Correlation of Solvolysis Rates 50 Years Later

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In 1948, Grunwald and Winstein[1] introduced the concept of "ionizing power of the solvent", ***Y***, based on the strong influence of the solvent on the solvolysis rate of alkyl halides in general and *tert*-butyl chloride in particular (Scheme 1).

Y is calculated from the following equation

$$\boldsymbol{Y} = \log k^{\mathrm{tBuCl}} - \log k_0^{\mathrm{tBuCl}} \qquad (1)$$

where k^{tBuCl} and k_0^{tBuCl} are the solvolysis rate constants at 25 °C for *tert*-butyl chloride in the solvent concerned and in an 80% v/v ethanol/water mixture; the latter datum is used as reference for the process.

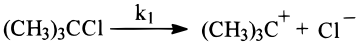
The strong solvent dependence of the solvolysis of *tert*-butyl chloride (e.g., the rate decreases by a factor of 90 from water, where $k = 3.3 \times 10^{-2}$ s^{-1}, to 50:50 v/v ethanol/water, where $k = 3.67 \times 10^{-4}$ s^{-1}, and by as much as 340 000 times from this mixture to pure ethanol, where $k = 9.70 \times 10^{-8}$ s^{-1}) was examined by Grunwald and Winstein[1,4] in the light of the Brönsted equation. They found the logarithmic coefficients of activity for the reactant (f_{tBuCl}) and transition state ($f^{\ddagger}_{\mathrm{tBuCl}}$) to vary linearly in a series of mixtures and the variation to be largely the result of changes in f_{tBuCl}. By contrast, in the more poorly ionizing solvents, changes in k are primarily due to changes in $f^{\ddagger}_{\mathrm{tBuCl}}$.

In a series of papers,[1−8] Grunwald and Winstein showed that, the solvolysis rate constant for organic halides which exhibit values differing by more than 6 orders of magnitude in this parameter can generally be accurately described by the following equation

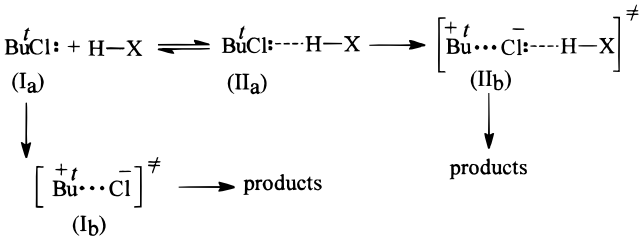
$$\log k = mY + \log k_0 \qquad (2)$$

where k and k_0 are the rate constants in the solvent concerned and the 80:20 ethanol/water mixture, and coefficient m represents the ease of solvation of the halide in question relative to *tert*-butyl chloride. In fact, the solvolysis of *tert*-butyl chloride is one of the cornerstones of physical organic chemistry.[9−11] Thus, some quantitative approaches to the kinetics of spontaneous reactions in various solvents (and, more interesting, solvent mixtures) are based on linear free-energy relations such as that of Grunwald and Winstein[1] or its extensions.[10,12−16] These equations allow one to interpolate or extrapolate rate constants that cannot be readily measured and also to derive mechanistically significant information in the process.

Scheme 1



Scheme 2



In the beginning, the mechanism by which *tert*-butyl chloride is solvolyzed[1−3] was assumed to depend on the polarity and electrophilicity of the reaction medium in a wide range of solvents. Koppel et al.[16] proposed a scheme for the process (Scheme 2) where H-*X* is the electrophilic agent, and structures $\mathrm{I_b}$ and $\mathrm{II_b}$ are the respective highly polar ($\mu^{\ddagger} \gg \mu$) ion-pair-like transition states. However, the initial assumption that *tert*-butyl chloride solvolysis is insensitive to solvent nucleophilicity was later questioned, and the process was considered to be influenced by the nucleophilic characteristics of the solvent as well.[11,13−15,17−21]

Several authors have correlated the solvolysis rate of *tert*-butyl chloride with various solvent property scales.[16,22−24] In 1972, Koppel and Palm[16] found log k values at 25 °C in 23 pure solvents to correlate with their

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polarity (Y), polarizability (P), and electrophilicity (E) solvent scales via the following equation[25]

$$\log k = 5.67(\pm 0.86)Y + 17.27(\pm 3.31)P + 0.379(\pm 0.034)E - 19.50(\pm 1.29) \quad (3)$$

with $n = 23$ and $r = 0.982$. They thus concluded that "the nucleophilic properties of the media are unimportant".

In 1981, Abraham et al.[22] used their solvatochromic model to analyze log k values for the solvolysis of *tert*-butyl chloride in 15 pure solvents and found it to depend exclusively on solvent polarity and acidity

$$-\log k = -6.94\pi^* - 5.25\alpha + 15.06 \quad (4)$$

with $n = 15$ and $r = 0.995$. They excluded trifluoroethanol from their solvent list because it was relatively poorly self-associated and could have resulted in increased stabilization of the reactant state (form II_a); solvation of such a reactant state would slow the forward rate and/or increase the fraction of internal return. In response to several criticisms,[15] these authors[23] revisited the problem by considering the data for this type of solvent and also the effects of basicity (nucleophilicity) and the Hildebrand solubility parameter, δ_H^2, a term related to the differential energies required to produce cavities in a solvent for reactant and transition states.[26] They obtained the following correlation equation for an overall 21 solvents:[28]

$$\log k = 5.10(\pm 0.37)\pi^* + 4.17(\pm 0.11)\alpha + 0.73(\pm 0.21)\beta + 0.48(\pm 0.07)\delta_H^2 - 14.60(\pm 0.29) \quad (5)$$

with $n = 21$, $r = 0.997$, and sd = 0.242.

In 1983, Swain et al.[24] correlated log k for eight solvents on the basis of their anion-solvating tendency (acity, A) and cation-solvating tendency (basity, B); they obtained the following equation

$$\log k = 4.74(\pm 0.37)A + 1.38(\pm 0.35)B - 2.18(\pm 0.38) \quad (6)$$

with $n = 8$ and $r = 0.995$. The dependence of k on B led them to assert that "this should dispel the long-standing myth that solvent nucleophilicity does not affect the rates of *tert*-butyl solvolyses".[29]

Because it is so sensitive to the solvent (or solvent mixture) characteristics (k increases by a factor of 6.6×10^{17} from the gas phase to water), this process is a suitable model for analyzing the solvent effect in broad terms, using both pure solvents and solvent mixtures. In the past few years, our group has developed pure solvent scales such as the polarity−polarizability (SPP), acidity (SA), and basicity (SB) scales. SPP for a solvent is computed from the solvatochromism of the probe 2-*N*,*N*-dimethyl-7-nitrofluorene and its homomorph 2-fluoro-7-nitrofluorene; SPP values range from 0 in the absence of solvent (i.e. in the gas phase) to 1 for DMSO.[31,32] SB is based on the solvatochromism of the probe 5-nitroindoline and its homomorph *N*-methyl-5-nitroindoline; values range from 0 for the gas phase to 1 for tetramethylguanidine.[30] Finally, SA is evaluated from the solvatochromism of the probe *o*-*tert*-butylstilbazolium betaine dye and its homomorph *o*,*o*′-di-*tert*-butylstilbazolium betaine dye and encompasses values from 0 for the gas phase to 0.4 for ethanol.[33] The acidity of solvents more acidic than methanol (SA = 0.6) is evaluated by applying the solvatochromic comparison method[34] to solvatochromism measurements of the probe 3,6-diethyl-1,2,4,5-tetrazine.[35]

The above-mentioned probes, which have provided so excellent scales for analyzing pure solvents, have also been used to determine SPP, SA, and SB for binary solvent mixtures. A detailed discussion of the measurements and their results, and the conclusions derived from the well-established preferential solvation model, will be presented in a future paper.

This paper reports on the analysis of 148 experimental log k values corresponding to the gas phase, 27 pure solvents,[36] and 120 aqueous binary mixtures of methanol (31 mixtures), ethanol (31), isopropyl alcohol (1), trifluoroethanol (8), dioxane (13), acetone (27), and acetic acid (9).[37] Of special interest is the inclusion of eight data for aqueous mixtures of trifluoroethanol on account of its role in the nucleophilic assistance to the process. The ensuing equation is[38]

$$\log k = 10.62(\pm 0.44)\mathrm{SPP} + 7.89(\pm 0.17)\mathrm{SA} + 1.71(\pm 0.22)\mathrm{SB} - 20.07(\pm 0.34) \quad (7)$$

with $n = 148$, $r = 0.990$, and sd = 0.40.

It should be noted that our solvent parameters (SPP, SA, and SB) provide accurate descriptions of the experimental data set examined [see eq 7 and Figure 1], especially if one considers that the set includes not only 27 pure solvents but also a substantial number of binary solvent mixtures.

On the basis of our equation, the solvolysis rate of *tert*-butyl chloride is increased by the solvent: all its effects contribute to accelerating the solvolytic process. The accelerating effect is largely the result of the solvent

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(28) This fit excludes aromatic solvents to avoid the need to include the polarizability term, δ, and also the gas phase for lack of parameter values.

(29) This conclusion should be taken cautiously as the basicity scale of Swain et al. is known to describe not solvent basicity but rather solvent polarity−polarizability (see Figures 9 and 10 in ref 30).

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(36) The experimental data values for log k corresponding to solvents (water, methanol, ethanol, *n*-butanol, *n*-hexanol, *n*-octanol, 2-propanol, 2-methyl-2-propanol, ethylene glycol, glycerol, 2,2,2-trifluoroethanol, formamide, *N*,*N*-dimethylformamide, *N*,*N*-dimethylacetamide, *N*-methylpyrrolidone, acetonitrile, acetone, acetic acid, ethyl acetate, 1,4-dioxane, tetrahydrofuran, benzene, chlorobenzene, nitrobenzene, nitromethane, diethyl ether, *n*-heptane) and the gas phase were compiled from the following: (a) References 22 and 23 and references therein. (b) *Tables of Rate and Equilibrium Constants of Heterolytic Organic Reactions*; Palm, V. A., Ed.; Moscow, 1977; Tom. II, Vol. II.

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(38) This equation has been determined using the program MINITAB. Inc. State College PA (USA) v. 9.

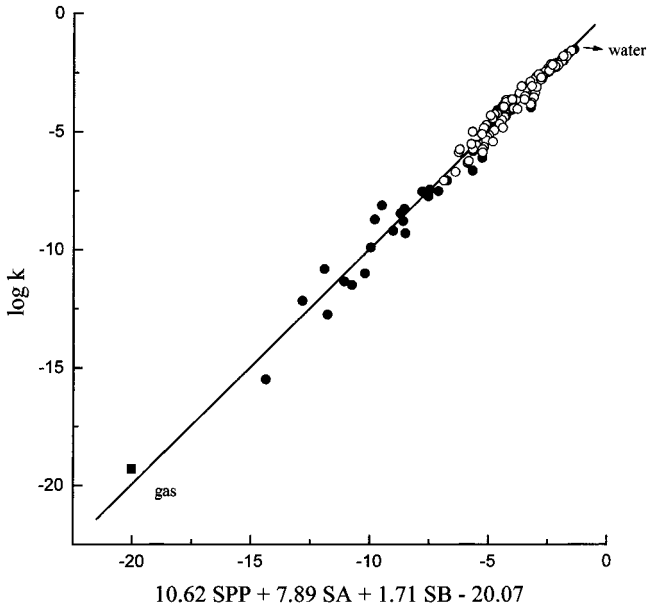

Figure 1. Plot of the experimental log *k* values at 25 °C for the solvolysis of *tert*-butyl chloride versus the predicted values by eq 7 corresponding to the gas phase (■), 27 pure solvents (●), and 120 binary solvent mixtures (○).

polarity−polarizability (e.g., the kinetics is 6300 faster in *n*-heptane than in the gas phase). In the condensed phase, however, acidity contributes only slightly less than polarity (10.62 vs 7.89) to the effect. One other fact worth noting is that, based on our scales, the process is favored by an increased basicity of the medium (i.e. nucleophilically assisted). Figure 1 confirms the applicability of the proposed equation to account for vast changes in polarity, acidity, and basicity, taking into account that the rate of the process varies over a range of about 20 orders of magnitude.

The favorable results with this kinetics data provided by our solvent scales, and additional evidence currently being obtained by our group,[39] confirm that the scales are suitable for describing the solvolytic behavior of solvent mixtures. This makes the proposed approach a highly useful tool for understanding and rationalizing other phenomena of chemical and biochemical interest such as protein folding and unfolding in aqueous mixtures of denaturing agents.

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