Reaction Constants Derived from Activation Parameters for the Evaluation of Substituent and Solvent Effects

Ferenc Ruff*

Department of Organic Chemistry, L. Eötvös University P. O. Box 32, H-1518 Budapest 112, Hungary

Received xxx; Preprint published xxx; Accepted xxx ; Published xxx

Internet Electron. J. Mol. Des. 2003, 1, 000–000

Abstract

In order to separate the effect of substituents into two parts, referring to the interaction of the reacting molecules and the solvation, the $\delta\Delta G^{\ddagger}$, $\delta\Delta H^{\ddagger}$ and $\delta\Delta S^{\ddagger}$ reaction constants were defined and determined from the dependence of ΔG^{\ddagger} , ΔH^{\ddagger} and ΔS^{\ddagger} activation parameters on the σ substituent constants, by analogy with the Hammett equation. The new reaction constants give the effect of the substituents on the reaction in energy units. $\delta\Delta G^{\ddagger}$, $\delta\Delta H^{\ddagger}$ and $\delta\Delta S^{\ddagger}$ can be divided into internal ($\delta\Delta X_{int}^{\ddagger}$, X = G, H, S) and external ($\delta\Delta X_{ext}^{\ddagger}$,) parts which refer to the bond formation and the solvation, respectively. The contribution of the substituents to the internal part of entropy of activation ($\delta\Delta S_{int}^{\ddagger}$), and the external part of free energy of activation ($\delta\Delta G_{ext}^{\ddagger}$), originated from solvent reorganization were supposed to be zero. Thus $\delta\Delta G^{\ddagger}$ and $\delta\Delta S^{\ddagger}$ present a good approximation to $\delta\Delta H_{int}^{\ddagger}$ and $\delta\Delta S_{ext}^{\ddagger}$, describing the effect of substituents on the energy barrier of the reaction and on the solvation, respectively. The $\delta\Delta G^{\ddagger}$ reaction constant reflects the change in solvation with the substituents in the Hammett equation. The $\delta\Delta S^{\ddagger}$ reaction constant reflects the change in solvation with the substituents in the reaction. A tentative interpretation of $\delta\Delta S^{\ddagger}$, based on the solvation of charged species in organic solvents and the rearrangement of the solvent structure in water containing mixtures is discussed for some nucleophilic addition, nucleophilic substitution and acid-catalysed reactions. A break of the $\delta\Delta H^{\ddagger} vs$. σ and $\delta\Delta S^{\ddagger} vs$. σ plots at about $\sigma \sim$ 0 is diagnostic for the change of solvation with the electronic effect of the substituents.

Keywords. Substituent effect; Solvent effect; Activation parameters; Reaction constants; QSPR; Isokinetic relationships.

Abbreviations and notations β , isokinetic temperature $\delta\Delta G^{\ddagger}$, r. c. of free energy of activation $\delta\Delta H^{\ddagger}$, r.c. of enthalpy of activation $\delta\Delta S^{\ddagger}$, r. c. of entropy of activation $\delta\Delta X_{int}^{\ddagger}$, internal r. c. $\delta\Delta X_{ext}^{\ddagger}$, external r. c.QSPR, quantitative structure-property relationshipsr. c. reaction constant

^{*} Correspondence author; phone: +36-1-2090-555; fax: +36-1-3722-620; E-mail: ruff@szerves.chem.elte.hu

1 INTRODUCTION

In previous papers [1,2] the reaction constants $\delta \Delta G^{\ddagger}$, $\delta \Delta H^{\ddagger}$ and $\delta \Delta S^{\ddagger}$ were defined by Eqs. (1)–(3) indicating the dependence of the activation parameters on substituent constants, by the analogy with the Hammett equation (Eq. 4, [3–6]).

$$\Delta G^{\ddagger} = \delta \Delta G^{\ddagger} \sigma + \Delta G_{o}^{\ddagger} \tag{1}$$

$$\Delta H^{\ddagger} = \delta \Delta H^{\ddagger} \sigma + \Delta H_{o}^{\ddagger} \tag{2}$$

$$\Delta S^{\ddagger} = \delta \Delta S^{\ddagger} \sigma + \Delta S_{o}^{\ddagger} \tag{3}$$

$$\log k = \rho \sigma + \log k_0 \tag{4}$$

 ΔG^{\ddagger} , ΔH^{\ddagger} , ΔS^{\ddagger} and ΔG_{o}^{\ddagger} , ΔH_{o}^{\ddagger} , ΔS_{o}^{\ddagger} are the activation parameters obtained for the substituted and unsubstituted compounds, respectively. In Eqs. (1)–(3) σ substituent constants giving the best correlations with the Hammett equation were used. The units of $\delta \Delta G^{\ddagger}$ and $\delta \Delta H^{\ddagger}$ reaction constants are kJ mol⁻¹ σ^{-1} and that of $\delta \Delta S^{\ddagger}$ is J mol⁻¹ K⁻¹ σ^{-1} , but σ can be replaced by any other substituent constant. The standard errors of the new reaction constants were discussed earlier [1]; the relation between them is the same as that of the activation parameters (Eq. 5).

$$\delta \Delta G^{\ddagger} = \delta \Delta H^{\ddagger} - T \,\delta \Delta S^{\ddagger} \tag{5}$$

The ratio of $\delta \Delta H^{\ddagger}$ and $\delta \Delta S^{\ddagger}$ reaction constants is equal to the β isokinetic temperature (Eq. 6, [1]), which is the slope of the linear ΔH^{\ddagger} vs. ΔS^{\ddagger} plots (Eq. 7) and the temperature of intersection of the log (*k*/*T*) vs. (1/T) plots of a reaction series [7–11].

$$\delta \Delta H^{\ddagger} / \delta \Delta S^{\ddagger} = \beta \tag{6}$$

$$\Delta H^{\ddagger} = \beta \Delta S^{\ddagger} + \text{const.}$$
 (7)

The new reaction constants can be determined by Eqs. (1)–(3) or from the β isokinetic temperature, as described earlier [1]. The reaction constants $\delta\Delta G^{\ddagger}$ and ρ have opposite signs and are proportional to each other (Eq. 8, [1]). $\delta\Delta G^{\ddagger}$ and ρ are calculated at the *T* temperature. $\delta\Delta G^{\ddagger} = -2.303RT\rho$ (8)

If $\delta \Delta G^{\ddagger}$, $\delta \Delta H^{\ddagger}$ and $\delta \Delta S^{\ddagger}$ are positive, the electron-withdrawing substituents ($\sigma > 0$) increase and the electron-donating groups ($\sigma < 0$) decrease the value of the corresponding activation parameters (Eqs. 1–3) and vice versa for the case when these reaction constants have a negative sign. The decrease of ΔG^{\ddagger} and ΔH^{\ddagger} and the increase of ΔS^{\ddagger} accelerate the reaction.

On the basis of the theory developed by Heppler [12–14] the reaction constants can be divided into internal and external parts [1], referring to the bond formation and the solvation process, respectively (Eqs. 9–11).

$$\delta \Delta G^{\ddagger} = \delta \Delta G_{\text{int}}^{\ddagger} + \delta \Delta G_{\text{ext}}^{\ddagger}$$
⁽⁹⁾

$$\delta \Delta H^{\ddagger} = \delta \Delta H_{\text{int}}^{\ddagger} + \delta \Delta H_{\text{ext}}^{\ddagger}$$
(10)

$$\delta \Delta S^{\ddagger} = \delta \Delta S_{\text{int}}^{\ddagger} + \delta \Delta S_{\text{ext}}^{\ddagger}$$
(11)

The internal part of entropy of activation was supposed to be independent of the substituents [12–14] (*i.e.* $\delta\Delta S_{int}^{\dagger} \approx 0$), and the external part of free energy of activation, due to solvent reorganisation, to be zero ($\delta\Delta G_{ext}^{\dagger} \approx 0$) [15–17]. If these approximations are valid, then $\delta\Delta S^{\dagger} \approx \delta\Delta S_{ext}^{\dagger}$, $\delta\Delta H_{ext}^{\dagger} \approx T\delta\Delta S_{ext}^{\dagger}$ and $\delta\Delta G^{\dagger} \approx \delta\Delta H_{int}^{\dagger}$. This means that the change of entropy with the substituents is determined by the solvation. The value of $\delta\Delta H^{\dagger}$ is also influenced by the solvation and the change of free energy of activation by the substituents is a good approximation of the internal part of enthalpy of activation, which is characteristic of the effects of substituents on the reaction.

Earlier it was supposed [1] that $\delta \Delta H_{int}^{\ddagger}$ does not change with a small change of the composition of the solvent and the so-called isosolvent temperature (β_{ext}), which can be obtained from a $\Delta H^{\ddagger} = \beta_{ext} \Delta S^{\ddagger} + \text{const.}$ plot of a reaction measured in different solvents, describes better the proportionality of $\delta \Delta H_{ext}^{\ddagger}$ and $\delta \Delta S_{ext}^{\ddagger}$. However, a more thorough analysis of the solvent effect [2] revealed that the latter approximation ($\delta \Delta H_{ext}^{\ddagger}/\delta \Delta S_{ext}^{\ddagger} \approx \beta_{ext}$) is valid only in a few special cases and the former approximation ($\delta \Delta H_{ext}^{\ddagger}/\delta \Delta S_{ext}^{\ddagger} \approx T$) gives regularly a much better description of the phenomena.

On the basis of the previous discussion the most valuable information can be expected from $\delta\Delta G^{\ddagger}$ and $\delta\Delta S^{\ddagger}$ reaction constants, which characterize the effects of substituents on the energy barrier of activation and on the difference of solvation between the reactants and the transition state, respectively. The interpretation of the $\delta\Delta H^{\ddagger}$ parameter is less straightforward, because it contains contributions not only from the internal but also from the external part of the enthalpy of activation, which is related to the entropy of activation and for a reaction may show considerable changes with the solvent. In this paper some simple organic reations are discussed to find the first approximate correlations between the reaction constants and the mechanism of the reactions as well as the solvation of the participating species.

2 MATERIALS AND METHODS

Activation parameters were calculated from the temperature dependence of rate constants, by using the Eyring equation (Eq. 12).

log $(k/T) = \log (R/Nh) + \Delta S^{\ddagger}/2.303R - \Delta H^{\ddagger}/2.303RT = \log (R/Nh) - \Delta G^{\ddagger}/2.303RT$ (12) Regularly only two activation parameters, ΔG^{\ddagger} and ΔH^{\ddagger} (seldom ΔG^{\ddagger} and ΔS^{\ddagger}) give good correlations (r > 0.950) with the substituent constants (Eqs.1–3, [1]). The third reaction constant ($\delta \Delta S^{\ddagger}$ or $\delta \Delta H^{\ddagger}$) can be calculated from Eq. (5). Only those compounds (given in Tables 1–4) were omitted from the caculations, which caused a change in the mechanism of the reaction, or whose activation parameters showed a decided difference from the expected values, presumably because of experimental errors. The $\delta\Delta G^{\ddagger}$, $\delta\Delta H^{\ddagger}$, $\delta\Delta S^{\ddagger}$ and ΔG_{o}^{\ddagger} , ΔH_{o}^{\ddagger} , ΔS_{o}^{\ddagger} values of the studied reaction series, in which only a substituent of one of the reactants was varied, are shown in Tables 1–4. In some cases the change of activation parameters with the substituents are also illustrated in $\Delta G^{\ddagger}/\Delta H^{\ddagger}/-T\Delta S^{\ddagger}$ vs. σ plots. For the evaluation of the $\delta\Delta G^{\ddagger}$, $\delta\Delta H^{\ddagger}$ and $\delta\Delta S^{\ddagger}$ reaction constants, the rate constants published earlier were used. References are given in Tables.

3 RESULTS AND DISCUSSION

The interpretation of the reaction constant $\delta \Delta G^{\ddagger}$ is analogous to that of the well known ρ constant, which is widely used [3–6] since Hammett published his famous equation (Eq. 4). The advantage of $\delta \Delta G^{\ddagger}$ is revealed in giving the change of reactivity in energy units. We will also discuss the reaction constants $\delta \Delta S^{\ddagger}$ which shows the dependence of solvation on substituents.

Solvation is a highly complicated process which depends on structure of the reactants, the mechanism of the reaction and the solvent [18]. Each of the reactions may represent a special case, therefore only some general principles may be discussed here. During the reaction the reactants are desolvated, the transition state is solvated and some part of the solvent is reorganized. The desolvation of the reactants increases, the solvation of the transition state decreases the entropy of activation. Charged and dipolar species require stronger solvation than nonpolar molecules. The entropy change connected with the rearrangement of the solvent depends on its structure. In less polar solvents, the solvation of charged species give rise to stronger rearrangement of the solvent and a greater decrease of entropy of activation because the solvent molecules are only slightly ordered in the pure solvents. In polar protic solvents, especially in water, where the solvent molecules are highly ordered, the ordering can be smaller in the solvation shell of large ions or polar molecules, than in the pure solvent. In this way, given substituents in the reactant may either increase or decrease the entropy of activation for the solvent.

3.1 Reaction of Carboxylic Acids Derivatives with Nucleophiles

The structure of aromatic carbonyl compounds can be characterized by two Lewis structures (1, 2). The attack of the nucleophile on the carbonyl carbon atom leads to a

tetrahedral intermediate (3) and the product (4) is formed with the splitting of the L leaving group [19]. From the Hammond principle [20] it follows that the structure of the transition state may be similar to that of the intermediate 3. Electron-withdrawing and electron-donating substituents increase the contribution of Lewis structures 1 and 2, respectively, and compounds with the latter substituents may bring about a greater negative charge on the carbonyl oxygen atom than the former ones. In the transition state, with a nearly complete negative charge on the oxygen, the substituents have smaller effect on the charge distribution because only inductive effects are operative for the lack of delocalization. Thus the differences in the charges of the carbonyl oxygen atom of the different substituted compounds are greater in the reactant state than in the transition state.

$$\begin{bmatrix} O & O^{-} \\ Ar - C - L & \longleftrightarrow & Ar - C^{-}L \end{bmatrix} \xrightarrow{Nu^{-}} \begin{bmatrix} O^{-} \\ Ar - C - L \\ Nu \end{bmatrix} \xrightarrow{Nu^{-}} Ar - C^{-}Nu + L^{-}$$

In reactions solvation can be changed in different ways; some cases are discussed below.

1. If the solvation is influenced mainly by the size of the charge of the substrate in less polar solvents, then the decrease of entropy at the formation of the transition state is smaller, ΔS^{\ddagger} is greater for compounds with electron-donating groups ($\sigma < 0$); *i.e.* $\delta \Delta S^{\ddagger} < 0$ (*cf.* Eq. 3). Compounds with electron-donating groups are solvated stronger in the reactant state than those having electron-withdrawing substituents and they can be transferred to the transition state with a smaller change in the rearrangement of the solvent molecules.

2. If the nucleophile is strongly solvated in a polar protic solvent and its attack on less reactive compounds with electron-donating groups must be promoted by a special solvation of the carbonyl oxygen in the transition state, then entropy of activation shows a greater decrease, ΔS^{\ddagger} is smaller for the given compounds ($\sigma < 0$) than in other cases; *i.e.* $\delta \Delta S^{\ddagger} > 0$ (*cf.* Eq. 3). In polar protic solvents (*e.g.* in water) the solvent molecules in the solvation shell of large ions are less ordered than in the bulk of the solvent. Because the electron-withdrawing groups decrease the negative charge of the oxygen atom in the transition state, this phenomenon can also lead to a less ordered solvent shell and to an increase in ΔS^{\ddagger} for these reactants ($\sigma > 0$); *i.e.* $\delta \Delta S^{\ddagger} > 0$ (*cf.* Eq. 3).

3. If the splitting of the leaving group (L) is rate-determining and promoted by solvation, electron-withdrawing substituents in the aromatic ring (Ar) linked directly to the C=O group hinder the departing of L⁻. These compounds ($\sigma > 0$) need stronger solvation which is connected with the decrease in ΔS^{\ddagger} value; *i.e.* $\delta \Delta S^{\ddagger} < 0$. On the other hand, electron-

withdrawing groups in the L leaving group promote the reaction and need smaller solvation, therefore ΔS^{\ddagger} increases; *i.e.* $\delta \Delta S^{\ddagger} > 0$.

In the alkaline hydrolysis (Nu = OH⁻) of ArCOOEt (L = OEt) substrates, the values of $\delta\Delta G^{\ddagger}$ reaction constants are similar in different solvents (Table 1, No. 1). $\delta\Delta G^{\ddagger} < 0$ was found because electron-withdrawing groups decrease the value of ΔG^{\ddagger} and increase the rate of the reaction. The values of $\delta\Delta H^{\ddagger}$ are not characteristic of the reaction, but depend clearly on the solvent. In aqueous solvent mixtures $\delta\Delta S^{\ddagger} > 0$, if the concentration of water is higher than about 20 %, and it increases with the increase of the water content of the solvent. In 85 wt % ethanol-water $\delta\Delta S^{\ddagger} \sim 0$, the change of solvation in this medium seems to be independent of the substituents. The increasing leaving group ability increases the value of entropy reaction constant. $\delta\Delta S^{\ddagger} = 27,0$ J mol⁻¹ K⁻¹ σ^{-1} was obtained for the hydrolysis of ArCOOAr' benzoic acid esters with the Ar'O = 2,4-(NO₂)₂-C₆H₃O leaving group in 50 vol % dioxane-water mixture ($\delta\Delta G^{\ddagger} = -13.5$ kJ mol⁻¹ σ^{-1} , $\delta\Delta H^{\ddagger} = -5.81$ kJ mol⁻¹ σ^{-1} , [27]). The change of solvation with the substituents may be explained by reasons discussed above as case 2 and 3. The ΔG_0^{\ddagger} value of the unsubstituted compound shows only smaller changes with the solvent composition (Table 1, No.1). ΔS_0^{\ddagger} is much higher in alcohol-water mixtures, the solvation is changed more slightly at the formation of the transition state in these media.

If substituents are bonded to the phenyl ring of the Ar'O leaving group in MeCOOAr' (Table 1, No. 2), they have smaller effect (the absolute value of $\delta\Delta G^{\ddagger}$ decreases as compared to that of ArCOOEt) and do not change solvation as shown by $\delta\Delta S^{\ddagger} \approx 0$ in 56 wt % acetone-water mixtures. The change in the solvation of the transition state with the substituents is the same as that of the reactant state.

In the basic hydrolysis of PhCOOAr' esters (Table 1, No. 3) $\delta\Delta G^{\ddagger}$ shows considerable change with the solvent. $\delta\Delta S^{\ddagger}$ has a small positive value in water and high negative values in 80 vol % DMSO-water mixtures or in 2.25 M aqueous Bu₄NBr solution of high ionic strength. The OH⁻ ion is less solvated and most reactive in DMSO-water and most solvated and less reactive in 2.25 M Bu₄NBr solution (*cf.* ΔG_0^{\ddagger} values in Table 1, No. 3). The change of solvation is the smallest in the reaction at high ionic strength (*cf.* ΔS_0^{\ddagger} values). The observed change in entropy of activation with the substituents may be explained for water ($\delta\Delta S^{\ddagger} > 0$) and for the other two media ($\delta\Delta S^{\ddagger} < 0$) as described in case 2 and case 1, respectively.

In some other reactions of substituted carboxylic acid derivatives with nucleophiles (Table 1, Nos. 4–8) $\delta\Delta G^{\ddagger} < 0$ and $\delta\Delta S^{\ddagger} < 0$ were found in less polar solvents or in solvent mixtures containing small amount of protic solvent, and solvation is controlled by charges (case 1). The

	nucleopinies									
No	Reaction	Ref.	Solvent ^{<i>a</i>}	n ^b	$\delta\Delta G^{\ddagger c,d} (r)$	$\delta\Delta H^{\ddagger d}$ (r)	$\delta\Delta S^{\ddagger e}$	$\Delta G_0^{\ddagger cf}$	$\Delta H_{\rm o}^{\ddagger f}$	$\Delta S_{o}^{\ddagger g}$
1.	ArCOOEt $+ OH^{-h}$	[21-23]	56 wt % $a-w^{k}$	18	-13.2 (0.991)	-11.2 (0.984)	6.7	87.5	58.2	-98.3
	011	[23]	50 vol % a–w	5	-12.3 (0.996)	-7.98 (0.987)	14.5	87.1	55.4	-106
		[23]	40 vol % a–w	5	-12.7 (0.998)	-6.58 (0.969)	20.5	86.4	52.6	-113
		[24]	71.2 wt % m–w	6 ^{<i>l</i>}	-12.5 (0.998)	-6.77 (0.975)	19.2	91.5	71.8	-66.1
		[25]	85 wt % e–w	8	-14.7 (0.997)	-15.8 (0.998)	-3.7	93.3	71.5	-67.4
		[26]	85 wt % e–w	6	-14.6 (0.996)	-14.4 (0.991)	~0	91.3	71.5	-66.5
2.	MeCOOAr' $+ OH^{-i}$	[21]	56 wt % a–w	5 ^m	-8.43^{n} (0.999)	-8.35 (0.999)	~0	73.8 ^{<i>n</i>}	51.0	-78.8
3.	PhCOOAr' $+ OH^{-i}$	[28,29]	W	7	-6.07 (0.993)	-5.19 (0.981)	2.95	75.2	42.5	-110
		[30]	80 vol % dm–w	6 °	-9.43 (0.996)	-16.0 (0.991)	-22.0	69.7	36.5	-111
		[31]	2.25 M Bu ₄ NBr (w)	6 °	-13.1 (0.998)	-24.9 (0.976)	-39.6	79.3	63.3	-53.3
4.	$ArCONH_2 + OH^{-h}$	[32]	60 vol % e–w	4	-8.49^{p} (1.000)	-12.6 (0.991)	-12.5	111.7 ^p	75.2	-112
5.	$(ArCO)_2O + H_2O^h$	[33]	75 vol % d–w	9	-19.8 ^{<i>q</i>} (0.994)	-31.3 (0.971)	-34.7	102.7 ^{<i>q</i>}	64.1	-151
6.	ArCOCl + H_2O^h	[34]	95 vol % a–w	4 ^{<i>r</i>}	-11.3 (1.000)	-23.0 (0.998)	-39.3	97.4	49.0	-163
7.	ArCOCl + EtOH ^h	[35]	e	7 ^r	-8.83 (0.989)	-15.4 (0.989)	-21.9	90.9	61.5	-98.7
		[36]	60 vol % eth–e	7 ^r	-9.14 (0.995)	-20.4 (0.981)	-37.8	95.7	57.9	-127
8.	ArCOC1 + PhNH ₂ ^h	[37]	b	4	-6.85 (0.993)	-9.35 (0.994)	-8.39	79.5	28.9	-170
9.	$ArNH_2$ + PhCOCl ^j	[37]	b	6	15.0 (0.990)	14.9 (0.983)	~ 0	79.9	30.7	-165
		[38]	eth	4	14.6 (0.983)	19.3 (0.999)	15.7	77.5	22.9	-183

TABLE 1. Reaction constants and activation parameters for the reactions of carboxylic acid derivatives with mualaamhilaa

^a Solvents: (a) acetone, (b) benzene, (d) dioxane, (dm) DMSO, (e) ethanol, (eth) ether, (m) methanol, (w) water. Values of solvent composition refer to the first solvent.

^b Number of compounds .

^c The values of $\delta\Delta G^{\ddagger}$ and ΔG_{0}^{\ddagger} were calculated at 298 K, if not otherwise stated.

^d In kJ mol⁻¹ σ^{-1} unit. ^e In J mol⁻¹ K⁻¹ σ^{-1} unit. ^f In kJ mol⁻¹ unit. ^g In J mol⁻¹ K⁻¹ unit.

 ${}^{h}\sigma$ constants were used in correlations.

 ${}^{i}\sigma^{o}$ constants were used in correlations.

 ${}^{j}\sigma^{-}$ constants were used in correlations.

^{*k*} 56 wt % a–w and 60 vol % a–w are identical.

^{*l*}*p*-Cl substituted compound omitted.

 \overline{m} p-NH₂, m-COO⁻ and p-COO⁻ substituted compounds omitted.

^{*n*} The value of $\delta\Delta G^{\ddagger}$ and ΔG_{0}^{\ddagger} was calculated at 288 K.

 o *m*-NH₂ substituted compound omitted.

^{*p*} The values of $\delta\Delta G^{\ddagger}$ and ΔG_{o}^{\ddagger} were calculated at 326 K. ^{*q*} The values of $\delta\Delta G^{\ddagger}$ and ΔG_{o}^{\ddagger} were calculated at 331 K. ^{*r*}*p*-MeO substituted compound omitted.



FIGURE 1. $\Delta G^{\ddagger} vs. \sigma (\bullet - \bullet), \Delta H^{\ddagger} vs. \sigma (\bullet - \bullet), \text{ and } -T\Delta S^{\ddagger} vs. \sigma (\blacktriangle - \bigstar) \text{ plots of the reaction of aniline (PhNH₂)}$ with substituted benzoyl chlorides (X-C₆H₄COCl, X = *p*-Me, H, *p*-Cl, *p*-NO₂) in benzene, [37]. Slopes: $\delta \Delta G^{\ddagger} = -6.85 \pm 0.6 \text{ kJ mol}^{-1} \sigma^{-1} (r = 0.993), \delta \Delta H^{\ddagger} = -9.35 \pm 0.74 \text{ kJ mol}^{-1} \sigma^{-1} (r = 0.994), -T\delta \Delta S^{\ddagger} = 2.70 \pm 0.56 \text{ kJ mol}^{-1} \sigma^{-1} (r = 0.960), \delta \Delta S^{\ddagger} = -9.06 \pm 1.9 \text{ J mol}^{-1} \text{ K}^{-1} \sigma^{-1}, \delta \Delta S_{\text{calc}}^{\ddagger} = -8.39 \text{ J mol}^{-1} \text{ K}^{-1} \sigma^{-1} (T = 298 \text{ K}).$



FIGURE 2. ΔG^{\ddagger} vs. σ^{-} ($\blacksquare -\blacksquare$), ΔH^{\ddagger} vs. σ^{-} ($\bullet -\bullet$), and $-T\Delta S^{\ddagger}$ vs. σ^{-} ($\blacktriangle -\blacktriangle$) plots of the reaction of substituted anilines (X-C₆H₄NH₂, X = H, *p*-Cl, *m*-Cl, *m*-NO₂, *p*-NO₂) with benzoyl chloride (PhCOCl) in benzene, [37]. Slopes: $\delta \Delta G^{\ddagger} = 15.0 \pm 0.8$ kJ mol⁻¹ (σ^{-})⁻¹ (r = 0.990), $\delta \Delta H^{\ddagger} = 14.9 \pm 1.0$ kJ mol⁻¹ (σ^{-})⁻¹ (r = 0.983), $-T\delta \Delta S^{\ddagger} = -0$ kJ mol⁻¹ (σ^{-})⁻¹, $\delta \Delta S^{\ddagger} = -0$ J mol⁻¹ K⁻¹ σ^{-1} , (T = 298 K).

effect of substituents of the substrate on the activation parameters *e.g.* in the reaction of ArCOCl with PhNH₂ in benzene (Table 1, No.8) is shown in Fig. 1. By varying the substituents of the nucleophile in the reaction of PhCOCl with ArNH₂, $\delta\Delta G^{\ddagger} > 0$ was obtained, indicating that electron-donating groups ($\sigma < 0$) promote the reaction (Table 1, No. 9, Fig. 2). In benzene solvation does not change with the substituents ($\delta\Delta S^{\ddagger} \sim 0$). In ether, however, aniline derivarives substituted with electron-withdrawing groups form stronger H-

bonds than those with electron-donating substituents, and the desolvation of the nucleophiles in the reaction increases the value of ΔS^{\ddagger} , *i.e.* $\delta \Delta S^{\ddagger} > 0$ (Table 1, No. 9, *cf.* Eq. 3).

3.2 Aliphatic Nucleophilic Substitutions

In S_N2 type solvolysis reactions of alkyl benzenesulfonate (ArSO₃R) the water or alcohol (R'OH) nucleophiles attack the α -carbon atom of the R alkyl group with the formation of alcohols (ROH) or ethers (ROR'), respectively [39,40]. Electron-withdrawing substituents ($\sigma > 0$) bonded to the ArSO₃⁻ leaving group promote the nucleophilic attack ($\delta\Delta G^{\ddagger} < 0$) and, by decreasing the charge and the solvation of the ArSO₃⁻ ion, increase the entropy of activation ($\delta\Delta S^{\ddagger} > 0$). The less polar the solvent is, the greater the values of $\delta\Delta S^{\ddagger}$ and ΔG_{0}^{\ddagger} , and the smaller those of $\delta\Delta G^{\ddagger}$ and ΔS_{0}^{\ddagger} (Table 2, Nos. 1–4).

When the substituents in the nucleophile were varied in the $S_N 2$ reaction of MeI with dimethylaniline derivatives (ArNMe₂), electron-donating groups ($\sigma < 0$) were found to promote the reaction ($\delta \Delta G^{\ddagger} > 0$) and to decrease the entropy of activation ($\delta \Delta S^{\ddagger} > 0$), which may be ascribed to the increased solvation of the transition state (Table 2, No. 5). The $\delta \Delta S^{\ddagger}$ values obtained may be reasoned in two ways. Dimethylaniline derivatives with electron-withdrawing groups are more polar ($X^{\delta-}-C_6H_4-NMe_2^{\delta+}$) in the reactant state than the unsubstituted analogue and need a smaller change in solvation to reach the transition state. In contrast the charge separation for dimethylaniline derivatives with electron-donating groups is greater in the transition state ($X^{\delta+}-C_6H_4-NMe_2^{\delta+}\cdots Me^{\cdots}I^{\delta-}$) and needs greater solvation. Both effects give rise to a greater decrease of entropy values at the formation of the transition state and produce both a smaller value of ΔS^{\ddagger} for ArNMe₂ compounds with electron-donating groups ($\sigma < 0$) in Ar and a positive $\delta \Delta S^{\ddagger}$ reaction constant.

In the $S_N 2$ type nucleophilic displacement reaction involving N,N-dimethylaniline (5) and N-chloroacetyl arylamines (6) electron-withdrawing substituents on the Ar aromatic ring of

$$\begin{array}{cccc}
 & & & & & \\
 & & & \\
 & PhNMe_2 & + & ArNH-C-CH_2Cl & \longrightarrow & \begin{bmatrix} & O \\ & & & \\ ArNH-C-CH_2-N^+Me_2Ph & + & Cl^- \end{bmatrix} & \longrightarrow \\
 & & 5 & 6 & 7 & & \\
\end{array}$$

 \xrightarrow{O}_{II} $ArNH \xrightarrow{C} CH_2 - NMePh + MeCl$ $8 \qquad 9$

the substrate help the nucleophilic attack ($\delta \Delta G^{\ddagger} < 0$) and increase the solvation of the transition state ($\delta \Delta S^{\ddagger} < 0$; Table 2, No. 6, Fig. 3). The absolute value of $\delta \Delta G^{\ddagger}$ is small, because

		onotanto	und dott vati	on pui	uniteter	5 of unpilue	te nuereopn.	* /	* -	* -	+ <i>I</i> .
No.	Reaction ^{<i>a</i>}	Ref.	Solvent	n^{c}	T/	$\delta\Delta G^{\downarrow e}$	$\delta \Delta H^{\ddagger e}$	$\delta \Delta S^{\ddagger J}$	$\Delta G_{\mathrm{o}}^{\ \downarrow g}$	$\Delta H_{o}^{\downarrow g}$	$\Delta S_0^{\ddagger n}$
			b		\mathbf{K}^{d}	(r)	(r)	(r)			
1.	$ArSO_3Me + H_2O$	[39]	W	6	323	-5.72	-1.53	12.9	102.3	86.1	-50.2
						(0.974)		(0.973)			
2.	ArSO ₂ Me + EtOH	[40]	e	5	343	-9.29	-2.16	20.6	111.8	84.2	-80.3
		[]	-			(0.999)		(0.956)		• • • •	
						(****)		(0.500)			
3.	$ArSO_3nPr + ROH$	[41]	m	6	313	-7.75	-2.35	17.2	111.8	88.9	-73.3
						(0.989)		(0.975)			
			e	6	313	-8.05	-0.50	24.2	113.3	86.7	-84.9
						(0.984)		(0.963)			
			<i>n</i> -p	6	313	-8.32	0.3	27.6	113.7	84.7	-92.6
						(0.986)		(0.977)			
			<i>n</i> -b	6	313	-8.39	-1.77	21.1	114.0	85.9	-89.6
						(0.988)		(0.955)			
			<i>i</i> -p	6	313	-9.16	-1.00	26.1	115.6	75.1	-127.0
						(0.987)		(0.957)			
			<i>t</i> -b	6	313	-9.78	-0.64	29.2	118.6	76.3	-135.2
						(0.990)		(0.990)			
4.	$ArSO_2CH_2CH=CH_2$	[41]	m	8	303	-8.38	-7.51	2.87	100.6	86.9	-45.1
	+ ROH					(0.998)	(0.928)				
			<i>n</i> -p	8	303	-8.95	-4.78	13.8	103.1	86.3	-55.6
						(0.998)	(0.796)	(0.782)			
			<i>n</i> -b	8	303	-9.23	-2.46	22.3	103.5	86.9	-54.9
						(0.997)	(0.868)	(0.970)			
			<i>i</i> -p	8	303	9.36	-1.05	27.4	104.8	82.6	-73.3
					• • •	(0.998)	• • • •	(0.961)		~ — .	
			<i>t</i> -b	8	303	-10.4	-2.93	24.7	106.1	67.4	-127.7
-		E 403		-		(0.998)	1 < -	(0.963)	100.0	(1.(100
5.	$ArNMe_2 + Mel$	[42]	m	7	328	13.8	16.7	8.97	100.9	61.6	-120
						(0.994)	(0.974)				
6	ArNHCOCH ₂ Cl	[43]	0	9	461	-0.70	-36.1	-77.2	137.0	81.5	-131.5
0.	$+ PhNMe_2$	[10]	U		101	(0.977)	(0.993)	(0.992)	127.0	01.0	101.0
						(0.277)	(0.570)	(()))=)			
7.	$ArNHQ + H_2O$	[44]	pH: 7.2	14	298	13.6	26.0	41.4	87.9	76.1	-38.4
	$(Q=CH_2C(NO_2)_2Me)^{-1}$		(w)			(0.982)	(0.984)	(0.978)			

TABLE 2. Reaction constants and activation parameters of aliphatic nucleophilic substitution reactions

^{*a*} The σ constants were used in correlations if not otherwise stated.

^b Solvents: (b) BuOH, (e) EtOH, (m) MeOH, (p) PrOH, (o) octanol, (w) water. Values of solvent composition refer to the first solvent.

^{*c*} Number of compounds. ^{*d*} The values of ΔG_0^{\ddagger} and $\delta \Delta G^{\ddagger}$ were calculated at the given temperatures.

^{*e*} In kJ mol⁻¹ σ^{-1} unit.

^{*f*} In J mol⁻¹ K⁻¹ σ^{-1} unit.

^g In kJ mol⁻¹ unit. ^h In J mol⁻¹ K⁻¹ unit.

^{*i*} The σ^{-} constants were used in correlations.

the substituents in Ar is far from the CH₂ center of the reaction and the temperature of the measurements (T = 461 K) is close to the isokinetic temperature ($\beta = 467$ K). Both ΔS^{\ddagger} and $\delta \Delta H^{\ddagger}$ values are changed on a much larger scale because of solvation. The reason may be similar to that mentioned Section 3.1. Compounds with electron-donating groups have higher negative charge on the carbonyl oxygen atom (cf. Lewis structure 2) and are solvated more strongly, therefore the rearrangement of the solvent molecules is smaller, and the entropy of activation is greater for the given compounds. The opposite can be expected for compounds with electron-withdrawing substituents.



FIGURE 3. ΔG^{\ddagger} vs. σ (\blacksquare - \blacksquare), ΔH^{\ddagger} vs. σ (\bullet - \bullet), and $-T\Delta S^{\ddagger}$ vs. σ (\blacktriangle - \blacktriangle) plots of the reaction of substituted N-chloroacetyl arylamines (X-C₆H₄NHCOCH₂Cl, X = *p*-MeO, 3,4-Me₂, *p*-Me, *m*-Me, H, *p*-I, *p*-Br, *p*-CH₃CO, *m*-NO₂, *p*-NO₂) with N,N-dimethylaniline (PhNMe₂) in octanol, [43]. Slopes: $\delta\Delta G^{\ddagger} = -0.7 \pm 0.05$ kJ mol⁻¹ σ^{-1} (r = 0.977), $\delta\Delta H^{\ddagger} = -36.1 \pm 1.6$ kJ mol⁻¹ σ^{-1} (r = 0.993), $-T\delta\Delta S^{\ddagger} = 35.6 \pm 1.6$ kJ mol⁻¹ σ^{-1} (r = 0.992), $\delta\Delta S^{\ddagger} = -77.2 \pm 1.9$ J mol⁻¹ K⁻¹ σ^{-1} , (T = 461 K).

The N-(2,2-dinitropropyl) arylamines (10) hydrolyse in an unimolecular S_N1 reaction in buffered neutral aqueous solution to give ionic intermediates (12,13), which react with water in a fast step to give the products (14,15). Electron-donating substituents accelerate the

$$\operatorname{ArNHCH}_{2}C(\operatorname{NO}_{2})_{2}CH_{3} \longrightarrow \left[\operatorname{ArNHCH}_{2}^{\delta_{+}-\delta_{-}}C(\operatorname{NO}_{2})_{2}CH_{3}\right]^{\sharp} \longrightarrow \left[\operatorname{ArNHCH}_{2}^{+} + {}^{-}C(\operatorname{NO}_{2})_{2}CH_{3}\right] \longrightarrow 10 \qquad 11 \qquad 12 \qquad 13$$

$$\xrightarrow{H_2O} \text{ArNHCH}_2OH + \text{HC(NO}_2)_2CH_3$$
14 15

reaction ($\delta\Delta G^{\ddagger} > 0$, Table 2, No. 7), but activation parameters correlate with the σ^{-} constants because electron-withdrawing groups with through conjugation (*e.g. p*-NO₂) hinder the reaction in a greater degree than it would be expected on the basis of the σ constants. Electron-withdrawing groups increase the value of ΔS^{\ddagger} ($\delta\Delta S^{\ddagger} > 0$, Table 2, No. 7). The explanation may be the same as in the case of the S_N2 reaction of ArNMe₂ derivatives with MeI. As compared with the unsubstituted compounds the polarity of the reactants with electron-withdrawing substituents is greater in the reactants state, the change of their solvation is smaller at the formation of the transition state (**11**). When electron-donating substituents are present, the charge separation in the transition state is more extensive, requiring stronger solvation. Both effects produce a positive $\delta \Delta S^{\ddagger}$ value.

3.3 Acid-catalysed Reactions

In acid-catalysed reactions the first step is the equilibrium protonation of the substrate (16), which is followed by the nucleophilic attack in the second, rate-determining step (17-20). Activation parameters (ΔX^{\ddagger} , X = G, H, S), calculated from the observed rate constants are composed of the enthalpy and entropy changes (ΔX_1°) of the equilibrium and the activation parameters (ΔX_2^{\ddagger}) of the second step $(\Delta X^{\ddagger} = \Delta X_1^{\circ} + \Delta X_2^{\ddagger}, [1])$. If the protonation is a fast equilibrium, the change of free energy of activation with the substituents $\delta\Delta G^{\ddagger}$ has small absolute value, e.g. in the hydrolysis of esters and amides or in the esterification of carboxylic acids (Table 3, No. 1–6). In the hydrolysis of ArCOOEt esters the nucleophilic attack ($\delta \Delta G^{\ddagger} <$ 0, Table 3, No. 1), in that of the MeCOOAr' and ArCONH₂ substrate the protonation has greater substituent effect ($\delta \Delta G^{\ddagger} > 0$, Table 3, Nos. 2,3), and they are promoted by electronwithdrawing and electron-donating groups, respectively. In the esterification of ArCOOH acids with methanol (Table 3, No. 5) the protonation, in the reaction of the same substrates with the bulky cyclohexanol (Table 3, No. 6) the nucleophilic attack has greater influence on the substituent effect. The value of $\delta \Delta S^{\ddagger}$ (and therefore that of $\delta \Delta H^{\ddagger}$) depends on the effect of the substituents on solvation. In the hydrolysis of esters (Table 3, Nos. 1,2) and N-acyl hydrazones (Table 3, No. 4) and in the esterifications (Table 3, Nos. 5,6) the reactants substituted with an electron-donating group in Ar (cf. Lewis structure 17) are solvated stronger, therefore the change of the solvation at the formation of the transition state is smaller for the given compounds ($\delta \Delta S^{\ddagger} < 0$). In the case of amides (Table 3, No. 3) for which

 $L = OEt, OAr', NH_2; R = H, Me, C_6H_{11}$

 $\delta\Delta S^{\ddagger} > 0$, compounds with electron-withdrawing substituents (cf. Lewis structure 18) have more polar structure and are solvated in a greater extent in the reactant state and require therefore smaller reorganisation in the solvation shell at the formation of the transition state. These compounds exhibit higher entropy of activation.

	TABLE 3. reac	tion cons	tants and activation	n para	meters	of acid cal	alysed rea	ctions		4	
No	Reaction ^a	Ref.	Solvent ^b	n^{c}	T/	$\delta \Delta G^{\ddagger e}$	$\delta \Delta H^{\ddagger e}$	$\delta \Delta S^{\ddagger f}$	$\Delta G_{\mathrm{o}}^{\ \mathrm{I} g}$	$\Delta H_0^{\ \ \ g}$	$\Delta S_0^{\ddagger h}$
					K ^d	(r)	(r)	(r)			
1.	ArCOOEt	[45]	56.74 wt %	8	353	-1.74	-12.1	-28.8	118.7	81,5	-105
	$+ H_3O^+$		e-w			(0.937)	(0.978)				
		[45]	56 wt %	8	353	-1.67	-3.33	-4.7	118.7	81.5	-105
			a–w			(0.950)	(0.954)				
2.	AcOAr	[46,	56 wt %	5	298	0.94	-2.01	-9.89	99.2	69.1	-101
	$+ H_3O^{+ i}$	47]	a–w			(0.976)	(0.951)	(0.985)			
3.	ArCONH ₂	[32]	60 vol %	4	326	3.17	11.3	24.9	115.4	93.8	-65.3
	$+ H_3O^+$		e-w			(0.998)	(0.957)				
4	ArCONHN=CHPh	[48]	nH· 1 15	6	298	-0.81	-40.4	-133 5	77 1	66 7	-34.8
	$+ H_2 O^{+j}$	[10]	p11. 1.10	Ū	270	(0.999)	(0.995)	(0.995)	,,	00.7	5 1.0
	11,0	[48]	pH: 4.01	6	298	0.95	-36.7	-125.8	89.2	36.5	-177
		[]	P		_, ,	(0.989)	(0.998)	(0.998)			
5.	ArCOOH	[49]	MeOH	16	298	1.33	1.10	~ 0	94.3	61.7	-109
	+ MeOH ₂					(0.464)					
6.	ArCOOH	[50]	C ₆ H ₁₁ OH	15	328	-3.46	-5.96	-7.87	110.7	79.0	-96.7
0.	$+ C_6 H_{11} O H_2^+$		0,111,011	10	020	(0.871)	0.50	1.01	110.7	12.0	2011
7		[51]	toluene	8	208	12.0	0.03	12.5	8/1 1	54.4	100
1.	+ Ph ₂ CN ₂ ^{k}	[51]	tolucile	0	298	(0.000)	-9.03	15.5	04.1	54.4	-100
	Γ II ₂ CN ₂	5513			• • • •	(0.999)	(0.779)				100
8.	PhCOOH	[51]	toluene	8	298	9.59	5.16	-14.8	84.1	54.4	-100
	$+ \operatorname{Ar_2CN_2}^{n}$					(0.996)	(0.919)				
9.	PhNH ₂	[52]	94 vol % e-w	5	329	-8.79	-21.2	-37.4	98.3	21.9	-232
	$+ \text{ArNO}^{l}$		acetate buffer ^m			(0.984)	(0.999)	(0.996)			
10.	ArNH ₂	[52]	94 vol % e-w	5	329	15.7	20.0	12.1	98.3	21.9	-232
	$+ PhNO^{l}$		acetate buffer <i>m</i>			(0.998)	(0.998)	(0.959)			
								. ,			

^{*a*} The σ constants were used in correlations if not otherwise stated.

^b Solvents: (a) acetone, (e) EtOH, (w) water. Values of solvent composition refer to the first solvent.

^c Number of compounds.

^{*d*} The values of ΔG_o^{\ddagger} and $\delta \Delta G^{\ddagger}$ were calculated at the given temperatures. ^{*e*} In kJ mol⁻¹ σ^{-1} unit.

^{*f*} In J mol⁻¹ K⁻¹ σ^{-1} unit.

^g In kJ mol⁻¹ unit.

^h In J mol⁻¹ K⁻¹ unit.

^{*i*} The σ_{o} constants were used in correlations.

^{*j*} Products: ArCONHNH₂ + PhCHO

^k Products: ArCOOCHPh₂ or PhCOOCHAr'₂

^{*l*} Product: PhN=NAr

^m 0.88 M AcOH + 0.25 M AcONa

In the reaction of aromatic carboxylic acids (ArCOOH) with diaryldiazometanes (Ar'₂CN₂) the proton transfer to the C-atom of Ar'₂CN₂ is the rate-determining step, which is promoted by the electron-withdrawing groups in ArCOOH ($\delta \Delta G^{\ddagger} < 0$) and by the electron-donating substituents in Ar'₂CN₂ ($\delta\Delta G^{\ddagger} > 0$, Table 3, Nos. 7,8). The delocalisation of the charge in the ArCOO⁻ intermediate is aided by electron-withdrawing groups ($\delta\Delta S^{\ddagger} > 0$). If Ar'₂CN₂ is the reactant, the electron-donating groups have similar effect on the Ar'₂CHN₂⁺ intermediate ($\delta\Delta S^{\ddagger} < 0$), decreasing the solvation and increasing the value of ΔS^{\ddagger} .

In the reaction of arylamines (ArNH₂) with aromatic nitroso compounds (Ar'NO) acid catalysis takes place mainly by H-bond formation with Ar'NO. The rate-determining step is the nucleophilic attack of the amino-nitrogen atom on the nitroso group (products are ArN=NAr' + H₂O). The reaction is facilitated by the electron-donating groups of ArNH₂ ($\delta\Delta G^{\ddagger} > 0$, Table 3, No. 10) and the electron-withdrawing groups of Ar'NO ($\delta\Delta G^{\ddagger} < 0$, Table 3, No. 9). The electron-donating groups in Ar'NO and the electron-withdrawing groups in ArNH₂ increase the charge separation and the solvation in the reactant state and this way increase the value of ΔS^{\ddagger} (cf, $\delta\Delta S^{\ddagger}$ values for reactions No. 9 and 10 in Table 3, respectively).

3.4 Reactions with Changing Solvation

In some reactions the $\Delta H^{\ddagger} vs. \sigma$ and $\Delta S^{\ddagger} vs. \sigma$ plots have two linear parts with a break at about $\sigma \approx 0$ (Figs. 4 and 5. Note that entropy is plotted in $-T\Delta S^{\ddagger}$ units, to have the plot on the same scale as ΔG^{\ddagger} and ΔH^{\ddagger}). The same type of plots were obtained in every known cases. Here Eqs. (1)–(3) should be applied separately for compounds having electron-donating or electron-withdrawing groups. Some examples are collected in Table 4, *e.g.* the hydrolysis and solvolysis reactions of esters of carboxylic acids (Nos. 1–3) and sulfonic acids (Nos. 4,5) and the thermal decomposition of an urethane (No. 6)



FIGURE 4. ΔG^{\ddagger} vs. σ ($\blacksquare -\blacksquare$), ΔH^{\ddagger} vs. σ ($\bullet -\bullet$), and $-T\Delta S^{\ddagger}$ vs. σ ($\blacktriangle -\blacktriangle$) plots of the alkaline hydrolysis of p-XC₆H₄-C₆H₄COOEt esters (X = p-MeO p-Me, H, p-Cl, p-Br, m-Br, p-NO₂) in 88.7 wt % ethanol-water, [53]. Slopes are given in Table 4. (T = 298 K).



FIGURE 5. $\Delta G^{\ddagger} vs. \sigma$ ($\bullet-\bullet$), $\Delta H^{\ddagger} vs. \sigma$ ($\bullet-\bullet$), and $-T\Delta S^{\ddagger} vs. \sigma$ ($\blacktriangle-\blacktriangle$) plots of the alkaline hydrolysis of p-XC₆H₄SO₃Et esters (X = p-MeO p-Me, H, p-Cl, p-Br, p-NO₂) in 70 vol % dioxane-water, [56]. Slopes are given in Table 4. (T = 323 K).

* *	Tał	ole 4	. Reaction	i constants	of reaction	ons with	changing	solvation
-----	-----	-------	------------	-------------	-------------	----------	----------	-----------

No.	Reaction ^{<i>a</i>}	Ref	Solvent ^b	n ^c	T/		$\sigma \leq 0$			$\sigma \ge 0$	
					К"	a* a	a	a cat f	a * .	a	a . et f
						$\delta \Delta G^* e$	$\delta \Delta H^* e$	$\delta \Delta S^{*J}$	$\delta \Delta G^* e$	$\delta \Delta H^* e$	$\delta \Delta S^{*j}$
						(<i>r</i>)	(<i>r</i>)	(r)	(r)	(<i>r</i>)	(<i>r</i>)
1.	4-Ar-C ₆ H ₄ COOEt	[53]	88.7 wt %	6	298	-3.95	-8.03	-13.6	-3.34	-0.71	8.85
	+ OH -		e-w			(0.993)	(0.994)		(1.000)		(0.963)
2.	ArCOOEt +OH ⁻	[54]	30 vol %	5	298	-11.0	-8.17	9.54	-12.1	-2.21	32.6
		[]	d–w	-	_, ,	(0.998)	(0.998)	(1.000)	(0.995)		(0.966)
			40 vol %	5	298	-12.0	-12.3	-1.24	-12.5	-5.38	24.0
			d–w			(0.999)	(0.995)		(0.994)	(0.995)	(0.993)
			50 vol %	5	298	-12.7	-16.3	-12.4	-13.2	-6.81	21.1
			d–w			(0.999)	(1.000)	(0.989)	(0.994)	(0.959)	(0.996)
3.	$ArCOSQ + OH^{-g}$	[55]	50 vol %	9	293	-11.0	-25.2	-48.1	-11.2	22.9	117
	$Q = 2,4-(NO_2)_2C_6H_3$		d-w			(0.981)	(0.689)	(0.482)	(0.984)	(0.845)	(0.912)
4.	$ArSO_3Et + OH^-$	[56]	70 vol %	6	323	-8.51	-28.5	-61.9	-7.37	-2.14	16.2
			d-w			(0.981)	(0.999)	(0.991)	(1.000)	(0.555)	(0.851)
5.	ArSO ₃ CH ₂ CH=CH ₂	[41]	e	8	303	-10.3	-14.1	-12.6	-8.61	1.61	33.7
	+ EtOH					(0.998)	(0.992)	(0.848)	(0.995)	(0.410)	(0.965)
6.	ArNHCOOCH ₂ Ph	[57]	eta	9	423	-8.72	-48.4	-92.9	-2.62	-5.67	-6.9
	(decomposition) ^h					(0.974)	(0.976)	(0.971)	(0.864)	(0.870)	(0.768)

^{*a*} The σ constants were used in correlations.

^b Solvent: (d) dioxane, (e) ethanol, (eta) ethanolamine (w) water. Values of solvent composition refer to the first solvent.

^d The values of $\delta \Delta G^{\ddagger}$ were calculated at the given temperatures.

^{*e*} In kJ mol⁻¹ σ^{-1} unit.

^{*f*} In J mol⁻¹ K⁻¹ σ^{-1} unit.

^{*g*} Products: $ArCOO^- + 2,4-(NO_2)_2C_6H_3SH$ ^{*h*} Products: $ArN=C=O + PhCH_2OH$

The $\delta\Delta G^{\ddagger}$ reaction constants are only slightly different for compounds having the two types of substituents (Table 4. Nos. 1-5), and in many cases they have the same value within

^c Number of compounds.

the experimental errors. Much greater and systematic changes can be observed for $\delta\Delta H^{\ddagger}$ and $\delta\Delta S^{\ddagger}$. Both electron-withdrawing and electron-donating substituents increase the value of ΔH^{\ddagger} and ΔS^{\ddagger} , or decrease them in a smaller extent than it would be expected on the basis of a linear ΔH^{\ddagger} and ΔS^{\ddagger} vs. σ plot (*e.g.* Table 4, No. 2, 30 vol % dioxane-water). $\delta\Delta S^{\ddagger}$ and $\delta\Delta H^{\ddagger}$ have regularly smaller value for electron-donating substituents ($\sigma < 0$) and higher for electron-withdrawing substituents ($\sigma > 0$).

In conection with the Hammett equation it is well known that if the log (k) vs. σ plot is concave upwards the mechanism is changed with the substituents, and if the given plot is concave downward, then the rate-determining step of the reaction becomes different [4,5,58]. For the ΔG^{\ddagger} vs. σ plots the opposite arrangement is expected, because the sign of ρ and $\delta \Delta G^{\ddagger}$ are different (Eq. 8). In the decomposition of ArNHCOOCH₂Ph (Fig. 6, Table 4, No. 6) the rate-determining step of the reaction and probably also the solvation change with the substituent, because the ΔG^{\ddagger} vs. σ plot is concave upwards and the ΔH^{\ddagger} and ΔS^{\ddagger} vs. σ plots show breaks at $\sigma \approx 0$.



FIGURE 6. $\Delta G^{\ddagger} vs. \sigma (\blacksquare-\blacksquare), \Delta H^{\ddagger} vs. \sigma (\bullet-\bullet), \text{ and } -T\Delta S^{\ddagger} vs. \sigma (\blacktriangle-\blacktriangle) \text{ plots of the decomposition of X-C₆H₄-NHCOOCH₂Ph urethanes (X = p-MeO p-Me, m-Me, H, m-MeO, p-Cl, m-Cl, m-NO₂ p-NO₂) in ethanolamine, [57]. Slopes are given in Table 4. (T = 423 K).$

If ΔG^{\ddagger} gives a linear correlation with the σ constants ($\delta \Delta G^{\ddagger}$ is constant within the experimental errors), but $\delta \Delta H^{\ddagger}$ and $\delta \Delta S^{\ddagger}$ change with them, solvation may become different, due to the electronic effects of the substituents. $\delta \Delta H^{\ddagger}$ and $\delta \Delta S^{\ddagger}$ change together with the solvation because of the external contribution of enthalpy of activation (*cf.* Eq. 10). One may suppose that electron-donating groups increase the polarity of the reactant state and so diminish the difference between the reactant and the transition state, by decreasing the

difference of solvation and increasing the entropy of activation (case 1 in Section 3.1). Electron-withdraving substituent decrease the negative charge of the reactant and transition states and so the difference of the of solvation of the two states, by increasing in this way the value of ΔS^{\ddagger} (case 2 in Section 3.1).

The above explanation suggests that the break of the given ΔH^{\ddagger} and $\Delta S^{\ddagger} vs. \sigma$ plots are not caused by a change in the mechanism or in the rate-determining step of the reaction, but by a change in the solvation. This is regularly not reflected or cause only slight differences in the free energy of activation because of the enthalpy-entropy compensation of the external parts of these activation parameters.

4 CONCLUSIONS

The ΔG^{\ddagger} , ΔH^{\ddagger} and ΔS^{\ddagger} activation parameters (or at least two of them) give good linear correlations with the substituent constants. The $\delta \Delta G^{\ddagger}$, $\delta \Delta H^{\ddagger}$ and $\delta \Delta S^{\ddagger}$ reaction constants derived from activation parameters can be used for the characterization of the effects of substituents on the reactivity and solvation in energy units. $\delta \Delta G^{\ddagger} \approx \delta \Delta H_{int}^{\ddagger}$ is a good approximation of the effect of substituents on bond formation in the reaction. $\delta \Delta S^{\ddagger} \approx \delta \Delta S_{ext}^{\ddagger}$ characterizes the change of solvation by the functional groups bonded to the reactants. $\delta \Delta H^{\ddagger}$ is less informative for the reaction because it has components from both the bond formation and the solvation.

 $\delta \Delta G^{\ddagger}$ can be interpreted in the same way as the ρ constant in the Hammett equation. From the $\delta \Delta S^{\ddagger}$ reaction constant conclusions can be drawn on the change in solvation during the reacton, depending on the substituents in the reactants. Broken $\delta \Delta H^{\ddagger}$ and $\delta \Delta S^{\ddagger} vs. \sigma$ plots refer to a change in solvation with the electronic effect of the substituents. A tentative explanation, based on the solvation of charged species and the reorganisation of the solvent, is also offered for the evaluation of the $\delta \Delta S^{\ddagger}$ reaction constant.

Acknowledgment

The author thanks Professor Árpád Kucsman for fruitful discussions. This work was supported by the Hungarian Scientific Research Foundation (OTKA No. 043639).

5 REFERENCES

- F. Ruff, J. Mol. Struct. (Theochem), 2002, 617, 31-45.
 F. Ruff, J. Mol. Struct. (Theochem), 2003, 625, 111-120.
 L. P. Hammett, *Physical Organic Chemistry*, 2nd. Ed. McGraw-Hill, New York, 1970.
 J. Shorter, *Correlation Analysis of Organic Reactivity*, Wiley, New York, 1982;
- [5] O. Exner, Correlation Analysis of Chemical Data, Plenum Press, New York, 1988; and references therein.

- [6] P.R. Wells, *Linear Free Energy Relationships*, Academic Press, New York, 1968.
- [1] J. E. Leffler and E. Grunwald, Rates and Equilibria of Organic Reactions, Wiley, New York, 1963, Ch. 9.
- [2] O. Exner, Prog. Phys. Org. Chem. 1973, 10, 411-482, and references therein.
- [3] W. Linert and R.F. Jameson, Chem. Soc. Rev. 1989, 18, 477-506.
- [4] W. Linert, Chem. Soc. Rev. 1994, 23, 430-438.
- [5] L. Liu and Q.-X. Guo, Chem. Rev. 2001, 101, 673-695, and references therein.
- [6] L. G. Hepler, W. F. O'Hara, J. Phys. Chem. 1961, 65, 811-814.
- [7] L. G. Hepler, J. Am. Chem. Soc. 1963, 85, 3089-3092.
- [8] J. W. Larson and L. G. Hepler, J. Org. Chem. 1968, 33, 3961-3966.
- [9] E. Grunwald and C. Steel, J. Am. Chem. Soc. 1995, 117, 5687-5692.
- [10] E. Gallicchio, M. M. Kubo and R. M. Levy, J. Am. Chem. Soc. 1998, 120, 4526-4527.
- [11] M. Rekharsky, Y. Inoue, Chem. Rev. 1998, 98, 1875-1917.
- [12] C. Reichardt, Solvent and Solvent Effects in Organic Chemistry, 2nd Ed. Verlag Chemie, Weinheim, 1988.
- [13] J. March, Advanced Organic Chemistry, Wiley, New York, 3rd Ed, pp, 334-338, and references therein.
- [14] M. Farcasiu, J. Chem. Educ. 1975, 52, 76-79.
- [15] E. Tommila and C. N. Hinshelwood, J. Chem. Soc. 1938, 1801-1810.
- [16] E. Tommila, Ann. Acad. Sci. Fennicae, A57, 1941, No. 13, 3-15.
- [17] E. Tommila, A. Nurro, R. Muren, S. Merenheim and E. Vuorinen, Suomen Kemistilehti, 1959, B32, 115-120.
- [18] E. Tommila and L. Ketonen, Suomen Kemistilehti, 1945, B18, 24-30.
- [25] C. K. Ingold and W. S. Nathan, J. Chem. Soc. 1936, 222-227.
- [26] D. P. Evans, J. J. Gordon and H. B. Watson, J. Chem. Soc. 1937, 1430-1435.
- [27] L. S. Prangova, L. S. Efros and I. Ya. Kvitko, Reakts, Sposobnost, Org, Soedin. (Tartu), 1971, 8, 381-388.
- [28] T. C. Püssa and V. M. Nummert, V. A. Palm, Reakts. Sposobnost, Org. Soedin. (Tartu), 1972, 9, 697-702.
- [29] V. Nummert and M. Piirsalu, Org. React. 1995, 29, 109-115.
- [30] V. Nummert and M. Piirsalu, Org. React. 1996, 30, 95-101.
- [31] V. Nummert and M. Piirsalu, J. Chem. Soc., Perkin Trans. 2. 2000, 583-593.
- [32] I. Meloche and K. J. Laidler, J. Am. Chem. Soc. 1951, 73, 1712-1714.
- [33] E. Berliner and L. H. Altschul, J. Am. Chem. Soc. 1952, 74, 4110-4113.
- [34] D. A. Brown and R. F. Hudson, J. Chem. Soc. 1953, 883-887.
- [35] A. Kivinen, Ann. Acad. Sci. Fennicae, A. II. No. 108.1961, 1-71.
- [36] G. E: K. Branch and A. C. Nixon, J. Am. Chem. Soc. 1936, 58, 2499-2504.
- [37] E. G. Williams, C. N. Hinshelwood, J. Chem. Soc. 1934, 1079-1081.
- [38] E. Tommila and T. Vihavainen, Acta Chem Scand. 1968, 22, 3224-3230.
- [39] R. E. Robertson, A. Stein and S. E. Sagamori, Can. J. Chem. 1966, 44, 685-690.
- [40] R. E. Robertson, Can. J. Chem. 1953, 31, 589-594.
- [41] R. V. Sendega, R. V. Vizgert and M. V. Mikhalevitch, *Reakts. Sposobnost, Org. Soedin. (Tartu)*, **1970**, *7*, 512-518.
- [42] D. P. Evans, H. B. Watson and R. Williams, J. Chem. Soc. 1939, 1345-1350.
- [43] Yu. V. Svetkin and M. M. Mursa, Reakts. Sposobnost, Org. Soedin. (Tartu), 1971, 8, 875-881.
- [44] B. V. Ghidaspov, P. A. Ivanov, Yu. A. Povarov and V. F. Selivanov, *Reakts. Sposobnost, Org. Soedin.* (*Tartu*), **1970**, *8*, 49-55.
- [45] E. W. Timm and C. N. Hinshelwood, J. Chem. Soc. 1938, 862-869.
- [46] E. Tommila and M Sippola, Suomen Kemistilehti, 1956, B29, 64-70.
- [47] J. Martinmaa and E. Tommila, Suomen Kemistilehti, 1967, B40, 222-228.
- [48] A. B. Dekelbaum and B. V. Passett, Reakts. Sposobnost, Org. Soedin. (Tartu), 1974, 11, 383-395.
- [49] R. J. Hartman and N. M. Gassmann, J. Am. Chem. Soc. 1940, 62, 1559-1560.
- [50] R. J. Hartman, N. M. Hoogstein and J. A. Moede, J. Am. Chem. Soc. 1944, 66, 1714-1718.
- [51] C. K. Hancock and E. Földváry, J. Org. Chem. 1965, 30, 1180-1184.
- [52] Y. Ogata and Y. Tagaki, J. Am. Chem. Soc. 1958, 80, 3591-3597.
- [53] E. Berliner and L. H. Liu, J. Am. Chem. Soc. 1953, 75, 2417-2420.
- [54] E. Tommila and M.-L.Savolainen, Suomen Kemistilehti, 1967, B40, 212-215.
- [55] L. S. Prangova, I. Ya. Kvitko and L. S. Efros, Reakts. Sposobnost, Org. Soedin. (Tartu), 1971, 8, 371-376.
- [56] R. V. Vizgert and E. K. Savchuk, Zh. Obsch. Khim. 1956, 20, 2261-2270.
- [57] T. Mukaiyama and M. Iwanami, J. Am. Chem. Soc. 1957, 79, 73-76.

[58] F. Ruff and I. G. Csizmadia, Organic Reactions, Equilibria, Kinetics and Mechanism, Elsevier, Amsterdam, 1970, 170-177.

Biography

Author is professor of chemistry at the Eötvös University, Budapest, Hungary. After obtaining a Ph. D. degree in 1965, Dr. Ruff joined the research group of Prof. Á. Kucsman and worked in the field of organic sulfur chemistry and physical organic chemistry. He obtained D.Sc. degree from Hungarian Academy of Sciences in 1991and become full professor in 1992. Dr. Ruff published 95 papers and two books.