A Study of Solvolyses of ortho- and para Carboxybenzyl Bromides
Using the Extended Grunwald-Winstein Equation

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Solvolyses of benzyl halides have been studied extensively. However, the reaction mechanism of the isomeric carboxybenzyl halides is not well established. Accordingly, a study of the mechanism of the isomeric carboxybenzyl bromides under solvolytic conditions is one of the subject of continuing interest.

Recently, the extended Grunwald-Winstein equation [eqn. (1)] has been applied to a very useful mechanistic tool for solvolysis reactions.2-5

\[
\log(k/k_o) = lN_T + mY_B + c \tag{1}
\]

In equation (1), \(k\) and \(k_o\) are the specific rates of solvolysis in a given solvent and in the standard solvent (80% ethanol), respectively; \(l\) is the sensitivity towards changes in solvent nucleophilicity \((N_T); m\) is the sensitivity towards changes in solvent ionizing power \((Y_B); c\) is a residual term. The equation is a very useful indicator of the extent of nucleophilic participation by the solvent, as expressed in the parameter, \(l\), which, in turn, is directly related to whether a substitution reaction is unimolecular \((S_N1)\) or bimolecular \((S_N2)\). Also, there is a general tendency for a decrease in \(m\) values as \(l\) values increase.

For \textit{para} carboxybenzyl bromide (\textit{p}-isomer, I), it is to be expected that the electron withdrawing carboxylic acid group will favor \(S_N2\) reaction, which is already known to be the favored pathway for benzyl bromide in the absence of substituents. Applying the extended Grunwald-Winstein equation [eqn. (1)] using \(N_T\) and \(Y_B\) values, one would expect an \(l\) value approaching unity and an \(m\) value in the 0.4 to 0.5 range.6 There are indications that, in 80% aqueous dioxane as solvent, the \textit{ortho} carboxybenzyl bromide (\textit{o}-isomer, II) reacts about 80 times faster than the \textit{p}-isomer(I), which suggests the possibility of an intramolecular assistance to the substitution process.6 If intramolecular assistance operates, it would be expected to operate as in eqn. (2):

\[
\text{CH}_2\text{Br}\quad \overset{\text{S_N2}}{\text{+Br}} \quad \rightarrow\quad \text{CH}_2\text{O} \quad \overset{\text{S_N1}}{\text{O}} \quad \text{O} \tag{2}
\]

If the mechanism operates according to eqn. (2), or some closely related variant, one would expect the influence of ionizing power (ion-pair-like species). If intramolecular assistance should not operate for solvolyses of \textit{o}-isomer(II), one would predict an \(l\)-value close to that operating for solvolyses of \textit{p}-isomer(I), reflecting extensive nucleophilic assistance from a solvent molecule.

In the present study, we report concerning the application of the extended Grunwald-Winstein equation [eqn. (1)] to the solvolyses of \textit{para} and \textit{ortho} carboxybenzyl bromides in wide variety of hydroxyl solvents. This is the first time that this eqn. (1) has been used as a tool in a study of possible intramolecular nucleophilic participation during solvolyses.

Results and Discussion

The specific rate constants, \(k_{obs}\), of solvolyses for \textit{p}-isomer (I) and \textit{o}-isomer(II), at 25.0 °C or 45.0 °C, in binary solvent mixtures are reported in Table 1, together with the \(N_T\) and \(Y_B\) values. The solvents consisted of ethanol (EtOH), binary mixtures of water with ethanol, methanol (MeOH), 2.2.2-trifluoroethanol (TFE) and acetone. As shown in Table 1, the \(k_{obs}\) for reaction of the \textit{o}-isomer(II) in all the solvents is solvolyzed much more rapidly than its \textit{p}-isomer(I). The high reactivity of \textit{o}-isomer(II) reverses the usual order of reactivity among isomers of this type. Andrews and co-workers5 have demonstrated that the high reactivity of the \textit{o}-isomer(II) is rationalized in terms of internal participation by a neighboring carboxylic acid group (\textit{o}-COOH). Such participation is not possible for \textit{p}-isomer(I) because of unfavorable molecular geometry.

An analysis in terms of the simple Grunwald-Winstein equation [eqn. (1) without the \(N_T\) term] to the specific rates of solvolysis of \textit{p}-isomer(I) (from Table 1) leads to an extremely poor correlation with value of 0.170 for the correlation coefficient(\(r\)). Again, analysis of the data using the extended Grunwald-Winstein equation [eqn. (1)] leads to a good linear correlation with values of 1.24 ± 0.09 for \(l\), 0.59 ± 0.05 for \(m\), 0.10 ± 0.05 for \(c\), 0.973 for the correlation coefficient, and 107 for the F-test value (Figure 1). These \(l\) and \(m\) values (or \(l/m\) ratio) are similar to those obtained to reflect the bimolecular pathway within the analyses of the solvolyses of \textit{p}-nitrobenzyl \textit{p}-toluenesulfonates96 and haloformates.5(c)

Application of the equation (1) to solvolyses of \textit{o}-isomer(II) leads to a poor correlation with values of 0.90 ± 0.14 for \(l\), 0.49 ± 0.10 for \(m\), 0.007 ± 0.14 for \(c\), 0.933 for the
Table 1. Specific rate constants \(k_{obs}(sec^{-1})\) for the solvolyses of p-carboxybenzyl bromide(I) (at 45.0 °C) and o-carboxybenzyl bromide(II) (at 25.0 °C) in binary hydroxyl solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>(10^3k_{obs}(sec^{-1}))_p</th>
<th>(10^3k_{obs}(sec^{-1}))_o</th>
<th>(N)^{1}</th>
<th>(Y_{br})</th>
</tr>
</thead>
<tbody>
<tr>
<td>100EtOH</td>
<td>0.188 ± 0.003</td>
<td>3.04 ± 0.1</td>
<td>0.37</td>
<td>-2.40</td>
</tr>
<tr>
<td>90EtOH</td>
<td>0.455 ± 0.02</td>
<td>4.92 ± 0.06</td>
<td>0.16</td>
<td>-0.84</td>
</tr>
<tr>
<td>80EtOH</td>
<td>0.752 ± 0.03^{h}</td>
<td>15.1 ± 0.2</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>70EtOH</td>
<td>1.09 ± 0.04</td>
<td>27.1 ± 0.2</td>
<td>-0.20</td>
<td>0.68</td>
</tr>
<tr>
<td>50EtOH</td>
<td>2.45 ± 0.08</td>
<td>-</td>
<td>-0.58</td>
<td>1.88</td>
</tr>
<tr>
<td>90MeOH</td>
<td>0.853 ± 0.02</td>
<td>3.93 ± 0.2</td>
<td>-0.01</td>
<td>-0.14</td>
</tr>
<tr>
<td>80MeOH</td>
<td>1.46 ± 0.01</td>
<td>10.7 ± 0.3</td>
<td>-0.06</td>
<td>0.70</td>
</tr>
<tr>
<td>50MeOH</td>
<td>3.76 ± 0.09</td>
<td>47.7 ± 0.4</td>
<td>-0.54</td>
<td>2.04</td>
</tr>
<tr>
<td>50Acetone</td>
<td>0.127 ± 0.009</td>
<td>4.25 ± 0.1</td>
<td>-0.37</td>
<td>-0.70</td>
</tr>
<tr>
<td>60Acetone</td>
<td>0.606 ± 0.02</td>
<td>25.3 ± 0.2</td>
<td>-0.52</td>
<td>1.03</td>
</tr>
<tr>
<td>50Acetone</td>
<td>1.06 ± 0.08</td>
<td>-</td>
<td>-0.7</td>
<td>1.74</td>
</tr>
<tr>
<td>97TFE</td>
<td>-</td>
<td>0.275 ± 0.03</td>
<td>-3.3</td>
<td>2.53</td>
</tr>
<tr>
<td>90TFE</td>
<td>0.0127 ± 0.002</td>
<td>0.385 ± 0.02</td>
<td>-2.55</td>
<td>2.58</td>
</tr>
<tr>
<td>70TFE</td>
<td>0.210 ± 0.01^{i}</td>
<td>11.3 ± 0.3^{3}</td>
<td>-1.98</td>
<td>2.79</td>
</tr>
<tr>
<td>50TFE</td>
<td>0.781 ± 0.03</td>
<td>-</td>
<td>-1.73</td>
<td>3.04</td>
</tr>
</tbody>
</table>

^{h}Substrate concentration of ca. 5.40 × 10^{-4} M. ^{i}Substrate concentration of ca. 5.00 × 10^{-2} M. ^{1}Volume/volume basis at 25.0 °C, except for TFE:H₂O mixtures, which are on a weight/weight basis. ^{2}Based on the specific rates of solvolysis of the S-methylidenbenzothiophenium ion, from ref. 6 and ref. 8. ^{3}Values of 1-adamantyl bromide from ref. 3 and ref. 7. ^{4}Percentage of products for the solvolysis of these substrates: p-isomer, 100%EtOH; p-carboxybenzyl ethyl ether (retention time: 44.86 min, 100%); 80%EtOH; p-carboxybenzyl ethyl ether (retention time: 44.86 min, 47.00%); p-carboxybenzyl alcohol (retention time: 71.24 min, 95.3%); o-isomer: 100%EtOH; o-carboxybenzyl ethyl ether (retention time: 41.61 min, 8.52%); phthalide (retention time: 49.11 min, 91.5%); 80%EtOH; o-carboxybenzyl ethyl ether (retention time: 41.61 min), phthaladile (retention time: 49.11 min, 97.7%), 50%EtOH, phthalide (retention time: 49.11 min, 100%). ^{5}TFE is 2,2,2-trifluoroethanol. ^{6}At 55 °C, 68 °C, and 73 °C, values of 1.87 × 10^{-3} sec^{-1}, 5.76 × 10^{-3} sec^{-1}, and 8.97 × 10^{-3} sec^{-1}, respectively, were obtained. ^{7}At 55 °C, 68 °C, and 73 °C, values of 0.602 × 10^{-5} sec^{-1}, 1.09 × 10^{-5} sec^{-1}, and 1.43 × 10^{-5} sec^{-1}, respectively, were obtained. ^{8}At 35 °C and 45 °C, values of 30.6 × 10^{-4} sec^{-1} and 44.2 × 10^{-4} sec^{-1} were obtained. ^{9}Value of 33.0 × 10^{-4} sec^{-1} at 45 °C was obtained. ^{10}Value of ΔS^f=19.6 kcal·mol^{-1} and ΔS^s= -41.3 cal·K^{-1}·mol^{-1}. ^{11}The values of the enthalpies and entropies of activation for the solvolyses of p-isomer(I) and o-isomer(II) in 80% aqueous ethanol and 70% aqueous 2,2,2-trifluoroethanol are reported in the footnotes to Table 1. These values are consistent with the finding by Andrews,9 Pribat12 and our previous study,13,14 with the very negative entropies of activation, and with the bimolecular nature of the proposed rate-determining step. From the data of ΔH^f for p-isomer(I) and o-isomer(II), it appears the energy barrier for reaction of o-isomer(II) is significantly less than p-isomer(I), and this is presumed to reflect the contribution of the o-carboxylic acid group. For reactions of p-isomer(I) and o-isomer(II), product studies were carried out in ethanol, 80% and 50% aqueous ethanol with the analyses employing gas chromatography and those results are reported in the footnotes to Table 1. The fact that the product obtained from the o-isomer(II) was identified as phthalide supports the possibility of an intramolecular participation due to assistance of the carboxyl group. From p-isomer(I), p-carboxybenzyl ethyl ether and alcohol were obtained. In conclusion, the specific rates of solvolyses of p-isomer(I) and o-isomer(II) are very well correlated by the equation (1) and (3) over a wide range of solvents, respectively. The solvolysis of p-isomer(I) (l = 1.24, m = 0.59, l/m = 2.1), where bond making (l-value) is more progressed than bond breaking (m-value), is indicated to proceed by the bimolecular pathway (associated S_2), reflecting nucleophilic assistance from a solvent molecule. The bond making (l-value) of o-isomer(II)(l/m = 1.8) is less progressed than p-isomer(I) (l/m = 2.1). Therefore, the solvolysis of o-isomer(II) is

![Figure 1](image_url)
considered to reflect the operation of both the intramolecular assistance of \( o \)-carboxylic acid group (ion-pair like species) and the nucleophilic assistance from a solvent molecule.

**Experimental Section**

\( o \)-Carboxybenzyl bromide (\( o \)-HOOC\( \text{C}_6\text{H}_4\text{CH}_2\text{Br} \)) was prepared from the corresponding \( o \)-toluic acid (Aldrich, \( o \)-HOOC\( \text{C}_6\text{H}_4\text{CH}_3 \)) according to previously published procedures.\(^{15}\) \( p \)-Carboxybenzyl bromide (Aldrich, \( p \)-HOOC\( \text{C}_6\text{H}_4\text{CH}_2\text{Br} \)) was recrystallized from benzene (Aldrich) before using. Solvents were purified and the kinetic runs carried out as previously described.\(^{13}\) All runs were performed at least in duplicate. The \( l, m \) and \( h \) values were calculated using the multiple regression analyses. The products were directly analyzed by gas chromatography as previously described.\(^{5(b)}\)

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**References**