Nucleophilic Displacements on a Phospholane: a Case of Inversion of Configuration

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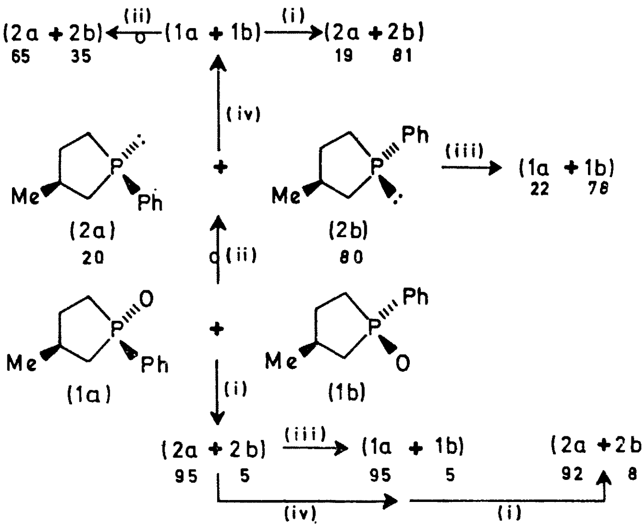
Summary The stereochemical direction of nucleophilic displacements at phosphorus in phospholanium ions is shown to depend on the nature of the entering and leaving groups, as well as on constraints imposed by the ring.

NUCLEOPHILIC displacements on tetraco-ordinate phosphorus in small-membered rings, phosphetanes[1] and phospholanes,[2] in contrast to the same displacements in acyclic systems,[3,4] have been reported to proceed with retention of configuration. We report the results of a study on a phospholane, in which both the retention and inversion mechanisms are operative, depending on the combined nature of the nucleophile and leaving group.†

The parent compound for this study, 3-methyl-1-phenylphospholane 1-oxide (**1a**) was prepared by condensation of isoprene and PhPCl$_2$ followed by hydrolysis[5] and hydrogenation (Raney nickel catalysis, 50 lb/in^2 of H$_2$). Subsequent transformations on (**1a**) were effected using known procedures.[2,4] The diastereomeric ratio of phosphines was determined by n.m.r. analysis of the –CH$_2$I signals of the methylene iodide derivatives in trifluoroacetic acid. The phosphine oxide ratios were determined by reduction with PhSiH$_3$, followed by derivatization as above. As previously found,[2b] this reduction proceeds with complete retention of configuration. Our results are summarized in the Scheme.‡

The benzyl salts of the epimeric 3-methyl-1-phenylphospholanes, (**2a**) and (**2b**), in accord with the previous finding for the 1-methyl analogue,[2] are hydrolysed with complete retention of configuration. By contrast, the deoxygenation of (**1a**) and (**1b**) by Si$_2$Cl$_6$[4] proceeds with predominant *inversion of configuration*. The lack of complete stereospecificity may be the result of stereomutation of either the starting phosphine oxide or product phosphine by reductant by-products, *e.g.*, SiCl$_4$;[4]§ alternatively, dual mechanisms may operate.

This stereochemical dichotomy illustrates the relative importance of substituent electronic and ring strain effects in controlling displacement stereochemistry.[10] Previous studies on phosphoranes have shown that highly electronegative groups prefer axial (*a*), and electropositive groups, *e.g.*, alkyl or aryl, equatorial (*e*) positions.[11] Taking into consideration the strain introduced when a small ring spans the *ee* positions, the initial phosphorane resulting from *a* attack of hydroxide on the *benzyl*phospholanium ion is predictably one in which the ring spans the *ae* positions, and by avoiding the unfavourable *ee* disposition of the ring, retention stereochemistry for *benzyl* displacement is thus assured.[2,10] However, when both the nucleophile and the departing group (in the present instance, trichlorosilyl anion and trichlorosiloxide ion, respectively) are highly electronegative relative to the "non-reacting" ligands, a competition arises between a ring terminus and an electronegative group for the remaining apical position, to relieve ring strain and stereoelectronic strain, respectively. For the phospholanium (in contradistinction to the phosphetanium) system, relief of stereoelectronic strain more than compensates for the induced ring strain, and inversion of configuration should thus be the norm for five and higher membered ring systems.[12]



SCHEME. Reagents: (i) PhSiH$_3$; (ii) Si$_2$Cl$_6$–benzene for 0·5h at room temp.; (iii) PhCH$_2$Br followed by 1·0 N-NaOH; (iv) H$_2$O$_2$. The *cis*- and *trans*-designations are arbitrary; they represent relative configurations and are not intended to denote absolute stereochemistry. The numbers found below compounds (**1a**, **b**) and (**2a**, **b**) represent the diastereomeric ratios (± 5%), determined as stated in the text.

A similar stereochemical dependence on the nature of the leaving and entering groups has been noted in the alkaline hydrolysis of the benzyl- and ethoxy-t-butylmethylphenylphosphonium ions: the former[13] is hydrolysed with predominant retention and the latter[14] with predominant inversion of configuration of configuration. In

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† All new compounds gave acceptable elemental analyses and n.m.r. spectra consistent with their reported structures.

‡ Assuming retention of configuration for the H$_2$O$_2$ oxidation (ref. 6), inversion and retention of configuration for the Si$_2$Cl$_6$ and PhSiH$_3$ reductions, respectively, are established, irrespective of the stereochemical course of quaternization. Stereochemical assignments for the hydrolysis of the benzyl salts entail the additional assumption of retention of configuration for alkyl halide quaternization (ref. 6).

§ In support of this possibility, the phosphine oxide is epimerized by SiCl$_4$ (ref. 4), as well as by LiAlH$_4$ (ref. 7) and N$_2$O$_4$ (ref. 8), to give approximately the same (50 : 50) epimeric mixture. The phosphine is also epimerized by SiCl$_4$ (ref. 4) (**2a** :**2b** = 45 : 55).

this case ring strain is replaced by the steric effect of the t-butyl group in controlling displacement stereochemistry.

We thank the Air Force Office of Scientific Research and the National Science Foundation for support of this work, the National Aeronautics and Space Administration for a predoctoral fellowship (W.E.), and NATO and CNRS for a postdoctoral fellowship (G.C.).

(*Received, April 20th*, 1970; *Com.* 567.)

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