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Additivity Rules Using Similarity Models for Chemical Reactivity: Calculation and Interpretation of Electrofugality and Nucleofugality

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Abstract: A recently proposed, multiparameter correlation: log k (25 °C) $= s_f$ $(E_f + N_f)$, where E_f is electrofugality and N_f is nucleofugality, for the substituent and solvent effects on the rate constants for solvolyses of benzhydryl and substituted benzhydryl substrates, is re-evaluated. A new formula ($E_f =$ log $k_{\mathrm{RCl/EtOH/25^\circ C}}$ -1.87), where RCl/EtOH refers to ethanolysis of chlorides, reproduces published values of E_f satisfactorily, avoids multi-parameter optimisations and provides additional values of E_f. From the formula for E_f, it is shown that the term $(s_f \times E_f)$ is compatible with the Hammett–Brown (ρ^+ σ^+) equation for substituent effects. However, the previously published values of N_f do not accurately account for solvent and leaving group effects (e.g. nucleofuge Cl or X), even for benzhydryl solvolyses; alternatively, if the more exact, two-parameter term, $(s_f \times N_f)$ is used, calculated effects are less accurate. A new formula ($N_f = 6.14$ + log $k_{\mathrm{BX/any\ solvent/25^\circ C}}$), where BX refers to solvolysis of the parent benzhydryl as electrofuge, defines improved N_f values for benzhydryl substrates. The new formulae for E_f and N_f are consistent with an assumption that $s_f = 1.00$, and so improved correlations for benzhydryl substrates can be obtained from the additive formula: log $k_{\mathrm{RX/any\ solvent/25^\circ C}} = (E_f + N_f)$. Possible extensions of this approach are also discussed.

Keywords: kinetics · leaving group effects · nucleophilic substitution · solvent effects · substituent effects

Introduction

Structure and reactivity are key aspects of chemistry. For decades, additivity rules have played an important role in organising, storing and correlating experimental data for applications in structure elucidation (e.g. NMR,[1] and UV[2]) and for thermochemical data.[3] Nowadays, such rules can be linked to computer packages for organic structures (e.g. NMR chemical shifts from Chemdraw[4]). Although organic reactivity is a more diverse topic, simple additivity relationships have been observed for the rates of reactions of relatively stable carbocations with nucleophiles,[5] and for nucleophilic additions to organometallic compounds.[6] Similar relationships for many other polar organic and organometallic reactions, have subsequently been devised.[7]

In a further extension of previous investigations,[5–7] a series of benzhydrylium cations ($\mathrm{ArAr'CH^+}$) have recently been proposed as reference electrofuges for the development of a general nucleofugality scale.[8] Based on Equation (1), an electrofuge is defined as a leaving group that does not depart with the bonding electrons, and electrofugality (E_f) mainly depends on the ability of the aryl groups to stabilise the cation; nucleofugality (N_f) is a measure of the reactivity of the leaving group ($\mathrm{X^-}$) and it depends on the solvent and leaving group.

$$\mathrm{ArAr'CHCX} \rightarrow \mathrm{ArAr'CH^+} + \mathrm{X^-} \qquad (1)$$

A statistical analysis using Equation (2), in which log k refers to the rate constant for solvolysis, gave many optimised values of E_f, N_f and a slope/sensitivity term (s_f).[8]

$$\log k\ (25\,^\circ\mathrm{C}) = s_f\ (E_f + N_f) \qquad (2)$$

Solvolytic reactions have played a major role in the critical assessment of many aspects of mechanism and reactivity in organic chemistry.[9] We recently compared simple linear free-energy relationships, using one parameter for solvent effects on reactivity, with those based on multi-parameter correlations (MPCs);[10] a tendency to underestimate the errors in MPC was illustrated,[10] and the organic chemists' concept of similarity and analogy were applied. Equation

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(2) is an unusual type of MPC, because only one freely adjustable parameter (s_f) accommodates the response of log k to both E_f and N_f . In addition, s_f is the most likely parameter in which residual errors can be "placed"; unlike other equations for correlating organic reactivity, Equation (2) has no "hidden" term for residual errors.[10]

Also in the previous work,[8] a large amount of experimental data was needed to evaluate the parameters. Values of E_f and N_f were corrected to account for the s_f term, but the s_f term was then set to unity (so, in effect it was excluded) in predictive applications of Equation (2). A simpler, more transparent and consistent approach, based on additivity, is now suggested.

As Equation (2) includes both solvent and substituent effects on solvolytic reactivity, comparisons with simpler equations are important. Comparisons were made briefly with the Hammett–Brown[11a,b] ($\rho^+\sigma^+$) treatments of substituent effects,[8a] and various Grunwald–Winstein (mY)[12] correlations for solvent effects were shown.[8b] Connections between Equation (2) and simpler equations[11,12] will now be explored further.

New equations defining E_f and N_f are now proposed, consistent with simple additivity relationships to calculate log k. These allow: 1) convenient extension of the E_f scale by simple calculation; 2) a derivation showing direct links between E_f and σ^+, providing an interpretation of E_f values; 3) a link to published σ^+correlations for benzhydryl solvolyses, showing that some of the published N_f values[8] contain systematic errors; 4) interpretations of N_f and s_f values.

Results and Discussion

Kinetic data were assembled directly from published rate constants, as described in the footnotes to Tables. All statistical calculations were performed by using Microsoft Excel. In addition to typically quoted statistical results, Excel shows the upper and lower limits for the values of optimised variables (slopes/coefficients and intercepts) for a 95% confidence level; these are typically about 2–3 times greater than the standard errors.[10] Even then, errors are underestimated, because it is assumed that there are no errors in the independent/explanatory variables (e.g. E_f); since E_f was obtained by MPC,[8] there will be significant errors (e.g. see Table 1).

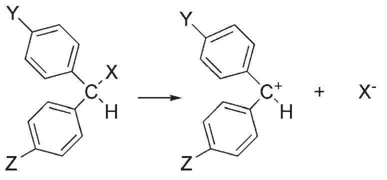
Definition of electrofugality (E_f): The key reference point (E_f=0) for Equation (2) is the electrofuge (Ar_2CH^+ where Ar=4-methoxyphenyl), and s_f=1.00 is assumed to correlate data for solvolyses of all benzhydryl chlorides (ArAr′CHCl) in ethanol at 25°C.[8a] Each benzhydryl electrofuge is assumed to have a unique value of E_f, and each pair of solvent and leaving group was assumed to have unique values of s_f and N_f. An MPC, in which 167 rate constants were fitted to Equation (2), gave 20 values of E_f (input parameter on the x axis), as well as 25 values of slopes (s_f) and 26 values of intercepts ($s_f \times N_f$).[8a]

Table 1. Values of Electrofugality (E_f) from Equation (3) and from multi-parameter correlations (MPC) for 3- or 4-Z-monosubstituted benzhydryl cations (**2**, Y=H).

Z	E_f [Eq. (3)][a]	E_f MPC[b]	E_f MPC[c]
4-Me	−4.78[d]	−4.71[d]	−4.68[d]
4-F	−5.90[e]	−5.81[e]	−5.78[e]
3-Me	−5.82	−5.83	−5.78
H	−6.14	−6.09	−6.05
4-Cl	−6.55	−6.55	−6.52
4-Br	−6.66	−6.67	−6.67
3-Cl	−7.77	−7.80	−7.74
4-NO_2	−9.24	−9.05[f]	−9.26[g]

[a] Kinetic data from ref. [14]; additional values of E_f are: 3-OMe (−6.16), 3-F (−7.63), 3-Br (−7.77), 3-CN (−8.67), 4-CN (−8.88), 3-NO_2 (−8.82). [b] Ref. [8c]. [c] Ref. [8a]. [d] The earlier experimental value of $1.23\times10^{-3}\,s^{-1}$ (ref. [14]) is supported by three other values (ref. [15]), but a significantly higher value (1.54) was input for MPC (ref. [8a]). [e] The earlier experimental value is $9.3\times10^{-5}\,s^{-1}$ (ref. [14]), but a significantly higher, newer value (10.7) was input for MPC (ref. [8a]). [f] Based on only two values for rate constants for 4-nitrobenzhydryl solvolyses (bromides in 80% ethanol and 80% acetone), that is, excluding the value for the chloride in ethanol (ref. [14]). [g] Based on four values for rate constants for 4-nitrobenzhydryl solvolyses, including the value for the chloride in ethanol used for Equation (3).

The important experimental rate constant for solvolysis of 4,4′-dimethoxybenzhydryl chloride (**1**, Y=Z=OMe, X=Cl) in ethanol at 25°C is very difficult to measure, and the published value (log k=1.76[13a,b]) was extrapolated from data at lower temperatures, and reported only in a thesis;[13a] the kinetic experiments were carried out at relatively high substrate concentrations (10^{-2} M),[13a] with no allowance for the possibility of common ion rate depression. A higher value of log k=1.87 was obtained from the MPC [Eq. (2)].[8a] Recent direct measurements of cation reactivities show that cation **2** (Y=Z=OMe) reacts faster with 10^{-2} M chloride ion in ethanol at 20°C than with solvent alone.[13c]



1 **2**

To simplify the following discussion, the value of 1.87 from MPCs will be used. However, judging by σ^+ correlations (discussed later), even the higher value of 1.87 may still be too low. As the published values[8] of E_f (as well as s_f and N_f) are a complex function of the whole set of input data, the value of every parameter would be affected by revision of any input data: for example, when the input data in the preliminary communication[8c] were extended,[8a] 7 of the 8 values for mono-substituted substrates changed (Table 1).

Throughout the following discussion, equations are proposed to reproduce the values obtained using the MPC.

These equations are designed to provide interpretations of, and further insights into, the parameters obtained by the MPC. As the MPC involves over 200 interdependent numbers, exact interpretations of the data obtained by the MPC are virtually impossible. Even the definition that $s_f = 1.00$ for chlorides cannot be shown as an exact equation, because 1.00 refers to the slope of a correlation (with associated errors) of log k with E_f. The main supporting argument for the interpretations given below is that the equations are shown to reproduce (within relatively small errors) the numerical values of the parameters in the MPC.

A precise definition of E_f based on solvolyses of chlorides (RCl) in ethanol at 25 °C can be obtained by rearranging Equation (2): substituting $s_f = 1.00$ and $(s_f \times N_f) = 1.87$, gives Equation (3). Then, instead of affecting all values of E_f and N_f, any future revision of the rate constant for ethanolysis of 4,4′-dimethoxybenzhydryl chloride (**1**, Y = Z = OMe, X = Cl), could most simply be handled by a revision of the value of E_f for the 4,4′-dimethoxybenzhydryl cation (**2**, Y = Z = OMe). No other values of E_f, nor the values of N_f proposed here (see later), would be affected.

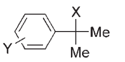
$$E_f = \log k_{\mathrm{RCl/EtOH}}\ (25\,^{\circ}\mathrm{C}) - 1.87 \qquad (3)$$

Values of E_f, calculated by using Equation (3) and data from one reliable source,[14] compare well with values obtained by multi-parameter optimisations (Table 1); significant discrepancies (>0.1) in the values can be explained by different choices of input data (Table 1, footnotes d–g). Importantly, Equation (3) refers to any substrate (RCl), where R can be any group (e.g. alkyl or aryl), so new values of E_f can be readily obtained (e.g. see Table 1, footnote a).

A statistical approach to the selection of parameters from various model reactions may be preferred to the use of data from "reliable" sources for a well-defined model reaction. Selection of "reliable" data may be considered either negatively (perhaps too subjective), or positively (based on experience); for example, one result (for **1**, Z = OMe, Y = H, X = Cl) has not been included in Equation (3) because a high rate constant was obtained titrimetrically at one low temperature (−31.6 °C).[14]

However, statistical treatments using MPC are not necessarily more reliable than using data "subjectively",[10,16] and the rejection of experimental data is not unique to the "subjective approach". Whilst the published paper[8a] shows 167 rate constants included in the correlation (Equation (2)), the associated supporting information[15] shows that 90 data points were eventually rejected, following several rounds of optimisations. Over two thirds of the pruned 167 point data set[8a] are from the authors' own laboratory, and their results are not always in agreement with others (e.g. for 4-methylbenzhydryl chloride (**1**, Z = Me, Y = H, X = Cl) in ethanol, the selected value ($k = 1.54 \times 10^{-3}\,\mathrm{s}^{-1}$) differs by over 20% from four independent values in very close agreement ($10^3 k = 1.27$, 1.24, 1.23 and 1.23), although there is also a much lower value of 0.72.[15] A simple alternative procedure is to average results from various sources, but this leads to equal weightings of data independent of source. As the main sources of error are systematic (e.g. solvent batch, especially traces of water in alcohols, and temperature calibration), selection of data from one source can be justified. Alternatively, a fully statistical approach would allow an input of all of the data, and could also provide estimates of random errors.

If it is assumed that Equation (3) provides an exact definition of E_f for any substrate, a direct link with the $\rho^+\sigma^+$ equation can be established (see Supporting Information; Section S1). After separating the $(s_f \times E_f)$ term, it is shown that s_f refers to the solvent effect on a substituent effect; s_f is close to 1.00 for mono-substituted benzhydryl chlorides (**1**, X = Cl, Y = H)[14] and for a range of substituted cumyl chlorides (**3**, X = Cl),[11a] the reference compounds for the σ^+scale.



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Solvent and leaving group effects—the correction terms N_f or ($s_f \times N_f$): Values of $(s_f \times N_f)$ are obtained from Equation (2) when $E_f = 0$; that is, the electrofuge ($\mathrm{Ar_2CH^+}$ where Ar = 4-methoxyphenyl) anchors one end of the range of data. Equation (2), like various other MPCs for solvent effects,[10] has an important reference point at an extreme end of the correlation, where the availability of supporting experimental data is limited. In contrast, the reference points for simpler $\rho^+\sigma^+$ and mY treatments (e.g. $\sigma^+ = 0$ for H,[11] and $Y = 0$ for 80% ethanol/water[12]) are well-defined experimentally, and are usually well within the range of data to be correlated; consequently errors, especially those from non-linear correlations, are reduced.

Substituting $E_f = 0$ into Equation (2) gives Equation (4), where $(s_f \times N_f)$ refers to solvolyses of 4,4′-dimethoxybenzhydryl substrates (**1**, Y = Z = OMe).

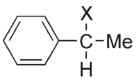
$$\log k\ (25\,^{\circ}\mathrm{C}) = (s_f \times N_f) \text{ for solvolyses of } (\mathbf{1}, \mathrm{Y} = \mathrm{Z} = \mathrm{OMe}) \qquad (4)$$

Most of the experimental data for solvolyses of 4,4′-dimethoxybenzhydryl substrates (**1**, Y = Z = OMe) were unavailable; of the 13 values required, as few as 5 may be reliable (X = dinitrobenzoate in four solvents and X = trifluoroacetate in ethanol), and others were obtained by extrapolations.[8a] Although Equation (4) is derived exactly from Equation (2), inconsistencies in the results can be seen by subtracting pairs of values of $(s_f \times N_f)$, which give unreliable predictions for leaving group effects (see Table S1 in the Supporting Information) and solvent effects (see Table S2 in the Supporting Information) for solvolyses of (**1**, Y = Z = OMe).

To reduce the extrapolation errors, published values of N_f were calculated[8] from Equation (4) by dividing the intercept term $(s_f \times N_f)$ by the slope s_f, obtained for each combination of solvent and leaving group (s_f varies from 0.75 for tosylates in ethanol to 1.18 for dinitrobenzoates in 90% acetone). In effect, values of N_f are obtained from the difference between two values of E_f on the x axis, when log k =

0.[7a] In typical measures of leaving group effects,[17] the reactivities of a common organic moiety attached to two different leaving groups are compared directly. However, when s_f differs from 1.00, leaving group effects from values of N_f refer to two different organic moieties, as discussed in the Supporting Information (Section S2). Values of N_f give more realistic predictions of solvent effects (see Table S1 in the Supporting Information) and leaving group effects (see Table S2 in the Supporting Information) than ($s_f \times N_f$), but are still not reliable.

The predicted log k (TFA/DNB) rate ratios of <3 (ref. [8a] and Table S1 in the Supporting Information) are two orders of magnitude less than previous estimates based on 1-phenylethyl solvolyses (**4**).[17] Also, the predicted[8a] values of log k (Cl/TFA) of 0.57–1.82 (see Table S1 in the Supporting Information) are large compared with data for 1-phenylethyl (**4**),[17] *tert*-butyl (**5**) and 1-adamantyl (**6**) solvolyses;[18] at 75 °C, 1-phenylethyl trifluoroacetate in 80 % ethanol shows the opposite trend, as it is 2.5 times *more reactive* than the chloride.[17] Unusual results for trifluoroacetates are discussed further in the Supporting Information (see Section S2).



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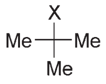

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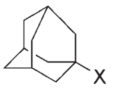

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Two equations were investigated to try to define more transparent and reliable values of N_f. Benzhydryl chloride (BCl) in ethanol was selected as a new anchor point for the N_f scale (log $k_{\mathrm{EtOH/25^\circ C}} = -4.27$[14]) to provide a more accessible range of data; N_f was then obtained from Equation (5), using kinetic data for other benzhydryl solvolyses (BX/any solvent) to provide the correction term (i.e. N_f) for solvent and leaving group effects. Similarly, if 1-phenylethyl chloride (**4**, X=Cl, log $k_{\mathrm{EtOH/25^\circ C}} = -6.67$[19]) is selected, N_f is then obtained from Equation (6), using kinetic data for other 1-phenylethyl solvolyses (**4**, coded 1-PEX/any solvent).

$$\begin{aligned} N_f &= 1.87 \pm \text{correction terms} \\ &= 1.87 + \log k_{\mathrm{BX/any\ solvent}} - \log k_{\mathrm{BCl/EtOH}} \qquad (5) \\ &= 6.14 + \log k_{\mathrm{BX/any\ solvent/25\,^\circ C}} \end{aligned}$$

$$N_f = 1.87 - (-6.67) + \log k_{\mathrm{1-PEX/any\ solvent}} \qquad (6)$$

Equations (5) and (6) are designed to be consistent with the proposal[8b] that $s_f = 1.00$ in Equation (2) is a reasonable approximation. This simplified and general "semi-quantitative" approach[8b] is abbreviated SQA in the following discussion. Logarithms of solvolysis rate constants for any substrate (RX) are then obtained[8b] simply by adding values of two parameters (E_f and N_f). When values of N_f from Equations (5) or (6) are added to the new values of E_f (Equation (3), Table 1), the questionable ethanolysis rate constant for solvolyses of (**1**, Y=Z=OMe, X=Cl) cancels out (log $k = 1.87$, discussed above).

Values of N_f, obtained in four different ways, are compared in Table 2, and there is satisfactory agreement for tosylates, chlorides, and bromides. Agreement for carboxylate leaving groups is less satisfactory, and some of the data required for Equations 5 and 6 are not reliable because of extrapolation errors. The most anomalous results are for trifluoroacetate, and an additional five values of N_f (including four carboxylate values) from the MPC are omitted from Table 2, because data for neither Equations (5) nor (6) were available. Also, Equation (5) shows that a plot of N_f versus various Y values will be virtually the same as a plot of log k for benzhydryl substrates versus Y, as observed in Figures 2 and 3 of reference [8b].

Table 2. Values of Nucleofugality (N_f) from Equations (5) and (6) and from multi-parameter correlations (MPC) for combinations of leaving groups (X) and solvents.

X[a]	solvent[b]	N_f [Eq. (5)][c]	N_f [Eq. (6)]	N_f MPC[d]	N_f MPC[e]
OTs	90A	5.62			5.42
	80A		6.43[f]		5.94
	EtOH	6.30[f]	6.42[f]		6.05
	80E	7.30	7.67[f]		7.46
Br	90A	2.41		2.27	2.31
	80A	3.45		3.26	3.04
	EtOH	3.27	3.18[g]	3.09	2.97
	80E	4.62	5.09[g]	4.69	4.39
	MeOH	4.39	4.25[g]		4.27
	TFE	6.18			6.20
Cl	90A	0.85		0.73	0.69
	80A	1.97	2.37[h]	1.95	1.98
	EtOH	1.87[i]	1.87[i]	1.87[i]	1.87[i]
	80E	3.45	3.53[j]	3.36	3.28
	MeOH	3.06	2.89[j]		2.95
	TFE	5.93			5.56
CF_3CO_2	80A	1.45		0.54	0.70
	EtOH	1.11		0.32	0.30
	80E	2.33	3.9[k]	1.45	1.46
DNB	80A	−3.2[l]		−2.49	−2.23
PNB	80E	−2.2	−1.7[m]		−2.84

[a] Codes for leaving groups (X) are: DNB=2,4-dinitrobenzoate; PNB=4-nitrobenzoate. [b] Solvent codes are: A= % v/v acetone/water; E= % v/v ethanol/water; TFE=2,2,2-trifluoroethanol. [c] Kinetic data from ref. [8a], except where stated otherwise. [d] MPC (ref. [8c]). [e] MPC (ref. [8a]). [f] Calculated from kinetic data for the corresponding mesylates (refs. [17b,20]) and OTs/OMs rate ratios (ref. [12b]). [g] Kinetic data from ref. [21]. [h] Kinetic data from ref. [22]; this data point was plotted incorrectly in Figure 1 of ref. [23], and the correct value of log (k/k_0) of −1.16 fits the correlation with data for 4-methoxybenzyl chloride as similarity model. [i] Anchor point. [j] Kinetic data from ref. [19]. [k] Approximate value because kinetic data from ref. [17a] refer to 75 °C, and the rate ratios are temperature dependent. [l] Based on questionable data; it was calculated from experimental data at higher temperatures, and it deviates from a σ^+ plot (see Table S3, footnote f). [m] Approximate value based on a PNB/Cl rate ratio of 6×10^{-6} at 75 °C (ref. [17]).

The discrepancies between N_f values from Equation (5) and from MPC are explained mainly by the s_f parameter. If $s_f = 1.00$ is assumed (Equation (2), combining the N_f value from Equation (5) with E_f from Equation (3) gives (by design) the correct rate constant for (parent) benzhydryl solvolyses; in contrast, when N_f and E_f values from MPC are used, a suitable value of s_f is obtained to improve the accuracy of the calculated rate constant. Consequently, N_f values from Equation (5) are more closely compatible with the convenient assumption that $s_f = 1.00$.

If it is assumed that $s_f = 1.00$, as proposed for the SQA,[8b] then the difference in the N_f values from Equation (5) and from MPC (Table 2) is due mainly to an error in the SQA, and partly due to the small differences between E_f values from Equation (3) and from MPC (Table 1). Among the data in Table 2, the largest error in SQA is probably the result for benzhydryl trifluoroacetate in 80E ($\Delta\log k = 0.87$). The larger discrepancy for DNB in 80A is probably due partly to experimental errors (for evidence that this is a "rogue" data point, see Table 2, footnote l and Table S3, footnote f). It is appropriate here to reiterate that the MPC approach does avoid undue reliance on individual, potentially "rogue", data points.

Deviations from $s_f = 1.00$ are explained in Section S3 in the Supporting Information by the known complexities[11c] of solvolyses of substituted benzhydryl chlorides. Also, there may be a significant error in the experimental rate constant for solvolyses of **1** (Y = Z = OMe, X = Cl),[13] which is the key anchor point for the MPC, as $E_f = 0$ is assumed for the reference electrofuge (**2**, Y = Z = OMe). If curvature of the plot (see Figure 4 in reference [8a]) of E_f versus $\Sigma\sigma^+$ for electron-rich substrates is ignored, by analogy with a more extensive data set,[11c] an E_f of 0.88 is calculated from the slope and intercept. A steeper slope (giving a higher value of E_f) could be justified from the more precise correlation for symmetrically substituted benzhydryl compounds.[11c]

A comparison of the published $\Sigma\sigma^+$ plot[11c] with data from Equation (2)[8a] further illustrates the failure of multiparameter correlations to detect novel effects, whilst at the same time achieving moderately good correlations.[23]

Extension to other solvolyses: The scope of the SQA[8b] can now be predicted. Since published values of E_f are reproduced within (± 0.1) by Equation (3) (Table 1), and most values of N_f are close to those predicted by Equation (5) (Table 2), Equation (2) can be written as Equation (7) (if $s_f = 1.00$), where all rate constants refer to 25 °C.

$$\begin{aligned}&\log k_{\mathrm{RX/any\ solvent}} - \log k_{\mathrm{RCl/EtOH}}\\&= \log k_{\mathrm{BX/any\ solvent}} - \log k_{\mathrm{BCl/EtOH}}\end{aligned} \tag{7}$$

According to Equation (3), E_f is simply a disguised form of the rate constants for ethanolyses of chlorides. Equation (7) shows that identical corrections for changes in solvent (from ethanol) and/or leaving group (from chloride) are applied to an unknown substrate (RX) and to the reference electrofuge (benzhydryl). In effect, Equation (7) is one of many possible examples of a similarity model,[12d] and by implication (with approximations noted above), so is SQA (Equation 2, with $s_f = 1.00$).[8b] These equations will have the similar defects, and fail to take account of: 1) differences in solvation between alkyl and aryl groups;[12c,d,24] 2) the lower sensitivity to changes in solvent polarity due to delocalized transition states involving neighbouring group or nucleophilic solvent participation;[25] 3) steric differences between secondary and tertiary sulfonates.[17b,26]

Relaxing the condition that $s_f = 1.00$ allows more flexibility, and a s_f term then appears in 3 of the 4 terms in Equation (7); even then, the equation still could not account for unrelated changes in slopes and intercepts, observed in applications of the Grunwald-Winstein equation.[12,24] To retain the attractive simplicity of calculating solvolysis rate constants simply by adding two numbers together,[8b] one extra set of values (N'_f, Equation (9), analogous to Equations (5) and (6)) based on solvolyses of *tert*-butyl chloride can be defined for use with substrates more similar to *tert*-alkyl than secondary benzhydryl.

Log k for *tert*-butyl chloride in any solvent is given by Equation (8), where Y refers to the original Y values.[12a] Based on the derivation of Equation 5, N'_f is given in Equation (9), where the log k(X/Cl) term is a leaving group correction. Logarithms of rate constants for a *tert*-alkyl substrate would then be given by Equation (10).

$$\log k_{t\mathrm{BuCl/any\ solvent}} = \log k_{t\mathrm{BuCl/EtOH}} - Y_{\mathrm{EtOH}} + Y_{\mathrm{any\ solvent}} \tag{8}$$

$$N'_f = 3.90 + Y_{\mathrm{any\ solvent}} + \log k(\mathrm{X/Cl}) \tag{9}$$

$$\log k_{tert\text{-}\mathrm{alkylX/any\ solvent}=}E_f + N'_f \tag{10}$$

The authors[8b] alternative SQA was to calculate individual values of E_f from Equation (2), using up to ten known values of log k in other solvents and appropriate values of s_f and N_f; for *t*BuX, values of E_f varied from −9.2 for *t*BuCl in MeOH to −7.2 for *t*BuBr in 90 % acetone: that is, the uncertainty in E_f, corresponding to 100-fold in rate, is very large for an input parameter. The uncertainty has arisen from calculations in solvents (EtOH, 80 % ethanol/water, MeOH, 90 % and 80 % acetone/water) having a relatively small range in Y values (only 2, that is, 100-fold in rate); consequently, even larger errors are possible. In the absence of a clear definition of E_f, the SQA allows the selection of a suitable choice of E_f to improve "predictions". Therefore, SQA "works" mainly because E_f is a disguised form of log k (with or without the assumption that $s_f = 1.00$). Overall, many accurately known experimental rate constants may be used to calculate an average value of E_f, which may be used later in SQA to "predict" a less reliable value for one of the known experimental results.

A questionable implication of Equations (5)–(9) is that electrofugality does not depend on the solvent or leaving group, whereas a specific parameter for "aromatic ring solvation" is known to improve many correlations of solvolytic data.[24b,27] Therefore, for a precise approach, it is reasonable to propose various values of E_f,[8b] but then it is not clear why an 'average' value of E_f should later be selected.[8b] A further inconsistency is that specific values of s_f are used to calculate E_f, but then $s_f = 1.00$ is assumed in the SQA.[8b] Because of the oversimplification arising from correlating kinetic data using only two parameters (E_f and N_f), it is reasonable (as in the SQA[8b]) to allocate the structural effect to one term (E_f), and the combined solvent and leaving group effect to another term (N_f).

Conclusion

A recent attempt[8a] to obtain 71 optimum values of parameters in Equation (2) from 167 experimental values of log k gave some unreliable values of s_f and N_f (see Section S2 in the Supporting Information). A major cause of errors is the variation in electron demand for benzhydryl solvolyses (4-methoxy-monosubstituted < symmetrically disubstituted < 4-nitro-monosubstituted[11c] (see also Section S3 in the Supporting Information). When electronic effects in the substrate are less complex (e.g. for cumyl (**3**)), solvent effects on E_f are known to make only a small contribution to s_f (see Section S1 in the Supporting Information).[11a] Other contributions to s_f are difficult to separate, but the main one is probably residual errors.

A more promising suggestion,[8b] based on Equation (2), allows the correlation and/or prediction of solvolysis rates simply by adding two parameters (assuming that the slope parameter $s_f = 1.00$). Electrofugality (E_f) for benzhydryl electrofuges is closely related to log k for ethanolysis of chlorides (Equation (3), Table 1); this new definition of E_f is relatively robust and transparent (as it is not dependent on multi-parameter correlations[8]) and it can readily be extended to other electrofuges. Nucleofugality (N_f) is a correction term, allowing for changes in solvent (from ethanol) and leaving group (from chloride). Equation (5) provides a new definition of N_f, suitable for solvolyses of benzhydryl chlorides, bromides and tosylates.

The accuracy of predictions of log k, assuming $s_f = 1.00$, based on Equations (2), (3) and (5), depends on the suitability of solvolyses of benzhydryl substrates (i.e. secondary diaryl) as similarity models. Of the various possible modifications, which are needed to account for other solvolyses when similarity is less close, an alternative set of N_f values based on solvolyses of *tert*-butyl subtrates (N'_f, Equation (9)) is suggested. Predicted values of log k would then be obtained from Equation (10).

Many other additivity rules for chemical reactivity can be devised,[7] but caution is needed if multi-parameter correlations are used.[10] Although the complexity of structure/reactivity relationships might be used to justify the use of many parameters (e.g. for solvent effects[10]), the range of available experimental data may often be inadequate.

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