When ethanol solutions of the purple compound are treated with sodium bisulfite or sodium dithionite ($Na_2S_2O_4$) the purple color fades to yellow. Treatment of the yellow solution with a solution of hydrogen peroxide or shaking it in the presence of air restores the original purple color. Reaction of a chloroform solution of the purple compound with lead tetraacetate results in the formation of a yellow solution which cannot be restored to its original purple color by treatment with reducing agents.

Formation of Gossycaerulin During Cooking of Cottonseed.—As shown in Table V, the gossypol content of two lots of seed heated at 115° decreased sharply during the initial period of heating, increased slightly over a short period, and then decreased slowly as the period of heating was prolonged. On the other hand, the gossycaerulin contents of the cooked seed increased slowly throughout the entire period of cooking, and the *p*H decreased at approximately the same rate.

Summary

A blue pigment, gossycaerulin, has been prepared by heating acidified solutions of gossypol, and reaction conditions which favor the formation of this pigment have been determined.

The properties of purified gossycaerulin have shown it to be a polar, alpha hydroxy, quinonoid, oxidation product of gossypol. It exhibits a maximum blue color having an absorption maximum at 605 mμ in acid solution and is reversibly convertible into a non-polar, yellow, neutral form.

A yellow pigment has been detected as a by-product formed from gossypol during its conversion to gossycaerulin. A purple compound resulting from the reaction of gossycaerulin with sulfuric acid has been shown to exhibit the reactions of a quinonoid compound.

Gossycaerulin has been detected in cooked cottonseed, and the extent of its formation has been shown to be correlated with the disappearance of gossypol, the length of heating, and the *p*H developed during heating of the seed.

NEW ORLEANS, LOUISIANA RECEIVED JULY 26, 1946

[CONTRIBUTION FROM THE NORTHERN REGIONAL RESEARCH LABORATORY[1]]

The Preparation of Acetopropyl Alcohol and 1,4-Pentanediol from Methylfuran[2]

BY L. E. SCHNIEPP, H. H. GELLER AND R. W. VON KORFF[3]

Development of practical methods[4,5] for the conversion of furfural to methylfuran makes it of interest to investigate this material as an intermediate for organic syntheses.

Although methylfuran can be catalytically reduced to tetrahydromethylfuran,[5,6] the dihydrofurans appear to be more attractive starting materials, since they hydrolyze to give hydroxycarbonyl derivatives. It has been shown by Wilson,[7] for example, that δ-hydroxybutyraldehyde can be prepared from 2,3-dihydrofuran. Earlier work by Paul[8] had demonstrated that 4,5-dihydro-2-methylfuran hydrolyzes to acetopropyl alcohol which was later obtained by Topchiev[9] directly from methylfuran by a combination of hydrogenation and hydrolysis reactions.

Since Topchiev did not report the details of his experimental work, his method was reinvestigated to establish optimum conditions for this conversion. The complete hydrogenation of the reaction mixture to produce 1,4-pentanediol was also studied.

Results obtained show that acetopropyl alcohol can be prepared in 25–35% yields or 1,4-pentanediol in 50–60% yields by hydrogenating methylfuran in the presence of water and a very small amount of acidic materials. Hydrogenation in the presence of water alone did not effect cleavage of the furan ring. Small amounts of acidic materials were necessary to produce the desired difunctional aliphatic derivatives. Best yields and most readily reproducible results were obtained by using formic acid in concentrations of 0.01–0.10% by weight of the reaction mixture.

Investigations were carried out in dioxane or alcohol solutions and with water alone. The conversion of methylfuran to 1,4-pentanediol was conveniently accomplished by conducting the reaction in a two-phase, methylfuran–water mixture. The products were readily separated by fractional distillation of the aqueous solution of tetrahydromethylfuran and 1,4-pentanediol produced by the reaction. Use of a blending solvent was advantageous when acetopropyl alcohol was the desired product. This hydrogenation was interrupted when approximately 1 mole of hydrogen/mole of methylfuran had been absorbed and less unreacted methylfuran was recovered than from the two-phase water system.

Results of this investigation substantiate the mechanism of acetopropyl alcohol formation proposed by Topchiev.[9] Available evidence is in accord with the sequence of reactions

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(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

(2) Presented under the title "The Hydrogenation of Methylfuran in Aqueous Media" before the Division of Organic Chemistry, 109th Meeting of the American Chemical Society, Atlantic City, New Jersey.

(3) Present address: 712 Lincoln Avenue West, Minneapolis, Minnesota.

(4) W. A. Lazier, U. S. Patent 2,077,422 (April 20, 1937).

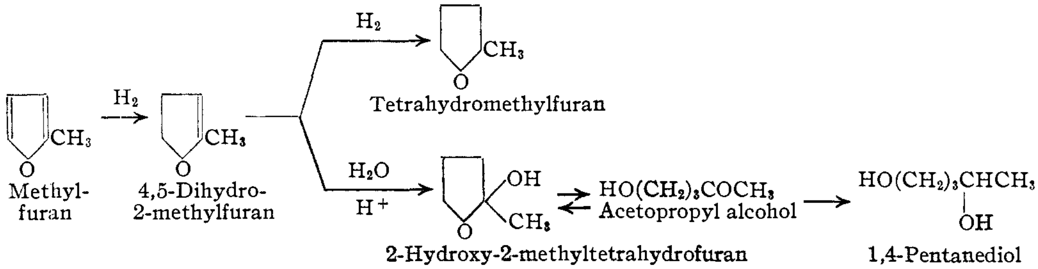
(5) L. W. Burnette, *Iowa State Coll. J. Sci.*, **19**, 9 (1944).

(6) R. Connor and H. Adkins, THIS JOURNAL, **54**, 4678 (1932).

(7) C. L. Wilson, *J. Chem. Soc.*, 48–51 (1945).

(8) R. Paul, *Bull. soc. chim.*, **53**, 417 (1933).

(9) K. Topchiev, *Compt. rend. Acad. Sci. U. R. S. S.*, **19**, 497–498 (1938); [*C. A.*, **32**, 8411 (1938)].



The reactions of 4,5-dihydro-2-methylfuran were studied on samples of this material prepared by dehydration of acetopropyl alcohol by the method of Kyrides and Zienty.[10] The ease with which this material hydrolyzed back to acetopropyl alcohol on treatment with water and a trace of acid indicates why it was impossible to isolate it from partially hydrogenated reaction mixtures.

This method of converting methylfuran to acetopropyl alcohol or 1,4-pentanediol appears to be applicable to the preparation of other δ-keto-alcohols, or 1,4-diols from other α-substituted furans. Furan, with its equivalent double bonds, does not undergo ring cleavage. Furfuryl alcohol, which might be expected to yield 1,4,5-pentanetriol, yielded only tetrahydrofurfuryl alcohol. Furfuryl acetate gave a very small yield of 1,4-dihydroxypentanol-5-acetate and vinylfuran was converted to 1,4-hexanediol in 37% yield, the other product being 2-ethyltetrahydrofuran.

Experimental

Methylfuran.—Methylfuran was prepared by the vapor phase hydrogenation of furfural over a copper chromite-on-activated charcoal catalyst by the method of Burnette.[4] Since this author did not give complete experimental details, further investigation was necessary. From numerous small-scale experiments the following apparatus was developed.

The reactor consisted of a 4-inch brass tube, 16 inches long, with short lengths of 2-inch copper tubing silver-soldered to the ends. These ends were machined to fit 55–50 ground glass joints. The tube was wrapped in four separate sections with Nicrome ribbon, so that heat could be applied to only the cooler sections of the reactor. Temperatures were measured by two thermocouples, one extending down the center of the reactor and the other near the wall.

The catalyst was prepared by intimately mixing 200 g. of copper chromite[11] with 2000 cc. of moist activated charcoal. The lower three sections of the reactor were filled with catalyst and porcelain Raschig rings were packed into the top section. This ring-packed section served as a preheater. The reactor was heated to a catalyst temperature of 250° and a slow stream of hydrogen was passed through the system for several hours before the furfural feed was started.

When the furfural feed was started, the reaction on the catalyst was highly exothermic and great care had to be exercised to prevent inactivation due to overheating. After this initial period of excessive activity the catalyst temperatures could be controlled by regulating the feed rate. A typical run was conducted as follows:

Freshly distilled furfural (1015.2 g.) was fed into the top of the catalyst chamber by means of a bellows-type proportioning pump at the rate of 2.24 g./min. Hydrogen measured by a gas flowmeter was fed concurrently to the reactor at the rate of 3.5 liters/min. (200% excess over theory). Heat was supplied to only the preheater and the bottom section of the tube since the heat of reaction was sufficient to maintain a temperature of 250° in the two center sections. The vapors from the bottom of the reactor entered a coil condenser in which the unreacted furfural, furfuryl alcohol, some of the methylfuran, and most of the water condensed. Uncondensed vapors consisting of hydrogen, methylfuran, and water were passed through Dry Ice cooled traps which removed the methylfuran and water. The total weight of condensed material was 1036.1 g. Fractional distillation gave 804 g. of methylfuran (92.5%) and small amounts of furfural and furfuryl alcohol.

1,4-Pentanediol. (1) **Dioxane–Water Solution.**—A solution of 41 g. (0.5 mole) of methylfuran in 400 cc. of dioxane, 100 cc. of water, and 0.5 cc. of formic acid was mixed with 5 g. of a freshly reduced nickel-on-Celite catalyst in a 3-liter rocking-type hydrogenation bomb.

The catalyst consisted of approximately 20% nickel on a Celite carrier and was prepared by precipitating nickel carbonate on Celite and reducing the washed and dried precipitate at 450° for one hour in a slow stream of hydrogen. The freshly reduced catalyst was kept in an atmosphere of nitrogen during transfer to the bomb.

The hydrogenation was conducted at an initial pressure of 1200 p. s. i. and a temperature of 150°. The theoretical amount of hydrogen was absorbed (2 moles per mole of methylfuran) in eight hours. The catalyst was removed by filtration and the reaction mixture carefully distilled through a 14-inch helices-packed column. The distillates consisted of the water azeotropes of tetrahydromethylfuran (b. p. 72–75°, 15 g., 35.7% yield) and dioxane (b. p. 87°). The residue (approximately 50 cc.) was distilled under reduced pressure to give 32 g. (61.6% yield) of 1,4-pentanediol (b. p. 114–115° at 14 mm.), d^{25}_4 0.982; n^{25}_D 1.4452.

By decreasing the formic acid from 0.5 to 0.2 cc. the reaction was completed in two to three hours and a 50% yield of 1,4-pentanediol was obtained.

(2) **Water Alone.**—A mixture of 410 g. of methylfuran, 500 cc. of water, 0.3 cc. of formic acid, and 10 g. of nickel-on-Celite catalyst was charged into a 3-liter hydrogenation bomb. The reaction was complete in four hours. Distillation of the reaction mixture as described above gave 187.9 g. of tetrahydromethylfuran (43.6% yield) and 260.0 g. of 1,4-pentanediol (50.0% yield).

Acetopropyl Alcohol.—Acetopropyl alcohol was prepared from methylfuran by stopping the hydrogenation of a dioxane solution of water and methylfuran when 40–50% of the theoretical amount of hydrogen had been consumed.

A mixture of 246 g. of methylfuran, 1000 cc. of dioxane, 300 cc. of water, 0.3 cc. of formic acid, and 5 g. of nickel-on-Celite catalyst was hydrogenated in a 3-liter bomb at 150° and a hydrogen pressure of 1500 p. s. i. The reaction was stopped when in ninety minutes approximately 1 mole of hydrogen/mole of methylfuran had been absorbed. The catalyst was removed by filtration and 0.2 *N* sodium hydroxide added to the filtrate to a phenolphthalein alkalinity. Fractional distillation of the reaction mixture at atmospheric pressure gave 73.3 g. (30.5% of original) of methylfuran, 76.6 g. (29.7% yield) of tetrahydromethylfuran, dioxane, water, and a higher boiling residue.

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[10] L. P. Kyrides and F. B. Zienty, THIS JOURNAL, **68**, 1385 (1946).

[11] W. A. Lazier and H. R. Arnold, "Organic Syntheses," Coll. Vol. II, p. 142.

This residue was distilled under reduced pressure to give 94.6 g. (30.9%) of acetopropyl alcohol and 12.2 g. (3.9%) of 1,4-pentanediol. The acetopropyl alcohol had the properties: b. p. 75° (3 mm.); $d^{25}{}_4$ 0.993; $n^{25}{}_D$ 1.4350.

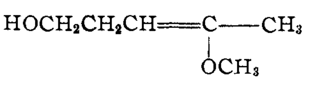
4,5-Dihydro-2-methylfuran.—This dihydromethylfuran was prepared from acetopropyl alcohol by the method of Kyrides and Zienty.[10] Acetopropyl alcohol (25 g.) was heated to boiling at atmospheric pressure in a flask equipped with a 14" × 3/4" helices-packed column. Distillate temperature did not exceed 72°. Near the end of the distillation heat was applied to the column to prevent excessive holdup.

The distillate consisting of water and dihydromethylfuran was transferred to a separatory funnel and the water layer removed. The dihydromethylfuran (19 g., 92.3%) contained a trace of water. After standing for twelve hours this water had reacted; redistillation gave pure dihydromethylfuran (b. p. 80°, $n^{25}{}_D$ 1.4290, $d^{25}{}_4$ 0.895) and a trace of acetopropyl alcohol.

This method was used by Kyrides and Zienty[10] to separate acetopropyl alcohol from 1,4-pentanediol. The dihydromethylfuran is readily converted back to acetopropyl alcohol by reaction with water catalyzed by a trace of acid.

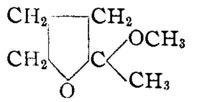
2-Methoxy-2-methyl-tetrahydrofuran.—4,5-Dihydro-2-methylfuran (10 g.) was dissolved in 10 cc. of methyl alcohol containing two drops of acetic acid. The temperature of the solution rose to 39° and remained there for fifteen minutes. The reaction mixture was then refluxed on a steam-bath for an additional fifteen minutes after which the acid was neutralized by addition of an excess of sodium methoxide. The undissolved solid was removed by filtration and the filtrate distilled. 2-Methoxy-2-methyl-tetrahydrofuran, having a menthol-like odor, was obtained in 88.6% yield: b. p. 114.5°; $n^{25}{}_D$ 1.4110; $d^{25}{}_4$ 0.932. *Anal.* Calcd. for $C_6H_{12}O_2$: C, 62.07; H, 10.34; OCH_3, 26.72. Found: C, 61.96; H, 10.36; OCH_3, 25.90.

Reasoning by analogy with the hydrolysis product from 4,5-dihydro-2-methylfuran the alcoholysis product may have either an open-chain or cyclic structure illustrated by formulas I and II



$$\mathrm{HOCH_2CH_2CH{=\!=}\underset{\displaystyle OCH_3}{C}{-\!-}CH_3}$$

I



II

Molar refractivity of the compound obtained indicates the cyclic form (II). *Anal.* M_D found, 30.90. M_D calcd. for I, 32.61; for II, 30.99.

Treatment of 10 g. of 2-methoxy-2-methyl-tetrahydrofuran with 10 cc. of water effected a rapid hydrolysis to give methanol and acetopropyl alcohol (6.5 g.).

Summary

Methylfuran has been converted to 1,4-pentanediol in 50–60% yields by hydrogenation in the presence of water and a trace of acid.

Acetopropyl alcohol was prepared in 25–35% yield by interrupting the reaction after absorption of 1 mole of hydrogen/mole of methylfuran.

The reversible conversion of acetopropyl alcohol to 4,5-dihydro-2-methylfuran confirms a previously proposed mechanism by which 2-methylfuran is converted to acetopropyl alcohol.

2-Methoxy-2-methyl-tetrahydrofuran, a new compound having a menthol-like odor, has been prepared by methalcoholysis of 4,5-dihydro-2-methylfuran.

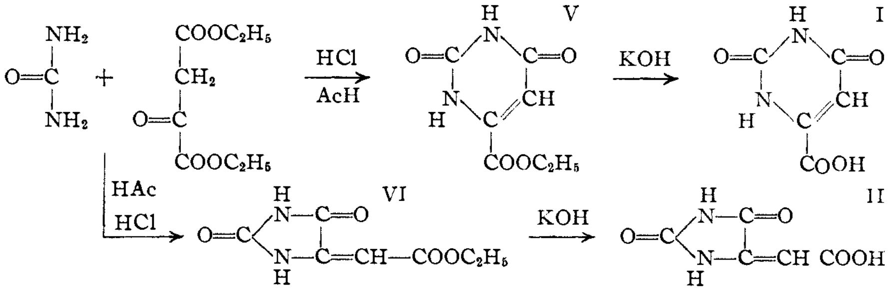
PEORIA 5, ILL. RECEIVED SEPTEMBER 30, 1946

[CONTRIBUTED FROM KERCKHOFF LABORATORIES OF BIOLOGY, CALIFORNIA INSTITUTE OF TECHNOLOGY]

Intermediates in the Synthesis of Orotic Acid from Oxalacetic Ester and Urea

BY HERSCHEL K. MITCHELL AND JOSEPH F. NYC

Müller in 1897[1] reported the synthesis of a compound, through condensation of oxalacetic ester and urea, to which he assigned a structure corresponding to an ester of 4-carboxy-uracil. This substance received little attention until after the isolation from milk, by Biscaro and Belloni,[2] of a nitrogenous heterocyclic acid (orotic acid). Although these investigators assigned a seven-membered ring structure to the acid, it was pointed out by Wheeler, Johnson and Johns[3] that the empirical formula was identical with that of a carboxyl derivative of uracil. The latter workers synthesized 5-carboxyuracil and found that this substance was not identical with orotic acid. The ester prepared by Müller[1] was then re-examined by Wheeler,[4] who considered that the synthesis might result in either a pyrimidinecarboxylic acid (I) or a substituted hydantoin (II) in accordance with the reactions



The acid obtained was identified as 4-carboxyuracil by conversion to 5,5'-dibromo-barbituric acid (III) with bromine water. On treatment with bromine water 5-(carboxy-methylidene)-

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(1) R. Müller, *J. prakt. Chem.*, **56**, 480 (1897).

(2) G. Biscaro and E. Belloni, *Ann. Soc. Chim. Milano*, XI, fasc I and II (1905); *Chem. Zentr.*, [II] **63**, 64 (1905).

(3) R. L. Wheeler, T. B. Johnson and C. O. Johns, *Am. Chem. J.*, **37**, 392 (1907).

(4) H. L. Wheeler, *ibid.*, **38**, 358 (1907).