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# Electrolytic Methoxylation of 2-Acetylfuran

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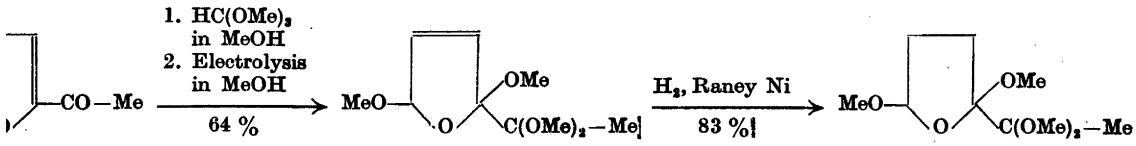
2-Acetylfuran has been methoxylated by transformation into the dimethyl ketal and electrolysis in methanol. Reaction of the resulting 2,5-dimethoxy-2-(α,α-dimethoxyethyl)-2,5-dihydrofuran (I) with an aqueous solution of hydroxylamine hydrochloride gave 2-methyl-3,6-pyridinediol-1-oxide (IV). This compound has previously been prepared by Vargha, Ramonczai and Bite, who believed it to be an aldoxime of 2-hexene-4,5-dione-1-al(III). I was catalytically hydrogenated to 2,5-dimethoxy-2-(α,α-dimethoxyethyl)-tetrahydrofuran (II), which by heating with dilute hydrochloric acid yielded pyrocatechol.

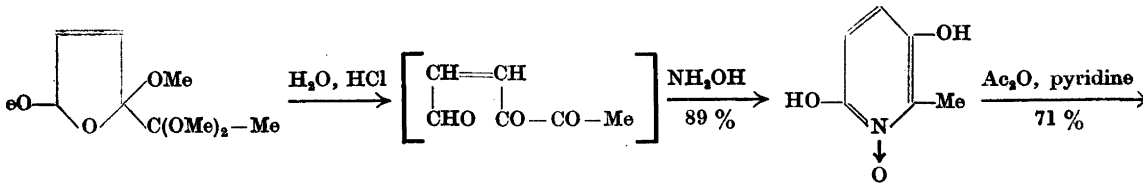
As part of an investigation of the electrolytic methoxylation of furans, reaction conditions have been worked out for the methoxylation of 2-acetylfuran. The furan is first heated under reflux with methanol, methyl orthoformate and a trace of *p*-toluenesulfonic acid, and the resulting solution, which probably contains 2-acetylfuran dimethyl ketal, is then electrolyzed. Analyses showed the reaction product to be the expected 2,5-dimethoxy-2-(α,α-dimethoxyethyl-2,5-dihydrofuran (I). Catalytic hydrogenation of I gave the corresponding tetrahydrofuran II.



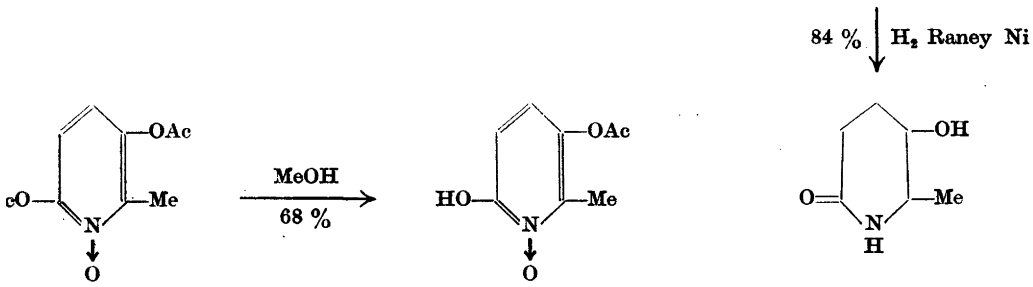

I II

By reaction of I with an aqueous solution of hydroxylamine hydrochloride an 89 % yield of a compound $C_6H_7O_3N$ (m.p. 236°), which was soluble in alkali, sparingly soluble in water and alcohol and insoluble in ether, was obtained. It gave a strong violet ferric chloride reaction. Acetylation of this compound yielded a diacetate, which was transformed by solution in methanol into a monoacetate. The diacetate gave a red ferric chloride reaction after some seconds, while the monoacetate gave the same reaction immediately. Catalytic

hydrogenation of the $C_6H_7O_3N$-compound yielded a compound $C_6H_{11}O_2N$, which gave no ferric chloride reaction. Assuming the $C_6H_7O_3N$-compound to be 2-methyl-3,6-pyridinediol-1-oxide (IV), these experiments may be explained as shown below.

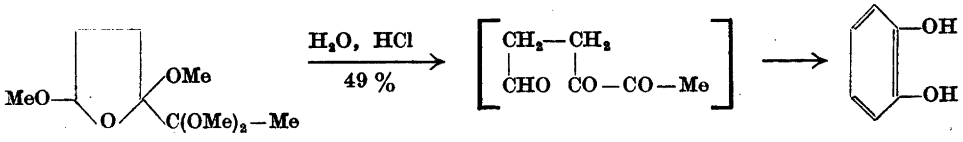



I III IV




V VI VII

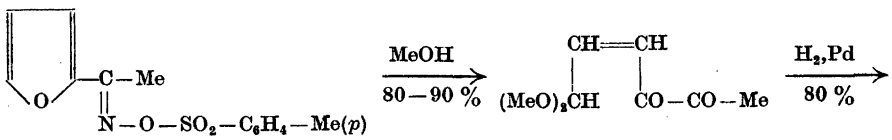
By heating of II with dilute hydrochloric acid, pyrocatechol is formed in a 49 % yield. Evidently hydrolysis to hexane-4,5-dione-1-al (VIII) followed by intramolecular condensation takes place.



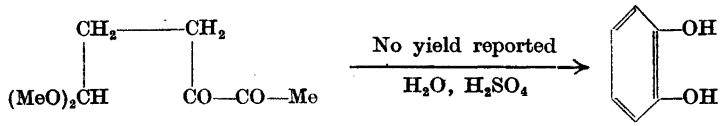

II VIII

Vargha, Ramonczai and Bite[1] have reported that treatment of the *p*-toluenesulfonate of 2-acetylfuran oxime (IX) with methanol results in the formation of a liquid $C_8H_{12}O_4$, which may be catalytically hydrogenated to another liquid $C_8H_{14}O_4$. The $C_8H_{12}O_4$-liquid gave, with an aqueous solution of hydroxylamine hydrochloride, a compound $C_6H_7O_3N$ with properties similar to our $C_6H_7O_3N$-compound (2-methyl-3,6-pyridinediol-1-oxide (IV)). The $C_8H_{14}O_4$-liquid gave pyrocatechol by heating with dilute sulfuric acid. These reactions were explained by Vargha, Ramonczai and Bite as shown below.

The $C_6H_7O_3N$-compound was assumed to be an aldoxime of 2-hexene-4,5-dione-1-al (III).




IX X




XI

Vargha, Ramonczai and Bite did not report any spectra, refractive indices or methoxy values for their liquids, so that it is not certain whether these actually have been pure compounds with the proposed structures (X and XI) or not. It is, however, apparent from the published data, and also in conformity with our findings, that the liquids as claimed are derivatives of 2-hexene-4,5-dione-1-al (III) and hexane-4,5-dione-1-al (VIII), respectively. The $C_6H_7O_3N$-compound, which evidently is identical with our $C_6H_7O_3N$-compound, must on the other hand be 2-methyl-3,6-pyridinediol-1-oxide (IV).

## EXPERIMENTAL

Microanalyses by E. Boss and K. Glens

*2,5-Dimethoxy-2-(α,α-dimethoxyethyl)-2,5-dihydrofuran (I).* 2-Acetylfuran (3.30 g, 0.030 mole) and methyl orthoformate (3.50 g, 0.033 mole) was added to a solution of *p*-toluenesulfonic acid (8.6 mg) in anhydrous methanol (10 ml) and the mixture heated under reflux (10 min). After cooling a solution of ammonium bromide (0.60 g) in methanol (30 ml) was added and the mixture electrolyzed in the small cell described previously [2] (temperature of cooling-bath −18°).

| Time hr | Current amp | Potential across the cell during electrolysis volt | Ampere hours (per cent of theoretical amount) | |
|---|---|---|---|---|
| 0.1 | 1.0 | 4.8 | 0.09 | (6 %) |
| 0.5 | 0.9 | 5.0 | 0.43 | (27 %) |
| 1.0 | 0.8 | 5.1 | 0.81 | (50 %) |
| 2.5 | 0.6 | 5.2 | 1.68 | (104 %) |

After electrolysis the yellow liquid was poured into a solution of sodium methoxide (from sodium (147 mg) in methanol (5 ml)) and the methanol and the ammonia evaporated in a vacuum. Anhydrous ether (50 ml) was added, the precipitate removed by filtration and the filtrate distilled in a vacuum.

| Fraction (g) | B.p.$_{14}$ °C | $n_D^{25}$ |
|---|---|---|
| 1 (0.30) | 108–112 | 1.4502 |
| 2 (3.37) | 112–113 | 1.4498 |
| 3 (0.48) | 113–115 | 1.4499 |

The yield (all fractions) was 4.15 g (64 %, current efficiency 62 %) of I (colorless liquid). A portion of fraction 2 was analyzed.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $C_6H_8O(OCH_3)_4$ (218.2) | Calc. | C | 55.0 | H | 8.3 | $OCH_3$ | 56.9 |
| | Found | » | 55.1 | » | 8.2 | » | 55.4 |

All fractions gave a positive Beilstein test for halogens, thus indicating, that the product is contaminated by a small amount of some bromine-containing impurity.

*2,5-Dimethoxy-2-(α,α-dimethoxyethyl)-tetrahydrofuran (II).* I (3.00 g), anhydrous methanol (15 ml) and potassium hydroxide (11 mg) were shaken (4 hr) with Raney nickel (0.3 g) under hydrogen (100 atm). The product was isolated by distillation.

| Fraction (g) | B.p.$_{14-15}$ °C | $n_D^{25}$ | Calc. for $C_6H_8O(OCH_3)_4$ (220.3) | | |
|---|---|---|---|---|---|
| | | | C 54.5% | H 9.2% | $OCH_3$ 56.4% |
| 1 (0.31) | 116 | 1.4390 | 54.2 | 9.2 | 54.0 |
| 2 (2.21) | 118–119 | 1.4387 | 54.7 | 9.0 | 55.3 |

The yield (both fractions) was 2.52 g (83 %) of II (colorless liquid).

*2-Methyl-3,6-pyridinediol-1-oxide (IV).* I (0.44 g, 0.002 mole) was dissolved in water (5 ml) and the solution added to a solution of hydroxylamine hydrochloride (0.21 g, 0.003 mole) in water (2 ml). The mixture was left standing for 15 minutes whereby white crystals precipitated. The crystals were removed by filtration, washed twice with water and dried. The yield was 0.25 g (89 %) of IV (white needles, m. p. 220–230° (dec.) (Hershberg apparatus, corr.)) Crystallization from ethanol gave 0.21 g (75 %), m. p. in evacuated tube 234–236° (dec.). Vargha, Ramonczai and Bite[1] found m. p. 236° for their $C_6H_7O_2N$-compound.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $C_6H_7O_2N$ (141.1) | Calc. | C | 51.1 | H | 5.0 | N | 9.9 |
| | Found | » | 50.8 | » | 5.4 | » | 10.0 |

IV was sparingly soluble in water and insoluble in ether. It gave a strong violet color with ferric chloride.

*2-Methyl-3,6-diacetoxypyridine-1-oxide (V).* A mixture of IV (0.42 g), pyridine (5 ml) and acetic anhydride (5 ml) was heated to boiling, left standing for 5 minutes, cooled and evaporated in a vacuum. Addition of ether to the residue gave 0.32 g of V (almost colorless crystals, m. p. 96–98°).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $C_6H_5O_2N(COCH_3)_2$ (225.2) | Calc. | C | 53.3 | H | 4.9 | N | 6.2 | $COCH_3$ 38.2 |
| | Found | » | 53.2 | » | 4.9 | » | 6.0 | » 39.0 |

From the filtrate another 0.16 g of V (white crystals, m. p. 96—98°) was obtained, the total yield of V thus being 0.48 g (71 %).

Found C 53.4 H 5.2 N 6.2 $COCH_3$ 38.4

V gave a red color with aqueous ferric chloride after some seconds.

*2-Methyl-3-acetoxy-6-pyridinol-1-oxide (VI).* V (90 mg) and methanol (2 ml) were heated to boiling and twice partly evaporated with ether, whereby white crystals were obtained. The yield was 50 mg (68 %) of VI (white crystals, m. p. 129—131°).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $C_6H_6O_2N(COCH_3)$ | (183.2) | Calc. | C | 52.5 | H | 5.0 | N 7.7 | $COCH_3$ 23.5 |
| | | Found | » | 52.5 | » | 5.2 | » 7.5 | » 23.3 |

VI gave instantaneously a red color with aqueous ferric chloride.

*5-Hydroxy-6-methyl-2-piperidone (VII).* IV (1.00 g) and anhydrous methanol (30 ml) were shaken (1 hr) with Raney nickel (0.4 g) under hydrogen (100 atm, 100° C). The Raney nickel was removed by filtration and the filtrate evaporated in a vacuum. The white crystalline residue was crystallized from methanol. The yield was 0.67 g of VII (white crystals, m. p. 178—180°; recrystallization from methanol-ether did not change the m. p.).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $C_6H_{11}O_2N$ | (129.2) | Calc. | C | 55.8 | H | 8.6 | N 10.9 |
| | | Found | » | 56.0 | » | 8.9 | » 10.7 |

Addition of ether to the mother liquor and crystallization from methanol of the crystals obtained gave another 0.10 g of VII (white crystals, m. p. 177—179°), the total yield of VII thus being 0.77 g (84 %).

VII gave no coloration with aqueous ferric chloride.

*Acetate of VII.* A mixture of VII (100 mg), pyridine (2 ml) and acetic anhydride (2 ml) was heated to boiling and then evaporated in a vacuum. The white crystalline residue was boiled with ether. The yield was 90 mg (68 %) of 5-acetoxy-6-methyl-2-piperidone (white crystals, m. p. 169—172°).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $C_6H_{10}O_2N(COCH_3)$ | (171.2) | Calc. | C | 56.1 | H | 7.7 | N 8.2 | $COCH_3$ 25.1 |
| | | Found | » | 56.5 | » | 8.0 | » 8.0 | » 25.2 |

*Hydrochloride of VII.* VII (100 mg) dissolved in methanol (2 ml) and methanol (1 ml), to which had been added acetyl chloride (0.08 ml), were mixed and the hydrochloride precipitated with ether, removed by filtration, washed with ether and dried. The yield was 120 mg (94 %) of 5-hydroxy-6-methyl-2-piperidone hydrochloride (white crystals, m. p. 146—149°).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $C_6H_{12}O_2NCl$ | (165.6) | Calc. | C | 43.5 | H | 7.3 | N 8.5 | Cl 21.4 |
| | | Found | » | 43.1 | » | 7.4 | » 8.0 | » 21.3 |

*Pyrocatechol from II.* II (4.56 g) and *N* hydrochloric acid (45 ml) were mixed and heated under reflux (2 hr). The light-brown mixture was cooled and saturated with sodium hydrogen carbonate. A small amount of an insoluble oil was removed and the mixture extracted continuously with ether. The etheral extract was dried with magnesium sulfate and distilled in a vacuum. The yield was 1.12 g (49 %) (light-brown crystals, b. $p._1$ 88—90°, m. p. 97—102°). Crystallization of 200 mg from ether-petroleum ether gave 160 mg of almost white crystals, m. p. 100—103°.

| | | | | | | |
|---|---|---|---|---|---|---|
| $C_6H_6O_2$ | (110.1) | Calc. | C | 65.4 | H | 5.5 |
| | | Found | » | 65.1 | » | 5.6 |

The crystals gave no m. p. depression when mixed with an authentic specimen of pyrocatechol.

## REFERENCES

1. Vargha, L., Ramonczai, J. and Bite, P. *J. Am. Chem. Soc.* **70** (1948) 371.
2. Limborg, F. and Clauson-Kaas, N. *Acta Chem. Scand.* **7** (1953) 234.

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