

Transformation of 2-(Hydroxymethyl)-5-(aminomethyl)-furan into 6-Methyl-3-pyridinol *

NIELS ELMING

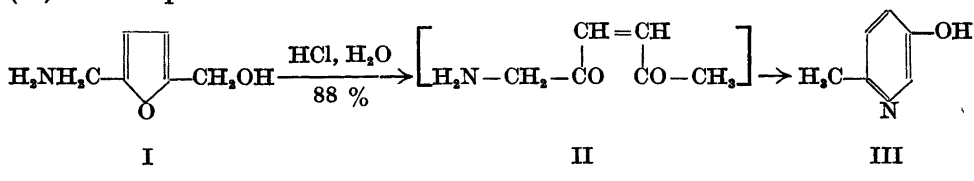
Centrallaboratoriet, Sadolin & Holmblad A/S, Copenhagen, Denmark

NIELS CLAUSON-KAAS

Department of Chemistry, Israel Institute of Technology, Haifa, Israel

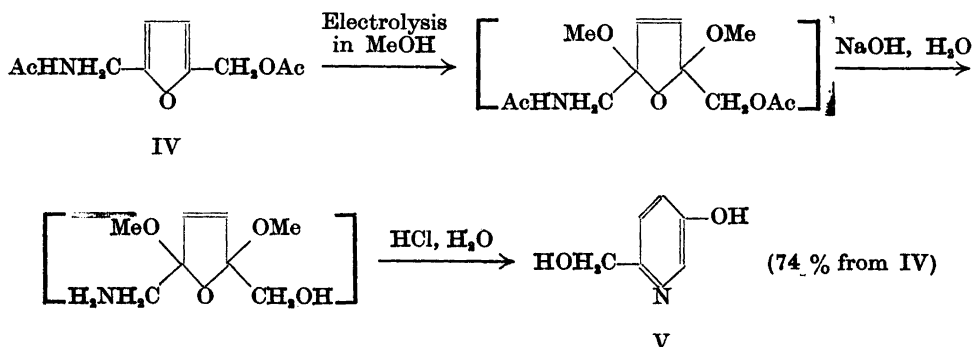
6-Methyl-3-pyridinol has been prepared from 2-(hydroxymethyl)-5-(aminomethyl)-furan by the action of hydrochloric acid. Electrolytic methoxylation of 2-(acetoxymethyl)-5-(acetamidomethyl)-furan followed by alkaline hydrolysis and treatment with hydrochloric acid gave 6-(hydroxymethyl)-3-pyridinol.

Furfuryl alcohol is transformed by the action of methanolic hydrogen chloride into a mixture of distillable products (yield 42 %) consisting of 2,3 (or 4), 5-trimethoxytetrahydrofuran, methyl levulinate, methyl levulinate dimethyl ketal and 2 (or 3)-methoxylevulinylaldehyde dimethyl acetal¹. It has been proved^{1,2} that this transformation proceeds through *cis*-3-acetylacrolein or its equivalent. We have now found that 2-(hydroxymethyl)-5-(aminomethyl)-furan (I) forms 6-methyl-3-pyridinol (III) by the action of hydrochloric acid. It is reasonable to assume that this transformation also takes place through an unsaturated 1,4-dicarbonyl compound, *viz.* 1-amino-3-hexene-2,5-dione (II) or its equivalent.



* Presented before the Division of Organic Chemistry at the 9th Scandinavian Chemical Meeting, Århus, Denmark, August 1956.

I is a new compound which was prepared by reductive amination of 5-(hydroxymethyl)-furfural (yield 72 %). It was characterized by the hydrochloride, the diacetate [2-(acetoxymethyl)-5-(acetamidomethyl)-furan (IV)] and by transformation of IV into the known 6-hydroxymethyl-3-pyridinol (V) by the sequence of reactions shown below (*cf.*³).



EXPERIMENTAL

Microanalyses by E. Boss and K. Glens

2-(Hydroxymethyl)-5-(aminomethyl)-furan (I). 5-(Hydroxymethyl)-furfural⁴ (12.8 g), methanol (30 ml), liquid ammonia (5 ml) and Raney nickel (0.4 g) were mixed and shaken (1 h) under 100 atmospheres of hydrogen at 65–75°. After cooling, the reaction mixture was filtered and the filtrate distilled. The yield was 9.30 g (72 %) of I (pale yellow liquid, b.p. d_4^{20} 102–105°, n_D^{20} 1.5278). (Found: C 56.8; H 7.4; N 11.1. Calc. for $C_6H_9O_2N$ (127.1): C 56.7; H 7.1; N 11.0).

2-(Hydroxymethyl)-5-(aminomethyl)-furan hydrochloride. Gaseous hydrogen chloride was passed into a solution of I (130 mg) in ether. The precipitate was removed by filtration, washed with ether and dried. The yield was 120 mg (72 %) of 2-(hydroxymethyl)-5-(aminomethyl)-furan hydrochloride [almost white crystals, m.p. 118–121° (Hershberg apparatus, *corr.*)]. (Found: C 44.3; H 6.2; N 8.5; Cl 21.2. Calc. for $C_6H_{10}O_2NCl$ (163.6): C 44.1; H 6.2; N 8.6; Cl 21.7).

2-(Acetoxymethyl)-5-(acetamidomethyl)-furan (IV). I (1.27 g) was dissolved in a mixture of acetic anhydride (15 ml) and pyridine (15 ml). The reaction mixture was left standing for 2 days and then evaporated in a vacuum. The residue was crystallized from ether. The yield was 1.93 g (92 %) of IV (white crystals, m.p. 65–67°). (Found: C 56.9; H 6.2; N 6.3; COCH₃ 38.5. Calc. for $C_{12}H_{17}O_5N_2$ (211.2): C 56.9; H 6.2; N 6.6; COCH₃ 40.8).

6-Methyl-3-pyridinol (III). I (1.27 g) was dissolved in a mixture of N hydrochloric acid (60 ml) and water (40 ml). The reaction mixture was heated under reflux (15 h) and then evaporated in a vacuum. The residue was dissolved in water (15 ml), solid potassium carbonate was added and the mixture continuously extracted with ether overnight. The ether extract was evaporated, the residue washed twice with ether and dried. The yield was 0.96 g (88 %) of III (light-brown crystals, m.p. 168–170°, previously found⁵ 167–169°). III gave a red color with aqueous ferric chloride. (Found: C 66.0; H 6.5; N 12.7. Calc. for C_6H_7ON (109.1): C 66.0; H 6.5; N 12.8). Sublimation (150°, 0.05 mm) gave white crystals, m.p. 169–171°.

Picrate. After crystallization from ethanol the m.p. was 205–208° (decomp.), previously found⁶ 203°. (Found: C 42.8; H 3.2; N 16.3. Calc. for $C_{11}H_{10}O_5N_4$ (338.2): C 42.6; H 3.0; N 16.6).

6-Methyl-3-pyridinol hydrochloride. In another experiment the reaction mixture was evaporated as described above. The residue was then sublimed (160°, 0.1 mm). The yield

was 75 % of 6-methyl-3-pyridinol hydrochloride (white crystals, m.p. 145–150°). (Found: C 49.6; H 5.7; N 9.9; Cl 24.1. Calc. for C_6H_7ONCl (145.6): C 49.5; H 5.5; N 9.6; Cl 24.4).

6-(Hydroxymethyl)-3-pyridinol (V). IV (1.70 g) and ammonium bromide (200 mg) were dissolved in methanol (15 ml) and the solution electrolyzed with the set-up described previously⁷ (temperature of cooling-bath -21°).

Time h	Current Amp.	Potential across the cell during electrolysis Volt	Ampere hours (% of theoretical amount)	
0.1	0.30	4.6	0.02	(5 %)
0.2	0.29	4.7	0.05	(12 %)
0.5	0.29	4.9	0.14	(33 %)
1.0	0.29	4.9	0.26	(60 %)
2.0	0.22	5.1	0.48	(111 %)

After electrolysis the liquid was poured into a solution of sodium methoxide (from 250 mg of sodium) in methanol (5 ml) and the methanol and the ammonia evaporated in a vacuum. Sodium hydroxide (3 N, 14 ml) was added, the mixture heated under reflux (18 h) and then continuously extracted with ether for 20 h. The ether was evaporated in a vacuum and the mixture heated under reflux (20 min) with hydrochloric acid (N, 15 ml). The mixture was evaporated to dryness in a vacuum and the residue then dissolved in water (15 ml). Solid potassium carbonate was added and the mixture continuously extracted with ether overnight. The ether extract was evaporated, the residue washed twice with ether and dried. The yield was 0.74 g (74 %) of V (light-brown crystals, m.p. 123–125°, previously found⁶ 124–125°). V gave a red color with aqueous ferric chloride (Found: C 57.6; H 5.8; N 10.8. Calc. for $C_6H_7O_2N$ (125.1): C 57.6; H 5.6; N 11.2). Sublimation (125°, 0.05 mm) gave white crystals, m.p. 123–125°.

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Received September 13, 1956.