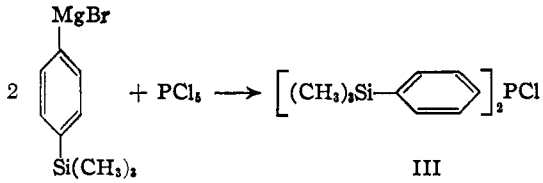
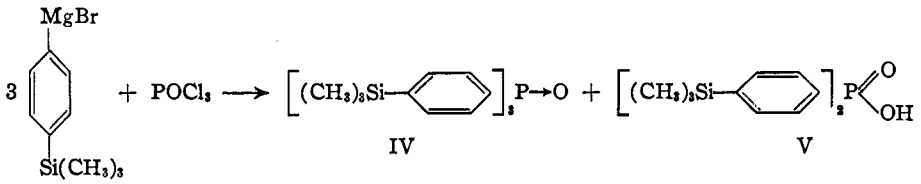


(II) with potassium permanganate in aqueous and in pyridine solution did not result in the formation



of the corresponding phosphine oxide. This result is not surprising in view of the well-known resistance of aromatic phosphines toward oxidation.

*p*-Trimethylsilylphenylmagnesium bromide (I) when treated with phosphorus oxychloride yields both the phosphine oxide (IV) as well as the diphosphonic acid (V). The procedure was essentially that of Kosolapoff.[2]

## Experimental

*p*-Trimethylsilylphenylmagnesium bromide (I) was prepared from 12.2 g. of magnesium turnings, 114.5 g. of *p*-bromophenyltrimethylsilane and 550 cc. of anhydrous ether. The reaction was initiated by means of a small amount of ethylmagnesium bromide.

**Tris-(*p*-trimethylsilylphenyl)-phosphine (II).** (A).—In a three-necked flask, equipped with stirrer, reflux condenser and dropping funnel, were placed 34.4 g. of phosphorus trichloride and 100 cc. of ether. Half of the above prepared Grignard solution was added gradually through a dropping funnel. Afterwards the mixture was refluxed for three hours. The inorganic precipitate was filtered off and washed with ether. The solvent was then removed from the filtrate. The weight of the residual material was 68.1 g. On standing in the refrigerator, crystals formed which were recrystallized from alcohol, yielding colorless needles, m.p. 95–96° (uncor.).

B.—Half of the above described Grignard solution was added slowly to a solution of 52.1 g. of phosphorus pentachloride in 100 cc. of ether. The product was worked up in the same way as described in A. The residual material weighed 63 g. It was vacuum distilled. Tris-(*p*-trimethylsilylphenyl)-phosphine (II) distilled at 112–117° at 31 mm. It was recrystallized from alcohol, yielding colorless needles, m.p. 95–96° (uncor.). A mixed melting point taken with the products obtained by procedures A and B showed no depression, establishing thereby the identity of the two materials. The yields of the pure product ranged from 35–45%.

*Anal.* Calcd. for $C_{27}H_{39}PSi_3$: Si, 17.6; P, 6.5. Found: Si, 17.2; P, 6.8.

In the above distillation, another fraction was isolated, distilling at 72° at 43 mm. as a colorless liquid.

*Anal.* Calcd. for $C_{18}H_{26}ClPSi_2$: Si, 15.4; P, 8.5. Found: Si, 13.1; P, 8.9.

While this compound evidently was not pure, it probably contained bis-(*p*-trimethylsilylphenyl)-chlorophosphine (III). The presence of chlorine was proven by means of a qualitative test.

**Tris-(*p*-trimethylsilylphenyl)-phosphine Oxide (IV).**—*p*-Trimethylsilylphenylmagnesium bromide, prepared from 57 g. of *p*-bromophenyltrimethylsilane, was added gradually to a solution of 38 g. of phosphorus oxychloride in 300 cc. of ether which was brought to reflux before the addition. The reaction mixture was then refluxed for 15 hours. After cooling, the yellow liquid was decanted from the residual solid. The solid was hydrolyzed in ice-water forming a white precipitate. The yellow liquid was concentrated on the steam-bath and formed a yellowish-white solid. Both the white precipitate and the residual solid obtained from the liquid portion of the reaction mixture were combined and washed first with dilute sodium hydroxide and then with water. The residual product was extracted with ether and the ether extract dried over anhydrous sodium sulfate. After removal of the ether, the remaining solid was recrystallized from alcohol, yielding a colorless, crystalline product, m.p. 259° (uncor.). The yield was 30%.

*Anal.* Calcd. for $C_{27}H_{39}OPSi_3$: Si, 17.0; P, 6.3. Found: Si, 17.4; P, 6.8.

**Bis-(*p*-trimethylsilylphenyl)-phosphonic Acid (V).**—The sodium hydroxide extract from the combined solid products of the reaction of *p*-trimethylsilylphenylmagnesium bromide and phosphorus oxychloride was acidified with dilute hydrochloric acid, resulting in a colorless, crystalline product, m.p. 213–214.5° (uncor.). The yield was 15%.

*Anal.* Calcd. for $C_{18}H_{27}O_3PSi_2$: Si, 15.5; P, 8.6. Found: Si, 16.5; P, 8.9.

NEW PRODUCTS DEVELOPMENT LABORATORY
GENERAL ELECTRIC COMPANY
PITTSFIELD, MASS.

(2) G. M. Kosolapoff, THIS JOURNAL, 64, 2982 (1942).

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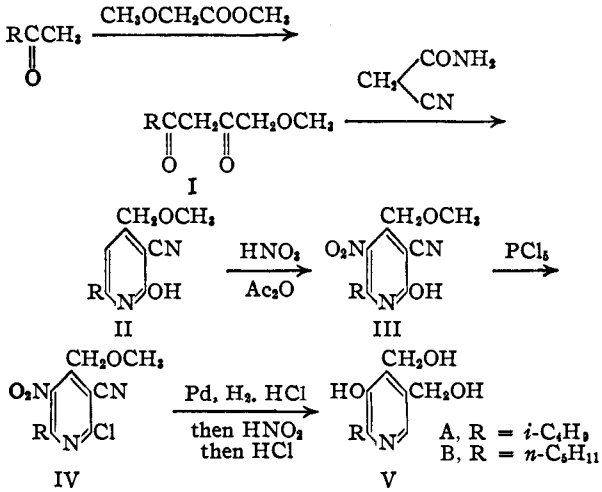
# Chemistry of Vitamin $B_6$. X. Some Homologs of the Vitamin $B_6$ Group

BY DOROTHEA HEYL, EILEEN LUZ, STANTON A. HARRIS AND KARL FOLKERS

RECEIVED APRIL 22, 1953

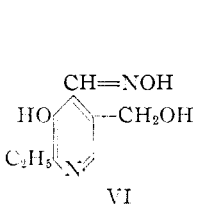
An ethyl homolog of pyridoxine, 2-ethyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine, was reported previously.[1] Two higher homologs have been prepared: the corresponding isobutyl and *n*-amyl derivatives. These compounds were synthesized in general by the sequence of reactions which was used for preparation of the ethyl homolog, the main difference being that several of the intermediates were not isolated. The compounds actually isolated are represented by the formulas I through V.



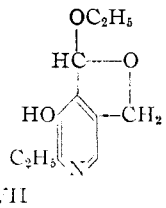
2-Ethyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine[1] was oxidized to 2-ethyl-3-hydroxy-4-formyl-5-hydroxymethylpyridine, which was isolated as the oxime VI. The latter was con-

(1) S. A. Harris and A. N. Wilson, THIS JOURNAL, 63, 2526 (1941).

verted to the monoethyl acetal VII. These reactions are analogous to those previously described for the corresponding pyridoxal derivatives.[2,3]



VI



VII

## Experimental[4]

The reactions carried out for the preparations of 2-isobutyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine and 2-*n*-amyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine were similar to reactions previously described.[1,5] Only the physical properties of the intermediates and products are listed here.

**2-Isobutyl-4-methoxymethyl-5-cyano-6-hydroxypyridine** (IIA) was prepared from 1-methoxy-7-methyl-2,4-heptanedione (IA) (b.p. 113° (24 mm.), $n^{29}D$ 1.4596). After one recrystallization from ethyl alcohol, the product melted at 204–205°.

*Anal.* Calcd. for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32; N, 12.72. Found: C, 65.68; H, 7.25; N, 12.71.

**2-Isobutyl-3-nitro-4-methoxymethyl-5-cyano-6-hydroxypyridine** (IIIA) was purified by two recrystallizations from ethyl alcohol, accompanied by decolorization with Darco; m.p. 167–168°.

*Anal.* Calcd. for $C_{12}H_{15}N_3O_4$: C, 54.33; H, 5.70; N, 15.84. Found: C, 54.62; H, 5.50; N, 15.83.

**2-Isobutyl-3-nitro-4-methoxymethyl-5-cyano-6-chloropyridine** (IVA) was recrystallized three times from petroleum ether (b.p. 30–60°). It melted at 42–43°.

*Anal.* Calcd. for $C_{12}H_{14}N_3O_3Cl$: C, 50.80; H, 4.96; N, 14.82. Found: C, 50.82; H, 5.12; N, 15.08.

**2-Isobutyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine hydrochloride** (VA) was recrystallized from hot water, with decolorization with Darco; m.p. 213–214°.

*Anal.* Calcd. for $C_{11}H_{18}NO_3Cl$: C, 53.33; H, 7.32; N, 5.66. Found: C, 53.35; H, 7.25; N, 5.90.

**1-Methoxy-2,4-nonanedione** (IB).—Condensation of methyl methoxyacetate with methyl *n*-amyl ketone yielded 1-methoxy-2,4-nonanedione; b.p. 138° (28 mm.), $n^{25}D$ 1.4602.

*Anal.* Calcd. for $C_{10}H_{18}O_3$: C, 64.48; H, 9.74. Found: C, 64.50; H, 9.72.

**2-*n*-Amyl-4-methoxymethyl-5-cyano-6-hydroxypyridine** (IIB) was recrystallized twice from absolute alcohol; m.p. 131–132°.

*Anal.* Calcd. for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.74; H, 7.64; N, 12.05.

**2-*n*-Amyl-3-nitro-4-methoxymethyl-5-cyano-6-hydroxypyridine** (IIIB) was recrystallized twice from alcohol and once from dilute alcohol. It melted at 161–162°.

*Anal.* Calcd. for $C_{13}H_{17}N_3O_4$: C, 55.90; H, 6.14; N, 15.05. Found: C, 56.25; H, 5.79; N, 15.24.

**2-*n*-Amyl-3-nitro-4-methoxymethyl-5-cyano-6-chloropyridine** (IVB) was recrystallized twice from petroleum ether (b.p. 30–60°); m.p. 42–43°.

*Anal.* Calcd. for $C_{13}H_{16}N_3O_3Cl$: C, 52.44; H, 5.42; N, 14.11. Found: C, 52.16; H, 5.00; N, 14.20.

**2-*n*-Amyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine hydrochloride** (VB) was recrystallized from alcohol containing a trace of hydrogen chloride. The product melted at 186–187°.

*Anal.* Calcd. for $C_{12}H_{20}NO_3Cl$: C, 55.05; H, 7.70; N, 5.35. Found: C, 54.93; H, 7.82; N, 5.47.

**Oxime of 2-Ethyl-3-hydroxy-4-formyl-5-hydroxymethylpyridine** (VI).—2-Ethyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine hydrochloride[1] (10.7 g.) was oxidized with manganese dioxide and sulfuric acid in a manner exactly analogous to the preparation of pyridoxal oxime.[2] The yield of the oxime of 2-ethyl-3-hydroxy-4-formyl-5-hydroxymethylpyridine was 4.8 g. (50%). After one recrystallization from water–alcohol and one from alcohol, the oxime melted at 225–226°.

*Anal.* Calcd. for $C_9H_{12}N_2O_3$: C, 55.09; H, 6.17; N, 14.28. Found: C, 55.22; H, 6.00; N, 14.12.

**Monoethyl Acetal of 2-Ethyl-3-hydroxy-4-formyl-5-hydroxymethylpyridine Hydrochloride** (VII).—Conversion of 3.4 g. of the oxime of 2-ethyl-3-hydroxy-4-formyl-5-hydroxymethylpyridine (VI) to the corresponding monoethyl acetal was carried out in the manner previously described for the conversion of pyridoxal oxime.[3] The yield of the monoethyl acetal of 2-ethyl-3-hydroxy-4-formyl-5-hydroxymethylpyridine hydrochloride was 1.66 g. (39%); m.p. 137.5–138.5°. After one recrystallization from alcohol–ether containing a little hydrogen chloride and another recrystallization from alcohol containing a little hydrogen chloride, the material melted at 132–133°.

*Anal.* Calcd. for $C_{11}H_{16}NO_3Cl$: C, 53.77; H, 6.56; N, 5.70. Found: C, 54.00; H, 6.29; N, 5.63.

RESEARCH LABORATORIES
MERCK AND CO., INC.
RAHWAY, NEW JERSEY

(2) D. Heyl, *ibid.*, **70**, 3434 (1948).

(3) S. A. Harris, D. Heyl and K. Folkers, *ibid.*, **66**, 2088 (1944).

(4) We are indebted to Mr. Richard Boos and his associates for the microanalyses.

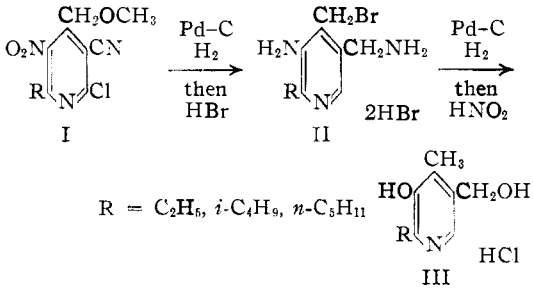
(5) S. A. Harris and K. Folkers, THIS JOURNAL, **61**, 1245, 3307 (1939).

## Chemistry of Vitamin $B_6$. XI. Homologs of 4-Desoxypyridoxine

BY DOROTHEA HEYL, EILEEN LUZ, STANTON A. HARRIS AND KARL FOLKERS

RECEIVED APRIL 22, 1953

4-Desoxypyridoxine was shown to be a potent vitamin $B_6$ inhibitor.[1] Because of the biological interest in this compound, the preparation of homologs for further biological study was undertaken. Three homologs, represented by structure III, in which the methyl group in position 2 of 4-desoxypyridoxine has been replaced by ethyl, isobutyl and *n*-amyl groups, have now been prepared by synthesis through the intermediates I and II.



I II III

2-Ethyl-3-hydroxy-4-methyl-5-hydroxymethylpyridine hydrochloride and 2-isobutyl-3-hydroxy-4-methyl-5-hydroxymethylpyridine hydrochloride have also been prepared by the direct hydrogenolysis of the 2-ethyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine hydrochloride[2] and 2-isobutyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine hydrochloride.[3] Hydrogenolysis of pyridoxine hydrochloride to form 4-desoxypyridoxine hydrochloride was described previously.[4]

(1) W. H. Ott, *Proc. Soc. Exp. Biol. Med.*, **61**, 125 (1946); W. W. Cravens and E. E. Snell, *ibid.*, **71**, 73 (1949).

(2) S. A. Harris and A. N. Wilson, THIS JOURNAL, **63**, 2526 (1941).

(3) D. Heyl, E. Luz, S. A. Harris and K. Folkers, *ibid.*, **75**, 4079 (1953).

(4) S. A. Harris, *ibid.*, **62**, 3293 (1940).