

Nuclear Oxidation of Furfural

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It has been demonstrated that 1,4-addition products come into existence when furan is oxidized under proper conditions with the following reagents:

- a. Bromocyanogen ¹.
- b. Atmospheric oxygen ².
- c. Nitric acid in acetic acid anhydride ³ (Marquis' reagent ⁴).
- d. Osmium tetroxide and hydrogen peroxide in alcohol ⁵ (Milas' procedure ⁶).
- e. Bromine in alcohol ⁷ (Meinel's procedure ⁸).
- f. Lead tetraacetate ⁷.
- g. Bromine in acetic acid in the presence of potassium acetate ⁹.
- h. Peracids.

It was concluded that, in general, reactions between furans and oxidizing reagents as a rule are initiated by a 1,4-addition of the reagent to the double bonds of the furan nucleus, the only alternative being a so-called direct β -substitution ⁷.

In this communication the oxidation of furfural is discussed with special regard to the structure of addition products which have earlier been obtained from furfural by oxidation. The preparation of the stable 2,5-dimethoxy-2,5-dihydrofurfural diacetate is described and the structure proved by oxidative degradation.

Furfural has frequently been oxidized to maleic acid or to compounds, which are formed by further action of the reagent on maleic acid. In some cases maleic acid aldehyde has been isolated together with formic acid ^{10, 11} or carbon dioxide ¹². An explanation of the formation of these compounds based upon the conception of 1,4-addition has earlier been given (Milas ¹², Dunlop, Stout and Swadesh ¹¹ and Clauson-Kaas ⁷). The well known oxidations of furfural to mucobromic and mucochloric acid with warm aqueous solutions of the halogens belong to the same type of reactions.

Cross, Bevan and Heiberg¹³ have oxidized furfural in water with Fenton's reagent at about 40°. The authors suggest that 3-hydroxyfurfural and 3-hydroxyfuroic acid are formed by the reaction. We believe that their 3-hydroxyfurfural, which was isolated as a phenylhydrazone in a 93 % yield, calculated on furfural, actually is maleic acid aldehyde. The proposed hydroxyfuroic acid, which was isolated as a barium salt, was obtained in a 5 % yield. It is highly improbable, that the acid is 3-hydroxyfuroic acid and we suggest that it has the formula I and is a product of hydrolysis of an intermediate 2,5-hydroxy-2,5-dihydrofuroic acid II. In this connection it should be mentioned that Milas¹² by the oxidation of furfural with vanadium pentoxide and sodium chlorate isolated the barium salt of a dicarboxylic acid with the formula $C_5H_4O_5$ which might have been formed by oxidation of I and consequently be a ketoglutaconic acid (III).

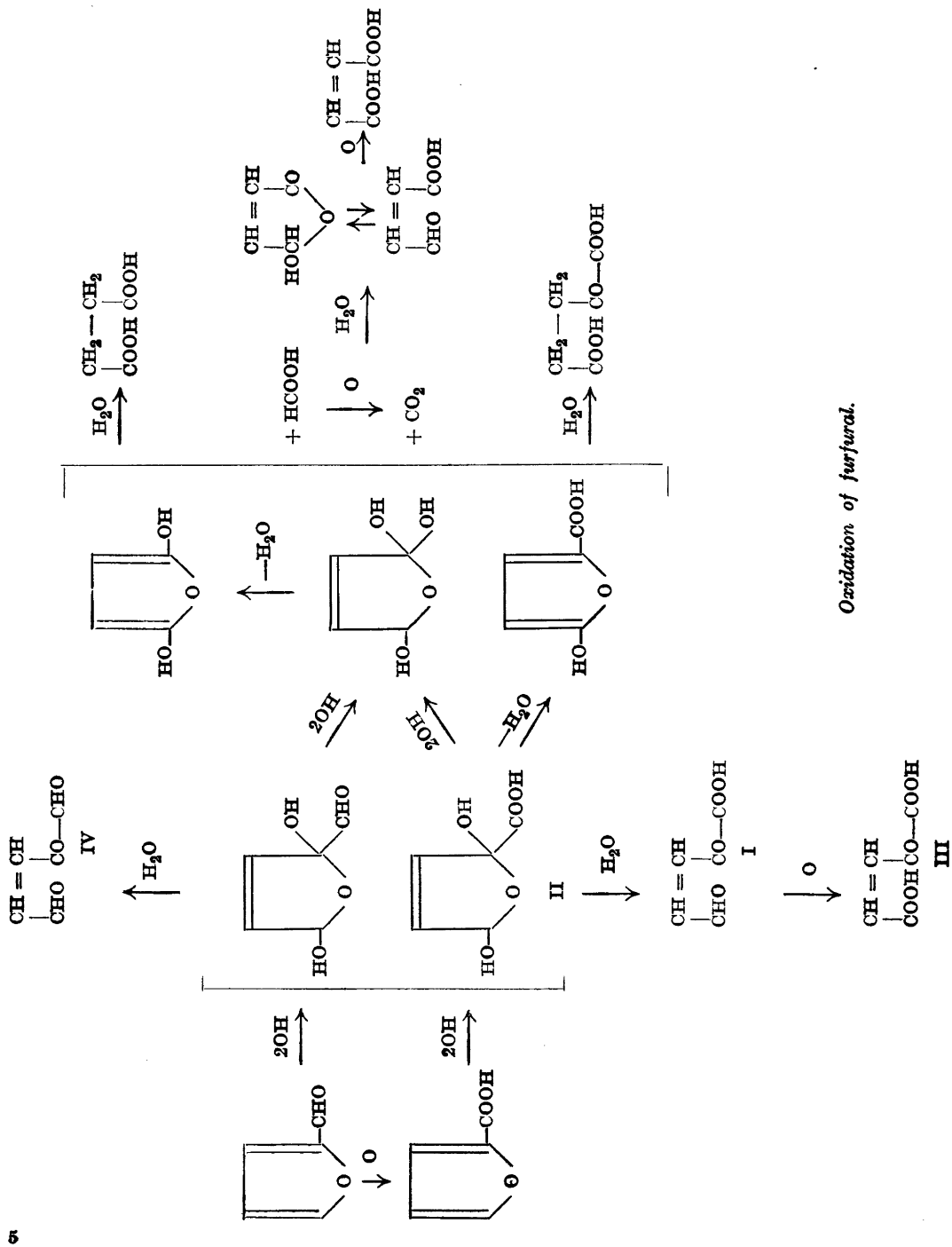
By the oxidation of furfural with Fenton's reagent, formic acid and acetic acid as well as compounds, which could be oxidized to iodoform, were also shown to be present in the reaction mixture. The identification of formic acid is in agreement with our interpretation of the reaction mechanism, but we are not able to explain how the other products may arise from the oxidation of furfural. Probably their formation is due to a content of 5-methylfurfural in the furfural employed.

Cross, Bevan and Briggs¹⁴ oxidized furfural with Caro's acid. Formic acid and succinic acid were obtained together with the barium salt of an acid with the formula $C_5H_6O_5$ and what was claimed to be 5-hydroxyfurfural, precipitated as phenylhydrazone and methylphenylhydrazone. We believe that the aldehyde isolated from this oxidation also is maleic acid aldehyde, while the acid probably is α -ketoglutaric acid. The formation of this acid as well as of succinic acid has previously been formulated as the result of a 1,4-elimination of water from the intermediate 2,5-dihydroxy-2,5-dihydrofurans⁷.

Hughes and Acree¹⁵ oxidized furfural with bromine in water at low temperature. Addition of phenylhydrazine to the reaction mixture yielded a red bis-phenylhydrazone of what was proposed to be a ketodihydrofurfural. We believe that furfural by this reaction is oxidized to 2-pentene-1,5-dial-4-one (IV) which in some way or other has condensed with two moles of phenylhydrazine.

‡ The formation of all above mentioned oxidation products of furfural may be expressed by the following sequence of reactions (see pag. 417; cf. Milas¹², Dunlop, Stout and Swadesh and Clauson-Kaas⁷).

Scheibler, Jeschke and Beiser¹⁶ have obtained an epoxide of furfural diacetate in an analytically pure state by the action of perbenzoic acid (yield 8 %). This compound was indifferent to bromination and catalytic hydrogenation



Oxidation of furfural.

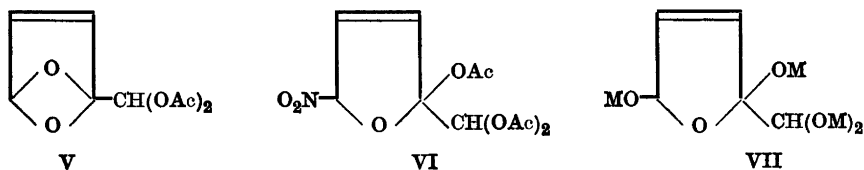
and was therefore assumed to possess a formula containing a diepoxycyclobutane ring and no double bonds. However, in view of what is known about the inertness of the 3,4-double bonds of certain 2,5-dihydrofurans⁷, the oxide may as well be a 1,4-addition compound with the formula V which would be consistent with the findings of Böeseken *et. al.*¹⁰ that furfural is oxidized with peracetic acid to maleic acid aldehyde (yield 40 %), maleic acid (7 %) and formic acid (100 %).

We have not repeated the experiments of Scheibler, Jeschke and Beiser but investigated the action of peracids on furan. It was found that when equimolar amounts of furan and peracid interact, the bis-phenylhydrazone of malealdehyde may be precipitated in a pure state by addition of phenylhydrazine to the reaction mixture. The highest yield obtained was 23 % of the theoretical amount. In spite of numerous preparations under various conditions it was not possible to improve this figure, but in judging the yield the lability and reactivity of the substances involved in the reaction should be considered.

The isolation of malealdehyde-bis-phenylhydrazone proves, that the peracids have been added to furan to yield 2,5-epoxy-2,5-dihydrofuran or its equivalent whereafter the addition product, either spontaneously or by the action of phenylhydrazine rearranges to malealdehyde.

The isolation of several oxidation products formed by the interaction of peracids and furans has been reported by Böeseken *et al.* and by Milas and McAlevy¹⁷, but the experimental evidence from these investigations is not sufficient to permit any deductions concerning the mechanism of this type of reaction. It therefore seems, that peracids behave like other oxidizing agents towards furans. It is of special interest in this connection to mention that this is also the case with atmospheric oxygen according to the experiments of Ciamician and Silber¹⁸, Schenk² and Dunlop, Stout and Swadesh.

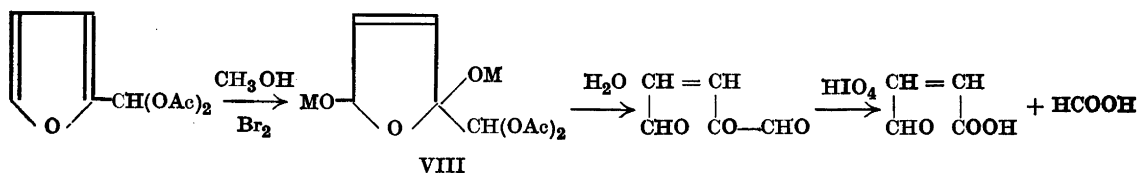
So far two stable addition products of furfural have been isolated in good yields and analyzed. Gilman and Wright¹⁹ prepared the nitroacetate of furfural diacetate by nitration of this compound according to the directions of Marquis, and Meinel¹⁸ obtained dimethoxy-dihydrofurfural dimethylacetal by methoxylation of furfural with methanolic bromine. We have earlier proposed formulas VI and VII for these compounds although other formulas were suggested by the above authors^{3, 7}.



Meinel reported that furfural diacetate can not be methoxylated, but we encountered no difficulties in preparing a dimethoxydihydrofurfural diacetate

by the action of bromine in methanol on furfural diacetate. The addition compound was a colourless, extremely viscous oil which could be purified by distillation in vacuum. The yield of the pure product was as high as 81 %. The addition of two methoxy groups was confirmed by analysis, methoxy, acetoxy and molecular weight determination.

In order to elucidate the structure, the dimethoxydihydrofurfural diacetate was hydrolyzed and oxidized with one mole of periodic acid. Maleic acid aldehyde was hereby isolated as phenylhydrazone (yield 70 %) and methylphenylhydrazone (yield 71 %). The identification of maleic acid aldehyde proves that the addition compound is 2,5-dimethoxy-2,5-dihydrofurfural diacetate (VIII). The periodic acid oxidation at the same time supports the theory, that the oxidation of furfural to maleic acid aldehyde proceeds through a 1,4-addition product.



The methylphenylhydrazone of maleic acid aldehyde melted at about the same temperature as the methylphenylhydrazone prepared by Cross, Bevan and Briggs. This substantiates the opinion expressed above that the 5-hydroxyfurfural of these authors is in fact maleic acid aldehyde.

EXPERIMENTAL

Oxidation of furan with peracids

The action of peracetic acid and perbenzoic acid on furan was investigated under various conditions. Moist and dry chloroform, ether, acetic acid anhydride and water were tested as solvents and the temperature was varied from zero to 40°. When the peracid had disappeared, phenylhydrazine was added and the malealdehyde bis-phenylhydrazone filtered off and weighed. Several preparations yielded about 20 % of the theoretical amount of the hydrazone, but this figure was never surpassed substantially. No difference in the action of the two peracids was observed. Details of a typical experiment are given below:

280 mg of freshly distilled furan were added to 9.8 ml of 0.42 *M* perbenzoic acid in moist chloroform and the mixture left standing over night at zero. The next day 95 % of the peracid had disappeared. 2.00 ml of the reaction mixture were added to a solution of 0.2 ml of phenylhydrazine in 0.3 ml of alcohol. The hydrazone precipitated immediat-

ely and was filtered off, washed with benzene and dried in vacuum; yield 44 mg = 20 %. Yellow crystals, m. p. 172° (Kofler stage, corr.); previously³ found 171°.

$C_{16}H_{16}N_4$ (264) Calc. N 21.21 Found N 21.23

2,5-Dimethoxy-2,5-dihydrofurfural diacetate

Preparation. 19.8 g (0.1 mole) of furfural diacetate were methoxylated and the reaction product isolated in the usual manner⁷. The methanolic solution of bromine was added during 45 minutes and the temperature kept at about 15°. The ethereal layer was shaken with 50 ml of a saturated solution of acid potassium carbonate instead of the normal salt employed for the isolation of dimethoxydihydrofuran. The final product was distilled in vacuum at 1 mm and obtained as a practically colourless, very viscous oil; b. p. 122—26°; yield 21 g = 81 %. The freezing point depression of a benzene solution was measured.

$C_{11}H_{16}O_7$ (260) Calc. C 50.74 H 6.21 CH_3COO 45.3 CH_2O 23.8 Mol.wt. 260
Found » 50.44 » 6.21 » 45.8 » 23.5 » 252

Hydrolysis and oxidation with periodic acid; identification of maleic acid aldehyde. 260 mg of 2,5-dimethoxy-2,5-dihydrofurfural diacetate and 240 mg of potassium metaperiodate were weighed into a 50 ml volumetric flask. 10 ml of 0.1 N sulfuric acid were added and the flask filled to the mark with water and shaken for one hour at room temperature. At this time the mixture was homogenous. The solution was left standing for 40 hours at room temperature and was then heated for 5—6 hours at 75° on the water bath. After cooling 25 ml of the mixture were added to a solution of 0.30 ml of phenylhydrazine and 0.30 ml of glacial acetic acid in 10 ml of water. The hydrazone, which precipitated almost immediately, was filtered off after shaking for two minutes, washed with water and dried in vacuum over phosphorous pentoxide at 80°; yield 66 mg = 70 %. The crude product was recrystallized from acetone-benzene; yield 45 mg = 47 %; m. p. 149° (tube, corr.). When recrystallized once more from acetone-ligroin the melting point was raised to 150°. (Fecht²⁰ 158—59°; Ciamician a. Silber¹⁸ 157°; Milas¹² 157.5—58°; Böeseken *et. al.*¹⁰ 155°). The phenylhydrazone prepared by Cross, Bevan a. Briggs melted at 155°.

The fraction melting at 149° was analyzed:

$C_{10}H_{10}O_2N_2$ (190) Calc. C 63.16 H 5.32 N 14.74
Found » 62.52 » 5.28 » 14.45

The methylphenylhydrazone was prepared in the same manner by adding 25 ml of the reaction mixture to a solution of 0.30 ml of methylphenylhydrazine and 1 ml of glacial acetic acid in 10 ml of water; yield 72 mg = 71 %. The crude product was washed with ligroin and recrystallized from methanol-water and then twice from benzene-ligroin; faintly yellow crystals; yield 28 mg = 28 %; m. p. 145° (tube, corr.). The methylphenylhydrazone prepared by Cross, Bevan a. Briggs melted at 143°.

$C_{11}H_{14}O_2N_2$ (204) Calc. C 64.67 H 5.93 N 13.72
Found » 65.30 » 6.02 » 13.28

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SUMMARY

The oxidation of furfural is discussed. 2,5-Dimethoxy-2,5-dihydrofurfural diacetate is prepared by methoxylation of furfural diacetate and the structure is proved by oxydative degradation.

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