[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY]

The Dielectric Constants of Solutions of Glycine and Pyridine Betaine in Water–Dioxane Mixtures

BY GERALD OSTER,[1] DONNA PRICE,[2] LESLIE G. JOYNER[3] AND JOHN G. KIRKWOOD

Introduction

The amino acids, betaines, and proteins exhibit certain properties similar to those of ionic compounds although their molecules in solution are electrically neutral. There is convincing evidence[4] that such molecules in aqueous solution have very large dipole moments of from about 15×10^{-18} e. s. u. for α-amino acids to as high as 1300×10^{-18} e. s. u. for the protein γ-pseudo globulin. Molecules of this type are called dipolar ions or zwitterions. One of the best indications of their dipolar structure is to be found in the dielectric properties of solutions of these substances. When amino acids, betaines, and proteins are dissolved in water they produce strikingly large dielectric constant increments. Wyman[5] found that this increase in dielectric constant of the water $\epsilon - \epsilon_0$, where ϵ is the dielectric constant of the solution and ϵ_0 that of pure water, is proportional to the concentration c of the solute, *i. e.*, $\epsilon = \epsilon_0 + \delta c$ where δ, the dielectric increment, is a constant. However, as the dielectric constant ϵ_0 of the solvent is lowered by the addition of a liquid of lower dielectric constant (*e. g.*, addition of ethanol or dioxane to water, or the addition of benzene to ethanol) the dielectric increment δ, *i. e.*, the relative lowering, decreases markedly and approaches zero as the dielectric constant ϵ of the solvent mixtures decreases. In any solvent mixture the relation $\epsilon = \epsilon_0 + \delta c$, nevertheless, is obeyed quite closely. This lowering of δ which corresponds to an apparent decrease in the dipole moment of the dipolar ions was thought to be due to an actual movement of the charged groups toward each other since lowering the dielectric constant of the solvent medium increases the coulombic attraction between the charges. It was thought that either there was an equilibrium between dipolar ions and completely uncharged molecules due to the movement of charged groups, or else a gradual decrease in dipole moment due to the distortion of chemical bond angles, so that the charges could come close together.

In order to examine these hypotheses two types of dipolar substances were examined, glycine and pyridine betaine. Glycine $^+NH_3CH_2COO^-$ offers the possibility of a shift of a hydrogen atom to the COO^- group thereby forming a nondipolar molecule, while pyridine betaine  $N^+—CH_2—COO^-$ contains no groups which can shift to form the un-ionized molecule.

Experimental

Apparatus.—The apparatus used to measure the dielectric constant was similar to that of Geddes and Kraus[6] with some modifications. The method is a resonance method due to Wyman.[7] The technique consists essentially in completely immersing in the medium a resonator of fixed inductance and capacity. The resonator is coupled inductively to an oscillator, the frequency of which is adjusted by a variable capacity until it corresponds to the natural period of the resonator. From the frequency of the resonator in vacuum (air) or in a standard of known dielectric constant and its frequency in the unknown medium the dielectric constant of the latter may be determined.

Certain features of the apparatus will be described briefly.

The resonator was of the shielded type used by Wyman for measurements in benzene. Due to the corrosive action of glycine solutions on many metals the resonator was constructed of platinum–10% iridium alloy.

The resonator was suspended in a cell containing 400 cc. of fluid. This cell was set in a double walled flask through which oil from a constant temperature bath was circulated. The double-walled flask was in turn surrounded by a Dewar flask. Thus the temperature of the solution was maintained at 25.0 ± 0.01°.

Since the dielectric constant of a water-dioxane mixture is very sensitive to the composition, it was necessary to take elaborate precautions to avoid evaporation of the dioxane during a run. A system of pipets, completely closed except for a small capillary hole, was used for filling and making dilutions. Ground glass joints were used throughout. Nitrogen was used to force the solutions into the pipets which were calibrated to ±0.01 ml.

Materials.—Practical dioxane was purified by the modified method of Vingee and Kraus.[8] Ammonia-free glycine was purified by three recrystallizations from water–alcohol solutions. The pyridine betaine was prepared by the general method of von Gerichten[9] and was purified by recrystallizations from absolute alcohol; decomposition point, 204°. Conductivity water whose specific conductivity was less than 10^{-6} ohm^{-1} was used in the solutions. The concentrations of the glycine solutions were determined to an accuracy of 0.1% by a micro-Kjeldahl analysis. Pyridine betaine exhibited greater solubility than glycine in the lower dielectric constant solvent mixtures so that its solutions were made by dissolving a known weight of the substance.

Experimental Results

In these experiments the dielectric constants of solutions of glycine and of pyridine betaine in water–dioxane (ϵ_0 from 5.7 to 78.5) were measured. The results are presented in Table I and illustrated in Figs. 1 and 2.

In the case of glycine there was some decrease in the dielectric increment δ with concentration

---

[1] Present address: Department of Electrical Engineering, Massachusetts Institute of Technology.

[2] Present address: Hercules Powder Co.

[3] Present address: Gulf Research Laboratory.

[4] E. J. Cohn and J. T. Edsall, "Proteins, Amino Acids and Peptides," Reinhold Publishing Corp., New York, N. Y., 1943.

[5] J. Wyman, Jr., *Chem. Rev.*, **19**, 213 (1936).

[6] J. Geddes and C. A. Kraus, *Trans. Faraday Soc.*, **32**, 585 (1936).

[7] J. Wyman, Jr., *Phys. Rev.*, **35**, 623 (1930).

[8] R. A. Vingee and C. A. Kraus, THIS JOURNAL, **55**, 21 (1933).

[9] E. von Gerichten, *Ber.*, **15**, 1251 (1882).

TABLE I

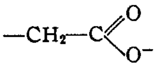
DIELECTRIC INCREMENTS IN WATER-DIOXANE MIXTURES AT 25°

ϵ_0	δ	Range of concentration, moles/liter
	Glycine	
13.397	3.27	0.00092-0.00939
15.795	6.77	.00075- .0154
18.967	10.23	.00125- .01574
22.632	13.93	.00196- .01544
25.953	16.02	.00305- .02062
30.457	18.01	.00209- .01756
40.020	19.96	.00110- .01646
78.54	22.58	(Wyman and McMeekin)[10]
	Pyridine Betaine	
5.680	6.76	.00911- .01175
6.808	8.89	.00631- .00753
9.230	10.17	.02502- .03509
9.437	10.78	.01306- 0.1783
11.537	11.25	.02101- .02627
16.467	15.22	.01743- .02902
27.500	17.25	.0385 - .0709
78.54	18.5	(Edsall and Wyman)[11]

at very low concentrations (below 0.005 mole/liter) of glycine. The values of δ presented in Table I, therefore, represent the extrapolated values at infinite dilution. The δ values for pyridine betaine remained constant with concentration over the concentrations range measured.

Discussion

The decrease in δ with ϵ_0 for glycine and pyridine betaine are both of the general form of the decrease of that for glycine betaine and the benzbetaines in ethanol-water and ethanol-benzene mixtures as observed by Edsall and Wyman.[11] However, before seeking a common mechanism for this decrease in dielectric increment with decreasing dielectric constant of the medium it would be well to examine in the case of pyridine betaine the possibility of reversion to the un-ionized form in low dielectric constant media, thus accounting for the decrease in increment.

The positive charge in pyridine betaine is probably located near the nitrogen in the pyridine ring. Due to resonance the pyridine ring is a very stable structure and its stability is further enhanced by the resonance in the carbon-oxygen bonds of the  $-CH_2-C{\scriptstyle\begin{matrix}\nearrow O\\ \searrow O^-\end{matrix}}$ side group. Therefore it does not seem possible (except at considerably elevated temperatures) that a bond rupture between the nitrogen and a carbon atom could take place with a consequent movement of the positive charge toward the negative charge.

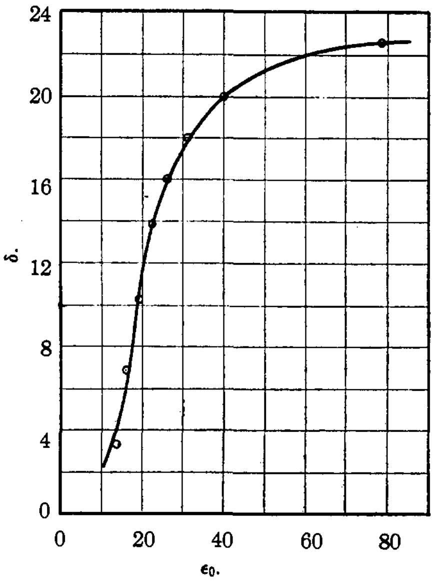


Fig. 1.—Dielectric increment of glycine in water-dioxane mixtures.

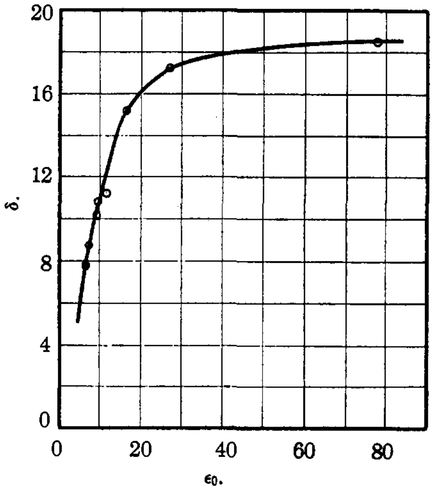
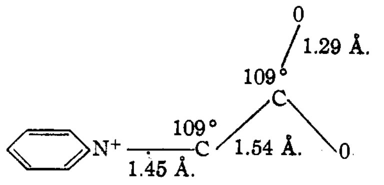


Fig. 2.—Dielectric increment of pyridine betaine in water-dioxane mixtures.

Another possibility is that since the carbon-carbon bond is $-CH_2-COO^-$ has nearly free rotation possibly by rotating the atoms about, some favorable position might be achieved in which the positive and negative charges would be very close to each other. However, from structural considerations this proves not to be the case. Below is a diagram of the pyridine betaine molecule, the atomic distances and angles being those



$d = 1.45 \cos (180-109) + 1.54 + 1.29 \cos (180-109)$

---

[10] J. Wyman, Jr., and T. L. McMeekin, THIS JOURNAL, 55, 915 (1933).

[11] J. T. Edsall and Jeffries Wyman, Jr., *ibid.*, 57, 1964 (1935).

determined from X-ray data. The positive charge is assumed at the nitrogen atom and the negative charge is taken as being on the oxygen atom closest the nitrogen atom. Although X-ray crystal structure studies[12] indicate that the negative charge is probably located halfway between the two oxygens, the diagram here indicates the closest position of the negative charge to the nitrogen atom. The configuration of the —C—COO$^-$ group illustrated in the diagram corresponds to the distance of closest approach of the negative and positive charges while still retaining the normal bond angles and bond lengths. This configuration corresponds to a positive to negative charge distance of 2.48 Å. or a dipole moment of this length times the charge on the electron or 11.9×10^{-18} e. s. u.—still a very large dipole moment to account for small values of δ.

The possibility of bond angle distortion was raised by Edsall and Wyman.[11] However, the bond angle deformation necessary to account for such small dipole moments would be tantamount to breaking the chemical bonds.

Of course, dipole association could account for an apparent decrease in moment of the dipole. However, this would be expected to be dependent on the concentration of the dipoles giving a decrease in δ with increasing concentration. In these experiments no such effects were observed.

An explanation for the "anomalous" lowering of δ with lowering of ϵ_0 lies in the electrostatic behavior of dipoles in mixed solvents, a general theory of which is presented in the following paper.

Summary

1. The dielectric constants of solutions of glycine and of pyridine betaine in mixtures of water and dioxane were determined.

2. The dielectric increments both of glycine and of pyridine betaine showed a regular decrease with decreasing dielectric constant of the solvent mixture. This decrease is similar to that exhibited by glycine betaine and the benzbetaines.

3. The possibility of reversion of pyridine betaine to the un-ionized was examined. Calculations show that the charged groups could approach each other (and thus account for the experimental results) only if the valence bonds were tremendously distorted.

CAMBRIDGE, MASS. RECEIVED NOVEMBER 5, 1943

(12) G. Albrecht and R. B. Corey, THIS JOURNAL, 61, 1087 (1939).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY]

The Dielectric Properties of Dipolar Ions in Mixed Solvents

BY GERALD OSTER[1]

Introduction

The similarity of physical properties of all the amino acids and betaines manifests itself in many ways. Their high melting points[2] as compared with their uncharged isomers, their relative insolubility in many organic solvents, and their dielectric behavior in various solvents,[3a,b] all indicate together with considerable supplementary evidence,[4] the presence of a common property, namely, the existence of these substances in the form of dipolar ions.

In this paper the dielectric properties of these dipolar ions (or zwitterions, as they are sometimes called) in solution will be considered since it is these properties which are so closely similar among the various amino acids and betaines. Glycine and different betaines when in mixed solvents exhibit similar behavior of the dielectric increment, the change in dielectric constant of the solution with concentration of solute, with changing dielectric constant of the solvent mixture. With all the amino acids and betaines studied (ortho, meta and para benzbetaines,[3a] glycine, pyridine betaine)[3b] a regular decrease in the dielectric constant of the solvent mixture (alcohol-water, dioxane–water, or benzene–alcohol mixtures) was observed. A decrease in the dielectric increment corresponds to an effective decrease in dipole moment, the quantitative relation being shown below. A detailed study of the structure of one of these substances[3b] indicates that rearrangement of the charged groups within the molecule to form an uncharged molecule is probably not possible. The argument presented in reference (3b) may be carried over to other betaines and amino acids. In fact, there is further evidence[5] that the benzbetaines and glycine betaine do not exist in the uncharged form in solvent mixtures of low dielectric constant in that the known uncharged isomers (esters of these dipolar ions, prepared by heating the dipolar solid to very high temperatures) have solubility properties vastly different from the dipolar substances.

A theory of the behavior of dipolar ions in mixed solvents will now be presented in which the existence (in any appreciable quantities) of the uncharged dipolar ion need not be assumed. The

(1) Present address: Department of Electrical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts.

(2) E. J. Cohn and J. T. Edsall, "Proteins, Amino Acids and Peptides," Reinhold Publishing Co., New York, N. Y., 1943; especially Chapter 8 by Edsall and Scatchard.

(3) (a) J. Wyman, Jr., *Chem. Rev.*, **19**, 213 (1936); (b) D. Price, L. G. Joyner and G. Oster, THIS JOURNAL, **66**, 946 (1944).

(4) Reference 2, Chapter 2 by J. T. Edsall.

(5) J. T. Edsall and J. Wyman, Jr., THIS JOURNAL, **57**, 1964 (1935).