Conformations of Saturated Cyclic Phosphorus Heterocycles. II.[1] 5-*tert*-Butyl-2-amino-1,3,2-dioxaphosphorinanes. Apparent Effects of P–N Vicinal Interactions on the Conformational Energy of Amino Groups on Trivalent Phosphorus and the Influence of Lone Pair Orientation on $^3J_{H_{eq}P}$

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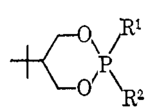
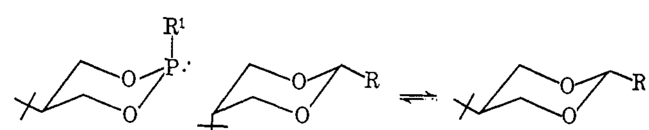
Abstract: Cis and trans isomeric mixtures of 2-dimethylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane (**2**) and 2-methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane (**4**) have been synthesized and their conformations studied by ^{1}H, ^{13}C, and ^{31}P nmr. At equilibrium at 25°, **2** is shown to have a trans : cis (**2a** : **2b**) ratio of isomers of 83 : 17; thus $\Delta G°_{25}$ (cis → trans) = −0.92 kcal/mol. For the isomers of **4**, the trans : cis ratio (**4a** : **4b**) is 55 : 45; and $\Delta G°_{25}$ (cis → trans) = −0.12 kcal/mol. **2a** and **4a** are found to exist predominantly as chair-form conformers with both ring substituents equatorial. The cis isomers, **2b** and **4b**, probably have the 5-*tert*-butyl substituent equatorial or pseudoequatorial so that any relief of 1,3-syn-axial repulsive interaction must involve population of twist-form conformers rather than a chair with 5-*tert*-butyl axial and Me_2N or MeNH equatorial. The equatorial preferences of Me_2N and MeNH are rationalized in terms of greater minimization of vicinal interactions along the phosphorus–nitrogen bond when these groups are equatorial than when they are axial. This factor is not present with phosphorus substituents of similar size such as Me_2CH and CH_3 which display axial preferences. The oxides (**3a**, **3b**) of **2a** and **2b** and the sulfide (**5a**) of **4a** were also investigated by ^{1}H, ^{13}C, ^{31}P, and by use of the shift reagent Eu(dpm)$_3$. The trans oxide (**2a**) and trans sulfide (**5a**) populate chair conformers with both ring substituents equatorial. The cis oxide most probably populates three conformers, the chair with *tert*-butyl equatorial (**9**), a twist form with both substituents pseudoequatorial (**10**), and the chair with *tert*-butyl axial and Me_2N equatorial (**11**). The ratio **9** : **10** : **11** is approximately 3 : 6 : 1. The trivalent isomers **2a** and **4a** with phosphorus lone pair axial show $^3J_{HCOP}$ values (19.6 and 20.2 Hz) nearly double those noted for such 1,3,2-dioxaphosphorinanes with equatorial phosphorus lone pairs. $^3J_{HCOP}$, therefore, depends on both the HCOP dihedral angle and lone-pair orientation.

Earlier work from our laboratories[1b,2] and others[3] has established that alkoxy,[1b,3a–c] chloro,[1b,3] alkyl,[2b] and phenyl[2a] substituents on *trivalent* phosphorus in the 1,3,2-dioxaphosphorinane series in general prefer an axial rather than equatorial orientation. As a result, for the 5-*tert*-butyl substituted compound (**1**) with R^1 = Cl,[1b] OMe,[1b] CH_3,[2b] *i*-Pr,[4] and Ph,[2a] the cis



1, R^1 = Cl, OMe, CH_3, *i*-Pr; R^2 = lone pair
2, R^1 = Me_2N; R^2 = lone pair
3, R^1 = Me_2N; R^2 = O
4, R^1 = MeNH; R^2 = lone pair
5, R^1 = MeNH; R^2 = S

isomer is more stable than the trans form. The cis compounds exist very predominantly, if not exclusively, as chair conformers with the 5-*tert*-butyl group equatorial and R^1 axial as shown in **6**. This is in sharp contrast to 5-*tert*-butyl-2-alkyl-substituted-1,3-dioxanes, **7**,



6 7a 7b

which possess[5] the conformations shown in **7a** and **7b**. The trans isomer (**7b**) is the thermodynamically more stable species as would be predicted if **7a** is subject to repulsive, 1,3-syn-axial interactions. Thus, the conformations of the 1,3,2-dioxaphosphorinanes are not determined primarily by 1,3-steric repulsive interactions. We have suggested[1,2] that vicinal interactions along the P–O bonds including those involving the phosphorus lone pair may be responsible for the unusual conformational preferences in **1**.

In this paper we report the results of a study of the conformations of the stereoisomers of the amino-substituted compounds **2**, **3**, **4**, and **5**. Of particular interest is the finding that the amino substituents in **2** and **4** have an equatorial preference and that with both **2** and **4** the trans isomer is more stable than the cis form.

Results

Syntheses. Phosphoramidite **2**, 2-dimethylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane, was synthesized by reaction of $(Me_2N)_3P$ with 2-*tert*-butyl-1,3-propanediol. Pmr analysis (*tert*-butyl and dimethylamino resonances) of freshly distilled **2** showed the presence of

(1) (a) A portion of the work reported in this paper was published in preliminary form: W. G. Bentrude and H.-W. Tan, *J. Amer. Chem. Soc.*, 94, 8222 (1972); (b) for part I in this series, see W. G. Bentrude and J. H. Hargis, *ibid.*, 92, 7136 (1970).

(2) (a) W. G. Bentrude and K. C. Yee, *Tetrahedron Lett.*, 3999 (1970); (b) W. G. Bentrude, K. C. Yee, R. D. Bertrand, and D. M. Grant, *J. Amer. Chem. Soc.*, 93, 797 (1971).

(3) (a) D. W. White, R. D. Bertrand, G. K. McEwen, and J. G. Verkade, *J. Amer. Chem. Soc.*, 70, 7125 (1970); (b) C. L. Bodkin and P. Simpson, *J. Chem. Soc. B*, 1136 (1971); (c) M. Haemers, R. Ottinger, J. Reisse, and D. Zimmermann, *Tetrahedron Lett.*, 461 (1971); (d) K. Bergesen and P. Albriktsen, *Acta Chem. Scand.*, 26, 1680 (1972).

(4) W. G. Bentrude, H.-W. Tan, and K. C. Yee, unpublished results.

(5) E. L. Eliel and M. C. Knoeber, *J. Amer. Chem. Soc.*, 90, 3444 (1968); F. G. Riddell and M. J. T. Robinson, *Tetrahedron*, 23, 3417 (1967).

two isomers in 61 : 39 ratio (**2a** : **2b**). Oxidation at 0–5° with N_2O_4 in CH_2Cl_2 gave near-quantitative amounts of the corresponding 2-oxo-1,3,2-dioxaphosphorinanes (**3a** and **3b**), in 60 : 40 ratio (pmr and vpc analyses). After about 3 weeks in benzene solution at room temperature, a 60 : 40 ratio of **2a** : **2b** was converted to 83 : 17 as shown both by pmr analysis and N_2O_4 oxidation. In $CDCl_3$ the equilibration to an 83 : 17 ratio (**2a** : **2b**) required less than 2 days, presumably because the interconversion **2a** $\rightleftharpoons$ **2b** is catalyzed by traces of acid in $CDCl_3$. When an 83 : 17 **2a** : **2b** isomeric mixture in $CDCl_3$ was heated to 75° for 2 hr, a 77 : 23 equilibrium ratio of **2a** : **2b** was established (nmr probe temperature, 75°). On cooling to room temperature, the **2a** : **2b** ratio returned to 82 : 18. When the sample was kept at about 0° in a refrigerator for 2 months, the ratio changed to 86 : 14 (probe temperature, 0°). The oxides, **3a** (mp 114.5–115.0°) and **3b** (mp 117.5–118.0°) were separated by column chromatography.

The methylamino analog of **2**, 2-methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane (**4**), was prepared as a mixture of isomers from reaction of 2-chloro-5-*tert*-butyl-1,3,2-dioxaphosphorinane with excess methylamine. Distillation of the products gave an initial **4a** : **4b** ratio of about 90 : 10 (by pmr analysis of the *tert*-butyl absorptions). After equilibration of a benzene-d_6 solution of the isomers of **4** at room temperature, the **4a** : **4b** ratio was 55 : 45. On heating a benzene solution of **4** the ratio decreased considerably and on return of the sample to room temperature was reestablished at 55 : 45. (At the higher temperature the *tert*-butyl resonances were not sufficiently well enough separated to allow accurate determination of **4a** : **4b**.) Addition of a trace of CF_3CO_2H failed to change the room-temperature isomer ratio. After 1 month at about 0°, the **4a** : **4b** was 62 : 38. This ratio had changed to 55 : 45 (28° probe temperature) when the sample was reexamined after 1 week at room temperature.

Attempted N_2O_4 oxidation of **4** gave an ill-defined mixture of products. However, reaction of a 90 : 10 **4a** : **4b** mixture with S_8 at 5–10° in benzene gave quantitative amounts of the derivative, 2-methylamino-5-*tert*-butyl-2-thio-1,3,2-dioxaphosphorinane (**5**), in ratio 91 : 9 (**5a** : **5b**) as determined by vpc.

Several types of evidence, to be outlined below, established that the thermodynamically more stable isomer of **2** and **4** in both cases is the trans form (**2a** or **4a**) with both substituents equatorial on a chair-form ring. Results of pmr studies of the isomers of **2** and **4** are followed by pmr evidence (including shift reagent work) which establishes the geometries (cis or trans) of the pentacovalent compounds derived stereospecifically by oxidation of **2** and **4** and hence the geometries of **2** and **4** themselves. Additional details concerning the conformations of the isomers of **2** and **4** revealed by ^{13}C and ^{31}P nmr investigations then are presented.

^{1}H Nmr Studies. The methylene portions of the pmr spectra (100-Hz sweep width) of pure **3a** and **3b** and of 83 : 17 (**2a** : **2b**) and 90 : 10 (**4a** : **4b**) isomer mixtures of the trivalent compounds **2** and **4** were analyzed by hand as ABXY systems. (The methylene hydrogens were designated nuclei A and B, the methine hydrogen as X, and the phosphorus nucleus as Y.) The hand-calculated coupling constants, J_{AX}, J_{BX}, J_{AY}, J_{BY}, and J_{AB} and chemical shifts, ν_A and ν_B along with ν_X (center of the methine spectrum), and J_{XP} (obtained from the methine spectrum), were employed as input parameters for an iterative AA'BB'XY analysis of the methylene region of the spectrum using the LAOCN3 program. $J_{AA'}$, $J_{AB'}$, $J_{A'B}$, and $J_{BB'}$ were taken as zero. The methine spectrum generated from the parameters obtained in this way fit closely the experimental one in each case. This procedure provided a valuable cross-check of the parameters. We have found that J_{AX} and J_{BX} values determined by iterative fitting of the methine spectrum generally differ by less than 0.05 Hz from those obtained iteratively from the methylene region. A negative sign for J_{XP} was required to faithfully simulate the methine spectra of the oxides and sulfides.

The ABXY approximation applied to these systems neglects cross-ring couplings, $J_{AA'}$, $J_{AB'}$, and $J_{BB'}$, which are evident in the methylene region of certain spectra and often result in triplet-like splittings. In certain instances analysis of the wings of the methylene portion of the spectra allowed determination of values for these cross-ring couplings which ranged from 0.5–1.5 Hz. However, in view of the complexity of the spectra and uncertainties of line assignments, it is not certain that the values determined for $J_{AA'}$, $J_{AB'}$ ($=J_{A'B}$), and $J_{BB'}$ are unique even when experimental spectra are accurately simulated. Therefore, we have not reported them. Spectral parameters for **2**, **3**, **4**, and **5a** appear in Table I. We have checked the validity of the above approximation in similar systems. Thus, computer-generated 100-MHz or 220-MHz spectra based on parameters determined in LAOCN3 analysis neglecting cross-ring couplings of a 60-MHz spectrum were in close agreement with experimental 100- or 220-MHz spectra. A useful aspect of the cross-ring splittings is that they result in clearly discernible splittings of the 16 transitions of the AB portion of the ABXY spin system only when a given isomer is strongly biased energetically toward a single conformer (anancomeric system[6]). Mobile systems with two or more conformers present in appreciable amounts show only line-broadening effects of cross-ring couplings.

The J_{AX} and J_{BX} values for **2a** *and* **4a** *indicate that the 5-tert-butyl group is predominantly equatorial in both compounds.* Also the combination of small J_{AP} and large J_{BP} for **2a** and **4a** is the pattern noted[1-3] for other trivalent systems of this type in which the isomer in question exists largely in one chair-form conformation. The magnitude of J_{BP}, however, is nearly double that normally encountered in other 1,3,2-dioxaphosphorinanes with the exception of *trans*-2,5-di-*tert*-butyl-1,3,2-dioxaphosphorinane (J_{BP} = 19.8 Hz, C_6D_6[4]) which for steric reasons must assume a chair conformation with both *tert*-butyl groups equatorial. *We interpret the large J_{BP} values found for* **2a** *and* **4a** *as being evidence for the equatorial orientation of the Me_2N and MeNH groups in the thermodynamically more stable isomers of* **2** *and* **4**. (This apparent dependence of J_{HCOP} on lone-pair orientation will be discussed later.) Thus, both ring substituents are assigned the equatorial positions in **2a** and **4a**, the trans isomers.

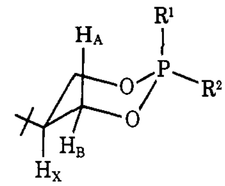
A further effect of lone-pair orientation is seen in the relative chemical shifts of H_A and H_B. With polar axial substituents, Cl and MeO, H_A is downfield of

(6) M. Anteunis, D. Tavernier, and F. Borremans, *Bull. Soc. Chim. Belg.*, **75**, 396 (1966).

Table I. Pmr and ^{31}P Spectral Parameters for 2–4[a,k]

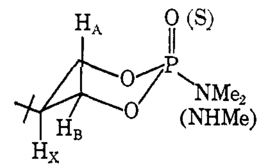
Compd	R^1	R^2	Solvent	J_{AB}[b]	J_{AX}	J_{BX}	J_{AP}	J_{BP}	J_{XP}[e]	J_{PNCH}	δ_A[c]	δ_B	δ_X	$\delta_{t\text{-Bu}}$	$\delta_{X \text{ or } Y}$	$\delta_{^{31}P}$[f]
2a	Lone pair	Me_2N	C_6D_6	−11.36 (0.042)[d]	10.68 (0.063)	4.08 (0.072)	2.50 (0.069)	19.62 (0.094)	1.1	8.7	3.94 (0.0005)	4.09 (0.0004)	1.72	0.635	2.63	142.4
2b	Me_2N	Lone pair	C_6D_6							8.4			1.65[g]	0.690	2.49	135.4
3a	O	Me_2N	$CDCl_3$	−11.12 (0.037)	11.57 (0.057)	4.06 (0.055)	2.34 (0.064)	21.37 (0.074)	−0.80	10.0	4.41 (0.0004)	4.29 (0.0004)	1.97	0.960	2.71	6.96
3b	Me_2N	O	$CDCl_3$	−10.97 (0.023)	10.18 (0.031)	4.80 (0.035)	8.68 (0.031)	13.70 (0.036)	−0.90	10.6	4.14 (0.0002)	4.42 (0.0002)	2.23	0.955	2.68	5.34
4a	Lone pair	MeNH	C_6D_6	−11.36 (0.036)	10.24 (0.058)	4.58 (0.055)	2.32 (0.11)	20.24 (0.11)	0.8	h	3.92 (0.0001)	4.08 (0.0001)	1.70	0.650	2.55	137.8
4b	MeNH	Lone pair	C_6D_6											0.667	h	129.3
5a	S	$NHCH_3$	$CDCl_3$	−11.13 (0.030)	11.64 (0.050)	4.19 (0.044)	3.88 (0.058)	24.81 (0.065)	−0.8	13.0	4.52 (0.0005)	4.28 (0.0005)	1.98	0.967	2.69[i] 3.17 (broad)[j]	

[a] Measured at ambient probe temperatures, Varian Associates XL-100-12 spectrometer, except for **4a**, **4b**, and **5a** measured on a Varian A-60 instrument. [b] Coupling constants in Hz. Absolute values given except for J_{AB}, assumed negative, and J_{XP} (see text). [c] Chemical shifts in ppm downfield from TMS as internal standard. [d] Number in parentheses is probable error of parameter determined from LAOCN3 iterative analysis of AB (methylene) spectrum, ABXY approximation. RMS errors of line positions: **2a**, 0.127; **3a**, 0.104; **3b**, 0.091; **4a**, 0.099; and **5a**, 0.078. [e] From X spectrum (methine H), error estimated <0.3 Hz. [f] In ppm downfield from external 85% H_3PO_4 (C_6D_6 solvent). [g] From a 220-MHz spectrum. [h] Could not be determined with confidence from spectrum of 90:10 mixture because of apparent overlap of CH_3NH and CH_3NH resonance and uncertainty of $^3J_{HCNH}$. [i] CH_3NH (d of d, J_{HH} = 5.2 Hz). [j] $NHCH_3$. [k] See structure at top of page.



H_B by 0.3–0.4 ppm.[1b] Even *cis*-**1** with R^1 = Me has δ_A at 3.89 and δ_B at 3.83 ppm (*o*-dichlorobenzene).[2b] But *trans*-2,5-di-*tert*-butyl-1,3,2-dioxaphosphorinane with the lone pair on phosphorus clearly axial shows δ_A and δ_B reversed at 3.82 and 4.12 ppm, respectively.[4] The relative chemical shifts of these protons in **2a** and **4a** are consistent with the *axial phosphorus lone-pair configuration* assigned to these compounds.

The values of J_{AX} and J_{BX} for oxides **3a** and **3b** and sulfide **5a** indicate that the orientation of the 5-*tert*-butyl group in these rings, like **2a** and **4a**, is largely equatorial or pseudoequatorial, although J_{AX} for **3b** is slightly reduced. That the conformations of **3a** and **5a** are best represented by a single chair-form isomer, **8**, is



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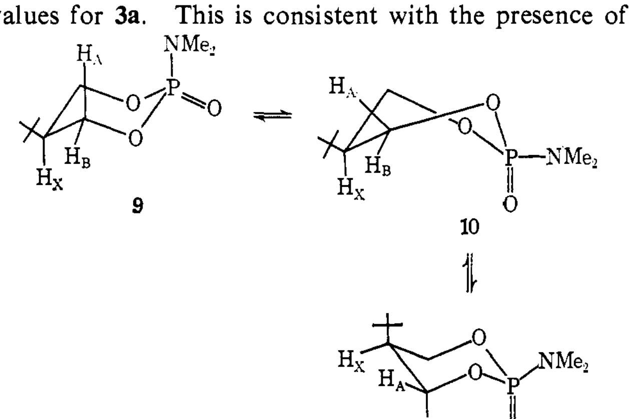
confirmed by the parameters J_{AP} and J_{BP} which are similar to those for other[7] 2-oxo- and 2-thio-1,3,2-dioxaphosphorinanes thought to exist in a single chair conformation. By contrast, **3b** shows values for J_{AP} and J_{BP} which are intermediate between the extreme values for **3a**. This is consistent with the presence of



9 **10** **11**

two or more conformations in rapid equilibrium with each other. (That this is true is indicated also by the influence (*vide infra*) of added shift reagent on the position of equilibrium.) If one assumes the values of J_{AP} and J_{BP} in **3a** to be equivalent to $J_{H_{ax}P}$ and $J_{H_{eq}P}$,

(7) A great number of such studies have been reported. Some of the more recent ones include: (a) L. D. Hall and R. B. Malcolm, *Can. J. Chem.*, **50**, 2092, 2102 (1972); (b) J.-P. Majoral, R. Pujol, and J. Navech, *Bull. Soc. Chim. Fr.*, 606 (1972); (c) P. C. Maria, L. Elegant, M. Azzaro, J.-P. Majoral, and J. Navech, *ibid.*, 3750 (1971); (d) J.-P. Majoral and J. Navech, *ibid.*, 2609 (1971); (e) *ibid.*, 1331 (1971); (f) *ibid.*, 95 (1971); (g) J.-P. Majoral, R. Pujol, J. Navech, and F. Mathis, *Tetrahedron Lett.*, 3755 (1971); (h) J.-P. Majoral, R. Pujol, and J. Navech, *C. R. Acad. Sci., Ser. C*, **272**, 1913 (1971); (i) D. W. White, G. K. McEwen, R. D. Bertrand, and J. G. Verkade, *J. Chem. Soc. B*, 1454 (1971); (j) A. R. Katritzky, M. R. Nesbit, J. Michalski, Z. Tulimowski, and A. Zwierzak, *ibid.*, 140 (1970); (k) R. S. Edmundson and E. W. Mitchell, *J. Chem. Soc. C*, 752 (1970).

respectively, *i.e.* that J_{H_AP} in structure **9** is equal to J_{H_BP} in **11**, then it is easy to show that values of J_{AP} (9.57 Hz) and J_{BP} (14.14 Hz) approximating those found for **3b** could result from the presence of the two conformers **9** and **11** with a **9**:**11** ratio of 62:38.

However, assuming that in **9** and **11** $J_{ax-ax} = 11.6$ Hz, $J_{eq-ax} = 4.0$ Hz, and $J_{eq-eq} = 1.5$ Hz, time-averaged values of 7.8 and 4.0 Hz are calculated for J_{AX} and J_{BX}, respectively, for a 62:38 ratio of **9**:**11**. These results obviously are in poor agreement with the experimental parameters, 10.18 and 4.80 Hz. Another piece of evidence consistent with the presence of only a small percentage of **11** among the conformers of **3b** (and for that matter **3a** and **5a**) is the magnitude of J_{XP} (−0.8 Hz). For other pentavalent 1,3,2-dioxaphosphorinanes, it has been found[7a,e,8] that $|^4J_{XP}| \leq 1$ Hz for axial H_X and 2–3 Hz when H_X is equatorial.

An alternate possibility is that a mobile equilibrium exists between **9**, **11**, and a twist–boat form **10**. We earlier reported[9] that *cis*-2,5-di-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane is largely in a boat or twist conformation (see below) as shown by the coupling constants $J_{AX} = J_{AP} = J_{BP} = 10$ Hz and $J_{BX} = 5$ Hz. Using these parameters and those assumed for **9** and **11**, time-averaged couplings, J_{AX}, J_{BX}, J_{AP}, and J_{BP} of 9.6, 4.6, 8.8, and 12.6, respectively, are predicted for an assumed equilibrium conformer mixture of 30% **9**, 60% **10**, and 10% **11**. The 1:2 ratio of **9**:**10** suggests that these conformers are approximately equal in conformational enthalpy, since there are two identical twist conformations readily accessible to **10**.

An equilibrium analogous to **9** $\rightleftharpoons$ **10** $\rightleftharpoons$ **11** is also noted[4] for *cis*-2-isopropyl-5-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane. Based on *A* values[10] for cyclohexane system, the isopropyl and Me_2N groups should have similar sizes, and on this basis this finding is not surprising. *trans*-2-Isopropyl-5-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane, however, shows no signs of the presence of more than one conformer and displays coupling constants similar to those for **3a** and **5a**. This is evidence for the correctness of the assigned geometries of **3a**, **3b**, and **5a**. The cross-ring coupling patterns (*vide supra*) exhibited by these compounds also show the strong conformational bias of **3a** and **5a** toward a single chair form. (This also applies to **2a** and **4a**.) Steric 1,3-syn-axial repulsions involving an axial Me_2N or *i*-Pr substituent apparently are relieved in these systems by ring reversal to a twist–boat conformation.

Also consistent with these assignments are the relative shifts of the A and B protons in **3a**, **3b**, and **5a**, *i.e.* $\delta_A > \delta_B$ in **3a** and **5a** and $\delta_B > \delta_A$ in **3b**. This ordering of chemical shifts has been noted [4,9,11] without exception for all pairs of 2-R-5-*tert*-butyl-2-oxo- and 2-thio-1,3,2-dioxaphosphorinanes (R = CH_3O, Me, *i*-Pr, *t*-Bu, Ph) whose structures are known from X-ray[12] or other evidence. The same may be said for the frequencies of the methine hydrogens, *i.e.*, δ_X(cis) > δ_X(trans).

The oxides **3a** and **3b** and sulfide **5a** are formed from the stereospecific, retentive,[15] oxidation of phosphoramidites **2a**, **2b**, and **4a**, respectively. Therefore, *the evidences for the trans geometries of* **3a** *and* **5a** *and cis geometry of* **3b** *also offer further support for the geometries assigned above to* **2a**, **2b**, **4a**, *and* **4b**.

Shift Reagent Studies. We earlier reported[17] the usefulness of the shift reagents $Eu(dpm)_3$ and $Eu(fod)_3$ for the simplification of the pmr spectra of oxides similar to **3a** and **3b**. (Unfortunately, shift reagents do not yield useful information with 2-thio-1,3,2-dioxaphosphorinanes.) These reagents also were shown[17] to be helpful in establishing cis or trans geometry in such systems. It also was noted that when two or more conformers of similar energies are present the equilibrium between these species is perturbed by coordination with europium. Application of these ideas to the oxides **3a** and **3b** further confirms the above structural assignments.

Structural assignments based on the effects of added shift reagents or proton chemical shifts have sometimes been made by plotting observed shift change $\Delta_{obsd}(H_i)$, *vs.* mole ratio of total shift reagent to total substrate (E_t/S_t) and then comparing $\Delta_{obsd}(H_i)$ for various hydrogens at $E_t/S_t = 1$. The latter $\Delta_{obsd}(H_i)$ value is sometimes called the gradient, G_i. This method has certain limitations which are partially overcome by an internal referencing method.[18] Plots of $\Delta_{obsd}(H_i)$ *vs.* $\Delta_{obsd}(H_j)$ where i and j are two different protons on the same molecule are generally linear, and their slopes are equal to $\Delta_{max}(H_i)/\Delta_{max}(H_j)$. We have used H_X as the reference proton in the 2-oxo-1,3,2-dioxaphosphorinanes. If H_X and H_A or H_B are in the same relative environments in a pair of *cis*- and *trans*-2-substituted-5-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinanes, then similar values of $\Delta_{max}(H_A)/\Delta_{max}(H_X)$ and $\Delta_{max}(H_B)/\Delta_{max}(H_X)$ should be obtained. Comparison of these two ratios also gives a direct measure of the relative responses of H_A and H_B to added shift reagent. These parameters for **3a** and **3b** are compiled in Table II. Plots of $\Delta_{obsd}(H_i)$ *vs.* $\Delta_{obsd}(H_j)$ gave correlation coefficients of 0.9999 and had intercepts $<|6$ Hz$|$. Also included in Table II are data for analogous 1,3,2-dioxaphosphorinanes (**12–14**) whose cis or trans geometries are known with considerable certainty.[19] Table II clearly shows the similarity of the values of $\Delta_{max}(H_A)/$

(8) L. D. Hall and R. B. Malcolm, *Chem. Ind.* (*London*), 92 (1968).

(9) W. G. Bentrude and K. C. Yee, *J. Chem. Soc.*, *Chem. Commun.*, 169 (1972).

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(11) W. G. Bentrude and J. H. Hargis, *Chem. Commun.*, 1113 (1969).

(12) X-Ray structures have been determined for *cis*-2-methyl-5-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane,[13] *trans*-2-methoxy-5-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane,[14] *cis*-2-phenyl-5-*tert*-butyl-2-thio-1,3,2-dioxaphosphorinane,[14] and *cis*-2,5-di-*tert*-butyl-2-thio-1,3,2-dioxaphosphorinane.[14]

(13) M. Haque, C. N. Caughlan, J. H. Hargis, and W. G. Bentrude, *J. Chem. Soc. A*, 1786 (1970).

(14) C. N. Caughlan and coworkers, unpublished work, Montana State University, Bozeman, Mont.

(15) D. Z. Denney, G. Y. Chen, and D. B. Denney, *J. Amer. Chem. Soc.*, 91, 6838 (1969); J. Michalski, A. Okruszek, and W. Stec, *Chem. Commun.*, 1495 (1970); W. E. McEwen, *Top. Phosphorus Chem.*, 2, 29 (1965). The accompanying paper[16] provides strong evidence for the retentive N_2O_4 oxidations.

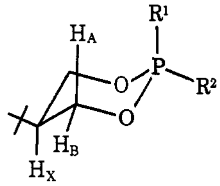
(16) The same conclusion concerning the equatorial preference of the dimethylamino substituent on phosphorus in trivalent 1,3,2-dioxaphosphorinanes has been reached independently by Professor J. G. Verkade and his group as reported in the accompanying paper: J. A. Mosbo and J. G. Verkade, *J. Amer. Chem. Soc.*, 95, 4659 (1973). A preliminary account of their work appeared earlier: J. A. Mosbo and J. G. Verkade, *ibid.*, 94, 8224 (1972).

(17) K. C. Yee and W. G. Bentrude, *Tetrahedron Lett.*, 2775 (1971); W. G. Bentrude, H.-W. Tan, and K. C. Yee, *J. Amer. Chem. Soc.*, 94, 3264 (1972).

(18) D. R. Kelsey, *J. Amer. Chem. Soc.*, 94, 1764 (1972).

(19) The stereochemistries of **12a** and **12b** are based on X-ray evidence.[13] Those of **13a**, **13b**, and **14a** are inferred from X-ray structures of the corresponding sulfides[12,14] and assorted spectroscopic data.

Table II. Effects of Added Eu(dpm)$_3$ on Proton Chemical Shifts



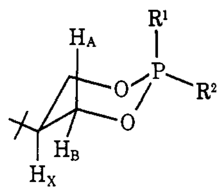
Compd	R[1]	R[2]	$\Delta_{max}(H_A)/\Delta_{max}(H_X)$	$\Delta_{max}(H_B)/\Delta_{max}(H_X)$	G_A	G_B	G_X
3a[a]	O	Me$_2$N	1.30	0.769	290	178	236
3b[b]	Me$_2$N	O	1.09	1.30	208	249	196
12a[c]	O	Me	1.82	0.912	500	248	276
12b[d]	Me	O	1.04	1.61	198	307	188
13a[e]	O	Ph	1.45	0.819	425	244	292
13b[f]	Ph	O	1.10	1.25	257	296	237
14a[g]	O	*t*-Bu	1.44	0.794	349	196	235

[a] Addition of Eu(dpm)$_3$ to a 0.24 *M* solution of **3a** in CDCl$_3$, 25°. [b] Addition of Eu(dpm)$_3$ to a 0.25 *M* solution of **3b** in CDCl$_3$, 25°. [c] Addition of Eu(dpm)$_3$ to a 0.34 *M* solution of **12a** in CCl$_4$, ambient temperature. [d] Addition of Eu(fod)$_3$ to a 0.20 *M* solution of **12b** in CCl$_4$, ambient temperature. [e] Addition of Eu(dpm)$_3$ to a 0.24 *M* solution of **13a** in CCl$_4$, ambient temperature. [f] Addition of Eu(dpm)$_3$ to a 0.24 *M* solution of **13b** in CDCl$_3$, ambient temperature. [g] Addition of Eu(dpm)$_3$ to a 0.25 *M* solution of **14a** in CDCl$_3$, 36°.

$\Delta_{max}(H_X)$ and $\Delta_{max}(H_B)/\Delta_{max}(H_X)$ for **3a** to those of **12a**, **13a**, and **14a**, particularly the greater response of H_A. Similarly, the parameters for **3b** closely resemble those for **12b** and **13b**. The conclusion that **3a** is a trans isomer is again confirmed.

The effects of adding Eu (dpm)$_3$ on the coupling constants in **3a** and **3b** are recorded in Table III. The *J* values of **3a** are essentially unchanged by added Eu(dpm)$_3$ even at an E_t/S_t ratio of 0.82. This also is consistent with its assigned trans structure, since it is the result observed with **12a**, **13a**, and **14a**, all of which are trans isomers and whose potential conformational equilibria are strongly biased in favor of the chair form with substituents 5-*t*-Bu and 2-Me, 2-Ph, or 2-*t*-Bu equatorial. The conformational mobility of **3b** and the presence of reasonably high concentrations of more than one conformer of **3b** are well demonstrated by the variation in J_{AX}, J_{AP}, and J_{BP}. Clearly, the equilibrium between conformers of complexed **3b** (**9**-E, **10**-E, **11**-E) is

Table III. Effects of Added Eu(dpm)$_3$ on *J* Values



Compd	Mol of Eu(dpm)$_3$/mol of compd	J_{AB}[a]	J_{AX}	J_{BX}	J_{AP}	J_{BP}
3a	0.00	−11.12	11.57	4.06	2.34	21.37
	0.82	−11.5	11.5	4.0	2.5	22.3
3b	0.00	−10.97	10.18	4.80	8.68	13.70
	0.37	−11.0	9.5	5.0	11.5	12.0
	0.56	−11.0	9.0	5.0	*b*	11.0
	0.70	−11.0	8.5	5.0	*b*	11.0
	0.95	−11.0	8.5	5.0	*b*	10.5
	1.36	−11.5	8.0	*b*	14.5	*b*

[a] Coupling constants in Hz, measured at 60 MHz to nearest 0.5 Hz. Estimated error, ±0.5 Hz. [b] Resonance obscured by overlap of Me$_2$N spectrum at this ratio of Eu(dpm)$_3$/compound.

$$\begin{array}{ccccc} \mathbf{9} & \rightleftharpoons & \mathbf{10} & \rightleftharpoons & \mathbf{11} \\ -E \uparrow\downarrow E & & -E \uparrow\downarrow E & & -E \uparrow\downarrow E \\ \mathbf{9}\text{-E} & \rightleftharpoons & \mathbf{10}\text{-E} & \rightleftharpoons & \mathbf{11}\text{-E} \end{array}$$

different than that between uncomplexed forms of **3b**. The decrease in J_{AX} on Eu(dpm)$_3$ addition suggests a shift on complexation toward **11**-E. This effect would be consistent with a lessening of the equatorial preference[8] of the P=O bond and the presence of unfavorable steric interactions in complexed **10**. The same types of changes in *J* values are found with the cis oxides **12b** and **13b**.[4] *Thus the effects of adding Eu(dpm)$_3$ on both chemical shifts and coupling constants confirm the trans structure for* **3a** *and the cis structure for* **3b**.

^{13}C Nmr Studies. Applications of ^{13}C nmr to studies of cyclic compounds, *e.g.*, cyclohexanes[20] and 1,3-dioxanes,[21] have yielded results which have proved valuable in understanding conformations in these systems. This method is especially useful with inseparable mixtures of isomers such as **2a,b** and **4a,b**. In fact, as we will show, the assignment of the trans and cis geometries to **4a** and **4b**, respectively, can be made solely on the basis of their ^{13}C spectra, their ^{31}P shifts (see below) and the unusually large $J_{H_{eq}P}$ of **2a** and **4a** previously noted. Detailed consideration of the application of ^{13}C to systems like **2–4** will be presented elsewhere. The important features of the ^{13}C spectra of **2** and **4** (Table IV) which confirm the geometry assigned and which pertain to their conformations will be discussed here.

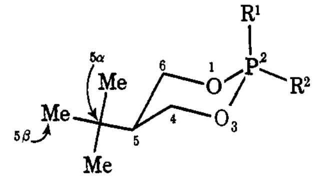
It should first be noted that the values of $\delta_{4,6}$ for **2b** and **4b** are larger than those for the isomers **2a** and **4a**. The upfield shift of ring carbon atoms γ to an axial ring substituent, the so-called γ effect,[22] is commonly noted in cyclohexanes. We have also noted it in the trivalent

(20) See, *e.g.*, the following papers and references therein: F. A. L. Anet, C. H. Bradley, and G. W. Buchanan, *J. Amer. Chem. Soc.*, **93**, 258 (1971); D. K. Dalling, D. M. Grant, and L. F. Johnson, *ibid.*, **93**, 3678 (1971).

(21) G. M. Kellie and F. G. Riddell, *J. Chem. Soc. B*, 1030 (1971); A. J. Jones, E. L. Eliel, D. M. Grant, M. C. Knoeber, and W. F. Bailey, *J. Amer. Chem. Soc.*, **93**, 4772 (1971); F. G. Riddell, *J. Chem. Soc. B*, 331 (1970).

(22) J. D. Roberts, F. J. Weigert, J. I. Kroschwitz, and H. J. Reich, *J. Amer. Chem. Soc.*, **92**, 1338 (1970); D. K. Dalling and D. M. Grant, *ibid.*, **89**, 6612 (1967); G. W. Buchanan, D. A. Ross, and J. B. Stothers, *ibid.*, **88**, 4301 (1966).

Table IV. ^{13}C Chemical Shift Data for 1,3,2-Dioxaphosphorinanes **2** and **4** in C_6H_6[a]



Compd	R¹	R²	$\delta_{2\beta}$[d]	$\delta_{4,6}$	δ_5	$\delta_{5\alpha}$	$\delta_{5\beta}$
2a[b]	Lone pair	Me_2N	93.59 (21.5)[e]	62.84 (4.5)	82.05 (8.5)	97.77	100.95
2b	Me_2N	Lone pair	93.05 (19.9)	66.53 (<2)	82.02 (6.7)	96.89	101.04
4a[c]	Lone pair	MeNH	103.90 (2.5)	63.38 (3.8)	82.01 (8.6)	97.65	100.97
4b	MeNH	Lone pair	101.95 (21.9)	67.48 (<2)	81.94 (4.9)	97.14	101.06

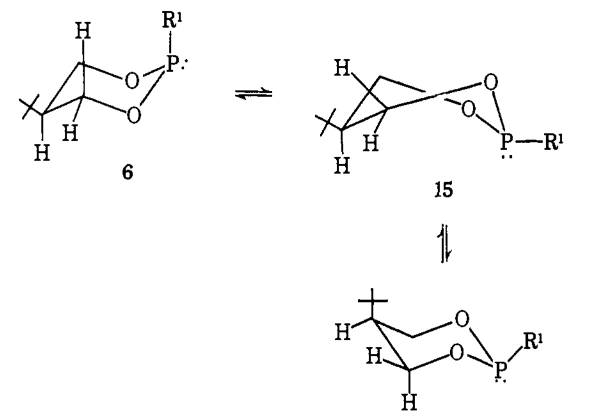
[a] Measured at ambient probe temperatures. Chemical shifts in ppm upfield from internal C_6H_6. [b] Measured on 65:35 (**2a**:**2b**) mixture, 40% (v/v) solution. [c] 65:35 mixture (**4a**:**4b**), 35% (v/v) solution. [d] 2β refers to carbon of Me_2N or MeNH group. [e] Coupling constants J_{CP} in parentheses.

1,3,2-dioxaphosphorinane series, *e.g.*, for *cis*-5-*tert*-butyl-2-methyl-1,3,2-dioxaphosphorinane[2b] (axial Me) $\delta_{4,6}$ is 67.38 (J_{COP} = 4.0 Hz), while for the trans isomer $\delta_{4,6}$ is 63.95 (J_{COP} = 1.2 Hz). Likewise for *cis*-2-isopropyl-5-*tert*-butyl-1,3,2-dioxaphosphorinane,[23] $\delta_{4,6}$ = 65.95 (J_{COP} = 3.3 Hz), and for the trans isomer, $\delta_{4,6}$ = 62.61 ($J_{COP} \cong 0$). The failure of the carbon shifts in Me_2N of **2a** and **2b** to be affected by changes in orientations also was noted with the 2-isopropyl-5-*tert*-butyl-1,3,2-dioxaphosphorinanes. With both Me_2N and Me_2CH, it seems likely that the β-methyls are not subject to steric interactions leading to upfield when axial, because the smaller methine hydrogen (Me_2CH) or lone pair (Me_2N) is preferentially held in proximity to the axial ring hydrogens at C-4 and C-6.

Secondly, the pmr data of Table I show the 5-*tert*-butyl groups on **2b** and **4b** to be equatorially oriented. ^{13}C studies [21] in the 1,3-dioxane ring system have shown that an equatorial to axial reorientation of a 5-*tert*-butyl group results in a 2 ppm *downfield* shift of the 5α and 5β carbon resonances; and our ^{13}C investigations[23] of 1,3,2-dioxaphosphorinane rings indicate that a similar effect is operative in these rings. For five cis trivalent derivatives analogous to **2b** and **4b** with J_{AX} (phosphorus substituent = Cl, CH_3O, Me, *i*-Pr, Ph) in the range 11.0–11.9 and J_{BX} 3.10–3.76, average values of $\delta_{5\alpha}$ = 97.22 ± 0.27 and $\delta_{5\beta}$ = 101.15 ± 0.10 were noted. The values of these shifts for **2b** and **4b** are quite in agreement with the ranges noted.

The ^{13}C data, therefore, support the idea that if 1,3-syn-axial repulsions for **2b** and **4b** in conformation **6** are relieved in any way by conversion to another conformer, it is unlikely that **16** is involved to any great degree. In **16** the $\delta_{5\alpha}$ and $\delta_{5\beta}$ resonances should be shifted considerably downfield. As an example, *trans*-2-methoxy-5-*tert*-butyl-1,3,2-dioxaphosphorinane, the diaxial chair conformer which pmr analysis shows to be highly populated,[1b] has $\delta_{5\beta}$ = 99.95 and $\delta_{5\alpha}$ = 96.03. For **2a** and **4a** shifts $\delta_{5\alpha}$ and $\delta_{5\beta}$ are about those found for other equatorially 2,5-disubstituted-1,3,2-dioxaphosphorinanes.

(23) W. G. Bentrude, K. C. Yee, R. D. Bertrand, H. W. Tan, A. J. Jones, and D. M. Grant, unpublished work. Not including compounds 2–4, ^{13}C shift and carbon–phosphorus coupling data have been collected on 14 pairs of cis–trans isomeric 2-substituted-5-*tert*-butyl-1,3,2-dioxaphosphorinanes, oxides, and sulfides.



6 **15** **16**

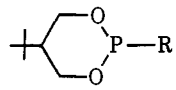
^{31}**P Measurements.** Table I also records ^{31}P chemical shifts for **2** and **4**. Previous studies in our laboratory with six other pairs of isomeric trivalent compounds have shown that without exception the resonance for the cis isomer with the phosphorus substituent axial occurred upfield of that for the trans isomer.[4] Likewise for the pentavalent oxides analogous to **3**, $\delta_{^{31}P}$ (cis) was found[4] to be upfield of $\delta_{^{31}P}$ (trans). The ^{31}P data of Table I thus reinforce the stereochemical (cis or trans) assignments made to the isomers of **2**, **3**, **4**, and **5**.

Discussion

Me_2N and MeNH Orientations. The above results show that the Me_2N and MeNH substituents of 2-dimethylamino- and 2-methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinanes (**2** and **4**) have a preference for the equatorial orientation with the consequence that the trans isomer is more stable than its cis counterpart.[16] From the equilibrium ratios of **2a** : **2b** (83 : 17) and **4a** : **4b** (55 : 45) at room temperature, one may estimate a $\Delta G°_{25}$ (trans → cis) value of 0.94 kcal/mol for **2a** → **2b** and 0.12 kcal/mol for **4a** → **4b**. It seems evident from the nmr results that only one conformer of **2a** or **4a** is highly populated, the chair form with both ring substituents equatorial. However, with the cis isomers, **2b** and **4b**, the only inference which can be drawn from the present data is that conformers with the 5-*tert*-butyl equatorial or pseudoequatorial are predominant at the temperature studied. Since this does not exclude a boat or twist conformer like **15** in which 1,3-syn-axial repulsions are relieved, however, it would not be correct to assume that $\Delta G°_{25}$ (trans → cis) in these systems is equivalent to the conformational energy (*A* value) of either Me_2N or MeNH on phosphorus.

In Table V are listed for comparison the values of

Table V. $\Delta G°_{25}$ (cis → trans) for 2-R-5-*tert*-Butyl-1,3,2-dioxaphosphorinanes



Compd	R	$\Delta G°_{25}$ (cis → trans)[e]	*A* values[a] (cyclohexane)
17	OCH_3	1.4[b] ($CDCl_3$)	0.6
18	CH_3	1.0[c] (benzene, ODCB[f])	1.7
19	*i*-Pr	0.65[d] (benzene)	2.2
20	Ph	1.3[d] (benzene, $CDCl_3$)	3.0
21	*t*-Bu	−1.5[d] (benzene, ODCB[f])	>5
4	MeNH	−0.12 (benzene, $CDCl_3$)	0.9
2	Me_2N	−0.94 (benzene, $CDCl_3$)	2.1

[a] Conformational energies, $\Delta G°_{25}$ (equatorial–axial) for substituent on cyclohexane ring, ref 10. [b] Reference 1b. [c] Reference 2b. [d] Reference 4. [e] Solvent in parentheses. [f] *o*-Dichlorobenzene.

$\Delta G°_{25}$ (cis → trans) for **2** and **4** and for the series of trivalent 2-R-5-*tert*-butyl-1,3,2-dioxaphosphorinanes we have studied previously. Also listed are the conformational energies (*A* values) for these substituents when attached to a cyclohexane ring. The most striking aspect of these results is that the amino substituents prefer to be equatorial rather than axial. This finding is in sharp contrast to that for systems **17–20**. In **17–20** the substituent R on phosphorus preferentially occupies the axial position, and the cis isomer is more stable than the trans by 0.65–1.4 kcal/mol. We have suggested[1,2] previously that for **17–20** 1,3-syn-axial repulsions which arise when the substituent R is axial (A_P) are outweighed by vicinal interactions along the P–O bonds in the ring which are more favorable when the substituent is axial [E_{VPO}(ax)] than when it is equatorial [E_{VPO}(eq)] (see expressions 1–3). Thus, according to eq 3, when [E_{VPO}-

$$E_{ax} = A_P + E_{VPO}(ax) \qquad (1)$$

$$E_{eq} = E_{VPO}(eq) \qquad (2)$$

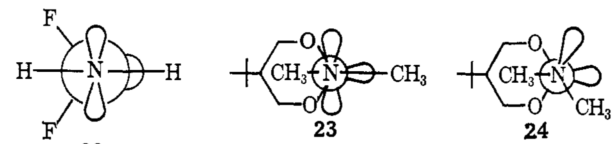
$$E_{ax} - E_{eq} = A_P + [E_{VPO}(ax) - E_{VPO}(eq)] \qquad (3)$$

(ax) − E_{VPO}(eq)] is sufficiently negative, $E_{ax} - E_{eq}$ will be negative, and R will prefer to be axial. By contrast, if A_P is sufficiently positive, this repulsive interaction term cannot be overcome by the P–O vicinal interactions. An example is provided by the *tert*-butyl group attached to phosphorus.[4] This substituent is equatorial in both the cis and trans isomers. Although *A* values for cyclohexanes are certainly not good absolute measures of A_P, it is likely that they do predict *relative* A_P values. Thereby, one expects for MeNH and Me_2N that their A_P values would be less or at least no greater than those for OCH_3, CH_3, and *i*-Pr. We are forced to look elsewhere, therefore, for an explanation of the unusual $\Delta G°_{25}$ (cis → trans) values for **2** and **4**.

On the basis of the following considerations, we propose that yet another term (E_{VPN}) be added to eq 1–3. E_{VPN} allows for differences in vicinal interactions in various conformers which are attainable by rotation about the P–N bond when the dimethylamino group is axial (E_{VPN}(ax)) or equatorial (E_{VPN}(eq)). In this way eq 4 may be formulated

$$E_{ax} - E_{eq} = A_P + [E_{VPO}(ax) - E_{VPO}(eq)] + [E_{VPN}(ax) - E_{VPN}(eq)] \qquad (4)$$

In this regard investigations of H_2NPF_2 (microwave[24]) and Me_2NPCl_2 (infrared and Raman[25]) in the gas phase and X-ray crystallographic studies[26] of Me_2NPF_2 all show the conformation of lowest energy to be that pictured for H_2NPF_2 by **22**. Electron diffraction work[27] on gaseous Me_2NPF_2 indicates a 32° angle exists between the CNC plane and the phosphorus–nitrogen bond and that there is a similar small deviation from planarity about nitrogen in H_2NPF_2. A staggered pyramidal conformation otherwise like **22** was proposed. Further, nmr investigations[28] have demonstrated that rotations about P–N bonds in various trivalent phosphorus compounds,



22 **23** **24**

Z_2PNMe_2, are subject to barriers in the range $\Delta G^{\ddagger}$ = 6–13 kcal/mol. At low temperatures in some systems it is possible to slow rotation so that the methyls of a Me_2N on phosphorus become nonequivalent. This also is consistent with a structure like **22**. Whether these phenomena are the result of true pπ–dπ bonding interactions or not, they do show that vicinal interactions, attractive and repulsive, fluctuate over fairly wide ranges on rotation about the P–N bond. The result is that certain conformations in which the two methyls are in different environments are considerably more favored than others.

If similar vicinal forces are at work in the cyclic systems, *e.g.*, **2**, then presumably when Me_2N is equatorial (**2a**), a conformation analogous to **22** can be assumed in which E_{VPN}(eq) is minimized. However, for **2b** minimization of P–N vicinal interactions, as shown in structure **23**, obviously results in severe destabilizing steric interaction between the methyl group and the syn-axial ring hydrogens. The Me_2N will assume by P–N rotation some conformation in which the most favorable balance between P–N vicinal interactions and steric repulsions is attained. Thus an axial Me_2N will be destabilized with respect to an equatorial one; *i.e.* [E_{VPN}(ax) − E_{VPN}(eq)] > 0. If the latter term of eq 4 is large enough, the

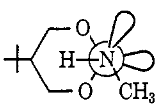
(24) A. H. Brittain, J. E. Smith, P. L. Lee, K. Cohn, and R. H. Schwendeman, *J. Amer. Chem. Soc.*, **93**, 6772 (1971).
(25) J. R. Durig and J. M. Casper, *J. Phys. Chem.*, **75**, 3837 (1971).
(26) E. D. Morris, Jr., and C. E. Nordman, *Inorg. Chem.*, **8**, 1673 (1969).
(27) G. C. Holywell, D. W. H. Rankin, B. Beagley, and J. M. Freeman, *J. Chem. Soc. A*, 785 (1971).
(28) M.-P. Simonnin, C. Charrier, and R. Burgada, *Org. Magn. Resonance*, 113 (1972); A. H. Cowley, M. J. S. Dewar, W. R. Jackson, and W. B. Jennings, *J. Amer. Chem. Soc.*, **92**, 1085, 5206 (1970); J. E. Bissey, H. Goldwhite, and D. G. Rowsell, *Org. Magn. Resonance*, **2**, 81 (1970); J. Nelson, R. Spratt, and B. J. Walker, *Chem. Commun.*, 1509 (1970); H. Goldwhite and D. G. Rowsell, *ibid.*, 713 (1969); D. Imbery and H. Friebolin, *Z. Naturforsch. B*, **23**, 759 (1968); A. H. Cowley, M. J. S. Dewar and W. R. Jackson, *J. Amer. Chem. Soc.*, **90**, 4185 (1968); M.-P. Simonnin, J. J. Basselier, and C. Charrier, *Bull. Soc. Chim. Fr.*, 3544 (1967).

phosphorus vicinal interactions $[E_{\mathrm{VPO}}(\mathrm{ax}) - E_{\mathrm{VPO}}(\mathrm{eq})]$ will be outweighed, and the Me_2N will be equatorial.

It may be that the planarity observed about nitrogen in **22** is a result of pπ–dπ bonding. (An alternate view is that the planar geometry is a consequence of inductive release from the PH_2 group.[29]) In compound **2**, the geometry about nitrogen then may well be more nearly pyramidal as a result of a reduction in π bonding as a consequence of replacement of the strongly electronegative fluorines in **22** by oxygens. However, the following arguments similar to those based on **23** can be made using **24**. Considerations based on the gauche effect[30] predict that P–N vicinal interactions are often optimized by maximizing the number of electron pair–electron pair and polar bond–polar bond interactions and thus would designate conformation **24** as the most stable for an axial Me_2N. The steric consequences of **24** obviously are quite similar to those of **23**.

The conformational preference of the methylamino substituent in **4** for the equatorial position is reduced (Table V) as would be predicted if in eq 4 the vicinal interaction terms are similar to those for **2**, and the value of A_P is lower for MeNH than for Me_2N. This is a reasonable expectation in view of the relative A values for the two substituents (Table V). But a more careful consideration of the conformations available to the methylamino substituent suggests that this may be an oversimplification.

The axial MeNH group can attain conformation **25** or **26** in which vicinal interactions presumably are opti-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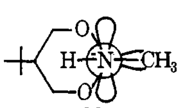
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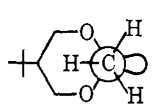
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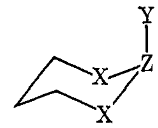
mized with no more apparent steric strain than that experienced by an axial methyl group (structure **27**). In this view MeNH should behave like CH_3. This points up the fact that our understanding of the interactions in these systems is not yet complete.

A part of the difference between MeNH and Me could result from reduced rotational freedom in the axial position for MeNH. The methyl group should be essentially freely rotating in both positions. Furthermore, although the P–N vicinal interactions are minimized with respect to the dihedral angles between the lone pairs on the nitrogen and phosphorus atoms when the methylamino substituent is axial and conformation **25** or **26** is populated, it does not necessarily follow that $E_{\mathrm{VPN}}(\mathrm{ax}) = E_{\mathrm{VPN}}(\mathrm{eq})$. Because of the ring structure, the directional orientations of the bond dipoles and lone pairs associated with the ring oxygens with respect to the substituents on nitrogen are fixed and are different when the MeNH is axial than when it is equatorial. Therefore, the sum of *all* vicinal interactions about the phosphorus–nitrogen bond will not be the same in **4a** and **4b** though in both cases the most stable rotamer is populated. Thus $E_{\mathrm{VPN}}(\mathrm{ax}) \neq E_{\mathrm{VPN}}(\mathrm{eq})$. If $E_{\mathrm{VPN}}(\mathrm{ax}) > E_{\mathrm{VPN}}(\mathrm{eq})$, then the somewhat unexpected size of the axial MeNH is rationalized.

The possible role of solvation on the $\Delta G°_{25}$ values for the systems of Table V has not been considered to now. As seen in Table V, change from a π-electron rich solvent (benzene) to one with significant hydrogen bonding properties ($CDCl_3$) or increased polarity ($CDCl_3$ or ODCB) has no measurable effect on $\Delta G°_{25}$. Solvation effects seem to be minor in the limited range of solvents studied.

Other Heterocyclic Systems. Axial preferences for substituents on heteroatoms in six-membered rings have been noted also for 1,3,2-dithiaphosphorinanes[31]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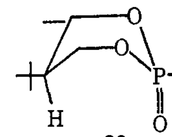
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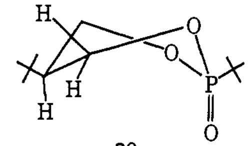
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(**28**, X = S; Z = P; Y = MeO, Ph, Me, Et), phosphorinanes[32] (**28**, X = CH_2; Z = P; Y = H), sulfites[33] (**28**, X, Y = O; Z = S), thiane 1-oxide[34] (**28**, X = CH_2; Z = S; Y = O), protonated thiane[35] (**28**, X = CH_2; Z = S; Y = H), and selenane[36] derivatives (**28**, X = CH_2; Z = Se; Y = H, CH_3, O).

In the crystal both axial and equatorial orientations have been noted[37] for phenyl substituents on phosphorus in phosphorinanes, and methyl substituents[38] at phosphorus in these systems appear to have little orientational preference in solution. It has been suggested[36] that for all these systems, including the 1,3,2-dioxaphosphorinanes, the axially oriented heteroatom substituent is further from the syn-axial ring hydrogens than in cyclohexanes and 1,3-dioxanes, and as a result the 1,3-syn-axial interactions are attractive rather than repulsive. In support of this view are the increased axial preferences of substituents in selenane derivatives[36] compared to the corresponding thiane derivatives.

It seems to us that another explanation is possible. The structural feature common to all these systems is a lone-pair substituent on the heteroatom (P, S, or Se). Vicinal interactions about the ring heteroatom involving the lone pair could favor the axial substituent orientation, even though the exact interactions are different in each ring. Reduced *repulsive* 1,3-syn-axial interactions may well play a role as well in allowing the sub-

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(30) S. Wolfe, *Accounts Chem. Res.*, **5**, 102 (1972).

(31) R. O. Hutchins and B. E. Maryanoff, *J. Amer. Chem. Soc.*, **94**, 3266 (1972).

(32) J. B. Lambert and W. L. Oliver, Jr., *Tetrahedron*, 27, 4245 (1971).

(33) See, *e.g.*: C. H. Green and D. G. Hellier, *J. Chem. Soc., Perkin Trans. 2*, 458 (1972); G. Wood, G. W. Buchanan, and M. H. Miskow, *Can. J. Chem.*, **50**, 521 (1972); P. Albriktsen, *Acta Chem. Scand.*, **25**, 478 (1971); G. Wood, J. M. McIntosh, and M. H. Miskow, *Can. J. Chem.*, **49**, 1202 (1971); W. Wucherpfennig, *Justus Liebigs Ann. Chem.*, 737, 144 (1970); R. F. M. White, *J. Mol. Struct.*, 6, 75 (1970); H. F. van Woerden, H. Cerfontain, C. H. Green, and R. J. Reijerkerk, *Tetrahedron Lett.*, 6107 (1968); J. W. L. van Oyen, R. C. D. E. Hasekamp, G. C. Verschoor, and C. Romers, *Acta Crystallogr., Sect. B*, **24**, 1471 (1968); H. F. van Woerden and E. Havinga, *Recl. Trav. Chim. Pays-Bas*, **86**, 341, 353 (1967); C. Altona, H. J. Geise, and C. Romers, *ibid.*, **85**, 1197 (1966).

(34) J. B. Lambert and R. G. Keske, *J. Org. Chem.*, **31**, 3429 (1966); C. R. Johnson and D. B. McCants, Jr., *J. Amer. Chem. Soc.*, **87**, 1109 (1965); J. C. Martin and J. J. Uebel, *ibid.*, **86**, 2936 (1964).

(35) See J. B. Lambert, D. S. Bailey, and C. E. Mixan, *J. Org. Chem.*, **37**, 377 (1972); J. B. Lambert, R. G. Keske, and D. K. Weary, *J. Amer. Chem. Soc.*, **89**, 5921 (1967).

(36) J. B. Lambert, C. E. Mixan, and D. H. Johnson, *Tetrahedron Lett.*, 4335 (1972).

(37) A. T. McPhail, J. J. Breen, J. C. H. Steele, Jr., and L. D. Quin, *Phosphorus*, 1, 255 (1972); A. T. McPhail, J. J. Breen, and L. D. Quin, *J. Amer. Chem. Soc.*, **93**, 2574 (1971); A. T. McPhail, J. J. Breen, J. H. Somers, J. C. H. Steele, Jr., and L. D. Quin, *Chem. Commun.*, 1020 (1971).

(38) L. D. Quin and J. H. Somers, *J. Org. Chem.*, **37**, 1217 (1972).

stituent to become axial. The latter effect could explain the results of replacing sulfur with selenium in six-membered rings. A full understanding of the origin of the axial orientations of substituents on heteroatoms is yet to be gained.[38a]

Nonchair Conformations. The ease with which the pentavalent *cis*-dimethylamino compound, **3b**, assumes a twist–boat conformation is worthy of some further comment. We previously reported[9] that *cis*-2,5-di-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane in solutions exists primarily in a boat conformation, **29**. It now seems more likely that a skew boat with a small degree of twist, **30**, better represents the structure of this compound. Our earlier estimate that $\Delta G_{25}°$ for interconversion of a chair conformer analogous to **11** to a twist conformer, **10** or **30**, is about 1 kcal/mol is reconfirmed by this study. If the ratio **10**:**11** of **6**:1 used to approximate the coupling constants observed for **3b** is considered reasonably accurate, and $\Delta G°_{25}$ for axial to equatorial reorientation of the 5-*tert*-butyl group is -1.5 to -1.8 kcal/mol as it is for 1,3-dioxanes and cyclic sulfites, then $\Delta G°_{25}$ **11** → **10** is calculated to be 0.7–1.0 kcal/mol. The tendency of **3b** in conformation **9** to escape to higher energy forms **10** and **11** shows that if equilibration **3a** ⇌ **3b** could be carried out, **3a** *would be shown to be the thermodynamically more stable isomer.*[39]

Effects of Lone-Pair Orientation on $^3J_{HCOP}$. The very large $^3J_{HP}$ values noted for **2a** and **4a** should prove to be very valuable in assigning configuration. Thus $^3J_{HCOP}$ is dependent on both the dihedral angle (Karplus-like relation) *and* the orientation of the phosphorus lone pair in 1,3,2-dioxaphosphorinanes. The effects of lone-pair orientation on $^3J_{HCCP}$ have been noted earlier.[40] Larger couplings are found when the hydrogen-substituted carbon β to phosphorus is cis to the lone pair. Likewise, the increase in $^3J_{HCOP}$ for H_{eq} noted in **2a**, **4a**, and *trans*-2,5-di-*tert*-butyl-1,3,2-dioxaphosphorinane[4] is for hydrogen on a cis β-CH_2 group. That the lone-pair orientation should influence $^3J_{HCOP}$ has been suggested earlier.[41] Our results appear to be the first to verify this prediction. We interpret the very large $^3J_{H_{eq}P}$ noted[41b] for 5,5-dimethyl-2-dimethylamino-1,3,2-dioxaphosphorinane (19.6 Hz) compared to the corresponding values for the 2-alkoxy, 2-fluoro, 2-chloro, and 2-phenyl analogs as resulting from the axial orientation of the phorphorus lone pair in the amino compound. The phosphorus lone pair doubtless is equatorial in all the other compounds in the series.

Experimental Section

Proton nmr spectra were taken on Varian A-60, A-56/60, and XL-100-12 spectrometers. Chemical shifts are reported in δ, parts per million downfield from tetramethylsilane as internal standard. Variable-temperature ^{1}H nmr spectra were obtained using a Varian A-60 spectrometer equipped with Model V-6040 temperature controller. The probe temperature was monitored by measuring the temperature dependence of the chemical shift of methanol or ethylene glycol. The ^{31}P magnetic resonance data were obtained on a Varian XL-100-12 spectrometer operating at 40.5 MHz. Proton decoupling was accomplished with either a Hewlett Packard 5105A frequency synthesizer (aided by a Boonton Radio Co. 230A power amplifier) or a Varian XL-100 Gyrocode decoupler. Pulse Fourier transform proton decoupled ^{13}C spectra were recorded at 25.2 MHz with a Varian XL-100-15 spectrometer equipped with a Gyrocode decoupler. Samples were contained in 10-mm o.d. thin-walled tubes which were placed inside 12-mm o.d., 11-mm i.d. tubes containing approximately 0.5 ml of benzene-d_6 for internal field frequency lock. Chemical shifts are reported in parts per million upfield from internal C_6H_6. Infrared spectra were taken on a Beckman-IR5A infrared spectrophotometer. Vapor phase chromatography was performed on a Hewlett-Packard Model 700 gas chromatograph equipped with flame detectors. The column was $^1/_8$ in. × 6 ft 10% SE-30 on 80–100 mesh Chromosorb W. Ratios of products were not corrected for possible sensitivity differences of cis and trans isomers. Preparative vapor phase chromatography was performed on an Aerograph A-90 P-3 instrument using a 0.25 in. × 6 ft 20% SE-30 on 60–80 mesh Chromosorb W column. Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. All melting points are uncorrected. All reactions involving trivalent phosphorus were carried out under an atmosphere of dry nitrogen, and the solvents used were deoxygenated by a dry nitrogen flush. Nmr samples of trivalent phosphorus compounds were deoxygenated with nitrogen flush and sealed under reduced pressure.

Synthesis of 2-Dimethylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane (2). Hexamethylphosphorus triamide (6.53 g, 40.0 mmol) in 40 ml of toluene and 2-*tert*-butyl-1,3-propanediol[42] (5.29 g, 40.01 mmol) in 40 ml of ethyl acetate were dripped simultaneously from two addition funnels into 80 ml of stirred refluxing toluene. The addition was carried out over a period of 2 hr after which the solution was refluxed and stirred for an additional hour. Vpc analysis indicated that the reaction was complete. After removal of the solvent, distillation of the residue yielded a mixture of two isomers of 2-dimethylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane (**2**) in 89.4% yield (7.34 g, 35.8 mmol), bp 80–92° (2.5 mm). The ratio of the two isomers, as determined from integrated intensities of the *tert*-butyl and dimethylamino protons in the pmr spectrum, was 61:39. The major isomer (**2a**) was subsequently proved to be *trans*-2-dimethylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane: pmr (benzene-d_6) δ 0.635 (9 H, singlet, *t*-Bu), 1.72 (1 H, multiplet, methine H), 2.63 (6 H, doublet, J_{HP} = 8.7 Hz, Me_2N), and 3.79–4.28 (4 H, multiplet, CH_2O). The only resonances that could be assigned to the cis isomer (**2b**) were at δ 0.690 (9 H, singlet, *t*-Bu), and 2.49 (6 H, doublet, J_{HP} = 8.4 Hz, Me_2N).

Oxidations of *trans*- and *cis*-2-Dimethylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinanes with N_2O_4. To a stirred solution of 4.94 g (24.07 mmol) of a mixture of *trans*- and *cis*-2-dimethylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane of ratio 61:39 (trans/cis) in 25 ml of reagent methylene chloride (dried over molecular sieve) at 0–5° was added 10 ml of a saturated solution of N_2O_4 in methylene chloride over a period of 20 min to give a green reaction solution. Vpc analysis indicated the reaction to be complete. A mixture of the two corresponding oxides (**3**) of trans:cis ratio 60:40 (determined by pmr and vpc) resulted. (The major oxide (**3a**) has shorter vpc retention time compared to that of the minor oxide.) The solvent was removed under reduced pressure to give 5.28 g (99%) of product **3**. The two oxides were separated by column chromatography using a 3.2 cm × 88 cm column packed with 280 g of Florisil (100–200 A mesh) and eluted with ether–ligroin (bp 60–

(38a) Note Added in Proof. The conformations of 1-methylphosphorinane have been studied recently by ^{31}P nmr as a function of temperature [S. I. Featherman and L. D. Quin, *J. Amer. Chem. Soc.*, **95**, 1699 (1973)]. The chair-form conformer with equatorial methyl was shown to have a *lower* enthalpy than that with methyl axial. This is just the opposite of what we have observed for the 5-*tert*-butyl-2-methyl-1,3,2-dioxaphosphorinanes. That the methyl group in 1-methylphosphorinane has a slight axial preference at room temperature was shown to be a result of entropy effects.

(39) See ref 16. Certain 5,5-disubstituted-2-dimethylamino-2-oxo-[7f] and 2-thio-[7i] 1,3,2-dioxaphosphorinanes display $^3J_{HP}$ values which indicate that a high proportion of one conformer is present in solution. The $(ClCH_2CH_2)_2N$ group in cyclophosphamide is equatorial in the solid form: J. C. Clardy, J. A. Mosbo, and J. G. Verkade, *J. Chem. Soc. D*, 1163 (1972).

(40) J. B. Robert and J. D. Roberts, *J. Amer. Chem. Soc.*, **94**, 4902 (1972); C. H. Bushweller, J. A. Brunelle, W. G. Anderson, and H. S. Bilofsky, *Tetrahedron Lett.*, 3261 (1972); J. P. Albrand, D. Gagnaire, M. Picard, and J. B. Robert, *ibid.*, 4593 (1970); L. D. Quin and T. P. Barket, *J. Amer. Chem. Soc.*, **92**, 4303 (1970); W. McFarlane, *Chem. Commun.*, 229 (1968); S. E. Cremer and R. J. Chorvat, *J. Org. Chem.*, **32**, 4066 (1967).

(41) (a) J. P. Albrand, A. Cogne, D. Gagnaire, and J. B. Robert, *Tetrahedron*, **28**, 819 (1972); (b) D. Gagnaire, J. B. Robert, and J. Verrier, *Bull. Soc. Chim. Fr.*, 2392 (1968); (c) D. Gagnaire and J. B. Robert, *ibid.*, 2240 (1967).

(42) Prepared by $NaBH_4$ reduction of *tert*-butyl diethylmalonate: P. Boldt and L. Schultz, *Naturwissenschaften*, **51**, 288 (1964).

90°). The ether concentration was increased gradually during elution. The major oxide, *trans*-2-dimethylamino-5-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane (**3a**), was recrystallized from ether–ligroin (60–90°): mp 114.5–115.0°; ir (KBr) 2959, 2907, 2825, 1473, 1330, 1239, 1143, 1058, 1011, 898, 814, and 702 cm^{-1}; pmr ($CDCl_3$) δ 0.960 (9 H, singlet, *t*-Bu), 1.97 (1 H, multiplet, methine H), 2.71 (6 H doublet, J_{HP} = 10.0 Hz, Me_2N), and 4.09–4.57 (4 H, multiplet, CH_2O).

Anal. Calcd for $C_9H_{20}O_3PN$: C, 48.86; H, 9.11; P, 14.00. Found: C, 48.73; H, 9.38; P, 14.50.

The minor oxide, *cis*-2-dimethylamino-5-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane (**3b**), was recrystallized from ether–ligroin (60–90°): mp 117.5–118.0°; ir (KBr) 2967, 2915, 2825, 1486, 1460, 1374, 1309, 1261, 1181, 1140, 1081, 1054, 1012, 991, 893, 848, 814, 784, and 680 cm^{-1}; pmr ($CDCl_3$) δ 0.955 (9 H, singlet, *t*-Bu), 2.23 (1 H, multiplet, methine H), 2.68 (6 H, doublet, J_{PH} = 10.6 Hz, Me_2N), and 3.98–4.58 ppm (4 H, multiplet, CH_2O).

Anal. Calcd for $C_9H_{20}O_3PN$: C, 48.86; H, 9.11; P, 14.00. Found: C, 49.06; H, 8.91; P, 14.00.

Synthesis of 2-Methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane (4). Anhydrous ether (25 ml) was added to a 100-ml, round-bottom, three-necked flask equipped with a Dry Ice condenser, a 50-ml addition funnel topped with nitrogen bubbler, and an adapter with a disposable pipet connected to the valve of a methylamine gas cylinder (Matheson), and the flask was then chilled to −20°. A solution of 4.78 g (24.3 mmol) of 2-chloro-5-*tert*-butyl-1,3,2-dioxaphosphorinane[1b] in 40 ml of anhydrous ether was added dropwise over a period of 30 min. Simultaneously, methylamine was bubbled through the disposable pipet into the ether solution. A white precipitate of amine hydrochloride was formed. The mixture was stirred with continued methylamine addition at −20° for another 30 min. The addition of $MeNH_2$ was discontinued, and the reaction mixture was stirred under nitrogen at methylamine reflux for a final 3.5 hr. The solution was then quickly filtered under nitrogen pressure through a glass wool filter plug to remove the amine salt into a flask protected from moisture by a $CaCl_2$ drying tube. Most of the ether was short path distilled under nitrogen. The remaining liquid was then distilled under reduced pressure to give a mixture of two isomers of 2-methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane (**4**) in 60% yield (2.80 g, 14.64 mmol), bp 82° (1.0 mm). Vpc analysis showed only one peak. However, pmr (benzene-d_6) showed the presence of two isomers in ratio about 90:10 as determined from the integrated intensities of the *tert*-butyl protons. The pmr (benzene-d_6) spectrum of the major isomer (**4a**) showed resonances at δ 0.650 (9 H, singlet, *t*-Bu), 1.70 (1 H, multiplet, methine H), 2.55 (4 H, broad multiplet, MeNH), and 3.65–4.41 (4 H, multiplet, CH_2O). The only resonance that could be assigned accurately to the minor isomer (**4b**) was at δ 0.667 (9 H, singlet) which is due to the *tert*-butyl protons. The resonances of the rest of the protons for the minor isomer overlap with those of the major isomer.

Synthesis of 2-Methylamino-5-*tert*-butyl-2-thio-1,3,2-dioxaphosphorinane (5). To a stirred solution of 0.24 g (1.26 mmol) of a 90:10 trans:cis mixture of 2-methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane in 1 ml of benzene at 5–10° was added under nitrogen 0.04 g (1.26 mmol) of sulfur in small portions. The reaction was followed by vpc analysis. After the reaction was complete, vpc analysis (temperature programmed at 10°/min) showed two products at retention temperatures 201 and 204° in area ratio 91:9. Removal of solvent gave 0.28 g (~100%) of product. After purification by preparative vpc, a 91:9 (trans:cis) ratio mixture was used for analysis: pmr (**5a**, major isomer, $CDCl_3$) δ 0.967 (9 H, singlet, *t*-Bu), 1.98 (1 H, multiplet, methine H), 2.69 (3 H, quartet, J_{HP} = 13.0 Hz, J_{HH} = 5.2 Hz, MeNH), 3.17 (1 H, broad multiplet, MeNH), and 3.93–4.79 ppm (4 H, multiplet, CH_2O).

Following the above procedure, a 55:45 (trans:cis) ratio mixture of 2-methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane was converted to the corresponding sulfides in a 58:42 (trans:cis) ratio.

Anal. Calcd for $C_8H_{18}PO_2NS$: C, 43.04; H, 8.13; P, 13.87. Found: C, 43.04; H, 8.27; P, 14.16.

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Relative Energetics of Modes for Phosphorane Formation and Decomposition in Nucleophilic Displacement Reactions at Acyclic Phosphorus. Alkaline Hydrolysis of Alkoxy(alkylthio)phosphonium Salts

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Abstract: A stereochemical and product study was carried out on the alkaline hydrolysis of various alkoxy(alkylthio)methylphenylphosphonium hexachloroantimonates (**1**). Two products, an alkyl phosphinothiolate (**3**) and an alkyl phosphinate (**2**), from cleavage of the alkoxy group or the alkylthio group, respectively, were obtained from all compounds studied except when the alkoxy group is menthoxy. The ratio of the two products was affected by the nature of the substitution in the alkoxy group but insensitive to substitution in the alkylthio group. In addition, when (*S*)-**1** (R = R′ = Me) was hydrolyzed, the two products, **2** (R = Me) and **3** (R′ = Me), were of the *R* configuration indicating cleavage of the alkoxy group with inversion and cleavage of the alkylthio group with retention of configuration at phosphorus. A mechanism involving axial attack of hydroxide ion in the face of the tetrahedral phosphonium salt opposite the alkoxy ligand, followed by a competition between direct loss of the axial alkoxy ligand and an isomerization with subsequent loss of the alkylthio ligand from an axial position, is implicated from the results.

There now appears to be ample evidence that pentacoordinate intermediates are involved in many nucleophilic displacement reactions at tetracoordinate phosphorus in both cyclic[1–4] and acyclic[5–10] phosphorus

(1) (a) F. H. Westheimer, *Accounts Chem. Res.*, 1, 70 (1968), and references therein; (b) R. Kluger, F. Covitz, E. Dennis, L. D. Williams,