# *Theory of the Influence of the Dielectric Constant on the Rate of Reaction in Solution with Application to Enzyme Reactions. I. Development of the Theory and its Application to Some Simple Systems**

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The rate of the reaction in solution involving ions or dipolar molecules is generally influenced by the dielectric constant of the medium, and this effect, termed the solvent effect, has been quantitatively interpreted by various authors in conformity to the electrostatic theories[1-5]. There is, however, marked inconsistency between the prediction of Amis-Jaffé's theory and that of Laidler-Eyring's for reactions between a negative ion and a dipolar molecule[2]. Recently Laidler and Landskroener developed a more general theory of the solvent effect[6] based on Kirkwood's model for a spherical solute molecule having an arbitrary charge

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[1] S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes", McGraw-Hill, New York (1954), p. 400.

[2] E. S. Amis, "Kinetics of Chemical Change in Solution", MacMillan Co., New York (1949), p. 153.

[3] E. S. Amis, *J. Chem. Educ.*, **28**, 635 (1951); **29**, 337 (1952); **30**, 351 (1953).

[4] E. A. Moelwyn-Hughes, "The Kinetics of Reactions in Solution", Oxford University Press, London (1947), p. 90, 120, 202.

[5] G. Scatchard, *J. Am. Chem. Soc.*, **52**, 52 (1930).

[6] K. J. Laidler and P. A. Landskroener, *Trans. Faraday Soc.*, **52**, 200 (1956).

distribution[7,8], considering the microscopic distribution of charges in the reactants and the activated complexes, which had not been taken into account explicitly in the previous treatments[1-5]. Their theory was applied to the interpretation of the effect of solvent on the rates of the acid and base hydrolyses of esters, amides and anilides, and the results were considered to be successful[6].

The influence of the dielectric constant upon the rates of several enzyme reactions have been treated quantitatively on the basis of simple models[9,10], which seem evidently inadequate to a large complex ion such as protein. The Kirkwood's model may be a suitable one for the treatment of the electrostatic properties of protein molecules[11-13]. Although Laidler-Landskroener's theory is based on this model, it is not applicable to enzyme reactions, because of the approximation made in its derivation, which is not adequate for the large molecules with their charges near the surface of the sphere.

In this paper, a theory of the solvent effect which is applicable to enzyme reactions as well as to reactions involving small ions or molecules is developed, based on the Kirkwood's model. The theory is applied to the interpretation of the effect of solvent on the dissociation constants of carboxylic acids and on the rate constants of unimolecular and bimolecular reactions of simple organic compounds. Application of the theory to enzyme reactions will be treated in the following paper.

## Theoretical

Kirkwood[7] obtained an expression for the work of charging, or the electrostatic free energy, of a spherical solute molecule of radius $b$, having a low dielectric constant $D_i$, within which are situated $M$ discrete point charges $e_1 \cdots e_M$, and which is immersed in a solvent of dielectric constant $D$, as illustrated in Fig. 1.

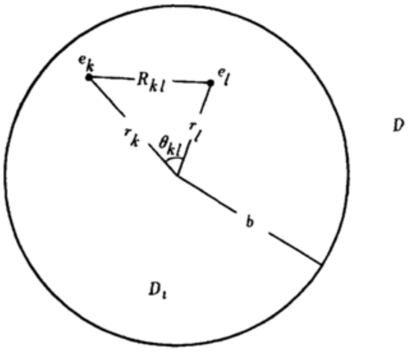

Fig. 1. Kirkwood's model for a spherical solute species having an arbitrary charge distribution.

For zero ionic strength, the work of charging, $W_0$, with respect to the energy zero for the completely discharged state, is expressed as follows[7,8,12,14]:

$$W_0=\frac{1}{2D_i}\sum_{k=1}^{M}\sum_{l=1}^{M}e_ke_l/R_{kl}+\frac{1}{2}\left(\frac{1}{D}-\frac{1}{D_i}\right)\sum_{n=0}^{\infty}\frac{(n+1)Q_n}{b^{2n+1}[(n+1)+nD_i/D]} \tag{1}$$

$$Q_n=\sum_{k=1}^{M}\sum_{l=1}^{M}e_ke_lr_k{}^nr_l{}^nP_n(\cos\theta_{kl}) \tag{2}$$

where $R_{kl}$ is the distance between the charges $e_k$ and $e_l$, $r_k$ and $r_l$ the distances of charges $e_k$ and $e_l$ from the center of the sphere, $\theta_{kl}$ the angle between $r_k$ and $r_l$, and $P_n(\cos\theta_{kl})$ is the Legendre polynomial. $Q_0$ is simply the square of the total net charge of the ion, and $Q_1$ is equal to the square of the dipole moment of the molecule. The succeeding $Q_n$'s involve the higher multipole moments, and depend not only upon the relative position of the charges, but also upon the distance of the charges from the surface of the sphere.

When the charges are situated not so near to the surface of the sphere, i. e., $r_k/b$ is not so close to unity, the summation in Eq. 1 converges rapidly, and the terms beyond $n=1$ can be dropped without serious error. This is the case in Laidler and Landskroener's treatment[6]. However, this approximation is not a reasonable one, especially when $b$ is large and the charges are situated near the surface, as is the case of a large complex ion such as protein. Now it is necessary to take the sum of the infinite series in Eq. 1. Since $D_i \ll D$ ($D_i$ was taken by Kirkwood to be 2), in a similar manner to Kirkwood's treatment[8], the sum is obtained by expanding the second term of Eq. 1 in increasing powers of $D_i/D$, and dropping all terms

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[7] J. G. Kirkwood, *J. Chem. Phys.*, **2**, 351 (1934).

[8] J. G. Kirkwood and F. H. Westheimer, ibid., **6**, 506 (1938).

[9] Y. Ogura et al., *Symposia on Enzyme Chem.* (*Kôso Kagaku Shimpojiumu*), **5**, 28 (1950); Y. Tonomura, *J. Japan. Biochem. Soc.*, (*Seikagaku*), **25**, 157 (1953).

[10] M. L. Barnard and K. J. Laidler, *J. Am. Chem. Soc.*, **74**, 6099 (1952); K. J. Laidler and M. C. Ethier, *Arch. Biochem. Biophys.*, **44**, 338 (1953).

[11] T. L. Hill, *J. Phys. Chem.*, **60**, 253 (1956); *J. Am. Chem. Soc.*, **78**, 3330 (1956); ibid., **78**, 5527 (1956).

[12] C. Tanford and J. G. Kirkwood, ibid. **79**, 5333 (1957).

[13] C. Tanford, ibid., **79**, 5340 (1957).

[14] The first term in Eq. 1 represents the work of charging in an unbounded medium of dielectric constant $D_i$, and is independent of the solvent. It contains self-energy terms (i. e., $k=l$), which are infinite because of the assumption of point charges. But this term does not appear in the final expression for the activity coefficient (Eq. 8 below). The second term represents the mutual electrostatic energy of the molecule and the solvent medium, and is the important term in the present treatment.

higher than the first. Finally we have[15]

$$W_0=\frac{1}{2D_i}\left[\sum_{k=1}^{M}\sum_{l=1}^{M}\frac{e_ke_l}{R_{kl}}-\frac{1}{b}\left(\sum_{k=1}^{M}e_k^2f'_{kk}+\sum_{k=1}^{M}\sum_{l\neq k}e_ke_lg'_{kl}\right)\right]+\frac{1}{2Db}\left[\sum_{k=1}^{M}e_k^2f_{kk}+\sum_{k=1}^{M}\sum_{l\neq k}e_ke_lg_{kl}\right] \tag{3}$$

where

$$\left.\begin{aligned} f_{kk}&=\frac{2}{1-x_{kk}}+\frac{1}{x_{kk}}\ln(1-x_{kk})\\ g_{kl}&=\frac{2}{(1-2\alpha_{kl}x_{kl}+x_{kl}^2)^{1/2}}\\ &\quad+\frac{1}{x_{kl}}\ln\frac{1-\alpha_{kl}}{(1-2\alpha_{kl}x_{kl}+x_{kl}^2)^{1/2}+x_{kl}-\alpha_{kl}}\end{aligned}\right\} \tag{4}$$

$$\left.\begin{aligned} f'_{kk}&=\frac{1}{1-x_{kk}}\\ g'_{kl}&=\frac{1}{(1-2\alpha_{kl}x_{kl}+x_{kl}^2)^{1/2}}\end{aligned}\right\} \tag{5}$$

where

$$\begin{aligned} x_{kl}&=r_kr_l/b^2;\quad x_{kk}=(r_k/b)^2\\ \alpha_{kl}&=\cos\theta_{kl}\end{aligned} \tag{6}$$

For zero ionic strength, the activity coefficient $\gamma$ of a solute species in the solvent of dielectric constant $D$ with respect to a standard solvent of dielectric constant $D_0$ ($D_0\gg D_i$) is related to the work of charging $W_0$ and $W_0^0$ in each solvent, respectively, in the following manner

$$\ln\gamma=(W_0-W_0^0)/\boldsymbol{k}T \tag{7}$$

where $\boldsymbol{k}$ is the Boltzmann constant and $T$ the absolute temperature. Insertion of Eq. 3 into Eq. 7 gives rise to

$$\ln\gamma=\frac{\varepsilon^2L}{2b\boldsymbol{k}T}\left(\frac{1}{D}-\frac{1}{D_0}\right) \tag{8}$$

where $\varepsilon$ is the protonic charge and $L$ is a new dimensionless parameter defined as

$$L=\sum_{k=1}^{M}\xi_k^2f_{kk}+\sum_{k=1}^{M}\sum_{l\neq k}\xi_k\xi_lg_{kl} \tag{9}$$

where $\xi_k$ is the valence of the charge $e_k$, i. e., $\xi_k=e_k/\varepsilon$. The value of $L$ is determined by the charge configuration of the species, i. e., $L$ is a function of $\xi$'s, $r$'s, $\theta$'s of the charges and the radius $b$. Thus $L$ will be conveniently termed "charge configuration function". $L/b$ represents the susceptibility of the electrostatic free energy of the solute species to the change in dielectric constant of the medium.

By the use of this new parameter $L$, a relationship between the rate or the equilibrium constant of a chemical change in solution and the dielectric constant of the solvent can readily be obtained. For example, let us consider the reaction

$$\mathrm{A+B}\rightleftharpoons\mathrm{X}_{\ddagger}\rightarrow\text{Products}$$

where the reactants A, B and the activated complex $X_{\ddagger}$ may be either ions or molecules with particular charge configuration. Let $k_0$ denote the rate constant in the standard solvent of dielectric constant $D_0$ ($D_0\gg D_i$), then the rate constant $k$ in a solvent of dielectric constant $D$ is[1]

$$k=k_0\gamma_A\gamma_B/\gamma_{\ddagger} \tag{10}$$

where the $\gamma$'s are the activity coefficients of the corresponding species. Using Eq. 8 we have

$$\ln k=\ln k_0+\frac{\varepsilon^2}{2\boldsymbol{k}T}\left(\frac{1}{D}-\frac{1}{D_0}\right)\left(\frac{L_A}{b_A}+\frac{L_B}{b_B}-\frac{L_{\ddagger}}{b_{\ddagger}}\right) \tag{11}$$

where $L$'s and $b$'s are the charge configuration functions and the radii of the species, respectively. This equation indicates that the plot of $\log k$ against $1/D$ gives a straight line and that the slope is

$$\frac{\mathrm{d}\log k}{\mathrm{d}(1/D)}=\frac{\varepsilon^2}{2.303\,(2\boldsymbol{k}T)}\left(\frac{L_A}{b_A}+\frac{L_B}{b_B}-\frac{L_{\ddagger}}{b_{\ddagger}}\right) \tag{12}$$

Thus the slope is determined by the charge configuration functions and the radii of the species.

In a similar manner, the relationship between the equilibrium constant $K$ and the dielectric constant of the medium, $D$, can be obtained. For the equilibrium

TABLE I. VALUES OF $f$ FOR VARIOUS VALUES OF $x$

| $x$ | $f$ | $x$ | $f$ |
|---|---|---|---|
| 0 | 1.000 | 0.925 | 23.866 |
| 0.05 | 1.079 | 0.930 | 25.712 |
| 0.1 | 1.169 | 0.935 | 27.846 |
| 0.2 | 1.384 | 0.940 | 30.340 |
| 0.3 | 1.668 | 0.945 | 33.294 |
| 0.4 | 2.056 | 0.950 | 36.847 |
| 0.5 | 2.614 | 0.955 | 41.197 |
| 0.6 | 3.473 | 0.960 | 46.647 |
| 0.7 | 4.947 | 0.965 | 53.669 |
| 0.8 | 7.988 | 0.970 | 63.052 |
| 0.83 | 9.630 | 0.975 | 76.217 |
| 0.85 | 11.101 | 0.980 | 96.008 |
| 0.88 | 14.257 | 0.985 | 129.070 |
| 0.90 | 17.442 | 0.990 | 195.348 |
| 0.91 | 19.576 | 0.995 | 394.675 |
| 0.92 | 22.255 | 1 | ∞ |

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15) Eq. 2 can be written as

$$Q_n=\sum_{k=1}^{M}e_k^2r_k^{2n}+\sum_{k=1}^{M}\sum_{l\neq k}e_ke_lr_k^nr_l^nP_n(\cos\theta_{kl})$$

When this is inserted into Eq. 1 and the summation is performed, the first term gives the $f$ and $f'$ terms and the second term gives the $g$ and $g'$ terms in Eq. 3.

TABLE II. VALUES OF $g$ FOR

| $\alpha \diagdown x$ | 0.1 | 0.2 | 0.3 | 0.4 | 0.5 | 0.6 | 0.7 | 0.8 | 0.85 | 0.90 |
|---|---|---|---|---|---|---|---|---|---|---|
| −1 | 0.865 | 0.755 | 0.664 | 0.587 | 0.522 | 0.467 | 0.418 | 0.376 | 0.357 | 0.339 |
| −0.9 | 0.876 | 0.772 | 0.683 | 0.607 | 0.542 | 0.485 | 0.436 | 0.392 | 0.372 | 0.354 |
| −0.8 | 0.887 | 0.789 | 0.703 | 0.628 | 0.563 | 0.505 | 0.454 | 0.409 | 0.389 | 0.370 |
| −0.7 | 0.899 | 0.807 | 0.725 | 0.651 | 0.585 | 0.527 | 0.475 | 0.428 | 0.407 | 0.387 |
| −0.6 | 0.911 | 0.827 | 0.748 | 0.676 | 0.610 | 0.551 | 0.497 | 0.449 | 0.427 | 0.406 |
| −0.5 | 0.924 | 0.847 | 0.773 | 0.702 | 0.637 | 0.577 | 0.522 | 0.473 | 0.450 | 0.428 |
| −0.4 | 0.936 | 0.868 | 0.799 | 0.732 | 0.667 | 0.607 | 0.551 | 0.499 | 0.475 | 0.452 |
| −0.3 | 0.950 | 0.891 | 0.828 | 0.764 | 0.700 | 0.639 | 0.582 | 0.528 | 0.503 | 0.479 |
| −0.2 | 0.963 | 0.915 | 0.859 | 0.799 | 0.737 | 0.677 | 0.618 | 0.562 | 0.536 | 0.510 |
| −0.1 | 0.977 | 0.941 | 0.893 | 0.838 | 0.779 | 0.719 | 0.659 | 0.601 | 0.573 | 0.546 |
| 0 | 0.992 | 0.968 | 0.930 | 0.882 | 0.826 | 0.767 | 0.706 | 0.646 | 0.617 | 0.588 |
| 0.1 | 1.007 | 0.997 | 0.971 | 0.931 | 0.881 | 0.823 | 0.762 | 0.699 | 0.668 | 0.637 |
| 0.2 | 1.022 | 1.028 | 1.015 | 0.986 | 0.943 | 0.889 | 0.828 | 0.763 | 0.730 | 0.697 |
| 0.3 | 1.038 | 1.061 | 1.065 | 1.050 | 1.017 | 0.968 | 0.909 | 0.842 | 0.807 | 0.771 |
| 0.4 | 1.055 | 1.096 | 1.120 | 1.123 | 1.104 | 1.065 | 1.009 | 0.941 | 0.904 | 0.865 |
| 0.5 | 1.072 | 1.135 | 1.182 | 1.209 | 1.211 | 1.187 | 1.138 | 1.071 | 1.032 | 0.990 |
| 0.6 | 1.090 | 1.176 | 1.253 | 1.311 | 1.344 | 1.345 | 1.312 | 1.250 | 1.209 | 1.163 |
| 0.7 | 1.108 | 1.222 | 1.333 | 1.435 | 1.515 | 1.561 | 1.562 | 1.515 | 1.475 | 1.426 |
| 0.8 | 1.128 | 1.271 | 1.427 | 1.590 | 1.747 | 1.877 | 1.956 | 1.960 | 1.931 | 1.883 |
| 0.9 | 1.148 | 1.325 | 1.537 | 1.789 | 2.080 | 2.398 | 2.702 | 2.916 | 2.961 | 2.953 |
| 0.92 | 1.152 | 1.336 | 1.561 | 1.836 | 2.166 | 2.547 | 2.945 | 3.270 | 3.363 | 3.388 |
| 0.94 | 1.156 | 1.348 | 1.586 | 1.886 | 2.260 | 2.720 | 3.248 | 3.750 | 3.930 | 4.021 |
| 0.96 | 1.160 | 1.360 | 1.613 | 1.939 | 2.365 | 2.925 | 3.640 | 4.450 | 4.810 | 5.058 |
| 0.98 | 1.164 | 1.372 | 1.640 | 1.995 | 2.482 | 3.171 | 4.172 | 5.597 | 6.433 | 7.208 |
| 0.99 | 1.166 | 1.378 | 1.654 | 2.025 | 2.546 | 3.313 | 4.518 | 6.527 | 7.980 | 9.679 |
| 0.995 | 1.168 | 1.381 | 1.661 | 2.041 | 2.579 | 3.391 | 4.720 | 7.163 | 9.210 | 12.123 |
| 0.997 | 1.168 | 1.382 | 1.664 | 2.047 | 2.593 | 3.423 | 4.808 | 7.466 | 9.859 | 13.671 |
| 0.998 | 1.168 | 1.383 | 1.665 | 2.050 | 2.600 | 3.439 | 4.853 | 7.630 | 10.231 | 14.671 |
| 0.999 | 1.168 | 1.384 | 1.667 | 2.053 | 2.607 | 3.456 | 4.899 | 7.804 | 10.643 | 15.895 |
| 1 | 1.169 | 1.384 | 1.668 | 2.056 | 2.614 | 3.473 | 4.947 | 7.988 | 11.101 | 17.442 |

* When $x$ is zero, the value of $g$ is equal to unity for any value of $\alpha$.

$$\mathrm{A+B \rightleftharpoons C+D}$$

the final expression is

$$\frac{\mathrm{d}\log K}{\mathrm{d}(1/D)}=\frac{\varepsilon^2}{2.303(2kT)}\left[\left(\frac{L_\mathrm{A}}{b_\mathrm{A}}+\frac{L_\mathrm{B}}{b_\mathrm{B}}\right)-\left(\frac{L_\mathrm{C}}{b_\mathrm{C}}+\frac{L_\mathrm{D}}{b_\mathrm{D}}\right)\right] \tag{13}$$

Assuming that the molecule or ion is a sphere within which each point charge is located at the center of each constituting atom, the value of $L$ of the molecule or ion with known charge configuration can be calculated using Eqs. 4, 6 and 9. For convenience of calculation, the values of $f$ and $g$ for various values of $x$ and $\alpha$ are tabulated in Tables I and II. For $x=0$, $f$ and $g$ are both equal to unity. The value of $g$ for $\alpha=1$ is equal to that of $f$ for the corresponding value of $x$. The value of $L$ is dependent on the position of the center to be chosen. It may be most reasonable to choose the center at the geometrical center of the

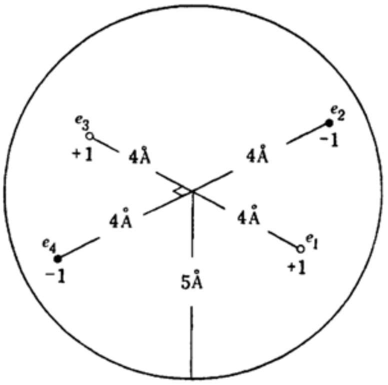

Fig. 2. A hypothetical dipolar ion. Two sets of charges, unit positive charges, $e_1$ anp $e_3$, and unit negative charges $e_2$ and $e_4$, are situated at equal distance 4 Å from the center, on the two diameters which are perpendicular to each other. The radius of the sphere is 5 Å.

VARIOUS VALUES OF $x$ AND $\alpha$*

| 0.91 | 0.92 | 0.93 | 0.94 | 0.95 | 0.96 | 0.97 | 0.98 | 0.99 | 1 | $x$ / $\alpha$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 0.336 | 0.333 | 0.329 | 0.326 | 0.323 | 0.319 | 0.316 | 0.313 | 0.310 | 0.307 | −1 |
| 0.350 | 0.347 | 0.343 | 0.340 | 0.336 | 0.333 | 0.330 | 0.326 | 0.323 | 0.320 | −0.9 |
| 0.366 | 0.362 | 0.359 | 0.355 | 0.351 | 0.348 | 0.344 | 0.341 | 0.338 | 0.334 | −0.8 |
| 0.383 | 0.379 | 0.376 | 0.372 | 0.368 | 0.364 | 0.361 | 0.357 | 0.354 | 0.350 | −0.7 |
| 0.402 | 0.398 | 0.394 | 0.390 | 0.386 | 0.383 | 0.379 | 0.375 | 0.371 | 0.368 | −0.6 |
| 0.424 | 0.419 | 0.415 | 0.411 | 0.407 | 0.403 | 0.399 | 0.395 | 0.391 | 0.387 | −0.5 |
| 0.447 | 0.443 | 0.439 | 0.434 | 0.430 | 0.426 | 0.422 | 0.417 | 0.413 | 0.409 | −0.4 |
| 0.474 | 0.470 | 0.465 | 0.460 | 0.456 | 0.451 | 0.447 | 0.442 | 0.438 | 0.434 | −0.3 |
| 0.505 | 0.500 | 0.495 | 0.490 | 0.486 | 0.481 | 0.477 | 0.471 | 0.467 | 0.462 | −0.2 |
| 0.541 | 0.535 | 0.530 | 0.525 | 0.520 | 0.515 | 0.510 | 0.505 | 0.500 | 0.495 | −0.1 |
| 0.582 | 0.576 | 0.571 | 0.565 | 0.560 | 0.554 | 0.549 | 0.544 | 0.538 | 0.533 | 0 |
| 0.631 | 0.625 | 0.619 | 0.613 | 0.607 | 0.602 | 0.596 | 0.590 | 0.584 | 0.578 | 0.1 |
| 0.691 | 0.684 | 0.678 | 0.671 | 0.665 | 0.658 | 0.652 | 0.646 | 0.639 | 0.633 | 0.2 |
| 0.764 | 0.757 | 0.750 | 0.743 | 0.736 | 0.729 | 0.722 | 0.714 | 0.708 | 0.701 | 0.3 |
| 0.858 | 0.850 | 0.842 | 0.834 | 0.826 | 0.818 | 0.810 | 0.803 | 0.795 | 0.787 | 0.4 |
| 0.981 | 0.972 | 0.964 | 0.955 | 0.946 | 0.937 | 0.928 | 0.919 | 0.910 | 0.901 | 0.5 |
| 1.154 | 1.144 | 1.134 | 1.124 | 1.114 | 1.104 | 1.093 | 1.083 | 1.072 | 1.062 | 0.6 |
| 1.415 | 1.404 | 1.393 | 1.381 | 1.369 | 1.357 | 1.344 | 1.332 | 1.319 | 1.306 | 0.7 |
| 1.871 | 1.858 | 1.845 | 1.831 | 1.817 | 1.802 | 1.786 | 1.770 | 1.753 | 1.736 | 0.8 |
| 2.944 | 2.933 | 2.921 | 2.905 | 2.888 | 2.869 | 2.848 | 2.824 | 2.799 | 2.772 | 0.9 |
| 3.383 | 3.376 | 3.365 | 3.352 | 3.335 | 3.315 | 3.293 | 3.267 | 3.239 | 3.208 | 0.92 |
| 4.026 | 4.027 | 4.022 | 4.013 | 3.999 | 3.981 | 3.957 | 3.929 | 3.897 | 3.860 | 0.94 |
| 5.088 | 5.111 | 5.125 | 5.131 | 5.128 | 5.116 | 5.095 | 5.066 | 5.029 | 4.983 | 0.96 |
| 7.335 | 7.448 | 7.544 | 7.622 | 7.678 | 7.711 | 7.720 | 7.706 | 7.666 | 7.602 | 0.98 |
| 10.018 | 10.343 | 10.645 | 10.917 | 11.149 | 11.330 | 11.454 | 11.514 | 11.504 | 11.425 | 0.99 |
| 12.808 | 13.512 | 14.222 | 14.915 | 15.565 | 16.137 | 16.594 | 16.900 | 17.026 | 16.955 | 0.995 |
| 14.665 | 15.740 | 16.884 | 18.074 | 19.270 | 20.407 | 21.399 | 22.143 | 22.542 | 22.531 | 0.997 |
| 15.909 | 17.295 | 18.832 | 20.513 | 22.300 | 24.113 | 25.811 | 27.192 | 28.027 | 28.138 | 0.998 |
| 17.486 | 19.352 | 21.549 | 24.134 | 27.148 | 30.572 | 34.241 | 37.713 | 40.216 | 40.899 | 0.999 |
| 19.576 | 22.255 | 25.712 | 30.340 | 36.847 | 46.647 | 63.052 | 96.008 | 195.348 | ∞ | 1 |

molecule or ion concerned. As an example, $L$ of a hypothetical dipolar ion such as that depicted in Fig. 2 is calculated to be 11.8. The procedure of the calculation is illustrated in Appendix I.

For a spherical ion including a charge $Z\varepsilon$ at its center, $L$ is simply $Z^2$ (since $x=0$ and $f$ is unity). Thus for a reaction between such unipolar ions Eq. 12 reduces to the familiar expression of Laidler-Eyring for reactions between ions[1].

For the purpose of comparison, Laidler-Landskroener's equation[6], which corresponds to Eq. 12, is cited below;

$$\frac{\mathrm{d}\log k}{\mathrm{d}(1/D)}=\frac{\varepsilon^2}{2.303(2\boldsymbol{k}T)}\left[\left(\frac{Z_A{}^2}{b_A}+\frac{Z_B{}^2}{b_B}-\frac{(Z_A+Z_B)^2}{b_\ddagger}\right)+\frac{3}{2}\left(\frac{G_A}{b_A{}^3}+\frac{G_B}{b_B{}^3}-\frac{G_\ddagger}{b_\ddagger{}^3}\right)\right] \qquad (14)$$

where $b$ and $Z$ represent the radius and the net charge of the species, respectively, and $G$ is a quantity determined by the given charge distribution in the species, which is proportional to the square of the dipole moment.

## Application of the Theory to Some Simple Systems

Before applying the theory to enzyme reactions, it is desirable to test its applicability to some simple systems, for which the structure and the charge distribution in the species concerned can be visualized with considerable certainty. Three examples will be treated here; first, the dissociation equilibria of carboxylic acids; second, the $S_N1$ solvolysis; and third, the acid and base catalyzed hydrolyses of esters, amides and anilides.

**Dissociation of Carboxylic Acids.** — The dissociation constants of some carboxylic acids have been measured by several authors in

TABLE III. THE INFLUENCE OF THE DIELECTRIC CONSTANT UPON THE DISSOCIATION CONSTANTS OF CARBOXYLIC ACIDS

| Acid | Temp. °C | Solvent[a] | Dissociation constant | $\frac{d(pK)}{d(1/D)}$ | $b$(Å)[b] |  | $d$(Å)[b] |  |
|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | I | II | I | II |
| Acetic | 25 | (W, W-E<br>W-D) | $K$ | 118 | 2.97 |  | 1.33 |  |
| Benzoic | 20 | (W, W-E<br>W-D) | $K$ | 170 | 3.75 |  | 0.65 |  |
| Succinic | 20 | (W, W-E<br>W-M, W-D) | $K_1$ | 133<br>150 | 4.30<br>4.07 | 4.40<br>4.10 | 1.09<br>0.86 | 1.19<br>0.89 |
|  |  |  | $K_2$ | 178<br>200 | 3.73<br>3.48 | 3.80<br>3.50 | 1.01<br>0.76 | 1.08<br>0.78 |
| Adipic | 20 | (W, W-E<br>W-D) | $K_1$ | 147 |  | 4.84 (all *trans*)<br>3.95 (di-*cis*) |  | 0.99<br>0.94 |
|  |  |  | $K_2$ | 164 |  | 4.88 (all *trans*)<br>4.06 (di-*cis*) |  | 1.03<br>1.05 |
| Azelaic | 20 | (W, W-E<br>W-M, W-D) | $K_1$ | 135 |  | 6.84 (all *trans*)<br>5.84 (tri-*cis*) |  | 1.23<br>1.21 |
|  |  |  | $K_2$ | 140 |  | 6.98 (all *trans*)<br>6.03 (tri-*cis*) |  | 1.37<br>1.40 |

a) W: water, E: ethanol, M: methanol, D: dioxane.

b) $b$ (or $d$) indicates the radius (or the depth of the charge on the oxygen atom in $COO^-$) of $A^-$, $AH^-$ or $A^=$ corresponding to the dissociation constant $K$, $K_1$ or $K_2$, respectively.
I: Calculated by Method I. II: Calculated by Method II.

various mixed aqueous solvents. The apparent dissociation constant $K_a$ of an acid AH ($K_a = [H^+][A^-]/[AH]$) in various mixed solvents having equal dielectric constants does not give the same value in different media having different water concentrations[16,17]. Yasuda[18] proposed that the dissociation constant $K$ of an acid in aqueous mixed solvents should be given by the following equation:

$$K = [A^-][H_3O^+]/[AH][H_2O]$$

corresponding to the equilibrium

$$AH + H_2O \rightleftharpoons H_3O^+ + A^-$$

He found that the plot of p$K$, instead of p$K_a$, of an acid against $1/D$ becomes a single straight line, irrespective of the sort of mixed solvent used, unless $1/D$ exceeds ca. 0.02[18]. Therefore, it may be reasonable to conclude that the variation in p$K$ is essentially due to the change in the dielectric constant of the medium, at least in the range stated above. The slope d(p$K$)/d($1/D$) is written as follows;

$$-\frac{d(pK)}{d(1/D)} = \frac{\varepsilon^2}{2.303(2kT)}\left(\frac{L_{AH}}{b_{AH}} + \frac{L_{H_2O}}{b_{H_2O}} - \frac{L_{A^-}}{b_{A^-}} - \frac{L_{H_3O^+}}{b_{H_3O^+}}\right) \qquad (15)$$

Values of the slopes obtained from Yasuda's results for several carboxylic acids are summarized in Table III, where $K_1$ and $K_2$ are the first and the second dissociation constants of dibasic acids, respectively.

$$K_1 = [AH^-][H_3O^+]/[AH_2][H_2O]$$

$$K_2 = [A^=][H_3O^+]/[AH^-][H_2O]$$

Procedure of testing the theory is as follows; first, for the three species, $H_2O$, $H_3O^+$ and AH (or $AH_2$ for the dibasic acid), $L/b$'s are calculated from the charge configurations and the radii of these species; insertion of these values together with the value of the slope into Eq. 15 leads to an equation for $L_{A^-}/b_{A^-}$; if the magnitudes and the relative positions of the charges in $A^-$ are known, $L_{A^-}$ and $L_{A^-}/b_{A^-}$ are the functions of $b_{A^-}$ only; then the equation can be solved for $b_{A^-}$[19]. If the theory is correct, $b_{A^-}$ thus obtained should be of reasonable magnitude as is expected from the structure of $A^-$. The geometry and the charge distribution of the species which are necessary for the calculation of $L$'s are summarized in Appendix II.

Succinic acid was treated by the following two methods. In Method I, the charge distribution in the COOH group was considered explicitly in the evaluation of $L_{AH_2}$ and $L_{AH^-}$ as in the case of acetic acid and benzoic acid. Since $L_{AH_2}$ was found to be appreciably small,

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[16] J. C. Speakman, *J. Chem. Soc.*, **1943**, 270.

[17] M. L. Dondon. *J chim. phys.*, **54**, 290, 304 (1957).

[18] M. Yasuda, This Bulletin, **32**, 429 (1959).

[19] Practically $b_{A^-}$ is obtained in the following manner. For several fixed values of $b_{A^-}$ suitably chosen, $L_{A^-}$'s are calculated and $L_{A^-}/b_{A^-}$ is plotted against $b_{A^-}$. By graphical interpolation $b_{A^-}$ to be solved is readily found.

TABLE IV. THE INFLUENCE OF SOLVENT UPON THE RATE CONSTANTS OF $S_N1$ SOLVOLYSIS

| Compound | Temp. °C | Solvent[a] | $\frac{d \log k_1}{d(1/D)}$ | Model | Type | Present theory $b_{\ddagger}$(Å) | Present theory $d$(Å)[b] | L-L theory $b_{\ddagger}$(Å)[c] |
|---|---|---|---|---|---|---|---|---|
| *tert*-Butyl chloride | 25 | (W-E, W-M<br>W-A, HCOOH) | −179 | I | (1)<br>(2) | 3.12<br>3.10 | 0.48<br>0.46 | 1.92 |
| | | | | II | (1)<br>(2) | 2.41<br>2.36 | 0.47<br>0.42 | |
| *tert*-Butyl bromide | 25 | (W-E, W-A) | −127 | I | (1)<br>(2) | 3.50<br>3.46 | 0.64<br>0.60 | 2.27 |
| | | | | II | (1)<br>(2) | 2.72<br>2.65 | 0.62<br>0.55 | |
| Benzhydryl chloride | 25 | W-E | −122 | I | (2) | 3.84 | 0.60 | 2.19 |
| | | W-A | −137 | I | (2) | 3.79 | 0.55 | 2.10 |
| α-Phenethyl chloride | 50 | W-E | −166 | I | (2) | 3.92 | 0.45 | 1.99 |
| | | W-A | −150 | I | (2) | 3.96 | 0.49 | 1.92 |
| Neopentyl bromide | 95 | (W-E<br>HCOOH) | −162 | I | (2) | 3.62 | 0.42 | 1.96 |
| Pinacolyl-*p*-bromobenzene sulfonate | 70 | (W-E, W-A<br>$Ac_2O$-AcOH) | −103 | I | (2) | 8.05 | 0.60 | 2.34 |
| α-Methylallyl chloride | 25 | (W, W-E) | −161 | I | (2) | 3.48 | 0.49 | 1.99 |

a) W: water, E: ethanol, M: methanol, A: acetone.

b) The depth of the charge on the halogen atom from the surface.

c) $b_{\ddagger}$ calculated by the present author with Laidler-Landskroener's equation (Eq. 14).

in Method II, $L_{AH_2}$ and $L_{AH^-}$ were evaluated assuming that the charge on every atom in the COOH group is zero. This greatly simplifies the calculation, without affecting the results seriously (compare *b*'s for I and II in Table III). Hence, adipic acid and azelaic acid were treated by Method II. For these two acids calculations were made for the all *trans* form and the di-*cis* or tri-*cis* form (see Appendix II).

The results of the calculations are summarized in Table III. In the last two columns are presented the values of *d*, the depth of the charge on the oxygen atom in the $COO^-$ group from the surface of the sphere[20]. It is noted that *d*'s are nearly constant for the acids in spite of the wide variation in *b*'s.

**$S_N1$ Solvolysis.** — The influence of the dielectric constant of the medium upon the rate constant $k_1$ of $S_N1$ solvolysis has been discussed by Shingu and Okamoto[21]. The linear relationship between $\log k_1$ and $1/D$ was interpreted quantitatively on the basis of an ion-pair model for the activated complex. In the present study, the activated complex itself is treated as a sphere, within which positive and negative charges are assumed to be located at the centers of the carbon and halogen atoms, respectively. The equation to be used is as follows;

$$\frac{d \log k_1}{d(1/D)} = \frac{\varepsilon^2}{2.303\,(2kT)}\left(\frac{L_A}{b_A} - \frac{L_{\ddagger}}{b_{\ddagger}}\right) \tag{16}$$

where $L_A/b_A$ and $L_{\ddagger}/b_{\ddagger}$ are concerned with the reactant molecule and the activated complex, respectively. In the manner similar to that of the preceding example, the radius of the activated complex $b_{\ddagger}$ was determined to fit the experimentally obtained slope.

For *tert*-butyl chloride and *tert*-butyl bromide the charge distributions were calculated from the observed dipole moments[22,23] considering the inductive effect[24], and the $L_A$'s were estimated. Since it was found that they are sufficiently small (see Appendix II), and the final values of $b_{\ddagger}$ are only slightly affected by ignoring them (by 0.01 Å or less), $L_A/b_A$ in Eq. 16 was approximated to zero for the present example. In the activated complexes the carbon-halogen bond lengths were assumed to be increased 50% (Model I) or 10% (Model II) over the normal bond lengths. In calculating *L*, two types of charge distribution were assumed for the activated complexes. Type 1

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[20] *d* is equal to *b* minus *r* for the oxygen atom.

[21] H. Shingu and K. Okamoto, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **78**, 558 (1957).

[22] L. E. Sutton, "Determination of Organic Structures by Physical Methods", edited by E. A. Braud and F. C. Nachod, Academic Press, New York (1955), p. 392.

[23] C. P. Smyth, "Dielectric Behavior and Structure", McGraw-Hill, New York (1955).

[24] R. P. Smith, T. Ree, J. L. Magee and H. Eyring, *J. Am. Chem. Soc.*, **73**, 2263 (1951); R. P. Smith and H. Eyring, ibid., **74**, 229 (1952).

consists of a unit negative charge on the halogen atom, and compensating positive charges distributed on the remaining atoms in the same proportion to those in the normal molecules. In Type 2, simplification was made, so that a unit positive charge is localized solely on the $\alpha$-carbon atom, neglecting the charges on the remaining atoms except for a unit negative charge on the halogen atom. Calculation showed that the solved $b_{\ddagger}$'s are somewhat smaller in Type 2. Since the difference in $b_{\ddagger}$'s is not serious, the other five compounds were treated with the simplified models (Type 2), assuming that the carbon-halogen bond lengths in the activated complexes are increased 50% over the normal ones (Model I).

The results are listed in Table IV, where $b_{\ddagger}$'s calculated with Laidler-Landskroener's equation (Eq. 14) are also included. $d$ indicates the depth of the charge on the halogen atom from the surface of the sphere. It is noticed that $d$'s, in contrast to $b_{\ddagger}$'s, are not affected appreciably by the choice between Models I and II.

**III. Acid and Base Catalyzed Hydrolyses of Esters, Amides and Anilides.**—As an example of bimolecular reactions, and for the purpose of comparing the applicability of the present theory with that of Laidler-Landskroener's, the acid and base hydrolyses of certain esters, amides and anilides are treated along the same line and on exactly the same models for the activated complexes as those they proposed[6]. The relevant equation is

$$\frac{\mathrm{d}\log k}{\mathrm{d}(1/D)}=\frac{\varepsilon^2}{2.303(2kT)}\left(\frac{1}{b_{\mathrm{A}}}-\frac{L_{\ddagger}}{b_{\ddagger}}\right) \tag{17}$$

where $k$ denotes the bimolecular rate constant, $b_{\mathrm{A}}$ the radius of a hydronium or hydroxyl ion, and $L_{\ddagger}$ and $b_{\ddagger}$ refer to the activated complex. In accordance with Laidler-Landskroener's treatment, it was assumed that the hydronium and the hydroxyl ions are unipolar ions (the charge is located at the center of the ion) with the radii of 1.70 Å[25] and 1.40 Å[26],

TABLE V. THE INFLUENCE OF SOLVENT UPON THE RATE CONSTANTS OF THE ACID AND BASE HYDROLYSES OF ESTERS, AMIDES AND ANILIDES

| Compound | Catalyst | Temp. °C | Solvent[a] | $\frac{\mathrm{d}\log k}{\mathrm{d}(1/D)}$ | $b_{\ddagger}$ (Å) L-L theory[b] | $b_{\ddagger}$ (Å) Present theory C[c] | $b_{\ddagger}$ (Å) Present theory P[d] |
|---|---|---|---|---|---|---|---|
| Ethyl acetate | $H_3O^+$ | 35 | W-D | −11 | 4.6 | 5.39 | 4.29 |
| | | 35 | W-A | −34 | 4.1 | 5.08 | 3.97 |
| Methyl propionate | $H_3O^+$ | 35.3 | W-A | −31 | 4.2 | 5.11 | 4.00 |
| Ethyl acetate | $OH^-$ | 25 | W-D | −24 | 1.9 | 4.47 | 3.56 |
| | | | W-A | −32 | 1.8 | 4.45 | 3.51 |
| | | | W-*i*Pr | −50 | 1.7 | 4.41 | 3.42 |
| | | | W-*t*Bu | −61 | 1.7 | 4.39 | 3.38 |
| | | | W-*n*Pr | −74 | 1.6 | 4.37 | 3.34 |
| | | | W-E | −96 | 1.5 | 4.35 | 3.29 |
| | | | W-M | −155 | 1.3 | 4.31 | 3.20 |
| Formanilide | $H_3O^+$ | 30 | W-E | −13.8 | 3.7 | 4.33 | 3.65 |
| Form-*o*-toluidide | $H_3O^+$ | 30 | W-E | −14.5 | 3.7 | 4.32 | 3.64 |
| Form-*p*-toluidide | $H_3O^+$ | 40 | W-E | −13.8 | 3.7 | 4.32 | 3.65 |
| *o*-Nitro-acetanilide | $H_3O^+$ | 80 | W-E | − 5.5 | 3.9 | 4.42 | 3.76 |
| Acetanilide | $H^3O^+$ | 80 | W-E | − 5.4 | 3.9 | 4.42 | 3.76 |
| Aceto-*m*-toluidide | $H_3O^+$ | 80 | W-E | − 7.8 | 3.8 | 4.38 | 3.72 |
| Acetamide | $H_3O^+$ | 80 | W-E | −42.1 | 3.2 | 4.09 | 3.37 |
| Propionamide | $H_3O^+$ | 80 | W-E | −39.7 | 3.2 | 4.10 | 3.38 |
| Acetamide | $OH^-$ | 80 | W-E | −71.3 | 1.6 | 4.39 | 3.34 |
| Propionamide | $OH^-$ | 80 | W-E | −68.4 | 1.6 | 4.39 | 3.35 |

a) W: water, E: ethanol, M: methanol, D: dioxane, *i*Pr: isopropanol, *n*Pr: *n*-propanol, *t*Bu: *tert*-butanol.

b) Values calculated by Laidler and Landskroener[6].

c) Center: Carbonyl carbon atom.

d) Center: Point P depicted in Fig. A-5 in Appendix II.

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[25] J. D. Bernal and R. H. Fowler, *J. Chem. Phys.*, **1**, 515 (1933).

[26] J. Buchanan and S. D. Hamann, *Trans. Faraday Soc.*, **49**, 1425 (1953).

respectively. Hence their $L$'s are unity. $L$'s of the substrate molecules were also approximated to zero. By Eq. 17, $b_{\ddagger}$'s were determined to fit the observed slopes using their models for the activated complexes (see Fig. A-5 in Appendix II). The results are listed in Table V. In the column of $b_{\ddagger}$, L-L indicates Laidler-Landskroener's values[6], and C or P denotes the results of the present study when the center of the activated complex is taken at the carbonyl carbon atom as in Laidler-Landskroener's calculation, or at the point P depicted in the models, respectively.

## Discussion

In the previous theories of the solvent effect[1-5], an ion or a molecule was treated as a uniformly charged sphere or a dipole, respectively, disregarding the actual distribution of charges within them. It is more reasonable to treat the reactants and the activated complex as those having the particular distribution of charges. In this sense, Laidler-Landskroener's treatment[6] and the present one may be said to be more accurate and general than the previous treatments.

However, as seen from Tables IV and V, the radii of the activated complexes calculated according to Laidler-Landskroener's formula are unreasonably too small for the $S_N1$ solvolysis and the base hydrolysis of esters and amides. These values of radii would lead to an improbable situation where some of the charges are extruded out of the sphere, which is obviously inconsistent with the Kirkwood's model on which the theory is based. On the other hand, the application of the present theory to the above three examples has revealed that the radii of the species concerned are of quite reasonable magnitude as are to be expected from the structures of the species. It is evident from Example III that this discrepancy has come from the approximation made in the derivation of Laidler-Landskroener's equation in which the higher terms were dropped in the sum in Eq. 1, the other circumstances being equal in both treatmnets. The difference between the two theories may be most clearly illustrated in the following example. Suppose a unimolecular reaction in which the reactant is a neutral molecule having no distribution of charge and the activated complex is such as is shown in Fig. 2. Since both the net charge and the dipole moment are zero, the slope $\mathrm{d}\log k/\mathrm{d}(1/D)$ predicted by Laidler-Lands-kroener's equation (Eq. 14) is zero. On the other hand, the slope predicted by the present theory at 25°C is

$$\frac{\mathrm{d}\log k}{\mathrm{d}(1/D)}=-\frac{\varepsilon^2}{2.303(2kT)}\left(\frac{L}{b}\right)=-121.7\times\frac{11.8}{5}$$

$$=-286 \qquad (18)$$

The value of $L$ depends sensitively upon the depth of the charge, $d$, at which the charge is located within the sphere. It is worthwhile to examine the values of $d$ determined to fit the observed slopes in the above examples, since they serve as a more rigorous check for the validity of the theory than the radii do.

In treating the interaction energies between charges on organic ions, as reflected in p$K$'s of dibasic acids and amino acids, based on the Kirkwood's model, Tanford[27] showed that the interaction energies critically depend upon the depth, $d$, of the charges, and it is necessary that $d$ be assigned a value close to 1.0 Å to account for experimentally observed interaction energies. He also found[13] that in calculating titration curves for simple protein model molecules using the Kirkwood model, merely by placing charges about 1 Å below the surfaces the titration curves can be obtained with a slope whose order of magnitude is in the best agreement with that observed experimentally.

Application of the present theory to the dissociation of carboxylic acids showed, as seen from Table III, that $d$'s of the charge on the oxygen atom in the carboxylate group are of nearly constant value around 1.0 Å within the error of the slope[28]. It is of interest to see that these values of $d$ are in good agreement with Tanford's value obtained from the calculation of interaction energies stated above, although different lines of approach have been made. These values of $d$ are comparable to the van der Waals radius (1.40 Å) or the ionic radius (1.4 Å) of oxygen atom[29]. Considering the simplicity of the Kirkwood model, the agreement may be considered to be satisfactory.

The depths, $d$'s calculated for the $S_N1$ solvolysis are also nearly constant for the series of compounds, but are considerably smaller compared with the van der Waals or ionic radii of the halogen atoms[29]. However, we have good reasons to accept the first example (variation of p$K$ of carboxylic acids with $D$) as the most reliable one, for in the remaining two examples the structures and the charge configurations of the activated complexes are essentially speculative in nature and are not so definitely established. In addition there is

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27) C. Tanford, *J. Am. Chem. Soc.*, **79**, 5348 (1957).

28) The error in the slope may amount to ca. 10%, which leads to an uncertainty of 0.2 Å in $b$ or $d$.

29) L. Pauling, "The Nature of the Chemical Bond", Cornell University Press, New York (1940).

some possibility that an influence other than that of the dielectric constant might be included in the experimentally determined slopes. In fact, for the $S_N1$ solvolysis of *tert*-butyl chloride, Okamoto and Shingu[30] have pointed out that the solvent molecules containing one or more hydroxyl groups have some specific effect in accelerating the solvolytic reaction, and this effect is to be distinguished from the dielectric constant effect. Therefore, the observed slopes may be, at least in part, attributed to this specific effect caused by changing the composition of mixed solvents. The true slopes may be less negative, which may lead to larger values of $d$ in the above calculations.

Since the present theory has been developed for zero ionic strength, a comment will be needed about the influence of ionic strength, $\mu$, on the theoretical expressions. According to Kirkwood, the work of charging $W$ of the spherical molecule stated above in the presence of external ions in the solvent is[7]

$$W = W_0 + W_{\text{ion}} \tag{19}$$

where $W_0$ is a work of charging at zero ionic strength which was already expressed in Eq. 1, and $W_{\text{ion}}$ is a term arising from the presence of external ions and is given in the following formula[7,12]

$$W_{\text{ion}} = -\frac{\varepsilon^2}{2a}\sum_{k=1}^{M}\sum_{l=1}^{M}\xi_k\xi_l\,C_{kl} \tag{20}$$

where $a$ is the mean distance of closest approach of ions in the solvent to the solute species and $C_{kl}$ is a complex function of $D$, $D_i$, $a$, $\mu$ and the charge configuration of the species, and is difficult to manage in a simple manner. However, at low ionic strength[31] it is a good approximation to write $C_{kl}$ as

$$C_{kl} \simeq \frac{1}{D}\cdot\frac{\kappa a}{1+\kappa a} \tag{21}$$

where $\kappa$ is the Debye-Hückel parameter

$$\kappa = \sqrt{8\pi N\varepsilon^2\mu/1000DkT} \tag{22}$$

and is also a function of $D$. In a manner similar to that of Eq. 7 through Eq. 13, an expression for $\mathrm{d}\log k/\mathrm{d}(1/D)$ in the presence of ions, corresponding to, e. g., Eq. 12, is obtained as follows;

$$\frac{\mathrm{d}\log k}{\mathrm{d}(1/D)} = \frac{\varepsilon^2}{2.303(2kT)}\left[\left(\frac{L_A}{b_A}+\frac{L_B}{b_B}-\frac{L_\ddagger}{b_\ddagger}\right) - \frac{\mathrm{d}}{\mathrm{d}(1/D)}\left(\frac{\Phi_A}{a_A}+\frac{\Phi_B}{a_B}-\frac{\Phi_\ddagger}{a_\ddagger}\right)\right] \tag{23}$$

where

$$\Phi = \sum_{k=1}^{M}\sum_{l=1}^{M}\xi_k\xi_l C_{kl} \simeq \frac{Z^2}{D}\cdot\frac{\kappa a}{1+\kappa a} \tag{24}$$

since $\sum_{k=1}^{M}\sum_{l=1}^{M}\xi_k\xi_l$ is equal to the square of the total net charge $Z^2$ of the species. The second term in the right hand side in Eq. 23 represents a contribution of the term dependent on ionic strength to the slope. The contribution at various ionic strengths was estimated for the reaction

$$\mathrm{A}+\mathrm{B} \rightleftharpoons \mathrm{X}_\ddagger \rightarrow \text{Products}$$

for which $a_A = a_B = 5\,\text{Å}$ and $a_\ddagger = 6\,\text{Å}$, at 25°C and $D$=78.5. The results are summarized in Table VI, where $\varphi$ designates the contribution of the term dependent on ionic strength to the slope.

$$\varphi \equiv \frac{\varepsilon^2}{2.303\,(2kT)}\cdot\frac{\mathrm{d}}{\mathrm{d}(1/D)}\left(\frac{\Phi_A}{a_A}+\frac{\Phi_B}{a_B}-\frac{\Phi_\ddagger}{a_\ddagger}\right) \tag{25}$$

TABLE VI. THE CONTRIBUTION OF THE TERM DEPENDENT ON IONIC STRENGTH TO THE SLOPE

| $\mu$ | $\varphi$ | | |
|---|---|---|---|
| | $Z_A=+1$<br>$Z_B=+1$ | $Z_A=+1$<br>$Z_B=-1$ | $Z_A=\pm1$<br>$Z_B=0$ |
| 0.01 | − 9.2 | 9.9 | 0.17 |
| 0.04 | −14.7 | 16.7 | 0.49 |
| 0.09 | −18.2 | 21.6 | 0.83 |
| 0.25 | −23.1 | 28.1 | 1.26 |
| 0.49 | −24.9 | 32.2 | 1.83 |
| 1.0 | −26.0 | 37.0 | 2.75 |

$\varphi$ is seen to be positive or negative according as the charges of the reactant ions are of opposite or like sign, and to be small if one of the reactants has no net charge. Although the $\varphi$ is only approximate especially at high ionic strengths, it may serve as a rough estimate of the contribution of the term dependent on ionic strength to the slope.

## Summary

A theory has been developed on the relationship between the equilibrium constant or the rate constant of a reaction and the dielectric constant of the solvent based on the Kirkwood's model. It is applicable to equilibrium states or reaction processes in which ions or molecules having arbitrary charge distributions are involved, including enzyme reactions. The theory predicts that there is a linear relationship between the logarithm of the equilibrium or rate constant and the reciprocal of the dielectric constant of the solvent. The slope is determined by the new parameter $L$, termed the charge

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[30] K. Okamoto and H. Shingu, reported at the Symposium on Mechanisms of Organic Reactions, Tokyo, 1959.

[31] Ionic strength up to $\kappa a$=0.5 with charges near the surface, and to even higher values of $\kappa a$ for charges appreciably below the surface[12].

configuration function, and the radius of each species involved. $L$ of a species is a function of the magnitudes and the relative positions of charges in it and its radius. Tables have been presented in order to facilitate the evaluation of $L$.

The applicability of the theory has been tested for the dissociation of carboxylic acids, the $S_N1$ solvolysis of organic halides, and the acid and base hydrolyses of esters, amides and anilides, and the results are found to be satisfactory.

The influence of ionic strength on the theoretical expressions has also been discussed.

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### Appendix I

**Evaluation of *L*.** — The charge configuration function $L$ of the hypothetical dipolar ion depicted in Fig. 2 is evaluated as follows; $L$ is written as

$$L=\xi_1^2f_{11}+\xi_2^2f_{22}+\xi_3^2f_{33}+\xi_4^2f_{44}+2\xi_1\xi_2g_{12}+2\xi_1\xi_3g_{13}$$
$$+2\xi_1\xi_4g_{14}+2\xi_2\xi_3g_{23}+2\xi_2\xi_4g_{24}+2\xi_3\xi_4g_{34}$$

where

$$\xi_1=\xi_3=-\xi_2=-\xi_4=1$$

And

$$b=5\text{ Å}$$
$$r_1=r_2=r_3=r_4=4\text{ Å}$$
$$x_{11}=x_{22}=\cdots\cdots=x_{12}=\cdots\cdots=x_{34}=(r/b)^2=0.64$$
$$\alpha_{12}=\alpha_{14}=\alpha_{23}=\alpha_{34}=\cos 90°=0$$
$$\alpha_{13}=\alpha_{24}=\cos 180°=-1$$

The values of $f(x)$ and $g(x,\alpha)$ are given from Tables I and II as follows;

$$f_{11}=f_{22}=f_{33}=f_{44}=3.98$$
$$g_{12}=g_{14}=g_{23}=g_{34}=0.743$$
$$g_{13}=g_{24}=0.447$$

Hence $L$ is evaluated to be

$$L=4\times3.98-2\times4\times0.743+2\times2\times0.447=11.76$$

### Appendix II

The geometry and the charge distribution necessary for the calculation of $L$'s in the above three examples are summarized here. $r$'s and $\theta$'s are readily computed from them with trigonometry. A–B designates the distance between atoms A and B, $\xi_A$ the valence of the charge on A. The positions of the centers of the species are also shown. The procedure of determining $b$ to fit the observed slope is illustrated for the acetate ion.

**Dissociation of Carboxylic Acids.**

1) $H_2O$ :— O–H $=0.96$ Å, $\angle$HOH $=105°$[29]. $\xi_0=-0.66$, $\xi_H=0.33$ (calculated from the dipole moment[23]). Center: Oxygen atom. $b=1.40$ Å[32]. $L$ calculated $=0.263$.

2) $H_3O^+$ :— O–H $=1.01$ Å, $\angle$HOH $=117°$[33] (pyramidal structure with equivalent H). $\xi_H=0.50$, $\xi_0=-0.50$. Center: Oxygen atom. $b=1.70$ Å. $L$ calculated $=1.266$.

3) Carboxyl group :—The structure of the carboxyl group[23] for acetic acid, benzoic acid and succinic acid (Method I) is shown in Fig. A-1. All the atoms are assumed to lie on the same plane[34]. The charge distribution is shown in the individual articles below.

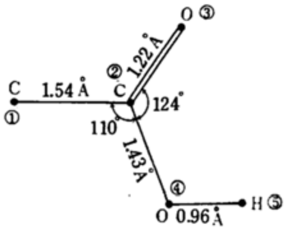

Fig. A-1. The structure of the carboxyl group. The atoms are numbered as indicated.

4) Carboxylate group :—The structure[35] and the charge distribution of the carboxylate group is depicted in Fig. A-2. This was used as the carboxylate model in every acid anion throughout this

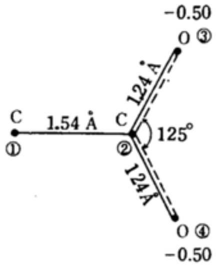

Fig. A-2. The structure of the carboxylate group. The atoms are numbered as indicated. The valences of the charges on the oxygen atoms are also shown.

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32) R. W. Gurney, "Ionic Processes in Solution", McGraw-Hill, New York (1953), p. 16.

33) S. Seki et al., "Gendai Kagaku", VIG, Iwanami, Tokyo (1956), p. 51.

34) R. F. Curl, *J. Chem. Phys.*, **30**, 1529 (1959).

35) G. A. Jeffrey and G. S. Parry, *J. Chem. Soc.*, **1952**, 4864.

example. The two oxygen atoms are equivalent[36]. It was assumed that the four atoms are coplanar, and $\xi_1=\xi_2=0$, $\xi_3=\xi_4=-0.50$.

5) Acetic acid (AH):—The charge distribution was calculated from the bond moments[23] and the dipole moment[23] considering the inductive effect[24]. $\xi_1=0.110$, $\xi_2=0.409$, $\xi_3=-0.412$, $\xi_4=-0.435$, $\xi_5=0.325$. Center: Carboxyl C atom. $b=3.00$ Å. $L$ calculated$=0.097$.

6) Acetate ion ($A^-$): — Center: Point on the $C_1$-$C_2$ line at 0.64 Å apart from $C_2$ atom. $L_{A^-}/b_{A^-}$ calculated for various values of $b_{A^-}$ are as follows;

| $b_{A^-}$(Å) | 2.40 | 2.70 | 3.00 | 3.30 |
|---|---|---|---|---|
| $L_{A^-}/b_{A^-}$(Å$^{-1}$) | 0.689 | 0.529 | 0.437 | 0.376 |

Insertion of the observed slope $d(pK)/d(1/D)$, $L$'s and $b$'s for $H_2O$, $H_3O^+$ and HA into Eq. 15 gives

$$\frac{L_{A^-}}{b_{A^-}}=\frac{118}{121.7}+\frac{0.263}{1.40}+\frac{0.097}{3.00}-\frac{1.266}{1.70}=0.445\ (\text{Å}^{-1}) \tag{A-1}$$

$L_{A^-}/b_{A^-}$ is plotted against $b_{A^-}$, and the value of $b_{A^-}$ which fulfils Eq. A-1 can be obtained graphically. $b_{A^-}$ thus obtained is 2.97 Å.

7) Benzoic acid (AH):—The charge distribution was determined to fit the observed dipole moment[23] assuming that $\xi_3$, $\xi_4$ and $\xi_5$ are the same as those in acetic acid and the remaining charges are shared by the $C_2$ atom and the center of the ring, Q. $\xi_2=0.455$, $\xi_3=-0.412$, $\xi_4=-0.435$, $\xi_5=0.328$, $\xi_Q=0.064$. Center: Point on the $C_2$-Q line at 1.88 Å apart from $C_2$. $b=4.60$ Å. $L$ calculated$=0.102$.

8) Benzoate ion ($A^-$): — Center: Point on the $C_2$-Q line at 2.32 Å apart from $C_2$ atom.

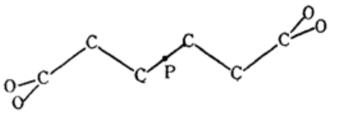
9) Succinic acid ($AH_2$) (Method I):—*trans* Form, symmetric with respect to the middle point of the C-C bond in $CH_2$-$CH_2$ group, was assumed. The four carbon atoms lie on the same plane, to which the planes including each carboxyl group are perpendicular. $\xi_1=0$, $\xi_2=0.519$, $\xi_3=-0.412$, $\xi_4=-0.435$, $\xi_5=0.328$. The charge distribution in the two carboxyl groups are the same. Center: Center of symmetry. $b=4.60$ Å. $L$ calculated$=0.210$.

10) Bisuccinate ion ($AH^-$) (Method I):—*trans* Form similar to $AH_2$ except that one of the carboxyl groups is replaced by carboxylate group. Center: C atom adjacent to the carboxyl C atom. The charge distribution in the carboxyl group is the same as that in $AH_2$.

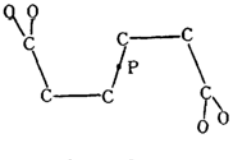
11) Succinate ion ($A^=$) (Method I):—Symmetric *trans* form similar to $AH_2$ except that the carboxyl groups are replaced by the carboxylate groups. Center: Center of symmetry.

12) Succinic acid ($AH_2$, $AH^-$, $A^=$) (Method II): —The geometry of each species is the same as that of the corresponding species treated in Method I. The charges on all the atoms in COOH group were assumed to be zero.

13) Adipic acid ($AH_2$, $AH^-$, $A^=$) (Method II): —The structures assumed are schematically depicted in Fig. A-3. In both forms, all the carbon atoms lie on the same plane, to which the two planes including each carboxyl group are perpendicular.

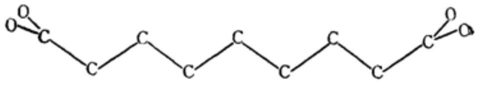


all *trans* form

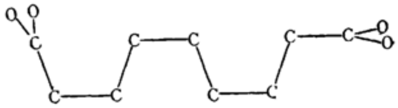


di-*cis* form

Fig. A-3. Schematic representation of the structures of adipic acid.



all *trans* form



tri-*cis* form

Fig. A-4. Schematic representation of the structures of azelaic acid.

Center: Middle point of C-C bond, P, as shown in Fig. A-3.

14) Azelaic acid ($AH_2$, $AH^-$, $A^=$) (Method II): The structures assumed are depicted in Fig. A-4. All the carbon atoms were assumed to lie on the same plane, to which the two COOH planes are perpendicular. Center: Center of the rectangle formed by the four oxygen atoms in $A^=$ form.

### SN1 Solvolysis.

In *tert*-butyl chloride and *tert*-butyl bromide, the atoms are numbered as follows; methyl carbon atom 1, α-carbon atom 2, and halogen atom (X) 3. The carbon atoms were all assumed to be tetrahedral. The center was chosen at $C_2$ atom in both normal state and activated state.

1) *tert*-Butyl chloride.

Normal state: — C-X=1.76 Å, C-C=1.54 Å. $\xi_1=0.0417$, $\xi_2=0.0882$, $\xi_3=-0.213$. (The small charges

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[36] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules", Methuen & Co., London (1958), p. 161.

on the methyl hydrogen atoms were included in $\xi_1$). $b=3.00$ Å. $L$ calculated$=0.048$.

Activated state:— C-X$=2.64$ Å (Model I); C-X $=1.94$ Å (Model II). $\xi_1=0.196$, $\xi_2=0.414$, $\xi_3=-1.0$ (Type 1), $\xi_1=0$, $\xi_2=1.0$, $\xi_3=-1.0$ (Type 2).

2) *tert*-Butyl bromide.

Normal state:— C-X$=1.91$ Å, C-C$=1.54$ Å. $\xi_1=0.0403$, $\xi_2=0.085$, $\xi_3=-0.206$. $b=3.00$ Å. $L$ calculated$=0.057$.

Activated state:— C-X$=2.86$ Å (Model I); C-X $=2.10$ Å (Model II). $\xi_1=0.195$, $\xi_2=0.414$, $\xi_3=-1.0$ (Type 1); $\xi_1=0$, $\xi_2=1.0$, $\xi_3=-1.0$ (Type 2).

The following five compounds were treated by the simplified type of charge distribution for the activated complexes (Type 2), $\xi_2=1$, $\xi_3=-1$, ignoring every small charge on the remaining atoms. The C-X bond distance in the activated complex was taken as 2.86 Å for bromide, and 2.64 Å for chloride (Model I).

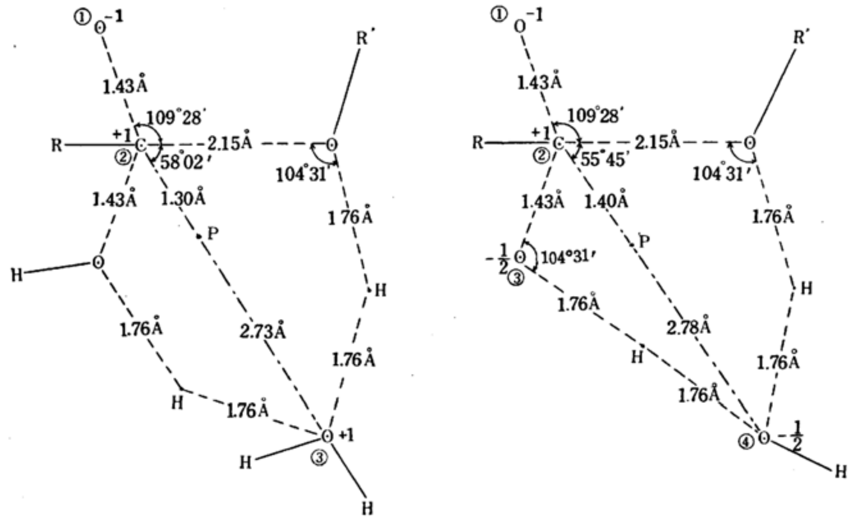
3) Neopentyl bromide:—Center: Middle point between $\alpha$-C and $\beta$-C atoms.

4) Benzhydryl chloride:—Center: Middle point between the two aromatic C atoms to which the $\alpha$-C atom is attached.

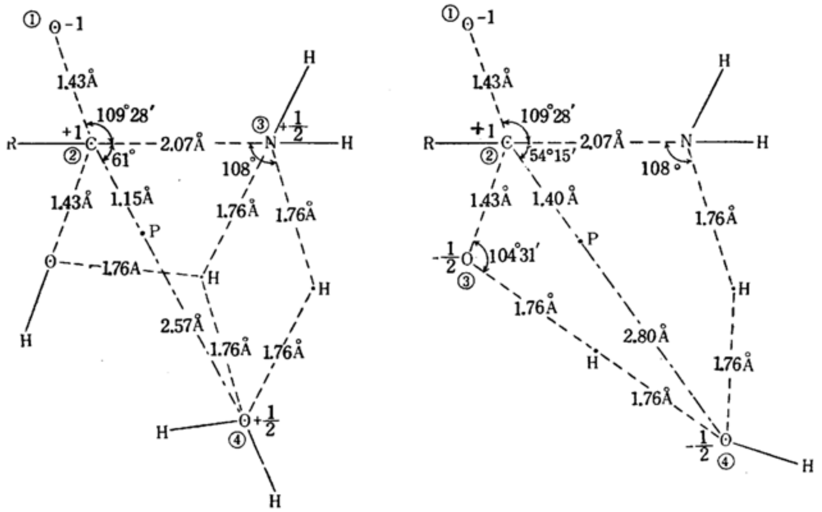
5) $\alpha$-Phenethyl chloride:—Center: $C_1$ atom of phenyl group.

6) Pinacolyl-$p$-bromobenzenesulfonate:—Center: Sulfur atom.

7) $\alpha$-Methylallyl chloride:—Center: Middle point between the $\alpha$-C atom and the adjacent double bonded C atom.



(1) Acid hydrolysis of an ester (2) Base hydrolysis of an ester



(3) Acid hydrolysis of an amide or anilide (4) Base hydrolysis of an amide or anilide

Fig. A-5. Laidler-Landskroener's models for the activated complexes in the acid and base hydrolyses of esters, amides and anilides.

### III. Acid and Base Hydrolyses of Esters, Amides and Anilides.

Laidler-Landskroener's models for the activated complexes are shown in Fig. A-5. It was assumed that the $C_2$ atoms are tetrahedral, and the following four atoms lie on the same plane;

$O_1$, $C_2$, $O_3$ and O(esteric) in Model (1)
$O_1$, $C_2$, $O_4$ and O(esteric) in Model (2)
$O_1$, $C_2$, $N_3$ and $O_4$ in Model (3)
$O_1$, $C_2$, N and $O_4$ in Model (4).

The center was chosen at $C_2$ atom or at point **P** depicted in the models (cf. Table V).