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METHOXIDE-INDUCED REARRANGEMENT OF SOME N-t-BUTYL α-CHLOROPHOSPHONAMIDATES EVIDENCE FOR AZAPHOSPHIRIDINE OXIDE INTERMEDIATES

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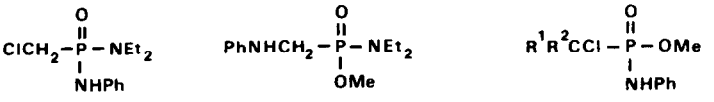
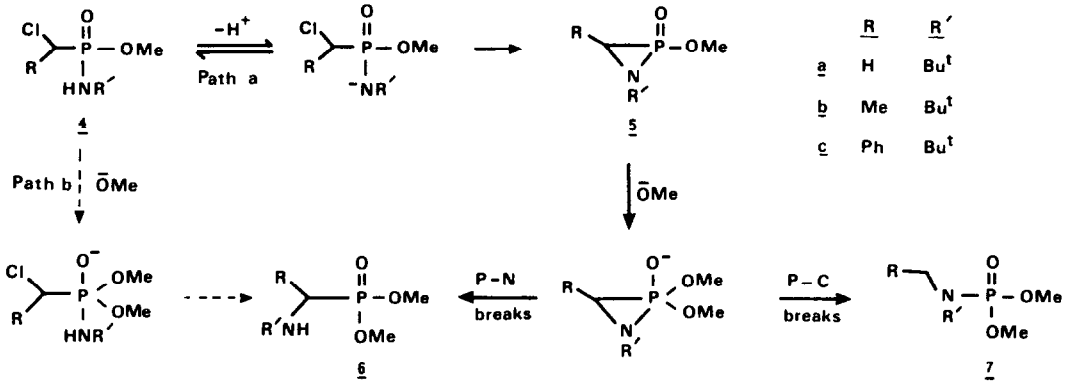
Summary: N-t-Butyl α-chlorophosphonamidates (4) undergo methoxide-induced rearrangement to give products (6 and 7) in which either the P-N or P-C bond has been broken. This implies the intermediacy of a cyclic azaphosphiridine oxide 5.

With NaOMe-MeOH the α-chlorophosphonic diamide 1 is converted into the α-(phenylamino)-phosphonate 2.[1] Recent work with the N-phenyl α-chlorophosphonamidates 3 (R^1, R^2=H or Me) has



shown that this useful type of rearrangement is not restricted to chloromethyl compounds.[2] Two reasonable mechanisms can be envisaged, depending on whether the methoxide acts initially as a nucleophile or a base (Scheme). In the latter case (path a) there would be formed an azaphosphiridine oxide intermediate 5, having carbon, nitrogen, and the phosphoryl group contained in a three-membered ring. Nothing seems to be known about this ring system (the phosphorus analogue of an α-lactam),[3] although it would be expected to react rapidly with nucleophiles, and no evidence of its involvement in the rearrangement has been found. Nonetheless, if 5 is formed it should be possible to demonstrate its intermediacy. In particular, by choosing suitable substituents at N and C it should be possible to induce the ring to open with P-C rather than P-N bond cleavage.



The N-t-butyl α-chlorophosphonamidates 4 (a-c) were prepared from the corresponding α-chlorophosphonic dichlorides by treatment first with Bu^tNH_2 (2 mol equiv.), then with methanolic NaOMe (slight excess; 0 °C). They were all crystalline, even though 4b and 4c were mixtures of diastereoisomers (^1H and ^{31}P n.m.r. spectroscopy).[4]

When dissolved in THF containing methanolic benzyltrimethylammonium methoxide (2 mol equiv. of 40% solution; 0.26 M initially) at 50 °C, the chloromethyl compound 4a was converted during 1.5 h into a 1.6:1 mixture of two products, δp 12.3 and 29.3.[5] The products were separated by partition between CH_2Cl_2 and aqueous HCl. The basic minor product (δp 29.3) had spectroscopic properties [including ν_{NH} 3300 cm^{-1}; δ($CDCl_3$) 2.90 (2H, d, J_{PH} 15 Hz) and 1.20 (br, NH); m/z 86 ($Bu^tNHCH_2^+$, 45%)] in accord with the aminophosphonate structure 6a. The neutral major product (δp 12.3) had m/z 195 (M^+, 1%) and 180 (M^+ - Me, 100), and δ($CDCl_3$) 3.59 (6H, d, J_{PH} 11 Hz), 2.67 (3H, d, J_{PH} 9 Hz), and 1.27 (9H, s) (no NH). Its identity as the phosphoramidate 7a was confirmed by comparison with an authentic sample obtained by N-methylation (NaH, MeI in DMF) of $Bu^tNHP(O)(OMe)_2$.[6]

The α-chloroethyl substrate 4b reacted at a similar rate and also gave two products. The major product (∿90%) was the aminophosphonate 6b (δp 30.3) but the phosphoramidate 7b (δp 12.4) [N-Et group: δ($CDCl_3$) 3.11 (2H, dq, J_{PH} 14, J_{HH} 7 Hz) and 1.14 (3H, t, J_{HH} 7 Hz)] was formed in significant yield (∿10%).[5]

The α-chlorobenzyl compound 4c reacted much more readily (0.5 h at 25 °C) and gave essentially a single product (δp 13.2). The phosphoramidate 7c [N-CH_2Ph group: δ($CDCl_3$) 7.4-7.1 (5H, m) and 4.33 (2H, d, J_{PH} 12 Hz)] was isolated in 96% yield. There was a trace of a second product (δp 26.0) (1-2%) which was not isolated but was found to have the same δp and g.l.c. retention time as an authentic sample of the aminophosphonate 6c prepared from $Bu^tN{=}CHPh$ and $HP(O)(OMe)_2$.

While either path in the Scheme can lead to the aminophosphonate products 6, the phosphoramidates 7 seem to demand the cyclic intermediate 5. And since opening of the ring in 5, as a result of nucleophlic attack at phosphorus, may entail either the C-P or N-P bond breaking, path a alone can account for both types of product. The behaviour of 4b and 4c relative to 4a is then as expected, viz the importance of C-P bond breaking decreases or increases as substituents on the α carbon atom decrease (R = Me) or increase (R = Ph) its ability to support negative charge.

References and Footnotes

1. K.A. Petrov, V.A. Chauzov, T.S. Erokhina, and I.V. Pastukhova, *J. Gen. Chem. USSR*, 1977, 47, 2501.
2. M.J.P. Harger and A.Williams, *J. Chem. Soc. Perkin Trans. 1*, in the press.
3. Some other types of compound containing the phosphoryl group in a three-membered ring have been postulated as short-lived intermediates or, in special cases, isolated e.g. P. Burns, G. Capozzi, and P. Haake, *Tetrahedron Lett.*, 1972, 925; H. Quast and M. Heuschmann, *Angew. Chem. Int. Ed.*, 1978, 17, 867; H. Quast, *Nachr. Chem. Tech. Lab.*, 1979, 27, 120 (review).
4. The new compounds 4, 6, and 7 (a-c) were fully characterised spectroscopically and by elemental analysis or high resolution mass spectrometry.
5. In the later stages of the reactions of 4a and 4b one of the products (δp 29.3 or 30.3) suffered some demethylation; the stated product ratios relate to the situation prevailing in the early stages, and at the end following remethylation with diazomethane.
6. c.f. S. Coulton, G.A. Moore, and R. Ramage, *Tetrahedron Lett.*, 1976, 4005.

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