sulfonate was collected by filtration of the cooled reaction mixture. The filtrate was concentrated to dryness and the residue was thoroughly extracted with cold benzene. The combined extracts were concentrated to a small volume and petroleum ether was added to turbidity. The crystalline product (mp 53–54°, 19.3 g, 60%) and an additional crop obtained from the mother liquor (mp 53°, 10.1 g, total yield 91.5%) were recrystallized from the same solvents: mp 54°; R_f (a) 0.58, (b) 0.36; $[\alpha]^{28}D$ −48.2° (*c* 1.0, chloroform) (lit.[2] mp 47–55°, $[\alpha]D$ −43.4°).

Anal. Calcd for $C_6H_{11}IO_3$ (258.95): C, 27.92; H, 4.29; I, 49.18. Found: C, 28.16; H, 4.30; I, 49.27.

2-Deoxy-3,5-*O*-ethylidene-D-*erythro*-pentononitrile (6).—1-Deoxy-2,4-*O*-ethylidene-1-iodo-D-erythritol (**5**, 5.16 g, 0.02 mole), sodium cyanide (1.078 g, 0.022 mole), and DMSO (20 ml) were stirred at 36° for 17.5 hr. The reaction mixture was passed through a silicic acid column (100 g) and eluted with a mixture of ethyl acetate–cyclohexane, 4:1. The eluate was collected in 5-ml fractions, which were analyzed by tlc. Fractions containing the product were pooled and concentrated. The residue was crystallized from ethyl acetate–petroleum ether (bp 40–60°) yielding the nitrile **6**, mp 102° (1.5 g, 48%). Two further crops from the mother liquor raised the total yield to 78%. Recrystallization of the first crop from the same solvents formed the pure nitrile: mp 102–103°; R_f (a) 0.39, (b) 0.13; $[\alpha]^{28}D$ −44° (*c* 0.9, chloroform); infrared 2245 cm^{-1} (C≡N) (lit.[2] mp 105–105.5°, $[\alpha]D$ −38°).

Anal. Calcd for $C_7H_{11}NO_3$ (157.17): C, 53.50; H, 7.05; N, 8.90. Found: C, 53.73; H, 7.16; N, 8.66.

2-Deoxy-*N*-phenyl-*erythro*-pentosylamine.—Raney nickel was prepared[8] from Raney's alloy (1.25 g), added in portions to 2 *N* sodium hydroxide (24 ml) with stirring. The suspension was stirred for 30 min and the catalyst was washed free of alkali with several changes of water (litmus). The catalyst was suspended in aqueous acetic acid (20%, 7.5 ml) and 2-deoxy-3,5-*O*-ethylidene-D-*erythro*-pentononitrile (**6**, 314 mg, 2 mmoles) was added. The mixture was stirred for 10 min. The catalyst was removed by gravity filtration and was washed with water until free of reducing material (Fehling). The combined filtrates and Amberlite IR-120(H) (4–5 g) were stirred for 2–3 hr in an oil bath (90°) while nitrogen was bubbled through the mixture. The original green solution turned colorless and tlc revealed a 2-deoxypentose, which could not be separated from 2-deoxy-D-*erythro*-pentose, R_f (c) 0.43 (Pfanstiehl). The resin was washed with water until free of reducing material. The filtrates were passed through a Duolite A-4 column (26 ml, 13 × 175 mm), and the column was washed with water until freed of reducing material. The eluate was concentrated under vacuum to a syrup, to which aniline (0.28 ml, 3 mmoles) was added, and the deoxy sugar derivative was crystallized from water and methanol, mp 164° (96 mg, 23%). Recrystallization from ethanol raised the melting point to 167–168°, $[\alpha]^{28}D$ +169° (*c* 0.58, pyridine, 10 min) [lit.[20] mp 171–172°, $[\alpha]^{17}D$ +164° (pyridine after 10 min)]. The product showed no change in melting point when mixed with a sample prepared from authentic 2-deoxy sugar.

Registry No.—2-Deoxy-D-*erythro*-pentose, 7640-21-3; **9**, 7718-67-4; **10**, 7721-91-7; **11**, 7705-70-6; **12**, 7705-71-7; **13**, 7718-68-5; **14**, 7705-72-8; **5**, 7284-12-0; **6**, 7705-74-0.

(20) L. Hough, *J. Chem. Soc.*, 3066 (1953).

Selective Demethylation of 3,4-Dimethoxy-Substituted Aromatic Aldehydes and Ketones

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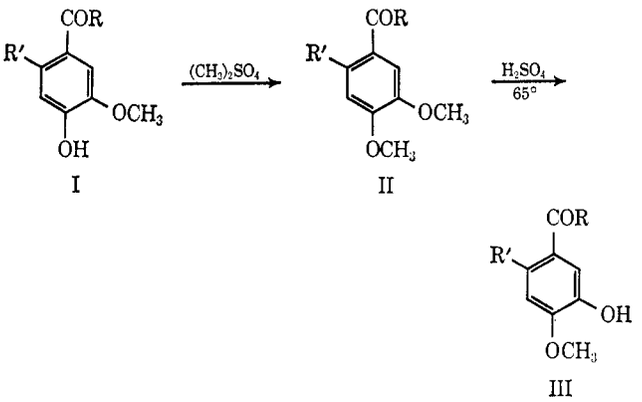
It has been shown that acid hydrolysis of 6,7-dimethoxy-3,4-dihydroisoquinolines causes preferential cleavage of the 7-methoxyl group.[1] These compounds may be visualized as aminocarbonyl derivatives in which ether cleavage occurs at the methoxyl group *meta* to the potential carbonyl function. The two 3,4-dimethoxy-substituted aromatic aldehydes, veratraldehyde (IIa) and 6-methylveratraldehyde (IIb), and the ketone, 3,4-dimethoxyacetophenone (IIc), which can be prepared easily from the readily available monomethyl ethers, vanillin (Ia), 6-methylvanillin (Ib), and 4-hydroxy-3-methoxyacetophenone (Ic), respectively, could be expected to react in an analogous fashion and were therefore chosen for model experiments. Our assumption proved to be correct[2] and we now wish to report a facile conversion of the two 4-hydroxy-3-methoxy-substituted aromatic aldehydes (Ia and Ib) and the ketone (Ic) into the corresponding 3-hydroxy-4-methoxy isomers (IIIa, IIIb, and IIIc, respectively) by acid hydrolysis of the intermediate O-dimethyl ether derivatives.



a, R = R′ = H
b, R = H; R′ = CH_3
c, R = CH_3; R′ = H

Thus veratraldehyde (IIa) and 6-methylveratraldehyde (IIb) on treatment with concentrated sulfuric acid at 65°, are converted to isovanillin (IIIa) and 6-methylisovanillin (IIIb) in yields of 61 and 64%, respectively. 6-Methylisovanillin (IIIb), a new compound, was different from the known isomeric 6-methylvanillin (Ib)[3] and both compounds on methylation gave the same known product (IIb).[4] Under the same conditions 3,4-dimethoxyacetophenone (IIc) is converted to acetoisovanillone (IIIc) in 58% yield.

Experimental Section[5]

6-Methylisovanillin (IIIb).—6-Methylveratraldehyde (IIb,[4] 225 g, 1.25 moles) was dissolved in 1125 ml of stirred, concentrated sulfuric acid at room temperature under nitrogen. The solution was heated to and stirred at 65° for 20 hr under nitrogen and then it was cooled and poured onto 7.5 kg of ice. After stirring for 15 min the mixture was filtered and the filter cake was washed with 500 ml of water. The filtrate, including the washes, was extracted with six 250-ml portions of methylene chloride. The combined methylene chloride extracts, the filter

(1) H. Bruderer and A. Brossi, *Helv. Chim. Acta.*, **48**, 1945 (1965).

(2) This is in marked contrast to the behavior of 3,4,5-trimethoxybenzaldehyde which, under acidic conditions, is preferentially cleaved at the *para* position to give syringaldehyde: I. A. Pearl and D. L. Beyer, *J. Am. Chem. Soc.*, **74**, 4262 (1952).

(3) J. P. Koetschet, *Helv. Chim. Acta.*, **13**, 479 (1930). This compound was kindly prepared by Dr. A. Focella and had mp 175–176°.

(4) A. St. Pfau, *ibid.*, **22**, 550 (1939).

(5) All melting points (corrected) were taken in open capillary tubes with a Thomas–Hoover melting point apparatus. Thin layer chromatography employed silica gel G plates and the infrared spectra were taken in chloroform.

cake obtained above, and 1.25 l. of 1 *N* sodium hydroxide were shaken in a separatory funnel and the methylene chloride layer was shaken again with 250 ml of 1 *N* sodium hydroxide and 250 ml of water. The combined aqueous phases were backwashed with 250 ml of methylene chloride and then acidified with 130 ml of concentrated hydrochloric acid. The mixture was cooled with an ice bath, filtered, washed with two 200-ml portions of water, and dried under vacuum at 50° to give 132.6 g (64%) of IIIb, mp 149–151°. Recrystallized from a mixture of 600 ml of ethanol and 1330 ml of water the product was analytically pure, mp 150.5–152.5°, and weighed 127.0 g (61.2%, 91.5% based on IIb consumed).

Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; N, 6.07. Found: C, 64.84; H, 6.18.

The combined methylene chloride extracts, after alkali treatment, were dried over magnesium sulfate and evaporated under vacuum to give 74.0 g of IIb, mp 74–76.

The melting point of the 6-methylisovanillin (IIIb) obtained above, on admixture with 6-methylvanillin (Ib),[3] was depressed to 137–140°. Methylation of our IIIb and Ib[3] with methyl sulfate gave the same product, authentic 6-methylveratraldehyde (IIb), as shown by mixture melting point and infrared spectra.

Isovanillin (IIIa).—By the same procedure described above for the preparation of IIIb, 5.6 g (61%) of isovanillin (IIIa), mp 110–113°,[6] was obtained from 10 g of veratraldehyde (IIa). Part of the veratraldehyde (4.2 g) was recovered unchanged.

Acetoisovanillone (IIIc).—When 119 g (0.66 mole) of 3,4-dimethoxyacetophenone (IIc)[7] was subjected to the hydrolysis conditions described for the preparation of IIIb above, 64.2 g (58.4%, 67.2% based on IIc consumed) of acetoisovanillone (IIIc), mp 92–93°,[8] and 18.6 g of recovered 3,4-dimethoxyacetophenone were isolated.

Registry No.—IIb, 7721-62-2; IIIb, 7721-61-1.

Acknowledgment.—We wish to thank David Malarek and Thomas Fraher for capable technical assistance.

(6) This material was identified by comparison (mixture melting point) with authentic material obtained from Monsanto Chemical Co.

(7) Prepared from acetovanillone and dimethyl sulfate by the method of F. F. Blicke and W. K. Johnson, *J. Am. Pharm. Assoc., Sci. Ed.*, **45**, 441 (1956).

(8) Identical (mixture melting point, tlc) with material prepared according to the method of R. Schwarz and K. Capek, *Monatsh. Chem.*, **83**, 889 (1952).

Preparation of Aldehyde Derivatives from Picoline N-Oxides

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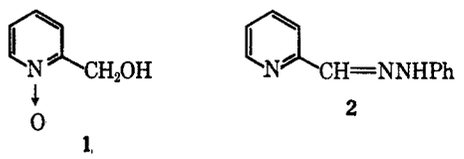
A number of methods are available for conversion of picolines to pyridine carboxaldehyde derivatives. Synthetically useful methods include selenium oxide oxidation,[1] oximation with butyl nitrite,[2] and double acylative rearrangement of picoline N-oxides.[3] A recent note on preparation of oximes of substituted pyridine-2-carboxaldehydes *via* a presumed NO heterolysis route[4] leads us to report preparation of pyridine-2- and -4-carboxaldehyde derivatives in good yields by a route involving a different type of NO heterolysis.

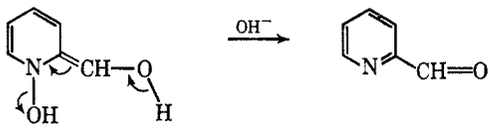
Hydroxymethylpyridine was prepared by the acylative rearrangement of picoline N-oxide[3,5] and oxidized to hydroxymethylpyridine N-oxide (**1**). When treated with phenylhydrazine in dilute sodium hydroxide, 2-hydroxymethylpyridine N-oxide is converted to pyridine-2-carboxaldehyde phenylhydrazone (**2**) in 79% yield.



1 **2**

Although hydrazines may serve as oxidants in some reactions (osazone formation, amination of tropones[8]), phenylhydrazine is not the oxidant in this reaction since a 72% yield of the hydrazone is obtained based on the amount of phenylhydrazine used. No phenylhydrazone is obtained by heating phenylhydrazine and 2-hydroxymethylpyridine N-oxide in the absence of sodium hydroxide, nor by heating phenylhydrazine and 2-hydroxymethylpyridine in dilute sodium hydroxide. Reaction of 2-hydroxymethylpyridine N-oxide, phenylhydrazine, and alkali in the presence of a 20-fold excess of 2-ethylpyridine N-oxide gave only the phenylhydrazone of pyridine-2-carboxaldehyde (61%) and no evidence of the possible intermolecular oxidation product, pyridine-2-carboxaldehyde N-oxide phenylhydrazone. Oxidation of the alcohol must therefore occur at the expense of the N-oxide in a base-catalyzed intramolecular reaction.

The oxidation of the alcohol and attendant reduction of the N-oxide may proceed *via* an elimination reaction involving enolization to enolamine **3**, followed by removal of a proton from the hydroxyl group and subsequent NO fission in a step bearing some resemblance to the oxidative step of the osazone reaction (NN fission).[9] As predicted by this mechanism no phenylhydrazone was obtained on treatment of the corresponding methyl ether, 2-methoxymethylpyridine N-oxide, with phenylhydrazine and dilute sodium hydroxide. The related oxidation of alkylhydroxylamines to imines by base-catalyzed elimination of the elements of water has been observed in several other instances.[4,10]



3

(1) W. Borsche and H. Hartmann, *Ber.*, **73**, 839 (1940).

(2) S. Forman, *J. Org. Chem.*, **29**, 3323 (1964).

(3) V. Boekelheide and W. Linn, *J. Am. Chem. Soc.*, **76**, 1286 (1954).

(4) F. A. Daniher, B. E. Hackley, Jr., and A. B. Ash, *J. Org. Chem.*, **31**, 2709 (1966).

(5) Distilled hydroxymethylpyridine, prepared by the acylative rearrangement of picoline N-oxide and subsequent hydrolysis of the acetate,[3] was found to contain 2% pyridine-2-carboxaldehyde. Although extensive investigations of the acylative rearrangement point to an ionic or radical-cage mechanism,[6] free radicals appear to be present in the reaction medium[7] and account for low yields of ethylpyridine, picoline, methane, carbon dioxide, and methyl acetate. Pyridine-2-carboxaldehyde may similarly result from abstraction of hydrogen from the major product, 2-acetoxymethylpyridine.

(6) S. Oae, T. Kitao, and Y. Kitaoka, *J. Am. Chem. Soc.*, **84**, 3359 (1962); V. J. Traynelis and P. L. Pacini, *ibid.*, **86**, 4917 (1964); T. Cohen and J. H. Fager, *ibid.*, **87**, 5701 (1965); V. J. Traynelis and A. I. Gallagher, *ibid.*, **87**, 5710 (1965); T. Koenig, *ibid.*, **88**, 4045 (1966).

(7) V. J. Traynelis and R. F. Martello, *ibid.*, **80**, 6590 (1958); V. J. Traynelis and R. F. Martello, *ibid.*, **82**, 2744 (1960).

(8) T. Mukai, H. Tsuruta, and T. Nozoe, *Tetrahedron Letters*, 1063 (1966).

(9) F. Weygand, *Ber.*, **73**, 1284 (1940); H. S. Isbell, *Ann. Rev. Biochem.*, **12**, 207 (1943).

(10) H. Feuer, B. F. Vincent, Jr., and R. S. Bartlett, *J. Org. Chem.*, **30**, 2877 (1965).