Kinetics of Peroxodisulphate Oxidation of *ortho*-Substituted *N,N*-Dimethylanilines, and the Mechanism of Boyland–Sims Oxidation

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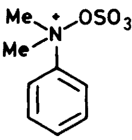
The kinetics of oxidation of some *ortho*-substituted *N,N*-dimethylanilines by peroxodisulphate have been studied in 50% (v/v) aqueous ethanol containing 0.025 mol dm^{-3} phosphate buffer (pH 7). The reaction is second-order overall, and first-order in each reactant. The rate is not influenced by the presence of the free-radical inhibitor allyl acetate. An increase in the polarity of the medium enhances the rate. The reactivities of *ortho*-substituted anilines lie in the order *o*-H > Me ~ MeO > F > Br > Cl > NO_2. Multiple regression analysis of the rate data reveals that the rate is susceptible to significant electronic and steric effects. All these observations are rationalised on the basis of attack of the oxidant at the *ipso*-position of the amine. Correlation analysis of reactivity data from the literature also indicates that the mechanism involves *ipso*-attack and not attack on nitrogen.

The reaction between aromatic amines and peroxodisulphate, (the Boyland–Sims oxidation) gives *ortho*-aminoaryl sulphates.[1,2] On the basis of substituent effects on the rates of oxidation of substituted anilines, attack of the oxidant at the *ortho*-carbon atom was excluded and a mechanism involving the electrophilic attack of the peroxodisulphate ion on the amine nitrogen was proposed.[2-4] The resulting intermediate arylhydroxylamine *O*-sulphonate was assumed to rearrange to the product.

Recent studies by Behrman[5] and by us[6] on substituent effects in the peroxodisulphate oxidation of *N,N*-dimethylanilines, however, have demonstrated *ipso*-attack. This suggestion also finds support in the observation[7] that the arylhydroxylamine *O*-sulphonate (1) did not rearrange to the *ortho*-sulphate under Boyland–Sims conditions. Here we report a novel approach to elucidation of the mechanism of the Boyland–Sims oxidation, by multiple regression analysis of the rate data obtained in the peroxodisulphate oxidation of *ortho*-substituted *N,N*-dimethylanilines. One would expect that peroxodisulphate oxidations of *N,N*-dimethylanilines and anilines would follow the same mechanism; therefore rate data reported in the literature[3] for the Boyland–Sims oxidation of substituted anilines were also analysed.



(1)

Results and Discussion

The rates of oxidation were measured at various initial concentrations of *N,N*-dimethylaniline and peroxodisulphate (PS) at pH 7. The plots of log [PS] *vs.* time are linear (*e.g.* Figure A), indicating that the reaction is first-order in the oxidant. The plot of pseudo-first-order rate constants (k_1) *vs.* [amine] affords a good straight line (Figure B; $r = 0.999$) passing through the origin.

The reaction with [PS] ≫ [amine] was studied by following the decrease in intensity (I) of the u.v. absorption at 250 nm. The plots of log $(I_t - I_\infty)$ *vs.* time are linear (*e.g.* Figure C), showing that the reaction is first-order in *N,N*-dimethylaniline. The linearity of the plot of pseudo-first-order rate constants (k_1) *vs.* [PS], passing through the origin (Figure D), also demonstrates the overall second-order nature of the reaction and the first-order dependence on [PS].

The rate of the reaction is not influenced by the addition of allyl acetate, as evident from the second-order rate constants: $2.36 \pm 0.11 \times 10^{-2}$ and $2.25 \pm 0.13 \times 10^{-2}$ in the absence and presence of allyl acetate (0.05 mol dm^{-3}), respectively.

The observation of (i) overall second-order kinetics, first-order in each substrate, (ii) a low activation energy and an appreciable negative entropy of activation, and (iii) the lack of effect of a radical trap on the rate are in agreement with the criteria suggested by Behrman and Edwards[8] for non-radical reactions of peroxides.

In order to demonstrate the effect of polarity of the medium, the oxidation of *N,N*-dimethylaniline by peroxodisulphate was studied in aqueous alcohols (pH 7) of various dielectric constants. The data in Table 1 clearly reveal that the rate increases with increase in the polarity of the medium, and lead to the inference that the transition state involves increased charge separation relative to the ground state, suggesting a polar mechanism. This effect of polarity has also been observed with some *meta*- and *para*-substituted *N,N*-dimethylanilines (Table 1).

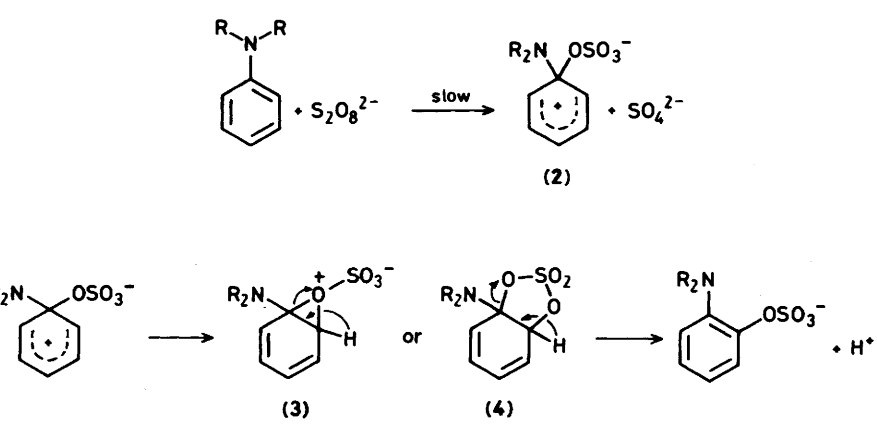
The product of the peroxodisulphate oxidation of *N,N*-dimethylaniline, obtained in 55—60% yield, was analysed as reported in the literature,[3] and found to be *ortho-N,N*-dimethylaminophenyl sulphate. However, *ca.* 40% of the total product was not characterised.

The second-order rate constants for the oxidation of *ortho*-substituted *N,N*-dimethylanilines by peroxodisulphate at 35, 40, and 45 °C and the activation parameters are listed in Table 2. The data reveal that all the *ortho*-substituted *N,N*-dimethylanilines are less reactive than the unsubstituted compound; the order of reactivity is *o*-H > Me ~ MeO > F > Br > Cl > NO_2.

With a view to understanding the contributions of inductive, resonance, and steric effects to the *ortho*-effect, the rate data have been analysed employing the substituent parameters (σ_I,[9] $\sigma_R{}^{\circ}$,[9] σ_R,[9] $\sigma_R{}^{+}$,[9] and v[10]) in the extended Hammett equation[11] in the form (1). The best fit is observed between the rate data and

$$\log k = \alpha\sigma_I + \beta\sigma_R + \varphi v + h \qquad (1)$$

σ_I, σ_R, and v, with the assumption that the nitro group is in an orthogonal orientation. The results are expressed in equation (2). This correlation is justified by the >99% confidence level of



(R = Me or H)

Scheme. Mechanism of peroxodisulphate oxidation of anilines

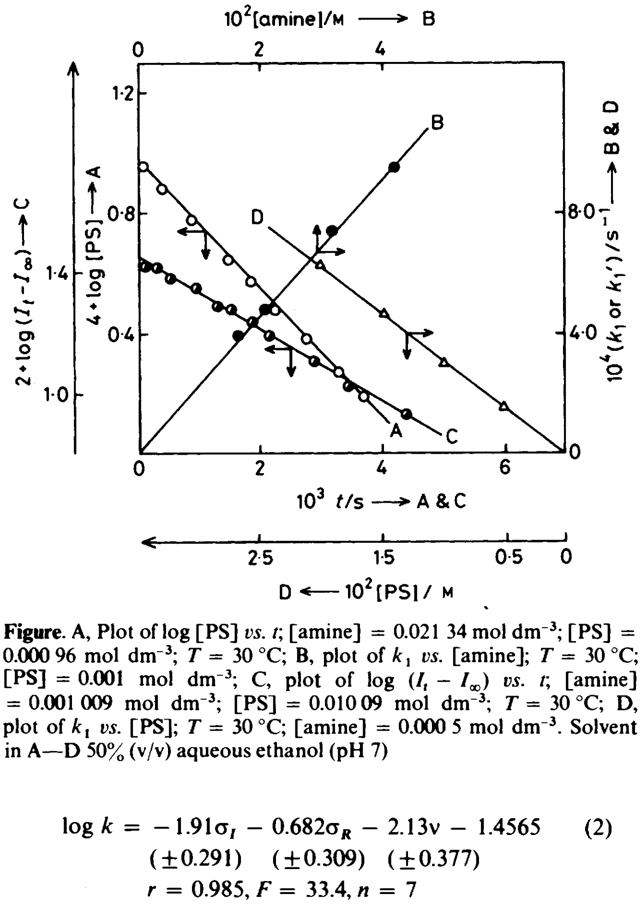


Figure. A, Plot of log [PS] *vs.* *t*; [amine] = 0.021 34 mol dm^{-3}; [PS] = 0.000 96 mol dm^{-3}; T = 30 °C; B, plot of k_1 *vs.* [amine]; T = 30 °C; [PS] = 0.001 mol dm^{-3}; C, plot of log ($I_t - I_\infty$) *vs.* *t*; [amine] = 0.001 009 mol dm^{-3}; [PS] = 0.010 09 mol dm^{-3}; T = 30 °C; D, plot of k_1 *vs.* [PS]; T = 30 °C; [amine] = 0.000 5 mol dm^{-3}. Solvent in A—D 50% (v/v) aqueous ethanol (pH 7)

$$\begin{aligned} \log k = -1.91\sigma_I - 0.682\sigma_R &- 2.13v - 1.4565 \qquad (2) \\ (\pm 0.291) \quad (\pm 0.309) &\quad (\pm 0.377) \\ r = 0.985, F = 33.4, &\, n = 7 \end{aligned}$$

the F test. The regression coefficients α, β, and φ are at >99%, <90%, and >98% confidence levels of Student's T test respectively.

The negative signs of α,β, and φ indicate that the reaction is (i) accelerated by the presence of electron-releasing substituents and (ii) retarded by an increase in steric crowding around the reaction site. The rate-retarding steric effect can be accounted for by *ipso*-attack, as the *ortho*-substituent is in close proximity to the *ipso*-carbon atom. If the attack were, however, to occur at the nitrogen atom, the *ortho*-substituent would be expected to enhance the rate of oxidation, as the steric inhibition of resonance would increase the electron density on the nitrogen atom, leading to a positive φ value. Behrman[5] has explained the low reactivities of 2-methyl-4-chloro-, 2-methyl-3-chloro-, 2,4-dimethyl-, and 2,3-dimethyl-*N*,*N*-dimethylanilines relative to *N*,*N*-dimethylaniline on this basis.

Mechanism.—The second-order kinetics, the absence of rate inhibition of addition of a free-radical inhibitor, the dependence of rate on the polarity of the medium, the effects of substituents on the rates of *meta*- and *para*-substituted *N*,*N*-dimethylanilines,[6] the results of correlation analysis of the rate data of *ortho*-substituted *N*,*N*-dimethylanilines, and the product formed in the reaction (*ortho*-*N*,*N*-dimethylaminoaryl sulphate) are all in accordance with a mechanism involving *ipso*-attack (Scheme). The intermediate (**2**) may rearrange to the *ortho*-sulphate through the further intermediate (**3**) or (**4**), with loss of a proton in a fast step to restore the aromaticity of the ring (Scheme).

In view of the fact that the peroxodisulphate oxidations of *meta*- and *para*-substituted *N*,*N*-dimethylanilines[6] and of the present *ortho*-substituted *N*,*N*-dimethylanilines have been shown to follow a mechanism involving *ipso*-attack, we were prompted to carry out a detailed correlation analysis of previously reported kinetic data[3] on the peroxodisulphate oxidation of *meta*- and *para*-substituted anilines. Correlation analyses of the reactivity data have been performed on the basis of three possible attacks of the oxidant, *viz.* at nitrogen, *ipso*-carbon, and *ortho*-carbon. For attack at nitrogen, log k_2 has been correlated with σ_m for *meta*-substituents and σ_p/σ_p^- for *para*-substituents, as in correlations carried out in studies of pK_a values and reactivities of anilines.[12] For attack at *ipso*-carbon, log k_2 is expected to correlate with σ_m for *meta*-substituents and σ_p^+/σ_p^- for *para*-substituents, as the *ipso*-carbon can conjugate with either a $+M$ or a $-M$ *para*-substituent. On similar grounds log k_2 is expected to correlate with σ_m for *para*-substituents and σ_p^+/σ_p^- for *meta*-substituents if the attack is at *ortho*-carbon. The results of these correlations are presented in Table 3. For attack at *ipso*-carbon, the correlation is better, as revealed by the fairly good correlation coefficient and low standard deviation. Consequently, it appears that Boyland–Sims oxidations of anilines and *N*,*N*-dimethylanilines involve initial rate-determining *ipso*-carbon attack by peroxodisulphate (Scheme).

Isokinetic Relationship.—The isokinetic temperature has been found to be −839 K by Exner's[13] method from a log–log plot of the rate constants at 35 and 45 °C (slope 0.977, r = 0.999, s = 0.02) for the peroxodisulphate oxidation of *N*,*N*-

Table 1. Second-order rate constants for the peroxodisulphate oxidation of *N*,*N*-dimethylanilines in alcohol–water solvent mixtures (pH 7) at 30 °C[a,b]

N,*N*-Dimethylaniline					
% EtOH–H_2O (v/v)	10^2k_2/dm^3 mol^{-1} s^{-1} [c]	% Pr^{i}OH–H_2O (v/v)	10^2k_2/dm^3 mol^{-1} s^{-1} [c]	% Bu^{t}OH–H_2O (v/v)	10^2k_2/dm^3 mol^{-1} s^{-1} [c]
30	8.58 ± 0.11	30	5.67 ± 0.10	30	4.58 ± 0.10
40	4.69 ± 0.09	40	2.70 ± 0.03	40	2.24 ± 0.04
50	2.36 ± 0.11	50	1.56 ± 0.04	50	1.44 ± 0.03
60	1.69 ± 0.05	60	1.07 ± 0.02	60	1.05 ± 0.02

	Substituted *N*,*N*-dimethylanilines		
Substituent	30% EtOH–H_2O (v/v) 10^2k_2/dm^3 mol^{-1} s^{-1} [c]	40% EtOH–H_2O (v/v) 10^2k_2/dm^3 mol^{-1} s^{-1} [c]	60% EtOH–H_2O (v/v) 10^2k_2/dm^3 mol^{-1} s^{-1} [c]
p-MeO		15.6 ± 0.24	6.65 ± 0.17
p-Me	16.0 ± 0.61	7.67 ± 0.37	
m-Me	10.3 ± 0.21	5.43 ± 0.10	
p-Cl	9.15 ± 0.39	4.17 ± 0.38	
m-MeO	7.52 ± 0.13	3.75 ± 0.06	
p-Br		3.86 ± 0.10	1.20 ± 0.06

[a] [amine] ≫ [PS]. [b] [phosphate buffer] = 0.025 mol dm^{-3}. [c] The error quoted in *k* is the 95% confidence limit of Student's *T* test.[18]

Table 2. Second-order rate constants and activation parameters for the oxidation of *ortho*-substituted *N*,*N*-dimethylanilines by peroxodisulphate ion[a]

	10^4k_2/dm^3 mol^{-1} s^{-1}			$\Delta H^{\ddagger}$ [b]	$-\Delta S^{\ddagger}$ [b]
Substituent	35 °C	40 °C	45 °C	kJ mol^{-1}	J K^{-1} mol^{-1}
H	318 ± 6.0	429 ± 19	569 ± 19	44.6 ± 5.7	129 ± 19
MeO	22.5 ± 0.90	32.9 ± 1.30	46.7 ± 1.40	56.7 ± 6.0	111 ± 20
Me	23.3 ± 0.52	33.7 ± 0.53	46.5 ± 2.50	53.7 ± 5.0	121 ± 16
F	15.7 ± 0.36	22.5 ± 0.55	29.8 ± 0.69	49.7 ± 3.8	138 ± 13
Cl	2.15 ± 0.06	3.29 ± 0.14	4.58 ± 0.22	60.1 ± 6.4	120 ± 21
Br	3.48 ± 0.19	4.83 ± 0.20	6.96 ± 0.20	53.8 ± 6.8	137 ± 21
NO_2	1.71 ± 0.15	2.40 ± 0.16	3.39 ± 0.09	53.2 ± 9.8	145 ± 32

[a] General conditions: [amine] ≫ [PS] in 50% (v/v) aqueous ethanol (pH 7); [b] The precision of ΔH‡ and ΔS‡ was calculated by the method of Petersen *et al.*[19]

Table 3. Results of correlation of rate data[a–c] with substituent parameters

	Substituent constants for				
Attack at	*para-*	*meta-*	ρ	*r*	*s*
Nitrogen	σ_p/σ_p^-	σ_m	−1.47	0.925	0.243
ipso-Carbon	σ_p^+/σ_p^-	σ_m	−1.26	0.960	0.178
ortho-Carbon	σ_m	σ_p^+/σ_p^-	0.766	0.553	0.532

[a] Data from ref. 3. [b] No. of substituents 17. [c] *ortho*-Substituents are excluded from the correlation.

dimethylanilines. The excellent correlation obtained indicates that the oxidations of all the substituted dimethylanilines follow the same mechanism.[14]

Experimental

Materials.—*ortho*-Nitro-*N*,*N*-dimethylaniline was prepared by the method of Campbell.[15] All the other *ortho*-substituted *N*,*N*-dimethylanilines were obtained by methylation of the corresponding anilines with dimethyl sulphate, and were purified by the method of Crocker and Jones.[16] The purity of all the compounds was checked by chromatographic and ^{1}H n.m.r. methods. Potassium peroxodisulphate (GR, Merck) was crystallised from water.

The buffered aqueous alcoholic solutions were prepared by mixing appropriate volumes of 0.025 mol dm^{-3} aqueous alcoholic solutions of potassium dihydrogen phosphate and disodium monohydrogen phosphate to give a pH of 7. The pH was measured using a digital pH meter (pH 5651, Electronic Corporation of India Limited).

Stoicheiometry.—Solutions of *N*,*N*-dimethylaniline containing an excess of peroxodisulphate were kept overnight at 30 °C. Estimation of the remaining oxidant showed that the stoicheiometry (amine:peroxodisulphate) is 1.2:1.

Kinetic Procedure.—The kinetic studies were carried out in buffered 50% aqueous ethanol (unless specified otherwise) under psuedo-first-order conditions with a large excess of amine over oxidant. The initial [amine] was in the range 0.02—0.06 mol dm^{-3}, depending on the reactivity and solubility of the amine, and the [PS] was kept at 0.001—0.002 mol dm^{-3} to maintain pseudo-first-order conditions. The reaction was followed by estimating the unchanged peroxodisulphate iodometrically.[17] The second-order rate constants were obtained by dividing the pseudo-first-order rate constants by [amine]. All the first-order plots were linear, with a correlation coefficient of at least 0.997. Duplicate runs were performed to confirm the rate constant at each temperature by taking different initial concentrations of the amine. The error quoted in *k* value is the 95% confidence limit of Student's *T* test. The least-squares and regression analyses were carried out using a Micro 2200 computer (Hindustan Computers).

The kinetic runs with a large excess of oxidant over amine were performed by following the u.v. absorption (250 nm) using a Perkin-Elmer 402 spectrophotometer. The initial concentrations of *N,N*-dimethylaniline and peroxodisulphate employed in a typical kinetic run (shown in Figure C) were 0.001 009 mol dm^{-3} and 0.010 09 mol dm^{-3}, respectively. Samples (1.5 ml) were withdrawn at convenient intervals and diluted to 10 ml with cold 50% aqueous ethanol (buffer pH 7) for optical density (I) measurement. The value of I_∞ was measured after 24 h.

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