The Stabilities of Meisenheimer Complexes. Part 42.[1] Kinetic Studies of the Reactions of Methyl 3,5-Dinitrobenzoate and of Methyl 4-Chloro-3,5-dinitrobenzoate with Hydroxide ions in Dimethyl Sulphoxide–Water Mixtures. Competitive Nucleophilic Attack at Aryl and Carbonyl Carbon Atoms

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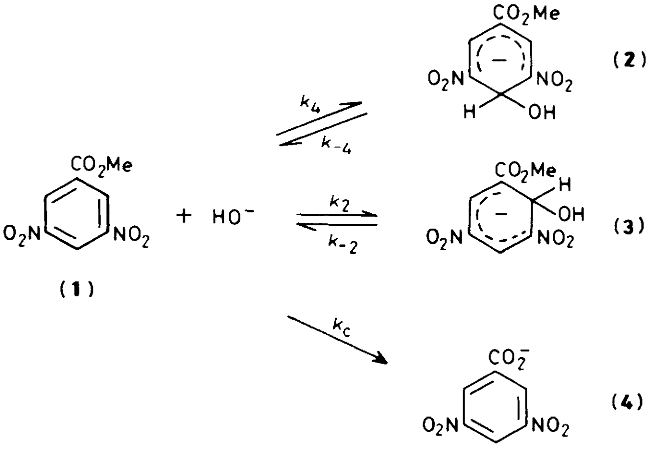
Kinetic and equilibrium data, obtained by stopped-flow spectrophotometry, are reported for the reactions of methyl 3,5-dinitrobenzoate (**1**) and methyl 4-chloro-3,5-dinitrobenzoate (**5**) with hydroxide ions in dimethyl sulphoxide–water mixtures. There is evidence for competition between attack at carbonyl and aryl carbon atoms, the latter becoming relatively favoured as the proportion of dimethyl sulphoxide in the solvent is increased. It is shown that the major pathway in the formation of 4-hydroxy-3,5-dinitrobenzoate from (**5**) involves hydroxide attack at the carbonyl function followed by slow attack at the ring carbon atom carrying chlorine.

We recently reported[1] kinetic and equilibrium studies of the reactions of 1-X-3,5-dinitrobenzenes (X = H, CO_2^-, CF_3, or NO_2) with hydroxide ions in water–dimethyl sulphoxide mixtures. These showed that there is little kinetic discrimination in nucleophilic attack at the isomeric 2- and 4-position. The higher thermodynamic stabilities observed for the 2-adducts as compared with the 4-adducts result mainly from lower rates of hydroxide expulsion.[2,3] The presence of the chlorine substituent in 1-X-3,5-dinitro-4-chlorobenzenes was shown[1] to result in a general reduction in the rate of nucleophilic attack, the effect being particularly large for *ipso*-reaction. Thus in similarly activated systems, values of k_4 for hydroxide attack at the 4-position are reduced by a factor of *ca.* 50 by the presence of the 4-chloro substituent. This reduction may be attributed to the steric and electrostatic repulsion between the chloro substituent and the incoming hydroxide ion.[4,5]

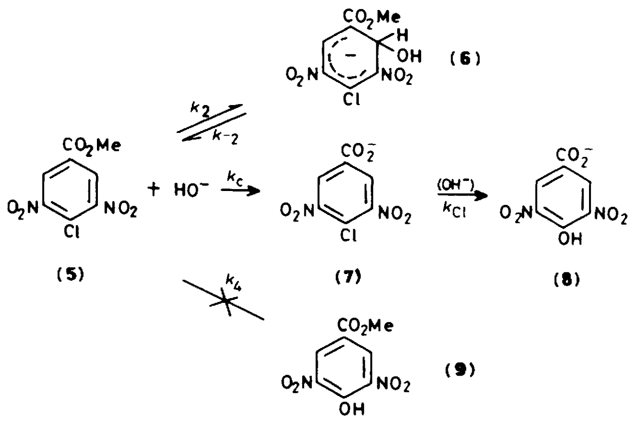
Equilibrium and ^1H n.m.r. studies have previously been reported for reactions of methyl 3,5-dinitrobenzoate with methoxide,[6,7] cyanide,[8] and oxocyclohexanide anions.[9] Isomeric reaction at the 2- and 4-position was observed with each nucleophile, equilibrium constants for formation of the 2-adducts being between three and six times larger than those for formation of their isomers.

We report here kinetic and equilibrium studies of the reactions of methyl 3,5-dinitrobenzoate and methyl 4-chloro-3,5-dinitrobenzoate with hydroxide ions in water–dimethyl sulphoxide mixtures. There is evidence for concurrent hydroxide attack at aryl and carbonyl carbon atoms, and our results allow quantitative comparisons of these reactions. Our results for methyl 3,5-dinitrobenzoate accord with Scheme 1, where there is eventually quantitative conversion into 3,5-dinitrobenzoate ions (**4**). This product may itself react with hydroxide ions to form σ-adducts,[1] but we have worked here with media insufficiently basic for their formation.

In media containing up to 90% (v/v) Me_2SO the two major rapid processes involved in the reaction of methyl 4-chloro-3,5-dinitrobenzoate with hydroxide are, as shown in Scheme 2, σ-adduct formation at the 2-position and ester hydrolysis to give 4-chloro-3,5-dinitrobenzoate (**7**). Slow substitution of the ring chlorine atom of (**7**) yields 4-hydroxy-3,5-dinitrobenzoate (**8**). Failure to observe direct substitution of ring chlorine in the substrate (**5**) may be attributed to the low rate expected for hydroxide attack at the chloro-substituted position.[1]



Scheme 1.



Scheme 2.

Results and Discussion

Methyl 3,5-Dinitrobenzoate.—Previously reported ^1H n.m.r. and u.v.–visible studies[6] of the reactions of (**1**) with methoxide ions in Me_2SO–MeOH indicate the rapid formation of a mixture of the 4-methoxy adduct, $\lambda_{max.}$ 550 nm, and the 2-methoxy adduct, $\lambda_{max.}$ 500 nm. Initially equal concentrations of the isomeric adducts are produced, but on equilibration the 2-methoxy adduct is favoured. With methoxide as nucleophile, attack at the carbonyl function is unproductive and hence not detected.

Our results for reaction of (**1**) with hydroxide ions in Me_2SO–H_2O provide evidence for the reactions of Scheme 1, involving the initial production of (**2**), $\lambda_{max.}$ 560 nm, and (**3**), $\lambda_{max.}$ 510 nm, followed by the equilibration of these adducts. However, here, hydroxide attack at the carbonyl function results in eventual conversion into 3,5-dinitrobenzoate (**4**). Kinetic measurements were made under first-order conditions with base in large excess over substrate. Observations by stopped-flow spectrophotometry revealed the presence of three relaxation times. Because the reactions are coupled the evaluation of individual rate coefficients from the observed relaxation times is not straightforward, in the general case.[10] We have therefore chosen to measure reaction rates under two sets of limiting conditions where simplified expressions are obtained.[10] The first limit involves work with media of relatively low basicity, achieved by using low hydroxide concentration and/or a low proportion of Me_2SO in the solvent. Here only small conversions of (**1**) into the adducts (**2**) and (**3**) are obtained, and it is then readily shown by standard methods[10] that the three observed rate coefficients (k_{fast}, k_{inter}, k_{slow}) can be identified as shown in equations (1)—(3).

$$k_{fast} = k_{-4} \tag{1}$$

$$k_{inter} = k_{-2} \tag{2}$$

$$k_{slow} = k_c[OH^-] \tag{3}$$

The other simplifying case involves media of relatively high basicity where the initial fast reaction consumes a high proportion of the substrate, which may subsequently be treated as a steady-state intermediate. Here equations (4)—(6) apply,[10] where k_{fast} involves the initial nucleophilic attack at the ring positions and the carbonyl group, k_{inter} the equilibration of adducts (**2**) and (**3**), and k_{slow} the formation of (**4**) from the equilibrated adducts *via* (**1**). A spectrum of the reaction system at completion of the most rapid reaction, k_{fast}, obtained in 90% (v/v) Me_2SO is shown in Figure 1. It indicates that the intensities of the bands at 510 nm, due to (**3**), and 560 nm, due to (**2**), are similar. It is known[6] that the extinction coefficients of the corresponding isomeric methoxide adducts are equal. If we make the reasonable assumption that the extinction coefficients of (**2**) and (**3**) are equal at their respective $\lambda_{max.}$ values, then we can conclude that these adducts are initially formed at equal rates so that the values of k_2 and k_4 are equal. Similar measurements in 70% and 80% Me_2SO, obtained with the condition of high basicity, indicated a similar result.

$$k_{fast} = (k_4 + k_2 + k_c)[OH^-] \tag{4}$$

$$k_{inter} = \frac{k_{-2} \cdot k_4 + k_{-4} \cdot k_2}{k_2 + k_4} \tag{5}$$

$$k_{slow} = \frac{k_c(k_2 + k_4)}{(k_2 + k_4 + k_c)(K_2 + K_4)} \tag{6}$$

40% and 50% (v/v) Me_2SO. In these media only very small concentrations of adducts (**2**) and (**3**) were produced. Independent measurements of the u.v. spectra of (**1**) and (**4**) indicate that formation of (**4**) produces an increase in absorption at 290 nm, and this wavelength was used to obtain values of k_{slow}. The data in Table 1, used with equation (3), give values for k_c of 22 l mol^{-1} s^{-1} in 40% Me_2SO and 42 l mol^{-1} s^{-1} in 50% Me_2SO.

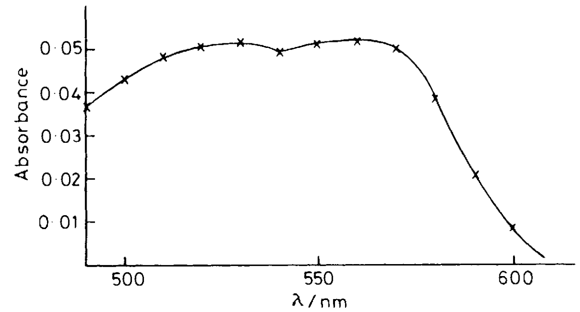


Figure 1. Visible spectrum, obtained by stopped-flow spectrophotometry, at the completion of the most rapid reaction of methyl 3,5-dinitrobenzoate (2×10^{-5}M) with NMe_4OH (2×10^{-3}M) in 90:10 (v/v) Me_2SO–H_2O (pathlength 2 mm)

60% Me_2SO. Values of observed rate coefficients are in Table 2. The results obtained at low base concentration yield k_{-4} 5.5 s^{-1}, k_{-2}, 1.4 s^{-1}, and k_c 80 l mol^{-1} s^{-1} by use of equations (1)—(3). The data for k_{fast} obtained at high base concentrations give a value for $k_2 + k_4 + k_c$ of 180 l mol^{-1} s^{-1}, which after subtraction of the known value for k_c yields values for k_2 and k_4 of 50 l mol^{-1} s^{-1}. Hence we obtain the equilibrium constants K_2 ($= k_2/k_{-2}$) 36 l mol^{-1} and K_4 ($= k_4/k_{-4}$) 9 l mol^{-1}. The value predicted by equation (5) for k_{inter} is 3.5 s^{-1}, in reasonable agreement with that observed. By substitution of known values of rate coefficients in equation (6) we obtain a value for $K_2 + K_4$ of 55 l mol^{-1}, again in reasonable agreement with the sum of independently obtained values.

70% Me_2SO. Extrapolation to zero base concentration of values, given in Table 3, for k_{fast} and k_{inter} yields k_{-4} 1.3 s^{-1} and k_{-2} 0.3 s^{-1}. Measurements at high base concentration of the fast colour-forming reaction give a value for $k_2 + k_4 + k_c$ of 650 l mol^{-1} s^{-1}. We were not able, in this solvent system, to obtain a value for k_c by direct observation. However, there is good evidence in the literature[1–3,7,10–14] that plots of the logarithms of rate and equilibrium constants *versus* the mole fraction of Me_2SO are linear. Hence by extrapolation we obtain a value for k_c of 200 l mol^{-1} s^{-1}. This leads to values of 225 l mol^{-1} s^{-1} for k_2 and for k_4. Combination of rate coefficients gives K_2 750 l mol^{-1} and K_4 170 l mol^{-1}. Values for k_{inter} and k_{fast} calculated from equations (5) and (6), respectively, using the known values for rate and equilibrium constants, are in good agreement with observed values.

80% Me_2SO. Here the condition of low basicity, where equations (1)—(3) apply, is unobtainable. The values of k_{fast} give, according to equation (4), a value for $k_4 + k_2 + k_c$ of 3 500 l mol^{-1} s^{-1}. Again by extrapolation we obtain a value for k_c of 700 l mol^{-1} s^{-1}, giving values for k_2, and k_4, of 1 400 l mol^{-1} s^{-1}. The value of k_{inter} yields, from equation (5), a value for $k_{-2} + k_{-4}$ of 0.30 s^{-1}, and, since results in 60% and 70% Me_2SO indicate that k_{-4} has a value four times that of k_{-2}, we can split this value to give k_{-2} 0.06 s^{-1} and k_{-4} 0.24 s^{-1}. The values obtained for K_2 and K_4 are 23 000 l mol^{-1} and 6 000 l mol^{-1}, respectively. We can have some confidence in the derived values since their use accurately predicts, by equation (6), the rate of the slow reaction. Data are in Table 4.

90% Me_2SO. The treatment of the data (Table 5) was exactly analogous to that described for 80% Me_2SO and yielded values for k_2 (and k_4) of 20 000 l mol^{-1} s^{-1}, k_c 6 000 l mol^{-1} s^{-1}, k_{-2} 0.0056 s^{-1}, and k_{-4} 0.022 s^{-1}. Combination of rate coefficients gave values for K_2 of 3.6×10^6 l mol^{-1} and K_4 of 9×10^5 l mol^{-1}.

Methyl 4-*Chloro*-3,5-*dinitrobenzoate*.—Examination by stopped-flow and conventional spectrophotometry of the

Table 1. Rate data for conversion of (**1**)[a] into (**4**) in 40% and in 50% (v/v) Me_2SO–H_2O at 25 °C

% Me_2SO (v/v)	$[NMe_4OH]$/M	$k_{\text{slow}}/\text{s}^{-1}$ [b]	k_c/l mol^{-1} s^{-1} [c]
40	0.0050	0.11	22
40	0.0075	0.17	23
40	0.0100	0.22	22
40	0.0150	0.31	21
50	0.0100	0.42	42
50	0.0200	0.84	42
50	0.0300	1.30	43

[a] Parent concentration 1 × 10^{-4}M. [b] Measured from increase in absorbance at 290 nm. [c] Calculated using equation (3).

Table 2. Rate data for reaction of (**1**)[a] with hydroxide ions in 60% (v/v) Me_2SO at 25 °C

$[NMe_4OH]$/M	$k_{\text{fast}}/\text{s}^{-1}$	$k_{\text{inter}}/\text{s}^{-1}$	$k_{\text{slow}}/\text{s}^{-1}$
0.001		1.4[c]	0.070[d]
0.002	5.5[b]	1.5[c]	0.16[d]
0.004		1.6[c]	0.32[d]
0.050	10[e]		0.75[g]
0.075	14[e]	4.0[f]	0.8[g]
0.100	19[e]	4.2[f]	0.8[g]

[a] Parent concentration 5 × 10^{-5}M. [b] Colour-forming reaction, at 600 nm. [c] Colour-forming, measured at 500 nm. [d] Increase in absorbance at 290 nm. [e] Colour-forming reaction; the value of k_{fast} is independent of the wavelength of measurement. [f] Measured as a fading reaction at 600 nm. [g] Fading reaction ot 500 nm.

Table 3. Rate data for reaction of (**1**) with hydroxide ions in 70% (v/v) Me_2SO at 25 °C

$[NMe_4OH]$/M	$k_{\text{fast}}/\text{s}^{-1}$	$k_{\text{inter}}/\text{s}^{-1}$	k_{calc}	$k_{\text{slow}}/\text{s}^{-1}$	k_{calc}
0.0002	1.4[a]	0.36[b]			
0.0004	1.47[a]	0.41[b]			
0.0006	1.51[a]	0.50[b]			
0.02	13[c]	0.7[d]	0.8[e]	0.14[f]	0.15[g]
0.04	26[c]	0.9[d]	0.8[e]	0.15[f]	0.15[g]

[a] Colour-forming reaction at 600 nm. [b] Colour-forming reaction at 500 nm. [c] Colour-forming reaction; value of k_{fast} is independent of wavelength. [d] Fading reaction at 600 nm. [e] Calculated from equation (5) with $k_2 = k_4$ and k_{-2} 0.3 s^{-1}, k_{-4} 1.3 s^{-1}. [f] Fading reaction at 500 nm. [g] Calculated from equation (6) with k_c 200 l mol^{-1} s^{-1}, $(k_2 + k_4)$ 450 l mol^{-1} s^{-1}, and $(K_2 + K_4)$ 920 l mol^{-1}.

Table 4. Rate data for reaction of (**1**)[a] with hydroxide ions in 80% (v/v) Me_2SO at 25 °C

$[NMe_4OH]$/M	$k_{\text{fast}}/\text{s}^{-1}$ [b]	$k_{\text{inter}}/\text{s}^{-1}$ [c]	$k_{\text{slow}}/\text{s}^{-1}$ [d]	k_{calc} [e]
0.005	17	0.17	0.021	0.019
0.010	35	0.15	0.018	0.019
0.020	69	0.15	0.018	0.019

[a] Parent concentration 2 × 10^{-5}M. [b] Colour-forming reaction; value is independent of the wavelength of measurement. [c] Fading reaction at 600 nm. [d] Fading reaction at 500 nm. [e] Calculated from equation (6) with k_c 700 l mol^{-1} s^{-1}, $(k_2 + k_4)$ 2 800 l mol^{-1} s^{-1}, and $(K_2 + K_4)$ 29 000 l mol^{-1}.

Table 5. Rate data for reaction of (**1**)[a] with hydroxide ions in 90% (v/v) Me_2SO at 25 °C

$[NMe_4OH]$/M	$k_{\text{fast}}/\text{s}^{-1}$ [b]	$k_{\text{inter}}/\text{s}^{-1}$ [c]	$k_{\text{slow}}/\text{s}^{-1}$ [d]	k_{calc} [e]
0.0010	46	0.014		
0.0020	95	0.014	0.0014	0.0012

[a] Parent concentration 2 × 10^{-5}M. [b] Colour-forming reaction, value is independent of wavelength of measurement. [c] Fading reaction at 600 nm. [d] Fading reaction, measured at 380 nm. [e] Calculated from equation (6) with k_c 6 000 l mol^{-1} s^{-1}, $(k_2 + k_4)$ 40 000 l mol^{-1} s^{-1}, and $(K_2 + K_4)$ 4.5 × 10^6 l mol^{-1}.

reactions of (**5**) with hydroxide ions in Me_2SO–H_2O revealed the presence of three time-dependent processes. The most rapid, designated k_{fast}, involves formation of a coloured species with $\lambda_{\text{max.}}$ *ca.* 480 nm and has low amplitude even in highly basic media. The absorption is at the wavelength expected for the adduct (**6**), and is not compatible with attack at the 4-position (the chloro-substituted position) since this would result[2,6] in absorption at *ca.* 550 nm. In the second process, k_{inter}, the absorption at 480 nm fades to zero and there is an increase in absorption at 290 nm. These two processes correspond to hydroxide attack at the 2-position to give (**6**) and at the carbonyl function to give (**7**). Since these are coupled, it may be shown by a standard treatment that equation (7) applies.[10]

$$k_{\text{fast}} + k_{\text{inter}} = k_{-2} + (k_2 + k_c)[OH^-] \qquad (7)$$

$$k_{\text{inter}} = k_{-2}k_c/(k_2 + k_c) \qquad (8)$$

$$k_{\text{slow}} = k_{\text{Cl}}[OH^-] \qquad (9)$$

When the initial reaction results in depletion of the parent concentration to such an extent that it may be treated as a steady-state intermediate then equation (8) will apply. The third process, k_{slow}, gives rise to an increase in absorption at 450 nm corresponding to conversion of (**7**) into (**8**).

50% *and* 60% (v/v) Me_2SO. Here conversion into adduct (**6**) was negligibly small, and the formation of (**7**) was followed by the increase in absorption at 290 nm. Formation of the phenol (**8**) was very slow and rates were not measured. Data are in Table 6.

70% (v/v) Me_2SO. Results are in Table 7. A linear plot according to equation (7) has intercept 0.3 ± 0.05 s^{-1} (k_{-2}) and slope 440 ± 20 l mol^{-1} s^{-1} ($k_2 + k_c$). The limiting value, 0.25 s^{-1}, of k_{inter} at high base concentration used in equation (8) with the known value of k_{-2} indicates that $k_c/(k_2 + k_c)$ is close to unity, so that k_2 may not be evaluated with any precision. However, we can make use of the absorbances at the completion of the rapid reaction to obtain a value for k_2. In the limit, at high base concentration, species (**6**) and (**7**) will be formed, in the initial reaction, in concentrations proportional to the values of k_2 and k_c, respectively. Also we may estimate[3,6,7] the value of the extinction coefficient of (**6**) at $\lambda_{\text{max.}}$ as 1.5 ± 0.5 × 10^4 l mol^{-1} cm^{-1}. Then use of equation (10) allows us to split the observed

$$\text{O.D.}/\varepsilon cl = k_2/(k_2 + k_c) \qquad (10)$$

value for $k_2 + k_c$ into the contributions for k_2 (40 ± 10 l mol^{-1} s^{-1}) and k_c (400 ± 20 l mol^{-1} s^{-1}). The low amplitude of the fast colour-forming reaction is thus explained in terms of the kinetic preference of the hydroxide ion for attack at the carbonyl function rather than at the ring. The results for k_{slow} lead to a value for k_{Cl} of 0.05 l mol^{-1} s^{-1}, in precise agreement with the value obtained previously[1] for the direct reaction of 4-chloro-3,5-dinitrobenzoate ions with hydroxide ions in 70% Me_2SO.

80% (v/v) Me_2SO. Application of equation (7) to the data in Table 8 yields a value for $k_2 + k_c$ of 1 650 ± 100 l mol^{-1} s^{-1}, but the value of k_{-2} is too small to be determined. Again using the absorbance at 480 nm at completion of the rapid reaction in equation (10) we obtain individual values for k_2 (250 ± 60 l mol^{-1} s^{-1}) and k_c (1 400 ± 100 l mol^{-1} s^{-1}). The use of the value of k_{inter} with equation (8) then yields a value for k_{-2} of 0.05 ± 0.01 s^{-1}. From the results for k_{slow} we obtain a value for

Table 6. Rate data for conversion of (**5**)[a] into (**7**) in 50% and 60% (v/v) Me_2SO at 25 °C

% Me_2SO	$[NMe_4OH]/M$	k_{obs}/s^{-1} [b]	$k_c/l\ mol^{-1}\ s^{-1}$ [c]
50	0.007	0.44	63
50	0.010	0.69	69
50	0.020	1.34	67
60	0.010	1.87	187
60	0.020	3.66	183

[a] Concentration $1 \times 10^{-4}M$. [b] Measured from increase in absorbance at 290 nm. [c] Calculated as $k_{obs}/[NMe_4OH]$.

Table 7. Rate data for reaction of (**5**)[a] with hydroxide ions in 70% (v/v) Me_2SO at 25 °C

$[NMe_4OH]/M$	k_{fast}/s^{-1} [b]	O.D. (480 nm)[c]	k_{inter}/s^{-1} [d]	k_{slow}/s^{-1} [e]
0.0020	1.0	0.0037	0.21	
0.0040	1.9	0.0045	0.22	
0.0080	3.6	0.0048	0.25	
0.0100	4.4	0.0049	0.25	
0.050				0.0025
0.100				0.0055

[a] Concentration $2 \times 10^{-5}M$. [b] Increase in absorption at 480 nm. [c] Absorbance at completion of fast reaction, measured with cell of 2 mm pathlength. [d] Fading reaction at 480 nm. [e] Colour-forming reaction at 450 nm.

k_{C1} of 0.19 l mol^{-1} s^{-1} using equation (9). This value is in exact agreement with the known value[2] for reaction of (**7**) with hydroxide ions.

90% Me_2SO. The data in Table 9 were treated in the same way as described for 80% solvent. Values obtained are k_2 5 000 ± 2 000 l mol^{-1} s^{-1}, k_c 11 000 ± 2 000 l mol^{-1} s^{-1}, and k_{-2} 0.007 ± 0.001 s^{-1}.

Comparisons.—Our results indicate competition between nucleophilic attack by hydroxide at ring and carbonyl carbon atoms as shown in Schemes 1 and 2. The mechanism of ester hydrolysis, the k_c step, is likely to involve rate-determining attack by hydroxide at the carbonyl carbon.[15,16] The relative ease of hydroxide attack at the acyl carbon casts doubt on the claim[17] that reaction of hydroxide ions with methyl 2,4,6-trinitrobenzoate results in initial formation of the 3-hydroxy adduct followed, after several hours, by isomerisation to the 1-hydroxy adduct; it seems likely that hydrolysis of the ester will have occurred.

Rate and equilibrium constants are summarised in Table 10. The values have been statistically corrected to take account of the fact that conversion of (**1**) into (**3**) and of (**5**) into (**6**) involves two equivalent ring positions. In agreement with previous work we find that plots of the logarithms of rate and equilibrium constants *versus* the mole percentage of Me_2SO are linear.[1-3,7,10-14] It is known[3] that Me_2SO has good solvating ability for large polarisable anions but not for small anions with localised charge. Hence the increases in value, with increasing proportion of Me_2SO, of equilibrium constants and of rate constants for reactions in the forward direction may be attributed to destabilisation of hydroxide ions and stabilisation of adducts or of the transition states leading to them. A plot shown in Figure 2 indicates that values of k_2 for attack at a ring carbon atom increase more rapidly than do values of k_c for attack at the carbonyl function. This may be a consequence of the better solvation by Me_2SO of the transition state leading to (**3**), where the negative charge may be delocalised about the ring and substituents, than of the transition state leading to (**1**), where the negative charge is localised on the carboxy function.

Table 8. Rate data for reaction of (**5**)[a] with hydroxide ions in 80% (v/v) Me_2SO at 25 °C

$[NMe_4OH]/M$	k_{fast}/s^{-1} [b]	O.D. (480 nm)[c]	k_{inter}/s^{-1} [d]	k_{slow}/s^{-1} [e]
0.000 25	0.35	0.0077		
0.000 50	0.77	0.0089	0.041	
0.001 00	1.6	0.0087	0.038	
0.002 00	3.4	0.0093	0.043	
0.004 00	6.8	0.0094	0.043	
0.010				0.0017
0.020				0.0039
0.030				0.0058

[a] Concentration $2 \times 10^{-5}M$. [b] Colour-forming reaction at 480 nm. [c] At completion of rapid colour-forming reaction. [d] Fading reaction at 480 nm. [e] Colour-forming reaction at 450 nm.

Table 9. Rate data for reaction of (**5**)[a] with hydroxide ions in 90% (v/v) Me_2SO at 25 °C

$[NMe_4OH]/M$	k_{fast}/s^{-1} [b]	O.D. (480 nm)[c]	k_{inter}/s^{-1} [d]
0.0010	13	0.017	
0.0020	31	0.017	0.0054
0.0040	68	0.017	0.0044
0.0050	82	0.016	0.0045

[a] Concentration $2 \times 10^{-5}M$. [b] Colour-forming reaction at 480 nm. [c] At completion of rapid colour-forming reaction. [d] Fading reaction.

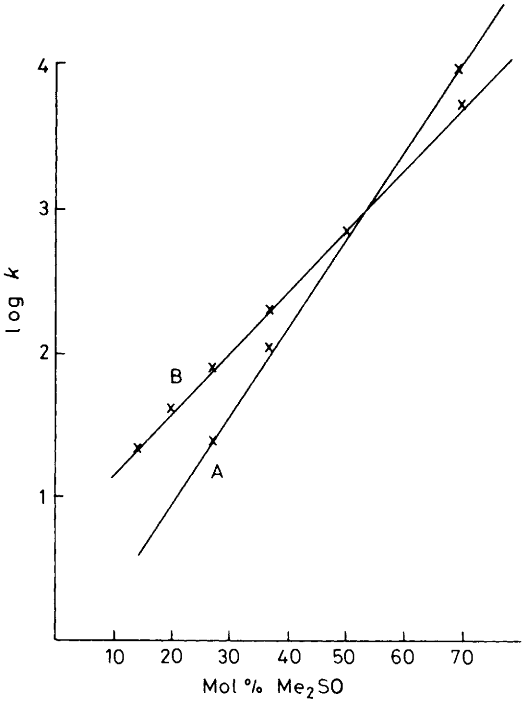


Figure 2. Variation with solvent composition of rate coefficients for hydroxide attack on (**1**): A, attack at ring carbon, k_2; B, attack at carbonyl carbon, k_c

Comparison of the values of K_2 and K_4 in Table 10 shows that the adduct (**3**) formed by hydroxide attack *para* to a nitro group in (**1**) has slightly higher thermodynamic stability than its isomer (**2**) where attack occurs *para* to the methoxycarbonyl substituent. The stabilising effect of a strongly electron-withdrawing group *para* to the position of base addition has been noted in other studies of σ-adduct formation.[2,3,6,7]

Table 10. Summary of statistically corrected kinetic and equilibrium data for reactions of (**1**) and (**5**) with hydroxide ions in Me_2SO-H_2O mixtures at 25 °C

		(**1**)						
% Me_2SO (volume)	% Me_2SO (mole)	k_2/l mol^{-1} s$^{-1\,a}$	k_{-2}/s^{-1}	K_2/l mol$^{-1\,a}$	k_4/l mol^{-1} s^{-1}	k_{-4}/s^{-1}	K_4/l mol^{-1}	k_c/l mol^{-1} s^{-1}
40	14.3							22
50	20.0							42
60	27.3	25	1.4	18	50	5.5	9	80
70	36.8	113	0.3	380	225	1.3	170	200
80	50.0	700	0.06	1.2×10^4	1 400	0.24	5 800	700
90	69.2	10 000	0.0056	1.8×10^6	20 000	0.022	9×10^5	6 000

		(**5**)			
% Me_2SO (volume)	% Me_2SO (mole)	k_2/l mol^{-1} s$^{-1\,a}$	k_{-2}/s^{-1}	K_2/l mol$^{-1\,a}$	k_c/l mol^{-1} s^{-1}
50	20.0				68
60	27.3				180
70	36.8	20	0.3	67	400
80	50.0	125	0.05	2 500	1 400
90	69.2	2 500	0.007	3.6×10^5	11 000

[a] Experimentally determined values of k_2 and K_2 have been divided by a factor of 2 (statistical correction).

Comparison of the results for (**1**) and (**5**) allows the effects of the chloro substituent to be examined. As discussed recently[1] the polar effect of the chlorine should encourage nucleophilic attack, while the presence in (**5**) of three groups at adjacent ring positions will cause steric strain. Thus the nitro groups at the 3- and 5-position will be forced from the ring plane so that they cannot exert their maximum electron-withdrawing influence.[3] The data in Table 10 show that the value of k_c for reaction of (**5**) is *ca.* twice as large as the value for reaction of (**1**). Hence for reaction at the external carbonyl function the polar withdrawal of the chlorine is more important. However for reaction at ring-carbon atoms the steric disruption of the chlorine is the more important factor. Thus the value of the equilibrium constant, K_2, for reaction at the unsubstituted ring position of (**5**) is *ca.* five times smaller than the corresponding value for (**1**), this reduction resulting almost entirely from a lower rate of hydroxide attack (k_2). Recently reported results[1] show that the rate of hydroxide attack at a ring-carbon atom carrying chlorine and flanked by two nitro-groups is reduced by a factor of *ca.* 50 as compared with attack at a similarly activated but unsubstituted ring position. This was attributed mainly to the steric and electrostatic repulsion expected between entering and leaving groups.[4] Hence we may calculate that in 80% (v/v) Me_2SO the value of k_4 for reaction at the chloro-substituted position of (**5**) will be *ca.* 28 l mol^{-1} s^{-1} [that is 1/50 of 1 400 l mol^{-1} s^{-1}, which is the corresponding value of k_4 for (**1**)]. Since in this medium values for (**5**) are k_c 1 400 l mol^{-1} s^{-1} and k_2 125 l mol^{-1} s^{-1}, it is seen that attack at the 4-position is not a major process. Hence, in the media we have used, the more important pathway in formation of the eventual product, (**8**) involves (**7**) rather than (**9**). As the proportion of Me_2SO in the solvent is increased k_4/k_c will increase and extrapolation of the data in Table 10 indicates that in 100% Me_2SO *ca.* 10% of the formation of (**8**) would occur *via* (**9**).

Experimental

Methyl 3,5-dinitrobenzoate[7] and methyl 4-chloro-3,5-dinitrobenzoate[18] were recrystallised specimens available from earlier work. Tetramethylammonium hydroxide was a commercial sample supplied as a concentrated solution (2.7M) in water; due account of the water content was taken when preparing dilute solutions in mixed solvents. Dimethyl sulphoxide was refluxed with calcium hydride and fractionated under reduced pressure. Solvents, degassed before use, were prepared by volume, and in stopped-flow work it was found most satisfactory to have solvents of the same composition in the two compartments. Visible spectra and kinetic measurements were made at 25 °C using a Hi-Tech SF3L stopped-flow spectrophotometer, or a Pye-Unicam SP8-100 recording spectrometer. Stock solutions of reagents were freshly prepared in Me_2SO-H_2O mixtures. All kinetic measurements were made under first-order conditions with the concentration of base in large excess over the concentration of substrate. Rate coefficients were evaluated by standard methods and are precise to ±5%.

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