

REACTIONS  
OF CHLORINATED FURANIDINES. VII.\*  
THE KINETICS  
OF FORMATION OF PYRIDINIUM SALTS

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The rate constants and Arrhenius activation parameters of formation of pyridinium salts from some  $\alpha$ -chloro ethers were measured. All the reactions studied were found to be of the first order in the  $\alpha$ -chloro ether. The results obtained in this study confirm the presumed mechanism of the reaction, which involves the dissociation of an  $\alpha$ -chloro ether to carboxonium ion in the rate-determining step.

Kinetic studies of some nucleophilic substitution reactions of noncyclic<sup>1-3</sup> and cyclic<sup>4</sup>  $\alpha$ -chloro ethers showed these reactions to be, in general, first-order reactions in the  $\alpha$ -chloro ether and to occur by  $S_N1$  mechanism.

Continuing our systematic study of the reactions of cyclic  $\alpha$ -chloro ethers we examined the kinetics of reactions of 2-chlorotetrahydrofuran (*I*), 2,3-dichlorotetrahydrofuran (*II*), 2-chlorotetrahydropyran (*III*), and 2,3-dichlorotetrahydropyran (*IV*) with pyridine in dimethylformamide. In order to compare the reactivity of the compounds *I-IV* with an acyclic analogue we measured also the reaction of pyridine with chloromethyl ethyl ether (*V*). The pyridinium salts formed by this reaction could be used in synthesis of other derivatives<sup>5</sup>.

## EXPERIMENTAL

### Chemicals Used

2-Chlorotetrahydrofuran (*I*) was prepared by chlorination of anhydrous tetrahydrofuran at  $-20$  to  $-25^\circ\text{C}$  according to lit.<sup>6</sup>; b.p.  $32-34^\circ\text{C}/10$  Torr,  $n_D^{20}$  1.4635 (reported<sup>6</sup> b.p.  $35-36^\circ\text{C}$ : 15 Torr,  $n_D^{20}$  1.4638).

2,3-Dichlorotetrahydrofuran (*II*) was prepared by chlorination<sup>7</sup> of anhydrous tetrahydrofuran; b.p.  $53-54^\circ\text{C}/12$  Torr,  $n_D^{20}$  1.4860 (reported<sup>7</sup> b.p.  $62^\circ\text{C}/20$  Torr).

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2-Chlorotetrahydropyran (III) was prepared by addition of hydrogen chloride to 2,3-dihydropyran at  $-20$  to  $-30^{\circ}\text{C}$ ; b.p.  $35-36^{\circ}\text{C}/12$  Torr,  $n_{\text{D}}^{20}$  1.4676 (reported<sup>8</sup> b.p.  $36-37^{\circ}\text{C}/12$  Torr,  $n_{\text{D}}^{20}$  1.4677).

2,3-Dichlorotetrahydropyran (IV) was obtained by addition of chlorine to 2,3-dihydropyran. at  $-20$  to  $-25^{\circ}\text{C}$ ; b.p.  $80-83^{\circ}\text{C}/13$  Torr,  $n_{\text{D}}^{20}$  1.4953 (reported<sup>8</sup> b.p.  $74^{\circ}\text{C}/11$  Torr,  $n_{\text{D}}^{25}$  1.4950).

Chloromethyl ethyl ether (V) was prepared by passing gaseous hydrogen chloride through a mixture of 30 g of paraformaldehyde and 50 ml of ethanol at  $20^{\circ}\text{C}$  according to ref.<sup>9</sup>; b.p.  $28^{\circ}\text{C}/15$  Torr,  $n_{\text{D}}^{20}$  1.4030 (reported<sup>8</sup> b.p.  $79-83^{\circ}\text{C}/760$  Torr,  $n_{\text{D}}^{20}$  1.40398).

Pyridine was dried by standing over solid potassium hydroxide for 10 days and then distilled. The fraction boiling  $114-119^{\circ}\text{C}$  ( $n_{\text{D}}^{20}$  1.5103) was used in the measurements. Dimethylformamide was dried by repeated azeotropic distillation with benzene<sup>10</sup>. The content of water (determined by Fisher method<sup>11</sup>) was lower than 0.01%.

#### Preparation of Pyridinium Salts

The pyridinium salts VI–X were prepared from the corresponding  $\alpha$ -chloro ethers by adding 0.1 mol of pyridine with efficient stirring to a solution of 0.1 mol of the  $\alpha$ -chloro ether in 10 ml of anhydrous diethyl ether. The pyridinium salts, which precipitated out of solution in nearly

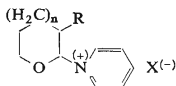
TABLE I  
Prepared Pyridinium Salts

Salt	Formula (m.w.)	Calculated/Found			
		% C	% H	% N	% Cl
VI	C <sub>9</sub> H <sub>12</sub> ClNO (185.6)	58.24	6.51	7.55	19.10
		58.42	6.41	7.43	20.08
VII	C <sub>9</sub> H <sub>11</sub> Cl <sub>2</sub> NO (220.0)	49.13	5.05	6.37	32.23
		48.92	5.13	6.57	32.06
VIII	C <sub>10</sub> H <sub>14</sub> ClNO (199.7)	60.15	7.06	7.01	17.75
		59.28	6.83	7.21	18.02
IX	C <sub>10</sub> H <sub>13</sub> Cl <sub>2</sub> NO (234.1)	51.30	5.59	5.98	30.28
		52.06	5.85	5.97	30.30
XI <sup>a</sup>	C <sub>9</sub> H <sub>11</sub> I <sub>3</sub> NO (530.9)	20.37	2.28	2.64	—
		18.96	2.32	2.56	—
XII <sup>b</sup>	C <sub>9</sub> H <sub>11</sub> I <sub>3</sub> ClNO (565.4)	19.12	1.96	2.48	—
		18.65	2.15	2.38	—

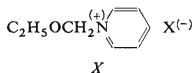
<sup>a</sup> M.p.  $89-90^{\circ}\text{C}$ . Calculated: 71.70% I; found: 69.44% I. <sup>b</sup> M.p.  $90-91^{\circ}\text{C}$ . Calculated: 67.33% I; found 67.55% I.

quantitative yield, are strongly hygroscopic, soluble in water and alcohols and insoluble in non-polar solvents. Their crystallization, which is difficult, is accompanied by their partial decomposition. For analysis, salts VI–IX were purified by multiple extraction with diethyl ether and chloroform and dried *in vacuo*.

By treating with an aqueous potassium triiodide, solution of salts VI–X can be easily transformed into crystalline, water-insoluble periodides of the pyridinium salts. In such a way the salts VI and VII were converted to the periodides XI and XII, which were purified for analysis by successive washing with water and ether followed by crystallization from ethanol. Elemental analyses of the salts are given in Table I.



R	X	n	R	X	n		
VI	H	Cl	0	IX	Cl	Cl	1
VII	Cl	Cl	0	XI	H	J <sub>3</sub>	0
VIII	H	Cl	1	XII	Cl	J <sub>3</sub>	0



Pyridinium salts VI–XII can be separated by paper chromatography using the system 1-butanol–1M-HCl (4 : 1). A solution of iodine in benzene may be used as a detecting agent.

#### Kinetic Measurements

The kinetics of the formation of pyridinium salts VI–X was followed by a conductivity method. A solution of a  $\alpha$ -chloroether in dimethylformamide was placed into a temperature-controlled conductivity cell equipped with platinum electrodes. As the start of the reaction we took the instant in which a solution of pyridine in dimethylformamide, warmed up to reaction temperature, was added. Dimethylformamide was used as the solvent due to its high dielectric constant (needed for good solvation of ions), inertness towards starting compounds, capability of dissolving reactants in required concentration, and possibility of working at low temperature. The conductivity of solutions was determined in regular time intervals, in case of rapid reaction it was automatically recorded with an EZ-4 recorder (Laboratorní přístroje). The conductivities were measured with a bridge compensatory Conductoscop LP (Laboratorní přístroje) instrument provided with magic eye as the indicator. The measurements were performed at frequency of 5 KHz. Initial concentration of compounds I, III and V was 0.25 mol/l and that of compounds II and IV 1.0 mol/l. The reaction of compound II with pyridine was also carried out using different ratios of the reactants at 30°C (Fig. 1). The concentration of the product was determined from calibration curve.

The first-order rate constants,  $k_1$ , were determined graphically from the integrated form of Eq. (1) (Eq. (2)),

$$\frac{d[D^+]}{dt} = k_1[A], \quad (1)$$

$$k_1 = 2.303 \log \frac{[A]}{[A] - [D^+]} 1/t, \quad (2)$$

where  $[A]$  is the initial concentration of  $\alpha$ -chloro ether,  $[D^+]$  is the concentration of pyridinium salt cation in time  $t$ , and  $k_1$  is the rate constant of unimolecular reaction. The results of kinetic measurements are given in Table II.

## RESULTS AND DISCUSSION

From the results it is seen that the course of the reaction can be well described by first-order kinetic equation which fits well even on using non-stoichiometric amounts of the reactants (Fig. 1). Rate constant of the reaction increases with increasing concentration of pyridine and is linearly dependent on reciprocal value of dielectric constant of the medium<sup>12,13</sup>. These findings support the assumption that the rate-determining step of the reaction is monomolecular dissociation of the  $\alpha$ -chloro ether (A), which is followed by the reaction of formed carboxonium ion ( $B^+$ ) with pyridine (C) to give pyridinium salt cation ( $D^+$ ):

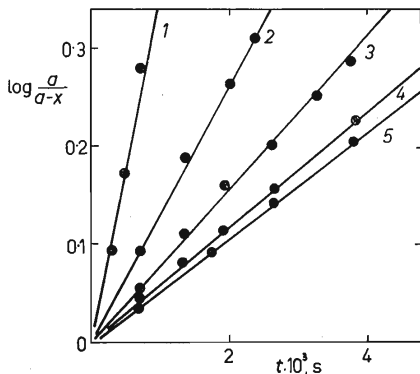


FIG. 1

Dependence of  $\log a/(a-x)$  on  $t$  for the Reaction of 2,3-Dichlorotetrahydrofuran (II) with Pyridine in Dimethylformamide at 30°C

1 Pyridine conc. 6.2 mol/l, conc. of compound II 1.0 mol/l; 2 pyridine conc. 1.8 mol/l, conc. of compound II 0.2 mol/l; 3 pyridine conc. 1.4 mol/l, conc. of compound II 0.6 mol/l; 4 pyridine conc. 0.6 mol/l; conc. of compound II 1.4 mol/l; 5 pyridine conc. 0.2 mol/l, conc. of compound II 1.8 mol/l.

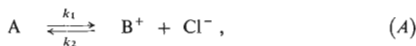


TABLE II

Arrhenius Activation Parameters,  $E_A$  and  $A$ , and Rate Constants,  $k_1$ , of the Reactions of  $\alpha$ -Chloro Ethers *I*–*V* with Pyridine in Dimethylformamide

$\alpha$ -Chloro ether	$E_A$ log $A$	Temperature °C	$k_1 \cdot 10^3$ $s^{-1}$
<i>I</i>	$5.65 \pm 0.45$ $4.2 \pm 0.3$	20	1 280
		14.6	840
		9.8	719
		5.4	515
		0.1	465
		– 7.3	268
		–27.0	161
<i>II</i>	$13.6 \pm 0.4$ $5.1 \pm 0.1$	50.5	0.642
		38.2	0.236
		36.0	0.201
		32.0	0.147
		30.0	0.127
		27.0	0.106
		24.0	0.083
<i>III</i>	$11.4 \pm 0.5$ $7.1 \pm 0.3$	31.0	88.7
		20.0	57.6
		0.0	10.0
		– 9.5	3.8
		–31.0	0.73
<i>IV</i>	$12.0 \pm 1.3$ $4.1 \pm 0.4$	51.9	0.123
		45.2	0.064
		35.6	0.0611
		24.3	0.0211
		18.8	0.0154
<i>V</i>	$5.7 \pm 0.4$ $2.5 \pm 0.2$	40.0	31.7
		30.0	21.4
		20.0	18.2
		9.5	11.7
		0.3	7.76

Differential equation (3) describing this process is identical

$$\frac{d[D^+]}{dt} = \frac{k_1 k_3 [A] [C]}{k_2 [Cl^-] + k_3 [C]} \quad (3)$$

with that for unimolecular reaction<sup>12</sup> and for initial stage of the reaction it can be re-written to the form (1).

The results obtained show also strongly deactivating effect of chlorine atom attached to the position  $\beta$ . So, compound *I* reacts at 20°C by factor of  $1.1 \cdot 10^4$  faster than compound *II* and, similarly, in tetrahydropyran series the reaction rate of compound *III* is increased by factor of  $3.5 \cdot 10^3$  over that of compound *IV*. The deactivating effect of the  $\beta$ -chlorine is compatible with monomolecular mechanism of the reaction: by its  $-I$  effect the chlorine atom increases electron deficiency on the carbon atom of carboxonium ion thus making its formation less advantageous.

The lower reactivity of tetrahydropyran derivatives relative to tetrahydrofuran ones (for the monochloro derivatives the ratio of the rate constants of tetrahydrofuran to tetrahydropyran derivative at 20°C equals to 22, and for the  $\alpha, \beta$ -dichloro derivatives 3.6) can be accounted for by energetically less suitable transformation of six-membered ring to carboxonium ion<sup>14</sup>.

The measured values of Arrhenius activation parameters are markedly low, especially when compared with those reported for solvolyses of other  $\alpha$ -chloro ethers. So, for instance, Salomaa found  $E_A = 19.79$  kcal/mol and  $\log A = 13.05$  for hydrolysis of 2,3-dichlorodioxane<sup>4</sup>,  $E_A = 24.52$  kcal/mol and  $\log A = 12.20$  for its ethanolysis<sup>4</sup>, and  $E_A = 14.51$  kcal/mol for the solvolysis of chloromethyl methyl ether in ethanol<sup>15</sup>. According to our opinion the low values obtained in the present work may be accounted for by the effect of the solvent (dimethylformamide). Changes in activation energies  $E_A$  between individual  $\alpha$ -chloro ethers *I*–*V* are roughly as expected, whereas the values of logarithms  $A$  are somewhat surprising; only the compounds *III* and *IV* have the values of  $\log A$  which fit expectation *i.e.*  $\log A$  for the dichloro derivative *IV* is lower than that for the monochloro derivative *III*, possibly due to lesser steric accessibility of the carbon of carboxonium ion of the former compound for pyridine molecule. For explanation of the fact that  $\log A$  for compound *I* is lower than the value for the corresponding dichloro derivative *II*, and especially that the value of  $\log A$  for compound *V* is extremely low, further experimental data are needed.

In conclusion, it can be said that the results obtained in the present work support the assumption that the reaction of the  $\alpha$ -chloro ethers with pyridine is a unimolecular process involving the formation of carboxonium ion in the rate-determining step.

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