THE DIELECTRIC CONSTANT OF SOLUTIONS OF DIPOLAR IONS

JEFFRIES WYMAN, JR.

The Biological Laboratories, Harvard University, Cambridge, Massachusetts

I. DIPOLAR IONS

In this paper we shall use the term "dipolar ion,"[1] in place of the German expression *zwitterion,* to refer to a particular type of ion usually arising from the dissociation of amphoteric molecules such as the amino acids. A typical dipolar ion is represented by the isoelectric form of glycine, NH_3^+ CH_2COO^-. Such ions are characterized by the possession of one or more pairs of opposite charges and are electrically neutral. There is now abundant evidence (7), of which that afforded by the study of the dielectric constant of solutions is outstanding, to show that many compounds exist in the form of dipolar ions. Notable among these are amino acids, peptides and proteins, a variety of betaines, and certain phospholipoids.

All the substances so far studied which appear to exist as dipolar ions are wholly insoluble in non-polar liquids;[2] indeed in general their solubility decreases with decreasing polarity (dielectric constant) of the solvent, an effect no doubt due to the very properties which underlie the formation of dipolar ions. On this account measurements of the dielectric constant of solutions of dipolar ions are restricted to solutions in polar solvents. This would at first seem to deprive the results of much of their value, owing to the lack of any exact theory by which to interpret the dielectric constant of polar liquids. Actually, however, when the subject is approached empirically the situation turns out to be unexpectedly simple, and we encounter certain regular and characteristic effects which not only afford one of the most convincing lines of evidence in favor of the existence of dipolar ions but throw much light on their properties and are moreover of interest in regard to the general problem of the dielectric constant of polar liquids.

[1] This term was first proposed by Ingold (33).

[2] Dimethylanthranilic acid, discussed below in section III, is a possible exception to this.

II. METHODS OF MEASUREMENT

Technically the problem of the measurement of the dielectric constant of the solutions is one of considerable difficulty, owing to conductivity. Water and most of the other solvents for dipolar ions are themselves appreciably conducting, and even with the best preparations available the conductivity of the solution is always greater still. Thus aqueous solutions of the purest preparations of amino acids which have been studied have a specific conductivity in the neighborhood of 50 to 100 $\times$ 10^{-6} mhos at a concentration of 1 mole per liter, or of the order of several hundred times that of ordinary distilled water.

Various methods are available for measuring the dielectric constant of slightly conducting liquids, and most of these have been used by the different investigators who have worked on the problem. The early work of Fürth (27) and Blüh (1) was done with Drude's second method at a wave length of about 76 cm., and more recently Frankenthal (25, 26) and Cavallaro (2, 3) have used the same method. Hedestrand (31) employed an alternating current bridge at a wave length of 300 meters, and Errera (23) also used a bridge in his studies on proteins. Devoto, in his very extensive work on dipolar ions and related molecules, has used throughout Drude's first method at a wave length of about 90 cm. Various forms of resonance method have been used by Walden and Werner (48), Errera (23), and Hausser (30). Shutt (43) has applied Fürth's ellipsoid method to the study of proteins.

There are, however, certain difficulties encountered, either singly or together, in the use of any of these methods in the study of solutions of dipolar ions:—the need of calibration of the circuits with accurately known standard liquids of dielectric constant greater than that of water; the problem of stray capacity effects at the high frequencies made necessary by the conductivity; the requirement of undue amounts of solution at all but very high frequencies (as in Drude's first method); the question of adequately satisfying the ideal conditions of the measurement (as in the ellipsoid method).

In order to avoid these troubles and at the same time to obtain absolute values of the dielectric constant, a new form of resonance method (49) was developed, specifically with a view to study of solutions of dipolar ions, which is adapted for use at high frequencies (3 to 20 meters). The resonant circuit, or resonator, is of fixed shape, designed to possess a suitable inductance and capacity for the frequencies employed, and is made of a single rigid piece of metal with no supporting dielectric material. Such a resonator, which may be gold-plated to give a permanent surface, can be completely immersed in the body of the liquid to be measured by

suspension with a very fine thread which occupies a negligible volume.   If this is done, its inductance of course remains unchanged, but its capacity is altered in accordance with the dielectric constant of the liquid.   If we denote this by ϵ and refer to the capacity of the resonator *in vacuo* (or, in practice, air) by C_0, then, since the electrostatic field is wholly included in the liquid, the new capacity is ϵC_0.   Since the resonant frequency of the circuit is given by $1/(2\pi\sqrt{LC})$, L denoting inductance,[3] it follows that if f is the frequency of the resonator in the liquid and f_0 its frequency *in vacuo* (or air) the dielectric constant of the liquid is given by $\epsilon = f_0^2/f^2$.   In order therefore to measure the dielectric constant of a given liquid, it is only necessary to determine the natural frequency of a suitably chosen resonator, first in air and then in the liquid.   Of course air may be replaced by any standard medium of known dielectric constant and the unknown dielectric constant determined in terms of this.   It should be noted that the dielectric constant is always given by the ratio of two frequencies; their absolute values do not matter.

In order to determine its natural frequency, the resonator, immersed in the desired medium, is brought into the field of a variable vacuum-tube oscillator, which is coupled with a piezoelectric oscillator of very constant period so as to give beats with it made audible by an amplifier and a pair of telephones.   The frequency of the oscillator is then altered by a tuning condenser until resonance is obtained.   This is recognized by a sudden change in the plate current of the oscillator, due to an energy exchange between the circuits.   The corresponding frequency is then determined by an interpolation based on various nearby beat combinations in terms of the standard frequency of the piezoelectric oscillator.

This method has been used by the author in all of his measurements given below except those on protein solutions discussed in section V.

III. THE DIELECTRIC INCREMENTS OF DIPOLAR IONS AND RELATED SUBSTANCES

A. Amino acids

We will consider first solutions of the monoamino monocarboxylic aliphatic amino acids in water.   These ampholytes form a very beautiful homologous series, the members of which differ from one another either in the number of carbon atoms in the chain or in the spacing of the carboxyl

---

[3] This assumes that at the frequency employed the effect of conductivity is negligible. Control experiments at wave lengths of about 5 meters with dilute aqueous solutions of potassium chloride indicate that any systematic errors in the determination of the resonant frequency arising from conductivity lie within the fringe of the experimental errors due to the dullness of the resonance.

and amino groups (as, for example, in the case of an α- and a β-form) or in both these respects. If they exist as dipolar ions there is a positive charge on the amino group and a negative charge on the carboxyl group. The positive charge may be supposed to be located at or close to the center of the nitrogen atom, and, on the basis of resonance, the negative charge midway between the two oxygen atoms of the carboxyl group. As a result of x-ray and electron-diffraction studies there is now fairly exact information as to the internuclear distances of adjacent atoms and the valence angles in the molecules. On the basis of this, assuming that there is no distortion, we may readily calculate[4] the distance between the positive and negative charges in an α-amino acid to be 2.92 A.U. This distance corresponds to an electric moment of 13.9 A.U. It is not possible to make a similar simple geometrical calculation for other forms in which there are one or more additional carbon atoms between the charged groups, because of the complicating effects of rotation about the valence bonds. The question remains open, therefore, how this distance varies among other members of the series, although it may reasonably be expected to increase with the length of the chain between the amino and carboxyl groups and indeed statistical considerations, discussed below, indicate that it may be, as an approximation, proportional to the square root of the number of intervening atoms. Apart from the amino and carboxyl groups there are no polar groups in the molecules. An outstanding feature of all these amino acids therefore is the extraordinarily large electric moments which they must be supposed to possess as dipolar ions, and which may be expected to find expression in the dielectric properties of their solutions.

The dielectric constant of aqueous solutions of all the amino acids is greater than that of water. The more consistent and apparently reliable results show that there is a linear increase of dielectric constant with the concentration of the amino acid, and a very careful study (52) reveals that this linearity is maintained with a precision equal to that of the best measurements (0.1–0.2 per cent) up to the highest concentrations obtainable—about 2 moles per liter in the case of α-aminobutyric acid, where the dielectric constant is 127, and 2.5 moles per liter in the case of glycine, where the dielectric constant is 135. This simple behavior greatly facilitates the description and comparison of the results, since in any given case these may be expressed in terms of the dielectric increment per mole of solute or the "molar dielectric increment," a quantity which has in various places been referred to by the symbol δ, but which we denote throughout this paper by $\Delta\epsilon/\Delta c$.

[4] In this calculation the C–C distance is taken as 1.54 A. U., the C–N distance as 1.4 A. U., the C–O distance as 1.29 A. U., the tetrahedral valence angle as 109° 28', and the angle subtended by the two oxygen atoms at the carboxyl carbon atom as 124°. See Stuart (45); also Pauling and Sherman (41).

The values of $\Delta\epsilon/\Delta c$ for all α-amino acids so far studied are not only positive and large, but are all very nearly the same. This may be seen from table 1, in which are summarized results of various workers on a large number of dipolar ions and related substances in water, and to which the reader is referred in connection with all the figures given below. There is a very satisfactory agreement between the results of Devoto at a wave length of 90 cm. ($\Delta\epsilon/\Delta c$ = 25–28), those of Hedestrand obtained with a bridge at 300 meters ($\Delta\epsilon/\Delta c$ = 23.0–23.6) and those of the author at wave lengths between 2.5 and 7 meters ($\Delta\epsilon/\Delta c$ = 22.6–23.2), which shows that there can be no question of anomalous dispersion in this range of frequency. The recent results of Hausser on glycine at 4 meters ($\Delta\epsilon/\Delta c$ = 30) are almost certainly too high.

When we consider acids with a greater number of carbon atoms between the amino and carboxyl groups, it is found, just as for the α-amino acids, that the values of $\Delta\epsilon/\Delta c$ are nearly the same for all forms in which this is the same (see table 1) and there is a regular increase of $\Delta\epsilon/\Delta c$ with the number of such intervening atoms. This increase is represented by the following figures, taken from the results of Devoto and of the author as given in table 1, in which n represents the number of intervening carbon atoms (1 for an α-amino, 2 for a β-amino acid, and so on). Because of the small systematic differences the values from the two sources are listed separately, those of Devoto being marked with a single, those of Wyman and McMeekin with a double asterisk.

n	1	2	3	4	5	6
$\Delta\epsilon/\Delta c$	26*, 23**	35*, 33**	51*, 55**	63*	73*, 78**	87*

A scrutiny of these figures shows that $\Delta\epsilon/\Delta c$ increases linearly with n, and indeed by almost exactly 13 for each additional carbon atom. This may be seen in figure 1, in which the averages are plotted.

These facts are at once intelligible if we suppose the amino acids in aqueous solution to exist predominantly as dipolar ions. In the first place the very large values of $\Delta\epsilon/\Delta c$ accord with the enormous moments predicted for such ions, for although it is true that in polar liquids the relation between polarization and dielectric constant cannot be stated quantitatively, there can hardly be any doubt that the two quantities increase together. In the second place the practical identity of $\Delta\epsilon/\Delta c$ for all the amino acids of a given type (α, β, or γ, etc. . . . .) suggests a corresponding identity of electric moment such as would be expected whenever the distance between the charged groups is the same, since apart from the effects of these groups there is no other considerable source of polarity in the molecules, and in any case moments of the order of those calculated for dipolar ions would be expected to overshadow everything else. Finally, the regu-

TABLE 1

Values of dielectric increment of dipolar ions and related substances in water

SUBSTANCE	DIELECTRIC INCREMENT
Glycine	22.6 (54),* 23.0 (31), 26.4 (8), 30 (30)
α-Alanine	23.2 (54), 23.6 (31), 27.7 (8)
α-Aminobutyric acid	23.2 (54)
α-Aminovaleric acid	22.6 (54)
dl-α-Valine	25 (9)
l-α-Leucine	25 (9)
β-Alanine	34.6 (54), 35 (11), 42.3 (31)
β-Aminobutyric acid	32.4 (54), 36 (16)
γ-Aminobutyric acid	51 (11)
γ-Aminovaleric acid	54.8 (54)
δ-Aminovaleric acid	63 (11)
ε-Aminocaproic acid	77.5 (54), 73 (11)
ζ-Aminoheptylic acid	87 (11)
l-Asparagine	28.4 (8), 20.4 (29)
l-Glutamine	20.8 (29)
d-Glutamic acid	26 (9)
l-Aspartic acid	27.8 (8)
dl-Proline	21 (9)
N-Phenylglycine	ca. 30 (17)
Ornithine	51 (16)
Sarcosine	24.5 (9)
d-Arginine	62 (15)
Taurine	41 (9)
Creatine	32.2 (29)
Glycocyamine	30 (29)
Acetylhistidine	62 (29)
Glycine dipeptide	70.6 (54), 70 (9), 70.5 (2), 80 (30)
Glycine tripeptide	113 (54), 128 (2)
Glycine tetrapeptide	159 (54)
Glycine pentapeptide	215 (54)
Glycine hexapeptide	234 (54)
Glycine heptapeptide†	290 (52)
Glycylalanine	71.8 (29)
Alanylglycine	71 (29)
Leucylglycine	62 (2), 68.4 (29)
Glycylleucine	54 (11), 74.6 (29), 70 (2)
N-Methylleucylglycine	67 (29)
Glycylphenylalanine	70.4 (29)
Phenylalanylglycine	56.7 (29)
d-Leucylglycylglycine	120.4 (29), 54 (11), 112 (2)
ε, ε'-Diguanidodi(α-thio-n-caproic acid)	151 (29)

* The figures in parentheses give the reference numbers.

† In 5.14 molar urea.

TABLE 1—*Continued*

SUBSTANCE	DIELECTRIC INCREMENT
ε,ε'-Diaminodi(α-thio-*n*-caproic acid)	131 (28)
Lysylglutamic acid	345 (28)
Glycine betaine	24–27 (16), 18.2 (22)
α-Aminovalerianic acid betaine	60 (30)
ξ-Aminopentadecylic acid betaine	220 (70°C.) (30)
π-Aminoheptadecylic acid betaine	190 (80°C.) (30)
Pyridine betaine	18.5 (22), 20.5 (30)
o-Benzbetaine	18.7 (22), 20 (17)
m-Benzbetaine	48.4 (22), 58 (17)
p-Benzbetaine	72.4 (22), 68 (17), 62 (30)
Thiobetaine	23 (16)
N-Dimethylanthranilic acid	12 (22), 16.7 (17)
Betaine *o*-aminophenol	5.6 (17)
Betaine *m*-aminophenol	32 (17)
Betaine *p*-aminophenol	45 (17)
Betaine of *p*-amino-*trans*-cinnamic acid	100 (17)
Betaine of *p*-sulfanilic acid	73 (17)
Betaine of *m*-sulfanilic acid	60 (17)
4,4'-Diphenylbetaine	155 (29)
Dimethylphenylglycine	17 (17)
o-Aminobenzoic acid	Low (13)
m-Aminobenzoic acid	41 (13)
p-Aminobenzoic acid	ca. 0 (13)
m-$(CH_3)_3N^+C_6H_4CH{=}CHCOO^-$	71 (18)
p-$(CH_3)_3N^+C_6H_4CH{=}CHCOO^-$ (*trans*)	100 (18)
p-$(CH_3)_3N^+C_6H_4CH{=}CBrCOO^-$ (*trans*)	102 (18)
m-$(CH_3)_3N^+C_6H_4CH{=}C(C_6H_5)COO^-$ (*cis*)	25 (18)
m-$(CH_3)_3N^+C_6H_4CH{=}C(C_6H_5)COO^-$ (*trans*)	90 (18)
Phenol	−6.6 (8)
Benzoic acid	−67 (8)
Aniline	−7.6 (8)
Urea‡	3.4 (8), 3.15 (12), 2.72 (51)
Thiourea	4 (8)
Methylurea	3.7 (9)
Ethylurea	1 (11)
Propylurea	1 (11)
Urethan	−4.3 (9)
Biuret	−6.3 (9)
Semicarbazide	0 (9)
Thiosemicarbazide	ca. 0 (9)
Dimethylurea (*asym.*)	ca. 0 (9)
Dimethylurea (*sym.*)	3 (9)
Malonamide	4.3 (9)
Succinamide	ca. −1 (9)

‡ The relation is not linear. Figures correspond to the limiting value of the increment at zero concentration.

TABLE 1—*Concluded*

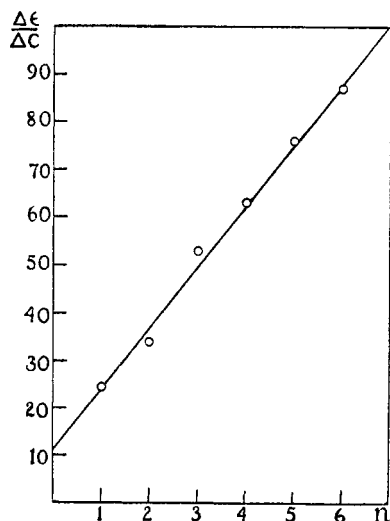| SUBSTANCE	DIELECTRIC INCREMENT
Acetamide	ca. −0.8 (9)
dl-Malamide	2 (16)
Benzamide	−4.1 (8)
Sulfamide	7 (10)
Nitromethane	−2 (16)
Hydantoin	−6.4 (11)
Pyrrolidine	−1.0 (11)
Pyridine	−4.2 (11)
Dimethylpyrone	ca. −3 (16)
2,5–Dioxopiperazine	−10 (9)
Glycine anhydride	−10 (9)
Succinimide	−10 (9)
Acetoacetic ether	−5.9 (16)
Hydroxylamine	−0.8 (16)
β-Indolepropionic acid§	−8 (29)
Acetanilide	−4 (8)
Acetonitrile	−1.74 (8)
m-Dihydroxybenzene	−6 (16)
o-Dihydroxybenzene	ca. −6 (16)
p-Dihydroxybenzene	−6.4 (16)
Methyl acetate	−5 (16)
1,2-*p*-Aminophenylarsenic acid	1.2 (16)

§ In 47.05 per cent ethanol.

FIG. 1. The dielectric increments of amino acids. n = number of carbon atoms between the amino and carboxyl groups.

lar increase of $\Delta\epsilon/\Delta c$ with the distance between the amino and carboxyl groups indicates a corresponding increase of moment. This would be expected on the basis of a dipolar ionic structure, but hardly otherwise; if the amino and carboxyl groups contribute to the moment simply as ordinary polar configurations there is no reason why the net effect should increase so consistently with their separation in the molecule. The exactly linear form of the increase of $\Delta\epsilon/\Delta c$ with n is more than could have been foreseen simply on the basis of the character of dipolar ions, and has implications which will be taken up later.

This interpretation of the behavior of the amino acids in aqueous solution is confirmed in a very satisfactory way by a study of the moments of their esters, which, unlike the acids themselves, are readily soluble in nonpolar liquids. Values of the moments of a number of such esters have been determined by Wyman and McMeekin (55), as given in table 2. Since it

TABLE 2

Electric moments of amino acid esters

SUBSTANCE	MOMENT
	e.s.u. $\times 10^{18}$
Glycine ethyl ester..	2.11
α-Alanine ethyl ester......................................	2.09
α-Aminobutyric acid ethyl ester.................................	2.13
α-Aminovaleric acid ethyl ester.................................	2.13
Valine ethyl ester..	2.11
α-Aminocaproic acid ethyl ester................................	2.13
β-Alanine ethyl ester..	2.14
β-Aminobutyric acid ethyl ester................................	2.11

is well known from a large number of cases that the replacement of a hydrogen atom by a methyl group does not appreciably alter the moment of a molecule,[5] we may accept the moments of these esters as the same as those of the corresponding amino acids in the unionized state, which cannot themselves be directly measured. If we do this it is apparent from the data in table 2 that unionized amino acids are molecules of very moderate electric moment, not at all such as would be expected to show the very large positive dielectric increments observed in aqueous solution. Various substances not capable of forming dipolar ions but with moments greater than these and soluble in water altogether fail to show such increments. Moreover there is no difference between the moments of the α- and β-forms to

[5] Thus, for example, the moments (E.S.U. $\times 10^{18}$) of acetic acid, methyl acetate, ethyl acetate, and ethyl propionate are, respectively, 1.73, 1.75, 1.81, and 1.79 (see Smyth (44), appendices).

correspond to the pronounced difference in the dielectric increments observed in aqueous solution. Devoto (11) has made a comparison of interest in this connection between γ-aminobutyric acid and its anhydride, pyrrolidone. In the anhydride the formation of dipolar ions is of course impossible, and the value of $\Delta\epsilon/\Delta c$ in water is found to be -1 (11). The moment of pyrrolidone in benzene is given as 2.3×10^{-18} E.S.U. (14), actually somewhat greater than that of amino acid esters.

B. Peptides

The peptides of glycine form a homologous series similar to the aliphatic amino acids, although containing an additional source of polarity due to the amide linkages. Like the amino acids, they may be expected to
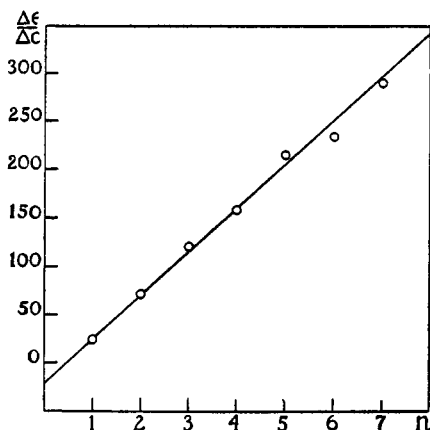
FIG. 2. The dielectric increments of peptides of glycine. n = number of glycine units in the molecule.

exist as dipolar ions, and this is in accordance with the dielectric increments. The first seven peptides of glycine have been studied, the seventh to be sure not in water, where it is very insoluble, but in a 5.14 molar aqueous solution of urea; and the values of $\Delta\epsilon/\Delta c$ are found to increase linearly with the number (n) of glycine units in the peptide, by an amount equal to about 45 for each additional unit, up to a value of 290 for the heptapeptide. This is shown in figure 2. Devoto (9) has found that, in contrast with its isomer glycylglycine, 2,5-dioxypiperazine has a negative molar dielectric increment, -10.

The study of the dielectric constant in the case of these two series not only affords very strong evidence that the compounds exist as dipolar ions, but suggests a simple correlation between the dielectric increment $\Delta\epsilon/\Delta c$ and the magnitude of the electric moment. This would not of course

enable us to calculate absolute values of the electric moments, but it would make it possible to estimate relative values. That the correlation holds from one series to another, and that $\Delta\epsilon/\Delta c$ does indeed reflect quite directly the magnitude of the moments, is borne out by the fact that the dielectric increment of glycylglycine (70.5) is about midway between that of ϵ-aminocaproic acid (73–77.5) and δ-aminovaleric acid (63), whereas the distance along the chain between the charged groups of the peptide is about the same as in a δ-amino acid. We have taken no account of the contribution to the moment due to the amide linkage. This point of view, which emerges from the study of amino acids and peptides, is greatly strengthened by the results of further studies on solutions of other compounds in water and in other solvents.

C. Betaines

The betaines form a class of compounds closely resembling the amino acids, and in view of their similarity of behavior they, too, must be supposed to exist as dipolar ions (22). For any given amino acid there is a corresponding betaine, which differs from it only in that the three hydrogens of the positively charged amino group are replaced by three organic radicals, represented, in all the cases with which we shall be concerned, by three methyl groups. If in these cases also, as would be expected, the positive charge of the dipolar ion is located at or near the center of the nitrogen atom, the moment of a betaine should be very close to that of the corresponding amino acid, and therefore on the basis of our empirical picture we should expect the dielectric increments of the two to be nearly the same. This turns out to be the case. For glycine $\Delta\epsilon/\Delta c = 23$; for its betaine $\Delta\epsilon/\Delta c = 18$; for δ-aminovaleric acid $\Delta\epsilon/\Delta c = 63$; for its betaine $\Delta\epsilon/\Delta c = 60$. Structurally pyridine betaine ($C_5H_5N^+CH_2COO^-$) and thiobetaine (($CH_3)_2{}^+SCH_2COO^-$) should have moments close to that of glycine betaine (though the S–C distance is 1.8 A.U. as compared with the N–C distance of about 1.4 A.U.) (45, p. 81); actually the corresponding values of $\Delta\epsilon/\Delta c$ are 18.5 and 23. The amino acid with the greatest separation of charged groups so far studied is ζ-aminoheptylic acid. Recently results have been published (30) on the betaines of ξ-aminopentadecylic acid and π-aminoheptadecylic acid, in which there are respectively fourteen and sixteen CH_2 groups between the amino and carboxyl groups (30). The values of $\Delta\epsilon/\Delta c$ are given as 220 at 70°C. and 190 at 80°C. for the ξ- and π-forms, respectively. It was necessary to work at these high temperatures because of the insolubility of the compounds, but it is known that values of $\Delta\epsilon/\Delta c$ do not change rapidly with the temperature. Thus for glycine the dielectric increment changes from 22.58 to only 23.80 between 25° and 0°C. (54). We may therefore consider these values in connection

with other results at room temperature. The fact that the dielectric increment is less for the π- than for the ξ-form is probably due to experimental errors or the presence of impurities. In any case both figures given are in approximate agreement with a continuous increase of $\Delta\epsilon/\Delta c$ by 13 for each additional intervening CH_2 group between the charges, as indicated by data over a more restricted range in the case of the amino acid series. Such an increase would imply values for $\Delta\epsilon/\Delta c$ of 192 and 218 for the ξ- and π-betaines, respectively.

Data are also available for the three benzbetaines (o-, m-, and p-$(CH_3)_3N^+C_6H_4COO^-$). The values of $\Delta\epsilon/\Delta c$ for the ortho, meta, and para forms obtained by Edsall and Wyman are 19, 48, and 72; the values given by Devoto are 20, 58, and 68. In accordance with our picture, therefore, these betaines also undoubtedly exist as dipolar ions. In these cases the amino and carboxyl groups are attached to the rigid benzene ring. Assuming the ring to be a plane hexagon, 1.39 A.U. on a side, the distances between the charged groups in the undistorted molecules should be 3.23, 5.49, and 6.36 A.U. On this basis the moment of the ortho compound should be slightly greater than that of an α-amino acid; the value of $\Delta\epsilon/\Delta c$ is actually slightly less. In contrast to o- and p-benzbetaines the o- and p-aminobenzoic acids have values of $\Delta\epsilon/\Delta c$ close to zero, and this accords with other properties. Thus the aminobenzoic acids have relatively low melting points (140–180°C.), they dissolve appreciably in non-polar solvents, and the dissociation constants of the ortho and para forms imply a ratio of dipolar ions to undissociated molecules in the neighborhood of one (20). Unlike the ortho and para forms m-aminobenzoic acid has a dielectric increment of 41, and it is reasonable to assume that in this case the dipolar ions outnumber the unionized molecules. This accords with data on its dissociation constants (20), with the fact that it shows considerable electrostriction (6), and with its heat of reaction with bases (19).

Another molecule closely related to the benzbetaines is N-dimethyl-anthranilic acid ($(CH_3)_2NC_6H_4COOH$). This shows quite unusual properties (22). Unlike amino acids and betaines it has a low melting point (70°C.), and gives rise to but little electrostriction in water (0.6 cc. as compared with 4.6 cc. for o-benzbetaine); moreover, it is very soluble in non-polar solvents. On the other hand its dissociation constants, at least in water and alcohol, indicate that it exists mainly as a dipolar ion, and its dielectric increment is 12, a value less to be sure than that of o-benzbetaine, a corresponding dipolar ion, but still indicative of highly polar properties. It is possible, as suggested by Pauling in conversation, that in the case of this molecule the polarity is due not to the structure of a true dipolar ion, but to the formation of a hydrogen bond between the carboxyl and methylated amino groups. This would account for the large moment

measured in benzene, 6.31×10^{-18} E.S.U. Such a value otherwise remains puzzling, for the acid is almost certainly not a dipolar ion in benzene and the moment of its methyl ester, which would ordinarily be expected to be the same as that of the unionized acid, is only 2.05×10^{-18} E.S.U. (22).

This methyl ester of dimethylanthranilic acid is also of interest in comparison with its isomers, the benzbetaines. Unlike them it is a liquid under ordinary conditions, having a boiling point of 139°C. at 16 mm. of pressure. Also quite unlike them it is insoluble in water but dissolves freely in non-polar liquids as well as in other organic solvents. In solvents of dielectric constant greater than about 10 it shows negative values of the dielectric increment, and in a mixture of 50 per cent water and ethyl alcohol, where it is still appreciably soluble, $\Delta\epsilon/\Delta c = -9.4$ (22). In the same solvent the benzbetaines all have large positive dielectric increments. From this it is clear that in the case of the betaines, owing perhaps to the bulk of a methyl group as compared with a proton, there is no labile equilibrium between dipolar ions and undissociated molecules governed by the properties of the solvent, such as is indicated for the corresponding amino acids by the study of dissociation constants.

D. Other dipolar ions

Results on various additional substances which have been studied in water are also given in table 1. These include a number of other betaines and related compounds, some of which show very large dielectric increments, as well as several other peptides. It is in accordance with our picture that all the peptides of α-amino acids, whether they contain substituted organic radicals or not, show dielectric increments close to those of the corresponding peptides of glycine. Three peptides, each containing two free amino and two free carboxyl groups, have also been investigated,—lysylglutamic acid, ϵ,ϵ'-diaminodi(α-thio-n-caproic acid), and ϵ, ϵ'-diguanidodi(α-thio-n-caproic acid). The exceptionally large value of $\Delta\epsilon/\Delta c = 345$ for lysylglutamic acid accords with an extended configuration with a considerable separation of the centers of gravity of the positive and negative charges. The much smaller values of $\Delta\epsilon/\Delta c$ observed for the two other peptides (131 and 151 respectively) imply smaller dipole moments and suggest a considerable amount of rotation about the S–S linkages. The fact that the increment of the diguanido- is greater than that of the diaminopeptide agrees with the fact that the separation of positive and negative charges in both halves of the symmetrical molecule is greater in the former than in the latter.

It may be pointed out here that although many of the cases we have discussed are those of relatively large molecules, there has been no evidence

of anomalous dispersion at wave lengths longer than 2.5 meters, such as have been used in the author's measurements, and only for glycylleucine and d-leucylglycylglycine do Devoto's results at 90 cm. seem significantly lower than results at longer wave lengths.

The point of view which we have developed enables us to deal empirically with a number of other molecules. Taurine ($NH_3^+CH_2CH_2SO_3^-$) has a dielectric increment of 41, somewhat greater than that of an aliphatic β-amino acid, and must certainly exist in the ionized form as we have written it. Sarcosine ($N(CH_3)H_2^+CH_2COO^-$) behaves like an α-amino acid. The same is true of dl-proline, a cyclic amino acid in which the distance between the nitrogen atom and the carboxyl group should be much the same as in an aliphatic α-amino acid. l-Aspartic and d-glutamic acids both have two carboxyl groups, and in each case the dielectric increment shows that it is the group in the α position with respect to the amino group which is ionized in the dipolar ion. This is in accordance with expectations based on dissociation constants (21). The three diamino acids l-asparagine ($NH_2COCH_2CHNH_2COOH$), l-glutamine ($NH_2CO(CH_2)_2$-$CHNH_2COOH$), and ornithine ($NH_2(CH_2)_3CHNH_2COOH$) have dielectric increments of 20 or 28, 21, and 51, respectively. In the two former compounds therefore it is the α-amino group, in the latter compound the more distant amino group which dissociates. This shows the effect of an amide linkage on the properties of the NH_2 group. The dielectric increments of creatine ($NH:C(NH_2)NCH_3CH_2COOH$) and glycocyamine ($NH:C(NH_2)NHCH_2COOH$), 32 and 30, respectively, are close to those of β-amino acids, although somewhat less, and the compounds must both be supposed to exist predominantly as dipolar ions. In these cases, owing to resonance, the positive charge should probably be regarded as located on the terminal carbon atom bearing the two nitrogens. d-Arginine ($NH:C(NH_2)NH(CH_2)_3CHNH_2COOH$) has a dielectric increment of 62, and here again, owing to resonance, it is probably the terminal carbon atom between the nitrogens which carries the positive charge. In acetylhistidine, also with an increment of 62, one of the nitrogens in the ring must bear a charge.

E. Amides

Carbamide and various substituted ureas which have been studied form an exceptional group of compounds. For the most part their aqueous solutions have dielectric constants greater than that of water, but the relation between dielectric constant and concentration, at least for carbamide itself, is not linear; and the values given for the dielectric increments, however estimated, are all much less than for amino acids, the greatest being 7 in the case of sulfamide, $SO_2(NH_2)_2$. In view of their positive

dielectric increments it has been suggested that they exist as true dipolar ions, for example,

$$\text{NH:C}\overset{\displaystyle \text{NH}_3^+}{\underset{\displaystyle \bar{\text{O}}}{\Big\langle}}$$
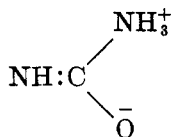
in solution (9). They do not however, so far as data are available, show the electrostriction characteristic of dipolar ions. It is probably more correct to interpret the behavior on the basis of a resonance effect, whereby the carbon atom may be regarded as bearing a negative, and either one of the nitrogens a positive, charge (42). This is in accordance with the rela-

TABLE 3

Electric moments of various amides

SUBSTANCE	MOMENT	REFERENCE
	e.s.u. $\times 10^{18}$	
Dimethylurea, symmetrical.........................	4.8	(32)
	5.1	(14)
Tetraethylurea......................................	3.3	(14)
Propylurea...	4.1	(14)
Acetamide..	3.6	(14)
Sulfamide..	3.9	(14)
Benzamide..	3.6	(14)
Valeramide...	3.7*	
Caproamide...	3.9*	

* From unpublished measurements of Wyman on benzene solutions. Polarizations decrease rapidly with concentration.

tively large moments of a number of these amides in non-polar solvents, given in table 3.

F. Dielectric increments in solvents other than water

A consideration of the dissociation constants of the amino acids and their esters in aqueous solution indicates an overwhelming preponderance of dipolar ions over undissociated molecules. Corresponding considerations in the case of solutions in alcohol–water mixtures indicate a steady diminution in the proportion of dipolar ions with an increase in the percentage of alcohol; nevertheless even in 90 per cent alcohol the ratio of dipolar ions to uncharged molecules should be of the order of 500 or 1000 to one (21). It is in accordance with this that the dielectric increments of amino acids in alcohol–water mixtures are all characteristically large. Beyond this

point of general agreement, however, there emerges the unexpectedly simple result that the numerical value of the dielectric increment of a given amino acid remains almost unchanged with varying composition of the alcohol–water solvent (52).   This fact, without regard to any theoretical implications it may have, is further evidence for our purely empirical conception of the dielectric increment as a very direct, simple, and significant expression of the polar properties of the dissolved molecules.   At the same time it at once raises the question how far this constancy of the values of the dielectric increments persists in other solvents, where the molecules may be expected to exist primarily in the form of dipolar ions and therefore possess the same characteristic moments.

Data in regard to this question are provided by studies (52) on the dielectric increments of two amino acids, glycine and α-aminobutyric acid, dissolved in aqueous solutions of urea and of each other.   Although the

TABLE 4

Solutions of α-aminobutyric acid (25°C.)

SOLVENT	ϵ_0*	$\Delta\epsilon/\Delta c$
80 per cent ethyl alcohol	35.37	24.0
60 per cent ethyl alcohol	47.20	22.1
40 per cent ethyl alcohol	59.41	22.6
20 per cent ethyl alcohol	69.82	23.6
Water	78.54	23.5
2.58 molar urea	87.37	20.9
0.961 molar glycine	99.8	23.1
1.993 molar glycine	124.05	19.0
2.510 molar glycine	134.9	18.4

* The dielectric constant of the solvent.

dissociation constants have not been determined under these conditions, the dielectric constants of the solutions are in all cases high, and it is reasonably certain that the amino acids exist overwhelmingly as dipolar ions. The results on α-aminobutyric acid, together with the results on solutions in alcohol–water mixtures, are given in table 4.   The results on glycine are essentially the same.   It is apparent that the dielectric increment remains remarkably constant in all these solvents.

Similar data are available for the three benzbetaines and glycine betaine, which, as we have pointed out, probably exist wholly in the form of dipolar ions under all conditions.   In figure 3 are shown the results of Edsall and Wyman (22) on solutions in ethanol–water and ethanol–benzene mixtures, and in figure 4 hitherto unpublished results of the author on solutions in

dioxane–water mixtures.[6]   It is apparent that in solvents of dielectric constant greater than 20 or 25 the values of the dielectric increment remain
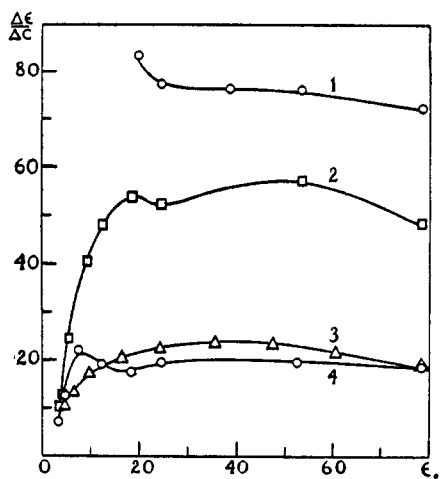
FIG. 3. The dielectric increments of betaines dissolved in ethanol–water and ethanol–benzene mixtures. ϵ_0 = dielectric constant of solvent.   1 = p-benzbetaine; 2 = m-benzbetaine; 3 = o-benzbetaine; 4 = glycine betaine.
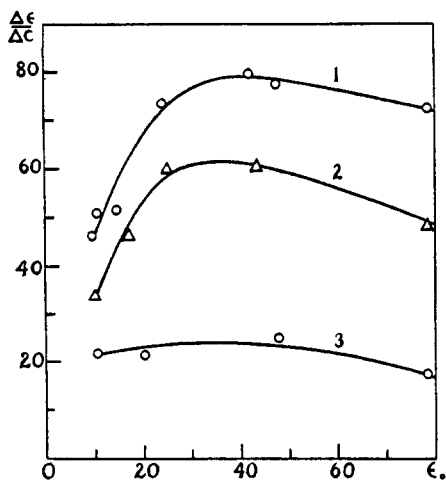
FIG. 4. The dielectric increments of betaines dissolved in dioxane–water mixtures. ϵ_0 = dielectric constant of solvent. 1 = p-benzbetaine; 2 = m-benzbetaine; 3 = o-benzbetaine.

[6] In certain cases, always in solvents of dielectric constant less than 25, the dielectric constant-concentration relation, $d\epsilon/dc$, is not linear, diminishing with the concentration.   In these cases the values of the dielectric increment plotted in the figure are the estimated values corresponding to zero concentration.

fairly constant and there is no considerable difference between the two sets of solvents. This is like the case of the two amino acids studied. In solvents of dielectric constant less than 20 or 25, the dielectric increments decrease markedly with the dielectric constant of the solvent, specific differences between the solvents become larger, and in general the situation is complicated. We shall not attempt to discuss it here.

All that we wish to emphasize at this point is the way in which the facts fit into an essentially simple picture, which emerges from a consideration of all the data on solutions of dipolar ions in solvents of high dielectric constant, and of which the main features are the following: linear variation of dielectric constant with the composition of the solution; characteristically large values of the dielectric increments; close correlation of these with the relative magnitudes of the electric moments; their approximate independence of the nature and dielectric constant of the solvent. From this picture it appears that to a certain unexpected extent, in the case of strongly polar liquid systems, the dielectric constant is an additive property.

III. THE INTERPRETATION OF THE DIELECTRIC CONSTANT OF POLAR LIQUIDS

In the previous section we have made no attempt to account for the character of the results in terms of the theory of the dielectric constant or to estimate numerical values of polarizations or moments. We have simply made use of the general point of view that the magnitude of the dielectric constant is positively correlated with the polarization. In this section we shall deal tentatively with both these matters.

It is clear at the start that the additive character of the dielectric constant, which is such an essential feature of the results, can hardly be accounted for on the basis of Debye's theory, developed primarily to deal with gases and dilute solutions in non-polar solvents. For in any system it is the polarization which is fundamentally the additive property, and in accordance with this theory the relation between dielectric constant and polarization per unit volume (p) is not linear but corresponds to a hyperbola:

$$p = \frac{\epsilon - 1}{\epsilon + 2} \tag{1}$$

In the case of a dipolar ion like α-aminobutyric acid, where the dielectric constant is so exactly linear in the concentration and the molar dielectric increment varies so little between different solvents, we should have to invoke an almost incredible degree of compensating variation in the polarizations to account for the facts in accordance with equation 1, for, owing to the nature of the function, ϵ is exceedingly sensitive to p in all media of high dielectric constant:

$$\frac{p d\epsilon}{\epsilon d p} = \frac{(\epsilon + 1)(\epsilon - 1)}{3\epsilon} \tag{2}$$

For example, if we assume the polarization of the solvent to be independent of the concentration of solute, this would be represented by a very exactly prescribed decrease in the polarization of the dipolar ions, on the one hand with increasing concentration in a given solvent and on the other hand with increasing dielectric constant of the solvent at a given concentration.

It is equally clear that the Debye theory fails to give satisfactory results when used to calculate the moments of the dipolar ions. Thus, taking account of optical polarizations, we arrive at the following moments (E.S.U. $\times 10^{18}$), based on data in water at a concentration of 0.2 mole per liter: glycine, 1.30; α-alanine, 1.51; α-aminobutyric acid, 1.67; α-amino-valeric acid, 1.79; β-alanine, 1.58; β-aminobutyric acid, 1.73. These results are unreasonably small, in all cases actually less than the moments of the esters of amino acids measured in benzene, which are close to 2.12 $\times$ 10^{-18} E.S.U. Moreover, the regularity which is so apparent in the values of the molar dielectric increment is completely lost; and the values for the moments of the larger α-amino acids are actually greater than those of the smaller β-amino forms.

This is only a particular instance of a general difficulty always encountered in the application of the theory to media of high dielectric constant. Owing to the nature of the equation (1), it follows that as the dielectric constant increases, the polarization per unit volume increases more and more slowly and approaches unity as a limit when ϵ tends to infinity.[7] It is for this reason that in highly polar media calculated values of polarizations per mole are limited by the partial molal volumes, which they approach whenever the dielectric constant is large; and this effect masks everything else. Indeed, even in the case of dilute solutions in non-polar solvents there is now evidence, owing to the very careful work of Müller (39), that this same difficulty is appreciable.

Various attempts have been made to deal with this effect in calculating the values of moments from data on solutions. For instance, van Arkel and Snoek (46) have attempted to do so by modifying the expression for the dipole portion of the polarization in terms of the electric moment. The phenomena exhibited by solutions of dipolar ions in polar liquids forcibly suggest quite another and more radical point of view. It appears that the only simple way to account for a body of facts which would otherwise constitute a set of very unlikely coincidences is to assume that in media of high dielectric constant the relation between dielectric constant and polarization is linear:

[7] This corresponds to the Curie point.

$$\epsilon = a + bp \tag{3}$$

where p denotes polarization per unit volume, a and b are constants, and $a < \epsilon$. If we accept this point of view it follows at once that whenever the volume polarization of a solution varies linearly with its composition the dielectric constant must do likewise. At the same time we have a ready explanation of the approximate constancy of the dielectric increment from solvent to solvent, and of its sameness for dipolar ions having moments of about the same size. If we assume the polarizations and partial molal volumes of solute and solvent to be independent of concentration, and if we denote by V the partial molal volume of the solute, by C its concentration in moles per liter, by P its molar polarization, and by ϵ the dielectric constant of the solvent, it follows from equation 3 that

$$\frac{d\epsilon}{dc} = \frac{bP - V(\epsilon_0 - a)}{1000} \tag{4}$$

The data show that the effect of the second term on the right is small for dipolar ions; thus in water the ratio

$$V\epsilon_0 / (1000 \, d\epsilon/dc)$$

is but 0.15 for glycine and 0.07 for the heptapeptide of glycine. From this it follows that the dielectric increment should be approximately proportional to the molar polarization, or, since the optical polarization is a negligible fraction of the total, to the square of the electric moment. This way of accounting for the situation was suggested by the writer, in a somewhat more specific form (52), and it has been adopted by Werner Kuhn (36). Recently it has been discussed further (53).

From a physical point of view the interesting implication of a linear relation between dielectric constant and polarization is in regard to the internal field. In accordance with the classical theory it follows that the ratio of this to the electric intensity increases without limit as the volume polarization approaches unity. On the basis of a linear relation it follows at once from the fundamental equations that the ratio remains finite when p increases indefinitely (53). This would be accounted for by the interaction of the molecules in the interior of the liquid, as Onsager (40) has attempted to do.

From a chemical point of view a linear relation has interesting implications with regard to the configuration of the dipolar ions in solution, although of course it is impossible to estimate numerical values of the moments without a knowledge of the constants. We have seen from the study of aliphatic amino acids and betaines and of peptides that the dielectric increment increases linearly with the length of the chain between the

oppositely charged groups in the molecule. Since it follows from equation 4 that the dielectric increment is approximately proportional to the square of the moment, this implies that in these cases the average value of the square of the distance between the charged groups also increases linearly with this length. This agrees with statistical deductions. Eyring (24) and Werner Kuhn (35) have both derived expressions for $\bar{C}^2$, the mean square distance between the ends of a "straight"-chain structure in which there is free rotation about valence bonds but no distortion of valence angles, and agree that as an approximation this quantity should be proportional to n, the number of atoms in the chain.[8] In these derivations no account is taken of the volume occupied by the chain or of the effects of forces between various parts of the molecule. In the case of dipolar ions the electrostatic attraction between the oppositely charged groups at the ends of the chain would be expected to reduce $\bar{C}^2$ considerably. In a more recent discussion Kuhn (36) has shown that this is so even in water where the dielectric constant is high, although the approximate proportionality of $\bar{C}^2$ and n is not affected. By taking account of this attraction and assuming a value of 1.5 A.U. for the distance of closest approach of the charged groups in amino acids, Kuhn calculates the following mean square values of the distance between the charges in relation to Z, where Z is 2 more than the number of CH_2 groups separating the amino and carboxyl groups:

Z..............	3	4	5	7	9	12	16	25
$\bar{C}^2(\text{A.U.}^2)$	3.88	5.54	7.3	11.6	16.4	24.5	38.2	69

Kuhn also develops an argument to show that any distortion of dipolar ions (e.g., stretching) due to the application of an external field makes no difference to their polarizations, so that the effective moments should be the same as those due to mean square distances as they exist in the absence of an external field.

These considerations lend support to the view that in strongly polar liquids the relation between dielectric constant and volume polarization is linear. Quite recently an attempt has been made to obtain other evidence in regard to this point from a consideration of pure liquids (53). One hundred and forty cases were considered in which there are data on the dielectric constant as well as on the electric moments. As a tentative pro-

---

[8] Eyring's formula is
$$\bar{C}^2 = C_1^2[n + 2(n-1)\cos\theta + 2(n-2)\cos^2\theta + \cdots + 2\cos^{n-1}\theta]$$
where θ is the supplement of the valence angle, C_1 is the distance between the centers of adjacent atoms of the chain, and the length of the chain is nC_1. Kuhn's formula is
$$\bar{C}^2 = nC_1^2\left(\frac{1+\cos\theta}{1-\cos\theta}\right)$$

cedure hypothetical values of the volume polarizations of the liquids were calculated by assuming for the liquid state the same molar polarizations as are found in the vapor or in solutions in non-polar solvents, and by taking account of the number of molecules per cubic centimeter. These hypothetical values of the volume polarization were then compared with the dielectric constant. Except in the case of relatively few liquids such as formic acid, prussic acid, water, formamide, and various alcohols, which are generally supposed to be strongly associated, owing to the formation of hydrogen bonds, and are anomalous in many respects (for example, see Kumler (37)), the results indicate a linear increase of dielectric constant with polarization which is fairly satisfactory in view of the nature of the procedure. A similar treatment of data on individual liquids over a range of temperature and pressure also gives results in accordance with a linear relation between polarization and dielectric constant.

We may try the effect of using these data to estimate rough values of the constants in equation 2. b then turns out to be between 6 and 10 and the best value appears to be close to 8.5; a is small, about equal to -1. Moments ($\times 10^{18}$ E.S.U) of several dipolar ions calculated from equation 4 on the basis of $b = 8.5$ and $a = -1$ are as follows: glycine, 12.2; β-alanine, 15; γ-aminobutyric acid, 18; δ-aminovaleric acid, 20; ϵ-aminocaproic acid, 22; glycine tetrapeptide, 31; glycine hexapeptide, 38. The corresponding moments calculated from the values of $\bar{C}^2$ given by Kuhn are 9.4, 11, 13, 15, 16, 24, and 32, respectively. For the longer chain molecules the agreement is moderate. Kuhn's values for the smaller molecules, such as glycine and β-alanine, are almost certainly too small, since the value of 1.5 A.U. assumed for the distance of closest approach of the amino and carboxyl groups is too small, and since in any case the treatment is not applicable to α-amino acids, where free rotation does not affect the moment, and is probably not well suited to the shorter chain molecules generally. As we have seen, on the basis of atomic dimensions we should predict a moment for glycine of 13.9×10^{-18} E.S.U., and recent calculations based on the application to solubility data of a model developed by Kirkwood (34) give a moment of 15.2×10^{-18} E.S.U.

Onsager (40) has very recently developed a treatment of the dielectric constant of liquids which would appear to account for all this in a most satisfactory way, indeed even to the numerical factors. According to his theory the value of b is determined by the "internal refractive index" of the molecules. If this is taken as 1.46, b turns out to be 8.5, the value obtained empirically from the data on the liquids. a is negligible in comparison with ϵ.

IV. ANOMALOUS DISPERSION OF DIPOLAR IONS

Among the ampholytes existing as dipolar ions the proteins may be expected to show exceptional dielectric properties, owing to their enormous size and the great number of dissociating groups possessed by even the most inert of them. The recent work of Svedberg and others shows that the molecular weights range from a value of 1700 to 3000 for clupein (38), the smallest protein molecule so far studied, up to values of several million in the case of certain hemocyanins. For molecules of this size we may expect large relaxation times and anomalous dispersion at radio frequencies.

The number of free dissociable groups in a protein is determined by the number of diacidic and dibasic amino acids which it contains, and if there is no ring formation it is two more than this number. The moment of the protein molecule as a dipolar ion is determined by the number of pairs of positive and negative charges which it carries as a result of the ionization of such groups and by their relative positions in the molecule. In all proteins this number appears to be considerable. For example, even in such an inert protein as zein it is about 6[9] and in egg albumin it is 27 (5, 47). Although little or nothing is known as to the spacial arrangement of these groups in the molecules, it is evident that in general the proteins may be expected to have unprecedentedly large resultant moments even among dipolar ions.

Fürth (27) early studied aqueous solutions of two proteins, "Kahlbaum's albumin" and gelatin, by means of Drude's second method at a wave length of 90 cm., and found that the dielectric constant of the solutions was less than that of water. The negative dielectric increments obtained by Fürth are in no way inconsistent with the character of the proteins as dipolar ions of large moment, for, as we have seen, it would be expected that at 90 cm. he was working within or below the region of anomalous dispersion. That this is the case has since been clearly shown by measurements of the author (50) on solutions of the plant protein zein in 70 per cent n-propyl alcohol over a range of temperatures and wave lengths, and by more recent work of Errera (23), Calvallaro (3), and Shutt (43). The results of all these investigators show that at longer wave lengths the proteins have large positive dielectric increments. Thus in the case of egg albumin dissolved in water Shutt's results (at 200 cycles per second) indicate a value of the dielectric increment of approximately 4000, and Errera's results (at wave lengths up to 20,000 meters) a value of about 10,000. In spite of the quantitative discrepancy it is evident from this that egg albumin must have an enormous moment: values calculated from these figures by means of equa-

[9] See Cohn, Berggren, and Hendry (4). The value 16, given in their paper, is based on a molecular weight now known to be about three times too large.

tion 4 are of the order of 200×10^{-18} E.S.U. Other proteins appear to have similarly large dielectric increments.

It is of interest to consider these results quantitatively in terms of Debye's theory of anomalous dispersion. In accordance with this the measured value of the dielectric constant drops from an upper static value ϵ_0 to a lower limiting value ϵ_∞ as the frequency of the measurement is increased to such a point that the dipoles can no longer follow the alternating field, in accordance with the following equation,

$$\epsilon = \epsilon_\infty + \frac{\epsilon_0 - \epsilon_\infty}{1 + x^2 \nu^2} \tag{5}$$

where

$$x = 2\pi\tau \frac{(\epsilon_0 + 2)}{(\epsilon_\infty + 2)}$$

and τ denotes the relaxation time and ν the frequency. The frequency ν_c at which the dielectric constant is midway between the upper and lower values, i.e., $\epsilon = (\epsilon_0 + \epsilon_\infty)/2$, is given by

$$\nu_c = \frac{1}{2\pi\tau} \frac{(\epsilon_\infty + 2)}{(\epsilon_0 + 2)}$$

If we are dealing with a solution there should be a region of anomalous dispersion for each component determined in accordance with equation 5 by the relaxation time of each. If instead of the classical relation between dielectric constant and polarization we assume any linear relation such as that apparently prevailing in highly polar media, it is easy to show that the expression for x is replaced by $x = 1/2\pi\tau$ and $\nu_c = 1/2\pi\tau$. The form of the dispersion curve is therefore the same whether one assumes the classical or the linear relation, and if ϵ_0 and ϵ_∞ are both large, as in the case of a protein in aqueous solution, the numerical value of ν_c is approximately the same on the basis of either interpretation of the dielectric constant.

The results on zein may be fitted satisfactorily by equation 5. This is shown in figure 5, in which is plotted the dielectric constant of a 4.2 per cent solution against the logarithm of the frequency at two temperatures. The smooth curves are calculated from equation 5 with the following choice of constants: at 69.5°C., $\epsilon_0 = 40.5$, $\epsilon_\infty = 27.0$, $x = 2.58 \times 10^{-7}$; at 50°C. $\epsilon_0 = 41.0$, $\epsilon_\infty = 29.8$, $x = 3.91 \times 10^{-7}$. On the basis of the classical theory these values of x correspond to relaxation times of 2.8×10^{-8} sec. and 4.6×10^{-8} sec. at 69.5° and 50°C., respectively; on the basis of a linear relation the corresponding values are 4.1×10^{-8} sec. and 6.2×10^{-8} sec. The measured viscosities at the two temperatures, to which of course the relaxa-
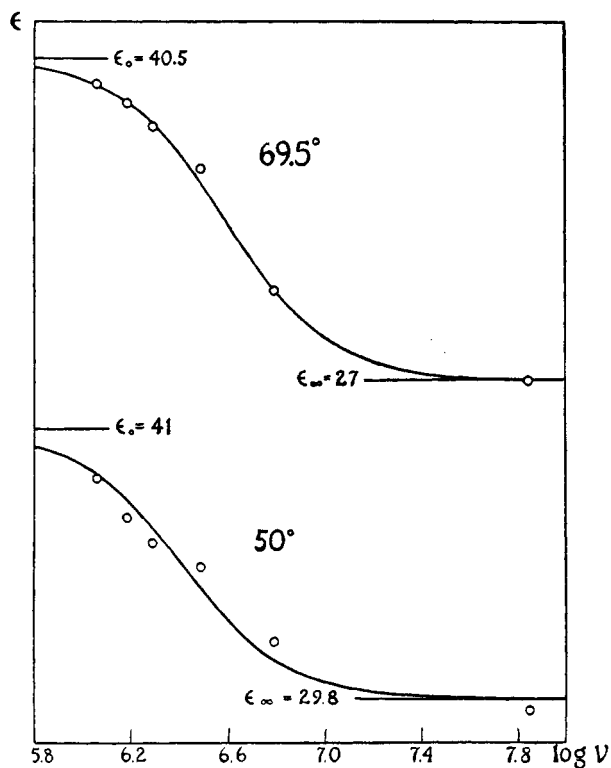
FIG. 5. The dielectric constant of a 4.2 per cent solution of zein in 70 per cent n-propyl alcohol as a function of frequency, ν. The smooth curves are calculated from equation 5.
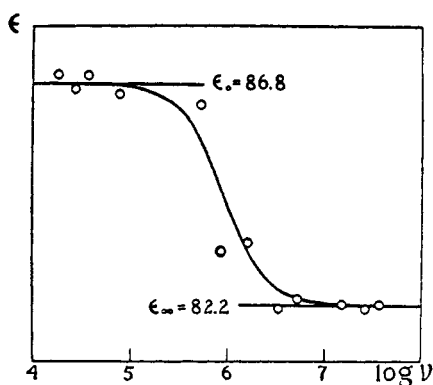

FIG. 6. The dielectric constant of a 0.4 per cent aqueous solution of hemoglobin as a function of temperature. The smooth curve is calculated from equation 5.

tion times should be proportional, are 0.017 and 0.034, respectively. If we assume the zein to have a molecular weight of 34,500 and to consist of spherical molecules, the relaxation times at the two temperatures calculated from Stokes' formula are 4.4×10^{-8} sec. and 9.2×10^{-8} sec., respectively, quite close to the experimental results. The values of the dielectric increments reckoned from the values of ϵ_0 and ϵ_∞ are approximately 12,000 at 69.5°C. and 10,000 at 50°C.

For comparison there are shown graphically in figure 6 Errera's results on a 0.4 per cent solution of hemoglobin in water at 13°C. The smooth curve corresponds to equation 5 with $\epsilon_0 = 86.8$, $\epsilon_\infty = 82.2$, and $x = 1.12 \times 10^{-6}$. The relaxation time corresponding to this value of x is close to 2×10^{-7} sec. on either interpretation of the dielectric constant. That calculated from Stokes' formula, taking account of the viscosity of the solution (= 0.0118 poise), on the basis of a molecular weight of 68,000 is 7.1×10^{-8}. Other results of Errera are fitted less closely by the theoretical curve, the region of dispersion extending in general over a longer range of frequency than is required by the simple theory, and the dielectric constant often showing an unexplained drop at the lowest frequencies.

REFERENCES

(1) Blüh: Z. physik. Chem. **106**, 341 (1923).
(2) Cavallaro: Arch. sci. biol. **20**, 567 (1934).
(3) Cavallaro: Arch. sci. biol. **20**, 583 (1934).
(4) Cohn, Berggren, and Hendry: J. Gen. Physiol. **7**, 81 (1924).
(5) Cohn: Physiol. Rev. **5**, 349 (1925).
(6) Cohn: J. Am. Chem. Soc. **56**, 784 (1934).
(7) Cohn: Annual Review of Biochemistry, Vol. IV, p. 93. Stanford University, California (1935).
(8) Devoto: Gazz. chim. ital. **60**, 520 (1930).
(9) Devoto: Gazz. chim. ital. **61**, 897 (1931).
(10) Devoto: Atti accad. Lincei **14**, 432 (1931).
(11) Devoto: Gazz. chim. ital. **63**, 50 (1933).
(12) Devoto: Gazz. chim. ital. **63**, 119 (1933).
(13) Devoto: Gazz. chim. ital. **63**, 247 (1933).
(14) Devoto: Gazz. chim. ital. **63**, 491 (1933).
(15) Devoto: Z. physiol. Chem. **222**, 227 (1933).
(16) Devoto: Gazz. chim. ital. **64**, 76 (1934).
(17) Devoto: Gazz. chim. ital. **64**, 371 (1934).
(18) Devoto: Z. Elektrochem. **40**, 641 (1934).
(19) Devoto: Atti accad. Lincei **19**, 50 (1934).
(20) Ebert: Z. physik. Chem. **121**, 385 (1926).
(21) Edsall and Blanchard: J. Am. Chem. Soc. **55**, 2337 (1933).
(22) Edsall and Wyman: J. Am. Chem. Soc. **57**, 1964 (1935).
(23) Errera: J. chim. phys. **29**, 577 (1932).
(24) Eyring: Phys. Rev. [2] **39**, 746 (1932).
(25) Frankenthal: Z. physik. Chem. **19**, 328 (1932).

(26) FRANKENTHAL: Z. physik. Chem. **21**, 310 (1933).

(27) FÜRTH: Ann. Physik **70**, 63 (1923).

(28) GREENSTEIN, WYMAN, AND COHN: J. Am. Chem. Soc. **57**, 637 (1935).

(29) GREENSTEIN AND WYMAN: J. Am. Chem. Soc. **58**, 463 (1936).

(30) HAUSSER: Sitzber. Heidelberg. Akad. Wiss. **6** (1935).

(31) HEDESTRAND: Z. physik. Chem. **135**, 36 (1928).

(32) HUNTER AND PARTINGTON: J. Chem. Soc. **1933**, 87.

(33) INGOLD: Chem. Rev. **15**, 225 (1934).

(34) KIRKWOOD: J. Chem. Physics **2**, 351 (1934).

(35) KUHN, W.: Kolloid-Z. **68**, 2 (1934).

(36) KUHN, W.: Z. physik. Chem. **175A**, 1 (1935).

(37) KUMLER: J. Am. Chem. Soc. **57**, 600 (1935).

(38) LINDERSTRÖM-LANG: Compt. rend. trav. lab. Carlsberg **20**, No. 10 (1935).

(39) MÜLLER, F. H.: Trans. Faraday Soc. **30**, 728 (1934).

(40) ONSAGER: J. Am. Chem. Soc. **58**, 1486 (1936).

(41) PAULING AND SHERMAN: Proc. Natl. Acad. Sci. **20**, 340 (1934).

(42) PAULING: J. Am. Chem. Soc. **57**, 2705 (1935).

(43) SHUTT: Trans. Faraday Soc. **30**, 893 (1934).

(44) SMYTH: Dielectric Constant and Molecular Structure. The Chemical Catalog Co., Inc., New York (1931).

(45) STUART, H. A.: Molekülstruktur. Julius Springer, Berlin (1934).

(46) VAN ARKEL AND SNOEK: Trans. Faraday Soc. **30**, 707 (1934).

(47) VICKERY AND SHORE: Biochem. J. **26**, 1101 (1932).

(48) WALDEN AND WERNER: Z. physik. Chem. **129**, 389 (1927).

(49) WYMAN: Phys. Rev. **35**, 623 (1930).

(50) WYMAN: J. Biol. Chem. **90**, 443 (1931).

(51) WYMAN: J. Am. Chem. Soc. **55**, 4116 (1933).

(52) WYMAN: J. Am. Chem. Soc. **56**, 536 (1934).

(53) WYMAN: J. Am. Chem. Soc. **58**, 1482 (1936).

(54) WYMAN AND McMEEKIN: J. Am. Chem. Soc. **55**, 908 (1933).

(55) WYMAN AND McMEEKIN: J. Am. Chem. Soc. **55**, 915 (1933).