





Additional examples recorded in the experimental section include monodebenzylation of dibenzyl *isoamyl* phosphate, *phenyl dibenzyl phosphate*, and *2-hydroxycyclohexyl dibenzyl phosphate*. The last named compound was originally prepared by Dr. F. R. Atherton, in this laboratory, by the reaction of dibenzyl hydrogen phosphate with *cyclohexene oxide*; the further development of this phosphorylation method in the preparation of sugar phosphates using anhydro-sugars as intermediates has also been studied and will form the subject of a separate communication. The quaternisation reaction\* can also be applied to dibenzyl phosphite which reacts readily with *N*-methylmorpholine or triethylamine with production of monobenzyl phosphite ( $\text{Ph}\cdot\text{CH}_2\cdot\text{O}\cdot\text{PO}_2\text{H}_2$ ), isolated as its *ammonium* salt. This is probably the most convenient method for preparing the monobenzyl phosphite which is an important intermediate in other phosphorylation studies now in progress and which we have hitherto prepared by partial hydrolysis of dibenzyl phosphite.

Since dibenzyl phosphite has few reactions of a trivalent phosphorus compound, it was of interest to examine the reaction of a tertiary base with tribenzyl phosphite in which the phosphorus atom is of necessity trivalent. It was not found possible to prepare this unstable ester in a pure condition, but by the use of material proved by assay to contain only some 13% of the dibenzyl ester it has been shown that it undergoes the normal quaternisation reaction with triethylamine, yielding dibenzyl phosphite as final product. The process of monodebenzylation by quaternisation can be applied only to neutral esters: esters such as dibenzyl hydrogen phosphate, which are ionic in character, do not undergo the reaction. That dibenzyl phosphite can be quaternised is, in our view, further evidence that it reacts as the neutral dibenzyl phosphonate [ $\text{HPO}(\text{O}\cdot\text{CH}_2\text{Ph})_2$ ]. It is of considerable interest that the quaternisation reaction applied to tribenzyl phosphite should yield dibenzyl phosphite; that the reaction stops at this stage is doubtless due to the dibenzyl phosphite being produced from an intermediate quaternary salt (VI) in which the dibenzyl phosphite is in the ionised form and so is resistant to further reaction with tertiary base. Only when the quaternary salt is decomposed will the dibenzyl phosphite revert to the normal non-ionised form.

The use of this reaction in the phosphorus series seems for all practical purposes to be confined to the removal of groups such as benzyl and substituted benzyl. Triphenyl phosphate did not react with *N*-methylmorpholine under the conditions employed with tribenzyl phosphate (cf. Morel, *Compt. rend.*, 1899, 128, 50). When refluxed for long periods with *N*-methylmorpholine, triethyl phosphate gave only minute yields of diethyl phosphate; when the reaction was carried out at 165° in an autoclave, both di- and mono-ethyl phosphate were produced. The formation of monoethyl phosphate was unexpected, but it had earlier been observed that, when heated alone above 140°, tribenzyl phosphate appeared to decompose, yielding dibenzyl ether and benzyl metaphosphate. A similar decomposition of triethyl phosphate would give ethyl metaphosphate which is known to yield both di- and mono-ethyl phosphate on hydrolysis (Langheld, Oppmann, and Meyer, *Ber.*, 1912, 45, 3753). In fact, virtually the same yield of these two products was obtained by heating triethyl phosphate alone at 165°; it is thus doubtful whether any appreciable quaternary salt formation occurs when it is heated with a tertiary base. Quaternary salt formation in the benzyl series may well be due, primarily, to the electrophilic character of the methylene group in the benzyl residue, and it is of interest that we were unable to effect any debenylation by quaternisation in the case of dibenzyl aminophosphonate; this lack of reactivity may be due to the amino-group exercising its effect not only on the phosphorus atom but also upon the benzyl groups. Further studies on the mechanism and scope of the quaternisation reaction will be described in a later paper, but the present work provides a new and valuable method for the selective debenylation of phosphites, phosphates, and pyrophosphates which should be capable of wide application.

Several substituted dibenzyl phosphates have been prepared and their reactions in various directions have been examined. The primary object in undertaking these studies was to ascertain whether or not the substituted benzyl esters offered marked advantages over the unsubstituted, either in ease of crystallisation or in reactivity. With this end in view, *ethyl di-p-nitrobenzyl phosphate*, *2-hydroxycyclohexyl di-p-nitrobenzyl phosphate*, and *2-hydroxycyclohexyl di-p-bromobenzyl phosphate* were prepared in addition to the other substituted benzyl esters mentioned earlier. Whilst it is true that these compounds showed some advantages (*e.g.*, in their ease of crystallisation) over corresponding unsubstituted benzyl esters, their expected slower rate of hydrogenolysis (cf. Baltzly and Buck, *J. Amer. Chem. Soc.*, 1943, 65, 1984) and greater difficulty of preparation put them at a relative disadvantage for general use. We were unable to prepare  $\alpha$ -naphthylmethyl phosphates, which might be expected to be more

\* The sense in which the term "quaternisation" is used is explained in this vol., p. 583, footnote.

labile than benzyl phosphates (Baltzy and Buck, *loc. cit.*); all attempts to condense  $\alpha$ -chloromethyl-naphthalene with silver phosphate led to polymeric materials.

Attention is drawn to the fact that *cyclohexylamine* gives highly crystalline salts with a number of the partly esterified phosphoric acids described in this paper as well as with dibenzyl hydrogen phosphate; these salts are useful for purposes of characterisation.

#### EXPERIMENTAL.

*Tribenzyl Pyrophosphate*.—*N*-Methylmorpholine (25 g.) was added to a solution of tetrabenzyl pyrophosphate (50 g.) in dry benzene (250 c.c.), and the mixture was refluxed for 2 hours. Benzene and *N*-methylmorpholine were removed under reduced pressure, and the residue washed twice with ether (250 c.c. in all). Aqueous silver nitrate (25 g. in 100 c.c. water) was added, followed by acetone (40 c.c.), and the mixture set aside at 0° for 3 hours with occasional shaking. The precipitated *silver tribenzyl pyrophosphate* (40 g.) was collected, washed with water and then with acetone, and dried in a desiccator at room temperature over phosphoric oxide (Found: Ag, 19.2.  $C_{21}H_{21}O_7P_2Ag$  requires Ag, 19.4%). The silver salt (5.1 g.) was dissolved in chloroform (25 c.c.), and the solution saturated with hydrogen sulphide. Silver sulphide was filtered off, and the filtrate evaporated. The syrup so obtained was dissolved in a minimum quantity of moist ether and set aside at 0°; *tribenzyl pyrophosphate* separated as its *monohydrate* in colourless needles, m. p. 65° (3.85 g.) (Found: C, 53.3; H, 4.8.  $C_{21}H_{22}O_7P_2 \cdot H_2O$  requires C, 54.0; H, 5.1%). When dried over phosphoric oxide at 100° the crystals changed to the syrupy anhydrous ester (Found: C, 55.4; H, 5.1.  $C_{21}H_{22}O_7P_2$  requires C, 56.1; H, 4.9%) from which they could be regenerated by trituration with a little water.

*Quaternisation of Tribenzyl Phosphate*.—Tribenzyl phosphate (2 g.) was refluxed for 2 hours with *N*-methylmorpholine (25 c.c.), the excess of base removed under reduced pressure and the residual syrup washed with ether and then dissolved in benzene. The benzene solution was shaken twice with dilute sulphuric acid (3*N*) then with water, dried ( $Na_2SO_4$ ), and evaporated. The residue was dissolved in warm ether, and *cyclohexane* was added until a cloudiness appeared. Dibenzyl hydrogen phosphate separated on standing (yield, 88%) as needles, m. p. and mixed m. p. 79–80°.

Addition of *cyclohexylamine* (0.72 g.) to a solution of the above product (2 g.) in alcohol (10 c.c.) caused separation of *cyclohexylamine dibenzyl phosphate*; recrystallised from alcohol it formed colourless needles, m. p. 173° (Found: C, 63.9; H, 7.2; N, 3.9.  $C_{20}H_{23}O_4NP$  requires C, 63.6; H, 7.4; N, 3.7%).

*2-Hydroxycyclohexyl Dibenzyl Phosphate* (by Dr. F. R. ATHERTON).—Dibenzyl hydrogen phosphate (5.56 g.) was added to *cyclohexene oxide* (2.0 g.) and dry carbon tetrachloride, and the mixture was set aside for 6 days with occasional shaking until the solution became homogeneous. Water (20 c.c.) was added, and then sufficient aqueous sodium hydroxide (1 c.c. of *N*) to make the aqueous layer alkaline to bromothymol-blue. The carbon tetrachloride phase was separated, washed with water, dried ( $Na_2SO_4$ ), and evaporated. The residue was dissolved in a minimum quantity of hot light petroleum (b. p. 60–80°), and the solution cooled. The ester separated as fine colourless needles (6.8 g., 91%), m. p. 78–80°, unchanged by further recrystallisation from light petroleum (Found: C, 64.2; H, 6.8.  $C_{20}H_{25}O_5P$  requires C, 63.8; H, 6.6%).

The same ester was obtained in 83% yield by reaction of silver dibenzyl phosphate with 2-iodocyclohexan-1-ol.

*Quaternisation of 2-Hydroxycyclohexyl Dibenzyl Phosphate*.—A solution of the ester (2 g.) in *N*-methylmorpholine (25 c.c.) was boiled under reflux for 1 hour, moisture being excluded by a silica-gel tube. Excess of base was removed under reduced pressure, and the residue worked up as described in the case of tribenzyl phosphate. Unchanged starting material (0.29 g., 15%) was recovered, the main product being an oil (1.06 g., 69%) which did not crystallise. The oil was dissolved in aqueous ammonia (10 c.c. of 5%), excess of ammonia removed by a current of dry nitrogen, and a solution of silver nitrate (1 g.) in water (2 c.c.) added. The slightly opalescent mixture was set aside in a refrigerator for 48 hours, by which time *silver 2-hydroxycyclohexyl benzyl phosphate* had separated in colourless prisms (0.25 g.) which were collected, washed with water, alcohol, and ether, and dried under reduced pressure at 60° in absence of light (Found: C, 39.8; H, 5.0; Ag, 27.1.  $C_{13}H_{18}O_5PAg$  requires C, 39.7; H, 4.6; Ag, 27.5%).

*Quaternisation of Dibenzyl isoAmyl Phosphate*.—The ester (4.57 g.; Atherton, Openshaw, and Todd, *J.*, 1945, 382) was dissolved in *N*-methylmorpholine (25 c.c.) and boiled under reflux for 2½ hours with exclusion of moisture. The yellowish solution was evaporated under reduced pressure, and the water-soluble oily residue shaken with a mixture of aqueous sodium hydroxide (20 c.c. of 5%) and ether (25 c.c.). The layers were separated, the aqueous one being again extracted with a further quantity of ether (25 c.c.). The aqueous layer was acidified with concentrated hydrochloric acid (10 c.c.), and the precipitated brown oil extracted with chloroform (3 × 25 c.c.). The chloroform extract was dried ( $Na_2SO_4$ ), shaken with charcoal at room temperature, filtered, and evaporated. The pale brown oil so obtained (2.84 g.) was dissolved in dry ether (20 c.c.), and *cyclohexylamine* (1.1 g.) in ether (5 c.c.) was added. There was considerable evolution of heat, and after a time the *cyclohexylamine benzyl isoamyl phosphate* separated (3.65 g., 78%). The salt, thrice recrystallised from acetone, formed colourless needles, m. p. 131–132° (Found: C, 60.5; H, 9.0; N, 3.6.  $C_{18}H_{32}O_4NP$  requires C, 60.6; H, 9.0; N, 3.9%).

*Phenyl Dibenzyl Phosphate*.—Dry powdered potassium phenoxide (8.6 g.) was placed in a flask cooled in an ice-bath, and an ice-cold solution of dibenzyl chlorophosphonate (prepared from 15 g. of dibenzyl phosphite in 150 c.c. carbon tetrachloride) was added gradually with stirring. The mixture was stirred at 0° for 6 hours and left overnight; no potassium chloride was precipitated. The solution was twice washed with aqueous sodium carbonate (250 c.c. of *N*) then with water, dried ( $Na_2SO_4$ ), and evaporated, traces of benzyl chloride and benzyl alcohol being removed at 100°/1 mm. On addition of *cyclohexane* to the residual oil, *phenyl dibenzyl phosphate* (11.9 g., 56%) separated. Recrystallised from light petroleum (b. p. 60–80°) it formed clusters of colourless needles, m. p. 42° (Found: C, 68.0; H, 5.7.  $C_{20}H_{19}O_4P$  requires C, 67.8; H, 5.4%).

*Quaternisation of Phenyl Dibenzyl Phosphate.*—The ester (2.05 g.) was refluxed for 3 hours with *N*-methylmorpholine (25 c.c.), and the mixture worked up as described in the case of dibenzyl *iso*amyl phosphate (above). The crude oily acid (1.4 g.) was treated with cyclohexylamine (525 mg.) in ether to give cyclohexylamine phenyl benzyl phosphate which crystallised from ethanol-acetone in long silky needles, m. p. 145° (Found: C, 62.6; H, 7.3; N, 4.0.  $C_{19}H_{26}O_4NP$  requires C, 62.8; H, 7.2; N, 3.9%).

Phenyl benzyl hydrogen phosphate itself did not crystallise, but it gave a *silver* salt, crystallising from water in colourless needles (Found: Ag, 28.8.  $C_{13}H_{13}O_4PAG$  requires Ag, 29.0%). Catalytic hydrogenation of the free acid ester regenerated from the cyclohexylamine salt yielded phenyl dihydrogen phosphate, m. p. 97–98° (Jacobsen, *Ber.*, 1875, 8, 1521, gives m. p. 97–98°) which was further characterised as its cyclohexylamine salt, m. p. 214–215° (colourless needles from ethanol) (Found: C, 53.3; H, 6.9; N, 5.5.  $C_{12}H_{20}O_4NP$  requires C, 53.0; H, 7.3; N, 5.2%).

*Tri-p-nitrobenzyl Phosphate.*—A mixture of *p*-nitrobenzyl bromide (108 g.), silver phosphate (70 g.), and dry methyl cyanide (450 c.c.) was heated under reflux with vigorous stirring during 6 hours, light being excluded. The slightly yellow solution was filtered from silver bromide and allowed to cool; *tri-p-nitrobenzyl phosphate* then crystallised. Further quantities of the same compound could be obtained by extracting the crude silver bromide with hot ethyl acetate. The combined material was recrystallised from ethanol, and the ester was obtained as pale yellow plates, m. p. 127–128° (Found: C, 50.3; H, 3.9; N, 8.5.  $C_{21}H_{18}O_{10}N_3P$  requires C, 50.1; H, 3.6; N, 8.4%) (yield, 72 g., 85%).

In order to obtain maximum yields in the above preparation vigorous stirring is essential, and methyl cyanide is the preferred reaction medium. *Tri-p-nitrobenzyl phosphate* is unaffected by 10 minutes' boiling with nitric acid (concentrated or dilute). It can be hydrogenated readily to phosphoric acid and *p*-toluidine, using a palladised charcoal catalyst at room temperature and atmospheric pressure.

*Quaternisation of Tri-p-nitrobenzyl Phosphate.*—The ester (2.0 g.) was dissolved in *N*-methylmorpholine (25 c.c.), and the solution heated with stirring on a boiling water-bath. After 10 minutes the solution became opalescent, and after 30 minutes pale yellow crystals separated. Heating was continued for 1½ hours in all, and the crystalline precipitate (1.85 g.; m. p. 179–180°) was collected and well washed with light petroleum (b. p. 60–80°) to remove any adhering base. Attempts to recrystallise this material from methanol-ethylene dichloride mixtures yielded only oily products, so it was analysed directly [Found: C, 50.9; H, 5.2; N, 8.9. Calc. for the quaternary salt (V)  $C_{26}H_{28}O_{11}N_4P$ : C, 51.7; H, 4.8; N, 9.3%].

It was soon clear that this product could not be the pure salt (V), because, on decomposing a quantity (770 mg.) with dilute hydrochloric acid, di-*p*-nitrobenzyl hydrogen phosphate (495 mg.; m. p. 171–172°) was obtained. This amount of product would correspond to an acid content of 64.2% in the quaternary salt which, if it has structure (V), has, in fact, a theoretical content of only 61%. If as seems probable the impurity is the *N*-methylmorpholine salt of di-*p*-nitrobenzyl hydrogen phosphate, then the figures quoted would suggest that the material isolated in the quaternisation contains ca. 80% of (V) and 20% of the *N*-methylmorpholine salt; it is perhaps significant that such a mixture should give analytical values (C, 50.9; H, 4.9; N, 9.2%) in good agreement with the observed figures. To obtain further evidence for the nature of the crystalline reaction product of *N*-methylmorpholine and *tri-p-nitrobenzyl phosphate* a small portion was decomposed with dilute hydrochloric acid, the precipitated di-*p*-nitrobenzyl hydrogen phosphate filtered off, and the aqueous acid solution evaporated to dryness. On dissolving the residue in methanolic acetone and allowing it to stand, colourless crystals separated, m. p. 217–218°. Recrystallisation from acetone gave needles, m. p. 223°, undepressed in admixture with an authentic sample of *N-p-nitrobenzyl-N-methylmorpholinium chloride* (m. p. 227°, prepared from *N*-methylmorpholine and *p*-nitrobenzyl chloride (Found: C, 52.6; H, 6.2; N, 9.9.  $C_{12}H_{17}O_3N_2Cl$  requires C, 52.8; H, 6.3; N, 10.3%).

In a separate experiment, *tri-p-nitrobenzyl phosphate* (15 g.) was heated with *N*-methylmorpholine (60 c.c.) at 80–85° during 2½ hours. The yellow crystalline precipitate was collected, washed, dissolved in water, and acidified with dilute hydrochloric acid. The crude acid which separated was purified by dissolving it in the minimum amount of aqueous sodium carbonate, boiling the solution with charcoal, filtering, and re-acidifying. The di-*p-nitrobenzyl hydrogen phosphate* so obtained crystallised from ethanol in yellow plates (9.0 g., 82%), m. p. 173–174° (Found: C, 45.6; H, 3.7; N, 7.3.  $C_{14}H_{13}O_8N_2P$  requires C, 45.7; H, 3.6; N, 7.6%). The compound gives a crystalline *silver* salt (Found: Ag, 22.7;  $C_{14}H_{12}O_8N_2PAG$  requires Ag, 22.7%) which is sparingly soluble in cold water (0.75 g. per 100 c.c.).

The yield of di-*p-nitrobenzyl hydrogen phosphate* obtained by quaternisation is considerably reduced when the reaction with *N*-methylmorpholine is carried out at the boiling point of the latter, owing to secondary decomposition.

*Tri-p-bromobenzyl Phosphate.*—A mixture of *p*-bromobenzyl bromide (110 g.; prepared in ca. 45% yield by bromination of *p*-bromotoluene in boiling carbon tetrachloride in presence of benzoyl peroxide), silver phosphate (62 g.), and methyl cyanide (500 c.c.) was heated under reflux with vigorous stirring for 1 hour. The product was isolated in the same way as the *tri-p-nitrobenzyl ester* (above). Recrystallised from ethyl acetate, *tri-p-bromobenzyl phosphate* (75 g., 84%) formed colourless needles, m. p. 132–133° (Found: C, 40.9; H, 3.0.  $C_{21}H_{18}O_4PBr_3$  requires C, 40.7; H, 3.0%).

*Di-p-bromobenzyl Hydrogen Phosphate.*—*Tri-p-bromobenzyl phosphate* (15 g.) was heated on a boiling water-bath for 3 hours with *N*-methylmorpholine. Evaporation of the solution gave a resin which was dissolved in water and acidified with dilute hydrochloric acid. The precipitate was suspended in water (100 c.c.), and dissolved by adding sodium carbonate until the liquid was alkaline to phenolphthalein. The resulting solution of sodium salt was boiled with charcoal, filtered, cooled, and acidified with hydrochloric acid. Di-*p-bromobenzyl hydrogen phosphate* separated as colourless needles; recrystallised from ethanol, the product (8.3 g., 79%) had m. p. 155–156° (Found: C, 38.6; H, 3.3.  $C_{14}H_{13}O_4Br_2P$  requires C, 38.6; H, 3.0%). The compound gave a sparingly soluble *silver* salt (Found: Ag, 19.5.  $C_{14}H_{12}O_4Br_2PAG$  requires Ag, 19.9%). Removal of the *p*-bromobenzyl groups from the ester by catalytic hydrogenation is much slower than hydrogenolysis of dibenzyl hydrogen phosphate.

*Tri-(5-chloro-2:3:1':3'-dioxatetramethylenebenzyl) Phosphate.*—5-Chloro-2:3:1':3'-dioxatetramethylenebenzyl chloride (6.57 g.; Buehler, Bass, Darling, and Lubs, *J. Amer. Chem. Soc.*, 1940, 62,

890) and silver phosphate (4.19 g.) were heated under reflux in benzene (70 c.c.) with vigorous stirring for 6 hours. The ester separated from the filtered solution on cooling, and was recrystallised from benzene. It formed colourless needles (5.1 g., 78%), m. p. 142—143° (Found: C, 50.4; H, 4.0.  $C_{27}H_{24}O_{10}Cl_3P$  requires C, 50.2; H, 3.7%). The compound is rather sparingly soluble in most solvents, and appears to be dimorphous since at times it separated as needles, m. p. 157—158°; the two forms were interconvertible, but their stability under different conditions was not investigated. Even after repeated recrystallisation the ester resisted all attempts at catalytic hydrogenation.

*Di-(5-chloro-2 : 3-1' : 3'-dioxatetramethylenebenzyl) Hydrogen Phosphate.*—The above tri-ester (2.36 g.) was heated on a boiling water-bath with *N*-methylmorpholine (20 c.c.) during 3 hours, and the product worked up as in the case of the *p*-bromobenzyl ester. The product crystallised from dioxan in colourless needles (1.22 g., 71%), m. p. 183—184° (Found: C, 46.6; H, 3.8.  $C_{18}H_{17}O_8Cl_2P$  requires C, 46.7; H, 3.8%).

*Attempted Quaternisation of Triethyl Phosphate.*—Triethyl phosphate (9.1 g.) was refluxed with *N*-methylmorpholine (25 c.c.) for 84 hours with exclusion of moisture. Excess of base was removed under reduced pressure, leaving a brown oil which was dissolved in water, boiled with charcoal, filtered, and the filtrate made strongly alkaline with barium hydroxide. After removal of excess of barium by passing carbon dioxide through the solution and filtering, the solution was concentrated under reduced pressure to small bulk (20 c.c.), and ethanol (200 c.c.) was added. The aqueous ethanolic solution was evaporated until crystallisation set in. On standing, barium diethyl phosphate (260 mg., 2.4%) separated in long needles [Found: C, 22.1; H, 4.6; Ba, 30.4. Calc. for  $Ba(C_4H_{10}O_4P)_2$ : C, 21.7; H, 4.5; Ba, 30.9%].

The above experiment was repeated under more drastic conditions, heating being carried out in an autoclave at 165° for 48 hours. On addition of ethanol to the aqueous solution of the barium salts, a sparingly soluble salt separated when the ethanol concentration reached 30%; this salt (530 mg., 3.3%), from its analysis, was evidently barium ethyl phosphate (Found: C, 7.6; H, 2.6; Ba, 45.8. Calc. for  $C_2H_5PO_3Ba \cdot 2H_2O$ : C, 8.1; H, 3.0; Ba, 46.2%). Evaporation of the mother liquors from the sparingly soluble salt gave barium diethyl phosphate (740 mg., 6.1%) (Found: C, 22.1; H, 4.7; Ba, 30.4%).

A third experiment was carried out in which triethyl phosphate (9.1 g.) was heated alone at 165°. On working up in the manner of the earlier experiments, barium ethyl phosphate (450 mg.) and barium diethyl phosphate (740 mg.) were again obtained.

*Ammonium Monobenzyl Phosphite.*—(a) *By partial hydrolysis of dibenzyl phosphite.* A series of experiments on the hydrolysis of dibenzyl phosphite using *N*/70-sulphuric acid showed that one benzyl group was much more readily removed than the other. The following method was adopted for preparative work.

Dibenzyl phosphite (5.24 g.) was dissolved in aqueous dioxan (600 c.c. of 75%) containing sulphuric acid at a concentration of *N*/70. The solution was boiled under reflux in an oil-bath until titration of aliquots showed a rise in acidity corresponding to the removal of one benzyl group from the ester (1½ hours). The sulphuric acid was removed quantitatively with barium hydroxide, barium sulphate spun off, and the solution neutralised with ammonia. The neutralised solution was concentrated to small bulk (80 c.c.) in a nitrogen atmosphere under reduced pressure, acidified with dilute hydrochloric acid, and extracted with chloroform (2 × 100 c.c.). The dried chloroform extract was then concentrated to 60 c.c., cooled to 0°, and saturated with gaseous ammonia. *Ammonium monobenzyl phosphite* separated and was recrystallised from "cellosolve"—dioxan. It formed colourless needles (1.74 g., 46%), m. p. 154° [Found: C, 44.6; H, 6.4; N, 7.4.  $NH_4(C_7H_9O_3P)$  requires C, 44.4; H, 6.4; N, 7.4%].

Monobenzyl phosphite itself was obtained as a pale yellow oil by acidifying an aqueous solution of the ammonium salt and extracting with chloroform. As it could not be purified by distillation or crystallisation, evidence for its identity was obtained by treatment with phenyldiazomethane. The product was evidently dibenzyl phosphite, for with carbon tetrachloride and ammonia, it gave dibenzyl aminophosphonate (overall yield on ammonium salt, 72%).

(b) *By quaternisation of dibenzyl phosphite.* Dibenzyl phosphite (2 g.) was dissolved in triethylamine (20 c.c.), and the solution heated under reflux with stirring in a nitrogen atmosphere for 1 hour, during which time it separated into two layers. Excess of base was removed under reduced pressure, and the residual oil was shaken with aqueous sodium hydroxide (10 c.c. of 5%) and ether (25 c.c.), and the layers separated. The aqueous layer was washed with ether, then acidified with concentrated hydrochloric acid (2 c.c.) and extracted with chloroform (3 × 25 c.c.). The combined chloroform extracts were dried ( $Na_2SO_4$ ), concentrated to smaller bulk (25 c.c.), and cooled to 0°. When ammonia was passed through the solution, *ammonium monobenzyl phosphite* separated (1.25 g., 87%). Recrystallised from "cellosolve"—dioxan, the salt formed long needles, m. p. 154°, undepressed in admixture with an authentic specimen prepared by partial hydrolysis of dibenzyl phosphite (see above).

When the period of refluxing was extended to 2 hours in the above experiment, the yield of pure product decreased to 51%; by allowing dibenzyl phosphite to stand at room temperature with *N*-methylmorpholine for 6 days a 73% yield of the above ammonium salt was obtained.

*Tribenzyl Phosphite.*—A solution of benzyl alcohol (32.4 g., 3 mols.) in pyridine (23.7 g., 3 mols.) and dry ether (50 c.c.) was cooled in an ice-salt mixture, and a solution of phosphorus trichloride (13.75 g., 1 mol.) in dry ether (20 c.c.) added gradually during 30 minutes, the mixture being vigorously stirred and moisture excluded by means of a silica-gel tube. Pyridine hydrochloride began to separate almost at once, and, after the mixture had been stirred at 0° for a further 2 hours, it was filtered (wt. of precipitated pyridine hydrochloride, 31.2 g., 91%), and the filtrate evaporated in a stream of dry oxygen-free nitrogen, any remaining traces of pyridine and phosphorus trichloride being removed at 70° under reduced pressure. The residual crude tribenzyl phosphite was a colourless oil (34.2 g.) which had a faint odour of dibenzyl phosphite. In order to determine the amount of dibenzyl phosphite in it, a portion (10.4 g.) was submitted to reaction with carbon tetrachloride and ammonia as described by Atherton, Openshaw, and Todd (*J.*, 1945, 660). From the reaction, dibenzyl aminophosphonate (1.38 g., m. p. 103°) was obtained corresponding to a content of 13% dibenzyl phosphite in the original ester (trialkyl phosphites do not react with carbon tetrachloride and ammonia).

The crude tribenzyl phosphite could not be purified by distillation in a nitrogen atmosphere, the product, which boiled at 225—230°/0.05 mm., containing 34% of dibenzyl phosphite. Purification by low-temperature crystallisation from acetone at -60° gave a product, possibly the pure ester, which liquefied at room temperature, and on exposure to air resolidified rapidly; the solid obtained had m. p. 59—61°, and, when recrystallised from *cyclohexane* gave needles, m. p. 64°, undepressed in admixture with an authentic specimen of tribenzyl phosphate (m. p. 64°). It was accordingly decided to use the crude tribenzyl phosphite directly for quaternisation experiments.

*Quaternisation of Tribenzyl Phosphite.*—The crude tribenzyl ester (10.3 g. containing ca. 13% dibenzyl phosphite) was dissolved in triethylamine (25 c.c.), and the solution refluxed for 1 hour in a stream of dry nitrogen. During the reaction, the solution separated into a colourless upper layer and a faintly yellow lower layer. Excess of base was removed under reduced pressure in a stream of nitrogen, the mixture foaming a good deal during this operation. The residual yellow oil dissolved completely in benzene (50 c.c.), and the benzene solution was shaken with dilute hydrochloric acid (2 × 40 c.c. of 2N), then with water, and dried. The benzene solution was then diluted with carbon tetrachloride (50 c.c.), and gaseous ammonia was passed through it for 35 minutes. Ammonium chloride (0.81 g.) was precipitated, and, from the benzene-carbon tetrachloride solution, dibenzyl aminophosphonate was obtained by evaporation. Recrystallised from carbon tetrachloride it had m. p. 102—103°, undepressed in admixture with an authentic specimen (m. p. 103—104°). The yield of dibenzyl aminophosphonate was 3.7 g. which, had the original tribenzyl phosphite been 100% pure and the conversion of dibenzyl phosphite into dibenzyl aminophosphonate quantitative, would correspond to a 46% yield in the quaternisation reaction.

*2-Hydroxycyclohexyl Di-p-nitrobenzyl Phosphate.*—(a) Silver di-*p*-nitrobenzyl phosphate (1.78 g.) and 2-iodocyclohexan-1-ol (0.95 g.) were heated under reflux in methyl cyanide (15 c.c.) during 1 hour. The cooled mixture was filtered, the precipitated silver iodide being well washed with methyl cyanide. The combined filtrate and washings were evaporated, and the residue was dissolved in hot ethanol (7 c.c.), boiled for a few minutes with charcoal, and filtered. The crystalline product (1.55 g., 89%) was precipitated by gradual addition of water and recrystallised from carbon tetrachloride. It formed pale yellow needles, m. p. 112—113° (Found: C, 51.9; H, 4.9; N, 5.8.  $C_{20}H_{23}O_9N_2P$  requires C, 51.5; H, 5.0; N, 6.0%).

(b) Di-*p*-nitrobenzyl hydrogen phosphate (3.68 g.) and freshly distilled *cyclohexene oxide* (1.0 g.) were dissolved in pure dioxan (30 c.c.), and the solution heated on the water-bath for 2 hours. Solvent was removed under reduced pressure, and the crystalline residue washed with water then with dilute ammonia and again with water. The crude product (4.45 g., 95%) had m. p. 110—112°, raised by one recrystallisation from a minimum quantity of ethanol to 112—113°, undepressed in admixture with material prepared by method (a).

*Di-p-nitrobenzyl Ethyl Phosphate.*—Silver di-*p*-nitrobenzyl phosphate (8 g.) was added to a solution of ethyl iodide (2.5 c.c.) in dry methyl cyanide (60 c.c.), and the mixture was refluxed for 15 minutes. The filtered solution was evaporated under reduced pressure, and the semi-crystalline residue dissolved in ethanol. The ethanolic solution was boiled with charcoal, filtered, cooled, and the *ester* precipitated in crystalline form by very cautious addition of water. Recrystallised from benzene-*cyclohexane*, di-*p*-nitrobenzyl ethyl phosphate formed pale yellow needles (5.83 g., 88%), m. p. 65—66° (Found: C, 48.6; H, 4.6; N, 7.4.  $C_{18}H_{17}O_8N_2P$  requires C, 48.5; H, 4.3; N, 7.1%).

A portion of the ester (3.5 g.) was dissolved in aqueous ethanol (200 c.c. of 80%) and hydrogenated at room temperature under atmospheric pressure, using a palladium oxide catalyst (0.05 g.); hydrogenation was complete in 1½ hours (hydrogen uptake ca. 1700 c.c.). After removal of catalyst by filtration, the solution was neutralised with barium hydroxide, *p*-toluidine removed by steam distillation, and barium ethyl phosphate isolated as its crystalline hydrate by concentration to small bulk (20 c.c.) and addition of ethanol. The anhydrous salt (2.07 g., 89%) was obtained by drying at 105—110°/0.1 mm. (Found: Ba, 52.0. Calc. for  $C_2H_5O_4PBa$ : Ba, 52.6%).

*2-Hydroxycyclohexyl Di-p-bromobenzyl Phosphate.*—This compound was prepared by two methods as described for the corresponding *p*-nitrobenzyl ester. Method (a) yielded colourless needles (yield, 73%), m. p. 104—105° from *cyclohexane* (Found: C, 44.7; H, 4.5.  $C_{20}H_{23}O_4Br_2P$  requires C, 45.0; H, 4.3%). The crude product from method (b) (yield, 95%) had m. p. 112—113°, undepressed with the product made by method (a). This unusual behaviour may be connected with the obvious possibility of a mixture of stereoisomers being present in the initial product.

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