

## Synthesis of functional furan derivatives by oxidation of furans and formylfurans with hydrogen peroxide\*

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The review analyzes the effects of the reaction conditions on the direction of the reactions between furans/formylfurans and hydrogen peroxide. The revealed dependences serve for the synthesis of the desired products and for development of new methods to access  $\alpha$ -hydroxy hydroperoxides of furan aldehydes, 2-furanoic acid and its esters and amides, a series of furoic acids bearing the substituent at the furan ring, 2(5*H*)-furanone and its homologs and functional derivatives, as well as 2,5-dialkoxydihydrofurans. The developed procedures are more advantageous than the conventional methods.

**Key words:** furans, formylfurans, furfural, hydrogen peroxide, oxidation, synthesis, furan derivatives, hydrofuran derivatives.

The reaction systems furfural—H<sub>2</sub>O<sub>2</sub> and furan—H<sub>2</sub>O<sub>2</sub> and the reactions occurring therein are very promising for the development of effective synthetic procedures to access poorly available compounds. The efficiency of this approach is attributed to the presence of several reaction centers in the molecules of furanic compounds as well as to the ability of hydrogen peroxide to form different reactive species (singlet and triplet oxygen, hydroxyl and perhydroxyl ions and radicals) depending on the decomposition conditions. The reactions between these reagents could be directed towards different types of the products by varying the reaction conditions (*e.g.*, reagent molar ratios, reaction temperature, solvent nature, and catalyst).

Our previous reviews<sup>1,2</sup> have summarized the advances in this field of chemistry. Oxidation of furfural (**1a**) with hydrogen peroxide was first reported in 1899. However, until our studies of the reactions of furan and furfural with hydrogen peroxide such systems were mainly used to synthesize aliphatic carboxylic acids (*e.g.*, succinic, maleic, fumaric, and  $\beta$ -formylacrylic acids). Also, synthesis of 2-furancarboxylic acid in 75 and 30% yields was enabled by oxidation of furfural in pyridine at 25 and 70 °C for 76 and 12 h, respectively.<sup>3,4</sup>

Synthetic scope of these reactions was not fully used due to the absence of experimentally confirmed data on the reaction mechanisms and transformations of the intermediate oxidation products. A breakthrough for tuning the processes occurring in the system furfural—H<sub>2</sub>O<sub>2</sub> was

brought by our findings of  $\alpha$ -hydroxy hydroperoxide **2a** and studies of its further transformations<sup>5–7</sup> (Scheme 1). For the synthesis of **2a**, 99% pure hydrogen peroxide was used in a ratio furfural : H<sub>2</sub>O<sub>2</sub> = 1 : 5. Hydrogen peroxide was added dropwise to the stirred furfural **1a** over a period of 30 min at –10—–15 °C and then the reaction was continued for 6 h. Peroxide **2a** was characterized by physicochemical, spectral, and chromatography methods.<sup>5</sup> Compound **2a** decomposes upon heating in water to give a mixture of furfural (**1a**), 2-formyloxyfuran (**3**), and acids **4**, **9b**, and **10** (see Scheme 1).

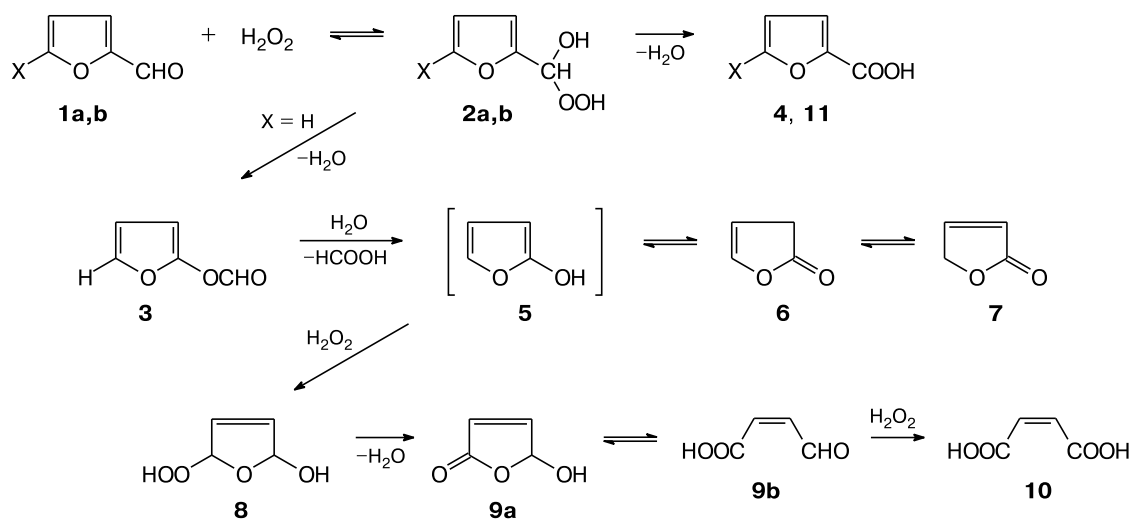
It is known<sup>1</sup> that  $\alpha$ -hydroxy hydroperoxides of aliphatic and aromatic aldehydes undergo intramolecular Baeyer–Villiger rearrangement to give either carboxylic acid or the corresponding ester depending on the structure of the starting aldehyde and the reaction conditions. The Baeyer–Villiger rearrangement of peroxide **2a** affords ester **3** and 2-furancarboxylic acid (**4**) found among the products of decomposition of **2a**.

Peroxide **2a** is the initial product of oxidation of furfural **1a** with aqueous H<sub>2</sub>O<sub>2</sub> (26–30%). This fact was confirmed using chromatographic and kinetic methods.<sup>6,7</sup> It is of note that formation of peroxides of type **2** occurs also in the reaction of furfural with H<sub>2</sub>O<sub>2</sub> mediated by compounds of group V and VI elements.<sup>7,8</sup>

Pure peroxide **2a** is very unstable and explosively decomposes at room temperature. In contrast, we succeeded in obtaining pure nitrofurfural hydroxy hydroperoxide **2b** following the below described procedure.<sup>9</sup> A solution of 5-nitrofurfural (**1b**) was mixed with 70% aqueous hydrogen peroxide in a molar ratio **1b** : H<sub>2</sub>O<sub>2</sub> of 1 : 2.2. A vigorously stirred reaction mixture was maintained at 45 °C for

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Scheme 1



X = H (**1a**, **2a**, **4**), NO<sub>2</sub> (**1b**, **2b**, **11**)

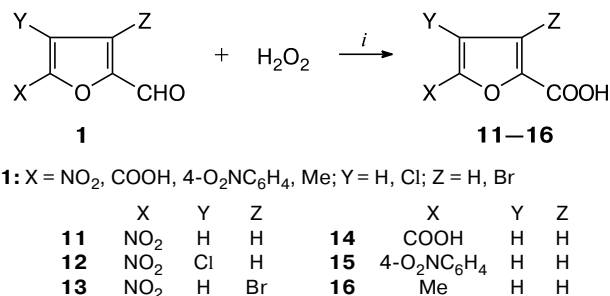
30 min. The yield of peroxide **2b** under these conditions was 95% (see Scheme 1). Heating (70 °C) and stirring peroxide **2b** in water for 3 h gives 5-nitro-2-furancarboxylic acid (**11**) in 93% yield.

It is clear that the presence of an electron-withdrawing substituent in the ring of furan aldehyde stabilizes hydroxy hydroperoxide **2b** and facilitates its rearrangement into furancarboxylic acid. Similar substituent effect was found for a series of substituted benzaldehydes.<sup>1</sup>

We used the effect of the electron-withdrawing substituent on the rearrangement of peroxide **2** in the synthesis of a series of furancarboxylic acids bearing the electron-withdrawing substituents<sup>6,10,11</sup> (Scheme 2). In all cases, the starting furan aldehyde was dissolved in dioxane with heating and slowly treated with 30% aqueous hydrogen peroxide; the reaction was carried out under vigorous stirring at 70 °C until complete consumption of aldehyde. For the synthesis of acids **11–14**, a reagent molar ratio was 1 : 2; while for the synthesis of acid **15**, 10-fold excess of hydrogen peroxide was needed due to poor solubility of the starting aldehyde. Acids **11–15** were obtained in the yields of 92–98%, physicochemical properties of these compounds are given in publications.<sup>6–10</sup>

It was found<sup>5</sup> that the yield of acid **4** formed by the rearrangement of peroxide **2a** was less than 2%. With the aim to synthesize acid **4** in high yields by oxidation of furfural with hydrogen peroxide, we studied the effects of the solvent basicity and pH of the reaction medium on the direction of the transformations of intermediate **2a**. We found,<sup>6–12</sup> that both the use of the solvents more basic than water (alcohols, dioxane, and tertiary amines) and maintaining pH of the reaction medium of about 7–8 when oxidizing furfural with aqueous hydrogen peroxide favor predominant formation of acid **4**. Taking these find-

Scheme 2



**1**: X = NO<sub>2</sub>, COOH, 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, Me; Y = H, Cl; Z = H, Br

Conditions: *i*. 60–70 °C, dioxane.

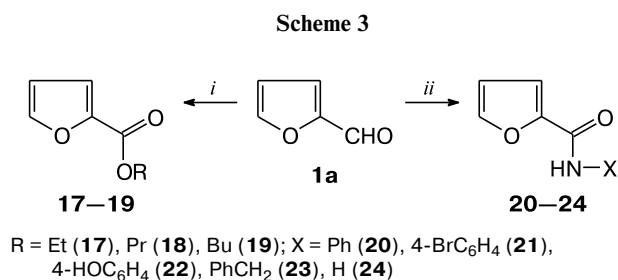
ings into account, we developed two procedures to synthesize acid **4** in a system furfural–H<sub>2</sub>O<sub>2</sub>.<sup>6,13,14</sup> The first procedure involves stirring a mixture of furfural, triethylamine, and 30% aqueous hydrogen peroxide in a molar ratio of 1 : 1 : 2 at 20–25 °C until complete consumption of furfural. In this case, the yield of acid **4** was 92%. Following the second procedure, a solution of aldehyde **1a** in *n*-butanol was treated portionwise with a solution of sodium acetate in 30% aqueous H<sub>2</sub>O<sub>2</sub> (**1a** : H<sub>2</sub>O<sub>2</sub> : AcONa = 1 : 2 : 0.5) over 2 h. The reaction was carried out under stirring with simultaneous azeotropic distillation of water; the water distilled off was periodically returned into the reaction. After complete conversion of furfural, the solvent was removed, the residue was treated with hydrochloric acid, and the crystals of acid **4** was collected by filtration; yield of **4** was 72%.

5-Methylfuran carboxylic acid **16** was synthesized similarly from 5-methylfurfural (see Scheme 2).

The possibility to direct the reaction of furfural with H<sub>2</sub>O<sub>2</sub> in the presence of alcohols and amines to produce

acid **4** was used for developing the procedures to access esters and amides of this acid from aldehyde **1a** without intermediate isolation of acid **4**.<sup>6,8,14</sup>

Esters **17–19** were synthesized by oxidation of furfural with 5% solution of hydrogen peroxide in ethanol (prepared from 90% aqueous hydrogen peroxide) in the presence of catalytic amounts of  $\text{SeO}_2$  (Scheme 3). The reaction was carried out under vigorous stirring at 50 °C using a molar ratio **1a** :  $\text{H}_2\text{O}_2$  :  $\text{SeO}_2$  = 1 : 3 : 0.05 until complete consumption of furfural. Then the same amount of the catalyst was additionally added and the reaction mixture was refluxed for 5 h. This method gives 60–62% yields of the target esters.<sup>6,14</sup>



**Reagents and conditions:** *i.*  $\text{H}_2\text{O}_2$ ,  $\text{SeO}_2$ , ROH. *ii.*  $\text{H}_2\text{O}_2$ , aqueous EtOH,  $\text{H}_2\text{N-X}$ .

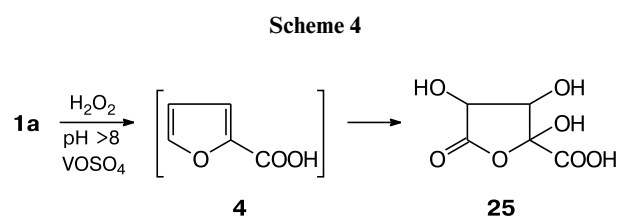
2-Furancarboxamides **20–23** were synthesized by the reaction of furfural with 30% solution of hydrogen peroxide in aqueous alcoholic solution catalyzed by primary aromatic amines (see Scheme 3). The reactions were performed under stirring at 0 °C using a molar ratio aldehyde **1a** :  $\text{H}_2\text{O}_2$  : amine = 1 : 2 : 1 until complete consumption of furfural.<sup>6,11,14</sup>

The first representative of a homologous series of amides of acid **4**, *i.e.*, unsubstituted amide **24**, was synthesized by oxidation of furfural with 30% solution of hydrogen peroxide in 25% aqueous ammonia in the presence of vanadium(IV,V) compounds<sup>8</sup> (see Scheme 3). A stirred mixture of the reagents (a molar ratio of **1a** :  $\text{H}_2\text{O}_2$  : ammonium : vanadium compound = 1 : (3–3.5) : (2–7) : (0.001–0.01)) was heated at 50–60 °C until complete consumption of furfural. The yield of amide **24** reached 84%. As compared with the catalyst-free conventional synthesis of amide **24** in the system aldehyde **1a**– $\text{H}_2\text{O}_2$ – $\text{NH}_4\text{OH}$ ,<sup>15</sup> the presence of vanadium catalysts results in a two-fold increase in the target product yield and a decrease in the reaction time to 6 h.

Thus, based on the reactions occurring in the system containing furfural (**1a**),  $\text{H}_2\text{O}_2$ , solvent, and catalyst, we elaborated synthetic procedures towards 2-furancarboxylic acid (**4**) as well as its esters and amides directly from aldehyde **1a** and requiring no isolation of acid **4** during the process. This synthetic protocol utilizes the readily available starting material and provides shorter reaction time and improved product yields than the earlier described

methods. From our viewpoint, this is very important since these compounds exhibit antibacterial, therapeutic, anti-fungal, herbicide, growth regulating, and some other useful biological activities and also can be used as intermediates in the chemical syntheses and in the production of plastics.<sup>11,16</sup>

Oxidation of furfural with aqueous hydrogen peroxide at pH of the reaction medium above 8 in the presence of catalytic amounts of vanadium compounds allows synthesizing hitherto unknown polyhydroxylated carboxyfuranone **25** in 60% yield (Scheme 4).<sup>14,17,18</sup> It should be emphasized that vanadium compounds at pH 7–8 suppress the formation of 2-furancarboxylic acid (**4**) which is the major product in the catalyst-free version. Using the model reactions involving acid **4**, we were able to show that furanone **25** is resulted from oxidative transformations of acid **4** under the selected reaction conditions.<sup>12</sup>



For the synthesis of 3,4,5-trihydroxy-5-carboxy-2(3*H*,5*H*)-furanone (**25**), furfural was oxidized with 30% hydrogen peroxide in the presence of  $\text{VOSO}_4$  at a molar ratio **1a** :  $\text{H}_2\text{O}_2$  :  $\text{VOSO}_4$  = 1 : 5 : 0.005 at pH 8–9 and temperature of 60 °C.

When the reaction of furfural with  $\text{H}_2\text{O}_2$  is carried out without additives increasing pH of the reaction medium, the early stages of oxidation quantitatively produce formic acid, while other carboxylic acids are formed later. During the oxidation process, pH of the reaction medium decreases up to 1–2 and the formed acids start to catalyze their own formation and the process becomes autocatalytic.<sup>6</sup> Under these conditions, furfural hydroxy hydroperoxide **2a** transforms into 2-formyloxyfuran **3** (see Scheme 1), which was isolated from the oxidate.<sup>19</sup> Ester **2a** and products of its hydrolysis, compounds **5–7**, determined the final products of oxidation of furfural with aqueous hydrogen peroxide in acidic medium.

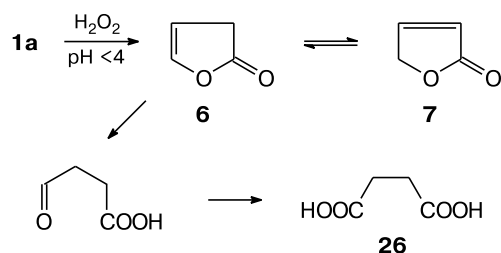
We failed to isolate pure enol **5** since conjugation between the cycle and hydroxy group causes its low stability. In acidic medium, enol **5** rapidly transforms into its more stable keto forms **6** and **7**. At the same time, enol **5** was detected by high-resolution NMR spectroscopy among the oxidation products and its stable forms, furanones **6** and **7**, were isolated.<sup>20</sup> Furanone **7** is stable under aqueous acidic conditions (pH < 4).<sup>12</sup> This provides possibility to synthesize compound **7** by autocatalytic oxidation of furfural with hydrogen peroxide.<sup>21,22</sup>

Furan-2(5*H*)-one (**7**) was synthesized by the reaction of furfural (**1a**) with either 15% or 30% hydrogen peroxide

at a molar ratio **1a** : H<sub>2</sub>O<sub>2</sub> of 1 : (2.0–2.2). The oxidation was carried out at 60–70 °C until complete consumption of furfural. Then the oxidate was concentrated, the crystalline product was filtered off, and the filtrate was extracted with chloroform to give lactone **7** in 40% yield.

The crystalline product is succinic acid (**26**) formed from unstable lactone **6** upon its hydrolysis to β-formylpropionic acid (Scheme 5). The latter compound is oxidized to acid **26** in 40% yield. Thus, under the described conditions the overall yield of the furfural oxidation products, compounds **7** and **26**, is 80%.

Scheme 5

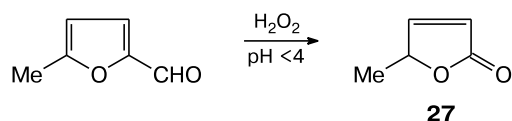


Earlier, furanone **7** was synthesized by a multistep protocol from substituted butyrolactones, which in turn were prepared from poorly available substituted butanoic acids or vinylacetic acid as well as by hydrolysis of 2-acetoxy- and 2-methoxyfuran. After our publication<sup>21</sup> appeared, Liu and co-workers<sup>23</sup> described synthesis of lactone **7** in 37% yield by oxidation of furfural with 30% hydrogen peroxide in heterogeneous system water–dichloroethane in the presence of sodium sulfate with all other conditions being identical to the earlier published.<sup>21</sup>

It is obvious that the direct synthesis of furanone **7** together with succinic acid (**26**) by the reaction of furfural with hydrogen peroxide is advantageous and makes compound **7** accessible for application as a biologically active substance and a starting material for different organic syntheses.<sup>14</sup>

Following the procedure described for the synthesis of lactone **7**, 5-methylfurfural was oxidized into 5-methyl-2(5*H*)-furanone (**27**) in 30% yield<sup>24</sup> (Scheme 6). This confirms the fact that oxidation of furan aldehydes bearing the electron-withdrawing substituents proceeds *via* transformations of the corresponding hydroxy hydroperoxides to give products similar in structure to compounds **3** and **5–7** (see Scheme 1).

Scheme 6



Tautomeric transformations of hydroxyfuran **5** into lactones **6** and **7** in the system furfural–H<sub>2</sub>O<sub>2</sub>–H<sub>2</sub>O compete with its oxidation with hydrogen peroxide into hydroxyfuranone **9a** *via* hydroperoxide **8** (see Scheme 1). In catalyst-free system, tautomeric transformations of enol **5** into its keto forms **6** and **7** are more preferable than oxidation reaction; therefore, in this case compound **9a** is a minor product formed in the yield less than 4%.<sup>25</sup>

Application of one of the following catalysts: vanadium(IV) or vanadium(V) compounds, molybdenum(VI) compounds, and SeO<sub>2</sub>, results in the formation of their peroxide species with H<sub>2</sub>O<sub>2</sub>, which are significantly more strong oxidizers than hydrogen peroxide.<sup>25</sup> Under these conditions, hydroxyfuran **5** rapidly oxidizes into hydroxyfuranone **9a** (see Scheme 1) and this process apparently predominates over the competing tautomeric transformations of enol **5** into lactones **6** and **7**. Taking these results into account, we elaborated synthetic procedure to obtain 5-hydroxy-2(5*H*)-furanone (**9a**).<sup>8,26,27</sup> The highest yield of **9a** (up to 90%) was achieved upon oxidation of furfural with 30% hydrogen peroxide in the presence of catalytic amounts of vanadium 2-oxonaphthenate (or other vanadium catalyst) and hydroquinone in a water–acetone mixed solvent at a molar ratio furfural : H<sub>2</sub>O<sub>2</sub> : catalyst : hydroquinone = 1 : 3 : 0.003 : 0.0003. The reaction was carried out at 55–60 °C for 6 h, then the oxidate was neutralized, concentrated, and extracted with diethyl ether. Drying the organic layers with Na<sub>2</sub>SO<sub>4</sub> and removal of the solvent afforded crystalline product **9a**, which melts at 55–57 °C.<sup>27</sup>

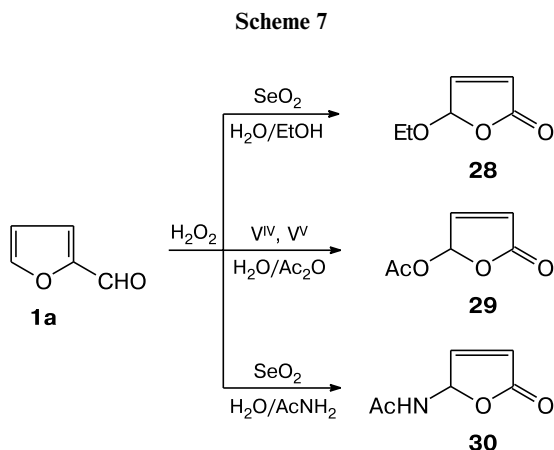
Other conditions<sup>8,26</sup> to synthesize compound **9a** by oxidation of furfural (**1a**) with hydrogen peroxide give target product in lower yields.

The cyclic form of hydroxyfuranone **9a** is contaminated with its open form **9b** (see Scheme 1). These forms exist in equilibrium, which is noticeably shifted towards the cyclic form<sup>28</sup> at acidic pH (pH 0–4) approached during oxidation of furfural with hydrogen peroxide.<sup>12</sup>

Synthesis of 5-hydroxy-2(5*H*)-furanone (**9a**) by the described above procedure is advantageous over both energy-consuming and time-consuming sensitized photo-oxidation of either furfural or furan with molecular oxygen<sup>29–31</sup> and unsafe furfural oxidation with nitric acid in the presence of vanadium catalyst.<sup>32</sup>

Based on the domination of oxidative transformations of enol **5** into hydroxyfuranone **9a** in the system furfural–H<sub>2</sub>O<sub>2</sub>–catalyst (SeO<sub>2</sub> or vanadium(IV,V) compounds) revealed by us, synthetic approaches towards derivatives **28–30** were elaborated (Scheme 7). These procedures involve catalytic oxidation of furfural with aqueous hydrogen peroxide in homogeneous water–organic mixtures.<sup>8,26,33</sup>

5-Ethoxy-2(5*H*)-furanone (**28**) was synthesized by stirring furfural with a solution of SeO<sub>2</sub> in 5% aqueous hydrogen peroxide for 2 h at 50 °C until complete conversion of aldehyde **1a**. Then the oxidate was concentrated under



vacuum to remove 80% of water, the residue was diluted with ethanol and chloroform, and the mixture was refluxed with simultaneous azeotropic distillation of water until its complete removal. The obtained residue was neutralized with concentrated aqueous  $\text{NaHCO}_3$  solution, extracted with diethyl ether, and vacuum distilled to give 70% yield of ethoxyfuranone **28** with b.p. 103–105 °C (16 Torr). For the reaction, a molar ratio furfural :  $\text{H}_2\text{O}_2$  : catalyst : EtOH : chloroform = 1 : 3 : 0.05 : 2 : 1 was used.<sup>26</sup>

To synthesize 5-acetoxy-2(5*H*)-furanone (**29**), a stirred mixture of furfural,  $\text{V}_2\text{O}_5$  or  $\text{VOSO}_4$ , acetone, and 30% aqueous hydrogen peroxide was heated at 50–60 °C for 6 h. The oxidate was concentrated *in vacuo*, the residue was treated with acetic anhydride and heated at 60 °C for 2 h. A molar ratio furfural :  $\text{H}_2\text{O}_2$  : catalyst : acetone : acetic anhydride was 1 : 3 : 0.003 : 10 : 2. Compound **29** was isolated in 76% yield by vacuum distillation of the reac-

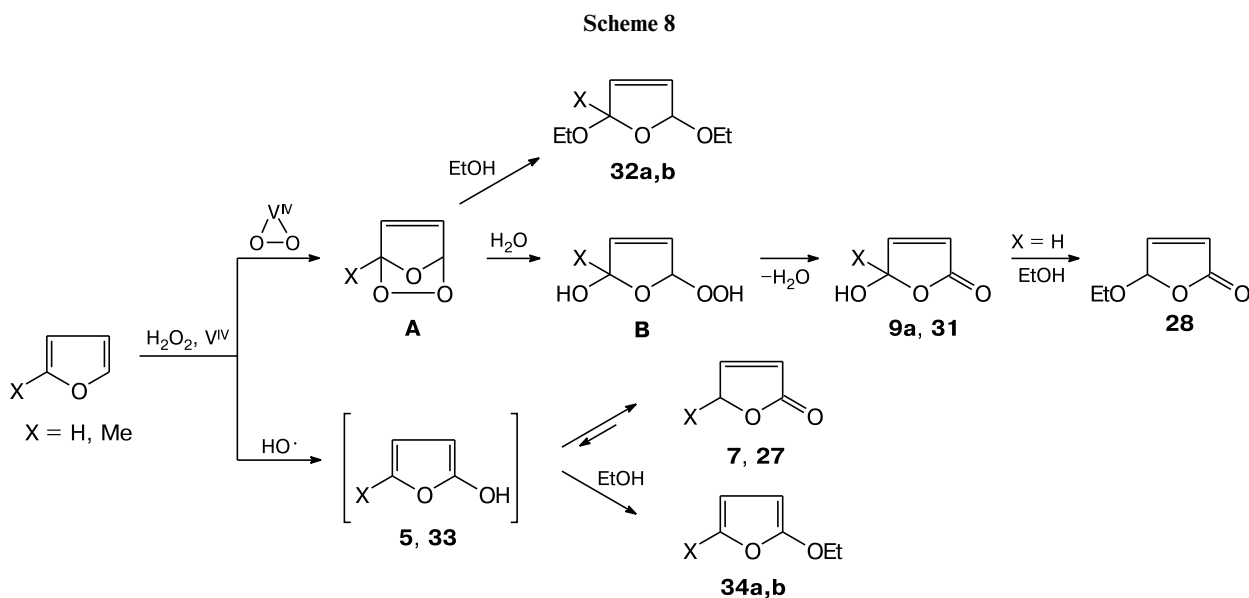
tion mixture to collect a fraction with b.p. 116–120 °C (5 Torr).<sup>33</sup>

5-Acetamido-2(5*H*)-furanone (**30**) was synthesized as described above for **28** by oxidation of furfural (**1a**) with 5% hydrogen peroxide in the presence of  $\text{SeO}_2$ .<sup>26</sup> After removal of 80% water from the oxidate, the residue was treated with acetamide (molar ratio furfural : acetamide = 1 : 1.2) and the mixture was refluxed for 1 h. Compound **30** was isolated in 60% yield by column chromatography (elution with chloroform) as crystals melting at 115–117 °C.

Thus, the finding of the synthetic conditions to access 5-hydroxy-2(5*H*)-furanone (**9a**) (see Scheme 1) prompts the synthesis of its derivatives **28**–**30** by catalytic oxidation of furfural without intermediate isolation of compound **9a** from the oxidate. The earlier described syntheses of compounds **28**–**30** started from either furanone **9a** or ethoxyfuranone **28**, which were synthesized as a rule by photochemical oxidation of furfural.<sup>30</sup>

A series of dihydrofuran derivatives (compounds **7**, **27**, **28**, **31**, and **32a,b**) were synthesized using the reactions occurring in the homogeneous systems furan (methylfuran)— $\text{H}_2\text{O}_2$ —vanadium compound—water—ethanol<sup>34–39</sup> (Scheme 8).

In contrast to furfural **1a**,  $\alpha$ -positions of unsubstituted furan have an increased electron density due to conjugation with the exocyclic oxygen atom. This facilitates substitution and addition reactions at the positions 2 and 5 of the furan ring. Note that hydrogen peroxide decomposes in the presence of vanadium(IV,V) compounds to give hydroxyl radicals, singlet oxygen, and vanadium peroxo complexes. All these species are capable of participating in the reactions with the furan ring to produce various furan and dihydrofuran derivatives.



X = H (**5**, **7**, **9a**, **32a**, **34a**), Me (**27**, **31**, **32b**, **33**, **34b**)

Along with the isolated individual products, the reactions in the specified above reaction systems proceed *via* the following intermediates: peroxy compounds **A** and **B** (detected by TLC), compounds **34a,b** and **6** (detected by GC/MS). Among the final oxidation products, compounds **7** and **9a** were also detected (see Schemes 1 and 8).<sup>34</sup> A detailed reaction mechanism of the reactions occurring in the described systems was discussed by us earlier.<sup>2</sup> Depending on the conditions of oxidation of either furan or 2-methylfuran, these reactions yield methylfuranone **27**, 5-hydroxy-5-methylfuranone **31**, ethoxyfuranone **28**, and diethoxydihydrofurans **32a,b**.

Oxidation of 2-methylfuran gives<sup>35</sup> also  $\beta$ -acetylacrylic acid (regarded as an open tautomeric form of hydroxyhydrofuranone **31**) and its ethyl ester.

5-Methyl-2(5*H*)-furanone (**27**) was synthesized by  $\text{KHW}_4$ -catalyzed oxidation of 2-methylfuran with 5% solution of hydrogen peroxide in *n*-butanol (was prepared from 30% hydrogen peroxide). A vigorously stirred reaction mixture was heated at 40–50 °C until complete consumption of 2-methylfuran. A molar ratio 2-methylfuran :  $\text{H}_2\text{O}_2$  : catalyst = 1 : 2 : 0.05 was used. Then the solvent was removed *in vacuo*, the residue was treated with triethylamine (3% based on the starting 2-methylfuran) and refluxed at 70 °C for 3 h. After removal of the catalyst, furanone **27** was isolated in 50% yield by vacuum distillation to collect fraction with b.p. 85–86 °C (10 Torr).<sup>36</sup> In a comparison with synthesis of lactone **27** by oxidation of 5-methylfurfural with hydrogen peroxide,<sup>4</sup> the use of 2-methylfuran as a starting material gives 1.7-times higher yield of the target compound.

5-Hydroxy-5-methyl-2(5*H*)-furanone (**31**) was synthesized from 2-methylfuran.<sup>8</sup> To a solution of 2-methylfuran in acetone, 30% aqueous  $\text{H}_2\text{O}_2$ , catalyst vanadyl acetylacetonate  $\text{VO}(\text{acac})_2$ , 18-crown-6, and hydroquinone were added. A molar ratio 2-methylfuran :  $\text{H}_2\text{O}_2$  :  $\text{VO}(\text{acac})_2$  : 18-crown-6 : hydroquinone was 1 : 3.2 : 2 : 0.002 : 0.0007. Oxidation was carried out at 60 °C for 6.5 h under vigorous stirring. Compound **31** was isolated in 75% yield as described above for **9a**. Compound **31** is a crystalline substance melting at 33–35 °C.

Oxidation of furan with hydrogen peroxide in aqueous ethanol in the presence of either  $\text{VOSO}_4$  or  $\text{VOCl}_2$  produces simultaneously 5-ethoxy-2(5*H*)-furanone (**28**) and 2,5-diethoxy-2,5-dihydrofuran (**32a**) in the yields of 55 and 40%, respectively.<sup>37,38</sup> To a vigorously stirred mixture of a catalyst in EtOH, 30% aqueous hydrogen peroxide was added and the resulting solution was maintained at 20 °C until the exothermic reaction ceased. Then furan was added and the reaction was carried out at 20 °C until complete consumption of  $\text{H}_2\text{O}_2$  and intermediate peroxides. A molar ratio furan :  $\text{H}_2\text{O}_2$  : catalyst : EtOH was 1 : 2 : 0.02 : 15. The oxidate was neutralized with saturated aqueous  $\text{NaHCO}_3$  and compounds **28** and **32a** were extracted with diethyl ether. The volatiles were removed under vacuum,

the residue was diluted with chloroform, and water was removed by azeotropic distillation. Removal of the solvent and subsequent vacuum distillation of the residue gives ethoxyfuranone **28** (b.p. 95–96 °C (12 Torr)) and diethoxydihydrofuran **32a** (b.p. 70–73 °C (12 Torr)).

The same procedure was used to oxidize 2-methylfuran in methanol at 60 °C to obtain 2-methyl-2,5-dimethoxydihydrofuran in 38% yield.<sup>38</sup>

Compounds **28**, **31**, and **32a,b** are apparently result from transformations of ozonides **A** and hydroperoxides **B** in aqueous alcoholic media. In turn, species **A** and **B** are formed from furan and 2-methylfuran (see Scheme 8).<sup>2,34,39</sup>

Syntheses of 2,5-dialkoxy-2,5-dihydrofurans by catalytic oxidation of furans with hydrogen peroxide in aqueous alcoholic media are advantageous over electrochemical alkoxylation of furan in the presence of bromine or bromine-containing catalytic systems<sup>29,30,40</sup> as well as over sensitized photooxidation of furan with oxygen in alcoholic media catalyzed by vanadium compounds.<sup>41–43</sup> These syntheses are time-consuming, require expensive materials for electrode fabrication and expensive equipment for photoreactions.

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The reactions of alkyl- and formylfurans with aqueous hydrogen peroxide are sensitive to the effects of different reaction variables. By changing pH of the reaction medium, applying vanadium(IV,V) or  $\text{SeO}_2$  catalyst, varying the reagent ratio and reaction temperature, and selecting the organic co-solvents soluble in water, it is possible to perform oxidation in homogeneous medium and to direct the reaction to obtain products of different types, namely,  $\alpha$ -hydroxy hydroperoxides of furan aldehydes, 2-furan-carboxylic acids and their esters and amides, 2(5*H*)-furanone and its various functional derivatives, as well as 2,5-dialkoxydihydrofurans.

All these compounds are of great interest as the intermediates in chemical synthesis and biologically active substances. The elaborated synthetic procedures are advantageous over earlier described approaches.

It is obvious that the revealed regularities of the reactions described in this review open prospects for application of their yet-unrealized synthetic possibilities and development of new synthetic procedures based on them.

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