

ION-PAIR EXTRACTION AS A TOOL FOR THE STUDY OF MECHANISMS OF REACTIONS RELATED TO PHASE TRANSFER CATALYSIS

Arne Brändström

Department of Organic Chemistry, AB Hässle, S-431 83 Mölndal, Sweden

Abstract - From distribution measurements using dilute solutions both the extraction equilibrium constant and the dissociation constant for the ion pair are obtained. The free energy of transfer of the two ions are also obtained from the same experiment. From these constants and distribution measurements in solutions, more concentrated than those above, the degree of dissociation in the organic layer is obtained without any use of the activity constant in the actual solution. From still more concentrated solutions constants can be obtained for the formation of adducts and triple ions in the organic layers and the formation of ion pairs in the aqueous layer. A knowledge of all these equilibrium constants is necessary for the interpretation of results obtained from kinetic measurements in two layer systems such as phase transfer catalysis.

INTRODUCTION

Ion-pair extraction is a process in which three compartments are involved, the aqueous layer, the organic layer, and the interphase (phase boundary). Our physical chemical knowledge of the behaviour of compounds in the aqueous layer can be considered as good, of that in the organic layer as fair, and of that in the interphase as almost nonexistent. However, by studying a reaction involving several compartments, knowledge of the physical chemical properties of one compartment can be used to deduce those of another, and for this reason ion pair extraction can be a very useful tool in physical organic chemistry. Curiously enough, ion pair extraction has not been used very much for that purpose.

THE FUNDAMENTAL EXTRACTION EQUATION

The distribution of a salt between two layers is often not well understood. More often than not, this is given as a ratio of the stoichiometric concentrations of an ion in the two layers. This is often called the "distribution constant". This is, however, not constant but is highly dependent on the nature and concentration of the counter-ion. Such approaches, which are an indication of lack of elementary knowledge of the concept of distribution, will not be discussed here.

From simple thermodynamic considerations (Ref.1) the fundamental equation 1 for ion pair extraction can be deduced.

$$K_{\text{ex}}(\text{QX}) = a_{\text{s}}(\text{QX}) / (a_{\text{w}}(\text{Q}^+) a_{\text{w}}(\text{X}^-)) = F(\text{Q}^+) F(\text{X}^-) / K_{\text{diss}}^{\text{s}}(\text{QX}) \quad (1)$$

For a given solvent *s* the factor $F(\text{Q}^+)$ depends on the structure of Q^+ only, and $F(\text{X}^-)$ on the structure of X^- only, provided that there is no specific interaction between X^- and Q^+ .

Activities are often not directly available for measurements and for practical purposes equation 2 is often used.

$$k_{\text{ex}}(\text{QX}) = C_{\text{s}}(\text{Q}) / ([\text{Q}^+]_{\text{w}} [\text{X}^-]_{\text{w}}) \quad (2)$$

where $C_{\text{s}}(\text{Q})$ is the stoichiometric concentration of *Q* in the organic layer. In this equation all concentrations can be measured and $k_{\text{ex}}(\text{QX})$ can thus be calculated. The variation of $k_{\text{ex}}(\text{QX})$ with $[\text{Q}^+]_{\text{w}}$ and $[\text{X}^-]_{\text{w}}$ can usually be used to calculate $K_{\text{ex}}(\text{QX})$ and several other constants. It will be demonstrated below how this can be done, but first a few fundamental facts will be pointed out.

THE POSSIBILITIES OF CONTROLLING THE DISTRIBUTION OF AN ION

The accuracy of a distribution measurement depends on the possibility of making true measurements of the concentrations in the two layers. It is always difficult to take samples of the two layers without crosscontaminations by micro drops. The most accurate measurements of *Q* are therefore obtained when the concentrations of *Q* are of the same magnitude in both layers. Equation 2 can be rewritten to give equation 3

$$D(\text{Q}) = C_{\text{s}}(\text{Q}) / [\text{Q}^+]_{\text{w}} = k_{\text{ex}}(\text{QX}) [\text{X}^-]_{\text{w}} \quad (3)$$

From this it can be seen that the distribution, $D(\text{Q})$, can be regulated at will within wide limits. By suitable choice of the structure of X^- and the solvents, $k_{\text{ex}}(\text{QX})$ can be varied by more than 20 powers of ten. An additional regulation of the distribution can be obtained by means of the concentration $[\text{X}^-]_{\text{w}}$. It is thus very often possible to perform experiments under conditions which makes accurate measurements possible.

THE CONCENTRATION UNITS

Equation 1 contains activities in two different solvents. This gives rise to a problem which is often overlooked. Activity is correlated to concentration by means of the activity coefficient and it is important to remember which unit is used for the concentrations in the two layers. The concentration unit most widely used is molarity *M*. When solutions in different solvents are compared, the mole fraction, N_{X} , is probably the most useful unit. For dilute solutions, we have $N_{\text{X}} = M V_{\text{s}} / 1000$ where V_{s} is the molar volume of the solvent, and this can be used for unit conversions. The concentration unit used in this paper and in most other papers published on ion pair extraction, is *M*.

DISSOCIATION IN THE ORGANIC LAYER

In dilute solutions of QX containing "uncomplicated" ions only C_s is the sum of the concentrations $[QX]_s$ and $[Q^+]_s$. Since $[Q^+]_s = [X^-]_s$ the dissociation equation gives

$$[Q^+]_s f_s = ([QX]_s K_{\text{diss}}^s(QX))^{1/2} \quad (4)$$

where f_s is the mean activity coefficient in the organic layer and $[QX]_s$ is assumed to be equal to $a_s(QX)$. If this is combined with equation 2 we obtain equation 5

$$\frac{C_s}{a_w(Q^+)a_w(X^-)} = K_{\text{ex}}(QX) + \frac{(K_{\text{ex}}(QX)K_{\text{diss}}^s(QX))^{1/2}}{(a_w(Q^+)a_w(X^-))^{1/2}f_s} \quad (5)$$

In this equation C_s , $a_w(Q^+)$ and $a_w(X^-)$ are measured or readily calculated. If equation 5 is combined with a suitable equation for the calculation of the activity coefficient f_s both $K_{\text{ex}}(QX)$ and $K_{\text{diss}}^s(QX)$ can be obtained by non linear least square regression (Ref.2).

Since both anions and ion pairs may be active nucleophiles a knowledge of the degree of dissociation is of fundamental importance in all discussions of the kinetics of a reaction involving these species. In such discussions the importance of the uncertainty in the calculation of f_s in solvents of low polarity is often overestimated. In contrast to common opinion f_s values for the ions in a solution are not required for the calculation of the degree of dissociation. This is readily seen from a very useful plot for the calculation of $K_{\text{ex}}(QX)$ and $K_{\text{diss}}^s(QX)$ from distribution experiments. Equation 5 is readily rearranged to give equation 6

$$D^* + D_{\text{korr}} = (a_w(Q^+)a_w(X^-))^{1/2}K_{\text{ex}}(QX) + (K_{\text{ex}}(QX)K_{\text{diss}}^s(QX))^{1/2}$$

$$D^* = \frac{C_s}{(a_w(Q^+)a_w(X^-))^{1/2}}; D_{\text{korr}} = (1 - 1/f_s)(K_{\text{ex}}(QX)K_{\text{diss}}^s(QX))^{1/2} \quad (6)$$

In this equation f_s appears in a correction term, D_{korr} , which is very small and rather unimportant for the calculation. Any reasonable equation for the calculation of f_s is therefore suitable in this calculation. This is readily seen from Fig.1 which demonstrates two plots, one with $f_s = 1$ and one with f_s values calculated using the equation of Marshall and Grunwald (3). In order to be able to demonstrate the difference between the two sets, a compound with a rather low $pK_{\text{diss}}^s(QX)$ value (4.70) has been selected for the plot. In compounds with higher $pK_{\text{diss}}^s(QX)$ values the difference between the two sets is much less and the two sets are indistinguishable when $pK_{\text{diss}}^s(QX) = 6.5$. It should also be observed that the f_s values that might be required for the plot are those for dilute solutions for which all activity coefficient equations give almost identical values.

The result of this is that $K_{\text{ex}}(\text{QX})$ values are available by methods which do not suffer from the uncertainty of f_s values in the organic solvent. If no species of QX other than the ions Q^+_s and X^-_s and the ion pair QX_s are present, the concentration of the ions can be calculated using equation 7.

$$[\text{Q}^+]_s = C_s(\text{Q}) - a_w(\text{Q}^+)a_w(\text{X}^-)K_{\text{ex}}(\text{QX}) \quad (7)$$

The concentrations of the ions are thus obtained without any knowledge of f_s in the actual solution. The presence of species of QX other than the ion pair and the ions is readily detected by a curvature in a plot according to equation 6.

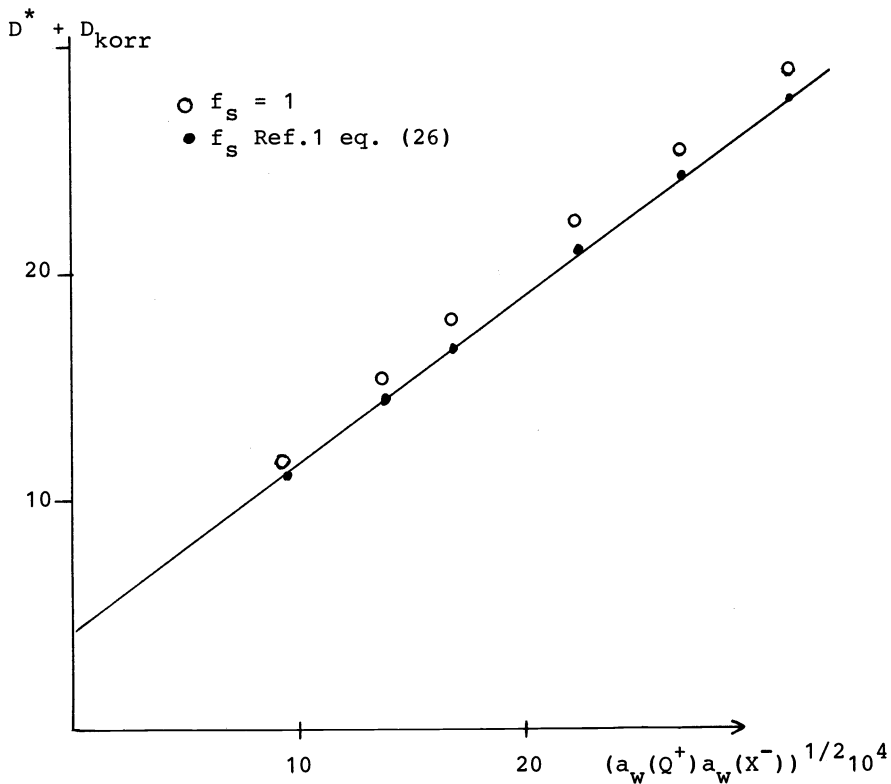


Fig. 1. Extraction and dissociation of tetrabutylammonium 3-nitrophenolate in dichloromethane plotted according to equation 6. Temperature 25°C.

TRIPLE ION FORMATION IN THE ORGANIC LAYER

According to theory (Ref.4) the maximum concentration C_{max} for which triple ion formation is below 0.1 per cent is given by equation 8

$$C_{\text{max}} = 1.19 \times 10^{-14} (\epsilon T)^3 \quad (8)$$

For wet dichloromethane ($\epsilon = 8.94$) this gives $C_{\text{max}} = 2.25 \times 10^{-4}$. Triple ion formation above 1 per cent can thus be expected only in solutions more

concentrated than 10^{-3} molar. We can also expect that triple ion formation is disfavoured if the ions are bulky.

Triple ion formation can be studied by ion pair extraction experiments. In principle, this is done by comparing C_s values calculated from equation 5 with those obtained by experiment. In this way it is possible to calculate triple ion formation constants, but it should be observed that f_s values for rather concentrated solutions are required for these calculations. Until more detailed information about the physical chemistry of triple ions is available, a combination of a triple ion formation equation and an activity coefficient equation is nothing but a complicated interpolation formula for the calculation of triple ion concentrations. Good agreement between found and calculated values is an indication that the underlying principles may be correct. Definitive proofs for the validity of the equations can only be obtained by independent measurement. Conductivity measurements might be used for this purpose, and an investigation along these lines has been started (Ref.5).

ION PAIR FORMATION IN THE AQUEOUS LAYER

As Bjerrum (6) has pointed out, ion pair formation between two univalent ions does not usually occur in water. A few cases have, however, been observed (Ref.7). Ion pair formation occurs when one of the ions contains an extended aromatic ring system. In an investigation of the extraction of sulfonic acids with amines (Ref.8) we observed some deviations in the extraction behaviour when the amine was quinoline or when the acid was 2-naphthalene sulfonic acid. A very strong effect was observed when these two compounds were combined. From simple calculations using structure-activity relationships for extractability we expected a high degree of extraction with dichloromethane but no extraction could be observed in our standard experiment. This was interpreted as being due to extensive formation of ion pairs in the aqueous layer, and additional evidence for this has been obtained from conductivity measurements (Ref.9) and from ^1H and ^{13}C NMR. (Ref.10).

With the theory of ion pair extraction presented here it is obvious that ion pair formation in the aqueous layer should result in a decreased degree of extraction. (The ion pair formation in the aqueous layer withdraws ions from the extraction equilibrium).

If the extraction is considered to be a distribution of the ion pair between the two layers the result is unexpected and an additional hypothesis is needed to explain the results.

The strong interaction between the quinoline - and the naphthalene-ring systems in the aqueous layer can be expected to give important information on the $\pi - \pi$ bond between aromatic rings and on the concept of hydrophobicity. Some investigations of these phenomena are under way (Ref.9).

ADDUCT FORMATION IN THE ORGANIC LAYER

When hydrogen donors are present in the slightly polar solvent often used in ion pair extractions, strong hydrogen bonds are often formed between the donor and the ion pair. One type of adduct is formed between water molecules and ion pairs containing hydrophilic anions such as OH^- , Cl^- and CN^- (Ref.11).

Another important type of adduct formation occurs between tetraalkylammonium phenolates and one or two mole equivalents of phenol. The importance of this type of side reaction on the extraction equilibrium has been discussed by Brändström (12) and several equilibrium constants have been measured by Johansson (13).

FREE ENERGY OF TRANSFER.

Equation 1 can be rearranged to

$$K_{\text{ex}}(\text{QX})K_{\text{diss}}^{\text{S}}(\text{QX}) = \frac{a_{\text{S}}(\text{Q}^+)a_{\text{S}}(\text{X}^-)}{a_{\text{W}}(\text{Q}^+)a_{\text{W}}(\text{X}^-)} = F(\text{Q})F(\text{X}) \quad (9)$$

Distribution experiments performed with dilute solutions give $(K_{\text{ex}}(\text{QX})K_{\text{diss}}^{\text{S}}(\text{QX}))^{1/2}$ as the intercept in a plot according to equation 6. Provided that no specific interaction occurs between Q^+ and X^- , F_{Q} and F_{X} are connected to the free energy of transfer $\Delta G_{\text{t}}^{\circ}$ of the two ions Q^+ and X^- from water to the solvent by equation 10

$$\begin{aligned} \Delta G_{\text{t}}^{\circ}(\text{Q}^+) &= -RT \ln F(\text{Q}) \\ \Delta G_{\text{t}}^{\circ}(\text{X}^-) &= -RT \ln F(\text{X}) \\ \Delta G_{\text{t}}^{\circ}(\text{Q}^+) + \Delta G_{\text{t}}^{\circ}(\text{X}^-) &= -RT \ln (K_{\text{ex}}(\text{QX})K_{\text{diss}}^{\text{S}}(\text{QX})) \end{aligned} \quad (10)$$

If this is combined with Parker's convention (Ref.14), equation 11

$$\Delta G_{\text{t}}^{\circ}(\text{Ph}_4\text{P}^+) = \Delta G_{\text{t}}^{\circ}(\text{Ph}_4\text{B}^-) \quad (11)$$

it is possible to obtain individual $\Delta G_{\text{t}}^{\circ}$ values for each ion. This has been done by Antoine et al (15) for the distribution of salts between dichloroethane and water. Dichloromethane is the only additional solvent for which sufficient distribution data are available for such a calculation. Unfortunately all data from the research group at the department of Analytical Pharmaceutical Chemistry in Uppsala are stoichiometric constants. My colleagues, Dr Klas Gustavii and Dr Anna-Maria Tivert, however, kindly provided me with their primary data which enabled me to calculate the values in Table 1-3.

No value for the distribution of salts containing the ions Ph_4B^- and Ph_4P^+ are available. Parker (16), however, found that the ion ClO_4^- is insensitive to changes in the acceptor properties (AN) (17) of the solvent. This means that we have good reason to believe that $\Delta G_{\text{t}}^{\circ}(\text{ClO}_4^-)$ has the

same value in dichloromethane as in dichloroethane. We can thus use $\Delta G_t^\circ(\text{ClO}_4^-) = 16.9 \text{ kJmol}^{-1}$ as a starting point in the calculation of individual ΔG_t° values, and the result of such a calculation is given in Table 4 together with the results obtained with dry and wet dichloroethane. It can be seen that the ΔG_t° values for the two wet solvents are approximately the same. This is certainly not valid for all wet solvents since Parker has demonstrated that $-\Delta \Delta G_t^\circ(Y^-) = n^1(Y^-)\Delta(\text{AN})$ where $n^1(Y^-)$ is the sensitivity of the anion Y^- to differences in the acceptor number, $\Delta(\text{AN})$ for the two solvents being compared.

TABLE 1. Thermodynamic $\text{Log } K_{\text{ex}}(\text{QX})$, $\text{Log } K_{\text{diss}}^{\text{S}}(\text{QX})$, and ΔG_t° values in KJ/mol calculated therefrom. Solvent dichloromethane and temperature 25°C .

Comp.	$\text{Log } K_{\text{ex}}(\text{QX})$	$\text{Log } K_{\text{diss}}^{\text{S}}(\text{QX})$	$\Delta G_t^\circ(\text{QX})$	$\Delta G_t^\circ(\text{Q}^+) + \Delta G_t^\circ(\text{X}^-)$
$(\text{C}_3\text{H}_7)_4\text{N NO}_3$	-0.02	-4.47	25.6	25.5
$(\text{C}_3\text{H}_7)_4\text{N I}$	1.35	-4.32	16.9	16.7
$(\text{C}_3\text{H}_7)_4\text{N ClO}_4$	2.60	-4.34	9.9	9.9
$(\text{C}_4\text{H}_9)_4\text{N NO}_3$	2.06	-4.40	13.4	13.5
$(\text{C}_4\text{H}_9)_4\text{N ClO}_4$	4.78	-4.42	-2.1	-2.1
$(\text{C}_4\text{H}_9)_4\text{N Cl}$	0.02	-4.34	24.6	24.6
$(\text{C}_4\text{H}_9)_4\text{N Br}$	1.42	-4.31	16.5	16.5
$(\text{C}_4\text{H}_9)_4\text{N I}$	3.49	-4.28	4.5	4.7
$(\text{C}_5\text{H}_{11})_4\text{N NO}_3$	4.39	-4.22	-1.0	-1.1
$(\text{C}_5\text{H}_{11})_4\text{N Br}$	3.76	-4.09	1.9	1.9

Y^-	Cl^-	Br^-	I^-	NO_3^-	ClO_4^-
$\Delta G_t^\circ(Y^-)$	43.6	35.5	23.7	32.5	16.9

Q^+	$(\text{C}_3\text{H}_7)_4\text{N}^+$	$(\text{C}_4\text{H}_9)_4\text{N}^+$	$(\text{C}_5\text{H}_{11})_4\text{N}^+$
$\Delta G_t^\circ(Q^+)$	-7.0	-19.0	-33.6

Ion pair extraction is thus a good and rapid method for measuring ΔG_t° values for ions in wet solvents. Parker et al (16) have demonstrated that ΔG_t° values are very useful in correlations of solvent effects on $\text{S}_{\text{N}}2$ reactions and should thus be very useful in the prediction of solvent effects in phase transfer catalysis. We can also expect that ΔG_t° values are an additive and to some extent, a constitutive property. From a few careful measurements it should thus be possible to predict the ΔG_t° values of a variety of ions. From Tables 2 and 3 it can thus be seen that ΔG_t° values are decreased by 3.54 KJ for each CH_2 group that is introduced.

If we are comparing chemically closely related compounds, e.g. mono- and dialkylammonium picrates, we can expect that $K_{\text{diss}}^{\text{S}}$ should be constant. (The radius of the cation is controlled by the NH_2 group.) The difference in $-\Delta G_t^\circ$ values should thus be equal to the difference in the $\text{RTln } K_{\text{ex}}$ values.

This is in principle what has been done in Table 3. ΔG_t° values for the introduction of a few groups such as Cl, Br, NO_2 , OH, OCH_3 and alkyl groups into aromatic sulfonic acids can therefore be calculated from the values of Brändström and Strandlund (8). This is, however, a field in urgent need of more experimental facts. When these are available the principles used by Brändström (18) for the calculation of group contributions to $\text{Log } K_D$ values should be useful.

TABLE 2. Thermodynamic $K_{\text{ex}}(\text{QX})$, $\text{Log } K_{\text{diss}}^{\text{S}}(\text{QX})$ and ΔG_t° values in KJ/mol calculated therefrom for tetraalkylammonium salts of some phenoles.

Q^+	Phenole	$\text{Log } K_{\text{ex}}(\text{QX})$	$\text{Log } K_{\text{diss}}^{\text{S}}(\text{QX})$	$\Delta G_t^\circ(\text{QX})$	$\Delta G_t^\circ(\text{X})$
$(\text{C}_4\text{H}_9)_4\text{N}$	2- NO_2	2.63	-4.33	9.7	28.7
$(\text{C}_4\text{H}_9)_4\text{N}$	3- NO_2	2.11	-4.62	14.3	33.3
$(\text{C}_4\text{H}_9)_4\text{N}$	4- NO_2	2.62	-4.25	9.3	28.3
$(\text{C}_3\text{H}_7)_4\text{N}$	2,4-(NO_2) ₂	2.73	-4.14	8.4	15.4
$(\text{C}_3\text{H}_7)_4\text{N}$	2,6-(Cl) ₂	0.99	-4.76	21.5	28.5
$(\text{CH}_3)_4\text{N}$	2,4,6-(NO_2) ₃	0.39	-5.02	26.4	
$(\text{C}_2\text{H}_5)_4\text{N}$	2,4,6-(NO_2) ₃	2.46	-4.28	10.4	
$(\text{C}_3\text{H}_7)_4\text{N}$	2,4,6-(NO_2) ₃	4.59	-4.12	-2.7	4.3

Q^+	$(\text{CH}_3)_4\text{N}$	$(\text{C}_2\text{H}_5)_4\text{N}$	$(\text{C}_3\text{H}_7)_4\text{N}$	$(\text{C}_4\text{H}_9)_4\text{N}$
$\Delta G_t^\circ(\text{Q}^+)$	22.1	6.1	-7.0	-19.0
$\Delta G_t^\circ_{\text{calc}}$	21.8	7.6	-6.5	-20.7

$$\Delta G_t^\circ(\text{calc}) = 35.9 - nx3.54$$

USE OF ION PAIR EXTRACTION FOR THE STUDY OF REACTION MECHANISMS

Only a few reactions involving two liquid layers have been carefully studied quantitatively. One of these is the alkylation of phenols, especially 4-nitrophenol (19). The equilibrium reactions involved are, when dichloromethane is used as the solvent and tetrapentylammonium as the cation.

$$\begin{aligned} [\text{HA}]_s &= K_D [\text{HA}]_w & \text{Log } K_D &= 0.64 \\ [\text{A}^-]_w^a \text{H}_2\text{O}^+ &= K_a [\text{HA}]_w & \text{p}K_a &= 7.02 \\ [\text{QA}]_s &= {}^3[\text{Q}^+]_w K_{\text{ex}}(\text{QA}) & \text{Log } K_{\text{ex}}(\text{QA}) &= 4.93 \\ [\text{QAHA}]_s &= [\text{QA}]_s [\text{HA}]_s K_{\text{QAHA}} & \text{Log } K_{\text{QAHA}} &= 4.08 \\ [\text{Q}^+]_s [\text{A}^-]_s &= f^2_s = K_{\text{diss}}^{\text{S}} [\text{QA}]_s & \text{p}K_{\text{diss}}^{\text{S}} &= 4.05 \end{aligned}$$

The alkylation reaction was studied using a total concentration of 10^{-3}M for the phenol and a concentration of about $5 \times 10^{-2}\text{M}$ for Q^+ in the aqueous layer. Equal phase volumes were used. The concentrations of all species involved at different pH values are given in Fig. 1. The construction of

this type of diagram is given in detail by Brändström (12). The kinetic investigation was performed at pH 10.1. At this pH about 75 per cent of A is present as QA_s , 25 per cent as A_s^- , and negligible quantities as $QAHA_s$. Concerning the reactivity of these species in the alkylation reaction, we can see that it should be impossible to detect the expected low reactivity of QAHA along with the high reactivity of A^- and QA_s , since QAHA is present in such low concentration. It should be much more simple to detect the nucleophilicity of QAHA if the alkylation is performed at a pH value of about 3, since at this pH about 90 per cent of A is present as QAHA. From a careful study of the extraction behaviour it is thus possible to select optimal conditions for a study of the alkylation kinetics. In the present case, the reaction was studied at pH 10.1 using different total concentrations of HA. In this way, a variation of the relative concentrations of A_s^- and QA_s was obtained, which did not result in any significant difference in the rate of alkylation. The obvious conclusion was that A_s^- and QA_s had the same reactivity. The reactivity of QAHA was tested in such a way that different quantities of HA were added to a solution of QA in dichloromethane and the alkylation followed in the single phase system. No reactivity of QAHA could be detected. Another possibility of revealing the dominant nucleophile is to perform the reaction at different pH values. In this case the pH region 2 to 12 is readily available for measurements.

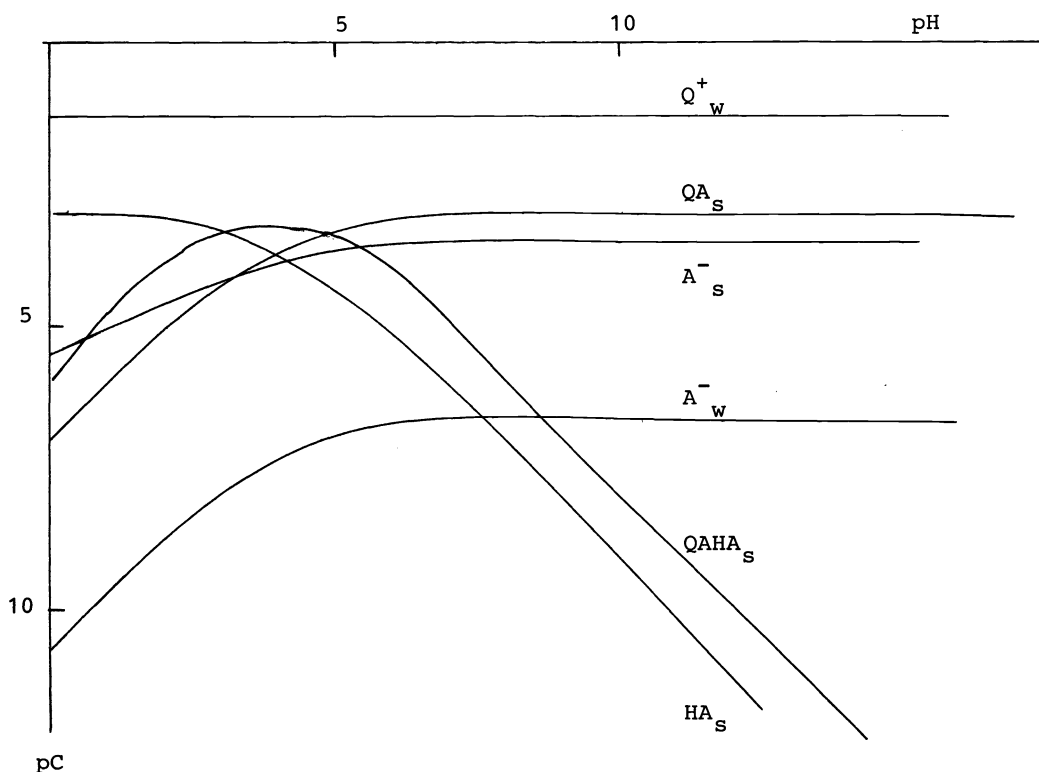


Fig. 2. The concentrations of the different species as a function of pH in a mixture of 1 mM 4-nitrophenol in dichloromethane with an aqueous solution 50 mM in tetrapentylammonium ions. Equal phase volumes, temperature 25°C.

TABLE 3. Thermodynamic $K_{\text{ex}}(\text{QX})$ and $K_{\text{diss}}^{\text{S}}(\text{QX})$ values together with $\Delta G_{\text{t}}^{\circ}$ values in KJ/mol calculated therefrom for some alkylaminium picrates.

Q	Log $K_{\text{ex}}(\text{QX})$	-Log $K_{\text{diss}}^{\text{S}}$	$\Delta G_{\text{t}}^{\circ}(\text{QY})$	$\Delta G_{\text{t}}^{\circ}\text{calc}$
$\text{C}_3\text{H}_7\text{NH}_3$	-0.34	6.53	39.2	38.9
$\text{C}_4\text{H}_9\text{NH}_3$	+0.38	6.54*	35.1	35.4
$\text{C}_5\text{H}_{11}\text{NH}_3$	+0.97	6.54	31.8	31.8
$\text{C}_6\text{H}_{13}\text{NH}_3$	1.69	6.54*	27.7	28.3
$\text{C}_8\text{H}_{17}\text{NH}_3$	2.69	6.54*	22.0	21.2
$\text{C}_{12}\text{H}_{25}\text{NH}_3$	5.35	6.54*	6.8	7.0
$(\text{CH}_3)_2\text{NH}_2$	0.15	6.54*	36.4	36.7
$(\text{C}_2\text{H}_5)_2\text{NH}_2$	1.29	6.43	29.3	29.6
$(\text{C}_3\text{H}_7)_2\text{NH}_2$	2.55	6.60	23.1	22.6
$(\text{C}_4\text{H}_9)_2\text{NH}_2$	3.78	6.54*	15.7	15.5
$(\text{C}_6\text{H}_{13})_2\text{NH}_2$	6.31	6.54*	1.3	1.3

* estimated value.

$$\Delta G_{\text{t}}^{\circ}\text{calc} = 49.5 - nx3.54 \text{ for } \text{C}_n\text{H}_{2n+1}\text{NH}_3\text{Y}$$

$$\Delta G_{\text{t}}^{\circ}\text{calc} = 43.8 - 2nx3.54 \text{ for } (\text{C}_n\text{H}_{2n+1})_2\text{NH}_2\text{Y}$$

TABLE 4. $\Delta G_{\text{t}}^{\circ}$ values in KJ/mol for some ions in water saturated dichloromethane or dichloroethane and in dry dichloroethane.

Ion	CH_2Cl_2 wet	$\text{ClCH}_2\text{CH}_2\text{Cl}$ wet	$\text{ClCH}_2\text{CH}_2\text{Cl}$ dry
Cl^-	43.6	45.2	53.6
Br^-	35.5	35.6	39.3
I^-	23.7	23.8	25.2
ClO_4^-	16.9		16.9
$4\text{-NO}_2\text{PhO}^-$	28.3	25.5	
$(\text{CH}_3)_4\text{N}^+$	22.1		15.4
$(\text{C}_2\text{H}_5)_4\text{N}^+$	6.1		4.7
$(\text{C}_3\text{H}_7)_4\text{N}^+$	-7.0		-8.8
$(\text{C}_4\text{H}_9)_4\text{N}^+$	-19.0	-19.2	-17.6
$(\text{C}_5\text{H}_{11})_4\text{N}^+$	-33.6	-33.1	

The equilibria involved in the phase transfer alkylation of a 1M solution of 4-chlorophenol in dichloromethane using an equal volume of a 0.01M aqueous solution of tetrabutyl ammonium ion as a catalyst are given in Fig. 3. We can see the tremendous difference between this and Fig. 2. From this we can understand that a careful consideration of the equilibria involved has to be made before results obtained under one type of

reaction conditions can be transferred to a reaction occurring under a different set of conditions.

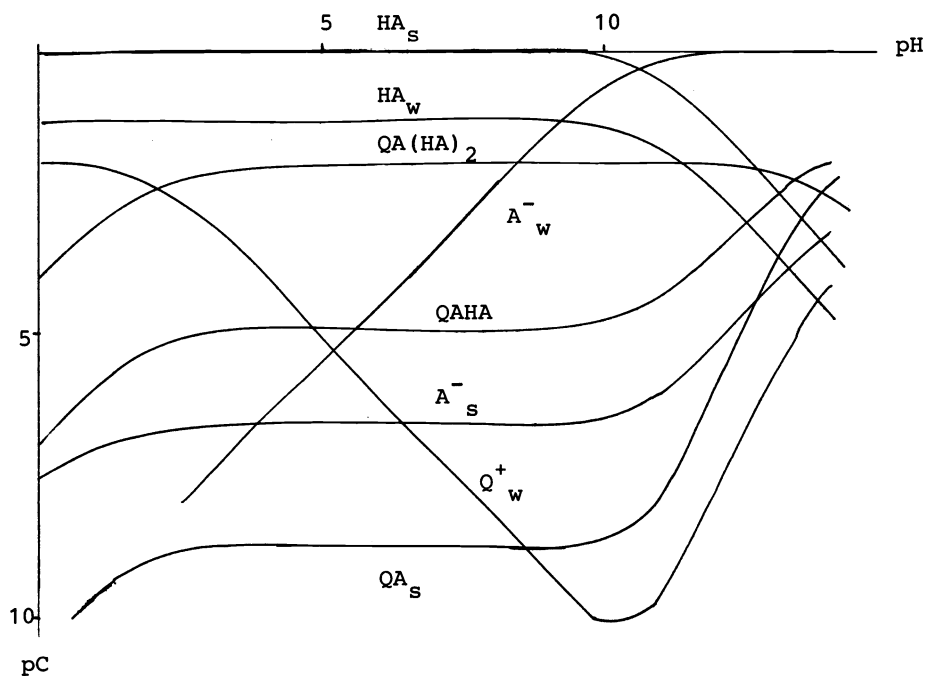


Fig. 3. The concentrations of the different species as a function of pH in a mixture of equal volumes of 1M 4-chlorophenol in dichloromethane and an aqueous solution' 10mM in tetrabutylammonium ions. Temperature 25°C.

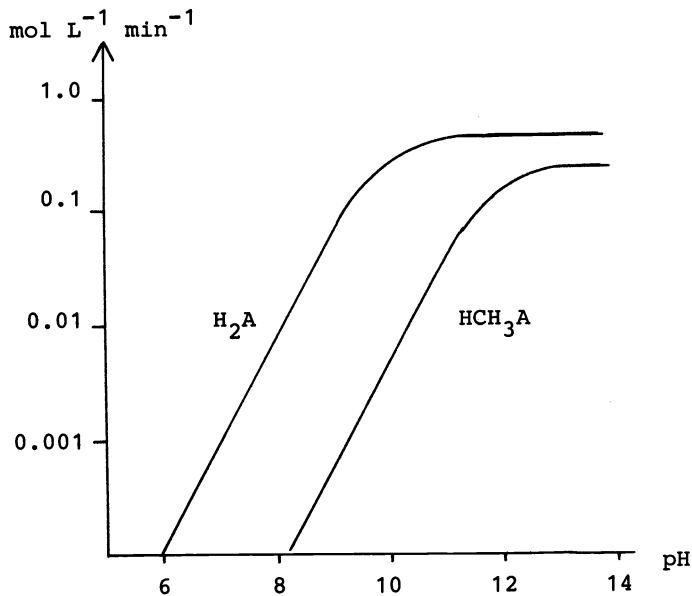


Fig. 4. Extractive methylation of 0.5M. 2,4-pentanedione H_2A or 3-methyl-2,4-pentanedione HCH_3A with methyl iodide and tetrabutylammonium ion, as a function of pH. Temperature 25°C.

TABLE 5. The extractive alkylation of 2,4-pentanedione using methyl iodide or dimethyl sulfate and tetrabutylammonium ions. Solvent dichloromethane. Temperature 25°C.

pH	QA _s mM	1/(f _s QA _s ^{1/2})	K _{Obs} CH ₃ I	% ion pair reaction	K _{Obs} (CH ₃) ₂ SO ₄	% ion pair reaction
5.5	0.00423	491	2.69	53	8.59	23
6.0	0.0134	279	2.11	68	5.75	35
6.5	0.0418	158	1.91	78	4.13	49
7.0	0.131	90	1.70	86	3.16	62
7.5	0.414	51	1.63	92	2.83	75
8.0	1.28	29	1.45	95	2.39	84
8.5	3.68	18	1.42	87	2.14	89
9.0	9.99	11	1.39	99	2.20	93

Alkylating agent	k _{QA}	k _A (K _{diss} ^S) ^{1/2}	Type of alkylation
CH ₃ I	1.42	0.00262	mainly C
(CH ₃) ₂ SO ₄	2.01	0.0134	0

The extraction and methylation kinetics of 2,4-pentanedione and 3-methyl-2,4-pentanedione has been studied by Brändström (20). The kinetic results obtained in the alkylation of 2,4-pentanedione with methyl iodide and with dimethyl sulphate are given in Table 5. In both reactions, both QA_s and A⁻s are the nucleophiles. The second order velocity constant observed k_{obs} is given by equation 12

$$k_{obs} = k_{QA} + k_A (K_{diss}^S / [QA]_s)^{1/2} / f_s \quad (12)$$

where k_{QA} and k_A are the second order velocity constant for the ion pair and the anion, respectively. Methyl iodide almost exclusively alkylated the carbon atom at pH 9. At pH 5.5, the alkylation with methyl iodide occurred to a greater extent at the oxygen atom than at pH 9.0, but due to the very low extent of reaction, about 1 per cent in 24 hours, an exact analysis could not be performed. (The product did not separate well from 2,4-pentanedione in the GLC analysis). With dimethyl sulphate the alkylation occurred at the oxygen atom. These results are in good agreement with the theory for alkylation advanced by Brändström (22).

Exact knowledge of the extraction behaviour and alkylation kinetics is of value for many reasons. From a theoretical point of view, this gives an information on the nucleophiles involved, and without such information, a discussion of the reaction mechanism is of limited value. It also seems for example inevitable that the hard - soft concept (21) will be adjusted to distinguish between anions and ion pairs.

Such a study of extraction behaviour and kinetics also yields much practical information. In the present case, for example, it has led to a simple method of purifying 3-methyl-2,4-pentanedione (22). More important is that this study has indicated a simple general method for selective monoalkylation, which is very useful in many cases. The principle behind this can be seen from the following.

If the alkylation rates in mole $L^{-1}min^{-1}$ observed or calculated, for the extractive methylation of 2,4-pentanedione and 3-methyl-2,4-pentanedione are plotted against pH, Fig. 4 is obtained. We can see that at low pH values there is about a hundred fold difference in rate of alkylation for the two compounds. At high pH values, however, this difference is less than a factor of 2. A selective monoalkylation is thus possible at low pH values but not at high pH values. From the equilibrium and velocity constants involved, it can be calculated that a 96 per cent yield of 3-methyl-2,4-pentanedione can be obtained in less than one hour if the methylation of acetylacetone is performed at $pH \leq 9$. This is in good agreement with experimental findings. The general method for selective alkylations based on this result is very simple in practice and is often also applicable to reactions other than extractive alkylations. All components except the base are mixed, and the base is then added slowly. It is advantageous, but not absolutely necessary, to follow the progress of the reaction by the pH or by other means. In the old standard method, all components except the alkylation agent were mixed and then the alkylation agent added slowly. The basicity of the solution was in this case very high and the selectivity poor. Despite certain obvious limitations to the "new" method, it has been used with success in many reactions in our laboratory.

REFERENCES

1. A. Brändström, Adv. in Physical Organic Chemistry **15**, 267-329, Academic Press, London (1977).
2. P. Beronius and A. Brändström, Acta Chem. Scand. **A30**, 687-691 (1976).
3. H.P. Marshall and E. Grunwald, J. Chem. Phys. **21**, 2143-2151 (1953).
4. R.M. Fouss and F. Accascina, Electrolytic Conductance Chapter XVIII, Interscience, London (1959).
5. T. Lindbäck and P. Beronius, Acta Chem. Scand. **A34**, 709-715 (1980).
6. N. Bjerrum, Kgl. Danske Videnskab. Selsk. **7**, N^o9 (1926).
7. G. Schill, J.A. Marinsky and Y. Marcus, Eds, Ion Exchange and Solvent Extraction **6**, 1-57, Dekker, New York (1974).
8. A. Brändström and G. Strandlund, Acta Chem. Scand. **B32**, 489-498 (1978).
9. T. Lindbäck, Private Communication.
10. G. Strandlund, Private Communication.
11. C.M. Starks and R.M. Owens, J. Am. Chem. Soc. **95**, 3613-3617 (1973).
12. A. Brändström, Preparative Ion Pair Extraction, 31-38, Apotekar-societeten S-111 81 Stockholm (1976).
13. P.A. Johansson, Acta Pharm. Suec. **14**, 345-362 (1977).

14. B.G. Cox and A.J. Parker, J. Am. Chem. Soc. 95, 402-407 (1973).
15. J.P. Antoine, I. de Aguirre, F. Janssens and F. Thyron, Bull. Soc. Chim. France 5-6, II 207-232 (1980).
16. A.J. Parker, U. Mayer, R. Schmid and V. Gutmann, J. Org. Chem. 43, 1843-1854 (1978).
17. U. Mayer, V. Gutmann and W. Gerger, Monatsh. Chem. 106, 1235-1257 (1975).
18. A. Brändström, Acta Pharm. Suec. In press.
19. A.-M. Tievert, Acta Pharm. Suec. 18, 1-10 (1981).
20. A. Brändström, Acta Chem. Scand. B30, 203-213 (1976).
21. R.G. Pearson and J. Songstad, J. Am. Chem. Soc. 89, 1827-1836 (1967).
22. A. Brändström, Ark. Kemi 6, 155-194 (1953).