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Ligand movement modulates the rate of proton transfer in reactions of $[Fe_4S_4Cl_4]^{2-}$

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Received (in Cambridge, UK) 23rd October 2001, Accepted 27th November 2001
First published as an Advance Article on the web 29th January 2002

Substitution of the first chloro-ligand in $[Fe_4S_4Cl_4]^{2-}$ by $4\text{-}RC_6H_4S^-$ (R = CF_3, Cl, H, Me or MeO), in the presence of $[H_2N(CH_2)_3CH_2]^+$, involves initial binding of thiolate, followed by protonation and finally chloride dissociation; the rate of protonation is facilitated by electron-withdrawing R-substituents indicating that Fe-thiolate bond length changes modulate proton transfer.

We have been studying the mechanisms of substitution, protonation and molecule binding reactions of natural[1–3] and synthetic Fe–S-based clusters.[4–6] One reaction, common to essentially all Fe–S-based clusters, is the substitution of terminal ligands on the Fe sites, which is accelerated in the presence of acid {eqn. (1)}.

$$[Fe_4S_4Cl_4]^{2-} + 4\text{-}RC_6H_4S^- \xrightarrow[-4Cl^-]{[NHR_3]^+} [Fe_4S_4(SC_6H_4R\text{-}4)_4]^{2-} \quad (1)$$

With acids such as $[NHEt_3]^+$ (pK_a = 18.46)[7] and $[lutH]^+$ (lut = 2,6-dimethylpyridine) (pK_a = 15.4)[8] protonation of the cluster (pK_a = 18.4 ± 0.5) in MeCN is sufficiently rapid to occur prior to the binding of the nucleophile,[9] and the substitution step. The pK_a of the cluster is independent of the terminal ligands indicating protonation occurs at the cluster core (presumably μ-S).[4,5]

Using the much weaker acid, $[H_2N(CH_2)_3CH_2]^+$ (pK_a = 21.5),[10] we recently showed that although protonation of $[Fe_4S_4Cl_4]^{2-}$ is thermodynamically-unfavourable, binding of a thiolate to the cluster increases the basicity sufficiently that protonation can now occur as shown in Fig. 1. By studying the rates of substitution, both in the absence and presence of $[H_2N(CH_2)_3CH_2]^+$, it is possible to calculate the rate constants for all the elementary steps in Fig. 1. Herein, we report results on the reactions between $[Fe_4S_4Cl_4]^{2-}$ and $4\text{-}RC_6H_4S^-$ (R = MeO, Me, H, Cl or CF_3) in the presence of $[H_2N(CH_2)_3CH_2]^+$, which show that the rates of nucleophile binding and proton transfer in the reaction are affected in an unexpected manner by the R-substituent. Specifically, both elementary reactions are facilitated by electron-withdrawing substituents indicating that Fe-thiolate bond length changes modulate the rate of proton transfer to the cluster.

As we have discussed before,[10] the rate law for the pathways shown in Fig. 1 is described by eqn. (2). All of the $4\text{-}RC_6H_4S^-$ (R = MeO, Me, H, Cl or CF_3) studied in this paper show behaviour consistent with this mechanism as illustrated by the typical data in Fig. 2. The kinetics were determined and analysed as described earlier.[4,5,9–13] Thus, the reaction exhibits a first order dependence on the concentration of thiolate, but the dependence on the concentration of $[H_2N(CH_2)_3CH_2]^+$ is markedly non-linear.

$$k_{obs} = \frac{k_1^R(k_2^R + k_5^R[NH_2(CH_2)_3CH_2^+])[4\text{-}RC_6H_4S^-]}{k_{-1}^R + k_2^R + k_5^R[NH_2(CH_2)_3CH_2^+]} \quad (2)$$

The kinetics of the reaction between $[Fe_4S_4Cl_4]^{2-}$ and $4\text{-}RC_6H_4S^-$, in the absence of acid, exhibit a non-linear dependence on the concentration of thiolate. This behaviour has been observed earlier[11] with R = H, and is consistent with the associative substitution pathway shown on the top line of Fig. 1, and the rate law of eqn. (3). Analysis of the kinetics both in the presence and absence of acid allows calculation of k_1^R, k_{-1}^R, k_2^R and k_5^R. The values of the rate constants are summarised in Table 1.

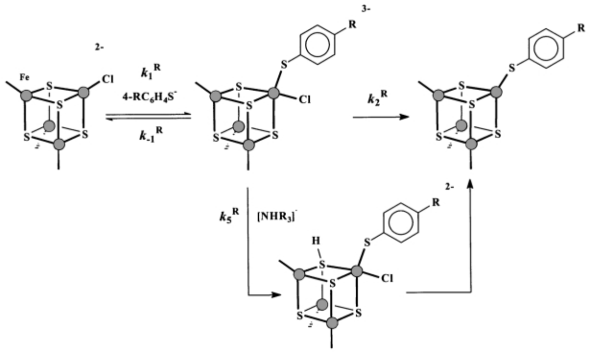

Fig. 1 Substitution in $[Fe_4S_4Cl_4]^{2-}$ by $4\text{-}RC_6H_4S^-$ in the presence of $[H_2N(CH_2)_3CH_2]^+$ in MeCN.

$$k_{obs} = \frac{(k_1^R k_2^R/k_{-1}^R)[4\text{-}RC_6H_4S^-]}{1 + (k_1^R/k_{-1}^R)[4\text{-}RC_6H_4S^-]} \quad (3)$$

The R-substituents on the thiolate can facilitate any of the elementary reactions in Fig. 1, either by destabilising the ground state or stabilising the transition state associated with that particular step. It is evident from Table 1 that k_1^R increases as R becomes more electron-withdrawing and this is not what would be anticipated if the dominant role of the R-group was to affect the ground state of the reaction. If ground state effects dominate, k_1^R would increase as the R-group becomes more electron-releasing, since the nucleophilicities of $4\text{-}RC_6H_4S^-$ would increase, in parallel with the substituent's effect on the basicity of the thiolate. That k_1^R, is facilitated by electron-withdrawing substituents is consistent with the predominant effect of the R-group being to stabilise the transition state of the nucleophile binding step. As anionic $4\text{-}RC_6H_4S^-$ approaches dianionic $[Fe_4S_4Cl_4]^{2-}$ there must necessarily be a build-up of a negative charge in the transition state. Electron-withdrawing R-groups which dissipate this unfavourable build-up of negative charge facilitate the rate of thiolate binding.†

The rate constant for dissociation of the coordinated thiolate (k_{-1}^R) is similarly facilitated by electron-withdrawing R-groups. Since the transition state for thiolate dissociation from $[Fe_4S_4Cl_4(SC_6H_4R\text{-}4)]^{3-}$ must be the same as that for the thiolate binding, R must have little effect on the intermediate, $[Fe_4S_4Cl_4(SC_6H_4R\text{-}4)]^{3-}$. Interestingly, a consequence of k_1^R and k_{-1}^R being similarly sensitive to the nature of R is that the binding constant, K_1^R is effectively independent of the thiolate.

Unexpectedly, the transfer of a proton from $[H_2N(CH_2)_3CH_2]^+$ to $[Fe_4S_4Cl_4(SC_6H_4R\text{-}4)]^{3-}$ (k_5^R) is also facilitated by electron-withdrawing groups. Proton transfer to the cluster is thus subject to the same electronic effects as nucleophile binding. This observation is counter-intuitive. It might be expected that k_5^R would be facilitated by electron-

DOI: 10.1039/b109668k

Table 1 Summary of elementary rate constants for the reaction of $4\text{-}RC_6H_4S^-$ with $[Fe_4S_4Cl_4]^{2-}$ in the presence of $[H_2N(CH_2)_3CH_2]^+$ or $[NHEt_3]^+$ in MeCN at 25.0 °C

	Studies with $[H_2N(CH_2)_3CH_2]^+$					Studies with $[NHEt_3]^+$	
4-R	$10^5k_1^R$/dm³ mol⁻¹ s⁻¹	$10^3k_{-1}^R$/dm³ mol⁻¹ s⁻¹	k_1^R/k_{-1}^R	k_2^R/s⁻¹	$10^6k_5^R$/dm³ mol⁻¹ s⁻¹	K_0	$10^3k_3^R$/dm³ mol⁻¹ s⁻¹
MeO	0.36 ± 0.02	0.69 ± 0.1	52.5	160 ± 10	0.47 ± 0.1	0.80 ± 0.1	6.8 ± 0.5
Me	1.4 ± 0.1	1.7 ± 0.2	83.6	200 ± 10	1.3 ± 0.1	0.82 ± 0.1	8.1 ± 0.5
H	1.4 ± 0.1	2.2 ± 0.2	63.6	300 ± 20	1.8 ± 0.1	0.87 ± 0.2	18.4 ± 1.0
Cl	5.5 ± 0.3	7.5 ± 0.3	73.3	480 ± 50	8.7 ± 1.0	1.10 ± 0.2	72.7 ± 5.0
CF_3	9.2 ± 1.0	19.2 ± 3	47.9 ± 5	1100 ± 100	26.4 ± 1.3	0.90 ± 0.2	106 ± 10

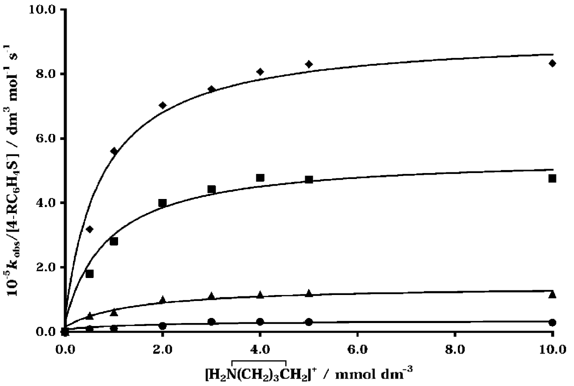

Fig. 2 Reaction of $[Fe_4S_4Cl_4]^{2-}$ with $4\text{-}RC_6H_4S^-$ in the presence of $[H_2N(CH_2)_3CH_2]^+$ in MeCN at 25.0 °C. Graph showing the dependence of the rate on the concentration of $[H_2N(CH_2)_3CH_2]^+$ ($[RC_6H_4S^-]$ = 5.0 mmol dm⁻³). Data correspond to: R = CF_3 (◆); R = Cl (■); R = Me (▲); R = MeO (●). Data for the reaction with R = H has already been reported.[10] Curves are those defined by eqn. (2) and the values listed in Table 1.

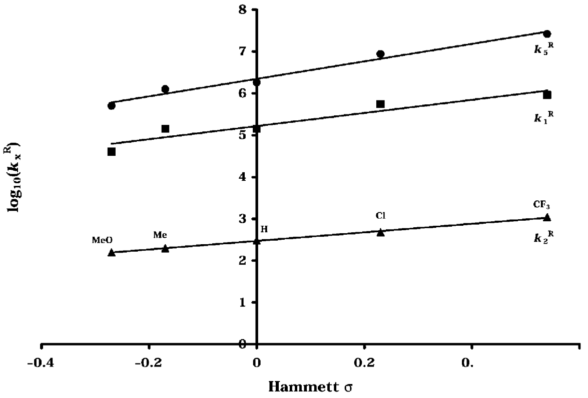

Fig. 3 The reaction of $4\text{-}RC_6H_4S^-$ with $[Fe_4S_4Cl_4]^{2-}$ in the presence of $[H_2N(CH_2)_3CH_2]^+$ in MeCN at 25.0 °C. Hammett plot[15] for the effect of the R-substituent on the rate constants for: binding of thiolate, k_1^R (■), ρ = 1.6; protonation of cluster, k_5^R (●), ρ = 2.1 and dissociation of chloride, k_2^R (▲), ρ = 1.0.

releasing groups which increase the basicity of the cluster site. That electron-withdrawing R-groups on a thiolate ligand favour the transfer of a proton to the cluster indicates that in the transition state of the proton transfer there must be an unfavourable build-up of negative charge.

In general, protonation of any site must involve shortening of the bond lengths of the ligands around that site. In our particular case, the shortening of the Fe-thiolate bond will be resisted by the build-up of negative charge as the thiolate and anionic cluster get closer. This negative charge can be dissipated by electron-withdrawing R-substituents, thus facilitating the Fe-thiolate bond length changes and hence the rate of proton transfer. Thus, Fe-thiolate bond-shortening prior to, or concomitant with, proton transfer is modulating the rate of proton transfer. Semi-quantitative representation of the effect that $4\text{-}RC_6H_4S^-$ has on k_1^R, k_2^R and k_5^R is shown in Fig. 3. Whilst it has been appreciated for a long time that bond length changes of spectator ligands is an important factor in proton transfer reactions, it is only in this study that it has been shown that bond distance reorganisation can affect the rate of proton transfer.

Finally, it is pertinent to note that although k_2^R is markedly less sensitive to the 4-substituent than k_5^R, dissociation of Cl^- is still facilitated by electron-releasing R-groups. It seems likely that, in the same way that protonation of the cluster is associated with a shortening of the Fe-thiolate bond, so is dissociation of Cl^-.

Notes and references

† Other studies indicate indirectly that electron-withdrawing R-substituents increase the rate of nucleophile binding. Our earlier studies[12,13] have shown that the kinetics for substitution of the terminal ligands of $[Fe_4S_4Cl_4]^{2-}$ by RC_6H_4SH in the presence of $[NHEt_3]^+$ are described by eqn. (4), where K_0 is the protonation constant and k_3^R is the rate constant for associative substitution of $[Fe_4S_3(SH)Cl_4]^-$.

$$k_{obs} = \frac{K_0k_3^R([NHEt_3^+]/[NEt_3])[4\text{-}RC_6H_4SH]}{1 + k_0[NHEt_3^+]/[NEt_3]} \qquad (4)$$

Table 1 shows that the initial protonation step (K_0) is independent of R, but the substitution step (k_3^R) is facilitated by electron-withdrawing substituents. Studies on the substitution of $[Fe_4S_4(SBu^t)_4]^{2-}$ by RC_6H_4SH also showed that the rate of the reactions increase as the R-substituent becomes more electron-withdrawing.[14]

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