

## ON GUAIACOL SOLUTIONS

### II. THE DISTRIBUTION OF SODIUM AND POTASSIUM GUAIACOLATES BETWEEN GUAIACOL AND WATER

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#### INTRODUCTION

In a series of studies related to the kinetics of penetration in living cells Osterhout and his coworkers<sup>1</sup> have used artificial cell models, consisting of a non-aqueous phase (guaiacol or guaiacol with *p*-cresol), representing the protoplasmic surface, in contact with aqueous phases, representing the cell sap and the external solution. In this connection the distribution of electrolytes between guaiacol and water, is particularly interesting.

The electrical conductivities of sodium and potassium guaiacolate solutions in guaiacol have been discussed in the previous paper.<sup>2</sup> It was shown that these salts are weak electrolytes in such solutions, and that their ionization constants can be computed from the conductivity measurements by taking into account the effect of interionic forces on the mobilities and activities of the ions.

This paper will deal with the partition of these salts between water and guaiacol, and will provide an independent means for computing these ionization constants. Starting from the assumptions that the salts are weak electrolytes in the guaiacol phase and strong electrolytes in the aqueous phase, and using the interionic attraction theory of Debye and Hückel, it is shown that the variation of the distribution coefficients with concentration can be explained. Furthermore, the ionization constants previously obtained from conductivity measure-

<sup>1</sup> Osterhout, W. J. V., *J. Gen. Physiol.*, 1932-33, **16**, 157, 529. Osterhout, W. J. V., and Stanley, W. M., *J. Gen. Physiol.*, 1931-32, **15**, 667. Osterhout, W. J. V., Kamerling, S. E., and Stanley, W. M., *J. Gen. Physiol.*, 1933-34, **17**, 445, 469.

<sup>2</sup> Shedlovsky, T., and Uhlig, H. H., *J. Gen. Physiol.*, 1933-34, **17**, 549.

ments are found to be in satisfactory agreement with the distribution determinations.

Also, it is shown that the magnitude of the distribution coefficients can be predicted from theoretical considerations, using only the properties of the solvent and the solute in the computations.

#### THEORETICAL

In discussing the distribution of sodium or potassium guaiacolate between guaiacol and water, we shall assume that the salt is practically completely dissociated in the aqueous phase, in which, therefore, the ionic activity is  $(C_1\gamma_1)$ ,  $- (C_1)$  being the total concentration of the salt in this phase, and  $(\gamma_1)$  the corresponding activity coefficient.

In the non-aqueous phase, the salt is only partially dissociated in accordance with the ionic equilibrium  $M^+ + G^- = MG$  ( $M$  referring to the metal and  $G$  to guaiacolate), for which the mass action expression is

$$K = \frac{[M^+][G^-]}{[MG]} = \frac{(C\theta\gamma)^2}{C(1-\theta)} \quad (1)$$

In this equation,  $K$  is the ionization constant, the brackets refer to activities,  $C$  is the total concentration in the non-aqueous phase,  $\theta$  is the degree of ionization, and  $\gamma$  is the mean ionic activity coefficient. We have assumed that the undissociated portion of the electrolyte behaves as an "ideal" solute, so that its activity is equal to its concentration. At equilibrium, the ratio of the activities of any solute species distributed between two phases, at a fixed temperature and pressure, is a constant,<sup>3</sup> independent of the concentration. Accordingly, for the dissociated portion of the solute

$$S_0 = \frac{C\theta\gamma}{C_1\gamma_1} \quad (2)$$

<sup>3</sup> In general this constant is not unity. This is because two standard states are involved, one for each phase. The actual "escaping tendency" of a solute species in equilibrium between two phases must, however, be equal. In other words, if the activities in the two phases were referred to a single standard state (in the gaseous or crystal state, for example), then the limiting partition coefficient would be unity. It is customary, however, to define the activity coefficient in such a manner as to render it equal to unity at infinite dilution, since by so doing the activity approaches the concentration as the solution becomes infinitely dilute. This procedure involves the fixing of a separate standard state for each solvent.

Also, it is assumed that the properties of the solvents remain essentially constant.

in which the numerator on the right hand side of the equation is the ionic activity in the non-aqueous phase, and the denominator is the corresponding activity in the aqueous phase. The value of  $(S_0)$ , the limiting partition coefficient, depends on the standard states for the two solvents.

We shall assume that the activity coefficients  $(\gamma)$  and  $(\gamma_1)$  are given by the familiar Debye-Hückel equations

$$\log_{10} \gamma = - \frac{a \sqrt{C\theta}}{1 + b \sqrt{C\theta}} \text{ for the non-aqueous phase} \quad (3)$$

and

$$\log_{10} \gamma_1 = - \frac{a_1 \sqrt{C_1}}{1 + b_1 \sqrt{C_1}} \text{ for the aqueous phase} \quad (3')$$

in which the coefficients in the numerators are equal to

$$\frac{0.4343 e^2}{2DkT} \left( \frac{8\pi N e^2}{1000 DkT} \right)^{\frac{1}{2}}$$

and the coefficients in the denominators are equal to

$$\left( \frac{8\pi N e^2}{1000 DkT} \right)^{\frac{1}{2}} d$$

where

- $e$  = electronic charge =  $4.77 \times 10^{-10}$  e.s.u.
- $k$  = Boltzmann's constant =  $1.371 \times 10^{-16}$  erg/degree
- $D$  = dielectric constant
- $T$  = absolute temperature
- $N$  = Avogadro's number =  $6.06 \times 10^{23}$
- $d$  = distance of closest approach for the ions

Combining (1) and (2), and substituting  $\frac{C}{C_1} = S$ , the partition coefficient, we obtain

$$S = \frac{(S_0)^2}{K} \cdot \frac{C_1(\gamma_1)^2}{(1 - \theta)} = \frac{\beta}{1 - \theta} C_1(\gamma_1)^2 \quad (4)$$

in which  $\frac{S_0^2}{K} = \beta$ . Taking logarithms in (1) and substituting from (3) and (3')

$$\log \theta = \log S_0 - \log S + \frac{a \sqrt{C\theta}}{1 + b \sqrt{C\theta}} - \frac{a_1 \sqrt{C_1}}{1 + b_1 \sqrt{C_1}} \quad (5)$$

The total salt concentrations,  $C$  and  $C_1$ , in the non-aqueous and aqueous phases respectively, have been determined by a method which will be described later in this paper. The ratio of these concentrations,  $S$ , is therefore also known, and  $\gamma_1$  can be computed from equation (3'). Assuming a provisional value for  $S_0$ , which may be obtained from a plot of  $S$  vs.  $C_1\gamma_1^2$ , extrapolated to  $C_1\gamma_1^2 = 0$ , values of  $\theta$  corresponding to the various distribution experiments, have been computed from equation (5) by a method of successive approximations. Then, using equation (4), values of  $S(1 - \theta)$  have been plotted against the corresponding values of  $C_1\gamma_1^2$ . If the correct value of  $S_0$  has been chosen, the plot will be linear, passing through the origin with a slope equal to  $\beta$  (see equation (4)). Successive values of  $S_0$  are assumed until this criterion is satisfied. Since the slope of the plot is  $\beta = \frac{(S_0)^2}{K}$ , the ionization constant,  $K$ , can thus be evaluated.

In this discussion we have neglected the possible effect of hydrolysis of the salts in the aqueous phase on the partition coefficients. Although guaiacol is such a weak acid that its salts are extensively hydrolyzed in pure water, it will be shown below that the solubility of guaiacol in the aqueous phase, which, of course, was always saturated with guaiacol in the partition experiments, is sufficiently great to reduce hydrolysis to a negligible extent for our purpose.

#### *Effect of Hydrolysis on the Partition Coefficients*

The hydrolysis of sodium and potassium guaiacolate:  $M^+ + G^- + H_2O = M^+ + OH^- + HG$  has a mass action constant

$$K_h = \frac{[OH^-][HG]}{[G^-]} = \frac{K_w}{K_{HG}} \quad (6)$$

$K_w$ , in this expression, is the dissociation constant for water ( $1 \times 10^{-14}$  at 25°) and  $K_{HG}$  is the corresponding dissociation constant of guaiacol in water.

Since we are interested only in the order of magnitude of the hydrolysis, we may neglect activity corrections. Thus, if  $C_1$  is the original concentration of guaiacolate in the aqueous phase, ( $X$ ) the concentration of salt hydrolyzed, and  $C_0$  the solubility of guaiacol in water, then

$$K_a = \frac{K_w}{K_{HG}} = \frac{(C_0)X}{(C - X)} \quad (6')$$

The solubility of guaiacol in water ( $C_0$ ) was determined by making successive additions of guaiacol from a weight burette to a weighed quantity of water contained in a glass-stoppered flask. After each addition of guaiacol, the solution was thoroughly shaken and allowed to stand in a constant temperature room at 25°C. The amount of guaiacol added to 116 gm. of water necessary for saturation was determined to within 1 drop.

$$\begin{aligned} \text{Solubility (weights in air) gm. HG/1000 gm. H}_2\text{O} &= 24.1 \pm 0.2 \\ \text{Moles guaiacol per 1000 cc. solution} &= 0.190 = C_0 \end{aligned}$$

The dissociation constant of guaiacol  $K_{HG}$  in water at 25°C. was determined in the following way. The pH of an aqueous solution 0.129 molal in guaiacol and 0.0195 molal in potassium guaiacolate was measured with the glass electrode, giving a value of 9.20.<sup>4</sup>

Taking logarithms in equation (6) we obtain  $\log K_{HG} = \log [G^-] - \log [HG] - \text{pH}$ , from which the value of the dissociation constant  $K_{HG}$  can be calculated by substituting the appropriate values for  $[G^-]$ , pH, and  $[HG]$ ;  $[HG] = 0.129$ , pH = 9.20, and  $\log [G^-] = \log (0.0195) + \log \gamma_{G^-}$ . The activity coefficient term,  $\log \gamma_{G^-}$  is given by the Debye-Hückel equation [equation (3')]. Thus,  $K_{HG}$  at 25°C. was found to be  $8 \times 10^{-11}$ .

Returning now to equation (6'), and substituting the proper values for  $K_w$ ,  $K_{HG}$ , and  $C_0$  we obtain:

$$K_a = \frac{10^{-14}}{8 \times 10^{-11}} = \frac{0.190 X}{C - X}$$

Solving for  $X$ , we get

$$X = (6.6 \times 10^{-4})C$$

which shows that the maximum error to be expected from neglecting hydrolysis is under a tenth of a per cent. For our purposes this small effect is entirely negligible.

#### *Partition Experiments*

The partition experiments were carried out in Pyrex glass tubes of about 50 cc. capacity, provided with a stop-cock at one end and a ground glass stopper at the

<sup>4</sup> We are indebted to Mr. D. Belcher for this measurement. Pure materials, and carbon dioxide-free conductivity water were used in preparing the solution.

other. With this arrangement, the two liquid phases could readily be separated from each other for subsequent analysis. Equilibrium between the aqueous and guaiacol solutions of the alkali guaiacolate<sup>5</sup> of various concentrations was attained by rotating the tubes containing the solutions in a constant temperature room at 25°C.  $\pm$  0.1° for 15 hours. The solutions turned from colorless to a yellow or brownish tint at the end of this period, due probably to an oxidation of a small amount of guaiacol to a quinoid structure.

*Analysis.*—The analysis of both the aqueous and guaiacol phases for sodium or potassium guaiacolate was carried out by adding distilled water to a known volume of solution and titrating with standard hydrochloric acid. Analyses of sufficient accuracy were only made possible by employing with glass electrodes a modification of the differential titration method described by MacInnes and Dole.<sup>6</sup> Glass electrodes were used since they are not "poisoned" by guaiacol. The procedure was to titrate the major portion of the solution with 0.1 N or 0.01 N acid delivered from a weight burette to within a few drops of the end-point, and then to complete the titration with a more dilute standard acid (0.001 to 0.002 N), delivered from a volumetric burette.

We are greatly indebted to Dr. D. A. MacInnes for the design of the differential titration apparatus which made the attainment of the required accuracy for this work possible. The apparatus is shown, diagrammatically, in Fig. 1. Two spiral electrodes (*A* and *B*) of the type described by MacInnes and Belcher<sup>7</sup> were used. The electrode (*A*) forms part of a gas lift pump for circulating the titrated solution. A jacket of Jena glass, sealed around this electrode, is filled with 0.1 N hydrochloric acid solution from which a silver-silver chloride electrode (*E*) makes contact to one terminal of the potentiometer. Another, larger, spiral electrode (*B*) entirely encircles the smaller "pump" electrode (*A*). It is filled with 0.1 N hydrochloric acid from which another silver-silver chloride electrode (*F*) completes the circuit to the potentiometer. The outer electrode (*B*) is rigid enough to be used as a hand-operated stirrer. Commercial nitrogen, after passing over soda-lime and through a cotton filter, enters through the stop-cock (*S*), operates the gas lift pump, and escapes at (*l*). Thus, solution is drawn up at (*M*) and is passed through the inner part of the spiral (*A*), returning to (*N*). The differential titrations were carried out with a student type Leeds and Northrup potentiometer and a vacuum tube (pliotron) electrometer.<sup>8</sup>

The potential differences corresponding to values near the end-point for a 2-drop addition of 0.001 N HCl amounted, in the case of the dilute guaiacol solutions, to

<sup>5</sup> The preparation of the salts and the purification of guaiacol have been described in the previous paper. Conductivity water was used for the aqueous phase.

<sup>6</sup> MacInnes, D. A., and Dole, M., *J. Am. Chem. Soc.*, 1929, **51**, 1119.

<sup>7</sup> MacInnes, D. A., and Belcher, D., *Ind. and Eng. Chem., Analytical Edition*, 1933, **5**, 199.

<sup>8</sup> Hill, S. E., *Science*, 1931, **73**, 529. We are indebted to Dr. S. E. Hill for putting this instrument at our disposal.

11–12 mv., and to 3–5 mv. in the case of the more concentrated solutions. It was thus always possible to estimate the end-point within 2 drops of 0.001 N acid.

The results of the partition experiments for potassium guaiacolate are given in Table I and those for sodium guaiacolate in Table II. No

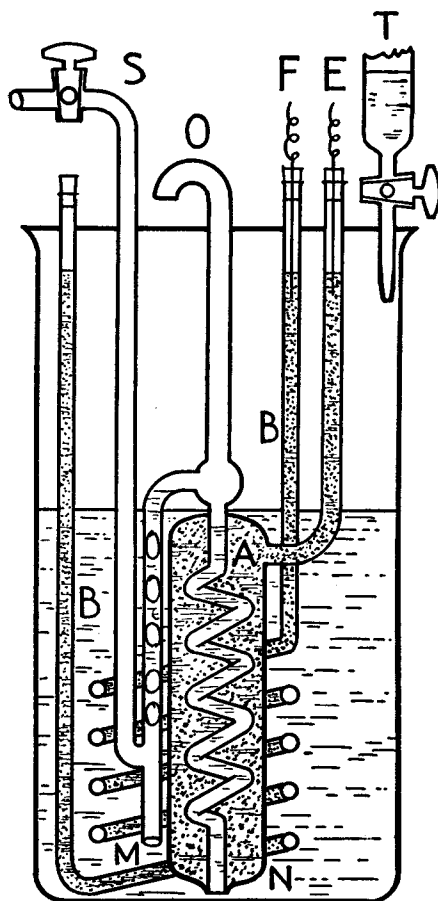


FIG. 1. Glass electrode differential titration apparatus

corrections were made for hydrolysis in the aqueous phase, since it was shown previously that the errors arising from this source were less than the probable experimental errors.

The method for calculating values of the dissociation constants of

the alkali guaiacolate in water-saturated guaiacol has already been discussed in this paper.

TABLE I  
*The Distribution of Potassium Guaiacolate between Water and Guaiacol at 25°C.*

| Non-aqueous phase |             | Aqueous phase       |                   | Partition coefficient<br>$S = \frac{C}{C_1}$ |
|-------------------|-------------|---------------------|-------------------|--|
| C (moles/liter)   |             | $C_1$ (moles/liter) | $C_1(\gamma_1)^2$ |  |
| Observed          | Calculated* |                     |                   |  |
| 0.0613            | 0.0594      | 0.1397              | 0.0860            | 0.439  |
| 0.03247           | 0.0322      | 0.1001              | 0.0643            | 0.324  |
| 0.02037           | 0.02037†    | 0.0780              | 0.0517            | 0.261  |
| 0.01073           | 0.01081     | 0.0550              | 0.0381            | 0.195  |
| 0.00924           | 0.00925     | 0.0505              | 0.0353            | 0.183  |
| 0.00283           | 0.00290     | 0.02652             | 0.0199            | 0.107  |
| 0.00093           | 0.00090     | 0.01347             | 0.0108            | 0.0690                                       |
| 0.00055           | 0.00052     | 0.00974             | 0.00802           | 0.0566                                       |
| 0.00034           | 0.00029     | 0.00683             | 0.00577           | 0.0490                                       |

\*  $K = 5.1 \times 10^{-5}$ .

† Reference point,  $\beta = 4.61$ ;  $S_0 = 0.0153$ .

TABLE II  
*The Distribution of Sodium Guaiacolate between Water and Guaiacol at 25°C.*

| Non-aqueous phase |             | Aqueous phase       |                   | Partition coefficient<br>$S = \frac{C}{C_1}$ |
|-------------------|-------------|---------------------|-------------------|--|
| C (moles/liter)   |             | $C_1$ (moles/liter) | $C_1(\gamma_1)^2$ |  |
| Observed          | Calculated* |                     |                   |  |
| 0.005575          | 0.00559     | 0.06437             | 0.0437            | 0.0866                                       |
| 0.002780          | 0.00283     | 0.04396             | 0.0312            | 0.0632                                       |
| 0.002789          | 0.00282     | 0.04384             | 0.0312            | 0.0636                                       |
| 0.001702          | 0.001702†   | 0.03285             | 0.0241            | 0.0518                                       |
| 0.000998          | 0.00099     | 0.02408             | 0.0183            | 0.0415                                       |
| 0.000518          | 0.00052     | 0.01585             | 0.0125            | 0.0327                                       |
| 0.000344          | 0.00031     | 0.01189             | 0.00963           | 0.0290                                       |

\*  $K = 4.3 \times 10^{-5}$ .

† Reference point,  $\beta = 1.75$ ;  $S_0 = 0.00855$ .

In computing the activity coefficients for the ions, according to the Debye-Hückel theory (equations (3) and (3')), a radius of 7 Å. has been assumed. This value was estimated with the aid of crystal



structure data,<sup>9</sup> and is sufficiently accurate since it enters as a correction term in the equations.

For the aqueous phase, saturated with guaiacol, the dielectric constant is 76.1, and for the non-aqueous phase, saturated with water, it is 14.3.<sup>10</sup> Accordingly,

$$\log_{10} \gamma_1 = - \frac{0.526 \sqrt{C_1}}{1 + 2.32 \sqrt{C_1}}$$

and

$$\log_{10} \gamma = - \frac{6.52 \sqrt{C\theta}}{1 + 5.36 \sqrt{C\theta}},$$

that is,  $a = 6.52$ ,  $b = 5.36$ ,  $a_1 = 0.526$ , and  $b_1 = 2.32$  in equations (3) and (3').

In Fig. 2, for potassium guaiacolate and sodium guaiacolate respectively, the solid lines show plots of the partition coefficients  $S$  (ordinates) against  $C_1\gamma_1^2$  (abscissae),  $C_1$  referring to the salt concentration in the aqueous phase and  $\gamma_1$  to the corresponding activity coefficients. The dotted lines in the figure show plots of  $S(1 - \theta)$  against the same abscissae. It will be recalled that to compute values of  $\theta$ , successive values for the limiting partition coefficient  $S_0$  are assumed; and the correct value of  $S_0$  is the one that sends the line,  $S(1 - \theta)$  vs.  $C_1\gamma_1^2$ , through the origin. The slope of this line is  $\frac{(S_0)^2}{K} = \beta$ , from which  $K$ , the ionic dissociation constant, is computed.

The calculated results for potassium guaiacolate give values of  $K = 5.5 \times 10^{-5}$  and  $S_0 = 0.016$ ; and for sodium guaiacolate  $K = 3.5 \times 10^{-5}$  and  $S_0 = 0.007$ . These values of  $K$  are in satisfactory agreement with those obtained from conductivity measurements, which were  $K = 5.1 \times 10^{-5}$  for potassium guaiacolate, and  $K = 4.3 \times 10^{-5}$  for sodium guaiacolate.

The agreement may, perhaps, be shown more clearly in another way. Equation (4) may be rewritten in the form

$$C = \beta C_1^2 (\gamma_1)^2 + \theta C \quad (4')$$

<sup>9</sup> Pauling, L., *J. Am. Chem. Soc.*, 1927, **49**, 765.

<sup>10</sup> We are indebted to Dr. S. O. Morgan of the Bell Telephone Laboratories for these values.

We shall assume that  $K$  has the value determined from the conductivity measurements for each salt. Now, taking the measured values of  $C$  and  $C_1$  for one partition experiment (a reference point), we calculate  $\beta$  in equation (4'), using equations (1) and (3). Taking this value of  $\beta$ , we then compute values of  $C$  corresponding to all the measured values of  $C_1$ . A comparison between the values of  $C$  (the alkali guaiacolate concentration in the non-aqueous phase) calculated

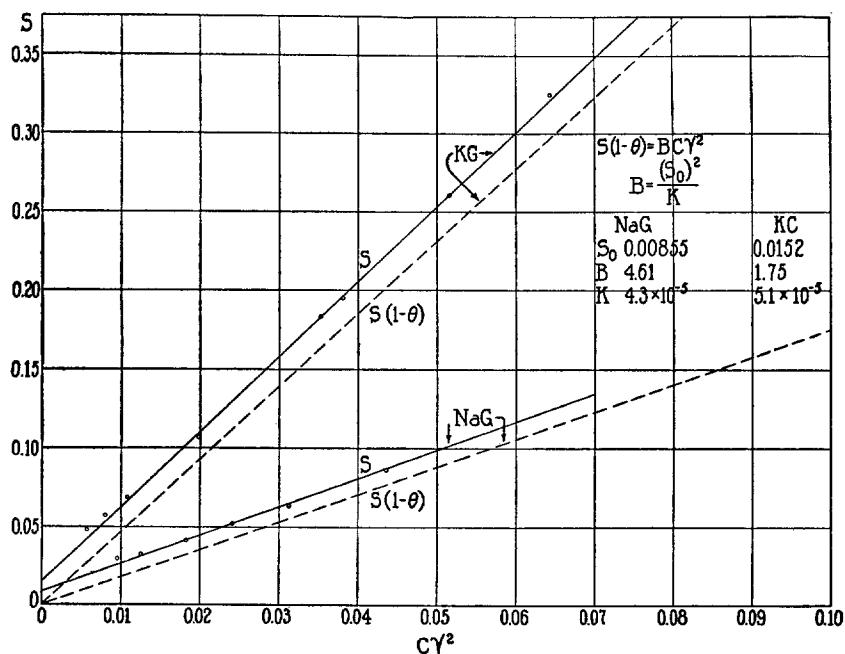


FIG. 2. Partition coefficients ( $S$ ) of sodium and potassium guaiacolates between guaiacol and water at 25°C.

in this manner and those obtained experimentally is shown in columns (2) and (1) respectively, of Tables I and II. The agreement is evidently quite satisfactory.

#### *The Theoretical Prediction of Limiting Partition Coefficients*

The relative concentrations of a solute species in two phases which are in equilibrium depend on the difference of the potential energy of

the solute in the two phases. In this discussion, we shall confine ourselves to the simplest case (infinite dilution) for which the concentration ratio is the limiting partition coefficient,  $S_0$ .

It has been shown by Born,<sup>11</sup> from classical electrostatic theory, that the difference in potential energy resulting from the transfer of a spherical ion from one solvent to another is given by the equation

$$\Delta E = \frac{e^2}{2r} \left( \frac{1}{D} - \frac{1}{D_1} \right) \quad (8)$$

in which  $\Delta E$  is the change of potential energy,  $e$  is the electrostatic charge of the ion,  $r$  is the ionic radius, and  $D$  and  $D_1$  are the dielectric constants of the two solvents. Furthermore, the Maxwell-Boltzmann distribution theorem gives us an expression for the concentration ratio:

$$\frac{C}{C_1} = \exp. -\frac{\Delta E}{kT} \quad (9)$$

$k$  is the Boltzmann constant, and  $T$  the absolute temperature.

Combining these two equations, we obtain

$$\log_e \frac{C}{C_1} = \frac{e^2}{2rkT} \left( \frac{1}{D} - \frac{1}{D_1} \right) \quad (10)$$

corresponding to the transfer of one kind of ion. However, since the electrical neutrality of the phases must be preserved, it is necessary to consider the simultaneous transfer of a negative and positive ion. Consequently, instead of equation (10) we have, for a simple univalent electrolyte

$$\log_e \left( \frac{C}{C_1} \right)^2 = \log_e S_0^2 = \frac{e^2}{2kT} \left( \frac{1}{D} - \frac{1}{D_1} \right) \left( \frac{1}{r^+} + \frac{1}{r^-} \right)$$

in which  $r^+$  and  $r^-$  are the respective radii of the positive and negative ions. This equation reduces to

$$\log_e S_0 = \frac{e^2}{4kT} \left( \frac{1}{D} - \frac{1}{D_1} \right) \left( \frac{1}{r^+} + \frac{1}{r^-} \right) \quad (11)$$

In the derivation of equation (11) it has been assumed that the properties of the solute depend only on its electrostatic charge and radius,

<sup>11</sup> Born, M., *Z. Phys.*, 1920, 1, 45.

and that those of the solvents depend on their dielectric constants alone. This means that all energy changes due to electrostriction, electrical saturation of solvent about the ions, ionic field asymmetries, electronic displacements, etc., have been neglected.

Since most of the factors neglected in this simple treatment are concerned with forces operating close to the ions, we shall make the following additional assumption. Let us assume that most of the "close range" forces are confined to a region corresponding to a single layer of solvent molecules polarized around the ions. It will be recalled that the concentration of water in the guaiacol phase, saturated with water, corresponds to a mole fraction of about 25 per cent. Water molecules, although smaller in size, have larger electrical dipole moments than guaiacol molecules. It is therefore reasonable to suppose that even in the guaiacol phase the ions will be preferentially "solvated" with water.

We shall assume, then, that for the case of salts distributed between guaiacol and water, the ions may be regarded as similarly hydrated with a single sheath of water molecules in both phases.

Returning to equation (11), and substituting the proper numerical values ( $k = 1.37 \times 10^{-16}$ ,  $e = 4.77 \times 10^{-10}$ ,  $T = 298^\circ$  (for  $25^\circ\text{C}.$ ),  $D = 14.3$ ,  $D_1 = 76.1$ ) we obtain

$$\log_{10} S_0 = -3.44 \left[ \frac{1}{r^+} + \frac{1}{r^-} \right] \quad (12)$$

in which, now,  $r^+$  and  $r^-$  are the radii, in Ångstrom units, of the solvated positive and negative ions. These values we shall obtain by adding 1 Å. (for the water sheath) to the crystallographic ionic radii.<sup>9</sup>

Thus  $r_{\text{Na}^+} = 1.95$  Å.,  $r_{\text{K}^+} = 2.33$  Å.,  $r_{\text{G}^-} = 7.0$  Å. Substituting these values in equation (12) for sodium guaiacolate (NaG) and potassium guaiacolate (KG) we obtain:

$$S_0 (\text{NaG}) = 0.0055; S_0 (\text{KG}) = 0.011$$

which are in as good agreement as can be expected with the experimentally determined values:<sup>12</sup>

$$S_0 (\text{NaG}) = 0.007; S_0 (\text{KG}) = 0.016$$

<sup>12</sup> Instead of equation (11) N. Bjerrum (*Tr. Faraday Soc.*, 1927, **23**, 447, 449) (see also *Z. phys. Chem.*, 1927, **127**, 358; 1932, **159**, 194) has used equation (10), with a value of  $r$  equal to the mean of the positive and negative ionic radii, and has shown that it fails to predict actual partition coefficients.

It is thus possible to predict from equation (12) that the smaller the ion sizes the smaller will be the limiting partition coefficients ( $S_0$ ). The stoichiometric partition coefficient ( $S$ ) (see equation (4)) is directly proportional to the square of ( $S_0$ ), and indirectly proportional to the dissociation constant ( $K$ ).

It can be shown<sup>13</sup> that the same factors which increase ( $S_0$ ) also increase ( $K$ ). However, since  $S$  is proportional to the first power of  $\left(\frac{1}{K}\right)$  and to the square of ( $S_0$ ), the latter primarily determines the change of ( $S$ ) with the concentration. Thus we may conclude that the slope  $\beta = \frac{(S_0)^2}{K}$  of equation (4) will be larger for salts having larger ions. This generalization is confirmed in the recent partition experiments of Osterhout, Kamerling, and Stanley,<sup>14</sup> who found that for the alkali guaiacolate distributed between water and guaiacol-*p*-cresol mixture,  $S$  increases in the order Cs > Rb > K > Na > Li, which is precisely what we should expect from the corresponding ion radii. The small partition coefficient for potassium chloride, measured by the same investigators can similarly be predicted from equation (12), since the "hydrated" chloride ion ( $r_{Cl^-} = 2.87 \text{ \AA.}$ ) is considerably smaller than the corresponding guaiacolate ion ( $r_{G^-} = 7.0 \text{ \AA.}$ ).

The effect of temperature on partition coefficients can be determined from equation (11). Since the logarithm in this equation is numerically negative, we can predict a greater partition coefficient at a higher temperature.

#### SUMMARY

1. Measurements are reported on the distribution of sodium and potassium guaiacolate between guaiacol and water at 25°C.
2. The variation of the partition coefficients with the concentration is explained with the aid of the Debye-Hückel interionic attraction theory and the assumption that the salts are strong electrolytes in water and weak electrolytes in guaiacol.

<sup>13</sup> Bjerrum, N., *K. Danske Vidensk. Selsk.*, 1926, **7**, No. 9. Fuoss, R. M., and Kraus, C. A., *J. Am. Chem. Soc.*, 1933, **55**, 1019.

<sup>14</sup> Osterhout, W. J. V., Kamerling, S. E., and Stanley, W. M., *J. Gen. Physiol.*, 1933-34, **17**, 469.

3. The dissociation constants of sodium and potassium guaiaculates in guaiacol previously computed from electrical conductivity determinations are shown to be in agreement with the corresponding values obtained from the distribution measurements.

4. From theoretical considerations an equation is derived with which it is possible to predict the magnitude of the limiting partition coefficients from the dielectric constants of the solvents, the size of the solute ions, and the temperature.