Kinetics and mechanism of in situ bromohydroxylation of cinnamic acids by sodium bromate-sodium bisulphite reagent in aqueous acetonitrile medium

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Rates of bromohydroxylation of 4-substituted cinnamic acids with HOBr, produced in situ from sodium bromate-sodium bisulphite reagent have been studied in aqueous acetonitrile medium iodometrically. Thermodynamic parameters for the adduct formation step and the activation parameters for the first order decomposition of the adduct step have been evaluated in the temperature range 303 to 318 K and discussed. The influence of the substituents on the first order decomposition rate constant (kls · l ) of the adduct has been investigated. The corresponding bromohydrins of cinnamic acids have been identified as the reaction products.

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Various authors have studied the kinetics of bromination of cinnamic acids (CA) by molecular bromine under various conditions extensively. Most often these reactions are promoted by light through a free radical mechanism. N-Bromoacetamide (NBA) has also been reported to add to the unsaturated compounds in the presence of hydroxylic solvents like water, giving rise to bromohydrins via an ionic mechanism. The kinetics of bromohydroxylation of cinnamic acids by NBA in aqueous methanol medium has also been reported from our laboratory. Here it was shown that HOBr is generated by hydrolysis of NBA, which later reacts with the substrate. However hypobromous acid (HOBr) was found to be easily generated in situ from NaBr03 in the presence of an appropriate reducing agent such as sodium bisulphite and which was successfully used in the synthesis of several organic compounds. Also we have reported recently the kinetic and mechanistic study of oxidation of DMSO by the same reagent. It was very easy to handle this reagent in aqueous solution compared to that of the aqueous solutions of several N-halo compounds. Since the aqueous solutions of N-halo compounds are not stable, everytime they have to be prepared afresh. A systematic kinetic investigation of the bromohydroxylation of cinnamic acids by sodium bromate-sodium bisulphite reagent has not been reported in literature hitherto. Hence we thought it worthwhile to undertake the title investigation.

Experimental Section

All the chemicals used were of AR grade. Sodium bromate and sodium bisulphite used in this study were BDH grade. All the cinnamic acids used were of Fluka grade. The solvent acetonitrile used was of AnalAR grade (H2O = 0.03%) from Merck and used as such. All the aqueous solutions were prepared in doubly distilled water. The reaction between cinnamic acids and sodium bromate-sodium bisulphite reagent was studied in water-acetonitrile (60:40 v/v) mixture. In this study, aqueous solutions of NaBr03 and NaHSO3 were allowed to react first together for 2 hr to generate HOBr completely and then kinetic runs were started with cinnamic acids. The kinetics of the reaction was studied in dark coloured reaction vessels by estimating the unreacted HOBr iodometrically at regular time intervals. To see the effect of dissolved oxygen on the rates, nitrogen gas was bubbled through reaction mixture to expel dissolved oxygen and the reaction was studied. It was found that there was no effect of oxygen on rates.

For stoichiometric runs, solutions of cinnamic acid 0.74 gm (0.05 mole), 1.51 g of NaBr03 (0.1 mole) and 2.08 g of NaHSO3 (0.2 mole) in 1:2:4 molar ratio were mixed in 100 mL of water-acetonitrile mixture (60:40 v/v) and set apart for 2 to 3 days, the resulting precipitate was filtered off and washed thoroughly with water until it was free from NaBr03 and NaHSO3. The product was recrystallised from aqueous methanol, m.p. 163°C. The product was characterized based on IR as 2-bromo-3-hydroxy-3-phenyl propanoic acid (i.e the corresponding bromohydrin of CA). The m.p. also corresponded with that reported. The weight of the product obtained is 1.12 g, which accounts for 91% of the yield. The stoichiometry was found to be 1:1 (CA:HOBr) in accordance with the Eq. 1.

\[ \text{Ph} \cdot \text{CH} \cdot \text{CH} \cdot \text{COOH} + \text{HOBr} \rightarrow \text{Ph} \cdot \text{CH} \cdot \text{CH} \cdot \text{COOH} - \text{Br} \cdot \text{OH} \]
Results and Discussion

Under the conditions \([\text{HOBr}] << [\text{CA}]\) the plot of \(\log [\text{HOBr}]\) versus time was linear indicating a first order dependence in \([\text{HOBr}]\). From the slopes of such plots, pseudo-first order rate constants \((k_{obs}/s^{-1})\) have been evaluated at different initial \([\text{CA}]\). The plot of \(\log k_{obs}\) versus \(\log [\text{CA}]\) was linear with a slope equal to 0.35, indicating the fractional order dependence in \([\text{CA}]\). This indicates the formation of an intermediate adduct between \text{CA} and \text{HOBr}, which could be a four-centered cyclic encounter pair. This fact was further supported by linearity in \(1/k_{obs}\) versus \(1/[\text{CA}]\) plot with finite intercepts. This adduct is supposed to decompose in the rate determining step to yield the products. Addition of acrylonitrile to the reaction mixture did not show any polymerization, thereby ruling out the possibility of a free radical mechanism.

The rates were unaffected by added \(\text{Na}_2\text{SO}_4\) indicating that the reaction may be between two dipoles i.e. \text{CA} and \text{HOBr}. In this study \text{HOBr} has been well-established to be the only effective bromohydroxylating species. Based on the foregoing discussion, product analysis and stoichiometry, a plausible mechanism for the bromohydroxylation has been proposed. Scheme I leads to rate law Eq. 5

\[
\text{rate} = \frac{kK[\text{CA}][\text{HOBr}]}{1 + K[\text{CA}]} \quad \ldots (5)
\]

or

\[
\frac{-2.303d \log[\text{HOBr}]}{dt} = k_{\text{obsd}} = \frac{kK[\text{CA}]}{1 + K[\text{CA}]} \quad \ldots (6)
\]

where \(k_{obs}\) is the observed pseudo-first order rate constant, \(k\) the first order rate constant for the decomposition of the adduct, and \(K\) the formation constant of the adduct. Eq. 5 accounts for the first order dependence of rate in \([\text{HOBr}]\) and fractional order dependence in \([\text{CA}]\).

Taking reciprocal of Eq. 6 at constant \([\text{CA}]\), we get

\[
\frac{1}{k_{\text{obs}}} = \frac{1}{kK[\text{CA}]} + \frac{1}{k} \quad \ldots (7)
\]

A plot of \(1/k_{obs}\) versus \(1/[\text{CA}]\) is linear, the slope of which is equal to \(1/kK\) and intercept equal to \(1/k\). The ratio of intercept to slope gives the value of \(K\) and the reciprocal of intercept gives the value of \(k\).

Effect of temperature

The reaction rates of bromohydroxylation of cinnamic acids increased with increase in temperature and the values of \(K\) and \(k\) also increased with temperature (Table I). Thermodynamic parameters for the adduct formation step were evaluated (for step 3). Activation parameters for the decomposition of the adduct (for step 4) were also evaluated from Eyring plots. These results are presented in Table II. The negative \(\Delta S\) and \(\Delta S^\neq\) values could be attributed to the greater rigidity of the transition state formed. It also implies formation of an ionic transition state with an extensive charge separation, which promotes a high degree of solvation (of the transition state) and hence loss of entropy.

Isokinetic phenomena

Plot of \(\Delta H^\neq\) versus \(\Delta S^\neq\) was linear \((r = 0.9868)\) which suggests that the bromohydroxylation of all cinnamic acids occurs by an identical mechanism. Isokinetic plots for the steps 3 and 4 in Scheme I are linear with isokinetic equilibrium temperature \((\beta_\text{eq} = 322 \text{ K})\) and isokinetic activation temperature \((\beta^* = 252 \text{ K})\). The value of \(\beta_\text{eq}\) is 322 K, which is above the
Table I — Effect of temperature on $K$ and $k$ in CA–HOBr reaction. $[\text{NaBrO}_3] = 1.00 \times 10^{-3}$ mol dm$^{-3}$; $[\text{NaHSO}_3] = 2.00 \times 10^{-2}$ mol dm$^{-3}$; $[\text{CA}] = 0.01-0.04$ mol dm$^{-3}$; $\text{H}_2\text{O}: \text{CH}_3\text{CN} = 60:40$ (v/v).

<table>
<thead>
<tr>
<th>Temp (K)</th>
<th>CA</th>
<th>4-OCH$_3$ CA</th>
<th>4-CH$_3$ CA</th>
<th>4-Cl CA</th>
<th>4-NO$_2$ CA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$K$</td>
<td>$k \times 10^5$</td>
<td>$K$</td>
<td>$k \times 10^5$</td>
<td>$K$</td>
</tr>
<tr>
<td>303</td>
<td>105</td>
<td>47.6</td>
<td>156</td>
<td>64.1</td>
<td>158</td>
</tr>
<tr>
<td>308</td>
<td>132</td>
<td>52.1</td>
<td>176</td>
<td>72.5</td>
<td>180</td>
</tr>
<tr>
<td>313</td>
<td>166</td>
<td>59.5</td>
<td>199</td>
<td>79.4</td>
<td>200</td>
</tr>
<tr>
<td>318</td>
<td>200</td>
<td>66.7</td>
<td>218</td>
<td>87.7</td>
<td>230</td>
</tr>
</tbody>
</table>

Units of $K$ are dm$^3$ mol$^{-1}$; units of $k$ are s$^{-1}$; the error limits in the formation and rate constants are ±3%.

Table II — Effect of substituents on $K$, $k$, thermodynamic and activation parameters.

$[\text{NaBrO}_3] = 1.00 \times 10^{-3}$ mol dm$^{-3}$; $[\text{NaHSO}_3] = 2.00 \times 10^{-2}$ mol dm$^{-3}$; $[\text{CA}] = 0.01-0.04$ mol dm$^{-3}$; $\text{H}_2\text{O}: \text{CH}_3\text{CN} = 60:40$ (v/v), Temp = 303 K.

<table>
<thead>
<tr>
<th>Substituent</th>
<th>$\sigma$</th>
<th>$K$ (dm$^3$ mol$^{-1}$)</th>
<th>$\Delta H$ (kJ mol$^{-1}$)</th>
<th>$\Delta S$ (J K$^{-1}$ mol$^{-1}$)</th>
<th>$k \times 10^5$ (s$^{-1}$)</th>
<th>$\Delta H^*$ (kJ mol$^{-1}$)</th>
<th>$\Delta S^*$ (J K$^{-1}$ mol$^{-1}$)</th>
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<tbody>
<tr>
<td>4-OCH$_3$</td>
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<td>-261</td>
</tr>
<tr>
<td>4-CH$_3$</td>
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<td>158</td>
<td>17.3</td>
<td>-147</td>
<td>50.5</td>
<td>18.8</td>
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</tr>
<tr>
<td>H</td>
<td>0.00</td>
<td>105</td>
<td>32.3</td>
<td>-101</td>
<td>47.6</td>
<td>15.8</td>
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</tr>
<tr>
<td>4-Cl</td>
<td>0.24</td>
<td>147</td>
<td>23.6</td>
<td>-127</td>
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<td>11.8</td>
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<tr>
<td>4-NO$_2$</td>
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<td>150</td>
<td>19.0</td>
<td>-142</td>
<td>27.8</td>
<td>10.1</td>
<td>-281</td>
</tr>
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</table>

Experimental temperature range 303-318 K. This means the formation of an intermediate adduct (Step 3) is largely influenced by enthalpy changes. The value of $\beta^*$ is well below the experimental temperature range, which means the decomposition of the adduct (step 4) is largely influenced by entropy changes$^{11,12}$.

Effect of substituents

The order of reactivity of various substituted cinnamic acids was found to be as follows: 4-OCH$_3$ CA > 4-CH$_3$ CA > CA > 4-Cl CA > 4-NO$_2$ CA. The values of $K$ did not show any systematic variation on changing the substituents, hence no attempt is made to give a qualitative interpretation to those values. But the values of first order decomposition rate constants ($k$) for the adduct (step 4) varied systematically. The Hammett's plot of log $k$ versus $\sigma$ was linear with $\rho = -0.34$ at 303 K (Figure 1). A negative value of $\rho$ suggests the development of an electron deficient reaction center in the activated complex (step 3). It also indicated that electron-donating substituents on benzene ring of cinnamic acids accelerated the reaction rates, while electron-withdrawing substituents retarded the rates. The substituent effect (p) for the decomposition of the adduct decreases with temperature indicating that it is an entropy controlled process$^9$. A negative $\rho$ value (-0.34) supports the electrophilic addition reaction of HOBr to the olefinic bond of cinnamic acids.

Figure 1 — Hammett plot for the decomposition of the 4-membered cyclic intermediate (conditions are same in Table I).
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References