STUDIES ON THE SYNTHESIS, REACTIVITY AND UTILITY OF ORGANOPHOSPHONATES AND CYCLODIPHOSPH(III)AZANES

A THESIS

SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

BY

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Dedicated

TO

My parents

&

Wife

Synopsis of the thesis entitled "Studies on the synthesis, reactivity and utility of organophosphonates and cyclodiphosph(III)azanes" *to be submitted by*

K. Praveen Kumar

(Supervisor: Prof. K. C. Kumara Swamy)

This thesis is divided into two parts: Part-A and Part B. Part A embodies the synthesis of various phosphonates and their utility in organic synthesis. The purpose of this part of the study is (i) to develop a simple methodology for the synthesis of a variety of organophosphonates by using the readily prepared (and cheap) key precursor (OCH_2CMe_2CHRO)PCl, (ii) to develop a simple and convenient method for the synthesis of di-substituted chloro/ bromo olefins and chloro-dienes by the Horner-Wadsworth-Emmons (HWE) reaction using phosphonates and (iii) to investigate the formation of phosphonates and pyrophosphates in the reaction of chlorophosphate esters with strong organic bases.

Part B involves (i) a study of the reaction of dialkyl azodicarboxylates with different cyclodiphosphosph(III)azanes in an effort to isolate and characterize compounds analogous to the intermediates proposed in the Mitsunobu reaction and (ii) investigations on the oxidative addition reactions of cyclodiphosphazanes followed by structural characterization of the resulting products.

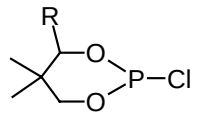
The compounds reported herein are characterized by IR and NMR (^{1}H, ^{13}C, ^{31}P) techniques, elemental analyses (representative examples) and X-ray structure determination (where feasible). References corresponding to each part are compiled after the respective experimental sections. In the appendix, selected atomic coordinates for compounds studied by X-ray crystallography are given as reference material.

PART-A

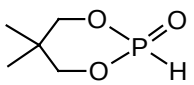
Chapter 1 reviews the literature on different methods for the synthesis of phosphonates and their utility in organic synthesis. Selected results from Chapter 2 (Results and Discussion) are described below:

(1) Phosphite Precursors

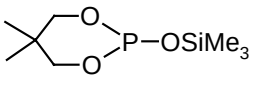
The precursors **1a-c** and **2-7** used in the present study are prepared by standard procedures available in the literature.



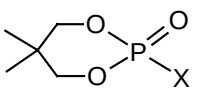
R = H; **1a** [bp 40°C/1 mm, δ(P): 145.8]
R = Ph; **1b** [δ(P):149.6]
R = 3-Br-C_6H_4; **1c** [δ(P):150.0, 151.2]
Yield: 85 - 95%



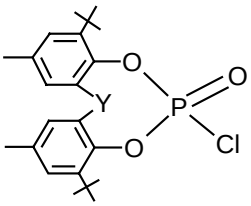
2 [δ(P): 2.3]
Yield: Quantitative



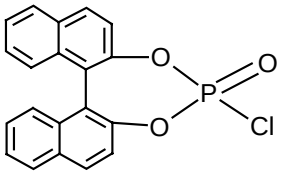
3 [δ(P): 108.6]
Yield: 94%



X = Cl [**4**: δ(P) -3.6]
X = N_3 [**5**: δ(P) -9.0]



Y = S [**6a**: δ(P) -8.2]
Y = CH_2 [**6b**: δ(P) -3.4]



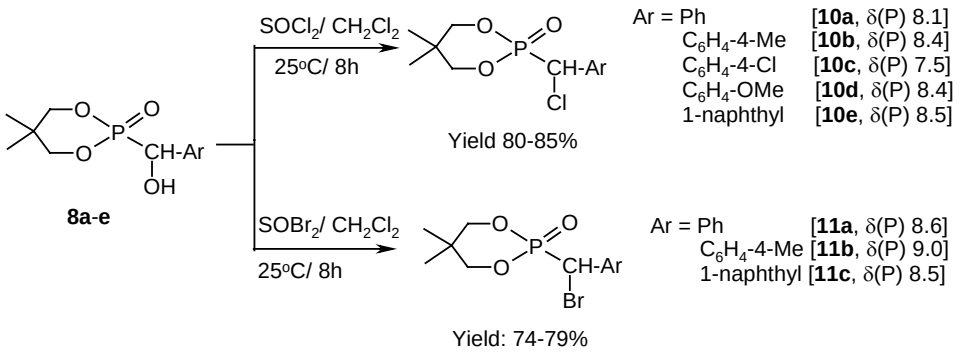
7 [δ(P): 11.1]

(2) Synthesis of Phosphonates

(a) *Synthesis of chloro- and bromophosphonates via α-hydroxyphosphonates*

The α-chlorophosphonates **10a-e** have been prepared by treating the α-hydroxyphosphonates **8a-e** (prepared by the Pudovik reaction of **2** with aldehydes) with thionyl chloride; the α-bromophosphonates **11a-c** have been prepared by treating the α-hydroxyphosphonates **8a-b** and **8e** with thionyl bromide in dichloromethane at room temperature (Scheme 1).

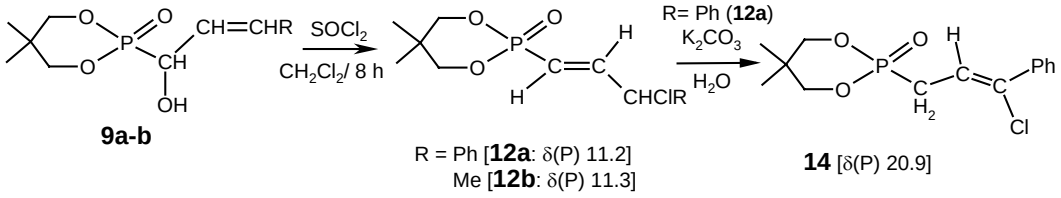
Scheme 1



In contrast to the above, the reaction of **9a-b** with thionyl chloride leads to the formation of the γ-chlorinated vinylphosphonates **12a-b**. A possible pathway for the formation of **12a-b** is discussed. The structure of **12a** is also unambiguously proved

by the X-ray crystallography. Compound **12a** rearranges to the phosphonate **14** (~ 95% purity) upon treatment with K_2CO_3/ xylene. This result has implications as regards the utility of **12a** in the HWE reaction (see below).

Scheme 2



9a-b

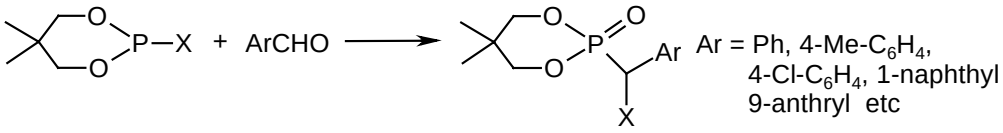
R = Ph [**12a**: δ(P) 11.2]
Me [**12b**: δ(P) 11.3]

14 [δ(P) 20.9]

(b) Direct synthesis of chloro and α-trimethylsilyloxyphosphonates

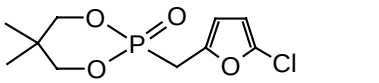
The compounds $(OCH_2CMe_2CH_2O)PX$ [X = Cl (**1a**), $OSiMe_3$ (**3**)] when reacted with various aromatic aldehydes afforded the α-chlorophosphonates (**10a-g**) in moderate yields (Scheme 3); in the reaction with 9-anthraldehyde, we also isolated *the rather unusual bisphosphonate* **15** (X-ray) in yields of ~35%. Interestingly, in the reaction of **1a** with cinnamaldehyde or furfuraldehyde, we again isolated γ-chlorophosphonate **12a** or the ring-chlorinated product **13**, respectively. The α-trimethylsilyloxyphosphonates **16a-h** were also readily obtained by treating **3** with various aldehydes (Scheme 3). Possible pathways for the formation of these α-chloro/ α-trimethylsilyloxyphosphonates as well as **15** are discussed.

Scheme 3

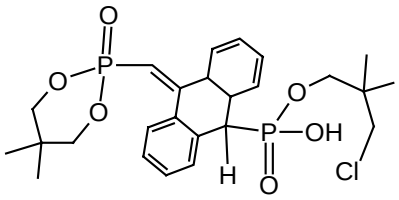


X = Cl (**1a**)
X = $OSiMe_3$ (**3**)

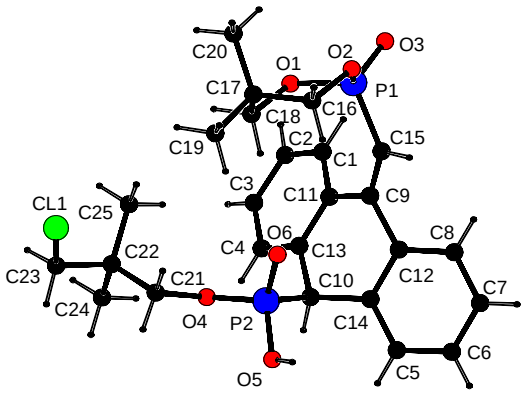
X = Cl (**10a-g**)
X = $OSiMe_3$ (**16a-h**)



13 [δ(P): 16.4]



15 [δ(P) 11.2, 24.1]

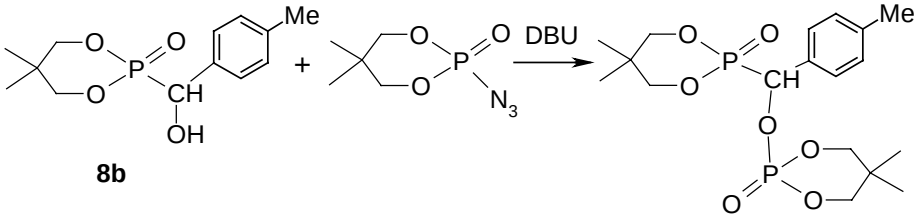


Compound **15**

(c) α-Phosphate esters of phosphonates, α-azidophosphonates and α-aminophosphonates

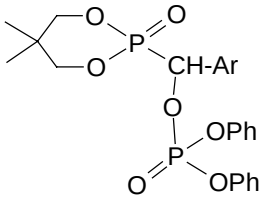
Treatment α-tosyl phosphonates $(OCH_2C(CH_3)_2CH_2O)P(O)CH(OTs)Ar$ (**17a-d**) (obtained from α-hydroxyphosphonates) with sodium azide did not lead to reproducible yields of α-azidophosphonates. Although the reaction of $(OCH_2CMe_2CH_2O)P(O)N_3$ (**5**) with 2-bromo-benzyl alcohol in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), afforded the azide $2\text{-Br-}C_6H_4CH_2N_3$ (**18**), attempts to convert the hydroxyphosphonate **8a-b** and **8h** to α-azidophosphonates using **5** or $(PhO)_2P(O)N_3$ resulted in the phosphate esters (of the phosphonate) **19** (using **8b**) or **20a-c** (Scheme 4) possibly because of the hydrolysis of the reacting azides. The structure of **20c** was also established by single crystal X-ray diffraction studies.

Scheme 4



8b

19 [δ(P) -8.7(d), 7.4 (d), ^3J(PP) = 30.0 Hz]



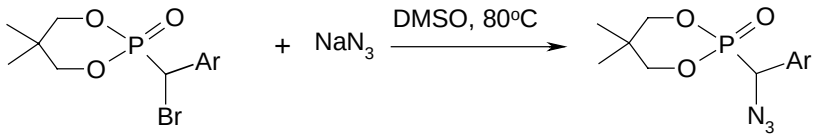
Ar = Ph [**20a** δ(P) -13.8(d), 6.3 (d)] ^3J(PP) = 41.7 Hz

C_6H_4-4-Me [**20b** δ(P) -13.8(d), 6.5 (d)] ^3J(PP) = 39.0 Hz

C_6H_4-2,6-Cl_2 [**20c** δ(P) -13.3(d), 4.3 (d)] ^3J(PP) = 39.0 Hz

However, we did succeed in preparing the α-azidophosphonates **21a-c** by reacting the bromophosphonates **11a-c** with sodium azide in 47-59% yield (Scheme 5). Our approach offers a convenient alternative to those available in the literature for other azidophosphonates.

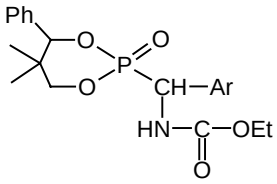
Scheme 5



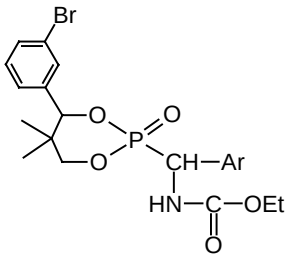
11a-c

Ar = Ph [**21a**: δ(P) 10.2]
C_6H_4-4-Me [**21b**: δ(P) 10.6]
1-Naphthyl [**21c**: δ(P) 10.6]

In view of the wide-ranging biological activity of the α-aminophosphonates and α-aminophosphonic acids, compounds **22a-f** were prepared by treating the P(III) precursors **1b-c** with urethane followed by an appropriate aldehyde in yields of 30-40%. Compounds **22a** and **22d** were obtained pure and **22b-c/22e-f** in a state of purity ~95%, because of the difficulty in separating them from the α-hydroxyphosphonates (formed via hydrolysis of **1b-c**). All these compounds are isolated as isomeric (probably diastereomeric) mixtures that can be distinguished by ^{31}P NMR. This route provides scope for preparing a wide variety of aminophosphonates.



Ar = Ph [**22a**: δ(P)19.1, 20.2 (2:3)]
C_6H_4-4-Me [**22b**: δ(P)19.3, 20.4 (3:1)]
C_6H_4-4-Cl [**22c**: δ(P)18.5, 19.5 (1:8)]



Ar = Ph [**22d**: δ(P)18.8, 20.3 (1:1)]
C_6H_4-4-Me [**22e**: δ(P)19.0, 20.4 (8:1)]
C_6H_4-4-Cl [**22f**: δ(P)18.3, 19.7 (2:3)]

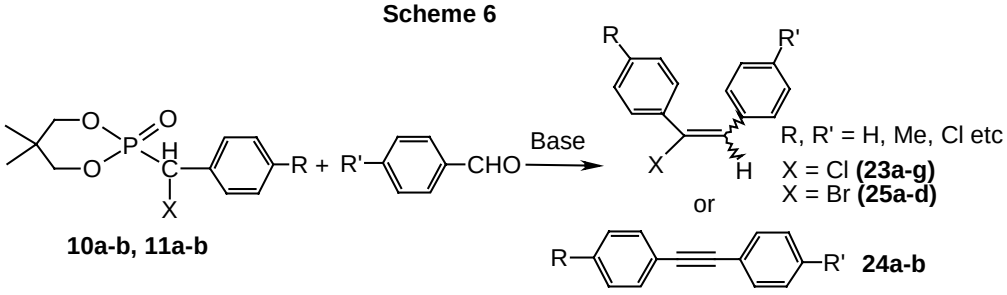
(3) Synthetic Utility of Phosphonates

Synthesis of disubstituted vinyl chlorides and chloro substituted dienes

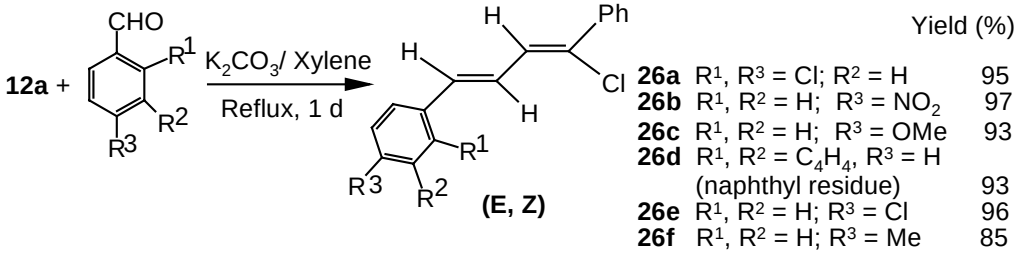
A comparative study of the efficiency of different bases and solvents in the reaction of α-chloro/ bromophosphonates with aldehydes for the Horner-Wadsworth-Emmons (HWE) reaction revealed that the system K_2CO_3/xylene/reflux gives the best

yields of substituted olefins and hence this method was used for the HWE reaction (Scheme 6). Thus we prepared compounds **23a-g, 25a-d** by reacting **10a-b, 10d** or **11a-b** with various aldehydes in the presence of K_2CO_3 in xylene at 140°C. The *E/Z* ratio is based on the $\delta(^1H)$ value for C_6H_4-OCH_3 or C_6H_4-CH_3 protons and the well-separated $\delta(^{13}C)$ values for the *ipso*-carbon. We also extended this method for synthesis of chloro substituted dienes.**26a-f** (Scheme 7). The identity of **26a** has been confirmed by X-ray crystallography.

Scheme 6

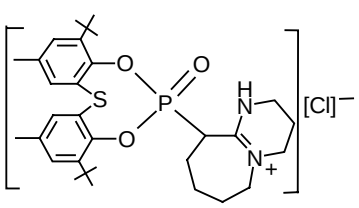


Scheme 7

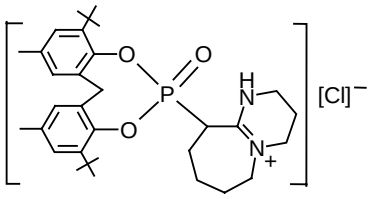


(4) Formation of phosphonates and pyrophosphates in the reactions of chlorophosphate esters with strong organic bases

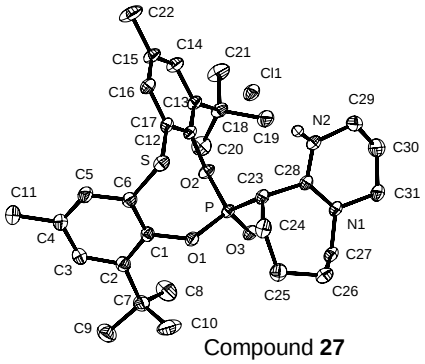
The reaction of **6a-b** and **7** with DBU in toluene (or THF for **7**) resulted in the phosphonate salts **27-29** (rather than the expected phosphoramidate salts with a P-N bond) are the major products. Compounds **27-28** could be isolated as pure solids. In the case of **29**, two isomeric products [δ(P) 29.4, 30.0; probably diastereomeric] are formed along with a product that showed a δ(P) of 5.4.



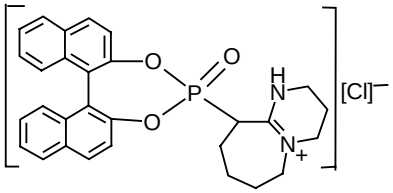
27 [δ(P): 6.4]



28 [δ(P): 7.2]

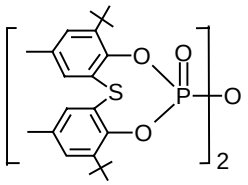


Compound **27**

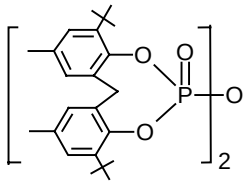


29[δ(P): 30.4, 29.2]

Although DBN is also a dinitrogen base similar to DBU, we did not observe a phosphonate salt in reactions using DBN. The only product that could be isolated in a pure state was the pyrophosphate **30** [δ(P) –31.1]. Even in the reaction using **6b**, the analogous pyrophosphate **31** is a major product. In the reaction of **6a** with N-methyl imidazole, the pyrophosphate (30%) along with two other peaks is observed in the ^{31}P NMR. In the analogous reaction of **7** with DBN or N-methyl imidazole, a peak at δ(P) -12.4, ascribable to the pyrophosphate **30**, was a major product. A possible rationale for these results is discussed.



30 [δ(P): -31.6]



31 [δ(P): -28.6]

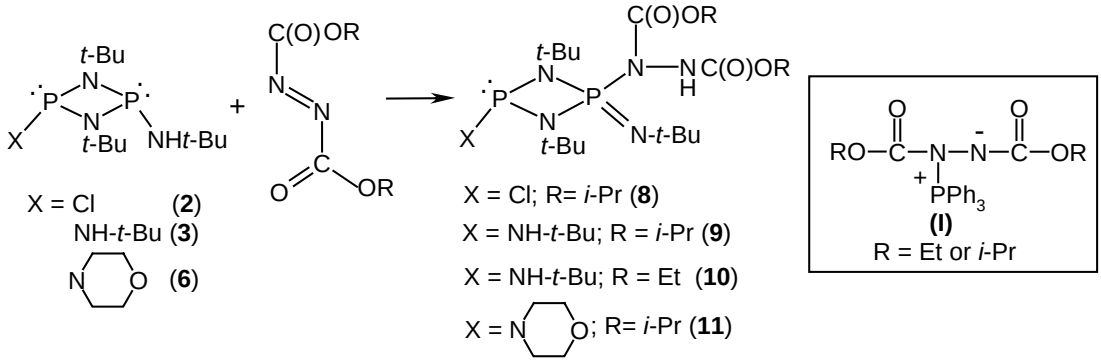
Chapter 3 describes the experimental details pertaining to part A.

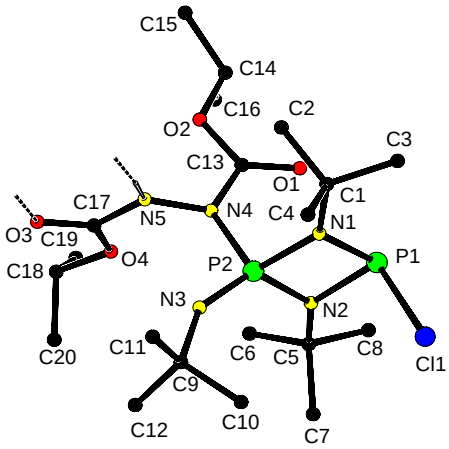
PART-B

Chapter 4 contains a review of literature on the general features of the Mitsunobu reaction and oxidative addition reactions of cyclodiphosphosph(III)azanes. The results obtained are discussed in Chapter 5.

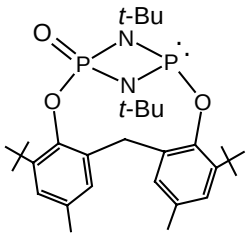
In connection with the isolation of Mitsunobu interemediates, we reacted cyclodiphosphazanes **2**, **3** or **6** with diethyl azodicarboxylate (DEAD)/ diisopropyl azodicarboxylate (DIAD). Rather than the intermediate of type **I** (proposed in the Mitsunobu reaction), we obtained the tautomeric forms **8-11** respectively (Scheme 8); the analogous compound [$(CO_2$-*i*-Pr)HNN(CO_2-*i*-Pr)](t-BuN)P(μ-N-*t*-Bu)$_2$POCH$_2$CMe$_2$CH$_2$O[P(μ-N-*t*-Bu)$_2$PN-*t*-Bu)(N(CO_2-*i*-Pr)-NH(CO_2-*i*-Pr)] (**12**) was obtained from its P(III) precursor (**7**). By contrast, the oxo-products **13** or **14**,were obtained by starting with their P(III) precursors (**4**, **5**). X-ray structures of **8** and **10**-**13** confirm these assertions.

Scheme 8



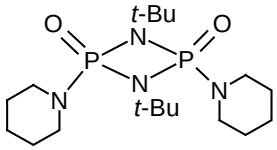


Compound **8**



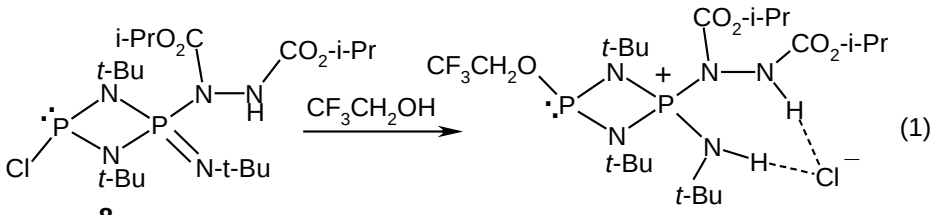
13 [δ(P) -2.5, 104.6]

(X-ray)



14 [δ(P) 1.5]

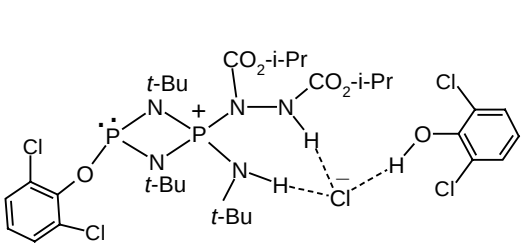
When compound **8** is treated with one mole equivalent of 2,2,2-trifluoroethanol, the P(III)-Cl end reacts and the proton from the liberated HCl adds to the nitrogen at P=N-*t*-butyl end to afford **15** (eq. 1; X-ray). The cation in this compound can be considered to be a protonated form of the betaine (CF_3CH_2O)P(μ-N-*t*-Bu)$_2$P$^+$(NH-*t*-Bu){N-(CO_2-*i*-Pr)-N$^-$(CO_2-*i*-Pr)}. This kind of species is *one of the intermediates proposed in the Mitsunobu reaction*.



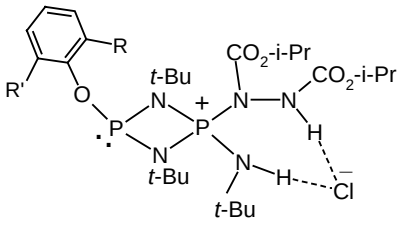
8

15 [δ(P) 11.7, 114.4; ^{2}J = 14.1 Hz] (X-ray)

We extended this reaction of **8** with the phenols 2,6-$Cl_2C_6H_3OH$, 2,6-$Me_2C_6H_3OH$, 2-Me-6-*t*-BuC_6H_3OH and 2,6-(*t*-Bu)$_2C_6H_3OH$ to yield **16-19**. An X-ray structural analysis **16** clearly reveals an additional 2,6-dichlorophenol moiety in the crystal stucture. There is a significant change in ^{31}P NMR chemical shifts when compound **9** is treated with various phenols as well as 2,2,2-trifluoroethanol (but not isopropanol), but attempted crystallization gave back **9** suggesting that the interaction is weak.



16 [δ(P) 10.9 (br), 115.9 (br)] (X-ray)

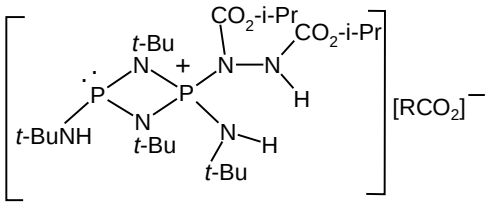


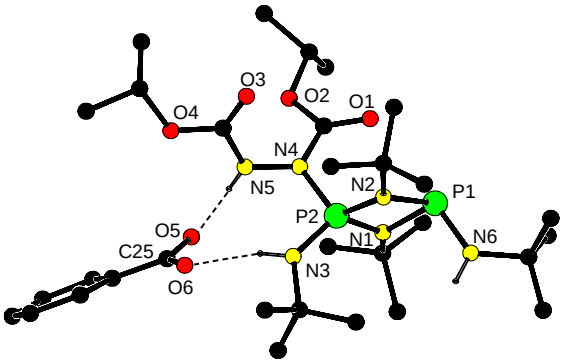
17 [R = R' = Me; δ(P) 10.7(d), 119.5(d), ^2J = 11.0 Hz]

18 [R = Me, R' = *t*-Bu; δ(P) 9.4(d), 114.6 (d), ^2J = 10.4 Hz]

19 [R = R' = *t*-Bu; δ(P) 9.4(d), 114.9(d), ^2J = 11.2 Hz]

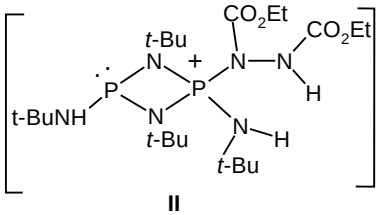
Addition of benzoic acid to **9**, prepared *in situ*, produced compound **20** (X-ray); analogous compounds **21-24** also could be obtained similarly. These structures are essentially the type of second stage intermediate proposed in the Mitsunobu reaction. Interestingly, we could effect esterification using the *in situ* formed analogous compound (*t*-BuNH)P(μ-N-*t*-Bu)$_2$P$^+$[(HN-*t*-Bu){N-(CO_2Et)-N(H)(CO_2Et)](4-NO_2-$C_6H_4CO_2^-$) [**II**: δ(P) 3.8 and 82.9] with ethanol leading to ethyl 4-nitrobenzoate, 4-$NO_2C_6H_4CO_2$Et (**25**) (Scheme 9).





R = Ph [**20**: δ(P) 1.1, 81.0]
4-Cl-$C_6H_4CH_2$ [**21**: δ(P) 0.1, 80.4]
4-Br-C_6H_4 [**22**: δ(P) 2.1, 81.5]
4-NO_2-C_6H_4 [**23**: δ(P) 2.9, 82.0]
4-Me-$C_6H_4SO_3^-$ instead of RCO_2^- [**24**: δ(P) 2.3, 82.2]

Scheme 9

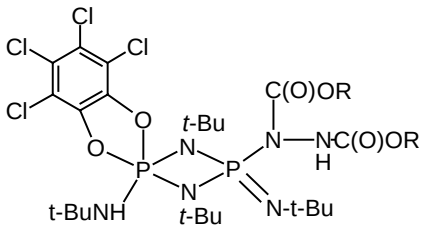


II

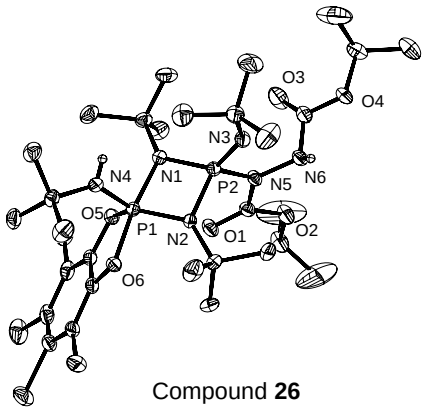
$[4\text{-}NO_2\text{-}C_6H_4CO_2]^-$ —EtOH→ 4-NO_2-$C_6H_4CO_2Et$ + other phosphorus products

25

Oxidative addition of tetrachloro-1,2-benzoquinone) to **9** and **10** leads to the novel compounds **26** and **27**, respectively, containing both tetra- and pentacoordinate phosphorus centres. The reaction of **3** with two mole equivalents of *o*-chloranil gives the bis-cycloaddition product $[(Cl_4C_6\text{-}1,2\text{-}O_2)(t\text{-BuNH})PN\text{-}t\text{-Bu}]_2$ (**28**) cleanly.



R = *i*-Pr [**26**, δ(P) -51.2, -35.1; ^2J = 89.6 Hz]
Et [**27**, δ(P) -51.9, -36.7; ^2J = 89.6 Hz]



Compound **26**

Chapter 6 gives the experimental details pertaining to Chapter 5.

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Appendix I

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.

K. Praveen Kumar

CERTIFICATE

This is to certify that the work described in this thesis entitled "Studies on the synthesis, reactivity and utility of organophosphonates and cyclodiphosph(III)azanes" has been carried out by Mr. *K. Praveen Kumar*, under my supervision and the same has not been submitted elsewhere for any degree.

Hyderabad

January 2005

K. C. Kumara Swamy

(Thesis supervisor)

Dean

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INDIA

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K. Praveen Kumar

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1. An Easy Access to Trisubstituted Vinyl Chlorides and Improved Synthesis of Chloro/ Bromostilbenes
   C. Muthiah, **K. Praveen Kumar**, S. Kumaraswamy and K. C. Kumara Swamy, *Tetrahedron*, 1998, **58**, 14315

2 Chlorophosphonates: Inexpensive Precursors for Stereodefined Chloro-Substituted Olefins and Unsymmetrical Disubstituted Acetylenes
   C. Muthiah, **K. Praveen Kumar**, C. Aruna Mani and K. C. Kumara Swamy, *J. Org. Chem*., 2000, **65**, 3733

3 Direct Synthesis of α-Substituted Phosphonates
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4 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
   N. S. Kumar, **K. Praveen Kumar**, K. V. P. P. Kumar, P. Kommana, J. J. Vittal and K. C. Kumara Swamy *J. Org. Chem*., 2004, **69**, 1880

5 Synthesis and Structures of New Oxidation/ Cycloaddition Products of Cyclodiphosph(III)azanes
   K. Praveen Kumar, Manab Chakravarty and K. C. Kumara Swamy,
   Z. Anorg. Allg. Chem., 2004, **630**, 2063

6 Formation of phosphonates and pyrophosphates in the reactions of chlorophosphate esters with strong organic bases
   K. V. P. P. Kumar, **K. Praveen Kumar**, M. Vijjulatha and K. C.

7 Characterization of second stage Mitsunobu-type intermediates
   K. Praveen Kumar, N. B. Kumar, K. C. Kumara Swamy (*to be submitted*)

Work not reported in this thesis:

8 The Reaction of Chlorophosphates with Strong Bases: Synthesis and Characterization of the Phosphonate Salts

M. Vijjulatha, K. Praveen Kumar, K. C. Kumara Swamy and J. J. Vittal, *Tetrahedron Lett.,* 1998, **39,** 1819

9 Oxidative Addition Reactions of Cyclodiphosph(III)azanes

K. C. Kumara Swamy, P. Kommana, M. Vijjulatha and **K. Praveen Kumar**, *Phosphorus, Sulfur and Silicon*, 2001, **169**, 31.

PAPERS PRESENTED IN SYMPOSIA

1. New Halogeno- and Pseudohalogeno-Phosphites and Phosphoranes

S. Kumaraswamy, C. Muthiah, **K. Praveen Kumar** and K. C. Kumara Swamy, *Frontiers in Inorganic Chemistry*, IISc, Bangalore, July, 8-10, **1998**.

2. New Cyclic Phosphoranes and Phosphonates: Synthesis, Structure and Reactivity

S. Kumaraswamy, **K. Praveen Kumar**, C. Muthiah, M. Vijjulatha, C. Arunamani and K. C. Kumara Swamy, *National Symposium in Chemistry*, IISc, Bangalore, Jan 27-30, **1999**.

3 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 6-8, **2004**.

Synopsis

This thesis is divided into two parts: Part-A and Part B. Part A embodies the synthesis of various phosphonates and their utility in organic synthesis. The purpose of this part of the study is (i) to develop a simple methodology for the synthesis of a variety of organophosphonates by using the readily prepared (and cheap) key precursor (OCH_2CMe_2CHRO)PCl, (ii) to develop a simple and convenient method for the synthesis of di-substituted chloro/ bromo olefins and chloro-dienes by the Horner-Wadsworth-Emmons (HWE) reaction using phosphonates and (iii) to investigate the formation of phosphonates and pyrophosphates in the reaction of chlorophosphate esters with strong organic bases.

Part B involves (i) a study of the reaction of dialkyl azodicarboxylates with different cyclodiphosphosph(III)azanes in an effort to isolate and characterize compounds analogous to the intermediates proposed in the Mitsunobu reaction and (ii) investigations on the oxidative addition reactions of cyclodiphosphazanes followed by structural characterization of the resulting products.

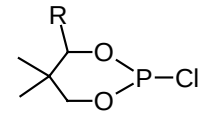
The compounds reported herein are characterized by IR and NMR (^{1}H, ^{13}C, ^{31}P) techniques, elemental analyses (representative examples) and X-ray structure determination (where feasible). References corresponding to each part are compiled after the respective experimental sections. In the appendix, selected atomic coordinates for compounds studied by X-ray crystallography are given as reference material.

PART-A

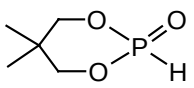
Chapter 1 reviews the literature on different methods for the synthesis of phosphonates and their utility in organic synthesis. Selected results from Chapter 2 (Results and Discussion) are described below:

(1) Phosphite Precursors

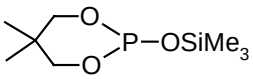
The precursors **1a-c** and **2-7** used in the present study are prepared by standard procedures available in the literature.



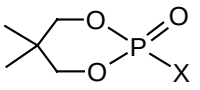
R = H; **1a** [bp 40°C/1 mm, δ(P): 145.8]
R = Ph; **1b** [δ(P):149.6]
R = 3-Br-C_6H_4; **1c** [δ(P):150.0, 151.2]
Yield: 85 - 95%



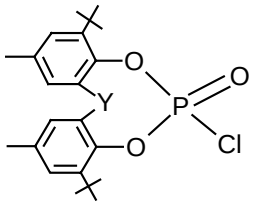
2 [δ(P): 2.3]
Yield: Quantitative



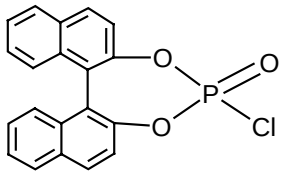
3 [δ(P): 108.6]
Yield: 94%



X = Cl [**4**: δ(P) -3.6]
X = N_3 [**5**: δ(P) -9.0]



Y = S [**6a**: δ(P) -8.2]
Y = CH_2 [**6b**: δ(P) -3.4]



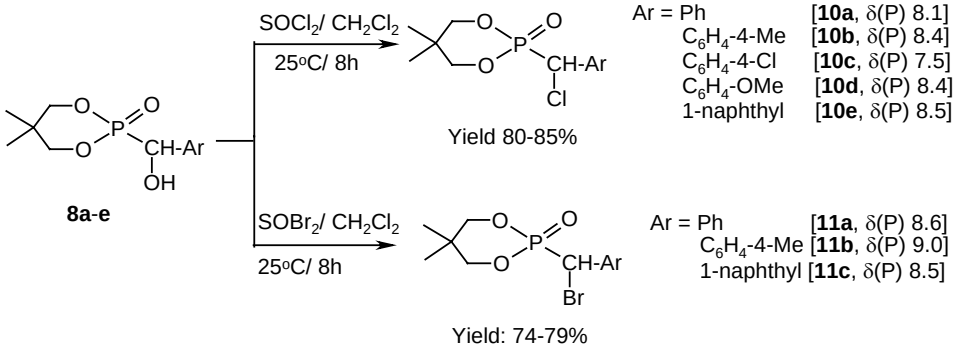
7 [δ(P): 11.1]

(2) Synthesis of Phosphonates

(a) *Synthesis of chloro- and bromophosphonates via α-hydroxyphosphonates*

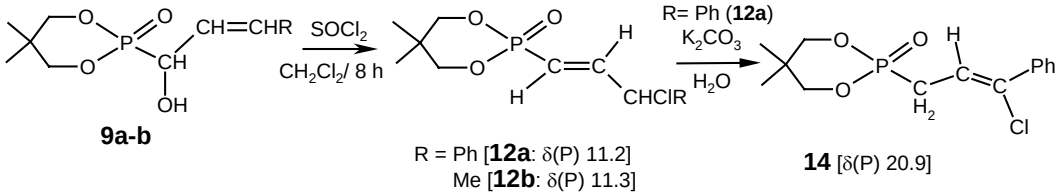
The α-chlorophosphonates **10a-e** have been prepared by treating the α-hydroxyphosphonates **8a-e** (prepared by the Pudovik reaction of **2** with aldehydes) with thionyl chloride; the α-bromophosphonates **11a-c** have been prepared by treating the α-hydroxyphosphonates **8a-b** and **8f** with thionyl bromide in dichloromethane at room temperature (Scheme 1).

Scheme 1



In contrast to the above, the reaction of **9a-b** with thionyl chloride leads to the formation of the γ-chlorinated vinylphosphonates **12a-b**. A possible pathway for the formation of **12a-b** is discussed. The structure of **12a** is also unambiguously proved by the X-ray crystallography. Compound **12a** rearranges to the phosphonate **14** (~ 95% purity) upon treatment with K_2CO_3/ xylene. This result has implications as regards the utility of **12a** in the HWE reaction (see below).

Scheme 2



9a-b

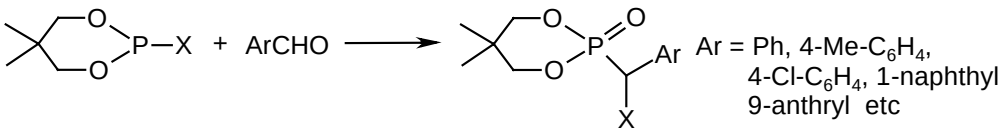
R = Ph [**12a**: δ(P) 11.2]
Me [**12b**: δ(P) 11.3]

14 [δ(P) 20.9]

(b) Direct synthesis of chloro and α-trimethylsilyloxyphosphonates phosphonates

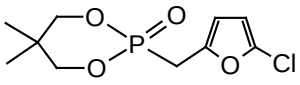
The compounds $(OCH_2CMe_2CH_2O)PX$ [X = Cl (**1a**), $OSiMe_3$ (**3**)] when reacted with various aromatic aldehydes afforded the α-chlorophosphonates (**10a-g**) in moderate yields (Scheme 3); in the reaction with 9-anthraldehyde, we also isolated *the rather unusual bisphosphonate* **15** (X-ray) in yields of ~35%. Interestingly, in the reaction of **1a** with cinnamaldehyde or furfuraldehyde, we again isolated γ-chlorophosphonate **12a** or the ring-chlorinated product **13**, respectively. The α-trimethylsilyloxyphosphonates **16a-h** were also readily obtained by treating **3** with various aldehydes (Scheme 3). Possible pathways for the formation of these α-chloro/ α-trimethylsilyloxyphosphonates as well as **15** are discussed.

Scheme 3

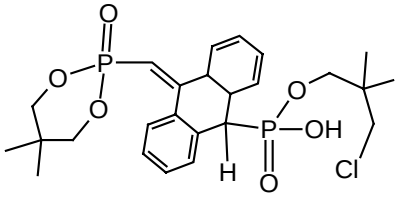


X = Cl (**1a**)
X = $OSiMe_3$ (**3**)

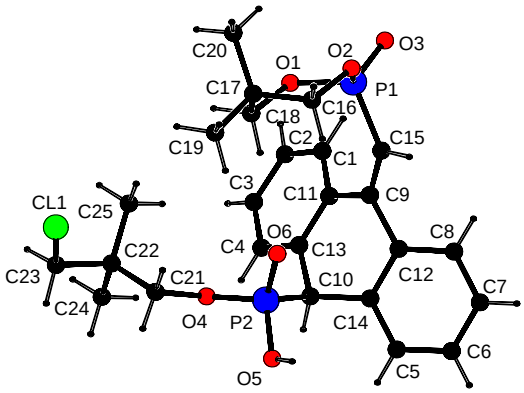
X = Cl (**10a-g**)
X = $OSiMe_3$ (**16a-h**)



13 [δ(P): 16.4]



15 [δ(P) 11.2, 24.1]

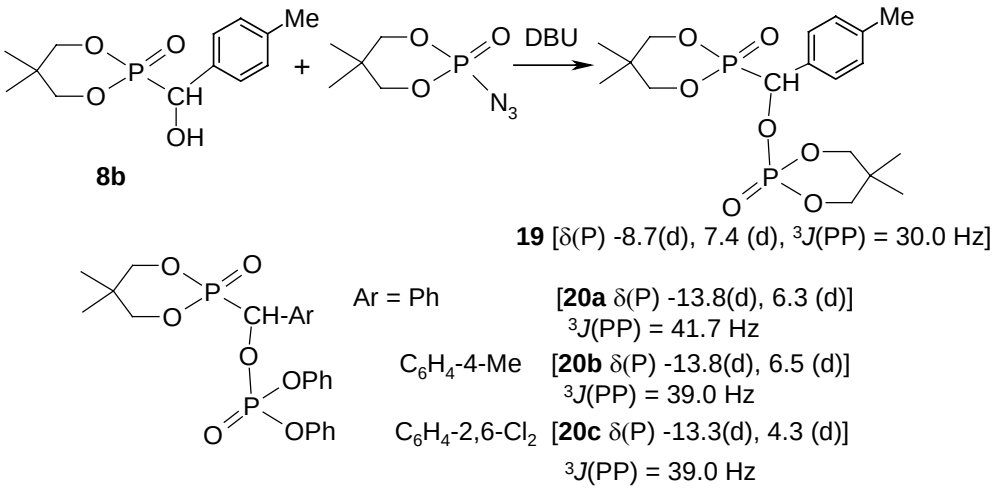


Compound **15**

(c) α-Phosphate esters of phosphonates, α-azidophosphonates and α-aminophosphonates

Treatment α-tosyl phosphonates $(OCH_2C(CH_3)_2CH_2O)P(O)CH(OTs)Ar$ (**17a-d**) (obtained from α-hydroxyphosphonates) with sodium azide did not lead to reproducible yields of α-azidophosphonates. Although the reaction of $(OCH_2CMe_2CH_2O)P(O)N_3$ (**5**) with 2-bromo-benzyl alcohol in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), afforded the azide 2-Br-$C_6H_4CH_2N_3$ (**18**), attempts to convert the hydroxyphosphonate **8a-c** to α-azidophosphonates using **5** or $(PhO)_2P(O)N_3$ resulted in the phosphate esters (of the phosphonate) **19** (using **8b**) or **20a-c** (Scheme 4) possibly because of the hydrolysis of the reacting azides. The structure of **20c** was also established by single crystal X-ray diffraction studies.

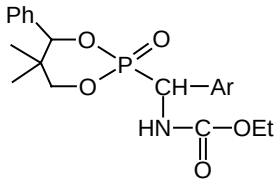
Scheme 4



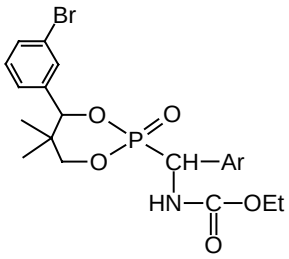
However, we did succeed in preparing the α-azidophosphonates **21a-c** by reacting the bromphosphonates **11a-c** with sodium azide in 47-59% yield (Scheme 5). Our approach offers a convenient alternative to those available in the literature for other azidophosphonates.

Scheme 5

In view of the wide-ranging biological activity of the α-aminophosphonates and α-aminophosphonic acids, compounds **22a-f** were prepared by treating the P(III) precursors **1b-c** with urethane followed by an appropriate aldehyde in yields of 30-40%. Compounds **22a** and **22d** were obtained pure and **22b-c/22e-f** in a state of purity ~95%, because of the difficulty in separating them from the α-hydroxyphosphonates (formed via hydrolysis of **1b-c**). All these compounds are isolated as isomeric (probably diastereomeric) mixtures that can be distinguished by ^{31}P NMR. This route provides scope for preparing a wide variety of aminophosphonates.



Ar = Ph [**22a**: δ(P)19.1, 20.2 (2:3)]
C_6H_4-4-Me [**22b**: δ(P)19.3, 20.4 (3:1)]
C_6H_4-4-Cl [**22c**: δ(P)18.5, 19.5 (1:8)]



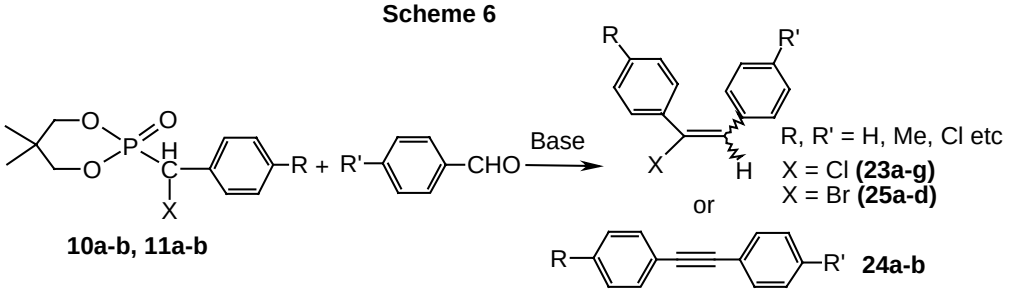
Ar = Ph [**22d**: δ(P)18.8, 20.3 (1:1)]
C_6H_4-4-Me [**22e**: δ(P)19.0, 20.4 (8:1)]
C_6H_4-4-Cl [**22f**: δ(P)18.3, 19.7 (2:3)]

(3) Synthetic Utility of Phosphonates

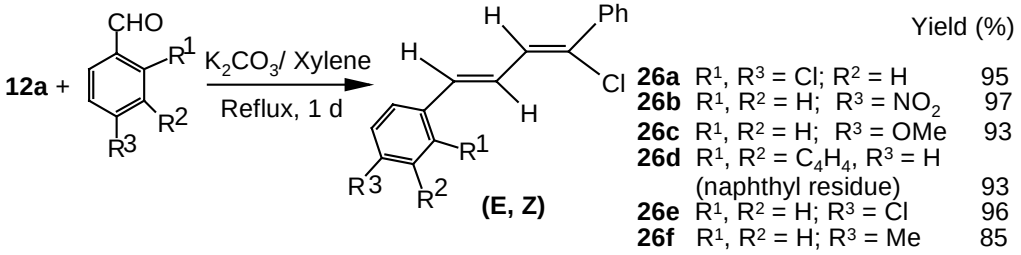
Synthesis of disubstituted vinyl chlorides and chloro substituted dienes

A comparative study of the efficiency of different bases and solvents in the reaction of α-chloro/ bromophosphonates with aldehydes for the Horner-Wadsworth-Emmons (HWE) reaction revealed that the system K_2CO_3/xylene/reflux gives the best yields of substituted olefins and hence this method was used for the HWE reaction (Scheme 6). Thus we prepared compounds **23a-g, 25a-d** by reacting **10a-b, 10d** or **11a-b** with various aldehydes in the presence of K_2CO_3 in xylene at 140^{o}C. The *E/Z* ratio is based on the δ(^{1}H) value for C_6H_4-OCH_3 or C_6H_4-CH_3 protons and the well-separated δ(^{13}C) values for the *ipso*-carbon. We also extended this method for synthesis of chloro substituted dienes.**26a-f** (Scheme 7). The identity of **26a** has been confirmed by X-ray crystallography.

Scheme 6

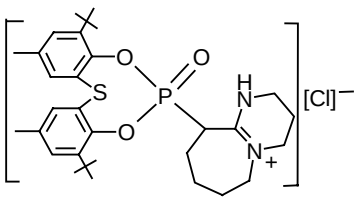


Scheme 7

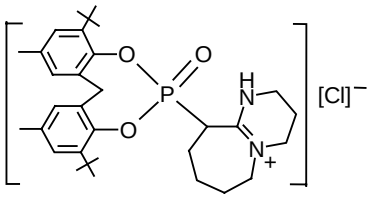


(4) Formation of phosphonates and pyrophosphates in the reactions of chlorophosphate esters with strong organic bases

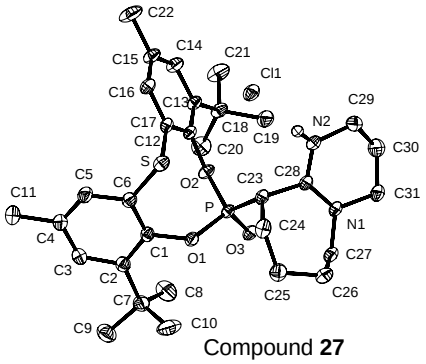
The reaction of **6a-b** and **7** with DBU in toluene (or THF for **7**) resulted in the phosphonate salts **27-29** (rather than the expected phosphoramidate salts with a P-N bond) are the major products. Compounds **27-28** could be isolated as pure solids. In the case of **29**, two isomeric products [δ(P) 29.4, 30.0; probably diastereomeric] are formed along with a product that showed a δ(P) of 5.4.



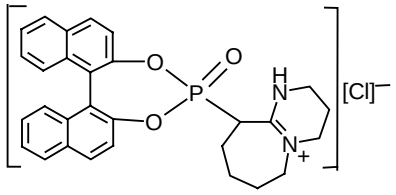
27 [δ(P): 6.4]



28 [δ(P): 7.2]

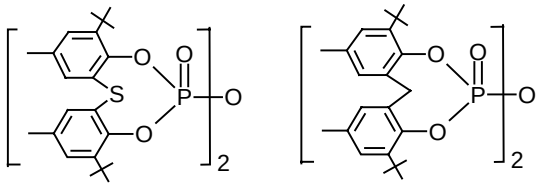


Compound **27**



29[δ(P): 30.4, 29.2]

Although DBN is also a dinitrogen base similar to DBU, we did not observe a phosphonate salt in reactions using DBN. The only product that could be isolated in a pure state was the pyrophosphate **30** [δ(P) –31.1]. Even in the reaction using **6b**, the analogous pyrophosphate **31** is a major product. In the reaction of **6a** with N-methyl imidazole, the pyrophosphate (30%) along with two other peaks is observed in the ^{31}P NMR. In the analogous reaction of **7** with DBN or N-methyl imidazole, a peak at δ(P) -12.4, ascribable to the pyrophosphate **30**, was a major product. A possible rationale for these results is discussed.



30 [δ(P): -31.6] **31** [δ(P): -28.6]

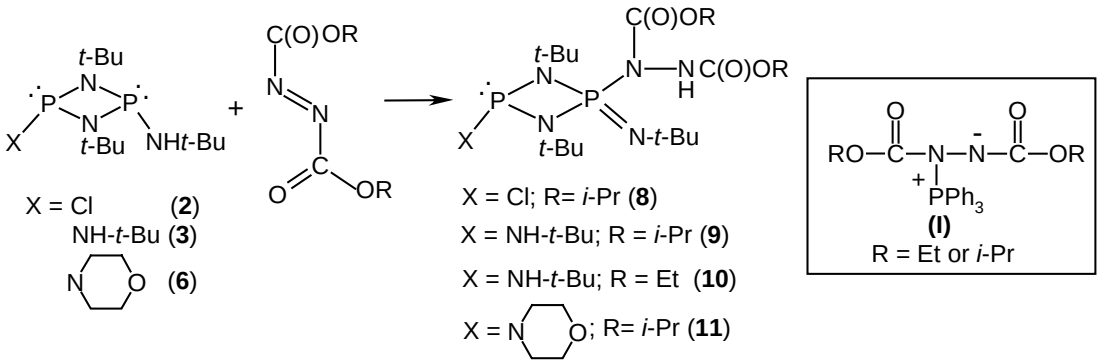
Chapter 3 describes the experimental details pertaining to part A.

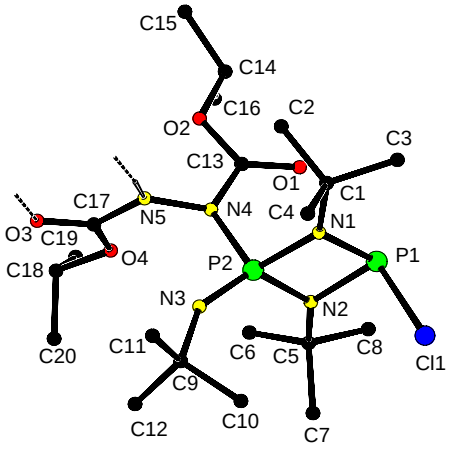
PART-B

Chapter 4 contains a review of literature on the general features of the Mitsunobu reaction and oxidative addition reactions of cyclodiphosphosph(III)azanes. The results obtained are discussed in Chapter 5.

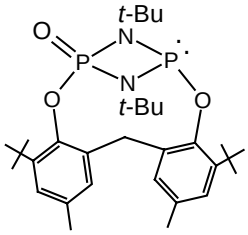
In connection with the isolation of Mitsunobu interemediates, we reacted cyclodiphosphazanes **2**, **3** or **6** with diethyl azodicarboxylate (DEAD)/ diisopropyl azodicarboxylate (DIAD). Rather than the intermediate of type **I** (proposed in the Mitsunobu reaction), we obtained the tautomeric forms **8-11** respectively (Scheme 8); the analogous compound [(CO_2-*i*-Pr)HNN(CO_2-*i*-Pr)](t-BuN)P(μ-N-*t*-Bu)$_2$POCH$_2$CMe$_2$CH$_2$O[P(μ-N-*t*-Bu)$_2$PN-*t*-Bu)(N(CO_2-*i*-Pr)-NH(CO_2-*i*-Pr)] (**12**) was obtained from its P(III) precursor (**7**). By contrast, the oxo-products **13** or **14**,were obtained by starting with their P(III) precursors (**4**, **5**). X-ray structures of **8** and **10-13** confirm these assertions.

Scheme 8



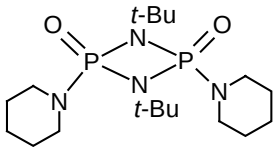


Compound **8**



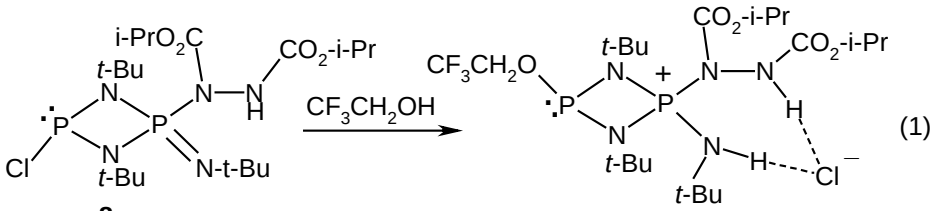
13 [δ(P) -2.5, 104.6]

(X-ray)



14 [δ(P) 1.5]

When compound **8** is treated with one mole equivalent of 2,2,2-trifluoroethanol, the P(III)-Cl end reacts and the proton from the liberated HCl adds to the nitrogen at P=N-*t*-butyl end to afford **15** (eq. 1; X-ray). The cation in this compound can be considered to be a protonated form of the betaine $(CF_3CH_2O)P(\mu\text{-}N\text{-}t\text{-}Bu)_2P^+(NH\text{-}t\text{-}Bu)\{N\text{-}(CO_2\text{-}i\text{-}Pr)\text{-}N^-(CO_2\text{-}i\text{-}Pr)\}$. This kind of species is *one of the intermediates proposed in the Mitsunobu reaction*.



8

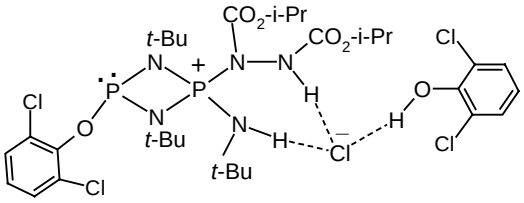
(1)

15 [δ(P) 11.7, 114.4; ^2J = 14.1 Hz]

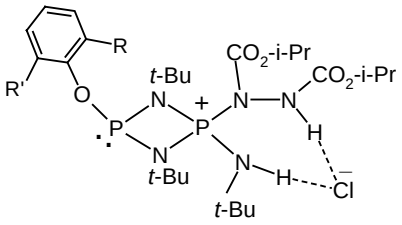
(X-ray)

We extended this reaction of **8** with the phenols $2,6\text{-}Cl_2C_6H_3OH$, $2,6\text{-}Me_2C_6H_3OH$, 2-Me-6-*t*-BuC_6H_3OH and $2,6\text{-}(t\text{-}Bu)_2C_6H_3OH$ to yield **16**-**19**. An X-

ray structural analysis **16** clearly reveals an additional 2,6-dichlorophenol moiety in the crystal stucture. There is a significant change in ^{31}P NMR chemical shifts when compound **9** is treated with various phenols as well as 2,2,2-trifluoroethanol (but not isopropanol), but attempted crystallization gave back **9** suggesting that the interaction is weak.

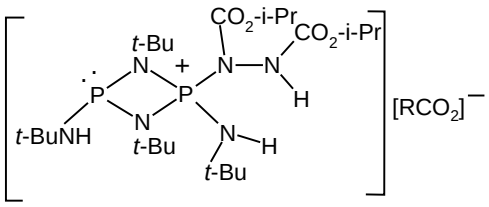


16 [δ(P) 10.9 (br), 115.9 (br)] (X-ray)

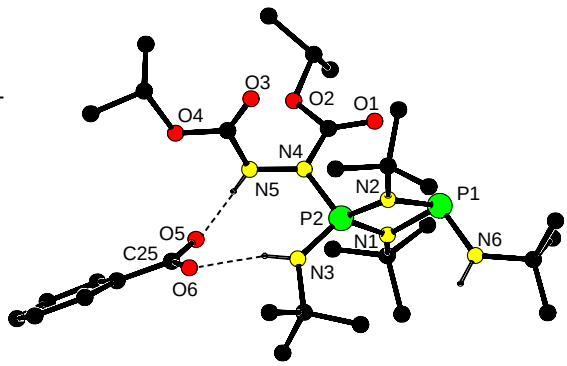


17 [R = R' = Me; δ(P) 10.7(d), 119.5(d), ^2J = 11.0 Hz]
18 [R = Me, R' = *t*-Bu; δ(P) 9.4(d), 114.6 (d), ^2J = 10.4 Hz]
19 [R = R' = *t*-Bu; δ(P) 9.4(d), 114.9(d), ^2J = 11.2 Hz]

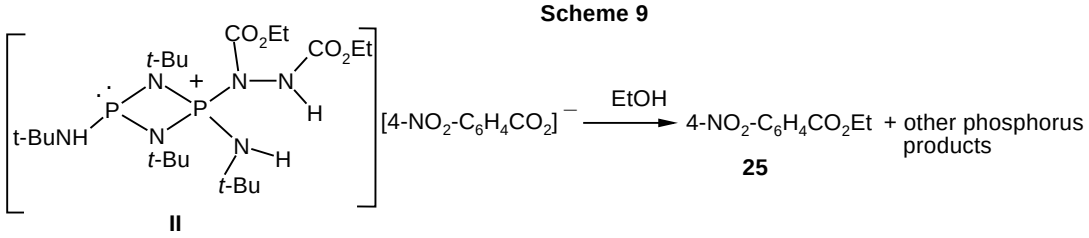
Addition of benzoic acid to **9**, prepared *in situ*, produced compound **20** (X-ray); analogous compounds **21**-**24** also could be obtained similarly. These structures are essentially the type of second stage intermediate proposed in the Mitsunobu reaction. Interestingly, we could effect esterification using the *in situ* formed analogous compound (*t*-BuNH)P(μ-N-*t*-Bu)$_2$P$^+$[(HN-*t*-Bu){N-(CO$_2$Et)-N(H)(CO$_2$Et)](4-NO$_2$-C$_6$H$_4$CO$_2^-$) [**II**: δ(P) 3.8 and 82.9] with ethanol leading to ethyl 4-nitrobenzoate, 4-NO$_2$C$_6$H$_4$CO$_2$Et (**25**) (Scheme 9).



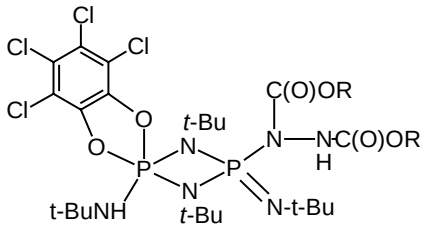
R = Ph [**20**: δ(P) 1.1, 81.0]
4-Cl-C$_6$H$_4$CH$_2$ [**21**: δ(P) 0.1, 80.4]
4-Br-C$_6$H$_4$ [**22**: δ(P) 2.1, 81.5]
4-NO$_2$-C$_6$H$_4$ [**23**: δ(P) 2.9, 82.0]
4-Me-C$_6$H$_4$SO$_3^-$ instead of RCO$_2^-$ [**24**: δ(P) 2.3, 82.2]



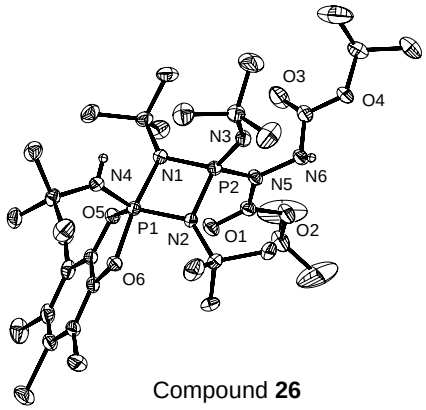
Scheme 9



Oxidative addition of tetrachloro-1,2-benzoquione) to **9** and **10** leads to the novel compounds **26** and **27**, respectively, containing both tetra- and pentacoordinate phosphorus centres. The reaction of **3** with two mole equivalents of *o*-chloranil gives the bis-cycloaddition product $[(Cl_4C_6\text{-}1,2\text{-}O_2)(t\text{-BuNH})PN\text{-}t\text{-Bu}]_2$ (**28**) cleanly.



R = *i*-Pr [**26**, δ(P) -51.2, -35.1; ^2J = 89.6 Hz]
Et [**27**, δ(P) -51.9, -36.7; ^2J = 89.6 Hz]



Compound **26**

Chapter 6 gives the experimental details pertaining to Chapter 5.

PART A

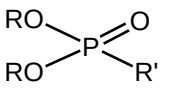
PHOSPHONATES – SYNTHESIS AND UTILITY

CHAPTER 1

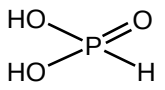
INTRODUCTION

1.1 General Introduction

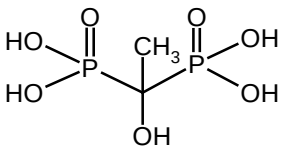
An organophosphonate ester (or simply organophosphonate) is a compound with the formula $(RO)_2P(O)R'$ (1.**1**)* containing a phosphorus-carbon bond and is a derivative of the phosphonic acid (1.**2**). An organophosphonic acid $RCH_2P(O)(OH)_2$ is a P-C bonded analogue of the organophosphate $ROP(O)(OH)_2$ and hence it can be expected that at least some organophosphonic acids may possess biological activity as regards to metabolic regulation or perturbation.[1,2] Etidronate (1.**3**) and Risedronate (1.**4**) are two phosphonates that are being used in the treatment of Paget's disease (bone desorption).[2f]



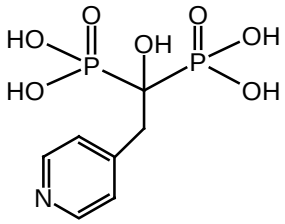
Phosphonate
(1.**1**)



Phosphonic acid
(1.**2**)



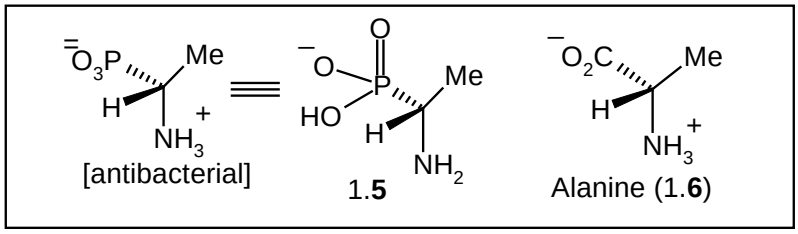
Etidronate (1.**3**)



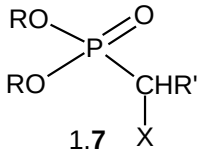
Risedronate (1.**4**)

A note on the 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 for compounds prepared in the present study; literature compounds as also intermediates/ transition state species are denoted by Roman numerals (**I**, **II,** etc.) in the order in which they appear in the text.

The α-aminophosphonic acids $(HO)_2P(O)CH(NH_2)(R)$ as well as their esters are also of tremendous current interest due to their varied biological activities that include antibacterial, antiviral, antifungal, pesticidal and glycine antagonism.[3] These compounds (e.g. 1.**5**) can be considered to be the phosphorus analogues of α-amino acids (e.g. 1.**6**).[4]



In addition to the above, it has been well recognized that phosphonate esters $(RO)_2P(O)CH(X)R^1$ (1.**7**) and related compounds containing stabilizing groups form anions which undergo a Wittig-like reaction with both aldehydes and ketones.[5] Unlike the Wittig reaction, this reaction (called Horner-Wadsworth-Emmons or simply HWE reaction) gives water-soluble by-products that can be easily separated from the required olefin. The phosphonates are also generally air-stable (*cf.* Wittig reagents). All these features have rendered phosphonates highly useful as synthons in C-C bond formation reactions and hence a vast amount of work has been reported in this area.[6,7]

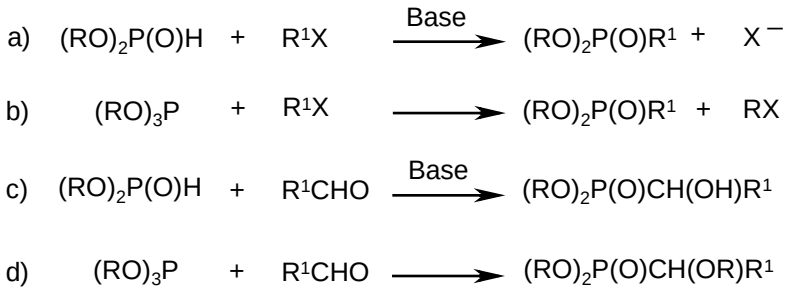


The focus of this chapter is to cover the literature on the synthesis and utility of phosphonate/ aminophosphonate esters that are relevant to this thesis.

1.2 Phosphonate Esters - Synthesis

The most widely used synthetic routes to phosphonate esters involve one of the following reactions: a) Michaelis-Becker reaction, b) Michaelis-Arbuzov reaction, c) Pudovik reaction or d) Abramov reaction (Scheme 1.1).[8]

Scheme 1.1



For method (a) sodium hydride, in general, works very nicely to generate the anion from the phosphite $(RO)_2P(O)H$. The preferred solvents are toluene, xylene and dioxane. The main problem here is the low solubility of the anion in the aprotic solvent. Method (b) remains the most common route for the formation of P-C bonds in quinquivalent organophosphorus compounds; this is due not only to the relatively easy availability of the required starting materials, but also to the relative ease of performing the reaction. Generally, methyl or diethyl esters of phosphorus and alkyl iodides are used. A limitation to either method (a) or (b) is the use of the alkyl halide itself; once the phosphonate is formed, further introduction of functionalities at the α-carbon is more difficult, although possible.

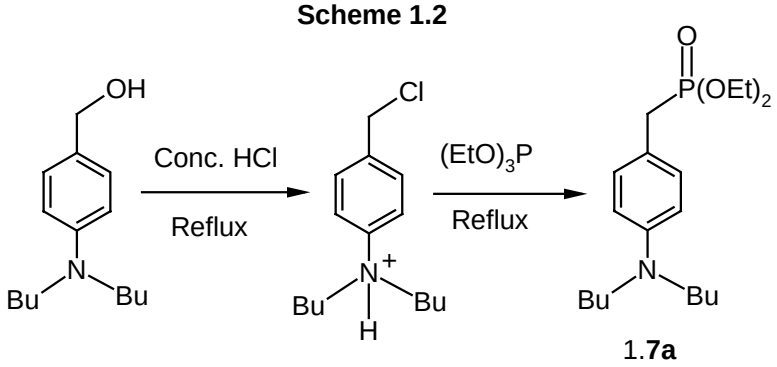
The addition of a phosphite [$(RO)_2P(O)H$ or $(RO)_3P$] to a carbonyl or carbonyl related groups leads directly to quinquivalent compounds [methods (c) and (d)] bearing a hydroxyl group or related polar functionality at the carbon attached to phosphorus (α-carbon). Such structural elements facilitate both further functionalization of that carbon and the ultimate cleavage of phosphorus from carbon. Thus the major plus point for the Pudovik and Abramov methods is the facility of synthesis of phosphonates bearing α-heterosubstitution.

The phosphonates described below are generally obtained by the variation of one or more of the above routes. Some of the recent publications are described below.

(i) Very electron-rich benzylic-type phosphonates $(RO)_2P(O)CH(X)R^1$ [X= H, R^1 = 4-N-(*n*-Bu)$_2$-C_6H_4, 1.**7a**] can be prepared by treating the corresponding alcohols in triethylphosphite with one equivalent of iodine at an appropriate temperature in a one-pot process (Scheme 1.2). The general Arbuzov route for these

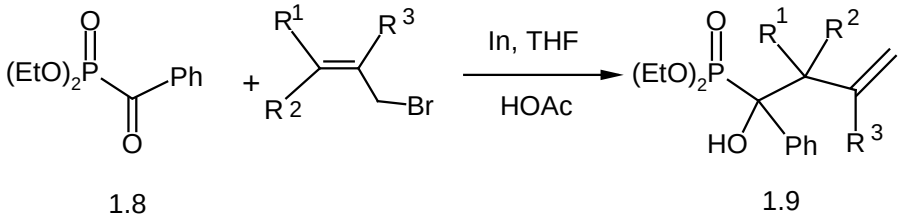
compounds is complicated by oxidative or electrophilic side-reactions, and isolation of the halides can be complicated by covalent/ ionic equilibria.[9]

Scheme 1.2



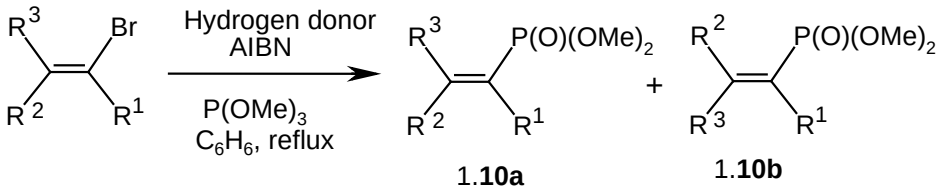
(ii) Treatment of acyl phosphonates 1.**8** with allylindium reagents in the presence of acetic acid afforded the corresponding α-hydroxy alkylphosphonates 1.**9** in good yields under mild conditions (Scheme 1.3). These studies have shown that it is possible to prepare tertiary α-hydroxy phosphonates from acyl phosphonates in high yield through an indium-mediated allylation. The reaction works well with several different allylic bromides, and does not appear to be sensitive to steric hindrance at the β-carbon.[10]

Scheme 1.3



(iii) The reaction of vinyl or aryl radicals under classical, thermal AIBN/n-Bu_3SnH conditions at 80°C with an excess of $(MeO)_3P$ gives rise to the corresponding vinyl- (or aryl) phosphonates 1.**10** in good yields (Scheme 1.4). This approach complements the photochemical reactions of the same systems previously used. Reactions with the individual stereo-isomers of MeCH=CMeBr (thermal AIBN/n-Bu_3SnH conditions) afford a *radical-equilibrated* 96/4 E/*Z* ratio of vinyl phosphonates. Substitution of $(Me_3Si)_3SiH$ for n-Bu_3SnH yields an approximately 1:1 ratio of separable *E* and *Z* vinyl phosphonate diastereomers.[11]

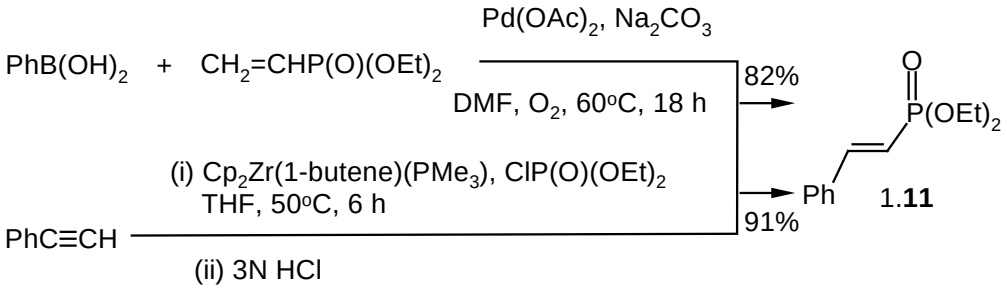
Scheme 1.4



1.**10a** 1.**10b**

(iv) Apart from the above, reaction of a vinylphosphonate with phenylboronic acid in the presence of $Pd(OAc)_2$/ Na_2CO_3 catalyst system is utilized to prepare substituted vinylphosphonates 1.**11** (Scheme 1.5).[12a] Interestingly, the same type of phosphonates can also be prepared by treating a terminal acetylene with $ClP(O)(OEt)_2$ in the presence of a suitable zirconyl catalyst.[12b]

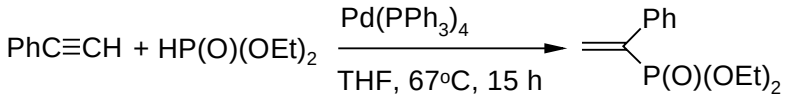
Scheme 1.5



1.**11**

In contrast to the above, hydrophosphorylation of terminal alkynes catalyzed by $Pd(PPh_3)_4$ is utilized to prepare α-substituted vinylphosphonates 1.**12** (Scheme 1.6).[13]

Scheme 1.6

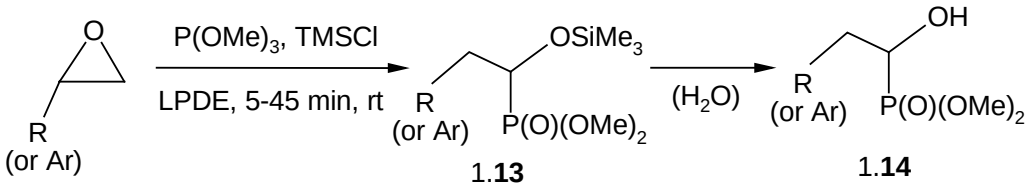


1.**12** (75%)

(v) A new method has been developed for the direct conversion of epoxides to α-hydroxyphosphonates 1.**14**, via the trimethylsilyloxyphosphonates 1.**13**, by the reaction of a trialkylphosphite with the epoxide in 5M lithium perchlorate in diethyl ether (LPDE) (Scheme 1.7). The reaction is highly regioselective and efficient with

excellent yields under mild and neutral conditions. It is claimed that the lithium perchlorate can be recovered.[14]

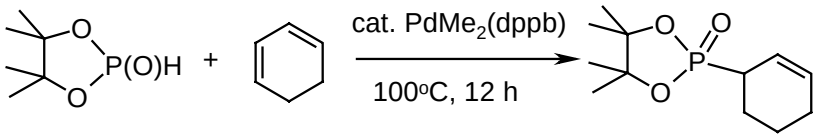
Scheme 1.7



1.**13** 1.**14**

(vi) Palladium catalyzed 1,4-hydrophosphonylation of 1,3-dienes efficiently takes place with 4,4,5,5-tetramethyl-1,3,2-dioxaphospholane-2-oxide (1.**15**) to afford the corresponding allylphosphonate 1.**16** selectively in high yields (Scheme 1.8).[15]

Scheme 1.8

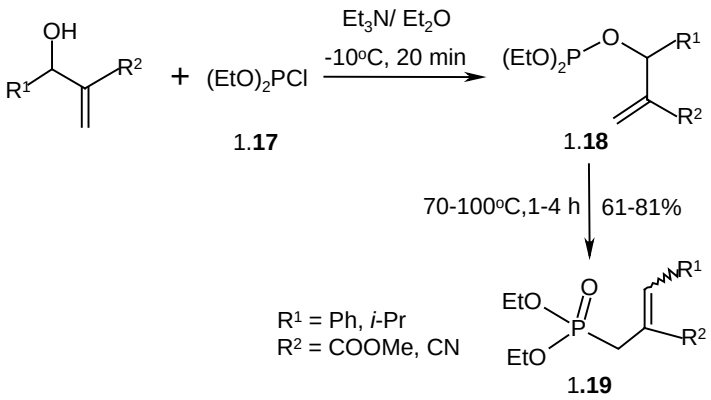


1.**15** 1.**16**

dppb = 1,4-bis(diphenylphosphino)butane

Allylphosphonates $(RO)_2P(O)CH_2C(R)=CR'R''$ which can form carbanions are useful in organic synthesis, particularly C-C bond forming reactions. One route for *Z*/*E* allylphosphonates 1.**19** is *via* the thermal Arbuzov rearrangement of allylphosphites 1.**18**, obtained by reacting diethylphosphorochloridite 1.**17** with Baylis-Hillman adducts (Scheme 1.9).[16a] The allylphosphite-allylphosphonate rearrangement is a stereoselective process with a *Z*/*E* isomer ratio of 95:5 for the ester (R^2 = COOMe) and 40:60 for the nitrile (R^2 = CN). However, diethylphosphorochloridite 1.**17** is not particularly stable and expensive. In this connection, from our laboratory, the use of much cheaper $(OCH_2CMe_2CH_2O)PCl$ has been developed;[16b-c] use of triethyl phosphite for the same purpose has also been reported.[16d]

Scheme 1.9

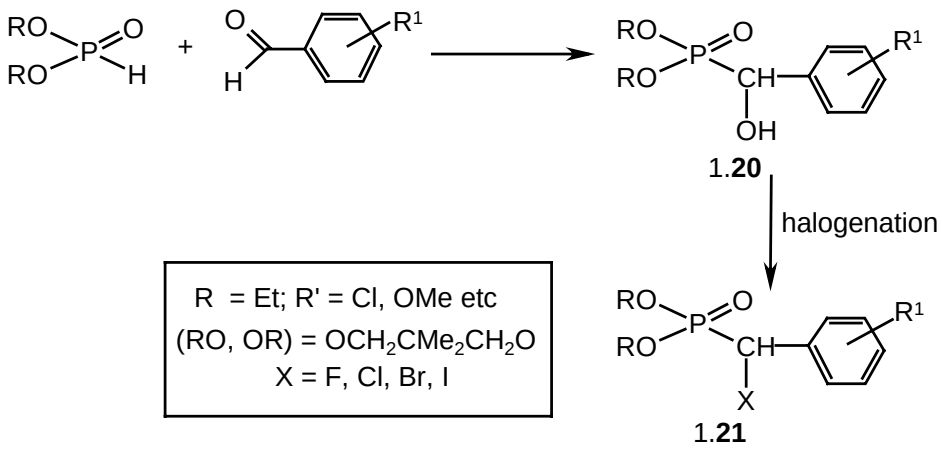


1.21 *Synthesis of α-halogenated/ pseudohalogenated/ trimethylsilyloxy phosphonates*

(a) By using dialkyl α-hydroxyphosphonates

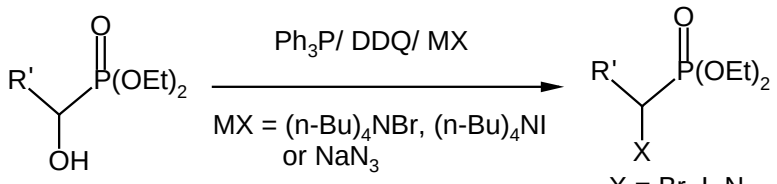
Dialkyl α-hydroxyphosphonates 1.**20** are readily prepared from dialkylphosphites and aldehydes (aryl, substituted aryl and heteroaryl) in the presence of triethyl amine (catalytic) by the Pudovik reaction.[8] Conversion of α-hydroxy phosphonates 1.**20** to α-halogenated phosphonates 1.**21** has been achieved by using a variety of halogenating agents, (i) Et_2NSF_3 for fluorination[17] (ii) $POCl_3$, PPh_3/ CCl_4 or $SOCl_2$ for chlorination[18] (iii) PPh_3/ CBr_4, Ph_3PBr_2/ Py, CH_2=$CHCH_2Br$/ CDI (N, N'-carbonyldiimidazole), or $SOBr_2$ for bromination[18e, 19] (iv) MeI/ CD_3I or PI_3 for iodination[18e, 19b] (Scheme 1.10). These methods have been employed for the preparation of a variety of α-substituted phosphonates in yields of 27-97%.

Scheme 1.10



The mixture of triphenylphosphine and 2,3-dichloro-5,6-dibenzoquinone as a neutral system has been utilized for the preparation of various types of α-bromo-, α-iodo, and α-azidophosphonates (1.**22**) from their corresponding diethyl α-hydroxyphosphonates in the presence of $(n\text{-}Bu)_4NBr$, $(n\text{-}Bu)_4NI$ and NaN_3 in good to high yields (Scheme 1.11). But the method has the disadvantage that the formed triphenylphosphine oxide is difficult to separate from the products.[20a] Essentially the same $Ph_3P/DDQ/NH_4SCN$ combination as a neutral system can be utilized for the direct preparation of diethyl α-thiocyanatophosphonates $(EtO)_2P(O)CH(NCS)R'$ (1.**23**) from diethyl α-hydroxyphosphonates (1.**20**; R = Et).[20b]

Scheme 1.11

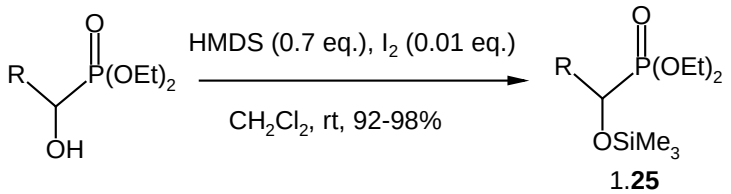


1.**22**

The same group also has reported copper triflate as a useful catalyst for the high-yielding preparation of α-acetyloxyphosphonates $(EtO)_2P(O)CH(OAc)R$ (1.**24**) under solvent-free conditions.[21]

The α-hydroxyphosphonates can be converted to α-trimethylsilyloxy phosphonates 1.**25** under mild conditions using hexadimethylsilazane (HMDS) in the presence of a catalytic amount of iodine (Scheme 1.12).[22]

Scheme 1.12



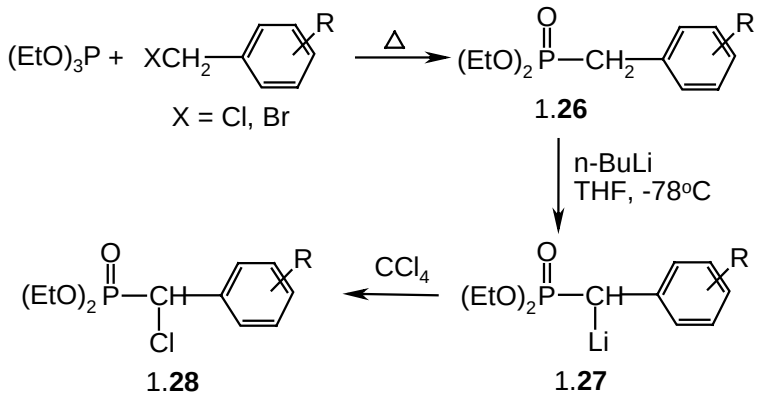
1.**25**

(b) By using diethyl benzylphosphonates

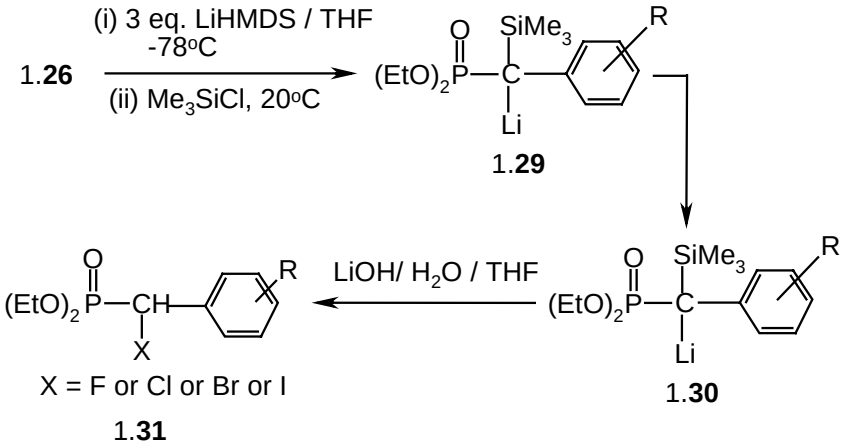
Diethyl benzylphosphonates 1.**26**, prepared by Michaelis-Arbuzov reaction of triethylphosphite with substituted benzyl halides, can be lithiated at the 2-position to give 1.**27**; the lithium can later be replaced by other groups to give substituted

phosphonates 1.**28** (Scheme 1.13).[23] Treatment of 1.**26** with three moles of LiHMDS followed by Me_3SiCl, halogenation and desilylation also offers a convenient route to α-halogenated phosphonates 1.**31** via 1.**29**-1.**30** (Scheme 1.14).[24]

Scheme 1.13



Scheme 1.14

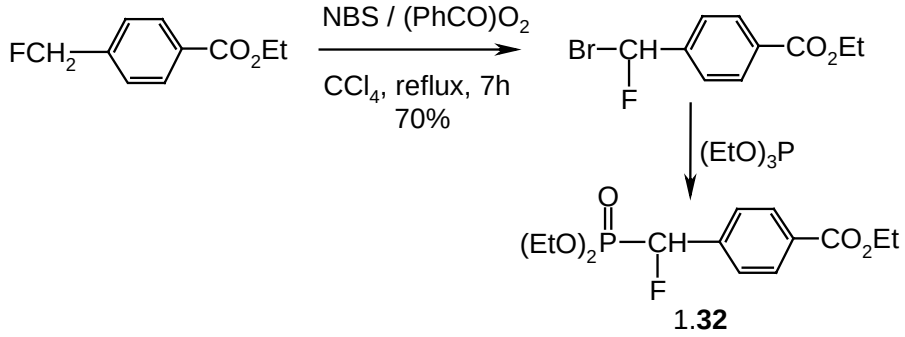


The main disadvantage of the routes shown in Scheme 1.13 and 1.14 is the use of rather expensive and air-sensitive lithium reagents.

(c) Direct formation of α-fluorobenzylphosphonates

Only one report involving the Michaelis-Arbuzov reaction is available for the synthesis of α-fluorophosphonates 1.**32** (Scheme 1.15). However, this is problematic in the case of secondary halides, and the presence of an electron-withdrawing group on the same carbon is needed for the success of the reaction.[25,26]

Scheme 1.15

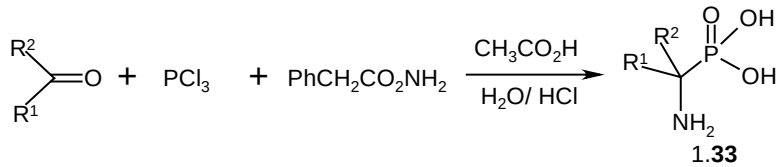


1.**32**

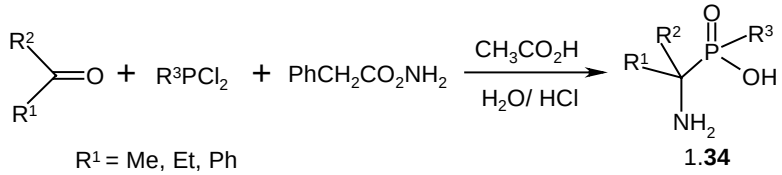
1.22 *Synthesis of α-aminophosphonates*

Amidoalkylation of trivalent phosphorus compounds (like a three component reaction mixture consisting of an amide, formaldehyde and PCl_3) for the preparation of aminomethanephosphonic acids is very well-known.[27] N-Hydroxymethylamide is formed as an intermediate in this reaction. This procedure was modified by Oleksyszyn who used benzyl carbamate and an aldehyde or ketone for the amidoalkylation of phosphorus trichloride to lead to the aminophosphonic (1.**33**) and aminophosphinic acids (1.**34**) (Scheme 1.16).[27c] Other alkyl carbamates/ amides can be used in place of benzyl carbamate; similarly, phosphorus trichloride can be replaced by dichlorophosphines. Hence this is one of the most commonly used reactions for the synthesis of structurally diverse aminophosphonates. A similar methodology can be utilized to prepare amino-bis(phosphonates) utilizing aniline, formic acid and PCl_3.[28]

Scheme 1.16



1.**33**

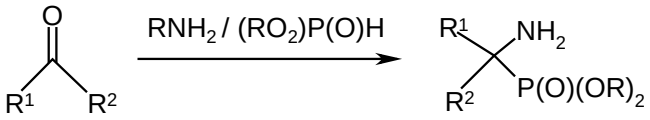


1.**34**

R^1 = Me, Et, Ph
R^2 = H, Me
R^3 = Me, Et, Ph

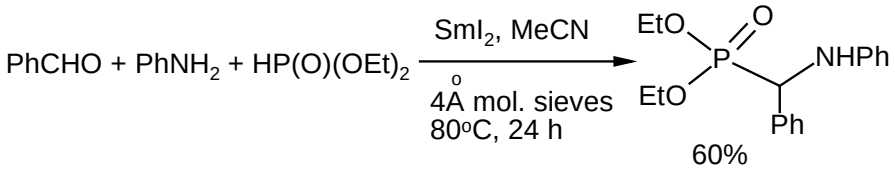
In the Kabachnik-Fields reaction, a three-component system of a carbonyl compound, ammonia (or a primary amine) and dialkyl phosphite is applied for the preparation of aminophosphonates 1.**35** (Scheme 1.**17**).[29-30] In place of ammonia, ammonium formate can also be used.[31] In a one-pot operation, wide ranging variations such as either ammonium hydrogen carbonate/ Silica gel/ microwaves or ceric ammonium nitrate can effectively catalyze the reaction.[32,33] Even SmI_2 (Scheme 1.**18**) or lithium perchlorate/ diethyl ether is a good catalyst (cf. compounds 1.**36**).[34,35]

Scheme 1.17



1.**35**

Scheme 1.18



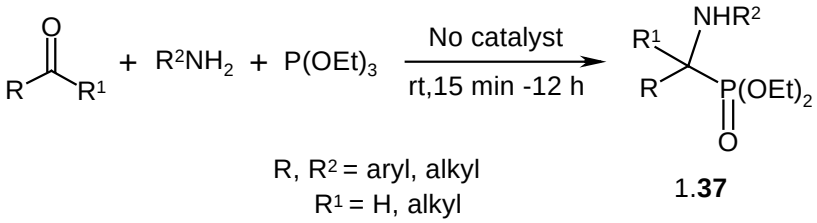
60%

1.**36**

Aldimines are proposed as intermediates in Kabachnik-Fields reaction. This led to the use of Schiff bases as substrates for the synthesis of aminophosphonates.[36] Although the nucleophilic addition reaction of phosphites to imines may proceed without a catalyst, the reaction is activated by base or by acid catalysis.[37] $InCl_3$ is a good Lewis acid catalyst and is efficient even in aqueous medium;[38] zirconium tetrachloride or lanthanum triflates can also be used as catalysts.[39,40]

The aminophosphonates 1.**37** can be synthesized by the three component coupling of carbonyl compounds, amines and triethylphosphite without using solvent or catalyst (Scheme 1.**19**).[41] A simple, efficient and general method has also been developed for the synthesis of α-aminophosphonic acids from hypophosphorous salts under solvent-free conditions using microwave irradiation.[42]

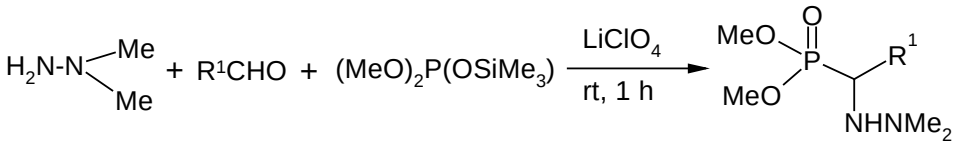
Scheme 1.19



1.**37**

Various α-hydrazinophosphonates 1.**38** were prepared on the basis of three-component (aldehydes, N,N-dimethylhydrazine, and dimethyl(trimethylsilyl)phosphite) coupling reactions via $LiClO_4$ catalyzed tandem reactions (Scheme 1.20). This method seems to be a good route to α-alkyl hydrazinophosphonates. However, aromatic aldehydes (e.g. benzaldehyde) or cinnamaldehyde are inert to nucleophilic addition.[43]

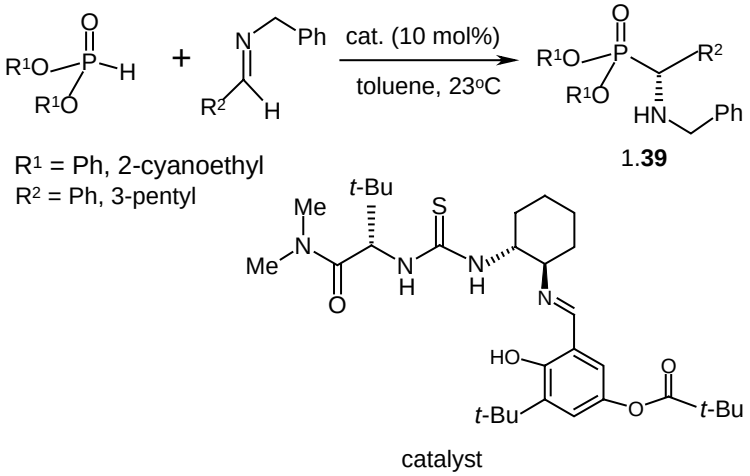
Scheme 1.20



1.**38**

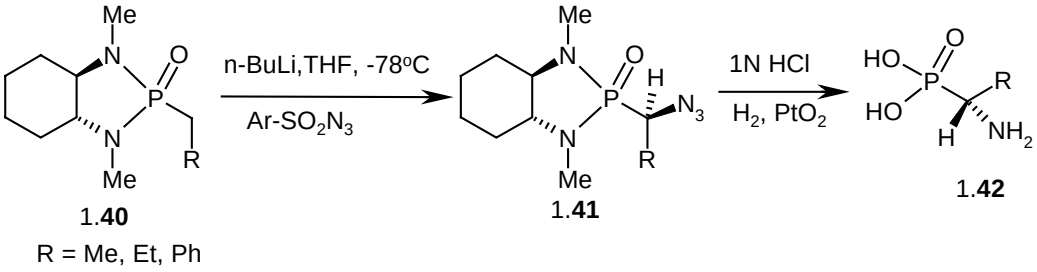
One of the recent methods for the preparation of chiral aminophosphonates involves the reaction of phosphites with N-benzylamines in the presence of a chiral thiourea catalyst leading to compounds 1.**39** (Scheme 1.21).[44] Catalytic asymmetric synthesis of α-aminophosphonates using enantioselective carbon-carbon bond-forming reactions is also reported recently by Kobayashi et al.[45]

Scheme 1.21



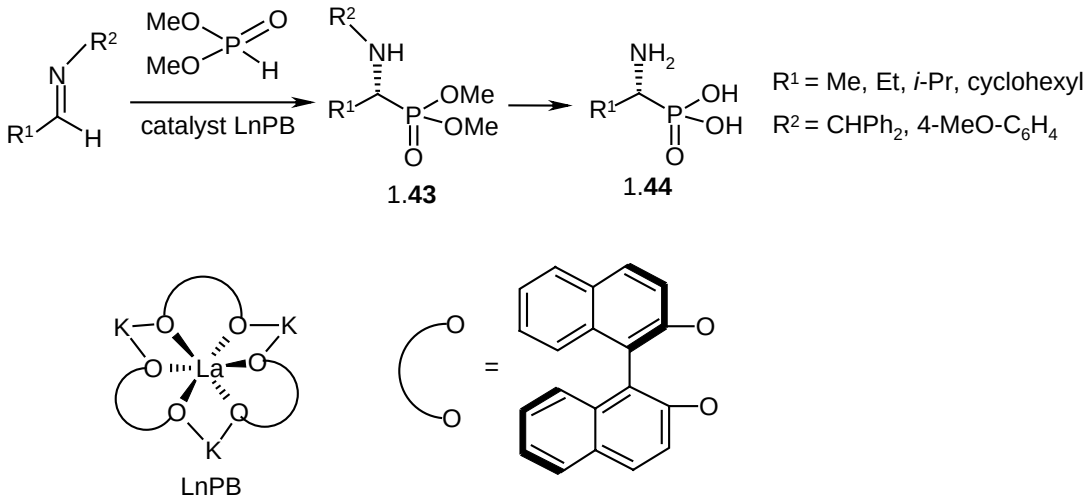
Hanessian *et al* have reported that chiral alkylphosphonamides (1.**40**), derived from N,N'-dimethyl (*R*,*R*)-1,2-diaminocyclohexane, undergo electrophilic azidation with trisylazide to give α-azidophosphonamides (1.**41**) with excellent enantioselectivity (Scheme 1.22). After deprotection and reduction of the azido group, various aminophosphonic acids (1.**42**) were obtained.[46]

Scheme 1.22



Shibasaki and his coworkers reported the first example of catalytic asymmetric hydrophosphonylation of imines using lanthanoid-potassium-BINOL heterobimetallic complexes (LnPB, Ln = lanthanide metal) leading to optically active aminophophosphonates (1.**43**) in modest to high enantiomeric excess (Scheme 1.23).[47] The use of 10-20 mol% lanthanum–potassium-(*R*)-BINOL complex (LnPB) showed high enantiomeric excess and good yields in the reaction of imines with dimethylphosphite in toluene-THF medium at room temperature. Phosphonates 1.**43** can be hydrolysed to give the aminophosphonic acids 1.**44**.

Scheme 1.23

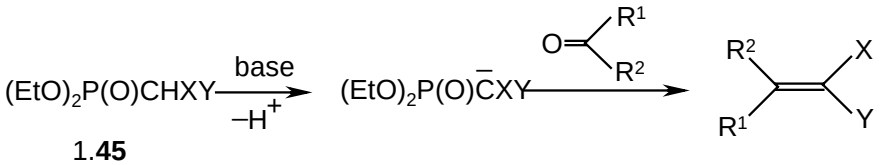


In addition to the above, there are several reports on the synthesis of chiral aminophosphonates/ aminophosphonic acids that use essentially the same principles.[48]

1.3 Phosphonates: Utility in Organic Synthesis

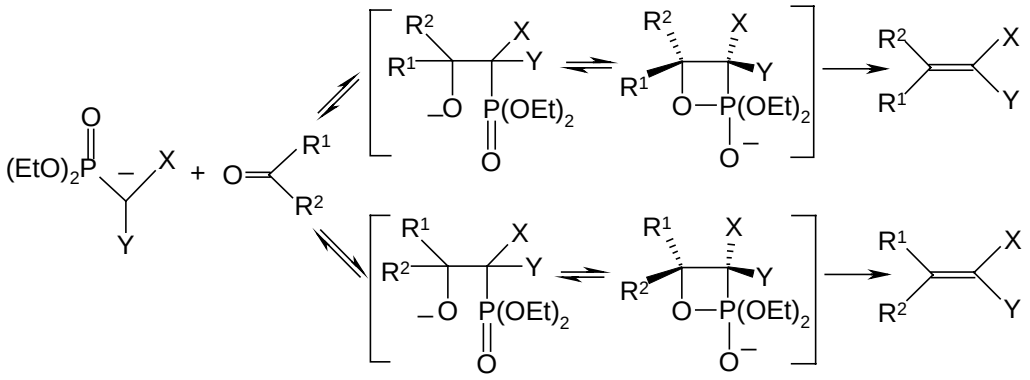
Although the Wittig reaction is one of the most effective and general methods of alkene formation from carbonyl derivatives,[49] it has a major disadvantage that the byproduct (e.g. $Ph_3P=O$) is water insoluble and hence the separation of products is not always convenient. Phosphonate esters 1.**45** and related compounds with a second stabilizing group form anions that undergo a Wittig-like reaction with both aldehydes and ketones (Scheme 1.24). Such reactions were originally described by Horner, but the general applicability of the reaction was shown by the work of Wadsworth and Emmons and hence this methodology is often referred to as the 'Horner-Wadsworth-Emmons' reaction (abbreviated as HWE reaction).[50]

Scheme 1.24



The addition of phosphonate anions to $R^1R^2C(O)$ gives a mixture of the *erythro* and *threo* isomeric β-hydroxyphosphonates as anionic intermediates (Scheme 1.25).[51] These intermediates lead to four-membered phosphetanes which are similar to those obtained from phosphonium ylides in the Wittig reaction.[52] These will then decompose by *syn* elimination of phosphate (or phosphinate) to give the alkene. The elimination is stereospecific, with the *erythro* form producing one isomer and *threo* form producing the other.

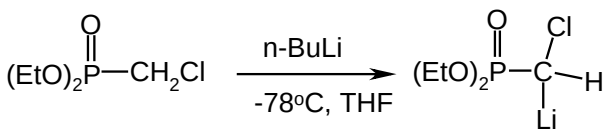
Scheme 1.25



In the above reaction, formation of the phosphonate anion $(EtO)_2P(O)\overline{C}(X)(Y)$ is favoured by electron withdrawing groups (X or Y). Also, the phosphono group confers less stability on the anion than does the positively charged triphenylphosphonio-group, with the result that Horner-Wadsworth-Emmons reagents are more reactive than the corresponding Wittig ylides.

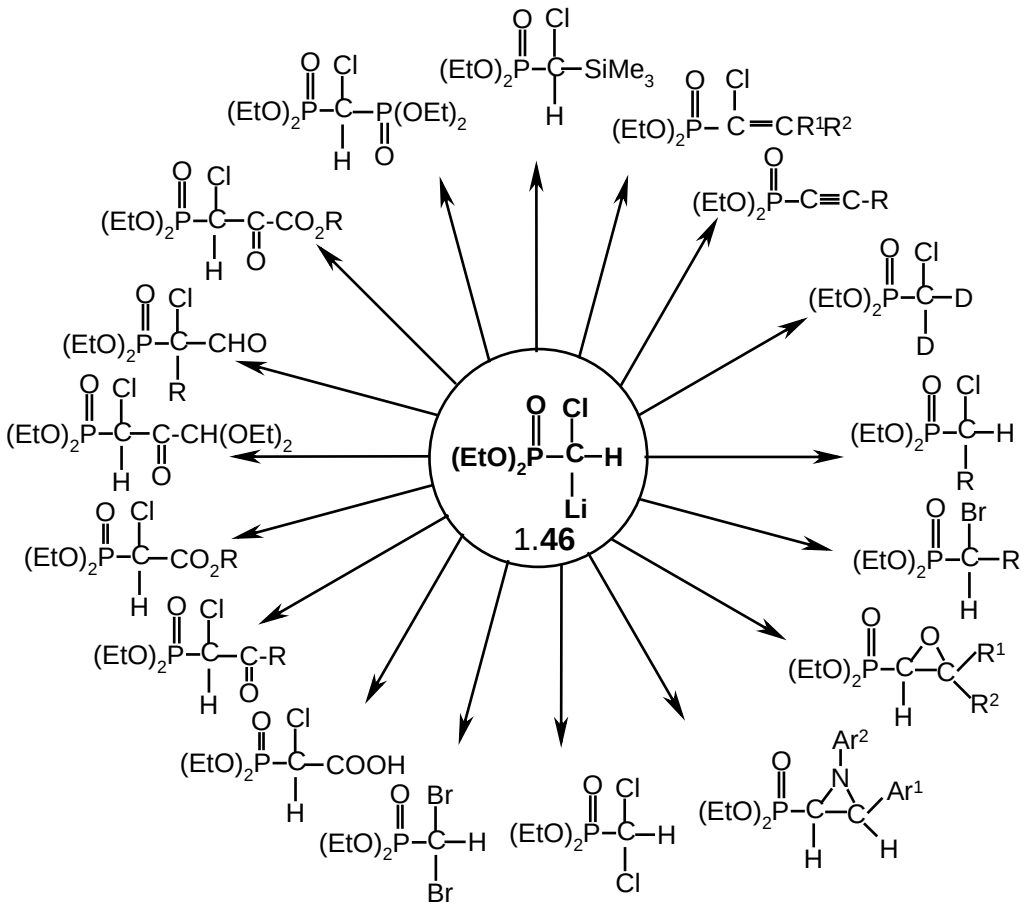
The phosphonate anions $(EtO)_2P(O)\overline{C}(X)(Y)$ are, in general, not very stable. Species 1.**46** is a stable anion isolated by Savignac and coworkers (Scheme 1.26)[53]; this compound can be kept at 0^oC for 30 min without apparent degradation. Compound 1.**46** itself is a useful synthon for preparing a variety of other phosphonates (Scheme 1.27) that have potential for use in HWE reactions.

Scheme 1.26



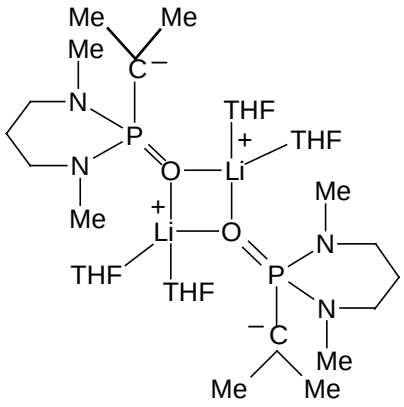
1.**46** [δ(P) 45.3]

Scheme 1.27
(from ref. 53)

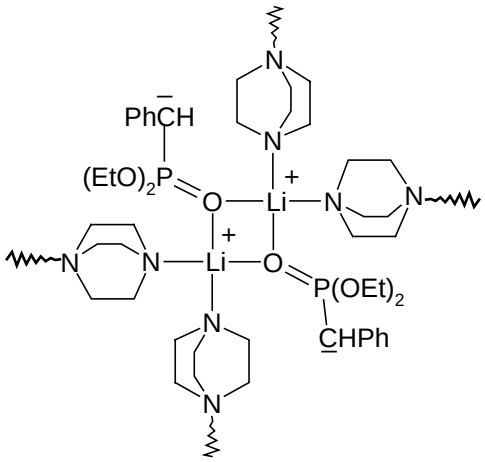


Several phosphonate anions have been characterized as lithium salts by X-ray structure determination; whereas $[Li.2THF]^{+}[(MeNCH_2CH_2CH_2NMe)P(O)(CHMe_2)]^{-}$ (1.**47**) is a dimer, the DABCO compound $[(EtO)_2P(O)CH(Ph)Li.N(CH_2CH_2)_3N]$ (1.**48**) is a polymer.[54]* Compound 1.**47** is a dimer in solution also [-100°C; ^{7}Li NMR: a triplet due to ^{2}J (^{31}P-^{7}Li); cryoscopy]. In the ^{13}C NMR spectrum of the anion, the carbon α- to phosphorus shows up as a doublet at δ 8.0, upfield to that of the neutral phosphonate [δ(C): 23.6 (d)] by 15.6 ppm.[54] Theoretical calculations also predict dimer formation in THF solution (in the absence of DABCO).[55]

*The other important points are: (i) anions are planar (ii) absence of metal (Li)-carbon contact and (iii) barrier to P-C bond rotation is very low (< 8 kcal/ mol).

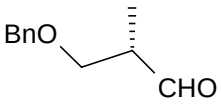
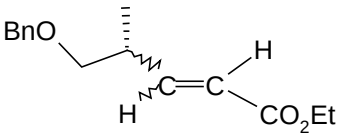
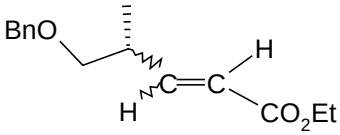


1.**47** (dimer)



1.**48** (polymer)

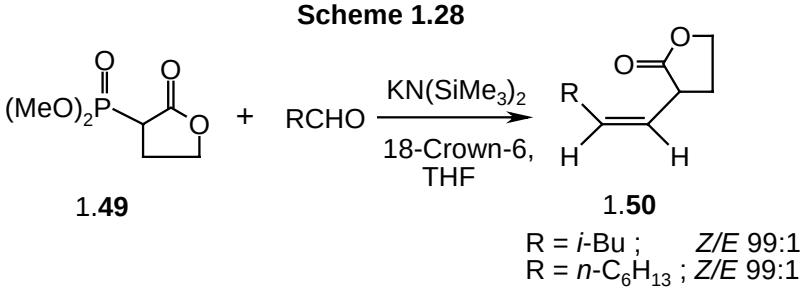
The most common application of the HWE reaction is in the synthesis of disubstituted (*E*)-alkenes. The (*E*)-stereoselectivity of the reaction can be maximized by increasing the size of the substituents on the phosphoryl portion; conversely, less bulk on the phosphonate is supposed to lead to *Z*-alkene formation.[51,56] An example to this effect is given below:

Aldehyde	Reagent	Product	*Z*/ E ratio
	$(Pr^iO)_2P(O)CH_2CO_2Et$, $KOBu^t$, THF, -78°C		5:95
	$(MeO)_2P(O)CH_2CO_2Et$, $KOBu^t$, THF, -78°C		3:1

The above information has been utilized for the synthesis of brefeldin-C and rifamycin-H which has an *E*-configured terminal double bond.[57] As far as the base is concerned, studies suggest that LiOH/ THF can give high *E*-selectivity.[58]

Dimethyl phosphonyl-γ-butyrolactone 1.**49**, which has less bulky methoxy groups on phosphorus, affords *Z*-olefins 1.**50** with very high selectivity in its reaction with aldehydes (Scheme 1.28). However, in the case of benzaldehyde the *Z*/*E* ratio was 1:1.

Scheme 1.28

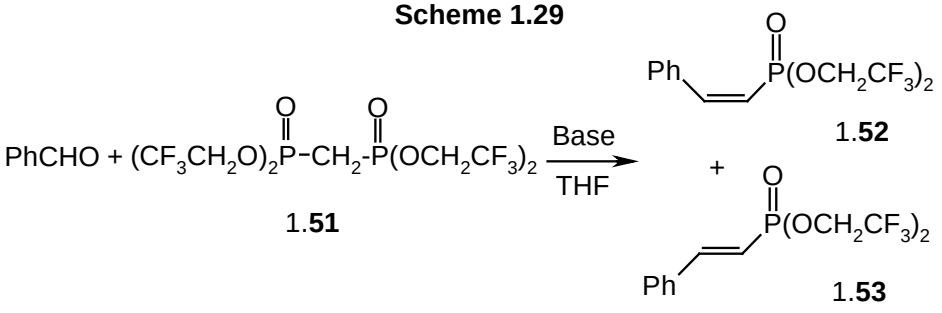


1.**49** 1.**50**

R = *i*-Bu ; *Z/E* 99:1
R = *n*-C_6H_{13} ; *Z/E* 99:1

Thus it appears that there is more left to be learnt as regards *Z/E* stereoselectivity. This statement is also corroborated by the results of Kiddle and coworkers[59] who obtained predominantly (*Z*)-isomers using the bisphosphonate $[(CF_3CH_2O)_2P(O)]_2CH_2$ 1.**51** (Scheme 1.29) which contains fairly bulky OCH_2CF_3 groups. Depending on the base used [KHMDS, KH, NaH; presence or absence of crown ethers], they obtained different ratios of *Z/E* isomers 1.**52**-1.**53**, with KHMDS/18-crown-6/ -78^{o}C giving the highest *Z/E* ratio (93:7). From the same studies, it appears that low temperature and presence of crown ether favour the formation of *Z*-isomers.

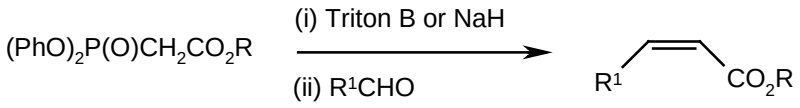
Scheme 1.29



1.**51** 1.**52** 1.**53**

Ando has studied the *Z*-selectivity in HWE reactions in greater detail.[60] In the studies on (diphenylphosphono) acetic acid esters 1.**54**, it was observed that a bulkier phosphonate ester gives higher *Z*-selectivity (to yield 1.**55**) (Scheme 1.30). Thus, it appears that *Z* or *E* selectivity is not easy to explain, despite a large number of studies.

Scheme 1.30



1.54 **1.55**

As far as bases are concerned, the following list represents the most widely used ones:[61]

(i) n-BuLi/ THF (ii) NaH/ THF (iii) LDA/ THF.

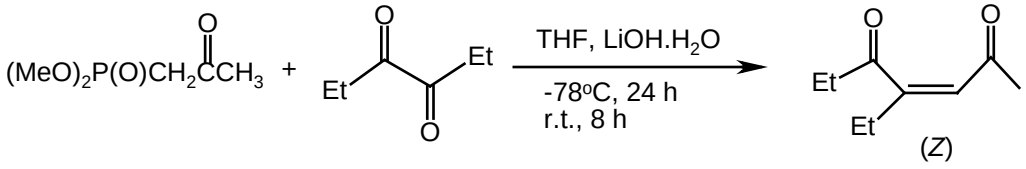
Other bases which have also found utility include (i) KO-*t*-Bu (ii) K_2CO_3 (iii) LiCl/ R_3N (iv) $MgCl_2.Et_3N$ and (v) KHMDS. In a report by Foucaud and coworkers a solid-liquid two phase system has also been used.[62]

As far as the solvent is concerned, it appears that THF is the most preferred one.

In the following paragraphs selected recent literature highlighting the potential of phosphonates is outlined.

(i) *Z*-Enedicarbonyl compounds 1.**57**, useful for the synthesis of cyclopentanone derivatives present in prostaglandins, have been synthesized by the HWE route in high stereoselectivity (Scheme 1.31).[63]

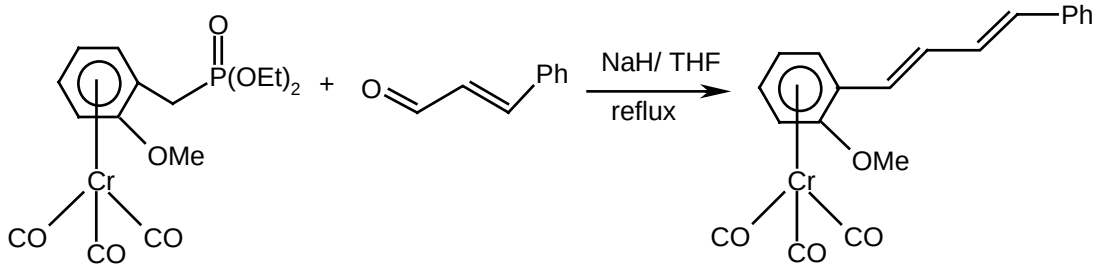
Scheme 1.31



1.**56** 1.**57**

(ii) Alkenyl substituted tricarbonylchromium arene complexes 1.**59** have been synthesized by the HWE approach (Scheme 1.32).[64] The isolated yields are moderate with both the *E* and *Z* isomers formed in comparable quantities.

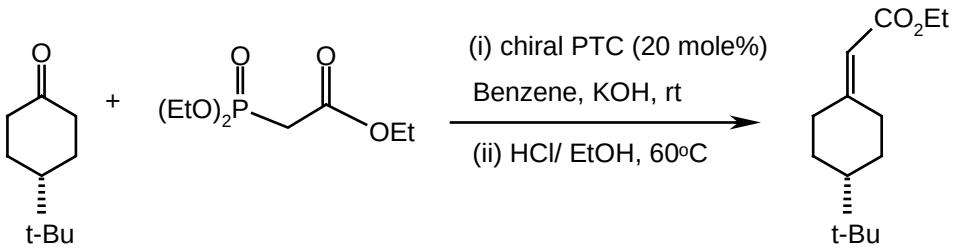
Scheme 1.32



1.**58** 1.**59** Yield: 87%

(iii) Catalytic asymmetric HWE reaction promoted by a chiral phase-transfer catalyst (quaternary ammonium bromide derived from cinchonine) can be utilized for the synthesis of optically active α,β-unsaturated esters 1.**61** (Scheme 1.33).[65]

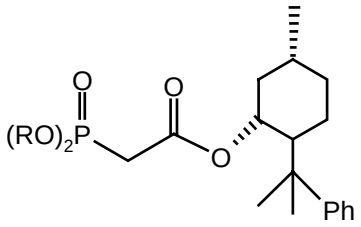
Scheme 1.33



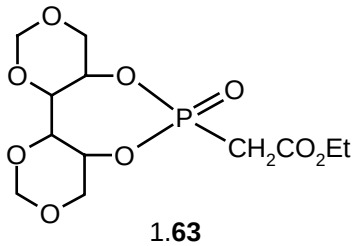
1.**60** 1.**61**

The desired products were obtained in moderate enantiomeric excess. It is also possible to use the optically active aluminium lithium bis(binapthoxide) complex in combination with *n*-BuLi for asymmetric HWE reactions.[66]

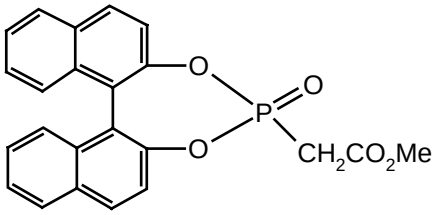
Chiral reagent based asymmetric HWE reaction is also possible as shown recently by Tullis *et* al;[67] they have used the chiral phosphonate reagents 1.**62** for this purpose. Other chiral phosphonates that have been used for asymmetric HWE reactions include 1.**63**,[68] 1.**64**[69] and 1,2-diaminocyclohexane derivatives.[70]



1.**62**



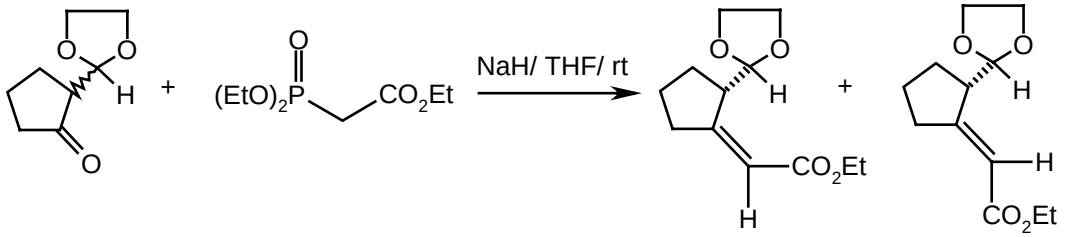
1.**63**



1.**64**

(iv) It is also possible to utilize the HWE reaction for base sensitive ketones that are enolizable; this approach has been useful for the synthesis of iridoid cyclopentapyranones 1.**65**- 1.**66** (Scheme 1.34).[71]

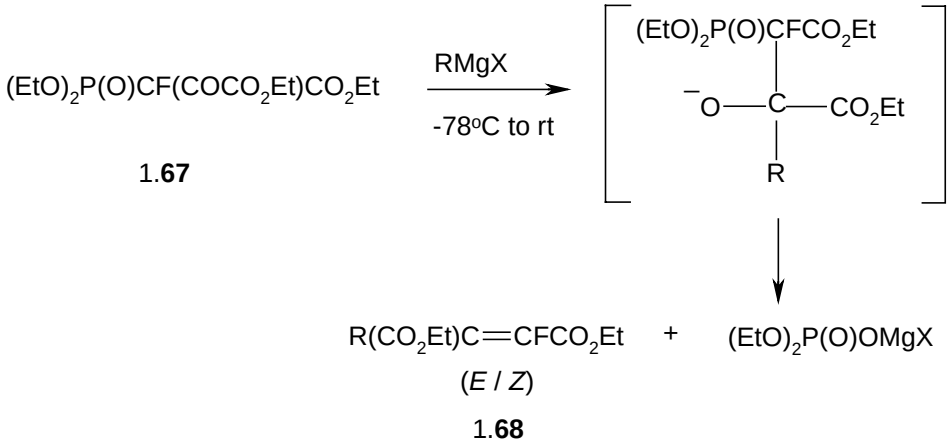
Scheme 1.34



1.**60** 1.**65** 1.**66**

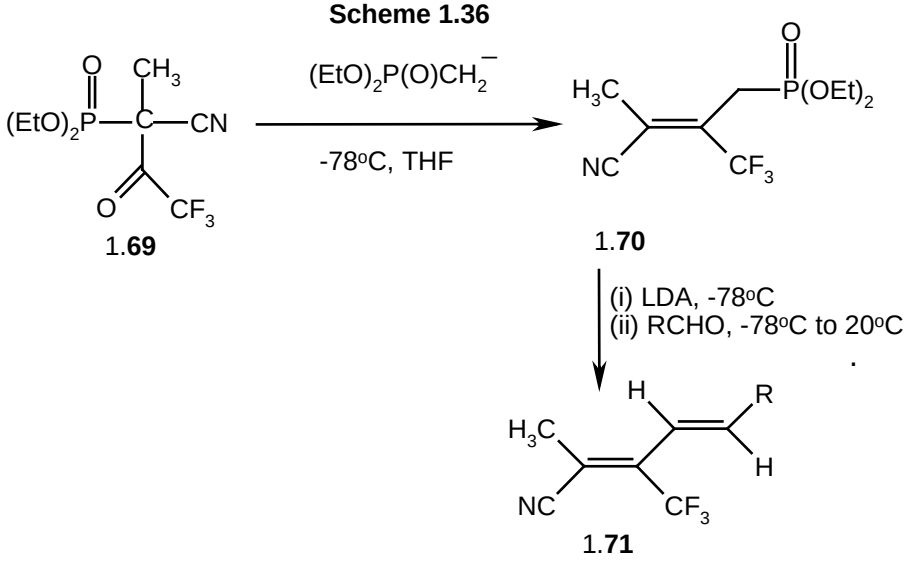
(v) A novel intramolecular HWE reaction leading to α-fluoro-α,β-unsaturated diesters 1.**68** has been reported by Tsai *et al* (Scheme 1.34).[72] It can be readily seen that the intermediate shown here is not too different from that shown in Scheme 1.25. Similar transformations using an alkyllithium in place of a Grignard reagent are also possible.[73]

Scheme 1.34



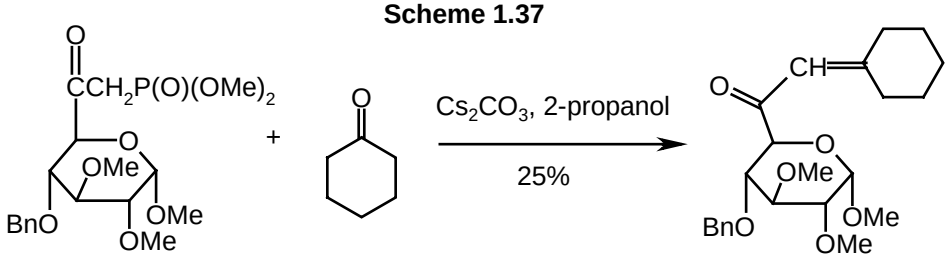
(vi) Substituted 1,3-dienes can be conveniently synthesized by using 2-alkenylphosphonates such as $(EtO)_2P(O)CH_2C(CN)=CHR$ (1.**69**).[74] The same result can also be achieved by using the double olefination approach- both the olefinations taking place *via* HWE reaction.[75] Here, in the first step, the carbonyl function of the neutral phosphonate acts as the ketone (Scheme 1.35).

Scheme 1.36



(vii) In carbohydrate chemistry also the HWE reaction is quite useful, with the restriction being that milder bases/ conditions have to be used (Scheme 1.37).[76]

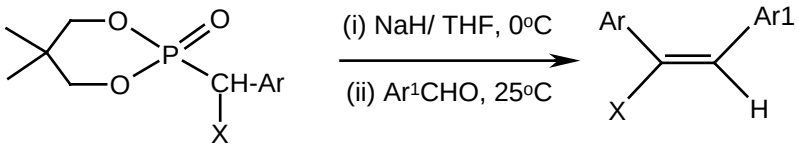
Scheme 1.37



1.**72** 1.**73**

(viii) For the synthesis of chloro and bromostilbenes 1.**75**, α-chloro or α-bromophosphonates 1.**74** bearing a 1,3,2-dioxaphosphorinane ring have been found useful (Scheme 1.38).[77]

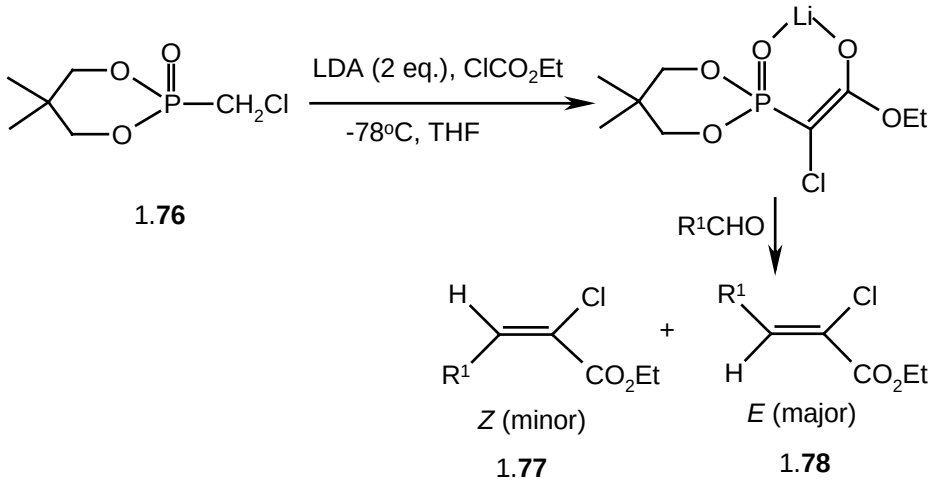
Scheme 1.38



1.74 1.75

Chloromethyl substituted phosphonates 1.**76** bearing the same six-membered ring have been useful in preparing α,β-unsaturated esters 1.**77**-1.**78** bearing an α-chloro group (Scheme 1.39).[78]

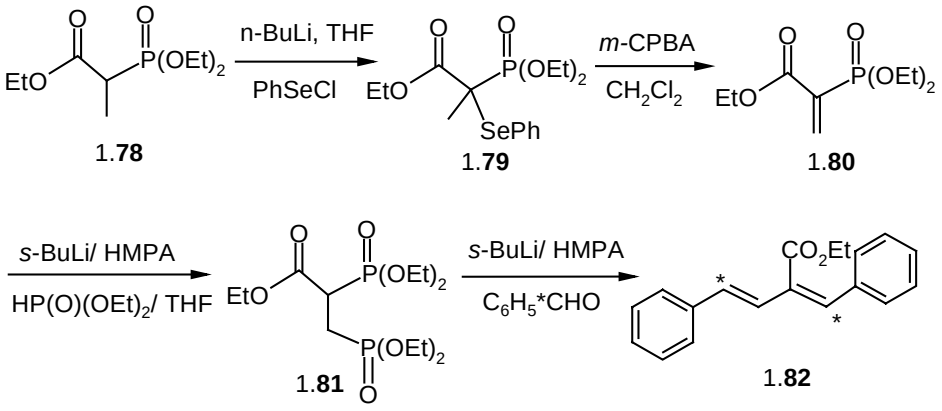
Scheme 1.39



1.**76** 1.**77** 1.**78**

(ix) The 1,4-bis-^{13}C labeled isomeric compounds (*Z*,*E*)-2-ethoxycarbonyl-1,4-diphenylbutadienes 1.**82** have been synthesized by a double HWE strategy (Scheme 1.40).[79]

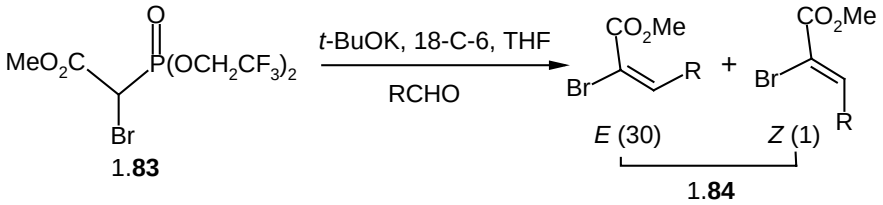
Scheme 1.40



1.**78** 1.**79** 1.**80** 1.**81** 1.**82**

(x) The novel reagent, methyl bis(2,2,2-trifluoroethoxy)bromophosphonoacetate 1.**83** is utilized for the synthesis of (*E*)-α-bromoacrylates 1.**84** (Scheme 1.41).[80]

Scheme 1.41

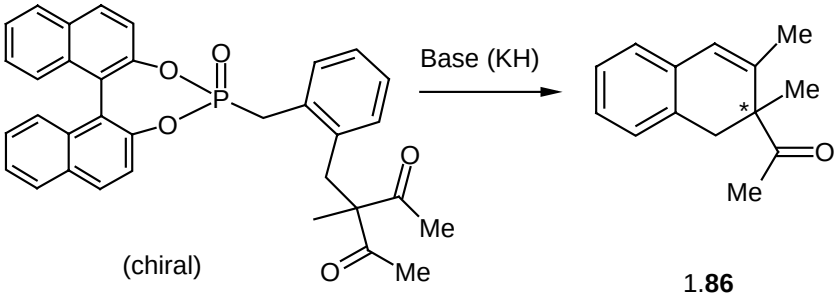


1.**83** 1.**84**

The above route was utilized for the synthesis of Plaunotol, a known anticancer drug via the bromoacrylates synthesized through the HWE reaction.[81]

(xi) Intramolecular asymmetric HWE reactions of some chiral binaphthyl phosphonates with 2,2-disubstituted 1,3-dicarbonyl groups 1.**85** have been effected in good yields and 82-88% ee (Scheme 1.42).[82]

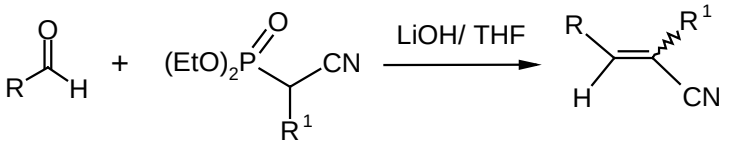
Scheme 1.42



1.**85** 1.**86**

(xii) A mild and practical procedure of HWE olefination promoted by lithium hydroxide and α-cyanophosphonates 1.**87** has been set up for the synthesis of α, β-unsaturated nitriles 1.**88** (Scheme 1.43). The reaction conditions are tolerated by functionalized ketones. The *E*-selectivity is predominant but *Z* isomer is also present in most cases.[83]

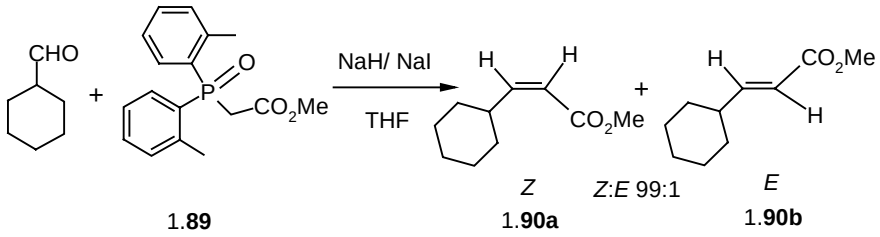
Scheme 1.43



1.**87** 1.**88**
R = Ar, PhCH=CH-
R^1 = Me or H
(Both *E* and *Z*)

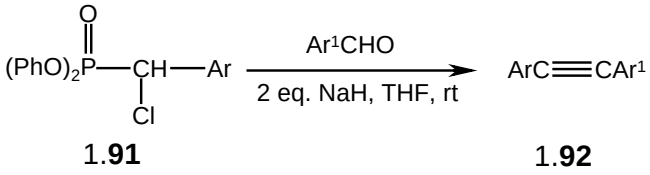
(xiii) New improved conditions for Z-selective HWE olefinations with Ando type (*o*-methylphenyl)phosphonates 1.**89** are reported. A combination of NaH and NaI affords Z olefins 1.**90a** in up-to >99:1 selectivity (Scheme 1.44). The fact that an excess of sodium ions is required for highest selectivities strongly suggests that these HWE reactions take place via cation-chelated intermediates and transition states.[84]

Scheme 1.44



(xiv) Although transition metal related routes are also available, α-chlorophosphonates 1.**91** offer a convenient route to a variety of unsymmetrical acetylenes 1.**92** *via* HWE reaction (Scheme 1.45).[86] Other α-halogenated phosphonates have also been subsequently developed for alkyne synthesis.

Scheme 1.45



(xv) Phosphonates can also be utilized for various organic syntheses without involving the HWE reaction. For example, vinylphosphonates $(EtO)_2P(O)C(E)=CHR$ [E=CN, SMe, CO_2Et etc.] are very useful precursors for a large number of carbocyclic and heterocyclic compounds; the double bond reactivity is made use of in these reactions. Since this and other applications[87] are not directly relevant to HWE reactions, they are not discussed further.[88]

(xvi) *Theoretical studies*: Ab Initio calculations by Ando on the HWE reaction of $(MeO)_2P(O)CH(Li)CO_2Me$ with acetaldehyde have shown that first the addition of lithium enolate to the aldehyde occurs followed by oxaphosphetane formation, pseudorotation, P-C bond cleavage and then O-C bond cleavage (*cf.* Scheme 1.24).[89] The oxaphosphetane formation is the rate-determining step both in the gas phase and in the presence of one dimethyl ether molecule. The transition state leading to the *trans* olefin is more stable than the transition state leading to the *cis* olefin. Brandt *et al* have evaluated the solvation contribution involved here.[90] In the free anionic system, the rate-determining step was again found to be the ring closure of the oxyanion to the oxaphosphetane. Several mechanistic alternatives have also been considered using the reaction of formaldehyde and

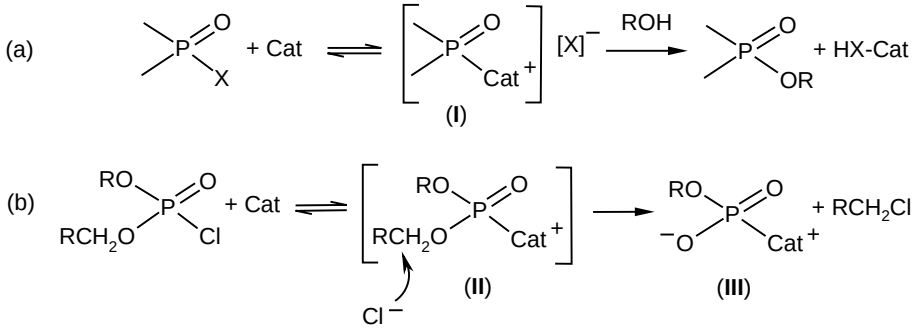
$(MeO)_2P(O)\overline{C}HCOOMe$ as a model system. When solvation was taken into account, it was predicted that the bimolecular formation of the oxyanion $(MeO)_2P(O)$-$CH(COOMe)$-CH_2O^- may be rate-determining.

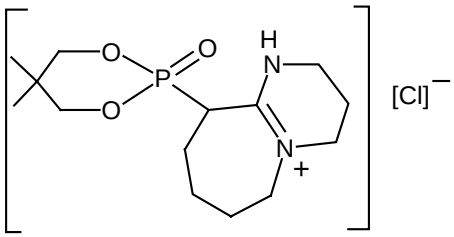
Another point as regards to the HWE reaction concerns the P-C bond rotation in phosphonate carbanions, which could play a role in the stereoselectivity. An *ab Initio* study suggests that the P-C bonds in the anion have low rotational barriers,[54b] and this may have a bearing on the nature of results inconclusive concerning *E*/*Z* stereoselectivity in HWE reaction (see above).

1.4 Reaction of Chlorophosphosphate Esters with Organic Bases

Nucleophilic substitution reactions of chlorophosphates are most often carried out in the presence of a base. In the absence of the base, this reaction will be slow and sometimes the base itself acts as a nucleophilic catalyst. The mechanism of rate enhancement (nucleophilic catalysis) of the nucleophilic substitution at phosphorus is commonly interpreted by two consecutive $S_N2(P)$ reactions (Scheme 1.46).[91-93] The leaving group X is substituted by the nucleophilic catalyst (Cat; can be N-methyl imidazole, imidazole or other bases) leading to a very reactive intermediate (**I**). The nucleophile then reacts with this intermediate giving the product. Although a species of type **I** has never been detected when the mixture of alcohol and catalyst was added to chlorophosphates, it is identified by NMR in the absence of alcohol. In the reaction of $(RO)(RCH_2O)P(O)Cl$ with the catalyst (Cat), formation of betaine **III** is observed and is assumed to occur *via* the intermediate **II**[94]. In the reaction of $(EtO)_2P(O)Cl$ with N-methyl imidazole, Corriu and coworkers have identified three products (**IV**-**VI**); salts **IV**-**V** (not isolated) are similar to **II** and **III**[93]. We have been interested in isolating intermediates of types **I**-**III**. One of the bases used by earlier workers work was 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU), but in a preliminary study from our laboratory had shown that this base could lead to ***phosphonate*** salts (e.g. 1.**93**) instead of betaines of type **I**.[95]. Since such a product was never reported prior to our work, we were curious to know whether this feature is common for other chlorophosphate esters also or not.

Scheme 1.46





1.**93**

OBJECTIVES OF THE PRESENT WORK

(Phosphonates)

The primary objectives of the present work are (i) to develop convenient routes to new organophosphonates and (ii) to find utility for the phosphonates thus obtained in organic synthesis, where possible. The following systems have been explored:

(i) Conversion of α-hydroxyphosphonates, obtained by the Pudovik reaction, to α-chloro/ α-bromophosphonates,

(ii) Use of a modified Abramov reaction to obtain α-substituted (α-Cl, α-$OSiMe_3$) phosphonates,

(iii) A one-pot synthesis of isomeric α- aminophosphonates, and

(iv) Reactivity of chlorophosphate esters with organic bases in an effort to understand the formation of phosphonate salts and pyrophosphates.

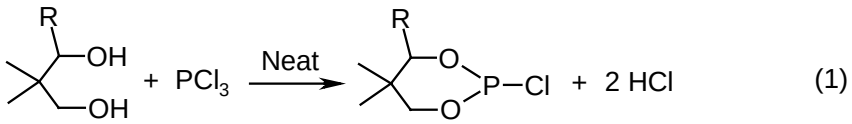
As far as the utility of phosphonates is concerned, only the Horner-Wadsworth-Emmons (HWE) reaction is investigated in this study. The aim is to synthesize chlorosubstituted olefins using conveniently prepared and cheap reagents.

CHAPTER 2

RESULTS AND DISCUSSION

2.1 Synthesis of Phosphites

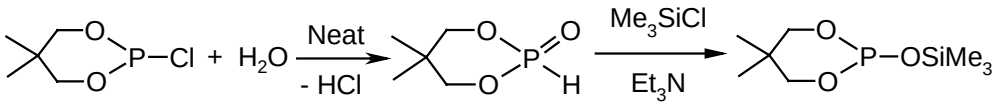
This part of the present work is essentially based on the precursors (OCH_2CMe_2CHRO)PCl [R = H (**1a)**, Ph (**1b**), (3-Br-C_6H_4) (**1c**)] which have a six-membered 1,3,2-dioxaphosphorinane ring.[96a-c] In the present study, compounds **1a-c** are prepared by treating the respective diol with phosphorus trichloride (slight excess) under neat conditions (eq. 1); compound **1a** is purified further by distillation in vacuum whereas **1b-c** are used as such after removal of unreacted PCl_3.



R = H; **1a** [b.p. 40°C/ 1 mm, δ(P): 145.8]
R = Ph; **1b** [δ(P):149.6]
R = 3-Br-C_6H_4; **1c** [δ(P):150.0, 151.2]
Yield: 85 - 95%

As is the case with many P(III) compounds containing a residual P-Cl bond, **1a** can be readily hydrolyzed by water to give the phosphite **2** (H-phosphonate; Scheme 1). Compound **2**, although can be distilled in vacuum, was used as such for further reactions in the present study without any difficulty. Upon reaction with trimethylsilyl chloride/ triethylamine, compound **2** gave the trivalent phosphite **3** (Scheme 1). This latter reaction has some precedence,[14,97] but is quite interesting since there are not many ways in which a phosphoryl (P=O) group is converted to a P(III) compound. The driving force is likely to be the formation of an Si-O bond stabilized by π-interaction of the vacant silicon *d*-orbitals with oxygen lone pair (or via hyperconjugative interactions[98]) of electrons.

Scheme 1

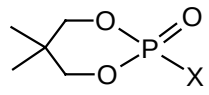


1a

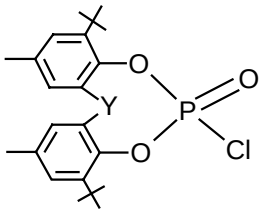
2 [δ(P): 2.3]
Yield: Quantitative

3 [δ(P): 108.6]
Yield: 94%

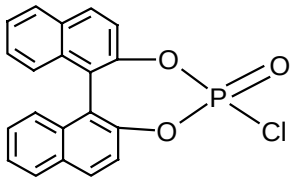
Compound **4** is prepared by the reaction of $P(O)Cl_3$ with 2,2-dimethyl-1,3-propanediol in the presence of a base while the azide **5** is prepared by treating **4** with sodium azide in methyl cyanide. Compounds S(6-*t*-Bu-4-Me-$C_6H_2O)_2$]P(O)Cl (**6a**),[99] CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2$P(O)Cl (**6b**)[95] and (2,2'-$C_{20}H_{12}O_2$)P(O)Cl [**7**, racemic][118] were prepared in a manner analogous to that of **4**. All these compounds are moisture-sensitive but can be preserved under nitrogen atmosphere.



X = Cl [**4**: δ(P) -3.6]
X = N_3 [**5**: δ(P) -9.0]



Y = S [**6a**: δ(P) -8.2]
Y = CH_2 [**6b**: δ(P) -3.4]



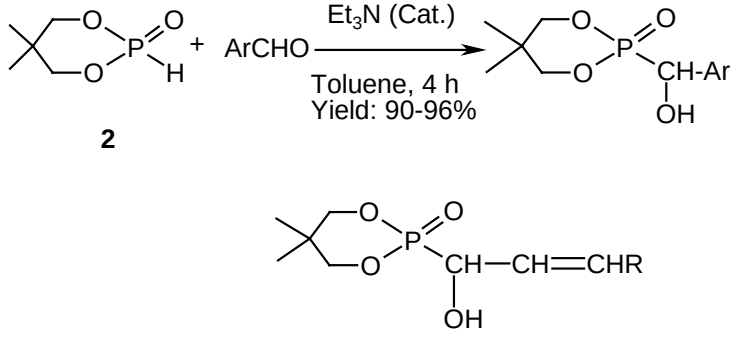
7 [δ(P): 11.1]

2.2 Synthesis of Phosphonates

2.21 *Synthesis of α-hydroxyphosphonates*

The α-hydroxyphosphonates **8a-h** have been synthesized by reacting **2** with aromatic aldehydes (Pudovik reaction; Scheme 2); compounds **9a-b** are also similarly obtained by treating **2** with cinnamaldehyde or crotonaldehyde respectively.

Scheme 2



Ar = Ph [**8a**, δ(P) 13.3]
C_6H_4-4-Me [**8b**, δ(P) 13.6]
C_6H_4-4-Cl [**8c**, δ(P) 12.9]
C_6H_4-4-OMe [**8d**, δ(P) 13.6]
1-naphthyl [**8e**, δ(P) 13.1]
9-anthryl [**8f**, δ(P) 16.9]
C_6H_4-3-Br [**8g**, δ(P) 13.4]
C_6H_3-2,6-Cl_2 [**8h**, δ(P) 14.1]

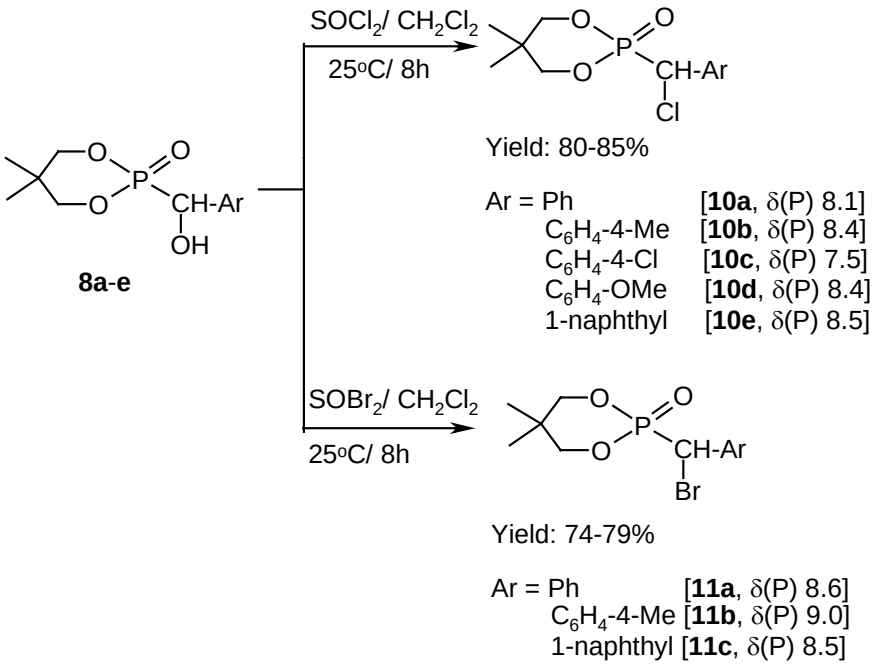
R = Ph [**9a**: δ(P) 13.9]
Me [**9b**: δ(P) 15.2]

Compounds **8a-h** and **9a-b** are stable in air in the solid state and in solution, but the solubility is less for some of these compounds. It can be noted that analogous ethoxyphosphonates are often liquids.[100] The IR spectra of show bands around 3300 (ν(OH)), 1250 (ν(P=O)) and 1050 (ν(P-O-C)) cm^{-1}. The ^1H NMR spectra show a characteristic doublet at δ 5.00-5.20 [^2J(P-H) ~12.0 Hz] for the P-C*H*-OH proton in **8a-h**; this proton is observed as a doublet of doublet at δ 4.90 in **9a** and as a doublet at δ 4.32 for **9b**. In the ^{13}C NMR, these phosphonates show a characteristic doublet around δ 71.0 [^1J(P-C) ~ 157 Hz] for the carbon 'α' to phosphorus. The ^{31}P NMR spectra show a single peak in the range δ 10-16.

2.22 *Synthesis of chloro and bromo substituted phosphonates by the reaction of 8a-e and 9a-b with $SOCl_2$/$SOBr_2$*

The α-chlorophosphonates **10a-e** have been prepared by treating the α-hydroxyphosphonates **8a-e** with thionyl chloride using dichloromethane as the solvent at room temperature; the α-bromophosphonates **11a-c** have been prepared by treating the α-hydroxyphosphonates **8a-b** or **8e** similarly with thionyl bromide (Scheme 3).[18e,19]

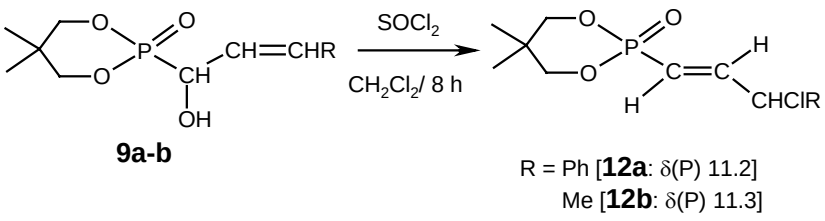
Scheme 3



Compounds **10a-e** and **11a-c** are air-stable solids. It is likely that the presence of the six-membered ring in our systems has facilitated the high yields. The ^{31}P NMR spectra exhibit peaks upfield to the α-hydroxyphosphonates **8a-e** [*cf.* Schemes 2 and 3]. This route, developed in our laboratory, is much superior to the use of PPh_3/DDQ/tetraalkyl ammonium halides as regards the isolation of the products.[20b] The $Ph_3P(O)$ formed in the latter reaction has an R_f value close to that of our phosphonates and hence hampers the isolation of pure products. In particular for the chlorophosphonates, our method is also very inexpensive.

In contrast to the above, the reaction of **9a-b** with thionyl chloride leads to the *γ chlorinated vinylphosphonates* **12a-b**. This reaction occurred in *a fashion different from that of the reaction of α-hydroxyphosphonates* **8a-e** *(normal aldehyde products) with thionyl chloride* (Scheme 4).

Scheme 4



9a-b

R = Ph [**12a**: δ(P) 11.2]
Me [**12b**: δ(P) 11.3]

The structures of compounds **12a-b** are proven by NMR spectroscopy and elemental analyses. Disappearance of the O-H functional group (from **9a**) is clearly shown by IR spectroscopy. The ^{1}H NMR spectrum of **12a** shows a doublet of doublet of doublet at δ 6.12 [^{4}J(HH), ^{3}J(HH), ^{2}J(PH) ~ 3.0, 19.1, 19.1 Hz] for the PC*H* proton, with the expected integrated intensities. Also in the ^{13}C NMR [Figure 1], compound **12a** shows a doublet at δ 117.2 [^{1}J(PC) = 186.0 Hz] for the P-*C*H carbon which is much downfield to that observed for **9a**. In **12b**, the PC*H* proton appears as a doublet of doublet at δ 6.00 in the ^{1}H NMR and the corresponding carbon appears at δ 116.1 [^{1}J(PC) = 186.5 Hz] in the ^{13}C NMR. Thus, compounds **12a-b** contain a P-CH= moiety instead of the P-CH(Cl) moiety present in the normal chlorinated derivatives **10a-e**. Finally, the structure of **12a** is unambiguously proved by X-ray crystallography (Figure 2).

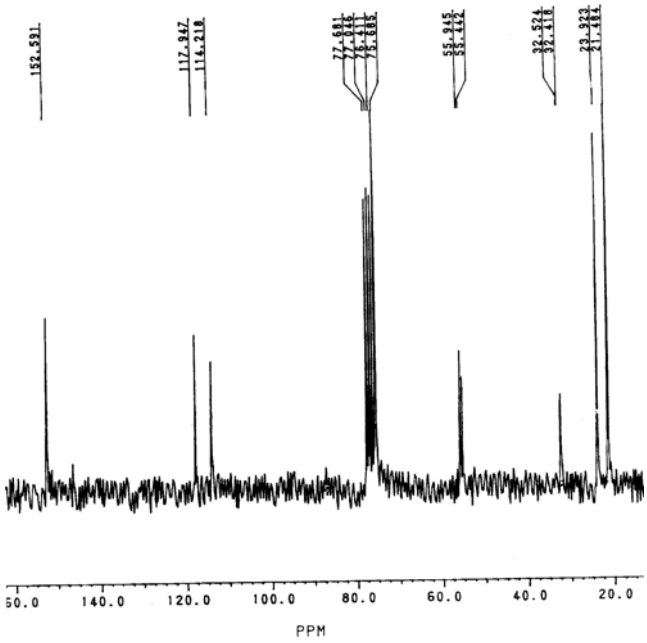


Figure 1. ^{13}C NMR spectrum of compound **12a**.

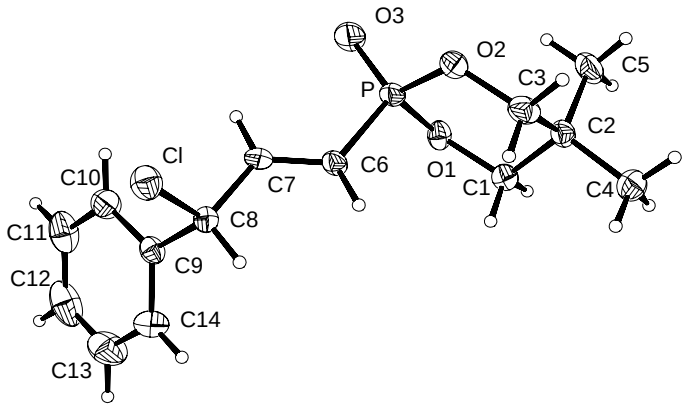
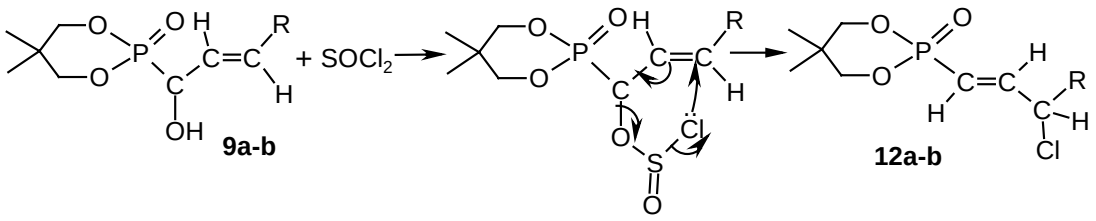


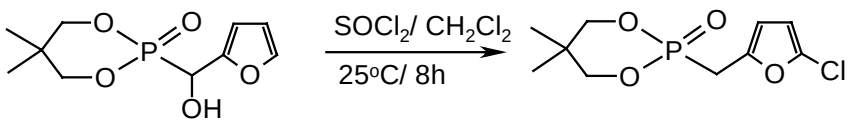
Figure 2. An ORTEP drawing of **12a**. Selected distances and angles: P-O(3) 1.445(4), P-O(1) 1.558(4), P-O(2) 1.577(4), P-C(6) 1.774(5), C(8)-C(7) 1.491(7), C(7)-C(6) 1.312(7) Å. O(3)-P-O(1) 111.8(2), O(3)-P-O(2) 112.6(3), O(1)-P-O(2) 104.9(2), O(3)-P-C(6) 114.0(3), O(1)-P-C(6) 106.5(2), O(2)-P-C(6) 106.5(2), C(1)-O(1)-P 121.7(3), C(3)-O(2)-P 120.5(3)^{o}.

A possible pathway for the formation of **12a-b** is given in Scheme 5. Formation of chlorinated products at a position different from α to the phosphorus (e.g. **13** from **8i**) was also observed in our laboratory in the case of furfuryl system (cf. Scheme 6), but this product is not a γ-chlorophosphonate.[101] The reaction of **9a** with thionyl bromide gives two products [δ(P) 6.4, 12.5], but no pure compound could be isolated.

Scheme 5

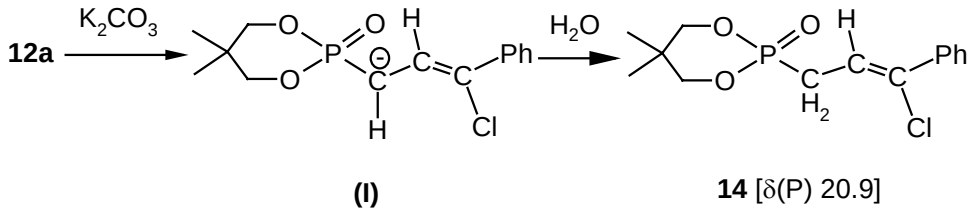


Scheme 6



Compound **12a** rearranges to the phosphonate **14** (~ 95% purity) upon treatment with K_2CO_3/ xylene. The ^{1}H [δ 3.10 (dd), 2 H, PC*H*$_2$)] [Figure 3] and ^{13}C NMR [δ 26.7 (d, ^1J(PC) = 136.5 Hz, P-*C*] spectra clearly show that the structural conversion has taken place via the carbanion **I** (Scheme 7); there is also a significant shift in the ^{31}P NMR chemical shift. This result has implications as regards the utility of **12a** (see section 2.32) in HWE reaction.

Scheme 7



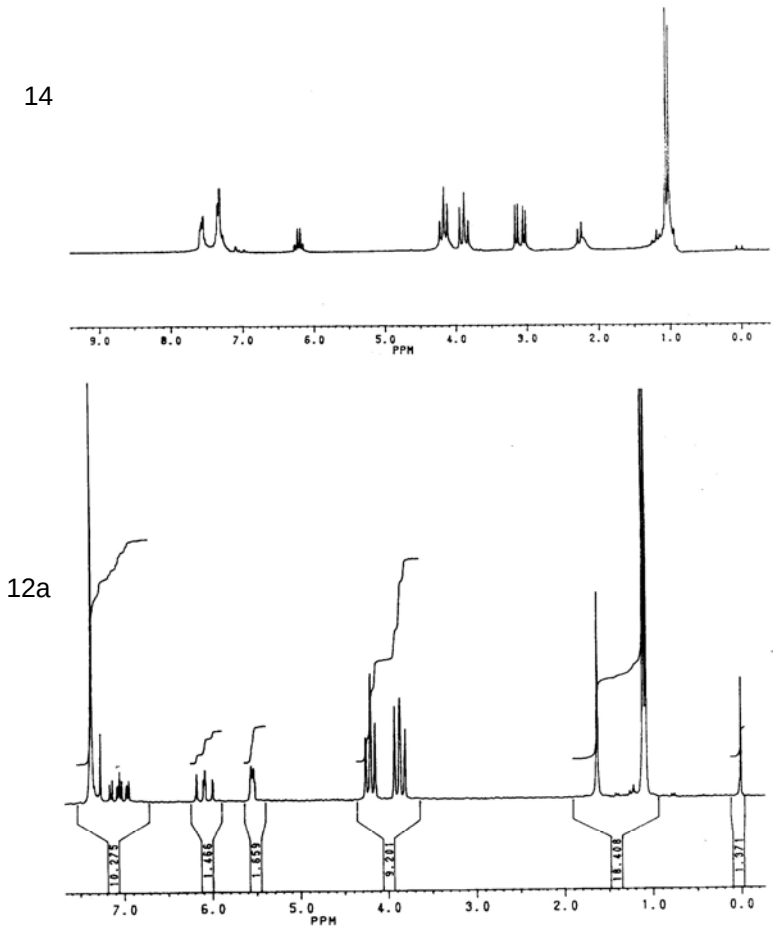
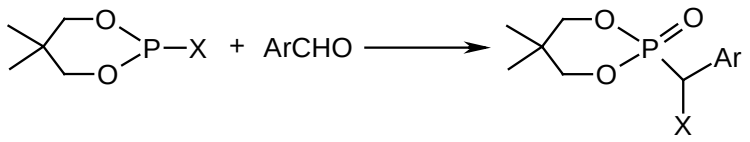


Figure 3. ^{1}H NMR spectra of compounds **12a** and **14**.

2.23 *Direct synthesis of chloro and α-trimethylsilyloxyphosphonates*

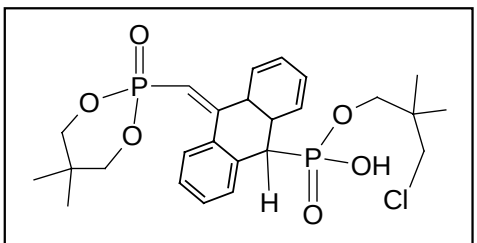
For the synthesis of compounds of type $(RO)_2P(O)CH(X)Ar$ (**II**), where X is a group other than a halogen, a procedure that uses a common, readily accessible precursor is not avaliable.[14,22] Species **II** can be regarded as an addition product of the corresponding phosphite $(RO)_2PX$ and an aldehyde ArCHO, formed by a modified Abramov reaction. As described before, the compounds $(OCH_2CMe_2CH_2O)PX$ [X = Cl (**1a**), $OSiMe_3$ (**3**)] are conveniently prepared and cheap, and so we felt that under suitable conditions, various α-substituted phosphonates may be directly accessible using these. Thus, we reacted the phosphite **1a** with various aromatic aldehydes and isolated the expected α-chlorophosphonates (**10a-g**) in moderate yields (Scheme 8, Table 1); in the reaction with 9-anthraldehyde, *we also isolated the* ***unusual*** *bisphosphonate* **15** in yields of ~35%. For this reason we checked the reaction of **8f** with thionyl chloride, but observed only the α-chlorophosphonate **10f** as a major product. Interestingly, in the reaction of **1a** with furfuraldehyde or cinnamaldehyde, we again isolated the ring-chlorinated product **13** (see Scheme 6 above for the other route[101]) or the γ-chlorophosphonate **12a**, respectively. The α-trimethylsilyloxyphosphonates **16a-h** are readily obtained by treating **3** with various aldehydes (Scheme 8; Table 1); the yields in this case are very good.

Scheme 8



X = Cl (**1a**)
X = $OSiMe_3$ (**3**)

X = Cl (**10a-g**)
X = $OSiMe_3$ (**16a-h**)



15 [δ(P) 11.2, 24.1]

Table 1. Details on the direct synthesis of chloro- and α-trimethylsilyloxyphosphonates

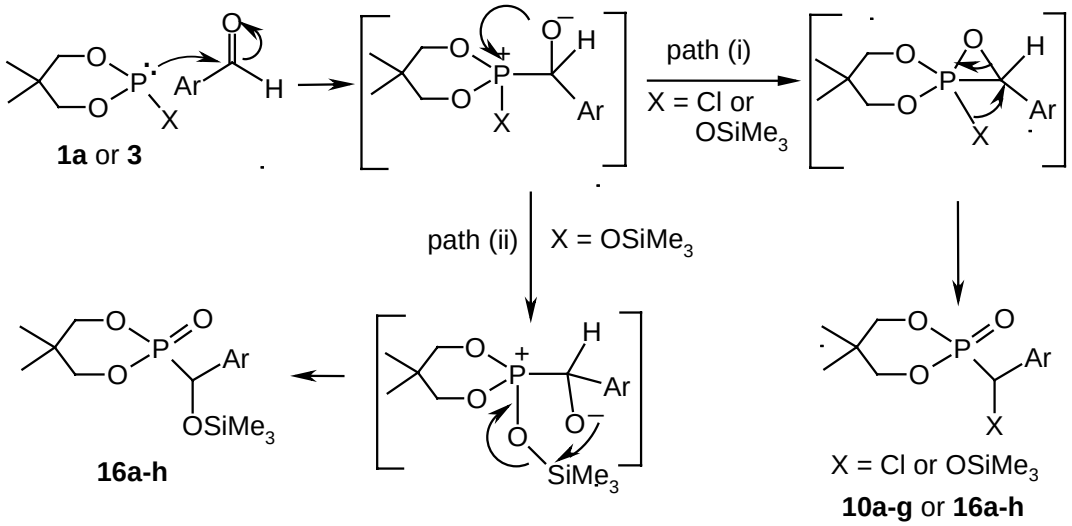
Entry	R	X	Product[-]	δ(P), ppm	Yield (%)[a]
1	Ph	Cl	**10a**	8.1	45
2	C_6H_4-4-Me	Cl	**10b**	8.4	55
3	C_6H_4-4-Cl	Cl	**10c**	7.5	45
4	C_6H_4-4-OMe	Cl	**10d**	8.4	60
5	1-Naphthyl	Cl	**10e**	8.6	40
6	2,4-$Cl_2C_6H_3$	Cl	**10f**	7.5	62
7	9-anthryl	Cl	**10g**	11.4	30
8	=CH-CH(Cl)Ph	Cl	**12a**[b]	11.2	65
9	C_4H_2ClO (Chlorofurfuryl)	Cl	**13**[c]	14.4	45
10	Ph	$OSiMe_3$	**16a**	11.0	89
11	C_6H_4-4-Me	$OSiMe_3$	**16b**	11.3	92
12	C_6H_4-4-Cl	$OSiMe_3$	**16c**	10.6	90
13	C_6H_4-4-OMe	$OSiMe_3$	**16d**	11.4	90
14	1-Naphthyl	$OSiMe_3$	**16e**	10.8	92
15	C_6H_3 –2,4-Cl_2	$OSiMe_3$	**16f**	8.9	91
16	C_6H_4-4-Br	$OSiMe_3$	**16g**	10.4	90
17	*iso* propyl	$OSiMe_3$	**16h**	18.4	86

[a]Isolated yields after crystallization from toluene.
[b]See Scheme 4 for structure.
[c] See Scheme 6 for structure.

Spectroscopic details on compounds **10a-g** and **12a** and **13** are already discussed above. The ^{1}H NMR spectra of the trimethylsiloxy compounds **16a-h** (solids) show a characteristic doublet at δ 5.10 - 6.10 [^2J(P-H) ≈ 16.0 Hz] for the P-C*H* proton; the ^{13}C NMR spectra show a doublet at δ 70.1-74.5 [^1J(P-C) ≈ 162.0 Hz] for the carbon 'α' to phosphorus.

A possible mechanism for the direct formation of α-chloro/ α-trimethylsilyloxyphosphonates is given in Scheme 9. Based on literature, for the formation of α-trimethylsilyloxyphosphonates, path (i) looks feasible.[102] However, path (ii) does not seem unrealistic [Distinction between the two pathways may probably be made only by using the ^{17}O substituted phosphite $(OCH_2CMe_2CH_2O)P(*OSiMe_3)$].

Scheme 9



For compound **15**, apart from the two signals in the ^{31}P NMR, the PC*H* (saturated) proton appears as a doublet at δ 4.48 with an unusually large coupling [^2J(PH) = 30.0 Hz] while the PC*H*= proton appears at δ 6.03 [^2J(PH) = 12.0 Hz]. The ^{13}C NMR spectrum shows the P*C*H(saturated) at δ 46.7 [^1J(PC) = 130.0 Hz] and P*C*H= at δ 110.0 [^1J(PC) = 149.0 Hz]. The structure has been confirmed further by single crystal X-ray diffraction [Figure 4]. The P(2)-C(10) distance is longer than P(1)-C(15) distance as expected for the P-C(sp^3)[cf. **12a**] and PC(sp^2) distances. The molecule is dimeric *via* hydrogen bond through O(5)-H…O(6'). This also shows that hydrolysis has occurred at the corresponding phosphorus center, P(2).

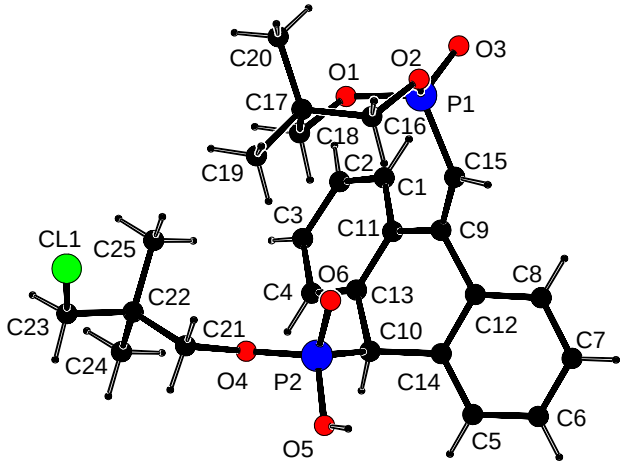
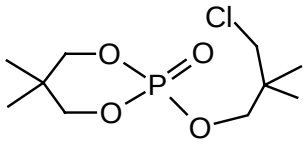


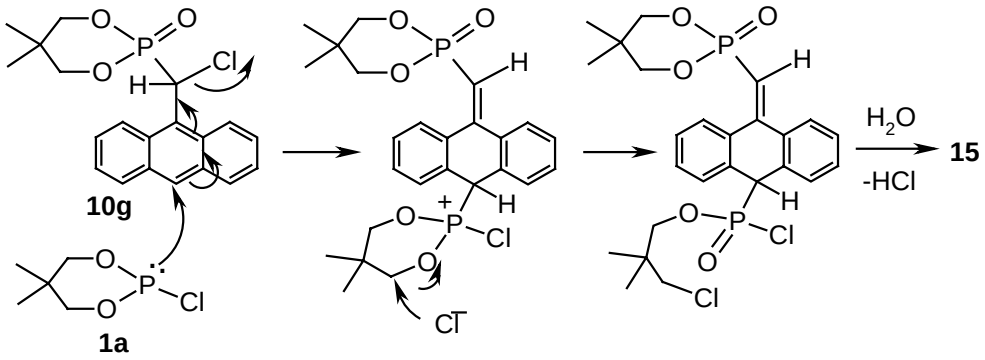
Figure 4. A diagram showing the molecular structure of **15**. Selected bond parameters (Å, °): P(1) – O(1) 1.569(2), P(1) – O(2) 1.583(2), P(1) – O(3) 1.456(2), P(1) – C(15) 1.775(2), P(2) – O(4) 1.563(1), P(2) – O(5) 1.536(1), P(2) – O(6) 1.497(1), P(2) – C(10) 1.815(2). Hydrogen bonded D-H, H..A, D…A and D-H…A parameters: O(5) – H(O5)…O(6') 0.69(4), 1.86(4), 2.548(2) Å, 175(4)°.

Formation of **15** is unexpected, but probably happens by the further reaction of **1a** with the chlorophosphonate **10g** formed in the reaction. The opening of the ring at P(2) [cf. Figure 4], is not due to hydrolysis, but from the attack of a chloride on the saturated OCH_2 carbon; this chloride anion must have come after the attack of **1a** on **10g** and subsequent de-aromatization of the central ring of the anthracene system. The colourless nature of **15** (**10g** is yellow) is also consistent with the loss of aromatization at the anthracene central ring. As regards the cleavage of 1,3,2-dioxaphosphorinane ring at P(2), we had earlier observed a similar phenomenon when **1a** was treated with 2,2-dimethyl-1,3-propanediol/ N-chlorodiisopropylamine (ClN-*i*-Pr_2) leading to $[(OCH_2CMe_2CH_2O)P(O)OCH_2C(CH_3)_2CH_2Cl]$ (**III**).[103] A possible pathway for the formation of **15** is shown in Scheme 10. Although activation of 10-position of the anthracenyl system is known in a few organic reactions,[104] isolation of a compound like **15** could open up a new way of obtaining bisphosphonates (currently pursued in the laboratory).



III

Scheme 10

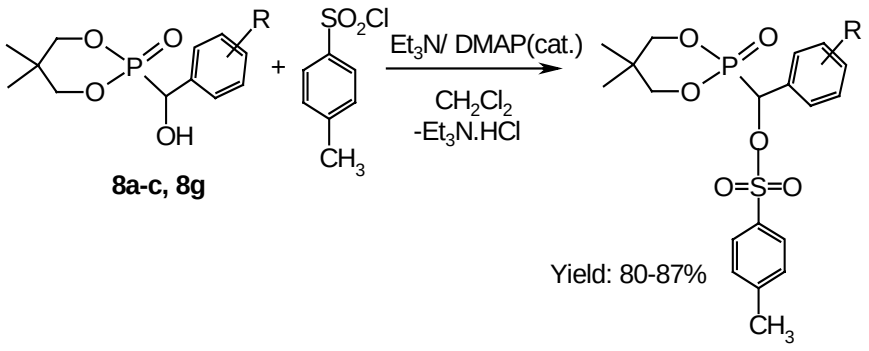


An important point to be noted here is the use of mild conditions coupled with good yields of the phosphonate products **10a-g**, **12**a, **13** and **16a-h**. Moreover, the starting phosphites **1a** and **3** themselves are conveniently prepared (and cheap). For the trimethylsilyloxy compounds of type **16**, only one other route is reported (Chapter 1, Scheme 1.21) subsequent to our work (cf. list of publications, p. vii). However, our route is more convenient and yields are high.

2.24 Synthesis of α-tosylphosphonates

Treatment of α-hydroxyphosphonates **8a-c** and **8g** with *p*-toluenesulfonyl chloride in the presence of Et_3N and catalytic amount of DMAP yielded the expected α-tosyl substituted phosphonate **17a-d** in 80-87% yield (Scheme 11). Compound **17a-d** are air-stable; they have been characterized by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy. The δ(P) values are 6–8 ppm up-field to that of the corresponding hydroxyphosphonates.

Scheme 11



R = H [**17a**: δ(P) 4.7]
4-Me [**17b**: δ(P) 5.1]
4-Cl [**17c**: δ(P) 4.3]
3-Br [**17d**: δ(P) 4.8]

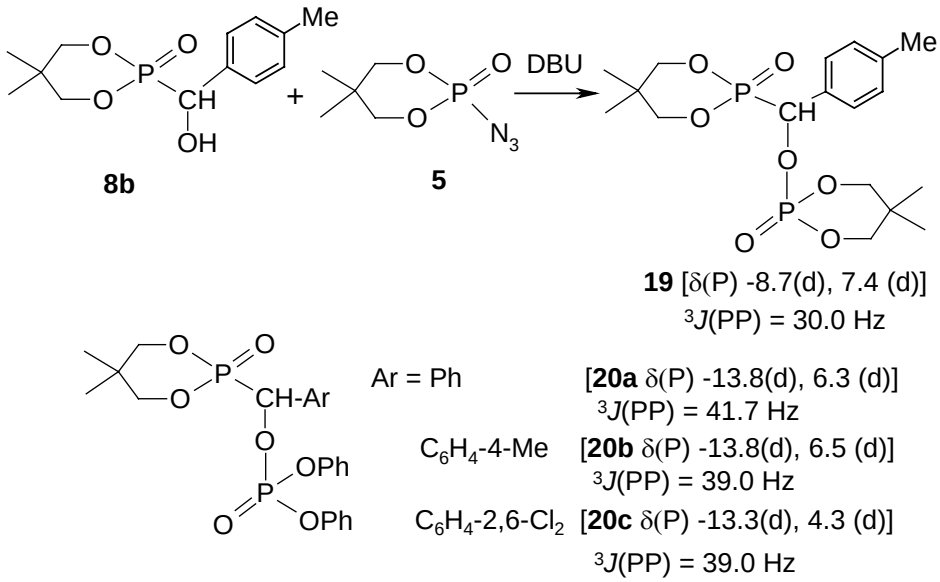
Since tosyl is a good leaving group, we felt that the above tosylphosphonates **17a-d** can be converted to azidophosphonates by reacting them with sodium azide. Only in the reaction using **17a**, we were able to identify the azidophosphonate **21a** (^{31}P NMR; see below for an alternative preparation) in low yields.

2.25 Attempted preparation of α-azidophosphonates via α-hydroxyphosphonates Formation of phosphate esters

In organic synthesis, it is known that the phosphoryl azide $(PhO)_2P(O)N_3$ is a very good reagent for the conversion of an alcoholic -OH group to an azide in organic chemistry.[105] For this reason we prepared the azide, $(OCH_2CMe_2CH_2O)P(O)N_3$ (**5**) and treated 2-bromo-benzyl alcohol with **5** in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), to know whether this compound also can be effectively utilized or not. The corresponding azide 2-Br-$C_6H_4CH_2N_3$ (**18**) could be isolated in ca 90% yield. However, when we tried to convert the hydroxyphosphonate **8b** to the corresponding azidophosphonate using **5** in the presence of DBU, the only product that could be isolated was the phosphate ester **19** of the phosphonate. Even when we treated $(PhO)_2P(O)N_3$ with the hydroxyphosphonates **8a-b** and **8h** similar phosphate esters **20a-c** (50-52% yield) were isolated. Apart from the observation of two doublets in the ^{31}P NMR, a doublet of doublet at δ ~5.90 (**20a-20b**) or 6.90 (**20c**) for PC*H* proton and a doublet at δ ca 77.6 for the P*C* carbon are characteristics of these compounds. In the reaction leading to **20b**, we observed the azidophosphonate **21b** [ca 5%, ^{13}C NMR: doublet at

δ 61.6 [^1J(P-C) ≈ 157.7 Hz; δ(P) 10.6; see below for alternative preparation]. Formation of **19** or **20a-c** must have occurred via the hydrolysis of **5** or $(PhO)_2P(O)N_3$ and subsequent condensation.

Scheme 12



The structure of **20c** was also established by single crystal X-ray diffraction [Figure 5].

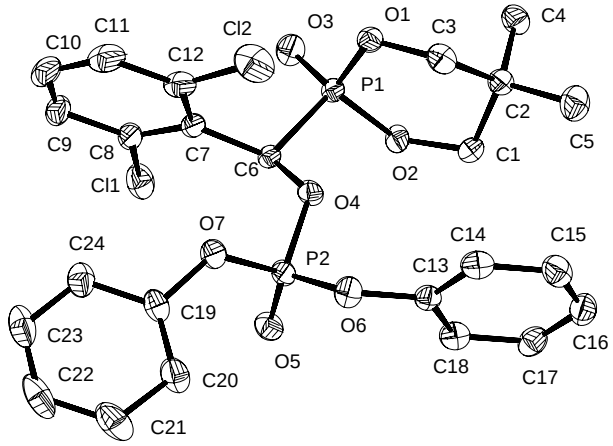
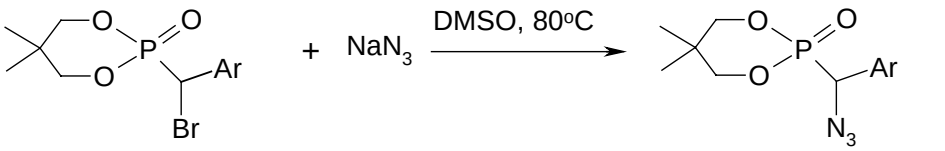


Figure 5. An ORTEP drawing of the molecule of **20c**. Selected bond distances (Å, °): P(1) – O(1) 1.561(1), P(1) – O(2) 1.562(1), P(1) – O(3) 1.455(1), P(1) – C(6) 1.828(2), P(2) – O(4) 1.580(1), P(2) – O(5) 1.445(2), P(2) – O(6) 1.573(1), P(2) – O(7) 1.565(1).

2.26 Synthesis of α-azidophosphonates from α-bromophosphonates

Although the above two approaches did not yield the intended α-azidophosphonates, we did succeed in preparing the latter by starting with the bromophosphonates **11a-c**. Thus treatment of **11a-c** with sodium azide yielded α-azidophosphonates **21a-c** in 47-59% yield (Scheme 13). The IR spectra of these compounds show a band at ~2095cm^{-1} due to the azide group. The NMR [^{1}H ^{13}C, ^{31}P] data are also consistent with the expected structures. Our approach offers a convenient alternative to those available in the literature for other azidophosphonates.[20a]

Scheme 13



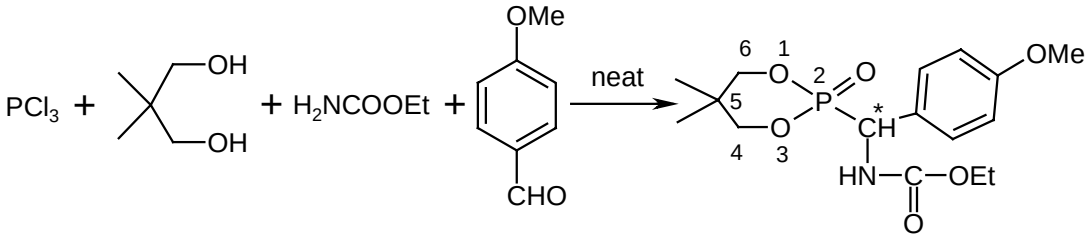
11a-c

Ar = Ph [**21a**: δ(P) 10.2]
C_6H_4-4-Me [**21b**: δ(P) 10.6]
1-Naphthyl [**21c**: δ(P) 10.6]

2.27 Synthesis of α-aminophosphonates

In our laboratory, a simple method, shown in (Scheme 14), has been developed for obtaining α-aminophosphonates of type **IV**[106].

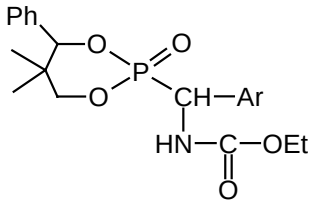
Scheme 14



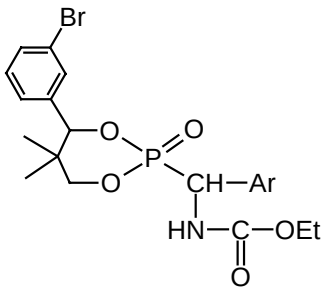
IV

Since these are chiral compounds, it was of interest to us to see if diastereomeric mixtures can be obtained if we substitute one of the hydrogen atoms of the ring (at C4 or C6 position) in such compounds and to check whether they are

distinguished clearly or not in the ^{31}P NMR. For this reason we prepared the P(III) precursors ($OCH_2CMe_2CH(Ph)O)PCl$ (**1b**) and ($OCH_2CMe_2CH(3\text{-}Br\text{-}C_6H_4)O)PCl$ (**1c**) and treated them with urethane followed by an appropriate aldehyde using the route shown in Scheme 14 to obtain the α-aminophosphonates **22a-f** (yields of 30-40%). Compounds **22a** and **22d** were obtained pure and **22b-c/22e** in a state of purity ~95%, because of the difficulty in separating them from the α-hydroxyphosphonates (formed via hydrolysis of **1b-c**). In the case of **22f**, the α-hydroxyphosphonate impurity was ~30%. Column chromatography could not be used in these cases because of extensive hydrolysis of the 1,3,2-dioxaphosphorinane ring and because of the non-volatility, purification by sublimation also was not fruitful. All these compounds exhibited two peaks in the ^{31}P NMR. Although the reaction mixture exhibited nearly equal amounts of the two peaks, the solids obtained after isolation had a different ratio, thus separation of these isomers should have been possible. Crystallization was attempted from different solvents (CH_2Cl_2-hexane, CH_2Cl_2-Et_2O, Et_2O, THF, CH_3CN, EtOH, MeOH), but crystals suitable for X-ray structure could not be obtained. Thus whether the two peaks (^{31}P NMR) are due to different diastereomers or conformational isomers (axial-equatorial disposition of the six-membered dioxaphosphorinane ring) could not be ascertained. The reaction however, worked.



Ar = Ph [**22a**: δ(P)19.1, 20.2 (2:3)]
C_6H_4-4-Me [**22b**: δ(P)19.3, 20.4 (3:1)]
C_6H_4-4-Cl [**22c**: δ(P)18.5, 19.5 (1:8)]



Ar = Ph [**22d**: δ(P)18.8, 20.3 (1:1)]
C_6H_4-4-Me [**22e**: δ(P)19.0, 20.4 (8:1)]
C_6H_4-4-Cl [**22f**: δ(P)18.3, 19.7 (2:3)]

2.3 Synthetic Utility of Phosphonates

2.31 *Synthesis of disubstituted vinyl chlorides/bromides*

In this study we have also compared the efficacy of different bases and solvents in the reaction of α-chloro/ bromophosphonates with aldehydes for the

Horner-Wadsworth-Emmons (HWE) reaction. The reaction of aldehydes with phosphonates has been checked in detail using different bases and solvents (Scheme 15, Table 2). As can be seen from Scheme 15, *Z*-olefins are also formed in significant quantities; this is in line with the observation made by Larsen and Aksnes that cyclic phosphonates increase *Z*-stereoselectivity.[107] The *E/Z* ratio is based on the δ(^{1}H) value for C_6H_4-OC*H*$_3$ or C_6H_4-C*H*$_3$ protons and the well separated δ(^{13}C) values for the *ipso*-carbon labeled as C(1) in Scheme 15 and diagram in Table 2; the *E*-isomer always showed the downfield chemical shift for C(1) in ^{13}C NMR spectroscopy [Here the comparison is made between the same *ipso* carbon of the two isomers and hence ^{13}C NMR gives an approximate ratio of the isomers].

Scheme 15

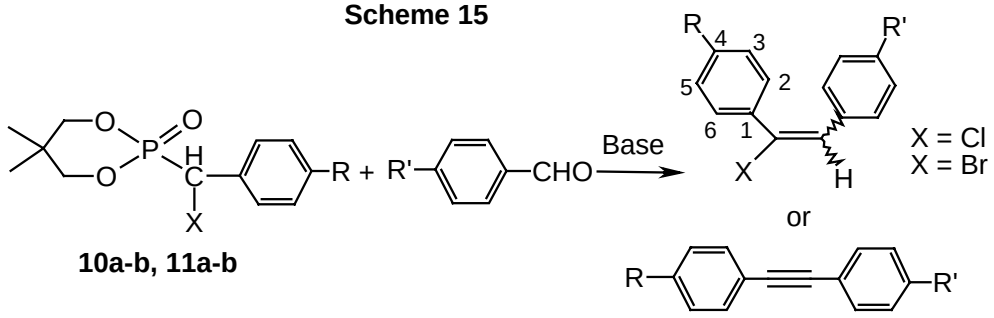


Table 2. Details on reactions of phosphonates with aldehydes using different bases

Compd	R'	Base	Solvent/ Temp/ Time	Pdt	Yield, % (*E/Z* ratio[a])
10a	4-OMe	NaH[b]	THF/0→20°C/13 h	**23a**	98 (65:35)
10a	4-OMe	NaH[b]/ DMSO (1:3)	THF/0°C/8 h	**23a**	65 (65:35)
10a	4-OMe	NaH[c]/ DMSO	DMSO/0→20°C/ 9 h	**23a, 24**	50 (total): 10% alkene (75:25); 40% alkyne
10a	4-OMe	NaH[c]/ DMSO	DMSO/75^{0}C/8 h	**24**	53 (alkyne only)
10a	4-OMe	CsF[c]	MeCN/reflux/3 d	**23a**	52 (40:60)
10a	4-OMe	K_2CO_3[c]	MeCN/reflux/3 d	**23a**	83 (55:45)
10b	H	K_2CO_3[c]	MeCN/reflux/3 d	**23b**	88 (60:40)
11a	4-OMe	K_2CO_3[c]	MeCN/reflux/5 d	**25a**	50 (50:50)[d]

11b	H	K_2CO_3[c]	MeCN/reflux/5 d	**25b**	52 (30:70)
10a	4-OMe	K_2CO_3[c]	Neat/150°C/1 h	**23a**	68 (55:45)
10a	4-OMe	KF or $HN(i\text{-}Pr)_2$	MeCN/reflux or neat/ 24 h	No reaction	

[a] Based on ^1H and ^{13}C NMR spectroscopy.

[b] 1.5 mole eq.

[c] 3 mole eq.

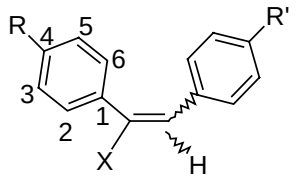
[d] Ph(Br)C=CPh(H) (6%) was obtained as a side product.

It can be noted that NaH in THF gives the best yield of the chloro olefin. Use of DMSO resulted in the formation of the alkyne in addition to the olefin.[108] There is a reversal of stereochemistry when CsF is used, but we have not been able to increase the yield of the predominant isomer. What attracted our attention more was the use of cheap K_2CO_3 in a suitable solvent.[109] We have further explored the effect of different solvents using K_2CO_3 as a base in the reaction of **10a** with *p*-anisaldehyde. Of the several solvents tried, xylene gives the best yield. In DMF the reaction did not work. The yields are in the order: THF (reflux, 3d, 33%) < acetone (reflux, 3d, 53%) < DMSO (80°C, 1d, 60%; 20% alkyne is also present) < CH_3CN + TMEDA (reflux, 3d, 80%) < CH_3CN (reflux, 3d, 83%) < xylene (reflux, 1d, 90%).

Since xylene as the reaction medium afforded the best results, we have used the K_2CO_3/ xylene method to synthesize other chloro- and bromostilbenes; also K_2CO_3 is much easier to handle than NaH. As can be seen from Table 3, excellent yields are obtained under these conditions. Noteworthy is the dramatic improvement in the yields of bromostilbenes over the NaH/THF method previously reported from our laboratory.[77]

We prepared compounds **23a-g, 25a-d** by reacting **10a-b, 10d** or **11a-b** with various aldehydes in the presence of K_2CO_3 in xylene/ 140°C [Table 3].

Table 3. Synthesis of chloro/ bromo stilbenes using K_2CO_3 as a base



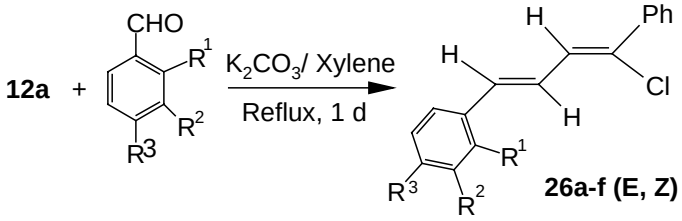
Sl. No.	Phosphonate	Aldehyde (R')	Product	Yield, % (*E/Z* ratio)[a]
1	**10a**	OMe	**23a** (X = Cl)	90 (40:60)
2	**10b**	H	**23b** (X = Cl)	91 (42:60)
3	**10a**	Me	**23c** (X = Cl)	97 (65:35)
4	**10b**	Cl	**23d** (X = Cl)	81(50: 50)
5	**10d**	Cl	**23e** (X = Cl)	89 (30:70)
6	**10d**	Me	**23f** (X = Cl)	90 (35:65)
7	**10d**	H	**23g** (X = Cl)	92 (50:50)
8	**11a**	OMe	**25a** (X = Br)	65 (60:40)
9	**11b**	H	**25b** (X = Br)	63 (55:45)
10	**11b**	Cl	**25c** (X = Br)	73 (60:40)
11	**11b**	OMe	**25d** (X = Br)	69 (50:50)

[a] Isomer ratio (by ^{1}H NMR and ^{13}C NMR spectroscopy) given in parentheses.

2.32 *Synthesis of chloro-substituted dienes*

We also extended the above K_2CO_3/ xylene method for synthesis of chloro substituted dienes **26a-f** (Scheme 16). The identity of **26a** is also confirmed by X-ray crystallography [Figure 6].

Scheme 16



		Yield (%)
26a	R^1, R^3 = Cl; R^2 = H	95
26b	R^1, R^2 = H; R^3 = NO_2	97
26c	R^1, R^2 = H; R^3 = OMe	93
26d	R^1, R^2 = C_4H_4 (naphthyl residue); R^3 = H	93
26e	R^1, R^2 = H; R^3 = Cl	96
26f	R^1, R^2 = H; R^3 = Me	85

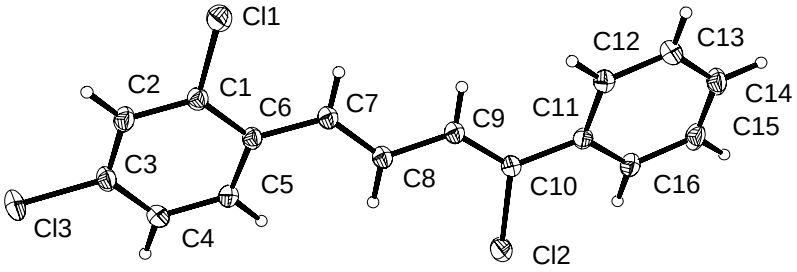
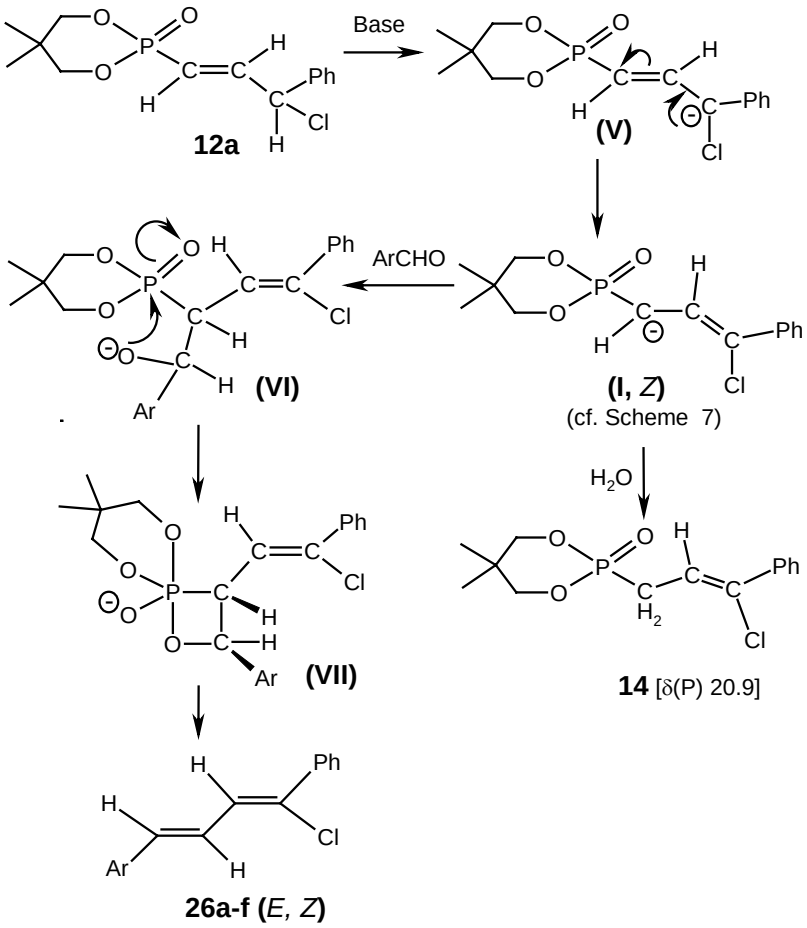


Figure 6. An ORTEP drawing showing the molecular structure of **26a**.

Formation of the (*E,Z*) dienes **26a-f** from **12a** must have occurred *via* the carbanion **I** (Scheme 7) since in a blank reaction of **12a** with K_2CO_3/ xylene without the aldehyde we were able to isolate the phosphonate **14** (Scheme 7) which has a P-CH_2 entity; the ^{13}C NMR spectrum of this compound shows a characteristic doublet at δ 26.7 [^1J(P-C) 136.5 Hz] which is different from that observed for **12a** [δ 117.2, ^1J(P-C) 186.0 Hz]. The (*E,Z*) stereospecificity is probably associated with the stabilization of the phosphorane transition state **VII** (*cf* Scheme 17). As yet we do not have a clear-cut explanation for the *Z* stereochemistry at the (Ph)C(Cl) end since in the reaction of **12a** with *p*-tolualdehyde using NaH/ THF also **26f** was found to be the only stereoisomer formed (^1H NMR). The stereospecificity observed here may be contrasted with that reported by Murray and coworkers in the reaction of α-methoxy allylphosphonates with aldehydes and ketones using LDA as the base to yield isomeric mixtures of dienes.[11]

Scheme 17

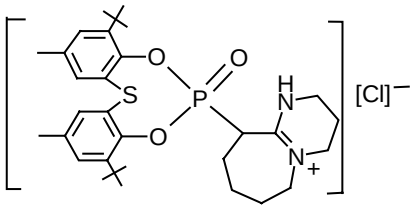


2.4 Formation of Phosphonates and Pyrophosphates in the Reactions of Chlorophosphate Esters with Strong Organic Bases

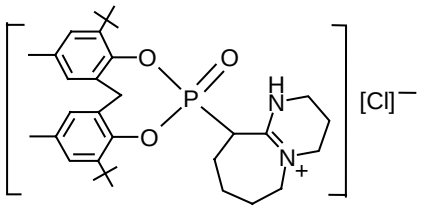
For this part of the study we have chosen, primarily, DBU, DBN [1,5-diazabicyclo(4.3.0)non-5-ene] and N-methyl imidazole, all with two nitrogen atoms as bases and compounds **6a-b** and **7** as phosphorus substrates.

The reaction of **6a-b** and **7** with DBU is conducted in toluene (or THF for **7**) as the solvent. The *phosphonate* salts **27-29** are the major products. Compounds **27-28** could be isolated as pure solids. In the case of **29**, two isomeric products [δ(P) 29.4, 30.0; probably diastereomeric] are formed along with another product that showed a δ(P) of 5.4. As mentioned in an earlier communication, assignment of structure for compound **28** could be done mainly by its downfield ^{31}P NMR chemical shift[95], the ^{13}C NMR is complex and in the ^{1}H NMR, a broad resonance appeared at δ 11.48 (ascribable to NH proton). The spectral features of **27** were analogous to those for **28**, but in this case the P-*C*H carbon was more readily

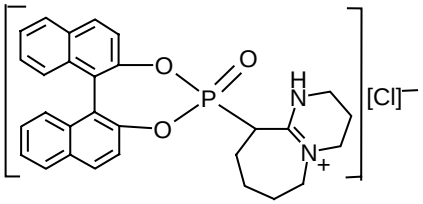
diagnosed at δ 44.4 [^{1}J(PC) = 130.0 Hz] in high-field ^{13}C NMR. For further confirmation, we have studied compound **27** by X-ray structure determination [Figure 7]. Attempted dehydrohalogenation of **27** in methanolic NaOH gave a mixture that showed two major peaks (total intensity >85%) at δ 24.8 and 31.4 (phosphonate region) in the ^{31}P NMR, but a pure compound could not be isolated.



27 [δ(P): 6.4]



28[δ(P): 7.2]



29[δ(P): 30.4, 29.2]

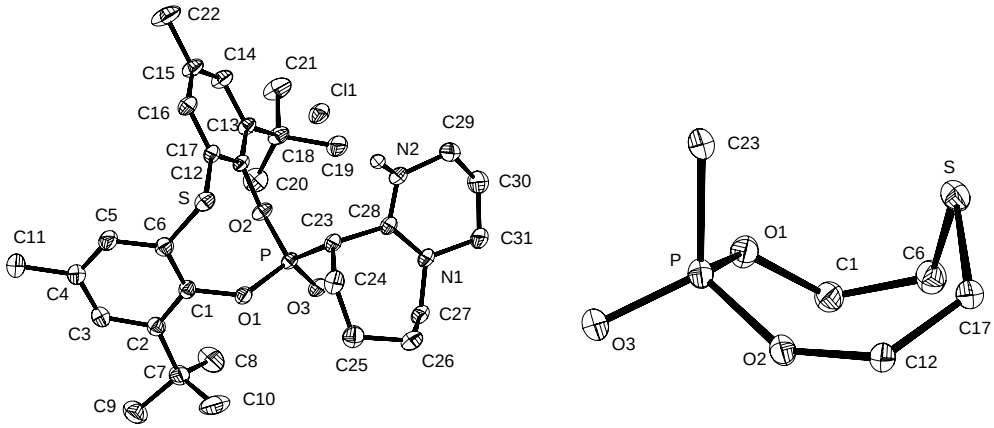
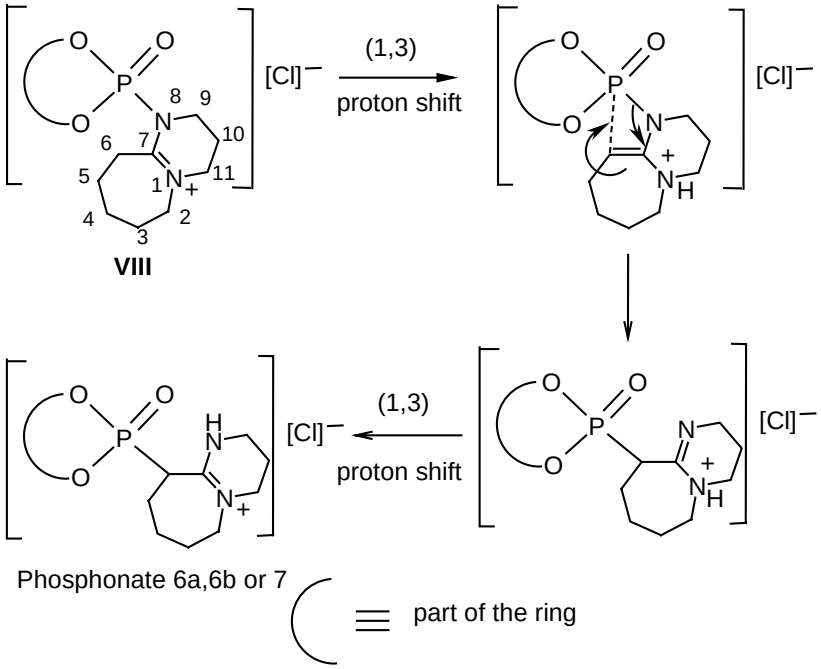


Figure 7. An ORTEP drawing of **27**.CH_2Cl_2.1/2$C_6H_5CH_3$. Solvent molecules are omitted. On the right hand side is shown the conformation of the eight-membered phosphocin ring. Selected bond distances (Å): P – O(1) 1.583(2), P – O(2) 1.568(2), P – O(3) 1.460(2), P – C(23) 1.822(3), N(1) – C(28) 1.328(3), N(2) – C(28) 1.303(3). Hydrogen bond parameters for N(2) – HN(2) – Cl(1): 0.72(3), 2.39(3) and 3.109(3) Å and 171(3)^{o}

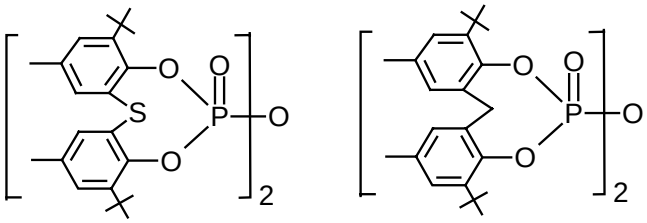
It is important to note that the use of DBU as a base is quite common and several studies using phosphate esters are also conducted in its presence.[110] To our knowledge, in these reports the possibility of formation of phosphonate salts is not mentioned, although it is known that DBU can be lithiated at the C(6) position (cf. Scheme 18 for numbering).[111] Formation of the phosphonate (*cf.* **27-29**), however, might have taken place *via* the intermediacy of a phosphoramidate salt **VIII** that undergoes 1,3-proton shift from C-6 to N-1 to give an enamine. This enamine could reorganize to **27** (or **28** or **29**) *via* a cyclic 4-membered transition state involving C-6, C-7, N-8 and P.

Scheme 18

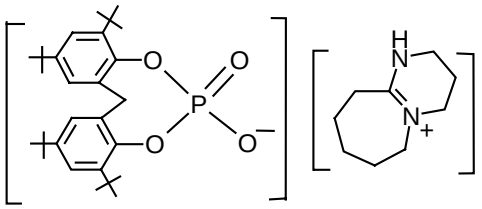


Although DBN is also a dinitrogen base similar to DBU, we did not observe a phosphonate salt in reactions using DBN. The reaction of **6a** with DBN initially showed peaks at δ -3.0, -11.4 and –12.1 in the ^{31}P NMR. However, the only product that could be isolated in a pure state was the pyrophosphate **30** [δ(P) –31.1; this was not present in the original reaction mixture but formed over a period of time]. Even in the reaction using **6b**, the analogous pyrophosphate **31** is a major product. In the reaction of **6a** with N-methyl imidazole, the pyrophosphate (30%) along with two other peaks at δ -7.0 and –11.7 are observed in the ^{31}P NMR. The pyrophosphate is

most likely produced by the reaction of the organophosphate salt (formed by the hydrolysis of phosphoramidate salt of type **VIII**) with the chlorophosphate **6a** or **6b**. The ^{31}P NMR peak at –11.5± 0.2 ppm in the reaction of **6a** with DBN or N-methyl imidazole is ascribable to the organophosphate salt S(6-*t*-Bu-4-Me-$C_6H_2O)_2$]P(O)(O^-)($HBase^+$); for comparison, the δ(P) value for the analogous salt CH_2(4,6-(*t*-$Bu)_2C_6H_2O)_2$]P(O)(O^-)($HDBU^+$) (**IX**) is –11.4.[112]



30 [d(P): -31.6] **31** [d(P): -28.6]



IX

The ^{31}P NMR peak at δ -3.0 or –7.0 in the reaction of **6a** with DBN or N-methyl imidazole, respectively, is likely to be due to the expected phosphoramidate salt. This assessment is based on our previous observation that in compounds containing the same eight-membered ring and phosphoryl oxygen, P-N bonded compounds show δ(P) values in between those for P-O and P-C bonded ones.[103,106,112, 113] The peak with δ(P) –12.1 (see above) is not assigned.

In the analogous reaction of **7** with DBN, several species are formed and the spectrum changed with time. A peak at δ -12.4, ascribable to the pyrophosphate, was a major component after 3 days; even with N-methyl imidazole, this compound was the major product [^{31}P NMR].

Brief discussion of the structures

In the structure of **27** (Figure 7 above), the phosphorus is connected to the carbon of the seven-membered ring that is at β-position to the nitrogen of the six-membered ring of the DBU residue. The P-O bond distances and the angles at phosphorus are in the normal range observed in similar compounds.[114] There is moderately strong hydrogen bonding between the N(2)-H and the chloride ion [*cf*. Figure 7]. However, the short N(1)- C(28) bond distance shows that the double bond is delocalized. The intra-molecular non-bonded P…S distance is 3.33Å which is less than the sum of van der Waals radii, but longer than that in several hexacoordinate phosphoranes with the same ring residue.[99,113] The eight-membered ring has a *tub* conformation that is analogous to that observed in many other tetracoordinate phosphorus compounds containing the CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2$]P(O) group, but different from the *boat-chair* conformation observed for P(III) compounds with similar rings. In compound **30** (*cf*. Figure 8), the intra-molecular P…S distance is 3.40 Å and the conformation of the eight-membered ring is again *tub*. Earlier, we had suggested that observation of *tub* conformation in compounds with the CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2$]P(O) group is related to the presence of weak intramolecular C-H…O interactions between the $ArCH_2$ protons and the phosphoryl oxygen[114,115] but such a feature is absent in **28** or **30** [In the absence of any additional interaction, the expected conformation is that of a *boat-chair*].[116] The possible intra-molecular C-H…O contacts in compound **31** are shown in Figure 9; here the bridging oxygen is closer to one of the $ArCH_2$ hydrogens and the conformation of the eight-membered ring is *tub*. A few more examples are necessary to conclude whether P…S (very weak, if at all) interaction in **28** or **30** has played a role (or not) in the observed *tub* conformation.

An interesting feature in **30** is the sulfur-sulfur non-bonded distance of *ca* 4.2Å within the molecule which suggests that **30** can be used as a soft bidentate ligand towards transition metals.

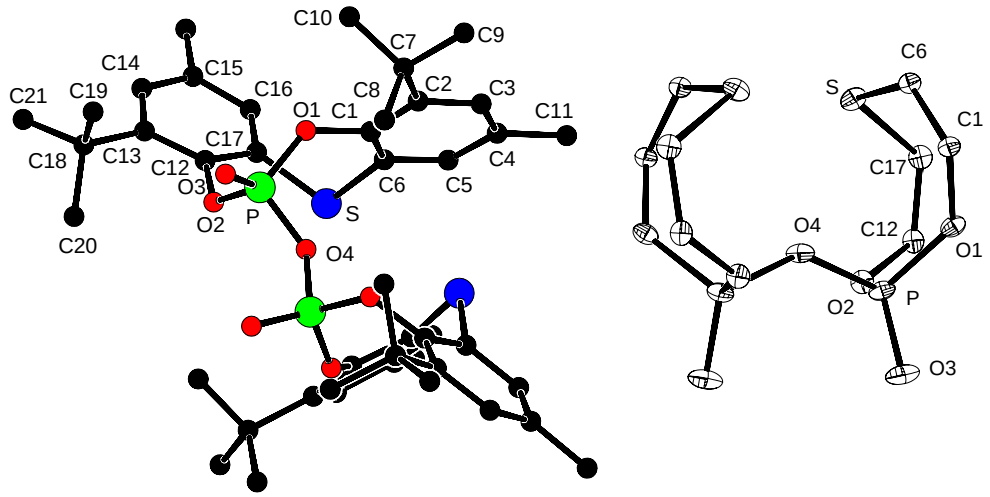


Figure 8. Molecular structure of **30**.CH_2Cl_2; solvent is not shown. Also shown on the right hand side is the conformation of the eight-membered ring. Selected distances and angles: P – O(3) 1.443(2), P – O(1) 1.563(2), P – O(2) 1.567(2), P – O(4) 1.583(1), O(3) – P – O(1) 113.49(11), O(3) – P – O(2) 113.33(10), O(1) – P – O(2) 106.81(9), O(30 – P – O(4) 114.68(12), O(1) – P – O(4) 104.06(8), O(2) – P – O(4) 103.47(7), P – O(4) – P' 134.17(14).

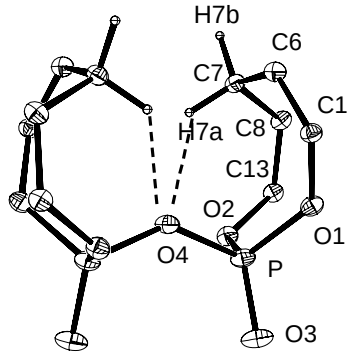


Figure 9. A picture showing the conformation of the phosphocin ring and possible interaction of the $ArCH_2$ hydrogen with the exocyclic non-phosphoryl oxygen in **31**. Other features are similar to that in **30** (*cf*. Figure **8**). Selected distances and angles (Å, ^{o}): P – O(1) 1.562(4), P – O(2) 1.563(4), P – O(3) 1.438(4), P – O(4) 1.591(2),. O(3) – P – O(1) 113.1(3), O(3) – P – O(2) 114.4(2), O(1) – P – O(2) 106.6(2), O(3) - P – O(4) 115.1(3), O(1) – P – O(4) 103.60(19), O(2) – P – O(4) 102.83(17), P – O(4) – P' 135.4(4). C(7)- H(7a)…O(4) parameters: 0.97, 2.51, 3.197(7)Å, 127.5^o.

2.5 Summary

(i) We have developed a convenient and practical synthesis of α-chloro and α-bromophosphonates from the reaction of simple α-hydroxy(aryl)phosphonates with $SOCl_2$/ $SOBr_2$. By contrast, the reaction of $(OCH_2CMe_2CH_2O)P(O)CH(OH)(CH=CHR)$ [R = Ph (**9a**), Me (**9b**)] with $SOCl_2$ leads to γ-chlorovinyl phosphonates $(OCH_2CMe_2CH_2O)P(O)CH=CH-CH(Cl)R$ [R = Ph (**12a**), Me (**12b**)]; compound **12a** is characterized by X-ray crystallography. A novel direct route utilizing the phosphites $(OCH_2CMe_2CH_2O)PX$ [X = Cl (**1a**), $OSiMe_3$ (**3**)] and aldehydes is developed for the synthesis of α-chloro and α-trimethylsilyloxyphosphonates $(OCH_2CMe_2CH_2O)P(O)CH(X)(Ar)$ (**10a-h**, **16a-h**). An unusual bisphosphonate, $[(OCH_2CMe_2CH_2O)P(O)CH(C_{14}H_8)P(O)(OH)\text{-}OCH_2CMe_2CH_2Cl]$ (**15**) [X-ray structure] was also obtained in the reaction of **1a** with 9-anthraldehyde. A viable synthetic route for the α-azidophosphonates has been developed by using α-bromophosphonates. Isomeric α-aminophosphonates $(OCH_2CMe_2CH(Ar)O)CH(NHCO_2Et)(Ar')$ (**22a-f**) were obtained in a one-pot reaction of $(OCH_2CMe_2CH(Ar)O)PCl$ [R = Ph (**1b**), 3-Br-C_6H_4 (**1c**)] with urethane and aromatic aldehydes.

(ii) The inexpensive K_2CO_3 in refluxing xylene is a good base (compared to NaH/THF) for the synthesis of chloro/bromostilbenes $ArCH=CX(C_6H_4\text{-}4\text{-}R)$ from the phosphonates $(OCH_2CMe_2CH_2O)P(O)CH(X)(C_6H_4\text{-}4\text{-}R)$ (X= Cl, Br) via the HWE reaction. The reaction of phosphonate **12a** with aromatic aldehydes using K_2CO_3/ xylene proceeds smoothly to give high yields of the chloro-substituted dienes and *only the (E,Z) isomer is obtained*; the stereochemistry was confirmed in the case of 2,4-$Cl_2C_6H_3$-CH=CH-CH=C(Ph)Cl (**26a**) by using X-ray crystallography.

(iii) It is shown that in the reaction of chlorophosphates with DBU, formation of P-C bonded (phosphonate) compound is a major pathway (e.g. **27**). When other bases like DBN are used, pyrophosphates (e.g. **30**) are the major products. The larger 7-membered ring in DBU, compared to the 5-membered ring DBN, might have brought the β (to the nitrogen of the six-membered ring) carbon of this ring in close proximity to the phosphorus resulting in the isolation of phosphonate salts.

CHAPTER 3

EXPERIMENTAL SECTION

General: Chemicals and solvents were procured from Aldrich/ Fluka or local manufacturers. Further purification was done according to standard procedures[117] wherever required. 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.

Elemental analysis: Elemental analyses were carried out on a Perkin- Elmer 240C CHN analyzer or Thermo Finnigan EA1112 analyser or obtained from elsewhere (IACS, Kolkata).

Mass spectra: Mass spectra were recorded on a CEC-21-110B double focusing mass spectrometer operating at 70 eV using direct inlet system.

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

Chromatography: Analytical thin layer chromatography (TLC) was performed on glass plates (8 x 2 cm^2) coated with Acme's silica gel (G254) containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapour or UV light. Column chromatography was carried out using Acme's silica gel (100-200 mesh).

3.1 Preparation of Phosphite/ Phosphate Precursors

The compounds $(OCH_2CMe_2CH_2O)PCl$ [**1a**; [bp 78-79°C/ 20 mm; δ(P) 145.8] and $(OCH_2CMe_2CH_2O)P(O)H$ [**2**; mp 52-54°C, bp: 93-94°C/ 0.05 mm; δ(P) 2.3] were prepared as reported earlier from the laboratory.[96a,119] Compounds

($OCH_2CMe_2CH(Ph)O)PCl$ [**1b**; δ(P) 149.6[96b]] and ($OCH_2CMe_2CH(3$-Br-$C_6H_4)O)PCl$ [**1c** δ(P) 150.0,151.2] were prepared in a manner similar to that for **1a**.[96c] The compounds S(6-*t*-Bu-4-Me-$C_6H_2O)_2P(O)Cl$ [**6a**; mp 184-187°C; δ(P) –8.2 (lit. –9.4)[99]], CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2P(O)Cl$ [**6b**; mp 206-208°C; δ(P) –3.4 (lit. -2.5)[95]] and (2,2'-$C_{20}H_{12}O_2$)P(O)Cl [**7**, racemic; mp 246-250°C; δ(P) 11.1 (lit. 11.5)][120] were prepared by following literature procedures.

(a) $(OCH_2CMe_2CH_2O)POSiMe_3$ (3)

Trimethylsilyl chloride (8.3 g, 76.4 mmol) was added drop-wise (10 min) to **2** (11.4 g, 76.4 mmol) and triethylamine (7.7 g, 76.4 mmol) in toluene (75 mL). The solution was stirred for 24 h, filtered, solvent was evaporated and the product **3** distilled at pump (75°C/0.5 mm Hg).

Yield: 15.9 g (94%).

^{1}H NMR: δ 0.23 (s, 9 H, SiCH_3), 0.71 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 3.18 – 3.28 (m, 2 H, OCH_2), 3.92 - 4.13 (m, 2 H, OCH_2).

^{13}C NMR: δ 1.1, 22.5, 22.8, 32.8, 67.7.

^{31}P NMR: δ 108.6.

Analytical data were not obtained due to the moisture sensitivity of the compound.

(b) $(OCH_2CMe_2CH_2O)P(O)Cl$ (4)

2,2-Dimethyl-1,3-propanediol (39.0 g, 0.37 mol) was added to phosphorus oxychloride (113.0 g, 0.74 mol) portion-wise (20 min) with continuous stirring at room temperature; the mixture was stirred further for 12 h and the excess phosphorus oxychloride was removed at pump. The product sublimed in vacuum (78-79°C/ 20 mm) to give pure **4**.

Yield: 57 g (90%).

^{1}H NMR: δ 0.92 and 1.32 (2 s, 6 H, 2 CH_3), 3.96 - 4.26 (m, 4 H, OCH_2).

^{31}P NMR: δ -3.6 (lit –3.4[121]).

(c) $(OCH_2CMe_2CH_2O)P(O)N_3$ (5)

Sodium azide (0.47 g, 7.32 mmol) was added to ($OCH_2CMe_2CH_2O)P(O)Cl$ (**4**) (0.45 g, 2.44 mmol) in acetonitrile (10 mL) and the mixture stirred for 12 h.

Solvent was removed at pump and heptane (20 mL) was added to the residue. Filtration followed by crystallization gave **5** as a solid.

Yield: 0.44 g (95%).

Mp: 46-48°C.

IR (cm^{-1}): 2166, 1308, 1059.

^{1}H NMR: δ 0.91 (s, 3 H, C*H*$_3$), 1.26 (s, 3 H, C*H*$_3$), 3.81 – 4.23 (m, 2 H, OC*H*$_2$).

^{13}C NMR: 19.9 and 21.5 (*C*H$_3$), 32.1 (d, ^{3}J(PC) = 6.0 Hz), 78.6 and 78.7 (O*C*H$_2$).

^{31}P NMR: δ -9.0.

The sample was hydrolytically unstable, but could be preserved under nitrogen atmosphere.

3.2 Synthesis of Phosphonates

3.21 Synthesis of α-hydroxy phosphonates 8a-h and 9a-b

The procedure was adapted from ref. 18e To a mixture of **2** (4.4 g, 29 mmol), benzaldehyde (3.1 g, 29 mmol) and toluene (20 mL) was added Et_3N (1.46 g, 14.5 mmol), cooling the flask when necessary. The mixture was stirred for 2 h at 25 °C and the white solid obtained was filtered, washed with toluene (5 mL) and recrystallized from CH_2Cl_2/toluene mixture (1:1) to give **8a** (6.9 g, 92%). Compounds **8b-e** were reported in literature prepared similarly and the relevant data are summarized below; the ^{31}P NMR data were identical to those in ref. 18e. Data for the new compounds **8f-h** are given afterwards.

Compound	M.p. (°C)	δ(P) ppm	yield (%)
$(OCH_2CMe_2CH_2O)P(O)CH(OH)Ph$ (**8a)**	151-153	13.3	92
$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_6H_4\text{-}4\text{-}Me)$ (**8b**)	164	13.6	96
$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_6H_4\text{-}4\text{-}Cl)$ (**8c**)	174-176	12.9	90
$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_6H_4\text{-}4\text{-}OMe)$ (**8d**)	155-157	13.6	94[119]
$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_{10}H_7)$ [$C_{10}H_7$ = 1-naphthyl] (**8e**)	172	13.1	90[119]

$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_{14}H_9)$ [$C_{14}H_9$ = 9-anthryl] (8f)

Yield: 59 % (using 58.4 mmol of **2**).

Mp: 156-158°C.

IR (cm^{-1}): 3287 (ν(OH)), 1464, 1248, 1198, 1082.

^{1}H NMR: δ 0.34 and 0.97 (2 s, 6 H, 2 CH_3), 3.03 and 3.27 (2 dd→t, $^{2,3}J$ = 8.8, 8.8 Hz, 2 H, OCH_AH$_B$ of one set), 3.52 (br s, 1 H, O*H*), 3.71 and 3.82 (2 dd→t, $^{2,3}J$ = 8.8, 8.8 Hz, 2 H, OCH_AH$_B$ of second set), 6.68 (d, ^2J(P-H) = 14.6 Hz, 1 H, P-C*H*-OH), 7.48-8.15 (m, 7 H, Ar-*H*). The four OC$H_A H_B$ protons show up separately in this compound.

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

^{31}P NMR: δ 16.9.

Anal. Calcd. for $C_{20}H_{21}O_4P$: C, 67.41; H, 5.94. Found: C, 67.80.45; H, 6.10.

Reaction of this compound with thionyl chloride led mostly to the chlorinated product **10g** (see below for details).

$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_6H_4$-3-Br) (8g)

Yield: 87% (using 58.4 mmol of **2**).

Mp: 202-204°C.

IR (cm^{-1}): 3277 (ν(OH)), 1474, 1250, 1186, 1078.

^{1}H NMR: δ 0.90 and 1.14 (2 s, 6 H, 2 CH_3), 3.00 ((br, 1 H, O*H*), 3.90 - 4.20 (m, 4 H, OCH_2), 5.18 (d, ^2J(P-H) ≈ 12.0 Hz, 1 H, P-C*H*-OH), 7.28 - 7.70 (m, 4 H, Ar-*H*).

Solubility was too low for recording ^{13}C NMR.

^{31}P NMR: δ 13.4.

$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_6H_3$-2,6-$Cl_2$) (8h)

Yield: 87% (using 58.4 mmol of **2**).

Mp: 176-178°C.

IR (cm^{-1}): 3272 (ν(OH)), 1471, 1243, 1184, 1072.

^{1}H NMR: δ 0.95 and 1.19 (2 s, 6 H, 2 CH_3), 3.09 ((br, 1 H, O*H*), 3.90 - 4.30 (m, 4 H, OCH_2), 5.4 (d, ^2J(P-H) ≈ 14.0 Hz, 1 H, P-C*H*-OH), 7.28 - 7.70 (m, 3 H, Ar-*H*).

Solubility was too low for recording ^{13}C NMR.

^{31}P NMR: δ 14.1.

$(OCH_2CMe_2CH_2O)P(O)CH(OH)(CH=CHC_6H_5)$ (9a)

Yield: 96% (using 14 mmol of **2**).

Mp 141-143°C.

IR (cm^{-1}): 3153 (br, ν(OH)), 1242, 1186

^{1}H NMR: δ 0.93 and 1.14 (2 s, 6 H, 2 CH_3), 3.90-4.10 (m, 2 H, 2 OCH_2), 4.20-4.35 (m, 2 H, 2 OCH_2), 4.87 (dd, 1 H, ^3J(HH) ~ 6.0 Hz, ^2J(P-H) = 16.0 Hz, P-C*H*-OH), 6.35 (ddd, *J* = 5.0, 6.0, 18.0 Hz, 1 H, C*H*=CHPh), 6.80 (dd, 1 H, ^3J~ 6.0, 18.0 Hz), 7.20-7.50 (m, 5 H, C_6H_5). The exact nature of *J* values was difficult to ascertain.

^{13}C NMR: δ 21.0 and 21.8 (2 s *C*H_3), 32.5 (d, ^3J(P-C) = 7.3 Hz, *C*Me_2), 71.1 (d, ^1J(P-C) = 159.7 Hz, *C*H(OH), 77.4 (d, ^2J(P-C) = 7.1 Hz, O*C*H_2), 123.8, 126.7, 127.9, 128.6, 132.5, 136.5.

^{31}P NMR: δ 13.9.

Anal. Calcd. for $C_{14}H_{19}O_4P$: C, 59.56; H, 6.79. Found: C, 59.45; H, 6.68.

$(OCH_2CMe_2CH_2O)P(O)CH(OH)(CH=CHCH_3)$ (9b)

Yield: 84% (using 14 mmol of **2**).

Mp 92-94°C.

IR (cm^{-1}): 3150 (br, ν(OH)), 1240, 1181

^{1}H NMR: δ 0.98 and 1.14 (2 s, 6 H, 2 CH_3), 1.74 (d, 3 H, ^3J(HH) ~ 8.0 Hz (CH_3)), 3.90-4.31 (m, 4 H, 2 OCH_2), 4.32 (m, 1 H, P-C*H*-OH), 5.54-5.70 (m, 1 H, C*H*), 5.78-6.00 (m, 1 H, C*H*).

^{13}C NMR: δ 17.9 (CH*C*H_3), 21.1 and 21.8 (2 s, *C*H_3), 32.5 (d, ^3J(P-C) ~ 7.3 Hz, *C*Me_2), 70.2 (d, ^1J(P-C) = 159.6 Hz, *C*H(OH)), 77.4 (O*C*H_2), 125.4, 130.4.

^{31}P NMR: δ 15.2.

Anal. Calcd. for $C_9H_{17}O_4P$: C, 49.08; H, 7.79. Found: C, 49.04; H, 7.68.

3.22 Synthesis of α-chloro and α-bromophosphonates [10a-e; 11a-c]

The procedure was essentially adapted from ref. 18e. To a solution of **8a** (0.4 g, 1.56 mmol) in dichloromethane (5 mL.) was added $SOCl_2$ (0.5 g, 0.3 mL, 4.2

mmol) (for **10a**) or $SOBr_2$ (0.8 g, 0.3 mL, 3.87 mmol) (for **11a**) and the mixture stirred at 25°C for 8h. Then water was cautiously added to destroy excess $SOCl_2$/$SOBr_2$ and the product was taken up in CH_2Cl_2 (10 mL). The solvent was removed and the residue crystallized from CH_2Cl_2/heptane to give **10a** or **11a**. The other compounds **10b-c** and **11b**, reported in the literature, were prepared similarly; the relevant data is summarized below. Data for the new compounds **10d-e** and **11c** are given afterwards.

Compound	Mp (°C)	δ(P) ppm	yield (%)
$(OCH_2CMe_2CH_2O)P(O)CH(Cl)Ph$ (**10a**)	150-152	8.1	81
$(OCH_2CMe_2CH_2O)P(O)CH(Cl)(C_6H_4$-4-Me) (**10b**)	184	8.4	86
$(OCH_2CMe_2CH_2O)P(O)CH(Cl)(C_6H_4$-4-Cl) (**10c**)	151-152	7.5	75
$(OCH_2CMe_2CH_2O)P(O)CH(Br)Ph$ (**11a**)	164-166	8.6	79
$(OCH_2CMe_2CH_2O)P(O)CH(Br)(C_6H_4$-4-Me) (**11b**)	184-188	9.0	74

$(OCH_2CMe_2CH_2O)P(O)CH(Cl)(C_6H_4$-4-OMe) (10d)

Yield: 80% (using 35.1 mmol of **8d**).

Mp: 126-128°C.

IR (cm^{-1}): 1264, 1062 (ν(P=O)).

^{1}H NMR: δ 0.95 and 1.16 (2s, 6 H, 2 C*H*$_3$), 3.79 (s, 3H, Ar-OC*H*$_3$), 4.13 (d, ^3J(P-H) = 10.0 Hz, 4 H, OCH_2), 5.09 (d, ^2J(P-H)= 13.4 Hz 1 H, P-C*H*Cl), 6.88, 7.46 (2 d, ^3J(H-H) = 8.0 Hz, 4 H, Ar-*H*).

^{13}C NMR: δ 21.1 and 21.8 (2 C*H*$_3$), 32.7 (d, ^3J(P-C) = 7.8 Hz, *C*Me$_2$), 53.6 (d, ^1J(P-C) = 158.6 Hz, P-*C*HCl), 55.3 (s, Ar-O*C*H$_3$), 77.9, 78.0 (2d, ^2J(P-C) ≈ 7.0 Hz, 2 O*C*H$_2$), 114.2, 125.7, 130.2, 130.3, 160.3.

^{31}P NMR: δ 8.4.

Anal. Calcd. for $C_{13}H_{18}ClO_4P$: C, 51.23; H, 5.96. Found: C, 51.45; H, 5.90.

$(OCH_2CMe_2CH_2O)P(O)CH(Cl)(C_{10}H_7)$ (10e) [$C_{10}H_7$ = 1-naphthyl]

Yield: 87% (using 35.1 mmol of **8e**).

Mp 167-168°C.

IR (cm^{-1}): 1260, 1060 (ν(P=O)).

^{1}H NMR: δ 0.89 and 1.18 (2 s, 6 H, C*H*$_3$), 3.99-4.20 (m, 4 H, OC*H*$_2$), 6.01 (d, 1 H, ^{2}*J*(P-H) = 14.0 Hz, C*H*Cl), 7.44-8.10 (m, 7 H, Ar-*H*).

^{13}C NMR: δ 21.0 and 21.7 (2 s, *C*H$_3$), 32.6, 51.0 (d, ^{1}*J*(P-C) = 155.0 Hz, P-*C*HCl), 78.2, 122.7, 125.3, 126.0, 127.0, 128.2, 128.3, 129.0, 130.0, 133.8.

^{31}P NMR: δ 8.5.

Anal. Calcd. for $C_{16}H_{18}ClO_3P$: C, 59.18; H, 5.60. Found: C, 59.12; H, 5.49.

Details on **10f-g**, prepared by another route, are given in section 3.24.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(Br))(C$_{10}$H$_7$) (11c) [C$_{10}$H$_7$ = 1-naphthyl]

Yield: 87% (using 35.1 mmol of **8e**).

Mp: 168-170°C.

IR (cm^{-1}): 1262, 1064 (ν (P=O)).

^{1}H NMR: δ 0.96 and 1.14 (2 s, 6 H, C*H*$_3$), 3.99 - 4.23 (m, 4 H, OC*H*$_2$), 5.94 (d, ^{2}*J*(P-H) = 16.0 Hz, 1 H, C*H*Br), 7.44 - 8.40 (m, 7 H, Ar-*H*).

^{13}C NMR: δ 21.2 and 21.7 (2 s, *C*H$_3$), 32.7 (d, ^{3}*J*(P-C) = 6.8 Hz, *C*Me$_2$), 37.9 (d, ^{1}*J*(P-C) ≈ 159.0 Hz, P-*C*HCl), 77.8, 122.7, 125.6, 126.2, 127.1, 130.0, 130.2, 133.9.

^{31}P NMR: δ 9.1.

3.23 Synthesis of γ-chlorovinylphosphonates 12a-b and compound 13

Thionyl chloride (16.45 g, 0.14 mol) was added to a stirred solution of **9a** (13.0 g 46 mmol) in dichloromethane (50 mL), the mixture stirred for 24 h, the solution washed with water, concentrated to 10 mL and heptane (5 mL) was added to the residue. Crystals of **12a** were isolated from this solution after slow evaporation of the solvent at room temperature. Compound **12b** was prepared similarly from **9b**.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH=CH-CH(Cl)C$_6$H$_5$) (12a)

Yield: 82 % (using 46 mmol of **9a**)

Mp: 120°C

^{1}H NMR: δ 1.08 and 1.10 (2 s, 6 H, C*H*$_3$), 3.87 (dd, ^{2}J(*HH*), ^{3}J(PH) ~ 11.0 Hz, 12.0 Hz, 2 H, OC*H*$_2$(A)), 4.20 (dd, ^{2}J(HH), ^{3}J(PH) ~11.0, 12.0 Hz, 2 H, OC*H*$_2$(B)), 5.55 (d, ^{3}J(HH) ~ 3.0 Hz, PhC*H*Cl), 6.12 (ddd, ^{4}J(HH), ^{3}J(HH), ^{2}J(PH) ~ 3.0, 19.1, 19.1 Hz, 1 H, PC*H*), 7.00, (ddd, ^{4}J(HH), ^{3}J(HH), ^{3}J(PH) ~ 8.5, 19.1, 19.1 Hz, 1 H, PCH=C*H*), 7.37 (br s, 5 H, Ar-*H*).

^{13}C NMR: δ 21.4 and 21.6 (2 s, CH$_3$), 32.5 (d, ^{3}J(PC) = 6.0 Hz, *C*Me$_2$), 61.7 (d, ^{3}J(PC)= 25.0 Hz, Ph*C*HCl), 75.7 (d, ^{2}J(PC) = 4.5 Hz, O*C*H$_2$), 117.2 (d, ^{1}J(PC) = 186.0 Hz, P-*C*H), 127.0, 127.7, 128.7, 129.0, 137.9, 150.7 (d, ^{2}J(PC) = 5.0 Hz, P-CH=*C*H).

^{31}P NMR: δ 11.2.

Anal. Calcd for $C_{14}H_{18}ClO_3P$: C, 55.91; H, 6.04. Found: C, 55.87; H, 6.15.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH=CH-CH(Cl)CH$_3$ (12b)

Yield: 52% (using 46 mmol of **9b**)

Mp: 120°C.

^{1}H NMR: δ 1.08 and 1.10 (2 s, 6 H, C*H*$_3$), 1.64 (d, ^{3}J(HH) ~ 6.7 Hz, 3 H, CHCl-C*H*$_3$), 3.87 (dd, ^{2}J(HH), ^{3}J(PH) = 11.0, 12.0 Hz, OC*H*$_2$(A)), 4.20 (dd, ^{2}J(HH), ^{3}J(PH) ~ 11.0, 11.0 Hz, OC*H*$_2$(B)), 4.60 (dqrt, ^{3}J(HH), ^{3}J(HH) = 6.7, 6.7 Hz, C*H*-Cl), 6.00 (dd, ^{3}J(HH), ^{2}J(PH) = 19.0, 19.0 Hz, 1 H, P-C*H*), 6.85 (ddd, ^{4}J(HH), ^{3}J(HH), ^{3}J(PH) ~ 8.5, 19.0, 19.0 Hz, PCH=C*H*) (Figure 10).

^{13}C NMR: δ 21.5 (s, C(*C*H$_3$)$_2$), 23.9 (s, CHCl*C*H$_3$), 32.5 (d, ^{3}J(PC) = 5.5 Hz, *C*Me$_2$), 55.6 (d, ^{3}J(PC) = 25.0 Hz, *C*HCl), 75.7 (O*C*H$_2$), 116.1 (P-*C*H, ^{1}J(PC) = 186.5 Hz), 152.6 (Figure 11).

^{31}P NMR: δ 11.3.

Anal. Calcd for $C_9H_{16}ClO_3P$: C, 45.29; H, 6.77. Found: C, 45.15; H, 6.64.

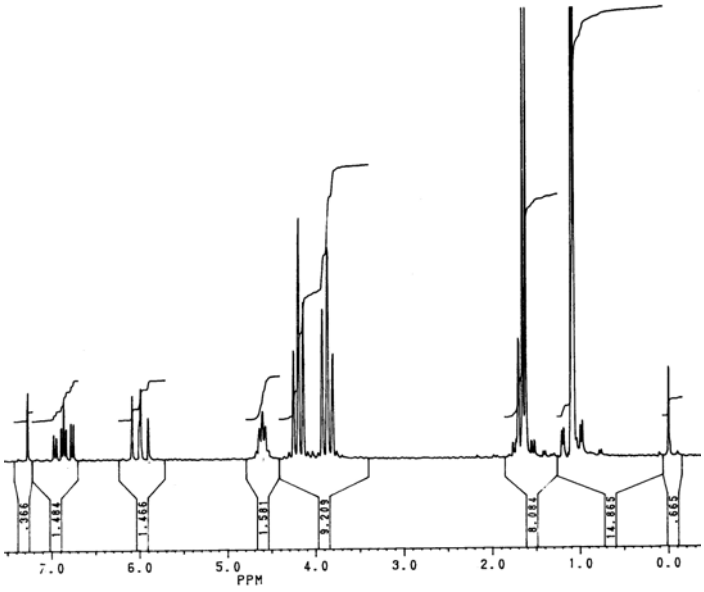


Figure 10. The ^{1}H NMR spectrum of **12b**

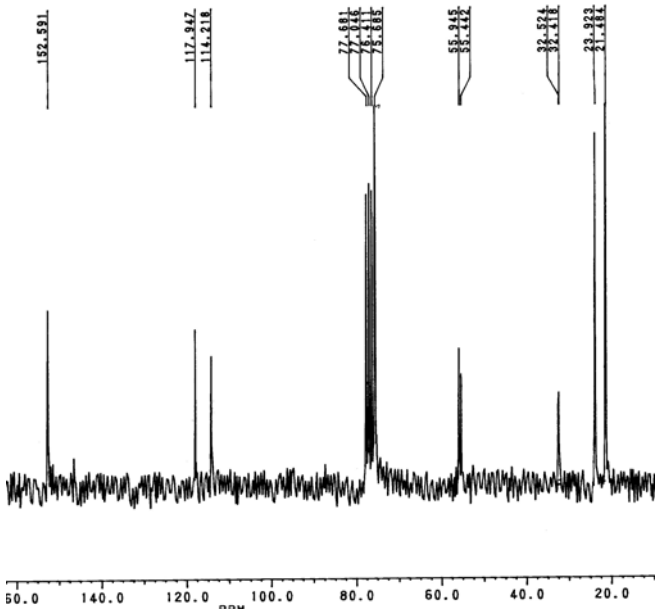


Figure 11. The ^{13}C NMR spectrum of **12b**

Compound **13** was prepared similarly from **8i** $(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_4H_3O)$[101,119] another route and NMR data are given in section 3.24.

Rearrangement of 12a to 14

Compound **12a** (0.6 g, 2.0 mmol) was heated with K_2CO_3 (0.5 g) in xylene (30 mL) at 80°C for 20 h. To the residue after removal of xylene, ether was added and the contents washed with water (3x10 mL). The ether portion was dried

(Na_2SO_4) and the solvent removed. The residue was essentially **14** (liquid) [NMR, >95%]. Attempted purification by column chromatography (for elemental analysis) was not successful.

Yield: 95% (using 2.0 mmol of **12a**)

^{1}H NMR: δ 1.03 and 1.06 (2 s, 6 H, CH_3), 3.10 (dd, ^3J(HH), ^2J(PH) = 7.8, 22.5 Hz, 2 H, PCH_2), 3.88 (dd, 2 H, OCH_2(A)), 4.17 (dd, 2 H, OCH_2(B)), 6.19 (td→qrt, 1 H, PCH$_2$-C*H*), 7.20-7.60 (m, 5 H, Ar-*H*). The exact nature of *J* values was difficult to ascertain.

^{13}C NMR: δ 21.4 (s, C(*C*H$_3$)$_2$), 26.7 (d, ^1J(PC) = 136.5 Hz, P-*C),* 32.5 (d, ^3J(PC)= 4.5 Hz, *C*Me$_2$), 75.5, (d, ^2J(PC) = 7.0 Hz, O*C*H$_2$), 115.9 (d, ^2J(PC) = 11.0 Hz, CH$_2$-*C*H), 126.5, 128.4, 129.0, 137.3.

^{31}P NMR: δ 20.9.

MS: 265 [M-Cl]$^+$.

3.24 Synthesis of chlorophosphonates (10a-g, 12a, 13), the bis-phosphonate 15 and α-trimethylsilyloxyphosphonates 16a-h by Abramov reaction of 1 or 3 with aldehydes

Typical procedure for (OCH$_2$CMe$_2$CH$_2$O)P(O)CH(Cl)(C$_6$H$_4$-2,6Cl$_2$) (10f)

A mixture of cyclic chlorophosphite **1a** (0.70 g, 4.2 mmol) and 2,6-dichlorobenzaldehyde (0.74 g, 6.88 mmol) was stirred at room temperature for 3 d. Then the product **10f** was crystallized from toluene or dichloromethane-hexane mixture.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(Cl)(C$_6$H$_3$-2,4-Cl$_2$) (10f)

Yield: 65% (using 4.2 mmol of **1a**).

Mp: 105-106°C.

^{1}H NMR: δ 1.02 and 1.20 (2 s, 6 H, 2 CH_3), 3.79 (s, 3 H, Ar-OCH_3), 4.10-4.30 (m, 4 H, 2 OCH_2), 5.65 (d, ^2J(P-H)= 13.4 Hz, 1 H, PC*H*Cl), 7.27-7.89 (m, 3 H, Ar-*H*).

^{13}C NMR: δ 21.1 and 21.7 (2 CH_3), 32.6 (*C*Me$_2$), 47.9 (d, ^1J(P-C) = 156.0 Hz, P*C*HCl), 78.1 (2d, ^2J(P-C) ≈ 7.0 Hz, 2 O*C*H$_2$), 128.0, 129.4, 130.8, 132.1, 135.9.

^{31}P NMR: δ 7.5 (lit 7.5[18e]).

Anal. Calcd for $C_{12}H_{14}Cl_3O_3P$: C, 41.95; H, 4.11. Found: C, 42.10; H, 4.21.

Compounds **10a-g** were obtained similarly in yields of 45-60% using the same molar quantities. Spectroscopic and analytical data for **10a-e** are given above (section 3.22).

$OCH_2CMe_2CH_2O)P(O)CH(Cl)(C_{14}H_9)$ (10g; $C_{14}H_9$ = anthryl) and $[(OCH_2CMe_2CH_2O)P(O)CH(C_{14}H_8)P(O)(OH)OCH_2CMe_2CH_2Cl]$ [$C_{14}H_8$ = anthryl residue] (15)

A mixture of **1a** (1.16 g, 6.88 mmol) and anthraldehyde (1.4 g, 6.88 mmol) was stirred at 80°C for 2 d. ^{31}P NMR of crude showed peaks at 11.2, 11.9, 12.3, 24.2, 35.7, 35.8. Excess of aldehyde was removed by passing the reaction mixture through a short silica gel column (ethyl acetate-hexane). Compounds corresponding to two spots (TLC) with R_f values lower than that of the aldehyde were collected and crystallized from dichloromethane hexane. The compounds **10g** (higher R_f, yellow crystals) and **15** (lower R_f, white crystals) were separated readily by hand picking.

$(OCH_2CMe_2CH_2O)P(O)CH(Cl)(C_{14}H_9)$ [$C_{14}H_9$ = 9-anthryl] (10g)

Yield: 30% (using 6.88mmol of **1a**)

Mp: 158-160°C.

^{1}H NMR: δ 0.97 and 1.05 (2 s, 6 H, 2 CH_3), 3.65 (t, $^{2,3}J$ = 8.0, 8.0 Hz, 1 H, OCH_AH$_B$), 4.01 (2 merged t, $^{2,3}J$ = 8.0, 8.0 Hz, 2 H, OCH_AH$_B$), 4.20 (2 merged t, $^{2,3}J$ = 8.0, 8.0 Hz, 1 H, OCH_AH$_B$), 6.75 (d, ^2J(P-H) = 14.6 Hz, 1 H, P-C*H*), 7.48-9.15 (m, 9 H, Ar-*H*).

^{13}C NMR: δ 21.2, 21.5 and 22.0 (3 s of differing intensity, CH_3), 32.5 (d, ^3J(P-C) = 2.0 Hz, *C*Me$_2$), 49.8 (d, ^1J(P-C) = 157.0 Hz, P*C*HCl), 58.7, 77.2 (2d, ^2J(P-C) ≈ 7.0 Hz, 2 O*C*H$_2$), 122.2, 124.2, 124.8, 125.2, 125.5, 126.1, 127.1, 128.0, 128.4, 129.1, 129.4, 129.9, 130.1, 130.8, 131.3, 131.9 (all aromatic *C*) (Figure 12).

^{31}P NMR: δ 11.4.

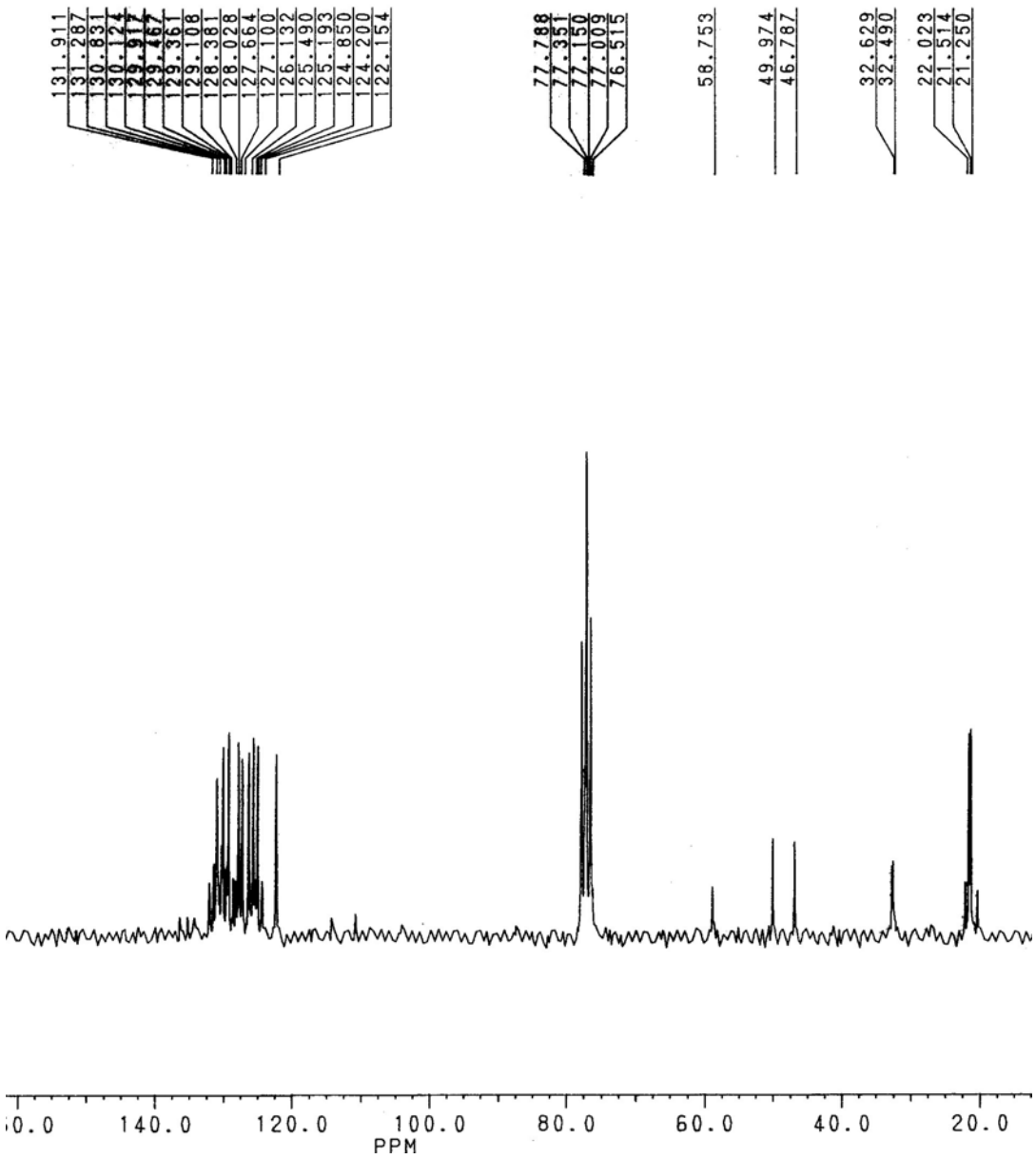


Figure 12. The ^{13}C NMR spectrum of **12b**.

[(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(C$_{14}$H$_8$)P(O)(OH)-OCH$_2$CMe$_2$CH$_2$Cl] [C$_{14}$H$_8$ = anthryl residue] (15)

Yield: 35% (using 6.88 mmol of **1a**).

Mp: 196-198°C.

^{1}H NMR: δ 0.82, 0.85, 0.93 and 1.29 (4 s, 12 H, C*H*$_3$), 3.06–3.34 (m, 4 H, OC*H*$_2$), 3.74–4.13 (m, 4 H, OC*H*$_2$), 4.47 (d, ^2J(P-H) = 30.0 Hz, 1 H, PC*H*), 6.03 (d, ^2J(P-H) = 15.0 Hz, 1 H, PC*H*=C), 7.11–8.20 (m, 8 H, Ar-*H*), 10.03 (br, 1 H, O*H*).

^{13}C NMR: 20.2 and 22.2 (2s, CH_3), 32.0 and 36.6 (2 s, CMe$_2$), 48.7 (d, ^1J(P-C) = 130.0 Hz, PCH), 51.1 and 69.5 (2d, ^2J(P-C) ≈ 7.0 Hz, 2 OCH$_2$), 75.5, 76.7, 111.0 (d, ^1J(P-C) ~ 149.0 Hz, PCH), 125.0, 127.2, 128.2, 128.3, 129.0, 129.6, 130.8, 131.9 (all aromatic *C*).

^{31}P NMR: δ 11.2, 24.2.

X-ray structural analysis was performed on this sample.

The γ chloro vinylphosphonate 12a and ring chlorinated furfuryl phosphonate 13

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH=CH-CH(Cl)C$_6$H$_5$) (12a)

Cinnamaldehyde (0.86 g, 6.51 mmol) was added all at once to (OCH$_2$CMe$_2$CH$_2$O)PCl (**1a**) (1.10 g, 6.51 mmol), the mixture stirred for 3 d upon which a white solid formed. This was washed with heptane (5 mL) and crystallized from a mixture of CH_2Cl_2 and heptane to get **12a**. Spectroscopic data are reported above.

With crotonaldehyde, a black gummy compound that showed ^{31}P NMR peaks at δ 11.7 for (**12b**) and 33.8 in 1:1 ratio (*ca* 38% each) along with other peaks. Attempts to isolate a pure product were unsuccessful.

Compound **13** was obtained in 45 % yield by the same route. This compound was reported from our laboratory by the thionyl chloride route described above.[101]

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH$_2$(5-Cl-C$_4$H$_2$O) (13)

Yield: 45% (using 6.51mmol of **1a**).

Mp. 98-100°C.

^{1}H NMR: δ 0.96 and 1.03 (2s, 6 H, CH_3), 3.29 (d, ^2J(P-H) = 22.0 Hz, 2 H, PCH_2), 3.80 (dd, ^2J(H-H), ^3J(P-H) ~ 11.0, 11.0 Hz, 2 H, OCH_2), 4.17 (dd, ^2J(H-H), ^3J(P-H) ~ 11.0, 11.1 Hz, 2 H, OCH_2), 6.10 (m, 1 H, furfuryl-*H*), 6.25 (m, 1 H, furfuryl-*H*)

^{13}C NMR: δ 21.2 and 21.4 (2 s, CH$_3$), 25.7 (d, ^1J(P-C) = 145.0 Hz, P-*C*), 32.4 (d, ^3J(P-C) ~ 5.0 Hz, CMe$_2$), 75.7 (d, ^2J(P-C) ~ 7.0 Hz, OCH$_2$), 107.4, 111.0, 111.1, 144.6.

^{31}P NMR: δ 16.4.

Anal. Calcd for $C_{10}H_{14}ClO_4P$: C, 45.37; H, 5.34. Found: C, 45.42; H, 5.38.

Typical procedure for $(OCH_2CMe_2CH_2O)P(O)CH(OSiMe_3)Ph$ (16a)

Benzaldehyde (0.52 g, 4.20 mmol) was added all at once to $(OCH_2CMe_2CH_2O)POSiMe_3$ (**3**) (0.94 g, 4.20 mmol) and the mixture stirred for 24 h. The white solid formed was washed with heptane (5 mL.) and crystallized from a mixture of CH_2Cl_2 and heptane. Compounds **16b-h** were prepared similarly. Compounds **16a-h** were hydrolytically unstable; leading to the hydroxyphosphonates. Hence *for purity check, ^{13}C NMR spectra were utilized in many cases*. Analytical data were obtained for **16f-g**.

Yield (**16a**): 89% (using 4.20 mmol of **3**)

Mp: 142-144°C.

IR (cm^{-1}): 2959, 1479, 1267, 1090, 1057, 1008.

^1H NMR: δ 0.10 (s, 9 H, $SiCH_3$), 0.91 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 3.81 - 4.36 (m, 4 H, OCH_2), 5.20 (d, 1 H, ^2J(P-H) = 17.0 Hz, C*H*), 7.30-7.50 (m, 5 H, Ar-*H*) (Figure 13).

^{13}C NMR: δ 0.2, 20.9, 22.0, 32.5 (d, ^3J(PC) = 7.5 Hz), 73.5 (d, ^1J(PC) = 164.8 Hz), 77.0, 78.4, 78.5, 127.0, 127.1, 128.2, 136.9 (Figure 14, next page).

^{31}P NMR: δ 11.0.

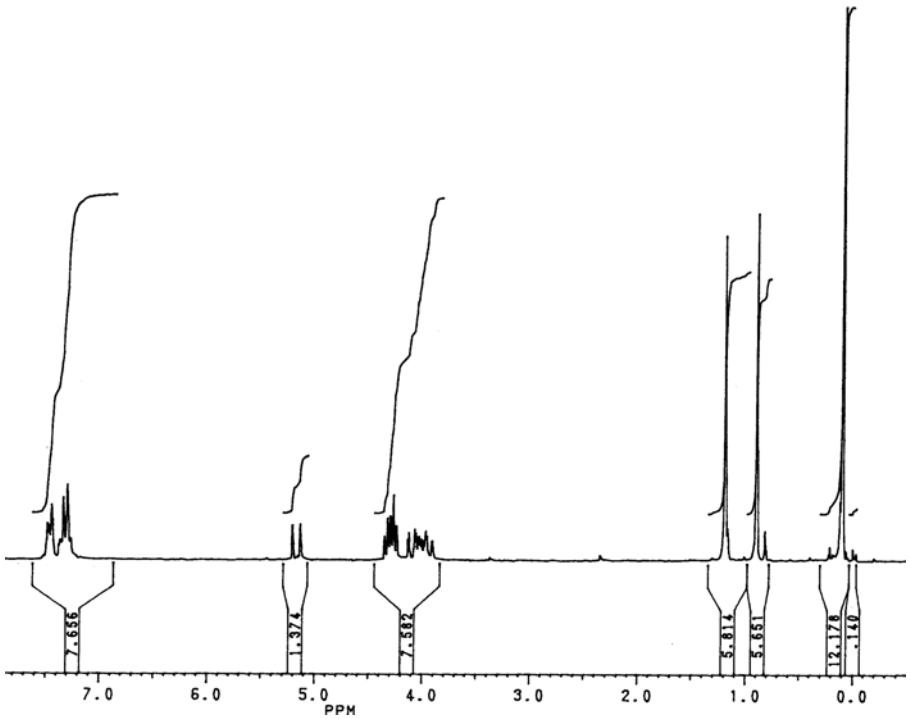


Figure 13. The ^1H NMR spectrum of **16a**

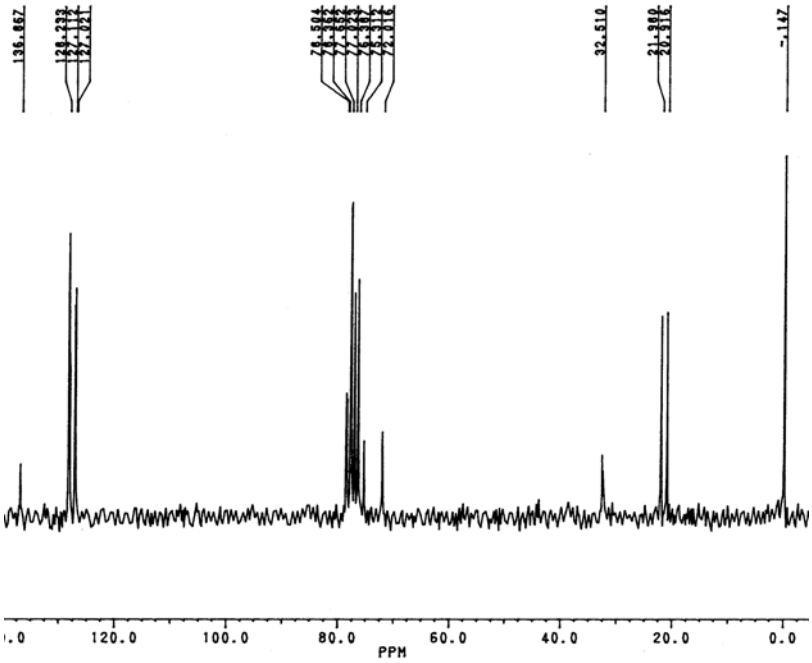


Figure 14. The ^{13}C NMR spectrum of **16a**

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(OSiMe$_3$)C$_6$H$_4$-4-Me (16b)

Yield: 92% (using 4.20 mmol of **3**).

Mp: 166-168°C.

^{1}H NMR: δ 0.10 (s, 9 H, SiC*H*$_3$), 0.90 (s, 3 H, C*H*$_3$), 1.20 (s, 3 H, C*H*$_3$), 2.34 (s, 3 H, C*H*$_3$), 3.80 - 4.32 (m, 4 H, OC*H*$_2$), 5.15 (d, 1 H, ^2J(P-H) = 14.0 Hz, C*H*), 7.02 and 7.32 (2 d, ^3J(H-H) = 8.0 Hz, 4 H, Ar-*H*).

^{13}C NMR: δ -0.12, 20.9, 21.1, 22.0, 32.4 (d, ^3J = 7.5 Hz), 73.5 (d, ^1J = 164.8 Hz), 78.4, 113.5, 126.9, 127.0, 129.0, 133.7, 137.8

^{31}P NMR: δ 11.3.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(OSiMe$_3$)C$_6$H$_4$-4-Cl (16c)

Yield: 90% (using 4.20 mmol of **3**).

Mp: 149-150°C.

IR (cm^{-1}): 2970, 2905, 1595, 1265, 1074, 1057.

^{1}H NMR: δ 0.12 (s, 9 H, SiC*H*$_3$), 0.95 (s, 3 H, C*H*$_3$), 1.27 (s, 3 H, C*H*$_3$), 3.95 - 4.21 (m, 4 H, OC*H*$_2$), 5.10 (d, 1 H, ^2J(P-H) = 14.0 Hz, C*H*), 7.26-7.50 (m, 4 H, Ar-*H*).

^{13}C NMR: δ -0.2, 20.9, 21.8, 32.4 (d, ^3J = 7.7 Hz), 73.2 (d, ^1J = 165.5 Hz), 76.4, 77.8, 128.3, 128.4, 133.9, 135.5.

^{31}P NMR: δ 10.6.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(OSiMe$_3$)C$_6$H$_4$-4-OMe (16d)

Yield: 90% (using 4.20 mmol of **3**).

Mp: 136-138°C.

^{1}H NMR: δ 0.10 (s, 9 H, SiC*H*$_3$), 0.90 (s, 3H, C*H*$_3$), 1.20 (s, 3 H, C*H*$_3$), 3.75 (s, 3 H, OCH$_3$), 3.81 - 4.40 (m, 4 H, OC*H*$_2$), 5.18 (d, 1 H, ^{2}J(P-H) = 17.0 Hz, C*H*), 6.88 and 7.46 (2 d, ^{3}J(H-H) = 8.0 Hz, 4 H, Ar-*H*).

^{13}C NMR: δ -0.12, 20.8, 21.8, 32.4 (d, ^{3}J(PC)= 7.5 Hz), 55.3, 55.5, 71.4 (d, ^{1}J(PC) = 164.8 Hz), 76.4, 77.3, 113.5, 113.9,114.3, 128.4, 128.5, 128.7, 131.9, 132.1, 159.6.

^{31}P NMR: δ 11.4.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(OSiMe$_3$)(C$_{10}$H$_7$) (16e) [C$_{10}$H$_7$=1naphthyl]

Yield: 92% (using 4.20 mmol of **3**)

Mp: 131-133°C.

IR (cm^{-1}): 3050, 2969, 1265, 1165, 1057, 1011.

^{1}H NMR: δ 0.13 (s, 9 H, SiC*H*$_3$), 0.90 (s, 3 H, C*H*$_3$), 1.20 (s, 3 H, C*H*$_3$), 3.90 - 4.28 (m, 4 H, OC*H*$_2$), 5.95 (d, 1 H, ^{2}J(P-H) = 19.0 Hz, C*H*), 7.40-8.18 (m, 7 H, Ar-*H*).

^{13}C NMR: δ -0.2, 20.9, 21.8, 32.3 (d, ^{3}J = 7.5 Hz), 70.1 (d, ^{1}J(PC) = 167.2 Hz), 77.7, 78.0, 78.1, 123.8, 124.9, 125.5, 125.9, 126.0, 126.1, 126.8, 128.5, 128.7, 130.7, 133.1, 133.7.

^{31}P NMR: δ 10.8.

OCH$_2$CMe$_2$CH$_2$O)P(O)CH(OSiMe$_3$)C$_6$H$_3$-2,4-Cl$_2$ (16f)

Yield: 91% (using 4.20 mmol of **3**).

Mp: 140-141°C.

IR(cm^{-1}): 1560, 1431, 1267, 1090, 1057, 1009.

^{1}H NMR: δ 0.08 (s, 9 H, SiC*H*$_3$), 0.92 (s, 3 H, C*H*$_3$), 1.26 (s, 3 H, C*H*$_3$), 3.96 - 4.65 (m, 4 H, OC*H*$_2$), 6.10 (d, 1 H, ^{2}J(P-H) = 19.0 Hz, C*H*), 7.20-7.35 (m, 3 H, Ar-*H*).

^{13}C NMR: δ 0.5, 20.8, 22.0, 32.4 (d, ^{3}J = 7.4 Hz), 70.5 (d, ^{1}J(PC) = 168.7 Hz), 78.4, 78, 78.7, 128.4, 129.6, 130.5, 132.1, 135.5, 135.6.

^{31}P NMR: δ 8.9.

Anal. Calcd for $C_{15}H_{23}Cl_2O_4PSi$: C, 45.35; H, 5.83. Found: C, 44.98; H, 5.45.

$(OCH_2CMe_2CH_2O)P(O)CH(OSiMe_3)C_6H_4$-4-Br (16g)

Yield: 90% (using 4.20 mmol of **3**).

M.p: 164-166°C

IR(cm^{-1}): 2968, 2903, 1487, 1265, 1057, 1008.

^{1}H NMR: δ 0.2 (s, 9 H, SiCH_3), 0.93 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 3.95 - 4.39 (m, 4 H, OCH_2), 5.10 (d, 1 H, ^{2}J(P-H) = 15.0 Hz, C*H*), 7.30-7.50 (m, 4 H, Ar-*H*).

^{13}C NMR: δ-0.2, 20.9, 21.9, 32.4 (d, ^{3}J = 7.5 Hz), 72.8 (d, ^{1}J = 166.2 Hz), 77.7, 77.9, 78.4, 78.5, 122.1, 128.5, 131.4, 136.0.

^{31}P NMR: δ 10.4.

MS: 406, 408 {1:1, $[M]^+$}.

Anal. Calcd for $C_{15}H_{24}BrO_4PSi$: C, 44.23; H, 5.93. Found: C, 43.50; H, 5.23.

$(OCH_2CMe_2CH_2O)P(O)CH(OSiMe_3)CH(CH_3)_2$ (16h)

Yield: 86% (using 4.20 mmol of **3**).

M.p: 74-76°C.

^{1}H NMR: δ 0.20 (s, 9 H, SiCH_3), 0.90-1.2 (many lines, 12 H, CH_3), 2.14 (m, 1 H, C*H*), 3.81 - 4.40 (m, 4 H, OCH_2), 5.11 (d, 1 H, ^{2}J(P-H) = 15.0 Hz, C*H*).

^{13}C NMR: δ 0.3, 18.2, 19.7, 21.2, 21.7, 32.5, 32.7, 74.5 (d, ^{1}J = 185.8 Hz), 75.7, 75.8, 76.5.

^{31}P NMR: δ 18.4.

3.25 Preparation of the α-tosyl phosphonates 17a-17d

Synthesis of $(OCH_2CMe_2CH_2O)P(O)CH(OTs)C_6H_5$ (17a)

To a well-stirred solution of **8a** (1.0 g, 3.92 mmol) and *p*-toluenesulfonyl chloride (TsCl) (0.78 g, 3.92 mmol) in CH_2Cl_2 (20 mL.) at 0°C was added triethylamine (0.59 g, 0.8 mL, 5.87 mmol) followed by 4-dimethylaminopyridine

(0.05 g, catalytic) under dry nitrogen atmosphere. After 0.5 h, the reaction mixture turned yellow; it was stirred further for 1 h, quenched with water (30 mL) and extracted with CH_2Cl_2 (2x20 mL). The CH_2Cl_2 layer was collected, dried (Na_2SO_4), filtered and then concentrated to give a solid which was crystallized from heptane to give **17a**.

Yield: 1.4 g (87%).

Mp: 176-178°C

IR (cm^{-1}): 1597, 1372, 1278, 1181, 1057.

^{1}H-NMR: δ 0.92 and 1.22 (2 s, 6 H, 2 C*H*$_3$), 2.33 (s, 3 H, Ar-C*H*$_3$), 3.96 - 4.40 (m, 4 H, 2 OC*H*$_2$), 5.85 (d, ^2J(P-H) = 20.0 Hz, 1 H, P-C*H*), 7.05 - 7.60 (m, 9 H, Ar-*H*).

^{13}C NMR: δ 20.7, 21.6 and 21.9 (s each, 3 *C*H$_3$), 32.5 (d, ^3J(P-C) = 8.4 Hz, *C*Me$_2$), 78.4 (d, ^2J(P-C) = 7.1 Hz, O*C*H$_2$), 78.8 (d, ^1J(P-C) = 167.0 Hz, P-*C*H), 78.9 (d, ^2J(P-C) = 7.3 Hz, O*C*H$_2$), 127.8, 127.9, 128.4, 129.1, 131.4, 133.3, 145.2.

^{31}P NMR: δ 4.7 (lit. 4.7[119]).

Reaction of this compound with an excess of sodium azide (4 mole equivalents) in dimethyl sulfoxide at 80°C resulted in the azidophosphonate **20a** in low yields.

Compounds **17b-d** were prepared by the same procedure. Analytical data were obtained for **17c-d**.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(OTs)C$_6$H$_4$-4-Me (17b)

Yield: 1.4 g (84%).

Mp: 172-174°C.

IR (cm^{-1}): 1472, 1372, 1281, 1181, 1059, 1007.

^{1}H-NMR: δ 0.96 and 1.24 (2 s, 6 H, 2 C*H*$_3$), 2.28 (s, 3 H, Ar-C*H*$_3$), 2.37 (s, 3 H, Ar-C*H*$_3$), 3.96 - 4.40 (m, 4 H, 2 OC*H*$_2$), 5.81 (d, ^2J(P-H) = 16.0 Hz, 1 H, P-C*H*), 7.05 - 7.60 (m, 8 H, Ar-*H*).

^{13}C NMR: δ 20.8, 21.1, 21.5 and 21.9 (s each, 4 *C*H$_3$), 32.5 (d, ^3J(P-C) = 8.4 Hz, *C*Me$_2$), 78.1 (d, ^2J(P-C) = 7.1 Hz, O*C*H$_2$), 79.1 (d, ^1J(P-C) = 167.0 Hz, P-*C*H), 127.9, 128.4, 129.1, 129.6, 131.4, 133.3, 145.2.

^{31}P NMR: δ 5.1.

$(OCH_2CMe_2CH_2O)P(O)CH(OTs)C_6H_4$-4-Cl (17c)

Yield: 1.2 g (80%).

Mp: 176-178°C.

IR (cm^{-1}): 1597, 1494, 1375, 1285, 1190, 1060.

^{1}H-NMR: δ 0.93 and 1.22 (2 s, 6 H, 2 CH_3), 2.36 (s, 3 H, Ar-CH_3), 3.90 - 4.40 (m, 4 H, 2 OCH_2), 5.80 (d, ^2J(P-H) = 19.0 Hz, 1 H, P-C*H*), 7.15 - 7.62 (m, 8 H, Ar-*H*).

^{13}C NMR: δ 20.7, 21.6 and 21.8 (s each, 3 *C*H_3), 32.5 (d, ^3J(P-C) = 8.4 Hz, *C*Me_2), 78.0 (d, ^1J(P-C) = 167.0 Hz, P-*C*H), 78.4 and 78.9 (d each, ^2J(PC) ~ 8 Hz, O*C*H_2), 127.9, 128.3, 128.6, 129.2, 129.3, 129.7, 130.1, 1302, 133.2, 135.1, 135.2, 145.5 (Figure 15).

^{31}P NMR: δ 4.3.

Anal. Calcd. for $C_{19}H_{22}ClO_6PS$: C, 51.29; H, 4.94; S, 7.19. Found: C, 50.76; H, 4.78; S, 6.95.

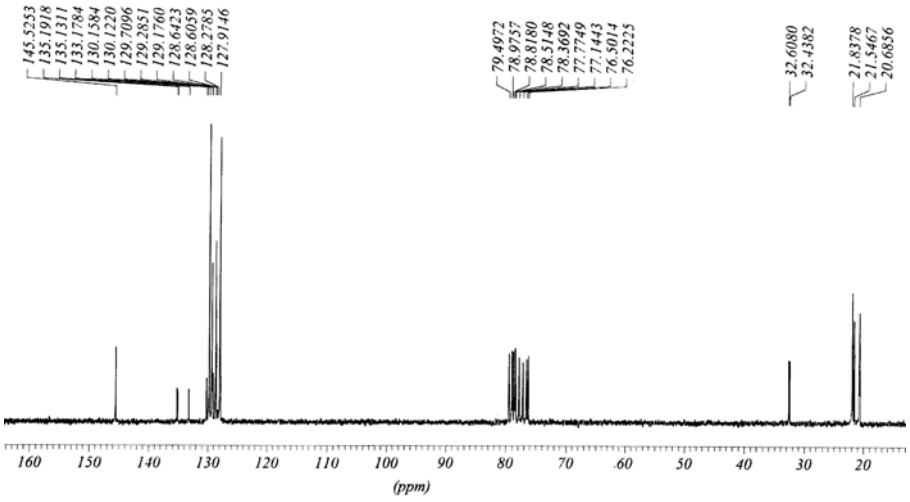


Figure 15. The ^{13}C NMR spectrum of **17c**.

$(OCH_2CMe_2CH_2O)P(O)CH(OTs)C_6H_4$-3-Br (17d)

Yield: 1.3 g (83%).

Mp: 156-158°C.

IR (cm^{-1}): 1595, 1379, 1283, 1194, 1055.

^{1}H-NMR: δ 0.97 and 1.25 (2 s, 6 H, 2 CH_3), 2.37 (s, 3 H, Ar-CH_3), 4.04 - 4.40 (2 m, 4 H, 2 OCH_2), 5.77 (d, ^2J(P-H) = 20.0 Hz, 1 H, P-C*H*), 7.05 – 7.57 (m, 8 H, Ar-*H*).

^{13}C NMR: δ 20.7, 21.6 and 21.9 (s each, *C*H_3), 32.5 (d, ^3J(P-C) = 8.4 Hz, *C*Me_2), 78.0 (^1J(PC) = 165.0 Hz, P*C*), 78.6 and 79.0 (d each, ^2J(PC) ~ 6.5 Hz, O*C*H_2) 122.4, 126.6, 126.7, 127.9, 129.7, 129.9, 130.6, 130.7, 132.0, 133.6, 145.6.

^{31}P NMR: δ 4.8.

Anal. Calcd for $C_{19}H_{22}BrO_6PS$: C, 46.60; H, 4.49, S; 6.54. Found: C, 47.05; H, 4.64; S, 6.68.

3.26 Reactions of phosphoryl azides with o-bromobenzyl alcohol and α-hydroxy phosphonates in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene

(a) Compound 18: To a solution of *o*-bromobenzyl alcohol (0.40 g, 2.10 mmol) and **5** (0.50 g, 2.61 mmol) in toluene (10 mL.), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.40 g, 2.61 mmol) was added and the mixture stirred for 1 d. Then crushed ice was added, the product extracted with ether and chromatographed over silica gel using hexane followed by CH_2Cl_2 - hexane (1:5) to afford **18** (liquid[122]).

Yield: 0.28g (88%)

IR (cm^{-1}): 2100, 1441, 1290, 1260, 1030.

^{1}H NMR: δ 4.52 (s, 2 H, C*H*$_2$), 7.12-7.70 (m, 4 H, Ar-*H*).

^{13}C NMR: δ 54.6 (*C*H_2), 123.8, 127.8, 129.8, 130.1, 133.1, 135.1 (aromatic carbons).

This is a known compound.[122]

(b) Compounds 19 and 20a-c: ***Procedure for* 20a**: To a solution of α-hydroxy phosphonate **8a** (0.50 g, 1.95 mmol) and diphenylphosphoryl azide (0.64 g, 2.34 mmol) in toluene (10 mL.), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.36g, 2.34 mmol) was added and the mixture stirred for 1 d. Then crushed ice was added, the product extracted with dichloromethane (DCM) and crystallized from dichloromethane-hexane (1:1) mixture to afford **20a** (see below for NMR data).

Compounds **19** and **20b-c** were obtained similarly.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH[OP(O)(OCH$_2$CMe$_2$CH$_2$O)]C$_6$H$_4$-4-Me (19)

Yield: 50% (using 1.95 mmol of **8b**)

Mp: 102-104°C.

IR (cm^{-1}): 1584, 1489, 1282, 1213, 1067.

^{1}H NMR: δ 0.84, 0.91 and 1.22 (3 s, 12 H, C*H*$_3$), 2.35 (s, 3 H, Ar-CH$_3$), 3.32 - 4.45 (m, 8 H, OC*H*$_2$), 5.72 (dd or t, ^{2}J(P-H) = 15.4 Hz, 1 H, P-C*H*OP), 6.90 - 7.50 (m, 4 H, Ar-*H*).

^{13}C NMR: δ 20.2, 20.7, 21.2 and 21.7 (4 s *C*H$_3$), 24.0, 32.0, 32.4, 38.0, 48.0, 54.3, 73.5 (dd, ^{1}J(PC) ~ 175 Hz, ^{2}J(PC) ~9.5 Hz, P-*C*-O-P), 77.8, 78.2, 127.9, 128.0, 129.0, 129.4. 129.8, 139.5, 166.2.

^{31}P NMR: δ -8.7 (d), 7.5 (d, ^{3}J(P-P) = 31.0 Hz).

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH[OP(O)(OPh)$_2$]C$_6$H$_5$ (20a)

Yield: 52% (using 1.95 mmol of **8a**)

Mp: 102-104°C.

IR (cm^{-1}): 1580, 1485, 1284, 1215, 1068.

^{1}H NMR: δ 0.85 and 1.21 (2 s, 6 H, 2 C*H*$_3$), 3.82 - 4.29 (m, 4 H, OC*H*$_2$), 5.91 (dd to t, ^{2}J(P-H) = 15.4 Hz, 1 H, P-C*H*OP), 6.90 - 7.59 (m, 10 H, Ar-*H*).

^{13}C NMR: δ 20.8 and 21.9 (2 s *C*H$_3$), 32.5 (d, ^{3}J(P-C) = 7.2 Hz, *C*Me$_2$), 76.6 (dd, ^{1}J(PC) ~ 155 Hz, ^{2}J(PC) ~9.5 Hz, P-*C*-O-P), 77.1, 78.5, 120.0, 125.5, 128.0, 128.2, 128.6, 129.4, 129.7, 132.4, 150.3.

^{31}P NMR: δ -13.8 (d), 6.3 (d, ^{3}J(P-P) = 41.7 Hz).

Anal. Calcd for C$_{24}$H$_{26}$O$_7$P$_2$: C, 64.28; H, 5.84. Found: C, 64.20; H, 5.78.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH[OP(O)(OPh)$_2$]C$_6$H$_4$-4-Me (20b)

Yield: 50% (using 1.48 mmol of **8b**).

Mp: 112-114°C.

IR (cm^{-1}): 1589, 1487, 1284, 1217, 1068.

^{1}H NMR: δ 0.84 and 1.20 (2 s, 6 H, 2 C*H*$_3$), 2.35 (s, 3 H, C*H*$_3$), 3.82 - 4.34 (m, 4 H, OC*H*$_2$), 5.91 (dd to t, ^{2}J(P-H) = 15.4 Hz 1 H, P-C*H*OP), 6.87 - 7.59 (m, 9 H, Ar-*H*).

^{13}C NMR: δ 20.7, 21.0 and 21.8 (3 s *C*H$_3$), 32.4 (d, ^{3}J(P-C) = 6.2 Hz, *C*Me$_2$), 76.7 (dd, ^{1}J(PC) = 167.5 Hz, ^{2}J(PC) = 10.0 Hz, P-*C*-O-P), 77.2, 77.8, 120.0, 125.4, 125.5, 128.0, 128.2, 129.3, 129.6, 129.8, 139.4, 150.1, 150.3, 150.4 (Figure 16).

^{31}P NMR: δ -13.8 (d), 6.5 (d); ^{3}J(P-P) ~ 39.0 Hz).

The azide is also probably formed in low yields; the ^{31}P NMR spectrum (Figure 17) showed a peak (ca 10 %) at δ 10.6. In the ^{13}C NMR also there was a minor doublet centered at δ 61.6 (^{1}J(PC) ~ 157.7 Hz) (cf. Figure 16); a weak band at 2097 cm^{-1} in the IR was also seen.

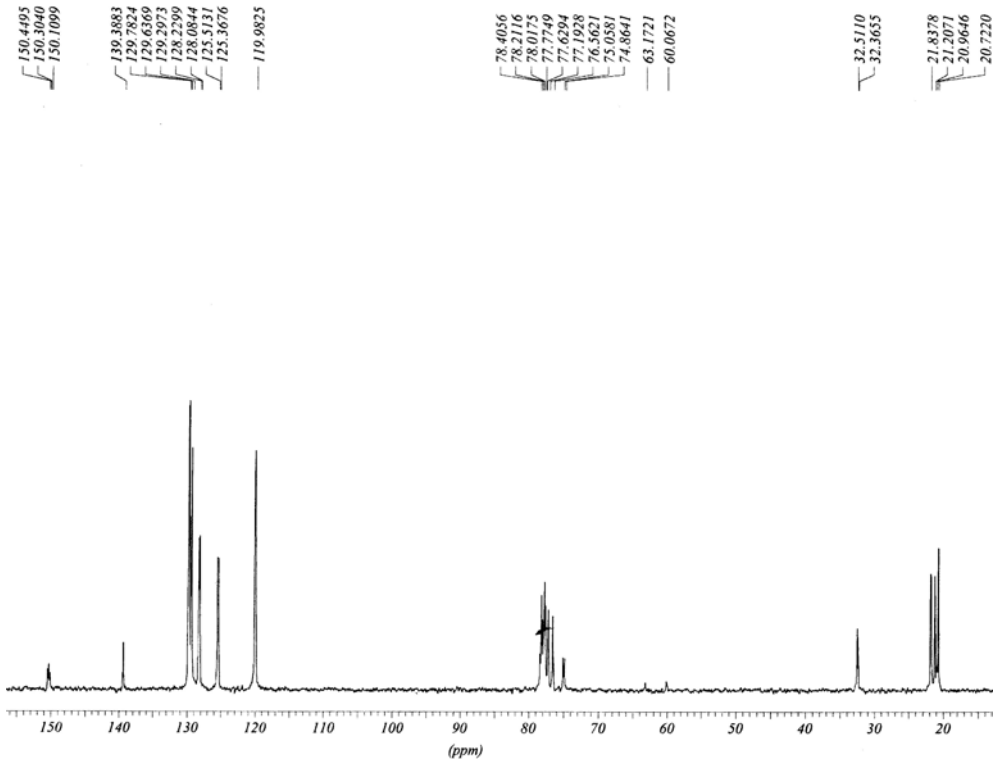


Figure 16. The ^{13}C NMR spectrum of **20b**.

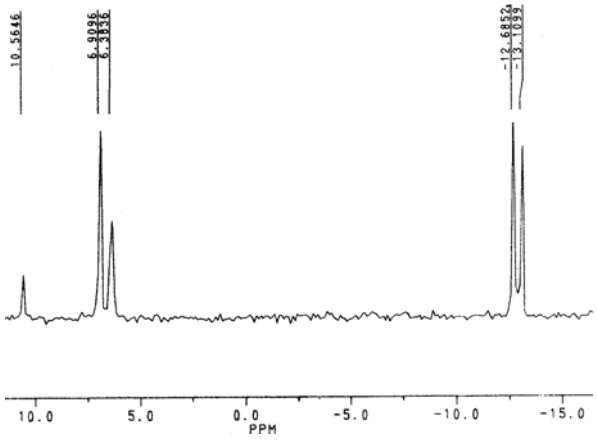


Figure 17. The ^{31}P NMR spectrum of the reaction mixture containing **20b** that also shows the formation of the azidophosphonate at δ 10.6.

$(OCH_2CMe_2CH_2O)P(O)CH[OP(O)(OPh)_2]C_6H_3$-2,6-$Cl_2$ (20c)

Yield: 50% (using 1.72 mmol of **8h**)

Mp: 120-122°C.

IR (cm^{-1}): 1582, 1485, 1279, 1217, 1068.

^{1}H NMR: δ 0.89 and 1.25 (2 s, 6 H, 2 C*H*$_3$), 3.89 - 4.46 (m, 4 H, OC*H*$_2$), 6.81 (dd to t, ^2J(P-H) = 16.4 Hz, 1 H, P-C*H*OP), 7.12 - 7.45 (m, 7 H, Ar-*H*).

^{13}C NMR: 21.6 and 21.9 (2 s, *C*H$_3$), 32.4 (d, ^3J(P-C) = 8.0 Hz, *C*Me$_2$), 73.4 (dd ^1J(PC) = 167.5 Hz, ^2J(PC) = 10.0 Hz, P-*C*-O-P), 77.2, 77.8 (O*C*H$_2$), 119.7, 119.8, 119.9, 125.5, 120.0, 125.5, 15.6, 128.4, 128.8, 129.7, 129.8, 130.4, 130.7, 136.0, 136.1, 149.9, 150.2, 150.3.

^{31}P NMR: δ -13.3 (d), 4.5, (d); ^3J(P-P) ~ 39.0 Hz.

Compound **20c** was also characterized by single crystal X-ray structure determination.

3.27 Synthesis of α-azidophosphonates 21a-c:

Typical procedure for 21b

A mixture of the α-bromophosphonate **11b** (1.16 g, 0.99 mmol) and sodium azide (0.32 g, 4.93 mmol) in dimethyl sulfoxide was stirred at 60°C for 3 h. Then crushed ice as added, the product extracted with dichloromethane and crystallized from dichloromethane hexane to get **21b**.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(N$_3$)C$_6$H$_4$-Me (21b)

Yield: 59% (Using 0.99 mmol of **11b**).

Mp: 146-148°C.

IR (cm^{-1}): 2097, 1269, 1059.

^{1}H NMR: δ 0.98 and 1.12 (2 s, 6 H, 2 C*H*$_3$), 2.35 (s, 3 H, Ar-C*H*$_3$), 3.92 – 4.20 (m, 4 H, OC*H*$_2$), 4.86 (d, ^2J(P-H) = 15.4 Hz 1 H, P-C*H*N$_3$), 7.20 and 7.36 (2 d, ^3J(H-H) = 8.0 Hz, 4 H, Ar-*H*).

^{13}C NMR: δ 21.0, 21.2 and 21.7 (s each *C*H$_3$), 32.5 (d, ^3J(P-C) = 7.2 Hz, *C*Me$_2$), 61.6 (d, ^1J(P-C) = 157.7 Hz, P-*C*HN$_3$), 77.2, 77.8 (2 s O*C*H$_2$), 128.2, 128.3, 128.7, 129.6, 139.0 (Figure 16, next page).

^{31}P NMR: δ 10.6.

Compounds **21a** and **21c** were prepared similarly.

Anal. Calcd. for C$_{13}$H$_{18}$O$_3$N$_3$P: C, 52.88; H, 6.14; N, 14.23. Found: C, 52.67; H, 6.01; N, 13.98.

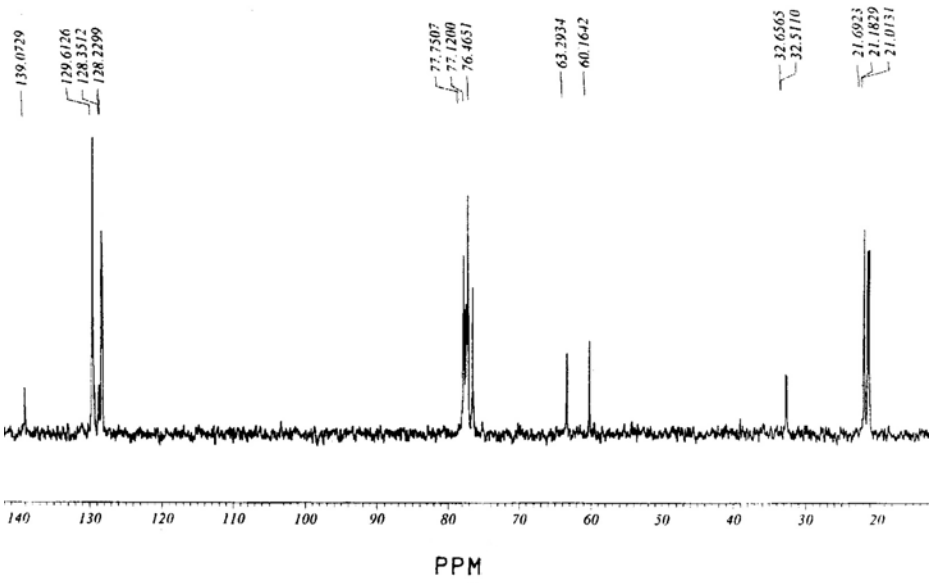


Figure 16. The ^{13}C NMR spectrum of **21b**.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(N$_3$)C$_6$H$_5$ (21a)

Yield: 52% (using 0.90 mmol of **11a**)

Mp: 118-120°C.

IR (cm^{-1}): 2095, 1267, 1059.

^{1}H NMR: δ 0.95 and 1.16 (2 s, 6 H, 2 C*H*$_3$), 3.92 - 4.19 (m, 4 H, OC*H*$_2$), 4.92 (d, ^{2}*J*(P-H) = 15.4 Hz 1 H, P-C*H*N$_3$), 7.19 - 7.56 (m, 5 H, Ar-*H*).

^{13}C NMR: δ 21.0 and 21.7 (2 s *C*H$_3$), 32.6 (s *C*Me$_2$), 61.4 (d, ^{1}*J*(P-C) = 155.2 Hz, P-*C*HN$_3$), 77.1, 77.3, 77.5, 128.2, 128.4, 128.9, 129.1, 132.0.

^{31}P NMR: δ 10.2.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(N$_3$)(1-C$_{10}$H$_7$) (C$_{10}$H$_7$ = Napth) (21c)

Yield: 47% (using 0.71 mmol of **11c**).

Mp: 128-130°C.

IR (cm^{-1}): 2105, 1273, 1059.

^{1}H NMR: δ 0.91, 1.11 (2 s, 6 H, C*H*$_3$), 3.78 - 4.20 (m, 4 H, OC*H*$_2$), 5.68 (d, ^{2}*J*(P-H) = 17.5 Hz, 1 H, PC*H*N$_3$), 7.34 - 8.20 (3 m, 7 H, Ar-*H*).

^{13}C NMR: δ 21.0 and 21.6 (2 s, *C*H$_3$), 32.5 (d, ^{3}*J*(P-C) = 6.8 Hz, *C*Me$_2$), 57.9 (d, ^{1}*J*(P-C) ≈ 159.0 Hz, P-*C*HN$_3$), 77.3, 77.4, 123.1, 125.2, 126.2, 126.6, 127.0, 127.2, 127.3, 127.7, 129.0, 130.5, 131.1, 134.0.

^{31}P NMR: δ 10.6.

3.28 Synthesis of aminophosphonates 22a-f

Procedure for ($OCH_2CMe_2CH(Ph)O)P(O)CH(NHCO_2Et)(Ph)$ (22a)

Compound ($OCH(Ph)CMe_2CH_2O)PCl$ (**1b**) (1.67 g, 5.97 mmol) and urethane (0.53 g, 5.97 mmol) were warmed to 80°C for 5 min and then benzaldehyde (0.63 g, 5.97 mmol) was added all at once the mixture upon which a white gummy solid formed. This was washed with hexane (15 mL) and the residue crystallized from a mixture of CH_2Cl_2 and hexane to get **22a** as a white solid. Compounds **22b-f** were prepared similarly from **1b** or **1c**.

Yield: 0.72g (30%)

Mp: 178-180°C.

IR (cm^{-1}): 3246, 1717, 1537, 1246, 1051.

^1H NMR: δ 0.76, 0.81 (2s, 6H, 2 C*H*$_3$), 1.22 (2 t merged, ^3J = 6.8 Hz, 3 H, OCH_2CH_3), 3.82 (m, 2 H, OCH_2), 4.12 (m, 2 H, OCH_2CH_3), 4.41 (m, 1 H, PhC*H*OP), 5.45 (m, 1 H, PC*H*NH), 5.91 (br, 1 H, N*H*), 7.16-7.40 (m, 10 H, Ar-*H*).

^{13}C NMR: δ 14.5 and 17.3 (2 s, CH_3), 21.2 (minor), 21.6 (CH_2CH_3), 30.9, 36.5 ($C(CH_3)_2$), 52.6 (d, ^1J(P-C) ≈ 154.0 Hz, P-*C*HNH), 61.7 (OCH_2CH_3), 75.6 and 75.8 (OCH_2), 84.6 and 84.7 (O*C*HPh), 127.2, 127.4, 127.8, 128.4, 128.7, 134.7, 135.2, 135.7 (all aromatic *C*), 156.0 (NH*C*(O)).

^{31}P NMR: δ 19.1, 20.2 [2:3 ratio].

Anal. Calcd. for $C_{21}H_{26}O_5NP$: C, 62.52; H, 6.45; N, 3.47. Found: C, 62.13; H, 6.10; N, 3.21.

($OCH_2CMe_2CH(Ph)O)P(O)CH(NHCO_2Et)(C_6H_4$-4-Me) (22b)

Yield: 32% (using the same molar quantities as for **22a**)

Mp. 192-194°C.

IR (cm^{-1}): 3239, 1719, 1534, 1244, 1046.

^1H NMR (major isomer): δ 0.75, 0.85 (2 s, 6 H, 2 C*H*$_3$), 1.20 (t, ^3J = 6.8 Hz, 3 H, OCH_2CH_3), 2.33 (s, 3 H, ArC*H*$_3$), 3.80 (dd, $^{2,3}J$ = 12.0, 18.0 Hz, 2 H, OCH_2), 4.12 (q, ^3J(HH) = 6.8 Hz, 2 H, OCH_2CH_3), 4.44 (d, ^3J = 13.6 Hz, 1 H, PhC*H*OP) 5.45 (m, 1 H, PC*H*NH), 5.90 (br, 1 H, N*H*), 7.16-7.40 (m, 9 H, Ar-*H*).

^{13}C NMR: δ 14.5, 17.3 (2 s, *C*H$_3$), 21.2 (Ar*C*H$_3$), 21.5 (CH$_2$*C*H$_3$), 36.5 (*C*(CH$_3$)$_2$), 52.4 (d, ^1J(P-C) = 154.0 Hz, P-*C*HNH), 61.6 (O*C*H$_2$CH$_3$), 75.7 and 75.8 (O*C*H$_2$), 84.6 and 84.8 (O*C*HPh), 127.4, 127.8, 128.0, 128.4, 129.4, 131.6, 135.7, 139.0, 138.2 (all Ar-*C*), 156.0 (NH*C*(O)).

^{31}P NMR: δ 19.3, 20.4 (3:1 ratio).

Anal. Calcd. for $C_{22}H_{28}O_5NP$: C, 63.31; H, 6.71; N, 3.35. Found: C, 63.75; H, 6.56; N, 3.25.

(OCH$_2$CMe$_2$CH(Ph)O)P(O)CH(NHCO$_2$Et)(C$_6$H$_4$-4-Cl) (22c)

Yield: 30% (using the same molar quantities as for **22a**)

Mp. 178-180°C.

IR (cm^{-1}): 3237, 1721, 1537, 1250, 1051.

^{1}H NMR (major isomer): δ 0.69, 0.76 (2 s, 6 H, 2 C*H*$_3$), 1.17 (t, ^3J = 4.0 Hz, 3 H, OCH$_2$C*H*$_3$), 3.78 (dd, $^{2,3}J$ = 12.0, 18.0 Hz, 2 H, OC*H*$_2$), 4.10 (m, 2 H, OC*H*$_2$CH$_3$), 4.34 (d, ^3J = 13.6 Hz, 1 H, PhC*H*OP) 5.35 (m, 1 H, PC*H*NH), 6.01 (br, 1 H, N*H*), 6.98-7.40 (m, 9 H, Ar-*H*).

^{13}C NMR: δ 14.5, 17.3 and 21.6 (3 s, *C*H$_3$), 36.5 (*C*(CH$_3$)$_2$), 52.1 (d, ^1J(P-C) ≈ 151.0 Hz, P-*C*HNH), 61.8 (O*C*H$_2$CH$_3$), 75.7 (s, O*C*H$_2$), 84.7 (d, ^2J(PC) =5.3 Hz, O*C*HPh), 127.1, 127.9, 128.5, 128.9, 129.2, 129.3, 134.5, 134.3, 135.3, 135.5 (all Ar-*C*), 155.7 (NH*C*(O)) (Figure 17).

^{31}P NMR: δ 18.5, 19.5 (1:8 ratio).

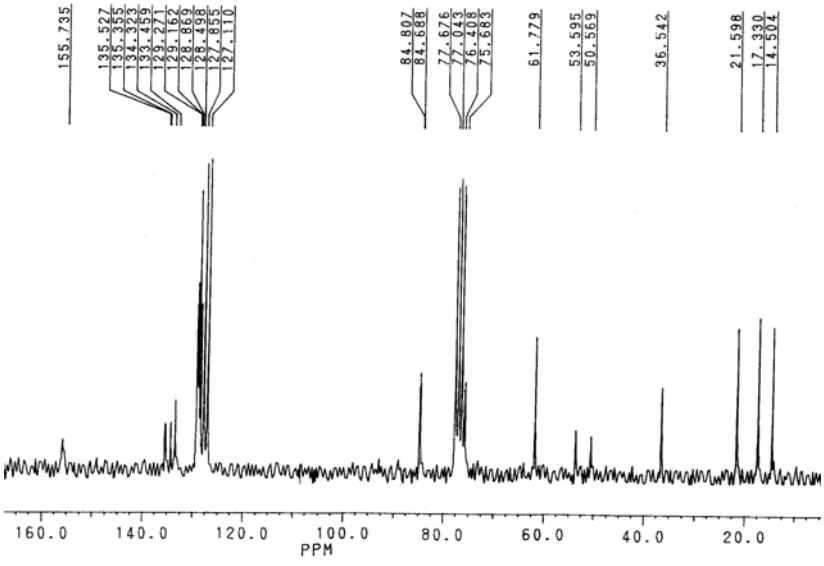


Figure 17. The ^{13}C NMR spectrum of **22c**.

($OCH_2CMe_2CH(C_6H_4$-3-Br$)O)P(O)CH(NHCO_2Et)(C_6H_5$) (22d)

Yield: 36% (using the same molar quantities as for **22a**)

Mp 198-200°C.

IR (cm^{-1}): 3258, 1753, 1228, 1066.

^{1}H NMR (1:1 mixture): δ 0.78, 0.81 (2 s, 6 H, 2 C*H*$_3$), 1.26 (m, 3 H, OCH_2CH_3), 3.83 (m, 2 H, O*CH*$_2$), 4.18 (m, 2 H, O*CH*$_2$CH$_3$), 4.46 (m, 1 H, PhC*H*OP) 5.40 (br m, 1 H, PC*H*NH), 5.88 (br, 1 H, N*H*), 7.00-7.51 (m, 9 H, Ar-*H*).

^{13}C NMR: δ 14.5, 17.2 and 21.5 (3 s, *C*H$_3$), 36.5 (*C*(CH$_3$)$_2$), 52.4 (d, ^1J(P-C) ≈ 149.0 Hz, P-*C*HNH), 61.8 (O*C*H$_2$CH$_3$), 75.5 (O*C*H$_2$), 83.7 (O*C*HPh), 122.2, 126.0, 127.9, 128.5, 128.8, 128.9, 129.4, 130.1, 130.3, 131.6, 134.6, 137.8, (all aromatic *C*), 155.7 (NH*C*(O)).

^{31}P NMR: δ 18.8, 20.3 (1.1 ratio).

($OCH_2CMe_2CH(C_6H_4$-3-Br$)O)P(O)CH(NHCO_2Et)(C_6H_4$-4-Me) (22e)

Yield: 32% (using the same molar quantities as for **22a**)

Mp: 190-192°C.

IR (cm^{-1}): 3237, 1719, 1534, 1244, 1049.

^{1}H NMR: δ 0.76, 0.84 (2 s, 6 H, 2 C*H*$_3$), 1.21 (t, ^3J = 6.8 Hz, 3 H, OCH_2CH_3), 2.35 (s, 3 H, ArC*H*$_3$), 3.83 (dd, $^{2,3}J$ = 12.0, 18.0 Hz, 2 H, O*CH*$_2$), 4.14 (m, 2 H, O*CH*$_2$CH$_3$), 4.49 (d, ^3J = 13.5 Hz, 1 H, PhC*H*OP), 5.41 (br, 1 H, PC*H*NH), 5.84 (br, 1 H, N*H*), 7.16-7.54 (m, 8 H, Ar-*H*).

^{13}C NMR: δ 14.4, 17.1, 21.1 and 21.3 (4 s, *C*H$_3$), 36.4 (*C*(CH$_3$)$_2$), 52.4 (d, ^1J(P-C) ≈ 155.0 Hz, P-*C*HNH), 61.6 (O*C*H$_2$CH$_3$), 75.4 (O*C*H$_2$), 83.7 (O*C*HPh), 122.0, 125.2, 125.9, 127.8, 128.1, 128.9, 129.3, 129.4, 130.2, 131.1, 131.4, 137.8, 138.3 (all aromatic *C*), 155.7 (NH*C*(O)).

^{31}P NMR: δ 19.0, 20.4 (8:1 ratio).

($OCH_2CMe_2CH(C_6H_4$-3-Br$)O)P(O)CH(NHCO_2Et)(C_6H_4$-4-Cl) (22f)

Yield: 32% (using the same molar quantities as for **22a**)

Mp. 180-182°C.

IR (cm^{-1}): 3256, 1705, 1539, 1244, 1043.

^{1}H NMR: δ 0.75, 0.85 (2 s, 6 H, 2 C*H*$_3$), 1.19 (br, 3 H, OCH$_2$C*H*$_3$) 3.78 (dd, $^{2,3}J$ = 12.0, 18.0 Hz, 2 H, OC*H*$_2$), 4.12 (m, 2 H, OC*H*$_2$CH$_3$), 4.42 (d, ^{3}J = 13.5 Hz, 1 H, PhC*H*OP), 5.35 (m, 1 H, PC*H*NH), 6.59 (br, 1 H, N*H*), 7.04-7.63 (m, 8 H, Ar-*H*). There were also peaks corresponding to the hydroxyphosphonate (see ^{31}P NMR).

^{13}C NMR: δ 14.2, 14.5 17.3, 21.0 and 21.3 (s each, *C*H$_3$), 36.5 (*C*(CH$_3$)$_2$), 52.2 (d, ^{1}J(P-C) ≈ 155.0 Hz, P-*C*HNH), 53.4, 61.8 (O*C*H$_2$CH$_3$), 75.7 (O*C*H$_2$), 84.0 (O*C*HPh), 122.2, 126.0, 129.0, 129.4, 130.2, 131.7, 133.1, 134.4, 137.8, 138.0 (all aromatic *C*), 155.9 (NH*C*(O)).

^{31}P NMR: δ 18.3, 19.7 (65% pure, the rest was the hydroxy phosphonate δ 13.0).

3.3 Utility of Chloro/ Bromophosphonates in HWE Reaction

3.31 Preparation of the chloro/bromo stilbenes and the acetylenes (23a-b, 24a, 25a-b)

For finding the best reaction conditions, several experiments using (OCH$_2$CMe$_2$CH$_2$O)P(O)CH(Cl)Ph (**10a**), and anisaldehyde (4-methoxybenzaldehyde) and different bases/ solvents (NaH, K$_2$CO$_3$, CsF, KF, diisopropylamine, THF, DMSO, acetonitrile and xylene) were conducted.

i) A solution of α-chlorophosphonate **10a** (0.50 g, 1.82 mmol) in THF (20 mL) was added rapidly to a slurry of NaH (0.11g, 60% dispersion, 2.73 mmol) in THF (20 mL) at 0°C, the mixture stirred for 30 min, and 4-methoxybenzaldehyde (0.25 g, 1.82 mmol) was added. After stirring at 0°C for 30 min, the mixture was brought to room temperature and stirred for 13 h. Then crushed ice was added, the product extracted with ether and chromatographed over silica gel using hexane followed by CH$_2$Cl$_2$ - hexane (1:5) to afford PhC(Cl)=C(C$_6$H$_4$-4-OMe) (**23a**; 0.44.g, 98%, *E*/*Z* 65:35).

ii) A solution of α-chlorophosphonate **10a** (0.50 g, 1.82 mmol) in THF (20 mL) was added rapidly to a slurry of NaH (0.11g, 60% dispersion, 2.73 mmol) and DMSO (0.60g 8.2 mmol) in THF (20 mL) at 0°C and 4-methoxybenzaldehyde (0.25 g, 1.82 mmol) in THF was added and stirring continued at 0°C for 8 h. Isolation of the product in a manner similar to procedure (i) afforded **23a** (0.29.g, 65%, *E*/*Z* 65:35).

iii) A solution of **10a** (0.50 g, 1.82 mmol) in DMSO (10 mL) was added rapidly to a slurry of sodium hydride (0.11g, 60% dispersion, 2.73 mmol) in DMSO

(10 mL) at 20°C and stirred for 30 min. 4-Methoxybenzaldehyde (0.25 g, 1.82 mmol) was added and the mixture stirred further for 9 h. Isolation of the product in a manner similar to procedure (i) afforded **23a** (0.05 g, 10% of olefin *E*/*Z* 75:25, 40% of alkyne **24a**).

iv) A solution **10a** (0.50 g, 1.82 mmol) in DMSO (10 mL) was added rapidly to a slurry of sodium hydride (0.11g, 60% dispersion, 2.73 mmol) in DMSO (10 mL) at 20°C and stirred for 30 min. 4-Methoxybenzaldehyde (0.25 g, 1.82 mmol) was added and the mixture stirred further at 75°C for 8 h. Isolation of the product in a manner similar to procedure (i) afforded **24a** (0.24g, 53% alkyne).

$C_6H_5C{\equiv}CC_6H_4$-4-OMe (24a)

Yield: 53%.

Mp: 56-58^oC

IR (cm^{-1}): 2216 (ν(C≡C).

^1H NMR: 3.80 (s, 3 H, C*H*$_3$), 6.80-7.60 (m, 9 H, Ar*H*)

^{13}C NMR: 55.3, 88.3, 89.7, 114.2, 115.5, 123.8, 128.0, 128.5, 131.6, 133.2, 159.8.

Anal. Calcd. for $C_{15}H_{12}O$: C, 86.50; H, 5.80. Found; C, 86.55; H, 5.85.

This is a known compound, but the ^{13}C NMR is not available.[123a]

Compound **24b** was prepared in similarly using **10b** and anisaldehyde using the same molar quantities.

CH_3-4-C_6H_4-C≡CC_6H_4-4-OMe (24b)

Yield: 55%.

IR (cm^{-1}): 2219 (ν(C≡C).

Mp: 121-123^oC.

^1H NMR: 2.40, 3.84 (2s, 6 H, C*H*$_3$ + OC*H*$_3$), 6.82-7.63 (m, 8 H, Ar*H*).

^{13}C NMR: 21.4, 55.3, 88.2, 89.7, 114.2, 115.7, 120.7, 129.1, 131.4, 133.0, 138.0, 159.8.

This is also a known compound, but the ^{13}C NMR is not available.[123b]

v) To a mixture of **10a** (0.50 g, 1.82 mmol) and anh. CsF (0.82 g, 5.46 mmol) in acetonitrile (20 mL) was added 4-methoxybenzaldehyde (0.25 g, 1.82 mmol) and the mixture heated under reflux for 3 d. Isolation of the product in a manner similar to procedure (i) afforded **23a** (0.22 g, 52%, *E*/*Z* 40:60).

vi) To a mixture of **10a** (0.50 g, 1.82 mmol) and anh. K_2CO_3 (0.75 g, 5.43 mmol) in acetonitrile (20 mL) was added 4-methoxybenzaldehyde (0.25 g, 1.82 mmol) and the mixture heated under reflux for 3 d. Isolation of the product in a manner similar to procedure (i) afforded **23a** (0.37 g, 83%, *E*/*Z* 55:45).

vii) To a mixture of the α-bromophosphonate **11b** (0.50 g, 1.57 mmol) and anhydrous K_2CO_3 (0.65 g, 470 mmol) in acetonitrile (20 mL) was added 4-methoxybenzaldehyde (0.25 g, 1.82 mmol) and the mixture heated under reflux for 3 d. Isolation of the product is same as procedure (i) to afford **25b** (0.21g, 50%, E/Z 50:50).

(viii) The reaction using K_2CO_3/xylene offered the best results; details are given below.

3.32 Preparation of the chloro/bromo stilbenes (23a-g and 25a-d)

Typical procedure for Ph(Cl)C=C(H)C_6H_4-4-OMe (23a)

To a mixture of **10a** (0.50 g, 1.82 mmol) and anhydrous K_2CO_3 (0.75 g, 5.43 mmol) in xylene (5 mL) at 20°C was added 4-methoxybenzaldehyde (0.25 g, 1.82 mmol) and the mixture heated under reflux for 24 h. Then, xylene was removed, water (25 mL) added, and the mixture extracted with ether (3 × 20 mL). The organic layer was dried (Na_2SO_4), solvent removed, and the residue chromatographed over silica gel (3% CH_2Cl_2 in hexane) to afford **23a** (liquid).

Yield: 0.40 g, 90%.

IR (cm^{-1}): 908, 1033, 1113, 1252, 1510, 1606.

^{1}H NMR: 3.76, 3.86 (2 s, ratio 2:3, 3 H, OC*H*$_3$), 6.70-7.90 (m, 10 H, Ar*H*, C=C*H*).

^{13}C NMR: δ 55.2, 55.3, 113.8, 125.7, 126.7, 128.0, 128.5, 128.6, 128.8, 129.3, 130.1, 131.1, 138.2 and 139.7 *(ipso* carbon at (Ar)(Cl)C=, ratio 2:3, *Z* and *E*-isomers respectively), 159.0, 159.5.

MS: 244, 246 $[M]^+$(^{35,37}Cl), 208, 165.

Anal. Calcd. for $C_{15}H_{13}ClO$: C, 73.60; H, 5.36. Found; C, 73.38; H, 5.45.

Data for the other compounds **23b-g** and **25a-d** prepared similarly, are given below.

(4-Me-C_6H_4)(Cl)C=C(H)C_6H_5 (23b) (liquid)

Yield: 88% (liquid; using 1.80 mmol of **10b**)

IR (cm^{-1}): 927, 1030, 1076, 1508, 1606.

^{1}H NMR: δ 2.30, 2.36 (2 s, ratio 3:2, 3 H, C*H*$_3$), 6.85-7.85 (m, 10 H, Ar*H*, C=C*H*).

^{13}C NMR: δ 21.2, 21.4, 125.3, 126.7, 127.3, 127.9, 128.3, 128.6, 128.8, 129.2 129.3, 129.5, 132.3, 132.4, 134.9, 135.5, 135.6, 136.6, 138.8 (*Z*), 138.9(*E*).

Anal. Calcd. for $C_{15}H_{13}Cl$: C, 78.70; H, 5.70. Found; C, 78.68; H, 5.71.

Ph(Cl)C=C(H)C_6H_4-4-Me (23c) (liquid)

Yield: 97% (E:Z 65:35; using 1.82 mmol of **10a**).

IR(cm^{-1}): 947, 1032, 1074, 1510, 1597.

^{1}H NMR: δ 2.30, 2.45 (2 s, ratio 2:3, 3 H, C*H*$_3$), 6.80-7.85 (m, 10 H, Ar*H* + C=C*H*).

^{13}C NMR: δ 21.1, 21.3, 125.8, 126.1, 126.7, 128.4, 128.6, 128.8, 129.0, 129.3, 131.4, 132.3, 132.6, 137.3, 138.0 (*Z*), 139.6 (*E*).

Anal. Calcd. for $C_{15}H_{13}Cl$: C, 78.70; H, 5.70. Found; C, 78.46; H, 5.26.

(4-Me-C_6H_4)(Cl)C=C(H)C_6H_4-4-Cl (23d)

Yield: 81% (E:Z 50:50; using 1.80 mmol of **10b**)

M.p: 56-58°C.

IR (cm^{-1}): 914, 1010, 1086, 1487, 1618.

^{1}H NMR: δ 2.37, 2.39 (2 s, ratio 1:1, 3 H, C*H*$_3$), 6.80-7.80 (m, 9 H, Ar*H* + C=C*H*).

^{13}C NMR: δ 21.1, 21.2, 124.0, 126.6, 127.2, 128.4, 129.0, 129.3, 129.9, 130.7, 133.0, 134.1, 139.0 (*Z* + *E*).

MS: 262, 264, 266 $[M]^+$ (^{35,37}Cl), 227, 192.

Anal. Calcd. for $C_{15}H_{12}Cl_2$: C, 68.46; H, 4.59. Found; C, 68.73; H, 4.80.

(4-MeO-C_6H_4)(Cl)C=C(H)C_6H_4-4-Cl (23e) (liquid)

Yield: 89% (E:Z 30:70; using 1.79 mmol of **10d**)

IR (cm^{-1}): 1030, 1086, 1138, 1250, 1510, 1605.

^{1}H NMR: δ 3.80, 3.82 (2 s, ratio 7:3, 3 H, OC*H*$_3$), 6.80-7.80 (m, 9 H, Ar*H* + C=C*H*).

^{13}C NMR: δ 55.3, 114.0, 128.6, 128.7, 131.8, 132.6, 133.0.

Anal. Calcd. for $C_{15}H_{12}Cl_2O$: C, 64.50; H, 4.30. Found; C, 64.23; H, 4.37.

(4-MeO-C$_6$H$_4$)(Cl)C=C(H)C$_6$H$_4$-4-Me (23f) (liquid)

Yield: 90% (E:Z 35:65; using 1.79 mmol of **10d**)

IR (cm^{-1}): 1116, 1172, 1284, 1508, 1610 cm^{-1}).

^{1}H NMR: 2.38, 2.39 (2 s, 3 H, 2 C-C*H*$_3$), 3.83, 3.86 (2 s, 3 H, 2 OC*H*$_3$), 6.80-7.70 (m, 9 H, Ar(*H*) + C*H*=CCl).

^{13}C NMR: 21.2, 21.3 (2 C-*C*H$_3$), 55.3, 55.4 (2 O*C*H$_3$), 113.8, 113.9, 124.5, 128.0, 128.6, 129.0, 129.3, 130.0, 130.2, 130.6, 131.1, 132.1, 132.7, 137.7, 160.0 (Ar(*C*) + *C*H=CCl).

MS: 258 (M$^+$) & 260 (M$^+$), 223, 208, 179, 178, 165, 152, 135, 115, 89, 77, 63, 39.

(4-Me-C$_6$H$_4$)(Cl)C=C(H)Ph (23g) (liquid)

Yield: 92% (E:Z 50:50; using 1.78 mmol of **10b**)

IR (cm^{-1}): 927, 1030, 1111, 1257, 1510, 1601.

^{1}H NMR: δ 0.80, 3.85 (2 s, 1:1, 3 H, C*H*$_3$), 6.85-7.85 (m, 10 H, Ar*H* + C=C*H*).

^{13}C NMR: δ 55.4, 113.7, 113.9, 116.2, 120.2, 124.4, 127.2, 127.7, 128.0, 128.2, 128.7, 129.3, 130.6, 131.9, 132.5, 135.6, 138.1, 140.7, 141.9, 141.9, 144.6, 149.7.

Anal. Calcd. for $C_{15}H_{13}ClO$: C, 73.60; H, 5.36. Found; C, 73.51; H, 5.30.

Ph(Br)C=C(H)C$_6$H$_4$-4-OMe (25a) (liquid)

Yield: 65% (60:40; using 1.68 mmol of **11a**)

IR (cm^{-1}): 966, 1030, 1109, 1249, 1510, 1605.

^{1}H NMR: δ 3.75, 3.85 (2 s, ratio 2:3, 3 H, OC*H*$_3$), 6.65-7.80 (m, 10 H, Ar*H* + C=C*H*).

^{13}C NMR: δ 55.2, 55.3, 113.7, 121.1, 122.1, 127.8, 128.3, 128.7, 129.3, 129.5, 130.0, 130.8, 132.6, 139.8 (*Z*), 141.4 (*E*), 159.5.

MS: 290, 288 [M]$^+$ (^{79,81}Br), 209.

Anal. Calcd. for $C_{15}H_{13}BrO$: C, 62.30; H, 4.50. Found; C, 62.60; H, 4.40.

4-Me-C_6H_4(Br)C=C(H)Ph (25b) (liquid)

Yield: 52% (30:70; using 1.67 mmol of **11b**)

IR (cm^{-1}): 814, 903, 1014, 1095, 1510, 1606.

^{1}H NMR: δ 2.35, 2.40 (2 s, ratio 3:7, 3 H, Ar-CH_3), 7.00-7.80 (m, 10 H, Ar*H* + C=C*H*).

^{13}C NMR: δ 21.1, 21.3, 124.3, 127.4, 127.7, 127.9, 128.2, 128.7, 129.0, 129.2, 131.6, 132.7, 136.5, 138.3 (*Z*), 138.8 (*E*).

MS: 290, 288 $[M]^+$ (^{79,81}Br), 209, 165.

Anal. Calcd. for $C_{15}H_{13}Br$: C, 65.90; H, 4.79. Found; C, 66.31; H, 4.95.

4-Me-C_6H_4(Br)C=C(H)C_6H_4-4-Cl (25c) (liquid)

Yield: 73% (60:40; using 1.67 mmol of **11b**).

IR (cm^{-1}): 903, 1009, 1086, 1487, 1608.

^{1}H NMR: δ 2.35, 2.40, (2 s with ratio 2:3, 3 H, Ar-CH_3), 6.90-7.70 (m, 9 H, Ar*H* + C=C*H*).

^{13}C NMR: δ 20.9, 21.1, 127.6, 128.4, 129.0, 129.4, 129.8, 130.5, 138.2 (*Z*), 138.8 (*E*).

MS: 310, 308, 306 $[M]^+$ (^{79,81}Br; ^{35,37}Cl), 229, 227 $[M\text{-}Br]^+$, 192 [M-Br-Cl]. Anal. Calcd. for $C_{15}H_{12}BrCl$: C, 58.59; H, 3.92. Found; C, 58.43; H, 4.07.

4-Me-C_6H_4(Br)C=C(H)C_6H_4-4-OMe (25d) (liquid)

Yield: 69% (50:50; using 1.67 mmol of **11b**).

IR (cm^{-1}): 905, 1024, 1252, 1510, 1608 cm^{-1}.

^{1}H NMR: δ 2.40, 2.42 (2 s, ratio 1:1, 3 H, Ar-CH_3), 3.77, 3.87 (2s, 3 H, OCH_3), 6.69-7.80 (m, 9 H, Ar*H* + C*H*=CBr).

^{13}C NMR: δ 21.2, 21.3 (2C-*C*H_3), 55.2, 55.3 (2s, O*C*H_3), 113.7, 121.5, 122.3, 127.7, 128.7, 129.0, 129.1, 129.3, 129.4, 130.0, 130.8, 132.2, 133.0, 136.9, 138.5 (*Z*), 138.6 (*E*), 138.7, 158.9, 159.4 (Ar*C* + *C*H=*C*Br) (Figure 18, next page).

MS: 302, 304 $[M]^+$(^{79,81}Br), 223, 179, 178, 165, 115.

Anal. Calcd. for $C_{16}H_{15}BrO$: C, 63.34; H, 4.90. Found; C, 63.42; H, 4.99.

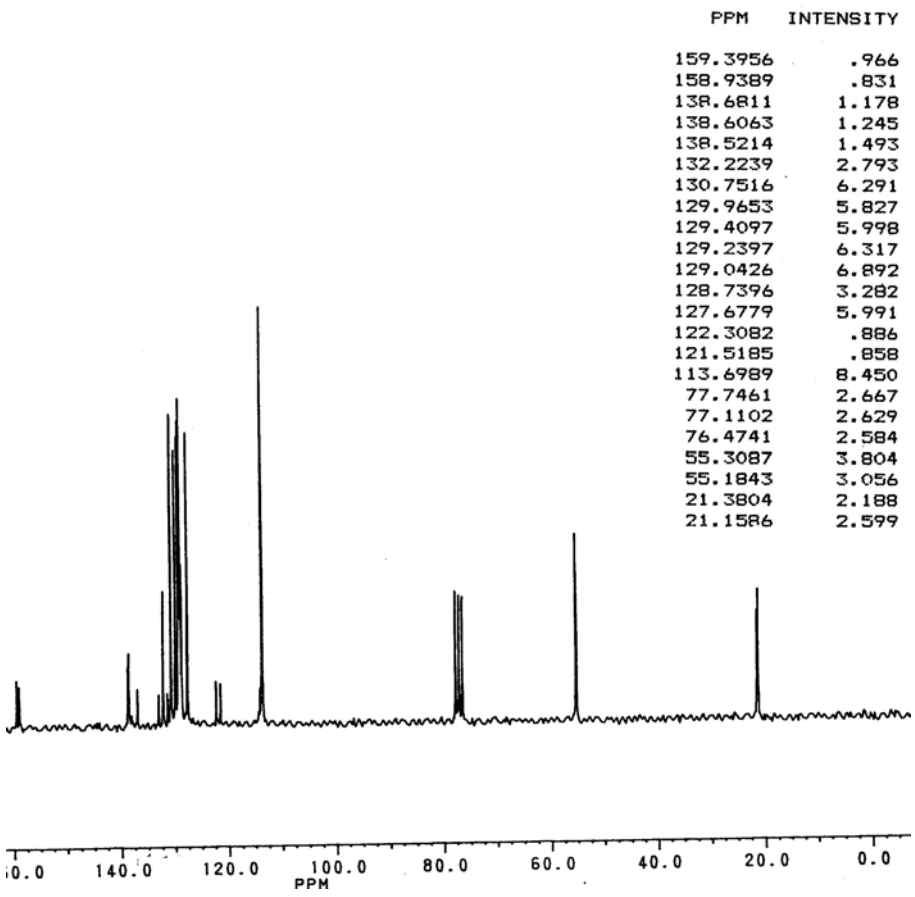


Figure 18. The ^{13}C NMR spectrum of **25d**

3.33 Synthesis of the chloro-dienes 26a-26f

Typical procedure for (2,4-Cl_2-C_6H_3)(H)C=C(H)-C(H)=C(Cl)Ph (26a)

A mixture of **12a** (0.50 g, 1.66 mmol), 2,4-dichlorobenzaldehyde (0.29 g, 1.66 mmol) and K_2CO_3 (0.68 g, 4.90 mmol) in xylene (10 mL) was heated under reflux for 24 h. After removal of xylene, water (10 mL) was added and the mixture extracted with ether (3 x 25 mL), washed with water (2 x 15 mL), dried (Na_2SO_4) and the solvent evaporated to get a semisolid which was purified by column chromatography (silica gel, hexane) to obtain **26a.**

Yield: 0.49 g (95%).

Mp: 129-131°C.

^1H NMR: δ 6.98 (d, ^3J(HH) = 9.3 Hz, 1 H, (Ph)ClC=C*H*), 7.11 (d, ^3J(HH) = 17.0 Hz, 1 H, Ar-C*H*=CH), 7.20-7.80 (m, 9 H, Ar-*H* + CH=C*H*-CH=).

^{13}C NMR: δ 121.2, 125.5, 126.4, 126.5, 127.0, 127.3, 127.7, 128.5, 129.0, 129.9, 131.7.

Anal. Calcd for $C_{16}H_{11}Cl_3$: C, 62.06; H, 3.58. Found: C, 62.00; H, 3.60.

(4-O_2N-C_6H_4)(H)C=C(H)-C(H)=C(Cl)Ph (26b)

Yield: 0.46 g (97%).

Mp: 158-160^{o}C.

^{1}H NMR: δ 6.83 (d, ^3J(H-H) = 15.6 Hz, 1 H, ArC*H*=CH), 6.97 (d, ^3J(H-H) = 15.6 Hz, 1 H, PhC*H*=CH), 7.30-8.30 (m 10 H, Phenyl-*H* + Ar-*H* +CH=C*H*-CH=).

^{13}C NMR: δ 124.1, 125.0, 127.1, 128.5, 129.3, 132.7, 136.1, 137.3, 143.4, 147.1.

Anal. Calcd. for $C_{16}H_{12}ClNO_2$: C,67.26; H, 4.24, N,4.90. Found: C, 67.28; H, 4.24; N, 4.94.

4-OMe-C_6H_4(H)C=C(H)-C(H)=C(Cl)Ph (26c)

Yield: 0.42 g (93%).

Mp: 135-137^{o}C.

^{1}H NMR: δ 3.85(s, 3 H, OC*H*$_3$), 6.76 (d, ^3J(H-H) = 18.0 Hz, 1 H, ArC*H*=CH), 6.90-7.00 (m 3 H, Ar-*H*.+Ph(Cl)C=C*H*), 7.20-7.80 (m 8 H, Ar-*H*.+ CH=C*H*-CH=).

^{13}C NMR: δ 55.3, 114.3, 123.1, 126.7, 128.1, 128.4, 135.3, 139.0.

Anal. Calcd. for $C_{17}H_{15}ClO$: C, 75.40; H, 5.59. Found: C, 74.84; H, 5.59.

(1-Naphthyl)(H)C=C(H)-C(H)=C(Cl)Ph (26d) (liquid)

Yield: 0.45 g (93%); liquid.

^{1}H NMR: δ 7.13-8.27 (m).

13C NMR: δ 122.6, 123.6, 124.1, 125.1, 125.9, 126.0, 126.6, 127.8, 128.5, 128.7, 131.9, 133.8, 134.5, 138.0.

Anal. Calcd. for $C_{20}H_{15}Cl$: C, 82.60; H, 5.19. Found: C, 82.45; H, 5.13.

4-Cl-C_6H_4(H)C=C(H)-C(H)=C(Cl)Ph (26e)

Yield: 0.44 g (96%).

Mp: 142-144 ^{o}C.

^{1}H NMR: δ 6.74 (d, ^3J(H-H) = 18.0 Hz, 1 H, ArC*H*=CH), 6.92 (d, ^3J(H-H) = 10.3 Hz, 1 H, Ph(Cl)C=C*H*), 7.30-7.70 (m 10 H, Ar-*H*.+ CH=C*H*-CH=).

^{13}C NMR: δ 125.6, 126.3, 127.9, 128.4, 128.8, 128.9, 133.6, 133.8, 134.1, 135.6, 137.6.

Anal. Calcd. for $C_{16}H_{12}Cl_2$: C, 69.84; H, 4.36. Found: C, 69.60.; H, 4.32.

4-Me-C_6H_4(H)C=C(H)-C(H)=C(Cl)Ph (26f)

Yield: 0.36 g (85%).

Mp: 112-114 ^{o}C.

^{1}H NMR: δ 2.40(s, 3 H, C*H*$_3$), 6.75 (d, ^{3}J(H-H) = 18.0 Hz, 1 H, ArC*H*=CH), 6.90 (d, ^{3}J(H-H) = 10.5 Hz, 1 H, ArC*H*=CH), 7.10-7.70 (m 10 H, Ar-*H*.+ Ph(Cl)C=C*H*-).

^{13}C NMR: δ 24.4, 124.2, 126.2, 126.3, 126.8.1, 128.5, 128.6, 129.5, 132.3, 134.4, 135.8, 137.9, 138.3

Anal. Calcd. for $C_{17}H_{15}Cl$: C, 80.17; H, 5.89. Found: C, 80.00; H, 5.78.

3.4 Reaction of Chlorophosphate Esters with Organic Bases

(a) Synthesis of [S(6-t-Bu-4-Me-$C_6H_2O)_2$P(O)(DBU)]$^{+}$[Cl]$^{-}$ (27)

To a stirred solution of S(6-*t*-Bu-4-Me-$C_6H_2O)_2$]P(O)Cl[99] (**6a**) (0.84 g, 1.90 mmol) in toluene (20 mL) was added DBU (0.29 g, 1.90 mmol) drop-wise over a period of 10 min at room temperature. After stirring overnight (the reaction mixture also showed peaks at δ –12.8 (10%) and –22.0 (5%) in the ^{31}P NMR), most of the solvent was removed in *vacuo* and compound **27** crystallized from dichloromethane – heptane (2:1) mixture.

Yield: 0.5 g (45%).

Mp: 210˚C.

IR (KBr): 3410, 3198, 2955, 1641, 1427, 1265, 1224 cm^{-1}.

^{1}H NMR: δ 1.35, 1.46 (2 s, 18 H, Ar-C(C*H*$_3$)$_3$), 1.90-2.00 (m, 8 H, C*H*$_2$), 2.27, 2.31 (2 s, 6 H, ArC*H*$_3$), 3.40-3.60 (m, 6 H, NC*H*$_2$), 7.12-7.48 (m, 4 H, Ar-*H*), 11.3 (br, 1 H, N*H*).

^{13}C NMR: δ 19.2, 19.5, 20.7, 20.7, 20.9, 21.4, 24.0, 24.5, 25.1, 26.4,26.8, 29.5, 29.9, 35.0, 35.1, 38.5, 44.3 [^{1}J(P-C) = 130.9 Hz], 50.4, 53.5, 53.8, 124.4, 125.1, 125.2, 128.1, 128.9, 129.6, 130.2, 134.7, 135.1, 135.3, 148.7, 148.9, 149.5, 149.6, 160.6.

^{31}P NMR: δ 6.4.

Anal. calcd for $C_{30}H_{44}ClN_2O_3PS$ (after drying): C, 62.22; H, 7.61; N, 4.84. Found: C, 61.95; H, 7.38; N, 4.62.

(b) Compound $[CH_2(6\text{-t-Bu-4-Me-}C_6H_2O)_2P(O)(DBU)]^+[Cl]^-$ (28)

The compound **28** [Mp: 220°C] was prepared in a manner similar to that given for **27** using **6b**; its ^1H and ^{31}P NMR [δ 7.2] were identical to the one we have reported before.[95]

(c) Compound $[(2,2'\text{-}C_{20}H_{12}O_2)P(O)(DBU)]^+[Cl]^-$ (29)

The reaction of $(2,2'\text{-}C_{20}H_{12}O_2)P(O)Cl$ (**7**, racemic)[120] with DBU was conducted in THF, because of low solubility of **7** in toluene. The ^{31}P NMR spectrum showed three peaks at δ 5.3 (25 %), 29.2 (30%) and 30.4 (40%) [rest ~ 5%]. The peaks at δ 29.2 and 30.4 are assigned to the diasteromeric phosphonate salts $[(2,2'\text{-}C_{20}H_{12}O_2)P(O)(DBU)]^+[Cl]^-$ (**29**) by comparing them with those for the analogous aminophosphonate $(+)\text{-}(C_{20}H_{12}O_2)P(O)CHNHCO_2Et)Ph$ [δ(P) 29.5][106]. A white solid with δ(P) 5.3 (>95%), that showed only the binol and DBU residues, was isolated in the reaction of **7** with DBU in the presence of $(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_6H_4\text{-}OCMe)$. This solid could not be purified further, but is likely to be the phosphate salt $(2,2'\text{-}C_{20}H_{12}O_2)P(O)(O^-)[HDBU^+]$ formed by hydrolysis [^1H NMR shows a peak at δ 10.9; ^{13}C NMR: complicated, but no doublet due to $^1J(PC)$ is observed].

(d) Reaction of $S(6\text{-t-Bu-4-Me-}C_6H_2O)_2P(O)Cl$ (6a) with DBN- Preparation of the pyrophosphate ester $[S(6\text{-t-Bu-4-Me-}C_6H_2O)_2P(O)]_2O$ (30)

To a stirred solution of **6a**[99] (0.85 g, 1.94 mmol) in toluene (20 mL) was added DBN (0.24 g, 1.94 mmol) drop-wise over a period of 10 min at room temperature. After stirring overnight the solvent was removed *in vacuo* and the compound crystallized from dichloromethane – heptane (2:1) mixture. In this reaction we got the crystals of the pyrophosphate **[**$S\{6\text{-}t\text{-Bu-4-Me-}C_6H_2O\}_2P(O)]_2O$ (**30**) but not of the expected compound.

Mp: 226-228°C.

IR (KBr): 2961, 2359, 1593, 1429, 1319, 1222 cm^{-1}.

^1H NMR: δ 1.39 and 1.46 (s each, 36 H, Ar-C(CH_3)$_3$), 2.29 (2 s, 12 H, ArCH_3), 7.20,7.25 (2 s, 8 H, Ar-*H*).

^{13}C NMR: δ 20.8 (s, Ar*C*H$_3$), 30.3 (Ar-C(*C*H$_3$)$_3$), 35.1 (Ar-*C*(CH$_3$)$_3$), 124.7, 129.9, 134.2, 135.0, 141.6, 150.0.

^{31}P NMR: δ –31.1.

Anal. calcd for $C_{44}H_{56}O_5P_2S_2$ (after drying): C, 66.84; H, 7.09. Found: C, 66.95, H, 6.98.

A reaction using N-methyl imidazole also resulted in the isolation of **30**.

The reactions of **6b** and **7** with DBN and N-methyl imidazole were done similarly, but in the latter case, THF was used as the solvent. ^{31}P NMR (major peaks, δ): (**a**) **6b** + DBN: -9.8 (46%), 0.1 (47%); (**b**) **6b** + N-methyl imidazole: -2.3 (65%), -9.8 (15%), -27.6 (20%); (**c**) **7** + DBN: -12.4 (30%), 3.2 (30%) and 14.8 (30%); (**d**) **7** + N-methyl imidazole: -12.4 (70%), 6.1 (28%). The peak at δ –27.6 in (**b**) is due to the pyrophosphate ester [CH$_2$(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$P(O)]$_2$O (**31**) and could be isolated in ca 40% yield [Mp 276^{o}C; ^{1}H NMR: Identical to that reported before;[95] ^{13}C NMR δ 20.9, 30.9, 34.6, 35.0, 127.7, 129.4, 131.4, 135.2, 141.3, 146.0. Anal. Calcd for $C_{46}H_{60}O_7P$: C, 70.23; H, 7.63. Found: C, 70.43, H, 7.81]. The peak at –12.4 in (**c**) and (**d**) is also assignable to the pyrophosphate ester [(2,2'-$C_{20}H_{16}O_2$)P(O)]$_2$O (**32**) on the same basis, but this compound was hydrolytically unstable [NMR evidence].

3.5 X-ray Crystallography

X-ray data were collected on a Bruker AXS SMART diffractometer (for **15, 20c, 27** and **30**) or an Enraf-Nonius-MACH3 (for **12a, 26f, 31**; up-to 2θ = 45) using Mo-K$_\alpha$ (λ = 0.71073 Å) radiation. The structures were solved by direct methods;[124] all non-hydrogen atoms were refined anisotropically. For the hydrogen atoms except the NH in **27**, the riding model was used; one of the solvent hydrogen atoms in **27** was not fixed because of symmetry. In **31** although there is a void and some residual electron density in the crystal packing, we could not model it with any suitable solvent. For this compound, the crystal data before had been given before,[95, 112] but the refinement could be improved and hence structure is better now; other details are discussed in a previous work and hence not given here. The data was not good because of the poor crystal quality. The crystal data are given in Tables 3-4.

Table 3. Crystal data for **12a, 15** and **20c**.

Compound	**12a**	**15**	**20c**
Emp. formula	$C_{14}H_{18}ClO_3P$	$C_{26}H_{33}Cl_3O_6P_2$	$C_{24}H_{24}Cl_2O_7P_2$
Formula weight	300.70	609.81	557.27
Crystal system	Orthorhombic	triclinic	Monoclinic
Space group	Pbca	$P\bar{1}$	$P2_1/c$
a /Å	8.7813(18)	11.5775(18)	14.3838(10)
b /Å	10.294(7)	11.6473(18)	11.4745(8)
c /Å	33.362(10)	12.4340(19)	16.1579(11)
α/deg	90.00	70.433(2)	90.00
β/deg	90.00	68.122(2)	106.262(1)
γ/deg	90.00	82.162(2)	90.00
V /Å^3	3016(2)	1465.9(4)	2560.1(3)
Z	8	2	5
D_{calc} /g cm^{-3}]	1.325	1.382	1.446
μ /mm^{-1}	0.360	0.460	0.421
F(000)	1264	636	1152
Crystal size [mm]	0.3 x 0.2 x 0.1	0.3 x 0.2 x 0.2	0.3 x 0.2 x 0.2
2θ max.	50	56	50
Observed reflections (I>2σ(I))	1388	5761	5107
Data/ restraints/ parameters	2644/0/174	6813/0/ 350	6127/0/ 318
S	1.076	1.011	1.040
R1 [I>2σ(I)]	0.0680	0.0523	0.0446
wR2 [all data]	0.1163	0.1569	0.0527
Max./min. residual electron dens. [eÅ^{-3}]	0.592/-0.373	0.507/ -0.553	0.465/-0.699

Table 3. Crystal data for **26f, 27** and **30**.

Compound	**26f**	**27**	**30**
Emp. formula	$C_{16}H_{11}Cl_3$	$C_{71}H_{100}Cl_6N_4O_6P_2S_2$	$C_{45}H_{58}Cl_2O_7P_2S_2$
Formula weight	309.60	1444.30	907.87
Crystal system	Monoclinic	triclinic	monoclinic
Space group	$P2_1/c$	$P\bar{1}$	$P2/n.$
a /Å	7.4728(15)	9.521(1)	12.509(1)
b /Å	11.6161(16)	14.310(1)	9.449(1)
c /Å	16.270(3)	14.533(1)	20.606(2),
α/deg	90.00	93.432(1)	90.00
β/deg	95.947(14)	92.521(1)	91.003(1),
γ/deg	90.00	98.959(1)	90.00
V /Å^3	1404.7(4)	1949.6(2)	2435.2(3)
Z	4	1	2
D_{calc} /g cm^{-3}]	1.464	1.230	1.238
μ /mm^{-1}	0.634	0.364	0.330
F(000)	632	766	960
2θ max.	50	56	56
Observed reflections (I>2σ(I))	2125	5058	4320
Data/ restraints/ parameters	2459/0/172	9130/ 5 / 427	5852 / 3 / 276
S	1.198	0.981	1.038
R1 [I>2σ(I)]	0.0312	0.0535	0.0590
wR2 [all data]	0.0360	0.1714	0.1922
Max./min. residual electron dens. [eÅ^{-3}]	0.200/-0.306	0.547 / -0.403	0.510/ -0.411

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PART B

OXIDATIVE ADDITION OF DIALKYL AZODICARBOXYLATES/ *o*-CHLORANIL TO CYCLODIPHOSPH(III)AZANES - IMPLICATIONS FOR THE MITSUNOBU REACTION

CHAPTER 4

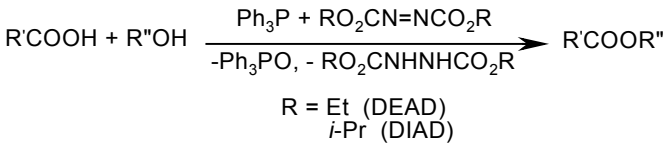
INTRODUCTION

In this chapter, relevant literature on the reactions of phosphorus (III) compounds with dialkyl azodicarboxylates (in the context of Mitsunobu reaction) is reviewed; this will be followed by a short survey of the chemistry of cyclodiphosph(III)azanes since these compounds are used in the present study.

4.1 Reactions of phosphorus (III) compounds with dialkyl azodicarboxylates

The triphenylphosphine (TPP)/ diethyl azodicarboxylate (DEAD) or diisopropyl azodicarboxylate (DIAD) mediated esterification of an acid with inversion of configuration for asymmetric alcohols, known as the Mitsunobu reaction, has proven useful in a wide variety of synthetic applications. This reaction has been subjected to considerable mechanistic scrutiny in recent years (Scheme 4.1).[1]

Scheme 4.1



Mechanistic discernment of the Mitsunobu reaction with respect to the initial redox chemistry has received substantial documentation.[2] Several other key features of this important reaction have been investigated by various groups.[3-5] The reaction is believed to proceed through the following steps (Scheme 4.2).[1a]

(a) Addition of phosphorus(III) compounds to DEAD/ DIAD to lead to the Morrison-Brunn-Huisgen intermediate **I**,

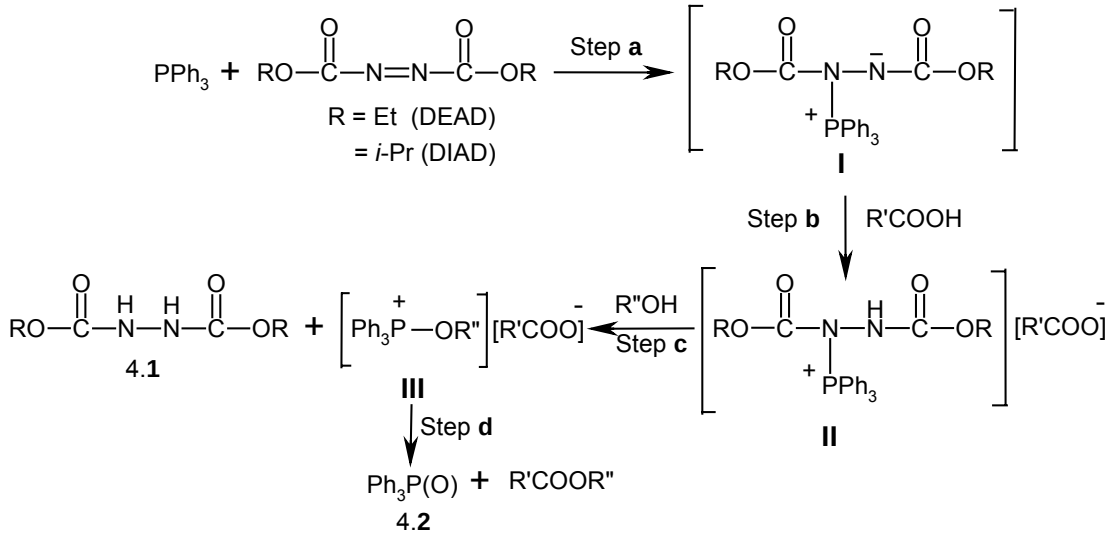
(b) Protonation of **I** to lead to **II**,

(c) Formation of the alkoxy phosphonium salt **III** and

(d) S_N2 Displacement of R'COOR" from **III**.

Details of these steps are discussed below.

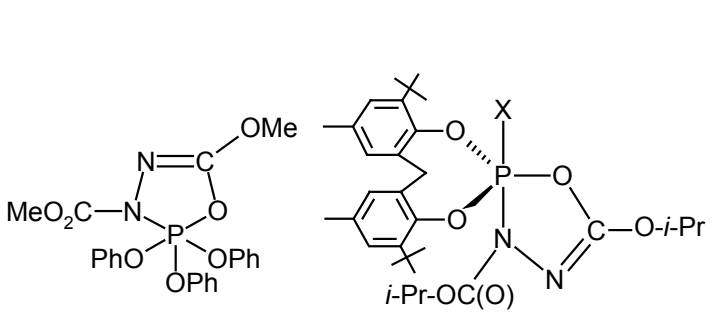
Scheme 4.2



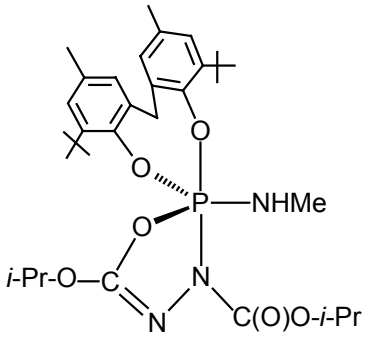
a) ***Addition of phosphorus(III) compounds to DEAD/ DIAD***

In earlier literature, Morrison reported that Michael type nucleophilic addition reaction of PPh_3 and DEAD/ DIAD leads to the formation of betaine **I**.[6] 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**.[7] This step is of primary interest in the present work.

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**.[8-13] Arbuzov *et al* reported that triphenyl phosphite reacts with dimethyl azodicarboxylate via N-O cycloaddition to give the pentacoordinate phosphorus compound 4.**3**.[8a] Later, Gonclaves *et al* prepared a series of pentacoordinate phosphoranes derived from the reaction of DEAD with various phosphites. The first structural characterization of many such pentacoordinate compounds (e.g. 4.**4**-4.**6**) was done from our laboratory.[14]



4.**3** X = N_3 [4.**4**, δ(P) -61.0, -69.7 (1:1)]
NCS [4.**5**, δ(P) -67.3]



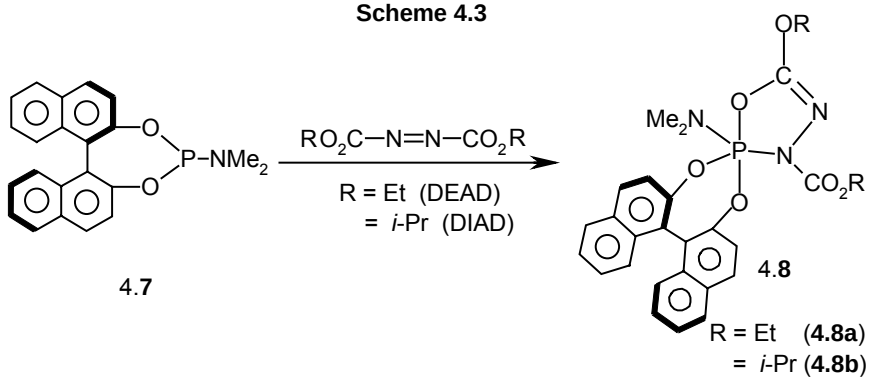
4.**6** [δ(P) -61.0, -61.7 (1:3)]

Various groups have monitored the progress of Mitsunobu esterification by ^{31}P NMR, and have strongly supported formation of the betaine **I.**[1,10] EPR spectroscopy suggests that formation of the betaine **I** can also occur through radical cations of type RO_2C-N-(Ph_3P^+)-$N^{\bullet}$-CO_2R.[12] Additionally, it is noted that treatment of DIAD with tributylphosphine gives a much weaker EPR signal relative to that with triphenylphosphine, while a much more intense signal could be detected in the reaction of DIAD with tris(dimethylamino)phosphine. As regards the esterification using PPh_3/ DIAD, it is reported that when the acid is added last, or when a large excess of azodicarboxylate and triphenylphosphine are used, radicals are certainly generated prior to the formation of the betaine **1**.[15]

The use of tri-*n*-butyl phosphine in place of the triphenyl phosphine offers different results in the coupling reaction of N-hydroxyphthalimide and 2,3,4,6-tetra-*O*-acetylglucofuranose with DEAD.[16] It is also observed that in the formation of 2-oxazolidones from CO_2 and ethanolamines using a Mitsunobu protocol, the use of triphenylphosphine and tributylphosphine affords different isomers[16] thus posing an intriguing question on the nature of the intermediate involved. Isolation of such intermediates will be an interesting aspect to study further.

Recently it is also shown that the dimethylamino derivative 4.**7** reacts with DEAD/ DIAD to yield the pentacoordinate phosphoranes 4.**8**, and not the betaine **I** (Scheme 4.3).[9b] This species 4.**8** has not been characterized by X-ray crystallography. Compound 4.**8** *does participate in the Mitsunobu coupling* between alcohol and acid.[9b]

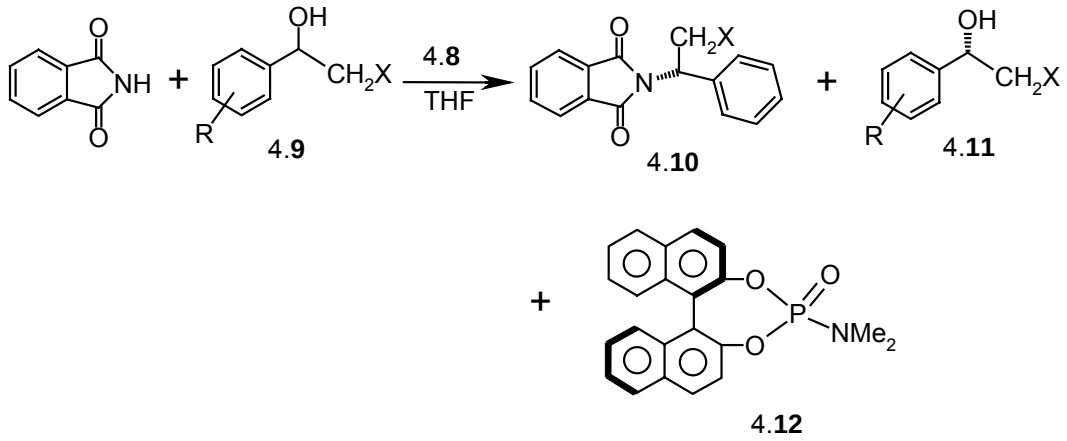
Scheme 4.3



Using a similar protocol, enantioselective reaction of racemic secondary alcohols with phthalimide in the presence of 4.**8** is effected resulting in unreacted,

enantiomerically enriched alcohols (Scheme 4.4).[17] These results also suggest that even when the initial products of the P(III) compound with DEAD/ DIAD are different from a betaine of type **I**, Mitsunobu reaction takes place smoothly, thus leaving room to explore other P(III) compounds for specific reactions.

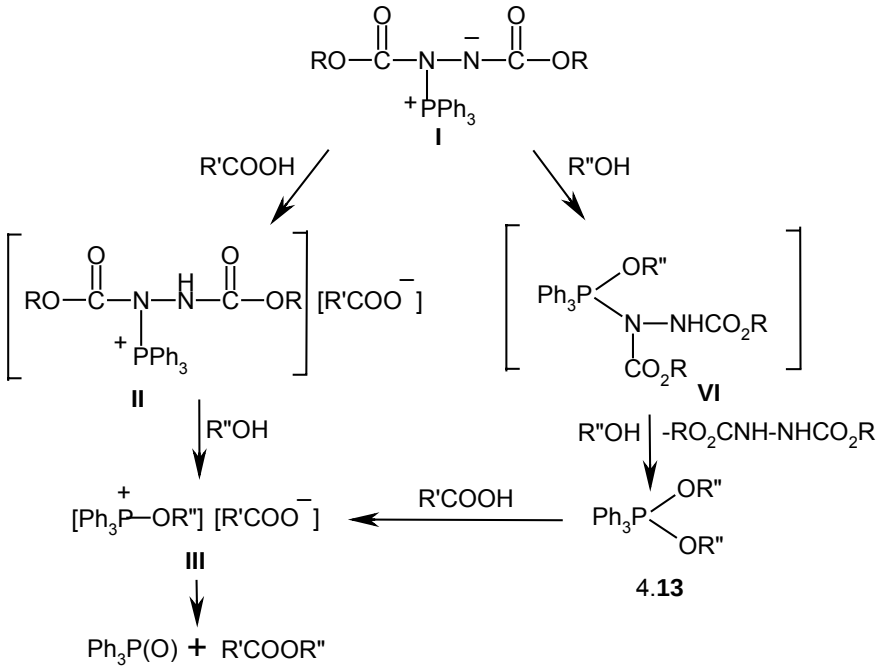
Scheme 4.4



b) Protonation of betaine I

The betaine **I** formed in the first step can react with either alcohols/ or carboxylic acids giving phosphoranes or oxophosphonium ions respectively. The order of addition of the acid and the alcohol to betaine **I** in the Mitsunobu esterification has a profound effect on the reaction pathway, implying potential duality of the mechanism.[2,10] Thus, different types of phosphorus intermediates could be involved depending upon the order of addition. The intermediate formed by the reaction of acid R'COOH and the betaine **I** is a species of type $[RO_2CN\text{-}(P^+Ph_3)\text{-}NHCO_2R][R'COO^-]$ (**II,** Scheme 4.5);[3] the stability of this species may be enhanced by hydrogen bonding. Oxaphosphorane intermediates $Ph_3P(OR'')_2$ (4.**13**) are formed by the reaction of **I** with alcohols R"OH (Scheme 4.5).[2]

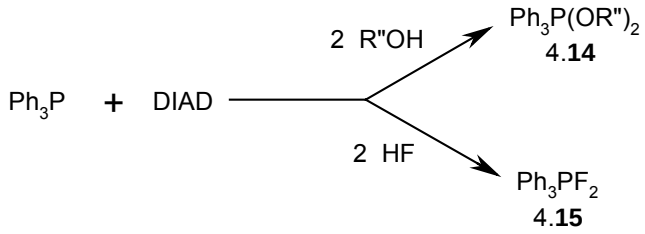
Scheme 4.5



Initial addition of alcohols/diols: Dialkoxytriphenylphosphoranes (4.**13**), dialkoxytributylphosphoranes and diaryloxytriphenylphosphoranes can be readily prepared from the reaction of betaine **I** with alcohols or phenols.[2a-d,3d,11,18-26] Walker has stated that a dialkoxytriphenylphosphorane is the only intermediate in the Mitsunobu reaction in the special case where the acid is added last.[18] An elegant use of this feature was reported by Trippett and coworkers for the synthesis of various cycic phosphoranes.[24] Later, this reaction was also utilized for probing the mechanism of the Mitsunobu reaction.[2] In fact, Mitsunobu protocol offers a simple procedure for the preparation of five (with 1,2-diols),[24,27] six (with 1,3-diols) and seven membered (with 1,4-diols) dioxytriphenylphosphoranes analogous to 4.**13**.[28]

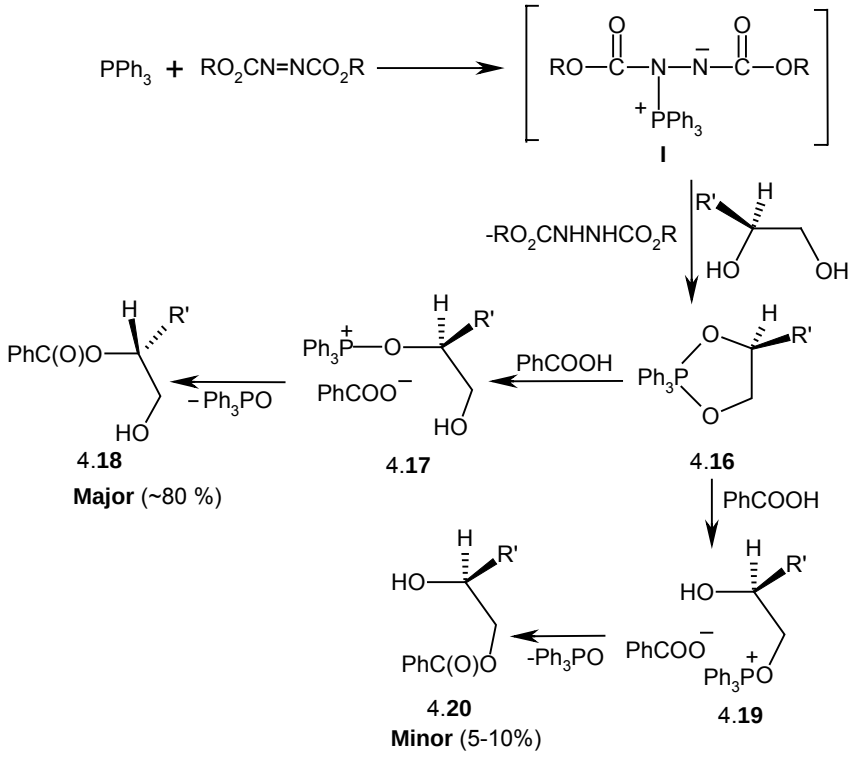
Besides the synthesis of oxyphosphoranes as described above, Mitsunobu reaction is also useful to prepare difluorophosphorane of type R_3PF_2 from a range of trivalent phosphorus compounds under mild conditions (Scheme 4.6).[29] Previous methods for the preparation of R_3PF_2 involved the use of reagents such as dimethylaminosulfur trifluoride,[30a] hexafluoroacetone,[30b] dinitrogen tetrafluoride,[30c] sulfur tetrafluoride,[30d] phenyl carbamoyl fluoride,[31a] and difluorodiaziridine.[31b] The method for the synthesis of R_3PF_2 under Mitsunobu conditions is cheap and the reagents can be handled very easily.

Scheme 4.6



Chemoselectivity: When unsymmetrical 1,2-diols (e.g. 1,2-propanediol and 1-phenyl-1,2-ethanediol) are used in the Mitsunobu reaction, monoesterification occurs affording thermodynamically least stable secondary ester as the major product (Scheme 4.7).[32,33] 1,3,2 λ^5-Dioxaphospholane 4.**16** is initially formed by the addition of diol to the betaine **I**, and is assumed to be the key intermediate. Hydrogen bonding interactions and ultimately proton transfer from the acidic component to the least hindered oxygen of phospholane 4.**16** initiates chemoselective ring opening to form the C-2 secondary phosphonium salt. Finally, attack of benzoate anion on the carbon center, followed by elimination of triphenylphosphine oxide (TPPO) affords predominantly the C-2 benzoate with inversion of configuration.[34]

Scheme 4.7



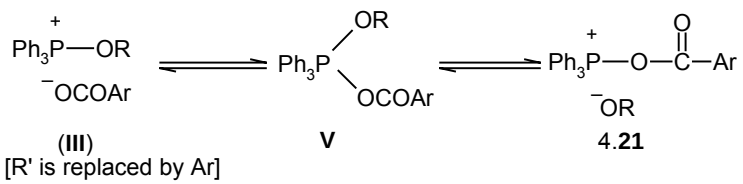
When a substrate containing both aliphatic and aromatic hydroxyls is involved, the Mitsunobu reaction serves as an extremely elegant tool to distinguish them in the esterification reactions.[35] Many other reagents poorly discriminate between the phenolic and aliphatic hydorxyl groups Mitsunobu conditions appear to be the best in the synthesis of vanillyl nonanoate from 3-MeO-4- OH-$C_6H_3CH_2OH$ in which the phenolic OH remains unreactive.[35]

Initial addition of acid and effect of strength of the acid: Protonation of the MBH betaine **I** can also be achieved by the addition of variety of carboxylic acids as mentioned previously.[36] Mitsunobu inversion of secondary alcohols are dramatically influenced by the strength of the acidic component (protonating agent). Stronger acids generally provide higher yields of the inverted product.[37] A similar effect is also demonstrated by other groups while comparing chloroacetic acid, benzoic acid and acetic acid (using menthol as alcohol). Better yields of the esters are obtained by starting with chloroacetic acid.[37-40]

c) Formation of the alkoxy phosphonium salt III

The reaction of MBH betaine **I** with an acid plus an alcohol or that of phosphorane 4.**13** (*cf.* Scheme 4.5) with an acid produces the alkoxy phosphonuim salt **III** (*cf.* Scheme 4.5). When a sterically hindered alcohol and an acid of high pK_a (weak acid) are used in the Mitsunobu reaction, more of acid anhydride and less of the desired ester are formed.[41] It is suggested that one of the reasons for the lower yields is the competitive formation of acid anhydride via acyloxyphosphonium salts 4.**21** (Scheme 4.8).[41] It is proposed that there is an equilibrium between alkoxyphosphonium intermediate **III** and acyloxyphosphonium salt 4.**21** through a phosphorane intermediate **V**. Equilibrium shifts towards **III** or 4.**21** depending on the pK_a of the acid. Strong acids give an increased preference for the formation of **III**.

Scheme 4.8



(**III**) **V** 4.**21**

[R' is replaced by Ar]

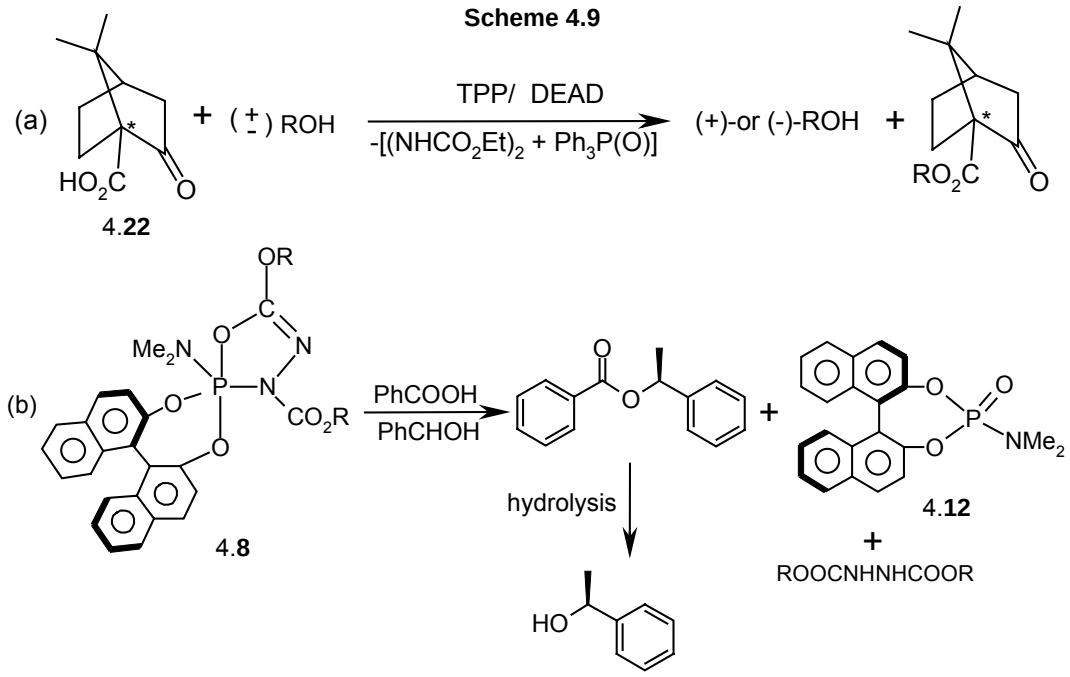
(d) S_N2 Displacement of R'COOR" from III:

S_N2 Displacement of R'COOR" from **III** or analogous species results in the inverted product.

4.2 Synthetic Applications of Mitsunobu Reaction

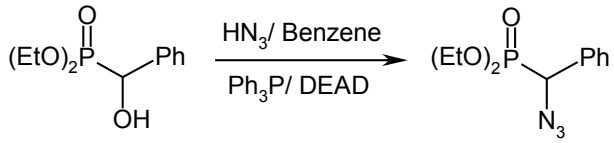
A few applications of the Mitsunobu reaction have already been discussed above. The Mitsunobu reaction has found widespread use in many fields because of its high reliability and extensive applicability.[1,42-44] Till recently, the chiral recognition and enantioselectivity were the least explored aspects of the Mitsunobu reaction. The design of chiral version of the Mitsunobu reaction is an interesting exercise. Among many available possibilities, the chiral auxiliary can be any one of the phosphine/ phosphite used, azodicarboxylate itself or the acidic component used. Scheme 4.9 demonstrates the kinetic resolution of the secondary alcohols with 4.**22** (a chiral acidic component) and 4.**8** (phosphorane derived from a chiral phosphite) in the Mitsunobu reaction.[45-46,9b] Use of the acidic component as a chiral auxiliary is the simplest of the all the possible choices.[45]

Scheme 4.9



Diethyl(1-azido)benzylphosphonate 4.**24** is obtained in high yield in the presence of Ph_3P/ DEAD (Mitsunobu conditions) by the reaction of diethyl-1-hydroxy benzylphosphonate 4.**23** with hydrazoic acid (Scheme 4.10).[47-50]

Scheme 4.10



4.**23** 4.**24**

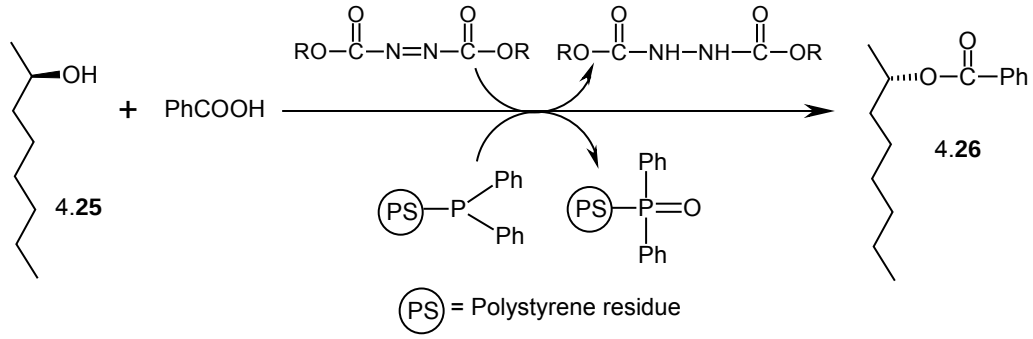
The versatility of the Mitsunobu reaction is also shown by replacing the traditionally used acidic component with a variety of nucleophiles such as metal halides (LiBr),[42a] silanols,[42b] amides/ imides,[42c] nitronates,[42d] fluorinated alcohols[42e] and mercury (II) or zinc halides,[42f-g] thus rendering the reaction widely applicable in organic synthesis.

Chiral aziridine sulfides and disulfides were synthesized from readily available and inexpensive *R*-cysteine by a Mitsunobu reaction; their application in the addition of diethylzinc to aldehydes provides secondary alcohols with up to 99% ee and *S*-configuration.[51] The total synthesis of anti-inflammatory active flavone C-glycoside isolated from oolong tea extract is achieved. Introducing a C-glucosyl moiety to an aryl system and constructing a fused tetracyclic ring characteristic to this natural product were conducted based on the O-to-C rearrangement of sugar moiety and the successive intramolecular Mitsunobu reaction, respectively.[52] The chain elongation of primary alcohol of saccharides has been achieved via a Mitsunobu reaction using bis(2,2,2-trifluoroethyl)-malonate as a nucleophile.[53] Reaction of 4-hydroxy-3-hydroxyalkyl-1-methyl-2(1H)quinolinones with Ph_3P/DEAD gives either C- or O-cyclized products depending on chain length. Hydroxyethyl group produces only spiro cyclopropylquinolinone, whereas hydroxypropyl group affords only pyranoquinolinone. Hydroxybutyl gives a 2:1 mixture of spiro cyclopentylquinolinone and oxepinoquinolinone.[54] Chiral 3,4-dibenzyloxy-5-hydroxymethyl-2-thiazolylpyrrolidines under Mitsunobu conditions (R-OH, Ph_3P, DIAD in THF) afforded the corresponding R-protected pyrrolidines and 2-deoxypiperidines in different ratios depending on the stereochemistry of the starting pyrrolidine and the nature of the acid R-OH.[55] A new method for separation. Tagging with cyclodextrin-binding groups is introduced and is exemplified in the context of the Mitsunobu reaction with adamantyl tags.[56] A new route for the solid-phase synthesis of N-aryl-N'-carboalkoxy guanidines using a Mitsunobu protocol is also described.[57] A mild method for the synthesis of

carbamates from amino alcohols involved sequential carboxylation with carbon dioxide, followed by a Mitsunobu reaction. Unexpectedly, the stereochemical course of the Mitsunobu reaction was dependent on whether the carbamic acid intermediate was N-substituted with hydrogen (retention) or carbon (inversion).[58] The unprotected L-arabinofuranosides, D-ribofuranosides and D-xylofuranosides are transformed into the corresponding S-acetyl-5-thio derivatives by the thio-Mitsunobu reaction.[59]

Separation of phosphine oxide as a by-product often haunts the isolation of the desired products in the traditional Mitsunobu reaction. When polystyryl diphenylphosphine is used in the Mitsunobu reaction in place of Ph_3P, the resulting phosphine oxide is anchored to the polystyrene resin and can be easily removed by means of filtration. Thus, the chiral 2-octanol (4.**25**) reacts with benzoic acid with complete inversion to give the corresponding ester 4.**26** that can be separated from the resin (Scheme 4.11).[60-62]

Scheme 4.11

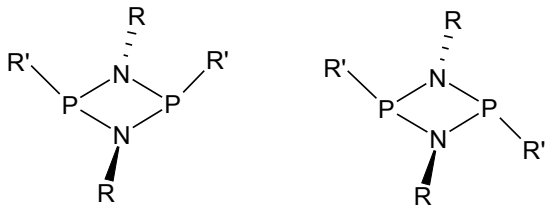


Two new second generation fluorous reagents bearing propylene spacers ($C_8F_{17}(CH_2)_3O_2CN{=}NCO_2$-t-Bu and $(C_6F_{13}(CH_2)_3O_2CN{=}NCO_2(CH_2)_3C_6F_{13}$ show expanded reaction scope while retaining the easy fluorous separation features.[63]

4.3 Cyclodiphosphazane Chemistry

Phosphorus and nitrogen form compounds of greater structural diversity than any other two congeners in the periodic table.[64] Among them, cyclophosphazanes, especially cyclodiphosph(III)azanes[65-68] having a formal P(III)-N bond constitute an important class of compounds known for their stability and ease of synthesis. Their important structural feature is a central four membered ring of alternating trivalent phosphorus and nitrogen atoms. Each atom has one exocyclic substituent; those on

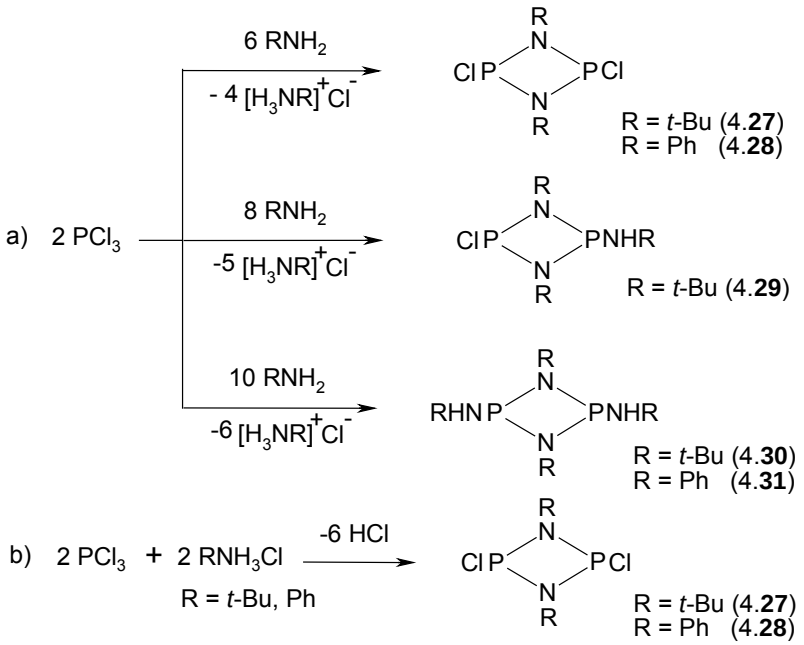
the nitrogen atoms lie approximately in the plane of the ring, while the substituents of the phosphorus atoms are almost perpendicular to it. This disposition of the substituents at phosphorus makes *cis* and *trans* isomers possible (**A**, **B**).



A (*cis*) **B** (*trans*)

There are several methods for the preparation of cyclodiphosph(III)azanes (or diazadiphosphetidines)[65b,69] and among them, the most convenient route is the condensation reaction of primary amines or their hydrochlorides with phosphorus trichloride (Scheme 4.12).[66-68, 70-72]

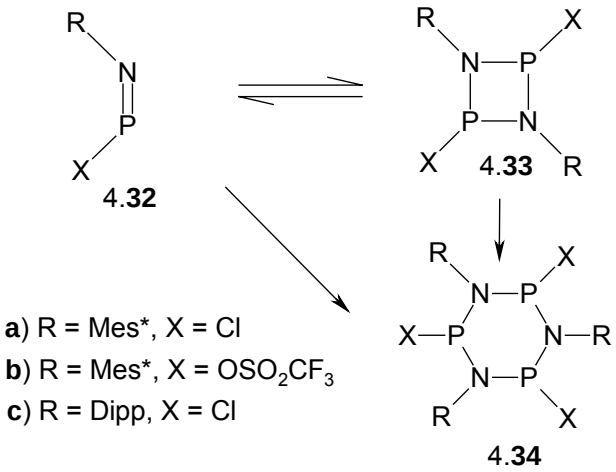
Scheme 4.12



Depending upon steric/ electronic factors, compounds with the empirical formula $[RNPX]_2$ can exist as monomers (iminophosphines), dimers [cyclodiphosph(III)azanes] or higher oligomers. An interesting case of monomer↔dimer equilibrium arises in some cases.[73] The compound Mes*NPCl

(Mes* = 2,4,6-tri-*tert*-butylphenyl) exists as a monomer 4.**32a** in the solid state, while the slightly smaller substituent at nitrogen (Dipp = 2,6-diisopropylphenyl) in DippNPCl allows the formation of dimer 4.**33c** (Scheme 4.13).[73] Evaporation of the hexane solution of 4.**32b** over a period of several days under vacuum at room temperature gives a mixture of crystals with different morphologies (of monomer 4.**32b** and dimer 4.**33b**). The solid state ^{31}P NMR spectra of 4.**32b** and 4.**33b** show signals at δ(P) 49 and 250 ppm respectively. Both crystals dissolve to give a peak at δ(P) 50 in the ^{31}P NMR spectrum (CD_2Cl_2), implying quantitative dissociation of the dimer in solution. The dimeric phosphazane 4.**33c** reacts rapidly with $GaCl_3$ to give [4.**34c**]**.**$GaCl_3$. This compound has been characterized by X-ray crystallography and is best described as the heterocyclic trimer of 4.**32c** associated with gallium trichloride. Thus the isolation and stability of iminophosphine compounds 4.**32** usually depend on the presence of sterically bulky substituents, which counter the thermodynamic preference for N-P single bonds over multiple N=P bonding.[74]

Scheme 4.13



Among these cyclodiphosph(III)azanes, compounds 4.**27**-4.**30** are the most studied. Important features in these compounds are (i) configurational and ring conformational preferences, (ii) substitution reactions and (iii) oxidative addition reactions. These are discussed below.

4.31 Configurational and ring conformational preferences

In the case of 4.**27** and 4.**28** single crystal X-ray structures confirm the *cis*-configuration of the chloro substituents.[75] The major structural difference between

the dichloro species 4.**27** and 4.**28** is in the $(P\text{-}N)_2$ ring, which is slightly puckered in 4.**27** but planar in 4.**28**. This feature suggests that the conformation of the $(P\text{-}N)_2$ ring may depend on the imino-nitrogen substituents.

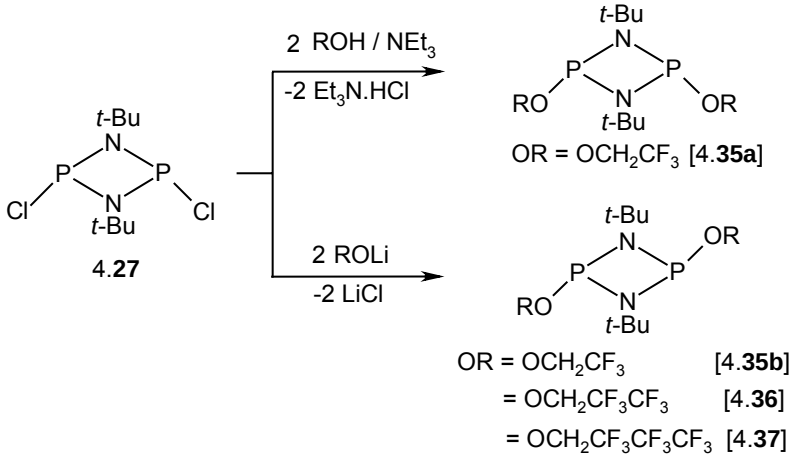
The solid state structure of 4.**29** demonstrates the *cis* configuration of the two phosphorus substituents Cl and NH-*t*-Bu; the $(P\text{-}N)_2$ ring is puckered.[69] The unique P-Cl bond is much longer than that in 4.**27** or 4.**28** (*cf*. Table 4.1). 1,3-Di-*tert*-butyl-2,4-di-*tert*-butylamino compound 4.**30** also has a *cis* configuration of the *tert*-butyl amino substituents. [75,76]

Table 4.1. Bond parameters in 4.**27**-4.**30**

Compound	$P\text{-}N_{endo}$ [mean (Å)]	$P\text{-}N_{exo}$ [mean (Å)]	P-Cl (Å)
$[ClPN\text{-}t\text{-}Bu]_2$ (4.**27**)	1.689(9)	_	2.105(7)
$[ClPNPh]_2$ (4.**28**)	1.695(10)	_	2.087(8)
$[(t\text{-}BuHN)P(\mu\text{-}N\text{-}t\text{-}Bu)_2PCl]$ (4.**29**)	1.674(3) to P-Cl 1.748(3) to P-N	1.659(3)	2.205(1)
$[(t\text{-}BuHN)PN\text{-}t\text{-}Bu]_2$ (4.**30**)	1.726(2)	1.664(2)	_

Both X-ray structural studies and solution state ^{31}P NMR studies have allowed the isomer assignment in the cyclodiphosph(III)azane derivatives. The ^{31}P NMR data indicate that the signal for the *trans* isomer is far downfield when compared to the *cis* isomer.[72, 77-83] Either *cis* or *trans* isomer may be formed as the major product in the reaction of 4.**27** with different reagents or under slightly altered conditions.[77, 84]

Scheme 4.14

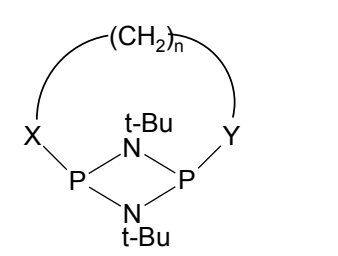


4.32 Substitution reactions of cyclodiphosph(III)azanes

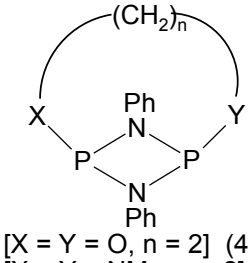
Compound 4.**27** reacts with alcohols or amines to give the substituted cyclodiphosph(III)azanes (see above, Scheme 4.14).[79,81,85,86] Either triethylamine or *n*-butyllithium is used as a base in these reactions. By suitably controlling the stoichiometry of the nucleophiles with respect to compound 4.**27**, partially substituted products can also be obtained.[72,77-81,86]

When difunctional reagents like diols/ diamines are made to react with the dichloro compounds 4.**27** or 4.**28**, bicyclic or macrocyclic derivatives are formed (chart 4.1, compounds 4.**38**-4.**48**).[84,87-89] Both the macrocycles 4.**46** and 4.**47** are well characterized. The recent claim by Wright et al[90] that they characterized the first dimeric species (4.**47**) is incorrect, because the X-ray structure of 4.**48** was already reported from our laboratory in 2003![91]

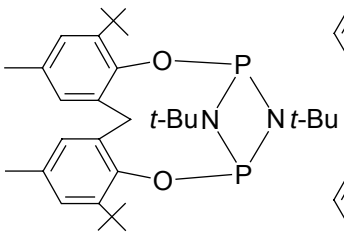
Chart 4.1



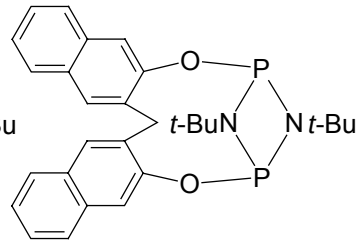
[X = Y = O, n = 2] (4.**38**)
[X = Y = O, n = 3] (4.**39**)
[X = Y = NMe, n = 2] (4.**40**)



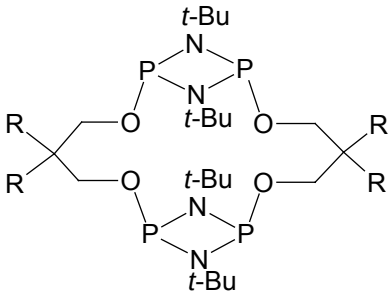
[X = Y = O, n = 2] (4.**41**)
[X = Y = NMe, n = 2] (4.**42**)
[X = O, Y = NMe, n = 2] (4.**43**)
[X = Y = O, n = 3] (4.**44**)



4.**45**



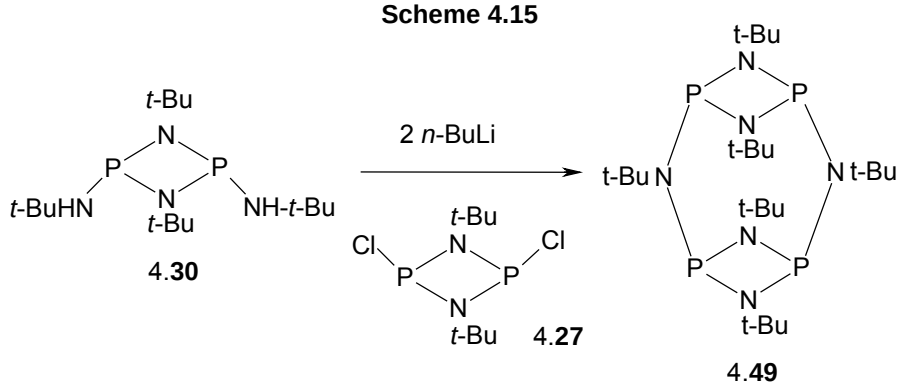
4.**46**



R = Me (4.**47**), Et (4.**48**)

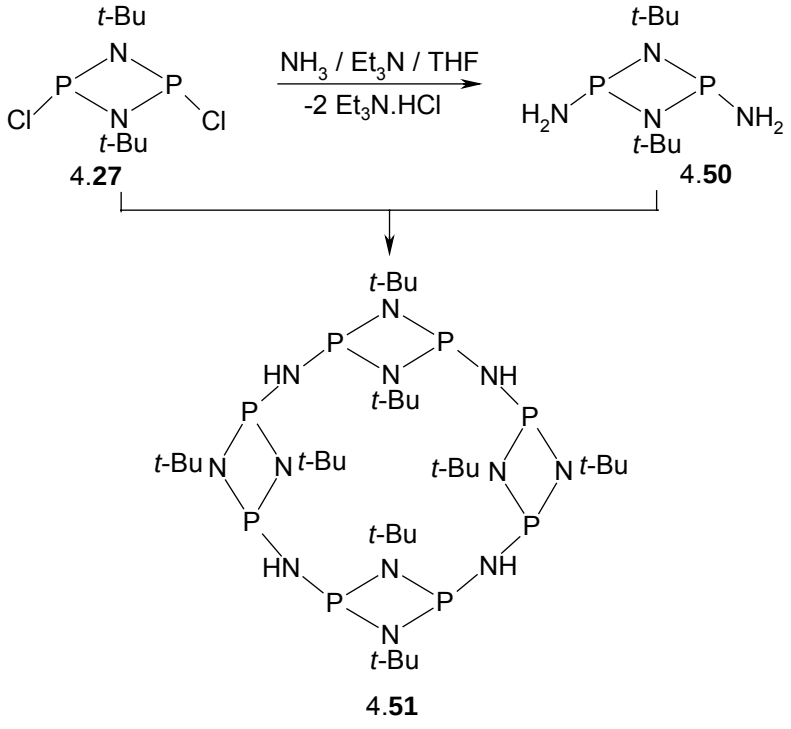
The macrocycle 4.**49** having two cyclodiphosphazane units has been synthesized by Stahl et al utilizing the reactivity of the dilithiated cyclodiphosph(III)azane 4.**30** (Scheme 4.15).[92,93]

Scheme 4.15



Recently, Wright and coworkers synthesized a macrocycle having four cyclodiphosph(III)azane skeletons from the reaction of $[ClPN(t\text{-Bu})]_2$ (4.**27**) with $[H_2NPN(t\text{-Bu})]_2$ (4.**50**) in the presence of excess of triethylamine.[94] The tetrameric macrocycle $[\{P(N\text{-}t\text{-Bu})\}_2NH]_4$ (4.**51**) thus obtained has been characterized X-ray crystallography. These reactions are shown in Scheme 4.16.

Scheme 4.16

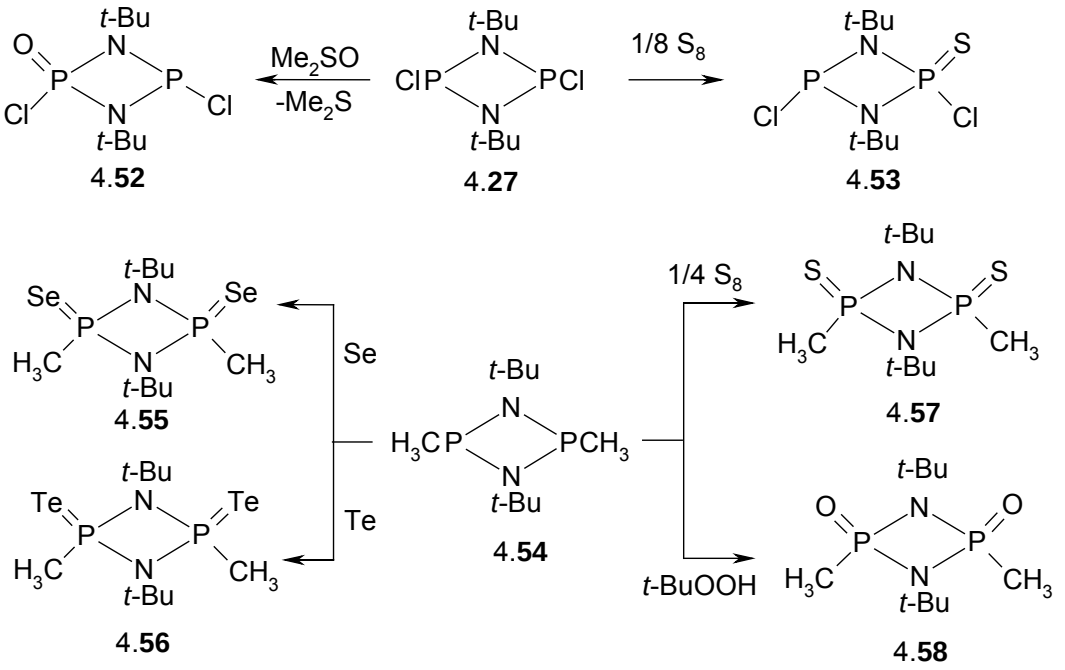


4.33 Oxidative addition reactions

The trivalent phosphorus atoms present in the cyclodiphosph(III)azane derivatives of the type discussed so far are susceptible to oxidation. Oxygen, sulfur, selenium and tellurium can be added on to the phosphorus atom. Compound 4.**27** reacts with dimethylsulfoxide or sulfur to give the mono-oxidized products 4.**52**,

4.**53** respectively (Scheme 4.17).[72,95] The dimethyl cyclodiphosph(III)azane 4.**54** undergoes oxidation with various reagents to yield compounds 4.**55**-4.**58**.[69] The dimethylamino derivative $[(Me_2N)PN\text{-}t\text{-}Bu]_2$, which is unreactive towards dimethylsulfoxide, undergoes oxidation with *t*-butylhydroperoxide to its dioxide easily (not shown in the Scheme).[79]

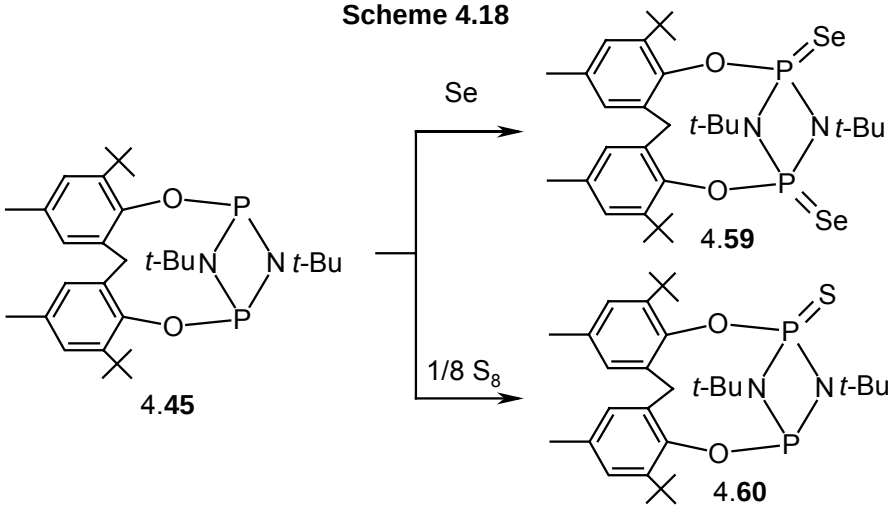
Scheme 4.17



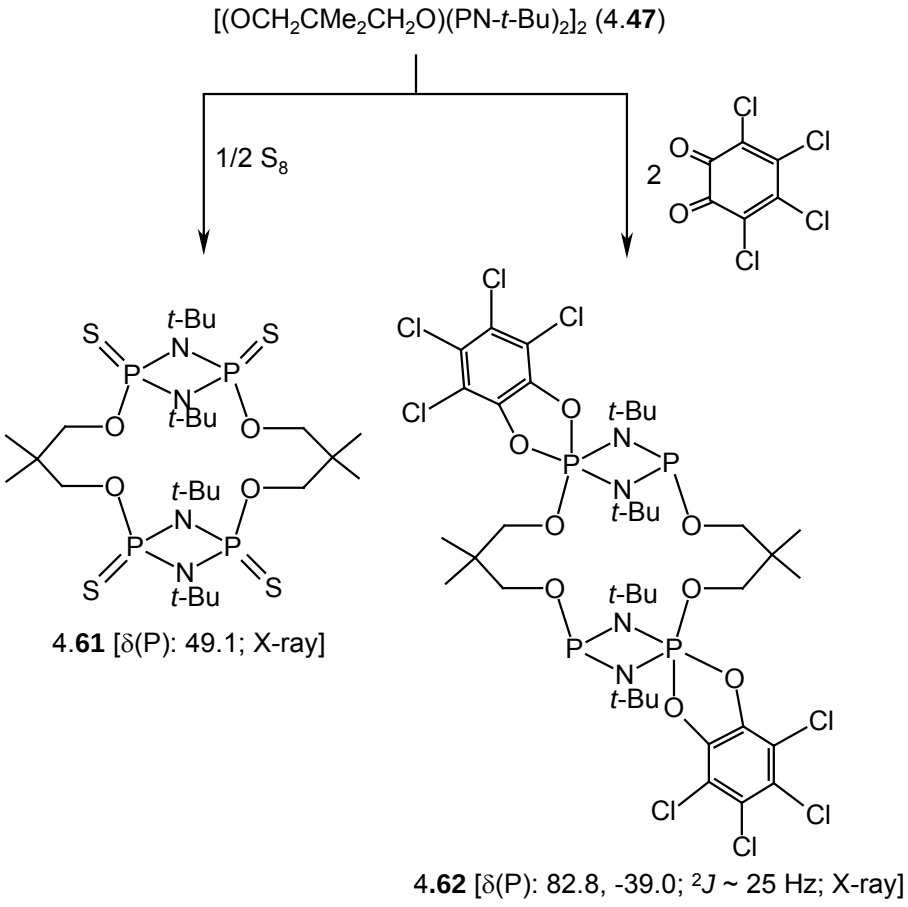
The bicyclic derivatives 4.**41**-4.**44** are resistant to oxidation with sulfur at room temperature.[87] Attempted oxidative addition reactions with 1,2-diketones led to ring cleavage and no identifiable product could be isolated.[88]

In contrast to the above, when the bicyclic compound 4.**45** is treated with selenium, the diseleno derivative 4.**59** is obtained. On the other hand, the same compound 4.**45** reacts with an excess of sulfur to give the mono substituted product 4.**60** (Scheme 4.18).[96] Upon addition of elemental sulfur to the macrocyle, 4.**47**, all the phosphorus atoms get oxidized to form 4.**61** while in the addition of *o*-chloranil, only two phosphorus atoms become pentavalent to form 4.**62**.[97]

Scheme 4.18



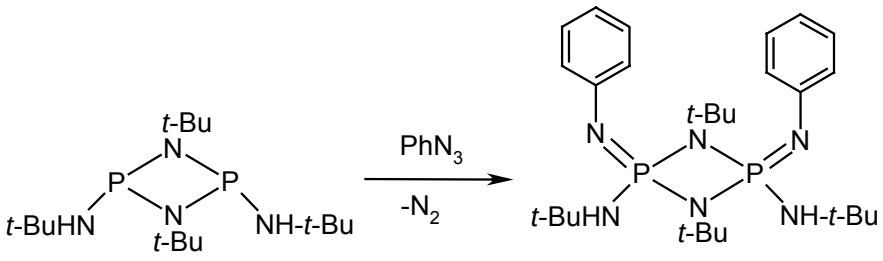
Scheme 4.19



The bis-*t*-butylamino compound [(*t*-BuNH)P-N-*t*-Bu]$_2$ (4.**30**) reacts with aryl azides to lead to the iminophosphoranes (e.g. 4.**63**) via the Staudinger reaction (Scheme 4.20).[98a] The P=N bonds in this compound are in the range 1.510-1.532 Å. In the novel tris-spirocyclic cyclotriphosphazene, $N_3P_3[(C_6H_{11}NP(Cl)NC_6H_{11})]_3$,

reported by Richards and Steiner, the quasi P=N distance (in the phosphazene residue) is 1.589 Å.[98b]

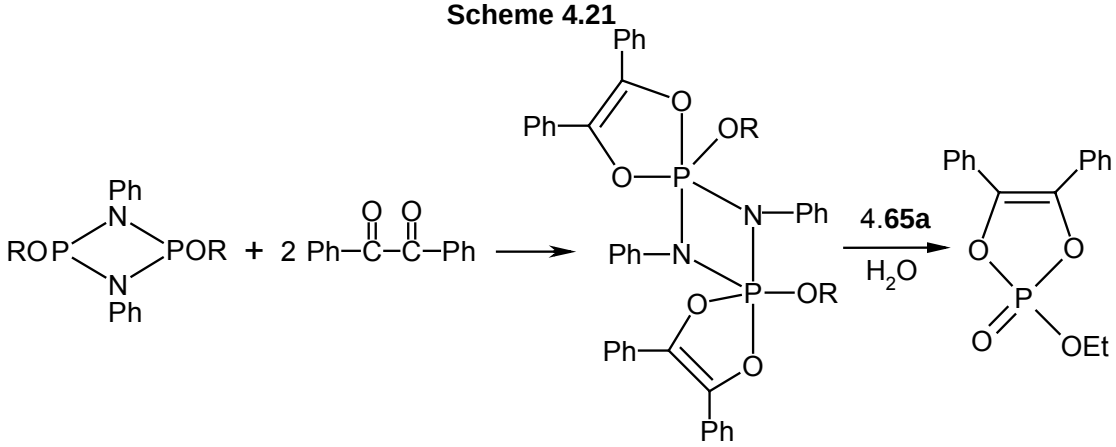
Scheme 4.20



4.**30** 4.**63**

Cyclodiphosph(III)azanes 4.**64a-b** react with benzil to afford the pentacoordinate phosphorus compounds 4.**65a-b** (Scheme 4.21).[99] Compound 4.**65a** on refluxing in *o*-dichlorobenzene gave the hydrolyzed product 4.**66** (cyclodiphosph(III)azane ring is cleaved). The reactions of 4.**65** with benzalacetophenone or α-phenyliminobenzyl phenyl ketone afforded products similar to 4.**66**.[99]

Scheme 4.21



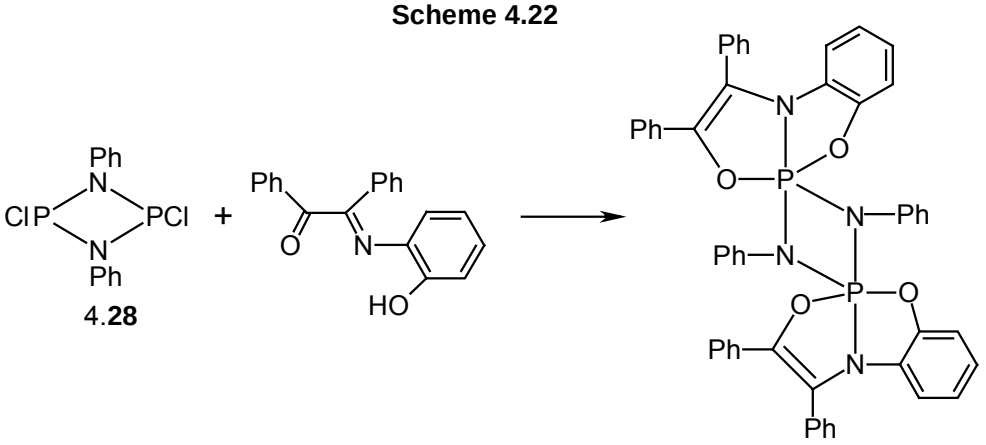
R = Et (4.**64a**)
R = Me (4.**64b**)

R = Et (4.**65a**)
R = Me (4.**65b**)

4.**66**

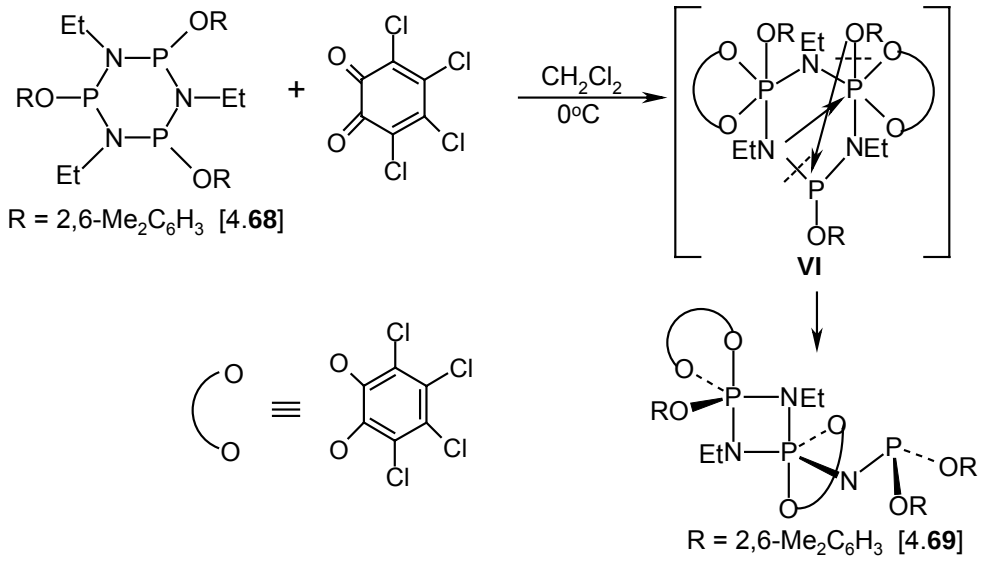
Treatment of benzilmonoanil with $[ClPNPh]_2$ (4.**28**) yields a stable pentacoordinated compound 4.**67**. In this reaction chlorine is replaced by the phenolic oxygen and oxidative addition occurs to give the pentacoordinated compound (Scheme 4.22).[100]

Scheme 4.22



Although the point of interest here is cyclodiphosph(III)azanes, an interesting reaction of cyclotriphosphazane is to be mentioned since the end product in this case is a cyclodiphosphazane. The cyclotriphosphazane 4.**68** on treatment with tetrachloro-*o*-benzoquinone undergoes a ring contraction-*cum*-rearrangement to the cyclodiphosphazane 4.**69**.[101] This transformation probably occurs *via* intermediate **VI** as depicted in Scheme 4.23.

Scheme 4.23



OBJECTIVES OF THE PRESENT WORK

1. To study the reaction of dialkyl azodicarboxylates with cyclodiphosphosphazane substrates in an effort to isolate and characterize compounds analogous to the proposed intermediates in the Mitsunobu reaction.

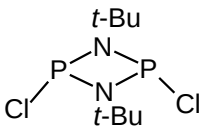
2. To investigate the oxidative addition reactions of cyclodiphosphazanes and structurally characterize the resulting products.

CHAPTER 5

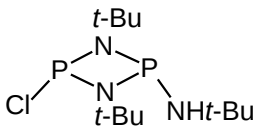
RESULTS AND DISCUSSION

5.1 Preparation of P(III) Precursors

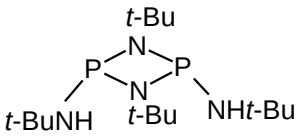
The precursors used in the present study $[ClP(\mu\text{-}N\text{-}t\text{-}Bu]_2$ (**1**),[102] $ClP(\mu\text{-}N\text{-}t\text{-}Bu)_2PNH\text{-}t\text{-}Bu$ (**2**),[103] $[(t\text{-}BuNH)P(\mu\text{-}N\text{-}t\text{-}Bu)]_2$ (**3**)[104] and $[(C_5H_{10}N)P(\mu\text{-}N\text{-}t\text{-}Bu]_2$ (**5**)[105] were synthesized by essentially following the procedures reported in the literature. The compound $[P(\mu\text{-}N\text{-}t\text{-}Bu)_2P][O\text{-}6\text{-}t\text{-}Bu\text{-}4\text{-}Me\text{-}C_6H_2]_2CH_2$ (**4**) was prepared by the method developed in our laboratory.[106] Synthetic routes to the morpholino and the bis-cyclodiphosphazane derivatives $[O(CH_2)_4N][P(\mu\text{-}N\text{-}t\text{-}Bu)_2P(NH\text{-}t\text{-}Bu)]$ (**6**) and $(OCH_2CMe_2CH_2O)[P(\mu\text{-}N\text{-}t\text{-}Bu)_2P[(NH\text{-}t\text{-}Bu)]_2$ (**7**) are shown in Scheme 1. The substituents on the two phosphorus atoms in the cyclodiphosphazane ring in **1**-**5** have been shown to be *cis* to each other by earlier workers. The assignment of *cis* geometry in **6**-**7** is based on the comparison of the ^{31}P NMR chemical shifts to those for **4** and **5**.



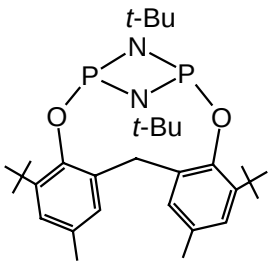
1 [δ(P) 206.5]



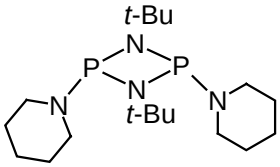
2 [δ(P) 135.4, 200.3]



3 [δ(P) 89.4]

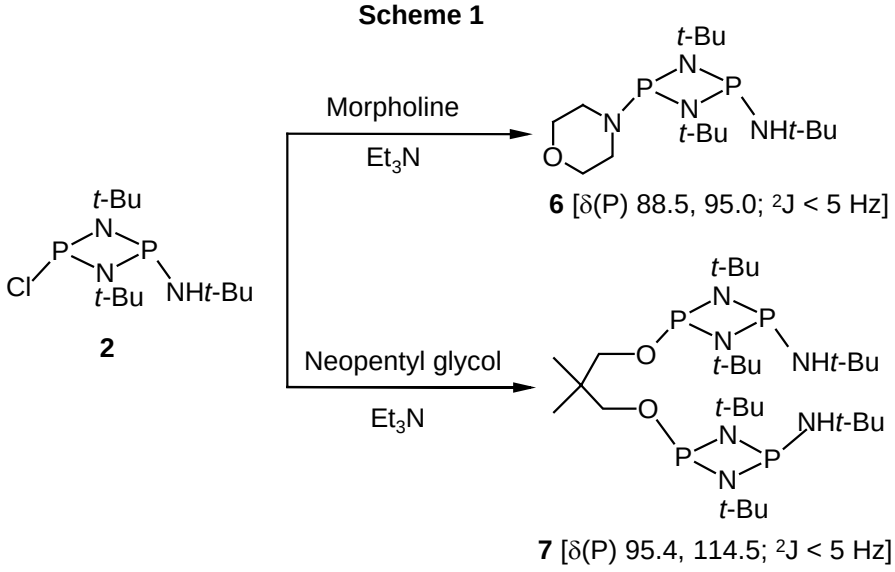


4 [δ(P) 143.9]



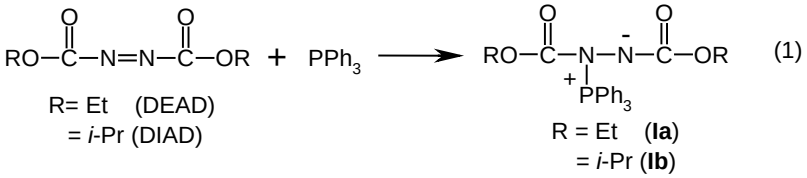
5 [δ(P) 93.4]

Scheme 1



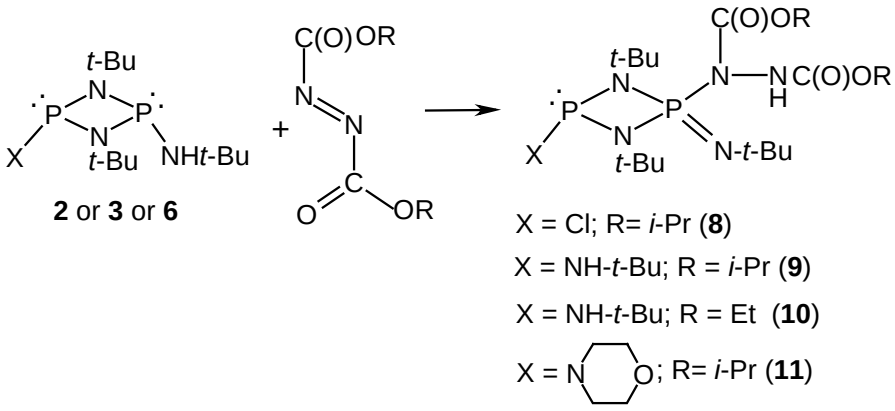
5.2 Reactions of Phosphorus(III) Compounds with Dialkyl Azodicarboxylates

In the original Mitsunobu reaction, triphenylphosphine that contains three carbons attached to phosphorus is utilized and the Morrison-Brunn-Huisgen (MBH) betaine **I*** is proposed as the intermediate in the first step (eq. 1).[1]



We have been interested in structurally characterizing compounds of type **I**. In this connection, we reacted cyclodiphosphazanes **2-7** (in which phosphorus atoms are bonded to nitrogen and chlorine/ oxygen atoms) with diethyl azodicarboxylate (DEAD) or diisopropyl azodicarboxylate (DIAD). In the reactions of **2**, **3**, or **6**, rather than a betaine of type **I**, we obtained tautomeric forms **8-11** in which the NH proton of the N*H*-*t*-Bu group is moved to the β-nitrogen of the DIAD/ DEAD residue (Scheme 2). A similar compound **12** was obtained by using **7** as the precursor. By contrast, an analogous reaction by using **4** or **5** led only to the oxo-products **13** or **14**, respectively. X-ray structures of **8** and **10**-**13** confirm these (see section 5.4).

Scheme 2



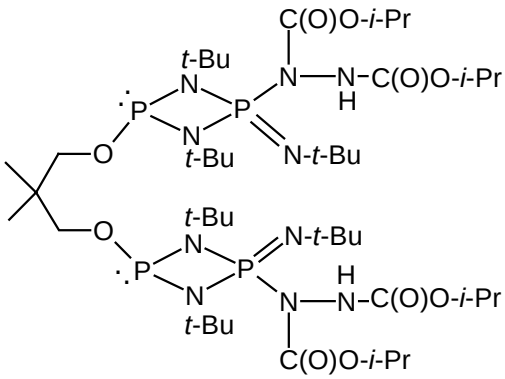
2 or **3** or **6**

X = Cl; R= *i*-Pr (**8**)

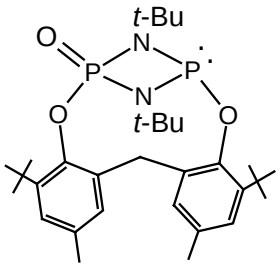
X = NH-*t*-Bu; R = *i*-Pr (**9**)

X = NH-*t*-Bu; R = Et (**10**)

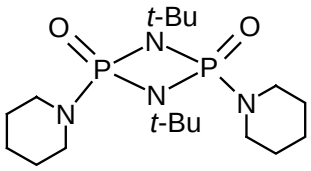
X = N O; R= *i*-Pr (**11**)



12



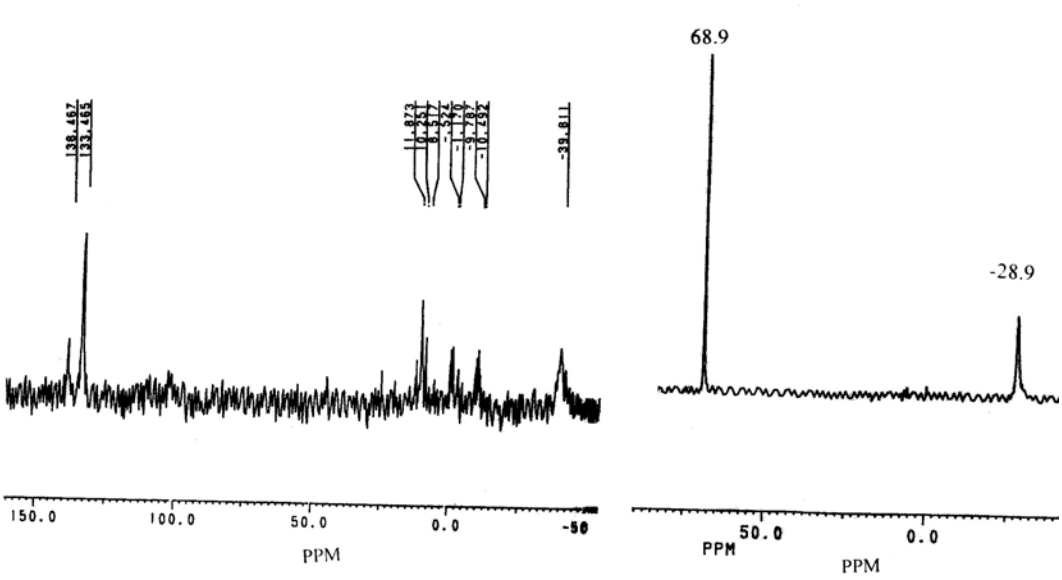
13 [δ(P) -2.5, 104.6]



14 [δ(P) 1.5]

The ^{31}P NMR data for **8**-**12** are summarized below; the spectra for **8** and **9** are illustrated in Figure 1.

Compound	^{31}P NMR data (δ)	
	tetra (penta?) coordinate P	tricoordinate P
8	(major peaks): -39.8, 11.9	133.4, 138.5
9	-28.9	68.9 (d) [^{2}J(PNP) < 5.0 Hz]
10	-28.7	68.9 [^{2}J(PP) < 5 Hz]
11	–51.6	69.7 [^{2}J(PP) < 5 Hz]
12	–40.6	92.8 [^{2}J(PP) < 5 Hz]

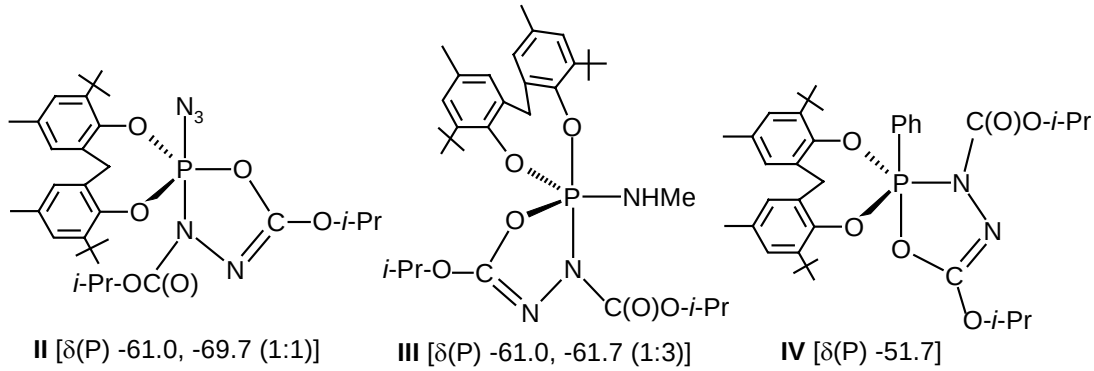


(a) (b)

Figure 1. The ^{31}P NMR spectra of (a) **8** and (b) **9**.

For these compounds, although the δ(P) values of the tricoordinate phosphorus are within the expected range, the chemical shifts for the tetracoordinate phosphorus connected to the dialkyl azodicarboxylate residue are rather up-field when compared to those available in the literature.[6,7,14] In fact they are closer to the range expected for pentacoordinate phosphorus [cf. structures **II-IV**].[**14**] Compound **8** exhibits broad (*solid* as well as *solution* state) signals in the ^{31}P NMR in tri-, tetra- and penta-coordinate regions [$CDCl_3$ (Figure 1a) as well as $C_6D_5CD_3$ (δ 138.6 and 10.5 with ^{2}J(PP) < 5.0 Hz, 133.6 and -34.6 with ^{2}J(PP) of ~16.0 Hz)]. There was no significant improvement in the quality of the solution spectra at lower temperatures and the compound could be recovered after removal of solvent from the solution. Thus for **8**, we think that all the three forms, imine-carbamate, betaine and penta-

coordinate structures are present in solution [cf. **11**, **11'** and **11''** below]. Compound **9**, however, exhibited relatively sharp signals (Figure 1b). In all the cases, the up-field peak is quite broad suggesting that in solution at least there is some exchange between the tetra- and penta-coordinate forms. In the IR spectra, at least two bands for the NH groups were observed at ~3270 and 3160 cm^{-1} which contrasts with one band (3383 cm^{-1}) observed for **III**.[14] In the ^{13}C NMR spectrum of **3**, the $C(CH_3)_3$ [δ 31.6; $^{3}J(PC)$ = 7.0 Hz] as well as the $C(CH_3)_3$ [δ 51.9; $^{2}J(PC)$ = 15.0 Hz] carbons at the ring nitrogen atoms show up as triplets due to coupling to the two equivalent phosphorus atoms (see experimental); in **9**-**10** the $C(CH_3)_3$ carbons appear at δ 31.0 (with some second order effects) and the $C(CH_3)_3$ carbons show up as distinct three signals [δ 51.3 (d, $^{2}J(PC)$ = 18.0 Hz), 51.4 (d, $^{2}J(PC)$ = 5.0 Hz), 52.6 (dd; $^{2}J(PC)$ = 9.5, 40.0 Hz; $C(CH_3)_3$ of the ring] [Figure 2].



II [δ(P) -61.0, -69.7 (1:1)] **III** [δ(P) -61.0, -61.7 (1:3)] **IV** [δ(P) -51.7]

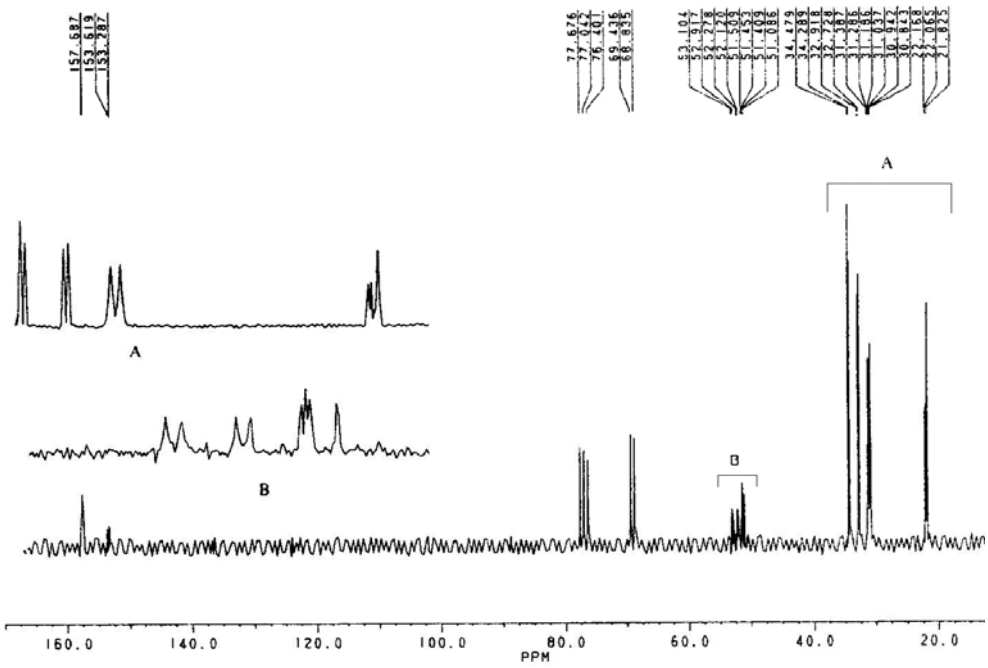
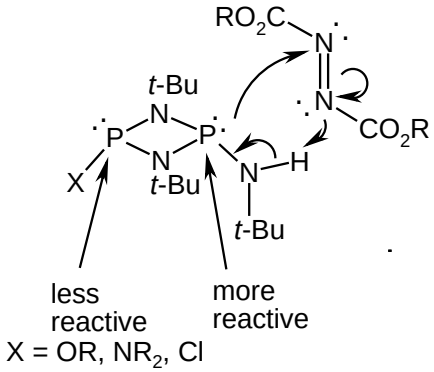
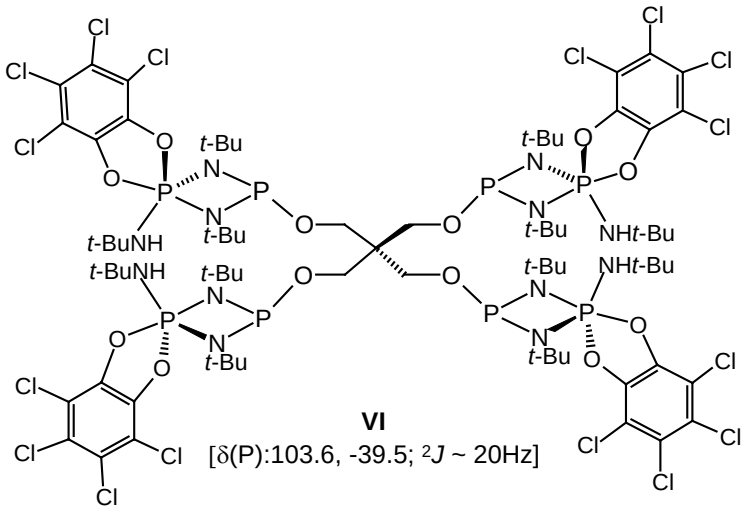


Figure 2. The ^{13}C NMR spectrum of **9**.

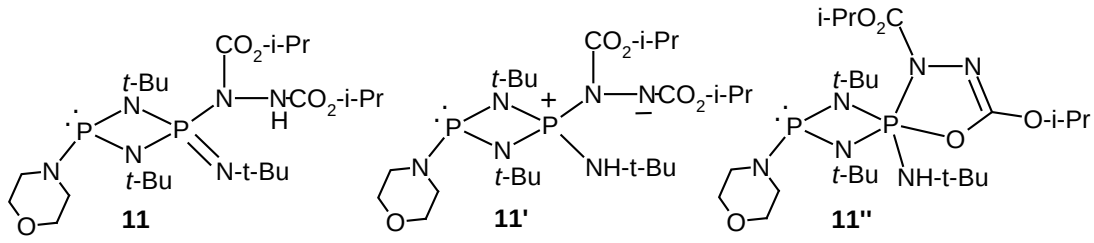
Despite the steric bulk, the electron-rich P(III) centre with the *t*-butylamino group is more reactive than the P-morpholino (secondary amino group) or P-alkoxy or P-chloro in the above reaction. This is to be expected because the *t*-butylamino group is more electron-donating thus facilitating the lone pair on the corresponding phosphorus to attack the electron deficient nitrogen of the dialkyl azodicarboxylate. All these reactions are complete within 1 h and in the synthesis of **9**-**10**, they are instantaneous [^{31}P NMR evidence]. The P-Cl end in **2** did not react (12 h) even when a second mole equivalent of DIAD was added. In the case of **3**, use of two mole equivalents of DIAD resulted in a product mixture that showed two broad humps in the ^{31}P NMR at δ -62.0 and –57.0, but no pure product could be isolated.



The greater reactivity at the P(III)-NH-*t*-Bu end relative to P(III)-OR end has also been noted by us in the reaction of analogous cyclodiphosphazane derivatives with *o*-chloranil. For example, treatment of C[CH$_2$OP(μ-N-*t*-Bu)$_2$PNH*t*-Bu]$_4$ (**V**) with four mole equivalents of *o*-chloranil led to the P(III)-N-P(V) compound **VI**, in which P(III)-OR end remains untouched.[97]

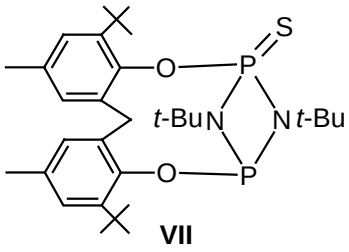


Compounds **8**-**12** can be considered to be the tautomers of the betaine forms [cf. **11'**] and are different from the pentacoordinate products [cf. **11''**]. The reason for the stability of **11** rather than **11'** is possibly the inductive effect of the *t*-butyl group and the presence of a fairly strong P=N bond in **11**.



From the reaction of **4** and **5** with DIAD, the only products that we could isolate were the mono- and the bis- oxo compounds **13** and **14**, respectively (see above). The NMR (^{1}H, ^{13}C and ^{31}P) spectra in these cases are as expected. In the reaction with **4**, even with an excess of DIAD, we isolated only **13** as the major product. Previously, DMSO or *t*-butyl hydroperoxide were used to obtain the P-oxo cyclodiphosphazanes.[79] A possible pathway for the formation of these oxo compounds involves rapid hydrolysis [resulting in the formation of *i*-$PrO_2CNHNHCO_2$-*i*-Pr] or decomposition of the intermediate betaine.

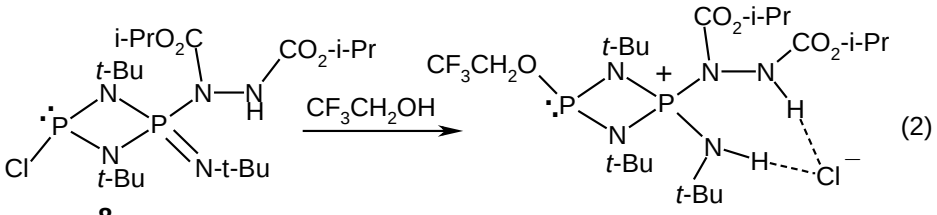
In this context, it is interesting to note that in an earlier study from our laboratory, it was found that only the mono-sulphur derivative **VII** was obtained in the reaction of {[*t*-BuNP]$_2$[6-*t*-Bu-4-Me-C_6H_2O]$_2CH_2$} (**4**) with (excess) sulfur.[96] Thus, although two reactive phosphorus (III) centers are available in **5**, only one reacts and the other end remains as such.



VII

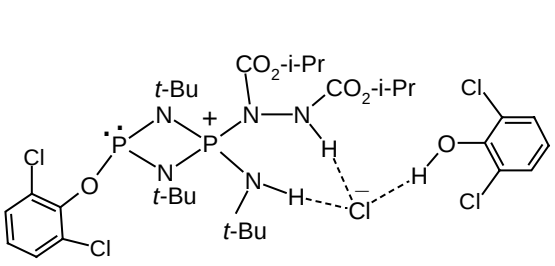
When compound **8** is treated with one mole equivalent of 2,2,2-trifluoroethanol, the P(III)-Cl end reacts and the proton from the liberated HCl adds to the nitrogen at P=N-*t*-butyl end to afford **15** (eq. 2). The cation in this compound

can be considered to be a protonated form of the betaine $(CF_3CH_2O)P(\mu\text{-}N\text{-}t\text{-}Bu)_2P^+[(NH\text{-}t\text{-}Bu)\{N\text{-}(CO_2\text{-}i\text{-}Pr)\text{-}N^-(CO_2\text{-}i\text{-}Pr)]$. An X-ray structural analysis clearly reveals the hydrogen-bonded chloride (see section 5.4). This kind of species [cf. structure $[ROC(O)N\{^+PPh_3\}NHC(O)OR][R'COO]^-$ (**II**) in Scheme 4.2 of Chapter 4] is *one of the intermediates proposed in the Mitsunobu reaction*.

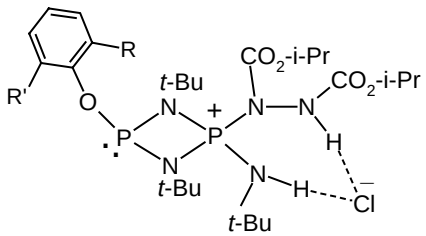


8 **15** [δ(P) 11.7, 114.4; ^2J = 14.1 Hz]

We extended this reaction of **8** with the phenols $2,6\text{-}Cl_2C_6H_3OH$, $2,6\text{-}Me_2C_6H_3OH$, $2\text{-}Me\text{-}6\text{-}t\text{-}BuC_6H_3OH$ and $2,6\text{-}(t\text{-}Bu)_2C_6H_3OH$. The ^{31}P NMR spectra of the products **16**-**19** [compound **19** was obtained in a state of purity ~90%; others were analytically pure] thus obtained showed two phosphorus signals in the region 10±2 and 116±4 ppm that correspond to a basic structure similar to **15**. Although analytical data obtained for **17**-**18** were consistent with a structure analogous to that of **15**, the data for **16** showed an additional 2,6-dichlorophenol moiety that was confirmed by X-ray structure determination (section 5.4). The assignment of structure for **19** is based on ^1H NMR integrated intensities. The ^{31}P NMR spectrum of the reaction mixture of **8** with benzoic acid showed mainly (>65%) two peaks at δ 10.5 and 103.3, which suggests that the product has a structure similar to **15** (with benzoate in place of the alkoxy group); however it could not be isolated.



16 [δ(P) 10.9 (br), 115.9 (br)]



17 [R = R' = Me; δ(P) 10.7(d), 119.5(d), ^2J = 11.0 Hz]

18 [R = Me, R' = t-Bu; δ(P) 9.4(d), 114.6 (d), ^2J = 10.4 Hz]

19 [R = R' = t-Bu; δ(P) 9.4(d), 114.9(d), ^2J = 11.2 Hz]

It would be interesting to see if a species analogous to **16** but with Cl^- replaced by a carboxylate anion can be isolated. Such a species would be important in the context of mechanism of Mitsunobu reaction, but we have not been successful as yet.

When we treated compound **9** with 2,2,2-trifluoroethanol and attempted to crystallize the product, the starting material **9** was recovered. However, when we monitored the same reaction using various phenols as well as trifluoroethanol by ^{31}P NMR, we found that there was a significant change in the spectra with both the signals of **9** moving significantly downfield [cf. Figure 3]. This, however, was not the case when isopropanol or water was treated with **9** and the spectrum remained essentially unchanged. Thus it appears that a more acidic proton like the ones in trifluoroethanol or phenols is required for a significant interaction; we assign the structure **VIII** for the products in these reactions.

Table 1. NMR data for the products from the addition of alcohols/ phenols to **9**

Sl. no	Phenol/ alcohol/ water	Product ^1H NMR for PNN*H* (δ)	Product ^{31}P NMR (δ)
1	NONE	2.45	-28.9, 68.9 (compound **9**)
2	Tetrachlorocatechol	3.14	-1.0, 81.2[a]
3	Catechol	3.08	-2.9, 80.2[b]
4	2,2'-Biphenol	3.02	-2.7, 80.6
5	Phenol	2.94	-9.7, 76.1
6	Trifluoroethanol	3.12	0.5, 81.2[c]
7	Isopropanol	2.59	-25.9, 69.4
8	Water	2.66	-26.6, 69.2

[a] ^1H NMR: δ 1.10-1.53 (many lines, ca 48 H, (CH(C*H*$_3$)$_2$) + PN*t*-Bu-*H*), 3.14 (d, ^3J(PH) ~ 4.0 Hz, PNN*H*), 5.02 (m, 2 H, C*H*(CH$_3$)$_2$), 7.60 (br, ~3 H, O*H* + NH). ^{13}C NMR: δ 21.5, 21.6, 21.7, 30.8, 30.9, 31.3, 32.3, 32.4, 52.6, 52.8, 54.8, 55.2, 55.4, 70.3, 70.8, 115.7, 116.9, 148.4, 152.4, 152.6, 156.5.

[b] ^1H NMR: δ 1.25-1.46 (many lines, ca 48 H, (CH(C*H*$_3$)$_2$) + PN*t*-Bu-*H*), 3.08 (d, ^3J(PH) ~ 4.0 Hz, PNN*H* 4.98 (m, 2 H, C*H*(CH$_3$)$_2$), 6.50- 6.90 (m, 4 H, Ar-*H*), 9.05 (br, ~3 H, O*H* + NH). ^{13}C NMR: δ 21.5, 21.6, 21.6, 25.0, 28.9, 30.3, 30.9, 31.0, 31.2, 31.7, 32.3, 32.4, 53.9, 54.5, 54.6, 64.2, 70.6, 77.2, 115.8, 119.4, 145.6, 152.6, 156.5.

[c] An additional set (ca 30 %) of broad peaks at δ -20.7 and 71.6 was noticed.

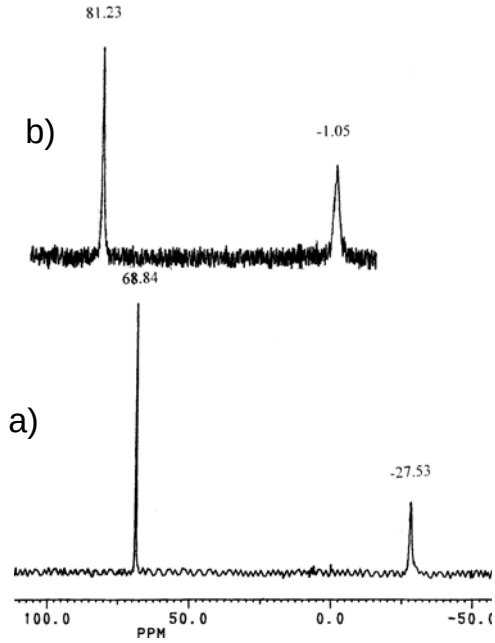
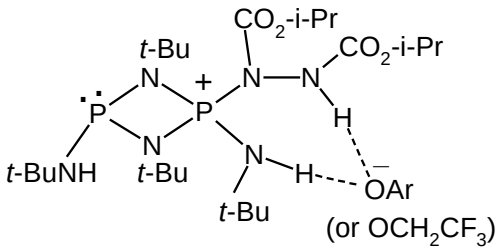


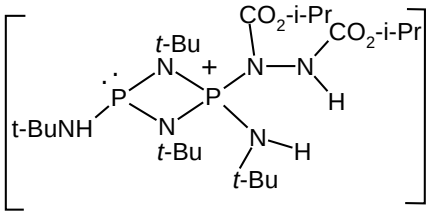
Figure 3. The ^{31}P NMR spectra of (a) **9** and (b) immediately after the addition of 1,2-tetrachlorocatechol to **9**.



VIII

When benzoic acid was added to a solution of **9** prepared *in situ*, the ^{31}P NMR of the solid obtained (after removal of all solvent) exhibited two major peaks (~ 95 %) at δ 80.7 and 1.1 (^{2}JPP < 7.0 Hz) that are quite different from that of **9**, but clearly in the tri- and tetra-coordinate region. The ^{1}H NMR spectrum is also different from that of **9** and the integrated intensities agree with structure **20**. Interestingly, the two methyl group protons of each $CHMe_2$ group show non-equivalence resulting in the observation of 4 doublets in the ^{1}H NMR [Figure 4; cf. expanded region]. The two ring N-*t*-butyl groups are also shown up separately and thus four different signals for the $C(CH_3)_3$ protons are observed; this situation is not common in the NMR spectra of cyclodiphosphazane derivatives. In the ^{13}C NMR such a difference is not very clearly seen. These data are consistent with the structure given below that is essentially the type of intermediate [cf. structures of **II** (in Scheme 4.2 in Chapter 4) and **15**] proposed in the Mitsunobu reaction. We were

able to obtain **20** and analogous compounds **21**-**24** by this route; compound **20** is characterized by X-ray crystallography (section 5.4).



$[RCO_2]^-$

R = Ph [**20**: δ(P) 1.1, 81.0]

4-Cl-$C_6H_4CH_2$ [**21**: δ(P) 0.1 (br), 80.4 (br)]

4-Br-C_6H_4 [**22**: δ(P) 2.1, 81.5]

4-NO_2-C_6H_4 [**23**: δ(P) 2.9, 82.0]

4-Me-$C_6H_4SO_3^-$ instead of RCO_2^- [**24**: δ(P) 2.3, 82.2]

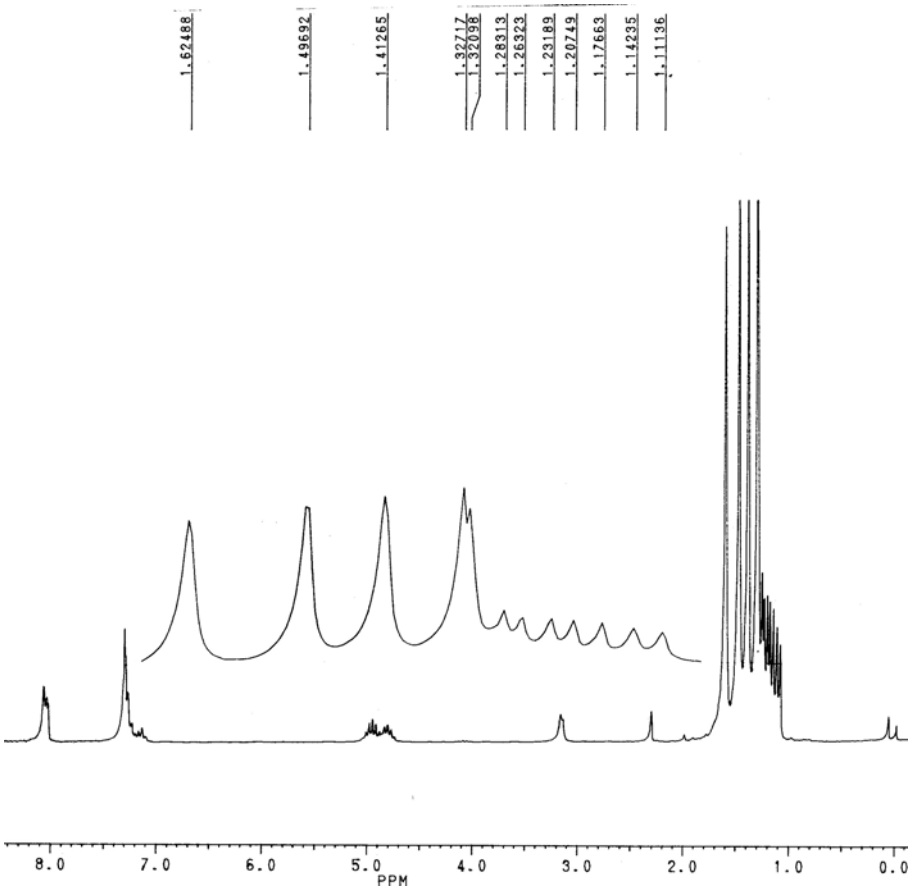
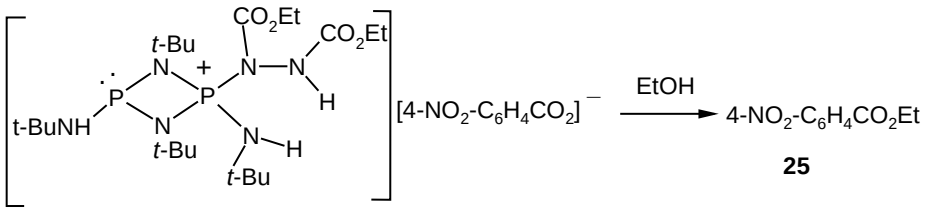


Figure 4. The ^{1}H NMR spectrum of **20**

We could effect esterification using the *in situ* formed (*t*-BuNH)P(μ-N-*t*-Bu)$_2$P$^+$[(HN-*t*-Bu){N-(CO_2Et)-N(H)(CO_2Et)](4-NO_2-$C_6H_4CO_2^-$) [**IX**: δ(P) 3.8 and 82.9(P); the structure should be analogous to that of the DIAD analogue **23**] and ethanol leading to the ester **25** (Scheme 3). Although the reaction did not take place

at room temperature [as expected, because we could isolate the intermediates as stable species], the esterification took place readily at 80°C.

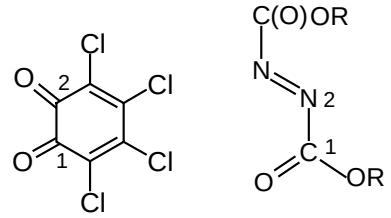
Scheme 3



IX

5.3 Oxidative Addition of *o*-Chloranil to Cyclodiphosphazane Compounds

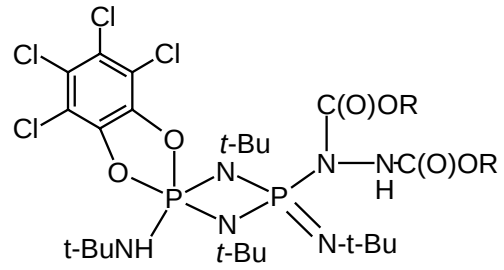
A second point of interest we had in the present study was to see if the P(III) centers undergo ready oxidation with *o*-chloranil to give rise to stable pentacoordinated compounds. It can be noted the both the dialkyl azodicarboxylates and *o*-chloranil possess 1,2-double bonds; although in our above reactions of cyclodiphosphazanes with DIAD/ DEAD pentacoordinate species were not isolated, in other studies conducted using cyclic phosphites, we did isolate several pentacoordinate phosphoranes with interesting 'apicophilicity' problems [compounds **II-IV** above are a few of them].[14]



o-Chloranil Dialkyl azodicarboxylate

Oxidative addition of *o*-chloranil (tetrachloro-1,2-benzoquione) to **9** and **10** leads to the novel compounds **26** and **27**, respectively, containing both tetra- and pentacoordinate phosphorus centres. The reaction is fairly clean which is unlike previous reports utilizing other 1,2-diketones.[107] Both **26** and **27** exhibit a pair of doublets each in the ^{31}P NMR [Figure 5]. with a large ^{2}J(PNP) value; the up-field signal is assigned to the pentacoordinate phosphorus [cf. δ(P) for **28** below: –51.6]. The downfield ^{31}P NMR signal (assigned to tetracoordinate phosphorus) is broad in

both the compounds suggesting some exchange at this center. In the ^{13}C NMR [Figure 6], the three types of $C(CH_3)_3$ and $C(CH_3)_3$ carbons were easily distinguished in these compounds, but not much information could be obtained from ^{1}H NMR. The reaction of **11** with *o*-chloranil did not give rise to a single product but the reaction mixture showed both tetra- and penta-coordinate phosphorus [^{31}P NMR].



R = *i*-Pr [**26**, δ(P) -51.2, -35.1; ^{2}J = 89.6 Hz]
Et [**27**, δ(P) -51.9, -36.7; ^{2}J = 89.6 Hz]

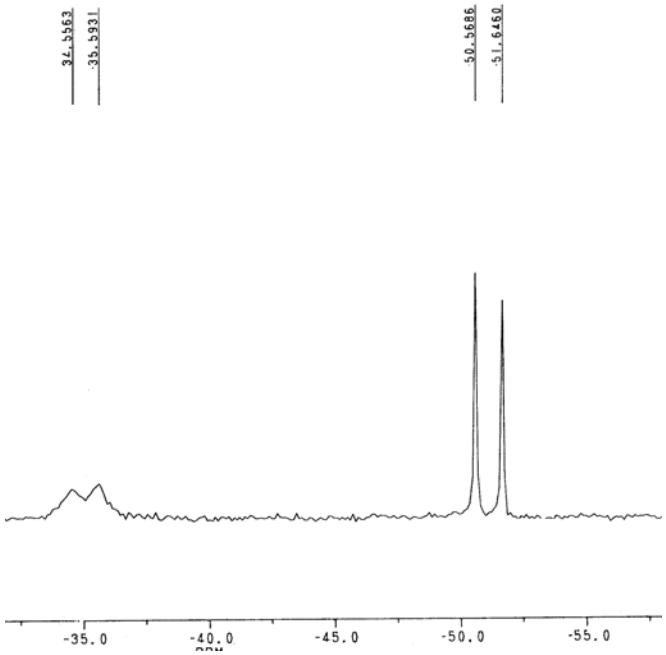


Figure 5. The ^{31}P NMR spectrum of **26**

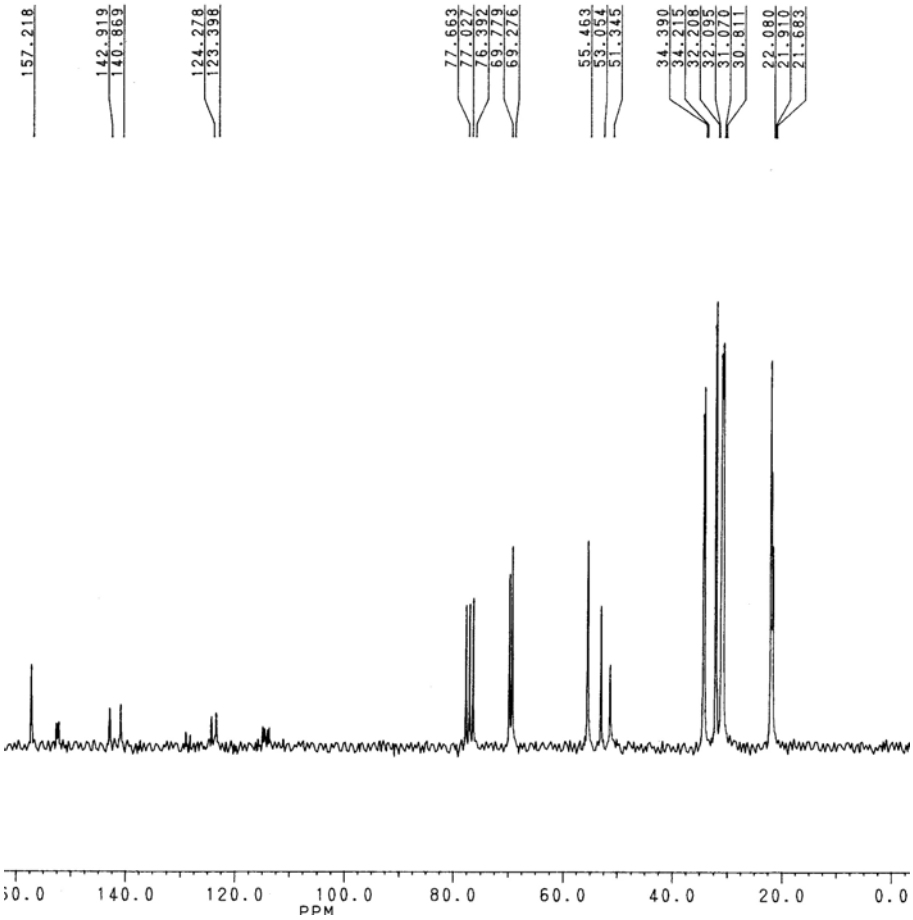
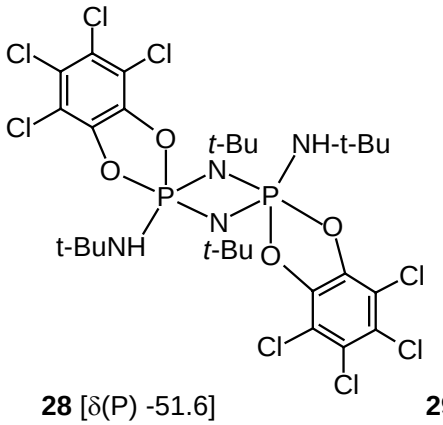
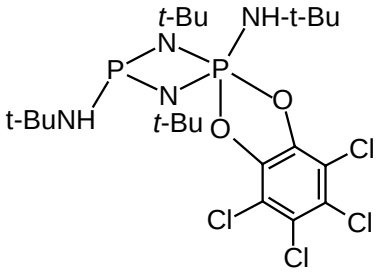


Figure 6. The ^{13}C NMR spectrum of **26**

The reaction of **3** with two mole equivalents of *o*-chloranil gives the bis-cycloaddition product **28** cleanly. By lowering the stoichiometry, we could also observe the mono-cycloadduct [$(C_6Cl_4$-1,2-$O_2)$(*t*-BuNH)P-(μ-N-*t*-Bu)$_2$PNH-*t*-Bu] (**29**) with P(III)-N-P(V) skeleton by ^{31}P NMR [δ 68.3, -39.5, ^2J(PP) = 16.0 Hz]. These were the only two products observed and thus, here also, the cycodiphosphazane ring remains intact.



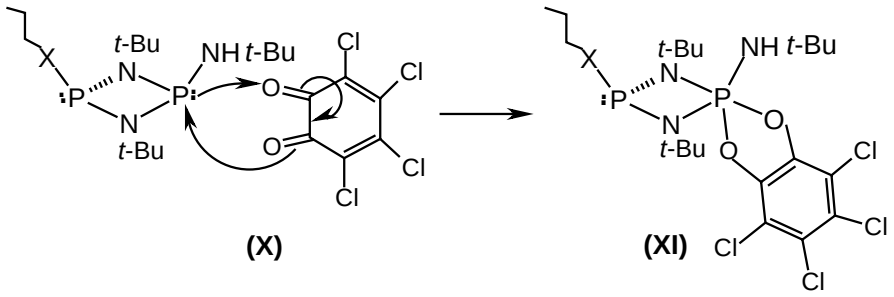
28 [δ(P) -51.6]



29 [δ(P) -39.5(d), 68.3(d); ^2J = 16.0 Hz]

A probable pathway for the oxidative addition of *o*-chloranil to **9-11** via species **X** and **XI** is depicted in Scheme 4.[109]

Scheme 4



5.4 X-ray Structural Studies

The molecular structures of **8** and **10-11** are shown in Figures 7-9. Selected geometrical parameters are given in Table 2. There are two molecules in the asymmetric unit of **8**, but only one is shown; the bond parameters in the second molecule are essentially identical to the first one. The methyl carbons of the *t*-butyl group at N(1) in **11** are disordered, but in the figure only one of the possible orientations is shown.

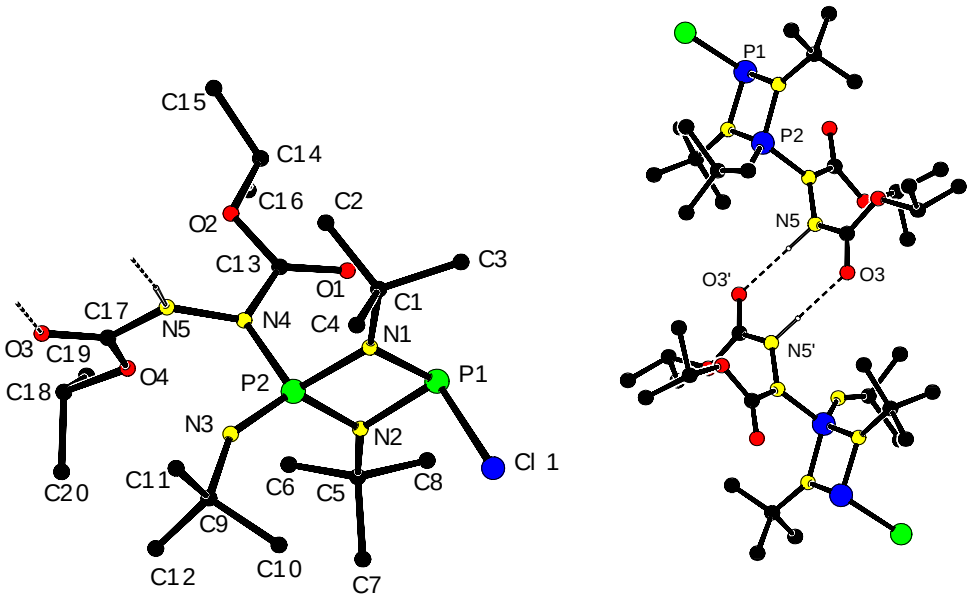


Figure 7. Molecular structure of **8**; only selected atoms are labeled. On the right hand side is shown the hydrogen bonded dimer. The second molecule in the asymmetric unit is not shown. Hydrogen bonded D-H, H..A, D…A and D-H…A parameters: N(5)-H(N5)…O(3') [dimer] 0.93(4), 1.96(4), 2.892(4)Å, 175(3)°. N(10)- H(N10)… O(7') [dimer, not shown] 0.91(4), 1.95(4), 2.862(4) Å, 179(3) °.

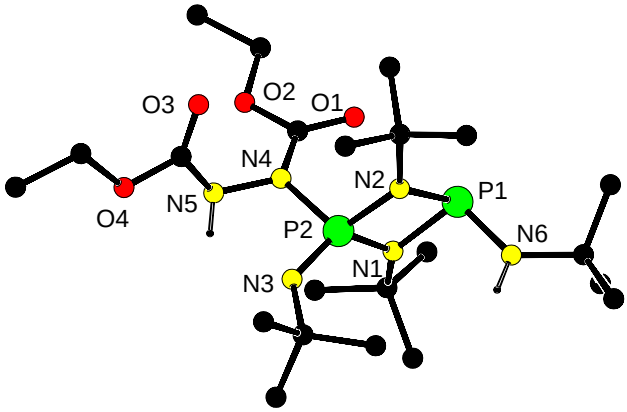


Figure 8. A plot showing the molecular structure of **10**; only selected atoms labeled with the hydrogen atoms [except on N(5)] not shown. There was no discernible hydrogen bonding in the structure.

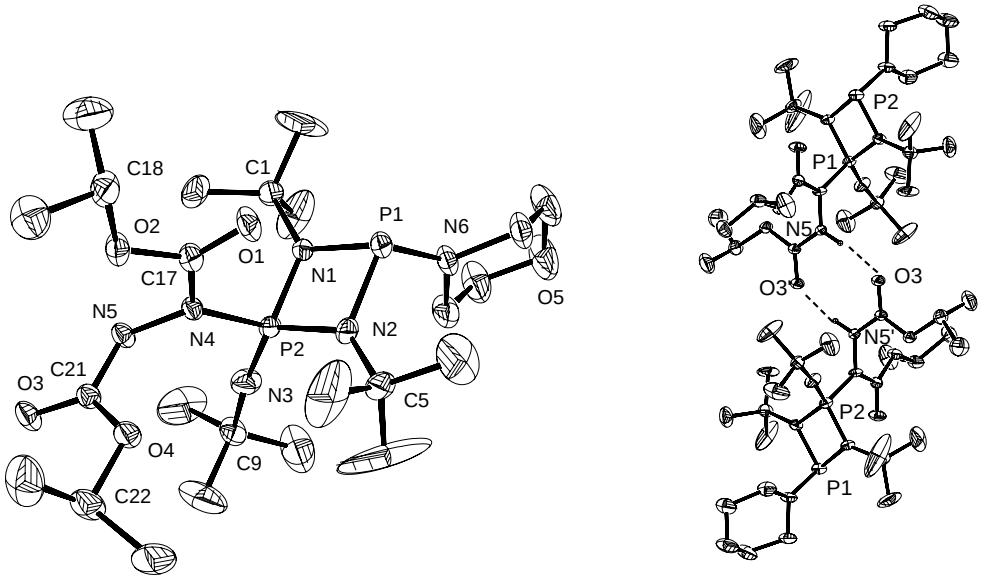


Figure 9. Molecular structure of **11**; only selected atoms labeled. On the right side is shown the dimer formation *via* N(5)-H(5)…O(3') hydrogen bonding. Hydrogen bond parameters [N-H, H…O, N…O, N-H…O]: 0.86Å, 2.05Å, 2.899(4) Å, 167.4^{o}

Table 2. Bond parameters (Å, ^{o}) with esd's in **8**, **10** and **11**

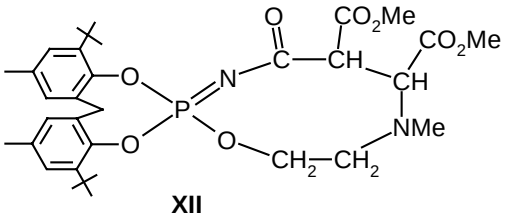
Bond parameter	Compound **8***	Compound **10**	Compound **11**
P(1)-N(1)	1.680(3)	1.742(1)	1.726(3)
P(1)-N(2)	1.695(3)	1.755(1)	1.741(3)
P(1)-Cl(1) (for **8**) or P(1)-N(6) (for **10**-**11**)	2.142(2)	- 1.668(1)	- 1.670(3)
P(2)-N(1)	1.681(3)	1.653(1)	1.657(3)
P(2)-N(2)	1.674(3)	1.659(1)	1.650(3)
P(2)-N(3)	1.488(3)	1.533(1)	1.464(3)
P(2)-N(4)	1.723(3)	1.729(1)	1.747(3)
N(1) - P(1) – N(2)	82.62(14)	79.74(5)	79.52(13)
N(2) – P(2) – N(1)	83.21(14)	85.21(5)	84.20(14)
C(1) – N(1) – P(1)	128.8(2)	129.0(1)	127.2(2)
C(1) - N(1) - P(2)	133.6(2)	132.2(1)	132.8(2)
P(1) – N(1) – P(2)	97.2(1)	97.67(5)	98.2(1)
C(5) - N(2) - P(2)	134.3(3)	131.7(1)	133.9(2)
C(5) – N(2) – P(1)	128.1(2)	126.8(1)	128.0(2)
P(2) - N(2) - P(1)	96.9(1)	96.9(1)	97.9(1)
C(9) – N(3) – P(2)	147.8(3)	133.3(1)	172.5(3)
ΣN4[a]	359.0	358.6	359.2
ΣN5	357.8	336.7	360.0
ΣN6	-	359.3	358.7

*For the second molecule in the asymmetric unit: P(3)-N(6) 1.686(3), P(3)-N(7) 1.684(3), P(3)-Cl(2) 2.160(2), P(4)-N(6) 1.676(3), P(4)-N(7) 1.668(3), P(4)-N(8) 1.481(3), P(4)-N(9) 1.720(3), N(7) - P(3) - N(6) 82.31(14), N(7) P(4) N(6) 83.09(14), C(29) - N(8) - P(4) 146.4(4), ΣN6 (ring) 359.0^{o}, ΣN7 (ring) 359.2^{o}, ΣN9 358.9^{o}, ΣN10 357.7^{o}.

[a] Σ represents the sum of the bond angles around this atom.

The X-ray structures of **8** and **11** show ***a very short*** P=N bond [P(2)-N(3) 1.488(3) Å in **8** and 1.464(3) Å in **11**] and the values are pretty close to that generally observed for P=O (cf. compound **13**). For further comparison, it can be noted that the P=N bond length in the monophosphazene $Ph_3P{=}NC_6H_4Br$ is 1.57

Å[108] and in **XII** is 1.550 Å[110] Thus it is possible that the nitrogen [N(3)] in these compounds is strongly involved in π-bonding with phosphorus; the linearity at the imino nitrogen N(3) in **11** also indicates such a possibility.



XII

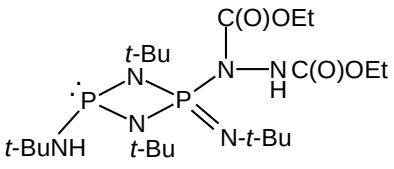
The structure of **10** reveals another interesting situation due to the following observations:

(a) The P(2)-N(3) distance of 1.533(1) Å is much longer than those found in **8** or **11**.

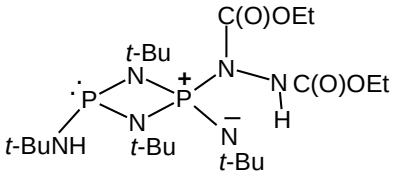
(b) It does not form a hydrogen bonded dimer which is unlike that exhibited by **8** or **11**. The N(5)-H and C=O(3) are *transoidal* in **10** whereas they are *cisoidal* in **8** and **11**. In fact in **10** the N(5)-H proton to is quite close to N(3) [2.215 Å].

(c) The sum (Σ) of the bond angles at N(5) is 336.7^{o} and hence this nitrogen is quite far from planar (or more pyramidal); the corresponding nitrogen in **8** or **11** are essentially planar (cf. Table 2).

Thus it is possible that in **10**, there is an additional contribution from the phosphonium isomer **10'**.



10



10'

The endocyclic P-N distances at the tricoordinate P(1) in **10**-**11** are close to that expected for a single bond[108] but longer than those at the tetracoordinate phosphorus P(2). The corresponding distances are shorter in **8**, possibly due to lesser competition for additional π-interaction (or due to negative hyperconjugation.[111]) with the nitrogen atoms. However all these P-N distances are in the normal range (1.65-1.74 Å) found for analogous compounds[96,108,112a-j].

For **13** (Figure 10; Table 3), we could not match the systematic absences with any of the orthorhombic space groups; however these agreed with that expected for the monoclinic space group $P2_1/a$ with twinning. An additional feature observed here is that the highest residual electron density is close [~1.3Å] to phosphorus at P(2) suggesting that there is partial oxidation at this centre. Although we did not attempt to refine the structure incorporating this slight nonstoichiometry [ca 7% of the bis oxidized product, based on ^{31}P NMR], it is interesting to note that analogous monosulfur product also showed this feature [96] The ^{31}P NMR spectra in both of these cases showed an additional sharp peak expected for the bis-oxidized (or sulfurized) product. The oxygen occupancy at P(2) increased upon further recrystallization of **13** in air [X-ray evidence].

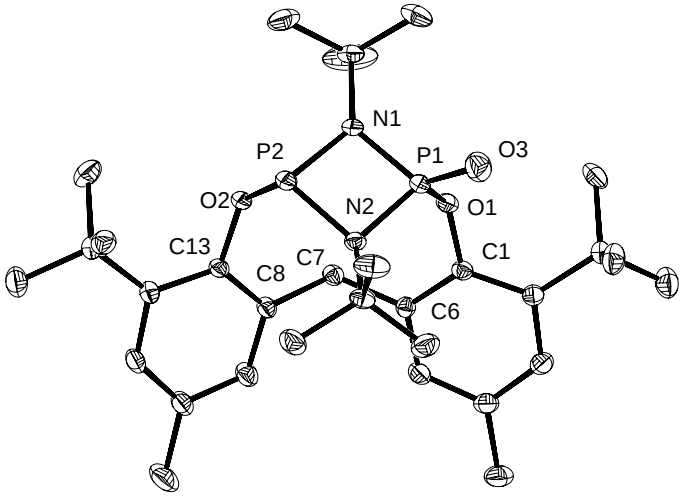


Figure 10. An ORTEP drawing of **13**; only selected atoms are labeled.

Table 3. Selected bond lengths (Å) and bond angles (^{o}) for **13** with esd's

P(1)-N(1)	1.660(3)	O(3)-P(1)-N(1)	119.87(19)
P(1)-N(2)	1.679(3)	O(3)-P(1)-O(1)	113.10(19)
P(1)-O(1)	1.618(3)	O(1)-P(1)-N(2)	109.26(15)
P(1)-O(3)	1.433(4)	O(3)-P(1)-N(2)	120.1(2)
P(2)-N(1)	1.697(3)	O(2)-P(2)-N(2)	105.63(14)
P(2)-N(2)	1.719(3)	N(1)-P(2)-N(2)	83.38(16)
P(2)-O(2)	1.642(3)	O(2)-P(2)-N(1)	102.55(16)

P(1)…P(2)	2.494(1)	N(1)-P(2)-N(2)	83.38(16)
		O(2)-P(2)-N(1)	102.55(16)
N(1)-P(1)-N(2)	85.76(15)	P(1)-N(1)-P(2)	95.99(17)
O(1)-P(1)-N(1)	105.15(18)	P(1)-N(2)-P(2)	94.43(15).

The P-N as well as the P-O single bond distances at the tetracoordinate phosphorus in **13** are distinctly shorter than those at the tricoordinate phosphorus. The mean P-N distances in **13** [1.678Å] are also shorter than those in its precursor [(*t*-BuN)P]$_2$[O-6-*t*-Bu-4-Me-C$_6$H$_2$]$_2$CH$_2$} (**4**) [1.712Å][112f], but closer to the monosulfur product [(S)P(μ-N-*t*-Bu)$_2$P][O-6-*t*-Bu-4-Me-C$_6$H$_2$]$_2$CH$_2$ (**VII**).[96]

The molecular structures of **15** and **16** are shown in figures 11 and 12 respectively; the bond parameters are shown in Table 4.

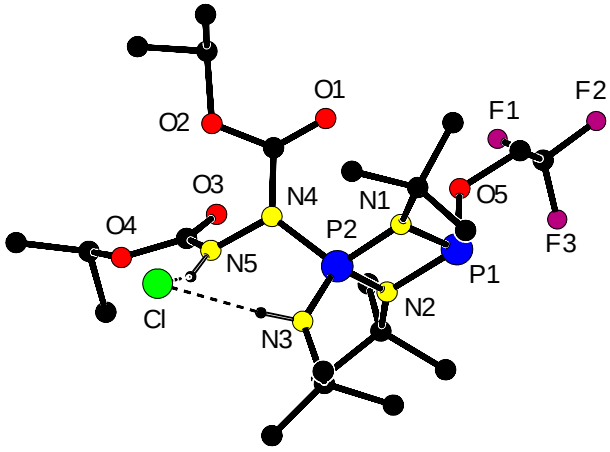


Figure 11 A plot showing the molecular structure of compound **15**. D-H, H..A, D…A and D-H...A parameters: N(3)-H(3)…Cl 0.86, 2.33, 3.166(2)Å, 162.9^o; N(5)-H(5)…Cl 0.86, 2.35, 3.084(1), 143.1^o.

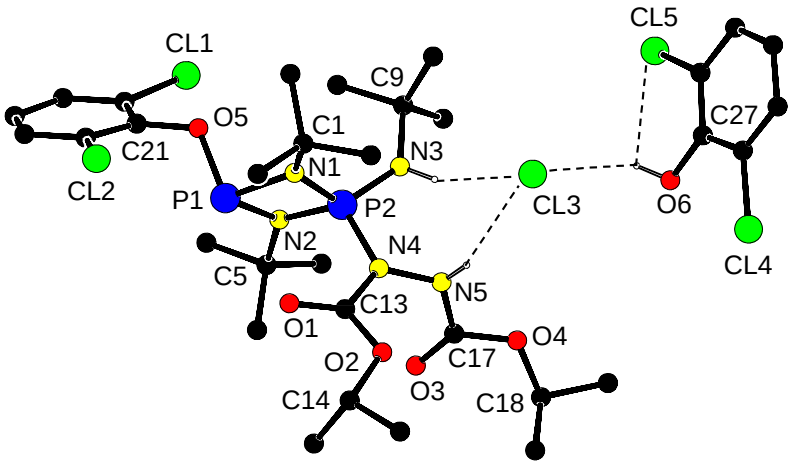


Figure 12. A plot showing the molecular structure of compound **16**. Hydrogen bond D-H, H..A, D…A and D-H...A parameters: N(3)-H(N3)…Cl(3) 0.81(5), 2.58(5), 3.313(4) Å, 150(5)^{o}; N(5)-H(N5)…Cl(3) 0.72(4), 2.45(5), 3.121(5) Å, 156(4)^{o}; O(6) – H(6)… Cl(3) 0.82, 2.33, 3.089(4) Å, 153.7^{o}; O(6) – H(6)…Cl(5) 0.82, 2.63, 2.997(5) Å, 109.1^{o}

Table 4. Selected bond lengths (Å) and bond angles (^{o}) with esd's for **15** and **16**

Compound	**15**	**16**
P(1)-N(1)	1.734(2)	1.733(3)
P(1)-N(2)	1.7240(17)	1.752(4)
P(1)-O(5)	1.6267(16)	1.670(3)
P(2)-N(1)	1.6242(16))	1.636(4)
P(2)-N(2)	1.6338(16)	1.642(3)
P(2)-N(3)	1.5888(16)	1.594(3)
P(2)-N(4)	1.6866(17)	1.691(4)
P(1)…P(2)	2.499(1)	2.505(1)
N(1)-P(1)-N(2)	80.78(7)	80.61(16)
N(1)-P(2)-N(2)	86.91(8)	86.92(17)
P(1)-N(1)-P(2)	96.14(8)	96.01(19)
P(1)-N(2)-P(2)	96.17(8)	95.05(19)
C(9)-N(3)-P(2)	134.44(13)	132.1(3)
ΣN1	359.0	358.9

ΣN2	359.6	353.2
ΣN3	360.0	359.7
ΣN4	359.8	360.0
ΣN5	360.0	359.3

In compounds **15** and **16**, the P-N distances at the tricoordinate phosphorus P(1) are longer than those at the tetracoordinate phosphorus P(2), as was the case for compounds **10** and **11**. The P(2)-N(3) distances are the shortest, but compared to the analogous distances in **8** or **11**, are significantly longer; this feature is in line with a P(2)-N(3) single bond in **15-16** with additional π-interaction (or hyperconjugative effects through the nitrogen lone pair of electrons).

A significant difference between the structures of **15** and **16** is the disposition of P(III)-OR (or OAr) and P-NH-*t*-Bu groups; whereas in the former the two groups are *transoidal*, in the latter they are *cisoida*l. Since the common starting compound **8**, has a *cisoidal* disposition of Cl and N-*t*-Bu groups, attack of nucleophile from the opposite direction would lead to *transoidal* disposition of incoming group with respect to the N-*t*-Bu group; this is observed in **15**. However, if there is isomerization (see Introduction, Chapter 4) leading to the thermodynamically stable form, a *cisoidal* geometry, as observed in **16** could result. Thus the two structures present an interesting point to study further (although not done here).

In the formation of both **15** and **16**, the proton of the liberated HCl is taken up by the P=N-*t*-Bu group, and the chloride anion is hydrogen bonded *intramolecularly* to the protons of the N*H*-*t*-Bu and P-N(COOR)-N*H*(COOR) groups. In **16**, the same chlorine is also involved in additional hydrogen bonding interactions with 2,6-dichlorophenol. These results suggest that even in the Mitsunobu reaction also, hydrogen bonding may play a significant role in holding different species together.

The molecular structure of **20** is shown in Figure 13. Only one of the two molecules present in the asymmetric unit is shown; the bond parameters in the other molecule are essentially the same. Selected bond parameters are given in Table 5.

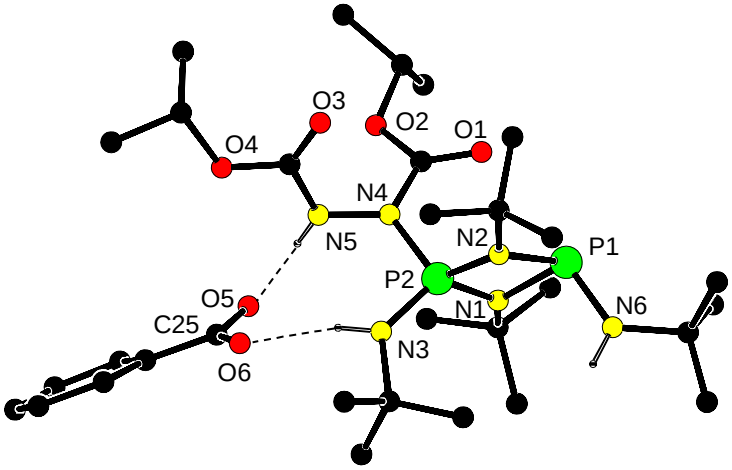


Figure 13. Molecular structure of **20**; only selected atoms are labeled. Hydrogen bond D-H, H..A, D…A and D-H...A parameters: N(3)-H(N3)…O(6) 0.85(2), 1.98(3), 2.807(2) Å, 166(2)°; N(5)-H(N5)…O(5) 0.88(3), 1.80(3), 2.678(2) Å, 172(3)°; N(9)-H(N9)…O(11) 0.89(2), 1.95(2), 2.804(2) Å, 161(2)°; N(11)-H(N11)…O(12) 0.73(3), 1.95(3), 2.673(2) Å, 169(3)°

Table 5. Selected bond lengths (Å) and bond angles (°) with esd's for **20**

Molecule 1		**Molecule 2**	
P(1)-N(1)	1.7616(15)	P(3)-N(7)	1.7621(16)
P(1)-N(2)	1.7672(16)	P(3)-N(8)	1.7706(16)
P(1)-N(6)	1.6521(19)	P(3)-N(12)	1.6534(19)
P(2)-N(1)	1.6280(15)	P(4)-N(7)	1.6267(16)
P(2)-N(2)	1.6367(15)	P(4)-N(8)	1.6303(15)
P(2)-N(3)	1.5900(17)	P(4)-N(9)	1.5959(17)
P(2)-N(4)	1.6913(15)	P(4)-N(10)	1.7021(16)
P(1)…P(2)	2.5378(7)	P(3)…P(4)	2.5336(8)
N(1)-P(1)-N(2)	78.71(7)	N(7)-P(3)-N(8)	78.58(7)
N(1)-P(2)-N(2)	86.54(8)	N(7)-P(4)-N(8)	86.76(8)
P(1)-N(1)-P(2)	96.88(8)	P(3)-N(7)-P(4)	96.69(8)
P(1)-N(2)-P(2)	96.34(8)	P(3)-N(8)-P(4)	96.22(8)

C(9)-N(3)-P(2)	129.81(15)	C(40)-N(9)-P(4)	129.22(15)
ΣN1	359.4	ΣN7	357.6
ΣN2	355.5	ΣN8	355.2
ΣN3	359.9	ΣN9	358.4
ΣN4	359.9	ΣN10	359.9
ΣN5	359.0	ΣN11	359.1
ΣN6	360.0	ΣN12	359.5

The P(III)-N bond distances in the cyclodiphosphazane ring in both the molecules of **20** are noticeably longer than those found in **8**, **10**, **11**, **15**, or **16**. The P-N(H-*t*-Bu) distances at the tetracoordinate phosphorus P(2) or P(4), although longer than those found in **8**, **10** or **11**, are still the shortest in each molecule. More significant is the hydrogen bonding that holds the carboxylate with the phosphorus substrate; one of the carboxylate oxygen atoms [O(6)] is connected to the N*H*-*t*-Bu proton while the other [O(5)] is connected to N-N*H*(COOR) proton. Other bond parameters are normal and the molecules retain the *cisoidal* geometry of the two NH-*t*-Bu groups.

In compounds **26** (Figure 14) and **27** (Figure 15a-b) both of which possess penta- and tetracoordinate phosphorus centres, the ring P-N bond distances are alternatively long and short, with the apical P-N at the pentacoordinate phosphorus [P(1)] being the longest, as expected (Table 6).[97,113] The geometry at P(1) is slightly distorted trigonal bipyramid. As regards the exocyclic P=N, the distances in **26** and **27** are longer than that observed in compound **11**; the bond angles, unlike in **11**, are also quite far from linearity.

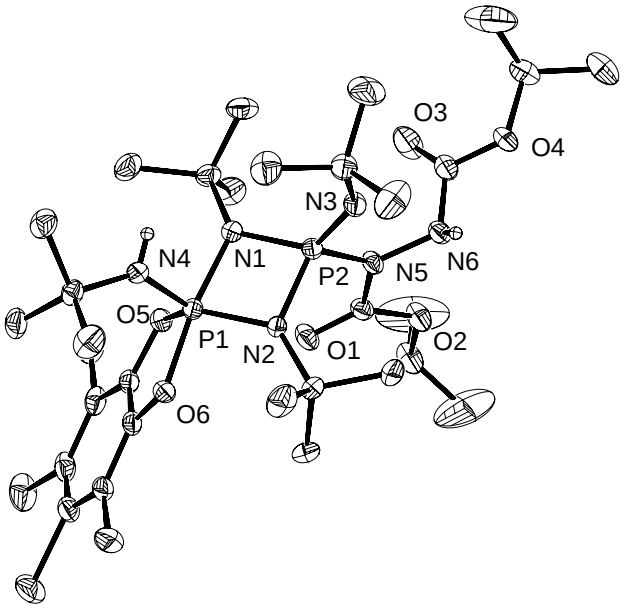


Figure 14. Molecular structure of **26**; only selected atoms labeled and the solvent is not shown.

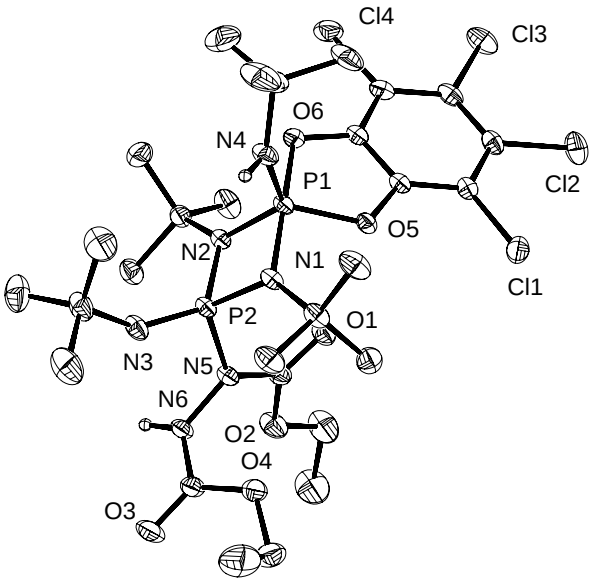


Figure 15a. Molecular structure of **27**; only selected atoms are labeled.

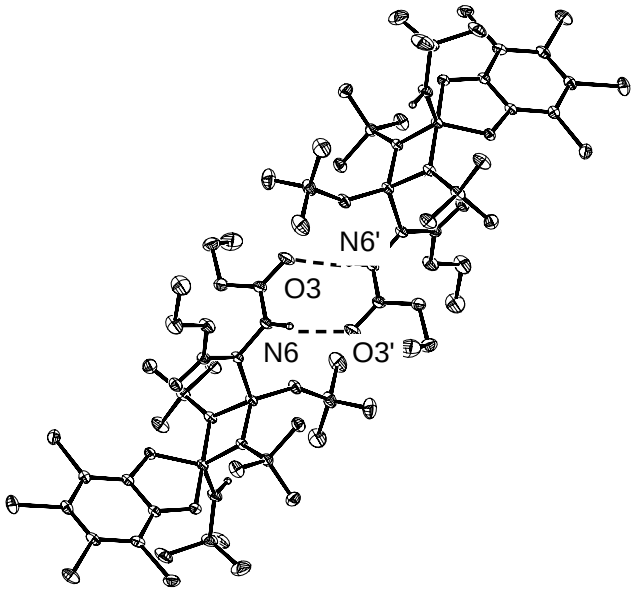


Figure 15b. Molecular structure of **27** showing the dimer *via* N(6)-H(6)…O(3') hydrogen bonding. Hydrogen bond parameters [N-H, H…O, N…O, N-H…O]: 0.86 Å, 2.03 Å, 2.865(3) Å, 163.7°.

Table 6. Selected bond parameters (Å, °) for **26** and **27**.$C_6H_5CH_3$ with esd's

Compound	**26**	**27**.$C_6H_5CH_3$
P(1)-N(1)	1.749(2)	1.755(2)
P(1)-N(2)	1.687(2)	1.688(2)
P(1)-N(4)	1.643(2)	1.637(2)
P(1)-O(5)	1.659(2)	1.664(2)
P(1)-O(6)	1.733(2)	1.738(2)
P(2)-N(1)	1.651(2)	1.654(2)
P(2)-N(2)	1.689(2)	1.694(2)
P(2)-N(3)	1.509(2)	1.503(2)
P(2)-N(5)	1.720(2)	1.727(2)
P(1)…P(2)	2.539(1)	2.541(1)
N(1)-P(1)-N(2)	81.35(10)	81.55(8)
N(1)-P(1)-N(4)	94.85(11)	94.74((9)

N(1)-P(1)-O(5)	90.44(9)	90.14(7)
N(1)-P(1)-O(6)	172.08(10)	172.65(8)
N(2)-P(1)-N(4)	119.87(11)	120.82(9)
N(2)-P(1)-O(5)	124.76(10)	123.20(8)
N(2)-P(1)-O(6)	92.36(9)	92.83(8)
N(4)-P(1)-O(5)	115.21(11)	115.82(9)
N(4)-P(1)-O(6)	92.46(11)	92.21(9)
O(5)-P(1)-O(6)	89.21(9)	89.00(7)
N(1)-P(2)-N(2)	84.22(10)	84.39(8)
N(1)-P(2)-N(3)	126.06(12)	125.80(9)
N(1)-P(2)-N(5)	113.32(11)	112.04(9)
N(2)-P(2)-N(3)	124.43(12)	125.08(10)
N(2)-P(2)-N(5)	107.05(10)	106.31(8)
N(3)-P(2)-N(5)	101.06(11)	102.08(9)
P(1)-N(1)-P(2)	96.61(11)	96.33(9)
P(1)-N(2)-P(2)	97.54(10)	97.41(8)
C(9)-N(3)-P(2)	137.8(2)	142.9(2)

In compound **11**, one phosphorus in the cyclodiphosphazane ring is tricoordinate whereas the other is tetracoordinate; in **26** and **27**, one is pentacoordinate and the other is tetracoordinate. In compound **28** (Figure 16, Table 7), both the phosphorus atoms are pentacoordinate and the geometry is trigonal bipyramidal with much less distortion than that found in **26** and **27**. The ring nitrogen which is apical with respect to P(1) is equatorial with respect to P(2) and *vice versa*; as expected, the apical bonds are longer. The exocyclic P-N(H)(*t*-Bu) bonds in **28** [mean 1.641Å] are shorter compared to those in its P(III) precursor [(*t*-BuNH)P-N-*t*-Bu]$_2$ (**3**) [1.664 Å];[114] even the mean cyclophosphazane P-N distance in **28** [1.698Å] is shorter than that in **2** [mean 1.728Å]. These observations suggest that the overall involvement of the nitrogen lone pair in additional bonding to phosphorus may be greater in pentacoordinate than in tricoordinate phosphorus.

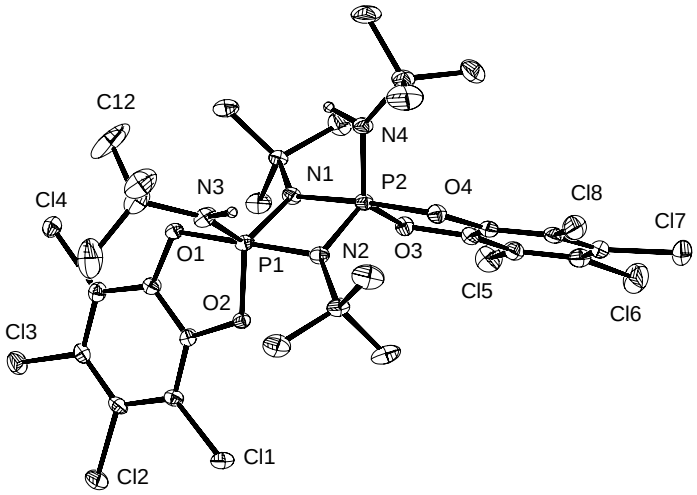


Figure 16. Molecular structure of **28**.½$C_6H_5CH_3$; only selected atoms are labeled and the solvent molecule is not shown.

Table 7 Selected bond parameters (Å, ^{o}) for **28**.½$C_6H_5CH_3$

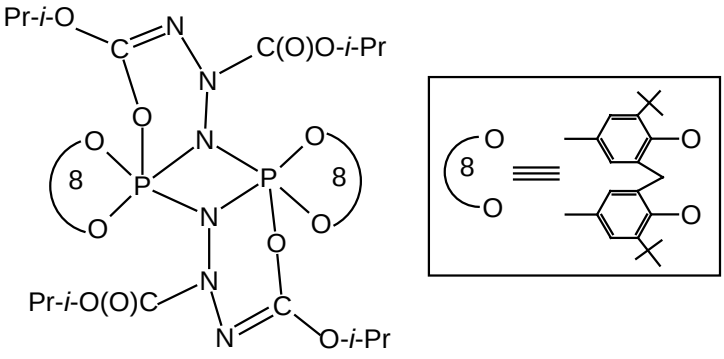
P(1)-N(1)	1.645(3)	N(2)-P(1)-O(1)	175.79(14)
P(1)-N(2)	1.758(3)	N(2)-P(1)-O(2)	90.28(14)
P(1)-N(3)	1.647(3)	N(3)-P(1)-O(1)	90.43(15)
P(1)-O(1)	1.743(2)	N(3)-P(1)-O(2)	119.05(15)
P(1)-O(2)	1.673(2)	O(1)-P(1)-O(2)	88.57(12)
P(2)-N(1)	1.753(3)	N(1)-P(2)-N(2)	82.05(15)
P(2)-N(2)	1.638(3)	N(1)-P(2)-N(4)	93.04(15)
P(2)-N(4)	1.636(3)	N(1)-P(2)-O(3)	89.71(14)
P(2)-O(3)	1.682(3)	N(1)-P(2)-O(4)	175.91(14)
P(2)-O(4)	1.742(3)	N(2)-P(2)-N(4)	121.36(16)
P(1)…P(2)	2.561(1)	N(2)-P(2)-O(3)	118.13(15)
N(1)-P(1)-N(2)	81.69(15)	N(2)-P(2)-O(4)	96.31(15)
N(1)-P(1)-N(3)	122.45(16)	N(4)-P(2)-O(3)	120.25(15)
N(1)-P(1)-O(1)	95.29(14)	N(4)-P(2)-O(4)	91.01(15)
N(1)-P(1)-O(2)	118.30(14)	O(3)-P(2)-O(4)	87.76(14)
N(2)-P(1)-N(3)	93.67(16)		

The carbamate type linkage –NH-C(O)OR present in compounds **11** and **27** leads to a hydrogen bonded dimer through the NH and the C=O moieties [cf. Figures 9 and 15]; however we did not infer such a feature in compound **26**. This observation suggests that preference for **11** to have the observed structure instead of the betaine **11'** is not associated with crystal packing/ hydrogen bonding (although this aspect needs further study).

The nitrogen atoms in the cyclodiphosphazane ring are planar for all the compounds except in the case of for **13** for N(1) [sum of the angles = 346.9^{o}]. This is likely to be restriction imposed because of the sterically encumbered 10-membered ring in **13**. In the corresponding P(III) precursor **4** both the ring nitrogen atoms were non-planar.[112f] However, it should be noted that in many other cyclodiphosph(III)azanes also, the ring nitrogen atoms are non-planar.[112e] The shorter P(1)…P(2) distance in **13** compared to the others may be due to restrictions imposed by the presence of the larger ring coupled with additional substituent (oxygen).

The P_2N_2 ring is close to planarity (max. deviation 0.046 Å) in all cases except **27** where a deviation of 0.13 Å from planarity is observed for P(2). As is the case with many amino/ aryloxy cyclodiphosph(III)azanes, the two amino groups in **11**, **26**, **27** and **28** are on the same side of the P_2N_2 ring [i.e. *cisoidal* orientation]. [112e, 114-115]

Interestingly, the N-P-N angles (in the four-membered cyclodiphosphazane ring) at the phosphorus bearing the DIAD residue in the compounds **8**, **15** and **26**-**28** are in the range 81.5-85^{o}, whereas it is 75.7(2)^{o} in the pentacoordinate compound **XIII**.[115] This difference is perhaps due to the (highly) sterically encumbered phosphorus in **XIII** (relative to **8**, **15** or **26**-**28**) forcing the N-P-N angle at the cyclophosphazane ring to contract.



XIII

5.5 Summary

1) What we have shown here is that the naive-looking reaction of DEAD/ DIAD with P(III) compounds, the key to the enormous synthetic utility of the Mitsunobu reaction, leads not just to the Morrison-Brunn-Huisgen (MBH) betaine $Ph_3P^+N(CO_2R)N^-(CO_2R)$ (**I**), but has the potential to open up new frontiers. Compounds with structures *quite different* from that of **I** have been characterized by using NMR spectroscopy and X-ray crystallography. Thus first examples of imino-phosphorus compounds [phosphinimine-carbamate type of products; X-ray evidence] $XP(\mu\text{-}N\text{-}t\text{-}Bu)_2P[(N\text{-}t\text{-}Bu)\{N\text{-}(CO_2R)\text{-}N(H)(CO_2R)]$ [R = *i*-Pr, X = Cl (**8**), NH-*t*-Bu (**9**), NC_4H_8O (**11**), R = Et, X = NH-*t*-Bu (**10**)] that have a structure halfway between the classical MBH betaine **I** and protonated betaine in the Mitsunobu reaction. By contrast, the reaction of $[(\mu\text{-}t\text{-}BuN)P]_2[O\text{-}6\text{-}t\text{-}Bu\text{-}4\text{-}Me\text{-}C_6H_2]_2CH_2$ (**4**) and $[(C_5H_{10}N)P\text{-}\mu\text{-}N\text{-}t\text{-}Bu]_2$ (**5**) with diisopropyl azodicarboxylate afforded the mono- and bis-oxidized compounds $[(O)P(\mu\text{-}N\text{-}t\text{-}Bu)_2P][O\text{-}6\text{-}t\text{-}Bu\text{-}4\text{-}Me\text{-}C_6H_2]_2CH_2$ (**13**) and $[(C_5H_{10}N)(O)P\text{-}\mu\text{-}N\text{-}t\text{-}Bu]_2$ (**14**), respectively. Thus, when a secondary amino or aryloxy substituent is present on phosphorus, the resulting DIAD adducts do not appear to be stable and lead to P(oxo) products.

2) Treatment of **8** with 2,2,2-trifluoroethanol or 2,6-dichlorophenol afforded the products $(CF_3CH_2O)P(\mu\text{-}N\text{-}t\text{-}Bu)_2P^+[(NH\text{-}t\text{-}Bu)\{N[(CO_2\text{-}i\text{-}Pr)(HNCO_2\text{-}i\text{-}Pr)]\}](Cl^-)$ (**15**) or $(2,6\text{-}Cl_2\text{-}C_6H_3\text{-}O)P(\mu\text{-}N\text{-}t\text{-}Bu)_2P^+[(NH\text{-}t\text{-}Bu)\{N[(CO_2i\text{-}Pr)(HNCO_2i\text{-}Pr)]\}](Cl^-)(2,6\text{-}Cl_2\text{-}C_6H_3\text{-}OH)$ (**16**) whose structures are close to one of the intermediates proposed in the Mitsunobu reaction. Reaction of **9** with carboxylic acids gave products of type $(t\text{-}BuNH)P(\mu\text{-}N\text{-}t\text{-}Bu)_2P^+[(HN\text{-}t\text{-}Bu)\{N\text{-}(CO_2iPr)\text{-}N(H)(CO_2iPr)](RCOO^-)$ (**20-23**) that are analogous to the second stage intermediates in the Mitsunobu reaction.

3) Oxidative addition of *o*-chloranil to **9-10** afforded $[(C_6Cl_4\text{-}1,2\text{-}O_2)(t\text{-}BuNH)P(\mu\text{-}N\text{-}t\text{-}Bu)_2P{=}N\text{-}t\text{-}Bu)(N(CO_2R)NHCO_2R]$ [R = *i*-Pr (**26**) and Et (**27**)] containing tetra- and penta-coordinate P(V) centers in the cyclodiphosphazane ring. For comparison, the X-ray structure of the double cycloaddition product $[(C_6Cl_4\text{-}1,2\text{-}O_2)(t\text{-}BuNH)PN\text{-}t\text{-}Bu]_2$ (**28**), obtained from the reaction of **3** with two mole equivalents of *o*-chloranil is also reported.

CHAPTER 6

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EXPERIMENTAL SECTION

The general experimental procedures and instruments used are already described in Chapter 3. Analytical data were obtained for representative compounds and X-ray structures were obtained where possible.

6.1 Preparation of Phosphorus(III) Precursors

The compounds [ClP(μ-N-*t*-Bu]$_2$ [**1**; mp 40-42^{o}C; δ(P): 206.5],[102] ClP(μ-N-*t*-Bu)$_2$PNH-*t*-Bu [**2**; mp 70-72 ^{o}C; δ(P) 135.4, 200.3][103] and [(*t*-BuNH)P(μ-N-*t*-Bu]$_2$ [**3**; mp 142-144 ^{o}C; δ(P): 89.4; ^{13}C NMR δ 31.6 (t, ^2J(PC) = 7.0 Hz) and 33.1 (d, ^2J(PC) = 15.0 Hz) (both C(*C*H$_3$)$_3$), 51.4 (d, ^2J(PC) = 12.5 Hz) and 51.9 (^2J(PC) = 15.0 Hz, *C*(CH$_3$)$_3$)],[3] and [(C$_5$H$_{10}$N)P-N-*t*-Bu]$_2$ [**5**; mp 170-172^{o}C; δ(P) 93.4][105] were synthesized by slightly altering the procedures reported in the literature. The compound [P(μ-N-*t*-Bu)$_2$P][O-6-*t*-Bu-4-Me-C$_6$H$_2$]$_2$CH$_2$ [**4**; mp 188-190^{o}C; δ(P): 143.9] was prepared by the method developed in our laboratory.[106]

[O(CH$_2$)$_4$N][P(μ-N-*t*-Bu)$_2$P(NH-*t*-Bu)] (6)

Morpholine (0.17 g, 1.74 mmol) in toluene (10 mL) was added drop-wise to a stirred solution of **2** (0.52 g, 1.75 mmol) and Et$_3$N in toluene (20 mL) at 0^{o}C. The mixture was allowed to attain room temperature, stirred for 24 h, concentrated to 2 mL and heptane (2 mL) was added to the residue. Crystals of **6** were obtained after ca 24 h by keeping the solution at 5^{o}C.

Yield: 0.46 g (73%).

Mp: 148 - 150^{o}C.

IR (cm^{-1}): 3335, 1456, 1360, 1221, 997.

^{1}H NMR: δ 1.22, 1.25, 1.26 (3 s, 27 H, PN*t*-Bu-*H*), 2.55 (d, 1 H, ^2J(P-H) = 10.0 Hz, N*H*), 3.20 (m, 4 H, NC*H*$_2$), 3.58 (t, ^3J(H-H) = 5.9 Hz, 4 H, OC*H*$_2$).

^{13}C NMR: 31.3-33.2 (many lines, NC(CH$_3$)$_3$), 43.5 (br s, NCH$_2$), 51.2 and 51.5 (merged t and d, NC(CH$_3$)$_3$), 68.1 (d, ^3J(P-C) = 9.4 Hz, OCH$_2$).

^{31}P NMR: δ 88.5, 95.0 [^2J(PP) < 5 Hz].

(OCH$_2$CMe$_2$CH$_2$O)[P(μ-N-*t*-Bu)$_2$P][(NH-*t*-Bu)]$_2$ (7)

To a stirred solution of **2** (1.10 g, 3.53 mmol) in toluene (10 mL), a solution of 2,2-dimethyl-propane-1,3-diol (0.18 g 1.76 mmol) and triethylamine (0.36 g 3.56 mmol) in toluene (10 mL) was added at room temperature, the mixture stirred for 24 h and filtered. The filtrate was concentrated to (5 mL) and heptane (2 mL) was added to the residue to obtain crystals of **7** after ca 24 h at 5^{o}C.

Yield: 0.92 g, 80%.

Mp: 158-160^{o}C.

IR (cm^{-1}): 3380 (vw), 3200 (vw), 1221, 1100, 1011.

^{1}H NMR: δ 1.30 (s, 18 H, PN*t*-Bu-*H*), 1.32 (s, 6 H, C(CH_3)$_2$), 1.36 (br s, 36 H, P(μ-N*t*-Bu-*H*), 3.34 (br s, OCH_2), 8.78 (d, ^2J(P-H) = 3 Hz, 2 H, NH).

^{31}P NMR: δ 95.4, 114.5 [^2J(PP) < 5 Hz]

6.2 Reaction of P(III) Compounds with Dialkylazodicarboxylates

Synthesis of ClP(μ-N-*t*-Bu)$_2$P[(N-*t*-Bu){N-(CO$_2$*i*-Pr)-N(H)(CO$_2$*i*-Pr)}] (8)

DIAD (0.59 g, 2.92 mmol) in toluene (10 mL) was added drop-wise to a stirred solution of **2** (0.91 g, 2.92 mmol) (bp 140^{o}C/3 mm) in toluene (20 mL). The mixture was stirred for 24 h at room temperature, concentrated to 2 mL and heptane (2 mL) was added to the residue. Crystals of **8** were obtained at 5^{o}C after *ca* 24 h.

Yield: 1.23 g (78%).

Mp: 118-120 ^{o}C.

IR (cm^{-1}): 3368, 3221, 1759, 1711, 1306, 1202, 899.

^{1}H NMR: δ 1.26-1.56 (many lines, 39 H, N*t*-Bu-*H* + CH(CH_3)$_2$), 4.92-5.18 (m, 2 H, CH(CH$_3$)$_2$).

^{13}C NMR: δ, 21.7 (s, CH(CH$_3$)$_2$), 27.8, 28.1, 30.8, 31.2, 51.8-57.0 (bunch of lines) 69.5- 70.3 (bunch of lines), 128.1, 128.9, 153.1, 155.5.

^{31}P NMR: δ -39.8, 11.8, 133.4, 138.5. ^{31}P NMR ($C_6D_5CD_3$): 138.6 and 10.5 with ^2J(PP) < 5.0 Hz, 133.6 and -34.6 with ^2J(PP) of ~16.0 Hz. At 240 K, major sharper signals were at δ -35.0, 10.3, 134.0, 140.0 in

addition to the other broad peaks. Solid state ^{31}P NMR: 80.0, 50.0, 9.5, -52.0 (all broad).

Anal. Calcd for $C_{20}H_{42}N_5O_4ClP_2$: C, 46.74; H, 8.23; N, 13.63. Found: C, 46.65; H, 8.32; N, 13.88.

_t_-Bu-HNP(μ-N-_t_-Bu)$_2$P[(N-_t_-Bu){N-(CO$_2$_i_-Pr)-N(H)(CO$_2$_i_-Pr)}] (9)

The procedure was the same as for **8** using **3** (2.26 g, 7.46 mmol) and DIAD (1.42 g, 7.46 mmol) to yield **9**.

Yield: 3.03 g, (74%).

Mp: 104-106 ^{o}C.

IR (cm^{-1}): 3380, 3192, 1761, 1720, 1665, 1391, 1308, 1260.

^{1}H NMR: δ 1.25 (d, ^{3}J(H-H) = 6.1 Hz, 6 H, CH(C*H*$_3$)$_2$), 1.29 (br s, 9 H, PN*t*-Bu-*H*), 1.32-1.34 (3 lines, 15 H, PN*t*-Bu-*H*) + CH(C*H*$_3$)$_2$), 1.38 (br s, 18 H, P(μ)N*t*-Bu-*H*), 2.70 (d, 2 H, ^{2}J(P-H) = 10.0 Hz, N*H*), 4.89-5.00 (m, 2 H, C*H*(CH$_3$)$_2$), 7.46 (br, 1 H, N*H*).

^{13}C NMR: δ 21.8 (s, CH(*C*H$_3$)$_2$), 22.1, 22.2 (2 s or d, CH(*C*H$_3$)$_2$), 30.9 (t, ^{3}J(P-C) = 5.0 Hz, NC(*C*H$_3$)$_3$), 31.0 (t, ^{3}J(P-C) = 5.0 Hz, NC(*C*H$_3$)$_3$), 32.7 (d, ^{3}J(P-C) = 9.0 Hz, NC(*C*H$_3$)$_3$), 34.4 (d, ^{3}J(P-C) = 9.0 Hz, NC(*C*H$_3$)$_3$), 51.3 (d, ^{2}J(P-C) = 18.0 Hz), 51.4 (d, ^{2}J(P-C) = 5.0 Hz) and 52.6 (dd; ^{2}J(P-C) = 9.5, 40.0 Hz) [all N*C*(CH$_3$)$_3$], 68.8 (s, O*C*HMe$_2$), 69.4 (s, O*C*HMe$_2$), 153.3, (d, ^{2}J(P-C) = 16.0 Hz, P-N-*C*(O)), 157.7.

^{31}P NMR: δ -28.9, 68.9 (^{2}J(PNP) = 7.0 Hz).

Anal. Calcd for $C_{24}H_{52}N_6O_4P_2$: C, 52.35; H, 9.51; N, 15.26. Found: C, 52.25; H, 9.56; N, 15.41.

(_t_-BuNH)P(μ-N-_t_-Bu)$_2$P[(N-_t_-Bu){N-(COOEt)-N(H)(COOEt)}] (10)

The procedure was the same as that for **8** using **3** (1.10 g, 3.16 mmol) and diethyl azodicarboxylate (DEAD, 0.54 g, 3.16 mmol).

Yield: 1.25g (76%).

Mp: 152-154^{o}C.

IR (cm^{-1}): 3366, 3192 (br), 1763, 1719, 1503, 1308, 1231.

^{1}H NMR: δ 1.12-1.30 (many lines, 42 H, CH_2CH_3 + PN*t*-Bu-*H*), 2.45 (br d, 1 H, ^{2}J(P-H) ~ 10.0 Hz, N*H*), 4.89-5.00 (m, 4 H, CH_2CH_3), 7.45 (br s, 1 H, N*H*).

^{13}C NMR: δ 14.4 (s, CH_2CH_3), 31.0 (m with some virtual coupling effects), $NC(CH_3)_3$), 32.7 (d, ^{3}J(P-C) = 9.6 Hz, $=NC(CH_3)_3$), 34.2 (d, ^{3}JP-C) = 9.1 Hz, $HNC(CH_3)_3$), 51.2 (d, ^{2}J(P-C) = 16.0 Hz, $NC(CH_3)_3$), 51.5 (br s, $NC(CH_3)_3$), 52.6 (dd, ^{2}J(P-C) = 8.5, 40.0 Hz, $NC(CH_3)_3$), 61.2 and 61.9 (s each, $OCHMe_2$), 153.8 (d, ^{2}J(P-C) = 15.0 Hz, P-N-*C*(O)), 158.0 (P-N-*C*(O)) [Figure 17].

^{31}P NMR: δ -28.7, 68.9 [^{2}J(PP) < 5 Hz].

Anal. Calcd for $C_{22}H_{48}N_6O_4P_2$: C, 50.56; H, 9.25; N, 16.08. Found: C, 50.60; H, 9.28; N, 16.15.

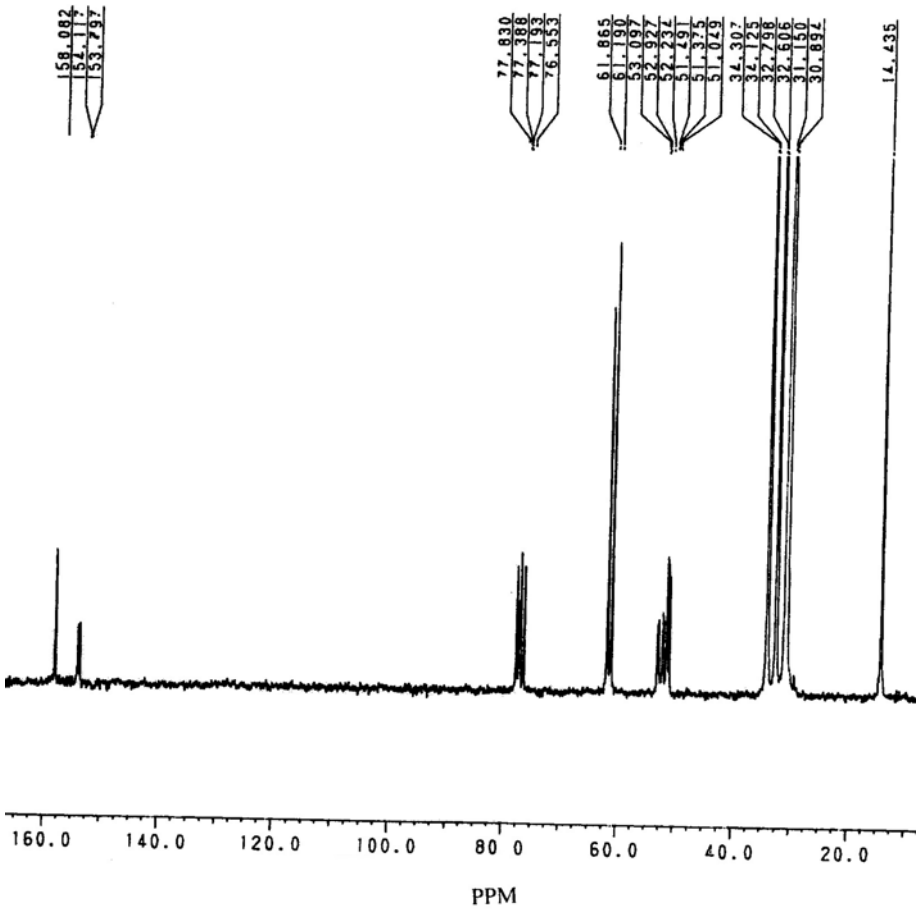

Figure 17. The ^{13}CNMR spectrum of **10**

[O(CH$_2$)$_4$N]-P(μ-N-*t*-Bu)$_2$P[(N-*t*-Bu){N-(COO-*i*-Pr)-N(H)(COO-*i*-Pr)}] (11)

DIAD (0.66 g, 3.24 mmol) in toluene (10 mL) was added drop-wise to a stirred solution of **6** (1.17 g, 3.24 mmol) in toluene (20 mL). The mixture was stirred for 24 h at room temperature, concentrated to 2 mL and heptane (2 mL) was added to the residue and a white solid of **11** was obtained at 5^{o}C after ca 24 h.

Yield: 1.46 g (80%).

Mp: 168-170^{o}C.

IR (cm^{-1}): 3266, 3154, 1703 (vs).

^{1}H NMR: δ 1.22-1.54 (many lines, 39 H, CH(C*H*$_3$)$_2$) + PN*t*-Bu-*H*), 3.03-3.34 (br, 4 H, NC*H*$_2$), 3.61-3.71 (br, 4 H, OC*H*$_2$), 4.95-5.10 (m, 2 H, C*H*(CH$_3$)$_2$), ~7.02 (v br, 1 H, N*H* (?)).

^{13}C NMR: δ 21.9, 22.1 (2 s, CH(*C*H$_3$)$_2$), 30.8, 35.1 and 35.2 (3 s, C(*C*H$_3$)$_3$), 41.5 and 46.4 (s and d, respectively, ^{2}J(PC) ~ 40.0 Hz, N*C*H$_2$), 51.1, 51.5 and 52.2 (d each, ^{2}J(P-C) ~ 9.0 Hz, N*C*(CH$_3$)$_3$), 66.6 and 68.2 (s and d respectively, ^{3}J(P-C) = 12.0 Hz, O*C*H$_2$), 69.1, 69.5 (s each, O*C*HMe$_2$), 153.3 and 156.7 (d and s respectively, ^{2}J(P-C) ~ 10.0 Hz, P-N-*C*(O)).

^{31}P NMR: δ –51.6, 69.7 [^{2}J(PP) < 5 Hz].

Anal. Calcd for $C_{24}H_{50}N_6O_5P_2$: C, 51.06; H, 8.92; N, 14.88. Found: C, 51.48; H, 9.02; N, 15.02.

[(CO$_2$-*i*-Pr)HNN(CO$_2$-*i*-Pr)](t-BuN)P(μ-N-*t*-Bu)$_2$POCH$_2$CMe$_2$CH$_2$O[P(μ-N-*t*-Bu)$_2$PN-*t*-Bu)(N(CO$_2$-*i*-Pr)-NH(CO$_2$-*i*-Pr)] (12)

The procedure was the same as that for **8** using **7** (0.38 g, 0.56 mmol) and DIAD (0.23 g, 1.21 mmol).

Yield: 0.48 g (80%).

Mp: 162-164^{o}C.

IR: (cm^{-1}): 3279, 3198, 1759, 1707, 1261, 1107.

^{1}H NMR: δ 0.92 (s, 6 H, C(C*H*$_3$)$_2$), 1.21-1.42 (many lines, 72 H CH(C*H*$_3$)$_2$) + P(μ)N*t*-Bu-*H*) + PN*t*-Bu-*H*), 3.59 (d, 1 H, ^{2}J(P-H) = 10.0 Hz, N*H*), 4.82-5.13 (m, 4 H, C*H*(CH$_3$)$_2$), ~7.20 (br, 1 H, N*H*).

^{13}C NMR: δ 21.9, 22.2 (2 s, CH(*C*H$_3$)$_2$), 31.1 (s, NC(*C*H$_3$)$_3$), 34.8 (d, ^{3}JP-C) = 7.7 Hz, NC(*C*H$_3$)$_3$), 36.3 (*C*Me$_2$), 51.3 (d, ^{2}J(P-C) = 4.9 Hz, NC(CH$_3$)$_3$), 52.2 (d, ^{2}J(P-C) = 8.5 Hz, NC(CH$_3$)$_3$), 52.9 (d, ^{2}J(P-C) =

9.7 Hz, N*C*$(CH_3)_3$), 69.1, 69.3 and 69.5 (O*C*H_2 + O*C*HMe_2), 156.4 and 157.1 (d and s respectively, ^2J(P-C) = 16 Hz, P-N-*C*(O)).

^{31}P NMR: δ –40.6, 92.8 [^2J(PP) < 5 Hz].

[(O)P(μ-N-*t*-Bu)$_2$P][O-6-*t*-Bu-4-Me-C_6H_2]$_2$$CH_2$ (13)

DIAD (0.167g, 0.82 mmol) was added to a THF solution of **4** (0.224 g, 0.41 mmol) and the reaction mixture was stirred overnight at room temperature. After removing the solvent under reduced pressure, the product was isolated by column chromatography (using 3 % ethyl acetate in hexane) and then crystallized from dichloromethane-hexane (1 mL) mixture.

Yield: 0.18 g (78.3%).

Mp: 194-196^{o}C.

IR: (cm^{-1}): 2969, 1605, 1435, 1275, 1204, 1130, 1053.

^{1}H NMR δ 0.95 (br), 1.51 and 1.57 (36 H, C(C*H*$_3$)$_3$), 2.36 and 2.37 (2 s, 6 H, Ar-C*H*$_3$), 3.41 (br, 1 H, Ar-C*H*$_A$H$_X$), 4.81 (br, 1 H, Ar-CH$_A$*H*$_X$), 7.05 – 7.35 (m, 4 H, Ar-*H*).

^{13}C NMR δ 21.2 and 21.3 (2 s, Ar-*C*H$_3$), 30.8, 31.5, 31.6 and 31.7 (4 s, Ar-C(*C*H$_3$)$_3$ + N-C(*C*H$_3$)$_3$), 35.0 (s, Ar-*C*H$_2$), 35.8 (s, Ar-*C*(CH$_3$)$_3$), 53.8 (d, ^{2}J(P-C) = 10 Hz, N-*C*(CH$_3$)$_3$), 126.6, 127.4, 128.8, 129.1, 132.4, 133.0, 133.8, 141.3, 142.4 and 147.3 (all Ar-*C*).

^{31}P NMR: δ –2.5 and 104.6 (d each, ^2J(PP) = 10.9 Hz). An additional peak (ca 7%) at δ –10.1 was also observed (see results and discussion). The ^{31}P NMR spectrum recorded for the reaction mixture also showed an analogous pattern.

An X-ray structure was obtained for this compound.

[(C_5H_{10}N)(O)P-N-*t*-Bu]$_2$ (14)

The procedure was the same as that for **8** using **5** (0.73 g, 1.96 mmol) and DIAD (0.79 g, 3.92 mmol).

Yield: 0.55 g (69%).

Mp: 134-136^{o}C.

IR (cm^{-1}): 1572, 1256, 1165, 1071, 958, 908.

^{1}H NMR: δ 1.30 (br, 4 H, -CH_2-), 1.41 (br s, 18 H, P(μ)N*t*-Bu-*H*), 1.58 (br s, 8 H, NCH_2), 3.21 (br s, 8 H, OCH_2).

^{13}C NMR: δ 24.2 (s, -*C*H_2-), 25.7 (s, *C*H_2), 30.4 (s, C(*C*H_3)$_3$), 45.9 (s, N*C*H_2), 53.6 (s, *C*$(CH_3)_3$).

^{31}P NMR: δ 1.5.

6.3 Reaction of 8 with 2,2,2-Trifluoroethanol and Phenols

(CF_3CH_2O)P(μ-N-*t*-Bu)$_2$P$^+$[(NH-*t*-Bu){N[(CO_2*i*-Pr)(H*N*CO_2*i*-Pr)]}](Cl$^-$) (15)

Trifluoroethanol (0.10 g, 0.97 mmol) was added drop-wise to a stirred solution of **8** (0.50 g, 0.97 mmol) in toluene (20 mL), the mixture was stirred for 2 d, concentrated to 2 mL and heptane (2 mL) was added to the residue. Crystals of **15** were obtained at 5^{o}C after *ca* 2 d.

Yield: 0.40 g (62%).

Mp: 171-173^{o}C.

IR (cm^{-1}): 3086, 1757.

^{1}H NMR: δ 1.22-1.76 (many lines, 39 H, N*t*-Bu-*H* + CH(CH_3)$_2$), 4.25-4.50 (m, OC$H_2$$CF_3$), 4.89-5.15 (m, 2 H, C*H*$(CH_3)_2$), 8.18 (d, ^{2}*J*(PH) ~ 9.0 Hz, P-N*H*), 9.95 (s, 1 H, N*H*) (Figure 18).

^{13}C NMR: δ 21.5, 21.9 (2s, CH(*C*H_3)$_2$), 27.7, 30.6, 30.8, 31.0, 55.6, 56.1, 57.5, 58.0 69.8, 70.5, 73.4, 156.2, 157.0 (2s, O*C*HMe_2).

^{31}P NMR: δ 11.7 (d), 114.4 (br d); ^{2}*J*(PP) = 16.0 Hz.

Anal. Calcd for $C_{22}H_{44}N_5O_5ClF_3P_2$: C, 43.08; H, 7.23; N, 11.43. Found: C, 43.12; H, 7.26; N, 11.55.

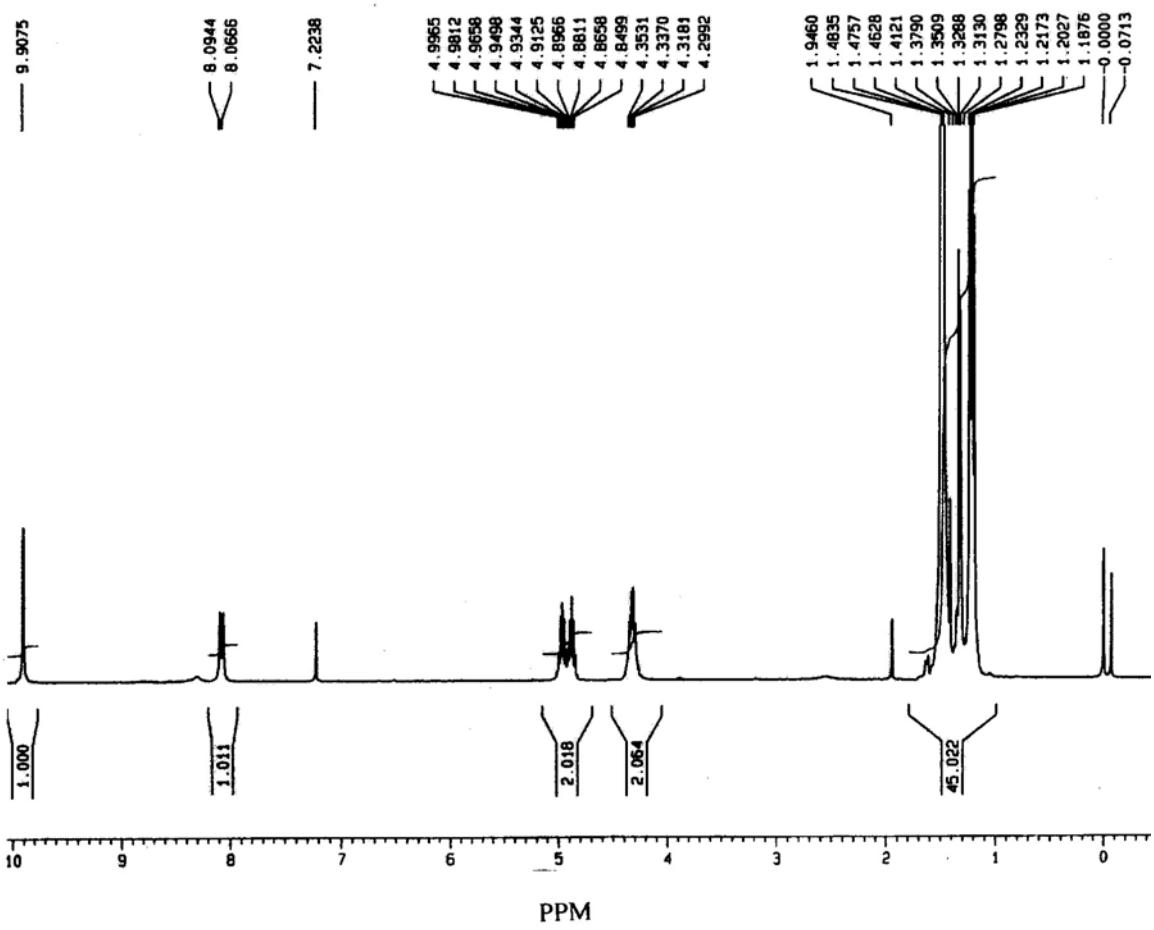

Figure 18. The ^{1}H NMR spectrum of **15**

(2,6-Cl_2-C_6H_3-O)P(μ-N-*t*-Bu)$_2$P$^+$[(NH-*t*-Bu){N[(CO_2*i*-Pr)(HNCO_2*i*-Pr)]}](Cl$^-$)(2,6-Cl_2-C_6H_3-OH) (16)

2,6-Dichlorophenol (0.54 g, 3.31 mmol) in toluene (10 mL) was added drop-wise to a stirred solution of **8** (1.70 g, 3.31 mmol) in toluene (20 mL), the mixture was stirred for 24 h, concentrated to 2 mL and heptane (2 mL) was added to the residue. Crystals of **16** were obtained at 5^{o}C after *ca* 2 d.

Yield: 1.08 g (ca 50% based on phosphazane).

Mp: 140-142^{o}C.

IR (cm^{-1}): 3428 (vw), 3083, 1742, 1229, 1190, 1092.

^{1}H NMR: δ 1.23 (br d, ^{3}J(HH) = 6.1 Hz, 6 H, CH(CH_3)$_2$), 1.30-1.55 (3 lines, 15 H, PN*t*-Bu-*H*) + CH(CH_3)$_2$), 1.68 (br s, 18 H, P(μ)N*t*-Bu-*H*), 4.75-5.10 (m, 2 H, C*H*), 6.92-7.60 (m, ~8 H, Ar*H* + O*H* + PN*H*), 11.26 (s, 1 H, N*H*).

^{13}C NMR: δ 21.3, 21.5, 21.8, 21.9 (4 s, CH(CH$_3$)$_2$), 30.4, 30.9, 31.5 and 31.6 (merged d and t, NC(CH$_3$)$_3$), 56.6 (d, ^2J(PC) = 9.0 Hz, NC(CH$_3$)$_3$), 57.4 (s, NC(CH$_3$)$_3$), 70.4 and 73.3 (s each, OCHMe$_2$), 120.7, 125.2, 126.3, 128.1, 130.0 (all aromatic *C*), 152.6 (d, ^2J(PC) = 20.2 Hz, P-N-*C*(O)), 155.6 (N*C*(O)O-*i*-Pr)

^{31}P NMR: δ 10.9, 115.9 (Figure 19).

An X-ray structure was obtained for this compound.

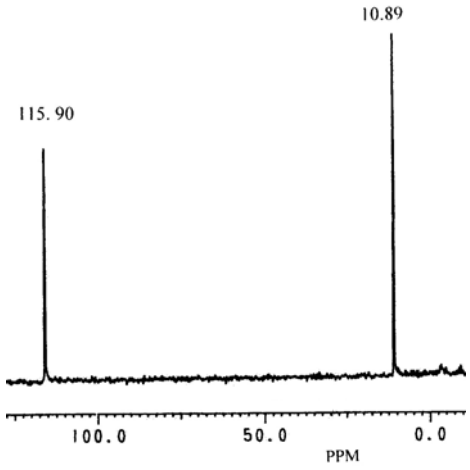

Figure 19. The ^{31}P NMR spectrum of **16**

(2,6-Me$_2$-C$_6$H$_3$-O)P(μ-N-*t*-Bu)$_2$P$^+$(NH-*t*-Bu){N(CO$_2$*i*-Pr)(HNCO$_2$*i*-Pr)}(Cl$^-$) (17)

This compound was prepared in a manner similar to that for **15** using 2,6-dimethylphenol (0.30 g, 2.30 mmol) and **8** (1.18 g, 2.30 mmol).

Yield: 1.11 g (75%).

Mp: 138-140^{o}C.

IR (cm^{-1}): 3090, 1750, 1235, 1182, 1065.

^{1}H NMR: δ 1.23-2.64 (many lines, 39 H, CH(CH_3)$_2$ + PN*t*-Bu-*H*), 2.43 (s, 6 H, ArCH_3), 4.78-5.09 (m, 2 H, C*H*Me$_2$), 6.92-7.60 (m, 3 H, Ar*H*), 7.60 (d, ^2J(PH) ~ 9.0 Hz), 9.95 (s, 1 H, N*H*).

^{13}C NMR: δ 21.5, 21.8, 21.9 and 22.0 (4 s, CH(CH$_3$)$_2$), 30.7 (d, ^2J(P-C) ~ 4.5 Hz, HNC(CH$_3$)$_3$), 31.0 (~t, ^2J(P-C) ~ 4.5 Hz, NC(CH$_3$)$_3$), 56.2 and 57.0 (NCMe$_3$), 70.3 and 73.5 (2 s, OCHMe$_2$), 119.8, 124.1, 128.4 and 130.0 (all aromatic *C*), 152.6 (d, ^2J(P-C) = 20.2 Hz, P-N-*C*(O)), 156.3 (N-*C*(O)O-*i*-Pr).

^{31}P NMR: δ 10.7, 119.5 (d each ^2J(PP) ~ 11.0 Hz).

Anal. Calcd for $C_{28}H_{52}N_5O_5ClP_2$: C, 52.86; H, 8.20; N, 11.00. Found: C, 52.82; H, 8.20; N, 11.00.

(2-Me-6-*t*-Bu-C_6H_3O)P(μ-N-*t*-Bu)$_2$P$^+$[(NH-*t*-Bu){N[(CO_2*i*-Pr)($HNCO_2$*i*-Pr)]}](Cl^-) (18)

This compound was prepared in a manner similar to that for **15** using 2-methyl-6-di-*t*-butyl-phenol (0.48 g, 2.92 mmol) and **8** (1.50 g, 2.92 mmol).

Yield: 1.60 g (81%).

Mp: 156-158^{o}C.

IR (cm^{-1}): 3138, 1757, 1305, 1229, 1186, 1074.

^{1}H NMR: δ 1.25-1.55 (many lines, 48 H, (CH(CH_3)$_2$) + PN*t*-Bu-*H*) + ArC(CH_3)$_3$), 2.23 (s, 3 H, Ar(CH_3), 4.78-5.09 (br, 2 H, C*H*), 6.72-7.60 (many lines, ca 4 H, N*H* +Ar*H*). 10.4 (br, 1 H, N*H*).

^{13}C NMR: δ 20.8 (s, ArC(*C*H$_3$)$_3$), 21.5, 21.7, 21.8, 22.0 (4 s, CH(*C*H$_3$)$_2$), 29.6, 30.5, 30.8, 31.0, 31.1, 31.2, 34.4 (ArC*H*$_3$), 34.9 (Ar*C*CH$_3$)$_3$), 56.3, 56.4, 57.3, 70.4 and 73.3 (s each O*C*HMe$_2$), 115.8, 116.6, 116.8, 127.0, 127.2, 129.3, 132.8, 135.5, 140.0 (all aromatic *C*), 150.5 (d, ^{2}*J*(P-C) = 19.2 Hz, P-N-*C*(O)), 155.3.

^{31}P NMR: δ 9.4, 114.6 (d each, ^{2}*J*(PP) = 10.4 Hz).

Anal. Calcd for $C_{31}H_{58}N_5O_5ClP_2$: C, 54.90; H, 8.62; N, 10.33. Found: C, 54.92; H, 8.75; N, 10.39.

The sample was not very stable and two additional doublets at δ -9.3 and 6.8 with a ^{2}*J*(PP) value of 40.0 Hz, probably due to the oxidation of P(III) end were observed in the reaction mixture.

(2,6-*t*-Bu_2-C_6H_3-O)P(μ-N-*t*-Bu)$_2$P$^+$[(NH-*t*-Bu){N[(CO_2Et)($HNCO_2$Et)]}](Cl^-) (19)

This compound was prepared in a manner similar to that for **15** using 2,6-di-*t*-butyl phenol (0.25 g, 1.20 mmol) and the product [likely to be the ethyl analogue ClP(μ-N-*t*-Bu)$_2$P[(N-*t*-Bu){N-(CO_2Et)-N(H)(CO_2Et)] of **8**; mp 120-122^{o}C; ^{31}P NMR spectrum was complicated as in **8**: δ -53.2, -10.9, -0.1, 9.9, 69.9, 102.0, 138.2; ^{1}H NMR was also not very clear, but showed the correct integration for the ethyl and *t*-butyl protons] obtained from the reaction of **2** with DEAD (0.58 g, 1.20 mmol).

Yield: 0.67 g (80%).

Mp: 140-142^{o}C.

IR (cm^{-1}): 3258, 1753, 1229, 1067.

^{1}H NMR: δ 1.26-1.57 (many lines, 57 H, (CH_2CH_3 + PN*t*-Bu-*H* + ArC(CH_3)$_3$), 4.12-4.56 (m, 4 H, CH_2), 6.67-7.6 (m, 3 H, Ar*H*), 10.52 (br, 1 H, N*H*).

^{13}C NMR: δ 14.0 and 14.5 (s each, CH_2CH_3), 27.7 (s, ArC(CH_3)$_3$), 30.6-31.6 (many lines, NC(CH_3)$_3$), 34.1, 34.4, 34.7, 35.1, 52.6, 56.3, 57.2, 57.3, 62.1, 62.4 and 64.7 (2s OCH_2), 115.3, 116.1, 123.3, 123.4, 123.5, 125.6, 145.9, 150.4, 152.7 (d, ^{2}J(P-C) = 11.2 Hz, P-N-*C*(O)).

^{31}P NMR: δ 9.4, 114.9 (d each, ^{2}J(PNP) = 11.2 Hz).

The compound was obtained only in a state of purity ~90%. There were two minor peaks (ca 10%) at δ 5.0 and 8.0.

6.4 Reaction of 9 with Phenols, Alcohols or Water

These reactions were conducted in an NMR tube by adding an equimolar quantity of tetrachlorocatechol, catechol, 2,2'-biphenol, phenol, 2,2,2-trifluoroethanol, isopropanol or water to **9** in an NMR tube in $CDCl_3$ solution. Although there was significant shift in the phosphorus resonances except in the case of isopropanol (even when two mole equivalents were used), we were unable to isolate the products; the starting material (**9**) could be recovered in the reaction with biphenol/ trifluoroethanol. Details of the spectral changes are given in Table 1 (section 5.1) of Results and Discussion.

6.5 Reaction of 9 with Aromatic Carboxylic Acids or *p*-Toluene sulfonic acid

(*t*-BuNH)P(μ-N-*t*-Bu)$_2$P^{+}[(HN-*t*-Bu){N-(CO_2*i*Pr)-N(H)(CO_2*i*Pr)]($C_6H_5COO^{-}$)(20)

Benzoic acid (0.25 g, 2.04 mmol) was added all at once to a stirred solution of **9** (1.12 g, 2.04 mmol) [prepared *in situ* also works well] in toluene (20 mL), the mixture stirred for 2 h, concentrated to ~2 mL and heptane (2 mL) was added to the residue. Crystals of **20** were obtained at 5^{o}C after *ca* 2 d.

Yield: 1.23 g (90%).

Mp: 86 - 88^{o}C.

IR (cm^{-1}): 3382, 1728, 1372, 1248, 1080.

^{1}H NMR: δ 1.14, 1.20, 1.25, 1.30 (4 d, ^{2}J(HH) = 6.2 Hz, 12 H, (CH(CH_3)$_2$), 1.34 (d, 9 H, ^{4}J(PH) ~ 3 Hz, PN*t*-Bu-*H*), 1.41, 1.50 and 1.62 (s each, 27 H, (PN*t*-Bu-*H*), 3.19 (d, ^{2}J(PH) = 4.3 Hz, 1 H, PN*H*), 4.84 and 4.99 (2 m, 2 H, OC*H*Me$_2$), 7.10-7.44 (m, 3 H, Ar-*H*), 8.09 (m 2 H, Ar*H*), 9.50 (br, 2 H, N*H*).

^{13}C NMR: δ 21.7, 21.9, 22.0 (s each CH*C*H$_3$)$_2$) 30.9, 31.2, 32.5 and 32.6 (s each, NC(*C*H$_3$)$_3$), 52.6 (d, ^{2}J(P-C) = 9.0 Hz, N*C*(CH$_3$)$_3$), 54.8, 55.4 and 55.8 (s each N*C*(CH$_3$)$_3$), 69.4 and 72.3 (s each O*C*HMe$_2$), 125.3, 127.3, 128.2, 129.6, 129.9, 137.4 (all aromatic *C*), 153.1 (d, ^{2}J(P-C) = 20.2 Hz, P-N-*C*(O)), 155.9 (N-*C*(O)), 171.6 (Ar*C*(O)).

^{31}P NMR: δ 1.1, 81.0.

(*t*-BuNH)P(μ-N-*t*-Bu)$_2$P$^+$[(HN-*t*-Bu){N-(CO$_2$-*i*-Pr)-N(H)(CO$_2$-*i*-Pr)](C$_6$H$_4$–4—Cl- CH$_2$COO$^-$) (21)

DIAD (0.52 g, 2.56 mmol) was added drop-wise to a stirred solution of **9** (0.90 g, 2.56 mmol) in toluene (20 mL) and the mixture was stirred for 30 min at room temperature. To this, (4-Cl-C$_6$H$_4$CH$_2$COOH) was added all at once, the mixture was stirred for 24 h at room temperature, concentrated to 2 mL and heptane (2 mL) was added. Crystals of **21** were obtained at 5^{o}C after ca 24 h.

Yield: 1.70 g (92%).

Mp: 80 - 82^{o}C.

IR (cm^{-1}): 3382, 1726, 1379, 1246, 1084.

^{1}H NMR: δ 1.17 – 1.28 (merged 4 d, ^{2}J(HH) ~ 6.2 Hz, 12 H, (CH(CH_3)$_2$), 1.29, 1.32, 1.42, 1.47 (s 36 H PN*t*-Bu-*H* + P(μ)N*t*-Bu-*H*), 3.15 (br, 1 H, N*H*), 3.47 (s, 2 H, ArCH_2), 4.78 - 5.13 (m, 2 H, OC*H*), 7.10-7.30 (m, 4 H, Ar*H*), 9.98 (br, 2 H, N*H*) (Figure 20).

^{13}C NMR: δ 21.6, 21.8, 22.0 (s each CH(*C*H$_3$)$_2$), 30.8, 30.9, 31.4, 32.4 and 32.5 (all NC(*C*H$_3$)$_3$), 44.6 (s, Ar*C*H$_2$), 52.3 (d, ^{2}J(P-C) = 15.0 Hz, N*C*(CH$_3$)$_3$), 55.2 and 55.4 (s each, N*C*(CH$_3$)$_3$), 69.1 and 71.9 (s each, O*C*HMe$_2$), 125.9, 127.7, 128.1, 128.9, 130.8, 131.0, 137.2 (all aromatic *C*), 153.1 (d, ^{2}J(PC) = 20.2 Hz, P-N-*C*(O)), 155.6, 176.3 (Ar*C*(O)) (Figure 21).

^{31}P NMR: δ 0.1 (br), 80.4 (br).

Anal. Calcd for $C_{32}H_{59}N_6O_6P_2Cl$: C, 53.29; H, 8.24; N, 11.37. Found: C, 53.39; H, 8.14; N, 11.37.

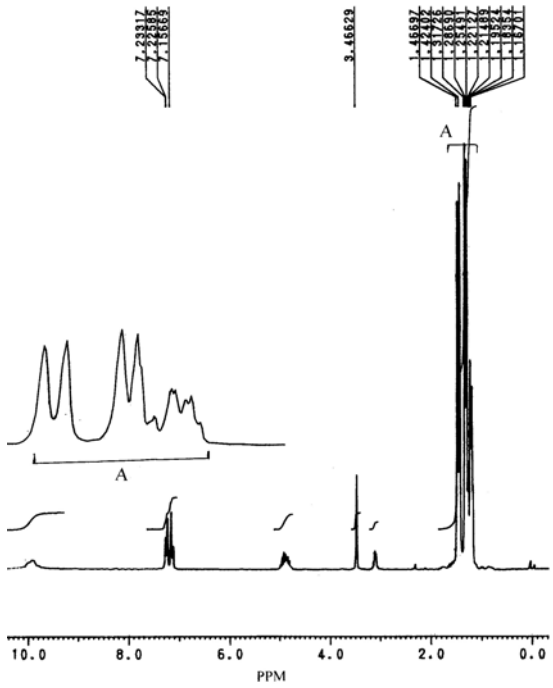

Figure 20. The ^{1}H NMR spectrum of **21**

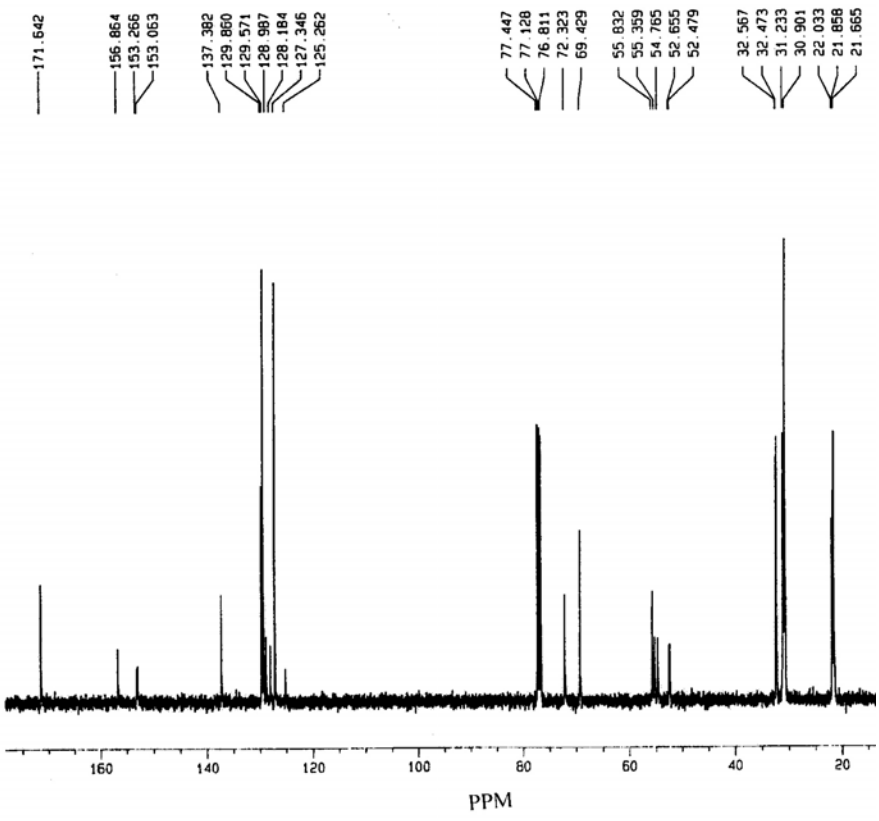

Figure 21. The ^{13}CNMR spectrum of **21**

(*t*-BuNH)P(μ-N-*t*-Bu)$_2$P$^+$[(HN-*t*-Bu){N-(COO-*i*-Pr)-N(H)(COO-*i*-Pr)](4-Br C$_6$H$_4$ COO$^-$) (22)

The procedure was same as that for **21** using DIAD (0.59 g, 2.92 mmol), **9** (1.02 g, 2.92 mmol) and (4-Br-C$_6$H$_4$CH$_2$COOH) (0.58 g, 2.92 mmol).

Yield: 1.97 g (90%).

Mp: 84 - 86 ^{o}C.

IR (cm^{-1}): 3383, 1725, 1368, 1304, 1219, 1080.

^{1}H NMR: δ 1.14, 1.21, 1.26, 1.31 (4 d, ^2J(HH) = 6.0 Hz, 12 H, CH(C*H*$_3$)$_2$), 1.34, 1.43, 1.51 and 1.64 (4 s, 36 H, PN*t*-Bu-*H*), 3.05 (d, ^2J(PH) = 6.0 Hz, 1 H, N*H*), 4.82 and 4.98 (2 m, 2 H, OC*H*), 7.35 and 7.98 (2 d, ^{3}J(HH) ~ 12.0 Hz, ArH). The NH proton signals were too broad.

^{13}C NMR: δ 21.6, 21.8, 21.9 and 22.0 (s each, CH(*C*H$_3$)$_2$), 30.9, 31.5, 32.4 and 32.6 (s each, NC(*C*H$_3$)$_3$), 52.5 (d, ^2J(P-C) = 17.0 Hz, N*C*(CH$_3$)$_3$), 55.7 (d, ^2J(P-C) = 7.0 Hz, N*C*(CH$_3$)$_3$), 55.2, 55.4 and 55.6 (N*C*(CH$_3$)$_3$), 69.4 and 72.2 (2 s, O*C*HMe$_2$), 123.9, 130.3, 131.2, 137.7 (all aromatic *C*), 153.2 (d, ^2J(P-C) = 20.5 Hz, P-N-*C*(O)), 155.7 (N-*C*(O)), 171.1 (Ar*C*(O)).

^{31}P NMR: δ 2.1, 81.5.

Anal. Calcd for $C_{31}H_{57}N_6O_6BrP_2$: C, 49.53; H, 7.64; N, 11.18. Found: C, 49.46; H, 7.76; N, 11.09.

(*t*-BuNH)P(μ-N-*t*-Bu)$_2$P$^+$[(HN-*t*-Bu){N-(COO-*i*-Pr)-N(H)(COO-*i*-Pr)](4-NO$_2$-C$_6$H$_4$COO$^-$) (23)

The procedure was same as that for **21** using DIAD (0.3.8 g, 1.90 mmol), **9** (0.65 g, 1.90 mmol) and (4-BrC$_6$H$_4$CH$_2$COOH) (0.31 g, 1.90 mmol).

Yield: 1.22 g, 90%).

Mp: 118-120^{o}C.

IR (cm^{-1}): 3370, 1734, 1227, 1082, 1030.

^{1}H NMR: δ 1.14, 1.21, 1.28 and 1.34 (4 d, ^2J(HH) = 6.0 Hz, 12 H, CH(C*H*$_3$)$_2$), 1.45, 1.49, 1.53, 1.68 (4 s, 36 H, PN*t*-Bu-*H*), 3.20 (d, ^2J(PH) = 6.0 Hz, 1 H, N*H*), 4.78 and 4.90 (2 m, 2 H, OC*H*), 8.20 (AB qrt, 4 H, Ar*H*). The NH proton signals were too broad.

^{13}C NMR: δ 21.6, 21.7, 21.8 and 22.0 (s each, CH(CH$_3$)$_2$), 30.9 (t, ^3J(P-C) = 4.5 Hz, NC(CH$_3$)$_3$), 31.3 (d, ^3J(P-C) = 3.7 Hz, NC(CH$_3$)$_3$), 32.5 (d, ^3J(PC) = 10.2 Hz, NC(CH$_3$)$_3$), 52.6 (d, ^2J(P-C) = 18.0 Hz, NC(CH$_3$)$_3$), 55.8 (d, ^2J(P-C) = 7.3 Hz, NC(CH$_3$)$_3$), 55.7 (NC(CH$_3$)$_3$), 69.5 and 72.3 (2 s OCHMe$_2$), 124.1, 128.2, 129.0, 130.4, 131.3, 137.2 (all aromatic *C*), 153.1 (d, ^2J(P-C) = 20.2 Hz, P-N-C(O)), 155.7 N-C(O)), 171.0 (ArC(O)).

^{31}P NMR: δ 2.9, 82.0.

Anal. Calcd for $C_{31}H_{57}N_7O_8P_2$: C, 51.87; H, 8.00; N, 13.66. Found: C, 52.00; H, 7.94; N, 13.89.

(*t*-BuNH)P(μ-N-*t*-Bu)$_2$P$^+$[(HN-*t*-Bu){N-(COO-*i*-Pr)-N(H)(COO-*i*-Pr)](4-Me-C$_6$H$_4$SO$_3^-$) (24)

The procedure was same as that for **21** using DIAD (0.48 g, 2.37 mmol), **9** (0.83 g, 2.37 mmol) and (4-Me-C$_6$H$_4$CH$_2$SO$_3$H) (0.37 g, 2.37 mmol).

Yield: 1.52 g, 91%).

Mp: 176-178^{o}C.

IR (cm^{-1}): 3372, 3152, 1740, 1302, 1167, 1080.

^{1}H NMR: δ 1.08-1.21 (many lines, 48 H, (CH(CH_3)$_2$) + PN*t*-Bu-*H* + P(μ)N*t*-Bu-*H*), 2.32 (s, 3 H, CH_3), 3.21 (d, ^2J(PH) = 4.0 Hz, 1 H, N*H*), 4.00-5.10 (m, 2 H, OC*H*), 6.66 (d, ^2J(PH) ~ 13.2 Hz, 1H, NH), 7.10 and 7.85 (d each, 4 H, ^3J(HH) = 7.0 Hz, Ar*H*), 10.71 (br, 1 H, N*H*).

^{13}C NMR: δ 21.2, 21.5, 21.7 and 21.9 (s each, CH(CH$_3$)$_2$), 30.8, 30.9, 31.1, 31.2, 32.3, 32.5 (all NC(CH$_3$)$_3$), 52.8 (d, ^2J(P-C) = 17.0 Hz, NC(CH$_3$)$_3$), 55.3 (d, ^2J(P-C) = 7.0 Hz, NC(CH$_3$)$_3$), 55.6 (d, ^2J(P-C) = 7.0 Hz, NC(CH$_3$)$_3$), 56.2 (s, NC(CH$_3$)), 69.5 and 72.3 (2 s OCHMe$_2$), 126.4, 128.1, 138.1, 144.0, 152.6 (d, ^2J(P-C) = 20.2 Hz, P-N-C(O)), 156.5.

^{31}P NMR (CDCl$_3$): δ 2.3, 82.2.

6.6 Esterification Reaction Using the *in situ* Formed (*t*-BuNH)P(μ-N-*t*-Bu)$_2$P$^+$[(HN-*t*-Bu){N-(CO$_2$Et)-N(H)(CO$_2$Et)](4-NO$_2$-C$_6$H$_4$CO$_2^-$) and Ethanol Leading to the Ester 25

DEAD (0.58 g, 3.44 mmol) was added drop-wise to a stirred solution of **10** (1.20 g, 3.44 mmol) in toluene (20 mL) and the mixture stirred for 30 min at room temperature. To this, (4-NO_2-C_6H_4COOH) was added all at once, the mixture was stirred for 2 h at room temperature. To this mixture, ethanol (0.16 g, 3.44 mmol) was added and the contents heated at 80 ^oC [no reaction at room temperature; ^{31}P NMR δ 3.8 and 82.9 (90%; cf. compound **23**] for 12 h. Solvent was removed, CH_2Cl_2 (20 mL) added to the residue and insoluble material was filtered off. Evaporation of the solvent gave a gummy material [^{31}P NMR δ(P) 6.5, 6.9, 8.4] that was chromatographed over silica gel (hexane followed by ethyl acetate - hexane (1:10)) to afford the ester (4-NO_2-$C_6H_4CO_2Et$) (**25**).

Yield: 0.26 g (40%)

Mp: 54-58^{o}C [Aldrich: 54-59^{o}C]

IR (cm^{-1}): 2965, 1725, 1527, 1262, 1101, 1019.

^{1}H NMR: δ 1.42 (t, ^2J(HH) = 7.0 Hz, 3 H, C*H*$_3$), 4.43 (q, ^2J(HH) .= 7.0 Hz, 2 H, C*H*$_2$), 8.19-8.28 (symmetric m, 4 H, Ar*H*).

^{13}C NMR: δ 14.2 (*C*H$_3$), 61.94 (*C*H$_2$), 123.5, 130.6, 135.8, and 150.5 (all aromatic *C*), 164.6 (*C*(O)).

This is a known compound (Aldrich).

6.7 Oxidative Addition of *o*-Chloranil to Cyclodiphosphazanes [(Cl$_4$C$_6$-1,2-O$_2$)(t-BuNH)]P(μ-N-*t*-Bu)$_2$P=N-*t*-Bu){N-(CO$_2$-*i*Pr)-N(H)(CO$_2$-*i*Pr)] (26)

o-Chloranil (0.77 g, 3.12 mmol) in toluene (10 mL) was added drop-wise (ca 10 min) to a stirred solution of **9** (172 g, 3.12 mmol) in toluene (20 mL). The mixture was stirred for 24 h at room temperature, concentrated to 5 mL and heptane (2 mL) was added to the residue. Crystals of **26** were obtained at 5^{o}C after 24 h.

Yield: 2.12 g (85%).

Mp: 196-198^{o}C.

IR (cm^{-1}): 3451, 3368, 1761, 1730, 1470, 1304, 1236, 1070.

^{1}H NMR: δ 1.20 - 1.25 (br, 21 H, (PN*t*-Bu-*H*, + CH(C*H*$_3$)$_2$), 1.37 and 1.50 (s each, 27 H, N*t*-Bu-*H*), 3.50 (d, ^{2}J(P-H) = 16.0 Hz, 1 H, N*H*), 4.89 (m, 2H, OC*H*(CH$_3$)$_2$).

^{13}C NMR: δ 21.7, 21.9 and 22.1 (3 s with one of the isopropyl groups showing nonequivalence, CH(*C*H$_3$)$_2$), 30.9 (d, ^{3}J(P-C) = 12.9 Hz, NC(*C*H$_3$)$_3$), 32.1 (d, ^{3}J(P-C) = 5.6 Hz, NC(*C*H$_3$)$_3$), 34.3 (d, ^{3}J(P-C) = 8.7 Hz, N*C*(CH$_3$)$_3$), 51.3, 53.1 and 55.5 (s each, N*C*(CH$_3$)$_3$), 69.3 and 69.8 (s each, O*C*H$_2$), 123.4, 124.3, 140.9, 142.9 (all Ar-*C*), 153.1 (d, ^{2}J(P-C) = 15.0 Hz, P-N-*C*(O)), 157.2 (P-N-*C*(O)).

^{31}P NMR: δ -51.2 and -35.1 (d each, ^{2}J(PNP) = 89.6 Hz).

Anal. Calcd for $C_{30}H_{52}N_6O_6Cl_4P_2$: C, 45.24; H, 6.58; N, 10.56. Found: C, 45.31; H, 6.61; N, 10.62.

An X-ray structure was obtained for this compound.

[(Cl$_4$C$_6$O$_2$-1,2)(t-BuNH)]P(μ-N-*t*-Bu)$_2$P=N-*t*-Bu)(N-(CO$_2$-Et)-N(H)(CO$_2$-Et) (27)

The procedure was the same as that for **2** using **10** (1.19 g, 2.30 mmol) and *o*-chloranil (0.57 g, 2.30 mmol).

Yield: 1.53 g (87%).

Mp: 182-184^{o}C.

IR (cm^{-1}): 3447, 3260, 3165, 1715, 1470, 1391, 1278, 1213.

^{1}H NMR: δ 1.22-1.28 (br, 15 H, CH$_2$C*H*$_3$ + PN*t*-Bu-*H*), 1.40 and 1.53 (s each, 27 H, N*t*-Bu-*H*), 3.38 (d, ^{2}J(P-H) ~ 14.6 Hz, 1 H, N*H*), 4.20 (m, 4 H, OC*H*$_2$).

^{13}C NMR: δ 14.6, 14.7 (2 s, CH$_2$*C*H$_3$), 21.4, 30.9 (d, ^{3}J(P-C) ~ 17.0 Hz, NC(*C*H$_3$)$_3$), 32.2 (d, ^{3}J(P-C) = 5.7 Hz, NC(*C*H$_3$)$_3$), 34.3 (d, ^{3}J(P-C) = 8.6 Hz, N*C*(CH$_3$)$_3$), 51.4 (br, N*C*(CH$_3$)$_3$), 53.2 (br, N*C*(CH$_3$)$_3$), 55.6 (br, N*C*(CH$_3$)$_3$), 61.8 and 62.6 (s, O*C*H$_2$), 125.3, 128.2, 129.0, 143.0 (all Ar-*C*), 153.3 (d, ^{2}J(P-C) = 16.0 Hz, P-N-*C*(O)), 157.8 (P-N-*C*(O)).

^{31}P NMR: δ -51.9 and -36.7 (^{2}J(PP) = 89.6 Hz).

An X-ray structure was obtained for this compound.

Analogous reaction using **11** gave a mixture of products (^{31}P NMR; 160 MHz) [A pair of doublets centred at δ(P) 8.4 and –68.9 (~40%, ^{2}J(PNP)~93.0 Hz). Other signals were at δ –36.8, -37.4, -71.7, -72.5].

[(Cl_4C_6-1,2-O_2)(*t*-BuNH)PN-*t*-Bu]$_2$ (28)

The procedure was the same as that for **26** using **3** (0.77g, 0.22 mmol) and *o*-chloranil (1.08, 0.44 mmol).

Yield: 1.71g (92%).

Mp: 212-214^{o}C.

IR (cm^{-1}): 3437, 1468, 1389, 1223, 1076.

^{1}H NMR: δ 1.27 and 1.45 (s each, 27 H, PN*t*-Bu-*H*), 3.11 (m, 1 H, N*H*).

^{13}C NMR: δ 32.4 (s, C(*C*H$_3$)$_3$), 52.7 and 55.4 (2 s, *C*(CH$_3$)$_3$), 125.3, 128.2, 129.0.

^{31}P NMR: δ –51.6.

The crystals obtained contained toluene as a solvent, as shown by X-ray structure determination.

By using 1:1 stoichiometry of **3** and *o*-chloranil the mono adduct **29** was identified clearly, but could not be isolated in a pure state, δ(P) –39.5 and 68.3 (d each, ^{2}J(PNP) ~ 13.0 Hz).

6.8 X-ray Crystallography

X-ray data were collected on an Enraf-Nonius-MACH3 or a Bruker AXS SMART diffractometer using Mo-K$_\alpha$ (λ = 0.71073 Å) radiation. The structures were solved by direct methods;[116] all non-hydrogen atoms, except the solvent in **14**, were refined anisotropically. For the hydrogen atoms except the NH hydrogen in some cases, the riding model was used. Crystallographic data are presented in Tables 1-3.

Table 1. Crystal data for **8**, **10**, **11** and **13**.

Compound	**8**	**10**	**11**	**13**
Emp. formula'	$C_{20}H_{42}ClN_5O_4P_2$	$C_{22}H_{48}N_6O_4P_2$	$C_{24}H_{50}N_6O_5P_2$	$C_{31}H_{48}N_2O_3P_2$
Formula weight	513.98	522.60	564.64	558.65
Crystal system	Triclinic	Monoclinic	Monoclinic	Monoclinic (twinned)[a]
Space group	$P\bar{1}$	$P2_1/c$	$P2_1/n$	$P2_1/a$
a /Å	11.439(2)	13.6582(12)	10.5745(18)	9.2547(7)
b /Å	14.028(3)	10.5579(9)	16.6512(16)	17.5157(12)
c /Å	19.909(2)	20.5262(18)	19.343(2)	19.6895(14)
α/deg	76.23(4)	90.00	90.00	90.0
β/deg	75.65(4),	93.1680(10)	104.30(4)	90.01(1)
γ/deg	80.66(2),	90.00	90.00	90.0
V /Å^3	2987.9(9)	2955.4(4)	3300.3(7)	3191.7(4)
Z	4	4	4	4
D_{calc} /g cm^{-3}]	1.143	1.175	1.136	1.163
μ /mm^{-1}	= 0.265	0.183	0.171	0.168
F(000)	1104	1136	1224	1208
Data/ restraints/ parameters	10535/ 0 / 585	6991/0/329	5808/ 0/ 361	5600/ 0/ 357
S	1.044	1.027	1.171	1.021
R1 [I>2σ(I)]	0.0605	0.0379	0.0577	0.0635
wR2 [all data]	0.2143	0.1104	0.1951	0.1775
max./min. residual electron dens. [eÅ^{-3}]	0.526 / -0.287	0.456/-0.388	0.48/ -0.31	0.97 / -0.57

[a]There was no orthorhombic space group matching with the systematic absences; the next possible space group was $P2_1/a$.

Table 2. Crystal data for.**15**, **16** and **20**.

Compound	**15**	**16**	**20**
Emp. formula	$C_{22}H_{45}ClF_3N_5O_5P_2$	$C_{32}H_{50}Cl_5N_5O_6P_2$	$C_{62}H_{116}N_{12}O_{12}P_4$
Formula weight	614.02	839.96	1345.55
Crystal system	monoclinic	Orthorhombic	Triclinic
Space group	$P2_1/c$	$P2_12_12_1$	$P\bar{1}$
a /Å	18.2506(18)	9.636(2)	15.035(3)
b /Å	9.7929(16),	16.662(4)	15.151(3)
c /Å	18.982(2)	26.283(2)	19.568(4)
α/deg	90.00	90.00	107.692(3)
β/deg	109.54(4)	90.00	107.430(3)
γ/deg	90.00	90.00	94.971(3)
V /Å^3	3197.2(7)	4220.0(14)	3973.6(13)
Z	4	4	2
D_{calc} /g cm^{-3}]	1.276	1.322	1.125
μ /mm^{-1}	0.275	0.465	0.154
F(000)	1304	1760	1456
2θ max.	50	50	56
Observed reflections (I>2σ(I))	5541	3451	12042
Data/ restraints/ parameters	7670 / 0 / 356	4168/0/460	18589/ 0 /871
S	1.040	1.073	1.010
R1 [I>2σ(I)]	0.0475	0.0415	0.0586
wR2 [all data]	0.1525	0.1337	0.1966
Max./min. residual electron dens. [eÅ^{-3}]	0.775/ -0.404	0.0332/ -0.299	0.617/ -0.377

Table 3. Crystal data for **26**.$C_6H_5CH_3$, **27** and **28**.½$C_6H_5CH_3$.

Compound	**26**.$C_6H_5CH_3$	**27**	**28**.½ $C_6H_5CH_3$
Emp. formula'	$C_{35}H_{56}Cl_4N_6O_6P$	$C_{30}H_{52}Cl_4N_6O_6$	$C_{31.50}H_{41.50}Cl_8N_4O$
Formula weight	860.60	796.52	885.73
crystal system	Triclinic	Triclinic	Monoclinic
space group	$P\bar{1}$	$P\bar{1}$	$P2_1/c$
a /Å	11.2386(10)	9.7466(10)	21.5990(14)
b /Å	12.9794(12)	13.2750(17)	10.0864(7)
c /Å	16.1146(15)	16.0446(17)	20.6260(14)
α/deg	93.015(2)	89.728(2)	90.0
β/deg	92.448(2)	78.379(2)	110.936(1)
γ/deg	106.144(2)	83.516(2)	90.0
V /Å^3	2250.8(4)	2020.0(4)	4196.8(5)
Z	2	2	4
D_{calc} /g cm^{-3}]	1.270	1.310	1.402
μ /mm^{-1}	0.380	0.418	0.652
F(000)	908	840	1826
Data/ restraints/ parameters	10548/ 19/ 478	9507/ 0/ 441	9985/ 4/ 444
S	1.045	1.031	0.927
R1 [I>2σ(I)]	0.0513	0.0538	0.0553
wR2 [all data]	0.1638	0.1381	0.1021
max./min. residual electron dens. [eÅ^{-3}]	0.37/-0.30	0.36/-0.30	0.62/-.36

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