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INVESTIGATION OF THE MECHANISM OF THE RECYCLIZATION OF FURANS TO THIOPHENES AND SELENOPHENES UNDER ACID-CATALYSIS CONDITIONS. 3.* INVESTIGATION OF THE RECYCLIZATION OF HOMOLOGS AND FUNCTIONAL DERIVATIVES OF FURAN. QUANTUM-CHEMICAL CALCULATIONS OF THE OBJECTS OF THE RECYCLIZATION

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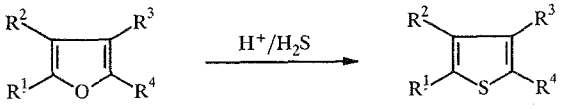
The kinetics of the conversion of di-, tri-, and tetraalkylfurans to the corresponding thiophenes were investigated. A correlation between the reactivities and structures of the investigated furans was established. Quantum-chemical calculations of the objects of the recyclization were made. The calculated and experimental data on the reactivities of the investigated compounds were compared. The most likely pathway of the protonation of furans in their recyclization was determined on the basis of calculations of the total energies of the protonated forms.

We have previously discovered the recyclization of furans to thiophenes and selenophenes by the action of nucleophiles under acid-catalysis conditions at 20-60°C [2-6]. Kinetic studies of the process in aqueous and absolute media were made. It was shown that, under the influence of nucleophiles in the presence of hydrochloric acid, recyclization proceeds via two parallel pathways to give intermediate dicarbonyl compounds and as a result of direct conversion of the furans to thiophenes and selenophenes. The primary occurrence of reaction via the latter pathway was established [7].

A study of the kinetics of the process in a nonaqueous medium showed that the reaction proceeds via a mechanism involving specific acid catalysis and is first order in the furan compound, zero order in the nucleophile, and second order in the acidic component [1]. The latter fact made it possible to propose a double-protonation mechanism as a model. The question as to the site of addition of the second proton remained open to discussion.

In the present research we thoroughly analyzed data on the recyclization of furans Ia-s to give the corresponding thiophenes:



Ia-y II b-n, r

Ia $R^1=R^2=R^3=R^4=H$ (unindicated R = H); I, IIb $R^1=CH_3$, c $R^1=R^4=CH_3$, d $R^1=CH_3$, $R^4=C_2H_5$, e $R^1=CH_3$, $R^4=C_3H_7$, f $R^1=CH_3$, $R^4=C_4H_9$, g $R^1=CH_3$, $R^4=CH(CH_3)C_3H_7$, h $R^1=CH_3$, $R^4=C(CH_3)_2C_3H_7$, i $R^1=R^4=C_2H_5$, j $R^1=C_2H_5$, $R^4=C_3H_7$, k $R^1=R^3=CH_3$, $R^4=C_2H_5$, l $R^1=R^3=R^4=CH_3$, m $R^1=R^4=CH_3$, $R^3=C_3H_7$, n $R^1=R^2=R^3=R^4=CH_3$, o $R^1=CH_3$, $R^4=CH_2NH_2$, p $R^1=CH_3$, $R^4=COOH$, q $R^1=CH_3$, $R^4=COCH_3$, r $R^1=CH_3$, $R^4=CH_2OH$, s $R^1=CH_3$, $R^4=NH_2$

*For Communication 2 see [1].

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TABLE 1. Rate Constants for the Recyclization of Furan Homologs

Compound	$k \cdot 10^{-4}$, sec^{-1}		Compound	$k \cdot 10^{-4}$, sec^{-1}	
Ic	7,75	0,57	Ii	7,72	0,10
Id	6,95	0,68	Ij	5,73	0,07
Ie	5,19	0,07	Ik	3,46	0,05
If	5,77	0,15	Il	1,55	0,06
Ig	5,41	0,11	Im	1,12	0,02
Ih	3,32	0,13	In	*	

*The degree of conversion after 14 h did not exceed 10%.

TABLE 2. Rate Constants for the Hydrolysis of Furan Homologs

Compound	$k \cdot 10^{-4}$, sec^{-1}		Compound	$k \cdot 10^{-4}$, sec^{-1}
Ic	4,60	0,25	Ik	*
If	2,39	0,29	Im	*
Ig	1,40	0,15	In	
Ih	0,82	0,20		

*The compound is not hydrolyzed.

It was established that 2,5-dialkyl- (Ib-k), 2,3,5-trialkyl- (Il, m), and 2,3,4,5-tetraalkyl(In)furans are capable of reacting with hydrogen sulfide in acidic media to give the corresponding alkyl-substituted thiophenes IIb-n [5]. The conversion of furans Ib, r gives the desired products in low yields [3, 5]. The recyclization of Ia, o-q, s could not be accomplished.

In the present research we determined the rate constants for the recyclization of Ic-n (Table 1). An analysis of the data obtained makes it possible to conclude that the reactivities of 2,5-dialkylfurans are virtually independent of the length of the carbon chain of the substituent. A certain decrease in the reaction rate is observed in the case of branched alkyl substituents; this is probably due to the steric factor.

The introduction of an alkyl substituent into the β position of the ring sharply decreases the recyclization rate. A significant decrease in the reactivity is observed when a methyl group in the β position of the ring is replaced by an ethyl group. Tetramethylfuran In undergoes 10% conversion to the corresponding thiophene.

For comparison, we studied the effect of the structure of alkyl-substituted furans Ic, f-h, k, m, n on the reactivity in the case of hydrolysis to 1,4-diketones under conditions identical to those in the recyclization. It was established that the rate of hydrolysis decreases with an increase in the length and degree of branching of the alkyl substituent in the α position of the furan ring (Table 2), while tri- and tetraalkylfurans are not hydrolyzed under the experimental conditions. The data obtained make it possible to assert that recyclization and hydrolysis proceed via different mechanisms.

As we noted, recyclization does not proceed when oxo and amino groups are present in the α position of the furan ring. We assumed that this is associated with the decrease in the electron density of the heteroring caused by introduction of the cited substituents. To shed some light on this problem we made quantum-chemical calculation of the electron structures of furans Ia-e, l, n-s (Table 3). A comparison of the results of the calculations with the experimental data does not make it possible to make a correlation between the reactivity and the charge distribution in the ring. Thus 2,5-dimethylfuran (Ic), which undergoes recyclization very readily, and tetramethylfuran (In), which undergoes no more than 10% recyclization, have the same type of charge distribution. The introduction of substituents such as NH_2, COOH, and $COCH_3$ increases the positive charge on the α-carbon atom; however, here also one cannot make an unambiguous selection. For example, in Io the charge distribution is similar to that in Ic; however, Io does not undergo recyclization, while Ic very readily undergoes conversion to thiophene IIc. This means that the magnitude of the charge on the α-carbon atom of the furan ring is not the determining factor in this reaction. The calculated values are in agreement with the results of quantum-chemical calculations of reactions involving electrophilic addition to the α position in five-membered heterocycles, where it was shown that this process is orbitally controlled [8].

TABLE 3. Charges on the Atoms of Furans with Various Substituents

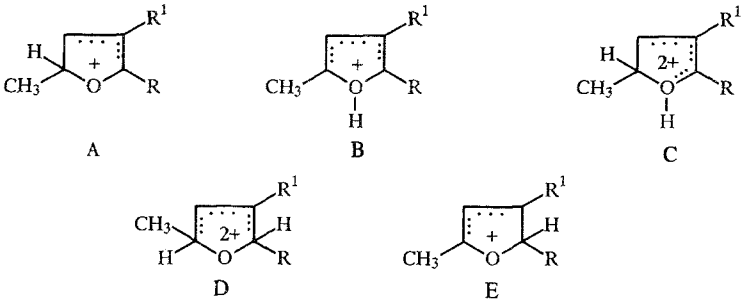
Compound	O	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$
Ia	-0.131	0,090	-0,031	-0,031	0,090
Ib	-0,145	0,154	-0,052	-0,033	0,090
Ic	-0,164	0,138	-0,039	-0,039	0,138
Id	-0,203	0,158	-0,066	-0,064	0,146
Ie	-0,203	0,158	-0,065	-0,065	0,148
If	-0,203	0,158	-0,077	-0,016	0,123
In	-0,206	0,136	-0,037	-0,037	0,136
Io	-0,168	0,140	-0,031	-0,050	0,129
Ip	-0,191	0,182	-0,070	-0,001	0,056
Iq	-0,173	0,184	-0.041	-0,020	0,070
Ir	-0,195	0,128	-0,044	-0,084	0,145
Is	-0,192	0,130	-0,038	-0,096	0,270

TABLE 4. Charges on the Atoms and Total Electron Energies of Furans Ia-c and Their Protonated Forms

Compound	Charges on the atoms					E, eV
	O	$C_{(2)}$	$C_{(3)}$	C(4)	C(5)	
Ia	-0,132	0,091	0,034	0,034	0,091	-135
Ia (A)	-0,109	0,265	-0,019	0,150	0,060	-1362,11
Ia (B)	-0,020	0,132	0,041	0,041	0,132	-1362,92
Ib	-0,145	0,154	-0,052	-0,033	0,090	-1587,98
Ib (A)	-0,146	0,083	0,151	-0,064	0,353	-1600,29
Ib (B)	-0,021	0,092	0,070	-0,045	0,207	-1599,95
Ic	-0,164	0,138	-0,039	-0,039	0,138	-1827,00
Ic (A)	-0,165	0,163	-0,186	-0,107	0,333	-1841,20
Ic (B)	-0,050	0,174	-0,035	-0,035	0,174	-1839,90
Ic (B)	-0,073	0,181	0,235	-0,074	0,373	-1846,00
Ic (D)	-0,108	0,184	0,166	-0,167	0,183	-1844,57

As regards the effect of functional groups in Io-s, they, in our opinion, may be additional protonation centers under the reaction conditions, i. e., unique "proton traps," since the heteroatoms of these groups have a large negative charge and contribute to the highest occupied molecular orbital (HOMO) of the indicated substances.

To solve the problem of the possibility of double protonation and the location of the second proton we calculated the total electron energies of furan (Ia), α-methylfuran (Ib), 2,5-dimethylfuran (Ic), and their protonated forms with respect to the α position (A) and the oxygen atom (B) (Table 4).



In the case of the 2,5-dimethylfuran molecule it is apparent that carbonium ion A, formed in the protonation of its α position, is energically more favorable than intermediate B, obtained by the addition of a proton to the oxygen atom; negative charge is retained on the oxygen atom in carbonium ion A, i. e., reprotonation at the oxygen atom to give intermediate C is possible. This process is energically more favorable than the addition of a second proton in the α′ position, which leads to dication D (Table 4).

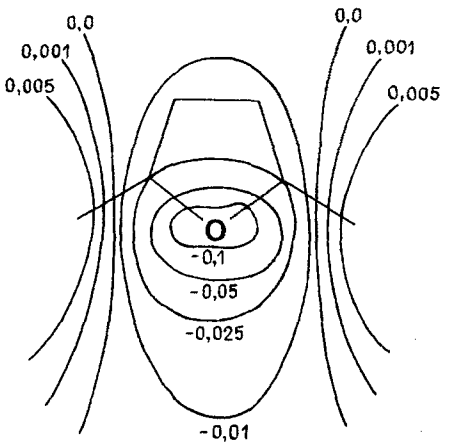


Fig. 1. Molecular electrostatic potential of dimethylfuran Ic above the plane of the molecule (2 Å).

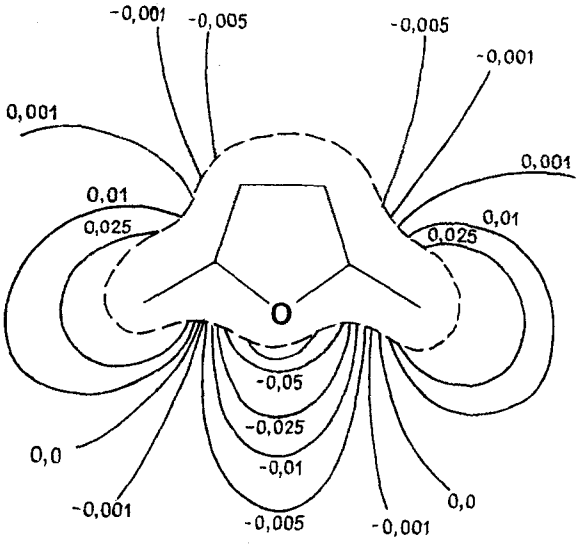


Fig. 2. Molecular electrostatic potential of dimethylfuran Ic in the plane of the molecule.

In the case of symmetrical α,α'-disubstituted furans Ic, i, n the α and α' positions are equivalent. A question regarding the preferred site of protonation arises for unsymmetrical alkylfurans Id, f, l. It is known that the protonation of 2-methyl-5-tert-butylfuran, according to PMR data, takes place at the ring $C_{(2)}$ atom [9]. We calculated the $C_{(2)}$- and $C_{(5)}$-protonated forms of Id, f, l. It was shown that the two positions are equivalent in Id — the energies of the corresponding carbonium ions of Id (A and E) are 2077.70 and 2077.71 eV. The difference in the energies for the carbonium ions of If (A) and If (E) is 10.55 eV, as compared with 10.99 eV for the carbonium ions of Il (A) and Il (E).

One should deal with the α- and O-protonated forms of the furan (Ia) and α-methylfuran (Ib) molecules separately. They have close energies (Table 4); this is probably the reason for their low reactivities, as compared with 2,5-dimethylfuran, in the recyclization reaction. We assume that two different intermediates based on the α- and O-protonated forms are formed with equal degrees of probability under the reaction conditions; these two intermediates then participate in two competitive processes — recyclization and cleavage with subsequent oligomerization.

It is known [10-13] that the reactivities of polar compounds with charged or polar reactants are determined by the molecular electrostatic potential (MESP). An analysis of the maps of the MESP of the model 2,5-dimethylfuran molecule (Figs. 1 and 2) showed that above the π bonds of the furan ring in a plane perpendicular to the plane of the molecule there

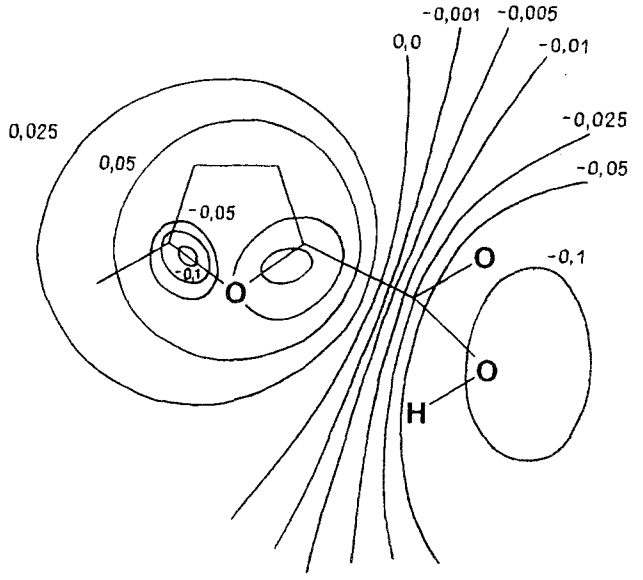


Fig. 3. Molecular electrostatic potential of 2-methyl-5-carboxyfuran (Ip) above the plane of the molecule (2 Å).

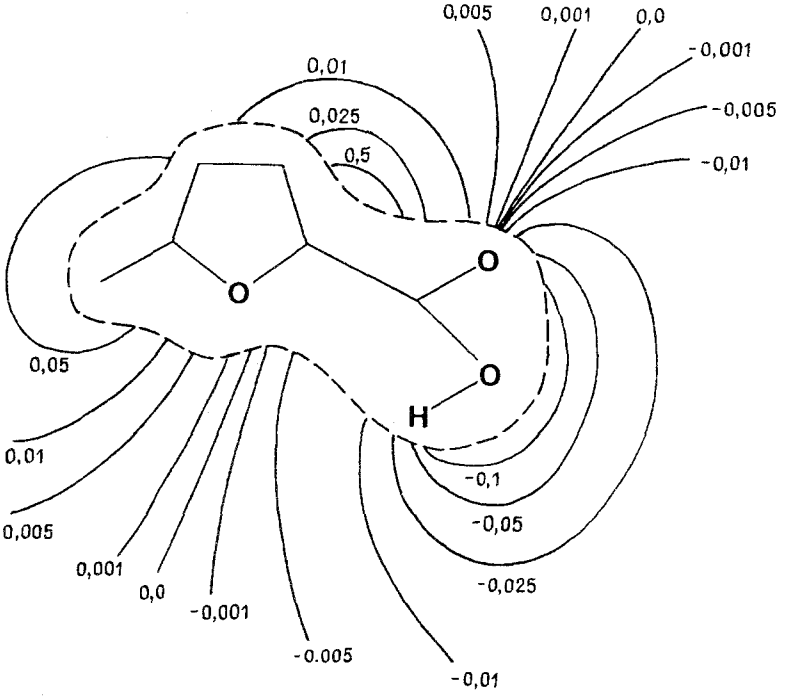


Fig. 4. Molecular electrostatic potential of 2-methyl-5-carboxyfuran (Ip) in the plane of the molecule.

is a narrow zone of negative values of the potential that allows the proton to approach the α-carbon atom. Calculation of the MESP for structures with functional groups in the case of Ip confirmed our experimental data on the impossibility of recyclization of Io-q, s: the presence of functional groups near the ring leads to that distribution of the MESP which promotes proton capture by the heteroatoms of these groups (Figs. 3 and 4).

The results obtained make it possible to work out in detail the previously proposed [1] mechanism of the recyclization of furans from the point of view of the structures of the intermediates. Thus we have shown that protonation of the substrate molecules takes place in the α position of the heteroring. O-Protonation is achieved in the case of realization of a step involving the addition of a second proton.

EXPERIMENTAL

The progress of the transformation of furans Ic-n during recyclization and hydrolysis was monitored with a Tsvet-101 chromatograph with a flame-ionization detector; the column length was 2 m, the diameter was 3 mm, the stationary phase was 15% Apiezon L on Chromaton N-AW-DMCS, the carrier gas was argon (helium), and the temperature was 160°C. The individuality of Ip-r and the results of recyclization were monitored by TLC on Silufol UV-254 plates in a hexane–chloroform–ether system (2:1:1) with development by iodine vapors.

The synthesis of I, IIb-n, and Io was described in [3, 5, 14]; Ip-r were commercial products.

Kinetic Studies of the Recyclization of Furans Ic-n. A 30-ml sample of a solution of dry hydrogen chloride in absolute ethanol was placed in a thermostatted (at 35°C) 50-ml three-necked reactor equipped with a magnetic stirrer, a reflux condenser with a gas-exit tube, a gas-bubbling tube, and a dropping funnel and saturated with hydrogen sulfide in the course of 1.5 h. A 0.006-mole sample of the starting furan was then added. At definite time intervals 0.5-ml samples were selected from the reaction mixture, neutralized with 2 ml of saturated sodium carbonate solution, and extracted with 0.5 ml of ether. Analysis of the percentages of the components in the extracts was carried out by GLC. The internal-standard method was used for the calculations; toluene was used as the internal standard. The recyclization rate constants were calculated from the slopes of the corresponding semilogarithmic anamorphoses of the curves of the consumption of starting furans Ic-n.

Kinetic Studies of the Hydrolysis of Furans Ic, f-h, k, m, n. Hydrolysis of the furans was carried out via the method described above, with the exception of saturation of the reaction mixture with hydrogen sulfide, starting with 0.006 mole of the starting furan compound and 0.06 mole of water. Monitoring of the progress of the reaction and calculation of the hydrolysis rate constants were accomplished as described above.

Quantum-Chemical Calculations. Quantum-chemical calculations were made by the SCF MO LCAO CNDO/2 method by means of the program of the VIKING complex [15]. The molecular electrostatic potentials were calculated within the diagonal approximation by means of the program in [11] using the charges on the atoms found by the CNDO/2 method.

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