

Methods of Synthesis of *O,O*-Bis[trimethylsilyl] Phosphorothiolates

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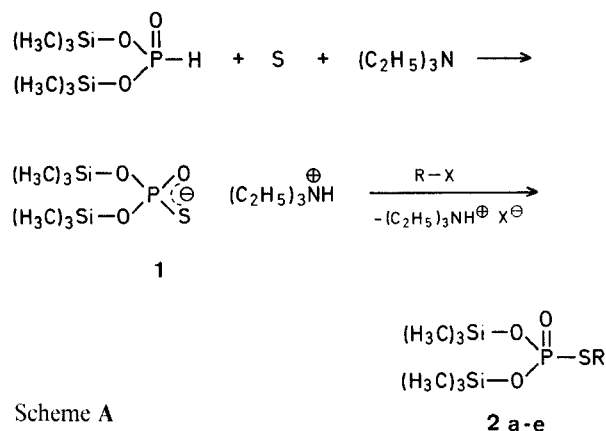
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There is growing interest in phosphoroorganic compounds containing silyl groups, as these substances give new possibilities in synthetic phosphorus chemistry. One of the properties important in this respect is the chemical lability of silyl groups which can be removed under mild conditions, without affecting the skeleton of the phosphorus compound. In connection with our interest in organosulfurphosphorus compounds, we examined several routes potentially leading to *S*-alkyl *O,O*-bis[trimethylsilyl] phosphorothiolates. Silyl groups in these compounds undergo hydrolytic or alcoholic cleavage to give P—OH functions which makes them convenient precursors for acids of the type (HO)₂P(O)SR and their salts.

Hata and Sekine^{1,2} described a synthesis of this type of compound based on the reaction of disulfides with tris[trimethylsilyl] phosphite or its analogues and found that such compounds can be easily desilylated without cleavage of the phosphorus-sulfur bond.

The present paper describes several other preparations of *O,O*-bis[trimethylsilyl] phosphorothiolates, including salts of *O,O*-bis[trimethylsilyl]phosphorothioic acid, which can act as nucleophilic thiophosphorylating agents (Route 1) and *O,O*-bis[trimethylsilyl]phosphorylsulfenyl chloride with pronounced electrophilic character (Route 2). We have also examined an Arbuzov-type reaction between tris[trimethylsilyl] phosphite and organosulfenyl chloride (Route 3) and have extended the scope of Hata and Sekine's method described above (Route 4).

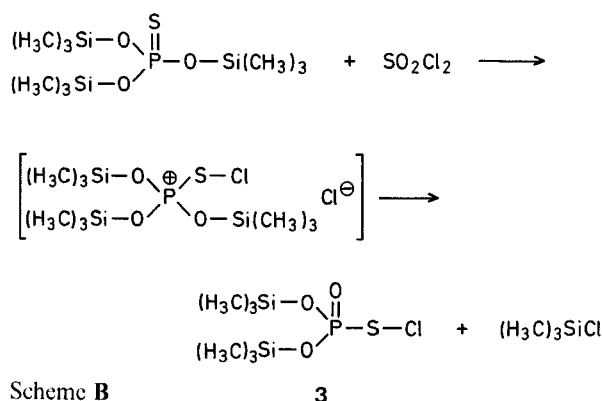
Route 1: The phosphorylation of organic halides with ammonium salts of *O,O*-bis[trimethylsilyl]phosphorothioic acid is a versatile and convenient method for *S*-alkyl *O,O*-bis[trimethylsilyl] phosphorothiolates. These salts may be obtained from bis[trimethylsilyl] phosphite according to Scheme A.



Scheme A

Triethylammonium *O,O*-bis[trimethylsilyl]phosphorothioate (**1**) was thus obtained in ~100% yield. Salt **1** forms white crystals which break down when exposed to the air but are stable if kept out of contact with the atmosphere, and dissolves easily in aromatic hydrocarbons and ethers; these solvents may be used as reaction media. The stability of **1** in benzene or diethyl ether solution is good (the solution darkens on standing for longer periods), in spite of the fact that silicon is a good electrophilic centre. However, any protolytic solvent decomposes the salt immediately. Salt **1** is a good thiophosphorylating agent in reactions with alkyl halides. Under the conditions used here, thiophosphorylation leads to the exclusive formation of a sulphur-carbon bond, as was found for the analogous reaction of *O,O*-dialkyl phosphorothioates³. The reaction between **1** and *n*-alkyl bromides proceeds smoothly at ambient temperatures and leads to the corresponding *S*-alkyl *O,O*-bis[trimethylsilyl] phosphorothiolate (~100% yield). The reaction is, however, subject to steric effects and the thiophosphorylation of secondary aliphatic bromides requires either a longer reaction time or a higher temperature. Alkyl bromides undergo thiophosphorylation more easily than the corresponding alkyl chlorides; reaction of **1** with *n*-propyl chloride in benzene in 80° gave only about 15% of the thiolate after 2 h, while the phosphorylation of *n*-propyl bromide at ambient temperature gave, after the same time, 70% of the thiolate.

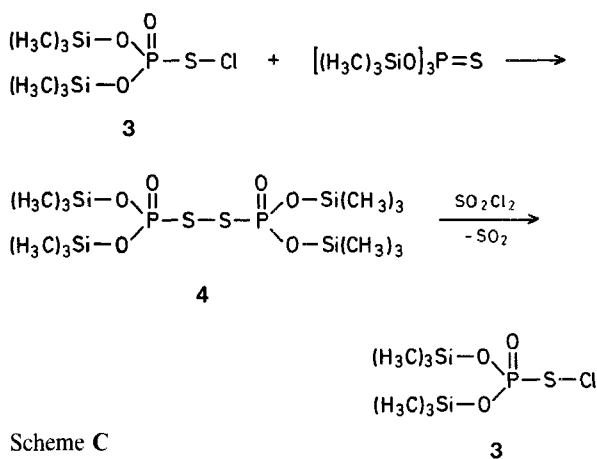
Route 2: *O,O*-Bis[trimethylsilyl]phosphorylsulfenyl chloride (**3**) may be obtained in 100% yield from tris[trimethylsilyl] phosphorothionate and sulfur chloride according to



Scheme B

a scheme similar to that described earlier⁴ for trialkyl phosphorothionates. Most probably an intermediate phosphonium salt is formed⁵ (Scheme B).

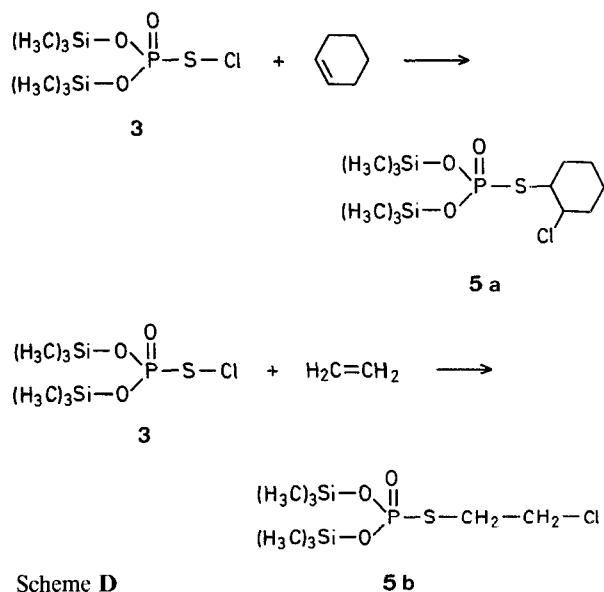
Scheme B represents a simplified mechanism of the formation of **3**. The sulfenyl chloride undergoes immediate reaction with the trisilyl phosphorothionate, which is in excess, giving di[bis(trimethylsilyl)phosphoryl] disulfide (**4**) in an analogous way to that described⁶. When the trisilyl phosphorothionate is consumed, further addition of the chlorinating agent results in splitting of the disulfide and **3** is reformed (Scheme C).



Scheme C

Thus no **3** appears in the reaction of the trisilyl phosphorothionate with SO_2Cl_2 when less than half the stoichiometric amount of chlorinating agent is used. Under these conditions, the reaction leads to a high yield of **4**, whose structure was confirmed by ^{31}P - and ^1H -N.M.R. spectra. Compound **3** appears to be less stable than its dialkyl analogues and a low temperature should be maintained during synthesis and the compound should be used immediately after preparation.

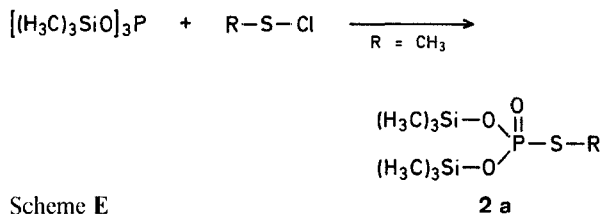
Compound **3** behaves similarly to other known phosphoryl-sulfenyl chlorides⁷, i.e., it undergoes addition to double bonds. The removal of the chlorotrimethylsilane, which is a by-product in the synthesis, is not necessary to bring about the addition. The reactions with ethene and with cyclohexene occur smoothly at low temperatures and lead to high yields of addition products (Scheme D).



Scheme D

The reaction of **3** with ethylmagnesium bromide follows rather complicated course and gives a variety of unidentified products.

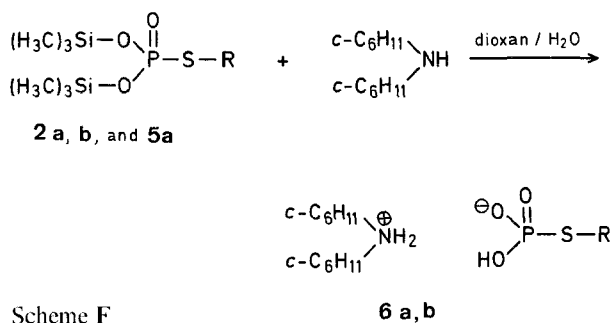
Route 3: The reaction of organosulfenyl chlorides with tris(trimethylsilyl) phosphite takes a course analogous to that of the reaction with trialkyl phosphite⁸, leading to the appropriate *O,O*-bis(trimethylsilyl) *S*-organyl phosphorothiolates, according to Scheme E.



Scheme E

This reaction, as was found for methanesulfenyl chloride, appears to be inferior to the other methods described here. An analogous reaction between the organosulfenyl chloride and bis(trimethylsilyl)phosphite does not lead to the expected phosphorothiolate.

Route 4: We have confirmed the usefulness of Hata and Sekine's method^{1,2} and have extended it to give *O,O*-bis(trimethylsilyl) *S*-methyl phosphorothiolate (**2a**) in 100% yield from tris(trimethylsilyl) phosphite and dimethyl disulfide. We also tried to obtain **2a** from an analogous reaction of the disulfide with the sodium salt of bis(trimethylsilyl) phosphite. The method cannot, however, be recommended as the reaction leads to many unidentified products. This is probably because of some fast consecutive reactions of mercaptides with **2a**.



Scheme F

As was observed earlier², *O*-trimethylsilyl in phosphorothiolates undergo very fast hydrolytic and alcoholic cleavage under mild conditions. We have noticed that the hydrolysis of *O,O*-bis(trimethylsilyl) *S*-alkyl phosphorothiolates with water in dioxan, in the presence of triethylamine, led to the precipitation of the ammonium salt of *S*-alkylphosphorothioic acid containing more than the stoichiometric amounts of the ammonium cation. Pure monoammonium salts were obtained by hydrolysis of the *O,O*-bis(trimethylsilyl) *S*-alkyl phosphorothiolate with an excess of water in dioxan and subsequent precipitation of the salt with a stoichiometric amount of the dicyclohexylamine (Scheme F).

All reaction vessels are filled with pure nitrogen and are protected towards the atmosphere.

Preparation of Triethylammonium Salt of *O,O*-Bis(trimethylsilyl)-phosphorothioic Acid (1):

A 1.5 litre four-necked, round-bottom flask equipped with a mechanical stirrer, a thermometer, a dropping funnel, and a reflux

Table. *S*-Organyl *O,O*-Bis[trimethylsilyl] Phosphorothiolates and Derivatives

Prod- uct	R	Route	Yield ^a [%]	b.p./torr or m.p.	n_D^{20}	Molecular formula ^b	³¹ P-N.M.R. ^c δ [ppm]	J_{PSCH} [Hz]	¹ H-N.M.R. (C ₆ H ₆) ^d δ [ppm]
1	—	1	(100)	40°	—	C ₁₂ H ₃₃ NO ₃ PSSi ₂ (358.6)	—35.9 (s)	—	0.2 [s, 18 H, Si(CH ₃) ₃]; 1.0, 3.0 [tq, 15 H, N(C ₂ H ₅) ₃]; 12.4 (s, 1 H)
2a	CH ₃	3 4	40 (60) 95 (100)	58°/1.5	1.4441	C ₇ H ₂₁ O ₃ PSSi ₂ (272.5)	—5.2 (q)	15	0.2 [s, 18 H; Si(CH ₃) ₃]; 1.7 (d, 3 H, S—CH ₃ , J_{PSCH} = 13 Hz)
2b	C ₂ H ₅	1	80 (98)	64°/1.6	1.4437	C ₈ H ₂₃ O ₃ PSSi ₂ (286.5)	—5.2 (t)	16	0.2 [s, 18 H, Si(CH ₃) ₃]; 0.95 (t, 3 H, —CH ₂ CH ₃); 2.0–2.3 (m, 2 H, —S—CH ₂)
2c	<i>n</i> -C ₃ H ₇	1	(67)	48°/0.02	1.4430	C ₉ H ₂₅ O ₃ PSSi ₂ (300.5)	—6.5 (t)	15	0.2 [s, 18 H, Si(CH ₃) ₃]; 0.77 (t, 3 H, —CH ₂ CH ₃); 1.4 (sext, 2 H, —CH ₂ CH ₃); 2.4–3.0 (m, 2 H, —CH ₂ CH ₂)
2d	<i>i</i> -C ₃ H ₇	1	(65)	48°/0.05	—	C ₉ H ₂₅ O ₃ PSSi ₂ (300.5)	—6.7 (d)	15	0.3 [s, 18 H, Si(CH ₃) ₃]; 1.3 [d, 6 H, CH(CH ₃) ₂]; 3.4 [oct, 1 H, CH(CH ₃) ₂]
2e	C ₆ H ₅ CH ₂	1	90	114°/0.05	1.4933	C ₁₃ H ₂₅ O ₃ PSSi ₂ (348.6)	—3.3 (t)	15	0.2 [s, 18 H, Si(CH ₃) ₃]; 3.3 (d, 2 H, S—CH ₂ , J_{PSCH} = 14.5 Hz); 7.2– 7.6 (m, 5 H _{arom})
3	—	2	(100)	—	—	C ₆ H ₁₈ ClO ₃ PSSi ₂ (292.9)	4.4 (s)	—	—
4	—	2	(87)	—	—	C ₁₂ H ₃₆ O ₆ P ₂ S ₂ Si ₄ (514.8)	1.4 (s)	—	0.3 [s, 36 H, Si(CH ₃) ₃]
5a	—	2	40 (60)	113°/0.1	1.4755	C ₁₂ H ₂₈ ClO ₃ PSSi ₂ (375.0)	—3.7 (d)	15	0.2 [s, 18 H, Si(CH ₃) ₃]; 0.9–1.8 (m, 9 H, cyclo- hexyl); 4.3 (bs, 1 H, >CH—Cl)
5b	—	2	65 (75)	76°/0.2	1.4562	C ₈ H ₂₂ ClO ₃ PSSi ₂ (320.9)	—3.9 (t)	18	0.2 [s, 18 H, Si(CH ₃) ₃]; 2.2–2.6 (m, 2 H, S—CH ₂); 2.9 (t, 2 H, —CH ₂ —Cl)
6a	CH ₃	—	75	168°	—	C ₁₃ H ₂₈ NO ₃ PS (309.4)	—18.9 (q)	15	—
6b	C ₂ H ₅	—	70	173°	—	C ₁₄ H ₃₀ NO ₃ PS (323.4)	—17.2 (t)	15	—

^a Yield of isolated product, value in brackets refers to yield estimated by ³¹P-N.M.R. analysis.

^b All products gave microanalyses with the following maximum deviations from the calculated values: C $\pm 0.9\%$, H $\pm 1.1\%$, N $\pm 0.1\%$, Cl $\pm 0.2\%$, P $\pm 0.8\%$, S $\pm 0.9\%$.

^c Measured with a Jeol JNM-FX 60 spectrometer.

^d Measured with a Perkin-Elmer R 12 spectrometer.

condenser is charged with bis[trimethylsilyl] phosphite⁹ (100 g, 0.44 mol), sublimed sulfur (25 g, 0.78 mol eq.) and dry benzene (300 ml). Triethylamine (100 g, 1 mol) is added dropwise to the vigorously stirred mixture during 3 h. During this period the temperature rises from 25 to 35°. Stirring is continued for 10 h with mild heating (30–35°) and the mixture is left for 12 h at room temperature. The solution is separated from excess sulfur by means of a syphon fitted with a sintered glass filter. The ³¹P-N.M.R. spectrum of the solution shows that bis[trimethylsilyl] phosphite is fully converted to one phosphorus-containing product, which is identified as **1**. Benzene and unreacted triethylamine

are distilled off under reduced pressure. After separation of a small amount of sulfur which is precipitated during this operation, a brown viscous liquid solidifying after some time is obtained. The salt is further purified by fractional crystallization from melt or by crystallization from diethyl ether.

Preparation of *O,O*-Bis[trimethylsilyl] *S*-Ethyl Phosphorothiolate (**2b**) from **1** and Ethyl Bromide:

A solution of **1** (10 g, 0.028 mol) in dry benzene (35 ml) is mixed with ethyl bromide (4.4 g, 0.04 mol). The mixture is kept in a closed vessel at ambient temperature for about 20 h. The precipitate of triethylammonium bromide (5 g, 0.028 mol) is separated and ³¹P-N.M.R. analysis of the solution reveals that **1** has been completely converted to one phosphorus containing product which is identified as **2b**. It is isolated and further purified by distillation under reduced pressure.

S-Benzyl, *S*-*n*-propyl and *S*-isopropyl esters of *O,O*-bis[trimethylsilyl]phosphorothioic acid (**2c–e**) are obtained analogously.

Preparation of Bis[trimethylsilyl]phosphorosulfonyl Chloride (3) and its Addition to C=C-Bonds:

A solution of tris[trimethylsilyl] phosphorothionate¹⁰ (33 g, 0.1 mol) in dry benzene (50 ml, diethyl ether is used as well) is placed in a four-necked round bottom 250 ml flask fitted with a thermometer, a mechanical stirrer, a reflux condenser, and a dropping funnel. The solution is cooled to about -5° and sulfuryl chloride (13.5 g, 0.1 mol) in benzene (50 ml) is added dropwise to the vigorously stirred reaction mixture at a rate such as to keep the temperature below 0° . ³¹P-N.M.R. analysis of the yellow solution obtained proves that the phosphorothionate has been completely converted to one phosphorus-containing product which is further identified as **3**. Dry cyclohexene (8.5 g, 0.1 mol) is placed in the dropping funnel and added dropwise to the vigorously stirred yellow solution until its decoloration. The temperature is kept in the range $0-5^{\circ}$. After chlorotrimethylsilane and sulfur dioxide are distilled off, vacuum distillation gives a fraction identified as *O,O*-bis[trimethylsilyl] *S*-2-chlorocyclohexyl phosphorothiolate (**5a**): yield: 20 g (40%); b.p. $112-113^{\circ}/0.1$ torr. Similarly, bubbling prepurified ethene through a solution of **3** gives *O,O*-bis[trimethylsilyl] *S*-[β -chloroethyl] phosphorothiolate **5b**.

Preparation of *O,O*-Bis[trimethylsilyl] *S*-Methyl Phosphorothiolate (2a) from Tris(trimethylsilyl) Phosphite and Methanesulfonyl Chloride:

A methanesulfonyl chloride solution¹¹ in benzene/diethyl ether (1:1 V/V) is prepared from dimethyldisulfide (4.7 g, 0.05 mol) and sulfuryl chloride (6.75 g, 0.05 mol) using the same apparatus as in the synthesis of **3**.

Tris[trimethylsilyl] phosphite (15.0 g, 0.05 mol) is added dropwise to vigorously stirred methanesulfonyl chloride solution until its orange colour disappeared. The temperature is kept below -10° . The ³¹P-N.M.R. analysis shows that the phosphite has been converted in to **2a** (60%) and other products (40%). After chlorotrimethylsilane and sulfur dioxide are distilled off, fraction boiling at $58^{\circ}/1.5$ torr is collected (yield: 40%).

Preparation of 2a from Dimethyl Disulfide and Tris[trimethylsilyl] Phosphite:

Tris[trimethylsilyl] phosphite (30 g, 0.1 mol) and dimethyl disulfide (9.5 g, 0.1 mol) are mixed and kept in closed vessel at ambient temperature. The ³¹P-N.M.R. analysis reveals that after about 100 minutes 15%, and after 24 h 100% of the phosphite is converted into one phosphorus-containing product, identified as **2a**. Distillation under reduced pressure gives **2a**: yield: 26 g (95%). An equivalent amount of $(\text{H}_3\text{C})_3\text{SiSCH}_3$ is collected as the first fraction.

Preparation of Dicyclohexylammonium Salt of *S*-Methylphosphorothioic Acid 6a:

Compound **3** (1.5 g, 5.5 mmol) is dissolved in prepurified dioxan (20 ml) containing water (6 mmol), and pure dicyclohexylamine (1.09 g, 0.006 mol) is added dropwise. The fine crystalline precipitate is filtered off, washed with ether, and dried under vacuum at $60-70^{\circ}$ to give **6a**: yield: 2 g (75%).

Analogously the *S*-ethyl (**6b**) derivative of the salt is obtained.

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