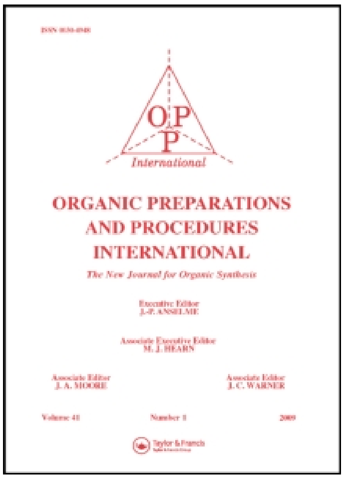

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PREPARATION OF TETRAETHYL (OXYDI-2,1-ETHANEDIYL)bisPHOSPHONATE AND 1,2-bis[2-(DIETHYLPHOSPHONO)ETHOXY]ETHANE

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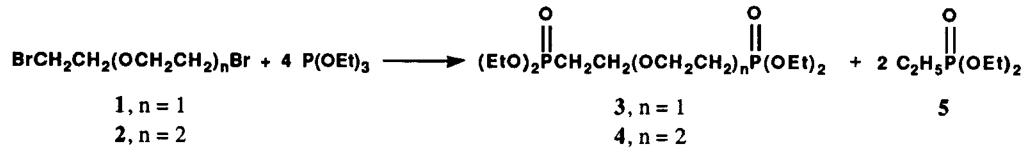
Tetraethyl (oxydi-2,1-ethanediyl)bisphosphonate **3** has previously been obtained in 34% yield by the reaction of bis(2-chloroethyl) ether with triethyl phosphite in the presence of $NiCl_2$ at 175-220° in an autoclave.[1] The procedure involves the removal of the nickel salt by the passage of an alcoholic solution of the crude product through an acidic ion exchanger. In the absence of $NiCl_2$, bis(2-chloroethyl) ether fails to react with triethyl phosphite even after refluxing for 22 hrs.[1] We have found that one mole of bis(2-bromoethyl) ether (**1**)[2] reacts with triethyl phosphite (4 moles) to yield a 2:1 mixture of diethyl ethylphosphonate **5** and compound **3** as indicated by ^{31}P NMR which contains two signals of equal intensity at +33.6 (compound **5**) and +28.3 ppm (compound **3**). These two compounds can be easily separated by distillation; compound **3** was characterized by ^1H and ^{31}P NMR (identical to those previously reported[1]) and ^{13}C NMR. Our method for the preparation of **3** is simple and results in higher yield (44%). bis-Phosphonates containing ether linkages such as compound **3** find applications as corrosion inhibitors[3] and chelating agents.[1]



$$BrCH_2CH_2(OCH_2CH_2)_nBr + 4\ P(OEt)_3 \longrightarrow (EtO)_2\overset{O}{\overset{\|}{P}}CH_2CH_2(OCH_2CH_2)_n\overset{O}{\overset{\|}{P}}(OEt)_2 + 2\ C_2H_5\overset{O}{\overset{\|}{P}}(OEt)_2$$

1, n = 1
2, n = 2

3, n = 1
4, n = 2

5

Similarly the reaction of 1,2-bis(2-bromoethoxy)ethane (**2**) with triethyl phosphite gave a 2:1 mixture of **5** (+33.6 ppm) and 1,2-bis[2-(diethylphosphono)ethoxy]ethane (**4**, +28.5 ppm). After the removal of **5**, the crude product exhibited ^1H, ^{13}C and ^{31}P NMR compatible with **4**. Attempted purification of **4** by distillation under reduced pressure resulted in extensive decomposition and even with careful distillation, pure **4** could be isolated in only 18% yield, compound **4** has previously been obtained[4] in 15% yield by the reaction of sodium diethylphosphonate with 1,2-bis(2-bromoethoxy)ethane.

EXPERIMENTAL SECTION

Elemental analyses were performed by Atlantic Microlab, Inc. Norcross, Georgia. ^1H and ^{13}C NMR Spectra were obtained in $CDCl_3$ on a Varian Gemini-300 Spectrometer, with operational frequencies of 300(^1H) and 75(^{13}C) MHz. The chemical shifts are given in ppm downfield from Me_4Si. ^{31}P NMR spectra were obtained in $CDCl_3$ with H_3PO_4 as external standard on a Jeol FX-60 spectrometer operating at 24.15 MHz.

Tetraethyl (oxydi-2,1-ethanediyl)bisphosphonate (3).- A mixture of bis(2-bromoethyl) ether[2] **1** (22.0 g, 95 mmol) [**CAUTION: Since bis(2-chloroethyl) ether is a cancer suspect agent, caution should be exercised in handling the related bis(2-bromoethyl) ether**] and triethyl phosphite (63.0 g, 380 mmol) was refluxed for 18 hrs. The reaction mixture showed two ^{31}P NMR signals at 28.3 and 33.5 ppm. The reaction mixture was then distilled under reduced pressure. The following fractions were collected. First fraction, diethyl ethylphosphonate, bp. 37-40°/0.3mm, 32.0 g; second fraction, bp. 145-147°/0.1mm, <1.0 g; third fraction, tetraethyl (oxydi-2,1-ethanediyl)bisphosphonate, bp. 167°/0.1mm, yield 14.5g (44%). MS: m/e 346 (calcd 346) ^{31}P +28.3 ppm. ^{13}C NMR: δ 16.45 (d, 6.1 Hz), 26.94 (d, 139.8 Hz), 61.60 (d, 6.5 Hz), 64.71.

Anal. Calcd for $C_{12}H_{28}O_7P_2$: C, 41.62; H, 8.09. Found: C, 41.78; H, 8.19

1,2-Bis[2-(diethylphosphono)ethoxy]ethane 4.- A mixture of 1,2-bis(2-bromoethoxy)ethane (27.6 g, 100 mmol) and triethyl phosphite (66.4 g, 400 mmol) was refluxed for 20 hrs. The reaction mixture was next distilled under reduced pressure. Diethyl ethylphosphonate (39.6 g) distilled over at 45-47°(0.5 mm of Hg). The remaining residual liquid was divided into three portions (ca. 10.5 g each). The distillation of one of these portions gave, after a small forerun, the following two fractions: **4**, bp. 200°/0.6mm, 2.3 g (17.7%); impure **4**, bp. 190-200°/0.6mm, 1.2 g. After the distillation of 2.3 g of **4**, decomposition started and temperature began to fall.

Spectral Data for 4: ^{31}P NMR: δ +28.46 ppm. ^1H NMR: δ 1.33(t, 7 Hz, 12H, CH_3), 2.12 (dt, 7.5 Hz, 18.7 Hz, 4H, P-$\underline{CH_2}$-CH_2), 3.60 (s, 4H,O-$\underline{CH_2}$-$\underline{CH_2}$O), 3.72 (dt, 7.5 Hz, 11.2 Hz, 4H $PCH_2\underline{CH_2}$), 4.10 (m, 8H, $PO\underline{CH_2}$). ^{13}C NMR 16.43 (d, 5.9 Hz, CH_3), 26.98 (d, 139.5 Hz, P-CH_2), 61.54 (d, 6.3 Hz, $POCH_2$), 65.13 (P-$CH_2\underline{CH_2}$), 70.05 (OCH_2CH_2O).

Anal. Calcd for $C_{14}H_{32}O_8P_2$: C,43.08; H,8.20. Found: C, 42.84; H, 8.08

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