Conformations of 6-Membered-ring Phosphorus Heterocycles: the 5-t-Butyl-2-oxo-1,3,2-dioxaphosphorinans

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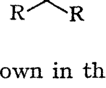
Summary The *cis*- and *trans*-isomers of 2-methoxy-2-oxo-, 2-methoxy-2-thio-, and 2-methyl-2-oxo-5-t-butyl-1,3,2-dioxaphosphorinan are shown to be predominantly chair-form rings with the t-butyl group equatorial in each case.

THE conformational requirements of substitituent groups in heterocyclic ring systems have been of great interest in recent years. Studies using *X*-ray[1] and dipole moment[2] techniques have suggested that for the unsubstituted or symmetrically-5,5-disubstituted 2-oxo-1,3,2-dioxaphosphorinans (I) with substituents (Z) such as alkylamino, phenoxy, alkoxy, or bromo the balance of competitive conformational preferences is such that there is generally an equatorial orientation of the phosphoryl oxygen. On the other hand it has been reported[3] that certain 2-arylalkyl-2-oxo-1,3,2-dioxaphosphorinans probably have the phosphoryl group axial in solution; this is suggested to be the case for both *cis*- and *trans*-5-chloromethyl-5-methyl-2-oxo-2-piperidino-1,3,2-dioxaphosphorinan.[4] However, up to now no information has been available as to the magnitude of the conformational bias of such systems.

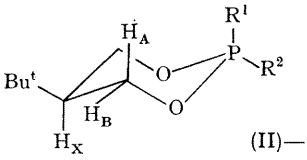
We report here ^{1}H n.m.r.-based analyses of the conformations of some *cis–trans* isomeric pairs of 2-substituted-2-oxo-1,3,2-dioxaphosphorinans of *known* geometry which contain a t-butyl group at the 5-position. Proton chemical shifts and coupling constants in these AA′BB′XY systems were determined using the LAOCN3 iterative computer program of Bothner-By and Castellano.[5] Such an analysis has not been reported previously for a 2-oxo-1,3,2-dioxaphosphorinan monosubstituted at carbon.



(I) R=H or Me

The values shown in the Table for J_{AX} (10·1—11·7 Hz.) and J_{BX} (3·25—4·74 Hz.) clearly establish the *trans* relationship of H_A and H_X which means that the t-butyl is equatorial in each case. The relatively large J_{HP} for H_B is consistent with a chair conformation with the H_BCOP system *trans* and coplanar.[6] Phosphate (II, *cis*) gives a deceptively simple spectrum as a result of the coincidence of δ_A and δ_B; hence only the sums of the coupling constants may be obtained. The sum $J_{AX} + J_{BX}$ (11·8 Hz.) is nearer that for the other cases (13—15 Hz.) in the Table than the range (3—6 Hz.) usually encountered for the equatorial 5-hydrogen in 5-t-butyl-1,3-dioxans.[7] Hence the orientational preferences suggested by studies of the symmetrically-5,5-disubstituted phosphorinans (I) are not great enough in any instance to cause either the *cis*- or *trans*-isomer to undergo ring inversion (flip) to a conformation with the t-butyl group axial. The free energy change ($\Delta G°$) for the equatorial–axial interconversion of the 5-t-butyl group in the 1,3-dioxan series[7] is 1·4 kcal./mole (25°) and might be expected to be similar here. Thus the conformational preferences of the individual members of each given pair of phosphorus substituents investigated appear to be rather closely balanced.

TABLE. *Coupling constants and chemical shifts for* 5-*t-butyl*-2-*substituted*-1,3,2-*dioxaphosphorinans*[a]



(II)—(IV)

Compound	R^1	R^2	Coupling constants, Hz.					Chemical shifts, Hz.			
			J_{AB}	J_{AX}	J_{BX}	J_{AP}	J_{BP}	δ_X	δ_A	δ_B	δ_{Bu^t}
(II, *cis*)	O	MeO	[b]	($J_{AX} + J_{BX}$ = 11·8)		($J_{AP} + J_{BP}$ = 23·4)		110	264	264	60
(II, *trans*)	MeO	O	−11·0	11·6	4·44	1·14	22·8	126	255	265	55
(III, *cis*)	S	MeO	−10·5	9·67	3·25	11·5	16·1	119	268	265	59
(III, *trans*)	MeO	S	−10·6	11·7	4·29	2·25	21·9	129	256	262	58
(IV, *cis*)	O	Me	−11·1	10·5	4·47	4·14	20·2	123	264	258	58
(IV, *trans*)	Me	O	−11·4	10·1	4·74	6·80	16·9	129	248	266	57
(IV, *trans*) (−54°)	Me	O	−11·5	10·8	5·5	6·40	22·7	—	—	—	—

[a] Spectra taken at 60 MHz. 35°, *ca.* 20% solutions in $CDCl_3$. Shifts in Hz. downfield from Me_4Si. [b] Indeterminate.

Examination of the data in the Table for the phosphonate (IV, *trans*) and thiophosphate (III, *cis*) shows the couplings J_{BP} and J_{AP} to be somewhat lower and higher, respectively, than those of the other compounds. These values are consistent with the presence of another conformation in equilibrium in which the ring has flipped at the phosphorus end of the molecule. Since the couplings to H_X do not vary much, the t-butyl end of the molecule seems to be fixed, the other conformer then being some type of boat form. Apparently the chair form predominated in (IV, *trans*) at −54°. The spectrum of (III, *cis*) is insensitive to temperature variation, hence the effect on J_{AP} and J_{BP} in this case may result from ring geometry distortion. Either distortion or ring inversion could be caused by steric repulsions resulting from the larger size of the axial substituent in (III, *cis*) and (IV, *trans*) compared to that of the other compounds.

The geometrical relationship of substituents in (II, *cis*) and (IV, *trans*) was established by *X*-ray crystallography.[8] Phosphate (II, *cis*) was formed in the stereospecific oxidation of its phosphite precursor at 0°. Since the t-butyl hydroperoxide[9] and sulphur oxidations[10] of optically-active phosphines are both believed to proceed with retention, the phosphite which gave phosphate (II, *cis*) is assumed to have given the thiophosphate (III, *cis*) on stereospecific oxidation with S_8.

The chemical shift values in the Table reveal that, except for (IV, *cis*), the value for H_B is relatively constant. However, the chemical shift for H_A is 9—16 Hz. further downfield in the *cis*-isomer (P=O or P=S axial) of a pair than it is in the *trans*-species. This is probably the result of the effect on the axial hydrogen of the difference in shielding or deshielding influence of the P=S or P=O bond and that of the other phosphorus substituent in each case. This trend appears to provide a valuable method for determining orientation of substituents at phosphorus in such systems.

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[10] Ref. 9, p. 29.