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THE ACIDITY OF SOME ALIPHATIC AMMONIUM IONS
IN DIMETHYL SULFOXIDE

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The potentiometric titration with the solu -
tion of tetrabutylammonium hydroxide in dimethyl-
sulfoxide (DMSO) was used for the determination
of the acidity of several ammonium cations of the
general formula $X_1X_2X_3NH^+$, where X_1, X_2, and X_3
are (the corresponding pK_a values are given in
parenthesis): 1. H, H, H (10.74); 2. Me, H, H
(10.7); 3. H, Me, OH (7.3); 4. H, H, CH_2COOEt
(8.96); 5. H, H, MeO (5.6); 6. H, Me, MeO (7.3);
7. H, H, OH (7.60); 8. Me, Me, OH (4.91); 9. H ,
H, CF_3CH_2 (5.84); 10. H, H, NH_2 (10.1); 11. H ,
H, NH_3^+ (4.0); 12. Me, Me, H (10.21); 13. Et, Et,
H (10.2); 14. Me, Me, Me (8.5); 15. CH_2Ph ,
CH_2Ph, CH_2Ph (4.15); 16. Me, Me, CH_2CN (3.3) ;
17. Me, Me, CH_2Ph (7.35); 18. Me, Me, CH_2CH_2OH
(8.2); 19. Me, Me, CH_2COOEt (6.35); 20. H, H ,
1-adamantyl (11.16); 21. ⬡ (10.6); 22. gua-
nidinium-ion (15.8).

The measured and literature pK_a values were
compared with the corresponding data for aqueous
solution and the gas phase. It was shown that the
transfer of the given reaction series from DMSO
into water changes only relatively insignificant-
ly its sensitivity towards the substituent effects.

On the other hand, however, the substitution of DMSO as a solvent for the gas phase increases more than two times the range of the influence of structural effects on the acidity of the ammonium ions, $X_1X_2X_3NH^+$.

The reaction series of the acidic dissociation of the substituted aliphatic ammonium ions (i.e., the basicity of the aliphatic amines) is of considerable interest in deal - ing with several fundamental problems of physical organic chemistry. So, the relatively high sensitivity of this reaction series towards the substituent effects is a precondi - tion for using it as one of the reference reactions for the establishment in the LFER framework of the so called sub - stituent constants (e.g., the Taft's inductive σ^*-con - stants, etc.)[1].

On the other hand, the literature analysis shows[2] that by the number of the solvents involved, the acidic dissocia- tion of the aliphatic ammonium ions occurs to be one of the most seldom studied "everyday" fundamental reaction series. It has been rather thoroughly studied in water, in some aqueous-organic mixtures, and in the gase phase[3,4]. More or less representative set of data exists also for acetoni - trile[1,5], HMPTA[1], and nitromethane[1,6].

The very first studies of the acidity of aliphatic am- monium ions in DMSO were performed already about 20 years ago[7,8].

Nevertheless, the presently existing collection of the pK_a values for the cationic acids of the above-mentioned type is still quite unsystematic and rather limited (see Ref. 1 for further references and Refs. 7-12). This situa - tion actually initiated the present work which was aimed at studying the possibility to use the earlier[13,14] elaborated potentiometric technique also for the determination of the acidity constants of the substituted aliphatic ammonium ions in the DMSO medium.

Experimental

Reagents. DMSO, benzene and i-PrOH were purified as described in Refs. 13, 14. The solution of the titrant, i.e. the solution of Bu_4NOH in the mixture (1 : 4) of i-PrOH and benzene, was prepared as described earlier[14].

As a rule, the perchlorate salts of amines (prepared by the interaction[7] of the corresponding amine with the 20-40% perchloric acid in 30% aqueous alcohol or acetic acid) were used for the determination of their pK_a values. In the case of $MeONH_3^+$, $Me_2(OH)NH^+$, $Me(OH)NH_2^+$ and $H_2N = C(NH_2)_2^+$ the hydrochlorides ("Aldrich" or "Eastman") were used, whereas in the case of hydrazine dihydrochloride as well as hydrosul - fate were used. For the H_2NOH, hydrochloride was also used. In most cases the commercial samples of amines were used for the synthesis of their perchlorates.

The synthesis of Me_2NCH_2COOEt was performed at inten - sive cooling in the medium of anhydrous benzene by reacting dimethylamine with the ethyl ester of chloroacetic acid[15]. The product (the yield was 28.5% from the theoretical value) was boiled at 149-151° (760 Torr), and had n_D^{20} = 1.4169, d_4^{20} = 0.9280, MR = 35.54 (theoretical - 35.50).

$MeCOCH_2NMe_2$ was prepared by reacting chloroacetone with dimethylamine[16] either in aqueous solution or in anhydrous benzene. The yield of the amine was 7.4% from the theoreti - cal value, whereas b.p. was 120-123°C, n_D^{20} = 1.4140 (Litera - ture - 1.4135), d_4^{20} = 0.8609.

Me_2NCH_2CN was synthesized according to the scheme[17]:

$$Me_2NH + H_2CO + NaHSO_4 + KCN \rightleftharpoons Me_2NCH_2CN + KNaSO_3 + H_2O$$

Its b.p. was 134-137°C, n_D^{20} = 1.4150, d_4^{20} = 0.8674 and the yield was 33.5% from the theoretical value.

Me_2NCH_2Ph was prepared from $PhCH_2Br$ and Me_2NH in aque - ous solution. The amine had b.p. 73-76°C (at 15 Torr), n_D^{20} = 1.5031, d_4^{20} = 0.9123, the yield was 60% from the theoreti - cal value.

For the measurement of the pK_a values of the acidic substances in DMSO solution was used the potentiometric technique[13,14] which in the present case uses the titration of the solutions of perchlorates, hydrochlorides or hydro - sulfates of amines in DMSO with the solution of Bu_4NOH in the mixture of benzene with i-PrOH. A Radiometer A 2222B or NST glass electrodes filled up with mercury were used. The concentrations of the solution of ammonium salts were in the range from 0.001 to 0.008 mol/l, whereas the concentration of the titrant was $(2-5) \times 10^{-2}$ mol/l.

The calibration of the glass electrode was made using the pK_a values of benzoic acid $(11.0)^{18}$ and $2,6-(NO_2)_2C_6H_3OH$ $(4.9)^{18}$ as references. Within the experimental errors of determination the slope of the calibration plot p_aH vs. $\log a_H^+$ does not differ from the theoretical value (59.1).

Before each series of experiments every day the check of the proper functioning of the electrode system was under-taken by the repeated titration of the standard substance - benzoic acid.

In the case of $H_2NNH_2 \cdot 2HCl$ two jumps on the titration plot were observed which correspond to the consecutive eli-mination of two protons from two amino-groups by the ad - dition of the two equivalents of the basic titrant. The mea-sured values of $pK_{a(1)}$ (4.0) and $pK_{a(2)}$ (10.0) differ signi-ficantly, however somewhat less than in aqueous solution , from each other. It should be noticed that the $pK_{a(2)}$ value calculated from the titration curve for the two-fold proto-nated hydrazine, $H_2NNH_2 \cdot 2HCl$, and the same quantity, cal-culated from the direct titration of the monoprotonated form of the hydrazine $(H_2NNH_3 \cdot HSO_4$ or $H_2NNH_3^+Cl)$ coincide with each other.

On the titration curve of $HONH_2 \cdot HCl$ also two bendings corresponding to the addition of two equivalents of Bu_4NOH were observed, whereas $pK_{a(1)} = 7.60 \pm 0.06$ and $pK_{a(2)} = 14.8 \pm 0.1$. There is no doubt that the former of these quantities refers to the elimination of the proton from the NH_3^+ -group of the cationic acid, $HONH_3^+$. The second pK_a value, however, might refer to the process of the acidic

dissociation of the neutral hydroxylamine by the scheme:

$$H_2NOH \rightleftharpoons H_2NO^- + H^+$$

Probably, this conclusion should be taken with some caution because the determined $pK_{a(2)}$ value (14.8) is only by one pK_a unit higher than the only available pK_a value (13.7)[18] for the aqueous solution whereas for the most hydroxylic acids XOH the difference between the pK_a values for aqueous solution and DMSO amounts from 5 $((CF_3)_3COH)$[13,18] to 15 (H_2O)[18] units of pK_a.

For each cationic acid the titration was repeated 3-5 times. From the mean pK_a values for the individual runs the arithmetic mean pK_a values were calculated. The latter are listed in Table 1 alongside with their confidence inter - vals. For the comparison some available literature data on the acidity of ammonium ions in DMSO and in aqueous solu - tion is also included in the same Table.

Table 1

pK$_a$ Values for Some Aliphatic Ammonium Ions
$X_1X_2X_3NH^+$ in DMSO and H_2O at $25^\circ C$

Ammonium Ion, $X_1X_2X_3NH^+$	DMSO		pK_a, H_2O	$\Delta pK_a =$ $pK_{a(DMSO)} - pK_{a(H_2O)}$
	pK_a, This work	pK_a, Lite- rature		
1 2	3	4	5	6
X_1, X_2, X_3				
1. H, H, H,	10.74 ± 0.20	10.5^7; 10.4^7	9.25	1.5
2. Me, H, H	10.7 ± 0.1	11.0^{10}	10.62	0
3. Et, H, H	-	10.9^{10}	10.63	0.3
4. Pr, H, H	-	10.7^{10}	10.53	0.2
5. Bu, H, H	-	11.1^{12}	10.60	0.5
6. MeO, H, H	5.6 ± 0.09	-	4.60	1.0
7. MeO(CH$_2$)$_2$,H,H	-	$10.2^{10,12}$	9.4	0.8

Table 1 continued

1	2	3	4	5	6
8.	CF_3CH_2,H,H	5.84 ± 0.10	5.8^{12}	5.7	0
9.	$EtOOCCH_2$,H,H	8.96 ± 0.11	-	7.7	1.3
10.	cy-Hex, H, H	-	11.7^2	10.68	1.0
11.	H_2N, H, H	10.1 ± 0.1	-	8.60	1.5
12.	H_3N^+, H, H	4.0 ± 0.05	-	-0.67	4.7
13.	HO, H, H	7.60 ± 0.06	-	5.96	2.6
14.	1-Ad, H, H	11.16 ± 0.04	-	-	-
15.	Ph, H,H	-	$3.6^{7,9}$; 3.7^8	4.60	-1
16.	Me, Me, H	10.21 ± 0.05	10.3^{10}	10.77	-0.6
17.	Et, Et, H	10.2 ± 0.1	10.5^7	10.93	-0.7
18.	Pr, Pr, H	-	10.1^9	11.0	-0.9
19.	Bu, Bu, H	-	10.0^7	11.25	-1.25
20.	$(H_2N)_2C = NH$	15.8 ± 0.2	-	14	1.8
21.	$(Me_2N)_2C=NH$	-	13.2^7	13.6	-0.4
22.	⬡NH	-	10.6^8,10.5^9,10.6^{12}	11.22	-0.6
23.	⬡NH	-	8.7^{12}	-	-
24.	⬠NH	-	10.8^7	-	-
25.	Me, OH, H	7.3 ± 0.2	-	5.96	1.3
26.	MeO, Me, H	7.3 ± 0.1	-	4.75	2.6
27.	Me, Me, Me	8.5 ± 0.2	8.4^{10}	9.80	-1.3
28.	Et, Et, Et	-	9.0^7	10.75	-1.8
29.	Bu, Bu, Bu	-	8.4^7	10.9	-1.5
30.	$PhCH_2$, $PhCH_2$, $PhCH_2$	4.15 ± 0.02	3.65^{11},4.1^{18}	-	-
31.	Me, Me, OH	4.91 ± 0.03	-	5.20	-0.3
32.	Me,Me,CH_2CN	3.3 ± 0.1	-	4.15	-0.9
33.	Me,Me,CH_2Ph	7.35 ± 0.05	7.59^{11}	5.2	2.1
34.	Me,Me,CH_2CH_2OH	8.2 ± 0.1	-	9.3	-1.1
35.	Me, Me, CH_2COOEt	6.35 ± 0.05	-	8.0	-1.7
36.	[N structure]	-	3.4^7	5.2	-1.8
37.	[N structure]	10.6 ± 0.1	-	-	-

Discussion

Already in the very first work of Kolthoff et al.[7] on the study of the dependence of the acidity constants of some ammonium cations on their structure in the DMSO solu - tion it was suggested on the basis of rather limited data that the absolute pK_a values of these compounds as well as their changes with the structure have a rather low suscep - tibility towards the transfer of the above-named reaction series from the aqueous solution into dimethylsulfoxide. This hypothesis has gotten further support also in some other pa- pers[8-12]. Similar behavior was noticed[19] for the same reac- tion series also in the concentrated aqueous solution of tetrabutylammonium bromide.

It was also shown by several authors[1,2,4-7] that while the absolute values of pK_a of the acidic dissociation of ammonium cations in acetonitrile and nitromethane increse significantly due to the transfer from water into these me- dia, the susceptibility of this reaction series towards the structural effects changes (increases) with such a transfer only rather insignificantly (in a sharp contrast with the analogous transfer of this reaction on series from the aque- ous solution into the gas phase[4,20,21]).

The comparison of the pK_a values for these two solvents with the inclusion of our new data does not contradict (see Fig. 1) either the hypothesis about the closeness of the absolute values of pK_a of the dissociation of ammonium ca- tions $X_1X_2X_3NH^+$ in DMSO and H_2O or the comparability of the susceptibilities of this reaction series towards the substituent effects in these media.

One can see that the majority of the data for the ter- tiary and primary ammonium ions in these two solvent does not disprove the hypothesis about the existence between the compared quantities of the very rough linear relationship with the slope practically indisdinguishable from unity. At the same time, from the straight line for the tertiary ali- phatic ammonium ions most significantly deviates the point for Me_2NCH_2Ph, whereas the point for pyridine fits the ge -
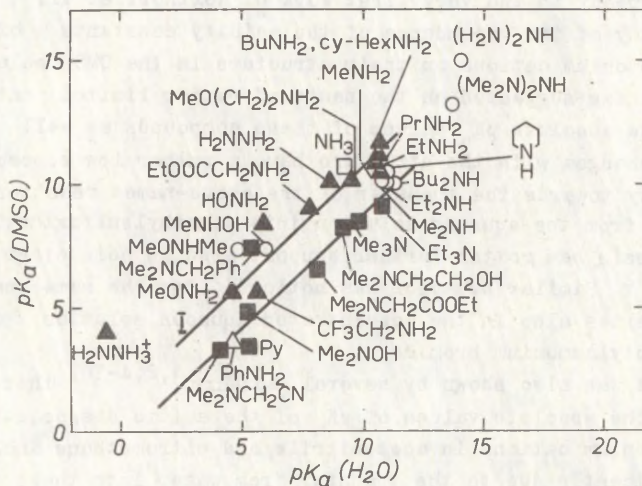
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Fig. 1. The comparison of the pK_a values for the
acidic dissociation of aliphatic ammonium
ions in DMSO and water.

neral plot for tertiary aliphatic ammonium ions. The largest
deviation (3.5 pK_a units) from the straight line I (the pri-
mary ammonium ions) in Fig. 1 belongs to $H_3NNH_3^{2+}$, the aci-
dity of which for the DMSO medium occurs to be much less
than expected. The same is true also for the monoprotonated
forms of hydroxylamines (deviations $\sim$ 1.5 pK_a units) and
hydrazine (1 pK_a unit) which behave analogously to $H_3NNH_3^{2+}$.

The situation about the behavior of the secondary am -
monium ions seems to be rather complicated and indefinite :
one can find it rather hard to declare that the straight
line in Fig.1, if put through the limited (and selected)
number of points (($Me_2N)_2CNH_2^+$, $Et_2NH_2^+$, $Me_2NH_2^+$, pyrrolidi -
nium ion, $Pr_2NH_2^+$), is located practically halfway between
the corresponding straight lines for the primary and tertia-
ry ammonium ions. So, from that imaginable straight line
would significantly deviate (about by 2 pK_a units) the

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points for $MeO(Me)NH_2^+$, $HO(Me)NH_2^+$ and $H_2NC(NH_2)_2^+$ the acidity of which in the DMSO medium again occurs to be too low.
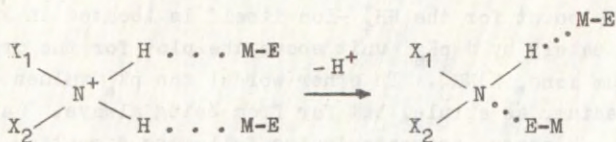
The point for the NH_4^+ -ion itself is located in Fig.1 approximately by 1 pK_a unit above the plot for the primary ammonium ions, $X_1NH_3^+$. In other words, the pK_a values for DMSO medium, as a rule, but far from being always, at $pK_{a(H_2O)}$ = const decrease in the following direction :

$NH_4^+ > X_1NH_3^+ > X_1X_2NH_2^+ > X_1X_2X_3NH^+$, whereas the $pK_{a(H_2O)}$ values, at $pK_{a(DMSO)}$ = const have the trend to increase in the same order. The comparison of the absolute values of pK_a for the substituted ammonium ions $X_1X_2X_3NH^+$ for DMSO and water shows (see Table 1, $\triangle pK_a$ values) that, on the average, those two quantities do not differ from each other by more than $\pm$ 1.2 pK_a units.

It follows from the above-said that in case of the transfer of the acidic dissociation reaction of cationic acids $X_1X_2X_3NH^+$ from water into DMSO a significant over - all compensation of contributions of nonspecific (polarity and polarizability)[22] and specific (general basicity,elec- trophilicity and steric characteristics of the solvent mo- lecules)[22], solvent-solute interactions in the gross sol - vent effects should take place[x] .

Such a compensation of various contributions of sol - vent-solute interactions in this case is rather hard to pre- dict because most frequently it is assumed (see Ref. 6 for literature references) that the major role is played by the nucleophilic solvation of the protonated form of the base which dominates over the electrophilic solvation of the neutral base while all other factors are less impor - tant (see the scheme):

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[x] It should be mentioned that the separate comparison of the data for the subseries of N-protonated forms of O- or N-substituted hydroxylamines shows that the suscep- tibility towards substituent effects in DMSO exceeds that for the aqueous solution almost twice.

2*

$$X_1 \diagdown \underset{X_2 \diagup}{\overset{+}{N}} \diagdown \begin{array}{l} H \cdot \cdot \cdot M-E \\ \\ H \cdot \cdot \cdot M-E \end{array} \quad \xrightarrow{-H^+} \quad X_1 \diagdown \underset{X_2 \diagup}{N} \diagdown \begin{array}{l} \overset{M-E}{H \cdot \cdot} \\ \\ \cdot \cdot E-M \end{array}$$

(1)

where M and E are the corresponding nucleophilic and elec-
tropilic solvation centers of the solvent molecule.

By its general basicity[22,23] DMSO (B = 362) signifi-
cantly exceeds water (B = 156) while by its electrophilic
solvating power[24] the latter is much more superior (E_{DMSO}=
3.2, E_{H_2O} = 21.8). Since ammonium ions are, as a rule ,
stronger acids than ME (e.g., HOH) or the nonprotonated ,
neutral form of the amine (X_1NH_2, X_1X_2NH, etc) then   one
might expect that the charged, cationic acid is better sta-
bilized by the nucleophilic solvation with the solvent mo -
lecules as Lewis' bases, than its deprotonated form due   to
the complex formation via the electrophilic center E of the
solvent molecule E-M. It follows from these   considerations
based only on the model of specific solvation that the trans-
fer of the process (1) from water into DMSO should result
in the extra-stabilization of the initial (cationic) state
relative to the deprotonated form of the acid.

The similar considerations refer also to the transfer
of the reaction (1) from the gas phase into DMSO or water.
It is not excluded that in the case of specific solvation
processes with the inclusion of several specifically solva-
ting, sometimes rather bulky solvent molecules, the steric
characteristics of the latter might play a significant role
hindering the complex formation between solute and solvent
molecules. So, in the case of the process (1) the access of
several pyramidal molecules of DMSO to the cationic acid
might be difficult (the specific solvation of the neutral
amine by the molecules of this solvent does not play   any

noticeable role) which could be a sufficient reason for the significant compensation of the solvent effects on the pK_a values while the reaction series (1) is transferred from water into DMSO.

As regards the influence of the nonspecific solvent-solute interactions, then their contribution should be the most noticeable for the transfer of the reaction series (1) from the gas phase into water or DMSO[6]. Due to the rather insignificant relative change of the polarity[22] ($\varepsilon_{DMSO} = 46.4$, $\varepsilon_{H_2O} = 78.2$) and polarizability[22] ($n_D^{25}(DMSO) = 1.4773$, $n_D^{25}(H_2O) = 1.3325$) factors of the latter two solvents one might expect that their influence on the transfer of the reaction series (1) from H_2O into DMSO will be mutually compensating and much less important than for the transfer of the reaction series (1) from the gas phase into any of these two solvents.

Earlier it was shown[4,20,21] that the acidity of the aliphatic ammonium cations in the gas phase could be de-scribed by the equation

$$A = a_0 + a_1 \sum \sigma^* + a_2 \sum \Delta R + a_3 \sum \sigma_R^0 + a_4 n_1 + a_5 \Delta n_2, \quad (2)$$

where A – is the measured quantity (gas phase basicity or acidity, ionization potential, pK_a, etc.), a_0, a_1, a_2, a_3, a_4, and a_5 – are the constants of the reaction series; $\sum \sigma^*$ and $\sum \sigma_R^0$ are the sums of the Taft's inductive and resonance substituent constants at the reaction center, $\Delta R = MR - MR(methyl)$ where MR is the calculated additive molecular refractivity of the substituent, which serves as an approximate measure of the polarizability of the latter, n_1 – is the number of hydrogen atoms, immediately attached to the reaction center, $\Delta n_2 = n_2 - n_{2(methyl)}$, where n_2 is the number of hydrogen atoms in the α-position to the reaction center ($n_{2(methyl)} = 3$)

which, besides the substituent inductive and resonance ef-

fects and the number of hydrogen atoms attached immediately on in the α-position to the protonization center, takes into account also the polarizability of the substituents. It was already noticed[4,14,20,21] that the relative con — tribution of the latter factor is much lower in the aque- ous solvent than in the gas phase, whereas the susceptibi- lity of the reaction series (1) towards the inductive ef- fect a, a_1, drops due to the transfer from the gas phase into water more than twice.

Similar conclusions could be drawn also from the sta- tistical analysis of the more representative and extensive data in terms of Eq. (2) conducted in the present work. The main results of the statistical check of this equation[+] could be summed up in the form of the following equations:

1. DMSO:

$$pK_a = (7.81 \pm 0.42) - (2.91 \pm 0.28)\sum \delta^* - (0.0444 \pm 0.0110)\sum \Delta R + (0.819 \pm 0.301)n_1 - (0.558 \pm 0.090)\Delta n_2 , \qquad (3)$$

$R = 0.985$, $s = 0.84$, $n = 26$, the maximum range of variation of pK_a was 7.6 pK_a units, $a_3 = 0$.

2. H_2O:

$$pK_a = (9.75 \pm 0.25) - (4.42 \pm 0.17)\sum \delta^* - (0.0756 \pm 0.015)\sum \Delta R + (1.00 \pm 0.17)n_1 - (0.407 \pm 0.050)\Delta n_2, \qquad (4)$$

$R = 0.988$, $s = 0.42$, $n = 20$ (the points for Me_2NCH_2Ph and Me_2NCH_2COOEt were excluded), the maximum range of the variation of pK_a was 7.4 pK_a units;

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x   The program, described in general features in Ref. 25   was used.

$a_3 = 0^+$.

One can see that both of these equations are rather approx-
imate and on their basis it is hardly reasonable to draw
some far-reaching conclusions about the exact relative con-
tributions of the different structural factors into the
gross acidity of the substituted aliphatic ammonium ions.
However, it should be noticed that in terms of the approach
based on Eq. (2) the absolute values of the susceptibili -
ties of the reaction series towards the inductive and po -
larizational effects of substituents are for the aqueous
solution somewhat higher than for the DMSO solution. At
the same time a_3 values for the both solvents are statis -
tically negligible while regression coefficients a_4 and a_5
in the limits of their combined confidence intervals are
practically the same for these two solvents.

It also seems reasonable to draw   attention   to the
direct comparison of pK_a values for $X_1X_2X_3NH^+$ in DMSO with
the gas phase basicity[3] (ΔG) of the corresponding
amines, $X_1X_2X_3N$ (see Fig. 2).

The significant scatter of the points seems to be ra-
ther expected because, in principle, the linear relation -
ship between the gross values of pK_a and ΔG should be
observed only in the case where two quantities depend only
on one and the same structural factor, e.g. on the induc -
tive effect of the substituents X_1, X_2 and X_3, which might
be expressed by the first term in Eq. (2). Therefore, such
a comparison is justified only on condition of the varia -
tion of only influencing structural factor at the fixed
contributions of the rest of the structural factors. Rough-
ly, these conditions are probably fulfilled (the values of
n_1, Δn_2, $\sum \sigma_R^o$ and $\sum \Delta R$ are practically constant ,

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[+] For cases R - correlation coefficient, s - standard de-
viation, n - the number of points, in the parentheses ,
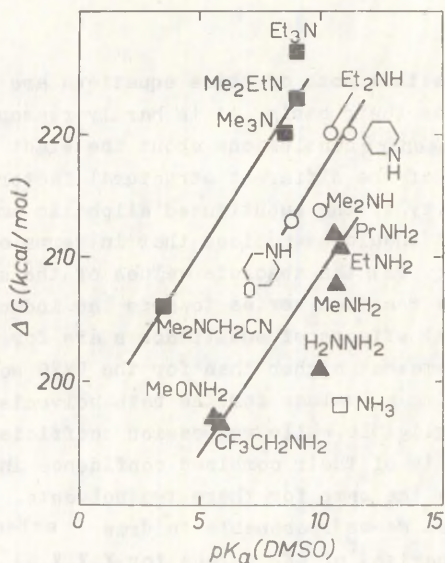after the regression coefficients are indicated their
confidence intervals.

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Fig. 2. The comparison of the gas phase basicity (ΔG) of amines with the acidity of their protona - ted forms in DMSO ($pK_{a(DMSO)}$).

the inductive effect of the substituents is variable) for the comparison of the following pairs of the points for the protonated forms of Me_2NCH_2CN and Me_2NEt, morpholine and piperidine, as well as $CF_3CH_2NH_2$ and $EtNH_2$. In Fig. 2 through the above-mentioned pairs of points are put the straight lines, the slopes of which are in the range from 2.0 to 2.4 and which actually should be roughly equal to the ratio of the a_1-coefficients from Eq. (2) for these two media, gas phase and DMSO. The results of the statistical treatment of the data on the acidity of substituted ammonium ions in gas phase[20] and in DMSO (this work, Eq. (3)) in terms of Eq. (2) do not contradict this finding.

In conclusion it is necessary to underline that the question about the influence of various structural effects

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on the acidity of substituted aliphatic amines in dimethyl-
sulfoxide could hardly be considered fully resolved. The
drawn conclusions, necessarily, need further verification
and refinement on the basis of an even more representative
and better balanced set of experimental data (one can see
from Table 1 that still insufficiently are represented the
secondary ammonium ions, much wider should also be the se-
lection of the primary, secondary and tertiary ammonium
ions containing the electronegative substituents, etc.).

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ISOKINETIC CORRELATION IN 2-(2,4-DINITRO-
ARYLOXY)-N-ETHYLPYRIDINIUM SALTS WITH SE-
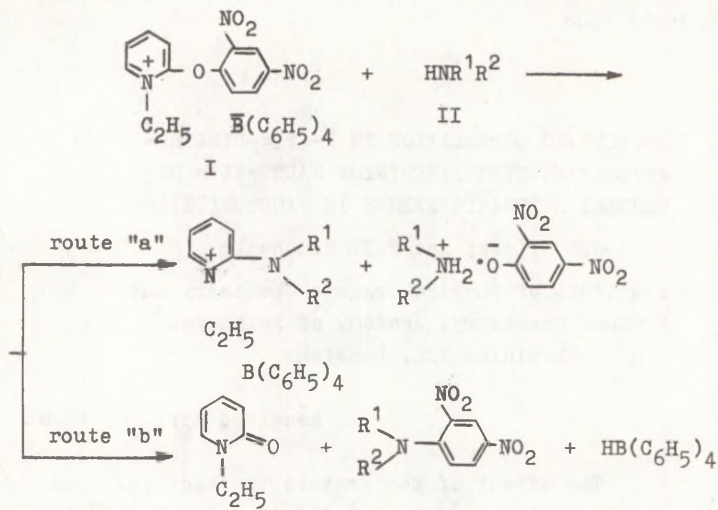CONDARY ALIPHATIC AMINES IN ACETONITRILE

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The effect of temperature in reactions   of
nucleophilic aromatic substitution (at $10-55^{\circ}C$)
has been studied in 2-(2,4-dinitroaryloxy) - N -
ethylpyridinium salt with secondary aliphatic
amines in acetonitrile. Substitution proceeds at
the activated carbon atom of benzene ring and is in
agreement with the regularities of the second or-
der reactions. Isoparametric correlation of the
type nucleophile-temperature has been observed .
Structural transition of a nucleophile exceeding
the isoparametric range has been carried out. Also,
we have traced violation of isoparametricity,which
is connected with rate-determining stage.

We have shown in[1] that the reactions of 2-(2,4-dinitro-
aryloxy)-N-ethylpyridinium salt (I) with aliphatic amines
(II) proceed according to two reaction centers of the sub -
strate: according to the carbon atom of pyridine ring with
formation of 2-(N-doalkyl)-N-ethylpyridinium salt and dinit-
rophenolate (route "a") and according to the carbon atom of
benzene ring with formation of the corresponding N-alkyl(aryl)
dinitro anilines and N-ethylpyridone (route "b").

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3*

The present work deals with the influence of temperature on the reactions of secondary aliphatic amines of 2-(2, 4-dinitroaryloxy)-N-ethyl pyridinium salt in acetonitrile.

It has been established on the basis of isolation of the reaction products and using the spectrophotometric analysis of the reaction mixture that the reaction of 2-(2,4-dinitroaryloxy)-N-ethylpyridinium salt with secondary aliphatic amines (piperidine, piperazine, hexamethylenimine , methylethylamine, methylbutylamine, morpholine, di-n-hexylamine, diethylamine) proceeds via nucleophilic substitution near the carbon atom of benzene ring, but in the case of dibenzylamine and diisobutyl amine at the α-atom of the carbon of pyridine ring.

These reactions are in agreement with the second order kinetic parameters. Thus, a concentration change of amines by more than one order does not bring about a change in the bimolecular rate constant, which was noticed in case of morpholine, methylbutylamine, dibenzyl amine and diisobutyl amine.

In Table 1 are given the bimolecular rate constants of

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Table 1

Rate Constants of 2-(2,4-Dinitroaryloxy)-N-Ethylpyridinium Salt Reaction
with Secondary Aliphytic Amines in Acetonitrile

	Amine	$\sum\sigma^*$	$-E_N^3$	$-E_N'^4$	$k\ l\cdot mol^{-1}\cdot s^{-1}$			
					283 K	298 K	313 K	328 K
1.	Piperidine	0.31	0.79	0.69	$7.3^{\pm}0.3$	$19.0^{\pm}1$	$46^{\pm}6$	$100^{\pm}10$
2.	Piperazine	0.38	0.79	0.69	$6.3^{\pm}0.2$	$14.0^{\pm}0.8$	$31^{\pm}1$	$54^{\pm}3$
3.	Hexamethyleneimine	0.29	1.10	0.92	$4.5^{\pm}0.2$	$10.0^{\pm}0.9$	$17.4^{\pm}0.6$	$35^{\pm}1$
4.	Methylethylamine	0.39	1.10	0.93	$2.5^{\pm}0.1$	$4.4^{\pm}0.2$	$7.2^{\pm}0.2$	$12.2^{\pm}0.6$
5.	Methylbutylamine	0.36	1.19	1.06	$2.25^{\pm}0.08$	$3.9^{\pm}0.1$	$6.0^{\pm}0.3$	$10.1^{\pm}0.3$
6.	Morpholine	$0.62^{1)}$	0.79	0.69	$1.00^{\pm}0.04$	$1.4^{\pm}0.6$	$2.27^{\pm}0.08$	$3.8^{\pm}0.1$
7.	Di-n-hexylamine	0.23	1.96	2.08	$0.27^{\pm}0.01$	$0.39^{\pm}0.01$	$0.56^{\pm}0.03$	$0.75^{\pm}0.02$
8.	Diethylamine	0.29	1.98	2.00	$0.22^{\pm}0.01$	$0.30^{\pm}0.01$	$0.48^{\pm}0.01$	$0.60^{\pm}0.02$
9.	Dibenzylamine	0.92	1.50	-	$0.025^{\pm}0.001$	$0.050^{\pm}0.001$	$0.16^{\pm}0.01$	$0.39^{\pm}0.01$
10.	Diisobutylamine	0.24	2.47	2.38	$0.033^{\pm}0.001$	$0.045^{\pm}0.002$	$0.045^{\pm}0.008$	$0.10^{\pm}0.04$

1) The value was calculated from the series of 2-bromo-N-ethylpyridinium bromide reactions
with aliphatic amines[5] and it agrees with the data of the present paper[6].

the reaction of salt (I) with amine in the temperature range
of 283-328 K. The dependence of reactivity on the structure
of nitrogen nucleophiles at a given temperature has been
studied in accordance with the two-parameter equation (1)[2],
considering the simultaneous influence of the inductive
($\sum \sigma^*$) and steric (E_N) factors of substituents in the vi -
cinity of nitrogen atom in the amine molecule.

$$\log k = \log k_o + \rho^* \sum \sigma^* + \delta E_N \tag{1}$$

The coefficient values found by means of Eq. (1), ob -
tained when applying E_N, which were determined according to
the isostericity principle from the E_s of Taft and E_s of
J.A. Macphee et al[4], are given in Table 2. If the temperature
rises, the absolute values of the sensitivity to the induc-
tive (ρ^*) and steric (δ) effects of substituents in the amine
molecule also tend to increase. The same concerns the reac-
tivity ($\log k_o$). Application of the E_N' values yields higher
statistical correlation characteristics. Processing of the
results without taking into account the inductive influence
of alkyl groups, as it has been suggested in[7] did not give
any positive results.

In the case of the present reaction series holds the
Arrhenius dependence. The dependence of log k on T^{-1} in the
reactions of salt (1) with secondary amines in acetonitrile
(Table 1, Nos 1-8) acts as a set of straight lines inter -
cepting in one common point (Fig. 1), which is situated in
a lower temperature range than that of the experiment. In
Table 3 are given the calculated activation parameters. As
to the reactions with participation of amines 1-8, absolute
value of a decrease in the activation enthalpy ($\Delta H^{\neq}$)
yields the decreasing absolute values of activation entropy
$\Delta S^{\neq}$. There is linear dependence between the $\Delta H^{\neq}$ and
$\Delta S^{\neq}$, thus referring to the existence of isokinetic corre-
lation. In order to check the reliability of this supposi -
tion, the reaction series was analyzed using the known tests:
$\log k_{T_2} - \log k_{T_1}$ $(T_2 > T_1)$; $\Delta H^{\neq} - \Delta S^{\neq}$; $\rho^* - T^{-1}$; $\delta - T^{-1}$

Table 2

Coefficient Values of Eq. (1) for Reaction of 2-(2,4-Dinitroaryloxy)-N-Ethylpyridinium Salt with Amines in 283-328 K Range, Taking into Consideration E_N and E_N'

T	$\log k_o$	$-\rho^*$	δ	r	s	n
		Considering E_N				
283	3.1 ± 0.2	3.0 ± 0.4	1.45 ± 0.09	0.989	0.10	8
298	3.9 ± 0.2	3.9 ± 0.4	1.70 ± 0.09	0.992	0.10	8
313	4.5 ± 0.2	4.2 ± 0.3	1.87 ± 0.08	0.995	0.09	8
328	5.1 ± 0.2	4.6 ± 0.3	2.06 ± 0.08	0.996	0.08	8
		Considering E_N'				
283	2.7 ± 0.1	2.9 ± 0.2	1.24 ± 0.04	0.997	0.05	8
298	3.5 ± 0.1	3.7 ± 0.2	1.45 ± 0.04	0.998	0.05	8
313	4.0 ± 0.2	4.0 ± 0.4	1.58 ± 0.07	0.994	0.09	8
328	4.5 ± 0.2	4.4 ± 0.3	1.74 ± 0.06	0.997	0.08	8

according to $y = a + bx^8$ type. The calculated values of pair-wise correlation are given in Table 4. The values of isokinetic temperature (β) were calculated from the depen - dence $\log k_{T_2} - \log k_{T_1}$ if $T_2 > T_1$, taking into account the deviation from (2)[9].
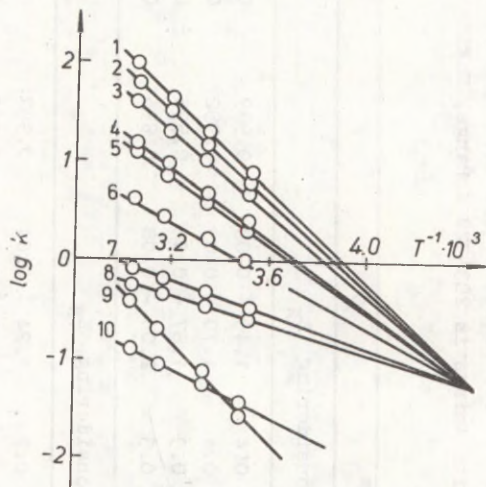

Fig. 1. Dependence $\log k - T^{-1}$ for reaction of 2-(2,4-dinitroaryloxy)-N-ethylpyridinium salt with secondary aliphatic amines in acetonitrile. Numeration of points cor - responds to that of Table 1.

The difference of the slope of straight line (b) from unity in the $\log k_{T_2} - \log k_{T_1}$ coordinates is taken as the accu - racy criterion for calculation of isokinetic temperature. The value of b-1 should at least 2-3 times exceed that of S_b (error). In our case, ratio $\frac{b-1}{S_b}$ equals 5-6.

The E_N values have been used when calculating pair-wise

Table 3

Activation Parameters of 2-(2,4-Dinitro-
aryloxy)-N-Ethylpyridinium Salt with Se-
condary Aliphatic Amines in Acetonitrile

Amine	log A	$B \cdot 10^3$ J/mol	$\Delta H^{\neq}$ $298 \cdot 10^3$ J/mol	$-\Delta S^{\neq}$ 298 · J/mol · degree
1. Piperidine	$9.2^{\pm}0.1$	$45.1^{\pm}0.9$	$42.6^{\pm}0.8$	$77^{\pm}1$
2. Piperazine	$7.7^{\pm}0.2$	$37.3^{\pm}0.9$	$35^{\pm}1$	$106^{\pm}2$
3. Hexamethylene- imine	$7.1^{\pm}0.3$	$35^{\pm}2$	$32^{\pm}2$	$118^{\pm}5$
4. Methylethyl- amine	$5.5^{\pm}0.2$	$28^{\pm}1$	$25^{\pm}1$	$148^{\pm}6$
5. Methylbutyl- amine	$5.0^{\pm}0.2$	$25^{\pm}1$	$23^{\pm}0.9$	$157^{\pm}6$
6. Morpholine	$4.2^{\pm}0.4$	$23^{\pm}2$	$21^{\pm}2$	$172^{\pm}13$
7. Di-n-hexyl- amine	$2.7^{\pm}0.1$	$17.5^{\pm}0.3$	$15.0^{\pm}0.2$	$202^{\pm}4$
8. Diethylamine	$2.2^{\pm}0.4$	$16^{\pm}2$	$13^{\pm}2$	$210^{\pm}35$
9. Dibenzyl- amine	$7.1^{\pm}0.2$	$47^{\pm}1$	$45^{\pm}1$	$117^{\pm}3$
10. Diisobutyl- amine	$2.2^{\pm}0.1$	$19.9^{\pm}0.7$	$17.4^{\pm}0.6$	$212^{\pm}12$

$$\beta = T_2 \frac{1 - b}{1 - b \frac{T_2}{T_1}} \tag{2}$$

correlations $\rho^{\ast} - T^{-1}$; $\delta - T^{-1}$, given in Table 4. The calculated ß values and the statistical parameters obtained after applying the E_N' do not practically differ from those for E_N. The value of isokinetic temperature $\beta_{average}$ = 213 K is lower than those falling into the studied temperature range and corresponds to the reaction series insensi - tivity to the structure of the secondary aliphatic amine ($\rho^{\ast} = 0$; $\delta = 0$).

The obtained results were processed in keeping with the polylinearity principle according to the multi-parameter equation (3), taking into consideration a common contribu - tion of inductive steric parameters of amine, the tempera - ture and their perturbing influence.

$$\log k = \log k_o + \rho^{\ast} \sum \hat{\delta}^{\ast} + \delta E_N + q \frac{298 - T}{298 \ T} +$$
$$+ k \sum \delta^{\ast} E_N + 1 \sum \delta^{\ast} \frac{298 - T}{298 \ T} + m E_N \frac{298 - T}{298 \ T} \qquad (3)$$

The standard temperature was 298 K. The numeric values of Eq. (3) in natural and in normed scales are given in Table 5. The statistical characteristics of Eq. (3) refer to its reliability.

Calculated critical values (Table 6) show that the value of isokinetic temperature $\hat{T}$ is in a satisfactory agreement with that found from partial correlations. The rate constant $\log \hat{k}$ isoparametric value can be equal to - 1.09 only in the case of amine, whose $\sum \delta^{\ast}$ and E_N are (1.0 $\pm$ 0.2); - (2.4 $\pm$ 0.5), respectively. It could have been expected that if the critical value of any of the parameters is ex - ceeded, it will lead either to the inversion of sensitivity coefficients $\rho^{\ast}$ and δ or to the breaking of isoparamet- ricity.

We have previously shown[10] that in the case of a simi- lar reaction of salt (1) with aromatic amines, nucleophilic substitution can be described by correlational relationship (4), assessing the additive contribution of inductive and temperature components.

Table 4

Correlation Coefficients of Eq. $y = a + bx$

	x	y	T(K)	a	b	β	R
1.	$\log k\ T_1$	$\log k\ T_2$	313	0.15 ± 0.02	1.10 ± 0.02	212 ± 4	0.999
2.	-"-	-"-	298	0.37 ± 0.02	1.20 ± 0.03	205 ± 5	0.998
3.	-"-	-"-	283	0.63 ± 0.04	1.39 ± 0.06	210 ± 9	0.995
4.	$-\Delta S^{\neq}$	$\Delta H^{\neq}$	283-328	58000 ± 1000	217 ± 7	217 ± 7	0.996
5.	$\frac{I}{T}$	$\rho^{\ast}$	283-328	$-(15 \pm 2)$	3200 ± 500	220 ± 60	0.971
6.	$\frac{I}{T}$	δ	283-328	5.9 ± 0.2	$-(1240 \pm 60)$	210 ± 20	0.997

$\beta_{average} = 213$

Table 5

Numeric Values of Eq. (3) in Natural and
Normalized Scales

Coefficients	Scale	
	Natural	Normalized
$\log k_o$	4.4 ± 0.1	6.0 ± 0.1
$\rho^{\ast}$	$-(5.7 \pm 0.3)$	0.87 ± 0.04
δ	2.31 ± 0.09	1.48 ± 0.06
q	4200 ± 300	1.04 ± 0.08
k	2.4 ± 0.4	0.34 ± 0.05
l	3300 ± 500	0.31 ± 0.05
m	1200 ± 100	0.4 ± 0.05
R	0.998	0.998
s	0.05	0.07
n	32	32

Table 6

Values of Critical Parameters

$\sum \hat{\delta}^{\ast}$	$\hat{E}_N$	$\dfrac{298 - T}{298\ T}$	$\hat{T}$
0	$-(3.3 \pm 0.6)$	(1.9 ± 0.3)	190 ± 30
1.3 ± 0.3	0	(1.7 ± 0.3)	200 ± 40
1.0 ± 0.2	$-(2.4 \pm 0.5)$	0	298

$$\log k = (7.4 \pm 0.3) - (6.9 \pm 0.2)\sum \sigma^* -$$
$$- (2600 \pm 200)\frac{1}{T}$$

$$r = 0.993; \quad s = 0.133; \quad n = 18 \tag{4}$$

The reaction series studied belongs to the isoentropic ones, and the absence of isokinetic relationship is explained by exceeding the limits of isoparametric range, as concerns the induction parameter ($\sum \sigma^*$ changes within range 1.20-1.64), which determines much lower reaction rate constant values . Thus, it becomes possible in the studied processes of nucleophilic substitution with participation of salt (1), secondary aliphatic and first-order aromatic amines to experimentally monitor the transition from the isokinetic to the enthalpic control, depending on the structure of nitrogen nucleophile.

Variations of energetic parameters of the reaction systems can probably be linked with the peculiarities of the stage-like mechanism of nucleophilic substitution. In the case of isokinetic correlation, the formation rate of the σ-complex by scheme (5) is in keeping with its decomposition rate.

$$\tag{5}$$
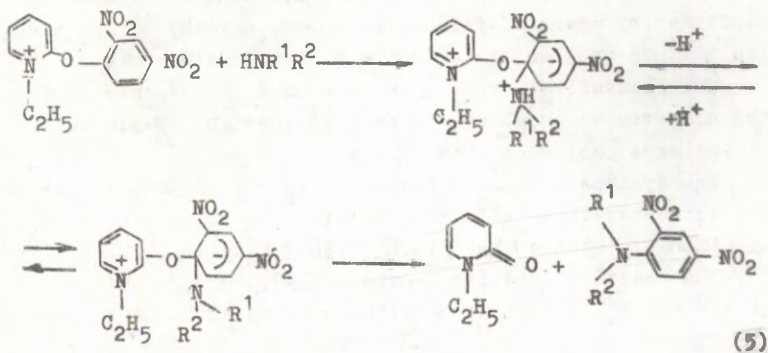
In the case of enthalpic control, in the reactions of aromatic amines having poor reactivity, the formation of the σ-complex becomes the limiting stage.

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For secondary aliphatic amines exceeding $\sum \hat{\sigma}^*$ and $\hat{E}_N$, the substitution process proceeds via the carbon atom of pyridine ring. The character of the variation constant, permits, depending on the temperature in the processes studied (Table 1, Fig. 1) also to predict the existence of isokinetic correlation in the case of substitution in the vi - cinity of the pyridine atom of carbon. Nevertheless we do not have any statistical parameters to prove the holding of isokinetics.

Experimental

Reaction rate was measured on a spectrophotometer "Spectromom-204", the thickness of the layer being 1 cm, at the accumulation of N-dialkyl-2,4-dinitroanilines within the range of 370-390 nm. In the case of dibenzylamine and diisobutylamine, the reaction was monitored by the accumulation of the 2,4-dinitrophenolate ion ($\lambda = 425$ nm). The concentration of amines (b, mol/l) varied in range $2 \cdot 10^{-4} - 0.15$, the concentration of pyridine salt (a, mol/l) in $6.10^{-5} - 1.5 \, r \, 10^{-4}$.

2,4-Dinitrophenol and N-dialkyl-2,4-dinitroanilines were identified by means of thin-layer chromatography of the reaction mixture on silufol (eluent - benzene) with markers.

The pseudofirst order rate constants in the case of stoichiometry were calculated as described in[5]. Basic calculations were performed on a DVK-2M.

The synthesis of 2-(2,4-dinitroaryloxy)-N-ethylpyridi - nium tetraphenylborate[10], the purification of acetonitrile[5] and aliphatic amines[5] have been already described.

The reaction products N-piperidyl-2,4-dinitroaniline and N,N-diethyl-2,4-dinitroaniline were obtained using similar methods. The (I) salt (0.0003M) with a ten-fold excess of the corresponding amine in 10 ml of acetonitrile was heated on a water bath during one hour. The mixture was concentrated by evaporation, the solid residue was recrystallized: N-Piperidyl-2,4-dinitroaniline (yield 74%) from ethanol, melting point $91-92^{\circ}C$[11]; N,N-diethyl-2,4-dinitroaniline

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(yield 72%) from butanol, melting point 79.5-80°C((80°C)[12].

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KINETICS OF OXIDIZING AMMONOLYSIS OF Cu^{2+}
2,6,8-TRIOXYPURINE IN AMMONIUM BUFFER
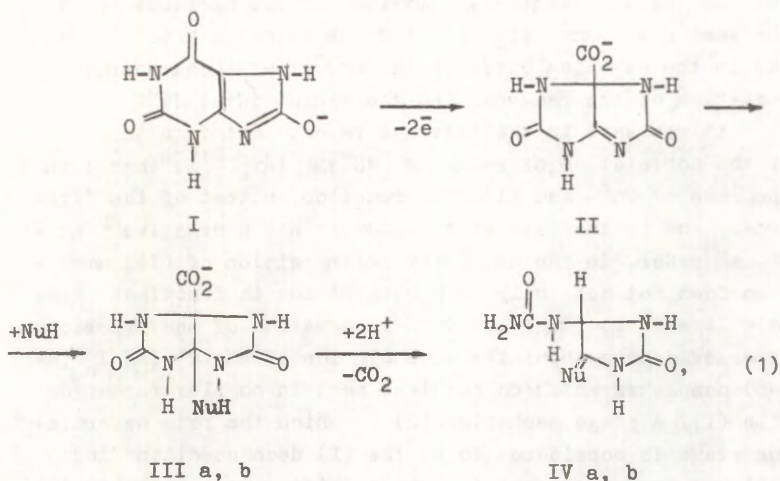
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The kinetics of oxidizing conversion of Cu^{2+}
2,6,8-trioxypurine (I) has been studied spectro -
photometrically in ammonium buffer (pH 8.5 - 10.8)
at 25°C. The process results from rapid oxidation
(I) with formation of 1-carbohydroxy-2,4,6,8 -
tetraaza-3,7-dioxo-4-en-bicyclo (3,3,0) octane (II)
which is bound into the (II-Cu^{2+} -NH_3) (II^x) com-
plex. Slow conversion of (II^x) takes place in two
parallel flows: intraspherical ammonolysis and
base-catalyzed ammonium.

The problem concerning the oxidizing conversion   of
2,6,8-trioxypurine or uric acid (I) - the product of the
oxidizing metabolism of nucleic acid, has been in the center
of attention of several researchers[1-5] mainly because of the
diseases caused by the disorders of nucleic metabolism re-
sulting from the accumulation of poorly soluble (I). Recent-
ly, the studies have been concentrated on (I) as a natural
antioxidant[6-8].

The analysis of the literature data on the fermentative
and electrochemical oxidizing conversion of (I) in the phos-
phate and borate buffers (pH 7-10) has yielded[9-11] the fol-
lowing scheme:

$$\text{I} \xrightarrow{-2\bar{e}} \text{II} \longrightarrow$$

$$\xrightarrow{+\text{NuH}} \text{III a, b} \xrightarrow[-CO_2]{+2H^+} \text{IV a, b}, \qquad (1)$$
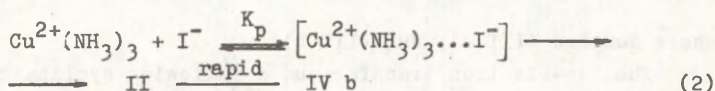
where $NuH-H_2O$ (III a); NH_3 (III b).

The two-electron transfer and a following cyclization results in the (I) anion ($pK_a = 5.75$[12]) conversion into 1-carboxy-2,4,6,8-tetraaza-3,7-dioxo-4-en-bicyclo (3,3,0) octane, which is attacked by a nucleophile (water), then forms the bicyclic intermediate (III a) whose decomposition yields 5-ureidohydantoin (allantoin, IV a). It should be stressed that in the 0.05 M phosphate buffer (pH = 8), the formation of (II) goes rapidly (k = 32.5 s$^-$), but the fol - fowing II conversion into IV a is a slow process (k = 3.5 · 10^{-3} s$^-$). 1-Dimethylamino-5-ureidohydantoin ($\lambda = 275$ nm)[13] was isolated at (I) oxidation in a 20% dimethyl amine solution in the presence of catalytic quantities of Cu^{2+} . The 1-amino-5-ureidohydantoin derivatives were obtained via (I) oxidation with potassium permanganate in the presence of aniline and piperidine[14] . We have assumed that scheme (1) also describes the aminolysis of (II) with the formation of the 1-amino-5-ureidohydantoin derivatives.

In order to check this hypothesis, it seemed to be worth-while studying the oxidizing ammonolysis of (I). Cu^{2+}

was used as the oxidizer, ammonium as the nucleophile. With
the same goal were also studied the reaction kinetics of
(I) in the ammonium buffer with Cu^{2+} at wide concentration
variation of the reagents and the medium pH at $25^{\circ}C$.

It was said in the previous report that[15] in the case
of the correlation of reagents $\left[NH_3^-\right] \gg \left[I\right] \gg \left[C^{2+}\right]$, then in
the case of Cu^{2+} and (I), the reaction is that of the first
order, and in the case of ammonium it has a negative frac -
tional order. In the oxidizing decomposition of (I), ammo -
nium does not act only as a reagent but it functions also
as a ligand, coordinating Cu^{2+} . Formation of the fractional
order evidences about the accumulation of the $C^{2+}(NH_3)_n$ (n=
4-6) complexes which do not take part in complex formation
with (I). A stage mechanism (2) in which the rate determin-
ing stage is considered to be the (I) decomposition into
(II) has been suggested for the oxidizing conversion of (I):

$$Cu^{2+}(NH_3)_3 + I^- \xrightarrow{K_p} \left[Cu^{2+}(NH_3)_3 \ldots I^-\right] \longrightarrow$$
$$\longrightarrow II \xrightarrow{rapid} IV\ b \tag{2}$$

As to the present work, the kinetics has been studied
if $\left[NH_3\right] \gg \left[Cu^{2+}\right] \gg \left[I\right]$. The reaction mixture can be charac -
terized by the following parameters: the absorption band de-
crease λ = 293 nm and the appearance of the absorption band
λ = 265 nm, which we can connect with 1-amino-5-ureidohy -
dantoin (IV b) absorption. The decrease in the absorption
(λ = 293 nm) is not linked with (I) anion loss but it is
caused by the rapidly forming (II), which is bound into the
$\left[II-Cu^{2+} - NH_3\right]$ complex of (II^x), having similar absorption
with (I) in the studied spectral region (cf.[9]). In the case
of the acidification of the reaction mixture after the ter-
mination of the reaction, selective absorption was not traced
in the ultra-violet spectral region, which is explained by
the (IV b) hydrolysis and (IV a) formation. The latter was
identified by means of the thin-layer chromatography.

It was established that at the given concentration of
Cu^{2+}, NH_3 and medium pH the pseudofirst order rate con -

stants (k_H) which were calculated from the decrease
of $\lambda = 293$ nm and the accumulation $\Lambda = 265$ nm remain constant during the process and are practically equal. Conse -
quently, the process proceeds quantitatively and it is not
complicated by hydrolysis.

In Table 1 are given the k_H values in the case of concentration variation of Cu^{2+} and pH. In the pH = 8.7-10.8
range and in the given concentration range of the ammonium
buffer, the k_H values do not change while changing the Cu^{2+}
concentration by one order of magnitude. Thus, it refers
to the Cu^{2+} zero order and confirms the hypothesis about
a complete bind of Cu^{2+} of the (II) intermediate into the
(II^x) complex.

The increase of the ammonium buffer concentration brings
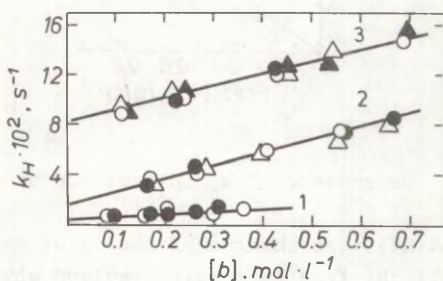about a remarkable increase of the k_H values (Table 2,Fig.1).

Fig. 1.   Dependence of k_H on ammonium buffer concen -
tration at pH 8.7 (1); 9.8 (2); 10.8 (3). C^{2+}
concentration (mol. 1^{-1}): $\bigcirc$ − $4.2 \cdot 10^{-4}$, $\bullet$ −
$1.7 \cdot 10^{-3}$, $\triangle$ − $2.5 \cdot 10^{-3}$, $\blacktriangle$ − $5 \cdot 10^{-3}$,
$\odot$ − $1 \cdot 10^{-2}$.

The linear dependences of k_H on the concentration of
ammonium buffer (Fig. 1) do not proceed from the origin in
the case of a wide variation range of the Cu^{2+} and pH con -
centrations. The intercepted sections on the ordinate show
the contribution of the flow with a pseudofirst order rate

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constant ($k_1^!$), conditioned by the intraspherical ammonolysis
of the double bond C = N of the (II) intermediate in the
($II^{\textbf{*}}$) complex. The values of $k_1^!$ tend to grow with the in -
crease of pH, approaching saturation. The character of the
dependence shows that the dissociated form of the ($II^{\textbf{*}}$) com-
plex appears to be its catalytically active form. The tan-
gents of the slope angles in Fig. 1 depict the second order
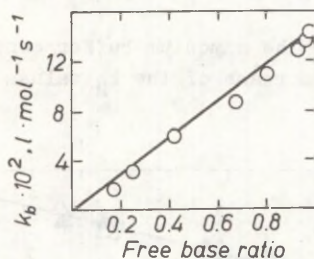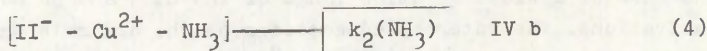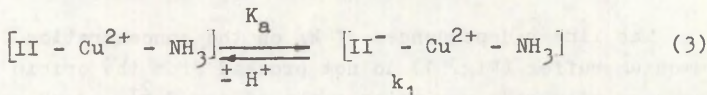rate constant (k_b), which has been brought about by the ca-
talytic effect in buffer.

Fig. 2. Dependence of k_b on fraction of free base (α).

Fig. 2 illustrates the changes of the value depending on
the buffer. If the free base mole fraction equals 1, then
the interception of the straight line with the right-hand
ordinate will yield the second order catalytic rate constant
value $k_2 = 0.156 \pm 0.01$ l $\cdot$ mol^{-1}, s^{-1}, caused by the am -
monium buffer catalysis with basic component.

It follows from the obtained results that the kinetic
scheme can be described with expressions (3) and (4).

$$\left[II - Cu^{2+} - NH_3\right] \underset{\pm\ H^+}{\overset{K_a}{\rightleftharpoons}} \left[II^- - Cu^{2+} - NH_3\right] \tag{3}$$

$$\left[II^- - Cu^{2+} - NH_3\right] \xrightarrow{\quad k_1 \quad} \boxed{k_2(NH_3)} \quad IV\ b \tag{4}$$

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In the case of the stationarity of the (II^{*}) anion formation, the reaction rate constants with consideration of the dissociation constant (K_a) and the material balance equation can be expressed by means of Eqs. (5) and (6)

$$k_H = \frac{K_a(k_1 + k_2 [NH_3])}{K_a + a_H^+} \tag{5}$$

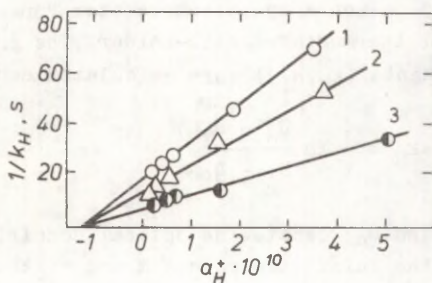$$\frac{1}{k_H} = \frac{1}{k_1 + k_2 [NH_3]} + \frac{a_H^+}{K_a(k_1 + k_2 [NH_3])} \tag{6}$$

Fig. 3. Dependence of $1/k_H$ on a_H^+ at free ammonium concentration $(mol \cdot l^{-1})$: 1-0, 2-0.1, 3-0.22.

In Fig. 3, are given the dependences on the activity of a_H^+ hydrogen ions in the $1/k_H$ coordinates at various ammonium concentrations. The interception of straight lines in a point on the abscess axis is numerically equal to the constant of (II^{*}) dissociation complex $(K_a = (7.4 \pm 1.1) \cdot 10^{-11}$ or $pK_a = 10.10 \pm 0.15)$. In Fig. 3, straight line 1, in the case of the zero free concentration of ammonium in - tercepts a section of the ordinate axis numerically equal to the rate constant of intraspheric ammonolysis $k_1 = (6.23 \pm 0.52) \cdot 10^{-2}$, which does not depend on pH. The $k_2 = 0.125 \pm$

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0.017, is calculated from straight lines 2 and 3, taking in-
to consideration the k_1 value. The latter somewhat deviates
from that found on the bases of the data of Fig. 2 (this
can be conditioned by complicated calculation by Eq. (6) .

Thus, the process of oxidizing ammonolysis of Cu^{2+} in
the ammonium buffer results from the rapid oxidation of (I)
with the formation of the (II^*) complex, whose slow rota -
tion proceeds in two parallel flows: the intramolecular am-
monolysis and base-catalyzed ammonium one..

Experimental

The process was controlled spectrophotometrically ac -
cording to the decrease in the 2,6,8-trioxypurine absorption
(λ = 293 nm); and to the accumulation of the reaction pro-
duct (λ = 265 nm) on a spectrophotometer "Spectromom-204"
with a special thermostated cell-holder. The pseudofirst or-
der rate constants (k_H, s^{-1}) were calculated according to (7)

$$k_H = \frac{1}{t} \ln \frac{D_o - D_\infty}{D_t - D_\infty}, \tag{7}$$

where D_o, D_t and D_∞ denote the optical densities of the
solutions at the inial time moment t and at the moment of
termination.

Uric acid marked "pure", twice recrystallized from
water, cupric chloride and ammonium chloride marked "che -
mically pure" were used. Ammonium was purified as described
in[16]. 1-Amino-5-ureidohydantoin was obtained and purified
according to methods[17]. In the reaction mixture, 1-amino-
5-ureidohydantoin was determined by means of thin-layer chro-
matography in the system of butyl alcohol-acidic acid-water
(2 : 1 : 1), as described in paper[18].

The reaction was carried out at 25^oC in ammonium buf -
fer in the pH range 8.5 $\pm$ 10.8. The pH value was kept con-
stant during the ammonium concentration change. by maintain-
ing the stability of the NH_4^+/NH_3 ratio. The ionic strength
of the solution was supported with monomolar potassium chlo-

ride.

In order to change the pH, a pH-meter of "Radelkis OP-211" was applied. The initial concentrations of the rea - gents were as follows: cupric chloride - $7 \cdot 10^{-4} + 2 \cdot 10^{-2}$ mol $\cdot$ 1^{-1}, ammonium - $1.1 \cdot 10^{-2} \div 0.6$ mol $\cdot$ 1^{-1}, ammonium chloride - $2.2 \cdot 10^{-2} \div 0.1$ mol $\cdot$ 1^{-1}, 2,6,8-trioxypurine - $5 \cdot 10^{-5}$ mol $\cdot$ 1^{-1}.

The ammonium fraction in the basic form (α) was found according to the Henderson-Hasselbach equation (8), using known[19] ammonium basicity constants in 1M KCl at 25° C ($pK_a = 9.21$).

$$pH = pK_a + \log \frac{\alpha}{1 - \alpha} \qquad (8)$$

Table 1

Effeots of Cu^{2+} Concentration and Medium pH on the Rate Constants of 2,6,8-Trioxypurine Oxidizing Conversion in Ammonium Buffer, 25°C

No	pH	$[NH_3],$ mol $\cdot$ 1^{-1}	$[Cu^{2+}] \cdot 10^3$ g $\cdot$ ion $\cdot 1^{-1}$	$k_H \cdot 10^2,$ s^{-1}
1	8.70	0.01	0.43	0.60 ± 0.02
2	8.70	0.01	0.80	0.58 ± 0.01
3	8.70	0.01	1.70	0.63 ± 0.01
4	9.80	0.16	1.70	4.72 ± 0.10
5	9.80	0.16	5.00	4.13 ± 0.07
6	9.80	0.16	9.77	4.36 ± 0.05
7	9.80	0.16	17.00	4.88 ± 0.08
8	10.80	0.43	1.25	12.2 ± 0.3
9	10.80	0.43	2.50	11.8 ± 0.3
10	10.80	0.43	5.00	11.8 ± 0.2
11	10.80	0.43	10.00	12.4 ± 0.2
12	10.80	0.43	17.00	11.7 ± 0.2

Table 2

Effect of Ammonium Buffer (b) Concentration on k_H
Values at pH 8.7; 9.8 and 10.8, 25°C.

No	pH	$[Cu^{2+}] \cdot 10^3$, $g \cdot ion \cdot l^{-1}$	$[b] \cdot 10^1$, $mol \cdot l^{-1}$	$k_H \cdot 10^2$, s^{-1}
1	8.70	1.7	0.8	0.63 ± 0.01
2	8.70	1.7	1.5	0.66 ± 0.02
3	8.70	1.7	2.0	0.73 ± 0.01
4	8.70	1.7	3.0	0.87 ± 0.01
5	9.80	1.7	1.4	2.93 ± 0.13
6	9.80	1.7	2.6	4.72 ± 0.13
7	9.80	1.7	5.7	6.60 ± 0.11
8	9.80	1.7	6.9	7.70 ± 0.39
9	10.80	5.0	2.5	8.40 ± 0.18
10	10.80	5.0	4.5	12.70 ± 0.15
11	10.80	5.0	5.4	13.30 ± 0.56
12	10.80	5.0	6.9	15.60 ± 0.49

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6

BASICITY AND STRUCTURE OF N-ALKYL- AND
N, N-DIALKYL ANILINES

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It is shown on the basis of the UV-spectra
(taken in hexane) and basicity constants (measured
in aqueous solutions) of aniline and its N-alkyl-
and N,N-dialkyl derivatives that the stepwise
substitution of alkyl radicals for the hydrogen
atoms of amino group leads to jump-like structural
changes of the amino group and, hence, the nature
of the lone electron pair of nitrogen atom. The
changes taking place enhance the conjugation of
alkyl- and dialkyl amino groups with the π-sys-
tem of phenyl ring, the aniline, N-alkyl and N,N
-dialkyl aniline derivatives fall on correlation
lines

$$pK_{BH}^+ = pK_{BH}^{o}{}^+ + \rho \sigma^- .$$

It has been shown in[1] that the increase of conjugation
of the lone electron pair of the nitrogen atom of methyl-
and dimethyl amino groups with the phenyl cycle π-system is
accompanied by the increase of the attenuation of electronic
substituent effects (ρ) in the ring into the basicity con-
stants in N-methyl and N,N-dimethylaniline series, if com-
pared with aniline derivatives.

In connection with the aforesaid, it was possible to
find out how the obtained regularities change in the case of

lengthening and branching of alkyl radicals at the nitrogen atom.

In order to get such data, in the present work, the basicity constants of the derivatives of N-ethyl and N,N -diethyl anilines, given in literature[2] and those for substituted N-isopropyl and N,N-diisopropyl anilines (Table 1) measured by the author (spectrophotometric method, wa - ter), as well as the data of the UV-spectra of the N-alkyl and N,N-dialkyl anilines have been used.

Table 1

Basicity Constants ($pK_{BH}+$) of Derivatives of N-iso- propyl and N,N-diisopropyl Anilines, $T = 298$ K

X in $XC_6H_4NHC_3H_7-iso$	$pK_{BH}+$	X in $(XC_6H_4N(C_3H_7-iso)_2$	$pK_{BH}+$
H	5.54	H	8.20
	5.77[3]		8.14[2]
m-CH$_3$	5.80	n-CH$_3$	8.59
m-Br	4.33	n-Cl	7.51
n-NO$_2$	1.21	n-Br	7.42
	1.32[3]	m-Br	6.94

Table 2 presents the parameters of correlation equa - tions $pK_{BH}+ = pK_{BH}^o+ + \rho\sigma^-$ for the N-ethyl, N-isopropyl, N,N -diethyl, and N,N-diisopropyl anilines. For comparison , ρ values in similar correlations of the aniline, N-methyl, and N,N-dimethyl anilines are given.

According to the correlation analysis data, only in the N,N-diisopropyl aniline the attenuation of the elec - tronic effects of substituents coincide with that of ani - line. In all other cases it is much higher. In the series of N-alkyl substituted anilines the N-isopropyl aniline has the highest conductivity of substituent effects, i.e. the branched hydrocarbon radical leads to more substantial changes of the amino group structure than usual. The fact that the isopropyl amino group can be characterized by the

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highest δ_R^o-constant values, exceeding those of other alkyl amino groups[7] also testifies this.

Table 2

Parameters of Correlation Dependences $pK_{BH}^+ = pK_{BH}^o{}^+ + \rho\delta^-$ of N-Alkyl and N,N-Dialkyl Anilines

Series	$pK_{BH}^o{}^+$	$-\rho$	s_{tot}	r	n
$XC_6H_4NH_2$		$2.767[4]$			
		$2.89[5]$			
		$2.82[6]$			
$XC_6H_4NHCH_3$		$3.56[1]$			
$XC_6H_4NHC_2H_5$	5.06 ± 0.03	3.24 ± 0.05	0.05	0.999	4
$XC_6H_4NHC_3H_7-iso$	5.59 ± 0.06	3.59 ± 0.09	0.09	0.999	4
$XC_6H_4N(CH_3)_2$		$3.64[1]$			
		$3.56[4]$			
$XC_6H_4N(C_2H_5)_2$	6.51 ± 0.06	3.71 ± 0.11	0.13	0.999	5
$XC_6H_4N(C_3H_7-iso)_2$	8.12 ± 0.02	2.94 ± 0.10	0.05	0.998	5

In Table 3 are given the λ_{max} and ε_{max} values of the p-bands of the UV spectra of aniline and its N-alkyl and N,N-dialkyl substituents in hexane solution.

It follows from these data that in the case of the introduction of alkyl groups, takes place the bathochromic shift of the p-band at the nitrogen atom in anilines, in the course of which the intensity of the band is increasing. The latter gives evidence of the strengthening conjugation of alkyl and dialkyl groups with the phenyl ring in comparison with the amino group conjugation[8].

Table 3 shows rather clearly that jump-like changes of the λ_{max} and ε_{max} values can be noticed after each successive substitution of the alkyl radical for the hydrogen atom of the amino group, and they do not actually depend on the alkyl nature.

In this respect, the exceptions are N-isopropyl and N,N-diisopropyl anilines. Among N-alkyl anilines, N-isopropyl

aniline has the highest ε_{max} value of the p-band. As to the p-band intensity for N, N-diisopropyl aniline, it is much lower than that for the other N, N-dialkyl anilines , the ε_{max} of the band being close to that of aniline.

We can suppose that there are two, almost equally strong though opposite, factors which influence the conjugation of the diisopropyl amino group with the π-system phenyl ring. On the one hand, the steric effect of isopropyl radicals worsens conjugation conditions, on the other hand, this steric effect favors the $sp^3 \longrightarrow sp^2$ rehybridization of the atomic orbitals of nitrogen; since the amino group structure becomes more planar-like and the p-character of the lone electron pair is expressed more clearly, there will be better conditions for conjugation.

As the increase in the conductivity of the substituent effects in the case of transition from the aniline series to that of N-alkaline and N,N-dialkyl anilines as well as the enhancement of the intensity of the UV-spectral p-bands of these compounds in comparison with aniline results from the improved conjugation between the alkyl and dialkyl amino groups and the π-system of the phenyl ring (the 6_R^o constants of alkyl and dialkyl amino groups also confirm the fact[7]), we can, evidently, draw the conclusion that the introduction of two isopropyl groups in the vicinity of the nitrogen atom leads to a somewhat perturbed conjugation. According to the data of[9], the diisopropyl amino group deviates by 24° from the phenyl ring plane.

It should be mentioned that in the succession of aniline, N-alkyl, and N,N-dialkyl aniline, the increase of ε_{max} is more remarkable in the case of aniline transition to N-alkyl anilines, i.e. if the first alkyl group is introduced, and not at the transition from N-alkyl to N.N-dialkyl derivatives on aniline.

Consequently, the substitution of any of hydrogen atoms of the amino group by the alkyl radical remarkably changes its structure. This statement was previously expressed in[1] where it was based on the analysis of the $pK_{BH}+ = pK_{BH}^o+ + \rho 6^o$ dependences in the series of aniline.

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Table 3

Data of UV-Spectra of Aniline and its N-Alkyl- and
N,N-Dialkyl Derivatives (Hexane)

Compound	λ_{max}, nm	ε_{max}	Compound	λ_{max}, nm	ε_{max}
$C_6H_5NH_2$	234	8 600	$C_6H_5(CH_3)_2$	251	15 800
$C_6H_5NHCH_3$	243	12 800	$C_6H_5N(C_2H_5)_2$	260	16 000
$C_6H_5NHC_2H_5$	245	12 900	$C_6H_5N(C_3H_7)_2$	258	16 000
$C_6H_5NHC_3H_7$	245	13 000	$C_6H_5N(C_3H_7\text{-iso})_2$	263	9 400
$C_6H_5NHC_3H_7\text{-iso}$	246	13 400	$C_6H_5N(C_4H_9)_2$	261	16 300
$C_6H_5NHCH_2C_6H_5$	244	12 600	$C_6H_5N(CH_2C_6H_5)_2$	251	16 000

N-methyl and N,N-dimethyl aniline derivatives.

The data of the present paper and those given in lite-
rature (see[1] and the references therein) refer to the fact
that the conjugation of alkyl and dialkyl amino groups   is
improved exceeding that of amino group. Thus, the basicity of
N-alkyl and N, N-dialkal anilines should be higher than   it
has been observed experimentally, but lower than the aniline
basicity.

One possible approach to explain the basicity   increase
in the case of transition from aniline to N-alkyl and N,N-
dialkyl aniline might be as follows: the intensification   of
the p-character of the lone electron pair of the nitrogen
atom, taking place thanks to the $sp^3 \longrightarrow sp^2$-rehybridization
in the case of the substitution of the amino group hydrogen
atoms by the alkyl radicals prevails over the delocaliza -
tion of the pair to the phenyl ring.

A sharp increase of the N,N-diisopropylaniline basici-
ty is most probably connected with a greater than usual in-
crease of the p-character of the lone electron pair on the one
hand, and with a certain breaking of the diisopropyl amino
group conjugation with the π-system of phenyl ring, on the
other hand.

Thus, the results of the correlation analysis of equation $pK_{BH}+ = pK^o_{BH}+ + \rho\delta^-$ (the basicity constants were mea - sured in water), the data of the UV spectra (in hexane) and the data on the δ^o_R substituent constants (found on the basis of the IR-spectra, measured in chloroform) published earlier[7] show that at the transition from aniline to N-alkyl and N,N-dialkyl aniline in the amino group structure, the character of the lone electron pair of the nitrogen atom changes drastically under the influence of alkyl radicals . The changes taking place appear in various physicochemical properties of the molecules of different solvents. These changes, actually, are the factors which determine that the derivatives of aniline, N-alkyl, and N,N-dialkyl anilines form separate correlation series, while the alkyl- and di - alkylamino group conjugation with the phenyl cycle π-system improvement,in comparison with that of amino group has been observed.

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REACTIVITY OF DERIVATIVES OF PHENYLANTHRANILIC ACID
VI. KINETICS OF ALKALINE HYDROLYSIS REACTION OF DE-
RIVATIVES OF ß-DIETHYLAMINOETHYL ESTER OF 4-CHLORO-
N-PHENYLANTHRANILIC ACID IN BINARY DIOXAN - WATER
SOLVENT

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The present paper is aimed to study the kine-
tics of the alkaline hydrolysis reaction of eight
ß-diethylaminoethyl ester derivatives of 4-chloro-
N-phenylanthranilic acid in binary solvent dioxan-
water within temperature range of 298-358 K. Bimo-
lecular reaction rate constants have also   been
found. As it was established, the reaction series
is in agreement with the equations of Hammett and
Arrhenius. Calculated thermodynamic activation pa-
rameters refer to the synchronic character of   al-
kaline hydrolysis reactions of esters. The isoki -
netic relationship should hold in the case of the
enthalpic control type. The isokinetic temperature
ß = 651 K. Multiple regression analysis has   been
applied to calculate the two-parameter correlation
equation with a cross term, isoparametric values of
the parameters being correlated have also   been
found.

In order to continue the studies on the reactivity[1,2] of biologically active derivatives of phenylanthranilic acid, the kinetics of alkaline hydrolysis of the ß-diethylamino - ethyl ester of 4-chloro-N-phenylanthranilic acid in the binary dioxan-water solution, containing 60 vol. % of dioxan has been studied in temperature range 298-358 K.

Reaction rate constants were calculated on the basis of variation of nucleophilic concentration (OH^-) in time. The methods of kinetic measurement were described in[1].

Table 1

Derivatives of ß-diethylaminoethylic Ester of 4-Chloro-N-Phenylanthranilic Acid
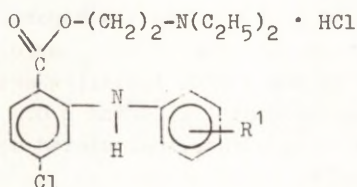
R^1	Melting point ^oC	% N found	Brutto formula	% N Calculated	R_f
H	108-109	7.2	$C_{19}H_{24}Cl_2N_2O_2$	7.3	0.58
4^1-Cl	181-182	6.9	$C_{19}H_{23}Cl_3N_2O_2$	6.7	0.63
4^1-CH_3	104-105	8.0	$C_{20}H_{26}Cl_2N_2O_2$	7.7	0.60
$3^1,4^1$-CH_3	158-159	6.9	$C_{21}H_{28}Cl_2N_2O_2$	6.8	0.66
4^1-OCH_3	102-103	6.2	$C_{20}H_{26}Cl_2N_2O_3$	6.3	0.51
2^1-Cl	161-162	6.8	$C_{19}H_{23}Cl_3N_2O_2$	6.7	0.61
2^1-CH_3	146-147	7.9	$C_{20}H_{26}Cl_2N_2O_2$	7.7	0.59
2^1-OCH_3	143-144	6.6	$C_{20}H_{26}Cl_2N_2O_3$	6.3	0.56

The reaction follows the second order kinetic equa - tion:

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$$\frac{dx}{dt} = k(a - x)(b - x) \qquad (1)$$

where   a, b — the corresponding initial concentrations of
                 ester and alkali (mol/l);

        x — current concentration of the reaction pro -
              duct (mol/l) at time moment t (sec);
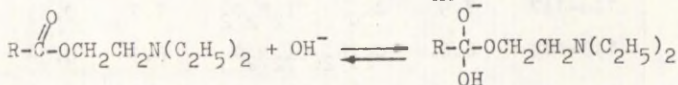
        k — reaction rate constant (1/mol sec).

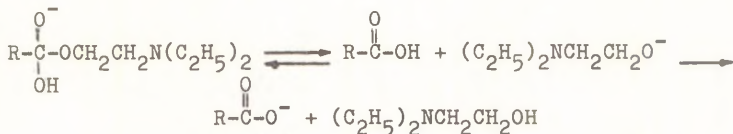The integration of Eq. (1) enables us to obtain   the
formula for calculating k:

$$k = \frac{1}{t(b-a)} \ln \frac{a(b-x)}{b(a-x)} \qquad (2)$$

The value of k is corrected by the expansion of the
solvent's volume during the temperature change from $25^{o}C$ to
$t^{o}C$, multiplying it by the d_{25}/d_t factor, where d_{25}, d_t de-
note the solvent densities at $25^{o}C$ and $t^{o}C$.

The reaction rate constants, calculated according   to
Eq. (2) and corrected by the expansion of the solvent's vol-
ume at various nucleophile substrate ratios remain stable
within the experiment error. Consequently, the reaction is
of the second order.

The values of rate constants of the reaction series are
determined by the substituent nature and position in the non-
anthranilic molecule fragment (Table 2). After the indroduc-
tion of donor substituents into the ester molecule, the k
values drop, the acceptor substituents favor the accelera -
tion of alkaline hydrolysis, i.e. they stabilize the anion
of 4-chloro-N-(R-phenyl) anthranilic acid on the expence of
a more significant charge delocalization. This leads to the
supposition that the alkaline hydrolysis of the studied es-
ters proceeds according to the $B_{AC}2$ mechanism:

$$R-\overset{\overset{O}{\|}}{C}-OCH_2CH_2N(C_2H_5)_2 + OH^- \rightleftharpoons R-\overset{\overset{O^-}{|}}{\underset{OH}{C}}-OCH_2CH_2N(C_2H_5)_2$$

$$R-\underset{\underset{OH}{|}}{\overset{\overset{O^-}{|}}{C}}-OCH_2CH_2N(C_2H_5)_2 \rightleftharpoons R-\overset{O}{\overset{\|}{C}}-OH + (C_2H_5)_2NCH_2CH_2O^- \longrightarrow$$

$$R-\overset{O}{\overset{\|}{C}}-O^- + (C_2H_5)_2NCH_2CH_2OH$$

The quantitative estimation of the substituent effect on the reactivity of esters is based on the Hammett equation:

$$\log k = \log k_o + \rho\sigma \tag{3}$$

The data obtained via the selective separate correlation for the 4^1- and 2^1-derivatives of ß-diethylamino ethyl ester of 4-chloro-N-phenylanthranilic acid, the values of the $\log k_o$ parameters and ρ turned out to be statistically identical. Therefore, an additional data correlation for 4^1 and 2^1- derivatives (Table 3) has been done. The correla - tion for 2^1-derivatives is probably connected with a re- lative remoteness of the substituents from the reaction cen- ter. The data of Table 3 evidence about the applicability of the Hammett equation to the reaction series studied. The ρ value is positive, thus once again confirming the exis - tence of the $B_{AC}2$-mechanism of alkaline hydrolysis of the esters studied. A negligible ρ value refers to the rela - tively low sensitivity of the substrate's electron system to structural changes, which is probably connected with either the remoteness of the substituents from the reaction center or with the isolating effect of the NH bridge group[3]. It is worth mentioning that the ρ value of the reaction se- ries studied, almost coincides with the ρ of the alkaline hydrolysis of both 4^1-derivatives of ß-dimethylamino ethyl ester of 4-chloro-N-phenylanthranilic acid[1] as well as with that of methyl ester derivatives of 4-nitro-N-phenylanthra- nilic acid. Consequently, the reaction mechanisms of these reactions are of the same type. The ρ value is decreasing with temperature increase.

The polyterms of rate constant logarithms are linear.

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Table 2

Rate Constants of Alkaline Hydrolysis of ß-diethylamino Ethyl Ester Derivatives of 4-Chloro-N-Phenylanthranilic Acid in Dioxan - Water Mixture at Various Temperatures

R^I \ T,K	$k \cdot 10^4$ 1 mol^{-1} s^{-1}						
	298	308	318	328	338	348	358
H	2.32 ± 0.04	3.62 ± 0.02	6.28 ± 0.08	10.31 ± 0.12	16.84 ± 0.15	26.20 ± 0.22	40.17 ± 0.24
4^1-Cl	6.86 ± 0.07	10.00 ± 0.09	16.3 ± 0.08	25.30 ± 0.14	39.10 ± 0.09	58.00 ± 0.15	84.70 ± 0.17
4^1-CH$_3$	1.41 ± 0.05	2.27 ± 0.05	4.05 ± 0.06	6.82 ± 0.03	11.40 ± 0.09	18.21 ± 0.08	28.43 ± 0.11
$3^1,4^1$-CH$_3$	1.15 ± 0.06	1.88 ± 0.03	3.38 ± 0.04	5.76 ± 0.04	9.72 ± 0.07	15.73 ± 0.07	24.70 ± 0.14
4^1-OCH$_3$	1.06 ± 0.04	1.73 ± 0.06	3.14 ± 0.04	5.37 ± 0.08	9.10 ± 0.05	14.71 ± 0.08	23.24 ± 0.12
2^1-Cl	4.16 ± 0.11	9.03 ± 0.09	10.60 ± 0.21	16.80 ± 0.18	25.52 ± 0.07	40.20 ± 0.09	60.05 ± 0.22
2^1-CH$_3$	1.36 ± 0.05	2.30 ± 0.07	4.11 ± 0.11	6.76 ± 0.09	12.03 ± 0.11	18.07 ± 0.16	27.80 ± 0.19
2^1-OCH$_3$	0.74 ± 0.08	1.33 ± 0.09	2.32 ± 0.12	4.03 ± 0.21	6.82 ± 0.17	11.36 ± 0.19	18.23 ± 0.16

Table 3

The Hammett Equation Parameters of Alkaline Hydro-
lysis of β-Diethylamino Ethylic Ester of 4-Chloro-
N-Phenylanthranilic Acid in the Binary Dioxan - Wa-
ter Solvent at Various Temperatures

T,K	ρ	$\log k_o$	r	s
298^a	1.278 ± 0.026	-3.638 ± 0.032	0.9953	0.0320
298^b	1.272 ± 0.003	-3.634 ± 0.003	0.9976	0.0049
298^c	1.276 ± 0.008	-3.636 ± 0.010	0.9961	0.0124
308^a	1.192 ± 0.033	-3.412 ± 0.029	0.9967	0.0597
308^b	1.193 ± 0.005	-3.441 ± 0.004	0.9994	0.0011
308^c	1.193 ± 0.011	-3.324 ± 0.012	0.9983	0.0241
318^a	1.115 ± 0.008	-3.199 ± 0.010	0.9994	0.0084
318^b	1.121 ± 0.004	-3.202 ± 0.004	0.9983	0.0073
318^c	1.118 ± 0.005	-3.200 ± 0.006	0.9991	0.0077
328^a	1.052 ± 0.010	-2.987 ± 0.013	0.9976	0.0124
328^b	1.055 ± 0.002	-2.987 ± 0.021	0.9965	0.0051
328^c	1.054 ± 0.002	-2.987 ± 0.016	0.9971	0.0084
338^a	0.989 ± 0.041	-2.770 ± 0.051	0.9991	0.0106
338^b	0.992 ± 0.009	-2.775 ± 0.004	0.9962	0.0076
338^c	0.991 ± 0.001	-2.772 ± 0.021	0.9981	0.0820
348^a	0.932 ± 0.008	-2.589 ± 0.010	0.9989	0.0121
348^b	0.933 ± 0.002	-2.582 ± 0.003	0.9973	0.0087
348^c	0.933 ± 0.006	-2.587 ± 0.005	0.9983	0.0091
358^a	0.882 ± 0.016	-2.399 ± 0.020	0.9975	0.0042
358^b	0.879 ± 0.008	-2.397 ± 0.011	0.9985	0.0055
358^c	0.881 ± 0.011	-2.398 ± 0.014	0.9985	0.0051

a - data for 2^1-derivatives were correlated

b - data for 4^1-derivatives were correlated

c - data for 2^1, 4^1-derivatives were correlated

This was proved also by high correlation coefficient values and by the test based on the Fischer F-criterion. Thus,using the Arrhenius equation,

$$\ln k = \ln A - \frac{E_A}{RT}$$ (4)

it was possible to find the activation energy E_A and the pre-expotential factor A (Table 4).

Table 4

Kinetic Activation Parameters (E_A and $\ln A$) of Alkaline Hydrolysis of Derivatives of ß-Diethyl-amino Ethyl Ester of 4-Chloro-N-Phenylanthrani-lic Acid in Dioxan - Water Mixture

R^I	E_A kcal/mol	$\ln A$	r	s
H	$10.22^{\pm}0.13$	$8.82^{\pm}0.31$	0.9939	0.0035
4^1-Cl	$9.03^{\pm}0.13$	$7.90^{\pm}0.32$	0.9991	0.0036
4^1-CH$_3$	$10.76^{\pm}0.12$	$9.24^{\pm}0.30$	0.9949	0.0034
$3^1,4^1$-CH$_3$	$10.98^{\pm}0.43$	$9.41^{\pm}0.30$	0.9990	0.0033
4^1-OCH$_3$	$11.07^{\pm}0.13$	$9.47^{\pm}0.32$	0.9962	0.0035
2^1-Cl	$9.02^{\pm}0.35$	$7.53^{\pm}0.09$	0.9969	0.0069
2^1-CH$_3$	$10.80^{\pm}0.11$	$9.29^{\pm}0.26$	0.9974	0.0070
2^1-OCH$_3$	$11.06^{\pm}0.23$	$9.21^{\pm}0.57$	0.9973	0.0076

Introduction of electron-acceptor substituents into the mo-lecule leads to the decrease in the energy activity, while the electron-donor substituents arise the opposite effect. The $\ln A$ value undergoes analogous changes. But the relation-ships $E = a_1 + b_1\bar{0}$ and $\ln A = a_2 + b_2\bar{0}$, studied by means of the regression analysis, appeared to be statistically doubt-ful.

Activation enthalpy ($\Delta H^{\neq}$) and entropy ($\Delta S^{\neq}$) were calculated according to the Eyring equation:

$$\ln \frac{k}{T} \cdot \frac{h}{K} = \frac{\Delta S^{\neq}}{R} - \Delta H^{\neq} \frac{1}{RT} \tag{5}$$

Free activation energy ($\Delta G^{\neq}$) was calculated by the second start of thermodynamics. These data are found in Table 5.

Table 5

Thermodynamic Activation Parameters of Alkaline Hydrolysis of Derivatives of ß-Diethylamino Ethyl Ester of 4-Chloro-N-Phenyl Anthranilic Acid in Dioxan - Water Mixture

R^1	$\Delta H^{\neq}$ kcal/mol	$-\Delta S^{\neq}$ e.u.	r	S	$\Delta G^{\neq}$ 298 K kcal/mol
H	9.57 ± 0.12	43.2 ± 1.1	0.9964	0.0067	22.4
4^1-Cl	8.39 ± 0.13	45.0 ± 0.3	0.9990	0.0036	21.8
4^1-CH_3	10.11 ± 0.12	42.3 ± 0.3	0.9985	0.0033	22.7
$3^1, 4^1$-CH_3	10.34 ± 0.12	42.0 ± 2.9	0.9994	0.0032	22.9
4^1-OCH_3	10.42 ± 0.14	41.9 ± 3.0	0.9972	0.0034	22.9
2^1-Cl	8.37 ± 0.34	45.7 ± 0.4	0.9966	0.0095	22.0
2^1-CH_3	10.15 ± 0.60	42.2 ± 1.4	0.9971	0.0028	22.7
2^1-OCH_3	10.71 ± 0.22	41.6 ± 0.6	0.9971	0.0063	23.1

The negative value of activation entropy has been confirmed by the $B_{AC}2$ mechanism of alkaline hydrolysis of esters. High absolute activation entropy values suggest the formation of a highly symmetric intermediate. The activation enthalpy values prove the synchronism of the reaction. The substituent effect in the substrate molecule on the $\Delta H^{\neq}$ and $\Delta S^{\neq}$ values nature is similar to their influence on the E_A and ln A. Nevertheless, the hypothesis about the li-

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nearity of relationships $\Delta H^{\neq} - f(\sigma)$, $\Delta S^{\neq} - f(\sigma)$ cannot be proved statistically. Free activation energy $\Delta G^{\neq}$ tends to increase when the donor substituents are conducted into the substrate molecule; but the changes are not significant.

The mutually exciting influence of both parameters (σ-substituent constants and temperature T) was quantitatively estimated using the equation with a cross term[3]:

$$f(x_1 x_2) = f_o + a_1 x_1 + a_2 x_2 + a_{12} x_1 x_2 \qquad (6)$$

where a_o, a_1, a_2, a_{12} are the constants characterizing the reaction series sensitivity to the effect of interacting parameters.

In order to find the constants of Eq. (6), the mul - tiple regression analysis using the algorithm given in[4] has been applied[4]. The statistical significance of the obtained results was assessed by the Fischer F-criterion. The calculations were conducted on a computer ES-1045. The data are presented in Table 6.

Table 6

Values of Susceptibility Constant of Eq. (6) and the Isoparametric Values (IPV) of Parameters Correlated

Equation parameters	Variable or cross term	Sensitivity factor	Numeric Value of sensitivity factor	IPV
f	log k		3.825 ± 0.017	$\beta = 646$
x_1	σ	a_1	-1.088 ± 0.039	$x_1 = 3.17$
x_2	$I/T \cdot 10^3$	a_2	-2.231 ± 0.035	$x_2 = 1.55$
$x_1 x_2$	$\sigma \cdot I/T \cdot 10^3$	a_{12}	0.703 ± 0.017	

Well-known formulae[5] were employed to calculate the IPV:

$$x_1 = -a_2/a_{12} \qquad x_2 = -a_1/a_{12} \qquad \beta = -a_{12}/a_1 \cdot 10^3 \tag{7}$$

It should be mentioned that the IPV found for the al - kaline hydrolysis reaction of the derivatives of ß-diethyl- aminoethyl ester of 4-chloro-N-phenyl anthranilic acid are identical with those for the same reaction of ß-dimethyl - amino ethyl ester derivatives of 4-chloro-N-phenylanthra - nilic acid.

It follows from the data of Table 6 that in this case the reaction is in agreement with the isokinetic correlation principle. The value of isokinetic temperature calculated according to (7) is practically identical with the ß values, calculated according to equation[5] (Table 7):

$$\log k_{T_2} = \text{const} + x \log k_{T_1} \tag{8}$$

Table   7

Determination of Isokinetic Temperature of Alkaline Hydrolysis Reactions of ß-Diethylamino Ethyl Ester Derivatives of 4-Chloro-N-Phenylanthranilic Acid

Temperature, K		x	r	s	ß,K
T_1	T_2				
298	318	0.881	0.9969	0.0061	634
298	338	0.780	0.9992	0.0075	645
298	358	0.691	0.9989	0.0045	650
318	338	0.885	0.9940	0.0047	655
318	358	0.784	0.9976	0.0081	658
338	358	0.886	0.9981	0.0035	661

$\bar{\beta} = 651$

The applicability of isokinetic correlation in the case of the reaction studied was once again tested by the ex - istence of linear correlation $\Delta H^{\neq} - \log k_T$, $\Delta H^{\neq} - \Delta s^{\neq}$, $E_A - \log A$, $\varrho - 1/T$ (Table 8).

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Table 8

Determination of Isokinetic Temperature. Correlation Parameters of Eq. $y = a + bx$ of Relationship of Kinetic and Activation Parameters of Alkaline Hydrolysis Reactions of ß-Diethylamino Ethyl Ester Derivatives of 4-Chloro-N-Phenylanthranilic Acid

x	y	a	b	r	s	ß,K
$\log k_{298}$	$\Delta H^{\neq}$	$(0.458\pm0.027) \cdot 10^3$	$(-2.51\pm0.05) \cdot 10^3$	0.9989	0.047	653
$\log k_{308}$	$\Delta H^{\neq}$	$(0.370\pm0.032) \cdot 10^3$	$(-2.67\pm0.03) \cdot 10^3$	0.9997	0.055	651
$\log k_{318}$	$\Delta H^{\neq}$	$(0.460\pm0.024) \cdot 10^3$	$(-2.84\pm0.03) \cdot 10^3$	0.9975	0.045	651
$\log k_{328}$	$\Delta H^{\neq}$	$(0.539\pm0.016) \cdot 10^3$	$(-3.03\pm0.02) \cdot 10^3$	0.9984	0.032	651
$\log k_{338}$	$\Delta H^{\neq}$	$(0.650\pm0.018) \cdot 10^3$	$(-3.21\pm0.02) \cdot 10^3$	0.9992	0.037	652
$\log k_{348}$	$\Delta H^{\neq}$	$(0.744\pm0.034) \cdot 10^3$	$(-3.42\pm0.09) \cdot 10^3$	0.9989	0.006	652
$\log k_{358}$	$\Delta H^{\neq}$	$(0.869\pm0.021) \cdot 10^3$	$(-3.63\pm0.06) \cdot 10^3$	0.9978	0.047	657
ΔS	$\Delta H^{\neq}$	$(37.6\pm0.3) \cdot 10^3$	648 ± 5	0.9972	0.167	649
$\log A$	E_A	1.201 ± 0.012	298 ± 7	0.9988	0.171	687
I/T	ρ	-1.073 ± 0.099	698 ± 8	0.9929	0.011	650

$\bar{\beta}=655$

In all cases, the dependence of the calculated corre-
lation parameters was tested by means of the Student t-test[4],
it has also been shown that all parameters are statistical-
ly valuable, their reliability exceeding 95%.

The value of ß is higher than that of the experimental
temperature range; i.e. the reaction studied belongs   to
the enthalpic type of control.

Experimental

Agents. The purification and purity level test of solvents
have been described in[1]. ß-Diethylamino esters of 4-chloro-
N-phenylanthranilic acid were synthesized using known meth-
ods[6,7]. The purity was checked by the TSH method (system
propanol-water 1 : 1), by the elemental analysis and   by
finding its melting point (Table 1).

Method[8] was applied for the preparation of the carbo-
nate-free sodium hydroxide solution.

Kinetic measurements have been described in[1]. The concen -
tration of sodium hydroxide was determined by means of po-
tentiometric titration on an pH meter EV-74 with either
glass ESP-43-074 or chlorosilver EVL-IM electrodes. Aqueous
HCl solution was used as a titrant. The kinetics of alka -
line hydrolysis reactions was studied at temperatures 25°,
35°, 45°, 55°, 65°, 75°, and $85^{o}C$. The experiments   were
repeated three times, including 6-8 measurements each (the
transformation degree amounted to 80%). The accuracy of the
obtained parameters was estimated by the statistics of small
sets (the reliability level being 0.95). The results   were
processed on a computer "Elektronika MK-52", using standard
programs[9].

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A SPECIALIZED SUBSYSTEM FOR CODING AND INPUT OF MOSAIC STRUCTURES

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Research and experimental work having been carried out during twenty years have by now re - sulted in creating the system "CIS-Tartu" at the department of organic chemistry. One component of the system is the subsystem for coding and input of mosaic structures, implementing the so called Geivandov method. The subsystem includes coding both standard and non-standard blocks. The soft- ware has been written in FORTRAN-77.

Substantial application of computers in a certain field of scientific research should be based upon a comprehensive data base. The problem is especially acute in organic che- mistry where millions of individual reactions have been studied and described.

At the department of organic chemistry of Tartu Uni - versity has been created a data bank "CIS-Tartu"[1], at pre- sent containing about 250 000 items of organic reactions . The bank contains the contents of the tables of rate and equilibrium constants issued by VINITI[2], as well as that of the supplementary volumes published by Tartu University . Since "CIS-Tartu" is first and foremost meant for theore- tical studies it takes into account specific features of

scientific research.

In the CIS-system, structural chemical objects are
presented in the form of graphs with labelled nodes and
arcs (so called ographs), thus being a generalization of
the notion of atomic structural formulae, whose data ele-
ments are the reaction ograph[6] and the parameter vectors
linked with it. Parameter vectors reflect certain reaction
procedure conditions, they also contain either a reaction
rate or an equilibrium constant (in these conditions). The
application of a common graph concept enables us to effec-
tively deal with such different objects as chemical com -
pounds, reaction equations, substituent solvents (in all
cases the ograph input language LINCS[3] can be applied) in-
ner representation[4], canonizing procedures[5], etc.

In the present paper we describe the DCOND subsystem
for coding and input of the chemical structural formulae
of cyclic compounds with conjugated bonds. The subsystem
is aimed to supplement the input language LINCS, being also
the implementation of the ring numeration by lines[6].

The blocks to be encoded by DCOND can be either stan-
dard or nonstandard. A standard block is a connected mosaic
chemical structure consisting of condenced six-membered
rings. Some of the block nodes can be labelled as exits
(see Fig. 1a) for realization of the possibility to con-
sider mosaic substructures.

A nonstandard block should be considered a modified
standard unit. The following four types of nonstandard
blocks are acceptable:

1) The nonstandard label of a node, the so-called he-
   tero atom. At the nodes of second order these la -
   bels differ from CH and at those of third order
   from C.

2) A node is linked with the other nodes of the block
   via single bonds only. Thus, this is the so called
   hydrated or saturated node. The CH2, CH and C la -
   bels are taken as the labels of the above-mentioned
   nodes of the 2nd, 3rd or 4th order, respectively .
   The DCOND also accepts the possibility of a hydra-

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ted heteroatom.
3) The cut absence of the 2nd order node.
4) Bridge - a structure with two exits added to the block, connecting two nodes of a ring.
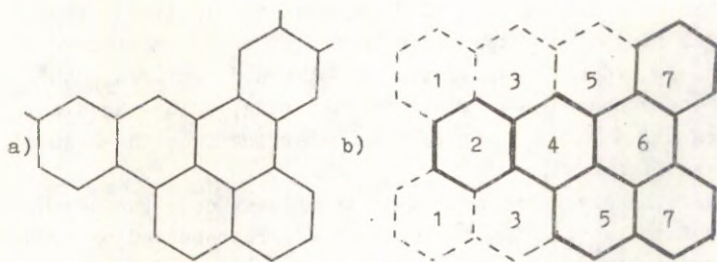
Fig. 1. A standard block with three exits (a) and an additional numbered unit (b).

An example of a nonstandard block is given in Fig. 2.
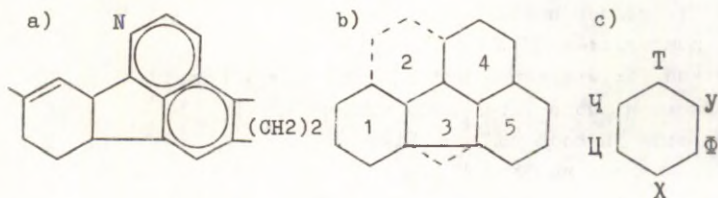
Fig. 2. A nonstandard block (a), the corresponding complemented block (b); local numeration of nodes in a ring (c).

Block coding proceeds as follows. The rings of a standard block, the modification of which is the coded block , are numbered. For that purpose, the standard block must be complemented to the left, up to the rectangular form (see Fig. 1 b, 2 b), then the rings should be numbered:odd lines, starting from the bottom 1, 3, 5...; even lines - 2, 4, 6... Actually, the linear code of a block is the list of the original ring attributes given in the order of their nume - ration. In order to locate the non-standard features, the nodes are numbered separately in each ring, using Russian letters Т,У,Ф,Х,Ц,Ч (clockwise, starting from the highest one; see Fig. 2 c).

Here is given the syntax of the linear code (using the Backus formulae), while the notions are represented by blankless word groups; the term "list" (of certain objects x) is interpreted traditionally:

$$list\_x : : = x \mid list\_x \ x$$

code_ of mosaic_ structure :: = 'COND list_ of_ring_ attributes

ring_attribute :: = ring_number exits list_of_nonstand.

ring_number :: = integer
exit :: = (node_numbers_list) | empty
node_number :: = Т | У | Ф | Х | Ц | Ч
nonstand. :: = hetero | hydro | cut | bridge | empty
hetero :: = node_label node_number
hydro :: = H node_numbers_list
cut :: = −node_numbers_list
bridge :: = node_number, LINCS − code_of_the_bridge. node_ number

In a ring attribute, nonstandard characteristics are always listed at random, but the node numbers, in the alphabetic order.

The codes of the structures (Fig. 1 a and 2 a)

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'COND   5 7 2(Ч) 4 6 7(ТУ)
'COND   1(Ч) НХЦ 3 -Х У.CH2. CH2.Ф 4 NЧ

The DCOND system translator operates according to the following scheme. The basic module is called the LINCS input information decoding system, in case there occurred the key word 'COND in the input stream. The first stage contains the input code scanning. As a result, a corresponding ograph can be compiled on the basis of the given mosaic structure code. The procedure starts from the first full ring, taking into consideration the level of the analysis of ring numbers in a code. At the same time, the previously determined links are corrected, and the nonstandard features of the ring node that are analyzed and processed in special module systems are added into the ograph storage operation area.

During the second stage, the ograph constructed in the first stage, is analyzed, and if necessary, special modules for processing various nonstandard features can be called. The following cases of nonstandards occur:

1) Exit. The processing of exits lies in the sorting of nodes: on the 1st place should be put the group of exit nodes - in turn, sorted in their order of occurrence in the given linear code. The exit node label is corrected according to the order changes.

2) Hetero atom. The standard label of the ograph node is replaced by the nonstandard input label. If the length of the label does not exceed 9 symbols, the very label is recorded instead of the standard one. In the opposite case, symbol "X" is substituted for the standard label, while the nonstandard label is recorded into the corresponding operation area.

3) Hydrated node. The standard node label correction depends on its order. Double bonds are replaced by single ones. If the hydrated node is a hetero atom, its label remains unchanged, these are only the bond levels that change.

4) <u>Cut</u>. If any of ring nodes is marked as being cut, the bonds are rearranged to eliminate the cut node from the ograph.

5) <u>Bridge</u>. On the basis of the "bridge" description can be compiled either one or several additional ograph nodes, attached to the given ring nodes, which ac - tually are the "bridge" ends. A correction of the involved nodes follows, in conformity with changes in their order.

The third, and final stage of the procedure consists in building the standard LINCS-code of the obtained ograph. For that purpose, all ograph nodes are numbered in the order of their succession. The number of each label and those of nodes being connected to the given node as well as the la - bels of these bonds are given. The address of the 1st symbol of the built LINCS-code is transmitted to the LINCS trans - lator for decoding instead of the COND-code.

The translator has been written in FORTRAN-77 and it has been implemented on a computer ND-100 of "NORSK-DATA".

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Examples of Coding of Standard Mosaic Structures
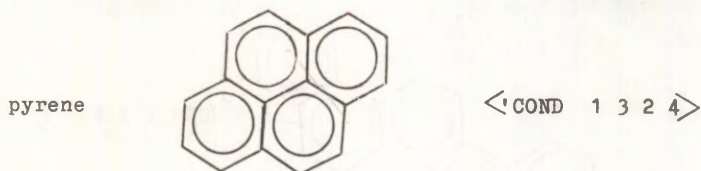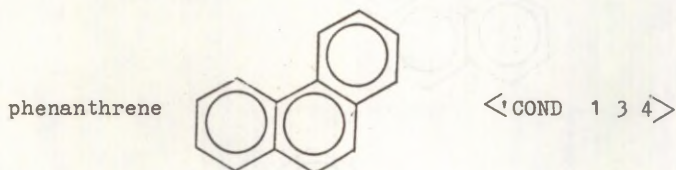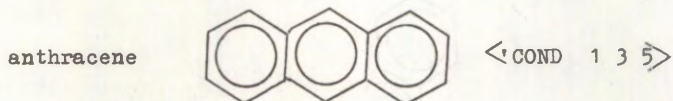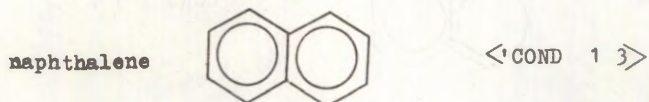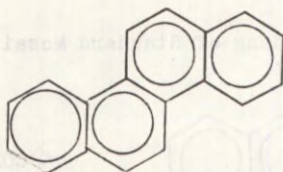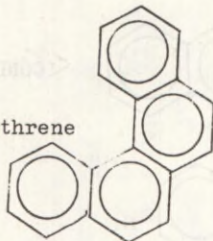
naphthalene $<$'COND 1 3$>$

anthracene $<$'COND 1 3 5$>$

phenanthrene $<$'COND 1 3 4$>$

triphenyl $<$'COND 5 2 4 5$>$

pyrene $<$'COND 1 3 2 4$>$

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chrysene ⟨COND 1 3 4 6⟩

benzo/s/phenanthrene ⟨COND 1 3 4 3⟩

benz/a/anthracene ⟨COND 1 3 5 6⟩

naphthacene ⟨COND 1 3 5 7⟩

pycene ⟨COND 1 3 4 6 7⟩

pentacene

⟨'COND 1 3 5 7 9⟩

benzo/e/
pyren

⟨'COND 5 2 4 6 5⟩

pentaphene

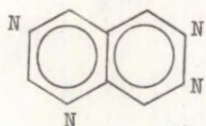⟨'COND 1 3 5 6 7⟩
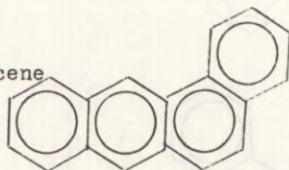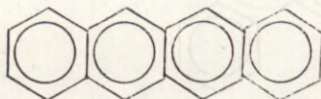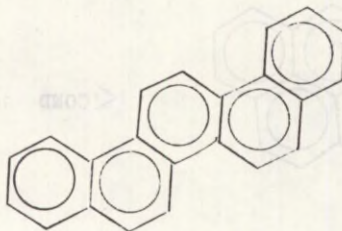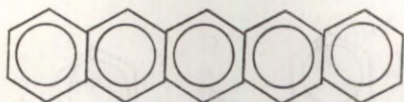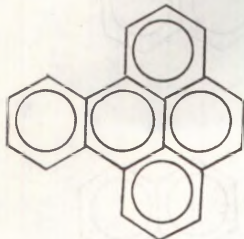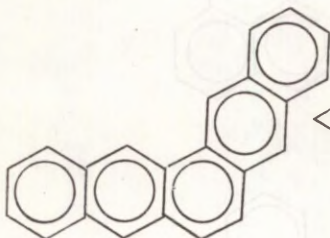
dibenzo/s,d/
phenanthrene

⟨'COND 1 3 4 1 3⟩

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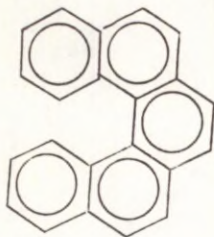
dibenzo/a,j/
anthracene

⟨'COND 3 5 7 2 8⟩
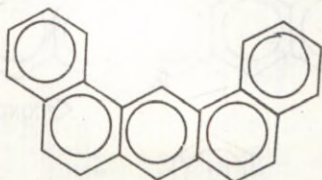
dibenzo/a,k/
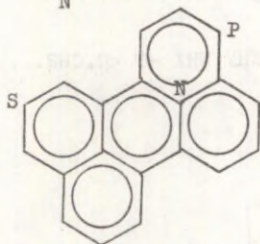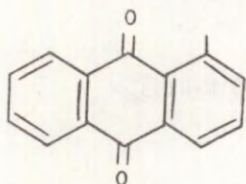perylene

⟨'COND 1 3 5 4 3 5 7⟩

perylene

⟨'COND 3 2 4 6 5⟩
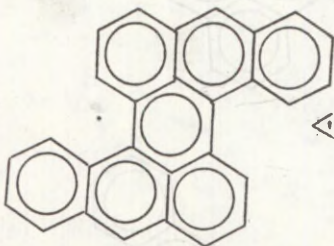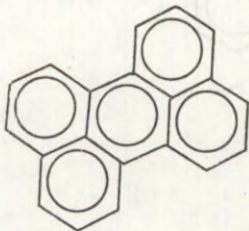
Examples of Coding of Nonstandard Mosaic Structures

⟨COND 1 NX NЧ 3 NУ NФ⟩

⟨COND 3 2 SЧ 4 NУ 6 5 PУ⟩

⟨COND 1 3 HTX COT COX 5(T)⟩

⟨COND 1(Ч) 3 -T NHX 5⟩

⟨COND 1 HTXЦЧ 3 N+HX 4 -T HУФЧ⟩
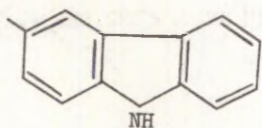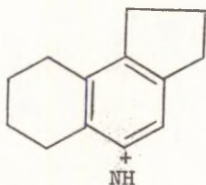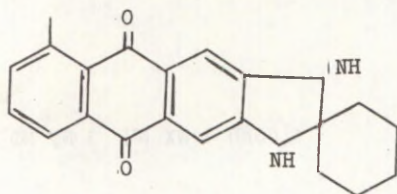
$\langle$ COND 1(T) 3 COT COX HTX 5 7 HУФX NHУ NHX -T $\langle$ C.CH2....$\rangle$ Ф $\rangle$

$\langle\!\langle$ COND 1 3(ТФ) N+HX$\rangle$[2.1] $\langle$ COND 1 (Ц) N+HX 3$\rangle\!\rangle$

$\langle$ COND 1(T) HTУФXЦЧ NX T. $\langle$ CH2.CH2$\rangle$ .X̄ $\rangle$

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MEDIUM EFFECT ON ENANTIOSELECTIVITY OF FOR-
MATION REACTIONS OF PEPTIDES AND AMIDES

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Institute of Physico-organic Chemistry and Coal Che-
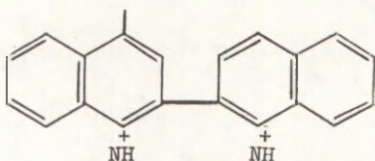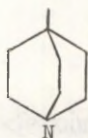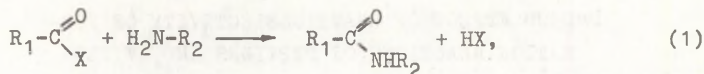mistry, Academy of Sciences of the Ukrainian SSR

Results concerning medium effect on rate of
p-nitrophenyl ester of N-carbobenzoxy-S-phenacyl
alanine reaction with racemate and enantiomers of
tertiary butyl ester of leucine have been con -
trasted with data of alkylphenylamines'acylation
reaction. We have established that there exists
ambiguity in medium effect (molar refraction of
solvent) on differences in reactivity of enantio-
mers (enantioselectivity) of amines, depending on
nature of acylating agents.

Studies devoted to the medium effect on the differences
in the reactivity of enantiomers to the chinal molecule be-
long to the means of getting a better conception of the na-
ture of enantiomeric differentiation. The information can
also be useful for finding the optimum conditions for the
kinetic decomposition of racemates via definite diastereo-
isomeric compounds.

In the present paper, we have studied the kinetics of
the reactions of p-nitrophenyl ether of N-carbobenzoxy-S-
phenylalanine with racemate and enantiomers of tertiary-bu-
tyl ester of leucine in dioxane, benzene, chlorobenzene
o-dichlorobenzene and the mixture of 50 vol. % chlorobenzene
with o-dichlorobenzene in benzonitrile. In all media stu -
died, the reaction was conducted under the conditions   of

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pseudofirst order at a manyfold excess of amino ether. In these conditions, the reaction proceeds quantiatively and irreversibly by scheme (1):

$$R_1-C\overset{\displaystyle O}{\underset{\displaystyle X}{\diagdown}} + H_2N-R_2 \longrightarrow R_1-C\overset{\displaystyle O}{\underset{\displaystyle NHR_2}{\diagdown}} + HX, \qquad (1)$$

where $R_1 = C_6H_5CH_2OCONHCHCH_2C_6H_5$;

$R_2 = (CH_3)_2CHCH_2CHCOOC(CH_3)_3$;

$X = p-O_2N-C_6H_4O-$.

The second order rate constants k_H ($1 \cdot mol^{-1} \cdot s^{-1}$), remaining the same during the whole process, reveal a significant growth, provided that the initial concentration of amino ester b ($mol \cdot 1^{-1}$) increases, being in keeping with Eq. (2),

$$k_H = k_2 + k_3b \qquad (2)$$

where k_2 ($1 \cdot mol^{-1} \cdot s^{-1}$) denotes the rate constant of noncatalytic order; k_3 ($1^2 \cdot mol^{-2} \cdot s^{-1}$) is the rate constant of the flow catalyzed by the initial amine. The rate constants of both flows (k_{2SS}, k_{2SR}, k_{3SS}, k_{3SR})[x] for the reactions studied in different solvents are presented in the Table. Drastic changes in the rate of the noncata - lytic rate constant k_2 in connection with the medium pola- rity could be observed both with the SS and SR pairs.

The values of kinetic enantioselectivity determined by the ratio of the SS-pair and the SR-pair rate constants for noncatalytic ($\varepsilon_2 = k_{2SS}/k_{2SR}$) and catalytic ($\varepsilon_3 = k_{3SS}/k_{3SR}$) reactions flows remarkably depend on the non-

---

[x] The first interlinear letter-index concerns electro - phetic reagent, the second one - nucleophilic reagent.

specific and specific medium properties. The most remar -
kable effect of enantiomeric differentiation in noncatalytic
reactions was observed in low-polarity, specifically sol -
vating dioxane[x] . At the same time, the higher enantiose -
lectivity of the catalytic processes is especially strongly
expressed in poorly solvating benzene. In the series of non-
specifically solvating related media (transition from chlo-
robenzene to o-dichlorobenzene), the behavior of enantiose-
lectivity of both reaction flows has similar character: the
higher the medium polarity, the lower enantioselectivity .
Hence, presumably, in the case of these reactions, the po-
lar properties of the solvent weaken the effects of non -
bonded interactions in transition state, which has resulted
in enantiomeric differentiation.

It would be interesting to compare the medium effect
on the enantioselectivity of amine acylation reactions, the
studied reaction of peptides' formation and on the reaction
of amides formation[1,2] being quite close to it. The molar
fraction values of solvents[3] have been chosen as the me -
dium parameters, characterizing its solvating properties .
This parameter ensures more favorable relations, in case
the observed enantioselectivity values are compared with
the medium properties. These relationships are shown in the
Figure, demonstrating their ambiguity for the reactions with
participation of various electrophiles. Thus, as concerns
the reactions of p-nitrophenyl ester of N-carbobenzoxy-S-
phenylaniline with the enantiomers of tertiary-butyl ester
of leucine (I) and 1-phenylethylamine (II)[I], there is cer-
tain agreement between the medium effect and enantioselec -
tivity values - the increase of the latter is proportional
to the molar refraction of the medium. In the case of (S)-
2-phenylbutyric anhydride reactions with 1-phenylethylamine

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[x] The larger the deviation of the rate constants' ratio of
    enantiomers from 1.0, the stronger is the enantioselec -
    tivity of the process.

Figure. Dependence of enantio-
selectivity log $\mathcal{E}$ (for
reactions I,II $\mathcal{E} = \mathcal{E}_2$,
for III,IV $= \dfrac{[SS]}{[SR]}$ - mo-
lar fraction of dias -
teroisomeric products)
on solvent molar re -
fraction (MR), $25°$.Sol-
vents: 1 - benzene ,
2 - chlorobenzene, 3 -
o-dichlorobenzene, 4 -
dioxane, 5 - acetonit-
rile, 6 - benzonitrile,
7 - acetone, 8 - ethyl-
acetate, 9 - methanol .
For curve numbers, see
text.
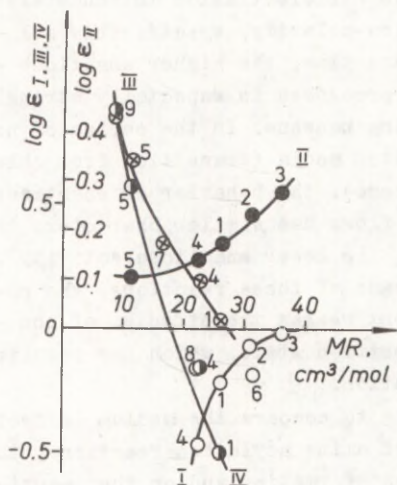
$(IV)^2$ enantiomers, the increase of this medium leads to
the weakening of the enantiomeric differentiation effect.
Although in reactions III and IV the enantioselectivity was
defined as the molar ratio of diastereoisomeric products ,
there still is connection between the medium effect on the
enantioselectivity and the transition state structure for
the reactions compared. It is known[4] that the aminolysis of
activated esters and anhydrides proceeds via essentially
different transition states; the reactions of. activated
asters have transition states with separated charges, while
the reactions of anhydrides are characterized by their cy-
clic. structure. This seems also to be the cause of different,
even oppositely directed sensitivities of enantioselecti -
vity values to the medium effects during the interaction of
these electrophiles with amine enantiomers.

$k_2 \cdot 10^4$ $(1 \cdot mol^{-1} \cdot s^{-1})$ and $k_3 \cdot 10^{-3}$ $(1^2 \cdot mol^{-2} \cdot s^{-1})$ Values for
Reactions of p-Nitrophenyl Ester of N-Carboxy-S-Phenylalanine with Enan-
tiomers and Racemate of Leucine Tertiary Butyl Ester in Various Solvents, $25^{\circ}C$

Solvent	k_{2SS}	k_{2SR}	ε_2	k_{3SS}	k_{3SR}	ε_3	k_{2S} rac.	k_{3S} rac.
1. Benzene	$2.15^{\pm}0.05$	$3.58^{\pm}0.08$	0.60	$1.41^{\pm}0.08$	$3.71^{\pm}0.13$	0.38	$2.85^{\pm}0.10$	$2.02^{\pm}0.11$
2. Chlorobenzene	$1.30^{\pm}0.02$	$1.54^{\pm}0.04$	0.84	$0.27^{\pm}0.03$	$0.61^{\pm}0.05$	0.44	$1.41^{\pm}0.01$	$0.35^{\pm}0.01$
3. 50 vol % chlo-robenzene in o-dichlorobenzene	$1.59^{\pm}0.01$	$1.81^{\pm}0.04$	0.88	$0.73^{\pm}0.02$	$1.21^{\pm}0.05$	0.60	$1.66^{\pm}0.04$	$1.03^{\pm}0.06$
4. o-dichloroben-zene	$1.82^{\pm}0.01$	$1.94^{\pm}0.02$	0.94	$0.79^{\pm}0.01$	$1.34^{\pm}0.03$	0.59	$1.89^{\pm}0.03$	$1.05^{\pm}0.02$
5. 1,4-dioxane	$1.43^{\pm}0.01$	$4.28^{\pm}0.08$	0.33	–	–	–	$2.85^{\pm}0.01$	–
6. Benzonitrile	$3.95^{\pm}0.01$	$6.11^{\pm}0.05$	0.64	$0.74^{\pm}0.02$	$1.00^{\pm}0.07$	0.74	$5.06^{\pm}0.02$	$1.03^{\pm}0.03$

Experimental

The solvents were purified using known methods[5].

R and S-tertiary butyl esters of leucine were obtained by the methods described in[6] and had the following specefic rotations: -22.7 (with 2, ethanol) and +22.7 (with 2, ethanol), respectively.

p-Nitrophenyl ester of N-carbobenzoxy-S-phenylaniline was obtained and identified analogously[1].

The reaction process was controlled spectrophotometrically at 310-320 nm (depending on a solvent) by its accumulation in the p-nitrophenol system.

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REACTIONS OF IMIDIC ACIDS' DERIVATIVES WITH NUC-
LEOPHILIC REAGENTS. ALKALINE HYDROLYSIS OF 4-NI-
TROPHENYL-N-BENZYLARYLIMIDATES IN DIOXANE-WATER
(1:1) MIXTURE

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Chemistry, Academy of Sciences of the Ukrainian
SSR, Donetsk

The kinetics of alkaline hydrolysis reac -
tion of 4-nitrophenyl-N-benzylarylimidates of
$R^1C_6H_4C(OC_6H_4NO_2-4) = NCH_2C_6H_5$ (I, R^1 = H,a; 3-Br,
b; 3-NO_2,c; 3,5-$(NO_2)_2$,d) has been studied   in
dioxane-water (1:1) mixture at the constant ion-
ic strength 0.2 M $NaClO_4$, at 25°C. S_N2 (TI) mech-
anism has been suggested; the rate limiting stage
of the hydroxide ion attack is either on the pro-
tonated or deprotonated substrate of I, depending
on the nature of substituent R^1. For Id imidate ,
a parallel reaction route via the fixed Meisen -
heimer б-complex, can be observed. The rate con -
stants of its accumulation and decomposition into
the reaction products in case of hydroxide ion
participation have been determined.

It was shown in our previous publications[1,2] that the
alkaline hydrolysis of aryl esters of diarylimidic acids
of $R^1C_6H_4C(OC_6H_4R^2) = NC_6H_4R^3$ (I) in the dioxane-water
(1:1) mixture proceeds according to the addition-elimina -
tion mechanism. The formation of a tetrahedral intermediate
was observed in the rate-limiting stage. In our case the un-

protonated imidate appeared to be the only reacting sub -
strate form, but as concerns the hydrolysis of aryl esters
of N-alkyl-substituted imidic acids of $AlkC(OAr) = NAlk$ (2),
in the pH range 1-12, the conjugated acid of the substrate[3]
functions as a reactant . This is confirmed by the pH-de -
pendence of the observed reaction rate constants, which has
either a sigmoid or a bell-shaped character with the plat-
eau at higher pH values. Participation of various substrate
forms of I and II in hydrolysis is evidently connected with
the acid-base properties of compared imidates.

Since N-alkyl- and N-aryl-substituted imidates show
drastic differences in their kinetic behavior, it was in-
teresting to study such substrates which according to their
basicity are between the former compounds. Here aryl-N-ben-
zylarylimidates of $R^1C_6H_4C(OC_6H_4R^2) = NCH_2C_6H_4R^3$ should be
considered most suitable (III). In contrast to alkylimidates
(II), whose structural change does not lead to essential
differences between the pK_a values, the structure of com-
pounds III enables to more extensively change the imidate
basicity by varying the R^1, R^2, R^3 substituents, thus also
making it possible for two flows to appear simultaneously
via the protonated and the unprotonated imidate.

With this aim in view, we have studied the alkaline
hydrolysis reaction of the compounds of group III (R^3 = H,
R^2 = 4-NO_2, R^1 = H,a; 3-Br,b; 3-NO_2,c; 3,5-$(NO_2)_2$,d) in the
dioxane-water (1:1) mixture, the constant ionic strength in
$NaClO_4$ being 0.2 M, at 25°C.

<center>Experimental</center>

4-Nitrophenyl-N-benzylarylimidates were synthesized
by well-known methods[4] from the corresponding imidoyl chlo-
rides and 4-nitrophenol. The obtained imidates were twice
recrystallized from alcohol. The characteristics of the
compounds which were synthesized first are given in Table 1.

The purification of solvents and preparation of solu -
tions for kinetic measurements were conducted as shown in[1,2].

Triethylamine labelled "pure" was distilled, collecting

Table 1

Characteristics of Synthesized 4-Nitrophenyl-N-Benzylarylimidates

of $R^1C_6H_4C(OC_6H_4NO_2-4)=NCH_2C_6H_5$

| R^1	Melting point ^{o}C	% found			Formula	% calculated		
		C	H	N		C	H	N
H	82 - 83	72.38	5.14	8.25	$C_{20}H_{16}N_2O_3$	72.29	4.82	8.43
$3-Br^{x)}$	72 - 73	58.33	3.75	6.92	$C_{20}H_{15}N_2O_3Br$	58.41	3.68	6.81
$3-NO_2$	91 - 92	63.71	4.20	11.02	$C_{20}H_{15}N_3O_5$	63.66	4.01	11.13
$3.5-(NO_2)_2$	103 - 105	56.45	3.20	13.34	$C_{20}H_{14}N_4O_7$	56.87	3.26	13.26

x) % Found: Br 19.52; % calculated: Br 19.43.

the average fraction; sodium perchlorate ("chemically pure") was used without an additional purification.

Kinetic measurements were carried out by the following methods. 0.01-0.02 ml of imidate solution in dioxane were added to 2.5 ml of alkaline solution in dioxane-water (1:1) mixture, so that its concentration in solution was $\sim 10^{-5}$ mol $\cdot$ 1^{-1}. The cell was put into the thermostatically con - trolled cell-unit of a spectrophotometer, the changes in the optical density of colored products were registered. All kinetic measurements were performed under pseudomonomolecu- lar conditions at a considerable alkaline excess, when com- pared with the initial substrate III.

The UV-spectra were recorded on a "Specord M 40", PMR- spectra were registered on a "Tesla BS-467" (60 MHz) in DMSO-d_6 (inner standard - HMDS), the electron-paramagnetic resonance spectra on a "RE 1308".

The analysis of the UV-spectra of reaction mixtures shows that the alkaline hydrolysis of IIIa-d imidates is quantitative and irreversible, proceeding by scheme (1):

$$III + OH^- \longrightarrow R^1C_6H_4\overset{O}{\overset{\|}{C}}NHCH_2C_6H_5 + 4\text{-}NO_2C_6H_4O^- \qquad (1)$$
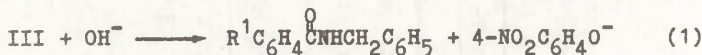
Mechanism and Kinetics of Alkaline Hydrolysis of IIIa-c Imidates

Under pseudomonomolecular conditions where $[NaOH] > [III]$ $\sim 10^{-5}$ mol $\cdot$ 1^{-1}, the observed reaction rate constants $k_{OH^-}^1(s^{-1})$, calculated on the bases of the 4-nitrophenolate anion accumulation at $\lambda = 400$ nm remain stable during the process. The values are presented in Table 2.

As concerns the IIIc imidate, the present relationship is linear in the variation range of alkaline concentration (Fig. 1, graph 1), which corresponds to the hydroxide ion first order. We can suppose on the basis of similar reactions of alkaline hydrolysis of imidates I studied previously[1,2] that in this case, the hydroxide ion attacks the unproto - nated substrate.

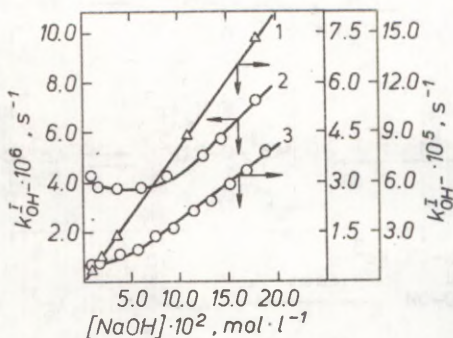In the cases of the IIIa,b compounds the $k_{OH^-}^1$ - $[NaOH]$

Fig. 1. Dependence of reaction rate constants k_{OH}^{I}-(s^{-1}) on the NaOH alkaline concentration for hydrolysis reaction of 4-nitrophenyl-N-benzylaryl imidates of $R^{1}C_6H_4C(OC_6H_4NO_2-4)= NCH_2C_6H_5$ in dioxane-water (1:1) mixture; $I = 0.2$ M $(NaClO_4)$; $25^{o}C$: $1-R^{1} = 3-NO_2$ (right section of the ordinate); $2-R^{1} = H$; $3-R^{1} = 3-Br$ (left section of the ordinate).

dependences cannot be considered linear, and they have two separate regions (Fig. 1, graphs 2,3). While in the region of small alkaline additions, the k_{OH}^{I}- values change but slightly, then further increasing of base concentration will make the dependences linear. The obtained results can be explained with its mechanism, including two parallel reaction routs via the protonated and unprotonated sub-strate forms:

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$$\text{Ar}^1-\text{C}\overset{\overset{+}{\text{NHCH}_2\text{Ar}^3}}{\underset{\text{OAr}^2}{\big/\big\backslash}} \quad \xrightarrow[k_3\text{H}_2\text{O}]{k_2[\text{OH}^-]} \quad \left[\text{Ar}^1-\underset{\text{OH}}{\overset{\overset{+}{\text{NHCH}_2\text{Ar}^3}}{\text{C}-\text{OAr}^2}} \rightleftharpoons \text{Ar}^1-\underset{-\text{O}}{\overset{\overset{+}{\text{NH}_2\text{CH}_2\text{Ar}^3}}{\text{C}-\text{OAr}^2}} \right]$$

$$K_a \big\updownarrow \pm\text{H}^+$$

$$\text{III} \quad \xrightarrow{k_1[\text{OH}^-]} \quad \left[\text{Ar}^1-\underset{\text{OH}}{\overset{\overset{-}{\text{NCH}_2\text{Ar}^3}}{\text{C}-\text{OAr}^2}} \rightleftharpoons \text{Ar}^1-\underset{-\text{O}}{\overset{\text{NHCH}_2\text{Ar}^3}{\text{C}-\text{OAr}^2}} \right]$$

$$\text{Ar}^1-\underset{}{\overset{\overset{\text{N}-\text{CH}_2\text{Ar}^3}{\|}}{\text{C}-\text{OH}}} \quad \xrightarrow{\text{fast}} \quad \text{Ar}^1-\underset{}{\overset{\overset{\text{O}}{\|}}{\text{C}-\text{NHCH}_2\text{Ar}^3}} \qquad (2)$$
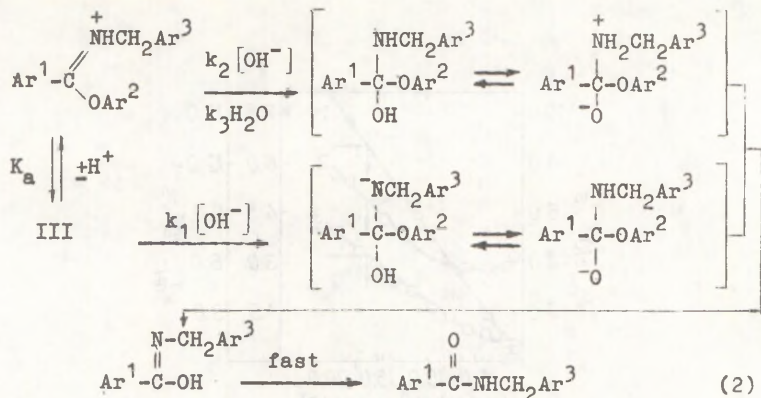
The kinetic regularities of these reactions with participation of the IIIa,b imidates have certain common features with the studied hydrolysis processes of the Shiff[5] bases, alkylimidates II[3] and thioimidates[6]. These are as follows: a) the existence of linear dependence "$k_{OH^-}^I$ [OH$^-$]" in the high concentration range of alkali; b) the existence of a plateau, corresponding to the hydrolysis which is not dependent on pH; c) the shift of the position of the plateau into the region of low alkali concentrations caused by the increase of the electron-donor properties of the R^1 substituents in the imidate molecule.

It follows from the results obtained in this study that all numerical parameters for the processes of alkaline hydrolysis of IIIa-c imidates meet the case.

Supposing that in Scheme (2), the formation of a tet - rahedral interval in various ionic forms acts as the rate limiting stage in Scheme (2), we can express (3) the reac - tion rate constant of pseudofirst order $k_{OH^-}^I$, where K_w and K_a are the corresponding constants of water and bound imidic acid:

$$k_{OH^-}^I = \frac{k_3[\text{H}^+] + k_2 K_w + k_1 K_a [\text{OH}^-]}{[\text{H}^+] + K_a} \qquad (3)$$

At high alkali concentrations, there can appear a situation when $\left[H^+\right] \ll K_a$, then Eq. (3) can be reduced to (4):

$$k_{OH^-}^I = k_3 \left[H^+\right] / K_a + \frac{k_2 K_w}{K_a} + k_1 \left[OH^-\right] \tag{4}$$

In Eq. (4), the first and the second terms correspond to the water molecule and hydroxide-ion attacks on the unpro - tonated imidate.

In the high concentration range of alkali (for the substrates studied, at $\left[OH^-\right] > 1.2 \cdot 10^{-1}$ mol $\cdot$ l^{-1}), the contribution of the first two terms of Eq. (4) is negligible in comparison with the third one. The situation is reflected by the graphs of the "$k_{OH}^I - \left[OH^-\right]$" relationship (Fig. 1). The rate constants of bimolecular interaction (k_1) of IIIa-c imidates with the hydroxide ion can be found in Table 2. Table 2 also contains the respective k_1 value for the IIId substrate, whose calculation methods will be discussed be - low.

The k_1 values can be described by the Hammett equation:

$$\log k_1 = -(4.62 \pm 0.19) + (2.55 \pm 0.23) \, \delta_R$$
$$r = 0.992; \quad S = 0.249; \quad n = 4 \tag{5}$$

The found value $\rho_R 1 = 2.55$ is quite close to the analogous parameter $\rho_R 1 = 2.0$ for the alkaline hydrolysis of 4-nitro-phenyl-N-phenylarylimidates of $R^1 C_6 H_4 C(OC_6 H_4 NO_2-4) = NC_6 H_5$ in the same solvent[1]. This is in keeping with the addition-detachment mechanism given in Scheme (2), where the forma - tion of the tetrahedral intermediate proceeds in the rate limiting stage (cf.[1]).

Table 2

Pseudofirst Order Rate Constants of $k_{OH^-}^{I}(s^{-1})$ and
Rate Constants of Bimolecular Interaction of
$k_1(l \cdot mol^{-1} \cdot s^{-1})$ of 4-Nitrophenyl-N-benzylaryli-
midates of $R^1C_6H_4C(OC_6H_4NO_2-4) = NCH_2C_6H_5$ with Hy-
droxide Ion in Dioxane-Water (1 : 1) Mixture ;
$I = 0.2$ M $(NaClO_4)$; $25^{\circ}C$

| [NaOH] $\cdot 10^2$, | $k_{OH^-}^{I} \cdot 10^5$, s^{-1} | | | |
mol $\cdot l^{-1}$	$R^1 = H$	$R^1 = 3\text{-}Br$	$R^1 = 3\text{-}NO_2$	$R^1 = 3,5\text{-}(NO_2)_2$
0.91	-	-	0.705	
0.95	0.416	0.518	-	
1.82	-	-	1.62	
1.90	0.383	0.577	-	
3.64	-	-	2.76	
3.80	0.374	0.862	-	
5.73	-	0.949	-	
6.20	0.378	-	-	
7.61	-	1.36	-	
9.05	0.428	-	-	
9.54	-	1.59	-	
10.9	-	-	8.78	
11.5	-	2.13	-	
12.7	0.501	-	-	
13.4	-	2.43	-	
14.5	0.569	-	-	
15.3	-	2.94	-	
17.2	-	3.29	-	
18.15	0.730	-	14.8	
19.1	-	3.99	-	
$k_1 \cdot 10^4$ $l \cdot mol^{-1} \cdot s^{-1}$	0.333 ± 0.045	2.35 ± 0.14	8.13 ± 0.06	1380 ± 90

Kinetics and Mechanism of Alkaline Hydro-
lysis Reaction of IIId Imidate

There are certain differences between the alkaline hy-
drolysis of the IIId imidate and that of the IIIa-c sub -
strates, containing weaker acceptor substituents with C-
phenyl fragment. The main difference is that immediately
after mixing reagents appear two additional absorption
bands at λ = 410-415 nm and λ = 539.4 nm. In both cases,
their optical density varies during the reaction: at λ =
410-415 nm the density is steadily increasing (Fig. 2, B)
while at λ = 439.4 nm, it initially increases but after
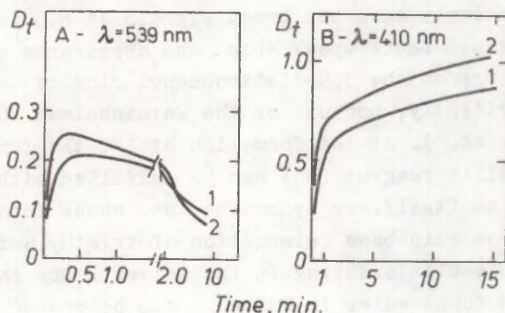achieving its maximum, starts slowly to decrease up to ze-
ro (Fig. 2, A).

Fig. 2. Changes of optical density in time for reac-
tion of 4-nitrophenyl-N-benzyl-3,5-dinitrophe-
nylimidate ($5 \cdot 10^{-5}$ mol $\cdot$ 1^{-1}) with hydroxide
ion in dioxane-water (1:1) mixture; I = 0.2 M
($NaClO_4$); $25^{\circ}C$; [NaOH] mol $\cdot$ 1^{-1}; 0.1 (1) ,
0.15 (2).

At 410-415 nm the absorption band undergoes a blue
shift of up to 400.1 nm during the reaction, which, con-
cerning its accuracy, corresponds to the absorption max-
imum of 4-nitrophenolate-ion. The character of the UV-spec-

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tra of the reaction mixture shows in the case of IIId the appearance of an intermediate, whose formation from the IIIa-c substrates seems to be thermodynamically unfavorable.

In order to find out the nature of this intermediate, the PMR and EPR spectra of the IIId compounds were studied in various media in the presence of bases.

After adding DMSO such a strong base as triethylamine, in the PMR spectra of the IIId imidate (DMSO-D$_6$; inner standard HMDS; $[IIId] = 2.0 \cdot 10^{-1}$; $[N(C_2H_5)_3] = 5.0 \cdot 10^{-1}$ mol $\cdot$ l^{-1}) weakens the intensity of the signals of the substrate methyl group protons (δ = 4.75 m.d.) as well as that of the 4-H-proton of 3.5-dinitrophenyl nucleus (δ = 8.91 m.d.). The signals of 3', 5' - and 2',6'-H-protons of 4-nitrophenyl ring (8.24 and 7.32 ppm, respectively) undergo a substantial shift ($|\Delta\delta|$ = 0.6 and $|\Delta\delta|$ = 0.18 ppm. In addition to that we have also noticed the appearance of two relatively weak but broad signals at 8.32 and 5.32 ppm. The obtained facts speak about the appearance of a nega - tive charge on the 3,5-dinitrophenyl ring of the IIId imidate, evidently, because of the Meisenheimer σ-complex of type IV (cf.[7]). At the formation of IV, the function of nucleophilic reagent (Nu) can be fulfilled either by tri - ethylamine itself, or hydroxide ion, whose formation re - sults from acid-base interaction of triethylamine with the water molecules existing in the solvent. The fact that there has been found water in DMSO-D$_6$ can be proved by the PMR-spectroscopy.

IVa   IVb   Va   Vb
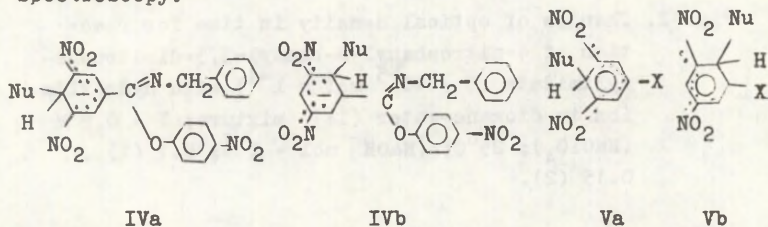
The formation of similar Va-b complexes was shown in the reactions of 3.5-dinitrosubstituted benzenes (X=COOH, COOCH$_3$, CN, NO$_2$) with anionic nucleophiles (Nu = OH$^-$,

CH_3O^-, SO_3^{-2}, $CH_3COCH_2^-$) in the media with high DMSO concen-
trations (DMSO-water, 50-95% (v/v) of organic compo-
nents)[7,8].

In the PMR-spectrum of the IIId imidate in DMSO in the
presence of alkali ([IIId] = 0.2 mol · l^{-1}, [NaOH] > 0.1
mol · l^{-1}) we have established that the signals of the
3.5-dinitrophenyl ring get fully extinguished. This pheno-
menon has usually been linked with[9] the formation of a pa-
ramagnetic moiety and hence, with certain broadening of re-
sonance lines and a drop in their intensity . Really, in
the EPR spectrum of the reaction mixture of the IIId imi-
date with NaOH in DMSO (Fig. 3) there are seven resonance
lines. The existence of these lines can be connected with
the structure of anion-radical particles VI, as to the lat-
ter, the hyper-fine interaction constants of the nitrogen
atom (Q_H) of the nitro-group and hydrogen (Q_H) nucleus
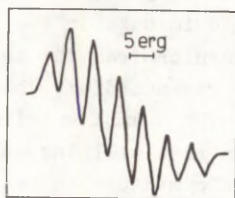equal 3 and 6 Gs, respectively.
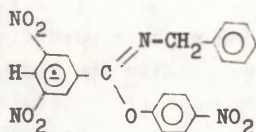
VI

Fig. 3. EPR spectrum of 4-
nitrophenyl-N-benzyl-3.5-di-
nitrophenylimidate (0.2 mol·
l^{-1}) and sodium hydroxide
(0.2 mol · l^{-1}) mixture in
DMSO at 20°C.

The existence of similar particles has been quite often postulated and in more rear cases these particles have even been observed during the processes of aromatic nucleophilic substituation[9-11], thus, evidently being the predicessor of the complexes of types IV-V.

It follows from the literature data (see e.g.[7]) that in the reactions of 3,5-dinitrosubstituted benzenes with anionic nucleophiles in the media with high DMSO concentration forms the mixture of isomeric products Va and Vb. Although the Vb complex formation proceeds slowlier, it is thermodynamically more stable. Unfortunately, we do not have any direct evidence, concerning the formation of two isomers - IVa-b from the PMR of spectral data.

Nevertheless, the analysis of the UV spectra of the reaction mixtures of IIId imidate and alkali in the solvents of various compositions (the volume ratio of DMSO-water 20:1, 3:1) confirms the existence of IV in forms a and b. At the initial time moment after mixing reagents ([IIId]$\simeq$ 10^{-5} mol $\cdot$ 1^{-1}; [NaOH] = 1.0 mol $\cdot$ 1^{-1}) three absorption peaks, at 410, 521 and 588 nm have been fixed. The optical density was noticed to drop quite sharply at 588 nm, while at 521 nm it tends to increase (the isobestic point is at 563 nm). Analogously with[12], at 521 and 588 nm, the absorption peaks correspond to the IVb and IVa isomers, respectively, while the latter rapidly transforms into IVb.The fact that there is only one absorption peak at 539.4 nm in the UV-spectrum of the mixture of the IIId imidate in the dioxane-water (1:1) solution, possibly results from the accumulation of the IVb isomer only in the given medium. This is in keeping with the conclusions drawn by Crampton et al.[8], saying that the Va$\rightleftarrows$Vb isomerization rate will increase if the water content in an aqueous-organic mixture increases.

Thus, the spectral data obtained by the authors of this paper evidence the formation of the Meisenheimer complex IVb in the reaction of the IIId imidate with alkali in the dioxane-water (1:1) mixture. During the following transformation the complex can form either final products (4-nitrophenolate-ion and N-benzyl-3,5-dinitrobenzamide), or act

as an inactive ballast complex. Since the concentration of the complex does not remarkably depend on the alkali concentration (Fig. 2), we can expect that its formation is a reversible process.

N-benzyl-3,5-dinitrobenzamide, forming during the hydrolysis reaction of IIId imidate is also able to form the complexes of types Va,b in the aqueous-organic media with high DMSO (> 60%) concentration, while in the dioxane-water mixtures we did not succeed in determining their accumula - tion by spectral methods.

$$\text{IIId} + \text{OH}^- \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} \text{IVb Equilibrium Studies}$$
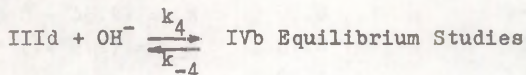
In order to find the equilibrium constants of the IVb complex formation, we used either kinetic or thermodynamic methods, depending on the initial reagents chosen.

In case of $[\text{NaOH}] > [\text{IIId}] \simeq 10^{-5}$ mol $\cdot$ l^{-1} pseudomono-molecularity, the rate constants $k_H(s^{-1})$ calculated by the IVb complex accumulation at $\lambda = 539.4$ nm remain stable during the process. Their values at various alkali concentration are brought in Table 3; where k_4 and k_{-4}, respectively, are the rate constants of the forward and back reactions:

$$k_4 = k_{-4} + k_4 \left[\text{OH}^-\right] \tag{6}$$

Considering the equivalence of 2 and 6-positions of 3,5-dinitrophenyl fragment of the IVd imidate, for the k_4 value was carried out a statistical correlation, dividing it by two. The equilibrium constant of complex IVb forma - tion equals $K_4 = k_4/k_{-4} = 88 + 35$ l $\cdot$ mol^{-1}.

The equilibrium constant K_4 can also be determined by some other methods from the spectral data according to Eq. (7), where D_i and D_{max} denote the optical densities of the complex at 539.4 nm after the equilibrium (D_i) has been established and at a full conversion of the substrate into to the IVb (D_{max}) complex, respectively:

Table 3

Pseudofirst Order Rate Constants $k_H(s^{-1})$ and Rate Constants of Forward k_4 ($1 \cdot mol^{-1} \cdot s^{-1}$) and Back $k_{-4}(s^{-1})$ Reactions Calculated by Eq. (6), of Meisenheimer Complex Formation from 4-Nitrophenyl-N-benzyl-3,5-dinitrophenyl Imidate and Hydroxide Ion in Dioxane-Water (1:1) Mixture; I = 0.2 M ($NaClO_4$); $25^{\circ}C$

[NaOH]$\cdot 10^2$, mol $\cdot 1^{-1}$	$k_H \cdot 10^2$, s^{-1}	Parameters of Eq. (6)
0.46	0.55	$k_4 = (2.54 \pm 0.09) \cdot 10^{-1}$
0.92	0.79	$k_{-4} = (2.9 \pm 1) \cdot 10^{-3}$
1.84	1.30	
3.69	2.01	
5.53	2.92	$K = \dfrac{k_4}{k_{-4}} = 88 \pm 35$ $1 \cdot mol^{-1}$
7.37	4.31	
11.0	5.84	

Table 4

Dependence of Optical Density at λ = 539.4 nm on Alkali Concentration for Formation Process of Meisenheimer (IV b) $\mathfrak{G}$-Complex from 4-Nitrophenyl-N-benzyl-3,5-dinitrophenylimidate and Hydroxide Ion in Dioxane-Water (1:1) Mixture; I = 0.2 M ($NaClO_4$); $25^{\circ}C$ ([III d]= = 9.59 $\cdot 10^{-5}$ mol $\cdot$ 1; cell thickness 1.00 cm)

[NaOH] $\cdot 10^2$, mol $\cdot 1^{-1}$	D_i	Equation Parameters (7)
0.61	0.083	$D_{max} = 0.348 \pm 0.064$
0.91	0.113	
1.06	0.127	$\varepsilon_{IVb} = 3630$
1.77	0.156	$K_4 = 49.9 \pm 5.5$
3.31	0.205	
3.74	0.219	
7.58	0.262	
10.2	0.284	
12.8	0.313	
17.1	0.325	

$$\frac{D_i}{[OH^-]} = K_4(D_{max} - D_i) \tag{7}$$

Primary data and the results of their procession by Eq. (7) are given in Table 4. The obtained $K_4 = 49.9\pm5.5$ is close to the analogous K_4 value found from kinetic measurements.

Kinetics of IIId Imidate Alkaline Hydrolysis (transformation of IV b complex into reaction products)

The rate constants k_H^I (s^{-1}) calculated on the basis of the complex decrease at $\lambda = 539.4$ nm remain stable during the reaction. Their values are presented in Table 5. Fig.4 shows that the k_H^I - $[NaOH]$ relation has two regions: non-linear region is characterized by a sharp rate increase as a result of the growth in alkali concentration, the linear region is connected with a slower rate increase from base concentration in solution.
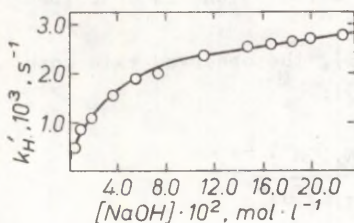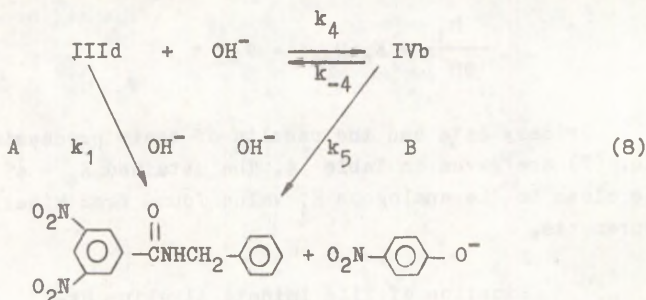

Fig. 4. Dependence of pseudofirst order rate constants k_H^I of complex IVb decomposition on alkaline concentration at 25°C, $I = 0.2$ M NaClO$_4$.

A rather similar character of this dependence with that of[13] makes us suppose that the formation of final products proceeds in two parallel flows A and B, shown in Scheme (8):

$$\text{IIId} \quad + \quad \text{OH}^- \quad \overset{k_4}{\underset{k_{-4}}{\rightleftharpoons}} \quad \text{IVb}$$

$$\text{A} \quad k_1 \diagdown \quad \text{OH}^- \qquad \text{OH}^- \diagup k_5 \quad \text{B} \tag{8}$$

$$O_2N\text{—}\underset{O_2N}{\overset{O_2N}{\bigcirc}}\text{—}\overset{\overset{O}{\|}}{C}NHCH_2\text{—}\bigcirc \quad + \quad O_2N\text{—}\bigcirc\text{—}O^-$$

The attack of hydroxide ion on the IIId imidate leads to a rapid equilibrium IVb complex formation, which in the reaction with hydroxide ion transforms into final products. Alongside with this, we can also observe the realization of the "ordinary" substrate consumption route in the reaction of hydroxide ion with the molecular form of the IIId imidate.

The alternative suggestion saying that the equilibrium IIId + OH$^-$ $\rightleftharpoons$ IVb is not in agreement with the character of the dependence of the rate constant of complex IVb decomposition on the alkali concentration. If the IVb complex acted as an inactive one (ballast), the k_H^I dependence on NaOH would take the form of a curve which is described by the first term in Eq. (9).

Proceeding from Scheme (8), the observed rate constant k_H^I can be presented by Eq. (9):

$$k_H^I = \frac{k_1 [OH^-]}{1 + K_4 [OH^-]} + \frac{k_5 K_4 [OH^-]^2}{1 + K_4 [OH^-]} \tag{9}$$

In case of low alkali concentrations, the contribution of flow B into the process rate can be neglected; then after a number of simple transformations:

$$\frac{1}{k_H^I} = \frac{K_4}{k_1} + \frac{1}{k_1 [OH^-]} \tag{10}$$

Table 5

Pseudofirst Order Rate Constants k_H^I (s^{-1}) of Complex
IVb Decomposition in Presence of Alkali in Dioxane-
Water (1:1) Medium; I = 0.2 M (NaClO$_4$); 25°C

[NaOH] · 10^2, mol·l^{-1}	k_H^I exp.·10^3, s^{-1}	k_H^I calc.·10^3, $s^{-1x)}$
0.461	0.500	0.505
0.921	0.86	1.01
1.84	1.18	1.26
3.69	1.57	1.70
5.53	1.89	1.99
7.37	1.98	2.11
11.06	2.37	2.46
14.74	2.55	2.53
16.59	2.61	2.60
18.43	2.67	2.68
19.9	2.72	2.74
22.5	2.77	2.83

x) For finding the k_H^I calc. values were used the follow-
ing values: K_4 = 57.4 l · mol^{-1}; k_1 = 1.38 · 10^{-1}
l · mol^{-1}·s^{-1} , k_5 = 2.83 · 10^{-3} l · mol^{-1} · s^{-1}.

In the alkali concentration range (0.4-7.4) · 10^{-2} mol ·
l^{-1}, the experimental data can be quite adequately described
by the latter equation, enabling us to find the values of
K_4 = 57.4 ± 10.5 l · mol^{-1} and k_1 = (1.38 ± 0.09) · 10^{-1}
l · mol^{-1} · s^{-1}.

At high alkali concentrations (> 0.1 mol · l^{-1}) , is
satisfied the condition K_4 [OH⁻]>1 and Eq. (9) will be trans-
formed as follows:

$$k_H^I = \frac{k_1}{K_4} + k_5[OH^-] \qquad (11)$$

For a rather narrow range of alkali concentration changes $(1.5 + 2.25) \cdot 10^{-1}$ mol $\cdot$ 1^{-1} it was possible to estimate from Eq. (11) the values $K_4/k_1 = 469 \pm 22$ (to compare this value from Eq. (10) equals 416 ± 49) and $k_5 = (2.89 \pm 0.57) \cdot 10^{-3}$ $1 \cdot$ mol$^{-1} \cdot$ s^{-1} .

Using the values of K_4, k_1 and k_5 found from Eqs. (10) and (11), and applying Eq. (9), we calculated a theoreti - cal curve of "k_H^I - [NaOH]" for whole variation range of al- kali concentration (Fig. 4), which quite well agrees with the experimentally obtained relationships. The data of Table 5 show that there are some deviations between the measured and calculated k_H^I values, not exceeding 10%.

One should pay attention to the process proceeding by route k_5 in Scheme (8). This is a reaction between two anionic particles. There have also been some cases of sub- stitution, in the case of the anionic nucleophiles' attack on the δ-anionic complexes of polynitro-substitud benze- nes[13] . Yet, as concerns the reaction center, situated near the aromatic ring, and the IVb complex, this substitution type was observed for the first time here. Since the pro - cess is formally a bimolecular one, so similarly to the IIIa-d substrates (see Scheme (2), route k_1), its mecha - nism can be described by Scheme (12), where two-charged anions VIIa and VIIb act as intermediates:

$$IVb + OH^- \underset{}{\overset{K_p}{\rightleftharpoons}} \left[\quad \right]$$
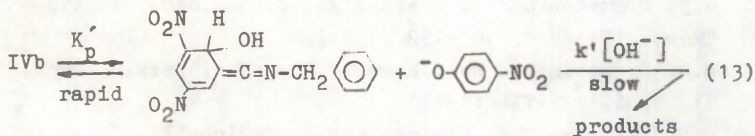
VIIa   VIIb

products ← (12)
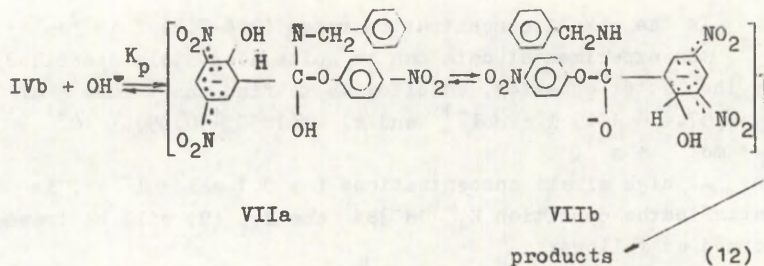
A somewhat lower reactivity of the IVb complex in com- parison with the initial IIId ($k_1/k_5 = 48$) imidate is quite clearly connected with the mechanism, being most probably

explained with a certain contribution into the activation free energy of electrostatic repulsion between interacting particles.

It is known[14] that in anion-radicals similar to VI , 3-nitro group does not reveal any acceptor properties . Quite contrary, it acts as a rather clearly expressed electron-donor ($\sigma_m^{NO_2^{\bar{}}}$ = -0.17). Thus, we might presume that in the IVb complex, where one 3-nitro group has been replaced by NO_2^- , its $\sigma_m^{NO_2}$ value should be still more negative . Proceeding from $\sigma_m^{NO_2^{\bar{}}} = \sigma_m^{NO_2^{\bar{}}}$ = -0.17, the maximum k_5 constant value found from Eq.(5) should equal $\leqslant 5.7 \cdot 10^{-4}$ $1 \cdot mol^{-1} \cdot s^{-1}$. The value is 4 times smaller than the experimental one ($2.89 \cdot 10^{-3}$ $1 \cdot mol^{-1} \cdot s^{-1}$) which could have two possible explanations: a) either the electron-donor influence of electrons in the anionic σ-complex is really weaker than that of an electron in the anion radi - cal complex, i.e., $\sigma_m^{NO_2^{\bar{}}} > \sigma_m^{NO_2^{\bar{}}}$, although this contradicts our logic ı; b) or the substitution mechanism does not correspond to Scheme (12), being equal to route k_1 in (2).

As an alternative version, we could, for instance , suggest a route through the ketiminic VIII intermediate:

$$IVb \xrightleftharpoons[\text{rapid}]{K_p'} \begin{array}{c} O_2N \quad H \\ OH \\ \langle\rangle=C=N-CH_2\langle\bigcirc\rangle \\ O_2N \end{array} + {}^-O\text{-}\langle\bigcirc\rangle\text{-}NO_2 \xrightarrow[\text{slow}]{k'[OH^-]} \quad (13)$$
$$\text{products}$$

In the case of small equilibrium constants of K_p and K_p' (or if the formation of VII determines the rate), routes (12) and (13) are kinetically identical. Therefore, without having any information on the thermodynamic formation of intermediates VII and VIII and without determining the rate limiting stage in Scheme (12), it would not be correct to say anything definite about the fine mechanism of route k_5 in Scheme (8).

Thus, it has been shown in the present paper that the

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alkaline hydrolysis of IIIa-d imidates in water-dioxane
(1:1) mixture can be characterized by the addition-detach-
ment mechanism with the formation of a tetrahedral inter -
medicate product in the rate limiting stage. Depending on
the structure of substrate III, either the protonated or
unprotonated forms or the anionic Ꝺ-complex of Meisenheimer
can act as an active form. The latter route of nucleophilic
substitution in the series of imidic acid derivatives was
obtained for the first time.

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REACTIONS OF IMIDO ACID DERIVATIVES WITH
NUCLEOPHILIC REAGENTS. ALKALINE HYDROLY-
SIS OF N-SUBSTITUTED 4-NITROPHENYL-3,5-
DINITROBENZIMIDATES IN DIOXAN - WATER
(1:1) MIXTURE

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The kinetics of alkaline hydrolysis reaction
of N-substituted 4-nitrophenyl-3,5-dinitrobenzi -
midates of $3,5-(NO_2)_2-C_6H_3-C(OC_6H_4-NO_2)$ = NR (III,
R = $CH_2C_6H_4-Br-3$, a; CH_3, b; $CH(CH_3)_2$, C; CH_2CH =
CH_2, d; in dioxan - water (1:1) mixture at the con-
stant ionic strength 0.2 M $NaClO_4$ has been stu -
ied. Step-line mechanism of addition-elimination
S_N2 (TI) with formation of a tetrahedral in -
termediate in rate limiting step has been sug-
gested for the processes studied. In case of IIIa
imidate, tetrahedral intermediate can be formed
both from molecular form and anionic Meisenheimer
δ-complex. For substrates IIIb-d, the contribu -
tion of the second route into observed rate was
negligible.

We have already reported in our previous publications[1]
about the kinetic peculiarities and quantitative regulari-
ties of alkaline hydrolysis reactions of N-benzyl-4-nitro-
phenylarylimidates in dioxan - water (1:1) mixture. As con-
cerns the given process a step-like addition-elimination

mechanism with the formation of a tetrahedral intermediate product (TIP) in the rate limiting step has been suggested. Depending on the acid-base properties of imidates, the TIP formation can proceed either from the neutral or from the protonated substrate forms. In the case of N-benzyl-4-nit-rophenyl-3,5-dinitrobenzimidate appears a parallel reaction route via the anionic σ-complex of Meisenheimer type I $(R = CH_2C_6H_5)$.

The formation of similar σ-complexes II was detected in the reactions of nucleophilic substitution in aromatic systems, for instance, in the case of anionic nucleophiles' $(OH^-$, $CH_3O^-)$ interaction with 3,5-dinitrobenzene $X-C_6H_3(NO_2)_2$-3.5 substituents $(X = CN$, NO_2, $COOCH_3$, CF_3, etc) in water-DMSO mixtures[2]. The stability constants of type II comp - lexes as well as their reactivity depends both on the nuc - leophilic reagent and substituent X nature, but also on the dissolving properties of the medium[2,3].

I   IIa   IIb
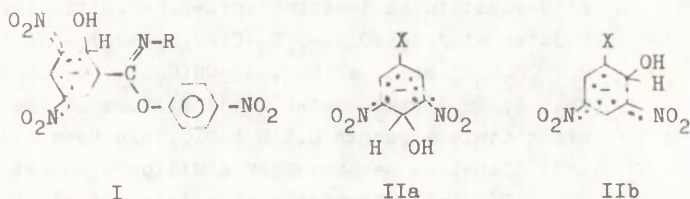
We have shown[1] that in contrast to the intermediates III studied earlier whose formation can take place only in water-DMSO mixtures containing more than 50% of organic com-ponent[3], the accumulation of complex I $(R = CH_2C_6H_5)$ pro-ceeds in the water-dioxan (1:1) mixture whose solvation properties are poorer. This refers to a better stability of the anionic particles belonging to type I, which can be linked with the azavinyl fragment effect stabilizing the negative charge. σ-complex I has another peculiarity in comparison with structural analogs of type II: if it is at-tacked by a nucleophilic reagent, this leaving group will not be replaced which is not connected with the activated ben-

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zene ring like in case of II (X), but the one situated near
the adjoining imidoyl center $(4-NO_2-C_6H_4O^-)$.

In our present paper we have tried to find the reali-
zation limits of alkaline hydrolysis mechanism via the an-
ionic δ-complex I in imidate series III thus obtaining some
additional information on the stability of such complexes
and their reactivity. With this aim in view was studied the
kinetics of alkaline hydrolysis of N-substituted 4-nitro -
phenyl-3,5-dinitrobenzimidates IIIa-d in dioxan —water (1:1)
mixture at constant ionic strength (0.2 M) of $NaClO_4$ at
$25^{\circ}C$.
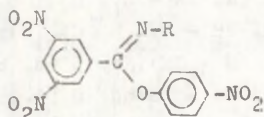
III, R = $CH_2C_6H_4$-Br-3, a; CH_3,
b; $CH(CH_3)_3$, c;
CH_2-CH = CH_2, d

Experimental

The PMR-spectra of 0.2 M of IIIa-d solutions were re -
gistered on a "Tesla BS 467" (DMSO - D_6: inner standard HMDS),
the EPR spectra were taken on PE 1308 spectrometer.

The reaction course was controlled spectrophotometri -
cally on a "Specord M-40" and on a SF-4a. The purification
of solvents and the methods of kinetic measuring have been
thoroughly described in[1].

The IIIa-d imidates were synthesized by the generally
accepted methods[4], the compounds were purified by repeated
recrystallization from alcohol.

4-nitrophenyl-N-3-bromobenzyl-3.5-dinitrobenzimidate

PMR (DMSO-D_6), δ_{ppm} = 8.79 (s, 1H - $C_{(4)}$H); 8.65 (s ,
2H - $C_{(2)}$H, $C_{(6)}$H; 8.15 (d, 2H - $C_{(3)}$H, $C_{(5)}$H); 8.05 - 6.75
(m, 6H - $C_{(2)}$H, $C_{(6)}$H, $C_{(Bz)}$H; 4.81 (d, 2H - CH_2-group).Mel-
ting point 135 - 136$^{\circ}C$. % found: C 47.82; H 2.67; Br
15.47, N 11.00; $C_{20}H_{13}BrN_4O_7$. % calculated: C 47.91; H 2.59;

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Br 15.95; N 11.18.

4-Nitrophenyl-N-methyl-3.5-dinitrobenzimidate

PMR (DMSO-D$_6$), δ_{ppm} = 8.76 (s, 1H - C$_{(4)}$H); 8.62 (s, 2H - C$_{(2)}$H, C$_{(6)}$H); 8.07 (d, 2H - C$_{(3)}$H, C$_{(5)}$H); 7.17 (d, 2H - C$_{(2)}$H, C$_{(6)}$H); 3.12 (s, 3H - CH$_3$-group. Melting point 129-130°C. % found: C 48.65; H 3.04, N 16.03 . C$_{14}$H$_{10}$N$_4$O$_7$. % calculated: C 48.56, N 2.91, N 16.18.

4-Nitrophenyl-N-isopropyl-3.5-dinitrobenzimidate

PMR (DMSO-D$_6$) δ_{ppm} = 8.85 (s, 1H - C$_{(4)}$H); 8.75 (s, 2H - C$_{(2)}$H, C$_{(4)}$); 8.18 (d, 2H - C$_{(3)}$H, C$_{(5)}$H);7.29 (d, 2H - C$_{(2)}$H, C$_{(6)}$H); 3.93 (k, 1H - CH); 1.15 (d, 6H-CH$_3$-group). Melting point 103-105°C. % found: C 51.15 ; H 3.83; N 14.74; C$_{16}$H$_{14}$N$_4$O$_7$. % calculated: C 51.34; H 3.77; N 14.97.

4-Nitrophenyl-N-allyl-3.5-dinitrobenzimidate

PMR (DMSO-D$_6$), δ_{ppm} = 8.77 (s, 3H - C$_{(2)}$H, C$_{(4)}$H , C$_{(6)}$H); 8.17 (d, 2H - C$_{(3)}$H, C$_{(5)}$H); 7.22 (d, 2H - C$_{(2)}$H, C$_{(6)}$H); 6.92 (d, 2H-CH$_2$-group); 6.48-5.93 (m, 1H - CH); 1.71 (d, 2H - CH$_2$). Melting point 153-154°C. % found: C 51.87; H 3.26; N 14.97. C$_{16}$H$_{12}$N$_4$O$_7$. % calculated: C 51.62; H 3.25; N 15.05.

Discussion

In order to find out the possibilities of formation of intermediates I during the alkaline hydrolysis of IIIa-d imidates, we studied the spectra of reaction mixtures in various media. Thus, in the PMR-spectrum of III a, b, d compounds in DMSO-D$_6$ and in the presence of sodium hydroxide ([III] $\sim$1 - 2·10^{-1} mol·l^{-1}, [NaOH] $\sim$5·10^{-2} mol·l^{-1}), the signals of the 3,5-dinitrophenyl ring disappear, evidently as a result of the formation of anion-radical par -

ticles III. Actually the EPR spectrum of the mixture consists of 7 bands with the intensities of 1:2:4:4:4:2:1 , respectively, which, like in paper[1], can be considered as belonging to structure IV. In the case of III c imidate in the PMR spectrum, when the signals of 2,6-protons of 3,5-dinitrophenyl fragment (δ = 8.75 ppm) disappear, appear three novel low-intensity signals (δ, ppm: 8.29, 7.29, 6.05) corresponding to structure 1. In adition to that, the signals of the CH_3-group protons in IIIc undergo a strong shift, $\Delta\delta_{CH_3}$ = 0.085 ppm. The obtained facts confirm the formation of the complexes of type I (R = $CH(CH_3)_2$) in the reactions of IIIa-d imidates with hydroxide ion in DMSO.

$$O_2N-\underset{O_2N}{\bigcirc}-\overset{N-R}{\underset{O-\bigcirc-NO_2}{C}}$$
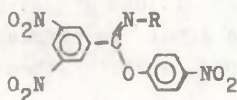
IV

In the UV-spectra of the reaction mixtures of IIIa-d imidates and alkali in the dioxan-water (1:1) medium (III) $\sim 1:0 - 5.0\cdot 10^{-4}$ mol·l^{-1} [NaOH] $\sim 1.0 - 2.0\cdot 10^{-1}$ mol·l^{-1}), more substantial formation of intermediate I was fixed also for IIIa compounds (λ_{max}=532 nm).In case of other substrates (IIIb-d) were registered only slight changes of optical density ($<$ 0.04) in the range of 500-550 nm, thus it was not possible to get more accurate spectral characteristics of these complexes. Nevertheless, as in ref.[1], a general reaction scheme, including the anionic δ-complex I functioning as an intermediate can be suggested for all IIIa-d imidates studied:

$$III + OH^- \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} I$$

$$k_1 \searrow \quad k_5 / OH^- \qquad (1)$$

$$O_2N-\underset{O_2N}{\bigcirc}-\overset{O}{\underset{NHR}{C}} + {}^-O-\bigcirc-NO_2$$
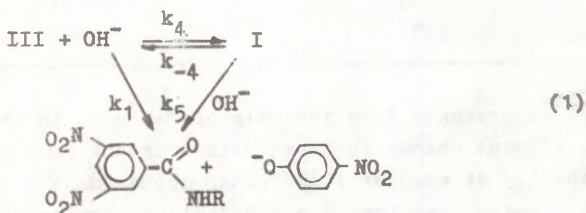
Kinetic method was used in order to determine the equilibrium constants of complex Ia formation. At a large alkali excess ($[NaOH] > [IIIa] \sim 10^{-5}$ mol·l^{-1}) the pseudofirst order constants k_H (s^{-1}) found spectrophotometrically, $\lambda = 532$ nm, remain the same during the process (Table 1) and they can be described by Eq. (2):

$$k_H = k_{-4} + k_4 [OH^-]$$ (2)

The forward and back reaction rate constants found from Eq. (2) are given in Table 2, which also contains analogous characteristics for N-benzyl-4-nitrophenyl-3,5-dinitrobenzimidate III ($R = CH_2C_6H_5$) obtained from the previous paper[1]. Since the 2,6-positions of 3,5-dinitrophenylic fragment of III imidates are equal, we carried out the statistic correction of k_4 values, dividing them by 2.

Table 1

Dependence of Reaction Rate Constants k_4 on Alkaline Correlation for Ia Complex Formation in Dioxan - Water (1:1) Mixture, I = 0.2 M (NaClO$_4$), 25°C

$[NaOH] \cdot 10^2$ mol · l^{-1}	$k_H \cdot 10^{-2}$, s^{-1}
0.45	1.48
0.91	2.26
1.21	2.66
1.83	3.82
2.72	5.35
3.65	7.03
5.51	10.4

As proceeds from the data of Table 2, in case of the substituent change in N-benzylic fragment from H to 3-Br, the stability of complex I increases approximately twice. At that, the forward reaction rate constant of complex I formation

Table 2

Rate Constants of Certain Steps in Scheme (2) for Alkaline Hydrolysis of
N-Substituted 4-Nitrophenyl-3.5-dinitrobenzimidates $3.5-(NO_2)_2-C_6H_3C(OC_6H_4-$
$-NO_2-4) = N-R$ in Water-Dioxan (1:1) Mixture, I = 0.2 (NaClO$_4$), 25°C

R	$k_4 \cdot 10^2$, $l \cdot mol^{-1} \cdot s^{-1}$	$k_{-4} \cdot 10^3$, s^{-1}	K_4, $mol \cdot l^{-1}$	$k_1 \cdot 10^3$ $l \cdot mol^{-1} \cdot s^{-1}$	$k_5 \cdot 10^3$ $l \cdot mol^{-1} \cdot s^{-1}$
$CH_2C_6H_5$	25.4 ± 0.9	2.9 ± 1.0	88 ± 35 [a] 57 ± 11 [b]	138 ± 9	2.9 ± 0.6
$CH_2C_6H_4-Br-3$	87.0 ± 1.6	6.71 ± 0.66	130 ± 15 [a] 135 ± 30 [b]	387 ± 42	16.9 ± 0.7
CH_3	-	-	-	0.55 ± 0.06	-
$CH(CH_3)_2$	-	-	-	0.49 ± 0.06	-
$CH_2CH=CH_2$	-	-	-	4.15 ± 0.14	-

[a] calculated from k_4/k_{-4}

[b] found from Eq. (3)

(ρ_{k_4} = 1.4 according to two points) increases a bit   more
(3.4 times). The absolute ρ_{k_4} value, considering the   re-
moteness of the R^1 substituent from the reaction center in
I to the $C = N-CH_2$ fragment evidences about comparatively
high sensitivity of the k_4 step to the nature of the men –
tioned substituent. This is in rather good agreement with
the earlier obtained data on the reactivity of 3,5-dinitro-
benzene substituents with anionic nucleophiles, during
which form the complexes of type IIa.

The transition rate of complex Ia into final products
was monitored spectrophotometrically at λ = 532 nm. The
pseudofirst order rate constants k_4' remain stable during the
reaction. Their values can be found in Table 3.

Table   3

Pseudofirst Order Rate Constants k_H' of Ia Complex
Transformation into Final Products in Alkaline Medium
in Dioxan – Water (1:1) Mixture, I = 0.2 M ($NaClO_4$) ,
$25^{\circ}C$

| $[NaOH] \cdot 10^2,$ mol $\cdot$ l^{-1}	k_H' exp. $\cdot 10^3$ s^{-1}	k_H' calc. $\cdot 10^3,$ s^{-1}
0.46	1.09	1.12
0.91	1.01	1.67
1.21	1.84	1.91
1.83	2.15	2.26
3.65	2.90	2.90
6.26	3.65	3.51
7.30	3.71	3.73
10.9	4.57	4.42
12.8	4.73	4.76
14.6	5.23	5.08
18.3	5.85	5.73

The character of the "k_H – $[NaOH]$" relationship is ana-
logous with that studied in[1], concerning the transformation

of complex I ($R = CH_2C_6H_5$). This fact can be linked with the realization of two parallel routes, A and B in scheme (2), with then sum of rates:

$$k_H' = \frac{k_1 [OH^-]}{1 + K_4[OH]} + \frac{K_4 k_5 [OH^-]^2}{1 + K_4[OH^-]} \qquad (3)$$

The k_1, k_5 and K_4 values (see[1]) found from the linear anamorphoses of Eq. (3) for various alkaline concentration ranges are presented in Table 2. Good agreement between the experimentally found rate constants and those calculated by Eq. (3) (Table 3) confirms the validity of the suggested scheme (2). Coinciding K_4 values obtained using independent ways (Table) also refer to the same situation; they were calculated from the data on the accumulation of the Ia intermediate, according to them was derived Eq.(2) and from those concerning its consumption – Eq. (3).

It follows from the data of Table 2 that the rate of hydroxide ion interaction with the anionic 6-complex (k_5 constant) is more sensitive to the substituent nature in N-benzyl ring (ρ k_5 = 1.97 in two points) than another analogous process (ρ k_5 = 1.15 in two points) where hydroxide ion attacks the initial imidate (constant k_1). Such a difference may be connected with the participation of the imidate azavinyl fragment in the distribution of negative charge in complex I owing to the formation of structure V.
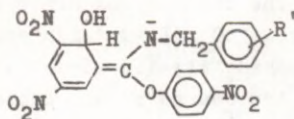
V

With the deepening of the acceptor properties of the R substituents the contribution of such a structure will certainly increase. This can also bring about a weakening of the differences in the reactivities of the molecular (III)

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and anionic ($\pm$) imidate forms. Really, it follows from k_1/k_5 of the compounds studied that the selectivity of the com - pared imidate forms towards the hydroxide ion will become remarkably poorer if the acceptor properties of the R' substituent are improved (R' = H, k_1/k_5 = 48; R' = 3-Br, k_1/k_5 = 23).

The peculiarities of route A in scheme (1) were reported in our previous works already[6,7]. The route presumably has the multi-step addition-elimination mechanism with the TIP formation in the rate limiting step. The closeness of the ρk_1 = 2.4 parameters[6] for the alkaline hydrolysis of 4-nitrophenyl-N-arylbenzimidates of $C_6H_5C(OC_6H_4-NO_2-4)$ = $N-C_6H_4R$ and ρk_1 = 1.15, for N-benzyl-derivatives of 4-nitrophenyl-3.5-dinitrobenzimidates of $3.5-(NO_2)_2-C_6H_3-(OC_6H_4-NO_2-4)$ = $N-CH_2C_6H_4R$, taking into account the inductive conductivity of methylene bridge ($Z^*_{-CH_2-}$ - 0.5[8]) provides evidence in support of the fact that N-aryl- and N-benzimidates III, have similar rate-limiting steps.

A priori, the addition-elimination mechanism with the TIP formation can also be suggested for the I σ-complex interaction with hydroxide ion. A comparatively high value ρk_5 = 1.97, concerning the substituents in the N-benzyl fragment of complex I for route B in scheme (2) agrees with this statement.

During the kinetic measurements ([NaOH]>[III] $\sim 10^{-5}$ mol · l^{-1}), in the water-dioxan (1:1) mixture we did not trace any remarkable accumulation of complex I in the case of IIIb-d imidates. The pseudofirst order rate constants of the alkaline hydrolysis of IIIb-d imidates, calculated considering the 4-nitrophenolate-ion accumulation at λ = 400 nm do not change in the course of the process. Their values are given in Table 4. The k_{OH}^1 values can quite well be described by Eq. (4). The values of k_1 calculated can be found in Table 2.

$$k_{OH^-}^1 = k_1[OH^-] \qquad (4)$$

Table 4

Pseudofirst Order Rate Constant k_{OH}^1- (s^{-1}) of Alkaline
Hydrolysis of N-Substituted 4-Nitrophenyl-3.5-dinitro-
benzimidates of $3.5-(NO_2)_2-C_6H_3-C(OC_6H_4-NO_2-4) = NR$ in
Dioxan-Water (1:1) Mixture, $I = 0.2$ M $(NaClO_4)$, $25^{\circ}C$

R	$[NaOH] \cdot 10^2, mol \cdot l^{-1}$	$k_{OH}^1- \cdot 10^4, s^{-1}$
CH_3	1.91	0.30
	5.42	0.46
	9.04	0.73
	14.5	1.05
	18.1	1.16
$CH(CH_3)_2$	1.91	0.18
	5.42	0.27
	9.04	0.46
	14.5	0.64
	18.1	0.93
$CH_2CH = CH_2$	0.92	0.35
	3.67	1.48
	9.18	3.40
	12.8	5.20
	18.4	7.64

Consequently, the kinetic regularities of the alkaline
hydrolysis of studied IIIb-d and IIIa imidates differ rather
substantially from each other. The essential difference is
that the kinetics of the hydrolysis of IIIa substrate cor -
responds to the realization of two parallel routes A and
B in scheme (1), but in the case of IIIb-d imidates to the
realization of route A only.

It is not possible to accurately estimate the reasons
of this phenomenon. The sensitivity of the formation of the
I σ-complex and the pK_a of the anionic component of imi -
date $(\beta_{RNH_2} = -0.66,$ R = $CH_2C_6H_5,$ $CH_2C_6H_4-Br-3)$ enables us

to expect the appearance of the route via the anionic σ-complex also in the case of IIIb-d substrates. Nevertheless, only route A (scheme 1) was established experimentally . Thus, we can come to the conclusion that alongside with the decrease of reactivity, owing to the weakening of the electron-acceptor strength of the substituent in the vicinity of nitrogen atom, there are some additional(most probably steric and conformational) factors hindering the reaction from proceeding via the I σ-complex.

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NUCLEOPHILIC SUBSTITUTION AT TETRACOOR-
DINATED ATOM OF PHOSPHORUS. REACTIVITY OF
PYRIDINE N-OXIDES IN HYDROLYSIS OF DIPHE-
NYLCHLOROPHOSPHATE IN ACETONITRILE

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Kinetics of hydrolysis of diphenylchloro -
phosphate, catalyzed by pyridine N-oxide in ace -
tone at $25^{\circ}C$ has been studied spectrophotometri -
cally and conductometrically. In a certain con -
centration range of water, interaction of diphe -
nylchlorophosphate with substituted pyridine N-
oxide acts as a rate limiting stage. Rate con -
stants of this interaction k_1 can more adequately
be described by correlation equation, considering
induction and resonance substituent effects ($\rho^{\circ} =
-3.92 \pm 0.23$; $\rho_R^+ = -2.31 \pm 0.51$), as well as Brøn-
sted equation ($\beta = 1.14 \pm 0.08$).

We have shown[1] that the diphenylchlorophosphate (DPCP)
interaction with different nucleophiles (NuH) in acetonit-
rile is catalyzed by pyridine N-oxide according to the nuc-
leophilic catalysis mechanism:

$$(C_6H_5O)_2P\!\!\diagup_{Cl}^{\diagup O} \;+\; O\!\leftarrow\!N\!\langle\rangle$$

$$k_1 \big\updownarrow\, k_{-1}$$

$$\left[(C_6H_5O)_2P\!\!\diagup_{O-N\langle\rangle}^{\diagup O}\!\!\!\!^+\right] \; Cl^- \;\underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}}\; (C_6H_5O)_2P\!\!\diagup_{O-N\langle\rangle}^{\diagup O}\!\!\!\!^+ \;+\; Cl^-$$

Ia $\qquad\qquad\qquad\qquad\qquad\qquad$ Ib

$$k_3\,\Big| \;NuH \qquad\qquad\qquad\qquad k_4\,\Big|\;NuH \qquad\qquad (1)$$

$$(C_6H_5O)_2P(O)Nu \;+\; O\!\leftarrow\!N\!\langle\rangle \;+\; HCl$$

$NuH = HN(C_2H_5)_2,\quad 3\text{-}NO_2C_6H_4NH_2,\quad H_2O,\quad CH_3OH.$

The kinetics of this reaction largely depends on the nucleophile's nature and concentration. At a wide variation range of nucleophilic concentration, the changes took place within the region of 1-0, i.e. the change of the rate li - miting step from the interaction of intermediates 1a and 1b with NuH, which is characterized by rate constants k_3 and k_4 in Scheme (1), up to catalyst (pyridine N-oxide) at- tack on the substrate (step k_1). Such a situation cannot be established in the case of analogous catalytic transi - tion processes of acyl and arensulphonyl groups in aprotic nedia[2-4]. It would not be possible to change the rate de- termining step (the interaction of I with NuH) of these systems within the limits of nucleophilic mechanism neither by changing the nucleophile concentration nor by varying its nature. It was possible to measure the k_1 rate constants only in some cases of formation of thermodynamically stable N-arenesulfonyloxypyridine salts[5].

Measuring of k_1 in the case of reaction (1) enables us to set a task of studying the nucleophilic reactivity of pyridine N-oxides in the series of other bases, including pyridines, N-substituted azoles, tertiary aliphatic amines,

which do not form thermodynamically stable products with co-
ordinationally unsaturated substrate. Therefore, it would
be rather complicated to study their nucleophilic reactivi-
ty in a wide range of structural variation, and the bases
of this type fall out of the "reactivity-nucleophility"ana-
lysis in the case of reactions including coordinationally
unsaturated substrates (C=O, C=N, C=C, SO_2, P=O, etc.). In
this sense, pyridine N-oxides are of special interest, since
they are widely known as "supernucleophilic" catalysts[6] in
the transition of acylic and arenesulphonylic groups, al -
though we have been the pioneers of studying them as the
catalysts of nucleophilic substitution reactions at the tet-
racoordinated phosphorus atom[1].

The present paper deals with the reactivity of pyri -
dine N-oxides (the pK_a variation range in water is -1.7 -
3.88) in DPCP hydrolysis (NuH = H_2O) in acetonitrile at
25°C.

In order to estimate the contribution of the DPCP non-
catalytic hydrolysis into the total reaction rate, we stud-
ied the reaction of DPCP with water in similar conditions.

Noncatalytic Hydrolysis

The rate of DPCP interaction with water in acetonitrile
was measured conductometrically, at [DPCP]$\ll$[H_2O]. The fact
that the interaction rate can be described by a second-order
reaction is confirmed by the linear dependence of the ob -
served pseudofirst order rate constant k_o^I on water concen -
tration. On the basis of the latter, and using the data of
Table 1, we calculated the bimolecular rate constant k_o va-
lues, given in the same table.

Catalytic Hydrolysis

In the presence of pyridine N-oxides (4-(N,N-dimethyl-
amino)pyridine N-oxide excl.), the hydrolysis rate of DPCP
in acetonitrile was studied conductometrically([DPCP]$\ll$[B])
at water concentration, being equal to 0.45 mol $\cdot$ 1^{-1} . As

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it has already been shown in[1], this is the intermediate
concentration within the range, in the case   of which
holds the zero order towards water in the case of unsub -
situted pyridine N-oxide. We have demonstrated by another
experiment, using 3-methyl-pyridine N-oxide that the in -
crease of water concentration up to 0.5 mol $\cdot$ l^{-1} does not
affect the interaction rate of DPCP with a catalyst(Table 2).

Table   1

Noncatalytic Interaction of DPCP with
Water in Acetonitrile at 25° C

$[H_2O]$, mol $\cdot$ l^{-1}	$k_o^I \cdot 10^5$, s^{-1}
0.035	0.24 ± 0.02
0.120	0.27 ± 0.01
0.150	0.27 ± 0.01
0.170	0.72 ± 0.03
0.360	1.52 ± 0.05
0.490	2.45 ± 0.18
0.840	4.29 ± 0.11
1.210	6.29 ± 0.11

$$k_o = (5.41 \pm 0.18) \cdot 10^{-5} \text{ l} \cdot \text{mol}^{-1} \cdot \text{s}^{-1}$$
$$s_o = 1.93 \cdot 10^{-6}; \quad r = 0.997; \quad N = 8$$

On the basis of the linear dependence of the pseudofirst
order rate constant k^I (s^{-1}) on B we calculated the k_1
values as the tangents of the slope curves of correspond -
ing lines (Table 2). In case of all studied pyridine N-ox-
ides (4-nitropyridine N-oxide excl.), the intercepted sec-
tion is statistically insignificant and, thus, the depen -
dence of k^I on the catalyst's concentration can be de -
scribed by Eq. (2), where the contribution of k_o^I is very
small (5.41 $\cdot$ 10^{-5} l $\cdot$ mol^{-1} $\cdot$ s^{-1} $\cdot$ 0.45 mol $\cdot$ l^{-1} =
2.43 $\cdot$ 10^{-5} s^{-1})

$$k^I = k^I_o + k_1 [B] \qquad (2)$$

For 4-nitropyridine N-oxide the intercepted section (k^I_o) equals $(2.5 \pm 0.5) \cdot 10^{-5}$ s^{-1}, which, according to Eq. (2) coincides with the k^I_o value in the DPCP noncatalytic hydrolysis.

In the reaction with participation of 4-(N,N-dimethylamino) pyridine N-oxide, the method of stopped flow with spectrophotometric registration of the optical density loss of the base was applied to determine the reaction rate .

Table 2

k^I (s^{-1}) and k_1 ($1 \cdot mol \cdot s^{-1}$) Values of Pyridine N-oxides Reactions with DPCP in Acetonitrile Containing 0.45 mol $\cdot 1^{-1}$ of Water at 25°C
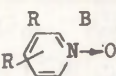
$R \underset{R}{\diagdown} N \rightarrow O$ R B	$[B] \cdot 10^3$ mol $\cdot 1^{-1}$	$k^I \cdot 10^3$, c^{-1}	k_1, $1 \cdot mol^{-1} \cdot s^{-1}$
1	2	3	4
H			4.16 ± 0.11[1]
$3-CH_3$	0.02	0.42 ± 0.11	
	0.035	0.67 ± 0.01	
	0.09^a	2.28 ± 0.04	
	0.11	2.18 ± 0.06	22.1 ± 0.8
	0.17^a	3.80 ± 0.12	$S_o = 2.8 \cdot 10^{-4}$;
	0.24	5.13 ± 0.05	$r = 0.996; N = 9$
	0.26^a	6.13 ± 0.11	
	0.35^a	7.44 ± 0.15	
	0.35	8.01 ± 0.18	
$3-Cl$	1.5	0.21 ± 0.01	
	2.6	0.41 ± 0.01	
	3.7	0.67 ± 0.01	0.14 ± 0.01
	7.7	0.96 ± 0.01	$S_o = 2.7 \cdot 10^{-4}$;

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Table 2 continued

1	2	3	4
	30.7	4.83 $^\pm$ 0.06	r = 0.997; N = 6
	53.8	7.43 $^\pm$ 0.08	
3-CN	2.1	0.78 $^\pm$ 0.01	$(2.6 \pm 0.4) \cdot 10^{-2}$
	14.9	3.38 $^\pm$ 0.05	$s_0 = 6.1 \cdot 10^{-5}$;
	21.3	5.82 $^\pm$ 0.09	r = 0.986; N = 3
4-Et	0.5	0.28 $^\pm$ 0.01	
	3.1	1.12 $^\pm$ 0.01	25.5 $^\pm$ 2.7
	5.1	1.24 $^\pm$ 0.02	$s_0 = 2.0 \cdot 10^{-4}$;
	7.1	1.82 $^\pm$ 0.05	r = 0.983; N = 5
	10.2	2.89 $^\pm$ 0.07	
4-NO$_2$	3.8	0.047$^\pm$ 0.005	
	7.7	0.061$^\pm$ 0.005	$(5.4 \pm 0.3) \cdot 10^{-3}$
	15.3	0.11 $^\pm$ 0.01	$s_0 = 4.8 \cdot 10^{-6}$;
	23.0	0.15 $^\pm$ 0.02	r = 0.996; N = 4
4-N(CH$_3$)$_2^b$		$(5.44 \pm 0.18) \cdot 10^3$	
		$(5.19 \pm 0.07) \cdot 10^3$	
		$(5.62 \pm 0.17) \cdot 10^3$	5490 $^\pm$ 110
		$(5.70 \pm 0.32) \cdot 10^3$	

^{a} [H$_2$O] = 0.5 mol $\cdot$ l^{-1}

^{b} k^I constants were found at a steady DPCP concentration being equal to 0.001 mol $\cdot$ l^{-1} and varying water concentration (see text).

Fig. 1 shows that the observed rate constants k^I do not actually depend on different water concentrations (provided that the DPCP concentrations remain fixed on the water concentration up to 0.34 mol $\cdot$ l^{-1}. The value is much smaller
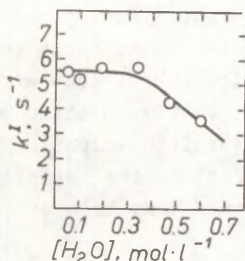
Fig. 1. Dependence of k^I on water concentration in ace-
tonitrile in DPCP hydrolysis reaction, cataly-
zed by 4-(N,N-dimethylamino)pyridine N-oxide at
$25^{\circ}C$.
$[DPCP] = 1 \cdot 10^{-3}$ mol $\cdot$ 1^{-1}.

than that obtained for other pyridine N-oxides (see the ex-
ample for 3-methylpyridine N-oxide in Table 2 and the data
on pyridine N-oxide[1]). A further rate increase at higher
water concentrations in a dipolar aprotic solvent can be
linked with a somewhat higher solvation level of a nucleo -
phile (4-(N-dimethylamino)pyridine N-oxide in this case)
caused by the effect of water molecules. Such a dependence
of reaction rate on the nucleophile (hydroxide ion) concen-
tration holds in the case of the alkaline hydrolysis of 4-
nitrophenyl esters of dialkyl and diaryl phosphoric acids
in acetonitrile with water additions (the hydrolysis rate
values reach their maximums at the concentration of water
0.02-0.3 mol $^-$ 1^{-1})[7,8], and that of DPCP hydrolysis in ace-
tonitrile, which is catalyzed by pyridine N-oxide[1]. In the
case of the latter, the retardation of the reaction was
traced starting from 0.7 mol $\cdot$ 1^{-1} of water. As to the reac-
tions of DPCP with 4-(N,N-dimethylamino) pyridine N-oxide
(Table 2), their k_1 value was calculated from $k^I(k^I [DPCP])$
values for the concentration range of water, during which

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the k^I values remained invariable.

It is known[9] that in pyridine N-oxides, the N-oxide grouping has a rather unique functional peculiarity: it interacts both with π-donor and π-acceptor substituents . Therefore, when describing the substituent effects in N-heteroaromatic systems, the duality of their resonance contribution should also be taken into account. Thus, the description of substituent effect on the basicity of pyridine N-oxides in water demonstrated[9] that this will be better achieved, using Eq. (3),

$$\log k = \log k_o + \rho^o \sigma^o + \rho_R^+ \sigma_R^+ + \rho_R^- \sigma_R^- \tag{3}$$

taking into account the polar resonance of para-substituents with the reaction center.

The processing of the k_1 values (Table 2) by Eq. (3) (the term with σ_R^- was left out, owing to a restricted set of π-acceptor substituents in the paraposition of pyridine N-oxide nucleus) yields quite good correlation with the following coefficient values[x]:

$$\log k = (0.78 \pm 0.10) - (3.92 \pm 0.23) \sigma^o -$$
$$- (2.31 \pm 0.51) \sigma_R^+ \tag{4}$$
$$s_o = 0.19; \quad R = 0.997; \quad N = 7$$

The reduction of multiple-regression coefficient to the standard (normed) scale[11], enables us to compare them directly with each other within the same reaction series. Regardless of the organic set of substituents, there still prevails the induction effect ($\sigma^o = -0.84$) over the effects of a direct polar conjugation ($\sigma_R^+ = -0.22$).

Rather good correlation parameters of Eq. (5) also confirm the aforesaid:

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[x] σ^o and σ_R^+ values were taken from[10]; in case of meta-substituents $\sigma_R^+ = 0.00$.

$$\log k_1 = (0.83 \pm 0.09) - (4.3 \pm 0.2) \bar{\delta}_{Py}, \qquad (5)$$
$$s_0 = 0.24; \quad r = 0.994; \quad N = 7$$

$\bar{\delta}_{Py}$[10] shows the sum of induction and resonance substituent effects and it is used for describing substituent effect in the pyridine nucleus. Realization of equations of type (5) is valid only in case of small resonance effeot contribu - tions into the total substituent effect.

Since pyridine N-oxides do not contain any hydrogen , attached to the nucleophilic center they attack the phospho- rylic group with the formation of highly reactive phospory- lic salts of type Ia (Ib), forming with water phosphoric acid in fast step. Therefore, in the present case the cor- relation of Brønsted-type between $\log k_1$ and the basicity of pyridine N-oxides[x], which is described by Eq. (6)

$$\log k_1 = -(0.40 \pm 0.15) + (1.14 \pm 0.08)pK_a \qquad (6)$$
$$s_0 = 0.37; \quad r = 0.987; \quad N = 7$$

is not connected with the process of proton transfer. If the ß value is more than 1, the sensitivity to the substi - tuent of introduction of the phosphorylic group into the pyridine N-oxides molecule exceeds that of proton addition to water. Taking into consideration the analogous statement by Jackson et al.[15], explaining a similar phenomenon in the aminolysis of acyl derivatives, we have come to the conclu- sion that in our case this is connected with the additional electronic stabilization of transition state by the phos - phorylic group if compared with the proton in the acid con- jugated of the base.

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[x] In correlation were used the pK_a values in water for $RC_5H_4N \rightarrow O$: R = H, 3-CH_3, 4-NO_2, 4-$N(CH_3)_2$[12]; R = 4-Et[13] R = 3-Cl_9[14]; R = 3-CN - calculated from correlation equa- tion[9].

The ρ^o and ß parameters obtained in the present paper will further be made use of in discussing the reactivities of different base classes, relative to the tetracoordinated phosphorus atom in aprotic media.

Experimental

Pyridine N-oxides, excluding 4-(N,N-dimethylamino)-and 4-nitropyridine N-oxides, were synthesized using similar methods, by oxidation of the pyridine of 30% hydrogen peroxide[16] ; 4-(N,N-dimethylamino)pyridine N-oxide[17], 4-nitropyridine N-oxide[18] and DPCP[19] were also obtained by known methods.

Acetonitrile was purified as suggested in[20], its residual water content was approximately $5 \cdot 10^{-3}$ mol $\cdot$ 1^{-1}, the latter was taken into account in the experiments with small water additions (up to 0.15 mol $\cdot$ 1^{-1}).

In all cases (4-(N-N-dimethylamino)pyridine N-oxide excl.), the reactions were controlled conductometrically according to the accumulation of hydrogen chloride in the reaction system. The resistance of the solvent was measured using the instalment described earlier[21]. The pseudofirst order rate constants k^I (s^{-1}) were calculated according to Eq. (7):

$$k^I = \frac{1}{t} \; \ln \; \frac{\dfrac{1}{R_\infty} - \dfrac{1}{R_o}}{\dfrac{1}{R_\infty} - \dfrac{1}{R_t}} \tag{7}$$

where R_∞ , R_o and R_t denote the resistance by the termination of the reaction, at the initial time moment and at time moment t, respectively.

In the case of 4-(N,N-dimethylamino)pyridine N-oxide, the process rate was monitored spectrophotometrically according to the optical density loss (λ = 313 nm, ε = 2400$\pm$ 500 1 $\cdot$ mol^{-1} $\cdot$ cm^{-1}, s_o = 2.65 $\cdot$ 10^{-2}, r = 0.999, N = 8)

on a high-speed spectrophotometer SP-176. The k^I (s^{-1}) constants were calculated by (8):

$$k^I = \frac{1}{t} \ln \frac{D_o - D_\infty}{D_t - D_\infty} \qquad (8)$$

In case of noncatalytic hydrolysis, the observed rate constants k^I_o were calculated by means of numerical diffe - rentiation on a computer ES-1020, of the dependence of conductivity on the time. The same calculation methods with determination of the rate at the zero time moment were also used in the case of the DPCP hydrolysis by N-oxide.

Mathematical processing of multiple regression was performed on a computer DVK-2.

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