Product Control in Nucleophilic Substitution at Tetrahedral Phosphorus by the Relative Apicophilicity of the Nucleophile

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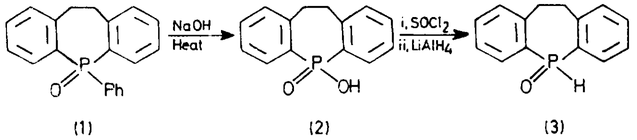
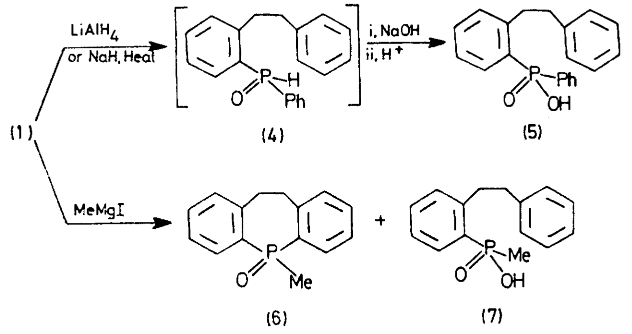
Summary A chemical probe for the study of the relative apicophilicity of groups in a trigonal bipyramidal phosphorane is suggested.

THE secondary phosphine oxide (**3**), required in a synthetic project, was prepared as shown in Scheme 1. An attempt[1] to prepare (**3**) directly from (**1**) by fusion with either $LiAlH_4$ or NaH, followed by oxidation,[2] resulted in the phosphinic acid (**5**) in good yields (Scheme 2). This was somewhat unexpected, since fusion of (**1**) with NaOH yielded only the heterocyclic phosphinic acid (**2**). Treatment of (**1**) with MeMgI in benzene gave a *ca.* 1:1 mixture of (**6**) and (**7**) (Scheme 2). These results could be rationalised as shown in Scheme 3.

Occasionally, square pyramidal rather than trigonal bipyramidal geometry has been found for stable phosphoranes[3a] or pentaco-ordinated intermediates (or transition states)[3b] in substitution reactions at phosphoryl phosphorus. However, it is usually assumed that bipyramidal intermediates are formed in such reactions, their formation and decomposition take place by apical attack and departure, and possible rearrangements occur *via* pseudorotation.[4] These assumptions are supported by kinetic, energetic,[4] and structural and permutational isomerisation studies.[5,6] Recently, an apicophilicity scale has been defined and tentatively outlined.[4]

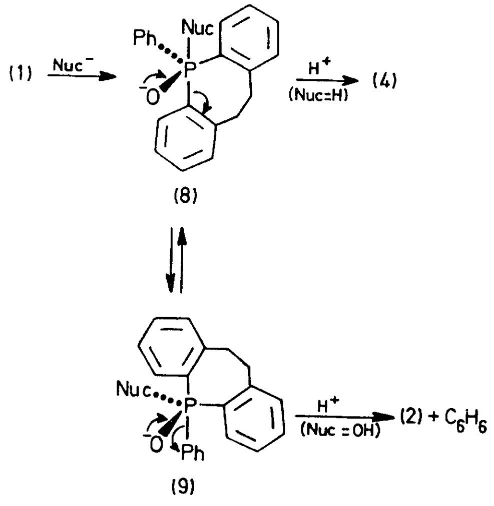


Scheme 1



Scheme 2

We now suggest that the relative apicophilicity of a nucleophile would be the major factor in product control where competing reactions proceed through a trigonal bipyramid, in systems such as the one shown in Scheme **3**. Apart from its application in rationalising the experimental results described, this approach can be used in a given system, *e.g.* (**1**), to study the relative apicophilicity of a nucleophile (group) by products analysis. Relatively high apicophilic nucleophiles would lead to substitution at tetrahedral phosphorus without (or with little) pseudorotation of the intermediate trigonal bipyramid, and with inversion of configuration at phosphorus[7] (measurable in chiral compounds). Accordingly, poorly apicophilic nucleophiles would give products *via* pseudorotated intermediates, accompanied by retention of configuration at phosphorus.



Scheme 3

Intermediate (or transition state) (**8**) (Scheme 3) provides a system free from ring-strain and steric hindrance which affect the permutational isomerisation of a trigonal bipyramid.[4] Thus, ring retention or ring fission, which are easily determined, *e.g.* by n.m.r. spectroscopy, are controlled by the relative apicophilicity of the nucleophile and the stability of the leaving group as a carbanion.[8] Consequently, we find O^-† to be a poorer apicophile than Me,[3b] while H is a relatively highly apicophilic atom.

(*Received*, 19*th November* 1975; *Com.* 1293.)

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† Under our reaction conditions, OH^- attack at phosphorus is almost certainly followed by a fast deprotonation (W. E. McEwen, 'Topics in Phosphorus Chemistry,' vol. 2, eds. M. Grayson and E. J. Griffith, Wiley, New York, 1965, p. 7).

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