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SYNTHESIS AND CIS-TRANS-GEOMETRY ASSIGNMENT IN DIASTEREOISOMERIC 2-t-BUTYLAMINO-4-METHYL-1,3,2-DIOXAPHOSPHORINANS AND THEIR 2-SELENO DERIVATIVES

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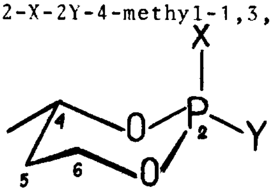
Stereochemical studies of 2-X-1,3,2-dioxaphosphorinans have shown that these systems exist in chair conformation and the steric orientation of X substituent depends on its chemical nature. It has been demonstrated that such X as halogen [1,2], alkoxyl [1], thiomethyl [3a], thiophenyl [3b], hydrogen [4], alkyl [5] and phenyl [6] prefer axial orientation, while alkylamino groups [7] are equatorially or axially orientated, depending on the nature of nitrogen substituents. Equatorial preference of the dimethylamino group in substituted 1,3,2-dioxaphosphorinans [7] has been ascertained from the determination and calculation of their dipole moments, ^{1}H, ^{13}C and ^{31}P nmr spectra analysis and deductive reasoning concerning stereochemistry of their chemical transformations. However, it was demonstrated recently that the phenylaminogroup prefers to occupy axial orientation [7f]. This fact prompted us to investigate systematically the factors govering the spatial orientation of alkylamino and dialkylamino substituents in dioxaphosphorinanyl ring systems.

In this communication we report the results of our studies on the configuration around the phosphorus atom in both diastereoisomeric 2-t-butylamino-4-methyl-1,3,2-dioxaphosphorinans (I) and on the conformation of their 2-selenoderivatives (II). Both cis- and trans-I were prepared in the reaction of trans-2-chloro-4-methyl-1,3,2-dioxaphosphorinan [8] (III) with t-butylamine. The product consisted of the mixture of two diastereoisomers in the ratio Ia:Ib = 26:74, which is left unchanged by distillation [9].
Product was investigated by means of gc-ms, ^{31}P, ^{13}C nmr spectroscopy; b.p. 43-4°/0,6; $n_D^{20} = 1,4665$; $\delta_{^{31}P} = -143.0$ (Ia) and -126,5 (Ib) ppm (C_6H_6)[10]. ^{31}P and ^{13}C nmr spectral analysis (TABLE) have shown that preponderant isomer (Ib) has the trans configuration with the 4-CH_3

equatorially and NHBu^t axially oriented while the minor one has an NHBu^t group in the equatorial disposition (Ia). This was concluded from the much lower value of $^{3}J_{P-C5}$ (TABLE) for trans- then cis-I[11], the observed γ effect for δC4 and δ C6 in both isomers[12] and also from chemical shift order of both Ia and Ib in the ^{31}P spectra[7b].

TABLE

^{13}C nmr Data [a] for 2-X-2Y-4-methyl-1,3,2-dioxaphosphorinans



Comp.	X	Y	Solvent	C_4	C_5	C_6	4-CH_3
Ia	lp	NHBu^t	$CDCl_3$	71.0 (7)	35.3 (10)	63.0 (7)	23.2 (5)
Ib	NHBu^t	lp	$CDCl_3$	63.8 (3)	35.9 (4)	58.0 (3)	23.2 (3)
IIa	Se	NHBu^t	C_6D_6	74.5 (8)	34.0 (5)	65.9 (5)	22.1 (10)
IIb	NHBu^t	Se	C_6D_6	75.7 (8)	31.6 (10)	64.6 (7)	21.8 (5)

a) Chemical shifts are relative to internal TMS (in ppm). Coupling constants (JPC, Hz) are given in parentheses. Proton decoupled spectra were obtained at 22.63 MHz with a Bruker HX-72 system using the Fourier transform technique

Addition of equimolar amounts of elemental selenium to a Iab mixture (cis:trans = 26:74) equilibrated at 25° gave a mixture of cis-and trans 2-t-butylamino-2-seleno-4-methyl-1,3,2-dioxaphosphorinans (II) in the ratio 30:70, respectively.

Addition of selenium to P^{III} derivatives is known to be fully stereospecific [13] but in this case an increase of content of cis-II in relation to the parent composition is probably due to higher Lewis basicity of axially orientated lone pair in Ia, as compared to the equatorially located lp in Ib [14], towards the selenium molecule.

Diastereoisomeric cis- and trans-II were separated by column chromatography (Silicagel 100-200 mesh, benzene as eluent) and characterized by m.ps, ^{31}P and ^{13}C nmr spectroscopy (TABLE). IIa: m.p. 120-120.5°; δ_{31P} = -66.5 ppm (C_6D_6), $^{1}J_{P-Se^{77}}$ = 900 Hz; δ_{4-CH_3} = 0.95 ppm (C_6D_6); $^{3}J_{CH_3-H}$ = 6.6 Hz; $^{4}J_{P-H}$ = 2.1 Hz. IIb: m.p. 81-82° ; δ_{31P} = -58.7 ppm (C_6D_6); $^{1}J_{P-Se}$ = 916 Hz; δ_{4-CH_3} = 1.24 ppm (C_6D_6); $^{3}J_{CH_3-H}$ = 6.9 Hz; $^{4}J_{P-H}$ = 1.2 Hz[15].

Recently we reported from this Laboratory the dependence of absolute values of spin-spin coupling constants between directly bonded magnetically active nuclei on their spatial disposition in the dioxaphosphorinanyl system e.i, $|^1J_{PX}|$ axial $<$ $|^1J_{PX}|$ equatorial for X = H, Se.[16] Thus the orientation of Se atom in cis-II is axial and equatorial in trans-II. Assignment of a cis- geometry for IIa and trans- for IIb is fully supported by their X-ray structure determination [17].

Although the X-ray structure determinations of IIa and IIb do not constitute proof of their conformation in solution nor that of their parent compounds Ia and Ib, they fully confirm the correctness of their cis-trans-geometry assignment. On the basis of stereo-chemical correlations and $^3J_{PC5}$ values extracted from ^{13}C nmr spectra [7e], we assume the axial and equatorial orientation of lone pairs in Ia and Ib, respectively. This structural conclusion supports the idea of two competing effects influencing the spatial orientation of the amino-substitutent in 1,3,2-dioxaphosphorinanyl ring systems, namely vicinal electron pair interactions and steric requirements of substituents bonded to the nitrogen atom. In the rationale of Verkade [7e] and Bentrude [7b], an Me_2N group prefers the equatorial orientation because of steric interaction of an axial nitrogen-methyl with the 4- and 6-hydrogens resulting from the requirement of perpendicularity of the nitrogen p electron pair and the lone pair of phosphorus [18]. In I, due to the lower steric requirements of the N-hydrogen atom, the $NHBu^t$ group can occupy the axial position. However, raising the temperatura of a mixture of Ia,b equilibrated at 25° (26:74) to 80° changed the ratio Ia : Ib to 44:56. This can be explained by the increase of thermal motion of the $NHBu^t$ group rotating around the P-N bond axis and which results in a shift to a higher content of cis- isomer wherein unrestricted rotation of $NHBu^t$ group in the equatorial disposition can occur.

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References and Notes

(1) W.G. Bentrude and J.H. Hargis, J.Am.Chem.Soc., 92, 7136 (1970); D.W. White, P.D. Bertrand. C.K. McEwen and J.G. Verkade, ibid., 92, 7125 (1970); W.G. Bentrude and J.G. Hargis, ibid., 92, 7136 (1970); M. Haemers, R. Ottinger, J. Reisse and D. Zimmermann, Tetrahedron Lett., 461 (1971).

(2) K. Bergesen and P. Albriksten, Acta Chem.Scand., 26, 1680 (1972).

(3) (a) A. Okruszek and W.J. Stec - Z. Naturforsch.- accepted for publication; (b) D.B. Denney and M.A. Moskal, Phosphorus, 4, 77 (1974).

(4) W.J. Stec, B. Uznański and J. Michalski, Phosphorus, 2, 237 (1973).

(5) W.G. Bentrude, K.C. Yee, R.D. Bertrand and D.M. Grant, J.Am.Chem.Soc., 93, 797 (1972).

(6) W.G. Bentrude and K.C. Yee, Tetrahedron Lett., 3999 (1970).

(7) (a) J.A. Mosbo and J.G. Verkade, J.Am.Chem.Soc., 94, 8224 (1972), ibid., 95, 4659 (1973); (b) W.G. Bentrude and Han Wan Tan, ibid., 94, 8222 (1972), ibid., 95, 4666 (1973); (c) W.J. Stec, A. Okruszek and J. Michalski, Bull. Acad. Polon. Sci., Ser.sci.chim., 21, 445 (1973); (d) E.E. Nifanteev, J.S. Nasonovskij and A.A. Kryuchkov, J.Gen.Chem., USSR, 43, 71 (1973); (e) A. Cogne, A. Guimaracs, J. Martin, J.B. Robert and W.J. Stec, Org. Magn. Res., 6 629 (1974); (f) W.J. Stec and A. Okruszek - J.Chem.Soc., accepted for publication.

(8) C.L. Bodkin and P. Simpson, J.Chem.Soc. (B) 1971, 1136.

(9) That the equilibrium ratio at 26:74 for I can be reached very quickly is concluded from the observation that slow addition of a 0.3 molar equivalent of Se to distilled I at 25^{o} gave only cis-II. Unreacted I retained the same isomer ratio as the starting material. This experiment was carried out in nmr tube and was followed by ^{31}P nmr.

(10) All new compounds described in this communication were identified by means of mass-spectrometry. δ_{31P} are listed in ppm relative to external 85% H_3PO_4. A positive shift is taken to occur at an applied magnetic field greater than that of the standard.

(11) (a) M. Haemers, R. Ottlinger, D. Zimmermann and J. Reisse, Tetrahedron Lett., 2241 (1973); ibid., Tetrahedron, 29, 3538 (1973); (b) E.E. Nifanteev, A.A. Borisienko and Sergeev, Dokl.Akad.Nauk USSR, 208 (3), 651 (1973).

(12) S.I. Featherman. S.O. Lee and L.D. Quin, J.Org.Chem, 39, 2899 (1973).

(13) W.J. Stec, A. Okruszek and J. Michalski, Angew.Chem., 83, 491 (1971).

(14) J.G. Verkade, Bioinorganic Chemistry, 3, 165 (1974).

(15) The value of ${}^{4}J_{PH}$(1.2 Hz) in IIb and the lower than average value of $\frac{\Delta J}{J_{min}}$[16] (1.8%) suggest that IIb exists in C_6D_6 solution in a chair-chair equilibrium. Axial tendency of sulphur in 2-thiono-2,5,5-trimethyl-1,3,2-dioxaphosphorinan was observed by J.B. Robert at al (J.B. Robert - private information).

(16) W.J. Stec, Z. Naturforsch., 29b, 109 (1974).

(17) T.J. Bartczak, A. Christensen, R. Kinas and W.J. Stec - manuscript in preparation.

(18) The requirement of perpendicularity of the nitrogen p-electron pair and localized electron pair of phosphorus is confirmed by our observations of exclusive axial preference of an aziridinyl group in the dioxaphosphorinanyl system, which possesses pronounced sp^3 nitrogen character [7e].