

**Furan derivatives. CLI.**  
**Synthesis**  
**of 2-Y-3-(5-methylthio- and 5-methylsulfonyl-2-furyl)acrylonitriles**  
**and kinetics of their reaction with nucleophilic reagents**

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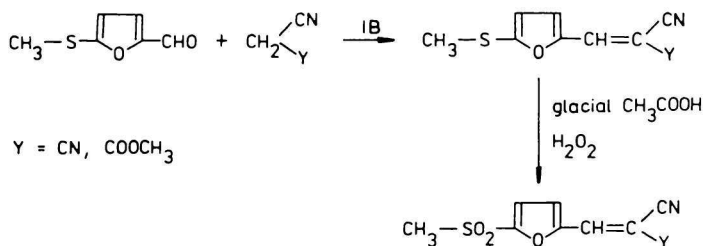
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2-Cyano-3-(5-methylthio- and 5-methylsulfonyl-2-furyl)acrylonitriles and methyl 2-cyano-3-(5-methylthio- and 5-methylsulfonyl-2-furyl)acrylates were prepared as model substances to study kinetics of nucleophilic replacement with secondary cyclic amines. Effects on the reaction rate of three different nucleophiles and of the electron-withdrawing group  $\text{CH}=\text{C}(\text{Y})\text{CN}$  at position 2 of the furan ring were investigated. The results obtained were compared with kinetic data of the  $\text{S}_{\text{N}}$  reaction of 5-(4-X-phenylsulfonyl- or -phenylthio)-2-furfurylidene malononitriles.

Описывается синтез 2-циано-3-(5-метилтио- и 5-метилсульфонил-2-фурил)акрилонитрилов и метиловых эфиров 2-циано-3-(5-метилтио- и 5-метилсульфонил-2-фурил)акриловой кислоты, которые были использованы в качестве модельных соединений для изучения кинетики реакции нуклеофильного замещения с вторичными циклическими аминами. Изучается влияние 3 различных нуклеофильных реагентов на скорость реакции, а также влияние электроноакцепторной группы  $\text{CH}=\text{C}(\text{Y})\text{CN}$  в положении 2 фуранового кольца. Полученные результаты сравниваются с кинетическими данными  $\text{S}_{\text{N}}$  реакции 5-(4-X-фенилсульфонил- или фенилтио)-2-фурфурилиденмалонитрилов.

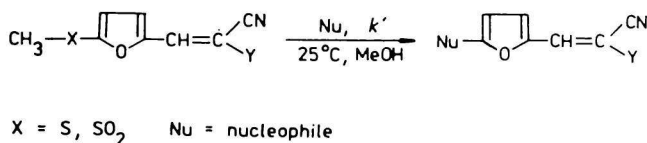
In our previous studies dealing with kinetics of nucleophilic replacement on the furan ring we have shown that the replaced group can be halogen, nitro [1], arylthio, and arylsulfonyl group [2]. Kinetic data of the  $\text{S}_{\text{N}}$  reaction of 5-(4-X-phenylthio- or 4-X-phenylsulfonyl)-2-furfurylidene malononitriles with secondary cyclic amines pointed out that the rate-determining step is the nucleophilic attack on position 5 of the furan ring. From these reasons, the reaction rate will be influenced by nucleophilicity of the reagent as well as by electron-withdrawing properties of the group to be released.

In the present work we report on the synthesis of model substances and their use in kinetic studies of an  $\text{S}_{\text{N}}$  reaction in which methylthio and methylsulfonyl are the



Scheme 1

groups to be replaced. The substances were prepared as shown in Scheme 1. The nucleophilic substitution was carried out under conditions of pseudomonomolecular reaction, *i.e.* in an excess of nucleophile (Scheme 2). Secondary cyclic amines of different nucleophilicity were used as the nucleophiles: morpholine (5.29), piperidine (5.59), and pyrrolidine (5.67). The reaction rate was followed spectrophotometrically at the wavelength corresponding to absorption maxima of the



Scheme 2

derivatives formed. Ultraviolet spectra of products of the  $S_N$  reaction were identical with those of standard compounds prepared in a different way. The rate constants  $k'$  and  $k_2$  of the  $S_N$  reaction with the used nucleophiles, calculated as described elsewhere [2], are listed in Table 1. They demonstrate that the reaction rate is proportional to increasing nucleophilicity of the reagents. The character of the substituted group is an additional factor affecting the exchange rate. As a rule, in all followed cases,  $k_2$  is higher with the derivatives having the methylsulfonyl group than with those having the methylthio group, apparently due to the electron-withdrawing character of the  $\text{CH}_3\text{SO}_2$  group. A comparison of the rate of nucleophilic replacement between derivatives *I* and *II* (Table 2) and piperidine with that of analogous aromatic derivatives *III* and *IV* showed that the derivatives having aromatic substituents (phenylthio and phenylsulfonyl groups) undergo the  $S_N$  reaction much easier than the aliphatic ones. This fact may be explained by higher stability of the released group  $\text{C}_6\text{H}_5\text{S}^-$  in comparison to that of the  $\text{CH}_3\text{S}^-$  group.

An important role in the course of the  $S_N$  reaction is played by the group  $-\text{CH}=\text{C}(\text{Y})\text{CN}$  at position 2 of the furan ring. The rate constants  $k_2$  for the reactions with all three nucleophiles are higher in the case of alkyl derivatives having  $\text{Y}=\text{CN}$  than in the case of those with  $\text{Y}=\text{COOCH}_3$  (Table 1). These

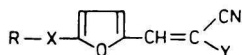
Table 1

Kinetic parameters of the  $S_N$  reaction of 2-Y-3-(5-methyl-X-2-furyl)acrylonitriles with nucleophiles in methanol at  $25 \pm 0.2^\circ\text{C}$ 

No.	X	Y	$k_2/l \text{ mol}^{-1} \text{ s}^{-1}$	Nucleophile
I	S	CN	0.657	PI
II	S	CN	0.1326	MO
III	S	CN	1.290	PY
IV	S	COOCH <sub>3</sub>	0.0381	PI
V	S	COOCH <sub>3</sub>	0.5454	MO
VI	S	COOCH <sub>3</sub>	0.6601	PY
VII	SO <sub>2</sub>	CN	10.731	PI
VIII	SO <sub>2</sub>	CN	0.784	MO
IX	SO <sub>2</sub>	CN	23.55	PY
X	SO <sub>2</sub>	COOCH <sub>3</sub>	3.372	PI
XI	SO <sub>2</sub>	COOCH <sub>3</sub>	10.824	PY
XII	SO <sub>2</sub>	COOCH <sub>3</sub>	0.0291	MO

PI — piperidine, PY — pyrrolidine, MO — morpholine.

Table 2

Rate constants of the  $S_N$  reaction of piperidine within methanol at  $25^\circ\text{C}$ 

No.	R	X	Y	$k_2/l \text{ mol}^{-1} \text{ s}^{-1}$
I	CH <sub>3</sub>	S	CN	0.657
II	CH <sub>3</sub>	SO <sub>2</sub>	CN	10.731
III	C <sub>6</sub> H <sub>5</sub>	S	CN	3.00
IV	C <sub>6</sub> H <sub>5</sub>	SO <sub>2</sub>	CN	11.36
V	C <sub>6</sub> H <sub>5</sub>	SO <sub>2</sub>	COOCH <sub>3</sub>	$0.44 \times 10^{-2}$

conclusions, which are in a good consonance with our previous results [3], follow from the fact that the group  $-\text{CH}=\text{C}(\text{CN})_2$  contributes more to decrease of  $E^{\text{LUMO}}$  at C-5 of furan than the group  $-\text{CH}=\text{C}(\text{CN})\text{COOCH}_3$ .

## Experimental

5-Methylthio-2-furaldehyde used in this work was prepared from 5-bromo-2-furaldehyde, sodium sulfide, and methyl iodide as described elsewhere [4].

Kinetic measurements were carried out on a registration spectrophotometer UV VIS (Zeiss, Jena) in the region of the last absorption maximum of the following products arising in the  $S_N$  reaction of 2-cyano-3-(5-X-2-furyl)acrylonitriles: X = piperidino (470 nm), morpholino (467 nm), and pyrrolidino (472 nm), or in the region of the last absorption maximum of methyl 2-cyano-3-(5-methylthio- and 5-methylsulfonyl-2-furyl)acrylates ( $\lambda_{\max}$  = 402 and 327 nm, respectively).

### 2-Y-3-(5-Methylthio-X-2-furyl)acrylonitriles

5-Methylthio-2-furaldehyde (1.42 g; 0.1 mol) was dissolved in ethanol (20 ml) and mixed with a solution of malonic acid dinitrile (0.01 mol) or methyl cyanoacetate (0.01 mol) in ethanol (10 ml). To agitated mixture a catalytic amount of sodium ethoxide was added and further stirred at room temperature for 2–3 h. The crystalline product formed during the reaction was sucked off and recrystallized from ethanol.

### Oxidation of 2-Y-3-(5-methylthio-2-furyl)acrylonitriles

To a solution of 2-Y-3-(5-methylthio-2-furyl)acrylonitriles (Y=CN or COOCH<sub>3</sub>, 0.005 mol) in glacial acetic acid (15 ml), 30% solution of hydrogen peroxide was added (3 ml). The mixture was stirred at room temperature for 30 min and then left to stand for 5 days. After this time the solution was concentrated to a half volume and diluted with water (4 ml). The precipitated crude product was sucked off and recrystallized from ethanol.

2-Y-3-(5-Methylthio- and 5-methylsulfonyl-2-furyl)acrylonitriles prepared in this way are listed in Table 3.

Table 3

Characterization of 2-Y-3-(5-methylthio-X-2-furyl)acrylonitriles

X	Y	Formula M	Calculated/found				Yield, % M.p., °C	$\lambda_{\max}$ /nm (log $\epsilon$ )		
			% C	% H	% N	% S				
S	CN	C <sub>9</sub> H <sub>6</sub> N <sub>2</sub> OS	56.83	3.17	14.74	16.87	72.8	238	260	415
		190.0	56.60	3.05	14.80	16.15				
S	COOCH <sub>3</sub>	C <sub>10</sub> H <sub>6</sub> NO <sub>3</sub> S	53.80	4.06	6.27	14.36	68.2	234	248	408
		223.2	53.51	3.98	6.20	14.20				
SO <sub>2</sub>	CN	C <sub>9</sub> H <sub>6</sub> N <sub>2</sub> O <sub>3</sub> S	48.64	2.72	12.60	14.43	70.0	211		328
		222.2	48.40	2.68	12.40	14.35				
SO <sub>2</sub>	COOCH <sub>3</sub>	C <sub>10</sub> H <sub>6</sub> NO <sub>3</sub> S	47.04	3.55	5.48	12.56	65.5	212		327
		255.2	46.95	3.48	5.30	12.40				

## References

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