23. Electrochemical Study of Phase-Transfer Catalysis Reactions: The *Williamson* Ether Synthesis

by **S. N. Tan**[a]), **R. A. Dryfe**[b])[1]), and **Hubert H. Girault**[a])*

[a]) Laboratoire d'Electrochimie, E.P.F. Lausanne, CH–1015 Lausanne
[b]) Department of Chemistry, University of Edinburgh, Edinburgh EH9 3JJ, United Kingdom

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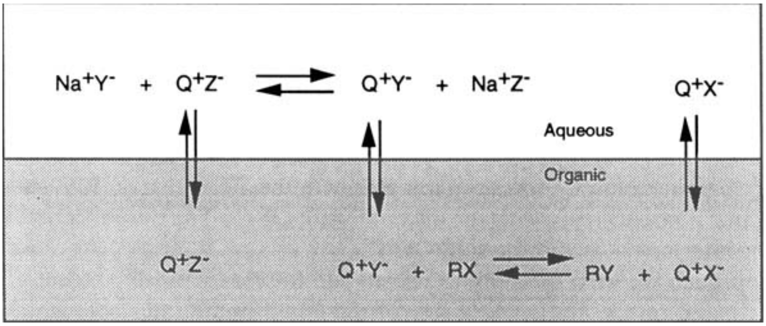
The transfer properties of the ionic species involved in the *Williamson* ether synthesis by phase-transfer catalysis were investigated using electrochemical techniques developed for the study of polarised liquid/liquid interfaces. This approach allows the measurement of the apparent partition coefficients of the transferring species. From these data, it is proposed that the role of the phase-transfer catalyst salt in the reaction mechanism is to establish a *Galvani* distribution potential difference between the two phases which in turn acts as the driving force for transferring the reactive aqueous ions to the organic phase.

Introduction. – The term phase-transfer catalysis (PTC) was coined by *Starks* [1] in 1971 and describes reactions where the reactants are present in different phases and brought into contact *via* a phase-transfer catalyst. The basic function of the catalyst is to facilitate the reaction between a species present often as an anion in an aqueous phase and a hydrophobic species which is often H_2O-insoluble. After *ca.* 20 years, PTC is now widely employed in organic synthesis, both in the laboratory and industry [2] [3]. PTC offers a distinct advantage over the classical homogeneous route as it requires milder reaction conditions. It avoids, *e.g.*, the use of anhydrous or expensive aprotic solvents. It also allows the reactions to be carried out at lower temperatures.

Various reaction models were proposed for PTC, but the overall scheme emerging in textbooks [2] is that described in *Scheme 1*, where *the catalytic ingredient allowing the transfer between phases is the quaternary onium cation (Q^+)*, where Y^- is the nucleophile,

Scheme 1



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[1]) Present address: Physical Chemistry Laboratory, South Parks Road, Oxford OX1 3QZ, United Kingdom.

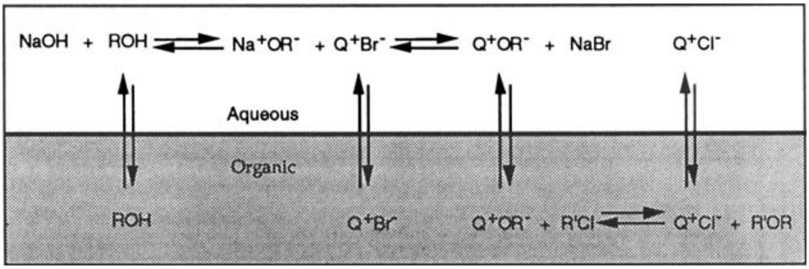
Z^- the chemically inert counter anion of the phase transfer catalyst salt, and RX the non-polar organic molecule with a leaving group X^-. The above model regards QY as a salt mainly dissociated in the aqueous phase and mainly ion-paired in the organic phase. The displacement reaction is proposed to occur in the organic phase. A question left open by this mechanism is whether the reaction in the organic phase is occurring with a free anion or with an ion pair. Both cases were reported in the literature [4] [5].

The purpose of the present paper is to investigate by electrochemical means the reaction mechanism of a simple, well characterised PTC reaction. For this illustrative purpose, we chose the phase-transfer catalytic approach for the traditional *Williamson* ether synthesis involving the nucleophilic substitution of a halide ion in an alkyl halide by an alkoxide anion.

$$\mathrm{BuOH_{water}} + \mathrm{PhCH_2Cl_{org.\,phase}} \longrightarrow \mathrm{BuOCH_2Ph_{org.\,phase}} + \mathrm{HCl_{water}}$$

The PTC route differs from the homogeneous reaction which requires the prior generation of the alkoxide anion, usually by the reaction of the alcohol with a strong and expensive base such as NaH, $NaNH_2$, or Na metal. Indeed, when the *Williamson* ether synthesis is carried out under phase-transfer catalytic conditions, 50% aqueous NaOH solution is sufficient to deprotonate the alcohol ROH, and the alkoxide RO^- is supposed to be solubilized in the organic phase by ion pairing with the quaternary ammonium ion (Q^+, see *Scheme 2*). The 'solubilized alkoxide' species QOR will react with the alkyl halide R′Cl in the organic phase [6]. *Scheme 2* differs slightly from *Scheme 1* due to the presence of the strong base needed to deprotonate the alcohol. The concentrations of the reactants usually involve a 5-fold excess of 50% NaOH solution over ROH. When using $PhCH_2Cl$ directly as the organic solvent, the reaction is pseudo-first order with respect to the ROH concentration. The concentration of the phase-transfer catalyst salt, *e.g.*, tetrabutylammonium bromide (Bu_4NBr) is then 3–5 mol-% with respect to ROH.

Scheme 2



If we apply the general philosophy of phase-transfer catalysis, we could say that the quaternary onium cation Q^+ forms an ion pair with the alkoxy anion RO^- as it transfers to the organic phase to react with the alkyl chloride, R′Cl. The onium cation is recycled back to the interface as a chloride salt (QCl).

The approach we wish to apply to investigate the mass-transfer aspect of this PTC reaction is based on the electrochemistry of the liquid/liquid interfaces which is a relatively new field of electrochemistry that was developed over the past two decades [7]. Indeed, *i*nterfaces between *t*wo *i*mmiscible *e*lectrolyte *s*olutions (ITIES) can be polarised by choosing for each phase a supporting electrolyte (hydrophilic for the aqueous side, and hydrophobic for the organic side) so as to form two back-to-back double layers. The polarisation window that can be obtained is several hundred millivolts, and it is limited by the transfer of the ionic species of the supporting electrolyte. The standard transfer potential of an ion from phase α to β, $\Delta_\beta^\alpha \phi_i^o$, is defined as the standard *Gibbs* energy of transfer (t) of this ion (i), $\Delta G_{t,i}^{o,\alpha\to\beta}$, divided by the molar charge (*Eqn. 1*) [7].

$$\Delta_\beta^\alpha \phi_i^o = \Delta G_{t,i}^{o,\alpha\to\beta}/z_i F \tag{1}$$

Since ion-transfer reactions are very fast compared to mass transport in the adjacent phases (*e.g.* diffusion, migration), the methodology developed to study electrode reactions can be transposed. In this way, it is possible to measure electrochemically the formal transfer potential $\Delta_\beta^\alpha \phi_i^{o'}$ by cyclic voltammetry in the same manner used to measure the formal redox potential of a redox couple. The formal potential is in fact an apparent standard transfer potential which takes into account the ion-ion interactions in the adjacent phases. It is related to the true standard transfer potential $\Delta_\beta^\alpha \phi_i^o$ by *Eqn. 2* where γ_i represent the activity coefficient of the transferring ionic species. The formal transfer

$$\Delta_\beta^\alpha \phi_i^{o'} = \Delta_\beta^\alpha \phi_i^o + \frac{RT}{z_i F} \ln\left(\frac{\gamma_i^\beta}{\gamma_i^\alpha}\right) \tag{2}$$

potential allows the definition of the apparent *Gibbs* energy of transfer, $\Delta G_{t,i}^{o',\alpha\to\beta}$ (*Eqn. 3*).

$$\Delta G_{t,i}^{o,\alpha\to\beta} = z_i F \cdot \Delta_\beta^\alpha \phi_i^{o'} \tag{3}$$

From the apparent *Gibbs* energy of transfer $\Delta G_{t,i}^{o',\alpha\to\beta}$ of a cation C^+ and of an anion A^-, we can calculate the apparent *Gibbs* energy of transfer or *Gibbs* energy of partition of the salt

$$\Delta G_{t,CA}^{o',\alpha\to\beta} = \Delta G_{t,C^+}^{o',\alpha\to\beta} + \Delta G_{t,A^-}^{o',\alpha\to\beta} \tag{4}$$

CA (*Eqn. 4*) and consequently, the apparent partition coefficient of the salt $P_{CA}^{\beta/\alpha}$ from *Eqn. 5*. By analogy, we define the apparent partition coefficient of an ionic species i (*Eqn. 6*).

$$P_{CA}^{\beta/\alpha} = \frac{c_{C^+}^\beta c_{A^-}^\beta}{c_{C^+}^\alpha c_{A^-}^\alpha} = \left(\frac{c_{CA}^\beta}{c_{CA}^\alpha}\right)^2 = \exp\left[\frac{-\Delta G_{t,CA}^{o',\alpha\to\beta}}{RT}\right] \tag{5}$$

$$P_i^{\beta/\alpha} = \exp\left[\frac{-\Delta G_{t,i}^{o',\alpha\to\beta}}{RT}\right] = \exp\left[\frac{-z_i F \cdot \Delta_\beta^\alpha \phi_i^{o'}}{RT}\right] \tag{6}$$

In the present study, we use this electrochemical approach to measure the apparent *Gibbs* energy of transfer of the species involved in the *Williamson* ether synthesis: the phase-transfer catalyst cation Bu_4N^+, the aqueous counter ion Br^-, the aqueous base OH^-, and the nucleophile butoxide BuO^-.

Since it is not possible to measure the standard transfer potential of BuO^- when the organic solvent is a reacting species, in this case $PhCH_2Cl$, we chose a solvent similar to $PhCH_2Cl$ from the physical properties point of view but chemically inert. *O*-Dichlorobenzene (*o*-$Cl_2C_6H_4$) was selected as the dielectric constant of the two solvents are quite similar ($\varepsilon^o_{PhCH_2Cl} = 7$, $\varepsilon^o_{o\text{-}Cl_2C_6H_4} = 10.0$) [8]. Therefore, the system studied in the present work differs from that described in *Scheme 2*, because the organic reactant is now dissolved in an inert solvent.

To ensure a certain conductivity in the organic phase when doing electrochemical measurements of standard transfer potentials, we added tetrabutylammonium tetraphenylborate ($Bu_4N(BPh_4)$) as a supporting electrolyte in the organic phase. The hydrophilic salt chosen as the supporting electrolyte in the aqueous phase was NaOH which is also required to deprotonate the alcohol to generate the RO^- ion.

Experimental. – *General.* All chemicals used were anal. grade or better. Bu_4NCl, $Bu_4N(BPh_4)$, BuOH, *o*-dichlorobenzene (*o*-$Cl_2C_6H_4$), and benzyl chloride ($PhCH_2Cl$) were all from *Fluka*. NaOH pellets, NaBr, and NaCl were from *Merck*.

The electrochemical system used to study ion-transfer reactions is defined by electrochemical cell 1,

$$\underbrace{\mathrm{Ag/AgCl/10\,mM\;Bu_4NCl/}}_{RE_o}\mathrm{10\,mM}\;\underbrace{\mathrm{Bu_4N(BPh_4)//12.5M\;NaOH}}_{\Delta_o^w\phi}\mathrm{/}\underbrace{\mathrm{1M\;NaCl/AgCl/Ag}}_{RE_w}$$

Electrochemical cell 1

and the cell voltage E is defined as the potential difference between the aq. and the org. reference electrode (*Eqn. 7*).

$$E = RE_w - RE_o \tag{7}$$

The cell-voltage scale depends on the choice of the reference electrodes and liquid junction used. It differs by a constant factor from the absolute scale defined by the *Galvani* potential difference $\Delta_o^w\phi$ across the H_2O/*o*-$Cl_2C_6H_4$ interface ($\Delta_o^w\phi = \phi^w - \phi^o$ in which ϕ^w and ϕ^o are the inner *Galvani* potential of the aq. and org. phase, resp.). $\Delta_o^w\phi$ can be calculated from the value of the cell voltage E on the assumption that it is equal to zero at the potential of zero charge which can be measured using a streaming electrode [7].

Measurements of Apparent Gibbs *Energy of Transfer.* The formal transfer potentials of OH^-, Na^+, and Bu_4N^+ were determined directly using cell 1 by a method called end-of-the-window technique [9]. In separate experiments, BuOH and NaBr were added to the aq. phase of cell 1 for the determination of the formal transfer potentials of

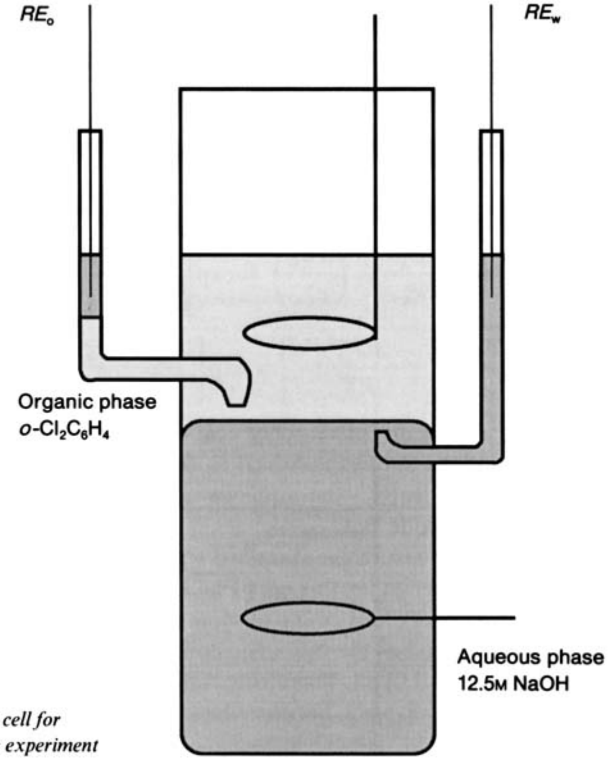


Fig. 1. *Electrochemical cell for the cyclic-voltammetric experiment*

BuO^- and Br^-, resp. In the former case, both aq. and org. phases were left to equilibrate overnight. Cyclic-voltammetry measurements were performed with a four-electrode potentiostat system with a waveform generator (*PPR1*, *HITEK*, England) [9]. Due to the high density of the aq. phase (12.5M NaOH), the aq. phase was at the bottom of the electrochemical cell (see *Fig. 1*).

Constant Potential Electrolysis. A controlled-potential electrolysis was performed using the above instrumentation in the cell illustrated in *Fig. 1*. The bottom aq. phase containing 100 mM BuOH in 12.5M NaOH was stirred with a magnetic stirrer during electrolysis. GC experiments were performed on a *Hewlett-Packard* (model *5890*) gas chromatograph. GC/MS Experiments on a *Hewlett-Packard* (model *5992B*) analyser system allowed the identification of the species generated after electrolysis.

All experiments were performed in a thermostated bath maintained at 25 ± 1°.

Results and Discussion. – *Fig. 2* shows the cyclic voltammograms for electrochemical cell 1 with different concentrations of NaOH in the aqueous phase. There is a significant increase of the polarisation window in the negative direction as the concentration of NaOH increases. To identify the ionic species limiting the potential window, we repeated the experiment at a liquid/liquid interface supported at the tip of a micropipette (tip diameter is $\leqslant 30$ µm). In this way, we observed that a low NaOH concentration, the potential window is limited at negative potentials by the transfer of Bu_4N^+ from o-$Cl_2C_6H_4$ to H_2O. Similarly, at positive potentials, the window is limited by the transfer of BPh_4^- from o-$Cl_2C_6H_4$ to H_2O. As the concentration of NaOH increases, the potential window widens as the apparent *Gibbs* energies of transfer of the organic ions increase due to the salting out effect as described by *Schiffrin* and coworkers [10]. This effect is such that when the NaOH concentration reaches 12.5M, the window at negative potentials becomes limited by the transfer of OH^- from H_2O to o-$Cl_2C_6H_4$ and at positive potentials by the transfer of Na^+ from H_2O to o-$Cl_2C_6H_4$. At high NaOH concentration, it is possible to observe, after a certain time, the transfer of CO_3^{2-} and HCO_3^- resulting from the equilibration of the atmospheric CO_2, as illustrated in *Fig. 2c*. This side point illustrates the sensitivity of the electrochemical approach to detect ionic species. These results show that even hydrophilic OH^- ions can be transferred to an organic phase if the appropriate *Gibbs* energy of transfer is provided to the ions (in the present case, the energy is supplied by polarising the interface).

The formal transfer potential for OH^- obtained by the end of the window method [9] is equal to −584 mV on the relative scale of cell voltage which is determined by the choice of the reference electrodes and liquid junction potentials illustrated in electrochemical cell 1. The Bu_4N^+ crosses at a more negative potential than OH^-, thus the formal transfer potential for Bu_4N^+, $E^{1/2}_{Bu_4N^+}$, is less than −584 mV and is estimated to be *ca.* −600 mV. This estimated figure is only proposed to clarify the argumentation developed below and should not be taken as an experimental value.

The apparent standard *Gibbs* energy of transfer of the $Bu_4N(OH)$ species (see *Eqn. 8*) is obtained by summing the apparent *Gibbs* energy transfer of Bu_4N^+ and OH^- (see

$$\Delta G^{o',w\to o}_{t,Bu_4N(OH)} = \Delta G^{o',w\to o}_{t,Bu_4N^+} + \Delta G^{o',w\to o}_{t,OH^-} = -RT\ln P^{o/w}_{Bu_4N(OH)} \tag{8}$$

Eqn. 4), where $P^{o/w}_{Bu4N(OH)}$ is the apparent partition coefficient of $Bu_4N(OH)$ between the o-$Cl_2C_6H_4$ and H_2O. This apparent *Gibbs* energy of transfer of the salt is obtained on an absolute scale although the formal transfer potentials are expressed on an arbitrary scale. Indeed, it is expressed as a difference of formal transfer potentials (*Eqn. 9*) and, therefore, the arbitrary choice of an origin on the potential axis does not matter.

$$\Delta G^{o',w\to o}_{t,Bu_4N(OH)} = \Delta G^{o',w\to o}_{t,Bu_4N^+} + \Delta G^{o',w\to o}_{t,OH^-} = F(E^{o'}_{Bu_4N^+} - E^{o'}_{OH^-}) \tag{9}$$

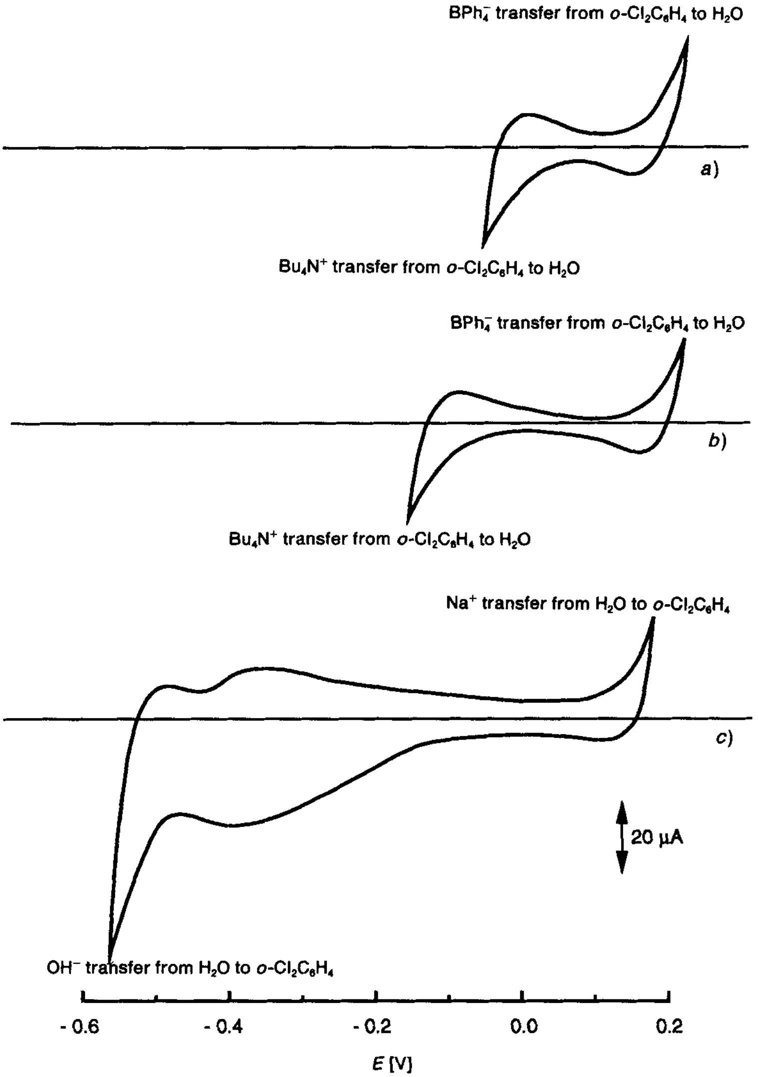


Fig. 2. *Cyclic voltammogram of electrochemical cell 1 with* a) *0.125* M, b) *1.25* M, *and* c) *12.5* M *NaOH.* Scan rate 50 mV s^{-1}.

The apparent partition coefficient of the $Bu_4N(OH)$ salt is, therefore, found to be 1.86. This value indicates that if $Bu_4N(OH)$ was added to a 12.5M $NaOH/o\text{-}Cl_2C_6H_4$ system, about four times as much salt would be present in the organic phase compared to the aqueous phase. This value also shows the strong salting-out effect taking place the present situation.

Fig. 3 shows the cyclic voltammogram of the electrochemical cell 1 when 100 mM BuOH was present in the aqueous phase. A good reversible transfer voltammogram which is assigned to the BuO^- transfer can be observed. The formal transfer potential for

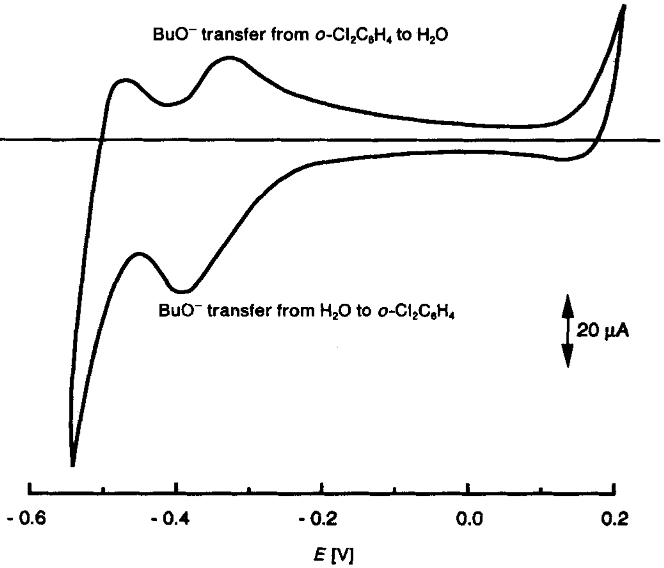


Fig. 3. *Cyclic voltammogram of electrochemical cell 1 with 100* mM *BuOH in 12.5* M *NaOH.* Other conditions as in *Fig. 2c*.

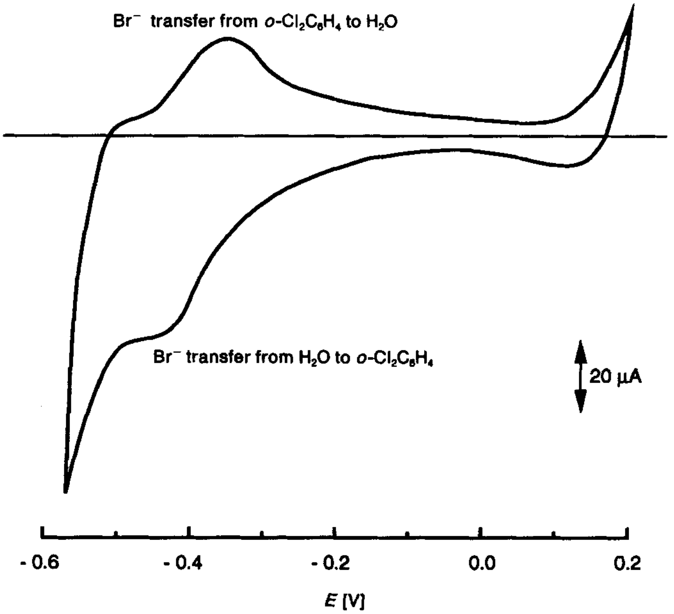


Fig. 4. *Cyclic voltammogram of electrochemical cell 1 with 0.5* mM *NaBr in 12.5* M *NaOH.* Other conditions as in *Fig. 2c*.

BuO^-, $E^{o'}_{BuO^-}$, obtained from the voltammogram directly at the mid-peak potentials is equal to −365 mV, still on the arbitrary potential scale of electrochemical cell 1. By the same method, we calculate the apparent partition coefficient $P^{o/w}_{Bu_4N(OBu)}$ of $Bu_4N(OBu)$ to be 9430. Similarly, we measured the apparent *Gibbs* energy of transfer of the aqueous counter ion (Br^-) of the phase-transfer catalyst salt and found a value of $E^{o'}_{Br^-} = -430$ mV; the cyclic voltammogram of Br^- is shown in *Fig. 4*. This value shows that Br^- is more hydrophilic than BuO^-. This in turn yields an apparent partition coefficient for Bu_4NBr of *ca.* 750.

With these results, we can examine how all the reactants would partition in the absence of chemical reactants in the organic phase, *i.e.* in the absence of benzyl chloride in o-$Cl_2C_6H_4$. If the initial concentrations of the various reacting species in the system before mixing are, *e.g.*, as follows: $7.35 \cdot 10^{-2}$ M Bu_4NBr in H_2O (none in o-$Cl_2C_6H_4$), 0.1M BuOH, *i.e.* $1.25 \cdot 10^{-4}$ M BuO^- in H_2O (none in o-$Cl_2C_6H_4$), and 12.5M NaOH in H_2O (none in o-$Cl_2C_6H_4$); then the equilibrium partition concentrations would be as follows (see *Appendix*):

in H_2O:	in o-$Cl_2C_6H_4$:
$1.0 \cdot 10^{-4}$ M Bu_4N^+	$7.34 \cdot 10^{-2}$ M Bu_4N^+ (99.85%)
$3.5 \cdot 10^{-2}$ M Br^-	$3.82 \cdot 10^{-2}$ M Br^- (52.1%)
$1.25 \cdot 10^{-4}$ M BuO^-	$1.7 \cdot 10^{-3}$ M BuO^- (93.1%)
12.5M OH^-	$3.3 \cdot 10^{-2}$ M OH^- (2.6%)

This equilibrium distribution, established from the electrochemical data, shows that the phase-transfer catalyst cation Bu_4N^+ is totally dissolved in the organic phase, that the phase-transfer catalyst anion Br^- is equally partitioned, that the BuO^- concentration is greater in the organic phase than in the aqueous phase as the partition displaces the acid-base equilibrium of BuOH in 12.5M NaOH, and that the concentration of OH^- in o-$Cl_2C_6H_4$ is small in proportion but far from being negligible. This illustrates how an electrochemical approach can provide all the thermodynamic partition data relative to a PTC reaction.

To analyse what are the driving forces which cause the transfer of nucleophile from the aqueous to the organic phase, let us consider the following hypothetical experiment. A solution of Bu_4NBr in 12.5M NaOH is in contact with a solution of $PhCH_2Cl$ in o-$Cl_2C_6H_4$. Calculations based on the apparent partition coefficients determined above shows that more than 99% of the phase-transfer catalyst cation would be dissolved in the organic phase. The question is what would happen if we added BuOH to the aqueous phase. According to the conventional theory based on ion-pair formation, BuO^- forms an ion pair at the interface with Bu_4N^+, and the neutral ion pair formed diffuses inside the organic phase. The problem with this mechanism is that the organic phase would act as an anion sink breaking the electroneutrality of the two adjacent immiscible phases.

Another explanation for the role of the phase-transfer catalyst salt we wish to propose is based on electrochemical arguments. Considering that we have principally one salt distributed between two immiscible electrolyte solutions (*i.e.* the phase-transfer catalyst salt), the liquid/liquid interface becomes polarised, and a *Galvani* potential difference, in this case called the distribution potential, will be established. Its value can be calculated from standard transfer potential values according to *Eqn. 10* below [7]. In the present

$$\Delta^{w}_{o} \phi_{Bu_4NBr} = \frac{\Delta^{w}_{o} \phi^{o}_{Bu_4N^+} + \Delta^{w}_{o} \phi^{o}_{Br^-}}{2} \tag{10}$$

case, we can consider, to a first approximation, that the potential difference is controlled solely by the distribution of the phase-catalyst salt Bu_4NBr, and we shall neglect for the simplicity of the argument developed below the contribution of the distribution of $Bu_4N(OH)$. In this way, the cell voltage is given by *Eqn. 11.*

$$E_{Bu_4NBr} = \frac{E^{o'}_{Bu_4N^+} + E^{o'}_{Br^-}}{2} = -515\,\mathrm{mV} \qquad (11)$$

Fig. 5 illustrates how the different ionic species partition between the two phases depending on the cell voltage. We see that if the potential difference between the aqueous phase and the organic phase is −515 mV, then Cl^- and OH^- are energetically more stable in the aqueous phase, and no transfer of these two species from H_2O to o-$Cl_2C_6H_4$ will be induced by the polarisation established by the distribution of Bu_4NBr. The same applies to Bu_4N^+ which at this potential difference will prefer to remain in the organic phase. However, we see that if Br^- or RO^- were added to the aqueous phase, then the polarisation of the interface will drive their transfer to the organic side. This electrochemical argument, therefore, explains how the phase-transfer-catalysed reaction proceeds in our hypothetical experiment.

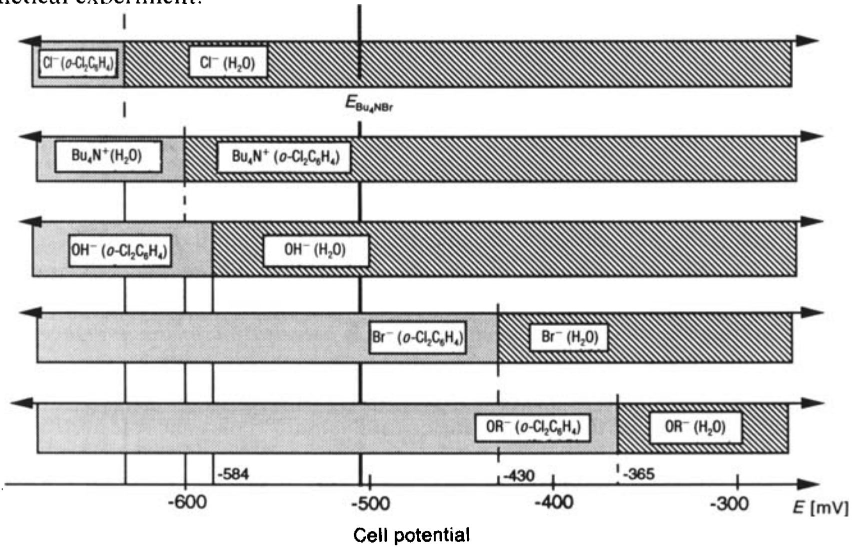


Fig. 5. *Partition diagram of the species in the phase-transfer catalysis reaction for the* Williamson *ether synthesis.* E_{Bu_4NBr} is the cell voltage corresponding to the distribution potential of Bu_4NBr.

This electrochemical approach clearly shows that the Galvani *distribution potential difference established by the partition of the phase-transfer catalyst salt* (Bu_4NBr) *is in turn acting as a driving force for the anions which have standard transfer potential less negative than the distribution potential.* Of course, the concentration of the transferring ion should be less than that of the phase-transfer catalyst salt so that only the partition of the latter controls the polarisation of the interface. This applies to BuO^- for which the concentration will not exceed 0.2 mM based on the pK_a of BuOH and the pH employed [11]. Consequently, ion-transfer reactions will take place on their own and will not necessarily require the phase-transfer catalyst cation Bu_4N^+ to act as a shuttle as usually assumed in

[1]. It can be seen that the proposed theory gives equal importance to the cation and the anion of the phase-catalyst salt as the distribution potential between the two phases established by the partition of the salt is the half sum of the standard *Galvani* ion-transfer potentials of the two ions. The present approach deviates then from the hitherto accepted theories which give more importance to the cation, since a lot of emphasis is usually given to the ion pairing of this cation with the anion to be transferred.

Of course, in a closed system as that shown in *Scheme 2*, there is no external circuit to allow the electric current carried by the ion-transfer reaction to flow. To maintain the electroneutrality of the phases, either a cation must also cross from the H_2O to the organic phase or an anion must cross from the organic to the H_2O phase. The former process is possible by the co-transfer of the PTC cation, *i.e.* Bu_4N^+. This process is usually described in the older PTC literature as the ion pair ($Bu_4N(OR)$) transport across the interface. Although thermodynamically possible, this scenario will be hindered first by the negligible concentration of ion pairs in H_2O (*vide infra*), but more importantly by the negligible concentration of Bu_4N^+ in the aqueous phase ($< 1\%$). On the other hand, the electroneutrality can also be achieved by the transfer in the opposite direction of Br^- from the organic to the H_2O phase, since Br^- is more hydrophilic than BuO^-. The latter scenario is more likely than the former, because a relatively large proportion of the Br^- ions are present in the organic phase. *In this way, we see that what is often described as ion-pair extraction is in fact an anion exchange.*

Of course, as soon as the nucleophilic substitution occurs in the organic phase, *i.e.* after reaction of BuO^- with $PhCH_2Cl$, Cl^- will cross the interface since Cl^- is more hydrophilic than Br^- as illustrated in *Fig. 5*.

Our work, therefore, shows that the transfer of the reactive anion is not a consequence of the presence of the PTC cation at the interface which leads to the transfer of an ion pair from the H_2O to the organic phase. Indeed *the driving force for the reactive-anion transfer is a gradient of electrochemical potential generated by the distribution of the PTC salt* (Bu_4NBr) *between the two phases which results in a polarisation of the interface.* In other words, the role of the phase-transfer catalyst salt is to establish by its spontaneous distribution a gradient of electrochemical potential, which in turn will induce the respective transfer reactions. For the phase-transfer catalyst salt to play the role ascribed here, it is evident that it should be in excess of the concentrations of the free transferring ions. If not, the equilibrium potential would be a mixed potential where every ionic species contributes.

To corroborate the proposed theory, we carried out an electrolysis experiment by fixing the potential difference across the liquid/liquid interface *via* a potentiostat rather than by the distribution of the phase-transfer catalyst salt. The solution used for the electrolysis comprised an aqueous solution of 12.5M NaOH with 100 mM BuOH. It should be stressed that there is no phase-transfer catalyst salt in the system. The organic phase was a solution of 10 mM $Bu_4N(BPh_4)$ and 10 mM $PhCH_2Cl$ in o-$Cl_2C_6H_4$. The organic salt is totally insoluble in H_2O and was simply used to maintain the conductivity of the organic phase. In this set up, the interface can be polarised as shown in *Fig. 2*. The electrolysis potential expressed on the arbitrary scale defined by electrochemical cell 1 was set at −500 mV. In this way, we were able to synthesize benzyl butyl ether ($PhCH_2OBu$) simply by polarising the interface externally, and this product was identified by a GC/MS experiment during the course of the bulk electrolysis experiment. No trace of $PhCH_2OBu$ was detected when the interface was polarised at a potential more positive than −300 mV. This qualitative experiment of electrosynthesis of $PhCH_2OBu$ illustrates that the reaction proceeds *via* anion transfer and corroborates our model of the role of the PTC salt.

Perhaps it is worthwhile discussing the role of ion pairing in the respective phases in cell 1. If one adapts the theory of *Bjerrum* [12] and its inherent definition of an ion pair, *i.e.* an ion pair exists when the distance between the centre of the two ions is less than a critical distance q defined by *Eqn. 12*, where e is the electronic charge of the proton. In the

$$q = \frac{z_+ z_- e^2}{8\pi\varepsilon_0\varepsilon_r kT} \tag{12}$$

case of a univalent salt 1:1 ($z_+ = z_- = 1$), this critical distance of *Bjerrum* in H_2O is 357 pm at 25°. Since the radius of the phase-transfer catalyst cation Bu_4N^+ is equal to 380 pm [13], it is clear from the *Bjerrum* theory that the concentration of Bu_4NX (where X = OH^-, Br^-, or RO^-) is negligible in the aqueous phase. On the other hand, the critical *Bjerrum* distance in the organic phase is much greater (*e.g.* 2.8 nm if $\varepsilon_r = 10$) and, consequently, ion pairing takes place more readily. It is possible to calculate by the *Bjerrum* theory the fraction θ of ion pairs, and in the case of Bu_4NBr in an organic solvent of dielectric constant equal to 10, such as o-$Cl_2C_6H_4$, we have for $c = 10^{-4}$M a $\theta = 0.223$, for $c = 10^{-3}$M a $\theta = 0.545$, and for $c = 10^{-2}$M a $\theta = 0.791$. This shows that for the conditions of the *Williamson* ether synthesis studied above, where the concentration of Bu_4NBr in the organic phase is *ca.* 0.04M, the ion-pair fraction is greater than 80%. Since the concentration of BuO^- in the organic phase is also *ca.* 0.001M, it is clear that the ion-pairing fraction of $Bu_4N(OBu)$ is in the range of 50%, whereas that of $Bu_4N(OH)$ is more than 90% due to the high concentration of $Bu_4N(OH)$ of 0.03M and the small size of the OH^- anion.

This calculation has important bearing on the mechanistic aspect of the nucleophilic substitution as it shows that the reacting nucleophile is more likely to be a single ion rather than an ion pair. This consideration of ion-pair formation shows that although the concentration of OH^- in the organic phase is greater than that of BuO^-, the latter is more reactive than the former as shown in the product distribution of the PTC reactions.

Conclusion. – We have employed a liquid/liquid electrochemical technique to study a model reaction for the *Williamson* ether synthesis. This approach allows the measurement of the relevant partition coefficients of the various reacting species used under the phase-transfer catalysis conditions. A new mechanistic model is proposed, the gist of which is *the key role played by the phase-transfer catalyst salt as a chemical means to onset a* Galvani *potential difference between the two immiscible phases, equal to the distribution potential of the phase-transfer catalyst salt.* This *Galvani* potential difference is in turn the driving force for the transfer of the reactive anion like BuO^- from the aqueous to the organic phase and for the return of the displaced anion from the organic to the aqueous phase. As a consequence, we postulate that the phase-transfer catalyst cation is not required to act as an 'anion transporter' during the course of the *Williamson* ether synthesis here above studied. This work also illustrates the role of the phase-transfer catalyst counter anion since the distribution potential generated by the phase-transfer catalyst salt is determined by the hydrophobicity of both the cations and the anions.

Appendix. – Let us consider the equilibrium situation for the system used in the *Williamson* ether synthesis by phase-transfer catalysis with o-$Cl_2C_6H_4$ in the absence of $PhCH_2Cl$ so as to avoid chemical reactions.

The conservation of Bu_4N^+ and Br^- after partitioning can be written as:

$$[Bu_4N^+]_w + [Bu_4N^+]_o = [Bu_4NBr]_i, \qquad [Br^-]_w + [Br^-]_o = [Bu_4NBr]_i$$

Let x and y be the fraction of Bu_4N^+ and Br^- in the organic phase, respectively:

$$(1-x)[Bu_4NBr]_i + x[Bu_4NBr]_i = [Bu_4NBr]_i, \qquad (1-y)[Bu_4NBr]_i + y[Bu_4NBr]_i = [Bu_4NBr]_i$$

The apparent partition coefficient of Bu_4NBr defined by *Eqn. 5* reads:

$$P_{Bu_4NBr} = 750 = \left(\frac{[Bu_4N^+]_o[Br^-]_o}{[Bu_4N^+]_w[Br^-]_w}\right) = \frac{xy}{(1-x)(1-y)} \tag{13}$$

Let p and q be the concentrations of OH^- in the organic and aqueous phase, respectively, then the apparent partition coefficient of $Bu_4N(OH)$ is given by *Eqn. 14*,

$$P_{Bu_4N(OH)} = 1.86 = \left(\frac{[Bu_4N^+]_o[OH^-]_o}{[Bu_4N^+]_w[OH^-]_w}\right) = \frac{xp}{(1-x)q} \tag{14}$$

with $q = 12.5$ M the concentration of NaOH in the aqueous phase.

Let u and v be the concentrations of the BuO^- species in the organic and aqueous phase, respectively. Similarly, the apparent partition coefficient of $Bu_4N(OBu)$ reads:

$$P_{Bu_4N(OBu)} = 9430 = \left(\frac{[Bu_4N^+]_o[BuO^-]_o}{[Bu_4N^+]_w[BuO^-]_w}\right) = \frac{xu}{(1-x)v} \tag{15}$$

Considering the acid-base equilibrium of BuOH, we have:

$$v = K_a[BuOH][H^+]$$

or by taking the pK_a of BuOH to be equal to 18, and [BuOH] = 0.1 M, we obtain:

$$v = 1.25 \cdot 10^{-4}\,\text{M} \tag{16}$$

The electroneutrality of the organic phase is given by:

$$[Bu_4N^+]_o = [BuO^-]_o + [Br^-]_o + [OH^-]_o \quad \text{or} \quad x[Bu_4NBr]_i = u + p + y[Bu_4NBr]_i \tag{17}$$

Eqns. 13–17 yield a third-order equation in x which was solved numerically using Maple software. The concentrations of the various species were based on the following conditions used for the PTC reaction: 5 mol-% of Bu_4NBr with respect to 1 mol each of $PhCH_2Cl$ and BuOH, respectively, and 5-fold excess of 12.5 M NaOH. By employing the density of $PhCH_2Cl$ and BuOH of 0.81 and 1.1 $g \cdot cm^{-3}$, respectively, the concentration of Bu_4NBr in molarity is thus equal to $7.35 \cdot 10^{-2}$ M.

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