MECHANISM OF RECYCLIZATION OF FURANS TO THIOPHENES AND SELENOPHENES UNDER ACID-CATALYSIS CONDITIONS.

2.* KINETIC INVESTIGATIONS OF THE REACTION OF 2,5-DIALKYLFURANS WITH HYDROGEN SULFIDE AND HYDROGEN SELENIDE IN AN ANHYDROUS MEDIUM

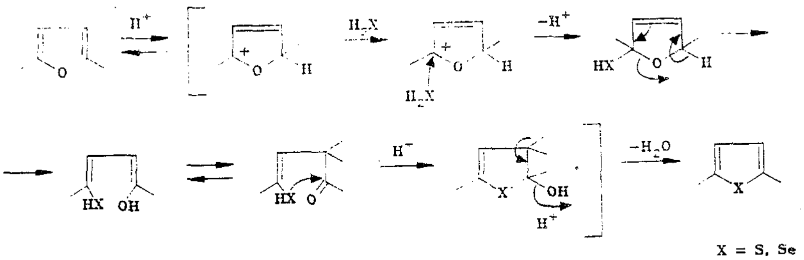
S. P. Voronin, T. I. Gubina,
S. A. Trushin, I. A. Markushina,
and V. G. Kharchenko

UDC 547.739'732'722.07:541.127

The effect of the concentration of the acidic component on the rates of recyclization of 2,5-dialkylfurans to thiophenes and selenophenes was studied. On the basis of the direct correlation of log k on $(H_0)_I$ and the isotope effect of the solvent it was established that the reaction proceeds via a mechanism of specific acid catalysis. It was shown that the rates of the reactions with the participation of hydrogen sulfide and hydrogen selenide coincide at equal acidities and temperatures. A scheme for the mechanism of the reaction that includes a step involving the formation of the doubly protonated form of the substrate is proposed.

It has been previously shown [1] that the recyclization of 2,5-dialkylfurans to thiophenes and selenophenes in the presence of hydrochloric acid proceeds via two parallel pathways: with the formation of intermediate dicarbonyl compounds and as a result of the direct conversion of furans to thiophenes.

In the present research we investigated the kinetics of the process in an anhydrous medium; to describe its mechanism we propose the following scheme:



According to this mechanism the rate-determining step should follow a step involving rapid and reversible protonation, i.e., equilibrium between the protonated and unprotonated forms of the substrate should be reached, which is determined by the acidity of the medium.

For experimental confirmation of the proposed scheme we determined the dependence of the rates of recyclization of 2,5-dimethylfuran (I) to 2,5-dimethylthiophene (II) and to 2,5-dimethylselenophene (III) on the Hammett acidity function in its modified form $(H_0)_I$ for low-polarity solvents [2].

The rates of the reactions were evaluated from the change in the concentration of the starting furan from GLC data. The quantitative compositions of the samples were calculated by the internal-standard method. 2,5-Dimethylselenophene was used as the internal standard in the recyclization of I to product II, while 2,5-dimethylthiophene was used as the internal standard in the recyclization of I to III. On the basis of the results of the rates of the investigated reactions on the hydrogen chloride concentration (Table 1) it may be concluded that the rates of the two reactions depend to the same extent on the concentration of the acidic component and virtually coincide at the same hydrogen chloride concentration.

---

*See [1] for Communication 1.

N. G. Chernyshevskii Saratov State University, Saratov 410026. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1458-1462, November, 1989. Original article submitted April 20, 1988; revision submitted December 1, 1988.

0009-3122/89/2511-1216$12.50

TABLE 1. Dependence of the Rates of the Reactions of 2,5-Dimethylfuran with Hydrogen Sulfide and Hydrogen Selenide on the Hydrogen Chloride Concentration

c_{HCl}, N	Selectivity, $k \cdot 10^{-4}$, sec^{-1}	
	with H_2S	with H_2Se
1,4	0,98±0,02(80) 0,94±0,12(83)	0,8±0,03(82) 0,81±0,04(82)
1,9	1,54±0,12(80) 1,44±0,008(78)	1,71±0,09(81)
2,4	2,28±0,30(80) 3,40±0,14(87)	2,53±0,17(80) 3,51±0,08(80)
3,2	8,41±0,40(85) 8,85±0,33(88)	8,16±0,85(80) 8,89±0,49(76)

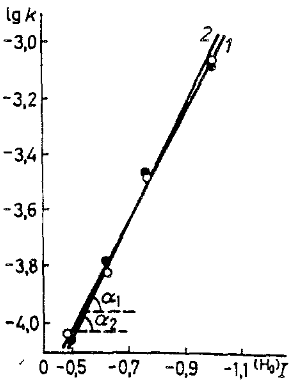


Fig. 1. Dependence of the rates of recyclization of I to II (1) and III (2) on the acidity of the medium [tan α_1 = 1.91 (I → II); tan α_2 = 1.96 (I → III)].

A directly proportional dependence of the rate constant on $(H_0)_I$ (Fig. 1), which constitutes evidence that recyclization proceeds via a mechanism of specific acid catalysis, was established. The slopes of the lines obtained that depict this dependence are close to two, which indicates a reaction that is second order in the acidic component. The isotope effect of the solvent $k_{C_2H_5OH}/k_{C_2H_5OD} = 1.9$, which is known to be characteristic for reactions that proceed via a mechanism of specific acid catalysis [3]. Zero order in the nucleophile was established: the rate constants for recyclization of 2,5-dimethylfuran to the corresponding thiophene and selenophene are virtually equal.

The effect of the temperature on the rates of recyclization of I to II and of a derivative of I to product III was studied. The experimental data obtained (Table 2) provide evidence that the reaction rates coincide at the same temperature. The energies of activation calculated from the slopes of the corresponding lines constructed in Arrhenius coordinates are close and are equal to, respectively, 18.4 (for I → II) and 18.9 kcal/mole (for I → II). These values are characteristic for heterolytic reactions that take place in solutions and constitute evidence for an identical energy barrier of the rate-determining steps of the two processes. On the basis of this it may be concluded that the investigations were carried out in the kinetic region.

An analysis of the experimental data obtained provides evidence that reaction of the nucleophile with a molecule of the substrate does not occur in the rate-determining step of the reaction (the reaction is zero order in the nucleophile). This assumption is also based on the different nucleophilicities of hydrogen sulfide and hydrogen selenide and their different solubilities in organic solvents [4]. Thus the scheme presented above is not justified since it does not reflect the kinetic principles of the process that we obtained.

TABLE 2. Dependence of the Rates of the Reaction of 2,5-Dimethylfuran with Hydrogen Sulfide and Hydrogen Selenide on the Temperature

T, °C	$k\cdot10^{-4}$, sec^{-1}	lg k	E_{act}, kcal/mole	$k\cdot10^{-4}$, sec^{-1}	lg k	E_{act}, kcal/mole
	with H_2S			with H_2Se		
25,0	1,04±0,12	−3,98	18,4	0,98±0,10	−4,01	18,9
35,4	3,19±0,40	−3,50		2,84±0,31	−3,54	
40,2	4,68±0,32	−3,33		4,45±0,35	−3,35	
45,0	7,33±0,24	−3,13		7,43±0,47	−3,13	

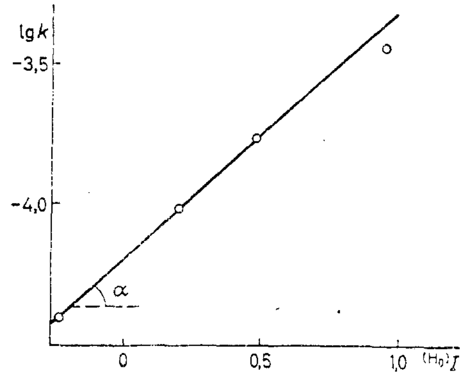
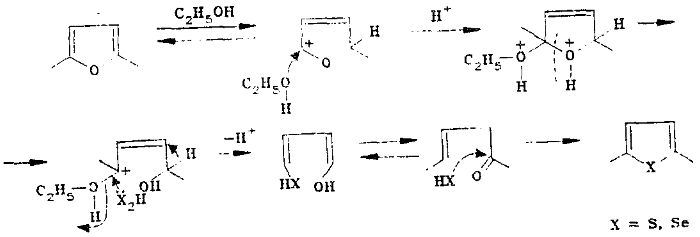


Fig. 2. Dependence of the rate of hydrolysis of 2,5-dimethylfuran in 95% ethanol on the acidity of the medium (tan α = 0.9).

The following hypothetical scheme may correspond to zero order in the nucleophile and second order in the acidic component:



According to this scheme a molecule of the alcohol acts as a competing nucleophile. Cleavage of the cyclic acetal with the formation of a carbonium ion, which then reacts with a molecule of hydrogen sulfide or hydrogen selenide, occurs under the influence of a second proton.

Assuming identical character of the mechanisms of hydrolysis and recyclization one expected to obtain similar kinetic principles for the two reactions at comparable concentrations of the nucleophilic reagents.

The dependence of the rate of hydrolysis of 2,5-dimethylfuran on the concentration of the acidic component in 95% ethanol was studied. The initial concentration of I was lower by a factor of 25 than the initial concentration of water in the 95% ethanol. The hydrolysis of furans under these conditions is a "pseudo-first" order reaction. The graphical dependence of the rate constant on $(H_0)_I$, which is a straight line with a slope close to one (Fig. 2), was constructed from data that describe the change in the rate of hydrolysis of I as a function of the hydrogen chloride concentration. On the basis of this it may be concluded that the hydrolysis of 2,5-dimethylfuran (I) under the conditions presented above proceeds via a mechanism of specific acid catalysis and is first order in the acidic component, i.e., despite the considerably lower concentration of water as compared with ethanol, the latter does not prove to be a nucleophile in either hydrolysis or recyclization.

On the basis of the kinetic data obtained it may be concluded that there is a difference in the mechanisms of hydrolysis and recyclization and it may be assumed that opening of the furan ring is associated with the formation of a doubly protonated form of the substrate. The facts of double protonation established from the slopes of the correlation lines log k as a function of $(H_0)_I$ have been described for the benzidine rearrangement [5] and the decarboxylation of phenylglyoxylic acid [6]. As regards the site of addition of the second proton in the recyclization of furans to thiophenes, this question requires additional research, which we will attempt to accomplish by means of quantum-mechanical calculations.

EXPERIMENTAL

The course of the conversion of 2,5-dimethylfuran to 2,5-dimethylthiophene and 2,5-dimethylselenophene was monitored with a Tsvet-101 chromatograph with a flame-ionization detector; the 2 m by 3 mm steel column was packed with 15% Apiezon L on Chromaton N-AW-DMCS, the carrier gas was argon, the flow rate was 2 liters/h, and the temperature was 160°C.

Compounds I-III were obtained by the methods in [7, 8].

Study of the Effect of the Hydrogen Chloride Concentration on the Rates of Recyclization of I to II and III (Table 1). A 30-ml sample of a 1.4 N (1.9 N, 2.4 N, 3.2 N) solution of hydrogen chloride in absolute ethanol was placed in a 50 ml three-necked thermostatically heated (35 ± 0.1°C) reactor equipped with a magnetic stirrer, reflux condenser, and bubbling tube and saturated with hydrogen sulfide or hydrogen selenide for 2 h, after which 0.30 g (3.2 mmole) of I and 0.15 g of III or II (the internal standard) were added to the reaction mixture. The reaction time was reckoned from the moment at which the 2,5-dimethylthiophene was added to the reaction mixture. Samples (1 ml) were selected from the reaction mixture at definite intervals of time and neutralized with 2 ml of a saturated solution of sodium carbonate, and the neutralized samples were extracted with 0.5 ml of ether. The concentrations of the components in the sample were determined by means of GLC using the internal-standard method for the calculations. The experiment was carried out twice. The rate constants were calculated from the slopes of the straight lines (Fig. 1).

Study of the Effect of the Temperature on the Rates of Recyclization of I to II and III (Table 2). The reaction of 2,5-dimethylfuran (I) with hydrogen sulfide was carried out by the method described above in two thermostatically controlled reactors connected in parallel to the same thermostat; the reaction was carried out in 20 ml of 2.4 N solution of hydrogen chloride in absolute ethanol starting from 0.2 g of 2,5-dimethylfuran. The rate constants of the two reactions were determined at 25.0°C, 35.4°C, 40.2°C, and 45.0°C.

Determination of the Isotope Effect of the Solvent. The reaction of I with hydrogen sulfide was carried out in two parallel thermostatically controlled (at 35°C) reactors. Samples (30 ml) of solutions of hydrogen chloride in ethanol and C_2H_5OD with a concentration of 1.9 N were placed in each reactor. The solutions were saturated in the course of 1 h: the first with H_2S, and the second with D_2S [the latter was obtained by the action of D_2SO_4 (20% in D_2O) on iron sulfide]. After saturation, weighed samples of I [0.3 g (3 mmole)] and toluene [0.15 g (1 mmole)] (the internal standard) were added to each of the reactors. The rate constants of the reactions being compared were determined by the method described above and were calculated from the slopes of the corresponding anamorphoses. The isotope effect of the solvent $k_{C_2H_5OD}/k_{C_2H_5OH} = 2.92/1.49 = 1.9$.

Study of the Effect of the Hydrogen Sulfide Concentration on the Rate of Recyclization of I to II. The reaction was carried out in a thermostatically controlled (at 35°C) reactor starting from 0.2 g of I in 30 ml of a 2.4 N solution of hydrogen chloride in absolute ethanol at hydrogen sulfide concentrations of 0.10 and 0.15 mole/liter. The hydrogen sulfide concentration was determined by iodometric titration. The rate constants were, respectively, $(1.39 \pm 0.05)\cdot 10^{-4}$ sec^{-1} and $(1.41 \pm 0.06)\cdot 10^{-4}$ sec^{-1}.

Study of the Effect of the Hydrogen Chloride Concentration on the Rate of Hydrolysis of I in 95% Ethanol. The reaction was carried out in a thermostatically controlled (at 35°C) reactor starting from 0.2 g of I in 20 ml of solutions of hydrogen chloride in 95% ethanol with concentrations of 1.4, 1.9, 2.4, and 3.2 N.

The $(H_0)_I$ values for the various concentrations of hydrogen chloride in absolute and 95% ethanol were determined by graphical extrapolation from the data in [9, 10].

LITERATURE CITED

1. S. P. Voronin, T. I. Gubina, I. A. Markushina, and V. G. Kharchenko, Khim. Geterotsikl. Soedin., No. 10, 1333 (1989).
2. I. Rocek, Coll. Czech. Chem. Commun., 22, No. 1, 2 (1957).
3. C. A. Bunten and V. J. Shiner, J. Am. Chem. Soc., 83, 3214 (1961).
4. G. G. Devyatykh, A. E. Ezheleva, A. D. Zorin, and M. V. Zueva, Zh. Neorg. Khim., 8, 1307 (1963).
5. N. M. Émanuél and D. P. Knorre, Course in Chemical Kinetics [in Russian], Vyssh. Shkola, Moscow (1974).
6. W. W. Elliott and D. L. Hammick, J. Chem. Soc., 3402 (1951).
7. V. G. Kharchenko, T. I. Gubina, and I. A. Markushina, Zh. Org. Khim., 18, 394 (1982).
8. V. G. Kharchenko, I. A. Markushina, and S. P. Voronin, Khim. Geterotsikl. Soedin., No. 2, 219 (1983).
9. B. Nahlovsky and V. Chvalovsky, Coll. Czech. Chem. Commun., 33, 3122 (1968).
10. B. Nahlovsky and V. Chvalovsky, Coll. Czech. Chem. Commun., 33, 3391 (1968).

SYNTHESES BASED ON FURANCARBOXYLIC ACID AMIDES.

1. SYNTHESIS AND STRUCTURE OF 2-(5-R-2-FURYL)-4-OXOQUINAZOLINES

I. N. Kozlovskaya, L. A. Badovskaya,
V. E. Zavodnik, and Z. I. Tyukhteneva

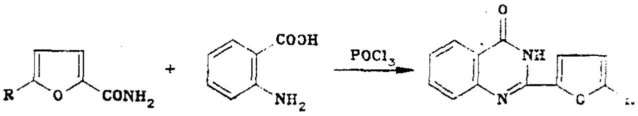
UDC 547.856.1'725'583.5.07:543.51'422:
548.737

2-(5-R-2-Furyl)-4-oxoquinazolines are formed in the condensation of furancarboxylic acid primary amides with anthranilic acid in the presence of phosphorus oxychloride. It was determined by x-ray diffraction analysis, IR and PMR spectroscopy, and mass spectrometry that a labile hydrogen atom is bonded to the nitrogen atom in the 3-position and that the molecule has an s-NH,O-trans conformation.

Compounds with pronounced biological activity are found in the oxoquinazolines series [1-4]. Little-investigated oxoquinazolines that contain a furan fragment in their structures are of interest in this respect.

The aim of the present research was the synthesis of 2-(5-R-2-furyl)-4-oxoquinazolines on the basis of furancarboxylic acid primary amides and the study of their structures.

2-(5-R-2-Furyl)-4-oxoquinazolines IIa-h (Table 1) were obtained in high yields by condensation of 5-R-furan-2-carboxylic acid primary amides Ia-h with anthranilic acid in the presence of phosphorus oxychloride.



I a-h

II a-h

I, II a R=H, b R=CH_3, c R=C_6H_5, d R=Br, e R=I, f R=NO_2, g R=4-BrC_6H_4, h R=4-$NO_2C_6H_4$

Oxoquinazoline IIa (Fig. 1, Table 2) was subjected to an x-ray diffraction study to establish the structures of the synthesized compounds.

Compound IIa exists in the form of the s-N,O-trans isomer. The quinazoline ring is planar within the limits of 0.02 Å. The deviation of the $O_{(4)}$ atom from the mean plane drawn through the $N_{(1)}C_{(2)}N_{(3)}C_{(4)}-C_{(10)}$ atoms is 0.7 Å. The maximum deviation of the ring atom from the mean plane of the five-membered heteroring is 0.003 Å for the $O_{(2)}$ atom. The geometry

---

Krasnodar Polytechnic Institute, Krasnodar 350072. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1463-1466, November, 1989. Original article submitted April 4, 1988; revision submitted January 17, 1989.

0009-3122/89/2511-1220$12.50