Isokinetic relationships for nucleophilic substitution reactions at the saturated carbon atom. Reactions in aqueous solutions

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An isokinetic relationship (IKR) with the parameters T_{iso} = 6145 K and $\log k_{iso}$ = 10.622 is valid for nucleophilic substitution reactions at the saturated carbon atom with the participation of anionic nucleophiles in aqueous solutions. The IKR describes the rate constants of the reactions with different anionic nucleophiles, leaving groups, and substituents at the electrophilic reaction center. Similar reactions with neutral nucleophiles, which follow another mechanism, are described by a separate IKR with T_{iso} = −1232 K and $\log k_{iso}$ = 16.226. The reactions of haloforms with hydroxide ion, which proceed by a specific mechanism involving the haloform ionization equilibrium followed by α-elimination of the halide ion, are described by yet another IKR with T_{iso} = −1463 K and $\log k_{iso}$ = 21.057.

Key words: isokinetic relationship, compensation effect, rate constants, activation parameters, nucleophilic substitution reactions, aqueous solutions.

Analysis of temperature dependences of physicochemical parameters of various processes in the liquid, solid, and gas phases (*e.g.*, rate constants of chemical reactions) revealed the isokinetic relationship (IKR) or compensation effect.[1–3] The existence of IKR is evidence for a linear free energy relationship (LFER) in the series of analyzed reactions. In this case, the free energy of a particular member of the series can be expressed as a sum of increments determined by structural factors.[1] Additionally, the IKR indicates the homogeneity of the reactions constituting the series and that they proceed by a common mechanism.[2,4] Determination of the values of isokinetic parameters (the isokinetic temperature, T_{iso}, and the rate constant for the process at $T = T_{iso}$, k_{iso}) for various reaction series can serve as a basis for quantitative classification of chemical reactions since the T_{iso} values are dependent on the height of the potential barrier calculated as an arithmetic mean for the reactions constituting the series.[5] It should be noted that often only T_{iso} values are reported,[4] despite the fact that any reaction series is characterized by two parameters (T_{iso} and $\log k_{iso}$). The knowledge of the coordinates of isokinetic point is required for predicting the temperature dependences of the rate constants.[6]

In this work, the applicability is considered of IKR to nucleophilic substitution reactions at the saturated carbon atom with participation of anionic nucleophiles N^{z-} (z is the charge of the anion) proceeding by the S_N2 mechanism

$$YCH_2X + N^{z-} = YCH_2N^{1-z} + X^-, \qquad (1)$$

where X and X^- is the leaving group and its anion, respectively, and Y is the substituent at the electrophilic reaction center. The series analyzed comprises reactions proceeding in aqueous solutions by the mechanism described by Eq. (1). The rate constants of several reactions (1) at different temperatures have been determined previously.[7–20] We will also consider the applicability of isokinetic relationships to the series of reactions of methyl iodide with amines,[21–23] which are neutral nucleophiles, and to those of haloforms with hydroxide ion.[24,25] These reactions are of interest for comparison. The mechanism of the last-named reactions proceeding in aqueous solutions is specific and involves the ionization equilibrium followed by α-elimination of halide ion.

Calculation procedure

If the IKR is valid for a particular series of reactions, then for any reaction in the series the temperature dependences of the second-order rate constants (k/L mol^{-1} s^{-1}) described by the conventional Arrhenius equation $\log k = \log A - E_a/(2.303RT)$ (A/L mol^{-1} s^{-1} is the pre-exponential factor, E_a/kJ mol^{-1} is the energy activation, and R is the universal gas constant) should also satisfy the equations of the straight lines passing through the isokinetic point[2,4] with coordinates $\log k_{iso}$, $1/(2.303RT_{iso})$:

$$\log k - \log k_{iso} = -E_{iso}[(2.303RT)^{-1} - (2.303RT_{iso})^{-1}], \qquad (2)$$

where T/K and T_{iso}/K is the current and isokinetic temperature, respectively. The T_{iso} and $\log k_{iso}$ values are the same for all members of the reaction series, whereas the isokinetic

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activation energy, E_{iso}, is specific to each member of the reaction series.

Isokinetic parameters T_{iso} and $\log k_{iso}$, as well as the E_{iso} values for the reaction series in question, were calculated using the least squares method (LSM) by varying the T_{iso} and $\log k_{iso}$ values until the minimum sum was reached of the squares of deviations $S = \Sigma(\log k - \log k')^2$, where $\log k'$ are the logarithms of the rate constants k' calculated from the equation

$$\log k' = \log k_{iso} - E_{iso}[(2.303RT)^{-1} - (2.303RT_{iso})^{-1}]. \quad (3)$$

Calculations were carried out using an original ISOKIN program written in the Turbo Pascal programming language. The program made it possible to include in calculations the k values at any T for the members of the reaction series, to determine the T_{iso} and $\log k_{iso}$ values, and to perform for the whole reaction series the LSM calculations of the parameters of Arrhenius equations (E_a and $\log A$), isokinetic activation parameters E_{iso} and $\log A_{iso} = \log k_{iso} + E_{iso}/(2.303RT_{iso})$, and the corresponding standard deviations (s). In addition, the program made it possible to assess the parameters and statistical characteristics of the regression between the $\log k$ values used in the calculations and the $\log k'$ values calculated from Eq. (3) at the minimum S value.

Results and Discussion

The temperature dependences of the rate constants for reactions (1) have been determined for many anionic nucleophiles with different structure and charges (Table 1). The influence of the structure of leaving groups X and substituents Y in substrates (Table 2) on the reaction rates has been less studied. The reaction series considered in this work included the reactions (1) with monatomic and polyatomic anions; therefore, calculations were carried out using the corrected rate constants obtained by division of the k values by statistical factors (F) of nucleophiles, which were defined as the number of equivalent nucleophilic atoms in the anions (see Table 1). For hydroxide ion, which exists in aqueous solutions as a $H_3O_2^-$ hydrate in which the negative charge is evenly divided between the oxygen atoms,[26] we accepted $F = 2$. Statistical factors corresponding to the number of equivalent leaving groups in the molecules of substrates were also taken into account for the reactions with participation of CH_2Cl_2 [14] and haloforms.[24,25]

Table 1. Statistical factors (F) of anionic nucleophiles (N^{z-}) used for correcting the rate constants, k, of reactions (1)

N^{z-}	F	N^{z-}	F	N^{z-}	F
I^-	1	AcO^-	2	HSO_3^-	2
Br^-	1	HS^-	1	SO_3^{2-}	3
Cl^-	1	MeS^-	1	SO_4^{2-}	4
F^-	1	PhS^-	1	$S_2O_3^{2-}$	3
NC^-	1	NCS^-	1	NO_2^-	2
N_3^-	2	$MeC(O)S^-$	1	NO_3^-	3
HO^-	2	HCO_3^-	2	HPO_4^{2-}	3
PhO^-	1	CO_3^{2-}	3	PO_4^{3-}	4

The initially considered reaction series included the reactions for which the number (m) of k values at different temperatures exceeded 2 and the temperature range (ΔT), in which they were measured, was at least 15 K. However, our analysis showed that the deviations of two $\log k$ values (for the reactions of MeI with HCO_3^- at 60 °C and of $MeOSO_2Ph$ with NO_2^- at 60 °C) from Eqs. (2) are larger than those statistically admissible. After exclusion of these values from the series, the remaining data for these (at $m = 2$) and other reactions satisfied the IKR (see Table 2).

The $\log k$ values ($n = 225$) constituting the series were described by a general IKR with a standard deviation $s = [S/(n - 2)]^{0.5}$ of 0.056, which corresponds to the reproducibility of the rate constants determined by different authors. For instance, the $\log k$ values for the $MeOSO_2Ph + HO^-$ reaction at 40 °C differ by 0.075,[8,15] whereas the $\Delta\log k$ value for the reaction of MeI with N_3^- at 40 °C is 0.044.[9,27]

The isokinetic parameters $T_{iso} = 6145$ K and $\log k_{iso} = 10.622$ determined for a series of 60 reactions of the type (1) were used in calculations of E_{iso} and $\log A_{iso}$ values. The quality of the IKR obtained is characterized by the regression between the $\log k$ and $\log k'$ values calculated using Eq. (3) for reactions (1):

$$\log k = (1.000\pm0.003)\log k' + (0.001\pm0.011),$$

$$n = 225,\ s = 0.056,\ r = 0.999.$$

The regression plot is presented in Fig. 1. The regression coefficient equal to unity, the statistical insignificance of the absolute term, the small s value, and the high correlation coefficient (r) are evidence for applicability of the IKR to the series of $\log k$ values in

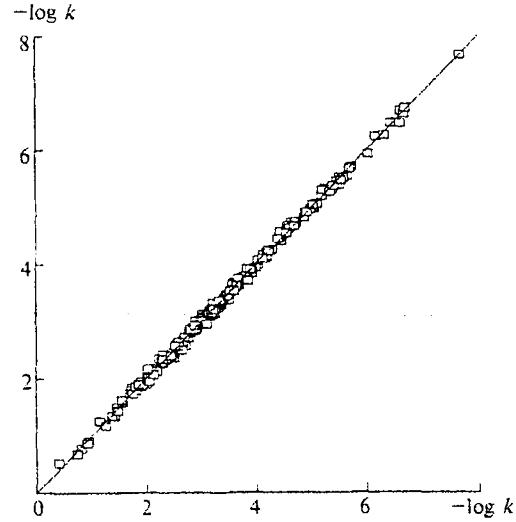

Fig. 1. Correlation between the $\log k$ values corrected by division by statistical factors F and the $\log k'$ values calculated using Eq. (3) for reactions (1) with anionic nucleophiles in aqueous solutions.

Table 2. Activation parameters of reactions (1) calculated using the Arrhenius equation (E_a and $\log A$) and using the IKR (E_{iso} and $\log A_{iso}$)

Reaction	$m/\Delta T$	Reference	E_a /kJ mol^{-1}	$\log A$	E_{iso} /kJ mol^{-1}	$\log A_{iso}$
$MeF + I^-$	5/30	7	96.25±4.17	9.18±0.62	112.36±0.32	11.577±0.003
$MeCl + I^-$	5/37	7	91.08±7.19	11.15±1.10	92.78±0.26	11.410±0.002
$MeOSO_2Ph + I^-$	3/35	8	85.33±0.36	11.65±0.06	83.44±0.06	11.331±0.001
$MeCl + Br^-$	3/40	9	96.69±2.22	10.94±0.37	99.82±0.15	11.470±0.001
$^-O(O)CCH_2Br + Br^-$ *	5/43	10	93.26±7.43	11.39±1.21	93.40±0.29	11.416±0.002
$MeOSO_2Ph + Br^-$	3/35	8	82.04±0.10	10.25±0.02	88.79±0.23	11.376±0.002
$MeBr + Cl^-$	3/40	9	100.80±4.80	12.40±0.80	95.00±0.29	11.429±0.002
$MeI + Cl^-$	5/37	7	99.01±7.82	11.74±1.19	97.08±0.28	11.447±0.002
$^-O(O)CCH_2Cl + Cl^-$ *	4/28	11	113.75±1.88	11.85±0.27	111.83±0.06	11.572±0.000
$MeOSO_2Ph + Cl^-$	3/40	8	89.38±2.37	10.98±0.40	91.91±0.14	11.403±0.001
$MeCl + F^-$	3/43	7	114.11±3.98	13.14±0.61	103.32±0.44	11.500±0.004
$MeBr + F^-$	4/53	7	105.69±2.29	11.00±0.35	109.24±0.18	11.550±0.001
$MeI + F^-$	3/40	7	106.82±0.48	11.55±0.07	106.71±0.02	11.529±0.000
$MeF + NC^-$	4/23	12	97.13±6.01	11.20±0.88	98.89±0.13	11.462±0.001
$MeCl + NC^-$	7/41	12	89.83±1.14	11.45±0.18	89.40±0.04	11.382±0.000
$MeBr + NC^-$	8/40	12	87.02±0.96	12.37±0.17	80.96±0.12	11.310±0.001
$MeI + NC^-$	7/34	12	86.26±0.79	11.90±0.13	82.85±0.06	11.326±0.001
$MeOSO_2Ph + NC^-$	3/40	8	73.20±2.17	10.45±0.39	77.83±0.21	11.283±0.002
$MeI + N_3^-$	3/40	9	89.39±2.91	11.22±0.49	90.39±0.12	11.390±0.001
$MeOSO_2Ph + N_3^-$	3/35	8	93.60±2.77	12.76±0.46	85.11±0.30	11.345±0.003
$MeCl + HO^-$	5/29	13	102.20±0.43	12.42±0.07	96.09±0.10	11.438±0.001
$MeBr + HO^-$	6/30	13	96.02±0.41	12.69±0.07	88.33±0.12	11.373±0.001
$MeI + HO^-$	6/40	13	93.35±0.55	11.85±0.09	90.51±0.06	11.391±0.001
$CH_2Cl_2 + HO^-$	5/51	14	110.04±0.52	11.01±0.07	114.32±0.11	11.593±0.001
$MeOSO_2Me + HO^-$	3/20	15	82.96±1.80	10.84±0.30	86.05±0.07	11.353±0.001
$MeOSO_2Ph + HO^-$	4/60	8	86.36±1.13	11.77±0.20	83.85±0.13	11.334±0.001
$EtOSO_2Ph + HO^-$	4/35	16	88.67±2.05	12.45±0.33	81.56±0.18	11.315±0.002
$MeI + PhO^-$	3/40	9	100.96±0.48	13.24±0.08	89.87±0.43	11.386±0.004
$MeOSO_2Ph + PhO^-$	3/40	8	87.78±4.11	12.29±0.74	82.37±0.28	11.322±0.002
$MeI + AcO^-$	3/40	9	106.70±3.08	12.34±0.52	101.62±0.23	11.485±0.002
$EtCl + AcO^-$	3/20	17	98.51±8.47	10.17±1.15	108.56±0.21	11.544±0.002
$BuCl + AcO^-$	3/30	17	103.18±1.12	10.16±0.14	114.29±0.26	11.593±0.002
$MeOSO_2Ph + AcO^-$	3/40	8	86.30±7.61	10.46±1.28	91.93±0.37	11.403±0.003
$MeOSO_2Ph + HS^-$	4/30	18	59.59±2.20	9.02±0.40	71.77±0.30	11.232±0.003
$MeOSO_2Ph + MeS^-$	3/20	18	49.94±5.62	8.40±1.04	64.95±0.34	11.174±0.003
$MeOSO_2Ph + PhS^-$	4/30	18	73.63±2.93	11.77±0.53	70.62±0.12	11.222±0.001
$MeOSO_2Ph + NCS^-$	3/40	8	74.20±3.55	9.81±0.59	83.26±0.38	11.329±0.003
$MeOSO_2Ph + MeC(O)S^-$	3/40	18	72.67±5.23	11.40±0.94	71.72±0.22	11.231±0.002
$MeI + HCO_3^-$	2/20	9	110.73	12.99	102.05±0.30	11.489±0.003
$MeOSO_2Ph + HCO_3^-$	3/40	8	90.19±0.90	11.00±0.15	92.61±0.10	11.409±0.001
$MeI + CO_3^{2-}$	3/40	9	102.86±0.53	12.99±0.09	93.46±0.37	11.416±0.003
$MeOSO_2Ph + CO_3^{2-}$	3/40	8	83.83±4.20	11.22±0.70	84.53±0.17	11.340±0.001
$MeI + HSO_3^-$	3/40	9	86.91±1.05	9.94±0.18	95.85±0.35	11.436±0.003
$MeI + SO_3^{2-}$	3/20	9	81.22±1.66	12.34±0.31	75.40±0.13	11.263±0.001
$MeOSO_2Ph + SO_3^{2-}$	3/40	8	71.15±2.33	10.35±0.42	76.27±0.23	11.270±0.002
$MeI + SO_4^{2-}$	3/40	9	109.74±3.24	11.86±0.54	107.81±0.15	11.538±0.001
$MeOSO_2Ph + SO_4^{2-}$	3/40	8	97.10±3.58	11.57±0.60	96.34±0.14	11.441±0.001
$MeCl + S_2O_3^{2-}$	5/30	13	86.51±0.62	11.64±0.11	84.78±0.04	11.342±0.000
$MeBr + S_2O_3^{2-}$	6/25	13	81.41±0.67	12.37±0.12	75.39±0.09	11.263±0.001
$MeI + S_2O_3^{2-}$	4/16	13	79.50±3.32	11.91±0.60	75.93±0.08	11.267±0.001
$EtI + S_2O_3^{2-}$	4/27	19	91.01±3.23	12.56±0.54	83.71±0.17	11.333±0.001
$^-O(O)CCH_2Br + S_2O_3^{2-}$	4/37	20	66.80±0.15	9.06±0.03	79.21±0.36	11.295±0.003
$MeOSO_2Ph + S_2O_3^{2-}$	3/30	8	67.37±3.57	9.80±0.65	75.47±0.29	11.263±0.002
$MeI + NO_2^-$	3/40	9	92.59±0.90	11.23±0.15	93.71±0.06	11.418±0.000
$MeOSO_2Ph + NO_2^-$	2/20	8	75.58	9.52	86.17±0.37	11.354±0.003
$MeOSO_2Ph + NO_3^-$	3/40	8	88.84±0.50	9.35±0.08	101.54±0.49	11.485±0.004
$MeI + HPO_4^{2-}$	3/40	9	105.76±3.12	12.61±0.52	98.89±0.29	11.462±0.002
$MeOSO_2Ph + HPO_4^{2-}$	3/40	8	91.86±6.33	11.88±1.06	88.89±0.27	11.377±0.002
$MeI + PO_4^{3-}$	3/40	9	94.88±0.53	11.99±0.09	91.35±0.14	11.398±0.001
$MeOSO_2Ph + PO_4^{3-}$	4/60	8	81.18±3.68	11.32±0.64	81.14±0.23	11.311±0.002

* Isotope exchange reaction.

question. Because of the positive T_{iso} value, the E_{iso} and $\log A_{iso}$ parameters of the series of reactions (1) change with compensation effect,[1,2] which is confirmed by the correlation

$$E_{iso} = (117.71\pm0.04)\log A_{iso} - (1250.31\pm0.46),$$

$$n = 60,\ s = 0.031,\ r = 0.9999.$$

From the results obtained (see Table 2) it follows that the standard deviations of the E_{iso} and $\log A_{iso}$ parameters calculated using the IKR are much smaller than the s values for corresponding E_a and $\log A$ parameters of the Arrhenius equation. The E_{iso} and $\log A_{iso}$ values, calculated for very wide ($T_{iso}-T$) temperature ranges, must be closer to the true values; therefore, differences between the E_a and E_{iso} values, as well as those between the $\log A$ and $\log A_{iso}$ values, are mainly due to actual errors of determination of the E_a and $\log A$ values. It should also be taken into account that the standard deviations of E_a and $\log A$ values do not adequately characterize experimental errors, since at small number m the deviations of boundary $\log k$ values both to the various sides from the straight line described by the Arrhenius equation lead to a decrease in the s value because of introducing an error into the E_a value. This factor is responsible for the largest differences between the E_a and E_{iso} parameters for the reactions with $m = 3$ and 2 (see Table 2), as well as for the substantial decrease in these errors at $m = 5$ and at larger m values. It has been reported[28] that the errors of determination of E_a values affect the $\log A$ errors. As a consequence, a correlation exists between the differences of the $\Delta\log A = \log A - \log A_{iso}$ and $\Delta E_a = E_a - E_{iso}$ parameters for reactions (1)

$$\Delta\log A = (0.166\pm0.002)\Delta E_a + (0.019\pm0.015),$$
$$n = 60,\ s = 0.11,\ r = 0.995,$$

which is satisfied at both positive and negative $\Delta\log A$ and ΔE_a values.

The rate constants for reactions with $^{-}O(O)CCH_2Br$ and other anionic substrates (see Table 2) are described by the IKR for reactions (1), which indicates that the mechanism of processes proceeding involving these substrates has no characteristic features. In essence, the reaction of hydroxide ion with dichloromethane, which results in the formation of formaldehyde,[14] does not belong to the reactions of the type (1). However, its limiting stage involves the attack of hydroxide ion on the C atom according to the S_N2 mechanism; thus, the $\log k$ values for this reaction also satisfy the IKR for reactions (1). At the same time, the reactions of haloforms with hydroxide ion in aqueous solutions are described by a separate IKR. This is due to a specific mechanism of these reactions, which involves the haloform ionization equilibrium followed by α-elimination of the halide ion at the monomolecular limiting stage[24,25] according to the scheme

$$\mathrm{Hal_3CH} + \mathrm{HO^-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Hal_3C^-} + \mathrm{H_2O},$$

$$\mathrm{Hal_3C^-} \xrightarrow{k_2} \mathrm{Hal_2C} + \mathrm{Hal^-}.$$

In this case, the observed second-order rate constant is described by the equation $k = k_1k_2/(k_{-1} + k_2)$. It is likely that $k_{-1} \gg k_2$ and $k = Kk_2$, where K is the constant of the haloform ionization equilibrium.

The $\log k$ values of 12 reactions with participation of haloforms ($n = 31$) are described by a separate IKR with the parameters $T_{iso} = -1463$ K, $\log k_{iso} = 21.057$, and the standard deviation $s = 0.037$. The following regression between the $\log k$ values used in calculations and the $\log k'$ values calculated using Eq. (3) was obtained for this reaction series

$$\log k = (1.0003\pm0.0051)\log k' + (0.001\pm0.018),$$
$$n = 31,\ s = 0.037,\ r = 0.9996.$$

It indicates that the IKR holds for this series.

Table 3. Activation parameters calculated using the Arrhenius equation (E_a and $\log A$) and using the IKR (E_{iso} and $\log A_{iso}$) for the reactions of haloforms with hydroxide ion in aqueous solutions

Haloform	$m/\Delta T$	Reference	E_a /kJ mol^{-1}	$\log A$	E_{iso} /kJ mol^{-1}	$\log A_{iso}$
$CHClI_2$	2/17	25	134.19	18.35	123.24±0.23	16.623±0.009
$CHCl_3$	4/50	25	118.15±1.27	15.91±0.22	122.40±0.14	16.656±0.005
$CHBr_3$	3/25	25	119.53±0.04	16.76±0.01	119.56±0.00	16.764±0.000
$CHCl_2I$	2/10	25	128.06	18.77	116.99±0.15	16.862±0.006
$CHBr_2Cl$	3/50	25	119.29±0.82	17.33±0.14	116.66±0.12	16.875±0.005
$CHCl_2F$	2/20	25	114.68	16.72	115.72±0.03	16.911±0.001
$CHBrCl_2$	4/50	25	114.84±1.28	17.14±0.22	113.91±0.06	16.980±0.002
$CHFI_2$	2/21	25	118.73	18.58	110.71±0.24	17.102±0.009
$CHBrClF$	2/15	25	106.09	17.41	105.52±0.01	17.300±0.000
$CHBr_2F$	2/20	25	110.14	18.20	105.32±0.14	17.308±0.005
$CHBrF_2$	2/20	24	95.68	15.62	104.92±0.27	17.323±0.010
$CHClF_2$	2/25	24	110.65	16.29	114.33±0.13	16.964±0.005

Table 4. Activation parameters calculated using the Arrhenius equation (E_a and log$A$) and using IKR (E_{iso} and logA_{iso}) for the reactions of amines with methyl iodide in aqueous solutions

Amine	$m/\Delta T$	Reference	E_a /kJ mol^{-1}	log$A$	E_{iso} /kJ mol^{-1}	logA_{iso}
NH_3	3/20	21	100.98±4.46	13.67±0.77	92.96±0.14	12.285±0.006
$MeNH_2$	3/20	21	91.23±0.35	13.31±0.07	87.06±0.07	12.535±0.003
Me_2NH	3/20	21	88.22±3.07	13.42±0.57	84.11±0.09	12.660±0.004
Me_3N	3/20	21	85.87±0.90	13.45±0.17	82.05±0.07	12.747±0.003
H_2NNH_2*	4/40	22	84.80±0.43	11.62±0.07	89.66±0.11	12.425±0.005
H_2NNMe_2	2/10	23	71.24	10.41	84.26±0.17	12.654±0.007

* Calculated using $F = 2$.

The so-called anticompensation effect[1] between the E_{iso} and logA_{iso} parameters of this reaction series (Table 3) is described by the following regression

$$E_{iso} = (-27.996\pm0.010)\log A_{iso} + (589.58\pm0.16),$$

$$n = 12,\ s = 0.0073,\ r = 0.9999.$$

It is known that the anticompensation effect is observed in the reaction series whose mechanism involves the reversible equilibrium.[1] Analogously to the reactions series (1), a correlation is observed between the Δlog$A$ and ΔE_a values for the reactions involving haloforms

$$\Delta\log A = (0.175\pm0.004)\Delta E_a - (0.017\pm0.020),$$

$$n = 12,\ s = 0.069,\ r = 0.998.$$

The coefficient at ΔE_a is close to that obtained for a similar correlation for reactions (1).

The kinetics of substitution reactions at the sp^3-hybridized carbon atom involving neutral nucleophiles in water has been little studied. The available data for six reactions of methyl iodide with amines[21–23] do not satisfy the IKR for reactions (1). According to calculations, the reactions with amines are described by a separate IKR with the parameters $T_{iso} = -1232$ K, logk_{iso} = 16.226, and the standard deviation s = 0.035. The IKR in this series is confirmed by the regression

$$\log k = (1.0003\pm0.0102)\log k' + (0.001\pm0.030),$$

$$n = 18,\ s = 0.034,\ r = 0.9992.$$

The activation parameters for these reactions are listed in Table 4. Unlike the reaction series (1), the anticompensation effect between the E_{iso} and logA_{iso} parameters is observed for this reaction series because of the negative T_{iso} value. It is described by the following regression

$$E_{iso} = (-23.607\pm0.014)\log A_{iso} + (382.97\pm0.18),$$

$$n = 6,\ s = 0.0055,\ r = 0.9999.$$

The anticompensation dependence between the activation parameters of a particular reaction series indicates that they proceed by a mechanism which involves a reversible equilibrium.[1] It is likely that the nucleophilic attack of amine on a haloalkane results in the formation of an ionic pair, which dissociates into either products of initial reagents (in accordance with the Hofmann reaction) following the scheme

$$R_3N + MeI \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R_3NMe^+I^- \xrightarrow{k_2} R_3NMe^+ + I^-.$$

In this case, the rate constants are described by the expression $k = k_1k_2/(k_{-1} + k_2)$.

The isokinetic parameters obtained from the IKR calculations can find some applications. Comparison of the T_{iso} and logk_{iso} parameters for the three reaction series considered shows that they are strongly dependent on the reaction mechanisms. Therefore, it is helpful to establish whether the kinetic parameters of the reactions under study belong to the series with known IKR when studying their mechanisms.

Additionally, the T_{iso} and logk_{iso} values can be used for assessing the activation parameters of (kinetically) little studied reactions proceeding by known mechanisms. This is possible owing to the following characteristic feature of IKR. If the IKR holds, the E_{iso} and logA_{iso} values of a particular reaction are determined by the T_{iso} and logk_{iso} parameters and by the known log$k$ values. Therefore, it is sufficient to know the only log$k$ value, which can be substituted into corresponding formulas for calculation of E_{iso} and logA_{iso} values, in particular, without resort to the LSM calculations:

$$E_{iso} = (\log k_{iso} - \log k)/[(2.303RT)^{-1} - (2.303RT_{iso})^{-1}], \quad (4)$$

$$\log A_{iso} = \log k_{iso} + E_{iso}/(2.303RT_{iso}). \quad (5)$$

This procedure can be illustrated taking calculations of activation parameters of the reactions of methyl perchlorate and methyl nitrate with anionic nucleophiles in water as an example. The reaction mechanism is described by Eq. (1). The E_{iso} and logA_{iso} values for these reactions calculated from Eqs. (4) and (5) using the known data[29] are listed in Table 5. The E_{iso} values obtained for the reactions of anionic nucleophiles with $MeClO_4$ are much lower than those obtained for the reactions with participation of $MeOSO_2Ph$, MeI, and

Table 5. Activation parameters E_{iso} and $\log A_{iso}$ calculated using Eqs. (4) and (5) for the reactions of $MeClO_4$ and $MeNO_3$ with anions in aqueous solutions (according to the data taken from Ref. 29)

N^{z-}	$MeClO_4$		$MeNO_3$	
	E_{iso} /kJ mol^{-1}	$\log A_{iso}$	E_{iso} /kJ mol^{-1}	$\log A_{iso}$
$S_2O_3^{2-}$	65.2	11.18	94.4	11.42
SO_3^{2-}	67.9	11.20	90.9	11.39
I^-	71.0	11.23	104.1	11.51
NCS^-	71.3	11.23	104.0	11.51
PO_4^{3-}	71.4	11.23	100.8	11.49
PhO^-	72.2	11.24	100.3	11.47
HO^-	73.3	11.24	101.6	11.49
CO_3^{2-}	73.9	11.25	103.0	11.50
N_3^-	75.0	11.26	105.8	11.52
NO_2^-	75.2	11.26	107.5	11.54
Br^-	76.0	11.27	109.0	11.55
p-$NO_2C_6H_4O^-$	77.2	11.28	109.2	11.55
HPO_4^{2-}	77.8	11.28	109.2	11.55
HSO_3^-	—	—	110.1	11.56
AcO^-	80.3	11.30	111.0	11.57
Cl^-	81.7	11.32	111.7	11.57

$MeNO_3$ (on the average, by 10.8±1.2, 16.8±4.3 and 30.2±2.6 kJ mol^{-1}, respectively, see Tables 2 and 5). When varying the leaving groups, the E_{iso} values change by constant increments, which confirms the applicability of the LFER principle to the reaction series (1).

Thus, knowledge of the rate constants (at least at one temperature) for the S_N2 substitution reactions at the saturated carbon atom proceeding with participation of anionic nucleophiles in aqueous solutions makes it possible to assess their activation parameters using the IKR obtained for reactions (1). The same conclusion is also valid for other IKR.

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