INVESTIGATION OF FURAN ACETAL COMPOUNDS

V.* SYNTHESIS AND KINETICS OF THE FORMATION OF 5-NITRO-2-(α-FURYL)-5-ETHYL-1,3-DIOXANES AND THEIR REDUCTION TO THE CORRESPONDING AMINO DERIVATIVES

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New 1,3-dioxanes, which are derivatives of 2-nitro-2-ethylpropane-1,3-diol and aldehydes of the furan series, were synthesized. The nitrodioxanes were reduced by means of sodium amalgam to the corresponding amines. The kinetics of the formation of the nitrodioxanes was studied. The accelerating action of the electron-acceptor diol substituent on the reaction rate was established. The rate constants in the aldehyde series increase on passing from α'-methylfurfural to α'-nitrofurfural, and they correlate satisfactorily with Brown's σ_p^+ constants.

Nitro derivatives of furan compounds are attracting attention because of their extensive synthetic possibilities and practical application as physiologically active preparations [2]. Amino derivatives that contain a dioxane ring in addition to a furan ring are equally valuable [3,4].

We have synthesized 5-nitro-2-(α-furyl)-5-ethyl-1,3-dioxanes by condensation of 2-nitro-2-ethylpropane-1,3-diol with various aldehydes of the furan series (Table 1).

The corresponding amino derivatives (VI-X) were obtained by electrochemical reduction of I-V on sodium amalgam in aqueous alcohol.

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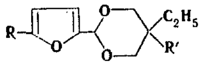
*See [1] for communication IV.

TABLE 1



Comp.	R	R'	mp, °C	Empirical formula	Found, %				Calc., %				Yield, %
					C	H	N	Hal	C	H	N	Hal	
I	H	NO_2	57	$C_{10}H_{13}NO_5$	52,7	6,0	6,5	—	52,9	5,7	6,2	—	66
II	CH_3	NO_2	99	$C_{11}H_{15}NO_5$	54,5	6,6	6,0	—	54,8	6,2	5,8	—	70
III	Br	NO_2	116	$C_{10}H_{12}BrNO_5$	39,1	4,0	4,7	26,0	39,2	3,9	4,6	26,1	81
IV	I	NO_2	125	$C_{10}H_{12}INO_5$	33,9	3,7	4,0	35,9	34,0	3,4	4,0	36,0	79
V	NO_2	NO_2	139	$C_{10}H_{12}N_2O_7$	43,8	4,6	10,3	—	44,1	4,4	10,3	—	82
VI	H	NH_2	73—74	$C_{10}H_{15}NO_3$	60,7	7,9	7,3	—	60,9	7,6	7,1	—	56
VII	CH_3	NH_2	49—50	$C_{11}H_{17}NO_3$	62,0	8,3	6,6	—	62,5	8,1	6,6	—	23
VIII	Br	NH_2	106	$C_{10}H_{14}BrNO_3$	43,5	5,3	5,4	28,7	43,5	5,8	5,1	29,0	18
IX	I	NH_2	76	$C_{10}H_{14}INO_3$	37,4	4,5	4,4	39,3	37,2	4,3	4,3	39,4	14
X	NH_2	NH_2	62—63	$C_{10}H_{16}N_2O_3$	58,8	8,0	13,6	—	59,0	7,9	13,9	—	10
XI	H	$NHCOCH_3$	190	$C_{12}H_{17}NO_4$	60,1	7,2	6.0	—	60,3	7,1	5,9	—	88
XII	$NHCOCH_3$	$NHCOCH_3$	194	$C_{14}H_{20}N_2O_5$	56,3	7,0	9,5	—	56,8	6,8	9,5	—	87

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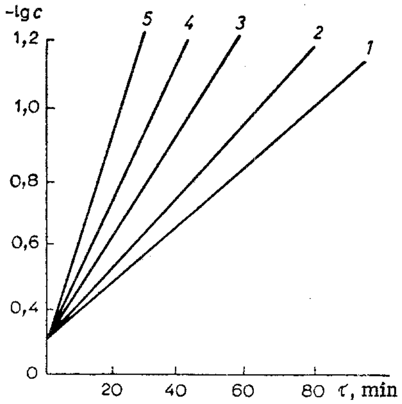


Fig. 1. Semilogarithmic anamorphoses of the kinetic curves of the reaction of α'-substituted furfurals with 2-nitro-2-ethylpropane-1,3-diol: 1) CH_3; 2) H; 3) Br; 4) I; 5) NO_2.

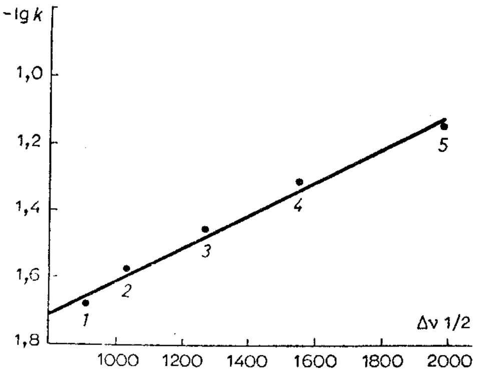


Fig. 2. Correlation of the rates of formation of 1,3-dioxanes with the σ_p^+ constants of substituents in the 5 position of the furan ring: 1) CH_3; 2) H; 3) Br; 4) I; 5) NO_2.

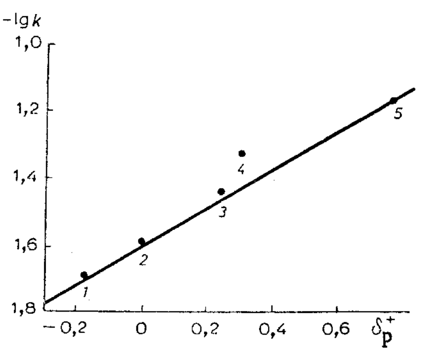


Fig. 3. Correlation of the rates of formation of 1,3-dioxanes with the magnitude of the solvatochromic effect of furan aldehydes with substituents in the 5 position of the ring: 1) CH_3; 2) H; 3) Br; 4) I; 5) NO_2.

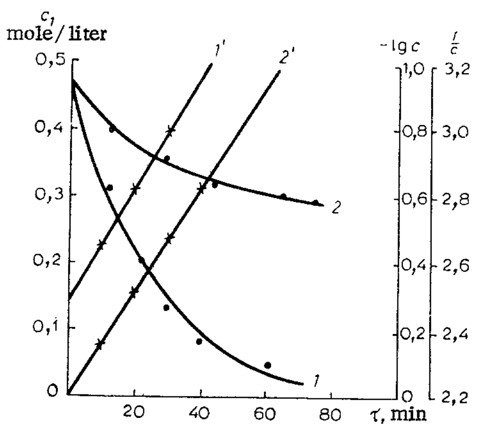


Fig. 4. Consumption of 5-nitrofurfural during its reaction with 2-ethyl-2-(hydroxymethyl)-propane-1,3-diol: 1) in the presence of a catalyst; 2) in the absence of a catalyst; 1', 2') dependences of log c on τ and of 1/c on τ, respectively.

In addition to the bands that characterize the furan and dioxane rings, the IR spectra of I-V contain bands of a nitro group (1534 and 1345 cm^{-1}) of very high intensity. The absence of absorption at 3300-3700 cm^{-1} (ν_{OH}) and at 1660-1720 cm^{-1} ($\nu_{C=O}$) indicates the proposed structure. A less intense band is observed at 1550 cm^{-1} (δ_{NH_2}) in the IR spectra of VI-X. Broad bands that characterize the stretching vibrations of associated and free NH_2 groups are present at 3200-3700 cm^{-1}.

In order to establish the effect of a substituent in the diol molecule on its reactivity and to accurately specify the reaction mechanism, the kinetics of the formation of furyldioxanes during the condensation of substituted furfurals with 2-nitro-2-ethylpropane-1,3-diol were examined. The reaction is described by a first-order kinetic equation, which is confirmed by the character of the curves, the rectilinearity of their semilogarithmic anamorphoses (Fig. 1), and by the fact that the rate constant does not change under the investigated conditions as the concentration of starting reagents is changed (Table 2).

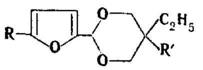
The dependence of the rate constants for the formation of 1,3-dioxanes on the substituents in the α' position of the furan ring and the 5 position of the dioxane ring is presented in Table 3.

It should be noted that the reaction rate is described by a first-order equation when the ratio of starting components is stoichiometric and the mechanism is bimolecular. This is explained by the fact that the aldehyde adsorptively saturates the catalyst surface during the reaction, and its surface concentration remains practically constant; in this case, the adsorption step proceeds more rapidly than the diffusion and

TABLE 2. Rate Constants for the Condensation of 2-Nitro-2-ethylpropane-1,3-diol with Furfural

Conc., mole/liter		k, min^{-1}
furfural	alcohol	
0,7	0,5	0,0200
0,5	0,5	0,0200
0,3	0,5	0,0201

TABLE 3. Rate Constants for the Formation of



R	k, min^{-1}	
	$R'=CH_2OH$	$R'=NO_2$
CH_3	0,0116	0,0200
H	0,0127	0,0250
Br	0,0230	0,0345
I	0,0250	0,0479
NO_2	0,0413	0,0718

and chemical reaction steps, while the limiting step of the process is nucleophilic attack by alcohol of the carbon of the protonated complex $>\overset{+}{C=O}\cdots H$. It is considered that protonation occurs at the carbonyl group, but one cannot exclude the possibility that the proton can also interact with the alcohol. Two cations – the protonated furfural molecule, which accelerates the formation of 1,3-dioxanes, and the $H_2\overset{+}{O}CH_2CR(C_2H_5)CH_2OH$ oxonium ion, which inhibits the condensation of polyols with aldehydes – will be competitive.

The introduction of a nitro group into the alcohol molecule reduces the electron density on the oxygen of the hydroxyl group due to the –I effect and diminishes the probability of the formation of the oxonium ion. In this case, protonation proceeds primarily at the carbonyl group of the aldehyde. The latter accelerates the nucleophilic interaction, and the rate constant for condensation of the nitro alcohol increases (Table 3).

A change in the structure of the carbonyl compounds is reflected appreciably in the rate of the process. The effects of substituents in the furan ring on the magnitude of the rate constant of the reaction under consideration can be arranged in the following order with respect to decreasing reactivity: $NO_2 > I > Br > H > CH_3$, which is in agreement with the conclusions in [5]. The rate constants correlate satisfactorily with Brown's σ_p^+ constants [6] (Fig. 2). The correlation coefficient (r) is 0.986, and the reaction constant (ρ), determined from the slope of the line, is +0.6. The positive ρ value for the formation of 1,3-dioxanes confirms our conclusion regarding the effect of electron-donor and electron-acceptor substituents, as well as the nucleophilic character of the process. The low absolute value of ρ is evidence in favor of molecular interactions and the formation of an intermediate polarized complex.

The correlation with the solvatochromic effect (Fig. 3) is satisfactory. The rate constant can be calculated from the equation $k = -1.71 + 4.9 \cdot 10^{-4} \cdot \Delta\nu_{1/2}$ (r = 0.97).

The acceleration that is observed when a nitro group is introduced into the furan ring is associated not only with the action, in the same direction, of the inductive and mesomeric effects but also with the decrease in the interaction of the furan ring with the carbonyl group, which additionally promotes an increase in the magnitude of the fractional positive charge on the carbon atom. In this case, the increase in the electron deficit is so significant that the reaction proceeds without a catalyst (Fig. 4), although at a somewhat slower rate. However, carrying out the reaction of furfural with the nitro alcohol in the absence of a catalyst does not lead to any changes whatsoever in the initial concentrations of the aldehydes. The destabilization of the nucleophilic reagent is so great that even the introduction of a strong acceptor into the furan ring does not promote the reaction in the absence of a catalyst.

EXPERIMENTAL

2-(α-Furyl)-5-ethyl-5-nitro-1,3-dioxane (I). A 4.8-g (0.05 mole) sample of furfural was added with stirring and heating on a water bath to 7.45 g (0.05 mole) of 2-nitro-2-ethylpropane-1,3-diol and 0.96 g of KU-2 (H form) cation-exchange resin in 100 ml of absolute benzene. The end of the reaction was determined by spectrophotometry. At the end of the reaction, the exchange resin was removed by filtration, and the dioxane crystallized out from the benzene solution to give 7.5 g (66%) of colorless needles that were only slightly soluble in alcohol, benzene, and ether. Nitrodioxanes II-V were similarly obtained.

2-(α-Furyl)-5-amino-5-ethyl-1,3-dioxane (VI). A solution of 8 g (0.035 mole) of dioxane I in 150 ml of 70% ethanol was added with continuous stirring at the rate of 10 ml/min to 250 ml of sodium amalgam (1.7 g-eq of Na in 1 liter of mercury; the mirror area of the amalgam was 140 cm^2). At the end of the reduction, the amines were extracted with 250 ml of ether. The ether extracts were dried with sodium sulfate, and the ether was removed by distillation to give 3.9 g (56%) of yellow crystals that were unstable in air. Aminodioxanes VII-X were similarly obtained.

2-(α-Furyl)-5-ethyl-5-acetamido-1,3-dioxane (XI). A 1.27-g (0.01 mole) sample of dioxane VI was mixed with 2.04 g (0.02 mole) of acetic anhydride at room temperature. Colorless crystals [2.11 g (88%)] precipitated immediately. Compound XII was similarly obtained.

The kinetic experiments were carried out in a thermostatted (80 ± 0.1°) flask with a stoichiometric ratio of components (0.5 g-mole/liter of aldehyde and 0.5 g-mole/liter of alcohol) with KU-2 (20% of the weight of the aldehyde) in absolute benzene at a constant rate of stirring. The mathematical analysis of the kinetic curves was performed graphically and analytically. The reaction was monitored spectrophotometrically via the method in [7].

The IR spectra of mineral oil suspensions of the compounds were obtained with an IKS-14 spectrophotometer.

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