Ortho Effect in the Kinetics of Boyland-Sims Oxidation of Aniline

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The influence of diverse ortho-substituents in the oxidation of aniline by peroxydisulphate ion in aqueous base has been explained in terms of polar and steric factors. The greater importance of the polar effects over the steric factors in the present reaction series, in general, is brought to light. A good Hammett correlation exists between log \( k \) and \( \sigma \) (Taft's substituent constant) establishing the mechanism of the Boyland-Sims oxidation, viz. the initial attack in the reaction is at the amine nitrogen and it is also the rate limiting step.

**Materials and Methods**

The various ortho-substituted anilines (BDH/Flu've) were purified either by distillation or by recrystallization.

The kinetic runs were carried out in aq. t-BuOH (40:60, v/v) and the unused peroxydisulphate was estimated by the iodometric procedure due to Kolthoff and Carr, with the difference that the aliquots of the reaction mixture were run into glacial acetic acid instead of a mineral acid.

A knowledge of the \( pK_a \) values of the aromatic amines is necessary for the present investigation, since the \( pK_a \) could be expected to be an indication of the nucleophilicity of the amine nitrogen towards peroxydisulphate. The \( pK_a \) values of aniline, \( o\)-fluoro-, \( o\)-chloro-, \( o\)-bromo- and \( o\)-iodo-anilines, \( o\)-aminobenzoic acid, \( o\)-aminocetophenone, \( o\)-nitroaniline, \( o\)-anisidine and \( o\)-phenetidine in 100% water are known\(^7\) (Table 1).

The \( pK_a \) values of a few compounds like \( o\)-toluidine, \( o\)-isopropylaniline and 2,6-disopropylaniline were determined by potentiometric titration and the values are 3-50, 3-15 and 2-80 respectively.

**Results and Discussion**

A wide variety of anilines with both electron-releasing and electron-withdrawing groups at the 2 and/or 6 position were taken for the present investigation. Aqueous t-butanol was chosen to keep the solvent oxidation at a minimum in a few slow reactions, while its high percentage in the mixture was to obviate solubility difficulties with some of the substrates.

Since stoichiometric determinations show that reasonable yields of the product (the sulphate ester) are obtained, only if the amine is in large excess over the peroxydisulphate, the \([\text{amine}] : [\text{S}_2\text{O}_8^{2-}]\) ratio was kept at least 10:1. Under this condition, it has been already shown\(^5\) in a number of organic bases that the reaction is first order with respect to the peroxydisulphate as well as the amine, i.e. rate = \( k[\text{amine}] [\text{S}_2\text{O}_8^{2-}]\). The second order rate constant \( k \) for each ortho-substituted aniline in the present study (Table 2) was calculated by dividing the pseudo-first order constant \( k_1 \) for the disappearance of \( S_2O_8^{2-} \) by \([\text{amine}]\).

The \( pK_a \) values indicate that all the orthoalkyl groups decrease the basic strength of aniline and that the bulkier the group, the less is the basicity. The trend in the relative reactivities of these anilines is, however, not in this direction, though we may normally expect a correlation between the \( pK_a \) values and the reactivities, the reaction being an electrophilic attack at the amine nitrogen. Thus both \( o\)-toluidine and \( o\)-ethylaniline are more reactive than aniline; \( o\)-isopropylaniline is less reactive than the above ortho compounds and is nearly as reactive as aniline.

<table>
<thead>
<tr>
<th>Amine</th>
<th>( pK_a )</th>
<th>Amine</th>
<th>( pK_a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aniline</td>
<td>4·60</td>
<td>( o)-Aminobenzoic acid</td>
<td>2·04</td>
</tr>
<tr>
<td>( o)-Fluoroaniline</td>
<td>2·96</td>
<td>( o)-Aminocetophenone</td>
<td>2·16</td>
</tr>
<tr>
<td>( o)-Chloroaniline</td>
<td>2·62</td>
<td>( o)-Nitroaniline</td>
<td>-0·280</td>
</tr>
<tr>
<td>( o)-Bromoaniline</td>
<td>2·60</td>
<td>( o)-Anisidine</td>
<td>4·49</td>
</tr>
<tr>
<td>( o)-Iodoaniline</td>
<td>2·60</td>
<td>( o)-Phenetidine</td>
<td>4·47</td>
</tr>
</tbody>
</table>

It has been confirmed that the same trend in the \( pK_a \) values of the above amines is followed in 40% t-BuOH-60%\( H_2O \) (v/v) mixture also, which is the reaction condition.

**Table 1 — \( pK_a \) Values of the Various Amines in Water**

[Data from references 9, 10]
as aniline, while 2,6-diisopropylaniline is significantly more reactive than the parent compound. This order of reactivity can be explained on the basis of the following factors:

(i) Polar effects — The +I and hyperconjugative effects of the ortho-alkyl groups will increase the reactivity of the substrate.

(ii) Steric effect in the free base (i.e. substrate) — This effect, in the form of steric inhibition of resonance, will tend to increase the reactivity of the substrate. But this is not usually significant, as shown by Brown and McDaniel in explaining the basicities of o-alkylanilines. Wepster have also drawn the same conclusion on the basis of spectroscopic evidence.

(iii) Steric hindrance at the reaction site — This effect in the transition complex will obviously retard the reaction rate. The situation here may be compared to the F-strain that Brown refers to in an acid-base reaction. According to Wepster, if the reference acid is a simple protonic one, without any bulky group, the F-strain in the conjugate acid may not be appreciable and yet the base may be weak due to steric hindrance to solvation of the conjugate acid.

In the light of the factors (i-iii) the relative reactivities of the various anilines towards $\text{S}_2\text{O}_8^{2-}$ can now be reviewed. The enhanced reactivities of o-methyl- and o-ethyl-anilines over aniline are due to the +I and hyperconjugative effects of the alkyl groups, any steric effect being less important. That o-isopropylaniline is less reactive than the o-methyl- or o-ethyl-aniline and yet nearly as reactive as aniline itself indicates the simultaneous operation of polar effects in the free base and the steric hindrance to solvation of the activated complex. In the 2,6-diisopropylaniline, the rate retarding steric factor is more than compensated by the two rate enhancing factors, viz. the polar effects as well as the steric inhibition of resonance in the free base.

All ortho-halogen substituted anilines are less reactive than aniline and the reactivity decreases from F to I. The decrease is not gradual, as seen from the nearly equal reactivities of the bromo, and the iodo-anilines. Here again we have the combined operation of several factors: (a) The +I effect of the ortho-halogen, tending to decrease the reactivity, decreases from F to I; (b) the hydrogen bonding between the amino group and the ortho-halogen tending to increase the reactivity, has its decreasing order of influence from F to I; and (c) the steric inhibition of resonance in the free base, which is very significant in the case of the bulky iodine atom tending to increase the reactivity, possibly explains why the decreasing trend of reactivity stops at bromine. The order of reactivities of these halogen compounds is also reflected in their $\text{pK}_a$ values.

Anisidine and phenetidine are less basic than aniline (Table 1). There are two opposing polar effects here, viz. —I and +M effects of the alkoxy groups. According to Ingold, the —I effect of the ortho-alkoxy group usually outweighs the +M effect and hence one would expect these compounds to be less reactive than aniline. However it is not so. A possible reason for this lies in the operation of the ‘alpha-effect’ studied and systematized by Edwards. Though the alkoxyl group is not at a position alpha to the amine nitrogen, there is a possible transmission of the alpha-effect of the alkoxyl group, according to Edwards, from the para-position to the reaction site through conjugation.

The considerably diminished reactivity of o-nitroaniline can be attributed to the powerful —I and —M effects of the NO₂ group from the ortho-position. There is an additional rate-retarding influence due to resonance stabilization through chelation between the NO₂ and the NH₂ groups.
The powerful electron-withdrawing influence \((-I, -M)\) of the acetyl group from the ortho position in \(\alpha\)-aminobenzophenone is responsible for the lowered reactivity of this compound.

The reactivity of \(\alpha\)-aminobenzoic acid is only slightly less than that of aniline. Since the medium for the present reaction series is 0.25N NaOH, this substrate will be present in the form of the carboxylate ion, which does not possess any appreciable electron-withdrawing influence, in contrast to free COOH group.

One can thus conclude that for a majority of the reactions in the present series, the relative rates are primarily determined by the polar effects of the ortho-substituents and not to any appreciable degree by steric factors. This is also in accordance with Taft's overall observations on the ionization constants of ortho-substituted anilines and benzoic acids\(^{15,16}\). A fairly linear plot between \(\log k_2\) and \(\sigma_{\text{ortho}}\) (Taft's substituent constant) is obtained (Fig. 1) the slope \(p\) being \(-1.48\) (\(c.c = 0.95\)), which is nearly the same as that obtained for the \(\text{S}_2\text{O}_8^2-\) oxidation of various anilines with substituents in all positions\(^8\) and also of substituted aminopyridines\(^9\). This is in accordance with the mechanism proposed for the Boyland-Sims oxidation, namely that the initial rate limiting attack is at the amine nitrogen by the electrophilic centre of the peroxydisulphate ion.

References