KINETICS OF NUCLEOPHILIC DISPLACEMENT OF 2,5-DISUBSTITUTED FURANS*

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Received July 24th, 1978

5-Nitro- and 5-bromo-2-furfurylidenemalonitriles react with secondary saturated amines in an S_N reaction to replace bromo or nitro groups. The effects of nucleophilic reagent, solvent and temperature on the reaction rate were investigated. The results were contrasted with kinetic data of the S_N reaction of 5-(4-X-phenylsulfonyl- or phenylthio)-2-furfurylidenemalonitriles.

As followed from the kinetic of S_N reaction of 5-(4-X-phenylthio- or 4-X-phenylsulfonyl)-2-furfurylidenemalonitriles with secondary cyclic amines[1], the rate determining step is the nucleophilic attack at position 5 of the furan ring and therefore, the rate of the S_N reaction is considerably influenced by both the nature of the leaving group (phenylthio- or phenylsulfonyl) and the nucleophility of reagent.

This paper deals with the examination of kinetics of the S_N reaction involving Br and NO_2 as leaving groups. The kinetics of nucleophilic replacement of bromine in 5-bromofurfurylideneaniline and 5-halogen-2-furaldehydes by aromatic and aliphatic secondary amines was already studied[2]. A characteristic feature of mechanisms of these reactions is an electrophilic attack on the C=N bond prior to the nucleophilic attack at position 5 of the furan ring resulting in a considerable increase of the electron-accepting capability of azomethine grouping. The nucleophilic replacement of bromine or nitro groups takes place without a preceding protonization when using a strong electron-accepting substituent as $—CH=C(CN_2)$ in position 2 of the furan ring.

Piperidine, morpholine, N-phenylpiperazine and pyrrolidine were the nucleophilic reagents used in reaction with 5-bromofurfurylidenemalonitrile. Kinetics of this reaction was measured by a spectroscopic method in methanol under conditions of pseudomonomolecular reaction with an excess of nucleophilic reagent. The UV spectra of products of kinetic measurement were identical with those of 5-piperidino-, 5-morpholino-, 5-N-phenylpiperazino- and 5-pyrrolidino-2-furfurylidenemalonitriles, the physico-chemical properties of which were already published[1].

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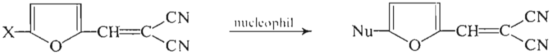
* Part CXXV in the series Furan Derivatives; Part CXXIV: This Journal *44*, 2417 (1979).

The rate constants of the S_N reaction of *I* and *II* with various nucleophilic reagents, listed in Table I, show the rate of the S_N reaction to be markedly influenced by the nucleophility of the reagent; its increase is proportional to the rate of S_N reaction (the nucleophility of reagents: piperidine 5·59, morpholine 5·29, pyrrolidine 5·67 and piperazine 5·59, ref.[4]). A greater activation effect of the NO_2 group on the S_N reaction course with piperidine is seen from comparison of k_2 of the replacement of bromine and nitro groups with derivatives *I* and *II*, respectively (Table I). The rate of nucleophilic displacement at position 5 of the furan ring markedly depends, according to results presented and those published[1], on the character of the leaving group. As seen in Table II, the replacement ability decreases in the order $NO_2 >$ $>$ Br $>$ $C_6H_5SO_2 > C_6H_5S$. The solvent effect on the kinetics of the S_N reaction was investigated with 5-nitro-2-furfurylidenemalonitrile and piperidine in methanol, dimethyl sulfoxide and sulfolane. Results obtained with methanol were reproducible,



I; X = Br, Nu = piperidine, morpholine, N-phenylpiperazine, pyrrolidine
II; X = NO_2, Nu = piperidine

TABLE I

Kinetic and Thermodynamic Parameters of an S_N Reaction of 5-X-2-Furfurylidenemalonitriles with Nucleophiles

Concentration 2–5 . 10^{-2}M, k_2 in l mol^{-1} s^{-1}, E_a in kJ mol^{-1}; ΔH^* in kJ mol^{-1}; ΔS^* n J grad^{-1} mol^{-1}.

X Reagent	$k_2 . 10^3$ 18°C	$k_2 . 10^3$ 25°C	$k_2 . 10^3$ 35°C	E_a	ΔH^*	$-\Delta S^*$
Br Piperidine	11·66	20·63	31·70	48·77	46·29	215·11
Br Morpholine	6·90	12·46	21·50	49·50	47·23	219·35
Br N-Phenylpiperazine	7·73	13·33	23·96	49·33	46·95	218·55
Br Pyrrolidine	19·60	28·70	58·66	47·94	45·34	205·65
NO_2 Piperidine	26·00	42·80	125·9	68·91	66·44	206·32

whilst with the remaining solvents the rate constants were found to decrease with increase of both concentration of the nucleophilic reagent and temperature. On the basis of UV spectra it could be assumed that at higher concentrations of piperidine ($\sim 10^{-2}$M) a concurrent reaction of solvents with piperidine occurred in addition to the S_N reaction; consequently, a decrease in concentration of the nucleophilic reagent takes place. Table I lists the thermodynamic parameters of the investigated S_N reactions.

EXPERIMENTAL

5-Bromo- and 5-nitrofurfurylidenemalonitriles were prepared by condensation of the respective 5-substituted 2-furaldehyde with malodinitrile according to[5]. All compounds were purified either by crystallization or distillation prior to kinetic measurements. The kinetics was measured with a spectrophotometer UV VIS, Zeiss, at 18°, 25° and 35° ± 0·2°C in the region of the last maximum of the S_N reaction product of 5-X-furfurylidenemalonitrile as follows: X (λ_{max}, nm) piperidino (470) morpholino (467), N-phenylpiperazino (453), pyrrolidino (472). The reaction mixture consisted of 0·1—0·5 ml of methanolic solution of *I* and *II* and 9·5—9·9 ml of methanolic (dimethyl sulfoxide, sulfolane) solutions of the appropriate secondary amine. Final concentrations of the substrate and the nucleophilic reagent in the mixture were $1-5 \,.\, 10^{-5}$M and $1-5 \,.\, 10^{-2}$M, respectively. The apparent rate constants k' (s^{-1}) were calculated from the line slope of the linear relationship $\log \Delta E = f(t)$ by the least squares method. Rate constants k_2 ($l \,.\, mol^{-1} \,.\, s^{-1}$) were calculated from the line slope of the nucleophilic reagent concentration and the apparent rate constants k'.

TABLE II

Kinetic Parameters of an S_N Reaction of 5-X-2-Furfurylidenemalonitriles with Piperidine in Methanol

$t = 25° \pm 0{\cdot}2°C$, k_2 in $l\ mol^{-1}\ s^{-1}$; E_a in kJ mol^{-1}; ΔH^* in kJ mol^{-1}; ΔS^* in J $grad^{-1} \,.\, mol^{-1}$.

X	$k_2 \,.\, 10^3$	E_a	ΔH^*	$-\Delta S^*$
Br	20·63	48·77	46·29	215·11
NO_2	42·80	68·91	66·44	206·32
C_6H_5S	3·00[a]	68·45	65·98	207·08
$C_6H_5SO_2$	11·36[a]	39·90	37·43	156·75

[a] According to[1].

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Translated by Z. Votický.