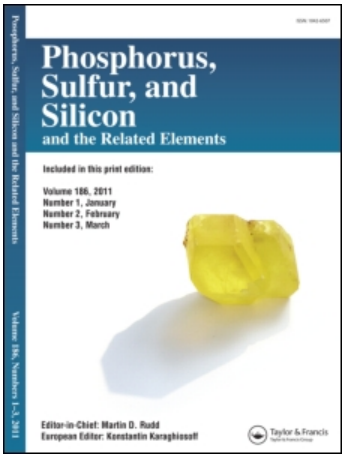

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REACTION OF TRIS(TRIMETHYLSILYL) PHOSPHITE WITH EPOXIDES AND GLYCIDOL DERIVATIVES

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Tris(trimethylsilyl) phosphite deoxygenates styrene epoxide and tritylglycidol. The same phosphite with glycidyl mesylate gave bis(trimethylsilyl) ester of 3-mesyl-2-trimethylsiloxypropylphosphonic acid by attack at the epoxide methylene carbon. The ester was not stable and reacted further intramolecularly. With glycidyl tosylate and glycidyl 3-nitrobenzenesulfonate, however, the reaction was more complicated and glyceryl 1,3-bis(arenesulfonate) was one of the products. With these activated glycidols deoxygenation and reduction of the nitro group were also observed.

Key words: Tris(trimethylsilyl) phosphite, styrene epoxide, tritylglycidol, activated glycidols, phosphonates, Arbuzov reaction.

In a previous communication[1] we reported on the reaction of tris(trimethylsilyl) phosphite, **1**, with epichloro- and epibromohydrins which gave, after workup, 3-halo-2-hydroxypropylphosphonic acids by attack of the phosphite at the epoxide methylene carbon.

In this communication we report on the behaviour of the same phosphite, **1**, towards protected and activated glycidols as well as towards simple epoxides.

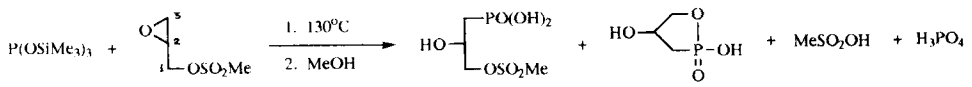
RESULTS AND DISCUSSION

Reaction of $P(OSiMe_3)_3$, **1**, with styrene epoxide at 130–150°C gave nearly quantitatively tris(trimethylsilyl) phosphate which was identified and determined by magnesia mixture precipitation. Deoxygenation of certain epoxides can be effected by triethyl phosphite[2,3] and by **1**[4,5] but some phosphonylation takes place when the trialkyl phosphite contains one or more secondary or tertiary alkyl groups.[6]

There is no report on the reaction of glycidol derivatives with trialkyl phosphites.[7] The reaction of protected glycidol, tritylglycidol, with **1** at 130°C/20 h lead to the recovery of a non-phosphonylated compound which was not identified. More forcing conditions gave 24% deoxygenation of tritylglycidol.

Sulfonates will give the Arbuzov reaction with trialkyl phosphites[8] provided that the sulfonate anion can attack the phosphonium intermediate. Tosylates,[9] but not triflates,[10,11] do give the Arbuzov reaction, albeit in a more complicated way. We, therefore, tried the reactions of **1** on glycidyl derivatives activated by sulfonate groups hoping to obtain products suitable for phosphonolipid synthesis.

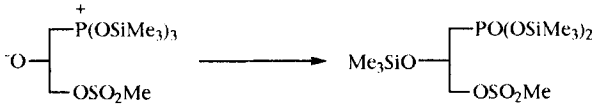
Glycidyl mesylate, **2**, reacted smoothly with **1** at 130°C till TLC (Et_2O) showed complete disappearance of the mesylate. The crude product contained no epoxide



1 2 3 4 5 6

ring (by NMR). Some loss of weight occurred due to the volatility of $MeSO_2OSiMe_3$ (b.p. ~210°C). Methanolysis[12] of the crude product and addition of methanolic lithium hydroxide precipitated the dilithium salt of **3** in 41% yield, contaminated with 8% Li_3PO_4 (indicating deoxygenation of **2**) while the lithium salts of the cyclic phosphonate **4** and methyl sulfonic acid **5** remained in the supernatant liquid. Although the lithium salt of **4** was not obtained in a pure state in any experiment, its spectral characteristics [IR: 1352 s, 1147 s, 962 s] and ^{1}H-NMR [1.8–2.2, m, CH_2P; 3.7–4.1, m, CH_2O; 4.9, m, CHOH] check well with the proposed structure (see also Reference 13 for sodium propylphostonate] and its hydrolysis[14] gave pure dilithium 2,3-dihydroxypropylphosphonic acid.[15]

As in the case of epihalohydrins[1] the phosphite attacked at C_3 selectively giving the intermediate **7**, which afforded the Arbuzov product **8**. No attack at C_1 (epoxide ring intact) was observed even when the reaction was done at 115°C. However, contrary to the epihalohydrin case,[1] the ester **8** was not stable and underwent partial cyclization giving the trimethylsilyl esters of **4** and **5**. Analogous cyclizations have been observed.[13,16]

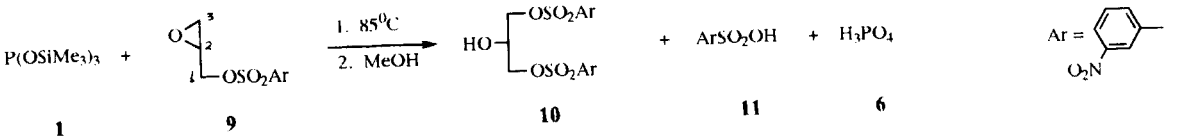


7 **8**

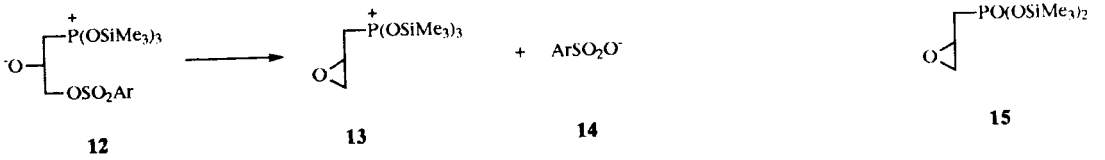
It is known[17] that the 3-nitrobenzenesulfonyl group favours attack by aryl oxide nucleophiles at the C_1 of glycidyl 3-nitrobenzenesulfonate. We tried the reaction of **1** with **9** in spite of the complications which may arise from the propensity of phosphites[5,18,19] to reduce nitro groups.

Reaction of glycidyl 3-nitrobenzenesulfonate **9** with **1** under mild conditions, after work up, gave 17% glyceryl 1,3-bis(3-nitrobenzenesulfonate), **10**, (thus consuming 34% of **9**), 30% of **11** and 24% of H_3PO_4. The H_3PO_4 most probably arose from the reduction of the nitro groups, as evidenced by the colouration of the system. The bis(sulfonate) ester, **10**, probably arose as follows. The bulky phosphite **1** again attacked the C_3 of **9** (and not the C_1) giving the intermediate **12**. Now, the negatively charged oxygen in **12** attacked the C_1 carbon (instead of desilytating the phosphonium group as in **7** → **8**) because the 3-nitrobenzenesulfonate anion, **14**, is an excellent leaving group.[17] The anion **14** then attacked another molecule of **9** giving the anion of **10** which can desilylate **13** to afford the trimethylsilyl ester of **10** and the Arbuzov product **15**, which in turn can react with the remaining **1**.

Glycidyl tosylate, **9** (Ar = *p*-MeC_6H_4) reacted completely with **1** (130°C/7.5 h) to give 9% of glyceryl 1,3-bis(4-toluenesulfonate) as an oil,[20] and a phosphonic



1 **9** **10** **11** **6**



12 **13** **14** **15**

acid analogous to **3** contaminated with 7% of H_3PO_4 and other phosphonylated compound(s) as the low carbon and hydrogen elemental analyses revealed.

Summarizing, while activated glycidol was attacked by oxygen nucleophiles[17] mainly or exclusively at C_1 the phosphorus nucleophile **1** showed C_3 preference, which can be attributed to the bulkiness of the reagent. Moreover, the reaction products depended on the leaving group ability of the sulfonate anion.

EXPERIMENTAL

The following compounds were prepared by the literature methods: styrene epoxide,[21] tritylglycidol,[22] glycidyl 4-toluenesulfonate,[17] glycidyl mesylate (or 3-mesyloxy-1,2-epoxypropane),[23] glycidyl 3-nitrobenzenesulfonate,[17] tris(trimethylsilyl) phosphite containing 20% bis(trimethylsylilyl) phosphonate.[24] Estimation of PO_4^{3-} was effected by precipitation with magnesia mixture.[25] TLC was run on microslides coated with silica gel (Merck). IR and ^{1}H-NMR spectra were recorded on a Perkin Elmer model 16PC FT-IR and a Varian model T-60A NMR spectrometer. Elemental analysis were conducted by C.N.R.S., Vernaison, France.

Reaction of styrene epoxide with **1**: Reaction of 1.508 g (12.6 mmol) of styrene epoxide with 3.755 g (12.6 mmol) of **1** at 130°C/8 h and 150°C/2 h followed by fractional distillation yielded three fractions, all impure. After methanolysis, 1.205 g (12.3 mmol) of phosphoric acid were found in the fractions corresponding to 98% deoxygenation.

Reaction of tritylglycidol with **1**: Reaction of 0.747 g (2.37 mmol) of tritylglycidol with 0.707 g (2.37 mmol) of **1** at 130°C/5 h and 145°C/8 h gave a very viscous orange oil which was solvolysed with methanol, evaporated and the residue extracted with water. The aqueous extracts contained 24% of phosphate. The organic phase was analysed by TLC (toluene/ether 85:15 v/v) and showed the presence of unreacted tritylglycidol.

Reaction of glycidyl mesylate with **1**: Glycidyl mesylate (1.52 g, 10 mmol) and **1** (2.98 g, 10 mmol) were stirred at 130°C/5 h. Distillation removed bis(trimethylsilyl) phosphonate and some trimethylsilyl mesylate (bp 50–70°C/0.6 mm Hg) leaving a pale yellow oil (3.55 g) as residue. The oil was solvolysed with methanol (20 ml) for 30 min, evaporated and dried to give 2.11 g of a very viscous colorless oil. This was dissolved in methanol (5 ml) and a solution of 480 mg (20 mmol) of lithium hydroxide in methanol (50 ml) was added. The precipitated solvate of dilithium salt of **3** was centrifuged, washed with methanol, and dried in vacuo over P_2O_5 to give 1.10 g of an off-white solid containing 8% of Li_3PO_4. Yield 41%. The mixture did not melt up to 280°C, it was insoluble in MeOH and moderately soluble in H_2O and DMSO. Calculated for $C_4H_9O_7PSLi_2$ C 19.53, H 3.69%; found C 18.13, H 3.99%. IR (KBr): 3442 broad, m, 1350 m, 1176 m, 1117 s, 1076 s, 1001 m. ^{1}H-NMR (D_2O) δ: 1.80 (m, 2H, CH_2P), 2.90 (s, 3H, CH_3S), 4.20 (m, 3H, $CHOHCH_2OS$).

The supernatant liquid was evaporated, dried and extracted with acetone for 24 h to give an insoluble mass, which contained lithium mesylate, LiOH and impurities, and a solution, which contained the lithium salt of **4** and impurities.

Reaction of glycidyl 3-nitrobenzenesulfonate with **1**: Reaction of 4.518 g (17.5 mmol) of glycidyl 3-nitrobenzenesulfonate with 5.215 g (17.5 mmol) of **1** at 85°C/8 h, solvolysis and evaporation gave a foamy sticky gum which was extracted with water (30 ml). The insoluble yellow mass (1.72 g) was purified by boiling with chloroform (60 ml) for 30 min, decantation from an insoluble brown gum, evaporation and drying. The compound, glyceryl 1,3-bis(3-nitrobenzenesulfonate), **10**, (1.392 g) is a pale yellow solid, m.p. 103–4°C, soluble in Me_2CO, MeCN and DMSO and sparingly soluble in CH_2Cl_2 and $CHCl_3$. Calculated for $C_{15}H_{14}N_2O_{11}S_2$ C 38.96, H 3.05%; found C 39.24, H 3.17%. IR (KBr): 3564 m, 3104 w, 1610 m, 1538 vs, 1354 vs, 1188 vs, 1130 m, 1074 m, 960 s, 884 m, 816 m, 734 m, 662 m, 606 m, 586 m. ^{1}H-NMR (DMSO-d_6) δ: 4.15 (s, broad, 5H, $CH_2CH(OH)CH_2$), 8.3 (m, 8H, $C_6H_4NO_2$).

The dark red aqueous extracts contained 24% of H_3PO_4. Impure lithium salt of **11** (1.02 g) was isolated by evaporating the water, adding lithium hydroxide in methanol, evaporating the supernatant liquid, extraction with acetone, and evaporation of the acetone phase. IR (KBr) of pure hydrated lithium salt of **11**: 3474 broad, s, 1644 s, 1542 s, 1356 s, 1244 s, 1176 s, 1150 s, 1050 s, 670 s, 630 s.

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