DIFFUSION OF SALTS ACROSS A BUTANOL-WATER INTERFACE

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ABSTRACT Diffusion of the chloride salts of Li, Na, K, Rb, and Cs from water into 1-butanol and from 1-butanol into water was examined at temperatures from 13–40°C. Distribution coefficients, interfacial transfer coefficients, Arrhenius activation energy, free energy of activation, enthalpy, and entropy of activation were determined for the diffusion of these salts across the alcohol-water interface. The results indicate that the entropy decrease made the major contribution to the change in the free energy of activation.

INTRODUCTION

Diffusion of solute from the bulk medium to the membrane surface is fundamental to solute transport. Diffusion, as it is usually studied, involves only the movement of the solute through a homogeneous medium. However, as the solute approaches an interfacial region, e.g. between the medium and the cell membrane, a more or less abrupt change in the dielectric occurs and the diffusion of an electrolyte is measurably different from that in the bulk medium. In a recent discussion of surface energy terms, Schulman (1966) pointed out that classical membrane thermodynamics ignore these surface properties, and yet these properties are important in regard to the selectivity of ion fluxes.

Rosano, Duby, and Schulman (1961) have developed a method for the study of diffusion across liquid-liquid interfaces. The investigation reported here extends their work and indicates the nature of the difference in the diffusion of electrolytes across interfaces as compared with diffusion in the bulk solution. The butanol-water interface offers a greater resistance to the movement of salts as compared with bulk diffusion. The data indicate that the resistance depends upon the fact that salts in solution require a reduction in entropy prior to crossing the interface either from water to butanol or from butanol to water. Comparison of the Arrhenius energy both for salts crossing the butanol-water interface and for crossing the cell membrane shows significant agreement.

MATERIALS AND METHODS

Experimental. The apparatus (Fig. 1) consisted of battery jars with glass covers and double-bladed stirrers on each stirring shaft. The stirring blades were rotated at a constant speed of 10 RPM. A six unit Phipps and Bird electric stirrer (Phipps & Bird, Richmond, Virginia) allowed six simultaneous experiments at any one temperature. For experiments involving a net flux of ions from the aqueous to the nonaqueous phase, 230 ml of distilled water and 200 ml of 1-butanol mutually saturated were placed in the jars and allowed to equilibrate to the temperature of the thermostated room. Then 20 ml of a 1 M solution of a specific salt was injected into the aqueous phase. The exact salt concentration of each experiment was measured, and these were in the range of 80 mM per liter. The area of the interface between the water and butanol was 75.2 cm^2. Five or six 1-ml samples were taken from the butanol phase at definite time intervals between one-fourth and three-fourths attainment of equilibrium. After the samples were collected, the whole system was then vigorously stirred and allowed to clear before samples were drawn from both phases for the determination of the distribution coefficient (P_{ow}). All samples from the alcohol phase were evaporated and then diluted to 10 ml with water.

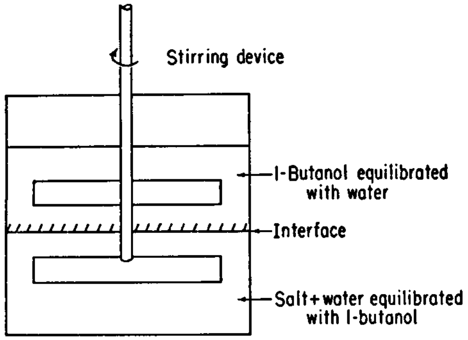

FIGURE 1 Diagram of the diffusion cell.

Experiments were also performed by equilibrating 1-butanol with a 1 M solution of the salt and then carefully pouring 200 ml of this over 250 ml of distilled water previously saturated with butanol. Samples of 0.1 ml were taken from the aqueous phase and diluted to 10 ml. The Li$^+$, Na$^+$, K$^+$, and Rb$^+$ concentrations were determined by using a Model 21 Coleman Flame Photometer (Coleman Instruments, Inc., Maywood, Illinois). Diffusion of CsCl was determined by analysis of chloride by using an Aminco-Chloride Titrator (American Instrument Co., Inc., Silver Spring, Maryland).

Theoretical. For experiments involving a net flux of salt from alcohol to water, the kinetic equation for the interfacial transfer coefficient was derived as follows:

Where C_o = concentration of the salt in the alcohol phase at time, t; C_o^e = concentration of the salt in the alcohol phase at equilibrium, $t = \infty$; C_w = concentration of the salt in the aqueous phase at time, t; C_w^e = concentration of the salt in the aqueous phase at equilibrium, $t = \infty$; C^i = initial concentration, i.e., $t = 0$; n_o = number of moles of salt in alcohol phase; n_w = number of moles of salt in aqueous phase; P_{ow} = distribution coefficient = C_o^e/C_w^e; A = area of the interface; k_{ow} = interfacial transfer coefficient from alcohol to water, (cm hr^{-1}); k_{wo} = interfacial transfer coefficient from water to alcohol, (cm hr^{-1}); V_o = volume of the alcohol phase; and V_w = volume of the aqueous phase.
Assuming that

$$-dn_o/dt = A(k_{ow}C_o - k_{wo}C_w) \tag{1}$$

with

$$V_oC_o + V_wC_w = V_wC_w^i \tag{2}$$

and

$$C_w = C_w^i - (V_o/V_w)C_o \tag{3}$$

and since by definition at equilibrium

$$dn_w^e/dt = 0 \quad \text{and} \quad C_o^e/C_w^e = k_{wo}/k_{ow} = P_{ow}, \tag{4}$$

then

$$C_w^e = C_w^i - aC_o^e$$

where

$$a = V_o/V_w \quad \text{and} \quad k_{wo} = k_{ow}[C_o^e/(C_w^i - aC_o^e)]. \tag{5}$$

Substituting (5) in (1) and

$$dn_o/dt = V_o\, dC_o/dt$$

$$-V_o(dC_o/dt) = A\{k_{ow}C_o - k_{ow}[C_o^e/(C_w^i - aC_o^e)][C_w^i - aC_o]\},$$

then

$$-V_o(dC_o/dt) = [Ak_{ow}/(C_w^i - aC_o^e)][C_oC_w^i - aC_oC_o^e - C_o^eC_w^i + aC_oC_o^e]$$

or

$$-V_o(dC_o/dt) = [Ak_{ow}C_w^i/(C_w^i - aC_o^e)][C_o - C_o^e]. \tag{6}$$

Since

$$C_w^i = C_w^e + aC_o^e,$$

then

$$-V_o(dC_o/dt) = Ak_{ow}[(C_w^e + aC_o^e)/C_w^e][C_o - C_o^e].$$

Simplifying by means of equation 4,

$$-V_o(dC_o/dt) = Ak_{ow}(1 + aP_{ow})(C_o - C_o^e). \tag{7}$$

Integrating between 0, C_o and $t = 0$ to t gives

$$-\ln|1 - (C_o/C_o^e)| = A/V_o[(aP_{ow} + 1)k_{ow}t] \tag{8}$$

$$[-\ln|1 - (C_o/C_o^e)|][(A/V_o)(aP_{ow} + 1)t]^{-1} = k_{ow}. \tag{9}$$

Absolute reaction rate theory suggests that the proper form for the interfacial transfer coefficient in this investigation is

$$k_{ow} = L(kT/h)\exp(-\Delta F^{\ddagger}/RT) \tag{10}$$

where L is the distance of the barrier which must be crossed in the activation process (Glasstone, Laidler, and Eyring, 1941). For diffusion through an interface, Sinfelt and Drickamer (1955) estimated L from $(\bar{V}/N)^{1/3}$ where $\bar{V}$ is the mean volume of a gram molecular weight of water and alcohol and N is 6.023×10^{23}. The value calculated for the butanol and water interface is 3.93 A. In equation (10), kT/h is a frequency factor and $\Delta F^{\ddagger}$ is the free energy of activation for the diffusion. The exponential factor represents the probability that a molecule striking the interface will possess sufficient free energy to surmount the energy barrier. The enthalpy of activation $\Delta H^{\ddagger}$ can be obtained from the Arrhenius equation:

$$k_{ow} = A \exp(-E_a/RT) = A \exp -(\Delta H^{\ddagger} + RT)/RT \tag{11}$$

where A is a constant, E_a the Arrhenius activation energy, R the gas constant, and T the absolute temperature. Then the entropy of activation[1] may be obtained from

$$\Delta F^{\ddagger} = \Delta H^{\ddagger} - T\,\Delta S^{\ddagger}. \tag{12}$$

RESULTS

The flux of KCl was examined at 30°C with variation of the independent parameters of equation (9) to test the validity of the application of a first order kinetic expression to this experimental system. Variation in interfacial area, in the ratio of the volume of alcohol to water, in the concentration of KCl, and in the direction of flux of the KCl had no marked effect on the interfacial transfer coefficients measured. The error of the mean of the coefficients obtained was 1.2% of the mean.

Since water flux occurred during the flux of salt into the alcohol, it was necessary to determine whether this water flux altered the interfacial transfer coefficient of the salt. An 80 mM sodium chloride solution was equilibrated with butanol. Then approximately 80 μc of Na^{24} was injected into the aqueous phase. Samples were taken from the alcohol phase and counted for radioactivity. Under these conditions the net fluxes of both salt and water were zero. The interfacial transfer coefficients for the labelled NaCl in this experiment were the same as those determined in the nonequilibrium condition.

Values that we determined for the interfacial transfer coefficients of KCl and NaCl agreed with those obtained by Rosano, Duby, and Schulman (1961) who used a different design of the diffusion cell. Their values for k_{ow} and k_{wo} (Table I) must be multiplied by 2.303 to correct for the use of log instead of ln in solving their equation 13.

Experiments were performed where the rates of flux of LiCl, NaCl, KCl, RbCl and CsCl, were measured at six different temperatures from 13.1°–39°C. The interfacial transfer coefficients k_{ow} and k_{wo} plotted against the reciprocal of the absolute temperature are shown in Figs. 2 and 3.

At the end of each experiment, equilibrium concentrations of the salt in the water and alcohol were determined. Values for P_{ow} were found to be independent of temperature within the range 13.1°–39°C. This temperature independence is in agreement with the results of Rosano et al., (1961). P_{ow} values are listed on Table I.

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[1] As one of the referees points out, the quantity that is determined as $\Delta S^{\ddagger}$ is actually $\Delta S^{\ddagger} + R \ln (L/L_{assumed})$, since $k_{ow} = L(kT/h)\exp(-\Delta H^{\ddagger}/RT)\exp(\Delta S^{\ddagger}/R)$, and an assumed value of L is used in estimating $\Delta S^{\ddagger}$. A change of L by a factor of 10, however, would change the estimated $\Delta S^{\ddagger}$ by less than 5 eu.

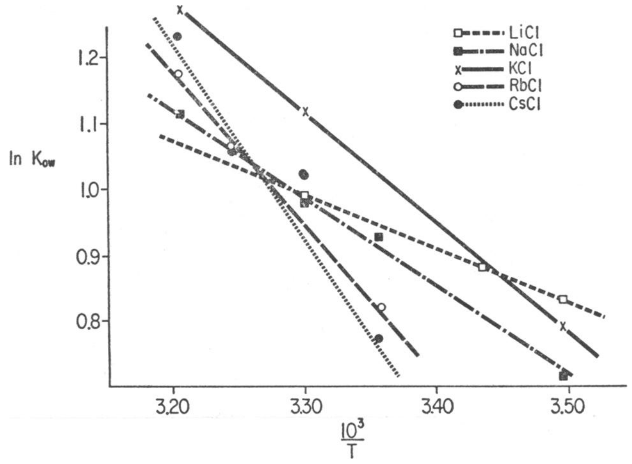

Figure 2 Natural logarithm of interfacial transfer coefficients of salts (k_{ow}) diffusing from 1-butanol to water plotted against $1/T$°K.

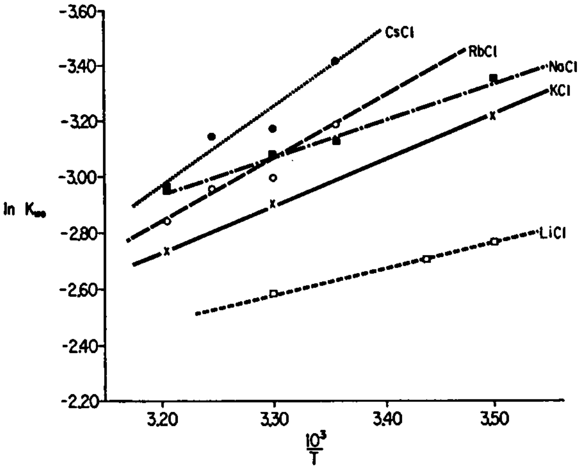

Figure 3 Natural logarithm of interfacial transfer coefficients of salt diffusing from water to 1-butanol (k_{wo}) plotted against $1/T$°K.

TABLE I
DISTRIBUTION COEFFICIENTS FOR THE SALTS STUDIED

Salt	P_{ow}
LiCl	2.78×10^{-2}
NaCl	1.73×10^{-2}
KCl	1.80×10^{-2}
RbCl	1.80×10^{-2}
CsCl	1.50×10^{-2}

Values obtained for interfacial transfer coefficients were used to determine the free energy of activation ($\Delta F^{\ddagger}$) from equation (10) and the enthalpy of activation ($\Delta H^{\ddagger}$) was then determined from equation (11). Values for free energy of activation, enthalpy of activation, entropy of activation, and for the activation energy derived from the Arrhenius plot (E_a) are given in Tables II and III for the two different directions of the salt flux; i.e., from water to alcohol and alcohol to water. The entropy term is given in entropy units; i.e., calories per mole per degree.

TABLE II

ENERGY BARRIERS FOR THE DIFFUSION OF SALTS FROM 1-BUTANOL TO WATER AT 25°C

Salt	E_a	$\Delta H^{\ddagger}_{25^\circ C}$	$\Delta F^{\ddagger}_{25^\circ C}$	$\Delta S^{\ddagger}_{25^\circ C}$
	kcal/mole	*kcal/mole*	*kcal/mole*	*eu*
LiCl	1.75	1.15	11.63	−35.15
NaCl	2.59	2.00	11.65	−32.37
KCl	3.41	2.89	11.58	−29.39
RbCl	4.29	3.70	11.71	−26.86
CsCl	5.64	5.04	11.73	−22.45

TABLE III

ENERGY BARRIERS FOR THE DIFFUSION OF SALTS FROM WATER TO 1-BUTANOL AT 25°C

Salt	E_a	$\Delta H^{\ddagger}_{25^\circ C}$	$\Delta F^{\ddagger}_{25^\circ C}$	$\Delta S^{\ddagger}_{25^\circ C}$
	kcal/mole	*kcal/mole*	*kcal/mole*	*eu*
LiCl	1.78	1.19	13.75	−42.14
NaCl	2.68	2.09	14.05	−40.13
KCl	3.40	2.81	13.96	−37.41
RbCl	4.37	3.78	14.08	−34.56
CsCl	5.40	4.81	14.22	−31.58

The effect of six different anions on the interfacial transfer coefficients of sodium salts and potassium salts was examined. These experiments were performed at 30°C, and consequently only free energy of activation ($\Delta F^{\ddagger}$) can be obtained from the data presently available. These results are shown in Table IV.

The role of the volume of the salts in determining the energy required to cross the interface was examined by plotting the Arrhenius energy of activation against the intrinsic volume of the salt. This volume is defined by Gluechauf (1965) as

$$V^0 = (4/3)\pi N(r_o + a)^3$$

where r_0 is the crystallographic radius of the ion, N is 6.023×10^{23}, and the increment (a) of 0.55 A is due to the open structure of water and is obtained from the molar volume of water (ϕ_w) and r_w the radius of the water molecule.

TABLE IV

INTERFACIAL TRANSFER COEFFICIENTS AND FREE ENERGIES OF ACTIVATION OF SELECTED SALTS OF Na^+ AND K^+ DIFFUSING FROM 1-BUTANOL TO WATER AND FROM WATER TO BUTANOL

Salt	Experiments at 30°C $\Delta F^{\ddagger}_{o \to w}$	k_{ow}	$\Delta F^{\ddagger}_{w \to o}$	k_{wo}
	kcal/mole	*cm/hr*	*kcal/mole*	*cm/hr*
$NaHCO_3$	11.94	2.15	14.47	3.20×10^{-2}
$KHCO_3$	12.04	1.82	14.56	2.82×10^{-2}
NaCl	11.81	2.66	14.21	4.60×10^{-2}
KCl	11.73	3.06	14.15	5.51×10^{-2}
NaF	11.78	2.80	14.67	2.30×10^{-2}
KF	11.84	2.53	14.73	2.13×10^{-2}
NaAc	11.75	2.96	14.25	4.82×10^{-2}
KAc	11.73	3.06	14.21	4.99×10^{-2}
NaOH	10.90	4.48	14.18	5.24×10^{-2}
KOH	11.62	3.66	14.26	4.68×10^{-2}
NaBr	11.74	3.02	13.95	7.55×10^{-2}
KBr	11.72	3.10	13.95	7.66×10^{-2}
NaI	11.84	4.62	13.13	22.18×10^{-2}
KI	11.72	3.12	13.54	15.16×10^{-2}

$$
\begin{aligned}
a &= \left(\frac{3\phi_w}{4\pi N \times 10^{-24}}\right)^{-1/3} - r_w \\
&= \left(\frac{18.02}{2.52}\right)^{-1/3} - 1.38 \\
&= 0.55\text{A}.
\end{aligned}
$$

The plot of the Arrhenius energy of activation against the intrinsic volume of the salt is shown on Fig. (4).

DISCUSSION

Energy barriers at the interface. The diffusion of molecules across an interface can be visualized as a process involving an intermediate activated state of the molecule striking the interface; only those molecules with sufficient energy to surmount the energy barrier will penetrate the interface. From the tables of values of $\Delta F^{\ddagger}$ (Tables II and III) it can be seen that the free-energy barrier to diffusion through a water-butanol interface is large. The values of $\Delta F^{\ddagger}$ for ordinary bulk diffusion are much lower, approximately 3 kcal/per mole (*vide*: Glasstone et al., 1941). Evidence has been reviewed by Davies and Rideal (1963), that water

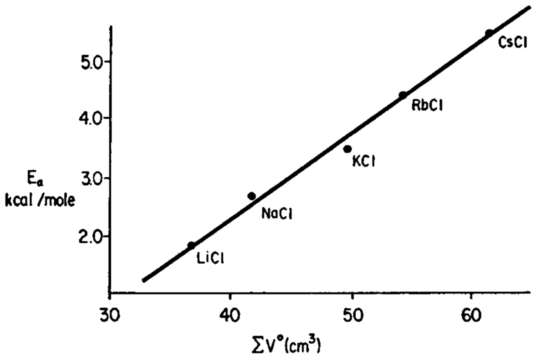

FIGURE 4 Arrhenius activation energies (E_a) plotted against the intrinsic molar volumes of the salts. The value of Cl^- (33.15 cm^3) was added to the intrinsic molar volumes calculated for the cations.

structuring occurs at an interface between water and a region of different dielectric. Within the several molecules approaching the interface, the viscosity of the water molecules increases markedly. This structure has been referred to as a region of "soft ice." This "soft ice" may cause the great resistance to diffusion across the interface.

Variation in the interfacial transfer coefficients with temperature. Heating a system both increases the kinetic energy of the molecules and decreases the order of the system. Both these factors play a role in the increased rate of interfacial transfer which occurred at higher temperatures. The enthalpy of activation was found for the chloride salts of the alkali metals to be directly related to the intrinsic volume of the salt (Fig. 4). The entropy of activation was found to be inversely related to the ideal partial molal entropy of the cations in the bulk of the solution (Fig. 5).

Values obtained for $\Delta F^\ddagger$ were in the range of 10 to 14 kcal per mole and the enthalpy of activation was found to be only 1 to 5 kcal per mole. By far the greater amount of free energy of activation goes into the reduction of entropy which occurs with the transfer of these salts. The $T\Delta S^\ddagger$ for LiCl in kcal per mole at 25°C is -12.56, for NaCl is -11.96, KCl is -11.28, for RbCl is -10.3, and for Cscl is -9.41. On the basis of the change in entropy required for activation, CsCl should move more easily across an interface than RbCl which in turn, would pass more readily than NaCl and KCl. At the interface, the decrease in entropy required for passage of these ions is such that CsCl would more frequently present the necessary configuration for transfer than Rb, K, Na, or Li chlorides, but would fail to cross the interface owing to insufficient heat content. Increase in the thermal energy of the system would provide this requisite energy and consequently at higher temperature the movement of the larger ions is facilitated. The increase in magnitude of energy required to reduce the entropy and to present the necessary configuration

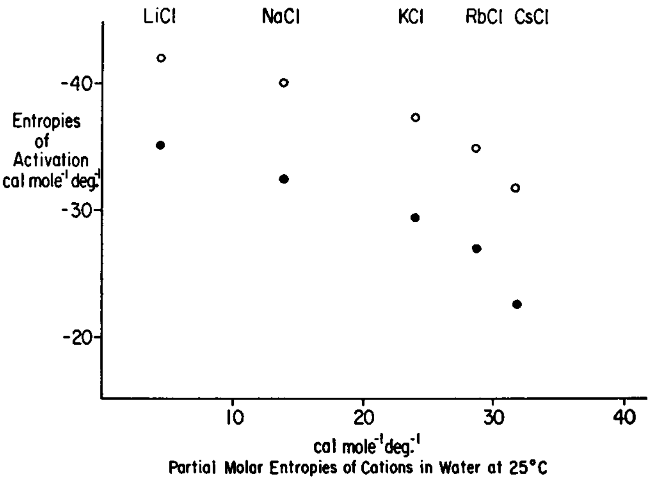

FIGURE 5 Entropies of activation ($\Delta S^{\ddagger}$) for the interfacial diffusion of the salts plotted against the partial molal entropies of the cations in water at 25°C (*vide*: Gurney, R. W., 1962, Ionic Processes in Solution, Dover Publications, Inc., New York, N. Y., 267). ● butanol to water; ○ water to butanol.

at the interface restricts the flux of the small ions relative to the larger at higher temperatures.

Since the ability of biological membranes to distinguish between K^+ and Na^+ is of biological importance it seems worthwhile to inquire whether these studies will aid in understanding how the cell or cell membrane accomplishes the separation.

Rosano et al. (1961) have suggested that differences in hydration energies may determine the rate of interfacial diffusion. On the basis of hydration energy alone the rate of transfer should be in the order $K^+ > Na^+$ and in the present studies the rates of transfer were $K^+ > Na^+$. However we cannot explain the rapidity of Li^+ diffusion nor the slow diffusion rates of Rb^+ and Cs^+ at low temperatures on the basis of hydration energy regulating the diffusion.

The ion size does not play a major role as K^+ is larger than Na^+ at the interface according to the work of Sears and Schulman (1964) and according to the relation between $\Delta H^{\ddagger}$ and intrinsic volume reported here. The results of this study show that the entropy of K^+ in the activated state plays the major role in producing the greater rate of diffusion of K^+ as compared with Na^+.

Interfacial vs Fick diffusion. The activation entropy term seems to distinguish the diffusion across an interface from the standard Fick diffusion in the bulk phase. From the available information (Glasstone, Laidler, and Eyring, 1941) the activation entropy is approximately 1 eu for diffusion of a solute through a solvent. The $\Delta S^{\ddagger}$ for NaCl, KCl, LiCl, HCl, urea, and mannitol were calculated from data available in the literature (International Critical Table, Vol. V, 1st edition,

1929) for diffusion in water. These calculations show the values for $\Delta S^{\ddagger}$ scatter about 1 eu (Table V). Large negative entropies of activation occurred at the interface.

Comparison with biological data. To compare the results of the salt transfer across the water-butanol interface with uptake of salts by a biological system, we examined data presented by Ling (1962). From these data Arrhenius activation energies (E_a) were calculated for the uptake by frog muscle of the chloride salts of Na^{22}, K^{42}, Rb^{86}, and Cs^{134}. Table VI shows these values together with the Arrhenius activation energy for the movement of the salts across the water-butanol interface from water to alcohol and also the values for the energy required to cross the interface twice ($w \rightarrow o$ then $o \rightarrow w$). The activation energies of the penetration by Na^{22} and Cs^{134} agree with those obtained in the interface studies for crossing one interface (i.e., $w \rightarrow o$), whereas K^{42} activation energy agrees with that for crossing both interfaces (i.e., $w \rightarrow o \rightarrow w$). This suggests Na^+ and Cs^+ were dissolved in the mem-

TABLE V

REPRESENTATIVE VALUES FOR ENTROPY OF ACTIVATION FOR DIFFUSION OF SOLUTES IN WATER AT 25°C

Data taken from International Critical Tables.

Substance	$\Delta S^{\ddagger}$
	eu
NaCl	4.81
KCl	3.13
LiCl	−2.29
HCl	−6.03
Urea	−1.82
Manitol	−2.19

TABLE VI

COMPARISON OF THE ARRHENIUS ACTIVATION ENERGIES (E_a) FROM INTERFACIAL DIFFUSION STUDIES WITH E_a CALCULATED FROM DATA FOR THE UPTAKE OF Na^{22}, K^{42}, Rb^{86}, AND Cs^{134} BY FROG MUSCLES (LING, 1962)

Salt	E_a (Muscle)	E_a (Interface) $w \rightarrow o \rightarrow w$	E_a (Interface) $w \rightarrow o$
	kcal/mole	*kcal/mole*	*kcal/mole*
Na^{22}	3.08	5.27	2.68
K^{42}	7.76	6.81	3.40
Rb^{86}	4.72(15° → 30°C) 12.58(0° → 15°C)	8.66	4.37
Cs^{134}	5.62	11.04	5.40

brane, and K+ had penetrated into the cell. Rb+, gave two straight lines on an Arrhenius plot with a break at 15°C. The values for Rb for 15°–30°C agree with the energy required to cross only one interface (w→o).

The data obtained thus far and presented here suggests that an interfacial region serves as a barrier to select salts on the basis of the entropy of activation for the diffusion.

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REFERENCES

Davies, J. T., and Rideal, E. K., 1963, Interfacial Phenomena, New York, Academic Press, Inc., 2nd edition.

Glasstone, Q., Laidler, K. J., and Eyring, H., 1941, The Theory of Rate Processes, New York, McGraw-Hill Book Co., Inc.

Gluechauf, E., 1965, *Tr. Farad. Soc.*, **61**, 914.

Ling, G. N., 1962, A Physical Theory of the Living State: The Association-Induction Hypothesis, New York, Blaisdell Publishing Co.

Rosano, H. L., Duby, P., and Schulman, J. H., 1961, *J. Physic. Chem.*, **65**, 1704.

Schulman, J. H., 1966, *Ann. New York Acad. Sc.*, **137**, 860.

Sears, D. F., and Schulman, J. H., 1964, *J. Physic. Chem.*, **68**, 3529.

Sinfelt, J. H., and Drickamer, H. G., 1955, *J. Chem. Physic.*, **23**, 1095.