Definition of Reaction Sequences Resulting in Self-Assembly of $[Fe_4S_4(SR)_4]^{2-}$ Clusters from Simple Reactants

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Abstract: Several reaction systems which result in the assembly of the biologically relevant $[Fe_4S_4(SPh)_4]^{2-}$ cluster (**1**) from simple reactants have been examined by spectrophotometry and ^1H NMR spectroscopy in order to define reaction sequences and identify intermediates. Systems I and II were based on the reactant mole ratios $PhS^-/FeCl_3/S = 3.5/1/1$ and $\geq 5/1/1$, respectively, and were conducted in acetonitrile and methanol solutions. In system I the first identifiable intermediate is the adamantane-like species $[Fe_4(SPh)_{10}]^{2-}$ (**4**), which reacts with sulfur in an all-or-nothing process in both solvents to afford **1**. No other intermediates were identified in this system. In system II the first recognizable species formed is tetrahedral $[Fe(SPh)_4]^{2-}$ (**2**). Reaction of **2** with sulfur in acetonitrile yields binuclear $[Fe_2S_2(SPh)_4]^{2-}$ (**3**), but in methanol **3**, which also results from **2** and sulfur, spontaneously forms **1** in a slow reaction. Thus system II provides the first demonstrated instance of elaboration of a tetranuclear cluster through mononuclear and binuclear intermediates. In methanol the overall reactions affording **1** from initial reactants are quantitative when assayed spectrophotometrically. Salts of intermediates **2**, **3**, and **4** have been independently synthesized, and the reactions **4** + S → **1** and **2** + S → **3** have been executed in good yield on a preparative scale. Reaction system III, having the reactant mole ratio $PhS^-/FeCl_3/S^{2-} = 1.5/1/1$, affords **1** in 82% spectrophotometric yield but proceeds too rapidly for detection of intermediates by the methods employed. The results are used to interpret reaction sequences in previously reported preparative methods for $[Fe_4S_4(SR)_4]^{2-}$ clusters. Certain limitations of the investigation are noted.

The preparation of the first synthetic analogue $[Fe_4S_4(SCH_2Ph)_4]^{2-}$ of an iron-sulfur protein active site was accomplished in 1972.[2] Shortly thereafter the synthetic procedure was shown to be general for a variety of R = alkyl and aryl substituent groups,[3] affording a portion of the now extensive family of cubane-type $[Fe_4S_4(SR)_4]^{2-}$ clusters[4,5] (**1**, Figure 1). These species are readily prepared anaerobically from simple, cheap reagents at ambient temperature in a process whose limiting stoichiometry is that of reaction 1 (Table I). Clusters are readily isolated from the methanol reaction solution and purified as quaternary ammonium salts; 50-80% yields of purified products are common in this laboratory. Clusters formed by direct synthesis are frequently useful as precursors to differently substituted species by means of the thiolate ligand substitution reaction (2)[4-7] or by treatment with the general electrophile YX (reaction 3).[8,9] Reaction 2 has proven of particular use in incorporating cysteinyl peptides around the Fe_4S_4 core unit,[10-12] thereby more closely simulating the terminal ligation of protein $[Fe_4S_4(S\text{-}Cys)_4]$ sites.

The preparative route to $[Fe_4S_4(SR)_4]^{2-}$ clusters remained unaltered until 1979 when Christou and Garner[13] showed that elemental sulfur in the presence of sufficient thiolate reductant afforded the clusters from Fe(II) or Fe(III) salts (reactions 4 and 5). Reactions 1[14] and 4[15] have been extended to the synthesis of $[Fe_4Se_4(SR)_4]^{2-}$ clusters. It is now abundantly clear that all such clusters form as a consequence of being the thermodynamically most stable, soluble product in the methanol reaction systems 1, 4, and 5. The term "spontaneous self-assembly" has recently been applied[16] to the outcome of these reaction systems as a euphemistic reminder that, as in the initial synthesis of most metal clusters,[17] the nature of the principal reaction product could not have been uniquely predicted.

In view of the importance of $[Fe_4S_4(SR)_4]^{2-}$ clusters as accurate synthetic representations of protein 4Fe-4S sites[4,5,18] and the unanswered question as to their biosynthesis,[19] we have undertaken an investigation directed toward elucidation of the reaction sequence leading to their formation. On the premise that the clusters are very likely elaborated in a stepwise fashion from other stable species, which may be of smaller nuclearity, certain independent results were considered to render such an investigation more feasible than at the time of the original cluster synthesis. Chief among these are (i) the synthesis of $[Fe(SPh)_4]^{2-}$ (**2**)[20] and its characterization as a mononuclear tetrahedral species,[21] (ii) the formation of the binuclear Fe(III) complexes $[Fe_2S_2(SR)_4]^{2-}$ (**3**) (R = Ph, *p*-tolyl (*p*-tol)) initially by reaction 6,[22] and very recently by reaction 7[23] using elemental sulfur as the source of sulfide,

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Table I. Reactions Pertinent to the Assembly of $[Fe_4S_4(SR)_4]^{2-}$ Clusters

no.	stoichiometric reaction[a]	ref
(1)	$4FeCl_3 + 6NaSR + 4NaHS + 4NaOMe \xrightarrow{MeOH} Na_2[Fe_4S_4(SR)_4] + RSSR + 12NaCl + 4MeOH$	2, 3
(2)[b]	$[Fe_4S_4(SR)_4]^{2-} + nR'SH \rightleftharpoons [Fe_4S_4(SR)_{4-n}(SR')_n] + nRSH$	6, 7
(3)[b]	$[Fe_4S_4(SR)_4]^{2-} + nYX \dashrightarrow [Fe_4S_4(SR)_{4-n}X_n]^{2-} + nYSR$	8, 9
(4)[g]	$4FeCl_3 + 14LiSR + 4S \xrightarrow{MeOH} Li_2[Fe_4S_4(SR)_4] + 5RSSR + 12LiCl$	13
(5)[g]	$4FeCl_2 + 10LiSR + 4S \xrightarrow{MeOH} Li_2[Fe_4S_4(SR)_4] + 3RSSR + 8LiCl$	13
(6)[d]	$2FeCl_3 + 4NaSR + 2NaHS + 2NaOMe \xrightarrow{MeOH} Na_2[Fe_2S_2(SR)_4] + 6NaCl + 4MeOH$	22
(7)	$2FeCl_3 + 8NaSR + 4S \xrightarrow{MeOH} Na_2[Fe_2S_2(SR)_4] + 2RSSR + 6NaCl$	23
(8)[i]	$4FeCl_3 + 14NaSR \longrightarrow Na_2[Fe_4(SR)_{10}] + 2RSSR + 12NaCl$	24, *c*
(9)	$4FeCl_2 + 10NaSR \xrightarrow{MeOH} Na_2[Fe_4(SR)_{10}] + 8NaCl$	*c*
(10)[i]	$FeCl_3 + 5NaSR \longrightarrow Na_2[Fe(SR)_4] + {}^1/_2RSSR + 3NaCl$	*c*
(11)[e]	$[Fe_4(SR)_{10}]^{2-} + nS \longrightarrow (n/4)[Fe_4S_4(SR)_4]^{2-} + ((4-n)/4)[Fe_4(SR)_{10}]^{2-} + (3n/4)RSSR$	*c*
(12)	$2[Fe(SR)_4]^{2-} + nS \xrightarrow{MeCN} (n/2)[Fe_2S_2(SR)_4]^{2-} + (2-n)[Fe(SR)_4]^{2-} + (n/2)RSSR + nRS^-$	*c*
(13)[f]	$2[Fe_2S_2(SR)_4]^{2-} \longrightarrow [Fe_4S_4(SR)_4]^{2-} + RSSR + 2RS^-$	30, *c*
(14)	$2[Fe_2S_2(SR)_4]^{3-} \longrightarrow [Fe_4S_4(SR)_4]^{2-} + 4RS^-$	30
(15)[h]	$2[Fe(SPh)_4]^{2-} + 2PhCH_2SSSCH_2Ph \xrightarrow{MeCN} [Fe_2S_2(SPh)_4]^{2-} + 2PhCH_2SSCH_2Ph + PhSSPh + 2PhS^-$	36

[a] All reactions are conducted under anaerobic conditions. Limiting stoichiometries are given but in practice excesses of certain reactants may be used; cf. references. [b] Aprotic solvents usually employed. [c] This work. [d] Succeeds with 2 $RS^- = 1,2\text{-}C_6H_4(CH_2S)_2^{2-}$ but fails with monothiolates. [e] Methanol or acetonitrile solvent. [f] Requires protic solvent. [g] Li^+ salts are specified because they were used in the original reports of these reactions; however, Na^+ salts may also be used. [h] Proposed stoichiometry. [i] Methanol or ethanol solvent.

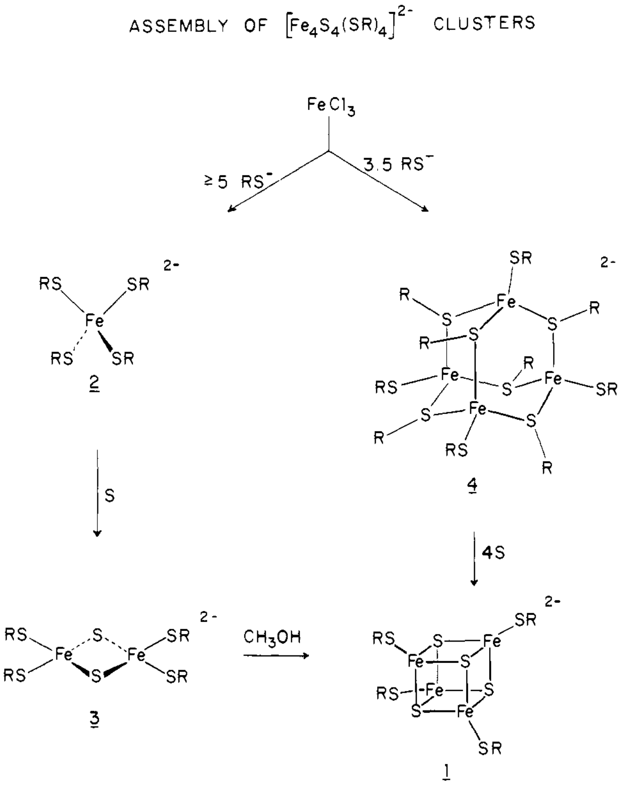

Figure 1. Depiction of the course of reactions resulting in assembly of $[Fe_4S_4(SR)_4]^{2-}$ clusters (**1**) via the intermediates $[Fe(SR)_4]^{2-}$ (**2**), $[Fe_2S_2(SR)_4]^{2-}$ (**3**), and $[Fe_4(SR)_{10}]^{2-}$ (**4**).

analogously to reaction 4, and (iii) the preparation by reaction 8 of $[Fe_4(SPh)_{10}]^{2-}$ (**4**),[24] containing an adamantane-like structure very similar to that of $[Co_4(SPh)_{10}]^{2-}$ characterized earlier.[25] As will be seen, each of these species is a detectable, isolable intermediate in the formation of tetranuclear clusters. Herein we report characterization of the reaction sequences involving intermediates **2**, **3**, and **4** which result in the assembly of $[Fe_4S_4(SR)_4]^{2-}$ clusters in methanol reaction systems comprised initially of $FeCl_3$, NaSPh or Na(S-*p*-tol), and elemental sulfur.

Experimental Section

Preparation of Compounds. $(Et_4N)_2[Fe_2S_2(SR)_4]$[23] and $(Et_4N)_2[Fe_4S_4(SR)_4]$[3,13] (R = Ph, *p*-tol) were prepared as previously described. All preparations and purifications were conducted under anaerobic conditions owing to the sensitivity of the preceding and the new compounds to dioxygen.

$(Et_4N)_2[Fe_4(SPh)_{10}]$. (a) By Reaction 8. A solution of 7.6 g (28 mmol) of $FeCl_3\cdot6H_2O$ in 50 mL of ethanol was added to a stirred solution of 99 mmol of NaSPh (from 10.5 mL of benzenethiol and 2.3 g of sodium) in 100 mL of ethanol. The initial black solution became an intense yellow-brown within 5 min, after which time addition of 3.2 g (15 mmol) of Et_4NBr in 50 mL of ethanol to the vigorously stirred solution caused precipitation of the crude product as yellow-brown microcrystals. After the reaction mixture was cooled to −20 °C the solid was collected by filtration and washed with ethanol until the washings were colorless. For removal of NaCl and NaBr, the solid was dissolved in 30 mL of acetonitrile and the mixture was filtered. Addition of 150 mL of warm ethanol to the filtrate caused separation of the product as golden brown microcrystalline flakes. After the mixture was cooled to −20 °C, the solid was collected by filtration, washed with ethanol, and dried in vacuo; 8.8 g (80%) of pure material was obtained. Anal. Calcd for $C_{76}H_{90}Fe_4N_2S_{10}$: C, 57.93; H, 5.76; N, 1.78; S, 20.30. Found: C, 57.88; H, 5.85; N, 1.96; S, 20.35. Absorption spectrum (acetonitrile): λ_{max} 256 (ϵ_M 74 000), 430 (sh 9200), 1850 (400) nm. **(b) By Reaction 9.** A solution of 3.2 g (20 mmol) of $FeCl_2\cdot2H_2O$ in 50 mL of ethanol was added to a stirred solution of 50 mmol of NaSPh (from 5.3 mL of benzenethiol and 1.2 g of sodium) in 100 mL of ethanol, forming an intense yellow-brown solution. A solution of 2.1 g (10 mmol) of Et_4NBr in 25 mL of ethanol was added, producing a yellow precipitate which upon being stirred for several min assumed a microcrystalline form. The crude product was collected by filtration, washed with isopropyl alcohol, and dissolved in ~30 mL of acetonitrile. To the filtrate of this solution was added 120 mL of warm ethanol, resulting in separation of the product as small red-brown needles. This material was collected, washed with 10:1 v/v isopropyl alcohol/acetonitrile and then ether, and dried in vacuo; 6.0 g (76%) of pure product was obtained, in all respects identical with that obtained from the preceding method.

$(n\text{-}Bu_4N)_2[Fe_4(SPh)_{10}]$. This compound was prepared by method b. The acetonitrile filtrate was evaporated to dryness in vacuo, and the residue was recrystallized from methanol to afford the pure compound as red-brown needles in 63% yield. It is substantially more soluble in organic solvents than the Et_4N^+ or Me_4N^+ salts. Anal. Calcd for $C_{92}H_{122}Fe_4N_2S_{10}$: C, 61.39; H, 6.83; N, 1.56. Found: C, 61.29; H, 6.92; N, 1.76.

$(Me_4N)_2[Fe_4(SPh)_{10}]$. Method b was used. Volume reduction of the acetonitrile filtrate followed by cooling caused separation of the pure

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Table II. Quantitation of Reactions in Acetonitrile and Methanol Solutions at ~25 °C by Absorption and ^{1}H NMR Spectra

reaction	solvent	method	$[Fe_4(SPh)_{10}]^{2-}$ or $[Fe(SPh)_4]^{2-}$ initial concn, mM	*n* equiv of S	% conversion to $[Fe_4S_4(SPh)_4]^{2-}$ or $[Fe_2S_2(SPh)_4]^{2-}$ obsd	theor ($25n$)[j]	theor ($50n$)[k]
(11)	MeCN	vis[a]	3.66, 5.65	1.00	26.7[c]	25	
(11)	MeCN	vis		2.00	51.4	50	
(11)	MeCN	vis		3.00	77.8	75	
(11)	MeCN	vis		4.00	99.8	100	
(11)	MeCN	near-IR[a]	10.0	1.00	25.3	25	
(11)	MeCN	near-IR		2.00	49.7	50	
(11)	MeCN	near-IR		3.00	74.4	75	
(11)	MeCN	near-IR		4.00	100	100	
(11)	MeCN	NMR[b]	2.31[d]	1.03	25	26	
(11)	MeCN	NMR	1.33	1.60	45	40	
(11)	MeCN	NMR	1.21	2.14	58	54	
(11)	MeCN	NMR	1.59	2.79	73	70	
(11)	MeCN	NMR	1.29	3.61	96	90	
(8) + (11)	MeOH[g]	vis	4.00, 5.00	1.00	23.6[c]	25	
(8) + (11)	MeOH	vis		2.00	44.8	50	
(8) + (11)	MeOH	vis		3.00	74.1	75	
(8) + (11)	MeOH	vis		4.00	99.3	100	
(12)	MeCN	vis	11.2	1.00	49.7[e]		50
(12)	MeCN	vis	5.00–7.42	2.00	84.2[c,f]		100
(12)	MeCN	NMR	3.44[d]	0.96	52		48
(10) + (12) + (13)	MeOH	vis	20.0	2.00	99.5	100	
(1)	MeOH	vis	2.00 ($FeCl_3$)[h]	1.50[h]	81.8[i]		

[a] Visible or near-infrared spectrophotometry; observed % conversions determined by using extinction coefficients of authentic product compounds. [b] Observed % conversions based on integrated signal intensities. [c] The set of values consists of mean values at *n* equivalents for the concentrations or concentration range indicated. [d] For all NMR runs this quantity is millimole of reactant in solution samples; accurate concentrations were not determined. [e] Mean for two reactions at 45 °C. [f] Two reactions at 25 °C and two at 45 °C. [g] All observed % conversions in methanol solution based on initial $FeCl_3$ concentration. [h] Mole ratio of reactants as in reaction 1. [i] Small quantity of black solid removed by centrifugation before measurement; mean value of three reactions. [j] Reaction 11. [k] Reaction 12.

product as red-brown crystals. Anal. Calcd for $C_{68}H_{74}Fe_4N_2S_{10}$: C, 55.81; H, 5.10; Fe, 15.27; N, 1.91; S, 21.91. Found: C, 55.49; H, 5.13; Fe, 15.00; N, 2.06; S, 21.70. This compound was used in the X-ray structural determination of $[Fe_4(SPh)_{10}]^{2-}$.[24]

$(Et_4N)_2[Fe_4(S\text{-}p\text{-tol})_{10}]$. Method b was employed using Na(S-*p*-tol). Recrystallization of the crude product from 1:4 v/v acetonitrile/methanol gave the pure compound in 72% yield as red-brown crystals. Anal. Calcd for $C_{86}H_{110}Fe_4N_2S_{10}$: C, 60.20; H, 6.46; N, 1.63. Found: C, 60.11; H, 6.48; N, 1.73.

$(Et_4N)_2[Fe_4(SCH_2Ph)_{10}]$. This compound was prepared by method b. A solution of 3.2 g (20 mmol) of $FeCl_2\cdot 2H_2O$ in 50 mL of methanol was added to a solution of 70 mmol of $NaSCH_2Ph$ (from 8.3 mL of benzylthiol and 1.6 g of sodium) in 100 mL of methanol, forming a brown solution and some yellow-brown solid. After being stirred for 15 min, the mixture was filtered and the filtrate was treated with 2.1 g (10 mmol) of Et_4NBr in 50 mL of methanol, resulting in the separation of a brown microcrystalline solid. After the filtrate volume was reduced by ca. half, 50 mL of isopropyl alcohol was added and the solid was collected. Recrystallization from acetonitrile with slow cooling to −20 °C gave 5.2 g (63%) of pure product as brown-black crystals. Anal. Calcd for $C_{86}H_{110}Fe_4N_2S_{10}$: C, 60.20; H, 6.46; N, 1.63. Found: C, 60.16; H, 6.47; N, 1.68.

$(Et_4N)_2[Fe(SPh)_4]$. This compound was prepared by reaction 10. A solution of 120 mmol of NaSPh (from 12.7 mL of benzenethiol and 2.8 g of sodium) in 100 mL of ethanol was added to a stirred solution of 5.4 g (20 mmol) of $FeCl_3\cdot 6H_2O$ in 30 mL of ethanol over a 10-min period. A solution of 9.3 g (44 mmol) of Et_4NBr in 30 mL of ethanol was then introduced, causing separation of a microcrystalline solid that was collected by filtration, washed with ether, and dried in vacuo. This material was recrystallized from warm acetonitrile, yielding 11 g (53%) of pure product as light greenish tan crystals which lost their crystallinity upon drying in vacuo. Anal. Calcd for $C_{40}H_{60}FeN_2S_4$: C, 63.80; H, 8.03; N, 3.72. Found: C, 64.09; H, 7.82; N, 3.77. Absorption spectrum (acetonitrile): λ_{max} 337 (ϵ_M 16 300), 390 (sh, 2800), 1700 nm (110). Voltammetry (acetonitrile): $E_{1/2} = -0.53$ V vs. SCE (ΔE_p = 100 mV, $i_{p,c} = i_{p,a}$ at 100 mV/s).

$[Fe_4S_4(SPh)_4]^{2-}$ from $[Fe_4(SPh)_{10}]^{2-}$ and Sulfur. This preparation proceeds by reaction 11 (*n* = 4) and was conducted in two solvents.

(a) In Methanol. A solution of 1.80 g (1.00 mmol) of $(n\text{-}Bu_4N)_2[Fe_4(SPh)_{10}]$ in 100 mL of methanol was stirred with 0.128 g (4.00 mmol) of elemental sulfur for 3 h. Upon volume reduction to 10 mL a black microcrystalline product separated which was collected and washed thoroughly with methanol, affording 1.11 g (87%) of $(n\text{-}Bu_4N)_2[Fe_4S_4(SPh)_4]$. In this and the following preparations the products were identified by their characteristic ^{1}H NMR[23,26,27] and/or UV–visible spectra.[22,28]

(b) In Acetonitrile. A solution of 5.00 g (3.17 mmol) of $(Et_4N)_2[Fe_4(SPh)_{10}]$ in 50 mL of acetonitrile was stirred with 0.407 g (12.7 mmol) of elemental sulfur for 6 h. Addition of ether caused precipitation of $(Et_4N)_2[Fe_4S_4(SPh)_4]$, which was collected and washed with ether; 2.93 g (88%) was obtained. A second crop of 0.14 g was realized by cooling the filtrate to −20 °C, affording a total yield of 93%.

$[Fe_2S_2(SPh)_4]^{2-}$ from $[Fe(SPh)_4]^{2-}$ and Sulfur. This preparation proceeds by reaction 12 (*n* = 2). A solution of 5.00 g (6.64 mmol) of $(Et_4N)_2[Fe(SPh)_4]$ in 50 mL of acetonitrile was stirred with 0.213 g (6.64 mmol) of elemental sulfur for 3 h at 70 °C. After the reaction mixture was cooled slowly to −25 °C, black flakes were collected, washed with cold acetonitrile, and dried in vacuo, affording 2.06 g (71%) of $(Et_4N)_2[Fe_2S_2(SPh)_4]$.

Monitoring of Reactions. The reaction systems initially containing, in varying mole ratios, $FeCl_3$/NaSPh/S in methanol, $[Fe_4(SPh)_{10}]^{2-}$/S and $[Fe(SPh)_4]^{2-}$/S in acetonitrile, and $[Fe_2S_2(S\text{-}p\text{-tol})_4]^{2-}$ in acetonitrile/methanol were monitored spectrophotometrically and/or by ^{1}H NMR spectroscopy at ambient temperature. All systems were maintained under anaerobic conditions. Further experimental details are given in Table II and in appropriate figure legends. Specified reaction times are not necessarily the minimum values required to reach equilibrium. NaSPh was prepared by the anaerobic reaction of benzenethiol and sodium in hexane or THF. The resulting white solid was collected by filtration, washed with the same solvent, and thoroughly dried in vacuo. Acetonitrile-d_3 (Merck) was dried over 3A molecular sieves. $FeCl_3$ (Cerac, Fisher Scientific), methanol-d_4 (Merck), and other reagents and solvents (degassed) were used as received. Absorption spectra were recorded on Cary Models 17 and 219 spectrophotometers. ^{1}H NMR spectra were obtained on Varian XL-100-15 and Bruker HXS-360 spectrometers by using the procedures described.[26,29]

Results and Discussion

In seeking to define the sequence of reactions resulting in formation of $[Fe_4S_4(SR)_4]^{2-}$ clusters, we have concentrated on

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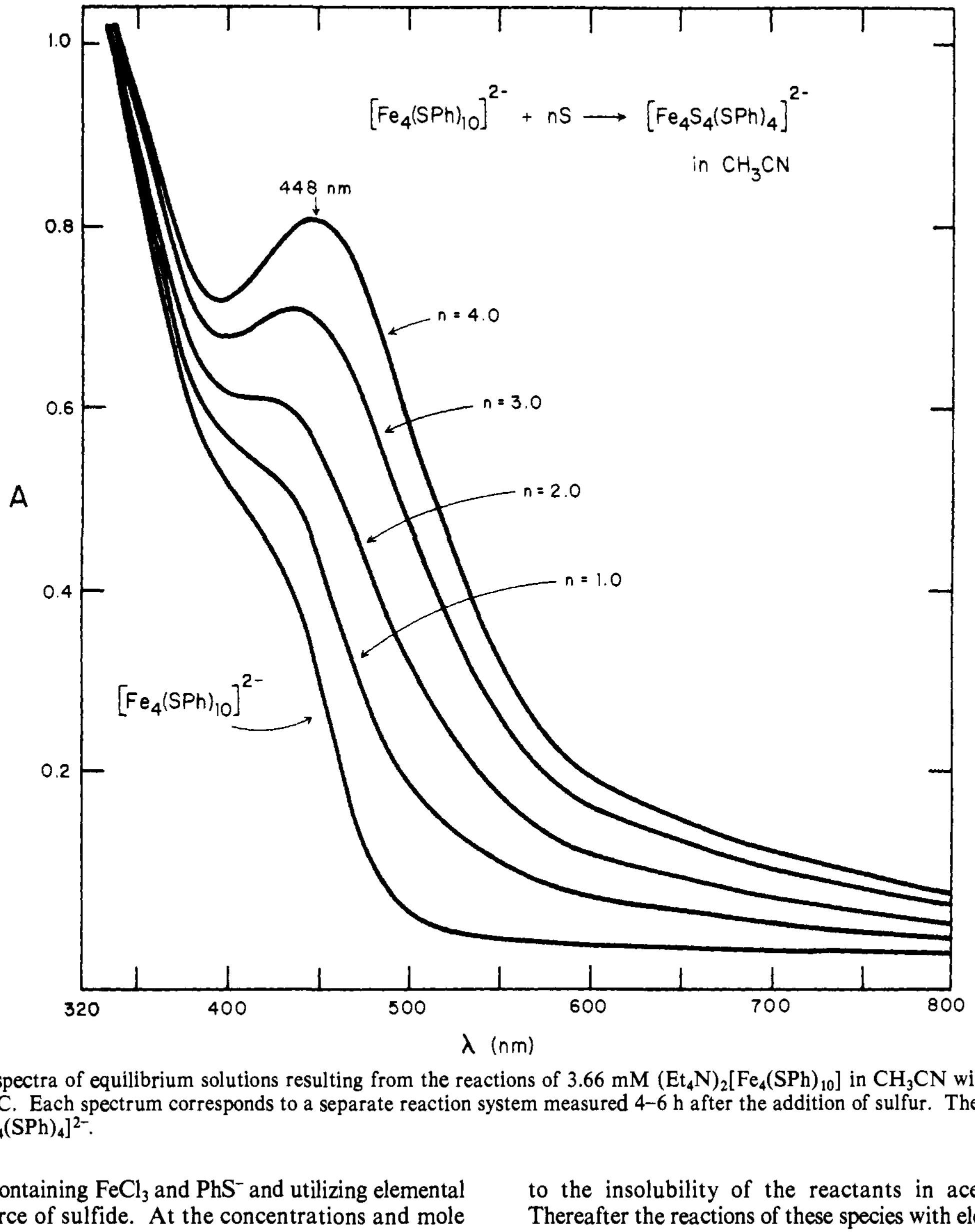

Figure 2. Visible spectra of equilibrium solutions resulting from the reactions of 3.66 mM $(Et_4N)_2[Fe_4(SPh)_{10}]$ in CH_3CN with n = 1.0–4.0 equiv of sulfur at ~25 °C. Each spectrum corresponds to a separate reaction system measured 4–6 h after the addition of sulfur. The n = 4.0 curve is the spectrum of $[Fe_4S_4(SPh)_4]^{2-}$.

systems initially containing $FeCl_3$ and PhS^- and utilizing elemental sulfur as the source of sulfide. At the concentrations and mole ratios required for monitoring reactions by spectrophotometry and ^1H NMR spectroscopy, intermediate iron benzenethiolate species proved to be soluble and to react smoothly with the only insoluble component, sulfur, to afford homogeneous systems. This behavior obtained in methanol solution where sodium salts of intermediates and products were formed and in acetonitrile solutions if quaternary ammonium salts of these same species were employed. Certain other systems tested, based on $FeCl_3$, alkylthiolates, and sulfur or sulfide, gave precipitates which hindered examination of reactions. Both intermediates and products are identifiable by their absorption spectra and, in some cases, are even more clearly recognized by their ^1H NMR spectra. Because all such species are paramagnetic, the latter spectra are rendered distinctive by isotropic interactions, affording the isotropic shift patterns evident from the data of Table III for acetonitrile solutions. Shifts in methanol solutions differ slightly from these values. Alternating signs of ring proton shifts, sign inversion on p-H/p-Me substitution, and relative shifts ensure that the isotropic shifts of $[Fe(SR)_4]^{2-}$ and $[Fe_4(SR)_{10}]^{2-}$ species, whose spectra have not been described in full previously, are dominantly contact in origin as has been shown for $[Fe_4S_4(SR)_4]^{2-}$[26,27] and $[Fe_2S_2(SR)_4]^{2-}$.[23]

Reaction sequences have been found to depend on the initial $PhS^-/FeCl_3$ mole ratios, 3.5/1 and $\gtrsim$5/1, and on the nature of the solvent, aprotic (acetonitrile) vs. protic (methanol). Dependence on mole ratios arises as a consequence of different initial species formed, which were produced in methanol solutions owing to the insolubility of the reactants in acetonitrile solution. Thereafter the reactions of these species with elemental sulfur were examined with their sodium salts in situ in methanol and with their quaternary ammonium salts in acetonitrile. Reactions conducted under these conditions are considered in turn, with attention directed to the listing of reactions pertinent to cluster assembly in Table I and quantitation of reaction products in Table II. Table I contains all presently known reactions for assembly of $[Fe_4S_4(SR)_4]^{2-}$ clusters from simple reactants or complexes formed therefrom. As will be seen, reactions 11 and 13[30] represent the final identifiable steps in cluster formation under different experimental conditions.

Reaction System: PhS^-/Fe(III) = 3.5/1 + Sulfur. Reaction of NaSPh and $FeCl_3$ in the indicated mole ratio in ethanol (reaction 8), followed by addition of R'_4N^+ cations affords crystalline $(R'_4N)_2[Fe_4(SPh)_{10}]$ salts in ca. 60–80% purified yields. The structure **4** was demonstrated by X-ray crystallography.[24] It contains six bridging and four terminal ligands and an adamantane-like Fe_4S_6 core dimensionally similar to those in $[Co_4(SPh)_{10}]^{2-}$[25] and $Zn_4(SPh)_8(MeOH)$.[31] Each Fe atom is located in an approximately tetrahedral FeS_4 site.

(a) In Acetonitrile. The reaction of preisolated $(Et_4N)_2[Fe_4(SPh)_{10}]$ with n = 1–4 equiv of sulfur was examined by spectrophotometry in the visible and near-infrared regions and by ^1H

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(30) J. Cambray, R. W. Lane, A. G. Wedd, R. W. Johnson, and R. H. Holm, *Inorg. Chem.*, **16**, 2565 (1977).

(31) I. G. Dance, *J. Am. Chem. Soc.*, **102**, 3445 (1980).

Table III. Isotropic Shifts of Fe–S Complexes in CD_3CN Solutions at ~27 °C

complex	($\Delta H/H_0$), ppm[a] o-H	 m-H	 p-H, $-CH_3$
$[Fe(SPh)_4]^{2-}$	+9.60	−15.1	+16.8
$[Fe(S\text{-}p\text{-tol})_4]^{2-}$	+8.80	−13.2	−17.9
$[Fe_2S_2(SPh)_4]^{2-}$	+2.30	−2.11	+3.82
$[Fe_2S_2(S\text{-}p\text{-tol})_4]^{2-}$	+2.42	−2.10	−3.74
$[Fe_4(SPh)_{10}]^{2-}$	+10.4 (t)[c]	−9.00 (t)[d]	+16.2 (t)
	+16.2 (b)[c]	−9.00 (b)[d]	+19.2 (b)
$[Fe_4(S\text{-}p\text{-tol})_{10}]^{2-}$[b]	+10.2 (t)	−9.07 (t)	−16.9 (t)
	+16.4 (b)	−8.88 (b)	−19.3 (b)
$[Fe_4S_4(SPh)_4]^{2-}$	+1.34	−1.03	+1.91
$[Fe_4S_4(S\text{-}p\text{-tol})_4]^{2-}$[e]	+1.28	−0.91	−1.63

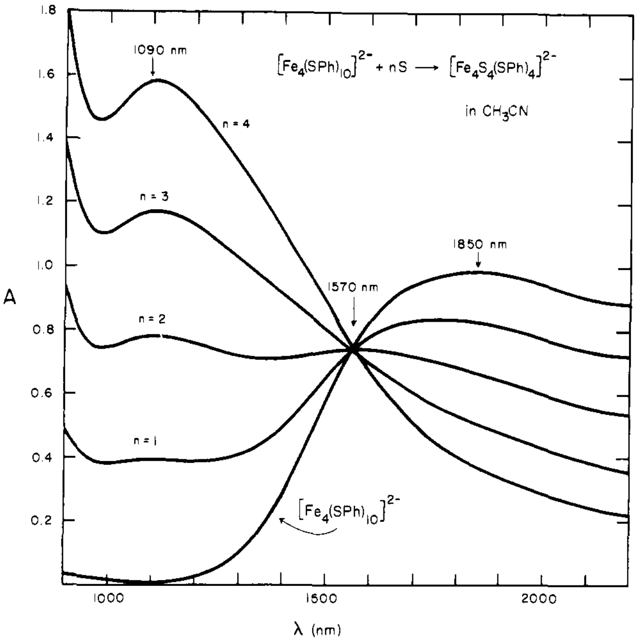

Figure 3. Near-infrared spectra of equilibrium solutions resulting from the reactions of 10.0 mM $(Et_4N)_2[Fe_4(SPh)_{10}]$ with n = 1.0–4.0 equiv of sulfur at ~25 °C. Other details are as in Figure 2 except that spectra were measured 12–15 h after the addition of sulfur.

NMR spectroscopy. Absorption spectra of equilibrium solutions are shown in Figures 2 and 3. Upon the addition of sulfur the nearly featureless visible spectrum of $[Fe_4(SPh)_{10}]^{2-}$ (430 nm (sh)) becomes progressively more intense until, at 4.0 equiv of sulfur, the final spectrum (λ_{max} = 448 nm) becomes identical with that of an authentic sample of $[Fe_4S_4(SPh)_4]^{2-}$ in acetonitrile. Similarly, in the near-infrared region the broad tetrahedral Fe(II) band ($^5E \rightarrow {}^5T_2$) of $[Fe_4(SPh)_{10}]^{2-}$ at 1850 nm decreases, and absorption due to $[Fe_4S_4(SPh)_4]^{2-}$ increases, in intensity as the amount of sulfur is increased. The n = 4.0 equiv spectrum lacks the 1850 nm band and is fully consistent with formation of $[Fe_4S_4(SPh)_4]^{2-}$ (λ_{max} = 1090 nm).

A complementary view of the reaction system is afforded by the NMR spectra in Figure 4. Upon addition of 1.0 equiv of sulfur new signals appear at −8.23, −5.86, and −5.29 ppm and intensities of the features at −16.2, 3.2, 9.0, and 12.0 ppm are attenuated. Assignment of the latter as resonances of $[Fe_4(SPh)_{10}]^{2-}$ follows from separate examination of this complex at 360 MHz and a lower temperature, under which conditions spectral resolution in greatly improved. One such spectrum is shown in Figure 5; assignments of bridging and terminal p-H and m-H resonances are made on the basis of ~3:2 signal intensities. Also included is the spectrum of $[Fe_4(S\text{-}p\text{-tol})_{10}]^{2-}$, in which the lack of signal overlap in the upfield region allows the indicated assignments of the two relatively broad o-H resonances. Returning to Figure 4, systems with higher equivalents of sulfur display progressively diminished $[Fe_4(SPh)_{10}]^{2-}$ resonances, which are

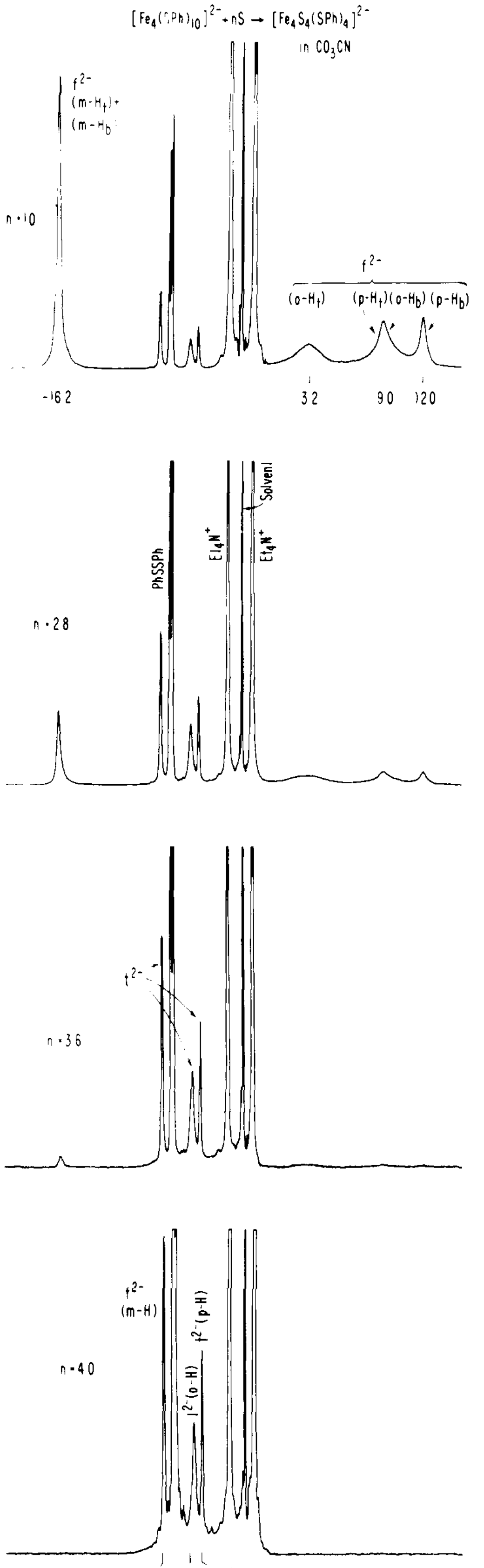

Figure 4. ^1H NMR spectra (100 MHz) of equilibrium solutions resulting from the reactions of $(Et_4N)_2[Fe_4(SPh)_{10}]$ (f^{2-}) with 1.0–4.0 equiv of sulfur in CD_3CN at ~27 °C, yielding $[Fe_4S_4(SPh)_4]^{2-}$ (t^{2-}). Each spectrum corresponds to a separate reaction system measured ~1 h after the addition of sulfur. Spectral amplitudes are not constant; signal assignments are indicated (cf. Figure 5). In this and other NMR spectra shifts (ppm) downfield and upfield of Me_4Si reference are designated as − and +, respectively.

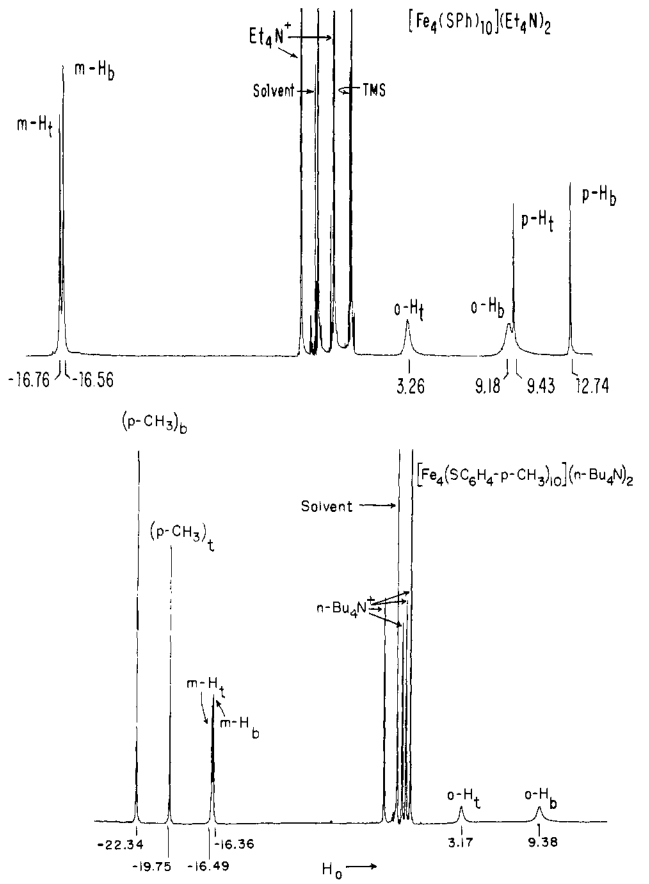

Figure 5. ^1H NMR spectra (360 MHz) in CD_3CN of $(Et_4N)_2[Fe_4(SPh)_{10}]$ at -10 °C (top) and $(n\text{-}Bu_4N)_2[Fe_4(S\text{-}p\text{-}tol)_{10}]$ at -5 °C (bottom). Signal assignments are indicated for bridging (b) and terminal (t) ligands.

absent in the $n = 4.0$ equiv spectrum. The signal multiplet near −7.1 ppm, from PhSSPh formed in the reaction, shows a concomitant increase in intensity. The only isotropically shifted resonances present in the final spectrum are in the aforementioned set of three, which is found in the spectrum of $[Fe_4S_4(SPh)_4]^{2-}$ measured separately in acetonitrile.[26]

Spectral features of reaction systems initially containing the mole ratios $0 < S/[Fe_4(SPh)_{10}]^{2-} \leq 4$ indicate the presence of only two Fe–S species, $[Fe_4(SPh)_{10}]^{2-}$ and $[Fe_4S_4(SPh)_4]^{2-}$, in detectable concentrations at equilibrium. The existence of a clean isosbestic point at 1570 nm in the near-infrared spectra (Figure 3) and the observation of the same point in reacting systems with 4 equiv of sulfur (not shown) are consistent with this situation. Further, no resonances other than those assignable to these two complexes were observed in equilibrium solutions. Consequently, the reactions of $[Fe_4(SPh)_{10}]^{2-}$ with sulfur in acetonitrile solutions are interpreted in terms of the "all-or-nothing" stoichiometry of reaction 11; i.e., at a given value of n equiv of sulfur $[Fe_4S_4(SPh)_4]^{2-}$ is formed at the expense of unreacted $[Fe_4(SPh)_{10}]^{2-}$. Absorption spectral changes and relative NMR signal intensities can be accounted for quite satisfactorily on this basis, as may be seen from the excellent agreement between theoretical and observed percents conversion to $[Fe_4S_4(SPh)_4]^{2-}$. Results from near-infrared spectra are particularly convincing owing to the complete separation of the 1090 nm band from other absorptions. Reactions with $n = 4.0$ equiv of sulfur are quantitative (mean value 99.8%), a matter confirmed on the preparative scale by isolation of a product salt of $[Fe_4S_4(SPh)_4]^{2-}$ in 93% yield.

(b) In Methanol. Reaction 8 affords a solution of $Na_2[Fe_4(SPh)_{10}]$. Spectra of equilibrium solutions after addition of n = 1–4 equiv of sulfur, shown in Figure 6, resemble those in acetonitrile solution. Absorbance in the visible region increases with increase in n, and the $n = 4.0$ equiv spectrum has a well-defined maximum at 434 nm. The NMR spectrum of $[Fe_4(SPh)_{10}]^{2-}$, given in Figure 7, is substantially broadened and less well-resolved than in acetonitrile. However, all signals, which include that of PhSSPh produced in reaction 8, are identifiable. Addition of n = 4.0 equiv of sulfur[32] abolishes all $[Fe_4(SPh)_{10}]^{2-}$ resonances and

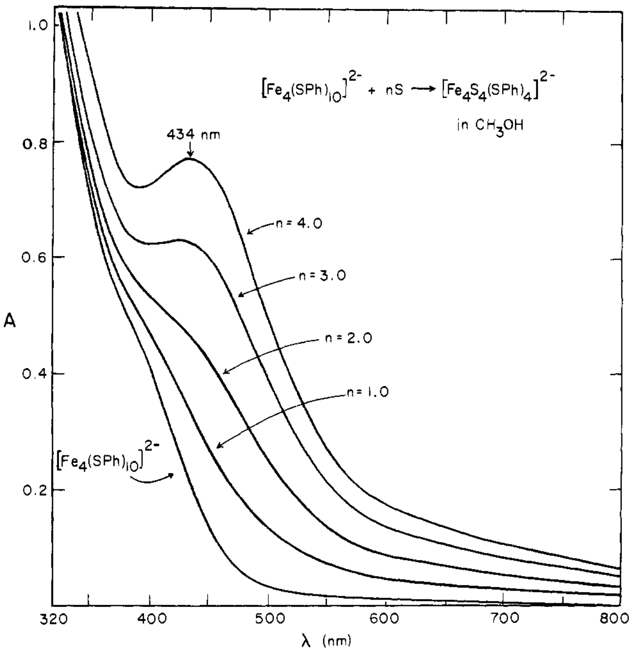

Figure 6. Visible spectra of equilibrium solutions resulting from the reactions of 5.00 mM $Na_2[Fe_4(SPh)_{10}]$ (from 20.0 mM $FeCl_3$ + 3.5 equiv of NaSPh) with n = 1.0–4.0 equiv of sulfur in CH_3OH at ~25 °C. Each spectrum corresponds to a separation reaction system measured 0.5–1 h after the addition of sulfur. The $n = 4.0$ curve corresponds to the spectrum of $[Fe_4S_4(SPh)_4]^{2-}$.

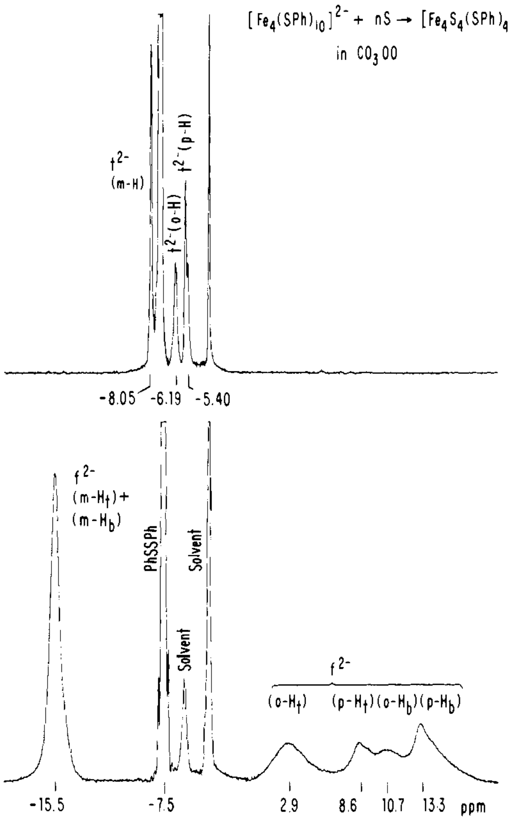

Figure 7. ^1H NMR spectra (100 MHz) of equilibrium solutions in CD_3OD at ~27 °C: bottom, ~0.05 M $Na_2[Fe_4(SPh)_{10}]$ (f^{2-}, from ~0.20 M $FeCl_3$ + 3.5 equiv of NaSPh); top, 1 h after addition of 4.0 equiv of sulfur/f^{2-}, demonstrating formation of $[Fe_4S_4(SPh)_4]^{2-}$ (t^{2-}). Signal assignments are indicated.

produces signals at -8.05, -6.19, and -5.40 ppm, which are assigned to *m*-H, *o*-H, and *p*-H, respectively, of $[Fe_4S_4(SPh)_4]^{2-}$.

In these and other methanol reaction systems described subsequently, sodium salts of reactants and products have proven difficult to isolate in tractable form. Their identification in situ follows from obvious similarities of absorption and ^{1}H NMR spectra with those of isolated analytical specimens of R'_4N^+ salts examined in acetonitrile solutions. The blue-shifted band of $[Fe_4S_4(SPh)_4]^{2-}$ in methanol (434 nm) vs. acetonitrile (448 nm) is one example of a common characteristic of $[Fe_4S_4(SR)_4]^{2-}$ spectra when compared in protic and aprotic solvents.[33]

Reactions of the $[Fe_4(SPh)_{10}]^{2-}/S$ systems in methanol may also be diagnosed in terms of the stoichiometry of reaction 11, as supported by the agreement of theoretical and observed yield data in Table II. The preparative cluster assembly reaction 4, involving the initial mole ratios $PhS^-/Fe(III)/S = 3.5/1/1$, may now be interpreted as the sum of two distinct processes: rapid formation of $[Fe_4(SPh)_{10}]^{2-}$ by the homogeneous reaction 8 followed by conversion to $[Fe_4S_4(SPh)_4]^{2-}$ by the very much slower, heterogeneous reaction (11) with $n = 4$. On a preparative scale a purified yield of 76% for $(n\text{-}Bu_4N)_2[Fe_4S_4(SPh)_4]$ has been reported.[13] Although we have not done so, this yield could doubtless be optimized in view of the fact that the spectrophotometrically determined yield of the overall reaction (8) + (11) = (4) is quantitative (99.3%, based on $FeCl_3$). However, we have obtained the same compound in 87% yield by reaction of methanol-soluble $(n\text{-}Bu_4N)_2[Fe_4(SPh)_{10}]$ with sulfur. Reaction 5, which has been shown to give $(n\text{-}Bu_4N)_2[Fe_4S_4(SPh)_4]$ in 66% yield,[13] may be similarly interpreted as the reaction sum (9) + (11) = (5) inasmuch as we have demonstrated the preparation of $[Fe_4(SPh)_{10}]^{2-}$ salts by reaction 9.

Reaction System: $PhS^-/Fe(III) \geq 5/1$ + Sulfur. Reaction 10, but with NaSPh and $FeCl_3$ in 6:1 mole ratio, followed by addition of Et_4NBr afforded $(Et_4N)_2[Fe(SPh)_4]$ in 53% yield after purification. Thus in this reaction system the initial recognizable species formed is $[Fe(SPh)_4]^{2-}$ rather than $[Fe_4(SPh)_{10}]^{2-}$. The tetrahedral structure **2** has been established by X-ray diffraction,[21] and certain spectroscopic properties have been examined in detail.[34] Retention of a tetrahedral structure in acetonitrile solution is indicated by the $^5E \rightarrow {}^5T_2$ band at 1700 nm observed by Holah and Coucouvanis[20] and confirmed in this work.

(a) In Acetonitrile. Reaction of preisolated $(Et_4N)_2[Fe(SPh)_4]$ with $n = 1$ and 2 equiv of sulfur in the stoichiometry of reaction 12 results in replacement of the nearly featureless spectrum of the initial complex (390 nm (sh)) with the characteristic spectrum of $[Fe_2S_2(SPh)_4]^{2-}$ (λ_{max} = 478, 530 (sh) nm; not shown). Corresponding results were obtained when reaction systems were examined by ^{1}H NMR, as seen in Figure 8. Upon introduction of $n = 1.0$ equiv of sulfur, resonances of $[Fe(SPh)_4]^{2-}$ at -22.3, 16.8, and 23.5 ppm are reduced in intensity. Signals at -9.33 and -5.06 ppm, from *m*-H and *o*-H of $[Fe_2S_2(SPh)_4]^{2-}$,[23,35] appear together with that at -7.1 ppm from PhSSPh/PhS^- produced in the reaction. No signals from other Fe-S species were observed at equilibrium. The quantitated spectrophotometric and NMR yield data in Table II for $n = 1.0$ equiv support adherence of the reaction systems to the all-or-nothing stoichiometry of reaction 12. In the NMR spectrum after reaction of $n = 2.0$ equiv of sulfur the only isotropically shifted resonances are those of $[Fe_2S_2(SPh)_4]^{2-}$, suggesting quantitative conversion to product. However, the spectrophotometric yield, while relatively high, was not quantitative in repetitive reactions at 25 and 45 °C (mean value 84.2%). When reaction 12 with $n = 2.0$ equiv of sulfur was performed on a preparative scale, $(Et_4N)_2[Fe_2S_2(SPh)_4]$ was obtained in 71% yield. Formation of $[Fe_2S_2(SPh)_4]^{2-}$ by this reaction is foreshadowed by the preparation of its Ph_4P^+ salt from $[Fe(SPh)_4]^{2-}$ and dibenzyl trisulfide,[36] for which the stoichiometry of reaction 15 is proposed.

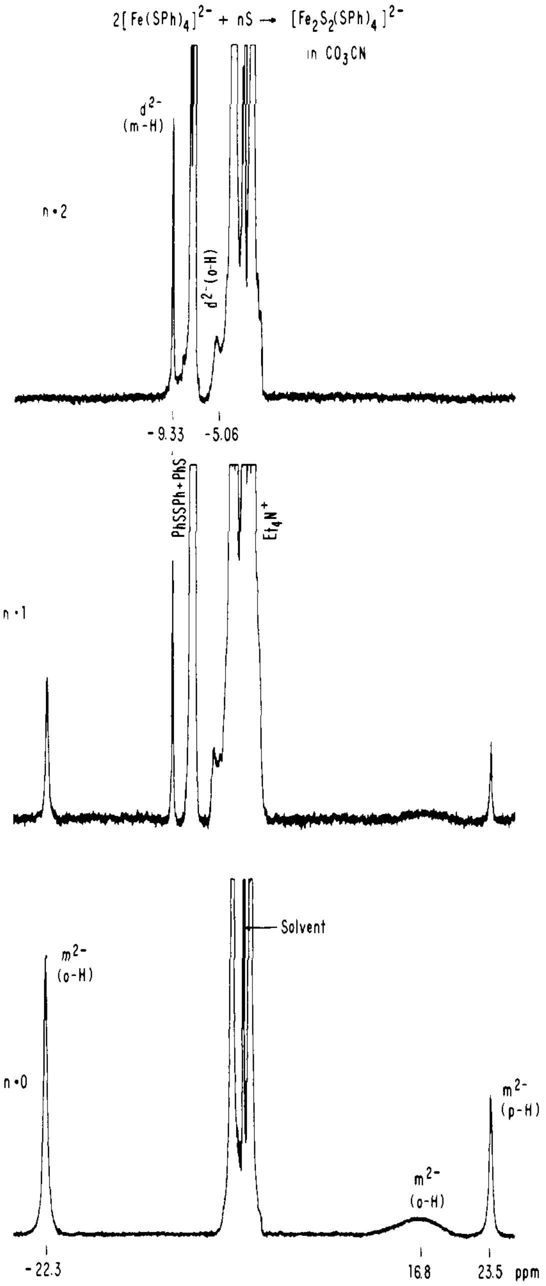

Figure 8. ^{1}H NMR spectra (100 MHz) of equilibrium solutions resulting from the reactions of $(Et_4N)_2[Fe(SPh)_4]$ (m^{2-}) with $n = 1.0$ and 2.0 equiv of sulfur/$2m^{2-}$ in CD_3CN at ~27 °C, yielding $[Fe_2S_2(SPh)_4]^{2-}$ (d^{2-}). The two upper spectra correspond to separate reaction systems 1 h after addition of sulfur. Spectral amplitudes are not constant; signal assignments are indicated.

(b) In Methanol. Reaction 10, conducted as described above, affords solutions of $Na_2[Fe(SPh)_4]$. Addition of $n = 2.0$ equiv of sulfur in the stoichiometry of reaction 12 results in a behavior different from that in the acetonitrile reaction system, a matter evident from the time-dependent visible spectra in Figure 9. After 5 min reaction time the spectrum of $[Fe(SPh)_4]^{2-}$ is replaced by

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(32) Solutions containing ~0.05 M $Na_2[Fe_4(SPh)_{10}]$ and $n \approx$ 1-3 equiv of sulfur were somewhat viscous and did not afford well-resolved spectra, which for this reason are not shown. This behavior did not occur at the lower concentrations used in spectrophotometric experiments such as those in Figure 6.

(33) C. L. Hill, J. Renaud, R. H. Holm, and L. E. Mortenson, *J. Am. Chem. Soc.*, **99**, 2549 (1977).

(34) A. Kostikas, V. Petrouleas, A. Simopoulos, D. Coucouvanis, and D. G. Holah, *Chem. Phys. Lett.*, **38**, 582 (1976); P. M. Champion and A. J. Sievers, *J. Chem. Phys.*, **66**, 1819 (1977).

(35) The *p*-H resonance of $[Fe_2S_2(SPh)_4]^{2-}$ at -3.4 ppm[23] is barely evident as a shoulder on the intense cation signal in the $n = 2$ equiv spectrum of Figure 8.

(36) D. Coucouvanis, D. Swenson, P. Stremple, and N. C. Baenziger, *J. Am. Chem. Soc.*, **101**, 3392 (1979).

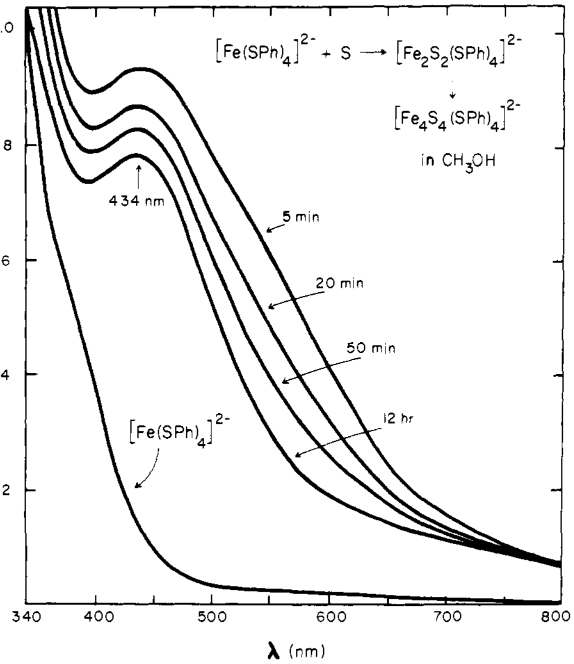

Figure 9. Visible spectra of solutions resulting from the reaction of 20.0 mM $Na_2[Fe(SPh)_4]$ (from 20.0 mM $FeCl_3$ and 6 equiv of NaSPh) with 1 equiv of sulfur in CH_3OH at ~25 °C. The spectrum recorded at 12 h reaction time is that of an equilibrium solution containing $[Fe_4S_4(SPh)_4]^{2-}$.

one with pronounced visible absorption exhibiting a shoulder near 530 nm, possibly due to $[Fe_2S_2(SPh)_4]^{2-}$. At longer reaction times band shapes and intensities change until at 12 h the spectrum of $[Fe_4S_4(SPh)_4]^{2-}$ is fully developed (λ_{max} = 434 nm, compare with the n = 4.0 equiv spectrum in Figure 6). Analysis of the reaction at this point shows quantitative formation of $[Fe_4S_4(SPh)_4]^{2-}$ (99.5%, based on $FeCl_3$). NMR spectra of the reacting system, set out in Figure 10 for a solution 10-fold more concentrated in iron than that in Figure 9, provide definite information as to the sequence of events. Addition of n = 2.0 equiv of sulfur affords, after 10-min reaction time, a spectrum devoid of $[Fe(SPh)_4]^{2-}$ resonances. The most intense new feature is that at −9.19 ppm, which is due to *m*-H of $[Fe_2S_2(SPh)_4]^{2-}$ (*p*-H and *o*-H resonances are obscured by cation and solvent signals). Subsequent spectra show a progressive decrease in the intensity of this signal and concomitant increase in the intensities of the PhSSPh/PhS⁻ resonance near −7.1 ppm and the signals at −8.06, −6.19 (sh), and −5.40 ppm. At 90-min reaction time this set of signals, which arises from $[Fe_4S_4(SPh)_4]^{2-}$ (compare with Figure 7), is dominant and the resonance at −9.19 ppm has nearly disappeared. Final evidence that the last step in the sequence involves the spontaneous dimer → tetramer conversion of reaction 13 is given by the NMR spectra in Figure 11. Preisolated $(Et_4N)_2[Fe_2S_2(S\text{-}p\text{-tol})_4]$ in a 2:1 v/v CD_3CN/CD_3OD solution[37] is observed to convert slowly to $[Fe_4S_4(S\text{-}p\text{-tol})_4]^{2-}$ with attendant formation of *p*-tolSS-*p*-tol/*p*-tolS⁻. Changes in *m*-H and *p*-CH_3 resonances, in particular, readily identify the overall reaction. Chemical shifts of the product cluster differ only slightly from those of authentic $[Fe_4S_4(S\text{-}p\text{-tol})_4]^{2-}$ in pure CD_3CN.[26,27]

Cluster formation in the methanol reaction system having the initial mole ratios PhS⁻/Fe(III)/S ≳ 5/1/1 may now be recognized to occur by means of three distinct reactions: production of $[Fe(SPh)_4]^{2-}$ by homogeneous reaction 10, formation of $[Fe_2S_2(SPh)_4]^{2-}$ by the slower reaction 12 with n = 2, and conversion to $[Fe_4S_4(SPh)_4]^{2-}$ by reaction 13. The reaction sum 4 × (10) + 2 × (12) + (13) = (4); consequently, this reaction system is equivalent to the cluster assembly reaction (4). As such

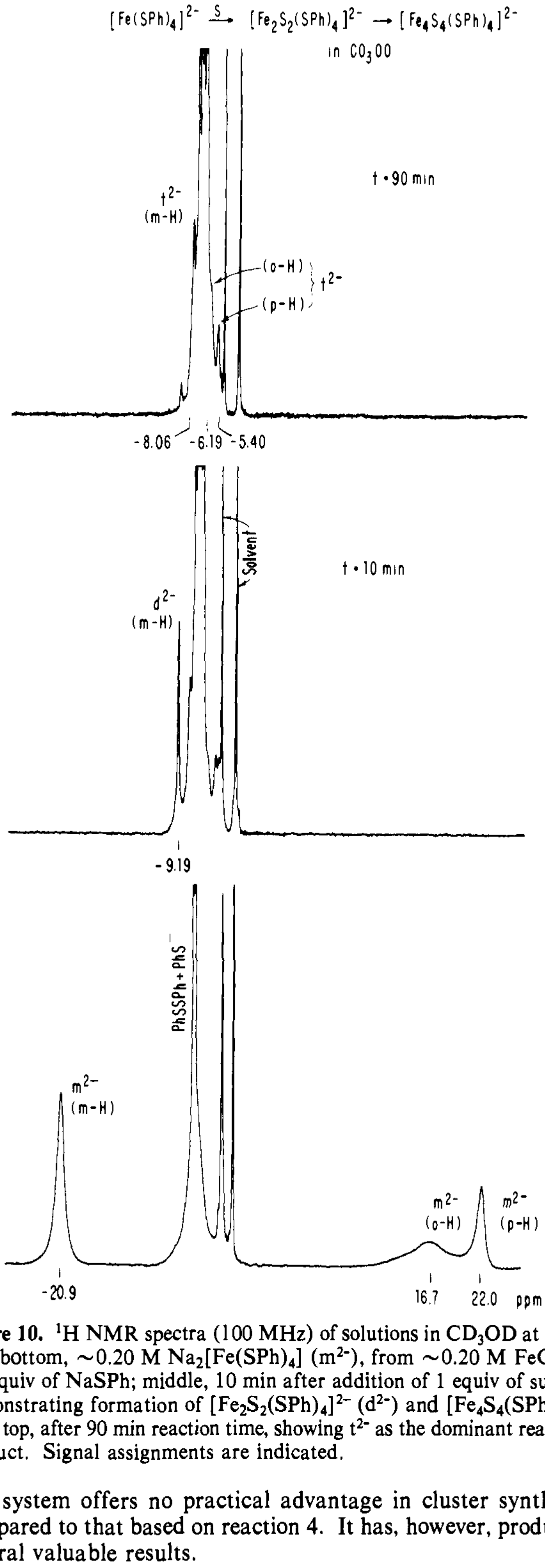

Figure 10. ¹H NMR spectra (100 MHz) of solutions in CD_3OD at ~27 °C: bottom, ~0.20 M $Na_2[Fe(SPh)_4]$ (m^{2-}), from ~0.20 M $FeCl_3$ + ≳6 equiv of NaSPh; middle, 10 min after addition of 1 equiv of sulfur, demonstrating formation of $[Fe_2S_2(SPh)_4]^{2-}$ (d^{2-}) and $[Fe_4S_4(SPh)_4]^{2-}$ (t^{2-}); top, after 90 min reaction time, showing t^{2-} as the dominant reaction product. Signal assignments are indicated.

this system offers no practical advantage in cluster synthesis compared to that based on reaction 4. It has, however, produced several valuable results.

Chief among these results is the demonstration that tetranuclear clusters can be built up by a series of spontaneous irreversible reactions 16 commencing with trivial reagents and passing through

$$FeCl_3 \xrightarrow[(10)]{PhS^-} [Fe(SPh)_4]^{2-} \xrightarrow[(12)]{S} [Fe_2S_2(SPh)_4]^{2-} \xrightarrow[(13)]{} [Fe_4S_4(SPh)_4]^{2-} \quad (16)$$

successive mononuclear and binuclear intermediates. Owing to the stoichiometry of reaction 4 the latter two species were not detected as intermediates in that system. Certain parts of, or related to, the sequence (16), which is schematically depicted in Figure 1, have been seen earlier but the individual steps have not been resolved in any other system. The dimer → tetramer con-

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[37] Acetonitrile was required to provide adequate solubility of the complex; comparison of Figures 10 and 11 indicates that it retards the rate of dimer → tetramer conversion.

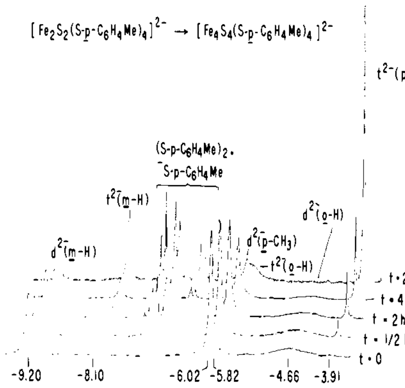

Figure 11. ^{1}H NMR spectra (100 MHz) demonstrating the conversion $[Fe_2S_2(S\text{-}p\text{-tol})_4]^{2-}$ (d^{2-}) → $[Fe_4S_4(S\text{-}p\text{-tol})_4]^{2-}$ (t^{2-}) at ~27 °C. The reaction system at zero time consisted of 1 mL of 5 mM d^{2-} in CD_3CN + 0.5 mL of CD_3OD. Signal assignments are indicated.

version (13) was observed in aqueous HMPA.[30] The only monomer → dimer conversion found previously is reaction 17[30] which,

$$2[Fe(S_2\text{-}o\text{-xyl})_2]^{1-} + 2HS^- + 2OMe^- \rightarrow [Fe_2S_2(S_2\text{-}o\text{-xyl})_2]^{2-} + 2(S_2\text{-}o\text{-xyl})^{2-} + 2MeOH \quad (17)$$

in terms of initial oxidation states, is an inverse version of reaction 12. Presumably because of its chelate structure,[22] the product dimer does not convert to a tetramer in protic solvents and forms a stable trianion upon reduction.[38] In contrast, reaction 14 proceeds rapidly upon reduction of $[Fe_2S_2(SPh)_4]^{2-}$.[30] Christou et al.[39] have observed a monomer → tetramer conversion in a system containing the reactant mole ratio Cys$_4$-peptide ($\equiv 4RS^-$)/$FeCl_3/S^{2-}$ = 1.5/1.2/2.0 in Me_2SO. In the absence of sulfide reaction 18 occurs, followed by decay of the product to a species whose spectrum is more consistent with $[Fe(SR)_4]^{2-}$,[40] as in reaction 19, than with the proposed $[Fe_2(SR)_6]^{2-}$.[39] Addition

$$FeCl_3 + 4RS^- \rightarrow [Fe(SR)_4]^{1-} + 3Cl^- \quad (18)$$

$$[Fe(SR)_4]^{1-} + RS^- \rightarrow [Fe(SR)_4]^{2-} + {}^1/_2RSSR \quad (19)$$

$$4[Fe(SR)_4]^{2-} + 4S^{2-} + RSSR \rightarrow [Fe_4S_4(SR)_4]^{2-} + 14RS^- \quad (20)$$

of sulfide at this point afforded essentially quantitative generation of the $[Fe_4S_4(SR)_4]^{2-}$ chromophore in a process represented here as reaction 20. Intermediate species were not detected. The reaction sum (18) + (19) = (10), suggesting on this basis and from the reversible oxidation of $[Fe(SPh)_4]^{2-}$ in acetonitrile ($E_{1/2}$(1-/2-) = −0.53 V) that $[Fe(SPh)_4]^{1-}$ is the first species formed in reaction 10. Evidently $[Fe(SPh)_4]^{1-}$ lacks the stability, likely imparted by chelation, of the oxidized peptide complex and $[Fe(S_2\text{-}o\text{-xyl})_2]^{1-}$. Indeed, the 1-/2- potential of the latter (−1.02 V[40]) shows the higher relative stability of the Fe(III) state. Lastly, the occurrence of $[Fe_2S_2(SPh)_4]^{2-}$ in reaction sequence (16) has led to a preparation more convenient than the original reaction 6.[22] Introduction of an appropriate R'_4N^+ cation at the outset of reaction 7 (=2 × (10) + (12) (n = 2)) results in trapping of the binuclear complex as a sparingly soluble $(R'_4N)_2[Fe_2S_2(SPh)_4]$ salt.[23]

Reaction System: $PhS^-/Fe(III)/S^{2-}$ = 1.5/1/1. This stoichiometry of reactants corresponds to that of reaction 1, the original preparative method for $[Fe_4S_4(SR)_4]^{2-}$ clusters.[2,3] Although in practice a 3/1/1 mol ratio has been usually employed, the net stoichiometry of the originally suggested reaction scheme,[3,41] is that of reaction 1. Consequently, the course of this reaction was examined in methanol. Addition of $FeCl_3$ solution to a solution of NaSPh, NaHS, and NaOMe resulted in a very rapid reaction which was complete within ~15 min. The final spectrum (λ_{max} = 435 nm, not shown) is unambiguously that of $[Fe_4S_4(SPh)_4]^{2-}$. Triplicate runs gave yields of 80.1–83.9% (mean 81.8%), obtained from absorbances measured after separation of a small quantity of insoluble black solid. This material, which is presumably an iron sulfide, was minimized by the specified order of addition of reactants. The spectrophotometric yields are consistent with those usually obtained on a preparative scale. While the reaction sum 4 × (18) + 4 × (19) + (20) = (1), the sequence of events, albeit incompletely defined, in the peptide reaction system[39] cannot apply to reaction 1 owing to different reactant mole ratios. The latter reaction proceeded too rapidly to allow detection of intermediates by conventional spectrophotometry.

Summary

The course of self-assembly reactions affording $[Fe_4S_4(SR)_4]^{2-}$ clusters from simple reactants is dependent on the mole ratio of those reactants. For the system $PhS^-/Fe(III)/S$ = 3.5/1/1 the assembly reaction consists of the steps

$$\text{reaction } 4 = (8) + (11) \ (n = 4)$$

Similarly, the system $PhS^-/Fe(II)/S$ = 2.5/1/1 is now recognized to proceed in the steps

$$\text{reaction } 5 = (9) + (11) \ (n = 4)$$

The only identifiable intermediate, $[Fe_4(SPh)_{10}]^{2-}$, has been independently synthesized. Reaction 11 in acetonitrile and the overall reaction in methanol are quantitative. For the system $PhS^-/Fe(III)/S \geq 5/1/1$ the assembly reaction has been resolved into the sequence

$$\text{reaction } 4 = 4 \times (10) + 2 \times (12) \ (n = 2) + (13)$$

thereby demonstrating elaboration of tetranuclear clusters from mononuclear and binuclear intermediates, which have been independently synthesized. Reaction 12 in acetonitrile results in less than quantitative yield (84%), but the overall reaction (4) in methanol is quantitative. The original system for cluster synthesis, when conducted according to the stoichiometry of reaction 1, results in yields of 82%. No intermediates were detected in this reaction.

While this investigation has provided the first information as to the sequence of events resulting in $[Fe_4S_4(SR)_4]^{2-}$ cluster assembly, certain limitations are noted. Emphasis has been placed on the examination of reaction systems at equilibrium. Identifiable intermediates[42] and products are those which could be separately synthesized. Other, shorter lived species such as those which must intervene in, e.g., reaction 8 (itself a cluster assembly problem) and reaction 11, were not detected. In systems containing elemental sulfur (described above as heterogeneous) it is unclear whether sulfur itself and/or a soluble species such as $PhSS^-$ is the actual reactant. The reaction schemes given above and summarized in Figure 1 remain to be demonstrated as general for a variety of thiolates RS^-. (However, the observation that soluble species are produced when $FeCl_2$ is reacted with $\gtrsim$2.5 equiv of EtS^-, $PhCH_2S^-$, and $t\text{-}BuS^-$ in methanol, together with the isolation of $(Et_4N)_2[Fe_4(SCH_2Ph)_{10}]$ by reaction 9, suggests that the schemes apply in at least these additional cases.) Kinetic studies of individual reactions are lacking, as are studies of possible equilibria between reactant species, such as $[Fe_4(SPh)_{10}]^{2-} + 6PhS^- \rightleftharpoons 4[Fe(SPh)_4]^{2-}$. Nonetheless, establishment of reaction stoichiometries and identification of products in all reactions and of at least some intermediates in coupled reactions are prerequisite

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[39] G. Christou, B. Ridge, and H. N. Rydon, *J. Chem. Soc., Chem. Commun.*, 908 (1977). The peptide used was Ac-Gly$_2$-Cys(Gly$_2$-Cys)$_3$Gly$_2$-NH$_2$.

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[41] The use of a 3/1/1 mol ratio usually leads to precipitation of an iron thiolate polymer (prior to reaction with sulfide), rendering such systems unsuitable for observation at all stages of the cluster formation reaction.

[42] A definite example of a detected but unidentified intermediate is found in reaction 11 (R = p-tol) in CD_3OD. Resonances at −100, −62, and 60 ppm emerge immediately after addition of sulfur and gradually diminish as the reaction proceeds.

to further, more detailed investigations of cluster assembly.

The biosynthesis of $[Fe_4S_4(SR)_4]^{2-}$ clusters, as well as those of the $[Fe_2S_2(SR)_4]^{2-}$ type, remains an open question. The spontaneous occurrence of reactions such as (1) and (4)–(7) makes it obvious that no protein is required to guide the construction of a cluster from simple reactants. Iron is a ubiquitous component of cells, and sulfide has been demonstrated in bacterial, plant, and fungal cells.[19] The possible role of S(0) in protein cluster synthesis has been noted,[36] and 2-Fe ferredoxins have been reconstituted from apoproteins containing S(0) in the presence of a thiol reductant.[43] As noted at the outset cysteinyl peptides can be placed around Fe_4S_4 units by reaction 2. Consequently, one view that must be entertained is that in vivo Fe–S cluster synthesis may occur by reactions the same or similar to those examined here and that cluster insertion into a peptide environment may be a nonenzymatic process. Interception and stabilization of a particular type of unit (1Fe, 2Fe–2S, 4Fe–4S) would then be a function of the selectivity or specificity of the apoprotein. Examples of the instability of an iron site in an "unnatural" peptide[44] and the selectivity of several apoproteins for the "natural" Fe–S clusters,[45] as in the ligand substitution reaction (2) with nR′SH = apoprotein, are available.

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Actinide–Carbon Bonds: Insertion Reactions of Carbon Monoxide, *tert*-Butyl Isocyanide, and *tert*-Butyl Cyanide into $[(Me_3Si)_2N]_2MCH_2Si(Me)_2NSiMe_3$

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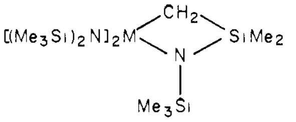
Abstract: The thorium or uranium metallacycles $[(Me_3Si)_2N]_2MCH_2Si(Me)_2NSiMe_3$ (I) react with *tert*-butyl cyanide to give the six-membered ring compounds $[(Me_3Si)_2N]_2MN{=}C(t\text{-}Bu)CH_2Si(Me)_2NSiMe_3$. The metallacycles (I) also react with the isoelectronic molecules *tert*-butyl isocyanide and carbon monoxide to give the unique five-membered ring compounds with exocyclic carbon–carbon double bonds, $[(Me_3Si)_2N]_2MXC({=}CH_2)Si(Me)_2NSiMe_3$, where X is t-BuN or oxygen. The four-membered ring metallacycles (I) give simple coordination complexes of the type $[(Me_3Si)_2N]_2MCH_2Si(Me)_2NSiMe_3(N_3SiMe_3)$ with trimethylsilyl azide.

The four-membered ring metallacycles of thorium or uranium (I) are formed by γ elimination of methane or hydrogen from



I, M = Th or U

$[(Me_3Si)_2N]_3MMe$ or $[(Me_3Si)_2N]_3MH$, respectively.[1] The polarity of the actinide–carbon bond and the ring strain inherent in the four-membered ring suggest that 1,2-dipolar organic molecules will insert into the metallacyclic ring. Insertion of the isoelectronic molecules carbon monoxide, *tert*-butyl isocyanide, and *tert*-butyl cyanide into the actinide–carbon bond has been realized, and the results are described herein.

tert-Butyl cyanide reacts with I (M = Th) to give a 1:1, monomeric, diamagnetic complex. The ν(CN) stretching frequency in the infrared spectrum (1617 cm^{-1}) shows that the complex is not a simple coordination complex but one in which the carbon–nitrogen bond order has been reduced from 3 in the uncomplexed alkylcyanide to 2 in the complex. The nuclear magnetic resonance spectra show that insertion has occurred into the thorium–carbon bond rather than into the thorium–nitrogen bonds. The ^{1}H and

Table I. ^{1}H Nuclear Magnetic Resonance Data[a]

compd	$(Me_3Si)_2N$	Me_3SiN	Me_2Si	CH_2	Me_3C
I, M = Th[d]	0.37	0.38	0.56	0.49	
II, M = Th	0.36	0.90	0.33	2.04	1.29
VI, M = Th	0.54	0.44	0.61	5.51 and 5.43[b] (J = 13 Hz)	1.56
IX, M = Th	0.48	0.41	0.63	5.49 and 4.15[b] (J = 13 Hz)	
X, M = Th	0.46	0.64[e] 0.45[e]	0.23	1.04	
I, M = U[d]	−23.3	−9.90	+2.08	−128.6	
II, M = U	−5.85	−19.9	+8.58	+33.6	−11.8
VI, M = U	−3.88	−10.8	+5.91	+8.71[c]	−14.1
IX, M = U	−6.69	−17.0	+2.74	−11.0[c]	
X, M = U	−3.59	−19.6[e] −27.9[e]	−11.8	72.9	

[a] In benzene-d_6 at 28 °C, chemical shifts are expressed in δ units (positive numbers are to high frequency) relative to Me_4Si. [b] A AB spin system, see text. [c] Broadened resonance ($\nu_{1/2}$ is ca. 10 Hz). [d] See ref 1. [e] These equal-area resonances are due to Me_3SiN of the metallacycle and coordinated Me_3SiN_3. Free Me_3SiN_3 resonates at δ 0.20.

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