in benzene (50 ml.) was stirred while a solution of triphenylphosphine (11.4 g., 0.043 mole) in benzene (50 ml.) was added at such a rate that the temperature remained below 40°. The solution was heated at 50° for 15 min. and the benzene was removed *in vacuo*. Distillation produced a colorless liquid which on redistillation gave N-ethylbenzimidoyl chloride (2.7 g., 0.016 mole, 37%), b.p. 89–91° (9 mm.), $n^{21}D$ 1.5508; reported[24] b.p. 110–111° (15 mm.). The distillation residue was dissolved in hot benzene. Chilling and the addition of hexane separated triphenylphosphine oxide (11.0 g., 0.040 mole, 93%).

B. From N-Ethylbenzamide and Phosphorus Pentachloride.[24]—A solution of N-ethylbenzamide (7.5 g., 0.05 mole) and phosphorus pentachloride (10.4 g., 0.05 mole) in benzene was heated at 50° for 1 hr. The benzene and phosphorus oxychloride were removed *in vacuo* and distillation gave a yellow liquid which on redistillation gave N-ethylbenzimidoyl chloride (3.7 g., 0.022 mole, 44%), b.p. 51° (0.25 mm.), $n^{21}D$ 1.5507. The infrared spectrum was identical with that of the sample prepared as described in part A.

Reaction of N,N-Diethyl-2,2,2-Trichloroacetamide with Tributylphosphine in the Presence of tetrapropylammonium Bromide.—A solution of tetrapropylammonium bromide (26.6 g., 0.10 mole) and N,N-diethyl-2,2,2-trichloroacetamide (21.9 g., 0.10 mole) in chloroform (150 ml.) was stirred while tributylphosphine (30.3 g., 0.15 mole) was added dropwise in a nitrogen atmosphere. The solution was heated at 85° for 7 hr. and then the chloroform was removed *in vacuo*. Distillation gave two arbitrary fractions, I, 7.5 g., b.p. 25–64° (0.3 mm.), and II, 17.6 g., b.p. 64–130° (0.3–0.7 mm.). Fractions I and II were found to contain less than 1% bromine, if any.[8] Vapor phase and infrared analysis of the fractions showed them to contain: N,N-diethyl-1,2,2-trichlorovinylamine[1] (3.2 g., 0.016 mole, 16%), tributylphosphine (11.5 g., 0.057 mole, 38%), N,N-diethyl-2,2,2-trichloroacetamide (1.8 g., 0.0082 mole, 8%), an unknown (1.8 g.) and tributylphosphine oxide (6.2 g., 0.028 mole, 28%). The unknown substance decomposed before it could be characterized.

The residue was extracted with hexane (100 ml. and evaporation of the hexane gave impure tributylphosphine oxide. Extraction of the residue with ethyl acetate separated a tan solid. Recrystallization from acetone–ethyl acetate gave somewhat impure tetrapropylammonium bromide (25.4 g., 0.095 mole, 95%), m.p. 245–254°, reported[25] m.p. 252°. The infrared spectrum was essentially identical with that of an authentic sample.

Reaction of N,N-diethyl-2,2,2-trichloroacetamide and Tributylphosphine in Chloroform.—A solution of N,N-diethyl-2,2,2-trichloroacetamide (21.9 g., 0.10 mole) in chloroform (150 ml.) was stirred in a nitrogen atmosphere while tributylphosphine (30.3 g., 0.15 mole was added dropwise. The solution was heated at 70° for 3 hr. and the chloroform was evaporated *in vacuo*. Distillation produced N,N-diethyl-1,2,2-trichlorovinylamine[1] (11.5 g., 0.057 mole, 57%), $n^{25}D$ 1.4864.

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(24) G. Lander, *J. Chem. Soc.*, **83**, 320 (1903).

(25) S. Sugden and H. Wilkins, *ibid.*, **132**, 1297 (1929); Eastman Kodak Co. sample decomposed at 267–269°.

[CONTRIBUTION FROM MONSANTO CHEMICAL CO., RESEARCH DEPARTMENT, INORGANIC CHEMICALS DIVISION, ST. LOUIS, MO.]

N.m.r. Study of the P–C(OH)–P to P–C–O–P Rearrangement: Tetraethyl 1-Hydroxyalkylidenediphosphonates[1]

BY STEVEN J. FITCH AND KURT MOEDRITZER

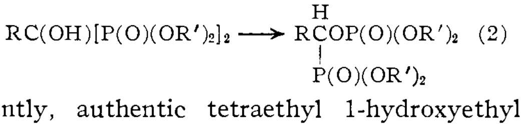
RECEIVED JANUARY 9, 1962

Compounds previously reported to be tetraalkyl 1-hydroxyalkylidenediphosphonates are found to be isomeric rearrangement products of the reported materials. Authentic tetraethyl 1-hydroxyethylidenediphosphonate was prepared, and its rearrangement was demonstrated. P^{31} and H^1 n.m.r. spectra, infrared spectra and chemical evidence are presented in support of the rearrangement, and the rearrangement is related to other reactions of 1-hydroxyalkylphosphonates.

Introduction

The synthesis of 1-hydroxyalkylidenediphosphonate esters by the base-catalyzed addition of dialkyl phosphonates to dialkyl acylphosphonates has been reported.[2a,b] However, our attempts to prepare diphosphonates by the reported methods led to the formation of isomeric compounds containing two chemically different kinds of phosphorus atoms. This finding was interpreted as meaning that the initially formed diphosphonates had rearranged to the isomeric phosphates. Subsequently, authentic tetraethyl 1-hydroxyethylidenediphosphonate was isolated and characterized, and direct evidence of its rearrangement was obtained.

$$RC(O)P(O)(OR')_2 + HP(O)(OR')_2 \longrightarrow RC(OH)[P(O)(OR')_2]_2 \quad (1)$$



$$RC(OH)[P(O)(OR')_2]_2 \longrightarrow R\underset{P(O)(OR')_2}{\overset{H}{C}}OP(O)(OR')_2 \quad (2)$$

Results and Discussion

P^{13} N.m.r. Spectra.—The distilled products of reaction 1 with R = CH_3 or C_6H_5 and R′ = C_2H_5 give spectra having two peaks of approximately equal size, showing that equal numbers of phosphorus atoms are in the two chemical states. The chemical shift of one peak is about +1 p.p.m., which is characteristic of trialkyl orthophosphate esters.[3] The other peak occurs at −16 (R = C_6H_5) or −21 (R = CH_3) p.p.m. As can be seen from Table I, this second chemical shift is appropriate for a diethyl alkylphosphonate having

TABLE I

CHANGE IN CHEMICAL SHIFT OF $RP(O)(OC_2H_5)_2$ WITH INCREASING ELECTRONEGATIVITY OF α-SUBSTITUENTS[a]

R	Chemical shift, p.p.m.	R	Chemical shift, p.p.m.
C_2H_5	−32.5	$ClCH_2$	−18
CH_3	−30	Cl_2CH	− 9.3
n-$C_9H_{19}CH(OH)$	−25.5	Cl_3C	− 6.5
$C_2H_5O_2CCH_2$	−19		

[a] These chemical shifts are abstracted from ref. 3 and from unpublished data in this Laboratory.

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(1) Presented at 140th Meeting of the American Chemical Society, Chicago, Ill., September, 1961.

(2) (a) R. L. McConnell and H. W. Coover, Jr., *J. Am. Chem. Soc.*, **78** 4450 (1956); (b) J. A. Cade, *J. Chem. Soc.*, 2272 (1959).

(3) J. R. Van Wazer, C. F. Callis, J. N. Shoolery and R. C. Jones, *J. Am. Chem. Soc.*, **78**, 5715 (1956).

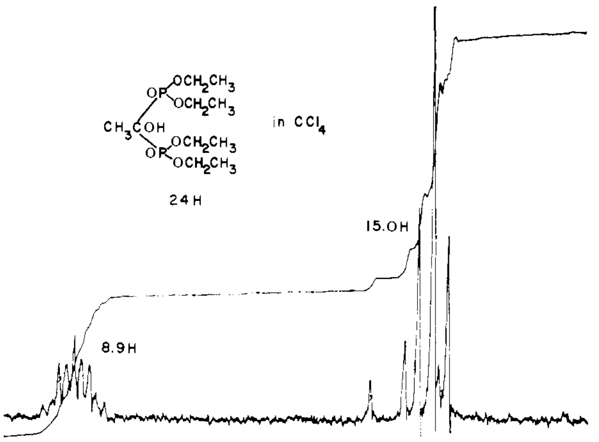


Fig. 1.—H^1 n.m.r. spectrum of the diphosphonate.

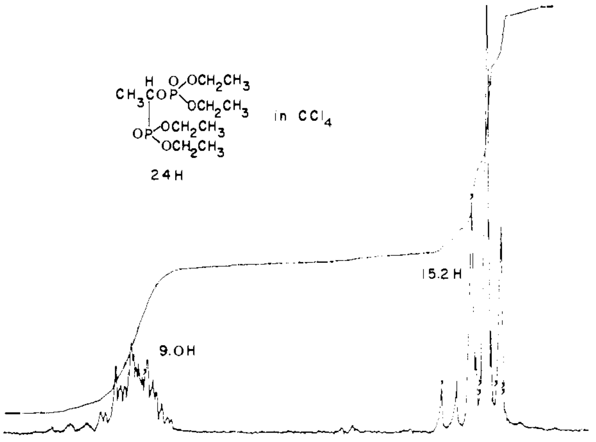


Fig. 2.—H^1 n.m.r. spectrum of the rearranged product.

an electron-withdrawing substituent, such as $-OP(O)(OC_2H_5)_2$, on the α-carbon. Both resonances show partly resolved fine structure from coupling of phosphorus nuclei to protons on neighboring groups. The presence of both phosphate and phosphonate groups in the molecule supports the structure of the rearrangement product of eq. 2.

If the products of eq. 1 with $R = CH_3$ are not heated above *ca.* 80°, tetraethyl 1-hydroxyethylidenediphosphonate can be isolated by crystallization at 0°. Its aqueous solution gives a single n.m.r. peak with a chemical shift of -20.8 p.p.m., as would be expected from a symmetrical diphosphonate. The fine structure of the resonance could not be resolved. However, when the ester was converted to the corresponding acid, only the protons on the methyl group remained to couple with phosphorus, and the expected quartet centered at -19.8 p.p.m. was obtained.

No reaction conditions could be found for preparing the diphosphonate with $R = C_6H_5$ without extensive rearrangement.

H^1 N.m.r. Spectra of the Diphosphonate.—The diphosphonate (Fig. 1) with $R = CH_3$ gave methyl resonances consisting of two overlapping triplets of total area equal to 15.0 H atoms/molecule. The large triplet ($J = 7$ c.p.s.) corresponds to the four equivalent methyl groups coupled to methylene protons, and the small triplet corresponds to the odd methyl group coupled symmetrically to two equivalent phosphorus atoms with $J = 16$ c.p.s.

These assignments were verified by a double resonance experiment: the H^1 n.m.r. spectrum was taken while the phosphorus nuclei were being irradiated at their resonant frequency with a high power level. This eliminated the phosphorus–hydrogen coupling and left only hydrogen–hydrogen coupling. Under these conditions, the small triplet collapsed to a singlet, showing that it had arisen from phosphorus–hydrogen coupling, while the large triplet was unchanged.

The downfield multiplet of 8.9 H was assigned to the eight methylene hydrogens plus the hydroxyl hydrogen. This was verified by removing the hydroxyl hydrogen through exchange with deuterium oxide, leaving a methylene resonance of 8.0 H. Under double resonance conditions, this methylene resonance, complicated by both phosphorus–hydrogen and hydrogen–hydrogen coupling, became simplified to the expected quartet.

H^1 N.m.r. Spectra of the Rearrangement Products.—The rearrangement product with $R = CH_3$ (Fig. 2) showed a methyl resonance of 15.2 H. It consisted of a predominant triplet from the four equivalent methyl groups plus a doublet and some partly obscured peaks from the odd methyl group. The more complex structure of the odd methyl resonance is in accord with its coupling to the odd hydrogen and to one or both of the non-equivalent phosphorus atoms. The resonance from the odd methyl group appeared to simplify to the expected doublet overlapping the triplet under double resonance conditions.

The complex multiplet of 9.0 H was assigned to the eight methylene protons plus the odd proton. The complexity arises from coupling of these nine protons to non-equivalent phosphorus atoms and to neighboring methyl protons. In a double resonance spectrum, the expected methylene quartet appeared along with small, partly obscured peaks from the odd proton.

The rearrangement product with $R = C_6H_5$ gave a phenyl resonance of 4.9 H, a double doublet of 1.0 H for the odd hydrogen and multiplets of 7.9 and 12.6 H for the eight methylene and twelve methyl protons. The form of the resonance from the odd proton is consistent with its location, two atoms removed from one phosphorus atom and one atom removed from the other. Impurities made a more exact analysis of this spectrum difficult.

Infrared Spectra.—McConnell and Coover[2] used the presence of a hydroxyl band of variable intensity at 3400–3500 cm.$^{-1}$ as proof of the diphosphonate structure with its P–C(OH)–P backbone. However, diethyl 1-hydroxyethylidenediphosphonate has a hydroxyl frequency of 3180 cm.$^{-1}$. The latter frequency is in the range of 3180–3285 cm.$^{-1}$ established[4] for hydroxyl groups which are intramolecularly hydrogen-bonded to phosphoryl groups in α-hydroxyalkylphosphonates.

(4) C. D. Miller, R. C. Miller and W. Rogers, Jr., *ibid.*, **80**, 1562 (1958).

Furthermore, the rearrangement products gave no hydroxyl frequency in the infrared, as would be expected. However, very strong hydroxyl bands at 3400–3500 cm.$^{-1}$ were observed after the same samples were exposed to the laboratory air for only two minutes. Other investigators have also questioned[4] this assignment of the 3400–3500 cm.$^{-1}$ frequency to the diphosphonates, and it can be concluded that McConnell and Coover probably observed the hydroxyl frequency of water absorbed by their hygroscopic rearrangement products. The infrared data are summarized in Table II.

TABLE II

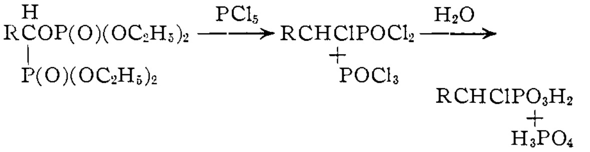
INFRARED ABSORPTION, CM.$^{-1}$

$RCH[P(O)(OC_2H_5)_2]$ $[OP(O)(C_2H_5)_2]$ R =	OH	P=O	P–O–C_2H_5
CH_3	Absent	1265	1163
CH_3[a]	3400(strong)	1265	1163
C_6H_5	Absent	1270	1170
C_6H_5[a]	3450(strong)	1270	1170
$RC(OH)$ $[P(O)(OC_2H_5)_2]_2$			
CH_3	3180(strong)	1260	1163

[a] 2-min. air exposure of the sample on the sodium chloride disk was permitted before the spectrum was taken.

Cade[2] cited molar refractivities as the only evidence for a P–C(OH)–P structure. However, he did not compare his experimental values with those calculated for the P–C–O–P isomer. The calculated values for the two isomers are not greatly different, and a careful comparison of the molar refractivities of both isomers is needed for a convincing structure proof.

Chemical Evidence.—Diethyl 1-(diethoxyphosphinyl)-ethyl phosphate was chlorinated with phosphorus pentachloride and hydrolyzed. The P^{31} n.m.r. spectrum showed 1-chloroethylphosphonic acid and orthophosphoric acid, as would be expected from the reactions



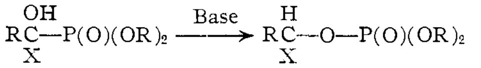
$$\underset{P(O)(OC_2H_5)_2}{\overset{H}{RCOP(O)(OC_2H_5)_2}} \xrightarrow{PCl_5} \underset{POCl_3}{\underset{+}{RCHClPOCl_2}} \xrightarrow{H_2O} \underset{H_3PO_4}{\underset{+}{RCHClPO_3H_2}}$$

The phosphoric acid came partly from the excess phosphorus pentachloride, of course. Such treatment of the diphosphonate would be expected to produce 1-chloroethylidenediphosphonic acid.

Conditions for Rearrangement.—A sample of molten tetraethyl 1-hydroxyethylidenediphosphonate was heated at 123–125° for 10 min. without change in its P^{31} n.m.r. spectrum. However, after a trace of sodium ethoxide in ethanol was added, the same treatment caused complete rearrangement, as shown by equal n.m.r. peaks at -20.2 and $+1.3$ p.p.m.

Rearrangement was also observed in the same system under actual synthesis conditions. A reaction mixture held at 50° showed gradually decreasing P^{31} n.m.r. peaks from the starting materials and gradually increasing peaks from the diphosphonate and a little of the rearrangement product. Distillation gave starting materials and the rearrangement product.

Reaction of 1-Hydroxyalkylphosphonates with Base.—The reaction



$$\underset{X}{\overset{OH}{RC}}\text{—}P(O)(OR)_2 \xrightarrow{Base} \underset{X}{\overset{H}{RC}}\text{—}O\text{—}P(O)(OR)_2 \qquad (3)$$

has been observed earlier for X = $C(O)CH_3$,[5] CN[6] and, in this paper, for X = $P(O)(OR)_2$.

When the rearrangement of the diphosphonate is written in the form of eq. 3, it can be recognized as an example of the third possibility in the reaction scheme proposed by Bengelsdorf[7] for dialkyl 1-hydroxyalkylphosphonates. The other possibilities are cleavage into aldehyde plus phosphite, or HX plus olefinic phosphate.

Bengelsdorf's rules apply to neutral esters of 1-hydroxyalkylphosphonates, but not to the ionized salts which are stable toward base. For example, 1-hydroxydecylphosphonic acid was not degraded in hot 6 *N* NaOH, but the corresponding diethyl ester was completely decomposed into phosphite and condensed aldehyde under those conditions. The ionized form presumably is stabilized by the spreading of the phosphoryl π-bond over the three unshared oxygen atoms. Related stabilization of ionized forms is found in the rapid hydrolysis of branching phosphate groups to ionized groups in condensed phosphate salts (the antibranching rule[8]), and in the basic hydrolysis of trialkyl to dialkyl phosphates[9] and dialkyl to monoalkyl alkylphosphonates.[10]

Experimental

The P^{31} spectra were taken on a Varian high resolution spectrometer with model V-4311 fixed frequency r.f. unit operating at 24.3 megacycles/sec. Eighty-five per cent. orthophosphoric acid was used as the reference standard in reporting chemical shifts.[3] The double resonance proton spectra were observed at 40 megacycles/sec. with a V-4310 r.f. unit while decoupling phosphorus at 16.2 megacycles/sec. with an auxiliary Varian n.m.r. spin decoupler. The other proton spectra were taken on a Varian A-60 n.m.r. spectrometer. Infrared spectra were taken on a Beckman IR-4 spectrometer. The diethyl phosphonate and triethyl phosphite were commercial products and were fractionally distilled before use.

Tetraethyl 1-Hydroxyethylidenediphosphonate.—A mixture of 30.0 g. (0.167 mole) of diethyl acetylphosphonate[2] (P^{31} n.m.r.: + 3.0 p.p.m.) and 23.0 g. (0.167 mole) of diethyl phosphonate (P^{31} n.m.r.: doublet at -21.4 and $+$ 6.5 p.p.m.) was treated with a drop of sodium ethoxide in ethanol. The temperature rose spontaneously to 72°, and the liquid became yellow. N.m.r. showed a large peak at -19.8 p.p.m., small peaks from the reactants and a trace of phosphate ester at *ca.* 0 p.p.m. Cooling overnight at *ca.* 0° gave a crop of white crystals which were filtered in the cold through a pre-cooled sintered-glass filter, removing the coloration. Upon warming to room temperature, the crystals began to liquefy due to their hygroscopicity, and they were filtered again and dried by evacuation over P_4O_{10}. Further handling was performed in a dry-box. Calcd. for $C_{10}H_{24}P_2O_7$: C, 37.74; H, 7.60; P, 19.47. Found: C, 37.94; H, 7.90; P, 19.3; m.p., 38.0–38.9°, reversible; n.m.r. of aqueous solution: -20.8 p.p.m. The same n.m.r. sample was treated with concd. HCl and heated at 100° for 2 hr.;

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(5) V. A. Kukhtin, V. S. Abramov and K. M. Orekhova, *Proc. Acad. Sci. U.S.S.R.*, **128**, 903 (1959); English translation.

(6) L. A. R. Hall and C. W. Stephens, *J. Am. Chem. Soc.*, **78**, 2565 (1956), and L. A. R. Hall, C. W. Stephens and J. J. Drysdale, *ibid.*, **79**, 1768 (1957).

(7) I. S. Bengelsdorf, *J. Org. Chem.*, **21**, 475 (1956), and M. S. Kharasch, R. A. Mosher and I. S. Bengelsdorf, *ibid.*, **25**, 1000 (1950).

(8) J. R. Van Wazer, "Phosphorus and Its Compounds," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1958, pp. 437–441.

(9) Reference 8, pp. 586–590.

(10) R. Rabinowitz *J. Am. Chem. Soc.*, **82**, 4564 (1960).

n.m.r. of the resulting ethylidenediphosphonic acid solution showed a quartet centered at −19.8 p.p.m. with coupling constant *ca.* 17 c.p.s.

Diethyl 1-(Diethoxyphosphinyl)-ethyl Phosphate.—(a) A reaction mixture identical to the above was held at 50° (by initial cooling) for 30 hr. Periodic n.m.r. spectra showed a gradual decrease in area of the reactant peaks and growth of the diphosphonate peak along with a small phosphate peak from the rearrangement product. The phosphonate peak of the rearrangement product was hidden in the large diphosphonate peak. Distillation gave reactants in the forerun, an intermediate fraction (8.1 g., 130° (0.07 mm.)) containing rearrangement product with some diethyl phosphonate, and a fraction (2.3 g., 137° (0.08)) containing nearly pure rearrangement product (−19.9 and +1.9 p.p.m.). All fractions contained a little phosphate ester at *ca.* +1 p.p.m. (b) A mixture of 648 g. (3.6 moles) of diethyl acetylphosphonate and 600 g. (4.4 moles) of diethyl phosphonate was treated with sodium ethoxide catalyst. The temperature rose to 65° and was held at 105° for 4 hr. Distillation gave 260 g. (24%) of rearrangement product having equal n.m.r. peaks at −21.1 and +1.7 p.p.m.; b.p. 130–136° (0.1 mm.) mostly 132°; $n^{25}{}_{D}$ 1.4275. Comparable values for supposed diphosphonate[1,2]: b.p. 140–150° (0.07 mm.) and 125° (0.06 mm.); $n^{20}{}_{D}$ 1.4350. Calcd. for $C_{10}H_{24}P_2O_7$: C, 37.74; H, 7.60; P, 19.47. Found: C, 37.24; H, 7.65; P, 18.28.

Diethyl 1-(Diethoxyphosphinyl)-benzyl Phosphate.—A mixture of 242 g. (1 mole) of diethyl benzoylphosphonate and 138 g. (1 mole) of diethyl phosphonate was treated as in part b above. Distillation gave 210 g. (55%) of rearrangement product having equal n.m.r. peaks at −16.2 and +1.4 p.p.m. with impurity at −17.3 p.p.m.; b.p. 171–174° (0.1 mm.), $n^{25}{}_{D}$ 1.4776. Comparable values for supposed diphosphonate[2]: b.p. 149° (0.07 mm.), $n^{25}{}_{D}$ 1.4798. Calcd. for $C_{15}H_{26}P_2O_7$: C, 47.37; H, 6.90; P, 16.29. Found: C, 45.46; H, 6.82; P, 16.15. Five attempts to prepare the diphosphonate in this system showed that rearrangement is rapid at the lowest usable reaction temperatures (about 50°) and slow at room temperature; that repeated additions of ethoxide catalyst are necessary because of its reaction with the benzoylphosphonate (demonstrated independently); and that distillation *increases* the amount of impurity at −17 p.p.m. Therefore, the H^1 n.m.r. spectrum discussed in the text was run on an undistilled reaction product containing a little diethyl phosphonate, but no other impurities visible in P^{31} n.m.r.

Chlorination of Diethyl 1-(Diethylphosphinyl)-ethyl Phosphate.—This phosphate was heated with an excess of PCl_5 in CCl_4 and hydrolyzed. The hydrolysate showed 1-chloroethylphosphonic acid (−20.1 p.p.m.) and H_3PO_4 (0 p.p.m.).

Reactions of 1-Hydroxydecylphosphonic Acid and Its Ester with Base.—Diethyl 1-hydroxydecylphosphonate (m.p. 46°, from hexane; n.m.r., −25.5 p.p.m.) was prepared by the ethoxide-catalyzed addition of diethyl phosphonate to an equimolar amount of freshly distilled decylaldehyde. A mixture of 2.1 g. of this ester with 19 g. of 6 *N* NaOH was heated at 97° for 1 hr. On cooling, a yellow semi-solid upper layer of condensed aldehyde formed, and the lower layer showed only the sodium phosphite doublet at −21.3 and + 13.6 p.p.m.

A portion of the ester was hydrolyzed in concd. HCl and purified by water and hexane washes. Calcd. for $C_{10}H_{24}PO_4$: C, 50.41; H, 9.73; P, 13.00; neut. equiv., 238. Found: C, 50.08; H, 9.53; P, 13.15; neut. equiv., 234 g./equiv. N.m.r.: −23.0 p.p.m. in ethanol; m.p. 155° with decomposition.

A mixture of 3.0 g. of the acid and 26 g. of 6 *N* NaOH was heated at 97° for 19 hr. No phase separation occurred on cooling, and the free acid was precipitated with HCl, filtered and dried; recovery: 2.9 g. (97%), identified by m.p. and mixed m.p.

Acknowledgments.—The authors wish to thank Mr. J. T. Yoder for some of the n.m.r. spectra, Mr. D. Bisno for part of the synthetic work, Mr. G. F. Brautigam for some of infrared spectra, and Drs. C. F. Callis, R. R. Irani and M. M. Crutchfield for helpful discussions. This work was supported in part by the Air Research and Development Command, United States Air Force, under Contract AF 33(616)-6950 monitored by the Materials Laboratory, Wright Air Development Center, Wright-Patterson Air Force Base, Ohio.

[CONTRIBUTION FROM THE FACULTY OF PHARMACEUTICAL SCIENCES, THE UNIVERSITY OF TOKYO, TOKYO, JAPAN]

Organic Phosphates. XVII.[1] Syntheses of Nucleotides by Condensation of Phosphorylated Sugar and Bases

BY TYUNOSIN UKITA AND HIKOYA HAYATSU

RECEIVED SEPTEMBER 23, 1961

Crystalline 2,3,4-tri-*O*-acetyl-6-di-*p*-nitrophenylphosphoryl- (VIII) and 2,3,4-tri-*O*-acetyl-6-diphenylphosphoryl-α-D-glucopyranosyl bromides (IX) were obtained. On condensation of these bromides with dithyminylmercury, VIII afforded an *O*-glucoside which contained two glucosyl residues attached on one thyminyl residue, while the similar condensation of IX with dithyminyl- or *N*-acetylcytosine-mercury gave the respective *N*-glucosides, 1-(2′,3′,4′-tri-*O*-acetyl-6′-diphenylphosphoryl-β-D-glucopyranosyl)-thymine and 1-(2′,3′,4′-tri-*O*-acetyl-6′-diphenylphosphoryl-β-D-glucopyranosyl)-4-acetamido-2(1H)-pyrimidinone. The former product was converted to 1-β-D-glucopyranosylthymine-6′ phosphate by catalytic hydrogenation and subsequent deacetylation. The 2,3-di-*O*-benzoyl-5-diphenylphosphoryl-D-ribofuranosyl bromide was condensed with dithyminylmercury (A) as well as with chloromercuri-6-benzamidopurine (B). The product obtained from A, 1-(2′,3′-di-*O*-benzoyl-5′-diphenylphosphoryl-β-D-ribofuranosyl)-thymine, was converted to 1-β-D-ribofuranosylthymine-5′ phosphate after removal of phenyl groups by catalytic hydrogenation and subsequent deacylation. The condensation product of B, 6 benzamido-9-(2′,3′-di-*O*-benzoyl-5′-diphenylphosphoryl-β-D-ribofuranosyl)-purine, gave adenosine-5′ phosphate on its successive treatment with 0.5 *N* sodium hydroxide and methanolic sodium methoxide to remove one phenyl and three benzoyl groups and subsequent removal of a phenyl group attached at phosphoryl residue with phosphodiesterase from Russel's viper.

Recent progress in nucleotide chemistry has included the total syntheses of several naturally occurring as well as some unnatural nucleotides. These syntheses involve, as general procedures, the phosphorylation of nucleosides having suitably protected sugar moieties and thus require prior syntheses of the nucleosides.[2]

However, when the synthesis of a desired nucleoside requires numerous steps[3,4] or proceeds in

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(1) Part XVI of this series: T. Ukita and R. Takeshita, *Chem. Pharm. Bull.* (*Tokyo*), **9**, 606 (1961).

(2) (a) J. Baddiley in "The Nucleic Acids," Vol. I, E. Chargaff and J. N. Davidson, Editors, Academic Press, Inc., New York, N. Y., 1955, p. 137. (b) A. R. Todd in "Methods in Enzymology," Vol. III, S. P. Colowick and N. O. Kaplan, Editors, Academic Press, Inc., New York, N. Y., 1957, p. 811. (c) F. Cramer, *Angew. Chem.*, **72**, 236 (1960); (d) H. G. Khorana, *Federation Proc.*, **19**, 931 (1960); (e) J. Davoll and B. A. Lowy, *J. Am. Chem. Soc.*, **73**, 1650 (1951); (f) J. J. Fox and I. Wempen, *Adv. in Carbohydrate Chem.*, **14**, 283 (1959)