Synthesis of substituted dibenzophospholes. Part 9.[1] Preparation of two water-soluble phosphinic–polyphosphonic acids

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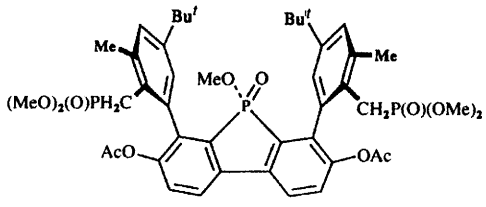
Several improvements, including a generally applicable method for reduction of aromatic nitro compounds to amines, were made to the preparation from 2,2′,4,4′-tetranitrobiphenyl of the *meso* atropisomer 1 of a bis-phosphonomethylated 4,6-diaryldibenzophosphole 5-oxide, previously obtained in impure form.[2] A concomitant product 12 containing one phosphonomethyl group was formed by a novel intramolecular displacement. Both products were converted by a specially developed method[3] into crystalline phosphinic–polyphosphonic acids, containing respectively four and three phosphonomethyl groups, which formed stable monodisperse solutions in water at pH 2–4. These solutions catalysed the hydration of 2-methylpropene to *tert*-butyl alcohol somewhat more efficiently than a toluene-4-sulfonic acid solution of equivalent acidity.

Part 7 of this series[2] reported an amorphous preparation of the phosphinic–phosphonic ester **1**, which was required in substantial amounts for further elaboration into a candidate catalyst for alkene hydration in aqueous solution. Resynthesis of this compound, starting from 2,4,2′,4′-tetranitrobiphenyl, led to several improvements. A convenient procedure for nitrating



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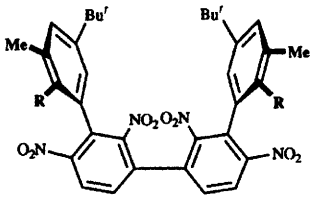
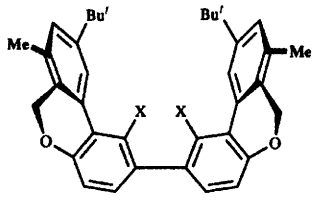


2 R = H
3 R = CH_2Cl
4 R = CH_2OAc

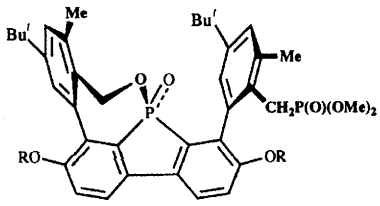


5 X = NO_2
6 X = NH_2
7 X = I
8 X,X = —NH—
9 X,X = —P(O)(OMe)—

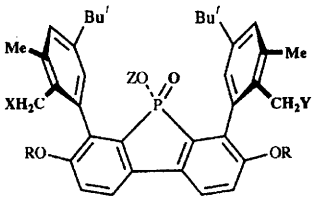
biphenyl and recrystallizing the product yielded tetranitrobiphenyl in purer form than has previously been reported. Reaction with copper(I) *tert*-butoxide and 3-*tert*-butyl-5-iodotoluene as usual yielded the quaterphenyl **2**, converted as before[2] *via* the bis-chloromethyl compound **3** into the bis-acetoxymethyl derivative **4** and thence to the bibenzochromenyl **5**. Reduction of this dinitro compound on a larger scale proved capricious and the earlier procedure using hydrazine and Raney nickel was replaced by a novel method using zinc–copper couple in toluene–acetic acid. This reagent has smoothly reduced all 2,2′-dinitrobiphenyls so far tried, including the parent compound. Since smooth reduction to diamines is exceptionally difficult with this class because benzo[*c*]cinnolines and their *N*-oxides and dihydro compounds tend to be formed, the general method is recommended as quick and convenient for use with aromatic nitro compounds in general. Conversion of the diamine **6** into the diiodide **7** remained the least satisfactory stage (50% yield); a minor by-product was identified as the carbazole **8**.

Reaction of the diiodide with butyllithium and then phosphorus trichloride proceeded as before[2] but conversion of the intermediate chlorophosphole into the cyclic phosphinic ester **9** was much improved by methanolysis followed by oxidation with iodine in wet tetrahydrofuran; this new generally applicable procedure replaces the laborious hydrolysis, oxidation with alkaline hydrogen peroxide, and diazomethane methylation previously employed. The chromane rings were opened by boron tribromide and the intermediate dibromide **10** was acetylated by pyridine–acetyl chloride in benzene. This was more satisfactory than 2,4,6-trimethylpyridine (2,4,6-collidine)–acetic anhydride[2] but led to some replacement of bromine by chlorine if the product **11** was left long in the reaction mixture.

With adequate supplies of the dibromo diacetate **11** the Arbuzov reaction with trimethyl phosphite was re-examined. Comparable amounts of two crystalline esters were found. One was the *meso* ester **1** (the methoxy group is thought to be oriented as shown because of a small (1%) NOE interaction with the *tert*-butyl hydrogens) in pure form; the other was identified as a product in which, apparently, bromide anions formed as intermediates in a normal Arbuzov reaction had attacked the phosphinic ester methyl group, leading to a phosphinate anion which then underwent intramolecular reaction with a surviving bromomethyl group and led to the endocyclic ester **12**. If formed by this mechanism the product **12** could probably be suppressed by substituting ethanolysis for methanolysis in the preparation of the phosphinic ester **9**, but since it was easily isolated the synthesis was continued with it in parallel with the ester **1**. Chirality had been introduced by the intramolecular cyclization but resolution of the racemate would have been pointless for the present purposes.



12 R = Ac
14 R = H
16 R = $CH_2P(O)(OEt)_2$



1 R = Ac; X = Y = $P(O)(OMe)_2$; Z = Me
10 R = H; X = Y = Br; Z = Me
11 R = Ac; X = Y = Br; Z = Me
13 R = H; X = Y = $P(O)(OMe)_2$; Z = Me
15 R = $CH_2P(O)(OEt)_2$; X = Y = $P(O)(OMe)_2$; Z = Me
17 R = $CH_2PO_3H_2$; X = Y = PO_3H_2; Z = H
18 R = $CH_2PO_3H_2$; X = I; Y = PO_3H_2; Z = H
19 R = $CH_2PO_3H_2$; X = H; Y = PO_3H_2; Z = H

The acetyl groups were selectively removed by brief treatment with methanolic alkali and the crystalline phenols **13** and **14** were converted by reaction with diethyl 4-chlorophenylsulfonyloxymethylphosphonate, a reagent specially developed for the purpose,[3] to phosphonate esters **15** and **16**. Cleavage with iodotrimethylsilane then led to the crystalline acid **17** and the amorphous iodomethyl compound **18** which was reduced by zinc–copper couple in acetic acid to a crude crystalline product in which traces of macrocyclic ester persisted. Hydrogenation over palladium on carbon gave the homogeneous crystalline product **19**.

Both acids **17** and **19** were slightly soluble in water and gave colourless, clear, blue-fluorescent solutions on addition of alkali. They were apparently monodisperse in solution although foam formation on boiling indicated surface activity. Since both of them originated from a quaterphenyl **11** of *meso* conformation, the *tert*-butyl groups on the two benzene rings flanking the phosphinic acid function are certainly in **17**, and presumably in **19**, on the same side of the dibenzophosphole ring plane as shown. This geometry was designed to be complementary to the alkene 2-methylpropene, whereas chiral analogues with butyl groups on opposite sides would complement (*E*)-but-2-ene.

Both compounds contain ionizing hydrogen of five different kinds. Each aryloxymethylphosphonic acid function has two hydrogens corresponding to the first and second dissociations. The constants pK_1 and pK_2 for the prototype phenoxymethylphosphonic acid are respectively 1.37 and 6.84.[4] The prototype, benzylphosphonic acid, of the other phosphonic acid functions has pK_1 1.85 and pK_2 7.4.[5] The prototype 5-hydroxydibenzophosphole 5-oxide, representing the phosphinic acid groups, has pK_1 2.8 (all these values are for aqueous solutions). Hence in the experimental conditions described below, using aqueous solutions of the acids **17** and **19** between pH 2.8 and 3.9, substantially all phosphonic acid groups would exist as the very weakly acid monoanions and a high proportion of the phosphinic acid groups were undissociated, especially since ionization yielding oxonium ion would be disfavoured in the shielded phosphinic acids. The effectiveness of the acids **17** and **19** in catalysing the hydration of 2-methylpropene in aqueous solution was examined by heating dilute (0.05 mol l^{-1}) aqueous solutions of the acids, partly neutralized to pH around 3, with excess of the alkene at 50 °C. Conversion (which did not approach the equilibrium) into *tert*-butyl alcohol was measured after the experiment by NMR comparison of the product signal with suitable catalyst peaks, and was compared with conversion effected by toluene-4-sulfonic acid solutions of comparable ionic strength and pH. The acid-catalysed hydration of 2-methylpropene in aqueous solution has been extensively studied[6] and is regarded as a pure oxonium-ion catalysis when strong acids are used. With due reservations it could therefore be concluded that at similar levels of pH and ionic strength, hydration rates in excess of that found with the strong sulfonic acid could be attributed to catalysis by the most electrophilic hydrogen available: that is, by undissociated phosphinic acid. Such catalysis, however, was unremarkable. All solutions of the two acids gave somewhat faster rates of hydration than was observed with the strong acid, but the maximum effect was seen with a solution of the acid **19** at pH 3.88, which catalysed hydration at three times the rate calculated for oxonium-ion catalysis and also at nearly three times the rate calculated on the basis of pH for catalysis by the same acid at lower pH (2.92).

It was also possible to test, with these water-soluble acids, the extent of complexation of 2-methylpropene by the catalysts. Deuterium oxide solutions of the partially neutralized acids were sealed in NMR tubes with 2-methylpropene. In the conditions of the experiment, the molar concentration of the dissolved alkene was smaller than that of the catalyst. Appreciable complexation between the alkene and the phosphinic acid groups would have affected the proton signals from the alkene because of shielding by the pendant aryl rings, as seen invariably in esters of similar phosphinic acids including, *e.g.* the esters **1**, **10**, **11**, **13** and **15**. In fact no disturbance of the 2-methylpropene signals was observed in comparison with a similar solution of orthophosphoric acid. Thus no complexation comparable to that of an enzyme with, *e.g.* a substrate or a competitive inhibitor was achieved. Taken together the results suggest that to reach useful levels of catalysis the cleft flanking the phosphinic acid function must be better designed.

Experimental

Mps were observed in an Electrothermal apparatus and are uncorrected. NMR Spectra were determined, on Bruker WM-360 or Bruker AMX-500 instruments, in deuteriochloroform unless stated otherwise; ^{31}P chemical shifts are referred to 85% orthophosphoric acid. 'Hexanes' means light petroleum, bp 60–80 °C. Solvents were purified by routine methods; proportions of mixed solvents are by volume.

2,4,2′,4′-Tetranitrobiphenyl

Biphenyl (77.1 g) was added to stirred, ice-cooled sulfuric acid (400 ml; *d* 1.84). Nitric acid (300 ml; *d* 1.5) was added dropwise (*ca.* 20 drops min^{-1} at first) so that the temperature did not rise above 12 °C (total time 2 h). The ice bath was removed, whereupon the temperature rose slightly above ambient. After 1 h the mixture was warmed; at 35 °C a sample on TLC (silica; ethyl acetate–hexanes 1:2; twice developed) showed only the tetranitro compound with a small faster-running spot. Heating was continued up to 93 °C; the cooled mixture was poured on ice (2 kg) and dichloromethane (1 l). The upper layer was decanted into a 5 l separatory funnel, diluted with water (1 l) and shaken with dichloromethane (2 × 50 ml). The combined dichloromethane solution was washed with water (1 l), brine (250 ml), saturated aqueous sodium carbonate (50 ml) and brine, filtered through magnesium sulfate and concentrated at around 350 mmHg to *ca.* 400 ml. Ethyl acetate (750 ml) was added (immediate crystallization) and concentration was continued at around 250 mmHg until no more dichloromethane condensed. Collection after overnight refrigeration yielded tetranitrobiphenyl (112 g, 67%); pale cream crystals, mp 168.5–169.5 °C

(lit.,[7] 163–164 °C); homogeneous by TLC. A second crop (39 g), pale yellow, had mp 125–135 °C and yielded further pure material on recrystallization.

1,1′-Dimethyl-3,3′-di-*tert*-butyl-10*H*,10′*H*-9,9′-dioxa-6,6′-biphenanthryl-5,5′-diamine 6

Zinc powder (20 g) was quickly washed successively by swirling, settling and decantation with aqueous hydrochloric acid (3 × 15 ml of 3% w/v), water (2 × 15 ml), aqueous copper sulfate (2 × 30 ml of 2%), water (2 × 30 ml) and acetic acid (2 × 15 ml, then 30 ml), then transferred using acetic acid (30 ml) into toluene (20 ml) in a three-necked flask fitted with mechanical stirrer, thermometer, reflux condenser and port for addition of liquids. A stream of nitrogen was passed over the mixture and a solution of the dinitrobibenzochromenyl **5** (5 g) in the minimum of boiling toluene (25 ml) was added in small portions. The strong exotherm was controlled as necessary to *ca.* 60 °C by regulating the addition and by ice-cooling; it ceased soon after addition was complete and a water bath at 60 °C was used to maintain heating for 10–15 min thereafter (total reaction time 0.5 h). The ice-cooled mixture was diluted (to 250 ml) with water, dichloromethane was added, the solids were filtered off and washed with dichloromethane. The non-aqueous layer was washed (2 × water, sat. aq. sodium hydrogen carbonate, water), filtered through magnesium sulfate and evaporated. Collection by means of diethyl ether gave the crystalline diamine **6** (4.5 g, 100%), chromatographically homogeneous.

4,13-Dimethyl-2,15-di-*tert*-butyl-5*H*,12*H*,17*H*-bis[2]benzopyrano[4,3-*a*: 3′,4′-*i*]carbazole 8

When the diiodide **7** was prepared on a larger scale from the diamine **6** by the published procedure,[2] a small fraction containing the *carbazole* **8** was separated by chromatography along with the diiodide and the cinnoline already reported. It crystallized from carbon tetrachloride as slightly discoloured prisms, unaltered by heating above 360 °C *in vacuo* (Found: C, 83.7; H, 6.9; N, 2.6. $C_{36}H_{37}NO_2$ requires C, 83.8; H, 7.2; N, 2.7%); δ_H(360 MHz) 1.33 (18 H, s), 2.44 (6 H, s), 5.16 (4 H, s), 7.01 (2 H, d, *J* 8.4), 7.24 (2 H, s), 7.74 (2 H, s), 7.88 (2 H. d, *J* 8.4), 9.25 (1 H, s).

Methyl 4,13-dimethyl-2,15-di-*tert*-butyl-17-methoxy-17-oxo-5*H*,12*H*,17*H*-17λ^5-phospholo[2″,3″:3,4;5″,4″:3′,4′]dibenzo-[1,2-*c*:1′,2′-*c*′]bis[2]benzopyran 9

The diiodide **7** (40 g) in anhydrous tetrahydrofuran (1200 ml) was stirred at −70 °C under nitrogen during addition of butyllithium (80 ml of 1.33 mol l^{-1} in hexanes). After 75 min phosphorus trichloride (15 ml) was added and the temperature rose briefly to −60 °C. After a further 30 min the mixture was allowed to warm to −40 °C and after 5 min at this temperature the cooling bath was replaced. Dry methanol (75 ml) and then dry pyridine (37.5 ml) were added, the mixture was allowed to come to +10 °C, and a solution of iodine (42 g) and water (3 ml) in tetrahydrofuran (60 ml) was added gradually. When decolorization became slow pyridine (15.5 ml) was added and the mixture was stirred overnight whereupon all the iodine had reacted. The solution was washed with brine, water, aqueous hydrochloric acid (2 mol l^{-1}) and finally with brine containing a little sodium thiosulfate. The residue after evaporation of solvents at low pressure was taken up in a mixture of chloroform and dichloromethane, filtered, treated with ethereal diazomethane until excess was present (*ca.* 10 mmol required) and evaporated at low pressure. The yellow crystalline residue on addition of diethyl ether afforded the methyl phosphinate **9** (19.2 g with an additional 1 g from the filtrate), which was recrystallized from chloroform–hexanes; mp 300–302 °C (vacuum, no apparent decomp.). The previous figure, 320 °C (decomp.), was determined in air. The ^{1}H NMR spectrum agreed with that already recorded.[2]

***meso*-4,6-Bis(2-bromomethyl-3-methyl-5-*tert*-butylphenyl)-5-methoxy-5-oxo-5*H*-5λ^5-dibenzophosphole-3,7-diyl diacetate 11**

The methyl phosphinate **9** (9 g) in dry dichloromethane (240 ml) was stirred at −70 °C under nitrogen during addition (25 min) of boron tribromide in dichloromethane (64 ml of 1 mol l^{-1}). After a further 50 min below −70 °C the mixture was allowed to warm during 45 min to −20 °C; disappearance of the initial red colour was rapid around −35 °C and the final colour was lemon yellow. The solution was poured into vigorously stirred iced water (1.2 l). After 1 h of stirring the dichloromethane layer was washed twice with water, filtered through magnesium sulfate and concentrated to a small volume. Benzene (100 ml) was added and remaining dichloromethane was removed at low pressure. Next day the crystals of dihydroxy dibromo ester **10** were collected and a small further crop obtained by concentrating the filtrate at low pressure. The solid was partially dissolved in chloroform (100 ml) and added to stirred benzene (50 ml) to which pyridine (3 ml) and (with cooling) acetyl chloride (6 ml) had been added. A clear solution formed after 2 h; 1 h later, the mixture was poured on ice and the non-aqueous layer was washed (brine, sat. aq. sodium hydrogen carbonate), filtered through magnesium sulfate and evaporated at low pressure. Addition of hexanes (20 ml) caused immediate crystallization; the diacetoxy dibromo ester **11** (5.97 g) showed a ^{1}H NMR spectrum identical with that reported earlier.[2] The benzene mother liquor of the dihydroxy dibromo ester was similarly acetylated; the product (6.5 g; apparently a stereoisomeric mixture) did not crystallize.

***meso*-4,6-Bis(2-dimethoxyphosphorylmethyl-3-methyl-5-*tert*-butylphenyl)-5-methoxy-5-oxo-5*H*-5λ^5-dibenzophosphole-3,7-diyl diacetate 1 and 2-*tert*-butyl-8-(5-*tert*-butyl-2-dimethoxyphosphorylmethyl-3-methylphenyl)-7-oxo-5*H*-7λ^5-benzo[2,3]phosphindolo[1,7a,7-*c*,*d*][2,3]benzoxaphosphepine-9,14-diyl diacetate 12**

The diacetoxy dibromo ester **11** (5.62 g) and trimethyl phosphite (11 ml) were heated in a bath at 115 °C; a slow stream of nitrogen was passed through to entrain methyl bromide. After 20 h, TLC (silica; ethyl acetate–hexanes 1:1) showed two spots only. Water, diethyl ether and dichloromethane were added; the organic layer was washed with water, filtered through magnesium sulfate and evaporated. The residue, a foam, crystallized on addition of carbon tetrachloride (8 ml); after refrigeration overnight the white product **1** (1.375 g) was collected. The filtrate was evaporated and dissolved in moist diethyl ether whereupon a second product **12** (1.2 g) crystallized. The diethyl ether-soluble residue (3.5 g) was put on a column of silica gel (200 g) and eluted first with ethyl acetate (which yielded more **12**) and then with methanol–ethyl acetate 1:1, yielding more **1**.

The bis-phosphonate **1** crystallized from benzene–hexanes as large colourless prisms of a benzene solvate. It half-melted around 100 °C and resolidified; mp 248–250 °C (lit.,[2] amorphous, mp 210–215 °C) (Found: C, 60.8; H, 6.5; P, 10.6. $C_{45}H_{57}O_{12}P_3$ requires C, 61.2; H, 6.5; P, 10.5%); δ_H(360 MHz) 1.20 (18 H, s, Bu′), 1.93 (6 H, s, Ac), 2.46 (6 H, d, J_{PH} 1.7, 3′-Me), 2.53 (3 H, d, J_{PH} 12.1, 5-OMe), 3.27 and 3.32 (4 H, 2 dd, J_{HH} 10.7, J_{PH} 15.8, CH_2P), 3.53 (6 H, d, J_{PH} 11.1, 2 × phosphonate Me), 3.57 (6 H, d, J_{PH} 10.8, 2 × phosphonate Me), 6.86 (2 H, m, dd when irradiated at δ 2.45, J_{HH} 2.2, J_{PH} 1.0, H-6′), 7.15 (2 H, m, dd when irradiated at δ 2.45, J_{HH} 2.2, J_{PH} 0.9, H-4′), 7.37 (2 H, dd, J_{HH} 8.3, J_{PH} 0.9, H-2, -7) and 7.78 (2 H, dd, J_{HH} 8.3, J_{PH} 4.0, H-1, -8). Irradiation of the P–OMe signal produced a 6% NOE enhancement of the H-6′ signal, suggesting that the relative orientations of the aromatic rings and the phosphinate oxygens are as shown in **1**.

The oxophosphindolobenzoxaphosphepine **12** crystallized from aqueous methanol; mp 276–278 °C (decomp.) (Found: C 66.2; H, 6.3; P, 8.2. $C_{42}H_{48}O_9P_2$ requires C, 66.5; H, 6.4; P, 8.2%); δ_H(360 MHz, [$^2H_6$]DMSO) 1.22 and 1.29 (each 9 H, s, Bu′), 1.95 and 2.12 (each 3 H, s, Ac), 2.45 and 2.51 (each 3 H, s, Ar*Me*), 3.29 (2 H, 2 dd overlapped, J_{HH} 10.7, J_{PH} 15, CH_2P), 3.51 (3 H, d, J_{PH} 10.8, P–OMe), 3.52 (3 H, d, J_{PH} 10.8, P–OMe),

4.51 (1 H, dd, J_{HH} 11.8, J_{PH} 1.5, ArCH*H*OP), 5.16 (1 H, dd, J_{HH} 11.8, J_{PH} 27.9, ArC*H*HOP), 7.01 (1 H, s, 6′-H), 7.22 (2 H, d, J ~1.5, 3- and 4′-H), 7.38 (2 H, app. t, J 8.5, 10- and 13-H), 7.50 (1 H, d, J 1.9, 4-H), 7.80 (2 H, 2 dd presenting as quintet, J_{HH} 8.5, J_{PH} 4.0, 11- and 12-H).

meso-4,6-Bis(2-*dimethoxy*phosphorylmethyl-3-methyl-5-*tert*-butylphenyl)-3,7-dihydroxy-5-methoxy-5*H*-5λ^5-dibenzophosphol-5-one 13

The diacetate **1** (1.282 g) in methanol (50 ml) was cooled in ice. Aqueous sodium hydroxide (12.5 ml of 2 mol l^{-1}) was added without further cooling. After 1 min, hydrochloric acid (4.3 ml of 6 mol l^{-1}) was added, then sat. aq. sodium hydrogen carbonate (1 ml). The crystallizing mixture was concentrated to *ca.* 30 ml at low pressure, then cooled in ice. The product was collected and washed quickly with ice cold methanol–water (6:4). The white crystals of a dihydrate of the *diol* **13** (1.055 g) were dried *in vacuo*; mp 182 °C (Found: C, 59.0; H, 6.9; P, 11.2. $C_{41}H_{53}O_{10}P_3 \cdot 2H_2O$ requires C, 59.0; H, 6.85; P, 11.2%). The NMR spectrum (at 60 MHz) was similar to that of the diacetate **1** without the signal at δ 1.93.

2-*tert*-Butyl-8-(5-*tert*-butyl-2-dimethoxyphosphorylmethyl-3-methylphenyl)-9,14-dihydroxy-5*H*-7λ^5-benzo[2,3]phosphindolo-[1,7a,7-*c*,*d*][2,3]benzoxaphosphepin-7-one 14

The diacetate **12** (2.461 g) was hydrolysed with methanol (105 ml) and aqueous sodium hydroxide (26 ml of 2 mol l^{-1}) essentially as described for the *meso* diacetate **1**. After the acidification chloroform (70 ml) and then water (140 ml) were added. The chloroform layer was separated and the upper layer was extracted thrice with small amounts of chloroform. The united extracts were swirled with sat. aq. sodium hydrogen carbonate (50 ml), filtered through magnesium sulfate and evaporated at low pressure to a thin syrup which was warmed at *ca.* 60 °C and treated with ethyl acetate (70 ml) in a thin stream. An ethyl acetate solvate of the *diol* **14** (2.468 g) separated as small prisms, unmelted at 330 °C after reddening from 200 °C; δ_H(360 MHz, [$^2H_6$]DMSO) 1.17 (3 H, t, J 7.1, *Me*CH$_2$OAc), 1.22 and 1.30 (each 9 H, s, 2 Bu′), 1.98 (3 H, s, *Me*CO$_2$Et), 2.37 and 2.45 (each 3 H, br s, 2 Ar*Me*), 3.18 (2 H, 2 dd overlapped, ArCH$_2$P), 3.30 and 3.35 (each 3 H, d, J_{PH} 10.8, P–OMe), 4.02 (2 H, q, MeC*H*$_2$OAc), 4.30 (1 H, dd, J_{HH} 12.0, J_{PH} 2.2, ArC*H*HOP), 5.04 (1 H, dd, J_{HH} 12.0, J_{PH} 28.5, ArCH*H*OP), 7.10 (1 H, d, J 8.3, H-10 or -13), 7.17 (1 H, half-obscured d, J ~8.5, H-13 or -10), 7.19 (2 H, s, H-1 and -3), 7.27 (1 H, d, J 1.8, H-4′), 7.72 (2 H, 2 dd presenting as quintet, J_{HH} ~8.4, J_{PH} ~4.2, H-11 and -12), 7.76 (1 H, d, J 1.9, H-6′), 9.65 and 10.13 (each 1 H, s, OH).

meso-4,6-Bis(5-*tert*-butyl-2-dimethoxyphosphorylmethyl-3-methylphenyl)-3,7-bis(diethoxyphosphorylmethoxy)-5-methoxy-5*H*-5λ^5-dibenzophosphol-5-one 15

The hydrated diol **13** (816 mg) and diethyl 4-chlorophenylsulfonyloxymethylphosphonate (1.24 g) were dissolved in benzene (50 ml). From the pink-fluorescent solution benzene (10 ml) was distilled to remove water of crystallization. To the cooled stirred solution sodium hydride (0.24 g of 60% in mineral oil), followed by dry hexamethylphosphoramide (4 ml), was added. A yellow colour soon developed and hydrogen was evolved. After 22 h at 40 °C the solution was almost colourless. Ethyl acetate (40 ml) and water were added (hydrogen evolved) and the aqueous layer was extracted with ethyl acetate (2 × 40 ml), then acidified and extracted again with ethyl acetate which was washed with sat. aq. sodium hydrogen carbonate before being combined with the organic layers for further washing (2 × water, 1 × brine). Filtration through magnesium sulfate and evaporation left a residue (1.2 g), which crystallized on warming with hexanes (20 ml). Recrystallization from carbon tetrachloride (3 ml) by addition of diethyl ether gave a monohydrate of the *tetraphosphonate ester* **15** (795 mg); mp 195–197 °C (shrinking at 115–120 °C and resolidifying) (Found: C, 54.7, 55.0; H, 7.0, 6.9; P, 14.3, 14.5. $C_{51}H_{75}O_{16}P_5 \cdot H_2O$ requires C, 54.8; H, 6.95; P, 13.9%); δ_H(360 MHz) 1.15 (12 H, dt, J_{HH} 7.1, J_{PH} 0.5, 4 × C*H*$_3$CH$_2$), 1.23 (18 H, s, 2 × Bu′), 2.03 (~3 H, br s, H$_2$O), 2.41 (6 H, d, J 1.5, 2 × ArMe), 2.60 (3 H, d, J_{PH} 11.9, 5-OMe), 3.18 (2 H, dd, J_{HH} 11.5, J_{PH} 16, 2 × C*H*HP), 3.37 (2 H, dd, J_{HH} 11.5, J_{PH} 16, 2 × CH*H*P), 3.50 (6 H, d, J_{PH} 10.5, 2 × P–OMe), 3.53 (6 H, d, J_{PH} 10.5, 2 × P–OMe), 3.81 (8 H, m, ABX$_3$P system, 4 × MeC*H*$_2$OP), 4.23 (2 H, dd, J_{HH} 12.8, J_{PH} 10.0, 2 × ArOC*H*HP), 4.34 (2 H, dd, J_{HH} 12.8, J_{PH} 10.8, 2 × ArOCH*H*P), 6.97 (2 H, br s, 2 × H-6′), 7.11 (2 H, br s, 2 × H-4′), 7.17 (2 H, d, J 8.5, H-2 and -8), 7.68 (2 H, dd, J_{HH} 8.5, J_{PH} 4.2, H-1 and -9); δ_P + 38.9 (1 P, phosphinate), +28.8 (2 P, 2 × ArCH$_2$P), +16.9 (2 P, 2 × OCH$_2$P).

2-*tert*-Butyl-8-(5-*tert*-butyl-2-dimethoxyphosphorylmethyl-3-methylphenyl)-9,14-bis(diethoxyphosphorylmethoxy)-5*H*-7λ^5-benzo[2,3]phosphindolo[1,7a,7-*c*,*d*][2,3]benzoxaphosphepin-7-one 16

The diol **14** (ethyl acetate solvate, 731 mg) and diethyl 4-chlorophenylsulfonyloxymethylphosphonate (1.23 g), in benzene (75 ml; distilled down to 40 ml to remove ethyl acetate) were treated with sodium hydride (0.24 g of 60% in mineral oil) followed by dry hexamethylphosphoramide (4 ml). The mixture became orange–yellow and evolved hydrogen. After 18 h at 44 °C it was almost colourless. Water and ethyl acetate were added; the upper layer was shaken twice with water to clear it. The aqueous layers were extracted twice with ethyl acetate which after being washed with water was united with the benzene–ethyl acetate layer. Filtration through magnesium sulfate and evaporation left a residue (1.6 g) which was dissolved in ethyl acetate–methanol (9:1) and put on a column of silica (35 g) and eluted first with the same solvent and then with ethyl acetate–methanol (4:1). The second eluate on evaporation yielded a colourless foam (756 mg) of the *triphosphonate* **16**, homogeneous by TLC (silica; ethyl acetate–methanol 9:1, twice developed); δ_H(360 MHz) 1.13, 1.16, 1.19, 1.23 (each 3 H, t, J 7, C*H*$_3$CH$_2$), 1.26 (9 H, s, Bu′), 1.32 (9 H, s, Bu′), 2.43 (3 H, s, ArMe), 2.46 (3 H, d, J 1.4, ArMe), 3.32 (2 H, 2 dd overlapped, CH$_2$P), 3.45 and 3.47 (each 3 H, d, J_{PH} 10.8, 2 × P–OMe), 3.72–4.46 (9 H, m, 4 × MeC*H*$_2$OP and ArCH*H*OP), 5.10 (1 H, dd, J_{HH} 11.9, J_{PH} 28.6, ArC*H*HOP), 7.15–7.27 (5 H, m, H-3, -10, -13, -4′ and -6′), 7.66–7.71 (3 H, m, H-1, -11 and -12); δ_P +38.1, +28.6, +17.6, +16.8.

meso-4,6-Bis(5-*tert*-butyl-3-methyl-2-phosphonomethylphenyl)-5-hydroxy-3,7-bis(phosphonomethoxy)-5*H*-5λ^5-dibenzophosphol-5-one 17

The tetraphosphonate–phosphinate tetraethyl–pentamethyl ester **15** (111.5 mg) was distilled almost to dryness with benzene (2 ml). Dry chloroform (2 ml) was added and followed, under nitrogen, by iodotrimethylsilane (0.2 ml). After 3.5 h the mixture was evaporated at low pressure, methanol was added and, 20 min later, removed at low pressure. Water and some methanol were added and traces of iodine were boiled off with the methanol and some of the water. The aqueous residue then contained a white crystalline solid which was collected after 3 d. The *tetraphosphonic–phosphinic acid* **17** (87 mg), a monohydrate, had mp 355 °C (vacuum); it was recrystallized without change in mp by concentrating a filtered solution in ethanol–methanol–water to *ca.* 50 mg ml^{-1} and adding 0.25 vol. of hydrochloric acid (1 mol l^{-1}) (Found: C, 48.9, 48.9; H, 5.45, 5.5. $C_{38}H_{49}O_{16}P_5 \cdot H_2O$ requires C, 48.8; H, 5.5%). For the NMR spectra the solid in deuterium oxide was brought into solution by addition of 2 equiv. of sodium deuteroxide; δ_H(360 MHz) 1.03 (18 H, s, 2 × Bu′), 2.20 (6 H, s, 2 × ArMe), 2.90 and 3.08 (each 2 H, dd, J_{HH} 12, J_{PH} 21, 2 × ArCH$_2$P), 3.85 (4 H, d, J_{PH} 10.1, OCH$_2$P), 6.90 (2 H, d, J 8.5, H-2 and -8), 7.03 (2 H, s, H-6′), 7.14 (2 H, s, H-4′), 7.37 (2 H, dd, J_{HH} 8.5, J_{PH} 3.5, H-1, -9); δ_P +34.1 (1 P), +24.1 (2 P), +14.0 (2 P). A satisfactory proton spectrum could also be obtained in water by suppressing the water peak by pre-saturation.

4-(5-*tert*-Butyl-2,3-dimethylphenyl)-6-(5-*tert*-butyl-3-methyl-2-phosphonomethylphenyl)-5-hydroxy-3,7-bis(phosphonomethoxy)-5*H*-5λ^5-dibenzophosphol-5-one 19

The triphosphonate **16** (738 mg) was dried by evaporation with benzene and dissolved in dry chloroform (16 ml), cooled under nitrogen, and treated with iodotrimethylsilane (1.6 ml). After 25 h the solution was evaporated at low pressure, dissolved in dry methanol, added to a suspension of zinc–copper couple (from 10 g zinc powder as described earlier) in dry methanol (total volume 50 ml), stirred overnight under nitrogen, cooled in ice and treated dropwise with hydrochloric acid (56 ml of 6 mol l^{-1}). Effervescence ceased after 0.5 h; the residue was filtered off and washed with methanol. The filtrate was concentrated to *ca.* 40 ml. After refrigeration the white solid was collected, washed with ice cold hydrochloric acid (1 mol l^{-1}) and dried over sodium hydroxide. The product (574.5 mg) could be obtained crystalline and fairly pure by dissolution in methanol, addition of hydrochloric acid (1 M) and slow evaporation of most of the methanol, and this was the preparation used as a hydration catalyst; but NMR spectra indicated slight contamination with transannular ester (as in **16**). A sample was therefore dissolved in methanol and hydrogenated (1 atm)† over an equal weight of palladium-on-carbon (10%) overnight. Recovery by filtration and evaporation gave a crystalline product which was recrystallized from methanol–hydrochloric acid to yield the pure *phosphinic–triphosphonic acid* **19** as colourless needles of a dihydrate which charred but did not melt at 350 °C (Found: C, 52.5, 52.7; H, 5.8, 6.0. $C_{38}H_{48}O_{13}P_4{\cdot}2H_2O$ requires C, 52.3; H, 6.0%); δ_H(500 MHz, CD_3OD) 1.25 and 1.26 (total 18 H, 2 s, Bu^t), 1.93 and 2.22 (each 3 H, s, ArMe-3′ and -3″), 2.42 (3 H, d, *J* 1.0, ArMe-2″), 3.04 and 3.24 (each 1 H, dd, J_{HH} 12, J_{PH} 21.5, $ArCH_2P$), 4.16 (4 H, m, 2 × OCH_2P), 7.10 and 7.11 (2 H, 2br s, H-6′, -6″), 7.15 and 7.18 (each 1 H, s, H-4′, -4″), 7.36 (2 H, 2d overlapped, *J* 8.5, H-2, -8), 7.83 (2 H, m, H-1, -9); δ_P +18.5 (1 P, t, J_{PH} 10.0), +18.7 (1 P, t, J_{PH} 9.7), +27.0 (1 P, t, J_{PH} 11.8), +39.4 (1 P, t, J_{PH} 3.9).

Experiments on catalysis of hydration of 2-methylpropene

The acids **17** and **19** proved very difficult to seal in NMR tubes with 2-methylpropene since the tubes regularly burst on freezing. Finally the acid **17** (60 mg, 0.064 mmol) was dissolved in sodium hydroxide (0.025 mol l^{-1} in water; 2 equiv.), evaporated in a vacuum desiccator to avoid foaming, and redissolved in deuterium oxide (1.2 ml). Part of this solution was introduced drop by drop into an NMR tube held nearly horizontally in a bath at −50 °C, so that each separate drop froze and did not fill the lumen. Finally the tube was cooled in liquid nitrogen and evacuated; 2-methyl propene (*ca.* 0.5 mmol) was then introduced and the tube was sealed. A similar tube containing the acid **19** was prepared with the same precautions, and a control tube of 2-methylpropene and orthophosphoric acid (0.1 mol l^{-1}) in deuterium oxide was prepared without trouble. The tubes contained enough aqueous layer to ensure that only dissolved 2-methylpropene was inspected. The spectra at 360 MHz were examined shortly after filling and at intervals for two months thereafter. All tubes showed evidence of *tert*-butyl alcohol formation after a few days. The spectrum of 2-methylpropene was also seen; the molar concentration in the deuterium oxide at room temperature was around 5 mmol l^{-1}. The chemical shift of the methyl groups in 2-methylpropene was invariant in all three tubes and no significant signal unattributable to dissolved 2-methylpropene, its hydration product or the catalyst was seen. To examine the rate of hydration of 2-methylpropene at different pH, aqueous solutions (0.05 mol l^{-1}) of the two acids were prepared as above and adjusted to different pH (measured with a microelectrode calibrated against 0.05 mol l^{-1} buffers of similar pH range) with small amounts of sodium hydroxide. A partially neutralized solution of toluene-4-sulfonic acid (0.05 mol l^{-1} in water) was the control. Each sample (volume 0.65 ml) was cooled in liquid nitrogen and sealed in a heavy-walled tube under vacuum after introduction of 2-methylpropene (0.2 ml). All tubes (volume *ca.* 5 ml) were sheathed in iron pipe and immersed horizontally in a constant-temperature bath at 50 °C for 24 h, then refrigerated for later opening, when each tube was cooled in ice while 2-methylpropene evaporated. The pH were checked (unchanged, within experimental error), and the spectra were examined at 360 MHz. Concentrations of *tert*-butyl alcohol were measured by integration of its signal and comparison with peaks of the catalyst spectrum. Toluene-4-sulfonic acid at pH 2.35 produced 0.73 mol *tert*-butyl alcohol per mol catalyst and this was taken as the standard for H_3O^+ catalysis. Conversions for the acids **17** and **19**, in mol *tert*-butyl alcohol per mol catalyst, are shown below (calculated figures for hydroxonium ion catalysis in parentheses). Acid **17**: pH 2.25, 1.85 (1.0); pH 2.82, 0.61 (0.43); pH 3.64, 0.11 (0.05). Acid **19**: pH 2.92, 0.44 (0.41); pH 3.88, 0.13 (0.042).

† 1 atm = 101 325 Pa.

Acknowledgements

I thank Dr A. G. Avent for skilled NMR measurements, and the University of Sussex for laboratory facilities.

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Paper 6/04318F
Received 20*th June* 1996
Accepted 19*th August* 1996