etry of the azaborine ring found experimentally agrees well with the description of the bonding presented here.

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Supplementary Material Available: Structures and energies of the calculated molecules in the form of archive entries (3 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

A Semitheoretical Multiparameter Approach To Correlate Solvent Effects on Reactions and Equilibria

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A solvent rate effect equation which uses four physical properties of the solvent for parameters has been applied with good success to solvolysis reactions, solvent E_t values, Claisen Rearrangements, Diels–Alder reactions, endo–exo ratios in Diels–Alder reactions, azo-Cope rearrangements, and enol–ketone equilibria of the dimedone and pyridone variety. The coefficients of the parameters, which are the Kirkwood–Onsager function, the solvent cohesive energy density, the specific solvation of chloride ion, and the specific solvation of potassium ion, lead to differences in dipole moments, in volumes between initial and final states, and in the extent of specific solvation of anionic and cationic sites relative to the solvation of chloride ion and potassium ion, respectively.

Concern for solvent effects on chemical reactions has led to more than a few theoretical constructs and empirical correlations to provide not only rationalization but prediction of equilibrium and rate data.[1] For instance, in solvolysis reactions, Winstein–Grunwald solvent Y values[2] have proven remarkably useful not only for correlation purposes, but to assess the sensitivity of the reaction to solvent relative to the standard. The sensitivity of the reaction to Y might appear to be a measure of change in ionic character from ground state to transition state. However, Abraham has provided quantitative data on the stability of *tert*-butyl chloride in various solvents relative to that in DMF and found significant destabilization in the more polar, hydroxylic media.[3b] Indeed, ground-state destabilization is an important contributor to the S_N1 rate differences in polar media as was suggested by Winstein[2] and demonstrated by Arnett.[4] In addition, Abraham found that the solvent cohesive energy density, ced, as defined by Hildebrand, $(\Delta H_{vap} - RT)/V_m$,[5] is the major correlator of the stability of *tert*-butyl chloride in a wide range of solvents. Further, by subtraction Abraham could determine the relative stability of the *tert*-butyl chloride solvolysis transition state in different solvents relative to that in DMF and found behavior which correlated with the Taft solvatochromic π^* parameter.[3a] However, some solvents stabilize the transition state by what has been recognized as a specific hydrogen bonding effect; these solvents include trifluoroethanol, hexafluoroisopropanol, and formic acid. Thus, the coefficient of the hydrogen bonding term, α, in the Taft multiparameter correlation of the *tert*-butyl chloride solvolysis reaction is not insignificant compared to the coefficient of the π^* parameter (eq 1; note that Taft uses δ^2 for the ced term).[3c]

$$\ln k = 5.10\pi^* + 4.17\alpha + 0.73\beta + 0.0048\delta^2 - 14.60 \qquad (1)$$

Interestingly, the ced term appears to be insignificant in the Taft correlation of the solvolysis data despite its importance in correlating the ground-state destabilization. Abraham argues that there is destabilization of the transition state by the ced term so that only the π^* and α terms are important overall. However, there should be concern over the extent to which the ced term is also included in the π^* term as admitted by Taft.[3a] Interestingly, increases in the ced have also been argued to be responsible for increased apolar binding of pyrene with cryptans.[6] References are scattered throughout the literature to the potential interchangeability of rate responses to ced and external pressure studies,[7] although le Nobel's recent review argues vigorously against this.[8]

A particularly relevant approach to solvent effects on enol–ketone tautomeric equilibria was provided by Beak[9] who used the Kirkwood–Onsager function, $[(\epsilon - 1)/(2\epsilon + 1)]$,[10] and Taft's α and β parameters of early 1980's vintage. Remarkable correlations were found for cyclohexane-1,3-dione systems and related rigid systems. This equation with the addition of a ced term and the inclusion of the

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(1) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH: Weinheim, 1988.

(2) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc.* **1948**, *70*, 846. See also: Smith, S. G.; Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1961**, *83*, 618.

(3) (a) For the most recent review of parameter values with extensive comments, see: Abraham, M. H.; Grellier, P. L.; Abboud, J.-L. M.; Doherty, R. M.; Taft, R. W. *Can. J. Chem.* **1988**, *66*, 2673. (b) Abraham, M. H.; Grellier, P. L.; Nasehzadeh, A.; Walker, R. A. C. *J. Chem. Soc.* **1988**, 1717. (c) Multiparameter correlation approaches to solvent effects were pioneered by Koppel and Palm.[1]

(4) Arnett, E. N.; Bentrude, W. G.; Burke, J. J.; Duggleby, P. M. *J. Am. Chem. Soc.* **1965**, *87*, 1541 and references contained therein.

(5) (a) Hildebrand, J. H.; Prausnitz, J. M.; Scott, R. L. *Regular and Related Solutions*; Van Nostrand-Reinhold: Princeton, 1970. Hildebrand, J. H.; Scott, R. L. *Regular Solutions*; Prentice-Hall: Englewood Cliffs, NJ, 1962. Hildebrand also called the ced an internal solvent pressure, and many use both terms interchangeably. More recently the internal solvent pressure has been defined as $(dU/dV)_T$. Measured values for this are distinctly different from the ced (see ref 1). (b) For a correlation with the square root of the solvent cohesive energy density, see also; Herbrandson, H. F.; Neufeld, F. R. *J. Org. Chem.* **1966**, *31*, 1140.

(6) Smithrud, D. B.; Diederich, F. *J. Am. Chem. Soc.* **1990**, *112*, 339.

(7) Ouellette, R. J.; Williams, S. H. *J. Am. Chem. Soc.* **1971**, *93*, 466. Dack, M. R. J. *J. Chem. Educ.* **1974**, *51*, 233. Snyder, J. P.; Harpp, D. N. *J. Am. Chem. Soc.* **1976**, *98*, 7821.

(8) le Nobel, W. J. *Chem. Rev.* **1989**, *89*, 549.

(9) (a) Mills, S. G.; Beak, P. *J. Org. Chem.* **1985**, *50*, 1216. (b) Beak, P.; Covington, J. B.; White, J. M. *J. Org. Chem.* **1980**, *45*, 1347.

(10) Kirkwood, J. G. *J. Chem. Phys.* **1934**, *2*, 351. Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486. For applications of this solvent property see ref 1, Chapter 5.

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latest values for α and β will be used as a comparison for the equation developed below. The Taft equation will also be used with the change of the units of the ced term. Other approaches to correlate solvent effect data include a two-term equation by Swain[11] which uses empirically determined "acity" and "basity" parameters and a one-term equation championed by Reichardt involving solvatochromically determined E_t values.[1] These will be discussed below.

The KOPMH Equation. Concern that currently popular correlation equations may not represent all factors in solvation or may not provide direct physical insight into the solvent effect led to the use of a four-parameter equation (eq 2) which includes only physically measurable

$$\ln k = c_1\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + c_2\alpha' + c_3\beta' + c_4\text{ced} + c_5 \quad (2)$$

properties of the solvent whose coefficients provide semitheoretical information about the difference between the initial state and transition or final state. These parameters are the Kirkwood–Onsager function, $[(\epsilon - 1)/(2\epsilon + 1)]$,[10] the solvent ced an anion relative stabilization term, and a cation relative stabilization term. The coefficient of the Kirkwood–Onsager function may be related to the difference in ground-state and transition-state dipole moments assuming a reasonable cavity radius for each state. The solvent ced term has a coefficient that is a volume difference between ground state and transition state *in the context of the cohesive energy density*. The α' and β' terms are derived from Parker's and Marcus'[12] compilations of the relative free energy of solvation of chloride ion and potassium ion, respectively, in a variety of solvents—all with a Kirkwood–Onsager term near 0.5 although with different cohesive energy terms. The α' and β' terms for other solvents are roughly interpolated from Taft's α and β terms. They are the relative free energies of solvation in cal/mol divided by $100RT$. Thus, the coefficients of the α' and β' terms measure the percent specific solvation difference between the initial and final or transition state relative to the solvation of the two reference ions. The coefficients of eq 2 can be rewritten as in eq 3.

$$\ln k = f(\mu^2/r^3)\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + a\alpha' + b\beta' + \Delta V\text{ced} + c \quad (3)$$

The parameters are given in Table I. It is important to note that pairs of parameters are moderately noncovariant over a large range. The Kirkwood–Onsager function rises steeply in the low dielectric extreme but plateaus for polar solvents while the solvent ced rises only with highly internally hydrogen-bonded solvents. The parameter α' goes to a maximum with solvents that donate hydrogens in hydrogen bonds but are poor hydrogen bond acceptors. Just the opposite is true for the the β' values which go to a maximum with good Lewis base electron pair donors. Unfortunately, while the α' and β' terms are not correlated ($r = 0.08$), each is weakly correlated to the Kirkwood–Onsager function ($r = 0.54$ and $r = 0.30$, respectively), and the solvent ced is weakly correlated to the Kirkwood–Onsager function ($r = 0.424$), so some care is necessary in not only choosing solvents but interpreting the results of a correlation.

Because of the different behavior of each of these parameters, it is important to choose a wide range of solvents to provide coefficients indicative of the nature of the ground state and transition state in a reaction. Thus, the choice of water, ethylene glycol, or formamide, trifluoroethanol or hexafluoroisopropanol, methanol or ethanol, DMSO or DMF, diethyl ether or THF, and benzene or carbon tetrachloride should be appropriate for a solvent effect study using the KOPMH (Kirkwood, Onsager, Parker, Marcus, Hildebrand) equation (eq 3). And, of course, the use of two or more solvents in each category would provide more accuracy and precision. It would be inappropriate to use a large number of solvents in only a few categories.

The KOPMH equation was applied to a variety of reactions with moderate success to provide a useful insight into the mechanism of each reaction. In every case a correlation coefficient was calculated according to the procedure emphasized by Swain.[11] Care should be exercised in interpreting the standard deviations and range of values since they are given in the units of natural logarithms. Thus, what would appear to be a standard deviation that is 10% of the range is really less than a 2% standard deviation in a rate or equilibrium constant itself.

***tert*-Butyl Chloride Solvolysis.** Application of the KOPMH equation to 20 solvents included in Abraham's data for the difference in free energy between *tert*-butyl chloride and the S_N1 transition state (see Appendix) using the parameters of Table I gives:

$$\ln k_{\text{rel}} = 18.9\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 52.8\alpha' - 0.76\beta' - 10.1\text{ced} - 15.4$$

$$\text{SD} = 1.1 \text{ (range 25.5)};\ r = 0.989$$

The coefficient of the Kirkwood–Onsager function is substantial and corresponds to a transition-state dipole moment of roughly 7 D at a distance of 4.0 Å. The coefficient of the hydrogen-bonding term suggests that nearly 90% of the hydrogen-bonding solvation of chloride ion is present in the S_N1 transition state. Importantly, the ced coefficient is substantial and is nearly the activation volume observed for the S_N1 reaction from external pressure studies.[8] This is the solvophobic factor which is responsible for destabilization of the ground state in highly hydrogen bonded media. The coefficient of the β' term may represent some stabilization of the ground state by electron donors although it is the least important term in the correlation.

For comparison purposes, the Taft, Beak, Swain, and E_t equations were applied to the same data

$$\text{Taft: } \ln k = 11.9\pi^* + 9.93\alpha + 3.32\beta - 6.75\text{ced} - 15.6$$

with SD = 1.37; $r = 0.981$ (ced scales exactly the same as δ^2)

$$\text{Beak: } \ln k = 31.4\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 7.42\alpha - 1.27\beta - 13.5\text{ced} - 19.5$$

with SD = 1.42; $r = 0.980$

$$\text{Swain: } \ln k = 23.8A + 8.11B - 16.10$$

with SD = 1.40; $r = 0.981$

$$E_t \text{ values: } \ln k = -0.765E_t/RT - 16.10$$

with SD = 1.28; $r = 0.984$.

That any of these correlations are reasonable is unexpected given the rather substantial change in transition-state structure that must occur over such a wide range of

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[11] Swain, C. G.; Swain, M. S.; Powell, A. L.; Alunni, S. *J. Am. Chem. Soc.* **1983**, *105*, 502.

[12] Cox, B. G.; Hedwig, G. R.; Parker, A. J.; Watts, D. W. *Aust. J. Chem.* **1974**, *27*, 477. Marcus, Y. *Pure Appl. Chem.* **1983**, *55*, 977.

Table I. Parameters[b] for the Kirkwood, Onsager, Parker, Marcus, Hildebrand Equation

$$\ln k = f(\mu^2/r^3)^c\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + a\alpha' + b\beta' + \Delta V\text{ced} + c$$

	solvent	$\epsilon - {}^1/{}_{2\epsilon} + 1$	α'	β'	ced
32	pyridine	0.444	0.000	0.203	0.188
31	Et_3N	0.243	0.000	0.220	0.100
30	ethyleneglycol	0.480	0.198[a]	0.177[a]	0.358
29	HCOOH	0.487	0.282	0.000	0.360
28	HOAc	0.386	0.169	0.101	0.343
27	HFIP	0.499	0.321	0.000	0.151
26	H_2O	0.491	0.234[a]	0.169[a]	0.927
25	TFE	0.472	0.275[a]	0.011[a]	0.231
24	MeOH	0.477	0.181[a]	0.130[a]	0.346
23	EtOH	0.470	0.153[a]	0.103[a]	0.274
22	iPrOH	0.463	0.135	0.135	0.225
21	tBuOH	0.442	0.118	0.135	0.189
20	DMSO	0.484	0.072[a]	0.221[a]	0.285
19	$HCONH_2$	0.493	0.179[a]	0.186[a]	0.610
18	DMF	0.480	0.039[a]	0.210[a]	0.234
17	$PhNO_2$	0.479	0.093[a]	0.101[a]	0.206
16	CH_3NO_2	0.479	0.085[a]	0.092[a]	0.268
15	PhCN	0.471	0.000	0.125	0.207
14	CH_3CN	0.480	0.065[a]	0.136[a]	0.233
13	CH_3COCH_3	0.465	0.014[a]	0.153[a]	0.153
12	EtOAc	0.385	0.000	0.101	0.134
11	CH_2Cl_2	0.422	0.034	0.000	0.165
10	$CHCl_3$	0.359	0.051	0.000	0.150
9	HMPA	0.475	0.000[a]	0.234[a]	0.124
8	THF	0.407	0.000	0.101	0.146
7	dioxane	0.223	0.000	0.101	0.169
6	Et_2O	0.345	0.000	0.076	0.095
5	nBu_2O	0.292	0.000	0.076	0.100
4	Ph-H	0.230	0.008	0.034	0.141
3	CCl_4	0.226	0.000	0.000	0.125
2	c-C6	0.202	0.000	0.000	0.113
1	gas	0.000	0.000	0.000	0.000

[a] Relative ΔG(solvation)/100RT of chloride ion (α') and of potassium ion (β') from Marcus (ref 12); the rest of the α' and β' values are interpolated using Taft's α and β parameters. [b] A DOS program with these parameters and the multiparameter fitting routine along with the other parameters and equations discussed is available for math coprocessor equipped machines. Send the author a formatted disk. [c] $f(\mu^2/r^3) = 24.2(\mu(fs)^2/r(fs)^3 - \mu(gs)^2/r(gs)^3)$; μ is in Debye and r is in Å.

solvents. Indeed, the correlation might appear fortuitous so it is instructive to examine the rate data over a more limited range of polar solvents where more "standard" S_N1 behavior might occur. Thus, with the solvents water, ethylene glycol, trifluoroethanol, methanol, ethanol, dimethyl sulfoxide, formamide, dimethylformamide, nitromethane, acetonitrile, and acetone, the following correlation with the KOPMH equation is found:

$$\ln k_{\text{rel}} = -20.38\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 50.1\alpha' + 3.08\beta' - 11.2\text{ced} + 3.1$$

$$\text{SD} = 1.3 \text{ (range 19.0)}; r = 0.977$$

It must be recognized that the coefficient of the Kirkwood–Onsager (K–O) term is practically meaningless since the range of K–O parameter is very small with the solvents used. Indeed, if the K–O term is dropped the correlation becomes:

$$\ln k_{\text{rel}} = 49.8\alpha' + 1.91\beta' - 10.8\text{ced} - 6.3$$

$$\text{SD} = 1.19 \text{ (range 19.0)}; r = 0.98$$

This correlation describes the *tert*-butyl chloride solvolysis under conditions normally encountered and described in undergraduate textbooks. The parameters used are not generated by a fitting routine, they are measured properties of the solvent scaled to give the proper units of the dependent variable. They reveal a small effect of transition-state stabilization by the dielectric properties of the medium. They reveal substantial effects of hydrogen bonding to the transition state and of solvent cohesive energy density in destabilizing the ground state.

Correlation of E_t Values. An interesting application of the KOPMH equation is to the E_t values provided by Reichardt[1] where E_t expressed as an equilibrium constant (see Appendix).

$$-E_t/RT = 44.4\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 113\alpha' + -0.59\beta' - 16.5\text{ced} + 42.7$$

$$\text{SD} = 2.20 \text{ (range: } 53.27); r = 0.989$$

Here the contribution from three terms is important for reasons that are not obvious. Since the solvatochromic shift is presumably a vertical transition, no rearrangement of solvent should occur in the process. Yet the solvent cohesive energy contribution is substantial. For comparison purposes, the Taft and Beak equations give:

$$\text{Taft: } -E_t/RT = 10.0\pi + 12.8\alpha + 3.61\beta - 9.07\text{ced} + 28.8$$

$$\text{SD} = 2.39; r = 0.969$$

$$\text{Beak: } -E_t/RT = 27.0\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 10.6\alpha + 0.214\beta - 13.8\text{ced} + 25.7$$

$$\text{SD} = 2.36; r = 0.970$$

The fits are about the same, and the large coefficient of the solvent ced term is unmistakable. What gives rise to E_t values is not totally clear but hydrogen-bonding ability is the most important term. Finally, for comparison purposes, the Swain equation gives:

$$-E_t/RT = 26.3A + 6.44B + 29.1$$

$$\text{SD} = 2.88; r = 0.955$$

Polar Solvent Effects in the Claisen Rearrangement. Application of the KOPMH equation with the parameters of Table I to the Claisen Rearrangement rate data provided by Brandes[13] in 10 critically chosen solvents (see Appendix) reveals that

$$\ln k_{\text{rel}} = 3.70\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 6.10\alpha' - 7.15\beta' - 4.51\text{ced} - 0.952$$

$$\text{SD} = 0.41 \text{ (range: } 5.37); r = 0.967$$

When the β' term is removed the correlation becomes:

$$\ln k_{\text{rel}} = -1.04\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 10.82\alpha - 3.35\text{ced} + 0.089$$

$$\text{SD} = 0.433; r = 0.963$$

Alternatively, if the Kirkwood–Onsager term is deleted the correlation becomes:

$$\ln k_{\text{rel}} = 9.55\alpha' - 2.44\beta' - 3.77\text{ced} - 0.071$$

$$\text{SD} = 0.406; r = 0.968$$

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(13) Brandes, E. B.; Grieco, P. A.; Gajewski, J. J. *J. Org. Chem.* **1989**, 515. The data for the ester-substituted allyl vinyl ether and the sodium carboxylate were combined with the rate constant in TFE being the average value for both substrates (whose rates differed by less than 50% in TFE).

The equally good correlations in all three cases should make clear that the Kirkwood–Onsager term and the β' term are partly inversely correlated and both would appear to contribute near negligibly to the solvent response observed by Brandes. Clearly the hydrogen-bonding term and the solvent ced terms are most important. Since this sigmatropic shift has a negative activation volume from external pressure studies (-10 cm^3/mol)[8] the solvent ced coefficient is not unreasonable. The coefficient of the hydrogen bonding term is ca. 15% of that providing hydrogen-bonding stabilization of chloride ion and may well be due to the partial formation of the hydrogen-bond-accepting carbonyl group in the transition state. The lack of a dielectric effect is not inconsistent with the transition-state dipole moment resulting from partial formation of the carbonyl group which is about the same as the dipole moment of the starting vinyl ether which may be reversed in direction pointing toward C-1 which receives electron density from the vinyl ether oxygen.

Other solvent effect correlation equations can be applied with results varying from better (Taft) to equivalent (Beak) to much worse (Swain and E_t values).

$$\text{Taft: } \ln k = 1.273\pi^* + 1.69\alpha - 0.77\beta - 2.6\text{ced} - 0.344$$

$$\text{SD} = 0.172;\ r = 0.994$$

$$\text{Beak: } \ln k = 2.97\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 1.93\alpha - 1.01\beta + 0.639\text{ced} - 14.2$$

$$\text{SD} = 0.308;\ r = 0.968$$

$$\text{Swain: } \ln k = 0.42A + 0.827B - 0.823$$

$$\text{SD} = 0.65;\ r = 0.914$$

$$E_t \text{ values: } \ln k = -0.141E_t/RT - 4.87$$

$$\text{SD} = 0.725;\ r = 0.893$$

The Taft equation correlation also indicates that the dominant terms are hydrogen bonding and solvent ced.

Diels–Alder Reaction. The most extensive set of solvent effects on Diels–Alder reactions has been provided by Blokzijl, Blandamer, and Engberts who studied the reaction of cyclopentadiene with 5-methoxy-1,4-naphthoquinone.[14] Fifteen of the solvents have parameters defined (cyclohexane was used for hexane) and give according to the KOPMH equation:

$$\ln k\ (\text{L/mol-s}) = 0.304\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 13.1\alpha' - 2.52\beta' - 6.82\text{ced} - 7.53$$

$$\text{SD} = 0.54\ (\text{range: } 8.82);\ r = 0.974$$

The good correlation suggests little change in dipole moment from ground to transition state, but it does show a significant effect of hydrogen bonding, a point made by Jorgensen in his simulation of Diels–Alder reactions.[15] The solvent cohesive energy density effect is not insignificant. Indeed, if both the dielectric and β' parameters are removed, the correlation improves slightly and gives virtually the same coefficients of α' and ced: ced:

$$\ln k\ (\text{L/mol-s}) = 13.5\alpha' - 6.31\text{ced} - 7.53$$

$$\text{SD} = 0.52;\ r = 0.977$$

For comparisons the other correlation equations give

$$\text{Taft: } \ln k = 1.51\pi^* + 2.23\alpha - 0.686\beta - 6.06\text{ced} - 8.07$$

$$\text{SD} = 0.44;\ r = 0.983$$

$$\text{Beak: } \ln k = 1.77\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 2.10\alpha - 0.663\beta - 7.06\text{ced} - 3.95$$

$$\text{SD} = 0.056;\ r = 0.972$$

$$\text{Swain: } \ln k = 6.44A + 1.62B - 8.63$$

$$\text{SD} = 0.94;\ r = 0.920$$

$$E_t \text{ values: } \ln k = 0.209E_t/RT - 14.1$$

$$\text{SD} = 1.05;\ r = 0.900$$

Origin of Endo–Exo Diels–Alder Preferences: Berson ω-Values. Berson examined the solvent effect on endo–exo preferences of addition of various dienophiles to cyclopentadiene and introduced the ω scale, namely the logarithm$_{10}$ of the endo–exo ratio (see Appendix).[16] The KOPMH equation gives

$$2.303\omega = 0.692\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 1.15\alpha' - 0.214\beta' - 1.95\text{ced} + 0.722$$

$$\text{SD} = 0.083\ (\text{range: } 0.920);\ r = 0.958$$

The dominant term in the correlation is the cohesive energy density term whose coefficient suggests that the volume of the transition state for endo product formation is ca. 2 mL/mol smaller than that for the transition state to the exo product. However, equally good correlations can be obtained if only the hydrogen bonding and the ced terms are used or if only the Kirkwood–Onsager and hydrogen-bonding terms are used. These observations make it clear that the data set, though containing 10 entries,[1] is insufficient to distinguish between the possibilities except that hydrogen bonding is important.[15] However, generally the largest endo selectivity is observed for Diels–Alder reactions in water,[17] and this is more consistent with dominance of the ced term rather than a dielectric term since the dielectric term is virtually the same for water, methanol, and ethanol. Further, the endo–exo ratio for methyl acrylate reacting with cyclopentadiene in trifluoroethanol was measured[18] to be 7.1[18] which is similar to that in methanol. The fit is slightly improved with the addition of the trifluoroethanol point:

$$2.303\omega = 0.808\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 1.73\alpha' - 0.262\beta' - 1.40\text{ced} + 0.767$$

$$\text{SD} = 0.078\ (\text{range: } 0.935);\ r = 0.967$$

Exclusion of the β' and ced terms gives a worse fit:

$$2.303\omega = 1.146\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 2.54\alpha' + 0.839$$

$$\text{SD} = 0.104;\ r = 0.942$$

Exclusion of the dielectric and β' terms gives an intermediate fit with coefficients similar to those from use of all terms

$$2.303\omega = 1.92\alpha' - 1.87\text{ced} + 0.951$$

$$\text{SD} = 0.096;\ r = 0.951$$

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[14] Blokzijl, W.; Blandamer, M. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1991**, *113*, 4241.

[15] Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1991**, *113*, 7430.

[16] Berson, J. A.; Hamlet, Z.; Mueller, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 297.

[17] Breslow, R.; Guo, T. *J. Am. Chem. Soc.* **1988**, *110*, 5613.

[18] I thank Leif P. Olson for this experiment.

For comparison purposes, the other correlation equations give

$$\text{Taft: } 2.303\omega = 0.355\pi^* + 0.351\alpha + 0.003\beta - 1.503\text{ced} + 0.812$$

$$\text{SD} = 0.085;\ r = 0.962$$

$$\text{Beak: } 2.303\omega = 1.003\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 0.274\alpha - 0.155\beta - 1.51\text{ced} + 0.732$$

$$\text{SD} = 0.054;\ r = 0.983$$

$$\text{Swain: } 2.303\omega = 1.085A + 0.354B + 0.830$$

$$\text{SD} = 0.070;\ r = 0.974$$

$$E_t\text{: } 2.303\omega = -0.035E_t - 0.075$$

$$\text{SD} = 0.074;\ r = 0.971$$

Hydrogen-Bond-Insusceptible Behavior. Mitsuhashi proposed that the relative rate behavior of a reaction in methanol and DMSO denoted the importance of hydrogen bonding in the reaction.[19] The ionization of (*p*-nitrophenyl)azo-*tert*-cumylmalononitrile, where the leaving group is carbon, was studied (range of rates: 25-fold from acetone to DMSO at 60 °C) and was noted as a reaction requiring little hydrogen bonding in contrast to the ionization of *tert*-butyl chloride. Application of the KOPMH equation to the reaction gives:

$$\ln k = 2.42\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) - 66.5\alpha' - 7.90\beta' - 72.5\text{ced} - 8.612$$

$$\text{SD} = 0.279\ (\text{range: } 3.26);\ r = 0.970$$

When the β' term is removed the correlation becomes:

$$\ln k = 0.5\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) - 51.2\alpha' - 72.5\text{ced} - 6.67$$

$$\text{SD} = 0.39;\ r = 0.979$$

If the Kirkwood–Onsager term is also deleted the correlation becomes:

$$\ln k = -51.6\alpha' - 60.1\text{ced} - 6.74$$

$$\text{SD} = 0.2;\ r = 0.985$$

Thus, the reaction rate is enormously retarded by hydrogen bonding and accelerated by the solvent ced; i.e., the volume change from ground state to transition state is very negative. However, there is little dipole moment change from ground state to transition state.

Similar behavior is revealed by correlation with the Taft and Beak equations except that the β term contributes positively so that the ced coefficient is not as negative

$$\text{Taft: } \ln k = -0.30\pi^* - 3.42\alpha + 2.39\beta - 21.3\text{ced} - 0.92$$

$$\text{SD} = 0.049;\ r = 0.999$$

$$\text{Beak: } \ln k = -0.157\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) - 3.29\alpha + 2.28\beta - 21.0\text{ced} - 0.967$$

$$\text{SD} = 0.0620;\ r = 0.999$$

Application of the Swain and E_t equations to this data is unsatisfactory.

In the same paper the ionization of *p*-methoxyneophyl tosylate was noted as a hydrogen-bond-susceptible reaction, and a solvent polarity scale was proposed based on the relative rate of ionization of this tosylate in various solvents versus methanol (range of rates: 136-fold from acetone to methanol at 75 °C). Thus, W_{ion} was defined as $RT \ln k_{\text{ion}}/k_{\text{ion}}(\text{methanol})$. Various other solvent polarity scales were compared to W_{ion}, and it was applied to 3,3-shifts and related reactions. Correlation of W_{ion}/RT with the KOPMH equation gives

$$W_{\text{ion}}/RT = -10.0\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 0.98\alpha' - 3.28\beta' - 24.9\text{ced} - 3.58$$

$$\text{SD} = 0.066\ (\text{range: } 4.95);\ r = 0.999$$

Thus, the major factor in the solvolysis is the solvent ced. The smaller dipole moment of the transition state is also noteworthy. For comparison the Taft and Beak equations give

$$\text{Taft: } W_{\text{ion}}/RT = 2.80\pi^* + 2.0\alpha - 0.661\beta - 18.5\text{ced} - 9.56$$

$$\text{SD} = 0.098;\ r = 0.998$$

$$\text{Beak: } W_{\text{ion}}/RT = -7.72\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 0.438\alpha - 0.493\beta - 24.5\text{ced} - 4.89$$

$$\text{SD} = 0.0362;\ r = 0.9998$$

Azo-Cope Rearrangement. Mitsuhashi studied the 3,3-shift of (*m*-chlorophenyl)azo(α,α-dimethyl)malononitrile at 60 °C and found a modest solvent polarity dependence (rate range: 20-fold from CCl_4 to DMSO) where methanol had a rate retarding effect relative to DMSO.[19] Application of the KOPMH equation to this data gives

$$\ln k = 4.93\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) - 17.8\alpha' - 1.86\beta' - 16.0\text{ced} - 0.081$$

$$\text{SD} = 0.40\ (\text{range: } 3.49);\ r = 0.887$$

The Taft and Beak equations give

$$\text{Taft: } \ln k = 3.12\pi^* + -0.437\alpha - 0.119\beta - 5.0\text{ced} - 1.00$$

$$\text{SD} = 0.15;\ r = 0.985$$

$$\text{Beak: } \ln k = 4.94\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) - 1.63\alpha - 0.149\beta - 7.18\text{ced} + 1.01$$

$$\text{SD} = 0.350;\ r = 0.918$$

And the Swain equation gives

$$\ln k = 2.70A - 5.54B + 0.893$$

$$\text{SD} = 0.177;\ r = 0.980$$

Enol–Ketone Tautomeric Equilibria. Beak successfully modeled the equilibrium between dimedone and its enol tautomer as a function of solvent[9a] using the Kirkwood–Onsager function and the Taft α and β terms of the early 1980's. Application of the Beak equation using the latest Taft parameters and without any contribution from ced gives the following equation

$$\text{Beak: } \ln K_{\text{eq}} = 1.09\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 2.23\alpha + 9.41\beta - 3.40$$

$$\text{SD} = 0.853\ (\text{range: } 7.98);\ r = 0.953$$

The Taft equation gives

$$\text{Taft: } \ln K_{\text{eq}} = 0.241\pi^* + 0.510\alpha + 9.60\beta - 4.63\text{ced} - 3.86$$

$$\text{SD} = 0.337;\ r = 0.993$$

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[19] Mitsuhashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 2394, 2400.

Table II.

tert-butyl chloride solvolysis[3]

solvent#	ln k rel
30	8.96789977
28	4.20839989
27	13.32659966
26	15.96519959
25	10.40409973
24	5.57779986
23	3.37339991
22	1.83699995
21	.63459998
20	-1.03539997
19	9.45219976
18	.00000000
16	.98529997
14	-.30059999
13	-3.07279992
12	-6.71339983
11	-4.32529989
8	-5.57779986
6	-9.55239975
4	-8.21639979

Claisen Rearrangement[13]

solvent#	ln k rel
26	5.36597602
25	3.82000000
24	2.15176220
20	1.16315081
23	1.80828877
22	1.60943791
14	1.13140211
13	.74193734
4	.69314718
2	.00000000

E_t values[1]:

solvent#	$-E_t$*1000/RT
32	-66.0
31	-54.0
26	-105.37699729
25	-99.36499745
19	-94.52199757
30	-94.02099758
24	-92.68499762
23	-86.67299777
28	-85.50399780
22	-81.16199791
16	-77.32099801
14	-76.81999803
20	-75.14999807
21	-73.31299812
18	-73.14599812
13	-70.47399819
11	-68.63699824
10	-65.29699832
12	-63.62699836
8	-62.45799839
7	-60.11999846
6	-57.78199852
4	-57.61499852
5	-55.77799857
3	-54.27499861
2	-52.10399866

Cyclopentadiene + 5-methoxy-1,4-naphthoquinone (ref 14).

solvent #	ln k (1/mol-sec)
2	-7.16523151
4	-6.48904494
3	-6.55008083
7	-6.32553966
8	-7.02092398
10	-5.08159438
11	-5.64362855
13	-6.35963387
14	-5.45146855
20	-4.84342738
23	-4.23360663
24	-4.02295457
25	-2.07068004
30	-2.02041820
26	1.66013103

ln k reported for the ionization of (*p*-nitrophenyl) azo-*tert*-cumylmalononitrile, ref. 19:

solvent #	ln k
24	4.57677071
20	6.64898455
18	5.50125821
32	4.34120464
14	4.05352257
7	3.38777436

ln k for the 3,3-shift of (*m*-chlorophenyl)azo(α,α-dimethylmalononitrile at 60°C as reported in ref 19:

solvent #	ln k
20	5.52545294
18	4.99721227
14	4.53044664
32	4.45898768
24	4.14154616
13	4.09100566
10	3.47506723
4	3.46260601
3	2.58021683

ln Keq for the enolization of acetonylacetone (ref 9a):

solvent #	ln Keq
26	-1.46967597
20	.69314718
14	.18232156
24	1.06471074
23	1.75785792
22	1.91692261
11	1.43508453
10	1.78170913
3	3.36729583
8	1.97408103
7	1.56861592
32	1.30833282
4	2.68784749
2	3.73766962

W_{ion} /RT defined as ln kion of *p*-methoxyneophyl tosylate/kion(MeOH) in ref 19:

solvent #	W_{ion}/RT
24	.00000000
20	-2.04600000
18	-3.17200000
32	-4.03000000
14	-3.00000000
13	-4.95000000

ln Keq for the enolization of dimedone (ref 9a):

solvent #	ln Keq
26	2.92249992
24	4.85969988
23	4.99329987
14	.85169998
13	1.38609996
20	5.00999987
7	1.03539997
6	1.13559997
8	1.95389995
4	-2.03739995
10	-2.90579993
11	-2.65529993
18	4.32529989

ln Keq for 6-chloro-2-hydroxypyridine-6-chloro-2-pyridone equilibrium (ref 9b):

solvent #	ln Keq
1	-3.50699991
2	-2.67199993
3	-2.67199993
7	-3.67399991
4	-2.50499994
10	-.78489998
12	-3.50699991
8	-3.84099990
11	-1.50299996
21	-1.33599997
22	-1.58649996
23	-1.33599997
24	-1.00199997
26	2.83899993

Omega values from ref 16:
as reported in ref 1:

solvent#	omega*2.303
16	1.59367598
24	1.94603498
14	1.59367598
28	1.89536898
23	1.65355398
13	1.42555698
18	1.42785998
32	1.37028498
31	1.02483499
4	1.14459099
25	1.96 (Leif Olson)

The KOPMH equation is not as good for reasons that are not obvious

$$\ln K_{eq} = -5.38\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 35.1\alpha' + 37.7\beta' + 9.40\text{ced} - 0.195$$

$$\text{SD} = 1.19;\ r = 0.907$$

When attempts are made to correlate the equilibrium between acetonylacetone and its enol, the Beak equation with the latest Taft parameters gives a poor correlation

$$\text{Beak:}\ \ln K_{eq} = -9.98\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) - 0.349\alpha + 1.22\beta + 5.06$$

$$\text{SD} = 0.90\ (\text{range: } 5.21);\ r = 0.719$$

(The earlier Taft parameters did much better for this equilibrium.) The Taft equation gives

$$\text{Taft:}\ \ln K_{eq} = -2.85\pi^* - 0.309\alpha - 0.171\beta + 2.30\text{ced} + 4.09$$

$$\text{SD} = 0.502;\ r = 0.922$$

The KOPMH equation does slightly worse than the Taft equation

$$\ln K_{eq} = -6.45\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 6.95\alpha' - 1.23\beta' - 5.18\text{ced} + 5.00$$

$$\text{SD} = 0.588;\ r = 0.891$$

In 1980, Beak published a quantitative model for solvent effects on the 6-chloro-2-hydroxypyridine, 6-chloro-2-pyridone equilibrium which invoked the Kirkwood–Onsager term and early values of α and β.[9b] The Beak equation with the latest Taft α and β parameters gives

$$\text{Beak:}\ \ln K_{eq} = 1.99\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 4.05\alpha - 2.53\beta - 3.19$$

$$\text{SD} = 0.535\ (\text{range: } 6.68);\ r = 0.951$$

The Taft equation gives

$$\text{Taft:}\ \ln K_{eq} = 0.334\pi^* + 3.34\alpha - 1.82\beta - 2.0\text{ced} - 3.12$$

$$\text{SD} = 0.478;\ r = 0.961$$

The KOPMH equation does as well as the Beak and Taft equations and further indicates not only the larger dipole moment and smaller volume of the pyridone, but the importance of hydrogen bonding to the pyridone and the acceptance of a hydrogen bond from the phenol all relative to the effects of solvent on chloride ion and potassium ion

$$\ln K_{eq} = 1.805\left(\frac{\epsilon - 1}{2\epsilon + 1}\right) + 12.6\alpha' - 14.5\beta' - 5.15\text{ced} - 3.47$$

$$\text{SD} = 0.477;\ r = 0.961$$

The α' and β' terms can be converted to energies relative to the gas phase by directly multiplying each coefficient by the parameter for the particular solvent.

Polarizability Considerations. Solvent polarizability has been occasionally cited as an important contributor to solvent effects, and equations including refractive indices have been proposed. Carbon disulfide has the highest refractive index among the most common organic solvents, yet Swain's parameters and E_t values make it equivalent to carbon tetrachloride. Indeed, its dielectric constant, solvent ced, and anticipated α' value are nearly the same as CCl_4. S_N2 reactions of the Menschutkin type (RI + tertiary amines) represent the cases where the KOPMH equation is inadequate to the task. If solvent polarizability were to be included, the correlation might be better. However, whether a five-parameter equation must be used for this purpose or whether other factors like variable transition-state structures are important remain as questions for the future.

Concluding Remarks

While not giving correlations of solvent–rate data that are always superior to the Taft and Beak equations, the KOPMH equation has the virtue of providing physically significant coefficients to factors that appear to be chemically orthogonal. Concern that the correlations are inadequate might be tempered by the consideration of the effect of solvents on transition-state structure. Perturbations of this sort are not unexpected and must lead to less than superb correlations. Further, the current paper makes no attempt to assess the temperature dependences and assumes that the temperatures are not very different from room temperature.

It should be recognized that Swain has emphasized the utility of the *acity* and *basity* parameters and the unique ability of these parameters to reproduce many solvent effects thereby calling into question the need for equations with more parameters.[11] However, the poor quality of fits by the Swain dual parameter equation for many of the data sets presented here must call into question the dual parameter approach. Further, the dissection of E_t values[1] provided here must raise awareness of the limited scope of this parameter; it is primarily hydrogen bond parameter modified by a dielectric and a cohesive energy density term. Finally, the contributions of Taft[3a] and Beak[9] should be recognized as important steps to the current approach which attempts to focus on orthogonal factors responsible for solvent effects on equilibria and rates.

Appendix

Solvolysis data (Table II).

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