Stereochemistry of the Alkaline Hydrolysis of Dialkoxyphosphetanium Salts: Nature and Energetics of the Pentaco-ordinate Intermediates

By KENNETH E. DEBRUIN* and MARTIN J. JACOBS

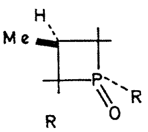
(*Department of Chemistry, Colorado State University, Fort Collins, Colorado* 80521)

Summary The observed lack of stereospecificity in the alkaline hydrolysis of 1,1-dialkoxyphosphetanium salts implies rapid pseudorotation of the pentaco-ordinate intermediates.

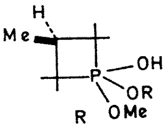
THE transesterification of 1-trideuteriomethoxy-2,2,3,4,4-pentamethylphosphetan oxide (I)† with sodium methoxide in MeOH proceeds with retention of configuration.[1] Presumably, a pentaco-ordinate intermediate containing three exocyclic P–O bonds (II) is involved. We find that when a similar intermediate (III) is formed in the alkaline hydrolysis of a dialkoxyphosphetanium salt, 1-ethoxy-1-methoxy-2,2,3,4,4-pentamethylphosphetanium hexachloroantimonate (IV), decomposition to products proceeds with a nearly complete lack of stereospecificity.

Reaction of diastereomerically pure $(R)_P$-1-chloro-2,2,3,4,4-pentamethylphosphetan oxide (V)[2,3] with sodium methoxide in MeOH produced diastereomerically pure $(R)_P$-1-methoxy-2,2,3,4,4-pentamethylphosphetan oxide (VI).[1,4] Similarly, the reaction of $(R)_P$-(V) with sodium ethoxide in EtOH produced $(R)_P$-1-ethoxy-2,2,3,4,4-pentamethylphosphetan oxide (VII). The ^1H n.m.r. signals (60 MHz, C_6D_6, Me_4Si) of the ring methyl groups in $(R)_P$-(VII) were superimposable on the signals of the methyl groups in $(R)_P$-(VI).[1]

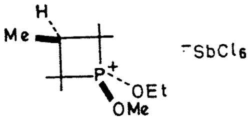
$(S)_P$-(IV),‡ prepared by *O*-ethylation of $(R)_P$-(VI) with triethyloxonium hexachloroantimonate,[5] reacted with 0·05 M-NaOH in 50 vol % aqueous dioxan for 1 min at room temperature. Work-up by extraction with methylene chloride and evaporation of the solvent yielded four neutral products, $(R)_P$-(VI), $(S)_P$-(VI), $(R)_P$-(VII), and $(S)_P$-(VII), in > 80% yield. When $(R)_P$-(IV), prepared by *O*-methylation of $(R)_P$-(VII) with trimethyloxonium hexachloroantimonate,[5] reacted under these conditions. the same four products were formed in similar ratios (Table). The relative amounts of the four products were obtained by



R
(I) OCD_3
(V) Cl
(VI) OMe
(VII) OEt



R
(II) CD_3
(III) Et



(IV)

Products from hydrolyses of phosphetanium salts

Phos-phetanium salt	Yield of products (%)[a]			
	$(S)_P$-(VII)	$(R)_P$-(VII)	$(S)_P$-(VI)	$(R)_P$-(VI)
$(S)_P$-(IV)	36	39	9	16
$(R)_P$-(IV)	33	49	7	11

[a] % of non-acidic products. The standard deviation of five determinations is ±2%.

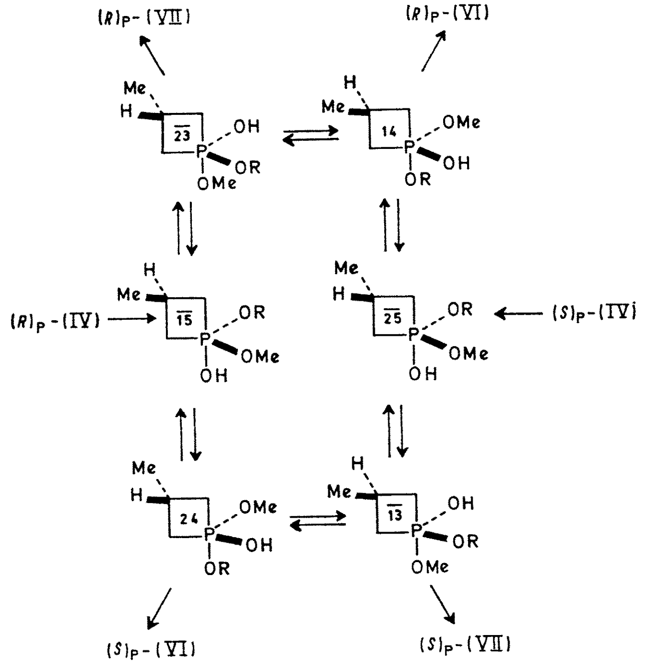
---

† The absolute configuration shown for compounds (I) and (IV)—(VII) is $(R)_P$. $(R)_P$ and $(S)_P$ refer to enantiomers at phosphorus.

‡ $(R)_P$- and $(S)_P$-(IV) were identified by elemental analyses and gave similar but different n.m.r. spectra consistent with that expected for a phosphonium salt.

integration of the 3—5 p.p.m. region in the n.m.r. spectrum of the crude product mixture. For each ester, (VI) or (VII), the signals of the POC*H* protons of the $(R)_{\mathrm{P}}$ isomer were downfield by *ca.* 2—3 Hz from those of the $(S)_{\mathrm{P}}$ isomer with those of (VI)[1] centred around 3·6 p.p.m. and those of (VII) at 4·0 p.p.m. The observed product ratios were unaffected by further differential hydrolysis to the acid as shown by submitting known ratios of the products to the reaction conditions.

These results provide information on the pentacoordinate intermediates (phosphoranes) involved in the displacement reactions. In the Scheme,§ if one assumes attack and departure occur at the apical position of the phosphorane,[6,7] $\overline{25}$ and $\overline{15}$ would be the initially formed phosphoranes from $(S)_{\mathrm{P}}$-(IV) and $(R)_{\mathrm{P}}$-(IV), respectively. Loss of the apical alkoxide from 14 and $\overline{23}$ would give $(R)_{\mathrm{P}}$-(VI) and $(R)_{\mathrm{P}}$-(VII), while $(S)_{\mathrm{P}}$-(VII) and $(S)_{\mathrm{P}}$-(VI) would be formed from $\overline{13}$ and 24, respectively. Thus, in order for $(S)_{\mathrm{P}}$- and $(R)_{\mathrm{P}}$-(IV) to yield all four ester products upon hydrolysis, pseudorotation from $\overline{15}$ and $\overline{25}$ to the remaining four phosphoranes must occur.



SCHEME

Cremer and Trivedi[1] have obtained results that indicate the phosphorane intermediates exist as the mono-anion under these alkaline conditions. They found that displacement of $^{-}OCD_3$ in $(R)_{\mathrm{P}}$-(I) by methoxide ion in MeOH (0·65 M) proceeds with retention of configuration at phosphorus. Presumably, the anion of $\overline{23}$ (R=CD_3 in the Scheme) is formed initially and then undergoes pseudorotation to 14 and loss of $^{-}OCD_3$ to yield $(R)_{\mathrm{P}}$-(VI). The phosphorane must remain as the anion so that further pseudorotation to $\overline{25}$ and $\overline{15}$ is blocked by the necessity of placing the relatively electropositive O^{-} in an unfavourable apical position.[6] The observation of complete retention puts an upper limit of 13 on the pK_a of these cyclic phosphoranes.[9] Thus, in the alkaline hydrolysis of (IV), the intermediate is probably in the form of the anion and the pseudorotations from $\overline{15}$ to $\overline{23}$ and 24 as well as from $\overline{25}$ to 14 and $\overline{13}$ are irreversible.

The relative energy barriers for pseudorotation of $\overline{23}$ to 14 and 24 to $\overline{13}$ compared to the barriers for loss of alkoxide can be obtained by analysis of the product ratios from $(R)_{\mathrm{P}}$-(IV) and from $(S)_{\mathrm{P}}$-(IV). Complete equilibration of phosphoranes 24 and $\overline{13}$ must be established prior to loss of alkoxide since $(S)_{\mathrm{P}}$-(VI) and $(S)_{\mathrm{P}}$-(VII) are formed in the same ratio from $(S)_{\mathrm{P}}$-(IV) as from $(R)_{\mathrm{P}}$-(IV). Thus, pseudorotation of 24 to $\overline{13}$ is a lower energy pathway than loss of alkoxide. A different ratio of $(R)_{\mathrm{P}}$-(VII) to $(R)_{\mathrm{P}}$-(VI) is obtained from the hydrolysis of $(S)_{\mathrm{P}}$-(IV) than from the hydrolysis of $(R)_{\mathrm{P}}$-(IV), indicating that here, loss of alkoxide competes with pseudorotation between $\overline{23}$ and 14. Reaction of hydroxide on $(R)_{\mathrm{P}}$-(IV) results in a relatively higher ratio of $(R)_{\mathrm{P}}$-(VII) to $(R)_{\mathrm{P}}$-(VI) than is obtained from $(S)_{\mathrm{P}}$-(IV). However, the pseudorotation must still be of lower energy in order to explain the degree of equilibration observed. It should be pointed out that a delicate balance does exist and small changes may affect the relative energies.

The above results indicate that pseudorotations of the type $\overline{23}$ to 14 and 24 to $\overline{13}$ are not rate-limiting steps in the transesterification of these cyclic phosphinate esters. In addition, alkaline hydrolysis of these esters[10] most reasonably proceeds by rate-limiting attack of hydroxide ion under similar conditions.

This work was supported by a F.I.C. Grant from Colorado State University.

(*Received, October* 26*th*, 1970; *Com.* 1855.)

---

§ Only the phosphoranes which contain a ring spanning an apical and an equatorial position and their connecting pseudorotations are considered. See ref. 7 for the development of the Scheme.[8]

[1] S. E. Cremer and B. C. Trivedi, *J. Amer. Chem. Soc.*, 1969, **91**, 7200.
[2] J. J. McBride, Jun., E. Jungermann, J. V. Killheffer, and R. J. Clutter, *J. Org. Chem.*, 1962, **27**, 1833.
[3] M. Hague, *J. Chem. Soc.* (*B*), 1970, 934.
[4] W. Hawes and S. Trippett, *J. Chem. Soc.* (*C*), 1969, 1455.
[5] H. Meerwein, E. Battenburg, H. Gold, E. Pfeil, and G. Willfang, *J. prakt. Chem.*, 1939, **154**, 83.
[6] F. H. Westheimer, *Accounts Chem. Res.*, 1968, **1**, 70.
[7] K. E. DeBruin, G. Zon, K. Naumann, and K. Mislow, *J. Amer. Chem. Soc.*, 1969, **91**, 7031.
[8] P. C. Lauterbur and F. Ramirez, *J. Amer. Chem. Soc.*, 1968, **90**, 6722.
[9] J. H. Ridd, *Chem. and Ind.*, 1957, 1268.
[10] K. Bergesen, *Acta Chem. Scand.*, 1967, **21**, 1587; W. Hawes and S. Trippett, *Chem. Comm.*, 1968, 577; P. Haake, R. D. Cook, W. Schwarz, and R. D. McCoy, *Tetrahedron Letters*, 1968, 5251.