

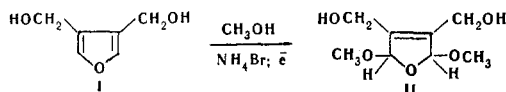
# ELECTROLYTIC METHOXYLATION OF 3,4-BIS(HYDROXY-METHYL)FURAN AND SYNTHESIS OF 4,5-BIS-(HYDROXYMETHYL)PYRIDAZINE

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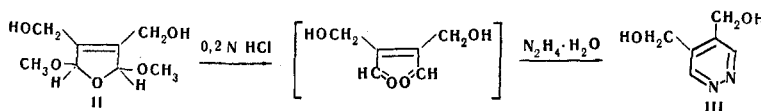
3,4-Bis(hydroxymethyl)furan was electrolytically methoxylated during intense cooling. 4,5-Bis(hydroxymethyl)pyridazine was obtained by reaction of the methoxylation product - 2,5-dimethoxy-3,4-bis(hydroxymethyl)-2,5-dihydrofuran - with hydrazine hydrate.

Previously one of us, together with Sadovaya and Baskina [1], has developed a method for the synthesis of 3,6-bis(hydroxymethyl)pyridazine from methoxylated 2,5-bis(hydroxymethyl)furan and hydrazine hydrate. To synthesize 4,5-bis(hydroxymethyl)pyridazine we subjected 3,4-bis(hydroxymethyl)furan (I) to electrolytic methoxylation [2,3] and found that the reaction proceeds successfully during intense cooling of the reaction mixture ( $-60^{\circ}\text{C}$ ) to give 57% of 2,5-dimethoxy-3,4-bis(hydroxymethyl)-2,5-dihydrofuran (II). At higher temperatures ( $-15$  to  $-20^{\circ}$ ) a significant amount of side products is formed, and the yield of II decreases sharply (to 25%).



We note that our attempts to methoxylate a homolog of I - 2,5-dimethyl-3,4-bis(hydroxymethyl)furan - were unsuccessful: only resinification products are formed, even on cooling to  $-60^{\circ}$  [4].

Hydrolysis of methoxylated diol II and subsequent reaction with hydrazine hydrate leads to a low yield (10%) of the previously unreported 4,5-bis(hydroxymethyl)pyridazine (III); the low yield is associated with the difficulty in isolating III from the reaction mixture.



## EXPERIMENTAL

**2,5-Dimethoxy-3,4-bis(hydroxymethyl)-2,5-dihydrofuran (II).** Electrolytic methoxylation was carried out in an electrolyzer with a nickel cathode and a graphite anode at 24 V and a current strength of 4-5 A [5]. A solution of 10 g (0.008 mole) of 3,4-bis(hydroxymethyl)furan (I) [bp  $108-109^{\circ}$  (1 mm),  $n_D^{20}$  1.5080] and 2.5 g of ammonium bromide in 150 ml of methanol was cooled to  $-60^{\circ}$  and electrolyzed for 3 h. The mixture was then poured into a sodium methoxide solution (0.8 g of sodium in 30 ml of methanol), the alcohol was distilled off in vacuo, a mixture of 300 ml of ether and 50 ml of acetone was added to the residue, and the inorganic precipitate was removed by filtration. After removal of the solvents the  $140-150^{\circ}$  (1 mm) fraction (10.5 g), which partially crystallized, was collected. The crystals of 2,5-dimethoxy-3,4-bis-(hydroxymethyl)-2,5-dihydrofuran (II) were isolated (4 g), and the viscous liquid was mixed with aluminum oxide and charged into a column filled with aluminum oxide. The contaminants were washed out with a chloroform-acetone mixture (2:1), and an additional quantity of II was extracted with an acetone-methanol

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mixture (10:1). The overall yield of II, which was colorless crystals with mp 108° (from benzene-hexane), was 8.4 g (57%). Found %: C 50.18, 50.72; H 7.53, 7.42.  $C_8H_{14}O_5$ . Calculated %: C 50.53; H 7.42. PMR spectrum\*:  $\delta$  3.12 (OH),  $\delta$  3.39 (OCH<sub>3</sub>),  $\delta$  4.28 (CH<sub>2</sub>),  $\delta$  5.72 (CH).

4,5-Bis(hydroxymethyl)pyridazine (III). Compound II (5 g) was heated for 10 min with 50 ml of 0.2 N hydrochloric acid on a boiling water bath, the mixture was cooled to 10-15°, and 3.5 ml of 95% hydrazine hydrate was added with stirring. After heating for 0.5 h on a boiling water bath, the mixture was cooled and extracted with ethyl acetate in a liquid extractor for 50 h. After removal of solvent 0.38 g (10%) of III was obtained in the form of light-yellow crystals with mp 123-124° (from ethyl acetate). Found %: C 51.09, 51.31; H 5.61, 5.70; N 20.31.  $C_6H_8N_2O_2$ . Calculated %: C 51.43; H 5.71; N 20.00.

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\*The spectrum was obtained with a JNM-4H-100 spectrometer, the solvent was deuteriochloroform, and the chemical shifts are given in parts per million with respect to the signal of tetramethylsilane, which is taken as zero.