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Kinetics of the Solvolyses of Benzhydryl Derivatives: Basis for the Construction of a Comprehensive Nucleofugality Scale

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This and the following article are dedicated to Professor Henning Hopf on the occasion of his 65th birthday

Abstract: A series of 21 benzhydrylium ions (diarylmethylium ions) are proposed as reference electrofuges for the development of a general nucleofugality scale, where nucleofugality refers to a combination of leaving group and solvent. A total of 167 solvolysis rate constants of benzhydrylium tosylates, bromides, chlorides, trifluoroacetates, 3,5-dinitrobenzoates, and 4-nitrobenzoates, two-thirds of which have been determined during this work, were subjected to a least-squares fit according to the correlation equation $\log k_{25\,^\circ C} = s_f(N_f + E_f)$, where s_f and N_f are nucleofuge-specific parameters and E_f is an electrofuge-specific parameter. Although nucleofuges and electrofuges characterized in this way cover more than 12 orders of magnitude, a single set of the parameters, namely s_f, N_f, and E_f, is sufficient to calculate the solvolysis rate constants at 25 °C with an accuracy of ±16%. Because $s_f \approx 1$ for all nucleofuges, that is, leaving group/solvent combinations, studied so far, qualitative discussions of nucleofugality can be based on N_f.

Keywords: carbocations · kinetics · nucleophilic substitution · reaction mechanisms · solvent effects

Introduction

The knowledge of leaving group abilities is of similar importance for the understanding of nucleophilic substitution reactions as the knowledge of nucleophilic properties. While the latter aspect has been the topic of numerous investigations for more than half a century,[1] much less attention has been paid to the quantification of nucleofugalities,[2,3] and most textbooks confine themselves to the qualitative rule that leaving group abilities of X^- increase with increasing acidities of the conjugate acids HX.[4]

It is obvious that a general nucleofugality scale cannot exist. Relative leaving group abilities do not only depend on the mechanism—S_N1 or S_N2—but even within one type of mechanism they depend on substrate and solvent.

Nucleofuge: A leaving group that carries away the bonding electron pair[43] (for example, X^- in Equation (1) below).

Electrofuge: A leaving group that does not carry away the bonding electron pair[43] (for example, R^+ in Equation (1) below, or H^+ in the nitration of benzene by NO_2^+).

Nucleofugality and **electrofugality** are kinetic terms describing leaving group abilities. They are related to the kinetic terms nucleophilicity and electrophilicity and the thermodynamic terms Lewis basicity and Lewis acidity, respectively.

Specifically in this work **nucleofugality** is defined for combinations of leaving groups and solvents, while differential effects of solvents on electrofugality are neglected.

In S_N1-type solvolyses, for example, large leaving groups (tosylates) come off particularly fast from bulky substrates, due to steric repulsions in the ground state (back strain).[5] Furthermore, geminal interactions between the leaving group and other substituents at the reaction center are variable (e.g., anomeric effect)[6] and, therefore, account for the dependence of relative nucleofugalities on the nature of the electrofuges.

The observation that benzhydryl bromides solvolyze about 30 times faster in ethanol than the corresponding chlorides (see below), while the leaving group abilities of bromide and chloride are comparable in trifluoroethanol, illustrate the dependence of relative leaving group abilities on the solvent. Even more pronounced solvent effects on

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relative leaving group abilities are encountered when anionic and neutral leaving groups are compared.[7,8] Thus, a change from ethanol to 20% aqueous ethanol increases the solvolysis rate of 1-adamantyl chloride by a factor of $10^{6.6}$ (at 25 °C),[9] whereas the same variation of solvents accelerated the solvolysis of the 1-adamantyldimethylsulfonium ion by a factor of only 1.7 (at 70.4 °C).[8]

For these reasons, comparisons of leaving group abilities have to refer to certain reference reactions, for example, the rate constants for the reaction in Equation (1) for a given R in a certain solvent at a certain temperature.

$$R{-}X \xrightarrow[k]{EtOH/25\,^{o}C} R^{+} + X^{-} \rightarrow \text{Products} \qquad (1)$$

However, nucleofugality scales derived in this way cover only narrow ranges. For the determination of solvolysis rates, the substrate has to be dissolved in the corresponding medium, and because of the mixing problem, it is very difficult to investigate solvolysis reactions with $k > 10^2\ s^{-1}$. While rate constants of this order of magnitude may be obtained for solvent mixtures by means of stopped-flow techniques, the limitation for pure solvents is even lower. On the other hand, the study of reactions with $k < 10^{-5}\ s^{-1}$ takes a long time, and even when investigations at variable temperature are considered, it is difficult to develop nucleofugality scales based on single reference electrofuges R^+, which exceed ten orders of magnitude. In practice, this range is even smaller, and the core of the well-known nucleofugality scale by Noyce,[2a] which is based on solvolysis rates of 1-phenylethyl derivatives in 80% aqueous ethanol, covers only six orders of magnitude. Noyce extended this scale to 14 orders of magnitude by including substituted 1-phenylethyl derivatives and assuming constant reactivity ratios.

We now report that a comprehensive nucleofugality scale may be constructed by the same procedure that had rendered the most extended nucleophilicity scales presently available.[10]

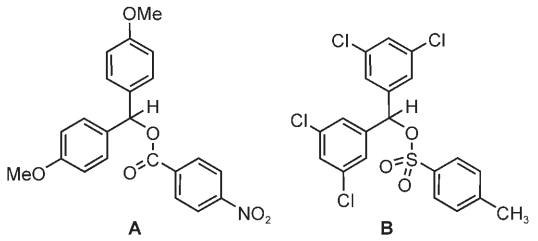
Results and Discussion

By using highly stabilized benzhydrylium ions for characterizing strong nucleophiles and non- or weakly stabilized benzhydrylium ions to characterize weak nucleophiles, the method of overlapping reactivity series had allowed us to quantitatively compare nucleophiles as weak as benzene with nucleophiles as strong as malonate and thiolate ions.[11–16] Equation (2), where s and N are nucleophile-specific parameters and E is an electrophile-specific parameter, presently includes electrophiles and nucleophiles that differ by almost 30 orders of magnitude.

$$\log k = s(N + E) \qquad (2)$$

In analogy to this procedure, which employed benzhydrylium ions as the reference electrophiles, we now use *p*- and *m*-substituted benzhydrylium ions as reference electrofuges. In this way, the steric requirements of the electrofuges are kept constant. Furthermore, the use of benzhydrylium ions as reference electrophiles in electrophile/nucleophile combinations and as reference electrofuges in heterolysis reactions will allow us to elucidate the relationships between the two types of scales.

Combinations of poor leaving groups (weak nucleofuges) with highly stabilized benzhydrylium ions (good electrofuges), for example, **A**, and combinations of good leaving groups (good nucleofuges) with destabilized benzhydrylium ions (poor electrofuges), for example, **B**, give substrates that solvolyze at rates that can be measured conveniently.[17]



Because of the variable solvent effects on the leaving group abilities of different groups X, the nucleofuge-specific parameters s_f and N_f, defined by Equation (3), will generally refer to combinations of leaving groups and solvents, for example, Cl^- in EtOH or dinitrobenzoate in 80% aqueous acetone.

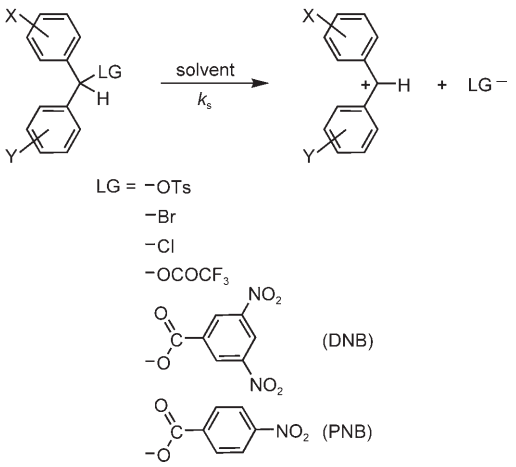
$$\log k_s = s_f(N_f + E_f) \qquad (3)$$

s_f, N_f: *n*ucleo*f*uge-specific parameters,
E_f: *e*lectro*f*uge-specific parameter.

As previously discussed for Equation (2),[10,11] the special types of the linear free-energy relationships [Eq. (2) and Eq. (3)], which define N (or N_f) as the negative intercepts on the abscissa (E or E_f axis), render nucleophilicity parameters N or nucleofugality parameters N_f that are not strongly dependent on the slopes. This is because the intersections of the correlation lines with the abscissa are within or close to the experimental range and never require long-ranging extrapolations, which would be inevitable if nucleophilicity or nucleofugality would be defined as intercepts on the ordinate.

By selecting common leaving groups (LG), for example, *p*-tosylate (OTs), bromide, chloride, trifluoroacetate, 3,5-dinitrobenzoate (DNB), and 4-nitrobenzoate (PNB), and common solvents (ethanol, methanol, 80% aqueous ethanol, 80 and 90% aqueous acetone, and trifluoroethanol) for our investigations (Scheme 1), it is possible to employ a manifold of literature data for the correlations.

Kinetics: All solvolysis rate constants determined during this work were derived from conductivity measurements. Whenever possible, the experiments were carried out at



Scheme 1. Solvolysis reactions of X,Y-substituted benzhydryl derivatives with different leaving groups.

25 °C. If the reactions were too fast or too slow at this temperature, the kinetics were determined at lower or at elevated temperatures, and the Eyring equation was used to extrapolate to 25 °C.

Table 1[18–30] summarizes all solvolysis rate constants k_s (s^{-1}) that were employed to calculate the electrofugality and nucleofugality parameters according to Equation (3). In cases where different solvolysis rate constants for the same substrate under the same conditions are given in the literature, only the k_s that is closest to the calculated value from the correlation equation (k_{calcd}) is given in Table 1. All available rate constants are listed in Table S1 of the Supporting Information.

The solvolysis rate constants given in Table 1 were subjected to a least-squares fit according to Equation (3): $\Sigma\Delta^2$, as defined in Equation (4), was minimized[31] to yield the optimized parameters N_f and s_f (Table 2) as well as E_f (Table 3). In order to link Equation (3) to Equation (2), E_f

Table 1. Solvolysis rate constants of X,Y-substituted benzhydryl derivatives in different solvents (25 °C).

Nucleofuge Leaving group	Solvent[b]	Electrofuge X, Y	k_s [s^{-1}]	k_{calcd} [s^{-1}][a]	Ref.
TsO	90A10W	H	3.01×10^{-1}	2.74×10^{-1}	–
		3-Cl, 4′-Cl	2.60×10^{-3}	3.31×10^{-3}	–
		3-Cl, 3′-Cl	2.05×10^{-4}	1.77×10^{-4}	–
Br	90A10W	4-Me, 4′-Me	6.24×10^{-2}	6.98×10^{-2}	–
		4-OPh	6.86×10^{-2}	5.87×10^{-2}	–
		4-Me	4.08×10^{-3}	4.40×10^{-3}	–
		4-F	3.60×10^{-4}	3.50×10^{-4}	–
		H	1.87×10^{-4}	1.88×10^{-4}	–
		4-Cl	6.45×10^{-5}	6.40×10^{-5}	–
Cl	90A10W	4-Me, 4′-Me	1.83×10^{-3}	1.79×10^{-3}	–
		4-Me	1.11×10^{-4}	1.16×10^{-4}	–
		4-F	9.78×10^{-6}	9.47×10^{-6}	–
		H	5.07×10^{-6}	5.11×10^{-6}	[18]
CF_3CO_2	90A10W	4-OMe	1.44×10^{-2}	1.52×10^{-2}	–
		4-Me, 4′-Me	7.97×10^{-4}	7.12×10^{-4}	–
		4-Me	4.95×10^{-5}	5.26×10^{-5}	–
DNB	90A10W	4-OMe, 4′-OMe	9.42×10^{-4} [c]	9.33×10^{-4}	–
		4-OMe, 4′-OPh	1.01×10^{-4} [c]	1.04×10^{-4}	–
		4-OMe, 4′-Me	2.87×10^{-5} [c]	2.82×10^{-5}	–
TsO	80A20W	3-Cl, 4′-Cl	1.41×10^{-2}	1.45×10^{-2}	–
		3-Cl, 3′-Cl	1.07×10^{-3}	1.01×10^{-3}	–
		3,5-$(Cl)_2$, 3′-Cl	4.05×10^{-5}	4.16×10^{-5}	–
Br	80A20W	4-OPh	2.59×10^{-1}	3.54×10^{-1}	[19a]
		4-Me	4.54×10^{-2}	3.45×10^{-2}	–
		3,5-$(Me)_2$	8.99×10^{-3}	6.62×10^{-3}	[19b]
		4-OPh, 4′-NO_2	5.19×10^{-3}	4.73×10^{-3}	[20]
		4-F	3.71×10^{-3}	3.55×10^{-3}	–
		3-Me	4.08×10^{-3}	3.53×10^{-3}	[19a]
		H	2.03×10^{-3}	2.02×10^{-3}	–
		4-Cl	6.81×10^{-4}	7.69×10^{-4}	–
		4-Br	4.60×10^{-4}	5.58×10^{-4}	[19a]
		4-Cl, 4′-Cl	2.72×10^{-4}	3.09×10^{-4}	–
		3-Cl	4.42×10^{-5}	6.14×10^{-5}	[19a]
		4-NO_2	3.33×10^{-6}	2.67×10^{-6}	[21]
Cl	80A20W	4-Me, 4′-Me	2.79×10^{-2}	2.96×10^{-2}	–
		4-OPh	2.64×10^{-2}	2.55×10^{-2}	–
		4-Me	1.76×10^{-3}	1.74×10^{-3}	–
		3,5-$(Me)_2$	2.25×10^{-4}	2.65×10^{-4}	[22]
		4-OPh, 4′-NO_2	2.05×10^{-4}	1.81×10^{-4}	[20]
		4-F	1.34×10^{-4}	1.30×10^{-4}	–

Table 1. (Continued)

Nucleofuge Leaving group	Solvent[b]	Electrofuge X, Y	k_s [s^{-1}]	k_{calcd} [s^{-1}][a]	Ref.
Cl	80A20W	3-Me	1.22×10^{-4}	1.29×10^{-4}	[22]
		H	6.82×10^{-5}	6.86×10^{-5}	–
		4-Cl	2.31×10^{-5}	2.27×10^{-5}	[23]
		4-Br	1.66×10^{-5}	1.58×10^{-5}	[18]
		4-Cl, 4′-Cl	8.40×10^{-6}	8.03×10^{-6}	[18]
		3-Cl	1.20×10^{-6}	1.27×10^{-6}	[24]
CF_3CO_2	80A20W	4-Me, 4′-Me	3.77×10^{-3}	3.59×10^{-3}	–
		4-Me	2.85×10^{-4}	3.11×10^{-4}	–
		4-F	3.24×10^{-5}	3.32×10^{-5}	–
		H	2.04×10^{-5}	1.91×10^{-5}	[19a]
DNB	80A20W	4-OMe, 4′-OMe	2.99×10^{-3} [c]	3.09×10^{-3}	–
		4-OMe, 4′-OPh	3.34×10^{-4} [c]	3.79×10^{-4}	–
		4-OMe, 4′-Me	1.08×10^{-4} [c]	1.09×10^{-4}	–
		4-OMe	1.85×10^{-5} [c]	1.47×10^{-5}	–
		H	4.39×10^{-10}	4.65×10^{-10}	[19a]
TsO	ethanol	3-Cl	5.57×10^{-2}	5.47×10^{-2}	–
		3-Cl, 4′-Cl	2.83×10^{-2}	2.47×10^{-2}	–
		3-Cl, 3′-Cl	1.83×10^{-3}	2.12×10^{-3}	–
		3,5-$(Cl)_2$, 3′-Cl	9.65×10^{-5}	1.12×10^{-4}	–
		3,5-$(Cl)_2$, 3′,5′-$(Cl)_2$	5.81×10^{-6}	5.06×10^{-6}	–
Br	ethanol	4-Me	2.95×10^{-2}	2.67×10^{-2}	–
		4-OPh, 4′-NO_2	3.55×10^{-3}	3.45×10^{-3}	[20]
		4-F	2.38×10^{-3}	2.56×10^{-3}	–
		H	1.34×10^{-3}	1.44×10^{-3}	–
		4-Cl	5.00×10^{-4}	5.32×10^{-4}	–
		4-Cl, 4′-Cl	2.10×10^{-4}	2.08×10^{-4}	–
		3-Cl, 4′-Cl	1.58×10^{-5}	1.48×10^{-5}	–
Cl	ethanol	4-OMe, 4′-OMe	5.72×10^{1}	7.36×10^{1}	[25]
		4-OMe, 4′-OPh	1.52×10^{1}	1.15×10^{1}	[25]
		4-OMe, 4′-Me	5.14	3.81	[25]
		4-OMe	5.00×10^{-1}	6.44×10^{-1}	[25]
		4-Me, 4′-Me	2.17×10^{-2}	2.48×10^{-2}	–
		4-OPh	2.22×10^{-2}	2.09×10^{-2}	[25]
		4-Me	1.54×10^{-3}	1.55×10^{-3}	–
		3,5-$(Me)_2$	2.25×10^{-4}	2.46×10^{-4}	[26b]
		4-OPh, 4′-NO_2	2.67×10^{-4}	1.69×10^{-4}	[20]
		4-F	1.07×10^{-4}	1.23×10^{-4}	–
		3-Me	1.12×10^{-4}	1.22×10^{-4}	[26a]
		H	5.54×10^{-5}	6.57×10^{-5}	–
		4-Cl	2.06×10^{-5}	2.23×10^{-5}	[26a]
		4-Br	1.61×10^{-5}	1.56×10^{-5}	[26a]
		4-Cl, 4′-Cl	8.07×10^{-6}	8.05×10^{-6}	[26b]
		3-Cl	1.25×10^{-6}	1.33×10^{-6}	[26a]
		3-Cl, 4′-Cl	5.03×10^{-7}	4.58×10^{-7}	[26c]
		4-NO_2	4.24×10^{-8}	4.03×10^{-8}	[26a]
CF_3CO_2	ethanol	4-OMe	2.86×10^{-2}	2.95×10^{-2}	–
		4-Me, 4′-Me	1.89×10^{-3}	1.73×10^{-3}	–
		4-Me	1.40×10^{-4}	1.54×10^{-4}	–
		4-F	1.84×10^{-5}	1.69×10^{-5}	–
		H	9.37×10^{-6}	9.81×10^{-6}	–
DNB	ethanol	4-OMe, 4′-OMe	5.79×10^{-3} [c]	5.64×10^{-3}	–
		4-OMe, 4′-OPh	7.52×10^{-4} [c]	7.23×10^{-4}	–
		4-OMe, 4′-Me	1.88×10^{-4} [c]	2.14×10^{-4}	–
		4-OMe	3.22×10^{-5} [c]	3.01×10^{-5}	–
TsO	80E20W	3-Cl	6.54×10^{-1}	5.99×10^{-1}	–
		3-Cl, 4′-Cl	2.72×10^{-1}	2.60×10^{-1}	–
		3-Cl, 3′-Cl	1.59×10^{-2}	1.96×10^{-2}	–
		3,5-$(Cl)_2$, 3′-Cl	9.13×10^{-4}	8.93×10^{-4}	–
		3,5-$(Cl)_2$, 3′,5′-$(Cl)_2$	3.64×10^{-5}	3.45×10^{-5}	–
Br	80E20W	4-OPh, 4′-NO_2	4.72×10^{-2}	6.75×10^{-2}	[20]
		4-F	5.88×10^{-2}	4.99×10^{-2}	[27]
		H	3.04×10^{-2}	2.78×10^{-2}	[27]
		4-Cl	1.21×10^{-2}	1.01×10^{-2}	–

Table 1. (Continued)

Nucleofuge Leaving group	Solvent[b]	Electrofuge X, Y	k_s [s^{-1}]	k_{calcd} [s^{-1}][a]	Ref.
Br	80E20W	4-Cl, 4′-Cl	4.81×10^{-3}	3.90×10^{-3}	–
		3-Cl	6.48×10^{-4}	7.24×10^{-4}	[27]
		3-Cl, 4′-Cl	2.59×10^{-4}	2.67×10^{-4}	–
		4-NO_2	2.63×10^{-5}	2.74×10^{-5}	[27]
		3-Cl, 3′-Cl	8.99×10^{-6}	1.23×10^{-5}	–
		3,5-$(Cl)_2$, 3′-Cl	3.84×10^{-7}	3.10×10^{-7}	–
Cl	80E20W	4-Me	4.64×10^{-2}	4.26×10^{-2}	–
		3,5-$(Me)_2$	5.84×10^{-3}	6.98×10^{-3}	[22]
		4-OPh, 4′-NO_2	4.26×10^{-3}	4.83×10^{-3}	[20]
		4-F	3.67×10^{-3}	3.52×10^{-3}	–
		3-Me	3.40×10^{-3}	3.50×10^{-3}	[22]
		H	2.04×10^{-3}	1.91×10^{-3}	–
		4-Cl	7.29×10^{-4}	6.60×10^{-4}	–
		4-Cl, 4′-Cl	2.86×10^{-4}	2.43×10^{-4}	–
		3-Cl	3.56×10^{-5}	4.14×10^{-5}	[24]
		3-Cl, 4′-Cl	1.53×10^{-5}	1.45×10^{-5}	–
		4-NO_2	1.30×10^{-6}	1.33×10^{-6}	[24]
CF_3CO_2	80E20W	4-Me, 4′-Me	2.30×10^{-2}	2.23×10^{-2}	–
		4-Me	2.10×10^{-3}	2.28×10^{-3}	–
		4-F	3.27×10^{-4}	2.83×10^{-4}	–
		H	1.55×10^{-4}	1.69×10^{-4}	–
DNB	80E20W	4-OMe, 4′-OMe	3.93×10^{-2}	3.78×10^{-2}	–
		4-OMe, 4′-OPh	5.59×10^{-3}	5.95×10^{-3}	–
		4-OMe, 4′-Me	1.98×10^{-3}	1.99×10^{-3}	–
		4-OMe	3.50×10^{-4}	3.40×10^{-4}	–
PNB	80E20W	4-OMe, 4′-OMe	2.65×10^{-3}	2.12×10^{-3}	–
		4-OMe, 4′-OPh	3.35×10^{-4}	3.69×10^{-4}	–
		4-OMe, 4′-Me	1.11×10^{-4}	1.31×10^{-4}	–
		4-OMe	2.38×10^{-5}	2.46×10^{-5}	–
		4-Me, 4′-Me	1.19×10^{-6}	1.15×10^{-6}	[28]
		H	4.50×10^{-9}	4.32×10^{-9}	[2c]
Br	methanol	4-OPh, 4′-NO_2	4.74×10^{-2}	4.47×10^{-2}	[20]
		4-F	2.92×10^{-2}	3.26×10^{-2}	[27]
		H	1.76×10^{-2}	1.76×10^{-2}	[27]
		3-Cl	4.22×10^{-4}	3.78×10^{-4}	[27]
		4-NO_2	1.14×10^{-5}	1.21×10^{-5}	[27]
Cl	methanol	4-Me	1.98×10^{-2}	2.01×10^{-2}	[24]
		3,5-$(Me)_2$	3.87×10^{-3}	3.29×10^{-3}	[26b]
		4-OPh, 4′-NO_2	2.18×10^{-3}	2.28×10^{-3}	[20]
		4-F	1.38×10^{-3}	1.66×10^{-3}	[26a]
		3-Me	1.74×10^{-3}	1.65×10^{-3}	[26a]
		H	8.33×10^{-4}	8.97×10^{-4}	[29]
		4-Cl	2.97×10^{-4}	3.11×10^{-4}	[26a]
		4-Br	2.39×10^{-4}	2.18×10^{-4}	[26a]
		4-Cl, 4′-Cl	1.15×10^{-4}	1.14×10^{-4}	[26b]
		3-Cl	1.93×10^{-5}	1.94×10^{-5}	[24]
		3-Cl, 4′-Cl	8.21×10^{-6}	6.83×10^{-6}	[26c]
		4-NO_2	5.50×10^{-7}	6.25×10^{-7}	[30]
TsO	TFE[f]	3,5-$(Cl)_2$, 3′-Cl	4.36×10^{-2}	4.36×10^{-2} [d]	-
		3,5-$(Cl)_2$, 3′,5′-$(Cl)_2$	1.07×10^{-3}	1.07×10^{-3} [d]	-
Br	TFE[f]	H	1.10	1.36	–
		4-Cl, 4′-Cl	1.52×10^{-1}	1.97×10^{-1}	–
		3-Cl	6.62×10^{-2}	3.76×10^{-2}	–
		3-Cl, 4′-Cl	1.40×10^{-2}	1.41×10^{-2}	–
		4-NO_2	2.89×10^{-4} [e]	(1.50×10^{-3})	[27]
		3-Cl, 3′-Cl	6.70×10^{-4}	6.82×10^{-4}	–
		3,5-$(Cl)_2$, 3′-Cl	1.99×10^{-5}	1.82×10^{-5}	–
		3,5-$(Cl)_2$, 3′,5′-$(Cl)_2$	3.41×10^{-7}	4.00×10^{-7}	–
Cl	TFE[f]	4-OPh, 4′-NO_2	6.34×10^{-1}	8.60×10^{-1}	[20]
		H	6.17×10^{-1}	3.94×10^{-1}	–
		4-Cl, 4′-Cl	6.40×10^{-2}	6.98×10^{-2}	–
		3-Cl	1.52×10^{-2}	1.58×10^{-2}	–
		3-Cl, 4′-Cl	4.85×10^{-3}	6.59×10^{-3}	–

Table 1. (Continued)

Nucleofuge Leaving group	Solvent[b]	Electrofuge X, Y	k_s [s^{-1}]	k_{calcd} [s^{-1}][a]	Ref.
Cl	TFE[f]	4-NO_2	5.44×10^{-5} [e]	(8.87×10^{-4})	[24]
		3-Cl, 3′-Cl	7.20×10^{-4}	4.38×10^{-4}	–

Table 2. Nucleofugality parameters N_f and s_f for leaving groups (LG) in various solvents.[a]

LG	N_f/s_f					
	90A10W	80A20W	EtOH	80E20W	MeOH	TFE
TsO	5.42/0.89	5.94/0.81	6.05/0.75	7.46/0.79	–	9.82/0.89[b]
Br	2.31/1.00	3.04/0.90	2.97/0.92	4.39/0.94	4.27/0.98	6.20/0.92
Cl	0.69/0.99	1.98/1.02	1.87/1.00[c]	3.28/0.98	2.95/0.98	5.56/0.82
CF_3CO_2	0.12/0.94	0.70/0.88	0.30/0.87	1.46/0.82	–	–
DNB	−2.57/1.18	−2.23/1.13	−2.04/1.10	−1.43/0.99	–	–
PNB	–	–	–	−2.84/0.94	–	–

[a] Mixtures of solvents are given as (v/v); solvents: A = acetone, E = ethanol, TFE = 2,2,2-trifluoroethanol, W = water. [b] Only two solvolysis rate constants were available for a tentative determination of N_f and s_f. [c] The predefined slope parameter for chloride in ethanol ($s_f = 1.00$) was kept constant during the optimization procedure.

for the dianisylcarbenium ion (X, Y = 4-OMe, 4′-OMe) was set to 0.00 (as was E for this carbocation), and s_f for the leaving group/solvent combination chloride/ethanol was set to 1.00. Details of the optimization procedure are given in the Supporting Information.

$$\sum\Delta^2 = \sum(\log k_s - \log k_{calcd})^2 = \sum(\log k_s - s_f(N_f + E_f))^2 \quad (4)$$

The good agreement between experimental and calculated rate constants shown in Table 1 and the graphical representation of some of the linear correlations (Figure 1) show that Equation (3) is indeed well-suited for correlating the solvolysis rate constants listed in Table 1.

Table 3. Electrofugality (E_f) and electrophilicity (E) parameters of X,Y-substituted benzhydryl derivatives.

No.	X	Y	E_f	E[a]
1	4-OCH_3	4-OCH_3	0.00[b]	0.00
2	4-OCH_3	4-OPh	−0.81	0.61
3	4-OCH_3	4-CH_3	−1.29	1.48
4	4-OCH_3	H	−2.06	2.11
5	4-CH_3	4-CH_3	−3.47	3.63
6	4-OPh	H	−3.55	2.90
7	4-CH_3	H	−4.68	4.59
8	3,5-$(CH_3)_2$	H	−5.48	–
9	4-OPh	4-NO_2	−5.64	–
10	4-F	H	−5.78	5.60
11	3-CH_3	H	−5.78	–
12	H	H	−6.05	5.90
13	4-Cl	H	−6.52	–
14	4-Br	H	−6.67	–
15	4-Cl	4-Cl	−6.96	6.02
16	3-Cl	H	−7.74	–
17	3-Cl	4-Cl	−8.21	–
18	4-NO_2	H	−9.26	–
19	3-Cl	3-Cl	−9.63	–
20	3,5-$(Cl)_2$	3-Cl	−11.34	–
21	3,5-$(Cl)_2$	3,5-$(Cl)_2$	−13.14	–

[a] From ref. [10a]. [b] The predefined electrofugality $E_f = 0$ was kept constant during the optimization procedure.

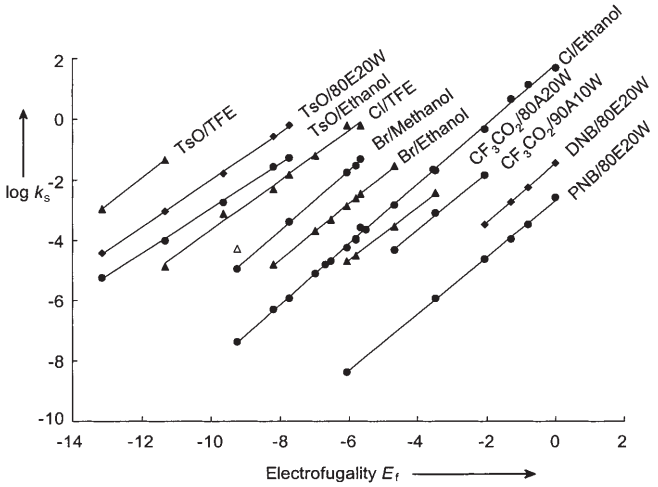


Figure 1. Plot of $\log k_s$ (25 °C, from Table 1) vs E_f (from Table 3) for the solvolysis reactions of X,Y-substituted benzhydryl derivatives in various solvents. Mixtures of solvents are given as (v/v); solvents: W = water, A = acetone, E = ethanol, M = methanol, TFE = 2,2,2-trifluoroethanol. The solvolysis rate constant for the 4-nitrobenzhydryl chloride in TFE (△) was not used for the correlation. In order to avoid overlaps, only 11 of the 26 correlations are shown; all correlation lines are depicted in the Supporting Information.

The similarity of the slopes s_f implies that variation of the carbocations has similar effects on the ionization rates of different esters in different solvents. So far, we have not been able to interpret the small differences in s_f, which are neglected in the following qualitative treatments.

Figure 2 illustrates the increase of nucleofugality from 4-nitrobenzoate to tosylate in 80% aqueous ethanol by more

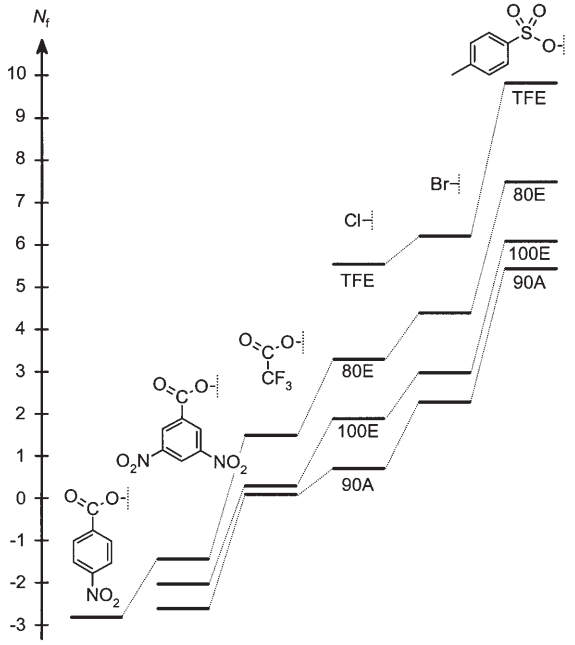


Figure 2. Nucleofugalities N_f for typical leaving groups in the reference solvents used in this work (data from Table 2). Mixtures of solvents are given as (v/v); solvents: 90A = 90% aq. acetone, 80E = 80% aq. ethanol, 100E = ethanol, TFE = 2,2,2-trifluoroethanol.

than ten orders of magnitude. Since, for most leaving groups, the reactivities in 100% ethanol and 80% aqueous acetone are very similar (Tables 1 and 2), the latter parameters could not be included in the graphical presentation of Figure 2. Our method of assigning nucleofugality parameters to combinations of leaving groups and solvents is an alternative to previous approaches that employ different Y scales for different leaving groups.[3c,32–34]

The solvent effect on ionization rates, which is illustrated by N_f in Table 2 and Figure 2, is alternatively illustrated in Figure 3. It can be seen that the solvent dependence is strongest for Cl and decreases in the order Cl > Br ≈ OTs > CF_3CO_2 > DNB. This order correlates qualitatively with the localization of charge in the anionic leaving group, that is, the necessity of anion solvation, and not with the nucleofugality N_f. In agreement with this observation, Bentley and Roberts reported a slope of 0.7 when solvolysis rates of 1-adamantyl trifluoroacetate in a variety of solvents were plotted against the solvolysis rates of 1-adamantyl chloride (25 °C).[35] An analogous correlation between the solvolysis rate constants for 1-adamantyl picrate[36] and 1-adamantyl chloride,[9] with a slope of 0.5, reflects the even better delo-

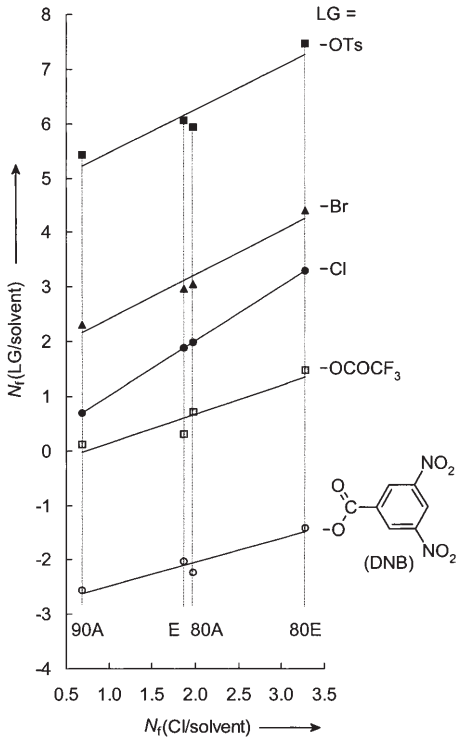


Figure 3. Plot of N_f(LG) vs N_f(Cl) in different solvents. Mixtures of solvents are given as (v/v); solvents: 90A = 90% aq. acetone, 80A = 80% aq. acetone, E = ethanol, 80E = 80% aq. ethanol.

calization of charge density in the picrate leaving group. Because of the small number of data points for the correlations in Figure 3, we refrain from a quantitative discussion of the slopes.

The linear correlation between the electrofugality parameters E_f versus the Hammett σ[37] constants, with a slope of $\rho = -4.39$ (Figure 4), is in agreement with previous analyses by Tsuno and Fujio, who systematically studied the deviations of donor/acceptor-substituted benzhydrylium systems from this correlation.[38]

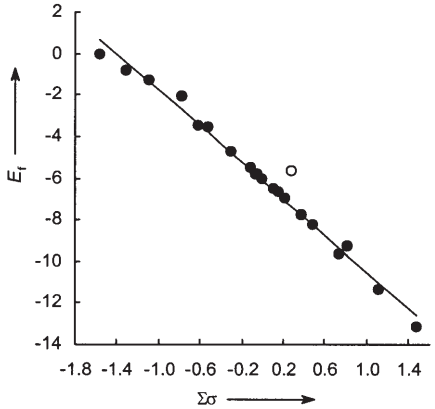


Figure 4. Correlation of the electrofugality parameters E_f of benzhydrylium ions (Table 3) with Hammett σ constants (from ref. [37]). $E_f = -4.39\Sigma\sigma - 6.14$, $n = 20$, $r^2 = 0.9917$; the deviating point of 4-nitro-4′-phenoxybenzhydrylium (○) is not included in the correlation.

A comparison of the electrofugality parameters E_f with the available electrophilicity parameters E (Table 3) shows that in most cases $E_f \approx -E$, but that the 4-phenoxy- and 4,4′-dichloro-substituted benzhydrylium ions are poorer electrofuges than expected on the basis of their electrophilicities (Figure 5). The reason for these deviations is not clear at present. It now has to be examined whether the good correlation between electrofugality E_f and electrophilicity E shown in Figure 5 also holds for other types of carbocations and for systems with $E_f > 0$ and $E_f < -6$.

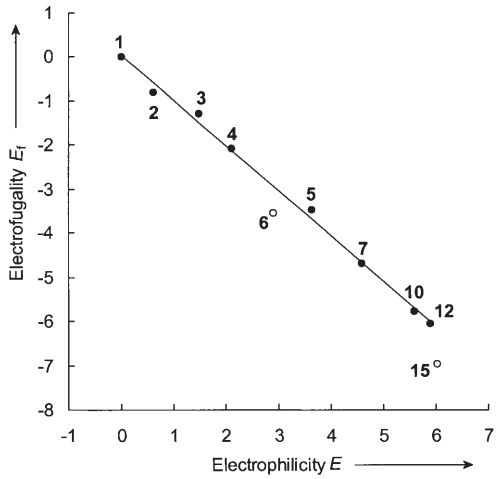


Figure 5. Linear correlation of the electrofugality parameters E_f with the electrophilicity parameters E ($E_f = -1.02E + 0.04$, $n = 8$, $r^2 = 0.9962$; electrofuges **6** and **15** are not considered in the correlation).

Conclusion

The excellent correlations shown in Figure 1 indicate that our goal of developing a basis for a general nucleofugality scale has indeed been achieved. In the succeeding paper, we will show how this method can be employed for characterizing other nucleofuges and electrofuges and for estimating absolute solvolysis rate constants.

Experimental Section

Caution: One or more of the chloro-substituted benzhydryl compounds cause severe irritation of the skin and should be handled with extreme care.

Benzhydryl derivatives: Chloro-substituted benzhydrols were prepared by reactions of substituted benzaldehydes with Grignard reagents, which were obtained from bromoarenes. Treatment of benzhydrol solutions in benzene with 4-nitrobenzoyl chloride or 3,5-dinitrobenzoyl chloride in the presence of pyridine furnished benzhydryl 4-nitrobenzoates and 3,5-dinitrobenzoates, respectively.[39,40] Benzhydryl trifluoroacetates were prepared from benzhydrols and trifluoroacetic anhydride in dry diethyl ether according to the procedure published by Bunton and Hadwick.[41] Benzhydryl chlorides were obtained from the reaction of benzhydrols with thionyl chloride in dichloromethane. Benzhydryl bromides were prepared by treatment of benzhydrols with phosphorus tribromide in dichloromethane. 3,3′,5-Trichlorobenzhydryl tosylate was obtained from 3,3′,5-trichlorobenzhydrol by treatment with *n*-butyllithium at −78 °C and subsequent addition of tosyl chloride. All other benzhydryl tosylates were prepared according to the procedure published by Cheeseman and Poller[42] by addition of silver tosylate to solutions of the benzhydryl chlorides in diethyl ether. Detailed procedures and characterizations of the new compounds are given in the Supporting Information.

Kinetics: Solvolysis rates of benzhydrylium derivatives (Table 1) were monitored by following the increase in the conductivity of the reaction mixtures (conductimeters: WTW LF530 or Tacussel CD 810, Pt electrode: WTW LTA 1/NS). In the cases of 4-nitrobenzoates, 3,5-dinitrobenzoates, and trifluoroacetates, organic bases were added to ionize the weak acids produced by the solvolysis reactions. Details of the kinetic measurements are given in the Supporting Information.

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