Ion Pair Extraction in Preparative Organic Chemistry. IX.
Kinetic Evidence for an Ion Pair Mechanism in the
Halogen Exchange of Alkyl Halides Catalyzed by
Tetrabutylammonium Halides

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The kinetics of the reaction between a methylene chloride solution of benzyl chloride and an
aqueous solution of sodium iodide in the presence of tetrabutylammonium iodide has been
studied. When the mixture is properly stirred, the rate-determining step occurs within the
organic layer. The dominating nucleophile was found to be the ion pair. An excellent preparative
method is given for the conversion of alkyl iodides into alkyl chlorides, as well as a method
for the reverse reaction.

The halogen exchange in alkyl halides with an
alkali halide has been studied under a variety
of conditions. In most cases, the main reaction
is proved, or believed, to be an attack on the
alkyl halide by the free halide anion. A careful
discussion of the problems involved in the
identification of the nucleophile has recently
been given by Beronius, Isacsson and Nilsson. 1
We have studied the reaction of benzyl chloride
RCI in methylene chloride with an aqueous
solution of sodium iodide, in the presence of
tetrabutylammonium iodide QI, to benzyl iodide
RI by the formula

$$\text{RCI}_a + \text{I}_w^- \rightarrow \text{RI}_a + \text{Cl}_w^-$$

where the subscripts w and s indicate that the
c molecule or ion is present in water or solvent.

The reaction was followed by taking samples
from the aqueous layer and analyzing for Cl-
by potentiometric argentimetry. When the

Fig. 1. The sudden stop. The circles are the
experimental quantities of benzyl iodide formed
from a mixture of 25 ml of a 0.4 M solution of
benzyl chloride in methylene chloride and 25
ml of a solution 0.156 M in NaI and 0.25 M in
NaCl with 4.00 g of tetrabutylammonium iodide
as a catalyst. The curve represents the values that
should be obtained with an excess of
sodium iodide in the aqueous layer. The
horizontal line is the total quantity of NaI
available.
Table 1. Reaction of benzyl chloride with aqueous sodium iodide in the presence of 4.000 g of tetrabutylammonium iodide.

<table>
<thead>
<tr>
<th>t min</th>
<th>Aqueous volume ml</th>
<th>a ml</th>
<th>a + b ml</th>
<th>mmol Cl⁻</th>
<th>mmol RCl</th>
<th>RCl calc</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>25.0</td>
<td>0</td>
<td>0</td>
<td>10.00</td>
<td>10.00</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>25.0</td>
<td>0.080</td>
<td>0.787</td>
<td>0.99</td>
<td>8.01</td>
<td>8.05</td>
</tr>
<tr>
<td>30</td>
<td>24.5</td>
<td>0.143</td>
<td>0.788</td>
<td>1.75</td>
<td>8.25</td>
<td>8.18</td>
</tr>
<tr>
<td>45</td>
<td>24.0</td>
<td>0.210</td>
<td>0.763</td>
<td>2.57</td>
<td>7.43</td>
<td>7.40</td>
</tr>
<tr>
<td>60</td>
<td>23.5</td>
<td>0.257</td>
<td>0.740</td>
<td>3.29</td>
<td>6.71</td>
<td>6.69</td>
</tr>
<tr>
<td>75</td>
<td>23.0</td>
<td>0.325</td>
<td>0.773</td>
<td>3.95</td>
<td>6.05</td>
<td>6.05</td>
</tr>
<tr>
<td>90</td>
<td>22.5</td>
<td>0.380</td>
<td>0.781</td>
<td>4.53</td>
<td>5.47</td>
<td>5.47</td>
</tr>
<tr>
<td>105</td>
<td>22.0</td>
<td>0.429</td>
<td>0.782</td>
<td>5.06</td>
<td>4.94</td>
<td>4.94</td>
</tr>
<tr>
<td>120</td>
<td>21.5</td>
<td>0.474</td>
<td>0.780</td>
<td>5.56</td>
<td>4.44</td>
<td>4.47</td>
</tr>
<tr>
<td>137</td>
<td>21.0</td>
<td>0.516</td>
<td>0.783</td>
<td>5.98</td>
<td>4.02</td>
<td>3.99</td>
</tr>
<tr>
<td>150</td>
<td>20.5</td>
<td>0.556</td>
<td>0.786</td>
<td>6.36</td>
<td>3.84</td>
<td>3.65</td>
</tr>
<tr>
<td>180</td>
<td>20.0</td>
<td>0.618</td>
<td>0.785</td>
<td>6.99</td>
<td>3.01</td>
<td>2.99</td>
</tr>
</tbody>
</table>

\[ k([QI]_s) = 67.1 \times 10^{-4} \text{ min}^{-1}. \] \[ \text{S.E.}(k([QI]_s)) = 0.41 \times 10^{-4} \text{ min}^{-1}. \]

The calculated value of RCl was obtained from this constant. \(a\) and \(b\) are the ml of AgNO₃ used to titrate Cl⁻ and I⁻.

Table 2. Reaction of benzyl chloride with aqueous sodium iodide in the presence of different quantities of tetrabutylammonium iodide.

<table>
<thead>
<tr>
<th>QI g</th>
<th>[QI]₅₈ M</th>
<th>(k([QI]_s)) min⁻¹</th>
<th>S.E. (k) min⁻¹</th>
<th>(k) M⁻¹ min⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.250</td>
<td>0.0271</td>
<td>4.16 \times 10^{-4}</td>
<td>2.6 \times 10^{-4}</td>
<td>1.56 \times 10^{-2}</td>
</tr>
<tr>
<td>1.000</td>
<td>0.1083</td>
<td>16.3 \times 10^{-4}</td>
<td>6.4 \times 10^{-4}</td>
<td>1.51 \times 10^{-2}</td>
</tr>
<tr>
<td>2.309</td>
<td>0.2500</td>
<td>38.0 \times 10^{-4}</td>
<td>1.4 \times 10^{-4}</td>
<td>1.52 \times 10^{-2}</td>
</tr>
<tr>
<td>4.000</td>
<td>0.4332</td>
<td>67.1 \times 10^{-4}</td>
<td>1.0 \times 10^{-4}</td>
<td>1.55 \times 10^{-2}</td>
</tr>
</tbody>
</table>

mixture was properly stirred, the reaction showed the following features:

1. The quantity of QI used remains in the organic layer throughout the reaction.
2. For a given quantity of QI, the reaction velocity follows first order kinetics with the rate proportional to the concentration of RCl in the organic layer.
3. The pseudo first-order velocity constant according to point 2 is directly proportional to the quantity of QI added to the organic layer.
4. The velocity of the reaction is independent of the concentration of I⁻ in the aqueous layer, provided that this concentration is above a low critical value (about \(10^{-4}\) M).
5. As soon as the concentration of I⁻ in the aqueous layer has fallen below the critical value, the reaction suddenly stops.

The results of the kinetic measurements are given in Tables 1 and 2 and in Fig. 1. From these experimental facts we can draw the following conclusions:

The rate-determining step occurs within the organic layer between RCl and a nucleophile dissolved in the organic layer. As will be demonstrated, this nucleophile is the ion pair QI. The rate determining step is therefore

\[
\text{RCI} + \text{QI} \xrightarrow{\text{slow}} \text{RI} + \text{QCl} \\
\text{QCl} + \text{I} \xrightarrow{\text{rapid}} \text{QI} + \text{Cl} 
\]

This reaction is coupled with a very rapid ion exchange step.

\[
\text{QCl} + \text{I} \xrightarrow{\text{rapid}} \text{QI} + \text{Cl} 
\]

The equilibrium constant for this exchange has been independently determined to be about \(4 \times 10^4\). This means that the equilibrium is displaced far to the right unless the concentration of I⁻ in the water layer is very low. The
concentration of QCl in the organic layer is thus very low and the reverse reaction

$$\text{RI}_s + \text{QCl}_s \rightarrow \text{RCI}_s + \text{QI}_s$$

is so slow that it can be neglected as long as there is enough $\Gamma^-$ present in the aqueous layer. When $\Gamma^-$ in this layer has been consumed to a low critical value, however, the reverse reaction suddenly becomes of importance and the reaction stops.

The extraction equilibrium for QI has been studied by Gustavii. He describes the total equilibrium by the equations:

$$\begin{align*}
Q_w^+ + I_w^- & \rightleftharpoons QI_s \quad [QI]_s = E_{QI}[Q^+][I^-]_w \\
QI_s & \rightleftharpoons Q_s^+ + I_s^- \quad [Q^+]_s[\Gamma^-]_s = K_{diss}[QI]_s \\
2QI_s & \rightleftharpoons QI_2s \quad [QI]_s = K_s[QI]_s^2
\end{align*}$$

with the constants $E_{QI} = 3200$

$K_{diss} = 7.6 \times 10^{-5}$ and $K_s = 6.3$.

In his calculations, the deviation from unity of the activity coefficient $\gamma_s$ in the organic layer was not taken into consideration. It was found that an introduction of the activity coefficients obtained by the equations of Debye, Hückel or Marshall and Grünwald gave rise to only minor changes in the constants.

The dimerization describes the behaviour in the high concentration range in a very satisfactory way, especially when the activity coefficients $\gamma_s$ are considered to be unity. The physical existence of this dimer can be highly questioned, however. The dimerization constant calculated by either method is so low that the lifetime of the dimer must be of the same magnitude as the contact time in molecular collisions, and the physical significance of the dimer is therefore lost.

An alternative explanation of the increased extraction in the high concentration region is a small medium effect. (A methylene chloride solution of QI is a better extraction solvent than pure methylene chloride). This medium effect becomes detectable in solutions stronger than about $10^{-5}$ M and is rather low even at high concentrations. There is thus no reason to introduce other nucleophiles than the ion pair QI and the free anion $\Gamma^-$ into the discussion.

Denoting the total concentration of QI in the organic layer by $C_{QI}$, we have in the concentration range used in the kinetic experiments

$$[QI]_s \simeq C_{QI} \text{ and } [Q^+]_s = [\Gamma^-]_s \simeq (K_{diss}C_{QI})^{1/2}$$


Assuming second order kinetics, we obtain the velocity for the formation of RI

$$\frac{d[R]}{dt} = k_{QI}[QI]_s[RCl]_s \simeq k_{QI}C_{QI}[RCl]_s$$

$$\frac{d[R]}{dt} = k_{\Gamma^-}[\Gamma^-]_s[RCl]_s \simeq k_{\Gamma^-} \frac{(K_{diss}C_{QI})^{1/2}}{\gamma_s} \times [RCl]_s$$

depending on whether the ion pair or the anion is the dominating nucleophile. Since the velocity has been found to be directly proportional to $C_{QI}$ and not to $C_{QI}^{1/2}$, we can conclude that the ion pair is the dominating nucleophile in this concentration range.

As a complement, we have also briefly studied the reaction

$$\text{RI}_s + \text{QCl}_s \rightarrow \text{RCI}_s + \text{QI}_s$$

in an homogenous methylene chloride solution. The reaction was rapid and the quenching procedure far from satisfactory. The experimental values therefore showed a considerable scattering. It was obvious, however, that the reaction was of second order with the equilibrium shifted far to the right. The velocity constant was about 200 times higher than that of the reverse reaction.

When making a comparison of the two reactions, it should be remembered that, in the presence of a water layer, QCI is extracted together with several molecules of water of solvation which may decrease the reactivity of the ion pair, whereas QI is extracted without any water of this type. The kinetic facts open the curious possibility of an excellent method to convert alkyl iodides to alkyl chlorides, as well as a good method for the reverse reaction.

**EXPERIMENTAL**

The kinetic measurements in a two-layer mixture

A carefully weighed quantity of pure tetrabutylammonium iodide was added to a 100 ml flask with a very efficient stirrer and a replaceable stopper. The flask was placed in a water thermostat at 25.0 °C. 25.00 ml of a prethermostated 0.3902 M solution of NaI in water was added, followed by 25.00 ml of a 0.400 M solution of benzyl chloride in methylene chloride. The time was taken from the moment when the last mentioned solution was added. At intervals the stirrer was stopped for a few seconds, the
layers were allowed to separate and 0.500 ml of the upper layer was withdrawn. This was added to a few ml of dilute nitric acid and the contents of Cl\(^{-}\) and I\(^{-}\) were determined by potentiometric argentimetry.

**Calculations.** Due to the difficulties in removing 0.500 ml samples accurately and rapidly, the concentration of QI in the sample was calculated in the following way: The apparent extraction constant of QI is about 4000 for all the solutions used. The concentration of Q\(^{+}\) in the aqueous layer is thus \(<10^{-4}\) M, as long as the concentration of I\(^{-}\) in the water layer is above 0.025 M. This is valid during the first 95\% of the reaction. Since the concentration of Q\(^{+}\) is low, the total concentration of halide ions in the sample is almost exactly equal to that of sodium ions, which is 0.3902 M. Assume that the volume of AgNO\(_3\), used to titrate Cl\(^{-}\) is \(a\) and that used to titrate I\(^{-}\) is \(b\). The concentration of Cl\(^{-}\) in the sample is thus

\[
[\text{Cl}^{-}]_w = \frac{a}{a+b} 	imes 0.3902
\]

Since the extraction constant of QCl is very low (about 1 under the present conditions), and the concentration of Q\(^{+}\) in the water layer is very low, the fraction of Cl\(^{-}\) present in the organic layer is very low, \(<1\%\), and can thus be neglected in the calculations. The total quantity of Cl\(^{-}\) formed is thus equal to the concentration of Cl\(^{-}\) found in the sample, multiplied by the aqueous volume from which the sample was withdrawn, plus the quantity of Cl\(^{-}\) in all samples previously taken.

Since the velocity of the reaction is proportional to the constant concentration [QI] \(_s\) of QI and to the concentration [RCl] \(_s\) of RCl, the following equation is valid

\[
[RCl]_s = [RCl]_s^0 \times e^{-k[QI]_s} t
\]

where [RCl] \(_s^0\) is the starting concentration of RCl. We can expect that the error in [RCl] \(_s\) is normally distributed. Since the reaction is followed to a high degree of conversion, the normal way of calculating the velocity constant \((k[QI]_s)\) from the linear transform \(\ln [RCl]_s = \ln [RCl]_s^0 - k[QI]_s t\) by the method of least squares should not be used. (The errors in \(\ln [RCl]_s\) are far from normally distributed). \(k[QI]_s\) was instead calculated by a least squares computer program for nonlinear regression based on normal distribution of the error in [RCl] \(_s\) and the iterative method of Gauss.\(^{4}\) This method gives both \(k[QI]_s\) and the standard error S.E. of this constant.

A typical run is given in Table 1 and a summary of 4 runs at different [QI] \(_s\) values is given in Table 2. Fig. 1 demonstrates the sudden stop in the reaction that occurs when an insufficient quantity of NaI is used.

The kinetic measurements in a homogeneous solution

A carefully weighed quantity of pure anhydrous tetrabutylammonium chloride was dissolved in methylene chloride to make a standard solution, about 0.16 molar. A second solution of the same molarity was prepared by dissolving benzyl iodide in methylene chloride. The two solutions were placed in a water thermostat at 25.0 °C. Ten ml portions of each solution were rapidly mixed. The progress of the reaction was followed by taking 1.00 ml samples which were rapidly added to 10 ml of water contained in centrifuge tubes, and the mixture was immediately vigorously shaken for one minute. The layers were then rapidly separated by centrifugation. A 5.00 ml sample of the aqueous layer was analyzed for Cl\(^{-}\) by potentiometric argentimetry. A calculation of the phase equilibria shows that less than 1\% of the Cl\(^{-}\) was present in the organic layers.

**Calculations.** Since the concentrations of the two reacting species are almost equal to the mean concentration \(A\), we obtain, according to Widequist,\(^{4}\) the following equation

\[
\frac{1}{A - [RCl]_s} = \frac{1}{A} + kt
\]

which is valid provided that the reverse reaction can be neglected. This, in fact, was found to be the case.

The errors in [RCl] \(_s\) can be expected to be normally distributed and the constants \(A\) and \(k\) were calculated by a least squares computer program for nonlinear regression considering this fact. The results are given in Tables 3 and 4.

**Preparation of alkyl chlorides from alkyl iodides.** 0.1 mol of an alkyl iodide and 0.108

\[
\text{[Table 3. The reaction of benzyl iodide with tetrabutylammonium chloride in methylene chloride [RCl] \(_s^0\) = 0.0904 M, [QCl] \(_s^0\) = 0.0814 M. Mean concentration } A = 0.0859 M.}
\]

\[
\begin{array}{ccc}
| t & [QCl]_s & [RCl]_s & [RCl]_\text{calc} \\
<table>
<thead>
<tr>
<th>M</th>
<th>M</th>
<th>M</th>
<th>M</th>
</tr>
</thead>
</table>
| 0   & 0.0814 & 0 & 0  \\
| 0.88 & 0.0700 & 0.0115 & 0.0079  \\
| 0.82 & 0.0670 & 0.0145 & 0.0154  \\
| 1.17 & 0.0610 & 0.0205 & 0.0504  \\
| 1.47 & 0.0550 & 0.0265 & 0.0241  \\
| 1.73 & 0.0530 & 0.0285 & 0.0270  \\
| 2.02 & 0.0530 & 0.0285 & 0.0300  \\
| 2.30 & 0.0485 & 0.0330 & 0.0325  \\
| 2.63 & 0.0435 & 0.0380 & 0.0353  \\
\end{array}
\]

\(k = 3.16 M^{-1} \text{ min}^{-1}\). SE(k) = 0.19 M^{-1} \text{ min}^{-1}\. A = 0.0851 M. SE(A) = 0.0016 M. [RCl] \(_\text{calc}\) is calculated from these constants.

Table 4. The reaction of benzyl iodide with tetrabutylammonium chloride in methylene chloride $[\text{RCl}]_s = [\text{QCl}]_s$.

<table>
<thead>
<tr>
<th>$t$ min</th>
<th>$[\text{QCl}]_s$ M</th>
<th>$[\text{RCl}]_s$ M</th>
<th>$[\text{RCl}]_{\text{calc}}$ M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.0833</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2.10</td>
<td>0.0532</td>
<td>0.0301</td>
<td>0.0305</td>
</tr>
<tr>
<td>3.92</td>
<td>0.0416</td>
<td>0.0417</td>
<td>0.0432</td>
</tr>
<tr>
<td>6.05</td>
<td>0.0314</td>
<td>0.0519</td>
<td>0.0521</td>
</tr>
<tr>
<td>8.02</td>
<td>0.0251</td>
<td>0.0582</td>
<td>0.0574</td>
</tr>
<tr>
<td>10.02</td>
<td>0.0211</td>
<td>0.0622</td>
<td>0.0612</td>
</tr>
</tbody>
</table>

$k = 3.28 \text{ M}^{-1} \text{ min}^{-1}$. SE($k$) = 0.102 M$^{-1}$ min$^{-1}$.

$A = 0.0835$ M. SE($A$) = 0.0012 M.

[\text{RCl}]_{\text{calc}}$ is calculated from these constants.

mol of anhydrous tetrabutylammonium chloride were mixed in a flask arranged for distillation. The mixture was heated and distilled directly from the reaction mixture, eventually at reduced pressure, so that the temperature does not exceed 140 °C. In this way over 90% of the n-alkyl chloride is obtained in a few minutes. For the preparation of butyl chloride, the distillation started at atm. pressure at ≤72 °C and was finished at 50 °C/190 Torr. For the preparation of octyl chloride, the distillation was performed at 7 Torr, and the product was collected up to 70 °C. Both products contained a small droplet of water that was readily removed. Apart from this, they were pure when tested by gas chromatography.

Preparation of iodoacet-2,6-xylidine. A mixture of 19.77 g (0.1 mol) of chloroacet-2,6-xylidine, 16.49 g (0.11 mol) of sodium iodide, and 5 g (0.014 mol) of tetrabutylammonium iodide was added to 100 ml of chlorobenzene and 50 ml of water. The resulting suspension was refluxed for 90 min. The mixture was chilled to 0 °C and the product collected by filtration, washed with cold water and cold methylene chloride yielding 26.5 g (92%) of iodoacetoxyldide. The product was pure and was readily recrystallized from 1,2-dichloroethane. The melting point was 170 °C.

REFERENCES
