UDC 547.636' 118.5 : 547.964 : 612.145

182. Tyunosin Ukita, Nobumasa Imura, Kinzo Nagasawa,[*2] and Norio Aimi : Organic Phosphates. XIX.[*3] A Novel Phosphorylation of Nucleosides and Related Compounds with Hydrobenzoin Cyclic Phosphate activated by Diphenyl Phosphorochloridate.[*4]

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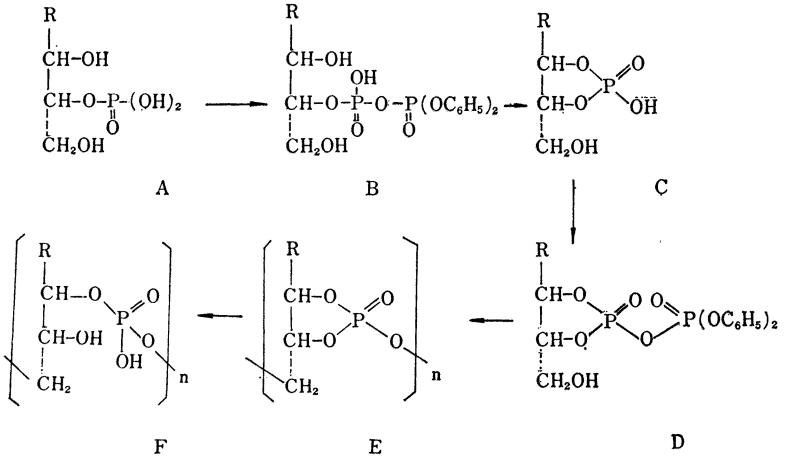
The Michelson's method in chemical synthesis of polyribonucleotides[1] involves a general reaction mechanism, that is, a trihydroxylic compounds which has a phosphorylated hydroxyl group attached adjacent to another hydroxyl bearing carbon and a primary hydroxyl group (A) by reaction with diphenyl phosphorochloridate gives a diphenyl pyrophosphate (B). The product, in the next step, forms a five-membered cyclic phosphate (C) with a simultaneous liberation of the diphenyl phosphoryl group. And the cyclic phosphate thus formed reacts with another molecule of the reagent giving an unstable pyrophosphate (D) which reacts intermolecularly with primary hydroxyl groups to give ultimately a mixture of polymers.

In this series of reactions the polymerisation occurs by an alcoholysis of the intermediate (D) by primary hydroxyl group at the pyrophosphate bond with an accompanied liberation of diphenyl phosphate.



If the intermediate (D) does not involve the primary hydroxyl group in the same molecule and if a similar alcoholysis occurs with another kind of hydroxylic compound (ROH), the products corresponding to the polymers E and F are represented by G and H, respectively.

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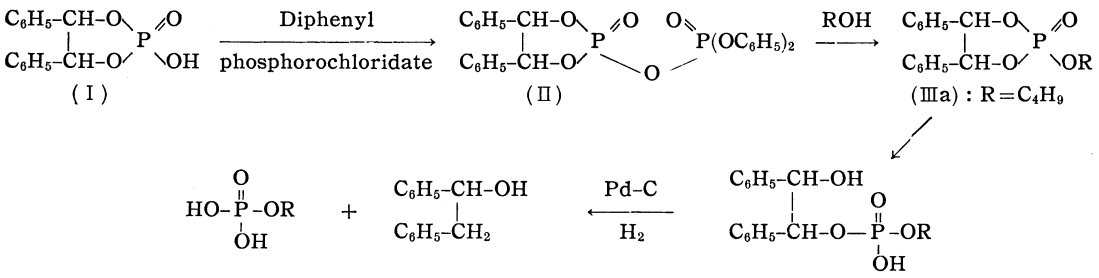
*3 Part XVIII. T. Ukita, H. Hayatsu : This Bulletin. **9**, 1000 (1961).
*4 This work was reported at the 14th Annual Meeting of the Pharmaceutical Society of Japan, July, 1961.

1) A. M. Michelson : J. Chem. Soc., **1959**, 1371; *Idem* : *Ibid.*, **1959**, 3655.

As each reaction step from A to F involves no drastic condition and F is reportedly obtainable in a considerable yield, compound G or H might be an excellent precursor in preparation of an phosphorylated hydroxylic compound, provided their glycol group could be removed under a mild condition.

In a previous paper of this series, Ukita *et al.*[2] reported that hydrobenzoin cyclic phosphotriester (III) (R_1, R_2=phenyl in G), and hydrobenzoin phosphodiester (IV) (R_1, R_2= phenyl in H) by hydrogenation catalyzed with palladium-charcoal can readily liberate dihydrostilbene and 1,2-diphenylethanol respectively to give phosphomonoester.

The present report communicates a novel phosphorylation method of hydroxylic compound (ROH) by its reaction with hydrobenzoin cyclic phosphate (I) and diphenyl phosphorochloridate and by subsequent catalytic hydrogenation of the resulting hydrobenzoin phosphodiester (IV). The reactions are summarized as followings :



(V a) : R=C_4H_9
(V b_1) : R=methyl ribofuranoside-2(+3)
(V b_2) : R=methyl ribofuranoside-5
(V c) : R=methyl 2,3-O-isopropylidene-ribofuranoside-5
(V d) : R=2′,3′-O-isopropylideneuridine-5′
(V e) : R=uridine-2′(+3′)

(IV a) : R=C_4H_9
(IV d_1) : R=methyl ribofuranoside-2(+3)
(IV b_2) : R=methyl ribofuranoside-5
(IV c) : R=methyl 2,3-O-isopropylidene-ribofuranoside-5
(IV d) : R=2′,3′-O-isopropylideneuridine-5′
(IV e) : R=uridine-2′(+3′)

In practice, tributylammonium hydrobenzoin cyclic phosphate (THCP) was reacted in an anhydrous condition with equimolar amounts of diphenyl phosphorochloridate and a hydroxylic compound in the presence of twice the molar amount of tributylamine for 24 to 50 hours at 37°. The solvent used for the reaction was dry dioxane or a mixture of dioxane and dimethylformamide (DMF) depending on the solubility of the hydroxylic compound used. The reaction mixture before and after catalytic hydrogenation was analyzed for mobility on paper electrophoretic pattern, Rf values, for phosphorus by coloration with Hanes-Isherwood reagent[3], for α-glycol group with periodate-Schiff's reagent[4] and for pyrimidine moiety of the spots by ultraviolet absorption at 260 mμ on paper partition chromatograms.

On phosphorylation of butanol by this reaction, after catalytic hydrogenation, butyl phosphate was detected by paper chromatography and the yield was estimated to be 30 to 42%. The incubation mixture of butanol with hydrobenzoin cyclic phosphate, diphenyl phosphorochloridate and tributylamine gave a crystalline phosphorus product which was soluble in ether and gave an electrophoretically inert (M=0[*5]) spot. The product was so unstable that, on keeping, it was converted into an acidic compound (M= 0.95) which, on catalytic hydrogenation, afforded butyl phosphate. From these results, the neutral compound with M value of 0 and the acidic intermediate with M value of

[*5] See the Experimental Part.

2) T. Ukita, K. Nagasawa, M. Irie : J. Am. Chem. Soc., **80**, 1373 (1958).
3) R. S. Bandurski, B. Axelrod : J. Biol. Chem., **193**, 405 (1951).
4) J. Baddiley, J. G. Buchanan, R. E. Handschumacher, J. F. Prescott : J. Chem. Soc., **1956**, 2818; J. G. Buchanan, C. A. Dekker A. G. Long : *Ibid.*, **1950**, 3162.

0.95 were assumed to be butyl hydrobenzoin cyclic phosphate (IIIa) and butyl 1,2-diphenyl-2-hydroxyethyl phosphate (IVa), respectively.

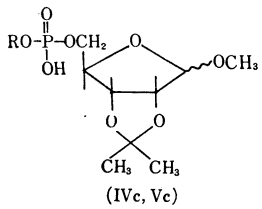
When methyl $\alpha(+\beta)$-ribofuranoside[5] was used as a hydroxylic compound, the reaction mixture before catalytic hydrogenation revealed an acidic product which gave an electrophoretic migration of M=0.90 and positive reactions for both Hanes-Isherwood and periodate-Schiff's reagents.

After catalytic hydrogenation, however, this product was separated by paper chromatography into two compounds having respective Rf_1 values (and yield) of 0.23 (17.5%) and 0.15 (46%)which werei dentified to be methyl ribofuranoside 2(+3)-phosphate (Vb_1) and methyl ribofuranoside 5-phosphate (Vb_2) respectively. Thus, the intermediate compound with M=0.90 was a mixture of 1,2-diphenyl-2-hydroxyethyl ester of methyl ribofuranoside 2(+3)- and 5-phosphate (IVb_1+IVb_2).

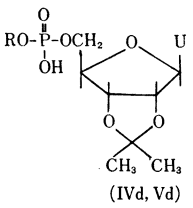
The above findings showed that in this series of reaction, alcoholysis of type II compound occurs not only by the primary but also by the secondary hydroxyl group although the yield of the product by the former was higher than that by the latter.

In order to use this type of phosphorylation reaction for the synthesis of some nucleoties and related compounds, the reactions were performed in preparative scale using methyl 2,3-O-isopropylideneribofuranoside,[6] 2′,3′-O-isopropylidene-[7] and 5′-O-trityluridine.[7]

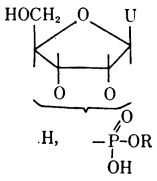
In the case of methyl 2,3-O-isopropylideneribofuranoside, the reaction mixture revealed an electrophoretically neutral phosphoryl compound, which on hydrolysis with diluted hydrochloric acid gave phosphodiester (IVc). On catalytic hydrogenation, (IVc) furnished a phosphate (Vc) in a yield of 76% : The structure of (Vc) was confirmed by identification of ribose 5-phosphate obtained after removal of the protecting groups by acid hydrolysis.



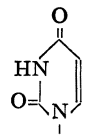
(IVc, Vc)



(IVd, Vd)



(IVe, Ve)

U : 

(IVc), (IVd), (IVe), R=1,2-diphenyl-2-hydroxyethyl (Vc), (Vd), (Ve) : R=H

The reaction for 2′,3′-O-isopropylideneuridine was performed in a mixture of dioxane and dimethylformamide and the acidic product, phosphodiester (IVd) was isolated as barium salt in a yield of 70% on removal of hydrobenzoin moiety by catalytic hydrogenation gave 2′3-O-isopropylideneuridine 5′-phosphate (Vd) which was subsequently converted to uridine 5′-phosphate.

The phosphorylation of 5′-O-trityluridine by this procedure led to the successful phosphorylation of its 2′ or 3′ hydroxyl group although the yield was not so excellent as in the above two cases presumably depending on the less reactivity of secondary hydroxyl group. In this case, the reaction mixture was treated with 80% acetic acid at room temperature to remove the trityl group and the phosphodiester type product (IVe), was isolated in a yield of 13%. The hydrobenzoin moiety of (IVe) was removed

5) H.M. Kissman, C. Pidacks, B.R. Baker : J. Am. Chem. Soc., **77**, 18 (1955).
6) P.A. Levene, E.T. Stiller : J. Biol. Chem., **104**, 299 (1934).
7) P.A. Levene, R.S. Tipson : *Ibid.*, **104**, 385 (1934).

by catalytic hydrogenation to give a mixture of uridine 2'- and 3'-phosphate which was identified with an authentic specimen.

Experimental

Paper Partition Chromatography (PPC)——A sample containing 10~40 γ of phosphorus was applied on Toyo Roshi No. 53 paper and run ascendingly for 16 hr., using the following solvent systems: (1) iso-PrOH-conc. NH_4OH-H_2O (7 : 2 : 1); (2) iso-PrOH-conc. NH_4OH-H_2O (7 : 1 : 2). For the preparative isolation of compounds, sheets of Toyo Roshi No. 26 paper were used. The Rf values of each solvent system used are represented by abbreviations of Rf_1 and Rf_2, respectively. For the detection of spots, the Bandurski-Axelrod method[3] for phosphate, the periodate-Schiff's reagent[4] for α-glycol group and ultraviolet absorption for pyrimidine nucleosides were employed.

Paper Electrophoresis (PEP)——The sample was applied onto a strip of Toyo Roshi No. 53 paper and after being moistened with buffer solution of pH 5.6 (BuOH-pyridine-AcOH-H_2O=20 : 10 : 2 : 968)), the strips were subjected to electrophoresis at a potential of 700 v/16 cm. for 40 min. The detection of the spots on paper was made by the same technique as that used in PPC. The mobility (M) for each spot was represented by the ratio of the distance of the spot from the start line to that of dinitro phenylglycine used as a standard.

Phosphorylation of BuOH——A mixture of 700 mg. (1.5 m mole) of THCP, 490 mg. (1.8 m mole) of diphenyl phosphorochloridate, and 0.14 cc. (1.5 m mole) of BuOH was dissolved in 4 cc. of dry dioxane. The mixture was added with 670 mg. (3.6 m mole) of tributylamine and kept at 37° for 24 hr. An aliquot of the reaction mixture was applied for PEP to observe two phosphorus positive spots having M values of 0 and 0.90. The spot with M=0 was extracted with Et_2O and the extract, after removal of the solvent, gave colorless crystals which, by keeping at room temperature, were converted to a product giving a spot of M=0.95 on PEP. This new product was catalytically hydrogenated with Pd-C. The reaction mixture on PPC with solvent (1) revealed one phosphorus positive spot which had the same Rf value as that of authentic butyl phosphate[2].

Another aliquot from the reaction mixture was treated with 5% NH_4OH to hydrolyze phosphotriester and the mixture, after removal of the solvent by evaporation, was catalytically hydrogenated with Pd-C. On application of the hydrogenated mixture to PPC, two phosphorus positive spots, those of butyl phosphate (Rf_1=0.38) and of inorganic phosphate (Rf_1=0.05), were obtained. The yield of butyl phosphate, calculated from the quantitative determination of phosphorus from the extracts of these two spots, was 42%.

Phosphorylation of $\alpha(+\beta)$-Methyl Ribofuranoside——A mixture of 290 mg. (1.8 m mole) of methyl ribofuranoside, 820 mg. (1.8 m mole) of THCP and 670 mg. (3.6 mmole) of tributylamine was dissolved in a mixed solvent of 3 cc. of dry dioxane and 2 cc. of dimethylformamide (DMF). To the mixture was added 490 mg. (1.8 m mole) of diphenyl phosphorochloridate and the reaction was carried out in a manner similar to that for BuOH. An aliquot was taken from the reaction mixture and applied for PEP. The phosphorus positive spot with M=0.90 appeared colored bluish violet with periodate-Schiff's reagent. Another aliquot from the reaction mixture was taken and after evaporation of the solvent, the residue obtained was catalytically hydrogenated, and applied to PPC to give two phosphorus positive spots (Rf_1=0.15 and 0.23), besides those for inorganic phosphate and diphenyl phosphte.

The spot with Rf_1 value of 0.15 colored bluish-violet with periodate-Schiff's reagent and was identified with that of authentic methyl ribofuranoside 5-phosphate ($V b_2$) while the spot with Rf_1 value of 0.23 was inert to that reagent and assumed to be that of methyl ribofuranoside 2(+3)-phosphate ($V b_1$). The respective yields of ($V b_2$) and ($V b_1$) calculated from phosphorus determination were 46 and 17 %.

Synthesis of Methyl Ribofuranoside 5-Phosphate used as Standard——A solution of 2 g. of methyl 2,3-di-O-acetylribofuranoside 5-diphenyl phosphate[8] in 30 cc. of anhyd. MeOH was catalytically hydrogenated with 200 mg. of Adams' platinum. After completion of H_2 consumption (5 hr.), the catalyst was removed by filtration and the filtrate was kept overnight after addition of 17 cc. of methanolic MeONa. When the solution was refluxed on a water bath for 30 min., a white precipitate appeared which was filtered and washed successively with anhyd. MeOH and anhyd. Et_2O to give 390 mg. of hygroscopic white powder (sodium methyl ribofuranoside 5-phosphate).

To the combined filtrate and washings, was added 30 cc. of H_2O and the solution was carefully neutralized by adding Dowex-50 (H form) resin. After removal of resin by filtration the neutral filtrate was evaporated to ca. 20 cc. and washed with Et_2O. The aqueous layer on evaporation gave additional 800 mg. of sodium methyl ribofuranoside 5-phosphate. *Anal.* Calcd. for $C_6H_{11}O_8PNa \cdot 3H_2O$, C, 21.05; H, 4.97. Found C, 20.74; H, 5.15. Rf_1=0.15, Rf=0.17 (BuOH•AcOH•H_2O (4 : 1 : 5)).

8) T. Ukita, H. Hayatsu : J. Am. Chem. Soc., 84, 1879 (1962).

Phosphorylation of Methyl 2,3-O-Isopropylideneribofuranoside——A mixture of 0.75 g. (3.7 m mole) of methyl $\alpha(+\beta)$-2,3-O-isopropylideneribofuranoside[5], 1.70 g. (3.7 m mole) of THCP and 2 cc. (8.4 m mole) of tributylamine was dissolved in 10 cc. of dry benzene and the solvent was removed by distillation under reduced pressure. The residue was dried twice by azeotropical distillation with 10 cc. of dry dioxane and finally dissolved in 6 cc. of dry dioxane. To this solution was added 1.18 g. (4.4 m mole) of diphenyl phosphorochloridate and the mixture was kept at 37° for 50 hr. The reaction mixture revealed on PEP a neutral, phosphorus positive spot which disappeared on neutralization with dil. HCl; while after this treatment a new spot with a mobility of 0.83 appeared. The neutral solution was extracted with Et_2O, and the extract was washed with H_2O and the residue obtained by the removal of Et_2O was cataytically hydrogenated with Pd-C in dioxane.

On PPC of the hydrogenated mixture, besides the spots of the reagent and inorganic phosphate, a new phosphorus positive spot, having a Rf_1 value of 0.39 was observed. This spot, on succesive spraying *N* HCl and keeping 15 min. at 60°, colored violet with periodate-Schiff's reagent. This new spot was identified with authentic sample of methyl 2,3-O-isopropylideneribofuranoside 5-phosphate and the yield calculated from phosphorus determination of phosphorus positive spots was 76%.

From the hydrogenated mixture, solvent was removed by distillation and the residue was dissolved in 100 cc. of H_2O, passed through a column of 60 cc. of Dowex-50 (pyridinium form) resin and the column was washed with 100 cc. of H_2O. The effluent and washings were combined and lyophilized. The pyridinium salt of the phosphorylated compound thus obtained were dissolved in 50 cc. of iso-PrOH and dry NH_3 was passed through the solution to convert the pyridinium salt to ammonium salt. As the ammonium salt contaminated with ammonium phosphate, it was dissolved in 5 cc. of H_2O and the inorganic phosphate was precipitated as Ba salt by addition of 1*M* $(AcO)_2Ba$. After removal of barium phosphate by centrifugation, to the supernatant was added 1*M* $(NH_4)_2CO_3$ to remove Ba ions. The soluble portion was concentrated in a reduced pressure and, after addition of *N*/3 H_2SO_4 kept at room temperature for 24 hr. to hydrolyze isopropylidene and methyl groups. To the solution was added a saturated $Ba(OH)_2$ solution and $BaSO_4$ precipitated was removed by centrifugation. On addition of 7 cc. of 99% EtOH, 60 mg. of white precipitate appeared from the supernatant. The product was reprecipitated from H_2O-EtOH and dried over P_2O_5 at 40° for 8 hr. *in vacuo* and analyzed. *Anal.* Calcd. for $C_5H_9O_8PBa \cdot H_2O$ (barium ribose 5-phosphate): C, 15.66; H, 2.89; P, 8.08. Found C, 16.01; H, 3.23; P, 8.15.

Phosphorylation of 2',3'-O-Isopropylideneuridine——A mixture of 0.89 g. (3.1 m mole) of 2', 3'-O-isopropylideneuridine, 1.45 g. (3.4 m mole) of THCP and 1.75 cc. (7.4 m mole) of tributylamine was dissolved in a mixed solvent of 16 cc. of dioxane and 2 cc. of DMF, and 7 cc. of the solvent was azeotropically distilled off. To the solution was added 1.01 g. (3.7 m mole) of diphenyl phosphorochloridate dissolved in 3 cc. of dioxane and 1 cc. of DMF, and the mixture was kept at 37° for 50 hr. After addition of dilute NH_4OH, the reaction mixture revealed on PEP an ultraviolet absorbing, phosphorus positive spot with M value of 0.85 besides the spots of the starting material and reagents. (Prior to this treatment an electrophoretically inert spot which was presumed to be that of phosphotriester was observed).

The yield of the product with M value of 0.85 was ca. 80% when calculated from the spectrophotometrical determination at 260 mμ of the spots of M=0.85 and of uridine.

Isolation of Phosphodiester (IVd)——From ca. 1/6 volume of the reaction mixture, the solvent was removed in a reduced pressure and the residue was dissolved in 15 cc. of dioxane containing 10% NH_4OH after addition of 1 cc. of 1*M* $(AcO)_2Ba$, the mixture was kept cool overnight. The colorless needles of Ba salt of (IVd) appeared were collected, washed with a small quantity of H_2O and dried in a desiccator under reduced pressure, yield 230 mg. (70%). *Anal.* Calcd. for $C_{26}H_{28}O_{10}N_2PBa_{1/2}$: N, 4.53; P, 4.93. Found N, 4.41; P, 4.68. $Rf_1=0.84$.

Isolation of 2',3'-O-Isopropylideneuridine 5'-Phosphate——To ca. 2/3 volume of the reaction mixture was added 20 cc. of dioxane containing 10% NH_4OH and the resulting mixture was kept at room temperature for 1 hr. Solvent was removed in a reduced pressure and the residue was catalytcially hydrogenated at 25~28° in 30 cc. of dioxane with 1 g. of Pd-C. After 15 hr. when H_2 uptake was completed, the catalyst and solvent were removed and the residue was shaken with Et_2O and H_2O. The aqueous layer was washed twice with Et_2O and passed through a column (2×20 cm.) of Dowex-50 (pyridinium form) resin. The column was washed with H_2O and the effluent and washings were combined and then lyophilized to obtain a colorless syrup, which was dissolved in a mixture of 5.5 cc. of MeOH and 33 cc. of iso-PrOH. Dry NH_3 was passedt hrough the solution and the mixture was kept cold overnight to precipitate a white solid which was collected by centrifugation. The precipitate was washed thoroughly with iso-PrOH to remove ammonia and dried in a desiccator. To this dry product dissolved in 4 cc. of H_2O was added 1*M* $(AcO)_2Ba$ to remove inorganic phosphate. From the soluble part exess Ba ions were removed as $BaCO_3$ by the addition of 1*M* $(NH_4)_2CO_3$ and subsequent centrifugation. The supernatant upon removal of the solvent gave 726 mg. (87%) of light yellow syrup which on PPC gave one spot having a Rf_1 value of 0.16 identical with that of authentic 2',3'-O-isopropylideneuridine 5'-phosphate. On PEP, this compound revealed one spot (M=1.0)

identical with that of the authentic specimen. The syrup was converted to Ba salt by addition of 1*M* $(AcO)_2Ba$ and barium 2′,3′-O-isopropylideneuridine 5′-phosphate was reprecipitated from aqueous solution by the addition of 99% EtOH. *Anal.* Calcd. for $C_{12}H_{15}O_9N_2PBa \cdot H_2O$: C, 27.84; H, 3.31; N, 5.41; P, 5.99; Ba, 26.54. Found C, 27.88; H, 3.40; N, 5.51; P, 5.63; Ba, 26.09.

Uridine 5′-Phosphate——Fifty miligrams of barium 2′,3′-O-isopropylideneuridine 5′-phosphate was dissolved in 15 cc. of *N* H_2SO_4 and warmed at 90° for 90 min. After neutralization of the mixture with $Ba(OH)_2$, $BaSO_4$ precipitated was removed by centrifugation and the supernatant was evaporated to ca. 3 cc. To the solution was added three times volume of anhyd. EtOH and the white precipitate formed was collected and reprecipitated form aqueous solution with anhyd. EtOH. The preparation was dried over P_2O_5 under reduced pressure. *Anal.* Calcd. for $C_9H_{11}O_9N_2PBa \cdot 3H_2O$: C, 21.05; H, 3.34; N, 5.46; P, 6.03. Found C, 20.62; H, 2.66; N, 5.16; P, 6.09. This product was identified with authentic uridine 5′-phosphate on PPC using solvent (1) ($Rf_1=0.05$) and a solvent system EtOH-1*M* $AcONH_4$ (5 : 2) ($Rf=0.53$).

Phosphorylation of 5′-*O*-Trityluridine——A mixture of 1.91 g. (3.9 m mole) of 5-O-trityluridine, 1.81 g. (3.9 m mole) of THCP and 2.26 cc. (9.5 m mole) of tributylamine was dissolved in 10 cc. of dry dioxane. To the solution was added 1.30 g. (4.8 m mole) of diphenyl phosphorochloridate and the mixture was kept at 37° for 24 hr. Thirteen mililiters of the reaction mixture was taken, added with 10 cc. of 80% AcOH and kept at room temperature for 24 hr. to hydrolyze trityl group. The reaction mixture on PPC revealed, besides the spots of reagents and the starting material, two phosphorus positive and ultraviolet absorbing spots with $Rf_2=0.63$ and 0.12. By spectrophotometrical estimation at 263 mμ of the extracts obtained from these spots, the respective yield of the products giving Rf_2 value of 0.63 and 0.12 was found to be 33 and 10%.

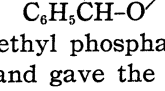
The reaction mixture was applied onto 30 sheets of Toyo Roshi No. 26 (15×40 cm.) and run ascendingly with solvent (2). The bands having Rf_2 value of 0.63 on the paper were cut and the combined cuttings were extracted with 50% MeOH. After evaporation of the solvent, the residue obtained was lyophilized to give white powder which was precipitated from EtOH by adding 4 times volume of Et_2O. The precipitation was repeated twice to give pure ammonium salt of (IVe) in an yield of 114.4 mg. (12%). The sample was dried in a desiccator over P_2O_5 under reduced pressure. *Anal.* Calcd. for $C_{23}H_{28}O_{10}N_3P$: N, 7.82; P, 5.76. Found N, 7.41; P, 5.74. M=0.78.

A part of this product was catalytically hydrogenated with Pd-C in H_2O and the reaction mixture on PPC gave a spot with Rf_2 value of 0.12 which was identical with that appeared from the above reaction mixture.

The bands with Rf value of 0.12 were also collected and extracted with H_2O. After lyophilization of the aqueous solution, the residue obtained was dissolved in 10 cc. of H_2O and passed through a column (1×10 cm.) of Dowex-50 (H form) resin. The column was washed with 20 cc. of H_2O and the effluent was combined with the washings. The acidic solution was neutralized with *N* NaOH and evaporated to ca. 2 cc. On addition of 8 cc. of Me_2CO to the neutral solution, appeared white precipitates of Na salt of (Ve) which weighed, after washing and drying, 53 mg. (8%). The white powder thus obtained gave Rf_2 value of 0.12 and Rf value of 0.55 with solvent, EtOH-1*M* $AcONH_4$ (5 : 2), which were respectively identical with those of authentic uridine 2′(+3′)-phosphate.

The authors are indebted to Dainippon Vitamin Co., Ltd. for their kind supply of uridine. Thanks are also due to Mr. D. Ōhata of the Sasaki Institute for carrying out the micro-analyses.

Summary

Hydrobenzoin cyclic phosphate, diphenyl phosphorochloridate, and tributylamine were reacted with several hydroxylic compounds (ROH) at 37° for 24~50 hours and the resulting phosphotriesters of type  were hydrolyzed to phosphodiesters (esters of 1,2-diphenyl-2-hydroxyethyl phosphate) which were catalytically hydrogenated to liberate hydrobenzoin moiety and gave the phosphoryl esters of the hydroxylic compounds used.

The reaction was applied to butanol, methyl ribofuranoside to detect the corresponding phosphates. And the method was used for the preparative phosphorylation of methyl 2,3-O-isopropylideneribofuranoside, 2′,3′-O-isopropylideneuridine and 5′-O-trityluridine.

(Received July 24, 1962)