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# Thermodynamic Properties, Propensity Laws, and Solvent Models in Solutions in Self-Associating Solvents. Application to Aqueous Alcohol Solutions

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**Abstract:** First, second, and third partial derivatives of the free energy of liquid solutions with respect to any variable(s) of state are related to partial derivatives of the free energy with respect to the microscopic variables of any solvent model. Partial molar thermodynamic properties are thus dissected into two additive terms. The first term expresses the effect of adding the component under conditions where, by hypothesis of the model, the solvent network remains constant; the second term expresses the effect of the associated change of solvent network. When the second term is relatively large for an entire reaction series, the equations predict a variety of propensity laws, including, for example, the "compensation law", $T\delta\Delta\bar{S}^\circ \approx \delta\Delta\bar{H}^\circ$. Some of these propensity laws are quasithermodynamic; others are model specific. The general equations are solved specifically for a familiar two-state model of liquid water in which the hydrogen bonding is treated as a sitewise 1:1 equilibrium. The specific equations are then applied to solutions of alcohols in water, and to solutions of other substrates in water-rich mixed alcohol-water solvents. The equations permit a plausible, consistent interpretation of some extraordinarily complex solution thermodynamics.

As is well-known, the molecular liquid or lattice structure of self-associating liquid solvents can be changed by the addition of solutes—the hydrophobic effects of solutes in water provide good examples.[1a,3] Such solute-induced changes of the solvent network cause specific deviations of the thermodynamic partial molal properties of the solution components from normal or regular values. While it is common experience that partial molal free energies are not greatly affected, partial molal enthalpies, heat capacities, volumes, and indeed all derivatives of $\bar{G}_i$ with respect to $T$, $P$, and/or concentration show considerable deviations from normal patterns.[1-5] In extreme cases, the deviations become so large that they outgrow and dwarf the normal values.[5c,6,7]

In theoretical models for describing these phenomena it is assumed that the properties of the solvent network depend on a single microscopic variable or a small number of microscopic variables. In chemical models, convenient variables are the mole fractions of the relevant solvent subspecies. In aqueous solutions such subspecies might be water molecules, or water lattice sites, in different states of hydrogen bonding.[8-10] In physical models, the microscopic variables express the result of physical interactions. Examples are internal pressure[11] or electric dipole correlation.[12]

In the following, I shall derive general equations which express the partial molal properties of solutions at equilibrium as functions of the microscopic variables ($\alpha_1$, $\alpha_2$, etc.) that characterize the solvent network.[13a] In the application of theoretical models one usually begins with the theoretical expression for the free energy, $G$, of the solution and then obtains partial molal properties by appropriate partial differentiation with respect to $T$, $P$, and/or mole number, $n_i$, of a component. Familiar examples are $\bar{G}_i = \partial G/\partial n_i$, $\bar{H}_i = \partial G/\partial n_i - T(\partial^2 G/\partial n_i \partial T)$, $\bar{C}_{Pi} = -T(\partial^3 G/\partial n_i \partial T^2)$. It is therefore sufficient to analyze the derivatives of the free energy. Such analysis shows that partial molal properties can generally be resolved into two conceptually simple additive terms. One term involves partial derivatives of $G$ with respect to the macroscopic variables ($T$, $P$, $n_1$, $n_2$, etc.) at constant $\alpha_1$, $\alpha_2$, etc. It represents the thermodynamics of adding the component to the solution in such a way that, by hypothesis of the chosen model, the solvent network does not change. In order to stress that constancy of solvent network is *predicted* rather than maintained experimentally, I shall call this term *isodelphic*, cf. Delphic Oracle.

The other term involves partial derivatives of $G$ with respect to the microscopic variables ($\alpha_1$, $\alpha_2$, ...) at constant $T$, $P$, $n_1$, $n_2$, etc. as well as partial derivatives of the $\alpha$'s with respect to macroscopic variables. It consistently evaluates the contribution to the partial molal property due to the change in solvent network caused by the addition of the component. I shall call this term *lyodelphic*.[13b]

It turns out that for solutions at equilibrium at constant $T$ and $P$, the partial molal free energy is purely isodelphic—the lyodelphic

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[3] (a) Tanford, C. "The Hydrophobic Effect: Formation of Micelles and Biological Membranes"; Wiley: New York, 1980. (b) Ben-Naim, A. "Hydrophobic Interactions"; Plenum Press: New York, 1980. (c) Franks, F. "Water, A Comprehensive Treatise"; Franks, F., Ed.; Plenum Press: New York, 1975; Chapter 1, p 4.

[4] (a) Blandamer, M. J.; Robertson, R. E.; Scott, J. M. W.; Vrielink, A. *J. Am. Chem. Soc.* **1980**, *102*, 2585. (b) Ramadan, M. S.; Evans, D. F.; Lumry, R. *J. Phys. Chem.* **1983**, *87*, 4538. (c) Lumry, R.; Battistel, E.; Joliceur, C. *Faraday Symp. Chem. Soc.* **1982**, *17*, 93-108, 200-213, 231-238.

[5] Leung, C. S.; Grunwald, E. *J. Phys. Chem.* **1970**, *74*, 687. (b) *Ibid.* **1970**, *74*, 696. (c) Grunwald, E. *Ibid.* **1963**, *67*, 2208, 2211.

[6] Alexander, D. M.; Hill, D. J. T. *Aust. J. Chem.* **1969**, *22*, 347.

[7] Arnett, E. M.; McKelvey, D. R. *J. Am. Chem. Soc.* **1966**, *88*, 5031.

[8] (a) Nemethy, G.; Scheraga, H. A. *J. Chem. Phys.* **1962**, *36*, 3382. (b) *Ibid.* **1962**, *36*, 3401. (c) *Ibid.* **1964**, *41*, 680.

[9] (a) Frank, H. S. "Water, A Comprehensive Treatise"; Franks, F., Ed.; Plenum Press: New York, 1972; Chapter 14, Section 5, p 1. (b) Eisenberg, E.; Kauzmann, W. "The Structure and Properties of Water"; Oxford University Press: London, 1969.

[10] Angell, C. A. *J. Phys. Chem.* **1971**, *75*, 3698.

[11] (a) Tammann, G. *Z. Anorg. Allg. Chem.* **1926**, *158*, 25. (b) McDevit, W. F.; Long, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 1773. (c) Grunwald, E.; Butler, A. F. *Ibid.* **1960**, *82*, 5647, eq 26.

[12] (a) Oster, G.; Kirkwood, J. G. *J. Chem. Phys.* **1943**, *11*, 175. (b) Grunwald, E.; Pan, K.-C. *J. Phys. Chem.* **1976**, *80*, 2929. (c) *Ibid.* **1976**, *80*, 2941.

[13] (a) Any model that predicts physical properties must be consistent with the laws of thermodynamics. When the properties to be predicted are *thermodynamic* properties, consistency with the laws of thermodynamics leads to further general equations, including those to be derived in this paper, which apply to any model. Such equations are useful for testing the experimental validity of a given model. Moreover, by specifying the partial derivatives that must be evaluated by using the model, the equations also test whether the model is adequately complete. (b) A reviewer has pointed out that the isodelphic and lyodelphic terms introduced here correspond closely, though not exactly, to Ben-Naim's "frozen" and "relaxed" states. (c) Hildebrand, J. H.; Scott, R. L. "The Solubility of Nonelectrolytes", 3rd ed.; Reinhold: New York, 1950; p 135.

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term is identically zero, regardless of model[13c]—while all other partial molal properties have both isodelphic and lyodelphic terms and thus are inherently more complicated, in agreement with experience.

Although the equations to be derived do not represent new thermodynamic knowledge, they formulate existing knowledge so as to facilitate the testing of solvent models and guide the analysis of solution mechanisms. When, for a series of substrates, the magnitude of the lyodelphic terms are large relative to the isodelphic ones, the equations predict a variety of propensity laws whose validity can be tested. Some of them are quasithermodynamic, others depend on the specific model chosen for the solvent network. For instance, the propensity law that aqueous salt effects on nonelectrolytes follow a regular sequence, known as the Hoffmeister series,[14] can be derived only for specific solvent models. On the other hand, the propensity law that $\delta\Delta H^\circ \approx T\delta\Delta S^\circ$, known as the compensation law,[15] is quasithermodynamic and becomes exact as the isodelphic terms become relatively negligible.

## Solvent Networks Defined by One Variable

Mathematically, the simplest solution models are those in which the structure of the solvent network depends on a single microscopic variable, $\alpha$. Although the analysis in this section applies to both chemical and physical models, I shall, for sake of definiteness, consider a chemical model in which the solvent network is made up of solvent molecules in two states, A and B, present at mole fractions $\alpha$ and $1 - \alpha$, respectively. The properties of the solvent network thus depend on a single variable, $\alpha$. Let $n_1$ denote the total number of moles of solvent, and $n_2$, $n_3$, etc., denote the mole numbers of the solutes.

**Independent Variables and Definitions.** I shall assume that the liquid is a homogeneous phase but that the $B/A$ ratio and hence $\alpha$ are variables. That is, the Gibbs free energy ($G$) of the liquid is a function $G(T, P, n_1, \alpha, n_2, \text{etc.})$, and the liquid is at thermodynamic equilibrium when $\partial G/\partial\alpha = 0$.[16a]

To simplify the notation, let $G = G(x_1, x_2, ..., \alpha)$, where a subscripted $x$ denotes either $T$, $P$, or the mole number of a component, and let $y = \partial G/\partial\alpha$ at constant $x_1$, $x_2$, etc. The existence of thermodynamic equilibrium at constant $T$ and $P$ then requires that $y = 0$.[16b]

Because our interest is in properties at equilibrium, let $\alpha = \alpha(x_1, x_2, ..., y)$. Thus, in the language of the calculus, $x_1, x_2, ..., \alpha$ are variables of the first class, and $x_1, x_2, ..., y$ are variables of the second class.[17] Physically, partial derivatives at constant $\alpha$ represent changes under isodelphic conditions because the $B/A$ ratio of states of the solvent molecules remains constant. Partial deriatives at constant $y = 0$ represent the results of real measurements at thermodynamic equilibrium. Our problem will be to relate the two.

Partial derivatives with respect to variables of the first class will be written without subscripts. Partial derivatives with respect to variables of the second class will be written in parentheses followed by a $y$ subscript. For instance,

$$\frac{\partial G}{\partial x_1} = \left(\frac{\partial G}{\partial x_1}\right)_{\alpha,x_2,...}$$

$$\left(\frac{\partial G}{\partial x_1}\right)_y = \left(\frac{\partial G}{\partial x_1}\right)_{y,x_2,...}$$

For solutions at equilibrium we shall write either $(\partial G/\partial x_i)_{y=0}$ or $(\partial G/\partial x_i)_{\text{eq}}$.

**First Derivatives.** On writing $dG(x_1, x_2, ..., \alpha)$ and introducing $d\alpha(x_1, x_2, ..., y)$, one obtains eq 1. The first term on the right

$$\left(\frac{\partial G}{\partial x_i}\right)_y = \frac{\partial G}{\partial x_i} + \frac{\partial G}{\partial \alpha}\left(\frac{\partial \alpha}{\partial x_i}\right)_y \tag{1}$$

is the isodelphic term, the second is the lyodelphic term. However, at equilibrium $\partial G/\partial\alpha = 0$; hence, the first derivative of $G$ with respect to any variable of state at equilibrium (eq 2) is purely isodelphic, no matter how large the accompanying change in $\alpha$ might be. We shall find that this conclusion goes beyond the

$$\left(\frac{\partial G}{\partial x_i}\right)_{\text{eq}} = \frac{\partial G}{\partial x_i} \tag{2}$$

two-state model and applies to any model.

In particular, when $x_i = n_2$, $(\partial G/\partial n_2) = \bar{G}_2$, the formal partial molal free energy of the solute component at equilibrium. Thus, $\bar{G}_2$ is purely isodelphic. Moreover, because the *standard* partial molal free energy $\bar{G}_2{}^\circ = \bar{G}_2 - RT \ln m_2$ (where $m_2$ is highly dilute at constant $T$ and $P$), $\bar{G}_2{}^\circ$ is likewise purely isodelphic; and so are standard free energy changes $\Delta\bar{G}^\circ = -\text{RT} \ln K$ of chemical reactions.

**Second Derivatives.** In differentiating eq 1 with respect to any variable of state $x_j$ at constant $y$, I made use of eq 3, in which $\phi$ is any function of variables of the first kind, such as $\partial G/\partial x_i$ or $\partial G/\partial\alpha$. The result was then simplified by introducing (4),

$$\left(\frac{\partial \phi}{\partial x_j}\right)_y = \frac{\partial \phi}{\partial x_j} + \frac{\partial \phi}{\partial \alpha}\left(\frac{2\alpha}{\partial x_j}\right)_y \tag{3}$$

which was derived by noting that $(\partial\alpha/\partial x_j)_y = -(\partial y/\partial x_j)_\alpha/(\partial y/\partial\alpha)_{x_j}$. The general expression obtained for the second derivative

$$\frac{\partial^2 G}{(\partial\alpha\partial x_j)} = -\frac{\partial^2 G}{\partial\alpha^2}\left(\frac{\partial \alpha}{\partial x_j}\right)_y \tag{4}$$

was (5). At equilibrium it reduces to (6). The first term on

$$\left(\frac{\partial^2 G}{\partial x_i \partial x_j}\right)_y = \frac{\partial^2 G}{\partial x_i \partial x_j} - \frac{\partial^2 G}{\partial\alpha^2}\left(\frac{\partial \alpha}{\partial x_i}\right)_y\left(\frac{\partial \alpha}{\partial x_j}\right)_y + \frac{\partial G}{\partial \alpha}\left(\frac{\partial^2 \alpha}{\partial x_i \partial x_j}\right)_y \tag{5}$$

$$\left(\frac{\partial^2 G}{\partial x_i \partial x_j}\right)_{\text{eq}} = \frac{\partial^2 G}{\partial x_i \partial x_j} - \frac{\partial^2 G}{\partial\alpha^2}\left(\frac{\partial \alpha}{\partial x_i}\right)_{\text{eq}}\left(\frac{\partial \alpha}{\partial x_j}\right)_{\text{eq}} \tag{6}$$

the right in (6) is the isodelphic term, the second is the lyodelphic term.

**Third Derivatives.** The full expression for the second derivative was differentiated with respect to any variable of state $x_k$ at constant $y$, making use of eq 3. The result was simplifed on the basis of eq 4 and its partial derivatives (eq 7). For further

$$\frac{\partial^3 G}{\partial\alpha\partial x_i \partial x_j} + \frac{\partial^3 G}{\partial\alpha^2\partial x_i}\left(\frac{\partial \alpha}{\partial x_j}\right)_y + \frac{\partial^2 G}{\partial\alpha^2}\left(\frac{\partial^2 \alpha}{\partial x_i \partial x_j}\right)_y + \frac{\partial^3 G}{\partial\alpha^2\partial x_j}\left(\frac{\partial \alpha}{\partial x_i}\right)_y + \frac{\partial^3 G}{\partial\alpha^3}\left(\frac{\partial \alpha}{\partial x_i}\right)_y\left(\frac{\partial \alpha}{\partial x_j}\right)_y = 0 \tag{7}$$

simplification it was convenient to introduce a function $h$ whose

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(14) (a) Randall, M.; Failey, C. F. *Chem. Rev.* **1927**, *4*, 285. (b) Long, F. A.; McDevit, W. F. *Ibid.* **1952**, *51*, 119. (c) Bergen, R. L.; Long, F. A. *J. Phys. Chem.* **1956**, *60*, 1131.

(15) (a) Lumry, R.; Rajender, S. *Biopolymers* **1970**, *9*, 1125. (b) Lumry, R. "Bioenergetics and Thermodynamics: Model Systems"; Braibanti, A., Ed.; Reidel: Dordrecht, Holland, 1980; pp 405–423, 435–452. Some errors on pp 416–422 were corrected in the 1981 reprint of this work.

(16) (a) The analysis must begin with the free energy $G$ of the solution rather than with the partial molal free energy $\bar{G}_i$ of a component, for the following reason: By definition, $\bar{G}_i = (\partial G/\partial n_i)_{T,P,n_j}$. When the addition of the $i$th component to the solution at constant $T$ and $P$ changes the microscopic variable $\alpha$ which defines the structure of the solvent network, $(\partial G/\partial n_i)_{n_j}$ and $(\partial G/\partial n_i)_\alpha$ are different functions, which intersect at equilibrium. However, if one is interested in higher order derivatives at constant $\alpha$, one has to operate on $(\partial G/\partial n_i)_\alpha$. If one operates on $(\partial G/\partial n_i)_{n_j}$, one is likely to get the wrong answer. A typical error of this kind has been discussed by: Grunwald, E.; Butler, A. F. *J. Am. Chem. Soc.* **1960**, *82*, 5647, 5652–3. (b) This approach dates back at least to the work of P. Debye on salting-out of nonelectrolytes. Debye, P. *Z. Phys. Chem.* **1927**, *130*, 55.

(17) Sherwood, G. E. F.; Taylor, A. E. "Calculus"; Prentice-Hall: New York, 1943; p 328.

definition is given in (8). Physically, the $h$ function is convenient,

$$h_j = \frac{\partial^2 G}{\partial \alpha^2}\left(\frac{\partial \alpha}{\partial x_j}\right)_y \tag{8}$$

as seen in a later section, because in an often used two-state model of liquid water $h$ is independent of $\alpha$. Mathematical simplification of the expression for the third derivative resulted by introducing eq 9.

$$\left(\frac{\partial h_j}{\partial x_i}\right)_y = \frac{\partial^3 G}{\partial \alpha^2 \partial x_i}\left(\frac{\partial \alpha}{\partial x_j}\right)_y + \frac{\partial^3 G}{\partial \alpha^3}\left(\frac{\partial \alpha}{\partial x_i}\right)_y\left(\frac{\partial \alpha}{\partial x_j}\right)_y + \frac{\partial^2 G}{\partial \alpha^2}\left(\frac{\partial^2 \alpha}{\partial x_i \partial x_j}\right)_y \tag{9}$$

The general expression obtained in this way for the third derivative was (10). At equilibrium it reduces to (11). The first term on the right in (11) is the isodelphic term; the other terms together constitute the lyodelphic term.

$$\left(\frac{\partial^3 G}{\partial x_i \partial x_j \partial x_k}\right)_y = \frac{\partial^3 G}{\partial x_i \partial x_j \partial x_k} + \frac{\partial G}{\partial \alpha}\left(\frac{\partial^3 \alpha}{\partial x_i \partial x_j \partial x_k}\right)_y + \frac{\partial^3 G}{\partial \alpha^3}\left(\frac{\partial \alpha}{\partial x_i}\right)_y\left(\frac{\partial \alpha}{\partial x_j}\right)_y\left(\frac{\partial \alpha}{\partial x_k}\right)_y - \left(\frac{\partial h_j}{\partial x_i}\right)_y\left(\frac{\partial \alpha}{\partial x_k}\right)_y - \left(\frac{\partial h_k}{\partial x_j}\right)_y\left(\frac{\partial \alpha}{\partial x_i}\right)_y - \left(\frac{\partial h_i}{\partial x_k}\right)_y\left(\frac{\partial \alpha}{\partial x_j}\right)_y \tag{10}$$

$$\left(\frac{\partial^3 G}{\partial x_i \partial x_j \partial x_k}\right)_{\text{eq}} = \frac{\partial^3 G}{\partial x_i \partial x_j \partial x_k} + \frac{\partial^3 G}{\partial \alpha^3}\left(\frac{\partial \alpha}{\partial x_i}\right)_{\text{eq}}\left(\frac{\partial \alpha}{\partial x_j}\right)_{\text{eq}}\left(\frac{\partial \alpha}{\partial x_k}\right)_{\text{eq}} - \left(\frac{\partial h_j}{\partial x_i}\right)_{\text{eq}}\left(\frac{\partial \alpha}{\partial x_k}\right)_{\text{eq}} - \left(\frac{\partial h_k}{\partial x_j}\right)_{\text{eq}}\left(\frac{\partial \alpha}{\partial x_i}\right)_{\text{eq}} - \left(\frac{\partial h_i}{\partial x_k}\right)_{\text{eq}}\left(\frac{\partial \alpha}{\partial x_j}\right)_{\text{eq}} \tag{11}$$

## More Than One Microscopic Variable

In cases of two or more microscopic variables, the analysis is a direct extension of the one just described. For definiteness, let there be two independent variable, $\alpha_1$ and $\alpha_2$. Let $G = G(x_1, x_2, ..., \alpha_1, \alpha_2)$, $y_1 = \partial G/\partial \alpha_1$, and $y_2 = \partial G/\partial \alpha_2$. At thermodynamic equilibrium, $y_1 = y_2 = 0$. Let $\alpha_1 = \alpha_1(x_1, x_2, ..., y_1, y_2)$ and $\alpha_2 = \alpha_2(x_1, x_2, ..., y_1, y_2)$. The first derivative of $G$ with respect to any macroscopic variable $x_i$ is then given by (12a). In case of $m$ microscopic variables, the same approach leads to eq 12b. At equilibrium at constant $T$ and $P$, the $y$'s are all zero; hence, both (12a) and (12b) reduce to (13). Since, in deriving (13), no restriction was placed on the nature of the model or of the independent microscopic variables, we may conclude that any first derivative of $G$ with respect to any variable of state at equilibrium is isodelphic.

$$\left(\frac{\partial G}{\partial x_i}\right)_{y_1,y_2} = \left(\frac{\partial G}{\partial x_i}\right)_{\alpha_1,\alpha_2} + y_1\left(\frac{\partial \alpha_1}{\partial x_i}\right)_{y_1,y_2} + y_2\left(\frac{\partial \alpha_2}{\partial x_i}\right)_{y_1,y_2} \tag{12a}$$

$$\left(\frac{\partial G}{\partial x_i}\right)_{y_1,\ldots,y_m} = \left(\frac{\partial G}{\partial x_i}\right)_{\alpha_1,\ldots,\alpha_m} + \sum_{l=1}^{m} y_l\left(\frac{\partial \alpha_l}{\partial x_i}\right)_{y_1,\ldots,y_m} \tag{12b}$$

$$\left(\frac{\partial G}{\partial x_i}\right)_{\text{eq}} = \left(\frac{\partial G}{\partial x_i}\right)_{\alpha_1,\ldots,\alpha_m} \tag{13}$$

**Second Derivatives.** To obtain an expression for the second derivative of $G$ in case of two microscopic variables, (12a) was differentiated with respect to $x_j$, and the result was simplified by introducing eq 14 and its analogue in which the subscripts $i$ and $j$ are interchanged. The subscript $l$ is either 1 or 2. In deriving (14), $x_i$, $x_j$, $\alpha_1$, and $\alpha_2$ are variables of the first class, and $x_i$, $x_j$, $y_1$, and $y_2$ are variables of the second class. The result, for equilibrium at constant $T$ and $P$, is (15). There is a close similarity between eq 15 and its single-variable analogue (6). Both equations are consistent with the more general expression (16), which is proposed as a theorem, yet to be proved for $m > 2$.

$$\left(\frac{\partial y_l}{\partial x_i}\right)_{y_1,y_2,x_j} = \left(\frac{\partial y_l}{\partial x_i}\right)_{\alpha_1,\alpha_2,x_j} + \left(\frac{\partial y_l}{\partial \alpha_1}\right)_{\alpha_2,x_i,x_j}\left(\frac{\partial \alpha_1}{\partial x_i}\right)_{y_1,y_2,x_j} + \left(\frac{\partial y_l}{\partial \alpha_2}\right)_{\alpha_1,x_i,x_j}\left(\frac{\partial \alpha_2}{\partial x_i}\right)_{y_1,y_2,x_j} = 0 \tag{14}$$

$$l = 1, 2$$

$$\left(\frac{\partial^2 G}{\partial x_i \partial x_j}\right)_{\text{eq}} = \left(\frac{\partial^2 G}{\partial x_i \partial x_j}\right)_{\alpha_1,\alpha_2} - \sum_{s=1}^{2}\sum_{t=1}^{2}\left[\frac{\partial^2 G}{\partial \alpha_s \partial \alpha_t}\left(\frac{\partial \alpha_s}{\partial x_i}\right)_{\text{eq}}\left(\frac{\partial \alpha_t}{\partial x_j}\right)_{\text{eq}}\right] \tag{15}$$

$$\left(\frac{\partial^2 G}{\partial x_i \partial x_j}\right)_{\text{eq}} = \left(\frac{\partial^2 G}{\partial x_i \partial x_j}\right)_{\alpha_1,\ldots,\alpha_m} - \sum_{s=1}^{m}\sum_{t=1}^{m}\left[\frac{\partial^2 G}{\partial \alpha_s \partial \alpha_t}\left(\frac{\partial \alpha_s}{\partial x_i}\right)_{\text{eq}}\left(\frac{\partial \alpha_t}{\partial x_j}\right)_{\text{eq}}\right] \tag{16}$$

## Compensation Law: Isokinetic Relationship

Let $\delta Z$ for a substrate in a reaction series denote the difference between the value of $Z$ for the substrate and that for the reference substrate. For many reaction series and biophysical processes in aqueous solutions it is found that $\delta\Delta\bar{H}°$ is large compared to $\delta\Delta\bar{G}°$, so that $T\delta\Delta\bar{S}° \approx \delta\Delta\bar{H}°$.[15] This relationship is known as the compensation law because the separately large contributions to $\delta\Delta\bar{G}°$ from $T\delta\Delta\bar{S}°$ and $\delta\Delta\bar{H}°$ tend to compensate each other.

The compensation law can be derived from the results of the preceding sections as a special case in which the lyodelphic contributions to $\delta\Delta\bar{H}°$ and $\delta\Delta\bar{S}°$ are large compared to the isodelphic ones. To show this, the thermodynamic relation (17a) is dissected into separate isodelphic (17b) and lyodelphic (17c) relationships, and use is made of the fact that $\delta\Delta\bar{G}°$ is purely isodelphic. The compensation law then emerges as an approximation which is valid when $\delta\Delta\bar{H}° >> \delta\Delta H°_\alpha$.

$$\delta\Delta\bar{H}° = \delta\Delta\bar{G}° + T\delta\Delta\bar{S}°$$

$$\delta\Delta H°_\alpha + \delta\Delta H°_{lyo} = \delta\Delta G°_\alpha + T\delta\Delta S°_\alpha + T\delta\Delta S°_{lyo} \tag{17a}$$

$$\delta\Delta H°_\alpha = \delta\Delta G°_\alpha + T\delta\Delta S°_\alpha \tag{17b}$$

$$\delta\Delta H°_{\text{lyo}} = T\delta\Delta S°_{\text{lyo}} \tag{17c}$$

I regard the compensation law as a quasithermodynamic relationship. For the compensation law to apply, it it necessary and sufficient that the substrates in the reaction series interact with the solvent so as to produce a genuine change in some intrinsic solvent property, with relatively large enthalpic and entropic consequences. No specific theory is required as to the nature of the interaction or of the solvent property.

Many other reaction series, in both aqueous and nonaqueous solutions, display an enthalpy–entropy relationship known as the *isokinetic relationship*.[18] In such series, $\delta\Delta\bar{H}° \approx \beta\delta\Delta\bar{S}°$ for equilibria, or $\delta\Delta H^\ddagger \approx \beta\, \delta\Delta S^\ddagger$ for reaction rates. The parameter $\beta$ is called the isokinetic temperature. When $T = \beta$, $\delta\Delta\bar{G}°$ or $\delta\Delta G^\ddagger = 0$, for all members of the series.

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[18] (a) Leffler, J. E. *J. Org. Chem.* **1955**, *20*, 1202. (b) Leffler, J. E.; Grunwald, E. "Rates and Equilibria of Organic Reactions"; Wiley: New York, 1963; Chapter 9.

To derive the isokinetic relationship, the inequality $\delta\Delta\bar{H}^\circ \gg \delta\Delta H^\circ_\alpha$ may be relaxed to $\delta\Delta\bar{H}^\circ > \delta\Delta H^\circ_\alpha$, but there must now be a significant correlation between lyodelphic and isodelphic terms. As a result, $\delta\Delta\bar{H}^\circ$ is nearly proportional to $\delta\Delta\bar{S}^\circ$, but the slope $\beta$ is different from $T$. A correlation between iso- and lyodelphic terms may be expected if, for a series of substituents, perturbations of the reaction zone and of the solvent network are at least approximately proportional to each other.

## Two-State Chemical Model Applied to Aqueous Solutions

Except for specifying the number of microscopic variables, the equations obtained so far have been general. In this section we shall examine their use by applying them to an often used two-state chemical model of water in aqueous solutions.[9,10,19,20] There will be a single microscopic variable, the mole fraction $\alpha$ of one of the states. Before formulating a mass-action expression for equilibrium between the states, however, let us briefly discuss the model.

**Sitewise Equilibrium in Three-Dimensional Solvent Networks.** Solvents such as water and the alcohols, which associate to hydrogen-bonded polymers, share the physical complexities of all polymers, and their thermodynamic properties can be described by a simple two-state model only as a first approximation. Nevertheless, the two-state models are useful for semiquantitative purposes, including the derivation of propensity laws.

A reasonable approach within the two-state framework is to formulate the equilibrium as sitewise.[10,21] The mass-action expression then depends simply on the dimensionality of the solvent polymers. For *linear* polymers consisting of hydrogen-bound chains, the breaking of a chain-hydrogen bond results in the formation of two independent kinetic molecular units. Sitewise equilibrium is therefore formulated with 2:1 stoichiometry, as in (18). The 2:1 stoichiometry successfully reproduces, for example,

$$\text{OH(donor site)} + \text{O(acceptor site)} = \text{OH...O} \tag{18}$$

the breaking of solvent structure by hydrogen bond acceptor solutes in 1-octanol.[12c,21]

For *three-dimensional* hydrogen-bonded polymers such as liquid water, the breaking of an internal hydrogen bond produces an isomer of the original polymer molecule. In terms of molecular kinetic units, the product is a single molecule. Sitewise equilibrium is therefore formulated with 1:1 stoichiometry, as in (19), where [W] denotes an acceptor site. It is implied that the state on the

$$\text{OH...[W]} = \text{OH}\cdot\text{[W]} \tag{19}$$

left in (19) has a relatively low energy and entropy, since it represents a normal hydrogen bond. The state on the right has a relatively high energy and entropy; it represents an interaction of OH with [W] in which there is considerable flexibility in the configuration of the local polymer environment.

The two-state model with 1:1 stoichiometry reproduces many thermodynamic and spectroscopic properties of liquid water with fair-to-good accuracy.[10,19,20] It should be noted, however, that there is some spectroscopic evidence for the occurrence of cooperative processes in which *two* hydrogen bonds to a given water molecule break *simultaneously*.[19a] If such processes are stoichiometrically significant (as compared to the independent sitewise ones envisaged in (19)] one may need a three-state[22] or higher[8] model, with appropriate stoichiometry, to accommodate the facts.

**Mathematical Formulation.** Relevant equations are summarized in Table I. Two key assumptions are made: (a) The two solvent states interact with 1:1 stoichiometry. (b) The solvent equilibrium is perturbed by added solutes. Owing to (a), Table I shows familiar equilibrium expressions (20) for whose use there is ample precedent. To account for (b) one introduces activity coefficients, as in (20a), which allow $K$ to vary with the solute molality.

**Table I.** Two-State Model Applied to Sitewise 1:1 Equilibrium[a,b]

Definitions

$m$ = molality; $m_1 = 1000/\mathrm{M}_1$

$f$ = molal activity coefficient

$\delta\mathrm{X}_1 = \mathrm{X}_{1\mathrm{B}} - \mathrm{X}_{1\mathrm{A}}$, for any solvent state property X

Assumptions: at Equilibrium

$$(1-\alpha)/\alpha = K = K_0 f_{1\mathrm{A}}/f_{1\mathrm{B}} \tag{20a}$$

$$\partial \ln K/\partial T = \delta\bar{H}_1/RT^2 \tag{20b}$$

$$\partial \ln K/\partial P = -\delta\bar{V}_1/RT \tag{20c}$$

$$\ln (f_{1\mathrm{B}}/f_{1\mathrm{A}}) = \delta j_{21} m_2 \text{ (one solute)} \tag{21a}$$

$$\ln (f_{1\mathrm{B}}/f_{1\mathrm{A}}) = \textstyle\sum_i \delta j_{i1} m_i \text{ (} i \text{ solutes)} \tag{21b}$$

$$\ln K = \ln K_0 - \textstyle\sum_i \delta j_{i1} m_i \tag{21c}$$

$$\partial \ln K/\partial n_i = (m_1/n_1)\, \partial \ln K/\partial m_i = (-m_1 \delta j_{i1})/n_1 \tag{21d}$$

$$\partial \ln K/\partial n_1 = (\textstyle\sum_i \delta j_{i1} m_i)/n_1 \tag{21e}$$

Approximations

$$\partial j_{i1}/\partial m_k = 0 \tag{22a}$$

$$\partial \delta\bar{H}_1/\partial m_i = -RT^2(\partial \delta j_{i1}/\partial T) = 0 \tag{22b}$$

$$\partial \delta\bar{H}_1/\partial T = \delta\bar{C}_{p1} = 0 \tag{22c}$$

$$\partial \ln (f_{1\mathrm{B}}/f_{1\mathrm{A}})/\partial\alpha = 0 \tag{22d}$$

Relations of $G$ to $\alpha$

$$G = n_1(\alpha\bar{G}_{1\mathrm{A}} + [1-\alpha]\bar{G}_{1\mathrm{B}}) + \textstyle\sum_i n_i \bar{G}_i \tag{23a}$$

$$\partial G/\partial\alpha = n_1(\bar{G}_{1\mathrm{A}} - \bar{G}_{1\mathrm{B}}) \tag{23b}$$

$$\bar{G}_{1\mathrm{A}} = \bar{G}_{1\mathrm{A}}{}^\circ + 2RT \ln (2m_1 \alpha f_{1\mathrm{A}}) \tag*{(24a)$^a$}$$

$$\bar{G}_{1\mathrm{B}} = \bar{G}_{1\mathrm{B}}{}^\circ + 2RT \ln (2m_1[1-\alpha]f_{1\mathrm{B}}) \tag*{(24b)$^a$}$$

$$\partial^2 G/\partial\alpha^2 = (2n_1RT)/[\alpha(1-\alpha)] \tag{25a}$$

$$\partial^3 G/\partial\alpha^3 = [2n_1RT(1-2\alpha)]/[\alpha^2(1-\alpha)^2] \tag{25b}$$

$$(\partial\alpha/\partial x_i)_{\mathrm{eq}} = [-K/(1+K)^2][(\partial \ln K)/\partial x_i] = -\alpha(1-\alpha)[(\partial \ln K)/\partial x_i] \tag{26a}$$

$$h_i = -2n_1RT[(\partial \ln K)/\partial x_i] \tag{26b}$$

Results

$$(\bar{G}_i)_{\mathrm{eq}} = (\bar{G}_i)_\alpha, \text{ for any component} \tag{27a}$$

$$(\bar{G}_i{}^\circ)_{\mathrm{eq}} = (\bar{G}_i{}^\circ)_\alpha, \text{ for any component} \tag{27b}$$

$$(T\bar{S}_2)_{\mathrm{eq}} = (T\bar{S}_2)_\alpha - 2\alpha(1-\alpha)m_1\delta j_{21}\delta\bar{H}_1 \tag{28}$$

$$(\bar{H}_2)_{\mathrm{eq}} = (\bar{H}_2)_\alpha - 2\alpha(1-\alpha)m_1\delta j_{21}\delta\bar{H}_1 \tag{29}$$

$$(\bar{V}_2)_{\mathrm{eq}} = (\bar{V}_2)_\alpha - 2\alpha(1-\alpha)m_1\delta j_{21}\delta\bar{V}_1 \tag{30}$$

$$(\partial\bar{G}_i/\partial m_k)_{\mathrm{eq}} = (\partial\bar{G}_i/\partial m_k)_\alpha - 2RT\alpha(1-\alpha)m_1\delta j_{i1}\delta j_{k1} \tag{31}$$

$$(\bar{C}_{p2})_{\mathrm{eq}} = (\bar{C}_{p2})_\alpha - 2R\alpha(1-\alpha)(1-2\alpha)m_1\delta j_{21}(\delta\bar{H}_1/RT)^2 \tag{32}$$

$$T(\partial\bar{S}_i/\partial m_k)_{\mathrm{eq}} = T(\partial\bar{S}_i/\partial m_k)_\alpha + 2\alpha(1-\alpha)m_1\delta j_{i1}\delta j_{k1}([1-2\alpha]\delta\bar{H}_1 + RT) \tag{33}$$

$$(\partial\bar{H}_i/\partial m_k)_{\mathrm{eq}} = (\partial\bar{H}_i/\partial m_k)_\alpha + 2\alpha(1-\alpha)(1-2\alpha)m_1\delta j_{i1}\delta j_{k1}\delta\bar{H}_1 \tag{34}$$

[a] For the water lattice (Bernal–Fowler model) the number of sites equals 2 $m_1$.

I shall assume that $\ln (f_{1\mathrm{B}}/f_{1\mathrm{A}})$ is proportional to the solute molality. For solutions with a single solute this is expressed in eq 21a, for those with two or more solutes it is expressed in (21b). The functional form of (21a) and (21b) is consistent with dilute-solution theory and implies that solute-induced changes in the partial molal free energies of the solvent states are proportional to the solute concentrations.

The parameter $\delta j_{i1}$ is an important property. It will appear as a factor in all lyodelphic terms. Its magnitude measures the relative effectiveness of the solute at changing the solvent network. Its sign indicates the direction of the change—a positive sign indicates network-structure making. We shall refer to $\delta j_{i1}$ as the network-interaction constant for the given solute in the given solution.

Table I also lists, as eq 22 a–d, some partial derivatives whose neglect seems justified at low-to-moderate solute concentrations.

Equations 23–25 are equations for the free energy and its derivatives with respect to $\alpha$. These equations do not require the existence of equilibrium between the two solvent states. Equilibrium is introduced starting with eq 26. Unusual factors of two, which appear beginning with eq 24, come from the assumption of sitewise equilibrium. In the Bernal-Fowler structure of liquid water, the number of hydrogen-bonding sites is twice the number of water molecules, as noted particularly by Angell in his important paper.[18]

Some useful results of the model are given in eq 27–34. As required, first derivatives of $G$ are purely isodelphic; second and third derivatives have both an iso- and a lyodelphic term. The lyodelphic terms are the source of propensity laws. In all second

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(19) (a) Walrafen, G. E. *J. Chem. Phys.* **1966**, *44*, 1546. (b) *Ibid.* **1967**, *47*, 114. (c) *Ibid.* **1968**, *48*, 244. (d) Walrafen, G. E. "Water, A Comprehensive Treatise"; Franks, F., Ed.; Plenum Press: New York, 1972; Chapter 5, p 1.

(20) Worley, J. D.; Klotz, I. M. *J. Chem. Phys.* **1966**, *45*, 2868.

(21) Grunwald, E.; Pan, K.-C.; Effio, A. *J. Phys. Chem.* **1976**, *80*, 2937.

(22) Senior, W. A.; Verrall, R. E. *J. Phys. Chem.* **1969**, *73*, 4242.

**Table II.** Interpretation of $\Delta C_p$ for Solution of Alcohol Vapors in Water

| | *t*-BuOH | | *n*-BuOH | | *i*-PrOH | |
|---|---|---|---|---|---|---|
| temp, °C | $\Delta C_P$, eu | $\delta j_{21}$, $m^{-1}$ | $\Delta C_P$, eu | $\delta j_{21}$, $m^{-1}$ | $\Delta C_P$, eu | $\delta j_{21}$, $m^{-1}$ |
| 5 | 116.4 | 0.46 | 91.3 | 0.36 | 76.6 | 0.30 |
| 15 | 103.5 | 0.46 | 86.3 | 0.38 | 71.5 | 0.31 |
| 25 | 90.6 | 0.46 | 81.3 | 0.41 | 66.4 | 0.33 |
| 35 | 77.7 | 0.46 | 76.9 | 0.45 | 61.3 | 0.35 |
| $\sigma$/mean | 10[a] | 0.46 | | 0.40 | 10[a] | 0.32 |
| | *n*-PrOH | | EtOH | | MeOH | |
| 5 | 69.4 | 0.26 | 50.3 | 0.19 | 24.0 | 0.08 |
| 15 | 67.2 | 0.29 | 47.4 | 0.20 | 25.0 | 0.09 |
| 25 | 65.0 | 0.32 | 45.5 | 0.21 | 25.9 | 0.11 |
| 35 | 62.8 | 0.36 | 43.1 | 0.24 | 26.9 | 0.13 |
| $\sigma$/mean | 9[a] | 0.31 | 7[a] | 0.21 | 6[a] | 0.10 |

$10^6\alpha(1-\alpha)(1-2\alpha)/T^2$: 1.184 (5 °C), 1.045 (15 °C), 0.908 (25 °C), 0.775 (35 °C)

[a] Experimental standard deviation.

derivatives they are proportional to $\alpha(1-\alpha)$. In third derivatives there is always a lyodelphic component that is proportional to $\alpha(1-\alpha)(1-2\alpha)$ and sometimes an additional lyodelphic component that is proportional to $\alpha(1-\alpha)$.

Depending on the macroscopic variables ($T$, $P$, number and nature of solutes) and the consequent magnitudes of iso- and lyodelphic terms, the equations in Table I predict a wide range of propensities, from proportionalities to uncorrelated scatter. The validity of the underlying model can therefore be tested. To provide a severe test, and to demonstrate the usefulness of this kind of analysis, I shall examine some of the thermodynamic complexities of aqueous solutions of alcohols.

## Selected Results for Alcohols in Water

Thermodynamic parameters for two-state sitewise equilibrium in water were taken from the work of Angell.[10] The following values were used: $\delta\bar{H}_1$ = 1900 cal per mol of sites, $\delta\bar{S}_1$ = 4.8 cal K$^{-1}$ per mol of sites. At 298 K, $\alpha = 0.688$.

**$\Delta C_p$ for ROH(g) → ROH(aq).** Results reported by Alexander and Hill[6] for a series of aliphatic alchols are listed in Table II. The values are relatively large, much larger than the upper limit of 12 cal K$^{-1}$ mol$^{-1}$ (12 eu) which has been estimated for the process $g \rightarrow 1$ of normal liquids.[23] To estimate lyodelphic contributions I shall write $\Delta C_p = (C_{p_2})_{lyo} + [(C_{p_2})_\alpha - C_p°(g)]$, and I shall let $[(C_{p_2})_\alpha - C_p°(g)]$ = 6 eu, i.e., half the upper limit for normal condensation. This leads to $(C_{p_2})_{lyo} = \Delta C_p - 6$ eu. On applying (32) and introducing appropriate numbers, one then obtains (35).

$$\Delta C_p - 6 = (C_{p_2})_{lyo} = -2.02\cdot10^8\ \mathrm{T}^{-2}\ \alpha(1-\alpha)(1-2\alpha)\delta j_{21}\ \mathrm{eu} \tag{35}$$

The variable $\mathrm{T}^{-2}\ \alpha(1-\alpha)(1-2\alpha)$ decreases consistently with increasing temperature, by over 30% in the experimental range. $(C_{p_2})_{lyo}$, which is expected to be proportional to it, also decreases consistently for all alcohols except methanol, and (35) reproduces the data within their experimental error.

Mean values of the interaction constants $\delta j_{21}$ are included in Table II. For straight-chain alcohols, $H(CH_2)_nOH$, the empirical equation $\delta j_{21} = 0.10n$ reproduces the interaction constants well. If this indication that $\delta j_{21}$ is an additive-constitutive property is correct, then the contribution to $\delta j_{21}$ from the H + OH part structure has the plausible value of zero. The positive sign of the interaction constants indicates that alcohols in dilute aqueous solution are water-network structure makers.

Of special interest is the *magnitude* of the interaction constants, which I find to be surprisingly large. It follows from (20a) and (21c) that $\partial\alpha/\partial m_2 = \alpha(1-\alpha)\delta j_{21}$. The number of hydrogen-bonded water lattice sites is $2m_1\alpha$. Thus, the change in the number of hydrogen-bonded water lattice sites per mole of added solute is $2m_1(\partial\alpha/\partial m_2)$, or 23.9 $\delta j_{21}$ at 25 °C. For straight-chain alcohols, the structure making is therefore about 2.4 hydrogen bonds per $CH_2$ group, or ≈10 hydrogen bonds per mol of *n*-butyl alcohol. No wonder that experts warn us that measurements must be made in very dilute solution!

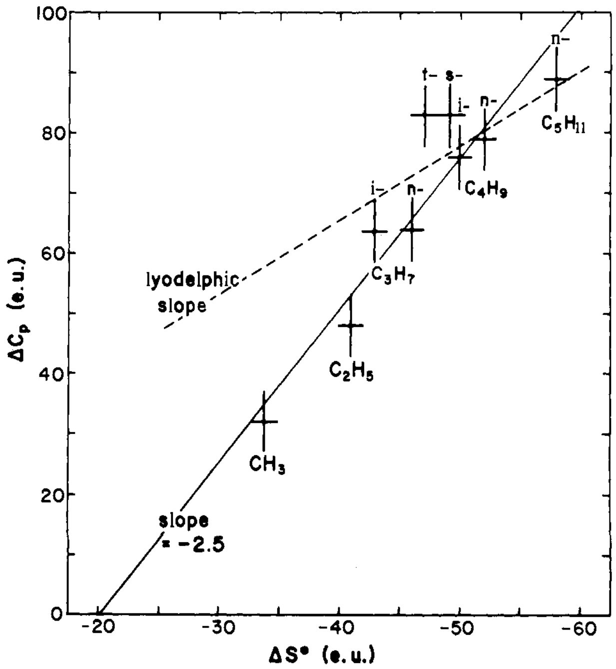

**Figure 1.** $\Delta C_p$ vs. $\Delta S°$ for solutions of gaseous aliphatic alcohols in water. Data from ref 1c. The dashed line is drawn with the slope predicted for a purely lyodelphic substituent effect.

**$\Delta C_p$ Compared with $\Delta S°$.** Just as $\Delta C_p$ for the solution of gaseous alcohols in water is considerably larger than expected for normal solution processes, so $\Delta S°$ is considerably more negative. Results at, or near 25 °C have been reported by Arnett, Kover, and Carter[1c] and are plotted in Figure 1. There is a strong linear trend. I now wish to show that the two-state sitewise equilibrium model predicts this trend.

Let $\delta\Delta C_p = \Delta C_p(\mathrm{ROH}) - \Delta C_p(\mathrm{MeOH})$, and $\delta\Delta S° = \Delta S°(\mathrm{ROH}) - \Delta S°(\mathrm{MeOH})$. Let these quantities be dissected into iso- and lyodelphic terms, as in (36). Because $[(C_{p_2})_\alpha - C_p°(g)]$

$$\delta\Delta C_p = \delta[(C_{p_2})_\alpha - C_p°(g)] + \delta(C_{p_2})_{lyo} \tag{36a}$$

$$\delta\Delta S° = \delta[(S°_2)_\alpha - S°(g)] + \delta(S°_2)_{lyo} \tag{36b}$$

is relatively small—its upper limit is 12 eu[23]—the first term on the right in (36a) is relatively negligible, and $\delta\Delta C_p = \delta(C_{p_2})_{lyo}$, in good approximation. On the other hand, $[(S°_2)_\alpha - S°(g)]$ for isodelphic condensation is relatively greater. Its value is of the order of −22 eu (the Trouton's rule value for the condensation of normal liquids), and substituent effects, though smaller, may be considerable.[24] The approximation that the first term on the right in (36b) is negligible thus may not be a good one. If that term is neglected none the less, and if lyodelphic terms are expressed according to (28) and (32), one obtains (37).

$$\delta\Delta C_p = \delta\Delta S°\ [(1-2\alpha)\delta\bar{H}_1/RT] \tag{37}$$

Because of the approximations made in its derivation, eq 37 is not expected to give precise fits, but it should be valid as a propensity law. This is indeed the case. First, eq 37 predicts a linear variation of $\Delta C_p$ with $\Delta S°$ for a series of alcohols, in agreement with observation. Second, the slope of the line is predicted to be negative, in agreement with observation. Finally, on the quantitative level, the slope at 25 °C is predicted to be −1.2,

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[23] Benson, S. W. *J. Am. Chem. Soc.* **1978**, *100*, 5640.

[24] (a) Frank, H. S. *J Chem. Phys.* **1945**, *13*, 493. (b) Frank, H. S.; Evans, M. W. *Ibid.* **1945**, *13*, 507.

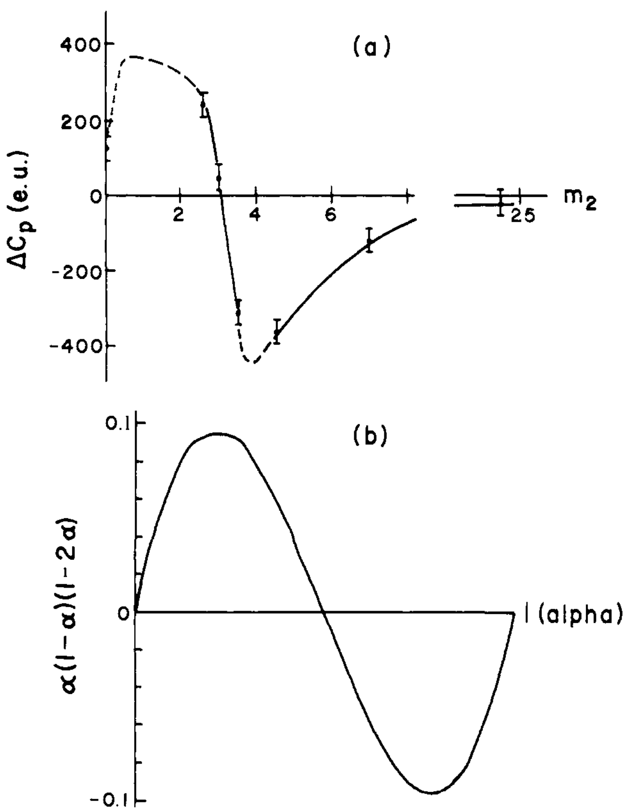

**Figure 2.** (a) $\Delta C_p$ for solution of solid sodium tetraphenylboride in *tert*-butyl alcohol ($m_2$)/water mixed solvents. Data from ref 7. The dashed segments are science fiction. (b) Plot of $\alpha(1 - \alpha)(1 - 2\alpha)$ vs. $\alpha$ for comparison.

which can be compared with an experimental slope (Figure 1) of −2.5.

**$\Delta C_p$ for Solution of Sodium Tetraphenylboride.** Arnett and McKelvey[7] have reported $\Delta C_p$ for the solution of solid sodium tetraphenylboride (NaTPB) in aqueous solutions containing up to 30 mol % *tert*-butyl alcohol. The data of interest to us are in the range 4.5–11 mol % *tert*-butyl alcohol, in which the alcohol molality $m_2$ varies from 2.6–7.0 *m*. The results, which are plotted in Figure 2a, are remarkable because they seem to violate two theorems of normal solution thermodynamics. First, the magnitudes of $\Delta C_p$ are large, ranging up to nearly 400 eu. This violates the theorem that enthalpies of solution are, in first approximation, independent of the temperature. Second, the values of $\Delta C_p$ vary strongly with $m_2$; they even change sign! This violates the theorem that solutes in similar solvents have similar thermodynamic properties.

These hitherto unexplained results would lose their mystery if one could explain them in terms of well-founded theory. I shall try to do so, by assuming that abnormal values of $\Delta C_p$ in solution represent lyodelphic effects. In particular, if one may apply the two-state solvent model and considers the lyodelphic term in eq 32, $\Delta C_p$ is expected to vary as $\alpha(1 - \alpha)(1 - 2\alpha)$. Accordingly, Figure 2 places a graph of the function $\alpha(1 - \alpha)(1 - 2\alpha)$ next to the plot of the experimental results. There is an obvious qualitative resemblance, including even the change of sign.

One can adapt the two-state solvent model to apply to these experiments by asssuming that the OH groups of the alcohol molecules become incorporated in the hydrogen-bonded solvent networks. At moderate alcohol concentrations, where there is still a large excess of water molecules, the solvent networks almost certainly remain three-dimensional polymers, so that sitewise equilibrium will continue to proceed with 1:1 stoichiometry. Thus, the basic model of Table I remains intact. Some revision will be required, however, to allow for the second solvent component. In principle, the parameters $\alpha$, $\delta j_{21}$, and $\delta\bar{H}_1$ now are functions of alcohol concentration.

I shall assume that these parameters are continuous functions of $m_2$ and that neither $\delta j_{21}$ nor $\delta\bar{H}_1$ changes algebraic sign in the range of interest. Since $\alpha = 0.688$ and $\delta\bar{H}_1 = 1900$ cal in pure water, it follows that $\delta j_{21} > 0$. A positive value of $\Delta C_p$ for solution of NaTPB therefore indicates that $\alpha > 0.5$, a negative value that $\alpha < 0.5$. Thus, in Figure 2a, $\alpha > 0.5$ at 2.6 $m_2$, $\alpha = 0.5$ near 3.0 $m_2$, and $\alpha < 0.5$ above 3 $m_2$ and approaching 0 with increasing alcohol concentration.

In summary, the gist of this approach is to use $\Delta C_p$ for the solution of NaTPB in the mixed solvent as a probe for $\alpha$ in the solvent network, and to deduce as much quantitative information concerning $\alpha$ as knowledge of other parameters permits. The approach leads clearly to the conclusion that in the range $m_2 > 2.6$, $\alpha$ decreases continuously from an initial value above 0.5 to a final value of, or near, 0. In other words, *tert*-butyl alcohol is a solvent-network structure breaker, in this range. On the other hand, it was found earlier in this section that in highly dilute solution in water, *tert*-butyl alcohol is a strong solvent structure maker with $\delta j_{21} = 0.46$. To complete the explanation, I must show that these seeming contradictions can be reconciled.

In water, the change in the number of hydrogen-bonded lattice sites per mole of added solute was found to be 23.9 $\delta j_{21}$, or 11.0 sites per mol of *tert*-butyl alcohol. The total number of water lattice sites in which 11.0 sites are *not* hydrogen-bonded is $11.0/(1 - \alpha)$, of 35.2 sites at 25 °C. Per mole of alcohol, this corresponds to a volume of 320 mL of water, which may be said to be the molar hydration shell of *tert*-butyl alcohol.

When two molecular hydration shells interpenetrate, the region of overlap is almost certainly a region of hydrogen-bond breaking. The "excluded volume" $Vx$, if all overlap is to be avoided, is 8 times the volume of the hydration shells,[25a] or about 2.5 L/mol. This is a relatively large volume, and overlap is therefore negligible only at very high dilutions. At all other concentrations, overlap of hydration shells and hydrogen-bond breaking are statisticalily significant, and at high enough concentrations they become dominant.

A rough estimate of the *tert*-butyl alcohol concentration $m_2{}^*$ at which $\partial\alpha/\partial m_2$ changes sign is $m_2{}^* \approx 1/Vx$.[25b] On introducing 2.5 L/mol for $Vx$, one finds that $m_2{}^* \approx 0.4\ m$. Thus, solvent structure breaking should be dominant at concentrations above $\approx 0.4\ m_2$. Since the data which indicate that $\partial\alpha/\partial m_2$ is negative lie above 2.6 $m_2$, the decrease of $\alpha$ with increasing $m_2$ is plausible. This argument would be stronger, of course, if it could be supported by direct measurements at 0.01–2.6 *m* aqueous concentrations of *tert*-butyl alcohol.

**Enthalpy in the Solvolysis of *tert*-Butyl Chloride.** There are independent measurements in ethanol–water solutions which, if interpreted similarly, indicate that $\alpha$ indeed goes through a maximum at an alcohol molality of the order of $1/Vx$. Using the same method as before, I estimate from the value, 0.21, obtained for $\delta j_{21}$ of ethanol in water (Table II) that the hydration-shell volume is 145 mL/mol, that $Vx$ is 1.16 L/mol, and that $m_2{}^* = 0.86$, which is equivalent to 1.5 mol % or 4.8 vol % of ethanol.

The evidence that $\alpha$ goes through a maximum near $1/Vx$ comes from activation enthalpies of solvolysis of *tert*-butyl chloride[26] and enthalpies of solution of *tert*-butyl chloride.[27] Making use of eq 29, dissection into iso- and lyodelphic terms leads to (38), in which the factor of $\alpha(1 - \alpha)$ can serve as a probe for $\alpha$.

$$\Delta H^{\ddagger} = (\Delta H^{\ddagger})_{\alpha} - 2\alpha(1 - \alpha)m_1\delta\bar{H}_1[\delta j_{21}(\ddagger) - \delta j_{21}(\mathrm{RCl})] \quad (38a)$$

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(25) (a) If overlap must be excluded, $Vx$ is identical with the collision volume for hard-sphere collisions. For a description of the latter, see: Moore, W. J. "Basic Physical Chemistry"; Prentice-Hall: New York, 1983; Section 15.1. (b) When $m_2 = 1/Vx$, the fraction of alcohol molecules with non-overlapping hydration shells is roughly $^1/_2$. (c) Standard experimental error in $\Delta H^{\ddagger}$ is 0.15 kcal.

(26) Winstein, S.; Fainberg, A. H. *J. Am. Chem. Soc.* **1957**, *79*, 5937.

(27) Arnett, E. M.; Duggleby, P. McC.; Burke, J. J. *J. Am. Chem. Soc.* **1963**, *85*, 1350.

$$\Delta H_s = (\Delta H_s)_\alpha - 2\alpha(1-\alpha)\mathrm{m}_1\delta\bar{H}_1\delta j_{21}(\mathrm{RCl}) \qquad (38b)$$

The probe function $\alpha(1 - \alpha)$ goes through a maximum of 0.25 when $\alpha = 0.5$. In water at 25 °C, its value is 0.215.

Experimental results are plotted in Figure 3. The upper figure shows $\Delta H^\ddagger$ and $\Delta H_s$ for the solvent range in which $\alpha$ is expected to decrease with increasing $m_2$. The two curves have very similar absolute shapes, indicating that the lyodelphic terms (which are proportional to each other) are relatively large. Extrema are found at 14.3 mol % ethanol, at (or near) which concentration $\alpha = 0.5$.

The fact that the plot for $\Delta H_s$ goes through a maximum indicates that $\delta j_{21}(\mathrm{RCl})$ is negative. Therefore, *tert*-butyl chloride tends to *break* hydrogen bonds in three-dimensional water networks. To account for this, I suggest that the solute-network interaction is dominated by the electronegative chlorine atom, which polarizes the OH groups so as to disrupt the OH...[W] hydrogen-bonded alignments.

The fact that the plot for $\Delta H^\ddagger$ goes through a minimum indicates that $[\delta j_{21}(\ddagger) - \delta j_{21}(\mathrm{RCl})]$ is positive.

The lower part of Figure 3 shows data for a solvent range which includes 4.8 vol % ethanol where $\alpha$ is predicted to go through a maximum. Comparison with the upper figure shows that if $\alpha$ were indeed passing through a maximum, $\Delta H^\ddagger$ would be passing through a maximum as well. The data plotted in the lower Figure 3 do show a small maximum, of marginal statistical significance[25c] and happily at the predicted ethanol concentration.

## Relevancy to Structure–Energy Relationships

I foresee relevancy mainly in three areas: interpretation of structure–enthalpy relationships, prediction of propensity rules, and refinement of models of solvent structure.

**Classification of Solvent Conditions. Structure–Enthalpy Relationships.** Let us define *isodelphic conditions* as solution conditions under which lyodelphic contributions to thermodynamic partial molal properties are negligible. The solvents which provide isodelphic conditions are not limited to normal solvents but also include self-associated solvents, provided that the structure of the self-associated solvent networks is too strong to be perturbed by the added solutes. A case in point is octanoic acid, whose typically nonpolar dielectric constant indicates strong head-to-head association of the carboxyl groups. At room temperature, octanoic acid is isodelphic; electric dipole moments measured for ion pairs in octanoic acid are close to values obtained in the gas phase.[28]

Returning to the realm of solvent models, we note that the lyodelphic terms in Table I go to zero as $\alpha$ approaches either zero or unity. Thus, one may predict that most, if not all, real solvents tend to become isodelphic as the temperature is lowered.

When solvent conditions are isodelphic, standard enthalpy changes in reaction series may be expected to correlate well with standard free energy changes. In fact, good linear correlations have been observed between free energies of protonation of bases in water and enthalpies of protonation of the same bases in sulfolane, dimethyl sulfoxide, and fluorosulfuric acid.[29]

**Propensity Laws.** Illustrative examples have been given, so this topic needs little further discussion. When lyodelphic contributions to partial molal properties are substantial, proportional or linear tendencies among $\delta$ quantities in reaction series will be common.

**Models of Solvent Structure.** Among theoreticians, the liquid state holds a special fascination because scientific truth about liquid structure is so hard to come by. The present approach is useful because it encourages quantification of qualitative models for the interpretation of thermodynamic solution properties.

In chemical models, a key requirement of the present approach is the formulation of a mass action expression for equilibrium among the solvent states. This can be diagnostic. Let me return briefly to two-state models of liquid water structure and discuss the effect of cooperativity of hydrogen bonding.

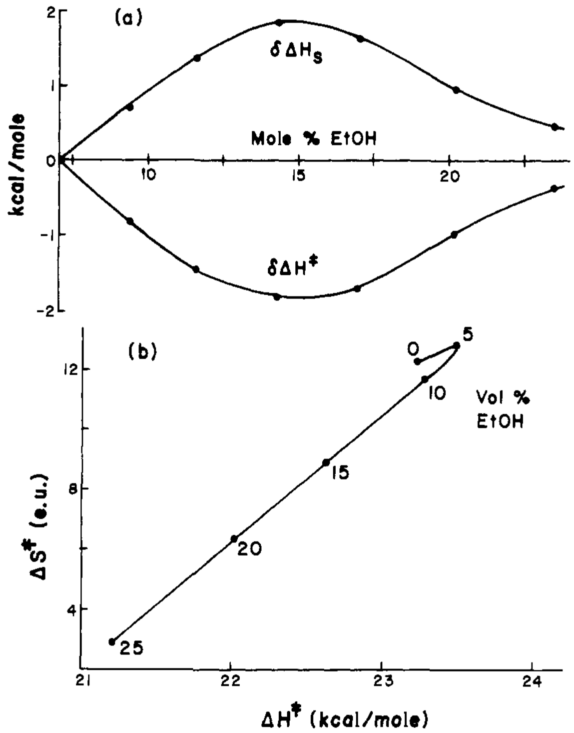

**Figure 3.** (a) $\Delta H^\ddagger$ for solvolysis and $\Delta H_s$ for solution of *tert*-butyl chloride in ethanol/water mixed solvents. In this range $\alpha$ is expected to decrease with increasing ethanol concentration. Data from ref 26 and 27. (b) $\Delta S^\ddagger$ and $\Delta H^\ddagger$ for solvolysis of *tert*-butyl chloride at low ethanol concentrations. $\Delta H^\ddagger$ and $\alpha$ are expected to pass through a maximum at ≈4.8 vol % ethanol.

The 1:1 sitewise equilibrium model applied in the preceding section neglects possible cooperativity of hydrogen bonding. By contrast, the "flickering cluster" model of Frank and Wen[30] stresses it. From a mass-action point of view, there are two ways in which a number of water molecules can interact cooperatively to form a hydrogen-bonded cluster. One way is for the entire cluster to either be hydrogen-bonded or Van der Waals bonded—that is, bound by interactions other than hydrogen bonds. One would formulate this process as in (39). As shown in (39), this cooperative change is analogous to, say, the transition from one crystalline form of a solid to another. There should be a sharp transition temperature.

$$\text{Van der Waals } [(\mathrm{HOH})_n] = \text{H-bonded } [(\mathrm{HOH})_n] \qquad (39)$$

The other way is for the hydrogen-bonded clusters to be formed cooperatively from a number of water molecules and to "melt" cooperatively. Because by hypothesis the association process is cooperative, any nonassociated water molecules are monomeric and are treated in mass-action expressions as independent kinetic units. One would therefore formulate this process as in (40). As shown in (40), this cooperative change is analogous to, say, the formation of nonelectrolytic micelles from their monomeric precursors in aqueous solution.[31] The mass-action expression will be $(1 - \alpha) = K(T)$, where $(1 - \alpha)$ is the fraction of monomeric water molecules. This expression is distinctly different from that for equilibrium among two kinds of cooperative clusters (eq 39) and also from that for noncooperative 1:1 sitewise equilibrium. It will be instructive to quantify the cooperative models and to see if, and to what extent, they succeed at reproducing thermodynamic properties.

$$n \text{ monomeric HOH} = \text{H-bonded } [(\mathrm{HOH})_n] \qquad (40)$$

**Registry No.** Water, 7732-18-5.

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