Solvent Effects in Organic Chemistry. V. Molecules, Ions, and Transition States in Aqueous Ethanol[1]

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Kinetic studies of many solvolysis reactions by other workers have shown remarkable minima in ΔH^* at 0.8 to 0.9 mole fraction of aqueous ethanol. Partial molal heats of solution at infinite dilution are reported herein for a number of carefully chosen salts and nonelectrolytes through the same solvent range. These show endothermic maxima where ΔH^* for solvolysis usually give minima. The size of the maximum depends primarily on the volume which the solute molecules occupy. Furthermore, the size of the maximum is greater for nonelectrolytes than for salts of comparable molecular size. This gives an empirical explanation of the ΔH^* minima which are observed for reactions in which a nonpolar ground state goes to a polar transition state. Data are cited from a recent review to support the idea that addition of alcohols to water increases the structuredness of the solution to a maximum in the region noted above. Addition of a small amount of a third component to highly aqueous ethanol solutions appears to result in less structure formation than when addition is made to pure water. By addition of the heat of solution of the ground state to ΔH^* it is possible, in some cases, to calculate exactly how the heat of solution of the transition state changes with solvent composition. Several such cases are discussed. These results are interpreted qualitatively in terms of the Frank–Evans picture of aqueous solutions.

Introduction

The most powerful means for influencing rates and yields of many reactions is through solvent variation. The effect of such a change on rate is often many-fold larger than that produced by a change of molecular structure and has the great practical advantage, for synthetic purposes, that the unmodified substrate molecule is used. The past 30 years have seen enormous progress in the empirical correlation of substituent effects on rates and equilibria through linear free energy relationships.[2,3] During the same period it has become increasingly clear that the interaction of solvents with molecules, ions, and radicals often cannot be accounted for satisfactorily by continuum properties of the solvent, such as dielectric constant, but that quite specific interactions between substrate and solvent molecules are also important.

Solvation through hydrogen bonding, ion–dipole, or dipole–dipole interactions occurs by means of the close association of suitable functional groups on the substrate and solvent molecules and so has many of the characteristics of a chemical reaction. Thermodynamically, solvation may be considered in the same general terms as the modification of the properties of the substrate molecule by substituent changes, the solvating molecules being equivalent to loosely attached substituents.[3] It is therefore to be hoped that empirical correlations of the linear free energy type may be developed which will be useful for predicting solvent effects and that eventually something approaching a useful structural theory of solvation on a par with our present structural theory of substitution may develop. We would like nothing better than to have this paper contribute to such a theory. However, even a detailed thermodynamic dissection of the energy and entropy changes produced by adding a solute to a solvent will only reflect the combined effects of solvent–solute, solvent–solvent, and solute–solute interactions.[3] Although solute–solute interactions can be cancelled out of the following treatment, it will be seen that solvent–solvent interactions are probably very important. For the introduction of a third component to a binary solvent the number of mixed solvent–solute and solvent–solvent interactions is so large that even in favorable cases (and that discussed here is not one) it would be dangerous to suggest molecular structures for solvation complexes from over-all thermodynamic properties alone.

The most ambitious attempt to correlate reaction rates (free energies of activation) with solvent composition is that of Winstein[4a–i] and his students. However, it is clear from the classic contribution of Winstein and Fainberg[4d] that apparently simple solvent effects on free energy often obscure dramatic and complicated changes in the enthalpy and entropy of solvation (because of the compensation phenomenon).[3,5,6] The latter two properties must therefore be carefully examined if we wish to understand the fundamentals of solvent effects.

The influence of solvent variation on reaction rate may be examined in terms of changes in the activation parameters ΔF^*, ΔH^*, and ΔS^*. However, each of these quasi-thermodynamic properties merely represents the difference between the corresponding properties of the transition state and the ground state in the medium. Generally, for the activation parameter P^*

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[1] This research was supported by grants from the National Science Foundation (G-14583 and GP-2014) and National Institutes of Health (GM-10872).

[2] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940.

[3] J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963.

[4] (a) E. Grunwald and S. Winstein, *J. Am. Chem. Soc.*, 70, 846 (1948); (b) S. Winstein, E. Grunwald, and H. W. Jones, *ibid.*, 73, 2700 (1951); (c) A. H. Fainberg and S. Winstein, *ibid.*, 78, 2770 (1956); (d) S. Winstein and A. H. Fainberg, *ibid.*, 79, 5937 (1957); (e) A. H. Fainberg and S. Winstein, *ibid.*, 79, 1597 (1957); (f) A. H. Fainberg and S. Winstein, *ibid.*, 79, 1602 (1957); (g) A. H. Fainberg and S. Winstein, *ibid.*, 79, 1608 (1957); (h) S. Winstein, A. H. Fainberg, and E. Grunwald, *ibid.*, 79, 4146 (1957); (i) M. Cocivera, Thesis, University of California at Los Angeles, 1963.

[5] J. E. Leffler, *J. Org. Chem.*, 20, 1202 (1958).

[6] R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, pp. 69–73.

$$\Delta P^* = \Delta\bar{P}^t - \Delta\bar{P}^g \qquad (1)$$

where $\Delta\bar{P}^t$ corresponds to the partial molal property for transferring the transition state from a reference state to the medium and $\Delta\bar{P}^g$ represents a similar value for the ground state. The effect of variation of a binary solvent on an activation parameter is best considered then in terms of how ΔP^*, $\Delta\bar{P}^t$, and $\Delta\bar{P}^g$ change as the medium is altered from one of its pure components through the series of mixtures[7] under examination. Plainly, no firm conclusions can be drawn about property changes ($\Delta\Delta\bar{P}^t$) associated with the transition state from changes in the activation parameter ($\Delta\Delta P^*$) unless the corresponding change for the ground state property ($\Delta\Delta\bar{P}^g$) is known. However, it also follows that *if both* $\Delta\Delta P^*$ *and* $\Delta\Delta\bar{P}^g$ *are measured, then a complete analysis is possible*, and the effect of changing the transition state property $\Delta\Delta\bar{P}^t$ may be calculated directly with as much precision as the less precise of its two components $\Delta\Delta P^*$ or $\Delta\Delta\bar{P}^g$.

Over the past decade some very careful measurements of the effect of binary solvent change on the activation parameters for a number of reactions have been made in the laboratories of Winstein,[4] Robertson,[8] Tommila,[9] and Hyne.[10] Particular attention should be drawn to SN1 solvolytic reactions since for them the observable ground state goes to an easily visualized ion-pair-like (henceforth called salt-like) transition state. Hopefully, the study of solvent effects will contribute to a further understanding of this simple organic reaction.

In several cases[11-18] analyses of free energy changes including $\Delta\Delta\bar{F}^t$ have been made since $\Delta\Delta\bar{F}^g$ may be obtained with relative ease from Henry's law constants for the substrate (if it is sufficiently volatile) over the same part of the solvent spectrum used for the study of rate variations ($\Delta\Delta F^*$). However, the much more revealing values of $\Delta\Delta\bar{H}^t$ and $\Delta\Delta\bar{S}^t$ have not been examined until very recently because of the problems associated with measuring $\Delta\Delta\bar{H}^g$.

It has usually been suggested that $\Delta\Delta\bar{H}^g$ be gotten from the temperature coefficient of Henry's law for the reacting solute.[4i,8e,9e] This is undesirable theoretically since it requires very precise data and assumes that $\Delta\bar{H}^g$ does not vary with temperature. From a practical point of view it is to be avoided because of the appalling amount of labor required, and because it cannot be applied to some of the most important cases involving nonvolatile substrates or those that undergo very rapid solvolysis; for example, *t*-butyl chloride in highly aqueous ethanolic solutions.

Recently, we described a direct approach to the problem through measurement of the partial molal heat of solution ($\Delta\bar{H}_s$) of the substrate in relevant solvent mixtures by means of a special solution calorimeter.[19] This was applied to the solvolysis of *t*-butyl chloride in aqueous ethanol. Since that time we have made similar measurements on other compounds for which the variations of ΔH^* with changing medium have already been determined. We shall present here some of our results for the heats of solution of appropriate nonelectrolytes and salts for comparison with some solvolytic transition states. A rough interpretation of the results will be advanced.

We may relate ΔH^* for the reaction in solution to $\Delta\bar{H}_s{}^g$ for the ground state based on itself as a pure liquid or solid by the following cycle,[4d,8e] where the superscripts *, g, and t again refer to the activation process, the ground state, and transition states, respectively, while s, l, and v apply to the process or species in solution, pure liquid, or vapor state. For interpreting the effect of changing solvent on the transition state the term $\Delta\Delta\bar{H}_s{}^t$ is desired. This represents the enthalpy change associated with conveying the transition state from the vapor phase to the solution being studied. It is easily obtained from the cycle if $\Delta\Delta H_s{}^*$ (change in heat of activation in solution) and $\Delta\Delta\bar{H}_s{}^g$ (change in heat of solution of the ground state) are known, since the heat of vaporization of the ground state ($\Delta\bar{H}_v{}^g$) and the heat of activation in the vapor phase ($\Delta H_v{}^*$) are constant. The *variation* in heat of solution of the ground state with solvent composition ($\Delta\Delta\bar{H}_s{}^g$) is independent of the standard state chosen since it is possible to make as many hypothetical transfers as desired from one state to another to get from the vapor to the solution. However, this is not true for the actual ΔH values themselves. Since we shall usually measure $\Delta H_s{}^g$ from a pure liquid or solid ground state this will differ by $\Delta H_v{}^g$ from the value which might be obtained from temperature variation of Henry's law.

$$\begin{tikzcd}
RX_v{}^g \arrow[r, "\Delta H_v{}^*"] & R\text{- - -}X_v{}^t \arrow[dd, "\Delta\bar{H}_s{}^t"] \\
RX_l{}^g \arrow[u, "\Delta\bar{H}_v{}^g"'] & \\
RX_s{}^g \arrow[u, "-\Delta\bar{H}_s{}^g"'] \arrow[r, "\Delta H_s{}^*"] & R\text{- - -}X_s{}^t
\end{tikzcd}$$

Experimental[20]

I. Calorimeter. The calorimetric equipment that is needed for the program outlined above must meet a number of requirements. It should be capable of giving results rapidly so that many compounds in many solvent mixtures can be studied. Compared to modern high precision calorimeters[21,22] it need not be very

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[7] In contrast to variation of substituents, which is discontinuous, solvent variation is (at least macroscopically) a continuous process.

[8] (a) R. E. Robertson, *Can. J. Chem.*, **31**, 589 (1953); **33**, 1536 (1955); (b) P. M. Laughton and R. E. Robertson, *ibid.*, **33**, 1207 (1955); (c) J. B. Hyne and R. E. Robertson, *ibid.*, **34**, 863 (1956); (d) *ibid.*, **34**, 931 (1956); (e) R. E. Robertson, R. L. Heppolette, and J. M. W. Scott, *ibid.*, **37**, 803 (1959).

[9] (a) E. Tommila, *Suomen Kemistilehti*, **B25**, 37 (1952); (b) L. Pekkarinen and E. Tommila, *Acta Chem. Scand.*, **13**, 1019 (1959); (c) J. Murto and E. Tommila, *ibid.*, **16**, 63 (1962); (d) E. Tommila, *et al.*, *Ann. Acad. Sci. Fennicae, Ser A. II*, **No. 91** (1959); (e) E. Tommila and M. Murto, *Acta Chem. Scand.*, 17, 1947, 1957, 1985 (1963).

[10] (a) J. B. Hyne, *J. Am. Chem. Soc.*, **85**, 304 (1963); (b) J. B. Hyne and R. Wills, *ibid.*, **85**, 3650 (1963); (c) J. B. Hyne, R. Wills, and R. E. Wonkka, *ibid.*, **84**, 2914 (1962); (d) J. B. Hyne, *ibid.*, **82**, 5129 (1960).

[11] A. R. Olson and R. S. Halford, *ibid.*, **59**, 2644 (1937).

[12] A. R. Olson, W. O. Ruebsamen, and W. E. Clifford, *ibid.*, **76**, 5255 (1954).

[13] P. D. Bartlett, *ibid.*, **61**, 1630 (1939).

[14] S. Winstein, *ibid.*, **61**, 1635 (1939).

[15] R. Clement, J. N. Naghizadeh, and M. R. Rice, *ibid.*, **82**, 2449 (1960).

[16] R. Clement and J. N. Naghizadeh, *ibid.*, 81, 3154 (1959).

[17] D. N. Glew and E. A. Moelwyn-Hughes, *Discussions Faraday Soc.*, **15**, 150 (1953).

[18] D. N. Glew and E. A. Moelwyn-Hughes, *Proc. Roy. Soc.* (London), **211**, 254 (1952).

[19] E. M. Arnett, P. McC. Duggleby, and J. J. Burke, *J. Am. Chem. Soc.*, **85**, 1350 (1963).

[20] A description of the apparatus and techniques given here was presented at the Pittsburgh Analytical Conference in March 1964.

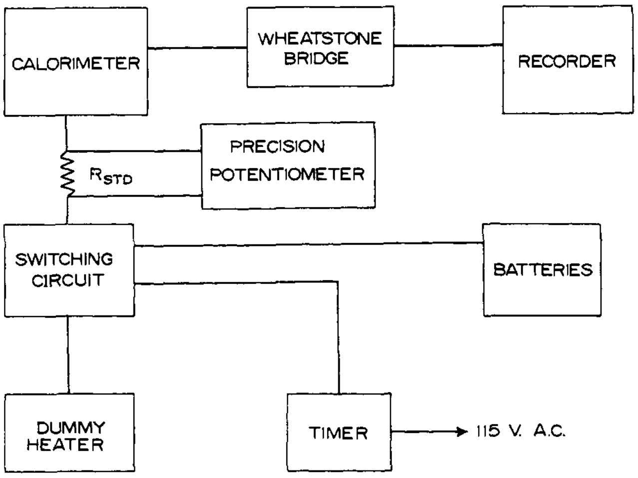

Figure 1. Block diagram of calorimeter system.

accurate nor precise since heats of activation are rarely known to better than the nearest 0.1 kcal./mole. It should be sensitive enough so that partial molal heats of solution can be obtained directly without the need of multiple runs at different concentrations. This is made more difficult by the practical necessity of keeping the total volume of the solution low in order to avoid the handling of enormous amounts of mixed solvents. The calorimeter should record the heat of solution rapidly so that errors from heat of reaction will not be a problem in the cases of compounds that solvolyse rapidly. Rapid response will also reduce errors from base line drifts due to heat of stirring and heat leaks. Although this has not been a problem in the work described here, the usefulness of this simple calorimeter is limited to rapid heat changes. Finally, it is desirable that the calorimeter be easy and inexpensive to construct. The apparatus to be described below meets all of these requirements. Our equipment is shown schematically in the block diagram Figure 1 and will be discussed in terms of its component parts.

The calorimeter vessel (Figure 2) is a standard 300-ml. dewar jar of 4.5-in. depth and 2.5-in. i.d. To reduce heat exchange between the contents of the calorimeter and its environment even further, all experiments were conducted in a room held at 25 ± 2°, and the contents of the calorimeter were routinely kept at 25 ± 0.5°. The temperature coefficient of $\Delta\bar{H}_s$ for the reactions under study is too small to introduce error due to slight deviations from 25.0° at our level of precision.[23] This is an important point since it means that the calorimeter and its contents need not be completely immersed in a constant temperature bath

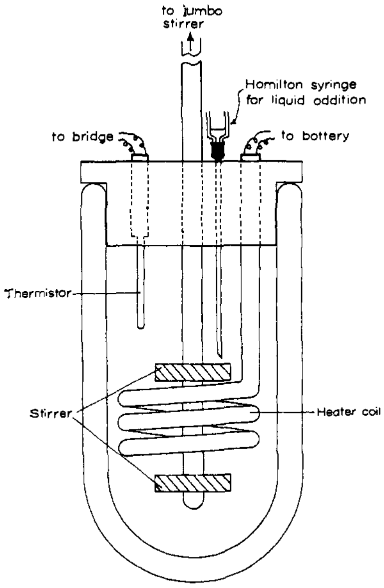

Figure 2. The solution calorimeter.

as would be required for high precision work. The saving in time normally required for long equilibration periods and the avoidance of complicated apparatus for sample introduction is a major reason for our ability to gather results rapidly.

The top of the calorimeter is machined from a piece of 3.25-in. diameter Teflon rod to fit snuggly into the top of the dewar jar. This serves as thermal and electrical insulation, prevents evaporation, and supports the thermistor, electrical heater (and cooling well if necessary) while providing an excellent bearing surface for the stirrer shaft. A small hole is also drilled through this stopper for introduction of liquid samples or, if solid samples are to be used, a larger hole is drilled to accommodate the apparatus used for that purpose (see Procedure). A terminal strip for electrical contacts is also screwed onto this stopper.

The temperature-sensing element is a VECO No. 32A1 thermistor with a resistance of 2000 ohms ± 20% at 25° (or 5000 ohms, see below) purchased from the Victory Engineering Corp., Springfield, N. J. Two 3-in. leads of 24 enameled manganin wire are soldered to the themistor after first cutting the original leads quite short. The thermistor is now mounted in the end of a $1^3/_8$-in. length of 7-mm. o.d. Pyrex tubing by means of a machined Teflon adaptor, manganin leads emerging from the top of the tube, and the thermistor from the bottom. The tube is filled with paraffin wax and mounted in the Teflon calorimeter head. This method of assembly is required in order to have the thermistor element properly placed about half-way down in the dewar and also to permit easy replacement of broken thermistors.

A spiral heater jacket is made from a 2-ft. length of 8-mm. o.d. Pyrex tubing. It is sealed at the lower end (after the heating coil has been inserted), and the upper end is bent so as to parallel the projection of the axis of the coil. The heater is suspended perpendicularly in the calorimeter by thrusting this extension through a tight-fitting hole in the Teflon top. The heater resistance is made[22] by winding about 100 ohms (9 ft.) of 36 enameled manganin wire on a mandrel into

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(21) J. M. Sturtevant, "Physical Methods of Organic Chemistry," Vol. I, A. Weissberger, Ed., 3rd. Ed., Interscience Publishers, Inc., 1959, Chapter 10.

(22) W. F. O'Hara, C. Wu, and L. G. Hepler, *J. Chem. Educ.*, **38**, 512 (1961).

(23) Recent direct measurements of heats of hydrogen bonding by Mr. Norman Edelstein in our laboratory have shown an easily detectable variation of ΔH with temperature. In order to maintain constant temperature, when necessary, a well is introduced into the calorimeter in the form of a 15 cm. × 10 mm. glass tube sealed at the bottom and supported by the calorimeter head. This extends down toward the bottom of the calorimeter. After the recorder has traced a temperature rise, a long, 7-mm. o.d. tube carrying a small charge of Dry Ice is introduced into the 10-mm. well and is removed as soon as the recorder pen has returned to the base line. In this way many measurements may be made in a day without changing the temperature in the calorimeter as much as a hundredth of a degree.

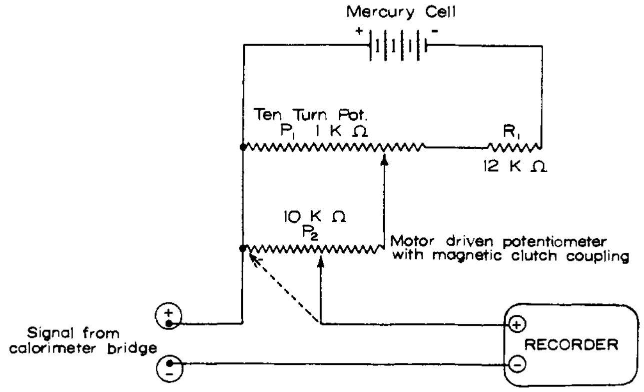

Figure 3. Diagram of the base-line compensator.

a bifilar coil of small enough diameter to allow an easy fit inside the heater jacket. Three-inch lengths of copper 24 wire are then soldered on to provide leads of low electrical resistance while still keeping thermal leakage small. After the solder joints are varnished and insulated, the coil is removed from the mandrel and carefully worked into its spiral jacket with the aid of an aspirator vacuum at its lower end. Before assembly, the heater unit may be aged in an oven at 120–140° for 24–48 hr. to reduce drifting resistance when it is in operation. After the lower end of the jacket has been sealed off, it is nearly filled with paraffin oil and the last inch is sealed with paraffin wax with the copper leads emerging. The resistance of the heater is determined accurately by calibration against an NBS one by means of the potentiometer. If the heater is properly cured, its calibration need be checked only every 3 months.

A dummy heater is also included in the circuit to stabilize the batteries when the calorimeter heater is not being used. This is made of 36 manganin wire of sufficient length to give a resistance equivalent to that of the calorimeter heater (100 ohms) plus the 10-ohm standard resistance (R_s) used to measure the current through the calorimeter during a thermal calibration. The dummy heater is enclosed in a straight length of Pyrex tubing, sealed at its lower end, filled with paraffin oil, and capped at the top with paraffin wax. It is suspended through a rubber stopper in a 500-ml. flask filled with paraffin oil and at all times, except during thermal calibration, the batteries (two 6-v. Willard DD-3-3 low-discharge type in series) are discharged through it. Its resistance need not be known with accuracy and can be measured with an ohmeter.

Good stirring is probably the most difficult problem in designing a calorimeter for this work. Many of the substrates are of low solubility in the aqueous ethanol solutions considered here, and some also dissolve slowly. It is necessary to be sure that a saturated solution is not approached too closely when the chosen quantity of substrate is injected. This can be tested by seeing that the measured heat of solution is independent of sample size for small samples. It is especially important that samples of light, difficultly soluble substrates should not rise to the surface in single drops and float there without dissolving. Furthermore, the heat of solution or heat from thermal calibration must be dissipated swiftly and evenly through the calorimeter so that the thermistor soon registers the average temperature of the contents.

The effectiveness of agitation should be tested in questionable cases by replacing the dewar flask with an unsilvered glass container of the same dimensions and then injecting a sample under normal agitation conditions while observing the behavior of the sample through the wall of the simulated calorimeter.

After considerable trial and error with many kinds of stirrers over several years we find the most effective one for a calorimeter of the type described here to be that shown in Figure 2. A pair of 20-mm. o.d. Teflon impellors are made to fit on an 8-mm. o.d. Pyrex shaft. Ten blades are cut, each about 5 mm. deep and slightly pitched to drive liquid toward the bottom of the calorimeter. These are slid on the shaft into the positions shown, slightly above and below the heating coil. In operation, the shaft is driven by a Fisher Jumbo stirrer at a constant speed. We find that this arrangement gives superior circulation and speed of solution with low base-line noise and surprisingly little heat of stirring.

A Sargent Model S-R recorder with 1.0-, 2.5-, and 5.0-mv. range plugs and a Leeds and Northrup No. 8687 potentiometer are used. The Wheatstone bridge circuit is that described by Jordan.[24] We have also used a Sargent bridge (S-81601) successfully with a 5000-ohm thermistor.

Time is measured with a Standard timer (Model S-1-3H-15) purchased from the Standard Electric Timer Co., Springfield 2, Mass. This is synchronized to the passage of current through the heater coil by means of a heavy silver, low-resistance switch (4620-S) purchased from Shallcross Manufacturing Co., Selma, N. C., designed to eliminate switching lag or slight variation of resistance in the switch.

Our standard 10-ohm resistor (General Radio) was calibrated against an NBS standard and found to be 10.0022 ohms at 25°.

Great care must be taken to see that all parts of the apparatus are thoroughly grounded and that stray fields are prevented by twisting the lead wires for compensation.

II. Base-Line Compensator. In order to measure a heat change precisely, it is necessary that a straight base line be displayed on the recorder both before and after addition of the solute. Heat of stirring and constant heat leaks to or from the outside cause the base line to drift steadily, usually in a positive direction. It is, therefore, likely that a quarter or a third of the width of the chart will be effectively wasted by base-line drift before and after introducing the heat change to be measured. Since the precision of our method depends on the size of pen displacement, it is obviously desirable to reduce or eliminate systematic base-line drifts. This is accomplished through the simple apparatus shown in Figure 3 which supplies a gradually changing voltage to the recorder to oppose that from the thermistor bridge. In this manner flat base lines before and after heat injections are obtained easily, and full utilization of the chart paper is realized. This base-line compensator has obvious application to other laboratory techniques such as gas chromatography.

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(24) J. Jordan, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **19**, 193 (1958).

Table I. Measurement of Heat of Solution of Potassium Chloride in Water at 25°

Calibration measurements				Wt. of KCl, mg.	Heats of solution		
E, v.	Time, sec.	Δ_c,[a] mm.	Q_e/Δ_c × 10^2		Δ_R,[b] mm.	Q,[c] cal.	ΔH, kcal./mole
1.12532	45.06	220	6.202	84.0	75	4.673	4.15
1.12532	45.01	219	6.223	165.1	145	9.035	4.08
1.13196	44.98	218	6.248	118.2	107	6.667	4.21
1.13196	44.99	218	6.249	159.8	143	8.910	4.16

[a] Recorder deflection from passage of current through heater for time t to produce heat Q_e. [b] Recorder deflection from introduction of sample. Heat of solution of sample in calories; $Q = Q_e\Delta_R/\Delta_c$.

III. Procedure. About 1.5 hr. is required for the recorder, the bridge, the potentiometer, and the battery discharge through the dummy heater to become stabilized before measurements can be made. While these components are warming up, the calorimeter is filled with the solvent for study (at 25 ± 0.5°) to a point which will leave only a small dead space between the liquid and the calorimeter top, which is now put in place. The stirrer is started and the recorder pen is brought to the lower end of its scale by means of the bridge.

With proper stirring, the calorimeter and its contents soon reach thermal equilibrium at which point the recorder traces a steady line with slight exothermic drift due to heat of stirring. Now the base-line compensator may be adjusted to remove this drift. When operating properly, the apparatus should be able to record a straight line for at least 0.5 hr. when undisturbed.

A calibration is now made by introducing a measured number of calories through the heater coil. The silver switch is thrown starting the timer and heater, and the potential drop across the standard resistance is measured at once with the potentiometer. Heating is continued for a long enough period to give a full pen displacement (250 mm.) when allowance is made for establishment of a straight base line both before and after the heating period. The length of time will vary with the specific heat of the solution and its volume, the heater resistance, and range plug of the recorder; aqueous solutions in our apparatus usually require 25–45 sec. Use of the base-line compensator permits a longer heating period since allowance need not be made for base-line drift before and after heating. This gives a more accurate calibration. The current (I) through the heater circuit may be easily calculated from the standard resistance and the voltage drop across it during the heating period.[22] The electrical heat introduced in terms of calories thus is $Q_E = I^2Rt/4.184$ where I is the current through the heater of resistance R and t is the time of heating in seconds; R is usually constant over a period of 6 months. The system has now been calibrated in terms of cal./mm. of recorder scale. (Although we originally made three such calibrations before each sample introduction and three afterwards, agreement between them was usually so good that this has been reduced to two before and one after.)

Presented in Table I are data for a typical run with solid sample injection. Probably the most important factor in permitting rapid measurements of heats of solution is the technique of sample introduction which avoids the usual sealing in thin-walled ampoules.[21,22] For liquids, a 250-μl. Hamilton syringe with Chaney adapter is employed. Calibration with water shows that these impliments have a high accuracy and precision when nearly full, the error being less than 1%. Much depends on the technique of introduction. The liquid is drawn into the barrel through the 4-in. (N720 purchased from Hamilton Co., Whittier, Calif.) needle considerably beyond the volume that is ultimately to be delivered. Some of the excess is now forced out with the syringe held vertically, needle up, to eliminate air bubbles, and wiped dry. It is now lowered carefully through the hole for the needle until it comes to rest in a vertical position. The plunger is forced down gently until it is stopped by the Chaney adapter and the syringe is left untouched in position while the base line again stabilizes, usually for about 2 min. This hiatus is necessary to dissipate heat absorbed from the operator's hands. The sample is now introduced by twisting the adapter to the delivery position and then rather quickly pushing the plunger down—slow delivery tends to make less soluble materials emerge in large drops that dissolve slowly. Under optimum conditions the heat of solution may be recorded within 1 sec.—even if the pen overshoots, the heat is measured by the difference between the base lines before and after sample introduction.

Solids are introduced conveniently by means of the device shown in Figure 4. The needle end of a plastic disposable syringe is sliced off with a razor, and the plunger is fitted with a short glass cylindrical stop to prevent pushing the rubber tip into the solution when the sample is delivered. A Teflon wafer, cut with a cork borer from sheet stock, is placed on the rubber plunger tip and a glass collar is slid inside the barrel. This serves as a container for the solid sample and prevents its being crushed or compressed when the plunger is pushed during delivery. The collar is secured to the end of the plunger by a short length of fine nichrome or platinum wire so that it will not be tossed about in the calorimeter after injection. The sample (30–100 ± 0.2 mg.) is weighed into the collar chamber. The tight-fitting Teflon plug is now seated firmly in the end of the barrel and the assembly is mounted in the calorimeter head through an appropriate hole in such a way that it is immersed only to the level of the Teflon wafer. After thermal equilibration has occurred, as shown by the recorder trace, the plunger is depressed until it hits the stop, whereupon the plug at the end falls out, and the collar drops a short distance into the solvent until it is arrested by its wire leash. At this point, most of the solid in the collar has fallen into the swirling solvent, and any residue in the collar is immediately flushed out so that

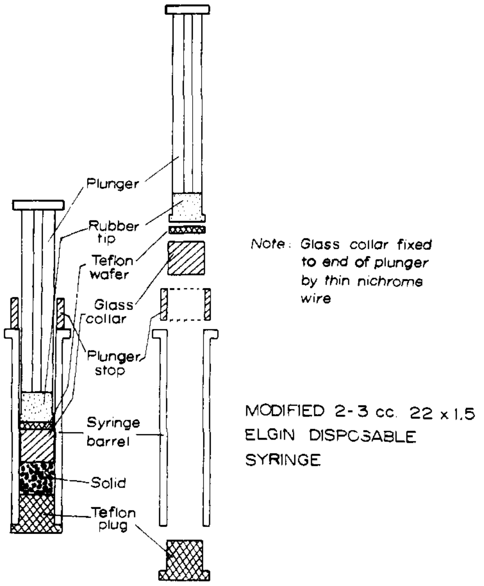

Figure 4. Device for the addition of solid samples.

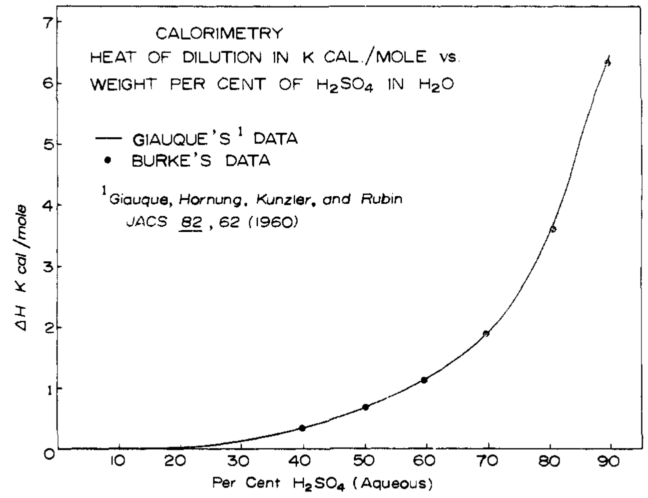

Figure 5. Comparison of our results with those from high-precision calorimetry.

complete solution is usually almost instantaneous unless the solute is fairly insoluble. Suitable control experiments in which no sample is used show that no measurable heat change is produced by the sample introduction apparatus itself, provided that equilibration time is allowed and work is done close to ambient temperature. In practice, the gathering of data is only about half as fast with solid solutes as with liquid ones.

IV. Errors. The size of the deflection, and therefore of the error, depends upon the size of the sample, the heat of solution, and the specific heat of the system, as well as instrumental factors, so no single estimate of error can be applied to our experiments. Although temperature changes as such are not considered in our calculations, we have found that for aqueous solutions a full 250-mm. deflection (1 mv.) generally corresponds to *ca.* 0.070° so that 0.0003° may be detected.[24a]

Many systematic errors such as unexpected electrical fluctuations or thermal leaks can cause inaccurate results, although precision is maintained. Frequent checks for accuracy are therefore recommended. We have used the work of Giauque, *et al.*,[25] on the partial molal heat of solution of water in aqueous sulfuric acid solutions. A typical comparison of our results with theirs is shown in Figure 5. As another check, our average value for the heat of solution of potassium chloride in water is 4.15 ± 0.03 compared to the accepted value of 4.185 ± 0.001.[26]

Our measurements are effectively *partial molal heats of solution at infinite dilution* as shown by our ability to inject five to ten samples of the more soluble substrates into the same solution without producing any change in the measured heat of solution outside experimental error. In practice we never inject more than three replica samples in the same solution and, of course, use only one sample of the less soluble substrates (less than enough for saturation).

V. Materials. Aqueous ethanol solutions of $x\%$ ethanol were prepared by mixing in the proportions of x ml. of absolute ethanol and $(100 - x)$ ml. of distilled water at 25°. At first graduated cylinders were used but more recently appropriate combinations of volumetric flasks were employed to obtain greater accuracy. This change made no perceivable difference in our results or in the refractive indices of the solutions.

The liquid solutes *t*-butyl chloride, *n*-butyl chloride, isopropyl bromide, *t*-butyl alcohol, carbon tetrachloride, ethyl acetate, and benzyl chloride were of the best grade available from Fisher or Eastman. They were dried over Drierite and distilled to a proper, constant boiling point. The fraction to be used was routinely tested for purity by gas chromatography. Methyl and *n*-propyl benzenesulfonates were prepared from benzenesulfonyl chloride and the alcohols according to the method of Robertson.[8a] They were distilled and the cut with proper refractive index used.

The potassium halides were Baker and Adamson reagent grade and were vacuum dried at 160°. Tetraphenylarsonium chloride was used as received from Eastern Chemical Corp. The tetramethyl- and tetrabutylammonium salts were Eastman White Label materials. They were recrystallized, the former from ethanol and the latter from ethyl acetate, and then vacuum dried at 80°. Fisher reagent grade sodium tetraphenylboride was used without further purification.

Dimethyl *t*-butyl sulfonium iodide was generously provided by Professor J. B. Hyne. It was recrystallized from ethanol and dried before use.

Results and Discussion

Before examining our results in detail, it may be wise to put them in perspective against some relevant facts about the media we are using.

1. Solvent Structure in Aqueous Alcohol Solutions. Aqueous solutions command a special position in

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[24a] NOTE ADDED IN PROOF. Recently we have improved our sensitivity by a factor of 30- to 50-fold by means of a variable recorder amplifier purchased from Instruments and Communications, Inc., Wilton, Conn. This will permit us to extend our range of measurements to a number of compounds which were too insoluble for consideration in the present report.

[25] W. F. Giauque, E. W. Hornung, J. E. Kunzler, and T. R. Rubin, *J. Am. Chem. Soc.*, **82**, 62 (1960).

[26] (a) G. Somson, J. Coops, and M. W. Tolk, *Rec. trav. chim.*, **82**, 231 (1963); (b) R. J. Irving and I. Wadsö, *Acta Chem. Scand.*, 18, 195 (1964).

chemistry due to water's natural abundance, biological importance, and excellence as a medium for electrolytes. Because of the formal similarity of alcohols to water, their aqueous solutions have received particular attention. However, in view of the poor state of solution theory at present, it is asking too much that binary mixtures of these useful but complex solvents containing a third component should not only be useful but also be amenable to facile and detailed interpretation.

The Ingold–Hughes[27] theory of solvent effects gives a helpful picture of the influence of medium on SN1 reactions predicting that the salt-like transition state will be more strongly solvated relative to a nonpolar ground state as the solvent polarity increases, thus speeding the reaction. Although ΔF^* generally does behave in conformity with this principle, ΔH^* and ΔS^* often undergo variations which indicate that more complicated interactions are occurring.[4–10] To our knowledge, the wild fluctuations of ΔH^* and ΔS^* (especially the extrema in the high water end of the solvent spectrum) are peculiar to aqueous solutions but not to aqueous alcohols alone.[9]

Realization of this has prompted some workers in the field to introduce new refinements of the Ingold–Hughes theory in terms of specific solvation of ground and transition states,[8,10,28] and these have often been quite detailed. These views are related to the Debye[29] theory of Coulombic solvent sorting for salts giving special priority to water as an ion solvator. That this cannot always be so is demonstrated by the fact that dioxane may be a better cation solvator than water in aqueous dioxane solutions.[30]

These theories have tended to emphasize the role of solvation of the salt-like transition state in considering the chemical details of the events taking place. This was natural, since the necessary thermodynamic properties for solution of the ground states were lacking, and intuitively one would suppose their contributions to activation parameters would be small compared to those for the more polar transition state. However, a number of facts cast doubt on this interpretation. (a) The heats of solution for salts in highly aqueous methanol[31] solutions show only modest changes in $\Delta\bar{H}_s$ in the same solvent mixtures where activation parameters may change sharply. If the transition state in an SN1 reaction is salt-like and if the large minima in heats of activation are due to selective solvation of it, we should have expected salts themselves to show larger extrema. Furthermore, the effect on salts is in an endothermic rather than an exothermic direction as they pass through the high water region in methanol. (b) A good portion of the difference in activation parameters for *t*-butyl chloride solvolysis when going from methanol to 70.5% methanol is due to change in ground state solvation.[4d] (c) It has been observed recently for the solvolysis of *t*-butyl chloride in highly aqueous ethanol solutions that changes in the heat of solution for the ground state are almost wholly responsible for the observed change in the heat of activation.[19] (d) There is no evidence at all that we know of from careful product studies for solvolysis reactions in the extrema region of highly aqueous alcohol solutions[4i] that the *composition* of the solvent shell around the transition state is different from that around the ground state. However, the *interaction* of the two different states with the solvent must be different or there would be no variation in ΔH^* as the solvent changes.

The results to be described below were anticipated in our previous publication[19] which showed that nonpolar ground states may cause endothermic maxima in the same solvent region of aqueous ethanol (*ca.* 0.9 mole fraction of water) where heats of activation are most apt to show minima. The magnitude of such a maximum for a given nonelectrolyte is related to the size of the nonelectrolyte molecule (just as Slansky's work[31] shows the effect of ionic size for salts) and is greater than that for salts of the same molar volume. Roughly speaking then, the primary factor determining the size of the $\Delta\Delta\bar{H}_s$ maxima for the compounds we have examined is the size of the molecular entities being introduced into the solvent, and their polarities are an important but secondary consideration. Also, specific solvent–solute interactions due to the shape of the particle and functional groups attached to it are, doubtless, of some moment. This at once suggests that the main effect of adding the solute arises from its influence on the solvent. It would seem suitable, therefore, to digress at this point to consider the known facts about the aqueous alcohol solutions into which our solutes will be put. Fortunately, this complex matter has recently been the subject of a review article.[32]

Of primary importance to us is the fact that the extrema like those for activation parameters and heats of solution in highly aqueous alcohol solutions are found also for other physical properties related to solvent structure that take place in the absence of chemical events. *The introduction of a molecule, ion, or transition state is, therefore, just another means of perturbing the solvent structure.*

The exact nature of liquid water is by no means well understood.[33] However, there is general agreement that it is a very highly structured liquid. Many of its properties suggest that it is a mixture of fluctuating regions of three dimensional hydrogen-bonded polymers in equilibrium with randomly arranged H_2O monomer molecules.[34]

At room temperature and pressure pure aliphatic alcohols also have a considerable fraction of their molecules joined in rings and chains, but they do not seem to participate in formation of the three-dimensional clusters that are characteristic of water.[32]

It would be natural to suppose that as alcohol is added to pure water the structure of the latter would be destroyed progressively as the alcohol content increased. If this were so, the introduction of a third solute would assist in structure breaking and heat would be absorbed in proportion to the size of the hole produced by the added solute molecules. The attractive simplicity of

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(27) C. K. Ingold, "Structure and Mechanism in Organic Chemistry, Cornell University Press, Ithaca, N. Y., 1953, Chapter 7.

(28) G. Kohnstam, Special Publication No. 16, The Chemical Society, London, 1962.

(29) P. Debye, *Z. physik. Chem.* (Leipzig), 130, 56 (1927).

(30) E. Grunwald, G. Baughman, and G. Kohnstam, *J. Am. Chem. Soc.*, **82**, 5801 (1960).

(31) C. Slansky, *ibid.*, **62**, 2430 (1940).

(32) F. Franks, *Quart. Rev.* (London), in press. We are very grateful to Professor Franks for much helpful criticism and discussion and for permitting us to use a preprint of his article.

(33) G. Nemethy and H. A. Scheraga, *J. Chem. Phys.*, **36**, 3382 (1962).

(34) H. S. Frank, National Academy of Sciences Publication 942.

Table II. $\Delta\Delta\bar{H}_s$ for Various Nonelectrolytes

Compd.	Mole fraction of water											
	0.582	0.684	0.726	0.765a	0.798	0.830	0.857	0.884	0.906	0.929	1.00	$\Delta\bar{H}_s^{g}$ [a]
t-BuCl	−1.56	−0.94		0.00		+1.04	+1.06	+0.81	+0.54	−0.03		+3.35
n-BuCl	−1.67	−1.02		0.00		+1.29		+1.03		−0.05		+3.54
i-PrBr	−1.49	−1.02		0.00		+0.93		+1.10		−0.49		+3.28
CCl_4	−1.45	−1.08	−0.40	0.00	+0.55	+0.40	−0.10	−0.50	−2.01	−2.65		+2.65
t-BuOH	−0.28	−0.08	+0.12	0.00	−0.28	−0.28	−0.67	−0.98	−2.04	−2.84	−4.49	+0.28
$MeOSO_2C_6H_5$			−0.43	0.00	+0.61	+1.15	+1.74	+2.55				+4.68
EtOAc	−0.72	−0.41	−0.35	0.00	−0.03	+0.17	+0.11	−0.19	−0.85	−1.74	−4.33	+1.97
$C_6H_5CH_2Cl$	−1.90	−0.98	−0.62	0.00	+0.62	+1.46	+1.88	+1.61	+0.68	+1.43		+4.58
EtOH	0.00	+0.044		0.00		−0.096			−0.93		−2.40	0.00
H_2O	0.00	−0.02	0.00[b]	0.00	+0.02[b]	+0.03	+0.07[b]	+0.11[b]	+0.15[b]	+0.18[b]	+0.230	−0.23

[a] Reference solvent; 50 vol. % ethanol. [b] Interpolated from values provided through generosity of Professor L. G. Hepler.

this notion, however, is challenged by the very maxima and minima to which our attention has been directed which suggest that structure breaking must go through a maximum in the high water region of the solvent spectrum. However, if the only effect of adding alcohol to water were to break down its structure, we would expect this to gradually reach a plateau, and then level off until nearly pure alcohol was reached, at which point the disrupting effect of adding water on the structure of pure alcohol would begin to be felt.

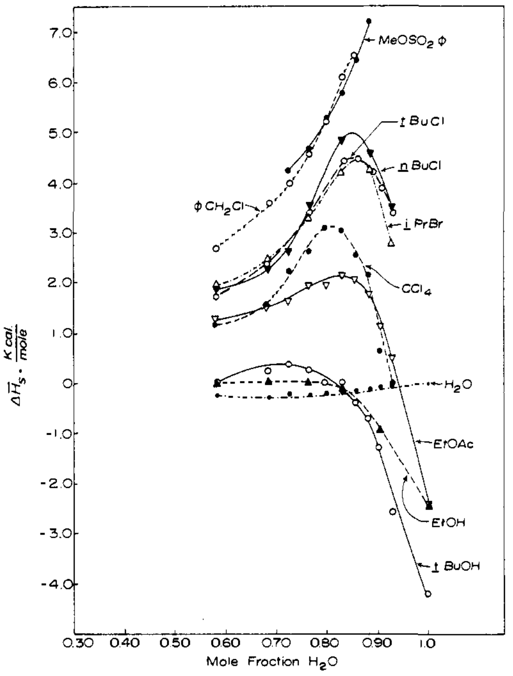

Figure 6. Variation of partial molal heat of solution at infinite dilution ($\bar{H}_s$) with composition of aqueous alcohol solvent for selected nonelectrolytes.

Franks'[32] recent evaluation of the voluminous and diffuse literature on aqueous alcohol solutions reveals clearly, however, that addition of the first increments of a low molecular weight alcohol (and very likely other cosolvents) to water produces at first an increase in the degree of structuredness. Hints of this have been available for many years, but the most important facts are as follows. (a) Far from tending in an endothermic (structure-breaking) direction, the heat of mixing for methanol, ethanol, propanol, and *t*-butyl alcohol actually show exothermic maxima in the high water region. From the addition of the first increments of alcohol an exothermic interaction is found and only after this has gone through a maximum is the structure-breaking trend anticipated in the previous paragraph seen. (b) The partial molal volumes of ethanol and *t*-butyl alcohol in highly aqueous solutions go through minima in the same 0.9 mole fraction of water region. (c) Ultrasound absorption and velocity, which are measures of compressibility and structuredness, go through maxima in water-rich solutions of ethanol and *t*-butyl alcohol. (d) Although it would be expected that solutes would lower the temperature of maximum density of water, addition of small quantities of alcohols actually raise it. This has been related to the expansibility and other structural factors by Frank and Franks.[32] In the case of the first three properties, the positions of the extrema are closer to pure water for *t*-butyl alcohol than they are for the lower alcohols, and the extrema are less pronounced in each case at higher temperatures than they are at room temperature, as would be expected if thermal energy were destroying structure.

The burden of this evidence is that *addition of alcohol to water causes at first an increase in the degree of solvent structuredness.* The larger the alcohol molecules, the sooner the structure-making effect becomes saturated and then becomes opposed by further additions of alcohol so that structure making goes through a maximum. Naturally, the structure making is opposed as temperature increases. Apparently, the effect of adding a third component to an aqueous alcohol solution is greatly affected by the structure of the solvent mixture. The endothermic maxima for heats of various solutes in aqueous ethanol occur in about the position of maximum structuredness of the solvent.

2. *Nonelectrolytes.* In Figure 6 are shown the partial molal heats of solution for various organic solutes going from the pure substance as standard state to aqueous ethanol mixtures at that temperature. The molecules must be separated widely on going from the standard state to highly dilute solution. Therefore, the heat of vaporization is part of each heat term for each compound and this difference, which is irrelevant to our discussion, accounts partially for the positions of the various curves on the plot. It is the shapes of the curves rather than their relative positions with which we are concerned, and one is struck at once with how similar they are. The effect of solvent change on heat of solution is shown more quantitatively in Table II where heats of solution for each nonelectrolyte are

Table III. $\Delta\Delta\bar{H}_s$ for Various Electrolytes

Compd.	0.457	0.582	0.684	0.726	0.765	0.798	0.830	0.857	0.884	0.906	0.929	0.967	1.00	$\Delta\bar{H}_s^{g\,a}$
KCL		−1.01	−0.23		0.00		+0.19		0.32		−0.09		−1.05	+5.18
KBr		−1.36	−0.57		0.00		+0.65		+0.40		+0.02		−0.58	+5.07
KI		−0.94	−0.21		0.00		+0.86		+1.49		+1.39		+0.52	+4.27
$NaOSO_2C_6H_5$	−1.69	−1.21	−0.48		0.00		+0.40		+0.49		−0.64	−2.15	−3.18	+4.99
t-$Bu(Me)_2S^+I^-$	−1.52	−1.03	−0.33		0.00		+0.10		+0.71		+0.06	−0.24	−1.02	+6.69
$(C_6H_5)_4As^+Cl^-$					0.00		+1.60		+2.90		+0.90		−6.00	+3.40
$(C_6H_5)_4As^+Cl^- \cdot 2H_2O$			−0.89	−0.68	0.00	+1.03	+1.49		+2.54		+1.09		−5.75	+8.71
$Na^+B(C_6H_5)_4^-$			−2.08	−0.98	0.00	+1.58	+3.04	+4.22	+4.46	+3.24	+1.59		−6.28[b]	+1.68
$Me_4N^+Cl^-$		−0.52	−0.25		0.00		+0.19		+0.02		−0.30		−1.54	+2.49
n-$Bu_4N^+I^-$		−1.02	−0.44		0.00		+0.54		−0.76		−3.70		−9.23	+12.76

[a] Reference solvent; 50 vol. % ethanol. [b] Values listed here were obtained with early apparatus. A recent measurement a year later gives probably a better value of −5.24 ± 0.05 kcal./mole in water, which would give a relative value of −6.92 instead of −6.28 in water.

taken relative to the value in the 0.765 mole fraction water solution as 0.00. This choice was made because some of the compounds were too insoluble in water (which would have been a better reference medium) to permit good $\Delta\bar{H}_s$ measurements. Those that could be carried all the way to pure water suggest how large the maxima might be for the other compounds if we had been able to measure them.

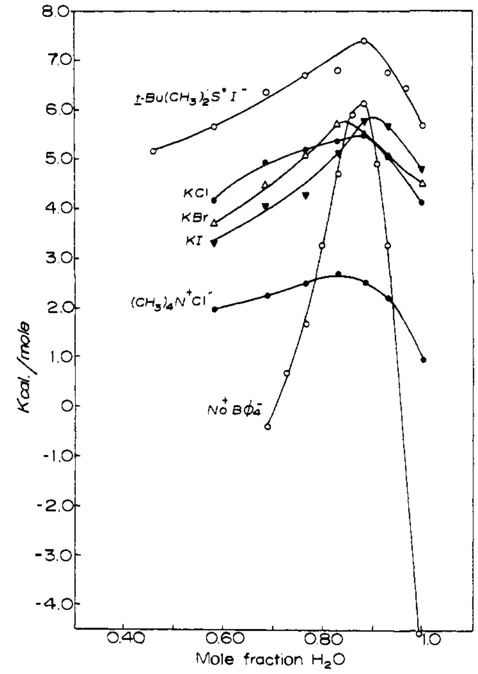

Figure 7. Variation of $\bar{H}_s$ with solvent composition for selected salts.

The most important facts that emerge from examination of the data are the following. (a) Most of the compounds show endothermic maxima in solutions of 0.80 to 0.90 mole fraction of water—the very ones where heats of activation and many physical properties show extrema. Methyl benzenesulfonate and benzyl chloride reach their solubility limits before we can be sure that a maximum has been reached, but one has every reason to expect their curves to break downwards by analogy to the other compounds described here. (b) The size of the maximum is roughly a function of the volumes of the solute molecules. Carbon tetrachloride, t-butyl chloride, isopropyl bromide, and n-butyl chloride probably occupy about the same volume per molecule, and are seen to give curves of about the same size and shape. Benzyl chloride and methyl benzenesulfonate should be of roughly the same molecular size and appear to be headed toward peaks of roughly equivalent size and shape, but which are larger than those for the smaller molecules.

Although we do not think that the data are accurate enough to warrant detailed comparison of the exact shapes of the curves, it seems that ethyl acetate and t-butyl alcohol are truly different, reflecting their different shape, polarity distribution, and perhaps specific solvation. Ethanol and water will be referred to under Interpretation.

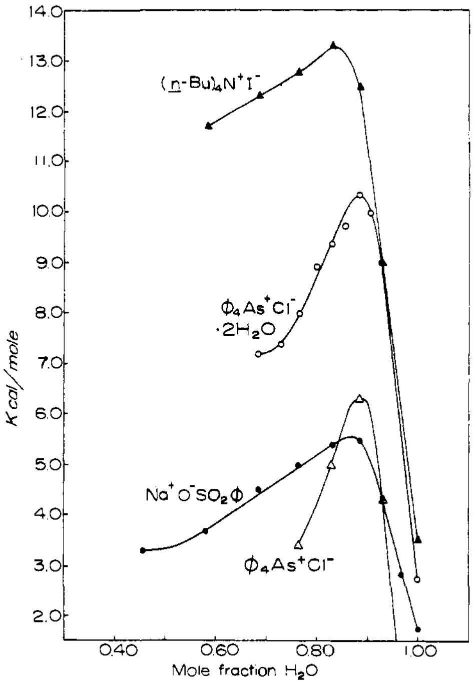

Figure 8. Variation of $\bar{H}_s$ with solvent composition for several "large salts."

3. Salts. Table III and Figures 7 and 8 show the results of adding electrolytes of various molar volumes. Once again endothermic maxima are found between 0.80 and 0.90 mole fraction of water. The "small salts" (potassium halides) behave very much in aqueous ethanol as Slansky[24] found them to in aqueous methanol. Comparison of the curves for tetramethylammonium chloride and dimethyl t-butylsulfonium iodide with the "small salts" and nonelectrolytes shows that although the volume occupied by a salt is related

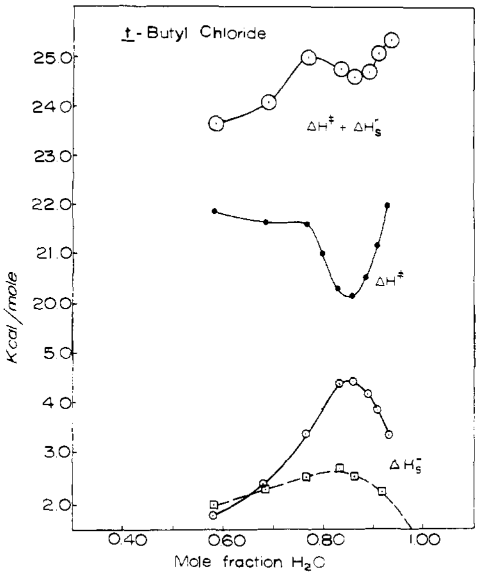

Figure 9. Dissection of enthalpy contributions to solvent variation of ΔH^* for *t*-butyl chloride solvolysis. The dotted line at the bottom is for tetramethylammonium chloride. Note the slight difference between this result and earlier measurements in ref. 19.

to the size of its endothermic maximum, salts produce smaller maxima than do nonelectrolytes of the same size. Thus, although tetramethylammonium chloride doubtless is somewhat "bigger" than *t*-butyl chloride, its $\Delta\Delta\bar{H}_s$ going from $N_{H_2O} = 0.96$ to $N = 0.85$ is only 0.7 kcal./mole while $\Delta\Delta\bar{H}_s$ for *t*-butyl chloride is about 2.0 kcal./mole over the same range. As would be expected, tetra-*n*-butylammonium iodide has a much larger maximum than the tetramethyl compound.

The extreme effect of molecular size is shown by the salts with tetraphenyl cations and anions—sodium tetraphenylboron giving a change of $\Delta\bar{H}_s$ amounting to about 11 kcal./mole between water and $N_{H_2O} = 0.884$. We also note the intriguing fact that the large cation, $(C_6H_5)_4As^+$, gives a smaller maximum than the similarly large $(C_6H_5)_4B^-$ anion suggesting that the sign of an ion's charge may be of importance.

4. Transition States. Some of the compounds described above have been used as substrates in solvolysis reactions in these media, and the variation of ΔH^* may be combined with $\Delta\Delta\bar{H}_s$ for the ground state in order to analyze changes in the heat of solution for the transition state ($\Delta\Delta\bar{H}_s^t$). This can only be done rigorously for cases where activation parameters have been measured at 25° because of the large variation of heat terms with temperature, which may be expected from what is known about ΔC_p^* in aqueous binary solvents[25] reflecting the structure-breaking effects of temperature. One should also know the composition of the transition state and the heats of solution of its components at each solvent composition. This requirement is only approached here for SN1 substrates such as *t*-butyl chloride. We do not have enough information at present to discuss heats of solution of SN2 transition states for benzyl halides or benzenesulfonates with rigor.

Figure 9 shows the results of a complete analysis of enthalpy variations for *t*-butyl chloride. Although preliminary results have been published previously,[19] their significance can now be examined from a better perspective in the light of the foregoing material about nonelectrolytes and salts. The results clearly demand that the heat of solution of the *t*-butyl chloride solvolysis transition state will scarcely change in the region of the high water minimum of ΔH^*. Our work of 2 years ago indicated that all of the decrease in ΔH^* on going through the minimum results from an increasing endothermic interaction of the solute in the solvent—the ground state is increasingly "unwelcome" as the maximum is approached from the high water side. Since then, our original measurements have been repeated by three different workers with greatly improved calorimetric techniques. The results in Table II are our best values. In Figure 9 it is seen that, if they are used to estimate the behavior of the transition state, it may actually be somewhat complex, but our original conclusion is essentially borne out. This result is in sharp contrast to the original arguments of the Hughes–Ingold theory[27] although the rate behavior agrees well with its predictions. Referring back to Figure 7, however, we see that from $N_{H_2O} = 0.70$ to 0.97, potassium chloride and tetramethylammonium chloride exhibit small, gentle, endothermic maxima in $\Delta\bar{H}_s$ so that if the *t*-butyl chloride transition state here resembled the trimethylcarbonium chloride ion pair (as is widely believed), it is acting true to form, and this is strong evidence for such a model. The result, of course, does not mean at all that the salt-like transition state is not solvated nor even that its interaction with the solvent is not changing—there is simply very little net change in heat of solution in this case as solvent composition varies through this region. One may guess from Figure 7 that the dramatic result in this case occurs fortuitously because *"trimethylcarbonium chloride" is of just the right size and shape to give practically no change in* $\Delta\bar{H}_s$ *here.*

In their consideration of ΔH^* extrema in water-rich ethanol solutions, Hyne and Wonkka[10d] suggested that sulfonium salt solvolysis should show a ΔH^* maximum in the same solvent region where ΔH^* minima are usually observed. This is because the sulfonium case involves an ionic ground state going to a less polar transition state—the reverse of the usual SN1 situation. The result bore out their prediction and is treated in Figure 10, although their kinetic results at 50° are not exactly compatible with ours, which were made at 25° where the solvent is more structured.

Since molecules produce larger $\Delta\bar{H}_s$ maxima than do ions of the same size, the results in both of the above cases are explained empirically in terms of the trends noted in Figures 6 and 7. Since *t*-butyl chloride goes from molecule to "ion" there is a minimum in ΔH^* at just the point where there is a ΔH^* maximum for the "ion-to-molecule" sulfonium salt reaction.

Even greater liberties are taken by us in treating the data by Hyne and Robertson[8d] for methyl benzenesulfonate solvolysis as shown in Figure 11. Their ΔH^* data were calculated for 50°, and the transition state in this case probably has much SN2 character. If we dare to take the trends shown in Figure 11 at face value, we can at least say that they are consistent with what we might have expected. Methyl benzenesulfonate is a large polar molecule. Its solvolysis transition state will surely be somewhat larger and may be more polar. Figure 11 shows clearly that the

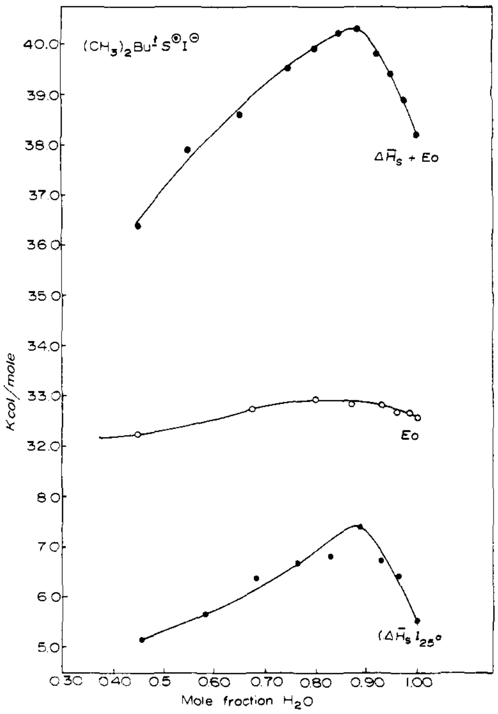

Figure 10. Dissection of solvent effects on enthalpy factors for dimethyl *t*-butyl sulfonium iodide solvolysis.

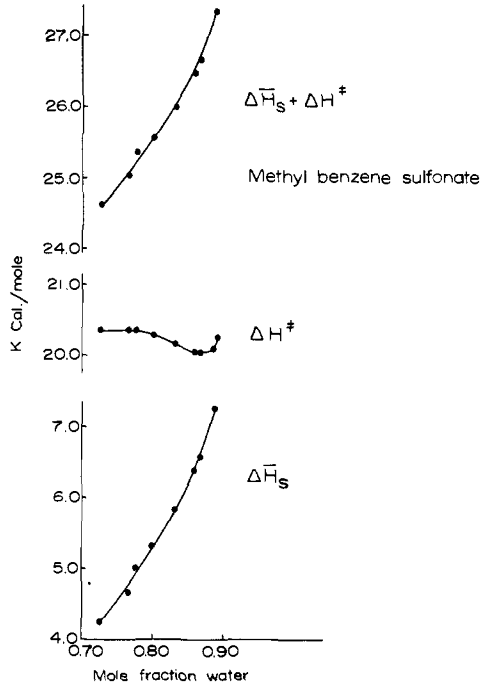

Figure 11. Dissection of solvent effects for the solvolysis of methyl benzenesulfonate.

small change in ΔH^* obscures the fact that the ground and transition states are both undergoing fairly large parallel shifts in heat of solution so that, again, trends in ΔH^* tell little about transition state behavior. We note in passing that sodium benzenesulfonate (Figure 8) is a good deal less sensitive to solvent change between 0.7 and 0.9 mole fraction of water than is methyl benzenesulfonate.

We were unable to get good $\Delta\bar{H}_s$ measurements for benzyl chloride in highly aqueous media because of its insolubility. There seems to be no doubt that an endothermic maximum is being approached which will more than account for the minimum in ΔH^*. Although Hyne[10c,d] has published considerable data for the variation of activation parameters of benzyl halides in this solvent spectrum, insolubility has so far precluded our examination of their ground state behavior with our present apparatus. We note, however, that the operational consequences of his detailed analysis of benzyl systems largely fit the behavior which we would expect of them on empirical grounds, even though our data do not support some of his interpretations which were based, of necessity, on activation data alone.

Cocivera[4i] refers to a complete dissection of activation parameters for isopropyl bromide solvolysis done in the UCLA laboratories—the heats of solution having been gotten from the temperature variation of Henry's law. The data presented there were gotten by extrapolation of data from many sources and are only comparable with ours over a small part of the solvent spectrum. However, the magnitude and directions of their estimated changes in $\Delta\bar{H}_s$ for S_N2 ground states composed of an isopropyl bromide and one molecule of water or ethanol agree nicely with our measurements.

In view of the significantly different behavior of salts and nonelectrolytes noted in this paper, it would seem that comparison between solvent effects on ($\Delta H^* + \Delta\bar{H}_s$) for a given solvolysis reaction and that for a salt which would be a good model for the transition state may be a powerful new criterion for solvolysis mechanisms. We are examining this possibility.

5. Interpretation. At this point, the following generalizations seem to hold for the systems we have considered above. (a) Heats and entropies of activation for many solvolysis reactions show extrema in highly aqueous binary solvents. In aqueous alcohols the extrema become larger and occur at higher mole fractions of water as the size of the alcohol molecules is increased. (b) Heats of solution for a number of nonelectrolytes and salts show endothermic maxima in the same region of water-rich binary solvents where other properties show extrema. The size of the maximum produced by a solute depends on the size and polarity of its molecules—the bigger the molecules, the larger is the change in $\Delta\bar{H}_s$ on going from water to the maximum. Nonelectrolytes cause larger maxima than do salts of equal molecular volume—anions may cause larger maxima than do comparable cations (although this is not certain). (c) A number of physical properties show changes indicating that the solvent goes through a maximum degree of structuredness in the same solvent region where heats of solution and activation give maxima. (d) Free energies of activation[4d] and solution[32] do not reflect the sudden variations described above.

The general pattern described here may be accommodated qualitatively to what is probably the best current picture of solute behavior in aqueous solutions—that derived from the important paper of Frank and Evans.[35-37] On the basis of entropies of solution,

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(35) H. S. Frank and M. W. Evans, *J. Chem. Phys.*, **13**, 507 (1945).

(36) For a good resumé of this approach, see R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," 2nd Ed., Butterworth and Co., (Publishers) Ltd., London, 1959, pp. 14–17.

(37) H. S. Frank and W. Y. Wen, *Discussions Faraday Soc.*, **24**, 133 (1957).

and numerous other properties, these workers conclude that most (but not all) small ions have a *structure-breaking* effect when dissolved in water, which partially compensates for the entropy losses due to free volume change, covalent solvation, and dielectric orientation on going from gaseous to hydrated ions. The observed entropy of solution for salts in water is therefore less negative than might be expected. Nonelectrolytes (especially hydrocarbons) for the most part tend to increase water structure in their immediate neighborhood. Large organic ions, such as tetraalkylammonium ones, will give a net effect depending on their size and carbon content.

The structure-forming propensities which we have already noted for alcohols in highly aqueous solution fit the nonelectrolyte pattern suggested by the Frank–Evans theory—the hydroxyl group serving mainly as a solubilizing function. However, it appears that only a limited amount of "extra structure" can be called forth by introduction of nonelectrolyte (alcohol) molecules. The microscopic act here is probably akin to building clathrate cages[36–38] around parts of the hydrocarbon chains, and there are a limited number of vacancies (potential or preexisting as the case may be) into which guest particles can fit before destruction of order begins.

Looked at in this way we see at once that the trend of $\Delta\bar{H}_s$ from pure water toward 0.8–0.9 mole fraction of aqueous ethanol for nonelectrolytes is endothermic because the solute is progressively less able to compete with the excess ethanol in the formation of structure.

Molecules and ions with large nonpolar appendages have the most to lose from this competition, so they will show the largest endothermic trend on going from water to the $\Delta\bar{H}_s$ maximum (*i.e.*, the largest exothermic trend on going from the maximum to pure water) Ions have structure-breaking tendencies generally related to their size, and, as we have seen, salts show smaller $\Delta\bar{H}_s$ maxima than do nonelectrolytes of the same carbon content, small salts showing the least effect. Structure-breaking ions give endothermic maxima because there is more structure to break in highly aqueous alcohol than in pure water. Thus, endothermic maxima such as we have seen for both nonelectrolytes and salts on going from water to highly aqueous alcohol can result *either because the solute is a more effective structure maker in water than in the binary solvent or a more effective structure breaker in the latter.* The behavior of ions carrying large nonpolar groups will be determined by the mixing of these effects.[39]

This interpretation assumes that enthalpy can be taken as an indicator of net structural change. More properly, entropies should be used, but these are not available at present. However, in view of the striking tendency for enthalpy and entropy changes to mirror each other in highly aqueous media,[4d] our assumption is probably a safe one. Since ΔH and ΔS are related to ΔF as derivatives, it is natural that they show sharper fluctuations. Furthermore, the mobile equilibria between different species of water act as a strong damper to changes in ΔF, although ΔH and $T\Delta S$ may undergo large (and opposite) fluctuations as conditions are varied. This simple fact goes far to explain the "compensation effects" underlying the linear correlations of free energies in aqueous systems which are so important to physical organic chemistry. Very few values for $\Delta\Delta\bar{F}_s$ are available for solutes in highly aqueous alcohol at present, but it appears that when suitably treated, solubilities show very small but definite irregularities here.[32]

Returning again to Figure 6, several further facts which might otherwise be puzzling are found to harmonize with this interpretation. Both *t*-butyl alcohol and ethanol give *endothermic* maxima for $\Delta\bar{H}_s$ here, although as noted[32] above, both alcohols give *exothermic* maxima for their heats of mixing in this region. In the case of ethanol, the difference is that between heat of mixing itself and the partial molal heat of solution which corresponds to the rate of change of heat of mixing as a function of solvent composition. Our curve shows, in agreement with known values of ΔH^E mixing, a steady decrease in exothermicity relative to the effect from adding the first increment of ethanol to pure water. This would be expected if structure formation were becoming saturated at about 0.85 mole fraction of ethanol. Similarly, the maximum effect of *t*-butyl alcohol as a structure maker is exerted when the first increment is added to pure water. As the amount of ethanol in the solvent increases, *t*-butyl alcohol (like the other nonelectrolytes) is increasingly ineffective at further structure making.

Additions of small amounts of water to this highly aqueous system have no noticeable effect, because the change with respect to water content on going through this range of solvent is so small. A fundamental requirement for such a two component system is that[40]

$$\frac{\partial\bar{H}_1/\partial X_2}{\partial\bar{H}_2/\partial X_2} = -X_2/X_1$$

It is easily seen from Figure 6 that the curve for variation of $\Delta\bar{H}_s$ for water is indeed related to the composition and the curve for ethanol in the way required by this equation. Thus, the curves have equal and opposite slopes as they approach the 0.5 mole fraction point; a small minimum in the water curve is found beneath the maximum in the ethanol curve, and the gentle positive slope for water in highly aqueous solutions is the direct consequence of the negative sign and low ratio on the right side of the equation above.

It will be recalled that the extrema in physical properties for highly aqueous alcohol solutions are apt to be more pronounced and occur at a higher mole fraction of water for *t*-butyl alcohol solutions than for ethanolic ones. This is explained here by the greater hydrocarbon content of *t*-butyl alcohol relative to ethanol, which makes it able to reach its structure-forming maximum in a more highly aqueous solution (on the mole fraction scale) than ethanol and so be a better competitor for structure making with other nonelectrolytes in water-rich solutions. It is an obvious prediction from this that heats of solution curves for the compounds and salts we have discussed above would show sharper

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(38) D. N. Glew, *Nature*, 195, 698 (1962).

(39) The *t*-butyl chloride transition state appears to strike just the right balance to give very little net change through the region of observation.

(40) G. N. Lewis and M. Randall, "Thermodynamics," 2nd Ed., revised by K. S. Pitzer and L. Brewer, McGraw-Hill Book Co., Inc., New York, N. Y., 1961, p. 212.

endothermic maxima in aqueous *t*-butyl alcohol than they do in aqueous ethanol and show them in more highly aqueous solutions. Very recent measurements by Dr. Donald McKelvy in our laboratory (which will be presented fully elsewhere) completely fulfill this prediction. He has also demonstrated that the same pattern of $\Delta\bar{H}_s$ results described in this paper for ethanolic solutions carries over to aqueous acetone and dioxane as well as *t*-butyl alcohol.

We have said little about the contribution of specific solvation of functional groups up to this point. Several facts show that these less easily generalized influences must play a role which may be important. Although the over-all shapes of our curves in Figures 6, 7, and 8 are similar, there are distinct differences which seem to be related to functional variation (*e.g.*, ethyl acetate and *t*-butyl alcohol in Figure 6). Only further experimentation will delineate the importance of this factor relative to the more general ones given above—in the present series it is not large.

We have also avoided discussion of the solute behavior in solutions on the more alcoholic side of the $\Delta\bar{H}_s$ maximum. Here the present situation is unmanageably complex, and specific interactions may play a greater role because the solvent structure has collapsed.

Finally, we do not feel that these experiments say anything definitive pro or con on the subject of "solvent sorting," in the sense of selective covalent binding of one solvent component to the solute, except that it need not be involved in the thermodynamic or kinetic phenomena discussed here. It does seem reasonable however that the difference between the behavior of cations and anions of the same size is derived from their modes of interaction with the hydroxylic solvent components. The cations would be expected to interact with the negative end of the O–H dipole and so have hydrogens directed out while anions should be acting as hydrogen bond acceptors.[35,41]

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(41) A. Allerhand and P. von R. Schleyer, *J. Am. Chem. Soc.*, **85**, 1233 (1963).

Effect of Structural Changes in Reactants on the Position of Hydrogen-Bonding Hydrogens and Solvating Molecules in Transition States. The Mechanism of Tetrahydrofuran Formation from 4-Chlorobutanol[1]

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Reasons are advanced for expecting that a proton being transferred in an organic reaction from one oxygen (or nitrogen) to another should lie in an entirely stable potential at the transition state and be closer to the more basic atom, but increasingly remote as substituents are changed to make this atom less basic. This "solvation rule" predicts no ordinary primary isotope effect for such "hydrogen-bonding" hydrogens, and a dependence of position on structure of the reactants which is opposite to that for hydrogens which separate "reacting bonds," e.g., the α-hydrogens of ketones undergoing enolization, which follow the "reacting-bond rule" previously proposed. However, secondary hydronium ($DO^+ + HO \rightarrow DO + HO^+$) or hydroxide ($DO^- + HO \rightarrow DO + HO^-$) isotope effects cannot be ignored. The simplest procedure for calculating them is described. The k_H/k_D isotope effects in the reactions of water or hydroxide ion with 4-chlorobutanol to form tetrahydrofuran are quantitatively interpretable as secondary and solvent isotope effects, with no ordinary primary isotope effect from the alcoholic hydrogen being transferred. The change in structure of the transition state for reaction of hydroxide ion with 2-chloroethanol is in accord with the reacting-bond rule. A fundamental fallacy in anthropomorphic arguments used to choose among reaction mechanisms is illustrated by the hydrolysis of Schiff bases. The decomposition of hyponitrous acid, the Cannizzaro reaction, the benzilic acid rearrangement, and the alkaline cleavage of 2,6-dihalobenzaldehydes illustrate further the method for calculating isotope effects from assumed transition states.

Proton transfers from electronegative atoms such as oxygen are extremely rapid whereas those from carbon are kinetically slow. This is understandable from transition-state models for the reaction of hydroxide ion with an alcohol (I) or ketone (II). The low electronegativity or Coulomb integral of carbon necessitates delocalization of the negative charge on the enolate

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