# 220. *Studies on Phosphorylation. Part IV. Further Studies on the Use of Dibenzyl Chlorophosphonate and the Examination of Certain Alternative Phosphorylation Methods.*

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Investigations directed to the improvement of phosphorylation procedures using dibenzyl chlorophosphonate as phosphorylating agent have been carried out. An improved method for the purification of dibenzyl phosphite and an alternative method for its conversion into dibenzyl chlorophosphonate are described. The action of tertiary bases on dibenzyl chlorophosphonate is discussed, and 2 : 6-lutidine is shown to have advantages over pyridine in the phosphorylation of alcohols with this reagent. *Dibenzhydryl phosphite* has been prepared, and from it, by reaction with carbon tetrachloride and amines, several substituted aminophosphonates have been obtained. Hydrogenolysis of benzyl esters of phosphoric acid, for which general conditions are given, proceeds, as expected, more readily than that of benzhydryl esters. Substituted diazomethanes can be used with advantage for the preparation of phosphites and phosphates, but the method is limited by the accessibility of the diazo-compounds.

In Part I of this series (Atherton, Openshaw, and Todd, *J.*, 1945, 382) the preparation of dibenzyl chlorophosphonate and its application to the phosphorylation of amines and alcohols was described; the same reagent, prepared by a different route, has also been employed as a phosphorylating agent by Deutsch and Fernö (*Nature*, 1945, **156**, 604). The choice of this reagent was dictated largely by our intention to apply it in a variety of synthetic studies on nucleotides and other physiologically active phosphates and polyphosphates. In these studies it was necessary to have a reagent which would phosphorylate under mild conditions at low temperature and which would yield initial products from which the protecting groups could be removed readily by either hydrolysis or hydrogenolysis, since syntheses were envisaged in which these two methods would have to be applied at different stages. Dibenzyl chlorophosphonate possesses, from this point of view, advantages over most other reagents which have been employed for phosphorylation, the more so as it has been shown that partial debenzylation of the intital reaction products can be effected by either hydrogenolysis (Part I, *loc. cit.*) or hydrolysis (Baddiley and Todd, *J.*, 1947, 648). The technique of partial debenzylation offers a route to polyphos-

phates which has been utilised in the synthesis of adenosine-5′ pyrophosphate (adenosine diphosphate) (Baddiley and Todd, *loc. cit.*). Phosphorylation with dibenzyl chlorophosphonate has been widely employed in these laboratories, and in consequence considerable attention has been paid to the improvement of the method and its reduction to a routine procedure for general use. As described in Part I (*loc. cit.*), the procedure, although fairly satisfactory, had certain defects; first, purification of the dibenzyl phosphite used as starting material was rather tedious; secondly, the yields obtained in the phosphorylation of alcohols were only moderate; and thirdly, removal of benzyl groups from the initial products by hydrogenation was, at times, unaccountably slow. These points, among others, have been the subject of closer study.

In order to ascertain whether the complete decomposition of dibenzyl phosphite, which usually occurred on attempting to purify it by normal vacuum distillation, was due to the presence in the crude material of impurities produced in the reaction between phosphorus trichloride and benzyl alcohol, an alternative method of preparation was examined. Pallazo and Maggiacomo (*Gazzetta*, 1908, **38**, II, 115) showed that diethyl phosphite can be prepared by the action of diazoethane on phosphorous acid, the latter presumably reacting as the tautomeric phosphonic acid, $HPO(OH)_2$. Phenyldiazomethane reacted smoothly with phosphorous acid, but the product decomposed as before on attempted distillation by ordinary methods at $10^{-2}$ mm.; low temperature purification by the method already described (Part I, *loc. cit.*) gave, however, a high yield of pure dibenzyl phosphite. Since then the difficulty of distillation could not be attributed simply to by-products formed in the phosphorus trichloride route, the next possibility to be considered was that it might have its origin in the formation of traces of acidic material in the preliminary heating of the dibenzyl phosphite. Accordingly, crude dibenzyl phosphite was saturated with gaseous ammonia and filtered from the small amount of solid material formed; a small amount of *N*-methylmorpholine was then added and the mixture rapidly distilled under reduced pressure in a nitrogen atmosphere. This procedure, which is described in the experimental section, was found quite satisfactory, and by it large quantities of dibenzyl phosphite have been purified without difficulty. A possible reason for the formation of acidic material on heating dibenzyl phosphite, which seems to have been the source of our earlier difficulties, is mentioned later in this paper in connection with work on *dibenzhydryl phosphite*.

The preparation of dibenzyl chlorophosphonate by the action of chlorine on dibenzyl phosphite (Part I, *loc. cit.*) is satisfactory, although it has to be carried out below 0°. With the object of making available an alternative route which might proceed at room temperature, the use of sulphuryl chloride, a mild chlorinating agent, was examined. In preliminary experiments it was found that diethyl and di*iso*propyl phosphites were readily converted into the corresponding chlorophosphonates by being warmed with this reagent. The same conditions were unsuitable for dibenzyl phosphite; in this case a diluent had to be employed, and reaction then occurred at room temperature, giving dibenzyl chlorophosphonate in good yield. An observation made in the course of experiments aimed at the preparation of dialkyl chlorophosphonites is worthy of mention. Treatment of diethyl or di*iso*propyl phosphite with thionyl chloride yields not the chlorophosphonite but the corresponding chlorophosphonate, together with unidentified halogen-free products; the mechanism of this reaction is obscure and warrants further study.

Phosphorylation of amines by dibenzyl chlorophosphonate is almost quantitative, but phosphorylation of alcohols in presence of pyridine under the conditions described in Part I (*loc. cit.*) gives variable yields often as low as 50%. Dibenzyl chlorophosphonate can be heated to 55° for at least 1½ hours without noticeable decomposition, and it is quite stable to ethanol in the absence of tertiary bases. It seemed, therefore, that the comparatively low yields obtained on phosphorylating alcohols must be due to some reaction between the tertiary base, or its hydrochloride, and dibenzyl chlorophosphonate, or the initial product. The speed at which the reaction was carried out seemed to be one factor affecting the results, since dibenzyl chlorophosphonate gave a higher yield with *n*-butanol in presence of pyridine when the reaction was carried out within 3 hours at 40° than after 18 hours at room temperature. When *N*-methylmorpholine was substituted for pyridine in the reaction with *n*-butanol, the low temperature reaction gave a large amount of *N*-benzyl-*N*-methylmorpholinium chloride, and reaction at the higher temperature apparently a mixture of this substance with *N*-methylmorpholine hydrochloride; in neither case could the other products of reaction be hydrogenated. These observations suggest that the main reaction competing with that leading to dibenzyl *n*-butyl phosphate and *N*-methylmorpholine hydrochloride is one between base and reagent,

leading to *N*-benzyl-*N*-methylmorpholinium chloride and, presumably, benzyl metaphosphate according to the scheme :

$$R_3N + (Ph{\cdot}CH_2{\cdot}O)_2POCl \longrightarrow R_3\overset{+}{N}(CH_2Ph){\cdot}\overset{-}{O}{\cdot}PO(O{\cdot}CH_2Ph)Cl \longrightarrow R_3\overset{+}{N}(CH_2Ph)\overset{-}{Cl} + Ph{\cdot}CH_2{\cdot}O{\cdot}PO_2$$

Support for this view was provided by the observation that a high yield of *N*-benzyl-*N*-methylmorpholinium chloride is obtained when an equimolar mixture of dibenzyl chlorophosphonate and *N*-methylmorpholine is kept at room temperature. An analogous reaction almost certainly occurs, although doubtless to a lesser extent, in phosphorylations using pyridine, since it was found that dibenzyl chlorophosphonate is completely destroyed by pyridine in 2½ hours at 34°. It was evident that as a step towards increasing yields obtained in phosphorylating alcohols it would be desirable to find some tertiary base causing less destruction of dibenzyl chlorophosphonate than pyridine. Accordingly, several common tertiary bases were mixed with dibenzyl chlorophosphonate at room temperature, and the amount of reagent remaining after 1 hour was determined by treating the mixture with ammonia and weighing the dibenzyl aminophosphonate produced. The percentage yields of dibenzyl aminophosphonate were : pyridine, 58% ; α-picoline, 70% ; quinoline, 77% ; dimethylaniline, 83% ; 2 : 6-lutidine, 85% ; quinaldine, 86%. A control experiment in absence of tertiary base gave a 90% yield of dibenzyl aminophosphonate. Of the three bases causing least decomposition in 1 hour, only 2 : 6-lutidine satisfied the requirements of availability and volatility for general use, and we have employed it with advantage in place of pyridine in many phosphorylations. With it, the yields of, *e.g.*, barium ethyl phosphate and barium glucose-6 phosphate were increased by some 15% over our earlier figures. The nature of the alcohol has, of course, an effect and in some cases—*e.g.*, *n*-butanol, 2′ : 3′-*iso*propylideneadenosine—the yields with 2 : 6-lutidine are not so markedly improved ; nevertheless, 2 : 6-lutidine is, in general, preferable to pyridine as a tertiary base in alcohol phosphorylations. Even in the best cases examined by us, however, the yields obtained with alcohols still fall considerably short of those obtained in phosphorylating amines. The tendency for tertiary base hydrochloride produced in the reaction to debenzylate the initial reaction product is doubtless one adverse factor which operates. Another will obviously be the speed at which the alcohol employed undergoes reaction, since the stability of the quaternary phosphorylating intermediate will be low in presence of excess of tertiary base It is probable that, in order to get maximum yields, optimum conditions would have to be determined for each individual case, but the general procedure indicated in this paper may be taken as reasonably satisfactory.

In view of the difficulty occasionally encountered in our early work of removing benzyl groups from the dibenzyl phosphates obtained as initial products in phosphorylation, a careful study has been made of the various factors influencing hydrogenolysis. Hydrogenolysis proceeds best in ethanol or dioxan solution, preferably in presence of a little water. It is accelerated by traces of mineral acid and retarded by bases, and platinum, palladium, or nickel catalysts can be employed. For general use we recommend a palladium oxide catalyst in amount 2—5% of the material to be hydrogenolysed in presence of a trace of sulphuric acid. Under these conditions no difficulty has been encountered, and hydrogen uptake proceeds at a rate of 30—100 c.c./min. A point of interest is that, where 2 : 6-lutidine is used as tertiary base in phosphorylating alcohols, the reaction products are quite colourless and hydrogenation proceeds smoothly and rapidly even in the absence of any acid.

Since it would sometimes be useful to prepare substituted phosphates containing groups other than benzyl, which could nevertheless be removed by selective hydrogenolysis, dibenzhydryl phosphite was prepared by the action of diphenyldiazomethane on phosphorous acid. Dibenzhydryl phosphite, unlike dibenzyl phosphite, is a high-melting solid. It is, however, very unstable, and on being kept or on recrystallisation it gradually decomposes with formation of dibenzhydryl ether ; decomposition is very rapid on heating. Since one would expect, on general grounds, that dibenzyl phosphite, although more stable, would resemble the dibenzhydryl ester in properties, it is probable that the former will undergo at higher temperatures a similar decomposition yielding dibenzyl ether. Such a decomposition would involve the simultaneous formation of acidic material and may explain the tendency of dibenzyl phosphite to decompose violently on distillation as mentioned above. The chlorination of dibenzhydryl phosphite was examined, but no dibenzhydryl chlorophosphonate could be obtained ; it was probably formed initially but was so unstable that it decomposed immediately. By treatment of the ester with carbon tetrachloride and the appropriate amine (Atherton, Openshaw, and Todd, *J.*, 1945, 660 ;

Atherton and Todd, *J.*, 1947, 674), however, *dibenzhydryl aminophosphonate*, *dibenzhydryl benzylaminophosphonate*, and *dibenzhydryl* cyclo*hexylaminophosphonate* were prepared in good yield. Hydrogenolysis of the last named compound showed that, as anticipated, the benzhydryl groups were more slowly removed than benzyl groups.

It is obvious that substituted diazomethanes could be employed for the preparation of organic phosphates. This method has been used, for example, by Reichstein and Schindler (*Helv. Chim. Acta*, 1940, **23**, 669), who prepared deoxycorticosterone phosphate by interaction of 21-diazoprogesterone and phosphoric acid. By using dibenzyl hydrogen phosphate in place of phosphoric acid in such reactions, not only would the protecting benzyl groups in the products be of advantage in various directions, but yields would doubtless be better, since there would be no danger of the formation of di- or tri-esters. By this means we prepared in model experiments *benzhydryl dibenzyl phosphate* and *desyl dibenzyl phosphate* from diphenyldiazomethane and phenylbenzoyldiazomethane in excellent yield; in the same way, ethyl dihydrogen phosphate was readily prepared by interaction of diazoethane with dibenzyl phosphate and hydrogenation of the initial product. The use of this method of phosphorylation is severly restricted by the inaccessibility of many substituted diazomethanes, but it may be of value in special cases.

## EXPERIMENTAL.

*Preparation of Dibenzyl Phosphite by the Use of Phenyldiazomethane.*—Phenyldiazomethane( 5·9 g., 2 mols.) dissolved in dry ether (100 c.c.) was gradually added (*ca.* 20 minutes) to an ice-cold stirred solution of phosphorous acid (2·05 g., 1 mol.) in dry ether (200 c.c.). After removal of ether, an attempt was made to distil the liquid residue at $10^{-2}$ mm.; the product began to distil at 160° but almost immediately violent decomposition occurred. Accordingly, the preparation was repeated and the product purified by low-temperature distillation as described in Part I (*loc. cit.*); dibenzyl phosphite (5·5 g., 84%), m. p. 17°, was thus obtained.

*Purification of Dibenzyl Phosphite.*—Crude dibenzyl phosphite (300 g.) prepared as in Part I (*loc. cit.*) is saturated with gaseous ammonia, filtered from any solid which separates, and *N*-methylmorpholine (3% by weight) added. The apparatus used for distillation is a two-necked retort with a long side arm; the two necks are fitted respectively with a thermometer and a capillary admitting nitrogen, and the side-arm is connected by a three limbed " pig " leading to the receivers. The above mixture is placed in the retort, the thermometer and capillary sealed in with polythene, and the retort immersed in an oil-bath and attached to a high-vacuum system giving a pressure of *ca.* $10^{-1}$ mm. *N*-Methylmorpholine distils off and is collected in a liquid-air trap, and the bath is then heated as rapidly as possible to 180—190°, at which temperature dibenzyl phosphite begins to distil; a small fore-run is usually obtained during the heating. Distillation is carried out as rapidly as possible, care being taken to keep the bath temperature uniform and to avoid local overheating. Should any sign of decomposition occur in the retort, or should distillation appear to slacken, the operation is interrupted *immediately*, the vacuum cut off, the bath removed, and the system flooded with nitrogen. With this procedure and the above quantities, pure dibenzyl phosphite (*ca.* 240 g.), b. p. 165°/$10^{-1}$ mm. (bath temp. 180—190°), is obtained.

*Action of Sulphuryl Chloride on Dialkyl Phosphites.*—(a) *Di*iso*propyl phosphite.* The phosphite (33·2 g.) was stirred while sulphuryl chloride (28 g.) was added so as to maintain the temperature at 35—40°. The mixture was stirred for a further 90 minutes, sulphur dioxide and hydrogen chloride removed by reducing the pressure, and the product distilled through a short Vigreux column. Di*iso*propyl chlorophosphonate (33 g., 82%) distilled at 95—96°/14 mm. For characterisation, a portion (4 g.) was allowed to react with aniline; di*iso*propyl anilinophosphonate (5 g., 97%) was obtained, m. p. and mixed m. p. 120—121°.

(b) *Diethyl phosphite.* In exactly similar fashion diethyl phosphite (27·6 g.) gave diethyl chlorophosphonate (31 g., 90%), characterised by conversion into diethyl anilinophosphonate, m. p. and mixed m. p. 95—96°.

(c) *Dibenzyl phosphite.* A slow stream of nitrogen was passed through a stirred solution of dibenzyl phosphite (13·1 g.) in carbon tetrachloride (150 c.c.) while sulphuryl chloride (7 g.) in carbon tetrachloride (25 c.c.) was added during 20 minutes, the temperature being maintained at 17—19° by external cooling. Nitrogen was blown through the solution at a more rapid rate for 90 minutes, and the content of dibenzyl chlorophosphonate determined by addition of aniline (15 c.c.). On working up in the usual manner, dibenzyl anilinophosphonate (16·3 g., 92%) was isolated; recrystallised from *cyclo*hexane it had m. p. 91—92°, undepressed by an authentic specimen.

*Reaction of Dibenzyl Chlorophosphonate with* n-*Butanol in Presence of Pyridine.*—(a) *Low-temperature reaction.* A solution of dibenzyl chlorophosphonate (from 5·24 g. of dibenzyl phosphite) in carbon tetrachloride (20 c.c.) was added to an ice-cold mixture of *n*-butanol (1·62 g.), dry pyridine (4 c.c.), and chloroform (15 c.c.) at such a rate that the temperature did not exceed 10°. After standing overnight the mixture was washed with dilute acid, alkali, and water, dried ($Na_2SO_4$), and evaporated under reduced pressure. The colourless oil so obtained (6 g.) was dissolved in ethanol (100 c.c.) and hydrogenated with palladium oxide (0·1 g.) in presence of dilute sulphuric acid (1 c.c. of N); hydrogen uptake (900 c.c.) was complete in 30 minutes. Catalyst was removed by filtration, and the solution exactly neutralised (phenolphthalein) with saturated aqueous barium hydroxide and evaporated to dryness under reduced pressure. The residue was extracted with boiling water, and the extract filtered and concentrated under reduced pressure until crystallisation set in. On standing, barium *n*-butyl phosphate separated as its dihydrate (2·65 g., 56%) (Found : Ba, 42·2. Calc. for $C_4H_9O_4PBa,2H_2O$ : Ba, 42·2%).

(b) *High-temperature reaction.* An exactly comparable experiment to that described in (a) was carried out, but the temperature during the addition of the dibenzyl chlorophosphonate was maintained

at 35—40° and the product worked up after 3½ hours. The yield of barium *n*-butyl phosphate (4·13 g., 63%) was appreciably higher than in (a) (Found : Ba, 42·1. Calc. for $C_4H_9O_4PBa,2H_2O$ : Ba, 42·2%).

*Reaction of Dibenzyl Chlorophosphonate with* n-*Butanol in Presence of* N-*Methylmorpholine.*—Reactions exactly parallel to (a) and (b) above were carried out using *N*-methylmorpholine in place of pyridine.

*Low-temperature reaction.* A considerable quantity (3·85 g.) of crystalline solid separated and was filtered off. It proved to be *N*-benzyl-*N*-methylmorpholinium chloride, m. p. 236° (decomp.) (Found : Cl, 15·6. Calc. for $C_{12}H_{18}ONCl$ : Cl, 15·6%). The liquid product obtained from the filtrate resisted hydrogenation.

*High-temperature reaction.* The crystalline material (3·2 g.) which separated during the reaction appeared from its properties and chlorine content (Found : Cl, 19·0%) to be a mixture of *N*-methylmorpholine hydrochloride and *N*-benzyl-*N*-methylmorpholinium chloride. The oily product again could not be hydrogenated.

*Barium Ethyl Phosphate.*—Ethanol (4 c.c.) and 2 : 6-lutidine (4 c.c.) were added to a solution of dibenzyl chlorophosphonate (from 5·24 g. of dibenzyl phosphite) in dry carbon tetrachloride (100 c.c.), and the mixture left at room temperature for 5 hours. The neutral oily product was isolated and hydrogenated in aqueous ethanol using a palladium oxide catalyst. Traces of chloride were removed with silver sulphate, and excess of silver precipitated with hydrogen sulphide. The filtered solution was neutralised to phenolphthalein with aqueous barium hydroxide, barium sulphate spun off, and the solution concentrated to small bulk. On addition of ethanol, barium ethyl phosphate separated as its crystalline dihydrate (3·8 g., 64%) (Found : Ba, 45·4. Calc. for $C_2H_5O_4PBa,2H_2O$ : Ba, 46·2%). With pyridine in place of lutidine, the yield was 50% (Part I, *loc. cit.*). A similar experiment with *n*-butanol in place of ethanol gave barium *n*-butyl phosphate in 62% yield.

*Barium Glucose-6 Phosphate.*—(a) *By the use of pyridine.* Dibenzyl chlorophosphonate (from 13·1 g. of dibenzyl phosphite) in dry chloroform (50 c.c.) was added dropwise to a solution of 1 : 2-*iso*propylidene D-glucose (11 g.) in pyridine (100 c.c.) at −10° during 75 minutes. Stirring was continued while the mixture was allowed to warm to room temperature. The mixture was then set aside overnight, and evaporated under reduced pressure to a syrup, which was taken up in chloroform, washed with dilute sulphuric acid, then water, dried ($Na_2SO_4$), and evaporated. The residue was dissolved in ethanol, the solution refluxed for 30 minutes with Raney nickel (5 g.) to remove possible catalyst poisons, filtered, and then hydrogenated with the use of a mixture of palladium oxide (0·5 g.) and palladised charcoal (1·0 g.) as catalyst. Hydrogenation was at first rapid (70 c.c./min.), but it became slow (3 c.c./min.) after 1500 c.c. had been absorbed, and ceased after a total of 2160 c.c. hydrogen had been taken up. The *iso*propylidene group was removed from the product, and glucose-6 phosphate isolated as its barium salt (8 g., 42%; $[\alpha]_D^{30°}$ + 11·8°) by the procedure of Levene and Raymond (*J. Biol. Chem.*, 1930, **89**, 479).

(b) *By the use of* 2 : 6-*lutidine.* Dibenzyl chlorophosphonate (from 5·24 g. of dibenzyl phosphite) in chloroform (25 c.c.) was added dropwise to a stirred ice-cold solution of 1 : 2-*iso*propylidene D-glucose (4·4 g.) in 2 : 6-lutidine (100 c.c.) during 3 hours. The mixture was stirred at 0° for 4 hours and set aside overnight. Chloroform and the main bulk of lutidine were removed under reduced pressure, aqueous barium hydroxide added until the mixture was alkaline to phenolphthalein, and liberated lutidine removed by concentrating the mixture under reduced pressure to *ca.* 100 c.c. Methanol (100 c.c.) was added, together with sufficient sulphuric acid to make the acid concentration N/5, and the homogeneous solution heated on the steam-bath for 2 hours. From the resulting solution, glucose-6 phosphate was isolated as its barium salt (3·25 g.). The mother liquors from the barium salt were freed from barium by titration with sulphuric acid, using rhodizonic acid as indicator, and filtration from barium sulphate. The solution was evaporated, and the residue dissolved in aqueous ethanol (75%) and hydrogenated with the use of a palladium oxide catalyst. From the product a further quantity of barium glucose-6 phosphate (1·25 g.) was obtained. (Total yield, 4·5 g., 59%; $[\alpha]_D^{20°}$ + 12·3°.)

In a similar way barium glucose-6 phosphate was prepared from 3 : 5-benzylidene-1 : 2-*iso*propylidene D-glucose; the yield was 38% with pyridine and 49% with 2 : 6-lutidine. The preparation of glucose-6 phosphate by direct treatment of unprotected D-glucose with dibenzyl chlorophosphonate in presence of pyridine, followed by hydrogenation, was unsatisfactory, the yield being only *ca.* 15%.

*Dibenzhydryl Phosphite.*—A solution of phosphorous acid (13·7 g.) in dry ether (150 c.c.) was added gradually to an ice-cold solution of diphenyldiazomethane in light petroleum (prepared from 62 g. of benzophenone hydrazone according to Staudinger, Anthes, and Pfenninger, *Ber.*, 1916, **49**, 1932) until the red colour of the diazo-compound was discharged. The bulky colourless crystalline precipitate (52 g., 75% calculated on benzophenone hydrazone) was collected, washed with ether–light petroleum, and dried at room temperature in a desiccator (Found : C, 74·7; H, 5·9. $C_{26}H_{23}O_3P$ requires C, 75·4; H, 5·6%). On being heated, the product decomposed gradually above 60° and melted completely at 105°; placed in a pre-heated bath it decomposed sharply at 78°, resolidified, and ultimately melted again at 105°. Recrystallisation from hot solvents gave dibenzhydryl ether, m. p. 108—109°. The phosphite could be obtained as long felted needles by adding light petroleum to an ice-cold solution in ethyl acetate, but then showed the same behaviour on being heated as the initial product, and gave similar analytical figures.

*Dibenzhydryl* cyclo*Hexylaminophosphonate.*—*cyclo*Hexylamine (1·5 g., 3 mols.) was added to a solution of dibenzhydryl phosphite (2·1 g., 1 mol.) in carbon tetrachloride (10 c.c.). The mixture was set aside for 4 hours, extracted with dilute acid, washed with water, and dried ($Na_2SO_4$). Evaporation gave a resin (2·5 g.) which crystallised on trituration with light petroleum. Recrystallised from *cyclo*hexane, the *product* formed colourless needles, m. p. 101—102° (Found : C, 75·1; H, 6·5; N, 2·8. $C_{32}H_{34}O_3NP$ requires C, 75·1; H, 6·7; N, 2·7%).

*Dibenzhydryl Benzylaminophosphonate.*—Prepared in a similar way with the use of benzylamine, this *ester* formed colourless needles, m. p. 104—105°, from hexane–*cyclo*hexane (Found : C, 76·2; H, 5·9; N, 2·5. $C_{33}H_{30}O_3NP$ requires C, 76·3; H, 5·8; N, 2·7%).

*Dibenzhydryl Aminophosphonate.*—Prepared by passing gaseous ammonia into a solution of dibenzhydryl phosphite in carbon tetrachloride, this *ester* formed colourless needles, m. p. 145°, from *cyclo*hexane (Found : C, 72·1; H, 5·5; N, 3·1. $C_{26}H_{24}O_3NP$ requires C, 72·8; H, 5·6; N, 3·3%).

*Dibenzyl Hydrogen Phosphate.*—The following method is more convenient than the literature procedures (Lossen and Köhler, *Annalen*, 1891, **262**, 196; Lynen, *Ber.*, 1940, **73**, 367). A mixture of crude dibenzyl phosphite (225 g. of 80% purity), carbon tetrachloride, and aqueous pyridine (200 g. in 600 c.c. of water) was cooled to 0°, and a solution of bromine (110 g.) in carbon tetrachloride (150 c.c.) was added with stirring during 3 hours so that the temperature did not rise above 10°. Stirring was continued for a further hour, concentrated hydrochloric acid (250 c.c.) added, and the layers separated. The carbon tetrachloride layer was washed with water and then neutralised to phenolphthalein with aqueous sodium hydroxide (170 c.c. of 10%). Acidification of the neutral aqueous layer with hydrochloric acid precipitated dibenzyl hydrogen phosphate, which was extracted with chloroform (3 × 150 c.c.), the extract evaporated, and the product recrystallised from ether. Colourless prisms (100 g.) were obtained, m. p. 79—80°, undepressed in admixture with material, m. p. 79—80°, prepared by the method of Lynen (*loc. cit.*). The impurities normally present in crude dibenzyl phosphite apparently have an adverse effect, since the yield of product is higher (75%) when distilled material is employed.

*Benzhydryl Dibenzyl Phosphate.*—Ethereal diphenyldiazomethane was added to a suspension of dibenzyl hydrogen phosphate (4·7 g.) in ether (50 c.c.) until a permanent pink colour was produced. After addition of more dibenzyl hydrogen phosphate (0·1 g.) to discharge the colour, the solution was washed with aqueous sodium hydroxide, dried, and evaporated. On adding a little light petroleum and allowing to stand overnight in the ice-chest, the oily product solidified. Recrystallised from light petroleum, the *ester* had m. p. 72—72·5° (Found: C, 73·1; H, 5·6. $C_{27}H_{25}O_4P$ requires C, 73·0; H, 5·6%). The yield was almost theoretical.

*Desyl Dibenzyl Phosphate.*—Phenylbenzoyldiazomethane (4·44 g., 1 mol.) was added to a solution of dibenzyl hydrogen phosphate (5·56 g., 1 mol.) in benzene (50 c.c.). After 48 hours the pale yellow solution was washed with aqueous sodium hydroxide, dried, and evaporated. The residual oil crystallised on standing with light petroleum and then had m. p. 53—54° (yield, 7·6 g.) (Found: C, 71·1; H, 5·8. $C_{28}H_{25}O_5P$ requires C, 71·2; H, 5·4%). Attempts to purify the *ester* by further recrystallisation led to decomposition with production of oily material.

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