Contribution from the Department of Chemistry,
Stanford University, Stanford, California 94305

Improved Syntheses of the Dimeric Complexes $[Fe_2X_2(SC_6H_4Y)_4]^{2-}$ and $[Fe_2X_2((SCH_2)_2C_6H_4)_2]^{2-}$ (X = S, Se), Analogues of the 2-Fe Sites of Oxidized Ferredoxin Proteins

JOHN G. REYNOLDS and R. H. HOLM*

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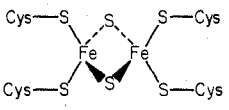
Improved syntheses of the complexes $[Fe_2X_2(S_2\text{-}o\text{-xyl})_2]^{2-}$ (**1**, **6**; $S_2\text{-}o\text{-xyl} = o\text{-}C_6H_4(CH_2S)_2^{2-}$) and $[Fe_2X_2(SC_6H_4Y)_4]^{2-}$ (**2**, **7**; Y = H, Me) with X = S, Se, analogues of the 2-Fe sites of oxidized ferredoxin proteins, have been developed by using simple reagents in methanol solution at ambient temperature. The reaction system $FeCl_3/X/Na_2(S_2\text{-}o\text{-xyl})$ (1:1:2) affords **1** and **6**, which are isolated as Et_4N^+ salts, and the system $FeCl_3/X/NaSC_6H_4Y/R'_4N^+$ (1:1:4:2) gives the R'_4N^+ salts (R' = Me, Et) of **2** and **7**. In the latter case the chalcogen and the quaternary ammonium cation are co-introduced to the reaction mixture containing the initially formed Fe thiolate species in order to precipitate the sparingly soluble salts $(R'_4N)_2[Fe_2X_2(SC_6H_4Y)_4]$. In the absence of R'_4N^+ the tetranuclear clusters $[Fe_4S_4(SC_6H_4Y)_4]^{2-}$ are the final reaction products. These syntheses result in 50–55% yield of purified products and are more expedient than earlier syntheses of Fe_2S_2 complexes in that they do not require prior preparation of Fe–S precursor compounds. The Se-containing complexes $[Fe_2Se_2(S_2\text{-}o\text{-xyl})_2]^{2-}$ (**6**) and $[Fe_2Se_2(SC_6H_4Y)_4]^{2-}$ (**7**) have been prepared for the first time and exhibit absorption and ^1H NMR spectra and redox potentials which do not differ markedly from those of **1** and **2**. Comparative properties of Fe_2X_2 complexes are tabulated, and limitations and other aspects of the synthetic procedures are discussed. These procedures, together with existing synthetic methods for tetranuclear clusters, provide ready synthetic access to a wide variety of the Fe–S protein site analogues $[Fe_nX_n(SR)_4]^{2-}$ (n = 2, 4).

Introduction

The binuclear complexes bis[*o*-xylyl-α,α'-dithiolato-μ-sulfido-ferrate(III)], $[Fe_2S_2(S_2\text{-}o\text{-xyl})_2]^{2-}$ (**1**), and bis[bis-(arylthiolato)-μ-sulfido-ferrate(III)], $[Fe_2S_2(SC_6H_4Y)_4]^{2-}$ (**2**), were originally synthesized[1,2] as part of a program directed at the isolation of analogues of the various types of redox sites in iron–sulfur proteins.[3,4] Structures of $[Fe_2S_2(S_2\text{-}o\text{-xyl})_2]^{2-}$ and $[Fe_2S_2(SC_6H_4\text{-}p\text{-Me})_4]^{2-}$ have been determined[1,2] and are shown in Figure 1. The structures are closely similar, with each containing a planar rhomboidal $[Fe_2S_2]^{2+}$ core of virtually equal dimensions. In the biological context complexes **1** and **2** have proven to be of considerable value in at least two respects. The close relationship between their magnetic and spectroscopic properties[1-3,5] and those of 2-Fe sites in oxidized ferredoxin proteins (Fd_{ox})[3] has provided additional pursuasive evidence for the correctness of the proposed formulation **3** for



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protein sites, which has recently been confirmed for the 2-Fe Fd_{ox} protein from *Spirulina platensis* by X-ray crystallography.[6,7] In the core extrusion method for identifying site structures in Fe–S proteins, the spectroscopic properties of the complexes **2** serve to identify them in the extrusion reaction system, thereby leading to establishment of 2-Fe sites in the native proteins.[9-12]

Synthetic routes affording complexes **1** and **2** are outlined in Figure 1; in all cases the complexes were isolated as R'_4N^+, Ph_4P^+, or Ph_4As^+ salts. $[Fe_2S_2(S_2\text{-}o\text{-xyl})_2]^{2-}$ was originally prepared in fair yield by the direct reaction (1) utilizing the dithiol **4**.[1,2] Subsequently, reaction 2 was devised and resulted in a 93% conversion of the preisolated monomer $[Fe(S_2\text{-}o\text{-xyl})_2]^-$ (**5**)[13] to **1**.[14] $[Fe_2S_2(SC_6H_4Y)_4]^{2-}$ species were first obtained by the ligand substitution reaction (3).[2] More recently, the representative complex $[Fe_2S_2(SPh)_4]^{2-}$ has been produced by reactions 4[15] and 5[16] which utilize as starting materials $[Fe_2S_2Cl_4]^{2-}$[15] and $[Fe(SPh)_4]^{2-}$,[17] respectively.

In view of the continuing utility of complexes **1** and **2** in this and other laboratories, more convenient synthetic routes to these species which do not require prior preparation of Fe–S precursor compounds are clearly desirable. In our investigation of the course of reactions in methanol solutions leading to the assembly of the tetranuclear clusters $[Fe_4S_4(SC_6H_4Y)_4]^{2-}$ from elementary reagents,[18] we have observed intermediate formation of the dimers **2** and found conditions allowing their isolation prior to significant conversion to tetramers. As a result the direct reaction (6) and the analogous reaction (7) have been developed as convenient syntheses of complexes **2** and **1**, respectively, and have been adapted to the synthesis of the corresponding Fe_2Se_2 complexes. Here we report synthetic details and characterization data for new compounds. This work, together with facile preparations of tetranuclear clusters by several methods,[19-22] provides ready synthetic access

* To whom correspondence should be addressed at the Department of Chemistry, Harvard University, Cambridge, MA 02138.

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Table I. Spectroscopic and Redox Potential Data for $[Fe_2X_2(SR)_4]^{2-}$ Complexes (X = S, Se)

complex	λ_{max}, nm (ϵ_M)[a]	$(\Delta H/H_0)_{iso}$, ppm[b]	$E_{1/2}$, V (vs. SCE)[a]
$[Fe_2S_2(S_2\text{-}o\text{-xyl})_2]^{2-}$	338 (16 200), 414 (17 000), ~455 (sh, 9200), 590 (4800)[c]	−37.4 (CH_2); −0.25, +0.15 (ring H)[d]	−1.51, −1.77
$[Fe_2Se_2(S_2\text{-}o\text{-xyl})_2]^{2-}$	342 (19 600), 432 (13 600), 488 (sh, 11 300), 630 (5800)	−42.2 (CH_2); −0.23, +0.09 (ring H)[d]	−1.45[e]
$[Fe_2S_2(SPh)_4]^{2-}$	333 (19 500), 490 (11 200)[c]	+2.30 (*o*-H), −2.11 (*m*-H), +3.82 (*p*-H)	−1.19, −1.50[f]
$[Fe_2Se_2(SPh)_4]^{2-}$	335 (22 800), 498 (13 600)	+2.78 (*o*-H), −2.51 (*m*-H), +4.40 (*p*-H)	−1.18, −1.45[f]
$[Fe_2S_2(SC_6H_4\text{-}p\text{-Me})_4]^{2-}$	336 (18 600), 502 (11 200)[c]	+2.42 (*o*-H), −2.10 (*m*-H), −3.74 (*p*-Me)	
$[Fe_2Se_2(SC_6H_4\text{-}p\text{-Me})_4]^{2-}$	340 (20 800), 510 (13 200)	+2.99 (*o*-H), −2.51 (*m*-H), −4.44 (*p*-Me)	−1.22, −1.49[f]
$[Fe_4S_4(SR)_4]^{2-}$	461 (18 600)[c,g]	+1.28 (*o*-H), −0.91 (*m*-H), −1.63 (*p*-Me)[h,i]	−1.04, −1.75[g,j]
$[Fe_4Se_4(SR)_4]^{2-}$	466 (18 110)[g,j]	+1.60 (*o*-H), −1.09 (*m*-H), −1.99 (*p*-Me)[h,k]	−1.01, −1.62[g,j]

[a] DMF solution. [b] CD_3CN solution unless noted otherwise; $(\Delta H/H_0)_{iso} = (\Delta H/H_0)_{obsd} - (\Delta H/H_0)_{dia}$, ~25 °C. [c] Reference 2. [d] Me_2SO solution. [e] Second reduction highly irreversible. [f] Both processes irreversible, $E_{p,c}$ values given. [g] R = Ph. [h] R = *p*-C_6H_4Me. [i] Reference 26. [j] Reference 21. [k] Reference 29.

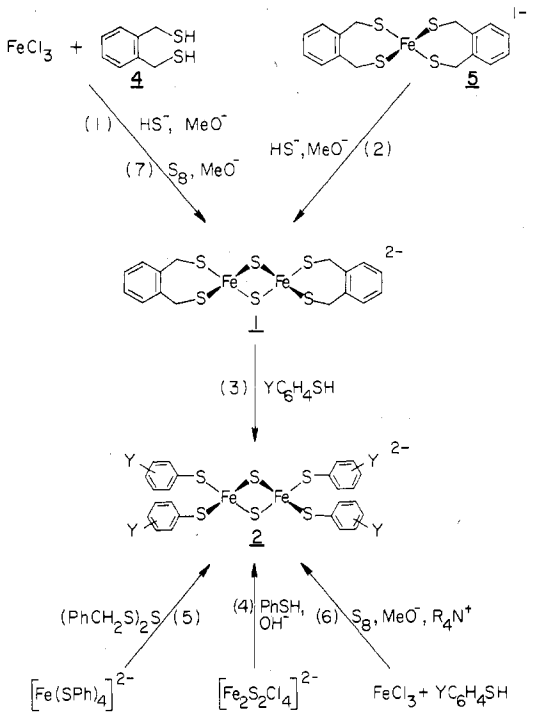

Figure 1. Synthetic routes to $[Fe_2S_2(S_2\text{-}o\text{-xyl})_2]^{2-}$ (**1**) and $[Fe_2S_2(SC_6H_4Y)_4]^{2-}$ (**2**). Reactions 1–5 have been previously reported.[2,14-16]

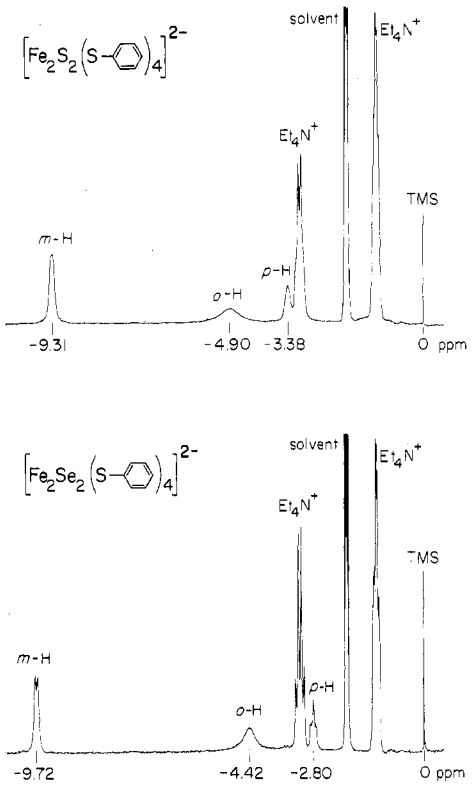

Figure 2. ^1H FT NMR spectra of Et_4N^+ salts of $[Fe_2S_2(SPh)_4]^{2-}$ and $[Fe_2Se_2(SPh)_4]^{2-}$ in CD_3CN solution at ~25 °C. Signal assignments are indicated.

to a wide variety of $[Fe_2X_2(SR)_4]^{2-}$ and $[Fe_4X_4(SR)_4]^{2-}$ species (X = S, Se) by direct reactions of simple reagents.

Experimental Section

Preparation of Compounds. All manipulations were performed under a dry, dioxygen-free dinitrogen or argon atmosphere with use of thoroughly degassed solvents and reagents. Methanol was dried over and distilled from $Mg(OMe)_2$; acetonitrile and DMF were dried over and distilled from CaH_2. *o*-Xylyl-α,α'-dithiol (**4**) was prepared as described[2] and was doubly sublimed before use. Benzenethiol and *p*-tolylthiol (Aldrich Chemical Co.) and $FeCl_3$ (anhydrous, Fisher Scientific Co.) were commercial samples and were used as received. Spectroscopic and redox potential properties of compounds prepared by reactions 6 and 7 are summarized in Table I. Of these compounds $(Et_4N)_2[Fe_2S_2(SC_6H_4Y)_4]$ (Y = H, *p*-Me)[2] and $(Et_4N)_2[Fe_2S_2(S_2\text{-}o\text{-xyl})_2]$[1,2] were previously prepared by other methods (Figure 1).

(a) $(R'_4N)_2[Fe_2X_2(SC_6H_4Y)_4]$ (Y = H, *p*-Me; X = S, Se). To a solution of 81 mmol of sodium thiolate (from 1.86 g of sodium metal and 81 mmol of thiol) in 100 mL of methanol was added the filtrate from a mixture of 3.24 g (20 mmol) of $FeCl_3$ in 50 mL of methanol. A dark solution formed immediately together with the separation of an amorphous solid. Upon being stirred overnight (≳12 h), the reaction mixture slowly assumed a dark green color. Filtration afforded an off-white solid (mainly NaCl and $(YC_6H_4S)_2$) and a dark green filtrate. To the latter was added 21 mmol of R'_4NBr dissolved in a minimal amount of methanol followed by 21 mmol of sulfur or selenium powder. The reaction mixture was then stirred for 12–24 h during which time the product separated as a black crystalline solid. Pure $(R'_4N)_2[Fe_2S_2(SC_6H_4Y)_4]$ compounds were obtained in 50–55% yield by one or two recrystallizations from warm (40–45 °C) acetonitrile. So that substantial formation of $[Fe_4S_4(SC_6H_4Y)_4]^{2-}$ is avoided, the reaction time should be ≲24 h; in the recrystallization procedure, which separates dimer salt from any tetramer salt (more soluble) formed, temperatures should not be higher than the specified range. Et_4N^+ and Me_4N^+ salts were obtained in comparable yield and equivalent purity as judged from ^1H NMR spectra, several of which are shown in Figure 2. The former salts were analyzed.

Anal. Calcd for $(Et_4N)_2[Fe_2Se_2(SPh)_4]$, $C_{40}H_{60}Fe_2N_2S_4Se_2$: C, 49.69; H, 6.26; Fe, 11.55; N, 2.98; S, 13.27; Se, 16.33. Found: C, 49.55; H, 6.24; Fe, 11.47; N, 3.00; S, 13.18; Se, 16.09.

Anal. Calcd for $(Et_4N)_2[Fe_2Se_2(SC_6H_4\text{-}p\text{-Me})_4]$, $C_{44}H_{68}Fe_2N_2S_4Se_2$: C, 51.66; H, 6.70; Fe, 10.92; N, 2.74; S, 12.54;

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Se, 15.44. Found: C, 51.53; H, 6.56; Fe, 10.95; N, 2.87; S, 12.46; Se, 15.21.

(b) $(Et_4N)_2[Fe_2X_2(S_2$-*o*-xyl$)_2]$ (X = S, Se). The preceding method and the same amounts of reagents were employed except that 40 mmol of *o*-xylyl-α,α'-dithiol was used in 250 mL of methanol. Addition of $FeCl_3$ produced a slurry of the iron thiolate compound. The products slowly separated as dark solids after the addition of Et_4NBr and the chalcogen powder. Pure products were obtained as red-black crystalline solids in ~50% yields after one or two recrystallizations from warm (40–45 °C) DMF.

Anal. Calcd for $(Et_4N)_2[Fe_2Se_2(S_2$-*o*-xyl$)_2]$, $C_{32}H_{56}Fe_2N_2S_4Se_2$: C, 44.35; H, 6.51; Fe, 12.89; N, 3.23; S, 14.80; Se, 18.22. Found: C, 44.21; H, 6.48; Fe, 12.77; N, 3.24; S, 14.75; Se, 18.23.

For a demonstration of the importance of the point of addition of cation in the preparative scheme, preparation a with *p*-tolylthiol was conducted as described except that Me_4NBr was added to a filtered solution of the reaction mixture *after* 12–24-h reaction time. A red-black crystalline solid was obtained in 92% yield after recrystallization from acetonitrile. This material was identified as $(Me_4N)_2[Fe_4S_4(SC_6H_4$-*p*-Me$)_4]$, previously prepared[23] by a related method with NaHS/NaOMe as the source of sulfide.[19] Under the same conditions the thiols RSH (R = Ph, *p*-C_6H_4OMe, Et, *t*-Bu) afforded the clusters $[Fe_4S_4(SR)_4]^{2-}$, all of which have been previously reported,[19,20,24] in good yield. Addition of R'_4NBr (R = Me, Et) and sulfur to $FeCl_3$/RSH/NaOMe reaction products (R = *p*-C_6H_4OMe, Et, *t*-Bu), as in system a, failed to yield detectable quantities of $[Fe_2S_2(SR)_4]^{2-}$ salts by ^1H NMR examination of reaction systems and products. The iron thiolate polymers formed from $FeCl_3$/RSH/NaOMe (R = CH_2Ph, $CH_2C_6H_4$-*p*-OMe) did not react with sulfur at ambient temperature but have been shown to react readily in the presence of NaHS/NaOMe to give the appropriate $[Fe_4S_4(SR)_4]^{2-}$ clusters.[19,25] Addition of NaSH/NaOMe and Et_4NBr to the benzylthiolate polymer gave after 12–24-h reaction times only $(Et_4N)_2[Fe_4S_4(SCH_2Ph)_4]$.

Physical Measurements. Absorption spectral, ^1H NMR, and electrochemical measurements were made as previously described.[14,26] Potentials in Table I measured in this work were determined at ~25 °C by cyclic voltammetry at a glassy carbon electrode using DMF solutions, 0.1 M $(n$-$Bu_4N)ClO_4$ supporting electrolyte, and a 100 mV/s scan rate.

Results and Discussion

Although the preparations of starting materials for reactions 1 and 2 in Figure 1 are straightforward, the synthesis of $[Fe_2S_2(S_2$-*o*-xyl$)_2]^{2-}$ (**1**) by reaction 7 is much more convenient.

$$2FeCl_3 + 2S + 4Na_2(S_2\text{-}o\text{-xyl}) \rightarrow Na_2[Fe_2S_2(S_2\text{-}o\text{-xyl})_2] + 2o\text{-xylS}_2 + 6NaCl \quad (7)$$

The product is readily obtained in ~50% yield after purification as its Et_4N^+ salt. The arylthiolate complexes $[Fe_2S_2(SC_6H_4Y)_4]^{2-}$ (**2**) were first prepared by the ligand substitution reaction (3), which in the presence of excess thiol rapidly

$$[Fe_2S_2(S_2\text{-}o\text{-xyl})_2]^{2-} + 4YC_6H_4SH \rightleftharpoons [Fe_2S_2(SC_6H_4Y)_4]^{2-} + 2o\text{-xyl(SH)}_2 \quad (3)$$

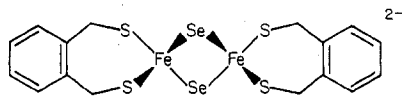
proceeds to completion in an aprotic solvent such as acetonitrile. Complexes with Y = H, *p*-Me, *p*-Cl[2] and *m*-CF_3, *p*-CF_3[11] have been prepared in this way. For cases with X = H and *p*-Me, reaction 6 is far more expedient than reactions 3–5 and affords the desired complexes in 50–55% yield after purification.

$$2FeCl_3 + 2S + 8NaSC_6H_4Y + 2R'_4NBr \rightarrow (R'_4N)_2[Fe_2S_2(SC_6H_4Y)_4] + 2(YC_6H_4S)_2 + 6NaCl + 2NaBr \quad (6)$$

The success of reaction 6 depends upon the co-introduction of an appropriate quaternary ammonium salt and sulfur to the $FeCl_3$/RSH/NaOMe reaction mixture, effecting the trapping of the complexes **2** as sparingly soluble salts in methanol. If the cation is withheld until reaction with sulfur is complete, reaction 8 ensues, as shown by the preparation of $(Me_4N)_2$-$[Fe_4S_4(SC_6H_4$-*p*-Me$)_4]$ in 92% yield under such conditions. This reaction was introduced by Christou and Garner[20] for the synthesis of $[Fe_4S_4(SR)_4]^{2-}$ (R = Ph, *t*-Bu) and earlier by Christou et al.,[22] with elemental selenium in place of sulfur, for the preparation of $[Fe_4Se_4(SPh)_4]^{2-}$. In the case of reaction 7 the Et_4N^+ cation may be added at the beginning or at the completion of the reaction. With this cation, tetranuclear species have not been found as soluble reaction products. As observed earlier,[2] the bite distance of the dithiolate ligand, while flexible, is not large enough to span the S···S distance (range 6.0–6.7 Å) found in $[Fe_4S_4(SR)_4]^{2-}$ structures[19,27] and in its dianion form promotes the formation of the binuclear complex.

$$4FeCl_3 + 4S + 14NaSR \rightarrow Na_2[Fe_4S_4(SR)_4] + 5RSSR + 12NaCl \quad (8)$$

As with reaction 8,[22] reactions 6 and 7 readily proceed with elemental selenium as the chalcogenide source. The previously unknown[28] complexes $[Fe_2Se_2(S_2$-*o*-xyl$)_2]^{2-}$ (**6**) and $[Fe_2Se_2$-$(SC_6H_4Y)_4]^{2-}$ (**7**; Y = H, *p*-Me) were obtained as R'_4N^+ salts in yields and purities equivalent to those of their sulfur congeners.



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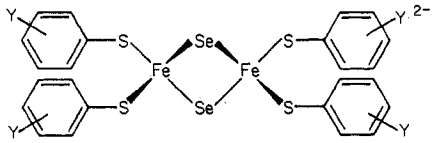

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Access to complexes **6** and **7** permits comparative examination of the influence of core atom (X = S, Se) in $[Fe_2X_2$-$(SR)_4]^{2-}$ species. Toward this end certain spectroscopic properties and redox potentials are collected in Table I, which also includes corresponding data for $[Fe_4X_4(SR)_4]^{2-}$ clusters.[2,21,26,29] ^1H NMR spectra of $[Fe_2X_2(SPh)_4]^{2-}$ are directly compared in Figure 2. The signs and magnitudes of the isotropic shifts demonstrate that, as with $[Fe_4X_4(SR)_4]^{2-,3-}$ clusters,[21,26] these shifts arise mainly from hyperfine contact interactions consequent to ligand → core (Fe) antiparallel spin transfer. These effects of core selenide vs. sulfide are evident from the data: (i) small red shifts of charge-transfer absorption bands; (ii) larger isotropic shifts but with nearly constant X = Se/S shift ratios for a given ring position (1.19–1.24), indicating that the X = Se species are more paramagnetic; (iii) slightly less negative redox potentials for the couples 2−/3− and 3−/4−. These comparative effects have also been observed for $[Fe_4X_4(SR)_4]^{2-}$ species (data for several of which are included in Table I) and doubtless arise from the same factors, which have been discussed.[21] The few selenium-substituted 2-Fe Fd_{ox} proteins which have been characterized[30–34] were

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(27) L. Que, Jr., M. A. Bobrik, J. A. Ibers, and R. H. Holm, *J. Am. Chem. Soc.*, **96**, 4168 (1974); H. L. Carrell, J. P. Glusker, R. Job, and T. C. Bruice, *ibid.*, **99**, 3683 (1977).
(28) Similar species have apparently been generated in solution but were not isolated: Y. Sugiura, K. Ishizu, T. Kimura, and H. Tanaka, *Bioinorg. Chem.*, **4**, 291 (1975).
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obtained by reconstitution reactions of apoproteins with iron and selenium reagents. All such proteins exhibit effect i, but when they are compared to native proteins, the redox potential differences, while small, are variable in sign (−14 to +38 mV[33,34]). NMR and magnetic data have not been determined. At present firm evidence is lacking for the occurrence of selenium as a core constituent or as a terminal ligand (selenocysteinate) in Fe–S proteins of any type. However, the comparative data reported here for complexes **1**/**6** and **2**/**7**, as well as results for the protein 4-Fe site analogues $[Fe_4X_4(ZPh)_4]^{2-,3-}$ (X, Z = S, Se),[21] support the proposition that selenium could act as a functional substitute for sulfur in native proteins. Indeed, several Se-substituted 2-Fe proteins have proven active in bioassays.[30,32]

Lastly, it is observed that reaction 6 should be capable of extension to other aromatic thiols. The requirements are that the initially formed iron thiolate species be reactive toward elemental sulfur and that a suitable cation be employed to precipitate the desired 2-Fe complex before $[Fe_4S_4(SR)_4]^{2-}$ formation, by reaction 8 or other means, proceeds to an undesirable extent. A current limitation of the method is the inability to obtain $[Fe_2S_2(SR)_4]^{2-}$ complexes derived from monofunctional alkylthiols. Chelate complexes **1** and **6** are the only stable 2-Fe alkylthiolate species yet encountered. The first of these requirements also provides a limitation on $[Fe_4S_4(SR)_4]^{2-}$ synthesis by reaction 8, e.g., in the case of R = CH_2Ph at ambient temperature. It is the experience of this laboratory that virtually all iron alkyl- and arylthiolate species, including insoluble polymers, react with NaHS/NaOMe as the sulfide source in methanol at ambient temperature, in the absence of R'_4N^+ salts, to form $[Fe_4S_4(SR)_4]^{2-}$. The limiting stoichiometry is represented by reaction 9. In the R = alkyl

$$4FeCl_3 + 4NaHS + 6NaSR + 4NaOMe \rightarrow Na_2[Fe_4S_4(SR)_4] + RSSR + 12NaCl + 4MeOH \quad (9)$$

systems tested, co-introduction of the sulfide source and a R'_4N^+ salt, as in reaction 6, impeded further reaction to form tractable species (R = Et, *t*-Bu) or gave the tetrameric cluster (R = CH_2Ph) as the only identifiable product. A subsequent report will deal with the course of formation of $[Fe_4S_4(SR)_4]^{2-}$ by reaction 8, including the possible role of $[Fe_2S_2(SR)_4]^{2-}$ as an intermediate species.[18]

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Registry No. $(Et_4N)_2[Fe_2S_2(S_2\text{-}o\text{-}xyl)_2]$, 56083-11-5; $(Et_4N)_2[Fe_2Se_2(S_2\text{-}o\text{-}xyl)_2]$, 74752-86-6; $(Et_4N)_2[Fe_2S_2(SPh)_4]$, 55939-70-3; $(Et_4N)_2[Fe_2Se_2(SPh)_4]$, 74752-88-8; $(Et_4N)_2[Fe_2S_2(SC_6H_4\text{-}p\text{-}Me)_4]$, 55939-64-5; $(Et_4N)_2[Fe_2Se_2(SC_6H_4\text{-}p\text{-}Me)_4]$, 74752-90-2.

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Contribution from the Chemistry Department, University College, Belfield, Dublin 4, Ireland

Design of Metal Chelates with Biological Activity. 2.[1] Solution Properties of Iron(III) Glycinehydroxamate

DAVID A. BROWN,* M. V. CHIDAMBARAM, and J. D. GLENNON

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Chemical criteria proposed previously as indicators of biological activity by a metal chelate as a source of a trace element are applied to ferric glycinehydroxamate, $Fe(GHA)_3$. The species distribution and the relevant stability constants of species present in aqueous solutions of $Fe(GHA)_3$ were obtained by analytical potentiometry. Together with magnetic susceptibility measurements, these results show the absence of any polymeric species at physiological pH values. The complex is shown also to donate iron rapidly to apotransferrin and the free ligand to effectively depolymerize iron citrate polymers. Biological potential is thus strongly indicated by all the proposed chemical criteria. In vitro studies indicate absorption of the undissociated chelate by rat intestines.

Introduction

This paper is the second part of a series devoted to finding in vitro chemical criteria which can be used as indicators of biological activity with the eventual aim of designing metal chelates as suitable sources of various trace elements essential in animal nutrition. In this paper, iron is the trace element considered, and we discuss ferric glycinehydroxamate as a possible source.

In living systems, the absorption, secretion, and retention of iron are largely controlled by the intestinal mucosa. A specific iron protein, transferrin, exists in the blood serum and serves as a carrier for iron.[2] Another iron protein, ferritin, functions both in iron absorption from the intestine and in iron storage in the liver, kidney, and spleen.[3] The normal iron content of men and women is 50 and 35 mg/kg of body weight respectively, giving an approximate total of 2–5 g of iron in the normal adult. When the level of iron falls below these levels, a state of iron deficiency is present. Apart from porphyrins, the other major class of naturally occurring iron complexing agents are the hydroxamic acids which complex as dihydroxamic acids (forming the mycobactins, mycelianamide, and pulcherrimic acid) and the trihydroxamic acids (forming the ferrichrome and ferrioxamine groups). These

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