Mechanism of the alkaline hydrolysis of *O*-ethyl *S*-(2,4,6-trinitrophenyl) thio- and dithiocarbonates

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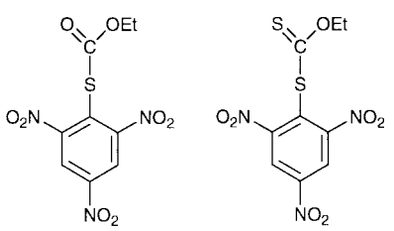
The alkaline hydrolysis of *O*-ethyl *S*-(2,4,6-trinitrophenyl) thio- and dithiocarbonates, **1** and **2**, respectively, were studied kinetically in 5% dioxane in water, at 25.0 °C, and ionic strength 0.2 mol dm^{-3} (KCl). Two kinetic processes, well separated in time, were detected. The fast process involves the formation of a σ-complex by addition of HO$^-$ to one of the unsubstituted positions of the aromatic ring, followed by fast ionisation of this complex. The slow process leads to the formation of a mixture of 2,4,6-trinitrophenoxide and 2,4,6-trinitrobenzenethiolate ions in a 10:1 ratio, respectively, in the reaction of **2**, and to a mixture in a 2:1 ratio in the reaction of **1**, independent of KOH concentration. Although the substrates show different kinetic behaviour with KOH concentration, the results can be discussed on the basis of a common reaction mechanism.

Introduction

Although the aminolysis reactions of thio- and dithiocarbonates have received some attention,[1,2] little is known about the mechanism of the basic hydrolysis of these compounds.[3] We have recently examined the reactions of *O*-ethyl *S*-(2,4,6-trinitrophenyl) thiocarbonate, **1**, and *O*-ethyl *S*-(2,4,6-trinitrophenyl) dithiocarbonate, **2**, with secondary alicyclic amines and pyridines.[2] We have found that, under all conditions, the reactions lead mainly to the aminolysis products and only in the reactions of **1** with nicotinamide[2c] and **2** with 3-chloropyridine[2d] and piperazinium ion,[2a] was the hydrolysis reaction detected. Likewise in the reactions of **1** with anilines and phenoxide ions the hydrolysis reaction was of minor importance compared to the aminolysis or phenolysis reactions.[4] In all these reactions[2,4] the main reaction product is that corresponding to nucleophilic attack on the carbonyl or thiocarbonyl group with no indication, within the detection limits, of nucleophilic aromatic substitution. Since **1** and **2** have an aromatic ring strongly activated for nucleophilic aromatic substitution,[5] we considered it to be of interest to study the hydrolysis reaction of these compounds in order to see if we could detect the formation of Meisenheimer intermediates which are often observed in other reactions of trinitrophenyl derivatives with various substituents in the 1-position.[6–10] Therefore, in the present work we carry out a kinetic study of the hydrolysis of **1** and **2**. In fact, both compounds give substitution on the aromatic ring and in both cases this is the predominant reaction. Besides, addition of HO$^-$ to an unsubstituted position of the aromatic ring takes place and the Meisenheimer complex formed, and its conjugate base, can be detected at short reaction times.



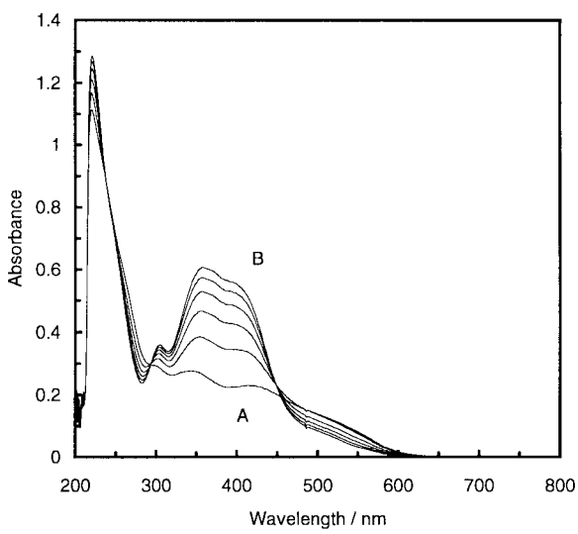


Fig. 1 Spectra for the hydrolysis of **1** in basic solution at different reaction times. [HO$^-$] = 0.1 mol dm^{-3}, time interval 1 s, first cycle (A).

Results

Reactions of *O*-ethyl *S*-(2,4,6-trinitrophenyl) thiocarbonate, 1

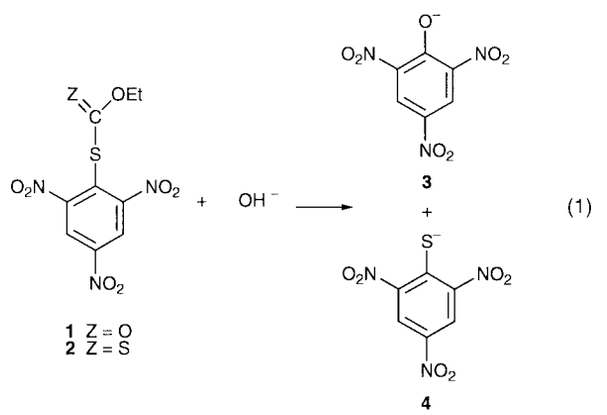
The spectrum of **1** in 5% dioxane in water showed no absorption in the visible region. When KOH was added a coloured species was rapidly formed. The spectrum of the reaction mixture showed an increase in absorbance beyond 450 nm. After 1 s (in the reaction with KOH 0.2 mol dm^{-3}), two isosbestic points developed, one around 290 nm and another at 450 nm with a broad absorption band between them (Fig. 1).

Two kinetic processes, well separated in time, were measured at 400 nm. The results are summarised in Table 1. Analysis of the products gave 67% of 2,4,6-trinitrophenoxide ion (**3**) and 33% of 2,4,6-trinitrobenzenethiolate ion (**4**), eqn. (1). The ratio

Table 1 Values of the rate constants for the alkaline hydrolysis of **1** for the fast (k_{fast}) and the slow (k_{slow}) processes[a]

[KOH]/mol dm^{-3}	k_{fast}/s^{-1}[b] (400 nm)	k_{slow}/s^{-1}[c] (400 nm)
0.010		0.037 ± 0.003
0.040	11 ± 1	0.148 ± 0.001
0.050	8.1 ± 0.6	
0.070		0.274 ± 0.001
0.100	14.0 ± 0.5	0.40 ± 0.02
0.125	17 ± 1	
0.130		0.47 ± 0.02
0.150	19 ± 0.9	
0.160	21 ± 2	0.58 ± 0.05
0.190	28 ± 2	
0.200	25.2 ± 0.9	0.71 ± 0.06

[a] Solvent: 5% dioxane in water, temperature 25.0 °C, ionic strength 0.2 mol dm^{-3}. [b] Errors represent the deviation of the mean of 5–10 determinations. [c] Errors are the standard deviation of the absorbance *vs.* time plot from a single exponential.



(1)

[3]:**[4]** = 2:1 was independent of HO^- concentration, within experimental error.

Reaction of *O*-ethyl *S*-(2,4,6-trinitrophenyl) dithiocarbonate, 2

The spectrum of this substrate in 5% dioxane in water showed a band at 270 nm. When KOH was added, the first spectrum that could be taken after mixing showed a decrease in absorbance at 270 nm and an increase in absorbance at 500 nm (Fig. 2, line A). Thereafter, two isosbestic points were observed, at 285 and 430 nm, with an increase in absorbance between them. The band at 270 nm and the absorbance beyond 430 nm also decreased (Fig. 2).

At 480 nm, two kinetic processes were measured while at 300 nm there was only one, which corresponds to the slowest observed at 480 nm. Since the absorbance changes at 480 nm were too small, better results were obtained from the absorbance changes at 300 nm, which correspond to the maximum absorption of potassium *O*-ethyl dithiocarbonate. Both processes exhibit a nonlinear dependence on KOH concentration (Table 2). Products analysis gave 91% of **3** and 9% of **4**. The ratio **[3]**:**[4]** = 10:1 was independent of the HO^- concentration, within experimental error.

Discussion

The fast absorbance increase observed beyond 450 nm for the reaction of **1** and beyond 430 nm for that of **2** is consistent with a mechanism involving the formation of a σ-complex by addition of hydroxide ion to one of the unsubstituted positions of the aromatic ring (Scheme 1).

Similar adducts have been reported in related systems. Some examples are the hydrolysis reactions of 2,4,6-trinitrophenyl aryl sulfides and the corresponding ethers,[9a] and 1-amino-2,4-dinitrobenzenes.[10] For this mechanism two relaxation times may be expected,[11] however only one (k_{fast} in Tables 1 and 2) is observable since the proton transfer will be a very rapid equilibrium on the stopped-flow timescale. Assuming that the process observed corresponds to the formation of **5**, in rapid equilibrium with **6** or **7**, the observed rate constant is given by eqn. (2).

Table 2 Values of the rate constants for the alkaline hydrolysis of **2** for the fast (k_{fast}) and the slow (k_{slow}) processes[a]

[KOH]/mol dm^{-3}	k_{fast}/s^{-1} (480 nm)	k_{slow}/s^{-1} (480 nm)	k_{slow}/s^{-1} (300 nm)
0.011			0.072 ± 0.003
0.019	5.47 ± 0.03	0.142 ± 0.007	0.141 ± 0.005
0.040		0.338 ± 0.009	0.281 ± 0.003
0.049	5.64 ± 0.09		
0.060	5.9 ± 0.04	0.373 ± 0.004	0.39 ± 0.02
0.079	6.1 ± 0.1	0.45 ± 0.01	0.49 ± 0.02
0.100	6.1 ± 0.1	0.494 ± 0.006	0.55 ± 0.01
0.119	6.63 ± 0.04	0.510 ± 0.006	
0.120			0.65 ± 0.02
0.139			0.66 ± 0.02
0.140	6.9 ± 0.3	0.52 ± 0.01	
0.159			0.67 ± 0.03
0.160	7.64 ± 0.07	0.524 ± 0.005	
0.180		0.53 ± 0.01	0.67 ± 0.04
0.190	8.34 ± 0.07		
0.193	8.5 ± 0.2		

[a] Solvent 5% dioxane in water, temperature 25.0 °C, ionic strength 0.2 mol dm^{-3}. Errors are the standard deviation of the absorbance *vs.* time plot from a single exponential.

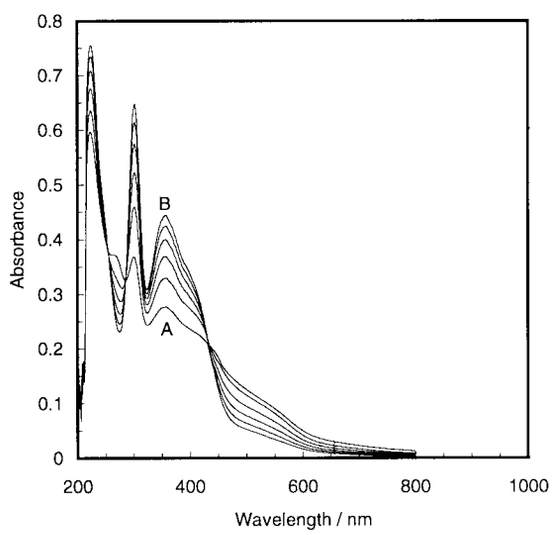


Fig. 2 Spectra for the hydrolysis of **2** in basic solution at different reaction times. [HO^-] = 0.1 mol dm^{-3}, time interval 1 s, first cycle (A).

$$k_{fast} = k_1[OH^-] + \frac{k_{-1}}{1 + K_2[OH^-]} \quad (2)$$

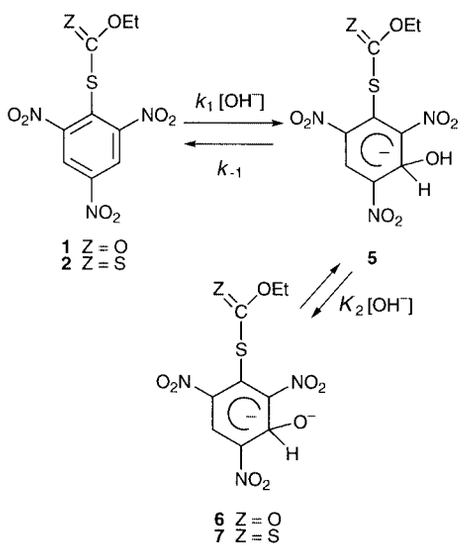
By fitting† the data to eqn. (2), the values of k_1, k_{-1} and K_2 for the reactions of **1** and **2** could be determined and from the two former values the equilibrium constant K_1 was also calculated; these values are collected in Table 3. Fig. 3 shows the plot of k_{fast} *vs.* [OH^-] for the reaction of **2**. The line was drawn through eqn. (2) with the data of Table 3, which shows the very good agreement between the experimental and calculated data. In Table 3, it can be seen that the K_2 value for the reaction of **2** is about 5 times greater than that of **1**, reflecting the higher acidity

† Sigmaplot, version 1.0, 1995.

Table 3 Calculated rate and equilibrium constants for the hydrolysis reactions of **1** and **2**[a]

	1	**2**
k_1/dm^3 mol^{-1} s^{-1}	114.2 ± 4	32.4 ± 0.6
k_{-1}/s^{-1}	4.1 ± 0.6	5.8 ± 0.2
K_1/dm^3 mol^{-1}	27.9 ± 4.2[b]	5.6 ± 0.2[b]
K_2/dm^3 mol^{-1}	1.6 ± 0.6	8.8 ± 0.8
$(k_3 + k'_3)$/dm^3 mol^{-1} s^{-1}	3.9 ± 0.4	8.3 ± 0.8
$(k_4 + k'_4)$/dm^3 mol^{-1} s^{-1}	4.3 ± 0.3	5.4 ± 1.0
$(k_5 + k'_5)$/dm^3 mol^{-1} s^{-1}	0.72 ± 0.5	0.13 ± 0.06
k_3; k'_3/dm^3 mol^{-1} s^{-1}	2.6; 1.3[c]	7.5; 0.8[d]
k_4; k'_4/dm^3 mol^{-1} s^{-1}	2.9; 1.4[c]	4.9; 0.5[d]
k_5; k'_5/dm^3 mol^{-1} s^{-1}	0.48; 0.24[c]	0.12; 0.01[d]

[a] Errors shown are standard errors. [b] Calculated as k_1/k_{-1}. [c] Assuming $k_3/k'_3 = k_4/k'_4 = k_5/k'_5$ = [**3**]/[**4**] = 2/1. [d] Assuming $k_3/k'_3 = k_4/k'_4 = k_5/k'_5$ = [**3**]/[**4**] = 10/1.

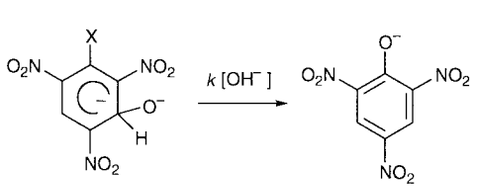


Scheme 1

of the dithio complex **5** (with Z = S). On the other hand, the value of k_1 is larger for the reaction of **1** than that of **2**, in agreement with the findings in aminolysis reactions: the thiol derivative **1** is more reactive than the dithio derivative **2**.[2a,b]

For the slow hydrolysis of **1** and **2** we suggest the mechanism depicted in Scheme 2. In this scheme, **1** and **2** have reached equilibrium with **5**. This mechanism is proposed on the basis of: i) the product analysis, which indicates that the nucleophilic reaction takes place at the aromatic as well as at the carbonyl (or thiocarbonyl) carbon; ii) the dependence of the rate constant on HO^- concentration; and iii) the mechanism just described for the fast process.

The upper part of Scheme 2 represents the attack of HO^- at the 1-aromatic carbon and the lower part of the scheme depicts its nucleophilic reaction at the carbonyl or thiocarbonyl centre. A similar reaction to that for the k_5 step of Scheme 2 is the reaction of the 1:1 Meisenheimer complex shown in eqn. (3),



(3)

which has been reported in the hydrolysis of 1-X-2,4,6-trinitrobenzenes.[12]

It should be noted that the paths with rate constants k_3, k'_3, k_4, k'_4, k_5 and k'_5 do not represent elementary steps. All the steps that lead to product **3** in Scheme 2 must involve the attack

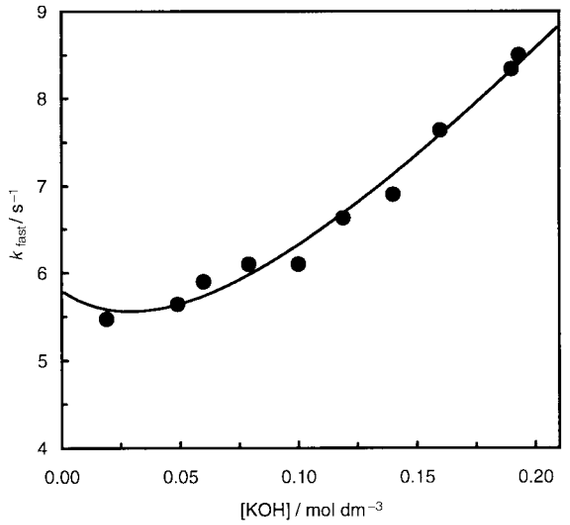
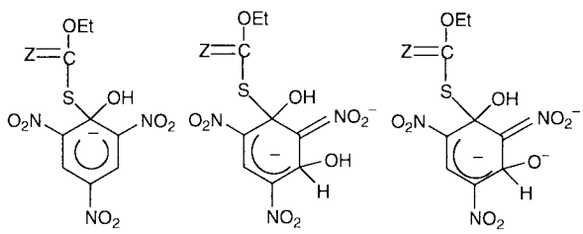


Fig. 3 Dependence of the rate constant for the fast process, k_{fast}, on the HO^- concentration for the hydrolysis of **2**. The line was calculated with eqn. (2) and the data of Table 3.



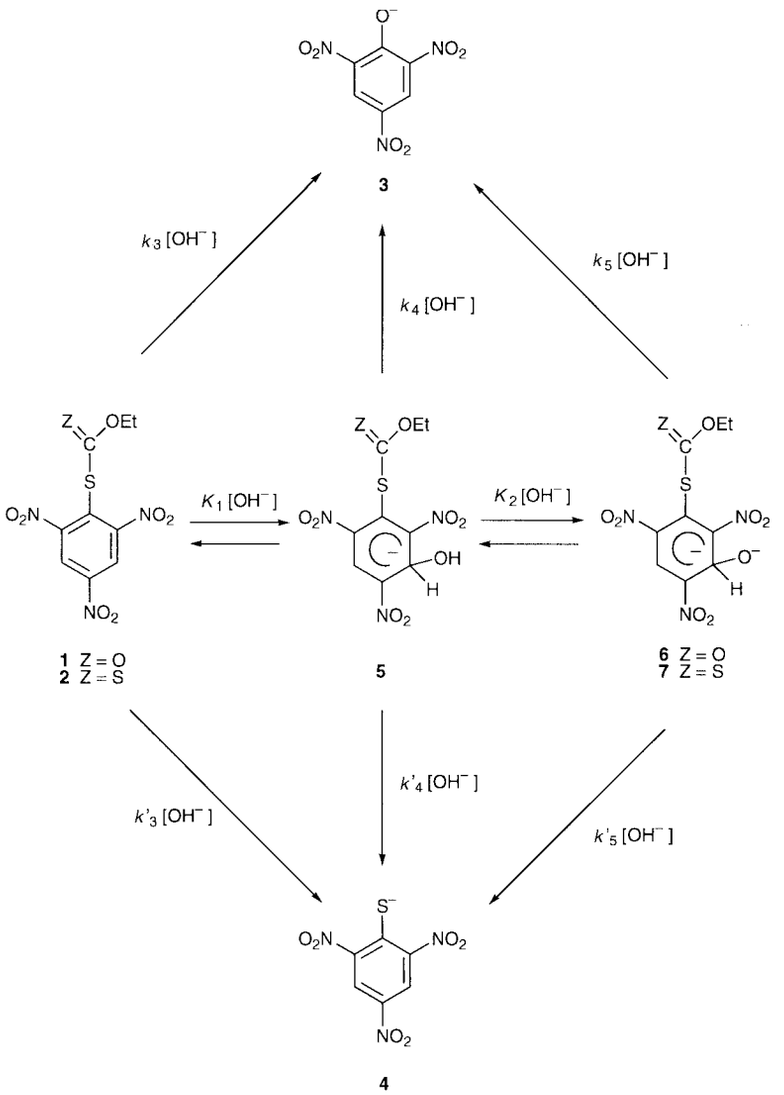
of HO^- on C-1 of the aromatic ring, and therefore, the formation of intermediates **8**, **9** and **10**. However, these intermediates do not accumulate under the reaction conditions and only an overall rate constant can be determined. Highly charged Meisenheimer complexes are not unusual in polar solvents. For instance, trinitrobenzene adds two sulfite ions giving a Meisenheimer complex with four negative charges.[13]

According to Scheme 2, the observed rate constant for the slow hydrolysis of **1** and **2** (k_{slow}), is given by eqn. (4).

$$k_{slow} = \frac{(k_3 + k'_3)[OH^-] + (k_4 + k'_4)K_1[OH^-]^2 + (k_5 + k'_5)K_1K_2[OH^-]^3}{1 + K_1[OH^-] + K_1K_2[OH^-]^2} \quad (4)$$

By fitting the k_{slow} *vs.* $[OH^-]$ data to eqn. (4) for the reactions of **1** and **2** the values of $(k_3 + k'_3)$, $(k_4 + k'_4)$ and $(k_5 + k'_5)$ could be determined; these are shown in Table 3. Fig. 4 shows the fitting of eqn. (4), using the values in Table 3, to the experimental points for the reaction of compound **1**. Assuming that the [**3**]:[**4**] ratios (2:1 and 10:1, for the reactions of **1** and **2**, respectively) reflect the rate constant ratios for the formation of **3** and **4**, all the rate microcoefficients in eqn. (4) can be calculated; they are also summarised in Table 3.

The ratio of the nucleophilic rate constants for attack at the aromatic/carbonyl carbons (k_{arom}/k_{co}) for **1** is lower (2:1) than the ratio k_{arom}/k_{cs} for **2** (10:1). This could be due to the fact that HO^- is a hard base that prefers to bind to the relatively hard CO group compared to the softer CS group.[14] The regioselectivity observed for these reactions contrasts that observed with amines where addition to the aromatic ring was never detected.[2] The different behaviour of amines and HO^- as nucleophiles may be attributed to the higher steric effect in the reactions of the amines which are bulkier than HO^-. Important steric effects were observed in other nucleophilic aromatic substitution reactions.[15]



Scheme 2

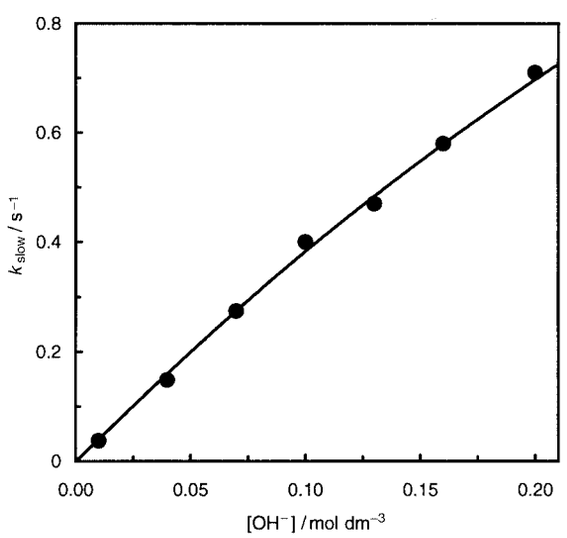


Fig. 4 Dependence of the rate constant for the slow process, k_{slow}, on the HO^- concentration for the hydrolysis of **1**. The line was calculated with eqn. (4) and the data of Table 3.

On the other hand, it can be seen (Table 3, k_3) that for the addition of hydroxide anion to the C-1 position of the aromatic ring, substrate **2** is three-fold more reactive than **1**. This result may be explained by the fact that in going from the Meisenheimer complex **8** to **3** there is more steric release in the case of compound **2** than **1** due to the bulkier C=S group in the former complex compared to the C=O group in the latter.

Another possible mechanism for the fast process is that shown in Scheme 3, where there is an equilibrium between **1** or **2** and **5**.

The existence of Meisenheimer 1:2 σ-complexes (similar to **11**) is well documented. These have been found in the hydrolysis of 1,3,5-trinitrobenzene and 1-X-2,4,6-trinitrobenzenes,[6b] ethyl dinitrobenzoates[6c] and 1-amino-2,4,6-trinitrobenzenes,[7] and in the reactions of sulfite ions with alkyl and aryl ethers and thioethers.[9b] Aqueous solutions favour the formation of the 1:2 σ-complexes.[16]

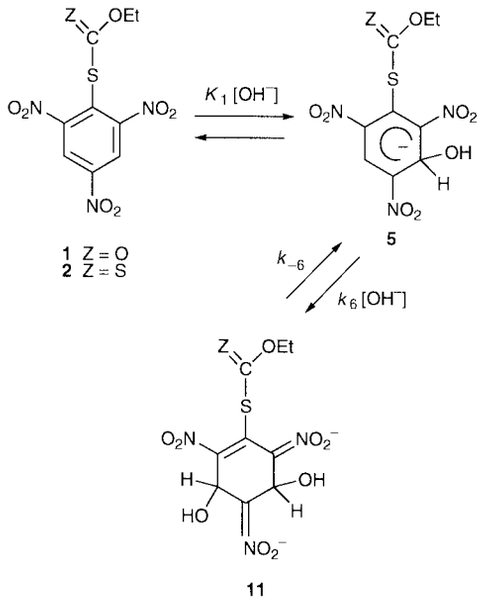
From Scheme 3, eqn. (5) can be derived. Reasonable fits can also be found with this mechanism.

$$k_{fast} = \frac{K_1 k_6 [OH^-]^2}{1 + K_2[OH^-]} + k_{-6} \qquad (5)$$

For the slow process, assuming equilibrium for the two steps in Scheme 3, a similar mechanism to that depicted in Scheme 2 and a similar rate law to that in eqn. (4) can be obtained.

The formation of the aromatic substitution product **3** by the reaction of HO^- with a 1:2 Meisenheimer complex has been shown to occur in the hydrolysis reactions of picramides[7] and 2,4-dinitroanilines.[10]

Although satisfactory fits are found for the fast and slow processes for the mechanisms with and without the dihydroxy



Scheme 3

Meisenheimer complex **11**, we prefer the mechanisms without it (Schemes 1 and 2). The reasons for this preference are:‡ i) by using the values of the microcoefficients found in the fitting through eqn. (5), the fraction of **11** calculated, after equilibration with **5**, is very small at low OH^- concentration. Substantially larger fractions of **6** or **7** are found for the mechanism in Scheme 1, using the data in Table 3. ii) The visible spectra (400–600 nm) of the initially produced adducts in Figs. 1 and 2 show absorption bands that correspond more to a 1 : 1 adduct than to a 1 : 2 complex. iii) The data in Table 1 show a minimum in a plot of k_{fast} *vs.* $[OH^-]$. This is predicted by eqn. (2) but not by eqn. (5). iv) The values of K_1, for monoadduct formation, are usually larger than those of K_6, for diadduct formation. Hence, two relaxations should have been found for the fast process; however, we observed only one relaxation.

Experimental

Materials

Compounds **1** and **2** were available from previous work.[2a,b] KOH and KCl, Merck a.r., were used as purchased and dioxane was purified as described previously.[17]

Kinetic measurements

Spectral and kinetic measurements were recorded on a Shimadzu UV-2101PC spectrophotometer or a Hewlett Packard HP-8453 diode array equipped with a Hi-Tech SFA-20 rapid kinetic accessory. An Applied Photophysics SF 17MV stopped-flow spectrofluorimeter was used to measure the rate coefficients of the fast processes. All the reactions were studied in 5% dioxane in water, 25.0 ± 0.1 °C, and ionic strength 0.2 mol dm^{-3}, with KCl used as compensating electrolyte. All kinetic runs were carried out under pseudo-first-order conditions, the initial substrate concentration being *ca.* 2×10^{-5} mol dm^{-3}.

In a typical stopped-flow experiment, two solutions were prepared in 5% dioxane in water at twice the concentrations required for the final solution: one containing the substrate and the other the nucleophile and KCl. The reaction was initiated by mixing equal volumes of both solutions. All relaxation times represent the average of five to ten determinations.

Product studies

The final products of the reactions of **1** were identified as a mixture of 2,4,6-trinitrophenoxide and 2,4,6-trinitrobenzenethiolate ions in a 2 : 1 ratio, independent of KOH concentration. This was achieved by comparing the final spectra of the reactions with those of various mixtures of authentic 2,4,6-trinitrophenoxide and 2,4,6-trinitrobenzenethiolate ions under the same experimental conditions.

On the other hand, in the reactions of **2**, the presence of potassium *O*-ethyl dithiocarbonate and a mixture of 2,4,6-trinitrophenoxide and 2,4,6-trinitrobenzenethiolate ions in a 10 : 1 ratio as products was inferred by comparison of the final reaction spectra with those of authentic samples of these products under identical experimental conditions. The formation of **4** was detected and quantified by HPLC using an instrument equipped with a Knauer Model 64 pump with an RP-18 column and Perkin Elmer LC-15 UV detector (254 nm), under the following conditions: eluant, methanol in the isocratic mode; flow rate, 0.5 ml min^{-1}; room temperature. Under these conditions, the retention times for 2,4,6-trinitrophenol and 2,4,6-trinitrobenzenethiol were 3.2 and 5.7 min, respectively.

Acknowledgements

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