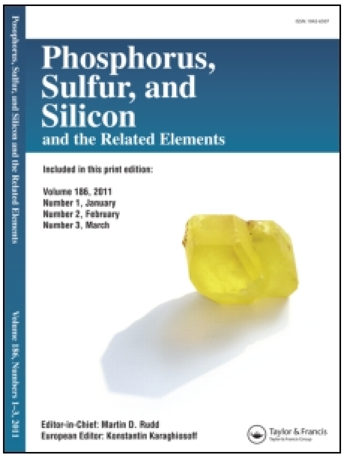

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REACTION OF PENTAERYTHRITOL WITH DIETHYL PHOSPHOROCHLORIDATE PENTAERYTHRITOL BIS-, TRIS- AND TETRAKIS(DIHYDROGEN PHOSPHATES)[1,2]

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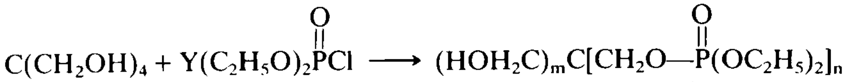
Reaction of pentaerythritol **1** with 1, 2 or 3 equivalents of diethyl phosphorochloridate **2** yielded pentaerythritol tris(diethyl phosphate) **5**. Treatment of pentaerythritol with 4 or more equivalents of **2** gave pentaerythritol tetrakis(diethyl phosphate) **6**. Transesterification of **5** and **6** with trimethylsilyl chloride and sodium iodide in acetonitrile followed by treatment with water gave pentaerythritol tris (dihydrogen phosphate) **7** and pentaerythritol tetrakis(dihydrogen phosphate) **8** respectively. Pentaerythritol bis(dihydrogen phosphate) **9** was prepared by the hydrolysis of 3,9-dichloro-2,4,8,10-tetraoxa-3,9-diphosphaspiro [5,5] undecane 3,9-dioxide **10**. The compounds **7**, **8** and **9** were isolated as anilinium salts and characterized by ^1H, ^{13}C and ^{31}P NMR spectra.

Reaction of pentaerythritol **1** with 1, 2, or 3 equivalents of diethyl phosphorochloridate[3] **2** generated in situ by the reaction of diethyl phosphonate, carbon tetrachloride and triethylamine gave exclusively pentaerythritol tris(diethyl phosphate) **5**. **5** was formed in quantitative yield by the reaction of **1** with 3 equivalents of **2**. The structure of **5** was confirmed by ^1H, ^{13}C and ^{31}P NMR spectra and mass spectrum. The ^{13}C NMR spectrum of **5** contained a singlet at 60.22 ppm due to $\underline{C}H_2OH$ and a quartet at 46.95 ppm due to $\underline{C}[CH_2O\underset{\underset{O}{\|}}{P}(OC_2H_5)_2]_3$ that is coupled to phosphorus of the phosphate ester groups.



$$C(CH_2OH)_4 + Y(C_2H_5O)_2\overset{\overset{O}{\|}}{P}Cl \longrightarrow (HOH_2C)_mC[CH_2O{-}\overset{\overset{O}{\|}}{P}(OC_2H_5)_2]_n$$

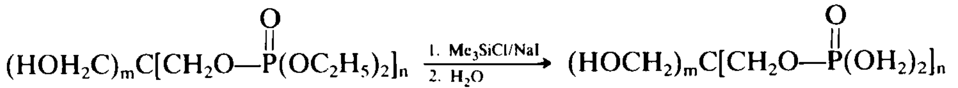
1 **2**
Y = 1, 2, 3, or 4

3 m = 3; n = 1
4 m = 2; n = 2
5 m = 1; n = 3
6 m = 0; n = 4

The formation of a single product **5** came as a surprise to us but is not unexpected because **1** is practically insoluble in the reaction mixture and as it reacts with **2** to form first pentaerythritol mono(diethyl phosphate) **3**, it goes in solution. Once in solution, **3** reacts faster than **1** with **2** to form pentaerythritol bis(diethyl phosphate) **4** and finally **5**. At this stage, the molecule probably becomes sterically crowded and further reaction to pentaerythritol tetrakis(diethyl phosphate) **6** is very slow. This was supported by the observation that when **1** was treated with 4 equivalents of **2** under similar conditions, significant amount of **5** was formed along with **6**.

An attempt to distil **5** under reduced pressure led to its decomposition yielding triethyl phosphate as distillate (identified by comparison with an authentic sample by IR, ^{1}H NMR, ^{13}C NMR, and MS).

Treatment of **5** with trimethylsilyl chloride and sodium iodide in acetonitrile[4] followed by hydrolysis with water gave pentaerythritol tris(dihydrogen phosphate) **7** which was isolated as its tetraanilinium salt and characterized by ^{1}H, ^{13}C and ^{31}P spectra (Table II) and elemental analysis (Table I).



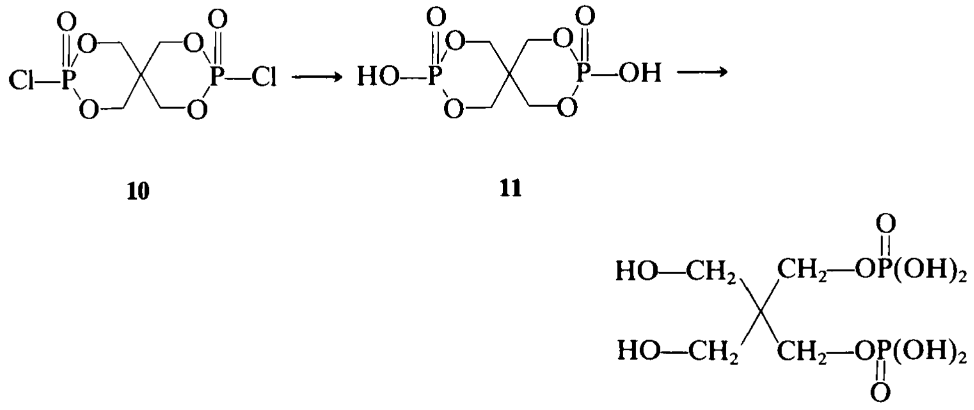
$$(HOH_2C)_mC[CH_2O-\overset{O}{\overset{\|}{P}}(OC_2H_5)_2]_n \xrightarrow[2.\ H_2O]{1.\ Me_3SiCl/NaI} (HOCH_2)_mC[CH_2O-\overset{O}{\overset{\|}{P}}(OH_2)_2]_n$$

5
6

7 m = 1, n = 3
8 m = 0, n = 4

Similar treatment of **6** gave pentaerythritol tetrakis(dihydrogen phosphate)[5] **8** which was isolated as its trianilinium salt (Tables I and II). This method of hydrolysis of **5** and **6** via transesterification with Me_3SiCl/NaI resulted in poor yields of **7** and **8** respectively owing to the indiscriminate cleavage of P—O—C bonds. No attempts were made to improve the yields.

Pentaerythritol bis(dihydrogen phosphate) **9** was prepared by the hydrolysis of 3,9-dichloro-2,4,8,10-tetraoxa-3,9-diphosphaspiro [5,5] undecane 3,9-dioxide **10**. Treatment of **10** with water at 90°C for 30 min has been reported[6] to yield 3,9-dihydroxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro [5,5] undecane 3,9-dioxide **11**, 57%. We followed the published procedure in detail but prior to the isolation of **11** examined the reaction mixture by ^{31}P NMR. Two phosphorus signals at 0.00 ppm and −3.39 ppm were observed. Work up as described by Rätz and Sweeting gave a 49% yield of **11** whose properties were in complete accord with those reported.[6] Pure **11** exhibited a ^{31}P signal at −3.15 ppm. From the ^{31}P NMR study, it also became evident that the signal at 0.00 ppm was developing at the expense of the signal at −3.39 ppm. After refluxing **10** with water[7] for 5 h, ^{31}P of the reaction mixture indicated 96% conversion of **10** to **9**. The compound **9** was isolated as its trianilinium salt and characterized by ^{1}H, ^{13}C and ^{31}P NMR spectra (Table II) and elemental analysis (Table I).



10 **11**

9

TABLE I

Physical properties and analytical data of compounds **7–9**

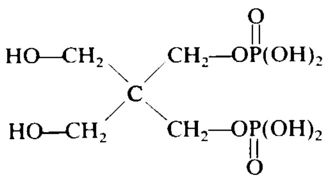
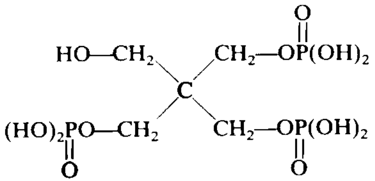
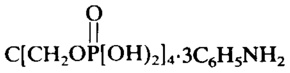
Compound	Structure (Isolated Salt)	mp (°C)	Mol. Formula	Analysis Calcd (Found)				
				C	H	N	P	H_2O
9	 $\cdot 3C_6H_5NH_2$	108–110	$C_{23}H_{35}N_3O_{10}P_2$	48.00 (47.77)	6.08 (6.14)	7.30 (7.27)	10.78 (11.02)	
7	 $4C_6H_5NH_2\cdot 2H_2O$	103–104	$C_{29}H_{47}N_4O_{15}P_3$	44.38 (44.10)	5.99 (5.80)	7.14 (7.07)	11.86 (12.43)	4.59 (4.75)
8	 $C[CH_2O\overset{O}{\overset{\|}{P}}[OH)_2]_4\cdot 3C_6H_5NH_2$	151.5–153	$C_{23}H_{37}N_3O_{16}P_4$	37.55 (37.15)	5.03 (5.16)	5.03 (5.16)	16.87 (16.68)	

TABLE II

Spectral data of compounds **7–9** (anilinium salts)

Compound	H^1 NMR (D_2O/TMSPAS)[a]	C^{13} D_2O/TMS(cap)	P^{31}(D_2O/H_3PO_4cap)
9	3.60 (s,4H,ÇH̦$_2$OH), 3.84 (d,4H,J_{PH} = 6 Hz,ÇH̦$_2$OP) 7.15–7.60 (m,15H, aromatic)	46.34 (t,J_{PC} = 7.32 Hz, POCH$_2$Ç) 60.87 (s,ÇH$_2$OH),64.20 (d,J_{PC} = 4.88 Hz,POÇH$_2$) 121.98,127.34,130.91 and 135.54	+0.859
7	3.60 (s,2H,ÇH̦$_2$OH) 3.82 (d,6H,J_{PH} = 6 Hz,ÇH̦$_2$OP) 7.16–7.60 (m,20 H, aromatic)	46.30 (quartet, J_{PC} = 7.32 Hz,POCH$_2$Ç) 61.36 (s,ÇH$_2$OH), 64.69 (d,J_{PC} = 4.88 Hz,POÇH$_2$) 123.21,128.80,131.32,134.00	+0.707
8	3.84 (d,8H,J_{PH} = 6 Hz,ÇH̦$_2$OP) 7.15–7.55 (m,15H,aromatic)	45.72 (quintet,J_{PC} = 7.32 Hz,POCH$_2$Ç) 63.87 (d,J_{PC} = 3.66 Hz,POÇH$_2$) 124.10,130.35,131.25	+0.2525

[a] TMSPAS = sodium salt of 3-(trimethylsilyl)propionic acid

EXPERIMENTAL

Melting points were obtained on a Fisher–Johns melting point apparatus and are uncorrected. The elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee and Petrolite Corporation, Analytical Section. ^{31}P and ^{13}C spectra were obtained with a Jeol FX–60 spectrometer operating at 24.15 and 15.04 MHz, respectively. The chemical shift ($+\delta$) values are downfield from H_3PO_4(cap) for ^{31}P spectra and from Me_4Si for ^{13}C spectra. ^1H NMR spectra were obtained with a Perkin–Elmer R-32 spectrometer (90 MHz).

Pentaerythritol tris(diethyl phosphate) **5**

To a magnetically stirred mixture of pentaerythritol (13.6 g, 0.1 mol), carbon tetrachloride (70 mL) and diethyl phosphonate (41.43 g, 0.3 mol) cooled in an ice-bath was added dropwise triethylamine (30.6 g, 0.3 mol). The mixture was stirred at rt for 16 h. Water (100 mL) and methylene chloride (100 mL) were next added. The organic layer was separated, dried over anhydrous sodium sulfate and the solvents were removed on rotary evaporator to yield 54.0 g (99%) of **5**. MS, m/e 544 M(+) ^1H NMR ($CDCl_3$/TMS) 1.35 (t,J_{HH} = 7 Hz, 18 H, CH_3), 3.60 (2H, CH_2OH), 3.95–4.45 (m,18H,CH_2). ^{13}C NMR ($CDCl_3$/TMS) 17.20 (d,J_{PC} = 7.32 Hz, POCH$_2$ÇH$_3$), 46.95 (q,J_{PC} = 7.32 Hz, POCH$_2$Ç) 60.22 (s,ÇH$_2$OH) 65.13 (d,J_{PC} = 6.10 Hz, POÇH$_2$CH$_3$) 65.94 (d, J_{PC} = 6.10 Hz, POÇH$_2$-C). ^{31}P NMR ($CDCl_3/H_3PO_4$Cap). 0.0.

Pentaerythritol tetrakis(diethyl phosphate) **6**

To a magnetically stirred mixture of pentaerythritol (13.6 g, 0.1 mol), carbon tetrachloride (90 mL) and diethyl phosphonate (55.24 g 0.4 mol) cooled in an ice bath was added dropwise triethylamine (40.8 g, 0.4 mol). The reaction mixture was stirred for 60 h and worked up as described for **5**. If the crude product contained significant amount of **5**, it was treated further with diethyl phosphonate (13.6 g), carbon tetrachloride (30 mL) and triethylamine (10.2 g). ^1H NMR 1.35 (t,J_{HH} = 7 Hz,24 H,CH_3), 3.80–4.45 (m,24H,CH_2). ^{13}C NMR ($CDCl_3$/TMS) 16.19 (d,J_{PC} = 6.10 Hz, $POCH_2CH_3$), 45.37 (quintet, J_{PC} = 8.55 Hz,POCH$_2$Ç), 64.20 (d,J_{PC} = 4.88 Hz,POÇH$_2$CH$_3$) 65.17 (s).

Tetraanilinium salt of pentaerythritol tris(dihydrogen phosphate) **7**

To a stirred mixture of **5** (16.32 g, 0.03 mol) and sodium iodide (27 g) in acetonitrile (60 mL) under nitrogen was added trimethylsilyl chloride (19.55 g, 0.18 mol). The reaction mixture was stirred at rt for 40 min and then held at 40°C for 20 min. It was next filtered to remove sodium chloride and volatiles were removed on a rotary evaporator to obtain crude silyl ester. The crude ester was stirred with 30 mL of water for 18 h. The aqueous layer was separated and freeze-dried to get a red syrup which was dissolved in 50 mL ethanol and aniline (16.75 g) dissolved in ethanol (20 mL) was added. The white solid that separated out as a first crop was anilinium phosphate (2.8 g), 'H NMR showed only aromatic protons. Tetraanilinium salt of **7** crystallized out as a second and third crops, 5.5 g and was purified by recrystallization from ethanol to give 4.2 g (18%) of pure tetraanilinium salt of **7**.

Trianilinium salt of pentaerythritol tetrakis(dihydrogen phosphate) **8**

Trimethylsilyl chloride (21.72 g) was added to a stirred mixture of **6** (17.0 g, 0.025 mol) and sodium iodide (30 g) in acetonitrile (60 mL) under nitrogen atmosphere. The reaction mixture was held at 40°C for 30 min and then stirred at rt for 90 min. The workup as described for **7** above gave crude silyl ester that was stirred with 30 ml water for 18 h. Work up as described for **7** gave a red syrup that was dissolved in ethanol (50 mL) and treated with aniline (18.6 g) dissolved in ethanol (20 mL). The solution was warmed and then allowed to stand whereupon anilinium phosphate (4.7 g) separated out as a first crop. The next three crops that separated were combined and crystallized from ethanol to give 1.25 g (7%) of pure trianilinium salt of **8** (colorless needles).

Trianilinium salt of pentaerythritol bis(dihydrogen phosphate) **9**

A solution of 10 g of compound **10** in 75 mL water was refluxed for 5 h. Removal of water on rotary evaporator gave a thick syrup (10 g). A 3.5 g portion of this syrup was dissolved in 30 mL ethanol and

4.5 g of aniline in 20 mL ethanol was added. The solution was warmed and then allowed to stand whereupon trianilinium salt of **9** (4.0 g, 59%) crystallized out as a white solid.

REFERENCES AND NOTES

1. The systematic names for these compounds are **7** 2,2-Bis [(phosphonooxy)methyl]-1,3-propanediol, mono (dihydrogen phosphate), **8** 2,2-Bis [(phosphonooxy)methyl]-1,3-propanediyl bis (dihydrogen phosphate), **9** 2,2-Bis (hydroxymethyl)-1,3-propanediyl bis (dihydrogen phosphate).
2. We are indebted to Dr. Joy E. Merritt of Chemical Abstracts Services for her guidance in questions concerning the nomenclature of these compounds.
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4. (a) D. A. Predvoditelev, L. I. Smirnova and E. E. Nifantev, *Zh. Org. Khim.*, **15,** 2223 (1979). (b) G. A. Olah and S. C. Narang, *Tetrahedron,* **38,** 2225 (1982).
5. (a) G. C. Daul and J. D. Reid, U.S. Patent, 2,583,549. C.A. **46,** 7584i (1952). (b) V. Bellavita and O. Tiberi, *Ricerca Sci.*, **22,** 69 (1952) C.A. **48,** 3889a (1954).
6. R. Ratz and O. J. Sweeting, *J. Org. Chem.*, **28,** 1608 (1963).
7. R. R. Nicholson, R. E. Smith, J. G. Shukla. U.S. Patent 4,205,022 C.A. **94,** 32527j (1981), report the hydrolysis of **10** to **9** but the characterization of **9** is not given.