Kinetics and mechanism of the oxidation of some \(\alpha\)-hydroxy acids by benzyltrihlyammonium chlorochromate

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The oxidation of glycollic, lactic, malic and a few substituted mandelic acids by benzyltrihlyammonium chlorochromate (BTEACC) in dimethyl sulfoxide leads to formation of the corresponding oxoacids. The reaction is first order in BTEACC. Michaelis-Menten type of kinetics is observed with respect to the hydroxy acids. Polymerisation of acrylonitrile is not induced in this reaction. The oxidation of \(\alpha\)-deutermandelic acid shows primary kinetic isotope effect \((k_H/k_D = 5.51 \text{ at } 298 \text{ K})\). The reaction does not exhibit the solvent isotope effect. The reaction is catalysed by hydrogen ions and hydrogen ion dependence has the form: \(k = a \times b \text{ [H}^+\text{]}\). The oxidation of \(p\)-methyl mandelic acid has been studied in 19 different organic solvents. The solvent effect has been analysed using Kamlet’s and Swain’s multiparametric equations. A mechanism involving a hydride ion transfer via a triethylammonium cation is proposed.

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Pyridinium and quinolinium halochromates have long been used as mild and selective oxidizing reagents in synthetic organic chemistry\(^1\). Benzyltrihlyammonium chlorochromate (BTEACC) is one such compound used for the oxidation of benzyl alcohol\(^2\). BTEACC is a milder oxidant as compared to other halochromates like PCC and PFC. We have been interested in the kinetic and mechanistic aspects of the oxidation by complexed Cr(VI) species and several studies, including that of \(\alpha\)-hydroxy acids by halochromates have already been reported\(^3\). \(\alpha\)-Hydroxy acids may be oxidized either as alcohols, yielding the corresponding oxoacids\(^4\) or they may undergo oxidative decarboxylation to yield a ketone. There are only a few reports on the oxidation aspects using benzyltrihlyammonium chlorochromate (BTEACC) available in the literature\(^5\). In continuation of our earlier work, we now report the kinetics and mechanism of oxidation of some hydroxy acids by BTEACC in DMSO as solvent. A suitable mechanism has also been proposed.

Experimental

The hydroxy acids were commercial products of the highest purity available and were used as such. The preparation and specification of the substituted mandelic acids have been described earlier. BTEACC was prepared by earlier reported method\(^2\) and its purity was checked by an iodometric method. \(\alpha\)-Deutermandelic acid (PhCD(OH)COOH or DMA) was prepared by the reported method. Its isotopic purity, ascertained by NMR spectra, was 95±4%. Due to the non-aqueous nature of the solvent, toluene \(p\)-sulphonic acid (TsOH) was used as a source of hydrogen ions. Solvents were purified by their usual methods.

Product analyses were carried out under kinetic conditions i.e., with an excess of the reductant over BTEACC. In a typical experiment mandelic acid (7.6 g, 0.05 mol) and BTEACC (3.27 g, 0.01 mol) were dissolved in 100 ml of DMSO and allowed to stand in dark for \(=24\) h to ensure completion of the reaction. It was then treated with an excess (250 ml) of a freshly prepared saturated solution of 2,4-dinitrophenylhydrazine in 2 mol dm\(^{-3}\) HCl and kept overnight in a refrigerator. The precipitated 2,4-dinitrophenylhydrazone (DNP) was filtered off, dried, weighed, recrystallised from ethanol and weighed again. The product was identical (m. pt. and mixed m. pt.) to an authentic sample of DNP of phenylglyoxylic acid. Similar experiments with the other hydroxy acids yielded the DNP of the corresponding oxoacids in 78-88% yield, after recrystallization. The oxidation state of chromium in completely reduced reaction mixtures, determined by an iodometric method, was 3.95±0.10. The spent reaction mixture was tested with aqueous silver nitrate solution. No precipitate was formed indicating the absence of free chloride ions.

Kinetic measurements

The pseudo-first order conditions were attained by keeping a large excess \((\geq 15\) or greater\) of the hydroxy acid over BTEACC. The temperature was
kept constant to ±0.1 K. The solvent was DMSO, unless specified otherwise. The reactions were followed by monitoring the decrease in concentration of BTEACC spectrophotometrically at 370 nm for up to 80% of the reaction. No other reactant or product has any significant absorption at this wavelength. The pseudo-first order rate constants, \( k_{\text{obs}} \), were computed from the linear least square plots of \( \log[\text{BTEACC}] \) versus time. Duplicate kinetic runs showed that the rates were reproducible within ±3%. The second order rate constants, \( k_2 \), were calculated from the relation: 
\[
k_2 = \frac{k_{\text{obs}}}{[\text{hydroxy acid}]}.
\]
All experiments, other than those for studying the effect of hydrogen ions, were carried out in the absence of TsOH.

**Results and discussion**

The rate and other experimental data were obtained for all the hydroxy acids studied. Since the results were similar, only representative data are reproduced here.

The oxidation of hydroxy acids resulted in the formation of the corresponding oxoacids. Product analysis and stoichiometric determinations indicated that the overall reaction may be written as below (Eq. 1).

\[
\begin{align*}
\text{ArCH(OH)COOH} + \text{O}_2\text{CrClO} & \rightarrow \text{ArCOCOOH} + \text{H}_2\text{O} + \text{CrOCIO} \text{bteN}^+ \quad \text{(1)}
\end{align*}
\]

The reactions are of first order with respect to BTEACC. Further, the pseudo-first order rate constant, \( k_{\text{obs}} \), is independent of the initial concentration of BTEACC. The reaction rate increases with increase in the concentration of the hydroxy acid but not linearly (Table 1). A plot of \( 1/k_{\text{obs}} \) versus \( 1/[\text{hydroxy acid}] \) is linear \( (r > 0.995) \) with an intercept on the rate-ordinate. Thus, Michaelis-Menten type kinetics are observed with respect to the alcohols. This leads to the postulation of the following overall mechanism (Eqs 2 and 3) and rate law (Eq. 4).

\[
\begin{align*}
K & \quad \text{Hydroxy acid + BTEACC \rightarrow [complex]} \quad \text{(2)}
\end{align*}
\]

\[
\begin{align*}
k_2 & \quad \text{[complex] \rightarrow Products} \quad \text{(3)}
\end{align*}
\]

\[
\begin{align*}
\text{Rate} = k_2 K [\text{HA}][\text{BTEACC}] / (1 + K [\text{HA}]) \quad \text{(4)}
\end{align*}
\]

The dependence of reaction rate on the reductant concentration was studied at different temperatures and the values of \( K \) and \( k_2 \) were evaluated from the double reciprocal plots. The thermodynamic parameters of complex formation and activation parameters of decomposition of the complexes were calculated from the values of \( K \) and \( k_2 \) respectively at different temperatures (Table 2).

The oxidation of hydroxy acids, by BTEACC, in an atmosphere of nitrogen failed to induce the polymerisation of acrylonitrile. Further, addition of acrylonitrile had no effect on the rate (Table 1).

The reaction is catalysed by hydrogen ions. \( p \)-Toluene sulphonic acid (TsOH) was used as the source of hydrogen ions. The hydrogen ion dependence has the following form:

\[
k_{\text{obs}} = a + b [\text{H}^+] \quad \text{(5)}
\]

The values of \( a \) and \( b \) for \( p \)-methyl mandelic acid are \( 1.07 \pm 0.06 \times 10^5\) s\(^{-1}\) and \( 1.91 \pm 0.10 \times 10^7\) mol\(^{-1}\) dm\(^3\) s\(^{-1}\) respectively \( (r^2 = 0.9980) \).

To ascertain the importance of the cleavage of the \( C-H \) bond in the rate-determining step, the oxidation of \( \alpha \)-deuteriomandelic acid (DMA) was studied. Results showed the presence of a substantial primary kinetic isotope effect (Table 3). The value of \( k_0/k_\beta \) is 5.51 at 298 K.

The oxidation of mandelic acid was studied in 95% deuterium oxide under identical conditions. Results showed the absence of solvent isotope effect.

The rate of oxidation of mandelic acid was determined in the following nineteen organic solvents: chloroform, toluene, dichloromethane, acetonitrile, acetonitrile, THF, DMSO, tert-butyl alcohol, acetone, dioxane, DMF, dimethoxyethane, butanone, carbon disulphide, nitrobenzene, acetic acid, benzene, ethyl acetate, cyclohexane. The choice of

<table>
<thead>
<tr>
<th>Table 1 - Rate constants for the oxidation of ( p )-methyl mandelic acid by BTEACC at 288 K</th>
</tr>
</thead>
<tbody>
<tr>
<td>( 10^4 [\text{BTEACC}] ) (mol dm(^{-1}))</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>1.00</td>
</tr>
<tr>
<td>1.00</td>
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<tr>
<td>1.00</td>
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</tr>
<tr>
<td>8.00</td>
</tr>
<tr>
<td>1.00</td>
</tr>
</tbody>
</table>

\( ^* \) Contained 0.001 mol dm\(^{-3}\) acrylonitrile
Table 2 – Formation constants for the BTEACC-hydroxyacid complexes and thermodynamic parameters

<table>
<thead>
<tr>
<th>R</th>
<th>K (dm³ mol⁻¹)</th>
<th>ΔH° (kJ mol⁻¹)</th>
<th>ΔS° (J mol⁻¹ K⁻¹)</th>
<th>ΔG° (kJ mol⁻¹)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>288K</td>
<td>298K</td>
<td>308K</td>
<td>318K</td>
</tr>
<tr>
<td>H</td>
<td>6.17</td>
<td>5.23</td>
<td>4.35</td>
<td>3.40</td>
</tr>
<tr>
<td>p-F</td>
<td>6.03</td>
<td>5.26</td>
<td>4.45</td>
<td>3.55</td>
</tr>
<tr>
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<td>4.80</td>
<td>4.00</td>
<td>3.65</td>
</tr>
<tr>
<td>p-Br</td>
<td>5.63</td>
<td>4.70</td>
<td>3.92</td>
<td>3.11</td>
</tr>
<tr>
<td>p-Me</td>
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<td>5.09</td>
<td>4.21</td>
<td>3.41</td>
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<tr>
<td>p-Pr</td>
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<td>4.50</td>
<td>3.86</td>
<td>3.06</td>
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<tr>
<td>p-OMe</td>
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<td>4.92</td>
<td>4.05</td>
<td>3.33</td>
</tr>
<tr>
<td>m-Cl</td>
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<td>5.30</td>
<td>4.44</td>
<td>3.55</td>
</tr>
<tr>
<td>m-NO₂</td>
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<td>4.60</td>
<td>3.81</td>
<td>3.06</td>
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<tr>
<td>p-NO₂</td>
<td>6.27</td>
<td>5.40</td>
<td>4.55</td>
<td>3.63</td>
</tr>
<tr>
<td>GA</td>
<td>5.53</td>
<td>4.81</td>
<td>4.00</td>
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<tr>
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<tr>
<td>MLA</td>
<td>5.35</td>
<td>4.58</td>
<td>3.80</td>
<td>3.15</td>
</tr>
<tr>
<td>DMA</td>
<td>5.76</td>
<td>4.86</td>
<td>3.90</td>
<td>3.15</td>
</tr>
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</table>

Table 3 – Rate constants for the decomposition of BTEACC-hydroxyacid complexes and activation parameters

<table>
<thead>
<tr>
<th>R</th>
<th>10²kₐ (dm³ mol⁻¹ s⁻¹)</th>
<th>ΔH° (kJ mol⁻¹)</th>
<th>ΔS° (J mol⁻¹ K⁻¹)</th>
<th>ΔG° (kJ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>288K</td>
<td>298K</td>
<td>308K</td>
<td>318K</td>
</tr>
<tr>
<td>H</td>
<td>6.39</td>
<td>13.5</td>
<td>27.2</td>
<td>56.7</td>
</tr>
<tr>
<td>p-F</td>
<td>9.02</td>
<td>18.8</td>
<td>37.1</td>
<td>75.6</td>
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<td>p-Cl</td>
<td>3.60</td>
<td>8.01</td>
<td>16.2</td>
<td>34.2</td>
</tr>
<tr>
<td>p-Br</td>
<td>3.06</td>
<td>6.57</td>
<td>13.5</td>
<td>29.0</td>
</tr>
<tr>
<td>p-Me</td>
<td>28.8</td>
<td>57.6</td>
<td>108</td>
<td>198</td>
</tr>
<tr>
<td>p-Pr</td>
<td>42.3</td>
<td>49.5</td>
<td>93.6</td>
<td>171</td>
</tr>
<tr>
<td>p-OMe</td>
<td>306</td>
<td>522</td>
<td>873</td>
<td>1470</td>
</tr>
<tr>
<td>m-Cl</td>
<td>1.01</td>
<td>2.34</td>
<td>5.21</td>
<td>11.0</td>
</tr>
<tr>
<td>m-NO₂</td>
<td>0.48</td>
<td>0.47</td>
<td>1.14</td>
<td>2.90</td>
</tr>
<tr>
<td>p-NO₂</td>
<td>0.13</td>
<td>0.34</td>
<td>0.84</td>
<td>2.16</td>
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<tr>
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<td>4.14</td>
<td>7.74</td>
<td>14.0</td>
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<tr>
<td>LA</td>
<td>4.32</td>
<td>8.55</td>
<td>17.1</td>
<td>33.3</td>
</tr>
<tr>
<td>MLA</td>
<td>3.51</td>
<td>6.57</td>
<td>12.4</td>
<td>22.5</td>
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<td>DMA</td>
<td>1.11</td>
<td>2.45</td>
<td>5.13</td>
<td>11.1</td>
</tr>
<tr>
<td>kₐ/k₀</td>
<td>5.76</td>
<td>5.51</td>
<td>5.30</td>
<td>5.11</td>
</tr>
</tbody>
</table>
solvents was limited by the solubility of BTEACC and reaction with primary and secondary alcohols. There was no noticeable reaction with any of the solvents chosen.

The entropy and enthalpy of activation of the oxidation of ten substituted mandelic acids are linearly related (r² = 0.9998). The value of isokinetic temperature evaluated from this plot is 706±32 K. The correlation was tested and found genuine by Exner's criterion. The isokinetic temperature, calculated from Exner's plot of log k₂ at 288 K versus log k₂ at 318 K (r² = 0.9929) is 698±30 K. A linear isokinetic relationship is a necessary condition for the validity of linear free energy relationship, which suggests that all the hydroxy acids are oxidised by the same mechanism.

The observed H⁺ dependence suggests that reaction follows two mechanistic pathways, one acid-independent and other acid-dependent. The acid catalysis may well be attributed to a protonation of BTEACC to give stronger oxidant and electrophile.

\[
[O_2CrClO_4\text{bteN}^+] + H^+ \rightarrow [HCOC\text{OCIO}_2\text{bteN}^+] \quad \ldots \ldots \ldots (6)
\]

The rate constants of oxidation, k₂, in eighteen solvents (CS₂ was not considered, as the complete range of solvent parameters was not available) were correlated in terms of the linear solvation energy relationship (Eq. 7) of Kamlet et al.\(^\text{10}\)

\[
\log k_2 = A_0 + \pi^* + b \beta + a \alpha \quad \ldots \ldots \ldots (7)
\]

where \(\pi^*\) represents the solvent polarity, \(\beta\) the hydrogen bond acceptor basicity and \(\alpha\) is the hydrogen bond donor acidity and \(A_0\) is the intercept term. It may be mentioned here that out of the 18 solvents, 12 have a value of zero for \(\alpha\). The results of correlation analyses in terms of Eq. 7, a biparametric equation involving \(\pi^*\) and \(\beta\), and separately with \(\pi^*\) and \(\beta\) are given below (Eqs 8-11).

\[
\log k_2 = -4.24 + (1.76 \pm 0.20) \pi^* + (0.19 \pm 0.16) \beta - (0.09 \pm 0.15) \alpha \quad \ldots \ldots (8)
\]

\(R^2 = 0.8784; \text{sd} = 0.18; n = 18; \Psi = 0.24\)

\[
\log k_2 = -4.27 + (1.79 \pm 0.18) \pi^* + (0.16 \pm 0.15) \beta \quad \ldots \ldots (9)
\]

\(R^2 = 0.8754; \text{sd} = 0.18; n = 18; \Psi = 0.37\)

\[
\log k_2 = -4.23 + (1.84 \pm 0.18) \pi^* \quad \ldots \ldots (10)
\]

\(r^2 = 0.8662; \text{sd} = 0.18; n = 18; \Psi = 0.38\)

\[
\log k_2 = -3.22 + (0.48 \pm 0.39) \beta \quad \ldots \ldots (11)
\]

\(r^2 = 0.0882; \text{sd} = 0.46; n = 18; \Psi = 0.98\)

Here \(n\) is the number of data points and \(\Psi\) is the Exner's statistical parameter.

Kamlet's\(^\text{10}\) triparametric equation explains ca. 88% of the effect of solvent on oxidation. However, by Exner's criterion the correlation is not even satisfactory (cf. Eq. 8). The major contribution is of solvent polarity. This alone accounted for ca. 87% of the data. Both \(\beta\) and \(\alpha\) play relatively minor roles.

The data on the solvent effect were analysed in terms of Swain's equation\(^\text{11}\) of cation- and anion-solvating concept of the solvents also (Eq. 12).

\[
\log k_2 = aA + bB + C \quad \ldots \ldots (12)
\]

Here \(A\) represents the anion-solvating power of the solvent, \(B\) the cation-solvating power and \(C\) is the intercept. \((A + B)\) is postulated to represent the solvent polarity. The rates in different solvents were analysed in terms of (Eq. 12), separately with \(A\) and \(B\) and with \((A + B)\).

\[
\log k_2 = (0.75 \pm 0.03) A + (1.81 \pm 0.02) B - 4.45 \quad \ldots \ldots (13)
\]

\(R^2 = 0.9976; \text{sd} = 0.03; n = 19; \Psi = 0.05\)

\[
\log k_2 = 0.49(\pm 0.60) A - 3.21 \quad \ldots \ldots (14)
\]

\(r^2 = 0.0383; \text{sd} = 0.48; n = 19; \Psi = 1.00\)

\[
\log k_2 = 1.76(\pm 0.13) B - 4.21 \quad \ldots \ldots (15)
\]

\(r^2 = 0.9096; \text{sd} = 0.15; n = 19; \Psi = 0.31\)

\[
\log k_2 = 1.46+0.14 (A + B) - 4.41 \quad \ldots \ldots (16)
\]

\(r^2 = 0.8696; \text{sd} = 0.18; n = 19; \Psi = 0.37\)

The rates of oxidation of p-methylmandelic acid in different solvents showed an excellent correlation in Swain's equation (cf. 12) with the cation-solvating power playing the major role. In fact, the cation-solvation alone accounts for ca. 99% of the data. The correlation with the anion-solvating power was very poor. The solvent polarity, represented by \((A + B)\), also accounted for ca. 87% of the data. In view of the fact that solvent polarity is able to account for ca. 87% of the data, an attempt was made to correlate the rate with the relative permittivity of the solvent. However, a plot of \(\log k_2\) against the inverse of the relative permittivity was not linear \((r^2 = 0.5268; \text{sd} = 0.34; \Psi = 0.71)\).

The rate of oxidation of substituted mandelic acids correlated well with Brown's \(\sigma^*\) values\(^\text{12}\), the reaction constant being negative. The correlation with Hammett's \(\sigma^*\) values was not very significant. The large negative reaction constants and correlation with \(\sigma^*\)
values indicate a carbocationic reaction centre in the transition state.

**Mechanism**

Absence of any effect of added acrylonitrile on the reaction discounts the possibility of a one-electron oxidation, leading to the formation of free radicals. The presence of a substantial kinetic isotope effect in the oxidation of mandelic acid confirms the cleavage of the \( \alpha\)-C-H bond in the rate determining step. The large negative reaction constant together with the excellent correlation with Brown's \( \sigma^+ \) values point to a highly electron-deficient carbon centre in the transition state. The transition state, thus, approaches a carbocation in character. This is supported by the solvent effect also. Greater role played by the cation-solvating power of the solvents supported the postulation of a carbocationic transition state. Therefore, the correlation analysis of substituent and solvent effects on the oxidation of mandelic acid supports the mechanism involving a hydride-ion transfer via a chromate ester.

It has been shown that a study of the dependence of the kinetic isotope effect on temperature can be gainfully employed to resolve this problem. The data for protio- and deuteriomandelic acids, fitted to the familiar expression \( k_i/k_i = \exp[(E_i/RT)] \) show a direct correspondence with the properties of a symmetrical transition state in which the activation energy difference \( E_i \) for \( k_{1d}/k_{1h} \) is equal to the zero-point energy difference for the respective C-H and C-D bonds (\( \approx 4.5 \) kJ/mol) and the frequency factors and the entropies of activation of the respective reactions are nearly equal. Similar phenomena have been observed earlier in the oxidation of diols by BPCC and that of hydroxy acids by PFC.

Very cogent evidence against the occurrence of concerted one-step biomolecular processes by hydrogen transfer has been documented and it is evident that in the present study also the hydrogen transfer does not occur by an acyclic biomolecular process. It is well established that intrinsically concerted sigmatropic reactions, characterized by transfer of hydrogen in a cyclic transition state, are the only truly symmetrical processes involving a linear hydrogen transfer. It has also been shown that a cyclic hydride transfer, in the oxidation of alcohols by Cr(VI), involves six electrons and, being a Hückel-type system, is an allowed process. Thus the overall mechanism is proposed involving the formation of a chromate ester in a fast equilibrium and then a decomposition of the ester in a subsequent slow step via a cyclic concerted symmetrical transition state leading to the product (Scheme 1). The observed negative value of entropy of activation also supports a polar transition state.

The observed negative entropy of activation also supports this. As the charge separation takes place, the charged ends become highly solvated. This results in immobilization of a large number of solvent molecules reflected in the loss of entropy.

It is of interest to compare the mode of oxidation of hydroxy acids by PFC and BTEACC. The oxidation

\[
\begin{align*}
\text{ArC} = \text{O} + \text{H} - \text{O} - \text{H} \rightarrow \text{ArC} = \text{O} - \text{Cr} - \text{O} - \text{bteN}^+ \rightarrow \text{ArC} = \text{O} - \text{Cr} - \text{O} - \text{bteN}^+ + \text{H}_2\text{O} & \\
\text{HOOC} + \text{O} - \text{bteN}^+ \rightarrow \text{HOOC}O - \text{bteN}^+ & \\
\end{align*}
\]

**Scheme 1**
by PFC and BTEACC exhibited a similar kinetic picture, i.e., Michaelis-Menten type kinetics with respect to hydroxy acids. The rate laws, hydrogen ion dependence and kinetic isotope effect are similar in both the cases. In the oxidation by PFC and BTEACC, excellent correlations were obtained in terms of Swain's equation with the cation solvating power of the solvents playing the major role. In all the three oxidations the polar reactions are negative.

Acknowledgement

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References