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Combined *versus* individual labilising effects of H^+, Na^+ and nucleophile on catalysed substitution reactions: studies on $[Fe_4S_4X_4]^{2-}$ (X = Cl or PhS)†

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The reactions between $[Fe_4S_4X_4]^{2-}$ (X = PhS or Cl) and $Et_2NCS_2^-$ to form $[Fe_4S_4X_2(S_2CNEt_2)_2]^{2-}$ have been studied in MeCN. The kinetics are consistent with a dissociative mechanism under all conditions. The addition of Na^+ led to an increase in rate for $[Fe_4S_4(SPh)_4]^{2-}$ and analysis of the kinetics indicates that a single Na^+ binds and labilises the cluster. Comparison is drawn with the established effect of H^+ on the lability of this cluster. The presence of a thiolate ligand is necessary to bind Na^+ since the reaction between $[Fe_4S_4Cl_4]^{2-}$ and $Et_2NCS_2^-$ is unaffected by the addition of Na^+. The addition of acid to $[\{Fe_4S_4(SPh)_4\}Na]^-$ further accelerates the rate of substitution. Quantitative analysis shows that the combined labilising effect of Na^+ and H^+ is no more than that expected from the individual labilisation afforded by each cation. Similar analyses show the same is true for H^+ and nucleophile in acid-catalysed associative substitution mechanisms, and two H^+ in the acid-catalysed dissociative mechanisms of Fe–S-based clusters. The generality of these observations is discussed.

Introduction

There are many substitution reactions which are catalysed or inhibited in the presence of other species; for example, substitution reactions[1] in the presence of H^+. Elaborations of this chemistry could involve catalysis by several components [A, B, C, *etc.* . . ., as illustrated in equation (1)]. For example, A and B could both be H^+.

$$\text{M–X} + \text{Y} \xrightarrow{\text{A, B, C, } etc. \ldots} \text{M–Y} + \text{X} \qquad (1)$$

An important mechanistic question in such systems is, "Is the combined labilising effect of all these species different to that expected from each contributor or is there a cooperative effect when all the components A, B, C, *etc.* are present?" Specifically, for the acid-catalysed reactions, "Is the effect of two H^+ different from that expected from compounding the effect from one H^+ with another H^+?" Although these are fundamental mechanistic questions which relate to the reactions of many compounds, we are unaware of any study which addresses this problem. This is because such a study requires that the elementary rate constants for the dissociation of M–X to be determined in the presence of A, in the presence of B, as well as in the presence of A and B together. In most systems it is not possible to 'dissect' kinetically the dissociation rate constants from the binding constants of A and B. However, our studies on the acid-catalysed substitution reactions of synthetic Fe–S-based clusters[2–7] have shown that the binding of H^+ or nucleophile are rapid equilibrium reactions which are followed by the slow dissociation of the leaving group. Analysis of the kinetic data invariably allows us to determine the dissociation rate constants. Herein, we report kinetic studies on the substitution reaction shown in equation (2) (X = Cl or PhS) and: (i) compare the effects that Na^+ and H^+ have on the lability of the clusters; (ii) quantify the combined effect of binding Na^+ and H^+ on the lability of the cluster in terms of the individual labilising effects of these two cations, and (iii) a quantitative analysis of the relative labilising effects of binding H^+ and PhSH in the associative substitution mechanisms of $[Fe_4S_4Cl_4]^{2-}$.

$$[Fe_4S_4X_4]^{2-} + 2Et_2NCS_2^- \xrightarrow{H^+,\ Na^+,\ etc.} [Fe_4S_4(S_2CNEt_2)_2X_2]^{2-} + 2X^- \qquad (2)$$

In order to investigate the effect of Na^+ it has been necessary to use $Et_2NCS_2^-$ as the nucleophile. Previously similar studies used RS^- or ArS^- as the nucleophile.[2–7] However, both NaSR and NaSAr are very poorly soluble in MeCN, and precipitation of these compounds precludes studying the reactions. NaS_2CNEt_2 is sufficiently soluble in MeCN to avoid this complication. Clearly, in the reactions of $[Fe_4S_4(SPh)_4]^{2-}$ in the presence of Na^+, some NaSPh will be produced. However, the low amounts of NaSPh formed ($[NaSPh] \leq 0.2$ mmol dm^{-3}) are sufficiently soluble in MeCN for the reaction to remain homogeneous.

Results and discussion

Effects of H^+ on the reactivity of $[Fe_4S_4(SPh)_4]^{2-}$

In a series of kinetic studies we have been studying the acid-catalysed substitution reactions of a variety of synthetic Fe–S-based clusters: reactions essential in understanding the multi-proton, multi-electron, substrate transformation chemistry of these compounds.[8] The generalised picture which has emerged from these studies is exemplified by that of $[Fe_4S_4(SPh)_4]^{2-}$ shown in Fig. 1.

Initial protonation occurs at the thiolato-S and subsequently at two μ_3-S atoms. It is protonation of these μ_3-S which labilises the cluster towards substitution. Protonation of the thiolate ligand is, apparently, not appreciably labilising. The reasons for this have been discussed in detail earlier[5,8] but, briefly, are a consequence of protonation at this site decreasing the σ-donor but increasing the π-acceptor abilities of the ligand. The nett

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† *Supplementary data available*: kinetic data. For direct electronic access see http://www.rsc.org/suppdata/dt/1999/119/, otherwise available from BLDSC (No. SUP 57466, 5 pp.) or the RSC Library. See Instructions for Authors, 1999, Issue 1 (http://www.rsc.org/dalton).

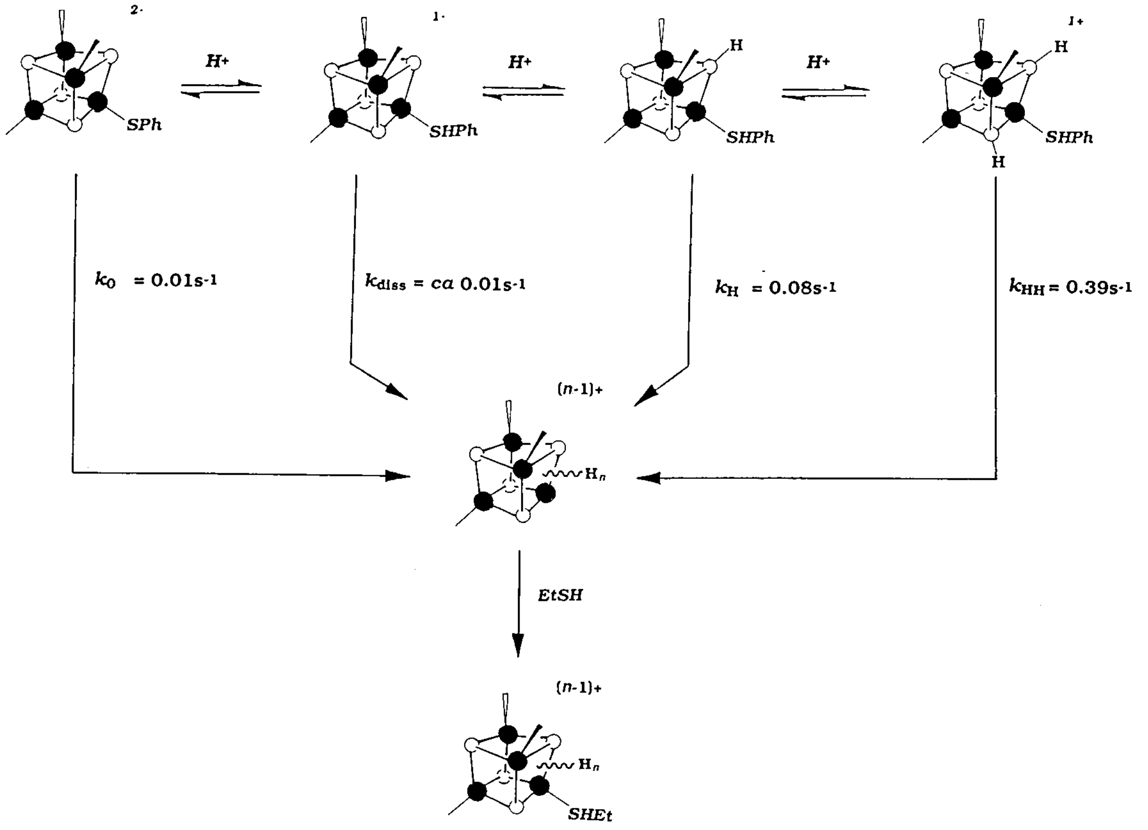

Fig. 1 Effect of successive addition of H^+ to $[Fe_4S_4(SPh)_4]^{2-}$ on the lability of the cluster in the dissociative substitution reactions with EtS^-. For simplicity only one PhS ligand is shown; ● = Fe, ○ = S.

effect is that the Fe–thiolate and Fe–thiol bond strengths are very similar, and consequently the lability is unchanged. This proposal is consistent with structural studies on mononuclear thiolate complexes.[9]

These reactions of $[Fe_4S_4(SPh)_4]^{2-}$ operate by an acid-catalysed dissociative substitution mechanism and analysis of the kinetics gives the values of $k_0 = 1.0 \pm 0.2 \times 10^{-2}$ s^{-1}, $k_H = 8.0 \pm 0.2 \times 10^{-2}$ s^{-1} and $k_{HH} = 0.39 \pm 0.02$ s^{-1}. The ratio, $k_H/k_0 = 8.4 \pm 1.6$, describes the labilising effect a single protonation has on the dissociation of the leaving group. Similarly $k_{HH}/k_0 = 41 \pm 8$ describes the effect of diprotonation. It is evident, that to a reasonable approximation, $k_{HH}/k_0 = (k_H/k_0)^2$. That is, the labilising effect of each successive H^+ is compounded. Clearly, we are not looking for an exact relationship here. Merely a guide as to whether there are orders of magnitude difference between the combined and the individual labilising effects of each contributor to the activated complex. In the remainder of this paper we will see that similar equations describe the labilisation of the leaving group in Fe–S clusters by the combined effects of: (i) H^+ and Na^+ and (ii) H^+ and nucleophile.

The clusters studied in this work[10,11] and the products of the reactions [equation (2)] have already been structurally well characterised. Earlier synthetic studies showed that the addition of at least two mole equivalents of $Et_2NCS_2^-$ to $[Fe_4S_4X_4]^{2-}$ (X = Cl or PhS) results in the formation of $[Fe_4S_4(S_2CNEt_2)_2X_2]^{2-}$ and X-ray crystallography has established that the Et_2NCS_2-ligands are bound in a bidentate fashion to the Fe atoms.[12]

Effect of Na^+ on the reactivity of $[Fe_4S_4(SPh)_4]^{2-}$ and $[Fe_4S_4Cl_4]^{2-}$

When studied on a stopped-flow apparatus, the reaction between $[Fe_4S_4(SPh)_4]^{2-}$ and an excess of $[NBu^n_4]S_2CNEt_2$ is associated with a biphasic absorbance–time curve, provided $[Et_2NCS_2^-] < 20$ mmol dm^{-3}. The initial absorbance is that of $[Fe_4S_4(SPh)_4]^{2-}$ and the final absorbance corresponds to $[Fe_4S_4(SPh)_2(S_2CNEt_2)_2]^{2-}$. At higher concentrations of $Et_2NCS_2^-$ the absorbance–time curve becomes more complicated, with an increasing absorbance over protracted times (>20 s). For simplicity we have: (i) studied the kinetics only when $[Et_2NCS_2^-] < 20$ mmol dm^{-3} and (ii) restricted the discussion to the first substitution reaction, corresponding to the initial phase of the absorbance–time curve. In order to get accurate rate constants for this first phase a method has been adopted, used in earlier studies, involving fitting the entire curve to two exponentials, and from this analysis obtaining the rate constant for the faster phase.

The rate of the initial substitution reaction exhibits a first order dependence on the concentration of $[Fe_4S_4(SPh)_4]^{2-}$ but is independent of the concentration of $Et_2NCS_2^-$ ($k_{obs} = 2.0 \pm 0.5 \times 10^{-2}$ s^{-1}). This value is in good agreement with the rate constant measured using EtS^- or Bu^tS^- in earlier studies. The first-order dependence on the concentration of cluster is indicated by the exponential shape of the absorbance–time curve, and is confirmed by experiments in which the concentration of the cluster was varied ($[Fe_4S_4(SPh)_4{}^{2-}] = 0.02$–$0.2$ mmol dm^{-3}) whilst keeping the concentration of $Et_2NCS_2^-$ constant (5.0 mmol dm^{-3}). Under these conditions the value of k_{obs} did not vary. These kinetics are consistent with the uncatalysed dissociative mechanism shown in the centre of Fig. 2, in which dissociation of the Fe–SPh bond has to occur before $Et_2NCS_2^-$ binds to the cluster.

The addition of $Na[BPh_4]$ results in an increase in the rate of the reaction as shown in Fig. 3. The dependence on the concentration of Na^+ is complicated. At low concentrations of Na^+ the rate exhibits a first order dependence on the concentration of Na^+, but at high concentrations the rate becomes independent of the concentration of Na^+. Experiments in which the concentration of $Et_2NCS_2^-$ was varied (maintaining $[Na^+] = 10.0$ mmol dm^{-3}), showed that the rate of the reac-

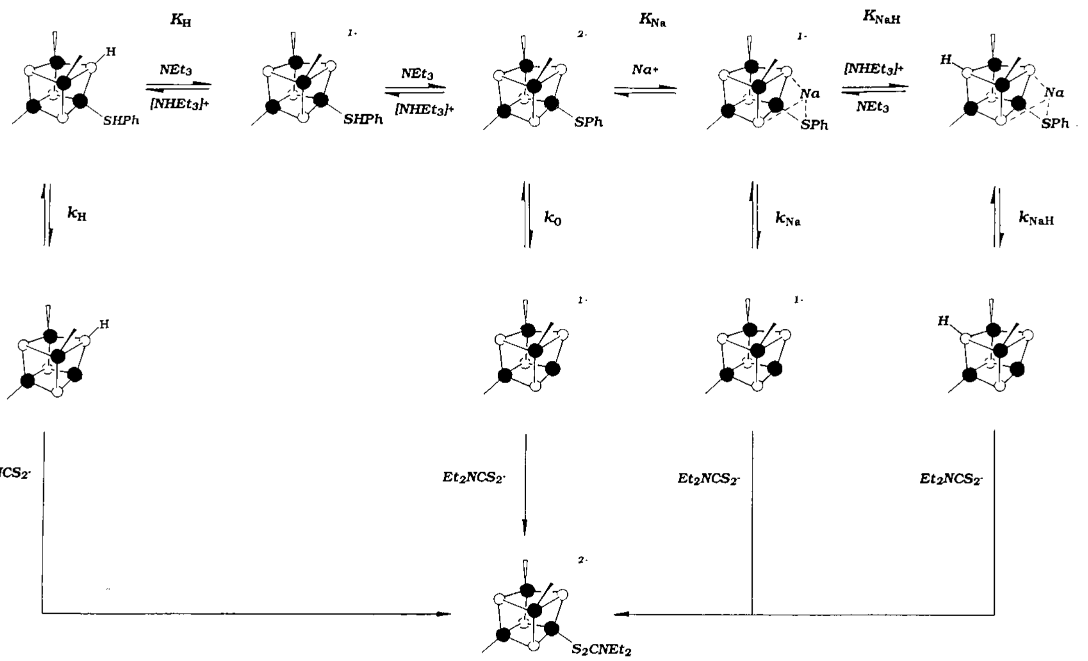

Fig. 2 Dissociative substitution pathways in the reactions of $[Fe_4S_4(SPh)_4]^{2-}$ with $Et_2NCS_2^-$ in MeCN at 25.0 °C. Shown (from left to right) are: (i) acid-catalysed pathway; (ii) uncatalysed pathway; (iii) Na^+-catalysed pathway and (iv) Na^+- with acid-catalysed pathway. Only one PhS ligand is shown for simplicity; ● = Fe, ○ = S.

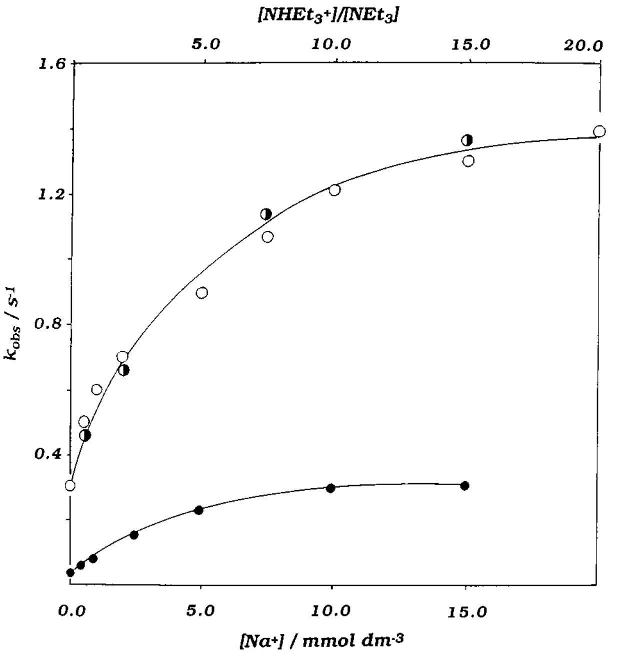

Fig. 3 Kinetics for the reaction between $[Fe_4S_4(SPh)_4]^{2-}$ (0.1 mmol dm^{-3}) and $Et_2NCS_2^-$ in MeCN at 25.0 °C. The bottom curve illustrates the effect of Na^+ on the rate of the reaction (●); the curve is that defined by equation (3). The top curve shows the combined effect of Na^+ and H^+; data points correspond to: $[NHEt_3^+] = 10$ mmol dm^{-3} (○), $[NHEt_3^+] = 20$ mmol dm^{-3} (◑); $[Et_2NCS_2^-] = 2.0$ mmol dm^{-3}, $[NEt_3] = 1$–20 mmol dm^{-3}. The curve is that defined by equation (6).

tion is independent of thiolate. Analysis of these data by the usual "double reciprocal" graph[13] gives the rate law shown in equation (3).

$$\frac{-d[Fe_4S_4(SPh)_4{}^{2-}]}{dt} = \frac{\{(2.0 \pm 0.5) \times 10^{-2} + (1.5 \pm 0.1) \times 10^2[Na^+]\}}{1 + (5.1 \pm 0.3) \times 10^2[Na^+]}[Fe_4S_4(SPh)_4{}^{2-}] \qquad (3)$$

This behaviour is consistent with the pathway shown in Fig. 2 in which Na^+ rapidly binds to the cluster and this labilises the Fe–SPh bond to dissociation. This behaviour is directly analogous to that observed with H^+, and the effects of Na^+ and H^+ will be compared below. First, the way Na^+ binds to $[Fe_4S_4(SPh)_4]^{2-}$ will be considered.

The binding of Na^+ to other Fe–S clusters has been observed crystallographically. Thus, in $[Na_2\{Fe_6S_9(SMe)_2\}_2]^{6-}$, each Na^+ is bound to three μ_3-S;[14] in $[\alpha\text{-}Na_2Fe_{18}S_{30}]^{8-}$ and $[\beta\text{-}Na_2Fe_{18}S_{30}]^{8-}$, each Na^+ is bound to four μ-S[15,16] and in $[Na_9Fe_{20}Se_{38}]^{9-}$ each Na^+ is bound to four μ-Se.[16] Finally, there is evidence that Na^+ interacts with the "double-cubane" $[\{MoFe_3S_4(SEt)_2(Cl_4cat)\}_2(\mu\text{-}SEt)_2]^{4-}$ ($Cl_4cat = C_6Cl_4O_2{}^{2-}$).[17] Molecular modelling studies indicate that a Na^+ could bind to two μ_3-S and two μ-SEt residues. With these precedents in mind, it seems likely that Na^+ binds to $[Fe_4S_4(SPh)_4]^{2-}$ using one SPh and two μ_3-S as shown in Fig. 2.

The rate law for the reactions in the presence of Na^+ is readily derived by assuming that binding Na^+ is a rapid equilibrium reaction (complete within the dead-time of the stopped-flow apparatus, 2 ms), and that subsequent dissociation of the Fe–SPh bond is rate-limiting. The result is shown in equation (4), and comparison of equations

$$\frac{-d[Fe_4S_4(SPh)_4{}^{2-}]}{dt} = \frac{\{k_0 + k_{Na}K_{Na}[Na^+]\}}{1 + K_{Na}[Na^+]}[Fe_4S_4(SPh)_4{}^{2-}] \qquad (4)$$

(3) and (4) gives $k_0 = 1.5 \pm 0.5 \times 10^{-2}$ s^{-1}, $k_{Na} = 0.30 \pm 0.04$ s^{-1} and $K_{Na} = 5.1 \pm 0.3 \times 10^2$ dm^3 mol^{-1}. A quantitative measure of the labilising effect of Na^+ is given by $k_{Na}/k_0 = 31 \pm 6$.

Equation (4) is directly comparable to the rate law describing the effect of $[NHEt_3]^+$ on the substitution reactions[2] of $[Fe_4S_4(SPh)_4]^{2-}$. In this case the total 'proton' concentration is expressed as $[NHEt_3^+]/[NEt_3]$, and the rate law is that shown in equation (5), with $k_0 = 1.0 \pm 0.2 \times 10^{-2}$ s^{-1}, $k_H = 8.0 \pm 0.1 \times 10^{-2}$ s^{-1} and $K_H = 1.2 \pm 0.1$.

$$\frac{-\mathrm{d}[\mathrm{Fe_4S_4(SPh)_4}^{2-}]}{\mathrm{d}t} = \frac{\{k_0 + k_\mathrm{H}K_\mathrm{H}[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]\}}{1 + K_\mathrm{H}[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]}[\mathrm{Fe_4S_4(SPh)_4}^{2-}] \quad (5)$$

By comparing k_Na and k_H derived from equations (4) and (5) respectively, a quantitative measure of the relative labilising effects of $\mathrm{H^+}$ and $\mathrm{Na^+}$ is obtained, $k_\mathrm{Na}/k_\mathrm{H} = 4.1 \pm 0.3$. Although this is not a large difference it is, at first sight a surprising result. Intuitively, it might be expected that $\mathrm{H^+}$ would be more labilising than $\mathrm{Na^+}$ since $\mathrm{H^+}$ is a more polarising cation. In addition, in the reactions with acid, $\mathrm{H^+}$ is labilising a thiol ligand (Fig. 1) whereas $\mathrm{Na^+}$ is labilising a thiolate ligand (Fig. 2), making the greater labilising power of $\mathrm{Na^+}$ even more unexpected. The reasons for this are not entirely clear but we suggest that (at least) part of the reason is because a single $\mathrm{Na^+}$ is sufficiently large to interact with both the thiolate ligand and two μ_3-S simultaneously. Consequently, the labilising interactions of $\mathrm{Na^+}$ with the leaving group and μ_3-S are always in concert. In contrast, with the smaller $\mathrm{H^+}$, such a concerted interaction is not possible and multiple protonations must occur to attain the same effect.

The importance of the thiolate ligand in facilitating the binding of $\mathrm{Na^+}$ to $[\mathrm{Fe_4S_4(SPh)_4}]^{2-}$ is emphasised in studies with $[\mathrm{Fe_4S_4Cl_4}]^{2-}$. The kinetics of the reactions of $[\mathrm{Fe_4S_4Cl_4}]^{2-}$ with $[\mathrm{NBu^n{}_4}]\mathrm{S_2CNEt_2}$ are independent of the concentration of $\mathrm{Et_2NCS_2}^-$, with $k_0{}^\mathrm{C} = 3.0 \pm 0.5\ \mathrm{s^{-1}}$. This rate constant is in good agreement with that observed earlier for the dissociative substitution pathway using $\mathrm{PhS^-}$ as the nucleophile ($k_0{}^\mathrm{C} = 2.0 \pm 0.3\ \mathrm{s^{-1}}$).[4]

The rate of the reaction of $[\mathrm{Fe_4S_4Cl_4}]^{2-}$ with $\mathrm{Et_2NCS_2}^-$ is unaffected by the presence of $\mathrm{Na^+}$. Since the geometries of the cluster cores of $[\mathrm{Fe_4S_4(SPh)_4}]^{2-}$ and $[\mathrm{Fe_4S_4Cl_4}]^{2-}$ are essentially identical, this indicates that Cl is a poorer ligand than PhS for $\mathrm{Na^+}$. Assuming that the rate law shown in equation (4) operates in the reactions of $[\mathrm{Fe_4S_4Cl_4}]^{2-}$, a limit for the value of $K_\mathrm{Na}{}^\mathrm{C}$ (the binding constant of $\mathrm{Na^+}$ to $[\mathrm{Fe_4S_4Cl_4}]^{2-}$) can be calculated. Since, there is no evidence for the binding of $\mathrm{Na^+}$ even when $[\mathrm{Na^+}] = 20.0\ \mathrm{mmol\ dm^{-3}}$, $K_\mathrm{Na}{}^\mathrm{C} < 5\ \mathrm{dm^3\ mol^{-1}}$ (*i.e.* $\mathrm{Na^+}$ is bound to $[\mathrm{Fe_4S_4Cl_4}]^{2-}$ at least 100 times more weakly than it is to $[\mathrm{Fe_4S_4(SPh)_4}]^{2-}$).

Combined effect of $\mathrm{Na^+}$ and $\mathrm{H^+}$ on the lability of $[\mathrm{Fe_4S_4(SPh)_4}]^{2-}$

When $[\mathrm{Na^+}] \geq 10\ \mathrm{mmol\ dm^{-3}}$, all of the $[\mathrm{Fe_4S_4(SPh)_4}]^{2-}$ in solution has a $\mathrm{Na^+}$ bound to it, *i.e.* $[\{\mathrm{Fe_4S_4(SPh)_4}\}\mathrm{Na}]^-$. Under these conditions, the addition of $[\mathrm{NHEt_3}]^+$ results in a further increase in the rate as shown in Fig. 3. Analysis of the kinetics shows that the reaction exhibits a non-linear dependence on, $[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]$, such that at low values of this ratio the rate exhibits a first order dependence on $[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]$, but is independent of the ratio at high values of $[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]$. In additional experiments, $[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]$ was kept constant and the concentration of PhSH varied. Under these conditions the rate of the reaction does not depend on the concentration of PhSH. The rate law which fits these data is shown in equation (6).

$$\frac{-\mathrm{d}[\mathrm{Fe_4S_4(SPh)_4}^{2-}]}{\mathrm{d}t} = \frac{\{0.30 \pm 0.03 + (0.38 \pm 0.04)[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]\}}{1 + (0.25 \pm 0.02)[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]} \times [\mathrm{Fe_4S_4(SPh)_4}^{2-}] \quad (6)$$

This rate law is identical to that observed with essentially every Fe–S-based cluster we have studied to date,[2–8] the only difference is that in this case $\mathrm{Na^+}$ is additionally bound to the cluster. The mechanism is shown in Fig. 2. Rapid protonation of $[\{\mathrm{Fe_4S_4(SPh)_4}\}\mathrm{Na}]^-$ labilises the cluster towards dissociation of the Fe–SPh bond. The kinetics clearly demonstrate that $\mathrm{H^+}$ does not displace the bound $\mathrm{Na^+}$, otherwise k_obs at high $[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]$ would correspond to the value observed in the presence of $[\mathrm{NHEt_3}]^+$ and defined by equation (5).

By considering all the pathways shown in Fig. 2, the general rate law shown in equation (7) can be derived, assuming that

$$\frac{-\mathrm{d}[\mathrm{Fe_4S_4(SPh)_4}^{2-}]}{\mathrm{d}t} = \frac{\{k_0 + k_\mathrm{Na}K_\mathrm{Na}[\mathrm{Na^+}] + k_\mathrm{NaH}K_\mathrm{Na}K_\mathrm{NaH}[\mathrm{Na^+}][\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]\}}{1 + K_\mathrm{Na}[\mathrm{Na^+}] + K_\mathrm{Na}K_\mathrm{NaH}[\mathrm{Na^+}][\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]} \times [\mathrm{Fe_4S_4(SPh)_4}^{2-}] \quad (7)$$

binding of $\mathrm{Na^+}$ and $\mathrm{H^+}$ are rapidly established equilibria complete within the dead-time of the stopped-flow apparatus, and dissociation of the Fe–SPh bonds are the rate-limiting steps.

Under conditions where $[\mathrm{Na^+}] > 10\ \mathrm{mmol\ dm^{-3}}$, $K_\mathrm{Na}[\mathrm{Na^+}] \gg 1$ and equation (7) simplifies to equation (8).

$$\frac{-\mathrm{d}[\mathrm{Fe_4S_4(SPh)_4}^{2-}]}{\mathrm{d}t} = \frac{\{k_0 + k_\mathrm{Na} + k_\mathrm{NaH}K_\mathrm{NaH}[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]\}}{1 + K_\mathrm{NaH}[\mathrm{NHEt_3}^+]/[\mathrm{NEt_3}]} \times [\mathrm{Fe_4S_4(SPh)_4}^{2-}] \quad (8)$$

Comparison of equations (6) and (8) gives $(k_0 + k_\mathrm{Na}) = 0.30 \pm 0.03\ \mathrm{s^{-1}}$, and using $k_0 = 1.5 \pm 0.5 \times 10^{-2}\ \mathrm{s^{-1}}$ (the mean value of k_0 derived from this and earlier studies), $k_\mathrm{Na} = 0.28 \pm 0.03\ \mathrm{s^{-1}}$. This value is in good agreement with that derived from studies in the presence of only $\mathrm{Na^+}$ [equation (4)]; in addition, $k_\mathrm{NaH} = 1.5 \pm 0.2\ \mathrm{s^{-1}}$ and $K_\mathrm{NaH} = 0.25 \pm 0.02$.

The question which must now be addressed is, “Where does this proton bind?” Using the value of $K_\mathrm{NaH} = 0.25 \pm 0.02$ derived from these studies together with the pK_a of $[\mathrm{NHEt_3}]^+$ in MeCN (18.46),[18] the pK_a = 17.9 of $[\{\mathrm{Fe_4S_4(SPh)_4}\}\mathrm{Na}]^-$ can be calculated. This value is slightly smaller than for the parent $[\mathrm{Fe_4S_4(SPh)_4}]^{2-}$ (pK_a = 18.6),[5] consistent with the presence of the electron-withdrawing $\mathrm{Na^+}$ bound to the cluster. Most important the pK_a associated with $[\{\mathrm{Fe_4S_4(SPh)_4}\}\mathrm{Na}]^-$ falls in the range $17.9 \leq \mathrm{p}K_\mathrm{a} \leq 18.9$, observed for all Fe–S-based clusters in MeCN.[5] This is consistent with protonation occuring at the cluster core; most probably a μ_3-S.

Since, the above analyses have yielded the values of k_NaH and k_Na, and earlier work[2] gave k_H we are in a position to discuss quantitatively the relative labilising effects of $\mathrm{Na^+}$, $\mathrm{H^+}$ and the combined effect of both $\mathrm{Na^+}$ and $\mathrm{H^+}$ on the cluster.

From the studies with $[\mathrm{NHEt_3}]^+$ alone [equation (5)], $k_\mathrm{H}/k_0 = 8.4 \pm 1.6$, and in studies where only $\mathrm{Na^+}$ is added [equation (4)], $k_\mathrm{Na}/k_0 = 31 \pm 6$. The addition of both $\mathrm{Na^+}$ and $\mathrm{H^+}$ results in an increase in the rate [equation (8)], $k_\mathrm{NaH}/k_0 = 170 \pm 20$. This is close to the value which can be calculated using the simple equation, $k_\mathrm{NaH}/k_0 = (k_\mathrm{Na}/k_0)(k_\mathrm{H}/k_0) = 260 \pm 50$. That is, the labilising effect of $\mathrm{Na^+}$ and $\mathrm{H^+}$ together is not appreciably different from the product of the individual labilising components.

We will see in the next section that similar behaviour is observed in the effects of $\mathrm{H^+}$ and nucleophile on the lability of the cluster in an associative mechanism.

Effect of $\mathrm{H^+}$ on the dissociative lability of $[\mathrm{Fe_4S_4Cl_4}]^{2-}$

Previous studies showed that the substitution reaction between $[\mathrm{Fe_4S_4Cl_4}]^{2-}$ and $\mathrm{PhS^-}$ occurs predominantly by an associative mechanism, and protonation (by $[NHEt_3]^+$) accelerates the rate.[4] Previously, the relative contributions to the labilisation of the cluster from binding H^+ and PhSH could not be assessed. However, because $Et_2NCS_2^-$ is a poor nucleophile the substitution reaction with $[Fe_4S_4Cl_4]^{2-}$ occurs exclusively by a dissociative pathway. This permits a quantification of the effect H^+ alone has on the rate of dissociation of the chloro-group. Comparison with the earlier studies allows us to estimate the individual effects that binding H^+ and PhSH have on the labilisation of the chloro-group in the associative pathway.

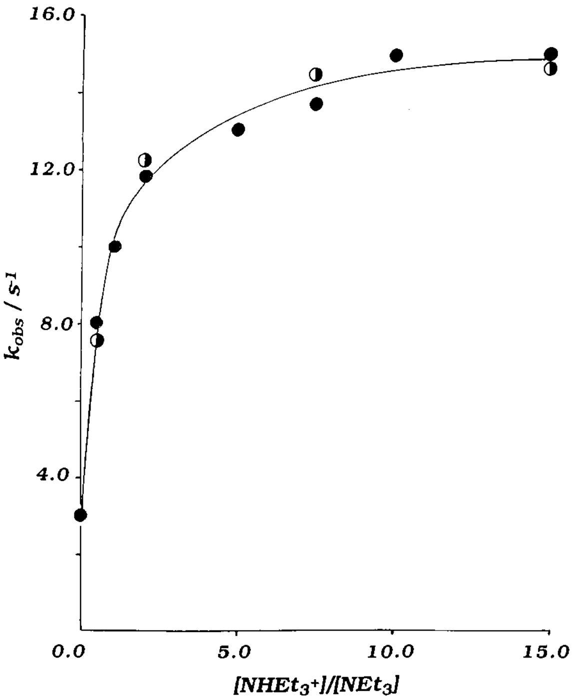

Fig. 4 Kinetics for the reaction between $[Fe_4S_4Cl_4]^{2-}$ (0.1 mmol dm^{-3}) and $Et_2NCS_2^-$ in the presence of $[NHEt_3]^+$ in MeCN at 25.0 °C. Data shown: $[NHEt_3^+]$ = 10.0 mmol dm^{-3} (●), $[NHEt_3^+]$ = 20.0 mmol dm^{-3} (◑); $[Et_2NCS_2^-]$ = 2.0 mmol dm^{-3}, $[NEt_3]$ = 0.7–20 mmol dm^{-3}. Curve drawn is that defined by equation (9).

The addition of $[NHEt_3]^+$ to the reaction between $[Fe_4S_4Cl_4]^{2-}$ and $Et_2NCS_2^-$ leads to an increase in the rate of reaction as shown in Fig. 4.

The rate of reaction exhibits a first order dependence on the concentration of $[Fe_4S_4Cl_4]^{2-}$ (as indicated by the exponential shape of the absorbance–time curve) and the usual non-linear dependence on the ratio, $[NEt_3^+]/[NEt_3]$. The rate law consistent with these data is shown in equation (9).

$$\frac{-d[Fe_4S_4Cl_4^{2-}]}{dt} = \frac{\{3.0 \pm 0.5 + (30.2 \pm 0.2)[NHEt_3^+]/[NEt_3]\}}{1 + (2.0 \pm 0.2)[NHEt_3^+]/[NEt_3]} \times [Fe_4S_4Cl_4^{2-}] \quad (9)$$

This is consistent with the dissociative mechanism shown in Fig. 5. The rate law associated with this mechanism is shown in equation (10), assuming that protonation is a rapidly established equilibrium and dissociation of the chloro-group is rate-limiting.

$$\frac{-d[Fe_4S_4Cl_4^{2-}]}{dt} = \frac{\{k_0^C + k_H^C K_H^C[NHEt_3^+]/[NEt_3]\}}{1 + K_H^C[NHEt_3^+]/[NEt_3]}[Fe_4S_4Cl_4^{2-}] \quad (10)$$

Comparison of equations (9) and (10) gives: $k_0^C = 3.0 \pm 0.5$ s^{-1}; $k_H^C = 15.0 \pm 1.0$ s^{-1} and $K_H^C = 2.0 \pm 0.2$. The value of

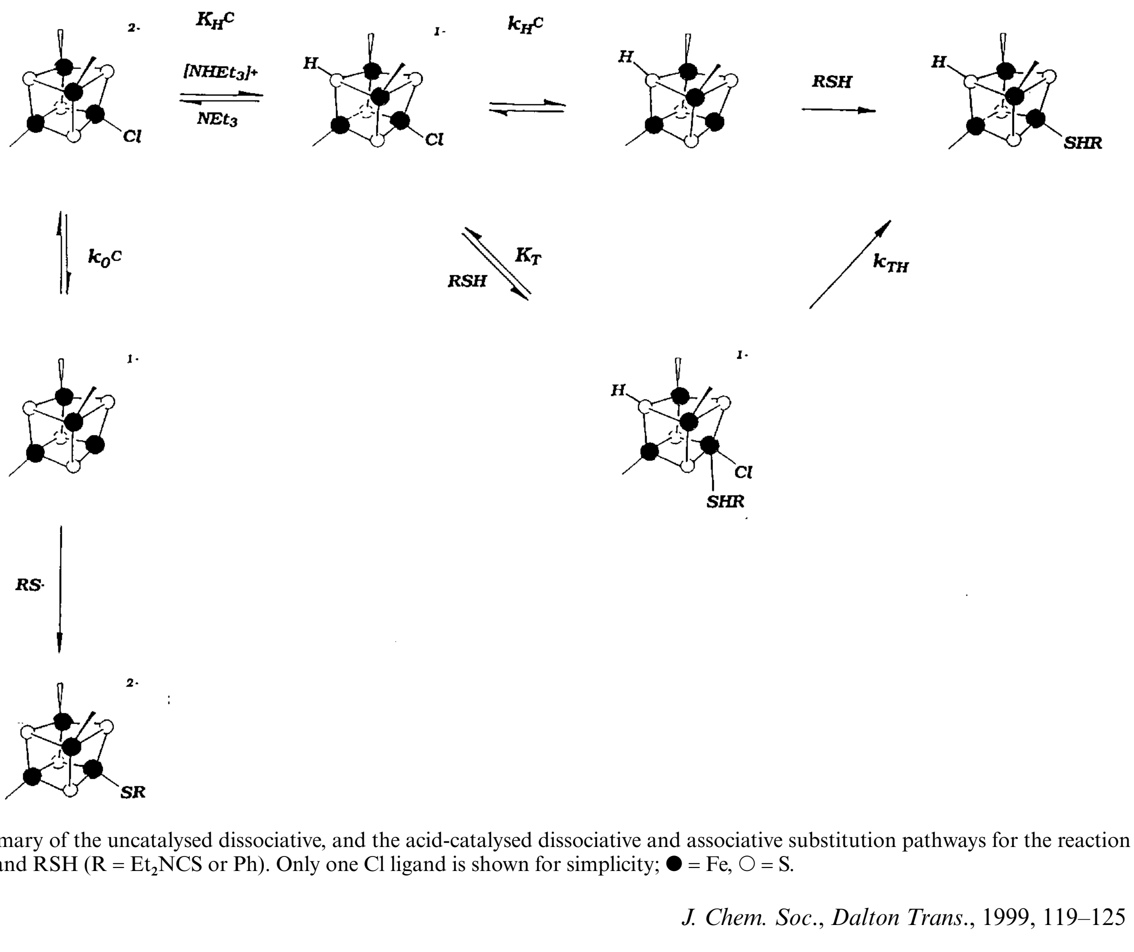

Fig. 5 Summary of the uncatalysed dissociative, and the acid-catalysed dissociative and associative substitution pathways for the reaction between $[Fe_4S_4Cl_4]^{2-}$ and RSH (R = Et_2NCS or Ph). Only one Cl ligand is shown for simplicity; ● = Fe, ○ = S.

Table 1 Comparison of the individual and combined effects of H^+, Na^+ and PhSH on the dissociation of the leaving group in the substitution reactions of $[Fe_4S_4X_4]^{2-}$ (X = Cl or PhS)

Cluster	A	k_A/k_0 [a]	B	k_B/k_0	k_{AB}/k_0 Obs.	k_{AB}/k_0 Calc.
$[Fe_4S_4(SPh)_4]^{2-}$	H	8.4 ± 1.6	H	8.4 ± 1.6	41 ± 8	71 ± 13
	H	8.4 ± 1.6	Na	31 ± 6	170 ± 20	260 ± 50
		$k_Ak_0^{C}$ [b]		$k_Bk_0^{C}$	k_{AB}/k_0^{C} Obs.	k_{AB}/k_0^{C} Calc.
$[Fe_4S_4Cl_4]^{2-}$	H	5.0 ± 0.3	PhSH	83 ± 4	≥250	415 ± 20

[a] $k_0 = (1.0 \pm 0.2) \times 10^{-2}\ s^{-1}$, for studies with $[Fe_4S_4(SPh)_4]^{2-}$. [b] $k_0^C = 3.0 \pm 0.5\ s^{-1}$, for studies with $[Fe_4S_4Cl_4]^{2-}$.

K_H^C is in good agreement with that determined in the earlier studies with PhSH ($K_H^C = 2.2 \pm 0.1$).[4]

Earlier studies on the reaction between $[Fe_4S_4Cl_4]^{2-}$ and PhSH in the presence of $[NHEt_3]^+$ showed that the mechanism involved rapid protonation of the cluster, followed by the binding of PhSH (K_T), then rate-limiting cleavage of Fe–Cl (k_{TH})[4] (Fig. 5). Analysis of the kinetics gave $K_Tk_{TH} = 1.5 \times 10^4$ $dm^3\ mol^{-1}\ s^{-1}$. A limit to the value of K_T can be estimated since, even at the highest concentration of PhSH used ([PhSH] = 5.0 mmol dm^{-3}), there is no kinetic evidence for the accumulation of appreciable amounts of the cluster with PhSH bound; hence $(5.0 \times 10^{-3})K_T \leq 0.1$, and $K_T \leq 20$ mol dm^{-3}; consequently $k_{TH} \geq 7.5 \times 10^2\ s^{-1}$. The labilisation afforded by binding H^+ and PhSH is $k_{TH}/k_0^C \geq 250$.

We are now in a position to estimate the individual labilising effects of H^+ (k_H^C/k_0^C) and nucleophile (k_T/k_0^C). The studies with $Et_2NCS_2^-$, reported herein, show that protonation of the cluster core labilises the chloro-group to dissociation, $k_H^C/k_0^C = 5.0 \pm 0.3$. Earlier studies[4] showed that the dissociation of the chloro-group after binding of PhS^- was associated with a rate constant, $k_T = 2.5 \pm 0.1 \times 10^2\ s^{-1}$. Consequently, labilisation afforded by binding of PhS^- is $k_T/k_0^C = 83 \pm 4$. Although, strictly, this is the labilisation afforded by PhS^- rather than PhSH, currently it is the best we can do, and does at least give an estimate of the effect of PhSH. Using these values we can calculate $(k_T/k_0^C)(k_H/k_0^C) = 415 \pm 20$, consistent with the simple relationship, $k_{TH}/k_0^C = (k_T/k_0^C)(k_H/k_0^C)$.

Previously, in a study[5] on the acid-catalysed substitution reactions of the linear trinuclear cluster, $[Cl_2FeS_2VS_2FeCl_2]^{3-}$ we came to the conclusion that H^+ alone was not particularly labilising but for maximum labilisation both protonation and binding a thiol was necessary. Herein, a detailed quantitative analysis confirms our earlier proposal.

Labilisation by multiple components

Throughout this paper we have emphasised that the labilising effect of adding more than one reactant (H^+, Na^+ or nucleophile) to a cluster is not appreciably more labilising than that expected from the individual effects of each contributor. This is born out by the summary of the results shown in Table 1, where we return to the generalised designations (A, B, C, *etc.* . . .) introduced in equation (1).

Thus, two species A and B will affect the lability of the leaving group by an amount described by the simple relationship shown in equation (11), where k_0 is the rate constant associated with the uncatalysed reaction.

$$k_{AB}/k_0 = (k_A/k_0)(k_B/k_0) \qquad (11)$$

Close inspection of Table 1 reveals that our (perhaps over-simplistic) equations consistently over-emphasise the labilising power of the combination of several components. This is probably not too surprising considering the electronic origins of the effects we are discussing. The strength, and hence lability, of Fe–Cl, Fe–SPh or Fe–SHPh bonds are defined by the σ- and π-orbital overlap between ligand and Fe. The electron density distribution within these σ- and π-orbital components is perturbed by the presence of H^+, Na^+ or nucleophile. It seems likely that in the presence of several components the electron distribution is distorted predominantly by one component such that the others do not have the effect (when acting in concert) that they do when acting individually. However, it is clear that this is a rather minor effect and that (at least in these systems) there is no cooperative labilising effect from having several components present.

Experimental

All manipulations were routinely performed under an atmosphere of dinitrogen using Schlenk or syringe techniques as appropriate. $[NBu^n_4]_2[Fe_4S_4(SPh)_4]$[19] and $[NBu^n_4]_2[Fe_4S_4Cl_4]$[11] were prepared by the literature methods and characterised as described earlier.

MeCN was dried by distillation from CaH_2 under an atmosphere of dinitrogen.

$Na[BPh_4]$ was purchased from Aldrich and used as received. $NaS_2CNEt_2 \cdot 3H_2O$ (Aldrich) was recrystallised from methanol–diethyl ether and dried *in vacuo*.

$[NHEt_3]BPh_4$ was prepared by the literature method.[20]

Preparation of $[NBu^n_4]S_2CNEt_2$

$[NBu^n_4]Br$ (2.9 g, 8.9 mmol) was added to a solution of $NaS_2CNEt_2 \cdot 3H_2O$ (2.0 g, 8.9 mmol) in methanol (*ca.* 50 mL), and the solution stirred for 30 min. The solvent was then removed *in vacuo* to leave a pale yellow solid. MeCN (*ca.* 20 mL) was added to the solid and after stirring for 30 min the mixture was filtered through Celite to remove NaBr. Diethyl ether (*ca.* 60 mL) was added to the clear filtrate which went cloudy (a further small amount of NaBr). The mixture was again filtered through Celite, then addition of a large excess of diethyl ether (*ca.* 200 mL) to the clear solution produced no further cloudiness. The solution was cooled to −20 °C overnight to produce fine, pale yellow needles of the product, which was removed by filtration, washed with diethyl ether and then dried *in vacuo*.

Kinetic studies

The reactions were studied on a Hi-Tech Stopped-Flow apparatus modified to handle air-sensitive solutions.[21] The temperature was maintained at 25.0 °C using a Grant LE8 thermostat tank. The spectrophotometer is interfaced to a Viglen computer *via* an analogue-to-digital convertor.

All solutions were prepared immediately prior to study and used within 1 h.

Under all conditions the reactions exhibited exponential absorbance–time curves which were fitted using a computer program. The dependence on the concentration of other reagents was established using conventional graphical methods as presented in Results and discussion.

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