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The First Hydrogen Bonded Anionic Phosphates Exhibiting Sulfur Donor Coordination[1]

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Donor atom interaction at phosphorus has been found to increase from phosphates to phosphites to pentaoxyphosphoranes in bringing about the formation of higher coordinate geometries.[2−5] Sulfur atoms as part of flexible ring systems have been amply studied in this regard.[2−15] Though less studied, a similar conclusion has been reached regarding oxygen[2,3,9,16−18] and nitrogen[19] as donor atoms. In nucleophilic displacement reactions at active sites of phosphoryl transfer enzymes, phosphate substrates are proposed to form pentaoxyphosphoranes as intermediates with trigonal bipyramidal (TBP) geometries.[20−25] On the basis of our recent studies, it is postulated that active site residues may act in a donor fashion and increase the coordination geometry of both the substrate and proposed intermediate.[2]

Studies thus far have been carried out in the absence of additional enzyme interactions such as those posed by hydrogen bonding, salt bridges, and electrostatic interactions. Furthermore, the studies in the absence of an enzyme environment have been confined to neutral phosphates, whereas those representing ground state configurations at active sites are anionic.

In this Communication, we have synthesized the first anionic phosphates undergoing sulfur donor action in the presence of hydrogen bonding. Their structures from X-ray analyses establish the degree of interaction encountered. The synthesis of the two anionic phosphates **2**[27] and **3**[28] resulted from the reaction of the neutral phosphite **1**[26] with the amino−diol $[CH_2(C_6H_4)OH]_2NMe$ (**4**)[19] and amino−triol $[CH_2(C_6H_4)OH]_2N$ (**5**),[29] respectively.

All three phosphates **1**−**3** show sulfur coordination at phosphorus which displaces the geometry from a tetrahedron toward a TBP.[30] For **1**, the displacement is 30% TBP while for **2** and **3**,

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(1) (a) Pentacoordinated Molecules. 129. (b) Part 128: Chandrasekaran, A.; Sood, P.; Day, R. O.; Holmes, R. R. *Inorg. Chem.* **1999**, *38*, 3369−3376.

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(26) The neutral phosphate **1** was prepared as follows: To an ice-cold solution of phosphorus oxychloride (1.00 mL, 10.7 mmol) in diethyl ether (250 mL) were added 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) (3.84 g, 10.7 mmol) and triethylamine (3.00 mL, 21.6 mmol) dropwise in diethyl ether (50 mL). The system was stirred for 44 h and filtered. Pentafluorophenol (1.97 g, 10.7 mmol) and triethylamine (1.50 mL, 10.7 mmol) in diethyl ether (50 mL) were added dropwise to the filtrate with stirring for a further 24 h. The system was filtered and left to concentrate under a nitrogen flow. The solution was then treated with water (2 × 50 mL). Phosphate **1** formed by concentration of the resultant solution: yield 1.5 g (27%), mp > 250 °C. ^{1}H NMR: 1.38 (s, 18 H, $C(CH_3)_3$), 2.27 (s, 6 H, CH_3), 7.14−7.31 (4 H, Ar(H)). ^{31}P NMR: −11.57. Anal. Calcd for $C_{22}H_{29}O_4PS$: C, 62.84; H, 6.95. Found: C, 63.01; H, 7.00.

(27) Synthesis of the anionic phosphate **2**: A solution of phosphate **1** (0.30 g, 0.68 mmol) and amino−diol **4** (0.20 g, 0.67 mmol) in dichloromethane−heptane (1:1, 50 mL) was stirred for 1 h and left for crystallization. The powdery solid that formed was recrystallized from toluene−dichloromethane (40:10 mL). The solid was washed with toluene and pentane and dried under vacuum: yield 0.40 g (74%), mp 235−237 °C. ^{1}H NMR: 1.38 (s, 18 H, *t*-Bu), 2.10 (s, 6 H, aryl-*Me*), 2.19 (s, 6 H, aryl-*Me*), 2.25 (s, 6 H, aryl-*Me*), 3.77 (d, 2 H, NCH_2, 12 Hz), 4.44 (d, 2 H, NCH_2, 12 Hz), 6.67 (s, 2 H, aryl), 6.91 (s, 2 H, aryl), 7.06 (s, 2 H, aryl), 7.30 (s, 2 H, aryl) (there was also a toluene molecule). ^{31}P NMR: −12.9. Anal. Calcd for $C_{41}H_{54}NO_6PO{\cdot}C_7H_8$: C, 71.00; H, 7.70; N, 1.72. Found: C, 69.04; H, 7.56; N, 1.83 (after 1 h of vacuum drying).

(28) Synthesis of the anionic phosphate **3**: A solution of phosphate **1** (0.30 g, 0.68 mmol) and amino−triol **5** (0.30 g, 0.71 mmol) in dichloromethane−toluene (40: 10 mL) was stirred for 1 h and left for crystallization. A microcrystalline solid was obtained: yield 0.50 g (79%), mp 232−234 °C. The crystal used for the X-ray study was obtained from methanol. ^{1}H NMR: 1.42 (s, 18 H, *t*-Bu), 2.07 (s, 9 H, aryl-*Me*), 2.16 (s, 9 H, aryl-*Me*), 2.26 (s, 6 H, aryl-*Me*), 4.03 (s, 6 H, NCH_2), 6.64 (s, 3 H, aryl), 6.85 (s, 3 H, aryl), 7.08 (s, 2 H, aryl), 7.29 (s, 2 H, aryl) (there was also a toluene molecule). ^{31}P NMR: −12.1. Anal. Calcd for $C_{49}H_{62}NO_7PS$: C, 70.06; H, 7.44; N, 1.67. Found: C, 69.55; H, 7.35; N, 1.66 (after 1 h of vacuum drying).

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(30) Crystal data for **1**: triclinic, $P\bar{1}$, colorless, $a = 12.489(2)$ Å, $b = 12.512(3)$ Å, $c = 16.870(5)$ Å, $\alpha = 108.00(2)°$, $\beta = 101.87(2)°$, $\gamma = 96.99(2)°$, $V = 2404(1)$ Å^3, $Z = 4$, $R = 0.0402$, $R_w = 0.1101$. Crystal data for **2**: monoclinic, $P2_1/c$, colorless, $a = 13.314(3)$ Å, $b = 12.016(5)$ Å, $c = 29.493(6)$ Å, $\beta = 99.90(2)°$, $V = 4648(2)$ Å^3, $Z = 4$, $R = 0.0586$, $R_w = 0.1596$. Crystal data for **3**: tetragonal, $I4_1/a$, colorless, $a = 38.530(8)$ Å, $b = 38.530(14)$ Å, $c = 13.271(10)$ Å, $V = 19702(17)$ Å^3, $Z = 16$, $R = 0.1386$, $R_w = 0.2510$.

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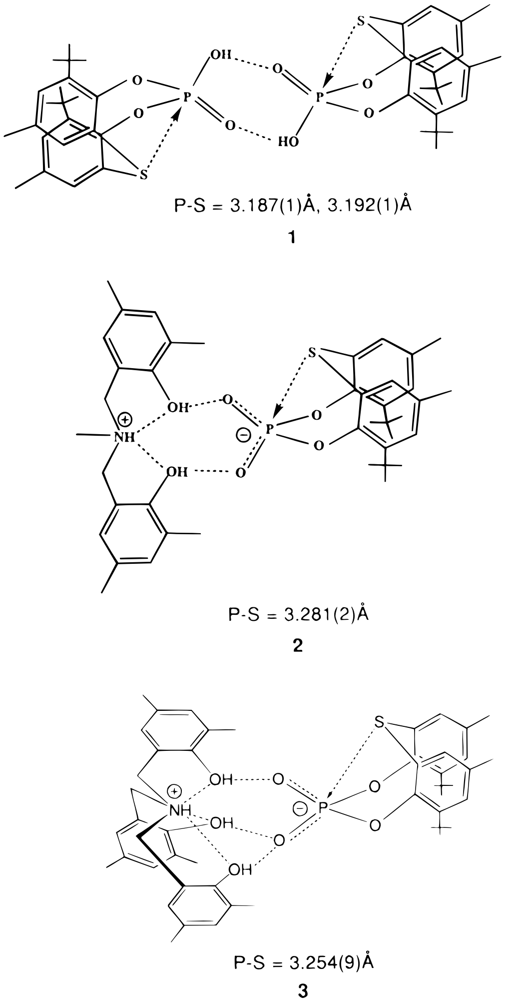


Figure 1. Schematic representations of the structures of **1**−**3** exhibiting hydrogen bonding and P−S interaction.

it is 23% and 26%, respectively. Figure 1 shows a schematic representation of the hydrogen-bonded structures illustrating the boat conformation of the cyclic system as a consequence of P−S coordination. An ORTEX plot of **2** (Figure 2) is taken as representative of the main structural features for these phosphates.

The P−S distance for the anionic phosphates **2** and **3**, respectively, are 0.092 and 0.065 Å longer than that for **1**. The P−S distances shown in Figure 1 compare with 3.65 Å for the sum of the van der Waals radii[31] and 2.12 Å for the covalent sum.[32] If coordination was entirely absent, the rings would reside in an anti chairlike conformation, as previous work has shown.[2]

Neutral phosphate **1** exists as a hydrogen-bonded dimeric unit. In comparison with the similarly constructed anionic phosphates **2** and **3** relative to the neutral entity **1**, the average lengthening of the P−S distance is 0.078 Å. In the anionic phosphates **2** and **3**, hydrogen bonding is expected to increase the electrophilicity at phosphorus. This presumably is countered to a greater extent by the presence of a negative charge that decreases the Lewis acid character of phosphorus.

The most remarkable feature stemming from the inclusion of hydrogen bonding and anionicity in these phosphates is that they still allow sulfur donor action to be expressed, especially since donor action with neutral phosphates is weak to begin with. We can anticipate that the introduction of these two effects in the much more strongly coordinating pentaoxyphosphoranes will not effectively reduce the degree of formation of octahedral geometries. In the presence of a similar sulfur-containing ring system, P−S distances for pentaoxyphosphoranes are observed in the range 2.89−2.33 Å (averaging 2.53 Å)[2,3,9] which is much closer to the sum of the covalent radii, 2.12 Å.[31] For example, compare this distance in **7** of 2.331(1) Å[10] to that for **6**, 3.114(2) Å.[5] The displacement toward an octahedron for **7** is 79%.

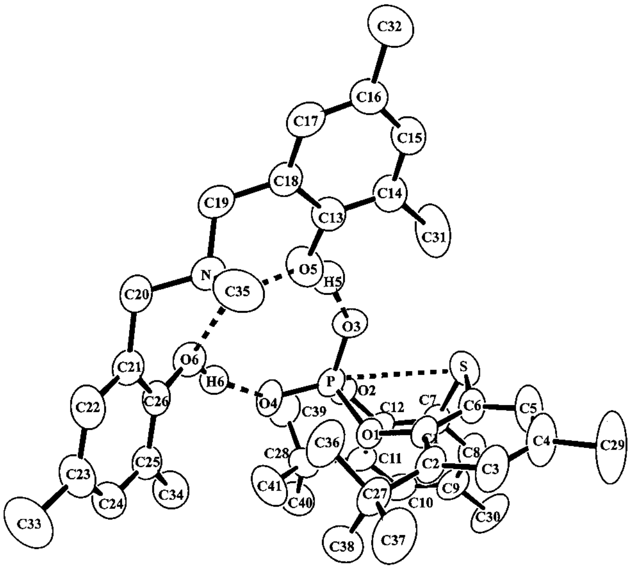
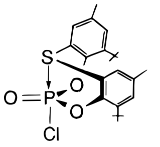
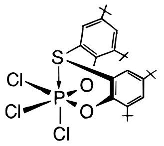


Figure 2. ORTEX diagram of the anionic phosphate **2** with thermal ellipsoids shown at the 40% probability level. All hydrogens are omitted for clarity. Hydrogen bonding and P−S interaction are indicated by dashed lines.



P-S = 3.114(2)Å
% TBP, 35

6 [5]



P-S = 2.331(1)Å
% octa, 79

7 [10]

On the basis of this present work, donor action from available residues at active sites of phosphoryl transfer enzymes is an increasingly likely possibility and one that has not been considered previously. As stated before, the increased degree of donor interaction in proposed intermediates in causing an increase in coordination geometry relative to that for phosphate substrates is a factor that may cause a rate enhancement as a result of tighter nucleophile bonding in the transition state.[2] Thus, donor action may be viewed as a nucleophilic assisted nucleophilic displacement process.

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Supporting Information Available: Tables of crystal data, atomic coordinates, anisotropic thermal parameters, bond lengths and angles, and hydrogen atom parameters and ORTEX diagrams for **1**−**3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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