# Reaction of 4-Benzylidene-2-methyl-5-oxazolone with Amines, Part 2: Influence of Substituents in Para-Position in the Phenyl Ring and a Substituent on Amine Nitrogen Atom on the Reaction Kinetics

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ABSTRACT: An influence of a structure of the amine (benzylamine, N-methyl-benzylamine, N-isopropyl-benzylamine, N-methyl-butylamine, N-ethyl-butylamine, sec-butylamine, and tertbutylamine) on a rate constant of the ring-opening reaction of 4-benzylidene-2-methyl-5oxazolone (Ox) was studied. The good correlation between logarithm of the rate constants and Charton's steric substituent constant  $\nu$  as well as good correlation with a form of the simple branching equation indicate that there is a steric effect because of substitution at C1 carbon atom of nucleophile which decreases the reaction rate. Additionally, an influence of a structure of the benzylidene moiety of Ox on a rate of the oxazolone ring-opening reaction was studied.

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The substituents (-OH,  $-OCH_3$ ,  $-N(CH_3)_2$ , -Cl,  $-NO_2$ ) in para-position of the phenyl ring of Ox substantially modified the rate of the reaction with benzylamine in acetonitrile. The rate of the Ox ring-opening reaction decreased with increase of the electron-donating properties of the substituent. A good correlation between the rate constants of the reaction of 4-(4'-substituted-benzylidene)-2-methyl-5-oxazolones with benzylamine and the electron density at the reaction center (carbon C5 of the oxazolone ring), calculated using ab initio method, and the Hammett substituent constants, and CR equation were established. © 2002 Wiley Periodicals, Inc. Int J Chem Kinet 34: 148–155, 2002; DOI 10.1002/kin.10039

# INTRODUCTION

Oxazolones, the activated form of carboxylates formed from amino acids, are applied for the peptide bond formation. They are widely used especially in synthesis of dehydropeptides. 4-Benzylidene-substituted oxazolones are very suitable intermediates for synthesis of peptides containing dehydrophenylalanine (dehydropeptides) [1,2]. Disappearing, after treatment with an amine, a characteristic absorption band of 4-benzylidene-2-methyl-5-oxazolone (Ox) at 325 nm was utilized to study the kinetics and mechanism of the ring-opening reaction of oxazolone [3]. The spectrokinetic method can be also used to study the influence of structural modifications of amines on the rate of this reaction. The influence of structural modification on the reactivity of molecules is often interpreted qualitatively in terms of steric effects. Many different scales of steric subsituent constants were proposed. The Taft's  $E_s$ [4–7] and Hancock's  $E_s^{c}$  [8] constants were based on the rate constants of the acidic hydrolysis of a substituted ester and a reference ester, while Fellous' and Luft's  $E_s^*$  constants were based on hydroboration reaction of alkenes by bis(1,2-dimethylpropyl)borane [9]. Charton [10–13] defined the steric parameter,  $\nu$ , from the intrinsic size of the substituent defined by its average van der Waals radius, while Beckhouse [14,15] based his parameter on differences between the heat of formation of the tert-butyl derivative of R  $[R-C(CH_3)_3]$  and that of the methyl derivative [R-CH<sub>3</sub>]. Statistical evidence was put forward, suggesting that v was the better measure of steric effects than  $E_s^{c}$  [16,17]. Because the steric effects cannot be analyzed using a single steric parameter, the expanded branching equation was introduced by Charton [18-20].

In organic chemistry many empirical models for a description of relations between structure and reactivity have emerged. The most successful model describing an influence of substituents on the reaction rate was based on the classical Hammett equation [21–25] and its further modifications [6,26–29]. The Hammett model assumed a direct correlation between the influence of substituents on the reaction rate and substituent





Figure 1 Structure of 4-benzylidene-2-methyl-5-oxazolone and reaction scheme.

constants  $\sigma$ , which were defined as independent in the studied reaction.

In this paper we used the Hancock's  $E_s^c$  [8] and Charton's  $\nu$  [10–13] substituent constants, simple branching equation [18–20] for the qualitative interpretation of the influence of the steric effects on the ring-opening reaction of Ox with different amines. The Hammett equation as well as the CR equation [29] were applied for quantitative analysis of the influence of substituents in 4-(4'-substituted-benzylidene)-2-methyl-5-oxazolones (Fig. 1) on the reaction rate with benzylamine. For the purpose of our studies, we prepared Ox analogues with electron-donating or electron-withdrawing substituents in the phenyl ring, such as -OH,  $-OCH_3$ ,  $-N(CH_3)_2$ , -Cl, and  $-NO_2$ .

#### MATERIALS AND METHODS

## Synthesis of 4-(4'-Substitutedbenzylidene)-2-methyl-5-oxazolones

The synthesis of 4-benzylidene-2-methyl-5-oxazolone (Ox) and its purification was described in the previous paper [3], and therefore in this paper we include only a brief description of the synthesis. The general procedure of the oxazolone preparation is as follows: 0.183 mol of sodium acetate and 0.62 mol of acetic anhydride were added to a round-bottom flask (500 ml) containing 0.25 mol of acetylglycine and

0.37 mol of an appropriate benzaldehyde. The resulting mixture was refluxed under nitrogen for 1.5 h. After that, the obtained solution was cooled and placed into a refrigerator for crystallization. The formed crystals were filtered off, washed with water, and dried. The crude product was recrystallized from carbon tetrachloride.

## <sup>1</sup>H NMR and FT-IR Analysis of Para-Substituted 4-Benzylidene-2-methyl-5oxazolones

4-(*p*-Dimethylamino)benzylidene-2-methyl-5-oxazolone ((CH<sub>3</sub>)<sub>2</sub>N-Ox, yield 78%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) = 2.43 (s, 3H, CH<sub>3</sub>-C=), 3.10 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>-N), 6.72 (d, 2H, J<sup>H</sup> = 9.0 Hz, aromatic), 7.16 (s, 1H, Ar-CH=,  $\gamma$ -lactone), 8.00 (d, 2H, J<sup>H</sup> = 9.0 Hz, aromatic); FT-IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3070.1 (w, H-C=,  $\gamma$ -lactone), 2907.7, 2823.6 (w, w, (CH<sub>3</sub>)<sub>2</sub>N-), 1776.2 (s, C=O,  $\gamma$ -lactone), 1655.7, 1601.9, 1492.6 (s, m, w, -C=N- in ring), 1450.8, 1425.9 (aromatic ring), 1303.6, 1263.7, 1230.5 (w, s, s, -C-O-C- in  $\gamma$ -lactone), 1192.5 (s, -C-N-).

4-(*p*-Methoxy)benzylidene-2-methyl-5-oxazolone (CH<sub>3</sub>O-Ox, yield 68%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) = 2.40 (s, 3H, CH<sub>3</sub>-C=), 3.98 (s, 3H, CH<sub>3</sub>O-), 6.97 (d, 2H,  $J^{\rm H} = 9.0$  Hz, aromatic), 7.12 (s, H, Ar-CH=,γ-lactone), 8.07 ppm (d, 2H,  $J^{\rm H} = 9.0$  Hz, aromatic); FT-IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3070.1 (w, H-C=, γ-lactone), 3009.0, 2832.9 (w, w, CH<sub>3</sub>O-Ar), 1776.2 (s, C=O, γ-lactone), 1655.7, 1601.9, 1492.6 (s, m, w, -C=N- in ring), 1450.8, 1425.9 (aromatic ring), 1303.6, 1263.7, 1230.5 (w, s, s, -C-O-C-, γ-lactone).

4-(*p*-Nitro)benzylidene-2-methyl-5-oxazolone (NO<sub>2</sub>-Ox, yield 70%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) = 2.46 (s, 3H, CH<sub>3</sub>-C=), 7.14 (s, H, Ar-CH=, γ-lactone), 8.27 (d, 4H,  $J^{\rm H} = 1.3$  Hz, aromatic); FT-IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3070.1 (w, H-C=, γ-lactone), 1776.2 (s, C=O, γ-lactone), 1655.7, 1601.9, 1492.6 (s, m, w, -C=N- in ring), 1519.8, 1343.9, 764.7, 748.9 (s, m, m, m, NO<sub>2</sub>-Ar), 1450.8, 1425.9 (aromatic ring), 1303.6, 1263.7, 1230.5 (w, s, s, -C-O-C-, γ-lactone).

4-(*p*-Chloro)benzylidene-2-methyl-5-oxazolone (Cl-Ox, yield 75%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) = 2.44 (s, 3H, CH<sub>3</sub>-C=), 7.11 (s, H, Ar-CH=, γ-lactone), 7.43 (d, 2H,  $J^{H} = 8.6$  Hz, aromatic), 8.05 (d, 2H,  $J^{H} = 8.6$  Hz, aromatic); FT-IR (KBr):  $\nu$ (cm<sup>-1</sup>) = 3070.1 (w, H-C=, γ-lactone), 1776.2 (s, C=O, γ-lactone), 1655.7, 1601.9, 1492.6 (s, m, w, -C=N- in ring), 1450.8, 1425.9 (aromatic ring), 1303.6, 1263.7, 1230.5 (w, s, s, -C-O-C-, γ-lactone), 529.7 (s, Cl-). 4-(*p*-Hydroxy)benzylidene-2-methyl-5-oxazolone (HO-Ox, yield 72%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) = 2.33 (s, 3H, CH<sub>3</sub>-C=), 7.12 (s, H, Ar-CH=, γ-lactone), 7.20 (d, 2H,  $J^{\rm H}$  = 8.8 Hz, aromatic), 8.12 (d, 2H,  $J^{\rm H}$  = 8.8 Hz, aromatic); FT-IR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3431.5, 3291.8, 918.9, 892.2 (O-H), 3070.1 (w, H-C=, γ-lactone), 1776.2 (s, C=O, γ-lactone), 1655.7, 1601.9, 1492.6 (s, m, w, -C=N- in ring), 1450.8, 1425.9 (aromatic ring), 1303.6, 1263.7, 1230.5 (w, s, s, -C-O-C-, γ-lactone).

All amines used in kinetic measurements were purchased form Aldrich and were used without any additional purification.

#### **Kinetic Measurements**

A course of the ring-opening reaction of Ox with an amine was studied by recording an absorbance decrease of the substrate at an absorbance maximum of the longwavelength band and at a maximum of the increased absorbance of a product using a Specord UV/VIS Carl Zeiss Jena spectrophotometer equipped with 12-bytes analogue-to-digital converter and the computer program Mult ver. 3.12 (Ambex, Warsaw, Poland). For one experimental curve 4096 data points were collected. In the kinetic measurements, concentration of the oxazolone ( $c = 5.25 \times 10^{-5}$  M) was the same in all experiments. The ring-opening reaction was performed in acetonitrile (MeCN) at 293 K. The concentrations of benzylamine (BzA), N-methylbenzylamine (MBzA), and N-methylbutylamine (MBuA) were varied in a range from 0.025 to 0.36 M, whereas the kinetic measurements with application of sec-butylamine (s-BuA), tert-butylamine (t-BuA), N-isopropylbenzylamine (i-PrBzA), and N-ethylbutylamine (EtBuA) were performed for the amine concentration equal to 0.059 M. In the case of kinetic studies of the reaction of an appropriate para-substituted in the benzylidene moiety oxazolone with BzA, the molar ratio of BzA to an appropriate oxazolone was about 500.

The reaction was monitored until more than 98% of the substrate disappeared. The rate constant calculations with assumed pseudo-first-order kinetic model as well as the correlation calculations were performed using the Origin ver. 6.1 program (Microcal Software, Inc., Northampton, MA).

## **Theoretical Calculations**

The PM3 method (MOPAC 6 packet) was used for the oxazolones' geometry optimization [30]. The atomic charges were calculated from Mulliken populations computed from the ab initio 6-31G\* wave function, using the GAMES program [31].

#### **RESULTS AND DISCUSSION**

# Influence of a Substituent on Amine Nitrogen Atom

The reaction spectra of oxazolone (Ox) with BzA (c = 0.014 M) in acetonitrile recorded at the wavelengths range 230–370 nm are presented in Fig. 2. A disappearance of a long-wave band with maximum at  $\lambda = 325$  nm (a band related to the substrate) and a building-up of an absorption band at the wavelength shorter than 300 nm (connected with an absorption of a product) with isosbestic point at  $\lambda = 295$  nm are observed (Fig. 2).

Additionally, the course of the reactions with all amines studied were also monitored by HPLC method. The reaction's chromatogram was always a sum of the substrates and one product only.

Reaction rates v (the oxazolone absorbance decays versus time) were analyzed assuming a pseudo-first-order kinetics, because of the 500 times higher concentration of the amine than that of the oxazolone. The obtained relationships between the pseudo-first-order rate constant and amine concentration  $k_{obs} = f(C_{amine})$  for *n*-BuA, BzA, MeBuA, and MeBzA are illustrated in Fig. 3.

The dependence of  $k_{obs}$  vs  $C_{amine}$  (*n*-BuA, BzA, MeBuA, and MeBzA) as can be observed in Fig. 3



Figure 2 Reaction spectra of 4-benzylidene-2-methyl-5-oxazolone with benzylamine ( $c_{BZA} = 0.059$  M) in acetonitrile.



**Figure 3** The dependence of the reaction rate constants as a function of the concentration of butylamine, benzylamine, *N*-methylbutylamine, and *N*-methylbenzylamine.

is nonlinear. As it was discussed in the previous paper [3], the nonlinear dependence of the rate constant on an amine concentration could be described assuming that the Ox ring-opening reaction with an amine proceeded as parallel reactions according to the equation

$$-d[Ox]/dt = k_0 + k_1[Ox][amine] + k_2[Ox][amine]^2$$
(1)

in which the  $k_0$  rate constant is connected with the ring-opening reaction caused by other nucleophile than amine present in a solution [32,33]. The calculated, based on Eq. (1), rate constants and statistical parameters describing the quality of the fit are presented in Table I. As can be seen from the data presented in Table I, the first two terms in Eq. (1) are not meaningful from the statistical point of view and can be disregarded, thus simplifying Eq. (1) to the form

$$-d[Ox]/dt = k_2[Ox][amine]^2$$
(2)

The fit of experimental data to that equation gives almost the same  $k_2$  and statistical parameters of the fit as obtained using Eq. (1). However, the fit of the experimental data to the equation

$$-d[Ox]/dt = k[amine]^n$$
(3)

gives a very good correlation coefficient, but because of the high correlation between the fitting parameters (k and n) calculated from this equation, the rate constant and the exponent differ substantially from those obtained from Eq. (2) (see Table II). All these fits indicate that the ring-opening reaction of Ox with an amine in acetonitrile solution is the second-order reaction according to an amine. The lack of possibility to record

4-Benzylidene-2-methyl-5-oxazolone with Amines and Statistical Parameters Describing the Quality of the Fit								
Amine	$k_0$	$k_1$	$k_2$	$100r^{2}$	F	Sest	N <sub>dp</sub>	
<i>n</i> -BuA <sup><i>a</i></sup>	$4 \times 10^{-4}  (\pm 5 \times 10^{-4})$	$-0.011(\pm 0.045)$	8.46 (±0.45)	99.79	1630	$1 \times 10^{-3}$	10	
N-MeBuA	$5 \times 10^{-5}  (\pm 3 \times 10^{-4})$	$5.7 \times 10^{-2}  (\pm 1.3 \times 10^{-2})$	$1.34(\pm 0.07)$	99.84	3532	$8 \times 10^{-4}$	14	
BzA	$-1 \times 10^{-4}  (\pm 6 \times 10^{-4})$	$1.3 \times 10^{-3}  (\pm 1.6 \times 10^{-3})$	0.87 (±0.06)	99.76	1640	$1.5  imes 10^{-3}$	11	
N-MeBzA	$-3.5 \times 10^{-6}  (\pm 8.8 \times 10^{-5})$	$1.2 \times 10^{-3}  (\pm 1.9 \times 10^{-3})$	$0.119(\pm 0.007)$	99.75	1401	$2 \times 10^{-4}$	11	

**Table I**Calculated [according to Eq. (1)] Rate Constants of the Ring-Opening Reaction of4-Benzylidene-2-methyl-5-oxazolone with Amines and Statistical Parameters Describing the Quality of the Fi

<sup>*a*</sup>Data from preceding paper in this series [3].

an intermediate product spectrum did not allow, in accordance to Polster and Mauser [34,35] and Vajda and Rabitz [36,37], to predict exact mechanism of the reaction studied.

For all amines studied, the rate constant of Ox disappearing at one amine concentration (0.059 M) was also measured. The calculated pseudo-first-order rate constants are presented in Table III. Introduction of a second substituent on nitrogen atom or use of an amine with branched alkyl chain caused a decrease in the reaction rate. The decrease of the rate constants of this reaction depends mostly on the size of a substituent, whereas the influence of an amine basicity is significantly lower. The basicities of benzylamines, in terms of  $pK_b$ , are about 4.4, whereas  $pK_b$  for butylamines are in a range 3.40-3.55. However, in spite of almost one order lower basicity of BzA than n-BuA, the observed rate constants of the Ox ring-opening reaction for both amines are comparable. Moreover, within the same type of amines (benzylamines, butylamines) the differences between the rate constants are more diversified than their  $pK_b$ 's. Therefore, in the case of the studied reaction, the reactivity of the amines should be interpreted in terms of the steric effects. Several different scales can be used for quantitative and qualitative interpretation of the steric effects [4,8,9,11,14,18-20,38]. In our paper for the qualitative interpretation of the influence of the steric effects on the ring-opening reaction of Ox with different amines, the Hancock's  $E_s^{c}$  [8] and Charton's  $\nu$  [10–13] substituent constants and simple branching equation [18-20] were used. The obtained

**Table II**Calculated [according to Eq. (3)] Rate Constants of the Ring-Opening Reaction of 4-Benzylidene-2-methyl-5-oxazolone with Amines and StatisticalParameters Describing the Quality of the Fit

Amine	k	п	$100r^{2}$
<i>n</i> -BuA <sup><i>a</i></sup>	15.8 (±2.7)	2.37 (±0.08)	99.9
N-MeBuA	$1.07(\pm 0.10)$	$1.75(\pm 0.05)$	99.79
BzA	0.85 (±0.08)	$1.98(\pm 0.08)$	99.76
N-MeBzA	0.114 (±0.008)	1.94 (±0.06)	99.72

<sup>a</sup>Data from preceding paper in this series [3].

data for Hancock's  $E_s^{c}$  substituent constant were fitted according to equation

$$\log(k_{\rm X}/k_{\rm Me}) = a + bE_{\rm s}^{\ \rm c} \tag{4}$$

where *a* and *b* are fitted parameters,  $k_X$  and  $k_{Me}$  refer to a substituent X and a reference subsituent (methyl group), respectively. For the Charton's  $\nu$  substituent constant we applied the equation

$$\log k_{\rm X} = c + dv \tag{5}$$

As in Eq. (4) *c* and *d* are fitted parameters, and  $k_X$  is the rate constant that refers to a substituent X. The best correlation was found for Charton's  $\nu$  substituent constant (Fig. 4) especially in the series of primary amines (log  $k_X = 3.09(\pm 0.69) - 8.11(\pm 0.88) v$ ;  $100r^2$ , 97.71; *F*, 85.14; *S*<sub>est</sub>, 0.209; *N*<sub>dp</sub>, 4).

For series of *N*-substituted amines the correlation was moderate (log  $k_{\rm X} = -2.18(\pm 1.27) - 3.89$  $(\pm 2.38) v$ ;  $100r^2$ , 73.69; *F*, 2.80;  $S_{\rm est}$ , 1.309;  $N_{\rm dp}$ , 3 for benzylamine series and log  $k_{\rm X} = -2.29(\pm 0.60) 1.45(\pm 1.36) v$ ;  $100r^2$ , 52.96; *F*, 1.13;  $S_{\rm est}$ , 0.602;  $N_{\rm dp}$ , 3 for butylamine series). In the case of Hancock's  $E_{\rm s}^{\rm c}$  substituent constant, the correlation was also moderate. The correlations are as follows:  $\log(k_{\rm X}/k_{\rm Me}) =$  $0.74(\pm 0.60) - 0.66(\pm 0.22) E_{\rm s}^{\rm c}$ ;  $100r^2$ , 89.51; *F*, 8.54;  $S_{\rm est}$ , 0.472;  $N_{\rm dp}$ , 3 for benzylamine series, and  $\log(k_{\rm X}/k_{\rm Me}) = 0.33(\pm 1.47) + 1.43(\pm 1.21) E_{\rm s}^{\rm c}$ ;

**Table III** The Pseudo-First-Order Rate Constants of the Ring-Opening Reaction of 4-Benzylidene-2-methyl-5-oxazolone with Amines (c = 0.059 M) in Acetonitrile at 298 K

Amine	$k  (s^{-1})$
BzA	$3.11 \times 10^{-3}$
N-MeBzA	$6.24 \times 10^{-4}$
<i>N</i> -iPrBzA	$4.19 \times 10^{-6}$
BuA	$4.80 \times 10^{-3}$
N-MeBuA	$2.52 \times 10^{-3}$
s-BuA	$4.66 \times 10^{-4}$
N-EtBuA	$3.75 \times 10^{-4}$
t-BuA	$1.59 \times 10^{-5}$



**Figure 4** The correlations between log  $k_X$  and Charton's steric substituent constants  $\nu$  for primary amines.

 $100r^2$ , 58.28; *F*, 1.40; *S*<sub>est</sub>, 1.51; *N*<sub>dp</sub>, 3 for butylamine series.

The rate constants for all amines studied in the reaction with Ox can be correlated with a form of the simple branching equation [18–20]

$$\log k_{\rm NX1X2} = B_{\rm N} n_{\rm N} + B_{\rm C1} n_{\rm C1} + B^0 \tag{6}$$

where  $n_N$  is the number of C–N bonds on the N atom of the amine, and  $n_C$  is the total number of C–C bonds on C1 atom of X1 and X2. Correlation with Eq. (6) gave the regression equation log  $k_{NX1X2} = -0.413(\pm 0.250)n_N - 1.171(\pm 0.151)n_{C1} 0.778(\pm 0.476), 100R^2, 92.36; A100R^2, 89.68; F,$  $31.42; S_{est}, 0.354; N_{dp}, 8; r_{nN,nC}, 0.$  As  $B_N$  was not significant, the term in  $n_N$  was dropped from Eq. (6). Correlation then gave the regression equation log  $k_{NX1X2} =$  $-1.171(\pm 0.171)n_{C1} - 1.397(\pm 0.332), 100R^2, 88.62;$  $A100R^2, 86,73; F, 46.73; S_{est}, 0.402; N_{dp}, 8.$  Thus, there is a steric effect because of substitution at C1 which decreases the reaction rate, in agreement with the correlation with the v parameters, and it is additive.

# Influence of the para-Substituents in the Phenyl Ring

Absorption spectra of substituents in the para-position of 4-benzylidene-2-methyl-5-oxazolones, normalized to unity at maximum of long-wave absorption band in acetonitrile, are presented in Fig. 5.

The position of maximum of long-wave absorption band depends on the type of substituent in the phenyl ring of the oxazolone. The electron-donating substituents cause batochromic shift of the maximum of absorption band as compared with unsubstituted



**Figure 5** Absorption spectra of substituted 4-benzylidene-2-methyl-5-oxazolones in acetonitrile.

Ox. The absorption spectrum of the nitro-substituted Ox is also long-wave-shifted but in this case the strong auxochromophoric effect of the strong electronwithdrawing group is manifested. Such changes of the position of the absorption band indicate the interaction between the phenyl ring, possessing the electrondonating character, and the oxazolone moiety of the compound, exhibiting electron-withdrawing character, in spite of nonplanar conformation of Ox structure. Semiempirical calculations using PM3 method revealed that the dihedral angle between phenyl and oxazolone rings is about 40° (from 37.7° for *p*-methoxy-Ox to 47.7° for unsubstituted Ox).

A kind of a substituent in the phenyl ring has distinct influence on the reaction rate of Ox with BzA. The calculated pseudo-first-order rate constants of the reaction of oxazolone ( $c = 5 \times 10^{-5}$  M) with benzylamine (c = 0.029 M) are presented in Table IV.

The fastest decrease of the Ox absorbance was observed for the nitro-subsituted compound, whereas the slowest decrease was observed for the dimethylamino one. Thus, the electron-donating substituents which increase the electron density at the reaction center (carbon C5 in the oxazolone ring) distinctly slow down the

**Table IV** The Pseudo-First-Order Rate Constants of the Ring-Opening Reaction of Substituted at the Phenyl Ring 4-Benzylidene-2-methyl-5-oxazolones ( $c = 5 \times 10^{-5}$  M) with Benzylamine (c = 0.029 M) in Acetonitrile at 298 K

Substituent	$k ({ m s}^{-1})$
$-N(CH_3)_2$	$6.26  imes 10^{-6}$
-OCH <sub>3</sub>	$6.20 \times 10^{-5}$
-ОН	$4.98 \times 10^{-4}$
—н	$3.66 \times 10^{-4}$
—Cl	$1.06 \times 10^{-3}$
-NO <sub>2</sub>	$2.37 \times 10^{-2}$

ring-opening reaction with the nucleophile. An influence of substituents on a reaction rate is usually correlated with the substituent constants using the Hammett equation [21–25] or its modifications [6,26–28]. In our studies we used the classical Hammett equation  $\log(k/k_0) = \rho\sigma$ , where k and  $k_0$  are rate constants obtained for substituted and unsubstituted Ox, respectively,  $\rho$  is a reaction constant, and  $\sigma$  is a substituent constant. The Hammett plot of the oxazolone ringopening reaction with benzylamine are presented in Fig. 6.

The log( $k/k_0$ ) correlates well with the classical Hammett substituent constants log( $k/k_0$ ) = 1.573 (±0.293) $\sigma$ , 100 $r^2$ , 87.79; *F*, 28.77; *S*<sub>est</sub>, 0.469;  $N_{dp}$ , 6. The correlation can be better after discarding the data obtained for the hydroxyl substituent, log( $k/k_0$ ) = 1.712(±0.154) $\sigma$ , 100 $r^2$ , 97.62; *F*, 123.2; *S*<sub>est</sub>, 0.239;  $N_{dp}$ , 5. The deviation observed for the hydroxyl group can be explained as a result of existing specific interactions between the substituent and the solvent (hydrogen bonding) which cause decrease of electron density at the reaction center and thereby increase of the reaction rate. Furthermore, a very good correlation between log ( $k/k_0$ ) and an atomic charge ( $\delta$ ) at the reaction center (carbon C5 in the oxazolone ring) was obtained according to the equation

$$\log(k/k_0) = a + b\delta(C5) \tag{7}$$

The calculated correlation is  $\log(k/k_0) = -538$ (±57) + 667(±88) $\delta$ (C5); 100 $r^2$ , 93.48; *F*, 57.34; *S*<sub>est</sub>, 0.239; *N*<sub>dp</sub>, 6, when all data points are included and log (*k*/*k*<sub>0</sub>) = -563(±26) + 698(±32) $\delta$ (C5); 100 $r^2$ , 99.38; *F*, 478.0; *S*<sub>est</sub>, 0.122; *N*<sub>dp</sub>, 5, after exclusion of the data point for OH (Fig. 7).



**Figure 6** Plot of the Hammett equation  $\log(k/k_0) = \sigma \rho$  of the reaction of substituted 4-benzylidene-2-methyl-5-oxazolones with benzylamine in acetonitrile.



**Figure 7** Plot of  $log(k/k_0)$  vs atomic charge at C5 carbon atom of the oxazolone ring.

The outstanding correlations between  $\log(k/k_0)$ and Hammett's substituent constant  $\sigma$ , and between  $\log(k/k_0)$  and the atomic charge at the reaction center  $\delta$  (C5) are a result of the good correlation between the substituent constant  $\sigma$  and the atomic charge at carbon C5,  $\delta$ (C5) = 0.80703(±0.00011) + 0.00241(±0.00017) $\sigma$ , 100 $r^2$ , 98.04; *F*, 200.5; *S*<sub>est</sub>, 0.0003, *N*<sub>dp</sub>, 6.

We also performed studies in which we took into account field (*F*) and mesomeric (*M*) effect of the substituents separately [25,39], contrary to the previously used classical Hammett approach combining all substituent-promoted effects into one substituent constant  $\sigma$ . For that approach we applied multiple regression method to the equation

$$\log(k/k_0) = a + bF + cM \tag{8}$$

where *F* and *M* are field effect constant and mesomeric effect (Dewar–Grisdale) constant, respectively [25,39]. The values of *F* and *M* constants were taken from Ref. [39]. Satisfactory correlation between log  $(k/k_0)$  and substituent constants *F* and *M* was established: log  $(k/k_0) = -0.668(\pm 0.439) + 2.023$  $(\pm 0.613)F + 0.036(\pm 0.195)M$ ,  $100r^2$ , 83.48; *F*, 7.58; *S*<sub>est</sub>, 0.631; *N*<sub>dp</sub>, 6; *r*<sub>F,M</sub>, 0. As the value of constant *c* was not significant, the term *M* was dropped from Eq. (8). Correlation then gave the regression equation  $\log(k/k_0) = -0.726(\pm 0.273) +$  $2.080(\pm 0.466)F$ ,  $100r^2$ , 83.28; *F*, 19.93; *S*<sub>est</sub>, 0.549; *N*<sub>dp</sub>, 6, which indicated that the substituent constant *F* (field effect) had dominant significance.

The rate constants for the reaction of 4-(4'-substituted-benzylidene)-2-methyl-5-oxazolones with benzylamine can be correlated with the CR equation in the form [29]

$$\log k_{\rm X} = C\sigma_{\rm CX} + R\sigma_{\rm eX} + h \tag{9}$$

where  $\sigma_{eX}$  is the electronic demand sensitivity electrical effect parameter and  $\sigma_{CX}$  is a parameter defined by the relationship  $\sigma_{CX} = l\sigma_{IX} + d\sigma_{dX}$  (where  $\sigma_{I}$  is the localized electrical effect parameter and  $\sigma_{d}$  is the intrinsic delocalized electrical effect parameter). The obtained correlation gave, on exclusion of data point for OH, the regression equation  $\log k_{X} = 2.37(\pm 0.03)\sigma_{CX} + 2.60(\pm 0.17)\sigma_{eX} + 2.57(\pm 0.0195); 100R^{2}, 99.98; A100R^{2}, 99.97, F, 4187, S_{est}, 0.0244, N_{dp}, 5; P_{D}, 50; \eta, 1.10(\pm 0.071); <math>r_{\sigma CX,\sigma eX}$ , 0.456 (for the meaning and method of calculation of  $P_{D}$  and  $\eta$  parameters see Ref. [29]). The value of  $\eta$  has the sign and magnitude expected for nucleophilic attack on a carbonyl carbon.

#### CONCLUSIONS

The steric hindrance due to the substitution at C1 carbon atom of amine seems to be a main factor responsible for the modification of the reaction rate constants of the ring-opening reaction of 4-benzylidene-2-methyl-5-oxazolone with different amines, even though it does not completely explain all observed differences. The original Hammett's substituent constants take into account all effects connected with an influence of the substituents in the phenyl ring of 4-benzylidene-2-methyl-5-oxazolones on the charge distribution at the reaction center; but although the Hammett approach is good enough for accurate description of the substituents influence on the reaction rate, the CR equation gave more information about the electrical effects introduced by substituents.

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