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Chemistry of selected cyclic P(III) compounds possessing a P–Cl bond

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Abstract. The compounds $[CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2]PCl$ (**1**), $(OCH_2CMe_2CH_2O)PCl$ (**2**), and $[ClPN(t\text{-Bu})]_2$ (**3**) have been utilized as precursors in the synthesis of (i) new pentacoordinate phosphorus compounds [e.g. $CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2P(NRR')(O_2C_6Cl_4)$, $CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2PX[OC(O\text{-}i\text{-Pr})N{=}N(C(O)O\text{-}i\text{-Pr})]$, (ii) cyclic phosphates and their complexes [e.g. $\{imidazolium\}^+\{CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2PO_2\}^-.MeOH$], (iii) new cycloaddition products [e.g. $\{CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2\}P\{C(CO_2Me)C(CO_2Me)C(O)N\}$, (iv) macrocyclic compounds [e.g. $\{[(t\text{-BuN})P]_2[-OCH_2CMe_2CH_2O-]\}_2$] and (v) phosphonates [e.g. $(OCH_2CMe_2CH_2O)P(O)CH_2C(CN){=}CHC_5H_4FeC_5H_5$]. The synthetic and structural aspects of these new products are discussed.

Keywords. Pentacoordinate phosphorus; phosphates; hydrogen bonding; cycloaddition, macrocycles; phosphonates.

1. Introduction

Cyclic P(III) compounds with a P–Cl bond are useful substrates for exploring new reactions that involve substitution, coordination or oxidation. In recent years we have exploited three such substrates, $[CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2]PCl$ (**1**)[1], $(OCH_2CMe_2CH_2O)PCl$ (**2**)[2] and $[ClPN(t\text{-Bu})]_2$ (**3**)[3] for different purposes. While **1** and **2** are readily prepared by the reaction of the respective diols with phosphorus trichloride, compound **3** is a product of the reaction of phosphorus trichloride with *t*-butylamine. Compound **1** features a flexible eight-membered ring with sterically protecting *t*-butyl groups that could lend kinetic stability for reactive intermediates[4]. Compound **2** is perhaps the cheapest P(III) chloro precursor that is fairly reactive. Compound **3** has two reactive P–Cl ends making it a useful precursor for macrocyclic synthesis in its reaction with di-/polyfunctional reagents. In this report we highlight our work utilizing **1–3** that pertain to the following systems: (a) Pentacoordinate phosphorus; (b) hydrogen bonding involving phosphates; (c) cycloaddition reactions of P(III) azides and isocyanates; (d) macrocyclic cyclodiphosphazanes; and (e) phosphonates – synthesis and utility.

2. Pentacoordinate phosphorus

In compounds containing trigonal bipyramidal phosphorus as the central atom, it is often stated in the literature that sterically bulky substituents prefer to stay at the equatorial

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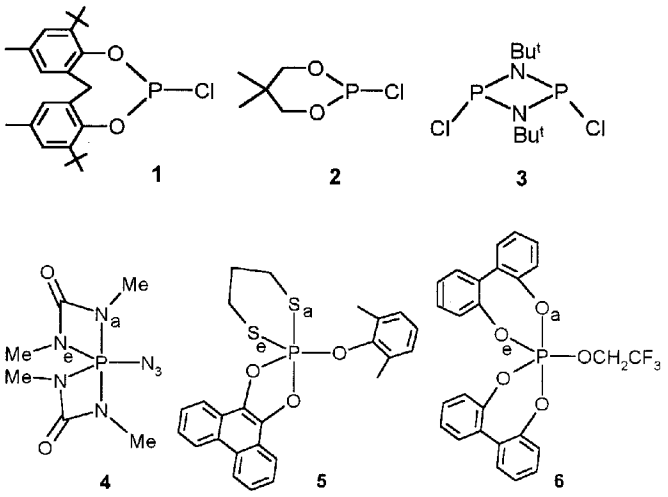


position, whereas sterically small ones go to apical positions [5–7]. It is also emphasized that more electronegative substituents prefer the apical sites; in cases where phosphorus is part of a 4–7 membered ring (e.g. **4–6**), this rule is not followed because of the general preference of these rings to span an apical-equatorial site [8,9]. The flexibility offered by the eight-membered ring present in **1** can make it occupy either apical-equatorial or diequatorial disposition, depending on the other substituents, when this ring is a part of trigonal bipyramidal phosphorus. Based on this notion, we have characterized compounds **7–15** by X-ray crystallography to ascertain the relative tendency of various substituents to occupy the apical position in trigonal bipyramidal phosphorus (the so called 'apicophilicity') [10,11]. Compounds **7–13** and **15** are prepared by reacting the appropriate P(III) precursor with *o*-chloranil, while compound **14** is obtained by the Staudinger reaction of the azide **10** with triphenylphosphine. It is found that the sterically small $-NH_2$ group occupies an equatorial position (compound **12**) whereas the sterically bulky $-N(i\text{-}Pr)_2$ group occupies an apical position (compound **7**). This feature contrasts the site preferences often emphasized for trigonal bipyramidal phosphorus [6]. The results also reveal the higher apicophilicity of a phenyl group over a methyl group (compounds **11** and **15**). Furthermore, it is shown for the first time that an –SAr group has a high apicophilicity (compound **9**).

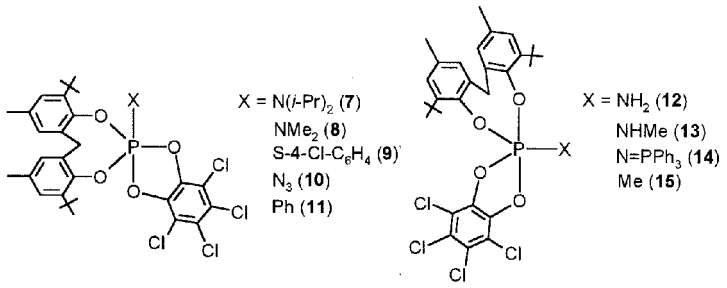


Chart 1.

Many of the pentacoordinate phosphorus compounds thus synthesized show interesting exchange processes in solution as evidenced from variable temperature NMR spectra. For example, the ^{31}P NMR spectrum of the methyl compound **15** in toluene-d_8 shows two dominant peaks at δ –15·8 and –21·0 and a small peak at δ –27·2 at 233 K; the peaks at δ –15·8 and –27·2 broaden and eventually disappear at higher temperatures (figure 1). These features suggest the preference for one of the stereoisomers at higher temperatures; such a phenomenon is different from the normal Berry pseudo-rotation where at the high temperature limit, an averaged out spectrum at the middle of the coalescing peaks is expected. Based on the available X-ray structures and NMR data on related compounds, it is suggested that a process like that shown in scheme 1 is taking place. It can be noted that the local environment at phosphorus in **I** and **II** can be significantly different because of the change in the (i) O–P–O angle involving the eight-membered ring when located apical-equatorially (structure **I**) to that when it is located diequatorially (structure **II**) and (ii) position of the methyl in **I** and **II** (equatorial vs apical).

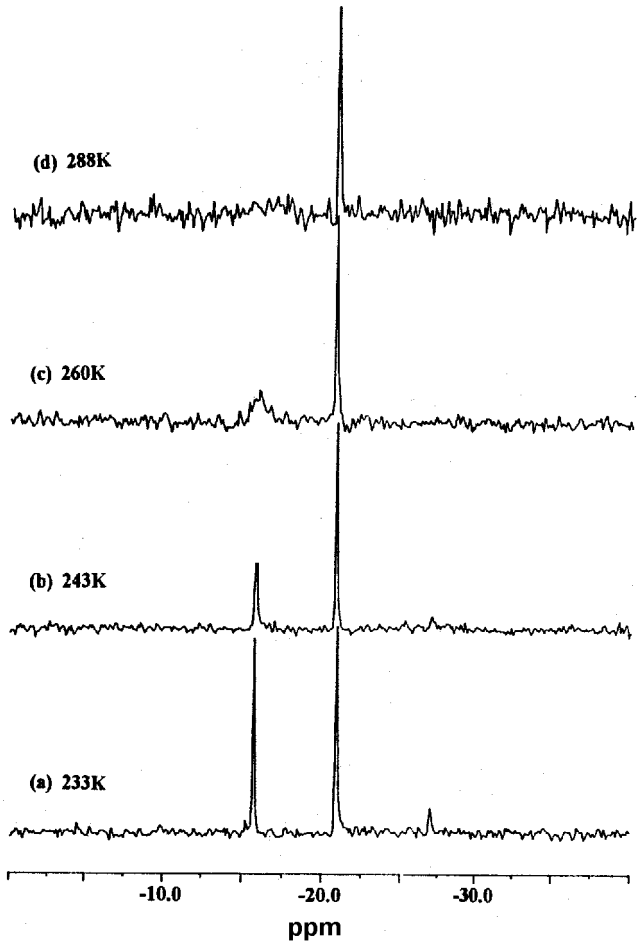
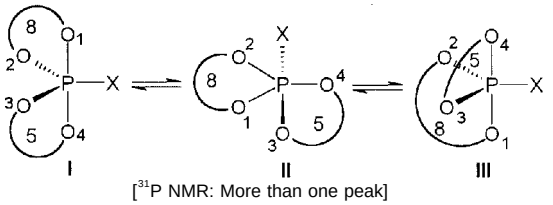
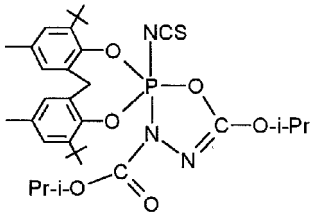


Figure 1. Variable temperature ^{31}P NMR spectra for **15**.



Scheme 1.

Another related reaction that we have investigated is that of the substituted derivatives of **1** (Cl replaced by Ph, NCS, N_3 etc.) with diisopropyl azodicarboxylate (DIAD); the products in general, contain pentacoordinate phosphorus [12]. An example is **16** in which the less electronegative and sterically more encumbered nitrogen of the five-membered ring, rather than the more electronegative oxygen, occupies an apical position of the trigonal bipyramidal phosphorus, in contrast to normal expectations [6].



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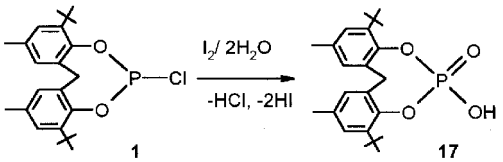
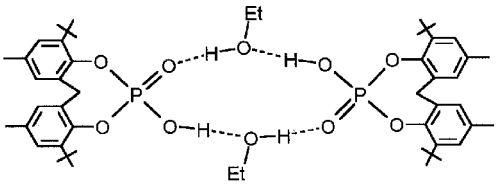
3. Strong hydrogen bonding involving/assisted by the cyclic phosphate $CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2PO_2H$ (17)

The phosphoryl bond in phosphates participates in fairly strong hydrogen bonds (with suitable donors) that are relevant in the context of applications like ferroelectric materials or in proton-transfer reactions in chemical and biological systems [13]. However, studies related to a detailed analysis of structural diversity imparted due to hydrogen bonding by fixing a phosphate and changing its partners are rather limited. Since a substrate like H_3PO_4 or $(RO)P(O)(OH)_2$ will have too many sites for hydrogen bonding, to begin with, we have chosen the cyclic phosphate $CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2PO_2H$ (**17**; 1) for such a study [14]. Compound **17** is fairly stable and is soluble in most of the organic solvents. In the solid state it exists as a dimer, as expected, with the O(H)…O distance of 2·481(2) [triclinic form] or 2·507(3) Å [monoclinic form]. The ethanol and the methanol solvates are also dimers with the alcohol inserted in between the two phosphates; what is perhaps more significant is that one of the O–H…O hydrogen bonds in the ethanol solvate **17**.EtOH is extremely short [O…O 2·368(4) Å][14]. Such a feature is extremely rare for a neutral molecule with no metal involvement.



1 **17** (1)



17.EtOH Dimer

In the imidazole complex of **17**, {imidazolium}$^{+}${CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2PO_2$}$^{-}$ MeOH (**18**), the two nitrogens of the imidazolium ion are engaged in extended hydrogen bonding as expected [14]. However, the methanolic oxygen is involved in hydrogen bonding to a phosphate oxygen on the one side and a C–H, located in between the two nitrogens of the imidazolium ion, on the other side (figure 2). This feature leads to a helical structure. The observation of fairly strong C–H...O hydrogen bond [C...O 3·090(4) Å] suggests that in bio-systems involving the hydrolysis/cyclization of RNA derivatives, the C^{e} of the histidine imidazolyl ring could be involved in similar interactions [15].

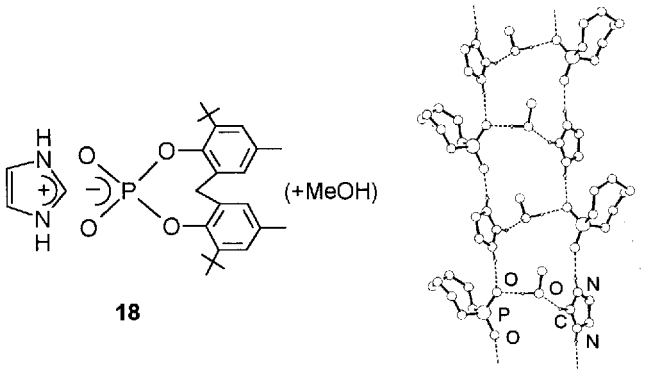


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Figure 2. A picture of **18** showing the hydrogen bonding. Only selected atoms are shown.

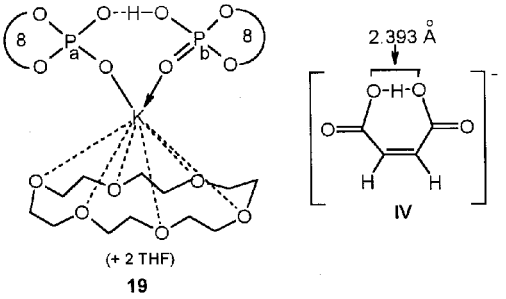

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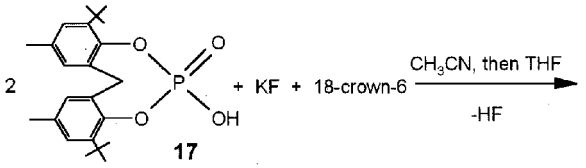
Figure 3. A drawing of **19** as well as the monodeprotonated maleate anion showing the overall structures. The phosphate at P_a is deprotonated; THF molecules do not have any discernible interaction with the phosphate.

In a reaction using equimolar amounts of **17**, KF and 18-crown-6, a complex with 1:1 stoichiometric ratio of the phosphate to the crown is initially obtained; this compound, upon reacting further with one more equivalent of the phosphate **17** leads to **19** (2). In the structure of **19**, the phosphate and its anion are held on one side by potassium cation and on the other side by a hydrogen bond as shown in figure 3 [14]. This situation is comparable to monodeprotonated maleic acid [HO(O)CCH=CHC(O)O$^-$] (**IV**) wherein the proton of the OH is involved in a very strong intramolecular hydrogen bond. In fact, in **19** also a very strong O–H…O hydrogen bond is indicated by the short O…O distance [2·397(4) Å].

That the phosphate **17** often engages itself in strong hydrogen bonding is evidenced in the compounds $[HNC_5H_4\text{-}N{=}N\text{-}C_5H_4NH]^{2+}[\{CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2PO_2\}_2]^{2-}.4CH_3CN.H_2O$ (**20**), **17**.adenine.1/2MeOH (**21**), and **17**.S-(–)-proline (**22**) [14]. In all these compounds a very strong N–H…O hydrogen bond is present [e.g. N…O distance in **20** 2·558(3) Å]. In the light of these results, the range of N(H)…O hydrogen bond lengths can safely be given as 2·55–3·20 Å instead of 2·66–3·20 Å [16].



(2)

[K, 18-C-6]{**17**, $CH_2[4\text{-Me-}6\text{-}t\text{-Bu-}C_6H_2O]_2PO_2$}.2THF

19

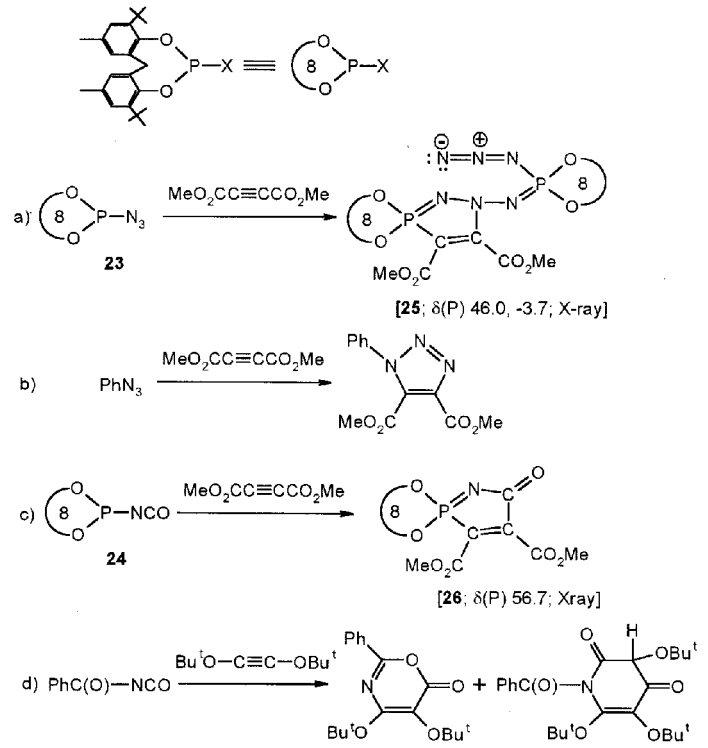
4. Cycloaddition reactions of P(III) azides and isocyanates

A major difference between a P(III) azide and an organic azide is that in the former, the phosphorus can be oxidized to P(V) whereas in the latter, the relevant carbon is already tetravalent. Since an isocyanate group can be considered to be electronically equivalent to an azide, we may expect the reactivity of a P(III) isocyanate also to be different from an organic isocyanate. Bearing this in mind, to start with, we wanted to compare the reaction of a P(III) substrate versus that of its organic counterpart with an activated acetylene. For this purpose, we chose the phosphorus precursors $CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2PX$ [X = N_3 (**23**) and NCO (**24**)] that can be readily prepared by treating **1** with sodium azide or isocyanate respectively. Reaction of **23** and **24** with dimethyl acetylenedicarboxylate (DMAD) indeed proceeds in a manner different from their organic analogs (scheme 2) [17–19]. Interestingly, the product **25** obtained by starting with **23** is quite different from **27** which is obtained from the reaction of the P(III) azide $\{(i\text{-Pr})_2N\}_2PN_3$ with DMAD [20].

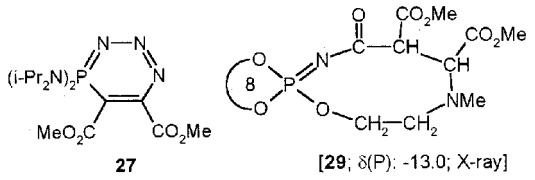
Compound 26 is a useful substrate for further reactions. It has a P–N double bond across which an alcohol can be added; it can also be considered as an ***a,b***-unsaturated ketone. While the first feature is realized in its reaction with 2,2,2-trifluoroethanol to lead to the pentacoordinated phosphorane $CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2P(OCH_2CF_3)(NHC(O)C(CO_2Me){=}C(CO_2Me)$ (**28**; X-ray), the second feature is the one that leads to the ring expanded product **29** when **26** is treated with N-methylethanolamine [17]. Currently, these aspects are being explored further.

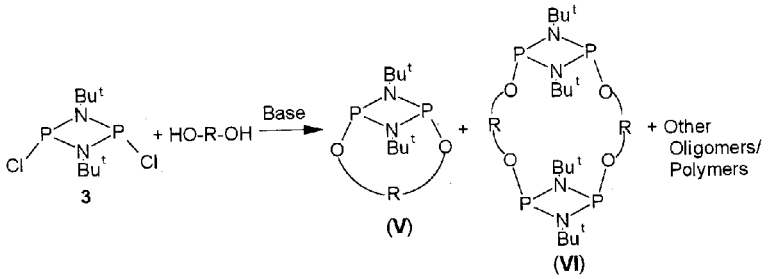
5. Macrocyclic and polydentate cyclodiphosphazanes

The two reactive P–Cl ends of the cyclodiphosphazane **3** are useful for constructing macrocycles, if one reacts it with a difunctional reagent (e.g. a diol). This apparently simple-looking reaction can lead to monomeric, dimeric or other oligomeric products (scheme 3). In most of these reactions we, as well as others, have isolated monomeric products of type **V**; compound **30** is one such compound synthesized by us from the reaction of **3** with the diol $CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2OH)_2$ in the presence of triethylamine[21]. The first example of a macrocycle **31** which is of type **VI** has been prepared in our laboratory by treating 2,2-dimethyl-1,3-propanediol with **3**; although we could not get the X-ray structure of **31** itself, the fully sulfurized compound **32** was amenable for an X-ray structural investigation thus proving the identity of **31** (chart 2)[22]. Reaction of **31** with half mole equivalents of *o*-chloranil afforded **33** in which the macrocyclic skeleton



Scheme 2.





Scheme 3.

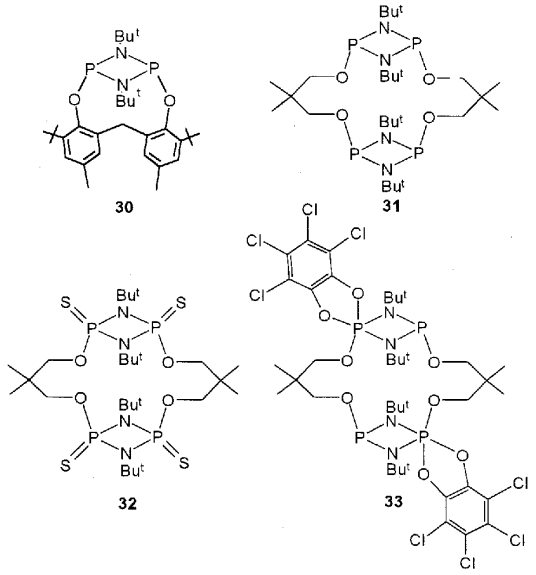
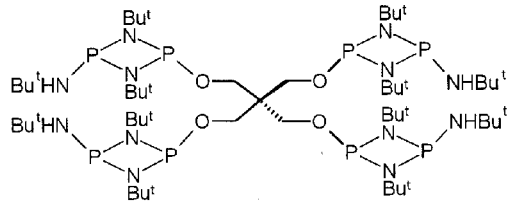


Chart 2.

is retained. However, the macrocyclic skeleton is not retained in all the reactions of **31**; in the reaction with 9,10-phenanthrene quinone, the macrocycle is cleaved and the product isolated has only a single phosphorus atom.

Replacement of one of the chlorines in **3** by a *t*-butylamino group leads to (*t*-BuNH)P(*t*-BuN)$_2$PCl (**34**) which, when treated with one fourth mole equivalents of pentaerythritol, leads to **35** that can be a useful multidentate phosphine type of ligand[23]. More work in this direction is in progress.



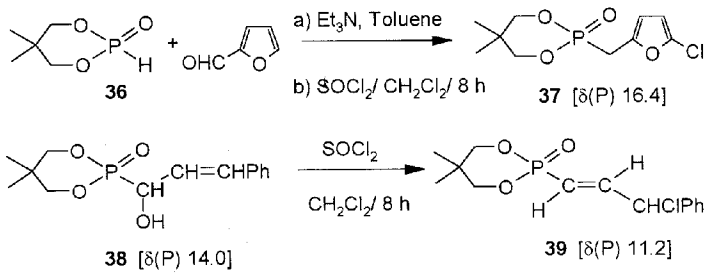
35; δ(P) 117.9; 94.7

6. Phosphonates: Synthesis and utility

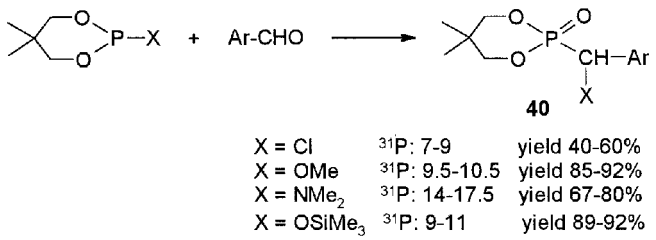
Phosphonates with a hydrogen on the α-carbon are very useful precursors in Horner–Wadsworth–Emmons reaction. For this purpose, we have prepared many phosphonates of the type $(OCH_2CMe_2CH_2O)P(O)CHClAr$ from the reaction of $(OCH_2CMe_2CH_2O)P(O)H$ [**36**, obtained by the hydrolysis of $(OCH_2CMe_2CH_2O)PCl$ (**2**)] with aromatic aldehydes followed by treating the α-hydroxy phosphonates obtained with thionyl chlorides [24]. In reactions using furfuraldehyde and cinnamaldehyde, the chlorination occurred differently as shown in scheme 4 [2]. In an attempt to find alternative routes to these phosphonates, we treated the precursors $(OCH_2CMe_2CH_2O)PX$ [X = Cl(**2**), NMe_2, OMe, $OSiMe_3$] directly with aromatic aldehydes and obtained the corresponding α-substituted phosphonates $(OCH_2CMe_2CH_2O)P(O)CHXAr$ [**40**, X = Cl, NMe_2, OMe, $OSiMe_3$] [25] (scheme 5). Interestingly, compounds **37** and **39** were obtained in the reaction of **2** with furfuraldehyde and cinnamaldehyde respectively.

Another approach we have used is to treat our chloro precursor **2** with a suitable allyl alcohol derived from the Baylis–Hillman reaction [26]. By this means, we could obtain the ferrocenyl substituted phosphonate **41**. Utility of such a phosphonate is realized by the synthesis of the conjugated diene with two ferrocenyl moieties via the Horner–Wadsworth–Emmons reaction (scheme 6) [27].

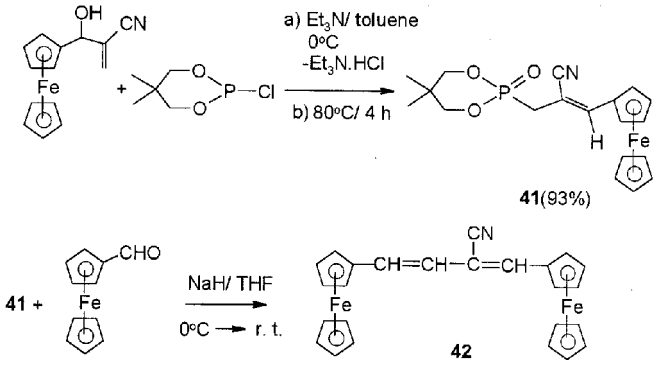
The above synthetic methodologies are feasible because of the convenient and economically viable route to **2** developed by us. Currently we are exploring the synthetic potential of **2** and its substituted derivatives in the preparation of aminophosphonic acids, which are phosphorus analogues of biologically very important amino acids.



Scheme 4.



Scheme 5.



Scheme 6.

7. Summary

In this report we have described the synthetic potential of the readily accessible precursors **1–3** that lead to several novel reactions as well as structures. In particular, the cycloaddition reactions, hydrogen bonding patterns and the phosphonate synthesis mentioned above appear to offer a fertile ground for further research.

Acknowledgements

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