Is the *tert*-Butyl Chloride Solvolysis the Most Misunderstood Reaction in Organic Chemistry? Evidence Against Nucleophilic Solvent Participation in the *tert*-Butyl Chloride Transition State and for Increased Hydrogen Bond Donation to the 1-Adamantyl Chloride Solvolysis Transition State

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Abstract: Despite theoretical calculations to the contrary, it has been argued that the 1-adamantyl cation is more stable than the *tert*-butyl cation in media of high dielectric constant. This argument has been utilized to suggest that the higher rate of solvolysis of *tert*-butyl chloride in aqueous ethanol is evidence for nucleophilic solvent participation in this classic reaction. Further, in “more highly ionizing” solvents, the rate of 1-adamantyl chloride is nearly the same as that of *tert*-butyl chloride, which is interpreted as a manifestation of the relative stabilities of the cations. However, the evidence cited does not explain the increased sensitivity of the rate of solvolysis of 1-adamantyl chloride over *tert*-butyl chloride to solvents which are better able to donate hydrogen bonds. The hypothesis developed here is that 1-adamantyl chloride solvolysis is assisted by hydrogen bond donation departing chloride ion to a greater extent than that of *tert*-butyl chloride solvolysis, most likely due to lessened steric interactions in a developing pyramidal cation. This hypothesis is supported by multiparameter solvent effect factor analyses utilizing the KOMPH2 equation which, in addition, quantifies the important role of ground-state destabilization due to strong solvent−solvent interactions. An important result from the good correlation of free energies of transfer of the *tert*-butyl chloride solvolysis transition state is that there is no change in mechanism, and, in particular, no nucleophilic participation even in non-hydroxylic basic solvents. The equation is also applied to the case of dimethylsulfonium ion solvolyses where the *tert*-butyl salt reacts substantially faster than the 1-adamantyl salt in ethanol and the gas phase. The decreased rate of the former in hydrogen bond donating solvents relative to the gas phase is as yet unclear. Solvent *N* values that were generated to characterize solvent nucleophilicity are shown not to be correlated by measures of solvent basicity but rather by the negative of measures of solvent hydrogen bond donor ability.

Introduction

The S_N1 reaction[1a] serves as an introduction to kinetics, carbocations, and solvent effects, and *tert*-butyl chloride, **tbucl**, is the substrate given the greatest focus. However, beyond the fact that the reaction rate is faster in polar solvents consistent with a more polar transition state only occasionally is noted the importance of hydrogen bond donating solvents to stabilize developing anion in the transition state.[1a,b] Further, little attention is given, except in one text,[1c] to the remarkable observation by Winstein[2a] and later by Arnett[2b] that the reaction in water is accelerated by ground-state destabilization. However, there is a substantial literature on the importance of nucleophilic solvent participation in the solvolysis of **tbucl**[3] and the development of solvent *N* values which appears to ignore the factors described above.

The Case *for* Nucleophilic Solvent Participation in *tert*-Butyl Chloride Solvolysis

A recent paper serves as a point of departure.[4] Building on concepts summarized in ref 3, the paper concludes that the solvolysis of **tbucl** in alcohol solvents is substantially assisted by nucleophilic participation by the solvent. The argument begins with the observation that the solvolysis reaction of **tbucl** in 80% aqueous ethanol (80% ethanol, 20% water v/v) is roughly 1000 times faster at ambient temperature than the solvolysis of 1-adamantyl chloride, **admcl**, eq 1. This was

$$k^{\text{tbucl}}/k^{\text{admcl}}\ (80\%\ \text{aqueous ethanol}) = 1000 \qquad (1)$$

thought to be remarkable since the authors determined that in exchange reactions of the chlorides (and the hydrides) in the gas phase, the cation derived from **admcl** (or adamantane) is more stable than the cation from **tbucl** (or isobutane).[4] That is,

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[1] (a) Streitwieser, A., Jr. *Solvolytic Displacement Reactions*; McGraw-Hill Book Company, Inc.: New York, 1962; in this review, solvent polarity in the form of the Kirkwood-Onsager function (ref 9 below) is used to correlate solvolysis rate data (p 48), and hydrogen bond donation from the solvent is noted on p 171. (b) For an early, more explicit possible description of hydrogen bond donation to departing anions see: Dannenberg, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 6261. (c) Harris, J. M.; Wamser, C. C. *Fundamentals of Organic Reaction Mechanisms*; John Wiley & Sons: New York, 1976; p 143.

[2] (a) Winstein, S.; Fainberg, A. H. *J. Am. Chem. Soc.* **1957**, *79*, 5937. (b) Arnett, E. N.; Bentrude, W. G.; Burke, J. J.; Duggleby, P. M. *J. Am. Chem. Soc.* **1965**, *87*, 1541.

[3] For a summary of the origins and arguments for *N* values see: Bentley, T. W.; Llewellyn, G. In *Progress in Physical Organic Chemistry*; Taft, R. W., Ed.; John Wiley & Sons: New York, 1990; Vol. 17, pp 120−158. See also: Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd. ed.; Harper Collins Publishers: New York, 1987; pp 335−340.

[4] Takeuchi, K.; Takasuka, M.; Shiba, E.; Kinoshita, T.; Okazaki, T.; Abboud, J.-L. M.; Notario, R.; Castaño, O. *J. Am. Chem. Soc.* **2000**, *122*, 7351.

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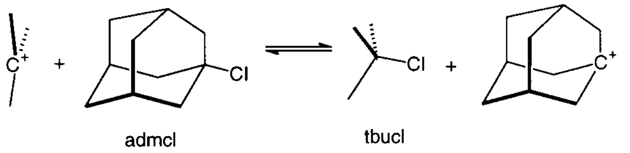
Scheme 1



the equilibrium constant for the reaction of Scheme 1 is about 10^7. Therefore, it was argued that the solvolysis reaction of **tbucl** must be assisted by the basicity of the alcohol solvents, apparently from the backside in an S_N2-like fashion, since this mode of solvation is, of course, not available to **admcl**.

It must be recognized, and some attention to this is paid by the authors,[4] that in the gas phase, small ions such as *tert*-butyl cation are generally less stable than bigger ions because of polarizability. The more the charge can be delocalized through both π and σ bonds in bigger molecules, the more stabilized is the charge. Indeed, ref 4 reports a calculation of the equilibrium constant of the exchange reaction above using the polarizable continuum model to mimic the dielectric effect of water on the cation stabilities, and it reveals that the *tert*-butyl cation is more stable than the 1-adamantyl cation by roughly 2 kcal/mol in this medium relative to the chloride ground states.

There is the further observation[3,4] that in more "ionizing, less nucleophilic solvents" like trifluoroethanol, **tfe**, and hexafluoroisopropyl alcohol, **hfip**, the difference in the solvolysis rates of **tbucl** and **admcl** diminishes to the point where less than a factor of 3 separates the two chlorides in **hfip**. This is used to reinforce the argument that the two cations are at least equally stable in nonnucleophilic solvents.

N Values

To quantify the extent of nucleophilic assistance in the **tbucl** solvolysis a second term, *N*, was added[3] to the venerable solvent *Y* value equation proposed by Winstein and Grunwald.[5] The Winstein−Grunwald *Y* values are directly the ratio of the logarithms (base 10) of the rate of solvolysis of **tbucl** in a solvent and that in 80% aqueous ethanol. Representative *Y* values are −2.0 (EtOH), −1.6 (HOAc), −1.0 (MeOH), 1.3 (**tfe**), and 3.7 (H_2O). The derivation of the *N* values begins with the use of *Y* values obtained from both 1- and 2-adamantyl solvolysis with an *N* value to allow the equation to correlate the **tbucl** solvolysis data although its quantitative origins begin with the effect of solvent on the S_N2 reaction of methyl tosylate with some additional considerations.[3] Representative *N* values are 0.06 (EtOH), −0.04 (MeOH), −0.44 (H_2O), −2.28 (HOAc), and −3.07 (**tfe**).

Concerns and Alternative Hypothesis

The Takeuchi−Bentley arguement for nucleophilic participation in **tbucl** solvolyses has been addressed more than a few times by Fárcaşiu, and Taft and Harris.[6] In particular, the need for electrophilic assistance to stabilize the departing anion has been emphasized, and it was recognized to be more important with 1-admantyl derivatives than with *tert*-butyl derivatives. An explanation for greater sensitivity of 1-admantyl derivatives to electrophilic catalysis follows from observations of increased hydride donor rates from the bridgehead carbon of adamantane relative to that from isobutane which was attributed to steric effects.[6d]

In this paper, the relative sensistivity of the two systems to electrophilic assistance by solvent will be quantified by multiparameter correlation equations employing parameters derived from different sources than that of ref 6b. Further, to address nucleophilic assistance hypothesis, two-part hypothesis will be pursued to deal with the facts:

(a) In solvents of moderate to high dielectric constant, the *tert*-butyl cation is more stable than the 1-adamantyl cation presumably because of less angle strain in the former case and because solvation by a dipolar medium is important with charged molecules and is more effective with smaller charged species. The calculations in ref 4 support this.

(b) In solvents which can donate hydrogen bonds much more effectively than alkyl alcohol solvents and water, especially in **hfip** where both **tbucl** and **admcl** have similar solvolysis rates, the transition state for solvolysis of **admcl** is better stabilized by hydrogen bonding to the departing chloride ion than is the transition state for formation of the *tert*-butyl cation. This is most easily explained by less steric inhibition of hydrogen bonding to the chloride ion in a developing pyramidal cation relative to that in a developing cation whose arms of attached carbons are free to move into a planar arrangement, see Scheme 2.

What facts support this "new" hypothesis over the nucleophilic assistance hypothesis? It is significant that the solvolysis rate of **admcl** is much more sensitive to variation in the hydrogen bond donating ability of solvents than is the solvolysis of *tert*-butyl chloride. For instance, the rate ratio for solvolysis of **admcl** in **hfip** and **tfe** is 170 while that for solvolysis of **tbucl** in these same two solvents is only 20. This is consistent with more hydrogen bond donation to the transition state for ionization of **admcl** than that from **tbucl**. The observation of the greater hydride donor ability of the bridgehead adamantyl hydride to cations[6d] supports this hypothesis. The alternative hypothesis that **hfip** is "more highly ionizing" than **tfe**, which allows the greater stability of the 1-adamantyl cation to manifest itself, is at odds with the calculations of ref 4. However, rather than argue from a comparison of just two solvents it is more insightful to examine a large range of solvents which reveal the importance of other factors, in particular, ground state destabilization, especially in water, that may have obscured the variable extent of hydrogen bond donation in *tert*-alkyl chloride solvolysis transition states.

Correlation of Solvolysis Rate Data

To analyze the **tbucl** and **admcl** solvolyses it is useful to attempt to correlate the rate data with various measures of solvent polarity. One popular measure of solvent "polarity" is the E_t30 value of the solvent.[7] This is defined as the shift in the UV absorption maximum of a dipolar dye upon changing solvent polarity, and this value is claimed to correlate **tbucl** rate data. However, of what physical meaning is the change in UV wavelength of a dipolar dye to a nonpolar excited state when the solvent is in a nonequilibrium distribution about the neutral excited state due to the vertical nature of the UV transition? Unfortunately, a popular (and insightful) multiple parameter solvent/rate correlation equation that was developed by Taft and

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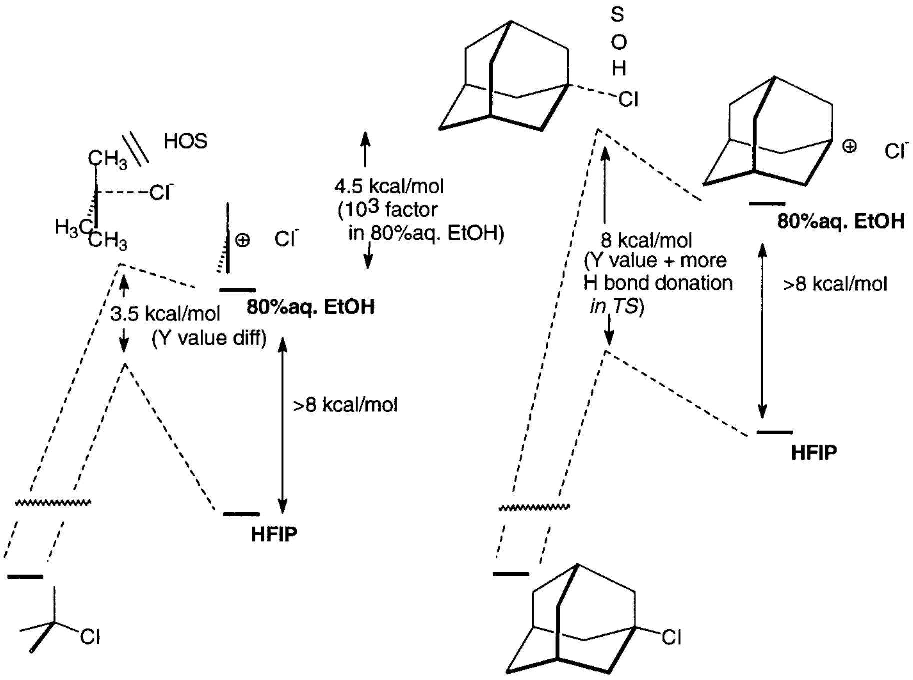
(5) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc.* **1948,** *70,* 846.

(6) (a) Fárcaşiu, D.; Jähme, J.; Rüchardt, C. *J. Am. Chem. Soc.* **1985**, *107*, 5717; *see also* Fárcaşiu, D.; Marino, G.; Harris, J. M.; Hovanes, B. A. *J. Org. Chem.* **1994**, *59*, 154. (b) Harris, J. M.; McManus, S. P.; Sedaghat-Herati, M. R.; Neamati-Mazraeh, N.; Kamlet, M. J.; Doherty, R. M.; Taft, R. W.; Abraham, M. H. In *Nucleophilicity*; Advances in Chemistry Series No. 215; Harris, J. M., McManus, S. P., Eds.; American Chemical Society: Washington, DC, 1987, pp 247−294. (c) Abraham, M. C.; Doherty, R. M.; Kamlet, M. J.; Harris, J. M.; Taft, R. W. *J. Chem. Soc., Perkin Trans. 2* **1987**, 913, 1097. (d) Kramer, G. M. *Tetrahedron* **1986**, *42*, 1071. (e) Similar conclusions have recently been reached through different considerations, see: Richard, J. P.; Toteva, M. M.; Amyes, T. L. *Org. Lett.* **2001**, *3*, 2225.

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

Scheme 2



co-workers[8] utilizes a parameter, π^*, that is also derived from solvochromic studies, so correlation with Taft's multiparameter equation provides a partly clouded insight into what might be responsible for the rate effects induced by solvent. Nonetheless, Taft and co-workers[6b] concluded that solvent electrophilicity is more important than solvent nucleophilicity in **tbucl** solvolysis after correlation of solvent rate data with their equation. Similar conclusions were drawn by Fárcaşiu.[6a]

It would appear appropriate to attempt to correlate the N (nucleophilicity) values of ref 3 with some measure of solvent basicity. Indeed, Taft and co-workers measured the spectroscopic responses of an OH bond to equimolar amounts of various solvents to assess the hydrogen bond basicity of the solvents. These responses were cast in terms of β values. However, an attempted correlation of N values with Taft's β values is, at best modest, $r = 0.76$ (Supporting Information).

KOMPH2

For mechanistically meaningful analysis of reactions it would seem reasonable to correlate solvent-induced rate effects by bulk physical and chemical properties of the solvents or well-defined functions of them. Thus we proposed the KOMPH multiparameter equation[9a] where solvent polarity is characterized by the Kirkwood–Onsager function of dielectric constant, $(\epsilon - 1)/(2\epsilon + 1)$,[9c,d] which is used in all of the standard Quantum Mechanics packages to address solvent polarity effects from a continuum dielectric medium. Also included in the KOMPH equation is the solvent cohesive energy density, CED, as defined by Hildebrand, namely, $(\Delta H_{vap} - RT)/V_{molar}$, which must be involved to characterize reactions involving interconversion of nonpolar with polar species or involve volume changes.[9g] And finally, solvent hydrogen bond donor and basicity parameters must be used that characterize the specific role of the solvent over and above its "polarity". These parameters, α' and β', respectively, are, in our view, best described by the free energies of transfer of chloride ion and potassium ion, respectively, between bulk solvents corrected for the solvent Kirkwood–Onsager function and its CED. The data are provided in a compilation by Marcus.[9e] Some of the initial ion transfer data were obtained by A. J. Parker, who utilized large counterions to lessen the effect of the counterion in each solvent.[9f]

KOMPH2 and *N* Values

Unfortunately, the β' values of the KOMPH equation and its updated version, KOMPH2,[9b] which anchors the α' and β' parameters to the gas phase, do not provide any better correlation of N values than the Taft β values. However, a reasonable correlation of N values (from ref 3, Table 5) can be obtained for the solvents, ^{i}PrOH, EtOH, MeOH, **tfe**, H_2O, **hfip**, HOAc, and HCO_2H, using more parameters, namely, the Kirkwood–Onsager function of dielectric constant, and α' values, along with the β' values. The correlation[10] is given in eq 2. The origin

$$2.303N = 37.0[(\epsilon - 1)/(2\epsilon + 1)] - 33.8\alpha' + 22.3\beta' - 14.0 \quad r = 0.987 \tag{2}$$

of the negative contribution of hydrogen bond donation is of concern particularly since the total contribution of negative

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[8] (a) For the most extensive set of parameters see: Abraham, M. H.; Grellier, P. L.; Abboud, J.-L. M.; Doherty, R. M.; Taft, R. W. *Can. J. Chem.* **1988**, *66*, 2673.

[9] (a) Gajewski, J. J.; Brichford, N. L. In *Structure and Reactivity in Aqueous Solution*; Cramer, C. J., Truhlar, D. G., Eds.; ACS Symposium Series No. 568; American Chemical Society: Washington, DC, 1994; pp 229–242. To obtain a copy of this version (KOMPH2) go to: http://php.indiana.edu/~gajewski/. (b) Gajewski, J. J. *J. Org. Chem.* **1992**, *57*, 5500. This equation was named the KOMPH equation after refs 9c–g: (c) Kirkwood, J. G. *J. Chem. Phys.* **1934**, *2*, 351. (d) Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486. (e) Marcus, Y. *Pure Appl. Chem.* **1983**, *55*, 977. (f) Cox, B. G.; Hedwig, G. R.; Parker, A. J.; Watts, D. W. *Aust. J. Chem.* **1974**, *27*, 477. (g) Hildebrand, J. H.; Prausnitz, J. M.; Scott, R. L. *Regular and Related Solutions*; Van Nostran Reinhold: Princeton, NJ, 1970. (h) A referee was concerned about the relative importance of various terms in the KOMPH2 equation. The Supporting Inforamtion also includes the total contribution to ln k of each term (coefficient times parameter value) for each solvent. The referee was also concerned about the dependence of the H-bonding ability on CED. These are poorly correlated parameters provided that alcohols, water, and fluorinated alcohols are used. Trifluoroethanol and hexafluoroisopropyl alcohol are superb hydrogen bond donating solvents but have low CEDs. Water and low molecular weight alcohols are good hydrogen bond donor solvents, but the CED of water is nearly three times that of methanol.

hydrogen bond donation (α') in each solvent is more than twice as large in an absolute sense as the solvent basicity (β') contribution. It would appear that the *N* values are more a compensation for the increased hydrogen bonding in the 1-admantyl chloride solvolysis transition state than a measure of the nucleophilic assistance in the *tert*-butyl chloride solvolysis transition state.

KOMPH2 and *tert*-Butyl Chloride Solvolyses

More significant in connection with solvent nucleophilicity is the correlation of the *tert*-butyl chloride solvolysis *Y* values for the solvents, EtOH, MeOH, **tfe**, **hfip**, H_2O, HOAc, and HCO_2H (ref 3, Table 6), with the KOMPH2 parameters. A good correlation is obtained, eq 3 , but the solvent basicity coefficient

$$2.303Y(\mathbf{tbucl}) = 30.4[(\epsilon - 1)/(2\epsilon + 1)] + 29.3\alpha' - 34.1\beta' + 17.4\mathrm{CED} - 24.5r = 0.987 \tag{3}$$

is *negative*; further, it has a substantial standard deviation. If the basicity term is omitted to determine if the rate changes of the **tbucl** solvolysis could be analyzed in terms of the other parameters, a reasonable correlation is still obtained (see eq 4

$$2.303Y(\mathbf{tbucl}) = 45.3[(\epsilon - 1)/(2\epsilon + 1)] + 44.4\alpha' + 12.4\mathrm{CED} - 36.4r = 0.943 \tag{4}$$

). In this correlation the coefficients are consistent with the importance of solvent polarity as defined by the Kirkwood−Onsager function of dielectric constant as well as hydrogen bond donation to the transition state, and ground-state destabilization by strong solvent−solvent interaction as defined by the Cohesive Energy Density.

Discussion of the KOMPH2 Correlation of *Y* Values

It should be noted that the standard deviations in the coefficients of eq 4 are roughly 40%, 20%, and 10%, respectively, of the values reported. The high standard deviation with the Kirkwood−Onsager coefficient is most likely the result of the narrow range of solvent polarities used, since only acetic acid has a modestly different Kirkwood−Onsager parameter from the others. It is reasonable that solvents which are much less polar should be included in the rate data measurements to assess the contribution of solvent polarity to the reaction. On the other hand, with the solvents used, the range of α' values is substantial, i.e., the value for **tfe** is 50% higher than that of ethanol and that of **hfip** is 2.5 times that of ethanol. Further, the range of solvent CED parameters is substantial in the data set, and the standard deviation reflects it. It is important to note as well that the β' values of the solvents used represent an enormous range from water to **hfip**. It is also useful to note that the β' parameters for the solvents used in eqs 3 and 4 are modestly correlated by the other three parameters with a coefficient of 0.758, and the α' parameters for the solvents used are poorly correlated by the other three parameters having a coefficient of 0.443. Finally, if the hydrogen bond donor parameter, α', were excluded in the analysis of the **tbucl** *Y* values used in eq 3, a poorer correlation is obtained (see eq 5

$$2.303Y(\mathbf{tbucl}) = 27.6[(\epsilon - 1)/(2\epsilon + 1)] - 67.0\beta' + 20.7\mathrm{CED} - 13.9r = 0.9 \tag{5}$$

); however, again, the coefficient of this basicity term is negative. Equation 5 would appear to be an excellent example of correlation without causality unless it is recognized that the basicity parameters, being modestly correlated with other parameters, reflect the contribution of these other parameters in the reaction with, of course, the hydrogen bond donating parameter contributing in a positive way. The conclusion from these analyses, eqs 3−5, is that solvent nucleophilicity plays no significant specific role in stabilizing the transition state for the **tbucl** solvolysis.

KOMPH2 Correlation of Ground States and Transition States in *tert*-Butyl Chloride Solvolyses

Concern about the lack of orthogonality of the parameters in the KOMPH2 equation should recognize that part of the problem is the range of solvents used in the reaction. If data over a much larger range of solvents is dissected into both ground state and transition state contributions,[11] a clearer picture emerges. For the ground state there is a small contribution from solvent basicity, but the dominant effect is destabilization as witnessed by a negative contribution of the CED term (see eq 6). So

$$\ln K_{\mathrm{transfer}}(\mathbf{tbucl}) = -0.2[(\epsilon - 1)/(2\epsilon + 1)] + 0.5\alpha' + 5.2\beta' - 11.5\mathrm{CED} - 2.0r = 0.946 \tag{6}$$

dominant is the CED term that a correlation of equivalent quality is obtained with only this parameter (see eq 7).

$$\ln K_{\mathrm{transfer}}(\mathbf{tbucl}) = -10.7\mathrm{CED} - 2.4r = 0.948 \tag{7}$$

In analyzing the effect of solvents on the transition state, a reasonable correlation is obtained where the dominant terms are the dielectric effect and the hydrogen bond donation of the solvents. The solvent basicity term contributes to a small extent but the standard deviation in its coefficient is 75% of the coefficient, and the CED term is small with an even larger percent standard deviation (see eq 8). If the basicity and CED

$$\ln K_{\mathrm{transfer}}(\mathbf{tbuclTS}) = 11.9[(\epsilon - 1)/(2\epsilon + 1)] + 43.2\alpha' + 10.6\beta' + 1.1\mathrm{CED} - 11.2r = 0.962 \tag{8}$$

terms are omitted in the analysis, the correlation is still reasonable (see eq 9). However, if the hydrogen bond donation

$$\ln K_{\mathrm{transfer}}(\mathbf{tbuclTS}) = 16.3[(\epsilon - 1)/(2\epsilon + 1)] + 41.6\alpha' - 11.4r = 0.959 \tag{9}$$

term is removed, a poor correlation is obtained and the coefficient of the β' term is again negative, indicating destabilization of the transition state which is compensated, *albeit* poorly, by increased contributions by both the dielectric effect and the CED (see eq 10).

$$\ln K_{\mathrm{transfer}}(\mathbf{tbuclTS}) = 40.6[(\epsilon - 1)/(2\epsilon + 1)] - 33.7\beta' + 14.3\mathrm{CED} - 17.3r = 0.709 \tag{10}$$

Concerns about Mechanism of *tert*-Butyl Chloride Solvolysis in More Nucleophilic Solvents: Correlation of *tert*-Butyl Chloride Transition State Free Energies in Solvents of Substantial Dielectric Constant with only the Hydrogen Bond Donating Parameter, α'

In any attempted correlation of *tert*-butyl chloride solvolysis data, there is concern that in solvents such as ethanol and isopropyl alcohol, which are not highly electrophilic nor have

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[10] The correlation coefficient equation used is that defined in the following: Swain, C. G.; Swain, M. S.; Powell, A. L.; Alunni, S. *J. Am. Chem. Soc.* **1983**, *105*, 502.

[11] Abraham, M. C.; Grellier, P. L.; Nasehzadeh, A.; Walker, R. A. C. *J. Chem. Soc.* **1988**, 1717.

high dielectric constants but are nonetheless Lewis bases, that the mechanism of solvolysis changes to one involving more nucleophilic participation so that the rates are substantially higher than what might have been anticipated for the pure ionization process. Further, the evidence for internal return in ion pairs with rate-determining nucleophilic attack and rearrangement out of ion pairs is well-established in secondary systems.[12] Thus, in *tert*-butyl chloride solvolyses, the rate-determining step may be different than in the 1-admantyl solvolyses in the less polar, more nucleophilic solvents. It should be noted that changes in rate-determining steps often result in poor responses to Linear Free Energy relations such as the Hammett equation. However, this is not the case in the analysis of the effect of solvent on the free energy of transfer of the *tert*-butyl chloride solvolysis transition states from solvents such as benzene through water using only the Kirkwood−Onsager function and the hydrogen bond donation parameter (see eq 9). To avoid any compensating behavior by the Kirkwood−Onsager function, removal of the solvents with low dielectric constant from Abraham's data for the relative transition state provides a data set that is correlated with only the hydrogen bond donating parameter (eq 11). The correlation includes the solvents **hfip**,

$$\ln K_{\text{transfer}}(\mathbf{tbuclTS}) = 39.8\alpha' - 2.8r = 0.965 \qquad (11)$$

tfe, water, ethylene glycol, formamide, methanol, ethanol, 2-propanol, 2-methyl-2-butanol, nitromethane, dimethyl sulfoxide, dimethylformamide, acetonitrile, and benzonitrile. The range of experimental free enegies is roughly 10 kcal/mol and the greatest deviation is with ethanol, which is calculated at what would be a rate factor of only 6.7 out of a range of 3.1×10^7! It is hard to make a case for a change in mechanism that necessarily must change the nature of the transition state in the *tert*-butyl chloride solvolysis. Further, the deviation in ethanol is such that the transition state is calculated to be more stable than it actually is so there is no evidence that ethanol's nucleophilicity stabilizes the transition state beyond the effect of hydrogen bond donation.

In this connection, it is appropriate to attempt a correlation of the rate data for solvolysis of 2-propyl tosylate using the KOMPH2 parameters. The result is a correlation coefficient of 0.996 where solvent dielectric constant, hydrogen bond donation, and basicity are important but not the cohesive energy density of the solvent. However, equally good correlations are obtained by removal of the α' or the β' or the CED term, which provide very different results. This multiple minimum result suggests that the solvent data set is insufficient to make distinctions (the solvent data set consists of only water, formic acid, acetic acid, methanol, and ethanol from ref 10).

Summary of *tert*-Butyl Chloride Solvolyses

If the correlation **tbucl** *Y* values by eq 4 represents causality in the solvolyses of *tert*-butyl chloride in the standard hydroxylic solvents, then it is clear that the solvent dielectric constant is important to stabilize a dipolar transition state, which in solvents of modest to high polarity appears to be constant in structure; that hydrogen bond donor ability is important, presumably to stabilize the developing chloride ion in the transition state; and that the ground state is destabilized in solvents of high cohesive energy density, especially in water. The latter effect would appear to be due to disruption of the hydrogen bonding network by the few nonpolar molecules that do dissolve. This disruption, which is also present to smaller, but variable extents in other alcohol solvents, is relieved upon formation of the dipolar transition state which can interact positively with these solvents.

KOMPH2 Correlation of 1-Adamantyl Chloride Solvolyses

The correlation of **admcl** solvolysis data in the same solvents as utilized for the **tbucl** solvolyses (ref 3, Table 8) is as good as that represented by eq 4. Here, of course, the solvent basicity parameter must be omitted (see eq 12). If solvent basicity is

$$2.303Y(\mathbf{admcl}) = 57.0[(\epsilon - 1)/(2\epsilon + 1)] + 72.1\alpha' + 12.6\text{CED} - 47.6r = 0.939 \quad (12)$$

included, a better correlation is obtained as in the **tbucl** solvolysis analysis; again, however, the coefficient of this term is negative and its standard deviation is large (50% of the coefficient, see eq 13). Clearly, solvent nucleophilicity in the

$$2.303Y(\mathbf{admcl}) = 38.2[(\epsilon - 1)/(2\epsilon + 1)] + 52.9\alpha' - 43.1\beta' + 18.9\text{CED} - 32.5r = 0.967 \quad (13)$$

1-adamantyl solvolysis should play no role so the correlation of eq 13 does not represent causality, but, in this case, it provides the suggestion that hydrogen bond donation is even more important than the coefficient of the α' term would indicate. Indeed, an important result of these correlations is that the magnitude of the solvent hydrogen bond donation is much greater in the **admcl** solvolysis than it is in the **tbucl** solvolysis whether the basicity parameter is included. This confirms part b of the hypothesis described above.

The conclusion here is that solvolyses of both **tbucl** and **admcl** have little if any component of solvent nucleophilic assistance, but hydrogen bond donation is more important in **admcl** solvolyses presumably because of greater access of the solvent to the developing chloride ion. And finally, besides the obvious dielectric effect, solvent−solvent interaction, particularly in water, can destabilize the ground state leading to enhanced rates of solvolyses.

Solvolyses of Dimethylsulfonium Salts

It is useful to examine solvolysis reactions where the leaving group is charged in both the ground state and the transition state to assess the relative stabilities of the cations. In these reactions the effects of solvent dielectric constant, hydrogen bond donation, and CED should be substantially less than in the solvolyses of the chlorides. The solvolysis of *tert*-butyldimethylsulfonium chloride, **tbudmscl**, was studied by Swain[13] and was found to be not very dependent on the counterion. Further, the rates were remarkably independent of solvent polarity from acetic acid to water, indeed, the rate range is only a factor of 2. However, the reaction is roughly 15% faster in ethanol than in methanol, unlike **tbucl** solvolysis where the reaction is roughly 10 times faster in methanol than in ethanol. Kevill has provided additional data on this solvolysis (using the triflate counterion which does not affect the rate relative to chloride ion) and this reveals that the reaction is slower in **tfe** by a factor of roughly 6,[14] and in **hfip** the reaction is slower by another factor of

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(12) (a) Winstein, S.; Robinson, C. G. *J. Am. Chem. Soc.* **1958**, *80*, 169. (b) Winstein, S.; Appel, B.; Baker, R.; Diaz, A. *Special Publication No. 19*; The Chemical Society: London, 1965; p 109. (c) Shiner, V. J., Jr. In *Isotope Effects in Chemical Reactions*; ACS Monograph 167; Collins, C. J., Bowman, N. S., Eds.; Van Nostrand Reinhold Company:, New York, 1970; Chapter 2.

(13) Swain, C. G.; Kaiser, L. E.; Knee, T. E. C. *J. Am. Chem. Soc.* **1958**, *80*, 4092.

(14) Kevill, D. N.; Kamil, W. A.; Anderson, S. W. *Tetrahedron Lett.* **1982**, 4635.

roughly 3.5.[15] So hydrogen bond donor solvents which are also weakly basic significantly slow the reaction. This observation has been interpreted in terms of less nucleophilic participation in solvents such as **tfe** and **hfip**.[15]

For comparison, 1-adamantyl dimethylsulfonium triflate, **addmstf**, has been studied by Kevill[15] and found to undergo solvolysis slower than **tbudmscl** in ethanol at 50 °C by a factor of roughly 200. While the rate factor is not as large as in the solvolysis of chlorides, it is substantial. Further, the response of the rate to solvents is very small with the largest effect being rate increases in the better hydrogen bond donor (or it is emphasized the less basic) solvents. Thus the rate of solvolysis of the *tert*-butyl dimethyl sulfonium salt in **hfip** is only a factor of roughly 3 faster than that of **addmstf**. This then is cited as evidence for nucleophilic solvent participation in *tert*-butyl cases, particularly in ethanol solvent.[15]

To examine the rate effect of all pure solvents used, the rate data at 50 °C from **tbudmscl** and the corresponding triflate salt, remembering that the counterion makes little difference, were analyzed with the KOMPH2 equation described above to give a modest correlation, eq 14 , where both hydrogen bond donation and solvent basicity retard the rate.

$$\ln k_{\mathrm{rel}}(\mathbf{tbudmscl}) = -2.4[(\epsilon - 1)/(2\epsilon + 1)] - 12\alpha' - 2.4\beta' - 0.7\mathrm{CED} + 6.0r = 0.913 \quad (14)$$

However, the standard deviations in all coefficients except that for hydrogen bond donation are large so a better correlation could be obtained by using only that term (see eq 15). It is remarkable that the coefficient of the hydrogen bond donor parameter is negative. The explanation for diminished hydrogen bond stabilization of the transition state relative ground state is not obvious. It is important to note, however, that at best a poor correlation of the rate data can be obtained by excluding the α′ term but retaining the solvent basicity term (see eq 16), which suggests that nucleophilic participation by the solvent is not involved. The solvolysis of **tbudmscl** therefore is easily dissected into only one important contributing factor, namely, hydrogen bond loss from ground state to transition state and not nucleophilic solvent participation.

$$\ln k_{\mathrm{rel}}(\mathbf{tbudmscl}) = -11.3\alpha' + 4.8r = 0.95 \quad (15)$$

$$\ln k_{\mathrm{rel}}(\mathbf{tbudmscl}) = 0.4[(\epsilon - 1)/(2\epsilon + 1)] + 13.4\beta' - 1.3\mathrm{CED} - 1.0r = 0.437 \quad (16)$$

Examination of the rate data from solvolyses of 1-adamantyl dimethylsulfonium triflate, **addmstf**,[15] at 70 °C with KOMPH2 yields only a poor correlation with substantial standard deviation in the Kirkwood−Onsager, the basicity, and the CED terms (see eq 17). If only the α′ parameter is used the correlation is better (see eq 18). The correlation, such as it is, suggests that the dominant factor is a small degree of hydrogen bond donation to the transition state. The dimethylsulfonium solvolyses are remarkable in that the rate differences diminish in more hydrogen bond donating, less basic, solvents just as in the case of the chlorides. The contrast between the chlorides and the dimethylsulfonium salts, however, is that in those hydrogen bond donating, weakly basic solvents, the chlorides increase in rate with the adamantyl chloride increasing faster, but with the dimethylsulfonium ions, the major change is rate retardation of the *tert*-butyl derivatives. It is important to note that the intercept in eqs 15 and 17 indicates that in the gas phase, the *tert*-butyl salt would solvolyze roughly 100 times *faster* than the 1-adamantyl salt even though the temperature is 20 deg lower. This, of course, is not what would actually be observed because of the increased stability of the 1-admantyl cation relative to the *tert*-butyl one in the gas phase due to polarizability effects as described above. However, as extrapolated from solutions of high dielectric constant, the intercepts reveal the increased stability of the *tert*-butyl cation over the 1-adamantyl case in the high dielectric constant media.

$$\ln k_{\mathrm{rel}}(\mathbf{addmstf}) = 2.7[(\epsilon - 1)/(2\epsilon + 1)] + 5.7\alpha' + 1.9\beta' - 0.1\mathrm{CED} - 1.7r = 0.573 \quad (17)$$

$$\ln k_{\mathrm{rel}}(\mathbf{addmstf}) = 5.1\alpha' - 0.1r = 0.787 \quad (18)$$

Further Arguments for Nucleophilic Solvent Participation and Responses

Bentley (p 134 of ref 3) argued against the Fárcaşiu/Taft/Harris suggestion of increased solvent electrophilicity in 1-adamantyl chloride solvolyses[6a,b] stating: "but it is not explained why the additional electrophilicity term for fluorinated alcohols is *absent* in comparisons of Y_{OTs} and Y_{Cl}. ... Also, for solvolyses of alkyldimethylsulfonium ions, solvent electrophilicity is relatively unimportant and the effects of the low nucleophilicities of fluorinated alcohols can be observed."

To address Bentley's first concern, there should be hydrogen bonding to the oxygens of a departing tosylate group just as there is with chloride. Indeed, a correlation of the Y_{OTs} values given in Bentley's chapter[3] (Table 5) which are derived from solvolysis of 1- and 2-adamantyl tosylates reveals substantial solvent hydrogen bond donation (solvent electrophilicity) to the transition state (see eq 19). Here the β′ term is excluded because nucleophilic assistance should be absent, and indeed, the standard deviation in its coefficient in an analysis which includes it is large (Supporting Information).

$$2.303Y_{\mathrm{OTs}} = 36.9[(\epsilon - 1)/(2\epsilon + 1)] + 58.3\alpha' + 12.5\mathrm{CED} - 34.9r = 0.975 \quad (19)$$

However, what is actually necessary is a comparison of 1-adamantyl tosylate to *tert*-butyl tosylate to find the same enhanced electrophilicity in the 1-adamantyl case. Unfortunately these data are not available because of the instability of the material so the Bentley argument cannot be totally discounted, but its basis seems incorrect. Finally, there does appear to be a small increase in electrophilicity, i.e., increased hydrogen bond donation from the solvent in the transition state for 1-adamantyl dimethylsulfonium ion solvolyses relative to that of *tert*-butyldimethylsulfonium ion solvolyses; however, the correlations appear to suffer from lack of data or perhaps incorrect data to make a strongly defendable hypothesis.

The proponents of solvent nucleophilic participation have tried to dismiss the Taft multiparameter approach to solvolyses which long ago pointed out the lack of dependence of the rate on solvent basicity, and, as developed above, the KOMPH2 equation shows the same behavior. Kevill[15] implies that the solvent nucleophilic participation is small but not inconsequential: "A problem with multiparameter equations is that inclusion of a minor contributor will not meaningfully improve the correlation if its contribution is significantly less than the sum of the deviations associated with the other parameters." The concern should be focused on a rationalization of the negative (or inverse) dependence on solvent basicity in the *tert*-alkyl

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[15] Kevill, D. N.; Anderson, S. W. *J. Am. Chem. Soc.* **1986**, *108*, 1579.

chloride solvolyses reflected in the KOMPH2 approach if there is reluctance to allow the dismissal of a contributor with a large standard deviation. An inverse dependence on solvent basicity, if actually involved, would appear to require increased stabilization of the ground state not the transition state by more basic solvents in *both* the *tert*-butyl chloride and 1-adamantyl chloride solvolyses.

Finally it is worthy of note that the methanolysis of a tertiary phthalate studied by Doering and Zeiss resulted in 54% inversion and 46% racemization.[16] In a recent, exhaustive study Müller found that a *tertiary* chloride underwent solvolysis with 60 ± 20% net inversion in methanol, ethanol, formic, and acetic acid with similar results for a *p*-nitrobenzoate leaving group.[17] However, in TFE, both substrates gave net retention to the extent of 13% and 40%, respectively. The extent of olefin formation was 50 ± 25% in all solvents. The inversion noted in ethanol is substantially less than what might be expected for a factor of roughly 10^3 that is claimed to be the backside nucleophilic component of the solvolysis of *tertiary* chlorides in ethanol, i.e., the fact that *tert*-butyl chloride undergoes solvolysis roughly 10^3 times faster in ethanol than does 1-adamantyl chloride. However, while these results indicate that the classical planar cation is not the product-forming intermediate from *tertiary* derivatives in solvolysis, they indicate remarkable consistency in the fate of whatever intermediate is formed, except in the case of the very good hydrogen bond donor solvents. What is striking is that on an energy scale, the differences between the various reaction pathways pale into insignificance against the dramatic response of the rates to changes in solvent that are addressed here.

Concerns about Multiparameter Correlation Approaches to Solvent Effects

Standard criticisms of multiparameter correlations revolve about the need for many data points, the nature of the parameters, and therefore the meaningfulness of any correlation. Almost no recognition is given to the fact that statistics, and therefore meaningful evaluations, result from the use of a factor analysis provided there are $N + 1$ more solvent data points than parameters and the intercept. Almost no recognition is given to the need to use parameters or factors that are as orthogonal as possible, or at least to consider the impact of lack of orthogonality, and the need to utilize solvents which represent extremes of each parameter or factor. The cases where the data seem insufficient or inadequate for unambiguous analysis are noted in the discussion. For instance, the use of just ethanol, methanol, acetic acid, and formic acid provides little insight into the importance of any of the factors utilized in KOMPH2. The addition of water would help to address the CED contribution and the further addition of TFE and HFIP would address the hydrogen bond donation.[9h] To assess the importance of solvent basicity, DMSO and DMF should be used. To assess the importance of solvent dielectric constant, cyclohexane and benzene should be used.

There should also be concern about the involvement of other factors, among them, polarizability. However, except for the acid−base reactions of solvent molecules in the gas phase, in our hands, no solution correlation has benefited from the additional use of a polarizability parameter. Further, the KOMPH2 equation is incomplete. For instance, the solvophobic nature of fluorocarbons toward hydrocarbon solutes cannot be addressed with the factors in KOMPH2. In addition, surface tensions are only modestly correlated with KOMPH2, and reactions whose rates depend on solvent viscosity cannot be treated yet. This is not an exclusive list, but it does represent some of the continuing challenges to understand the important role of solvents in chemical reactions.

Conclusions

(1) increasing solvent dielectric constant promotes faster S_N1 reactions of all *tert*-alkyl chlorides and may alter the relative stabilities of cations compared with those in the gas phase particularly if there is a size difference in the cations. The Kirkwood−Onsager function provides a measure of the effect of dielectric constant on the reaction.

(2) Increased hydrogen bond donation to the leaving group promotes faster S_N1 reaction with all *tert*-alkyl chlorides, especially those which give rise to more pyramidal cations. Hydrogen bond donation is quantifiable using the free energies of chloride ion transfer between solvents.

(3) Water is a unique solvent for these reactions. The enormous rate increase of solvolysis reactions in water is a result of substantial destabilization of the neutral ground state in water and in other solvents which are highly associated due to hydrogen bonding. Further, this effect is quantifiable by the Hildebrand Cohesive Energy Density.

(4) There is no evidence for significant nucleophilic participation of the solvent in the S_N1 reaction of any *tert*-alkyl chloride ***in any solvent*** given the excellent correlations of the *tert*-butyl chloride transition state with only the hydrogen bond donor parameter and the Kirkwood−Onsager Function. Secondary halides are a different story, and this is well-documented. Solvent basicity can be gauged by the free energy of transfer of potassium ion between different solvents.

(5) Correlation of solvent effects with fundamental physical and chemical properties of bulk solvents provides insight into the nature of differences between ground state and transition state that help move mechanistic analysis from correlation to understanding at a more fundamental level provided that a sufficient number of different types of solvents are utilized in rate and equilibrium studies.

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Supporting Information Available: All of the data and statistical analyses (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[16] Doering, W. von E.; Zeiss, H. H. *J. Am. Chem. Soc.* **1953**, *75*, 4733.

[17] Müller, P.; Rossier, J. C. *J. Chem. Soc., Perkin Trans. 2* **2000**, 2232.