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Rearrangements and Tautomeric Transformations of Heterocyclic Compounds in Homogeneous Reaction Systems Furfural–H_2O_2–Solvent

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Abstract—General information on the reactions of furfurals with hydrogen peroxide is given. We have discussed the Baeyer–Villiger rearrangement of furan 2-hydroxyhydroperoxides and tautomeric transformations with proton transfer of 2-hydroxyfuran and β-formylacrylic acid formed in a homogeneous reaction system furfural–H_2O_2–solvent under the catalysis with the formed acids. The factors affecting these rearrangements and tautomeric transformations as well as their specificity in comparison with benzene type compounds, and the pathway of the reactions of furan aldehydes with H_2O_2 in water have been analyzed. Keto-enol tautomerism of cyclic hemiacetal form of β-formylacrylic acid leading to its transformation into succinic anhydride has been described for the first time.

Keywords: furan aldehydes, hydrogen peroxide, tautomerism, the Baeyer–Villiger reaction, peroxides, molecular rearrangement

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Development of ideas on furan aldehydes reactions with hydrogen peroxide. A series of rearrangements and tautomeric transformations of furan and hydrofuran compounds may occur in a homogeneous furfural–H_2O_2–solvent reaction mixture, determining the direction of processes in the mixture. Review [1] gives a historical overview of the research on furfural reactions with hydrogen peroxide. Even though these reactions have been studied since 1899, their mechanism have long been controversial and not coinciding with the data on the H_2O_2 reactions with other aromatic oxo compounds. It is known [1–3] that the oxidation of benzene-type aldehydes and ketones occurs through the formation of their α-hydroxyhydroperoxides. These intermediates undergo an intramolecular Baeyer–Villiger rearrangement affording either the corresponding benzoic acids (esters) or formylphenols which are further hydrolyzed into phenols and formic acid. It is notable that the oxidation of benzaldehyde yields mainly benzoic acid, evidencing the ease of the hydrogen atom transfer to the electron-deficient α-oxygen atom of the peroxide moiety in comparison with phenyl radicals during rearrangements of the α-hydroxyhydroperoxides.

The data on formation of furan-type α-hydroxyhydroperoxides and their transformations have remained unknown until publication of our studies [1]. Such peroxides have been discovered in the reaction mixtures during oxidation of furfural **1** and 5-substituted (CH_3, NO_2) furan aldehydes with hydrogen peroxide [4].

Further studies [5–8] have discussed the formation and transformations of α-hydroxyhydroperoxides of furfural, 5-methylfurfural, and 5-nitrofurfural in their reactions with H_2O_2 in water, ethanol, *n*-butanol, and dioxane. Individual peroxides of furfural and 5-nitrofurfural have been isolated [6].

The oxidation of aldehyde **1** with 30% aqueous solution of H_2O_2 has given a mixture containing the product of rearrangement of furfural α-hydroxyhydroperoxide **2**: 2-formyloxyfuran **3** [9]. Hydrolysis of the latter affords formic (**6**) and β-formylacrylic (**8a**+**8b**) acids, along with an unidentified compound.

The final products of furfural oxidation in different solvents are listed in Table 1. Distinct features of these reactions are as follows: the stability of the formed

Table 1. Composition of products of the reaction between furfural **1** and 30% H_2O_2 in different solvents[a]

Compound	Yield, mol% (with respect to furfural)		
	water	ethanol	dioxane
	180 min	210 min	440 min
Furfural α-hydroxyhydroperoxide **2**	10.8	70.1	98.0
β-Formylacrylic acid (**8a** and **8b**)	6.6	0.8	Traces
Maleic acid (**9**)	10.8	3.1	–
Fumaric acid (**10**)	0.2	0.6	–
β-Formylpropionic acid (**14**)	4.0	1.0	–
Succinic acid (**15**)	20.0	3.0	–
2-Furoic acid (**4**)	1.3	8.1	–
Formic acid (**6**)	86	20	Traces
2(3*H*)-Furanone (**11**) and 2(5*H*)-furanone (**12**)	40	12	–

[a] [**1**] : [H_2O_2] = 1 : 2, 60±1°C, conversion of furfural at the given reaction duration 70%.

peroxides in dioxane, the predominance of 2-furoic acid **4** in the products in ethanol, and the formation of 2(3*H*)- and 2(5*H*)-furanones (**11**, **12**) along with succinic acid (**15**) as the major products in water [5, 7, 8, 10]. Based on these data, furanone **12** and acid **15** have been prepared simultaneously with 30 and 35% yield, respectively, via oxidation of furfural **1** with 15% aqueous hydrogen peroxide (furfural–H_2O_2 1 : 2.3 mol/mol, 4 h, 70±1°C) [11, 12].

Scheme 1 has been suggested for the reactions occurring in a homogeneous aldehyde **1**–H_2O_2–water system in view of the available data. Most of the products and stages in this scheme have been experimentally confirmed [7–11].

It is notable that the pH of reaction mixture is reduced to 1–2 during oxidation of furfural, due to the formation of the acids (Scheme 1) which act as acid catalysts in most of the involved stages. Formic acid **6** formed at the beginning of the oxidation is of special importance. Hence, the considered reaction is acid-autocatalytic.

The study of the furan aldehydes containing substituents which do not react with aqueous H_2O_2 (5-methylfurfural **16** and 5-nitrofurfural **17**) has allowed elucidation of the role of electron-donor (CH_3) and electron-acceptor (NO_2) groups [8, 10, 13]. These reactions occur through the formation of α-hydroxyperoxides of 5-methylfurfural (**18**) and 5-nitrofurfural (**19**).

The final products of oxidation of aldehyde **16** are methyl-substituted homologs of hydrofuranones **11** and **12** [5-methyl-2(3*H*)-furanone **20** and 5-methyl-2(5*H*)-furanone **21**] and methyl-substituted structural analogs of acids **14** and **8b** [acetylpropionic (levulinic) acid **22** and β-acetylacrylic acid **23**] (Scheme 1) [8, 10]. The reaction of aldehyde **16** with aqueous H_2O_2 does not yield 5-methyl-2-furoic acid **24**.

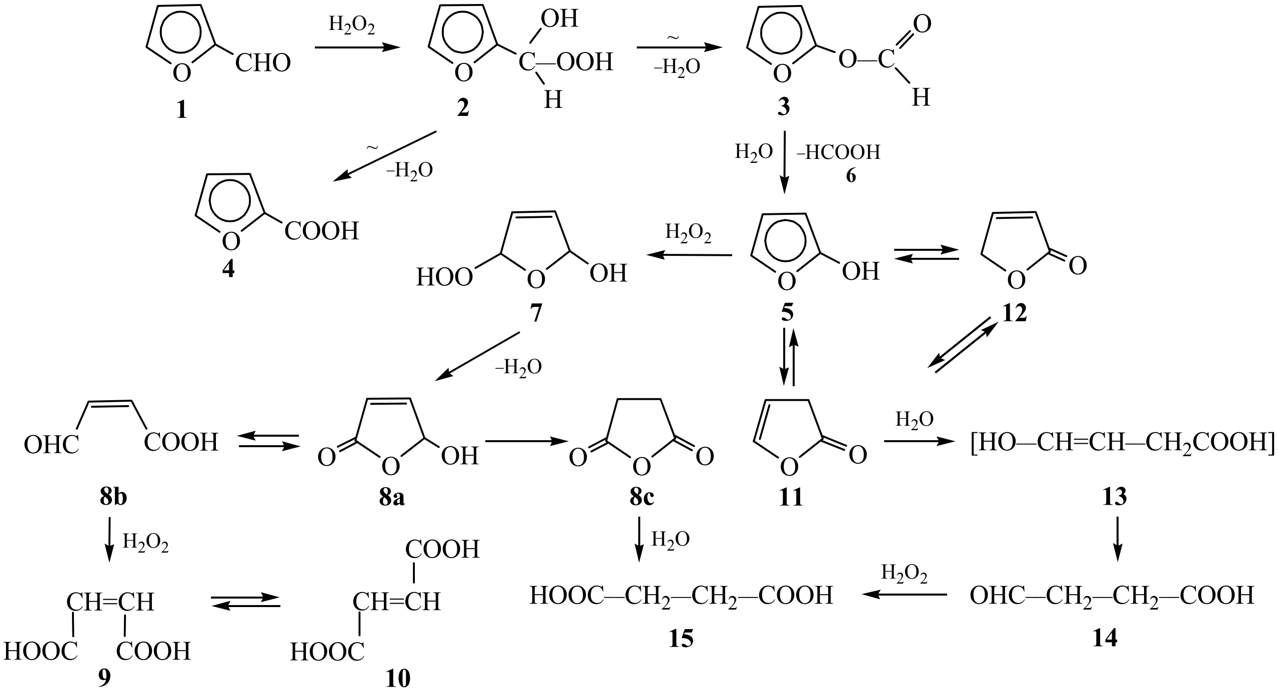
The oxidation of aldehyde **17** with 28% aqueous hydrogen peroxide diluted with dioxane gives exclusively 5-nitro-2-furoic acid **25** in a quantitative yield [13].

Besides the considered oxidation processes, homogeneous reactions of furfural with H_2O_2 in the presence of compounds of V and VI group elements have been described [14–20].

The addition of catalytic amount of a soluble compound of V^{+5}, Nb^{+2}, Nb^{+5}, Mo^{+6}, Cr^{+6}, or Se^{+4} to the aldehyde **1**–H_2O_2–water reaction system immediately affords the peroxo complexes of these elements, as confirmed in the study of the model systems by means of spectroscopy and chromatography. These complexes vigorously react with the carbonyl group of furfural with the formation of the corresponding furyl-containing organometal ozonides which are likely transformed into 2-formyloxyfuran **3**. Furfural α-hydroxyhydroperoxide **2** is not formed in these reactions.

The reactions are the fastest in the presence of Se^{+4} or V^{+5} compounds, being the slowest in the presence of

Scheme 1.



niobium compounds [15, 20]. The rates of the reaction in the presence of Nb^{+2} and Nb^{+5} were equal and close to that in the absence of any catalyst. This observation can be explained by the negative oxidation potential of niobium in its compounds, regardless of the oxidation state. The final composition of the products of the catalytic oxidation of furfural **1** in the presence of V^{+5}, Mo^{+6}, Cr^{+6}, or Se^{+4} differs from that under the acid autocatalysis conditions [20]. In the presence of V^{+5}, β-formylacrylic acid (as a mixture of two tautomeric forms **8a** and **8b**) is predominantly formed, its yield being insignificant in the absence of the catalyst. The reactions in the presence of Cr^{+6} give mainly acids **8** and **15**, whereas the presence of Mo^{+6} triggers the formation of furanone **12** and hydroxyacids (tartaric **26** and malic **27**). Niobium compounds do not significantly affect the composition of the major products of the furfural oxidation as compared to the catalyst-free process (Table 2).

The oxidation of furfural with 5% H_2O_2 at 50±1°C in the presence of SeO_2 (furfural:H_2O_2:catalyst molar

Table 2. Composition of major products formed in a homogeneous reaction mixture furfural–H_2O_2–water–catalyst upon complete decomposition of peroxide compounds[a]

Catalyst	Yield, %[b]					
	8a+8b	**9**	**12**	**15**	**26**	**27**
Acid autocatalysis	4	8	22	48	–	1
Nb_2O_5	1	12	29	17	–	–
$Nb(CH_3COO)_2$	1	8	34	14	–	–
$NaVO_3$[c]	33	9	8	15	3	4
$Na_2Cr_2O_7$	22	9	25	10	4	1
Na_2MoO_4	7	1	33	11	8	27

[a] [**1**] : [H_2O_2] : [catalyst] = 1 : 3.2 : 0.05, 60±1°C. [b] A mixture of β-formylpropionic, malonic, and oxalic acids is also formed (overall yield 20% in the presence of Nb^{+2} and Nb^{+5}, 10% in the presence of V^{+5}); 1–6% of malonic acid is formed in the presence of Mo^{+6} and Cr^{+6}.

[c] The catalyst loading was reduced tenfold due to the vigorous reaction.

ratio 1 : 3 : 0.05) leads to the formation of β-formylacrylic acid **8** (as a mixture of tautomers **8a** and **8b**, yield 60%) along with maleic (**9**) and fumaric (**20**) acids (total yield 22%), succinic (**15**) and β-formylpropionic (**14**) acids (total yield 8%), and 2(5*H*)-furanone **12** (yield 8%) [14–16].

In all the mentioned cases, formic acid **6** is formed with a quantitative yield.

The well-known epoxidizing ability of molybdenum peroxo complexes and characteristic transformation of vanadium peroxo complexes into the complexes with singlet oxygen $V^{+5}(O_2)$ determined the differences in the pathway and mechanism of the stage the ester **3** and hydroxyfuran **5** oxidation as compared to the acid autocatalysis conditions, which leads to the formation of compounds **8**, **26**, and **27** in significant amounts (Table 2) [20]. A procedure to prepare acid **8** in up to 60% yield [16] has been developed basing on the reaction of furfural with H_2O_2 in the presence of V_2O_5.

Since the yield of 2(5*H*)-furanone **12** is the highest in the presence of niobium compounds (Table 2), the optimal conditions of the furfural reaction in the H_2O_2–H_2O–$Nb(CH_3COO)_2$ system affording this lactone in up to 64% yield have been elaborated [19].

Besides the above-described homogeneous reactions of furfural with H_2O_2, heterogeneous oxidation of aldehyde **1** with hydrogen peroxide has been described [21–28]. These studies aimed to optimize the conditions favoring the increase in the yield of target oxidation products. The oxidation with 30% hydrogen peroxide in a water–1,2-dichloroethane two-phase system in the presence of Na_2SO_4 at 70°C, followed by boiling in the organic phase has given a mixture of furanones **11** and **12** (Scheme 1). Heating of these mixtures with triethylamine resulted in 67% yield of furanone **12**, total reaction duration being 14 h [21]. The process intermediates have not been studied, and the reaction mechanism has been explained using the scheme from [10].

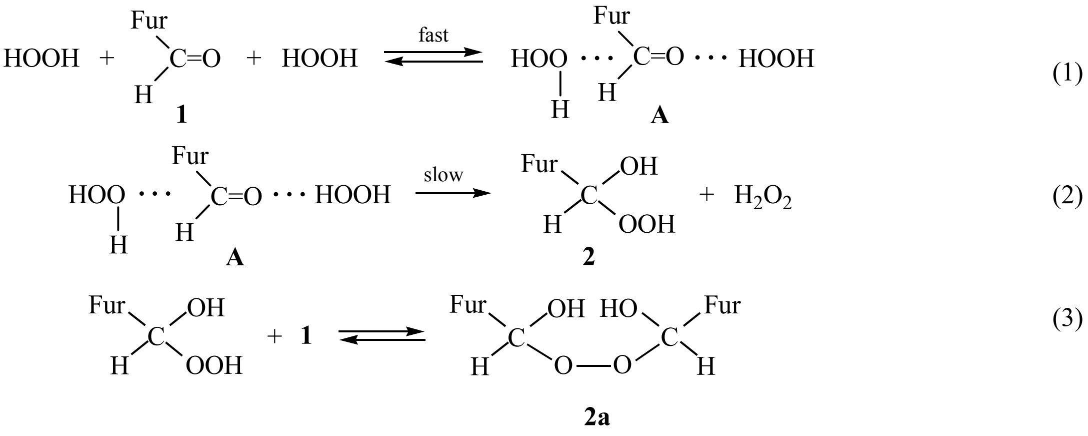
Comparative study of oxidation of aldehyde **1** with H_2O_2 in water–1,2-dichloroethane and water–ethyl acetate two-phase systems in the presence of formic acid (1 : 0.8 molar ratio with respect to furfural) has been reported [22]. The yield of furanone **12** has been up to 60–62%, and the total yield of acids **9** and **15** has been 15–20%. The suggested mechanism of their formation has been based on the schemes elaborated in our studies [9–11]. Peroxyformic acid has been considered the oxidant in an organic phase. Alternatively, splitting of the cycle in a molecule of aldehyde **1** assisted by water in acidic medium has been suggested. This seems unlikely in view of stability of furan cycle in furfural owing to the conjugation with the carbonyl group [1].

The oxidation of furfural **1** with hydrogen peroxide in the presence of homogeneous acid catalysts in two-phase aqueous-organic systems has been performed [23]. The conditions favoring predominant formation of furanone **12** have been elaborated; it has been further hydrogenated in the presence of heterogeneous metal complex catalysts to afford γ-butyrolactone. The formation of intermediate furanone **12** and acids **9**, **15** has been found coinciding with the scheme in [11].

Strongly acidic ion-exchange resin (Amberlist-15) has been used as solid catalyst in oxidation of furfural and other furan derivatives with hydrogen peroxide [24, 25]. The use of such catalyst has directed the reaction towards predominant formation of the acid **15**, its yield being up to 74% under the optimized conditions. It has been suggested [25] that π,π-interaction between the tosyl cycle of the catalyst and that of the furan compound occurs in the first stage, leading to the formation of an intermediate containing five-membered cycle built of carbon and oxygen atoms of the carbonyl group of the furan compound as well as sulfur and oxygen atoms of the sulfonic group of the catalyst. Under the action of H_2O_2, this intermediate is further transformed into 2-formyloxyfuran **3**, earlier isolated as a product of homogeneous oxidation of aldehyde **1** under acid autocatalysis conditions [9]. The mechanism of formation of this ester during oxidation in the presence of Amberlist-15 has not been considered by the authors. The transformation of ester **3** into furanone **11** and further into acid **15** has been shown in the schemes in [9, 11].

Catalytic oxidation of furfural with hydrogen peroxide in an aqueous medium in the presence of titanium silicalite (TS-1) as catalyst (50°C, aldehyde **1** to H_2O_2 molar ratio 1 : 7.5, 24 h) has afforded acid **9** in 78% yield [26]. Sequential use of these catalysts (TS-1 and Amberlist-70) at different stages of the process has increased the yield of acid **9** to 80%, the process duration being 28 h, and the H_2O_2 excess being reduced to 4.4. The suggested reaction mechanism includes as the first stage the epoxidation of one of the double bonds of the furan ring of furfural with

Scheme 2.



Fur = furyl.

hydrogen peroxide [26]. This seems unlikely, since epoxidation of the furan cycle is known for furan and its derivatives containing electron-donor substituents [1] but is not possible for furfural, due to the reduced electron density in the cycle of aldehyde **1** and disturbance of the cycle conjugation with the carbonyl group upon epoxidation.

It has been shown that oxidation of furfural with H_2O_2 in the presence of polystyrene sulfonic acid as the acid catalyst affords acids **9** and **15** (yield 46 and 28%, respectively) [27]. The oxidation mechanism has not been discussed.

Another procedure of furfural oxidation with 10% hydrogen peroxide in methanol has been performed in the presence of photogenerated iron catalyst $[FeCp(C_6H_5R)]PF_6$ at 20°C [28]: the mixture has been irradiated with visible light during 2 h, and then the process has been carried out in dark over 4 days with addition of H_2O_2 by portions [28]. The oxidation has given methyl 2-furanoate (yield 90%). Advantages of this method include the high yield of the ester and the possibility of regeneration of the catalysis for repeated use. At the same time, the process is quite time consuming and involves toxic methanol. Mechanism of the reaction has not been discussed.

As seen from the presented data, rearrangements of furan hydroxyperoxides and tautomeric transformations of the products of deep oxidation of furan aldehydes with hydrogen peroxides have not been considered so far. At the same time, the experimental data are available on homogeneous oxidation in the furfural–H_2O_2–water systems, including mechanism of formation and products of transformations of furan α-hydroxyhydroperoxides, hydrofurans, and aldehyde-acids. This has allowed the analysis of rearrangements and tautomerism of a series of heterocyclic compounds in the mentioned systems.

Formation and rearrangements of furan α-hydroxyperoxides. Pure furfural α-hydroxyhydroperoxide **2** has been isolated upon oxidation of furfural with concentrated H_2O_2 on cooling (–15°C). Peroxide **2** is very unstable and explodes at room temperature in pure form [6]. In view of this, peroxide **2** has been prepared and studied in the form of a solution in *n*-butanol [17, 29]. Under these conditions oxidation of aldehyde **1** is fast enough, and the peroxide compounds are exclusively accumulated in the solution at certain moment. Besides peroxide **2**, furfural α,α'-dihydroxyperoxide **2a**, a product of the reaction between aldehyde **1** and peroxide **2**, is also formed (Scheme 2).

Kinetics of oxidation of furfural in *n*-butanol with 30% hydrogen peroxide prepared by dilution of 99% H_2O_2 with *n*-butanol [17] has revealed the pseudo first rate order with respect to furfural and the second rate order with respect to H_2O_2, i. e. overall the third reaction rate order. This has allowed description of the formation of peroxides **2** and **2a** by Scheme 2.

In view of the kinetic data, the rate of the process in Scheme 2 is determined by stage 2. The formation of complex **A** (stage 1) is in agreement with the activation parameters of the reaction between furfural and H_2O_2 in *n*-butanol [29] and suggest the association between the carbonyl group of furfural and H_2O_2 molecules [30]. The third reaction rate order in the reaction of nucleophilic addition at the carbonyl group

Table 3. Parameters of transformation of furfural α-hydroxyhydroperoxide **2** into 2-furoic acid **4** in basic medium of amine (c_{start} = 0.1 mol/L)

Solvent	T, °C	$k\times10^{-2}$, s^{-1}	E_a, kcal/mol	$A\times10^{-5}$, s^{-1}	ΔS_a, e. u.
Pyridine	24	1.65	10.0	3.7	–26
Triethylamine	25	1.75	10.0	3.9	–25

for synchronous addition of the nucleophile and proton, which is the case of the considered process as well [31].

It is notable that the formation of α-hydroxyhydroperoxides of furan aldehydes during oxidation of these aldehydes with hydrogen peroxide in dioxane is accelerated by electron-donor (CH_3) as well as electron-acceptor (NO_2) substituents [8], which is in line with the reaction through the formation of complex **A** (Scheme 2).

The oxidation of furfural in water gives exclusively peroxide **2**, whereas peroxide **2a** is formed in trace amount [7]. In this case, the formation of peroxide **2** is accompanied by its decomposition into furanones and acids (Scheme 1 and Table 1). At the same time, the third reaction rate order is preserved: the first with respect to furfural, the first with respect to H_2O_2, and the first with respect to formic acid formed via hydrolysis of ester **3** and acting as a protogen in the formation of complex **A** (Scheme 2) [8]. This fact confirms that the formation of α-hydroxyhydroperoxide **2** limits the overall rate of the multistage reaction between furfural and H_2O_2 in an aqueous medium.

The products of α-hydroxyhydroperoxide **2** transformations in water have been compared with these obtained upon addition of water to its solutions in *n*-butanol, ethanol, and dioxane. The prepared aqueous-organic solutions containing 25% of water have been heated at 60°C until complete decomposition of the peroxides [7, 8]. A mixture of acids and hydrofuranones is formed in water (Table 1). In the case of the alcohols and dioxane with addition of water, qualitative composition of the products is the same but 2-furoic acid **4** predominates among the acids (yield up to 60%), the yield of formic acid being reduced.

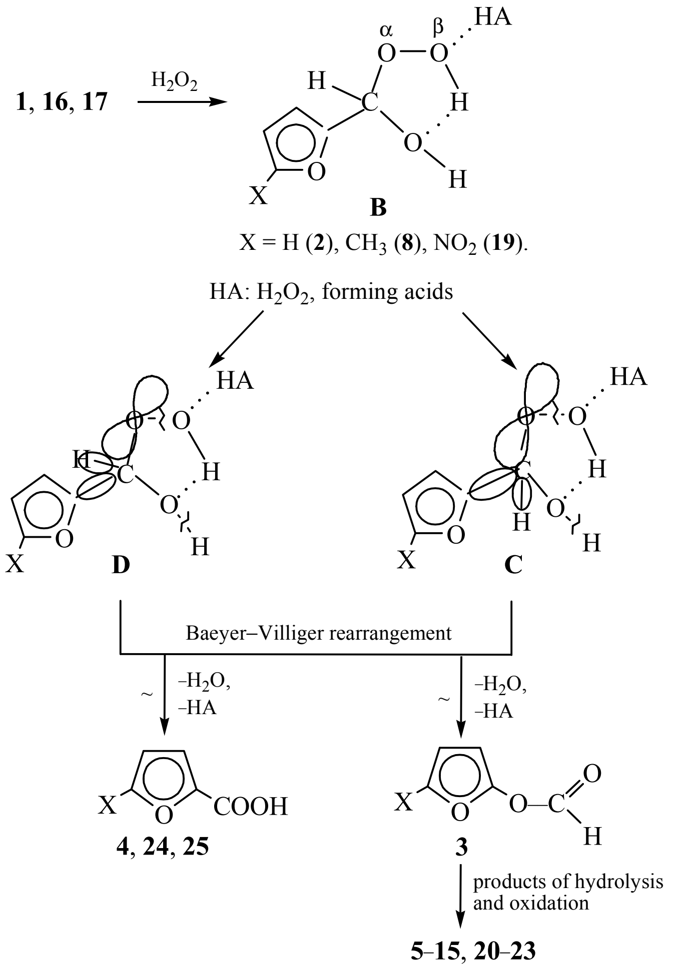
It is notable that the oxidation of 5-methylfurfural **16** with aqueous hydrogen peroxide does not give 5-methyl-2-furoic acid **24**. At the same time, the oxidation of aldehyde **16** in a more basic solvent (water : triethylamine = 1 : 1) yields acid **24** as the major product [32].

The study of transformations of α-hydroxyhydroperoxide **2** in pyridine and triethylamine at 24–25°C has revealed that it is completely consumed during 15–20 min with quantitative formation of acid **4**. The decomposition of peroxide **2** follows the first-order kinetics, and the rate as well as activation parameters in both solvents are almost equal (Table 3). The activation parameters point at the formation of a highly polar transition state during the transformation of peroxide **2** into acid **4**. Hence, the transformation of furfural and 5-methylfurfural α-hydroxyhydroperoxides into the corresponding 2-furoic acids is the major pathway in the basic solvents.

In contrast to peroxide **2**, 5-nitrofurfural α-hydroxyhydroperoxide **19** is relatively stable. It has been prepared via oxidation of 5-nitrofurfural **17** with 35% H_2O_2 in a water–dioxane medium at 45°C in 95% yield [6]. Peroxide **19** is a stable crystalline compound of mp 79–80°C. Upon 2 h heating in water at 70°C it is quantitatively transformed into 5-nitro-2-furoic acid **25** [6, 13]. It is notable that the oxidation of aldehyde **17** with 30% H_2O_2 gives peroxide **19** as the only intermediate, which is further transformed into acid **25** in 98% yield [13].

Comparison of the reactions of H_2O_2 with aldehydes **1**, **16**, furan ketones **28**, and 5-methyl-2-acetylfuran **29** has shown the identity of their products and oxidation mechanisms [33]. Chromatographic analysis of the reaction mixture has revealed the presence of α-hydroxyhydroperoxides with structure and properties analogous to these of peroxides **2** and **18** formed from furfural and 5-methylfurfural, respectively. The products of deep oxidation of ketones have been isolated as well: 2(3*H*)-furanone **11**, 2(5*H*)-furanone **12**, 5-methyl-2(3*H*)-furanone **20**, and 5-methyl-2(*5H*)-furanone **21**; β-formylacrylic **8a**, maleic **9**, succinic **15**, β-acetylacrylic **23**, and β-acetylpropionic **22** acids. The furanones **20** and **21** are major products of the ketones oxidation. The oxidation of furan ketones is accompanied by quantitative formation of acetic acid. Esters of 2-furoic or 5-methyl-2-furoic acid are not formed.

Scheme 3.



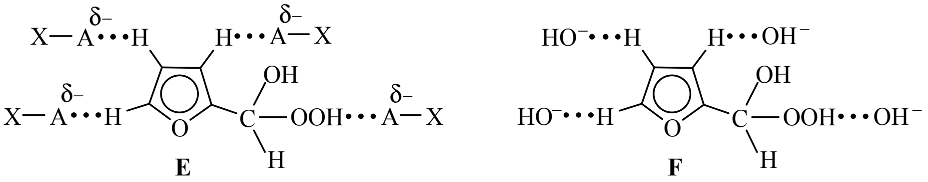
X = H (**4**), CH_3 (**14**, in alcohols, dioxane, pyridine, or triethylamine); X = NO_2 (**25**, in water); X = H, CH_3 (**5**–**15**, **20**–**23**, in water).

The oxidation of furan ketones is slower in comparison with furan aldehydes, as expected in view of the effect of the methyl group increasing the electron density at the carbon atom of the carbonyl group and sterically hindering the nucleophilic attack of this atom by hydrogen peroxide.

The discussed data have suggested the concept of the rearrangements of furan α-hydroxyhydroperoxides in homogeneous reaction mixtures containing the furan aldehyde, H_2O_2, and solvent. The formation of such hydroxyhydroperoxides occurs through the formation of type **A** complexes (Scheme 2), with hydrogen peroxide acting simultaneously as nucleophile and electrophile. In the case of reactions of furfural and 5-methylfurfural in water, the forming organic acids (mainly formic one) begin to act as protogen in complexes **A** (Scheme 2). α-Hydroxyhydroperoxides are protonated (by hydrogen peroxide and then with the formed acids) at the α-oxygen atom of the peroxide fragment (Scheme 3). This enhances the polarization of the peroxide bond and additionally reduces the electron density at its α-oxygen atom. The formation of an intramolecular hydrogen bond between the hydroxyl and peroxide groups with the formation of a sufficiently stable five-membered cycle is also probable (complex **B**, Scheme 3).

It is to be seen that the Baeyer–Villiger rearrangements of α-hydroxyhydroperoxides of furfural, furan aldehydes with electron-donor substituents in the furan ring (as exemplified by 5-methylfurfural), and furan ketones **28** and **29** with an alkyl substituent or without other substituents in the ring proceeds with the migration of furyl radicals to the electron-deficient α-oxygen atom of the peroxide bond (Scheme 3). This is

Scheme 4.



(A–X) basic solvent (alcohols, dioxane, pyridine, or triethylamine).

a distinct feature of these rearrangements in comparison with the rearrangements of similar peroxides of benzaldehyde and benzene ketones. This fact can be explained by the enhanced electron density in the furan ring of furan peroxides owing to the conjugation with the heteroatom as well as lability of the π-electron system [34–36] not typical of the benzene cycle. Hence, rearrangements of the listed furan aldehydes involve the overlapping of the *p*-orbital of the electron-deficient α-oxygen atom of the peroxide bond in the molecule of peroxides **2** and **18** with the σ-orbital of the adjacent C–C bond (furyl), bonding electrons of which act as donor (transition state **C**, Scheme 3).

If the furan ring contains an electron-acceptor group (as in the case of 5-nitrofurfural), the electron density in the cycle is sufficiently reduced, and the formation of such transition state is impossible. In this case, hydrogen atom migrates to the electron-deficient atom of peroxide **19** through transition state **D** (Scheme 3), in which the bonding electrons of the adjacent C–H σ-bond act as donors, and 5-nitro-2-furoic acid **25** is the product of the Baeyer–Villiger rearrangement. This pathway of rearrangement of peroxide **2** during oxidation of furfural **1** in an aqueous medium is insufficient, being absent for the reaction of 5-methyl-furfural. However, 2-furoic (**4**) and 5-methyl-2-furoic acids (**24**) are the major products of oxidation in the reactions of these aldehydes with H_2O_2 in more basic organic media (alcohols, pyridine, or triethylamine) [32].

pH of the reaction medium also affects the direction of the rearrangement of furfural α-hydroxyhydroperoxide **2** [37]. As shown in Table 4, the reaction of aldehyde **1** with H_2O_2 in an aqueous medium, the formation of acid **4** starts only at pH 5, being the most pronounced at pH 7. In acid aqueous medium (pH 0–4) furanone **12** and acid **15** are mainly formed, as shown above. The presence of protons first favors the formation of peroxide **2** and then induces the polarization of the peroxide bond reducing the electron density at its α-oxygen atom. This, on the one hand, facilitates

Table 4. The effect of the medium pH on the formation of 2(5*H*)-furanone **12** and carboxylic acids **4** and **15** in the furfural–H_2O_2–H_2O system[a]

pH	Furfural conversion, %	Yield of oxidation products, %		
		12	**4**	**15**
0	100	38	–	40
1	100	50	–	40
2	98	40	–	40
3	80	22	–	43
4	65	13	–	45
5	52	–	30	50
6	48	–	50	40
7	50	–	65	20
7.5	58	–	45	4

[a] [Furfural] : [H_2O_2] = 1 : 10, 60°C, 4 h.

the rearrangement of peroxide **2** and, on the other hand, favors the formation of formyloxyfuran **3**. In an aqueous medium, the latter is hydrolyzed into hydroxyfuran **5**, which undergoes further transformations (Scheme 1).

The predominant formation of 2-furoic acid **4** via rearrangement of furfural α-hydroxyhydroperoxide **2** observed in basic organic media can be explained by the formation of hydrogen bonds between the molecules of the organic solvent and protons of the furan ring of the peroxide. The formation of such bonds upon dissolution of furfural in dioxane and DMSO has been confirmed by means of ^{1}H NMR spectroscopy [38]. Similarly, the formation of complexes **E** and **F** involving peroxide **2** (Scheme 4) during the reaction of furfural with H_2O_2 in basic media can be assumed. The formation of dioxane–5-nitrofurfural α-hydroxyhydroperoxide **19** complexes has been observed during the oxidation of 5-nitrofurfural with hydrogen peroxide in dioxane [38].

The formation of such bulky structures sterically hinders the migration of furan ring to the electron-deficient α-oxygen atom of the peroxide bond through complex **C** (Scheme 3) and, hence, the formation of formyloxyfuran **3**. In this case, migration of proton through complex **D** and formation of acid **4** are favorable.

The discussed data show that the Baeyer–Villiger rearrangement of a series of furan α-hydroxyhydroperoxides (which have been isolated in the reactions of furan aldehydes with H_2O_2) exhibits specific features in comparison with the rearrangements of similar benzene-type peroxides. This occurs owing to the differences in the structure and properties of the furan and benzene rings [1].

Further transformations of formyloxyfuran **3** and formyloxybenzene formed via rearrangement of the corresponding α-hydroxyhydroperoxides are significantly different as well. The products of hydrolysis of formyloxybenzene (formed via the oxidation of benzaldehyde with hydrogen peroxide) are formic acid **6** and phenol [1]. Hydrolysis of formyloxyfuran **3** yields acid **6** and 2-hydroxyfuran **5** (Scheme 1), electronic structure and properties of the furan ring of the latter strongly differing from these of the benzene ring. This is the reason for other differences in the transformations of formyloxybenzene and formyloxyfuran in the reaction systems where these are formed via the Baeyer–Villiger rearrangement.

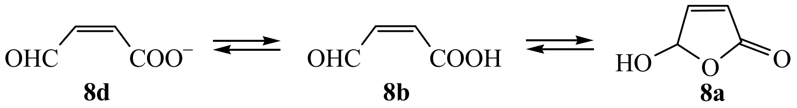
Products of hydrolysis of ester **3** are acid **6**, lactones **11** and **12**, and semialdehyde of succinic acid **14** found in the reaction mixture upon oxidation of furfural (Scheme 1). Compound **14** is formed from lactone **9** [10]. The hydrolysis is relatively fast (k = 13.0×10^{-3} min^{-1}). Lactone **12** has been isolated in a yield up to 40% during oxidation of furfural **1** with hydrogen peroxide in an aqueous medium [10, 11]. The freshly prepared furanone **12** contains up to 20% of furanone **11** as the admixture; the latter is transformed into lactone **12** upon heating or 2 months storage at room temperature [10]. High-resolution NMR spectrum recorded for the admixtures in lactone **12** contains relatively weak signals at δ 4.17, 5.80, 6.58, and 6.95 ppm [10]. They are attributed to the presence of 2-hydroxyfuran **5**, the tautomeric form of furanone **12**. This has been further confirmed by the observation of a weak band at 3500 cm^{-1} in the IR spectrum of lactone **12**, typical of the OH group of aromatic enols. The enol **5** has been observed also in the products of the oxidation by means of chromato–mass spectrometry [39].

Tautomeric and isomeric transformations of products of furfural oxidation with hydrogen peroxide. The available data have allowed the explanation of the mechanism of the lactones and acids formation in the furfural–H_2O_2–H_2O reaction system. The readily proceeding hydrolysis of ester **3**, in contrast to this of formyloxybenzene, is due to the formation of unstable enol **5** from ester **3**.

Positive effect of the hydroxyl group conjugation with the π-system of the furan ring occurs in the molecule of hydroxyfuran **5**. As a result, the electron density in the cycle is enhanced, its aromaticity is reduced, and the diene system reactions become characteristic of it. This leads to the easy mobility of the hydroxyl group hydrogen to the position 3 of the furan cycle (adjacent to the hydroxyl group) and to the opposite position 5, explaining the tautomeric transformation of enol **5** into lactones **11** and **12** (Scheme 1).

The equilibrium in this keto-enol tautomerism is shifted towards the lactone forms, because the total energy of the bonds in lactones is higher than in hydroxyfuran **5**, and the conjugated system is partially preserved in the molecules of unsaturated lactones **11** and **12**. Such transformations have been described in the literature [40]. At the same time, as mentioned above, lactone **12** contains minor amount of the enol **5**. This is a typical case when the enol double bond is

Scheme 5.



conjugated with other double bonds [41], as in the mole-cule of intermediate **5**.

Hydrofuranone **11** is readily hydrolyzed into acid **13** which exists in the stable tautomeric form of aldehyde-acid **14** (Scheme 1). The formation of acid **14** from 2(3*H*)-furanone **11** has been confirmed experimentally [10, 42]. The aldehyde-acid **14** is oxidized with hydrogen peroxide in the reaction mixture into succinic acid **15**, which has been isolated from the products of the furfural reaction with H_2O_2 in up to 40% yield [11].

In contrast to lactone **11**, compound **12** is stable in acidic aqueous media, including the conditions of furfural oxidation with hydrogen peroxide in water. It does not undergo acid hydrolysis and is not oxidized by hydrogen peroxide in acid media [11].

The product of oxidation of tautomer **5** is β-formylacrylic acid **8** existing in the reaction medium in two tautomer forms **8a** and **8b**. It is formed via the addition of H_2O_2 at the diene system of 2-hydroxy-furan **5** through the formation of hydroperoxide **7** (Scheme 1). Its yield is low upon oxidation of furfurol **1** with hydrogen peroxide in water in the absence of a catalyst (Table 1). However, the oxidative ability of the medium is enhanced when the reaction of aldehyde **1** with H_2O_2 is performed in the presence of selenium, vanadium, molybdenum, or niobium compounds, and the oxidation of hydroxyfuran **5** becomes competitive to its tautomeric transformations into lactones **11** and **12**. Under these conditions, acid **8** is formed in significant yield [15, 16, 18, 20].

Acid **8b** is further oxidized into maleic acid **9**, which it slightly isomerized into fumaric acid **10**. The ease of transformation of hydroxyfuran **5** into stable products **8a**, **8b**, **12** and further **9** and **15** favors the shift of the equilibrium of hydrolysis of ester **3** towards the intermediate **5** and the products of its tautomeric and oxidative transformations. The formed acids **6**, **8b**, **9**, and **15** act as catalysts at all the stages of the reaction in an aqueous medium shown in Scheme 1.

Oxidation of benzene with hydrogen peroxide stops at the formation of phenol, the phenol–ketone tautomeric equilibrium of which is shifted towards phenol due to aromaticity of the benzene ring [41]. This fact rules out any further transformations of phenol analogous to these shown in Scheme 1 for furan aldehydes. Hence, it is the keto-enol tautomerism of 2-hydroxyfuran **5**, intermediate of furfural oxidation with hydrogen peroxide, which determines the dramatic difference of this process from benzaldehyde oxidation.

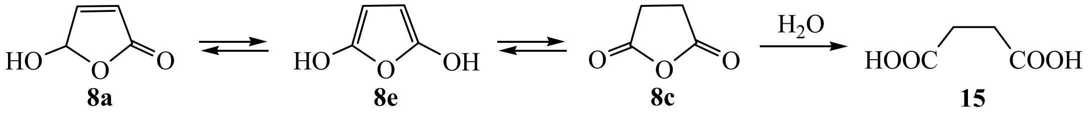
In the furfural–H_2O_2–solvent reaction system the tautomeric transformations involving the proton transfer are observed also for the products of hydroxyfuran **5** oxidation (Scheme 1). β-Formylacrylic acid **8** has been isolated from the reaction medium in two forms: open carbonyl (**8b**) and cyclic hemiacetal (**8a**) ones, their ratio being changed in the course of the reaction. Initially, when the reaction medium pH is close to neutral, the carbonyl form **8b** is predominant. As the medium becomes more acidic, the ratio is changed in favor of the cyclic form **8a** which is prevailing in the final products [18]. pH of the reaction medium is reduced from 6.5 to 1 due to the formation of acids **6**, **8b**, and **15** (Scheme 1). To explain the observations, the equilibrium between compounds **8a** and **8b** has been studied by means of polarography [43]. The reduction has been performed using a dropping mercury electrode with m 2.01 mg/s and t_1 3.41 s. Only the **8b** form can be reduced under the experiment conditions, which allows monitoring the ratio of the forms by measuring the current of reduction.

It has been found that β-formylacrylic acid exists in almost exclusively open neutral **8b** and anionic **8d** forms in basic to weakly acidic media (Scheme 5). At pH 0–4, 30–60% of it is in the cyclic form **8a**. The *trans*-form of acid **8** has not been observed.

The obtained data on the pH effect on the cycle-chain tautomerism of acid **8** are in agreement with the behavior of other acylacrylic acids [44].

The observed partial transformation of the hemiacetal form **8a** into succinic acid **15** [45] has not been known before. Heating of a neutral aqueous solution of compound **8a** (c = 1.2 mol/L) at 60°C has afforded acid **15** with 3% yield after 3 h and 13% yield after 24 h. At pH 9–10 and 70–80°C, hemiacetal **8a** is

Scheme 6.



completely transformed into acid **15** within minutes; the latter has been isolated as such and in the form of diethyl ester [45]. Scheme 6 of the transformations has been suggested.

Hemiacetal **8a** containing a carbonyl group is in equilibrium with the enol form **8e** which can have a keto form **8c,** succinic anhydride. Hydrolysis of the latter gives acid **15**. In the basic media the equilibrium is shifted from the form **8a** towards form **8c** due to the hydrolysis of the latter into acid **15**. Hence, it can be suggested that acid **15** is partially formed from hemiacetal **8a** in the furfural–H_2O_2–H_2O system (Scheme 1) when the medium acidity has not yet significantly increased.

The above discussion has revealed that most of the stages of the reactions between furan aldehydes with hydrogen peroxides occur through rearrangements and tautomeric transformations of furan and hydrofuran compounds **2**, **5**, **8a**, **9**, and **12**. The predominant formation of 2-furoic acids or hydrofuranones **8a**, **9**, **12**, and acid **15** in this complex oxidation process is directed by the substitution in the furan cycle, nature and basicity of the solvent, and acid-base properties of the medium.

CONFLICT OF INTERESTS

No conflict of interest was declared by the authors.

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