

A MILD AND FACILE SYNTHESIS OF ALKYL- AND ARYLPHOSPHONYL DICHLORIDES
UNDER NEUTRAL CONDITIONS. REACTION OF BIS(TRIMETHYLSILYL) PHOSPHONATES
WITH PCl_5

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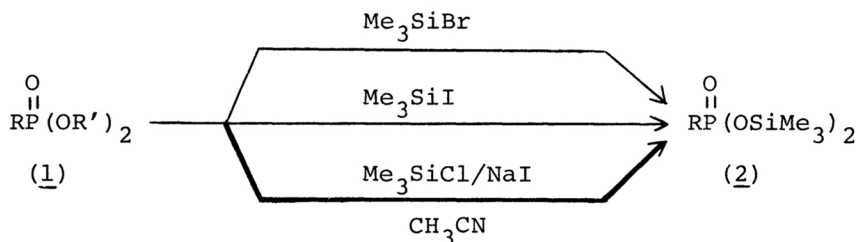
Bis(trimethylsilyl) phosphonates, which are prepared from the dialkyl esters with chlorotrimethylsilane/sodium iodide, are transformed in high yields into the corresponding phosphonyl dichlorides on the treatment with phosphorus pentachloride under mild and neutral conditions.

Various kinds of phosphonic acids and their derivatives, especially analogues of natural phosphates, are of current interest with regard to the synthesis and biological investigation.¹⁾ Phosphonyl dichlorides are well known as important intermediates for the preparation of the amides, thiophosphonyl dichlorides, and esters, especially phosphonate esters which can not be easily obtained by the Arbuzov reaction.^{2,3)}

Alkylphosphonyl dichlorides are conventionally prepared by the reaction of alkyl chlorides with phosphorus trichloride in the presence of aluminium chloride via two tedious steps. However, this method is inapplicable to vinyl halides and results in the formation of isomerized products in the case of *n*-alkyl chlorides ($> \text{C}_3$).⁴⁾ One of the most common route to the dichlorides is the reaction of phosphonic acids with phosphorus pentachloride (PCl_5) under acidic conditions. The yields are generally 60 - 80 % and in some cases, chlorination of aromatic nucleus occurs simultaneously.⁵⁾ Although dialkyl phosphonates, $\text{RPO}(\text{OR}')_2$ ($\text{R}' = \text{Me}$ or Et), are generally more readily obtained from trivalent phosphorus compounds by the direct reactions than the free acids, the conversion of dialkyl phosphonates into the dichlorides is usually accomplished only by heating them with PCl_5 at 100 - 120 °C for several hours.⁶⁾ Moreover, this preparative method is

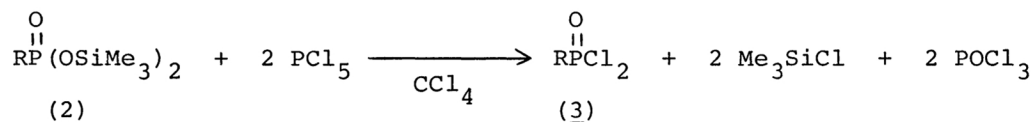
frequently accompanied by side reactions such as replacement of α -hydrogen of phosphonates with chlorine⁷⁾ and the yields of product are not always satisfactory.

On the other hand, new methods for the dealkylative silylation of dialkyl phosphonates using bromo- or iodotrimethylsilane have been recently developed⁸⁾ and widely applied to the synthesis of multifunctional phosphonic acids.⁹⁾ Our previous paper demonstrated the use of chlorotrimethylsilane/sodium iodide as a reagent for the dealkylation of dialkyl phosphonates (1) under mild and neutral conditions.¹⁰⁾



We wish to report here a very efficient method for the conversion of (1) into the phosphoryl dichlorides (3) via the corresponding silyl esters (2).

Bis(trimethylsilyl) phosphonates (2), which are conveniently and quantitatively prepared from (1), react smoothly with PCl_5 at 20 - 30 °C in carbon tetrachloride to give the corresponding dichlorides (3) in high yields.



Silyl phosphonate (2) (5 mmol) was added dropwise to PCl_5 (10 mmol) suspended in dry carbon tetrachloride (10 ml) with stirring at room temperature. The reaction proceeded exothermically and in most cases was essentially completed within 30 min. Dichloromethane is also suitable as solvent in this reaction. After removal of the resulting phosphoryl chloride and chlorotrimethylsilane in vacuo, the desired product (3) was isolated by distillation. The results of these reactions are summarized in Table. The products were characterized by comparison (bp, IR, NMR) with the authentic samples. Although volatile phosphoryl chloride and chlorotrimethylsilane were formed simultaneously, these compounds are unreactive to other functional groups of (3) under the present conditions and the product (3) was essentially pure. The dichloride (3) was treated directly with appropriate nucleophiles to provide the other phosphonic acid derivatives.

Table. Reaction of bis(trimethylsilyl) phosphonate with PCl_5 ^{a)}

| Compound | R | Time (h) | Yield (%) ^{b)} | Bp (°C/mmHg) |
|-----------|-----------------------------|----------|-------------------------|--------------|
| <u>3a</u> | Me | 1.0 | 98 | 65 - 67/20 |
| <u>3b</u> | Et | 0.5 | 95 | 54 - 55/10 |
| <u>3c</u> | Cyclohexyl | 1.0 | 81 | 90 - 92/1 |
| <u>3d</u> | PhCH_2 | 1.0 | 85 | 130 - 132/2 |
| <u>3e</u> | $p\text{-EtC}_6\text{H}_5$ | 0.5 | 82 | 120 - 123/2 |
| <u>3f</u> | EtOCOCH_2 | 0.5 | 61 ^{c)} | 119 - 122/3 |
| <u>3g</u> | $\text{CH}_2=\text{CH}$ | 0.5 | 95 | 67 - 69/15 |
| <u>3h</u> | $\text{CH}_2=\text{CHCH}_2$ | 0.5 | 94 ^{d)} | 70 - 71/12 |

a) Under these conditions, the reagent (PCl_5) has no effect on the benzylic hydrogen in 3d and 3e. b) Isolated yield.

c) The dichloride (3f) decomposed partially during the distillation.

d) Dichloromethane was used as the solvent in the place of CCl_4 .

When one equiv. of PCl_5 was used for the reaction, the yield of (3) was reduced (< 40 %) and viscous residue was formed in a considerable amount.

The present reaction system has an additional advantage that the produced chlorotrimethylsilane is recovered by distillation and can be utilized in the dealkylation of (1) again. Our new method can be widely employed in the synthesis of many kinds of phosphonyl dichlorides under neutral conditions.

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