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EQUILIBRIUM DISTRIBUTIONS AND STEREOCHEMISTRIES IN ISOMERIC 2-SUBSTITUTED-1,3,2-DIAZAPHOSPHORINANES

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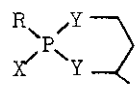
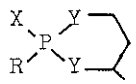
Considerable effort has been expended toward the determination of preferred phosphorus stereochemistries in 2-substituted-1,3,2-dioxaphosphorinanes[1], but only one inconclusive paper has reported a similar investigation of the diaza analogues.[2] This communication reports the results obtained from the isomeric pairs of compounds 1 and 2.



a or trans



b or cis

Compound	Y	R	X	Compound	Y	R	X
1	NMe	OMe	lone pair	5	O	OMe	lone pair
2	NMe	NMe_2	lone pair	6	O	NMe_2	lone pair
3	NMe	OMe	O	7	O	OMe	O
4	NMe	NMe_2	O	8	O	NMe_2	O

The reaction[2] of PCl_3 with N,N'-dimethyl-1,3-butanediamine[3] followed by MeOH or Me_2NH yielded isomeric mixtures of compounds 1 and 2, respectively. By integration of the proton NMR spectra, the isomer ratios of 56:44 for 1 and 61:39 for 2 were found. Similarly, a ratio of 59:41 was determined from the ^{31}P NMR spectrum of 2. For 1 the ratios could not be determined by the latter technique, however, since 1a and b have experimentally identical ^{31}P chemical shifts. This is the first report of such behavior that is not due to rapid equilibria. Two sets of OMe and NMe_2 resonances were observed in the proton NMR spectrum, and both were decoupled upon irradiation of the single phosphorus resonance.

The ratios appear to represent the room temperature equilibrium concentrations. Upon heating to 90°C for two hours, the ratios determined from proton NMR spectra (probe temperature 90°C) were 58:42 for 1 and 52:48 for 2. When cooled back to room temperature, the ratios returned to 56:44 and 59:41 for 1 and 2, respectively.

Although techniques are well established for identification of phosphorus stereochemistries and cis-trans geometries of 1,3,2-dioxaphosphorinanes,[1,4] it is not yet known if these can be applied to the diaza analogues. The observations of greater upfield ^{31}P chemical shifts in the trans isomers of 5 - 8, and the greater energy P=O absorption frequency from the trans isomers of 7 and 8 apparently result from the axial arrangements of the phosphorus substituents and/or equatorial orientations of the P=O links.[1,4] Since structural data have not been reported for the diaza analogues, however, it is not known whether the terms axial and equatorial appropriately describe the phosphorus substituent orientations. Also, due to the lack of NMR analyses, the effects of phosphorus and nitrogen substituent orientations upon ring conformations (e.g., axial vs. equatorial 4-methyl group) are not known.

The ^{31}P and ir spectral characteristics of the diaza compounds are sufficiently similar to those of the well characterized dioxa analogues to justify speculation as to phosphorus configurations. Then by assuming that the equatorial orientation of the 4-methyl group predominates in a chair-like ring, cis-trans geometries, as summarized in the Table and described as follows, can be assigned. The more abundant isomer of 2, having the greater upfield ^{31}P chemical shift, would appear to contain a significantly axial NMe_2 group orientation and thus be the trans isomer.[1] The identical chemical shifts of 1a and b, however, allow neither phosphorus stereochemical nor cis-trans geometrical assignments. Indeed, the single chemical shift may be indicative of identical phosphorus geometries. The geometrical assignments of 1 are apparently clarified and those of 2 substantiated by the 2-oxo derivatives. Compounds 3 and 4 were prepared by oxidation of 1 and 2, respectively, with NO_2, a procedure known to result in retention of phosphorus configuration.[1b] (Ratios of isomers determined from proton and

^{31}P NMR spectra were 56:44 and 57:43 for 3, and 58:42 and 57:43 for 4.) As for 2, the more abundant isomer of 4 displayed the greater upfield ^{31}P chemical shift and also caused the higher energy phosphoryl stretching frequency absorption. Both observations are consistent with an axially oriented NMe_2 group and thus trans geometry.[1,4] In contrast, the more abundant isomer of 3 displayed a lower field ^{31}P chemical shift and had the lower energy P=O stretching frequency absorption. This isomer of 3 and the more abundant isomer of 1 would therefore be assigned the cis arrangement.[1,4]

Table Infrared and NMR Data for 2-Methoxy- and 2-Dimethylamino-1,3,2-diazaphosphorinanes

Compound	$\bar{\nu}$(P=O)		^{31}P NMR		^{1}H NMR
	cm^{-1}	Rel. %[a]	δ[b]	Rel. %	Rel. %
1a	--	--	-130.1	100	44
1b	--	--	-130.1		56
2a	--	--	-109.9	59	61
2b	--	--	-124.8	41	39
3a	1282	40	-14.7	44	43
3b	1269	60	-16.4	56	57
4a	1194	60	-18.1	58	57
4b	1176	40	-19.8	42	43

[a]Calculated assuming equal extinction coefficients

[b]Relative to external H_3PO_4, where a negative value indicates a downfield shift

Independent of the assignments of phosphorus stereochemistries or cis-trans isomers, however, this study clearly indicates that a substantial difference exists between the behavior of 1,3,2-diaza- and 1,3,2-dioxaphosphorinanes. Whereas the isomer equilibrium distribution of 1a:b is 44:56 (or 56:44), that of 5a:b is about 100:0;[5] for 2a:b it is 60:40 (or 40:60), but for 6 it is 15:85.[6] The causes of these differences cannot be rationalized until structural data are available. It is worth noting, however, that

in addition to unfavorable steric interactions of an axial dimethylamino group with C4 and C6 axial protons (also predicted for dioxa compounds by Drieding models[1b]), models of diaza analogues indicate unfavorable interactions of a dimethylamino group with the N1 and N3 methyl protons when the former is equatorially, but not axially, oriented. These simple steric interactions, although probably contributory, are insufficient for rationalization of dioxa and diaza behavioral differences, since the methoxy compounds can avoid the interactions by rotation of the OMe group away from the ring.

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