

# Kinetics and Mechanism of Reaction between *N*-Polyfluorophenylcarbonimidoyl Dichlorides and Tertiary Amines in Acetonitrile

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**Abstract**—The reaction of *N*-polyfluorophenylcarbonimidoyl dichlorides with tertiary amines in acetonitrile afforded chloroamidines  $R^2NC(Cl)=NAr_F$  and alkyl chloride. The precursor of the products is the corresponding quaternary ammonium salt  $[R^3N+C(Cl)=NAr_F]-Cl^-$ . The rate of the salt formation is described by a second order equation; however with some amines a saturation effect was observed for the reaction rate with the growing amine concentration. This fact and also the influence of the amine and the substrate structure on the reaction rate suggests that reaction proceeds by addition–elimination mechanism with formation of a tetrahedral intermediate. The latter in the rate-limiting stage undergoes a stereomutation into an intermediate of a configuration favorable for conversion into a quaternary salt.

*N*-Substituted carbonimidoyl dichlorides ( $RN=CCl_2$ ) are applied as electrophilic agents to the synthesis of nitrogen-containing organic compounds, in particular, nitrogen-containing heterocycles [1–3]. Their reactions with nucleophiles depending on reaction conditions afford versatile products of replacement at the carbon atom. This is illustrated by Scheme 1 describing the intermediate and final products arising in reaction of carbonimidoyl dichlorides with primary and secondary amines [4].

In an aprotic medium secondary amines yield as final product chloroamidine **III**; the chlorine atom in the latter almost does not suffer substitution under the conditions of the experiment [3, 5]. In a dioxane–water mixture [6] and in aqueous acetone [7] the second chlorine atom in the chloroamidine **III** is readily replaced, and the main reaction product is guanidine **IV**.

The reaction of dichloride **I** with primary amines both in aprotic [3, 8, 9] and protic [10] solvents results in guanidine **VI** having as precursor carbo-diimide **V**. Products **V** were observed in the reaction mixture by spectral methods [3, 8, 9], and then they were preparatively isolated.

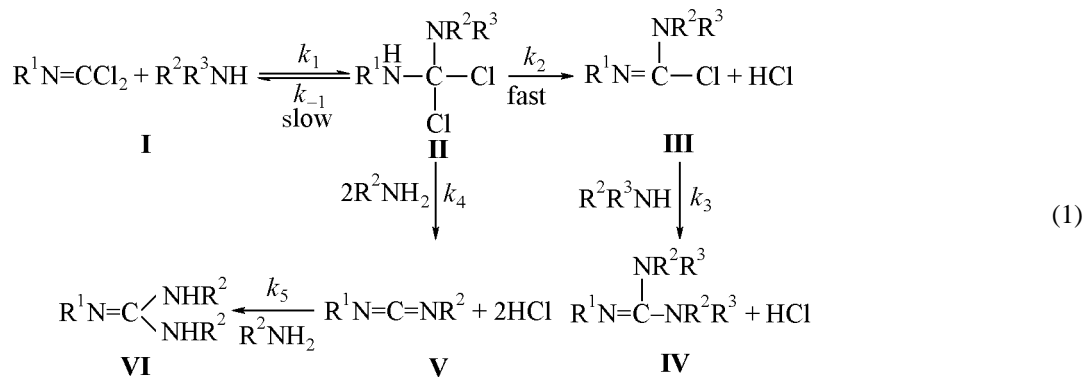
The investigation of aminolysis kinetics of *N*-polyfluorophenylcarbonimidoyl dichlorides by conductometric method revealed that although reaction products obtained from primary and secondary amines were different the reaction mechanism involved the same addition–elimination with formation of the

tetrahedral intermediate **II** in the limiting stage [5, 8]. This kinetic pattern ( $k_2 > k_{-1}$ ) arises apparently due to easy elimination of HCl at the stages  $k_2$  and  $k_4$ .

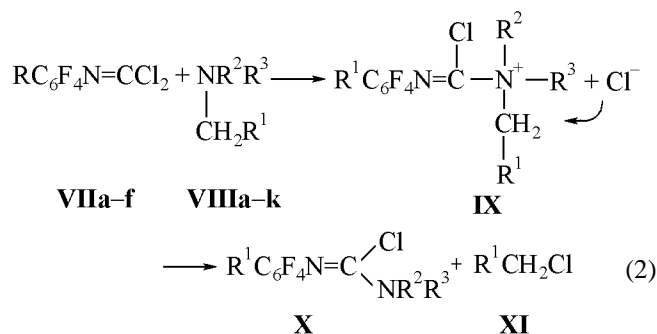
This opportunity is lacking in the reaction of dichlorides **I** with tertiary amines  $R_3N$ . The tertiary amines are known to serve as nucleophilic catalysts in hydrolysis [11] and alcoholysis [12] of *N*-arylcarbonimidoyl dichlorides. The limiting stage of these processes is a formation of quaternary ammonium salt  $[RN=C(Cl)-N^+R_3] \cdot Cl^-$  [12]. Quaternary salts of similar structure were isolated and characterized in reactions of imidoyl chlorides ( $R^1N=C(Cl)R^2$ ) with *N*-heterocyclic amines in aprotic media [13]; kinetics and mechanism of their formation was investigated (see review [4]). However the information on the reaction products obtained from carbonimidoyl dichlorides, in particular at the treatment with aliphatic tertiary amines is very scanty [2].

In the present study kinetics was investigated of reaction between *N*-polyfluorophenylcarbonimidoyl dichlorides  $RC_6F_4N=CCl_2$  [**VII**,  $R=4-CH_3$  (**a**),  $4-F$  (**b**),  $4-Br$  (**c**),  $4-CF_3$  (**d**),  $4-CN$  (**e**),  $4-NO_2$  (**f**)] with tertiary amines  $R^1R^2R^3N$  [**VIII**, trimethyl- (**a**), triethyl- (**b**), dimethylbenzyl- (**c**), dimethylbutyl- (**d**), diethylmethyl- (**e**), diethylisopropyl- (**f**), and diethylisobutylamines (**g**), *N*-methylmorpholine (**h**), *N*-ethylmorpholine (**i**), *N*-ethylpiperidine (**j**), diazabicyclooctane (**k**)] in acetonitrile [equation (2)].

In the  $^1H$  NMR spectrum of a mixture of *N*-pentafluorophenylcarbonimidoyl dichloride (**VIIb**) with



triethylamine (**VIIIb**) in  $\text{CD}_3\text{CN}$  (see EXPERIMENTAL) appeared two quartets at 4.2 and 3.7 ppm corresponding to the protons of the N-quaternized group in the intermediate product **IX** and to the protons of diethylamino group in chloroamidine **X** respectively. In the course of the reaction the intensity of the signal at 4.2 ppm first grows and then diminishes, and the intensity of the quartet at 3.7 ppm grows continuously. In 24 h when all triethylamine in the reaction mixture was consumed in the  $^1\text{H}$  NMR spectrum were revealed ethyl chloride (**XI**) signals (3.7 q, 1.47 t). Therefore the reaction of imidoyl dichlorides **VII** with tertiary amines **VIII** can be described as including two consecutive stages, as follows.

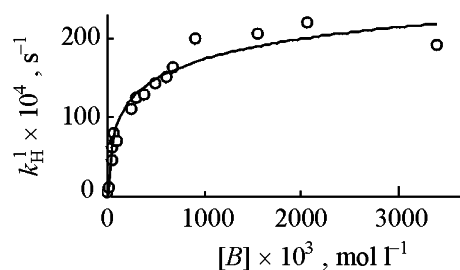


The kinetics of reaction between dichlorides **VII** and amines **VIII** was studied in excess amine:  $[\text{VIII}] \gg [\text{VII}] \sim 10^{-6} \text{ mol l}^{-1}$ . The reaction rate was measured by conductometric method as in the previously studied reactions with primary and secondary amines [5, 8]. Since according to Scheme 2 a ionic product forms only in the first stage, the use of the conductometric measurements makes possible to evaluate just the rate of this stage. Under the conditions of kinetic experiments the rate of conversion of the quaternary salt **IX** into non-ionic products **X** and **XI** may be neglected.

In all cases the apparent pseudofirst order rate constants  $k^1$  are constant in the course of the process and independent of imidoyl dichloride **VII** concentration indicating that in the given concentration range the reaction is first order with respect to substrate. As a rule the values  $k^1$  are proportional to amine concentration evidencing that reaction is also first order in amine. Thus for the majority of tertiary amines the kinetics is similar to that observed for primary and secondary amines [5, 8]. However sometimes (see Fig. 1) the linear relation " $k^1 - [B]$ " (where  $[B]$  is molar concentration of tertiary amine) is violated. We will discuss this phenomenon later.

In Table 1 are listed second-order rate constants ( $k^2$ ) for reaction of dichloride **VIIb** with tertiary amines **VIII** calculated proceeding from the linear parts of relations " $k^1 - [B]$ ". The effect on the reaction rate of amine structure is fairly described by Taft equation modified by Bogatkov, Popov, and Litvinenko [16]:

$$\log k^2 = (5.67 \pm 0.36) - (2.75 \pm 0.66 \Sigma \sigma^* + (1.95 \pm 0.13) E_N, \quad (3) \\
 r \ 0.975, \ S_0 \ 0.358, \ n \ 9,$$



**Fig. 1.** Apparent rate constant of pseudofirst order  $k_{\text{app}}^1$  for reaction of *N*-pentafluorophenylcarbonimidoyl dichloride with triethylamine as a function of the nucleophile concentration  $[B]$ , acetonitrile,  $25^\circ\text{C}$ .

**Table 1.** Second-order rate constants  $k^2$  for reaction of N-pentafluorophenylcarbonimidoyl dichloride (**VIIIb**) with tertiary amines **VIIIa-k** (acetonitrile, 25°C)

Amine	Range of amine concentration: [ <b>VIII</b> ] × 10 <sup>4</sup> , mol l <sup>-1</sup>	$k^2$ , 1 mol <sup>-1</sup> s <sup>-1</sup>	$n^a$	$\Sigma\sigma^*$ [14]	$-E_N$ [15]
<b>VIIIa</b>	0.0292...3.28	465 ± 20	7	0.0	1.54
<b>VIIIb</b>	56.6...3900	0.110 ± 0.006	31	-0.3	3.80
<b>VIIIc</b>	18.7...502	4.08 ± 0.12	21	0.215	2.23
<b>VIII d</b>	1.19...18.6	34.9 ± 1.3	7	-0.13	2.2
<b>VIII e</b>	25.2...111	1.07 ± 0.17	3	-0.20	3.0
<b>VIII f</b>	40.6...9340	0.0380 ± 0.0005	10	-0.38	-
<b>VIII g</b>	224...3150	0.0164 ± 0.0004	7	-0.325	-
<b>VIII h</b>	240...3050	0.704 ± 0.020	5	0.67 [15] (0.13) <sup>b</sup>	3.0
<b>VIII i</b>	503...10510	0.0179 ± 0.0017	4	0.57 [15] (0.03) <sup>b</sup>	3.5
<b>VIII j</b>	189...2570	0.260 ± 0.006	7	-0.28 [15]	3.5
<b>VIII k</b>	0.0956...0.307	3200 ± 120	5	0.39 [15] (-0.15) <sup>b</sup>	1.3

<sup>a</sup>  $n$  is the overall number of points. <sup>b</sup> Estimated  $\Sigma\sigma^*$  applied in this study for calculations along equation (3), (see text).

**Table 2.** Second-order rate constants  $k^2$  and first order one  $k_{lim}$  for reaction 4-substituted polyfluorophenylcarbonimidoyl dichlorides (**VIIa-f**) with tertiary amines (**VIIIb**) and dimethylbenzylamine (**VIIIc**) (acetonitrile, 25°C)

Compd. no.	R	$\sigma$ [14]	<b>VIIIb</b>		<b>VIIIc</b>
			$k^2 \times 10^2$ , 1 mol <sup>-1</sup> s <sup>-1</sup>	$k_{lim} \times 10^2$ , s <sup>-1</sup>	$k^2$ , 1 mol <sup>-1</sup> s <sup>-1</sup>
<b>VIIa</b>	4-CH <sub>3</sub>	-0.17	1.59 ± 0.14	1.39 ± 0.10	1.67 ± 0.03
<b>VIIb</b>	4-F	0.062	11 ± 0.6	2.23 ± 0.20	4.08 ± 0.12
<b>VIIc</b>	4-Br	0.232	11 ± 0.3	7.0 ± 2.0	9.67 ± 0.25
<b>VII d</b>	4-CF <sub>3</sub>	0.54	44 ± 4	65 ± 1	37.4 ± 1.3
<b>VII e</b>	4-CN	0.66 (0.89) <sup>a</sup>	66 ± 2	31 ± 14	125 ± 12
<b>VII f</b>	4-NO <sub>2</sub>	0.778 (1.25) <sup>a</sup>	81 ± 4	31 ± 5	102 ± 6

<sup>a</sup> The values of  $\sigma$  are given in parantheses. [18].

where  $\Sigma\sigma^*$  characterizes the inductive effect of substituents R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> at the nitrogen, and  $E_N$  is the steric constant of the amine; the factors before these variables characterize the sensitivity of the reaction to the inductive and steric effect respectively. The data of Table 1 for amines **VIII f** and **VIII g** are excluded from the correlation because the corresponding  $E_N$  data are lacking. In calculations by equation (3) the values  $\Sigma\sigma^*$  used for heterocyclic amines **VIII h, i, k** (see Table 1, in parentheses) were reduced by 0.54 compared with the published data [15]. This approach was justified for morpholine [5, 17] and proved to be efficient for tertiary amines. Evidently the increased nucleophilicity of morpholines (and diazacyclooctane) is caused by intramolecular (transannular) interaction of two heteroatoms.

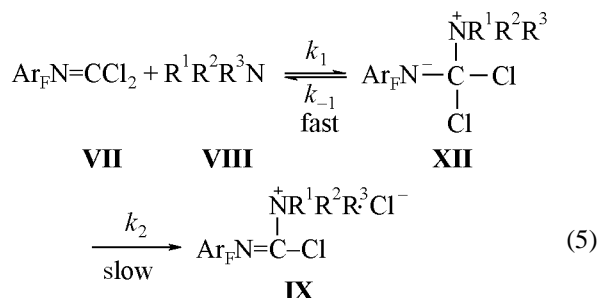
The corresponding correlation equation describing the combined effect of the structure of primary and

secondary amines in reaction with the same substrate has the following correlation parameters [8]:

$$\log k^2 = (7.35 \pm 0.34) - (5.09 \pm 0.33)\Sigma\sigma^* + (2.03 \pm 0.12)E_N, \quad (4)$$

$r$  0.983,  $S_o$  0.315,  $n$  14.

Our attention is engaged by the essentially smaller values of  $\log k_o^2$  and  $\rho^*$  in the reaction of tertiary amines as compared to that of primary and secondary amines. It was already noted that in the latter case a mechanism was substantiated consisting in addition-elimination with a limiting stage  $k_1$  in Scheme 1. The mentioned lower reactivity of the tertiary amines compared to primary and secondary ones (at equal  $\Sigma\sigma^*$  and  $E_N$ ) within the framework of the common mechanism of all the three amine classes may be attributed to the changed limiting stage of the reaction:  $k_2 \gg k_{-1}$  for primary and secondary amines (Scheme 1) and  $k_2 \ll k_{-1}$  for tertiary amines (Scheme 5):



Applying the method of stationary concentrations and taking into consideration the mass balance with respect to tetrahedral intermediate **XII** of Scheme 5 we obtain the following expression for  $k^l$ :

$$k^l = \frac{k_1 k_2 [B]}{k_{-1} + k_2 + k_1 [B]} \quad (6)$$

The dependence of  $k^l$  on amine concentration  $[B]$  predicted by equation (6) will be linear with the constraint  $k_{-1} + k_2 \gg k_1 [B]$ :

$$k^l = \frac{k_1 k_2}{k_{-1} + k_2} k_1 [B] = k^2 [B], \quad (7)$$

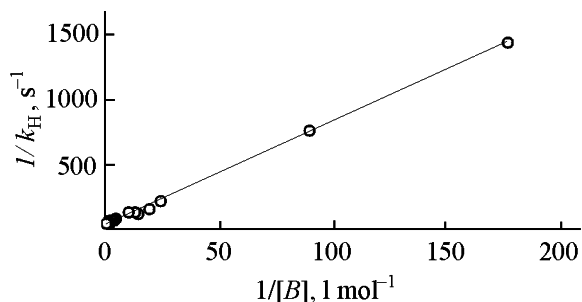
where  $k^2 = k_1 k_2 / (k_{-1} + k_2)$ ; if  $k_{-1} \gg k_2$ , then  $k^2 = K_1^* k_2$ , where  $K_1^* = k_1 / k_{-1}$ .

In the general case the dependence of  $k^l$  on amine concentration would be curvilinear. The limiting value of  $k^l$  designated hereinafter as  $k_{\text{lim}}$  is realized under condition  $(k_{-1} + k_2) \ll k_1 [B]$ . In order to estimate this value the expression (6) is transformed in reciprocal coordinates:

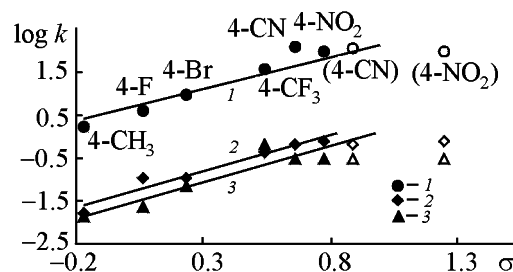
$$\frac{1}{k^l} = \frac{1}{k_2} + \frac{1}{k^2} \cdot \frac{1}{[B]} \quad (8)$$

Here the constant  $k_2$  plays the role of  $k_{\text{lim}}$ . The curvilinear  $k^l$  as a function of amine concentration is actually observed for three amines, **VIIIb**, **f**, **g** (see an example in Fig. 1). This curve can be linearized in the coordinates of equation (8) as shows Fig. 2. It is probable that such form of dependence (6) would have been observed with all the other amines if the reaction rate would be studied at higher concentration than that listed in Table 1. However it is difficult to perform for the reaction rates are too high.

If the outlined version is true then the values  $k_{\text{lim}}$  ( $k_2$ ) estimated by equation (8) characterize the unimolecular decomposition of intermediate **XII** in Scheme 5, and the values  $k^l$  listed in Table 1 in a sense correspond to combination of constants  $k_1 k_2 / (k_{-1} + k_2)$  or in a simpler case  $(k_{-1} \gg k_2)$  to a product  $K_1^* k_2$ , where  $K_1^*$  is the equilibrium constant of intermediate **XII** formation.



**Fig. 2.** Reciprocal values of rate constants of pseudofirst order  $1/k_{\text{app}}^l$  in reaction of *N*-pentafluorocarbonimidoyl dichloride with triethylamine as a function of reciprocal amine concentration  $1/[B]$ , acetonitrile, 25°C.



**Fig. 3.** Values of  $\log k^2$  (1, 2),  $\log k_{\text{lim}}$  (3) as functions of Hammett's  $\sigma$  constants for reaction of 4-substituted polyfluorophenylcarbonimidoyl dichlorides **VII** with dimethylbenzylamine (**VIIIc**) (1) and triethylamine (**VIIIb**) (2, 3) (acetonitrile, 25°C).

For the reaction of *N*-pentafluorophenylcarbonimidoyl dichloride (**VIIb**) with the three above amines the  $k_{\text{lim}}$  values are as follows:

Amine	<b>VIIIb</b>	<b>VIIIc</b>	<b>VIIIg</b>
$k_{\text{lim}} \times 10^3, \text{ s}^{-1}$	$22.3 \pm 2.1$	$3.16 \pm 0.08$	$3.34 \pm 0.17$
$K_1^*, \text{ l mol}^{-1}$	$4.9 \pm 3.1$	$12.0 \pm 0.4$	$4.9 \pm 0.4$

As seen, the values  $K_1^*$  estimated from the approximate expression  $k^2 = K_1^* k_{\text{lim}}$  are of relatively small absolute magnitude. It is clear that a significant amine excess is required for the accumulation of intermediate **XII** to become kinetically meaningful.

In order to support the above stated assumption that the stage  $k_2$  in Scheme 5 is rate-determining we studied the effect of substituent R in imidoyl dichlorides **VII** on the value of  $k^2$  in reaction with triethylamine (**VIIIb**) and dimethylbenzylamine (**VIIIc**), and also on the value of  $k_{\text{lim}}$  in reaction with triethylamine (Table 2). The effect of R substituents on the bimolecular rate constant  $k^2$  in reaction of

amine **VIIIc** with four dichlorides (**VII**, 4-R = CH<sub>3</sub>, F, Br, CF<sub>3</sub>) fits to Hammett's equation with excellent statistical parameters:

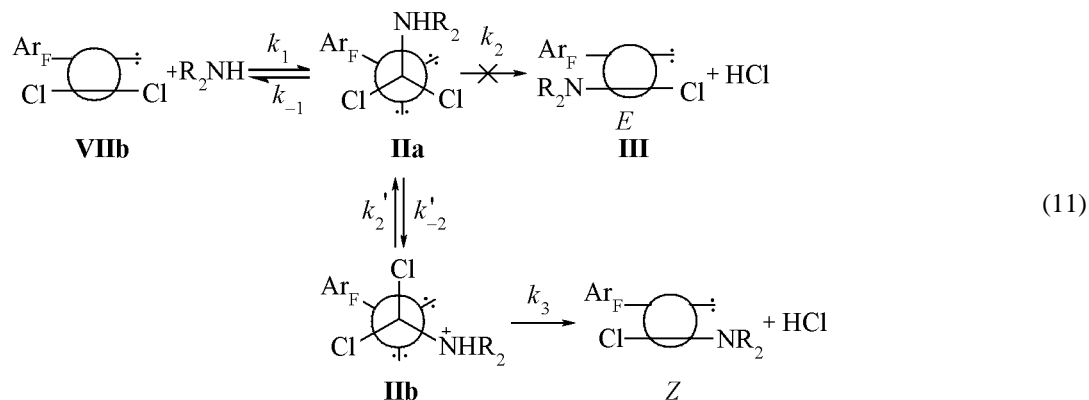
$$\log k^2 = (-1.47 \pm 0.02) + (1.91 \pm 0.06)\sigma \quad (9)$$

$r$  0.999  $s_0$  0.03  $n$  4

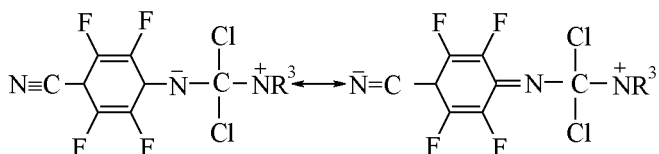
The point for R = CN fits well into correlation (9) if instead of Hammett's  $\sigma$  equal to 0.66 [1, 18] is used the value  $\sigma^-$  0.89 [18] (see Fig. 3, 1):

$$\log k^2 = (-1.46 \pm 0.03) + (1.80 \pm 0.06)\sigma \quad (10)$$

$r$  0.998  $s_0$  0.053  $n$  5.



This means that a significant contribution to transmission of the electronic effect of the substituent provides an effect of direct polar conjugation resulting in stabilization of the tetrahedral intermediate:



4-Nitro group also should possess a similar effect ( $\sigma^- + 1.25$  [18]). However it significantly falls out from the correlation (10) (see Fig. 3, 1). The cause of this deviation will be discussed further.

A positive sign of  $\rho$  in correlation (10) or (9) is expectable and in a good agreement with the published data on  $\rho$  values for bimolecular reactions of various imidoyl chlorides with nucleophiles [4]. It should be noted that in this reaction series no saturation of rate was observed with increasing amine **VIIIc** concentration.

The effect of substituents on  $k^2$  and  $k_{\text{lim}}$  values for dichlorides **VII** reactions with triethylamine (**VIIIb**) is more complicated (Fig. 3, 2, 3), and for six substituents basically cannot be described with Hammett equation. The qualitative pattern of  $k^2$  and  $k_{\text{lim}}$  dependence on  $\sigma$  is in general analogous. For four substituents (4-CH<sub>3</sub>, 4-F, 4-Br, 4-CF<sub>3</sub>) the trend in substituent effect coincides, and corresponds to the positive  $\rho$ . But with electron-withdrawing substituents (4-CN and 4-NO<sub>2</sub>) the sensitivity of the rate constant  $k^2$  to the R substituent effect sharply diminishes ( $\rho^- \sim 0$ ) even when are used values  $\sigma_{\text{CN}}$

0.66 and  $\sigma_{\text{NO}_2}$  0.78 and not  $\sigma_{\text{CN}}^-$  0.89 and  $\sigma_{\text{NO}_2}^-$  1.25 (Fig. 3, 2). And for the process described with  $k_{\text{lim}}$  it is possible to mark the change of  $\rho$  sign ( $\rho^- < 0$ ). It was already mentioned that a notable decrease in sensitivity of rate constant  $k^2$  to the influence of R was also observed in reaction of amine **VIIIc** with a substrate containing 4-NO<sub>2</sub> substituent (Fig. 3, 1). Such character of influence of substituent R in substrate does not agree with a mechanism of addition-elimination (Scheme 5) with a limiting stage of tetrahedral intermediate decomposition ( $k_2$ ).

This inconsistency may be apparently removed remaining in the framework of a unique mechanism for reactions of primary, secondary, and tertiary amines if a formation is assumed on the reaction coordinate of one more intermediate similar in structure to intermediate **XII** in Scheme 5 or intermediate **II** in Scheme 1 but unlike the final product. This assumption is built on the stereochemical result of the aminolysis of *N*-pentafluorophenylcarbonimidoyl dichloride (**VIIb**) with dibenzylamine in acetonitrile [19].

It was established that the arising chloroformamidine (**III**), R = C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>) had Z and not E-configuration (Scheme 11).

Quantum-chemical calculations of chloroformamidine (**III**, R = C<sub>2</sub>H<sub>5</sub>) showed that the Z-isomer is thermodynamically more favored [19]. Thus the observed stereochemical result is due to a thermodynamic control. A thermodynamic control of substitution stereochemistry was also observed in arylaminolysis of *N*-benzenesulfonylbenzimidoyl chloride [PhSO<sub>2</sub>N=C(Cl)Ph] in acetonitrile where as a limiting stage was postulated the decomposition of a tetra-

hedral intermediate [20]. This explanation of the stereochemical result assumes in its turn that in the intermediate **IIa** an internal rotation is possible providing the thermodynamically more stable configuration **IIb** whence *Z*-isomer forms in the stage  $k_3$  (Scheme 11) ensuring the thermodynamic control [19]. In this case either stage  $k'_2$  or  $k_3$  may be the limiting one.

Applying to Scheme 11 the method of stationary concentration and taking into account the mass balance for the intermediate products **IIa** and **IIb** we obtain the following expression for the rate constant of the pseudofirst order:

$$k^1 = \frac{k_1 k'_2 k_3 [B]}{(k_{-1} + k'_2)(k_{-2} + k_3) + k_1(k'_2 + k_{-2} + k_3)[B]} \quad (12)$$

It follows from this equation that to the linear part of the relation of  $k^1$  to  $[B]$  corresponds the following expression for the second order rate constant:

$$k^2 = \frac{k_1 k'_2 k_3}{(k_{-1} + k'_2)(k_{-2} + k_3)} \quad (13)$$

and equation (14) for the limiting value of the pseudo-first order rate constant:

$$k_{\text{lim}} = \frac{k'_2 k_3}{(k'_2 + k_{-2} + k_3)} \quad (14)$$

As seen, the value  $k^2$  is a combination of five constants corresponding to individual stages, and  $k_{\text{lim}}$  is a combination of three constants. This is a quite sufficient reason to expect that the principle of linearity of free energies might not be valid in the total range of  $\sigma$  variation, at least with respect to  $k^2$ .

However simpler versions of equations (13) and (14) are also possible providing the rate-determining stage is either the stereomutation of intermediate **IIa** [stage  $k'_2$  in Scheme 11] or the decomposition of intermediate **IIb** to the final product (stage  $k_3$ ).

If  $k_3 \gg k'_{-2}$ , then

$$k^2 = \frac{k_1 k'_2}{k_{-1} + k'_2} \quad (15)$$

The result is similar to that obtained in analysis of Scheme 5, but it means that the rate-determining stage is not the transformation of the primarily formed intermediate into the reaction products, but its stereomutation into the more thermodynamically stable form **IIb**. And when an additional constraint  $k'_2 \gg k_{-1}$  is valid then the rate-determining stage is

the amine attack on the substrate, i.e.  $k^2 = k_1$ . This is the case in the reactions of primary and secondary amines [5, 8], as has been already mentioned before. Under additional constraint  $k'_2 \ll k_{-1}$  an expression  $k^2 = K_1^* k'_2$  is valid. Under these conditions the value  $k_{\text{lim}}$  is numerically equal to  $k'_2$ :

$$k_{\text{lim}} = k'_2 \quad (16)$$

In a reversed situation when  $k_3 \ll k'_{-2}$  and  $k'_2$  the  $k^2$  is expressed by an equation

$$k^2 = \frac{k_1 k_3}{k_{-1} + k'_2} \quad (17)$$

and  $k_{\text{lim}}$  by an equation

$$k_{\text{lim}} = \frac{k'_2 k_3}{k_2 + k'_{-2}} = \frac{k_3}{1 + K_3^*} \quad (18)$$

where  $K_2^*$  is an equilibrium constant of stereomutation.

From the viewpoint of the above reasoning the influence of substituents R contained in the substrate on the processes described by the constants  $k^2$  and  $k_{\text{lim}}$  may be interpreted as follows. In reaction of carbonylimidoyl dichlorides (**VII**, 4-R = CH<sub>3</sub>, F, Br, CF<sub>3</sub>) with amines **VIIIb** and **VIIIc**\* the rate-determining stage is the stereomutation of intermediate **IIa** into **IIb** (stage  $k'_2$ ). In this case the constant  $k^2$  is determined by equation (15), and the constant  $k_{\text{lim}}$  by equation (16). The estimation of parameter  $\rho$  from three substituents\*\* (4-R = CH<sub>3</sub>, Br, CF<sub>3</sub>) for the bimolecular reaction with triethylamine ( $k^2$ ) gives a value of  $2.03 \pm 0.04$  which is close to that for the reaction with dimethylbenzylamine **VIIIc** [see  $\rho$  in equation (9)].

The estimation of  $\rho$  parameter for rate constant of the unimolecular reaction ( $k_{\text{lim}} = k'_2$ ) using the same points gave the value  $2.32 \pm 0.38$ . The positive  $\rho$  means here that the stereomutation ( $k'_2$ ) is facilitated by electron-withdrawing substituents, and the sensitivity to this effect is of the same order of magnitude as observed in the stage of nucleophilic attack (cf. with  $\rho$  value for the stage  $k_1$  in reaction of substrates **VIIa-f** with dibenzylamine in acetonitrile at 25°C that is equal to 2.11 [5]). Since from the above reasoning follows that in the simplest case  $k^2 = K_1^* k'_2$ , it is possible for reaction of dichlorides **VIIa-d** with triethylamine to make a rough estimation of the value  $\rho_1^*$  for the equilibrium of the intermediate formation:  $\rho_1^* \approx -0.5$ .

\* In the case of this amine to the series of R in parentheses should be added R = CN.

\*\* The point for 4-F-substituent strongly deviates from Hammett's correlation by obvious reasons (Fig. 3, 2).

**Table 3.** Rate constants of second order  $k^2$  and first order  $k_{\text{lim}}$  of reaction between *N*-pentafluorophenylcarbonimidoyl dichloride and triethylamine in acetonitrile at various temperatures

<i>T</i> , K	Range of amine concentrations, [B] × 10 <sup>3</sup> , mol l <sup>-1</sup>	$k^2 \times 10^2$ , l mol <sup>-1</sup> s <sup>-1</sup>	$k_{\text{lim}} \times 10^{-2}$ , s <sup>-1</sup>
298	5.66...3410	1.0 ± 1.0	2.2 ± 0.2
308	4.02...3400	15.0 ± 0.7	3.3 ± 0.7
318	4.88...3210	25.0 ± 1.0	6.3 ± 0.9
328	5.88...3020	26.0 ± 2.0	8.6 ± 0.9

With growing acceptor character of substituents (4-R = CN, NO<sub>2</sub>) the stage ( $k_3$ ) in Scheme 11 becomes rate-determining:  $k^2$  is described by equations (13) or (17), and  $k_{\text{lim}}$  by equations (14) or (18). Since in all the above equations the rate constant  $k_3$  is present characterizing the unimolecular decomposition of intermediate **Ib** (with negative  $\rho$ ), this fact will necessarily result in diminishing of  $\rho$  value at attempts to build up Hammett's correlations for the rate constants  $k^2$  and  $k_{\text{lim}}$  till  $\rho$  with a negative sign would be obtained as has been actually shown by an example of  $k_{\text{lim}}$  (Fig. 3, 3).

In Table 3 are compiled the data on the temperature effect in reaction of *N*-pentafluorophenylcarbonimidoyl dichloride (**VIb**) with triethylamine (**VIIIb**) on the processes described with the rate constants  $k^2$  and  $k_{\text{lim}}$ . The above reasoning indicates that in this  $\sigma$  range at 25°C (see Fig. 3, 2 and 3) are likely valid expressions (15) and (16) for  $k^2$  and  $k_{\text{lim}}$  respectively.

In the temperature range studied both data for  $k^2$  and  $k_{\text{lim}}$  are well consistent with Arrhenius equation.

$$\log k^2 = (4.33 + 0.46) - (1.57 + 0.14) \cdot 1/T \quad (19)$$

$$\log k_{\text{lim}} = \log k_2' = (5.08 + 0.40) - (2.01 + 0.13) \cdot 1/T \quad (20)$$

From parameters of equations (19) and (20) the activation energy ( $E_A$ ), enthalpy ( $\Delta H^\ddagger$ ), and entropy ( $\Delta S^\ddagger$ ) were estimated for the processes described with rate constants  $k^2$  and  $k_2'$ .

Process	$E_A$ , kJ mol <sup>-1</sup>	$\Delta H^\ddagger$ , ( $\Delta H^*$ ) kJ mol <sup>-1</sup>	$-\Delta S^\ddagger$ ( $-\Delta S^*$ ), J mol <sup>-1</sup> deg <sup>-1</sup>
$k^2$	30.0 ± 2.7	27.5 ± 2.5	170 ± 18
$k_2'$	38.5 ± 2.4	36.0 ± 2.2	156 ± 12
$K_1'$	-	-8.5 ± 3.4	14.0 ± 24

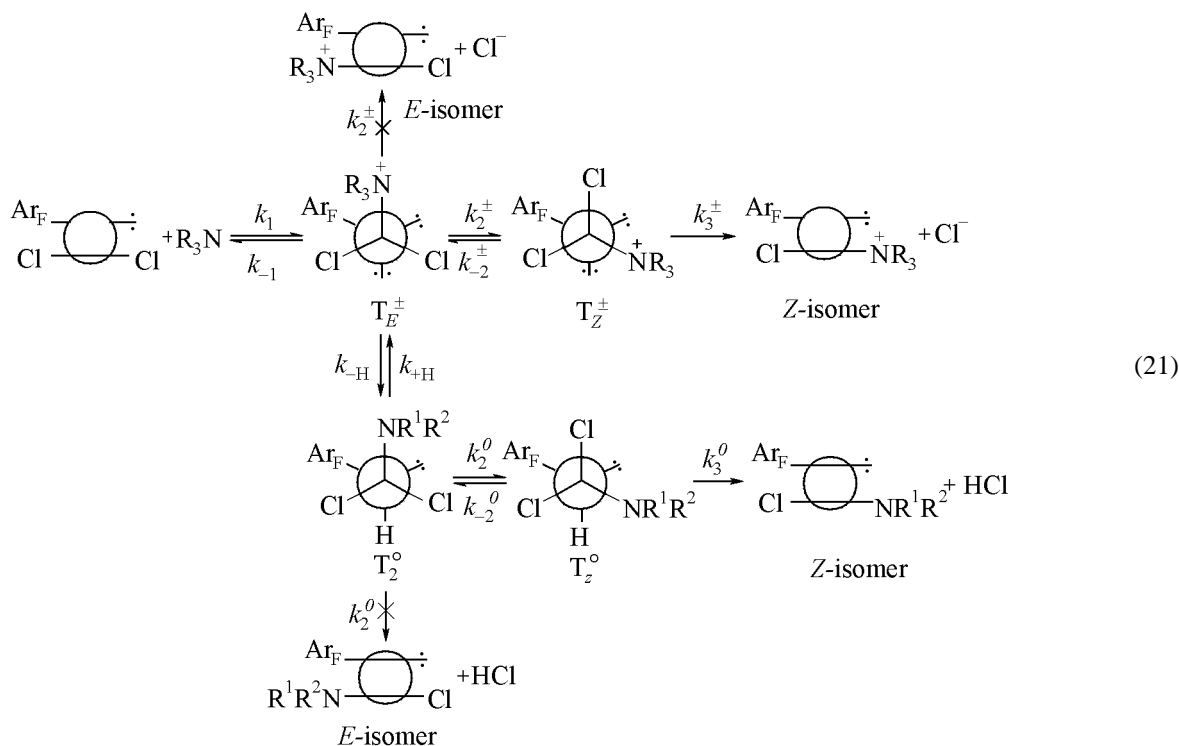
Since the  $k^2$  value is a combination of rate constants the calculated  $E_A$ ,  $\Delta H^\ddagger$ , and  $\Delta S^\ddagger$  also include the corresponding parameters of the individual stages. In the simplest case  $k^2 = K_1' k_2'$ . Therefore being in possession of  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  values for stereomutation stage ( $k_2'$ ) we were able to calculate the enthalpy ( $\Delta H^*$ ) and entropy ( $\Delta S^*$ ) of intermediate **Ia** formation in Scheme 11.

As seen, these figures should be regarded as rough estimation for the calculation errors would be necessarily high\*. Nonetheless, it is possible to state that the negative sign at  $\Delta H^*$  evidences the exothermic character of the formation equilibrium of intermediate  $T_E^*$  (see further Scheme 21). The latter process occurs virtually without entropy change ( $\Delta S^*$  is a statistical zero).

Summing up the data of this study and those from [5, 8] it is possible to build up a general scheme of replacement mechanism of the first chlorine atom in the *N*-substituted carbonimidoyl dichlorides by primary, secondary, and tertiary amines (Scheme 21) where in the general case  $R_3N = R^1R^2R^3N$ .

The difference between tertiary amines on the one hand and primary and secondary amines on the other hand consists in the existence of the tetrahedral intermediate in the former case only in a zwitter-ionic form  $T^\pm$ , and in the latter in the thermodynamically more stable neutral form  $T^0$  forming from the  $T^\pm$  through a fast proton transfer. This fact is decisive for the relative ratio of individual stages rates providing the same stereochemical result. In the charged intermediate  $T^\pm$  (with tertiary amines) the stereomutation of the primarily arising intermediate  $T_E^\pm$  into  $T_Z^\pm$  form occurs (all other factors being equal) significantly slower than the stereomutation of the neutral intermediate  $T_E^0$  into  $T^0$  (with primary and secondary amines). In the other words, the proton transfer in the intermediate makes all stages after  $k_1$  more energetically favorable. Therefore in reactions with primary and secondary amines the kinetic behavior follows a single pattern with rate-determining stage  $k_1$  disregarding the structure of amine or substrate. In contrast, for reactions with tertiary amines the stages  $k_2^\pm$  ( $k_{-2}^\pm$ ) and  $k_3^\pm$  are more significant from the energy viewpoint than  $k_1$ , and thus at certain reagents structure they become rate-determining.

\* Absolute value of errors in  $\Delta H^*$  and  $\Delta S^*$  were calculated as in [21].



## EXPERIMENTAL

$^1\text{H}$  NMR spectra were registered on spectrometers Gemini 200 (200 MHz) and Tesla BS467 (60 MHz).

The preparation of carbonimidoyl dichlorides was described in [1, 22].

The triethylamine was heated with *p*-toluenesulfonyl chlorides (about 5 wt%) for several hours, then it was twice distilled and the middle fraction was separated. The latter was refluxed for several hours over sodium metal and then distilled on a column 40 cm long separating the fraction of bp 89–89.5°C (publ. bp 89.5°C). In going to a new portion of triethylamine several kinetic measurements were performed for reaction with *N*-pentafluorophenylcarbonimidoyl dichloride in acetonitrile at 25°C (the most thoroughly studied reaction). If the results obtained did not fit to the previous data the purification was repeated.

Amines **VIIIc–j** were purified by the same procedure as triethylamine. Their boiling points were consistent with the published data.

Trimethylamine was obtained from its hydrochloride by treating with aqueous alkali, and it was collected as a solution in acetonitrile. To this solution

*p*-toluenesulfonyl chloride was added in amount of 3–5 wt% with respect to amine, and the mixture was kept for several hours. Then the mixture was heated in a flask with a reflux condenser, and the liberated trimethylamine was passed through a column packed with solid potassium hydroxide and was absorbed by acetonitrile. The concentration of the solution obtained was measured by acid–base titration. The working solutions were prepared by dilution.

1,4-Diazabicyclo[2,2,2]octane was sublimed in a vacuum from metallic sodium and immediately after sublimation it was dissolved in acetonitrile. The concentration of the solution obtained was measured by acid–base titration. The working solutions were prepared by dilution.

The acetonitrile for kinetic measurements was twice subjected to rectification on a column over phosphorus pentoxide and over freshly calcined potassium carbonate with separating the middle fraction. The electroconductivity of such solvent was no more than  $1 \times 10^{-6}$  Ohm  $\text{m}^{-1}$ .

**Reaction of *N*-pentafluorophenylcarbonimidoyl dichloride with triethylamine (preparative run).** To a solution of 0.6 g (2.3 mmol) of *N*-pentafluorophenylcarbonimidoyl dichloride in 3 ml of anhydrous



ether was added at stirring 0.92 g (9.1 mmol) of triethylamine in 3 ml of ether. The mixture was stirred at room temperature for 6 h. The precipitate was separated, the filtrate was evaporated. The residue was distilled in a vacuum (138–139°C at 10 mm Hg). We obtained 0.62 g (90%) of *N,N*-diethyl-*N*-pentafluorophenylchloroformamidine. The characteristics of the compound coincide with those published in [5].

**Reaction of *N*-pentafluorophenylcarbonimidoyl dichloride with triethylamine** ( $^1\text{H}$  NMR experiment). Dry deuteroacetonitrile used in the run was obtained by distillation of  $\text{CD}_3\text{CN}$  over phosphorus pentoxide in a distillation device dried for 4 h at 180°C in a drying cabinet just before use. The spectrum of thus prepared solvent contains only the signal from the residual protons of the methyl group. Into a freshly heated NMR tube was charged 0.140 g (0.54 mmol) of *N*-pentafluorophenylcarbonimidoyl dichloride and 0.4 ml of deuteroacetonitrile. The mixture was frozen in the liquid nitrogen, and 0.07 ml (0.05 g, 0.5 mmol) of triethylamine was added. The ampule was cautiously warmed till the lower layer melted, and then the mixture was stirred and became light-brown. Then the ampule was frozen again and it warmed already in the probe of the NMR spectrometer. Beside the resonances belonging to triethylamine (1.0 t and 2.6 q ppm) in the spectrum appears a signal from imidoilammonium salt (4.2 ppm q) and a lot more weak signal from chloroformamidine (3.7 ppm q). The upfield part of the spectrum is overlapped with stronger signals of triethylamine. The intensity of imidoilammonium salt resonance grew within 1 h, and then diminished; the intensity of chloroformamidine signal steadily increased. In 3 days in the mixture only signals of chloroformamidine (1.25 t, 3.7 q ppm) and those of ethyl chloride (1.47 t, 3.7 q ppm) were registered.

The procedure used in kinetic measurements was described before [23].

#### REFERENCES

- Savchenko, T.I., Kolesnikova, I.V., Petrova, T.D., and Platonov, V.E., *J. Fluor. Chem.*, 1983, vol. 22, p. 439.
- Petrova, T.D. and Platonov, V.E., *Usp. Khim.*, 1988, vol. 57, p. 405.
- Kolesnikova, I.V., Petrova, T.D., Platonov, V.E., Mikhailov, V.A., Popov, A.A., and Savelova, V.A., *J. Fluor. Chem.*, 1988, vol. 40, p. 217.
- Savelova, V.A. and Popov, A.F., *Zh. Org. Khim.*, 1999, vol. 35, p. 821.
- Mikhailov, V.A., Kolesnikova, I.V., Popov, A.A., Petrova, T.D., Platonov, V.E., and Savelova, V.A., *Zh. Org. Khim.*, 1989, vol. 25, p. 1030.
- Hegarty, A.F. and Digman, K.J., *J. Chem. Soc., Perkin Trans., II*, 1975, p. 1046.
- Bacaloglu, R. and Korodi, T., *Rev. Roum. Chim.*, 1979, vol. 24, p. 1165.
- Mikhailov, V.A., Popov, A.A., Savelova, V.A., Kolesnikova, I.V., Petrova, T.G., and Platonov, V.E., *Zh. Org. Khim.*, 1989, vol. 25, p. 1683.
- Kolesnikova, I.V., Petrova, T.D., Platonov, V.E., Ryabicheva, T.G., Mikhailov, V.A., Popov, A.A., and Savelova, V.A., *Zh. Org. Khim.*, 1989, vol. 25, p. 1689.
- Korodi, T. and Bacaloglu, R., *Bul. Sti. Sitehn. Inst., politehn. Timisoara, Ser. Chim.*, 1979, vol. 24, p. 84; *Ref. Zh. Khim.*, 1981, 21B963.
- Bacaloglu, R. and Korodi, T., Ostrogovich G., *Rev. Roum. Chim.*, 1979, vol. 24, p. 933.
- Bacaloglu, R., Korodi, T., Florescu, A., and Ostrogovich, G., *Rev. Roum. Chim.*, 1977, vol. 22, p. 877.
- Drizhd, L.P., Kryuchkova, E.N., Litvinenko, L.M., Savelova, V.A., and Chotii, K.Yu., *Ukr. Khim. Zh.*, 1984, vol. 50, p. 11948.
- Spravochnik khimika* (Chemist's Handbook), Moscow: Khimiya, 1964, vol. 3.
- Bogatkov, S.V., Belova, N.A., and Medved', S.S., *Reakts. Sposobn. Organ. Soedin.*, 1975, vol. 12, p. 267.
- Bogatkov, S.V., Popov, A.F., and Litvinenko, L.M., *Reakts. Sposobn. Organ. Soedin.*, 1969, vol. 6, p. 1011.
- Perepichka, I.F., Popov, A.F., Kostenko, L.I., and Piskunova, Zh.P., *Reakts. Sposobn. Organ. Soedin.*, 1986, vol. 33, p. 320.
- Gordon, A.J. and Ford, R.A., *The Chemist's Companion*, New York: Wiley, 1972.
- Mikhailov, V.A., Yufit, D.S., Balabanov, E.Yu., Struchkov, Yu.T., Popov, A.A., Savelova, V.A., Kolesnikova, I.V., Petrova, T.D., and Platonov, V.E., *J. Phys. Org. Chem.*, 1993, vol. 6, p. 319.
- Yufit, D.S., Struchkov, Yu.E., Mikhailov, V.A., Drizhd, L.P., and Savelova, V.A., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1988, p. 783.
- Kassandrova, O.N. and Lebedev, V.V., *Obrabotka rezul'tatov nablyudenii* (Processing of Measurements Results), Moscow: Nauka, 1970, p. 88.
- Savchenko, T.I., Petrova, T.D., Platonov, V.E., and Yakobson, G.G., *Zh. Org. Khim.*, 1979, vol. 15, p. 1018.
- Litvinenko, L.M., Mikhailov, V.A., Savelova, V.A., and Drizhd L.P., *Zh. Org. Khim.*, 1986, vol. 22, p. 2343.