like a simple phenol in water; however, since the pK_a of α-T in SDS micelles is greater than 14,[32,33] the concentration of the anion can not fully account for the pH dependence. Some other factor must be involved. One possible explanation is suggested by the observation that the pK_a of α-T in micellar solutions varies with the nature of the micelle.[33] It is possible that the micellar environment changes with pH, altering the extent of ionization of α-T. A pH-dependent change in the structure of the micelle also might change the rate of ozonation of the un-ionized form of α-T.

At this time we suggest that the available experimental facts on the reaction of ozone with α-tocopherol are most consistent with a mechanism in which ozone oxidizes α-T to the α-T-oxyl radical. Scheme I shows three possible mechanisms by which this oxidation could occur. Thermochemical considerations suggest that the direct hydrogen atom transfer (path *a*) is too endothermic to occur readily. However, the same result can be obtained by either an electron transfer followed by a proton transfer (path b–c) or by a proton transfer followed by an electron transfer (path d–e). One-electron oxidations of phenols are well-known,[34] and the proton transfer from the resulting cation radical (path c) could be fast enough so that it is not observed.[35] There is also ample precedent for charge transfer in ozonation reactions with electron-rich aromatic systems.[36] In either case, additional stabilization could be realized by solvation of the ozone radical anion and the proton. Clearly, the effect of pH suggests that path d–e predominates in aqueous media, although as discussed above, the pK_a of α-T may require that path d–e not be the sole pathway involved; in other words, the actual mechanism may involve a mixture of the two pathways shown in Scheme I.

Biological Significance. In biological membranes, the rate constant for ozonation of α-T would be at most comparable to that of a fatty acid. However, since unsaturated fatty acids are typically present in biological membranes at concentrations 100–1000 times higher than α-T,[37] α-T would not compete for direct reaction with ozone. Additionally, since the ozonation products of methyl oleate do not react with α-T at temperatures of 37 °C and below, α-T is not consumed by secondary reactions of this type.

Conclusions. When animals breath smoggy air, α-T is known to provide important protection.[7,8] Since ozone would be expected to react virtually exclusively with PUFA in membrane lipids and not with the α-T directly, the protection that α-T provides against ozone must arise because α-T scavenges radicals produced from an ozone–PUFA reaction,[3-8] as illustrated in eq 1 and 2. The

$$O_3 + \text{PUFA} \rightarrow \rightarrow \rightarrow \text{ROO}^{\bullet} \quad (1)$$

$$\text{ROO}^{\bullet} + \alpha\text{-T} \rightarrow \rightarrow \text{nonradical products} \quad (2)$$

direct, sacrificial reaction of ozone with α-T in biological membranes containing normal concentrations of unsaturated fatty acids does not occur.

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Registry No. α-T, 59-02-9; α-TQ, 7559-04-8; α-TAc, 58-95-7; α-T-oxyl, 23531-69-3; O_3, 10028-15-6; 1,4-pentadiene, 591-93-5; oleic acid, 112-80-1; methyl oleate, 112-62-9; linoleic acid, 60-33-3; methyl linoleate, 112-63-0.

(32) The pK_a of α-T is about 12 in cationic micelles and about 13 in zwitterionic micelles (see ref 33). In an attempt to measure the pK_a in SDS by the methods outlined in ref 33, we were only able to verify that the value was >13.

(33) Drummond, C. J.; Grelser, F. *Biochim. Biophys. Acta* **1985**, *836*, 275–278.

(34) (a) Grodkowski, J.; Neta, P. *J. Phys. Chem.* **1984**, *88*, 1205–1209. (b) Futamura, S.; Yamazaki, K.; Ohta, H.; Kamiya, Y. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3852–3855. (c) Hule, R. E.; Neta, P. *Chem.-Biol. Interact.* **1985**, *53*, 233–238. (d) Svanholm, U.; Bechgaard, K.; Parker, V. D. *J. Am. Chem. Soc.* **1974**, *96*, 2409–2413.

(35) The pK_a of phenoxyl cation radicals is ca. −5 (see: Land, E. J.; Porter, G.; Strachan, E. *Trans. Faraday Soc.* **1961**, 57, 1885–1893) and, by analogy to $HO_2^{\bullet}$ (pK_a = 4.7; see: Bielski, B. H. J. *Photochem. Photobiol.* **1978**, *28*, 645–649), the ozone radical anion can serve as a proton acceptor in the absence of other nucleophiles.

(36) (a) Pryor, W. A.; Ohto, N.; Church, D. F. *J. Am. Chem. Soc.* **1983**, *105*, 3614–3622. (b) Desvergne, J. P.; Bouas-Laurent, H. *J. Catal.* **1977**, *51*, 126–130. (c) Bailey, P. S.; Ward, J. W.; Carter, T. P., Jr.; Fischer, C. M.; Khashab, A. Y. *J. Am. Chem. Soc.* **1974**, *96*, 6136–6140.

(37) Underwood, B. A.; Denning, C. R.; Navab, M. *Ann. N.Y. Acad. Sci.* **1972**, *203*, 237–247.

^{17}O NMR Spectra of Cyclic Phosphites, Phosphates, and Thiophosphates

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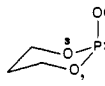
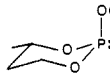
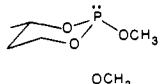
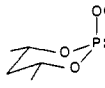
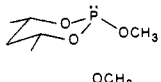
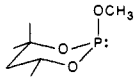
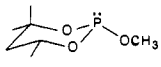
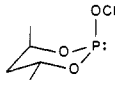
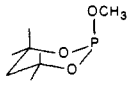
Abstract: The ^{17}O NMR spectra of a number of cyclic and bicyclic phosphites, phosphates, and thiophosphates are presented, and, in so far as possible, the ^{17}O chemical shifts are interpreted in terms of conformational factors.

Following the pioneering work of Christ and Diehl,[2] a number of groups have studied the ^{17}O spectra of various phosphorus derivatives including phosphites and phosphates.[3-10] However, despite the importance of cyclic phosphates in biochemical processes and of cyclic thiophosphates as phosphate analogues useful

(1) (a) University of North Carolina. (b) Iowa State University.
(2) Christ, H. A.; Diehl, P. *Helv. Phys. Acta* **1963**, *36*, 170.
(3) Grossman, G.; Gruner, M.; Selfert, G. *Z. Chem.* **1976**, *16*, 362.
(4) Gray, G. A.; Albright, T. A. *J. Am. Chem. Soc.* **1977**, *99*, 3243.
(5) McFarlane, H. C. E.; McFarlane, W. *J. Chem. Soc., Chem. Commun.*, **1978**, 531.
(6) Tsai, M.-D.; Huang, S. L.; Kozlowski, J. F.; Chang, C. C. *Biochemistry*, **1980**, *19*, 3531. Huang, S. L.; Tsai, M.-D. *Ibid.* **1982**, *21*, 951.
(7) Coderre, J. A.; Mehdi, S.; Demou, P. C.; Weber, R.; Traficante, D. D.; Gerlt, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 1870. Gerlt, J. A.; Demou, P. C.; Mehdi, S. *Nucleic Acids Res., Spec. Publ.* **1981**, *9*, 11; *J. Am. Chem. Soc.*, **1982**, *104*, 2848. Gerlt, J. A.; Reynolds, M. A.; Demou, P. C.; Kenyon, G. L. Ibid. **1983**, *105*, 6469.

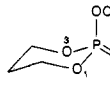
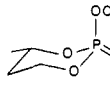
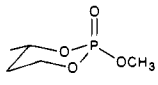
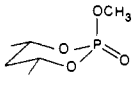
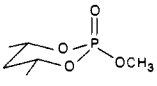
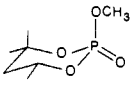
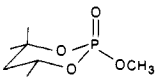
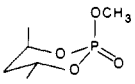
0002-7863/86/1508-6651$01.50/0

Table I. ^{17}O NMR Spectral Data for the Phosphites **1–9**[a]

	compounds	OCH_3	O-1	O-3
1		48 (149)	59 (173)	59 (173)
2		48 (170)	58 (160)	87 (170)
3		58[b] (c)	62[b] (c)	88 (180)
4		49 (150)	87 (173)	87 (173)
5		63 (166)	88 (166)	88 (166)
6		60 (155)	87 (164)	100 (181)
7		69 (c)	83 (c)	102 (c)
8		63 (151)	82[b] (c)	86[b] (c)
9		69 (155)	99 (166)	99 (166)

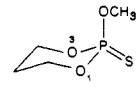
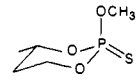
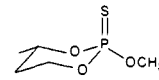
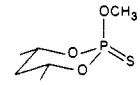
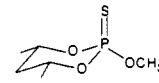
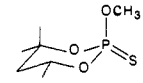
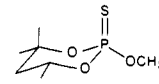
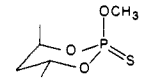
[a] Chemical shift in ppm relative to external H_2O at 100 °C, in parentheses one bond P–O coupling constant in Hz. [b] Chemical shifts were estimated from overlapping signals for O(1) and O(3). [c] Not clearly resolved.

Table II. ^{17}O NMR Spectral Data for the Phosphates **22–29**[a]

	compounds	OCH_3	O=P	O-1	O-3
22		21 (78)	82 (156)	47 (78)	47 (78)
23		22 (b)	83 (164)	45 (b)	76 (b)
24		29 (b)	88 (161)	46 (b)	74 (b)
25		23 (b)	81 (162)	73 (b)	73 (b)
26		29 (b)	88 (b)	73 (b)	73 (b)
27		31 (b)	89 (138)	74 (b)	87 (b)
28		34 (b)	94 (161)	73 (b)	89 (b)
29[d]		32 (b)	90 (156)	69[c] (b)	72[c] (b)

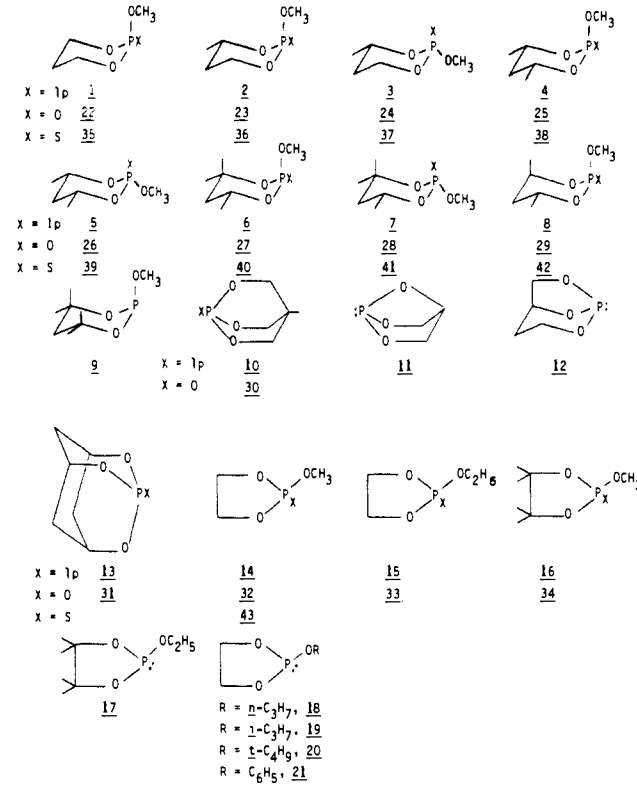
[a] Chemical shift in ppm relative to external H_2O at 100 °C; in parentheses, one-bond P–O coupling constant in Hz. [b] Not clearly resolved. [c] Chemical shifts and coupling constants were estimated from overlapping signal for O-1 and O-3. [d] Conformation uncertain, see text, probably a mixture of conformers.

Table III. ^{17}O NMR Spectral Data for the Thiophosphates **35–42**[a]

	compounds	OCH_3	O-1	O-3
35		48 (102)	69 (115)	69 (115)
36		48 (95)	65 (123)	93 (c)
37		54 (112)	73 (104)	101 (102)
38		48 (107)	91 (100)	91 (100)
39		53 (92)	101 (92)	101 (92)
40		59 (c)	93 (c)	104 (c)
41		64 (c)	94 (c)	107 (c)
42		60 (c)	90[b] (c)	90[b] (c)

[a] Chemical shift in ppm relative to external H_2O at 100 °C; in parentheses, one-bond P–O coupling constant in Hz. [b] Chemical shift were estimated from overlapping signal for O-1 and O-3. [c] Not clearly resolved.

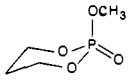
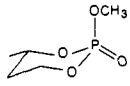
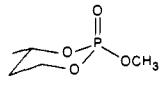
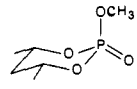
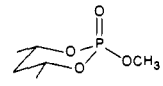
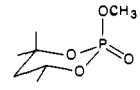
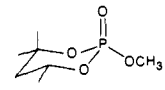
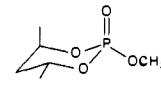
Chart I



in stereochemical studies,[11,12] in this category of compounds only ^{17}O-enriched cyclic 2′-deoxyadenosine-3′,5′-monophosphate seems

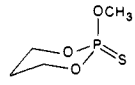
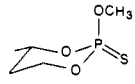
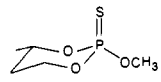
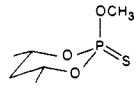
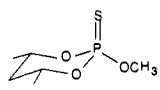
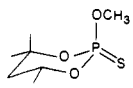
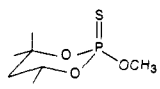
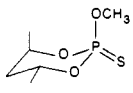
(8) Nieuwenhuizen, M. S.; Peters, J. A.; Sinnema, A.; Kieboom, A. P. G.; van Bekkum, H. *J. Am. Chem. Soc.* **1985**, *107*, 12.

Table IV. Dipole Moments of Cyclic Phosphates **22–29**

	compound	μ (debye)	ref
22		5.63	*a*
23		5.78	*a*
24		4.93	*a*
25		6.11 5.43	*a* *b*
26		4.69 4.73	*a* *b*
27		5.57	*b*
28		4.58	*b*
29		4.88	*b*

[a] Mosbo, J. A.; Verkade, J. G. *J. Org. Chem.* **1977**, *42*, 1549. [b] This work.

Table V. Dipole Moments of Cyclic Thiophosphates **35–42**

	compound	μ (debye)	ref
35		4.77	*a*
36		5.50	*b*
37		4.20	*b*
38		5.52	*a*
39		3.98	*a*
40		5.45	*a*
41		4.78	*a*
42		5.31	*a*

[a] This work. [b] Bodkin, C. L.; Simpson, P. *J. Chem. Soc. B* **1971**, 1136.

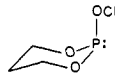
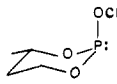
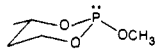
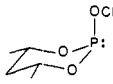
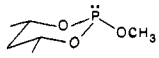
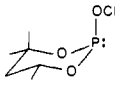
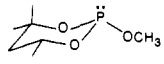
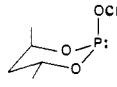
to have been examined by ^{17}O NMR spectroscopy.[7,8] We have now recorded the natural-abundance[13] ^{17}O spectra of the series of cyclic phosphites **1–21**, phosphates **22–34**, and thiophosphonates **35–43** (Tables I–III, X, XI). The structural formulas for these systems are given in Chart I. In a number of cases the $^{31}P^{17}O$ coupling constants as well as the ^{17}O chemical shifts were recorded; however, because of the large bandwidth, the reproducibility of the coupling values between our laboratories and on repeat recordings within one laboratory was only fair, thus leading to a precision of no better than ±10 Hz, and in some cases, notably for the C–*O* signals of phosphates, the coupling was not clearly resolved. The accuracy and reproducibility of the chemical shifts, however, are of the order of ±2 ppm or better.

Conformational Analysis. Before discussing the ^{17}O data, it is necessary to analyze the conformations of the compounds studied, especially those with six-membered rings. The conformations of the *cis*-4,6-dimethyl derivatives **4**, **5**, **25**, **26**, **38**, and **39** may be considered fixed as shown in Chart I. These compounds are the models in terms of which the conformations of the others may be discussed. Compounds **2**, **23**, and **36** clearly have the same conformation as **4**, **25**, and **38**, i.e., the one shown in Scheme I with axial methoxyl (anomeric effect) and equatorial methyl. The ^{17}O chemical shifts for OCH_3 and O(3) in the compounds of these two sets (Tables I–III) agree well.[14] In the case of the phosphates **23** and **25** (Table IV) and thiophosphates **36** and **38** (Table V), there is also fair agreement in the dipole moments which are characteristic of the methoxy orientation.[15] Unfortunately, the ^{13}C and ^{31}P spectra of the six-membered cyclic phosphates (Table VII), and thiophosphates (Table VIII) are not greatly affected by configuration or conformation, but in the case of the phosphites the $^{31}P^{13}C(5)$ coupling constant (Table VI) is characteristic, being of the order of 4–5 Hz for axial OCH_3 compounds and 11–14 Hz for equatorial ones.[16,17] By this criterion, compound **2** (like **4**) clearly has an axial methoxyl. Proton–proton coupling constants of **23**, **25**, **26**, **28**, and **38** and **39** (Table IX) are in accord with the assigned chair conformations.[18]

The situation for the stereoisomers **3**, **24**, and **37** is not so clear-cut. Phosphite **3** has been claimed, on the basis of proton

(9) Vasilev, V. V.; Dmitriev, V. E.; Ionin, B. I.; Mets, V. N. *J. Gen. Chem. U.S.S.R.* **1981**, *51*, 1836.
(10) Gerothanassis, I. P.; Sheppard, N. *J. Magn. Reson.* **1982**, *46*, 423.
(11) Eliel, E. L. "Prostereoisomerism (Prochirality)"; *Top Curr. Chem.* **1982**, *105*, 1.
(12) Floss, H. G.; Tsai, M.-D.; Woodward, R. W. *Top. Stereochem.* **1984**, *15*, 253.
(13) For earlier work, see: Eliel, E. L.; Liu, K.-T.; Chandrasekaran, S. *Org. Magn. Reson.* **1983**, *21*, 179. Manoharan, M.; Eliel, E. L. *Magn. Reson. Chem.* **1985**, *23*, 225.
(14) Regarding the effect of the additional ring-methyl substituent, see: Eliel, E. L.; Pietruslewicz, K. M.; Jewell, L. M. *Tetrahedron Lett.* **1979**, 3649.
(15) Mosbo, J. A.; Verkade, J. G. *J. Org. Chem.* **1977**, *42*, 1549.
(16) Infant'ev, E. E.; Borisenko, A. A.; Sergeev, N. M. *Proc. Acad. Sci. USSR, Phys. Chem. Sect.* **1973**, *208*, 100.
(17) (a) Haemers, M.; Ottinger, R.; Zimmermann, D.; Reisse, J. *Tetrahedron* **1973**, *29*, 3539. (b) Eliel, E. L.; Pietruslewicz, K. M. "^{13}C NMR of Nonaromatic Heterocyclic Compounds"; *Top C-13 NMR Spectrosc.* **1979**, *3*, 171.
(18) The proton–proton coupling constants in Table IX were recorded at room temperature. The referees have questioned whether the inference of one greatly predominant chair conformation is still justified at 100 °C. In the light of their comments we have also recorded the proton spectra of compounds **22–24**, **26**, **29**, **36**, **37**, and **40–42** at 25 and 100 °C in toluene-d_8 (there is an appreciable ASIS shift relative to $CDCl_3$ at 25 °C). The coupling constants for **23**, **26**, **36**, **37**, **40**, and **41** change very little with temperature, suggesting that the conformations at 100 and 25 °C are very similar (chair for **23**, **26**, **36**; chair or rigid boat for **40** and **41**; very predominantly diequatorial chair for **37**). The spectrum for **24** was too tightly coupled for a meaningful first-order analysis, but again there was little change in the basewidth of the peaks with temperature. Compound **22** showed a marked increase in basewidth for $H(5)_e$ and a decrease for $H(5)_a$, suggesting an increase in proportion of either an alternative chair (equatorial OCH_3) or twist form. This is somewhat at odds with the evidence from ^{17}O spectra (Table II) which suggests very predominantly axial OCH_3 even at 100 °C. Compounds **29** and **42** show increased conformational averaging at 100 °C as compared to room temperature, to the extent that the spectrum of **29** at 100 °C becomes difficult to analyze. This problem is less serious for **42** in which, however, $J_{H_AH_B}$ drops to 8.4 at 100 °C. Nonetheless, the axial OMe conformer appears to be favored in both compounds even at 100 °C, as indicated in the discussion. Comparison of ^{13}C spectra at 25 and 100 °C bears out the above conclusions. In most instances the shifts vary by 0.0–0.6 ppm. Exceptions are **29** [C(4) and C(5) vary by 0.7 ppm], **41** [C(5) varies by 0.7 ppm], and **42** [C(4) varies by 1.1 ppm, C(5) by 0.7 ppm]. However, because of the insensitivity of the ^{13}C spectra to conformation (see text), these results are less significant than those reported above for the proton spectra.

Table VI. ^{13}C and ^{31}P NMR Parameters for Cyclic Phosphites **1–8** at 25 °C[a]

	compound	solvent	C-4	C-5	C-6	C-4α	C-6α	C-2β	^{31}P	ref
1		none	59.5 (1.6)	29.4 (5.5)	59.5 (1.6)	–	–	49.8 (17.8)	131.0	*b, c, d*
2		none	66.0 (2.0)	36.5 (4.7)	60.0 (2.5)	23.4 (3.2)	–	49.8 (18.0)	129.8 125.9	*b, c, e*
3		none	69.8 (3.6)	34.0 (10.8)	59.0 (1.8)	23.5 (1.6)	–	49.2 (14.7)	123.5	*b, c, e*
		CD_2Cl_2	69.6	33.6 (12.0)	58.8	23.1		49.3 (15.0)	126.5	
4		$CDCl_3$	65.7	42.7 (4.2)	65.7	22.5 (3.2)	22.5 (3.2)	49.4	127.2 129	*c, d*
5		$CDCl_3$	69.7	40.8 (13.5)	69.7	23.3 (1.6)	23.3 (1.6)	48.2	131.5 133	*c, d*
		CD_2Cl_2	70.2	41.4 (13.8)	70.2	23.7	23.7	48.8 (10.0)		
6		CD_2Cl_2	75.7	46.8 (6.0)	62.3 (2.0)	28.5 eq 33.1 ax	23.1 (3.6)	49.6 (20.0)	129.9 128.6	*f, g*
7		CD_2Cl_2	75.2 (6.0)	44.4 (16.0)	67.3 (6.0)	28.6 eq 32.3 ax	24.1	49.1 (18.0)	131.1 129.7	*f, g*
8		CD_2Cl_2	69.3 (6.0)	39.9 (7.0)	61.6	23.0	23.1	49.6 (19.4)	131.9	*f*

[a] Values in parentheses are ^{31}P–^{13}C coupling constants in Hz. [b] Nifant'ev, E. E.; Borisenko, A. A.; Sergeev, M. M. *Proc. Acad. Sci. USSR Phys. Chem. Sect.* **1973**, *208*, 100. [c] ^{13}C and ^{31}P: Haemers, M.; Ottinger, R.; Zimmerman, D.; Reisse, J. *Tetrahedron* **1973**, *29*, 3539. [d] ^{31}P: White, D. W.; Bertrand, R. D.; McEwen, G. K.; Verkade, J. G. *J. Am. Chem. Soc.* **1970**, *92*, 7125. [e] ^{31}P: Mikolajczyk, M.; Luczak, J., *Tetrahedron* **1972**, *28*, 5411. [f] ^{13}C and ^{31}P: this work. [g] ^{31}P: Nifant'ev, E. E.; Sorokina, S. F.; Borisenko, A. A.; Zavalishina, A. I.; Komolova, G. V., *Zh. Obshch, Khim.* **1978**, *48*, 2378; *Engl. transl.*, p 2158.

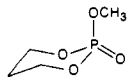
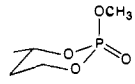
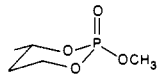
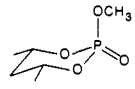
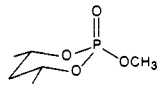
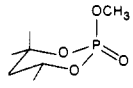
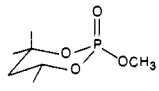
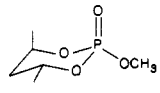
coupling constant, to be 16% in the diequatorial conformation, 44% in the diaxial, and 40% in the boat form.[19] Neither the ^{17}O spectrum (Table I) nor the ^{31}P–$^{13}C(5)$ coupling constants (Table VI) are in accord with so low a percentage in the diequatorial chair conformer. If one assumes, reasonably, that the boat form would resemble, in ^{17}O chemical shift and ^{31}P–^{13}C coupling constant, the chair conformer which possesses an axial OCH_3, the ^{17}O shift suggests about 70% and the coupling constant indicates ca. 70–80% diequatorial chair. An estimate of approximately 70% diequatorial chair and the rest diaxial chair or boat for phosphite **3** would seem reasonable and in qualitative accord with earlier work.[20] Phosphate **24** has been alleged,[21a] also on grounds of proton coupling, to be 60% in the diequatorial and 20% each in the diaxial and boat forms (where the terms equatorial and axial refer to the methoxyl group on phosphorus). However, the ^{17}O shifts for both the methoxyl and phosphoryl oxygen in **24** are very close to those in **26** and from the earlier measured dipole moments[15] of **23**, **24**, and **26**, over 80% of **24** would appear to be in the "diequatorial" conformation. Thus the estimate of only 60% of that conformation[21a] seems somewhat low. Nonetheless, it appears that neither **3** nor **24**[22] nor the thiophosphate **37** is conformationally homogeneous; in the case of the latter compound, dipole moments (Table V) suggest somewhat under 90% of the diequatorial Me–MeO conformation in accord with an earlier report.[20]

In the case of the ring-unsubstituted compounds, the phosphite **1** is believed, on the basis of its $^{13}C(5)$–^{31}P coupling constant (Table VI), to exist largely or exclusively in the MeO-axial conformation,[16,23] and this is borne out by comparison of the ^{17}O shifts of the methoxy group and the O(1) ring oxygen with the corresponding shifts in **2** and by comparison of the ^{17}O shift of the methoxy group in **4** (Table I). In the phosphate **22** the conformer with axial MeO has been found to be the predominating or exclusive one,[15,22,24] and again this is borne out by comparison of the ^{17}O shifts (Table II) of MeO, O=P, and O(1) with the corresponding shifts in **23** and by comparison of the ^{17}O shifts of the MeO and O=P groups in **25**. Less information is available in the literature[25] on the thiophosphate **35**, and the ^{17}O evidence for axial MeO (Table III) is not quite conclusive here. While the shift data for OMe agree with those of **36** and **38**, O(1) shifts of **35** and **36** are not in accord. The dipole moment of **35** (Table V) suggests that it exists as a conformational mixture.

The situation with the trimethyl compounds **6**, **7**, **27**, **28**, **40**, and **41** has not been extensively explored in the literature. In the case of the phosphites (**6**, **7**), ^{13}C NMR data (Table VI) point to predominant chair conformations with axial and equatorial alkoxyl groups, respectively. [The changes in chemical shift relative to **4** and **5** are reasonable for introduction of an additional axial methyl group, and the ^{31}P–$^{13}C(5)$ coupling constants differ in the expected way between the stereoisomers, though their absolute values are somewhat large in both cases.] The O(1) shift (Table I) in **6** agrees well with that in **4** but that in **7** is disturbingly far upfield (5 ppm) from that of **5**. The contribution of boat or twist forms cannot be excluded with either isomer. The low-field shift of MeO in **6** could be explained by a boat form, but it is equally consistent with a δ-compression effect in the chair (see below). The low-field ^{17}O shift of OMe in **7** is hard to explain on any grounds (see later discussion). In the case of the phenoxy

(19) Borisenko, A. A.; Sorokina, C. F.; Zavalishina, A. I.; Nifant'ev, E. E. *Proc. Acad. Sci. USSR, Chem. Sect.* **1978**, *241*, 359.
(20) Bodkin, C.; Simpson, P. *J. Chem. Soc., Chem. Commun.* **1969**, 829; *J. Chem. Soc. B* **1971**, 1136.
(21) (a) Mosbo, J. *Org. Magn. Reson.* **1978**, *11*, 281. (b) Bock, P. L.; Mosbo, J. A.; Redmon, J. L. *Ibid.* **1983**, *21*, 491.
(22) See also: Majoral, J.-P.; Navech, J. *Bull. Soc. Chim. Fr.* **1971**, 95, concerning the corresponding phenoxy compounds.
(23) See also: Maryanoff, B. E.; Hutchins, R. O.; Maryanoff, C. A. *Top. Stereochem.* **1979** *11*, 187.
(24) Regarding the corresponding phenoxy compound, see ref 22; the compound is in the chair conformation with axial C_6H_5O in the solid state: Geise, H. J. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 362.
(25) See ref 23, p 223.

Table VII. ^{13}C and ^{31}P NMR Parameters for Cyclic Phosphates **22–29** at 25 °C[a]

	compound	solvent	C-4	C-5	C-6	C-4α	C-6α	C-2β	^{31}P	ref
22		$CDCl_3$	69.2 (5.7)	26.1 (7.6)	69.2 (5.7)	–	–	53.6 (5.7)	−6.7	*b, c*
		toluene-d_8	68.8 (7.3)	26.2 (7.5)	68.8 (7.3)			53.0 (5.7)		
23		$CDCl_3$	77.5 (5.7)	33.4 (5.7)	68.3 (5.7)	22.3 (9.5)	–	53.6 (5.7)	−6.4	*b*
		toluene-d_8	76.9 (6.9)	33.2 (5.6)	68.0 (7.0)	22.1 (9.0)		52.9 (5.6)		
24		$CDCl_3$	76.4 (5.7)	32.6 (5.7)	66.7 (5.7)	21.7 (5.7)	–	54.6 (5.8)	−4.6	*b*
		toluene-d_8	76.0 (5.6)	32.7 (5.8)	66.6 (5.7)	21.6 (6.8)		54.2 (7.0)		
25		$CDCl_3$	76.1 (7.6)	40.5 (5.7)	76.1 (7.6)	22.1 (9.5)	22.1	53.4 (3.8)	−7.1	*b, d*
26		CD_2Cl_2	75.1 (7.0)	40.8 (5.8)	75.1 (7.0)	22.2 (8.0)	22.2 (8.0)	54.8 (7.6)	−4.9	*b, d*
		toluene-d_8	74.4 (4.8)	40.7 (5.4)	74.4 (4.8)	22.1 (9.3)	22.1 (9.3)	54.2 (5.8)		
27		CD_2Cl_2	83.4 (8.0)	44.6 (6.0)	72.9 (6.0)	31.8 eq (10.0) 25.8 ax	22.3 (9.8)	53.8 (6.0)	−7.6	*b*
28		CD_2Cl_2	82.6 (6.0)	44.6 (8.0)	73.1 (6.0)	30.9 eq (6.0) 27.3 ax	22.5 (8.0)	54.5 (6.0)	−6.1	*b*
29		$CDCl_3$	72.9 (7.6)	37.5 (7.6)	74.7 (7.6)	20.5	21.9 (7.6)	53.8 (5.7)	−6.1	*b*
		acetone-d_6	73.7 (6.4)	37.9 (4.1)	75.7 (6.5)	20.7	22.0 (12.3)	53.9 (5.7)		
		toluene-d_8	72.1 (7.4)	37.5 (7.6)	73.7 (7.3)	20.5	21.8 (7.4)	53.3 (5.8)		

[a] Values in parentheses are ^{31}P–^{13}C coupling constants in Hz. [b] ^{13}C and ^{31}P: This work. [c] ^{31}P: Mosbo, J. A.; Verkade, J. G. *J. Org. Chem.* **1977**, *42*, 1549. [d] ^{31}P: Mosbo, J. A.; Verkade, J. G. *J. Am. Chem. Soc.* **1972**, *94*, 8224.

analogues of the phosphates **27** and **28** (Table II), it has been suggested that the analogue of **27** exists as a chair, but that the analogue of **28** is possibly in a twist form.[26] However, the dipole moments of **27** and **28** (Table IV) are in the normal range for chair conformers (if perhaps slightly on the low side), their ^{13}C spectra (Table VII) show no obvious anomalies, and the proton spectra (Table IX) show a normal "backbone" thus excluding twist (but not classical boat) conformations. The ^{17}O spectra are not directly interpretable in terms of conformation and do not settle the question of twist or boat contributions. The proton–proton coupling constants in **27** and **28** as well as **40** and **41** exclude twist forms and suggest chair conformations as shown in Chart I for these compounds, though the high dipole moment of **41** (Table V) may point to a contribution from a rigid boat form with equatorial S and axial OCH_3.

No information appears to be available in the literature regarding the *trans*-4,6-dimethyl compounds **8**, **29** and **42**. In the phosphite **8**, the inequality of the C(4) and C(6) shifts (Table VI) and of the O(1) and O(3) signals (Table I) militates against a twist form and also against a near 50:50 conformer mixture. The $^{31}P^{13}C(5)$ coupling value of 7.0 Hz does suggest a mixture of conformers, but with the one having an axial MeO predominating. The proton–proton coupling constants (Table IX) support this hypothesis, as does the fact that the shift of the ^{17}OMe signal of **8** is somewhat downfield of that in **6** but appreciably upfield of that in **7**. The finding that the two methyl ^{13}C signals are nearly equal and occur near 23 ppm also speaks against the presence of a major amount of the conformer with equatorial OMe in which the axial MeC(6) would have to appear in the 17–19-ppm region. C(5) is somewhat downfield from the position it occupies in *trans*-4,6-dimethyl-substituted 1,3-dioxanes (i.e., 36.5–37.5 ppm).[27] This is typical of axial but not of equatorial OMe phosphites as is shown by comparing data in Table VI with C(5) in 1,3-dioxane (26.6 ppm) and its 4-methyl (33.7), *cis*-4,6-dimethyl (41.1), and 4,4,6-trimethyl (44.2 ppm) derivatives.[27] The situation is less clear for the phosphate **29**. Its dipole moment (Table IV) would seem to point either to a predominantly equatorial methoxyl or to a twist form. On the other hand, a proton NMR study[28] of the corresponding phenoxy compound suggests it to be a mixture of chair conformations in which the one with axial OPh predominates to the extent of 70–80% and the coupling constants in Table IX support an analogous situation in the case of the OMe compound **29**. The hypothesis of a conformer mixture is supported by the close similarity in chemical shifts of C(4) and C(6)[29] (Table VII) and of O(1) and O(3) (Table II), the upfield shift of the two methyl groups (Table VII) relative to those in the phosphite **8**, the intermediacy of the ^{17}OMe shift between those of **27** and **28** (Table II), and the effect of temperature on the proton spectrum.[18] The $^{17}O{=}P$ shift of **29** is closer to that of **27** (axial OMe), but the corresponding coupling constant is closer to that of **28**. The dipole moment (Table V) of the thiophosphate **42** suggests that it exists largely in the OMe-axial conformation, and this is supported by the proton–proton coupling pattern (Table IX), by the effect of temperature on the proton spectrum,[18] and by the ^{17}OMe shift relative to the corresponding data for **40** and **41** (Table III). The equivalency of the O(1) and O(3) signals is probably not significant since the (analogous) O(1) shifts in **40** and **41** also do not differ much from each other. The ^{13}C spectrum of **42** (Table VIII) is compatible with a predominantly axial OMe, but it cannot be claimed as strong evidence one way or the other. The ^{17}O

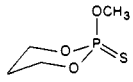
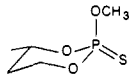
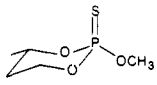
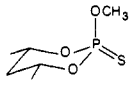
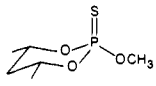
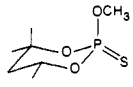
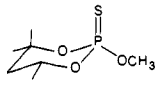
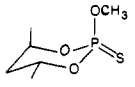
(26) Majoral, J.-P.; Navech, J. *C. R. Seances Acad. Sci.* **1969**, *268*, 2117; *Bull. Soc. Chim. Fr.* **1971**, 1331.

(27) Pihlaja, K.; Nurmi, T. *Isr. J. Chem.* **1980**, *20*, 160.

(28) Hall, L. D.; Malcolm, R. B. *Can. J. Chem.* **1972**, *50*, 2102.

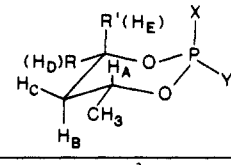
(29) This evidence must be viewed with caution since C(4) and C(6) are also nearly equal in *r*-2,*cis*-4,*trans*-6-trimethyl-1,3-dioxane, even though this compound is conformationally homogeneous.[27]

Table VIII. ^{13}C and ^{31}P NMR Parameters for Cyclic Thiophosphates **35–42** at 25 °C

compound		solvent	C-4	C-5	C-6	C-4α	C-6α	C-2β	^{31}P	ref
35		$CDCl_3$	67.9 (8.0)	26.3 (7.0)	67.9 (8.0)	– –	– –	54.3 (5.0)	64.4	*b*
36		$CDCl_3$	76.5 (8.0)	33.2 (7.0)	67.5 (8.0)	22.4 (9.0)	– –	53.9 (7.0)	64.1	*b, c*
		toluene-d_8	76.3 (7.7)	33.3 (6.0)	67.6 (9.4)	22.3 (9.5)	–	53.3 (5.1)		
37		$CDCl_3$	75.7 (7.0)	33.5 (5.0)	66.4 (6.0)	21.9 (9.0)	– –	54.9 (7.0)	66.1	*b, c*
		toluene-d_8	75.5 (4.0)	33.6 (5.3)	66.4 (5.2)	21.9 (9.2)	–	54.6 (5.7)		
38		$CDCl_3$	75.6 (8.0)	40.4 (5.5)	75.6 (8.0)	22.2 (10.0)	22.2 (10.0)	53.7 (5.5)		*b*
39		$CDCl_3$	74.7 (4.0)	41.2 (5.0)	74.7 (4.0)	22.1 (11.0)	22.1 (11.0)	54.9 (6.0)		*b*
40		$CDCl_3$	83.9 (9.9)	44.3 (5.7)	72.2 (7.8)	31.9 eq (9.3) 26.3 ax	22.4 (5.3)	54.1	62.5	*b*
		toluene-d_8	83.4 (10.9)	44.1 (5.7)	72.0 (7.8)	31.9 eq (9.4) 26.2 ax	22.3 (9.5)	53.7 (3.8)		
41		$CDCl_3$	83.6 (7.9)	43.8 (9.5)	72.8 (6.6)	31.1 eq (3.6) 27.3 ax	22.3 (9.1)	54.4	62.6	*b*
		toluene-d_8	82.9 (8.0)	43.8 (7.8)	72.2 (5.6)	31.2 eq (4.1) 27.1 ax (2.8)	22.4 (7.5)	54.1 (5.0)		
42		$CDCl_3$	75.5 (8.0)	37.9 (8.0)	72.8 (8.0)	21.1 –	22.2 (8.0)	54.5 (6.0)	63.9	*b*
		toluene-d_8	74.2 (9.3)	37.7 (7.6)	72.1 (7.6)	21.0 (3.7)	22.0 (7.5)	53.9 (3.7)		

[a] Values in parentheses are ^{31}P–^{13}C coupling constants in Hz. [b] ^{13}C and ^{31}P: this work. [c] ^{31}P: Mikolajczek, M.; Lucak, J. *Tetrahedron* **1972**, *28*, 5411.

Table IX. Backbone Coupling Constants in Hz (First-Order Analysis, $J_{^{31}PH}$, Not Included)



compd	R	R′	X	Y	$^3J_{H_AH_B}$	$^3J_{H_AH_C}$	$^2J_{H_BH_C}$	$^3J_{H_DH_C}$	$^3J_{H_DH_B}$
8	H	CH_3	OMe	:	9.4	3.2	−14.0	3.2	5.0
22[a]	H	H	OMe	=O	–	–	−14.8	2.6[b]	5.9[b]
23	H	H	OMe	=O	11.4	2.4	−14.8	2.4	6.2
24	H	H	=O	OMe	12	c	−17.3	*c*	*c*
25	CH_3	H	OMe	=O	11.3	2.4	−14.3		
26	CH_3	H	=O	OMe	11.3	2.4	−14.3		
27	CH_3	CH_3	OMe	=O	11.5	2.3	−14.3		
28	CH_3	CH_3	=O	OMe	11.7	2.6	−14.6		
29	H	CH_3	OMe	=O	9.0	4.1	−14.6	3.2	5.2
36	H	H	OMe	=S	11.5	2.2	−15.0	1.9[d]	1.9[d]
37	H	H	=S	OMe	10.7	2.8	−14.6	2.9	5.1
38	CH_3	H	OMe	=S	10.9	2.7	−14.5		
39	CH_3	H	=S	OMe	11.2	2.4	−14.4		
40	CH_3	CH_3	OMe	=S	11.5	2.3	−14.3		
41	CH_3	CH_3	=S	OMe	11.7	2.6	−14.5		
42	H	CH_3	OMe	=S	9.2	3.8	−14.6	3.8	5.2

[a] This compound has no methyl substituent. [b] $J_{H_EH_C}$ = 2.6, $J_{H_EH_B}$ = 9.3 Hz. [c] Spectrum not fully analyzed; $J_{H_EH_E}$ = 11.5, $J_{H_EH_C}$ = 4.2 Hz. [d] $J_{H_EH_E}$ 11.5, $J_{H_EH_C}$ 5.0, $J_{H_DH_E}$ −11.5 Hz.

spectrum of the 4,4,6,6-tetramethyl phosphite **9** is compatible with an all-chair form with axial methoxyl. The remaining compounds are either conformationally locked (bicyclic systems) or highly mobile (five-membered rings).

^{17}O–^{31}P Coupling Constants. Unfortunately, because of the large bandwidth of the ^{17}O signals, the reproducibility of the coupling data in Tables I–III (which in some instances contain data from two laboratories) is quite low and the accuracy of these constants is probably no greater than ±10 Hz (cf. ref 2, 4, and 5) overall. These data are somewhat less good (±15 Hz) for the ring oxygens whose signals tend to be particularly broad, and somewhat better (±5 Hz) for the rather narrow phosphoryl ox-

Table X. ^{17}O Resonances of Five-Membered Cyclic Phosphites, Phosphates, and Thiophosphate **43**[a]

compd	14	15	16	17	18	19	20	21	32[b]	33[c]	34[d]	43
δ_{P-OR}	67.4	104.6	77	125	100	133.4	151.0	156	28.7	60	34	61.8
J_{P-OR}	176	155	*e*	*e*	196	159	111	*e*	78	*e*	*e*	127
$\delta_{P-O\text{-ring}}$	78.7	78.6	127	125	78.4	79.6	79.3	81	46.1	48	96	71.5
$J_{P-O\text{-ring}}$	156	144	*e*	*e*	154	152	122	*e*	88	*e*	*e*	127

[a] Shifts in ppm, coupling constants in Hz. [b] P=*O*, 77.9 (166 Hz). [c] P=O, 80.2 (163 Hz). [d] P=*O*, 88.8 (159 Hz). [e] Not determined.

Table XI. ^{17}O Resonances in Bicyclic Phosphites and Phosphates[a]

compd	10	11	12	13	30	31
δ	71.4	91.6; 116.6	80; 84; 104.2	82.7	51; 68.4[c]	76; 93.0[c]
J	159	152; 133	189; 170; 129	152	b; 150	b; 150

[a] δ in ppm, J in Hz. [b] Not determined. [c] P=*O* resonance.

ygens. For the phosphites (Table I) the $^{31}P-^{17}O$ coupling constants fall into the 150–180-Hz range and are thus similar to that for $P(OMe)_3$ (154[2] or 153 Hz[5]). In most of the phosphates (Table II) $^{31}P^{17}O$ coupling constants for single-bonded P–O were not resolved.[30] The P=O coupling constants, in contrast, are well resolved; they fall in a narrow range (156–164 Hz except for **27**) which is in better agreement with one reported[2] $(MeO)_3P=O$ coupling constant of 165 Hz than with another report[4] of 145 Hz. The reason for the low P=O coupling constant for **27** is not obvious. The range for the thiophosphates (Table II) is 92–127 Hz for all P–O couplings.

^{17}O Chemical Shifts. Examination of the phosphite ^{17}O shifts in Table I, especially those for **4** vs. **5** and **2** vs. **3**, indicates substantial and easily detectable differences in the ^{17}O signal positions of axial and equatorial methoxyl groups. The axial ^{17}O nucleus resonates upfield of the equatorial, in accord with the earlier observation in conformationally locked cyclohexanols and their ethers.[13] This is of particular interest, since the ^{13}C and ^{31}P spectra of the isomers **4** and **5** (Table VI) are quite similar except for a small upfield shift (4 ppm) of C(4,6) in the axial isomer and the already-mentioned enhancement of the $^{31}P^{13}C(5)$ coupling in the equatorial one. The differences between stereoisomers for the ring oxygens [O(1,3)] is quite small (<3 ppm) implying that β_e and β_a effects of the exocyclic MeO on the ring oxygens are very similar. This is somewhat surprising, since the corresponding difference for exocyclic methyl (as in axially and equatorially substituted 2-methyl-1,3-dioxanes) is large (12.1 ppm[14]). By way of an analogy, the difference in β_e and β_a effects in the ^{13}C spectra of equatorially and axially substituted cyclohexanols[31] (2.4 ppm) is smaller than in methylcyclohexanes (3.6 ppm[32]) but not by as large a factor. We have already mentioned that the position of the ^{17}OMe signal for **1** strongly supports the axial conformation of the methoxyl group, as does the similarity in shift of O(1) for **1** and **2**. The β_e effects of the equatorial ring methyl groups on the adjacent oxygens in the ring in **2–5** amount to 25–30 ppm. Compound **6** displays a downfield shift of the axial methoxyl oxygen signal of about 12 ppm relative to **1**, **2**, and **4** which may be explained by a δ-compression shift.[13] A shift of a comparable magnitude is seen on O(3) as a result of combined β_a and gem-β_e effects (compare compounds **6** and **9** to **4** and **7** to **5**). It should be noted that the equatorial methyl groups in **2–5** exert a negligible δ effect on OMe. The effect of two axial methyl groups on the OMe shift in **9** is about twice as large as that of a single methyl in **6** relative to **4** as the standard.

The large downfield shift of ^{17}OMe in **7** has no obvious explanation. Three possibilities need to be considered. (1) The compound exists as a chair with equatorial methoxyl. In that case one must postulate a large δ_a effect of about 6 ppm (compare with **5**) even though there is no compression. Also, while the downfield shift of O(3) is reasonable, owing to the β_a and gem-β_e effects of the extra ring methyl substituent, the upfield shift of O(1) now requires the assumption of an upfield shifting δ effect. This does not appear very attractive, nor does the fact that, compared to **6**, O(1) is shifted upfield but O(3) downfield in **7**. On the other hand, the ^{13}C spectrum (Table VI) is quite compatible with the assumption of an equatorially substituted chair. The similarity of most ring carbon and methyl shifts with those of **6** [except for the absence of the γ-upfield shift at C(6)] points in this direction, as does the large (perhaps too large) $^{31}P^{13}C(5)$ coupling constant. Possibility 2 is that the compound exists as a boat. Although a number of ^{13}C spectra of 1,3-dioxanes existing in the skew-boat form have been recorded,[27] the spectral evidence either in favor or against this conformation is not decisive. A third possibility is that the compound exists as the alternate (triaxial) chair. This would be compatible with the very low-field OMe ^{17}O chemical shift and also with a very low-field MeC(6) ^{13}C shift but seems out of line with the rather low-field ^{13}C shift for C(6), an axial C(4) with nearly the same chemical shift as in **6**, and the large $^{31}P^{13}C(5)$ coupling, and it does not explain why O(1) and O(3) shift in opposite directions relative to **6**. Unfortunately this leaves the ^{17}O spectrum of **7** somewhat of a mystery. The possibility of a large δ_a effect on OMe certainly cannot be ruled out, with the effect on O(1) going in the opposite direction. If compound **8** is conformationally heterogeneous (vide supra) and the δ effect in **7** is real and is seen also in the OMe-equatorial conformation of **8**, the intermediacy of the ^{17}OMe chemical shift of **8** between those of **6** and **7** is reasonable. Moreover, if the axial conformer predominates in **8**, the ^{13}C spectrum (Table VI) may be readily interpreted with respect to the upfield shift of C(6) (point of attachment of an equatorial Me) relative to that in **4** as being due to a γ_a effect of the axial Me, and the nearly equal shift of the methyl groups may be interpreted as one being mainly equatorial and the other mainly axial, but with a syn-axial MeO exerting a downfield shifting δ-compression effect. The $^{31}P^{13}C(5)$ coupling value of 7.0 Hz is also in agreement with a predominantly axial conformation, but the C(4) ^{13}C shift, downfield from that in **4**, is somewhat puzzling since the α_a effect is generally less than α_e and the syn-axial (Me/OMe) compression is not known to produce a downfield shift at the γ position. The shifts of O(1) and O(3) are reasonable, the nucleus next to the equatorial methyl having about the same shift as in **4** and the other one being upfield ($\alpha_a < \alpha_e$).[14]

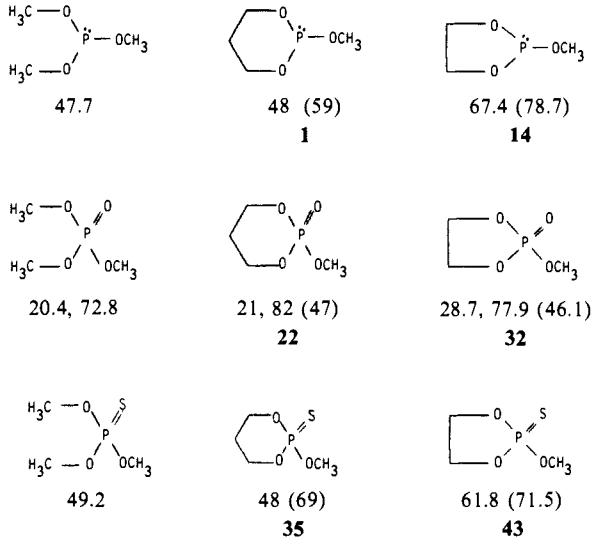
The ^{17}O chemical shifts in the phosphates (Table III) fall into four regions, 21–34 ppm for the P–*O*Me nuclei, 45–47 ppm for the oxygens adjacent to an unsubstituted carbon, 73–89 ppm for the ring oxygens adjacent to the methyl-substituted carbon, and (partially overlapping) 81–94 ppm for the P=*O* nuclei whose signals are readily discerned by their smaller bandwidth. Among the P–*O*Me nuclei, the axial ones (as in **22**, **23**, **25**) resonate at higher field than the equatorial ones **24**, **26**, but the difference (ca. 6 ppm) is less than that (ca. 13 ppm) in the phosphites. The trisubstituted compounds (**27**, **28**) conform to this pattern, though the δ-compression shift in **27** further reduces the difference. Altogether, the *O*Me signals in **27** and **28** are downfield of those in **25** and **26**. The δ-compression effect provides a logical ex-

(30) Resolution of P–O coupling constants seems to depend on the nature of the compound, the position of the oxygen nucleus, and the exact conditions under which the spectrum is recorded. In some instances, the coupling constants are masked (or, worse, simulated) by noise. We have only recorded coupling constants where such is not the case.

(31) Roberts, J. D.; Weigert, F. J.; Kirschwitz, J. I.; Reich, H. J. *J. Am. Chem. Soc.* **1970**, *92*, 1338.

(32) Levy, G. C.; Lichter, R. L.; Nelson, G. L. *Carbon-13 Nuclear Magnetic Resonance*, 2nd ed., Wiley-Interscience: New York, 1980, p 57.

Chart II



planation for **27** but the situation in **28** is puzzling, though it parallels that in the corresponding phosphite **7** (vide supra). Compound **29** displays an *O*Me shift intermediate between that of **27** and **28** supporting the assumption made earlier that it is a mixture of chair conformers. The phosphoryl oxygens display shift differences opposite to OMe, with axial P=*O* (**24**, **26**, **28**) resonating *down*field of equatorial (**23**, **25**, **27**). These results accord with those reported recently by Mosbo et al.[21b] for **25** and **26** although our chemical shifts differ by a few parts per million and are not as widely separated for the two isomers. Here, also, the trisubstituted compounds **27** and **28** resonate downfield of their conformational analogues (**22**, **23**, **25** vs. **27**; **24**, **26** vs. **28**). The intermediate P=*O* shift of **29** between **27** and **28** supports its presumed conformational heterogeneity. As in the corresponding phosphites the shift of the ring oxygen nuclei is insensitive to the configuration or conformation of the exocyclic OMe. Thus the ring oxygens resonate in a narrow range: 45–47 ppm if the adjacent carbon is unsubstituted, 73–76 ppm if substituted with one equatorial β-methyl group (a slightly lesser effect for the partially axial methyl group is seen in **29**), and 87–89 ppm when there is a pair of methyl groups (one equatorial, one axial) on the adjacent carbon. The ring oxygen shifts in the phosphates like the OMe shifts are upfield of those in corresponding phosphites (Table I). This trend and even the actual shift for POMe parallel those in acyclic compounds (e.g., $P(OMe)_3$, 47.7 ppm; $O{=}P(OMe)_3$, 20.4 ppm), but the P=*O* shift in trimethyl phosphate (72.8 ppm) is at higher field than that of the six-membered ring compounds in Table II. That the ring-oxygen signals are downfield of the P*O*Me signals in both phosphites and phosphates may be ascribed to the β effect of C(5).

The thiophosphates (Table III) show similar trends for axial and equatorial OMe ^{17}O chemical shifts as the phosphites and phosphates, and the magnitude of the axial–equatorial difference is small (5–6 ppm) as in the phosphates (compare **35**, **36**, **38** with **37**, **39** and **40** with **41**). Compound **42** seems to have predominantly axial OMe, its ^{17}OMe shift being closer to that of **40** than that of **41**. This is in agreement with dipole moment and proton–proton coupling evidence (vide supra). In the thiophosphate series, in contrast to the other two[33], the axial or equatorial OMe position reflects itself in the ring-oxygen shifts (upfield when OMe is axial, downfield when it is equatorial). However, this trend is greatly attenuated for **40** and **41**, supporting the earlier stated hypothesis that **41** may not be in the expected chair conformation with an axial sulfur and equatorial methoxyl. The OMe signals in the thiophosphates are in the same region as those of the phosphites and substantially downfield from those of the phosphates, in analogy with the acyclic analogue $SP(OMe)_3$ (see Chart II). However, the ring oxygen nuclei are actually *down*field from those in the phosphites. Thus the P=S moiety has either no effect at all compared to the P lone pair, or it has a downfield shifting effect, depending on orientation, whereas the effect of P=O relative to the P lone pair is upfield shifting.

A further comparison of cyclic and open-chain compounds (Chart II) is of interest. The similarity of the MeO shift in the open-chain and six-membered ring compounds in the two series suggests conformational analogy. The OMe in the six-membered rings is predominantly axial owing to the anomeric effect, and this influence may be expected to similarly enforce a gauche conformation (C–O–P–O) in the acyclic analogue. The downfield resonance of the ring oxygens could simply be a manifestation of the β effect of the C(5) carbon. Indeed, when β carbon atoms are introduced into phosphites and phosphates (compare **15** to **14** and **33** to **32**), the P–OR resonances do shift downfield. The large downfield shift in the ring oxygens of the five-membered phosphite **14** may be a hybridization effect. Although the average OPO bond angle in *trans-meso*-MeOPOCHPhCHPhO (98.9°) is only 1–2° smaller than in strainless phosphite esters,[34,35] the average of the ring POC angles (112.4°) is considerably smaller than the unstrained external POC angle (117.5°). Similar structural comparisons can be made with the corresponding phosphate *trans-meso*-MeO(O)POCHPhCHPhO (av OPO ≃ 104°, av ring POC = 111.6°[34]) and unstrained phosphate esters (av OPO = 105°, av POC = 120°[36]). However, the downfield shift of the ring oxygens seen in **14** compared to **1** is not seen in the corresponding phosphates and thiophosphates **32** and **43** compared to **22** and **35**. Thus the downfield shift of the MeO oxygens in all three of these compounds compared to their six-membered ring analogues is probably attributable to the loss of the upfield-shifting anomeric effect in the five-membered rings. Additional data for five-membered ring phosphites and phosphates are shown in Table X. On the whole these data are unexceptional except for the rather large downfield shifting effect of ring methyl substituents on exocyclic P—*O* and P=*O* (compare **16** with **14**, **17** with **15**, and **34** with **32**).

^{17}O shifts and $^{31}P^{17}O$ coupling constants for a few bicyclic compounds are listed in Table XI. Compound **10** in contrast to model phosphite **1** must exist in the boat form. However, this does not seem to explain the substantial downfield shift of the ^{17}O signals. In ^{13}C spectra, boat and twist forms usually resonate upfield of corresponding chair conformations. It is unlikely that hybridizational changes in the heteroatoms of **10** imposed by cage formation are responsible since an X-ray structural analysis of the analogue $P(OCH_2)_3CCH_2Br$[38] reveals an essentially strainless configuration (OPO = 100.1°, POC = 117.5°). Perhaps a β effect imposed by the boat forms of the rings in this cage structure (which we may call the "boat-β effect") is more pronounced than in a six-membered ring in the chair form. Assuming that the ring oxygens are nearly sp^2, it can be seen from models that the orientation of the back lobe of the C–H(eq) hybrid with respect to the back lobe of the sp^2 lone pair orbital on a ring oxygen is different in the chair and boat forms. In the strainless adamantoid system **13** the rings are chairs and the downfield chemical shift of the oxygens by 23.5 ppm from **1** could be associated with the axial substitution of each ring. Because each oxygen is present in two such rings and each ring is axially substituted, the deshielding effect may be expected to be larger than, for example, in going from **4** to **9** (~10 ppm) wherein each oxygen is β to only one axial substituent. The $^{31}P^{17}O$ coupling constant in **13** is certainly below the norm seen in Table I. The boat-shaped

(33) The same trend may, in fact, exist for the phosphites and phosphates, but the difference in the ring oxygen shifts between stereoisomers at phosphorus is so small as to be blurred by experimental uncertainty.

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compound **11** shows rather low-field shifts for both types of oxygen, but the shift for the one-oxygen bridge (116.6 ppm) is not greatly out of line, considering that it relates to a five-membered ring with a β substituent (compare **14** and **15** vs. **16** and **17** in Table X). The 91.6-ppm shift for the oxygens in the two-atom bridge is about 20 ppm lower than the corresponding shift in **10**.[9] Comparison with Chart II suggests that this may be due to the inclusion of these oxygen nuclei in a five-membered ring. Concomitantly there may be a boat-β effect operative, although its magnitude is impossible to assess owing to the different hybridization of these oxygens (POC = 105.8°[38]) compared with **10** (117.5°;[38] vide supra). Compound **12** is probably in the chair conformation and might be compared with **13**. The ^{17}O resonance at 104.2 ppm is assigned to the oxygen shared by both rings. Its chemical shift is about 20 ppm downfield from that in **13**, as might be expected since it is included in a five-membered ring. Of the other two ^{17}O resonances at 80 and 84 ppm, the downfield one ($J_{^{31}P^{17}O}$ = 170 Hz) is assigned to the five-membered ring oxygen since such oxygens tend to have lower $^{31}P^{17}O$ coupling constants (Table X) than six-membered ones (Table I). The remaining signal at 80 ppm ($J_{^{31}P^{17}O}$ = 189 Hz) does appear to be unaccountably far downfield if it is in a relatively undeformed and unsubstituted position in a six-membered ring (compare the shift of 59.2 ppm in **1**). Flipping the carbon α to this oxygen to the boat form in a rapid equilibrium with the chair cannot be ruled out, however.

Phosphates **30** and **31** correspond to the phosphites **10** and **13** and display the same downfield shift (although to a much lesser extent) of the ring oxygen atoms relative to the models **22** and **25**. However, a rather interesting difference is seen in the phosphoryl oxygen shifts. Thus the one in **30** is about 14 ppm upfield of that in the model **22** (boat-β effect) where in **31** the shift is about 12 ppm downfield of that in **25**. The coupling constants (150 ppm) are normal in both cases and the structural parameters for the cage moiety of **30**[39] and **43**[40] are very comparable thus ruling out changes in hybridization as the cause. It is possible that the boat-β effect is also operative on the chemical shifts of these bridgehead atoms. Thus $\delta^{31}P$ shifts downfield in the parent phosphites (by 46.2 ppm) from **10** to **13**,[41] the latter having a ^{31}P chemical shift typical of phosphite esters. A similar downfield ^{31}P chemical shift (by 7 ppm)[41] is noted in the corresponding thiophosphates. Strangely, however, the exception occurs from **30** to **31** where there is an *upfield* ^{31}P chemical shift although it is only 2.4 ppm.[42]

Conclusions

^{17}O chemical shift differences between axial and equatorial alkoxy oxygen signals in six-membered cyclic phosphites, phosphates, and thiophosphates in spectra recorded with the natural abundance of ^{17}O are large enough to assign configuration with confidence. In conformationally mobile systems, qualitative conformational analysis can be carried out using the same shift differences, even if the inaccuracies of the measurements do not permit quantitative conclusions. The relative shifts for the ring oxygens in the thiophosphates (upfield for axial RO, downfield for equatorial RO exocyclic substituents) can serve as additional indicators of configuration and conformation.

Ring oxygen nuclei resonate downfield of exocyclic ones for the methoxy compounds in each series. For analogously substituted compounds, the exocyclic oxygen resonates at considerably higher field (21–34 ppm) for phosphates than for phosphites or thiophosphates. The range for the latter two series (48–69 ppm) is comparable, with shifts for axial OMe being nearly identical but equatorial OMe resonating at slightly higher field in the thiophosphates than that in the corresponding phosphite. In the case of the ring oxygen nuclei, again those in the phosphates resonate at highest field but here the thiophosphate resonances are distinct (and downfield) from the phosphite resonances. Typical data for the conformationally well-defined set **4**, **5**, **25**, **26**, **38**, **39** are 87–88 ppm for the phosphites, 73 ppm for the phosphates, and 91–101 ppm for the thiophosphates.

As in the previously studied[2,4] acyclic phosphates, the phosphoryl (P=O) oxygen nuclei in the six-membered ring systems resonate downfield of the singly bonded (P—OR) ones. The relationship of the chemical shifts of the axial and equatorial phosphoryl oxygens are opposite of OR oxygens, with the axial P=*O* resonating downfield of the equatorial.

The usual β_e, β_a, and γ_a effects are seen although the difference in the β_e and β_a effects of the P—OMe moiety on the ring oxygen shifts in the phosphites and phosphates is unusually small. (A more normal effect is seen in the thiophosphates.) In the trimethyl compounds **6**, **27**, and **40** a δ-compression effect[13,43] on the P—*O*Me nucleus is clearly evident; a similar effect is seen on P=*O* in **28**. A corresponding downfield shift is seen in trimethylene sulfites with syn-axial S=*O* and CH_3 groups.[44] Rather surprisingly a consistent downfield shift of the methoxyl oxygen, not readily explainable on conformational grounds, is also seen in the equatorial OMe isomers **7**, **28**, and **41**, and a similar effect on equatorial P=O is observed in **27**. This effect, also, is seen in the shift of equatorial S=O in trimethylene sulfites.[44]

Comparison of six-membered with five-membered ring phosphites indicates a large downfield shift for both ring and exocyclic oxygen nuclei in the latter. In the thiophosphates the effect on the exocyclic *O*–R is smaller than in the phosphites and in the phosphate still smaller. The effect on the ring oxygen shifts is very small in the thiophosphate and nil in the phosphate. The phosphoryl oxygen shifts upfield as one goes from the six-membered to the five-membered ring.

In bicyclic systems there is a suggestion that phosphoryl oxygn nuclei in boat-shaped systems resonate substantially upfield of those in chair-shaped systems.

Experimental Section

Proton NMR spectra were recorded on a Perkin-Elmer R24B (60 MHz), a Varian XL-100 (100 MHz), or a Bruker Spectrospin WM-250 (250 MHz) spectrometer. Carbon-13 and phosphorous-31 NMR spectra were recorded on the Bruker instrument (at 62.89 MHz for carbon-13 and 101.27 MHz for phosphorus-31) operated in the pulsed Fourier transform mode and locked on solvent deuterium. Proton and carbon chemical shifts are reported with reference to Me_4Si as internal standard whereas phosphorus chemical shifts are referenced to 85% H_3PO_4 as external standard. Oxygen-17 NMR spectra were similarly recorded at 33.91 MHz but without a lock. Samples (natural ^{17}O abundance) were 1 M solutions in toluene (distilled from CaH_2), in 10-mm tubes, heated at 100 °C. The spectral settings were as follows: 6–10 kHz spectral width, 2000–4000 data points, 90° pulse angle corresponding to 30-μS pulse width, 13–205-ms acquisition time with a 250-μs acquisition delay, and 10^4–10^6 scans. Under these conditions, the observed signals had half-bandwidths in the range 20–220 Hz. Chemical shifts were measured without proton or phosphorus decoupling and are reported relative to external tap water reference at 100 °C.

Preparative HPLC was performed with a Waters Associates Prep LC/system 500 A liquid chromatograph. Dipole moments were measured by the heterodyne-beat method[45] in benzene. Dielectric constants were measured on a WTW Model DM 01 dipole meter and refractive indices on a Bausch and Lomb refractometer. Four solutions of each compound ranging in concentration from about 1 to 10 × 10^{-3} weight fraction in benzene solution were employed.

Syntheses. Phosphites **1**,[46,47] **2**,[20] **3**,[20] **4**,[48] **5**,[48] and **14**[46] and thiophosphates **36**[20] and **37**[20] were synthesized according to literature pro-

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cedures and were characterized by ^1H, ^{13}C, and ^{31}P NMR spectra. Most of the phosphites,[46-48] phosphates,[49] and thiophosphates[20] were prepared by general or specific methods reported in the literature. In some instances it proved preferable to synthesize phosphates directly from diols and $POCl_3$ followed by treatment with methanol and triethylamine rather than by the oxidation of phosphites[46] as described in the literature.[50]

Phosphites 6 and 7. A solution of 2-methyl-2,4-pentanediol (8.87 g, 0.0758 mol) and triethylamine (18.23 g, 0.181 mol) in anhydrous ether (50 mL) was added dropwise to a solution of phosphorus trichloride (10.30 g, 0.07500 mol) in anhydrous ether (1700 mL) at 0–5 °C, and the reaction mixture was stirred overnight at room temperature. The precipitate was filtered off and the filtrate concentrated on a rotary evaporator to leave a residue, which, on distillation under reduced pressure, gave 2-chloro-4,4,6-trimethyl-1,3,2-dioxaphosphorinane, presumably[51] as an isomer mixture, yield 4.07 g (30%): bp 66–68 °C (1 mm); ^{31}P NMR ($CDCl_3$) δ 147.6 [lit.[52] bp 53–55 °C (2 mm) (C_6D_6) δ 145.9].

Following the method described by Aksnes et al.,[47] the above phosphorochloridite (2.00 g, 0.0110 mol) in ether (10 mL) was treated with a solution of methanol (0.35 g, 0.011 mol) and triethylamine (1.21 g, 0.0119 mol) in ether (60 mL) to yield a 38/62 mixture of the phosphites **6** and **7**: yield 1.11 g (56%); bp 62–63 °C (4.3 mm); ^{31}P NMR (C_7D_8) δ 129.9 (6), 131.1 (7) [lit.[52] (solvent not stated) δ 128.6 (**6**), 129.7 (**7**)]; ^{13}C NMR, see Table VI. The ratio of the phosphites **6** and **7** is readily changed from 38/62 to 88/12 by the addition of a trace amount of *p*-TsOH.

Phosphite 8. A solution of methylphosphorodichloridite (2.55 g, 0.0192 mol) in anhydrous ether (10 mL) was added to a solution of *dl*-2,4-pentanediol (2.00 g, 0.0194 mol) and triethylamine (4.25 g, 0.0420 mol) in ether (30 mL) at 0–5 °C. After the mixture was stirred for 2 h at room temperature, the precipitated triethylamine hydrochloride was filtered and the filtrate concentrated to leave a residue, which, on distillation under reduced pressure, yielded **8**: yield 0.58 g (18%); bp 50 °C (9 mm); ^1H NMR (250 MHz) (CD_2Cl_2) δ 1.24 (d, J_{HCCH} = 7.5 Hz, 3 H, CH_3 at C-6 or C-4), 1.46 (d, J_{HCCH} = 6.8 Hz, 3 H, CH_3 at C-4 or C-6), 1.72 (1 H, H_4 or H_6), 2.02 (1 H, H_4 or H_6), 3.48 (d, J_{HCOP} = 12.2 Hz, 3 H, OCH_3), 4.27 (m, 1 H, eq or ax H_5), 4.61 (m, 1 H, ax or eq H_5); ^{31}P NMR (CD_2Cl_2) δ 131.9; ^{13}C NMR, see Table VI. Phosphite **8** was stereospecifically converted by treatment with sulfur to the corresponding thiophosphate **42** which displayed a parent peak of *m/e* 196 in its mass spectrum.

Phosphate 22. A solution of phosphorus oxychloride (20.17 g, 0.1315 mol) in anhydrous ether (150 mL) was added dropwise to a solution of 1,3-propanediol (10.00 g, 0.1314 mol) and triethylamine (26.62 g, 0.2636 mol) in anhydrous ether (250 mL) at 0–5 °C, and the reaction mixture was stirred overnight at room temperature. The precipitate was filtered and the filtrate was concentrated to leave the desired 2-chloro-2-oxo-1,3,2-dioxaphosphorinane (crude).

A solution of methanol (4.65 g, 0.145 mol) and triethylamine (14.07 g, 0.1390 mol) in anhydrous ether (20 mL) was added to a solution of the crude 2-chloro-2-oxo-1,3,2-dioxaphosphorinane in anhydrous ether (50 mL) at 0–5 °C. After the reaction mixture was stirred for 1 h at room temperature, the precipitated triethylamine hydrochloride was filtered and the filtrate concentrated to leave a residue, which, on distillation under reduced pressure, yielded **22**: yield 7.49 g (40% based on 1,3-propanediol); bp 67 °C (0.01 mm) [lit.[53] bp 120 °C (1 mm)].

Phosphates 23 and 24. Following the procedure described for the synthesis of **22**, a 60/40 mixture (crude) of phosphates **23** and **24** was synthesized in 50% yield from 1,3-butanediol. The isomers were separated by preparative HPLC (ethyl acetate). Phosphate **23** emerged first followed by **24**. ^{31}P NMR ($CDCl_3$): **23**, δ -6.4 [lit.[49] -5.30 (neat)]; **24**, δ -4.6 [lit.[49] δ -4.3 (neat)].

Phosphates 25, 26, and 29. Following the procedure described for the synthesis of **22**, a 40:40:20 mixture (crude) of phosphates was synthesized in 40% yield from a mixture of *meso*- and *dl*-2,4-pentanediol. The three stereoisomers were separated by preparative HPLC (ethyl acetate). Phosphate **25** emerged first, followed by **29** and **26**. ^{31}P NMR (C_7D_8) **25**, δ -6.4 [lit.[54] δ -7.1]; **26**, δ -4.5 [lit.[54] δ -4.9 (C_6D_6)]; phosphate **29**; ^1H NMR (250 MHz) (CD_2Cl_2) δ 1.41 (d of d, J_{HCCH} = 6.4 Hz, J_{HCCOP} = 2.2 Hz, 3 H, eq CH_3 at C-6 or C-4), 1.45 (d, J_{HCCH} = 6.7 Hz, 3 H, ax CH_3 at C-6 or C-4), 1.78 (m, 1 H, H_6 or H_4, 3.72 (d, J_{HCOP} = 11.3 Hz, 3 H, OCH_3), 4.72 (complex m, 2 H, ax and eq H_5); ^{31}P NMR ($CDCl_3$) δ -6.1; ^{13}C NMR, see Table VII. The mass spectrum of phosphate **29** displayed the parent peak of *m/e* 180; parent mass 180.0551 (calculated for $C_6H_{13}O_4P$, 180.0550).

Phosphates 27 and 28. Phosphates **27** and **28** have been reported in the patent literature[55] but have not been adequately characterized spectrally. Following the procedure described for the synthesis of **22**, an 80/20 mixture (crude) of phosphates **27** and **28** was synthesized in 35% yield from 2-methyl-2,4-pentanediol. The isomers were separated by preparative HPLC (ethyl acetate). Phosphate **27** emerged first, followed by **28**. 27: ^1H NMR (250 MHz) ($CDCl_3$) 1.39 (d of d, J_{HCCH} = 6.2 Hz, J_{HCCOP} = 2.4 Hz, 3 H, eq CH_3 at C-6), 1.46 (d, J_{HCCOP} = 2.5 Hz, 3 H, eq CH_3 at C-4), 1.51 (s, 3 H, ax CH_3 at C-4), 1.75 (m, 1 H, ax H_5), 1.92 (m, 1 H, eq or ax H_5), 3.77 (d, J_{HCOP} = 11.3 Hz, 3 H, OCH_3), 4.65 (m, 1 H, H_6); ^{31}P NMR ($CDCl_3$) δ -7.6; ^{13}C NMR, see Table VII. **28**: ^1H NMR (250 MHz) ($CDCl_3$) δ 1.39 (d of d, J_{HCCH} = 6.2 Hz, J_{HCCOP} = 2.0 Hz, 3 H, eq CH_3 at C-6), 1.46 (d, J_{HCCOP} = 1.8 Hz, 3 H, eq CH_3 at C-4), 1.57 (s, 3 H, ax CH_3 at C-4), 1.79 (m, 1 H, ax or eq H_5), 1.95 (m, 1 H, eq or ax H_5), 3.77 (d, J_{HCOP} = 11.3 Hz, 3 H, OCH_3), 4.78 (m, 1 H, H_6); ^{31}P NMR ($CDCl_3$) δ -6.1; ^{13}C NMR, see Table VII. The parent MS peaks of **27** and **28** appeared at 194.0703 ($C_7H_{15}O_4P$ requires 194.0706).

Thiophosphate 35. Sulfur (0.82 g, 0.0032 mol) was added to a solution of phosphite **1** (1.50 g, 0.0110 mol) in toluene (10 mL) at 0 °C. The mixture was stirred overnight at room temperature after which the excess sulfur was filtered off. The filtrate was concentrated and the residue distilled to yield **35**, yield 1.51 g (82%), bp 87 °C (0.01 mm) [lit.[56] bp 100 °C (0.05 mm)].

Thiophosphates 38, 39, and 42. A mixture of the phosphites **5** and **8** was synthesized in 76% yield from a mixture of *meso*- and *dl*-2,4-pentanediol.[48] A portion of the phosphite mixture was saved for reaction with sulfur and the rest was equilibrated to a mixture of **4** and **8** by the addition of one drop of trifluoroacetic acid.

The mixture of **5** and **8** (4.43 g, 0.0270 mol) was added to a solution of sulfur (1.36 g, 0.00530 mol) in carbon disulfide (10 mL) at 0–5 °C and stirred overnight at room temperature, after which the solution was concentrated and the residue passed through glass wool in a disposable pipet to remove excess sulfur. The filtrate containing **39** and **42** weighed 4.00 g (76% yield). The two products were separated by HPLC (80/20 hexane/ethyl acetate). Thiophosphate **39** emerged first, followed by **42**. The equilibrated phosphite mixture of **4** and **8** was treated with sulfur in a similar manner to yield thiophosphates **38** and **42**: yield 3.99 g (76%); separation also by HPLC (80/20 hexane/ethyl acetate). Thiophosphate **42** emerged first, followed by **38**: NMR (**38**) ^1H (250 MHz ($CDCl_3$) δ 1.39 (d of d, J_{HCCH} = 6.2 Hz, J_{HCCOP} = 2.3 Hz, 6 H, eq CH_3 at C-4 and C-6), 1.72 (m, 1 H, ax or eq H_5), 1.86 (m, 1 H, eq or ax H_5), 3.77 (d, J_{HCOP} = 13.3 Hz, 3 H, OCH_3), 4.62 (complex m, 2 H, ax H_6); ^{31}P ($CDCl_3$) δ 63.4; ^{13}C, see Table VIII. **39**: NMR ^1H (250 MHz) ($CDCl_3$) δ 1.25 (d of d, J_{HCCH} = 6.2 Hz, J_{HCCOP} = 2.0 Hz, 6 H, eq CH_3 at C-4 and C-6), 1.69 (m, 1 H, ax or eq H_5), 1.87 (m, eq or ax H_5), 3.86 (d, J_{HCOP} = 13.5 Hz, 3 H, OCH_3), 4.35 (complex m, 2 H, H_6); ^{31P} ($CDCl_3$) δ 66.1; ^{13}C, see Table VIII; MS parent peak of **38** and **39**, 196.0326 (calcd for $C_6H_{13}O_3PS$, 196.0321). **42**: NMR ^1H (250 MHz) (CD_2Cl_2) δ 1.41 (d of d, J_{HCCH} = 6.4 Hz, J_{HCCOP} = 1.9 Hz, 3 H, eq CH_3 at C-4 or C-6), 1.47 (d, J_{HCCH} = 6.8 Hz, 3 H, ax CH_3 at C-6 or C-4), 1.81 (m, 1 H, H_4 or H_6), 2.08 (m, 1 H, H_6 or H_4), 3.73 (d, J_{HCOP} = 13.1 Hz, 3 H, OCH_3), 4.75 (complex m, 2 H, ax and eq H_5); ^{31}P ($CDCl_3$) δ 63.9; ^{13}C see Table VIII; MS parent peak at 196.0325 (calcd for $C_6H_{13}O_3PS$ 196.0321).

Thiophosphates 40 and 41. Following the procedure described for the preparation of **8**, a mixture of the phosphites **6** and **7** was synthesized in 52% yield from 2-methyl-2,4-pentanediol and methylphosphorodichloridite. The mixture was treated with sulfur as in the synthesis of **39** and **42** to give a 65/35 mixture of **40** and **41** in 92% yield. The isomers were separated by preparative HPLC (80/20 hexane/ethyl acetate). Thiophosphate **41** emerged first, followed by **40**. **40**: NMR ^1H (250 MHz) ($CDCl_3$) δ 1.41 (d of d, J_{HCCH} = 6.2 Hz, J_{HCCOP} = 2.1 Hz, 3 H, eq CH_3 at C-6), 1.47 (d, J_{HCCOP} = 2.3 Hz, 3 H, eq CH_3 at C-4), 1.54 (s, 3 H, ax CH_3 at C-4), 1.74 (m, 1 H, ax or eq H_5), 1.98 (m, 1 H, eq or ax H_5), 3.75 (d, J_{HCOP} = 14.0 Hz, 3 H, OCH_3), 4.71 (complex m, 1 H, H_6); ^{31}P ($CDCl_3$) δ 62.5; ^{13}C, see Table VIII. **41**: ^1H (250 MHz) ($CDCl_3$) δ 1.41 (d of d, J_{HCCH} = 6.2 Hz, J_{HCCOP} = 1.6 Hz, 3 H, eq CH_3 at C-6), 1.47 (d, J_{HCCOP} = 1.0 Hz, 3 H, eq CH_3 at C-4), 1.62 (s, 3 H, ax CH_3 at C-4), 1.83 (m, 1 H, ax or eq H_5), 2.09 (m, 1 H, eq or ax H_5), 3.77 (d, J_{HCOP} = 14.0 Hz, 3 H, OCH_3), 4.81 (complex m, 1 H, H_6); ^{31}P ($CDCl_3$) δ 62.6;

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^{13}C, see Table VIII, MS parent peak of **40** and **41** 210.0475 (calcd for $C_7H_{15}O_3PS$, 210.0478).

Phosphate 32. Following a procedure described by Denney et al.[50] for the mercuric oxide oxidation of cyclic phosphites, phosphate **32** was prepared from phosphite **14**[46] in 29% yield, bp 60–62 °C (0.25 mm) [lit.[53] bp 85–86 °C (1 mm)].

Thiophosphate 43. Following the procedure described for the preparation of **35**, thiophosphate **43** was synthesized in 57% yield from phosphite **14** and sulfur. ^1H NMR (60 MHz, $CDCl_3$) δ 3.75 (d, J_{HCOP} = 14.0 Hz, 3 H, OCH_3), 4.75 (d, J_{HCOP} = 11.0 Hz, 4 H, ring protons).

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Registry No. 1, 31121-06-9; (±)-**2**, 103959-24-6; (±)-**3**, 103959-25-7; **4**, 7735-86-6; **5**, 7735-82-2; (±)-**6**, 103959-26-8; (±)-**7**, 103959-27-9; (±)-**8**, 95977-88-1; **9**, 69576-77-8; **10**, 1449-91-8; **11**, 279-53-8; (±)-**12**, 103959-28-0; **13**, 281-33-4; **14**, 3741-36-4; **15**, 695-11-4; **16**, 14812-60-3; **17**, 38206-24-5; **18**, 53969-09-8; **19**, 40928-00-5; **20**, 28950-17-6; **21**, 1077-05-0; **22**, 33554-05-1; (±)-**23**, 103959-29-1; (±)-**24**, 103959-30-4; **25**, 41158-22-9; **26**, 61248-12-2; (±)-**27**, 103959-31-5; (±)-**28**, 103959-32-6; (±)-**29**, 104012-92-2; **30**, 1449-89-4; **31**, 875-12-7; **32**, 2196-04-5; **33**, 823-31-4; **34**, 7443-26-7; **35**, 33148-57-1; (±)-**36**, 103959-33-7; (±)-**37**, 103959-34-8; **38**, 104012-93-3; **39**, 104012-94-4; (±)-**40**, 103959-35-9; (±)-**41**, 103959-36-0; (±)-**42**, 95932-59-5; **43**, 24453-84-7; (±)-$(H_3C)_2C(OH)CH_2CH(OH)CH_3$, 99113-75-4; PCl_3, 7719-12-2; Cl_2POCH_3, 3279-26-3; (±)-$H_3CC(OH)CH_2CH(OH)CH_3$, 1825-14-5; $POCl_3$, 10025-87-3; $HO(CH_2)_3OH$, 504-63-2; (±)-2-chloro-4,4,6-trimethyl-1,3,2-dioxaphosphorinane, 104012-95-5; 2-chloro-2-oxo-1,3,2-dioxaphosphorinane, 872-99-1.

Dynamic Stereochemistry of Hexakis(dimethylsilyl)benzene

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Abstract: Empirical-force-field (EFF) calculations show that hexakis(dimethylsilyl)benzene (**2**) has a C_{6h} ground-state geometry similar in most respects to the statically geared structure reported for hexaisopropylbenzene (**1**). Variable-temperature NMR measurements on the tricarbonylchromium π complex of **2** (**3**) yield a dimethylsilyl group rotation barrier of 14.2 kcal mol^{-1}. A 15.7-kcal mol^{-1} barrier is found for **2** by EFF calculations. According to these calculations, the rotation of the dimethylsilyl groups in **2** and, by extension, in **3** takes place by a stepwise mechanism rather than by correlated disrotation (dynamic gearing) of all six groups.

Hexaisopropylbenzene (**1**)[2,3] owes its exceptional conformational rigidity to a tightly interlocking cyclic tongue-and-groove arrangement of isopropyl groups in a structure of C_{6h} symmetry. The closely related hexakis(dimethylsilyl)benzene (**2**)[4] presumably adopts a similar structure, in which the SiH hydrogen of each dimethylsilyl group is tucked into the cleft formed by the two methyls of the neighboring group. However, because substitution of silicon for carbon significantly increases the interatomic distances in the side chains, the dimethylsilyl groups in **2** should be less tightly geared than the isopropyl groups in **1**, and the energy requirement for dimethylsilyl group rotation in **2** should therefore be considerably less than that for isopropyl group rotation in **1**. The present work was undertaken in order to place this comparison between the two systems on a quantitative basis.

The structural relationship between **1** and **2** was explored by use of the empirical force field (EFF) method,[5] which had previously been found to give results in satisfactory agreement with experimentally determined values for the ground state of **1**.[3] In accord with expectations, the structure of **2** calculated by this method[6-10] has C_{6h} symmetry and is a good deal less congested than that of **1**.[11] Inspection of Table I shows that, with the

Table I. Calculated Structural Parameters for **1** and **2**[a]

atoms[b]	hexaisopropylbenzene[c] (**1**)	hexakis(dimethylsilyl)benzene[d] (**2**)
	Bond Lengths	
C_{ar}–C_{ar}	1.419	1.415
C_{ar}–X	1.542	1.928
X–C_m	1.543	1.843
X–H	1.100	1.479
	Bond Angles	
C_{ar}–C_{ar}–C_{ar}	120.0	120.0
C_{ar}–C_{ar}–X[e]	121.1	120.4
C_{ar}–C_{ar}–X[f]	118.9	119.6
C_{ar}–X–C_m	115.8	111.1
C_m–X–C_m	115.6	116.3
C_m–X–H	99.6	99.8
C_{ar}–X–H	106.9	118.2
	Torsion Angle	
C_{ar}–C_{ar}–X–C_m	70.1	65.6

[a] Structural parameters calculated by the EFF method (see text). Bond lengths in angstroms, angles in degrees. [b] C_{ar} = aryl carbon, C_m = methyl carbon, X = methine carbon (**1**) or silicon (**2**). [c] Reference 3. [d] Present work. [e] Angle anti with respect to X–H. [f] Angle syn with respect to X–H.

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(6) Input geometries were based on standard bond lengths and bond angles. These structures were then optimized[7] by the program BIGSTRN-3[8] with use of the MM2 force field.[9] Final structures were characterized as minima by the absence of negative eigenvalues in the matrix of analytical second derivatives.

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