The Stabilities of Meisenheimer Complexes. Part 15.[1] The Interactions of 2,4,6-Trinitrobenzenesulphonate Ions with Sodium Sulphite and with Sodium Hydroxide in Water

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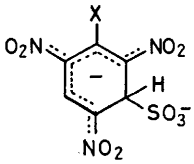
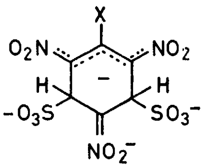
In the presence of aqueous sodium sulphite 2,4,6-trinitrobenzenesulphonate ions give 1 : 1 and 1 : 2 adducts by sulphite addition at unsubstituted ring positions; kinetic and equilibrium data are reported. It is shown that the initial fast reaction of 2,4,6-trinitrobenzenesulphonate ions with aqueous sodium hydroxide results in hydroxide attack at the unsubstituted 3-position, and that ionisation of the added hydroxy-group occurs. The slower addition of hydroxide at the 1-position leads to nucleophilic substitution giving picrate ions and the observation of base catalysis in this reaction is discussed.

THE reactions of 1-X-2,4,6-trinitrobenzenes with sodium sulphite [2-4] or with sodium hydroxide [5-7] in water usually result in the initial formation of 1 : 1 and 1 : 2 σ-complexes by nucleophilic addition at unsubstituted ring positions. Thus, with sulphite as nucleophile, complexes with structures (I) and (II) are formed. When the 1-substituent is a poor leaving group (X = H, O^-, NH_2, NMe_2, *etc.*) the complexes are time stable. When X is labile, *e.g.* Cl, nucleophilic substitution eventually occurs [8,9] although again the observed σ-complexes have structures (I) and (II).


(I)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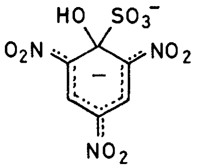

(III)

Bunton *et al.*[10] have recently made a kinetic study of the reaction of 2,4,6-trinitrobenzenesulphonic acid with aqueous sodium hydroxide to give picric acid. Reaction is likely to proceed *via* the intermediate (III). They found an increase with base concentration of the second-order rate constant which they interpreted as base catalysis of decomposition of the intermediate, and in aqueous dimethyl sulphoxide observed a coloured species which they thought might be the intermediate (III).

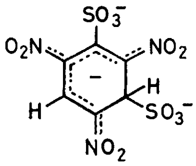
2,4,6-Trinitrobenzenesulphonic acid is of particular interest as it is widely used [11] as a reagent for the determination of amino-groups in amino-acids and proteins. We report here a study of the reversible reactions of this substrate with aqueous sodium sulphite and with sodium hydroxide in which we find that as with most other 1-X-2,4,6-trinitrobenzenes the initially formed and observable σ-complexes result from nucleophilic attack at unsubstituted ring positions.

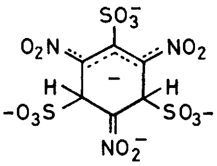
RESULTS AND DISCUSSION

Because of its high acid dissociation constant, solutions in water or alkaline media of 2,4,6-trinitrobenzenesulphonic acid will be very largely dissociated to 2,4,6-trinitrobenzenesulphonate ions.

Interactions with Sodium Sulphite.—Visible spectra in water indicate the presence of two equilibria between 2,4,6-trinitrobenzenesulphonate ions and sodium sulphite. At low sulphite concentrations (<0.1M) a pink species, $\lambda_{max.}$ 500 nm, is produced while in more concentrated sulphite solutions the rapid formation of the pink species is followed by formation of a yellow species with $\lambda_{max.}$ 395 nm. Both reactions are reversible. ^1H N.m.r. spectra show that these species have structures (IV) and (V) respectively.

The ^1H n.m.r. spectrum of the 2,4,6-trinitrobenzenesulphonate ion in water or deuterium oxide shows a single sharp peak at δ 8.97 due to the two equivalent ring protons. Spectra with added sodium sulphite were measured in deuterium oxide to minimise solvent peaks.


(IV)


(V)

They showed a sharp singlet at δ 5.95 attributed [2,4] to the ring protons of (V). There was no evidence for *cis–trans* isomerism in this adduct.[3,4] In water the equilibrium concentration of (IV) was too low to allow its detection by n.m.r. However in a hexadeuteriodimethyl sulphoxide–deuterium oxide mixture (60 : 40 v/v) containing sodium sulphite two doublets (J 1.5 Hz) were observed at δ 8.45 and 5.95 from the ring protons of (IV). Visible spectra indicate that in dimethyl sulphoxide–water mixtures the pink 1 : 1 adduct is preferentially formed; the change with solvent in the relative stability of the

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[1] Part 14, M. R. Crampton, *J.C.S. Perkin II*, 1977, 1442.

[2] M. R. Crampton, *J. Chem. Soc.* (*B*), 1967, 1341.

[3] C. F. Bernasconi and R. G. Bergstrom, *J. Amer. Chem. Soc.*, 1973, **95**, 3603.

[4] M. R. Crampton and M. J. Willison, *J.C.S. Perkin II*, 1976, 160.

[5] M. R. Crampton and V. Gold, *J. Chem. Soc.* (*B*), 1966, 893.

[6] M. R. Crampton and M. A. El Ghariani, *J. Chem. Soc.* (*B*), 1969, 330.

[7] C. F. Bernasconi and R. G. Bergstrom, *J. Amer. Chem. Soc.*, 1974, **96**, 2397.

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

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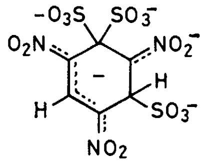
[10] C. A. Bunton, Y. Ihara, and J. L. Wright, *J. Org. Chem.*, 1976, **41**, 2520.

[11] C. L. Parrott and S. Shifrin, *Biochimica Biophysica Acta*, 1977, **491**, 114; C. A. Adams, T. C. Robberts and K. C. Butler, *Analyt. Biochem.*, 1976, **70**, 181; S. L. Snyder and P. Z. Sobocinski, *ibid.*, 1975, **64**, 284; A. Eklund, *ibid.*, 1976, **70**, 434.

complexes reflecting their different solvation requirements.[2] The n.m.r. spectra do not in themselves rule out structures for the complexes in which sulphite addition occurs at C-1 as well as at the unsubstituted ring positions [*e.g.* (VI)]. However, this possibility is eliminated by the kinetic and equilibrium data below, which show that the complexes contain one and two sulphite ions respectively.



(VI)

Kinetic measurements were made in water by the stopped-flow spectrophotometric method and showed the presence of two well separated relaxation times. Most measurements were made at 500 nm, where the rapid formation of colour was followed by a slower fading process, although some measurements were made at 400 nm where both processes gave increases in absorption. The measured relaxation times were independent of the wavelength of measurement. The data in Table 1 were obtained in solutions maintained at constant ionic strength 0.3 or 2.1M with sodium sulphate. They are in accord with processes involving one and two sulphite ions so that equations (1) and (2) will apply.[3,4]

$$1/\tau_1 = k_{-1} + k_1[SO_3^{2-}] \quad (1)$$

$$1/\tau_2 = k_{-2} + k_2K_1[SO_3^{2-}]^2/(1 + K_1[SO_3^{2-}] \quad (2)$$

TABLE 1

Kinetic and equilibrium data for formation of sulphite adducts from 2,4,6-trinitrobenzenesulphonate in water at 25°

$[Na_2SO_3]/M$	$[Na_2SO_4]/M$	τ_1^{-1}/s^{-1}	O.D.[a] (500 nm)	K_1/l mol^{-1}	τ_2^{-1}/s^{-1}	τ_2^{-1}(calculated)
0.02	0.08	44 ± 1	0.011	1.2		
0.04	0.06	44.5	0.024	1.3		
0.06	0.04	47	0.037	1.4		
0.08	0.02	48	0.046	1.3		
0.10	0	48	0.055	1.4		
0.02	0.68	45	0.026	2.9	0.16 ± 0.01	0.16
0.04	0.66	47	0.050	2.9	0.20	0.22
0.06	0.64	50.5			0.27	0.30
0.10	0.60	57	0.100	2.6	0.48	0.55
0.20	0.50	70	0.180	3.0	1.4	1.5
0.30	0.40		0.230	3.2	2.7	2.7
0.40	0.30		0.275	3.3	4.3	4.1
0.50	0.20		0.295	3.2	5.8	5.6
0.70	0		0.340	3.4	8.7	8.7

[a] Optical density at 500 nm for 3.6×10^{-5}M substrate after completion of fast colour forming reaction. For 1 cm pathlength.

Plots according to equation (1) of τ_1^{-1} *versus* sulphite concentration were linear and gave values at I 0.3M of k_1 60 ± 10 l mol^{-1} s^{-1} and k_{-1} 42 ± 2 s^{-1}, leading to K_1 1.4 ± 0.3 l mol^{-1}; and at I 2.1M of k_1 140 ± 20 l mol^{-1} s^{-1}, k_{-1} 42 ± 2 s^{-1} leading to K_1 3.3 ± 0.6 l mol^{-1}. An independent check on these values of K_1 is afforded by measurements (stopped-flow) at 500 nm of the optical densities after completion of the faster process. A Benesi–Hildebrand[12] plot of this optical density data gave an extinction coefficient of 1.35×10^4 l mol^{-1} cm^{-1}. The equilibrium constants thus calculated (Table 1) are in good agreement with the values calculated from kinetic data.

The variation with sulphite concentration of τ_2 at I 2.1M is well accommodated by equation (2) with k_2 18 l mol^{-1} s^{-1}, k_{-2} 0.14 ± 0.02 s^{-1} and K_1 3.0 l mol^{-1}. Thus K_2 has the value 130 ± 20 l mol^{-1}.

Due to the high charges of adducts (IV) and (V) the values of K_1 and K_2 increase with increasing ionic strength.[4] The value of 1.4 l mol^{-1} for K_1 at I 0.3M is similar to that for sulphite addition to the picrate ion[4] where the value is 2.5 l mol^{-1}. Both these values are considerably smaller than those for sulphite addition to uncharged 1-X-2,4,6-trinitrobenzenes. The value for K_2 is also similar to that for picrate ion (60 l mol^{-1}).

Interactions with Sodium Hydroxide.—In agreement with Bunton *et al.* we find that in aqueous sodium hydroxide solutions 2,4,6-trinitrobenzenesulphonate ions are fairly quickly converted to picrate ions ($\lambda_{max.}$ 355 nm). These workers observed the formation in dimethyl sulphoxide–water mixtures (65 : 35 v/v) of a coloured species ($\lambda_{max.}$ 505 nm). We find that a red species, $\lambda_{max.}$ 495 nm, is also observable during the reaction in water and the visible spectrum determined using stopped-flow spectrophotometry is shown in the Figure. It seems very probable that the same species is present in both media, the small bathocromic shift in solutions containing dimethyl sulphoxide being consistent with similar shifts in related compounds.[13]

The visible spectrum is very similar to that of the 1 : 1 adduct (IV) observed with sulphite and quite different from that of the 1 : 2 sulphite adduct (V). This argues strongly that the species is formed by addition at only one ring position. However, since the visible spectra of adducts formed by hydroxide addition at C-3 or at C-1 would be expected to be similar the observed spectrum does not allow a distinction to be made between these

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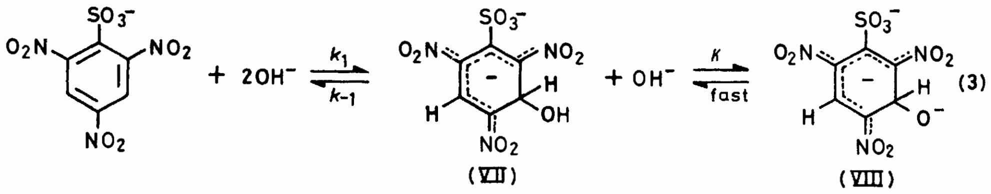
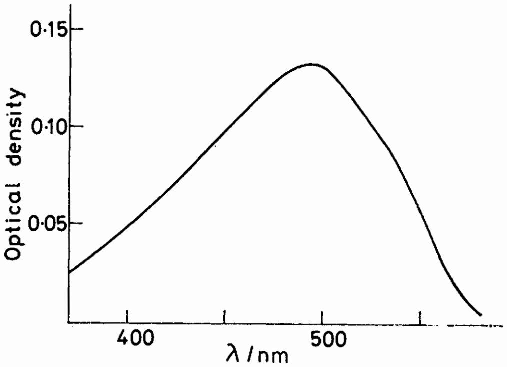
[12] H. A. Benesi and J. H. Hildebrand, *J. Amer. Chem. Soc.*, 1949, **71**, 2703.

[13] M. R. Crampton, *J.C.S. Perkin II*, 1973, 2157; M. R. Crampton and M. J. Willison, *ibid.*, 1976, 155.

possibilities. ^{1}H N.m.r. measurements were unhelpful because of the short lifetime of the complex. Nevertheless we will show later that the kinetic data are in better accord with addition at C-3.





Visible spectrum, determined by stopped-flow spectrophotometry, of the adduct initially produced from 2,4,6-trinitrobenzenesulphonate (8 × 10^{-5}M) and sodium hydroxide (0.5M) in water

Examination by stopped-flow spectrophotometry of the system in water shows the presence of two time dependent processes; a fast reaction producing the red species and a slower reaction giving the picrate ion.

Data corresponding to the faster process, determined with I 1M, are in Table 2. They are unusual in that increases in base concentration cause increases in the relaxation time (*i.e.* decreases in rate coefficient) and increases in value of the measured equilibrium constant. These effects are explained by the sequence of reactions in equation (3) in which hydroxide addition to give adduct (VII) is followed by a rapid equilibrium involving proton transfer from the added hydroxy-group to a second hydroxide ion.

The variation with hydroxide ion concentration of the relaxation time is given by equation (4). It turns out that in solutions where [NaOH] < 0.4M the k_1[NaOH] term can be neglected so that here equation (5) will apply. A plot of τ *versus* [NaOH] gave a good straight line whose intercept and slope yielded values for k_{-1} 45 ± 5 s^{-1} and K 32 ± 4 l mol^{-1}. The values of τ in

$$1/\tau = k_1[\text{NaOH}] + k_{-1}/(1 + K[\text{NaOH}]) \quad (4)$$

$$\tau = 1/k_{-1} + K[\text{NaOH}]/k_{-1} \quad (5)$$

more concentrated solutions gave a value for k_1 0.8 ± 0.1 l mol^{-1} s^{-1} which when combined with the value for k_{-1} gave K_1 0.018 ± 0.005 l mol^{-1}.

The variation of the measured equilibrium constant with base is given by equation (6). Although the extinction coefficient of the complex in water could not

$$K_c = K_1(1 + K[\text{NaOH}]) \quad (6)$$

be directly determined, measurements in dimethyl sulphoxide–water gave a value of 1.75 × 10^4 l mol^{-1} cm^{-1} and this value was used here. The assumption is made that the spectra of (VII) and (VIII) are similar, although except in the most dilute base solutions the complex will be largely in the form of (VIII). Values of K_c calculated using equation (6) with K_1 0.018 l mol^{-1} and K 32 l mol^{-1} are in good agreement with the experimental values. These are of course the values at I 1M and are higher than the thermodynamic equilibrium constants.

TABLE 2

Kinetic and equilibrium data for hydroxide ion addition to 2,4,6-trinitrobenzenesulphonate (TNBS) in water at 25°

[NaOH]^a/M	10^5[TNBS]/M	τ^{-1}/s^{-1}	τ^{-1}(calculated)^d	O.D.^{b} (495 nm)	$K_c{}^c$/l mol^{-1}	$K_c{}^d$(calculated)
0.02	400	28	27	0.040	0.029	0.029
0.035	400	21.5	21	0.090	0.037	0.038
0.07	80	14.4	14	0.051	0.053	0.058
0.10	80	11.3	10.8	0.100	0.072	0.075
0.20	16	6.3	6.3	0.075	0.14	0.14
0.40	8	3.3	3.7	0.133	0.26	0.25
0.60	4	2.5	2.7	0.138	0.41	0.37
0.80	1.6	2.2	2.3	0.082	0.51	0.48
1.00	1.6	2.3	2.2	0.114	0.68	0.60

[a] Solutions made up to constant ionic strength I 1.0M with sodium chloride. [b] After completion of fast process. For 1 cm cells. [c] Defined as O.D.(495 nm)/[NaOH]{[TNBS]$_{\text{stoich}}$ × 1.75 × 10^4 − O.D.(495 nm)}. [d] Calculated with k_1 0.8 l mol^{-1} s^{-1}, k_{-1} 45 s^{-1}, K_1 0.018, and K 32 l mol^{-1}.

Although the possibility of the ionisation of added hydroxy-groups in σ-complexes was suggested by Gold and Rochester[14] there has previously been no direct evidence for such ionisation in adducts derived from 1-X-2,4,6-trinitrobenzenes. However, it was found

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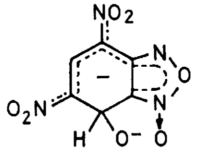
[14] V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1964, 1727.

recently[15] that the hydroxide adduct of 4,6-dinitrobenzofuroxan ionises in aqueous base to give the dianion (IX).



(IX)

The observed value for k_1, 0.8 l mol^{-1} s^{-1}, is 20 times larger than the value, 0.045 l mol^{-1} s^{-1}, found by Bunton *et al.*[10] for hydroxide ion attack at the 1-position of 2,4,6-trinitrobenzenesulphonate ions to give (III). This large difference clearly shows that the red species we have observed is (VII) and not (III). The slower rate of addition at Cl than at the unsubstituted ring positions is in line with previous results [8,9] and can be rationalised in terms of repulsion between entering and leaving groups.[16]

In Table 3 addition of hydroxide ions and sulphite ions to two substrates are compared. The data show that the sulphite adducts have considerably higher thermodynamic stabilities than the hydroxide adducts. Comparison of the k_{-1} values indicates that for 1,3,5-trinitrobenzene sulphite is a considerably better leaving group than is hydroxide although for 1,4,6-trinitrobenzenesulphonate the nucleofugicities are similar. Although these results refer to addition at unsubstituted ring positions they do suggest that the rates of cleavage of hydroxide ions and sulphite ions from (III) might not be too dissimilar. Hence the observation of base catalysis is a possibility. Ionisation of the hydroxy-group in (III) would provide a mechanism for such catalysis.

In fact Bunton *et al.*[10] found that the second-order rate coefficient for nucleophilic substitution of sulphite by hydroxide in 2,4,6-trinitrobenzenesulphonate doubled in the base concentration range 0—0.5M and interpreted this as base catalysis. However, addition of hydroxide ions to 2,4,6-trinitrobenzenesulphonate ions involves two negatively charged species so that rate increases similar to those found would be predicted purely from ionic strength effects. It is noteworthy that in solutions of constant ionic strength they found a very much smaller (15%) increase in rate coefficient. It thus seems probable that hydroxide ion addition is very largely rate limiting in the nucleophilic substitution reaction.

TABLE 3

Kinetic and equilibrium data for the addition of hydroxide ions and sulphite ions to unsubstituted ring positions of 1,3,5-trinitrobenzene and 2,4,6-trinitrobenzenesulphonate ions in water at 25°

	Hydroxide adducts			Sulphite adducts		
	k_1/l mol^{-1} s^{-1}	k_{-1}/s^{-1}	K_1/l mol^{-1}	k_1/l mol^{-1} s^{-1}	k_{-1}/s^{-1}	K_1/l mol^{-1}
1,3,5-TNB	37.5	9.8	3.8 [a]	3.5×10^4	125	290 [b]
2,4,6-TNBS	0.8	45	0.018 [c]	60	42	1.4 [d]

[a] Ref. 17. [b] Ref. 3. [c] Present work, *I* 1M. [d] Present work, *I* 0.3M.

EXPERIMENTAL

2,4,6-Trinitrobenzenesulphonic acid was obtained from B.D.H. Ltd. Aqueous solutions of sodium sulphite and sodium hydroxide were prepared from AnalaR reagent with carbon dioxide free water. ^{1}H N.m.r. measurements were made with Varian 60 MHz and Brüker 90 MHz instruments. In water and in deuterium oxide sodium 4,4-dimethyl-4-silapentane-1-sulphonate was used as internal reference. In water–dimethyl sulphoxide mixtures the reference was tetramethylsilane.

Kinetic measurements were made by mixing aqueous solutions of reagents in a Canterbury stopped-flow apparatus described previously.[13] All measurements were at 25°. Rate constants were reproducible to ±3%.

[7/1220 *Received*, 11*th July*, 1977]

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[15] F. Terrier, F. Millot, and W. P. Norris, *J. Amer. Chem. Soc.*, 1976, **98**, 5883.

[16] G. Bartoli and P. E. Todesco, *Accounts Chem. Res.*, 1977, **10**, 125.

[17] C. F. Bernasconi, *J. Amer. Chem. Soc.*, 1970, **92**, 4682.