³¹P NMR Chemical Shifts in Hypervalent Oxyphosphoranes and Polymeric Orthophosphates

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We report the first quantum chemical investigation of the solid- and solution-state ³¹P NMR chemical shifts in models for phosphoryl transfer enzyme reaction intermediates and in polymeric inorganic phosphates. The ³¹P NMR chemical shifts of five- and six-coordinate oxyphosphoranes containing a variety of substitutions at phosphorus, as well as four-coordinate polymeric orthophosphates and four-coordinate phosphonates, are predicted with a slope of 1.00 and an $R^2 = 0.993$ (N = 34), corresponding to a 3.8 ppm (or 2.1%) error over the entire 178.3 ppm experimental chemical shift range, using Hartree-Fock methods. For the oxyphosphoranes, we used either experimental crystallographic structures or, when these were not available, fully geometry optimized molecular structures. For the four-coordinate phosphonates we used X-ray structures together with charge field perturbation, to represent lattice interactions. For the three-dimensional orthophosphates (BPO₄, AlPO₄, GaPO₄), we again used X-ray structures, but for these inorganic systems we employed a self-consistent charge field perturbation approach on large clusters, to deduce peripheral atom charges. For pentaoxyphosphoranes, the solvent effect on ³¹P NMR chemical shieldings was found to be very small (<0.5 ppm). The ³¹P NMR chemical shielding tensors in the pentaoxyphosphoranes were in most cases found to be close to axially symmetric and were dominated by changes in the shielding tensor components in the equatorial plane $(\sigma_{22} \text{ and } \sigma_{33})$. The isotropic shifts were highly correlated $(R^2 = 0.923)$ with phosphorus natural bonding orbital charges, with the larger charges being associated with shorter axial P–O bond lengths and, hence, more shielding. Overall, these results should facilitate the use of ³¹P NMR techniques in investigating the structures of more complex systems, such as phosphoryl transfer enzymes, as well as in investigating other, complex oxide structures.

Introduction

The transition states or reactive intermediates of phosphoryl transfer enzymes and ribozymes are thought to feature fivecoordinate oxyphosphoranes,¹⁻³ and characterization of these active sites is desirable for improving our understanding of their modes of action and inhibition. The first X-ray crystal structure of such an intermediate was reported recently, but this structure raised questions as to the true identity of the species detected: did it contain a PO₃ or an MgF₃ group, coordinated to two oxygens?^{4,5} A theoretical study supported the idea of the presence of an MgF₃ group;⁶ however, the results of chemical analyses (of phosphorus) as well as further diffraction results⁷ now support the earlier interpretation of the presence of a pentavalent oxyphosphorane intermediate.⁴ Moreover, another pentavalent oxyphosphorane intermediate,⁸ and analogous hypervalent vanadates as well as tungstates, have been observed in other crystallographic structures of phosphoryl transfer proteins,⁹ again supporting the earlier interpretation.

Given these observations, it would clearly be of interest to use other complementary techniques to probe these systems in more detail, e.g., ³¹P or ⁵¹V NMR spectroscopy and, indeed, ³¹P NMR spectroscopy¹⁰ has been used to investigate model systems for phosphoryl transfer enzyme intermediates, having various coordination motifs, for over 4 decades.^{11–23} However, there have been no reports of the quantum chemical calculation of the ³¹P NMR shifts in these systems. Such calculations would be desirable in order to fully interpret the ³¹P NMR chemical shifts of reactive intermediates in proteins since the geometries of such species will have much larger errors than are found in more typical, small molecule crystal structures, necessitating the use of geometry optimization techniques in order to accurately reproduce the experimental spectroscopic observables.^{24–27} In this paper, we report the first quantum chemical investigation of the ³¹P NMR chemical shifts of a series of pentavalent oxyphosphoranes, containing O₅, O₄C₁, and O₄N₁ coordination spheres, using in some cases, geometry optimization techniques to deduce compound geometries. These results are complemented by additional studies of six-coordinate oxyphosphoranes as well as two other species: four-coordinate phosphonates and orthophosphates, to give a broad overview of the accuracy of chemical shift predictions which can currently be made using a variety of quantum chemical methods on a diverse range of P-O containing compounds.

Computational Details

We show in Figure 1 the structures of the systems investigated. There are 11 oxyphosphoranes containing an O₅ coordination sphere: $O_2S[(t-Bu)MeC_6H_2O]_2P(OCH_2CF_3)_3$ (1),¹⁹ $O_2S[(t-Bu)MeC_6H_2O]_2P(OPh)_3$ (2),¹⁹ (Xyl-O)_3P(O_2C_3H_4Me_2) (3),¹⁷ (Xyl-O)_3P(O_2C_{12}H_8) (4),¹⁷ (C_6H_5O)_3P(O_2C_{14}H_8) (5),¹⁶ (MeO)_3P[O_2(CMeCOMe)_2] (6),¹³ (MeO)_3P[(OCMeCOMe)-(OCMeEt)] (7),¹² (MeO)_3P[(OCMe)_2] (8),¹¹ (MeO)_3P(O_2C_{14}H_8) (9),¹⁶ P[(OCCF_3)_2](O_3C_6H_9) (10),²¹ and (PhO)P(O_2C_2H_4)-



Figure 1. Molecular structures of 1-18 (P, orange ball; O, red; C, cyan; N, blue; S, yellow; F, green; Cl, pink; H omitted for clarity).

system	$\delta^{ ext{expt}}$		$\sigma^{\rm calc}$	$\delta^{ m calc}_{ m abs}$	$\delta^{ m pred}_{ m reg}$	system	$\delta^{ ext{expt}}$		$\sigma^{\rm calc}$	$\delta^{ m calc}_{ m abs}$	$\delta^{ m pred}_{ m reg}$
1 O ₅	-84.1 [19]	solid	438.7	-110.4	-82.7	$18 O_5 N_1$	-145.6 [23]	soln	493.0	-164.7	-137.0
2 O ₅	-78.3 [19]	solid	436.6	-108.3	-80.6	19 O ₄	-29.5 [28]	solid	377.4	-49.1	-21.4
3 O ₅	-77.5 [17]	soln	434.4	-106.1	-78.4	20 O ₄	-24.5 [28]	solid	386.6	-58.3	-30.6
4 O ₅	-68.3 [17]	soln	416.7	-88.4	-60.7	21 O ₄	-9.8 [28]	solid	365.5	-37.2	-9.5
5 O ₅	-58.6 [16]	soln	417.5	-89.2	-61.5	$22 O_3 C_1$	18.4 [31]	solid	336.2	-7.9	19.8
6 O ₅	-54.8 [13]	soln	410.7	-82.4	-54.7	23 O ₃ C ₁	9.1 [31]	solid	344.8	-16.5	11.2
7 O ₅	-51.3 [12]	soln	407.8	-79.5	-51.8		3.9 [31]	solid	349.3	-21.0	6.7
8 O ₅	-48.9 [11]	soln	406.7	-78.4	-50.7	$24 O_3 C_1$	22.8 [31]	solid	332.2	-3.9	23.8
9 O ₅	-44.7 [16]	soln	402.4	-74.1	-46.4		16.8 [31]	solid	337.2	-8.9	18.8
10 O ₅	-41.7 [21]	soln	401.5	-73.2	-45.5	$25 O_3 C_1$	15.9 [31]	solid	341.6	-13.3	14.4
11 O ₅	-27.0 [16]	soln	389.1	-60.8	-33.1		12.8 [31]	solid	346.7	-18.4	9.3
$12 O_4 C_1$	-63.3 [18]	soln	418.9	-90.6	-62.9	26 O_3C_1	18.3 [31]	solid	339.5	-11.2	16.5
$13 O_4 C_1$	-34.2 [14]	soln	385.8	-57.5	-29.8	$27 O_3 C_1$	21.0 [31]	solid	335.5	-7.2	20.5
$14 O_4 C_1$	-17.9 [15]	soln	378.5	-50.2	-22.5	28 O ₃ C ₁	26.2 [31]	solid	326.9	1.5	29.1
$15 O_4 N_1$	-59.0 [22]	soln	411.8	-83.5	-55.8		24.7 [31]	solid	331.3	-3.0	24.7
$16 O_4 N_1$	-50.1 [22]	soln	408.4	-80.1	-52.4	29 O ₃ C ₁	32.7 [31]	solid	321.7	6.7	34.3
17 O ₆	-126.5 [20]	soln	489.0	-160.7	-133.0		32.7 [31]	solid	321.7	6.7	34.3

ſABL	E 1	l:	Experimental	and	Computed	³¹ P	NMR	Chemical	Shifts	and	Shieldings	(ppm) ^a
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^{*a*} References are in brackets. The first coordination shell atoms are indicated. The ³¹P NMR shifts are referenced to 85% phosphoric acid. Calculated shielding results (σ^{calc}) are from HF/6-311++G(2d,2p) as described in the text.

 $(O_2C_{14}H_8)$ (11).¹⁶ The shifts of several five-coordinate oxyphosphoranes containing O_4C_1 or O_4N_1 coordination motifs were also evaluated: Me₂C(CH₂O)₂P(OC₁₂H₈)(OXyl) (12),¹⁸ (MeO)₃P-(O₂C₆H₁₂) (13),¹⁴ P[OC(Ph)=NC(CF₃)₂](O₃C₆H₉) (14),¹⁵ H₂C-(6-*t*-Bu-4-Me-C₆H₂O)₂P(NCS)(O₂C₆Cl₄) (15),²² H₂C(6-*t*-Bu-4-Me-C₆H₂O)₂P(NH₂)(O₂C₆Cl₄) (16),²² in addition to two six-coordinate oxyphosphoranes, O₂S[(*t*-Bu)MeC₆H₂O]₂P(OC₆F₅)₃ (17)²⁰ and N[CH₂(Me(*t*-Bu)C₆H₂O)]₃P(OPh)₂ (18),²³ having O₆ and O₅N₁ coordination spheres, respectively. The coordination motifs investigated, O₅, O₄N₁, and O₄N₁, are the same as those reported in protein X-ray structures containing hypervalent phosphorus, vanadium, and tungsten species.^{4,8-9}

The hypervalent oxyphosphoranes contain a broad range of substituents (alkyl, aromatic; monocyclic, bicyclic, polycyclic; electron-donating, electron-withdrawing), and their ³¹P NMR shifts span a range of 128 ppm (Table 1)^{11–23} and, consequently, are expected to provide a good test of the quality of the ab initio chemical shift/shielding prediction methods.

We also investigated shieldings in three inorganic orthophosphates,²⁸ XPO₄, X = B (**19**), Al (**20**), Ga (**21**), having threedimensional polymeric structures.^{29,30} BPO₄, AlPO₄, and GaPO₄ all have the same cristobalite type structure as illustrated in Figure 2A: each P and X (=B, Al, Ga) coordinates to four oxygens and each oxygen coordinates to one P and one X.^{29,30} Their ³¹P NMR chemical shifts differ by 20 ppm,²⁸ however, and are clearly more deshielded than most of the ³¹P NMR shifts in the five- and six-coordinate oxyphosphoranes, Table 1.^{11–23}

On the basis of previous methodological investigations employing both HF and DFT methods,³¹ we chose to first use the HF method using the GIAO formalism³² in the Gaussian 03 program³³ to evaluate ³¹P NMR shielding properties. For the oxyphosphoranes (1–18), we used complete molecules (having up to 113 atoms) in the calculations, using a locally dense basis set scheme: 6-311++G(2d,2p) for P and its first coordination-shell atoms, and 6-31G(d) for the other atoms. This is basically the approach used previously to evaluate ³¹P NMR chemical shifts in a series of phosphonates.³¹ The X-ray structures of 1 and 2¹⁹ and the geometry optimized structures of 3–18 (see Supporting Information for the fully optimized structures, obtained by using the B3LYP functional³⁴ and a 6-31G(d) basis) were used to predict the solid-state and solution NMR shifts, respectively.



Figure 2. SC-CFP computational approach for GaPO₄: (A) crystal structure; (B) cluster structure; (C) first run data; (d) second run data; (E) third run data. In (C–E), real atoms and point charges are represented by sticks and balls, respectively (P, orange; O, red; Ga, gray).

For the polymeric orthophosphates (19-21), we use a selfconsistent charge field perturbation (SC-CFP) approach³⁵ in order to predict the solid-state ³¹P NMR shifts, as discussed in more detail below. The ³¹P NMR shifts of eight four-coordinate phosphonates (13 phosphorus sites having O₃C₁ coordination) studied previously (22–29, compounds 1-8 in ref 31) were also



calculated, using the same HF/6-311++G(2d,2p) method and the CFP approach^{36,37} as described in ref 31, but this time with the same GIAO formalism as used with the hypervalent oxyphosphoranes, for purposes of comparison. Bader's atomsin-molecules (AIM) theory³⁸ was used probe the nature of P-O bonding in the hypervalent oxyphosphoranes using the wave functions from the ab initio calculations and the AIM2000 program.³⁹ HF/6-311++G(2d,2p) calculations have been found to give good representations of the charge density and other chemical bond properties,⁴⁰ and AIM theory was used here to investigate bonding around the phosphorus sites⁴¹ in these systems. In addition to the above-described HF calculations of ³¹P NMR chemical shieldings, we also investigated the use of density functional theory (DFT) using the B3LYP functional with the same basis set scheme as used in the HF calculations to calculate the ³¹P NMR chemical shieldings in all these systems (1-29). Plus, to estimate possible solvent effects on the ³¹P shifts in the oxyphosphoranes, we used the self-consistent reaction field (SCRF) method using the COSMO formalism⁴² in the Gaussian 03 program, with different dielectric constants to represent different solvent environments. Calculations were performed on Silicon Graphics (Mountain View, CA) O-300 computers (using up to eight processors) as well as on a PQS (PQS Inc., Fayetteville, AR) workstation, equipped with 12 processors.

Results and Discussion

All of the computed ³¹P NMR chemical shieldings (σ^{calc}) are listed in Table 1, together with the corresponding experimentally measured chemical shifts (δ^{expt}). The compounds investigated

represent three rather different formal bonding situations: (1) conventional organic compounds, the oxyphosphoranes, typically P(OR)₅; (2) mixed organic/inorganic solids-phosphonates, containing P-C and P-O bonds, frequently with extensive electrostatic interactions in the crystal lattice, and (3) inorganic mixed oxides: $P_2O_5 \cdot X_2O_3 \equiv XPO_4$, e.g., AlPO₄. We used three methods to evaluate the NMR chemical shieldings: For the purely organic compounds we used single molecule structures in the HF calculations. For the phosphonates, the effects of electrostatic fields, or, equivalently, Coulombic interactions, become more important and consequently for these species we used a central phosphonate molecule while the rest of the crystal was represented by a charge field-the charge field perturbation (CFP) method^{36,37} described previously. This approach gives a good account of the lattice interactions for such mixed, organic/ inorganic solids and may be a good representation for phosphate, phosphonate, or oxyphosphorane species in proteins. For the polymeric inorganic solids, it might be possible to use simple cluster models, for example, P[OAl(OH)2]4 for AlPO4, or indeed the use of periodic boundary conditions,43 but based on earlier work with ⁶⁷Zn shifts in ZnO and ZnS,³⁵ we elected to use the self-consistent charge field perturbation (SC-CFP) method, which truncates clusters with a P atom whose charge is calculated in a self-consistent manner, as shown in Figure 2, an approach which could find utility in investigating the effects of bond length/bond angle effects on property calculations.

We show in Figure 2A the GaPO₄ lattice while Figure 2B shows the central PO₄ surrounded by GaO₄ tetrahedra in which each terminal oxygen in the cluster is capped with a P atom, treated as a point charge. In the cases of BPO₄, AlPO₄, and GaPO₄, all terminal atoms are equivalent to the central phosphorus atom and should therefore have the same atomic charges. All atoms in the clusters (except for the terminal atoms) were thus treated as real atoms (sticks in Figure 2C-E) with a 6-311++G(2d,2p) basis, while the terminal atoms (balls in Figure 2C-E) were treated as point charges, using natural bonding orbital (NBO) charges⁴⁴ obtained in a self-consistent manner (convergence set as 0.01 e). As shown in Figure 2C for GaPO₄, in the first run, the initial charge for phosphorus $(Q_{\rm P})$ was set as 5.00 e. After the calculation was complete, the computed NBO charge was found to be 2.79 e and the ³¹P NMR shielding (σ^{calc}), 358.2 ppm. This charge was then used in the input for the terminal atom's point charges in the second run, Figure 2D. From the output of the second run, we obtain $Q_{\rm P} =$ 2.85 e and $\sigma^{\text{calc}} = 365.5$ ppm. This new Q_{P} value was then used in the input for the terminal point charges in the third run. The output $Q_{\rm P}$ value in the third run was found to be the same as the input charge (at the precision used of 0.01 e), which means that convergence is manifest and consequently the final $\sigma^{\text{calc}} =$ 365.5 ppm value was used for the computed shielding for GaPO₄, as shown in Table 1. The same approach was then used for BPO₄ and AlPO₄.

The theoretically calculated chemical shieldings can be converted into calculated chemical shifts (δ_{abs}^{calc}) by using the absolute shielding of 85% H₃PO₄, reported previously by Jameson et al.⁴⁶ to be 328.35 ppm, Table 1. However, when the computed shieldings are plotted versus the experimental chemical shifts, we find an absolute shielding of 356.0 ppm, due presumably to basis set deficiencies or the neglect of electron correlation. Nevertheless, the actual correlation coefficient ($R^2 = 0.993$) and slope (-1.00) values are excellent. Consequently, we also show in Table 1 the theoretically predicted chemical shifts (δ_{reg}^{pred}) for compounds **1–29** obtained from the theoretical shieldings shown in Table 1 by using the



Figure 3. Plot of experimental versus predicted ³¹P NMR chemical shifts (HF results): circles, five-coordinate oxyphosphoranes; down triangles, six-coordinate oxyphosphoranes; up triangles, four-coordinate polymeric orthophosphates; squares, four-coordinate phosphonates. Solid and open data points stand for solid-state and solution ³¹P NMR shifts, respectively.

regression line between σ^{calc} and δ^{expt} , where we find

$$\delta_{\rm reg}^{\rm pred} = 356.0 - 1.00\sigma^{\rm calc} \tag{1}$$

As shown in Figure 3, there is an excellent correlation between these predictions and the experiment for all 34 phosphorus sites, for both the solid-state (solid data points) and solution NMR results (open data points), again of course with an $R^2 = 0.993$ and a slope of 1.00. Using this approach the root mean square error for δ_{reg}^{pred} is 3.8 ppm, or 2.1% of the whole experimental chemical shift range, of 178.3 ppm. Although the origins in the deviations in the absolute shielding are still not known, the absolute shielding of 85% H₃PO₄ (the ³¹P NMR shift reference) from these ab initio GIAO calculations is identical to that found in our previous CSGT⁴⁵ calculations,³¹ and from a practical standpoint does not affect our ability to make accurate shift predictions.

As may be seen from Figure 3, the shielding predictions (δ_{reg}^{pred}) for each of the different systems investigated (circles, five-coordinate oxyphosphoranes; down triangles, six-coordinate oxyphosphoranes; up triangles, four-coordinate polymeric orthophosphates; squares, four-coordinate phosphonates) are very promising. More specifically, the prediction of the solid-state ³¹P NMR chemical shifts (18 data points) for oxyphosphoranes (1, 2), orthophosphates (19-21), and phosphonates (22-29)cover a range of 116.8 ppm and provide a basis for the use of these computational methods in investigating a variety of related phosphorus-containing compounds. The predicted solution ³¹P NMR shifts (16 data points) for the oxyphosphoranes (3-18)cover a range of 127.7 ppm and lie on the same line as those for the solid-state NMR results, indicating that they also can be accurately predicted, even through in 16/18 cases their structures were obtained via gas-phase geometry optimization. For the polymeric orthophosphates, the SC-CFP approach dramatically reduced the errors in the shift predictions in 19-21 to 8.1, 6.1, 0.3 ppm, from the 45.0, 27.5, 17.3 ppm errors calculated for the PO₄³⁻ fragments alone in these XPO₄ crystals. The final prediction errors for these SC-CFP calculations are comparable to those of ⁶⁷Zn NMR shifts in polymeric zinc complexes reported previously.35

TABLE 2: Experimental and Computed ³¹P NMR Chemical Shifts and Shieldings (ppm)^a

system	$\delta^{ ext{expt}}$		$\sigma^{\rm calc}$	$\delta^{ m calc}_{ m abs}$	$\delta_{ m reg}^{ m pred}$	system	$\delta^{ ext{expt}}$		$\sigma^{\rm calc}$	$\delta^{ m calc}_{ m abs}$	$\delta^{ m pred}_{ m reg}$
1 O ₅	-84.1 [19]	solid	388.9	-60.6	-118.7	$18 O_5 N_1$	-145.6 [23]	soln	412.6	-84.3	-149.1
2 O ₅	-78.3 [19]	solid	363.9	-35.6	-86.7	19 O ₄	-29.5 [28]	solid	331.7	-3.4	-45.4
3 O ₅	-77.5 [17]	soln	350.7	-22.4	-69.7	20 O_4	-24.5 [28]	solid	338.9	-10.6	-54.6
4 O ₅	-68.3 [17]	soln	339.7	-11.4	-55.6	21 O ₄	-9.8 [28]	solid	316.3	12.1	-25.9
5 O ₅	-58.6 [16]	soln	342.6	-14.3	-59.4	$22 O_3 C_1$	18.4 [31]	solid	283.6	44.8	16.3
6 O ₅	-54.8 [13]	soln	331.8	-3.5	-45.5	$23 O_3 C_1$	9.1 [31]	solid	297.6	30.8	-1.7
7 O ₅	-51.3 [12]	soln	327.8	0.6	-40.4		3.9 [31]	solid	300.5	27.9	-5.4
8 O ₅	-48.9 [11]	soln	326.3	2.1	-38.5	$24 O_3 C_1$	22.8 [31]	solid	276.8	51.6	25.0
9 O ₅	-44.7 [16]	soln	320.7	7.7	-31.3		16.8 [31]	solid	285.6	42.8	13.7
10 O ₅	-41.7 [21]	soln	320.2	8.2	-30.6	25 O ₃ C ₁	15.9 [31]	solid	289.9	38.5	8.2
11 O ₅	-27.0 [16]	soln	304.7	23.7	-10.8		12.8 [31]	solid	298.5	29.9	-2.8
$12 O_4 C_1$	-63.3 [18]	soln	343.2	-14.9	-60.1	26 O_3C_1	18.3 [31]	solid	286.4	42.0	12.7
13 O ₄ C ₁	-34.2 [14]	soln	303.0	25.4	-8.6	27 O ₃ C ₁	21.0 [31]	solid	278.8	49.6	22.4
$14 O_4 C_1$	-17.9 [15]	soln	291.6	36.8	6.0	28 O_3C_1	26.2 [31]	solid	272.8	55.6	30.1
$15 O_4 N_1$	-59.0 [22]	soln	339.4	-11.1	-55.3		24.7 [31]	solid	278.4	50.0	22.9
$16 O_4 N_1$	-50.1 [22]	soln	332.4	-4.1	-46.3	29 O ₃ C ₁	32.7 [31]	solid	265.2	63.2	39.9
17 O ₆	-126.5 [20]	soln	402.2	-73.9	-135.8		32.7 [31]	solid	265.3	63.1	39.7

^{*a*} References are in brackets. The first coordination shell atoms are indicated. The ³¹P NMR shifts are referenced to 85% phosphoric acid. Calculated shielding results (σ^{calc}) are from B3LYP/6-311++G(2d,2p) as described in the text. The predicted shifts (δ^{pred}_{reg}) are based on the theory-versus-experiment correlation or fitting: $\delta^{pred}_{reg} = (296.3 - \sigma^{calc})/0.78$.



Figure 4. Plot of experimental shifts versus calculated ³¹P NMR chemical shieldings (B3LYP results): circles, five-coordinate oxyphosphoranes; down triangles, six-coordinate oxyphosphoranes; up triangles, four-coordinate polymeric orthophosphates; squares, four-coordinate phosphonates. The two dashed lines are regression lines for four-coordinate and five-coordinates systems, respectively.

The origins of the discrepancy in absolute shielding are, nevertheless, of interest, so to probe this question in more detail, we repeated all of the calculations using density functional theory, employing the popular hybrid functional B3LYP (which includes both electron correlation and Hartree-Fock exchange). On the basis of previous work on ¹³C NMR shifts, we expected small differences in slope and absolute shielding but with similar R^2 values. However, as can be seen in Table 2 and Figure 4, the results obtained were much worse, with slope = -0.78, R^2 = 0.923 and root mean square deviation = 7.1 ppm. As can also be seen in Figure 4, the three different types of compounds have shieldings which fall on different trend lines, which we attribute to very different bonding situations in the different types of compounds. For a given class (the five-coordinate oxyphosphoranes or four-coordinate phosphonates/phosphates) where there are numerous data points, the correlations ($R^2 = 0.916$, 0.972 for the five-coordinate and four-coordinate systems, respectively) are good, but there are clearly very different intercepts (absolute shieldings) between the classes. This implies that it will be necessary to adjust the amounts of HF exchange/

 TABLE 3: Solvent Effects on Computed ³¹P NMR Chemical Shieldings^a

	$\sigma^{ m calc}$ (ppm)									
system	$\epsilon = 1.0$	$\epsilon = 4.0$	$\epsilon = 10.0$	$\epsilon=20.0$	$\epsilon = 78.39$					
6 O ₅ 9 O ₅ 10 O ₅ 13 O ₄ C ₁	410.7 402.4 401.5 385.8	410.6 402.1 401.6 385.8	410.5 402.0 401.5 385.7	410.5 402.0 401.5 385.7	410.5 402.0 401.5 385.7					

^{*a*} HF/6-311++G(2d,2p) calculations.

electron correlation for each type of compound, something which seems undesirable given that the R^2 values within a class are no better than those obtained in the HF calculations ($R^2 =$ 0.966, 0.972 for the five-coordinate and four-coordinate systems, respectively). Therefore, the HF method was used in all following investigations and, at present, appears to be the method of choice for such shift predictions.

Another factor which might contribute to shift prediction errors in the hypervalent oxyphosphoranes is solvent effects. We thus carried out SCRF calculations using the COSMO formalism⁴² on compounds 6, 9, 10, and 13, using a variety of dielectric constants to represent different environments. Results are shown in Table 3, for ϵ values ranging from 1.0 (vacuum) to 78.39 (water). As can be seen from Table 3, solvent effects are quite small. For many molecules, gas-to-liquid shifts are large, but because the ³¹P atoms are essentially completely buried in these systems, and are thus unlikely to interact with solvent (CDCl₃, CH₂Cl₂, C₆D₆), these small shift differences are not entirely unexpected. In contrast to these results, it is worth noting that the exposed carbonyl oxygen atoms in compound **6** can have solvent effects of 30-40 ppm with $\epsilon =$ 4.0 and 44–55 ppm with $\epsilon = 78.39$ (data not shown), while their attached ¹³C atoms also have sizable shifts (in the opposite direction), consistent with solvation of these more exposed groups.

We next look at the effects of coordination number on ³¹P NMR chemical shifts. As shown in Figure 3, the ³¹P NMR shifts become more shielded when the coordination number increases from 4 to 5 to 6, a phenomenon also seen with ²⁹Si NMR shifts in silicates⁵¹ and for ⁶⁷Zn NMR shifts in zinc complexes.³⁵ This trend may be helpful in the NMR characterization of five-coordinate phosphoryl transfer enzyme intermediates, since the reactants and products of such reactions are generally four-



Figure 5. ³¹P NMR shielding tensor orientations (green) for **8** (P, orange; O, red; C, cyan; H omitted for clarity). σ_{11} is, in general, close to the axial P–O bond vector.



Figure 6. Plot of computed ³¹P NMR shielding tensor elements as a function of isotropic shielding for O₅ oxyphosphoranes (1–11). Except for 2 (open data points), the other 10 compounds are represented by solid data points with down triangle, up triangle and square points representing σ_{11} , σ_{22} , and σ_{33} , respectively.

coordinate systems, although of course a full quantum chemical investigation will be advisable since the effects of charge/ ionization state, the nature (O,N) of the ligands binding directly to phosphorus, metal—ion bonding, and the effects of electrostatic field effects on shielding, all of which can occur in proteins, are not immediately obvious.

Nevertheless, in the five-coordinate systems we have investigated here, there are already a variety of interesting substitution motifs at the phosphorus sites which produce very diverse ³¹P NMR shifts, and even for the O_5 species 1–11, the chemical shift range is large, some 60 ppm.^{11–13,16–18,21} We therefore next investigate in more detail the origins of these shifts, to obtain a better understanding of their correlations with geometric and electronic structural properties. As shown in Figure 5, for compound 8, a typical O_5 oxyphosphorane, the least shielded tensor component (σ_{11}) aligns close to the axial P–O bonds, while the two more shielded components (σ_{33} and σ_{22}) are basically in the equatorial plane. Figure 6 shows how each shielding tensor element varies with respect to the isotropic shielding and all computed shielding tensor element results are given in Table 4. As can be seen from Figure 6, σ_{33} and σ_{22} dominate the isotropic shielding trends. This means that the

 TABLE 4: ³¹P NMR Chemical Shielding Tensor Elements (ppm)

compound	$\sigma_{ m iso}$	σ_{11}	σ_{22}	σ_{33}
1	438.7	267.7	479.6	568.7
2	436.6	366.1	400.9	542.9
3	434.4	305.4	493.3	504.6
4	416.7	285.9	460.5	503.8
5	417.5	299.3	472.3	480.9
6	410.7	277.5	465.9	488.9
7	407.8	274.5	465.9	483.2
8	406.7	272.9	451.2	496.0
9	402.4	272.6	452.0	482.8
10	401.5	289.6	425.8	489.2
11	389.1	288.2	428.5	450.6
12	418.9	248.0	479.5	529.2
13	385.8	223.7	448.5	485.0
14	378.5	241.3	405.7	488.5
15	411.8	270.8	459.3	505.3
16	408.4	254.4	455.5	515.2
17	489.0	466.3	492.9	507.8
18	493.0	478.7	481.3	519.0
19	377.4	374.4	374.4	383.5
20	386.6	373.8	389.3	396.5
21	365.5	351.0	371.1	374.3
22	336.2	254.8	338.4	415.5
23	344.8	234.0	325.9	474.5
	349.3	250.8	326.1	470.9
24	332.2	280.0	301.8	414.9
	337.2	249.5	341.6	420.6
25	341.6	262.4	322.2	440.1
	346.7	235.5	325.2	479.6
26	339.5	244.4	326.5	447.6
27	335.5	281.1	322.4	402.9
28	326.9	268.6	298.9	413.3
•	331.3	276.6	298.6	418.7
29	321.7	267.0	297.2	400.9
	321.7	267.0	297.3	400.9

TABLE 5: ³¹P NMR Shifts, P–O Bond Lengths, and NBO Charges of 1–11^{*a*}

0				
compound	$\delta^{ ext{expt}}$ (ppm)	$R^{ m equ}$ (Å)	$R^{\mathrm{axi}}(\mathrm{\AA})$	$Q_{\mathrm{P}}\left(e ight)$
1	-84.1 [19]	1.603	1.647	2.819
2	-78.3 [19]	1.637	1.680	2.809
3	-77.5 [17]	1.647	1.695	2.781
4	-68.3[17]	1.642	1.699	2.788
5	-58.6 [16]	1.646	1.704	2.740
6	-54.8 [13]	1.640	1.699	2.747
7	-51.3 [12]	1.639	1.695	2.752
8	-48.9 [11]	1.641	1.702	2.739
9	-44.7 [16]	1.642	1.710	2.736
10	-41.7 [21]	1.644	1.714	2.721
11	-27.0 [16]	1.651	1.701	2.702

^a References are in brackets.

major contributions to the chemical shift changes observed must arise from bonding or structural changes orthogonal to σ_{22} , σ_{33} , i.e., along the apical P–O bond (collinear with σ_{11}). As can be seen in Table 5, the average axial P–O bond lengths (R^{axi}) are ca. 0.05 Å longer than the average equatorial P–O bond lengths (R^{equ}), and more importantly, R^{axi} has a larger variation as compared to R^{equ} , among the various compounds, consistent with ab initio results recently reported for other O₅ oxyphosphoranes.⁵²

There is, however, an outlier in Figure 6, O₅ compound 2. Upon close inspection of its structure, it can be seen that there is a sixth oxygen atom which is very close (2.49 Å) to the central phosphorus and the results of the AIM calculations clearly identify a (3,-1) bond critical point³⁸ between P and this sixth oxygen. This behavior is typical of a chemical bond, although this P–O bond is much weaker than the other five, more conventional P–O bonds. This sixth P–O bond aligns close to



Figure 7. Plot of experimental ³¹P NMR shifts versus phosphorus NBO charges for O₅ oxyphosphoranes (1–11). $R^2 = 0.923$.

 σ_{33} , and its effect is primarily to affect shieldings along σ_{11} and σ_{22} , as can be seen in Figure 6. In contrast, compound 1, though very similar to 2, has its sixth O at a much larger P–O distance (3.35 Å) and the AIM calculation indicates a (3,+1) critical point, not the (3,-1) critical point required for every chemical bond.³⁸ Consequently, compound 1 has normal shielding behavior. On the other hand, in the O₆ compound 17, the sixth P–O bond length (1.94 Å) is very much shorter than that found in 2 (2.49 Å), which results in a much larger effect on shielding, with σ_{11} and σ_{22} becoming 466.3 and 492.9 ppm in 17, to be compared to the values of 366.1 and 400.9 ppm in 2. These results clearly emphasize, then, the important effects of coordination geometry on ³¹P NMR shieldings/shifts.

When the experimental chemical shifts of the oxyphosphoranes are plotted as a function of P-O bond length, for either axial or equatorial P-O bonds, it is clear that the most shielded species, 1, has very short axial and equatorial bond lengths, Table 5. For the remaining species (2-11), there is a modest correlation between shielding and the average axial P-O bond length ($R^2 = 0.531$) but essentially no correlation with the average equatorial bond length ($R^2 = 0.153$), consistent with the discussion on the dominance of σ_{22} , σ_{33} on shielding described above. As to the actual origins of these variations in bond length (and the consequent correlations with shielding): our results suggest the possible importance of ring strain in influencing the observed shifts in that the most shielded species 10 and 11 have two or three small rings attached to P, which might be expected to cause strain, which could then be reduced by a slight lengthening of the P-O_{axi} bonds and a decrease in the phosphorus NBO charge. Most other species contain only one small ring, but in 1 and 2 there are two large rings, which would not be expected to be strained, consistent with the shorter P-O_{axi} bonds and an increased charge on P. In fact, as shown in Figure 7, we find a very good ($R^2 = 0.923$) correlation between phosphorus NBO charges and the experimental chemical shifts. More specifically, larger positive charges on P result in shorter axial P-O bond lengths and, consequently, larger shieldings in the equatorial plane (σ_{22} and σ_{33}) and upfield (more negative) isotropic chemical shifts, Figure 7.

Conclusions

The results we have described above are of interest for a number of reasons. First, these calculations give the first accurate predictions of ³¹P NMR chemical shifts in hypervalent oxy-

phosphoranes, of interest in the context of the structures of phosphoryl transfer enzyme transition state/reactive intermediates. Second, they enable calculation of ³¹P NMR shifts in polymeric orthophosphates, by means of a self-consistent charge field perturbation approach. Third, the ³¹P NMR chemical shifts of five- and six-coordinate oxyphosphoranes, as well as fourcoordinate polymeric inorganic orthophosphates and fourcoordinate phosphonates, are all well predicted, with a slope of 1.00 and an $R^2 = 0.993$, corresponding to a 3.8 ppm (or 2.1%) error over the entire 178.3 ppm range. Fourth, for pentaoxyphosphoranes, the solvent effect on ³¹P NMR chemical shieldings was found to be very small (<0.5 ppm). Fifth, the ³¹P NMR shifts in the O₅ systems were found to occur over a large chemical shift range and correlate with phosphorus NBO charges, providing an explanation for the dependence of shielding on P–O bond length. Taken together, these results should facilitate the use of ³¹P NMR techniques in investigating the structures of phosphoryl transfer enzyme intermediates and inhibitors, as well as polymeric orthophosphates.

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Supporting Information Available: Optimized geometries of compounds **3–18** given in PDB files. This material is available free of charge via the Internet at http://pubs.acs.org.

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