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# SYNTHESIS OF 4-(HYDROXYMETHYL)TETRAHYDRO-4-PYRANOL — A NEW INTERMEDIATE FOR THE PREPARATION OF SYNTHETIC CITRIC ACID

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The hydroxylation of 4-methylenetetrahydropyran with hydrogen peroxide in the presence of various acidic catalysts was investigated. The oxidation of 4-(hydroxymethyl)tetrahydro-4-pyranol with concentrated nitric acid leads to citric acid in 50% yield.

In the present communication we describe the results of the hydroxylation of 4-methylenetetrahydropyran (I) to 4-(hydroxymethyl)tetrahydro-4-pyranol (II). We became interested in the synthesis of tetrahydropyranol II in connection with the fact that citric acid, which, up until now, has been obtained almost exclusively by the biochemical oxidation of foodstuffs, can be synthesized by direct oxidation of II.

Taking into account data on the hydroxylation of olefins [1] and the double bond of dihydropyrans [2-4] we investigated the oxidation of I with hydrogen peroxide in the presence of various acidic catalysts. We showed that methylenetetrahydropyran I is readily oxidized by this reagent to give glycol II in good yields. The reaction is catalyzed by $Na_2WO_4 \cdot 2H_2O$, $NH_4NO_3$, $H_2MoO_4$, $H_2WO_4$, $Cr_2O_3$, and $CrO_3$. The best yields of glycol II were obtained when the reaction was carried out in the presence of sodium tungstate at 50-60°C and $H_2O_2$:I ratios of 1:1 to 1:1.5. It should be noted that even 2% (by mass) of this catalyst ensures a 96% yield of glycol II.

The $H_2O_2$—formic acid system is also a good reagent for the hydroxylation of II. Similar oxidation can be accomplished with aqueous potassium permanganate solution.

Taking into account the possibility of oxidation of primary alcohols [5] and oxacyclanes [6, 7] to carboxylic acids upon reaction with nitric acid, we investigated the behavior of 4-(hydroxymethyl)tetrahydro-4-pyranol under the influence of this reagent. We showed that, as expected, nitric acid readily oxidizes glycol II to give citric acid in 50% yield.

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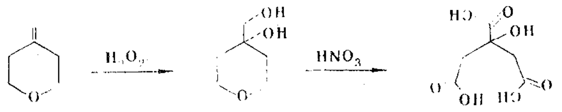
Thus we established that the synthesis of citric acid from I in practically acceptable yields is actually realizable.



## EXPERIMENTAL

The PMR spectra of solutions in $CHCl_3$ were obtained with a Perkin—Elmer R-12 spectrometer (60 MHz) with tetramethylsilane as the internal standard. Gas—liquid chromatography (GLC) was realized with 100- and 200-cm long columns packed with 10% PEG-20M on Inerton AW-HMDS and 5% SE-30 on Chromaton A-AW-HMDS; the carrier gas (helium) flow rate was 40-60 ml/min, and the temperature was 140-180°C.

4-(Hydroxymethyl)tetrahydro-4-pyranol (II). A 49-g (500 mmole) sample of 4-methyltetrahydropyran and the catalyst were placed in a flask equipped with a reflux condenser, a thermometer, and a dropping funnel, the mixture was heated with stirring to 45-50°C, and 85 ml of 30% hydrogen peroxide was added dropwise in the course of 1.5 h. Stirring was then continued for 25-30 h, after which the excess water was removed with a rotary evaporator at 45-50°C, and the residue was distilled *in vacuo* to give glycol II, with bp 129-130°C (6 mm), $n_D^{20}$ 1.4875, and $d_4^{20}$ 1.1864, in 45% yield. This product crystallized on standing to give a solid with mp 57°C. IR spectrum: 3300-3500 $cm^{-1}$ (OH). PMR spectrum: 1.68 (m, 3- and 5-H), 3.89 (m, 2- and 6-H), 3.54 (s, 4'-H), and 4.11 ppm (broad signal, OH). Found: C 54.3; H 9.8%. $C_6H_{12}O_3$. Calculated: C 54.5; H 9.1%. Oxidation with potassium permanganate was carried out by the method in [9].

Oxidation of Tetrahydropyran I with Hydrogen Peroxide in Formic Acid. A 20 ml (200 mmole) sample of 30% hydrogen peroxide was added dropwise slowly at 30-35°C to a solution of 9.8 g (100 mmole) of I in 50 ml of formic acid, after which the temperature was raised to 50°C, and stirring was continued for 40 h. The excess water was then removed by distillation, and the residue was distilled *in vacuo* to give 11.8 g (89%) of glycol II.

Citric Acid. A 100-ml sample of 65% nitric acid was heated until nitrogen oxides began to evolve (40-50°C), at which point 1 g of glycol II was added with stirring. An exothermic reaction ensued, and the reaction mixture was cooled to 30°C, and another 12.2 g (for a total of 100 mmole) of glycol II was added at this temperature. The temperature was raised to 60°C, and the mixture was stirred for another 24 h. The water and nitric acid were then removed by distillation, two 50-ml portions of water were added successively to the residue, and the aqueous mixture was distilled and evaporated to dryness on a water bath. The yield of citric acid, with mp 152°C (from water), was 9.6 g (50%).

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