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Enthalpies of transfer for amide-water-electrolyte systems

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ENTHALPIES OF TRANSFER FOR AMIDE–WATER–ELECTROLYTE SYSTEMS

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A Dissertation Presented

By

EVELYN REINHEIMER STIMSON

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ENTHALPIES OF TRANSFER FOR AMIDE-WATER-ELECTROLYTE SYSTEMS

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TO TOM

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Ithaca, New York
June 1971

Evelyn R. Stimson

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ENTHALPIES OF TRANSFER FOR AMIDE-WATER-ELECTROLYTE SYSTEMS

(June, 1971)

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The enthalpies of transfer for model amides, N,N -dimethylacetamide, N-methylacetamide, acetamide, formamide, N-methylformamide, N-acetylglycine-N-methylamide, N-acetylalanine-N-methylamide, N-acetylleucine-N-methylamide, and N-acetylglycylglycine-N-methylamide, from water to aqueous salt solution have been measured at 25° using the method of solution calorimetry. Measurements were done at limiting amide concentrations over a wide range of salt concentrations, 0.1 to 7.0 molal in some cases. Salts employed included alkali halides, alkaline earth halides, and guanidine hydrochloride. Trends in the heats of transfer were observed in an attempt to better characterize the forces responsible for isothermal denaturation by electrolytes.

From the dependence of the amide transfer upon 1) the total polarization density of the solvent, 2) the length of the peptide, 3) the configuration of the peptide, 4) the substituents on the peptide, and 5) the molecular symmetry of the amide, it is postulated that dispersion forces are important in these systems.

Finally, a model is presented for enzyme denaturation based upon the model compound data and this is tested for the case of lysozyme.

CHAPTER I

INTRODUCTION

A. Opening Remarks

Although it is known that inorganic salts as well as urea, guanidine hydrochloride, alcohols, organic solvents, etc., denature proteins and nucleic acids reversibly and isothermally in aqueous solutions,[1-5] the mechanisms or forces responsible for these conformational changes are the subject of uncertainty and controversy.[5] Nonetheless, it is clear that salts influence conformation and, consequently, the activity of enzymes and biological processes.

One of the most important biological systems, therefore, consists of salt-water-biopolymer. Proteins, nucleic acids, and other polyfunctional compounds exist and function, in vivo, in an environment of predominantly salt, water, and nonelectrolytes, such as sugars and lipids for instance. The understanding of the phenomenon of conformational changes of macromolecules in these media is basic to the understanding of biochemical systems.

Hydrogen bonding, hydration, hydrophobic bonding, changes in water structure, electrostatic interactions, ion binding and charge-transfer complexing are some of the possible modes of intermolecular interaction that have been postulated to be responsible for these changes in proteins.[1-5]

Systems such as aliphatic amide-salt - water represent a distinctly different degree of complexity from protein solutions. Yet the intermolecular forces responsible for dissolution and solvation of an amide group are similar to those for a peptide group on a protein which is changing its environment from a hydrophobic region to the surrounding aqueous medium in the course of a conformational change.

Although the applicability of model compound data to the elucidation of processes taking place in large molecules is not established on theoretical grounds, one approach in the attempt to predict the free energy changes and related quantities associated with conformational changes in salt solutions, if only in an empirical manner, has been to assume that the different groups of a protein molecule can be considered to a first approximation as sets of species components in a thermodynamic sense.[5-6] These group properties are obtained from small model compounds and are assumed applicable to more complex systems of interest. The results to be presented in this thesis provide enthalpy data for model compounds which may be used 1) to examine the additivity hypothesis considering a different thermodynamic property, 2) to shed more light on the forces operating in these systems, and 3) to predict the enthalpy of conformational change in protein-water-salt systems.

B. Isothermal Denaturation of Proteins by Electrolytes

Enzymes and other proteins have a three-dimensional structure or conformation which represents the biologically active ("native") form in solution. This conformation is dependent upon pH, temperature, added electrolytes, and other perturbing forces. Through such stresses the protein can denature or change conformation and become inactive.

In this work we will consider primarily the effect of adding electrolytes to an isothermal solution, at neutral pH and constant temperature (25°). Presumably the "native" structure is the state with minimum energy so that through the addition of electrolytes the protein-protein and protein-solvent interactions are energetically altered. Unfortunately, as is well known, the stability of protein conformations is largely determined by weak noncovalent forces, which are the most difficult to treat quantitatively in an *a priori* calculation of protein structure for a given peptide sequence.[7-8] Consequently the structure of a protein and the thermodynamic parameters of denaturation cannot be calculated *a priori* at present. Physico-chemical measurements, and a working theoretical hypothesis to relate denaturation to the observable properties arising from intermolecular forces, are still required.

C. Thermodynamic Quantities of Transfer from Model Compounds

If intermolecular forces between proteins and electrolytes are assumed to be only electrostatic, they are additive only in the absence of polarization.[9] Since in all real molecules and molecular systems, the addition of one charged group causes a redistribution of charges, the additivity of group contributions to intermolecular forces may not be realistic in all cases. Likewise, inductive effects between different molecules with conjugation or double bonds may cause an electron redistribution as well. In fact, it is known that stabilization through electron delocalization often increases more rapidly than expected from a linear relationship.[10] In these cases there results a breakdown in the additivity of intermolecular forces of groups so that collective terms must be considered.

But whenever it is realistic to consider the additivity of group contributions, it is assumed that each portion of the compound reacts independently and unperturbed by any group attached to it; i.e., minimal electron delocalization or overlap. This is equivalent to partitioning a protein into its component groups so that

$$\delta F_{tr} = \sum_j \delta f_{tr,j} \qquad (1)$$

where δF_{tr} represents the molecular thermodynamic property (free energy, enthalpy, entropy, or heat capacity) of transfer from water to electrolyte solution and δf_{tr} represents that for only a small group or portion of the molecule. With this simplified theory,[5-6] the individual thermodynamic group contributions may be experimentally measured using small model compounds that have a set of groups in common. It may not even be necessary that the model compounds are homologs of the more complex molecule under consideration, although homologs of comparable polarity are definitely preferable.

Variation and embellishment of the basic additivity concept can take many different theoretical forms to relate experimentally measured group enthalpies and the processes occurring in biological systems. The hypothesis does not predetermine:

1) Choice of model compounds or model systems,
2) Size of the group to be considered,
3) Whether one type of noncovalent bonding (e.g., hydrogen bonding, ion binding, etc.) can be considered in exclusion of all others,
4) Treatment of nonlinear contributions (e.g., cooperative effects).

In this work the model compounds are chosen on the basis of their simplicity. Formamide is used as the model

for a "bare" peptide group without the hydrophobic C_α carbon. Through measured enthalpies of transfer, the effects of varying the ionic radius and charge of both the electrolyte anion and cation in model systems are expected to provide information applicable to the backbone peptide groups in a macromolecule under similar circumstances. The effects of increasing the structural and electrostatic complexity, through additional hydrophobic and peptide groups, for an amide series are expected to indicate the forces upon these groups. These amide-electrolyte-water solutions serve as model systems for enzyme-electrolyte-water systems in which denaturation occurs within the concentration range of electrolytes studied in the model systems. Thus the transfer enthalpies derived from the model systems are expected to approximate that transfer enthalpy which results from a globular protein molecule, only peripherally exposed to the electrolyte solution, uncoiling and exposing all its internal units to the solvent. From this viewpoint

$$\Delta H_{\text{denaturation}} \simeq \sum \delta h_{tr} \qquad (2)$$

where a judicious choice of δh_{tr}'s is made.

D. Experimental Methods of Determining Enthalpies of Transfer

1. Calorimetric Method

Of the direct calorimetric methods for measuring ΔH_{tr} --i.e., heat capacity, differential and integral heats of solution and dilution--that involving the integral heat of solution[11] was selected because it could achieve the greatest accuracy considering the equipment which was available.

In the integral heat of solution method, we measure the heat change associated with the following process

$$\text{Amide } (m_1) + H_2O\ (55.51) \xrightarrow{q_3} \left|\begin{array}{l}\text{Solution of}\\ \text{Amide in}\\ \text{Water with}\\ \text{Molality of}\\ \text{Amide} = m_1\end{array}\right| \qquad (3)$$

In this process, the measured heat change, q, is related to the integral heat of solution as

$$\Delta H^{w}_{soln} = \frac{q_3}{m_1} \qquad (4)$$

The superscript "w" on the integral heat of solution refers to the fact that the amide has been dissolved in pure water.

Similarly, we measure the integral heat of the process

$$\text{Amide } (m_1) + \left|\begin{array}{c} H_2O\ (55.51) \\ + \\ \text{Salt } (m_2) \end{array}\right| \xrightarrow{q_5} \left|\begin{array}{l} \text{Solution of} \\ \text{Amide and Salt} \\ \text{in Water with} \\ \text{Molality of} \\ \text{Amide} = m_1 \\ \text{Salt} = m_2 \end{array}\right| \qquad (5)$$

as

$$\Delta H^{ws}_{soln} = \frac{q_5}{m_1} \qquad (6)$$

Here the superscript, "ws", implies that the amide has been dissolved in an aqueous salt solution.

The heat of transfer of the amide between water and the salt solution is given as

$$\Delta H_{tr} = \Delta H^{ws}_{soln} - \Delta H^{w}_{soln} \qquad (7)$$

In practice, the amide molalities are kept small to avoid any complication from short range amide-amide interactions. The molal enthalpy of transfer then is the enthalpy change accompanying the transfer of one mole of amide from water to an aqueous salt solution at amide molalities approximating infinite dilution.

Although there has been no systematic study of the behavior of amides in aqueous electrolyte solution, a few results do exist.[12] There are more extensive data for systems containing compounds other than amides.[13-17] However, these results are of varying levels of precision or at scattered salt concentrations.

2. Temperature Dependence of ΔG_{tr}

Although it is possible in principle to obtain ΔH_{tr} from the temperature dependence of ΔG_{tr}, it is difficult to obtain high precision over a sufficiently broad temperature range so that the derivative is meaningful. Furthermore, of the available methods for determining ΔG_{tr}--such as solubility, distribution, vapor-pressure, and electrochemical--all pose other inherent difficulties and limitations. The concentration range is severely limited in the solubility method, solubility and solvent effects are a problem with distributions and the vapor pressure of the solute may cause problems in isopiestic determinations. Of these methods, the electrochemical method is often considered to be better for measuring small differences; even so, because large differences in the nonelectrolyte concentrations must be utilized in order to obtain measureable $\delta\Delta E$ for systems with small transfer energies, the lower limit of the mean nonelectrolyte concentration is limited.

In view of these restrictions, the distribution,[6] isopiestic,[18] and electrochemical[19] methods have been applied only to a few compounds analogous to amides to obtain ΔG_{tr} but the temperature dependence of ΔG_{tr} has not been studied.

E. Estimates of Interactions from Spectroscopic Measurements

One possible method of investigating the nature of intermolecular forces and of determining thermodynamic quantities is the spectroscopic method.[20-21]

The spectral method has been applied successfully, for instance, in the ultraviolet region for the determination of the enthalpies of denaturation.[22-24] However, extension of the method to tyrosine as a model compound did not detect a salt perturbation of the position of absorption of the phenolic group.[25] Since most concentrated salt solutions are not transparent in the far ultraviolet, the consideration of other model compounds is not practical.

Another example where this method has been used is that for the gas phase study of intermolecular forces. For instance, the pressure-induced absorption shifts of the rotational lines in the vibrational-rotational bands of HCl by the addition of other gases have been shown to indicate that both long-range and short-range attractions are necessary to account for the experimental features in rotational analysis.[26] But as the intermolecular distances decrease, the frequency of collision increases so that liquids in general do not show rotational fine structure.

However, the observed alterations of the broad vibrational bands are resultants of electrostatic interactions

and may be attributed to any one or a combination of the following: 1) a shift or broadening when free rotation of the classical oscillating dipole is restricted, 2) a new band or species resulting from a strong attractive interaction, or 3) changed transition probabilities or energies due to vibronic or other perturbations.

Unfortunately, even though band position, shape, and intensity theoretically reflect all intermolecular interactions accurately in solution, the quantitative interpretation of the vibrational-rotational bands is difficult. For instance, McCabe and Fisher[27] treat binary solutions with near-infrared difference spectral methods but do not extend the study to three components.

Nonetheless, because spectra obtained in both the near and far infrared have been used in studies of hydrogen bonding[28] and other secondary interactions, and in view of the postulated importance of these interactions in polypeptide conformational stability, we decided to try an exploratory study in the practical near infrared spectroscopic region as an alternative means of estimating an order of magnitude for the transfer energy.

In order to apply this method, we will first make the following simplifying assumptions for an ideal amide-salt-water mixture:

1) A liquid mixture of noninteracting, nearly spherical molecules, is analogous to a condensed gas.
2) The ground state amide and ground state water molecules will retain the same energies in all ideal solutions at a given temperature.
3) The reference states chosen will be that of the average amide molecule in pure formamide solution at a given temperature, and likewise for the water molecules, without regard to species present.
4) Only one other amide electronic state is involved.
5) The vibrational sum rule holds so that the intensity is proportional to the number of molecules for collisional and thermal excitation.

Then from the measured density and concentration in a mixture, and the experimental absorbances of the pure reference solutions, it is possible to calculate an ideal absorbance for a mixture which can be compared to the experimental value. Any salt concentration or temperature dependent band shift or intensity change will qualitatively be attributed to some molecular interactions of otherwise unspecified origin. In brief, this is analogous to determining an excess property and could lead in the most favorable case to an estimate of ΔH_{tr}.

The actual description of the details involved will be deferred until the discussion of the results.

F. Aims of Research

Work was initiated to systematically determine enthalpies of transfer for some model amides in order 1) to seek correlations which might give insight into the nature of the intermolecular forces involved in the interactions occurring in electrolyte solutions, 2) to use this information for better understanding polyfunctional macromolecules such as proteins, and 3) to explore other possible ways of determining these energies for comparison.

CHAPTER II

EXPERIMENTAL METHODS

The materials, instruments, and experimental techniques used in this work are described briefly in this chapter.

A. Chemicals and Materials

1. Amides

Formamide, Scintillation Grade obtained from Nuclear Enterprises, or Reagent Grade obtained from Eastman Kodak Co., was fractionally recrystallized twice under dry nitrogen by the method outlined by Lagowski.[29] The material so obtained was chromatographically pure (>99.9%) when tested with a Beckman GC-4 Flame Ionization Gas Chromatograph using three different columns (Ten percent Carbowax-20 M on Chromosorb W, 25% SE-30 on Chromosorb P and 10% Versamid on Chromosorb W). This material had a melting point of 2.55° (uncorrected) and was stored under Linde 4A molecular sieves to maintain dryness. Karl Fisher titrations[30] detected less than 0.05% water.

N-methylformamide (NMF), purchased from Eastman Kodak Co., was vacuum distilled at approximately 51° and 1 mm pressure from phosphorus pentoxide. It was dried over molecular sieves and was shown to be chromatographically

pure and free from decomposition products, other amides, and water.

N,N -dimethylformamide (DMF), from Burdick & Jackson Laboratories, was vacuum distilled from that which had been dried over reagent grade potassium hydroxide pellets. The chromatographically pure amide was stored over molecular sieves but was not assayed for water content since only a few ppm are reported[31] for material treated similarly.

Acetamide purchased from Eastman Kodak Co. was dissolved in hot anhydrous methanol, filtered, diluted and recrystallized with anhydrous diethylether.[29] The crystals were filtered, washed, and stored over P_2O_5 in a vacuum desiccator for several weeks until all traces of solvents had been removed.

N-methylacetamide (NMA) received from Eastman Kodak Co. was purified by fractional freezing and the crystalline product stored over P_2O_5, in vacuo, to maintain dryness.

N,N -dimethylacetamide (DMA), distilled in glass and packed under nitrogen by Burdick & Jackson Laboratories, was chromatographically pure when received (>99.99%) and was used without further purification. Dryness again was maintained with molecular sieves.

N-acetylglycine-N-methylamide, purchased from Cyclo Chemical Corp., was recrystallized twice from hot methyl acetate solutions, filtered, ground to a fine powder and

stored for several weeks in a vacuum desiccator over P_2O_5 until all traces of methyl acetate and water were removed. This amide melted at 159.5° (uncorrected) under an atmosphere of nitrogen.

N-acetylglycylglycine-N-methylamide, custom synthesized by Fox Chemical Co., was dried and used without further purification.

N-acetylalanine-N-methylamide and N-acetyl-leucine-N-methylamide were purchased from Fox Chemical Co., dried in vacuo for at least 24 hr and used without further purification.

N-methylpropionamide (NMP) obtained from Eastman Kodak Co. was purified by vacuum distillation. The constant boiling middle third fraction was collected under nitrogen and stored over molecular sieves. The product purity (~99.99%) was determined chromatographically.

Egg White Lysozyme from Sigma Chemical Co., was Grade 1, 3 times crystallized, dialyzed and lyophilized. The water content was determined by heating a weighed sample in vacuum oven at 100° until a constant weight was obtained (about 24 hr).

2. Salts

Salts were routinely dried as needed but otherwise were used normally without further purification. Although

corrections were made in calculations of concentrations, it was found experimentally that certain impurities could not be tolerated and these batches of salts were eliminated or recrystallized as necessary. In Table 1 are listed the salts used, sources, and assays reported on the label or assayed by standard methods.

3. Other Materials

Acetone from Burdick & Jackson Laboratories was used as the reagent in the calorimetric determinations while acetone from J. T. Baker Chemical Co. was routinely used for washing the calorimeter cell. The former product was dry (~0.02%) whereas the latter product had a variable water content.

Nitrogen gas was obtained from different sources but was always of the highest purity and dryness.

Molecular sieves of Types 3A and 4A were obtained from Fisher Scientific Co. and were a product of Linde Air Products Co. These were regenerated as necessary by heating in a furnace at approximately 400° for 24 hr or longer.

Tris(methylhydroxy)aminomethane, abbreviated Tris or THAM, was purchased from Sigma Chemical Co. and used as received except for drying.

All concentrated and diluted hydrochloric acid used was Baker Analyzed Reagent Grade.

Table 1

Electrolyte Sources and Assays

Salt	Source	Assay
$BaCl_2 \cdot 2H_2O$	J. T. Baker Chemical Co.	99.8%
$CdCl_2$(anhyr.)	K & K Laboratories	95
CsCl	Fisher Scientific Co.	99.9
$CaCl_2$	J. T. Baker Chemical Co. Recrystallized from water	97.4
$LaCl_3$	Fisher Scientific Co.	99
LiCl	J. T. Baker Chemical Co.	99.9
$LiClO_4$(anhyr.)	K & K Laboratories	>99.8
$MgCl_2 \cdot 6H_2O$	J. T. Baker Chemical Co.	99.9
KCl	"	99.9, 100.0
KBr	"	99.9, 100.3
KI	"	100.0, 101.0
NaCl	"	99.9, 100.0
NaBr	"	99.6, 99.7, 99.9
NaI	"	>99.9, Iodine free
NaSCN	"	100.0
$AgNO_3$	"	100.5
$SrCl_2$	Fisher Scientific Co.	99.8
SrI_2	K & K Laboratories	95
GuHCl*	Eastman Kodak Co.	---
GuH_2SO_4*	"	---
GuHSCN*	"	---

*Gu = guanidine.

1-Propanol was kindly supplied by Floyd Wilcox who had purified it by distillation. The 97-97.5° midportion was checked chromatographically (>99.9%) and stored over molecular sieves. Less than 0.02% water content was maintained throughout the experiments.

Water, although distilled, was neither degassed nor carbon dioxide free. Originally an attempt was made to use degassed solutions but variable amounts of air were beat back into the solution by the stirrer. Since operation of the calorimeter with degassed solutions indicated a major redesign of both apparatus and procedure,[32] this precaution was dropped because air did not significantly affect the resulting transfer enthalpies. However, the pH of the salt solutions was always higher than pH 6 and was usually near pH 7.0 except for those solutions buffered elsewhere.

B. Instruments and Experimental Procedures

1. Calorimetric Method

a. General description of the calorimeter. All heats of solution used to calculate the heats of transfer were measured using a commercially available instrument--the LKB Model 8700-1 Precision Calorimeter.[33] This calorimetric system is one of the basic designs developed by Sunner and Wadsö.[34] This model is one of the shielded isothermal designs suitable for heats of solution in which the

materials dissolve rapidly in a narrow temperature range between twenty and forty degrees at atmospheric pressure.

The instrument consisted of three major components:

1) A thermostated bath, with a proportional heater and temperature controller (LKB #7600), and an external cooling bath (A Laude Model R-2 Bath was used in this case);

2) The calorimeter assembly (LKB #8721-1), including an automatically activated ampoule breaker (LKB #8722) and stirrer driver (LKB #8723); and

3) The electronic console with power supply (LKB #8701), galvanometer (Hewlitt Packard #419A), D.C. potentiometer (LKB #8704), Wheatstone bridge (LKB #8703), electronic timer (LKB #8705), standard reference cells (Muirhead & Co., Ltd.) and recorder (a Beckman 10" Linear-Log Recorder, Model #100502).

The assembled thin walled glass reaction vessel (100 ml) contained a temperature sensing thermistor (2K), an electrical heater (50Ω) for calibration, a combination gold stirrer-ampoule sample holder, and an embedded sapphire tip at the bottom for heat-free punctures. The reaction vessel was assembled in a reflective chrome washed brass jacket, which was sealed, evacuated, and submerged into the thermostating bath.

The reaction was initiated by the mechanical crushing of the thin walled ampoule (≈ 1 ml) on the sapphire tip and the heat liberated or absorbed was followed as a resistance change of the thermistor in the reaction vessel.

A detailed physical description of the instrument, the manufacturer's specifications and the company's recommended operational procedure can be found in their manual.[33]

b. Sample preparation. The most demanding step in the whole calorimetric procedure was that of preparing the sample. It is this step which determined the accuracy as well as the precision of the results. The difficulties encountered in sealing a sufficiently accurate weight of pure, dry compound under an inert atmosphere of gas could be attributed to: 1) the hygroscopic nature of the amides and 2) the variation in quality, cleanliness, size, and glass hardness of the ampoules supplied by the manufacturer. The first problem was largely circumvented by working in a dry box flushed with dry prepurified nitrogen. The second problem contributed a less consistent error; an error for which it is difficult to make corrections. The fact that the supplier's ampoules (especially those with ≈1 mm stems) were not "calorimetrically" clean inside was often visually observed and in other cases, was detected by the weight changes measured from the difference in weight of an empty ampoule before sealing with the miniature oxygen torch and

after sealing. Tests of this nature determined that the weights were only reliable to the nearest 0.1 mg.

Although it was desirable to approximate infinite dilution as nearly as possible, it was often necessary to compromise and use larger sample weights in order to reduce the percentage error in the weight and in the resulting molality. Thus, even though the detection of small heats were made as reliable as large ones, the sample weights throughout this work were in the 0.05 to 1.0 gram range, contributing errors of ≈0.1% or less to the final heats of solution. Larger sample sizes were avoided not only because the infinite dilution approximation was violated, but also because corrections for heat losses were considerable.

c. Techniques and modifications. Since the LKB operating procedure, as outlined in their manual,[33] was not used for most of the experiments reported here, a brief outline of the alternative operational procedure followed is included in the following discussion. This alternative method, adapted from adiabatic calorimetry experience,[34] was used only after it had proven to be more sensitive than the LKB procedure and to give identical results--both in precision and accuracy--for the particular problems of interest.

After the proper (proper is here equivalent to no random noise being generated) adjustment of the ampoule in

the cell holder, the 100 ml reaction vessel was weighed on a Mettler Analytical Balance, and reweighed with 100 ml of solution pipetted into the vessel from a 100-ml volumetric pipette. The reaction vessel was then coupled tightly (vacuum tight) and the thermistor and heater leads connected to the can cover; the components were then assembled. A partial vacuum (always 150 mm) was drawn on the can in order to retard conductional heat losses to the bath and to minimize effects from a variable bath temperature. (The inefficiencies in the mixing and equilibration of the bath were demonstrated by a simple ice cube test. An ice cube was placed into the bath and the length of the time necessary for the bath to register this imbalance was determined. The minutes required to re-equilibrate the system within the 0.001° company specification throughout the bath were also measured. In laboratories used with poor air-conditioning systems, hot or cold drafts of air upon the outside created bath fluctuations in the bath temperature.) A bath temperature of 25° was used throughout the series of experiments.

The stirrer motor was always set on the "high" (600 rpm nominal speed) position but the cable was modified to a free floating design after excessive and variable heating effects were observed to occur from variable turning rates caused by frictional constraints at the terminal couplings. Solution of all compounds investigated and reported here

took place in less than one minute under these conditions. Thus extrapolations and heat loss corrections were relatively small (<1%).

Although room temperature was maintained as closely to 25° as possible, experiments performed under ambient temperatures ranging from 19° to 29° gave the same heats of solution. The primary difference in runs at these extreme ambient temperatures was the longer pre-equilibration times necessary to bring the sample to the desired temperature. Final adjustments to bring the samples to within ±0.01° of 25.00° were usually made manually.

After the temperature inside the cell was stable at 25.00° for approximately ten minutes, the recorder was switched on and the galvanometer sensitivity turned up. The interfacing of the calorimeter with the recorder was done in a manner such that a full ten inch chart deflection was normally set equivalent to a 0.1 or 0.2 Ω shift (0.01 Ω was used in some trial experiments) with the recorder set on the 1 mv range. In this way a 0.002 cal heat change (5×10^{-6}° change in temperature), such as the heat of vaporization of water into a 1 ml ampoule filled with nitrogen, was observable. A recorder chart speed of two inches per minute was used. The heat of breaking the ampoule was small (<0.1%) relative to the heats measured and was cancelled out to a large extent in

the calculation of transfer heats. Glass corrections were also much smaller than errors from other sources and were not calculated.

When a linear recorder trace had been established and the Wheatstone bridge setting was recorded a 0.1 Ω shift was made on the bridge and the final bridge setting was recorded for chart calibration. After the base line was reestablished, the breaking of the ampoule was initiated manually. The bridge was again adjusted to bring the recorder trace on scale for the after-break base line. Extrapolation of these base lines through the mixing period was made and the half time difference value was used to correct the resistance recorded from the bridge.

The calibration adjust was made in every experiment before the heat capacity calibration. Furthermore, the heat capacity calibration was run for all samples. Only in the few cases where the heater lead was making intermittent contact was the heat capacity of the solution used from another duplicate sample in order to salvage the data. Subtle differences in the calorimeter conditions necessitated this repetition. For experiments reported here, the calibration time was always 80 ± 0.0003 sec, and either 200 or 500 mw power was used. The recording technique used for the heat capacity determinations was the same as

that for the heat of solution determinations except that the exponential heat losses necessitated use of a 0.63 "half-time."

The calorimeter thermistor was calibrated against a NBS certified platinum resistance thermometer (Leeds & Northrup #8163-B) in conjunction with a Mueller bridge (Rubicon Co. #1550) by fitting the thermistor-temperature data to the equation

$$R = \exp^{(\beta/T+\alpha)} \qquad (8)$$

for a slightly larger temperature interval than that used in the experiments (24-26°). These constants were used to convert observed resistance changes into temperature differences. Using the constants derived from the thermistor calibration, the resistance differences, weights, molecular weights, voltage, and time recordings, the ΔH_{soln}, temperatures, final molalities, etc., were calculated and printed out using a program on the IBM 360/40 computer.

d. Preliminary tests. Three calibration and test compounds were used initially to test the calorimeter, its operation and techniques. These were:

1) Tris(methylhydroxy)aminomethane titrated with 0.1 M HCl,
2) KCl solution in water, and
3) DMF (dimethylformamide) solution in water.

The results of these tests and the literature values are listed in Table 2. Considering the lack of "real" test compounds[35] for solution calorimetry as well as the concentration dependencies observed,[36] the agreement was considered to be satisfactory.

2. Spectroscopic Method

a. Apparatus and procedure. Because of the lack of an appropriate blank, all samples were run using dry air at room temperature in the reference compartment of a Cary 14 Spectrophotometer. All sample solutions were run with the same 0.1 cm cell (which, when cleaned thoroughly and routinely, required no corrections in the 6000 to 20000 Å region) under the same instrumental conditions (i.e., scan speed, chart speed, slit, slidewire, and damping conditions). All peaks were considered relative to the transparent region as a precautionary measure since there were occasions when the lamp characteristics changed during the series. The slit width was controlled between 0.15 and 0.2.

b. Preparation of solutions. Due to the relatively large temperature effects, as well as the greater accuracy obtained by weights, all solutions were prepared by weight. Densities of these solutions were measured as a function of temperature using a Christian Becker Density Balance and an Atkins Thermistor Probe as the temperature monitor.

Table 2

Calorimeter Tests

Compound	Molality x 10^2	ΔH_{soln} kcal $mole^{-1}$	Literature Value	Reference Number
Tris	2.745	-7.113	-7.101	36
	2.093	-7.115	-7.112 to 7.125	33
KCl*	2.0695	4.101	4.115 ± 0.010	37
	2.2165	4.083	4.104 ± 0.002	38
	3.2431	4.119		
	2.0812	4.084		
	4.8656	4.116		
	1.8379	4.096		
	1.3355	4.104		
	Average	4.100 ± 0.005		
DMF	2.6067	-3.637	-3.640 ± 0.029	39
	5.0240	-3.651		
	1.8954	-3.623		
	7.639	-3.631		
	9.0354	-3.631		
	Average	-3.635 ± 0.005		

* All values are corrected to infinite dilution.

C H A P T E R I I I

EXPERIMENTAL RESULTS

A. Calorimetric Measurements

1. Original (Reduced) Data

a. Discussion of format and symbols. The experimental data are tabulated in the section which follows. Each model system, either AMIDE-WATER SYSTEM or AMIDE-ELECTROLYTE-WATER SYSTEM, is given a separate page labeled accordingly, except where a table may contain a series of electrolytes. When a table contains a series, such as the FORMAMIDE-ALKALINE EARTH HALIDE-WATER SERIES, the individual salts are indicated within the text of the table.

These tables consist of four columns or less headed by the following symbols:

1) Amide Molality $m_1 \times 10^2$ — The amide concentration is given in moles per 1000 grams of water.

2) Salt Molality m_2 — The electrolyte concentration is given in moles per 1000 grams of water.

3) ΔH^{ws}_{soln} kcal $mole^{-1}$

or

ΔH^{w}_{soln} kcal $mole^{-1}$ — The amide molal heat of solution is as defined in equation 4 or 6.

4) ΔH_{tr} kcal mole^{-1} — This represents the amide molal transfer enthalpy calculated from the average values according to equation 7.

The precision of these values is indicated by the standard deviation.

Some of the transfer enthalpy data contained in these tables are presented in graphical form in the Figures (1-18) succeeding the tables.

b. Tables of Data.

Table 3

Enthalpies of Solution Per Mole of Formamide Dissolved to Give Various Molalities in Water

Amide Molality $m_1 \times 10^2$	ΔH^W_{soln} kcal $mole^{-1}$
1.5683	0.4843
2.0202	0.4876
5.6572	0.4825
	Ave. 0.4848 ± 0.0016

Table 4

Enthalpies of Solution Per Mole of N-Methylformamide Dissolved to Give Various Molalities in Water

Amide Molality $m_1 \times 10^2$	$-\Delta H^w_{soln}$ kcal mole^{-1}
1.0194	1.709
1.0958	1.701
1.2245	1.705
1.2287	1.711
1.2725	1.700
1.3694	1.709
	Ave. 1.706 ± 0.002

Table 5

Enthalpies of Solution Per Mole of Acetamide Dissolved to Give Various Molalities in Water

Amide Molality $m_1 \times 10^2$	ΔH^w_{soln} kcal mole^{-1}
2.3279	2.306
2.5055	2.305
	Ave. 2.305 ± 0.001

Table 6

Enthalpies of Solution Per Mole of N-Methylacetamide Dissolved to Give Various Molalities in Water

Amide Molality $m_1 \times 10^2$	$-\Delta H^w_{soln}$ kcal mole^{-1}
1.5295	0.9398
1.6378	0.9438
1.9118	0.9375
2.0865	0.9396
	Ave. 0.9402 ± 0.0013

Table 7

Enthalpies of Solution Per Mole of

N,N -Dimethylacetamide Dissolved to Give

Various Molalities in Water

Amide Molality $m_1 \times 10^2$	$-\Delta H^W_{soln}$ kcal mole^{-1}
Trial runs all on the same day with the same cell and conditions:	
1.8294	5.118
1.8691	5.108
3.0446	5.111
3.1409	5.121
4.2224	5.124
	Ave. 5.116 ± 0.003
Miscellaneous runs on different days with different cells and conditions:	
1.6251	5.124
2.1538	5.118
2.2004	5.124
2.2418	5.113
2.6545	5.122
3.2323	5.120
4.2723	5.104
4.7356	5.117
5.2598	5.113
	Ave. 5.116 ± 0.002

No concentration dependence was discernible within the region studied.

Table 8

Enthalpies of Solution Per Mole of N-Methylpropionamide Dissolved to Give Various Molalities in Water

Amide Molality $m_1 \times 10^2$	$-\Delta H^W_{soln}$ kcal mole^{-1}
1.0743	3.562
1.6836	3.577
1.8753	3.559
3.8299	3.579
	Ave. 3.569 ± 0.005

Table 9

Enthalpies of Solution Per Mole of N-Acetylglycine-N-methylamide Dissolved to Give Various Molalities in Water

Amide Molality $m_1 \times 10^2$	ΔH^w_{soln} kcal mole^{-1}
0.8532	0.4198
0.8671	0.4183
0.8922	0.4176
0.9132	0.4217
	Ave. 0.4194 ± 0.0013

Table 10

Enthalpies of Solution Per Mole of N-Acetylglycylglycine-N-methylamide Dissolved to Give Various Molalities in Water

Amide Molality $m_1 \times 10^2$	ΔH^w_{soln} kcal mole^{-1}
0.41144	4.556
0.42790	4.557
	Ave. 4.5565 ± 0.001

Table 11

Enthalpies of Solution Per Mole of N-Acetylalanine-N-methylamide Dissolved to Give Various Molalities in Water

Amide Molality $m_1 \times 10^2$	$-\Delta H^{w}_{soln}$ kcal mole^{-1}
0.47394	0.6569
0.64198	0.6566
	Ave. 0.6568 ± 0.0002

Table 12

Enthalpies of Solution Per Mole of N-Acetyl-leucine-N-methylamide Dissolved to Give Various Molalities in Water

Amide Molality $m_1 \times 10^2$	$-\Delta H^W_{soln}$ kcal mole^{-1}
0.24526	2.341
0.39945	2.341
0.43377	2.337
	Ave. 2.340 ± 0.001

Table 13

Enthalpies of Solution Per Mole of Formamide Dissolved to Give Various Molalities in Sodium Chloride Solutions. Calculated Enthalpies of Transfer of Formamide from Water to Sodium Chloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2		ΔH^{ws}_{soln} kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
3.5154	0.2787		0.4194	
3.6058	0.2787		0.4193	
		Ave.	0.4194±0.0001	-0.0654±0.0016
3.2744	0.5235		0.3731	
3.3887	0.5235		0.3744	
3.3909	0.5235		0.3745	
		Ave.	0.3740±0.0003	-0.1108±0.0016
2.6232	0.7556		0.3369	
3.1173	0.7556		0.3327	
		Ave.	0.3348±0.0021	-0.1500±0.0026
3.0058	1.0690		0.2875	
3.5858	1.0690		0.2849	
		Ave.	0.2862±0.0013	-0.1986±0.0021
3.3399	1.7821		0.1935	
3.5378	1.7821		0.1961	
3.6531	1.7821		0.1955	
3.8599	1.7821		0.1965	
		Ave.	0.1954±0.0007	-0.2894±0.0017
3.0846	3.4513		0.0790	
3.3005	3.4513		0.0796	
		Ave.	0.0793±0.0003	-0.4058±0.0016

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 3.

Table 14

Enthalpies of Solution Per Mole of Formamide Dissolved to Give Various Molalities in Sodium Bromide Solutions. Calculated Enthalpies of Transfer of Formamide from Water to Sodium Bromide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.3435	0.1059	0.4572	
1.4025	0.1059	0.4557	
1.6487	0.1059	0.4522	
		Ave. 0.4550±0.0015	-0.0298±0.0022
1.6154	0.3594	0.3930	-0.0918
1.7428	0.7013	0.3198	-0.1650
1.3552	1.5644	0.1816	
1.6084	1.5644	0.1752	
1.6606	1.5644	0.1682	
1.9033	1.5644	0.1733	
		Ave. 0.1746±0.0039	-0.3102±0.0041
1.6278	2.2015	0.0735	
2.3867	2.2015	0.0838	
2.4044	2.2015	0.0770	
3.4764	2.2015	0.0815	
		Ave. 0.790±0.0017	-0.4058±0.0023
1.2899	3.3087	0.0390	-0.5238

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 3.

Table 15

Enthalpies of Solution Per Mole of Formamide Dissolved to Give Various Molalities in Sodium Iodide Solutions. Calculated Enthalpies of Transfer of Formamide from Water to Sodium Iodide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
1.8563	0.5013	+0.3342	-0.1506
1.9509	0.7880	+0.2304	-0.2544
2.4067	1.0567	+0.1415	-0.3433
2.1218	3.8967	-0.1396	-0.6244

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 3.

Table 16

Enthalpies of Solution Per Mole of Formamide Dissolved to Give Various Molalities in Alkali Halide Solutions. Calculated Enthalpies of Transfer of Formamide from Water to Alkali Halide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
Lithium Chloride			
3.1880	0.5845	0.3966	
3.2654	0.5845	0.3939	
3.4654	0.5845	0.3935	
	Ave.	0.3947±0.0010	-0.0901±0.0019
2.8863	1.1489	0.3263	
3.2677	1.1489	0.3242	
	Ave.	0.3252±0.0011	-0.1596±0.0019
Potassium Chloride			
3.4595	0.4988	0.3709	-0.1139
3.6130	1.0341	0.2898	
3.6919	1.0341	0.2874	
5.7758	1.0341	0.2857	
6.1416	1.0341	0.2853	
	Ave.	0.2871±0.0010	-0.1977±0.0019
3.8878	3.4305	0.0382	
4.0613	3.4305	0.0298	
	Ave.	0.0340±0.0042	-0.4508±0.0044
Potassium Bromide			
2.6538	0.5074	0.3608	
2.8044	0.5074	0.3581	
	Ave.	0.3600±0.0006	-0.1248±0.0017

Table 16 (continued)

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
Potassium Iodide			
2.0037	0.5123	0.3457	
2.9868	0.5123	0.3454	
	Ave.	0.3456±0.0002	-0.1392±0.0016
Cesium Chloride			
2.8061	0.5167	0.3660	
3.5620	0.5167	0.3561	
	Ave.	0.3611±0.0050	-0.1237±0.0053

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 3.

Table 17

Enthalpies of Solution Per Mole of Formamide Dissolved to Give Various Molalities in Alkaline Earth Halide Solutions. Calculated Enthalpies of Transfer of Formamide from Water to Alkaline Earth Halide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
Magnesium Chloride			
2.9339	0.5043	0.2888	
2.9939	0.5043	0.2921	
	Ave.	0.2905±0.0017	-0.1943±0.0024
Calcium Chloride			
2.6001	0.4012	0.2886	
2.6180	0.4012	0.2949	
	Ave.	0.2918±0.0031	-0.1930±0.0035
Strontium Chloride			
3.1777	0.5112	0.2100	
3.3859	0.5112	0.2068	
	Ave.	0.2084±0.0016	-0.2764±0.0023
Barium Chloride			
2.7960	0.4895	0.1806	
3.0013	0.4895	0.1733	
3.0559	0.4895	0.1846	
	Ave.	0.1795±0.0033	-0.3053±0.0037
Strontium Iodide			
3.0256	0.50	0.2184	
3.5093	0.50	0.2176	
	Ave.	0.2180±0.0004	-0.2666±0.0020

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 3.

Table 18

Enthalpies of Solution Per Mole of Formamide Dissolved to Give Various Molalities in Miscellaneous Electrolyte Solutions. Calculated Enthalpies of Transfer of Formamide from Water to Electrolyte Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
Cadmium Chloride			
2.6021	0.49	0.2965	
2.9001	0.49	0.2952	
		Ave. 0.2959±0.0007	-0.1890±0.0017
Lanthanum Chloride			
2.8548	0.3822	0.1995	
3.1356	0.3822	0.2041	
		Ave. 0.2018±0.0023	-0.2430±0.0028
Sodium Thiocyanate			
2.7738	0.6343	0.3089	
3.1355	0.6343	0.3062	
3.1356	0.6343	0.3066	
		Ave. 0.3072±0.0008	-0.1776±0.0018
2.9620	0.9661	0.2402	
3.0894	0.9661	0.2379	
3.3053	0.9661	0.2439	
		Ave. 0.2407±0.0017	-0.2441±0.0023
Guanidine Hydrochloride			
3.2427	0.5163	0.3347	
3.3960	0.5163	0.3327	
		Ave. 0.3337±0.0005	-0.1511±0.0017

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 3.

Table 19

Enthalpies of Solution Per Mole of N-Methylformamide Dissolved to Give Various Molalities in Potassium Bromide Solutions. Calculated Enthalpies of Transfer of N-Methylformamide from Water to Potassium Bromide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.2047	0.3254	1.721	-0.015
1.1518	0.5200	1.761	
1.3070	0.5200	1.745	
		Ave. 1.753±0.008	-0.047±0.008
1.0804	1.0223	1.774	
1.8050	1.0223	1.762	
		Ave. 1.768±0.006	-0.066±0.006
1.0012	2.1637	1.773	
1.3135	2.1637	1.757	
1.4763	2.1637	1.762	
		Ave. 1.764±0.005	-0.058±0.005
1.2765	2.6934	1.777	
1.3111	2.6934	1.763	
1.3433	2.6934	1.750	
		Ave. 1.763±0.008	-0.057±0.008
1.4191	3.1937	1.732	
1.4346	3.1937	1.736	
1.4514	3.1937	1.738	
		Ave. 1.735±0.002	-0.029±0.003
1.4498	4.7719	1.679	
1.4544	4.7719	1.665	
		Ave. 1.672±0.007	+0.034±0.007

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 4.

Table 20

Enthalpies of Solution Per Mole of N-Methylformamide Dissolved to Give Various Molalities in Miscellaneous Salt Solutions. Calculated Enthalpies of Transfer of N-Methylformamide from Water to Salt Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
Sodium Chloride			
1.3003	1.0498	1.691	+0.015
1.1293	2.8840	1.657	
1.2265	2.8840	1.633	
		Ave. 1.645±0.012	+0.061±0.012
Potassium Chloride			
1.3872	4.7505	1.621	
1.4327	4.7505	1.623	
		Ave. 1.622±0.001	+0.084±0.002
Lithium Perchlorate			
1.2442	2.0218	1.785	
1.4271	2.0218	1.783	
		Ave. 1.784±0.001	-0.078±0.002

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 4.

Table 21

Enthalpies of Solution Per Mole of Acetamide Dissolved to Give Various Molalities in Sodium Chloride Solutions. Calculated Enthalpies of Transfer of Acetamide from Water to Sodium Chloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
2.0090	0.2631	2.294	
2.0361	0.2631	2.298	
2.3010	0.2631	2.295	
	Ave.	2.295±0.003	-0.010±0.002
1.8730	0.5160	2.290	
2.7131	0.5160	2.291	
	Ave.	2.290_5±0.001	-0.015±0.001
2.6621	1.0498	2.289	-0.016
1.9331	1.5985	2.294	
2.3639	1.5985	2.294	
	Ave.	2.294±0.000	-0.011±0.001
2.5069	2.0854	2.303	-0.002
1.7330	2.8840	2.324	+0.019

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 5.

Table 22

Enthalpies of Solution Per Mole of N-Methylacetamide Dissolved to Give Various Molalities in Sodium Bromide Solutions. Calculated Enthalpies of Transfer of N-Methylacetamide from Water to Sodium Bromide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
0.8491	1.0209	0.832	
1.0548	1.0209	0.806	
1.5205	1.0209	0.813	
	Ave.	0.817±0.008	0.123±0.008
1.1297	3.3003	0.500	
1.6366	3.3003	0.455	
	Ave.	0.477±0.022	0.463±0.022
1.5730	4.5304	0.237	
1.7972	4.5304	0.247	
	Ave.	0.242±0.005	0.698±0.005

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 6.

Table 23

Enthalpies of Solution Per Mole of N,N -Dimethylacetamide Dissolved to Give Various Molalities in Sodium Chloride Solutions. Calculated Enthalpies of Transfer of N,N'-Dimethylacetamide from Water to Sodium Chloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.3298	0.2787	5.110	0.006
1.1028	0.5235	5.098	
1.3591	0.5235	5.093	
1.3949	0.5235	5.097	
		Ave. 5.096±0.002	0.020±0.003
1.2681	0.7556	5.074	
1.5355	0.7556	5.085	
1.6036	0.7556	5.079	
		Ave. 5.079±0.003	0.037±0.004
1.3058	1.0690	5.056	
1.3379	1.0690	5.044	
1.5043	1.0690	5.064	
		Ave. 5.055±0.003	0.061±0.004
1.4452	1.7821	4.964	
1.4712	1.7821	4.966	
1.5821	1.7821	4.973	
2.3222	1.7821	4.972	
		Ave. 4.969±0.002	0.147±0.003
1.3566	3.2684	4.837	
1.4784	3.2684	4.848	
1.7018	3.2684	4.830	
		Ave. 4.838±0.005	0.278±0.005
1.3673	5.9681	4.383	
1.4048	5.9681	4.391	
		Ave. 4.387±0.004	0.729±0.005

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 7.

Table 24

Enthalpies of Solution Per Mole of N,N -Dimethylacetamide Dissolved to Give Various Molalities in Sodium Bromide Solutions. Calculated Enthalpies of Transfer of N,N'-Dimethylacetamide from Water to Sodium Bromide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
1.2707	0.1059	5.157	
1.3561	0.1059	5.139	
1.4913	0.1059	5.140	
		Ave. 5.145±0.006	-0.029±0.006
1.2950	0.3594	5.138	
1.3580	0.3594	5.137	
1.3968	0.3594	5.146	
		Ave. 5.140±0.003	-0.024±0.004
1.1510	0.5020	5.144	
1.7209	0.5020	5.169	
		Ave. 5.156±0.012	-0.040±0.012
1.0788	0.7013	5.139	
1.4298	0.7013	5.157	
		Ave. 5.148±0.009	-0.032±0.009
1.5225	1.0477	5.149	
1.5405	1.0477	5.126	
		Ave. 5.137±0.011	-0.021±0.011
1.1713	1.5644	5.106	
1.2746	1.5644	5.107	
1.3350	1.5644	5.107	
1.3832	1.5644	5.101	
1.4008	1.5644	5.105	
		Ave. 5.105±0.001	+0.010±0.002

Table 24 (continued)

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
1.3792	2.2015	5.058	
1.4761	2.2015	5.054	
1.4935	2.2015	5.050	
		Ave. 5.054±0.003	+0.062±0.004
1.2918	3.3087	4.955	
1.3314	3.3087	4.969	
1.3624	3.3087	4.962	
1.4063	3.3087	4.955	
1.4240	3.3087	4.953	
2.5820	3.3087	4.960	
		Ave. 4.959±0.002	+0.157±0.002
1.2847	4.4564	4.795	
1.5418	4.4564	4.790	
1.5775	4.4564	4.803	
		Ave. 4.796±0.004	+0.320±0.005
1.6885	6.9718	4.418	+0.698

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 7.

Table 26

Enthalpies of Solution Per Mole of N,N -Dimethylacetamide Dissolved to Give Various Molalities in Potassium Chloride Solutions. Calculated Enthalpies of Transfer of N,N'-Dimethylacetamide from Water to Potassium Chloride Solutions

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
1.0812	0.1014	5.127	
1.2138	0.1014	5.125	
3.2315	0.1014	5.121	
	Ave.	5.124±0.002	-0.008±0.003
0.7902	0.3041	5.103	
0.9414	0.3041	5.092	
1.6954	0.3041	5.107	
1.9170	0.3041	5.115	
1.9269	0.3041	5.117	
	Ave.	5.107±0.005	+0.009±0.005
3.5677	0.5076	5.114	
3.6794	0.5076	5.098	
4.6710	0.5076	5.100	
4.9192	0.5076	5.107	
6.6449	0.5076	5.116	
8.7185	0.5076	5.082	
	Ave.	5.103±0.005	+0.013±0.005
2.1826	0.7766	5.095	
4.4376	0.7766	5.096	
6.1945	0.7766	5.095	
	Ave.	5.095±0.001	+0.021±0.002
1.2685	1.0369	5.092	
2.2881	1.0369	5.070	
2.3476	1.0369	5.094	
3.3155	1.0369	5.070	
4.3309	1.0369	5.086	
5.6027	1.0369	5.069	
	Ave.	5.080±0.005	+0.036±0.005

Table 26 (continued)

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
2.3420	1.5728	5.034	
3.5585	1.5728	5.041	
4.2580	1.5728	5.041	
4.3170	1.5728	5.045	
7.1647	1.5728	5.040	
	Ave.	5.041±0.003	+0.075±0.004
1.8285	2.1282	5.007	
4.4858	2.1282	4.939	
4.5632	2.1282	4.967	
6.8108	2.1282	4.989	
	Ave.	4.976±0.015	+0.140±0.015
1.8879	3.3123	4.849	
1.9391	3.3123	4.854	
2.2879	3.3123	4.825	
5.5251	3.3123	4.845	
7.5536	3.3123	4.883	
7.4210	3.3123	4.833	
10.182	3.3123	4.873	
	Ave.	4.852±0.008	+0.264±0.008

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 7.

Table 27

Enthalpies of Solution Per Mole of N,N -Dimethylacetamide Dissolved to Give Various Molalities in Potassium Bromide Solutions. Calculated Enthalpies of Transfer of N,N'-Dimethylacetamide from Water to Potassium Bromide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
0.8443	0.1011	5.137	
1.3080	0.1011	5.137	
1.5481	0.1011	5.134	
	Ave.	5.136±0.001	-0.020±0.007
0.8986	0.2533	5.083	
1.1319	0.2533	5.191	
1.3262	0.2533	5.162	
1.5694	0.2533	5.148	
2.2132	0.2533	5.144	
	Ave.	5.145±0.015	-0.029±0.015
1.7546	0.5134	5.166	-0.050
1.2226	1.0404	5.164	
1.2390	1.0404	5.155	
1.4216	1.0404	5.162	
1.4796	1.0404	5.153	
1.5351	1.0404	5.159	
1.6537	1.0404	5.149	
	Ave.	5.157±0.003	-0.041±0.004
1.4761	1.5955	5.127	
1.4952	1.5955	5.129	
1.5544	1.5955	5.125	
	Ave.	5.127±0.001	-0.011±0.002

Table 27 (continued)

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.1283	2.1649	5.103	
1.3667	2.1649	5.095	
1.8536	2.1649	5.083	
1.9608	2.1649	5.102	
2.0470	2.1649	5.091	
	Ave.	5.095±0.004	+0.021±0.005
1.4918	3.3709	4.954	
1.6269	3.3709	4.956	
1.7620	3.3709	4.959	
	Ave.	4.956±0.001	+0.160±0.004
1.5570	4.4634	4.800	
1.6045	4.4634	4.791	
1.6815	4.4634	4.825	
	Ave.	4.805±0.010	+0.311±0.010

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 7.

Table 28

Enthalpies of Solution Per Mole of N,N -Dimethylacetamide Dissolved to Give Various Molalities in Potassium Iodide Solutions. Calculated Enthalpies of Transfer of N,N'-Dimethylacetamide from Water to Potassium Iodide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.3091	0.7799	5.217	
1.3893	0.7799	5.197	
1.6586	0.7799	5.206	
	Ave.	5.207±0.006	-0.091±0.006
1.4115	1.0519	5.202	
1.7219	1.0519	5.222	
1.7670	1.0519	5.220	
2.8428	1.0519	5.212	
	Ave.	5.214±0.005	-0.098±0.005
1.2764	2.2088	5.142	
1.4530	2.2088	5.136	
1.5217	2.2088	5.131	
	Ave.	5.136±0.003	-0.020±0.004
1.3502	3.5384	4.940	
1.5689	3.5384	4.960	
1.6315	3.5384	4.959	
1.6486	3.5384	4.951	
1.7022	3.5384	4.960	
	Ave.	4.954±0.004	+0.162±0.004
1.7959	4.5708	4.825	
1.9604	4.5708	4.821	
	Ave.	4.823±0.002	+0.293±0.003
1.7827	6.9355	4.421	
1.8263	6.9355	4.435	
2.3595	6.9355	4.438	
	Ave.	4.431±0.005	+0.685±0.005

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 7.

Table 29

Enthalpies of Solution Per Mole of N,N -Dimethylacetamide Dissolved to Give Various Molalities in Lithium Perchlorate Solutions. Calculated Enthalpies of Transfer of N,N'-Dimethylacetamide from Water to Lithium Perchlorate Solutions

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.3644	0.1837	5.097	
1.4677	0.1837	5.108	
	Ave.	5.103±0.005	0.013±0.005
1.2705	0.3875	5.108	
1.3349	0.3875	5.083	
	Ave.	5.096±0.012	0.020±0.012
1.0927	0.4968	5.067	
1.3738	0.4968	5.071	
1.7871	0.4968	5.084	
	Ave.	5.074±0.006	0.042±0.006
1.1937	0.9693	5.011	
1.2579	0.9693	5.012	
1.3388	0.9693	5.008	
1.4381	0.9693	5.002	
	Ave.	5.008±0.002	0.008±0.003
1.2848	2.0218	4.907	
1.4677	2.0218	4.898	
1.4726	2.0218	4.888	
	Ave.	4.898±0.005	0.218±0.005
1.5376	3.2839	4.495	0.621

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 7.

Table 30

Enthalpies of Solution Per Mole of N-Methylpropionamide Dissolved to Give Various Molalities in Sodium Chloride Solutions. Calculated Enthalpies of Transfer of N-Methylpropionamide from Water to Sodium Chloride Solutions

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
1.5290	0.1022	3.571	-0.002
1.3124	0.2631	3.520	
1.3328	0.2631	3.535	
1.4242	0.2631	3.508	
	Ave.	3.521±0.008	+0.048±0.009
1.2819	0.5160	3.478	
1.3973	0.5160	3.459	
	Ave.	3.468±0.010	+0.101±0.011
1.1895	0.9899	3.354	
1.3752	0.9899	3.353	
	Ave.	3.353±0.001	+0.216±0.005
1.1766	1.5985	3.204	
1.3324	1.5985	3.215	
	Ave.	3.210±0.005	+0.359±0.007
1.3312	2.0854	3.101	
1.4197	2.0854	3.093	
	Ave.	3.097±0.004	+0.472±0.006
1.3346	2.3822	3.046	
1.4339	2.3822	3.020	
1.8456	2.3822	3.034	
	Ave.	3.033±0.008	+0.536±0.009
1.4133	4.4087	2.519	
1.8298	4.4087	2.542	
	Ave.	2.531±0.011	+1.038±0.012

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 8.

Table 31

Enthalpies of Solution Per Mole of N-Methylpropionamide Dissolved to Give Various Molalities in Sodium Bromide Solutions. Calculated Enthalpies of Transfer of N-Methylpropionamide from Water to Sodium Bromide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
1.2643	0.1018	3.560	
1.4504	0.1018	3.557	
		Ave. 3.559±0.002	0.010±0.005
1.2628	0.2777	3.527	
1.5641	0.2777	3.515	
		Ave. 3.521±0.006	0.048±0.008
1.1662	0.5081	3.460	
1.6908	0.5081	3.495	
1.8590	0.5081	3.473	
		Ave. 3.476±0.010	0.093±0.011
1.4726	1.0209	3.361	
1.5309	1.0209	3.351	
		Ave. 3.356±0.005	0.213±0.007
1.2675	1.5898	3.212	
1.2955	1.5898	3.224	
1.3652	1.5898	3.233	
1.5984	1.5898	3.226	
		Ave. 3.224±0.004	0.345±0.006
1.3763	2.0697	3.119	0.450

Table 31 (continued)

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
1.2881	2.6900	2.953	
1.8220	2.6900	2.973	
2.0918	2.6900	2.967	
		Ave. 2.964±0.006	0.605±0.008
1.3936	3.3003	2.816	
1.5117	3.3003	2.811	
1.5840	3.3003	2.804	
		Ave. 2.810±0.004	0.759±0.006
1.1956	4.5304	2.492	
1.6588	4.5304	2.486	
2.3976	4.5304	2.499	
2.5086	4.5304	2.490	
		Ave. 2.492±0.003	0.877±0.006

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 8.

Table 32

Enthalpies of Solution Per Mole of N-Methylpropionamide Dissolved to Give Various Molalities in Sodium Iodide Solutions. Calculated Enthalpies of Transfer of N-Methylpropionamide from Water to Sodium Iodide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
1.3116	0.5073	3.430	
1.3626	0.5073	3.426	
	Ave.	3.428±0.002	0.141±0.006
1.0083	0.7880	3.370	0.199
1.3263	1.0775	3.308	
1.4703	1.0775	3.298	
	Ave.	3.303±0.005	0.266±0.007
1.9286	2.7323	2.871	0.698
1.4761	3.8967	2.577	
1.5486	3.8967	2.567	
	Ave.	2.572±0.005	0.997±0.007

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 8.

Table 33

Enthalpies of Solution Per Mole of N-Methylpropionamide Dissolved to Give Various Molalities in Potassium Chloride Solutions. Calculated Enthalpies of Transfer of N-Methylpropionamide from Water to Potassium Chloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.2637	0.4988	3.479	
1.3994	0.4988	3.484	
		Ave. 3.482±0.002	0.177±0.005
1.7466	1.0476	3.375	0.184
1.2989	1.6576	3.221	
1.6798	1.6576	3.248	
		Ave. 3.235±0.013	0.424±0.017
1.2110	3.3834	2.872	
1.3249	3.3834	2.830	
		Ave. 2.851±0.021	0.808±0.022

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 8.

Table 34

Enthalpies of Solution Per Mole of N-Methylpropionamide Dissolved to Give Various Molalities in Potassium Bromide Solutions. Calculated Enthalpies of Transfer of N-Methylpropionamide from Water to Potassium Bromide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
1.2229	0.1000	3.550	
1.2937	0.1000	3.546	
	Ave.	3.548±0.002	0.021±0.003
1.0718	0.2494	3.535	
1.1050	0.2494	3.527	
	Ave.	3.531±0.004	0.038±0.003
1.2149	0.5113	3.494	
1.2836	0.5113	3.491	
	Ave.	3.493±0.002	0.076±0.005
0.9271	0.7536	3.431	
1.5431	0.7536	3.436	
	Ave.	3.434±0.002	0.135±0.005
1.3331	1.0482	3.375	
1.5035	1.0482	3.384	
1.7802	1.0482	3.376	
	Ave.	3.378±0.003	0.191±0.006
1.4405	1.5805	3.261	0.308
1.1673	2.1782	3.139	
1.5947	2.1782	3.144	
	Ave.	3.142±0.002	0.427±0.005
1.5265	2.7745	3.013	0.556

Table 34 (continued)

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
1.6960	3.3874	2.869	0.700
1.3803	4.0710	2.694	
1.4755	4.0710	2.708	
	Ave.	2.701±0.007	0.868±0.008
1.2846	4.8251	2.522	
1.5228	4.8251	2.528	
1.5922	4.8251	2.539	
	Ave.	2.530±0.005	1.039±0.007

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 8.

Table 35

Enthalpies of Solution Per Mole of N-Methylpropionamide Dissolved to Give Various Molalities in Potassium Iodide Solutions. Calculated Enthalpies of Transfer of N-Methylpropionamide from Water to Potassium Iodide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.3819	0.2523	3.508	
1.3980	0.2523	3.518	
	Ave.	3.513±0.005	0.056±0.007
1.5106	0.5442	3.455	
1.6308	0.5442	3.455	
	Ave.	3.455±0.000	0.114±0.005
1.3387	0.7844	3.412	
1.4163	0.7844	3.410	
	Ave.	3.411±0.001	0.158±0.005
1.4515	1.0684	3.339	
1.5105	1.0684	3.344	
	Ave.	3.342±0.003	0.227±0.006
1.4195	1.6430	3.186	
1.6376	1.6430	3.192	
	Ave.	3.189±0.003	0.380±0.006
1.4703	2.8497	2.878	
1.5748	2.8497	2.878	
	Ave.	2.878±0.000	0.691±0.005
1.6970	3.5131	2.701	0.868
1.6259	4.9476	2.362	
1.9093	4.9476	2.355	
	Ave.	2.359±0.003	1.210±0.006

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 8.

Table 36 (continued)

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
1.6024	8.3454	-0.4746	
1.6243	8.3454	-0.4748	
		Ave. -0.4747±0.0001	-0.8941±0.0014

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 9.

Table 36

Enthalpies of Solution Per Mole of N-Acetylglycine-N-Methylamide Dissolved to Give Various Molalities in Guanidine Hydrochloride Solutions. Calculated Enthalpies of Transfer of N-Acetylglycine-N-Methylamide from Water to Guanidine Hydrochloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
0.9375	0.1309	0.3535	
0.9450	0.1309	0.3490	
1.1787	0.1309	0.3630	
	Ave.	0.3552±0.0019	-0.0642±0.0023
0.8197	0.2002	0.3244	
0.8493	0.2002	0.3224	
	Ave.	0.3234±0.0010	-0.0960±0.0016
0.9308	0.5163	0.2007	
1.0415	0.5163	0.2136	
	Ave.	0.2072±0.0065	-0.2122±0.0068
0.8678	0.5207	0.2032	-0.2162
0.9337	1.2170	-0.0076	-0.4270
1.0633	1.8211	-0.1279	-0.5473
1.0382	2.2080	-0.1938	
1.0766	2.2080	-0.1916	
	Ave.	-0.1927±0.0011	-0.6121±0.0017
1.0262	2.6637	-0.2442	-0.7136
1.4154	6.1229	-0.4407	
1.5545	6.1229	-0.4389	
	Ave.	-0.4398±0.0009	-0.8592±0.0018

Table 37

Enthalpies of Solution Per Mole of N-Acetylglycine-N-methylamide Dissolved to Give Various Molalities in Guanidinium Sulfate Solutions. Calculated Enthalpies of Transfer of N-Acetylglycine-N-methylamide from Water to Guanidinium Sulfate Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
0.9113	0.5467	0.2019	
0.9794	0.5467	0.2001	
1.1347	0.5467	0.2053	
	Ave.	**0.2024±0.0015**	**-0.2170±0.0020**
1.1032	1.1597	0.1045	-0.3149
1.0477	1.7975	-0.0360	
1.1537	1.7975	-0.0369	
	Ave.	**-0.0365±0.0005**	**-0.4559±0.0014**

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 9.

Table 38

Enthalpies of Solution Per Mole of N-Acetylglycine-N-methylamide Dissolved to Give Various Molalities in Guanidinium Thiocyanate Solutions. Calculated Enthalpies of Transfer of N-Acetylglycine-N-methylamide from Water to Guanidinium Thiocyanate Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.0041	1.0898	0.1150	
1.0118	1.0898	0.1099	
1.1153	1.0898	0.1082	
	Ave.	0.1110±0.0020	-0.5304±0.0026
1.3641	4.1745	0.5788	
1.5859	4.1745	0.5775	
	Ave.	0.5782±0.0006	-0.9969±0.0017

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 9.

Table 39

Enthalpies of Solution Per Mole of N-Acetylglycine-N-methylamide Dissolved to Give Various Molalities in Sodium Chloride Solutions. Calculated Enthalpies of Transfer of N-Acetylglycine-N-methylamide from Water to Sodium Chloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
0.7796	0.5235	0.3817	
0.9171	0.5235	0.3845	
	Ave.	0.3831±0.0014	-0.0363±0.0019
0.8066	0.7556	0.3763	
0.8388	0.7556	0.3873	
	Ave.	0.3818±0.0055	-0.0376±0.0056
0.8758	1.0690	0.3826	
0.8796	1.0690	0.3752	
0.9226	1.0690	0.3888	
	Ave.	0.3822±0.0039	-0.0372±0.0041
0.8670	1.7821	0.4074	
1.0059	1.7821	0.4099	
1.1334	1.7821	0.4075	
	Ave.	0.4083±0.0008	-0.0111±0.0015
1.0098	3.2684	0.5272	
1.0556	3.2684	0.5208	
1.2270	3.2684	0.5242	
	Ave.	0.5241±0.0018	+0.1047±0.0022
0.8668	5.9681	0.8576	
0.8886	5.9681	0.8587	
0.9593	5.9681	0.8591	
	Ave.	0.8585±0.0004	+0.4391±0.0014

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 9.

Table 40

Enthalpies of Solution Per Mole of N-Acetylglycine-N-methylamide Dissolved to Give Various Molalities in Sodium Bromide Solutions. Calculated Enthalpies of Transfer of N-Acetylglycine-N-methylamide from Water to Sodium Bromide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
0.6799	0.1018	0.4017	
0.7373	0.1018	0.4072	
	Ave.	0.4045±0.0027	-0.0149±0.0030
0.8163	0.2777	0.3664	
0.9561	0.2777	0.3700	
	Ave.	0.3682±0.0018	-0.0512±0.0022
0.9303	0.5020	0.3238	-0.0956
0.8157	1.0477	0.2904	
0.8900	1.0477	0.2873	
0.9315	1.0477	0.2920	
	Ave.	0.2899±0.0014	-0.1015±0.0015
1.0078	1.5898	0.2820	
1.0395	1.5898	0.2736	
	Ave.	0.2778±0.0042	-0.1515±0.0044
0.9437	2.0697	0.2817	-0.1377
0.9893	2.6900	0.2954	
1.0378	2.6900	0.2891	
	Ave.	0.2923±0.0031	-0.1271±0.0034
0.8568	3.3003	0.3345	
0.9458	3.3003	0.3302	
	Ave.	0.3324±0.0023	-0.0800±0.0027
1.0207	4.4564	0.4150	-0.0044

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 9.

Table 41

Enthalpies of Solution Per Mole of N-Acetylglycine-N-methylamide Dissolved to Give Various Molalities in Sodium Iodide Solutions. Calculated Enthalpies of Transfer of N-Acetylglycine-N-methylamide from Water to Sodium Iodide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
0.8466	0.2083	0.3555	
0.8928	0.2083	0.3509	
1.0709	0.2083	0.3541	
	Ave.	0.3535±0.0014	-0.0659±0.0019
0.9217	0.8270	0.2164	
1.3073	0.8270	0.2114	
	Ave.	0.2139±0.0025	-0.2055±0.0030
0.8005	1.0349	0.1885	
0.9072	1.0349	0.1904	
	Ave.	0.1895±0.0010	-0.2299±0.0016
0.9141	1.4218	0.1534	
0.9637	1.4218	0.1507	
	Ave.	0.1520±0.0014	-0.2674±0.0019
0.6950	2.1720	0.1086	
1.0253	2.1720	0.1074	
	Ave.	0.1080±0.0006	-0.3114±0.0014
0.9630	4.9085	0.2005	
1.1577	4.9085	0.1943	
1.2614	4.9085	0.1977	
	Ave.	0.1975±0.0018	-0.2219±0.0022
0.9939	5.7841	0.2895	
1.1622	5.7841	0.2828	
	Ave.	0.2862±0.0034	-0.1332±0.0036

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 9.

Table 42

Enthalpies of Solution Per Mole of N-Acetylglycine-N-methylamide Dissolved to Give Various Molalities in Potassium Chloride Solutions. Calculated Enthalpies of Transfer of N-Acetylglycine-N-methylamide from Water to Potassium Chloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
0.8201	0.1123	0.4120	-0.0074
0.7879	0.2698	0.3816	
0.9199	0.2698	0.3898	
0.9764	0.2698	0.3832	
	Ave.	0.3849±0.0025	-0.0345±0.0028
0.7485	0.4988	0.3740	
0.8592	0.4988	0.3657	
	Ave.	0.3699±0.0049	+0.0495±0.0051
0.8014	0.7988	0.3563	-0.0631
0.6958	1.0476	0.3502	-0.0692
0.9063	1.6576	0.3516	
1.1834	1.6576	0.3467	
	Ave.	0.3492±0.0024	-0.0702±0.0027
1.1858	2.6846	0.3846	
1.2524	2.6846	0.3811	
	Ave.	0.3829±0.0018	-0.0365±0.0022
0.8938	3.3834	0.4342	+0.0148
0.9298	3.4305	0.4402	+0.0208
0.9398	4.7505	0.5534	
1.0329	4.7505	0.5528	
1.1132	4.7505	0.5553	
	Ave.	0.5538±0.0007	-0.1344±0.0018

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 9.

Table 43

Enthalpies of Solution Per Mole of N-Acetylglycine-N-methylamide Dissolved to Give Various Molalities in Potassium Bromide Solutions. Calculated Enthalpies of Transfer of N-Acetylglycine-N-methylamide from Water to Potassium Bromide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
0.7956	0.3254	0.3561	
0.8901	0.3254	0.3471	
1.1935	0.3254	0.3411	
	Ave.	0.3481±0.0044	-0.0713±0.0046
0.8542	0.5200	0.3218	
0.8582	0.5200	0.3139	
	Ave.	0.3179±0.0040	-0.1005±0.0042
0.9473	0.7728	0.2983	-0.1331
0.7965	0.7898	0.2799	
0.8845	0.7898	0.2784	
0.9949	0.7898	0.2812	
	Ave.	0.2798±0.0010	-0.1396±0.0016
1.0199	1.0223	0.2471	
1.1714	1.0223	0.2529	
1.3104	1.0223	0.2539	
	Ave.	0.2513±0.0021	-0.1681±0.0025
0.8900	1.0404	0.2454	-0.1740
1.0256	2.1649	0.2256	-0.1938
0.9095	2.1637	0.2403	
0.9717	2.1637	0.2316	
0.9901	2.1637	0.2366	
	Ave.	0.2362±0.0025	-0.1832±0.0028

Table 43 (continued)

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
1.0324	2.6934	0.2512	
1.1051	2.6934	0.2311	
1.2649	2.6934	0.2465	
	Ave.	0.2429±0.0061	-0.1765±0.0062
0.9317	3.1940	0.2653	
1.1499	3.1940	0.2664	
1.2296	3.1940	0.2628	
	Ave.	0.2648±0.0011	-0.1546±0.0017
1.4604	3.3709	0.2611	-0.1583
0.7787	4.4634	0.3622	
1.1357	4.4634	0.3653	
	Ave.	0.3638±0.0016	-0.0556±0.0021
0.8788	4.7719	0.3910	
1.0065	4.7719	0.3836	
1.3104	4.7719	0.3862	
	Ave.	0.3869±0.0022	-0.0325±0.0026

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 9.

Table 44

Enthalpies of Solution Per Mole of N-Acetylglycine-N-methylamide Dissolved to Give Various Molalities in Potassium Iodide Solutions. Calculated Enthalpies of Transfer of N-Acetylglycine-N-methylamide from Water to Potassium Iodide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
0.8059	0.2523	0.3348	
0.8426	0.2523	0.3386	
	Ave.	0.3367±0.0019	-0.0827±0.0023
0.9106	0.5331	0.2551	
0.9665	0.5331	0.2560	
1.0600	0.5331	0.2579	
1.0818	0.5331	0.2552	
	Ave.	0.2560±0.0006	-0.1634±0.0014
0.8565	0.7798	0.2054	
1.0439	0.7798	0.2023	
	Ave.	0.2038±0.0015	-0.2156±0.0020
0.9796	1.0519	0.1713	
1.0016	1.0519	0.1703	
1.1194	1.0519	0.1704	
	Ave.	0.1717±0.0003	-0.2487±0.0013
0.8399	1.6103	0.1250	
0.8641	1.6103	0.1268	
1.0019	1.6103	0.1262	
	Ave.	0.1260±0.0005	-0.2934±0.0014
1.0788	2.2088	0.0821	
1.1376	2.2088	0.0833	
	Ave.	0.0827±0.0006	-0.3367±0.0014

Table 44 (continued)

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
1.1255	4.5708	0.2229	
1.1390	4.5708	0.2194	
	Ave.	0.2212±0.0018	-0.1982±0.0022
0.9493	6.9355	0.4714	
0.9861	6.9355	0.4753	
	Ave.	0.4733±0.0020	+0.0539±0.0024

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 9.

Table 45

Enthalpies of Solution Per Mole of N-Acetylglycylglycine-N-methylamide Dissolved to Give Various Molalities in Guanidine Hydrochloride Solutions. Calculated Enthalpies of Transfer of N-Acetylglycylglycine-N-methylamide from Water to Guanidine Hydrochloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
0.44831	0.5509	4.255	-0.301
0.40638	1.1459	4.005	-0.551
0.38009	1.6580	3.834	-0.722
0.44023	3.6967	3.269	-1.287
0.53983	3.9385	3.141	-1.415
0.71979	10.9708	2.829	-1.727

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 10.

Table 46

Enthalpies of Solution Per Mole of N-Acetylglycylglycine-N-methylamide Dissolved to Give Various Molalities in Potassium Iodide Solutions. Calculated Enthalpies of Transfer of N-Acetylglycylglycine-N-methylamide from Water to Potassium Iodide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	ΔH^{ws}_{soln} kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
0.43111	1.2698	3.863	-0.693
0.50310	2.7035	3.405	-1.151
0.43308	4.3468	3.278	-1.278
0.48093	6.2319	3.275	-1.281

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 10.

Table 47

Enthalpies of Solution Per Mole of N-Acetylalanine-N-methylamide Dissolved to Give Various Molalities in Guanidine Hydrochloride Solutions. Calculated Enthalpies of Transfer of N-Acetylalanine-N-methylamide from Water to Guanidine Hydrochloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
0.52538	0.5431	0.7890	-0.1322
0.58471	1.1987	0.8652	-0.2084
0.51717	2.6637	0.9457	-0.2889
0.67388	6.1229	0.8774	-0.2206

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 11.

Table 48

Enthalpies of Solution Per Mole of N-Acetylalanine-N-methylamide Dissolved to Give Various Molalities in Potassium Iodide Solutions. Calculated Enthalpies of Transfer of N-Acetylalanine-N-methylamide from Water to Potassium Iodide Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
0.51086	0.2523	0.6676	-0.0108
0.42848	0.7844	0.6674	-0.0106
0.48454	1.0684	0.6374	+0.0194
0.52954	1.6430	0.5881	+0.0687
0.46039	2.8497	0.4593	+0.1975

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 11.

Table 49

Enthalpies of Solution Per Mole of N-Acetyl-leucine-N-methylamide Dissolved to Give Various Molalities in Guanidine Hydrochloride Solutions. Calculated Enthalpies of Transfer of N-Acetyl-leucine-N-methylamide from Water to Guanidine Hydrochloride Solutions.

Amide Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
0.40219	0.5431	2.393	-0.053
0.38950	1.1987	2.364	-0.024
0.44540	2.6637	2.266	+0.074
0.47580	6.1229	1.998	+0.342

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 12.

Table 51

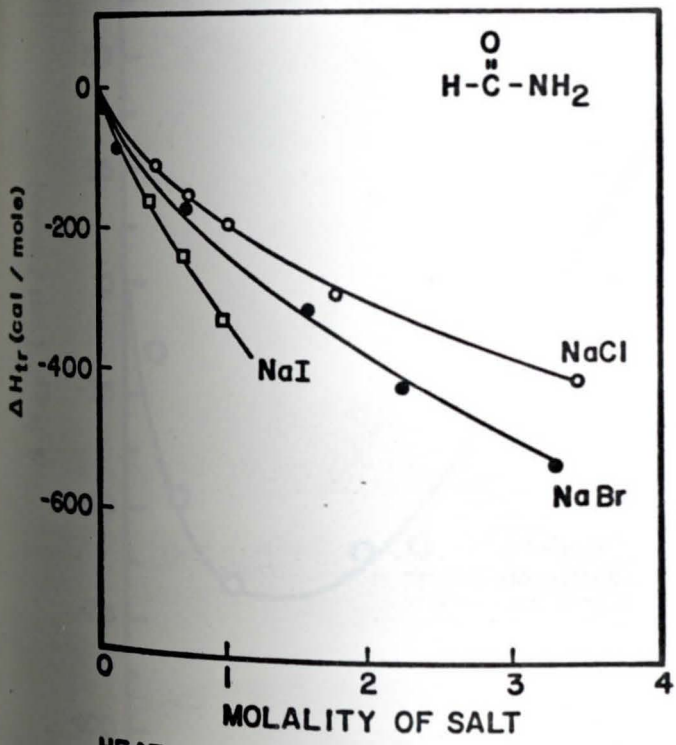
Enthalpies of Solution Per Mole of Lysozyme in pH 2.014 HCl Buffer Solutions. Enthalpy of Transfer of Lysozyme from pH 2.014 HCl Buffer to 3.5 m Guanidine Hydrochloride Solution, also at pH 2.014

Amide Molality $m_1 \times 10^5$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr} kcal mole^{-1}
2.0105	0	103.1	
2.2490	0	104.4	
		Ave. 103.7±0.6	
3.2277	3.5	127.4*	-23.7

* Although duplicate experiments were made to substantiate this value, pH variations of the poorly buffered system necessitated corrections for ionization and thus the additional data are omitted because of this ambiguity.

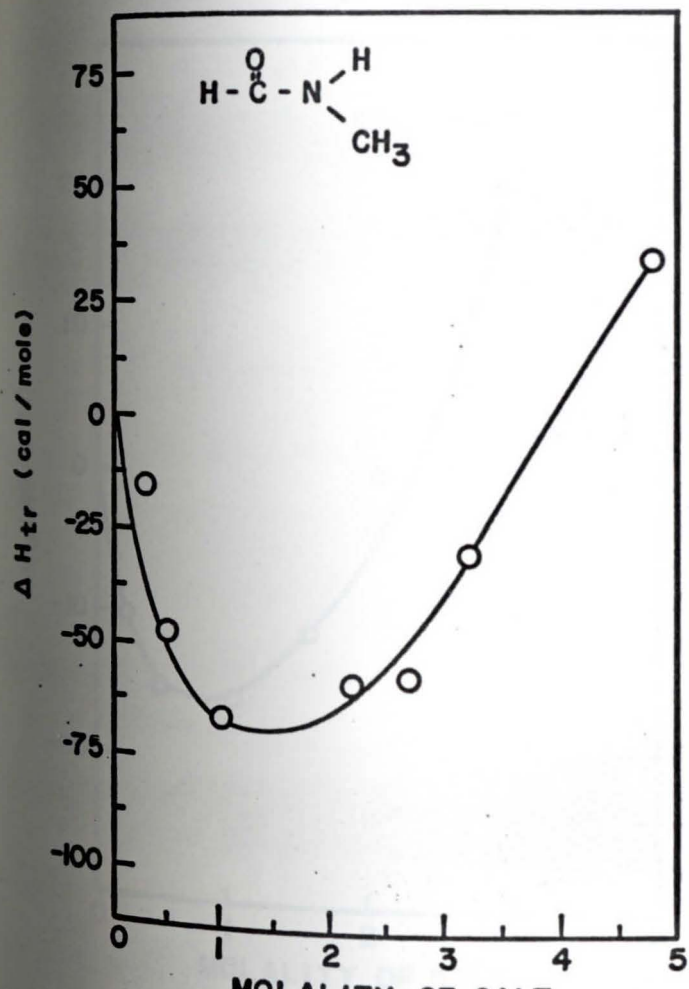
C. Figures

Figure 1



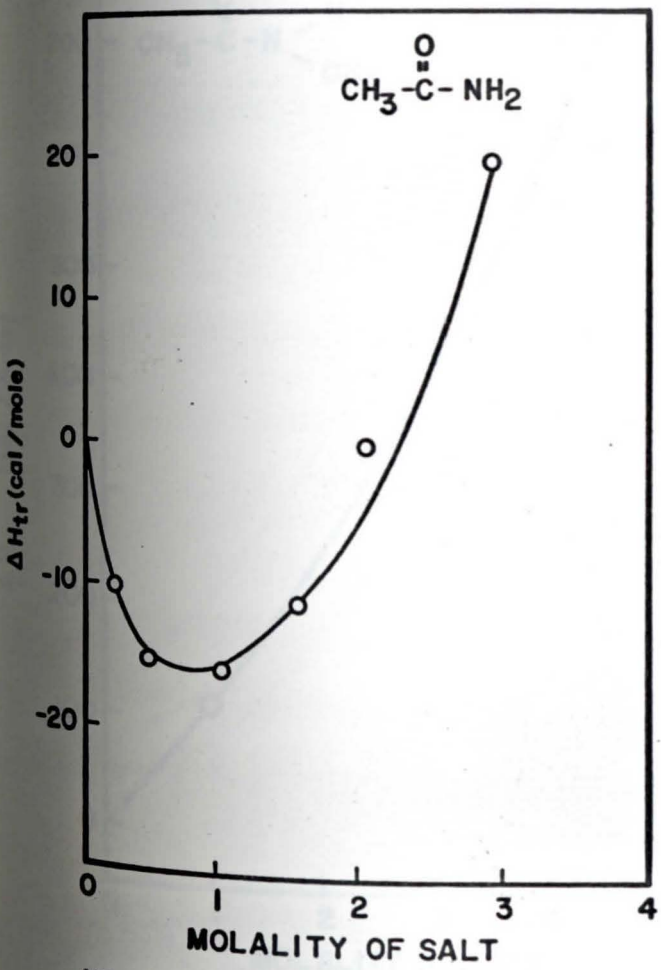
HEATS OF TRANSFER OF FORMAMIDE FROM WATER TO SODIUM HALIDE SOLUTIONS

Figure 2



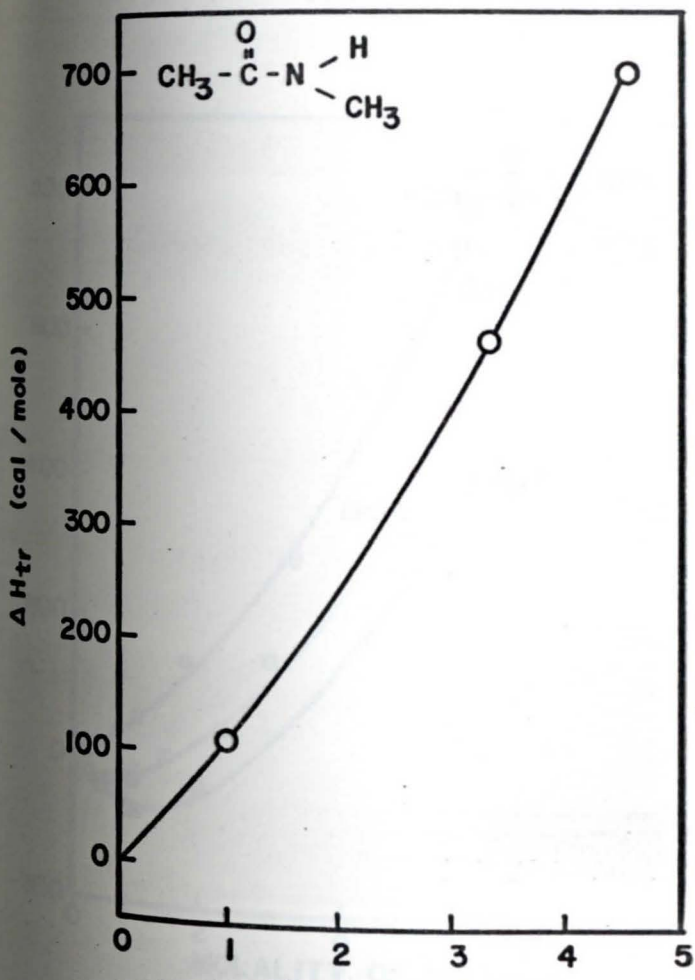
HEATS OF TRANSFER OF N-METHYL-FORMAMIDE FROM WATER TO POTASSIUM BROMIDE SOLUTIONS

Figure 3



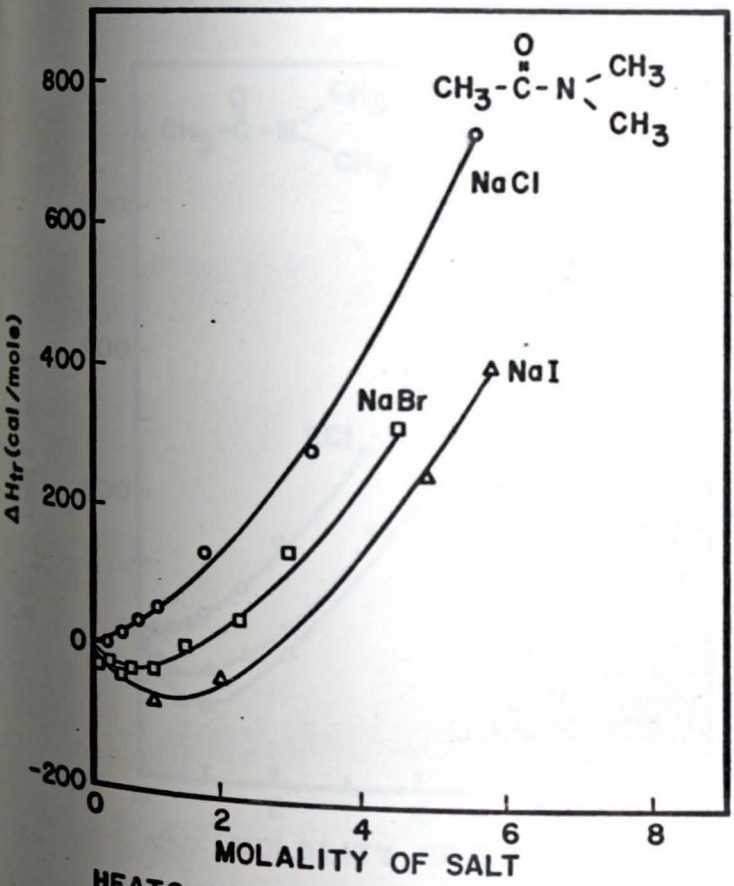
HEATS OF TRANSFER OF ACETAMIDE FROM WATER TO SODIUM CHLORIDE SOLUTIONS

Figure 4



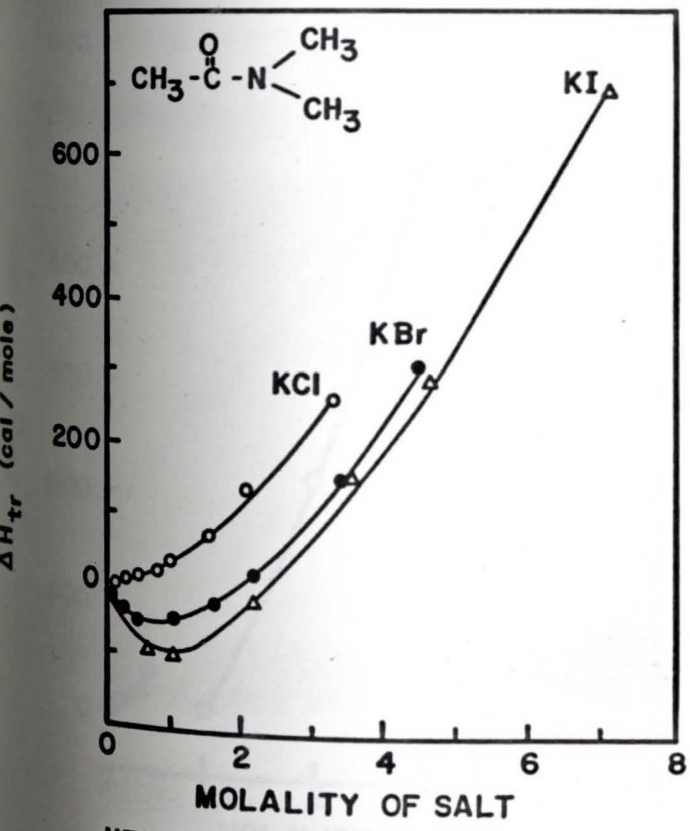
HEATS OF TRANSFER OF N-METHYL-ACETAMIDE FROM WATER TO SODIUM BROMIDE SOLUTIONS

Figure 5



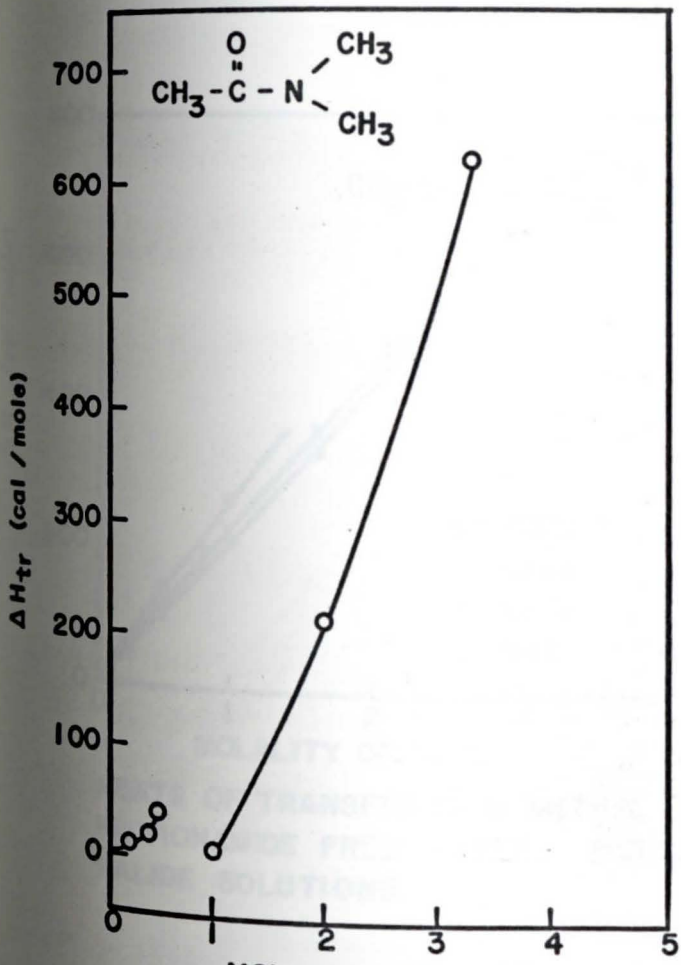
HEATS OF TRANSFER OF DIMETHYLACET-
-AMIDE FROM WATER TO SODIUM
HALIDE SOLUTIONS

Figure 6



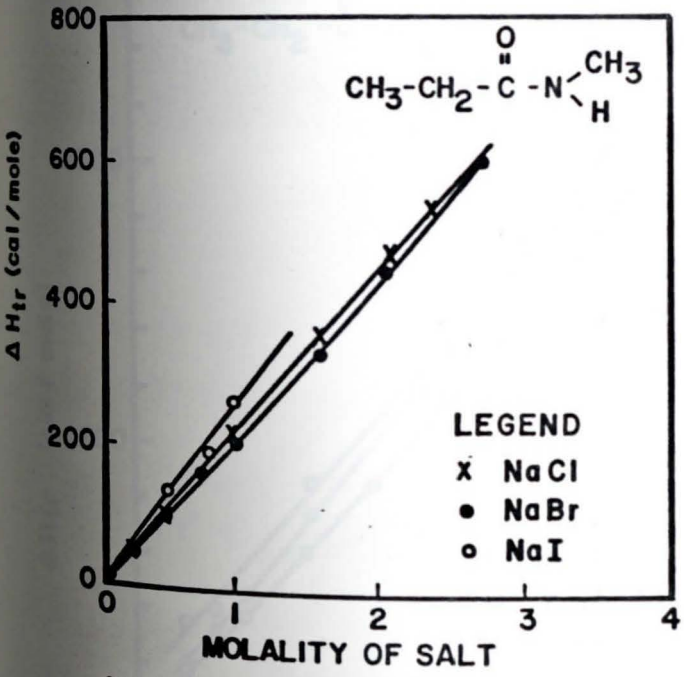
HEATS OF TRANSFER OF DIMETHYL-ACETAMIDE FROM WATER TO POTASSIUM HALIDE SOLUTIONS

Figure 7



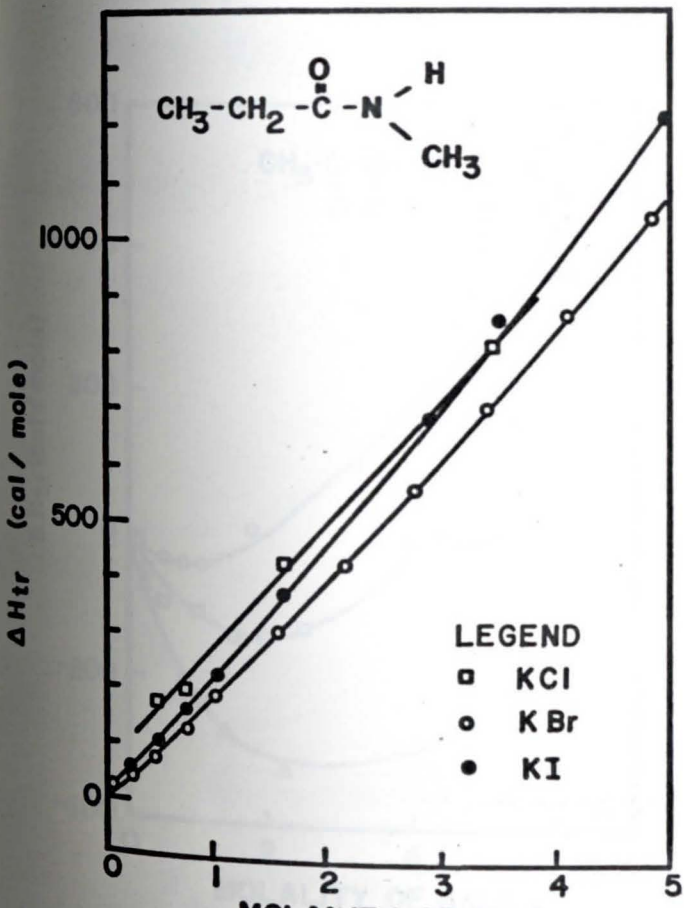
HEATS OF TRANSFER OF DIMETHYL-
-ACETAMIDE FROM WATER TO
LITHIUM PERCHLORATE SOLUTIONS

Figure 8



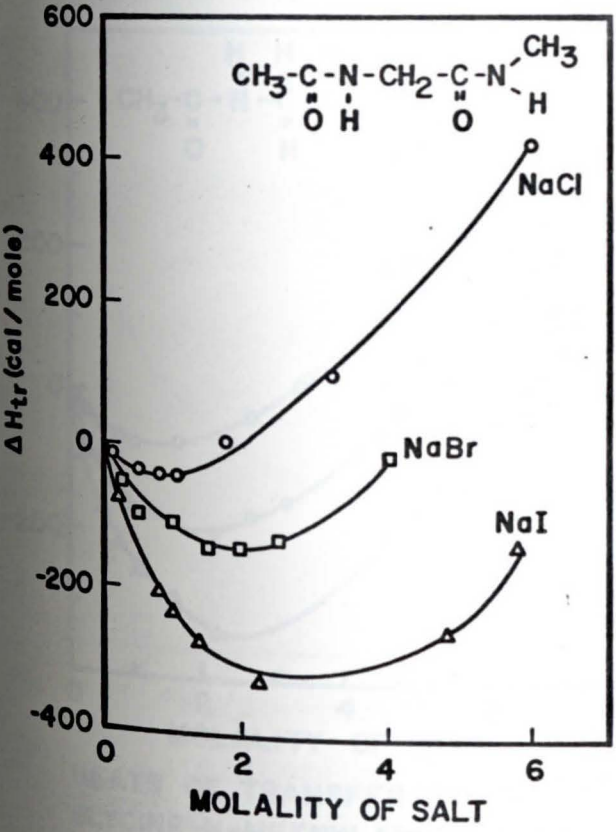
HEATS OF TRANSFER OF N-METHYL PROPIONAMIDE FROM WATER SODIUM HALIDE SOLUTIONS

Figure 9



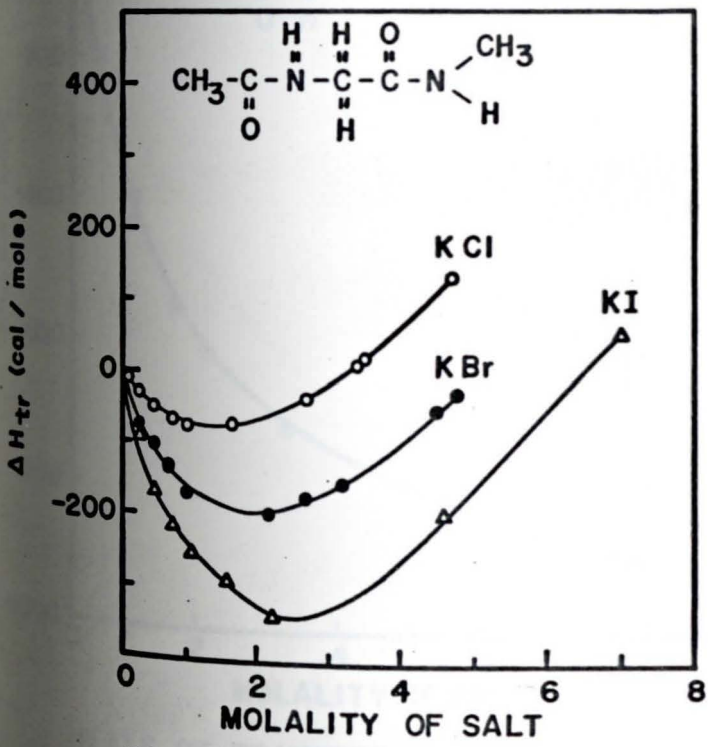
HEATS OF TRANSFER OF N-METHYL-PROPIONAMIDE FROM WATER TO POTASSIUM HALIDE SOLUTIONS

Figure 10



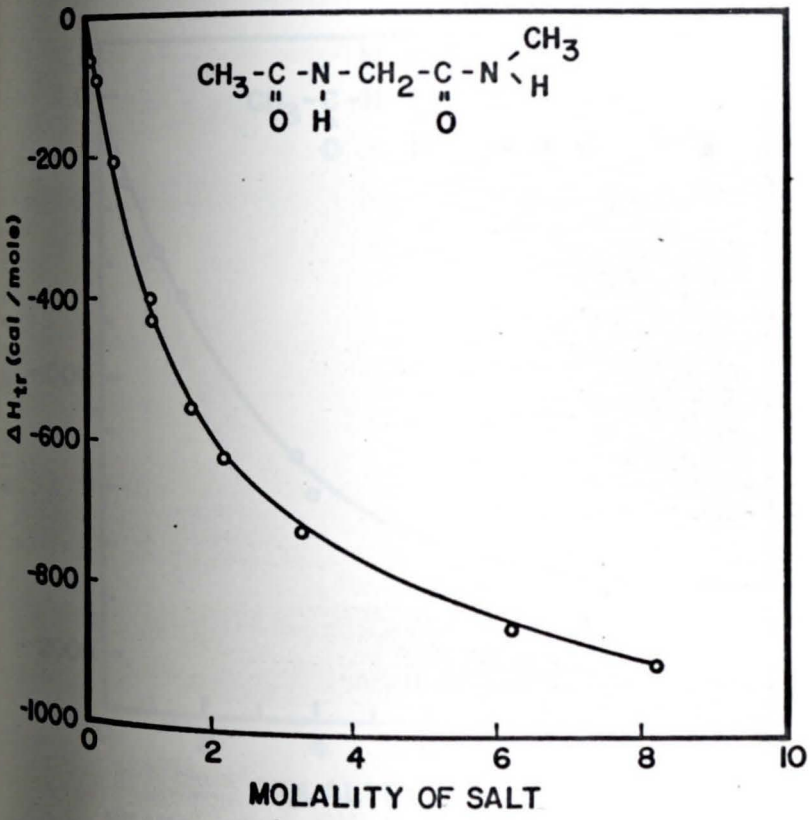
HEATS OF TRANSFER OF N-ACETYL GLYCINE-N-METHYLAMIDE FROM WATER TO SODIUM HALIDE SOLUTIONS

Figure 11



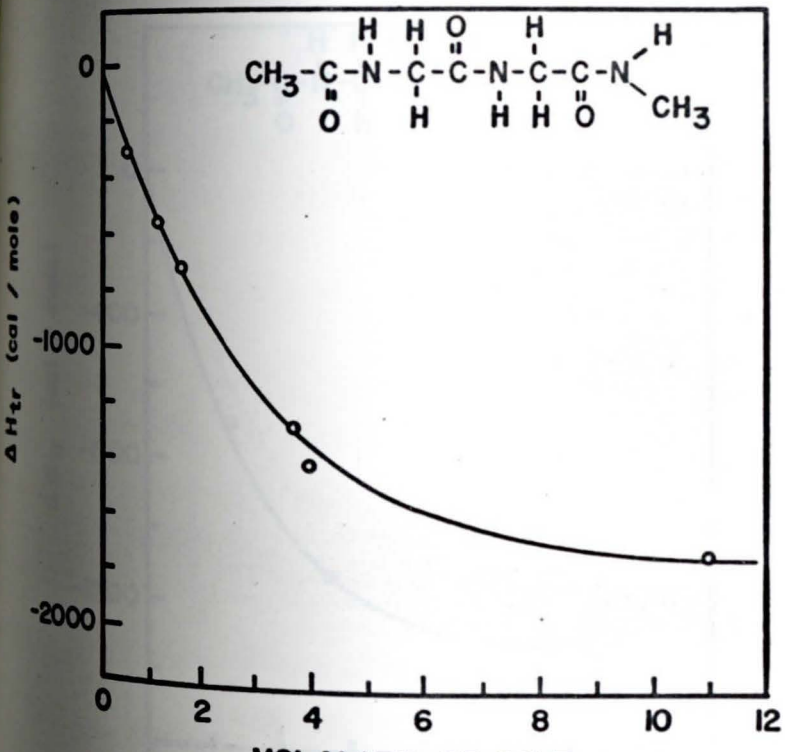
HEATS OF TRANSFER OF N-ACETYL-GLYCINE-N-METHYLAMIDE FROM WATER TO POTASSIUM HALIDE SOLUTIONS

Figure 12



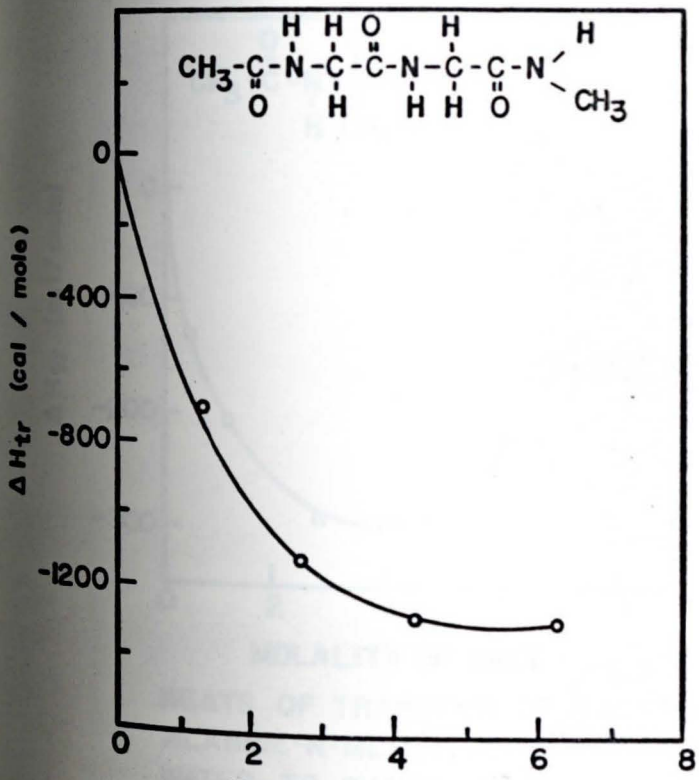
HEATS OF TRANSFER OF N-ACETYL GLYCINE N-METHYLAMIDE FROM WATER TO GUANIDINE HYDROCHLORIDE SOLUTIONS

Figure 13



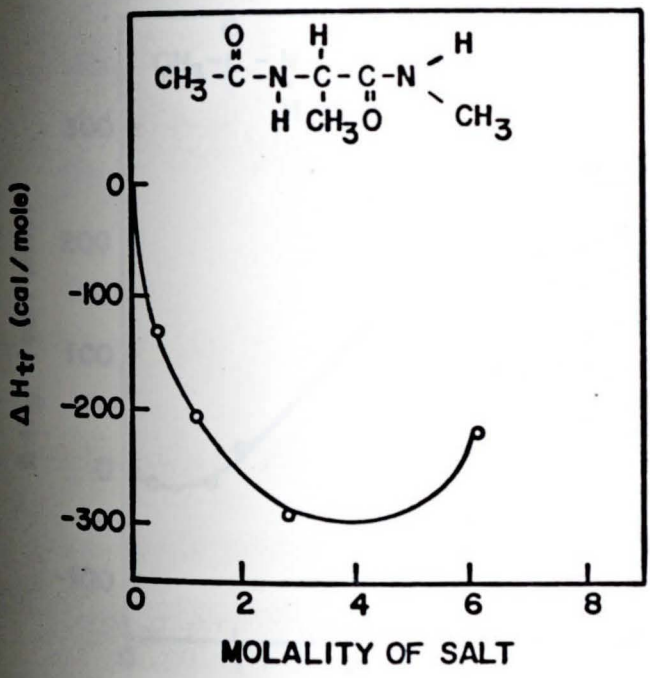
HEATS OF TRANSFER OF N-ACETYL--GLYCYLGLYCINE-N-METHYLAMIDE FROM WATER TO GUANIDINE HYDROCHLORIDE SOLUTIONS

Figure 14



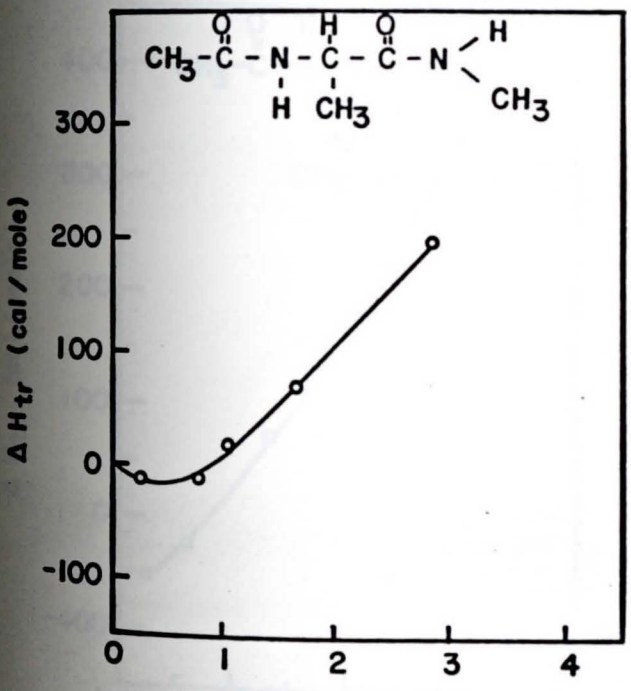
HEATS OF TRANSFER OF N-ACETYL-GLYCYLGLYCINE-N-METHYLAMIDE FROM WATER TO POTASSIUM IODIDE SOLUTIONS

Figure 15



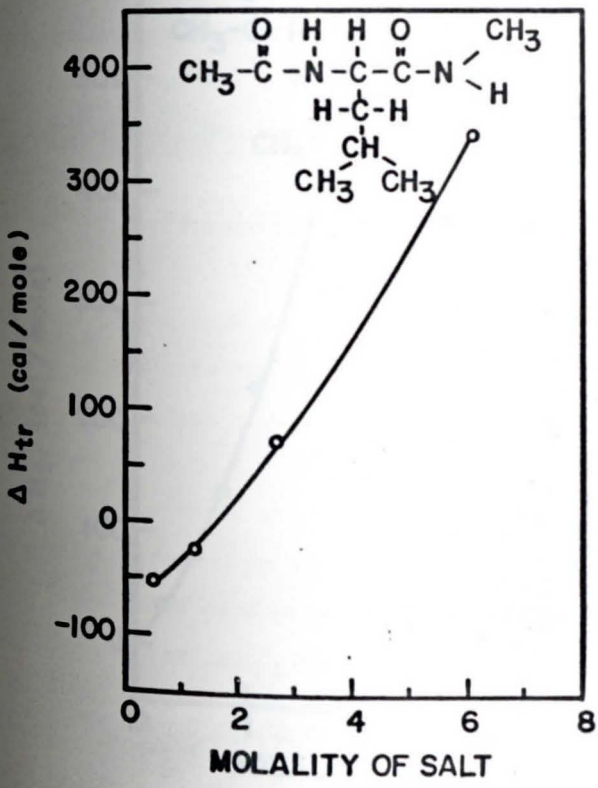
HEATS OF TRANSFER OF N-ACETYL-ALANINE-N-METHYLAMIDE FROM WATER TO GUANIDINE HYDRO--CHLORIDE SOLUTIONS

Figure 16



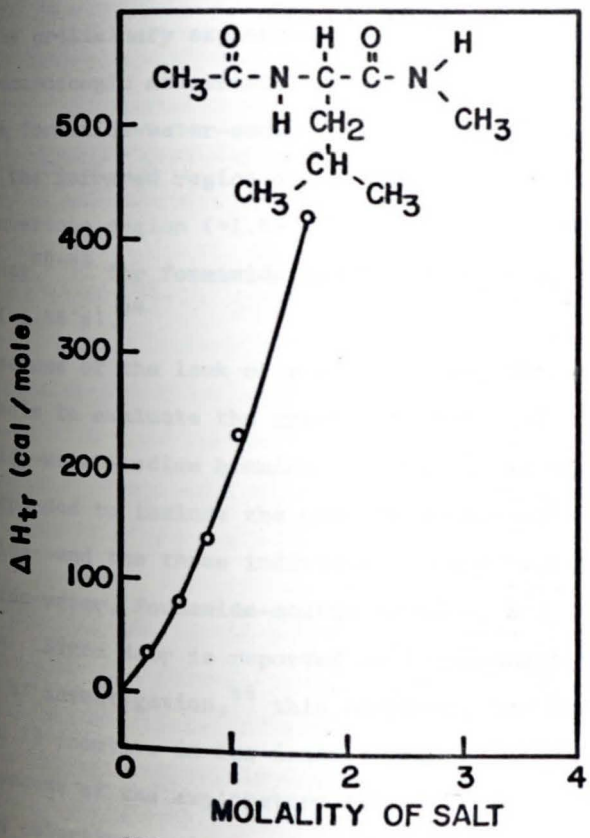
HEATS OF TRANSFER OF N-ACETYL-ALANINE-N-METHYLAMIDE FROM WATER TO POTASSIUM IODIDE SOLUTIONS

Figure 17



HEATS OF TRANSFER OF N-ACETYL-LEUCINE-N-METHYLAMIDE FROM WATER TO GUANIDINE HYDROCHLORIDE SOLUTIONS

Figure 18



HEATS OF TRANSFER OF N-ACETYL-LEUCINE-N-METHYLAMIDE FROM WATER TO POTASSIUM IODIDE SOLUTIONS

B. Spectroscopic Measurements

The preliminary exploratory spectral investigations and the spectroscopic measurements presented in this section, for the formamide-water-sodium bromide system, were carried out in the infrared region of what is often assigned as the first overtone region (≈1.49 μ) of the amide N-H stretching frequency[40-43] for formamide and as the $\nu_1 + \nu_3$ band of water (≈1.45 μ).[44]

Because of the lack of a good working theoretical hypothesis to evaluate the spectral studies of these formamide-water-sodium bromide solutions, the experiments were expanded to include the pure solvents--water and formamide--and the three individual binary systems as well--formamide-water, formamide-sodium bromide, and water-sodium bromide. Since NaBr is reported as transparent in the region of investigation,[45] this component has been considered IR inactive in its ionic forms.

Because of the exploratory nature of the work and its limited objectives only a representative portion of the data collected is presented here to illustrate the method.

1. Introduction

The first and foremost problem encountered in the application of spectral methods to multicomponent solutions with components of overlapping bands, is the separation of

spectral absorbances into their component parts or correlating the observations with the composition variables. The second problem, with such overlapping bands, is that the integrated intensities are difficult to measure. The third problem results from the normal double beam methods. These require a reference sample containing a suitable solution for comparison with the sample; or corrections are necessary.

Thus, the treatment for a ternary solution, consisting of formamide-water-sodium bromide, becomes considerably more involved than that for a binary solution such as the water-sodium bromide system[27] which has only one spectrally active component in the band region studied.

To overcome some of the forementioned difficulties, the following modifications of experimental design and assumptions were necessitated:

1) The reference did not contain the components of the sample and was completely inactive in the band region studied. Dry nitrogen gas was used in the reference beam which eliminated correcting sample spectra for reference contributions. The imbalance in scattering properties was ignored. Measurements of the absorbances of the pure components and densities of the mixed solutions allowed the calculations of the absorbance of the "ideal" reference solution for each mixture. Difference spectra were

calculated as the difference between the absorbance of the mixture and that of the "ideal" reference solutions.

2) The electrolyte concentration effects in the system were compared, on the basis of absorbance at various wavelengths enveloping the band, and assumed to yield the same qualitative conclusions as the consideration of the total integrated intensity would yield.

3) All the electrostatic or electrostriction terms will be removed from consideration as a result of (1) and the superposition principle of charge.

Briefly the scheme used to calculate the difference spectra followed this outlined procedure:

1) Measurement of the pure solvent spectra and respective absorptivities as a function of temperature,

2) Measurement of binary spectra and the calculation of spectra from component absorptivities and solution density,

3) Calculation of a difference spectra, and

4) Similar treatment, Steps 1-3, for ternary solutions.

2. Original (Reduced) Data

a. Discussion of tables, figures and symbols. In Table 52 are listed the absorptivities, a_{water}, calculated from the equation, $a_{water} = A/\ell c$, where c, the concentration, has been obtained from the density data of

Reference 27, and ℓ is the pathlength. Similarly Table 53 lists $a_{formamide}$ calculated in an analogous manner. The measured density data is included in the second line of the table as d. The temperature is denoted by T, and wavelength, λ, is given in μ or microns.

Tables 54, 55, and 56, contain the observed absorbances, A_{obs}, as a function of temperature, T, and wavelength, λ, for the three binary systems--water-formamide, water-sodium bromide, and formamide-sodium bromide respectively. Within each of the tables there are subdivisions where the various compositions are tabulated. Measured densities are again given in the second lines of the tables.

Representative A_{obs} data for the ternary system--formamide-water-sodium bromide--are tabulated in Table 57. A schematic spectra, showing the general blue shift with temperature, appears in Figure 19 for a ternary solution.

b. Tables and Figures of Original Data

Table 52

Measured Absorptivities for Water as a Function of Wavelength and Temperature*

T =	15.2	33.7	34.7	44.0	44.3	58.1	58.2	77.8
d =	0.9991	0.9945	0.9941	0.9907	0.9905	0.9842	0.9842	0.9730
λ(μ)								
1.42	208.3	230.1	240.3	238.8	245.8	244.0	237.3	239.8
1.46	241.8	238.1	240.5	229.3	228.7	215.5	210.7	196.1
1.49	186.5	172.9	175.5	164.2	166.1	151.6	153.1	134.4
1.52	127.3	116.7	119.3	108.4	108.6	101.1	99.2	87.4
1.56	78.8	71.9	75.2	66.9	66.6	62.1		53.0

* Average deviation is approximately ±2%.

Table 53

Measured Absorptivities for Formamide as a Function of Wavelength and Temperature*

T =	12.7	18.7	21.0	27.0	34.0	39.5	59.5	69.5	78.5
d =	1.1376	1.1325	1.1301	1.1239	1.1183	1.1118	1.0960	1.0900	1.0869
λ(μ)									
1.42	8.71	11.53	9.96	10.42	11.28	11.75	13.97	14.05	15.75
1.46	104.1	106.2	108.8	107.8	116.4	115.5	122.9	126.0	129.3
1.49	186.9	190.5	194.5	195.2	205.0	205.8	220.4	227.7	232.1
1.52	206.7	214.4	212.0	215.2	214.7	220.8	226.8	228.1	230.4
1.56	115.6	116.5	116.0	114.6	112.4	115.1	110.5	108.3	106.9

* Average deviation is approximately ±2%.

Table 54

Observed Absorbances for a Formamide-Water System as a Function of Solution Composition, Wavelength, and Temperature

Solution Composition:	11.2719 g Formamide; 15.3320 g H_2O					
T =	11.5	30.5	41.7	51.1	61.3	66.5
d =	1.0649	1.0527	1.0455	1.0394	1.0329	1.0303
λ(μ)						
1.42	0.649	0.710	0.730	0.753	0.763	0.771
1.46	0.935	0.914	0.895	0.886	0.858	0.849
1.49	0.872	0.830	0.803	0.796	0.768	0.760
1.52	0.667	0.636	0.611	0.598	0.578	0.570
1.56	0.402	0.371	0.347	0.339	0.319	0.311
Solution Composition:	11.2733 g Formamide; 9.9414 g H_2O					
T =	10.7	31.5	42.9	52.5	63.8	
d =	1.0811	1.0666	1.0568	1.0497	1.0419	
λ(μ)						
1.42	0.523	0.583	0.594	0.610	0.637	
1.46	0.818	0.801	0.783	0.772	0.760	
1.49	0.802	0.775	0.758	0.750	0.734	
1.52	0.642	0.628	0.605	0.597	0.576	
1.56	0.382	0.355	0.229	0.330	0.307	
Solution Composition:	16.8558 g Formamide; 10.2493 g H_2O					
T =	11.2	31.3	41.2	50.9	58.3	71.8
d =	1.0915	1.0767	1.0698	1.0630	1.0592	1.0531
λ(μ)						
1.42	0.424	0.467	0.483	0.497	0.510	0.501
1.46	0.710	0.706	0.700	0.690	0.685	0.661
1.49	0.748	0.733	0.730	0.720	0.711	0.702
1.52	0.632	0.616	0.608	0.595	0.584	0.573
1.56	0.370	0.350	0.338	0.324	0.320	0.302

Table 54 (continued)

Solution Composition: 22.5780 g Formamide; 5.0219 g H_2O

T =	31.2	41.8	52.0	62.7	74.1
d =	1.1033	1.0953	1.0839	1.0764	1.0650
λ(μ)					
1.42	0.239	0.250	0.258	0.269	0.270
1.46	0.492	0.496	0.493	0.492	0.491
1.49	0.625	0.625	0.628	0.632	0.635
1.52	0.594	0.592	0.583	0.586	0.579
1.56	0.334	0.326	0.309	0.302	0.293

Table 55

Observed Absorbances for a Sodium Bromide-Water System as a Function of Solution Composition, Wavelength, and Temperature

Solution Composition 1.0170 g NaBr; 24.7140 g H_2O

	T = 29.8	40.1	52.2	58.8	70.9
	d = 1.0255	1.0227	1.0180	1.0146	1.0075
λ(μ)					
1.42	1.245	1.292	1.333	1.361	1.418
1.46	1.326	1.294	1.265	1.243	1.210
1.49	0.999	0.956	0.896	0.872	0.836
1.52	0.662	0.626	0.584	0.563	0.534
1.56	0.413	0.383	0.354	0.343	0.325

Solution Composition: 1.6767 g NaBr; 24.6403 g H_2O

	T = 30.2	51.5	63.3	70.6
	d = 1.0457	1.0383	1.0319	1.0277
λ(μ)				
1.42	1.242	1.319	1.372	1.406
1.46	1.312	1.270	1.239	1.219
1.49	0.974	0.910	0.860	0.825
1.52	0.642	0.588	0.551	0.529
1.56	0.392	0.359	0.338	0.321

Solution Composition: 5.1685 g NaBr; 24.0278 g H_2O

	T = 30.3	41.3	51.1	61.8
	d = 1.1419	1.1376	1.1310	1.1259
λ(μ)				
1.42	1.187	1.236	1.283	1.316
1.46	1.246	1.222	1.202	1.174
1.49	0.895	0.856	0.824	0.796
1.52	0.558	0.531	0.508	0.484
1.56	0.327	-	0.300	0.287

Table 55 (continued)

Solution Composition: 7.7430 g NaBr; 22.7599 g H_2O

	T = 15.2	31.1	42.4	62.8	69.3
	d = 1.2261	1.2195	1.2144	1.2008	1.1961
λ(μ)					
1.42	1.120	1.171	1.219	1.278	1.300
1.46	1.256	1.210	1.177	1.141	1.114
1.49	0.902	0.848	0.803	0.760	0.735
1.52	0.563	0.511	0.485	0.448	0.429
1.56	0.326	0.294	0.281	0.258	0.247

Table 56

Observed Absorbances for a Sodium Bromide-Formamide System as a Function of Solution Composition, Wavelength, and Temperature

Solution Composition: 0.5938 g NaBr; 11.1847 g Formamide

T =	30.7	40.9	42.7	54.0	64.2	77.1
d =	1.1608	1.1525	1.1485	1.1419	1.1318	1.1189
λ(μ)						
1.42	0.057	0.060	0.060	0.065	0.060	0.067
1.46	0.278	0.288	0.296	0.300	0.302	0.313
1.49	0.492	0.503	0.502	0.520	0.525	0.546
1.52	0.555	0.557	0.557	0.562	0.562	0.573
1.56	0.309	0.303	0.300	0.296	0.285	0.285

Solution Composition: 1.3917 g NaBr; 11.1749 g Formamide

T =	34.0	47.8	60.7	75.9
d =	1.2158	1.2046	1.1932	1.1794
λ(μ)				
1.42	0.050	0.051	0.052	0.053
1.46	0.253	0.269	0.280	0.285
1.49	0.461	0.480	0.496	0.560
1.52	0.532	0.539	0.545	0.553
1.56	0.296	0.291	0.284	0.274

Solution Composition: 2.2388 g NaBr; 11.1837 g Formamide

T =	31.1	43.8	54.9	68.7
d =	1.2695	1.2601	1.2562	1.2411
λ(μ)				
1.42	0.051	0.057	0.057	0.058
1.46	0.241	0.253	0.268	0.267
1.49	0.439	0.453	0.465	0.478
1.52	0.512	0.524	0.527	0.528
1.56	0.291	0.285	0.284	0.271

Table 56 (continued)

Solution Composition: 2.9569 g NaBr; 10.9810 g Formamide

T =	30.6	44.1	54.3	60.8	71.7
d =	1.3149	1.3043	1.2913	1.2902	1.2812
λ(μ)					
1.42	0.057	0.056	0.057	0.055	0.057
1.46	0.240	0.245	0.254	0.254	0.258
1.49	0.429	0.433	0.448	0.451	0.460
1.52	0.499	0.510	0.512	0.512	0.515
1.56	0.288	0.286	0.278	0.272	0.270

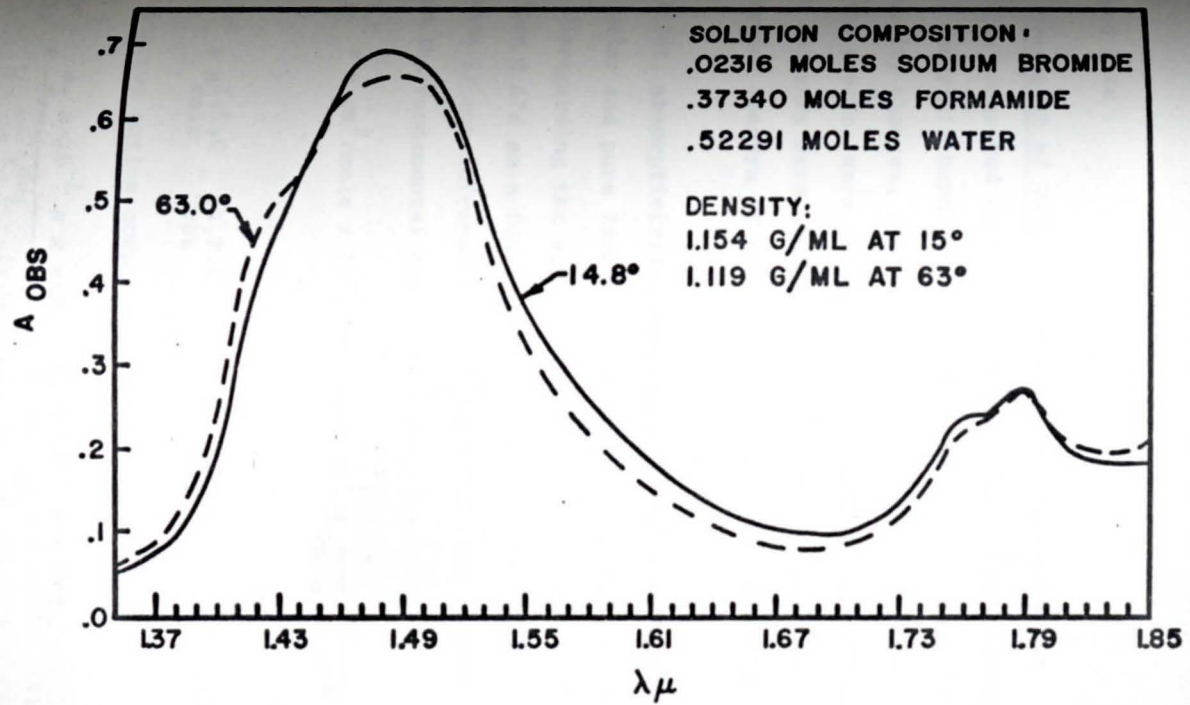
Table 57

Observed Absorbances for a Sodium Bromide-Water-Formamide System as a Function of Solution Composition, Wavelength, and Temperature

Solution Composition:	6.1175 g NaBr; 16.7920 g Formamide; 8.3270 g H_2O					
T = 12.9	31.7	40.4	48.6	59.2	69.8	73.2
d = 1.2660	1.2517	1.2454	1.2391	1.2306	1.2221	1.2190
λ(μ)						
1.42 0.336	0.374	0.390	0.403	0.406	0.419	0.460
1.46 0.579	0.590	0.590	0.586	0.577	0.571	0.602
1.49 0.614	0.623	0.620	0.620	0.611	0.607	0.637
1.52 0.532	0.540	0.535	0.528	0.514	0.518	0.548
1.56 0.290	0.297	0.289	0.282	0.266	0.261	0.293

Solution Composition:	3.0071 g NaBr; 16.7732 g Formamide; 9.2800 g H_2O				
T = 12.9	31.2	39.5	50.1	62.6	72.3
d = 1.1790	1.1653	1.1597	1.1521	1.1419	1.1336
λ(μ)					
1.42 0.423	0.412	0.425	0.432	0.439	0.438
1.46 0.686	0.633	0.628	0.620	0.605	0.584
1.49 0.721	0.660	0.660	0.650	0.638	0.627
1.52 0.622	0.559	0.552	0.543	0.539	0.528
1.56 0.372	0.302	0.293	0.281	0.271	0.264

Figure 19



CHARACTERISTIC SPECTRAL SHIFTS IN FORMAMIDE-SODIUM BROMIDE-WATER SYSTEMS AS A FUNCTION OF TEMPERATURE

1. Derived Data

a. Treatment of data. Because of all the inherent difficulties connected with this method--high concentration of amide, uncertain band assignments, broad bands, lack of a blank, density changes, etc.--the calculations and evaluation of the spectra were performed in the following manner.

Pure solvents were used as the bases for calculating the difference spectra of binary systems in the following manner:

1) First, absorptivities, $a(\lambda,T)$, were calculated for the pure water and pure formamide based on the total concentration, disregarding the specie or polymer types present;

2) Then δ A's as a function of λ,T,C for the binary systems with i) one infrared active component were calculated from the fundamental equations

a) $$A^{\lambda,T,C}_{calc} = a\ cm^2/mole \times 10^{-1}\ cm \times \rho\ g/cm^3 \times \frac{wt\%}{MW\ g\ mole^{-1}} \quad (9)$$

b) $$\delta^{\lambda,T,C} = A^{\lambda,T,C}_{calc} - A^{\lambda,T,C}_{obs} \quad (10)$$

and ii) with two active components

a) $$A^{\lambda,T,C}_{calc} = \frac{a_1 \times 10^{-1}\ \rho \times wt\%_1}{MW_1} + \frac{a_2 \times 10^{-1}\ \rho \times wt\%_2}{MW_2} \quad (11)$$

b) $$\delta^{\lambda,T,C} = A^{\lambda,T,C}_{calc} - A^{\lambda,T,C}_{obs} \quad (12)$$

where ρ is the density of the solution;

3) Likewise in the ternary system

$$A^{\lambda,T,C}_{calc} = \frac{a_1 \times 10^{-1} \rho \times wt\%_1}{MW_1} + \frac{a_2 \times 10^{-1} \rho \times wt\%_2}{MW_2} \qquad (13)$$

$$A^{\lambda,T,C}_{calc} - A^{\lambda,T,C}_{obs} = \Delta^{\lambda,T,C}_{HFS} \qquad (14)$$

The quantities

$\delta^{\lambda,T,C}_{HS}$ = δ for binary water-salt mixtures

$\delta^{\lambda,T,C}_{HF}$ = δ for binary water-formamide mixtures

$\delta^{\lambda,T,C}_{FS}$ = δ for binary formamide-salt mixtures

and $\Delta^{\lambda,T,C}_{HFS}$ might be expected to be zero if mixing without interaction were considered for spherical molecules. That is, it would be expected to be the A value normally seen by difference spectra for solution versus components in conventional tandem cells corrected for density changes.

Tables 58, 59, 60, and 61 list selected calculated δ's and Δ's for binary and ternary solutions. These are in the same format as used to list the observed A's. Figure 20 crudely plots Δ versus temperature for the two ternary solutions listed in Table 61. Since a blue shift occurs and 1.42 μ displays the largest increments, Δ's have been plotted for this wavelength.

b. Tables and Figures of Derived Data

Table 58

Calculated Difference Spectra for the Formamide-Water System as a Function of Solution Composition, Wavelength, and Temperature

Solution Composition: 1.2719 g Formamide; 15.3320 g H_2O

	T = 11.5	30.5	41.7	51.1	61.3	66.5
	d = 1.0649	1.0527	1.0455	1.0394	1.0329	1.0303
λ(μ)						
1.42	0.052	0.075	0.082	0.073	0.036	0.029
1.46	-0.005	-0.001	-0.005	-0.039	-0.050	-0.040
1.49	-0.042	-0.039	-0.041	-0.058	-0.057	-0.063
1.52	-0.021	-0.024	-0.021	-0.030	-0.036	-0.039
1.56	-0.012	-0.010	-0.003	-0.015	-0.010	-0.012

Solution Composition: 11.2733 g Formamide; 9.9414 g H_2O

	T = 10.7	31.5	42.9	52.5	63.8
	d = 1.0811	1.0666	1.0568	1.0497	1.0419
λ(μ)					
1.42	0.060	0.062	0.075	0.074	0.025
1.46	-0.004	0.003	-0.003	-0.020	-0.037
1.49	-0.033	-0.035	-0.043	-0.053	-0.059
1.52	-0.017	-0.030	-0.026	-0.035	-0.037
1.56	-0.009	-0.010	0	-0.016	-0.011

Solution Composition: 16.8558 g Formamide; 10.2493 g H_2O

	T = 11.2	31.3	41.2	50.9	58.3	71.8
	d = 1.0915	1.0767	1.0698	1.0630	1.0592	1.0531
λ(μ)						
1.42	0.060	0.063	0.071	0.068	0.037	0.048
1.46	0.083	0.001	-0.006	-0.018	-0.038	-0.033
1.49	0.111	-0.037	-0.046	-0.051	-0.050	-0.060
1.52	0.134	-0.030	-0.029	-0.032	-0.028	-0.039
1.56	-0.022	-0.018	-0.013	-0.015	-0.020	-0.035

Table 58 (continued)

Solution Composition: 22.5780 g Formamide; 5.0219 g H_2O

	T = 31.2	41.8	52.0	62.7	74.1
	d = 1.1033	1.0953	1.0839	1.0764	1.0650
λ(μ)					
1.42	0.085	0.039	0.036	0.017	0.016
1.46	-0.001	-0.007	-0.013	-0.026	-0.005
1.49	-0.026	-0.027	-0.030	-0.037	-0.042
1.52	-0.025	-0.028	-0.026	-0.038	-0.039
1.56	-0.026	-0.022	-0.017	-0.023	-0.026

Table 59

Calculated Difference Spectra for the Sodium Bromide-Water System as a Function of Solution Composition, Wavelength, and Temperature

Solution Composition: 1.0170 g NaBr; 24.7140 g H_2O

	T = 29.8	40.1	52.2	58.8	70.9
	d = 1.0255	1.0227	1.0180	1.0146	1.0075
λ(μ)					
1.42	0.025	0.013	-0.002	-0.077	-0.135
1.46	-0.010	-0.018	-0.065	-0.106	-0.139
1.49	-0.025	0.037	-0.040	-0.047	-0.079
1.52	0	-0.010	-0.020	-0.029	-0.036
1.56	-0.001	0.001	-0.007	-0.099	-0.059

Solution Composition: 1.6767 g NaBr; 24.6403 g H_2O

	T = 30.2	51.5	63.3	70.6
	d = 1.0457	1.0383	1.0319	1.0277
λ(μ)				
1.42	0.020	0.002	-0.096	-0.130
1.46	-0.003	-0.073	-0.130	-0.143
1.49	-0.006	-0.055	-0.065	-0.071
1.52	0.017	-0.033	-0.036	-0.039
1.56	0.017	-0.012	-0.093	-0.058

Solution Composition: 5.1685 g NaBr; 24.0278 g H_2O

	T = 30.3	41.3	51.1	61.8
	d = 1.1419	1.1376	1.1310	1.1259
λ(μ)				
1.42	0.025	0.007	-0.017	-0.093
1.46	0.010	-0.013	-0.054	-0.104
1.49	0.034	0.014	-0.003	-0.026
1.52	0.074	0.049	0.034	0.025
1.56	0.066	-	0.028	-0.057

Table 59 (continued)

Solution Composition: 7.7430 g NaBr; 22.7599 g H_2O

	T = 15.2	31.1	42.4	62.8	69.3
	d = 1.2261	1.2195	1.2144	1.2008	1.1961
λ(μ)					
1.42	-0.062	-0.025	-0.017	-0.095	-0.118
1.46	-0.028	0.008	-0.014	-0.110	-0.112
1.49	0.045	0.039	0.032	-0.021	-0.029
1.52	0.083	0.086	0.070	0.031	0.029
1.56	0.074	0.074	0.062	-0.032	-0.006

Table 60

Calculated Difference Spectra for the Sodium Bromide-Formamide System as a Function of Solution Composition, Wavelength, and Temperature

Solution Composition: 0.5938 g NaBr; 11.1847 g Formamide

	T = 30.7	40.9	42.7	54.0	64.2	77.1
	d = 1.1608	1.1525	1.1485	1.1419	1.1318	1.1189
λ(μ)						
1.42	-0.030	-0.031	-0.030	-0.034	-0.027	-0.030
1.46	-0.003	-0.005	-0.023	-0.014	-0.005	-0.009
1.49	-0.002	0.002	-0.007	-0.009	-0.007	0
1.52	-0.029	-0.019	-0.018	-0.024	-0.019	-0.030
1.56	-0.032	-0.025	-0.036	-0.024	-0.024	-0.032

Solution Composition: 1.3917 g NaBr; 11.1749 g Formamide

	T = 34.0	47.8	60.7	75.9
	d = 1.2158	1.2046	1.1932	1.1794
λ(μ)				
1.42	-0.023	-0.019	-0.019	-0.017
1.46	0.026	0.020	0.010	0.014
1.49	0.031	0.038	0.030	-0.022
1.52	-0.017	-0.002	-0.010	-0.018
1.56	-0.026	-0.026	-0.024	-0.024

Solution Composition: 2.2388 g NaBr; 11.1837 g Formamide

	T = 31.1	43.8	54.9	68.7
	d = 1.2695	1.2601	1.2562	1.2411
λ(μ)				
1.42	-0.025	-0.028	-0.027	-0.026
1.46	0.024	0.020	0.014	0.022
1.49	0.033	0.034	0.039	0.043
1.52	0.005	-0.006	-0.003	-0.005
1.56	-0.025	-0.019	-0.025	-0.022

Table 60 (continued)

Solution Composition: 2.9569 g NaBr; 10.9810 g Formamide

	T =	30.6	44.1	54.3	60.8	71.7
	d =	1.3149	1.3043	1.2913	1.2902	1.2812
λ(μ)						
1.42		-0.032	-0.028	-0.027	-0.023	-0.025
1.46		0.018	0.022	0.020	0.025	0.026
1.49		0.031	0.044	0.042	0.050	0.053
1.52		-0.005	-0.003	-0.004	0.002	-0.003
1.56		-0.025	-0.026	-0.025	-0.021	-0.027

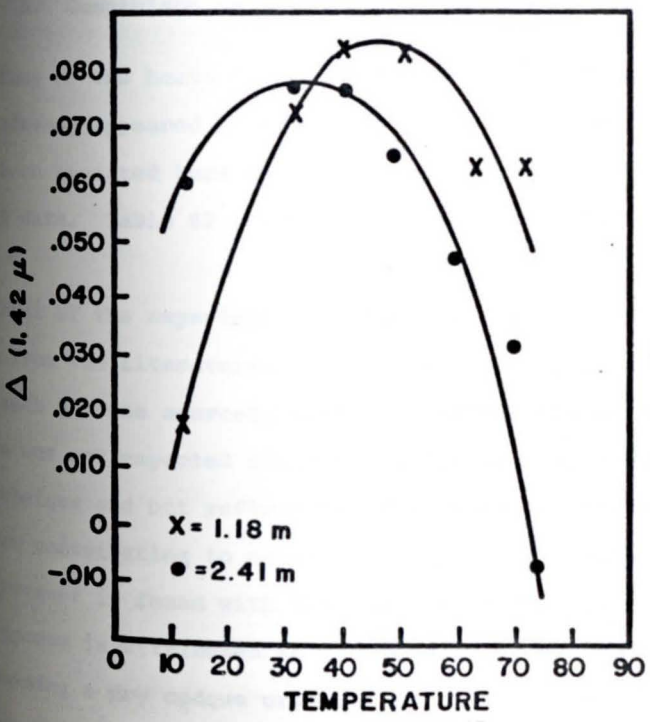
Table 61

Calculated Difference Spectra for the Sodium Bromide-Water-Formamide System as a Function of Solution Composition, Wavelength, and Temperature

Solution Composition:	6.1175 g NaBr; 16.7920 g Formamide; 8.3270 g H_2O						
T =	12.9	31.7	40.4	48.6	59.2	69.8	73.2
d =	1.2660	1.2517	1.2454	1.2391	1.2306	1.2221	1.2190
λ(μ)							
1.42	0.060	0.078	0.077	0.065	0.047	0.032	-0.007
1.46	-0.006	0.026	0.018	0.001	-0.005	-0.017	-0.039
1.49	-0.046	0.006	0.005	-0.011	-0.010	-0.012	-0.029
1.52	0.020	0.004	0.007	-0.003	-0.001	-0.014	-0.038
1.56	0.033	0.012	0.015	0.004	-0.025	-0.018	-0.045

Solution Composition:	3.0071 g NaBr; 16.7732 g Formamide; 9.2800 g H_2O					
T =	12.0	31.2	39.5	50.1	62.6	72.3
d =	1.1790	1.1653	1.1597	1.1521	1.1419	1.1336
λ(μ)						
1.42	0.018	0.073	0.084	0.083	0.063	0.064
1.46	-0.022	0.027	0.026	0.008	0.002	0.004
1.49	-0.044	0.003	-0.005	-0.011	-0.011	-0.011
1.52	-0.038	0.011	0.010	0.003	-0.011	-0.012
1.56	-0.032	0.018	0.024	0.017	-0.018	-0.003

Figure 20



CALULATED DIFFERENCE SPECTRA FOR TWO FORMAMIDE-WATER-SODIUM BROMIDE SOLUTIONS AS A FUNCTION OF TEMPERATURE

CHAPTER IV

DISCUSSION

A. Comparison of Results with Literature Data

Many of the heats of solution in water in this work have already appeared elsewhere in the literature. These have been repeated here only to provide a self consistent set of data. Table 62 summarizes these enthalpies of solution.

Most of the experimental values are close to those taken from the literature. Since the literature values are from such diverse sources, agreement within stated error limits was not expected since precision is only a function of technique and not reflective of chemical purity and other factors contributing to accuracy. A glaring example of disagreement is found with N-methylacetamide, however. This discrepancy is attributed to the difficulty encountered in maintaining a dry opaque crystalline substance in these experiments. When the N-methylacetamide crystals were damp, as indicated by greater transparency, larger exothermic enthalpies were observed. Because of the hygroscopic nature of N-methylacetamide and its own melting point, N-methylacetamide-electrolyte-water systems were not investigated more thoroughly in this work.

Table 62

A Comparison of the Enthalpies of Solution in Water with Literature Data (at 25° and atm pressure)

Compound	Exp. ΔH^{W}_{soln} kcal $mole^{-1}$	Lit. ΔH^{W}_{soln} kcal $mole^{-1}$	Ref
Formamide	0.4848 ± 0.0016	0.48 ± 0.01	46
N-Methylformamide	-1.706 ± 0.002	---	--
N,N-Dimethylformamide	-3.635 ± 0.005	-3.640 ± 0.029	39
Acetamide	2.305 ± 0.001	2.28 ± 0.03	46
N-Methylacetamide	-0.9402 ± 0.0013	-1.10 ± 0.03	46
		-1.195	47
N,N-Dimethylacetamide	-5.116 ± 0.002	-5.20 ± 0.03	46
		-5.010	47
N-Acetylglycine-N-methylamide	0.4194 ± 0.0013	0.400 ± 0.006	48
N-Acetylglycyl-glycine-N-methylamide	4.556 + 0.001	---	--
N-Acetylalanine-N-methylamide	0.6568 ± 0.0002	---	--
N-Acetyl-leucine-N-methylamide	2.340 ± 0.001	---	--
N-methylproprionamide	-3.569 ± 0.005	-3.540 ± 0.003	48

The polar liquid solute, formamide, in less polar solvent, water, gives an endothermic heat of solution (0.4848 kcal $mole^{-1}$) which might be interpreted to indicate that more energy is spent separating the highly hydrogen bonded formamide molecules than is returned by the water-formamide interactions. However, the heat of solution of polar crystals is unpredictable because it depends on the crystal's geometry and packing interactions. For example, the difference between the enthalpy of solution for N-acetylglycine-N-methylamide (0.4194 kcal $mole^{-1}$) and that of N-acetylglycylglycine-N-methylamide (4.556 kcal $mole^{-1}$) is approximately four kilocalories or nearly two times the heat for acetamide (2.305 kcal $mole^{-1}$). These compounds with large exothermic enthalpies of solution probably are compounds which solvate or create structure through hydrogen bonding, hydrophobic bonding, or dipole interactions. N,N-Dimethylacetamide, with little capacity to hydrogen bond, possesses about the same dipole moment as N-methylacetamide, for example, and could be classed as a structure maker. On the other hand, N-methylacetamide has all three capabilities --hydrogen bonding, hydrophobic bonding, and dipole interactions. Moreover, N,N-dimethylformamide (a liquid) has the same atomic constitution as NMA (a solid), but the enthalpy of solution is significantly larger than that for NMA. Thus very little information about solute-solvent interactions

can be gleaned from data on the solution of amide in a single solvent. Only the heats of transfer, from which short range amide-amide interactions have been removed from consideration permit assessment of amide-electrolyte interactions.

B. Correlation of Enthalpies of Transfer in Amide-Water-Salt Systems

Although coulombic effects are often assumed to be the predominating and only important effects,[5] it is possible that salts effect electrostatic interactions within macromolecules by shielding charges on the side chains from one another.[3] Consequently, salts are expected to differ in their effectiveness of denaturation according to their charge density in solution. With a shielding mechanism, the magnitude of interaction of a monopole anion or cation with the dipolar amide bonds might be expected to depend on the dipole moment and polarizability of the amide, and the size, charge, and polarization of the ions, as well as the temperature of the system.

Although such polarization effects or London dispersion forces have dynamic components and are not readily treated by electrostatics, these must be present in the systems investigated. The contrast between expectation and the actual measured results suggest this. From electrostatics

and the superposition of charge principle for noninteracting molecules, a zero heat of transfer should occur. If a specific interaction, such as hydrogen bonding, were present, the heat of transfer might be constant as a function of electrolyte concentration. However, a variable transfer enthalpy is experimentally observed. The following treatment is designed to indicate the reasons for suggesting the existence of dispersion forces in these systems.

The difficulties inherent in a purely electrostatic treatment may be appreciated from the following argument. A derivation[53] of a relationship for ΔH_{tr} from an ion-dipole model such as the Kirkwood equation[19] shows that the heat of transfer should depend inversely on the average radius of the ions in solution, i.e., Δ_{tr} should become less negative as the mean radius of the ions increases. The heat of transfer of formamide from water to the salt solutions, 0.5 m sodium chloride, 0.5 m sodium bromide and 0.5 m sodium iodide are -107 cal/mole, -130 cal/mole and -150 cal/mole respectively. This trend is opposite to that expected.

On the other hand, let us consider the situation of an amide of given moment and polarizability transferred to solutions of the same salt concentration but variable polarization densities. In this study the "bare" (i.e., no C_α carbon) peptide group interactions with the electrolyte, as

measured through the transfer enthalpies with formamide, were determined as a function of the total ionic polarization densities for a series of salts, with the data normalized to 0.5 molality salt for ready comparison. The enthalpies of transfer are interpolated from the data presented in Tables 13-18. The total molecular ionic polarizability density for guanidine hydrochloride is determined from the refractivity data of Kielley and Harrington[49] using the technique of Bottcher.[50] The set of ionic polarizability densities[51-52] and ionic radii[51-52] used for the other salts are those from the tabulation of Conway.[51] Tabulated heats of transfer as a function of the sums of the polarization densities of the ions appears in Table 63 and are presented in Figure 21.

In spite of the discrepancies among the literature values for solution polarizabilities (e.g., compare Li^+ = $.08 \times 10^{-24}$ cm^3 of Reference 51 and Li^+ = $.03 \times 10^{-24}$ cm^3 of Reference 52), a linear relationship results. This relationship has two interesting features. First, the correlation line extrapolates nearly to zero and second, the slope of the line is only a few percent less than the value of RT. Thus for an amide, at the infinite dilution approximation, in an electrolyte solution of constant concentration, the measured enthalpy is observed to be approximated by

Table 63

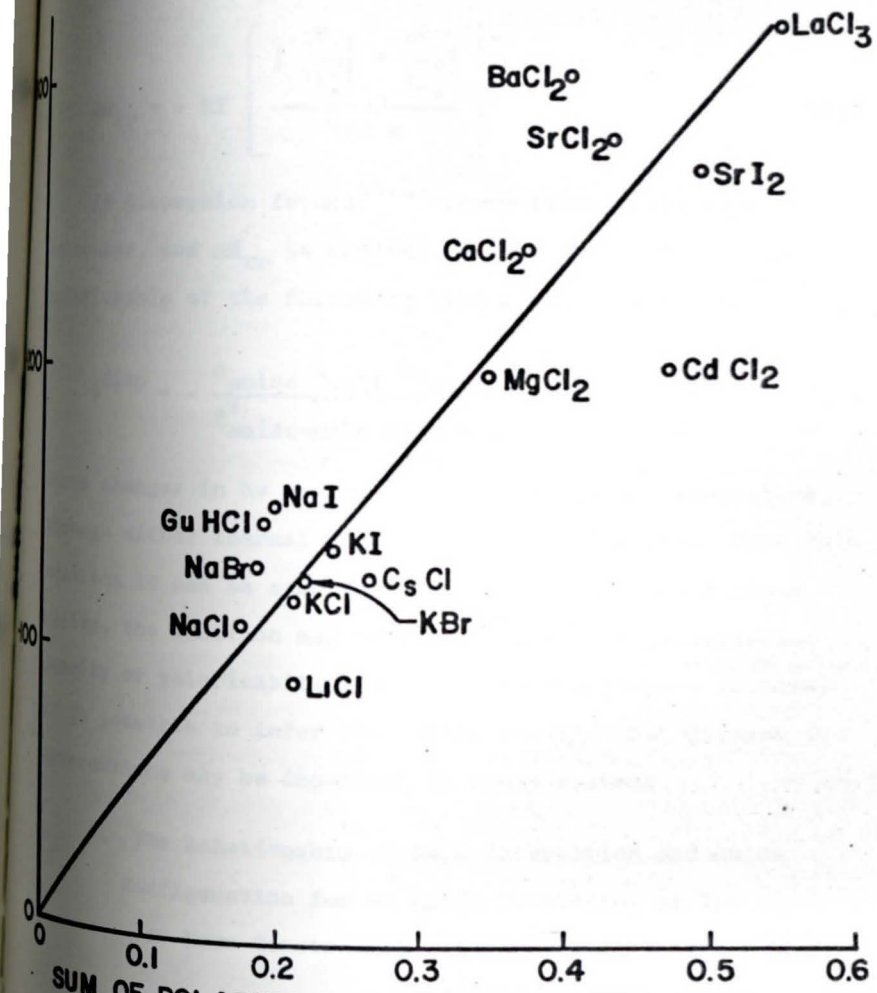
Sum of Polarization Density of Electrolyte Ions[a] for Various Salts

Salt (.5 m)	P_+ x 10^{24} cm^3	R_+ x 10^8 cm	P_- x 10^{24} cm^3	R_- x 10^8 cm	$\sum \frac{(P_+/R_+^3) + (P_-/R_-^3)}{4/3\ \pi}$	Formamide $\sim\Delta H_{tr}$ $cal\ mole^{-1}$
LiCl	0.08	0.60	3.02	1.81	0.21	-80
NaCl	0.21	0.95	3.02	1.81	0.17_5	-107
KCl	0.87	1.33	3.02	1.81	0.21	-114
CsCl	2.79	1.69	3.02	1.81	0.27	-119
$MgCl_2$	0.12	0.65	3.02	1.81	0.35	-194
$CaCl_2$	0.53	0.99	3.02	1.81	0.38	-240
$SrCl_2$	1.42	1.13	3.02	1.81	0.43	-278
$BaCl_2$	1.69	1.35	3.02	1.81	0.40	-310
$LaCl_2$	1.58	1.15	3.02	1.81	0.55	-316
NaBr	0.21	0.95	4.17	1.95	0.19	-130
KBr	0.87	1.33	4.17	1.95	0.22	-124
NaI	0.21	0.95	6.28	2.16	0.20	-150
KI	0.87	1.33	6.28	2.16	0.24	-136
SrI_2	1.42	1.13	6.28	2.16	0.49	-266
$CdCl_2$[b]	0.96	0.97	3.02	1.81	0.47	-193
GuHCl[c]	--	--	--	--	0.19	-146

a. Polarization and ionic radii data are from Ref. 51.

b. The presence of more than one ionic species has been ignored in the calculation of the sum of the polarization density for this salt.

c. Calculated from the refractive index data of Ref. 49.



VARIATION OF THE HEATS OF TRANSFER OF FORMAMIDE FROM WATER TO 0.5 m SALT SOLUTIONS WITH THE SUM OF POLARIZATION DENSITIES OF THE IONS, $\Sigma(P_+/V_+ + P_-/V_-)$

$$\Delta H_{tr} = - RT \left[\frac{\sum \left(\frac{P_+}{R_+^3}\right) + \left(\frac{P_-}{R_-^3}\right)}{4/3\ \pi} \right] \qquad (15)$$

If dispersion forces[54-55] occur between the ions and molecules, and ΔH_{tr} is reflecting this change in energy, a relationship of the following type might be expected

$$\phi^{disp} = - \frac{\alpha_{amide}\ \alpha_{salt}\ h\nu_{amide}}{R^6_{amide\text{-}salt\ distance}} \ , \qquad (16)$$

where changes in $h\nu$ energy can be effected by temperature through either thermal or collisional excitation. From this equation it can be seen that at constant amide polarizability, the function may tend to zero as the polarization density or polarizability of the electrolyte goes to zero. It is possible to infer from these results that dispersion interactions may be important in these systems.

C. The Relationship of Salt Interaction and Amide Configuration for an Amide Consisting of Two or More Constrained Dipolar Peptide Units

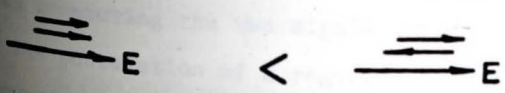
We have seen in the previous section that the transfer enthalpy data for a simple peptide unit, which has primarily only one axis of polarizability, can be shown to correlate better with the field density than with the field intensity. This has been shown through the total polarization density

relationship. We have also tried to show that a purely electrostatic argument was in contradiction to the experimental results, whereas a dispersion relationship is consistent with the experimental results. Let us turn our attention next to a dipeptide.

The interactions of an array of several or many dipoles, constrained by covalent linkages, presents a complicated theoretical problem. Even in a completely static field, it is difficult, but important, to see whether their general effect is to align parallel or nonparallel within the field. We must consider this before progressing to the situation in which dispersion effects may also occur.

If two dipole moments, such as the two dipolar components of a dipeptide, are in a horizontal position with respect to the field direction, they will have less mutual potential energy when parallel.

Pictorially, one can imagine dipoles as small vectors and the static field as a large vector so that



If the two dipoles are in a vertical orientation with respect to the field, they will have less mutual potential energy in an antiparallel alignment, such as

Thus when a dipeptide is placed into a static field in a given orientation with respect to the field, it will assume its minimum energy through rotation of its internal bond angles. Furthermore, if this dipeptide is allowed translational or molecular rotational freedom, its minimum energy becomes a function of its rotation and, therefore, internal rotation becomes a function of molecular translation. This situation of the interdependence of internal rotation and molecular translation will be termed as "coupling."

Now we are in a position to describe what should happen if a dipeptide is placed in a region or "domain" of fluctuating field. Since the field fluctuation has the same apparent result as translating the molecule, a field fluctuation also results in an internal rotation or change of bond angles connecting the two dipole segments.

The postulation of a region of microscopic local field fluctuation is reasonable considering what is known about ions. Electrolyte ions occur in solution with positive or negative charge and can be treated as individual species. Thus the smallest region in which

$$\int_{vol} dE = 0 \,, \qquad (17)$$

is that containing two ions of opposite charge. Thus the field not only fluctuates in going from the domain of an anion to that of a cation, but it can change sign as well. Consequently the field density changes as the amide moves from point to point in the solution due to thermal motion.

From the foregoing considerations it follows that N-acetylglycine-N-methylamide and N-acetylglycylglycine-N-methylamide, with predominantly one axis of polarization for parallel aligned dipoles and two or three axes for perpendicularly aligned dipoles, have two options open to them in a fluctuating field--translate (rotate externally) or rotate bonds internally. Yet for a given field density, the individual dipolar dipeptide bonds should reach the same minimum energy per peptide unit as two separate peptide units unconstrained by a covalent link, if excluded volumes for the dipeptide do not retard free rotation and losses in entropy are considered. Also conjugation may increase the dispersion effect per unit peptide slightly.

To demonstrate this, we will consider the heats of transfer for a monosubstituted amide series for two sodium bromide molalities as a function of the number of polarizable electrons in the molecule. This is shown in Table 64 and plotted in Figure 22.

Then we will consider the enthalpy of transfer for N-acetylglycine-N-methylamide versus the total number of

Table 64

Enthalpies of Transfer Versus the Number of Polarizable Amide Electrons for Some Amide-Sodium Bromide-Water Systems

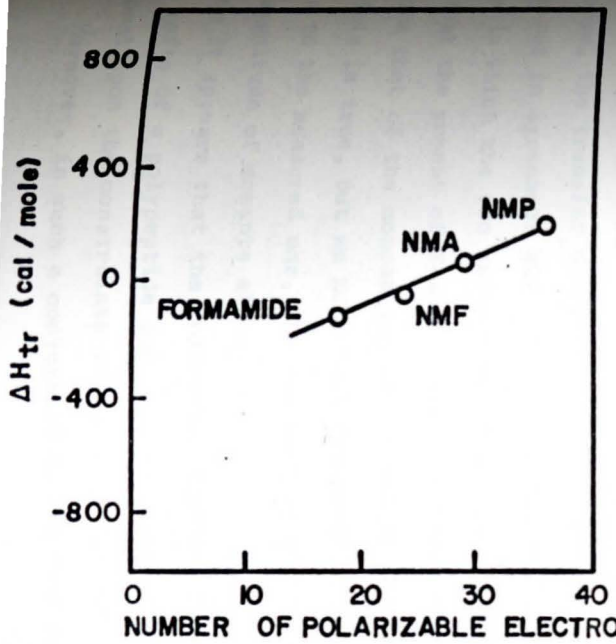
Amide	Number of Electrons	Dipole Moment[a]	ΔH_{tr}[b] cal $mole^{-1}$ 0.5 m NaBr	ΔH_{tr}[b] cal $mole^{-1}$ 4.0 m NaBr
Formamide	18	3.89	-120	-600
NMF[c]	24	3.80	-47	+35
NMA	29	3.68	+60	+400
NMP	36	3.55	+93	+800

a. R. Meighan, Diss. Abs. 25(8), 4427 (1965).

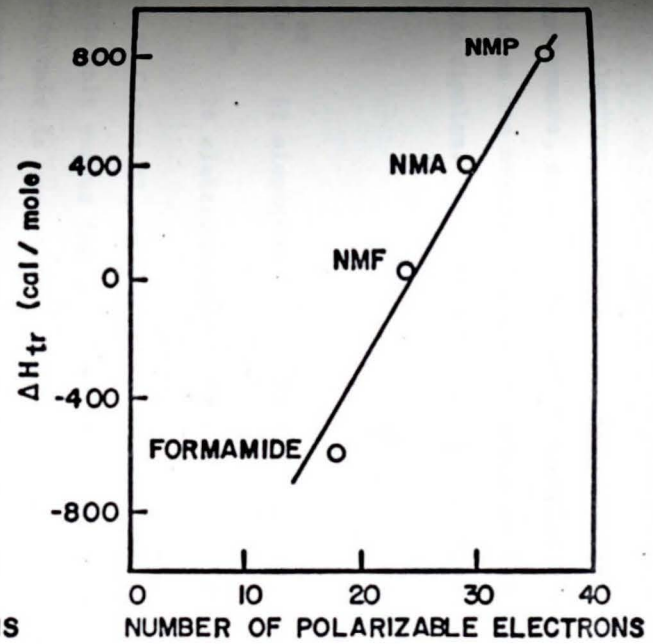
b. Values interpolated from Tables 14, 22, and 31; and Figures 1, 4, and 8.

c. Values approximated from Table 19 and Figure 2.

Figure 22



HEATS OF TRANSFER, AS A FUNCTION OF THE NUMBER OF POLARIZABLE AMIDE ELECTRONS, FROM WATER TO 0.5 m SODIUM BROMIDE SOLUTION



HEATS OF TRANSFER, AS A FUNCTION OF THE NUMBER OF POLARIZABLE AMIDE ELECTRONS, FROM WATER TO 4.0 m SODIUM BROMIDE SOLUTION

polarizable electrons for these two sodium bromide molalities. Furthermore, we will consider N-acetylglycine-N-methylamide as one overall dipole and again as two individual peptide dipoles. Then from Table 40 and Figure 10:

		$-\Delta H_{tr}$ 0.5 m NaBr	$-\Delta H_{tr}$ 4.0 m NaBr
molecule as as whole	52 electrons	96 cal/mole	32 cal/mole
as 2 peptide units	26 electrons/unit	48 cal/unit	16 cal/unit

Referring to Figure 22, we see that the transfer enthalpy per peptide unit versus the number of polarizable electrons per peptide unit is very nearly that predicted, on the basis of the monoamide sequence, for two independent peptide units. Furthermore, the transfer enthalpy for the molecule as a whole is not in agreement with the prediction for a rigid molecule in which the two units were parallel. It might be argued that the moment of N-acetylglycine-N-methylamide is then twice that of the monoamides and should not be in agreement. This is true, but we note that the predicted sign is opposite to the measured one, which cannot be accounted for by the magnitude of moments alone.

Thus it appears that the individual dipoles of the peptide units of a polypeptide can interact individually, conditional upon the constraints of the covalent bonds, of course. Moreover, in such a conjugated double bond system,

the dispersion energy is a function of the internal angles which determine the charge separation. Thus the dispersion energy may have a minimum or maximum with respect to the separation and relative orientations.

D. Effects of Substituent Groups on Amide-Salt Interactions

Previously we have considered peptides which were essentially polarizable along one peptide axis where the polarizabilities were very low in the other two directions. We now will try to indicate what should happen, on the basis of the hypothesized mechanism, when substituents are added to the peptide group.

For the case of a monopeptide, disubstitutions at the C_α carbon, and likewise disubstitution on the nitrogen, increases the polarizability along the second peptide axis. Furthermore, if these groups are bulky in relation to the hydrogen atom they displace, free rotation is restricted. Thus one peptide mode of minimizing its energy is effectively removed or reduced, which leaves the translational mode as the means of minimizing its energy in the fluctuating field. However, this too can be effectively removed if the peptide is so bulky that the field fluctuates at a faster rate than the average rate the molecule translates. (That is, two molecules--one of high molecular weight and the other a low molecular weight salt ion--will translate at

rates proportional to their respective molecular weights.) This leads to a "retarded" dipole with excess energy.

As the polarization density increases, however, a point may be reached where the excess energy of the retarded dipole is equal to the energy required to overcome the rotational barrier, thus reinstating this mode of interaction.

Similarly, if temperature were increased so that the translation were rapid, translation could be reinstated as the mode of interaction. In this manner, increased salt or electrolyte concentration (increased field density) is equivalent to added energy through an increased temperature.

From this it is expected that at some point the field fluctuation induces a perpendicular moment sufficient to overcome the moment causes by the hindered rotation. At this point, the dipole is no longer retarded and free rotation around the peptide bond occurs. If temperature is increased, the coupling between translational and rotational modes may be accessed through the vibrational modes.

We now turn to the experimental results of the DMA studies. In the absence of any external forces, the geometry expected may not possess the element of symmetry associated with a planar molecule since the rotational barrier is nonzero and relatively high. However, unlike NMF, NMA, and NMP, there may be a nonplanar molecular form that has an element of symmetry. This is the form in which

the amide methyl groups are perpendicular to the plane of the carbonyl methyl group and carbonyl group.

Either of these symmetrical forms would have one primary direction of polarization. This may account for the difference between NMP and DMA results; i.e., DMA displays an exothermic enthalpy region with certain of the electrolytes studied, whereas NMP always exhibited endothermic behavior. Thus dispersion forces are not only dependent upon electrolyte concentration, but may also be dependent upon symmetry.

Furthermore, in studies with the bulky dipeptide N-acetylglycine-N-methylamide, there is a very high rotational barrier and high moments perpendicular to that of the peptide bond moment. Thus it is unlikely that a small field density such as that from an electrolyte solution could overcome the barrier or the perpendicular moments. The internal bonds are so constrained that the peptide units within a molecule cannot interact with each other to reach a minimum energy. Experimentally, the exothermic contribution to the amide-salt interactions appears to have been destroyed, again only indicating that the interpeptide potential cannot be minimized. The increase in energy of such a "retarded" dipole or the constraints within a molecule can be related to the configurational entropy, which will be discussed in the next section.

E. Entropy-Enthalpy Relationships

It is shown in the previous section that additivity of peptide induction forces does occur when similar systems are compared in a judicious manner, i.e., the ΔH_{tr} for the interaction of N-acetylglycine-N-methylamide may be considered as the sum of two separate peptides, such additivity is assumed for the following pairs of systems:

1) N-Acetylglycine-N-methylamide - Potassium Iodide - Water and N-Acetylglycylglycine-N-methylamide - Potassium Iodide - Water,
2) N-Acetylglycine-N-methylamide - Guanidine Hydrochloride - Water and N-Acetylglycylglycine-N-methylamide - Guanidine Hydrochloride - Water,
3) N-Acetylglycine-N-methylamide - Potassium Iodide - Water and N-Acetylalanine-Methylamide - Potassium Iodide - Water,
4) N-Acetylglycine-N-methylamide - Guanidine Hydrochloride - Water and N-Acetylalanine-N-methylamide - Guanidine Hydrochloride - Water,
5) N-Acetylglycine-N-methylamide - Potassium Iodide - Water and N-Acetyl-leucine-N-methylamide - Potassium Iodide - Water, and
6) N-Acetylglycine-N-methylamide - Guanidine Hydrochloride - Water and N-Acetyl-leucine-N-methylamide - Guanidine Hydrochloride - Water.

The difference in transfer enthalpy, without reference to its source of origin, for any pair of systems is then calculated as the "group" contribution for that group not common to both members of the paired systems. The results of these calculations are shown in Tables 65-67 and Figure 23 for the alanine side chain, leucyl side chain and peptide (H-CH-C-N-H) groups.

In view of the fact that Tanford[56] has made similar assumptions and calculations for the transfer free energy for the leucyl and peptide groups resulting from the paired systems for

1) Diglycine-Guanidine Hydrochloride-Water and Glycine-Guanidine Hydrochloride-Water,
2) Triglycine-Guanidine Hydrochloride-Water and Diglycine-Guanidine Hydrochloride-Water,
3) Alanine-Guanidine Hydrochloride-Water and Glycine-Guanidine Hydrochloride-Water, and
4) Leucine-Guanidine Hydrochloride-Water and Glycine-Guanidine Hydrochloride-Water,

estimates of the group entropic contributions are calculated in Tables 68-69 from the equation $\Delta g_{tr} = \Delta h_{tr} - T\Delta s_{tr}$ and are shown as a function of the enthalpic group contribution in Figures 24-25.

Table 65

Calculated Enthalpies of Transfer of an Alanyl Side Chain from Water to Electrolyte Solutions

Δh_{tr} for an Alanyl Side Chain from Water to Potassium Iodide Solutions

m KI	.5	1.0	1.5
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylglycine-N-methylamide	-160	-250	-295
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylalanine-N-methylamide	-15	+20	+65
Difference Δh_{tr} (cal mole^{-1})	+145	+270	+360

Δh_{tr} for an Alanyl Side Chain from Water to Guanidine Hydrochloride Solutions

m GuHCl	.5	1.0	3.0	6.0
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylglycine-N-methylamide	-210	-400	-680	-850
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylalanyl-N-methylamide	-115	-200	-300	-220
Difference Δh_{tr} (cal mole^{-1})	+96	+200	+380	+630

Table 66

Calculated Enthalpies of Transfer of a Leucyl Group from Water to Electrolyte Solutions

Δh_{tr} for a Leucyl Side Chain from Water to Potassium Iodide Solutions

m KI	.5	1.0	1.5
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylglycine-N-methylamide	-160	-250	-295
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetyl-leucine-N-methylamide	+80	+210	+370
Difference Δh_{tr} (cal mole^{-1})	+240	+460	+665

Δh_{tr} for a Leucyl Side Chain from Water to Guanidine Hydrochloride Solutions

m GuHCl	.5	1.0	3.0	6.0
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylglycine-N-methylamide	-210	-400	-680	-850
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetyl-leucine-N-methylamide	-50	-25	+100	+330
Difference Δh_{tr} (cal mole^{-1})	+160	+375	+780	+1180

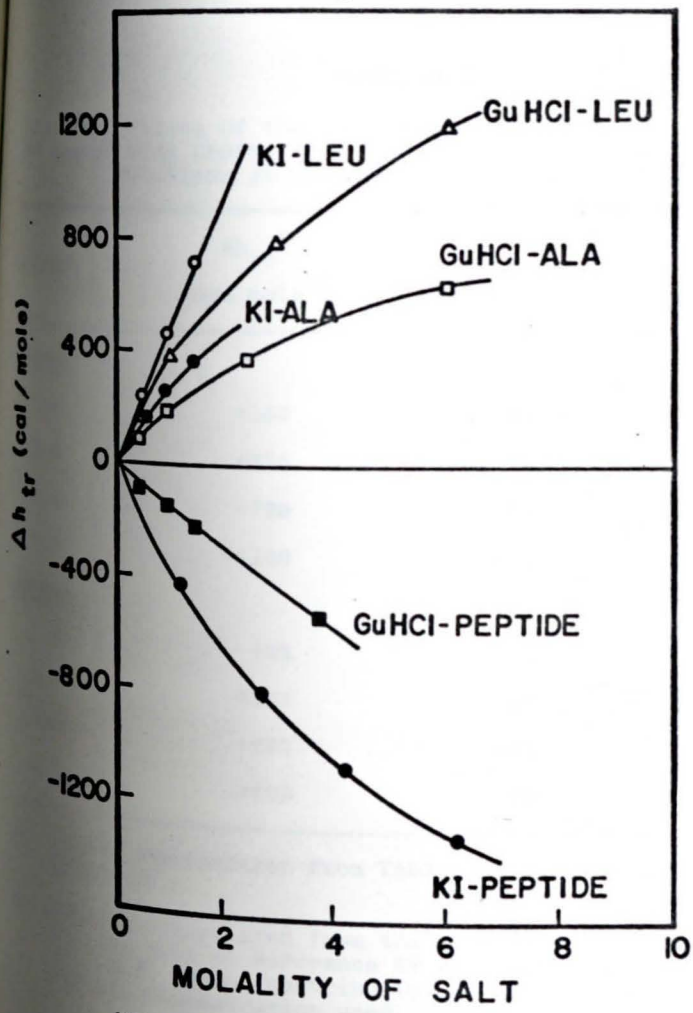
Table 67

Calculated Enthalpies of Transfer of a Peptide Group from Water to Electrolyte Solutions

Δh_{tr} for a Peptide Group (-$\overset{H}{\underset{H}{C}}$-C-$\overset{}{\underset{H}{N}}$-) from Water to Potassium Iodide Solutions				
m KI	1.25	2.75	4.30	6.25
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylglycylglycine-N-methylamide	-700	-1150	-1280	-1280
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylglycine-N-methylamide	-270	-345	-230	+25
Difference Δh_{tr} (cal mole^{-1})	-430	-805	-1050	-1305

Δh_{tr} for a Peptide Group from Water to Guanidine Hydrochloride Solutions				
m GuHCl	.50	1.0	1.5	3.8
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylglycylglycine-N-methylamide	-305	-560	-720	-1280
ΔH^{ws}_{soln} (cal mole^{-1}) N-Acetylglycine-N-methylamide	-210	-400	-510	-750
Difference Δh_{tr} (cal mole^{-1})	-95	-160	-210	-530

Figure 23



HEATS OF TRANSFER OF GROUPS
FROM WATER TO SALT SOLUTION

Table 68

Calculated Values of the Entropy for the Transfer of Leucyl and Alanyl Side Chains from Water to Guanidine Hydrochloride Solutions at Constant Temperature (25°C)

m GuHCl	Δh_{tr}[a] cal mole^{-1}	Δg_{tr}[b] cal mole^{-1}	$-T\Delta s^{calc}_{tr}$ cal mole^{-1}
Leucyl			
.5	+160	-60	+220
1.0	+375	-110	+485
3.0	+780	-260	+1040
6.0	+1180	-370	+1650
Alanyl			
.5	+95	-5	+100
1.0	+200	-10	+210
3.0	+380	-20	+400
6.0	+630	-30	+660

a. Values interpolated from Tables 65 and 66; and from Figure 23.

b. Values interpolated from the data in Reference 56 and density data of Reference 49 with the approximation that the amide volume contribution is negligible at the ~10-2 m concentration used.

Table 69

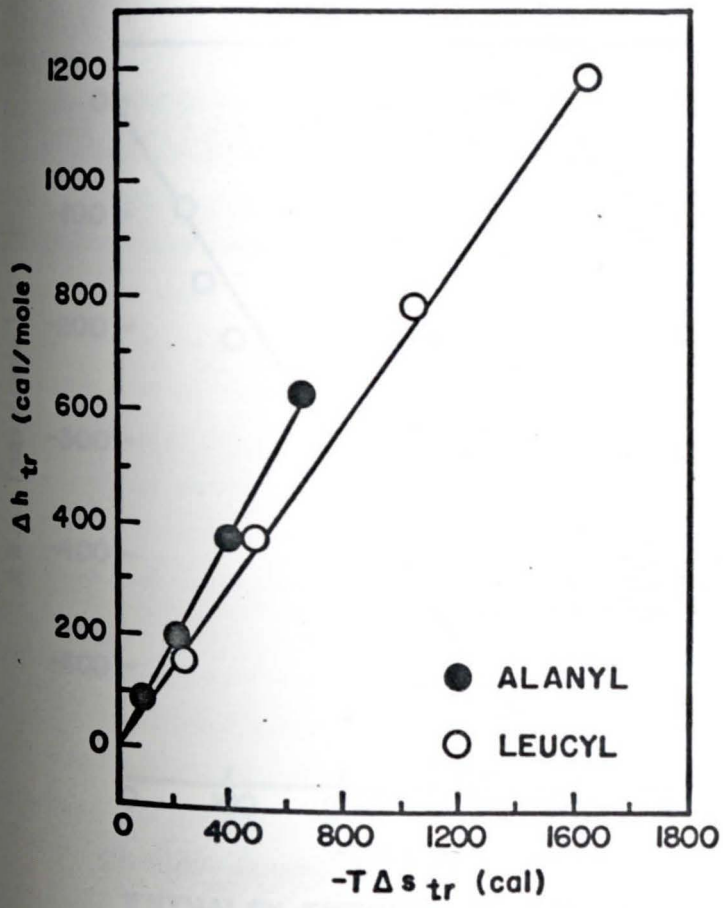
Calculated Values of the Entropy for the Transfer of a Peptide Group from Water to Guanidine Hydrochloride Solutions at Constant Temperature (25°C)

m GuHCl	Δh_{tr} [a] cal mole^{-1}	Δg_{tr} [b] cal mole^{-1}	$-T\Delta s_{tr}^{calc}$ cal mole^{-1}
.5	-95	-30	+65
1.0	-160	-10	+80
1.5	-210	-105	+105
3.8	-530	-175	+355

a. Values interpolated from Table 67 and Figure 23.

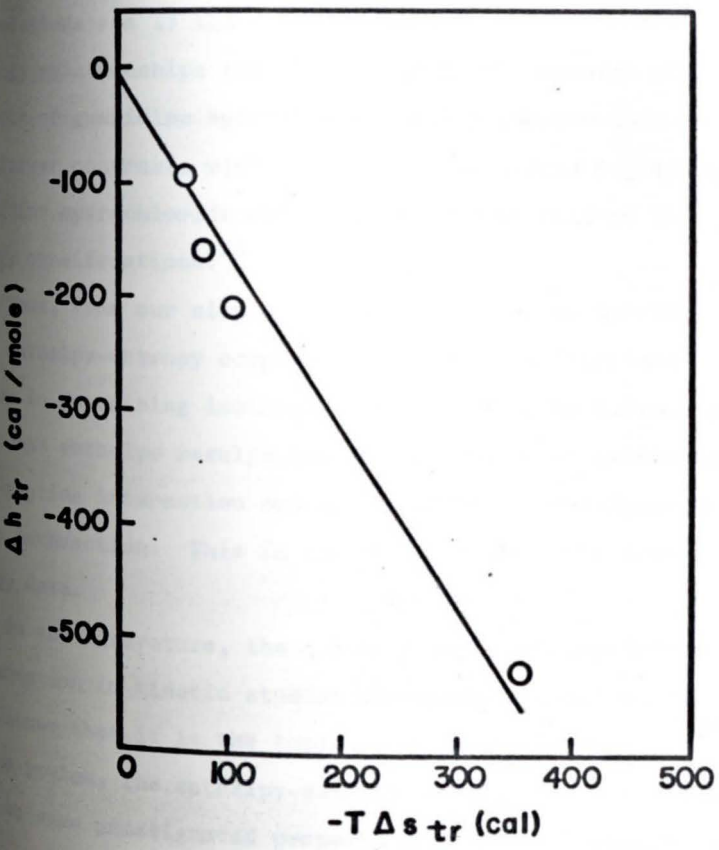
b. Values interpolated from the data in Reference 56 and the density data of Reference 49 with the approximation that the amide volume contribution is negligible at the $\sim 10^{-2}$ m concentration used.

Figure 24



ENTHALPY-ENTROPY RELATIONSHIP FOR THE TRANSFER OF LEUCYL AND ALANYL SIDE CHAINS FROM WATER TO GUANIDINE HYDROCHLORIDE SOLUTIONS AT CONSTANT TEMPER-ATURE

Figure 25



ENTHALPY-ENTROPY RELATIONSHIP FOR THE TRANSFER OF A PEPTIDE GROUP FROM WATER TO GUANIDINE HYDROCHLORIDE SOLUTIONS AT CONSTANT TEMPERATURE

The most interesting conclusions to result from these calculations are 1) the apparent large and linear enthalpy-entropy relationships and 2) the similarity between the effects of guanidine hydrochloride and potassium iodide. The latter contrasts with Tanford's conclusions regarding guanidine hydrochloride which are based entirely on free energy considerations.[56]

Thus, from our simple dipeptide models, we conclude that enthalpy-entropy compensation may be an important factor in describing isothermal denaturation by salts. At least the enthalpy results present a consistent exothermic salt-peptide interaction and an endothermic salt-hydrophobic group interaction. This is not the case with the free energy data.

In the literature, the evidence for enthalpy-entropy compensation in kinetic studies of aqueous solutions is so ubiquitous that it is the topic of an extensive review.[57] In the review, the enthalpy-entropy compensation is attributed to some undesignated property of water. However, the reviewers did not find any definite evidence that the theory for processes where changes in charge distribution occur, such as denaturation of proteins in aqueous electrolyte solution, involves both a basic electrostatic element and a manifestation of enthalpy-entropy compensation.

As we have tried to indicate here with model compounds, and will discuss further in the lysozyme denaturation model, the theory of isothermal denaturation probably needs to account for both the electrostatic effects within the macromolecule and enthalpy-entropy compensation. Unfortunately, more transfer free energy data is not presently available to calculate transfer entropies for the other model amide systems.

It is interesting to note, however, that acetone (C_3H_6O) displays enthalpy-entropy compensation whereas propanol (C_3H_8O) shows no change in entropy other than mixing ($-R \ln x$). This is in contrast to the heats of solution, which are very similar as would be expected from their similar sizes. (See Appendix I.) Also it is interesting that the salting out parameter is related to this enthalpy-entropy compensation phenomenon. We note that a limiting interaction parameter for acetone calculated from the enthalpy data is opposite in sign to that determined from free energy data (see Table 75 of Appendix I), whereas the same parameter for propanol for both the free energy and enthalpy calculations are quite similar in magnitude considering the difference in concentration ranges used to extrapolate to the infinite dilution approximation.

It appears therefore that the enthalpy-entropy compensation phenomenon is not exclusively a property of the amide

bond, but appears to be general for any molecule with a double bond and C_{2v} or less symmetry. Preliminary indications thus are that a double bond character for the solute is necessary, in aqueous solution, for the enthalpy-entropy compensation to occur, suggesting a bond rearrangement mechanism. There are not enough free energy data available to test this hypothesis. This is one area of investigation in additivity and salt effect phenomena where further study may be of interest.

F. A Consideration of Additivity as Applied to Enthalpies of Transfer and its Relation to the Enthalpy of Denaturation of Lysozyme by Electrolytes

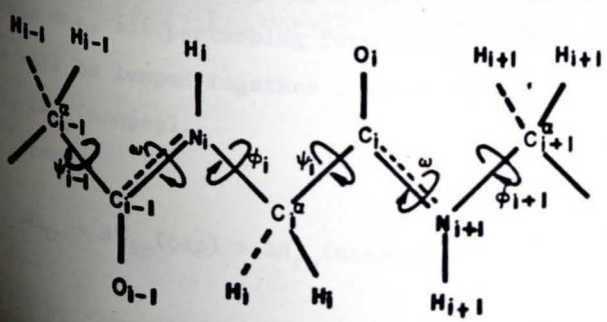
From the discussion in the previous section, the geometry of the molecule is an important factor determining the enthalpy of transfer. It is the angle dependencies of the group contributions and steric factors which cause the simple linear additivity for enthalpic group contributions to fail when considered over a wide electrolyte molality range. The amide-electrolyte interactions or the enthalpies of transfer are tensor quantities rather than scalar quantities.

Previously, free energy group contributions[6,54,55,58] appeared to be linearly additive for two reasons: 1) the hydrophobic enthalpy and entropy effects were largely com-

pensating and 2) the models used were of similar geometry and polarity at their minimum free energy configurations so that the electrostatic forces were comparable.

However, in general, entropic and enthalpic contributions are not so simply additive over an electrolyte molality range except for cases such as the formamide-electrolyte-water systems, and the inductive effects in the conjugated chain of the peptide "backbone" in which there is primarily only one axis of polarization.

Since it is at present impossible to determine, a priori, the detailed configuration of an enzyme, we consider the problem of applying the nonadditive or geometry dependent properties of the model systems to an enzyme system. Let us first assume the two state model, i.e., that in which only native or denatured molecules are present--no intermediate configurations, for the polyglycine-like backbone chain of the enzyme and also assume that in the native helix configuration there is only one angle of minimum energy allowed for each ω



This ω can be zero or a multiple of 180°. In a similar manner for the denatured state, no preferential conformation is assumed. The polyglycine-like backbone is in the random coil state. Since from the conjugated model amide, i.e., N-acetylglycylglycine-N-methylamide, enthalpic group contributions are approximately additive, the enthalpy of transfer of n peptide groups from water to salt solution will be approximately n times that found for a model peptide group. That is, as the salt concentration is increased, the angles characteristic of a helix would be stabilized by an increase in dipole moment--for parallel dipoles have been shown to predominate at high field strength or electrolyte concentration. In this way the inductive amide-electrolyte interaction becomes a measure of the helical content of the polyglycine backbone. When C_α substituents interfere with the rotation around the peptide bond, there results a decrease in the net possible inductive interaction. The decrease in inductive polarization is then a function of the orientational polarization.

Since the peptide group contribution is the only exothermic one, all perturbing forces due to C_α and N substituents will be lumped together into one general endothermic term, $\Delta H_{tr}(\text{nonpep})$.

Then

$$\Delta H_{tr} = \Delta H_{tr}(\text{pep}) + \Delta H_{tr}(\text{nonpep}) \qquad (18)$$

At the salt concentration midpoint for conformational change, C_m, $K = 1$,

$$\Delta G_{tr} = 0 = \Delta H_{tr} - T\Delta S_{tr} \tag{19}$$

where

$$\Delta H_{tr} = \sum_n \delta h_{tr}(pep) + \sum_n \delta h_{tr}(nonpep) \tag{20}$$

so that

$$\Delta G_{tr} = \sum_n \delta h_{tr}(pep) + \sum_n \delta h_{tr}(nonpep) - T\Delta S_{tr} \tag{21}$$

Then at the electrolyte concentration at which denaturation occurs

$$-\sum_n \delta h_{tr}(pep) = \sum_n \delta h_{tr}(nonpep) - T\Delta S_{tr} \tag{22}$$

However, $T\Delta S_{tr}$ is comprised of only one term in the case of transfer--an inherent term.[59] Thus,

$$-\sum_n \delta h_{tr}(pep) = \sum_n \delta h_{tr}(nonpep) - T\Delta S_{tr}(inherent) \tag{23}$$

Because of the large variety of hydrophobic groups involved, the right hand side of this equation is presently indeterminate.

But through the exothermic nature of the peptide interaction in opposition to the endothermic nature of the hydrophobic interactions, the maximum exothermic enthalpy of denaturation is

$$\Delta H_{den}(max) = -\sum_{n} \delta h_{tr}(pep) \quad (24)$$

$$= n[-\delta h_{tr}(pep)] \quad (25)$$

when the phenomenon of enthalpy-entropy compensation, as observed for the leucyl and alanyl side chains (Figure 24), holds so that

$$\sum_{n} \delta h_{tr}(nonpep) \approx -T\Delta S_{tr}(inherent) \quad (26)$$

Since transfer entropies for both peptide and hydrophobic groups are of the same sign, the total transfer entropy in equation 26 is considered even though that term could be split into its component parts. For such cases of compensation, this maximum (equation 24) may approximate the heat of denaturation.

On the other hand, for the cases where compensation doesn't occur, such as systems where all hydrophobic groups are exposed to the solvent before denaturation,

$$-T\Delta S_{tr}(inherent) = 0 \quad (27)$$

the minimum heat of denaturation would occur,

$$\Delta H_{den}(min) = \tfrac{1}{2}\, \Delta H_{den}(max) \quad (28)$$

That is, enthalpy of denaturation may be compensated by conformational entropy of the chain rather than that of the solvent.

Thus these approximations provide limiting values for the enthalpies of denaturation for enzymes, provided that model compound entropies apply in this case.

The enthalpy of lysozyme denaturation, at pH 2, by 3.5 m guanidine hydrochloride (Table 51) was experimentally determined as the enthalpy of transfer of lysozyme from a pH 2 ($\approx 10^{-2}$ HCl buffer) to a 3.5 m guanidine hydrochloride solution, also pH 2 ($\approx 10^{-2}$ HCl buffer). The denaturing salt concentration for pH 2 is slightly greater than that which has been determined by K. Aune[60] by spectroscopic measurements at 25°. As tabulated in Table 70, this calorimetric measurement agrees with the temperature dependence for the spectroscopic measurements of Aune.

Because of the heats of transfer, and presumably the heats of denaturation, are dependent on temperature and solvent, the heat capacity entry of Table 70 cannot be directly compared to the others. That is, the enthalpy of denaturation may not be an intrinsic property of the enzyme alone, but may be dependent on the solvent and temperature. This is possible because there may be two (or more) denatured states if biological activity loss is the only criterion. The one denatured state is that in which all bonds are free to rotate from the active configuration and the other in which the angles are fixed at minimum potential wells other than that in the native state.

Table 70

Comparison of the Enthalpies of Denaturation of Lysozyme

Method	Conditions	$+\Delta H_{den}$ kcal mole^{-1}	Ref.
Heat Capacity	pH 1 HCl-water 25° 3% soln.	55	61
Spectroscopic	pH 2 GuHCl var. Temp. var. ≈1% soln.	25	60
Transfer Enthalpy	pH 2 3.5 m GuHCl 25° ≈½% soln	24	This Work

From the transfer data for model compounds, a theoretical model has already been formulated which predicts the minimum and maximum limits for enthalpies of denaturation in an electrolyte system. A rough calculation of the ΔH_{den} using the model compound data and the theoretical model follows. This calculation includes the two limits--1) complete enthalpy-entropy compensation for the hydrophobic groups and 2) no compensation. Since lysozyme does not change volume significantly upon denaturation suggesting that nearly all the groups are already exposed to the solvent, case 2--no or little compensation--is expected for the calorimetric experiment of lysozyme in an isothermal determination.

From Figure 7 for the N-Acetylglycine-N-Methylamide--Guanidine Hydrochloride--Water system and Figure 10 for the N-Acetylglycylglycine-N-Methylamide--Guanidine Hydrochloride--Water system, the interpolated ΔH_{tr}'s at 3.5 m GuHCl are:*

$$\Delta H_{tr}(\text{NAGNMA at 3.5 m GuHCl})/2 \text{ peptides} \approx -720 \text{ cal} \quad (29)$$

or

$$\Delta h_{tr}/\text{one peptide unit} \approx -360 \text{ cal} \quad (30)$$

---

* Since lysozyme does not have a high helix content, this average is used for short helical runs rather than a higher value (-500) for a peptide within a longer helical segment.

and

$$\Delta H_{tr}(\text{NAGNMA at 3.5 m GuHCl})/3 \text{ peptides} \simeq 1220 \text{ cal} \quad (31)$$

or

$$\Delta h_{tr}/\text{one peptide unit} \simeq -410 \text{ cal} \quad (32)$$

for an average

$$\Delta h_{tr}/\text{peptide} \simeq -380 \text{ cal} \quad (33)$$

Lysozyme has 129 peptide units so that for the case where enthalpy-entropy compensation is nearly complete,

$$-\Delta H_{den}(\text{max}) \simeq 129 \times -383 \simeq 50 \text{ kcal} \quad (34)$$

and for the case where no compensation occurs,

$$-\Delta H_{den}(\text{min}) \simeq \tfrac{1}{2} \Delta H_{den}(\text{max}) \simeq 25 \text{ kcal} \quad (35)$$

This assumes no change in ionization of titratable groups with denaturation since the pH was fixed as a constant pH 2 throughout.

It is interesting to note that these two values are both represented experimentally, Table 70. The maximum, calculated from total hydrophobic enthalpy-entropy compensation, is approximated by the heat capacity measurements. The minimum, calculated from the assumption for no compensation, occurs as expected for the isothermal calorimetric case and again for spectroscopic measurements corrected for changes in activity of the solvent due to temperature

effects. Since the 25 kcal value was obtained very close to the transition point, we feel this is more representative of the denaturation process than the 55 kcal value which may include a further step to a different inactive configuration.

The finding that lysozyme does not require the enthalpy-entropy compensation is an indication that the number of hydrophobic groups, which are exposed to the electrolyte by the denaturation process, is probably small. On the other hand, ribonuclease with some buried groups in its 124 residues has a $\Delta H_{den} \approx 35$ kcal[62] for GuHCl, which is between the maximum and minimum extrema. The possibility that a number of groups are exposed during the denaturation of ribonuclease has been noted elsewhere.[62]

Finally, it is interesting to note that at 3.5 m GuHCl, that concentration at which lysozyme denatures at pH 2, the enthalpy of transfer for a model group is roughly -400 to -500 cal/residue. This is the order of magnitude calculated for the helix-coil transition per peptide unit for polyglycine (-488 cal/residue).[63] Although direct comparison cannot be made, this is at least consistent with the lysozyme picture presented.

G. Spectroscopic Considerations

The infrared spectra for formamide-sodium bromide-water systems indicate a general blue shift of the rotational-vibrational band which is increased both by an increase of salt concentration and an increase of temperature. The calculated difference spectra, with electrostriction effects removed, indicate very small absorbance differences, which show a characteristic dependence upon temperature. These facts are all consistent with dispersion and with the interpretation of the calorimetric data, but unfortunately do not permit a quantitative evaluation of the spectroscopic effects.

H. Conclusions

1) In an attempt to better characterize the forces responsible for isothermal denaturation by salts, we have calorimetrically measured the changes in enthalpy that occur for the transfer of a simple amide series from water to an aqueous salt solution for a series of salts and various electrolyte concentrations.

2) From the dependence of the amide transfer enthalpy of a "bare" peptide (based on formamide as a model compound) upon the total polarization density of the solvent, we have concluded that dispersion effects are present.

3) We postulate and find our data consistent with the idea that dispersion forces have angle dependent maxima and minima or that the conformation of a dipeptide is dependent on these forces subject to a number of constraints--covalent bonds, excluded volumes, charge groups, etc. Also a symmetry dependence, as for DMA, is noted.

4) We note that for dipeptides with large hydrophobic substituents, entropy-enthalpy compensation results. The dipeptide systems appear subject to dispersion forces but are incapable of relieving such stresses through the minimization of molecular energy with bond rotations.

5) We postulate that, in cases where the stresses are sufficiently large and the individual peptide units eventually reach a minimum energy in the electrolyte field, the enthalpy of the denaturation process or configurational change is directly related to the stress applied to achieve free rotation at the midpoint of transition.

6) We noted that the forces favoring configurational change were opposite to the constraints and have presented a model to estimate the possible maximum and minimum values of the enthalpy of denaturation. (Conversely, a model could be used to estimate the salt concentration range in which denaturation would occur if the heat of denaturation were known from other experiments.)

7) We have compared the two extreme values obtained from our model for lysozyme denaturation with literature

values and found a literature value in agreement with each of the extremes. This may be fortuitous.

8) We observed that spectroscopic results are consistent with the interpretation of calorimetric data.

9) Although the results of a detailed examination of the pertinent literature are too voluminous to report in this thesis, it is interesting to note that among peptide, polypeptide and enzyme data from spectroscopic, calorimetry, ultracentrifugation and other studies in the chemical literature we considered, we did not find any that contradict the dispersion hypothesis. On the contrary, there are occasional apparent contradictions which can be removed by our hypothesis; such as, the apparent discrepancies in the heats of denaturation obtained from the different methods, and the behavior of certain organic salts as protein denaturants.

10) Finally, we realize the difficulties the dispersion forces present in theoretical calculations, but nonetheless feel that these forces are possibly the configuration determining factors so that any successful theory must fully account for such forces. Obviously there is much to be done in order to achieve a general helix-coil theory which includes all forces.

APPENDIX I

Experimental values obtained from work concerning the peripheral studies with acetone and propanol are shown in Tables 71-74. For convenience, graphical representations of this information appear in Figures 26-27.

Furthermore, in order to make direct comparisons with the literature values for the "a" salting out parameters, Polyfit, a least square program stored in the SUNY/Binghamton IBM 360/40 Computer, was run with the ΔH_{tr} data using the equation

$$\Delta H_{tr} = am_1 + bm_1^{3/2} + cm_1^2 + dm_1m_2 \qquad (36)$$

which is the integrated form of the equation used by Schrier, et al.[64] These coefficients appear in Table 75 along with those for the ΔG_{tr} measurements as extracted from the literature. The calculated ΔS_{tr} that resulted from these measurements was the criterion used to judge the presence of enthalpy-entropy compensation. Although the free energy of transfer of acetone is predominantly determined by its molecular volume, a small contribution from the charge separation or induced moment is present, as is indicated by the transfer enthalpy.

This additional data is presented as evidence that the dispersion effect appears not to be unique to the peptide

linkage but may be general for all double bonded or conjugated molecules in aqueous solution.

Table 71

Enthalpies of Solution Per Mole of Propanol Dissolved to Give Various Molalities in Water

Alcohol Molality $m_1 \times 10^2$	$-\Delta H^{w}_{soln}$ kcal mole^{-1}
1.4753	2.429
5.1644	2.432
6.5376	2.423
6.9139	2.420
8.3800	2.424
9.8585	2.420
	Ave. 2.425±0.002

Table 72

Enthalpies of Solution Per Mole of Propanol Dissolved to Give Various Molalities in Sodium Chloride Solutions. Calculated Enthalpies of Transfer of Propanol from Water to Sodium Chloride Solutions.

Alcohol Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH^{a}_{tr} kcal mole^{-1}
1.5886	0.0143	2.422	0.003
1.5652	0.1175	2.395	
1.6556	0.1175	2.393	
1.8232	0.1175	2.389	
	Ave.	2.393±0.002	0.032±0.002
1.4388	0.2631	2.342	
1.6253	0.2631	2.334	
	Ave.	2.338±0.004	0.087±0.003
1.6529	0.5160	2.246	
1.6870	0.5160	2.250	
	Ave.	2.248±0.002	0.177±0.002
1.5060	0.9898	2.083	
1.8184	0.9898	2.080	
	Ave.	2.082±0.002	0.343±0.002
1.9362	1.5985	1.889	
2.6788	1.5985	1.891	
	Ave.	1.890±0.001	0.535±0.002
1.8544	2.0854	1.737	
1.9143	2.0854	1.737	
	Ave.	1.737±0.000	0.688±0.002
2.2902	2.3823	1.649	0.777

Table 72 (continued)

Alcohol Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	ΔH_{tr}[a] kcal mole^{-1}
1.9391	2.8840	1.499	
2.0644	2.8840	1.502	
		Ave. 1.501±0.002	0.924±0.002
2.1091	3.4513	1.320	
2.1610	3.4513	1.333	
		Ave. 1.327±0.006	1.098±0.003

a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 71.

Table 73

Enthalpies of Solution Per Mole of Acetone Dissolved to Give Various Molalities in Water

Acetone Molality $m_1 \times 10^2$	$-\Delta H^w_{soln}$ kcal $mole^{-1}$
1.0659	2.437
1.6053	2.436
	Ave. 2.436±0.001

Table 74

Enthalpies of Solution Per Mole of Acetone Dissolved to Give Various Molalities in Sodium Chloride Solutions. Calculated Enthalpies of Transfer of Acetone from Water to Sodium Chloride Solutions.

Acetone Molality $m_1 \times 10^2$	Salt Molality m_2	$-\Delta H^{ws}_{soln}$ kcal mole^{-1}	$\Delta H_{tr}{}^{a}$ kcal mole^{-1}
1.4559	0.0143	2.439	-0.003
1.6456	0.1175	2.433	
1.6949	0.1175	2.437	
	Ave.	2.435±0.002	+0.002±0.002
1.5534	1.0498	2.402	+0.034
1.6400	2.0854	2.359	+0.077
1.7469	2.3822	2.321	+0.115
1.7513	2.8840	2.294	+0.142
1.7229	3.4513	2.263	
1.7983	3.4513	2.263	
	Ave.	2.263±0.000	+0.173±0.001

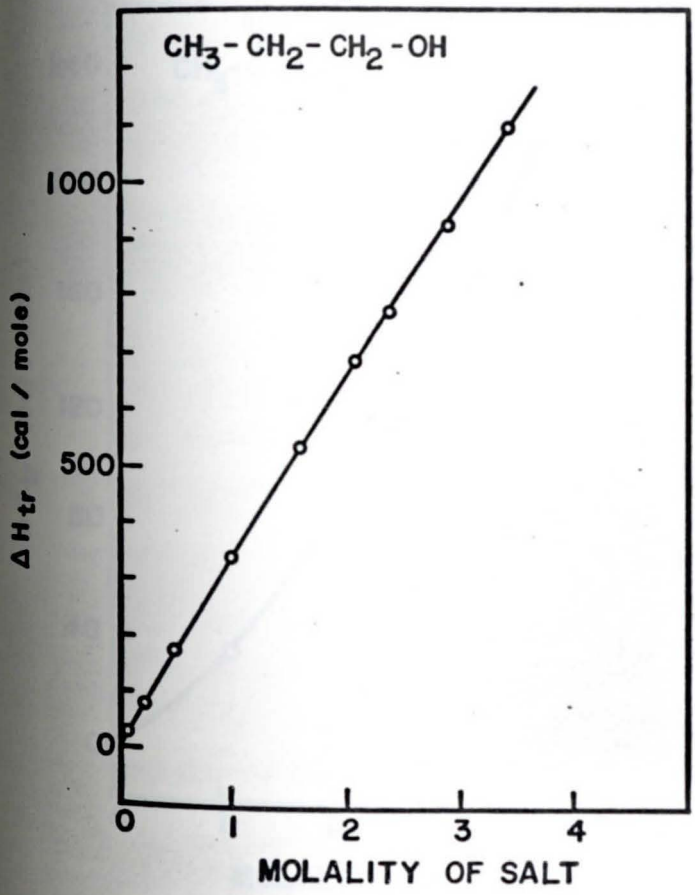
a. The ΔH^{w}_{soln} value used in obtaining ΔH_{tr} may be found in Table 73.

Table 75

Parameters for the Propanol and Acetone Systems

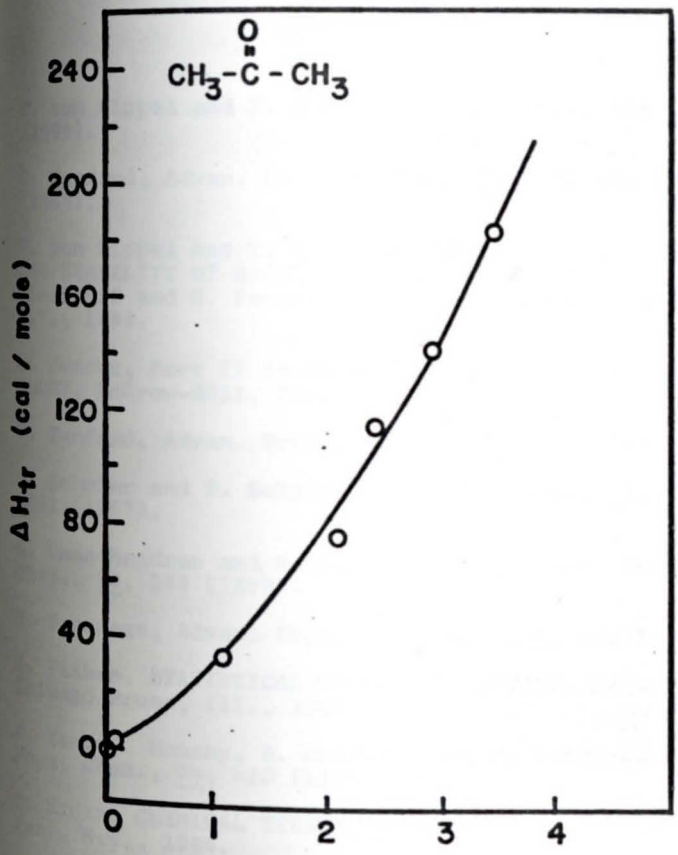
ΔH_{tr} From $\Delta H_{tr} = am_1 + bm_1^{3/2} + cm_1^2 + dm_1m_2$	ΔG_{tr} From $\Delta G_{tr} = -2.303\ RT\ (\delta \log \gamma_2/\delta m_1)_{m_2}$ $(\delta \log \gamma_2/\delta m_1)_{m_2} = a+bm_1^{1/2}+cm_1+dm_2$
Propanol[58]	
a = +.347	a = +.1654
b = +.006	b = -.0037
c = -.011	c = +.0070
d = -.132	d = -.0206
fit std dev = 6.2×10^{-3}	fit std dev = 1.2×10^{-3}
Acetone[64]	
a = -.060	a = +.1041
b = +.020	b = -.0121
c = -.0028	c = -.0016
d = +4.7	d = -.0053
fit std dev = 5.8×10^{-3}	

Figure 26



HEATS OF TRANSFER OF PROPANOL FROM WATER TO SODIUM CHLORIDE SOLUTIONS

Figure 27



HEATS OF TRANSFER OF ACETONE FROM WATER TO SODIUM CHLORIDE SOLUTIONS

CHAPTER V

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