t-Butylphosphonium Salts: Nucleophilic Displacement at Phosphorus with Inversion of Configuration

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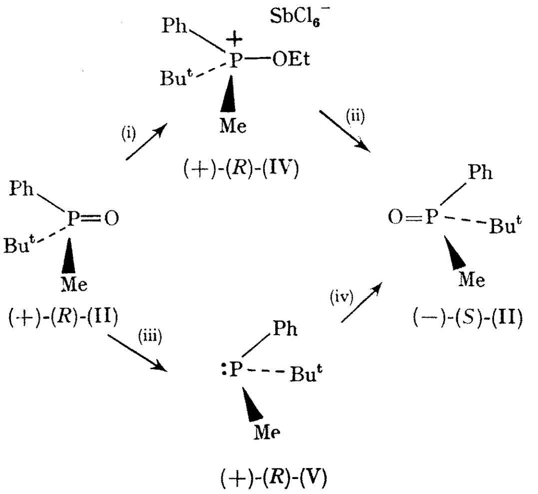
Summary The stereochemical direction (retention or inversion) of nucleophilic displacements at phosphorus in acyclic t-butylphosphonium salts depends on the nature of the leaving group.

DISPLACEMENT of the benzyl group in the alkaline hydrolysis of benzyl-t-*butyl*methylphenylphosphonium iodide (I) occurs with predominant retention of configuration on phosphorus,[1] in contrast to benzyl*ethyl*methylphenylphosphonium iodide, which undergoes the same reaction with inversion.[2] However, we find that other nucleophilic displacements at phosphorus in acyclic t-butylphosphonium salts proceed normally, *i.e.* with inversion.

Reaction of diastereomerically pure menthyl (*S*)-methylphenylphosphinate,[3] $[\alpha]_D - 94°$ (benzene), with t-butyllithium afforded (*R*)-t-butylmethylphenylphosphine oxide (II), $[\alpha]_D + 14{\cdot}9°$ (methanol), 71% optically pure by integration of ^{1}H n.m.r. signals due to enantiotopic methyl protons in (+)-1-phenyl-2,2,2-trifluoroethanol (III).[4] Loss of stereospecificity in the reaction of phosphinates with organolithium reagents has been noted before.[5] Ethylation (Scheme) and alkaline hydrolysis of the ethoxyphosphonium salt (IV), $[\alpha]_D + 19°$ (acetone), yielded (*S*)-(II), $[\alpha]_D - 14{\cdot}6°$

(methanol). The hydrolysis therefore proceeds with complete, or nearly complete, inversion of configuration.



SCHEME. Reagents: (i) $Et_3O^+SbCl_6^-/CH_2Cl_2$; (ii) $0\cdot5$M-NaOH in 50 *v/v* % aqueous dioxan for 10 min. at room temp.; (iii) Si_2Cl_6/benzene for 3 hr. at reflux temp.; (iv) H_2O_2.

Reduction of the same sample of (*R*)-(II) with hexachlorodisilane[6] afforded phosphine (V), $[\alpha]_D + 29\cdot5°$ (benzene), which, after oxidation with hydrogen peroxide, yielded (*S*)-(II), 62% optically pure by n.m.r. in (+)-(III). Partial racemization of phosphines and phosphine oxides under these reduction conditions has been noted before.[6] Since the oxidation proceeds with retention of configuration,[7] the reduction must proceed with net inversion.

In related but sterically unencumbered acyclic systems, displacement of ethoxide on phosphorus by hydroxide,[8] and displacement of trichlorosiloxide on phosphorus by trichlorosilyl anion (the inversion step in the reduction sequence),[6] also proceed with inversion of configuration. It follows that the anomalous stereochemistry (retention) observed[1] in the displacement of benzyl anion by hydroxide in (I) has its origin not only in the presence of the t-butyl group but is crucially dependent on the nature of the leaving group. We suggest that where the attacking nucleophile X (hydroxide, trichlorosilyl anion) and the displaced group Y (ethoxide, trichlorosiloxide) are both significantly more electronegative than alkyl or aryl, the lowest energy pathway leads, by way of apical attack, to an intermediate phosphorane in which X and Y occupy apical positions.[9] If loss of Y is an energetically favourable process relative to pseudorotation, the displacement will thus result in inversion of configuration. However, as in the case of benzyl, when Y is neither electronegative nor a good leaving group, these constraints are removed and pseudorotation may, *when steric factors favour the process*, lead to racemization and/or retention.

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