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A CONVENIENT DEALKYLATION OF DIALKYL PHOSPHONATES BY CHLOROTRIMETHYLSILANE IN THE PRESENCE OF SODIUM IODIDE

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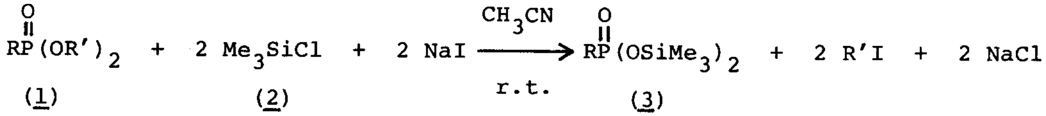
The efficient and convenient conversion of carboxylic acid esters to the corresponding acids using iodotrimethylsilane under mild conditions has been reported by some workers.[1)] Phosphonic acid silyl esters are also easily hydrolyzed by treating with water under mild conditions to give the corresponding phosphonic acids quantitatively.[2)] Recently, it has been reported that dialkyl phosphonates (1) reacted with chlorotrimethylsilane (2) or bromotrimethylsilane to afford the corresponding bis(trimethylsilyl) phosphonates (3) by Rabinowitz[2)] or Mckenna.[3)] This method via the silylation of 1 is very useful for the preparation of phosphonic acids having labile functional groups[4)] or the phosphonic acid derivatives of nucleosides, lipids, and carbohydrates.[5)] The silylation of 1 with 2 requires refluxing for several days with the large exess amount of the reagent, whereas the yield of the silyl esters (3) is less satisfactory. Bromotrimethylsilane is more reactive and the silylation of 1 is completed within one hour at room temperature. However, it must be prepared via two steps from readily available chlorosilane (2).[6)] Our interest was forcused on the facile dealkylation of phosphonates (1) with an equivalent amount of 2 under mild conditions.

We investigated the reaction of many kinds of 1, especially those having labile functional groups, with 2 in the presence of sodium iodide. When 2 (60 mmol) was added to phosphonates (1a - 1i)(30 mmol) in the presence of sodium iodide

(60 mmol) in acetonitrile (30 ml) with stirring at room temperature for 15 min, the exothermic reaction occurred immediately resulting in the precipitation of sodium chloride to afford the corresponding silyl phosphonates (3) in good yields



$$\underset{(1)}{\mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{P}}(\mathrm{OR'})_2} + \underset{(2)}{2\ \mathrm{Me_3SiCl}} + 2\ \mathrm{NaI} \xrightarrow[\mathrm{r.t.}]{\mathrm{CH_3CN}} \underset{(3)}{\mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{P}}(\mathrm{OSiMe_3})_2} + 2\ \mathrm{R'I} + 2\ \mathrm{NaCl}$$

The reaction of the dimethyl esters (1a - 1d), which could be monitored by taking the NMR spectrum of the mixture, went essentially to completion within 15 min, but further warming up to 40 °C for 15 min was required for the diethyl esters (1e - 1i). The results are summarized in Table 1.

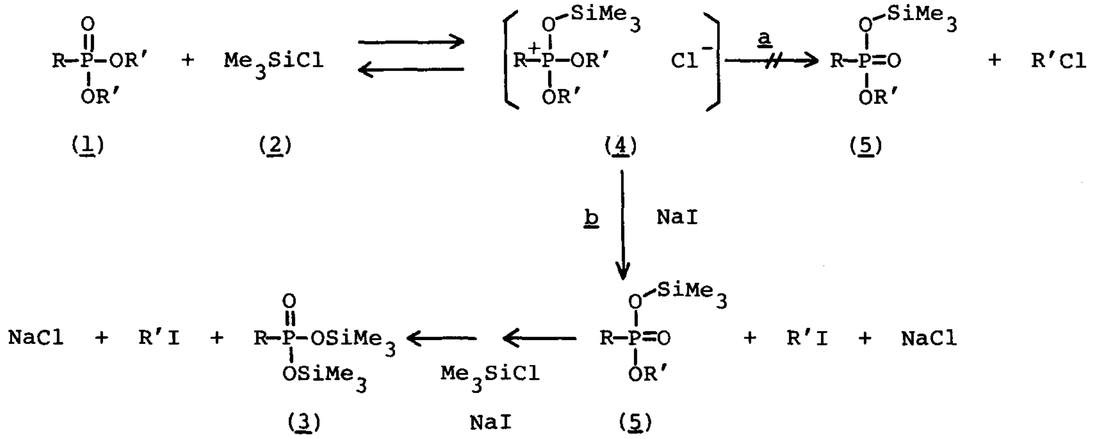
Table 1 Reaction of dialkyl phosphonates with chlorotrimethylsilane

Compound	R	R'	NaI (Equiv.)	Temp. (°C)	Time (min)	Yield[a)] (%)
1a	$PhCH_2$	Me	1.0	r.t.	15	100, 78[b)]
1b	Cl_3C	Me	1.0	r.t.	15	100
1c	$(MeO)_2CH$	Me	1.0	r.t.	15	100
1d	EtOCH=CH	Me	1.0	r.t.	15	100
1e	MeCO	Et	1.0	20 - 40	30	>98
1f	$MeOCOCH_2$	Et	1.0	20 - 40	30	>98
1g	Et_2NCO	Et	1.0	20 - 40	30	>98
1h	H_2NCOCH_2	Et	1.0	20 - 40	30	>98
1i	$NCCH_2$	Et	1.0	20 - 40	30	>98
1i	$NCCH_2$	Et	1.1	r.t.	15	100

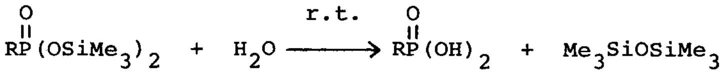
a) Yields were estimated on the reaction mixtures by NMR in CCl_4. b) Yield is for isolated product by distillation. In all cases, the silyl esters were identified by comparison (NMR) with authentic samples.[7)]

NMR spectrum on the reaction mixture exhibited the quantitative formation of methyl or ethyl iodide from 1a - 1d or 1e - 1i respectively. Using potassium bromide in the place of sodium iodide, silylation of 1i by 2 little occurred even at 60 °C for 1 h. Other solvents such as carbon tetrachloride or chloroform were unsuitable for this reaction.

We proposed the following mechanism for this dealkylation of phosphonates (1). Initial attack of phosphinyl sp^3 oxygen atom on silicon atom of 2, a fast and reversible step, forms a phosphonium type intermediate (4). Secondly, though the competitive attacks between chloride and coexistent iodide anion on 4, a slow and irreversible step a and b, are permitted, the reaction of 4 with more nucleophilic iodide anion (step b) occurs preferentially to give trimethylsilylated ester (5) and alkyl iodide. Bis(trimethylsilyl) phosphonate (3) is formed by a repetition of this process.



The obtained silyl esters (3a - 3i) readily converted to the corresponding phosphonic acids (6a - 6i) under mild conditions by the following manner. The resulting sodium chloride was filtered off and the silyl esters (3) were obtained by evaporating low boiling materials under reduced pressure. The hydrolysis of the residue by treating with water at room temperature gave the corresponding phosphonic acids (6a - 6i) immediately which were isolated as anilinium salts in 80 - 85 % overall yields.



$$\mathrm{R\overset{O}{\overset{\|}{P}}(OSiMe_3)_2 \;+\; H_2O \xrightarrow{r.t.} R\overset{O}{\overset{\|}{P}}(OH)_2 \;+\; Me_3SiOSiMe_3}$$

(**3**) (**6**)

The products were identified by comparison with authentic samples.[7)] Further application of this method, using chlorosilane (**2**) in the presence of sodium iodide, for other synthetic transformations are now in progress.

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7) Authentic samples were prepared by the reaction of dialkyl phosphonates with bromotrimethylsilane, followed by the hydrolysis of the resulting bis(trimethylsilyl) phosphonates.