Anal. Calcd. for $C_{27}H_{51}O_6N$: C, 66.76; H, 10.58; N, 2.88. Found: C, 67.13; H, 10.68; N, 2.78.

α,γ-Dihydroxy-β,β-dimethylbutyramide (Pantamide).—The synthesis of the pantamide was carried out by two different methods.

(A).—Ten grams of pantolactone was dissolved in 50 ml. of absolute methyl alcohol. This solution was saturated with dry ammonia, and was set aside for 48 hours. At the end of this period, the solvent was removed under vacuum, and the residue recrystallized from ethyl acetate; yield 8.5 g. (74.5%); m.p. 129.0–130.0°. *Anal.* Calcd. for $C_6H_{13}O_3N$: N, 9.51. Found: N, 9.30.

(B).—Ten grams of pantolactone was dissolved in 10 ml. of water and was added to 10 ml. of concentrated ammonium hydroxide solution. Such mixtures were allowed to stand for two hours, for 24 hours or were refluxed for 8 hours. The water was then removed under diminished pressure. The residue was recrystallized from 95% ethyl alcohol, ethyl acetate or a methyl alcohol–ethyl acetate mixture; yield (example) 7.3 g. (64.5%); m.p. 129.0–130.0°. No depression in m.p. was observed when mixed with the pantamide prepared by the preceding procedures.

Anal. Calcd. for $C_6H_{15}O_4N$: C, 43.62; H, 9.15; N, 8.48. Calcd. for $C_6H_{13}O_3N$: C, 48.97; H, 8.90; N, 9.51. Found: C, 49.17; H, 8.73; N, 9.38.

Approximately 166 mg. (one millimole as pantoic acid ammonium salt) of each preparation was accurately weighed and dissolved in 15 ml. of neutral 95% ethyl alcohol. This solution was further diluted with 20-ml. portion of absolute ethyl ether, and titrated with 0.1 *N* alcoholic potassium hydroxide solution with phenolphthalein. One hundred sixty six mg. was the amount of ammonium pantoate theoretically equivalent to 10 ml. of 0.1 *N* alkali solution. Both of these compounds prepared under (A) and (B), however, did not require a single drop of the alkali solution before it showed an alkalinity to phenolphthalein. Under the same conditions, one millimole of pure ammonium palmitate consumed the theoretical amount of the standard alkali solution. Thus the compounds must have been pantamide.

α,γ-Dipalmitoxy-β,β-dimethylbutyramide (Dipalmitoxypantamide).—One and a half grams (0.01 mole) of pantamide was acylated with 5.5 g. (0.02 mole) of palmitoyl chloride in a mixture of pyridine–chloroform. The reaction product was extracted with chloroform, and washed with 0.5 *N* hydrochloric acid, water, 5% sodium carbonate solution and with water until neutral. After the extract had been dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure. The residue was recrystallized from petroleum ether (b.p. 34–38°) and from 95% ethyl alcohol; yield 4.8 g. (77.0%); m.p. 74.0–75.0°; very fluffy amorphous powder. *Anal.* Calcd. for $C_{38}H_{73}O_5N$: C, 73.02; H, 11.77; N, 2.24. Found: C, 72.92; H, 11.77; N, 2.24.

α,γ-Dipalmitoxy-β,β-dimethylbutyric Acid (Dipalmitoxypantoic Acid).—Two grams of dipalmitoxypantamide was dissolved in 20 ml. of glacial acetic acid, and treated with 10 ml. of freshly prepared isoamyl nitrite.[15] The mixture was then placed on a steam-bath, and refluxed gently for two hours. The solvent was removed almost completely under vacuum, and the residue recrystallized from petroleum ether (b.p. 34–38°) in the refrigerator; yield 1.1 g. (55.0%); m.p. 62.0–63.0°. Calcd. for $C_{38}H_{72}O_6$: neut. equiv., 625. Found: neut. equiv., 627.

N-[α,γ-Dipalmitoxy-β,β-dimethylbutyryl]-3-amino-*n*-propyl Palmitate (Dipalmitoxypantothenyl Palmitate).—Two grams of *d*-pantothenyl alcohol (Nutritional Biochemical Corporation), was added to 30 ml. of chloroform containing 9 g. of palmitoyl chloride. To this mixture, 10 ml. of dry pyridine was added slowly with vigorous shaking at room temperature. As the reaction proceeded, the insoluble pantothenol went into the solution gradually and finally a clear reaction mixture was obtained, which was then set aside for 12 hours. The reaction product was extracted with chloroform and washed with water, 0.5 *N* hydrochloric acid, 5% potassium carbonate solution, and again with water successively. After drying the extract with anhydrous sodium sulfate, the solvent was removed and the residue recrystallized from 95% ethyl alcohol; yield 5.6 g. (60.9%); m.p. 49.0–53.0°; $[\alpha]^{34}D$ +9.5 (*c* 4.22%, in chloroform). *Anal.* Calcd. for $C_{57}H_{109}O_7N$: C, 74.37; H, 11.94; N, 1.52. Found: C, 74.59; H, 11.78; N, 1.56.

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URBANA, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF FOOD TECHNOLOGY, UNIVERSITY OF ILLINOIS]

The Synthesis of Long Chain Fatty Acid Derivatives of the Vitamin B_6 Group[1,2]

BY TAKETAMI SAKURAGI AND FRED A. KUMMEROW

RECEIVED AUGUST 16, 1955

The following long chain fatty acid derivatives of the vitamin B_6 group have been prepared: pyridoxine tripalmitate, pyridoxine trilinoleate, pyridoxine trioctanoate, pyridoxine tridecanoate, pyridoxal dipalmitate, pyridoxamine tripalmitate, pyridoxine 3,5-dipalmitate, pyridoxal 3-palmitate, pyridoxine 5-palmitate and 4-desoxypyridoxine dipalmitate. The ultraviolet spectra of these derivatives were essentially the same, having one maximum absorption peak in the neighborhood of 265–270 mμ or at 283 mμ (pyridoxine 5-palmitate) in diethyl ether as a solvent.

Since 1938, several workers have synthesized pyridoxine triacetate[3–8] and the tribenzoate.[3,6] Selective acetylation of pyridoxine also made it possible to prepare the diacetate of the vitamin.[5,9]

Three patent descriptions[6–8] deal with the preparation of the fat-soluble derivatives by acylating with short chain fatty acids, such as acetic and propionic acids. The esters of long chain fatty acids, however, have as yet not been prepared. The present paper describes the preparation of several long chain fatty acid derivatives of the vitamin B_6 group. These derivatives were biologically active as a source of vitamin B_6 for rats.[10]

The fully acylated compounds of the vitamin B_6 group, which are listed in Table I, have been prepared by treating the corresponding vitamin hydrochloride with the respective fatty acid chlorides in pyridine. Of these derivatives, pyridoxine trioctanoate (I) and pyridoxine trilinoleate (I) were liquid at room temperature; the latter compound solidified at −18 to −19°. Others were obtained as

(1) This work was supported by research grant No. A-257 from the National Institute of Health, U. S. Public Health Service, Department of Health, Education and Welfare.

(2) Portion of a thesis presented by T. Sakuragi as partial fulfillment of the requirement for the degree of Doctor of Philosophy in Food Technology.

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(5) S. A. Harris, THIS JOURNAL, **62**, 3203 (1940).

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(7) S. A. Harris and E. T. Stiller, U. S. Patent 2,349,267, May 23, 1944.

(8) J. C. Keresztesy and J. R. Stevens, U. S. Patent 2,412,272, Dec. 10, 1946.

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(10) T. Sakuragi and F. A. Kummerow, in press.

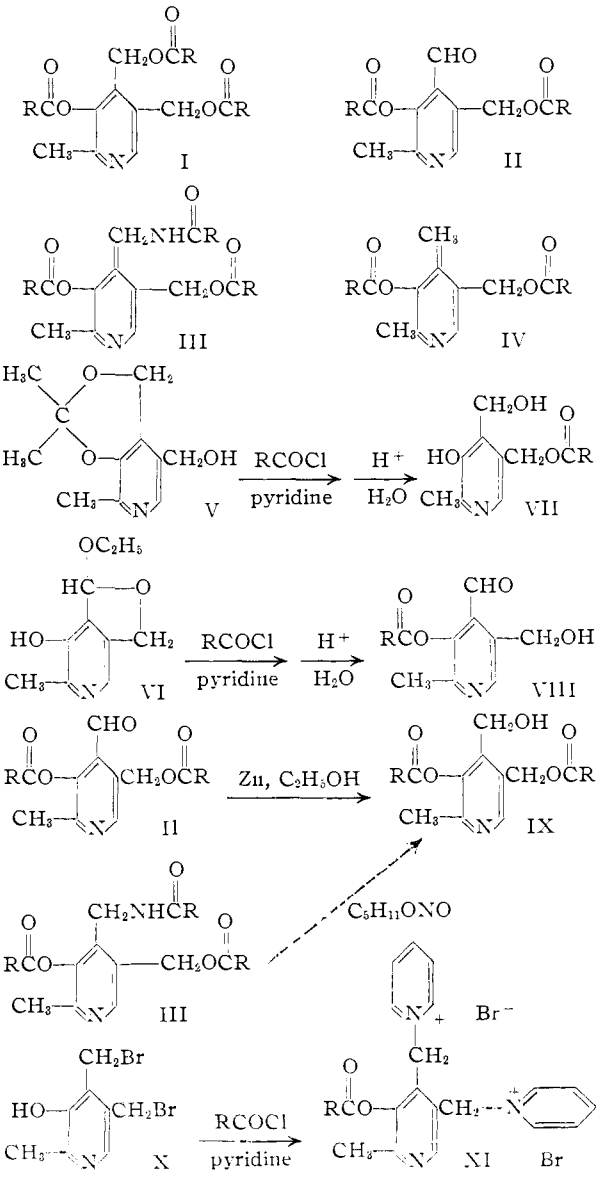
TABLE I

Acylated derivatives of vitamin B_6	Yield, %	M.p., °C.	UV spectra[a] Max, mμ	$E_{1m} \times 10^{-3}$	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
Pyridoxine tripalmitate[b,e] (I)	71.4	72.0–74.0	272	3.9	$C_{56}H_{101}O_6N$	76.04	76.15	11.51	11.32	1.58	1.59
Pyridoxine trilinoleate[c,f] (I)	65.2	Liquid	271	3.2	$C_{62}H_{101}O_6N$	77.85	77.85	10.64	10.75	1.46	1.47
Pyridoxine trioctanoate[g] (I)	..	Liquid	271	..	$C_{32}H_{53}O_6N$	70.16	70.15	9.75	10.00	2.74	2.66
Pyridoxine tridecanoate[h] (I)	..	47.5–48.5	271	..	$C_{38}H_{65}O_6N$	72.22	72.28	10.37	10.23	2.21	2.35
Pyridoxal dipalmitate[d,i] (II)	77.7	74.0	267	3.6	$C_{40}H_{69}O_5N$	74.60	74.84	10.80	10.93	2.19	2.40
Pyridoxamine tripalmitate[d,i] (III)	53.1	102.0–103.0	..	..	$C_{56}H_{102}O_5N_2$	76.22	75.70	11.64	11.37	3.17	3.17
4-Desoxypyridoxine dipalmitate[d,i] (IV)	95.9	59.5–61.0	264	3.2	$C_{40}H_{71}O_4N$	76.26	76.42	11.36	11.06	2.23	2.22

[a] Beckman DU spectrophotometer in 1-cm. silica cuvettes. Diethyl ether was used as a solvent. [b] We are indebted to Dr. G. E. Boxer, Merck and Co., Inc., for a supply of pyridoxine hydrochloride. [c] The linoleoyl chloride which was used for the synthesis of pyridoxine trilinoleate was prepared from oxalyl chloride and pure linoleic acid (T. R. Wood, F. L. Jackson, A. R. Baldwin and H. E. Longenecker, THIS JOURNAL, 66, 287 (1944)). The latter was isolated from corn oil as the tetrabromostearic acid by Rollet's method (A. Rollet, *Z. physiol. Chem.*, 62, 422 (1909)). [d] Pyridoxal·HCl, pyridoxamine·2HCl, and 4-desoxypyridoxine·HCl obtained from the Nutritional Biochemicals Corporation. [e] Recrystallized from 2-propanol. [f] The pyridoxine trilinoleate was purified as follows: approximately 3 g. of crude pyridoxine trilinoleate was dissolved in 500 ml. of hot ethyl alcohol, and cooled until the trilinoleate separated out as fine droplets. The mixture was centrifuged and the bottom layer collected. This purification was repeated twice, and the trace of the solvent was removed under high vacuum at room temperature overnight. [g] Recrystallized from abs. methanol at −20°. [h] Recrystallized from abs. methanol. [i] Recrystallized from abs. ethanol.

amorphous fatty powders, or flaky crystals. Pyridoxamine tripalmitate (III) was soluble in chloroform, but was insoluble in diethyl ether. Pyridoxine triacetate[6] and pyridoxine tripropionate[6] formed the hydrochlorides, whereas any compounds prepared in the present study did not appear to form salts except the intermediate compound, isopropylidene pyridoxine 5-palmitate and pyridoxal 3-palmitate (VIII). They were isolated as the hydrochloride and the hydrobromide, respectively.

Selective esterification of the vitamin by means of isopropylidenepyridoxine (V),[11,12] or the monoethylacetal of pyridoxal (VI)[13] had been attempted by some workers. The intermediates were involved in the synthesis of codecarboxylase or pyridoxal 5-phosphate. Pyridoxal 3-palmitate (VIII) was similarly prepared by esterifying the monoethylacetal of pyridoxal (VI) with palmitoyl chloride followed by acid hydrolysis. The 3-palmitate of pyridoxal (VIII) was then treated with zinc in alcohol. The amount used and obtained was too small to prepare pyridoxine 3-palmitate in the pure state. This reduction was confirmed by the conversion of pyridoxal to pyridoxine by refluxing in 95% ethyl alcohol for two hours in the presence of zinc powder in a good yield. The latter transformation has been carried out previously by a catalytic reduction,[9] though the yield was low. An attempt was also made to prepare pyridoxine 3-palmitate through a different pathway; pyridoxine was first converted to the dibromo compound X (2-methyl-3-hydroxy-4,5-dibromomethylpyridine), which was then treated with palmitoyl chloride in pyridine. Subsequent treatment of the reaction product with a silver salt seemed to be applicable to regenerate the two hydroxyl groups at 4- and 5-positions. The bromide, however, was reactive enough to form a pyridinium salt under the conditions applied and the compound obtained was not 2-methyl-3-palmitoxy-4,5-dibromomethylpyridine, but was 2,4,5-trimethyl-3-palmitoxy-4α,5α-bis-[pyridinium bromide] (XI). As was expected from the structure,



(11) J. Baddiley and A. P. Methias, *J. Chem. Soc.*, 2583 (1952).
(12) A. Cohen and E. G. Hughes, *ibid.*, 4384 (1952).
(13) P. Karrer and M. Viscontini, *Helv. Chim. Acta*, **30**, 52 (1947).

this compound was completely soluble in water as a cation active agent, and the solution showed surface activity.

Baddiley and Methias[11] met with difficulty when they attempted to esterify isopropylidenepyridoxine (V) through the 5-hydroxymethyl group which remained free. Their attempts to phosphorylate the isopropylidene derivative with phosphoryl chloride and with diphenyl chlorophosphonate were unsuccessful. They were also unable to esterify with *p*-toluenesulfonyl chloride, although the *p*-nitrobenzoate was formed very readily. In the present work, isopropylidenepyridoxine (V) was synthesized by treating pyridoxine hydrochloride with acetone which contained sulfuric acid as a catalyst, as reported by Cohen, *et al.*[12] It was of interest to note that the reaction was not catalyzed by dry hydrogen chloride, at least at room temperature. In the present experiment, the palmitoylation of isopropylidenepyridoxine (V) with palmitoyl chloride in a mixture of chloroform–pyridine was successful. Subsequent hydrolysis of the resultant compound gave pyridoxine 5-palmitate (VII). This hydrolysis was catalyzed by a trace of hydrogen ion in contrast to that of the monoethylacetal of 3-palmitoxypyridoxal, which required a higher level of the acid catalyst. One obvious explanation was available; once isopropylidenepyridoxine 5-palmitate hydrochloride was hydrolyzed, it released the hydrogen chloride, since free pyridoxine 5-palmitate (VII) could no longer form a salt with the acid. In the case of the monoethylacetal of pyridoxal 3-palmitate, however, the hydrolyzed product required a catalyst, hydrobromic acid, to form the hydrobromide of 3-palmitoxypyridoxal (VIII).

The dipalmitate of pyridoxine (IX), which was esterified through the 3-hydroxyl group and 5-hydroxymethyl group was prepared by the reduction of pyridoxal dipalmitate (II) following the procedure applied to the conversion of pyridoxal to pyridoxine with zinc in alcohol. The preparation of the 3,5-dipalmitate of pyridoxine (IX) also was attempted from pyridoxamine tripalmitate (III), which was treated with isoamyl nitrite in a medium of glacial acetic acid. The analytical results, however, seemed to indicate that the reaction product was a mixture of the dipalmitate and a monopalmitate of pyridoxine.

The ultraviolet spectra of some of these derivatives were observed. They were essentially the same, having one maximum absorption peak at 265–270 mμ or at 283 mμ in diethyl ether.

Acknowledgment.—The authors wish to thank Miss A. F. Schmidt and V. N. Schrodt for ultraviolet spectra.

Experimental

Acylation of Vitamin B_6 (I, II, III, IV).—Prior to acylation, the starting material, the water-soluble vitamin hydrochloride, was dried in a desiccator over sulfuric acid for 24 hours. The vitamin was then suspended in a mixture of dry chloroform and dry pyridine. To this suspension 1.2 to 3 moles of the respective fatty acid chloride dissolved in chloroform for 1 mole of the vitamin was added dropwise with stirring at room temperature or with cooling with ice. While the reaction proceeded, the particles of the vitamin disappeared and finally a clear solution was obtained. The mixture was then set aside for 4 to 48 hours at room temperature to complete the reaction. The acylated compound was extracted with diethyl ether or chloroform (for pyridoxamine tripalmitate). The extract was washed with 0.5 *N* hydrochloric acid, 5% sodium carbonate solution and with water successively, and was dried over anhydrous sodium sulfate. The reaction product was recrystallized from suitable solvents.

Seven fully acylated derivatives of the vitamin B_6 group are listed in Table I.

2-Methyl-3-palmitoxy-4-hydroxymethyl-5-palmitoxymethylpyridine (Pyridoxine 3,5-Dipalmitate) (IX).—Two hundred mg. of pyridoxal dipalmitate (II) was dissolved in hot 95% ethyl alcohol (100 ml.) and refluxed for two hours in the presence of 2 g. of zinc powder. After cooling, the mixture was filtered and the clear solution was poured into water. It was extracted with ether thoroughly and the extract washed with 5% sodium carbonate solution and with water until neutral. After drying over anhydrous sodium sulfate, the solvent was removed under diminished pressure; a white solid residue was obtained. It was recrystallized from 10 ml. of 95% ethyl alcohol; yield 50 mg. (24.9%), m.p. 58.0–61.0°, E_{264}^{Max} 4.1 × 10^3 in diethyl ether. *Anal.* Calcd. for $C_{40}H_{71}O_5N$: C, 74.37; H, 11.08. Found: C, 74.51; H, 11.16.

Nitrous Acid Oxidation of Pyridoxamine Tripalmitate.—One hundred fifty mg. of pyridoxamine tripalmitate (III) was dissolved in 10 ml. of glacial acetic acid and added to 5 ml. of freshly prepared isoamyl nitrite. The mixture was refluxed gently for 30 minutes. The solvent was removed almost completely under vacuum, and the residue was extracted with ethyl ether. The extract was washed with water, 5% potassium carbonate solution and with water successively. After drying over anhydrous sodium sulfate, the solvent was removed, and the residue was recrystallized from 70% ethyl alcohol; yield 35 mg., m.p. 56.5–60.0°. *Anal.* Calcd. for $C_{40}H_{71}O_5N$ (pyridoxine dipalmitate): C, 74.37; H, 11.08; N, 2.17. Found: C, 72.97; H, 10.19; N, 2.23. Thus the reaction product appeared to be a mixture of the dipalmitate and a monopalmitate of pyridoxine.

Monoethylacetal of 3-Palmitoxypyridoxal.—Two hundred thirty mg. of the monoethylacetal of pyridoxal hydrochloride was acylated with 500 mg. of palmitoyl chloride in a chloroform–pyridine mixture. The resultant compound was recrystallized from 60% ethyl alcohol; yield 200 mg. (46.1%), m.p. 56.0–57.0°. *Anal.* Calcd. for $C_{26}H_{43}O_4N$: C, 72.01; H, 10.00; N, 3.23. Found: C, 72.23; H, 9.93; N, 3.10.

2-Methyl-3-palmitoxy-4-formyl-5-hydroxymethylpyridine Hydrobromide (3-Palmitoxypyridoxal Hydrobromide) (VIII).—Approximately 100 mg. of the monoethylacetal of 3-palmitoxypyridoxal was dissolved in 7 ml. of ethyl alcohol, and this solution added to 3 ml. of water which contained 1 ml. of 40% hydrobromic acid. The mixture was refluxed for 10 minutes, and then diluted with 7 ml. of water. Upon cooling, fine needle-like crystals separated; yield 75 mg. (66.9%), m.p. 132.0°. *Anal.* Calcd. for $C_{24}H_{39}O_4N \cdot HBr$: N, 2.88; Br, 16.43. Found: N, 2.65; Br, 16.60.

Isopropylidenepyridoxine 5-Palmitate Hydrochloride.—The reaction product of isopropylidenepyridoxine hydrochloride (300 mg.) and palmitoyl chloride (500 mg.) in chloroform–pyridine was dissolved in a small portion of acetone containing dry hydrogen chloride. Petroleum ether (b.p. 34–38°) was added to the solution; flaky crystals were obtained. Recrystallization was repeated from the same solvent system without hydrogen chloride; yield 200 mg. (30.9%), m.p. 132.5–133.5°. *Anal.* Calcd. for $C_{27}H_{46}O_4N \cdot HCl$: N, 2.89; Cl, 7.32. Found: N, 2.87; Cl, 7.70.

2-Methyl-3-hydroxy-4-hydroxymethyl-5-palmitoxymethylpyridine (Pyridoxine 5-Palmitate) (VII).—One gram of isopropylidenepyridoxine 5-palmitate hydrochloride was dissolved in a mixture of 20 ml. of 95% ethyl alcohol and 10 ml. of water. To this solution 2 ml. of 4% aqueous hydrobromic acid solution was added and refluxed for 10 minutes. The solvent was then removed almost completely under reduced pressure, and the residue was recrystallized three times from acetone–water; yield 750 mg. (91.5%), m.p. 72.0–76.0°, ferric chloride test positive, E_{283}^{max} 5.1 × 10^3 in diethyl ether. *Anal.* Calcd. for $C_{24}H_{41}O_4N$: C, 70.72; H, 10.14; N, 3.44. Found: C, 70.80; H, 10.01; N, 3.28.

Complete Hydrolysis of Isopropylidenepyridoxine 5-Palmitate.—One hundred mg. of isopropylidenepyridoxine 5-

palmitate hydrochloride was dissolved in 65% ethyl alcohol containing 4.5% hydrogen chloride, and refluxed for 20 minutes. Upon addition of diethyl ether to the reaction mixture, white crystals separated. The latter were proved to be pyridoxine hydrochloride by means of a mixed melting point determination with authentic pyridoxine hydrochloride.

2,4,5-Trimethyl-3-palmitoxypyridine-4α,5α-bis-[pyridinium Bromide] (XI).—Eight hundred mg. of pyridoxine hydrochloride was dissolved in 20 ml. of 48% hydrobromic acid and refluxed for 10 minutes. The solution was then placed in the refrigerator for 12 hours. The crystals were collected and washed with acetone and with diethyl ether. The dibromo compound, 2-methyl-3-hydroxy-4,5-dibromomethylpyridine hydrobromide (X), yielded 800 mg., with a m.p. of 225–226° dec.

Seven hundred mg. of the dibromo derivative of pyridoxine was suspended in 20 ml. of alcohol-free chloroform and mixed with 570 mg. of palmitoyl chloride. With ice cooling, 3 ml. of dried pyridine was added to the mixture dropwise with strong stirring. The reaction proceeded immediately and the particles of the dibromide disappeared. The clear solution was set aside for 12 hours at room temperature. The solvent was then removed at low temperature *in vacuo* and the sirupy residue dissolved in a small amount of methyl alcohol. Upon cooling in the refrigerator, a precipitate formed, which was immediately removed by filtration and recrystallized from a methanol–acetone–petroleum ether system. Fine needle-like crystals were obtained, which were soluble in water and showed surface activity; yield 1.3 g. (94.2%), m.p. 146.0°. *Anal.* Calcd. for $C_{34}H_{49}O_2N_3Br_2$: N, 6.08; Br, 23.12. Found: N, 6.04; Br, 21.98.

URBANA, ILLINOIS

[CONTRIBUTION NO. 197 FROM JACKSON LABORATORY, E. I. DU PONT DE NEMOURS & CO.]

Organophosphorus Isocyanates

BY A. C. HAVEN, JR.

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The preparation and properties of several organophosphorus isocyanates are described.

Organophosphorus isocyanates, a new class of compounds, are available by reaction of phosphonic halides with silver cyanate in inert solvent.[1] The following diisocyanates of this class were prepared and characterized:

Ethylphosphonic	$-C_2H_5PO(NCO)_2$
Chloromethylphosphonic	$-ClCH_2PO(NCO)_2$
Isopropylphosphonic	$-(CH_3)_2CHPO(NCO)_2$
Hexadecylphosphonic	$-CH_3(CH_2)_{15}PO(NCO)_2$
Benzylphosphonic	$-C_6H_5CH_2PO(NCO)_2$
Phenylphosphonic	$-C_6H_5PO(NCO)_2$
Phenylphosphonous	$-C_6H_5P(NCO)_2$

In general, the appropriate chloride was heated several hours with a small excess of silver cyanate in benzene or acetonitrile. Removal of the silver salts and fractionation of the filtrate afforded the desired phosphonic isocyanate in yields varying from trace to 50%. These compounds are colorless liquids, boiling somewhat higher than the corresponding dichlorides. They polymerize slowly on standing and more rapidly when heated to give hard, glassy polymers. This behavior is in a large measure responsible for the low yields obtained.

Potassium cyanate was used in place of silver cyanate in one preparation of ethylphosphonic diisocyanate. The reaction was considerably slower and a reduced yield of diisocyanate was obtained.

The organophosphorus isocyanates exhibit the characteristic isocyanate reactions. When added to water they liberate carbon dioxide vigorously. Urethans and ureas are obtained from alcohols and amines, respectively. Both these reactions are very rapid at room temperature.

Combustion-resistant polymers were obtained by reaction of ethylphosphonic diisocyanate with hydroquinone, resorcinol, 1,6-hexanediol and *p*-phenylenediamine.

(1) Phosphorus triisocyanate and phosphoryl triisocyanate have been similarly prepared by G. S. Forbes and H. H. Anderson, THIS JOURNAL, **62**, 762 (1940); **64**, 1757 (1942).

Experimental

Ethylphosphonic Diisocyanate.—A suspension of 180 g. of fresh silver cyanate in 1.5 l. of dry benzene was treated with 73.5 g. of ethylphosphonic dichloride and refluxed with stirring for 15 hours. The suspension was filtered and the filtrate concentrated and fractionated to obtain ethylphosphonic diisocyanate, 38.3 g. (48%), b.p. 58–59° (0.70 mm.).

Anal. Calcd. for $C_4H_5N_2O_3P$: C, 30.0; H, 3.15; N, 17.5; P, 19.3. Found: C, 29.8, 29.8; H, 3.19, 3.21; N, 16.8, 16.8; P, 20.1, 18.6.

The bis-methylurethan was prepared by addition of the phosphonic diisocyanate to excess methanol. The resulting solution was evaporated to dryness and the product recrystallized from a mixture of methanol and absolute ether; m.p. 142–144°.

Anal. Calcd. for $C_6H_{13}N_2O_5P$: C, 32.1; H, 5.84; N, 12.5. Found: C, 32.6, 32.2, 31.9; H, 5.94, 5.98, 5.86; N, 12.2, 12.4.

The bis-ethylurethan was prepared similarly; m.p. 116–117°.

Anal. Calcd. for $C_8H_{17}N_2O_5P$: C, 38.1; H, 6.79; N, 11.1. Found: C, 37.9, 38.1; H, 6.86, 6.86; N, 11.6, 11.4.

The bis-phenylurea was prepared by addition of the diisocyanate to excess aniline. The resulting crude solid was washed thoroughly with 6 *N* hydrochloric acid, water, ethyl alcohol and ether (no solvent was found for recrystallization). The bis-phenylurea had m.p. 204–205°.

Anal. Calcd. for $C_{16}H_{19}N_4O_3P$: C, 55.5; H, 5.53; N, 16.3. Found: C, 55.4, 55.4; H, 5.39, 5.25; N, 16.6, 16.9.

The use of potassium cyanate is illustrated in the following experiment. A suspension of 85 g. of fresh, powdered potassium cyanate and 73.5 g. of ethylphosphonic dichloride in 700 ml. of acetonitrile (distilled over phosphorus pentoxide) was refluxed with stirring for 24 hours. The reaction mixture was filtered and the filtrate concentrated and distilled to give approximately 40 g. of unreacted ethylphosphonic dichloride and 8 g. of ethylphosphonic diisocyanate, b.p. 55–80° (3 mm.).

In some runs there was obtained a fraction boiling at 45–46° (0.75 mm.), intermediate between ethylphosphonic dichloride and ethylphosphonic diisocyanate. This material was tentatively identified as ethylphosphonisocyanatidic chloride, $C_2H_5PO(Cl)NCO$. It was converted to the diisocyanate by heating it in benzene with silver cyanate.