dodecyltrimethylphosphonium hydroxide with 1.0025 *N* hydrochloric acid gave a value of 0.26 *N*. Subsequent titration curves did not change even after refluxing 40 hr. Evaporation of a small sample led to decomposition to dimethyldodecylphosphine oxide.

Dodecyltrimethylphosphonium Methoxide.—A solution of 28 g of dodecyltrimethylphosphonium chloride (0.1 mole) in 40 ml of anhydrous methanol was added dropwise to a freshly prepared solution of potassium methoxide (0.1 mole) in 100 ml of methanol under argon. After stirring for 1 hr the potassium chloride was filtered under argon and the methanol was removed under vacuum overnight. The viscous liquid gave an infrared spectrum with a medium P^+CH_3 band at 7.73, a strong CH_3O band at 9.49, and a medium strong band at 10.2 μ characteristic of other dodecyltrimethylphosphonium compounds. The P^{31} nmr spectrum showed a singlet at −27.5 ppm relative to 85% phosphoric acid, characteristic of dodecyltrimethylphosphonium compounds. The proton nmr spectrum suggested the presence of about 3:1 ratio of methanol to dodecyltrimethylphosphonium methoxide. Care was required to prevent exposure to atmospheric moisture because hydrolysis and subsequent decomposition are rapid. Under a dry, inert atmosphere the dodecyltrimethylphosphonium methoxide showed little decomposition up to 160–170°. At this point, methane and dimethyl ether[20] (identified by their infrared spectra) were evolved. Upon heating to 200°, about 1.8 l. of gas was collected. Distillation gave 3.9 g of methanol, bp 67°, containing a trace of trimethylphosphine. Addition of excess methyl iodide and evaporation gave 0.4 g of tetramethylphosphonium iodide, mp >400°. The infrared spectrum was identical with that of an authentic sample of tetramethylphosphonium iodide prepared from trimethylphosphine and methyl iodide. Distillation of the remainder of the product under reduced pressure gave a 62% yield of slightly impure dimethyldodecylphosphine oxide, mp 78–81. The melting point was raised to 83–84° after recrystallization from hexane.

Registry No.—**1** and **2**, 7641-69-2; **3** and **4**, 7641-70-5; **5**, 2071-59-2; **6**, 7641-72-7; **7**, 7641-73-8; **8**, 7688-11-1.

Acknowledgments.—The authors wish to thank Dr. T. J. Logan and Dr. D. J. Peterson for their helpful discussions.

(20) Reference 17, Spectrum No. 1128.

A New Synthesis of Monoalkyl Phosphates

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Received March 8, 1966

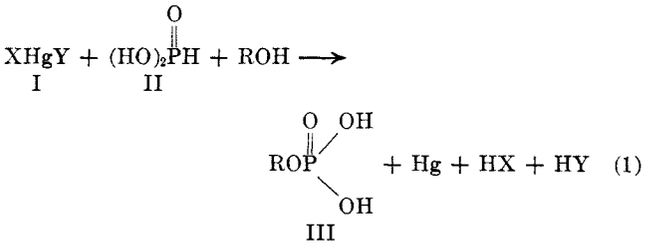
Various monoalkyl dihydrogen phosphates were prepared in good yields by the reaction of alcohols with inorganic phosphorous acid and mercury compounds in the presence of tertiary amines. The reaction can be explained by assuming an intermediate, metaphosphate, which reacts with alcohols to yield alkyl dihydrogen phosphates.

Various methods[1] have been reported for the phosphorylation of alcohols; however, there are few[2] which are well suited to the preparation of monoalkyl phosphates. One of the most simple and effective methods available is that of Kirby[3] in which the direct iodine oxidation of inorganic phosphorous acid in alcohols gives the corresponding monoalkyl phosphates in excellent yields, but this procedure is not applicable to most solid alcohols or those available in only small amounts, since the reaction has to be carried out in the presence of a large excess of alcohol.

It was found in our laboratory[4] that phosphorylation of simple alcohols by the use of monobenzyl phosphite or inorganic phosphorous acid and monobromocyanoacetamide gave the corresponding monoalkyl dihydrogen phosphates in good yields. However, when a slight excess of an alcohol was treated with either of these acids and monobromocyanoacetamide, the expected monoalkyl phosphates were always accompanied by small amounts of phosphoric acid and polyphosphoric acids which made the purification of the resulting phosphates more difficult.

The phosphorylation of alcohols was therefore investigated further by studying the use of some mercury compounds (I) as oxidizing reagents in the place of monobromocyanoacetamide in the above-mentioned experiment.

When mercuric acetate (I, X = Y = OAc) was brought into reaction with dry phosphorous acid (II) in refluxing ethanol, monoethyl phosphate (III, R = C_2H_5) was detected by paper chromatography together with orthophosphoric and unidentified polyphosphoric



$$\underset{\text{I}}{XHgY} + \underset{\text{II}}{(HO)_2\overset{\overset{O}{\|}}{P}H} + ROH \longrightarrow \underset{\text{III}}{ROP(O)(OH)_2} + Hg + HX + HY \quad (1)$$

acids. Among various compounds examined, mercuric chloride, acetate, and sulfate, and mercurous chloride were found to be effective for this type of reaction, while mercuric cyanide and dialkyl or diaryl mercury were ineffective. In view of these results, it might be said that mercuric compounds capable of releasing stable anions are effective for this reaction.

When mercuric chloride was treated with phosphorous acid in refluxing ethanol, a good deal of monoethyl phosphate and a small amount of unreacted phosphorous acid were detected by paper chromatography. On the other hand, when the reaction was carried out in the presence of more than 4 mole equiv of triethylamine, a quantitative yield of metallic mercury was deposited within a few minutes, and, in this case, chromatographically pure monoethyl dihydrogen phosphate (IV) was obtained as the bis(cyclo-

(1) D. M. Brown, "Advances in Organic Chemistry: Methods and Results," Vol. 3, Interscience Publishers, Inc., New York, N. Y., 1963, p 75.
(2) F. Cramer and G. Weimann, *Chem. Ber.*, **94**, 996 (1961).
(3) A. J. Kirby, *Chem. Ind.* (London), 1877 (1963).
(4) T. Obata, M. Ueki, and T. Mukaiyama, *Bull. Chem. Soc. Japan*, **39**, 1040 (1966).

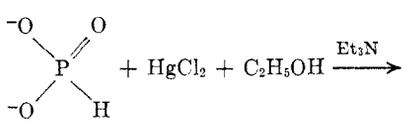
TABLE I

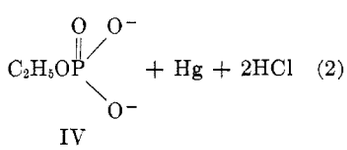
THE REACTION OF ALCOHOLS WITH PHOSPHOROUS ACID AND MERCURIC CHLORIDE IN THE PRESENCE OF TRIETHYLAMINE

Alcohol	Alkyl phosphate (anilinium salt)	Mp, °C	R_f value[a] A	R_f value[a] B	Anal., % C Calcd	C Found	H Calcd	H Found	N Calcd	N Found
CH_3OH	$C_7H_{12}NO_4P$	167–168	0.26	0.66	40.98	40.89	5.90	6.03	6.83	6.98
C_2H_5OH	$C_8H_{14}NO_4P$	164–166	0.37	0.70	43.84	44.00	6.49	6.63	6.39	6.59
$NCCH_2CH_2OH$	$C_9H_{13}N_2O_4P$	154–155	0.36	0.62	44.27	43.93	5.36	5.54	11.47	11.60
n-C_3H_7OH	$C_9H_{16}NO_4P$	137–139	0.45	0.73	46.35	46.69	6.92	7.19	6.01	6.12
i-C_3H_7OH	$C_9H_{16}NO_4P$	159–160	0.43	0.74	46.35	46.28	6.92	6.93	6.01	6.08
n-C_4H_9OH	$C_{10}H_{18}NO_4P$	138–140	0.54	0.77	48.58	48.49	7.34	7.52	5.66	5.61
i-C_4H_9OH	$C_{10}H_{18}NO_4P$	155–156	0.51	0.78	48.58	48.62	7.34	7.59	5.66	5.78
n-$C_5H_{11}OH$	$C_{11}H_{20}NO_4P$	135–137	0.63	0.72	50.56	50.62	7.72	7.62	5.36	5.57
i-$C_5H_{11}OH$	$C_{11}H_{20}NO_4P$	149–151	0.59	0.74	50.56	50.13	7.72	7.38	5.36	5.60
$C_6H_{11}OH$	$C_{12}H_{20}NO_4P$	168–169	0.56	0.78	52.74	52.42	7.38	7.45	5.13	5.11
$C_6H_5CH_2OH$	$C_{19}H_{18}N_2O_4P$	150–153	0.55	0.81	61.79	60.35	4.94	4.88	7.48	7.56
n-$C_8H_{17}OH$	$C_{14}H_{26}NO_4P$	129–130	0.74	0.89	55.43	54.68	8.64	8.47	4.62	4.77
Borneol	$C_{16}H_{26}NO_4P$	194–196	0.64		58.72	57.93	8.02	8.09	4.28	4.31

[a] Solvent systems: (A) *n*-propyl alcohol–concentrated NH_4OH–H_2O, 6:3:1; (B) *n*-butyl alcohol–CH_3CO_2H–H_2O, 5:2:3.

hexylammonium) salt[5] or what is more convenient to handle, as the monoanilinium salt in good yield. From the above results, it can be seen that tertiary amines play an important role in this type of reaction.





IV

In a similar manner, various alkyl phosphates were successfully synthesized from phosphorous acid and alcohols (see Table I).

The phosphate anilinium salts given in Table I were directly prepared by desalting the reaction mixtures with acidic ion-exchange resin, followed by treatment with aniline and recrystallization from ethanol. These salts have been found to be far easier to handle than the cyclohexylammonium salts, showing characteristic sharp melting points which differ widely for different substances.

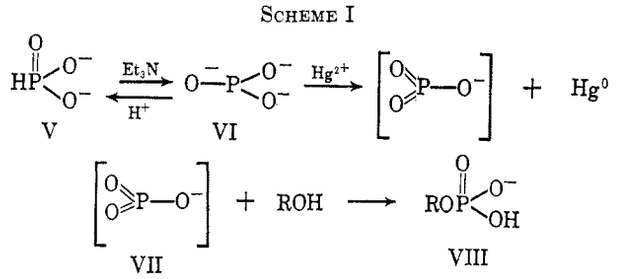
The mechanism of this reaction can be explained as shown in Scheme I.

In the presence of an excess of triethylamine, there can exist deprotonated phosphite ion (VI) in the reaction mixture. The ion can be oxidized readily by mercuric ion to metaphosphate ion (VII) to which an alcohol then adds to form a monoalkyl phosphate.

Two possible, alternative pathways for forming metaphosphate ion can be considered: one is through O-mercurated phosphonate (IX), and the other is through P-mercurated phosphonate (X), as shown in the Scheme II. However, it is difficult to state which

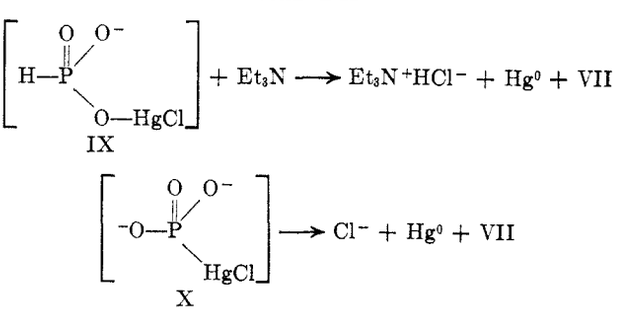
(5) Since the analytical carbon values of the resulting bis(cyclohexylammonium) salts of monoalkyl dihydrogen phosphates are lower by 2–4% than the calculated ones, it might be claimed that the isolated phosphates may be seriously contaminated by the other phosphate materials. Therefore, the purity of the substances was rechecked by testing whether or not the lower C values might result mainly from incomplete combustion. Combustion of the phosphates was tried at an elevated temperature (*ca.* 900°) in a platinum boat after coating the samples either with fine, powdered, dry tungsten trioxide or potassium dichromate. In both cases, the observed values of the carbon were less than the calculated ones. On the other hand, the conversion of cyclohexylammonium salts into anilinium salts was found to give satisfactory analytical results even at the combustion temperature of 750° (see Table I).

SCHEME I



intermediate is more plausible in this reaction, and therefore further investigation is needed. However,

SCHEME II



this metaphosphate (VII) could not be characterized by paper chromatography when mercuric chloride had been treated with phosphorous acid and triethylamine under a variety of conditions.

Next, a small excess of alcohols was treated with phosphorous acid and mercuric chloride in the presence of triethylamine. In these cases, monoalkyl phosphates, orthophosphoric acid, and unidentified polyphosphoric acids were formed so that the isolation of the expected phosphates became more difficult. However, it was found that the formation of by-products is minimized by employing acetonitrile as solvent and a slight excess of mercuric chloride in the above reaction; then, repeated recrystallization of the resulting phosphate anilinium salts or direct separation of by-products from the reaction mixture through a cellulose chromatographic column gave analytically pure samples in good yields. For example, benzyl and bornyl dihydrogen phosphates were successfully isolated as anilinium salts in 80 and 47% yields, respectively, after separation of by-products (mainly orthophosphoric acid) through Whatman Column Chromedia CF 11.

The effect of tertiary amines on this type of phosphorylation is illustrated as follows. When weak bases such as pyridine or 2,6-lutidine were used in the above experiment, the reaction proceeded slowly and the expected phosphates were obtained in low yields; on the other hand, strong bases such as hexamethylenetetramine and triethylenediamine were also found to be ineffective, because the preferential formation of stable mercury–amine complexes prevented the reaction.

In conclusion, all the common alcohols were easily phosphorylated in good yields by treating phosphorous acid with mercuric chloride and triethylamine in acetonitrile. Further, this procedure was proved to be applicable for the phosphorylation of alcohols available in only small amounts.

Experimental Section

Materials.—Phosphorous acid and mercury compounds were obtained from a commercial source. They were ground and dried over P_2O_5 *in vacuo* before use. Alcohols and solvents used were purified by the conventional procedures.

General Procedures for the Preparation of Monoalkyl Dihydrogen Phosphates. A. The Reaction of Mercuric Chloride with Phosphorous Acid and Alcohols.—Into a solution of mercuric chloride (2.72 g, 0.01 mole) and phosphorous acid (0.82 g, 0.01 mole) in dry alcohols (15 ml) was added excess triethylamine (5–6 ml) in one portion. The mixture was heated on a water bath at 80° for 15 min with vigorous stirring. After removal of metallic mercury (1.65–1.94 g, 82–96%) and triethylamine hydrochloride, the filtrate was concentrated and then acetone (10 ml) was added to remove residual ammonium salt (total yields amounted to more than 80%). The acetone solution was passed through an IR-200 ion-exchange column (25 × 1.8 cm) already prepared in water, and eluted with ethanol (50%). The eluates were concentrated, then ethanol (5 ml) and aniline (1.5 ml) were added. Recrystallization of the resulting anilinium salts from ethanol once or twice gave analytical samples. Crude yields amounted to 69–92%. Some of the mixture melting points were not depressed with authentic samples.[6] Both physical and analytical data are summarized in Table I.

(6) O. Mitsunobu, T. Obata, and T. Mukayama, *J. Org. Chem.*, **30**, 1071 (1965).

B. The Reaction of Mercurous Chloride with Phosphorous Acid and Alcohols.—To anhydrous solutions of mercurous chloride (4.78 g, 0.01 mole) and phosphorous acid (0.82 g, 0.01 mole) in alcohols (15 ml) was added triethylamine (6 ml) in one portion. The mixtures were heated at 80° and stirred constantly for an additional 30 min. After separation of mercury and ammonium salt, monoanilinium salts of the corresponding monoalkyl dihydrogen phosphates were obtained from those filtrates through the same procedure described in the above reaction.

Phosphorylation of Benzyl Alcohol and Borneol in Acetonitrile by the Reaction of Mercuric Chloride and Phosphorous Acid.—Into a clear solution of benzyl alcohol (1.4 g, 0.013 mole), phosphorous acid (0.82 g, 0.01 mole), and mercuric chloride (3.0 g, 0.011 mole) in dry acetonitrile (20 ml) was poured triethylamine (6 ml) in one portion, and the mixture was quickly warmed to 80°. After additional stirring for 30 min, the mixture was cooled. Precipitated metallic mercury (1.63 g, 82%) and triethylamine hydrochloride (1.18 g, 40%) were filtered out. The filtrate was evaporated under reduced pressure, and the oil was desalted through an IR-200 acidic ion-exchange resin column (25 × 1.8 cm) already prepared in 50% ethanol, followed by elution with the same solvent. The collected eluate (between 40 and 120-ml fractions) was concentrated, then the oil was chromatographed on a Whatman Column Chromedia CF 11 column (17 × 3 cm) which was prepared in water and then saturated with *n*-butyl alcohol. The first 40–90-ml fraction, eluted with *n*-butyl alcohol, contained free monobenzyl dihydrogen phosphate, which was characterized as its anilinium salt: mp 150–152°, 2.95 g (80%). *Anal.* Calcd for $C_{19}H_{23}N_2O_4P$: C, 61.79; H, 4.94; N, 7.48. Found: C, 60.36; H, 5.01; N, 7.50. The mixture melting point was not depressed with an authentic sample.

Similarly, bornyl dihydrogen phosphate was synthesized from 1.3 mole equiv of borneol, and it was isolated as the monoanilinium salt: mp 194–196°, 1.54 g (47%). *Anal.* Calcd for $C_{16}H_{26}NO_4P$: C, 58.72; H, 8.02; N, 4.28. Found: C, 57.94; H, 8.09; N, 4.31.

Registry No.—$C_{19}H_{23}N_2O_4P$, 7721-82-6; $C_{16}H_{26}NO_4P$, 7704-43-0; $C_7H_{12}NO_4P$, 7704-44-1; $C_8H_{14}NO_4P$, 2180-42-9; $C_9H_{13}N_2O_4P$, 7704-46-3; $C_9H_{16}NO_4P$ (mp 137–139), 2180-41-8; $C_9H_{16}NO_4P$ (mp 159–160), 1992-41-2; $C_{10}H_{18}NO_4P$ (mp 138–140), 1992-40-1; $C_{10}H_{18}NO_4P$ (mp 155–156), 7704-50-9; $C_{11}H_{20}NO_4P$ (mp 135–137), 7704-51-0; $C_{11}H_{20}NO_4P$ (mp 149–151), 7704-52-1; $C_{12}H_{20}NO_4P$, 7704-53-2; $C_{14}H_{26}NO_4P$, 7704-54-3.

Synthesis of D-*erythro*-Pentulose 1-Phosphate (D-Ribulose 1-Phosphate)

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Received November 8, 1966

The chemical synthesis of D-*erythro*-pentulose 1-phosphate (D-ribulose 1-phosphate) has been accomplished by the phosphorylation of 3,4,5-tri-*O*-benzoyl-D-*erythro*-pentulose dimethyl acetal, followed by the appropriate removal of the blocking groups. The pentulose acetal was prepared from the known 3,4,5-tri-*O*-benzoyl-1-deoxy-1-diazo-D-*erythro*-pentulose by hydrolysis to 3,4,5-tri-*O*-benzoyl-D-*erythro*-pentulose which was acetalated with trimethyl orthoformate.

The synthesis of phosphate esters of sugars has, since the early experiments of Fischer and Baer,[1] been a subject to challenge the imagination and ingenuity of chemists and biochemists. Many successful syntheses are recorded, but few general methods are known, particularly for the preparation of esters of reducing sugars with three, four, and five carbon atoms.

One method of rather wide applicability, developed mainly in this laboratory, makes use of the acyclic acetal derivatives of reducing sugars.[2] This approach eliminates interference from the oxane ring of the sugar, freeing all hydroxyl groups for reaction. In addition, the acetal structure stabilizes the final product against the decomposition characteristic of carbonyl phosphate esters, and, being sensitive to acid hydrolysis, permits the ready conversion of the derivative to the free sugar phosphate, as desired.

The success of this approach is attested by published syntheses of glycolaldehyde phosphate,[3] D-glyceralde-

(1) H. O. L. Fischer and E. Baer, *Ber.*, **65**, 337, 1040 (1932).

(2) C. E. Ballou and D. L. MacDonald, "Methods in Carbohydrate Chemistry," Vol. 2, R. L. Whistler and M. L. Wolfrom, Ed., Academic Press Inc., New York, N. Y., 1963, p 270.

(3) C. E. Ballou, *Arch. Biochem. Biophys.*, **78**, 328 (1958).