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REACTIONS OF ALDEHYDES OF THE FURAN SERIES.

2.* OXIDATION WITH SODIUM HYPOHALITES

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The conditions for the oxidation of formylfurans with sodium hypobromite and hypochlorite that promote an increase in the yields for the furancarboxylic acids were investigated. The usual composition of the hypohalite mixture [NaOH]:[X_2] = 3 gives low yields of the furancarboxylic acids, particularly on the basis of 5-methylfurfural. Doubling the relative percentage of alkali promotes an increase in the efficiency of the reaction. An interpretation of the process is given.

The corresponding furancarboxylic acids are formed in up to 90% yields in the oxidation of furfural [2, 3] and its halo derivatives [4], as well as 2,5-diforylfuran [5], with sodium hyperbromite or hypochlorite (NaOX). The oxidation of 5-methylfurfural (I) with hypohalites has not been described. Our attempt to oxidize this compound with sodium hypobromite under the conditions of the method in [3] showed that 5-methylpyromucic acid (II) is formed in no higher than 20% yield. The bulk of aldehyde I remains unchanged. An unidentified oil that decomposed with HBr evolution was extracted as a side product from the reaction mixture. Regulation of the temperature of the mixture over the range −10 to +5°C did not make a significant difference in the yield of acid II.

The known methods for the preparation of acid II are based on the oxidation of aldehyde I with molecular oxygen with catalysis by silver oxide [6-8] and potassium ferrate [9], its disproportionation via the Cannizzaro reaction [10], and on the chloromethylation of pyromucic acid ester (III) with subsequent reduction of the chloromethyl group to a methyl group and saponification of the ester [11]. These methods have little applicability because of the low yields of the acid or the preparative complexity. The development of an efficient method for the preparation of acid II, which can be used as the basis for the preparation of the industrially important compound furan-2,5-dicarboxylic acid, as well as for use in the syntheses of biologically active substances, makes it possible to make it more accessible. The starting compound, viz., 5-methylfurfural, is accessible, inasmuch as it is a side product of the hydrolysis industry.

In the present paper we present the results of a study of the conditions for the oxidation of 5-methylfurfural (I) with hypobromite and hypochlorite that facilitate the production of methylpyromucic acid in high yield, and we also give an interpretation of the oxidation of

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[*] See [1] for Communication 1.

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TABLE 1. Consumption of Sodium Hypobromite in the Oxidation of Furan Aldehydes and Yields of the Furancarboxylic Acids

Expt.	[NaOH] : [Br₂]	Starting NaOBr concn., moles/liter	Consumption of NaOBr per mole of aldehyde, moles/mole	Yields of furan carboxylic acids, %
		5-Methylfurfural		
1	3	4	3,6	13
2	3	2	3,0	24
3	3	1	3,0	21
4	4,5	1	1,3	76
5	6	1	1,2	94
6	9	1	1,2	95
		Furfural		
7	3	4	1,8	30
8	3	2	1,5	52
9	3	1	1,5	55
10	6	1	1,3	77

aldehyde I with hypohalites on the basis of their reactions with furfural and other compounds.

The composition of the hypohalite mixture that is usually employed for the oxidation of aldehydes of the furan series [2-5] specifies the ratio [NaOH]:[X_2] = 3:1 per carbonyl group of the substrate:

$$-CH{=}O + X_2 + 3NaOH \longrightarrow -COONa + 2NaX + 2H_2O$$

This overall reaction consists of two steps, viz., the formation of the hypohalite (1) and oxidation of the aldehyde (2):

$$X_2 + 2NaOH \longrightarrow NaX + NaOX + H_2O \tag{1}$$

$$-CH{=}O + NaOX + NaOH \longrightarrow -COONa + NaX + H_2O \tag{2}$$

The facts that in preliminary experiments on the oxidation of aldehyde I with hypobromite different products are formed, HBr is evolved, and the aldehyde remains unchanged indicate possible bromination in conformity with the halogenating ability of hypohalites [12, 13]. We have observed a similar phenomenon in the direct treatment of aldehyde I with molecular bromine in neutral aqueous solution. All of this made it possible to assume that an insufficient amount of the alkali that is necessary, in particular, for tying up the evolved HBr is developed in the investigated reaction mixture. We therefore set up a number of experiments on the oxidation of aldehyde I and furfural with hypobromite and hypochlorite in the presence of various amounts of alkali (Tables 1 and 2).

The experiments were carried out by titration of a solution of the hypohalite with the aldehyde, in which the aldehyde was added to the oxidizing agent in small portions, and the disappearance of the hypohalite was monitored spectrally from the absorption bands of the hypobromite at 330 nm and the hypochlorite at 292 nm [12]. The total disappearance of the spectrum of the hypohalite indicates the endpoint of the titration, and this makes it possible to establish the hypohalite:aldehyde ratio and to proceed with extraction of the furancarboxylic acid from the reaction mixture.

In experiments 1-3 and 7-9 (Table 1) we selected the degree of dilution of the reaction mixture of the hypobromite (its starting concentration) from the efficiency of the process. We found that the yield of the furancarboxylic acid is higher at a hypobromite concentration of 1 mole/liter than in the case of a hypobromite concentration of 4 moles/liter. All of the experiments were subsequently carried out precisely at this dilution or at values close to it (a precise starting concentration is more difficult to create in the preparation of the hypochlorite).

An incerase in the relative amount of the alkali (experiments 3-6 and 9 and 10) promote an increase in the yields of the furancarboxylic acids. The most efficient ratio is [NaOH]:[Br_2] = 6; the yield of acid II is increased to 94% in this case, and the yield of acid III is increased to 77%. An increase in this ratio to nine does not change the process.

The dependence of the specific consumption of hypobromite per mole of aldehyde on the excess amount of alkali should be regarded as particularly remarkable. When [NaOH]:[Br_2] = 3, 3 moles of hypobromite are consumed per mole of aldehyde I, i.e., three times the amount stipulated by Eq. (2). When furfural is treated with hypobromite, the consumption of NaOBr

TABLE 2. Consumption of the Hypochlorite in the Oxidation of Furan Aldehydes and Yields of the Furancarboxylic Acids

Expt.	[NaOH] : [Cl$_2$]	Starting NaOCl concn., moles/liter	Consumption of NaOCl per mole of aldehyde, moles/mole	Yields of furancarboxylic acids, %
		5-Methylfurfural		
11	3,0	2,5	2,0	13
12	4,5	1,7	1,7	56
13	6,0	1,5	1,5	70
		Furfural		
14	3,3	2,5	1,2	58
15	6,0	2,5	1,0	64

also exceeds the theoretical amount but only by a factor of 1.5. If, however, the amount of NaOH relative to Br$_2$ is increased to a factor of six, the consumption of hypobromite in the oxidation of both aldehydes decreases. In this case the results of the reaction are close to the stoichiometry of Eq. (2).

In the experiments with hypochlorite (Table 2) the yield of furancarboxylic acid also increases as the relative percentage of alkali is increased, and the relative consumption of the oxidizing agent per mole of the aldehyde decreases. However, the yield of acid II here reaches only 70%. However, in the case of the oxidation of furfural with hypochlorite, as in the case of oxidation with hypobromite, none of the indicated changes is as markedly expressed. However, one must note the lower yield of acid III as compared with the value indicated in the literature [2, 3].

To ascertain the possible reasons responsible for the pecularities of the hypohalite oxidation of aldehydes of the furan series we took into account the fact that in the complex mixture of reagents under consideration the reaction may take place simultaneously via several pathways. In addition to the indicated hypohalite oxidation and possible halogenation, one should take into account the increased tendency for aldehydes of the furan series to undergo Cannizzaro disproportionation in the presence of alkalies. The introduced excess alkali may promote disproportionation. In this case the increased yield of furancarboxylic acid may be associated with hypohalite oxidation of furfuryl alcohols as products of the Cannizzaro reaction:

$$2\,\text{–CH=O} \xrightarrow{\text{NaOH}} \text{–COONa} + \text{–CH}_2\text{OH} \xrightarrow{2\,\text{NaOX}} 2\,\text{–COONa} \tag{3}$$

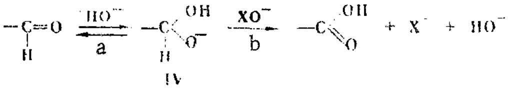
To verify this assumption we carried out the oxidation of 5-methylfurfuryl, furfuryl, and benzyl alcohols with hypobromite (Table 3). Benzyl alcohol was used for comparison.

The experimental results show that in the oxidation of furfuryl alcohols with hypobromite furancarboxylic acids are formed in very low yields. An increase in the amount of alkali has a small effect on the yield of the acid. Benzyl alcohol is oxidized to benzoic acid in rather high yield with much greater ease. In combination with the benzaldehyde detected in the mixture, the yield of products of oxidation of benzyl alcohol is close to 90%.

The data from experiments Nos. 16-21 are not in agreement with the proposed reaction Eq. (3). In addition to the yield of the acid, this is also indicated by the high degree of consumption of hypobromite per mole of alcohol, which computationally does not exceed two. In the case of the oxidation of benzyl alcohol the consumption of hypobromite is even smaller than two, since part of the intermediately formed benzaldehyde remained unoxidized. A comparison with the results of oxidation of benzyl alcohol makes it possible to assume that the increased consumption of hypobromite in the oxidation of furfuryl alcohols is associated with a reaction that proceeds with ring opening and a number of subsequent transformations.

Thus the assumption that the reaction proceeds through intermediate disproportionation via Eq. (2) is not confirmed, since the formation of furfuryl alcohols in this case does not lead to high yields of furancarboxylic acids.

A pathway involving hypohalite oxidation of the anion (IV) of the gem-diol, to which the aldehyde group is converted in an alkaline medium, is more likely:



(4)

TABLE 3. Consumption of Hypobromite in the Oxidation of Furan and Benzyl Alcohols and Yields of Furancarboxylic and Benzoic Acids

Expt.	$[NaOH] : [Br_2]$	Starting NaOBr concn., mole/liter	Consumption of NaOBr per mole of alcohol, moles/mole	Yield of aromatic acid, %
		5-Methylfurfuryl alcohol		
16	3,0	1,0	4,3	1
17	6,0	1,0	3,8	28
		Furfuryl alcohol		
18	3,0	1,0	4,0	4*
19	6,0	1,0	2,3	8*
		Benzyl alcohol		
20	3,0	1,0	1,9	74†
21	6,0	1,0	1,1	55†

*In addition, up to 10% furfural was detected.

†In addition, 10 and 35% benzaldehyde, respectively, were detected.

The amount of alkali that corresponds to the stoichiometry of Eq. (2) is not always sufficient for conversion of all of the aldehyde to anion IV. The donor effect of a methyl group in aldehyde I molecule decreases the ability of the carbonyl carbon atom to undergo nucleophilic addition of hydroxide ion even more. The role of excess alkali, which promotes a shift of equilibrium a in Eq. (4) to favor the formation of IV anions, as a result of which the primary occurrence of oxidative reaction b becomes possible, can therefore be understood.

The fact that the examined peculiarities of the oxidation with hypohalites are observed not only in 5-methylfurfural but also in furfural indicates that this phenomenon may be general for aldehydes of the furan series.

EXPERIMENTAL

The spectral monitoring of the reaction mixture was carried out with a Specord UV-vis recording spectrophotometer. The IR spectra were obtained with a Specord IR spectrometer.

5-Methylpyromucic Acid (II). A) A 34.12 g (0.21 mole) sample of Br_2 was dissolved at 0°C in 200 ml of water containing 50 g (1.2 moles) of NaOH and 16.5 g (0.15 mole) of aldehyde I was added dropwise in the course of 1.5 h. The reaction mass was maintained at 0-5°C. The side products were then extracted with ether 0.5 h after the end of the addition of the bromine, and the aqueous residue was refluxed for 5 min with 2 g of activated charcoal. The mixture was then acidified and filtered, and the precipitated crystals of acid II were removed by suction filtration and air dried. An additional amount of acid II was extracted from the aqueous solution. The overall yield was 18.4 g (16.3 g from precipitate and 2.1 g from the extract) or 97%.

B) Gaseous chlorine was bubbled at 0°C into 300 ml of water containing 72 g (1.8 moles) of NaOH until the gain in weight was 20 g (0.28 mole), after which 22 g (0.2 mole) of aldehyde I was added in the course of 2 h while maintaining the temperature at no higher than 5°C. The mixture was then stirred for another hour, after which the side products were removed by extraction with ether, and the mixture was worked up as described in method A. The yield of acid II was 17.2 g (69%).

The acid thus obtained had mp 108°C, and no melting-point depression was observed for a mixture with a sample obtained by the other method. The spectral characteristics (UV and IR) were also in agreement with the literature data [6-11].

The acids were extracted by a method similar to the described methods after oxidation of the other aldehydes and alcohols.

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SOLID-PHASE REARRANGEMENT OF AMINALS OF 5-HALOFURFURALS TO 5-N,N-DIALKYLAMINOFURFURLYIDENE-N,N-DIALKYLIMMONIUM SALTS

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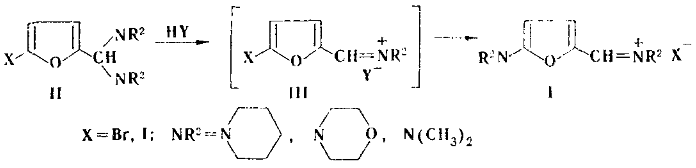
Aminals of 5-halofurfurals (products of the reaction of 5-halofurfurals with 2 moles of secondary amines) in the solid phase undergo rearrangement to 5-N,N-dialkylaminofurfurylidene-N,N-dialkylimmonium salts. The kinetics of the reaction were studied. A mechanism for the reaction is proposed.

It is known that 5-halo- and 4,5-dihalofurfurals [1-3], 5-halofurylacroleins [4], and 5-halofurfurylideneanilines [5] react with secondary amines to give 5-N,N-dialkylaminofurfurylidene-N,N-dialkylimmonium salts (I). Some of these salts have been obtained in crystalline form [1, 5]. The mechanism of this transformation was studied in [6-8]; in particular, it was established [8] that the reaction can be stopped at the step involving the formation of relatively stable aminals II. In [8] it was also noted that II are isolated from alcohol solutions in the form of white crystals; however, these crystals turn yellow rapidly during storage. It was found that the resulting salts I can be isolated in high yields with a high degree of purity. This reaction is of undoubted interest as a rare example of solid-phase nucleophilic substitution of halogen in the furan ring:



The kinetics of the rearrangement of aminals II are presented in Fig. 1. All of the kinetic curves are broken down into two sections: in the first section the reaction proceeds with acceleration, whereas in the second section it proceeds at a constant rate. The composition of the atmosphere in which the process takes place, particularly in the case of moisture, carbon dioxide, and traces of volatile mineral acids as impurities, has a pronounced effect on the rate. Most of the experiments were therefore carried out in a dry nitrogen atmosphere; the gaseous medium was varied intentionally only in a few cases. Thus II reacts in air approximately twice as fast as in dry nitrogen, whereas in a carbon dioxide atmosphere the reaction is accelerated to an even greater extent. However, varying the atmos-

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