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Prediction of interfacial transfer kinetics. II. Solute ionization and aqueous phase ionic strength effects in two-phase transfer and rotating diffusion cells

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Summary

Octanol–aqueous interfacial transfer kinetics of 5-allyl-5′-isopentylbarbituric acid and ethylparahydroxybenzoate are reported as functions of pH and ionic strength in the two-phase transfer cell. Solutes were selected to ensure that: (a) aqueous diffusional resistance at the interface was rate-determining; and (b) only the non-ionized solute partitioned. Transfer rate constants varied unpredictably with pH and fell significantly with increasing aqueous phase ionic strength. Results could not be explained by ionic strength-induced variations in partition coefficient, pK_a or kinematic viscosity of the phases. When the same solutes were studied in the rotating diffusion cell (RDC), however, transfer rate constants fell with increasing pH in accordance with an extension of our previous predictive theory. In the RDC, which has a mechanically stabilized interface, aqueous diffusivities were unaffected by pH or ionic strength. Interfacial resistance to transfer was negligible for both solutes. Interfacial instability, which was affected by the presence of ions in the aqueous phase, appeared to be the reason for the unpredictable results in the two-phase transfer cell. The octanol/water system displayed low interfacial tension which varied with aqueous ionic strength. The simpler two-phase cell is adequate for transfer studies with non-ionized solutes. Experiments involving variation in the ionic content of the aqueous phase, however, should employ a diffusion cell with a stabilized interface.

Introduction and Theory

In previous publications (Byron et al., 1980, 1981) we reviewed literature concerned with the study of interfacial transport in a variety of transfer cells. A theory was developed which enabled the prediction of non-ionized solute transfer kinetics in a symmetrically stirred two-phase transfer cell (TPTC, Fig. 1a). In paper I of this series (Byron and Rathbone, 1984) we developed and tested our theory in the presence of aqueous, organic and mixed diffusional control using three homologous series and octanol, chloroform or cyclohexane as the organic phase. The apparent first-order rate constant for partitioning, S ($= k_{12} + k_{21}$; Scheme I) could be predicted for non-ionized solutes as a continuous function of partition coefficient, K_D, from

$$S = \left[(D_1A)/(V_1h_1)\right]\left\{(K_D + r)/\left[K_D(1 + \gamma^{-1})\right]\right\} \quad (1)$$

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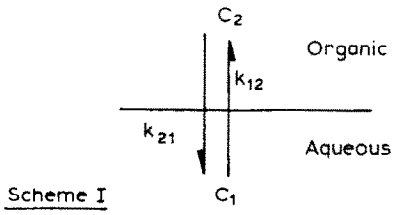
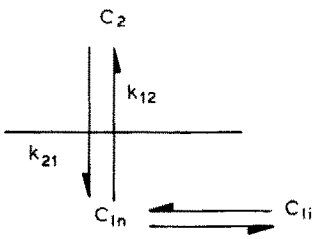


Scheme I



Scheme II

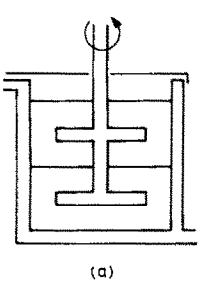
where symbols are defined in the Glossary of Terms. Eqn. 1 is a rearrangement of the original (Eqn. 14, Byron et al., 1981). It incorporates the term γ, which we introduced (Byron and Rathbone, 1984) to describe the diffusional resistance ratio (R_{aq}/R_{org}) at the interface. This publication is concerned only with "aqueous diffusional control" ($\gamma > 20$; Byron and Rathbone, 1984). Because, by definition,

$$\gamma = R_{aq}/R_{org} = (h_1 D_2 K_D)/(h_2 D_1) \quad (2)$$

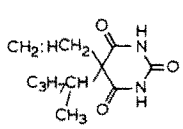
when K_D is sufficiently large, the resistance of the aqueous boundary layer dominates and S (Eqn. 1) tends to a K_D independent constant

$$S_{K_D \to \infty} = (D_1 A)/(V_1 H_1) \quad (3)$$

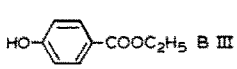
Under these circumstances in the TPTC, values for S ($S_{\gamma > 20} \to k_{12}$; Scheme I) had shown variations which we believed were due to changes in aqueous diffusivity, D_1 (Byron and Rathbone, 1984). We have investigated this phenomenon further, determined transfer kinetics with solute ionization and explored the effects of varying the ionic content of the aqueous phase.



(a)



A VI



B III

(b)

Fig. 1. (a) Two-phase transfer cell. Phase volumes $V_1 = V_2 = 90$ ml in a cell of internal diameter = 6.0 cm. Symmetric stirring employed a 3.7 cm diameter double-bladed paddle positioned 1.4 cm from the interface in each phase (b) 5-allyl-5'-isopentylbarbituric acid and ethylparahydroxybenzoate (AVI and BIII; abbreviations as in Byron and Rathbone, 1984). Values for pK_a were: 7.9 ± 0.01 (AVI), 8.28 ± 0.01 (BIII) and independent of ionic strength.

The dependence of the apparent first-order rate constant for partitioning, S, upon pH (partial solute ionization in the aqueous phase alone; Scheme II) can be derived by writing

$$d(a_n + a_i)/dt = da/dt = -f_n k_{12} a + k_{21} b \quad (4)$$

which is true because the ionization equilibrium is so rapidly achieved in the aqueous phase. This rate equation is directly analogous to that describing an A to B reversible transfer and integrates (Riggs, 1963) to give

$$(a - a^\infty) = (a^0 - a^\infty) e^{-(f_n k_{12} + k_{21})t} \quad (5)$$

Division of both sides of Eqn. 5 by V_1 and taking natural logarithms provides the first-order rate equation in terms of concentration

$$\ln(C_1 - C_1^\infty) = \ln(C_1^0 - C_1^\infty) - (f_n k_{12} + k_{21})t \quad (6)$$

Thus, a first-order plot of $\ln (C_1 - C_1^\infty)$ vs t is linear with a negative slope

$$S = f_n k_{12} + k_{21} \quad (7)$$

The non-ionized fraction, f_n, of the weakly acidic monoprotic solutes described in this publication (Fig. 1b) may be derived by exponentiating and rearranging the Henderson-Hasselbalch equation to give

$$f_n = 1/(1 + 10^{pH - pK_a}) \quad (8)$$

Substitution for f_n in Eqn. 7 then shows the theoretical dependence of the apparent first-order rate constant for partitioning, S, upon pH as

$$S = k_{12}/(1 + 10^{pH-pK_a}) + k_{21} \quad (9)$$

In the case of the high K_D solutes described here ($K_D > 235$; Byron and Rathbone, 1984) $k_{21} \rightarrow 0$ and thus, values for S should decrease sigmoidally from k_{12} toward zero as pH increases through the pK_a. One purpose of this publication is to report the dependence of S upon pH in two-phase transfer and rotating diffusion cells (Byron et al., 1980; Albery et al., 1976). The latter cell possesses a mechanically stabilized interface. Secondly, to document and explain the effects of increasing aqueous phase ionic strength upon the transfer of non-ionized solutes across the octanol/water interface.

Experimental

Two-phase transfer cell (TPTC)

Transfer kinetics were studied for solutes AVI and BIII (Fig. 1b) in the TPTC containing equal volumes of aqueous and organic phases according to Byron et al. (1981) with the following modifications. The organic phase was octan-1-ol (spectrograde, Fisons, Loughborough, U.K.) pre-equilibrated with an appropriate aqueous phase. The latter was either: (a) KCl solution with molality in the range 0–2 M; or (b) constant ionic strength phosphate buffers (Christian and Purdy, 1962). When buffers were not included in the aqueous phase, pH was maintained within 0.1 unit using a pH-stat (Models SBR3 and ABU 12, Radiometer, Copenhagen, Denmark). AVI and BIII were introduced into the aqueous phase in concentrations to produce an absorbance $\simeq 1$. Both solutes were stable and their partition coefficients concentration independent, under the experimental conditions employed during a kinetic run. A stirring speed of 100 ± 0.5 rpm was employed throughout and temperature held constant at 37 ± 0.1°C.

Rotating diffusion cell (RDC)

Interfacial transfer kinetics were also measured with an RDC. Aqueous and organic phases were identical to those described for the TPTC. The cell and technique has been described in detail by Albery et al. (1976). In summary, an inner aqueous phase (35 ml) was separated from the outer organic (160 ml) by an octan-1-ol saturated PTFE membrane (Type FHUP04700, pore size = 0.5 μm, thickness = 60 μm, porosity = 0.85; Millipore S.A., Molsheim, France). The exposed surface area was 3.14 cm^2. Solutes were introduced to the inner aqueous phase as a 0.25 ml methanolic bolus. Concentrations were monitored continuously by pumping the inner phase (Model RPD lab pump, Fluid Metering, Oyster Bay, NY, U.S.A.) through a flowcell in a spectrophotometer (Model CE 272, Cecil Instruments, Cambridge, U.K.). Studies were performed at 37 ± 0.1°C at a variety of rotation speeds.

Values for the apparent first-order rate constant for partitioning, S, were determined from plots of ln(transferable concentration) vs time after linear regression analysis. This procedure was identical for TPTC (Byron et al., 1981) and RDC. Albery et al. (1976) use the symbol k instead of S. Total diffusional resistance, to aqueous/organic transfer, R_T was determined at each rotation speed in the RDC from

$$R_T = A\left[V_1^{-1} + (V_2 K_D)^{-1}\right]/S \quad (10)$$

where the interfacial area, A = 2.67 cm^2, was given by the product of 3.14 cm^2 and the porosity, 0.85. Eqn. 10 is the reciprocal of Albery's Eqn. 13 after accounting for the case when $K_D \neq 1$. It can be derived by rearranging Eqn. 11 in Byron et al. (1980).

Partition coefficients of the solutes and viscosities and densities of the mutually saturated solvents were determined in triplicate at 37°C for all solute–solvent and solvent–solvent systems used in the present study, as described by Byron et al. (1981). Surface and interfacial tensions were determined for pre-equilibrated aqueous and organic phases using a modified Wilhelmy plate method (Jaycock and Parfitt, 1981). The apparent force required to detach a clean flat glass plate ($10 \times 5 \times 0.15$ mm) from the interface was determined at 20°C using a microforce balance (Model MK2B,

CI Electronics, Salisbury, U.K.). The device was counterbalanced and calibrated using a variety of solvent systems as standards.

Results and Discussion

Validity of Scheme II

The true oil–water partition coefficient, K_D, is defined

$$K_D = C_2^\infty / C_{1n}^\infty \quad (11)$$

Given the validity of Scheme II with insignificant ionized solute partitioning, the effect of pH upon the apparent partition coefficient, $(K_D)_{app}$, is given by

$$(K_D)_{app} = K_D f_n \quad (12)$$

which can be derived from Eqn. 8 and the definition

$$(K_D)_{app} = C_2^\infty / (C_{1n}^\infty + C_{1i}^\infty) \quad (13)$$

Rectilinear plots of $(K_D)_{app}$ vs f_n according to Eqn. 12 are shown in Fig. 2. Values for f_n were calculated from Eqn. 8 with pK_a values = 7.9 and 8.28 for AVI and BIII (Byron and Rathbone, 1984). The linearity of the data and absence of intercepts (Fig. 2) was consistent with Scheme II for both solutes in octanol/aqueous systems.

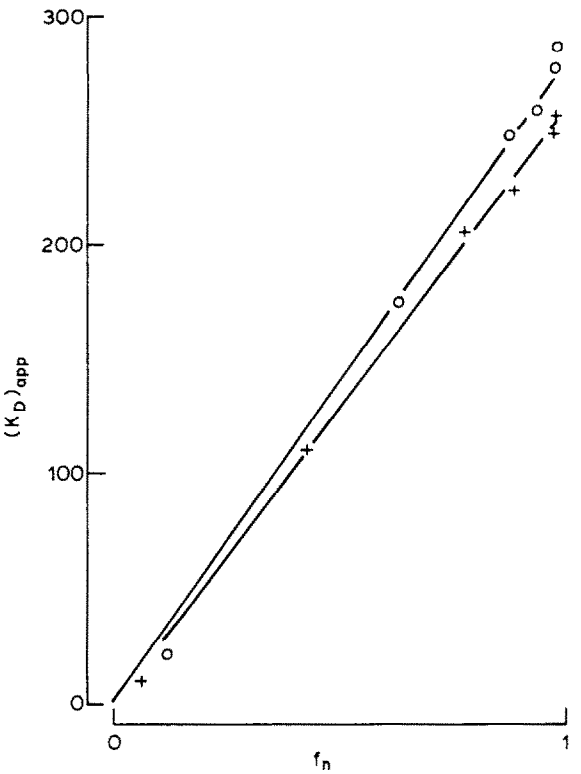


Fig. 2. Apparent partition coefficient vs fraction non-ionized for BIII (O) and AVI (+) in $\mu = 0.3$ M phosphate buffer at different pHs. Values for f_n were calculated using Eqn. 8.

Dependence of transfer kinetics on pH and ionic strength

Two-phase transfer cell

Our previous studies (Byron et al., 1981; Byron and Rathbone, 1984) have shown that non-ionized solutes transfered from aqueous to organic phases at rates predicted by Eqn. 1. Provided the ionic content of the aqueous phase was held constant during the study of each series of compounds, the presence or absence of buffer components did not cause departures from theory. Under conditions of partial ionization in the aqueous phase, however, we were unable to find one of the 16 compounds studied previously (Byron and Rathbone, 1984) whose transfer kinetics were adequately described by Eqn. 9. The pattern of results for S vs pH was similar for most compounds. For reasons of clarity, only those obtained with one compound are shown in Fig. 3. Errors in the determination of S under constant conditions were always < 5%. Typical replicates were usually within 3% of each other. The deviations from theory (Fig. 3, Eqn. 9) prompted further investigations in both the TPTC and the RDC in an attempt to resolve the conflict with theory.

Earlier determinations of S in the two-phase transfer cell with partial ionization (unpublished results) employed phosphate buffers as the aqueous phase in which pH and ionic strength, μ, varied simultaneously. Plots of S vs pH from these studies showed even larger deviations from theory than those represented by the closed symbols in Fig. 3. These were obtained using buffers with

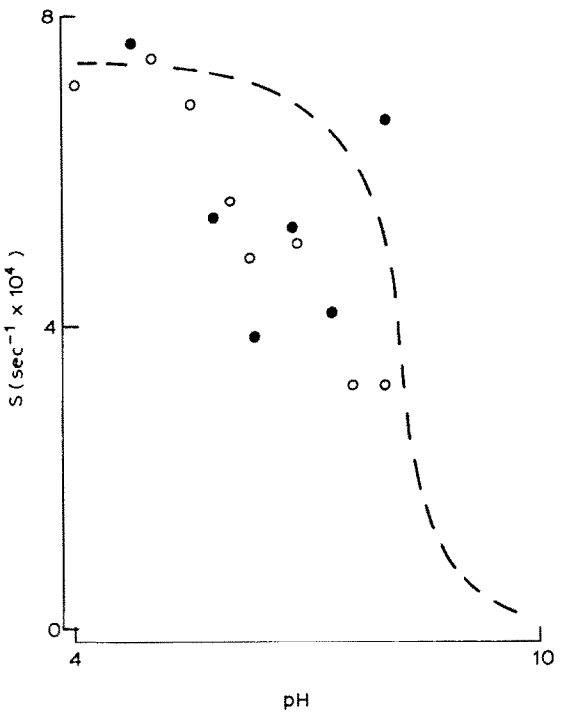


Fig. 3. Apparent first-order rate constants for partitioning, S vs pH for solute BIII in the TPTC. Values are shown following determinations in $\mu = 0.3$ M phosphate buffer (●) and 0.3 M KCl (○). The dashed line shows the theoretical dependence according to Eqn. 9.

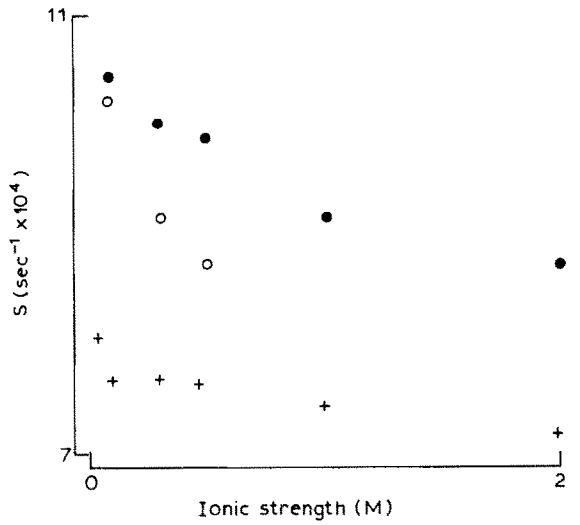


Fig. 4. S vs ionic strength, μ, for non-ionized A VI (●) and BIII (+) in the TPTC. Ionic strength was varied in the aqueous phase using KCl. In three cases (○) results are shown for AVI in phosphate buffer.

$\mu = 0.3$ M = constant (Christian and Purdy, 1962). The open symbols of Fig. 3 show values for S determined in the presence of 0.3 M KCl. In this case, pH of the aqueous phase was maintained by pH-stat. These values for S in the absence of buffer fell with increasing pH but remained poorly described by Eqn. 9. Deviation from theory could not be explained by ionic strength-induced changes in pK_a. Less than 0.05 unit variation in pK_a could be detected following titration at 37°C in KCl solutions with μ-values ranging from 0 to 2.0 M.

Values for S in the absence of ionization (pH = 5 ± 0.1) are shown for solutes AVI and BIII as a function of aqueous phase ionic strength in Fig. 4. It is clear that the ionic content of the aqueous phase affects the apparent transfer kinetics of the non-ionized compound even in the effective absence of solute ionization. Values for the resistance ratio, (proportional to K_D, Eqn. 2) in the case of both of these solutes > 60 (Table 2 of Byron and Rathbone, 1984) and thus S should be K_D-independent and described by Eqn. 3 [$S \rightarrow (k_{12})_{K_D \rightarrow \infty} \rightarrow (D_1A)/(V_1h_1)$]. Because the area : volume ratio, A/V_1, was held constant, we investigated the effect of aqueous phase ion content upon D_1 and factors believed to control boundary layer dimensions (kinematic viscosity of the aqueous and organic phases; Byron et al., 1981; Levich, 1947, 1962).

Values for viscosity, density and their ratio, kinematic viscosity are shown in Table 1 for the mutually saturated octanol and aqueous phases as functions of KCl-induced variations in aqueous ionic strength. At a fixed stirring speed in the two-phase transfer cell, aqueous diffusive boundary layer thickness, h, should be approximated by the Levich equation (Levich, 1947, 1962)

$$h = 0.643\, \nu^{1/6} D^{1/3} \omega^{-1/2} \qquad (14)$$

Thus, if stirring speed and aqueous diffusivity remain constant, the term $h_1\ \alpha(\nu_1)^{1/6}$. The magnitude of change in ν due even to the extremes of ionic strength (Table 1) could thus induce a change in $h \simeq 0.5\%$. Changes in kinematic viscosity can

TABLE 1

NORMAL AND KINEMATIC VISCOSITIES, DENSITIES [a], SURFACE AND INTERFACIAL TENSIONS FOR MUTUALLY SATURATED PHASES [b] AT DIFFERENT AQUEOUS PHASE IONIC STRENGTHS

Phase	μ [c]	η [d]	ρ [e]	ν [f]	Tension ($mN \cdot m^{-1}$)	
					Interfacial	Surface [g]
Aqueous KCl	0.0	0.693	0.994	0.697	8.36	32.1
	0.1	0.696	0.999	0.697	8.54	32.0
	0.3	0.697	1.008	0.691	8.68	32.3
	0.5	0.699	1.018	0.687	8.73	31.7
	1.0	0.705	1.040	0.678	9.18	33.3
	2.0	0.722	1.081	0.668	9.36	35.1
Octan-1-ol	0.0 [h]	4.73	0.819	5.775	8.36	27.5
	0.1	4.43	0.819	5.409	8.54	27.1
	0.3	4.42	0.819	5.397	8.68	27.5
	0.5	4.41	0.819	5.385	8.73	27.1
	1.0	4.39	0.819	5.360	9.18	27.1
	2.0	4.37	0.819	5.336	9.36	26.9

[a] Resistance ratio, γ (Eqn. 2) can be calculated using Eqn. 15 of Byron and Rathbone (1984). $\gamma > 60$ in all cases proving the rate determination of the aqueous boundary layer.
[b] 37°C.
[c] Molality.
[d] Viscosity; Poise $\times 10^2$.
[e] Density; $g \cdot cm^{-3}$.
[f] Kinematic viscosity; $cm^2 \cdot s^{-1}$, $\times 10^2$.
[g] Pure solvents gave 72.54 (H_2O) and 27.8 (oct) $mN \cdot m^{-1}$, respectively.
[h] Values for μ indicate ionic strength of aqueous phase during pre-saturation.

thus be excluded as a means of inducing the variations in S (Figs. 3 and 4; Eqn. 3).

Rotating diffusion cell

Solute transport measurements in the RDC yielded values for the total resistance to aqueous/octanol transfer, R_T (= reciprocal permeability, 1/P; Albery et al., 1976).

$$R_T = 1/P = h_1/D_I + R_1/\alpha + \ell/\alpha D_2 K_D + h_2/D_2 K_D \quad (15)$$

Because K_D is large in the case of solutes studied here, Eqn. 15 reduces to

$$R_T = h_1/D_1 + R_I/\alpha \quad (16)$$

The first and second terms on the right hand side of Eqn. 16 represent resistances to solute diffusion due to the aqueous diffusion layer and the interfacial barrier itself. The porosity, α, of the octanol-impregnated filters used in this study was 0.85. Because boundary layer thickness, h, is given by the Levich equation (Eqn. 14), substitution in Eqn. 16 gives

$$R_T = 0.643 \nu_1^{1/6} \omega^{-1/2} D_1^{-2/3} + R_I/\alpha \quad (17)$$

Experimentally, resistance to solute transfer is measured at several rotation speeds. A plot of R_T vs $\omega^{-1/2}$ should then be linear with a slope = 0.643 $\nu_1^{1/6}$ $D_1^{-2/3}$ and intercept R_I/α.

Significant diffusional resistance to interfacial transfer has been reported for some solutes at the octanol/water interface (Guy and Honda, 1984). The absence of a significant intercept in the plots of R_T vs $\omega^{-1/2}$ for either solute (Fig. 5) showed that interfacial resistance was negligible in these cases. Additional plots of R_T vs $\omega^{-1/2}$ at various ionic strengths as high as 2 molal could not be distinguished from those shown in Fig. 5. Thus, aqueous diffusion coefficients of non-ionized so-

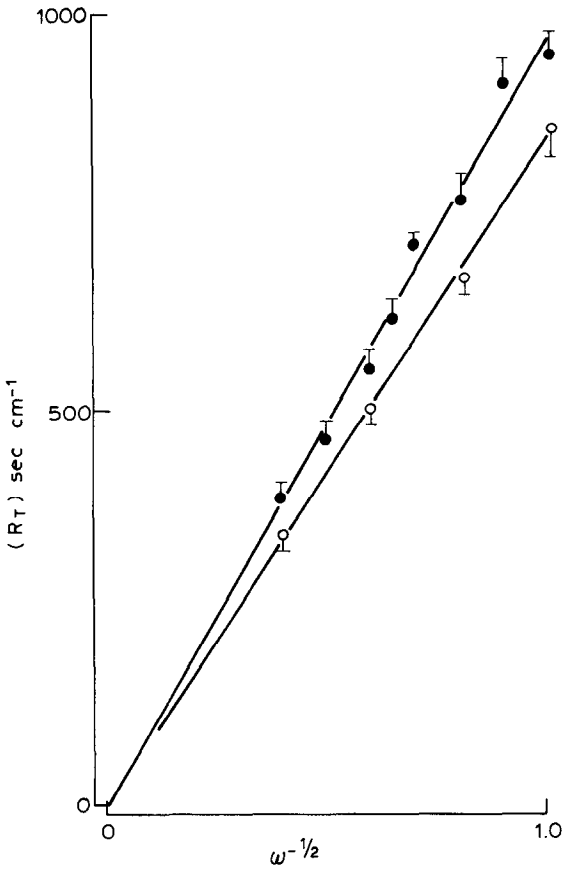


Fig. 5. Total resistance, R_T vs $\omega^{-1/2}$ for non-ionized solutes AVI (●) and BIII (○) in the RDC. Error bars are standard deviations. Aqueous phase was 0.3 M phosphate buffer.

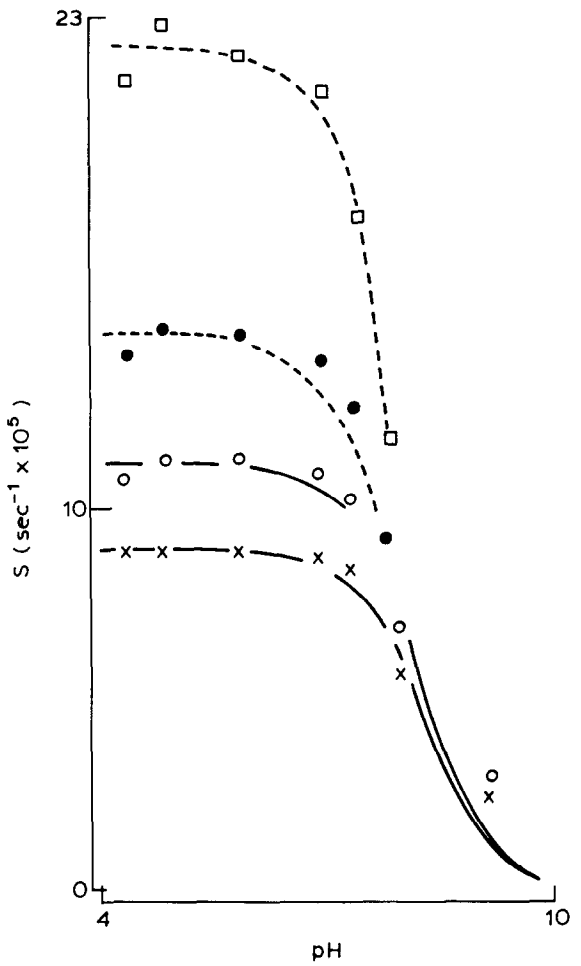


Fig. 6. S vs pH profiles for AVI (□, 375 rpm; ●, 167 rpm) and BIII (○, 94 rpm; ×, 60 rpm) partitioning in the RDC between 0.3 M phosphate buffers at constant μ and an octan-1-ol organic phase.

lutes AVI and BIII appeared to be constant and independent of μ.

Values for the overall diffusional resistance in the RDC, R_T, are determined in practice from apparent first-order rate constants for partitioning. These values for S were determined from plots of ln(transferable concentration) vs t according to Albery et al. (1976). We have used the RDC in a two-phase mode with A, V_1 and V_2 held constant. With one solute at constant stirring speed, the effect of partial ionization should thus be described by Scheme II. Under these circumstances, plots of S vs pH should also be described by Eqn. 9. Representative plots are shown in Fig. 6 for both solutes at different rotation speeds. These clearly conform to theory when the RDC is employed. A comparison of these results with those shown in Fig. 3 for the TPTC reveals the inadequacy of the latter for studies involving variations in the ionic content of the aqueous phase.

Interfacial instability

The existence of some instability at the aqueous/organic interface of the TPTC has never been in doubt. The work of Waterbeemd (1980, 1983) and ourselves (Byron et al., 1980, 1981; Byron and Rathbone, 1984), however, has established and proven a theoretical basis for non-ionized solute transfer in these cells. The previous validity of our

theories indicated that if interfacial instability existed, it remained constant and apparently unaffected when the transfer of different solutes was studied. We have explored a variety of explanations for the deviations from theory which occur in this cell in the presence of partial solute ionization and various ionic contents in the aqueous phase. Errors introduced by variation in partition coefficient with the content of the aqueous phase were avoided by choosing solutes whose transfer was subject to aqueous diffusional control and independent of K_D (Byron and Rathbone, 1984). The absence of interfacial resistance, significant variation in D_1, ν_1 and pK_a; finally the adherence to theory in the RDC, all point to variations in interfacial instability induced by different ionic contents in the aqueous phase.

Several workers using the RDC with its mechanically stabilized interface, advocate this cell as a means of reducing interfacial instability (Guy and Honda, 1984; Guy et al., 1982; Fleming et al., 1983). It is probable also, that the octanol/aqueous interface is more susceptible to instability problems than others. Most liquid/liquid interfacial tension values fall between the air/liquid surface tensions of the separate components (Glasstone and Lewis, 1961); a fact which indicates their absence of interaction. This is not true of octanol/aqueous systems. With these, interfacial and surface tensions vary as a function of aqueous phase ionic strength (Table 1). The low values for interfacial tension show that the octanol/water interface has little tendency to contract or resist deformation (Davies and Rideal, 1963; Davies, 1966; Lewis et al., 1953; Sherwood and Wei, 1957; Davies and Haydon, 1957; Sternling and Scriven, 1959) during mixing and solute transfer. Ionic strength-induced variations in interfacial tension are consistent with the observations of Guy and Honda (1984).

Interfacial instability in the TPTC appears to be variable and moderated by the ionic content of the aqueous phase in octanol/water systems. Although the TPTC was adequate for transfer studies with a variety of non-ionized solutes, experiments involving variation in the ionic content of the aqueous phase should employ a diffusion cell with a stabilized interface.

Glossary of terms

A	interfacial area
a	amount in the aqueous phase
b	amount in the organic phase
C	concentration
D	diffusion coefficient
f_n	solute fraction non-ionized
h	diffusive boundary layer thickness
k_{12}	first-order forward rate constant for partitioning (Schemes I and II)
k_{21}	first-order reverse rate constant for partitioning (Schemes I and II)
K_D	oil/water partition coefficient
$(K_D)_{app}$	apparent oil/water partition coefficient (pH-dependent)
ℓ	thickness of filter membrane
P	permeability
r	V_1/V_2
R_{aq}	aqueous diffusional resistance in boundary layer
R_{org}	organic diffusional resistance in boundary layer
R_I	interfacial diffusional resistance
R_T	total diffusional resistance
RDC	rotating diffusion cell
S	apparent first-order rate constant for partitioning
TPTC	two-phase transfer cell
t	time
V	volume
α	filter porosity
γ	R_{aq}/R_{org}
ω	speed of rotation (H_z)
μ	ionic strength
ν	kinematic viscosity (viscosity/density)
	Subscripts 1, 2, n and i refer to aqueous and organic phases, non-ionized and ionized solute respectively. Superscripts refer to time; ∞ represents equilibrium.

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