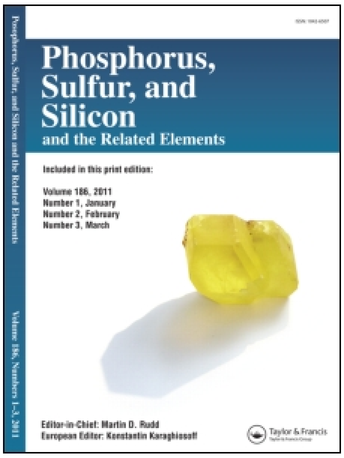

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REACTION OF TRIS(TRIMETHYLSILYL) PHOSPHITE WITH EPIHALOHYDRINS

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The reaction of tris(trimethylsilyl) phosphite with halohydrins does not lead to an Arbuzov product but to bis(trimethylsilyl) esters of 3-halo-2-trimethylsiloxypropylphosphonic acids. Methanolysis and neutralization affords the 3-halo-2-hydroxypropylphosphonic acids and their salts.

Key words: Tris(trimethylsilyl) phosphite; epichlorohydrin; epibromohydrin; 3-halo-2-hydroxypropylphosphonic acids.

The reaction of trialkyl phosphites with epiiodohydrin and epibromohydrin gave dialkyl 2,3-epoxypropylphosphonate[1,2] but with epichlorohydrin gave dialkyl methylphosphonate and dialkyl vinyl phosphate.[3]

Tris(trimethylsilyl) phosphite,[4] **1**, although difficult to obtain pure[5] [contaminant: bis(trimethylsilyl) phosphonate] is a useful phosphonylating agent, its main advantage being the extreme ease of hydrolysis of the resulting bis(trimethylsilyl) phosphonates to free phosphonic acids.

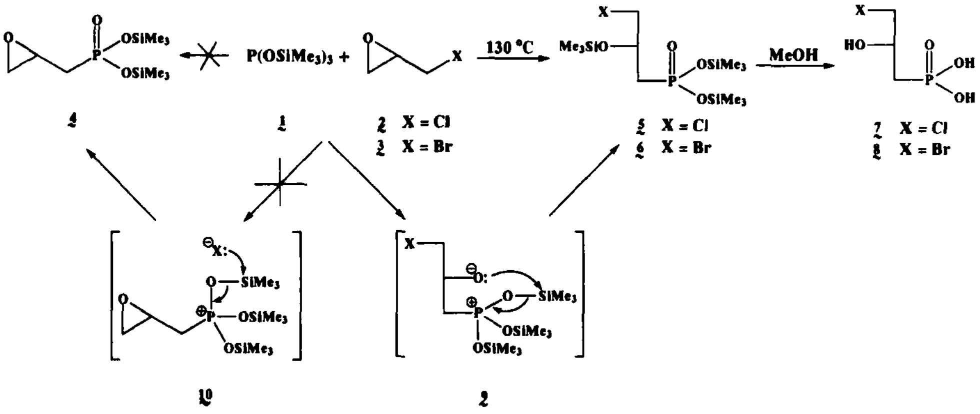
We thought that **1** would react with **2** or **3** in an Arbuzov fashion to give the epoxyphosphonate **4** which will give 2,3-dihydroxypropylphosphonic acid,[7] a key intermediate for the synthesis of phosphonolipids.[8] However, the reaction followed a different path giving fully protected 3-halo-2-hydroxypropylphosphonic acids, **5** and **6**.

The reaction of **1** (purity ~80%) with a slight excess of **2** or **3** at 130°C was smooth but it could not be easily followed by IR, ^{1}H-NMR or TLC. At the end of the heating there was practically no weight loss. Fractional distillation afforded the unreacted impurity, bis(trimethylsilyl) phosphonate, and the product, **5** or **6**, in 70–80% yields. The ^{1}H-NMR spectra of **5** and **6** showed the presence of —CH_2X[9] and the disappearance of the signals due to epoxide ring.[9] The IR (neat) spectra were not informative and some hydrolysis took place during the sample preparation.

The mechanism of the reaction evidently involves attack of the nucleophilic phosphorus on the electrophilic CH_2 of the epoxide ring and not on the —CH_2X. The driving force for such an attack may be that more energy is released by forming **5** or **6** (with strong Si—O bond) probably via the betaine **9** than by forming **4**, via **10**, releasing Me_3SiX which has weaker Si—X bonds.[10]

Reaction of **6** with excess methanol and evaporation gave the free acid **8** as an oil which retains tenacionsly methanol (by NMR). Its ^{1}H-NMR showed a doublet of doublets centered at δ 2.10 (J = 8 Hz), while its IR (neat) spectrum showed broad absorptions at 3271, 2844, 1650 and strong absorptions at 1140 and 996 cm^{-1}.

Deprotection of **6** with methanol followed by addition of 1 mol lithium hydroxide



in methanol gave the monolithium salt of **8** which is soluble in methanol. It also retains methanol, melts without decomposition at 165–8°C and its ^{1}H-NMR spectrum shows a doublet of doublets centered at δ 2.00 (J = 8 Hz). Its IR (KBr) spectrum showed a strong, broad absorption at 3416 cm^{-1} and strong absorptions at 1158, 1066 and 922 cm^{-1}. The monoammonium salt of **8** has been described in the literature.[11]

The dilithium salts of **7** and **8** precipitated from methanol as solvates, which upon prolonged drying in vacuo were obtained as white powders.

The scope of the reactions of **1** with epoxides and with glycidol derivatives is being investigated.

EXPERIMENTAL

Tris(trimethylsilyl) phosphite, **1**, containing ~20% bis(trimethylsilyl) phosphonate[5] was prepared from phosphorous acid and trimethylsilyl chloride in dry ether in the presence of triethylamine, b.p. 40–42°C/0.8 mm Hg. Epichlorohydrin and epibromohydrin were purified by distillation. IR and ^{1}H-NMR were run on a Perkin Elmer model 16 PC FT-IR and a Varian model T-60A spectrometers. Elemental analyses were done by C.N.R.S., Vernaison, France.

Preparation of dilithium salts of 3-halo-2-hydroxypropylphosphonic acids, **7** *and* **8**. Tris(trimethylsilyl) phosphite (4.179 g, ~80% pure) and epichlorohydrin (1.295 g, 14 mmol) were stirred gently at 130°C (oil bath temperature) for 10 h and then at 150°C for 2 h. Fractional distillation gave the product **5** (b.p. 98–100°C/0.6 mm Hg) as an oil (3.294 g, 75% on pure **1**). ^{1}H-NMR (CCl_4, internal $CHCl_3$) δ: 0.01 (s, 9H, Me_3SiOC), 0.15 (s, 18H, Me_3SiOP), 1.80 (m, 2H, CH_2P), 3.40 (m, 2H, CH_2Cl), 3.70 (m, 1H, HCO). Similarly prepared **6** (b.p. 109–110°C/0.6 mm Hg) (72% on pure **1**). ^{1}H-NMR (CCl_4 internal $CHCl_3$): similar to **5** except δ 3.20 (m, 2H, CH_2Br). Both compounds are moisture sensitive and have the same IR spectra. IR (neat) cm^{-1}: 3320 (variable intensity), 2960 m, 2902 w, 1254 s, 1050 s, 848 s, 760 m.

The ester **5** (3.109 g, 7.96 mmol) was dissolved in methanol (10 ml) and stirred at 25°C for 1 h. A solution of lithium hydroxide (0.382 g, 15.92 mmol) in methanol (45 ml) was then added and the system was stirred overnight. Centrifugation, washing the precipitated solvate with methanol and drying in vacuo for 2 days afforded the dilithium salt of **7** as a white powder (1.275 g, 85%) sparingly soluble in water. Calculated for $C_3H_6ClO_4PLi_2.H_2O$ C 17.62, H 3.94%; found C 17.86, H 3.24%. IR (KBr) cm^{-1}: 3386 broad, s, 1102 s, 1070 s. ^{1}H-NMR (DMSO-d_6, TMS) δ: 1.7 (m, 2H, CH_2P), 3.5 (m, 2H, CH_2Cl) 4.3 (m, 1H, CHOH).

Similarly prepared the dilithium salt of **8**. White powder (76%) moderately soluble in water. Calculated for $C_3H_6BrO_4PLi_2$ C 15.61, H 2.62%; found C 16.09, H 2.96%. IR (KBr) cm^{-1}: 3386 broad, s, 1102 s, 1070 s. ^{1}H-NMR (D_2O, DSS) δ: 1.7 (m, 2H, CH_2P), 3.6 (m, 2H, CH_2Br) 4.2 (m, 1H, CHOH).

Both compounds decomposed at ~245°C.

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