[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

THE STRUCTURE OF NITROFURAN AND THE MECHANISM OF NITRATION IN THE FURAN SERIES

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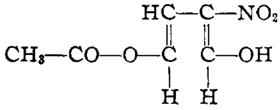
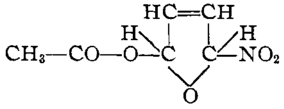
The nitration of furoic acid,[1] furfural diacetate,[2] 2-methylfuran[3] and many other furan derivatives, leads to the formation of nitro compounds in which it is reasonably certain that the nitro group has entered an *alpha* position. The nitration of furan itself gives a crystalline nitrofuran which Marquis[4] has formulated as β-nitrofuran. Since his work does not constitute an unequivocal demonstration of the position of the nitro group, and a large amount of indirect evidence would lead one to expect an α-nitrofuran, the validity of his formula is doubtful. The present study was undertaken with the object of establishing the structure of this nitrofuran and elucidating the mechanism of the nitration process.

In the nitration of furan, which is effected in the presence of acetic anhydride, there is formed an intermediate nitroacetate. This product corresponds in composition to the addition of a molecule of nitric acid and a molecule of acetic acid, with the elimination of a molecule of water. On treatment with pyridine, the unstable nitroacetate loses a molecule of acetic acid and is transformed into a crystalline nitrofuran. Marquis[4] found that the intermediate nitroacetate is decomposed by warm water with the production of nitrous and acetic acids and maleic dialdehyde, and this observation led him to formulate the intermediate product as an open-chain enol (I), produced by rupturing the oxygen bridge of the furan ring. It is difficult to concede that the formation of maleic dialdehyde is valid evidence for assigning the nitro group to the β-position and for assuming an open-chain enol structure. It seems more reasonable to assign to the intermediate nitroacetate a closed chain structure (II), which would be produced by 1,4-addition of nitric acid and subsequent acetylation. A similar 1,2-addition would give an alternative closed chain structure (III).

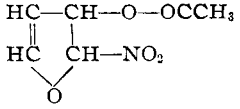


$$\begin{array}{lcc} & HC- & C-NO_2 \\ & \| & \| \\ CH_3-CO-O- & C & C-OH \\ & | & | \\ & H & H \end{array}$$

I



II



III

The formation of maleic dialdehyde can be explained more simply from the ring structures (II and III) than from the open-chain enol (I)

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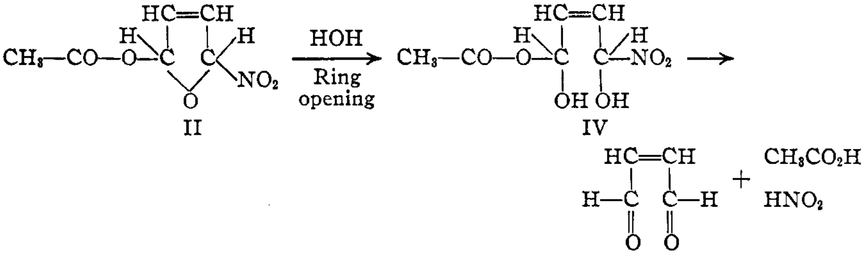
[1] Rinkes, *Rec. trav. chim.*, **49**, 1167 (1930).

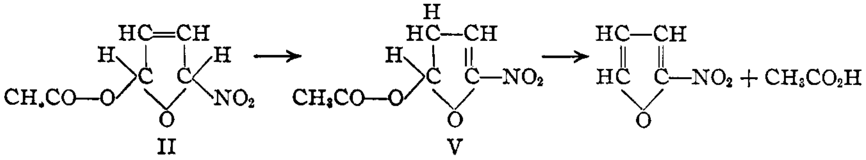
[2] Gilman and Wright, THIS JOURNAL, **52**, 2550 (1930).

[3] Ref. 1, p. 1118.

[4] Marquis, *Ann. chim. phys.*, [8] **4**, 216 (1905).

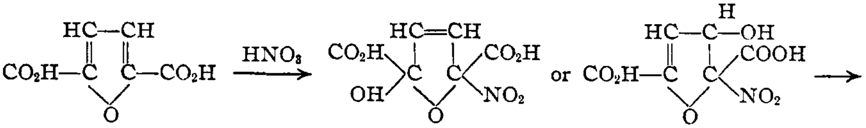


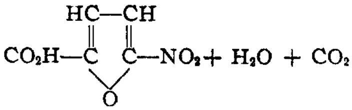
The decomposition of the unstable α-hydroxy nitro compound (IV) into an aldehyde and nitrous acid is analogous to the transformation of α-hydroxycarboxylic and α-hydroxysulfonic acids into aldehydes. The transformation of the intermediate nitroacetate (II) into 2-nitrofuran by the action of pyridine can be explained by 1,4-elimination of acetic acid or by a preliminary rearrangement into an isomeric nitroacetate (V), followed by 1,2-elimination of acetic acid



This type of rearrangement may be expected to occur readily since this shift of the double bond brings it into conjugation with the double bond of the nitro group. This reaction is analogous to the migration of the double bond from the β,γ- to the α,β-position in unsaturated carboxylic acids.

The behavior of certain substituted furan derivatives on nitration furnishes additional evidence for the formulation of the intermediate product as a ring compound. Although esters of furoic and furylacrylic acids form intermediate nitroacetates, the free acids do not form any intermediate product that can be isolated. It is highly probable that this difference is due to a greater lability of the intermediate product rather than to a fundamental difference in the mechanism of nitration. This view is supported by the observation that the nitration of furan derivatives containing a carboxyl group in the *alpha*-position often results in a displacement of the carboxyl group by the nitro group. Since the esters of these acids do not show this behavior, the decarboxylation is readily explained by the great instability of the intermediate α-nitro carboxylic acid





There is at present no direct evidence that favors the postulation of 1,4-addition of nitric acid rather than 1,2-addition. In the course of the present work one of the intermediate nitro compounds (obtained from methyl furoate) has been isolated in a pure state as a stable white crystalline solid. We hope to determine the structure of this intermediate compound in order to ascertain whether 1,4- or 1,2-addition has taken place.

In establishing the structure of the nitrofuran obtained by Marquis, 5-nitrofuroic acid was used as a reference substance. The position of the nitro group in this compound has been established with reasonable certainty by its formation from dehydromucic acid (furan-2,5-dicarboxylic acid) through the displacement of one carboxyl group and from 5-sulfofuroic acid through displacement of the sulfonic acid group.[5] It should suffice, therefore, to decarboxylate 5-nitrofuroic acid and to compare the resulting 2-nitrofuran with the compound produced by the direct nitration of furan. Accordingly, nitrofuroic acid (m. p. 185–185.5°) was decarboxylated by heating with copper bronze, in the presence of organic bases. The resulting 2-nitrofuran (m. p. 28.8–29.2°) proved to be identical with a specimen of nitrofuran (m. p. 28.8–29.2°) obtained from furan by nitration. Consequently, the nitrofuran described by Marquis should be designated as 2-nitrofuran instead of 3-nitrofuran.[6] Thus the nitration of furan occurs in an alpha position, in conformity with many furan derivatives and with its sulfur analog, thiophene.

Experimental

5-Nitrofuroic Acid.—This acid was prepared by hydrolysis of methyl or ethyl 5-nitrofuroate with strong sulfuric acid. Our experience showed that the yields were improved by using a solution of two parts by volume of concd. sulfuric acid in three parts of water, instead of the more concentrated acid (1:1) used by Marquis. In a typical preparation 55 g. of pure methyl 5-nitrofuroate was refluxed for fifty minutes with a solution of 250 cc. of concd. sulfuric acid in 375 cc. of water. The resulting 5-nitrofuroic acid after recrystallization from hot water melted at 185–185.5° (corr.) and weighed 40 g. (79% yield).

Intermediate Nitroacetate from Methyl Furoate.—In studying the nitration of

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[5] Hill and White, *Am. Chem. J.*, **27**, 193 (1902).

[6] This result has been anticipated by Rinkes (Ref. 1) who obtained a nitrofuran, m. p. 27.9°, by displacement of the carboxyl group of 2-furoic acid. He concluded that this product was 2-nitrofuran and showed that it was identical with the nitrofuran obtained by nitration of furan. To the intermediate nitroacetate, Rinkes assigns an open-chain enol formula which differs from that of Marquis merely in the position of the nitro group. We prefer to assign to this intermediate product a structure which differs from that of Marquis in the position of the nitro group *and* in having a closed chain (dihydrofuran) structure.

methyl furoate in acetic anhydride, it was observed that a white crystalline intermediate product could be obtained, along with a liquid product, if the excess of acetic anhydride was removed by prolonged contact with water. Although Marquis has described methyl 5-nitrofuroate, he did not report the isolation of this crystalline intermediate product.

A cooled solution of 50 g. of pure methyl furoate in 75 g. of acetic anhydride was added to a solution of 125 g. of fuming nitric acid (sp. gr. 1.50) in 200 g. of acetic anhydride, prepared and maintained at −5°. The temperature of the reaction mixture was kept at −5° during the course of this addition (two hours) and the resulting solution was stirred at −5° for two hours after all of the methyl furoate had been added. The reaction mixture was poured onto 500 g. of cracked ice and 2.5–3 liters of water was added. After stirring vigorously for twenty to thirty minutes the original viscous oil changed to a waxy mass containing white crystals and adhering drops of oil. This mass was separated and washed thoroughly, by stirring with cold water until the washings were free from acid. The waxy mass was pressed thoroughly on a suction filter in order to free the crystals from the adhering oil. The crystalline portion was washed with cold sodium bicarbonate solution and freed from alkali by repeated washing with cold water. After purification by several crystallizations from absolute methyl alcohol, the intermediate nitroacetate formed colorless needles which melted at 95.9° (corr.) in a capillary tube; on the electric bar[7] the crystals melted at 96.3° (corr.). This compound is very slightly soluble in petroleum benzine, and sparingly soluble in cold ether, carbon tetrachloride and methyl or ethyl alcohol. It is very soluble in acetone and in hot methyl or ethyl alcohol and glacial acetic acid.

Anal. Calcd. for $C_8H_9O_7N$: C, 41.54; H, 3.93. Found: C, 41.67, 41.48; H, 3.89, 3.92.

Upon catalytic hydrogenation, in the presence of platinum, the nitroacetate takes up approximately 2.5 moles of hydrogen. We have not yet studied the reactions of the reduced product.

This intermediate nitroacetate does not give an enol test with ferric chloride solution and does not decolorize a solution of bromine in carbon tetrachloride at 20°. The nitro-acetate shows the characteristic reducing action of aldehydes, with Fehling's solution and with ammoniacal silver oxide. It is decomposed on heating with water; on warming with pyridine it is converted almost quantitatively, by an *endothermic* reaction, into methyl 5-nitrofuroate. The latter, after one crystallization from methyl alcohol, formed colorless crystals, m. p. 81.6° (corr.). This product is evidently purer than that obtained by Marquis, who reported a melting-point of 78.5°.

In addition to the crystalline nitroacetate described above, there was obtained an almost equal quantity of a heavy yellow oil, which was obtained from the crystals by pressing on a suction filter and by adding water to the mother liquors from the crystallization of the solid nitroacetate. This oil was dissolved in ether, washed free from acid by means of cold sodium bicarbonate solution, and finally freed from alkali by repeated washing with cold water. The ether solution was allowed to stand at 0° for several days in order to separate an additional quantity of the crystals. After filtering these off and evaporating off the solvent under reduced pressure, there remained a yellow viscous oil from which no further quantity of crystals could be separated. On warming the oil with pyridine, a violent *exothermic* reaction occurs and the solution becomes very deeply colored (almost black). On pouring this into water, a highly colored insoluble precipitate is formed, from which only 25–30% of the calculated quantity of methyl 5-nitrofuroate could be isolated. The fact that a violent exothermic reaction occurs on

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[7] Dennis and Shelton, This Journal, 52, 3128 (1930).

treatment with pyridine, indicates that the oil contains a substance more reactive than the crystalline nitroacetate. The formation of methyl 5-nitrofuroate may be due to the presence of the crystalline nitroacetate dissolved in the oil.

Decarboxylation of 5-Nitrofuroic Acid: 2-Nitrofuran.—Five grams of the pure dry acid (m. p. 185–185.5°), 10 g. of high-boiling coal tar bases (b. p. 145–165° at 15 mm.) and 1 g. of copper-bronze (Kahlbaum's Naturkupfer C) were placed in a Wood's metal bath at 160–180°, and the temperature was finally raised to 220° after the original vigorous decomposition had subsided. The procedure was similar to that used for the decarboxylation of the halogenated furoic acids.[8] The distillates from several runs were combined and subjected to steam distillation. The volatile products were extracted with ether and the extract was washed thrice with cold dilute hydrochloric acid to remove any bases. After washing with cold water until the washings were free from acid, the ether solution was dried over anhydrous sodium sulfate. After removal of the solvent under diminished pressure, the residual crude 2-nitrofuran was dissolved in the minimum amount of petroleum benzine (b. p. 60–70°) at 50°. The warm solution was decanted from a small tarry residue and cooled to 0°, with vigorous stirring. The faintly pink crystals of 2-nitrofuran were filtered with suction, washed with a little of the cold solvent and then recrystallized in the same manner. The purified 2-nitrofuran formed almost colorless crystals melting at 28.8–29.2° (corr.). From 27 g. of 5-nitrofuroic acid there was obtained 2.8 g. of 2-nitrofuran (14% yield).

Nitration of Furan: 2-Nitrofuran.—The nitration of furan was carried out in acetic anhydride, according to the procedure of Marquis. After several crystallizations from petroleum benzine (b. p. 60–70°), the product formed pale yellow crystals, m. p. 28.8-29.2° (corr.). The identity of this nitrofuran with the specimen of 2-nitrofuran resulting from the decarboxylation of 5-nitrofuroic acid was established by a microscopical examination of the crystals and a mixed melting point determination. A mixture of the two substances in equal amounts melted at 28.8–29.2° (corr.), which is the melting point of the original pure substances.

Microscopical Examination of 2-Nitrofuran.[9]—Two samples of this compound, one prepared by the direct nitration of furan and the other by nitration of furoic acid and subsequent decarboxylation, exhibited exactly the same optical properties.

2-Nitrofuran was found to be very soluble in xylene at room temperature but it yielded well-formed crystals from this solvent when cooled to 0°. With this treatment, long, slender prisms were obtained as well as some smaller parallelograms. Both the prisms and the parallelograms were of two types, which will be designated as "type A" and "type B." Type A crystals were rectangular in shape, varying in length from squares to long prisms. In these, extinction was parallel. Type B crystals were parallelograms having an acute angle of about 68°. These, also, varied greatly in length. In this type, extinction was oblique to the direction of elongation and parallel to the shorter side. It was evident that the prisms were merely elongations of the shorter types. Type B crystals of both samples showed a marked tendency to form twins on the longer

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[8] Shepard, Winslow and Johnson, This Journal, **52**, 2083 (1930).

[9] The authors are indebted to Mr. P. P. McClellan for carrying out this microscopical examination.

side. Interference figures indicated that the crystals were biaxial, hence they must belong to the monoclinic system. The trace of the optic plane was parallel to the shorter side of type B crystals.

Summary

2-Nitrofuran has been prepared by the decarboxylation of 5-nitrofuroic acid and has been shown to be identical with the nitrofuran obtained from furan by nitration. The latter had been incorrectly formulated by Marquis to be 3-nitrofuran.

Evidence is presented to support the view that the intermediate nitroacetates, produced in the nitration of various furan derivatives in acetic anhydride solution, are ring structures rather than open chain enols.

The mechanism of the nitration process is suggested tentatively to be a 1,4-addition to the furan ring, without scission of the oxygen bridge.

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

THE ACTION OF PHENOL ON BENZOYLDIPHENYLMETHYL BROMIDE

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In a recent paper Schuster[2] reported that the reaction between benzoyldiphenylmethyl bromide and phenol gave phenylbenzoin monophenyl ether

$$(C_6H_5)_2CBrCOC_6H_5 + C_6H_5OH \longrightarrow HBr + \underset{(I)}{(C_6H_5)_2C(OC_6H_5)COC_6H_5} \qquad (1)$$

Subsequent treatment of the resulting product with phenylmagnesium bromide was reported to give benzopinacone monophenyl ether

$$(C_6H_5)_2C(OC_6H_5)COC_6H_5 + C_6H_5MgBr \longrightarrow (C_6H_5)_2C(OC_6H_5)C(OH)(C_6H_5)_2 \qquad (2)$$

A reaction such as that indicated in (1) would be remarkable indeed, since it is well known that phenol reacts in an acidic environment with certain compounds containing labile halogens to form nuclear substitution products; for example, phenol and triphenylchloromethane form *p*-hydroxytetraphenylmethane. It was then supposed that reaction (1) did not proceed as Schuster indicated, but rather

$$(C_6H_5)_2CBrCOC_6H_5 + C_6H_5OH \longrightarrow HBr + \underset{(II)}{(C_6H_5)_2C(C_6H_4OH)COC_6H_5} \qquad (3)$$

To test this supposition, Schuster's work was repeated in this Laboratory.

In the present paper it is shown that the reaction between benzoyldiphenylmethyl bromide and phenol proceeds neither according to (1) nor

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[1] Du Pont Fellow, 1930–1931.

[2] Schuster, *Ber.*, **63**, 2397 (1930).