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# NEW IDEAS ON PHASE TRANSFER CATALYSTS: $S_N2$ REACTION WITH A SOLID IONOPHORIC SALT

S. S. YUFIT AND I. A. ESIKOVA*

*N. D. Zelinsky Institute of Organic Chemistry, USSR Academy of Sciences, 47 Leninsky Prospect, Moscow, USSR*

**A new mechanism of substitution between *n*-hexyl bromide (RBr) and solid potassium chloride in toluene under phase-transfer catalysis conditions is suggested, involving the formation of intermediates, adsorbed on the solid phase, viz., two binary (KCl·QX and KX·QBr) and two ternary (QX·KCl·RBr and QBr·KX·RCl) complexes. According to this mechanism, the catalytic activity of onium salts (QX) in the substitution changes in the order QI > QBr > QCl. The nature of the catalyst cation has little or no effect on the reaction rate. A general rule is proposed according to which in this reaction the substrate is attacked by a stronger nucleophile whereas a weaker nucleophile accepts the leaving group of the substrate. These and earlier data are interpreted in term of the $S_N2$ process occurring on the solid-phase surface. The structure of the ternary complexes and the role of the phase-transfer catalyst are discussed.**

## INTRODUCTION

The $S_N2$ substitution mechanism at a saturated carbon atom is a cornerstone in the construction of the general phase-transfer catalysis (PTC) theory. However, only one heterophase system, viz. an organic/aqueous phase (l/l) has been studied well so far.[1-10] Also, little is known about the ways in which the substitution takes place in the organic/solid phase system, and sometimes the data obtained are conflicting.

This paper deals with the results of systematic studies[11-15] into the substitution reaction

$$\underset{\text{(RBr)}}{n\text{-}C_6H_{13}Br_{\text{org.ph.}}} + MCl_s \underset{\text{toluene}}{\overset{QX}{\rightleftharpoons}} \underset{\text{(RCl)}}{n\text{-}C_6H_{13}Cl_{\text{org.ph.}}} + MBr_s \qquad (1)$$

where MCl is a solid alkali metal chloride and QX is an onium salt.

Reaction (1) does not proceed in the absence of a catalyst. Anion exchange between solid KCl and $Bu_4NBr$ in toluene also does not occur, i.e. there is no $Cl^-$ nucleophile transfer to the organic phase.[11-15] The substitution kinetics conform to the behaviour of a reversible pseudo-first-order reaction and variable orders with respect to all the components. The free energy of substitution for reaction (1) depends on the nature of the solid MCl ionophore. The resulting data, as shown elsewhere,[14,15] are consistent with a substitution mechanism which includes the formation of two pairs of binary and ternary complexes obtained from RY, MX and QX adsorbed on the solid salt surface:

$$\begin{tikzcd}
\mathrm{MCl + QX} \arrow[d, shift left] & & & \mathrm{MBr + QX} \arrow[d, shift left] \\
\mathrm{MCl\cdot QX} \arrow[u, shift left] \arrow[r, shift left, "+\mathrm{RBr}"] & \mathrm{MCl\cdot QX\cdot RBr} \arrow[l, shift left, "K_{TC1}"] \arrow[r, shift left, "k_+"] & \mathrm{MBr\cdot QX\cdot NCl} \arrow[l, shift left, "k_-"] \arrow[r, shift left, "-\mathrm{RCl}"] & \mathrm{MBr\cdot QX} \arrow[u, shift left] \arrow[l, shift left, "K_{TC2}"] \\
\mathrm{(BC1)} & \mathrm{(TC1)} & \mathrm{(TC2)} & \mathrm{(BC2)}
\end{tikzcd} \qquad (2)$$

The overall reaction rate is controlled by the rate of the ternary complex rearrangement, which should be interpreted as a limiting factor. The possible structures of these ternary complexes are expected to provide for adherence to the detailed balancing principle in this reversible reaction.

The purpose of this study was to establish the functions of all the reagents involved, structures of the intermediates and features of the transition stage in the nucleophilic substitution reaction with participation of a solid ionophore and phase-transfer catalysts. To do so, we studied the effect of various catalysts on the rate of reaction (1).

## RESULTS AND DISCUSSION

In the construction of the ternary complex models, the following three factors were taken into account.

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* Author for correspondence.

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(1) the reaction proceeds via the $S_N2$ mechanism and it is assumed that the rear part of the carbon atom associated with the leaving $Y^-$ group is attacked by the $X^-$ ion;

(2) the quantum-chemical study of these systems[16,17] indicates that during such an attack the $X^-$ ion is capable of being diverted from the $X^- \cdots C{-}Y$ axis by up to 20° without a noticeable rise in the system's energy (10% maximum);

(3) the $Cl^- \cdots Q^+ \cdots Cl^- \cdots M^+$ and $Br^- \cdots M^+ \cdots Cl^- \cdots Q^+$ electrostatic interactions do not exhibit any predominant direction so that the arrangement of the component ions is controlled only by the strength of these interactions.

Note also that in the formation of ternary complexes the ion–ion and ion–dipole interactions impose some requirements on the geometry of the entering particles. The species TC1 and TC2 are assumed to have a cyclic structure with fixed bond lengths and angles.

In this context, the effect of the geometric factors will be significant, and the reaction rates depends on the size of the catalyst $Q^+$ ion (Table 1). The use of bulkier $Q^+$ cations results in a sharp deceleration of the substitution reaction. The reaction rate in the presence of $Bu_4NBr$ is four times that in the case of $Oct_4NBr$, although the latter is completely dissolved in toluene. The reaction rates in the presence of different QX have no connection with the solubility of the catalyst in toluene, since the addition of RBr to the system brings about complete dissolution of all the salts at 70 °C.

Special attention was paid to the effect of the catalyst anion. This is associated with the fact that the catalyst itself is capable of reacting as the nucleophile. Thus, in the RBr–QCl reaction the halogens are homogeneously substituted in the organic phase. This reaction proceeds practically irreversibly to give complete conversion of QCl to QBr (see the Experimental).

The reverse reaction, i.e. the RCl–QBr interaction under similar conditions, gives the substitution products with an equilibrium yield of less than 3·5%. The interaction of RBr with solid KCl or of RCl with solid KBr in toluene in the absence of a catalyst gives no substitution products. The situation is different when the substitution occurs under PTC conditions. In the QX catalysis (where X = Cl, Br or I) the reaction system contains two sources of nucleophiles, viz. $X^-$ from QX and $Cl^-$ from solid KCl.

It should be stressed that when using QI as the catalyst there are no indications of the appearance of even the modest amounts of RI. Analysis of the system containing QCl demonstrates that if QCl is used as the nucleophile, then one can observe first the homogeneous substitution and second that the role of the catalyst will be played by QBr appearing in the initial stage of the process. In this case no difference in the catalytic effects of QCl and QBr is expected to arise. However, Table 1 shows that QCl is a more active species and, hence, this route does not control the process kinetics. The absence of a homogeneous reaction in the case of the solid KCl phase can be attributed to strong catalyst adsorption on the surface.

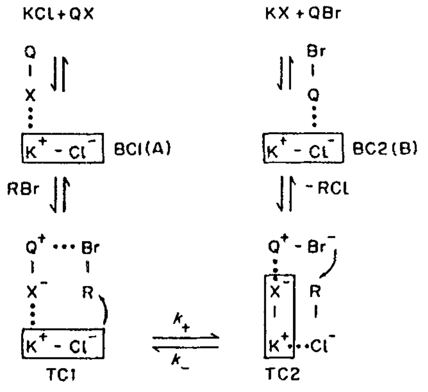
The energy of formation of the BC1 structures A and B (Scheme 1) will differ significantly owing to the difference in the radii of the $K^+$ and $Bu_4N^+$ ions ($r_+ = 0{\cdot}133$ nm and $0{\cdot}437$ nm, respectively), the structure A being preferred from the thermodynamic point of view. Therefore, the BC1(A)–RBr interaction seems

Scheme 1

Table 1. Effect of the nature of the catalyst on substitution rate constants[a]

| QX | Temperature (°C) | $K_{eq.}$ | $k_1 \times 10^6$ ($s^{-1}$) | $k_2 \times 10^6$ ($s^{-1}$) |
|---|---|---|---|---|
| $Bu_4NCl$ | 70 | 1·77 | 19·5 | 11·03 |
| $Bu_4NBr$ | 70 | 1·67 | 13·3 | 7·97 |
| $Bu_4NI$ | 70 | 1·69 | 10·4 | 6·14 |
| $Bu_4NClO_4$ | 70 | Reaction does not proceed | | |
| $Oct_4NBr$ | 70 | | 3·06 | |
| $Et_3(C_{15}H_{31})NBr$ | 70 | | 2·0 and 3·5 | |
| $Et_3CH_2PhNCl$ | 84 | | 1·39 | |
| $Bu_4NBr$ | 84 | 2·7 | 40·0 | 14·7 |
| $Me_3CetNBr$ | 84 | | 0·852 | |
| Quin[b] | 84 | | 1·763 | |
| $Ph_3MePBr$ | 84 | | 0·43 | |

[a] Toluene, KCl = 13 g, [RBr] = 0·9 M, [QX] = 0·02 M.
[b] N-Benzyl-3s-hydroxyquinuclidine chloride.



Scheme 2

to be more probable. Thus a successive formation of a binary and a ternary complex before the appearance of the final substitution product is assumed (Scheme 2). Here and in what follows X = Cl, Br or I. The arrows designate the direction of the nucleophilic attack. The rectangles show the crystalline lattice elements of the solid phase.

According to Scheme 2, it is the nature of the anion in QX that is responsible for the strength of the adsorption complex located on the solid salt surface.

It was established that the smaller the anion radius, the stronger is $X^-$–$K^+$ interaction and the complex formed. A satisfactory linear relationship between log $k_\pm$ and $1/r$ suggests the participation of the catalysts in the transition substitution state (Figure 1).

A correlation of the substitution rates in the course of QX catalysis permits the following principles to be derived:

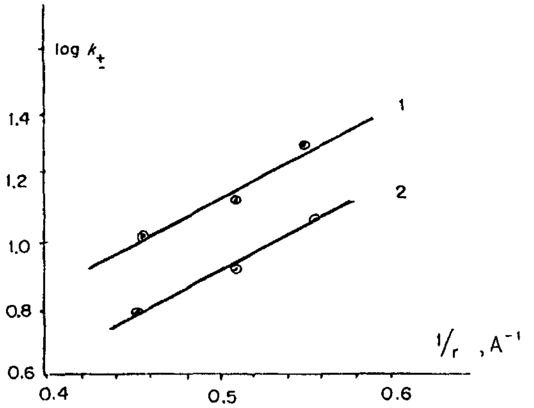
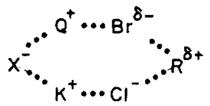


Figure 1. Relationship between log $k_\pm$ and $1/r$·1, RBr → RCl; 2, RCl → RBr. Toluene, 70°C, KCl = 13 g, organic phase volume = 25 ml, [RBr] = 0·9 M; $[Bu_4NX]$ = 0·02 M (X = Cl, Br, I)

(1) In the formation of TC1 and TC2 the substrate undergoes a nucleophilic attack by a stronger nucleophile. In the case of the forward reaction such a nucleophile is represented by an active $Cl^-$ from the solid ionophore and in the case of the reverse reaction a catalyst anion.

(2) A weaker nucleophile picks up the leaving substrate group. A need for a third particle to be involved in the biomolecular reaction has been advocated by Swain *et al.*[18] Most often such a particle is represented by a solvent molecule. If, as in our case, the solvent is inert toward all other components of the reaction mixture, then this role should be played by some reagent or phase, the so-called 'internal phase' according to Hinshelwood and co-workers.[19,20] In our studies we used as such a phase a catalyst and a solid phase for the forward and reverse reactions, respectively. Hence there is a difference in the ways in which TC1 and TC2 are formed and, hence, in functions fulfilled by the solid salt. This fact is indicated by the thermodynamic characteristics of the ternary complexes (Table 2).

Starting with the data on the dependences of $k_{obs}$ on $[QBr]_0$ and $[RBr]_0$[14] in the reaction with KCl, we determined the formation constant for TC1 ($K_{TC1} = 20{\cdot}48\ M^{-2}$) and its rearrangement constant ($k_+ = 0{\cdot}75\ M^{-2}s^{-1}$) at 84 °C. Using the equation $\Delta G = \Delta H - T\Delta S$, where $\Delta H = -11{\cdot}7\ \mathrm{kcal\,mol^{-1}}$ (1 kcal = 4·184 kJ),[15] we estimated the entropy of formation for TC1 and that of activation involved in the stage-by-stage rearrangement of all the TCs. It was found that $\Delta S_{TC1} = -26{\cdot}8$ e.u. and $\Delta S^{\neq} = +47$ e.u. A correlation of these values suggests that the structure of the TCs is more rigid than that of the transition state during the complex rearrangement. This agrees well with our idea that the solid-phase molecule forms part of the TCs. It is believed that a transition between the TC1 and TC2 occurs via a cyclic state with a delocalized bond system:



The surprisingly large difference between the entropy of formation for the TCs and the entropy of activation for their mutual transition can be attributed to the main role played by electrostatic forces and ion–dipole interactions in the formation of the TCs. These two bond types do not involve rigid requirements for the direction of the interactions and, hence, a low entropy of formation for the TCs is associated with a loss of those degrees of freedom which correspond to the adsorption of the two reacting molecules on the solid salt surface. However, in the transition state the interaction with the $sp^3$ carbon orbital calls for a more rigid orientation

Table 2. Potential energy changes for reaction (1) in the course of substitution[15a]

| | Potential energy (kcal mol$^{-1}$) | | | | |
|---|---|---|---|---|---|
| Cation M | Starting products (MCl + RBr) | TC1 | Transition state | TC2 | Final products (MBr + RCl) |
| Li$^+$ | −138·28 | −177·23 | −146·83 | −163·93 | −134·8 (calc.)<br>−140·0 (found) |
| Na$^+$ | −138·98 | −162·98 | −136·48 | −161·28 | −137·2 (calc.)<br>−139·11 (found) |
| K$^+$ | −144·98 | −156·68 | −139·08 | −145·78 | −144·98 (calc.)<br>−145·78 (found) |
| RBr$^+$ | −144·68 | −144·68 | −129·78 | −146·48 | −145·3 (calc.)<br>−146·48 (found) |
| Cs$^+$ | −146·38 | −140·38 | −126·48 | −146·48 | −147·8 (calc.)<br>−146·48 (found) |

[a]Toluene, MCl/RBr = 7, [RBr] = 0·9–1 M, [Bu$_4$NCl] = 0·04 M.

of the reacting dipoles and the attacking $Br^- \cdots C^{\delta+} \cdots Cl^{\delta-}$ or $Cl^- \cdots C^{\delta+} \cdots Br^{\delta-}$ ion. Then the only explanation of the large positive value of $\Delta S^{\neq}$ may be the destruction of the solid salt crystalline lattice, resulting in the appearance of lattice-free $M^+$ and $Cl^-$ (or $Br^-$) ions and, hence, a sharp rise in the entropy of the system.

Hence the above substitution mechanism with participation of TC1 and TC2 involves the destruction of the solid ionophore crystalline lattice by means of a catalyst. It is for this reason that the mechanism proposed can be of general significance as all reactions under PTC conditions occur in heterogeneous situations and involve adsorption at the interface, giving rise to intermediates that facilitate the process.

Is this correct if water is added to the system? Our data show that the reaction does not take place in the presence of 80 wt-% water in KCl and $Bu_4NBr$ solution. Replacement of $Bu_4NBr$ with $Oct_4NBr$ increases the substitution rate. The values of the rate constants are $k_{for.} = 4{\cdot}24 \times 10^{-5}\ s^{-1}$, $k_{rev.} = 3{\cdot}62 \times 10^{-5}\ s^{-1}$ at 60 °C and $[Oct_4NBr] = 0{\cdot}033$ M and $k_{for.} = 15{\cdot}73 \times 10^{-5}\ s^{-1}$, $k_{rev.} = 12{\cdot}42 \times 10^{-5}\ s^{-1}$ for 75 °C and $[Oct_4NBr] = 0{\cdot}033$ M. The activation energy is 18·2 kcal mol$^{-1}$ for the forward reaction and 17·1 kcal/mol$^{-1}$ for the reverse process. Also, it was found that type of salt cation ($M^+ = Li^+, Na^+, K^+, Rb^+, Cs^+$) does not affect the reaction rate constants. This indicates some differences between the reaction in the organic/aqueous and the organic/solid phase systems.

Addition of traces of water to the solid salt (KCl) has little or no effect on the initial substitution rate up to 7% (wt-% $H_2O$/KCl). Hence a 'dry' system ($H_2O < 0{\cdot}02$ wt-%) and systems with water added ($H_2O$ 0·13, 0·3 or 7 wt-%) behave in the same way. These preliminary results do not permit final conclusions to be made as to why water affects the kinetics and the mechanism of substitution.

The evidence obtained indicates that the mechanism suggested to occur in all cases on the solid phase surface is correct. Probably the main role in such a process is played by the binary and ternary complexes. Analysis of the energetics in the individual stages of the scheme points to a rigid structure of the given ternary complexes. The rearrangement of these complexes represents a rate-limiting stage. The high positive activation entropy for this stage is associated with the destruction of the solid ionophore crystalline lattice. The function of the phase-transfer catalyst in such a process consists in coordinating the reagents on the solid ionophore surface and activating the anion contained in this ionophore.

## EXPERIMENTAL

The bromine–chlorine substitution in hexyl bromide in the presence of solid MCl ionophores (M = Li, Na, K, Rb or Cs) was carried out in toluene, using a variety of phase-transfer catalysts ($Q^+X^-$) in the temperature range 50–106 °C. The solid salts (0·05–0·07 mm fractions) dried under vacuum at 260 °C just prior to the experiments were activated by crushing against the walls of a dry glass reactor. The MCl/RBr ratio was 7. The required intensity of stirring was effected with a PTFE device at 1900–2300 rpm. The reagents have been characterized elsewhere.[11,12] Traces of water in the solvent and the catalysts were determined by Fischer titration and by IR spectrometry, respectively. In both cases they did not exceed 0·01 wt-%. The kinetic methods used and analyses of the reaction mixtures have been described elsewhere.[12]

The activity of the phase-transfer catalysts was estimated by 70 and 84 °C; [RBr] = 0·9 mol l$^{-1}$, KCl = 13 g, organic phase = 25 ml, [QX] = 0·02 mol l$^{-1}$. The data obtained are listed in Table 1.

The homogeneous reactions between hexyl bromide (1 mol l$^{-1}$) and $Bu_4NCl$ (0·02 mol l$^{-1}$) and also between hexyl chloride ($1\,\mathrm{mol\,l^{-1}}$) and $Bu_4NBr$ ($0{\cdot}02\,\mathrm{mol\,l^{-1}}$) in toluene were studied at 70 °C. The reaction mixture was studied by titration to determine $Cl^-$ and $Br^-$ concentrations. Estimation of the constants for the homogeneous process

$$RCl + Bu_4NBr \underset{k_2}{\overset{k_1}{\rightleftharpoons}} RBr + Bu_4NCl$$

indicated that $K_{equi} = k_1/k_2 = 430$; $k_1 = 730 \times 10^{-3}\,\mathrm{M^{-1}\,s^{-1}}$ and $k_2 = 3{\cdot}11 \times 10^{-3}\,\mathrm{M^{-1}\,s^{-1}}$.

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