Reaction Kinetics

S_N1 Reactions with Inverse Rate Profiles**

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Dedicated to Professor Ingo-Peter Lorenz
on the occasion of his 60th birthday

Solvolysis reactions, which follow the S_N1 (or $D_N + A_N$)[1] mechanism, are usually considered to proceed through slow ionization and fast consecutive trapping of the intermediate carbocations [Eq. (1)].[2]

$$\text{R-X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{R}^+ + \text{X}^- \xrightarrow[k_2]{\text{SolvOH}} \text{R-OSolv} + \text{HX} \qquad (1)$$

Salt effects have been investigated to determine the reversibility of the ionization step.[2] Although Ingold and coworkers had already noted that the relative rates of the two steps may be reversed in the case of highly stabilized carbocations (S_N2C^+),[3] we recently reported the first example of a solvolysis reaction in which the rates of *both* steps can be measured directly.[4] We now report that fast ionization and slow reaction of the carbocation with the solvent is typical for a large variety of S_N1 solvolysis reactions. As we were able to study the two steps of Equation (1) separately, we can now

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[**] We thank the Deutsche Forschungsgemeinschaft (Ma-673/20-1), the Ministry of Science and Technology of the Republic of Croatia (Grant No. 0006451), and the Fonds der Chemischen Industrie for financial support and Professor D. N. Kevill for valuable suggestions.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

DOI: 10.1002/anie.200353468

define the borders between conventional S_N1 mechanisms and those with inverse rate profiles.

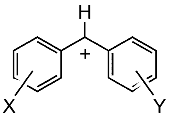
Equation (2) was previously demonstrated to be suitable for describing the rates of the reactions of carbocations R^+ with π, σ, and n nucleophiles (s and N are nucleophile-specific parameters, E is an electrophile-specific parameter).[5–9]

$$\log k(20\,^\circ\mathrm{C}) = s\,(N + E) \tag{2}$$

In view of the tremendous scope of Equation (2) for describing electrophile–nucleophile combinations, we examined whether an analogous approach might be used for describing heterolysis reactions. We now suggest Equation (3), which is not only mathematically analogous to Equation (2).[10]

$$\log k(25\,^\circ\mathrm{C}) = s_\mathrm{f}\,(N_\mathrm{f} + E_\mathrm{f}) \tag{3}$$

The nucleofuge-specific parameters N_f and s_f [Eq. (3)] refer to combinations of leaving groups and solvents, in the same way that the nucleophile-specific parameters N and s [Eq. (2)] are defined for anions and amines with respect to a certain solvent.[8] Electrofugality E_f, like electrophilicity E, is characterized by a single parameter. Furthermore, the same benzhydrylium ions (Scheme 1) that were previously employed as reference electrophiles[6] are now employed as reference electrofuges, which allows us to relate electrophilicity and electrofugality scales with each other in a simple way.[11–13]



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Scheme 1. Benzydrylium ions used as reference electrofuges and electrophiles.

The first-order solvolysis rate constants of benzhydryl bromides, chlorides, trifluoroacetates, and 3,5-dinitrobenzoates in 80% aqueous ethanol, 100% ethanol, 80% aqueous acetone, and 90% aqueous acetone, which were either determined in this work or collected from the literature, are summarized in the Supporting Information. These data were subjected to a least-squares fit on the basis of Equation (3)[14] by using the predefined parameters $E_\mathrm{f}[(4\text{-MeO-}C_6H_4)_2CH^+] = 0$ and $s_\mathrm{f}(\mathrm{Cl}^-/100\%\ \mathrm{EtOH}) = 1$. Figure 1 shows 10 of the 16 correlation lines (four leaving groups in four solvents) and reveals the applicability of Equation (3) for correlating rate constants of heterolysis reactions.

According to Table 1, the nucleofugality parameters obtained by this regression analysis range over eight orders of magnitude, from $N_\mathrm{f} = -3.4$ for 3,5-dinitrobenzoate in 90% aqueous acetone to $N_\mathrm{f} = 4.7$ for bromide in 80% aqueous ethanol. All slope parameters of chlorides, bromides, and 3,5-dinitrobenzoates are close to 1.0. The slope parameter s_f for trifluoroacetate is somewhat smaller in all solvents, indicating a slightly smaller carbocation character of the activated complexes of trifluoroacetate solvolyses.

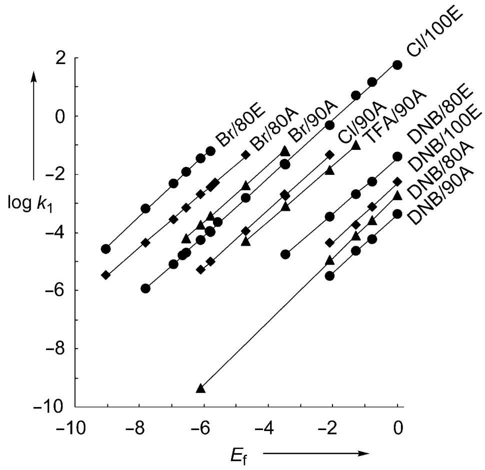


Figure 1. Plot of $\log k_1$(25 °C) versus the electrofugality parameter E_f for the solvolysis reactions of substituted benzhydrylium substrates (TFA = trifluoroacetate, DNB = 3,5-dinitrobenzoate). Only 10 of the 16 linear correlations evaluated are shown to avoid overlapping correlation lines. Mixtures of solvents are given as % v/v. Solvents: A = acetone, E = ethanol, W = water, 80E represents ethanol/water = 80:20, etc.

Table 1: Nucleofugality parameters $(N_\mathrm{f}/s_\mathrm{f})$[a] for four leaving groups in four solvents.[b]

Solvent	Bromide	Chloride	TFA	DNB
80E20W	4.69/1.04	3.36/0.99	1.45/0.81	−1.53/0.95
100E	3.09/0.96	1.87/1.00	0.32/0.87	−2.28/1.02
80A20W	3.26/0.95	1.95/1.01	0.54/0.85	−2.49/1.09
90A10W	2.27/0.98	0.73/0.99	0.22/0.96	−3.36/1.01

[a] As defined by Equation (3). [b] Abbreviations defined in Figure 1.

Table 2: Electrofugality (E_f) and electrophilicity (E) parameters of benzhydrylium ions **1–17**.

	Benzhydrylium ion X =	Y =	E_f[a]	E[b]
1	4-OCH$_3$	4-OCH$_3$	0.00[c]	0.00[c]
2	4-OCH$_3$	4-OC$_6$H$_5$	−0.79	0.61
3	4-OCH$_3$	4-CH$_3$	−1.27	1.48
4	4-OCH$_3$	H	−2.10	2.11
5	4-CH$_3$	4-CH$_3$	−3.48	3.63
6	4-OC$_6$H$_5$	H	−3.49	2.90
7	4-CH$_3$	H	−4.71	4.59
8	3,5-(CH$_3$)$_2$	H	−5.56	–
9	4-OC$_6$H$_5$	4-NO$_2$	−5.66	–
10	4-F	H	−5.81	5.60
11	3-CH$_3$	H	−5.83	–
12	H	H	−6.09	5.90
13	4-Cl	H	−6.55	–
14	4-Br	H	−6.67	–
15	4-Cl	4-Cl	−6.95	6.02
16	3-Cl	H	−7.80	–
17	4-NO$_2$	H	−9.05	–

[a] As defined by Equation (3). [b] As defined by Equation (2), from reference [6]. [c] By definition, see text.

The comparison of the electrofugality parameters E_f with the electrophilicity parameters E (Table 2) shows that in most cases $E_\mathrm{f} \approx -E$, but that the 4-phenoxy- and 4,4′-dichloro-substituted benzhydrylium ions **6** and **15** are poorer electrofuges than expected on the basis of their electrophilicities (see also Figure 2). The reasons for these deviations are presently not clear. Although an inverse relationship between E and E_f was expected, the slope of -1 is accidental and is a consequence of the choice of the predefined slope parameters

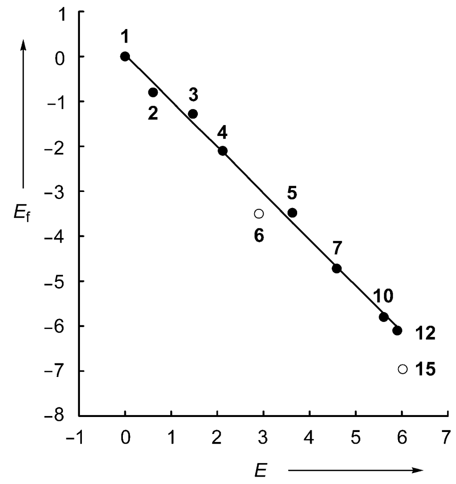
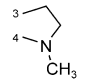
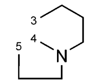


Figure 2. Linear correlation of the electrofugality parameter E_f with the electrophilicity parameter E ($E_f = -1.03\,E + 0.05$, $n = 8$, $r^2 = 0.9962$; electrofuges **6** and **15** are not considered in the correlation).

for nucleophiles ($s = 1.0$ for 2-methyl-1-pentene)[5,6a] and nucleofuges ($s_f = 1.0$ for Cl in 100% EtOH, see above).

To determine the rate constants k_2 of Equation (1), we measured the decay of the UV/Vis absorbances of the stable tetrafluoroborates of the benzhydrylium ions **18**–**24** in aqueous acetone (Table 3) by previously described methods.[8b] The linear correlation in Figure 3 shows that the reactions of carbocations with solvents can also be described by Equation (2), in accord with the work of Ritchie[15] and previous investigations by our group.[8b] It is thus possible to calculate N and s parameters for solvents, as listed in Table 4. Although these parameters were derived from reactions with benzhydrylium ions, they can also be employed to calculate the reaction rates of other types of carbocations.[16]

Table 3: First-order rate constants k_2 for the reactions of the benzhydrylium ions **18**–**24** with aqueous acetone at 20°C.

	Benzhydrylium ion X=Y=	E[a]	k_2 [s^{-1}] 80A20W	90A10W
18	4-NPh(CH_2CF_3)	−3.14	1.90×10^{2}	1.37×10^{2}
19	4-NMe(CH_2CF_3)	−3.85	1.90×10^{1}	1.78×10^{1}
20	4-NPh_2	−4.72	3.07×10^{1}	2.47×10^{1}
21	4-(*N*-morpholino)	−5.53	9.34×10^{-1}	7.75×10^{-1}
22	4-NPhMe	−5.89	1.20	9.40×10^{-1}
23		−8.76	2.08×10^{-3}	1.84×10^{-3}
24		−10.04	1.89×10^{-4}	2.21×10^{-4}

[a] As defined by Equation (2), from reference [6].

Because of the inverse relationship $E_f \approx -E$ shown in Table 2 and Figure 2, one can use the electrophilicity scale E as a common abscissa for plotting the rate constants of electrophile–nucleophile combinations as well as the rate constants for the reverse reactions (heterolyses). The four almost parallel lines (bottom right to top left) in Figure 4 reflect the leaving group abilities $Br^- > Cl^- > CF_3CO_2^- >$ 3,5-dinitrobenzoate (DNB) in 90% aqueous acetone. The ionization rates increase from right to left with increasing stabilization of the carbocations. In contrast, the rate constants for the reactions of carbocations with water increase from left to right as the stabilization of the carbocations

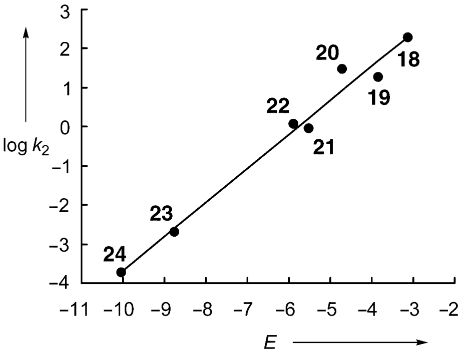


Figure 3. Linear correlation of the first-order rate constants $\log k_2$(20°C) of the reactions of benzhydrylium cations with 80% aqueous acetone versus the electrophilicity parameters E of the corresponding benzhydrylium ions ($\log k = 0.87\,E + 5.03$, $n = 7$, $r^2 = 0.9806$).

Table 4: Nucleophilicity parameters N and s for four solvents, frequently used for kinetic investigations of solvolysis reactions.

Solvent	N[a]	s[a]
90A10W	5.70	0.85
80A20W	5.77	0.87
80E20W	6.68[b]	0.85[b]
100E	7.44[b]	0.90[b]

[a] As defined by Equation (2). [b] From reference [16].

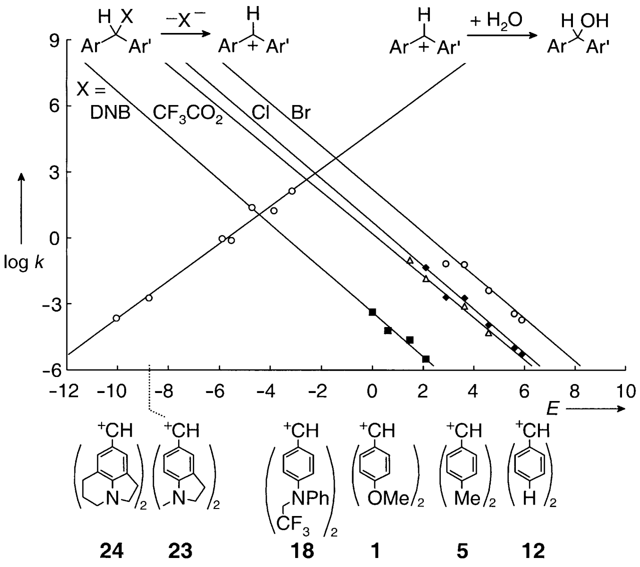


Figure 4. First-order rate constants for the ionization (25°C) and solvent combination (20°C) of benzhydrylium derivatives in 90% aqueous acetone. Abscissa: Electrophilicity parameters E of benzhydrylium ions.

decreases. If we neglect ion-pair recombinations and the fact that the combination rates refer to 20 °C whereas the ionization rates refer to 25 °C, the pseudo-first-order rate constants depicted in Figure 4 are directly comparable. Since the rate constants for ionization and trapping by the solvent are identical at the point of intersection, conventional S_N1 reactions (slow ionization, fast solvent trapping) are found on the right of the intersections, whereas reactions with inverse rate profiles (fast ionization, slow solvent trapping) are found on the left. With the approximations $k_{20^\circ\mathrm{C}} \approx k_{25^\circ\mathrm{C}}$, $E_\mathrm{f} \approx -E$ and s, $s_\mathrm{f} \approx 1$, Equations (2) and (3) can be combined to yield a rough estimate for the point of intersection at $E = (N_\mathrm{f} - N)/2$.

It is clear from this formula as well as from Figure 4 that accumulation of carbocationic intermediates must be expected in numerous solvolysis reactions (even with moderately stabilized carbocations) if solvents of low nucleophilicity (N) and systems with high nucleofugality (N_f) are employed. Figure 4 shows, for example, that alkyl bromide solvolysis reactions in 90 % aqueous acetone will proceed with accumulation of the intermediate carbocations if $E < -2$. In solvents of lower nucleophilicity,[16,17] this border is shifted towards less-stabilized carbocations. Accordingly, the 4,4′-dimethoxy-substituted benzhydryl cation **1** was observed by UV/Vis spectroscopy during the trifluoroethanolysis of the benzhydryl chloride **1**-Cl.[4] More solvent nucleophilicity and nucleofugality parameters are required for the general prediction of the borderline between the two mechanistic alternatives.

Received: December 5, 2003 [Z53468]

Keywords: carbocations · kinetics · linear free energy relationships · nucleophilic substitution · reaction mechanisms · solvent effects

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[10] Since most rate constants for electrophile–nucleophile combinations are reported for a temperature of 20 °C, whereas those for solvolysis reactions usually refer to 25 °C, it was necessary to use different temperatures for Equations (2) and (3).

[11] Because s_f as well as N_f are nucleofuge-specific parameters, one might ask the question as to why Equation (3) is used instead of the mathematically equivalent expression $\log k = N'_\mathrm{f} + s_\mathrm{f} E_\mathrm{f}$ ($N'_\mathrm{f} = s_\mathrm{f} N_\mathrm{f}$), in analogy to most common linear free-energy relationships.[12] As we have repeatedly discussed for Equation (2), it is this special term (with N as the negative intercept on the abscissa (E axis)) that renders nucleophilicity parameters N that are of immediate practical use.[5,13] Whereas the intersections of the correlation lines with the abscissa ($\log k = 0$) are always within or close to the experimental range, intersections with the ordinate (E or $E_\mathrm{f} = 0$) will often be far outside the experimental range. When the intercepts on the ordinate N' or N'_f are considered, even qualitative comparisons of compounds with large differences in reactivity are only possible in combination with the corresponding slope parameters. In contrast, nucleophilicity N and nucleofugality N_f (the intercepts on the abscissa) can *always* be qualitatively discussed without consideration of the slopes s or s_f.

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