# Structure–Basicity Relationships in 1-Phosphabicyclo[2.2.2]octane 1-Oxide and 1-Phosphabicyclo[2.2.1]heptane 1-Oxide

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Abstract: The relative constancy of the phenol hydrogen bonded OH stretching frequency shifts and of the P=O stretching frequencies for OPMe$_3$ (**1a**), OP(n-Bu)$_3$ (**1b**), and OP(CH$_2$CH$_2$)$_3$CH (**2**) suggests that constraint of acyclic phosphine oxides to bicyclic **2** involves little change in phosphoryl oxygen basicity. The phenol shift and P=O stretching frequency for OP(CH$_2$CH$_2$)$_2$CHCH$_2$ (**3**), however, is substantially smaller and larger, respectively, than for **1** or **2**, which is indicative of a substantially lower basicity of the phosphoryl oxygen in **3**. The resultant order **1** ≥ **2** > **3** contrasts with that of the analogous ester series OP(OR)$_3$ ≫ OP(OCH$_2$)$_3$CR > OP(OCH$_2$)$_2$C(R)O. The low basicity of **3** is ascribed to the abnormally small average CPC angle (96.2°) revealed by a crystal and molecular structure of this molecule.

In recent publications the relationship between the Lewis basicity of phosphorus and phosphoryl oxygen with molecular constraint has been explored in trialkyl phosphite and phosphate esters, respectively.[2] Pertinent to the present work on the title trialkylphosphine oxides is the observation in a series of phosphate esters that the Lewis basicity of the phosphoryl oxygen toward a proton[2a,e] is in the order
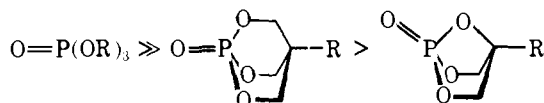
despite the accompanying reduction in the steric requirement of the triester moiety. The ordering of the first two members has been ascribed to the consequences of molecular constraint on the π character of the bonds of phosphorus to the esteratic oxygens, arising from rehybridization of these oxygens (the "hinge effect"), and on the orientation of the lone pairs on these oxygens relative to the O=P bond. In addition to these influences, strain-induced rehybridization of phosphorus in the third ester (which decreases the OPO angles and shifts more p character into the endocyclic P–O bonds) was suggested to account for the weakest basicity of this ester on the basis of a comparison of the structures determined by diffractional means for the two caged esters.[2c] The upward progression of O=P stretching frequencies that accompanies increased constraint (Table I) is also consistent with this rationale since the resultant positive charge which accumulates on phosphorus is expected to increase the ionic character of the σ bond and/or augment π back-donation from the phosphoryl oxygen.[2g]

The recent syntheses and study[3] of the bicyclic phosphine oxides **2** and **3**, which are analogous in structure to the above caged phosphate esters, allow a test of the postulated "hinge" and lone pair orientational effects since, unlike the oxygen it replaces, the tetravalent carbon atom is devoid of lone pairs. Here we present evidence from phenol shift studies of compounds **1–3** that their phosphoryl oxygen basicities follow the order shown below. The molecular structure determination of
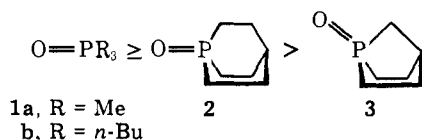
3 by means of x-ray diffraction is also reported, and the parameters relevant to the present study are compared with those for **1a** and the expected values of **2**.

Results and Discussion

The phenol shifts and O=P stretching frequencies of **1–3** in Table I reflect a substantially smaller difference in basicity between **1** and **2** than between **2** and **3**. In contrast, the substantially larger difference in the shifts for OP(OR)$_3$ and OP(OCH$_2$)$_3$C-n-Pent compared to **1** and **2** indicates that increasing constraint results in a greater difference in basicity of the phosphoryl oxygen in phosphate esters than in the analogous phosphine oxides. In the phosphate esters, however, constraint of OP(OR)$_3$ to OP(OCH$_2$)$_3$CR appears to involve a larger attenuation in basicity than further constraint of the latter compound to OP(OCH$_2$)$_2$CHO.

That phenol shift measurements are a quantitative measure of the basicity of oxygen and nitrogen donors, as measured from heats of their reaction with phenol, has been conclusively demonstrated by Drago et al.[4] Because a similar correlation was found for a series of sulfur donors,[5] it is reasonable to suppose that a correlation also exists for a series of phosphoryl oxygen donors such as those discussed here. This supposition is supported by the observation that the half-wave neutralization potentials in nitromethane give the basicity order PR$_3$ > P(OR)$_3$ > P(OCH$_2$)$_3$CMe.[6] The correlation of such measurements with aqueous pK values for amines has been shown to be essentially linear[7] and a similar correlation would be expected for phosphorus compounds. Finally, $\Delta\nu$(OH) for the P(OR)$_3$ and P(OCH$_2$)$_3$CR has been found[8] to follow the same trend as for the corresponding phosphates discussed here. It is also comforting to note from Table I that the phenol shifts for all the phosphine oxides are larger than those of the phosphates, which accords with the idea that phosphine oxides are expected to be more basic toward a proton than phosphates on inductive grounds. Evidence for this idea stems from an investigation of methyl proton chemical shifts in MeR$_2$P=O and Me(RO)RP=O compounds in aqueous H$_2$SO$_4$. In this study it was determined that substitution of a methoxy group for a methyl substituent resulted in a lowering of the phosphoryl oxygen basicity with respect to H$_2$SO$_4$.[8] Unfortunately the instability of the caged phosphates in aqueous acid rendered untenable a comparison of their basicity with the phosphine oxides **2** and **3** using this technique. The limited availability of **2** and **3** also precluded ordering their basicities with respect to **1** by this alternate procedure. It should be mentioned, however, that the approximate pK_a value of −1 determined for **3** as well as several four-, five-, and six-membered ring monocyclic phosphine oxides (by calculating the pK_a value which produces the most linear Bunnett plot for the acid hydrolysis of these compounds) suggests that basicity changes

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Table I. Trends in Spectroscopic Parameters Which Are a Measure of Basicity of 1–3 and Phosphates of Similar Structure

	Δν(O···H), cm⁻¹, Z = O		ν(O=P), cm⁻¹, Z = O		ν(HB),ⁱ cm⁻¹ Z = H₃B, Y = O	¹J¹H³¹P, Hz Z = H, Y = O	¹J⁷⁷Se³¹P, Hz Z = Se, Y = O
	Y = nothing in 1, CH₂ in 2, 3	Y = O	Y = nothing in 1, CH₂ in 2, 3	Y = O			
ZP(YMe)₃ (1a)	444	302	(1150–1183)ᵈ	(1252–1286)ᵈ	2382.3	826.2ᵏ	954.4ᵐ
ZP(Y-n-Bu)₃ (1b)	445ᶠ	300				812ˡ	
(difference)	25	55	19 to −14	41 to 75	20	73 to 87	99
ZP(YCH₂)₃CR (2)	420ᵃ	255ᵇ	1169a,e	1327f,g	2402.2ʲ	899.2f,k	1053.1f,m
(difference)	55		46	19 or 27	8	37	46
ZP(YCH₂)₂C(R)Y (3)	375ᵃ	c	1215a,e	1346 or 1354f,g,h	2410.2f	928.8ᵏ	1098.6f,m

ᵃ R = H. ᵇ R = n-Pent. ᶜ Insufficiently soluble. ᵈ Ranges quoted for acyclic trialkylphosphine oxides and phosphates (L. C. Thomas, "Interpretation of the Infrared Spectra of Organophosphorus Compounds", Heyden and Son, London, 1974, Chapter 1). ᵉ Reference 3b. ᶠ R = Me. ᵍ Measured in CHCl₃. ʰ Although a medium shoulder at 1314 cm⁻¹ appears on this band, only the strong absorption at 1327 cm⁻¹ is shifted in the spectrum of ¹⁸OP(OCH₂)₃CMe to 1287 cm⁻¹. ⁱ Weighted average of the A₁ and E nodes in CCl₄. ʲ R = Et. ᵏ Reference 2a. ˡ G. A. Olah and C. W. McFarland, *J. Org. Chem.*, 36, 1374 (1971). ᵐ Reference 11.
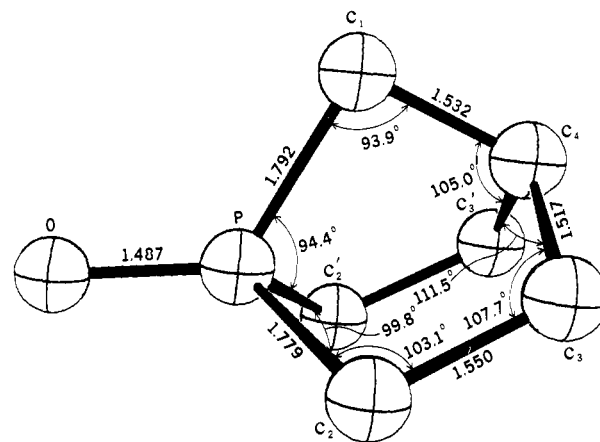
Figure 1. Computer drawing of 1-phosphabicyclo[2.2.1]heptane 1-oxide. None of the hydrogen atoms are shown.

among compounds 1–3 may actually be fairly small.[3d]

In addition to the phenol shift study reported herein which points to a comparatively large electron density decrease at the bridgehead phosphorus from OP(OR)₃ to OP(OCH₂)₃CR (in contrast to the change incurred from 1 to 2), a comparison of the changes in the weighted averages of the B–H stretching frequencies observed for the phosphite ester–borane adducts[9] and in the $^1JZ^{31}P$ spin–spin coupling constants (Z = ^1H[10] and ^{77}Se[11]) of the protonated and selenated phosphite esters lead to the same conclusion. Thus the phosphorus basicity decrease from an acyclic to a bicyclo[2.2.2]octane to a bicyclo[2.2.1]heptane structure appears in all cases to be a large one initially, followed by a substantially smaller decrease.

Since the absence of hybridizational effects on the phosphorus-bearing carbons appears to be responsible for the lack of substantial basicity change from 1 to 2, it could be assumed that the drop in basicity from 2 to 3 arises primarily from narrowing of the CPC bond angles in 3. The determination of the crystal and molecular structure of 3 is completely consistent with this assumption. The pertinent structural parameters given in Figure 1 for 3 reveal the presence of very much smaller CPC angles (96.2° av) in this molecule compared with those in 1a (106.0°).[12] This angular constriction accounts for the weak basicity of the oxygen in 3 since the resultant high degree of s character in the phosphorus lone pair is expected to reduce its donor character toward oxygen. Interestingly, both the PO and PC bond lengths in 3 are very close to those in 1a. The similarity in basicity of 1 and 2 can be ascribed to the maintenance of approximately tetrahedral CPC bond angles expected for a nearly strainless bicyclo[2.2.2]octane structure.[13] It seems reasonable to conclude that the structural and spectroscopic data are consistent with an oxygen "hinge effect" which sharply decreases basicity from OP(OMe)₃ to OP(OCH₂)₃CR but which is absent in 1 and 2. Furthermore, the substantial drop in basicity from 2 to 3 is largely associated with the strained endocyclic phosphorus angles. Such increased strain is also manifested from OP(OCH₂)₃CR to OP(OCH₂)₂C(R)O (angle OPO decreases from 104° to 99.9°[2c]) along with an augmented "hinge effect" (angle POC drops from 117.5° to 102°[2c]), although it is not possible presently to gauge the relative influences of these structural changes.

The question of the influence of conformation on the bonding characteristics of phosphorus esters has recently regained considerable interest.[2a,d–f,14] Germane to the work reported here is the expected decrease in energy of phosphoryl oxygen protonation and a rise in positive charge on phosphoryl oxygen with increasing constraint. This expectation is supported by CNDO/2 calculations in the case of O=P(OMe)₃

compared to $O=P(OCH_2)_3CMe$.[2f] Although a convergence problem precluded a comparison of $O=\overline{P(OCH_2)_2CMeO}$ in this respect, the expected trends in phosphorus protonation energy and phosphorus charge were observed in the phosphite series $P(OCH_3)_3$, $P(OCH_2)_3CMe$, and $\overline{P(OCH_2)_2CMeO}$.[2f] Similar trends in these parameters can thus be expected for the parent phosphines of **1–3**.

Experimental Section

Infrared spectra of the CCl_4–phenol–base solutions were recorded on a Beckman 4250 spectrometer. A 0.015 M phenol stock solution was made from CCl_4. The CCl_4 was purified by heating at reflux over and distilling from P_4O_{10}. The phenol was dried by azeotropic distillation of a benzene solution followed by removing the benzene and subliming the residue.

Isotopically substituted $^{18}OP(OCH_2)_3CMe$ was synthesized by treating an equimolar mixture of the parent phosphite and $H_2^{18}O$ (87.8% enrichment) in dry CH_3CN with an equimolar quantity of Br_2 in CCl_4 added dropwise at room temperature. Evaporation followed by sublimation of the residue under vacuum gave the product in 94% yield. A mass spectrum revealed the expected parent ion at m/e 166.

Crystals of **3** were grown by slow sublimation under vacuum in a sealed tube and mounted in Lindemann capillaries in a drybox to avoid hydration by atmospheric moisture. Preliminary examination of **3** showed the crystals to be orthorhombic with $a = 9.475$ (3), $b = 6.892$ (2), and $c = 10.308$ (4) Å and four units of **3** per unit cell. Systematic extinction of 0kl (absent if $k + l = 2n + 1$) did not allow the space group to be determined unambiguously since both a centrosymmetric group, *Pnma*, and a noncentrosymmetric group, *Pn2₁a* (alternate setting of *Pna2₁*), are consistent with these extinctions. Subsequent successful refinement in *Pnma* confirmed the centrosymmetric choice. Data were taken for 537 independent reflections using a computer-controlled four-circle diffractometer. After correction for Lorentz, background, and polarization effects, 414 reflections were judged to be observed ($F_o \geq 3(F_o)$). Routine application of MULTAN[15] revealed the positions of the phosphorus and oxygen atoms in the first phased E synthesis.[16] The rest of the nonhydrogen atoms were located in the succeeding electron density calculations. These positions were refined[15] to conventional crystallographic agreement factors of $R = 0.211$ and $R_w = 0.203$. The introduction of isotropic ($R = 0.108$ and $R_w = 0.115$) and anisotropic thermal parameters reduced these to $R = 0.091$ and $R_w = 0.098$. The hydrogen atoms were found by examination of difference Fourier calculations. Final full matrix refinement including both the hydrogen positions and their isotropic thermal parameters resulted in $R = 0.054$ and $R_w = 0.058$. The atomic scattering factors used in the refinements were those of Hansen et al.[17] Corrections,[18] real and imaginary, for anomalous dispersion of phosphorus were used in the calculations.

References and Notes

(1) (a) Iowa State University; (b) NIH Career Development Awardee, 1975–1980, AM 00014; (c) University of California, San Francisco.

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(9) See ref 2a for a discussion of such a study.

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(11) See ref 2a and 2f and R. D. Kroshefsky and J. G. Verkade, submitted, for a discussion for this type of study.

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(13) Disorder in the crystal prevented the solution of the structure of **2**. However, quinuclidinyl benzylate hydrobromide has been shown by x-ray diffraction to possess average CNC and NCC angles of 110 and 109°, respectively, in the quinuclidine moiety (A. Meyerhoffer and D. Carlstrom, *Acta Crystallogr., Sect. B*, **25**, 1119 (1969)). Also, previous studies[3b] have shown that **3** undergoes oxygen-18 exchange in water enormously faster than **2**, a fact consistent with much greater release of strain for **3** than for **2** in proceeding to the transition state in the exchange process.

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