Transesterification of Alkyl Phosphinates

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Summary Alkyl esters of phosphinic acid [$HOP(O)H_2$] undergo rapid transesterification at room temperature with primary, secondary, and tertiary aliphatic alcohols but not with phenol; trimethyl phosphate, dimethyl phosphonate, and the methyl esters of substituted phosphinic acids do not react under these conditions.

Though esters of both three-co-ordinate P^{III} and four-co-ordinate P^{IV} acids will undergo transesterification with added alcohols,[1] these reactions require fairly vigorous conditions and proceed best in the presence of catalysts, usually strong acids or bases. In marked contrast, we have observed that alkyl phosphinates (**1**) undergo rapid transesterification with aliphatic alcohols at room temperature in the absence of added catalysts. Thus, addition of a dry aliphatic alcohol to methyl or ethyl phosphinate (prepared from phosphinic acid and the corresponding trialkyl orthoformate[2,3]) affords a mixture of esters. This would seem to be an equilibrium mixture as the ratio of esters is unaltered on further standing.

$$\underset{(\mathbf{1})}{R^1OP(O)H_2} + R^2OH \rightleftharpoons R^2OP(O)H_2 + R^1OH$$

$$(R^1 = Me, Et;\ R^2 = Pr^i, Bu^t, PhCH_2)$$

The mixture is easily analysed by Fourier transform ^{31}P n.m.r. spectroscopy which also allows the unequivocal assignment of structure and the determination of approximate (±10%) values for the equilibrium constants by integration of the undecoupled spectra (Table).

TABLE. ^{31}P N.m.r. spectral data for the reaction $MeOP(O)H_2 + ROH \rightleftharpoons ROP(O)H_2 + MeOH$

R	δ[a]	$^1J_{PH}$[b]	$^3J_{POCH}$[b]	K_{eq}[c] (37 °C)
Me	19·2	569	13	—
Et	15·8	570	10	1·2
Pr^i	11·8	570	10	1·1
Bu^t	8·0	560	—	3·8
t-C_5H_{11}	6·3	552	—	0·58
$PhCH_2$	15·1	575	11	0·28

[a] In p.p.m. downfield of external H_3PO_4. These values vary with concentration by as much as ±0·5 p.p.m. [b] In Hz. [c] Mean of at least two determinations at different concentrations.

Particularly noteworthy is the ease of formation of t-butyl phosphinate; this would appear to be the first reported example of such a transesterification for any type of ester.

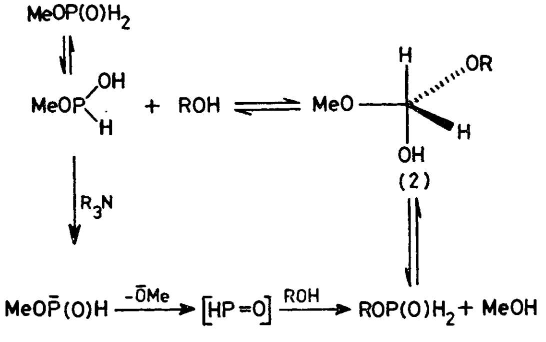
We have observed no uncatalysed exchange between t-butyl alcohol and dimethyl phosphonate or trimethyl phosphate even when they are refluxed together or heated in sealed tubes at 100 °C for several hours. Isopropyl alcohol does slowly exchange with dimethyl phosphonate and at molar concentrations comparable to the phosphinate reactions, the exchange of one methoxy for isopropoxy has a half-life of 6 h at 87 °C. The phosphinate exchange reaction is not immune to steric effects, however, as these presumably account for the low value of K_{eq} for 2-methylbutan-2-ol. Also with this alcohol the reaction is relatively slow in reaching equilibrium being only *ca.* 50% complete in samples examined as soon as possible (3—5 min) after mixing, whereas with the other alcohols used, reaction is essentially complete in the same period.

The reaction fails with phenol; even when a large excess of phenol is present no new compound can be detected by ^{31}P n.m.r. spectroscopy (limit *ca.* 1%). No exchange is observed, even on heating, between Bu^tOH and the methyl esters of phenylphosphinic, diphenylphosphinic, dimethoxymethylphosphinic, or 2-methoxycarbonylethylphosphinic acids.

The mechanism of the exchange reaction is obscure as indeed are the transesterification reactions of all phosphorus acids. Simple S_N2 type displacement at phosphorus seems unlikely in view of the relative insensitivity to steric effects. A possible explanation is that the reaction proceeds *via* a phosphorane intermediate (**2**), formed by reaction of the three-co-ordinate tautomer of the ester with the added alcohol. Intermediates analogous to (**2**) have been observed in the reactions of both three-co-ordinate P^{III}[4] and four-co-ordinate P^{IV}[5] species and hydroxy compounds. Recent work suggests that the three-co-ordinate tautomer is more readily formed from phosphinates than from phosphonates[3] and this feature, combined with the reduced steric demands of the three-co-ordinate forms, may account for the ease with which the reaction proceeds.

If the formation and decomposition of the intermediate phosphorane were concerted processes, the phosphorane (**2**) would be the most likely structure in view of the high apicophilicity of hydrogen,[6] and the anticipated diradial entry and departure of ROH.[7] Alkyl- or aryl-phosphinic acid esters would be expected to form an intermediate with the alkyl or aryl group in the radial position and would require at least one permutational isomerisation before collapse.† It should be noted, however, that no five-co-ordinate material could be seen by ^{31}P n.m.r. spectroscopy.

The thermal instability of the esters[2] and the complex nature of the mixture[3] makes more detailed study difficult. However, the rate of equilibration with 2-methylbutan-2-ol is apparently unaffected by the presence of phosphinic acid but is accelerated by ethyldi-isopropylamine (0·2 mol per mol of ester). This appears to be a genuine catalytic effect since K_{eq} is unaffected. It is unlikely that such a weak base would generate appreciable amounts of alkoxide ion and the formation of oxophosphine (**3**) by loss of an alkoxy group from the mono-anion of the alkyl phosphinate is suggested to account for this (Scheme). It seems unlikely, however, that (**3**) is responsible for the transesterification under neutral or acidic conditions.



SCHEME

The t-alkyl phosphinates are stable to added amines unlike the methyl and ethyl esters. This feature should considerably extend their synthetic utility.

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