Alkaline Hydrolysis of Alkoxy(methylthio)phosphonium Salts with Retention of Configuration at Phosphorus

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Summary Alkaline hydrolysis, with displacement of the methylthio-group, of the alkoxy(methylthio)phosphonium salts (2) and (6) proceeds with retention of configuration at phosphorus.

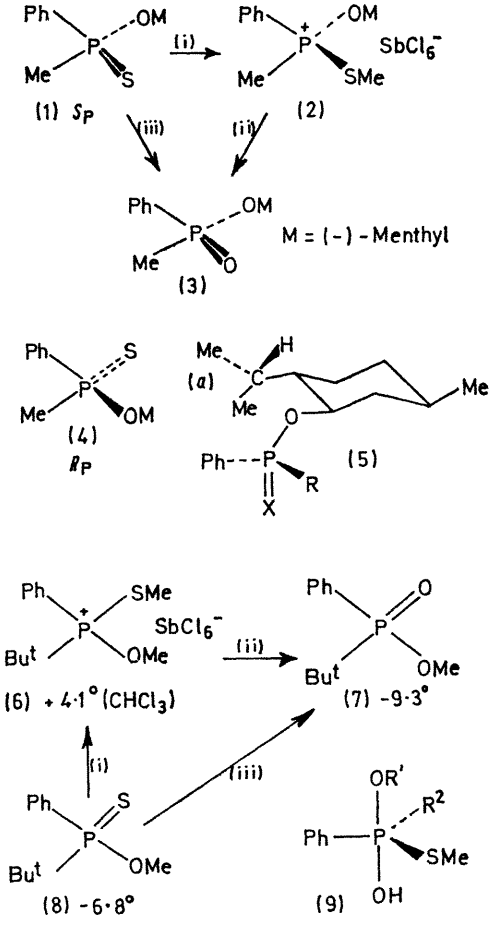
NUCLEOPHILIC substitution in acyclic phosphorus compounds usually proceeds with inversion of configuration at phosphorus, a consequence of apical attack and of the preference of electronegative substituents for the apical positions in the trigonal bipyramidal intermediates. We now report that hydrolysis of the salt (2) to give the phosphinate (3), and of the salt (6) to give the phosphinate (7), both hydrolyses involving displacement of the methylthio-group, proceed with *retention* of configuration at phosphorus.

O-Menthyl $(S)_P$-methylphenylthiophosphinate (1) was isolated by column chromatography and fractional crystallisation of the mixed diastereoisomers. It had m.p. 87—89° (from methanol), $[\alpha]_D$ −50·1°,† τ ($CDCl_3$) 1·80—2·63 (5H, m), 5·20—5·83 (1H, m), 8·05 (3H, d, J_{PH} 14 Hz), 8·17—8·87 (9H, m), and 8·87—9·53 (9H, m), and on alkaline hydrolysis gave (*R*)-(+)-methylphenylthiophosphinic acid[1] (dicyclohexylamine salt $[\alpha]_D$ + 11·3°). The n.m.r. spectrum of the other isomer, obtained on a mixture containing 70% of this isomer, showed τ ($CDCl_3$) 8·12 (3H, d, J_{PH} 14 Hz) and 9·56 (3H, d, J 7 Hz). The n.m.r. spectra of the diastereoisomers are very similar to those of the corresponding phosphinates; the second isomer (4) showed the high-field *pro*-(*S*)-methyl [(*a*) in (5)] characteristic[2,3] of the configuration (5) and is therefore the $(R)_P$-isomer.

Alkylation of (1) gave the hexachloroantimonate (2), τ ($CDCl_3$) 1·77—2·34 (5H, m), 5·17—5·77 (1H, m), 7·37 (3H, d, J_{PH} 12 Hz), 7·55 (3H, d, J_{PH} 15 Hz), 7·70—8·80 (9H, m), 8·80—9·34 (9H, m), which on alkaline hydrolysis in aqueous dioxan, gave menthyl $(R)_P$-methylphenylphosphinate (3) having the recorded[4] n.m.r. spectrum.

Alkylation of *O*-methyl phenyl-t-butylthiophosphinate‡ (8), $[\alpha]_D$ −6·8°, gave the hexachloroantimonate (6) which on alkaline hydrolysis at 0° gave the phosphinate (7), $[\alpha]_D$ −9·3°. Oxidation of (8), $[\alpha]_D$ −6·8°, with hydrogen peroxide in refluxing ethanol or with *m*-chloroperbenzoic acid in dichloromethane also gave the phosphinate (7), $[\alpha]_D$ −9·3°. That these oxidations involve retention of configuration at phosphorus is shown by the similar oxidations of the thiophosphinate (1) to the phosphinate (3).

The retention of configuration at phosphorus in the hydrolyses of (2) and (6) is consistent with attack of hydroxyl opposite to the alkoxy-group to give the intermediates (9) which then either lose SMe directly from an equatorial position or pseudorotate before losing this group from an



Reagents: (i) $Me_3O^+SbCl_6^-$; (ii) OH^-; (iii) H_2O_2 or RCO_3H

apical position. The preferential formation of the intermediates (9) may be a consequence of the greater electronegativity of the alkoxy over the alkylthio-group, despite the latter being the better leaving group.

(*Received, May 3rd,* 1971; *Com.* 688.)

† All rotations in methanol unless otherwise stated.

‡ The thiophosphinic acid was resolved *via* the quinine salt. Optically pure acid, as shown by the n.m.r. spectra of the salts with (−)-α-phenylethylamine,[5] had $[\alpha]_D$ ± 21·4°. The ester (8) was obtained from (+)-acid *via* the thiophosphinyl chloride, a process nvolving considerable racemisation. Alkaline hydrolysis of the ester (8), $[\alpha]_D$ −6·8°, gave thiophosphinic acid having $[\alpha]_D$ +4·2.

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