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Theory of Solutions of Molecules Containing Widely Separated Charges with Special Application to Zwitterions*

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The electrical contribution to the chemical potential of an ion having an arbitrary charge distribution is calculated with the aid of the Debye-Hückel theory. The calculation is based upon a general solution in polar coordinates of the approximate Debye-Hückel equation, $\Delta\psi - \kappa^2\psi = 0$. In addition, the Born relation between the free energy of solvation of a spherical ion and the dielectric constant of the solvent, is generalized to include ions of arbitrary charge distribution. Application of the theory to a study of the influence of simple electrolytes, and of the dielectric constant of the solvent on the solubilities of the aliphatic amino-acids in alcohol water mixtures, is discussed.

I.

THE aliphatic amino-acids, as well as a number of related compounds, exhibit many of the properties of strong electrolytes when dissolved in solvents of high dielectric constant such as water or alcohol. But unlike electrolytes, they do not appreciably increase the electrical conductivity of the solution. Evidently then, these substances do not produce real ions in solution. To account for this peculiar behavior, Adams[1] and Bjerrum[2] suggested that both the acidic and basic groups of an amino-acid molecule are completely ionized in certain solvents, giving rise to a hybrid ion with no resultant charge. Although it cannot contribute to the conductivity of the solution, the hybrid ion is surrounded by a strong electrostatic field, because of the wide separation of its charged groups. Therefore, large deviations from the ideal solution laws arising from electrostatic interaction between the hybrid ions, the solvent, and real ions present in the

solution, might be expected. Hybrid ions of this type have been called Zwitterions.

In recent years much evidence in favor of the Zwitterionic hypothesis has accumulated.[3] Perhaps the most convincing argument in its favor is furnished by measurements of the dielectric constants of amino-acid solutions.[4] The high dielectric constants of these solutions can be explained if one attributes an enormous electric moment of the order of 20×10^{-18} e.s.u. to an α-amino acid molecule and still larger moments to those of the β and γ-acids. Dipole moments of this magnitude could scarcely be produced except by amphoteric ionization leading to the formation of Zwitterions.

In an earlier article, the influence of salts upon the activity of Zwitterions in solution was investigated from the standpoint of the Debye-

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[1] E. Q. Adams, J. Am. Chem. Soc. **38**, 1503 (1916).

[2] N. Bjerrum, Zeits. f. physik. Chemie **104**, 147 (1923).

[3] E. J. Cohn, Ergebnisse der Physiologie **33**, 781 (1931); Naturwiss. **20** (36), 44 (1932).

[4] Hedestrand, Zeits. f. physik. Chemie **135**, 36 (1928); Wyman and McMeekin, J. Am. Chem. Soc. **55**, 915 (1933); **53**, 3292 (1931); Devoto, Gazz. Chim. Ital. **60**, 520 (1930); **61**, 897 (1932).

Hückel theory.[5] Although the theory predicts a large electrical contribution to the chemical potential of a Zwitterion, the logarithm of its activity coefficient is found to contain no term proportional to the square root of the ionic strength of the salt. It was therefore concluded that a Zwitterion behaves more like a highly polar non-electrolyte molecule than like a real ion in salt solutions of low ionic strength. The Zwitterion was represented by a highly simplified model consisting of two oppositely charged spheres with a rigid connection between their centers. This model was chosen because of its close resemblance to two independent ions. It has, however, certain disadvantages from a mathematical point of view. The electrostatic potential in the neighborhood of the Zwitterion is most conveniently expressed in terms of polar coordinates, and the boundary conditions lead to an infinite set of linear equations which are very difficult to solve unless the boundary of the ion has spherical symmetry.

In the present article the influence of salts and of the dielectric constant of the solvent upon the activity of a spherical ion, having a complex charge distribution, is investigated. When the net charge of the complex ion is zero, and its dipole moment is large, it corresponds to a Zwitterion. The discussion is limited to solutions in which the concentration of the complex ions, in particular Zwitterions, is so low that their mutual electrostatic interaction can be neglected. It should be possible to treat the mutual interaction of Zwitterions at least approximately by means of Keesom's theory of dipole gases.[6] This, however, will not be undertaken here.

II.

We consider a solution of complex ions at low concentration in a solvent of dielectric constant D. For the present purposes the ion is schematically represented by sphere of radius b, having a dielectric constant D_i, within which are situated M discrete point charges $e_1 \cdots e_M$. A polar coordinate system with origin at the center of the

sphere b may be conveniently employed to describe the configuration of the charges $e_1 \cdots e_M$. The position of each charge e_k is then given by three coordinates r_k, ϑ_k, and φ_k. The orientation of the coordinate system is quite arbitrary, and does not enter into the final result. The electrostatic potential at any point (r, ϑ, φ) inside the sphere b satisfies Laplace's equation and is given by

$$V_1 = \sum_{k=1}^{M} \frac{e_k}{D_i |r - r_k|} + \psi$$

$$\psi = \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} B_{nm} r^n P_n^m(\cos \vartheta) e^{im\varphi}, \qquad (1)$$

where $|r - r_k|$ is the distance of the charge e_k from the point (r, ϑ, φ), and ψ is the contribution to the potential arising from charge distributions in the solution outside of the sphere b. The $P_n^m(\cos \vartheta)$ are the associated Legendre functions and i is the imaginary unit, $(-1)^{\frac{1}{2}}$. The constants B_{nm} are to be determined by the proper boundary conditions. If there is no space charge in the surrounding solution, and the dielectric constant of the ion D_i is identical with that of the solvent D, then ψ vanishes. This, however, is not in general true.

We now suppose that in addition to the complex ions, the solution contains a simple electrolyte which produces ions of the valence types $Z_1 \cdots Z_i$, present at the molal concentrations $C_1 \cdots C_i$. These ions are supposed not only to be spherical in shape, but also to possess spherically symmetrical charge distributions. In other words their multipole electric moments, dipole, quadrupole, etc., are all assumed to be zero. If the mean distance of closest approach of these ions to the complex ion is a, there will exist a second spherical boundary of radius a, concentric with the sphere b, within which no ions penetrate. In the spherical shell, bounded by the spheres a and b, the potential V_2 must therefore satisfy Laplace's equation. When expanded in spherical harmonics it must have the form

$$V_2 = \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \{C_{nm}/r^{n+1} + G_{nm} r^n\} P_n^m(\cos \vartheta) e^{im\varphi}, \qquad (2)$$

[5] G. Scatchard and J. G. Kirkwood, Phys. Zeits. **33**, 297 (1932).

[6] W. H. Keesom, Phys. Zeits. **22**, 129, 643 (1921).

where r, ϑ, φ are the coordinates of a point in this region. We also remember that the dielectric constant in this region is D, that of the solvent.

In the solution outside of the sphere a, interaction of the complex ion with the simple electrolyte ions produces a mean space charge. The potential V_3 in this region satisfies Poisson's equation. If we assume that the mean space charge in the neighborhood of the complex ion is given by the Boltzmann distribution formula in the form employed by Debye, and further if nonlinear terms in V_3 appearing in the expansion of the Boltzmann factor are dropped, we may employ the approximate equation of the Debye-Hückel theory to determine this potential.

$$\Delta V_3 - \kappa^2 V_3 = 0, \qquad \kappa^2 = (4\pi N\epsilon^2/1000DkT)\sum_i Z_i^2 C_i, \tag{3}$$

where Δ is the Laplacian operator,* and κ^2 is a function of the ionic strength, $\sum_i Z_i^2 C_i/2$ of the electrolyte, as well as of Avogadro's number N, the electronic charge ϵ, Boltzmann's constant k, the absolute temperature T, and the dielectric constant of the solution D. If we ignore the influence of the electrolyte on the dielectric constant, D is equal to the dielectric constant of the solvent. After separation of variables, a general solution of Eq. (3) in polar coordinates can be effected.[5] All solutions which vanish at infinity, a necessary boundary condition, may be expressed in the form

$$V_3 = \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} (A_{nm}/r^{n+1})e^{-\kappa r}K_n(\kappa r)P_n^m(\cos \vartheta)e^{im\varphi}, \qquad K_n(x) = \sum_{s=0}^{n} \frac{2^s n!(2n-s)!}{s!(2n)!(n-s)!}x^s, \tag{4}$$

where r, ϑ, φ are the coordinates of any point in the solution outside the sphere a, referred to the polar system with origin at the center of this sphere.† The polynomials $K_n(x)$ and their first derivatives $K_n'(x)$ satisfy the following recurrence relations which will later be of use.

$$(2n+1+x)K_n(x) - xK_n'(x) = (2n+1)K_{n+1}(x),$$
$$K_{n+1}(x) - K_n(x) = x^2K_{n-1}(x)/(2n+1)(2n-1); \qquad n > 0. \tag{5}$$

In the three potentials V_1, V_2 and V_3 there are four constants A_{nm}, C_{nm}, G_{nm}, and B_{nm} to be determined for every set of indices n and m. These constants are fixed by the following boundary conditions. On the surface of the sphere a, V_3 and V_2 as well as their gradients shall be equal:

$$\begin{aligned} V_3 &= V_2 \\ &\qquad\qquad r = a. \\ \nabla V_3 &= \nabla V_2 \end{aligned} \tag{6}$$

On the surface of the sphere b, V_2 and V_1, the tangential components of their gradients, and the normal components of the dielectric displacement (dielectric constant multiplied by the field strength) shall be equal.[7]

$$V_2 = V_1; \qquad \frac{1}{r}\frac{\partial V_2}{\partial \vartheta} = \frac{1}{r}\frac{\partial V_1}{\partial \vartheta}$$

$$\frac{1}{r\sin\vartheta}\frac{\partial V_2}{\partial \varphi} = \frac{1}{r\sin\vartheta}\frac{\partial V_1}{\partial \varphi}; \qquad r = b \tag{7}$$

$$D\frac{\partial V_2}{\partial r} = D_i\frac{\partial V_1}{\partial r}.$$

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* For example in polar coordinates

$$\Delta = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial}{\partial r}\right) + \frac{1}{r^2\sin\vartheta}\frac{\partial}{\partial\vartheta}\left(\sin\vartheta\frac{\partial}{\partial\vartheta}\right) + \frac{1}{r^2\sin^2\vartheta}\frac{\partial^2}{\partial\varphi^2}.$$

† The radial factors of the solutions of Eq. (3) are related to the Bessel functions $r^{-\frac{1}{2}}I_{n+\frac{1}{2}}(\kappa r)$ or $r^{-\frac{1}{2}}J_{n+\frac{1}{2}}(i\kappa r)$. However, these functions as customarily defined do not satisfy the boundary conditions of the present problem.

[7] See for example Abraham-Becker, *Theorie der Elektrizität*, I, §32, p. 72.

Since some of them are equivalent, relations (6) and (7) furnish just four independent conditions. Before applying them we note that the first part of the potential V_1 may be expanded in spherical harmonics in the following form in the neighborhood of the surface of the sphere b, provided all of the r_k are less than b.

$$\sum_{k=1}^{M} \frac{e_k}{D_i|r-r_k|} = \sum_{n=0}^{\infty} \sum_{m=-n}^{+n} \frac{E_{nm}}{D_i r^{n+1}} P_n^m(\cos \vartheta)e^{im\varphi}, \tag{8}$$

where

$$E_{nm} = [(n-|m|)!/(n+|m|)!] \sum_{k=1}^{M} e_k r_k^n P_n^m(\cos \vartheta_k)e^{-im\varphi_k}. \tag{9}$$

We now apply the boundary conditions, which are at once seen to be satisfied independently by every harmonic component of the potentials. For every set of indices m and n, four equations are obtained:

$$A_{nm}e^{-\kappa a}K_n(\kappa a) = C_{nm}+a^{2n+1}G_{nm},$$

$$A_{nm}e^{-\kappa a}[(n+1+\kappa a)K_n(\kappa a) - \kappa a K_n'(\kappa a)] = (n+1)C_{nm}-na^{2n+1}G_{nm},$$

$$E_{nm}/D_i+b^{2n+1}B_{nm} = C_{nm}+b^{2n+1}G_{nm}, \tag{10}$$

$$(n+1)E_{nm}-nD_i b^{2n+1}B_{nm} = (n+1)DC_{nm}-nDb^{2n+1}G_{nm}.$$

Solution of these equations and use of the recurrence formulas (5) lead to the following expression for the constants B_{nm}, which are the only ones we require

$$B_{nm} = \frac{E_{nm}}{D_i b^{2n+1}} \frac{(n+1)(D_i-D)}{(n+1)D+nD_i}$$

$$-\frac{E_{nm}}{Da^{2n+1}} \frac{2n+1}{2n-1}\left[\frac{D}{(n+1)D+nD_i}\right]^2 \frac{\kappa^2 a^2 K_{n-1}(\kappa a)}{K_{n+1}(\kappa a)+\frac{n(D-D_i)}{(n+1)D+nD_i}\left(\frac{b}{a}\right)^{2n+1}\frac{\kappa^2 a^2 K_{n-1}(\kappa a)}{(2n-1)(2n+1)}} \tag{11}$$

except for $n=0$, where

$$B_{00} = \frac{E_{00}}{b}\left(\frac{1}{D}-\frac{1}{D_i}\right) - \frac{E_{00}}{Da}\frac{\kappa a}{1+\kappa a}.$$

It is to be noted that only B_{00} contains a term proportional to κ, the square root of the ionic strength. In every other B_{nm} the lowest power of κ is the second.

The mutual electrostatic energy of the complex ion and the medium in which it is immersed arises from the ionic space charge in the solution outside the sphere a, and from a surface charge of polarization on the sphere b depending upon the difference between D_i and D. This energy is determined by the potential ψ, the second term of Eq. (1). It can therefore be expressed as a function of the B_{nm} of Eq. (11), upon which ψ depends. It is easily verified that the B_{nm} are linear functions of the charges $e_1\cdots e_M$, constituting the ion, so that ψ also is a linear function of these charges. By a hypothetical charging process of the Guntelberg-Müller type, one finds that the mutual electrostatic energy of the ion and the medium, equal to a work of charging, is given by one-half the sum of the products of each e_l by the value of ψ at the point $(r_l, \vartheta_l, \varphi_l)$.*

$$W = \tfrac{1}{2}\sum_{l=1}^{M} e_l \psi(r_l, \vartheta_l, \varphi_l). \tag{12}$$

Introducing ψ from Eq. (1) and using the values of B_{nm} given by Eq. (10), we obtain

* Self-energy terms for the charge distribution $e_1\cdots e_M$ are omitted. They arise from the first term of V_1 and are independent of the medium. Further, because of the crudity of the molecular model, they have no physical significance.

$$W = W_0 + W(\kappa),$$

$$W_0 = \tfrac{1}{2} \sum_{n=0}^{\infty} \frac{(n+1)Q_n(D_i - D)}{D_i b^{2n+1}[(n+1)D + nD_i]},$$

$$W(\kappa) = -(Q_0/2D)\kappa/(1+\kappa a)$$

$$-\tfrac{1}{2} \sum_{n=1}^{\infty} \frac{Q_n}{Da^{2n-1}} \frac{2n+1}{2n-1}\left[\frac{D}{(n+1)D+nD_i}\right]^2 \frac{\kappa^2 K_{n-1}(\kappa a)}{K_{n+1}(\kappa a) + \dfrac{n(D-D_i)}{(n+1)D+nD_i}\left(\dfrac{b}{a}\right)^{2n+1} \dfrac{\kappa^2 a^2 K_{n-1}(\kappa a)}{(2n-1)(2n+1)}},$$

$$Q_n = \sum_{k=1}^{M}\sum_{l=1}^{M} e_k e_l r_k{}^n r_l{}^n \sum_{m=-n}^{+n} \frac{(n-|m|)!}{(n+|m|)!}P_n{}^m(\cos \vartheta_k)P_n{}^m(\cos \vartheta_l)e^{im(\varphi_k-\varphi_l)}.$$

(13)

By the addition theorem of spherical harmonics, the Q_n may be written more simply as

$$Q_n = \sum_{k=1}^{M}\sum_{l=1}^{M} e_k e_l r_k{}^n r_l{}^n P_n(\cos \vartheta_{kl}), \qquad (14)$$

where the $P_n(\cos \vartheta)$ are the ordinary Legendre functions and ϑ_{kl} is the angle between r_k and r_l, the lines drawn from the center of the sphere b to the charges e_k and e_l. Thus the final expression is independent of the orientation of the coordinate system (r, ϑ, φ). The early members of the function system $P_n(x)$ have the form

$$\begin{aligned} P_0(x) &= 1, \\ P_1(x) &= x, \\ P_2(x) &= (3x^2-1)/2, \\ P_3(x) &= (5x^3-3x)/2. \end{aligned} \qquad (15)$$

Thus we find that Q_0 is simply $(\sum_k e_k)^2$ or $Z^2\epsilon^2$ where Z is the valence of the complex ion. The terms in Eq. (13), corresponding to $n=0$, are seen to be identical with those of the ordinary Debye-Hückel theory, applied to an ion having a spherically symmetric charge distribution. If the net charge of the complex ion is zero, in which case it would correspond to a hybrid ion, the term for $n=0$ vanishes and the first term of importance is the one involving Q_1. Q_1 is readily seen to be equal to the square of the dipole moment of the ion. The succeeding Q_n's involve the higher order multipole moments.

It should be remarked here that the foregoing analysis is in no way restricted to ions consisting of discrete point charges e_k. A slight modification of the argument permits one to treat a complex ion whose charge distribution is a continuous function of position, $\rho_0(r, \vartheta, \varphi)$. Since we are interested here only in electrostatic contributions to the energy and do not take van der Waals forces into account, we may use a ρ_0 averaged over the high frequency motion of the electrons. Appropriate distribution functions of this type have been calculated with the aid of quantum mechanics by Hartree.[8] If ρ_0 is known the potential inside the ion must satisfy Poisson's equation

$$\Delta V_1 = -4\pi\rho_0. \qquad (16)$$

The solution of this equation which replaces the V_1 of Eq. (1) is

$$V_1 = \int \frac{\rho_0(r', \vartheta', \varphi')}{|r'-r|}dv' + \psi, \qquad (17)$$

where ψ is the same function as before, and the integration is extended over all of space. Actually, we may suppose $\rho_0(r, \vartheta, \varphi)$ to be effectively zero outside of a sphere of radius b. The potentials outside of the sphere b remain the same as before, and the same expression for W, Eq. (13), is obtained, except that the Q_n's are now given by integrals of the form

$$Q_n = \int\int \rho_0(r, \vartheta, \varphi)\rho_0(r', \vartheta', \varphi')r^n r'^n$$
$$\times P_n[\cos (\vartheta-\vartheta')]dv'dv \qquad (18)$$

instead of by sums over discrete point charges. One would still want to represent the atomic nuclei by point charges, so that in general the Q_n's would consist of an integral over the

[8] D. R. Hartree, Proc. Camb. Phil. Soc. **24**, 89 (1928).

electronic distribution and a discrete sum over the nuclear point charges. For the present purposes, this generalization is unimportant, since we do not try to calculate the multipole moments Q_n explicitly from atomic structure. However, it is of interest to know that the results have the same form, whether we employ the crude point charge model or a more refined one, consistent with modern theories of molecular structure.

We may inquire as to the significance of the dielectric constant of the ion D_i. By assigning a value greater than unity to D_i, we have a crude means of taking the polarization of the ion into account. Henceforth we shall neglect this effect and assign a value unity to D_i. Further, since we shall be interested in solutions having dielectric constants greater than 25, we may simplify our formulas by neglecting D_i/D in comparison with unity, without introducing much error.

We are now able to calculate the change in the chemical potential of a complex ion attending its transfer from one solution to another, under the assumption that this change is equal to the difference between the works of charging, Eq. (13), in the two mediums. If we choose a standard state as a solution in which the chemical potential of the complex ion is μ^0, the activity coefficient, γ,

in a second solution, in which the chemical potential is μ, is defined by the relation

$$\mu - \mu^0 = kT \log \gamma x/x^0$$
$$= kT \log \gamma + kT \log x/x^0, \quad (19)$$

where x^0 and x are the mol fractions of the complex ion type in the respective solutions. If in addition to the ideal term $kT \log x/x^0$, the only change in chemical potential is assumed to be that associated with electrostatic forces, we have

$$\log \gamma = (W - W^0)/kT, \quad (20)$$

where W and W^0 are the respective works of charging in the two solutions.

We shall first investigate the influence of simple electrolytes on the activity coefficient of the complex ion. We choose the standard state as a solution in which the ionic strength of the simple electrolyte is zero, and the concentration of the complex ions is sufficiently small to allow the neglect of their mutual interactions. From Eqs. (13) and (20) we obtain the following expression for $\log \gamma$ in a solution containing the simple electrolyte at an ionic strength proportional to κ^2, under the assumption that the dielectric constant of the solution is that of the pure solvent, D, and that the concentration of the complex ions remains small.*

$$\log \gamma = W(\kappa)/kT = -(Q_0/2DkT)\kappa/(1+\kappa a)$$

$$-\frac{\kappa^2}{2DkT} \sum_{n=1}^{\infty} \frac{(2n+1)Q_n}{(2n-1)(n+1)^2 a^{2n-1}} \frac{K_{n-1}(\kappa a)}{K_{n+1}(\kappa a) + \dfrac{nb^{2n+1}\kappa^2 K_{n-1}(\kappa a)}{(n+1)(2n-1)(2n+1)a^{2n-1}}}. \quad (21)$$

* The fact that we have employed the Guntelberg-Müller charging process rather than that of Debye perhaps requires some comment. The Guntelberg-Müller process yields the chemical potential of the complex ion directly, while the Debye process requires an intermediate calculation of the total free energy of the solution (complex ions and simple electrolyte). We cannot calculate the total free energy statistically, without first investigating the influence of complex ions upon the potential in a simple electrolyte ion. This problem is somewhat more complicated than that of the influence of the simple electrolyte on the potential in a complex ion. So far it has not been solved by means of the Debye theory.

We may assume that the two charging processes lead to the same result if the condition of integrability is fulfilled. If ψ_i is the potential in a simple electrolyte ion i, and ψ_s is

the potential in a complex ion s, this principle requires that

$$\partial\psi_s/\partial e_i = \partial\psi_i/\partial e_s,$$

where e_i is the charge on the ion i, and e_s is a common factor of the ensemble of charges making up the complex ion. It should be pointed out that e_i refers to the charge on a single ion i, and not to the charge of the ion type. (Onsager, Chem. Rev. 13, 73 (1933); Halpern, J. Chem. Phys. 2, 85 (1934).) Since solutions of the Debye linear equation, Eq. (3), generally satisfy the condition of integrability, we might reasonably suppose that the integrability condition is satisfied, without explicitly calculating ψ_i.

It is nevertheless interesting to investigate the matter further by means of a semi-thermodynamic argument suggested to the writer by Professor Scatchard. Without reproducing the argument in detail, we shall give an

In this expression, the above-mentioned approximation of neglecting D_i in comparison with D has been introduced. It is perhaps worth while at this point to give explicit expressions for some of the polynomials $K_n(x)$. We have from Eq. (4)

$$K_0(x) = 1,$$
$$K_1(x) = 1+x,$$
$$K_2(x) = 1+x+x^2/3,$$
$$K_3(x) = 1+x+2x^2/5+x^3/15,$$
$$K_4(x) = 1+x+3x^2/7+2x^3/21+x^4/105.$$
(22)

If we are interested in the influence of the simple electrolyte upon the solubility of Zwitterions, we have

$$\log (N/N_0) = -\log \gamma,$$
(23)

where N_0 is the solubility at zero ionic strength of the simple electrolyte, and N is the solubility at a finite ionic strength. The solubilities are to be expressed as mol fractions.

The influence of the complex ions upon the activity of a simple electrolyte ion may be obtained in a similar manner. We treat only the case in which the complex ion is a Zwitterion ($Q_0=0$), and the ionic strength of the electrolyte is very small. Under these conditions, each of the polynomials $K_n(\kappa a)$ is closely approximated by unity. Moreover, the mutual interaction of the electrolyte ions can be outline of it for the case when the complex ion is a Zwitterion. At Zwitterion concentrations sufficiently small that may neglect the dependence of the chemical potential, μ_z, on the Zwitterion concentration, we may write by thermodynamics

$$F = F_0 + \int_0^{n_z} \mu_z dn_z = F_0 + n_z \mu_z,$$

where F is the electrical free energy of the solution, F_0 the electrical free energy of the simple electrolyte solution in the absence of Zwitterions, μ_z the electrical part of the chemical potential of a Zwitterion, and n_z their number. The potential ψ_i in an ion may then be calculated from F by the following relation:

$$\psi_i = \partial F/\partial e_i = \psi_i^0 + n_z \partial \mu_z/\partial e_i,$$

$$\psi_i^0 = -(e_i/D)\kappa/(1+\kappa a_i).$$

To avoid undue complication, we neglect small terms in the denominators of Eq. (22) depending on $(b/a)^{2n+1}$, and write

$$\mu_z - \mu_z^0 = kT \log \gamma_z = -\frac{\kappa^2}{2D} \sum_{n=1}^{\infty} \frac{(2n+1)Q_n}{(2n-1)(n+1)^2 a^{2n-1}} \frac{K_{n-1}(\kappa a)}{K_{n+1}(\kappa a)}.$$

Differentiation with respect to e_i and multiplication by n_z yields

$$\psi_i = -(e_i/D)\kappa/(1+\kappa a_i) - \frac{4\pi e_i n_z}{D^2 kTv}\left\{\frac{3}{4}\frac{Q_1}{a}\frac{1-\kappa a/2+\kappa^2 a^2(1+\kappa a)/6}{1+\kappa a+\kappa^2 a^2/3}\right.$$

$$\left. + \sum_{n=2}^{\infty} \frac{(2n+1)Q_n}{(2n-1)(n+1)^2 a^{2n-1}} \frac{K_{n-1}(\kappa a)+\kappa^2 a^2[K_n(\kappa a)/(2n+1) - K_{n-2}(\kappa a)/(2n-1)]}{K_{n+1}(\kappa a)}\right\}.$$

The limiting form of this expression is used in the following section to obtain the influence of Zwitterions on the activity of slightly soluble salts.

The above value of ψ_i automatically fulfills the condition of integrability, when μ_z is calculated by the Guntelberg process, but it would be arguing in a circle to say that we have proved that the integrability condition is satisfied by this calculation. However, we can get at the matter in another way. Thus the chemical potential of the ion i is given by $\mu_i = \mu_i^0 + n_z(\partial \mu_z/\partial n_i)$. By the Guntelberg process,

$$\psi_i = \partial \mu_i/\partial e_i = \psi_i^0 + n_z(\partial^2 \mu_z/\partial e_i \partial n_i).$$

The ψ_i calculated by this relation agrees with the above expression to terms of order $1/n_i$, where n_i is the number of ions of the ith type present. Thus the two calculations of ψ_i agree except for a quantity of completely negligible order. Applying the condition of integrability to the latter expression for ψ_i, we find that it requires $\partial \psi_i/\partial e_i = \partial^2 \psi_s/\partial e_i \partial n_i$. We find that this condition is fulfilled by our ψ_s with the neglect of terms of order $1/n_i$, due to the fact that ψ_s is of the form $e_s f(\kappa)$. It should be remarked that this would not be true for an arbitrary ψ_s, for example, one containing terms of the Gronwall-La Mer type. Thus we have shown that the Guntelberg process gives a result which is consistent with the integrability condition, in the present case. Although the question cannot be definitely settled without an independent statistical calculation of ψ_i we may assume with some confidence that our result is independent of the charging process.

ignored. Choosing the standard state of the electrolyte as a solution in which the Zwitterion concentration is zero, we have for the activity coefficient of an ion of type i in a solution containing Zwitterions at a molal concentration C,

$$\log \gamma_i = -\frac{2\pi N Z_i^2 \epsilon^2}{1000 D^2 k^2 T^2} C \sum_{n=1}^{\infty} \frac{(2n+1)Q_n}{(2n-1)(n+1)^2 a^{2n-1}}. \tag{24}$$

This expression is useful in determining the influence of Zwitterions on the solubility of a slightly soluble salt. If N is the solubility of the salt in a solution containing Zwitterions, and N_0 is its solubility in the absence of Zwitterions, we have

$$\log (N/N_0) = -\log \gamma_\pm = -(1/\sum_i \nu_i)\sum_i \nu_i \log \gamma_i, \tag{25}$$

where $\gamma_\pm$ is the mean activity coefficient of the salt ions, and ν_i is the number of ions of the ith type produced by a salt molecule.

We now turn our attention to the influence of the dielectric constant of the solvent upon the chemical potential of the complex ion, in the absence of the electrolyte. In this case κ vanishes and W reduces to the first term, W_0, of Eq. (12). If we choose as the standard state a solution of the complex ion at low concentration in a solvent of dielectric constant D_0, we have from Eqs. (13) and (20),

$$\log \gamma = \frac{1}{2kT} \sum_{n=0}^{\infty} \frac{(n+1)Q_n}{b^{2n+1}} \left\{ \frac{1-D}{(n+1)D+n} - \frac{1-D_0}{(n+1)D_0+n} \right\} \tag{26}$$

as the expression for the activity coefficient in a solvent of dielectric constant D. Here again the dielectric constant of the complex ion has been assigned the value unity. The first term of Eq. (26) corresponds to Born's result for an ion having a spherically symmetrical charge distribution.[9] The remaining terms depend upon the multipole electric moments of the ion. For the ratio of the solubilities N and N_0 of Zwitterions in solvents having the respective dielectric constants D and D_0, we may write

$$\log (N/N_0) = -\log \gamma, \tag{27}$$

where $\log \gamma$ is given by Eq. (26). The rate of change of $\log (N/N_0)$ with the reciprocal dielectric constant is

$$\frac{d \log (N/N_0)}{d(1/D)} = -\frac{1}{2kT} \sum_{n=1}^{\infty} \frac{2n+1}{n+1} \frac{Q_n}{b^{2n+1}} \frac{1}{(1+n/(n+1)D)^2}. \tag{28}$$

Thus, as long as D is large, we may expect $\log (N/N_0)$ to be virtually a linear function of $1/D$.[10]

III.

We should expect Eqs. (21) and (26) to provide a refinement of the simple Debye-Hückel theory in the case of real ions possessing asymmetric charge distributions. Here, however, the terms depending upon the multipole moments of the ion would in general be of the nature of small corrections to the initial terms, depending

[9] M. Born, Zeits. f. Physik 1, 45 (1920).

[10] R. P. Bell, Trans. Faraday Soc. 27, 797 (1931), has obtained an equation corresponding to Eq. (26) for the influence of the solvent dielectric constant on the chemical potential of a dipole molecule. Bell's expressions for the electrostatic potentials near the boundary of the molecule agree with the dipole terms ($n=1$) of our potentials in the limit $\kappa=0$. However, his value for the electrostatic energy of the dipole differs from ours by a factor $\frac{1}{3}$. To obtain the electrostatic energy, he integrates $DE^2/8\pi$ over all of space.

This should and does give the same result as summing $\frac{1}{2}e\psi$ over all charges of the molecule, where ψ is the potential in the interior of the molecule due to external charge distributions. Bell's factor $\frac{1}{3}$ appears to arise from a faulty estimate of $\int DE^2/8\pi dv$ in the interior of the molecule. Thus he extends the integral over the volume occupied by the charges constituting the dipole, which is not permissible, and also uses an expression for the potential which does not converge near these charges.

upon the net charge. In the case of Zwitterions on the other hand, the total charge is zero, and the terms of Eqs. (21) and (26) containing Q_0 vanish. Thus the entire electrical contribution to the chemical potential arises from the multipole moments. For this reason, Eqs. (21) and (26) find their most interesting application to the case of Zwitterions. Of course the present theory is highly simplified and could only be expected to give precise results if the following conditions were exactly fulfilled. (1) The Zwitterions have spherical boundaries. (2) They are present in the solution at such low concentration that their mutual interaction is negligible. (3) Their multipole electric moments are very large relative to those of a solvent molecule. (4) Non-electrostatic deviations from the ideal solution laws are insignificant. (5) Corrections of the Gronwall-La Mer type arising from nonlinear terms in the Poisson-Boltzmann equation can be neglected. However, it often happens that these conditions are approximately fulfilled, so that our equations furnish the basis for a semi-quantitative theory of Zwitterionic solutions.

According to the Zwitterionic hypothesis, the aliphatic amino acids exist as hybrid ions in solvents of high dielectric constant. Thus an α-amino acid $RNH_2CHCOOH$ forms a Zwitterion of the structure $RN\overset{+}{H_3}CHC\overset{-}{OO}$. The simplest member of this class of substances is glycine which forms the Zwitterion $\overset{+}{N}H_3CH_2C\overset{-}{OO}$. Among the aliphatic amino acids, glycine furnishes the most favorable example for the application of the present theory. Not only may the nonelectrostatic deviation from the ideal solution laws be expected to be a minimum, but also the boundary of the glycine Zwitterion can be roughly approximated by a spherical surface. This is not obvious from the formula, but examination of a steric model makes it plausible. An extensive experimental study of the solubility relations of the aliphatic amino acids in alcohol-water mixtures has been carried out by E. J. Cohn and his co-workers.[11] Professor Cohn has kindly placed at our disposal his data, in part unpublished, relating to the influence of salts and

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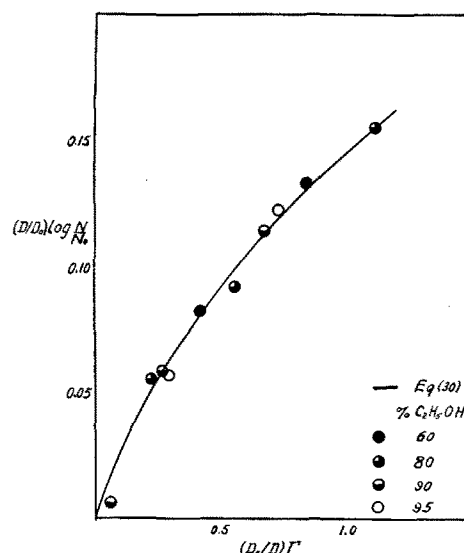[11] E. J. Cohn, Naturwiss. 20, 44 (1932).

FIG. 1. Solubility of glycine in alcohol-water mixtures containing LiCl at 25°C.

of the dielectric constant of the solvent upon the solubility of glycine.

An interesting property of Eq. (21) provides a means of correlating measurements of the influence of salts on the solubility of glycine in different solvents. By definition, Eq. (3), κ^2 is proportional to Γ/D, where Γ, the ionic strength of the salt, is defined as $\sum_i Z_i^2 C_i/2$. Thus according to Eq. (21), $D \log \gamma$ or $D \log (N/N_0)$ should be the same function of Γ/D for all solvents. This conclusion is confirmed by Cohn's measurements at 25°C of the solubility of glycine in alcohol-water mixtures containing lithium chloride. In Fig. 1, the experimental values of $(D/D_0) \log (N/N_0)$ in solutions of alcohol content varying from sixty to ninety-five percent, are plotted as a function of $(D_0/D)\Gamma$. The dielectric constant, D_0, of water at 25° has been introduced merely as a convenient scale factor. It is seen that the points fall very nearly upon a single curve up to ionic strengths, which doubtless lie beyond the region of validity of the present theory. Measurements in pure water do not fall upon the curve. This, however, is not to be expected. While the absolute solubility of glycine in solutions of high alcohol content is very low, its solubility in solutions of high water content is so high that the mutual interaction of the glycine hybrid ions can no longer be neglected, and Eq. (21) is no longer applicable.

Unless the charge distribution is concentrated very near the boundary of the ion, the sums in Eq. (21) and Eq. (26) converge quite rapidly, so that it is only necessary to retain the first few terms. For a Zwitterion, Q_0 is of course zero, while Q_1 is equal to the square of the dipole moment μ, and is independent of the position of the electric center of the charge distribution. The constants Q_2, Q_3, etc., are functions of the higher order multipole moments. They depend not only upon the relative charge distribution, but also upon the distance of the electric center from the boundary of the ion. If we approximate the charge distribution of a simple Zwitterion by two point charges $+e$ and $-e$ separated by a distance R, and situated at equal distances r from the center of the boundary sphere b, the constants Q_n have the following values

$$
\begin{aligned}
Q_0 &= 0, \\
Q_1 &= \mu^2 = e^2 R^2, \\
Q_2 &= 3\mu^2[r^2 - R^2/4], \\
Q_3 &= 6\mu^2[r^4 - 5r^2R^2/8 + 5R^4/48].
\end{aligned}
\tag{29}
$$

The Q_n of higher order may be calculated without difficulty from Eq. (14), for this or for any other simple charge distribution. If we neglect terms involving Q_n of higher order than the second, we obtain from Eqs. (21) and (23), after converting to common logarithms

$$
(D/D_0) \log_{10} N/N_0 = A\,\Gamma'\left\{ \frac{Q_1}{a} \frac{1}{1+(B\Gamma')^{\frac{1}{2}}+[1+\frac{1}{2}(b/a)^3]B\Gamma'/3} \right.
$$

$$
\left. + \frac{20}{81}\frac{Q_2}{a^3}\frac{1+(B\Gamma')^{\frac{1}{2}}}{1+(B\Gamma')^{\frac{1}{2}}+2[1+(1/9)(b/a)^5]B\Gamma'/5+[1+\frac{2}{3}(b/a)^5](B\Gamma')^{\frac{3}{2}}/15} \right\}
$$

$$
A = 3\pi N e^2/2303 D_0^2 k^2 T^2 = (3.00\times10^{34})/D_0^2 T^2,
\tag{30}
$$

$$
B = 8\pi N e^2 a^2/1000 D_0 k T = 2.53\times10^{19}(a^2/D_0 T),
$$

$$
\Gamma' = (D_0/D)\,\Gamma
$$

where Q_1 and Q_2 are given by Eq. (29), and the remaining symbols have their usual significance.

In the case of glycine, it is sufficient to retain only the first term of Eq. (30). With a proper choice of the constants Q_1, a and b, Eq. (30) yields the curve of Fig. 1, which fits the experimental points very satisfactorily. The radius, b, of the glycine hybrid ion is estimated from the partial molal volume to lie between 2.6 and 2.8A, depending upon whether a correction for the electrostriction of the solvent is made or not.[12] We therefore assign it a value of 2.7A. The course of the solubility curve is very insensitive to the explicit value of b, being chiefly determined by Q_1 and a. The limiting slope is determined by the ratio Q_1/a and the curvature by a. From the curve, Fig. 1, we obtain a value, 15.0×10^{-18} e.s.u. for the dipole moment, μ, of the glycine Zwitterion, and a value, 3.3A for the mean radius, a, of the salt ions and the Zwitterion. This value of the dipole moment differs but little from Wyman's estimate, 20×10^{-18} e.s.u., based upon measurements of the dielectric constants of an α-amino acid solution.[13] If we divide μ by the electronic charge, we obtain a value, 3.17A, for the effective separation of the positive charge on the basic group and the negative charge on the acidic group of the glycine Zwitterion. From a steric model of glycine, one finds that if the center of gravity of the positive charge is on the nitrogen atom of the amino group and that of the negative charge lies between the oxygen atoms of the carboxyl group, this distance should be about 3.3A. Due to internal polarization of the molecule, the effective separation of the two charges should certainly be less than this. Thus the value, 3.17A, obtained from solubility data with the aid of Eq. (30) furnishes a very reasonable estimate of the effective separation of the charged groups, although it is probably somewhat too large.

[12] E. J. Cohn, Science 79, 83 (1934).

[13] J. Wyman, J. Am. Chem. Soc. 56, 536 (1934).

We now turn our attention to the influence of the dielectric constant of the solvent upon the solubility of glycine in the absence of salts. If multipoles of higher order than the quadrupole are neglected and common logarithms are introduced, Eq. (28) becomes

$$\frac{d \log_{10} (N/N_0)}{d(1/D)} = -\frac{2.374 \times 10^{15}}{T} \left\{ \frac{Q_1}{b^3} \frac{1}{(1+1/2D)^2} + \frac{10}{9} \frac{Q_2}{b^5} \frac{1}{(1+2/3D)^2} \right\}. \quad (31)$$

If log (N/N_0) were plotted as a function of D^{-1}, the slope of the resulting curve should, according to Eq. (31), be independent of the choice of standard state. Moreover, in solvents of dielectric constant greater than that of alcohol, the factors $(1+n/(n+1)D)^{-2}$ vary only slightly from unity. Thus in alcohol-water mixtures, the curve, although slightly concave upward, should differ very little from a straight line. Cohn's measured values of log (N/N_0) for glycine in alcohol water mixtures at 25°C do not exhibit exactly this type of curve when plotted against $1/D$. In solvents rich in water, the curvature, although in the same direction, is much larger than could be accounted for by Eq. (31). This is probably due to mutual interaction of the glycine Zwitterions, not taken into account in this equation. In solvents rich in alcohol, on the other hand, there is a slight downward curvature not predicted by Eq. (31). This is probably due to a selective effect of the glycine Zwitterion upon the molecules of the mixed solvent, which would tend to make the solution in its immediate neighborhood richer in water than the bulk of the solution. This effect is also neglected in Eq. (31). However, in solvents ranging in alcohol content from forty to eighty percent, the slope is nearly constant, and has a mean value -96.4. If the quadruple term is neglected, and Eq. (31) is provisionally applied, this slope should be proportional to Q_1/b^3. Using the value of Q_1 previously obtained from the solubility of glycine in salt solutions, we calculate a value, 2.6A, for the radius b of the glycine Zwitterion. This is in good agreement with the estimates of this quantity from the molal volume, which range from 2.6 to 2.8A. The difference,

$a-b$, equal to 0.7A, furnishes an estimate of the effective radii of the lithium and chloride ions. If a^{-1} is calculated as the mean reciprocal of b and ionic radii obtained from crystal structure data, this difference, $b-a$, should be about 1A instead of 0.7A. This discrepancy could be removed by assigning a value, 3.6A, to a, instead of 3.3A. If this were done, the dipole moment calculated from the limiting slope of the salt curve, Fig. 1, would become 15.7×10^{-18} e.s.u., differing from the previous value by only five percent. However, the theoretical curve would then fall below the experimental points at the higher ionic strengths. This latter difficulty could perhaps be removed by taking the influence of higher multipole moments and the effect of the salt on the dielectric constant into account. However, such refinements do not seem worth while, in view of other approximations in the theory, such as the neglect of van der Waals forces and of the selective effect of the Zwitterion on the mixed solvent.

From the foregoing discussion, it is seen that the present theory gives an approximate account of the solubility relations of glycine in alcohol-water mixtures, both in the presence and in the absence of salts, as long as the glycine concentration is small. Moreover, it yields values of the dipole moment and of the size of the glycine Zwitterion, which are of reasonable magnitude. The calculated value of the dipole moment, 15×10^{-18} e.s.u., although it may be in error by fifteen or twenty percent, is perhaps the most reliable estimate as yet available. The theory also gives the qualitative aspects of the solubility relations of the other aliphatic amino acids, although, due to their hydrocarbon chains, the boundaries of these molecules cannot be approximated by spherical surfaces. Moreover, there is evidence that nonelectrostatic deviations from ideality in alcohol-water solutions of these acids increase with the length of the hydrocarbon chain. Quantitative agreement with the present theory is therefore not to be expected.

In conclusion, the writer wishes to acknowledge his indebtedness to Professor George Scatchard and to Professor E. J. Cohn for their interest and cooperation in this work.