than is true of normal hydrogen bonds. Normal hydrogen bonds are directly observable by a number of physical–chemical techniques such as infrared and nmr spectroscopy. So far, C–H···O interactions in molecules such as purines and pyrimidines have not been observed using these techniques.[39] Therefore, although the reality of C–H···O interactions in the solid state can no longer be denied,[18,22,40] they must be placed in a class apart from normal hydrogen-bonding interactions until it can be shown that they exhibit similar physical characteristics. Hence in this report short C–H···O contacts are referred to as hydrogen bond-*like* interactions.

There is no direct evidence to support the hypothesis that adenine–barbiturate base pairing has biological significance. Nevertheless, the great specificity and binding strength of this interaction[3] makes this hypothesis seem extremely plausible. The biological significance, if any, of the stacked dipoles found in I and II is less clear. In aqueous media, the free energies of such interactions are insignificant as are those of hydrogen bonds between bases. However, as was previously explained, it is quite likely that the barbiturate receptor site is in a nonpolar environment. The low dielectric constant of such a medium would stabilize any dipole–dipole interactions present. Hence, it may be that the barbiturate receptor site contains a group of atoms forming a strong dipole. This could be aligned so as to form an attractive interaction with the C-2–O-2 dipole of the barbiturate when it forms a hydrogen-bonded base pair with the adenine residue supposed to be at the receptor site. Such an interaction would enhance the strength of the adenine–barbiturate base pair and would therefore increase the already large specificity and binding strength of the barbiturate with its receptor site.

(39) G. C. Pimentel and A. C. McClellan, "The Hydrogen Bond," W. H. Freeman, San Francisco, Calif., 1960, p 197.
(40) N. C. Seeman, J. L. Sussman, and S.-H. Kim, *Nature (London), New Biol.*, **233**, 90 (1971).

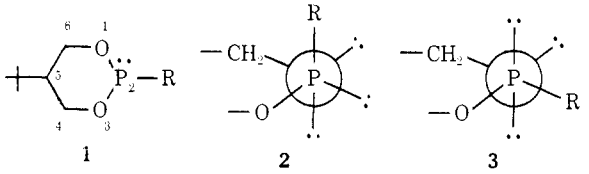
Acknowledgments. This work was supported by the National Institutes of Health (Grant No. GM18632) and by the Advanced Research Projects Agency, Office of the Secretary of Defense.

Communications to the Editor

Conformations of Saturated Phosphorus Heterocycles. Possible p_π–d_π Overlap Effects on the Apparent Conformational Energies of the Dimethylamino Group and the Influence of Phosphorus Lone-Pair Orientation on $^3J_{H_{eq}P}$

Sir:

Earlier work[1] has demonstrated that 2-R-5-*tert*-butyl-1,3,2-dioxaphosphorinanes **1** prefer to be in chair con-

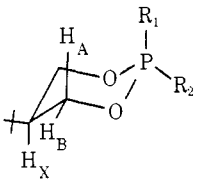


1 **2** **3**

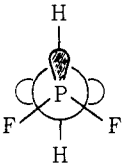
formations with the substituent on phosphorus *axial* rather than *equatorial* (for R = Cl,[1b] MeO,[1b] Me,[1a] *i*-Pr,[2] Ph[1c]). Consequently, the cis isomers (*t*-Bu equatorial, R axial) have been found to be more stable than the trans species. Thus, conformation about phosphorus is not determined primarily by 1,3-steric interactions but rather by the balance of vicinal interactions[3] between adjacent phosphorus and oxygen ring atoms and the substituent R (compare sturctures **2** and **3**).

We now report evidence that the dimethylamino group on phosphorus is more stable in the equatorial position with the consequence that *trans-2-dimethylamino-5-tert-butyl-1,3,2-dioxaphosphorinane* (**4a**) *is more stable than its cis isomer* **4b**.[4] This finding is quite surprising in that the Me_2N should have similar steric requirements to those of the isopropyl group[5] and also could impart to the system with axial Me_2N the stabilization usually ascribed to the anomeric effect.[6] In addition, results are presented that very strongly suggest that *the size of* $^3J_{H_{eq}P}$ *is greatly dependent on the axial or equatorial orientation of the lone pair on phosphorus.*

Compound **4** was synthesized by reaction of 2-*tert*-



4a, R_1 = e⁻ pair; R_2 = Me_2N
b, R_1 = Me_2N; R_2 = e⁻ pair
5a, R_1 = O; R_2 = Me_2N
b, R_1 = Me_2N; R_2 = O



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(1) (a) W. G. Bentrude, K. C. Yee, R. D. Bertrand, and D. M. Grant, *J. Amer. Chem. Soc.*, **93**, 797 (1971); (b) W. G. Bentrude and J. H. Hargis, *ibid.*, **92**, 7136 (1970); (c) W. G. Bentrude and K. C. Yee, *Tetrahedron Lett.*, 3999 (1970).
(2) W. G. Bentrude, H. W. Tan, and K. C. Yee, unpublished results.
(3) The so-called *gauche effect* may be operative: S. Wolfe, *Accounts Chem. Res.*, **5**, 102 (1972).
(4) This conclusion has been reached on the basis of independent evidence from a study of the *meso*-2-dimethylamino-4,6-dimethyl-1,3,2-dioxaphosphorinane system: J. A. Mosbo and J. G. Verkade, *J. Amer. Chem. Soc.*, **94**, 8224 (1972).
(5) J. A. Hirsch, *Top. Stereochem.*, **1**, 199 (1967). This review quotes a best value for the conformational energy of *i*-Pr in cyclohexane of 2.15 kcal/mol and a value for Me_2N of 2.1 kcal/mol (80% methyl Cellosolve).
(6) For recent discussions and references to the anomeric effect, see: H. Booth and R. U. Lemieux, *Can. J. Chem.*, **49**, 777 (1971); S. Wolfe, A. Rauk, L. M. Tel, and I. G. Csizmadia, *J. Chem. Soc. B*, 136 (1971); F. W. Nader and E. L. Eliel, *J. Amer. Chem. Soc.*, **92**, 3050 (1970).

Table I. Nmr Parameters[a] for **4a** and **4b** in Benzene-d_6

Compd	Coupling constants[b]						Chemical shifts[c]					
	J_{AB}	J_{AX}	J_{BX}	J_{AP}	J_{BP}	J_{PNCH}	δH_A	δH_B	δH_X	$\delta_{t\text{-Bu}}$	$\delta_{N(CH_3)_2}$	$\delta^{31}P^e$
4a[d]	−11.36	10.68	4.08	2.50	19.62	8.7	3.94	4.09	1.72	0.635	2.63	142.39
4b[d]						8.4			1.65	0.690	2.49	135.39

[a] Determined by ABXY analysis of the 100-MHz spectrum followed by LAOCN3 iterative analysis. [b] Values in Hz; absolute values of J given except for J_{AB} assumed to be negative. [c] Chemical shifts in ppm downfield from TMS. [d] A mixture of **4a** and **4b** of ratio 83:17 in benzene-d_6 was used for analysis; 25% (v/v). [e] In ppm downfield from external 85% H_3PO_4, benzene-d_6 solvent.

butyl-1,3-propanediol with $(MeN)_3P$ in refluxing toluene. Pmr analysis of freshly distilled **4** showed the presence of two isomers, **4a** and **4b**, in a 61/39 ratio (**4a**/**4b**) as did ^{31}P nmr spectroscopy. Oxidation with N_2O_4 in CH_2Cl_2 at 0–5° gave near-quantitative amounts of the two corresponding oxides (**5a** and **5b**) in a 60:40 ratio (vpc). After 3 weeks in benzene,[7] a 60:40 mixture of isomers of **4** changed to a presumably equilibrium 83:17 mixture (**4a**/**4b**) which was converted to the corresponding oxides in an 84:16 ratio (**5a**:**5b**). Pmr analysis of the more stable isomer **4a** gave the parameters shown in Table I. The values of J_{AX} and J_{BX} are clearly those expected if *the 5-tert-butyl is equatorial.*

The conclusion that **4a** is the trans isomer is based on several lines of evidence.

(a) $\delta^{31}P$(**4a**) > $\delta^{31}P$(**4b**). For all previous isomeric trivalent pairs, the ^{31}P shift for the cis isomer with R axial has been found[2] to be upfield of that for the trans isomer.

(b) The ^{13}C chemical shift of $C_{4,6}$ of **4a** is at 62.84 ppm upfield from internal C_6H_6 compared to a value of 66.53 ppm for **4b**. This is consistent with the γ effect[8] noted with axial substituents in cyclohexanes and also for the corresponding 1,3,2-dioxaphosphorinanes with R = CH_3[1a] [$\delta^{13}C_{4,6}$ = 63.95 ppm (equatorial), 67.38 ppm (axial)] and R = *i*-Pr[9] [$\delta^{13}C_{4,6}$ = 62.61 ppm (equatorial), 65.95 ppm (axial)].

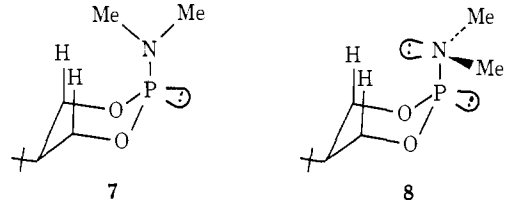
(c) The value of J_{BP} ($^3J_{H_{eq}P}$) for **4a**, 19.6 Hz, is nearly double that noted for the major isomer for all the analogs to **4** which have R axial. (A 19.6-Hz coupling was noted[10] previously for 2-dimethylamino-5,5-dimethyl-1,3,2-dioxaphosphorinane for which a chair form conformation is most reasonable.) The only other trivalent 5-*tert*-butyl-1,3,2-dioxaphosphorinane for which a comparable value for $^3J_{H_{eq}P}$ has been found is the thermodynamically more stable isomer of 2,5-di-*tert*-butyl-1,3,2-dioxaphosphorinane which undoubtedly exists in the chair conformation with both *tert*-butyl substituents *equatorial* [J_{BP} = 19.8 Hz (benzene)[2]].

(d) For the oxides **5a** and **5b** from stereospecific, presumably configurationally retentive[11] N_2O_4 oxidation of **4a** and **4b**, δH_A(4.41) > δH_B(4.29) for **5a** ($CDCl_3$) whereas δH_A (4.14) < δH_B (4.42) for **5b** ($CDCl_3$). This is exactly the effect of P=O orientation noted[2,12] for the oxide and sulfide pairs with R = CH_3O, CH_3, *i*-C_3H_7, *tert*-butyl, and C_6H_5 whose cis and trans geometries are known with absolute[13] or at least reasonable certainty. The same sorts of arguments apply to relative values of δH_X (1.97 for **5a**, 2.23 for **5b**).

(e) The effects on δH_A, δH_B, and δH_X of adding incremental amounts of Eu(DPM)$_3$ to **5a** and to **5b** were closely parallel to those previously reported[14] for the *trans*- and *cis*-5-*tert*-butyl-2-methyl-2-oxo-1,3-2-dioxaphosphorinanes, respectively.

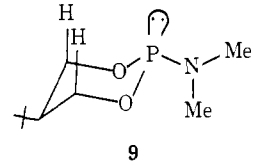
(f) $\delta^{31}P$(**5a**) > $\delta^{31}P$(**5b**). Without exception, as with the trivalent analogs, $\delta^{31}P$ for axial R has been found[2] to be upfield of $\delta^{31}P$ for equatorial R.

It seems possible that the surprising equatorial preference of Me_2N in these systems could result from steric hindrances to p_π–d_π bonding when Me_2N is axial. Microwave studies[15] show that F_2PNH_2 in the gas phase is most stable in the conformation depicted by **6**. Pmr studies[16] have demonstrated P–N rotation in trivalent phosphorus amides to be subject to barriers of the order of 6–13 kcal/mol. Both of these effects may be the result of p orbital back donation from nitrogen into the empty phosphorus d orbitals. Obviously, for **4b** a conformation such as that represented by **7** would be subject to severe steric interactions.



7

8



9

Thus, a conformation closely similar to **8** is likely to

(7) In $CDCl_3$ equilibration of a 60/40 mixture to an 83/17 ratio of **4a**/**4b** required only about 2 days. These equilibrations appear to be catalyzed by traces of acid.

(8) 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).

(9) W. G. Bentrude, K. C. Yee, R. D. Bertrand, and D. M. Grant, unpublished work.

(10) D. Gagnaire, J. B. Robert, and J. Verrier, *Bull. Soc. Chim. Fr.*, 2392 (1968).

(11) D. Z. Denney, G. Y. Chen, and D. B. Denney, *J. Amer. Chem. Soc.*, **91**, 6838 (1969).

(12) W. G. Bentrude and J. H. Hargis, *Chem. Commun.*, 1113 (1969); W. G. Bentrude and K. C. Yee, *ibid.*, 169 (1972).

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

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

(15) A. H. Brittain, J. E. Smith, P. L. Lee, K. Cohn, and R. H. Schwendeman, *J. Amer. Chem. Soc.*, **93**, 6772 (1971). Furthermore, Me_2NPF_2 exists in the crystal form in a very analogous conformation: E. D. Morris, Jr., and C. E. Nordman, *Inorg. Chem.*, **8**, 1673 (1969).

(16) 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); H. Goldwhite and D. G. Rowsell, *Chem. Commun.*, 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).

predominate for **4b**.[17] However, **4a** can assume the conformation **9** in which p_π–d_π stabilization is maximal. Thus, normal vicinal interactions which give rise to the axial preference for other substituents[1,2] may be outweighed by the conjugative effects available in **9**. We recognize that p_π–d_π bonding is likely to be considerably reduced in a molecule such as **4**, which is more similar to $(MeO)_2PNMe_2$ than to Me_2NPF_2. It seems likely nonetheless that the conformational preference peculiar to the Me_2N is in some way related to the presence of the lone pair on nitrogen and its interaction with the orbitals, occupied or empty, on phosphorus.[18]

That lone-pair orientation at phosphorus may affect $^3J_{H_{eq}P}$ was suggested[19] earlier. Our results appear to be the first to substantiate the idea that $^3J_{HCOP}$ depends on both the HCOP dihedral angle (Karplus-like relation) *and* the phosphorus lone-pair orientation. This approach may in fact turn out to be a very powerful one indeed for assignment of substituent configuration at trivalent phosphorus in 1,3,2-dioxaphosphorinanes.

Acknowledgment. This work was supported by a grant from the National Science Foundation (GP-22885).

(17) 1,3-Interactions in **8** may be relieved to some degree by ring reversal to the alternate chain with Me_2N equatorial or the analogous boat or twist form with Me_2N pseudoequatorial in which p_π–d_π bonding would be available.

(18) *E.g.*, a referee has suggested that the Me_2N in **7** and **9** may be pyramidal and that a stabilizing lone pair–lone pair gauche effect available to **9** is responsible for its lower energy.

(19) D. Gagnaire and J. B. Robert, *Bull. Soc. Chim. Fr.*, 2240 (1967).

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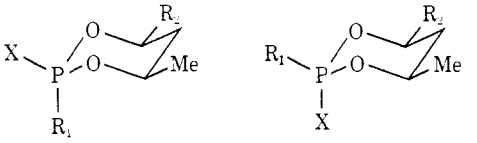
Phosphorus Stereochemistries in Isomeric 2-Dimethylamino-1,3,2-dioxaphosphorinanes

Sir:

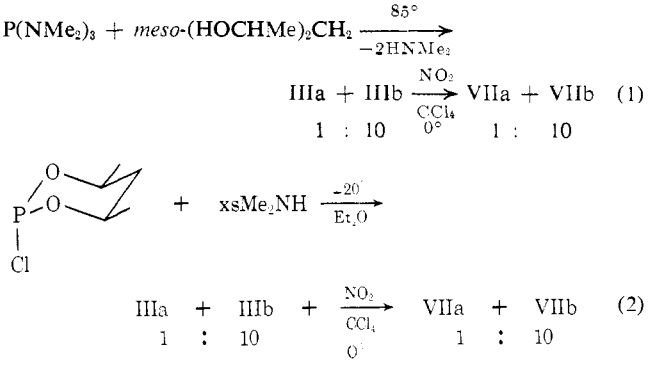
The factors governing the relative stabilities of the two possible configurations a and b at phosphorus in cyclic six-membered ring systems have received significant attention in a number of laboratories recently. In trivalent phosphorus systems (X = lone pair (lp)) strong evidence has been reported for the greater thermodynamic stability of configuration a compared to b for I and II.[1-3] While the bulk of the reported evidence supports the same phosphorus stereochemistry for several analogous systems, there have been reports contending for the greater stability of equatorial alkoxy substituents.[4] Although IIIa and b closely resemble Ia and b, we present in this communication evidence that the b isomer of the latter compound is the more thermodynamically stable as is also very probably the case for IVa and b.[5]



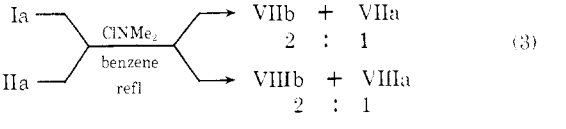
	X	R_1	R_2		X	R_1	R_2
Ia	lp	OMe	Me	Ib	lp	OMe	Me
IIa	lp	OMe	H	IIb	lp	OMe	H
IIIa	lp	NMe_2	Me	IIIb	lp	NMe_2	Me
IVa	lp	NMe_2	H	IVb	lp	NMe_2	H
Va	O	H	Me	Vb	O	H	Me
VIa	O	H	H	VIb	O	H	H
VIIa	O	NMe_2	Me	VIIb	O	NMe_2	Me
VIIIa	O	NMe_2	H	VIIIb	O	NMe_2	H
IXa	O	OMe	Me	IXb	O	OMe	Me
Xa	O	OMe	H	Xb	O	OMe	H

Pentavalent phosphorus a and b isomers where X = O are also known and the stereochemistry at phosphorus has been deduced from nmr results in solution and X-ray diffraction experiments in the solid state.[6] In the vast majority of cases where R = aryl, alkyl, or alkoxy, the P=O group prefers the equatorial position although chair–chair and chair–boat equilibria in solution can occur to varying degrees.[6,7] The preference of the P=O group to be equatorially disposed has also recently been shown when R_1 is H in Va,b and VIa,b.[2] In this communication we report the isolation and the phosphorus stereochemical assignments of the a and b isomers of VII and VIII.

The first steps in reactions 1 and 2 each produce a



10:1 ratio of IIIb to IIIa in overall yields exceeding 60% as shown by their pmr spectra, details of which will be published in due course. Pmr spectra also show that this ratio is preserved in the stereospecific and nearly quantitative oxidation to VIIb and VIIa. Reaction scheme 3 produces the indicated pentavalent



phosphorus systems in greater than 60% yield although the b to a ratio is now 2:1 as revealed from integration of the pmr spectra. The isomers of VII and VIII can

(1) J. Rodgers, D. W. White, and J. G. Verkade, *J. Chem. Soc. A*, 77 (1971).

(2) J. A. Mosbo and J. G. Verkade, *J. Amer. Chem. Soc.*, in press.

(3) M. G. B. Drew, J. Rodgers, D. W. White, and J. G. Verkade, *J. Chem. Soc. D*, 227 (1971).

(4) See D. W. White, R. D. Bertrand, G. K. McEwen, and J. G. Verkade, *J. Amer. Chem. Soc.*, **92**, 7125 (1970), for a recent summary of this controversy.

(5) W. G. Bentrude and H. W. Tan, *ibid.*, **94**, 8222 (1972), reach the same conclusion for the isomeric pair of 2-dimethylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinanes.

(6) See D. W. White, G. K. McEwen, R. D. Bertrand, and J. G. Verkade, *J. Chem. Soc. B*, 1454 (1971), for a recent summary of these results.

(7) (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).