CATALYTIC SYNTHESIS OF DIHYDROFURANS (REVIEW)

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Various methods for the preparation of 2,3-dihydrofuran, 2,5-dihydrofuran, 2-methylenetetrahydrofuran, and their alkyl and aryl derivatives are examined. The most promising method for the preparation of 2,3-dihydrofuran is the conversion of 1,4-butanediol on cobalt catalysts. 2,5-Dihydrofuran is obtained by dehydration of 2-butene-1,4-diol on Al_2O_3, cobalt-containing and other catalysts, while 2-methylenetetrahydrofuran is obtained by dehydrohalogenation of tetrahydrofurfuryl halides. The various methods for the isomerization of 2,5-dihydrofuran to 2,3-dihydrofuran are discussed. Examples of the application of dihydrofurans in organic synthesis are presented.

Dihydrofurans have recently become the subject of intensive studies due to their extensive use in fine organic synthesis. The presence of a double bond conjugated with an oxygen atom makes these cyclic vinyl ethers valuable intermediates in the synthesis of physiologically active substances, medicinal preparations, additives, etc. [1-3]. Thus, in particular, α-methyldihydrofuran is an intermediate for the synthesis of vitamin B_1, 5-chloro-2-pentanone, methyl cyclopropyl ketone, etc. [4].

Catalytic methods for the preparation of hydrogenated furan compounds have been elucidated in a number of monographs and review papers [5-10]. The principal products of hydrogenation of furan and furan compounds are tetrahydrofuran and its derivatives. In these processes dihydrofurans are formed in relatively small amounts or are not formed at all. In the present review we examine the catalytic methods for the synthesis of dihydrofurans by the dehydration and dehydrogenation of diols, keto alcohols, and other oxygen-containing compounds. Little discussion has been devoted to the problems mentioned above in reviews up until now [9].

1. Synthesis of 2,3-Dihydrofuran

1.1. Hydrogenation of Furan and Other Furan Compounds. Many attempts to hydrogenate furan to 2,3-dihydrofuran on Pt, Pd, and Ni catalysts have been unsuccessful [6]; hydrogenation of furan to tetrahydrofuran and hydrogenolysis of the C—O bond to give ketones have occurred in these attempts. The hydrogenation of the first double bond in the furan ring takes place with considerably greater difficulty than hydrogenation of the second bond. The accumulation of 2,3-dihydrofuran in the products of hydrogenation of furan is therefore unlikely, although a number of authors propose that 2,3-dihydrofuran is an intermediate in the hydrogenation of furan to tetrahydrofuran. It is interesting to note that products of hydrogenolysis of the C—O bond are primarily obtained in the hydrogenation of 2,3-dihydrofuran derivatives [11]. On a palladium catalyst at 200°C dihydrofurans give equimolar mixtures of furans and tetrahydrofurans, whereas at 300°C they give mixtures of furans and aliphatic ketones. It is assumed that both 2,5- and 2,3-dihydrofurans initially undergo catalytic dehydrogenation reactions, after which, depending on the temperature and the composition of the catalyst, the resulting furan ring undergoes either hydrogenation or hydrogenolysis [12, 13].

Up until recently it was assumed that dihydrofurans cannot be obtained by hydrogenation of tetrahydrofurans, since it was impossible to stop these reactions at the step involving the formation of dihydrofurans. Hydrogenation of the furan ring proceeds through a step involving the formation of a dihydrofuran; if water is present in the reaction mixture, the addition of water to the second double bond [15] may also take place in addition to its hydrogenation [14]:

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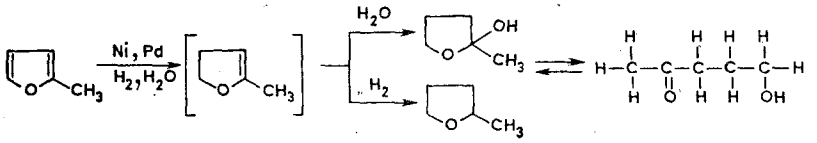
TABLE 1. Conversion of 1,4-Butanediol on a Cobalt Catalyst and on a Cobalt Catalyst Modified by Magnesium and Thorium Ions

Characteristics of the catalyst	Temp., °C	1,4-Butanediol: catalyst wt. ratio	Raw material charge, kg/kg·h	Nitrogen space velocity, kg/kg·h	S_{DMF}, %	S_{THF}, %	S_{DHF}/S_{THF}	Efficiency in the formation of 2,3-dihydrofuran, kg/kg·h
Cobalt	223	1 : 0,16	2,7	2,2	12,7	13,7	0,92	0,245
Cobalt modified by magnesium and thorium ions	225	1 : 0,16	2,7	2,2	49,0	24,6	1,99	0,520
	230	1 : 0,11	2,9	2,7	75,0	—	—	0,659
	232	1 : 0,07	4,5	2,8	62,0	—	—	1,195
	233	1 : 0,11	2,3	2,3	62,0	—	—	0,595
	237	1 : 0,13	3,0	2,3	65,6	12,2	5,37	0,887



Indirect evidence for the stepwise hydrogenation of the double bonds in the furan ring has been obtained [16].

The possibility of the formation of α-methyldihydrofuran was first established by Karakhanov and Blinov [17]. Thus 2-methyl-4,5-dihydrofuran was isolated for the first time in up to 5% yield in the hydrogenation of α-methylfuran in the vapor phase on a rhodium catalyst.

The fundamental possibility of the synthesis of 2,3-dihydrofuran by hydrogenation of furan was demonstrated in a patent [18]. Ruthenium catalysts applied to Al_2O_3 are promising catalysts for the hydrogenation of furan to 2,3-dihydrofuran. The reaction is carried out in the presence of dimethylformamide (DMF). In this case significant amounts of 2,3-dihydrofuran are detected along with tetrahydrofuran in the products of hydrogenation of furan. However, the method has not undergone further development.

2,3-Dihydrofuran was also obtained as an intermediate in the hydrogenation of furfural on a Pd/Al_2O_3 catalyst promoted by the addition of ruthenium or rhodium [19]. Furan, tetrahydrofuran, 2,3-dihydrofuran, and 2-methylfuran were detected in the reaction mixture. However, this method does not have practical value because of the low selectivity of the formation of 2,3-dihydrofuran.

1.2. Dehydrogenation of Tetrahydrofuran. Shimanskaya and co-workers [20] have proposed a method for the preparation of 2,3-dihydrofuran and 2-methyl-4,5-dihydrofuran by dehydrogenation of tetrahydrofuran and 2-methyltetrahydrofuran. A mixture of 2,3-dihydrofuran and furan in a ratio of 2:1 is formed on a zinc–chromium–manganese catalyst in the vapor phase with 5% conversion of the starting tetrahydrofuran.

1.3. Dehydration of 2-Hydroxytetrahydrofuran. 2-Hydroxytetrahydrofuran has been proposed as the raw material for the synthesis of 2,3-dihydrofuran [21]. The starting compound is obtained by hydroformylation of allyl alcohol in the presence of the $RhHCO(PPh_3)_3$ complex and excess PPh_3 [21] or by conversion of a mixture of 2-butene-1,4-diol and hydrogen on an Ni catalyst containing Se, Te, or Sn [22]. According to the latter method, the yield of 2-hydroxytetrahydrofuran is 73% vis-à-vis 82% conversion of the raw material. We have demonstrated the fundamental possibility of preparing 2-hydroxytetrahydrofuran by the liquid-phase oxidation of tetrahydrofuran [23]. Potassium pyrosulfate ($K_2S_2O_7$) is used as the dehydrating agent for the dehydration of 2-hydroxytetrahydrofuran [24]. The method is characterized by the use of a deficient amount of 2-hydroxytetrahydrofuran.

2,3-Dihydrofuran is also obtained by conversion of tetrahydrofuryl alcohol on a Cu–Co catalyst at 200-300°C [25]; tetrahydrofuran and 2,3-dihydrofuran are obtained in equal amounts in this case. A disadvantage of this method is the extremely low conversion of the raw material.

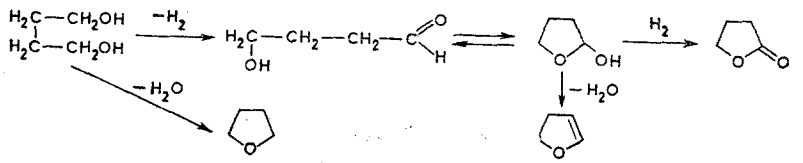
1.4. Conversion of 1,4-Butanediol. Selective catalysts for the dehydration of 1,4-butanediol to tetrahydrofuran are Al_2O_3, SiO_2–Al_2O_3, SiO_3–MgO [26, 27], ion-exchange resins [28], Cu–Al and Pd–Al catalysts of the Raney type [29, 30], catalysts containing K_2O, Al_2O_3, Nd_2O_3, MoO_3,

TABLE 2. Average Results of the Dehydration of γ-Acetopropyl Alcohol on a Cobalt Catalyst Promoted by the Addition of Zinc and Applied to γ-Al_2O_3 (at a nitrogen space velocity of 140-146 h^{-1} and for 60-80% conversion of the raw material)

Temp., °C	Raw material charge, g/liter·h	Yield of 2-methyl-4,5-dihydrofuran, %	Yield of 2-methyl-2,5-dihydrofuran, %	Efficiency of the formation of 2-methyl-4,5-dihydrofuran, g/liter·h
210	87	15	22	23,5
237	280	37	22	78
250	280	15,1	43	22
320	280	12,3	58	25

and NiO [31], etc. Compounds of Al, Zr, and other metals, in addition to dehydration, also catalyze the dehydrogenation of 1,4-butanediol to give 2,3-dihydrofuran [32]. Depending on the composition of the promoters and the nature of the support, cobalt-containing catalysts may have dehydrating ability in the reaction to form tetrahydrofuran and may also display high selectivity in the reaction to form 2,3-dihydrofuran.

Cobalt catalysts promoted by manganese, zinc, and magnesium ions and applied to carbon, silica gel, aluminum oxides, or kieselguhr are selective catalysts for the conversion of 1,4-butanediol to 2,3-dihydrofuran and other 1,4-alkanediols to 2,3-dihydrofuran derivatives [33]. According to this method, the reaction is carried out under periodic conditions with gradual raising of the temperature. The introduction of acidic additives into the reaction mixture has been proposed. The yield of 2,3-dihydrofuran reaches 89%. According to [34], the reaction proceeds via a parallel-consecutive scheme:



The conversion of 1,4-butanediol on Co catalysts applied to γ-Al_2O_3 and kieselguhr has been studied in detail [35, 36]. Tetrahydrofuran is obtained in quantitative yield when the reaction is carried out under flow conditions at atmospheric pressure on a cobalt catalyst promoted by zinc ions and applied to γ-Al_2O_3. It has been established that at 170-230°C on these catalysts 2,3-dihydrofuran is converted to tetrahydrofuran. Depending on the conditions, the process can be directed to favor the primary formation of 2,3-dihydrofuran (in up to 44% yield), γ-butyrolactone (in up to 43% yield), or tetrahydrofuran (in up to 60% yield) on a cobalt catalyst promoted by magnesium and applied to kieselguhr under continuous conditions in the liquid phase under pressure.

The catalytic synthesis of 2,3-dihydrofuran proceeds with the highest selectivity under periodic conditions at atmospheric pressure. In this case the resulting 2,3-dihydrofuran is removed rapidly from the reaction zone, and its further transformation is thereby avoided. The selectivity of the formation of 2,3-dihydrofuran increases at 180-230°C, whereas the selectivity of the formation of tetrahydrofuran decreases as the temperature is raised. The yield of 2,3-dihydrofuran reaches 73% vis-à-vis a process efficiency of 1.3 kg/liter·h when a mixture of two industrial cobalt catalysts is used under optimal conditions (at 230°C and a 1,4-butanediol:catalyst weight ratio of 1:0.46) [36].

Since the dehydration step (particularly the dehydration of 2-hydroxytetrahydrofuran to 2,3-dihydrofuran) may be of great significance in the overall synthesis of 2,3-dihydrofuran, a study of the effect of dehydrating additives on the activity and selectivity of the cobalt catalyst was expedient. It is known that thorium dioxide is an active dehydration catalyst [37]. The activity of an industrial cobalt–magnesium–thorium catalyst for the synthesis of alcohols in the conversion of 1,4-butanediol to 2,3-dihydrofuran was studied to verify this assumption (Table 1). The unpromoted cobalt catalyst is characterized by low selectivity of the formation of 2,3-dihydrofuran. The ratio of the selectivity of the formation of 2,3-dihydrofuran (S_{DHF}) and the selectivity of the formation of tetrahydrofuran (S_{THF}) is virtually

unity. Promotion of the cobalt catalyst by the addition of magnesium and thorium ions leads to a significant increase in the selectivity of the formation of 2,3-dihydrofuran.

It is interesting to note that the formation of γ-butyrolactone is not observed in the conversion of 1,4-butanediol on a cobalt catalyst modified with magnesium and thorium ions; this indicates acceleration of the steps involving dehydration of the intermediates to 2,3-dihydrofuran. Considering the high selectivity of the formation of 2,3-dihydrofuran, the cobalt catalyst promoted by magnesium and thorium should be considered to be promising for the catalytic synthesis of 2,3-dihydrofuran.

It has been established that the introduction of concentrated H_2SO_4 (at a 1,4-butanediol: H_2SO_4 molar ratio of $1:1.7\cdot10^{-2}$) does not have a positive effect on the course of the dehydration. Pronounced resinification of the reaction mixture is observed vis-à-vis a comparable yield of 2,3-dihydrofuran. The introduction of stearic acid under comparable experimental conditions leads to a significant increase in the yield of 2,3-dihydrofuran (by 13% or more). When stearic acid is used, the degree of resinification of the reaction medium is considerably lower than in the case of sulfuric acid. However, foam formation in the reaction mixture, which complicates carrying out the process in a periodically operating reactor, increases markedly when stearic acid is introduced [35, 36].

2. Synthesis of 2-Methyl-4,5-dihydrofuran and Other 2,3-Dihydrofuran Derivatives

2.1. Dehydration of γ-Acetopropyl Alcohol. One of the most selective and well-investigated methods for the preparation of 2-methyl-4,5-dihydrofuran is the dehydration of γ-acetopropyl alcohol.* Sodium amide ($NaNH_2$) [40], H_3PO_4 [41-43], Pd/ZrO_2 [44], and the oxides and hydroxides of alkaline earth metals [45] are used as the catalysts.

Furan derivatives are formed by slow distillation of γ-keto alcohols in the presence of $NaNH_2$. 2-Methyl-4,5-dihydrofuran was obtained in 50% yield by this method.

The periodic methods for the preparation of 2-methyl-4,5-dihydrofuran (in a rectification column) are also based on the use of H_3PO_4 and oxides and hydroxides of alkaline earth metals such as calcium [41, 42, 45]. In the case of phosphoric acid the reaction temperature is 175-185°C, as compared with 200-230°C when calcium hydroxide is used. The yield of the desired product is 73% with an efficiency of up to 650 g/liter·h [36]. A disadvantage of this method is that the process is carried out under periodic conditions.

Dehydration of γ-acetopropyl alcohol to give 2-methyl-4,5-dihydrofuran has been realized under continuous conditions in the vapor phase on a Pd catalyst applied to ZrO_2 [44]. Under the optimum conditions (at 300°C, a γ-acetopropyl alcohol space velocity of 0.5 h^{-1}, and a molar dilution of γ-acetopropyl alcohol with nitrogen of 1:3.0-3.8) the yield of 2-methyl-4,5-dihydrofuran reaches 82%. The useful lifetime of the catalyst is 500 h. On Cr_2O_3—Cu—C and Al_2O_3 catalysts in the presence of ammonia γ-acetopropyl alcohol is converted chiefly to nitrogen-containing heterocycles, and 2-methyl-4,5-dihydrofuran is formed in only small amounts (20-30%).

In addition to 2-methyl-4,5-dihydrofuran, γ-acetopropyl alcohol gives cyclopropyl methyl ketone with high selectivity (in up to 62% yield) [48]. The ketone is possibly a product of further transformation of 2-methyl-4,5-dihydrofuran.

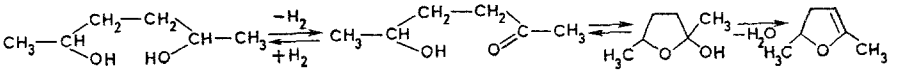
We have shown that cobalt catalysts promoted by zinc and applied to γ-Al_2O_3 have dehydrating ability with respect to γ-acetopropyl alcohol; 2-methyl-4,5-dihydrofuran and 2-methyl-2,5-dihydrofuran are formed in this case (Table 2). The highest selectivity of the formation of 2-methyl-4,5-dihydrofuran is observed at 237°C. The yield of 2-methyl-4,5-dihydrofuran is up to 37%. Over the 237-320°C range, the selectivity of the formation of 2-methyl-4,5-dihydrofuran decreases as the temperature is raised, and the selectivity of the formation of 2-methyl-2,5-dihydrofuran increases.

2.2. Transformation of 1,4-Alkanediols. On cobalt catalysts 1,4-pentanediols are dehydrogenated and dehydrated to give isomers, viz., 2-methyl-2,3-dihydrofuran and 2-methyl-4,5-dihydrofuran (in a ratio of 6:4 and in 89% yield). 1,1-Dimethyl-1,4-butanediol is converted to 2,2-dimethyl-2,3-dihydrofuran in 41% yield on a cobalt catalyst promoted by magnesium and

*γ-Acetopropyl alcohol is converted to 2-methyl-4,5-dihydrofuran even at room temperature (16% conversion after 54 days) [38]. Spectroscopic methods for the determination of γ-acetopropyl alcohol and 2-methyl-4,5-dihydrofuran are presented in [39].

applied to silica gel.

The activities of copper-containing catalysts in the conversion of 1,4-pentanediol and 2,5-hexanediol to 2,3-dihydrofuran derivatives have been investigated [49]. On copper catalysts 1,4-pentanediol is primarily dehydrated to give 2-methyltetrahydrofuran. On a Cu/SiO_2 catalyst at 200°C in the case of complete conversion of the raw material, the yield of 2-methyl-2,3-dihydrofuran does not exceed 8%. In contrast to this, 2,5-hexanediol is primarily dehydrogenated and dehydrated to give 2,5-dimethyl-2,3-dihydrofuran. Thus 2,5-dimethyl-2,3-dihydrofuran is obtained in 55% yield on a copper catalyst at 200°C. A possible mechanism for the formation of 2,5-dimethyl-2,3-dihydrofuran is represented by a scheme that includes, in contrast to [34], only successive steps:



2.3. Transformation of Ketones of the Tetrahydrofuran Series. Tetrahydrofuran-3-ones have been proposed as the raw material for the synthesis of methyl-substituted 2,3-dihydrofurans. They are initially converted to the corresponding tosylhydrazone [50]. The latter in ethylene glycol in the presence of sodium at 140-170°C form mixtures of the corresponding 2,3-dihydrofurans and 2,5-dihydrofurans. A mixture of methyldihydrofurans has been obtained in 58% yield by means of this method. The ratio of 2-methyl-4,5- and 2-methyl-2,5-dihydrofuran is 9:1. The same method has been used to obtain 2-methyl-2,3- and 2-methyl-2,5-dihydrofuran, as well as 3-methyl-2,3- and 3-methyl-2,5-dihydrofuran.

2.4. Dehydrohalogenation of Halotetrahydrofurans. The corresponding 3-chlorotetrahydrofurans have been used as the starting compounds to obtain alkyl- and aryldihydrofurans [51, 52]. Depending on the dehydrohalogenating agent and the reaction conditions, either individual alkyl- and aryl-2,3- and 2,5-dihydrofurans or mixtures of them can be obtained. Mixtures of alkyl- or aryl-substituted 2,3- and 2,5-dihydrofurans are primarily obtained when $NaNH_2$ is used [51, 53, 54]. Hydrolysis is used to separate the mixtures; 2,3-dihydrofurans form the corresponding γ-hydroxy aldehydes, whereas 2,5-dihydrofuran derivatives are not hydrolyzed [53]. This method has been used to obtain 2-methyl-4,5-dihydrofuran (in 53% yield), 2-ethyl-4,5-dihydrofuran (in 63% yield), 2-butyl-4,5-dihydrofuran (in 65% yield), and 2-phenyl-4,5-dihydrofuran (in 75% yield).

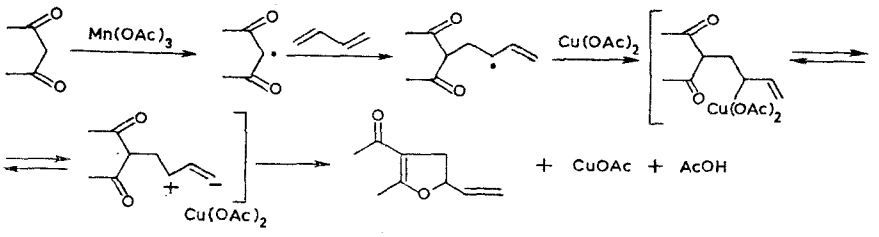
When $NaNO_2$ is used, 2-methyl-4,5-dihydrofuran (in 32% yield) is formed from 2-methyl-3-chlorotetrahydrofuran [52, 54]. 2-Alkyl-2,5-dihydrofurans have been obtained by distillation of 2-alkyl-3-chlorotetrahydrofurans over KOH [13].

2.5. Transformation of Unsaturated Alcohols or Acetals of α,β-Unsaturated Aldehydes. It has been proposed that acetylenic alcohols and acetals of α,β-unsaturated aldehydes be used as raw materials for the preparation of 2,3-dihydrofuran derivatives. 4-Pentyn-1-ol is converted to 2-methyl-4,5-dihydrofuran (in 48% yield) in the presence of $NaNH_2$ [51]. The selectivity of the process decreases when sodium methoxide is used [55].

Optically active 2,3-dihydrofuran derivatives are obtained by hydroformylation of allyl alcohols and acetals of α,β-unsaturated aldehydes in the presence of rhodium compounds [56]. This method was used to obtain 2-methyl-, 2-isobutyl-, 2,2-dimethyl-, 3-methyl-, and 3-phenyl-2,3-dihydrofuran in 36 to 70% yields.

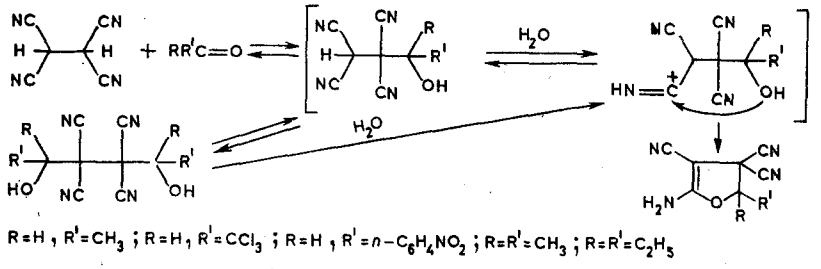
2.6. Transformation of Styrene and Its Derivatives. A promising method for the preparation of 2,3-dihydrofuran derivatives is the reaction of styrene or α-methylstyrene with acetone or acetylacetone in the presence of AgO and PbO_2 [57]; 2-phenyl-, 2-phenyl-3-acetyl-, 2-methyl-2-phenyl, and 2-metnyl-2-phenyl-3-acetyl-2,3-dihydrofuran are obtained in this reaction. The reaction proceeds via a radical mechanism.

2.7. Selective Radical 1,2 Addition of Carbonyl Compounds to Conjugated Dienes. Substituted 5-(1-alkenyl)-4,5-dihydrofurans have been obtained in the radical 1,2 addition of carbonyl compounds to conjugated dienes [58]:



It has been proposed that the reaction proceeds through a step involving the formation of a complex of the allyl-adduct radical with Cu(II) acetate. 2-Methyl-3-acetyl-5-vinyl-4,5-dihydrofuran was obtained in 90% yield by means of this method.

2.8. Condensation of Symmetrical Tetracyanoethane with Carbonyl Compounds. A new method for the synthesis of cyano derivatives of 2,3-dihydrofurans and other five-membered heterocycles based on symmetrical tetracyanoethane has been proposed [59]. The probable mechanism of the condensation of carbonyl compounds with tetracyanoethane is represented by the scheme



R=H, R'=CH_3; R=H, R'=CCl_3; R=H, R'=n-$C_6H_4NO_2$; R=R'=CH_3; R=R'=C_2H_5

Cyano derivatives of 2,3-dihydrofuran are raw materials in the synthesis of thermally stable high-molecular-weight compounds.

3. Synthesis of 2-Methylenetetrahydrofuran

2-Methylenetetrahydrofuran has been obtained by dehydrobromination of tetrahydrofurfuryl bromide by means of potassium or sodium hydroxide [60]. It has been shown that 2-methylenetetrahydrofuran undergoes isomerization to 2-methyl-4,5-dihydrofuran with high selectivity. The highest yield (up to 89%) of 2-methylenetetrahydrofuran was obtained by dehydrobromination of tetrahydrofurfuryl bromide with powdered KOH at 10-35°C. Comparable selectivity of the dehydrohalogenation of 2-tetrahydrofurfuryl chloride has also been achieved by using the potassium alkoxide of dimethylphenylcarbinol [61].

4. Synthesis of 2,5-Dihydrofuran

4.1. Dehydration of 2-Butene-1,4-diol. 2,5-Dihydrofuran has been obtained by dehydration of cis-2-butene-1,4-diol; sulfuric acid was used for this purpose, or dehydration was accomplished under continuous conditions on Al_2O_3 at 220-250°C [62]. 2,5-Dihydrofuran was obtained in up to 79% yield when the process was carried out at 220°C on activated Al_2O_3 [63-65].

A periodic process for the preparation of 2,5-dihydrofuran by dehydration of cis-2-butene-1,4-diol in the liquid phase at 170-220°C in the presence of Al_2O_3 is characterized by the highest selectivity [66]. The catalyst was obtained by heating bayerite. The yield of 2,5-dihydrofuran was 90.5%, and the percentage of 2,5-dihydrofuran in the isolated product was 98%. Aluminosilicates [67] and pyridine hydrochloride [68] have also been used as the dehydrating agent. However, the yield does not exceed 73% in these cases.

A method for the preparation of 2,5-dihydro-C_2^{14}-furan in 40% yield by dehydration of C_2^{14}-2-butene-1,4-diol on Raney nickel at 20°C has been proposed [69].

3-Butene-1,2-diol has also been used as the raw material, in addition to cis-2-butene-1,4-diol, for the preparation of 2,5-dihydrofuran [70]. However, the selectivity of the formation of 2,5-dihydrofuran is considerably lower in this case.

4.2. Transformation of 2-Butyne-1,4-diol. If the transformation of 2-butyne-1,4-diol is realized in one step (in ethanol in the presence of Raney nickel), a mixture of 2,5-dihydrofuran (8.5%), 2-buten-1-ol, 1,4-butanediol, and 2-butene-1,4-diol is obtained. Since the process is characterized by low selectivity, 2,5-dihydrofuran is synthesized from 2-butyne-1,4-diol in two steps, viz., hydrogenation of 2-butyne-1,4-diol to 2-butene-1,4-diol and dehydration of the latter [71].

2-Butyne-1,4-diol is hydrogenated in alcohol solution in the presence of Raney nickel. The dehydration of 2-butene-1,4-diol is carried out in the presence of dry HBr at 140-150°C. The yield of 2,5-dihydrofuran is 56%.

The dehydration of 2-butyne-1,4-diol derivatives in the presence of $CoMoO_4$ has also been used for the catalytic synthesis of 2-alkyl- and 2,5-dialkyl-2,5-dihydrofurans [72].

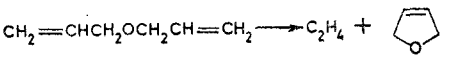
4.3. Transformation of 1,4-Butanediol Monoacetate. The dehydration of 1,4-butanediol monoacetate to 2,5-dihydrofuran is carried out in the presence of sulfuric acid [72, 73]. Pri-

marily tetrahydrofuran is obtained when the diacetate is used.

4.4 Transformation of Butadiene Monoxide. Butadiene monoxide is converted to 2,5-dihydrofuran [74, 75] in 84-93% yields with high selectivity in the presence of the (acetylacetonato)$_3$Al·HI·KI complex. N-Methylpyrrolidone has been recommended as the solvent.

In addition to aluminum acetylacetonate [and iron(III) acetylacetonate], magnesium acetylacetonate, $ZnCl_2$, $SnCl_2$, and $SnCl_4$ have been used as complexing agents.

4.5. Disproportionation of Diallyl Ether. The disproportionation of diallyl ether on an aluminum–rhenium catalyst containing 10-15% Re_2O_7 and promoted with 5% tetralkyltin (C_{1-4} alkyl groups) [76, 77] proceeds via the following scheme:

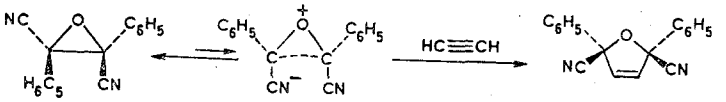


The conversion of the raw material was 31.9%, and the selectivity of the formation of 2,5-dihydrofuran was 90% [76]. The conversion of compounds with the general formula $MeCH{=}C{=}CHCH_2OH$ to 2,5-dihydrofuran and its derivatives has been investigated [78]. It is assumed that the first steps in the process are protonation of the hydroxy group and the subsequent formation of a carbonium ion with the structure $CH_3\overset{+}{C}HCH{=}CHCH_2OH$. Deprotonation of the latter leads to the formation of 2-methyl-2,5-dihydrofuran.

4.6. Transformation of 2-Alkyl-3-chlorotetrahydrofurans. 2-Alkyl-2,5-dihydrofurans are obtained by dehydrochlorination of 2-alkyl-3-chlorotetrahydrofurans by means of potassium hydroxide [79]. The yield of 2-methyl-2,5-dihydrofuran reaches 80%.

4.7. Cycloaddition of Carbonyl Ylids. Tetrasubstituted oxiranes, which exist in equilibrium with the corresponding carbonyl ylids, react at high temperatures with compounds with a triple bond to give 2,5-dihydrofuran derivatives [80].

α,β-Dicyano-trans-stilbene oxide reacts with acetylene to give cis-2,5-dicyano-2,5-diphenyl-2,5-dihydrofuran (in 91% yield).



At temperatures above 100°C α,β-dicyano-trans-stilbene oxide reacts with dimethyl acetylenedicarboxylate to give the corresponding 2,5-dihydrofuran derivative in 84% yield.

cis-2,5-Dicyano-2,3,4,5-tetraphenyl-2,5-dihydrofuran is obtained with high selectivity when diphenylacetylene is used as the acetylenic component.

5. Isomerization of 2,5-Dihydrofuran to 2,3-Dihydrofuran

Many authors have investigated the conversion of 2,5-dihydrofuran and its derivatives to more reactive compounds, viz., 2,3-dihydrofuran and its derivatives. According to [81], the isomerization is carried out in the presence of alkali metal alkoxides or alkalis at 100-250°C. The isomerization of 2,5-dihydrofuran, 2-methyl-2,5-dihydrofuran, and 2,2-dimethyl-2,5-dihydrofuran to the corresponding 2,3-dihydrofurans has been realized by means of this method. Thus 2,3-dihydrofuran was obtained in 51% yield vis-à-vis 79% conversion of the raw material in the isomerization of 2,5-dihydrofuran in the presence of potassium isobutoxide in sealed tubes at 180°C [82].

In a number of cases the isomerization of 2,5-dihydrofurans (and other β,γ-unsaturated ethers) is realized in the presence of alkalis or hydroxides of alkaline earth metals and iron pentacarbonyl. In this case the yield of 2,3-dihydrofuran reaches 90% [83]. The following materials have also been used as catalysts: KNH_2 Al_2O_3 [84], $Pd(PhCN)_2Cl_2$ [85], and $R_3MH\cdot H_2PtCl_6$ (R = C_2H_5, C_3H_7, C_4H_9, iso-C_3H_7, and iso-C_4H_9; M = Si and Ge) [86]. When these catalysts are used, the reaction is realized in the liquid phase under periodic conditions.

Methods for the isomerization of 2,5-dihydrofuran and its derivatives under continuous conditions have also been proposed. The active catalyst for isomerization is the catalyst obtained by coprecipitation and evaporation in the presence of a support (Al_2O_3) of soluble nickel salts such as $Ni(NO_3)_2$ and orthoarsenic acid [87]. The reaction is carried out in the presence of small amounts of CO. The isomerization of 2,5-dihydrofuran and 2-methyl-2,5-dihydrofuran under periodic conditions has been carried out on Pd, Pt, and Ni catalysts [88].

Thus 2,3-dihydrofuran was obtained in 63% yield vis-à-vis 75% conversion of the raw material when 0.1% Pd on Al_2O_3 was used at 150-170°C. Furan is present in the reaction mixture.

Thus a large number of methods is known for the preparation of 2,3-dihydrofuran, 2,5-dihydrofuran, and 2-methylenetetrahydrofuran and their derivatives. However, most of them are characterized by the use of a deficient amount of raw material. The most promising method for the preparation of 2,3-dihydrofuran is the transformation of 1,4-butanediol. The selection of more selective catalysts for this process and a study of the possibility of carrying out the reaction under continuous conditions are expedient. A selective process for the preparation of 2,5-dihydrofuran is the dehydration of 2-butene-1,4-diol on heterogeneous catalysts under continuous conditions. As regards the isomerization of 2,5-dihydrofuran to 2,3-dihydrofuran, it is evidently expedient to use this process as a method for the simultaneous preparation of furan and 2,3-dihydrofuran.

Fewer studies have been devoted to methods for the synthesis of 2-methylenetetrahydrofuran, although the latter can be obtained from a relatively accessible raw material, viz., tetrahydrofurfuryl alcohol, through a step involving the dehydrohalogenation of tetrahydrofurfuryl halides.

The fact that, despite their high reactivities, dihydro derivatives of furan have thus far found relatively little use in organic synthesis is evidently explained by the relatively great scarcity of these compounds. Concise information regarding some aspects of the use of dihydrofurans is presented below.

6. Characteristic Reactions of Dihydrofurans

The chemical properties of dihydrofurans are based primarily on the reactions of the double bond and the ether grouping.

The reactions of 2,5-dihydrofurans with halogens, hypochlorous acid, and aromatic hydrocarbons are discussed in a previous review [62].

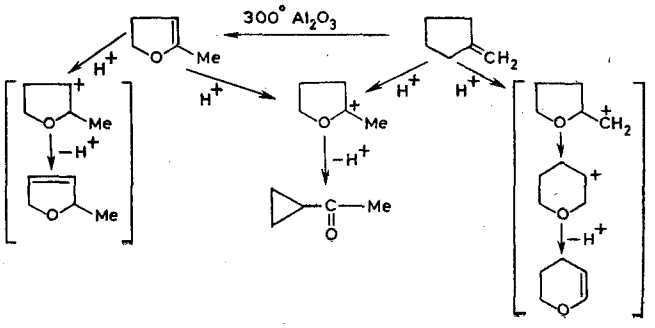
2,3-Dihydrofurans are more reactive than 2,5-dihydrofurans. They are readily hydrolyzed to give the corresponding hydroxy carbonyl compounds.

The hydrolysis of 2-methyl-4,5-dihydrofuran is an intermediate step in the practically important process for the production of γ-acetopropyl alcohol by the hydrogenation-hydration of 2-methylfuran [14].

In contrast to 2,3-dihydrofuran, 2,5-dihydrofuran and its derivatives do not undergo hydrolysis [89].

The thermal stabilities of 2,3- and 2,5-dihydrofurans also differ. 2,3-Dihydrofuran undergoes isomerization at 375°C to give cyclopropanecarbaldehyde. Cyclopropyl methyl ketone is obtained as a result of isomerization of 2-methyl-4,5-dihydrofuran at 300-500°C.

The isomerization of 4-methyl-5-phenyl-2,3-dihydrofuran in the vapor phase at 350°C on ZnO applied to kieselguhr leads to the formation of stereoisomers of 1-formyl-2-methyl-3-phenylcyclopropane and small amounts of 3-methyl-4-phenyl-3-butenal [90].

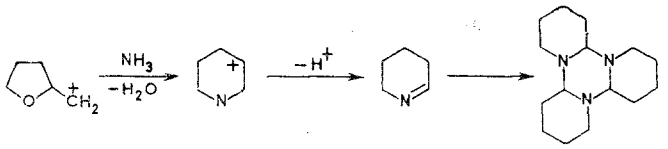


The transformation of 2-methylenetetrahydrofuran on Al_2O_3 in the presence and absence of ammonia has been investigated [91]. On Al_2O_3 at 300°C in the absence of ammonia, 2-methylenetetrahydrofuran is converted to cyclopropyl methyl ketone (73%) and 2-methyl-4,5-dihydrofuran (21%) vis-à-vis complete conversion of the raw material.

An intermediate form in the course of the formation of the principal reaction product, viz., cyclopropyl methyl ketone, is a tertiary carbonium ion, which develops as a result of

proton transfer from the catalyst to the double bond of 2-methylenetetrahydrofuran. Possible reaction pathways that lead to 2-methyl-2,5-dihydrofuran and 2,3-dihydropyran, which are formed in very small amounts in this process, are also shown in the scheme.

In the presence of ammonia the active intermediate form is a primary carbonium ion, the transformation of which leads to the formation of tetrahydropyridine and its trimerization product (α-tripiperideine):



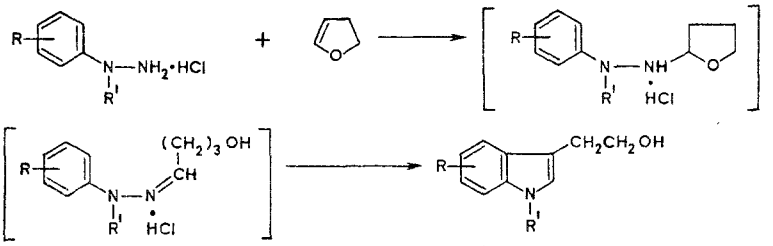
3-Alkylpyridines were detected as side products of the reaction.

An important aspect in the use of 2,3-dihydrofuran is its application in the synthesis of tetrahydrofuryl derivatives of purine and pyrimidine bases [2]. Tetrahydrofuryl derivatives of purine bases are obtained in the reaction of 6-substituted purines with 2,3-dihydrofuran in the presence of acidic catalysts (hydrogen chloride andp-toluenesulfonic acid) [92-94].

1-(2-Tetrahydrofuryl)uracils have been synthesized by the reaction of 2-chlorotetrahydrofuran with activated uracil derivatives [95, 96]. 2-Chlorotetrahydrofuran is obtained in turn by the reaction of HCl with 2,3-dihydrofuran. The reaction of 2-chlorotetrahydrofuran with fluorouracil leads to the antitumorigenic preparation ftorafur.

The condensation of thymidine with 2,3-dihydrofuran in the presence of p-toluenesulfonic acid gives, depending on the reagent ratio, 3- and 3'-O-(2-tetrahydrofuryl)thymidines or 3', 5'-di-O-(2-tetrahydrofuryl)thymidine [97].

2,3-Dihydrofuran has been used as a cyclic vinyl ether in the Fischer reaction with salts of arylhydrazines [98], which leads to the formation of tryptophols in 25-70% yields:



Dihydrofurans are used in the synthesis of vinyl sulfones [99], tetrahydrofuryl-substituted thioethers [100], pyrrolotetrazines [101], and the alkaloid isoretronecanol [102]. 2,5-Dihydrofuran derivatives are used as intermediates in the synthesis of prostaglandins [103].

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CHEMISTRY OF OXALYL DERIVATIVES OF METHYL KETONES.

28.* REACTION OF CARBONYL COMPOUNDS OF ADAMANTANE WITH 5-PHENYL-2,3-DIHYDROFURAN-2,3-DIONE

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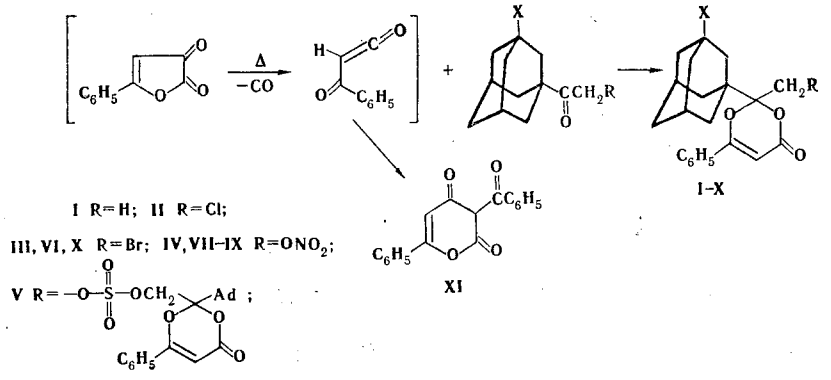
UDC 547.841'518.07:543.422

The reaction of substituted methyl 1-adamantyl ketones with an equimolar amount of 5-phenyl-2,3-dihydrofuran-2,3-dione under the conditions of the thermal decarbonylation of the latter leads to the corresponding 2-methyl-2-adamantyl-6-phenyl-1,3-dioxen-4-ones, 6-phenyl-3-benzoyl-2,4-dione, and the starting ketones. The steric and electronic factors that affect the yields of the dioxen-4-ones were examined. α-Hydroxymethyl 1-adamantyl ketones open up the furan ring to give 1-adamantoylmethyl benzoylpyruvate. Data from the IR, PMR, and UV spectra are presented.

It has been previously established that 5-aryl-2,3-dihydrofuran-2,3-diones form aroylketenes when they undergo thermal decarbonylation. The aroylketenes react with ketones to form 2,2,6-trisubstituted 1,3-dioxen-4-ones [1].

In order to search for new biologically active compounds of the adamantane series we subjected methyl 1-adamantyl ketones that contain halo, nitroxy, and sulfoxy groups attached to the methyl group to this reaction. 2-Methyl-2-adamantyl-6-phenyl-1,3-dioxen-4-ones with the corresponding substituents in the methyl and adamantyl groups (I-X), 6-phenyl-3-benzoylpyran-2,4-dione (XI) [2], and the starting ketones were isolated when equimolar amounts of the starting substances were refluxed in carbon tetrachloride for 2.5-3 h:



I—V X=H; VI, VII X=Br; VIII X=NO_2; IX X=C_6H_5; X X=ONO_2

*See [1] for communication 27.

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