964. *Coenzyme A. Part X.* Model Experiments on the Synthesis of Pyrophosphates of N-Pantoylamines. New Methods for the Debenzylation of Esters of Pyrophosphoric Acid.*

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Compounds now prepared in connection with a projected synthesis of 3′-dephospho-coenzyme A (I; R = H) include the 4-phosphate (III; R = H) and 4-pyrophosphate (V; R = H) of *N*-pantoyl*cyclo*hexylamine. The pyrophosphate was prepared from the 4-phosphate or its monobenzyl ester (III; R = CH_2Ph) by reaction with dibenzyl phosphorochloridate, followed by reduction.

Benzyl groups were readily removed from esters of pyrophosphoric acid and from nucleotides by reduction with sodium in liquid ammonia. Dibenzyl pyrophosphate gave inorganic pyrophosphate in high yield, tribenzyl pyrophosphate gave mainly pyrophosphate, and tetrabenzyl pyrophosphate gave mainly orthophosphate.

Some benzyl esters of ortho- and pyro-phosphoric acid are also debenzylated in alcoholic solution by irradiation with ultraviolet light.

There are several general procedures which might be applicable to the synthesis of coenzyme A (I; R = PO_3H_2) or 3′-dephospho-coenzyme A (I; R = H). These all involve condensation of two phosphoric esters, such as adenosine-5′ phosphate and pantetheine-4′ phosphate or their derivatives, to give a pyrophosphate. Reagents which effect similar condensations have been examined by us in model experiments on the synthesis of 3′-dephospho-coenzyme A. The presence of a thiol or sulphide group and of two amide groups in the pantetheine-4′ phosphate component usually interfered with pyrophosphate synthesis, but experiments described in this paper suggest that the pantothenic amide group does not preclude pyrophosphate synthesis through phosphorochloridates.

N-Pantoyl*cyclo*hexylamine (II) was chosen as a model for the introduction of a pyrophosphate group. This amide was readily phosphorylated with dibenzyl phosphorochloridate to give a neutral dibenzyl ester. It was shown earlier that phosphorylation of pantothenic acid derivatives with this reagent gives rise exclusively to 4-phosphates.[1] The neutral ester could not be purified but was hydrogenated catalytically to *N*-pantoyl*cyclo*hexylamine-4 phosphate (III; R = H), characterised as the crystalline mono*cyclo*hexylamine salt. Treating the triethylamine salt of this phosphate with dibenzyl phosphorochloridate and hydrogenating the product gave a mixture. Paper chromatography of the products showed that, besides inorganic ortho- and pyro-phosphates, unchanged *N*-pantoyl*cyclo*hexylamine-4 phosphate, and the 2 : 4-cyclic phosphate [2] (IV), there was a major spot of the required *N*-pantoyl*cyclo*hexylamine-4 pyrophosphate (V; R = H). This component was isolated by extraction from a number of paper chromatograms and converted into its crystalline *cyclo*hexylamine salt. Its structure was proved by analysis and by its conversion into the phosphate (III; R = H) and inorganic phosphate on short acid hydrolysis.

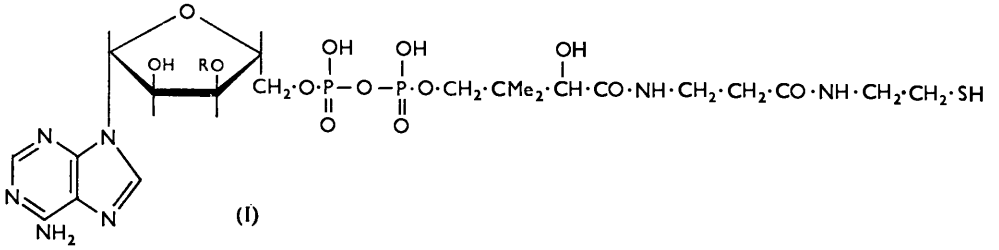
When the dibenzyl ester of *N*-pantoyl*cyclo*hexylamine-4 phosphate was heated with barium thiocyanate in 2-ethoxyethanol,[3] the monobenzyl hydrogen phosphate (III; R = CH_2Ph) was formed. It was isolated as its crystalline *cyclo*hexylamine salt. The triethylamine salt of this monobenzyl ester reacted with dibenzyl phosphorochloridate and the resulting mixture, after removal of benzyl groups by hydrogenation, was examined

* Part IX, *J.*, 1954, 2803.

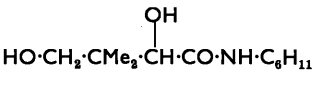
[1] Baddiley and Thain, *J.*, 1953, 1601.
[2] *Idem, ibid.*, p. 903.
[3] Morrison and Atherton, B.P. 675,779.

on paper. The products were very similar to those from the unprotected *N*-pantoyl-*cyclo*hexylamine-4 phosphate. A major product, with chromatographic properties identical with those of *N*-pantoyl*cyclo*hexylamine-4 pyrophosphate, was hydrolysed quantitatively to *N*-pantoyl*cyclo*hexylamine-4 phosphate and inorganic phosphate by short acid treatment.

The neutral dibenzyl ester obtained by phosphorylation of *N*-pantoyl*cyclo*hexylamine has interesting properties. Attempts to crystallise it led to the isolation of the *cyclo*hexylamine salt of dibenzyl phosphate. Even with rapid working under conditions as anhydrous as possible, debenzylation with a tertiary base [4] or with barium thiocyanate [3] led to the production of dibenzyl phosphate. The latter has solubilities very similar to those of the required monobenzyl ester and neither repeated crystallisation of the *cyclo*hexylamine salt nor purification through metal salts effected a separation. The presence of dibenzyl phosphate in chromatographically pure preparations of the monobenzyl ester (III; R = CH_2Ph) was shown by catalytic hydrogenolysis when, together with the 4-phosphate, a trace of inorganic phosphate was always produced. We envisage hydrolysis of the neutral ester (owing to its hyroscopic nature) leading to the production of pantolactone and the *cyclo*hexylamine salt of dibenzyl phosphate. We have noticed the formation of diphenyl phosphate and simultaneous fission of the amide linkage with several 4-(*OO*-diphenylphosphoric) esters of pantothenic acid derivatives during either prolonged storage or isolation procedures involving prolonged contact with aqueous solvents.



(I)



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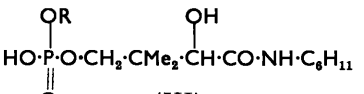

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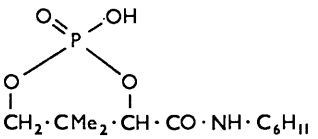

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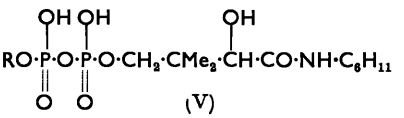

(V)

The above syntheses suggest that it might be possible to prepare 3′-dephospho-coenzyme A from a suitably protected derivative of pantetheine-4′ phosphate and 2′ : 3′-*iso*propylideneadenosine-5′ benzyl phosphorochloridate.[5] An intermediate in this synthesis would be an unsymmetrical pyrophosphate bearing one or two benzyl groups. The benzyl groups would have to be removed at a later stage in the synthesis. It was also thought that protection of both the 2′-hydroxyl group in the pantoyl residue and the terminal thiol group as their benzyl ethers might be necessary. These partially benzylated esters and ethers could occur in syntheses of the more direct type in which condensing agents such as carbodi-imides,[6] oxime sulphonates,[7] ethoxyacetylene,[8] etc., are used. In several routes, then, the need would arise for the removal under mild conditions of benzyl groups

[4] Cf. Baddiley, Clark, Michalski, and Todd, *J.*, 1949, 815.
[5] Corby, Kenner, and Todd, *J.*, 1952, 3669.
[6] Khorana and Todd, *J.*, 1953, 2254.
[7] Atherton, Morrison, Cremlyn, Kenner, Todd, and Webb, *Chem. and Ind.*, 1955, 1183.
[8] Arens and Doornbos, *Rec. Trav. chim.*, 1955, **74**, 79.

from a pyrophosphate. Hitherto, this has been done by catalytic hydrogenolysis,[9] quaternisation with a strong tertiary base,[4] anionic debenzylation,[3, 10, 11] or acid-catalysed transfer of benzyl to phenol.[12] The presence of sulphur in our compounds precluded hydrogenolysis with a palladium or platinum catalyst, and acidic phenol solutions caused extensive decomposition of some of the sulphur-containing model compounds. The former difficulty was overcome in earlier work on the synthesis of simple monophosphates of pantetheine by removing benzyl groups with sodium in liquid ammonia.[1] It was of interest to examine the effect of this reagent on pyrophosphates.

The various compounds were treated with sodium in liquid ammonia under anhydrous conditions and the products, after removal of ammonia by evaporation, were rapidly dissolved in water and passed through a column of a cation-exchange resin in the free acid form. The resulting solution of phosphates was neutralised with ammonia without delay and examined by paper chromatography. P^1P^2-Dibenzyl pyrophosphate was converted quantitatively into inorganic pyrophosphate. Tribenzyl pyrophosphate gave mainly inorganic pyrophosphate but also some orthophosphate. With tetrabenzyl pyrophosphate more orthophosphate was formed but even here a certain proportion of inorganic pyrophosphate was detected. A third product from tetrabenzyl pyrophosphate was recognised as inorganic phosphoramidate. This substance was identical in R_F with inorganic phosphoramidate produced by the action of sodium in liquid ammonia on dibenzyl phosphoramidate.[13]

These results are consistent with general ideas regarding the greater reactivity of the pyrophosphate linkage in neutral pyrophosphoric esters than in esters containing free acidic groups. The formation of inorganic phosphoramidate from tetrabenzyl pyrophosphate is not surprising, since ammonia reacts readily at room temperature with this ester to give dibenzyl phosphoramidate and ammonium dibenzyl phosphate.[14]

P^1-Benzyl P^2-*N*-pantoyl*cyclo*hexylamine-4 pyrophosphate (V; R = CH_2Ph), prepared by the action of barium thiocyanate on the neutral tribenzyl ester, was readily converted into *N*-pantoyl*cyclo*hexylamine-4 pyrophosphate by reduction with sodium in liquid ammonia, as well as by catalytic hydrogenolysis. This reagent also debenzylated 2′ : 3′-*iso*propylideneadenosine-5′ dibenzyl phosphate to 2′ : 3′-*iso*propylideneadenosine-5′ phosphate. Although the method could not be used with pyrimidine nucleotides because of reduction of the pyrimidine ring,[15] it is useful for the removal of benzyl groups from intermediates in many nucleoside pyrophosphate syntheses. It is already known that benzyl groups on the 2′-hydroxyl and the thiol group in pantetheine and its phosphates are removed under the conditions of reduction described above.[1]

Although complete removal of benzyl groups from a fully benzylated derivative of 3′-dephospho-coenzyme A by sodium in liquid ammonia would proceed in low yield, reasonable yields should be obtained from partially benzylated derivatives.

The relative ease of removal of benzyl as opposed to other alkyl and aryl groups by various techniques is sometimes attributable to the ready formation of benzyl radicals. This suggested to us the possibility of debenzylating pyrophosphates by irradiation with ultraviolet light. Dibenzyl phosphate and tetrabenzyl pyrophosphate were debenzylated smoothly in alcoholic solution by ultraviolet light, the latter giving inorganic pyrophosphate accompanied by only traces of orthophosphate. Adenosine-5′ benzyl phosphate, on the other hand, was completely unaffected under the experimental conditions employed. This relative stability is probably due to the strong absorption of ultraviolet light by the purine moiety.

[9] Baddiley and Todd, *J.*, 1947, 648.
[10] Clark and Todd, *J.*, 1950, 2023, 2031.
[11] Anand, Clark, Hall, and Todd, *J.*, 1952, 3665.
[12] Christie, Kenner, and Todd, *J.*, 1954, 46.
[13] Baddiley, Buchanan, and Letters, *J.*, 1956, 2812.
[14] Atherton and Todd, *J.*, 1947, 674.
[15] Burke, *Chem. and Ind.*, 1954, 1393.

Experimental

Evaporations were carried out *in vacuo*.

N-*Pantoyl*cyclo*hexylamine*.—DL-Pantolactone (7 g.), dissolved in *cyclo*hexylamine (*ca.* 50 c.c.), was refluxed for 30 min. Solvent was removed and a little ether was added. After decantation of the ether, the solid residue of *amide* recrystallised from aqueous alcohol as prisms, m. p. 111° (10 g., 80%) (Found: C, 62·8; H, 9·8; N, 6·3. $C_{12}H_{23}O_3N$ requires C, 62·8; H, 10·0; N, 6·1%).

A sample prepared from D(−)-pantolactone had m. p. 104°, $[\alpha]_D$ +51·4° (*c* 2·57 in EtOH) (Found: C, 62·6; H, 10·2; N, 6·1%).

cyclo*Hexylammonium Salt of* DL-N-*Pantoyl*cyclo*hexylamine*-4 *Phosphate*.—Dry DL-pantoyl-*cyclo*hexylamine (5·0 g.) was dissolved in dry pyridine (30 c.c.) and cooled in acetone–carbon dioxide. To the slurry was added dibenzyl phosphorochloridate (from 5·5 g. of dibenzyl phosphite) in carbon tetrachloride (5 c.c.). The mixture was allowed to reach room temperature and after an hour was treated with the same amount of the phosphorochloridate under identical conditions. After 2 days at −10° pyridine was removed by distillation. The syrup was dissolved in ethyl acetate (20 c.c.) and washed successively with water, 2N-sulphuric acid, and water. The solution was dried ($MgSO_4$), filtered, and evaporated to a clear syrup (15·7 g.).

A portion (10·0 g.) was hydrogenated in ethanol with palladium as catalyst. The catalyst was filtered off, water was added, and the ethanol evaporated. The solution was adjusted to pH8 with barium hydroxide solution, barium phosphate was filtered off, and the solution was passed through a column of Amberlite IR-120 (H^+ form) to remove barium ions. The effluent and aqueous washings were neutralised with *cyclo*hexylamine and evaporated to dryness. Trituration with ethanol gave a solid (8·8 g., 79%) which could not be recrystallised, although paper chromatography indicated that it was homogeneous. However, the *mono*cyclo*hexylamine salt*, m. p. 194—195°, readily crystallised from water (Found: C, 53·2; H, 9·1; N, 7·1; P, 7·7. $C_{18}H_{37}O_6N_2P$ requires C, 53·0; H, 9·1; N, 6·9; P, 7·6%) and gave one spot when chromatographed on paper in *n*-propyl alcohol–ammonia (see Table).

cyclo*Hexylammonium Salt of Benzyl* N-*Pantoyl*cyclo*hexylamine*-4 *Phosphate*.—D-*N*-Pantoyl*cyclo*hexylamine (11·5 g.) was phosphorylated with dibenzyl phosphorochloridate (from 15·0 g. of dibenzyl phosphite) in the usual way. The mixture, after evaporation of excess of pyridine, was dissolved in ether and washed exhaustively with water, N-sulphuric acid, water, N-sodium hydroxide, and finally water, dried ($MgSO_4$), and evaporated to a syrup (22·7 g.). Paper chromatography showed the absence of dibenzyl phosphate. The neutral ester was dissolved in 2-ethoxyethanol (100 c.c.), and barium thiocyanate (25 g.) added. The mixture was heated at 100° for 1 hr., during which it solidified. The following day it was treated with ether (500 c.c.) and filtered, and the solid was washed with ether and dried (P_2O_5). The product (37 g.), dissolved in 50% aqueous ethanol (400 c.c.), was poured through a column (2·7 × 90 cm.) of Amberlite IR-120 (H^+ form). Washing of the column was continued until the effluent was neutral, and the combined effluent was adjusted to pH 8 with *cyclo*hexylamine (*ca.* 13 c.c.). The solution was evaporated to 300 c.c. and the crystalline product was filtered off and washed with acetone and ether (15 g.; m. p. 189—190°). A further crop (1·0 g.; m. p. 183°) was obtained from the mother-liquors. Recrystallisation of the first crop from ethanol–ether lowered the m. p., but two crystallisations from water yielded a cyclo*hexylamine salt* with m. p. 190—191° (Found: C, 60·2; H, 8·7; N, 5·8; P, 6·3. $C_{25}H_{43}O_6N_2P$ requires C, 60·3; H, 8·6; N, 5·6; P, 6·2%).

Hydrogenolysis of the Monobenzyl Ester.—The above *cyclo*hexylamine salt (m. p. 190°; 0·5 g.) was hydrogenolysed in aqueous-alcoholic solution with palladium. Paper chromatography of the products in *n*-propyl alcohol–ammonia–water showed a strong spot identical with that from *N*-pantoyl*cyclo*hexylamine-4 phosphate, together with a trace of inorganic phosphate. Evaporation of the solution after removal of catalyst, followed by crystallisation from water, gave the mono*cyclo*hexylamine salt, m. p. 191—193°.

N-*Pantoyl*cyclo*hexylamine*-4 *Pyrophosphate*.—(a) *From* N-*pantoyl*cyclo*hexylamine*-4 *phosphate*. The mono*cyclo*hexylamine salt (0·5 g.) was converted into the free acid by passage through Amberlite IR-120 (H^+). The effluent was neutralised with triethylamine and evaporated to dryness. The water was evaporated and the residue dissolved in methyl cyanide (5 c.c.) and chloroform (10 c.c.). The solution was evaporated to dryness and the process was repeated, both chloroform and toluene being used. The residue crystallised. It was dissolved

in a mixture of dry methyl cyanide (3 c.c.) and carbon tetrachloride (5 c.c.) and cooled to −10°. To this solution was added dibenzyl phosphorochloridate (from 0·32 g. of dibenzyl phosphite; 1·1 mol.) and the whole was kept at 0° for 2·5 hr., then evaporated to dryness at 0°. The residue, dissolved in ethanol (96%), was hydrogenolysed in the presence of palladium black. Paper chromatography showed the formation of several compounds including inorganic ortho- and pyro-phosphate. A major spot having an R_F value slightly lower than that of *N*-pantoyl*cyclo*hexylamine-4 phosphate in the *iso*butyric acid–ammonia solvent was extracted from a chromatogram and shown to be hydrolysed completely by N-hydrochloric acid in 7 min. at 100° to inorganic phosphate and *N*-pantoyl*cyclo*hexylamine-4 phosphate. This compound was stable to hydrolysis in aqueous ammonia (*d* 0·88) under the same conditions. It was isolated by running as bands on Whatman No. 3 paper, first in *n*-propyl alcohol–ammonia–water (6 : 3 : 1) followed by *n*-butyl alcohol–acetic acid–water. It was converted into its *cyclo*hexylamine salt (42 mg.) by the usual ion-exchange procedure (see above), then further purified through the mercury salt and reconverted into the *dicyclohexylamine salt*, m. p. 130° (with previous shrinking) (Found: C, 49·5; H, 9·9; N, 8·3; P, 8·3. $C_{30}H_{64}O_9N_4P_2,2H_2O$ requires C, 49·8; H, 9·4; N, 7·8; P, 8·6%).

(b) *From benzyl* N-*pantoyl*cyclo*hexylamine-4 phosphate.* The *cyclo*hexylamine salt of the DL-monobenzyl ester (m. p. 189°) was treated with ether (10 c.c.) and 2N-sulphuric acid (10 c.c.), and then the ether layer was removed. After two further ether-extractions the combined extracts were dried (Na_2SO_4) and filtered, and triethylamine (0·2 c.c.) was added. The solution was evaporated to dryness, finally with chloroform and toluene. The residue was dissolved in dry chloroform (5 c.c.), and dibenzyl phosphorochloridate (from 0·27 g. of dibenzyl phosphite) in chloroform (15 c.c.) added. Triethylamine (1 drop) was added and the solution was left at room temperature for 2 hr. Evaporation left a semicrystalline gum which was rapidly dissolved in 95% ethanol and hydrogenolysed (palladium black). Hydrogen uptake was complete in 15 min. The catalyst was removed and the solution neutralised with ammonia, concentrated, and examined by paper chromatography.

The chromatographic analysis (in *n*-propyl alcohol–ammonia–water) was very similar to that given by the crude product obtained as in method (a). The material in the *N*-pantoyl*cyclo*hexylamine-4 pyrophosphate spot, which was present in slightly greater amount than before, was readily hydrolysed by N-hydrochloric acid in 7 min. at 100°, to give *N*-pantoyl*cyclo*hexylamine-4 phosphate and inorganic phosphate.

P^1-*Benzyl* P^2-(N-*Pantoyl*cyclo*hexylamine-4*) *Pyrophosphate.*—The neutral tribenzyl pyrophosphoric ester was prepared from the D-monobenzyl ester (0·5 g. of *cyclo*hexylamine salt, m. p. 190°) as in (b) above. The chloroform solution was evaporated to dryness and the residue dissolved in 2-ethoxyethanol (5 c.c.). Dry barium thiocyanate (1 g.) and triethylamine (1 drop) were added, and the mixture was heated at 100° for 15 min., then cooled. Light petroleum (b. p. 40—60°; 45 c.c.) was added, the mixture shaken, and the petroleum layer removed and discarded. Ether (50 c.c.) was added, whereupon a solid separated. The ether layer was decanted, the solid was washed with more ether (50 c.c.), and the ether extracts were discarded. The solid was ground with water (10 c.c.) and ether (10 c.c.) and filtered. The precipitate was washed successively with water (15 c.c.), acetone (10 c.c.), and ether. After drying, it was obtained as a pale yellow-green powder A (0·22 g.). The combined filtrates were evaporated to dryness, finally with benzene. The residual solid was triturated with acetone, filtered, and washed with acetone and then ether, to give a white powder B (0·27 g.).

Paper chromatography of product A in *n*-propyl alcohol–ammonia–water showed the presence of P^1P^2-dibenzyl pyrophosphate, some unchanged monobenzyl ester, and a spot with and R_F between these which was apparently the required compound. Solid B contained a small amount of the cyclic phosphate of *N*-pantoyl*cyclo*hexylamine together with unchanged monobenzyl ester. Dibenzyl phosphate would have the same R_F as the monobenzyl ester of *N*-pantoyl*cyclo*hexylamine-4 phosphate.

Product A (60 mg.) was converted into the free acid by treatment with Amberlite IR-120 (H^+ form) and hydrogenolysed in 50% aqueous ethanol over palladium black. The product, after removal of catalyst, was neutralised with ammonia and run on paper in *n*-propyl alcohol–ammonia–water. Together with inorganic ortho- and pyro-phosphate and *N*-pantoyl*cyclo*hexylamine-4 phosphate, was a major spot of *N*-pantoyl*cyclo*hexylamine-4 pyrophosphate, identified by its R_F value and ready hydrolysis with acid to the monophosphate and inorganic orthophosphate.

Products A (100 mg.) and B (100 mg.) were treated with sodium in liquid ammonia by the method described below for benzyl pyrophosphates. Chromatograms of the neutralised products showed that product A gave the same compounds as were obtained by catalytic hydrogenolysis. Product B yielded mainly the 4-phosphate together with some inorganic phosphate, cyclic phosphate, and a trace of the 4-pyrophosphate (characterised by acid hydrolysis as before).

Debenzylation of Pyrophosphoric Esters with Sodium in Liquid Ammonia.—Small pieces of sodium were added to the appropriate ester (0·001 mole) in liquid ammonia (50 c.c.) under anhydrous conditions until a permanent blue colour was obtained. After addition of a few drops of alcohol the solution was allowed to evaporate. Last traces of ammonia were evaporated and the residue was rapidly dissolved in water (20 c.c.), the dibenzyl filtered off, and the filtrate passed through Amberlite IR-120 (H^+ form). The effluent and aqueous washings of the column were neutralised with 2N-sodium hydroxide, and aliquot parts were examined by paper chromatography in *n*-propyl alcohol–ammonia–water (6 : 3 : 1). The product from P^1P^2-dibenzyl pyrophosphate showed the presence of only inorganic pyrophosphate, while the products from the other two esters showed that inorganic orthophosphate had been produced. The latter products were analysed for inorganic phosphate and total phosphate by Allen's method, the pyrophosphate being calculated by difference. Tetrabenzyl pyrophosphate yielded orthophosphate 76·2% and pyrophosphate 9·7%; for tribenzyl pyrophosphate the values were 22·2 and 58·7% respectively. The product from tetrabenzyl pyrophosphate gave a spot on chromatography corresponding to phosphoramidic acid which would behave on analysis as inorganic orthophosphate.

The debenzylation of 2′ : 3′-*iso*propylideneadenosine-5′ dibenzyl phosphate was carried out similarly. Amberlite IR-120 (ammonium form) was used in this case for the removal of sodium ions. The main product was 2′ : 3′-*iso*propylideneadenosine-5′ phosphate. Smaller amounts of unidentified products were also formed.

Action of Ultraviolet Light on Benzyl Phosphates.—Dibenzyl phosphates. Dibenzyl phosphate (50 mg.) in (*a*) dry ethanol (2 c.c.) and (*b*) 50% aqueous ethanol (2 c.c.) was irradiated in silica flasks by a " Mineralite " lamp, dry oxygen-free nitrogen being bubbled through the solutions. Aliquot parts were withdrawn at intervals and examined by paper chromatography in the *iso*butyric acid–ammonium *iso*butyrate solvent. In each case inorganic phosphate (R_F 0·37) and benzyl hydrogen phosphate (R_F 0·85) were produced from the starting material (R_F 0·93).

R_F values of phosphoric and pyrophosphoric esters of N-*pantoyl*cyclo*hexylamine.*

	R_F in Pr^nOH–aq. NH_3 (d 0·88)–H_2O	
	6 : 3 : 1	8 : 1 : 1
Pyrophosphate	0·08	0·0
Orthophosphate	0·17	0·02
Phosphoramidate	0·18	—
N-Pantoyl*cyclo*hexylamine-4 phosphate	0·67	0·29
N-Pantoyl*cyclo*hexylamine-4 pyrophosphate	0·56	0·16
N-Pantoyl*cyclo*hexylamine-2 : 4 phosphate	0·88	0·79
N-Pantoyl*cyclo*hexylamine-4 benzyl phosphate	0·93	0·92
P^1-Benzyl P^2-(*N*-pantoyl*cyclo*hexylamine-4) pyrophosphate	0·81	—
Dibenzyl phosphate	0·93	0·86
Dibenzyl pyrophosphate	0·77	0·60
Tribenzyl pyrophosphate	—	0·90

Tetrabenzyl pyrophosphate. The ester (0·2 g.) was dissolved in dry ethanol (10 c.c.) and nitrogen was passed through the solution in a silica flask. The solution was irradiated as before and samples were withdrawn at intervals and examined by paper chromatography. After 7 hr. there was a strong spot of inorganic pyrophosphate and only a trace of orthophosphate. Spots of intermediate benzyl esters of pyrophosphoric acid were detected.

Ultraviolet irradiation under these conditions had no effect on *S*-benzylcysteine or adenosine-5′ benzyl phosphate.

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