For the SOF and SO_2F substituents the calculated inductive values σ_I are slightly less than the literature values, but the resonance parameters $\sigma_{R°}$ agree exceptionally well. These results are comparable to the reported result for SO_2Cl. The parameters calculated for the SF_3 group at 25° show moderate agreement with the literature values, but in this case the σ_I value is high and the $\sigma_{R°}$ value is low. At −66°, the two shifts for the meta fluorine were calculated separately. Now the agreement between σ_I and $\sigma_{R°}$ is good from the higher field shift but very poor from the lower field value. A reasonable interpretation is that the lower field shift is for the meta fluorine on the side of the ring remote from the basal fluorine and that *m*-fluorophenylsulfur trifluoride is populated primarily with the configuration where the phenyl ring is oriented so that the meta fluorine is also remote from the basal fluorine. Low-temperature studies on *m*-fluorophenylsulfur trifluoride gave no indication of freezing out of the two ring conformation, but this result could also be interpreted on the basis that only one conformation predominates.

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Synthetic Analogs of the Active Sites of Iron–Sulfur Proteins. X.[1] Kinetics and Mechanism of the Ligand Substitution Reactions of Arylthiols with the Tetranuclear Clusters $[Fe_4S_4(SR)_4]^{2-}$

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Abstract: Previous work in this series has demonstrated that alkylthiolate tetramer dianions $[Fe_4S_4(SR)_4]^{2-}$ undergo facile ligand substitution reactions with added thiols R′SH. The rates and mechanism of initial thiolate substitution in reactions of R = Et and *t*-Bu tetramers with arylthiols in acetonitrile solution at 25° have been investigated by stopped-flow spectrophotometry. For the process $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-} + R'SH \rightarrow [Fe_4S_4(S\text{-}t\text{-}Bu)_3(SR')]^{2-} + t\text{-}BuSH$, reaction rates are second order, first order in tetramer and in thiol, and the following resolved second-order rate constants (R′, M^{-1} sec^{-1}) were determined: *p*-$C_6H_4NH_2$, 2.1 ± 0.2; *p*-tolyl, 4.5 ± 0.6; *o*-$C_6H_4NO_2$, 110 ± 8; *p*-$C_6H_4NO_2$, 3600 ± 200. Reaction rates parallel thiol acidities (in aqueous alcohol solutions), and it is proposed that the rate-limiting step is protonation of coordinated alkylthiolate followed by rapid separation of alkylthiol and coordination of arylthiolate. Rate constants for the reactions of the R = *t*-Bu and Et tetramers with *p*-$H_2NC_6H_4SH$ are within experimental error, indicating an absence of tetramer steric effects on reaction rates. Addition of benzoic or acetic acid to the system $[Fe_4S_4(SR)_4]^{2-}$–*p*-$H_2NC_6H_4SH$ produces significant increases in reaction rates but only the rate constant for the benzoic acid assisted process (250 ± 14 M^{-1} sec^{-1}, R = *t*-Bu) fits the rate-acidity correlation evident in systems containing tetramer and thiol. The relatively rapid rates and apparent mechanistic simplicity of the ligand substitution reactions, together with the previously observed lack of degradation of the Fe_4S_4 core over the course of full thiolate substitution, further emphasize the synthetic utility of these reactions based on alkylthiolate tetramers.

Recent investigations of the reactivity properties of the alkylthiolate tetramer dianions $[Fe_4S_4(SR)_4]^{2-}$, which are structurally[3-5] and electronically[3,5-8] related to the $[Fe_4S_4(S\text{-}Cys)_4]$ active centers in oxidized ferredoxin and reduced high-potential iron-sulfur proteins,[9] have shown that they undergo facile ligand substitution reactions with added thiols R′SH at ambient temperature in nonaqueous or partially aqueous media.[1,5,8,10] These reactions involve substitution of one or more thiolate ligands external to the Fe_4S_4 core which, from X-ray diffraction[3-5] and a variety of spectroscopic measurements,[11] is electronically fully delocalized and contains four equivalent metal sites. The typical complexes $[Fe_4S_4(SCH_2Ph)_4]^{2-}$ [3,4] and $[Fe_4S_4(SPh)_4]^{2-}$ [5] have the cubane-type stereochemistry with effective D_{2d} symmetry and approximately tetrahedral coordination at iron.

Spectrophotometric and pmr studies of equilibrium solutions have shown that the substitution reactions of

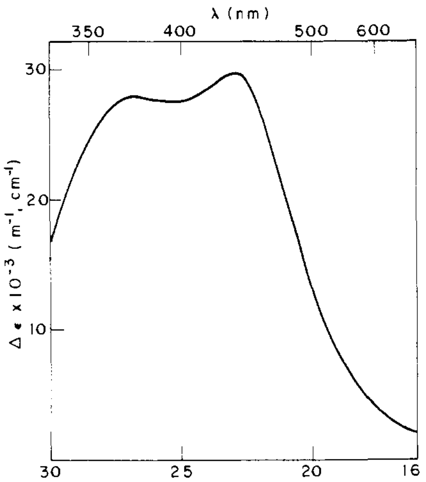

Figure 1. Electronic difference spectrum of $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ and $[Fe_4S_4(SC_6H_4\text{-}p\text{-}NO_2]^{2-}$ in DMF solution at 25°.

Table I. Protonation Constants of Thiols Used in This Study

Thiol acid	Log K_H (RSH)	Solvent
p-$O_2NC_6H_4SH$[a]	4.95	40% ethanol
o-$O_2NC_6H_4SH$[a]	5.99	48.9% ethanol
p-$CH_3C_6H_4SH$[a]	7.55	40% ethanol
p-$H_2NC_6H_4SH$[a]	7.95	40% ethanol
C_6H_5COOH[b]	5.98[c]	60% methanol

[a] J. P. Danehy and K. N. Parameswaran, *J. Chem. Eng. Data*, **13**, 386 (1968). [b] J. Chatt and A. A. Williams, *J. Chem. Soc.*, 4403 (1954). [c] Log K_H (RCOOH).

$[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ with arylthiols proceed stepwise (eq 1) and that only *ca.* 4.5-5 equiv of thiol are required to effect complete substitution (n = 4) of the initial tetramer.[5,8,10]

$$[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-} + nR'SH \rightleftharpoons [Fe_4S_4(S\text{-}t\text{-}Bu)_{4-n}(SR')_n]^{2-} + nt\text{-}BuSH \quad (1)$$

The substitution tendencies of aliphatic thiols are substantially less and, overall, the effectiveness of added thiols in ligand substitution was found to parallel roughly their aqueous acidities down to pK_a values of *ca.* 6.5.[5] Little discrimination could be detected among thiols of this or greater acidity. The positions of the ligand substitution equilibria were concluded to be dominated by the acid-base characteristics of *tert*-butylthiolate and R'SH.[5]

Most recently it has been demonstrated that reactions of $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ with acetyl-L-cysteine-N-methylamide and glycyl-L-cysteinylglycyl oligopeptides afford the corresponding Fe_4S_4-peptide dianions.[1] Their redox and spectral properties more closely resemble those of ferredoxin and high-potential proteins, especially when the latter is denatured in aqueous DMSO solution. Further, the peptide complexes can be converted to $[Fe_4S_4(SPh)_4]^{2-}$ upon treatment with excess benzenethiol. Similar ligand substitution reactions extend to the 2-Fe active site analog $[FeS(SCH_2)_2C_6H_4]_2^{2-}$,[12] affording $[Fe_2S_2(SPh)_4]^{2-}$ or other arylthiolate dimers.[13] As suggested earlier,[1,5,10] ligand exchange reactions with arylthiols offer a potential means of extruding Fe_2S_2 and Fe_4S_4 active site clusters from proteins and then identifying them in the form of their arylthiolate complexes. Such reactions have very recently been accomplished with a number of Fe-S proteins under denaturing conditions.[14] Consequently, the kinetics and mechanism of the ligand substitution process are matters of significance. Preceding observations have shown that ligand substitution is slow on the pmr time scale. In this work stopped-flow kinetic studies of the ligand substitution reactions of $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ and $[Fe_4S_4(SEt)_4]^{2-}$ with arylthiols in acetonitrile solution have been carried out in order to provide kinetic and mechanistic information.

Table II. Independence of $k_{initial}$ on $[Fe_4S_4(SR)_4]^{2-}$ for the reaction of $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ with p-$CH_3C_6H_4SH$ under pseudo-first-order conditions in acetonitrile solution ($[p\text{-}CH_3C_6H_4SH]$ = 1.61 (±0.01) × 10^{-2} *M*; 25°)[a]

$10^4[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$, *M*	$10^2k_{initial}$, sec^{-1}
1.29	7.0 ± 0.5
1.64	6.5 ± 0.3
2.06	9.3 ± 0.2
2.38	7.8 ± 0.7
2.57	9.5 ± 0.7

[a] Due to the large total change in absorbance, the high absorbancy of the $[Fe_4S_4(SR)_4]^{2-}$ tetramers, and the small change in absorbance which was utilized for the initial rate determinations, it was not experimentally feasible to vary the $[Fe_4S_4(SR)_4]^{2-}$ concentration as much as would normally be desirable.

Experimental Section

Preparation of Compounds. $(Ph_4As)_2[Fe_4S_4(S\text{-}t\text{-}Bu)_4]$ and $(n\text{-}Pr_4N)_2[Fe_4S_4(SEt)_4]$, employed as initial tetramers in the ligand substitution reactions with arylthiols, were prepared by the direct tetramer synthesis.[4] p-Nitrobenzenethiol[15] and o-nitrobenzenethiol[16] were prepared as described elsewhere. Other thiols were the best commercial grades available. Acetonitrile (Eastman Kodak Co., <0.1% H_2O), freshly distilled from calcium hydride and degassed prior to use, was the solvent employed in all kinetic runs. Protonation constants of thiols and acids employed in substitution reactions are collected in Table I.

Kinetic Measurements. Ligand substitution reactions were followed spectrophotometrically using a Durrum Instrument Corporation stopped-flow spectrophotometer with a 2.0-mm path length and operated at 25.0 ± 0.1°. A wavelength of 500 nm was chosen at which to monitor the reactions in order to allow the use of reasonable concentrations of $[Fe_4S_4(SR)_4]^{2-}$ (R = t-Bu, Et, 1-3 × 10^{-4} *M*) and still retain a large absorbance change. An example of a difference spectrum between an arylthiolate ($[Fe_4S_4(SC_6H_4NO_2)_4]^{2-}$) and an alkylthiolate tetramer ($[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$) is provided in Figure 1. Other examples of pronounced spectral changes in the 350-650-nm region upon adding 1 or more equiv of arylthiol to solutions of $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ have been given previously.[5,10] All manipulations were carried out under a nitrogen atmosphere and all solutions were freshly prepared for each series of kinetic measurements. During the course of the kinetic runs, nitrogen was introduced behind both drive syringes and the stop syringe to prevent oxidation of the tetramers. Kinetic data were obtained from treatment of oscilloscope traces. Due to the complexity of rate plots obtained for substitution of all four alkylthiolate ligands, initial rates for the first substitution only were determined in all cases. All reactions were conducted under pseudo-first-order conditions, and each constant is the average of at least three kinetic runs. Standard deviations of rate constants were calculated from the deviations of individual rate constants from the mean.

Results

The kinetics of the first ligand substitution of alkylthiolate tetramers by arylthiols in acetonitrile solution have been investigated by stopped-flow spectrophotometry. Inasmuch as $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ was used as the starting tetramer in previous studies of ligand substitution equilibria with arylthiols (eq 1), it was employed in the majority of the kinetic experiments. The initial reaction rates are second order, first order in tetramer (see Table II) and first order in thiol concentration. Concentrations of reactants and initial rate constants are given in Table III. In no case was an absorbance jump in the initial phase of a reaction observed. The resolved second-order rate constants were obtained by plotting the initial rate constants *vs.* thiol concentration and

Table III. Dependence of k_{initial} on Thiol Concentration for Ligand Substitution Reactions of $[Fe_4S_4(SR)_4]^{2-}$ in Acetonitrile Solution

$10^4[Fe_4S_4(SR)_4]$, M	$10^3[R'SH]$, M	10^2k_{initial}, sec^{-1} [a]
A. R = *t*-Bu, R′SH = *p*-$H_2NC_6H_4SH$		
1.45	9.28	2.13 ± 0.05
1.54	10.7	3.2 ± 0.2
1.45	13.9	2.54 ± 0.24
1.54	14.2	3.0 ± 0.04
1.87	17.4	6.0 ± 00.
1.54	18.3	4.7 ± 0.6
1.45	18.6	4.3 ± .2
1.87	21.8	6.2 ± 0.3
1.54	21.9	5.6 ± 0.3
1.45	23.2	7.04 ± 0.07
1.54	25.4	6.6 ± 0.3
1.87	25.7	5.2 ± 0.4
1.54	29.0	7.4 ± 0.3
1.87	30.0	6.6 ± 0.2
1.54	32.5	6.75 ± 0.01
1.87	34.4	7.3 ± 0.2
1.87	38.7	9.4 ± 0.2
B. R = *t*-Bu, R′SH = *p*-$CH_3C_6H_4SH$		
2.40	2.13	2.2 ± 0.2
2.57	3.20	1.63 ± 0.03
1.64	3.23	1.68 ± 0.09
2.40	5.32	3.2 ± 0.2
1.64	6.45	2.4 ± 0.2
1.29	6.45	2.30 ± 0.08
2.04	6.45	2.6 ± 0.2
1.64	10.2	3.5 ± 0.3
2.06	10.2	2.90 ± 0.04
2.40	10.6	4.8 ± 0.3
2.38	16.0	7.8 ± 0.7
2.06	16.1	9.3 ± 0.2
1.64	16.1	6.5 ± 0.3
1.29	16.1	7.0 ± 0.5
2.57	16.0	9.5 ± 0.7
C. R = *t*-Bu, R′SH = *o*-$O_2NC_6H_4SH$		
1.49	1.60	12.8 ± 0.9
1.46	2.01	14.6 ± 0.3
1.49	2.39	17.7 ± 0.1
1.49	3.19	25.1 ± 0.8
1.49	3.99	30 ± 2
1.46	4.02	26.3 ± 0.5
1.49	4.79	59 ± 5
1.46	5.03	46.6 ± 0.6
1.49	5.59	67 ± 3
1.49	6.38	71 ± 5
1.46	7.04	83 ± 2
1.49	7.18	75 ± 8
1.46	8.05	76 ± 7
1.46	9.05	92 ± 3
1.46	10.1	96 ± 2
D. R = *t*-Bu, R′SH = *p*-$O_2NC_6H_4SH$		
1.56	2.43	7.3 ± 0.5
1.60	2.43	6.9 ± 0.3
1.61	2.43	9.6 ± 0.3
1.79	2.43	7.0 ± 0.2
1.56	4.86	19.1 ± 0.1
1.60	4.86	17 ± 2
1.61	4.86	16.9 ± 0.9
1.79	4.86	15.4 ± 0.4
1.60	8.50	24.9 ± 0.5
1.61	8.50	33 ± 2
1.79	8.50	29.2 ± 0.9
1.56	12.2	44.6 ± 0.3
1.60	12.2	42 ± 2
1.61	12.2	46.7 ± 0.3
E. R = Et, R′SH = *p*-$H_2NC_6H_4SH$		
2.12	7.96	2.01 ± 0.08
2.24	8.84	3.4 ± 0.1
2.12	11.9	3.1 ± 0.2
2.24	13.3	4.5 ± 0.2
2.12	15.9	3.9 ± 0.2
2.24	22.1	6.24 ± 0.07
2.12	23.9	6.1 ± 0.1
2.12	27.9	6.6 ± 0.2
2.12	31.8	7.3 ± 0.1
2.12	35.8	8.2 ± 0.2

[a] Due to the fact that only the first few per cent of the absorbance change is utilized and the limited number of runs per data point (three), the number of significant figures varies in a somewhat random fashion and should not be taken to indicate a statistically more or less precise point.

Table IV. Resolved Second-Order Rate Constants for the Reactions of Arylthiols with $[Fe_4S_4(SR)_4]^{2-}$ in Acetonitrile Solution

R	R′SH	k_1, M^{-1} sec^{-1}
t-Bu	*p*-$H_2NC_6H_4SH$	2.1 ± 0.2
Et	*p*-$H_2NC_6H_4SH$	2.4 ± 0.2
t-Bu	*p*-$CH_3C_6H_4SH$	4.5 ± 0.6
t-Bu	*o*-$O_2NC_6H_4SH$	110 ± 8
t-Bu	*p*-$O_2NC_6H_4SH$	3600 ± 200

are listed in Table IV. As a typical example, the resolution of the second-order rate constant for the $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$–*o*-$O_2NC_6H_4SH$ reaction is shown in Figure 2. A plot of log K_H for the various thiols *vs.* the log of their respective resolved second-order rate constants is set out in Figure 3, in which a definite correlation between the acidity of the incoming thiol and its substitution rate is evident. The protonation constants in Table I were selected from the available data in order to provide an internal comparison in solvent media as nearly similar as possible. While available data do not allow direct comparison, the relative magnitudes of protonation constants in acetonitrile appear to parallel those determined in methanol–water solution. This correlation is interpreted to indicate that the rate-determining step in the initial phase of the reaction is protonation of bound thiolate by attacking thiol.

In order to investigate the generality of the acidity–reaction rate behavior, the reactions of both $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ and $[Fe_4S_4(SEt)_4]^{2-}$ with *p*-aminobenzenethiol were rerun in the presence of benzoic acid (Table V). The resolved rate constants, 250 ± 14 and 230 ± 17 M^{-1} sec^{-1}, respectively, when compared to the data in Table IV, demonstrate a significant (*ca.* 100-fold) acceleration of the reaction rate. From Figure 3 and Table I it is apparent that benzoic acid also fits the correlation of acidity with reaction rate.[17] In addition, as shown in Table VI, the rate of substitution becomes independent of thiol concentration in the presence of excess benzoic acid. When $[Fe_4S_4(SEt)_4]^{2-}$ was treated with excess benzoic acid in the *absence* of thiol, the principal visible absorption band at 420 nm[8] was completely removed. (Loss of the visible band has been observed under other conditions when tetramer solutions were acidified or otherwise caused to decompose.) Kinetic runs under these conditions revealed a *decrease* in absorbance at 500 nm (in contrast to an increase in the presence of thiol) at a rate roughly comparable to that of the substitution reactions. These results indicate that, at least within the interval of kinetic measurements (~1 min), the reactivity of benzoic acid is quite different in the presence and absence of thiol.

A series of experiments designed to promote intramolecular proton transfer and consequent rate acceleration was also attempted utilizing $[Fe_4S_4(SEt)_4]^{2-}$ and thiosalicylic acid in acetonitrile solution. Kinetic runs revealed only a

Table V. Dependence of k_{initial} on Benzoic Acid Concentration for Reaction of $[Fe_4S_4(SR)_4]^{2-}$ with *p*-Aminobenzenethiol[a] in Acetonitrile Solution

$10^4[Fe_4S_4(SR)_4]$, *M*	10^4[PhCOOH], *M*	$10^2 k_{\text{initial}}$, sec^{-1} [b]
	A. R = *t*-Bu	
1.76	1.62	5.1 ± 0.2
2.01	2.10	5.6 ± 0.6
1.76	3.25	8.8 ± 0.2
2.01	4.20	9.0 ± 0.2
1.76	4.87	13.5 ± 0.1
2.01	6.30	13.6 ± 0.5
1.76	6.50	18.6 ± 0.3
2.01	8.40	17.7 ± 0.5
1.76	9.74	23.9 ± 0.8
1.76	11.4	27 ± 1
2.01	12.6	30 ± 1
1.76	13.0	31.7 ± 0.5
1.76	14.6	40.6 ± 0.9
	B. R = Et	
2.14	1.61	11.2 ± 0.03
2.27	1.84	12.4 ± 0.5
2.44	2.12	16 ± 2
2.14	3.23	15.0 ± 0.6
2.27	3.69	15.6 ± 0.4
2.44	4.24	20.6 ± 0.4
2.14	4.84	19.9 ± 0.2
2.27	5.53	20.2 ± 0.3
2.44	6.36	27 ± 1
2.14	6.46	23 ± 1
2.27	7.38	24.7 ± 0.3
2.44	8.48	32 ± 2
2.14	9.68	27 ± 2
2.27	11.1	38 ± 2
2.14	11.3	31.2 ± 0.3
2.27	12.9	40.8 ± 0.7
2.14	12.9	34 ± 1
2.14	14.5	36 ± 1
2.27	14.8	48 ± 2
2.27	16.6	48.8 ± 0.8

[a] Concentration = (8.46 ± 0.01) × 10^{-3} *M*. [b] See Table III, footnote *a*.

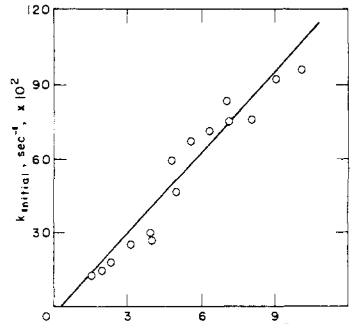

Figure 2. Resolution of the second-order rate constant for the reaction of *o*-nitrobenzenethiol with $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ in acetonitrile solution. The points are experimental, and the solid line is a linear least-squares fit to the data; $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]$ = 1.46–1.49 × 10^{-4} *M*.

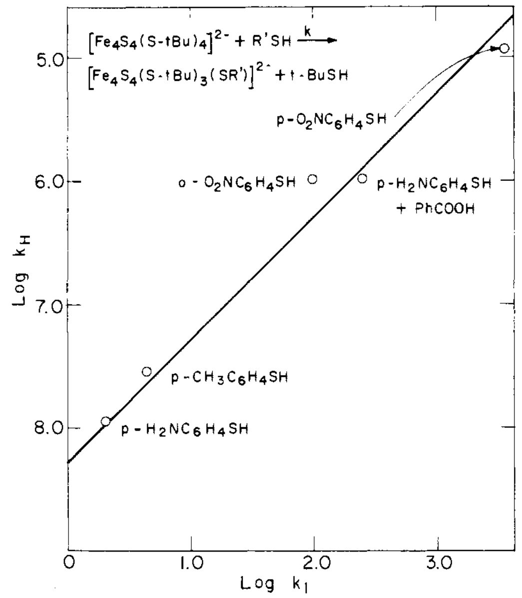

Figure 3. Dependence of resolved second-order rate constants on K_H (R′SH) for the ligand exchange reaction between thiols and $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ in acetonitrile solution. The solid line is constrained to a slope of unity.

very small change in absorbance at 500 nm. Subsequently, the spectrum of a solution of the tetramer with a tenfold excess of thiosalicylic acid revealed a shift of the principal visible absorption band from 420 to 360 nm while essentially preserving the ultraviolet absorption band at 290 nm. (No further kinetic experiments were conducted.) The effect of small amounts of water on the substitution rates in acetonitrile solution was investigated and found to be slight. For example, in a 20% water-acetonitrile solution the resolved second-order rate constant for the reaction of $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ with *p*-tolylthiol is *ca.* 12 M^{-1} sec^{-1}, less than a factor of 3 larger than the rate constant determined in pure acetonitrile solution (Table IV).

Discussion

In contrast to the ligand substitution reactions of planar complexes, the corresponding reactions of tetrahedral M(II, III) complexes have been much less extensively examined.[19,20] The processes investigated in this work involve the displacement of alkylthiolate ligands at tetrahedral iron sites by arylthiols. The only previous detailed study of reactions of this type with tetrahedral Fe(II, III) complexes is the pmr investigation of the phosphine exchange kinetics of several dihalobis(triarylphosphine)iron(II) species.[21]

$$[Fe_4S_4(SR)_4]^{2-} + R'SH \longrightarrow [Fe_4S_4(SR)_3(SR')]^{2-} + RSH \quad (2)$$

The absence of an absorbance jump in the kinetic runs tends to indicate that the process under observation is substitution of the first thiolate ligand, as indicated in eq 2 (R = *t*-Bu, Et), and that there are no rapid preequilibria taking place to form reactive intermediates such as, *e.g.*, $[Fe_4S_4(SR)_4(R'SH)]^{2-}$. It is apparent from the correlation of rate constants for thiolate substitution with the acidities of incoming thiols (Figure 3), and from the rate acceleration of the *p*-aminobenzenethiol reaction by benzoic acid (Table V), that the rate-determining step in the initial phases of these reactions involves protonation of bound thiolate. The lack of evidence for five-coordinate intermediates contrasts with the phosphine exchange of $[Fe(Ar_3P)_2X_2]$ where the results are consistent with an associative mechanism.[21] In addition, the observed rate acceleration by benzoic acid would require a concerted three-center reaction if a five-coordinate intermediate were involved, a process which is regarded as somewhat unlikely. It is concluded that an associative pathway does not apply either prior to or during the rate-determining step.

The proposed mechanism for initial thiolate substitution is described by eq 3 and 4 and is shown schematically in Figure 4. The slow protonation step is followed by fast separation of the alkylthiol from, and rapid capture of the generated arylthiolate anion by, the metal center. By assuming a steady-state concentration of $[Fe_4S_4(SR)_3(RSH)]^-$, the rate equation (5) may be derived. With the further assump-

Table VI. Independence of k_{initial} on Thiol Concentration in the Presence of Benzoic Acid ($[Fe_4S_4(SEt)_4] = 2.44 \times 10^{-4}$ *M*, $[PhCOOH] = 1.06 \times 10^{-3}$ *M*)

$10^3[p\text{-}H_2NC_6H_4SH]$, *M*	k_{initial}, sec^{-1}
1.69	41 ± 2
3.38	38.1 ± 0.6
5.07	40 ± 2
6.76	42 ± 2

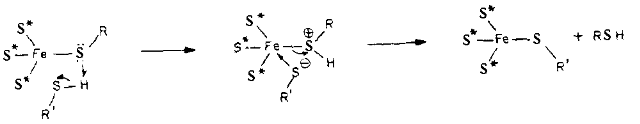

Figure 4. Proposed mechanism for the ligand exchange reaction between thiols and $[Fe_4S_4(SR)_4]^{2-}$ in acetonitrile solution. S* represents a sulfide sulfur in the Fe_4S_4 core.

$$[Fe_4S_4(SR)_4]^{2-} + R'SH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [Fe_4S_4(SR)_3(RSH)]^- + R'S^- \qquad (3)$$

$$[Fe_4S_4(SR)_3(RSH)]^- + R'S^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} [Fe_4S_4(SR)_3(SR')]^{2-} + RSH \qquad (4)$$

$$k_{\text{initial}} = k_1[R'SH]\left(1 - \frac{k_{-1}}{k_{-1} + k_2}\right) - \left(\frac{k_{-1}k_{-2}}{k_{-1} + k_2}\right)\frac{[Fe_4S_4(SR)_3(SR')][RSH]}{[Fe_4S_4(SR)_4]} \qquad (5)$$

tion that $k_2 \gg k_{-1}$ and because $[RSH] \equiv [Fe_4S_4(SR)_3(SR')]$, eq 6 is obtained in which $K_2 = k_2/k_{-2}$. Thus, if $k_1 > k_{-1}/K_2$, the proposed scheme satisfies the observed kinetic behavior. The rate limiting proton

$$k_{\text{initial}} = k_1[R'SH] - \frac{k_{-1}}{K_2}\frac{[Fe_4S_4(SR)_3(SR')]^2}{[Fe_4S_4(SR)_4]} \qquad (6)$$

transfer step (eq 3) could conceivably be affected by steric features of the metal site and the attacking thiol. As may be seen from the data in Table IV, the rates of reaction of $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ and $[Fe_4S_4(SEt)_4]^{2-}$ with *p*-aminobenzenethiol are within experimental error of each other, indicating that ethyl and *tert*-butyl groups near the metal center offer no steric discrimination to an unhindered arylthiol. That the reaction rates of *o*- and *p*-nitrobenzenethiol with $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ appear to fit the rate-acidity correlation (Figure 3) suggests a similar lack of significant steric effect due to incoming thiol. Rate determinations of reactions of benzenethiols having larger ortho substituents with little influence on acidity have not been carried out.

An alternate mechanism (suggested by one of the referees) which may be postulated is shown in eq 7-9. However,

$$[Fe_4S_4(SR)_4]^{2-} + H^+ \overset{K_H}{\rightleftharpoons} [Fe_4S_4(SR)_3(RSH)]^- \qquad (7)$$

$$[Fe_4S_4(SR)_3(RSH)]^- \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} [Fe_4S_4(SR)_3]^- + RSH \qquad (8)$$

$$[Fe_4S_4(SR)_3]^- + R'SH \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} [Fe_4S_4(SR)_3SR']^{2-} + H^+ \qquad (9)$$

this mechanism would appear to require that acetic acid accelerate the rate of the exchange reaction of *p*-aminobenzenethiol with $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ to a greater degree than benzoic acid since it is a stronger acid (at least in methanol-water solution). The rate of the acetic acid assisted reaction is, in fact, slower than the benzoic acid assisted reaction.[17] In addition, this mechanism implies that as the acidity of the exchanging thiol or assisting acid is increased, an absorbance jump should become evident which is contrary to the observation in this work.

The kinetic results, together with previous pmr and spectrophotometric studies,[5] reveal that both ligand substitution rates (eq 2) and equilibrium positions (eq 1), show a correlation with the acidities of the thiols R'SH. At parity of initial tetramer the rate of the first ligand substitution and the extent of fully substituted product formation increase with increasing acidity of R'SH. As mentioned at the outset, the methods thus far employed to assess the extent of equilibrium substitution are insufficiently sensitive to differentiate the effects of thiols with $pK_a < 6.5$. Hence the acidity-substitution correlation[5] was drawn mainly from the differences in substitution tendencies toward $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ displayed by aliphatic and the less acidic arylthiols *vs.* those of the somewhat more acidic arylthiols and thioacetic acid. Because of the close spectral similarity among aliphatic thiolate tetramers,[8] alkylthiols were not employed in the stopped-flow experiments and kinetic data were obtained for reactions involving arylthiols with an apparent span of 3.0 pK_a units. Consequently, the correlation of thiol acidities with rate and equilibrium properties is not as directly comparable at this stage as might be desired. However, the trends in both types of experiments are quite evident, suggesting that the proposed mechanism for initial substitution may be valid for successive substitution reactions albeit with different k_1 values. Rates for each subsequent thiolate substitution should decrease on statistical grounds and, intuitively, because attachment of the more electronegative arylthiolate ligands to the delocalized Fe_4S_4 core may decrease the basicity of the remaining alkylthiolate ligands. Although accurate rate constants could not be obtained, reaction rates were observed to decrease subsequent to the initial substitution process.

While no evidence was obtained for an associative ligand substitution pathway, several reactions have been observed in which it might occur. In methanol solution $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ is readily converted to $[Fe_4S_4(SPh)_4]^{2-}$ upon treatment with a small excess of sodium benzenethiolate. Equilibration of an acetonitrile solution of $[Fe_4S_4(S\text{-}t\text{-}Bu)_4]^{2-}$ and $[Fe_4S_4(S\text{-}p\text{-}tol)_4]^{2-}$ affords the various species $[Fe_4S_4(S\text{-}t\text{-}Bu)_{4-n}(S\text{-}p\text{-}tol)_n]^{2-}$ in roughly statistical amounts.[5] Coordinative unsaturation of the metal centers in $[Fe_4S_4(SEt)_4]^{3-}$ has been invoked in the first step of a recent abiological nitrogen fixation process wherein coordinated dinitrogen is bound to iron prior to or concomitant with electron transfer and subsequent conversion to ammonia.[22]

Lastly, the failure of acetic acid to follow the correlation of acidity with reaction rate[17] is puzzling and raises the possibility that the correlation for the benzoic acid assisted substitution process (Tables V and VI) may be fortuitous. If in this process coordinated thiolate is protonated by benzoic acid, as the acidity correlation implies, benzoate presumably assists the deprotonation of the incoming thiol. Possibly acetate is less effective in this respect. In any case the questions raised by this observation do not necessarily modify the central issue of the mechanism of thiolate substitution effected by thiols only. Protonation as a rate determining step is not usual but is invoked here in the scheme of Figure 4 as the simplest expression of the dependence of the reaction rates on thiol acidity consistent with available information. Added oxygen acids do enhance the reaction rates of alkylthiolate tetramer dianions with arylthiols, but in their absence partial or complete substitution can be achieved in a matter of minutes or less with no evident decomposition of the Fe_4S_4 core, further underscoring the synthetic utility[1,5] of the ligand substitution reactions based on alkylthiolate tetramers.

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Novel Octahedral Complexes of Nickel(II) with Thioether Derivatives of Cysteine Ethyl Ester

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Abstract: The green solid bis complex of cysteine ethyl ester and nickel(II), $Ni(Etc)_2$, has been prepared. Only the primary amine and thio groups appear to be coordinated. The complex is diamagnetic. Its spectrum in chloroform is interpreted to indicate weak thio bridging. The coordinated thio groups in this complex undergo alkylation with benzyl chloride, benzylthiomethyl chloride, and triphenylmethyl chloride. Octahedral nickel(II) complexes of the corresponding thioether derivatives of cysteine ethyl ester, $[NiL_2Cl_2]$, result. The infrared spectrum of the complex containing (*S*)-triphenylmethylcysteine ethyl ester, $[Ni(Ettpmc)_2Cl_2]$, indicates that one coordination position is occupied by the carbonyl oxygen of the ester group from one ligand. This result suggests that rearrangement has taken place, probably due to steric hindrance of triphenylmethyl groups initially in mutually cis positions.

There have been few studies of the solid bis nickel(II) complexes of cysteine methyl or ethyl esters.[2] The behavior of nickel(II) ion and cysteine methyl ester in aqueous solution has been interpreted to indicate coordination of the amine and thio groups.[3,4] There have been numerous reports of bis nickel(II) complexes with ligands containing only amine and thio groups.[5-10] These complexes generally exhibit diamagnetism, indicative of planar coordination.

Solid complexes of nickel(II) with thioether derivatives of cysteine ethyl ester contain three potential donor groups. Coordination of the ester group, if it occurs, is expected to be achieved through the carbonyl oxygen atom. When the carbonyl oxygen atom of a coordinated carboxylic acid group coordinates by bridging to an adjacent metal ion, its donor strength approximates that of a coordinated water molecule.[11] It is reasonable to assume that the carbonyl oxygen of an ester group has a similar, or smaller, donor strength. Hence, the relative donor strengths of the groups are expected to decrease in the order $-NH_2 > SR > -CO_2Et$.[12]

Octahedral nickel(II) complexes of thioether derivatives of cysteine ethyl ester were prepared by alkylation reactions between the appropriate organic chloride and bis(cysteine ethyl ester)nickel(II), $Ni(Etc)_2$. (Abbreviations for the names and formulas of all of the complexes examined in this study are given in Table I.) Similar alkylation reactions have been reported for bis(β-mercaptoethylamine)nickel(II), $Ni(MEA)_2$,[13,14] and other amine-thionickel(II) complexes.[15] There are several reports of the synthesis of similar octahedral nickel(II) complexes directly with the appropriate ligands.[16-19] In these cases, however, there was no ester group in the ligands.

Experimental Section

Preparation. The bis complexes $[Ni(SCH_2CH_2NH_2)_2]$[5] and $[Ni(SCH_2CH(NH_2)CO_2C_2H_5)_2]$ (see below) were made to react with several organic chlorides in an attempt to produce nickel complexes of the type $[NiL_2Cl_2]$. The organic chlorides were benzyl chloride ($PhCH_2Cl$), benzylthiomethyl chloride ($PhCH_2SCH_2Cl$),[20] triphenylmethyl chloride (Ph_3CCl), and diphenylmethyl chloride (Ph_2CHCl). With the exception of benzylthiomethyl chloride, the organic chlorides were used as reagent grade chemicals. Chloroform and DMF were used as solvents. Reagent inorganic salts were used without further purification.

$Ni(SCH_2CH(NH_2)CO_2C_2H_5)_2$. This complex was prepared by a