Tetrahedron Letters No.46, pp. 3999-4002, 1970. Pergamon Press. Printed in Great Britain.

POSSIBLE IMPORTANCE OF LONE PAIR INTERACTIONS IN THE PREFERRED AXIAL ORIENTATION OF PHENYL IN A 6-MEMBERED RING PHENYLPHOSPHONITE

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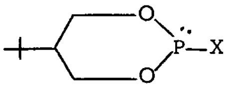
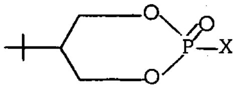
(Received in USA 20 August 1970; received in UK for publication 2 September 1970)

It has recently been noted[1,2] that in t-butyl substituted 6-membered ring phosphites (I) and in other ring-substituted analogs[2] the alkoxy shows an axial preference such that the 5-substituted cis isomer (I)[1] or 4-substituted trans isomer[2a] is the thermodynamically more stable species. This axial preference may be ascribed at least in part to the anomeric effect[3] also noted for the analogous 5-t-butyl-2-methoxy-1,3-dioxane.[3a] However, evidence[1] that the axial methoxy preference is probably greater in the t-butyl phosphite than with the corresponding dioxanes,[3b] suggests the possibility that other factors, such as the interaction of the adjacent electron lone pairs on oxygen and phosphorus, may exert an important orienting influence in such systems.



I $X = CH_3O$
II $X = C_6H_5$



III $X = CH_3$
IV $X = C_6H_5$

We have therefore thermally equilibrated the cis-trans pair of phenylphosphonites (II) with the unexpected result that the more stable form is the cis isomer with t-butyl equatorial and phenyl axial in a chair-form ring. This is especially surprising since the phenyl has considerably larger steric requirements than the methoxy and is not known to display the anomeric effect. ΔG°_{25} for the conversion axial→equatorial of the phenyl in 2-phenyl-4,6-dimethyl-1,3-dioxane is - 3.11 kcal/mol.[3b]

These conclusions concerning II arise from the following observations. A freshly prepared isomeric mixture of neat II shows at 40° t-butyl pmr absorptions at 42 and 65 Hz downfield from TMS. The area ratio is 90/10 with the major peak being the upfield one. On progressive heating, the ratio decreases monotonically until at 200° it is 70/30 and the peak separation is 16 Hz. On cooling again to 40° the equilibrium is slowly re-established[4] at 90/10. First order pmr analysis at 220 MHz of the 90/10 mixture gave the following results.[5]

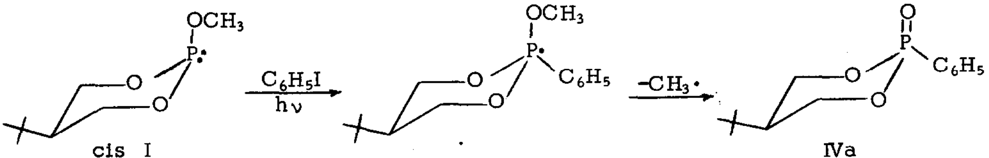
Pmr of IIa at 220 MHz

Chemical Shifts[a]			Coupling Constants[b]				
ν_A	ν_B	ν_X	J_{AB}	J_{BX}	J_{AX}	J_{AP}	J_{BP}
3.90	4.10	2.12	11	3.5	11	1.5	11

a) In ppm downfield from TMS internal standard. b) J in Hz.

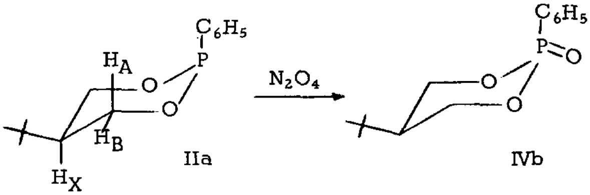
These results for the more stable isomer IIa are completely consistent with those expected[1,6] for a chair-form ring with t-butyl equatorial. The axial orientation of the phenyl is suggested by the reversal of the relative chemical shifts from that noted[1,6] for phosphites, probably as a result of the benzene ring current.[7] The axial phenyl orientation in IIa is confirmed by the following experiments.

Oxidation of the 90/10 mixture at 0° with N_2O_4 gave (vpc) at 90/10 mixture of the corresponding isomeric phenylphosphonates (IV). A sample of II which had been equilibrated at 140° to a 78/22 (nmr) mixture of isomers, quenched in ice water, and then oxidized at 0°, gave a 76/24 (vpc) mixture of isomers of IV. The minor isomer of IV is identical to the major isomer (95%, vpc) formed on photoreaction of a mixture of cis-I (90%, nmr) and trans-I (10%, nmr) with phenyliodide.



cis I IVa

Assuming that N_2O_4 oxidation of II proceeds with retention of configuration of phosphorus,[8] and that the isomer IVa formed above is that with t-butyl and phenyl trans, then the major isomer of II is the cis from IIa.



IIa IVb

Evidence for the trans stereochemistry of IVa is three-fold. First, the high stereoselectivity of the phenyl iodide photoreaction with I was shown above (90/10 cis/trans mixture of I gives 95/5 ratio of IVa/IVb). Second, we have recently shown[9b] that tBuS· and tBuO· oxidation of various cis/trans ratios of I is nearly stereospecific with retention at phosphorus and that the photoreaction with phenyl iodide in all probability involves phenyl radical.[10] Third, the isomer IVa shown has nmr identical in the methylene region to the corresponding trans-methylphosphonate III whose stereochemistry is firmly established by X-ray study of its cis analog.[11] This would not be true if the phenyl were in fact axial (IVb) in which position it should affect the relative chemical shifts of the A and B protons.

The strong downfield shift of the t-butyl protons in the minor isomer (IIb) suggests that the t-butyl is axial.[12] This is confirmed by the ^{13}C spectrum of the mixture.[13] The cis-trans equilibrium is most simply written as

IIa IIb

although some contribution from another conformer may be present in IIb. At 25°, ΔG° for IIa→ IIb is about 1.5 kcal/mol which is close to the range 1.4 - 1.8 kcal/mol for the equatorial → axial free energy change measured for the corresponding dioxanes[12] and sulfites.[14]

The likely role of adjacent lone-pair interactions in influencing torsional barriers is being increasingly well-recognized,[15] and we believe that such factors probably are important in determining orientational preferences in systems of the type we describe here. A special effect due to phenyl may also be present, since in the analogous 1,3-dioxanes the phenyl is less constrained to the equatorial position than is methyl.[3b] Our studies[16] with the methyl analog of II indicate that the cis isomer is the more stable form in that system as well.

Acknowledgement. This work was supported by National Science Foundation Grant GP-8363.

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4. We are not prepared to say anything at this time about the inversion barrier as it is possible that the process is being catalyzed by trace impurities.

5. We thank Dr. J. C. Martin and Mr. R. Thrift, University of Illinois, Urbana, Illinois for the 220 MHz spectrum.

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7. Intermolecular shielding and deshielding effects could also be important.

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