Bromide–Chloride Exchange between Alkyl Halides and Metal Halide Salts under Phase Transfer Conditions

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The equilibrium position of the phase transfer catalysed exchange reaction RCl + MBr $\rightleftharpoons$ RBr + MCl where R = primary alkyl group and M = Li, Na, K, Ca is strongly dependent on the nature of the metal cation M and the amount of water present in the reaction mixture; this has been applied in the synthetic use of the reaction in both directions.

Alkyl bromides are often much more reactive and therefore synthetically more useful than the corresponding chlorides. So the conversion of alkyl chlorides, generally cheaper and easily available, into alkyl bromides has received increasing attention recently.[1—5] It can be generally accomplished by exchange with a metal salt [Finkelstein reaction,[6] equation (1)] in homogeneous solutions when a polar solvent is used[1] or in a two phase system in the presence of a phase transfer agent.[4,5,7]

$$R\text{–}Cl + M^+Br^- \rightleftharpoons R\text{–}Br + M^+Cl^- \qquad (1)$$
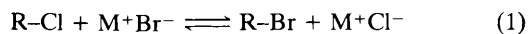
Another approach is direct halogen exchange between alkyl halides,[2] equation (2).

$$R\text{–}Cl + R'\text{–}Br \rightleftharpoons R\text{–}Br + R'\text{–}Cl \qquad (2)$$
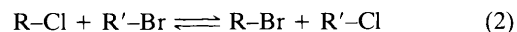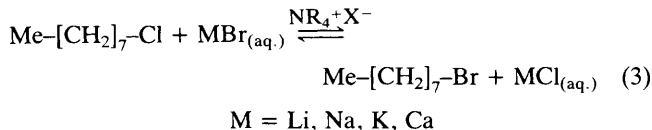
In this work, we show that high conversions into alkyl bromides can easily be obtained *via* reaction (1) using stoicheiometric amounts of metal bromides, under solid–liquid phase transfer catalysis (PTC) conditions if: (i) the amount of water present in the reacting system is carefully limited, and (ii) the metal cation is properly selected. Both

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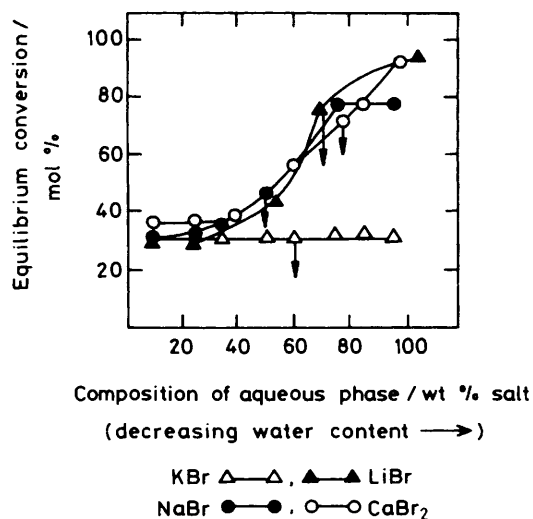
Figure 1. Equilibrium conversion of reaction (3) at 98 °C as a function of the initial aqueous phase composition. With 100% dry salt no reaction is observed at all. The arrows mark the point from which a solid phase is formed during the reaction.

factors strongly influence the equilibrium position of the exchange reaction.

We have studied the reactions of several metal bromides (Li, Na, K, and Ca) with n-octyl chloride in the presence of a quaternary ammonium phase transfer catalyst [equation (3)]. In these conditions, reactions were performed in the absence of organic solvent (n-octyl chloride and the product, n-octyl bromide being the organic phase).

$$Me\text{-}[CH_2]_7\text{-}Cl + MBr_{(aq.)} \underset{}{\overset{NR_4^+X^-}{\rightleftharpoons}}$$

$$Me\text{-}[CH_2]_7\text{-}Br + MCl_{(aq.)} \quad (3)$$

$$M = Li, Na, K, Ca$$

The reactions were carried out in sealed tubes equipped with magnetic stirrers which were placed in a thermostatic oil bath at 98 °C for 72 h which assured that the equilibrium composition was achieved. In each experiment 0.01 mol of n-octyl chloride was treated with an equivalent amount of a bromide salt in the presence of 5 mol% of tetrahexylammonium bromide (THAB) or Aliquat 336 and with a measured amount of water.

The final equilibrium composition of each experiment was determined by g.c. analysis of the organic phase and potentiometric titration of the inorganic phase. It was observed that in the total absence of water no exchange reaction took place at all, this observation is similar to findings in other phase transfer systems.[8] The measured equilibrium conversions of reaction (3) with four metal bromide salts as a function of the amount of water at 98 °C are shown in Figure 1. Only minor differences were observed in the equilibrium conversion with the two catalysts employed which can be attributed to the small difference in the bromide–chloride balance in the two systems.

It was observed that with a sufficient amount of water, the reaction mixture consists of two non-miscible liquid phases, but on decreasing the initial amount of water, a 'critical' concentration is reached, at which a precipitate is formed during the course of the reaction; this 'critical' concentration is marked with an arrow for each salt in Figure 1. Below this critical concentration, with even lower quantities of water the system was a slurry from start to finish.

It is clear from Figure 1 that reaction (3) is strongly dependent on the composition of the aqueous phase when lithium or calcium salts are involved. The effect is less pronounced with sodium bromide, and with potassium bromide the equilibrium conversion is almost independent of the initial amount of water.

We attribute the phenomenon shown in Figure 1 to the thermodynamic properties of the aqueous phase (namely the ternary system MBr–MCl–H₂O). When the inorganic phase is a real solution, the equilibrium position of reaction (3) is simply determined by the ratio of the activity coefficients $\gamma_{MCl}:\gamma_{MBr}$. The situation is far more complicated when slurries are formed but a qualitative idea can be obtained through the solubility and the affinity of the various salts towards water.

As it was shown for several other systems, water of hydration is essential for the extraction process by phase transfer catalysis to take place.[8] Salts, or rather anions, which are not in solution nor hydrated cannot be extracted. Lithium and calcium bromide are not only more soluble than the corresponding chloride salts but in high concentration the bromide salts force the chloride salts to precipitate out of solution. When only a limited amount of water is present, calcium bromide or lithium bromide will be hydrated owing to their higher affinity to water while the corresponding chlorides will remain dry and thus inert to the phase transfer exchange process. The equilibrium under these conditions is strongly shifted to the right. It should be noted that, with 95% dry calcium bromide the equilibrium conversion obtained in reaction (3) (92%) is not affected by addition of dry calcium chloride to the initial reaction mixture.

The above effects are weaker with sodium bromide but do not exist at all in the potassium bromide–potassium chloride system. Both potassium salts are almost not hydrated in the presence of water slurries.[9]

For practical purposes it is obvious that for bromination of various alkyl chlorides one would prefer lithium bromide which is commercially available in an almost anhydrous form which leads to the best conversions under the mildest conditions,[5] calcium bromide, which is more difficult to dry, being second best.[4]

For instance, using a slight excess of lithium bromide containing 1% of water and 5 mol% of Aliquat 336 at 85—110 °C, we were able to convert within about 6 h primary halides or 1,ω-dihalides (applied on a stoicheiometric basis) into the corresponding bromides in excellent yields (80—94%). Some secondary and tertiary alkyl chlorides were also converted in good yields, into their corresponding bromides.[5]

Electrophilic assistance by Li⁺ to the cleavage of the C–X bond may be also involved when lithium bromide is converted[10] in connection with the possibility of C–X ···· Li⁺ interactions.[11] This effect, which can occur at the solid–liquid interface and increases with the bond energy i.e. C–Cl > C–Br,[12] will be more pronounced for the reaction Br⁻ + C–Cl than for the reverse one, Cl⁻ + C–Br. It can thus contribute to shift the equilibrium (3) to the right. Electrophilic assistance by Ca²⁺ can also be involved in the case of CaBr₂ reaction as calcium salts were found to exhibit a strongly specific positive salt effect.[13]

For the reverse reaction, conversion of alkyl bromides into the corresponding chlorides, one would use 20—30% w/w aqueous solution of any of the chloride salts. Applying a 25% solution of sodium chloride on an equivalent amount of octyl bromide containing 5 mol% of Aliquat 336 at 95 °C we were able to achieve 98% conversion by replacing the aqueous phase two times with a fresh batch of solution and allowing each portion to react for 2½ h. Similarly 25% solutions of lithium, sodium, potassium, or calcium chlorides were con-

verted into bromides on contact with ethylene dibromide or 1,4-dibromobutane.

The observations presented here clearly indicate the important role of the metal cation in phase transfer catalysed reactions particularly in solid–liquid systems in the absence of added organic solvent. This aspect was not recognized in the literature where the main effects were attributed to the anions involved in the phase transfer process.[7]

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References

1 W. E. Willy, Dr. R. McKean, and B. A. Garcia, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 1989.
2 Y. Sasson and M. Yonovich-Weiss, *J. Mol. Catal.*, 1981, **10**, 357.
3 G. Cainelli, F. Manescalchi, and M. Panunzio, *Synthesis*, 1976, 472.
4 M. Yonovich-Weiss and Y. Sasson, *Synthesis*, 1984, 34.
5 A. Loupy and C. Pardo, to be published.
6 H. A. Finkelstein, *Ber. Dtsch. Chem. Ges.*, 1910, **43**, 1528.
7 C. M. Starks and C. Liotta, 'Phase Transfer Catalysis,' Academic Press, New York, 1978, pp. 117—122.
8 C. M. Starks and R. M. Owens, *J. Am. Chem. Soc.*, 1973, **95**, 3613; T. Ando, T. Kawater, J. Yamawaki, and T. Hanafusa, *Chem. Lett.*, 1982, 935; H. A. Zahalka and Y. Sasson, *J. Chem. Soc., Chem. Commun.*, 1984, 1652; F. Texier-Boullet, D. Villemin, M. Ricard, H. Moison, and A. Foucaud, *Tetrahedron*, 1985, **41**, 1259; Y. Le Bigot, M. Delmas, and A. Gaset, *ibid.*, 1986, **42**, 339; G. Bram, A. Loupy, and M. Pedoussaut, *Bull. Soc. Chim. Fr.*, 1986, 124; S. Dermeik and Y. Sasson, *J. Org. Chem.*, 1985, **50**, 879.
9 F. E. Harris and C. T. O'Konski, *J. Phys. Chem.*, 1957, **61**, 310.
10 S. Winstein, E. C. Friedrich, and S. Smith, *J. Am. Chem. Soc.*, 1964, **86**, 305.
11 R. H. Staley and J. L. Beuchamp, *J. Am. Chem. Soc.*, 1975, **97**, 5920.
12 J. A. Kerr, *Chem. Rev.*, 1966, **66**, 465.
13 T. Okuyama, K. Kumura, and T. Fueno, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 2285.