

CYCLIZATION AND ACID-CATALYZED HYDROLYSIS OF O-BENZOYL BENZAMIDOXIMES

František GRAMBAL and Jan LASOVSKÝ

*Department of Inorganic and Physical Chemistry,
Faculty of Natural Sciences, Palacký University, 772 00 Olomouc*

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Kinetics of formation of 1,2,4-oxadiazoles from 24 substitution derivatives of O-benzoylbenzamidoxime have been studied in sulphuric acid and aqueous ethanol media. It has been found that this medium requires introduction of the Hammett H^0 function instead of the pH scale beginning as low as from 0.1% solutions of mineral acids. Effects of the acid concentration, ionic strength, and temperature on the reaction rate and on the kinetic isotope effect have been followed. From these dependences and from polar effects of substituents it was concluded that along with the cyclization to 1,2,4-oxadiazoles there proceeds hydrolysis to benzamidoxime and benzoic acid. The reaction is thermodynamically controlled by the acid-base equilibrium of the O-benzoylated benzamidoximes.

Amidoximes and their O-acyl derivatives in particular are often mentioned in literature in the connection with synthesis of 3,5-disubstituted oxadiazoles. Since Tie-mann's works¹, the cyclization of O-acylated amidoximes has been the most frequent reaction for preparation of 1,2,4-oxadiazoles. In his review² and a later report³, Eloy gives various possible ways of the cyclization inclusive of the cyclization in dilute sulphuric acid medium. In a previous report⁴ we dealt with kinetics of cyclization of O-benzoylated benzamidoximes (*I-XXIV*) in neutral medium. The aim of this paper is to study kinetics and mechanism of the reaction of the same derivatives of these compounds in aqueous ethanol medium (50 g ethanol *per* 100 g solution) in the H^0 function range from -0.5 to 2.5 .

EXPERIMENTAL

The O-benzoylbenzamidoximes *I-XXIV* (Table I) were prepared according to ref.⁵. The kinetic measurements were carried out with $5 \cdot 10^{-4}$ mol dm⁻³ solutions of the compounds in sulphuric acid solutions of various concentrations (0.023 to 2.81 mol dm⁻³) in aqueous ethanol (50 g ethanol *per* 100 g solution). The reaction was followed at the temperature of 343.15 ± 0.05 K in an ultrathermostat. The rate constants were calculated from polarographic data by means of the least squares treatment. At regular time intervals 5 ml samples were withdrawn from the reaction mixture; after cooling the samples were mixed with 5 ml water or 0.1 mol dm⁻³ sulphuric acid solution in the same solvent, gelatine (0.05 ml) was added, the sample was deaerated with nitrogen, and the diffusion limit current was recorded of the O-benzoylated benzamidoximes⁶.

TABLE I

The hydrolysis rate constants (s^{-1}) of 4,4' substituted O-benzoylbenzamidoximes and the ionisation constants determined spectrophotometrically (pK_a) and kinetically (pK'_a)

Compound	R ¹	R ²	$k_{exp} \cdot 10^4$ for H^0										$k_n \cdot 10^5$	pK_a	pK'_a
			0.49	0.72	0.94	1.24	1.53	1.83	2.27	2.70	3.16	3.49			
I	H	H	1.56	1.48	1.36	1.14	0.92	0.71	0.49	1.70	3.20	1.42	1.44		
II	CH ₃	H	1.31	1.30	1.16	1.10	0.88	0.81	0.56	1.37	3.52	1.69	1.70		
III	Cl	H	2.11	1.93	1.62	1.22	0.84	0.58	0.37	2.64	2.17	1.08	1.48		
IV	Br	H	2.22	1.97	1.68	1.28	0.89	0.58	0.37	2.70	2.07	1.10	1.48		
V	CH ₃ O	H	1.12	1.10	1.05	0.96	0.83	0.72	0.53	1.16	3.49	1.74	1.80		
VI	NO ₂	H	2.90	2.00	1.38	0.80	0.46	0.28	0.16	7.58	0.85	0.43	0.26		
VII	H	Cl	2.51	2.24	1.93	1.77	1.55	1.03	0.74	2.82	5.23	1.20	1.17		
VIII	CH ₃	Cl	2.04	1.95	1.82	1.60	1.30	1.23	0.83	2.22	6.99	1.39	1.21		
IX	Cl	Cl	3.00	2.47	2.08	1.46	1.05	0.72	0.47	3.98	3.17	0.91	0.71		
X	Br	Cl	—	—	2.29	—	—	—	—	4.45	3.20	0.90	—		
XI	CH ₃ O	Cl	—	—	2.37	—	—	—	—	2.96	6.44	1.61	—		
XII	NO ₂	Cl	—	—	8.50	—	—	—	—	8.50	1.41	0.48	—		
XIII	H	CH ₃ O	0.71	0.67	0.61	0.54	0.47	0.34	0.24	0.76	1.69	1.60	1.51		
XIV	CH ₃	CH ₃ O	—	—	0.54	—	—	—	—	0.61	2.00	1.63	—		
XV	Cl	CH ₃ O	1.17	1.29	0.80	0.76	0.55	0.39	0.22	1.32	1.00	0.78	1.70		
XVI	Br	CH ₃ O	—	—	1.02	—	—	—	—	1.88	1.20	0.98	—		
XVII	CH ₃ O	CH ₃ O	0.48	0.47	0.44	0.41	0.36	0.31	0.26	0.50	2.13	1.85	1.90		
XVIII	NO ₂	CH ₃ O	2.53	2.09	1.53	1.18	0.74	0.44	0.23	3.39	0.54	0.77	0.87		
XIX	H	NO ₂	11.5	9.72	7.77	6.65	5.52	4.26	3.27	14.9	27.6	0.72	0.83		
XX	CH ₃	NO ₂	—	—	8.51	—	—	—	—	13.3	20.0	1.07	—		
XXI	Cl	NO ₂	—	—	5.44	—	—	—	—	15.3	15.2	0.54	—		
XXII	Br	NO ₂	—	—	4.77	—	—	—	—	14.2	15.0	0.48	—		
XXIII	CH ₃ O	NO ₂	10.2	8.89	9.11	7.40	5.70	5.22	4.32	12.4	33.2	1.21	0.87		
XXIV	NO ₂	NO ₂	—	—	4.65	—	—	—	—	33.10	3.97	—0.54	—		

At these conditions the presence of 1,2,4-oxadiazole and/or non-acylated amidoxime does not interfere with the polarographic estimation. The experimental rate constants were calculated from the relation $\ln(i_0/i_t) = k_{\text{exp}}t$, where i_0 and i_t mean the initial and the actual limit currents, resp., of the polarographic reduction of the reactants⁴. The values given in tables are mean values of 15–30 measurements each, the standard deviation of the rate constants being below 5%.

The dissociation constants of compounds *I*–*XXIV* were determined with the help of the H^0 function in aqueous ethanol. The H^0 functions were determined for the system sulphuric acid (perchloric acid)–water–ethanol (50 g ethanol *per* 100 g solution) from the absorbances ratio of the protonated and deprotonated forms of *p*-nitroaniline (*pK* 1.11) and *o*-nitroaniline (*pK* –0.29) (ref.⁷).

Two methods were adopted for analysis of the reaction products: *a*) 1 g compound *I* was dissolved in 200 ml warm aqueous-ethanolic 0.75 mol dm⁻³ sulphuric acid ($H^0 = 0.94$) and refluxed 17 h. After cooling and dilution with water to 500 ml, crystals were obtained (0.2 g) whose melting point (107°C), UV and IR spectra, and elemental analysis (for C₁₄H₁₀N₂O (222.2) calculated: 75.65% C, 4.50% H, 12.61% N; found: 75.69% C, 4.36% H, 12.60% N) were identical with those of 3,5-diphenyl-1,2,4-oxadiazole. The acid filtrate was extracted with ether and reextracted after alkalization with sodium carbonate to pH ~9; the respective extracts gave 0.30 g benzoic acid and 0.40 g benzamidoxime which were identified by IR spectra (the latter compound also by identical mixed melting point 79°C and by specific reaction with nickel(II) ion). *b*) The benzamidoxime content was determined spectrophotometrically by measuring the absorbance in the region where neither benzoic acid nor 3,5-diphenyl-1,2,4-oxadiazole absorb (λ 310 nm, $\epsilon = 2705$) (Table II).

The kinetic isotope effect was determined in the following way: 5 · 10⁻⁴ mol compound *I* was dissolved in 100 ml aqueous ethanol prepared from H₂O or ²H₂O and H₂SO₄ (H^0 0.94)⁴. The $k_{\text{H}}/k_{\text{D}}$ ratio was determined by measuring the reaction rates in both the media at 343.15 K.

The activation parameters were calculated from the rate constants measured at 343.15, 333.15, 323.15, and 313.15 K for compounds *I*–*XXIV* in aqueous ethanol at H^0 0.94. The effect of ionic strength was followed with compound *I* at the above-mentioned conditions (343.15 K) with addition of sodium perchlorate (Table III). The reaction order was also verified with compound *I* at the same conditions in the concentration region of the reactant from 10⁻⁵ to 10⁻² mol dm⁻³.

TABLE II

The amounts *m* (mg) of benzamidoxime obtained by hydrolysis of compound *I* and yields η (%) at various H^0 values

H^0	<i>m</i>		η
	Found	Calculated	
0.72	32.1	32.95	97.4
0.94	31.5	32.01	98.3
1.53	25.8	27.36	94.3
1.83	22.6	22.92	98.5
2.27	13.5	14.59	92.66

The ionic strength was adjusted with sodium perchlorate, all the chemicals used were of *p.a.* purity grade.

The apparatus used: an LP 7 polarograph (Laboratorní přístroje, Prague), an SP-8-100 spectrophotometer (Pye Unicam, Cambridge, Great Britain), a UR-20 infrared spectrophotometer (Zeiss Jena, G.D.R.), a U 10 ultrathermostat (Prüfgeräte, Medingen, G.D.R.).

<i>I</i>	$R^1 = R^2 = H$	<i>XIII</i>	$R^1 = H, R^2 = CH_3O$
<i>II</i>	$R^1 = CH_3, R^2 = H$	<i>XIV</i>	$R^1 = CH_3, R^2 = CH_3O$
<i>III</i>	$R^1 = Cl, R^2 = H$	<i>XV</i>	$R^1 = Cl, R^2 = CH_3O$
<i>IV</i>	$R^1 = Br, R^2 = H$	<i>XVI</i>	$R^1 = Br, R^2 = CH_3O$
<i>V</i>	$R^1 = CH_3O, R^2 = H$	<i>XVII</i>	$R^1 = R^2 = CH_3O$
<i>VI</i>	$R^1 = NO_2, R^2 = H$	<i>XVIII</i>	$R^1 = NO_2, R^2 = CH_3O$
<i>VII</i>	$R^1 = H, R^2 = Cl$	<i>XIX</i>	$R^1 = H, R^2 = NO_2$
<i>VIII</i>	$R^1 = CH_3, R^2 = Cl$	<i>XX</i>	$R^1 = CH_3, R^2 = NO_2$
<i>IX</i>	$R^1 = R^2 = Cl$	<i>XXI</i>	$R^1 = Cl, R^2 = NO_2$
<i>X</i>	$R^1 = Br, R^2 = Cl$	<i>XXII</i>	$R^1 = Br, R^2 = NO_2$
<i>XI</i>	$R^1 = CH_3O, R^2 = Cl$	<i>XXIII</i>	$R^1 = CH_3O, R^2 = NO_2$
<i>XII</i>	$R^1 = NO_2, R^2 = Cl$	<i>XXIV</i>	$R^1 = R^2 = NO_2$

RESULTS AND DISCUSSION

The compounds *I*–*XXIV* undergo parallel cyclization and hydrolysis to give the corresponding derivatives of 1,2,4-oxadiazole, benzamidoxime, and benzoic acid. In all the cases the reaction rate increases with the acid concentration and is first order in the reactant concentration c_T

$$v = -dc_T/dt = k_{\text{exp}} \cdot c_T \quad (1)$$

With sulphuric acid concentrations from 0.1 to 30% we must consider the acid-base equilibrium (*A*) and, hence, the simultaneous presence of both protonated and neutral forms of the reactant.

TABLE III

Effect of ionic strength μ on the rate constant $k_{\text{exp}}(\text{s}^{-1})$ for compound *I* at the conditions: $H^0 = 0.94$ and $T = 343.15 \text{ K}$

μ	2.26	2.36	2.76	3.26
$k_{\text{exp}} \cdot 10^4$	1.36	1.36	1.34	1.30



It can be presumed that the protonated form is preferably hydrolyzed by the mechanism of acid-catalyzed hydrolysis, whereas the basic form gives the oxadiazole⁴. The decomposition reaction rate of the two forms and the overall reaction rate are given by the following expressions:

$$K_a = [\text{B}][\text{H}^+]/[\text{BH}^+], \quad (2)$$

$$-d[\text{BH}^+]/dt = k_k[\text{BH}^+], \quad -d[\text{B}]/dt = k_n[\text{B}], \quad (3)$$

$$\begin{aligned} -dc_T/dt &= -d[\text{BH}^+]/dt - d[\text{B}]/dt = \\ &= c_T(k_k[\text{H}^+]/(K_a + [\text{H}^+]) + k_nK_a/(K_a + [\text{H}^+])), \end{aligned} \quad (4)$$

where c_T means the overall concentration of the benzoylated benzamidoxime, and K_a stands for the dissociation constant of the reactant. The proportion of the two reactions in the overall reaction is determined by the acidity of medium and pK_a values of the reactants (which we published earlier⁶). We found that in acid medium of aqueous ethanol (0.1 to 30% HClO_4 or H_2SO_4) the absorbance pH curves do not agree with the usual Henderson-Hasselbalch equation. Their course can be described by an analogous equation

$$m \text{ pH} = m \text{ pH} (\text{half protonation}) + \log [\text{B}]/[\text{BH}^+], \quad (5)$$

in which the m value is very close to two. This fact led us to the erroneous conclusion, that two protons take part in the acid-base reaction forming the product H_2B^{2+} , and in this sense we also formulated the dissociation constants⁶.

By measuring the absorbance curves of *p*- and *o*-nitroanilines (*i.e.* indicators which have pK_a values similar to those of the compounds studied and serve for construction of the Hammett acidity functions) in the presence of ethanol we observed the same anomalies of the absorbance curves due obviously to the effect of the mixed solvent on the activity coefficients. Therefore, we replaced the pH by H^0 function for aqueous ethanol and sulphuric or perchloric acid starting from 0.1% concentration (Fig. 1).

$$H^0 = -\log (a_{\text{H}^+}\gamma_{\text{B}}/\gamma_{\text{BH}^+}) = pK_a + \log ([\text{B}]/[\text{BH}^+]) \quad (6)$$

After this modification the acid-base equilibria of O-benzoylated benzamidoximes are simple and involve the exchange of a single proton. The corrected $\text{p}K_a$ values are given in Table I. On introducing the acidity function the experimental rate constant of the overall reaction becomes

$$k_{\text{exp}} = k_k h^0 / (K_a + h^0) + k_n K_a / (K_a + h^0), \quad (7a)$$

which can also be written as follows

$$1/(k_{\text{exp}} - k_n) = 1/(k_k - k_n) + K_a/h^0(k_k - k_n), \quad (7b)$$

$$H^0 = \text{p}K_a + \log(k_k - k_{\text{exp}})/(k_{\text{exp}} - k_n), \quad (7c)$$

where $H^0 = -\log h^0$.

The relation between acidity of medium and the reaction rate was studied with compounds I-IX, XIII, XIV, XVII-XIX, and XXIII. The acidity of medium was adjusted by addition of sulphuric acid which shows an extraordinary ability to protonate weak bases⁸. The k_n rate constant values can be determined directly by measuring the reaction rates in solutions in which the deprotonated form of the reactant is only present. These values can easily be obtained by polarography⁴ and are pH-independent within a broad interval (from 2.45 to 6.20). The k_k rate constants of the hydrolysis cannot be determined directly, because a complete protonation of the reactant necessitates an extremely strongly acidic medium, where the reaction mechanism is changed. Therefore, Eqs (7b) and (7c) were solved with respect to the unknown k_k and K_a : the results are presented in Table I. The linear course of Eqs (7b) and (7c) and the agreement of the dissociation constants determined spectrophotometrically ($\text{p}K_a$) with those obtained by kinetic method ($\text{p}K'_a$) confirm validity of the suggested kinetic scheme of parallel reactions according to Eq. (A).

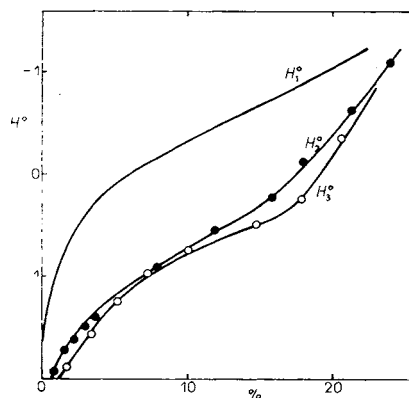


FIG. 1

The acidity functions in the systems: sulphuric acid-water (H_1^0), perchloric acid-water-ethanol (H_2^0), and sulphuric acid-water-ethanol (H_3^0)

In acid region the reaction is insensitive to increasing ionic strength. At high concentrations of electrolytes and in mixed media the activity coefficients are affected, the ratio of activity coefficients of the acidity function being changed, too. In such extreme media it is difficult to predict the effect of ionic strength. However, from the formalism suggested it follows that the particle reacting in the hydrolytic reaction is the ionised molecule of benzoylbenzamidoxime. This fact is in accordance with ref.⁹ stating that intramolecular catalysis of acylation of amidoximes is strongly suppressed in acid region.

After 20 h reaction course the yields of reaction products exceed 90%. According to the presumed formalism given in Eqs (1) through (4) the yields of the both forms depend on the dissociation degree of the reactants.

$$P/P_T = k_k/k_{c_{xp}}h^0/(K_a + h^0), \quad (8)$$

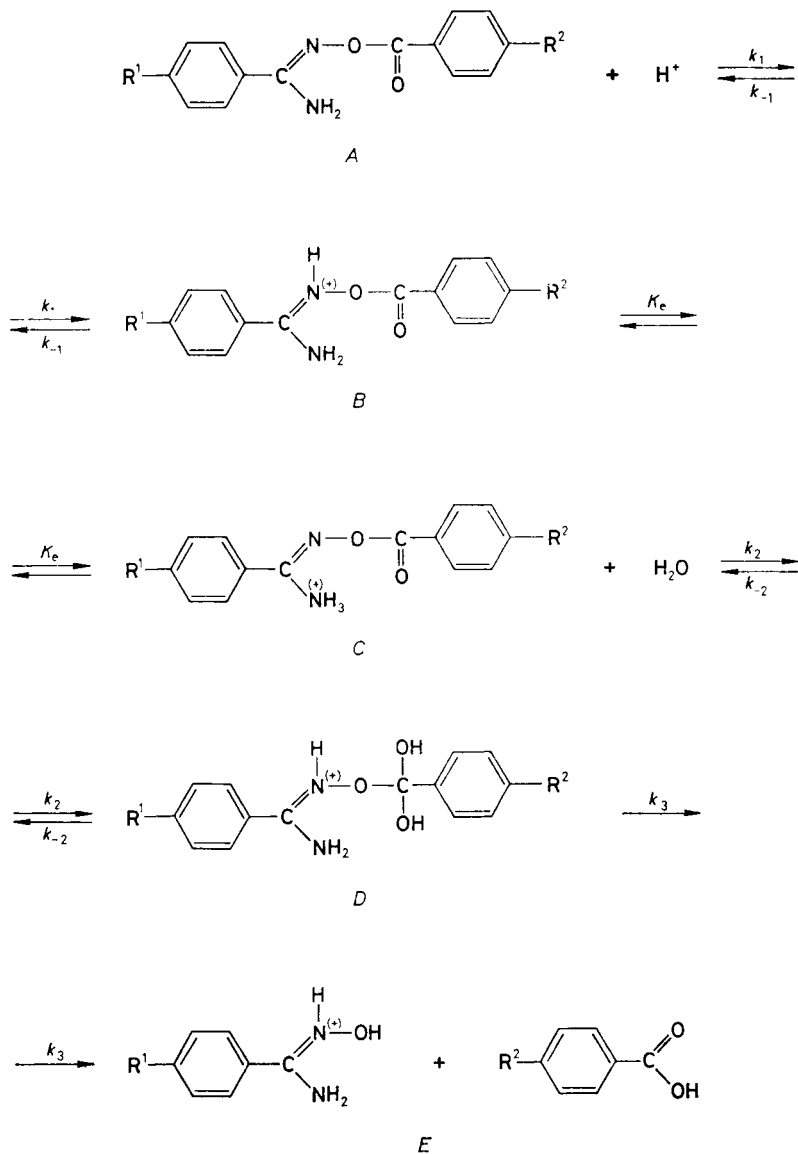
where P is the amount of the benzamidoxime obtained, P_T is the amount of all the products. Table III presents the experimental yields (%) of benzamidoxime obtained at different h^0 values along with the yields calculated from Eq. (8) which show very good agreement.

The k_k constants are the hydrolytic constants proper. Although benzoylated benzamidoximes can be considered analogues of esters, hydrolysis of these two types of compounds will differ somewhat, in spite of having some features in common.

The determining step can be any of the acid-catalyzed hydrolytic processes known with esters¹⁰. In order to verify the reaction molecularity we determined the activation quantities of all the compounds (Table IV): the activation entropies are considerably negative in all the cases, which indicates the bimolecular reaction¹¹. Hence, as a working hypothesis we can choose the reaction mechanism $A_{Ac}2$, which also agrees with the products of the hydrolysis reaction. This mechanism starting from the preequilibrium protonation of the substrate is characterized by slow addition of water with simultaneous proton transfer to carbonyl and subsequent rapid equilibria leading to the reaction product¹⁰. In contrast to the classic $A_{Ac}2$ mechanism, the benzoylated benzamidoximes are protonated in much less acidic region, and only the protonated molecule undergoes the hydrolysis. The non-protonated molecule reacts in another way to give the corresponding 1,2,4-oxadiazoles⁴. Hence, the hydrolysis depends on the presence of an equilibrium concentration of the protonated form given by the H^0 function. The protonated molecule adds a water molecule (or some other nucleophile) with subsequent formation of the transition state whose rapid transformation leads to the reaction products (Scheme 1).

The scheme involves an equilibrium K_c presuming the proton transfer to amidic nitrogen atom. Although at present there prevails the opinion that the protonation of amidoximes preferably proceeds at the imine nitrogen atom due to its greater basicity (in analogy to amidines), this presumed equilibrium would allow an explana-

tion for the fact that the reaction leading to formation of the cyclization product is practically stopped. It can be presumed that the protonation of the imine nitrogen will be connected with intramolecular catalysis by formation of the hydrogen bond with carbonyl oxygen atom, which would strongly support the acid-catalyzed cyclization presumed in the previous reports^{1,2}.



SCHEME 1

The addition of water (or ethanol) as the determining step of the reaction is confirmed first of all by polar effects of substituents at 4,4'-positions of substituted benzoylbenzamidoximes. Their effects on the hydrolysis were evaluated by means of the two-parameter equation for calculation of the rate constant k_k

$$\log (k_k)_{i,j} = \log k_0 + \rho_1 \sigma_{p,i} + \rho_2 \sigma_{p,j} \quad (9)$$

where $\sigma_{p,i}$ and $\sigma_{p,j}$ are constants of the substituents at the positions 4 and 4', respectively, and ρ_1 and ρ_2 are the corresponding reaction constants (Table V).

The substituent electronic effects on both benzamidoxime and benzoyl nucleus agree fully with the idea of the fundamental controlling role of the carbonyl carbon. Decreasing electron density results in increasing rate of the nucleophilic additions.

TABLE IV

The activation parameter values found for the compounds studied at $H^0 = 0.94$ and $T = 343.15$ K

Compound	ΔH^\ddagger , kJ mol ⁻¹	ΔS^\ddagger , J K ⁻¹ mol ⁻¹
<i>I</i>	70.49	-114.8
<i>II</i>	76.08	-115.8
<i>III</i>	70.58	-113.4
<i>IV</i>	82.99	-76.4
<i>V</i>	60.78	-144.6
<i>VI</i>	55.81	-157.7
<i>VII</i>	66.75	-122.8
<i>VIII</i>	68.86	-116.7
<i>IX</i>	78.43	-88.2
<i>X</i>	72.47	-94.3
<i>XI</i>	71.50	-106.3
<i>XII</i>	70.35	-110.7
<i>XIII</i>	77.15	-101.5
<i>XIV</i>	70.44	-122.5
<i>XV</i>	73.52	-109.9
<i>XVI</i>	83.6	-97.2
<i>XVII</i>	81.00	-92.3
<i>XVIII</i>	78.71	-89.7
<i>XIX</i>	59.20	-134.4
<i>XX</i>	62.24	-124.7
<i>XXI</i>	68.19	-109.6
<i>XXII</i>	67.39	-112.9
<i>XXIII</i>	65.62	-113.3
<i>XXIV</i>	81.85	-70.1

The magnitude of ρ_2 is comparable with that of ionization of substituted benzoic acids in accordance with the above-mentioned idea, and so is also the lower ρ_1 value with respect to the more difficult (and over a greater distance acting) transfer of electronic effects through imine group to carbonyl.

Similarly, the activation enthalpy values (Table IV) also confirm the addition as the determining step, being generally lower with the compounds carrying electron-acceptor groups. The enthalpies of the addition to carbonyl group are lower for compounds with such substituents^{12,13}. The activation entropy changes exhibit a compensation effect on the reaction velocity, which is connected with the pre-equilibrium reactions.

The found value of the kinetic isotope effect $k_H/k_D = 1.41$ stands in accordance with the generally acid-catalyzed reactions and, at the same time, brings the evidence that the reaction goes by some mechanism different from that in neutral media (where the kinetic isotope effect found⁴ has the value of 0.83). From the value of the kinetic isotope effects it also follows that the rate-limiting step of the reaction (the addition of water) is accompanied by a proton transfer (the $A_{Ac}2$ mechanism).

In order to make an overall evaluation of reactivity of the compounds studied we carried out calculations of linear correlations between the rate constants obtained, equilibrium and spectral data on O-benzoylated benzamidoximes. Some of the data used were taken from our previous reports^{4,6,14}. The evaluation of the matrix of correlation coefficients (Table VI) and the results obtained by the two-parameter correlation of properties of the disubstituted derivatives of benzoylbenzamidoximes lead to the following conclusions:

a) The equilibrium constants of acid-base and redox reactions (pK_a , $E_{1/2}$), the proton shifts of NH_2 group in 1H NMR spectra, and rate constants of the acid-catalyzed hydrolysis are mutually correlated, the polar effects of the same substituents at different positions (4,4') showing the same orientation in these interactions. The

TABLE V

The correlation characteristics between the $\log k_k$ and pK values measured and the substituent polarity coefficients

$x_{i,j}$	x_0	n	ρ_1	ρ_2	r_1	P_1	r_2	P_2	R	F
$\log k_k$	-3.720	24	0.59	1.09	0.44964	95	0.87853	99	0.9766	216.7
pK_a	1.30	24	-1.21	-0.67	-0.80390	99	-0.49866	95	0.935	73.04

n number of determinations; r_1 , r_2 the correlation coefficients; P_1 , P_2 the probability level (%); R the correlation coefficient between the dependent variable and the regression; F the Fisher criterion.

equilibrium constants (pK_a , $E_{1/2}$) and chemical shifts in the ^1H NMR spectra exhibit a higher ρ value for the substituents of the amidoxime aromatic nucleus, whereas the hydrolysis rate is more affected by substituents of the benzoyl part of the molecule. Substituents of the same orienting effects in the two positions have the same effects on electron densities, reactivity of heteroatoms, and bond orders. All these facts agree with the idea of the localized character of these interactions as represented in Fig. 2. The statistically significant linear dependence between pK_a and $\log k_k$ indicates that the structure of the transition state of the hydrolytic reaction approaches that of the protonated molecule⁹.

b) The electronic effects of substituents on the benzamidoxime nucleus exerted on the cyclization reaction rate are quite different, and the values of corresponding rate constants only correlate with the hydrolysis rate constants (Table VI). Both the cyclization and the hydrolytic reactions are substantially affected by the electron deficit at the carbonyl carbon. Whereas the cyclization reaction rate is increased

TABLE VI
The matrix of the correlation coefficients

Quantity	$\log k_n$	pK_a	δ	$E_{1/2}^a$
$\log k_k$	0.53651	-0.79857	0.75770	0.58348
$\log k_n$	—	-0.25268	0.32315	-0.28317
pK_a	—	—	-0.95753	-0.85359
δ	—	—	—	0.85038

^a The $E_{1/2}$ values for $\text{pH} = 5.18$ (all the nitro derivatives (VI, XII, XVIII—XXIV) were excluded from the correlation because of the reduction of NO_2 group taking place at more positive potentials before the reaction measured).

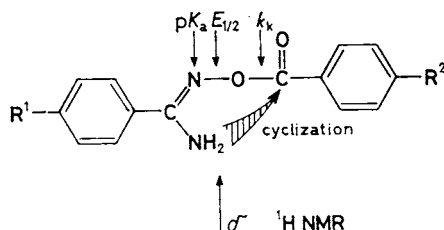


FIG. 2

Localization of the position of reaction in the case of equilibrium and kinetic processes

by electron-donor substituents at the benzamidoxime nucleus (the NH_2 group as a nucleophile), the opposite is true in the case of hydrolysis. The opposite direction of influence of the two substituents at 4,4'-positions on the cyclization rate indicates that the reaction is accompanied by an electron flow (push-pull effect) (Fig. 2).

REFERENCES

1. Tiemann F., Krüger P.: *Ber. Dtsch. Chem. Ges.* 17, 1685 (1884).
2. Eloy F., Lenaers R.: *Chem. Rev.* 62, 155 (1962).
3. Eloy F.: *Fortschr. Chem. Forsch.* 4, 807 (1965).
4. Grambal F., Lasovský J.: *This Journal*, 50, 2722 (1985).
5. Grambal F., Lasovský J., Bekárek V., Šimánek V.: *Chem. Zvesti* 33, 371 (1979).
6. Grambal F., Lasovský J.: *Chem. Zvesti* 33, 621 (1979).
7. Číhalík J., Dvořák J., Suk V.: *Přiručka měření pH*. Published by SNTL, Prague 1975.
8. Bell R. P.: *Proton v Khimii*. Mir, Moscow 1977.
9. Aubort J. D., Hudson R. F.: *J. Chem. Soc. D*, 1969, 22.
10. Ingold C. K.: *Structure and Mechanism in Organic Chemistry*. Cornell Univ. Press, Ithaca 1969.
11. Schaleger L. L., Long F. A.: *Adv. Phys. Org. Chem.* 1, 1 (1963).
12. Meloche I., Laidler K. J.: *J. Am. Chem. Soc.* 73, 1712 (1951).
13. Berliner E., Altschul L. H.: *J. Am. Chem. Soc.* 74, 4110 (1952).
14. Grambal F., Lasovský J., Bekárek V., Šimánek V.: *This Journal* 43, 2008 (1978).

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