

Preparation and Conformational Analysis of Geometric Isomers of 4,5-Dimethyl-2-ethoxy-2-oxo-1,2-oxaphosphorinane and Their 3,3,6,6-Tetradeuterio Analogs

KNUT BERGESEN and TROND VIKANE

Chemical Institute, University of Bergen, N-5000 Bergen, Norway

The geometric isomers of the title compounds have been prepared and separated on GLC. The 2,4-*cis*,4,5-*cis*-isomer is found to undergo a rapid ring inversion between two chair conformations, while ring rigidity has been observed for the 2,4-*trans*,4,5-*cis*-isomer. Equilibration studies of the isomers show that the 2,4-*trans*,4,5-*cis*-isomer is 0.9 kcal/mol more stable than the 2,4-*cis*,4,5-*cis* isomer.

The interest in conformational studies of six-membered ring systems containing one or more heteroatoms in the ring is at present rapidly growing.^{1,2} Like cyclohexane, heterocyclic six-membered ring compounds usually are most stable in chair form. Quantitative examinations, however, reveal important differences between cyclohexanes and corresponding heterocyclic compounds. The carbon-heteroatom bond in heterocycles is often appreciably different in length from the C-C bond, distorting the chair conformation as compared to cyclohexane. If more than one heteroatom is present in the ring, dipole-dipole interactions will also affect the ring conformation. In heteroatomic ring systems, the bending force constants for C-X-C angles, and torsional potentials about the C-X bond, are different as compared with the corresponding C-C-C arrangement in cyclohexane. This work reports the preparation, spectral properties, and conformational energies of geometric isomers of ring substituted 1,2-oxaphosphorinanes.

EXPERIMENTAL

The cyclic compounds 4,5-dimethyl-2-ethoxy-2-oxo-1,2-oxaphosphorinane (I) and 4,5-dimethyl-2-ethoxy-2-oxo-3,3,6,6-tetradeuterio-1,2-oxaphosphorinane (II) were prepared by heating triethyl phosphite together with *meso*-2,3-dimethyl-1,4-dibromobutane and *meso*-2,3-dimethyl-1,1,4,4-tetradeuterio-1,4-dibromobutane, respectively, according to the method of Garner.³

I: B.p._{1.5} 137°C, n_D^{20} 1.4552; GLC purity about 90 %.

II: B.p._{0.5} 105°C; n_D^{20} 1.4495; GLC purity about 90 %.

The isomers of I and II were separated on an Aerograph Autoprep A-700 gas chromatograph. GLC purity of the isomers was better than 99 %.

The PMR spectra were measured at 60 MC (JEOL-60H) in neat liquid at 25°C, in 20 % solution of the isomers in CCl₄ at 140°C, and in 20 % solution of the isomers in dichloromethane at -50°C.

The infrared spectra below 700 cm⁻¹ were recorded on a Unicam SP 100 instrument, from samples prepared as films between KBr-windows.

RESULTS AND DISCUSSION

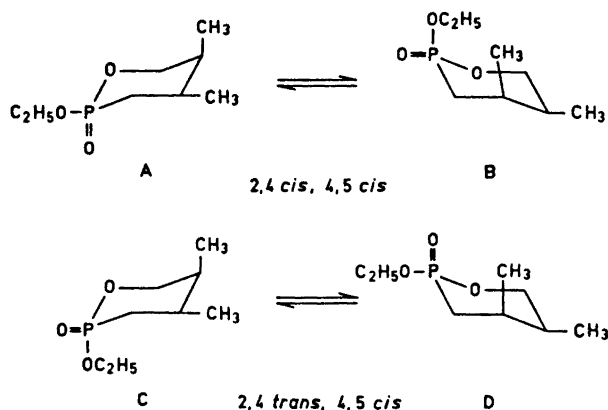
The phosphorinane compounds I and II were found by GLC to contain two isomers in the ratio approx. 1 : 2, and the isomers were separated by preparative GLC. The physical data, as refractive indexes, retention times, P=O frequencies, chemical shifts, and coupling constants of the isomers, are given in Table 1.

Table 1. Physical data, chemical shifts, and coupling constants for the geometric isomers of I and II.

Compound	Isomer	Retention time (min) 175°	n_D^{20}	$\nu_{P=O}$ cm ⁻¹	δ_{CH_3} Chemical shift ppm	Coupling constants Hz
I	2,4- <i>cis</i> ,4,5- <i>cis</i>	36	1.4573	1237	0.94	$^4J_{PH} = 2.1$
	2,4- <i>trans</i> ,4,5- <i>cis</i>	46	1.4565	1250 1256	1.06 0.96	$J_{H-C-CH_3} = 7.0$ $^4J_{PH} = 3.2$
II	2,4- <i>cis</i> ,4,5- <i>cis</i>	34	1.4579	1239	0.92	$^4J_{PH} = 1.9$
	2,4- <i>trans</i> ,4,5- <i>cis</i>	45	1.4573	1252	1.02 0.94 1.00	$J_{H-C-CH_3} = 6.8$ $^4J_{PH} = 3.1$ $J_{H-C-CH_3} = 6.9$

Each of the substituents, 2-ethoxy, 4- and 5-methyl in I and II may occupy either equatorial or axial positions in the ring, a total of 2³ isomers. Since *meso*-2,3-dimethyl-1,4-dibromobutane and *meso*-2,3-dimethyl-1,1,4,4-tetradeuterio-1,4-dibromobutane were used in the preparation of I and II, the 4- and 5-methyl groups are *cis* to each other. The isomers with both the methyl groups in equatorial or in axial position will therefore be ruled out and the remaining possible isomers are only 4. Two of these isomers may be derived from the other two by inversion of the chair conformations.

The PMR spectra of the isomers in dichloromethane showed no change over the temperature range -50° to +140°C. Below -55°C the isomers start

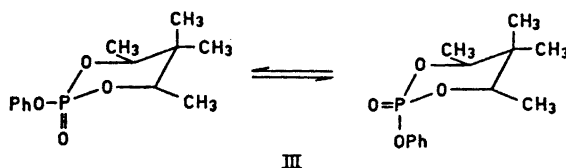


to crystallize from the solution. These observations point to the following three alternative explanations:

1. Ring rigidity, no inversion on the PMR time scale.
2. Equilibrium, greatly favouring one conformer.
3. Rapid equilibration over the whole temperature range.

Infrared spectra of the *cis* and *trans* dialkyl cyclohexanes⁴ show characteristic frequencies in the range 585–650 cm^{-1} only for those isomers having at least one axial substituent. Axial position of a methyl group has also been found for the *cis* isomer of 3-methyl-2-ethoxy-2-oxo-1,2-oxaphosphorinane⁵ and 5,5-dimethyl-2-methoxy-2-oxo-1,2-oxaphosphorinane.⁶ The infrared spectra of the assumed 2,4-*cis*,4,5-*cis* isomer of I show strong bands at 639 and 661 cm^{-1} and at 610 and 621 cm^{-1} for the assumed 2,4-*cis*,4,5-*cis* isomer of II. These band pairs are assigned to two axial methyl groups in different environments, believed to result from rapid equilibration between the two conformers A and B of the 2,4-*cis*,4,5-*cis* isomers. The band at 661 cm^{-1} in I (620 cm^{-1} in II) is assigned to the axial methyl group at position 5, and the band at 639 cm^{-1} (610 cm^{-1} in II) to the axial methyl group in position 4. The relative ratio between A and B is estimated from the area of the two absorption bands to be 2 : 3. Ring inversion ought to cause conformational change around the phosphorus atom. It is found that the phosphoryl absorption of the 2,4-*cis*,4,5-*cis* isomer of I gives a doublet, which might be due to equatorial as well as axial position of the phosphoryl group. Since atoms linked to six-membered rings usually give higher infrared stretching frequencies in equatorial position than in axial position, the phosphoryl absorption band at 1250 cm^{-1} is assigned to an equatorial position of the P=O group, and the frequency at 1237 cm^{-1} to an axial P=O group. This is also in agreement with the phosphoryl absorption frequency found for the geometric isomers of 4,5,5,6-tetramethyl-2-phenoxy-2-oxo-1,3,2-dioxaphosphorinane (III).⁸

The infrared singlet band of the assumed 2,4-*trans*,4,5-*cis*-isomer of I and II at 662 cm^{-1} and 620 cm^{-1} , respectively, is assigned to the axial methyl



group in position 5. In agreement with this assumption the phosphoryl absorptions of the isomers show singlets at 1256 cm^{-1} and 1253 cm^{-1} , respectively, pointing to an equatorial position of the phosphoryl group. According to the above arguments it seems reasonable to suggest a rigid structure of the 2,4-*trans*-4,5-*cis*-isomer, C.

The PMR signals of the methyl groups in position 4 and 5 of the 2,4-*cis*,4,5-*cis*- and 2,4-*trans*,4,5-*cis*-isomers of I and II consist of a double doublet at lower field and a doublet at higher field. The double doublet is due to the coupling to the methine proton as well as to the phosphorus atom, and is therefore assigned to the methyl group in position 4. From the chemical shift position of the doublet, and the lack of coupling to the phosphorus atom, the doublet is assigned to the methyl group in position 5.

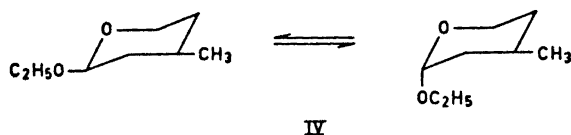
The conformational equilibria of the 2,4-*cis*,4,5-*cis*- and 2,4-*trans*,4,5-*cis*-isomers of I have been studied at 5 different temperatures over a range of approx. 100°C (Table 2). The equilibrations were carried out in sealed tubes catalyzed by trifluoroacetic acid, and each sample was analyzed by GLC.

Table 2. Equilibration data for 4,5-dimethyl-2-ethoxy-2-oxo-1,2-oxaphosphorinane.

Temp. $^\circ\text{C}$	% <i>trans</i>	Equilibrium constant, <i>K</i>	$-\Delta G^\circ$ kcal/mol	$-\Delta H^\circ$ kcal/mol
179	62.5	1.67	0.46	
204	61.2	1.58	0.43	
227	60.4	1.52	0.42	0.9 ± 0.1
258	58.6	1.42	0.37	
297	57.0	1.33	0.32	

The equilibrium was approached from both sides, or from the mixed isomers. The equilibration of the isomers shows that the 2,4-*trans*,4,5-*cis*-isomer, with an axial ethoxy group attached to the phosphorus atom, is 0.9 kcal/mol more stable than the 2,4-*cis*,4,5-*cis*-isomer.

The position of the equilibrium is different from that found for methoxycyclohexane⁷ where the isomer with equatorial orientation of the methoxy group is most stable. On the other hand, equilibration of 2-ethoxy-4-methyloxane (IV)⁹ has shown that the *trans*-isomer with an axial ethoxy group



is 0.75 kcal/mol more stable than the *cis*-isomer. Similar preferred axial placement of an alkoxy group has also been observed for 2-alkoxy-1,3-dioxanes.¹⁰ The preference for an axial 2-ethoxy group in oxane, 1,3-dioxanes, and in I may be due to the postulated "anomeric effect",^{9,11} involving the repulsions between lone-pair orbitals of the ring oxygen and the exocyclic alkoxy oxygen. The effect is solvent dependent, being largest in solvents of low dielectric constant. The effect gives larger preference for an electron withdrawing group (OEt) in axial position than in equatorial position when the group is attached to an atom in the α -position to the ring oxygen atom. Proton magnetic resonance analysis of the isomers of the tetradeuterio compound II is in progress in this laboratory.

REFERENCES

1. For reviews of heterocyclic conformational analysis, see Riddell, F. O. *Quart. Rev. (London)* **21** (1967) 364; Romers, C., Altona, C., Buys, H. R. and Havinga, E. In *Topics in Stereochemistry*, Interscience, New York, Vol. 4. *In press*.
2. Eliel, E. L. *Accounts Chem. Res.* **3** (1970) 1.
3. Garner, A. Y. *US Pat. 2953591*; *Chem. Abstr.* **55** (1961) 5346.
4. Zhizhin, G. N., Stein, Kh. E., Aleksayan, V. T. and Lieberman, A. L. *Zh. Strukt. Khim.* **6** (1965) 684.
5. Bergesen, K. and Vikane, T. *Acta Chem. Scand.* **25** (1971) 1147.
6. Bergesen, K. *To be published*.
7. Eliel, E. L. and Gilbert, E. C. *J. Am. Chem. Soc.* **91** (1969) 5487.
8. Majoral, I. P., Kraemer, R., Devillers, I. and Navech, I. *Bull. Soc. Chim.* **11** (1970) 3917.
9. Eliel, E. L. and Giza, C. A. *J. Org. Chem.* **33** (1968) 3754.
10. Nader, F. W. and Eliel, E. L. *J. Am. Chem. Soc.* **92** (1970) 3050.
11. a. Lemieux, R. U. In de Mayo, P., Ed., *Molecular Rearrangements*, Interscience, New York 1964, Chapter 12; b. Angyal, S. J. *Angew. Chem.* **81** (1969) 172.

Received May 24, 1971.