# The Differential Entropy of Dilution in Aqueous Solutions of Amino Acids

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not very close, it is about what one might expect. Likewise, the torsion constants of the *cis*- and *trans*-molecules differ somewhat. However, the pattern of constants shows such general consistency as to lend considerable support to their validity.

To examine the trend of the force constants in passing through the series of vinyl halides, it is informative to see whether or not a similar trend exists in some comparable series. The methyl halides afford such a comparison, and the force constants for bending of the $H-C-X$ angles in these molecules are given by Crawford and Brinkley.[12] Their values, expressed in terms

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[12] B. L. Crawford, Jr. and S. R. Brinkley, Jr., J. Chem. Phys. 9, 69 (1941).

of our units are as follows:

| | $CH_3F$ | $CH_3Cl$ | $CH_3Br$ | $CH_3I$ |
|---|---|---|---|---|
| $k$ | 0.41 | 0.31 | 0.28 | 0.24 |

The relative values of $k$ may be properly compared with those of $F_{22}$ in the vinyl compounds (see Table I). In both series, it is observed that progression from the fluoride to successively heavier halides leads to successively lower force constants.

We are aware that our assignment for vinyl fluoride will make it difficult to explain the published spectrum completely; however, any other assignment gives unreasonable force constants. Further investigation is needed here.

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# The Differential Entropy of Dilution in Aqueous Solutions of Amino Acids

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(Received July 22, 1946)

The relative partial molal entropy of water, $\bar{S}_1-\bar{S}_1^0$, in aqueous solutions of seven amino acids is calculated from existing data. For all solutions, $\bar{S}_1-\bar{S}_1^0=km^2$ approximately; $k$ is positive for glycine solutions and negative for solutions of the two alanines and four aminobutyric acids. The $\bar{S}_1-\bar{S}_1^0$ values are determined largely by the size and structure of the hydrocarbon part of the amino acid and only to a minor degree by its dipole moment. Positive $\bar{S}_1-\bar{S}_1^0$ values are interpreted as indicating a structure breaking effect of glycine on water; negative $\bar{S}_1-\bar{S}_1^0$ values indicate a structure strengthening effect which increases with size of the hydrocarbon residue. The data are consistent with the recent discussion of Frank. Heat capacity and viscosity values for some of these solutions qualitatively show expected behavior.

STUDIES of the heats of dilution of aqueous solutions of amino acids[1-3] have shown that the dipole moment is not the main factor determining the thermodynamic properties of these solutions. The quantity $\Phi_{L2}$ (apparent relative molal heat content) is negative for glycine, has positive values for $\alpha$-alanine and shows a further increment for $\alpha$-amino-*n*-butyric acid, although the dielectric increments for these three substances are approximately equal;[4] in

contrast, $\alpha$-amino-*n*-butyric and $\gamma$-aminobutyric acids show nearly identical $\Phi_{L2}$ values up to 1.2 *m* although the dielectric increment of the $\gamma$-acid is more than twice as large as that of the $\alpha$-acid. The hydrocarbon residue is evidently an important factor. Its influence may be exerted through hydrocarbon-hydrocarbon, hydrocarbon-dipole, and hydrocarbon-solvent interactions.

An examination of the differential entropies of dilution $(\bar{S}_1-\bar{S}_1^0)$ of aqueous electrolyte solutions[5] permitted an attempt to correlate the sizes, shapes, and hydrogen bonding powers of ions with changes in the structure of water in

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[1] W. E. Wallace, W. F. Offutt, and A. L. Robinson, J. Am. Chem. Soc. 65, 347 (1943).

[2] Data for $\alpha$- and $\beta$-alanine, L. S. Mason, H. Benesi, and A. L. Robinson, J. Am. Chem. Soc., to be published.

[3] Data for four aminobutyric acids, L. S. Mason and A. L. Robinson, J. Am. Chem. Soc., submitted for publication.

[4] E. J. Cohn and J. T. Edsall, *Proteins, Amino Acids, and Peptides* (Reinhold Publishing Corporation, New York, 1943), p. 146.

[5] H. S. Frank and A. L. Robinson, J. Chem. Phys. 8, 933 (1940). A recent paper by G. W. Stewart, J. Chem. Phys. 11, 72 (1943) is a particular interest in this connection.

TABLE I. Differential entropy of dilution $(\bar{S}_1-\bar{S}_1{}^0)$, in calorie-degree$^{-1}$-mole$^{-1}$, in aqueous solutions at 25°.

| amino acid \ $m$ | 0.2 | 0.4 | 0.6 | 0.8 | 1.0 | 1.2 |
|---|---|---|---|---|---|---|
| glycine | $0.0_312$ | $0.0_338$ | $0.0_382$ | 0.0015 | 0.0023 | |
| $\alpha$-alanine | $-0.0_488$ | $-0.0_335$ | $-0.0_379$ | $-0.0014$ | $-0.0022$ | $-0.0032$ |
| $\beta$-alanine | $-0.0_311$ | $-0.0_336$ | $-0.0_366$ | $-0.0013$ | $-0.0020$ | $-0.0026$ |
| $\alpha$-amino-$n$-butyric | $-0.0_323$ | $-0.0_391$ | $-0.0021$ | $-0.0037$ | $-0.0058$ | $-0.0084$ |
| $\alpha$-amino-$i$-butyric | $-0.0_330$ | $-0.0012$ | $-0.0027$ | $-0.0048$ | $-0.0076$ | $-0.0107$ |
| $\beta$-amino-$n$-butyric | $-0.0_325$ | $-0.0_395$ | $-0.0021$ | $-0.0037$ | $-0.0056$ | $-0.0080$ |
| $\gamma$-aminobutyric | $-0.0_335$ | $-0.0013$ | $-0.0029$ | $-0.0050$ | $-0.0076$ | $-0.0107$ |

the solutions. Recently Frank[6] has discussed entropies of vaporization of solutes from solutions and has interpreted the data to indicate that frozen patches or microscopic icebergs form around non-polar solutes and the non-polar parts of polar solute molecules in aqueous solutions. Data are now available for calculating $\bar{S}_1-\bar{S}_1{}^0$ values for aqueous solutions of seven amino acids. These values lead to some possible conclusions regarding the effect of the hydrocarbon residues on the structure of the solvent, which are consistent with the interpretations of Frank.

The $\bar{S}_1-\bar{S}_1{}^0$ values of Table I were calculated from

$$\bar{S}_1-\bar{S}_1{}^0 = (\bar{L}_1 - RT \ln (a_1/N_1))/T. \quad (1)$$

$\bar{L}_1$ is the relative partial molal heat content of the water $(\bar{H}_1 - \bar{H}_1{}^0)$ and $a_1$ is its activity, referred to pure water as the standard state. $N_1$, the mole fraction of water in the solution, takes account of the entropy of mixing; the values of Table I give the non-ideal part of the differential entropy of dilution. For consistent comparison all activity values were derived from the vapor pressure measurements of Smith and Smith.[7-9] For the same reason, all $\bar{L}_1$ values were derived from heat of dilution measurements made in this laboratory. Figure 1 shows the plots of the values of Table I against the molality.

There is no satisfactory theory to explain the thermodynamic behavior of these dipolar ions in aqueous solution.[10-13] Purely electrostatic inter-

actions, calculated for various simplified models, do not suffice. From a consideration of activity data Cohn[4] has concluded that the nature and number of polar and non-polar groups, and their positions in the molecule, must be considered in order to obtain a better explanation of the facts.

$\bar{S}_1-\bar{S}_1{}^0$ is the entropy change for the transfer of a mole of water from an infinitely dilute solution to a solution of finite concentration. Since entropy is related to structural order, the $\bar{S}_1-\bar{S}_1{}^0$ values should reflect the effect of the dipolar ions on the quasi-solid structure of water, positive values indicating structure weakening and negative values pointing to structure strengthening effects. For the seven amino acids studied the relation $\bar{S}_1-\bar{S}_1{}^0 = km^2$ holds fairly well, but only for glycine does the constant have a positive value.* The net effect of glycine is thus similar to that of sodium and potassium halides and nitrates at $1\,m$ while the behavior of the other six amino acids parallels the effect of ions such as $H_3O^+$, $OH^-$, $NH_4^+$, $Li^+$, and $F^-$, whose structure strengthening effect has been attributed to their small size or their hydrogen bridging capacity.[5]

The structure strengthening effect of the amino acids obviously cannot be attributed to these same factors. The order shown by glycine, $\alpha$-alanine, and $\alpha$-amino-$n$-butyric acid, and also by $\beta$-alanine and $\beta$-amino-$n$-butyric acid, is the reverse of the order expected from constant dipole moment and increasing size. Another factor, the non-polar hydrocarbon groups, seems to play the dominant role, giving rise to a structure strengthening interaction with the water. The values of Table I are derived from accurate data and the differences shown by the

[6] H. S. Frank, J. Chem. Phys. 13, 507 (1945).
[7] E. R. B. Smith and P. K. Smith, J. Biol. Chem. 117, 209 (1937).
[8] E. R. B. Smith and P. K. Smith, J. Biol. Chem. 121, 607 (1937).
[9] E. R. B. Smith and P. K. Smith, J. Biol. Chem. 132, 47 (1940).
[10] G. Scatchard and J. G. Kirkwood, Physik. Zeits. 33, 297 (1932).
[11] J. G. Kirkwood, Chem. Rev. 19, 275 (1936).
[12] R. M. Fuoss, J. Am. Chem. Soc. 56, 1027 (1934).
[13] R. M. Fuoss, J. Am. Chem. Soc. 58, 982 (1936).

* The dependence on $m^2$ is a reflection of the relative importance of the term in $\bar{L}_1$ in Eq. (1). There is some uncertain evidence that $\bar{L}_1$ for glycine[1] may also become negative at very small concentrations.
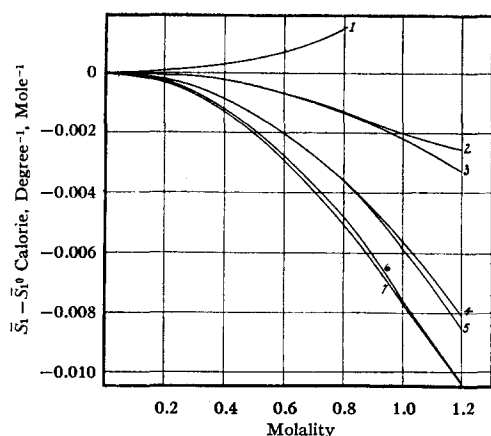
FIG. 1. Relative partial molal entropy of water, $\bar{S}_1 - \bar{S}_1^0$, in aqueous amino acid solutions: 1, glycine; 2, $\beta$-alanine; 3, $\alpha$-alanine; 4, $\beta$-$N$-butyric acid; 5, $\alpha$-$N$-butyric acid; 6, $\alpha$-iso-butyric acid; 7, $\gamma$-butyric acid.

members of an isomeric group are undoubtedly real, but it is interesting that $\Delta \bar{S}_1$ at $1\,m$ is $-0.0044$ in going from glycine to the alanines (average) and almost the same, $-0.0046$, in passing from the alanines to the aminobutyric acids (average). Small differences are noted between $\alpha$- and $\beta$-$n$-acids; hydrocarbon branching and the $\gamma$ position for the $NH_3^+$ group give the most negative values of $\bar{S}_1 - \bar{S}_1^0$, but further study will be required to clarify these effects.

The structure strengthening effect on water shown by the non-polar parts of these dipolar ions is consistent with the recent discussion by Frank[6] of the abnormally high entropies of vaporization of rare gases and hydrocarbon gases from water. Frank suggests that when a rare gas atom or a non-polar molecule or a polar molecule with non-polar parts dissolves in water at room temperature it modifies the water structure in the direction of greater "crystallinity." This effect increases with the size of the solute molecule. Our own study leads to similar conclusions and simply suggests that this "freezing" of the

water (Frank's calculations are for infinite dilution) increases with concentration in the range of this study. For glycine the structure breaking interaction, always present, is not compensated by the "iceberg" effect because of the small non-polar part.

The high apparent heat capacities of amino acids and fatty acids and alcohols in aqueous solutions have attracted comment.[14] In a homologous series of liquids the increment in $C_p$ per $CH_2$ group is only 6 to 8 cal./mole while in aqueous solution the increment in $\Phi(C_p)$ is 20 to 30 cal./mole. Similar behavior is shown by aqueous solutions of the rare gases, the effect also increasing with the size of the rare gas atom. The explanation for these large heat capacities given by Frank[6] should apply equally well to solutions of the amino acids. With increase of temperature the melting of the quasi-crystalline patches of water, which the entropy values indicate increase in size with increasing size of the hydrocarbon residue, will add an increasingly positive term to the heat capacities.

We may also call attention to the viscosities of aqueous solutions of glycine and $\alpha$-alanine.[15] Previous discussions of the effect of solutes[16, 6] on the structure of water have pointed to the relation between the viscosities of solutions and the structure weakening or strengthening influence of the solute. At 18° the relative viscosities of $1\,m$ solutions of glycine and $\alpha$-alanine are 1.153 and 1.310, respectively. Qualitatively such a difference would be expected in terms of the present discussion. More extensive data, both for entropies of dilution and viscosities, would be of interest for a further discussion of the effects of amino acids on the structure of water.

[14] J. T. Edsall, J. Am. Chem. Soc. **57**, 1506 (1935). See also reference 4, p. 168.

[15] G. Hedestrand, Zeits. f. anorg. Chemie **124**, 153 (1922).

[16] J. D. Bernal and R. H. Fowler, J. Chem. Phys. **1**, 515 (1933).