Separation of polar and steric effects in the oxidation of ortho-substituted benzaldehydes by ethyl chlorocarbamate

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Kinetics of oxidation of twelve ortho-substituted benzaldehydes by ethyl chlorocarbamate (ECC) to the corresponding benzoic acids have been studied. The reaction is first order each in [aldehyde], [ECC] and [H+]. Addition of ethyl carbamate has no effect on the reaction rate. (EtOC(OH)NHCl)⁺ has been postulated as the reactive oxidizing species. The correlation of rates with single substituent parameter equations is poor. The correlation with Charton’s equation of inductive, resonance and steric parameters is satisfactory. However, excellent correlations are obtained, when Charton’s steric parameter is used along with Taft’s σ and σ² substiuent constants. The polar reaction constants have negative values. The reaction is subject to steric hindrance by the ortho-substituents. Mechanistic aspects are discussed.

The correlation analysis of rate and structure of ortho-substituted aromatic compounds is complicated because of the possible interaction of the substituent with the ortho-site through polar effects, proximity effects, hydrogen bonding etc. Attempts have been made to quantitatively separate and analyse the contribution of various parameters to the ortho-effect. Of these, Charton’s treatment is considered the best method because of its wider applicability in explaining the nature of the ortho-effect.

A kinetic study of the oxidation of meta- and para-substituted benzaldehydes by ethyl chlorocarbamate (ECC) has been reported from this laboratory. The rates of oxidation showed excellent correlation in Taft’s dual substituent-parameter (DSP) equation. In this paper, we report the kinetics of oxidation of twelve ortho-substituted benzaldehydes by ECC. The rates were correlated with various single- and multi-parameter equations.

Materials and Methods

o-Methylthio, o-cyano-, o-acetylamino-benzaldehydes and methyl o-formylbenzoate were prepared by the reported methods. Specifications and purification of other benzaldehydes were described earlier. ECC was prepared by the reported method. Acetic acid was refluxed with CrO₃ for 3 hr and then distilled.

Product analysis—Freshly distilled o-methylbenzaldehyde (0.03 mol) and ECC (0.01 mol) were made up to 100 ml in 1:1 (v/v) acetic acid-water in the presence of 0.5 mol dm⁻³ HClO₄. The reaction mixture was allowed to stand for ca. 10 hr to ensure completion of the reaction. The solution was extracted with ether (3 × 100 ml). The ether solution was extracted with a saturated solution of NaHCO₃. The NaHCO₃ extract was concentrated by evaporating the solvent at 80°C, acidified with concentrated HCl and cooled in ice to furnish the crude acid (86%), which was recrystallised from hot water to produce pure o-toluic acid (m.p. and mixed m.p.). A similar experiment with o-(methylthio)benzaldehyde resulted in the formation of o-(methylthio)benzoic acid (m.p. 166°C).

Stoichiometry—To determine the stoichiometry, the aldehyde was treated with an excess of ECC. When the reaction was complete, unreacted ECC was determined iodometrically. Several determinations, using substituted benzaldehydes, indicated a 1:1 stoichiometry.

Kinetic measurements—The pseudo-first order conditions were attained by keeping a large excess (10-fold or greater) of the benzaldehyde over ECC. The reactions were carried out at constant temperature (±0.1°C) and in flasks blackened from the outside to prevent any photochemical reaction. The reactions were followed iodometrically up to 70% of the reaction. The solvent was 1:1 (v/v) acetic acid-water. The pseudo-first order rate constant, k₀, was computed from the linear (r>0.98) plots of log[ECC] versus time. Duplicate kinetic runs showed that the rates were reproducible to within ±3%. The specific rate constant, k, was obtained by the relation: \( k = k₀/[H⁺][aldehyde] \). Preliminary
experiments showed that the reaction is not sensitive to ionic strength and hence no attempt was made to keep it constant during the experiments.

Results and Discussion

Oxidation of the substituted benzaldehydes by ECC lead to the formation of corresponding benzoic acids. The overall reaction may be represented by Eq. (1).

\[
\text{ArCHO} + \text{EtOOCNHCl} + \text{H}_2\text{O} \rightarrow \text{ArCOOH} + \text{EtOOCNH}_2 + \text{HCl} \quad \ldots (1)
\]

The reaction is first order with respect to ECC. Further, the pseudo-first order rate constant, \(k_{\text{obs}}\), does not depend on the initial [ECC]. The reaction is of first order with respect to the aldehyde also. The rate varies linearly with \([\text{H}^+]\) (Table 1). The experimental rate law, therefore, has the following form (Eq. (2))

\[
-\frac{d[\text{ECC}]}{dt} = k_{\text{obs}}[\text{aldehyde}][\text{H}^+] \quad \ldots (2)
\]

The reaction rate is not affected by added ethyl carbamate, a reaction product (Table 1). Thus, hydrolysis and/or disproportionation of ECC is not involved in the oxidation process. The linear increase in the rate with acidity led us to postulate a pre-equilibrium protonation of ECC to yield a stronger oxidant and electrophile [Eq. 3].

\[
\text{EtOOCNHCl} + \text{H}^+ \rightarrow (\text{EtOC(OH)}\text{NHCl})^+ \quad \ldots (3)
\]

The specific rate constant, \(k\), for the twelve benzaldehydes were determined at different temperatures and the activation parameters were calculated (Table 2).

A linear isokinetic relationship between log \(k\) at 303 K and 318 K \((r=0.9995, \text{slope}=0.08463 \pm 0.0081)\) for the oxidation of benzaldehyde and ortho-substituted benzaldehydes showed that all the compounds are oxidized by the same mechanism\(^1\). The rates at 303 K were analysed separately in

<table>
<thead>
<tr>
<th>Subst.</th>
<th>(10^6 k) (dm(^6) mol(^{-2}) s(^{-1}))</th>
<th>(\Delta H^*) (kJ mol(^{-1}))</th>
<th>(\Delta S^*) (J mol(^{-1}) K(^{-1}))</th>
<th>(\Delta G^*) (kJ mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>H(^*)</td>
<td>187</td>
<td>570</td>
<td>-128 \pm 3</td>
<td>95.2 \pm 2</td>
</tr>
<tr>
<td>NO(_2)</td>
<td>5.18</td>
<td>25.0</td>
<td>-84 \pm 2</td>
<td>99.4 \pm 1.1</td>
</tr>
<tr>
<td>F</td>
<td>65.6</td>
<td>212</td>
<td>-118 \pm 3</td>
<td>93.4 \pm 1.8</td>
</tr>
<tr>
<td>Cl</td>
<td>23.0</td>
<td>84.0</td>
<td>-101 \pm 2</td>
<td>95.4 \pm 2.0</td>
</tr>
<tr>
<td>Br</td>
<td>16.3</td>
<td>67.2</td>
<td>-100 \pm 2</td>
<td>96.1 \pm 1.4</td>
</tr>
<tr>
<td>I</td>
<td>12.7</td>
<td>51.6</td>
<td>-102 \pm 2</td>
<td>96.1 \pm 1.4</td>
</tr>
<tr>
<td>OMe</td>
<td>382</td>
<td>937</td>
<td>-163 \pm 2</td>
<td>83.4 \pm 0.7</td>
</tr>
<tr>
<td>Me</td>
<td>113</td>
<td>355</td>
<td>-128 \pm 1</td>
<td>88.7 \pm 0.3</td>
</tr>
<tr>
<td>NHCOMe</td>
<td>103</td>
<td>302</td>
<td>-136 \pm 4</td>
<td>88.5 \pm 2.0</td>
</tr>
<tr>
<td>SME</td>
<td>88.8</td>
<td>267</td>
<td>-141 \pm 4</td>
<td>88.5 \pm 1.3</td>
</tr>
<tr>
<td>COOMe</td>
<td>13.1</td>
<td>55.1</td>
<td>-97 \pm 3</td>
<td>96.2 \pm 1.7</td>
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<tr>
<td>CN</td>
<td>6.58</td>
<td>31.1</td>
<td>-77 \pm 2</td>
<td>99.3 \pm 2.8</td>
</tr>
<tr>
<td>CF(_3)</td>
<td>3.19</td>
<td>17.1</td>
<td>-67 \pm 2</td>
<td>102 \pm 3</td>
</tr>
</tbody>
</table>

*Date from Ref. 6
terms of Taft's polar and steric parameter equations. The results are expressed as Eqs (4) and (5). The values of $\sigma_0$ and $E_s$ were those given by Charton$^2$ and Jones$^4$.

$$\log k = -1.63 (\pm 0.35) \sigma_0 - 4.14 \quad \ldots (4)$$
$$r^2 = 0.7841; sd = 0.32; n = 8$$

$$\log k = 0.62 (\pm 0.28) E_s - 3.90 \quad \ldots (5)$$
$$r^2 = 0.3485; sd = 0.58; n = 11$$

Here $r^2$ is the coefficient of determination and represents the fraction of the data explained by the regression; sd is standard deviation and $n$ is the number of data points. The rates of NHCOMe and COOMe compounds were not considered for Eq. (5) and those of the NHCOMe, COOMe, CF₃, CN, and SMe were not considered for Eq. (4), since the substituent constants were not available. The results of the correlation analysis showed that the observed reactivity of ortho-substituted benzaldehydes towards ECC was not compatible with either the size of the substituents or their Taft's polar substituent constant.

Since the single substituent-parameter equations failed to yield satisfactory correlations, the rate data were analysed using Charton's method$^4$. The rate constants were correlated in terms of Eqs (6) and (7). In Eqs (6) and (7), $\sigma_i$, $\sigma_R$, and $\nu$ represent inductive, resonance and steric substituent constants respectively and values used were those compiled by Aslam et al.$^5$; $h$ is the intercept term.

The results of the analysis of the rate data 303 K in terms of Eq. (6) are given in Eq. (8).

$$\log k_{ortho} = \alpha_{\sigma_i} + \beta_{\sigma_R} + h \quad \ldots (6)$$

$$\log k_{ortho} = \alpha_{\sigma_i} + \beta \sigma_R + \phi \nu + h \quad \ldots (7)$$

$$\log k = -1.97 (\pm 0.37) \sigma_i - 1.86 (\pm 0.32) \sigma_R - 4.09 \quad \ldots (8)$$

$$r^2 = 0.8725; sd = 0.26; n = 13$$

In multivariate linear regression using Eq. (6), the coefficient of determination is poor and the standard deviation is high. The absence of a significance correlation with Eq. (6) leads to the conclusion that the electric effects alone are not sufficient to account for the observed ortho-substituent effect in this reaction.

The correlation with Eq. (7) was performed using the rate data obtained at 303 K, 308 K, 313 K, and 318 K, assuming both planar and orthogonal conformations for $\sigma$-NO₂ and $\sigma$-COOMe groups. It was observed that the correlation is better with the orthogonal conformations of both $\sigma$-NO₂ and $\sigma$-COOMe groups. The coefficient of determination, $R^2$, varied between 0.85 to 0.96, and the standard deviation ranged from 0.15 to 0.28. The correlation obtained at 303 K is given in Eq. (9).

$$\log k = -1.81 (\pm 0.22) \sigma_i - 1.84 (\pm 0.18) \sigma_R - 0.81 (\pm 0.18) \nu - 3.73 \quad \ldots (9)$$

$$R^2 = 0.9612; sd = 0.15; n = 13$$

Thus the correlation is just satisfactory and not even good.

It may be recalled that the rates of oxidation of para-substituted benzaldehydes$^6$ showed excellent correlations with Taft's $\sigma_i$ and $\sigma_R$ substituent constants. Therefore, the rates of oxidation of the ortho-substituted benzaldehydes were correlated in a triparametric equation using Taft's $\sigma_i$ and $\sigma_R$ along with Charton's steric parameter, $\nu$. The values of Taft's $\sigma_i$ or $\sigma_R$ were those given by Ehrenson et al.$^5$ except that of $\sigma_R$ for the methylthio group. The value of $\sigma_R$ for the methylthio group as $-0.66$ was taken from our earlier report$^{16}$. The series of ortho-substituted benzaldehydes meet the minimal basic requirements of substituents for analysis by Taft's DSP equation$^{17}$. The behaviour of $\sigma$-NO₂ and $\sigma$-COOMe was consistent with their orthogonal conformations. The results, recorded in Table 3, showed that the reactivity of the ortho-substituted benzaldehydes correlate very well with the triparametric equation (Table 3).

The significance of the correlation was tested by

<table>
<thead>
<tr>
<th>Temp./K</th>
<th>$\rho_i$</th>
<th>$\rho_R$</th>
<th>$\phi$</th>
<th>$R^2$</th>
<th>sd</th>
<th>$P_R$</th>
<th>$P_S$</th>
</tr>
</thead>
<tbody>
<tr>
<td>303</td>
<td>$-1.58$</td>
<td>$-1.10$</td>
<td>$-1.06$</td>
<td>0.9999</td>
<td>0.004</td>
<td>41.4</td>
<td>28.3</td>
</tr>
<tr>
<td></td>
<td>($\pm 0.01$)</td>
<td>($\pm 0.01$)</td>
<td>($\pm 0.01$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>308</td>
<td>$-1.54$</td>
<td>$-1.05$</td>
<td>$-1.00$</td>
<td>0.9994</td>
<td>0.014</td>
<td>35.6</td>
<td>27.9</td>
</tr>
<tr>
<td></td>
<td>($\pm 0.04$)</td>
<td>($\pm 0.04$)</td>
<td>($\pm 0.04$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>313</td>
<td>$-1.52$</td>
<td>$-1.01$</td>
<td>$-0.94$</td>
<td>0.9978</td>
<td>0.031</td>
<td>39.9</td>
<td>27.1</td>
</tr>
<tr>
<td></td>
<td>($\pm 0.05$)</td>
<td>($\pm 0.03$)</td>
<td>($\pm 0.04$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>318</td>
<td>$-1.37$</td>
<td>$-0.90$</td>
<td>$-0.92$</td>
<td>0.9966</td>
<td>0.012</td>
<td>33.7</td>
<td>28.8</td>
</tr>
<tr>
<td></td>
<td>($\pm 0.01$)</td>
<td>($\pm 0.01$)</td>
<td>($\pm 0.01$)</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
means of an F-test. The confidence level of the F-test is > 99.9%. The confidence level for the significant of \( \rho_1 \), \( \rho_2 \) and \( \phi \) terms was obtained by a Student's \( t \)-test. The confidence level of the \( t \)-test is > 99.9%, indicating the operation of significant inductive, resonance and steric effects.

To test the significance of the three substituent constants, multiple linear regression analysis were carried out with Taft's \( \sigma_1 \) and \( \sigma_2 \), Taft's \( \sigma_R \) and \( \phi \), and with \( \sigma_1 \) and \( \phi \). The absence of significant correlation [Eqs (10)-(12)] showed that all the three \( \sigma \) and \( \sigma_R + \phi \) substituent constants are significant.

\[
\log k = -1.84 (\pm 0.40) \sigma_1 - 0.99 (0.21) \sigma_R^+ - 4.15
\]

\[
R^2 = 0.8533; \text{sd} = 0.27; n = 13
\]

\[
\log k = -1.31 (\pm 0.25) \sigma_R^2 - 1.35 (\pm 0.40) \phi - 4.19
\]

\[
R^2 = 0.7845; \text{sd} = 0.33; n = 13
\]

\[
\log k = -2.13 (\pm 0.66) \sigma_1 - 0.79 (\pm 0.55) \phi - 3.36
\]

\[
R^2 = 0.5974; \text{sd} = 0.45; n = 13
\]

There is no significant linearity between Taft's \( \sigma_1 \) and \( \phi \), \( \sigma_2 \) and \( \phi \), and between Taft's \( \sigma_1 \) and \( \sigma_R \) values \((R^2 = 0.1418, 0.1509\) and \(0.0546\) respectively) for the thirteen substituents.

The regression coefficients of \( \sigma_1 \) and \( \sigma_R \) terms are negative indicating that the electron-releasing groups accelerate the reaction and electron-withdrawing groups retard it. Similar results were obtained in the oxidation of \( \text{para-} \) and \( \text{meta-} \) substituted benzaldehydes also. The negative regression coefficient for the steric term indicates that the reaction is subject to steric hindrance by the \text{ortho-} substituents. The contribution \( P_R \) of the resonance effect to the total polar effect was calculated by Eq. (13).

\[
P_R = \frac{100 \times |\rho_R|}{|\rho_1| + |\rho_R|}
\]

The contribution of the steric parameter\( P_R \) to the total effect of the substituents, \( P_R \), was determined using Eq. (14).

\[
P_R = \frac{100 \times |\phi|}{|\rho_1| + |\rho_R| + |\phi|}
\]

The values of \( P_R \) and \( P_S \) are also recorded in Table 3. The value of \( P_R \) is \( \approx 40\% \). The value of \( P_R \) for the oxidation of \( \text{para-} \) substituted benzaldehydes is \( \approx 66\% \). This shows that the balance of inductive and resonance effects is different for the \text{ortho-} and \text{para-} positions, resonance effects being less pronounced in the former case. This may be due to the twisting away of the aldehyde group from the plane of the benzene ring. The value of \( P_S \) shows that the steric effect is considerable in this reaction.

The magnitude of all the reaction constants decreases with an increase in the temperature. This points to a decrease in the selectivity at higher temperatures. Out of the two polar effects, the decrease in the resonance effect is proportionately more. This is reflected in a gradual decrease in the value of \( P_R \). The contribution of the steric factor to the total effect of the \text{ortho-} substituent remains nearly constant over the temperature range.

The large negative polar reaction constants, a correlation involving \( \sigma_R \) and a substantial deuterium isotope effect observed \((k_d/k_0 = 5.2 \pm 0.1)\) in the oxidation of benzaldehyde point to a transition state in which the positive charge is highly localized on the aldehydic carbon atom. The transition state thus approaches a carbocation in nature. Therefore, a mechanism involving transfer of hydride ion from the aldehyde to the oxidant, in the rate-determining step, is proposed. The presence of an \text{ortho-} substituent hinders the approach of the oxidizing reagent to the aldehydic group. This causes the steric retardation in the reaction.

\[
\begin{align*}
&\text{Ar-}C\text{=H}+\text{Cl}^- \rightarrow \text{Ar-Cl}^-+\text{H}^+ \\
&\text{Ar-}C\text{=H}+\text{Cl}^- \rightarrow \text{Ar-Cl}^-+\text{H}^+ \\
&\text{Ar-}C\text{=H}+\text{Cl}^- \rightarrow \text{Ar-Cl}^-+\text{H}^+ \\
&\text{Ar-}C\text{=H}+\text{Cl}^- \rightarrow \text{Ar-Cl}^-+\text{H}^+
\end{align*}
\]

\[
\begin{align*}
&\text{Ar-C=O} + \text{H}^- \text{C(OH)}\text{OEt} \rightarrow \text{Ar-C=O} + \text{H}^- \text{C(OH)}\text{OEt} \rightarrow \text{Ar-C=O} + \text{H}^- \text{C(OH)}\text{OEt} \rightarrow \text{Ar-C=O} + \text{H}^- \text{C(OH)}\text{OEt} \\
&\text{Ar-C=O} + \text{H}^- \text{C(OH)}\text{OEt} \rightarrow \text{Ar-C=O} + \text{H}^- \text{C(OH)}\text{OEt} \rightarrow \text{Ar-C=O} + \text{H}^- \text{C(OH)}\text{OEt} \rightarrow \text{Ar-C=O} + \text{H}^- \text{C(OH)}\text{OEt}
\end{align*}
\]

\[
\begin{align*}
&P_R = \frac{100 \times |\rho_R|}{|\rho_1| + |\rho_R|}
\end{align*}
\]

\[
\begin{align*}
P_R = \frac{100 \times |\phi|}{|\rho_1| + |\rho_R| + |\phi|}
\end{align*}
\]

Acknowledgement

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References

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13 Exner O, Prog phys org Chem, 10 (1973) 1093.