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

M. Vijjulatha,[a] K. Praveen Kumar,[a] K. C. Kumara Swamy[a]* and J. J. Vittal[b]*

[a] School of Chemistry, University of Hyderabad, Hyderabad-500 046, India
[b] Department of Chemistry, National University of Singapore, Kent Ridge, Singapore 0511

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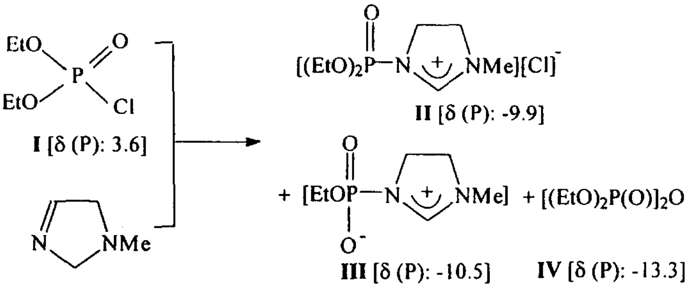
***Abstract*:** The reaction of $(OCH_2CMe_2CH_2O)P(O)Cl$ (**1**)with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) afforded the phosphonate salt $[(OCH_2CMe_2CH_2O)P(O)(DBU)]^+[Cl]$ (**3**)$^-$; the X ray structure of this compound as a hydrate shows that the C-6 (labeled as C1 in Fig.1) of the DBU is connected to the phosphorus. In an analogous manner the eight-membered ring compound $\{CH_2(4\text{-Me-2-}t\text{-Bu-}C_6H_2O)_2\}P(O)Cl$ (**2**) also afforded a phosphonate salt along with the pyrophosphate $[\{CH_2(4\text{-Me-2-}t\text{-Bu-}C_6H_2O)_2\}P(O)]_2O$ (**5**). By contrast, in the reaction of **1** with 1,5-Diazabicyclo[4.3.0]non-5-ene (DBN), N-methyl imidazole or 4-dimethylaminopyridine no phosphonate salt was observed; the pyrophosphate was found to be the end product and could be isolated. © 1998 Elsevier Science Ltd. All rights reserved.

In the reaction of diethyl chlorophosphate (**I**) with N-methyl imidazole, Corriu and coworkers have identified the ionic intermediate **II**, which is a phosphate-base complex [Scheme 1].[1,2] Reactions such as these may have relevance in the synthesis of biophosphate esters by the reaction of a chlorophosphate and an alcohol in the presence of a base.[3] Compounds analogous to **II** have also been isolated in a) the reaction of $(Me_3SiO)P(O)Ph(H)$ with 4-dimethylaminopyridine/CCl_4,[4] b) $(MeO)P(O)Cl_2$ with 4-dimethylaminopyridine[4,5] and c)$\{(Ph)(Br)CH\}_2P(O)Cl_2$ with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[6] Although it is said that these compounds (eg. **II**) may not be important in the nucleophilic catalysis of the nucleophilic substitution reactions at phosphorus,[1] they can be valuable intermediates as precursors for dioxaphosphoranes.[7] We are interested in studying the reaction chemistry of species of the type **II** and have chosen the readily synthesized substrates **1** and **2**.

Scheme 1



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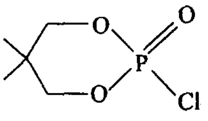
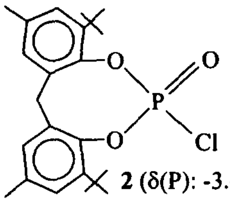
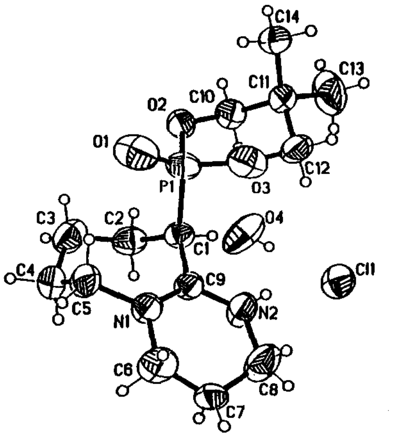
PII: S0040-4039(98)00096-3


1 (δ(P): -3.4)


2 (δ(P): -3.4)

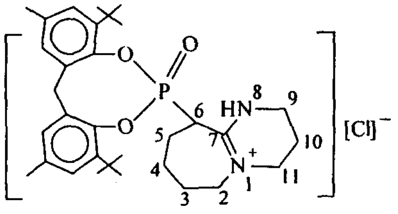
Interestingly, in the reaction of **1** with DBU, we observed the P-C bonded *phosphonate* salt $[(OCH_2CMe_2CH_2O)P(O)(DBU)]^+[Cl]^-$ (**3**) (Fig. 1) as the major product.[8] This type of P-C bonded product is different from the P-N bonded compounds mentioned above or the ones reported by Bertrand and coworkers in the reaction of $(R_2N)_2PCl$ with DBU.[9] Although it is known that DBU can be lithiated at C-6 position (labeled as C1 in Fig. 1) by *n*-butyl lithium,[10] P-C bond formation in the reaction of chlorophosphates with phenylethylamine/ DBU has not been inferred before.[11] Formation of **3** may involve a salt analogous to **II** which undergoes 1,3-proton shift from C-6 to N-1 to give an enamine (see structure of **4** for numbering sequence); this could reorganize to **3** *via* a cyclic 4-membered transition state involving C-6, C-7, N-8 and P.



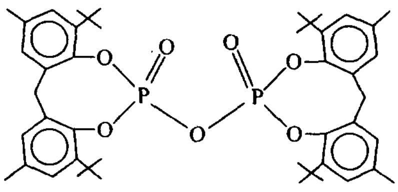
P(1) - O(1)	1.458 (2)
P(1) - O(2)	1.565 (1)
P(1) - O(3)	1.560 (2)
P(1) -C(1)	1.833 (2)
O(1) - P(1) - O(3)	111.98(11)
O(1) - P(1) - O(2)	112.09(10)
O(3) - P(1) - O2)	106.64 (8)
O(1) - P(1) - C(1)	115.30(10)
O(3) - P(1) -C(1)	105.46 (9)
O(2) - P(1) - C(1)	104.67 (8)

Fig. 1 An ORTEP picture of $3.H_2O$; also shown are selected bond parameters around phosphorus.

Reaction of the eight membered ring compound **2** with DBU also gave a phosphonate salt, **4**, along with the pyrophosphate $[\{CH_2(4\text{-}Me\text{-}2\text{-}t\text{-}Bu\text{-}C_6H_2O)_2\}P(O)]_2$ (**5**) (X-ray).[12]

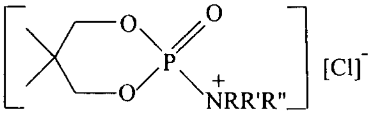


4 [δ (P): 7.2]


5 [δ (P): -28.6]

In contrast to the above, when **1** was allowed to react with 1,5-Diazabicyclo[4.3.0]non-5-ene (DBN), we could not detect a P-C bonded compound (*vide infra*); in the reaction of **1** with N-methyl imidazole,

imidazole and 4-dimethylaminopyridine, although intermediates are found, the pyrophosphate $[(OCH_2CMe_2CH_2O)P(O)]_2O$ (**6**) [13] is the end product and is the only one that could be isolated in a pure state. This latter result is analogous to that reported by Corriu and coworkers (*cf* compound **IV**).[1] Similar pyrophosphates are also obtained in the reactions of the eight-membered ring compounds $\{CH_2(4\text{-Me-}2\text{-}t\text{-Bu-}C_6H_2O)_2\}P(O)Cl$ (**2**) and $\{CH_2(2,4\text{-}(t\text{-Bu})_2\text{-}C_6H_2O)_2\}P(O)Cl$ (**7**) with these bases.[14] We believe that these pyrophosphates are formed *via* betaines of the type **V** and adventitious moisture.[15] We observe signals attributable to these; for example in the reaction of **1** with DBN two ^{31}P NMR signals at -6.7 and -12.0 which are different from those for a phosphonate (*cf* compound **3**) or for the pyrophosphate **6** [δ(P): -21.9] are seen. However, full characterization of these products has eluded us so far because of the extreme sensitivity of the intermediates in our hands.



(V)

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7. Quin, L. D. *Coord. Chem. Rev.* **1994**, *137*, 525.
8. Preparation of **3**: To a solution of **1** (0.77g, 4.21 mmol) in toluene (10 mL) a solution of DBU (0.64g, 4.21mmol) in toluene (10 mL) was added over a period of 10 min at 25°C and the mixture stirred overnight. The solid obtained (^{31}P NMR: single peak at 10.67 ppm) was filtered and washed with cold toluene (2 x 5 mL). Recrystallization was done from hot toluene to obtain **3**. Yield: 1.21g (84%). M. p. 184°C. ^1H NMR: 0.95 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.64-2.17 (m, 8H, CH_2), 3.00-3.10 (d, $^2J \approx 12$ Hz, PC*H*), 3.41 - 3.92 (m, 6H, NCH_2), 4.67 (d, $^2J = 11.1$Hz, OCH_AH_B), 4.78-4.97 (m, 2H, OCH_2), 5.34 (d, OCH_AH_B), 11.48 (br s, 1H, NH^+). ^{13}C NMR: 19.52, 19.97, 22.26, 23.55, 23.63, 24.35, 26.25, 32.83, 32.99, 38.37, 39.38 ($^1J(P\text{-}C) = 126.5$Hz), 49.96, 53.25, 78.59, 161.40. ^{31}P NMR: 10.67. Anal. calcd (**3** with one molecule of water that probably has entered during the process of crystallization) for $C_{14}H_{30}ClN_2O_4P$: C, 47.13; H, 8.41; N, 7.85. Found: C, 47.88: H, 8.09; N, 8.60. The filtrate showed a small quantity of the pyrophosphate **6** also (*ca* 0.05g).*Crystal data for* **3**.H_2O Formula: $C_{14}H_{28}CN_2O_4P$; M = 354.80; Monoclinic; Space group : C2/c; Diffractometer: Siemens SMART CCD. $a = 20.7477(3)$, $b = 9.6621(1)$, c = 18.1810 (3)Å, $\beta = 95.733\ (1)^0$. $V = 3626.41$ (8)

Å^3. $Z = 8$. D_c : 1.300 gcm^{-3}. θ range: 1.97 - 29.14. μ (Mo-K$_\alpha$) = 0.317mm^{-1}. Indep. reflections [R(int) = 0.0189]: 4347; Absorption correction: SADABS (Sheldrick, 1996). Max. and min. transmission: 0.945 and 0.830. Data/ restraints/ parameters: 4347/ 6/ 220. GooF: 1.032. $R_1(I > 2\sigma(I))$ 0.0483, wR2 = 0.1173 (SHELXTL, Version 5.03). Two orientations were found for C(7); only one of these is shown in the Fig. 1

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11. See, for example, Merckling, F. A.; Rüedi, P. *Tetrahedron Lett.* **1996**, *37*, 2217.
12. To a solution of **2** (0.328 g, 0.78 mmol), prepared by reacting 0.012 mol each of $POCl_3$, diol and triethylamine in benzene [60%. M. p. 162-164°C. ^{1}H NMR: 1.44 (s, 18H, *t*-Bu*H*), 2.31 (s, 6H, C*H*$_3$), 3.85-4.20 (AB qrt, 2H, ArC*H*$_2$), 7.07-7.10 (m, 4H, Ar-*H*). ^{31}P NMR: -3.4], in toluene (10 mL) a solution of DBU (0.118g, 0.78 mmol) in toluene (10 mL) was added dropwise at 25°C and the mixture was strirred overnight. Upon concentration to *ca* 10 mL compound **4** came out (0.2 g, 45%). The residue upon further concentration afforded **5** as a crystalline solid (0.15 g, 33 %). Compound **4**: M. p. 220°C (dec.). ^{1}H NMR: 1.38 (s, 9H, *t*-Bu*H*), 1.42 (s, 9H, *t*-Bu*H*), 1.80-2.30 (m, 8H, C*H*$_2$), 3.20 (br, 2H, C*H*$_2$), 3.45- 3.60, m, 6H, NC*H*$_2$), 4.90 (d, 1H, Ar-C*H*$_A$H$_B$), 5.50 (d, 1H, Ar-CH$_A$*H*$_B$), 7.00-7.25 (m, 4H, Ar-*H*), 11.48 (br, 1H, NH$^+$). An additional peak at 12.0 ppm was also observed. ^{31}P NMR : 7.21 (s). Note that this δ(^{31}P) value is in the range of our other phosphonates with phosphorus as a part of a 1,3,2-dioxaphosphorinane ring: Kumaraswamy, S.; Selvi, R. S.; Kumara Swamy, K. C. *Synthesis* **1997**, 207. Compound **5**: M. p. 276°C. ^{1}H NMR: 1.44 (S, 18H, *t*-Bu*H*), 2.31 (s, 6H, C*H*$_3$), 3.70 (d, ^{2}J = 15 Hz, Ar-C*H*$_A$H$_B$), 4.31 (d, ^{2}J = 15 Hz, 1H, Ar-CH$_A$*H*$_B$), 7.21- 7.24 (m, 4H, Ar-*H*). ^{13}C NMR: 20.94, 34.55, 34.99, 127.66, 129.41, 131.43, 135.21, 141.32, 146.0. ^{31}P NMR: -28.6. X-ray data for **5**: Empirical formula: $C_{23}H_{30}O_{3.5}P$; Formula weight: 393.44; Tetragonal; Space group: P4, Diffractometer: Enraf Nonius MACH3. $a = 15.996(2)$, $c = 9.3227$ (7)Å. $V = 2385.4$ (5) Å^3. $Z = 4$. D_c: 1.096 gcm^{-3}. θ range : 2- 22.5. μ (Mo-K$_\alpha$) = 0.135mm^{-1}. Indep. reflections [R(int) = 0.0569]: 1680. Data/ restraints/ parameters: 1680/ 0/ 249. GooF: 1.573. R_1 (I > 2 σ (I)] = 0.0698; wR2 = 0.1811 (SHELXL-97). More details including the ORTEPs are available from the authors.
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14. Compound **7** [δ (P): -2.4] was prepared in a manner analogous to that for **2**. Physical data for the pyrophosphate $[\{CH_2(2,4\text{-}(t\text{-}Bu)_2\text{-}C_6H_2O)_2\}P(O)]_2O$ (**8**): M. p. 276°C. ^{1}H NMR: 1.30 (s, 18H, , *t*-Bu*H*), 1.45 (s, 18H, *t*-Bu*H*), 3.75 (d, ^{2}J = 11.9 Hz, Ar-C*H*$_A$H$_B$), 4.41 (d, ^{2}J = 11.9 Hz, Ar-C*H*$_A$H$_B$), 7.20 and 7.30 (s each, 4H, Ar-*H*). ^{31}P NMR: -28.50. Anal. calcd for $C_{58}H_{84}O_7P_2$: C, 72.95, H, 8.86. Found: C, 72.77, H, 9.36.
15. A second possibility for the formation of pyrophosphates is *via* the reaction of the phosphate salts of the type $[(RO)_2PO_2]^-[Base]^+$ formed by hydrolysis *in situ* with the starting chlorophosphate. We did isolate such a salt in the reaction of **7** with DBU [X-ray.]. However, when we treated the phosphate $(OCH_2CMe_2CH_2O)P(O)(OH)$ with DBN (or DBU) in an NMR tube experiment the ^{31}P NMR peak for the mixture [-4.2 ppm in the reaction with DBN] was different from any of the two peaks [-6.8, -12.0] observed in the reaction of **1** with DBN. This, in conjunction with the fact that the concentration of the pyrophosphate increases over a period of time in the reaction of **1** with N-methylimidazole or imidazole or 4-dimethylaminopyridine, suggests the involvement of the betaines of type **III**. This aspect is currently under investigation.