# Kinetic and Thermodynamic Preferences in the Reactions of Thiolate Ions with 1-Substituted-2,4,6-trinitrobenzenes

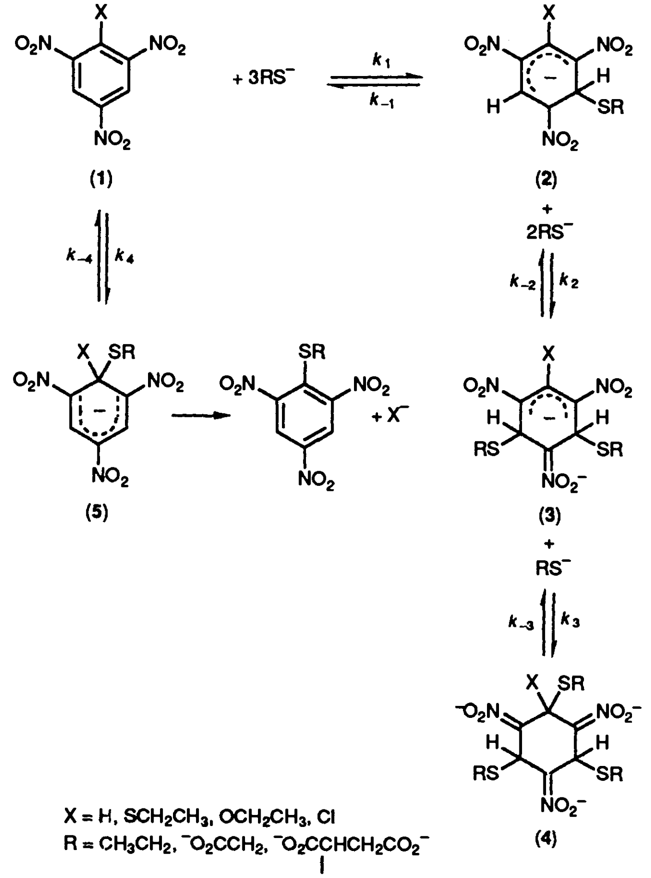
**Michael R. Crampton * and J. Andrew Stevens**
*Department of Chemistry, Durham University, Durham DH1 3LE*

Kinetic and equilibrium data are reported for reaction in water of ethanethiolate, thioglycolate, and thiomalate ions with 1-X-2,4,6-trinitrobenzenes (X = H, SEt, OEt, and Cl). The thiolate ions show strong kinetic preference for attack at unsubstituted ring positions. However, the isomeric 1:1 adducts formed by attack at substituted and unsubstituted positions have similar thermodynamic stabilities. The latter is in marked contrast with corresponding reactions of alkoxides. Adducts of stoicheiometry thiolate:nitro compound (2:1) are formed by thiolate attack at two unsubstituted ring positions and are stabilised in water by the good solvation of negative charge localised on the nitro groups. A 3:1 adduct has been identified by reaction of ethanethiolate ions with 1,3,5-trinitrobenzene and the kinetic data recorded. Comparison of nucleophilic attack by thiolate ions and by hydroxide ions indicates that the kinetic barrier to reaction with thiolates is considerably lower than for reaction with the oxygen base; a consequence is that (**5**; X = OEt) is an observable intermediate during nucleophilic substitution.

$^1$H NMR measurements in DMSO have been used to examine the structures of intermediates and reaction products; they show the irreversible displacement of nitro groups by thiolate ions.

There is now overwhelming evidence from NMR and kinetic studies that alkoxide ion attack at unsubstituted ring-positions of 2,4,6-trinitrophenyl ethers is a faster process than the isomeric attack at the subsituted 1-position, but leads to thermodynamically less stable products.[1] Similarly, it has been shown that hydroxide ion attack at the unsubstituted 3-position of 1-substituted-2,4,6-trinitrobenzenes is at least an order of magnitude more rapid than attack at the 1-position.[2,3]

In contrast with the wealth of information available for attack by oxygen nucleophiles, there have been few kinetic studies of the biologically important σ-adduct forming reactions of thiolate ions.[4,5] However we have recently measured[6] intrinsic reactivites, in the Marcus sense,[7] for the reactions in water of several thiolate ions at unsubstituted positions of trinitro-activated rings. Values for thioglycolate, thiomalate, and glutathione were all *ca.* 5 × $10^4$ and were considerably higher than corresponding values for sulphite ion (300) and for the hydroxide ion (10). Interestingly, Pietra and co-workers[8,9] have reported NMR measurements in dimethyl sulphoxide (DMSO) showing that the reactions of ethanethiolate ions with ethyl thiopicrate and with ethyl picrate yield mixtures of the 1- and 3-adducts in comparable concentrations, indicating similar thermodynamic stabilities for these isomeric adducts. We report here kinetic and equilibrium studies for the reactions in aqueous media of ethanethiolate ions and thioglycolate ions with 1-substituted-2,4,6-trinitrobenzenes. For comparison, some data for hydroxide ion attack are also included.



Scheme 1

## Results and Discussion

Our results for reaction of thiolate ions with trinitro-activated substrates indicate that in individual systems some or all of the processes shown in Scheme 1 are observed. Structures of adducts with 1:1 stoicheiometry were determined by NMR spectroscopy.

$^1$H *NMR Measurements.*—For reasons of solubility, measurements were limited to [$^2H_6$]DMSO as solvent, or to DMSO–$D_2O$ mixtures containing up to 15% by volume of deuterium oxide. Thiolate ions were generated *in situ* by addition of $OD^-$ in $D_2O$ to mixtures containing either ethanethiol or thioglycolate with the parent. The chemical shifts for the adducts obtained and for parent molecules are shown in Table 1. Adducts of general structure (**2**), where

**Table 1.** $^1H$ NMR chemical shifts [δ(ppm)] for parent structures and adducts.

| Parent | Ring | Methylene[a] | Methyl[a] | Other |
|---|---|---|---|---|
| (1; X = $OCH_2CH_3$) | 9.08 (s) | 4.26 (q) | 1.34 (t) | |
| (1; X = $SCH_2CH_3$) | 9.11 (s) | 2.95 (q) | 1.15 (t) | |
| (1; X = $SCH_2COOH$) | 9.08 (s) | 3.8 (s) | | |
| | | | | 11.3 (COOH) |
| Adducts | | | | |
| (2; X = $SCH_2CH_3$,<br>SR = $SCH_2CH_3$) | 5.97, 8.32 | 2.9 (q)<br>2.5 (q) | NM[b] | |
| (2; X = $SCH_2CH_3$,<br>SR = $SCH_2CO_2^-$) | 5.96, 8.30 | NM | NM | |
| (7; X = $SCH_2CH_3$) | 6.22, 8.34 | 2.8 (q) | NM | |
| (2; X = $OCH_2CH_3$,<br>SR = $SCH_2CH_3$) | 5.85, 8.32 | 4.0 (q)<br>2.5 (q) | NM | |
| (2; X = $OCH_2CH_3$,<br>SR = $SCH_2CO_2^-$) | 5.75, 8.33 | 4.1 (q)<br>3.1 (s) | 1.3 (t) | |
| (7; X = $OCH_2CH_3$) | 6.14, 8.38 | 4.0 (q) | 1.3 (t) | |
| (5; X = $SCH_2CH_3$,<br>SR = $SCH_2CH_3$) | 8.36 (s) | 2.5 (q) | NM | |
| (5; X = $OCH_2CH_3$,<br>SR = $SCH_2CH_3$) | 8.47 (s) | 3.26 (q)<br>2.37 (q) | NM | |
| (5; X = $OCH_2CH_3$,<br>SR = $SCH_2CO_2^-$) | 8.46 (s) | 3.27 (q)<br>2.9 | 1.80 (t) | |

[a] Coupling $J$ = 7 Hz is observed between methylene and methyl protons. [b] Not measured.

addition has occurred at an unsubstituted position, showed characteristic bands[1] of equal intensity at *ca.* δ 8.3 and 5.9 due to ring hydrogens. Adducts of type (5) gave a single band due to ring hydrogens at *ca.* δ 8.4. Small bands, slightly to high field of those from the adducts (2) were in some cases observed and are attributed to competitive addition of $OD^-$ at unsubstituted ring positions. Spectra were obtained within two minutes of mixing, before appreciable decomposition had occurred, which allowed the relative proportions of the 1-adducts (5) and 3-adducts (2) to be determined. They show that attack of ethanethiolate ion on ethyl thiopicrate favours the 3-adduct over the 1-adduct in a ratio of 3:1; with thioglycolate as the nucleophile no bands were observed for attack at the 1-position showing that the 3-adduct has appreciably greater thermodynamic stability. The spectra obtained with ethyl picrate show that for both ethanethiolate ions and thioglycolate ions the 1-adduct is favoured relative to the 3-adduct in the ratio of 1.2:1. These results, in general agreement with Pietra's findings,[8,9] show that the 1-adducts and 3-adducts have rather similar thermodynamic stabilities in these systems. Attempts to obtain spectra of adducts with 1:2 stoicheiometry using excess thiolate ions were unsuccessful. This can be attributed to the known ability[1] of the solvent, DMSO, to stabilise adducts of 1:1 stoicheiometry at expense of 1:2 adducts.

*Kinetics and Equilibria*.—Measurements were made in water containing 1% or 2% (v/v) of dioxane, which was used to prepare stock solutions of the nitro compounds. Unless otherwise stated, the ionic strength was maintained at 0.25 mol $dm^{-3}$ using sodium chloride. Kinetics were measured under first-order conditions using stopped-flow spectrophotometry. The results given are for the initial reversible adduct-forming reactions. These were often followed by slower irreversible processes.

*Trinitrobenzene and ethanethiolate ions.* Three reversible reactions were observed forming (2; X = H, R = Et) with $\lambda_{max}$ 460, 550 sh nm followed by (3; X = H, R = Et) with $\lambda_{max}$ 510 nm followed by (4; X = H, R = Et) which did not absorb in the visible region. Rate and equilibrium measurements are shown in Table 2. Absorbance values at completion of the most rapid colour forming reaction gave a value of 200 $dm^3$ $mol^{-1}$ for the equilibrium constant $K_1$, for formation of (2) but the rate of this reaction was too rapid for measurement by the stopped-flow method. Unfortunately temperature-jump measurements were not possible because the high equilibrium conversion to the 1:2 adduct (3), even at low nucleophile concentrations, resulted in very low equilibrium concentrations of the 1:1 adduct. The rate expression for the equilibration of (2) and (3) is shown in equation (1) and values calculated with $k_2$ = 3 × $10^4$ $dm^3$ $mol^{-1}$ $s^{-1}$, $k_{-2}$ = 3 $s^{-1}$, and $K_1$ = 180 $dm^3$

$$k_{obs,2} = k_{-2} + \frac{k_2K_1[SEt^-]^2}{1 + K_1[SEt^-]} \qquad (1)$$

$mol^{-1}$ gave an excellent fit with experimental values. The value calculated for $K_2(= k_2/k_{-2})$ of 1 × $10^4$ $dm^3$ $mol^{-1}$ is in good agreement with the literature value[10,11] determined from absorbance values. The high value obtained for $K_2$ relative to $K_1$ is attributed[11] to the excellent solvation by water of the negative charge localised on nitro groups in the di-adduct. Since there is virtually complete conversion to the 1:2 adduct the rate expression for conversion into the 1:3 adduct (4) simplifies to equation (2). A linear plot of the data in Table 2

$$k_{obs,3} = k_{-3} + k_3[SEt^-] \qquad (2)$$

gave values for $k_3$ of 900 $dm^3$ $mol^{-1}$ $s^{-1}$ and $k_{-3}$ 10 $s^{-1}$. Combination of these values gives $K_3$ (= $k_3/k_{-3}$) = 90 $dm^3$ $mol^{-1}$ in good agreement with the value obtained from equilibrium absorbance values. These results represent the first kinetic study of the formation of a σ-adduct with 1:3 stoicheiometry.

*Ethylthiopicrate* (1; X = SEt) *and ethanethiolate ions.* Visible spectra show that in water, even at very low nucleophile concentrations, there is extensive conversion to the 1:2 adduct which shows a single absorption maximum at 440 nm. Interestingly, $\lambda_{max}$ for this adduct shifts progressively to longer wavelength in solvents containing increasing proportions of DMSO reaching 490 nm in 60% (v/v) DMSO. In the latter medium the spectrum of a 1:1 adduct shows maxima at 460 nm, 540 sh. Stopped-flow measurements in water provided evidence for three reversible processes. The most rapid reaction, attributed to attack at an unsubstituted position

**Table 2.** Kinetic and equilibrium results for reaction of trinitrobenzene [a] with SEt$^-$ in water at 25 °C with $I$ = 0.25 mol dm$^{-3}$.

| [SEt$^-$]/$10^{-4}$ mol dm$^{-3}$ | $A^b_{460}$ nm | $K^c_1$/dm$^3$ mol$^{-1}$ | $k_{obs,2}$/s$^{-1}$ | $k^d_{calc}$ | $k_{obs,3}$/s$^{-1}$ | $A^e_{500}$ | $K^f_3$/dm$^3$ mol$^{-1}$ |
|---|---|---|---|---|---|---|---|
| 2.5 | — | — | 3.4 | 3.3 | — | — | — |
| 5.0 | 0.19 | 160 | 4.6 | 4.2 | — | — | — |
| 10 | 0.41 | 200 | 7.0 | 7.6 | — | — | — |
| 15 | 0.61 | 210 | 11.5 | 12.5 | — | — | — |
| 20 | 0.67 | 190 | 19 | 18.9 | — | — | — |
| 40 | 1.10 | 200 | — | — | 13.2 | — | — |
| 60 | — | — | — | — | 15.4 | — | — |
| 80 | — | — | — | — | 17.3 | 0.97 | 80 |
| 100 | — | — | — | — | 18.8 | — | — |
| 120 | — | — | — | — | 20.7 | 0.75 | 90 |
| 150 | — | — | — | — | 22.6 | — | — |
| 180 | — | — | — | — | 24.9 | — | — |
| 200 | — | — | — | — | — | 0.57 | 90 |
| 400 | — | — | — | — | — | 0.34 | 90 |
| 600 | — | — | — | — | — | 0.21 | 110 |

[a] Absorbances normalised to 1 × $10^{-4}$ mol dm$^{-3}$ trinitrobenzene. [b] At completion of rapid reaction forming 1:1 adduct. [c] Calculated as $A_{460}/(2.5 - A_{460})$(SEt$^-$). Assumes extinction coefficient for 1:1 adduct is 2.5 × $10^4$ dm$^3$ mol$^{-1}$ cm$^{-1}$. [d] Calculated from equation (1) with $k_2$ 30 000 dm$^3$ mol$^{-1}$ s$^{-1}$, $k_{-2}$ 3 s$^{-1}$ and $K_1$ 180 dm$^3$ mol$^{-1}$. [e] At completion of reaction forming 1:3 adduct. [f] Calculated as $(1.6 - A_{500})/A_{500}$[SEt$^-$]. Assumes extinction coefficient for 1:2 adduct is 1.6 × $10^4$ dm$^3$ mol$^{-1}$ cm$^{-1}$.

**Table 3.** Kinetic and equilibrium results for the reaction of ethyl thiopicrate with SEt$^-$ in water at 25 °C with $I$ = 0.25 mol dm$^{-3}$.

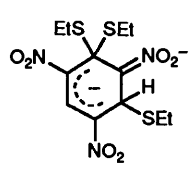
| [SEt$^-$]/$10^{-4}$ mol dm$^{-3}$ | $A^a_{440}$ | $K^b_1$/dm$^3$ mol$^{-1}$ | $k^c_{obs,2}$/s$^{-1}$ | $k^d_{calc}$ | $A^e_{440}$ | $A$(calc)$^f$ |
|---|---|---|---|---|---|---|
| 2.5 | 0.056 | 115 | 1.4 | 2 | 0.488 | 0.479 |
| 5.0 | 0.107 | 113 | 4.0 | 5 | 0.734 | 0.739 |
| 7.5 | 0.123 | 87 | — | — | — | — |
| 10 | 0.150 | 81 | 14 | 16 | 0.862 | 0.855 |
| 15 | 0.223 | 84 | 38 | 33 | — | — |
| 20 | 0.296 | 87 | 65 | 56 | 0.870 | 0.885 |
| 25 | — |  | 85 | 84 | — | — |
| 30 | — |  | 126 | 117 | — | — |

[a] At completion of very rapid reaction forming 1:1 adduct. [b] Calculated as $A_{440}/(2.0 - A_{440})$[SEt$^-$]. Assumes extinction coefficient for 1:1 adduct is 2 × $10^4$ dm$^3$ mol$^{-1}$ cm$^{-1}$. [c] For 1:2 adduct forming reaction. [d] Calculated from equation (1) with $k_2$ 1.9 × $10^5$ dm$^3$ mol$^{-1}$ s$^{-1}$, $K_1$ 85 dm$^3$ mol$^{-1}$ and $k_{-2}$ 1 s$^{-1}$. [e] At completion of adduct forming reactions. [f] Calculated with $K_1$ 85 dm$^3$ mol$^{-1}$, $K_2$ 2 × $10^5$ dm$^3$ mol$^{-1}$ and using a measured value of 9 × $10^3$ dm$^3$ mol$^{-1}$ cm$^{-1}$ for ε(1:2).

to give (**2**; X = SEt, R = Et), was too fast for kinetic measurements but the absorbance values at its completion gave (Table 3) a value for $K_1$ of 85 dm$^3$ mol$^{-1}$. At low nucleophile concentrations, [EtS$^-$] ≤ $10^{-3}$ mol dm$^{-3}$, a second process attributable to 1:1 adduct formation was observed. This process had very low amplitude and the value of the rate constant, 30 ± 10 s$^{-1}$, was independent of the nucleophile concentration. This process is thought to represent equilibration with the adduct (**5**; X = SEt, R = Et).

Our assignment of the faster, more intense process to formation of (**2**) is based on the NMR results given previously which show that at equilibrium (**2**) is quite strongly favoured relative to (**5**), and also by analogy with the results for attack of EtS$^-$ on trinitrobenzene where reaction at an unsubstituted position was found to be extremely rapid. On this basis, we may calculate a value of *ca.* 28 dm$^3$ mol$^{-1}$ for $K_4$ (one third of the value for $K_1$), so that the measured value of 30 s$^{-1}$ represents $k_{-4}$, leading to a value for $k_4$ (= $K_4k_{-4}$) of 840 dm$^3$ mol$^{-1}$, s$^{-1}$.

The major measurable rate process in water involved formation of the 1:2 adduct and when [SEt$^-$] > $10^{-3}$ mol dm$^{-3}$ this process became faster than the equilibration with (**5**) which was thus no longer observable. The rate data in Table 3 give a good fit with equation (1) with $k_2$ = 1.9 × $10^5$ dm$^3$ mol$^{-1}$ s$^{-1}$, $K_1$ = 85 dm$^3$ mol$^{-1}$ and $k_{-2}$ = 1 ± 1 s$^{-1}$. The high uncertainty in the value for $k_{-2}$ makes it unprofitable to obtain a value for $K_2$ by combination of rate coefficients. However the equilibrium absorbances at completion of these reactions are in accord with a value for $K_2$ of 2 × $10^5$ dm$^3$ mol$^{-1}$. The very high value obtained for the rate constant for formation of the 1:2 adduct is in accord with nucleophilic attack at an unsubstituted ring position and is more compatible with structure (**3**) rather than structure (**6**) for the 1:2 adduct.



(**6**)

*Ethyl picrate and ethanethiolate ions.* The behaviour in water was qualitatively similar to that observed with ethyl thiopicrate in that there was evidence for the formation of two isomeric 1:1 adducts, while formation of a 1:2 adduct, $\lambda_{max}$ 424 nm, was dominant. With the nucleophile concentration in excess of parent concentration three reversible processes were observable by stopped-flow. The most rapid process, attributed to formation of (**2**; X = OEt, R = Et), was too fast for kinetic measurements but absorbances gave a value for $K_1$ of 80 dm$^3$ mol$^{-1}$. With [SEt$^-$] < 2 × $10^{-3}$ mol dm$^{-3}$ two further processes were observed, both colour-forming at 445 nm. One is attributed to equilibration with (**5**; X = OEt, R = Et) and rate measurements lead to $k_{-4}$ = 13 s$^{-1}$. The second process is attributed to formation of (**3**; X = OEt, R = Et) and equation (1) is applicable. With [SEt$^-$] > 2 × $10^{-3}$ mol dm$^{-3}$ the latter

**Table 4.** Kinetic and equilibrium results for the reaction of ethyl picrate with ethanethiolate ions in water at 25 °C with $I$ = 0.25 mol dm$^{-3}$.

| [ethyl picrate]/10$^{-4}$ mol dm$^{-3}$ | [SEt$^-$]/10$^{-4}$ mol dm$^{-3}$ | $A_{445}^a$ | $K_1^b$/dm$^3$ mol$^{-1}$ | $k_{obs,4}^c$/s$^{-1}$ | $A_{445}^d$ | $k_{obs,2}^e$/s$^{-1}$ | $k_{calc}^f$ |
|---|---|---|---|---|---|---|---|
| 1.0 | 2.5 | — | — | 14 | — | 2.8 | 2.5 |
| 1.0 | 5.0 | 0.071 | 74 | 15 | 0.35 | 3.5 | 3.9 |
| 1.0 | 10 | 0.151 | 82 | 17 | 0.64 | — | — |
| 1.0 | 20 | 0.30 | 88 | — | — | — | 30 |
| 1.0 | 30 | — | — | — | 0.83 | 31 | 60 |
| 1.0 | 40 | 0.50 | 82 | — | — | 58 | 100 |
| 1.0 | 60 | 0.65 | 80 | — | 0.87 | 130 | |

| [ethyl picrate]/10$^{-4}$ mol dm$^{-3}$ | [SEt$^-$]/10$^{-4}$ mol dm$^{-3}$ | $A_{500}^a$ | $K_1^g$/dm$^3$ mol$^{-1}$ | $k_{obs,4}^c$/s$^{-1}$ | $A_{500}^h$ | $K_4^g$/dm$^3$ mol$^{-1}$ |
|---|---|---|---|---|---|---|
| 5.0 | 1.0 | 0.05 | 88 | — | 0.10 | 90 |
| 5.0 | 2.0 | 0.10 | 87 | 13 | 0.22 | 110 |
| 5.0 | 4.0 | 0.18 | 80 | 13 | 0.40 | 100 |
| 3.0 | 1.0 | 0.04 | 115 | — | 0.08 | 120 |
| 3.0 | 2.0 | 0.06 | 85 | 13 | 0.13 | 100 |

[a] At completion of most rapid reaction, forming (**2**; X = OEt, R = Et). [b] Calculated as $A_{445}/(2.0 - A_{445})[\mathrm{SEt}^-]$. Assumes extinction coefficient for (**2**) at 445 nm is 2.0 × 10$^4$ dm$^3$ mol$^{-1}$ cm$^{-1}$. [c] Rate process associated with formation of (**5**; X = OEt, R = Et). [d] At completion of reversible adduct-forming reactions. [e] Rate process associated with formation of (**3**; X = OEt, R = Et). [f] Calculated from equation (1) with $k_2$ 1 × 10$^5$ dm$^3$ mol$^{-1}$ s$^{-1}$, $k_{-2}$ 2 s$^{-1}$ and $K_1$ 80 dm$^3$ mol$^{-1}$. [g] Calculated values assuming that extinction coefficients for both (**2**) and (**5**) at 500 nm are 1.2 × 10$^4$ dm$^3$ mol$^{-1}$ cm$^{-1}$. [h] Total absorbance after formation of (**2**) and equilibration with (**5**).

**Table 5.** Kinetic and equilibrium data for reaction of ethyl picrate with thioglycolate ions at 25 °C with $I$ = 0.25 mol dm$^{-3}$.

| [ethyl picrate]/10$^{-4}$ mol dm$^{-3}$ | [thioglycolate]/10$^{-4}$ mol dm$^{-3}$ | $A_{440}^a$ | $K_1^b$/dm$^3$ mol$^{-1}$ | $k_{obs,4}^c$/s$^{-1}$ |
|---|---|---|---|---|
| 1 | 5 | — | — | 25 |
| 1 | 10 | — | — | 26 |
| 1 | 40 | 0.29 | 45 | — |
| 1 | 50 | 0.36 | 45 | — |
| 1 | 60 | 0.41 | 47 | — |
| 1 | 80 | 0.52 | 48 | — |
| 1 | 100 | 0.57 | 43 | — |

| [ethyl picrate]/10$^{-4}$ mol dm$^{-3}$ | [thioglycolate]/10$^{-4}$ mol dm$^{-3}$ | $A_{500}^a$ | $K_1^d$/dm$^3$ mol$^{-1}$ | $k_{obs,4}^c$/s$^{-1}$ | $A_{500}^e$ | $K_4^d$/dm$^3$ mol$^{-1}$ |
|---|---|---|---|---|---|---|
| 5 | 2 | 0.056 | 47 | 26 | 0.113 | 47 |
| 5 | 4 | 0.10 | 43 | 26 | 0.19 | 40 |
| 3 | 2 | 0.04 | 34 | 24 | 0.075 | 31 |

[a] At completion of most rapid reaction forming (**2**; X = OEt, R = $\mathrm{CH_2CO_2^-}$). [b] Calculated as $A/(1.9 - A)[^-\mathrm{SCH_2CO_2}^-]$. Using $\varepsilon_{440}$ = 1.9 × 10$^4$ dm$^3$ mol$^{-1}$ cm$^{-1}$. [c] Rate process for formation of (**5**). Values correspond to $k_{-4}$. [d] Values calculated for formation of 1:1 adducts, assuming $\varepsilon_{500}$ = 1.2 × 10$^4$ dm$^3$ mol$^{-1}$ cm$^{-1}$. [e] At completion of both adduct-forming reactions.

process 'overtakes' the formation (**5**) which is no longer observed. Data in Table 4 give values for $k_2$ of 1 × 10$^5$ dm$^3$ mol$^{-1}$ s$^{-1}$, $k_{-2}$ 2 s$^{-1}$ and $K_1$ 80 dm$^3$ mol$^{-1}$.

In order to limit formation of the 1:2 adduct and thus to obtain more information about formation of (**5**), measurements were also made with [ethyl picrate] > [ethanethiolate]. Here formation of (**5**; X = OEt, R = Et) was observed with a rate constant of 13 s$^{-1}$ ($\equiv k_{-4}$) following the very rapid formation of (**2**). The absorbances at completion of these two processes allowed the calculation of values of $K_1$ of 90 dm$^3$ mol$^{-1}$ and $K_4$ 100 dm$^3$ mol$^{-1}$, indicating slightly greater thermodynamic stability for the adduct formed by attack at the 1-position. This is in agreement with the NMR data in DMSO–water.

*Ethyl picrate and thioglycolate ions.* There was evidence for the formation of 1:1 complexes, $\lambda_{max}$ 440 nm, 520 sh, and of a 1:2 adduct $\lambda_{max}$ 426 nm. Stopped-flow measurements in water with nucleophile concentrations in large excess of substrate concentration indicated three reversible processes. The most rapid, attributed to formation of (**2**; X = OEt, R = $\mathrm{CH_2CO_2^-}$), was too fast for kinetic measurement but absorbances at completion gave a value for $K_1$ of 45 dm$^3$ mol$^{-1}$. Data are shown in Table 5. Unfortunately, there was strong interference between the rate processes forming (**3**; X = OEt, R = $\mathrm{CH_2CO_2^-}$) and (**5**; X = OEt, R = $\mathrm{CH_2CO_2^-}$) and it was possible only to determine a value for $k_{-4}$ of 25 s$^{-1}$. In water–DMSO (3:1 v/v) where the processes were better separated, values for $k_2$ of 2.5 × 10$^4$ dm$^3$ mol$^{-1}$ s$^{-1}$ and $k_{-2}$ 12 s$^{-1}$ were obtained.

Using solutions in water with [ethyl picrate] > [thioglycolate] where 1:2 adduct formation was relatively disfavoured we obtained the individual absorbances associated with formation of the isomeric 1:1 adducts leading to values for $K_1$ of 45 dm$^3$ mol$^{-1}$ and $K_4$ 40 dm$^3$ mol$^{-1}$.

*Picryl chloride and thioglycolate ions.* The very rapid formation of (**2**; X = Cl, R = $\mathrm{CH_2CO_2^-}$) was followed by the formation at a measurable rate of (**3**; X = Cl, R = $\mathrm{CH_2CO_2^-}$) with $\lambda_{max}$ 428 nm. Data in Table 6 lead to values for $K_1$ of 18 dm$^3$ mol$^{-1}$, $k_2$ 2.6 × 10$^4$ dm$^3$ mol$^{-1}$ s$^{-1}$, and $k_{-2}$ 25 s$^{-1}$. A third slower process was observed which we attribute to attack at the chloro-substituted position to give the product of nucleophilic substitution. It is expected that loss of chloride from the intermediate (**5**; X = Cl, R = $\mathrm{CH_2CO_2^-}$) will be rapid so that nucleophilic attack is rate-determining. Equation (3) applies to this process and values calculated with $k_4$ 1 000

**Table 6.** Kinetic and equilibrium data for reaction of picryl chloride (**1**; X = Cl) with thioglycolate ions in water at 25 °C with $I = 0.25$ mol dm$^{-3}$.

| [thioglycolate]/$10^{-3}$ mol dm$^{-3}$ | $A_{445}^{a}$ | $K_1^{b}$/dm$^3$ mol$^{-1}$ | $k_{\text{obs},2}^{c}$/s$^{-1}$ | $k_{\text{calc}}^{d}$ | $k_{\text{obs},4}^{e}$/s$^{-1}$ | $k_{\text{calc}}^{f}$ |
|---|---|---|---|---|---|---|
| 1 | 0.030 | 15 | 26 | 25 | 0.8 | 1.0 |
| 2 | 0.074 | 19 | 27 | 27 | 1.4 | 1.8 |
| 4 | 0.144 | 19 | 29 | 32 | 3.4 | 3.0 |
| 6 | 0.173 | 16 | 35 | 40 | 4.0 | 3.4 |
| 8 | 0.246 | 17 | 44 | 51 | — | |
| 10 | 0.318 | 19 | 65 | 65 | — | |
| 12 | — | — | 79 | 80 | — | |
| 16 | — | — | 130 | 117 | — | |

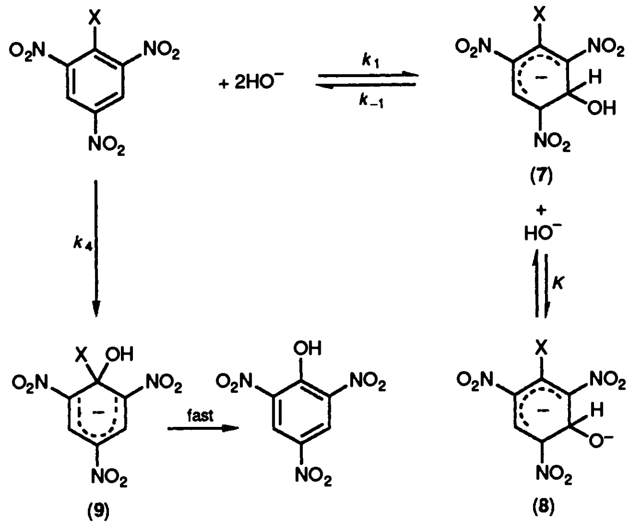
[a] At completion of formation of (**2**). [b] Calculated as $A/(2.0 - A)[\text{RS}^-]$, using a value for $\varepsilon_{445}$ of $2.0 \times 10^4$ dm$^3$ mol$^{-1}$ cm$^{-1}$. [c] Rate process associated with formation of (**3**). [d] Calculated from equation (1) with $k_2$ $2.6 \times 10^4$ dm$^3$ mol$^{-1}$ s$^{-1}$, $k_{-2}$ 25 s$^{-1}$ and $K_1$ 18 dm$^3$ mol$^{-1}$. [e] Nucleophilic displacement of chloride. [f] Calculated from equation (3) with $k_4$ 1 000 dm$^3$ mol$^{-1}$ s$^{-1}$, $K_1$ 18 dm$^3$ mol$^{-1}$ and $k_2$ 1 000 dm$^3$ mol$^{-1}$.

$$k_{\text{obs},4} = \frac{k_4[\text{RS}^-]}{1 + K_1[\text{RS}^-] + K_1K_2[\text{RS}^-]^2} \qquad (3)$$

dm$^3$ mol$^{-1}$ s$^{-1}$ are in reasonable agreement with observed values.

*Ethyl picrate and thiomalate ions.* Visible spectra indicate that with $[\text{RS}^-] < 0.03$ mol dm$^{-3}$ the parent is in equilibrium with 1:1 adducts, $\lambda_{\text{max}}$ 440 nm, 530sh. At higher nucleophile concentrations there is progressive conversion into a 1:2 adduct with $\lambda_{\text{max}}$ 430 nm. Stopped-flow measurements indicated the presence of two 1:1 adducts. Absorbances (not shown) led to values for $K_1$ of 8 dm$^3$ mol$^{-1}$ and for $K_4$ of 9 dm$^3$ mol$^{-1}$. The measurable rate process associated with formation of (**5**; X = OEt, R = $\text{CH}[\text{CO}_2^-]\text{CH}_2\text{CO}_2^-$) gives a value for $k_{-4}$ of 33 s$^{-1}$.

*Reactions of ethyl thiopicrate and ethyl picrate with hydroxide ions.* With each substrate the two major processes shown in Scheme 2 were observed on mixing with sodium hydroxide



**Scheme 2.**

solutions. The more rapid is associated with attack at an unsubstituted ring position to give (**7**) while the slower results in formation of picrate. Plots (Figure) of the rate coefficients of the faster reaction *vs.* hydroxide concentration showed distinct minima. This is interpreted as previously,[2,12] in terms of ionisation of the adducts (**7**), in rapid equilibria, to

$$k_{\text{obs},1} = k_1[\text{HO}^-] + \frac{k_{-1}}{1 + K[\text{HO}^-]} \qquad (4)$$

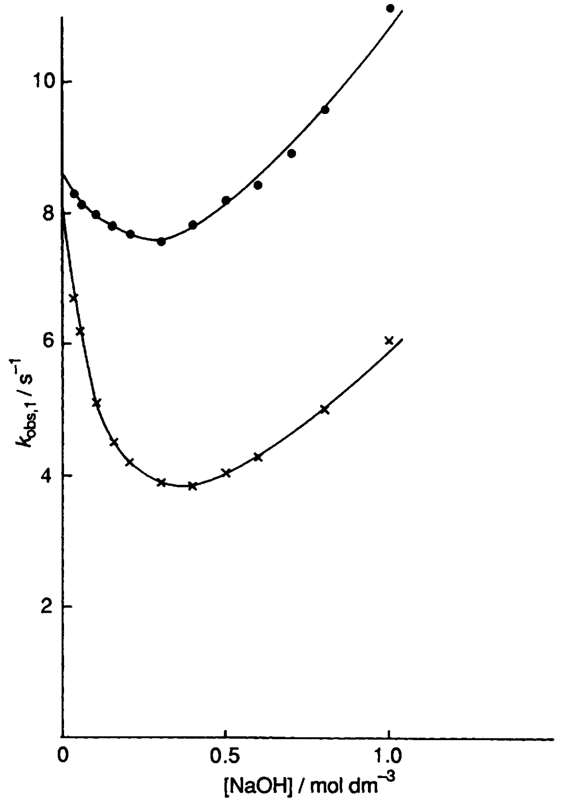


**Figure.** Dependence on base concentration, at $I = 1.0$ mol dm$^{-3}$ with NaCl, for $k_{\text{obs},1}$ for ethyl thiopicrate (X) and for ethylpicrate (●). The full lines are calculated using equation (4) and the values given in the text.

give the dianions (**8**). Equation (4) gives the base dependence expected. With ethyl thiopicrate values calculated with $k_1$ 4.8 dm$^3$ mol$^{-1}$ s$^{-1}$, $k_{-1}$ 8.3 s$^{-1}$ and $K$ 8 dm$^3$ mol$^{-1}$ gave excellent agreement with observed values at $I = 1.0$ mol dm$^{-3}$. With ethyl picrate, values were $k_1$ 8.1 dm$^3$ mol$^{-1}$ s$^{-1}$, $k_{-1}$ 8.6 s$^{-1}$, and $K$ 2.2 dm$^3$ mol$^{-1}$. Values of $k_4$, obtained by measuring the rate of picrate formation in dilute base solutions where there was little conversion into adducts (**7**), were 0.1 dm$^3$ mol$^{-1}$ s$^{-1}$ for ethyl thiopicrate and 0.8 dm$^3$ mol$^{-1}$ s$^{-1}$ for ethyl picrate.

*Comparisons.* Data are summarised in Table 7. They show that for a given nucleophile, values of the equilibrium constant $K_1$, for attack at an unsubstituted ring position, are reduced by the presence of a substituent at the 1-position; for example, with SEt$^-$ as the nucleophile, from 180 dm$^3$ mol$^{-1}$ for trinitrobenzene to 85 dm$^3$ mol$^{-1}$ for (**1**; X = SEt) and 80 dm$^3$ mol$^{-1}$ for (**1**; X = OEt). These small reductions are reasonably attributed to the steric effect of the 1-substituent which results in the twisting from the ring-plane of the adjacent nitro-groups,

**Table 7.** Summary of rate and equilibrium data[a] for adduct formation in water at 25 °C with $I = 0.25$ mol dm$^{-3}$.

| Parent | Nucleophile | $k_1$/ dm$^3$ mol$^{-1}$ s$^{-1}$ | $k_{-1}$/s$^{-1}$ | $K_1$/ dm$^3$ mol$^{-1}$ | $k_4$/ dm$^3$ mol$^{-1}$ s$^{-1}$ | $k_{-4}$/s$^{-1}$ | $K_4$/ dm$^3$ mol$^{-1}$ | $k_2$/ dm$^3$ mol$^{-1}$ s$^{-1}$ | $k_{-2}$/s$^{-1}$ | $K_2$/ dm$^3$ mol$^{-1}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| (1; X = H)[b] | SEt$^-$ | — | — | 180 | — | — | — | $3 \times 10^4$ | 3 | $1 \times 10^4$ |
| (1; X = SEt) | SEt$^-$ | — | — | 85 | 840 | 30 | 28 | $1.9 \times 10^5$ | 1 | $2 \times 10^5$ |
| (1; X = OEt) | SEt$^-$ | — | — | 80 | 1 300 | 13 | 100 | $1 \times 10^5$ | 2 | $5 \times 10^4$ |
| (1; X = H)[c] | $^-$SCH$_2$CO$_2$$^-$ | $1.4 \times 10^6$ | 5 500 | 250 | — | — | — | $3.3 \times 10^3$ | 8 | 400 |
| (1; X = OEt) | $^-$SCH$_2$CO$_2$$^-$ | — | — | 45 | 1 000 | 25 | 40 | $2.5 \times 10^4$ | 12 | 2 100[d] |
| (1; X = Cl) | $^-$SCH$_2$CO$_2$$^-$ | — | — | 18 | 1 000 | — | — | $2.6 \times 10^4$ | 25 | 1 000 |
| (1; X = OEt) | $^-$SCH(CO$_2$$^-$)CH$_2$CO$_2$$^-$ | — | — | 8 | 300 | 33 | 9 | — | — | — |
| (1; X = SEt)[e] | OH$^-$ | 4.8 | 8.3 | 0.6 | 0.1 | — | — | — | — | — |
| (1; X = OEt)[e] | OH$^-$ | 8.1 | 8.6 | 0.9 | 0.8 | — | — | — | — | — |

[a] The numbering of rate and equilibrium constants corresponds to Schemes 1 and 2. [b] Values also obtained for $k_3$ 900 dm$^3$ mol$^{-1}$ s$^{-1}$ and $k_{-3}$ 10 s$^{-1}$. [c] Ref. 12. [d] Values for $k_2$, $k_{-2}$, and $K_2$ refer to water–DMSO (3:1 v/v). [e] $I = 1.0$ mol dm$^{-3}$ NaCl.

thus reducing their electron-withdrawing ability. Unfortunately, attack by ethanethiolate ions at unsubstituted ring positions was too rapid for kinetic measurements by the stopped-flow method. However, values for three related thiolates are known[6] to be in the range 1–2 × $10^6$ dm$^3$ mol$^{-1}$ s$^{-1}$ and to show little dependence on the basicity of the thiolate. In related work, Bernasconi and Killion[13] have found and discussed the reasons for a very low value for $\beta_{\text{nuc}}$ for thiolate addition to α-nitrostilbenes which indicates a small dependence of the rate constant for thiolate attack on basicity. We therefore expect $k_1$ for thiolate attack at unsubstituted ring positions in these systems to have values of *ca.* $10^6$ dm$^3$ mol$^{-1}$ s$^{-1}$. Since values of $K_1$ are *ca.* $10^2$ dm$^3$ mol$^{-1}$ the values of $k_{-1}$ ($= k_1/K_1$) will be *ca.* $10^4$ s$^{-1}$. The measured values (Table 7) for $k_4$ for thiolate attack at the substituted 1-position are *ca.* $10^3$ dm$^3$ mol$^{-1}$ s$^{-1}$ and are much lower than corresponding values of $k_1$. Hence the thiolate ions, like alkoxides, show strong kinetic preference for attack at unsubstituted positions of the trinitro-substituted ring. In fact, the values of $k_4$ show little dependence on the structure of the attacking thiolate ion or, more surprisingly, on the nature of the group (OEt, SEt, or Cl) at the 1-position.

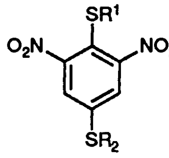
In a given system, the values obtained for $K_1$ and for $K_4$ in aqueous solutions are broadly similar. This indicates similar thermodynamic stability for the adducts formed by thiolate attack at unsubstituted positions and at SEt (or OEt) substituted positions. The NMR data indicate that in DMSO the adducts formed by attack at the 1- and 3-positions also have similar stabilities. This is in marked contrast with alkoxide attack on trinitrophenyl ethers where the 1,1-dialkoxy adducts have considerably greater thermodynamic stabilities than their isomers.[1] A major factor contributing to the high stability of 1,1-dialkoxy adducts is the special stabilising effect of two electronegative substituents attached to an sp$^3$ hybridised carbon atom.[14,15] The stabilisation will be much less important with two sulphur atoms at C-1 or with a combination of sulphur with oxygen. The two latter types of adducts will also be destabilised by increasing steric interactions as alkoxy groups are changed to the more bulky thioalkoxy groups.

Comparison (Table 7) of the kinetic and equilibrium values for hydroxide attack with those for corresponding attack of thiolate ions indicates the much lower kinetic and thermodynamic affinity of the oxygen base for aromatic carbon. The factors that favour the thiolate ions are their poor solvation relative to hydroxide,[16] so that less energy is expended on desolvation, and the favourable soft–soft interactions that result from reaction through the polarisable sulphur atom with aromatic carbon, a soft acid.

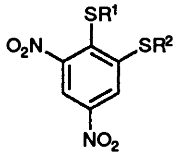
A consequence of the lower energy barrier to reaction with thiolate ions than for reaction with oxygen bases is that during the nucleophilic substitution of ethyl picrate (1; X = OEt) with thiolate ions, intermediates of structure (5; X = OEt) are observable. Thus, (5; X = OEt) will release thiolate ions in preference to ethoxide. In contrast, the intermediate (5; X = OH, R = Et) formed by hydroxide attack on ethyl thiopicrate is not observed since it is unstable with respect to loss of thioethoxide. These observations confirm theoretical predictions by Miller.[17]

*Irreversible reactions.* There is evidence in the literature[8,9,18,19] for the displacement by thiolate ions of *ortho-* and *para-*nitro groups activated by sulphide functions. Our results confirm that in DMSO the rapid and reversible formation of σ-adducts is followed by irreversible displacement of nitro-groups. Because of the low solubilities of reactant nitro compounds in water, we did not attempt to identify products in water.

Reaction of (1; X = SEt) with ethanethiolate ions in DMSO yielded (10; R$^1$ = R$^2$ = Et) as an eventual product which was identified by NMR spectroscopy and as a crystalline solid $\delta_H$ 8.10 (2 H, s, ring), 2.86 (2 H, q, CH$_2$), 3.18 (2 H, q, CH$_2$), 1.11 (3 H, t, CH$_3$), and 1.27 (3 H, t, CH$_3$). The NMR spectrum at completion of the reaction of ethyl picrate with excess ethanethiolate ions showed bands due to (10) and also to (11) [$\delta_H$ 8.51 (1 H, d, ring) and 8.22 (1 H, d, ring)]. Reaction here involves displacement of ethoxide by ethanethiolate followed by substitution of nitro groups. Addition of excess thioglycolate ions to a solution of ethyl thiopicrate in DMSO gave a mixture and the NMR spectrum showed bands due to (10; R$^1$ = Et, R$^2$ = CH$_2$CO$_2$H) [$\delta_H$ 8.17 (ring)], (11; R$^1$ = Et, R$^2$ = CH$_2$CO$_2$H) [$\delta_H$ 8.28, 8.50 (ring)], and (10; R$^1$ = R$^2$ = CH$_2$CO$_2$H) [$\delta_H$ 8.10 (ring)].



**(10)**



**(11)**

## Experimental

Ethyl thiopicrate (1; X = SEt) was prepared as before[20] by reaction of ethanethiolate ions with picryl chloride in ethanol. Recrystallisation gave yellow needles, m.p. 45 °C (lit.,[20] 45 °C). Ethyl picrate was available from previous work.[21] (10; R$^1$ = R$^2$ = Et) was prepared by reaction in DMSO of ethanethiolate ions with ethyl thiopicrate; recrystallisation from light petroleum gave material with m.p. 88 °C (lit.,[8] 90 °C). The thiols were the purest grade commercially available. The distilled water was boiled to remove carbon dioxide and subsequently protected from the atmosphere.

$^1$H NMR spectra were recorded using a Bruker 250 MHz instrument using $[^2H_6]$DMSO or $[^2H_6]$DMSO–$D_2O$ (9:1 v/v) as solvent. Substrate concentrations were 0.1–0.3 mol $dm^{-3}$ with nucleophile–parent mole ratios varying from 0–4. Thiolate ions were generated *in situ* by reaction of the parent thiol in $[^2H_6]$DMSO with deuterioxide ions in $D_2O$.

UV–visible spectra were measured with a Beckman Lambda 3 instrument. A Hi-Tech SF 3L stopped-flow spectrophotometer was used to measure rate coefficients. This instrument was also used to determine spectral shapes of species present after short reaction times. All kinetic measurements were made under first-order conditions with the concentration of nucleophile in large excess of that of the nitro compound. Reported rate coefficients are the mean of at least five separate determinations and are precise to $\pm 5\%$. Solutions of thiolate ions were, because of their instability, generated immediately before use from the parent thiol and sodium hydroxide solution. A slight excess, usually $5 \times 10^{-3}$ mol $dm^{-3}$, of hydroxide was used to ensure complete ionisation; checks were made to confirm that the excess hydroxide did not affect the observed kinetics.

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