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Partition of dissociable compounds in two-phase liquid systems: a theoretical and experimental study

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ABSTRACT: The partition at equilibrium, in a two-phase liquid system, of a compound dissociated in one phase, or both, is expressed in terms of general equations and analyzed. Dissociation in the second phase, even weak, has a non-negligible influence. The distribution ratio depends strongly on the concentration and can even be reversed in certain cases. All the partition and dissociation constants in each phase can be obtained from the concentrations at equilibrium measured under some given conditions. In less favorable cases, an apparent partition constant can still be estimated. This is illustrated by an experimental study, in the water/dichloromethane system, involving the partition of picric acid and cetyltrimethylammonium bromide (CTAB) followed by UV-Visible spectroscopy, and of a series of tetraalkylammonium bromides (ethyl, propyl, and butyl) assayed by mass spectroscopy. Copyright © 2006 John Wiley & Sons, Ltd.

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KEYWORDS: partition; dissociation; distribution ratio; extraction; mass transfer; quaternary ammonium

I. INTRODUCTION

When compounds are soluble in two immiscible solvents, they become split between the two phases. At equilibrium, the distribution ratio[1] is specific of the system. The solvents considered are most frequently water and an organic solvent. The fact that they are non-miscible and constitute a two-phase system does not imply that they are totally insoluble in each other, and so the properties of a solute in each phase of a two-phase system may differ from its properties in each of the phases alone. In the simplest case of a non-dissociable molecule, the distribution ratio is independent of the total concentration and equal to a constant, characteristic of the solute/two-phase system. But many molecules dissociate in at least one of the phases; the distribution ratio then depends on the total concentration involved.[2]

Out of equilibrium, deviation from this ratio is the driving force of mass transfer and of some external phenomena that may accompany it, like spontaneous agitation or interfacial turbulence.[3] We are interested in this kind of instability that has an important effect on transport rates and, therefore, plays an important role in industrial applications like Phase Transfer Catalysis[4] or extraction processes. The compounds for which we have studied the partition properties and dissociation constants are often involved in such applications[5] and give rise, under some experimental conditions to auto-oscillations of the interfacial tension and of the electrical potential between the two phases.[6] This phenomenon was observed in water/dichloromethane systems involving cetyltrimethylammonium bromide (CTAB) alone or associated to picric acid.[7,8] It was also observed when quaternary ammonium salts, tetraethylammonium bromide (TEAB), tetrapropylammonium bromide (TPAB), and tetrabutylammonium bromide (TBAB) are associated to sodium dodecylsulfate.

In some cases, for instance for polyacids, several dissociations are possible in each phase. Sometimes, other processes may occur like dimerisation,[9] heteroconjugation,[10], or aggregation.[11] The characteristics of such systems arise essentially from the coupling between bi-molecular (like association/dissociation) and monomolecular processes (like partition of the same species between the two phases). This is the reason why in this study we focus on the case where only one dissociation occurs in one phase or in both. When other processes occur, they must obviously be taken into account. The modeling of partition can then become significantly more complex. In some cases, the system of equations cannot be solved analytically; one then needs a numerical solver.

The aim of this work is to establish a clear basis for the comprehension and the determination of the different constants involved in partition, beyond the simple

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characterization of the hydrophilic/lipophilic balance expressed by log$P$ or log$D$[12] defined only in regard to octanol, usually for the sake of comparison and classification. We only consider the partition equilibrium between the two liquid phases, and assume that the volume of the two phases is large enough so that the quantity of the solute adsorbed at the interface is negligible. In these conditions, it is not necessary to take into account the interfacial phenomena although they obviously play a role in the kinetics of transfer.[13] On the other hand, as the purely 'chemical' approach is shown to be equivalent to the electrochemical one,[14] we only consider the concentrations, not the electrochemical potentials.

In a first theoretical part, we analyze in detail the equations related to the case involving one dissociation in each phase. We determine in particular the conditions under which an inversion point[15] exists: below a certain global concentration, the partition can be in favor of one phase whereas it is in favor of the other phase for higher concentrations. We discuss in parallel the particular case where dissociation only occurs in the aqueous phase, and also the case where the concentration of the associated species is negligible. We will show that it is possible to determine experimentally, by assaying one or the two phases, the partition coefficient and the dissociation constants. However, in some cases only an apparent partition coefficient can be reached. These different aspects will be illustrated in a second part by the treatment of the experimental data obtained by UV-Visible or by mass spectroscopy for the partition of picric acid, CTAB, TEAB, TPAB, and TBAB in a water/dichloromethane system.

II. THEORETICAL CONSIDERATIONS

1. Equations at equilibrium

The partition in a two-phase liquid system of a compound that dissociates in both phases is assumed to occur according to the following scheme:

$$AB_1 \leftrightarrows A_1^+ + B_1^- \tag{1}$$

$$AB_1 \leftrightarrows AB_2 \tag{2}$$

$$AB_2 \leftrightarrows A_2^+ + B_2^- \tag{3}$$

where A_1^+ and B_1^- represent the dissociated form[16] in Phase 1, AB_1 and AB_2 the associated forms, respectively, in Phases 1 and 2, A_2^+ and B_2^- the dissociated form in Phase 2. The partition itself (Step 2) is assumed to only involve the associated form. We will assume in the following that dissociation is greater in Phase 1. This phase could be considered as an aqueous one. We will also assume that there is no other source of ions, so that $[A_1^+] = [B_1^-]$ and $[A_2^+] = [B_2^-]$.

If no dissociation occurs in Phase 2, the above scheme reduces to Steps (1) and (2), that we will call *Scheme (1–2)* in the following discussion.

At equilibrium, the concentrations $x_1 = [A_1^+]_{\text{eq}}$, $y_1 = [AB_1]_{\text{eq}}$, $x_2 = [A_2^+]_{\text{eq}}$, and $y_2 = [AB_2]_{\text{eq}}$ are linked by the relations[17]:

$$K_{\text{d1}} = \frac{x_1^2}{y_1} \tag{4}$$

$$K_{\text{p}} = \frac{y_2}{y_1} \tag{5}$$

$$K_{\text{d2}} = \frac{x_2^2}{y_2} \tag{6}$$

K_{d1}, K_{d2} being the dissociation constants in Phases 1 and 2, respectively, and K_{p} the partition coefficient. Assigning n_{t} to the total number of moles involved, v_1 and v_2 to the volumes of Phases 1 and 2, the equation of conservation of mass is given by:

$$(x_1 + y_1)v_1 + (x_2 + y_2)v_2 = n_{\text{t}}$$

or, by using the volume ratio $r = v_2/v_1$, and the mean concentration $c_{\text{m}} = n_{\text{t}}/(v_1 + v_2)$:

$$x_1 + y_1 + r(x_2 + y_2) = c_{\text{m}}(1 + r) \tag{7}$$

The set of relations (4) to (7) provides the expression of the concentrations of the different species as a function of the mean concentration c_{m} (see Appendix A):

$$x_1 = \frac{d}{2}\left(\sqrt{m^2 + \frac{4(1+r)c_{\text{m}}}{d}} - m\right) \tag{8}$$

$$y_1 = \frac{1}{1 + rK_{\text{p}}}[(1 + r)c_{\text{m}} - mx_1] \tag{9}$$

$$y_2 = K_{\text{p}}y_1 = \frac{K_{\text{p}}}{1 + rK_{\text{p}}}[(1 + r)c_{\text{m}} - mx_1] \tag{10}$$

$$x_2 = px_1 \tag{11}$$

where the parameters $d = \frac{K_{\text{d1}}}{1+rK_{\text{p}}}$ and $m = 1 + rp$ are only used to simplify the notation while $p = \sqrt{K_{\text{p}}\frac{K_{\text{d2}}}{K_{\text{d1}}}}$ represents the partition constant between the dissociated species (relation 11).

The total concentrations in each phase are:

$$\begin{aligned} w_1 &= x_1 + y_1 \\ &= \frac{1}{1 + rK_{\text{p}}}[(1 + r)c_{\text{m}} - r(p - K_{\text{p}})x_1] \end{aligned} \tag{12}$$

$$\begin{aligned} w_2 &= x_2 + y_2 \\ &= \frac{1}{1 + rK_{\text{p}}}[K_{\text{p}}(1 + r)c_{\text{m}} + (p - K_{\text{p}})x_1] \end{aligned} \tag{13}$$

and the distribution ratio, defined as the ratio of the total concentration of solute in Phase 2 over its total concentration in Phase 1, without considering its chemical form[1], is:

$$D = \frac{w_2}{w_1} = \frac{K_p(1+r)c_m + (p - K_p)x_1}{(1+r)c_m - r(p - K_p)x_1} \qquad (14)$$

The Expressions (8) to (14) can be simplified when the dissociation takes place in Phase 1 only, following *Scheme (1–2)*, taking $K_{d2} = 0$ (and so $p = 0$, $m = 1$, and $x_2 = 0$).

2. Characteristics of the distribution ratio

The typical sigmoid shape of the curve $D(c_m)$ and the corresponding curves w_1 and w_2 are shown on Figure 1 (continuous lines).

The distribution ratio D tends to K_p when c_m infinitely increases, higher concentration favoring association. Inversely, it tends to p when c_m approaches zero and dissociation becomes almost total.[18]

In the special case of *Scheme (1–2)* ($K_{d2} = 0$, $p = 0$), D tends to zero when c_m decreases, with a slope of 1 (Figure 1A, dotted lines).

Increasing K_{d1}, the curve is horizontally translated toward the right and simultaneously its lower limit p is decreased. Inversely, this limit is increased by increasing K_{d2}.

The curve $D(c_m)$ crosses the line $D = 1$ when simultaneously $K_p > 1$ and $p < 1$, that is, taking into account the definition of p, when:

$$1 < K_p < K_{d1}/K_{d2} \qquad (15)$$

In these conditions, the distribution ratio is reversed by the effect of concentration.

The corresponding inversion mean concentration c'_m is expressed by (see Appendix B):

$$c'_m = \frac{(1-p)(K_p - p)K_{d1}}{(K_p - 1)^2} \qquad (16)$$

Partition is in favor of Phase 2 for concentrations above c'_m, and in favor of Phase 1 for concentrations below. When K_p approaches K_{d1}/K_{d2}, the inversion concentration approaches zero, whereas it increases to infinity for values of K_p very close to one. Note that, surprisingly, the inversion concentration does not depend on the volume ratio r. Also note the strong effect of even a relatively small value of K_{d2} ($10^{-6}\,\mathrm{mol \cdot L^{-1}}$) at low concentrations.

In the case of one dissociation only, *Scheme (1–2)*, the inversion point exists for all values of K_p greater than one, as the ratio K_{d1}/K_{d2} in the relation (15) tends to infinity and Expression (16) reduces to:

$$c'_m = \frac{K_p K_{d1}}{(K_p - 1)^2} \qquad (17)$$

In this case, when $K_p \gg 1$, c'_m approaches K_{d1}/K_p.

3. Apparent partition constant

For the sake of simplicity, we assume in this section that the dissociation in Phase 2 is negligible, following the *Scheme (1–2)*. However, the conclusions are still applicable in the general case.

Effective strong partition ($rK_p \gg 1$). If the term K_p is much greater than one, the parameter d reduces to $d \approx K_{d1}/rK_p = 1/rK_{app}$, $K_{app} = K_p/K_{d1}$ being the apparent partition constant, and, in the case of *Scheme (1–2)*,

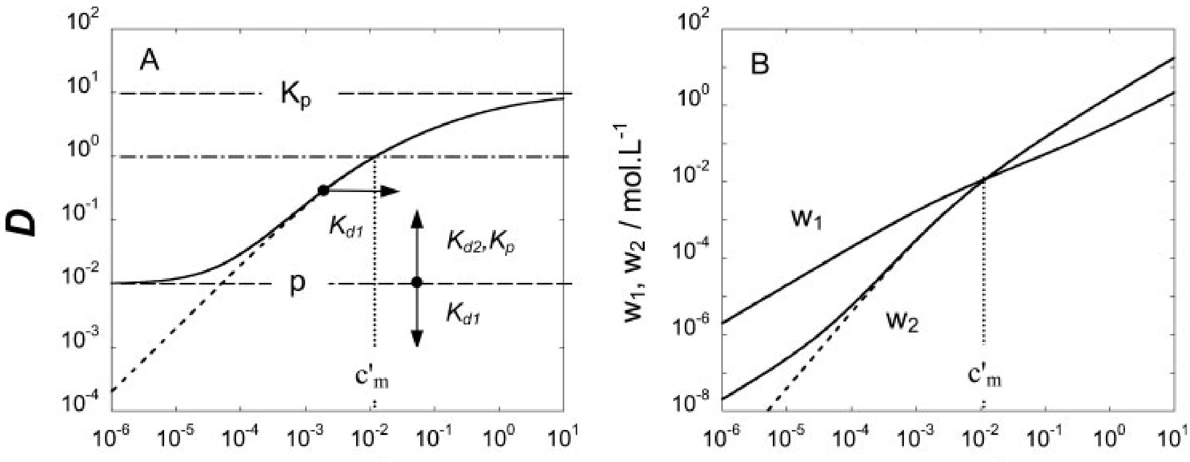

Figure 1. Typical variation of the distribution ratio D (A) and corresponding total concentrations w_1 and w_2 in the two phases (B) as a function of the mean concentration c_m. $K_p = 10$; $K_{d1} = 0.1\,\mathrm{mol \cdot L^{-1}}$; $K_{d2} = 10^{-6}\,\mathrm{mol \cdot L^{-1}}$ (continuous line), 0 (dotted line). The arrows indicate the displacement of the curve and its limits induced by increasing the mentioned constants. (On B, continuous and dotted lines of w_1 are superimposed, the difference between the two curves w_2 being very small)

Expressions (8) to (10) become:

$$x_1 \approx \frac{1}{2\, rK_{\mathrm{app}}}\left(\sqrt{1 + 4rK_{\mathrm{app}}(1+r)c_{\mathrm{m}}} - 1\right) \qquad (8')$$

$$y_1 \approx \frac{1}{rK_{\mathrm{p}}}[(1+r)c_{\mathrm{m}} - x_1] \qquad (9')$$

$$y_2 \approx \frac{1}{r}[(1+r)c_{\mathrm{m}} - x_1] \qquad (10')$$

As the parameter K_{p} only appears in the Expression (9′) of y_1, which is very small, only the apparent partition constant K_{app} can be determined experimentally from concentrations measurements.

Strong dissociation in phase 1 (K_{d1}). It is easy to verify that (8′) and (10′) are the exact expressions corresponding to the simplified model:

$$A_1^+ + B_1^- \leftrightarrows AB_2 \qquad (18)$$

where we assume that the dissociated form in Phase 1 is directly in equilibrium with the associated form in Phase 2, that is, considering that the concentration of AB_1 (y_1) is negligible. The apparent partition constant being defined in this case as $K_{\mathrm{app}} = y_2/x_1^2$, Expressions (8′) and (10′) are found again.

Hence, Expressions (8′) and (10′) do not only correspond to strong partition ($rK_{\mathrm{p}} \gg 1$), but in reality include all the cases where the concentration of the associated form in Phase 1 is negligible ($y_1 \approx 0$).

In the situation where y_1 is negligible, the simplified Expressions (8′) and (10′) apply and it is only possible to determine the apparent partition constant K_{app},[19] as we will see in the treatment of the experimental results obtained for CTAB and TBAB.

4. Determination of K_{d2}

Going back to the general case, but remaining in the hypothesis that dissociation is stronger in Phase 1, the possibility to determine K_{d2}, by using the complete Expressions (8) to (14), is relatively independent of the conditions analyzed above. It depends most of all on whether sufficiently precise measurements can be obtained for the weaker concentrations, for which the effect of dissociation in Phase 2 is the greatest, as shown in Figure 1. Hence, as we will see in the experimental examples, in the case of TPAB, the three constants K_{d1}, K_{p}, and K_{d2} could be determined, while in the case of TBAB, K_{d2} could be determined although only K_{app} was actually accessible.

5. Influence of the volume ratio

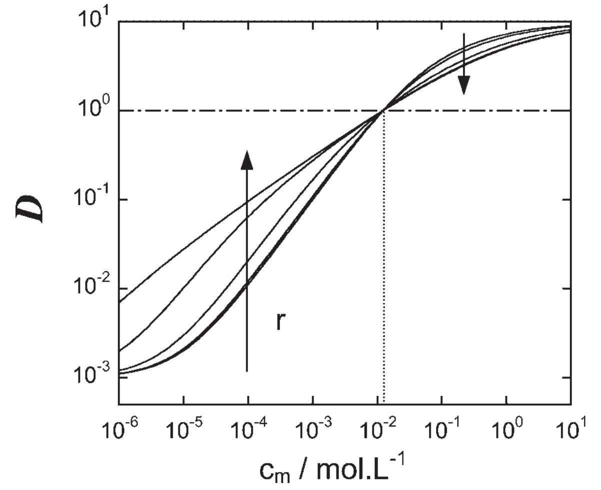

Figure 2. Effect of the volume ratio on the distribution ratio. In the direction of the arrows, $r = 1/99$, 1/9, 1, 9, and 99 ($K_{\mathrm{p}} = 10$; $K_{\mathrm{d1}} = 10^{-1}\,\mathrm{mol \cdot L^{-1}}$; $K_{\mathrm{d2}} = 10^{-8}\,\mathrm{mol \cdot L^{-1}}$). The curves $r = 1/99$ and $r = 1/9$ are superimposed

In the set of Eqns (8) to (13), the volume ratio r ($= v_2/v_1$) is the most often associated to K_{p} or p, and therefore, appears to be an external means of modulating the partition. This could be useful to determine parameters when difficulties arise as evoked above, a smaller value of r compensating for a high value of K_{p}, and vice versa. However, the decrease of the volume ratio leads to a lower variation of the concentrations in Phase 1, an increase of it has the same effect on Phase 2. So, in practice, no significant help can be gained by varying the volume ratio, as far as the determination of the constants is concerned. That is why in the following of this work we have systematically used $r = 1$. However, the volume ratio remains an important parameter for the extraction process, or, more generally, for any transfer phenomenon. Figure 2 shows how the distribution ratio typically depends on the volume ratio. It also illustrates the invariance of the inversion concentration. We do not consider in this work a volume ratio extremely large or small[20] because in these limit cases, contrarily to our hypothesis, the interface itself should be taken into account in the model.

III. EXPERIMENTAL EXAMPLES

The partition of the following compounds was studied in the two-phase system water/dichloromethane, with a volume ratio $r = 1$. For all compounds, concentration in the organic phase was measured as a function of the mean concentration, c_{m}. For picric acid and CTAB, concentration in the aqueous phase was also measured. The fitting of the experimental data was systematically performed first by neglecting the dissociation in the organic phase then by taking it into account. The scale of the experimental data covering several orders of magnitude, fitting was carried out on the logarithms of the

Table 1. Partition and dissociation constants in the water/dichloromethane system

	K_{d1}/mol·L^{-1}	K_p	K_{d2}/mol·L^{-1}	K_{app}(d)/mol^{-1}·L	p(e)	p(f)
Picric acid	*0.42*$_{(a)}$	**80**	1.0×10^{-5}	*1.9×10^2*	4.4×10^{-2}	—
CTAB	*$10^{-2}_{(b)}$*	*5.3×10^2*	—	$\mathbf{5.3\times10^4}$	—	—
TEAB	**0.11**	$\mathbf{7.2\times10^{-4}}$	—	*6.5×10^{-3}*	—	*1.5×10^{-4}*
TPAB	**0.8**	**0.17**	$\mathbf{3.8\times10^{-5}}$	*0.21*	2.8×10^{-3}	*2.1×10^{-3}*
TBAB	*1.6*$_{(c)}$	**28**	$\mathbf{3.6\times10^{-5}}$	*17*	2.5×10^{-2}	*3.0×10^{-2}*

Bold: Considered as new results of this work.
(a) Fixed value from Handbook of Chemistry and Physics.
(b) Fixed at a minimum value to obtain correct fitting.
(c) Fixed value from Fuoss, ref. 23.
(d) Calculated from our results, $K_{app}=K_p/K_{d1}$
(e) Calculated from our results, using the definition $p=(K_pK_{d2}/K_{d1})^{0.5}$.
(f) Calculated from the free energies of ions transfer in table 6.1 of ref. 26, using the relation $2\,RT\ln(p)=\Delta_2^1G^0_{trA+}+\Delta_2^1G^0_{trB-}$ (see Appendix C).

values, in order to correctly take into account the weaker and the stronger concentrations. Neglecting this precaution, the residuals at high or intermediate concentrations overwhelm the ones at low concentrations. In particular, it is not possible to correctly determine constant K_{d2}, which effect, particularly at low concentrations, may be totally ignored if a linear scale of concentration is used. Using logarithms seemed to us the best solution, however, a comparable result could be obtained by using weighted residuals.

The results are gathered in Table 1. The corresponding values of K_{app} and p are also indicated.

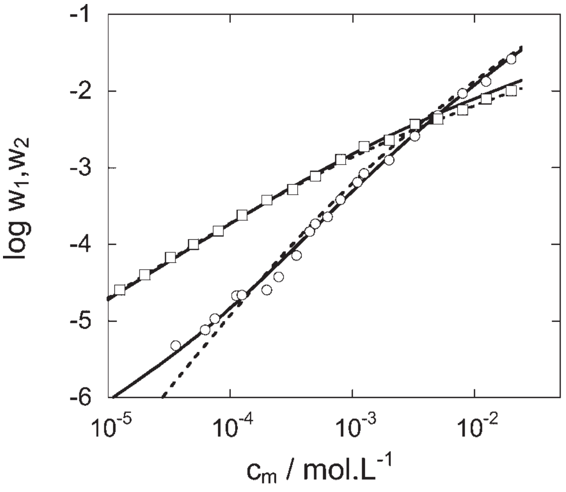

Figure 3. Partition of picric acid as a function of c_m. (□): total concentration in water, w_1; (○) total concentration in dichloromethane, w_2. Dotted line: without dissociation into the organic phase, K_{d2} fixed to 0, $K_p=140$ fitted; continuous line: $K_{d2}=1.0\times10^{-5}$ mol·L^{-1} fitted, $K_p=80$ fitted. The adjustment was performed simultaneously on the logarithm of the concentrations of the two phases; K_{d1} was fixed at its known value (0.42 mol·L^{-1})

1. Picric acid

In the case of picric acid, the dissociation constant in water is known ($pK_a=0.38$ at 25°C, i.e., $K_{d1}=0.42$ mol·L^{-1}), and the determination of the partition coefficient K_p can be expected, even in the case studied in section II-3, where the individual parameters K_p and K_{d1} cannot be individually reached. Moreover, quantitative analysis can be performed directly by UV-visible spectrophotometry in both water and dichloromethane (see experimental part). It was then possible to assay it, after partition, in the two phases, which allowed to experimentally show the existence of the inversion point, that appears for a mean concentration of 5×10^{-3} mol·L^{-1} (Figure 3). The accuracy of the assay has been evaluated by the difference between the sum of the values obtained in the two phases and the initial concentration. The mean difference was less than −2.8%, showing that the measured concentrations were very slightly underestimated.

The results of the measurements are plotted on Figure 3, together with their fitting obtained with and without dissociation in the organic phase using Eqns (12) and (13). K_{d1} being fixed, only K_p and K_{d2} were adjusted. It is clear that adjustment without dissociation in the organic phase (i.e., $K_{d2}=0$) does not take correctly into account data obtained for the lower concentrations. By fitting all the unknown parameters, we have obtained $K_p=80$ and $K_{d2}=10^{-5}$ mol·L^{-1}. When K_{d2} was fixed at zero, a three times higher residual error was obtained together with a higher K_p (140). This result can be explained by the fact that the dissociation in one phase 'helps' partition in favor of that phase. A close value, $K_p=125$, was found by direct fitting of the concentrations and not of their logarithm, K_{d2} being in this case impossible to determine.[21]

The value obtained for the dissociation constant in dichloromethane, $K_{d2}=1.0\times10^{-5}$ mol·L^{-1} can be compared to its value in water, obviously much higher as expected from their dielectric constants (78.48 and 9.08 for pure water and pure dichloromethane, respectively). The parameter p being close to 0.04 in these conditions, relation (11), $x_2=px_1$, indicates that the species dissociated in dichloromethane represents 4% of its counterpart in water. This relatively high value can be surprising for such a small value of K_{d2}.

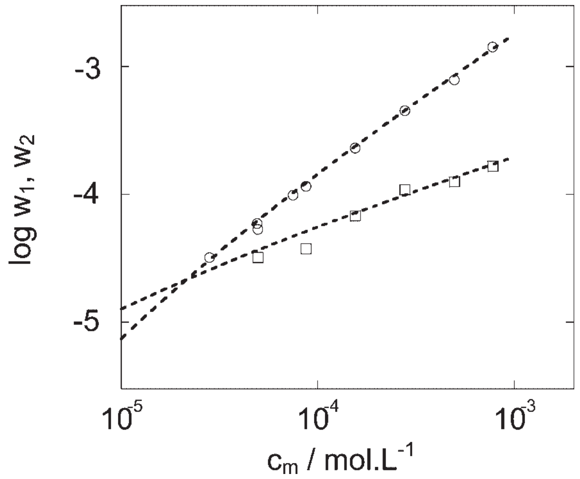

Figure 4. Partition of CTAB as a function of c_m. (□): total concentration in water, w_1; (○): total concentration in dichloromethane, w_2. Dotted line: simultaneous fitting of the logarithm of the concentrations in the two phases; $K_p = 5.3 \times 10^2$; K_{d1} arbitrarily fixed at 10^{-2} mol · L^{-1}; K_{d2} fixed at 0.

2. CTAB

CTAB cannot be directly assayed by UV-visible spectroscopy. A method of extraction (see experimental part) was used to perform the determination of CTAB in both the water and dichloromethane phases after partition (Figure 4). The mean difference between the sum of the values obtained in the two phases and the initial concentration was around −5.7%. This slight discrepancy could be explained by imperfect extraction of CTAB by this method, but it was assumed that this small difference did not significantly affect our conclusion. In order to avoid the difficulties due to micellization, the concentrations were lower than the critical micellar concentration in water, that is, $<8 \times 10^{-4}$ mol · L^{-1}. Figure 4 shows that in the concentration domain considered, the partition of CTAB is in favor of the organic phase. The inversion point was not reached but can be estimated at about 2×10^{-5} mol · L^{-1}.

As the dissociation constant of CTAB in water, K_{d1}, is not known, fitting was carried out only with K_p, while a fixed arbitrary value was attributed to K_{d1}. The fitting of these data allowed only the ratio K_p/K_{d1} to be determined ($K_{app} = 5.3 \times 10^4$ mol^{-1} · L). However, fitting becomes impossible for values of K_{d1} and K_p lower than 10^{-2} mol · L^{-1}and 5.3×10^2, respectively (Table 1). These values can be considered as lower limits for these unknown parameters. In these conditions, the value of rK_p is much greater than one, which explains why its actual value cannot be determined (see section II-3).

An attempt to fit the dissociation constant in dichloromethane, K_{d2}, led to a very small value (less than 3×10^{-6} mol · L^{-1}) which did not result in a significant decrease of the residual error. It can, therefore, be concluded that dissociation in the organic phase is negligible in the domain of concentration considered. Then, the parameter p cannot be calculated.

3. Quaternary ammonium salts

The series of quaternary ammonium bromides TEAB, TPAB, and TBAB, was assayed in the organic phase, after partition, by mass spectroscopy. This method presents the advantage of direct assay and provides accurate values at low concentrations (down to 10^{-6} mol · L^{-1}). Moreover, as the partition of these compounds is clearly less in favor of dichloromethane (Figure 5A) than for CTAB, the concentration in the aqueous phase varies very little and its assay does not give exploitable data.

TEAB: Thanks to the high sensitivity of the method it was possible to obtain precise values of the concentration

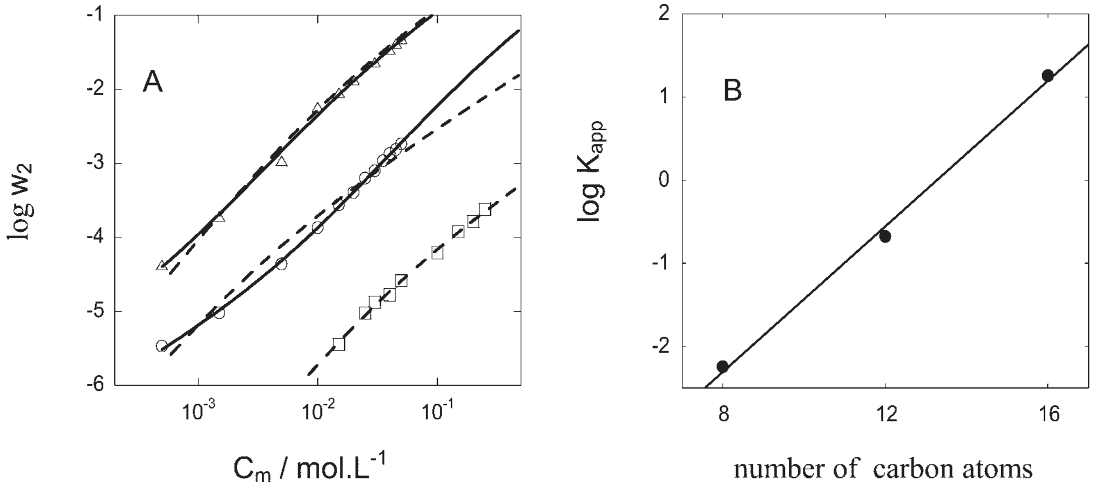

Figure 5. A: Log of the total concentrations, w_2, in CH_2Cl_2 after partition of TEAB (□), TPAB (○) and TBAB (△) *versus* the mean concentration c_m. Dotted lines: fitting without dissociation in Phase 2. Continuous lines: fitting with dissociation in both phases (see values of the constants in Table 1). B: Variation of the logarithm of the apparent partition constant $K_{app} = K_p/K_{d1}$ as a function of the number of carbon atoms of the alkyl groups of the quaternary ammonium.

in the organic phase, although 10 000 times lower than the concentrations in the aqueous phase (Figure 5A). In this example, the study of partition, clearly unfavorable to the organic phase, allowed the determination of the partition coefficient K_p itself, but also of the dissociation constant in the aqueous phase K_{d1}, K_{d2} being fixed to zero. The partition coefficient, K_p, is very low (7.4×10^{-4}) and K_{d1} is relatively high ($0.13\,\text{mol}\cdot\text{L}^{-1}$).

A value of $K_{d2} = 7 \times 10^{-5}\,\text{mol}\cdot\text{L}^{-1}$ is reported from conductance measurements in ethylene chloride.[22] However, we found that the attempt to fit K_{d2} did not result in any significant decrease of the residual error. Moreover, taking $K_{d2} > 10^{-7}\,\text{mol}\cdot\text{L}^{-1}$ did not allow a correct fitting of the data. It can, therefore, be concluded that, in our range of concentrations, the dissociation of TEAB in dichloromethane does not need to be taken into account as far as the partition is considered.

TPAB: The partition of TPAB is about 100 times more in favor of dichloromethane than TEAB (Figure 5A). Thanks to this more favorable situation, the three constants K_{d1}, K_p, and K_{d2} were determined without any ambiguity ($K_{d1} = 0.8\,\text{mol}\cdot\text{L}^{-1}$; $K_p = 0.17$; $K_{d2} = 3.8 \times 10^{-5}\,\text{mol}\cdot\text{L}^{-1}$). The residual error was 28 times higher if the dissociation in the organic phase (K_{d2}) was not taken into account (fixed to zero). Aberrant values of the corresponding constants K_p, K_{d1}, and even of their ratio, K_{app}, are reached in these conditions.

TBAB: The partition in favor of dichloromethane is again about 100-fold higher than for TPAB and fitting was only possible by arbitrarily fixing K_{d1}. As for CTAB, only the ratio K_p/K_{d1} could be determined. However, a correct fitting of the data could only be obtain for values of $K_{d1} > 1\,\text{mol}\cdot\text{L}^{-1}$. This is in agreement with the value $1.6\,\text{mol}\cdot\text{L}^{-1}$ given by Fuoss and Kraus.[23] Fixing K_{d1} at this value, K_p is found equal to 28. The dissociation constant in CH_2Cl_2 (K_{d2}) has been found at $3.4 \times 10^{-5}\,\text{mol}\cdot\text{L}^{-1}$, a value very close to that of TPAB. It was shown that the residual error was 3.3 times higher if this dissociation was neglected. Like for picric acid and CTAB, relation (15) being satisfied ($1 < K_p < K_{d1}/K_{d2}$), an inversion concentration exists and belongs to the experimental domain (about $6 \times 10^{-2}\,\text{mol}\cdot\text{L}^{-1}$).

Discussion on the series TEAB, TPAB, and TBAB. Several values of the dissociation constant in water K_{d1} are reported by the literature, coming from conductance measurements[5a,9,22,24] or dielectric spectroscopy[5a]. These values fluctuate from 0.26 to 0.42 (TEAB), 0.21 to 0.36 (TPAB), and 0.15 to 1.6 (TBAB) $\text{mol}\cdot\text{L}^{-1}$. The values given in Table 1 correspond to our best fit. However, an acceptable fit can still be obtained by fixing the above values of K_{d1} for TEAB and TPAB. On the contrary, for TBAB, a good fit cannot be obtained using the values 0.15–0.21 reported in reference 15(a). That is why we have taken the value given by Fuoss[23] ($1.6\,\text{mol}\cdot\text{L}^{-1}$).

The values of the dissociation constants in dichloromethane, K_{d2}, obtained for TPAB and TBAB (3.8×10^{-5} and $3.4 \times 10^{-5}\,\text{mol}\cdot\text{L}^{-1}$, respectively) are very close to the value $5 \times 10^{-5}\,\text{mol}\cdot\text{L}^{-1}$ ($K_{ass} = 2 \times 10^4\,\text{mol}^{-1}\cdot\text{L}$), reported for tetra-*n*-butylammonium iodide.[25]

Concerning both the dissociation constants, it is rather remarkable to obtain comparable values using two-phase assays on one hand, monophasic electrochemical measurements on the other hand.

As shown in Table 1, a very good agreement was found between the values of the partition constants p of dissociated species, calculated from our results and their values calculated from the standard Gibbs free energies of ions transfer from water to dichloromethane[26] (see Appendix C). This good correlation simultaneously validates our theoretical approach and our measurements.

Moreover, as shown in Figure 5B, the logarithm of the apparent partition coefficient K_{app} increases quasi-linearly as a function of the number of carbon atoms in the alkyl chains on the quaternary ammonium. This variation, due to increasing hydrophobicity is in agreement with the literature.[27] The slope of this line, representing the contribution of one methylene group ($\Delta\log K_{app}$/—CH_2—) is equal to 0.44. This value is in agreement with an estimation of log*P* for TEAB, TPAB, and TBAB obtained with the software miLogP1.2 (http://molinspiration.com) giving, $\log P = 0.3$, 2.04, and 3.8, respectively, that is, $\Delta\log P$/—CH_2— = 0.44. A slope of 0.43 is also reported for tetraalkylammonium picrates.[28]

IV. CONCLUSION

A detailed discussion of the equations governing the partition of a dissociable compound in both phases of a two-phase liquid system was presented. Dissociation was supposed to be much greater in one of the phases.

Particular attention was devoted to the aspects providing a better comprehension of the phenomena induced by the coupling between partition and dissociation, like the existence of an inversion point for the distribution ratio, clearly put forward experimentally in the case of picric acid. The influence of dissociation in the second phase, even weak, is demonstrated. We have also analyzed, first theoretically, then by dealing with experimental examples, the conditions for the determination of the different constants characterizing a given two-phase system from the quantitative assay in one phase or both:

1. It is always possible to determine an apparent partition coefficient (K_{app}), which is the ratio of the partition coefficient (K_p) over the dissociation constant in the more dissociative phase (K_{d1}). In the concentration domain used to determine it, this constant is sufficient to characterize the system as far as the distribution at

equilibrium of the solute between the two phases is concerned. If constant K_{d1} is known, it is then possible to deduce the value of K_p, as in the case of picric acid and TBAB.

2. In favorable cases, it is possible to obtain the true partition constant (K_p) and the dissociation constant in the more dissociative phase (K_{d1}). This was the case for TEAB and TPAB.
3. The determination of the dissociation constant in the less dissociative phase (K_{d2}) is relatively independent of the determination of the two other constants but needs to correctly take into account the data obtained at low concentrations. This is why it is necessary to obtain precise data in this domain, and to process their logarithm. Ignoring the second dissociation, even for values of K_{d2} of the order of $10^{-5}\,\mathrm{mol\cdot L^{-1}}$, leads to large errors on the other constants, including K_{app}.

In any case, the determination of the parameters is only possible if sufficiently precise method is used to assay the samples. The mass spectroscopy assay, developed for the tetraalkylammonium bromide series, provided accurate data at very low concentrations.

Although the main purpose of this work was not a detailed discussion of the results on the molecular level, they appear to be coherent and in agreement with the literature.

EXPERIMENTAL PART

Chemicals

All compounds used were analytical grade. Crystallized picric acid (Prolabo), cetyltrimethylammonium bromide (CTAB) 99+% (Aldrich), tetraethylammonium bromide (TEAB) 99+% (Acros Organics), tetrapropylammonium bromide(TPAB) 98% (Acros Organics), tetrabutylammonium bromide(TBAB) 99+% (Acros Organics), dichloromethane (Aldrich, HPLC grade), and methanol (Aldrich, HPLC grade) were used as received. All the aqueous solutions were prepared with ultra pure water filtered at 0.2 μm (resistivity $> 16\,\mathrm{M\Omega\cdot cm}$).

Preparation of the two-phase systems

All the solutions were initially prepared in the aqueous phase. 10 ml were put into contact with the organic phase (10 ml CH_2Cl_2, $\rho = 1.32$). The two-phase system was then placed under moderate stirring for at least 24 h at room temperature until equilibrium was reached.

Quantitative analysis of picric acid

All the measurements of UV-visible absorbance were performed with a Hewlett-Packard HP8452A diode array spectrophotometer. Picric acid was directly assayed by measuring its absorbance in water at 356 nm ($\varepsilon = 14400 \pm 150\,\mathrm{mol^{-1}\cdot L\cdot cm^{-1}}$) and in dichloromethane at 336 nm ($\varepsilon = 4200 \pm 55\,\mathrm{mol^{-1}\cdot L\cdot cm^{-1}}$). For the aqueous phase, all the measurements were performed in cells with an optical pathway of 1 cm. Higher concentrations were diluted (up to 100-fold) in order not to exceed an absorbance of 2. For the organic phase, the use of cells with an optical pathway of 5 cm was necessary for concentrations lower than 5×10^{-4} M. In this case, 25 ml of each phase was used. On the contrary, for concentrations higher than 2×10^{-3} M, cells of 0.1 cm optical pathway were used to avoid dilution and hence the risks of evaporation of dichloromethane.

Quantitative analysis of CTAB by extraction

After equilibration of the two-phase system under study (partition of the CTAB alone) the following extraction method was used. In water in the presence of picric acid, CTAB forms a totally hydrophobic ion pair with the picrate ion[8]. In the two-phase water/dichloromethane system, this ion pair is entirely dissolved in the organic phase. If picric acid is used in excess, all the CTAB is extracted in the organic phase as ion pairs that can be assayed by UV-visible spectrophotometry at 450 nm ($\varepsilon_{450\mathrm{nm}} = 6050 \pm 60\,\mathrm{mol^{-1}\cdot L\cdot cm^{-1}}$), where picric acid, which is also present, does not absorb.

Quantitative analysis of the quaternary ammonium salts

TEAB, TPAB, and TBAB were quantified by ESI-LC-MS. The set-up used was a triple quadripole Q-Trap from Applied Biosystems equipped with an electro-spray source. The mass spectrometer was coupled to an HPLC (Agilent 1100) with an automatic sampler. The acquisition system and the data processing for the set-up used Analyst 1.4 software.

Analysis was performed in FIA mode (flow injection analysis) at room temperature. The mobile phase was a mixture of H_2O/MeOH (20:80, v/v), the flow rate was 200 μl/min. The volume of the injected samples was 5 μl.

Analysis by mass spectrometry was performed in the MRM mode (multiple reaction monitoring) on the transitions 130▶86, 186▶114, and 242▶142 representing the precursor ion and a product ion of TEA^+, TPA^+, and TBA^+, respectively.

The precursor ion was selected in the first quadripole, the selected ion was decomposed in the second, and the product ion analyzed in the third. This mode of acquisition increased the selectivity and specificity of the analysis.

The main controls were the temperature of the source (300°C), the ionization potential (IS: 4800 V), the difference of potential between the skimmer and the inlet (DP: 40 V), and the energy of collision (CE: 30 V).

Assaying used a graded range of external standards comprising six solutions for each salt at concentrations between 10^{-6} and $10^{-5}\,\text{mol}\cdot\text{L}^{-1}$. The quantification limit was $10^{-7}\,\text{mol}\cdot\text{L}^{-1}$. The solutions to be analyzed were diluted in the mobile phase such that their concentrations fitted with the standards. The standards were used for calibration between each series of measurements; the relative error on the determined concentrations can be estimated to be less than 5%.

Processing the data. Parameters were fitted for the experimental data using home made simulation and fitting software (Sa3) based on an optimization algorithm of the Powell type. Fitting consisted in minimizing the residual error:

$$E = \frac{1}{n}\sum_{j=1}^{n}\left(c_j^{\text{calc}} - c_j^{\text{ex}}\right)^2$$

where c^{calc} and c^{ex} stand for the logarithms of the calculated concentration and of the experimental value, and n for the number of points considered. When analysis was performed in both phases, the data were fitted simultaneously. Care was taken to be insured that the results were robust and the set of optimized parameters unique. When the effect of one parameter on the fitting accuracy was shown to be non-significant, the corresponding parameter was systematically removed.

TABLE OF SYMBOLS

c_{m}	mean concentration: $n_{\text{t}}/(v_1 + v_2)$
c'_{m}	inversion mean concentration
d	$K_{\text{d1}}/(1{+}rK_{\text{p}})$, $\text{mol}\cdot\text{L}^{-1}$
D	distribution ratio: total concentration in Phase 1/ total concentration in Phase 2
K_{app}	apparent partition constant: $K_{\text{p}}/K_{\text{d1}}$ ($\text{mol}^{-1}\cdot\text{L}$)
K_{di}	dissociation constant in Phase i ($\text{mol}\cdot\text{L}^{-1}$)
K_{p}	partition constant (of associated species, y_2/y_1)
m	$1 + r\cdot p$
n_{t}	total number of moles involved
n'_{t}	total number of moles at inversion
p	$(K_{\text{p}}\cdot K_{\text{d2}}/K_{\text{d1}})^{0.5}$ (partition constant of dissociated species, x_2/x_1)
r	volume ratio: v_2/v_1
v_i	volume of Phase i
x_i	concentration of the dissociated form in Phase i ($\text{mol}\cdot\text{L}^{-1}$)
y_i	concentration of the associated form in Phase i ($\text{mol}\cdot\text{L}^{-1}$)
w_i	total concentration in Phase i: $x_{\text{i}} + y_{\text{i}}$ ($\text{mol}\cdot\text{L}^{-1}$)

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16. Compounds are assumed to dissociate into ions, because our experimental section is devoted to ions, but our conclusions also apply to all kind of association/dissociation processes.
17. The equilibrium constants take into account concentrations, not activities. However, our model correctly predicts the experimental data in a large concentration domain.
18. Theoretically, the constant p can be higher than K_p, reversing the shape of the curve of the figure 1A. However, it is only possible when $K_p < K_{d2}/K_{d1}$, i.e. K_p and p are very small, meaning that no actual partition occurs.
19. Following the definition of the extraction constant K_{ex} (ref 1), K_{app} can be considered as a self-extraction constant.
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21. Moreover, it has been verified that if K_{d1} is not attributed a fixed value it is then only possible to determine the apparent partition coefficient K_{app}. This is in agreement with the relatively high values of K_p (compared to 1) and K_{d1}, both contributing to make the concentration of the associated form in water (y_1) negligible (see section II-3).
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