The Stabilities of Meisenheimer Complexes. Part 41.[1] Kinetic Studies of Adduct Formation and Nucleophilic Substitution in the Reactions of Hydroxide Ions with 1-X-3,5-Dinitrobenzenes and with 1-X-4-Chloro-3,5-dinitrobenzenes (X = H, CF_3, CO_2^-) in Water–Dimethyl Sulphoxide Mixtures. The Effect of a Chloro-substituent on the Rate of Nucleophilic Attack

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Kinetic and equilibrium measurements are compared for the reactions of (**1**) and (**4**) (X = CF_3, CO_2^-, H) with hydroxide ions in dimethyl sulphoxide–water mixtures. The adducts (**3**), formed from (**1**), have higher thermodynamic stabilities than their isomers (**2**) although there is little kinetic discrimination in the rates of hydroxide attack at the three unsubstituted positions. The presence in (**4**) of the chlorine atom results in a general reduction in the rate of nucleophilic attack, the effect being particularly large for *ipso*-reaction (attack at the 4-position). Hence the reaction of (**4**) with base results in the initial formation of adducts (**5**). Contrary to a recent report the intermediates (**6**) on the reaction pathway to the phenols (**7**) are not sufficiently stable to allow spectrophotometric detection.

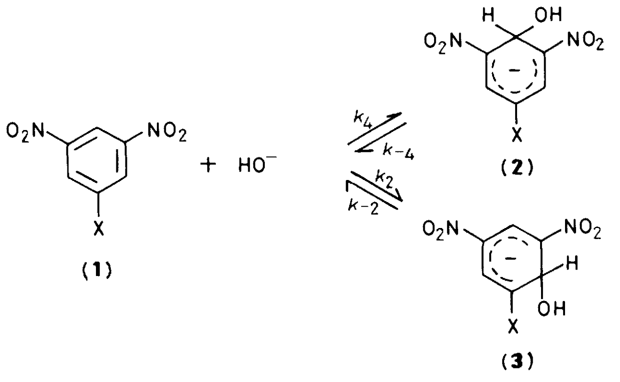
The reactions of unsymmetrically substituted benzene derivatives with nucleophiles frequently yield isomeric adducts.[2] ^1H N.m.r. and visible spectroscopic studies have shown that Scheme 1 is applicable to the reactions of 1-X-3,5-dinitrobenzenes with oxygen bases,[3–5] and kinetic data have been reported[6] for the reactions of 1-cyano-3,5-dinitrobenzene (1; X = CN) and 1-trifluoromethyl-3,5-dinitrobenzene (1; X = CF_3).

With 1-X-4-chloro-3,5-dinitrobenzenes isomeric reaction is again expected as shown in Scheme 2 although now, because of the instability with respect to loss of chloride ion of the intermediates (6), the substrates will eventually be converted into the substituted phenols (7). Studies involving the reaction of 1-substituted-2,4,6-trinitrobenzenes with hydroxide ions have shown that nucleophilic attack at unsubstituted ring positions is generally a faster process than at substituted positions,[7,8] and the observable adducts are of structure (5). Similarly in reactions of 1-substituted-2,4-dinitrobenzenes with hydroxide ions[9,10] and with sulphite ions[1,11] the observable coloured species result from attack at unsubstituted ring positions.

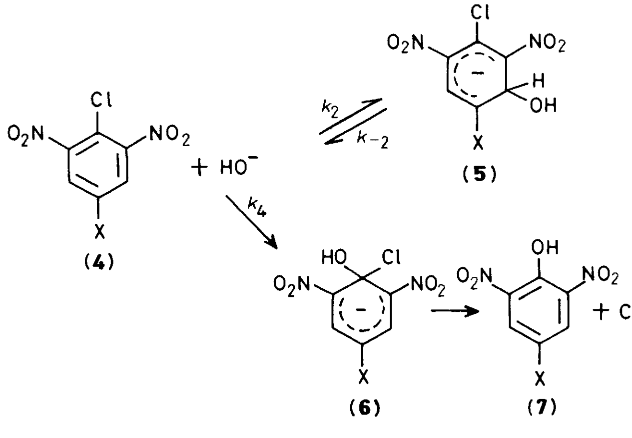
In this paper we compare the kinetics of the reactions with hydroxide ions of pairs of substrates (1) and (4) (X = H, CF_3, CO_2^-, NO_2) with the particular aim of quantifying the effect of the chlorine substituent on the rates of nucleophilic attack in similarly activated systems. Our results show that the values of k_4 corresponding to Scheme 2 are dramatically reduced compared to k_4 values for Scheme 1. We also examine the claim, recently made,[12] that the intermediates of structure type (6) may be *spectroscopically observed* during substitutions in aqueous dimethyl sulphoxide.

Results

All kinetic measurements were made under first-order conditions with the concentration of base in large excess over the concentration of substrate. The reported rate coefficients are the mean of at least five separate determinations and are precise to ±5%. Because of the wide variation in stabilities of the adducts formed it was not possible to make all measurements in a common solvent. It is known[2] that increasing the proportion of dimethyl sulphoxide (DMSO) in mixtures with water results in large increases in equilibrium constants for adduct formation and we have used such mixtures to find suitable solvents for the evaluation of rate coefficients.



Scheme 1.



Scheme 2.

We found it necessary to purify the DMSO carefully before use by refluxing over calcium hydride followed by distillation under reduced pressure. Both the DMSO and the distilled water used were degassed prior to use. We were careful to avoid the use of alcohols in the preparation of stock solutions of reagents since in the presence of base these will yield alkoxide ions,

Table 1. Kinetic and equilibrium data for the reaction of 1-trifluoromethyl-4-chloro-3,5-dinitrobenzene[a] with hydroxide ions in 70:30 (v/v) DMSO–water at 25°

$[NMe_4OH]$/M	k_{fast}/s^{-1} [b]	$k_{calc.}$ [c]	Absorbance[d] (480 nm)	K_2 [e]	k_{slow}/s^{-1} [f]	$k_{calc.}$ [g]
0.001	0.21	0.21	0.013	240		
0.002	0.27	0.26	0.024	270		
0.004	0.34	0.35	0.035	270		
0.007	0.49	0.49	0.044	260		
0.010	0.60	0.63	0.052	320		
0.020	1.10	1.11	0.058	290	0.011	0.010
0.050	2.53	2.54	0.063		0.011	0.011

[a] Concentration is 2 × 10^{-5}M. [b] Fast colour-forming reaction at 480 nm measured by stopped-flow method. [c] Calculated from equation (1) with k_2 47.5 l mol^{-1} s^{-1} and k_{-2} 0.16 s^{-1}. [d] At completion of rapid colour forming reaction. [e] Defined as (Absorbance)/(0.068 − Absorbance) $[NMe_4OH]$. [f] Fading reaction at 480 nm measured by stopped-flow method. [g] Calculated from equation (2) with k_4 3.6 l mol^{-1} s^{-1} and K_2 300 l mol^{-1}.

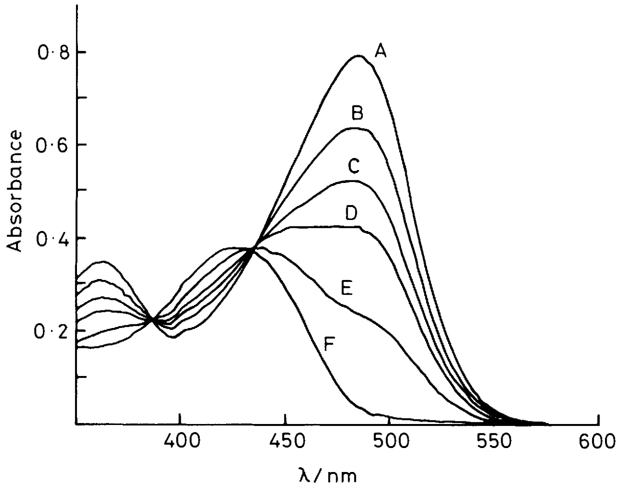


Figure 1. Visible spectra of 1-trifluoromethyl-4-chloro-3,5-dinitrobenzene (5 × 10^{-5}M) with tetramethylammonium hydroxide (5 × 10^{-3}M) in 80% (v/v) DMSO. Scans were started at the following times after mixing: A 10 s, B 100 s, C 190 s, D 280 s, E 500 s, F 2 000 s

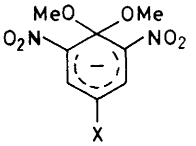
capable of themselves attacking the substrates.[2] Similarly we avoided the use of acetone in cleaning glassware since acetonate ions are known[2] to attack aromatic nitro-compounds.

1-*Trifluoromethyl*-4-*chloro*-3,5-*dinitrobenzene*.—Visible spectra in 80:20 (v/v) DMSO–water in Figure 1 show the rapid appearance of a band at 485 nm attributed[7] to (**5**; X = CF_3). This band gradually fades and a new band at 425 nm due to the phenol (**7**) appears. No absorption is observed in the region of 550 nm where the intermediate (**6**; X = CF_3) is expected to absorb.[7] Similarly spectra recorded in media containing 70—98% DMSO by volume also failed to show any absorption attributable to (**6**; X = CF_3). However the addition of small quantities of methanol to these reaction systems produced an absorption at 545 nm which may be attributed[7] to the dimethoxy adduct (**8**; X = CF_3).

Kinetics of the reactions with hydroxide ions were measured in 70:30 and 80:20 (v/v) DMSO–water solvent systems. Two processes, well separated in time, were observable corresponding to the reactions of Scheme 2. Treatment by standard methods[1,13] yields the rate expressions of equations (1) and (2).

$$k_{fast} = k_2[OH^-] + k_{-2} \qquad (1)$$

$$k_{slow} = k_4[OH^-]/(1 + K_2[OH^-]) \qquad (2)$$



(**8**)

Results are given in Tables 1 and 2 where the values calculated for rate and equilibrium constants are shown.

In 90% DMSO the system was less well behaved. The fast formation of (**5**; X = CF_3) occurred with k_2 4 400 l mol^{-1} s^{-1}. However, unlike the behaviour in more aqueous media, the fading reaction did not yield the phenol (**7**; X = CF_3) quantitatively. It is probable that because of the high stability of (**5**; X = CF_3) in this medium a decomposition reaction in addition to that shown in Scheme 2 may occur.

4-*Chloro*-3,5-*dinitrobenzoate*.—Measurements of visible spectra in 70:30 and 80:20 (v/v) DMSO–water, and also in 90:10 DMSO–water at low base concentrations ($[OH^-]$ < 0.005M) indicated the slow and quantitative formation of the phenol (**7**; X = CO_2^-) with $\lambda_{max.}$ 460 nm. No other coloured species were observed in these media. Here there is direct conversion of (**4**; X = CO_2^-) to (**7**; X = CO_2^-) and the kinetic results in Table 3 yield values for k_4 which, as expected, increase with increasing proportion of DMSO in the solvent.

In 90% DMSO at higher base concentrations (OH^- > 0.005M) and in 95% DMSO, visible spectra showed the formation of a transient species with $\lambda_{max.}$ 530 nm. In fact the spectrum, Figure 2, obtained by stopped-flow measurements at the completion of the rapid reaction indicates initial formation of a mixture of (**5**; X = CO_2^-) and (**7**; X = CO_2^-). There is then a slow reaction completing the conversion of the substrate to (**7**; X = CO_2^-). No absorption is observed attributable to the intermediate (**6**; X = CO_2^-) which would be expected[2,7] to absorb at *ca.* 600 nm. However the addition of small quantities of methanol to the reaction medium gave rise to a band at 595 nm which we attribute to the dimethoxy adduct (**8**; X = CO_2^-). Also the presence of acetone resulted in absorption in the region 550—600 nm, probably due to the formation of an acetonate adduct.[2]

Kinetic results for reaction with hydroxide in 90% and in 95% DMSO are in Tables 4 and 5. Two processes well separated in time were observed, but the spectroscopic evidence that the initial reaction yields a mixture of (**5**; X = CO_2^-) and (**7**; X = CO_2^-) indicates some coupling of the reactions. Standard treatments[13,14] yield equation (3) for the sum of the measured rate coefficients.

Table 2. Kinetic data for the reaction of 1-trifluoromethyl-4-chloro-3,5-dinitrobenzene with hydroxide ions in 80:20 (v/v) DMSO–water at 25°

$[NMe_4OH]$/M	k_{fast}/s^{-1} [a]	$k_{calc.}$ [b]	k_{slow}/s^{-1} [c]	$k_{calc.}$ [d]
0.000 25	0.10	0.10		
0.000 50	0.18	0.18		
0.001 00	0.33	0.33		
0.002 00	0.69	0.63	0.001 9	0.001 9
0.004 00	1.25	1.23	0.002 0	0.002 0
0.006 00	1.80	1.83	0.002 0	0.002 0

[a] Fast colour-forming reaction at 480 nm measured by stopped-flow method. [b] Calculated from equation (1) with k_2 300 l mol^{-1} s^{-1} and k_{-2} 0.03 s^{-1}. [c] Fading reaction at 480 nm measured with conventional spectrophotometer. [d] Calculated from equation (2) with k_4 20 l mol^{-1} s^{-1} and K_2 10 000 l mol^{-1}.

Table 3. Kinetic data for direct conversion of (**4**; X = CO_2^-)[a] to (**7**; X = CO_2^-) at 25°

DMSO (% v/v)	$[NMe_4OH]$/M	$k_{obs.}/s^{-1}$ [b]	$k_{obs.}$ $[NMe_4OH]^{-1}$/l mol^{-1} s^{-1} [c]
70	0.05	0.002	0.04
70	0.10	0.005	0.05
80	0.01	0.001 9	0.19
80	0.02	0.003 9	0.195
90	0.002	0.002 6	1.3
90	0.004	0.004 6	1.2

[a] Concentration is 5 × 10^{-5}M. [b] Measured as a colour-forming reaction at 460 nm by conventional spectrophotometry. [c] Corresponds to k_4 in Scheme 2.

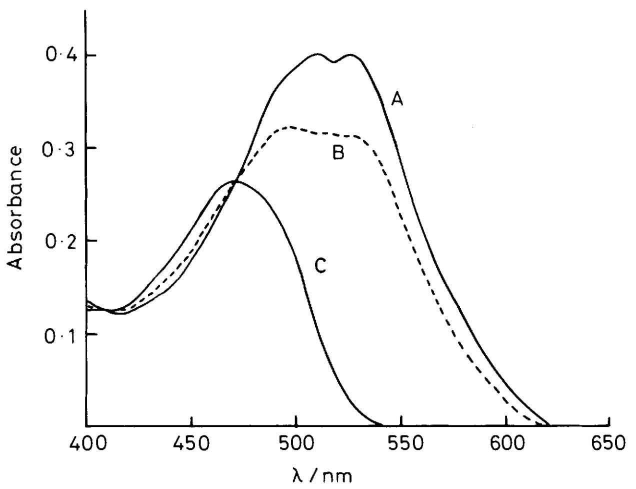


Figure 2. Visible spectra of 4-chloro-3,5-dinitrobenzoate (5 × 10^{-5}M) with tetramethylammonium hydroxide (0.04M) in 95% (v/v) DMSO. A, spectrum obtained by stopped-flow of species present at completion of rapid colour forming process. B, obtained by conventional spectrophotometer 10 s after mixing. C, stable reaction product (**7**; X = CO_2^-)

Table 4. Kinetic data for the reaction of 4-chloro-3,5-dinitrobenzoate[a] with hydroxide ions in 90:10 (v/v) DMSO–water at 25°

$[NMe_4OH]$/M	k_{fast}/s^{-1} [b]	k_{slow}/s^{-1} [c]	$k_{calc.}$ [d]
0.010	0.56		
0.020	0.60		
0.040	0.64	0.033	0.032
0.060	0.74	0.045	0.044
0.080	0.82	0.054	0.054

[a] Concentration is 5 × 10^{-5}M. [b] Measured at 530 nm or at a wavelength where an isosbestic point was observed between the two reactions. [c] Fading reaction at 530 nm. [d] Calculated from equation (2) with k_4 1 l mol^{-1} s^{-1}, and K_2 6 l mol^{-1}.

Table 5. Kinetic data for the reaction of 4-chloro-3,5-dinitrobenzoate[a] with hydroxide ions in 95:5 (v/v) DMSO–water at 25°

$[NMe_4OH]$/M	k_{fast}/s^{-1} [b]	k_{slow}/s^{-1} [c]	$k_{calc.}$ [d]
0.001 7	0.16	0.010	0.011
0.003 0	0.19	0.015	0.017
0.005 0	0.26	0.026	0.023
0.010 0	0.39	0.036	0.030
0.020 0	0.63	0.038	0.036
0.030 0	0.95	0.040	0.039

[a] Concentration is 2 × 10^{-5}M. [b] Measured at 530 nm or at a wavelength where an isosbestic point was observed between the two reactions. [c] Fading reaction at 530 nm. [d] Calculated from equation (2) with k_4 9 l mol^{-1} s^{-1} and K_2 200 l mol^{-1}.

$$k_{fast} + k_{slow} = k_{-2} + (k_2 + k_4)[OH^-] \qquad (3)$$

A plot according to equation (3) of the data in 90% DMSO gives k_{-2} 0.52 ± 0.01 s^{-1} (intercept) and $k_2 + k_4$, 4.4 ± 0.4 l mol^{-1} s^{-1} (slope). Since independent measurements (Table 3) give a value for k_4 of 1.25 l mol^{-1} s^{-1} in this solvent we obtain a value for k_2 of 3.2 ± 0.3 l mol^{-1} s^{-1}. Combination of rate coefficients for formation of (**5**) gives K_2 (= k_2/k_{-2}) 6 ± 1 l mol^{-1}. Values for k_{slow} calculated from equation (2) with values of k_4 1 l mol^{-1} s^{-1} and K_2 6 l mol^{-1} give a good fit with experimental data.

A plot according to equation (3) of the data in 95% DMSO (Table 5) gives k_{-2} 0.12 ± 0.01 s^{-1} and $k_2 + k_4$, 30 ± 3 l mol^{-1} s^{-1}. In order to separate values for k_2 and k_4 in this medium we make use of the known values for k_4 in more aqueous media. There is strong evidence[1,5,15–18] that plots of the logarithms of rate and equilibrium constants *versus* the mole fraction of DMSO are linear. Hence we obtain by extrapolation of the values in Table 3 a value of 5 ± 2 l mol^{-1} s^{-1} for k_4 in 95% DMSO. Use of this value leads to a value for k_2 of 25 ± 3 l mol^{-1} s^{-1}, which in combination with k_{-2} leads to a value for K_2 (= k_2/k_{-2}) of 200 l mol^{-1}. In fact to accommodate values of k_{slow} with equation (2) requires a value for k_4 of 9 l mol^{-1} s^{-1}. That this value is higher than that obtained by the extrapolation procedure may indicate an alternative decomposition mechan-

Table 6. Kinetic data for direct conversion of (**4**; X = H)[a] to (**7**; X = H) at 25°

DMSO (% v/v)	[NMe$_4$OH]/M	$k_{obs.}$/s^{-1} [b]	$k_{obs.}$ [NMe$_4$OH]$^{-1}$/l mol^{-1} s^{-1} [c]
70	0.05	0.000 98	0.020
70	0.10	0.001 9	0.019
80	0.010	0.001 5	0.15
80	0.020	0.002 8	0.14
90	0.000 7	0.001 5	2.1
90	0.001 0	0.002 3	2.3
90	0.001 5	0.003 1	2.1

[a] Concentration is 5 × 10^{-5}M. [b] Measured as a colour-forming reaction at 460 nm by conventional spectrophotometry. [c] Corresponds to k_4 in Scheme 2.

Table 7. Kinetic data for the reaction of 3,5-dinitrobenzoate[a] with hydroxide ions in 95:5 (v/v) DMSO–water at 25 °C

[NMe$_4$OH]/M	k_{fast}/s^{-1} [b]	k_{slow}/s^{-1} [c]
0.001		0.11
0.002	3.02	0.14
0.004	3.56	0.21
0.007	4.15	0.31
0.010	5.23	0.39
0.020	7.6	0.50

[a] Parent concentration is 1 × 10^{-5}M. [b] Fast colour-forming reaction at 630 nm measured by stopped-flow spectrophotometry. [c] Slow forming reaction at 540 nm measured by stopped-flow spectrophotometry.

ism for (**5**; X = CO$_2^-$) in addition to that shown in Scheme 2. The preferred value for k_4 in this medium is 5 ± 2 l mol^{-1} s^{-1}.

4-*Chloro* 3,5-*dinitrobenzene*.—Measurements are reported in Table 6 for the rates of formation of the phenol (**7**; X = H) in media where there is negligible formation of (**5**; X = H). These yield values of k_4 directly. Linear extrapolation, as before, yields a value in 95% DMSO for k_4 of 12 ± 2 l mol^{-1} s^{-1}.

Measurements in this solvent system indicate rapid formation of (**5**; X = H) with $\lambda_{max.}$ 510 nm. A linear plot, not shown, according to equation (1) yielded values for k_2 260 ± 20 l mol^{-1} s^{-1} and k_{-2} 0.1 ± 0.03 s^{-1}.

1-X-3,5-*Dinitrobenzenes*.—Previously reported ^{1}H n.m.r. results show that when the X-substituent is less strongly electron withdrawing than the nitro-group a mixture of adducts (**2**) and (**3**) is initially formed while the adducts of structure (**3**) predominate at equilibrium.[3–5] Visible spectra initially show two bands in the region 500—650 nm. Originally[4,5] both bands were attributed to adducts of structure (**2**). However Fyfe's work[3] has shown that the correct interpretation is that the band at longer wavelength is due to adducts of type (**2**) and that at shorter wavelength to adducts of type (**3**). With time the band at shorter wavelength increases in intensity at the expense of the longer wavelength band.

Two rate processes are expected for the reactions of Scheme 1, a fast process, k_{fast}, corresponding to the rapid formation of a mixture of adducts and a slower process, k_{slow}, corresponding to their equilibration. Since the reactions are coupled these rate coefficients are functions of all the rate processes in the system and Bernasconi[13] has shown that equations (4) and (5) will apply. Two limiting conditions are useful. First in media where only very small amounts of (**2**) are formed then there is a direct equilibration of (**1**) and (**3**) so that equation (6) applies. Second, in media of low base concentration the reverse rate coefficients dominate so that the two observed processes yield[13] k_{-4} and k_{-2} by equations (7) and (8).

$$k_{fast} + k_{slow} = k_{-4} + k_{-2} + (k_2 + k_4)[OH^-] \quad (4)$$

$$k_{fast}k_{slow} = k_{-2}k_{-4} + (k_2k_{-4} + k_4k_{-2})[OH^-] \quad (5)$$

$$k_{obs.} = k_{-2} + k_2[OH^-] \quad (6)$$

$$k_{fast} = k_{-4} \quad (7)$$

$$k_{slow} = k_{-2} \quad (8)$$

Table 8. Kinetic data for the reaction of 1,3-dinitrobenzene with hydroxide ions in 80:20 and in 90:10 (v/v) DMSO–water at 25 °C

DMSO % (v/v)	[NMe$_4$OH]/M	$k_{obs.}$/s^{-1} [a]	$k_{calc.}$ [b]
80	0.030	3.0	2.7
80	0.070	3.0	3.0
80	0.10	3.2	3.2
80	0.15	3.6	3.6
80	0.19	3.9	3.8
90	0.002	0.50	0.52
90	0.004	0.73	0.74
90	0.006	0.96	0.96
90	0.010	1.43	1.40
90	0.016	2.06	2.06
90	0.040	4.61	4.70

[a] Colour forming reaction at 530 nm, measured by stopped-flow spectrophotometry. [b] Calculated from equation (6) with k_2 7 l mol^{-1} s^{-1}, and k_{-2} 2.5 s^{-1} in 80% and with k_2 110 l mol^{-1} s^{-1} and k_{-2} 0.3 s^{-1} in 90% DMSO.

Table 9. Kinetic data for the reaction of 1,3-dinitrobenzene with hydroxide ions in 95:5 (v/v) DMSO–water at 25 °C

[NMe$_4$OH]/M	k_{fast}/s^{-1} [a]	k_{slow}/s^{-1} [b]
0.000 5	4 ± 1	0.4 ± 0.04
0.001 0	4	0.7
0.002 0	6	1.5
0.004 0	8	2.8

[a] Colour-forming reaction at 630 nm. [b] Slow colour-forming at 530 nm.

3,5-*Dinitrobenzoate*.—Visible spectra in 95% DMSO show that (**2**; X = CO$_2^-$) has an absorption maximum at 630 nm and (**3**; X = CO$_2^-$) at 540 nm. At equilibrium the latter isomer is strongly favoured. Kinetic data are in Table 7. Extrapolations to zero base concentration of the measured rate coefficients give values for k_{-4} of 2.4 ± 0.1 s^{-1} [equation (7)] and for k_{-2} of 07 ± 0.01 s^{-1} [equation (8)]. A linear plot according to equation (4) of k_{fast} + k_{slow} *versus* base concentration gives a value for k_2 + k_4 of 300 ± 20 l mol^{-1} s^{-1}, and use of equation

Table 10. Comparison of statistically corrected[a] values of rate and equilibrium constants for reaction of hydroxide ions at the 2-position in 1-X-3,5-dinitrobenzenes and in 4-chloro-1-X-3,5-dinitrobenzenes

	k_2/l mol^{-1} s^{-1}	k_{-2}/s^{-1}	K_2/l mol^{-1}		k_2/l mol^{-1} s^{-1}	k_{-2}/s^{-1}	K_2/l mol^{-1}	K_2(1)/K_2(4)	Medium
(1; X = NO_2)[b]	13	9.8	1.3	(4; X = NO_2)[c]	6	14	0.42	3.1	Water
(1; X = CF_3)[d]	63	0.086	730	(4; X = CF_3)	24	0.16	150	4.9	70% (v/v) DMSO
(1; X = CO_2^-)	30	0.07	430	(4; X = CO_2^-)	12	0.12	100	4.3	95% (v/v) DMSO
(1; X = H)	400	0.07	5 500	(4; X = H)	130	0.10	1 300	4.2	95% (v/v) DMSO

[a] Experimentally observed values of k_2 and K_2 have been divided by two, except in the case of 1,3,5-trinitrobenzene where values were divided by three. [b] Ref. 19. [c] Ref. 8. [d] Ref. 6.

Table 11. Comparison of the rates of nucleophilic attack by hydroxide at the 4-position in 1-X-3,5-dinitrobenzenes and 4-chloro-1-X-3,5-dinitrobenzenes

	k_4/l mol^{-1} s^{-1}		k_4/l mol^{-1} s^{-1}	k_4(1)/k_4(4)	Medium
(1; X = NO_2)	13[a]	(4; X = NO_2)[b]	0.4	32	Water
(1; X = CF_3)[c]	375	(4; X = CF_3)	3.6	104	70% (v/v) DMSO
(1; X = CO_2^-)	240	(4; X = CO_2^-)	5	48	95% (v/v) DMSO
(1; X = H)	700	(4; X = H)	12	58	95% (v/v) DMSO

[a] The value of 38 l mol^{-1} s^{-1} for reaction of 1,3,5-trinitrobenzene with hydroxide ions from ref. 19 has been divided by three (statistical correction). [b] Ref. 8. [c] Ref. 6.

Table 12. Comparison of statistically corrected[a] values for rate and equilibrium constants for reaction of hydroxide attack at the 2- and 4-positions of 1-X-3,5-dinitrobenzenes

Parent	k_4/lmol^{-1} s^{-1}	k_{-4}/s^{-1}	K_4/l mol^{-1}	k_2/l mol^{-1} s^{-1}	k_{-2}/s^{-1}	K_2/l mol^{-1}	K_2/K_4	Medium
(1; X = NO_2)[a]	13	9.8	1.3	13	9.8	1.3	1	Water
(1; X = CF_3)[b]	375	6	94	63	0.086	730	7.8	70% (v/v) DMSO
(1; X = CO_2^-)	240	2.4	100	30	0.07	430	4.3	95% (v/v) DMSO
(1; X = H)	700	3.5	200	400	0.07	5 700	28.5	95% (v/v) DMSO

[a] Experimental values of k_2 and K_2 for (1; X = CF_3, CO_2^-, and H) were divided by two. Values for 1,3,5-trinitrobenzene from ref. 19 were divided by three. [b] Ref. 6.

(5) allows the determination of values for k_2 60 ± 10 l mol^{-1} s^{-1} and k_4 240 ± 20 l mol^{-1} s^{-1}.

1,3-Dinitrobenzene.—In solvents containing 80 and 90% DMSO there is, at the base concentrations used, negligible formation of the adduct (2; X = H). The data in Table 8 correspond to the direct formation of (3; X = H) with $\lambda_{max.}$ 530 nm and treatment using equation (6) allowed the determination of values of k_2 and k_{-2} in these media. From the measurements, described below, in 95% DMSO it is not possible to obtain a value for k_{-2}. However there is strong evidence[1,5,15–18] that plots of the logarithms of rate and equilibrium constants *versus* the mole fraction of DMSO are linear. Hence by linear extrapolation we obtain values in 95% DMSO of 800 l mol^{-1} s^{-1} for k_2 and 0.07 s^{-1} for k_{-2}. Measurements in this medium indicate the transient formation of (2; X = OH) with $\lambda_{max.}$ 630 nm. Here the two reactions are strongly coupled and we assign relatively large errors to the rate coefficients reported in Table 9. A plot according to equation (4) has intercept, k_{-4}, of 3.5 ± 1 s^{-1} and slope, $k_2 + k_4$, of 1 700 ± 300 l mol^{-1} s^{-1}. From the slope of a plot according to equation (5) we obtain a value for k_2 of 1 000 ± 300 l mol^{-1} s^{-1}, in accord with that predicted by extrapolation from less basic media. Hence by difference we obtain a value for k_4 of 700 ± 300 l mol^{-1} s^{-1}.

Discussion

Visible spectra and kinetic results for the reaction of the chloro-substituted compounds (4; X = CF_3, CO_2^-, and H) are in accord with the processes of Scheme 2. Bands in the visible region are observed due to the adducts (5) and to the phenols (7), which will exist in the ionised form in basic media. Our results, obtained using carefully purified solvent, failed to substantiate the claim[12] that bands in the region of 600 nm are observed in these systems due to the intermediates (6). Hence the substitution of chloride by hydroxide will involve rate-determining attack of hydroxide to yield (6) which rapidly expels chloride to yield phenol (7).

Kinetic and equilibrium results relating to the chloro-substituted reactants of type (4) were obtained under conditions where there was eventually quantitative conversion to phenols (7). In media containing very high proportions of DMSO where the adducts (5) have high stability there was evidence for an alternative decomposition pathway which we did not investigate.

Data are summarised in Tables 10—12. Two points must be mentioned. We have applied statistical corrections so that rate and equilibrium constants apply to reaction at a single ring position of the substrates. This involves dividing by a factor of two the experimental values for k_2 and K_2 for both substrates (1) and (4) since two equivalent ring positions are available. Also, data obtained in DMSO–water mixtures of different composition are not comparable. Thus values for rate coefficients for forward reactions and equilibrium constants are expected[1,5,15–18] to increase with increasing proportion of DMSO while values for reverse coefficients are expected to decrease.

In Table 10 we compare rate and equilibrium constants for reaction at the unsubstituted 2-position in substrates (1) and (4). The effect of the 4-chloro substituent is to reduce equilibrium constants by factors ranging from 3.1 with $X = NO_2$ to 4.9 with $X = CF_3$; rate coefficients for hydroxide attack are reduced and rate coefficients for hydroxide expulsion are increased. The polar effect of the chlorine substituent would be expected to encourage attack at the 2-position. However, the results indicate that this is not the dominant factor so that the steric effect of the chlorine is more important. Thus the nitro-groups at the 3- and 5-positions will be forced from the ring-plane so that they cannot exert their maximum electron-withdrawing influence.[2] For comparison the value, 2.6 l mol^{-1}, for the equilibrium constant for reaction of methoxide ions in methanol at unsubstituted ring positions of picryl chloride[20] is lower by a factor of 4.4, after statistical correction, than the value, 17 l mol^{-1}, for the corresponding reaction of 1,3,5-trinitrobenzene.[5] The relative constancy of the values of the ratio $K_2(\mathbf{1})/K_2(\mathbf{4})$ in Table 10 indicates that the steric situation around the 1-position in the chloro-compounds is not much affected by the nature of the X-substituent.

The data in Table 10 do not allow direct comparison of the effects of the substituents X on K_2 values since they were measured in solvents of different composition. We would expect[2] values in each series, measured in a common solvent, to fall in the order $X = NO_2 > X = CF_3 > X = H$ reflecting the decreasing electron-withdrawing power of the substituent.[21] However, for compounds with $X = CO_2^-$ and H measurements relate to 95% DMSO and are thus directly comparable. They show that the presence of the CO_2^- group greatly reduces the values of rate and equilibrium constants for hydroxide attack at the *ortho*-position, an effect which may be attributed to the unfavourable electrostatic and steric interaction of the substituent with the incoming hydroxide ion.[21]

Perhaps the most interesting comparison is that in Table 11 which shows the effect of the chloro-substituent on the rate of *ipso*-attack by hydroxide. For similarly activated systems the effect of the chloro-substituent is to reduce the rate of hydroxide attack by factors ranging from 32 ($X = NO_2$) to 104 ($X = CF_3$). There are several factors to consider. The inductive effect of the chlorine atom should increase the rate of hydroxide attack. However, as mentioned previously, the chlorine will disrupt the planarity of the adjacent nitro-groups thus reducing their electron-withdrawing effect. This latter effect might be expected to reduce the rate of hydroxide attack by a factor of 2—4 (*cf.* Table 10). Probably the major effect is, however, the steric and electrostatic repulsion between the chloro-substituent and the approaching hydroxide ion.[8,22] In compounds of structure (**4**) each containing a chlorine substituent flanked by nitro-groups this effect should, as observed, remain essentially constant.

We also compare, in Table 12, the rate and equilibrium constants for attack at the 2- and 4-positions of 1-X-3,5-dinitrobenzenes. The importance of a strongly electron-withdrawing group *para* to the position of attack has been noted in studies of σ-adduct formation.[2] This effect is shown here by the increase in values of the ratio K_2/K_4 as the electron-withdrawing power of the X substituent decreases in the series NO_2, CF_3, H. The ratio for (**1**; $X = CO_2^-$) is out of sequence and is lower than expected on the basis of the electron-withdrawing power of the CO_2^- group.[21] The likely explanation is that the negative charge on the *ortho*-substituent results in a reduction in the value for K_2 here. In agreement with previous kinetic[6] and n.m.r. results[3] we find that values of k_4 are only slightly higher than values of k_2, showing that there is little kinetic discrimination in hydroxide attack at the three ring positions, but values of k_{-4} are much higher than corresponding values for k_{-2}.

Conclusions.—The kinetic results indicate that there is little discrimination in the rates of hydroxide attack at the three unsubstituted ring positions in (**1**). The presence in (**4**) of the chlorine atom results in a general reduction in the rates of nucleophilic attack, the effect being particularly large for *ipso*-reaction (attack at the 4-position). Hence adducts (**5**) are initially observed from the reaction of (**4**) with hydroxide. The presence in (**4**; $X = CO_2^-$) of the charged group results in a reduction in the value of k_2 for attack at the *ortho*-position so that here reaction with hydroxide yields, initially, a mixture of (**5**) and (**7**). There is no evidence in these systems for the build up of spectroscopically observable concentrations of intermediates (**6**) on the reaction pathway.

Experimental

Parent molecules were recrystallised commercial specimens or were available from previous work.[5] Visible spectra and kinetic measurements were made at 25 °C using a Hi-Tech SF 3L stopped-flow spectrophotometer, or a Pye–Unicam SP8-100 recording spectrometer. 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 satisactory to have solvents of the same composition in the two compartments. Tetramethylammonium hydroxide was a commercial sample supplied as a concentrated solution (2.7M) in water; due account was taken of the water content of the base when making dilute solutions in mixed solvents. Stock solutions of parent chloro compounds (**4**) were unstable in media rich in DMSO and fresh solutions were prepared as required.

References

1 Part 40, M. R. Crampton and C. Greenhalgh, *J. Chem. Soc., Perkin Trans. 2*, 1985, 599.

2 For reviews of σ-adduct formation see: M. R. Crampton, *Adv. Phys. Org. Chem.*, 1969, **7**, 211; M. J. Strauss, *Chem. Rev.*, 1970, **70**, 667; F. Terrier, *ibid.*, 1982, **82**, 77; G. A. Artamkina, M. P. Egorov, and I. P. Beletskaya, *ibid.*, 1982, **82**, 427; E. Buncel, M. R. Crampton, M. J. Strauss, and F. Terrier, 'Electron Deficient Aromatic- and Heteroaromatic–Base Interactions,' Elsevier, Amsterdam, 1984.

3 C. A. Fyfe, M. Cocivera, and S. W. H. Damji, *J. Am. Chem. Soc.*, 1975, **97**, 5707.

4 F. Terrier and F. Millot, *Tetrahedron Lett.*, 1971, 2933.

5 M. R. Crampton and H. A. Khan, *J. Chem. Soc., Perkin Trans. 2*, 1972, 733; 1973, 710.

6 F. Millot and F. Terrier, *Bull. Soc. Chim. Fr.*, 1974, 1823.

7 M. R. Crampton, M. A. El Ghariani, and H. A. Khan, *Tetrahedron*, 1972, **28**, 3299.

8 B. Gibson and M. R. Crampton, *J. Chem. Soc., Perkin Trans. 2*, 1979, 648.

9 Y. Hasegawa and T. Abe, *Chem. Lett.*, 1972, 985; *Bull. Chem. Soc. Jpn.*, 1973, **46**, 2756; Y. Hasegawa, *ibid.*, 1974, **47**, 2186.

10 K. Bowden and R. S. Cook, *J. Chem. Soc. B*, 1071, 1771.

11 J. F. Bunnett, M. Gisler, and H. Zollinger, *Helv. Chim. Acta*, 1982, **65**, 63.

12 Y. Hasegawa, *Chem. Lett.*, 1983, 129.

13 C. F. Bernasconi, 'Relaxation Kinetics,' Academic Press, New York, 1976.

14 C. F. Bernasconi and K. A. Howard, *J. Am. Chem. Soc.*, 1982, **104**, 7248.

15 A. P. Chatrousse, F. Terrier, and R. Schaal, *J. Chem. Res.*, 1977, (*S*) 228, (*M*) 2413.

16 W. L. Hinze, L.-J. Liu, and J. H. Fendler, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1751.

17 D. N. Brooke and M. R. Crampton, *J. Chem. Res.*, 1980, (*S*) 340, (*M*) 4401.

18 D. N. Brooke and M. R. Crampton, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1850.

19 C. F. Bernasconi, *J. Am. Chem. Soc.*, 1970, **92**, 4682.

20 L. H. Gan and A. R. Norris, *Can. J. Chem.*, 1974, **52**, 18.

21 G. B. Barlin and D. D. Perrin, *Chem. Soc. Quart. Rev.*, 1966, **20**, 75.

22 G. Bartoli and P. E. Todesco, *Acc. Chem. Res.*, 1977, **10**, 125.

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