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Binding small molecules and ions to $[Fe_4S_4Cl_4]^{2-}$ modulates rate of protonation of the cluster†

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The mechanism of the acid-catalyzed substitution reaction of the terminal chloro-ligands in $[Fe_4S_4Cl_4]^{2-}$ by PhS^- in the presence of $NHBu^n{}_3{}^+$ involves rate-limiting proton transfer from $NHBu^n{}_3{}^+$ to the cluster (k_0 = 490±20 $dm^3\ mol^{-1}\ s^{-1}$). A variety of small molecules and ions (L = substrate = Cl^-, Br^-, I^-, $RNHNH_2$ (R = Me or Ph), Me_2NNH_2, HCN, NCS^-, N_3^-, Bu^tNC or pyridine) bind to $[Fe_4S_4Cl_4]^{2-}$ and this affects the rate of subsequent protonation of $[Fe_4S_4Cl_4(L)]^{n-}$. Where the kinetics allow, the equilibrium constants for the substrates binding to $[Fe_4S_4Cl_4]^{2-}$ (K^L) and the rates of proton transfer from $NHBu^n{}_3{}^+$ to $[Fe_4S_4Cl_4(L)]^{n-}$ (k_0^L) have been determined. The results indicate the following general features. (i) Bound substrates increase the rate of protonation of the cluster, but the rate increase is modest (k_0^L/k_0 = 1.6 to ≥ 72). (ii) When K^L is small, so is k_0^L/k_0. (iii) Binding substrates which are good σ-donors or good π-acceptors lead to the largest k_0^L/k_0. This behaviour is discussed in terms of the recent proposal that protonation of $[Fe_4S_4Cl_4]^{2-}$ at a μ_3-S, is coupled to concomitant Fe-(μ_3-SH) bond elongation / cleavage.

Introduction

Small molecules and ions (*e.g.* protons, alkynes, hydrazines, CN^-, N_3^- *etc*) can bind to the Fe-S-based clusters in certain metalloenzymes (*e.g.* nitrogenases, CODH and aconitase) and to some synthetic Fe-S-based clusters.[1,2] However, there is little experimental information about how these substrates interact with either the natural or synthetic clusters or how they modulate the clusters' reactivity.[3] A major obstacle in studying substrate binding to Fe-S-based clusters is the difficulty in detecting the bound substrates using spectroscopy. There are several reasons for this, which have been discussed previously: the transient nature of the binding; the paramagnetism of the clusters (with multiple spin states) and the dominant intensity of the $\{Fe_4S_4\}$ chromophore in the UV-visible spectrum.[4] These problems are compounded in natural systems where various states of the enzyme occur during turnover. A kinetic method for detecting the binding of various small molecules and ions (henceforth called substrates = L) to synthetic Fe-S-based clusters has been developed, which avoids the problems of direct spectroscopic detection of the bound substrate. The method monitors binding of the substrate by the effect that it has on the rate of acid-catalyzed substitution of the cluster.[3-5]

The kinetics of the acid-catalyzed substitution reactions of terminal ligands have been studied for a variety of Fe-S-based clusters since the 1990s.[3-5] The mechanism involves initial protonation of a μ_3-S on the cluster which labilises terminal ligands to substitution. If a substrate binds to the cluster prior to either the protonation or substitution it will modulate the rate of the acid-catalyzed substitution. Using this approach, earlier studies detected binding of substrates to $[Fe_4S_4(SEt)_4]^{2-}$, $[\{MoFe_3S_4(SEt)_3\}_2(\mu\text{-}SEt)_3]^{3-}$ and $[Fe_6S_9(SEt)_2]$.[4–6] Analysis of the kinetic data gives information about: (i) how many molecules of substrate bind to a single cluster; (ii) how tightly the substrates bind (equilibrium binding constant) and (iii) how the bound substrate modulates the rate of acid-catalyzed substitution.

Recent, DFT calculations on cubanoid $[Fe_4S_4X_4]^{2-}$ (X = thiolate phenolate or halide) indicate that protonation of a μ_3-S is coupled to elongation/cleavage of an associated Fe-(μ_3-SH) bond (Fig. 1).[7,8] This suggestion consolidates the proposition that protonation and substrate binding in Fe-S-based clusters are intimately coupled since the 3-coordinate Fe site, generated upon protonation of μ_3-S, would appear to be a propitious site for the binding of a substrate. In this paper we report studies on $[Fe_4S_4Cl_4]^{2-}$, investigating the effects that various bound substrates have on the rate of subsequent protonation of the cluster. These results, together with earlier studies, define the mutual effects that proton and substrate have on the binding of one another at an Fe-S cluster.

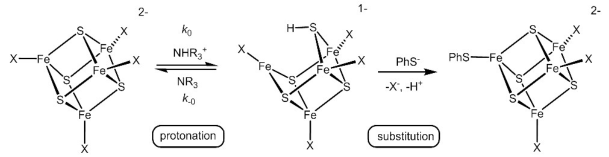

Fig. 1. Proposed mechanism for the acid-catalyzed substitution of $[Fe_4S_4X_4]^{2-}$.

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Results

We have recently shown that the acid-catalyzed substitution reaction of the terminal chloro-ligands in $[Fe_4S_4Cl_4]^{2-}$ by PhS^- in the presence of $NHBu^n_3{}^+$ involves rate-limiting proton transfer from $NHBu^n_3{}^+$ to $[Fe_4S_4Cl_4]^{2-}$ (k_0 = 490±20 dm^3 mol^{-1} s^{-1}).[9] Consequently, studies on the effects that substrates have on this reaction allow evaluation of whether substrates bind to the cluster before or after protonation by this acid and, if substrate binds before protonation, to measure how the bound substrate affects the rate of protonation of the cluster.

We have studied the effects that a variety of substrates {L = substrate = Cl^-, Br^-, I^-, $N_3{}^-$, NCS^-, CN^-, HCN, Bu^{t}NC, pyridine, $RNHNH_2$ (R = Me or Ph) and Me_2NNH_2} have on the rates of protonation of the cluster by $NHBu^n_3{}^+$. In order to analyze the kinetics of these reactions, it is important to consider what species are present in the solution.

In solutions containing mixtures of $NHBu^n_3{}^+$ (pK_a = 18.1)[10] and PhS^- (pK_a = 20.8)[11] the protolytic equilibrium shown in equation (1) is rapidly established and, in the presence of an excess of $NHBu^n_3{}^+$, the equilibrium lies to the right hand side. Consequently, in the presence of an excess of $NHBu^n_3{}^+$, the solution species are $NHBu^n_3{}^+$, NBu^n_3, PhSH and L. The concentrations of the species present in solution can be calculated from the simple relationships: $[NHBu^n_3{}^+]_e = [NHBu^n_3{}^+]_0 - [PhS^-]_0$ and $[PhSH]_e = [NBu^n_3]_e = [PhS^-]_0$ (subscript e denotes the concentration formed in the mixture and subscript 0 denotes the concentration prepared).

$$NHBu^n_3{}^+ + PhS^- \rightleftharpoons NBu_3 + PhSH \qquad (1)$$

The pK_a of the substrate is also an important parameter in the analysis of the kinetics presented herein. The pK_as of the various protonated substrates (LH) are collected in Table 1.[10-14] It is evident that the pK_a of $NHBu^n_3{}^+$ in MeCN (pK_a = 18.1)[14] is significantly larger than the pK_a of all LH except HCN. Consequently, of all the substrates studied herein, only CN^- is protonated by $NHBu^n_3{}^+$, and so the results for the kinetics in the presence of HCN/CN^- will be presented separately.

Kinetics of reactions with L = $RNHNH_2$ (R = Me or Ph), Me_2NNH_2, NCS^-, $N_3{}^-$, Bu^{t}NC or py. The absorbance-time traces for the reactions of $[Fe_4S_4Cl_4]^{2-}$ with PhS^- in the presence of L and $NHBu^n_3{}^+$ are biphasic and can be fitted to two exponential curves (see Experimental and ESI). This behaviour has been observed before for the substitution reactions of $[Fe_4S_4Cl_4]^{2-}$ and is a consequence of all the chloro-groups being substituted.[4] In this paper the focus is on the binding of L to $[Fe_4S_4Cl_4]^{2-}$ and so the following discussion relates only to the kinetics for the first (faster) phase. The kinetic data for both phases are presented in the ESI.[15]

That the absorbance-time traces can be fitted to exponential curves is consistent with the reaction exhibiting a first order dependence on the concentration of cluster. The dependence on the concentration of substrate (L) was determined from plots of $k_{obs}{}'/[NHBu^n_3{}^+]_e$ against the concentration of L ($k_{obs}{}'$ is k_{obs} corrected for the background uncatalysed substitution reaction which occurs with a rate constant of 2.5±0.5 s^{-1}; $k_{obs}{}' = k_{obs} - 2.5$).[16]

For the reactions with L = NCS^-, $N_3{}^-$, pyridine, or hydrazines, $k_{obs}{}'/[NHBu^n_3{}^+]_e$ increases in a non-linear fashion with the concentrations of L (Fig. 2). Analysis of these data by a plot of $[NHBu^n_3{}^+]_e/k_{obs}{}'$ versus 1/[L] gives a straight line graph from which the experimental rate law shown in equation (2) was derived. The values of the parameters a, b and c are presented in Table 1.

$$\text{Rate} = \left\{2.5 + \frac{(a + b[L])[NHBu^n_3{}^+]_e}{1 + c[L]}\right\}[Fe_4S_4Cl_4{}^{2-}] \qquad (2)$$

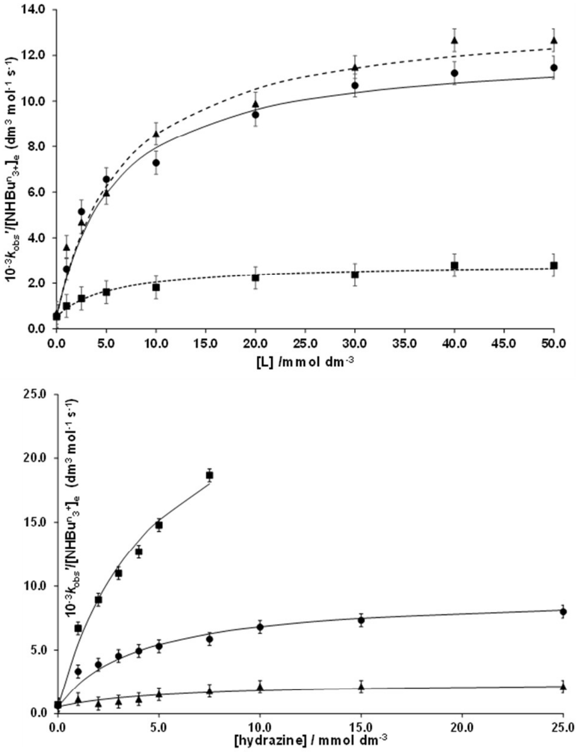

Fig. 2. TOP. Plots of $k_{obs}{}'/[NHBu^n_3{}^+]_e$ against the concentrations of: $N_3{}^-$ (▲), fit shown as dashed curve; NCS^- (●), solid curve fit; pyridine (■), fit shown as dotted curve, for the reaction of $[Fe_4S_4Cl_4]^{2-}$ (0.2 mmol dm^{-3}) with PhSH ($[PhSH]_e$ = 1.25 mmol dm^{-3}) in the presence of $NHBu^n_3{}^+$ ($[NHBu^n_3{}^+]_e$ = 3.75 mmol dm^{-3}) and the substrate at 25.0 °C in MeCN. Curves drawn are those defined by equation (2) and the parameters shown in Table 1. BOTTOM. Plot of $k_{obs}{}'/[NHBu^n_3{}^+]_e$ against the concentration of $PhNHNH_2$ (▲), Me_2NNH_2 (●) and $MeNHNH_2$ (■) for the reaction of $[Fe_4S_4Cl_4]^{2-}$ (0.2 mmol dm^{-3}) with PhSH ($[PhSH]_e$ = 1.25 mmol dm^{-3}) in the presence of $NHBu^n_3{}^+$ ($[NHBu^n_3{}^+]_e$ = 3.75 mmol dm^{-3}) and the hydrazine at 25.0 °C in MeCN. Curves drawn are those defined by equation (2) and the appropriate parameters shown in Table 1.

For the reaction with L = Bu^{t}NC, the plot of $k_{obs}{}'/[NHBu^n_3{}^+]_e$ versus [Bu^{t}NC] is linear (Fig. 3). This behaviour is also consistent with equation (2). If c[L] < 1, equation (2) simplifies to equation (3). A limit to the value of c can be estimated for the binding of Bu^{t}NC to the cluster and is presented in Table 1.

$$\text{Rate} = \{2.5 + (a + b[L])[NHBu^n_3{}^+]_e\}[Fe_4S_4Cl_4{}^{2-}] \qquad (3)$$

Table 1. Elementary rate and equilibrium constants for reaction of $[Fe_4S_4Cl_4]^{2-}$ with $NHBu^n{}_3{}^+$ in the presence of L, in MeCN at 25.0 °C

L	$pK_a{}^{LH}$	$E_L{}^a$	$a = k_0$ / dm^3 mol^{-1} s^{-1}	$b = K^L k_0{}^L$ / dm^6 mol^{-2} s^{-1}	$c = K^L$ / dm^3 mol^{-1}	$k_0{}^L$ / dm^3 mol^{-1} s^{-1}	$k_0{}^L/k_0$
Cl^-	8.9	-0.24	500±20	$1.6 \pm 0.4 \times 10^4$	≤ 50	$\geq 8 \times 10^2$	≥ 1.6
Br^-	5.5		540±20				
I^-	-2.3		560±20				
$N_3{}^-$	12.4	-0.30	530±20	$2.0 \pm 0.4 \times 10^6$	150±10	$1.3 \pm 0.2 \times 10^4$	24.5
NCS^-	10.2	-0.06	530±20	$2.0 \pm 0.4 \times 10^6$	170±10	$1.2 \pm 0.2 \times 10^4$	22.1
HCN^b	23.4		530±20		≤ 33		
Bu^tNC	–	+0.45	550±20	$7.5 \pm 0.5 \times 10^4$	≤ 2	$\geq 3.8 \times 10^4$	≥ 72
pyridine	12.6	+0.25	530±20	$4.3 \pm 0.4 \times 10^5$	180±10	$2.4 \pm 0.3 \times 10^3$	4.5
$MeNHNH_2$	15.5		530±20	$6.0 \pm 0.5 \times 10^6$	210±10	$2.9 \pm 0.3 \times 10^4$	53.9
Me_2NNH_2	14.9		530±20	$2.2 \pm 0.2 \times 10^6$	250±10	$8.8 \pm 0.5 \times 10^3$	16.6
$PhNHNH_2$	12.9		530±20	$3.7 \pm 0.4 \times 10^5$	190±10	$2.0 \pm 0.3 \times 10^3$	3.7

footnote: [a] E_L is a quantitative measure of whether bound L is a σ-donor/π-donor (negative E_L) or a σ-donor/π-acceptor (positive E_L).[18]
[b] with CN^- in the presence of HCN, rate = $7.1 \pm 0.5 \times 10^4[CN^-][Fe_4S_4Cl_4{}^{2-}]$.

It is worth noting that the analysis of the data for the reactions in the presence of $N_3{}^-$ and NCS^- yield slightly different values of K^L and $k_0{}^L$ (Table 1 and Fig. 2). However, the data for these two systems are so similar that they could both be fitted satisfactorily using $K^L = 160 \pm 10$ dm^3 mol^{-1} and $k_0{}^L = 1.25 \pm 0.05 \times 10^4$ dm^3 mol^{-1} s^{-1}.

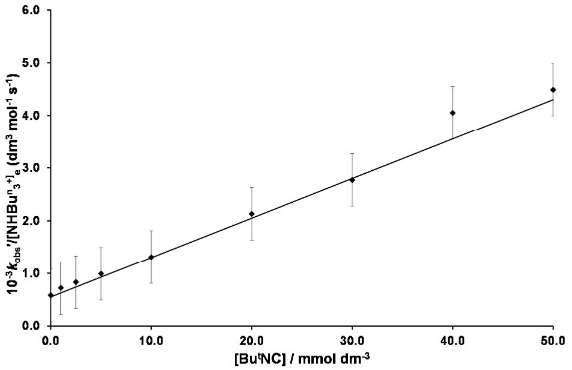

Fig 3. Plot of $k_{obs}'/[NHBu^n{}_3{}^+]_e$ against the concentration of Bu^tNC (♦) for the reaction of $[Fe_4S_4Cl_4]^{2-}$ (0.2 mmol dm^{-3}) with PhSH ($[PhSH]_e$ = 1.25 mmol dm^{-3}) in the presence of $NHBu^n{}_3{}^+$ ($[NHBu^n{}_3{}^+]_e$ = 3.75 mmol dm^{-3}) and Bu^tNC at 25.0 °C in MeCN. Line drawn is that defined by equation (3) and the appropriate parameters shown in Table 1.

Kinetics with L = Cl^-, Br^- or I^-. In the reaction of $[Fe_4S_4Cl_4]^{2-}$ with PhS^- in the presence of $NHBu^n{}_3{}^+$ and Cl^- the kinetics are those shown in Fig. 4. At low concentrations of Cl^- the rate decreases but at higher concentrations of Cl^- the rate increases in a linear fashion. Using an iterative method, the data was fitted to equation (4). In contrast, neither Br^- nor I^-, has a detectable effect on the rate of the reaction between $[Fe_4S_4Cl_4]^{2-}$ and PhS^- in the presence of $NHBu^n{}_3{}^+$.

$$\text{Rate} = \left\{ \frac{2.5}{1 + 6000[Cl^-]} + (500 + 1.6 \times 10^4[Cl^-])[NHBu^n{}_3{}^+]_e \right\} [Fe_4S_4Cl_4{}^{2-}] \qquad (4)$$

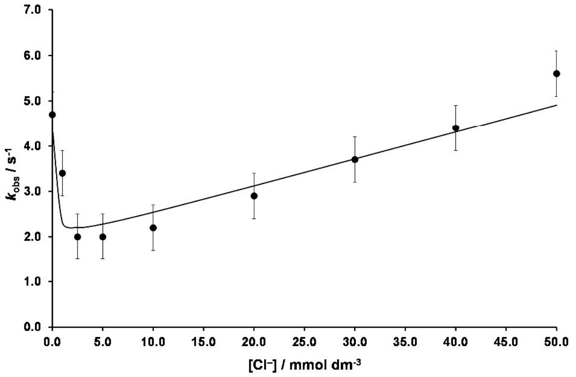

Fig 4. Plot of k_{obs} against the concentrations of Cl^- for the reaction of $[Fe_4S_4Cl_4]^{2-}$ (0.2 mmol dm^{-3}) with PhSH ($[PhSH]_e$ = 1.25 mmol dm^{-3}) in the presence of $NHBu^n{}_3{}^+$ ($[NHBu^n{}_3{}^+]_e$ = 3.75 mmol dm^{-3}) and Cl^- at 25.0 °C in MeCN. Curve is that defined by equation (4).

Kinetics with L = CN^-. The reaction between $[Fe_4S_4Cl_4]^{2-}$ (0.2 mmol dm^{-3}) and $NHBu^n{}_3{}^+$ (2.5 – 40.0 mmol dm^{-3}) with PhS^- (1.25 – 5.0 mmol dm^{-3}) was monitored in the presence of various concentrations of CN^-. The added complication in the studies with CN^- is that $NHBu^n{}_3{}^+$ (pK_a = 18.1 in MeCN)[14] is sufficiently strong to protonate CN^- ($pK_a{}^{HCN}$ = 23.4).[14] Consequently, it is necessary to analyse the kinetic data under two different conditions: (i) $[NHBu^n{}_3{}^+]_e \geq [CN^-]$ and (ii) $[NHBu^n{}_3{}^+]_e \leq [CN^-]$.

$[NHBu^n{}_3{}^+]_e \geq [CN^-]$. Under these conditions all CN^- is converted into HCN and, thus, the species present in solution are $NHBu^n{}_3{}^+$, PhSH and HCN. In order to calculate the concentrations of all solution species, the equilibrium reactions shown in both equations (1) and (5) need to be considered.

$$NHBu^n{}_3{}^+ + CN^- \rightleftharpoons NBu_3 + HCN \qquad (5)$$

When $[NHBu^n{}_3{}^+]_0 \geq ([PhS^-]_0 + [CN^-]_0)$, $[NHBu^n{}_3{}^+]_e = [NHBu^n{}_3{}^+]_0 - [PhS^-]_0 - [CN^-]_0$; $[PhSH]_e = [PhS^-]_0$ and $[HCN]_e = [CN^-]_0$. The plot of k_{obs} versus $[NHBu^n{}_3{}^+]_e$ is a straight line with an intercept {Fig.

5 (TOP)}. The rate is independent of the concentration of HCN, and the rate law derived from this graph {equation (6)} is in excellent agreement with that observed earlier for the reaction of $[Fe_4S_4Cl_4]^{2-}$ with PhS^- in the presence of $NHBu^n{}_3{}^+$, but no added substrate.[9]

$$\text{Rate} = \{2.0 + 500[NHBu^n{}_3{}^+]_e\}[Fe_4S_4Cl_4{}^{2-}] \qquad (6)$$

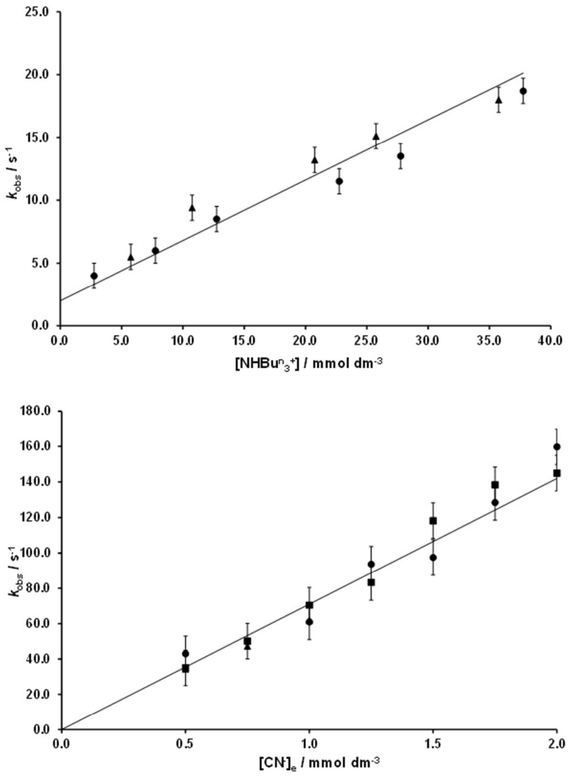

Fig. 5. TOP. Plot of k_{obs} against the concentration of $NHBu^n{}_3{}^+$ for the reaction of $[Fe_4S_4Cl_4]^{2-}$ (0.2 mmol dm^{-3}) with PhSH ($[PhSH]_e$ = 1.25 mmol dm^{-3}) in the presence of CN^- (when $[NHBu^n{}_3{}^+]_0 \geq ([PhS^-]_0 + [CN^-]_0)$ at 25.0 °C in MeCN. Line drawn is that defined by equation (6). BOTTOM. Plot of k_{obs} against the concentration of CN^- for the reaction of $[Fe_4S_4Cl_4]^{2-}$(0.2 mmol dm^{-3}) with PhSH ($[PhSH]_e$ = 1.25 mmol dm^{-3}) in the presence of CN^- {when $([NHBu^n{}_3{}^+]_0 - [PhS^-]_0) < [CN^-]_0$} at 25.0 °C in MeCN. Line drawn is that defined by equation (7).

$[NHBu^n{}_3{}^+]_e < [CN^-]$. When $[NHBu^n{}_3{}^+]_0 > [PhS^-]_0$, but $([NHBu^n{}_3{}^+]_0 - [PhS^-]_0) < [CN^-]_0$, the solution will contain PhSH and mixtures of HCN and CN^-, but no $NHBu^n{}_3{}^+$. The concentrations of the various species present in solution were calculated using the following relationships: $[PhSH]_e = [PhS^-]_0$; $[HCN]_e = [CN^-]_0 - ([NHBu^n{}_3{}^+]_0 - [PhS^-]_0)$; and $[CN^-]_e = [CN^-]_0 - [HCN]_e$. Under these conditions, a plot of k_{obs} versus $[CN^-]_e$ is a straight line (independent of the concentration of HCN) which passes through the origin (Fig. 5, BOTTOM). The rate law is that shown in equation (7).

$$\text{Rate} = 7.1 \times 10^4[CN^-]_e[Fe_4S_4Cl_4{}^{2-}] \qquad (7)$$

Discussion

With various substrates, L, the different kinetics reflect the effects that L have on the rate of protonation of $[Fe_4S_4Cl_4]^{2-}$ by $NHBu^n{}_3{}^+$. In the presentation that follows, we will first discuss the kinetics observed with the various L and how all the results can be accomodated by the pathways shown in Fig. 6. We will then discuss how initial binding of L affects the rate of protonation, and how initial protonation affects the rate of binding of L. Finally, the results from previous studies on substrate binding are considered in the light of the studies reported herein.

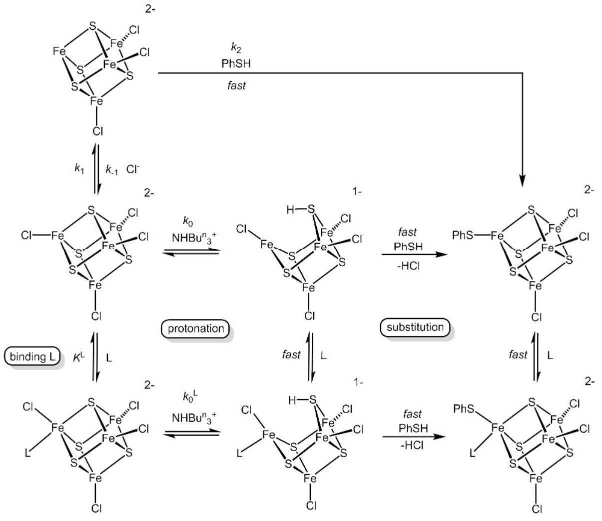

Fig. 6. Outline of the mechanism for the reaction between $[Fe_4S_4Cl_4]^{2-}$ and PhSH in the presence of $NHBu^n{}_3{}^+$ and substrate L.

Kinetics and Mechanism. The results presented herein indicate that the rate of proton transfer from $NHBu^n{}_3{}^+$ to $[Fe_4S_4Cl_4]^{2-}$ is modulated in the presence of L = Cl^-, $N_3{}^-$, NCS^-, Bu^tNC, pyridine, $RNHNH_2$ (R = Me or Ph) and Me_2NNH_2, indicating that these L bind to $[Fe_4S_4Cl_4]^{2-}$. Furthermore, this observation indicates that these L bind to $[Fe_4S_4Cl_4]^{2-}$ faster than protonation of this cluster by $NHBu^n{}_3{}^+$ (when $[NHBu^n{}_3{}^+]_e$ = 3.75 mmol dm^{-3}). Since the lowest concentration of L used was 1.0 mmol dm^{-3}, we can calculate that the rate of L binding is greater than *ca* 2 x 10^3 dm^3 mol^{-1} s^{-1}.

Of all the substrates studied only HCN, Br^- and I^- do not affect the rate of proton transfer from $NHBu^n{}_3{}^+$ to the cluster. We will discuss HCN later, and here just consider Br^- and I^-. That Br^- and I^- do not affect the rate of the reaction between $[Fe_4S_4Cl_4]^{2-}$ and $NHBu^n{}_3{}^+$ could be because: (i) Br^- and I^- do not bind to $[Fe_4S_4Cl_4]^{2-}$ or (ii) they bind more slowly than proton transfer from $NHBu^n{}_3{}^+$. Earlier studies showed that Br^- and I^- affect the rate of protonation of $[Fe_4S_4Cl_4]^{2-}$ by $pyrrH^+$ (pyrr = pyrrolidine),[16] indicating that Br^- and I^- do bind to $[Fe_4S_4Cl_4]^{2-}$. Furthermore, the rate of protonation of $[Fe_4S_4Cl_4]^{2-}$ by $pyrrH^+$ ($k = 2.1 \pm 0.5 \times 10^4$ dm^3 mol^{-1} s^{-1})[11,17] is significantly faster than that with $NHBu^n{}_3{}^+$, demonstrating that binding of Br^- and I^- to the cluster must be faster than protonation by $NHBu^n{}_3{}^+$. Consequently, it appears that although Br^- or I^- do bind to $[Fe_4S_4Cl_4]^{2-}$, their binding does not affect the rate of proton transfer from $NHBu^n{}_3{}^+$ appreciably.

For all substrates (except HCN and CN$^-$, *vide infra*) the experimental rate laws, equations (2), (3) and (4), are consistent with the mechanism shown in Fig. 6. In this mechanism the top and middle lines show the pathways which operate when no substrate L is present. These pathways have been established in earlier work and consist of (top line) the dissociative substitution pathway for $[Fe_4S_4Cl_4]^{2-}$ involving rate-limiting dissociation of a chloro-ligand to generate a vacant site on one of the Fe sites at which PhSH can attack.[16] The middle pathway shows (in simplified form) the acid-catalyzed substitution mechanism which, when the acid is $NHBu^n{}_3{}^+$, is rate-limited by proton transfer from $NHBu^n{}_3{}^+$ to the cluster.[9] The bottom line shows the pathway in which rapid binding of L to the cluster forms $[Fe_4S_4Cl_4(L)]^{3-}$ which is then protonated by $NHBu^n{}_3{}^+$. The general rate law associated with Fig. 6 is shown in equation (8) where, in the first term, $k_2' = k_2[PhSH]$. In equation (8), the first term describes the acid-independent pathway (Fig. 6, top line) whilst the second term describes the acid dependent pathways, both in the absence (Fig. 6, k_0, middle line) and presence (Fig. 6, $k_0{}^L$, bottom line) of L.

$$\text{Rate} = \left\{ \frac{k_1}{1 + k_{-1}[Cl^-]/k_2'} + \frac{(k_0 + k_0{}^L K^L[L])[NHBu^n{}_3{}^+]_e}{1 + K^L[L]} \right\} [Fe_4S_4Cl_4{}^{2-}] \qquad (8)$$

The rate law for the reaction in the presence of Cl$^-$ {equation (4)} is the only case where both terms shown in equation (8) are observed. Comparison of equations (4) and (8) gives $k_1 = 2.5\pm0.3$ s^{-1}, $k_{-1}/k_2' = 6\pm1 \times 10^3$, $k_0 = 500\pm20$ dm^3 mol^{-1} s^{-1} and $k_0{}^{Cl}K^{Cl} = 1.6\pm0.4 \times 10^4$ dm^6 mol^{-2} s^{-1}. The dependence on the concentration of Cl$^-$ is linear even at the highest concentration of Cl$^-$ ($[Cl^-]_{max}$ = 20 mmol dm^{-3}), and hence we can calculate $K^{Cl} \leq 50$ dm^3 mol^{-1}. It is worth noting that the values of k_1 and k_0 are in good agreement with those determined in earlier work ($k_1 = 2.0\pm0.3$ s^{-1} and $k_0 = 530\pm20$ dm^3 mol^{-1} s^{-1}).[9,16]

In the absence of added Cl$^-$, equation (8) simplifies to equation (9) and the reactions exhibit a non-linear dependence on the concentration of L (Fig. 2 and Table 1).

$$\text{Rate} = \left\{ k_1 + \frac{(k_0 + k_0{}^L K^L[L])[NHBu^n{}_3{}^+]_e}{1 + K^L[L]} \right\} [Fe_4S_4Cl_4{}^{2-}] \qquad (9)$$

When the binding of L to $[Fe_4S_4Cl_4]^{2-}$ is weak, $K^L[L] < 1$ and equation (9) simplifies to equation (10). This is the kinetic behaviour observed with L = Bu^{t}NC {Fig. 3, equation (3) and Table 1}.

$$\text{Rate} = \{k_1 + (k_0 + k_0{}^L K^L[L])[NHBu^n{}_3{}^+]_e\}[Fe_4S_4Cl_4{}^{2-}] \qquad (10)$$

Reactions with HCN and CN$^-$. Analysis of the kinetics of the reaction between $NHBu^n{}_3{}^+$ and $[Fe_4S_4Cl_4]^{2-}$ in the presence of CN$^-$ is complicated because $NHBu^n{}_3{}^+$ protonates this substrate. Consequently, it is only possible to study the reactions in solutions containing mixtures of $NHBu^n{}_3{}^+$ and HCN or mixtures of HCN and CN$^-$. The kinetics for the reaction of $[Fe_4S_4Cl_4]^{2-}$ with HCN in the presence of $NHBu^n{}_3{}^+$ {equation (6)} are identical to those observed for the reaction of $[Fe_4S_4Cl_4]^{2-}$ with only PhS$^-$ in the presence of $NHBu^n{}_3{}^+$, indicating that HCN neither protonates nor binds to the cluster. A limit for the value of $K^{HCN} \leq 33$ dm^3 mol^{-1} can be estimated, since there is no evidence that the rate is perturbed by HCN even at the highest concentration of HCN employed ($[HCN]_{max}$ = 3 mmol dm^{-3}). However, our studies cannot rule out the possibility that HCN binds slowly and hence binds to $[Fe_4S_3(SH)Cl_4]^-$.

The kinetics for the reaction of $[Fe_4S_4Cl_4]^{2-}$ with CN$^-$ in the presence of HCN {equation (7)} show that the reaction is independent of the concentration of HCN, consistent with the conclusion that HCN is neither an acid nor a substrate for $[Fe_4S_4Cl_4]^{2-}$. The simplicity of equation (7) makes unambiguous interpretation difficult, but we suggest that this rate law corresponds to an associative substitution mechanism, in which CN$^-$ displaces the chloro-ligand in $[Fe_4S_4Cl_4]^{2-}$ as shown in Fig. 7, with $K^{CN}k = 7.1\pm0.5 \times 10^4$ dm^3 mol^{-1} s^{-1}. A similar associative substitution mechanism has been proposed for the reaction of PhS$^-$ with $[Fe_4S_4Cl_4]^{2-}$.[16]

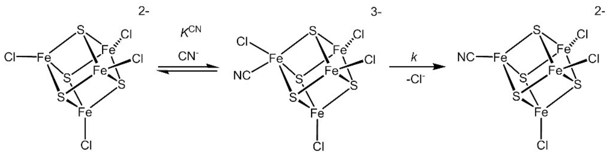

Fig. 7. Proposed mechanism for the substitution reaction of the chloro ligands in $[Fe_4S_4Cl_4]^{2-}$ by CN$^-$.

Protonation of $[Fe_4S_4Cl_4(L)]^{n-}$. The most notable feature of the data presented in Table 1 is that, in all cases, $[Fe_4S_4Cl_4(L)]^{n-}$ protonates faster than $[Fe_4S_4Cl_4]^{2-}$. Thus, the increase in the rate of proton transfer does not depend on the overall charge of $[Fe_4S_4Cl_4(L)]^{n-}$; for n = 2 (binding neutral L), we see a range for $k_0{}^L/k_0$ (*i.e.* L = PhNHNH$_2$, $k_0{}^L/k_0$ = 1.9; L = MeNHNH$_2$, $k_0{}^L/k_0$ = 53.9), and for n = 3 (binding anionic L) $k_0{}^L/k_0$ is essentially constant, $k_0{}^L/k_0$ = 22.1 – 24.5. Interestingly, for all substrates which are N-donor ligands {RNHNH$_2$ (R = Me or Ph), Me$_2$NNH$_2$, NCS$^-$, N$_3{}^-$ and py} the values of K^L and $k_0{}^L$ vary only slightly (K^L = 150 – 250 dm^3 mol^{-1} and $k_0{}^L = 0.2 \times 10^4 – 2.9 \times 10^4$ dm^3 mol^{-1} s^{-1}). This observation suggests that: (i) the binding affinity of L and the modulation of $k_0{}^L$ is principally defined by the donor atom and (ii) that NCS$^-$, coordinates using the N atom.

In the light of the recently proposed mechanism for acid-catalyzed substitution of cubanoid Fe-S-based clusters (Figs. 1 and 6), it might have been anticipated that binding L to $[Fe_4S_4Cl_4]^{2-}$ would facilitate subsequent proton transfer because the intermediate containing a 3-coordinate Fe site would be replaced by an intermediate containing a (presumably more stable) 4-coordinate Fe. The data in Table 1 certainly shows that the rate of proton transfer to $[Fe_4S_4Cl_4(L)]^{n-}$ is faster than to $[Fe_4S_4Cl_4]^{2-}$ but the increase in rate ($k_0{}^L/k_0$) is rather modest, suggesting that (in the absence of L) either formation of the 3-coordinate Fe site is not energeticallly very demanding or that a 'naked' 3-coordinate Fe site is never formed because the Fe-(μ_3-SH) bond only elongates but never breaks, or the incipient 3-coordinate Fe site binds a solvent MeCN molecule prior to or during protonation (Fig. 8). In the latter case, $k_0{}^L/k_0$ represents the difference in stabilities of the transition states for protonation in which the unique 'dissociated' Fe is 4-coordinate, bound to either a substrate or a MeCN.

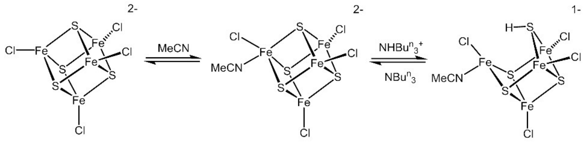

Fig. 8. Possible involvement of solvent (MeCN) binding to $[Fe_4S_4Cl_4]^{2-}$ prior to protonation.

The data in Table 1 indicate that k_0^L/k_0 varies with the bonding characteristics of L. The E_L parameter (included in Table 1 for selected substrates) is a quantitative measure of whether a ligand is a σ-donor/π-donor (negative E_L) or a σ-donor/π-acceptor (positive E_L).[18] Inspection of Table 1 shows that as the substrate becomes a stronger σ-donor/π-donor, the values of k_0^L/k_0 increase. A similar trend is evident when comparing the effect of the hydrazines. Although we do not have the E_L values for the hydrazines, it is to be noted that as the pK_a of the hydrazine increases so does the corresponding values of k_0^L/k_0.

Interestingly, it is evident that binding good σ-donor/π-acceptors (Bu^{t}NC) also results in a large k_0^L/k_0. This behaviour is not consistent with k_0^L/k_0 reflecting the electron-donating capability of the bound L. It is difficult to explain why good π-acceptor ligands would facilitate the rate of proton transfer to the cluster if protonation just involves simple addition of a proton to a μ_3-S with the cluster maintaining its structural integrity. However, this observation is consistent with the proposal that protonation of a μ_3-S is coupled to Fe-(μ_3-SH) bond elongation/cleavage. Binding Bu^{t}NC to a Fe site pulls π-electron density from the Fe, affecting the Fe-S bond and hence the activation energy for proton transfer. Previous work has also shown that other electron-withdrawing ligands facilitate the rate of proton transfer to $[Fe_4S_4Cl_4]^{2-}$.[19] In the reactions of $[Fe_4S_4Cl_4]^{2-}$ with 4-$RC_6H_4S^-$ (R = CF_3, Cl, H, Me or MeO) in the presence of pyrrH$^+$, the thiolate binds to the cluster prior to protonation by pyrrH$^+$. Binding R = CF_3 results in faster protonation (k^{CF3} = 26.4 x 10^6 dm^3 mol^{-1} s^{-1}) than binding R = MeO (k^{MeO} = 0.47 x 10^6 dm^3 mol^{-1} s^{-1}).

Binding L to $[Fe_4S_3(SH)Cl_4]^-$. Measuring the effect that protonation has on the rates of subsequent binding of L to $[Fe_4S_4Cl_4]^{2-}$ complements the studies presented herein (on the effect that bound substrates have on the rates of protonation). Earlier studies showed that protonation of $[Fe_4S_4Cl_4]^{2-}$ increases the rate of binding of Bu^{t}NC, but the effect is small (k_H^{BuNC}/k^{BuNC} = 3.8); for binding of Bu^{t}NC to $[Fe_4S_4Cl_4]^{2-}$ k^{BuNC} = 2.1 x 10^3 dm^3 mol^{-1} s^{-1} and binding to $[Fe_4S_3(SH)Cl_4]^-$, k_H^{BuNC} = 8.0 x 10^3 dm^3 mol^{-1} s^{-1}.[20,21] If protonation of a μ_3-S is coupled to Fe-(μ_3-SH) bond cleavage then it might be assumed that initial protonation of a μ_3-S would facilitate the binding of L because the 3-coordinate Fe site is primed to bind a substrate (Fig. 1). The small effect that protonation has on the rate of binding of Bu^{t}NC does not support this suggestion. However, the small effect observed may be because (as discussed above), in a coordinating solvent such as MeCN, a solvent molecule can bind to the incipient 3-coordinate Fe site prior to protonation (Fig. 8). Consequently, the effect measured in these experiments may not be comparing formation of a 3-coordinate and 4-coordinate Fe site. It is worth emphasising that whilst our studies show that protonation of the cluster has only a minor effect on the rate of substrate binding, our experiments do not address whether or not protonation increases the binding affinity of the substrate.

Earlier Studies on Substrate Binding. Finally, we will consider the results from some earlier studies on binding substrates to $[Fe_4S_4Cl_4]^{2-}$, and compare the results with those presented herein. Previous studies have investigated binding L = I^-, Br^-, PhS^-, EtS^- or Bu^{t}NC to $[Fe_4S_4Cl_4]^{2-}$ and the effects this has on the rates of protonation by pyrrH$^+$.[17] It was observed that some substrates increase the rates of proton transfer (L = PhS^- or Bu^{t}NC), whilst others inhibit the rate of proton transfer (L = I^-, Br^- or EtS^-). This is different to the behaviour reported herein for the reactions with NHBu$^n_3$$^+$. PyrrH$^+$ is a weaker acid (pK_a = 21.5 in MeCN)[22] than NHBu$^n_3$$^+$ (pK_a = 18.1 in MeCN),[14] and so proton transfer from pyrrH$^+$ to $[Fe_4S_4Cl_4]^{2-}$ is thermodynamically less favourable than the transfer from NHBu$^n_3$$^+$. Consequently, the effects that bound L has on the rates of subsequent proton transfer by pyrrH$^+$ may be due (at least in part) to the bound L modulating the pK_a of the cluster. For the thermodynamically-unfavourable proton transfer reactions with pyrrH$^+$, modulating the pK_a of the cluster would effect the rate.[23] In studies with the stronger acid, NHBu$^n_3$$^+$, where proton transfer must be thermodynamically more favourable, modulating the pK_a of the cluster by binding L is not reflected in the rate of the subsequent proton transfer. Rather, sterics may be a more important factor in reactions with NHBu$^n_3$$^+$.

Earlier studies showed that the rate of acid-catalyzed substitution of the terminal EtS ligands in $[Fe_6S_9(SEt)_2]^{4-}$ was inhibited when L = Cl^-, CN^-, N_3^- or Bu^{t}NC bind to the cluster. These studies were performed with $[NHEt_3^+]/[NEt_3]$ = 7.0.[6] Under these conditions all the cluster in solution is protonated and the rate law for acid-catalyzed substitution is that shown in equation (11) (k = rate constant for dissociation of EtS^- from $[Fe_6S_8(SH)(SEt)_2]^{3-}$ and k^L = rate constant for dissociation of EtS^- from $[Fe_6S_8(SH)(SEt)_2(L)]^{n-}$). In all cases, binding L to $[Fe_6S_8(SH)(SEt)_2]^{3-}$($K^L$) inhibits the rate of substitution of the protonated cluster (k^L)

$$\text{Rate} = \frac{(k + k^L K^L[L])[Fe_6S_8(SH)(SEt)_2{}^{3-}]}{1 + K^L[L]} \qquad (11)$$

The binding of L = Cl^-, Br^-, CO or N_2O to $[Fe_4S_4(SEt)_4]^{2-}$ has also been detected by the effect that it has on the rate of acid-catalyzed substitution of the terminal EtS^- ligands.[5] These experiments were performed using $[NHEt_3^+]_e/[NEt_3]_e$ = 2.0 and, under these conditions, a mixture of $[Fe_4S_4(SEt)_4]^{2-}$ and $[Fe_4S_3(SH)(SEt)_4]^-$ are present in solution. The rate law for the reaction under these conditions is that shown in equation (12). The binding of L to $[Fe_4S_4(SEt)_4]^{2-}$ results in a decrease in the rate of the acid-catalyzed substitution.

$$\text{Rate} = \frac{(kK_0 + k^L K_0^L K_L[L])\,[Fe_4S_4(SEt)_4{}^{2-}][NHEt_3{}^+]_e/[NEt_3]_e}{1 + K^L[L]} \qquad (12)$$

This decrease in rate indicates that $[Fe_4S_4(SEt)_4(L)]^{n-}$ undergoes acid-catalyzed substitution reactions slower than $[Fe_4S_4(SEt)_4]^{2-}$, either because the rate of substitution (k^L)

and/or the protonation constant (K_0^L) is smaller. However, because of the simplicity of the kinetics, it is not possible to establish which elementary step is affected.

The results presented in this paper on the reactions of $[Fe_4S_4Cl_4]^{2-}$ with $NHBu^n{}_3{}^+$ in the presence of L, together with the results from the studies with $[Fe_6S_8(SH)(SEt)_2]^{3-}$ suggest that, in general, binding L increases the rate of protonation but inhibits the rate of substitution. Thus, we conclude, that in studies with $[Fe_4S_4(SEt)_4]^{2-}$, the observed inhibition is because the rate of protonation is increased but the rate of substitution is inhibited, and the effect on the substitution step dominates**.**

Conclusions

In the acid-catalyzed substitution reactions of $[Fe_4S_4Cl_4]^{2-}$ by PhS^- in the presence of $NHBu^n{}_3{}^+$ the initial proton transfer from $NHBu^n{}_3{}^+$ to the cluster is rate-limiting. By studying the kinetics of this reaction in the presence of various substrates {L = Cl^-, N_3^-, NCS^-, CN^-, HCN, Bu^tNC, pyridine, $RNHNH_2$ (R = Me or Ph) and Me_2NNH_2} we have shown that binding L to the cluster increases the rate of protonation of the cluster. That both σ-donor/π-donor and σ-donor/π-acceptor ligands facilitate proton transfer is difficult to explain using a mechanism involving simple proton transfer to the cluster. Rather, this observation seems more consistent with the recent proposal that protonation of a μ_3-S site is coupled to Fe-(μ_3-SH) bond elongation/cleavage (Fig. 1), where both protonation and Fe-S bond weakening are important. However, it is surprising that the increase in the rate of proton transfer when L binds is rather small (Table 1). This observation, perhaps, suggests that in the absence of L, a solvent molecule binds to the incipient 3-coordinate Fe site prior to or during the protonation step (Fig. 8).

All the kinetic data (and in particular the dependence on the concentration of $NHBu^n{}_3{}^+$) can be accomodated entirely by the pathways shown in Fig. 6. Consequently, there is no evidence for protonation of L when bound to the cluster from these kinetic studies. If protonation of the bound L in $[Fe_4S_4Cl_4(L)]^{n-}$ does occur it must be slower than the rate-limiting steps associated with the pathways in Fig. 6.

Finally, the studies reported herein show that initial binding of L to $[Fe_4S_4Cl_4]^{2-}$ only increases the rate of subsequent proton transfer by a modest amount, and earlier studies showed that initial protonation of $[Fe_4S_4Cl_4]^{2-}$ only slightly increases the rate of subsequent L binding. However, we have no information about the effect that protonation has on the binding affinity of L. Future studies should explore if protonation of the cluster (either before or after L binding) affects the substrates' binding affinities.

Experimental

All manipulations in both the synthetic and kinetic aspects of this work were performed under an atmosphere of dinitrogen using Schlenk or syringe techniques, as appropriate. The following chemicals were purchased from Sigma-Aldrich and used as received without any further purfications: anhydrous $FeCl_3$, thiophenol, sulfur, $NBu^n{}_3$, $[NEt_4]N_3$, $[NEt_4]CN$, pyridine, Bu^tNC and sodium tetraphenylborate. CD_3CN was purchased from Goss Scientific and used as received. $[NBu^n{}_4]_2[Fe_4S_4Cl_4]$,[24] $[NHBu^n{}_3]BPh_4$,[9] $[NMe_4]NCS$[25] and $[NEt_4]SPh$[26] were prepared by the literature methods.

Kinetic Studies. All kinetic studies were performed using an Applied Photophysics SX.18 MV stopped-flow spectrophotometer, modified to handle air-sensitive solutions, connected to a RISC computer. The temperature was maintained using a Grant LTD6G thermostat tank with combined recirculating pump. The experiments were performed at 25.0 °C and the wavelength used was λ = 550 nm. All kinetics were studied in MeCN. The MeCN was dried over CaH_2 and distilled under an atmosphere of dinitrogen immediately prior to use.

The solutions of $[NBu^n{}_4]_2[Fe_4S_4Cl_4]$ and reagents {NHR_3^+, PhS^- and L = substrate = Cl^-, Br^-, I^-, $RNHNH_2$ (R = Me or Ph), Me_2NNH_2, HCN, NCS^-, N_3^-, Bu^tNC or pyridine} were prepared under an atmosphere of dinitrogen. The diluted solutions containing mixtures of NHR_3^+, PhS^- and L were prepared from freshly prepared stock solutions. All solutions were used within 1 h.

Under all conditions, the stopped-flow absorbance-time traces were biphasic and were an excellent fit to two exponentials, indicating a first-order dependence on the concentration of the cluster. Similar behaviour has been observed in the substitution reactions of most $[Fe_4S_4X_4]^{2-}$ (X = thiolate or halide).[4] The total absorbance changes observed herein, in the reactions of $[Fe_4S_4Cl_4]^{2-}$ are consistent with all four chloro-ligands being replaced by PhS^-. It has been suggested[4] that the absorbance-time curves can be fitted to two exponentials because either: (i) the first and second substitution steps are similar in rates but much slower than the rates of the third and fourth substitutions, or (ii) all four substitution steps occur at similar rates but the absorbance change for the first and second steps are appreciably larger than for the last two steps.

The dependences on the concentrations of NHR_3^+, NR_3 and PhSH were determined from analysis of the appropriate graphs as explained in Results**.**

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Notes and references

1 (a) R. H. Holm, P. Kennepohl and E. I. Solomon, *Chem. Rev*., 1996, ***96***, 2239; (b) H. Matsubara and K. Saeki, *Adv. Inorg. Chem*., 1992, ***38***, 223; (c) R. Cammack, *Adv. Inorg. Chem*., 1992, ***38***, 281; (d) B. Burgess and D. J. Lowe, *Chem. Rev*., 1996, ***96***, 2983; (e) T. Spatzal, M. Akoyoglu, L. Zhang, S. L. A. Andrade, E. Schleicher, S. Weber, D. C. Rees and O. Einsle, *Science*, 2011, ***334***, 940.

2 (a) Y. Hozumi, Y. Imasaka, K. Tanaka and T. Tanaka, *Chem. Lett*., 1983, 897; (b) R. S. McMillan J. Renauld, J. G. Reynolds and R. H. Holm, *J. Inorg. Biochem*., 1979, **11**, 213; (c) K. L. C. Gronberg, R. A. Henderson and K. E. Oglieve, *J. Chem. Soc., Dalton Trans*., 1998, 3093; (d) S. M. Malinak, K. D. Demadis and D. Coucouvanis, *J. Am. Chem. Soc*., 1995, **117**, 3129; (e) K. D. Demadis, S. M. Malinak and D. Coucouvanis, *Inorg. Chem*., 1996, **35**, 4038; (f) S. M. Malinak, A. M. Simeonov, P. E. Mosier, C. E. McKenna and D. Coucouvanis, *J. Am. Chem. Soc*., 1997, **119**, 1662; (g) R. E. Palermo, R. Singh, J. K. Bashkin and R. H. Holm, *J. Am. Chem. Soc*., 1984, **106**, 2600; (h) S. Ciurli, P. K. Ross, M. J. Scott, S.-B. Yu and R. H. Holm, *J. Am. Chem. Soc*., 1992, **114**, 5415; (i) T. A. Scott and H.-C. Zhou, *Angew. Chem. Int. Ed.*, 2004, **43**, 5628; (j) J. A. Weigel and R. H. Holm, *J. Am. Chem. Soc*., 1991, **113**, 4184.

3 (a) R. A. Henderson, *Bioinorg. React. Mech*., 2012, **8**, 1; (b) R. A. Henderson, *Bioinspired Catalysis,* W. Weigand and P. Schollhammer editors, 2015, Wiley-VCH, Weinheim, ch 11.

4 R. A. Henderson, *Chem. Rev*., 2005, **105**, 2365.

5 R. A. Henderon and K. E. Oglieve, *J. Chem. Soc., Dalton Trans*., 1993, 1473.

6 A. J. Dunford and R. A. Henderson, *J. Coord. Chem*., 2010, **63**, 2507.

7 I. Dance, *Inorg. Chem*., 2013, **52**, 10368.

8 (a) A. Alwaaly, I. Dance and R. A. Henderson, *Chem. Commun*., 2014, **50**, 4799; (b) I. Dance and R. A. Henderson, *Dalton Trans*., 2014, **43**, 16213; (c) I. Dance, *Dalton Trans*., 2015, **44**, 4707.

9 T. Al-Rammahi and R. A. Henderson, *Dalton Trans*., DT-ART-10-2015-004008.

10 B. G. Cox, *Acids and Bases Solvent Effects on Acid-Base Strength*, Oxford University Press, UK, 2013.

11 R. A. Henderson and K. E. Oglieve, *J. Chem. Soc., Dalton Trans*., 1999, 3927.

12 J. F. Coetzee, *Prog. Phy. Org. Chem*., 1967, **4**, 45.

13 Advanced Chemistry Development (ACD/Labs) Software V11.02 (© 1994-2014 ACD/Labs).

14 K. Izutsu, *Acid-Base Dissociation Constants in Dipolar Aprotic Solvents*, Blackwell Scientific, Oxford, UK, 1990.

15 For many L, the second phase appears to follow similar kinetics to that of the first phase, but is slower. However, for L = N_3^- or halide, the rates of the second phases appear to be independent of [L]. This behaviour could be because $[Fe_4S_4Cl_3(SPh)]^{2-}$ has a weak affinity for binding these L.

16 R. A. Henderson and K. E. Oglieve, *J. Chem. Soc., Chem. Commun*., 1994, 377.

17 K. Bates and R. A. Henderson, *Inorg. Chem*., 2008, **47**, 5850.

18 A. B. P. Lever, *Inorg. Chem*., 1990, **29**, 1271.

19 A. J. Dunford and R. A. Henderson, *Chem. Commun*., 2002, 360.

20 A. J. Dunford and R. A. Henderson, *Inorg. Chem*., 2002, **41**, 5487.

21 A. J. Dunford and R. A. Henderson, *J. Chem. Soc., Dalton Trans*., 2002, 2837.

22 R. A. Henderson and K. E. Oglieve, *J. Chem. Soc., Dalton Trans*., 1999, 3927.

23 R. P. Bell, *The Proton in Chemistry*, 2nd edition, Chapman Hall, London, 1973, p195, and references therein.

24 (a) K. S. Hagen, J. G. Reynolds and R. H. Holm, *J. Am. Chem. Soc*., 1981, **103**, 4054; (b) G. B. Wong, M. A. Bobrick and R. H. Holm, *Inorg. Chem*., 1978, **17**, 578.

25 D. Ford, L. F. Larkworthy, D. C. Povey and A. J. Roberts, *Polyhedron*, 1983, **2**, 1320.

26 R. E. Palermo, P. P. Power and R. H. Holm, *Inorg. Chem*., 1982, **21**, 173.

Binding small molecules and ions to $[Fe_4S_4Cl_4]^{2-}$ modulates rate of protonation of the cluster

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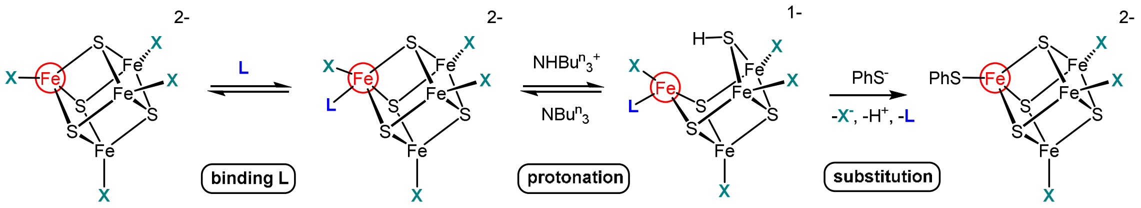
ABSTRACTS

Graphical Abstract



Textual Abstract

Binding various small molecules and ions (Cl^-, N_3^-, NCS^-, substituted hydrazines, Bu^{t}NC or pyridine) to $[Fe_4S_4Cl_4]^{2-}$ facilitates the subsequent protonation of the cluster.