Convenient Preparation of Long-Chain Dialkyl Phosphates: Synthesis of Dialkyl Phosphates

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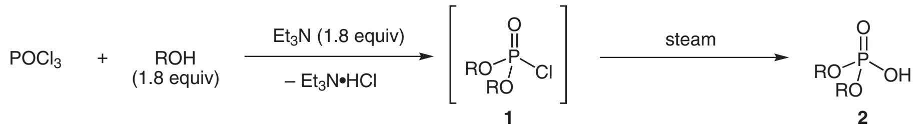
Abstract: Reaction of phosphorus oxychloride with a primary alcohol (1.8 equiv) and triethylamine (1.8 equiv) in toluene, followed by filtration and treatment with steam, gives dialkyl phosphates in good yield and essentially free from trialkyl phosphate contamination.

Key words: dialkyl phosphates, esterification, hydrolysis, hydraulic fracturing, enhanced oil recovery



Scheme 1

Dialkyl phosphates together with ferric salts are used as a key component of hydraulic fracturing fluids employed for enhanced oil and gas recovery.[1] In this application it is desirable that they should not be contaminated with trialkyl phosphates since these are volatile during subsequent refinery processing and may cause blockage of distillation columns leading to refinery shutdowns.[2] Despite this, much of the world production of dialkyl phosphates for this purpose is based on a process involving treatment of phosphorus pentoxide (P_2O_5) with an alcohol in the presence of a trialkyl phosphate,[3] typically triethyl phosphate, added to minimise the formation of monoalkyl phosphates. This process appears to involve initial interaction of the trialkyl phosphate with phosphorus pentoxide to form a mixture of polyphosphoric acid esters,[4] which undergo subsequent alcoholysis. The problem may be tackled downstream by removal of the phosphorus compounds from the oil, for example, using ceramic blocks containing basic metal oxides.[5] Replacement of triethyl phosphate by the less volatile tributyl and higher trialkyl phosphates reduces the problems somewhat,[6] but it would clearly be preferable to eliminate the trialkyl phosphates entirely from the production process. We describe here a convenient two-step process for synthesis of dialkyl phosphates, using inexpensive starting materials and conditions suitable for scale-up, which gives products free from any significant trialkyl phosphate impurities.

Various routes have been described for the synthesis of dialkyl phosphates including alkaline hydrolysis of trialkyl phosphates,[7] reaction of 2-chloro-2-oxo-1,3,2-benzodioxaphosphole (*o*-phenylene phosphorochloridate) with two equivalents of an alcohol followed by deprotection of the resulting dialkyl *o*-hydroxyphenyl phosphate with $PhI(OAc)_2$,[8] and for decyl and longer alkyl chains only, reaction of phosphorus oxychloride ($POCl_3$) with three equivalents of alcohol in benzene.[9,10] The last method, which proceeds in low yield (11–35%), appears to depend on selective crystallisation of the solid dialkyl phosphate from the complex mixture, including trialkyl phosphates, which is present and is not applicable for liquid compounds with less than ten carbons in the alkyl group.

We recently described the reaction of phosphorus oxychloride with two equivalents of an alcohol and pyridine in diethyl ether to give dialkylphosphoryl chlorides **1** and their subsequent hydrolysis in aqueous acetone to give dialkyl phosphates **2**.[2] However, various aspects of this procedure were unsuitable for large-scale operation and the product contained appreciable amounts of the undesired trialkyl phosphate. We therefore optimised the process by examining each parameter in turn. Toluene was found to be a highly satisfactory replacement for the volatile diethyl ether and had the additional advantage that its higher boiling point was compatible with steam hydrolysis, avoiding the need for evaporation to obtain **1** and its redissolution for hydrolysis to **2**. Triethylamine was found to give a more rapid reaction than pyridine. Hydrolysis of dialkylphosphoryl chlorides **1** under aqueous alkaline conditions is well known, but results in some degree of ester exchange leading to formation of the undesired trialkyl

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phosphates and monoalkyl phosphates.[11] We found that, while heating either the solution of **1** in toluene, directly obtained after filtering off the triethylamine hydrochloride, or pure **1** from its evaporation with water at various temperatures between 50 and 90 °C resulted in hydrolysis to give **2**; the most efficient and rapid procedure involved passing a current of steam through the heated toluene solution under reflux conditions (Scheme 1). Finally the influence of the reacting proportions on the amount of trialkyl phosphate in the final product was examined and it was found that by using 1.8 equivalents of alcohol and triethylamine the ratio of undesired trialkyl phosphate to dialkyl phosphate in the final product **2** could be reduced from 1:8 to 1:50 as determined by ^{31}P NMR spectroscopy. The results obtained under these optimised conditions are shown in Table 1.

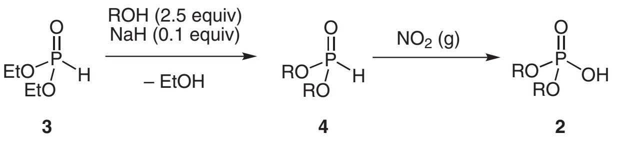
Table 1 Dialkyl Phosphates Prepared

R	^{31}P NMR of **1**, δ	^{31}P NMR of **2**, δ	Overall yield of **2** (%)
butyl	+5.1	+0.1	78
pentyl	+5.1	+0.2	80
hexyl	+4.6	+0.2	79
2-ethylbutyl	+4.9	+0.4	82
octyl	+4.9	+0.4	93
2-ethylhexyl	+4.9	+0.4	85
decyl	+4.7	+1.0	74
dodecyl	+5.0	+1.4	74

It should be noted that this gave the products directly in sufficient purity for further use, which was fortunate, since attempts to purify the liquid dialkyl phosphates by distillation, even under very high vacuum,[12] resulted in their decomposition with the formation of condensation products and distillation of the relevant alcohol.

The applicability of the method to secondary and tertiary alcohols was briefly examined. With butan-2-ol, the desired product was formed but in a much lower yield of 19%, and with *tert*-butyl alcohol none of the dialkyl phosphate was formed at all with all phosphorus-containing components ending up in the aqueous layer after the steam treatment. The method is thus limited to primary alcohols.

Although this procedure ultimately gave the best results, an alternative approach was also examined involving ester exchange of diethyl phosphite **3** with a longer chain alcohol to give **4**, which could then be oxidised (Scheme 2). The reaction of **3** with hexanol in the presence of catalytic sodium hydride did give dihexyl phosphite in good yield.[13]



Scheme 2

Recently both trichloroisocyanuric acid,[14] and a solid-supported *N*,*N*-dichlorobenzenesulfonamide,[15] have been reported to efficiently convert dialkyl phosphites such as **4** into the corresponding dialkylphosphoryl chlorides **1**, which could then be hydrolysed. However this adds and extra step to the synthesis and we preferred to examine direct oxidation of **4** to give **2**. A variety of oxidants for dialkyl phosphites have been reported including air in the presence of catalytic dibenzoyl peroxide,[16] but this method was not successful in our hands. Instead we chose to use gaseous nitrogen dioxide.[12,17] Passing this gas through pure dihexyl phosphite for 1.5 hours did afford the desired dihexyl phosphate in excellent yield and comparable purity to that obtained from the method of Scheme 1. However the hazards and environmental problems associated with the use of gaseous nitrogen dioxide meant that this method is unlikely to be viable on a large scale.

All NMR data were recorded in $CDCl_3$ on a Bruker instrument at 400 MHz (^{1}H), 100 MHz (^{13}C) and 162 MHz (^{31}P), and are referenced to internal Me_4Si (^{1}H and ^{13}C) or external 85% H_3PO_4 (^{31}P). Spectroscopic data were in good agreement with literature values where these were available for comparison as shown.

Dialkyl Phosphates; General Procedure

A solution of $POCl_3$ (30.7 g, 18.7 mL, 0.2 mol) in toluene (70 mL) was stirred at r.t. while a mixture of the appropriate alcohol (0.36 mol) and Et_3N (36.4 g, 50.2 mL, 0.36 mol) was added slowly so that the temperature did not rise above 60 °C. After the addition, the mixture was filtered to give $Et_3N \cdot HCl$ as a white solid (>95%). The filtrate containing the dialkyl chlorophosphate in toluene was stirred vigorously while steam from an external steam generator was passed through it for 1 h. The organic layer was separated, dried ($MgSO_4$), and the toluene evaporated to give the pure dialkyl phosphate as a colourless liquid (or colourless needles in the case of didecyl phosphate and didodecyl phosphate) (Table 1).

Dibutyl Phosphate

Yield: 29.5 g (78%); colourless liquid.

^{1}H NMR: δ = 0.93 (t, J = 7 Hz, 6 H), 1.42 (sext, J = 7 Hz, 4 H), 1.66 (quint, J = 7 Hz, 4 H), 4.02 (q, J = 7 Hz, 4 H), 10.51 (s, 1 H, OH) (Lit.[7,8]).

^{13}C NMR: δ = 13.6, 18.7, 32.2 (d, J = 7 Hz), 67.4 (d, J = 6 Hz) (Lit.[7,8]).

^{31}P NMR: δ = +0.1.

HRMS (CI^{+}): *m/z* [M + H^{+}] calcd for $C_8H_{20}O_4P$: 211.1099; found: 211.1098.

Dibut-2-yl Phosphate

This reaction was carried out on a threefold smaller scale than the general procedure. Yield: 2.4 g (19%); colourless liquid.

^{1}H NMR: δ = 0.94 (t, J = 7 Hz, 6 H), 1.32 (d, J = 6 Hz, 6 H), 1.66 (quint, J = 7 Hz, 4 H), 4.40 (m, 2 H), 12.50 (s, 1 H, OH) (Lit.[8]).

^{13}C NMR: δ = 9.3, 20.8 (d, J = 3 Hz), 30.2 (d, J = 6 Hz), 77.1 (d, J = 6 Hz) (Lit.[8]).

^{31}P NMR: δ = –0.4.

Dipentyl Phosphate

Yield: 34.3 g (80%); colourless liquid.

^{1}H NMR: δ = 0.91 (t, J = 7 Hz, 6 H), 1.32–1.40 (m, 8 H), 1.68 (quint, J = 7 Hz, 4 H), 4.01 (q, J = 7 Hz, 4 H), 9.72 (s, 1 H, OH).

^{13}C NMR: δ = 13.7, 22.0, 27.4, 29.7 (d, J = 7 Hz), 67.3 (d, J = 6 Hz).

^{31}P NMR: δ = +0.2.

HRMS (ES$^-$): m/z [M – H$^+$] calcd for $C_{10}H_{22}O_4P$: 237.1256; found: 237.1247.

Dihexyl Phosphate

Yield: 37.8 g (79%); colourless liquid.

^{1}H NMR: δ = 0.89 (t, J = 7 Hz, 6 H), 1.24–1.47 (m, 12 H), 1.59–1.74 (m, 4 H), 4.02 (q, J = 7 Hz, 4 H, OCH_2), 10.25 (s, 1 H, OH) (Lit.[8]).

^{13}C NMR: δ = 13.8, 22.4, 24.9, 30.0 (d, J = 6 Hz), 31.2, 67.4 (d, J = 6 Hz) (Lit.[8]).

^{31}P NMR: δ = +0.2.

HRMS (ES$^-$): m/z [M – H$^+$] calcd for $C_{12}H_{26}O_4P$: 265.1569; found: 265.1571.

Bis(2-ethylbutyl) Phosphate

Yield: 39.3 g (82%); colourless liquid.

^{1}H NMR: δ = 0.90 (t, J = 7 Hz, 12 H), 1.29–1.57 (m, 10 H), 3.94 (t, J = 6 Hz, 4 H), 10.65 (s, 1 H, OH).

^{13}C NMR: δ = 10.8, 22.6, 41.5 (d, J = 7 Hz), 69.0 (d, J = 7 Hz).

^{31}P NMR: δ = +0.4.

HRMS (ES$^-$): m/z [M – H$^+$] calcd for $C_{12}H_{26}O_4P$: 265.1569; found: 265.1573.

Dioctyl Phosphate

Yield: 53.9 g (93%); colourless liquid.

^{1}H NMR: δ = 0.88 (t, J = 7 Hz, 6 H), 1.22–1.48 (m, 20 H), 1.67 (quint, J = 7 Hz, 4 H), 4.02 (q, J = 7 Hz, 4 H), 10.53 (s, 1 H).

^{13}C NMR: δ = 13.9, 22.5, 25.3, 29.0, 29.1, 30.1 (d, J = 7 Hz), 31.7, 67.4 (d, J = 6 Hz).

^{31}P NMR: δ = +0.4.

HRMS (ES$^-$): m/z [M – H$^+$] calcd for $C_{16}H_{34}O_4P$: 321.2195; found: 321.2188.

Bis(2-ethylhexyl) Phosphate

Yield: 49.3 g (85%); colourless liquid.

^{1}H NMR: δ = 0.83–0.97 (m, 12 H), 1.22–1.48 (m, 16 H), 1.52–1.65 (m, 2 H), 3.90–4.00 (m, 4 H), 9.12 (s, 1 H, OH).

^{13}C NMR: δ = 10.6, 13.8, 22.8, 23.0, 28.7, 29.7, 39.9 (d, J = 8 Hz), 69.2 (d, J = 6 Hz) (Lit.[18]).

^{31}P NMR: δ = +0.4 (Lit.[19]).

HRMS (ES$^-$): m/z [M – H$^+$] calcd for $C_{16}H_{34}O_4P$: 321.2195; found: 321.2198.

Didecyl Phosphate

Yield: 50.3 g (74%); colourless solid; mp 47–48 °C (Lit.[20] mp 44–46 °C).

^{1}H NMR: δ = 0.88 (t, J = 7 Hz, 6 H), 1.22–1.42 (m, 28 H), 1.62–1.72 (m, 4 H), 4.01 (q, J = 7 Hz, 4 H), 7.27 (s, 1 H, OH) (Lit.[8,18]).

^{13}C NMR: δ = 14.0, 22.6, 25.4, 29.1, 29.3, 29.4, 29.5, 30.1 (d, J = 7 Hz), 31.9, 67.6 (d, J = 6 Hz) (Lit.[8,20]).

^{31}P NMR: δ = +1.4 (Lit.[20]).

HRMS (ES$^-$): m/z [M – H$^+$] calcd for $C_{20}H_{42}O_4P$: 377.2821; found: 377.2822.

Didodecyl Phosphate

Yield: 57.8 g (74%); colourless solid; mp 54–55 °C (Lit.[21] mp 56–58 °C).

^{1}H NMR: δ = 0.88 (t, J = 7 Hz, 6 H), 1.25–1.40 (m, 36 H), 1.67 (quint, J = 7 Hz, 4 H), 4.01 (q, J = 7 Hz, 4 H), 9.60 (br s, 1 H, OH) (Lit.[10]).

^{13}C NMR: δ = 14.1, 22.7, 25.4, 29.2, 29.4, 29.54, 29.60, 29.64, 29.66, 30.2 (d, J = 7 Hz), 31.9, 67.7 (d, J = 6 Hz) (Lit.[10]).

^{31}P NMR: δ = +1.0 (Lit.[10]).

HRMS: (CI$^+$): m/z [M + H$^+$] calcd for $C_{24}H_{52}O_4P$: 435.3603; found: 435.3594.

Dihexyl Phosphite

A mixture of diethyl phosphite (13.81 g, 0.1 mol), hexan-1-ol (25.54 g, 0.25 mol), and NaH (0.24 g, 0.01 mol) was heated in a flask set up for distillation at 160 °C for 3 h. During this time, EtOH steadily distilled over. The remaining hexane and EtOH were then removed by vacuum distillation (Kugelrohr) to leave a residue of dihexyl phosphite (22.4 g, 89%) as a colourless liquid.

^{1}H NMR: δ = 0.90 (t, J = 7 Hz, 6 H), 1.26–1.44 (m, 12 H), 1.64–1.75 (m, 4 H), 4.07 (q, J = 8 Hz, 4 H), 6.80 (d, $^1J_{\text{P-H}}$ = 693 Hz, 1 H).

^{13}C NMR: δ = 13.7, 22.3, 25.0, 30.1 (d, J = 6 Hz), 31.1, 64.6 (d, J = 6 Hz).

^{31}P NMR: δ = +7.6.

Dihexyl Phosphate

By Oxidation of Dihexyl Phosphite: Dihexyl phosphite (12.5 g, 50 mmol) was stirred in a cooling bath and the temperature maintained below 35 °C while NO_2 was bubbled through it from a cylinder for 1.5 h. After this time, N_2 was bubbled through the resulting green liquid for 2 h. This gave dihexyl phosphate (12.9 g, 97%) as a faintly yellow liquid. For spectroscopic data, see above.

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