

The Key Role of Water in Solid-Liquid Phase Transfer-catalysed Substitution Reactions

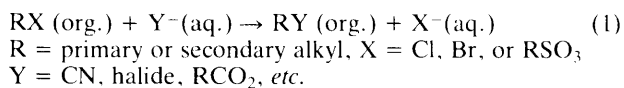
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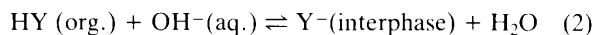
Traces of water are shown to be essential for substitution reactions catalysed by quaternary ammonium salts; in chloride-formate exchange maximum rate is observed with 0.2% water content of the formate salt, and addition of dehydrating agents reduces the maximum rate by 50%.

Heterogeneous displacement reactions of the general type (1) are known to be catalysed by lipophilic quaternary ammonium salts acting as phase transfer catalysts (P.T.C.).^{1,2} Several authors recommend that in order to achieve best results this type of exchange should be carried under the conditions known as solid-liquid phase transfer catalysis.³⁻⁵ namely, in the absence of water. The main reasons for this were as follows. (i) Decrease in the amount of water of hydration around the extracted ion pair results in higher nucleophilicity of the attacking anion and thus higher reaction rates.⁶ (ii)

Higher extraction coefficients and selectivity constants are observed particularly for hydrophilic anions that in liquid-liquid systems suffer from catalyst poisoning.^{7,8} (iii) With highly concentrated aqueous solutions simple pseudo-first-order rate equations are obtained which are independent of Y^- concentration.^{7,9} In more dilute aqueous solutions the rate is slower and follows a complicated rate equation. (iv) In some cases the (negative) free energy changes in reactions of type (1) are larger for dry systems resulting in higher equilibrium conversions.⁸



A second very common P.T.C. system is where the nucleophile Y⁻ is generated *in situ* by an equilibrium deprotonation process, usually in the presence of a hydroxide base^{1,2} [reaction (2)].



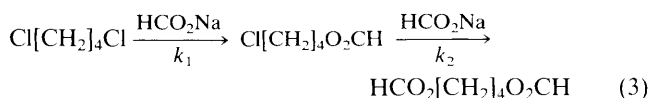
This type of mechanism is operative in alkylations and dichlorocarbene reactions. Here the removal of water has additional critical advantages. (i) Hydroxide ion is known to be a stronger base in the absence of hydration water.¹⁰ (ii) The presence of water shifts the equilibrium (2) to the left resulting in lower concentration of the active species Y⁻. (iii) The presence of HY in the system tends, in some instances, to deactivate the normal P.T.C. mechanism by hydrogen-bonding extraction of this compound.¹¹

These effects should always be carefully considered when designing a new P.T.C. system.

Despite all the listed advantages of solid-liquid processes we have now quantitatively verified that in the total absence of water reactions of type (1) with quaternary salts as catalysts do not take place at all. There are conflicting reports in the literature regarding this fact; some authors claim that an efficient reaction is obtained¹² while others report that no exchange is observed.¹³

We carried out reactions of type (1) with X = Cl or Br and Y = Br, Cl, F, HCO₂, or MeCO₂ (as K or Na salts), R = n-C₆H₁₃, n-C₈H₁₇, n-C₁₀H₂₁, or PhCH₂, in the presence of tetra-n-butylammonium hydrogen sulphate and bromide or tetra-n-hexylammonium chloride as catalysts in the presence and the absence of xylene or chlorobenzene as a solvent in a temperature range of 90–130 °C always with very efficient mixing. It was clear that when the reagents and solvents were carefully dried no exchange reaction took place. Attempts to extract, by anion exchange, the anion Y⁻ from the solid state into xylene or chlorobenzene containing the above quaternary salts also failed when the salt KY or NaY was freeze-dried prior to the experiment.

The consecutive exchange reaction (3) was carried out under controlled conditions, with chlorobenzene as solvent, in the presence of tetra-n-butylammonium hydrogen sulphate as catalyst, with varying amounts of water at 100 °C with mechanical mixing at 1000 rev./min. The reaction was followed by gas chromatographic analysis of samples taken at constant intervals.



The process was found to follow a consecutive first-order mechanism of the general type A → B → C and k₁ and k₂ were directly calculated from the reaction profiles. Figure 1 presents the measured pseudo-first-order rate constant k₁ as a function of the amount of water in the system under the specified reaction conditions. The precise amount of water in sodium formate was determined by thermogravimetric analysis and verified by Karl-Fischer titration of the reaction

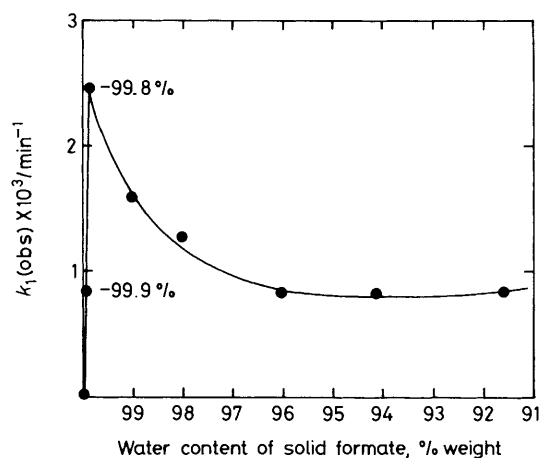


Figure 1. Effect of amount of water employed on the pseudo-first-order rate constant, k_1 (obs.), of reaction (3) catalysed by tetra-n-butylammonium hydrogen sulphate: 1,4-dichlorobutane (27.4 mmol), sodium formate (82.2 mmol), tetra-n-butylammonium hydrogen sulphate (1.6 mmol), and chlorobenzene (20 ml) at 100 °C, with mechanical stirring at 1000 rev./min.

Table 1. The effect of dehydrating agents on reaction (3).^a

Additive	$k_1 \times 10^3 / \text{min}^{-1}$	$k_2 \times 10^3 / \text{min}^{-1}$
None	3.1	1.3
CaCl ₂	1.8	0.9
MgSO ₄	1.5	0.7

^a Reaction conditions: dehydrating agent, (3.2 mmol), 1,4-dichlorobutane (27.4 mmol), 99.8% sodium formate (80.6 mmol), tetra-n-butylammonium bromide (1.6 mmol), and chlorobenzene (20 ml) at 110 °C with mechanical stirring at 1000 rev./min.

mixture. It can clearly be seen that no reaction takes place in totally dried system but the rate increases rapidly in the presence of traces of water and then drops again with larger amounts. A similar effect was observed by Starks.¹³

The importance of the traces of water in the reaction (3) could be again demonstrated by the addition of dehydrating agents. Landini and co-workers⁶ demonstrated rate increases in liquid-liquid systems on the addition of, e.g., KOH, which reduced the hydration of the extracted ion pair thus increasing the nucleophilicity and consequently the rate. We observed the opposite phenomenon in the solid-liquid systems. We were unable to use potassium hydroxide because it caused side hydrolysis reactions, but upon addition of calcium chloride or magnesium sulphate to the reaction (3) significantly lower rates were measured. Some results for reaction (3) catalysed by tetra-n-butylammonium bromide using the optimal 99.8% sodium formate are summarized in Table 1.

We conclude that traces of water are essential for phase transfer-catalysed reactions. Since catalytic amounts are optimal, we believe that the role of the water is kinetic rather than thermodynamic. Apparently a salt molecule in the solid lattice cannot be approached by the quaternary cation and it has to be hydrated in order to be extracted. Once the anion is extracted the water is released for another extraction cycle. When these water molecules are occupied with foreign dehydrating agent the reaction is naturally retarded.

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