A General Reagent for *O*-Phosphonomethylation of Phenols

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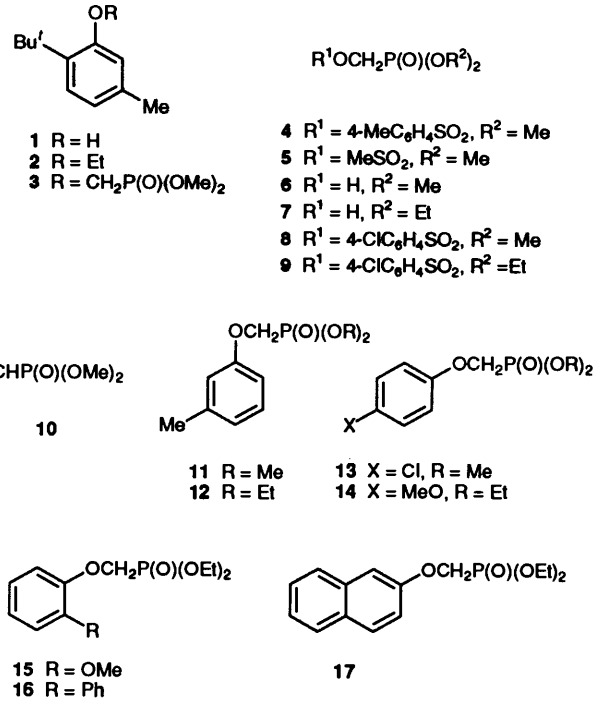
Diethyl 4-chlorophenylsulfonyloxymethylphosphonate, $ClC_6H_4SO_2OCH_2P(O)(OEt)_2$, has been established as the reagent of choice for conversion of phenols *via* alkali phenoxides into phenoxymethylphosphonates. With other leaving groups (iodide, methanesulfonate, toluene-4-sulfonate), or with the dimethyl instead of the diethyl ester, concomitant formation of alkyl phenyl ethers reduced the yields. The reactions proceeded easily in polar aprotic solvents, usually at room temperature, and yields were excellent. The products were easily converted by mild alkaline hydrolysis into monoesters, or into phosphonic acids *via* cleavage with iodotrimethylsilane. Some phenols were also converted into diethyl aryloxymethylphosphonates by incorporation into mixed formals by reaction with 2,4-dichlorophenoxymethyl chloride, followed by Lewis acid-catalysed transfer of an aryloxymethyl group to triethyl phosphite.

As part of a project[1] to synthesize water-soluble catalysts of alkene hydration, we needed methods for attaching water-solubilizing groups to rather large molecules. Phosphonomethoxy groups, $(HO)_2P(O)CH_2O$, are promising candidates since they have pK_1 around 1.37[2] and easily form aqueous solutions at pH 2–3, the target range for our catalysis. For convenience in synthesis, such groups would be added at a later stage by attachment of phosphonomethyl groups to phenols. Thus we needed a high-yielding method (especially since each molecule would usually present two phenolic groups for reaction), insensitive to the presence of most other functions; a survey of the literature disclosed no such method. The most direct[3] procedure, whereby disodium chloromethylphosphonate $ClCH_2P(O)(ONa)_2$ is heated at 160 °C with the sodium phenoxide in an excess of the phenol, can give high yields based on phosphonate but not on phenol. Diethyl iodomethylphosphonate $ICH_2P(O)(OEt)_2$ reacted[4] with sodium phenoxides at 160–200 °C to give indifferent yields of the monoester salts $ArOCH_2P(O)(OEt)(ONa)$, along with phenetoles ArOEt and other products. When aryloxymethyl chlorides are available, the Arbuzov reaction with a trialkyl phosphite can give dialkyl aryloxymethylphosphonates,[5] but this is not a general method; we tried a modification (see later) with limited success.

Re-examination of diethyl iodomethylphosphonate as a reagent, with hexamethylphosphoramide to speed up reaction, showed that with a test phenol, 2-*tert*-butyl-5-methylphenol **1**, the phenetole **2** was the main product, and that the disodium or dilithium salt $ICH_2P(O)(ONa$ or $OLi)_2$ did not react with the sodium phenoxide in hexamethylphosphoramide even at 100 °C. We then tried sulfonate esters of dialkyl hydroxymethylphosphonates: leaving groups more reactive than iodide might outweigh the tendency of phosphonic esters to etherify phenols.†

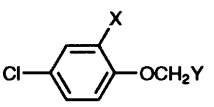
The first specimens (**4** and **5**) were made from the known[6] dimethyl diazomethylphosphonate **10** by reaction with anhydrous toluene-*p*-sulfonic acid or methanesulfonic acid in benzene. Later, we used the reaction of dialkyl hydroxymethylphosphonates (**6** and **7**) with sulfonyl chlorides and triethylamine to make the crystalline esters **8** and **9**. The esters **6** and **7** have usually been made by addition of dialkyl phosphites to paraformaldehyde (*e.g.*, ref. 7), but the use of aqueous formaldehyde is simpler[8] and crude products can be used for sulfonylation.



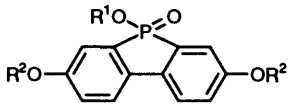
In general, the test phenol in dimethyl sulfoxide was converted into the sodium phenoxide with sodium hydride, the sulfonate ester was added and reaction proceeded at room temperature. The mesylate ester **5** was discarded after NMR analysis of its product with 3-methylphenol indicated a 4:1 molar ratio of ester **11** and 3-methylanisole. The tosylate dimethyl ester **4** gave a near-quantitative yield of product **11** after 1 h at room temperature, but with 4-chlorophenol and with the test phenol **1**, yields of the desired phosphonomethylated products were diminished by around 15% of the methyl ethers. These results are not further described.

A useful advance was made with the 4-chlorophenylsulfonyl dimethyl ester **8**, which formed dimethyl aryloxymethylphosphonates (**11**, **13**, **3**) from 3-methylphenol, 4-chlorophenol and the test phenol **1** without appreciable methylation; however,

† Other possible factors influencing the balance between products ArOR and $ArOCH_2P(O)(OR)_2$ in reactions between ArO^- and $XCH_2P(O)(OR)_2$ are: (i) nucleophilicity of the leaving X^- group (*e.g.*, I^-), which could generate RX from the phosphonate and thence lead to ArOR, regenerating X^- for further attack; (ii) (as suggested by a referee) the effect of X on the potential leaving group $XCH_2P(O)(OR)O^-$.



18 X = H, Y = OAlk
19 X = Cl, Y = OAr
20 X = Cl, Y= P(O)(OEt)$_2$



21 R^1 = Me, R^2 = H
22 R^1 = H, R^2 = $CH_2P(O)(OH)_2$

with 2-naphthol and with 2-phenylphenol a little methyl ether was detectable. The 4-chlorophenylsulfonyl diethyl ester **9** was best of all: this stable, crystalline reagent has so far phosphonomethylated all phenols tried without appreciable formation of *O*-ethyl side products. A preparation with a lower melting point has previously been reported.[9] The products (**15**, **16**, **17**) from 2-methoxyphenol, 2-phenylphenol, and 2-naphthol respectively were made in 92–94% yields.

The dialkyl aryloxymethylphosphonates produced in this study were easily purified by chromatography on silica, but being usually oils they were characterized, when required, by alkaline half-hydrolysis and isolation of the monoalkyl esters as crystalline benzylammonium or benzhydrylammonium salts. Phosphonic acids were made when required by an exceptionally clean and selective cleavage of the diesters with iodotrimethylsilane in dichloromethane or chloroform.[10] This completed the solution of our problem.

One of us[11] has reported a general synthesis of alkoxymethylphosphonic esters by Lewis acid-catalysed transfer of alkoxymethyl groups from alkoxy-4-chlorophenoxymethanes **18** to triethyl phosphite. We tried this method as a source of diethyl aryloxymethylphosphonates, preparing the intermediate formals **19** from 2,4-dichlorophenoxymethyl chloride and sodium phenoxides in tetrahydrofuran, and initiating the transfer to triethyl phosphite in dichloromethane at −78 °C by addition of titanium tetrachloride. Although 3-methylphenol, 2-phenylphenol, and 4-methoxyphenol afforded the expected diethyl aryloxymethylphosphonates (**12**, **16**, **14**) in reasonable yields (62–68%) the product from 2-methoxyphenol was exclusively **20**, from transfer of the dichlorophenoxymethyl group: remarkable, but no basis for a general method.

Application of the procedure to 3,7-dihydroxy-5-methoxy-5*H*-dibenzophosphole 5-oxide **21**, readily prepared from the 5-hydroxy analogue[12] by sequential treatment with thionyl chloride and methanol, gave in 80% overall yield after cleavage the crystalline bisphosphonic-phosphinic acid **22**. The disodio compound of **21** is exceptionally insoluble and here potassium carbonate was used *in situ* to promote reaction in hexamethylphosphoramide with the sulfonate ester **9**.

Experimental

M.p.s were observed in an Electrothermal apparatus and are uncorrected. ^{1}H NMR spectra were taken at 60 MHz in deuteriochloroform with a tetramethylsilane internal standard, and ^{31}P NMR spectra were taken at 32.43 MHz in deuteriochloroform and referred to 85% orthophosphoric acid as standard, except where otherwise stated. *J* values are recorded in Hz. Mass spectra were generated by electron impact. Sodium hydride as a 50% dispersion in mineral oil was washed with hexanes before use. 'Hexanes' means light petroleum, b.p. 60–80 °C; 'ether' means diethyl ether; 'brine' means saturated aqueous sodium chloride. Solvents were purified by routine methods; proportions of mixed solvents are by volume.

Reaction of Diethyl Iodomethylphosphonate with 2-tert-*Butyl-5-methylphenol.*—The phenol (164 mg, 1 mmol) in hexamethylphosphoramide (4 cm^3) was stirred with sodium hydride (50%; 60 mg) for 20 min, then diethyl iodomethylphosphonate (300 mg, 1.08 mmol; prepared from triethyl phosphite and diiodomethane at 190 °C)[13] was added. After a further 2.5 h, TLC (silica; hexanes–ethyl acetate, 4:1) showed no phenol and a fast-running component which was separated from excess of iodo ester by column chromatography in the same system, yielding 4-*tert*-butyl-3-ethoxytoluene (170 mg, 88%); δ_H 1.38 (9 H, s, Bu^t), 1.43 (3 H, t, *J* 7, CH_2*Me*), 2.28 (3 H, s, Me), 3.98 (2 H, q, *J* 7, CH_2), 6.58 (1 H, d, *J* 8, 6-H) overlapping 6.58 (1 H, s, 2-H) and 7.04 (1 H, d, *J* 8, 5-H).

Dimethyl p-*Tolylsulfonyloxymethylphosphonate.*—Toluene-*p*-sulfonic acid monohydrate (17 g) was dehydrated by heating at 60 °C and 0.1 mmHg for 2 h, followed by boiling in benzene (320 cm^3) for 4 h under a Dean–Stark trap. Dimethyl diazomethylphosphonate[6] **10** (12 g) was added slowly to this solution at room temperature. When no more gas was evolved ethyl acetate (150 cm^3) and water (50 cm^3) were also added to the solution. The upper layer was separated, washed with saturated aqueous sodium hydrogen carbonate (70 cm^3) and with brine (50 cm^3), and then dried ($MgSO_4$) and evaporated at low pressure, leaving the title ester **4** as an oil (12.8 g); δ_H 2.42 (3 H, s, Ar-Me), 3.73 (6 H, d, *J* 10.5, OMe), 4.16 (2 H, d, *J* 8.5, CH_2), 7.25 (2 H, d, *J* 8, 3′,5′-H) and 7.68 (2 H, d, *J* 8, 2′,6′-H). This sample was used directly for reaction with sodium phenoxides.

Dimethyl Methylsulfonyloxymethylphosphonate.—Methanesulfonic acid (0.9 cm^3, 13 mmol) was dissolved in benzene (60 cm^3), half of which was then distilled off under nitrogen. This solution was added in portions to a solution of the diazophosphonate **10** (1.05 g, 7 mmol) in benzene (2 cm^3). When gas was no longer evolved the mixture was evaporated at low pressure and dissolved in chloroform (100 cm^3) which was then washed with saturated aqueous sodium hydrogen carbonate (2 × 50 cm^3) and brine (50 cm^3), dried ($MgSO_4$) and evaporated to leave the title ester **5** (0.6 g); δ_H 3.1 (3 H, s, MeS), 3.8 (6 H, d, *J* 10.5, OMe) and 4.4 (2 H, d, *J* 8.5, CH_2), which was used without further purification.

Dimethyl and Diethyl 4-*Chlorophenylsulfonyloxymethylphosphonates.*—(i) Dimethyl phosphite (22.01 g, 0.2 mol) and aqueous formaldehyde (38%; 20 g, 0.25 mol) were mixed, cooled in ice, stirred, and treated with triethylamine (4 cm^3) added dropwise over 0.5 h. After a further 1.5 h at 5–10 °C the mixture was heated at 50 °C/14 mmHg for 1.5 h and finally at 100–110 °C/0.1 mmHg for 0.5 h. A portion (14 g) of this product was dissolved in dry ether (140 cm^3) containing triethylamine (15.3 cm^3, 0.11 mol) and stirred at −10 °C during dropwise addition of 4-chlorobenzenesulfonyl chloride (23.2 g, 0.11 mol). The mixture was stirred at 0 °C for 2 h and then overnight without cooling. The precipitate was filtered off and the filtrate on evaporation at low pressure left an oil (20.1 g) which was dissolved in chloroform–hexanes (2:3) and passed down a column of silica. When residual sulfonyl chloride ceased to be eluted the solvent was changed to chloroform and the dimethyl 4-chlorophenylsulfonyloxymethylphosphonate **8** (16.5 g) was collected and recrystallized from chloroform–hexanes, m.p. 66–67 °C (Found: C, 34.4; H, 3.9. $C_9H_{12}ClO_6PS$ requires C, 34.35; H, 3.8%); δ_H 7.84 (2 H, d, *J* 9, 2′,6′-H), 7.51 (2 H, d, *J* 9, 3′,5′-H), 4.26 (2 H, d, *J* 10, CH_2) and 3.78 (6 H, d, *J* 10, OMe); δ_P +16.6.

(ii) Using diethyl phosphite (27.3 g, 0.2 mol) instead of dimethyl phosphite and taking 16.8 g of crude product for sulfonylation, exactly the same procedure was followed except for the final work-up. After filtration water (200 cm^3) and ethyl acetate (200 cm^3) were added to the filtrate; the organic layer was washed with brine (150 cm^3), dried ($MgSO_4$) and

evaporated. The residue was chromatographed as for the dimethyl ester (chloroform–hexanes, 1:1, then chloroform). The solid product (17.5 g) on recrystallization from carbon tetrachloride gave the pure diethyl 4-chlorophenylsulfonyloxymethylphosphonate **9**, m.p. 48 °C (lit.,[9] 42–43 °C); δ_H 7.82 (2 H, d, *J* 10, 2',6'-H), 7.63 (2 H, d, *J* 10, 3',5'-H), 4.19 (2 H, d, *J* 9, CH_2P), 4.12 (4 H, dq, *J* 8, 8, OCH_2) and 1.32 (6 H, t, *J* 8, Me); δ_P +14.0.

General Methods for Phosphonomethylations with Dialkyl Arylsulfonyloxymethylphosphonates.—Sodium hydride (slight excess) was stirred with a solution (*ca.* 0.5 mol dm^{-3}) of the phenol in dry dimethyl sulfoxide. When reaction ceased, a solution (*ca.* 1.5 mol dm^{-3}) of the sulfonatophosphonate (usually 5–10% excess) was added to the mixture. The mixture was stirred at room temperature, whilst the reaction was monitored by TLC on silica, generally using ethyl acetate–hexanes mixtures for development and the phenol, the alkyl phenyl ether, and the sulfonatophosphonate as controls. Most of the reaction occurred in the first hour but stirring was usually continued overnight. When no phenol remained, the mixture was diluted with water and the product was extracted into ether or ethyl acetate. The extract was washed twice with brine, dried ($MgSO_4$) and evaporated. The crude product was put on a column of silica (flash chromatography grade) and eluted first with ethyl acetate–hexanes (1:3). Ethyl acetate then eluted the (generally oily) product, which was examined spectroscopically. For characterization as a crystalline solid a sample was dissolved in ethanol (15 cm^3 $mmol^{-1}$ ester) and aqueous sodium hydroxide (4%; 15 cm^3; $mmol^{-1}$ ester) and the mixture was kept at 50 °C for 5 h. The next day the ethanol was removed at low pressure and the residue was acidified with hydrochloric acid (2 mol dm^{-3}) and extracted thrice with ethyl acetate. The combined extracts after being washed with brine and dried ($MgSO_4$) were evaporated and the monoester after examination (NMR) was dissolved in a little methanol and treated with a slight excess of salt-forming amine (benzylamine or 1,1-diphenylmethylamine). The salt, recovered by evaporation at low pressure, was recrystallized and analysed. For complete dealkylation the diester was stirred under nitrogen in dry chloroform or dichloromethane (*ca.* 4 cm^3 $mmol^{-1}$) and iodotrimethylsilane (*ca.* 3.5 mmol $mmol^{-1}$ of diester) was added to the solution. After the red solution had been stirred for 2 h, methanol (6 cm^3 $mmol^{-1}$ of diester) was added to it and after a further 2 h it was evaporated at low pressure. The residue was boiled with water in an open flask until a colourless solution was obtained. The aryloxymethylphosphonic acid was recovered by evaporation at low pressure (sometimes, by addition of hydrochloric acid to the concentrated aqueous solution) and recrystallized.

Dimethyl 3-methylphenoxymethylphosphonate **11**. This was an oil, made in 95% yield from 3-methylphenol and the tosylate ester **4**; δ_H(80 MHz) 7.08 (1 H, m), 6.9–6.7 (3 H, m), 4.30 (2 H, d, *J* 10), 3.86 (6 H, d, *J* 10.7) and 2.33 (3 H, s); δ_P +20.92; *m/z* 230 (M^+, 45%), 199 (10), 121 (30) and 93 (100). A product identical with this (TLC, NMR) was obtained in 94% yield with the chloro analogue **8**. Methyl hydrogen 3-methylphenoxymethylphosphonate, an oil, was made from hydrolysis of **10**; its *benzylammonium salt* crystallized from ethyl acetate–hexanes; m.p. 115 °C (Found: C, 59.2; H, 6.7; N, 4.6. $C_{16}H_{22}NO_4P$ requires C, 59.4; H, 6.9; N, 4.3%); δ_P +14.41.

Dimethyl 2-tert-*butyl-5-methylphenoxymethylphosphonate* **3**. This was an oil, prepared in 94% yield from 2-*tert*-butyl-5-methylphenol **1** and the chlorophenylsulfonyl ester **8**, or in 80% yield (after separation from 15% of the anisole) from the tosylate ester **4**; δ_H 7.05 (1 H, d, *J* 8), 6.63 (1 H, br d, *J* 8), 6.57 (1 H, br s), 4.22 (2 H, d, *J* 10), 3.72 (6 H, d, *J* 11), 2.28 (3 H, s) and 1.38 (9 H, s); δ_P +11.86; *m/z* 286 (M^+, 78%), 271 (100), 161 (95) and 105 (90). Methyl hydrogen 2-*tert*-butyl-5-methylphenoxymethylphosphonate, from hydrolysis of **3**, showed δ_H 11.47 (1 H, br s), 7.04 (1 H, d, *J* 8), 6.6 (1 H, br d, *J* 8), 6.53 (1 H, br s), 4.18 (2 H, d, *J* 10), 3.75 (3 H, d, *J* 11), 2.23 (3 H, s) and 1.37 (9 H, s). Its *benzylammonium salt*, crystallized twice from ethyl acetate–hexanes, had m.p. 148–149 °C (Found: C, 63.0; H, 8.1; N, 3.9. $C_{20}H_{30}NO_4P$ requires C, 63.3; H, 8.0; N, 3.7%); δ_P +15.3.

Dimethyl 4-chlorophenoxymethylphosphonate **13**. This was an oil, made in 92% yield from 4-chlorophenol and the chlorophenylsulfonyl ester **8** and in 68% yield from the tosylate ester **4**; δ_H 7.03 (2 H, d, *J* 8), 6.72 (2 H, d, *J* 8), 4.15 (2 H, d, *J* 10) and 3.73 (6 H, d, *J* 10); δ_P +20.2; *m/z* 250 (M^+ for ^{35}Cl, 6%), 236 (40), 141 (23), 128 (100) and 111 (46).

Methyl hydrogen 4-chlorophenoxymethylphosphonate. This was an oil and showed δ_H 11.0 (1 H, br s), 7.1 (2 H, d, *J* 9), 6.71 (2 H, d, *J* 9), 4.15 (2 H, d, *J* 10) and 3.73 (3 H, d, *J* 9); δ_P +13.8; its *benzylammonium salt* had m.p. 159 °C after crystallization from ethyl acetate–hexanes (Found: C, 52.2; H, 5.7; N, 4.2. $C_{15}H_{19}ClNO_4P$ requires C, 52.4; H, 5.6; N, 4.1%).

Diethyl 2-methoxyphenoxyphosphonate **15**. This was an oil made in 92% yield from guaiacol and the chlorophenylsulfonyl ester **9** and showed δ_H 7.3 (4 H, br s), 4.37 (2 H, d, *J* 9), 4.27 (4 H, dq, *J* 7, 7), 3.85 (3 H, s) and 1.21 (6 H, t, *J* 7); δ_P +18.5; *m/z* 274 (M^+, 47%), 137 (60), 125 (75), 109 (35) and 95 (100). The 1,1-*diphenylmethylammonium salt* of the monoethyl ester from **15** had m.p. 94 °C (from carbon tetrachloride–hexanes) (Found: C, 64.3; H, 6.4; N, 3.6. $C_{23}H_{28}NO_5P$ requires C, 64.3; H, 6.6; N, 3.3%).

Diethyl 2-phenylphenoxymethylphosphonate **16**. This was an oil made in 92% yield from the chlorophenylsulfonyl ester **9** and 2-phenylphenol and showed δ_H 7.54–6.78 (9 H, m), 4.17 (2 H, d, *J* 10), 3.96 (4 H, dq, *J* 8, 8), 1.19 (6 H, t, *J* 8); δ_P +17.7. Iodotrimethylsilane produced *2-phenylphenoxymethylphosphonic acid*, m.p. 162 °C (from ethyl acetate–hexanes) (Found: C, 59.2; H, 5.3. $C_{13}H_{13}O_4P$ requires C, 59.1; H, 5.0%); δ_H(360 MHz, D_2O) 7.51 (2 H, dt, *J* 7, 1.6), 7.35–7.19 (5 H, m), 7.03–6.97 (2 H, m) and 4.12 (2 H, d, *J* 10.5); *m/z* 264 (M^+, 1%).

Diethyl 2-naphthyloxymethylphosphonate **17**. This was an oil, prepared in 94% yield from 2-naphthol and the chlorophenylsulfonate ester **9**; the ^1H NMR spectrum was uninformative since nearly all signals overlapped; δ_P +18.50; *m/z* 294.1027 (M^+ for $C_{15}H_{19}O_4P$ requires 294.1021); partial hydrolysis gave *ethyl hydrogen 2-naphthyloxymethylphosphonate* which crystallized from chloroform–hexanes; m.p. 104 °C (Found: C, 58.7; H, 5.6. $C_{13}H_{15}O_4P$ requires C, 58.65; H, 5.7%).

Diethyl Aryloxymethylphosphonates from Mixed Formals and Triethyl Phosphite.—A solution of a phenol (5 mmol) in dry tetrahydrofuran (12 cm^3) was added to sodium hydride (5 mmol) and the mixture was stirred under nitrogen for 1 h. 2,4-Dichlorophenoxymethyl chloride[14] (5 mmol) in tetrahydrofuran was added to the mixture which was then heated for 1 h at reflux and finally stirred overnight without heating. The mixture was then diluted with water and the product was extracted into ether (2 × 100 cm^3). The extract was washed with brine, dried ($MgSO_4$) and evaporated. The residue, with triethyl phosphite (1.4 cm^3), was dissolved in dichloromethane (10 cm^3) and the solution cooled to −78 °C; titanium tetrachloride (0.6 cm^3) was then added to it by syringe. The red solution after being allowed to attain room temperature was stirred for 20 h. It was then diluted with water (100 cm^3) and the product, worked up as above with ether, was put on a short flash column of silica. The phenol was removed by elution with ethyl acetate–hexanes (1:3) and the product was eluted with ethyl acetate. Hydrolysis or cleavage of the product was carried out as described above.

With 3-methylphenol, diethyl 3-methylphenoxymethylphosphonate **12**, an oil, was obtained in 68% yield; δ_H 7.2 (1 H, m), 6.83 (3 H, br s), 4.5–4.1 (6 H, m), 2.34 (3 H, s) and 1.33 (6 H, t,

J 7); δ_P +18.62; *m/z* 258 (M^+, 40%), 151 (15), 121 (100), 109 (25), 95 (30) and 91 (90). The 1,1-*diphenylmethylammonium salt* of the derived monoethyl ester had m.p. 54 °C after crystallization from chloroform–hexanes (Found: C, 66.5; H, 6.8; N, 3.7. $C_{23}H_{28}NO_4P$ requires C, 66.8; H, 6.8; N, 3.4%).

With 2-phenylphenol the product, obtained in 62% yield, was identical (TLC, NMR) with the diethyl 2-phenylphenoxymethylphosphonate **16** obtained from the same phenol by reaction with the chlorophenylsulfonyl ester.

With 4-methoxyphenol, diethyl 4-methoxyphenoxymethylphosphonate **14**, an oil, was obtained in 65% yield; δ_H 6.81 (4 H, s), 4.4–4.0 (6 H, m), 3.73 (3 H, s) and 1.36 (6 H, t, *J* 7); δ_P +18.68; *m/z* 274 (M^+, 42%) and 123 (100%).

With 2-methoxyphenol the sole product was diethyl 2,4-dichlorophenoxymethylphosphonate **20**, isolated in 60% yield; b.p. 135 °C/0.09 mmHg (lit.,[5] b.p. 162 °C/0.7 mmHg), identified by its NMR spectrum.

3,7-*Bis*(*phosphonomethoxy*)-5-*hydroxydibenzo*-5H-*phosphole* 5-*Oxide* **22**.—3,5,7-Trihydroxydibenzo-5*H*-phosphole 5-oxide[12] (687 mg) was boiled under reflux with thionyl chloride (8 cm^3). A clear solution formed after 10 min; the reagent was removed at low pressure and the residue was dissolved in dry methanol (5 cm^3) followed by pyridine (0.5 cm^3). After 5 min, water was added to the mixture and most of the methanol was removed at low pressure. The crystalline product was collected, triturated with cold aqueous sodium hydrogen carbonate (5%; 5 cm^3), and filtered off. The dried solid was recrystallized from acetic acid to yield yellow prisms of 3,7-dihydroxy-5-methoxy-5*H*-dibenzophosphole 5-oxide **21** (570 mg) in two crops; m.p. 275 °C (bubbling). A sample (262 mg, 1 mmol) and the diethyl chlorophenylsulfonyl ester **9** (767 mg, 2.2 mmol) in dry hexamethylphosphoramide (2 cm^3) with potassium carbonate (600 mg; freshly ignited) were stirred under nitrogen in a bath at 90 °C for 22 h. Ether was then added to the mixture until precipitation ceased; the mixture was then filtered. The filtrate and washings (ether) were evaporated and the residue was heated at 150 °C/0.2 mmHg to remove hexamethylphosphoramide. The residue was put on a column of silica and eluted first with ethyl acetate–methanol (9:1) to remove a minor fraction (150 mg); ethyl acetate–methanol (4:1) then eluted the major product (413 mg) which was dissolved in dry dichloromethane (9 cm^3) under nitrogen and treated with iodotrimethylsilane (0.8 cm^3). After 90 min the mixture was evaporated (cold trap) under reduced pressure, and treated with methanol (1 cm^3); and after evaporation the methanol treatment was repeated. The residue was boiled with water until all iodine had volatilized; the colourless solution was filtered, concentrated to 2–3 cm^3 and treated with hydrochloric acid (6 mol dm^{-3}; 1 cm^3). Next day the white crystals were collected, washed quickly with ice-cold hydrochloric acid (2 mol dm^{-3}), and dried *in vacuo* over sodium hydroxide to yield the *title compound* **22** as white woolly needles, m.p. 335 °C (decomp.) (Found: C, 38.2; H, 3.6. $C_{14}H_{15}O_{10}P_3$ requires C, 38.5; H, 3.5%); δ_H(360 MHz, D_2O) 7.10 (2 H, dd, *J* 8.6, 4.2, 1-, 9-H), 6.88 (2 H, dd, *J* 11.6, 2.5; 4-, 6-H), 6.69 (2 H, dd, *J* 8.6, 2.5; 2-, 8-H) and 3.95 (4 H, d, *J* 10.1, 2 CH_2). The pentamethyl ester, prepared with diazomethane, showed a single, blue fluorescent spot on TLC (silica; ethyl acetate–methanol, 9:1).

Acknowledgements

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