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The effect of the nature of the solvent on the direction and rate of oxidation of furfural by hydrogen peroxide was studied. The use of alcohol and dioxane as the solvents substantially increases the selectivity of the process and leads to the primary formation of furfural hydroxyperoxides (the α -hydroxyhydroperoxide in dioxane, and the α,α' -dihydroxyperoxide in alcohol). The polarity of the medium and specific solvation have a substantial effect on the rate of formation of the peroxides. The effect of specific solvation predominates.

The oxidation of furfural (I) with hydrogen peroxide, in conformity with modern concepts, is a complex consecutive process, occurs without the formation of free radicals, and includes a rearrangement of the Baeyer-Villiger type [1]. In contrast to similar reactions of aliphatic and aromatic aldehydes, the oxidation of furyl-substituted aldehydes proceeds specifically; this is associated with the peculiarities of furan derivatives. Furfural hydroxyperoxides are formed in the first step of the reaction [1, 2]. However, in the case of oxidation in water the reaction cannot be stopped at this step, since pyromucic acid and formylhydroxyfuran are formed in aqueous solutions as a result of decomposition and subsequent transformations of the peroxides. The formylhydroxyfuran is converted to α - and β -crotonolactones, which are hydrolyzed and oxidized for formylacrylic, formylpropionic, maleic, and succinic acids [1].

We have studied the effect of several organic solvents on the direction and rate of the individual steps of the process. The most interesting results were obtained in the case of oxidation in alcohols and in dioxane. In contrast to oxidation in water, in which the chief reaction products are acids, peroxide compounds are primarily formed in nonaqueous solutions (Table 1).

Two peroxides — the α -hydroxyhydroperoxide (II) and the α,α' -dihydroxyperoxide (III) — of furfural are formed in all of these cases. However, their amounts and ratios change as a function of the solvent (Fig. 1).

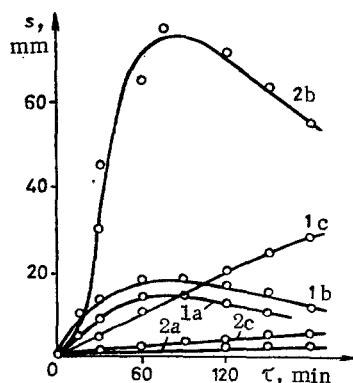


Fig. 1. Amounts of the α -hydroxyhydroperoxide (1) and α,α' -dihydroxyperoxide (2) in the oxidates in the oxidation of furfural with H_2O_2 : a) in water; b) in ethanol; c) in dioxane (s is the area of the spot on the chromatogram).

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TABLE 1. Oxidation of Furfural with Hydrogen Peroxide in Various Solvents at 60°C When $[I]_0 = 3.4$ moles/liter and $[H_2O_2]_0 = 6.8$ moles/liter

Solvent	τ , min	Converted I, moles/liter	Amounts formed, g-eq/liter	
			organic peroxides	acids
Water	180	1.9	0.65	2.7
Ethanol	210	2.0	3.45	0.5
Dioxane	440	2.0	3.90	0.0

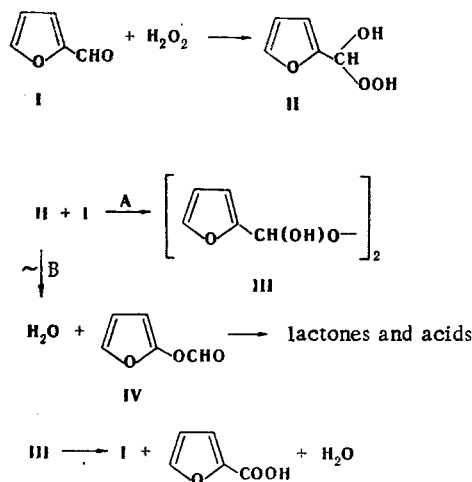
TABLE 2. Activation Characteristics of the Oxidation of Furfural with Hydrogen Peroxide When $[I]_0 = 0.5$ mole/liter and $[H_2O_2]_0 = 8$ moles/liter

Reaction characteristics	Solvent	
	ethanol	dioxane
E_a , kcal/mole	20.5	22.4
A , sec ⁻¹	$1.2 \cdot 10^{10}$	$6.1 \cdot 10^9$
ΔH (60°), kcal/mole	19.8	21.8
ΔS (60°), kcal/mole · deg	-14.6	-16.0

The primary product in the case of oxidation in dioxane and water is hydroxyperoxide II. Peroxide II is stable in dioxane, and its percentage is close to the stoichiometric value (Table 1). Peroxide II is unstable in water, and the products of rearrangement of the hydroxy hydroperoxide and their subsequent transformations are formed.

A distinctive feature of the reaction in alcohol is the primary formation of dihydroxyperoxide III. It is quite stable in alcoholic media. Intensive decomposition of the dihydroxyperoxide commences 90 min after the start of the reaction (Fig. 1) and is accompanied by the accumulation of pyromucic acid. The alcoholic oxidate contains six times as much pyromucic acid as the aqueous oxidate, and pyromucic acid constitutes 50% of the total of all of the acids.

The reaction evidently proceeds via the following scheme:



The tendency of peroxide I to undergo rearrangement via pathway B is associated with polarization of the O-O bond and increases as the polarity of the solvent increases. This may explain the predominance of pathway B in the case of oxidation in water ($\epsilon = 78.5$). In addition, water hydrolyzes ester IV formed during the rearrangement, as a result of which formic acid, which catalyzes pathway B, is formed.

The lower polarity of the alcohol ($\epsilon = 24$) and the absence of hydrolysis complicate the rearrangement of peroxide II. This creates conditions that favor the reaction of the hydroxyperoxide with furfural. Dihydroxyperoxide III is formed as a result of this reaction.

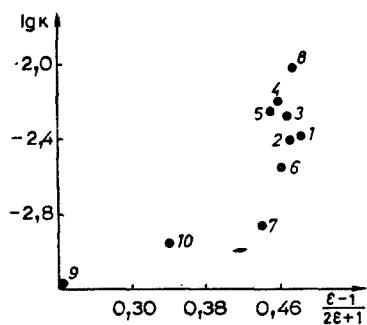


Fig. 2. Dependence of $\log k$ on the dielectric constant of the solvent for the reaction of furfural with H_2O_2 at 40°C when $[\text{I}]_0 = 0.5$ mole/liter and $[\text{H}_2\text{O}_2]_0 = 8$ moles/liter: 1) methanol; 2) ethanol; 3) propanol; 4) butanol; 5) pentanol; 6) 2-propanol; 7) 2-methyl-2-propanol; 8) ethylene chlorohydrin; 9) dioxane; 10) tetrahydrofuran.

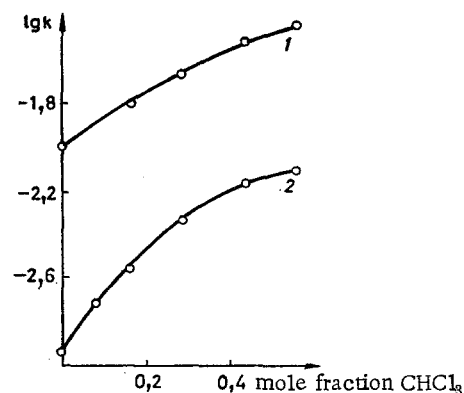


Fig. 3. Dependence of $\log k$ on the mole fraction of chloroform for the oxidation of furfural with H_2O_2 in a binary mixture of solvents: 1) ethanol-chloroform (50°C); 2) dioxane-chloroform (60°).

In addition to pathway A, pathway B is realized in alcohol, but the latter is expressed considerably more weakly, since only 10% formic acid and 8.5% oxo and dibasic acids are detected in the reaction mixture.

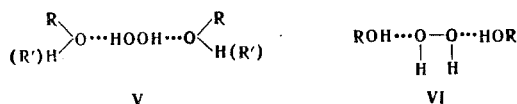
In the case of oxidation in dioxane, the low dielectric permeability of the medium ($\epsilon = 2.2$) and the absence of hydrolysis of the acids also make rearrangement B impossible. Solvation effects evidently hinder the reaction of hydroxyhydroperoxide II with furfural. In this case furfural hydroxyhydroperoxide is the final oxidation product.

To ascertain the character of the interaction of the solvent with the reacting particles we investigated the relationship between the rate of formation of furfural hydroxyperoxide and some properties of the solvent. The reaction rate constants increase as the dielectric permeability of the medium increases (Fig. 2). However, a linear relationship between the logarithms of the rate constants and the Kirkwood function is not observed. It follows from this that the change in the rate of oxidation of furfural with H_2O_2 in a series of different solvents cannot be explained purely by electrostatic interactions between the reacting particles and the medium.

To estimate the contribution of specific solvation, we carried out the oxidation of furfural with H_2O_2 in mixtures of chloroform with ethanol and dioxane (Fig. 3). The observed deviation from linearity of the dependence of $\log k$ on the mole fraction of one of the solvents in the binary mixture is an indication of specific solvation [3]. The addition of chloroform, which is relatively inert to specific solvation, in the case of oxidation in both ethanol and dioxane leads to an increase in the reaction rate, i.e., specific solvation hinders the oxidation process. The effect is manifested to a greater degree in dioxane. The addition of CHCl_3 to dioxane leads to a slight increase in the dielectric permeability from 2.2 to 3.6, whereas the rate constant increases in this case by a factor of seven. In ethanol-chloroform mixtures the rate increases as the mole fraction of CHCl_3 increases, despite the decrease in the dielectric permeability of the medium. This constitutes evidence that specific solvation has the predominant effect on the oxidation rate.

A study of the kinetics of the reaction in question [4] showed that the reaction of furfural with H_2O_2 proceeds through the formation of a furfural $\cdot 2\text{H}_2\text{O}_2$ complex. The inhibition of the reaction in solvents that are capable of specific solvation is then evidently associated with the interaction of the solvent with H_2O_2 molecules. Association of the V type hinders participation of H_2O_2 in the electrophilic act of the reaction, whereas association of the VI type reduces the nucleophilicity of H_2O_2 .

The activation energy increases on passing from ethanol to dioxane (Table 2), and this indicates an increase in this case of the energy barrier of the reaction, evidently due to



the solvation effects of the solvent. The increase in the negative value of the activation entropy constitutes evidence for greater structural limitations in the formation of the transition state in dioxane as compared with alcohol.

The lesser effect of specific solvation in the case of oxidation in alcohol as compared with dioxane is, in all likelihood, associated with the tendency of alcohols to undergo intermolecular association.

EXPERIMENTAL

Furfural purified with a column filled with aluminum oxide [5] and fractionated prior to the start of the experiments (n_D^{20} 1.5236 and d_4^{20} 1.1562) was used for the oxidation. Concentrated (99%) hydrogen peroxide was obtained by vacuum evaporation of perhydrol; the perhydrol used did not contain acid stabilizers. The solvents were purified and dried by the usual methods [6]. The dioxane and tetrahydrofuran (THF) were purified thoroughly to remove traces of peroxides by refluxing over lead dioxide and subsequent filtration through a dense paper filter and fractionation. The solvents themselves did not undergo oxidation under the reaction conditions, as verified by control experiments. The oxidation was carried out in a Heppler thermostat in which the temperature was maintained constant within $\pm 0.2^\circ$.

The comparison of the oxidation of furfural with H_2O_2 in the various solvents was made under identical conditions at a furfural- H_2O_2 molar ratio of 1:2 (60°). The concentrated hydrogen peroxide was diluted with the solvent to a concentration of 30%. The trend of the oxidation was followed by the sample-selection method. The reaction was stopped by rapid cooling of the samples in an ice-salt mixture.

The furfural consumption was determined spectrophotometrically with a Spektromom-203 spectrophotometer from the change in the optical density at λ_{max} 275 nm. The sum of the peroxide compounds was determined by iodometric titration, and the hydrogen peroxide content was determined by titration with cerium sulfate [7]. The difference in the results obtained by the two methods characterizes the amount of organic peroxides in the reaction mixture. Quantitative thin-layer chromatography [8] was used to establish the quantitative ratio between hydroxyhydroperoxide II and dihydroxyperoxide III. Separation was carried out on Silufol plates in a toluene-ethanol system (20:3). The volume of the mobile phase was 1% of the volume of the chromatographic chamber. The sample volume was 1-2 μl .

The sum of the acids in the oxidate was determined by titration with an 0.05 N alcohol solution of KOH in the presence of Bromthymol blue. Chromatography with a column filled with Cellite and silica gel [9] was used for the quantitative determination of the individual acids. The quantitative determination of crotonolactone was carried out with a PAKhV-03 gas-liquid chromatograph [9].

For the study of the effect of the nature of the solvent on the reaction rate and the determination of the activation characteristics, the oxidation was carried out at a furfural- H_2O_2 molar ratio of 1:15 (40°). The reaction rate was followed from the furfural consumption. The first-order rate constants were determined graphically from the slope of the semi-logarithmic anamorphoses in coordinates of $\log [I]_0/[I]$ and τ .

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RESEARCH IN THE ISOXAZOLE SERIES.

XXXIII.* REACTION OF PHENYLAZOTRIPHENYLMETHANE WITH METHYLISOXAZOLES

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The thermal decomposition of phenylazotriphenylmethane in 3,5-dimethyl- and 3,4,5-trimethylisoxazole was studied. In 3,5-dimethylisoxazole only the hydrogen atom of the methyl group in the 3 position is replaced by the $(C_6H_5)_3C^{\cdot}$ radical. The activities of the methyl groups of 3,4,5-trimethylisoxazole decrease in the order 3-C > 4-C >> 5-C. The specific direction of the reaction is associated with the orientation of the phenylazotriphenylmethane in the vicinity of the 3-C atom of the isoxazole ring owing to complexing of the azo group with the nitrogen atom. Complexes of 3,5-dimethyl- and 3,4,5-trimethylisoxazole with Eu^{3+} have a similar structure. The structures of the reaction products were established by means of their PMR and mass spectra.

In the course of a study of radical substitution in the isoxazole series we found an unusual reaction of phenylazotriphenylmethane (I). The aim of the present research was to study the specific reaction of azo compound I with methylisoxazoles.

2,5-Addition of $C_6H_5^{\cdot}$ and $(C_6H_5)_3C^{\cdot}$ radicals formed by thermal decomposition of azo compound I to furan was previously described in [2]. Benzene derivatives (even the alkyl homologs) undergo phenylation only in the ring [3]. In contrast to the indicated compounds, 3,5-dimethylisoxazole (II) reacts to give 3- β,β,β -triphenylethyl-5-methylisoxazole (IIa). The reaction must be carried out in a large excess of the isoxazole (>50 moles), and tetraphenylmethane (III) is formed at a reagent molar ratio of 1:10 because of the "cage effect" [4].

The structure of IIa was established by means of the PMR and mass spectra. Three singlets at δ 2.01, 3.99, and 4.73 ppm with an intensity ratio of 3:2:1 are observed in the PMR spectrum (in $CDCl_3$), along with the signals of aromatic protons at about 7.5 ppm. This sort of spectrum is possible only if substitution took place in one of the methyl groups. The shift to stronger field as compared with the starting isoxazole II of the signals of the protons of the CH_3 group and especially of the 4-H signal (by 1 ppm) constitutes evidence for shielding of the protons by the "umbrella" of the triphenylmethyl group. The choice between the two possible isomeric structures was made on the basis of the mass spectrum, in which one observes a molecular ion peak (m/e 339),[†] the most intense $(C_6H_5)_3C^+$ fragment ion peak (243), and less intense peaks of $H \begin{array}{c} \diagup \\ \text{N}^+ \\ \diagdown \end{array} CH_2C(C_6H_5)_3$ (296) and CH_3CO^+ (43) ions. The spectrum does

not contain peaks of fragment ions with mass numbers 285 and 54, which are formed in the fragmentation of the isomeric isoxazole (see [5] for the disintegration of isoxazole derivatives under the influence of electron impact):

*See [1] for communication XXXII.

[†]Here and subsequently, the numbers pertaining to the ions are the mass-to-charge ratios.

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