Specific Dealkylation of Phosphonate Esters using Iodotrimethylsilane

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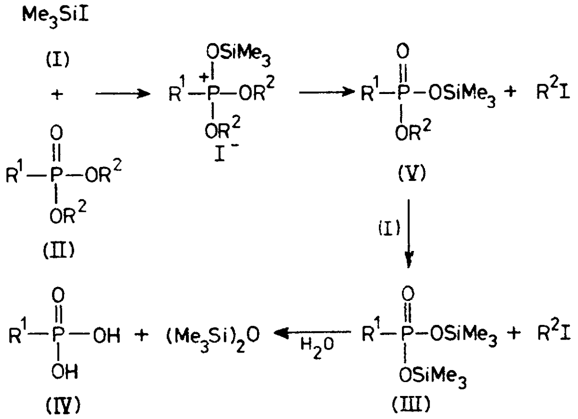
Summary Phosphonic acid dialkyl esters are transformed in high yield into the corresponding bistrimethylsilyl esters on treatment with iodotrimethylsilane; subsequent hydrolysis of these products affords the parent phosphonic acids under mild conditions without influence on a variety of other functional groups.

THE general development of phosphonates as analogues of natural phosphates[1] has been restricted by the terminal difficulties in their synthesis associated with the hydrolysis of phosphonate diesters to provide the parent phosphonic acids.[1,2] A variety of methods has been employed to circumvent the vigorous acidic conditions[3] usually required for such ester hydrolyses,[1] among which hydrogenolysis of aryl esters has been notably successful.[4]

Rabinowitz has devised the use of chlorotrimethysilane for de-esterification[5] though difficulties have been noted in its application to nucleoside,[3] carbohydrate,[6] and lipid[7] phosphonates. Bromotrimethylsilane is much more reactive and dealkylated simple phosphonate esters quantitatively[8] at 25 °C, though in our hands it appeared to be incompletely selective for dealkylation of phosphonate esters in species having multiple phosphonate and carboxylate ester groups. We have found the readily accessible iodotrimethylsilane to provide selective dealkylation of phosphonate diesters without modification of carboxylate esters[9] or a variety of other functionalities.†

The injection of 2 equiv. of iodotrimethylsilane[10] (I) into a solution of the dialkyl phosphonate (II) in dry chloroform or carbon tetrachloride under nitrogen initially at −40 °C and then at room temperature leads rapidly to the bistrimethylsilyl phosphonate esters (III) in virtually quantitative yield, as gauged by ^{1}H n.m.r. analysis of reactions performed in deuteriochloroform solution. After *in vacuo* removal of alkyl iodide and any excess of reagent the product can be either isolated by distillation or treated directly with water or methanol to provide the free phosphonic acids (IV), conveniently characterised as their *p*-anisidine salts.‡ Under these conditions, the reagent (I) has no effect on multiple carbon–carbon bonds (IIb, IIc), bromoalkane (IId), or ethoxycarbonyl (IIe) functions. It is especially valuable for dealkylation of acylphosphonate (IIf) and aroylphosphonate (IIg) diesters.

Attempts to isolate monoalkyl trimethylsilyl phosphonate intermediates (V) to achieve the monodealkylation of (II) using 1 equiv. of (I) led to mixtures of species (II), (III), and (V) which could be separated only by analytical g.l.c. It is thus apparent that the transformation of (V) into (III) is competitive with its formation from (II) as shown in the Scheme.



a; R^1 = PhCH$_2$, R^2 = Me or Et
b; R^1 = CH$_2$=CH, R^2 = Me or Et
c; R^1 = HC≡C, R^2 = Me or Et
d; R^1 = BrCH$_2$CH$_2$, R^2 = Me or Et
e; R^1 = (EtO$_2$C)$_2$CHCH$_2$, R^2 = Me or Et
f; R^1 = MeCO, R^2 = Me or Et
g; R^1 = PhCO, R^2 = Me or Et

SCHEME

Preliminary results indicate that aryl esters of phosphoryl acids are not cleaved by the reagent (I) which thus ought to provide a means of selective dealkylation of mixed alkyl aryl esters of phosphoric and phosphonic acids.

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† *Note added in proof:* a communication describing a related method for dealkylation of phosphonate esters has appeared since submission of this manuscript: T. Morita, Y. Okamoto, and H. Sakurai, *Tetrahedron Letters*, 1978, 2523.

‡ All new compounds have been characterised by spectroscopic and microanalytical methods.

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