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Hydrogen Peroxide Oxygenation of Furan-2-carbaldehyde by the Easy Method of Green Chemistry

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ABSTRACT

Derivatives of 2(5*H*)-furanone (*γ*-crotonolactone) are important intermediate synthetic products with a wide range of biological effects that have become widely used in the pharmaceutical industry, medicine and veterinary medicine, in particular in the prevention and treatment of fish diseases. However, the environmental issue of obtaining these compounds to reduce the negative impact on the surrounding environment remains relevant. The article describes for the first time the method of *γ*-

crotonolactone synthesis, which is based on the concept of green chemistry. Synthesis is carried out under mild conditions using non-toxic reagents by furfural oxidation. For the first time, a mixture of hydrogen peroxide and acetic acid for the oxidation of furfural was used in the ratio 1:0.05.

A mixture of organic acids (succinic, maleic, fumaric, formic acid and cinnamic acid), obtained as a by-product in the synthesis of *γ*-crotonolactone, can be used as a highly effective, eco-friendly organic fertilizer or preparation with a stimulating effect.

Keywords: furan-2-carbaldehyde, 2(5*H*)-furanone (*γ*-crotonolactone), green chemisty, hydrogen peroxide, acetic acid.

INTRODUCTION

The use of compounds of the furan series, namely derivatives of 2(5*H*)-furanone (*γ*-crotonolactone or 2-butenolide), in synthetic organic chemistry and in the national economy is known for a long time.[1,2] Compounds of this class are found in beer, kvass, fermented foods and especially in contaminated feeds exposed to mold.[3,4] They attract considerable attention as growth regulators of plants,[5] substances that inhibit the tumor growth in the organism, as they are inhibitors of cell metamorphosis[6] and promoters of the growth of industrial fish cultures.[7] 2(5*H*)-Furanones are known as compounds with the antifungal and antibacterial activities.[8-10]

Under the influence of γ-crotonolactone, the content of thiol groups in the intestinal mucosa is increased due to the increased biosynthetic processes in the gut associated with increased secretion of specific enzymes. The experiments for the determination of the total proteolytic activity of fish intestine, exposed to γ-crotonolactone, demonstrate it very clearly. The total proteolytic activity characterizing the number of enzymes in the intestinal mucosa has increased significantly (by 24%) for the 2nd day and continued to remain at a high level for 3 days. At 30th day it grew up to 30%. It is noted that the proteolytic activity of the intestine continues to remain high even after the end of γ-crotonolactone addition to the feed. 2(5*H*)-Furanone has not a negative effect on the fish body, on the contrary, this drug helps to suppress the growth of pathogenic microflora in the intestine.[11,12]

At the same time, formic, fumaric, maleic, succinic, and cinnamic acids as a product of the furfural oxidation are used in almost all fields of the industrial and food chemistry. Formic acid and its salts are used in the feed industry, textile dyeing and finishing, food additives, grass silage, natural rubber, leather tanning, etc.[13] Fumaric acid is nontoxic and versatility reagent, that used in the resin industry, green chemistry as an eco-friendly catalyst, and in the food industry as a nutritional additive and acidulant.[14] Maleic acid is not so widespread like fumaric acid. Maleic acid is used for the production of maleinate resins, copolymers, and generally as a chemical precursor of fumaric acid and maleic anhydride.[15] Moreover, cinnamic acid and its derivatives are known as natural occurring products.[16] They were found in all green plants.[17] Cinnamic acids are also used in medicinal chemistry as a perspective objects with a different useful spectrum of activities.[18]

Another promising direction for the use of 2(5*H*)-furanone is a fish breeding, which is particularly widespread in Central and Eastern Europe, as well as in Asia. Drugs based on 2(5*H*)-furanone inhibit the development of cyanobacteria, which prevents fish death in the ponds. In particular, there is a positive result in the use of drugs based on *γ*-crotonolactone and a mixture of the above-mentioned organic acids in the cultivation of fish in natural reservoirs and in recirculating aquaculture systems, which stimulate the development of a natural fodder base in fish-breeding ponds.[19] It allows the use of such drugs in the technologies of intensive cultivation of live feeds, in particular, freshwater planktonic crustaceans, such as daphniids. These organisms are widely used both in ornamental aquaculture and in the larviculture of many commercial fish species.[20]

Therefore, the aim of this study was to improve the synthesis of 2(5*H*)-furanone using non-toxic and environment-friendly hydrogen peroxide oxygenation in the presence of the catalytic amount of acetic acid in water.

MATERIALS AND METHODS

Chemicals. All alalytical grade chemicals were obtained from Sigma-Aldrich and were used without any further purification. Double distilled water was used in this study.

General Experimental Details

All melting points were determined in open capillary tubes on a Boetius apparatus and are uncorrected. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-500 spectrometer (500 MHz) in DMSO-d_6; the chemical shifts were measured relative to tetramethylsilane. Mass spectra were recorded on an Agilent 1100 Series G1956B LC/MSD SL LCMS system, using electrospray ionization at atmospheric pressure (70 eV). UV spectra were recorded on a "SPECORD M 40" spectrophotometer. IR spectra were recorded on a "SPECORD M 80" spectrophotometer in tablets with KBr. Elemental analysis was carried out on a Perkin Elmer 2400 CHN analyzer. The separate determination was carried out using a HPP4001 liquid chromatograph with two serially coupled glass columns (150 × 3.3 mm) packed with the Separon SC-X C-18 adsorbent (0.6% acetic acid as the mobile phase, flow rate of 0.3 cm^3/min). Monitoring of the reactions was performed by TLC method on "Silufol UV 254" plates.

Oxidation of furfural

The oxidation reaction with hydrogen peroxide was carried out in a three-necked round bottom glass flask equipped with reflux condenser and mechanical stirrer. The flask was loaded under stirring with the furfural (13.0 mL, 0.160 mol) and water (50 mL), and the mixture of H_2O_2 37.5% (14.7 mL, 0.192 mol) with acetic acid (0.55 mL, 0.0096 mol) was slowly added. The reaction mixture was kept under constant stirring for 24 h at a temperature below 60°C.

After completion of the reaction, water was removed under reduced pressure. The light yellow precipitate of organic acids was filtered off. 2(5*H*)-Furanone was obtained from the filtrate by vacuum distillation at a 12 mm Hg. The yield of 2(5*H*)-furanone – 71%.

2(5*H*)-Furanone (1): Colorless to slight light yellow liquid, bp. 85–88 ^{o}C / 12 mm Hg. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.88 (dd, ^{4}J = 2.2 Hz, ^{3}J = 1.7 Hz, 2H, 5-H), 6.10 (dt, ^4J = 2.2 Hz, ^3J = 5.8 Hz, 1H, 3-H), 7.58 (dt, ^4J = 1.7 Hz, ^3J = 5.8 Hz, lH, 4-H). ^{13}C NMR (125 MHz, $CDCl_3$,) δ 71.9, 121.1, 152.2, 173.7. IR (KBr, cm^{-1}): 1739, 1781 (C=O), 1053-1205 (–C–O–C–). Anal. Calcd. for $C_4H_4O_2$: C, 57.14; H, 4.80. Found: C, 57.10; H, 4.71. MS (EI) *m/z* 85.11 $[M+H]^+$.

Calculated and found data of succinic, maleic, fumaric, formic and cinnamic acids are confirmed by the literary data.

RESULTS AND DISCUSSION

Catalytic oxidation of furan-2-carbaldehyde (furfural) attracts the attention of many researchers. This aldehyde is derived from vegetable wastes[21–23] and is available on the market of chemical reagents. The furfural molecule contains several reaction centers, which implies a wide variety of syntheses. The projects on the oxidation of furfural by molecular oxygen after photoinitiation[24] and in conditions of heterogeneous catalysis, including the use of compounds of transitional and noble metals ($Cu(OAc)_2$, $Mn(OAc)_2$, $Pd(OAc)_2$, AgOAc, $FeSO_4$, $RuCl_3$, $NiCl_2$, V_2O_5, $Co(NO_3)_2$, TiO_2-ZrO_2, $Pb(OAc)_2$ are well known.[25–34] It was also reported about the oxidation of furfural with hydrogen peroxide in the presence of a photogenic iron catalyst in the form of a complex $[FeCp(C_6H_5R)]PF_6$ (R=H, Cl or CH_3).[35] However, insufficient attention was paid to the homogeneous reactions of furfural with aqueous hydrogen peroxide in the works mentioned above.

At the same time, it is known that in the process of furfural oxidation with hydrogen peroxide (Scheme 1), depending on the reaction conditions and the catalyst type, various reactive compounds are formed,[36,37] which provide means for the implementation of various synthetic pathways based on the reactions of furfural with aqueous H_2O_2 and catalysts.

All of the given above methods are multistage and include the use of hard-to-reach and in some cases toxic materials, such as organic solvents (dichloroethane, chloroform), complex salts of heavy and transition metals in the role of catalysts such as Cu^{2+}, Mn^{2+}, Pd^{2+}, Ag^{+}, Ru^{3+}, Ni^{2+}, V^{5+}, Co^{2+}. These catalysts are expensive and have a negative impact on the environment.

Therefore, in this work the method of *γ*-crotonolactone synthesis was based on the concept of green chemistry, namely the oxidation of furfural was carried out in an aqueous solution without the use of organic solvents, and for the first time an aqueous solution of hydrogen peroxide was used in the role of an oxidizer with a small amount of acetic acid as a promoter of reaction. Oxidation was carried out for 24 hours with vigorous stirring and at a temperature below 60°C. The process was controlled by UV spectroscopy (residual aldehyde) and TLC (acid formation). The composition of the reaction products was determined by high-performance liquid chromatography (HPLC) (using authentic samples). As a result, the target product *γ*-crotonolactone (**1**) was obtained with a yield of ~ 71% and a crystalline precipitate of by-products (**2-6**) mixture of light yellow color (Scheme 2).

Using HPLC it was determined that the crystalline precipitate contains mainly a mixture of organic acids, namely succinic (**2**), maleic (**3**), fumaric (**4**), formic (**5**), cinnamic (**6**). This mixture of organic acids can be used in agriculture as non-toxic ecologically pure organic fertilizer.

Thus, using the concept of green chemistry an important intermediate synthetic product with a wide range of biological effects *γ*-crotonolactone was synthesized by the oxidation of furfural under soft conditions and using non-toxic reagents. For the oxidation of furfural, a mixture of hydrogen peroxide and acetic acid was used in the ratio 1 : 0.05 for the first time. A mixture of organic acids in the role of a by-product, that can be used in the national economy as a highly effective, environmentally friendly organic fertilizer, was obtained.

Acknowledgments

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Notes

The authors declare no competing financial interest.

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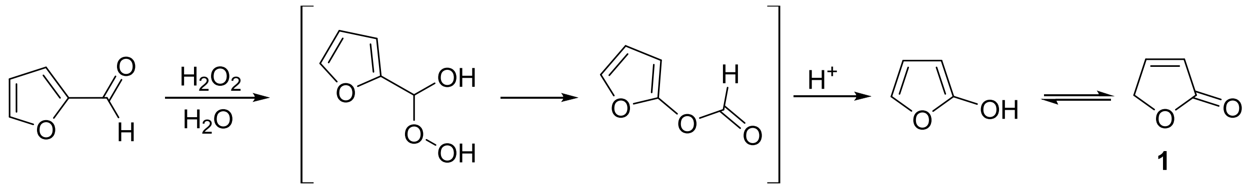
Figure captions

Scheme 1. Oxidation mechanism of furan-2-carbaldehyde.

Scheme 2. Oxidation of furan-2-carbaldehyde with H_2O_2 and acetic acid in water.

Scheme 1. Oxidation mechanism of furan-2-carbaldehyde.



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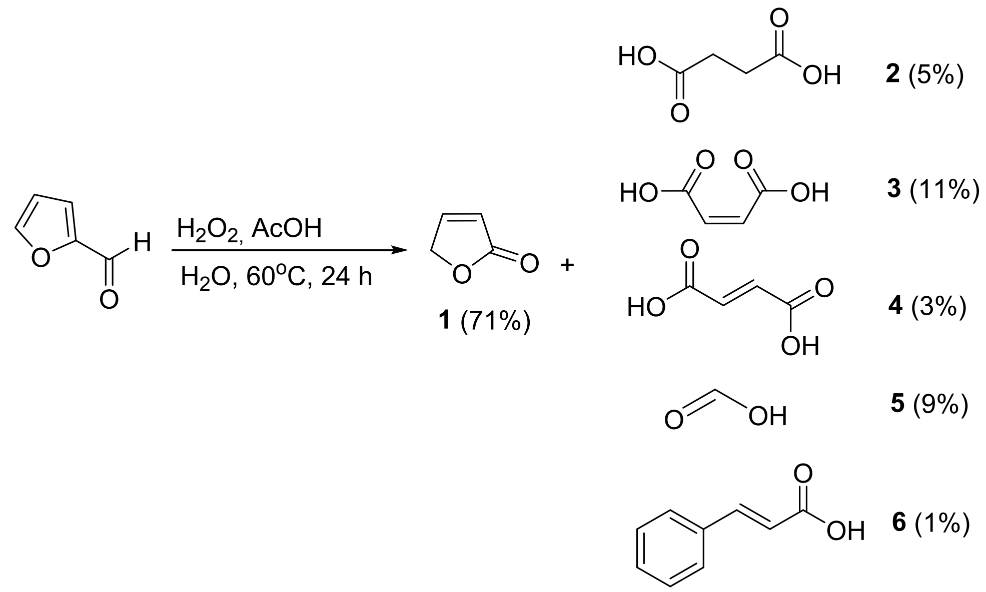
Scheme 2. Oxidation of furan-2-carbaldehyde with H_2O_2 and acetic acid in water.



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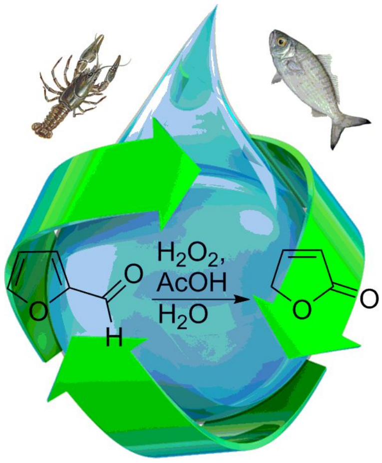

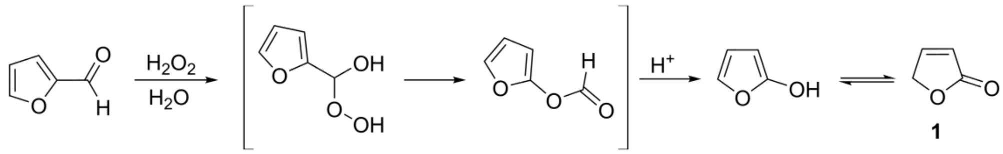

Oxidation mechanism of furan-2-carbaldehyde

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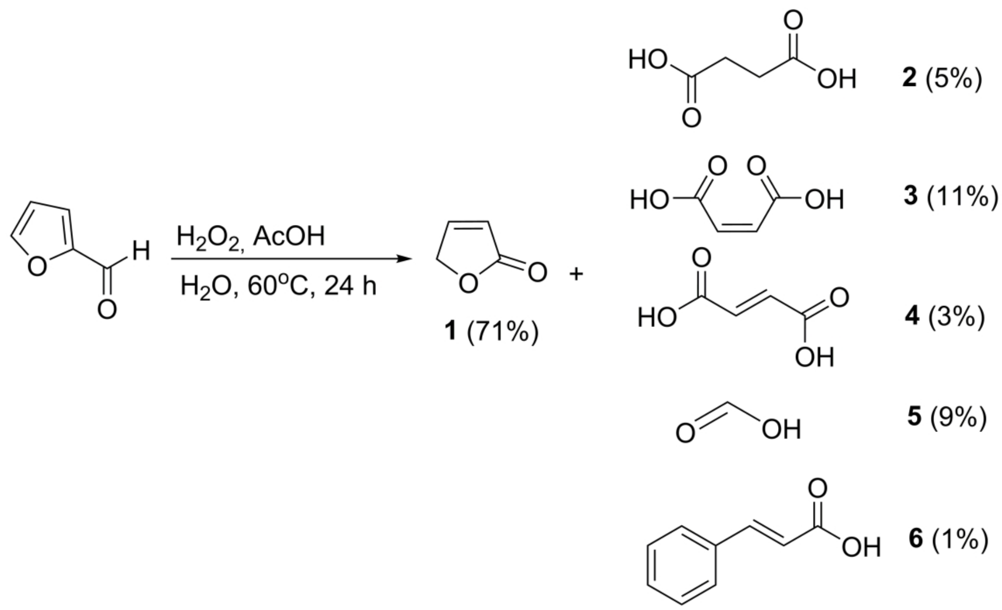

Oxidation of furan-2-carbaldehyde with H_2O_2 and acetic acid in water

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