Coordination of Carbonyl and Carboxyl Oxygen Atoms with Phosphorus in the Presence of Hydrogen Bonding. P−O Donor Action

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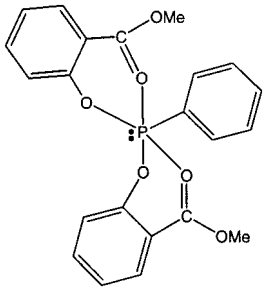
A series of phosphorus compounds **1**−**5** containing carbonyl or carboxyl groups was obtained and subjected to X-ray analysis. Syntheses of the phosphoranes **1** and **5** were effected by oxidation reactions using potassium permaganate, while the phosphine oxide **2** was obtained by oxidation with hydrogen peroxide. The readily available phosphines **3** and **4** were included in the study. The structures revealed that P−O coordination occurred for **1**−**3** in the presence of extensive hydrogen bonding and led to trigonal bipyramidal geometries. A similar structure was observed for **4** in the absence of hydrogen bonding. ^{31}P chemical shifts indicate retention of the basic coordination geometries in solution. Consideration of the chirality of the phosphoranes **1** and **5** leads to a pair of mirror images that are possible in solution but exist in preferred isomeric forms in the crystalline state. Evaluation of the energies of two competing bonding types indicated a range for P−O coordination above and below the hydrogen bond energy. The results suggest that phosphoryl transfer enzyme mechanisms should benefit by taking into account donor interactions to phosphorus by residues at active sites in addition to the inclusion of hydrogen bonding interactions.

Introduction

In an effort to establish the extent of donor action at phosphorus, we have been employing sulfur,[2−16] oxygen,[12,15−19] and nitrogen[20−22] containing donor groups, those common at active sites of phosphoryl transfer enzymes[23,24] and in enzyme actions involving cAMP.[23] It has been found that sulfur coordinates more strongly than oxygen atoms in increasing the coordination geometry at phosphorus,[18,23] and with sulfur as the donor atom, the degree of donor interaction increases from phosphates to phosphites to oxyphosphoranes in forming P−S bonds.[2,13,23] However, when the electrophilicity at phosphorus increases sufficiently, e.g., by the presence of pentafluorophenoxy ligands, a leveling effect occurs, and the sulfur and oxygen atoms exercise similar donor abilities for oxyphosphoranes.[15]

In recent work,[19] we have found that the carbonyl oxygen atom of the salicylate ligand coordinates with bis(methyl salicylate-*O*) phenylphosphine (**A**) to give a pseudo trigonal bipyramid (TBP) as a result of axial coordination.



A

This was the first example of a six-membered ring formation

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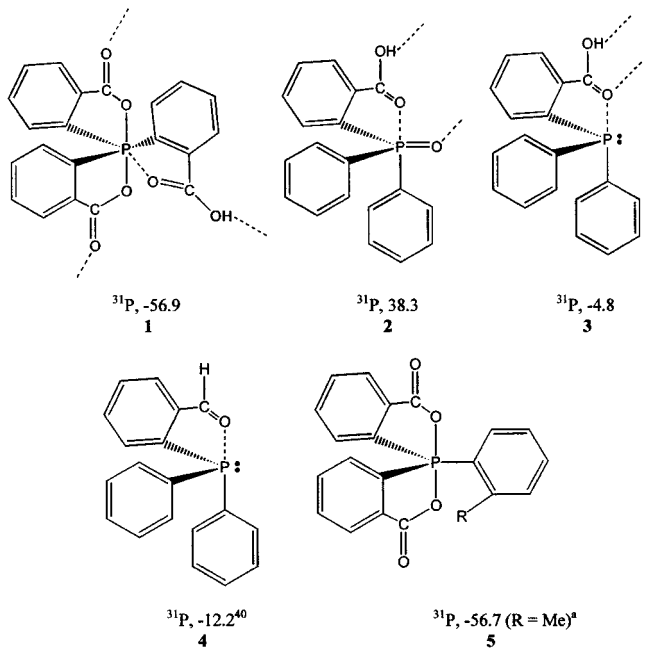
via carbonyl oxygen coordination. Earlier work[25−44] was concentrated on the formation of phosphorus compounds containing four- and five-membered cyclic systems showing oxygen coordination.

The amino acid residues, serine (Ser), threonine (Thr), asparagine (Asn), glutamine (Gln), glutamate (Glu), aspartate (Asp), and tyrosine (Tyr) are potentially oxygen atom donors that might influence active site interactions of phosphoryl transfer enzymes. For example, in phosphatase monoester hydrolysis by alkaline phosphatase, a serine residue at the active site is proposed to attack the phosphoryl group, leading to a transitional TBP.[45]

To extend our studies on oxygen atom donor action, we report here the study of a series (**1**−**4**) composed of phosphines, a phosphate, and phosphoranes interacting with oxygen atoms of carbonyl and carboxyl groups that serve as mimics for amino acid residues, in particular the carbonyl containing ones, Asn and Gln, and the carboxylate containing ones, Glu and Asp. Phosphoranes **5** and **5A**,[46] which lack any donor atoms, were included for comparison. The series we focus on is shown in Chart 1. Syntheses and X-ray and NMR measurements are performed to establish the structural arrangements of **1**−**5** and the extent of Lewis acid−base donor formation that takes place. The relative strengths of the P−O donor-accepting interactions are estimated and compared with hydrogen bonding interactions to evaluate their possible importance in mechanisms of phosphoryl transfer enzymes.

Chart 1[a]



[a] R = H, reference 46.

Experimental Section

Tri(*o*-tolyl)phosphine (Strem), diphenylphosphinobenzoic acid (**3**), diphenylphosphinobenzaldehyde (**4**) (Aldrich), and pyridine (EM Science) were used as supplied. Solvents were purified according to standard procedures.[47] All the reactions and crystallizations were carried out under atmospheric conditions. Proton NMR spectra were recorded on a Bruker AC200 FT-NMR spectrometer. ^{31}P NMR spectra were recorded on a Bruker DPX300 FT-NMR spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$, and the ^{31}P spectra were recorded in CH_2Cl_2 in the sweep-off mode. Chemical shifts are reported in ppm, downfield positive, relative to tetramethylsilane or 85% H_3PO_4, and were recorded at 23 °C. Elemental analyses were performed by the University of Massachusetts Microanalysis Laboratory.

Syntheses. $(C_6H_4CO_2)_2P(C_6H_4CO_2H)$ (**1**) and $(C_6H_4CO_2)_2P(C_6H_4Me)$ (**5**). Compound **1** was synthesized using a modified procedure of a literature method.[48] Potassium permaganate (40.0 g, 253 mmol) was added to a suspension of tri(*o*-tolyl)phosphine (5.00 g, 16.4 mmol) in pyridine (40 mL) and water (100 mL). The mixture was stirred at ambient conditions for 3 h and heated at 100 °C for 16 h. Water (100 mL) was added, and the mixture was filtered. The residue was washed with water (400 mL), and the washings were combined with the filtrate. Concentrated hydrochloric acid (75 mL) was added very slowly to the filtrate with stirring. Brisk effervescence was observed, probably due to the decomposition of hydrogen peroxide. The resultant white precipitate was filtered after 1 h, washed with water (100 mL), and air dried. Crystals of **1A** (**1**·H_2O) were obtained from the latter precipitated solid on crystallization from commercial acetone. The precipitated solid suspended in dichloromethane (100 mL) was boiled and concentrated to half the volume. It became a clear solution (due to the removal of water as an azeotrope) and a precipitate soon formed. The solvent was completely removed to obtain compound **1** as a colorless powder: yield 4.2 g (65%). ^{31}P NMR: −56.9. Anal. Calcd for $C_{21}H_{13}O_6P$: C, 64.30; H, 3.34. Found: C, 63.94; H, 3.39. Single crystals of **1B** (**1**·CH_2Cl_2) were obtained from a solution of this solid in heptane−dichloromethane (1:2) by slow evaporation.

The resulting filtrate (after removing **1**) was left overnight and filtered again to obtain **5** as a minor product: yield 0.40 g (6.7%); mp 212−215 °C. It was crystallized from acetone. ^{31}P NMR: −56.7. Anal. Calcd for $C_{21}H_{15}O_4P$: C, 69.62; H, 4.17. Found: C, 69.14; H, 3.98.

$(C_6H_4CO_2H)P(O)Ph_2$ (**2**). To a solution of diphenylphosphinobenzaldehyde, $(C_6H_4COH)PPh_2$ (**4**), (0.500 g, 1.72 mmol) in methanol (250

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mL) was added an aqueous solution of hydrogen peroxide (35%, 1.00 mL, 10.3 mmol). The yellow solution became colorless. It was kept for 24 h at ambient temperature to allow the solvent to evaporate slowly. The residue was extracted with dichloromethane (10 mL), filtered, and heptane (10 mL) was added. The solution was allowed to evaporate slowly to obtain compound **2** which resulted as a crystalline solid. The solid was washed with acetone (4 × 5 mL) and dried: yield 0.30 g (54%); mp >240 °C. ^{31}P NMR: 38.3. Anal. Calcd for $C_{19}H_{15}O_3P$: C, 70.81; H, 4.69. Found: C, 70.04; H, 4.64.

Single crystals of $(C_6H_4CO_2H)PPh_2$ (**3**) and **4** suitable for X-ray studies were obtained from acetone. Their ^{31}P shifts are −4.8 and −12.2 ppm,[40] respectively.

X-ray Studies. The X-ray crystallographic studies were performed using an Nonius Kappa CCD difractometer and graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). Data were collected at 23 ± 2 °C for $\theta_{\text{Mo K}\alpha} \leq 25°$. All data were included in the refinement. The structures were solved by direct methods and difference Fourier techniques and refined by full-matrix least-squares. Refinements were based on F^2, and computations were performed on a 600 MHz Pentium III computer using SHELXS-86 for solution[49a] and SHELXL-97 for refinement.[49b] All of the non-hydrogen atoms, except those of solvents, were refined anisotropically. The hydrogen atoms of the OH groups were located from difference Fourier techniques and refined isotropically. The remaining hydrogen atoms were included in the refinement as isotropic scatterers, riding in either ideal positions or with torsional refinement (in the case of methyl hydrogen atoms) on the bonded atoms. The final agreement factors are based on the reflections with $I \geq 2\sigma_I$. Crystallographic data are summarized in Table 1.

Results and Discussion

The atom-labeling schemes for **1**−**5** are given in the ORTEX[50] plots in Figures 1−5, respectively. The thermal ellipsoids are shown at the 40% probability level, and all hydrogen atoms are omitted for clarity. Selected bond parameters are given in Tables 2−7.

Syntheses. Phosporane **1** was synthesized by a modification of a literature method[48] involving permaganate treatment of tri(*o*-tolyl) phosphine. The sequence of steps is outlined in Scheme 1, eq 1. This process also yielded phosphorane **5** as a minor product. Formation of **1** is relatively fast compared to that of **5** (Scheme 1, eq 2) as noted from the dehydration of their respective phosphinoyl−carboxylic acids, the latter of which are represented as intermediates in the reaction sequences. The difference in relative dehydration rates allowed for the separation of the two phosphoranes by carrying out filtrations at different times. Phosphine oxide **2** was synthesized by the oxidation of dipheylphosphinobenzaldehyde (**4**) using an excess of hydrogen peroxide, which oxidizes both the phosphorus and the aldehyde group (Scheme 1, eq 3).

Structures. The crystal structures of the phosphoranes **1** and **5**, phosphine oxide **2**, and phosphines **3** and **4** were determined by single-crystal X-ray diffraction. Compounds **1**−**3** have a carboxyl group close to the phosphorus atom, whereas in **4**, a carbonyl (formyl) group is close to phosphorus. The structure of **4** has been reported earlier,[40] however, the donor interaction was not recognized, and the data reported here belong to a different crystalline form. Phosphorane **5** does not have any donor group. Its structure was determined to compare the geometrical changes that take place relative to the structure of **1**.

Due to donor coordination by the carbonyl groups in **2**−**4**, the structures are displaced toward TBP geometries, as the carbonyl oxygen atoms position themselves at axial sites, Figures 2−4. In **3** and **4**, a lone pair occupies an equatorial site, whereas in **2**, the phosphoryl oxygen atom is located at that position. For **1**, the structure is displaced toward an octahedron as a result of the carbonyl oxygen atom O5 coordinating to phosphorus essentially in-plane with the P−C bonds, Figure 1.

In forming P−O coordination, the % displacement toward a TBP is estimated as 18% for **2**, 36% for **3**, and 34% for **4** (Table 8). For the phosphine **A**,[19] displayed in the Introduction, the displacement was 37% toward a TBP as a result of one of the salicylate carbonyl oxygens coordinating at an axial site. Weaker coordination by the remaining salicylate carbonyl oxygen atom is observed. The P−O distance for this interaction is 3.049(6) Å.

These values are obtained by assuming a proportional displacement from the sum of the van der Waals radii[51] for phosphorus and oxygen toward that for the sum of the covalent radii,[52] i.e., 3.35 versus 1.83 Å. In a similar fashion, **1** is

Table 1. Crystallographic Data for Compounds **1**−**5**

compound	**1A**	**1B**[a]	**2**
formula	$C_{21}H_{13}O_6P.2H_2O$	$C_{21}H_{13}O_6P.CH_2Cl_2$	$C_{19}H_{15}O_3P$
fw	428.3	477.2	322.3
cryst syst	monoclinic	triclinic	monoclinic
space group	*C*2/*c*	*P*1	*C*2/*c*
cryst size, mm	0.45 × 0.25 × 0.10	0.70 × 0.50 × 0.50	0.75 × 0.10 × 0.05
a (Å)	29.3450(9)	7.9711(2)	26.1056(6)
b (Å)	8.2120(2)	8.3909(2)	8.5047(3)
c (Å)	18.4100(7)	9.5169(3)	19.1412(6)
α (°)	90	99.194(1)	90
β (°)	116.557(2)	108.748(1)	131.457(1)
γ (°)	90	110.617(1)	90
V (Å^3)	3968.4(2)	536.74(2)	3185.0(2)
Z	8	1	8
D_{calc} (g/cm^3)	1.434	1.476	1.344
$\mu_{\text{Mo K}\alpha}$ (cm^{-1})	1.86	4.14	1.85
total reflns	3462	3383	2800
reflns, $I > 2\sigma_I$	2839	3300	2213
R[b]	0.0407	0.0401	0.0471
R_w[c]	0.1144	0.1123	0.1325
compound	**3**	**4**	**5**
formula	$C_{19}H_{15}O_2P$	$C_{19}H_{15}OP$	$C_{21}H_{15}O_4P$
fw	306.3	290.3	362.3
cryst syst	triclinic	triclinic	monoclinic
space group	$P\bar{1}$	$P\bar{1}$	*C*2/*c*
cryst size, mm	0.45 × 0.25 × 0.05	0.70 × 0.35 × 0.20	0.40 × 0.20 × 0.20
a (Å)	5.6355(3)	8.5843(2)	30.4111(8)
b (Å)	11.1435(6)	10.1422(2)	8.4282(2)
c (Å)	13.2057(7)	10.6614(3)	15.3425(4)
α (°)	95.596(3)	107.198(1)	90
β (°)	100.257(3)	105.926(1)	114.966(1)
γ (°)	100.286(3)	107.949(1)	90
V (Å^3)	795.75(7)	772.33(3)	3565.0(2)
Z	2	2	8
D_{calc} (g/cm^3)	1.278	1.248	1.350
$\mu_{\text{Mo K}\alpha}$ (cm^{-1})	1.77	1.74	1.77
total reflns	2814	2694	3130
reflns, $I > 2\sigma_I$	2253	2296	2568
R[b]	0.0399	0.0394	0.0391
R_w[c]	0.1049	0.1150	0.1105

[a] The Flack parameter is 0.10(6). For the inverted structure, the Flack parameter is 0.87(6). R and R_w for the inverted structure are 0.0413 and 0.1168, respectively. [b] $R = \sum||F_o| - |F_c||/\sum|F_o|$. [c] $R_w(F_o^2) = \{\sum w(F_o^2 - F_c^2)^2/\sum wF_o^4\}^{1/2}$.

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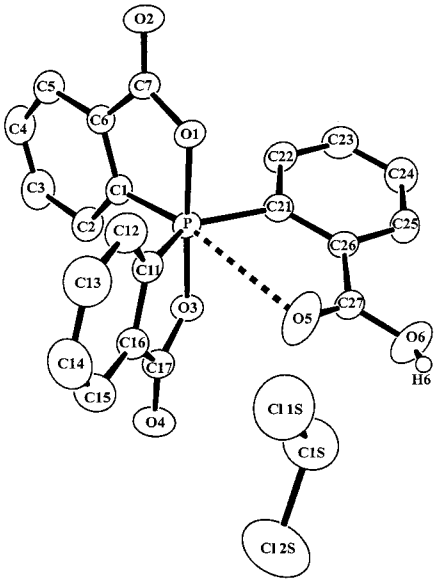

Figure 1. ORTEX diagram of **1B**.

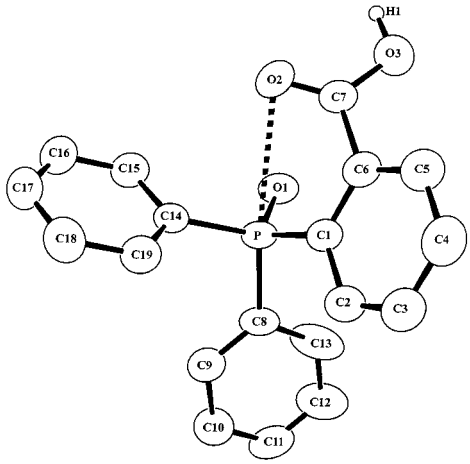

Figure 2. ORTEX diagram of **2**.

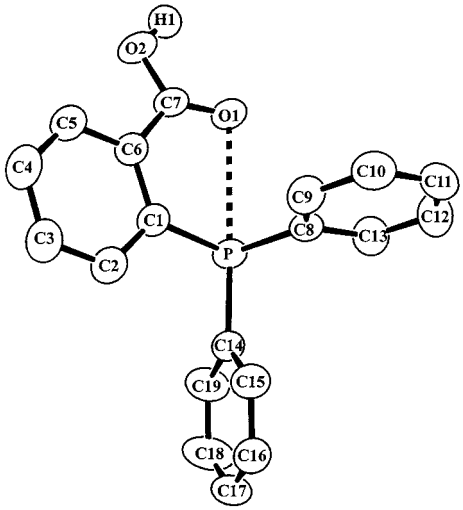

Figure 3. ORTEX diagram of **3**.

calculated to be displaced by about 24% toward an octahedron from a TBP. If the weaker salicylate P−O interactions

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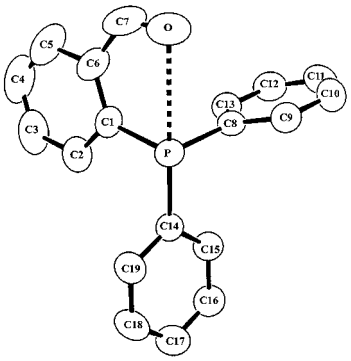


Figure 4. ORTEX diagram of **4**.

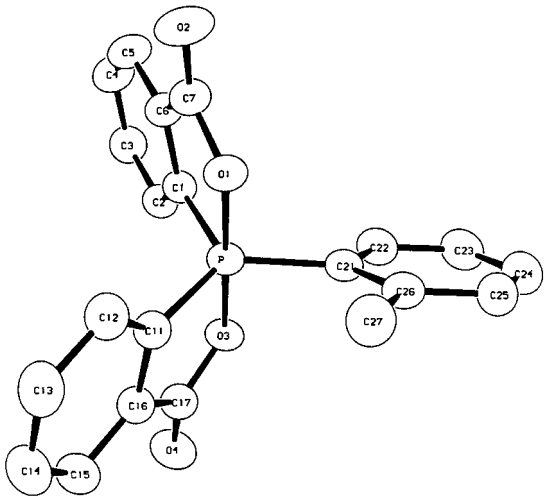


Figure 5. ORTEX diagram of **5**.

Table 2. Selected Bond Lengths [Å] and Angles [deg] for **1A**

P−O(1)	1.781(1)	P−O(3)	1.782(1)
P−C(1)	1.804(2)	P−C(11)	1.808(2)
P−C(21)	1.828(2)	P−O(5)	3.000(2)
O(1)−C(7)	1.326(2)	O(2)−C(7)	1.216(2)
O(3)−C(17)	1.342(2)	O(4)−C(17)	1.203(2)
O(5)−C(27)	1.192(2)	O(6)−C(27)	1.310(2)
O(1)−P−O(3)	178.40(7)	O(1)−P−C(1)	88.48(7)
O(3)−P−C(1)	92.30(7)	O(1)−P−C(11)	92.80(8)
O(3)−P−C(11)	88.14(8)	C(1)−P−C(11)	115.12(8)
O(1)−P−C(21)	89.98(7)	O(3)−P−C(21)	88.43(7)
C(1)−P−C(21)	112.76(8)	C(11)−P−C(21)	132.09(9)
O(1)−P−O(5)	74.49(6)	O(3)−P−O(5)	104.73(6)
C(1)−P−O(5)	162.97(7)	C(11)−P−O(5)	66.18(7)
C(21)−P−O(5)	68.66(7)	C(7)−O(1)−P	115.8(1)
C(17)−O(3)−P	116.1(1)	C(27)−O(5)−P	91.4(1)
C(2)−C(1)−P	128.9(2)	C(6)−C(1)−P	111.5(1)
C(2)−C(1)−C(6)	119.6(2)	C(12)−C(11)−P	128.6(2)
C(16)−C(11)−P	111.4(1)	C(16)−C(11)−C(12)	120.0(2)
C(22)−C(21)−P	115.1(1)	C(26)−C(21)−P	126.0(1)
C(26)−C(21)−C(22)	118.9(2)		

for **A** are considered, an octahedral character of about 20% is indicated.

The greater degree of coordination for the phosphines **3**, **4**, and **A**, relative to that for the phosphine oxide **2**, is consistent with earlier work[2,15] involving sulfur and oxygen donor action, which showed that the strength of such action is greater for phosphites compared to phosphates. The respective donor−acceptor P−O bond lengths for **3**, **4**, and **A** are 2.806(1), 2.834(2), and 2.788(6) Å, which are considerably smaller than that for **2**, 3.075(2) Å. It was suggested[2] that the presence of the

Table 3. Selected Bond Lengths [Å] and Angles [deg] for **1B**

P−O(1)	1.810(2)	P−O(3)	1.737(2)
P−C(1)	1.805(2)	P−C(11)	1.802(3)
P−C(21)	1.834(3)	P−O(5)	2.967(2)
O(1)−C(7)	1.319(3)	O(2)−C(7)	1.221(3)
O(3)−C(17)	1.344(3)	O(4)−C(17)	1.207(4)
O(5)−C(27)	1.174(4)	O(6)−C(27)	1.291(4)
O(3)−P−O(1)	177.95(9)	C(1)−P−O(1)	87.5(1)
C(11)−P−O(1)	90.5(1)	C(21)−P−O(1)	87.42(9)
O(3)−P−C(1)	94.5(1)	O(3)−P−C(11)	89.2(1)
O(3)−P−C(21)	91.4(1)	C(11)−P−C(1)	113.1(1)
C(21)−P−C(1)	112.8(1)	C(11)−P−C(21)	133.9(1)
O(1)−P−O(5)	104.31(9)	O(3)−P−O(5)	73.7(1)
C(1)−P−O(5)	168.1(1)	C(11)−P−O(5)	66.31(9)
C(21)−P−O(5)	69.65(9)	C(7)−O(1)−P	115.7(2)
C(17)−O(3)−P	116.3(2)	C(27)−O(5)−P	95.9(2)
C(2)−C(1)−P	127.3(2)	C(6)−C(1)−P	112.4(2)
C(2)−C(1)−C(6)	120.3(2)	C(12)−C(11)−P	129.4(2)
C(16)−C(11)−P	110.9(2)	C(12)−C(11)−C(16)	119.6(3)
C(22)−C(21)−P	115.0(2)	C(26)−C(21)−P	126.9(2)
C(22)−C(21)−C(26)	118.1(2)		

Table 4. Selected Bond Lengths [Å] and Angles [deg] for **2**

P−O(1)	1.488(2)	P−C(1)	1.814(3)
P−C(8)	1.812(2)	P−C(14)	1.800(2)
P−O(2)	3.075(2)	O(2)−C(7)	1.191(3)
O(3)−C(7)	1.308(3)		
O(1)−P−C(1)	113.0(1)	O(1)−P−C(8)	110.6(1)
O(1)−P−C(14)	114.2(1)	C(1)−P−C(8)	104.4(1)
C(1)−P−C(14)	107.0(1)	C(8)−P−C(14)	107.0(1)
O(1)−P−O(2)	70.51(8)	C(1)−P−O(2)	70.10(8)
C(8)−P−O(2)	174.1(1)	C(14)−P−O(2)	77.28(7)
C(7)−O(2)−P	83.1(1)	C(2)−C(1)−P	119.8(2)
C(6)−C(1)−P	122.1(2)	C(2)−C(1)−C(6)	118.1(2)
C(9)−C(8)−P	125.3(2)	C(13)−C(8)−P	116.9(2)
C(9)−C(8)−C(13)	117.8(2)	C(15)−C(14)−P	119.0(2)
C(19)−C(14)−P	121.8(2)	C(15)−C(14)−C(19)	119.2(2)

Table 5. Selected Bond Lengths [Å] and Angles [deg] for **3**

P−C(8)	1.833(2)	P−C(14)	1.836(2)
P−C(1)	1.849(2)	P−O(1)	2.806(1)
O(1)−C(7)	1.222(2)	O(2)−C(7)	1.313(2)
C(1)−P−C(8)	102.66(8)	C(1)−P−C(14)	102.22(9)
C(1)−P−O(1)	74.36(7)	C(8)−P−C(14)	100.31(8)
C(8)−P−O(1)	78.59(6)	C(14)−P−O(1)	175.97(7)
C(7)−O(1)−P	96.1(1)	C(2)−C(1)−P	121.3(1)
C(6)−C(1)−P	121.7(2)	C(2)−C(1)−C(6)	116.9(2)
C(9)−C(8)−P	125.2(2)	C(13)−C(8)−P	117.3(2)
C(9)−C(8)−C(13)	117.5(2)	C(15)−C(14)−P	125.6(2)
C(19)−C(14)−P	116.7(2)	C(15)−C(14)−C(19)	117.7(2)

Table 6. Selected Bond Lengths [Å] and Angles [deg] for 4

P−C(1)	1.840(2)	P−C(8)	1.832(2)
P−C(14)	1.835(2)	P−O	2.834(2)
O−C(7)	1.194(3)		
C(1)−P−C(8)	101.84(8)	C(1)−P−C(14)	102.22(8)
C(8)−P−C(14)	102.04(7)	C(8)−P−O	76.06(6)
C(14)−P−O	176.23(7)	C(1)−P−O	75.17(8)
C(7)−O−P	94.3(2)	C(2)−C(1)−P	121.9(2)
C(6)−C(1)−P	120.3(2)	C(2)−C(1)−C(6)	117.7(2)
C(9)−C(8)-P	117.8(1)	C(13)−C(8)−P	124.1(1)
C(9)−C(8)−C(13)	118.1(2)	C(15)−C(14)−P	124.4(1)
C(19)−C(14)−P	117.0(1)	C(15)−C(14)−C(19)	118.2(2)

phosphoryl groups reduces the electrophilicity at phosphorus due to back bonding.

The ^{31}P NMR chemical shifts for **1**−**5**, listed in Chart 1, are consistent with retention of their basic structures in solution. The phosphoranes **1** and **5** exhibit the most shielded phosphorus atoms, as expected for five coordination. The phosphines **3** and **4** are less shielded, and the phosphine oxide **2** has the least shielded phosphorus atom, as expected for lower coordinated structures. However, ^{31}P shifts do not reflect variations in P−O donor interactions for these molecules. Only in the case of bicyclic tetraoxyphosphoranes experiencing the much stronger donor−acceptor action found with sulfur coordination is there a noticeable influence on ^{31}P chemical shifts.[8] Here a correlation between an increase in ^{31}P shielding and an increase in octahedral character is observed. The present series **1**−**4**, with three aryl components each, results in a sizable reduction in the electrophilicity at phosphorus.

Table 7. Selected Bond Lengths [Å] and Angles [deg] for **5**

P−O(1)	1.774(1)	P−O(3)	1.784(1)
P−C(1)	1.806(2)	P−C(11)	1.812(2)
P−C(21)	1.817(2)	O(1)−C(7)	1.330(2)
O(2)−C(7)	1.211(2)	O(3)−C(17)	1.337(2)
O(4)−C(17)	1.206(2)		
O(1)−P−O(3)	179.26(6)	O(1)−P−C(1)	88.28(7)
O(3)−P−C(1)	91.42(7)	O(1)−P−C(11)	91.69(7)
O(3)−P−C(11)	87.87(7)	C(1)−P−C(11)	119.21(8)
O(1)−P−C(21)	91.16(7)	O(3)−P−C(21)	89.57(7)
C(1)−P−C(21)	117.42(8)	C(11)−P−C(21)	123.35(8)
C(7)−O(1)−P	116.4(1)	C(17)−O(3)−P	116.5(1)
C(2)−C(1)−P	128.6(1)	C(6)−C(1)−P	111.5(1)
C(2)−C(1)−C(6)	119.8(2)	C(12)−C(11)−P	128.4(2)
C(16)−C(11)−P	111.7(1)	C(12)−C(11)−C(16)	119.9(2)
C(22)−C(21)−P	115.8(1)	C(26)−C(21)−P	124.2(1)
C(22)−C(21)−C(26)	120.0(2)		

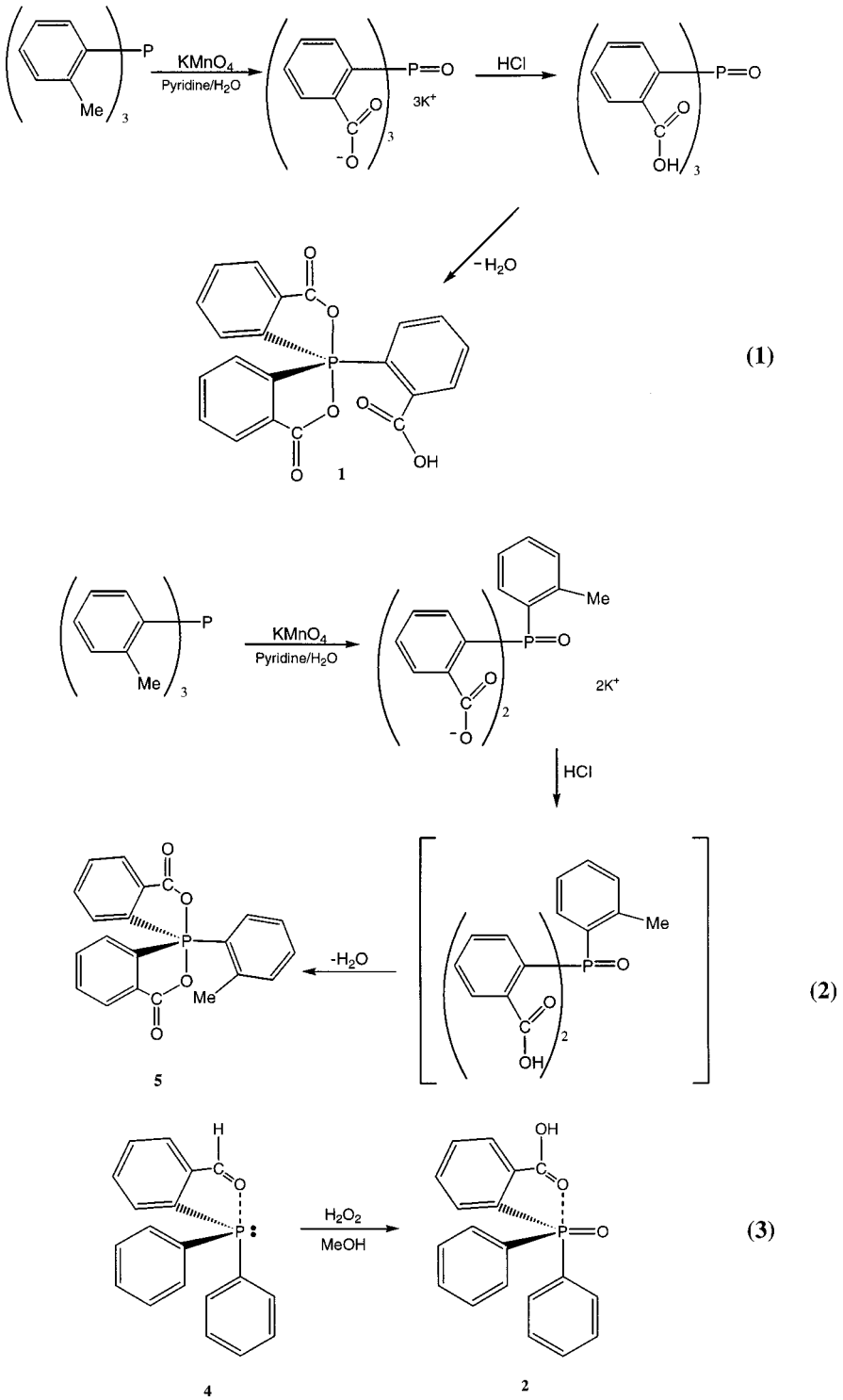
Table 9 compares bond parameters for the two crystalline modifications of phosphoranes **1** (**1A** and **1B**) that exhibit P−O donor coordination with similar bond parameters for phosphoranes **5** and **5A**,[46] which lack any donor interactions. Supporting weak P−O donor action is the presence of bond angles considerably reduced from 120° for the C1−P−C11 and C1−P−C21 values for **1A** and **1B** compared to **5** and **5A**. The greatest change is apparent for the C11−P−C21 angles, which are substantially increased for **1A** and **1B** relative to **5** and **5A**, i.e., by about 11°. This increase is attributed to the donor oxygen O5 approaching cis to C11. Other bond angles in Table 9 for the two kinds of phosphoranes are not that different from each other.

Chirality. Phosphoranes **1** and **5** have a chiral phosphorus atom as expected for a phosphorane with two axial−equatorial rings, a feature not considered by earlier workers.[47] The crystals obtained from acetone for **1A** and **5** are racemates, as established from their centrosymmetric space groups. However, the crystals of **1B**, obtained from dichloromethane, show an enantiometric excess of about 80% (90% is in one form and the remaining 10% being the enantiomer). This is based on the Flack parameter (see Table 1) and a batch scale factor of 0.10 obtained during the attempted twin refinement. Even though **1** is expected to be fluxional in solution, in the solid state it can show an isomeric preference. The two forms for phosphorus are displayed in Figure 6. Similar isomers are possible for **5**. Crystals of **1B** consist of Form I as the major isomer, whereas I and its enantiomer II are observed in equimolar quantities in the crystals of **1A** and **5**.

We plan to explore the chiral and chemical stability of **1** and exploit its use as a stable chiral acid. Studies so far show that **1** in the form of its salt is stable up to an equimolar concentration of potassium hydroxide in methanol, but in excess alkali it undergoes hydrolysis to form the phosphine oxide.

Hydrogen Bonding. In phosphorane **1**, phosphine oxide **2**, and phosphine **3**, hydrogen bonding manifests itself by way of the carboxyl hydrogen atoms. Table 10 lists the important hydrogen bonding interactions that are present in these compounds. Figures 7−10 illustrate the structures formed as a result of intermolecular hydrogen bonding in **1A**, **1B**, **2**, and **3**, respectively.

Scheme 1



For **1A**, a complex structural arrangement is formed, giving a hydrogen bonded planar polymer, Figure 7. The carboxyl hydrogen atom is hydrogen bonded to a water molecule and this water molecule is hydrogen bonded to a second water molecule. The water molecules are also involved in hydrogen bonding with the other carbonyl oxygen atoms (O2 and O4) but not to the carbonyl oxygen (O5), which interacts with the phosphorus atom. For **1B**, a simpler arrangement takes place, giving a linear hydrogen bonded polymer, Figure 8. Here the carboxyl hydrogen atom, H6, of one phosphorane molecule is involved in hydrogen bonding with one of the carbonyl oxygen atoms, O2, of an adjacent phosphorane molecule. The carbonyl oxygen atom O5 involved in donor action with phosphorus is hydrogen bonded to one of the dichloromethane hydrogens.

Both **2** and **3** form hydrogen bonded dimers, shown in Figures 9 and 10, respectively. The difference is that the phosphoryl oxygen atom O1 of **2** participates in hydrogen bonding, whereas the carbonyl donor oxygen atom O2 does not enter into hydrogen bonding. By contrast, the carbonyl donor oxygen atom O1 of phosphine **3** forms the hydrogen bonded dimer with the hydrogen atoms of the carboxyl groups.

It is significant that P−O donor−acceptor coordination persists in the presence of hydrogen bonding interactions in **1**−**3**,

Table 8. P−O Donor Distances (Å) and Torsion Angles (deg)

compound	P−O donor distance	O−C−C−C(P) torsion angle	% TBP[a]	% octa.[b]
1A	3.000(2)	29.0		23
1B	2.967(2)	12.3		25
2	3.075(2)	44.2	18	
3	2.806(1)	14.4	36	
4	2.834(2)	1.8	34	
4[c]	2.831	1.4	34	
A[d]	2.788(6)	7.4	37	
	3.049(6)	6.1		20

[a] Percent displacement toward a trigonal bipyramid. [b] Percent displacement toward an octahedron. [c] Reference 40. [d] Reference 19.

Table 9. Comparison of Bond Parameters[a] for Phosphoranes with and without P−O Donor Interaction

	1A	**1B**	**5**	**5A**[b]
O1−P−O3	178.40(7)	177.95(9)	179.26(6)	179.2
C1−P−C11	115.12(8)	113.1(1)	119.21(8)	120.5
C1−P−C21	112.76(8)	112.8(1)	117.42(8)	118.1
C11−P−C21	132.09(9)	133.9(1)	123.35(8)	121.4
O1−P−C21	89.98(7)	87.42(9)	91.16(7)	90.2
O3−P−C21	88.43(7)	91.4(1)	89.57(7)	90.6
O1−P−C1	88.48(7)	87.5(1)	88.28(7)	88.2
O3−P−C11	88.14(8)	89.2(1)	87.87(7)	88.4
O1−P−C11	92.80(8)	90.5(1)	91.69(7)	91.3
O3−P−C1	92.30(7)	94.5(1)	91.42(7)	91.4
P−C21−C22	115.1(1)	115.0(2)	115.8(1)	119.3
P−C21−C26	126.0(1)	126.9(2)	124.2(1)	121.4
C3P−Ph twist[c]	33.79(9)	20.2(2)	30.76(8)	36
P− C27	3.256(2)	3.302(2)	3.265(2)	−
P− O/H	3.000(2)	2.967(2)	3.09	−

[a] Distances are in Å and angles are in degrees. [b] Reference 46. [c] This angle refers to the angle between the equatorial plane containing phosphorus and the three carbon atoms and the plane of the single phenyl group whose carbon is attached to phosphorus.

especially since donor action with phosphorus compounds containing three aryl components leaves phosphorus at a considerably reduced electrophilicity compared to pentaoxyphosphoranes.[15,23] Phosphine **4**, which lacks hydrogen bonding, exhibits only a very small difference in the P−O donor distance when compared to the closely analogous structure of hydrogen bonded phosphine **3**. The P−O donor distance for **4** is 2.834(2) Å (2.831 Å, lit[40]) and this distance for **3** is 2.806(1) Å.

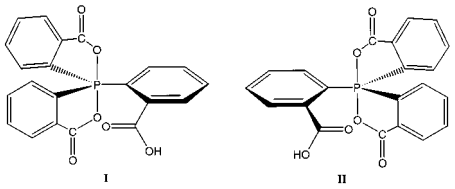


Figure 6. Isomeric representations for **1**.

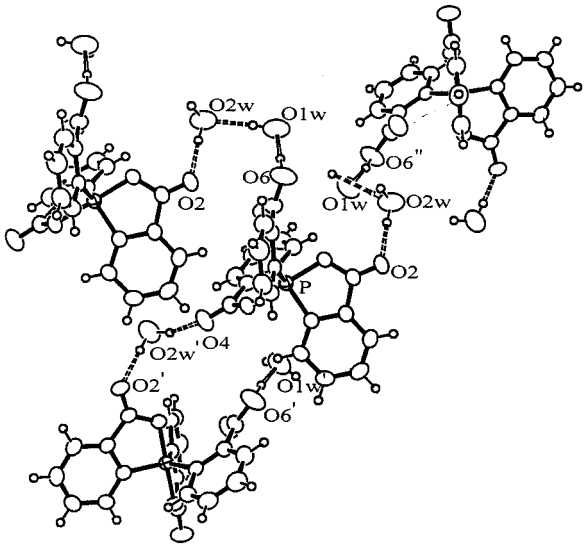


Figure 7. ORTEP-III for Windows diagram[64] of the hydrogen bonded two-dimensional polymeric representation of **1A**.

In **3**, by necessity, hydrogen bonding involves the donor oxygen atom. In **1A**, **1B**, and **2**, hydrogen bonding occurs with carbonyl oxygens not involved with donor carbonyl oxygen atoms. Thus, hydrogen bonding avoids the use of the donor oxygen atoms where possible and adds credence for P−O donor interaction to take advantage of the inherent electrophilicity present at phosphorus.

These results are in agreement with our earlier finding[14] that P−S donor coordination persists for a phosphate in the presence of hydrogen bonding no matter whether the phosphate exists as a neutral entity or is in its anionic form (Chart 2).

Table 10. Principal Hydrogen Bonding Interactions for **1**−**3**[a]

D−H···A[b]	*d*(D−H), Å	*d*(H···A), Å	*d*(D···A), Å	angle(DHA), deg
1A H−bonded 2-dimensional polymer in *yz* plane				
O2W−H3W···O2	0.92(2)	2.00(2)	2.919(3)	171(3)
O6−H1···O1W (w=water)	1.17(4)	1.47(4)	2.605(3)	161(4)
O1W−H1W···O2W ($x, y-1, z$)	0.93(2)	2.00(2)	2.899(3)	163(4)
O2W−H4W···O4 ($x, 1-y, {}^1/_2+z$)	0.92(2)	1.96(4)	2.820(3)	155(3)
O1W−H2W···O2W ($^1/_2-x, -^1/_2+y, {}^1/_2-z$)	0.94(4)	1.98(4)	2.891(3)	165(4)
1B. Linear H−bonded polymer along *z* axis (fixed hydrogen)				
O6−H6···O2 (x, y, 1+z)	0.82	2.00	2.624(3)	153
2. H−bonded dimer				
O3−H1···O1 ($^1/_2-x, {}^1/_2-y, 2-z$)	0.99(4)	1.67(5)	2.642(3)	169(4)
3. H−bonded dimer				
O2−H1···O1 ($1-x, 2-y, 1-z$)	0.93(3)	1.71(3)	2.630(2)	172(3)

[a] No C−H···O hydrogen bonds are included. [b] D = hydrogen atom donor and A = hydrogen atom acceptor.

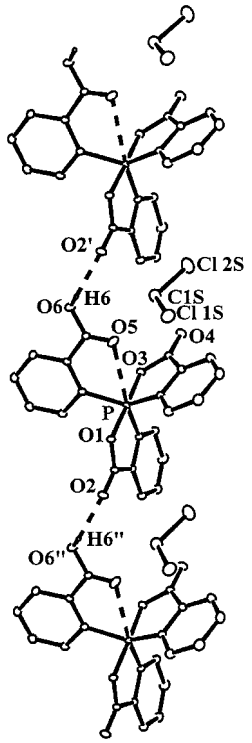


Figure 8. ORTEX diagram of the linear hydrogen bonded polymer arrangement of **1B**.

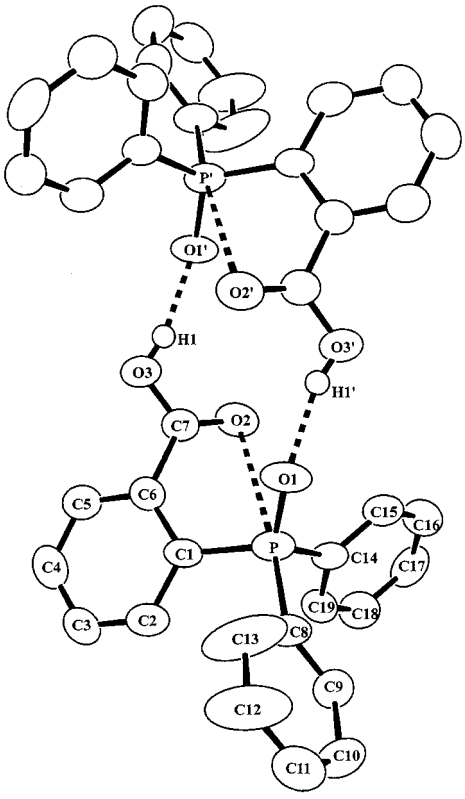


Figure 9. ORTEX diagram of the hydrogen bonded dimer formation of **2**.

It is possible to compare P−O donor coordination and hydrogen bonding in a more quantitative fashion. The hydrogen bond interactions that do not involve water or solvent molecules are shown in Table 10 for **1B**, **2**, and **3** and are seen to be confined to a narrow range, 2.624−2.642 Å. Examination of

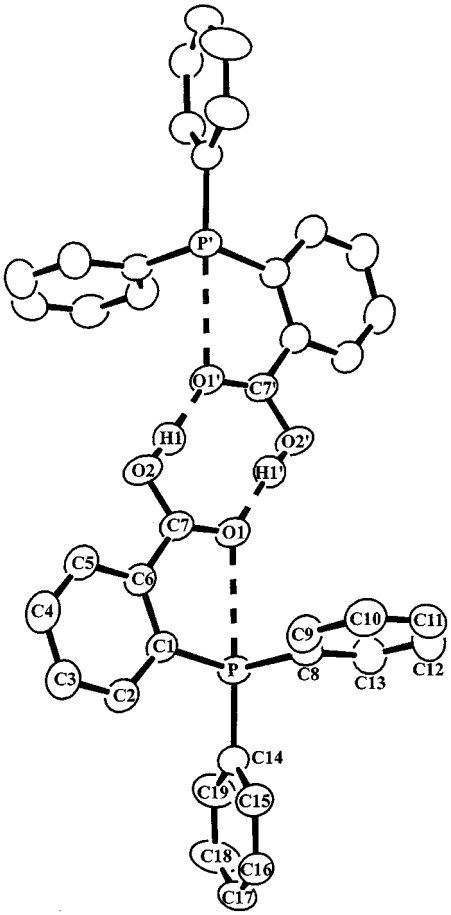


Figure 10. ORTEX diagram of the hydrogen bonded dimer formation of **3**.

literature on O−H···O hydrogen bonding with regard to the relation between enthalpy and O−O distance,[53] suggests that a value of about 5.5 kcal/mol applies in the present series. To establish a relationship between P−O bond distance and interaction energy, we employed an exponential function governing these two quantities. The P−O single bond energy is estimated as 80 kcal/mol, and the P−O single bond distance is about 1.63 Å.[54] With the use of the sum of the van der Waals radii of 3.35 Å for phosphorus and oxygen and setting this distance to correspond to a zero P−O bond energy, one may define the exponential relation to connect these limits.

This procedure allows an estimation of the P−O donor energies for **1**−**4**; these are in kcal/mol: 5.0 (**1**), 3.5 (**2**), 10 (**3**), and 9 (**4**). Based on this interpretation, P−O donor energies range from less than to more than the hydrogen bond energies. Thus, for **2**, with the P−O donor energy estimated to be less than the hydrogen bond energy, P−O donor action persists and is not involved in hydrogen bonding. The same is true for **1A** and **1B**, but here the P−O donor energies are estimated to be stronger than the energies associated with the hydrogen bonding. Only in the case of **3** (Figure 10) is the carbonyl oxygen atom (O1) involved in coordination to phosphorus and hydrogen bonding. One would expect the P−O energy to be reduced by the presence of hydrogen bonding since this process should remove some electron density at O1 and weaken the coordina-

(53) Pimintal, G. C.; McClellan, A. L. *The Hydrogen Bond*; W. H. Freeman and Co.: San Francisco, 1960.
(54) Huheey, J. E.; Keiter, E. A.; Keiter, R. L. *Inorganic Chemistry*, 4th ed.; Harper Collins: New York, 1993, Appendix E.

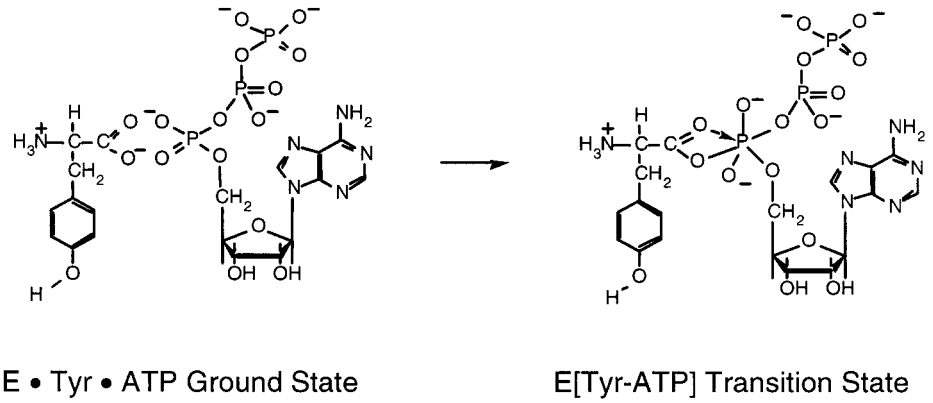
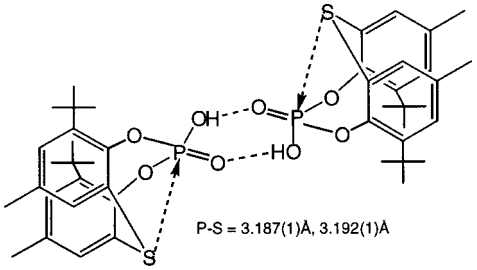
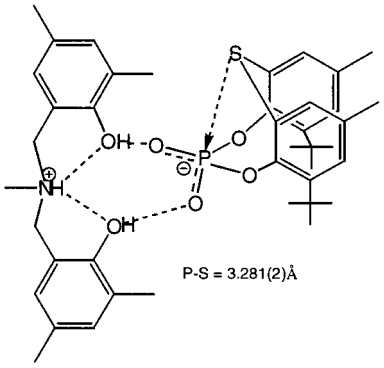
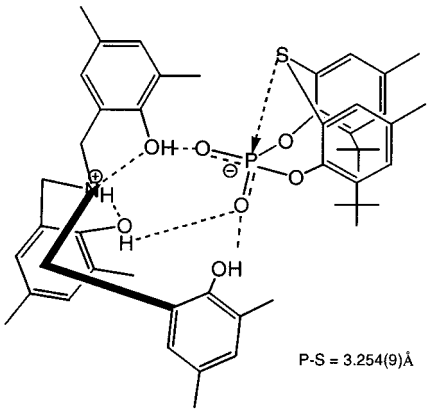


Figure 11. Ground-state complex[63] and proposed transition-state complex[19] in the activation of tyrosine by the tyrosyl−tRNA synthetase.

Chart 2. Schematic Representations of Phosphate Structures Exhibiting Hydrogen Bonding and P-S Interactions[14]







tion. However, as noted above, the P−O donor bond distance of **3** is very similar to that of **4**, which lacks any hydrogen bonding.

Application to Enzyme Active Sites. The work reported here shows that even weak P−O donor interactions persist in the presence of hydrogen bonding systems. Active sites of phosphoryl transfer enzymes and cAMP have postulated pentaoxyphosphoranes (TBP) as intermediates, for example, in hydrolysis mechanisms.[12,24,55−59] These intermediates have highly electrophilic phosphorus atoms capable of forming stronger P−O coordination than in the present study. This is evident from previous studies[2,13,18,23] of ours, conducted in the absence of hydrogen bonding, that show that donor coordination increases in the order: phosphates < phosphites < pentaoxyphosphoranes. Donor coordination with pentaoxyphosphoranes[3−13,15,17,18,20] leads to hexacoordinated phosphorus. These studies have included oxygen,[12,15,17,18] nitrogen,[20] and sulfur[3−13,15] donor atoms.

Enzyme active sites of phosphoryl transfer enzymes and cAMP invariably are portrayed with nearby residues involved in hydrogen bonding with the substrate but not with donor interactions.[23,24] Thus, knowledge of the coordination tendencies of phosphorus which might assist in describing mechanistic action of phosphoryl transfer enzymes and cAMP has not been utilized up to the present.

A number of enzymes, whose active sites have been mapped out, that contain potential oxygen donor groups include, e.g., alkaline phosphatase,[60,61] orotidine 5′-monophosphate decarboxylase,[62] and tyrosyl-tRNA synthetase.[63] In the latter enzyme operating on ATP, it has been proposed[63] that the carboxylate oxygen atom of tyrosine binds to phosphorus in the transition state, giving a pentacoordinate phosphorus atom. Consistent with our work is the likelihood that the carbonyl oxygen atom of

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the tyrosyl carboxylate groups also interacts with phosphorus.[19,23] This would result in a nucleophilic assisted nucleophilic attack in cleaving ATP in an in-line mechanism.

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Supporting Information Available: Tables of atomic coordinates, anisotropic thermal parameters, bond lengths and angles, and hydrogen atom parameters for **1**−**5** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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