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Synthesis and characterization of iron derivatives of dihydrolipoic acid and dihydrolipoamide

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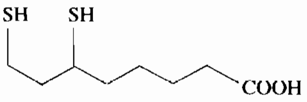
Abstract

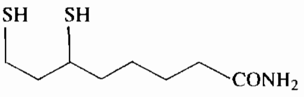
The preparation and properties of physiologically relevant complexes of iron(II) and iron(III) with dihydrolipoic acid and dihydrolipoamide are described. Data obtained from measurements of the magnetic properties of the compounds are discussed along with results obtained by vibrational, electronic, EPR and Mössbauer spectroscopy. While iron(III) compounds present a low-spin, d^5 configuration, iron(II) compounds present an intermediate spin state, $S=1$, d^6 configuration.

Introduction

Recent reports indicate that: (i) dihydrolipoic acid (**A**) and dihydrolipoamide (**B**), hereafter referred to as LH_3 and $L'H_2$ ($L=C_8H_{13}S_2O_2$; $L'=C_8H_{13}S_2ONH_2$), respectively, are able to mobilize iron rapidly and almost quantitatively from the iron storage protein, ferritin [1, 2], and from the iron transport protein, transferrin [3]; (ii) complexes of iron and LH_3 compare very favourably with other forms of complexed iron in the uptake of the metal by both apotransferrin and apoferritin [4]; (iii) the same complexes are the substrates for enzymatic synthesis of iron–sulfur clusters [5]; (iv) LH_3 takes part in the translocation of iron across biomimetic membranes in liposomes [6].



A



B

The present paper reports on the preparation and the properties of the same iron complexes with LH_3, which were found to be involved in the physiologically relevant reactions mentioned above.

In a separate paper, we reported on nickel(II), cobalt(II), mercury(II) and copper(I) complexes with LH_3 and $L'H_2$ [7]. Preliminary data on a compound of iron(III) with LH_3 were previously made available elsewhere [8].

Experimental

Preparation of ligands

Dihydrolipoic acid, LH_3, and dihydrolipoamide, $L'H_2$, were prepared as described previously [7], and their purity was assessed by IR, NMR spectroscopy and by potentiometric titration.

Preparation of compounds

To prevent the decomposition of the compounds all manipulations were performed on rigorously degassed solutions under an argon atmosphere. The isolated

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compounds were washed with water and dichloromethane, dried under dynamic vacuum and stored under argon. Buffer was 0.3 M Tritma Base (tris(hydroxymethyl)aminomethane), brought to pH 9.0 with HCl.

$Fe_2(LH)_3 \cdot 1.5H_2O$

One gram (4.83 mmol) of LH_3 was dissolved in 100 ml of buffer. To this solution, 20 ml of an aqueous solution of $FeCl_3$ (0.78 g, 2.88 mmol) were added. A green solution was obtained, with a pH around 8.0. By lowering the pH of the mixture to 5.0 with 0.1 N HCl, a green precipitate was obtained, which was decanted and isolated by filtration. The isolated compound is water soluble in the presence of an excess of LH_3.

Anal. Calc.: C, 38.06; H, 5.95; O, 15.86; S, 25.37; Fe, 14.76; H_2O, 3.57. Found: C, 37.60; H, 5.42; O, 15.60; S, 24.90; Fe, 14.82; H_2O, 4.00%. r.t. μ_{eff}(BM) 2.47.

$Fe_2L'_3 \cdot 2H_2O$

Ferric chloride hexahydrate (0.78 g, 2.88 mmol) and Tritma Base (1.20 g, 9.9 mmol) were suspended in 2 ml of DMF, and a solution of 1.0 g (4.83 mmol) of $L'H_2$ in 10 ml of DMF was added under magnetic stirring. Addition of 250 ml of water to the DMF solution resulted in the formation of a green precipitate, which was recovered by filtration.

Anal. Calc.: C, 37.76; H, 6.42; O, 10.48; S, 25.17; N, 5.51; Fe, 14.64; H_2O, 4.72. Found: C, 37.36; H, 6.37; O, 10.41; S, 25.03; N, 5.74; Fe, 14.65; H_2O, 4.53%. r.t. μ_{eff}(BM) 2.30.

$Fe_3L_2 \cdot 4H_2O$

To a slurry of 2.80 g (7.14 mmol) of $(NH_4)_2Fe(SO_4)_2 \cdot 6H_2O$, and 1.8 g (14.88 mmol) of Tritma Base in 2 ml of DMF, 10 ml of a DMF solution containing 1.0 g (4.81 mmol) of LH_3 were added. A brown–red compound precipitated upon dilution of the DMF solution with 100 ml of water. The compound was isolated by filtration, and found to be water soluble in the presence of an excess of LH_3.

Anal. Calc.: C, 29.56; H, 5.85; O, 19.71; S, 19.71; Fe, 25.77; H_2O, 11.08. Found: C, 29.33; H, 5.62; O, 19.51; S, 19.89; Fe, 25.86; H_2O, 10.00%. r.t. μ_{eff}(BM) 3.08.

$FeL' \cdot 0.5H_2O$

To a slurry of 1.90 g (4.84 mmol) of $(NH_4)_2Fe(SO_4)_2 \cdot 6H_2O$ in 2 ml of DMF, 1.17 g (9.67 mmol) of Tritma Base in 2 ml of DMF, and 1.0 g (4.83 mmol) of $L'H_2$ dissolved in 10 ml of DMF, were added in that order. Upon dilution of the mixture in DMF with 250 ml of water, a brown–red precipitate was obtained, and isolated by filtration.

Anal. Calc.: C, 35.60; H, 5.93; O, 8.89; S, 23.72; N, 5.19; Fe, 20.70; H_2O, 3.34. Found: C, 36.04; H, 6.23; O, 8.84; S, 23.79; N, 5.20; Fe, 20.75; H_2O, 3.16%. r.t. μ_{eff}(BM) 3.22.

Analytical and physical methods

Elemental analysis was carried out on a Perkin-Elmer elemental analyzer, model 2400. Sulfur was analyzed on a LECO sulfur determinator SC-132. Iron content of isolated compounds was determined by atomic absorption on a Perkin-Elmer Model 4000 instrument. The water content of isolated solids was determined from the weight loss during thermal analysis in a Dupont TG Model 1090 instrument.

Vibrational spectra were obtained in a Jasco FT/IR 5000 spectrophotometer on KBr pellets of samples. An exception was $Fe_2(LH)_3 \cdot 1.5H_2O$, for which the spectrum was recorded on Voltalef-3s mull in the range 4000–1300 cm^{-1}, and on Nujol mull in the range 800–1300 cm^{-1}. Electronic spectra of solutions in DMF or in water at a pH of about 9 were taken on a diode-array Hewlett-Packard spectrophotometer. EPR spectra were obtained at 123 K on a Varian E-9 spectrometer operating at X-band.

Mössbauer spectra were obtained on a conventional constant-acceleration spectrometer equipped with a room-temperature rhodium matrix ^{57}Co source. The spectra were fitted to Lorentzian line shapes by using standard least-squares computer minimization techniques. All the components of each spectrum were allowed to vary as symmetric doublets until the best fit was obtained.

Magnetic susceptibility was measured on solid samples according to the Faraday method, by using a Cahn apparatus equipped with a Cahn 1000 balance and an Oxford cryostat.

Potentiometric titration were performed at 25.0 ± 0.1 °C with a Metrohm 654 pH-meter equipped with a Metrohm Dosimat 665 automatic titrator, governed by the TITOBAS program [9], using a Whethron combined pH electrode for highly alkaline solutions. Titrations of LH_3 and $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$ or $FeCl_3$ in the molar ratios $[LH_3]/[M] = 2, 3, 4$ were performed with 0.1 M KOH. Potentiometric data for the electrode standardization were analyzed by the MAGEC program [10]. The formation constants of the complexes between LH_3 and Fe(II) or Fe(III) were calculated by a slightly modified version of the PSEQUAD program [11].

Results and discussion

Distribution curves for the formation of iron(III) and iron(II) complexes of LH_3 were determined from potentiometric titration and are presented in Figs. 1 and 2. In the case of iron(III), the following complexes were formed: $[Fe(LH_2)]^{2+}$, $[Fe(LH)]^{+}$, [FeL],

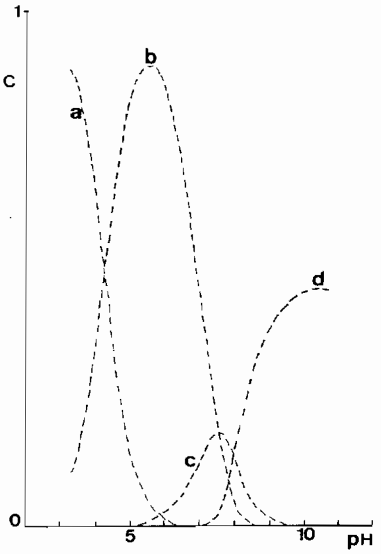

Fig. 1. Distribution curves for the formation of Fe(III) complexes: a, $[FeLH_2]^{2+}$; b, $[FeLH]^+$; c, [FeL]; d, $[Fe_2L_4H_4]^{2-}$ as functions of pH for a molar ratio $[LH_3]/[Fe]=2$.

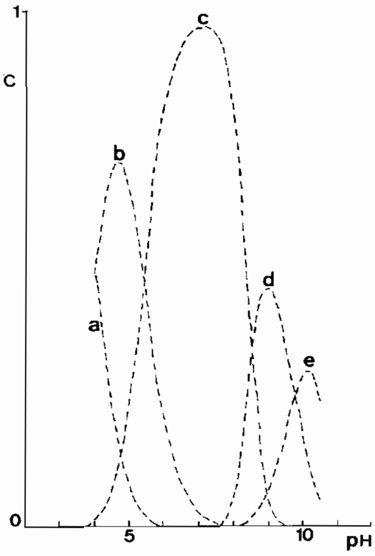

Fig. 2. Distribution curves for the formation of Fe(II) complexes: a, $[FeL_2H_6]^{2+}$; b, $[FeL_2H_5]^+$; c, $[FeL_2H_4]$; d, $[Fe_3H_4]^{3-}$; e, $[FeL_3H_3]^{4-}$ are functions of the pH for a molar ratio $[LH_3]/[Fe]=2$.

$[Fe_2(LH)_4]^{2-}$, in which $LH_2{}^{1-}$ represents the carboxylate anion of dihydrolipoic acid, LH^{2-} corresponds to the species deriving from deprotonation of both thiolic groups, and the trianion, L^{3-}, derives from complete deprotonation of the ligand. In the case of iron(II), the following compounds were observed: $[Fe(LH_3)_2]^{2+}$, $[Fe(LH_3)(LH_2)]^+$, $[Fe(LH_2)_2]$, $[Fe(LH_2)(LH)_2]^{3-}$ and $[Fe(LH)_3]^{4-}$. Formation constants for these complexes are reported in Table 1.

TABLE 1. Logarithms of the formation constants of the complexes[a] $M_mL_lH_h$ (standard deviations in parentheses)

Iron(II) compounds		Iron(III) compounds	
$[ML_2H_6]^{2+}$	61.23(2)	$[MLH_2]^{2+}$	28.51(1)
$[ML_2H_5]^+$	57.21(2)	$[MLH]^+$	24.52(1)
$[ML_2H_4]$	51.85(2)	[ML]	16.81(1)
$[ML_3H_4]^{3-}$	59.42(2)	$[M_2L_4H_4]^{2-}$	62.96(1)
$[ML_3H_3]^{4-}$	49.73(2)		

[a] The concentration values utilized were: iron(II); $10^4[LH_3]$, 5.585; $10^4[Fe]$, 5.152, 2.576, 1.538, 1.288; iron(III); $10^4[LH_3]$, 4.720; $10^4[Fe]$, 4.720, 2.360, 1.572, 1.176.

The electronic spectrum of a solution containing a molar ratio metal/$LH_3=1/2$ in aqueous buffer at pH 9.0 shows two maxima at 662 ($\epsilon=6500$) and 385 ($\epsilon=9560$) nm which, according to the literature [12], can be assigned to charge transfer interactions. The EPR spectrum of the same solution shows two signals at $g_1=2.133$ an $g_2=1.991$, which are characteristic of low-spin iron(III) complexes [13]. As reported in 'Experimental' four compounds were isolated in the solid state which corresponded to the following minimal formulae: $Fe_2(LH)_3 \cdot 1.5H_2O$, $Fe_2L'_3 \cdot 2H_2O$, $Fe_3L_2 \cdot 4H_2O$ and $FeL' \cdot 0.5H_2O$. Considering the wide range of bonding possibilities for the ligands, as well as the difficulties encountered in preparing the isolated material in a form suitable for single-crystal structural analysis, a variety of spectroscopic techniques was used to elucidate the properties of these compounds and to infer some structural information, not available otherwise.

Examination of the IR stretching frequencies for the carboxylic groups, assigned according to the literature [14], and reported in Table 2, made it evident that $Fe_2(LH)_3 \cdot 1.5H_2O$ shows values comparable to those of LH_3, while $Fe_3L_2 \cdot 4H_2O$ shows values comparable with those shown by the carboxylate anion in LH_2Na. This represents evidence for the presence of the LH^{2-} dianion in $Fe_2(LH)_3 \cdot 1.5H_2O$, and of the L^{3-} trianion in $Fe_3L_2 \cdot 4H_2O$. It appears therefore reasonable to hypothesize that both LH^{2-} and L^{3-} are coordinatively bound to the iron atom through their thiolate groups. A comparison of the difference $\Delta\nu=\nu_{as}-\nu_s$ between the stretching vibrations of $Fe_3L_2 \cdot 4H_2O$ and those of LH_2Na suggests that in the complex, as reported in the literature [15], the carboxylate group of L^{3-} either could act as a bidentate ligand or could form an ionic bond to the metal. Apparently, the possibility that the carboxylate could function as a monodentate ligand can confidently be ruled out.

By comparing the values for $[\nu(CO)+\delta(NH_3)]$ and $\nu(CN)$ [14] vibration frequencies the involvement of the amide group of $L'H_2$ in the binding of the metal can also be excluded.

Magnetic susceptibility values were measured on solid samples from 20 K to room temperature. All compounds were found to obey the Curie–Weiss law, $\chi_m=C/(T+\theta)$.

TABLE 2. Selected IR frequencies (cm^{-1})

Compound	$\nu_{as}(COO)$	$\nu_s(COO)$	$\nu(CO)+\delta(NH_2)$	$\nu(CN)$
LH_3	1710(vs)	1412(s)		
LH_2Na	1570(vs)	1440(ms)		
$L'H_2$			1659(vs) 1634(vs)	1418(ms)
$Fe_2(LH)_3 \cdot 1.5H_2O$	1700(s)	1415(ms)		
$Fe_2L'_3 \cdot 2H_2O$			1660(vs)	1415(m)
$Fe_3L_2 \cdot 4H_2O$	1546(vs)	1438(vs)		
$FeL' \cdot 0.5H_2O$			1662(vs)	1415(m)

vs = very strong; s = strong; ms = medium strong; m = medium.

The magnetic moment values for half of the minimal formula of $Fe_2(LH)_3 \cdot 1.5H_2O$ and $Fe_2L'_3 \cdot 2H_2O$ vary from 2.47 BM at 294 K to 2.02 BM at 20 K. Consequently it is clear that each iron of these compounds is iron(III), low spin, $S = 1/2$. In accordance to the temperature dependence of the magnetic moments, it is possible to establish that in the range of the investigated temperatures, these complexes do not show any magnetic interaction among iron ions.

The magnetic moment values for a third of the minimal formula of $Fe_3L_2 \cdot 4H_2O$ vary from 3.081 BM at 294 K to 2.057 BM at 20 K, with the room-temperature value being comparable to that calculated in the spin-only approximation for a compound of iron(II) with two unpaired electrons. Values close to these latter ones are reported in the literature [16] for compounds such as $[Fe(phen)_2ox] \cdot 5H_2O$ and $[Fe(phen)_2mal] \cdot 7H_2O$, which have a spin state $S = 1$. To explain how a triplet state can become the ground state of an iron(II) ion, it may be useful to refer to the Tanabe and Sugano diagram for the d^6 configuration. Since near the $^5T_{2g}$, $^1A_{1g}$ crossover the energy values of the $^3T_{1g}(^5t_{2g}e_g)$ and $^3T_{2g}(^5t_{2g}e_g)$ states are very close to that of the ground state, when the ligand field is greater than that of the crossover it may happen that, owing to the splitting of the $^3T_{1g}$ state as a consequence of the distortion from the octahedral geometry, a triplet state can become the ground state [16]. Hence, in D_{4h} symmetry, the possible ground states can be chosen among the states $^3A_{2g}$, ^3E_g (which derive from $^3T_{1g}$) and the states $^3B_{2g}$, ^3E_g (which derive from $^3T_{2g}$). As discussed in a later section of this paper, it was possible to propose the most probable ground state on the basis of the quadrupole splitting value obtained by Mössbauer spectroscopy,.

The EPR spectra of powdered samples of $Fe_2(LH)_3 \cdot 1.5H_2O$ and $Fe_2L'_3 \cdot 2H_2O$ from 120 to 4 K show two g values: $g_1 = 2.133$ and $g_2 = 1.991$. The two spectra are identical, and a typical tracing is presented in Fig. 3. These results indicate that both compounds contain low-spin ($S = 1/2$) iron(III) ions [13]. Furthermore, the observation of two g values confirms the hypothesis of a tetragonal distorted coordination around the iron atoms in these compounds. The weak signal which is present in the EPR spectrum of Fig. 3 at about 1500 G is surely due to the presence in the sample of impurities of high-spin iron(III) [17]. In fact, as it also will be pointed out later in the discussion of the Mössbauer spectra, this signal became more intense upon aging of the sample.

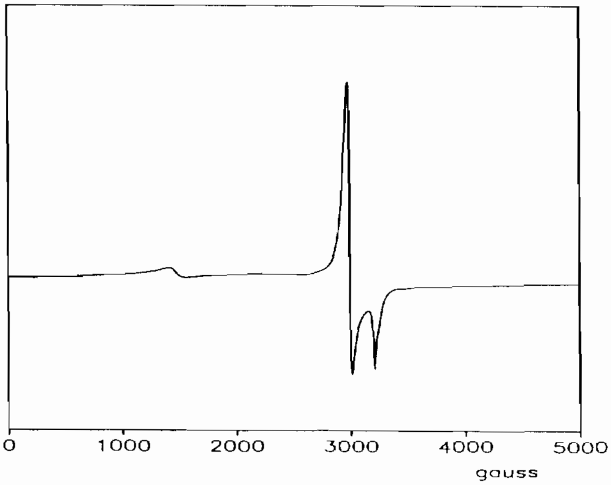

Fig. 3. EPR spectrum (20 K) of powdered sample of $Fe_2(LH)_3 \cdot 1.5H_2O$.

Several methods have been proposed for the calculation of the g expression for O_h and D_{4h} low-spin d^5 configurations [17–20]. Using the method of calculation proposed by Hudson and Kennedy [20], in D_{4h} symmetry, the ground Kramers' doublet could either be of type E′, for which $g_\parallel = g_\perp = 0$, or of type E″ for which the following expressions for g were calculated

$$g_\perp = 2[B^2 + K\sqrt{2}AB] \qquad g_\parallel = 2[A^2 - B^2 + KA^2]$$

where $A^2 + B^2 = 1$, K is the orbital reduction parameter (i.e. a measure of the covalence of the ligand–metal bond), and must assume values lower than 1.

Since from the EPR spectra it is not possible to obtain the signs of the g values, and taking into account that for compounds with a D_{4h} geometry the $g_{\perp}$ signal must always be more intense than that of $g_{\parallel}$, it was necessary to consider only the following possible pairs of g values

$$g_{\perp}=2.133,\ g_{\perp}=2.133,\ g_{\perp}=-2.133,\ g_{\perp}=-2.133$$

$$g_{\parallel}=1.991,\ g_{\parallel}=-1.991,\ g_{\parallel}=1.991,\ g_{\parallel}=-1.991$$

By imposing the condition, $K \leqslant 1$ the values of A, B and K which best reproduced the $g_{\parallel}$ and $g_{\perp}$ values were calculated through a computer simulation. The best fit corresponded to $g_{\parallel}=2.133$, $g_{\perp}=1.991$, $A=0.8069$, $B=0.5907$, $K=1.0$. Consequently, the ground Kramers doublet is

$$\Psi^{+}=0.8069|\overset{+}{1}\rangle+0.5907|\bar{\zeta}_1\rangle$$

$$\Psi^{-}=-0.8069|-\bar{1}\rangle-0.5907|\overset{+}{\zeta}_1\rangle$$

where $|\zeta_1\rangle$, $|1\rangle$ and $|-1\rangle$ represent the following d orbitals

$$|\zeta_1\rangle=i|xy\rangle$$

$$|1\rangle=-1/\sqrt{2}\,(|xz\rangle+i|yz\rangle)$$

$$|-1\rangle=1/\sqrt{2}\,(|xz\rangle-i|yz\rangle)$$

The ground state of each iron atom of $Fe_2(LH)_3 \cdot 1.5H_2O$ appears therefore as formed by a mixture of $(xy)^2(xz,yz)^3$ and $(xz,yz)^4(xy)$ configurations, with a slightly larger contribution from the first one.

It is important to note that no particularly evident EPR signal has been shown by iron(II) complexes from 298 to 20 K.

Table 3 reports the values for the isomer shift, δ, and for the quadrupole splitting, ΔE_a, obtained from Mössbauer spectra. The spectra of iron(III) complexes are shown in Fig. 4. Besides the main components of the signal, as reported in Table 3, other weak features were evident. These latter are likely due to contamination of the sample with impurities of high-spin iron(III) compounds (see, for instance, $\delta=0.56$ mm/s, $\Delta E_a=1.32$ mm/s in the case of $Fe_2(LH_3) \cdot 1.5H_2O$) as well as with impurities of high-spin iron(II) compounds ($\delta=1.44$ mm/s, $\Delta E_a=2.53$ mm/s for the same material). These minor components became more intense upon aging of the sample, suggesting that they derive from degradation processes. It is important to note that Mössbauer parameters for both $Fe_2(LH)_3 \cdot 1.5H_2O$ and $Fe_2L'_3 \cdot 2H_2O$ are very similar to those of the iron(III), low-spin compound $(Et_4N)_3[Fe_2S_4(S\text{-}p\text{-}C_6H_4Br)_4]$ [21] and that Mössbauer spectra of the iron(III) compounds did not shown any variation on going from 78 to 4 K, thus indicating the absence of any spin equilibrium.

TABLE 3. Isomer shift[a] and quadrupole splitting

Compound	δ (mm/s)	ΔE_a (mm/s)	T (K)
$Fe_2(LH)_3 \cdot 1.5H_2O$	0.40	1.84	78
	0.41	1.84	4
$Fe_2L'_3 \cdot 2H_2O$	0.40	1.85	78
	0.41	1.86	4
$Fe_3L_2 \cdot 4H_2O$	0.47	0.87	78
$FeL' \cdot 0.5H_2O$	0.48	0.78	78

[a] With respect to metallic iron at room temperature.

On the other hand, Mössbauer spectra of iron(II) compounds, such as the one of $Fe_3L_2 \cdot 4H_2O$ reported in Fig. 5, did not show any presence of impurities.

Previously in this paper it was emphasized that, on the basis of magnetic measurements, it was possible to assign to each iron atom of $Fe_3L_2 \cdot 4H_2O$ a triplet ground state to be chosen between the states $^3A_{2g}(e_g{}^4b_{2g}b_{1g})$ and $^3E_g(e_g{}^3b_{2g}{}^2a_{1g})$, which derive from the state $^3T_{1g}(t_{2g}{}^5e_g)$, and the states $^3B_{2g}(e_g{}^4b_{2g}a_{1g})$ and $^3E_g(e_g{}^3b_{2g}{}^2b_{1g})$, which derive from the state $^3T_{2g}(t_{2g}{}^5e_g)$, and that it was possible to single out the ground state when taking into account the experimental value of ΔE_a. While for the triplet states deriving from $^3T_{1g}$ one must expect $\Delta E_a=0$, for those deriving from $^3T_{2g}$ one must expect a value of ΔE_a very different from zero [16]. For example, $\Delta E_a=0.26$ was observed for the compounds $[Fe(phen)_2ox] \cdot 5H_2O$ and $[Fe(phen)_2mal] \cdot 7H_2O$ [16, 22], which have the ground state $^3A_{2g}$, while $\Delta E_a=2.68$ was reported for compounds such as phthalocyaninatoiron(II), which has the ground state $^3B_{2g}$ [23]. According to the experimental ΔE_a values, the ground state of our iron(II) atoms should originate from the mixing between two ^3E_g triplet states, one with $\Delta E_a=0$, and the other one with $\Delta E_a \gg 0$.

In agreement with the above hypotheses on the triplet ground state, the isomer shift values of our compounds are close to those measured for $[Fe(phen)_2ox] \cdot 5H_2O$ and $[Fe(phen)_2mal] \cdot 7H_2O$ [16, 22].

The possibility of chemical interconversion of the iron(III) compounds into the iron(II) ones was also investigated. This redox chemistry is of possible biological relevance, as mechanisms involving a modification of the redox state of the metal have been proposed for the mobilization of iron(III) from ferritin and transferrin as well as for the uptake of iron(II) by the apoform of either protein. As previously pointed out, it was possible to specify which chemical species were present in aqueous solutions at any given pH value. For example, at physiologically relevant pH values (i.e. $\simeq 8$), among the species characterized by the same metal/ligand ratio both oxidation states are represented: iron(III) is present as $[Fe(LH)_4]^{2-}$, and iron(II) as

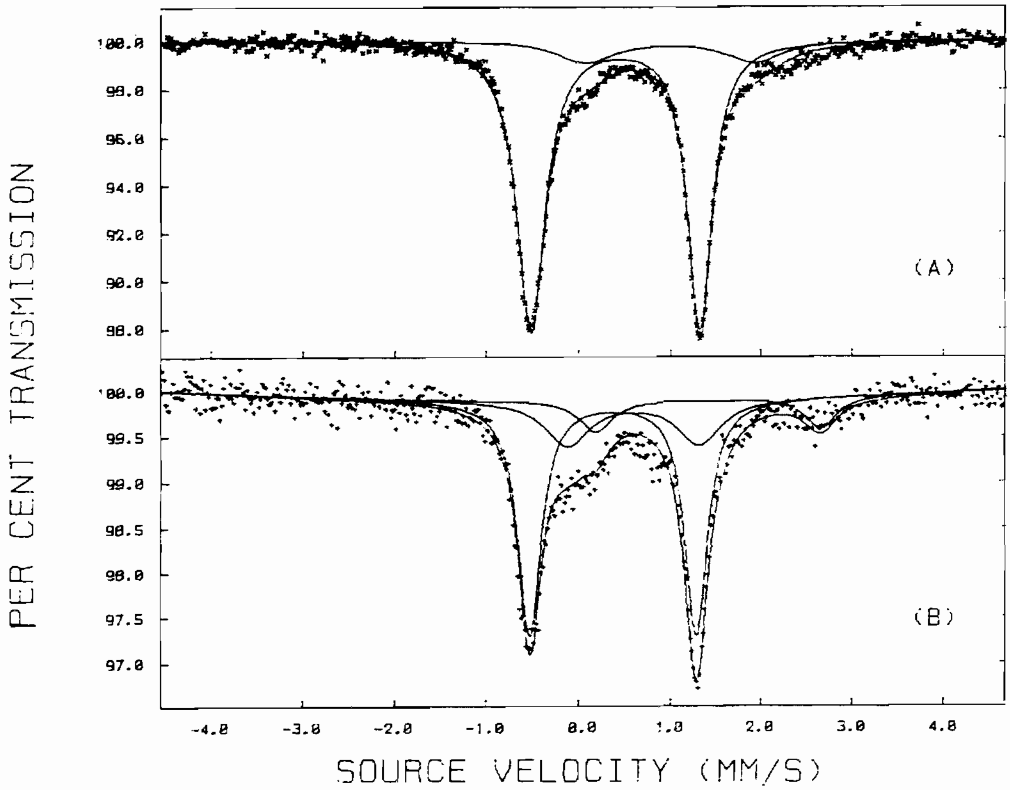

Fig. 4. Mössbauer spectra recorded at 78 K on solid samples of $Fe_2L'_3 \cdot 2H_2O$ (A) and $Fe_2(LH)_3 \cdot 1.5H_2O$ (B).

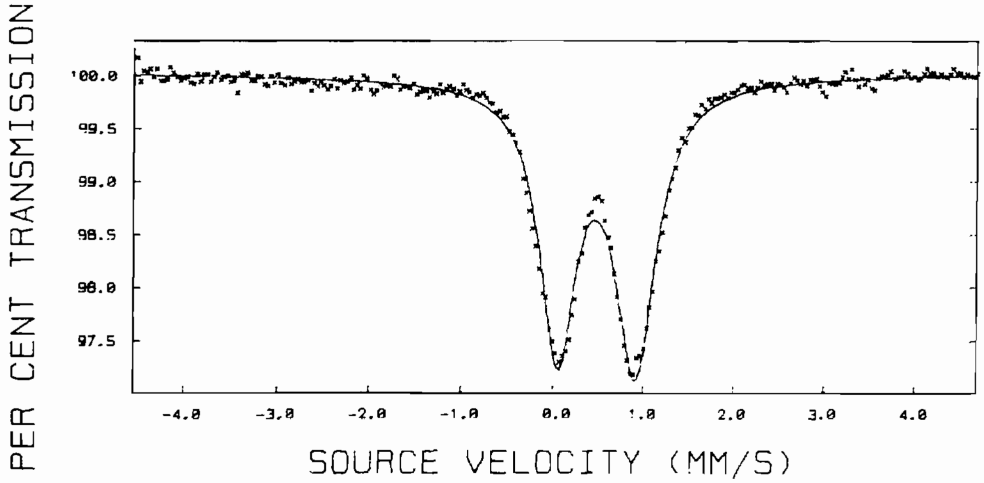

Fig. 5. Mössbauer spectra recorded at 78 K on solid samples of $Fe_3L_2 \cdot 4H_2O$.

$[Fe(LH_2)_2]$. On the basis of these observations, the interconversion between the two oxidation states of the metal was studied spectrophotometrically in aqueous solutions buffered at $pH \simeq 8$, using sodium dithionite and potassium ferricyanide as the reducing and the oxidizing agent, respectively. Upon addition of reductant, a deep green solution of the iron(III) compound turned to the brownish-yellow color characteristic of the iron(II) compound. The absorbance maximum at 385 nm was retained upon reduction, while the one at 662 nm was no longer evident. Addition of oxidant restored the typical spectrum of the iron(III) compound.

In conclusion, it has been demonstrated that dihydrolipoic acid and dihydrolipoamide can form complexes with either iron(II) and iron(III). The spin state of isolatable complexes was determined from spectroscopic and magnetic data, which also provided some information on the coordination geometry in these complexes.

The significance of the present work has to be found in the shuttle role hypothesized for the naturally occurring ligands used in the present work in the intracellular metabolism of iron. The chemical studies presented here support this hypothesis and complement previous biochemical and analytical observations. The capacity of these thiols in forming complexes with iron over a very broad pH range and in a variety of molar ratios to the metal, as well as the possibility that the bound metal undergoes easy redox chemistry without loss of coordination by the ligand represent indeed a rather unique combination of useful properties.

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References

1 F. Bonomi and S. Pagani, *Eur. J. Biochem., 155* (1986) 295.
2 F. Bonomi, A. Cerioli and S. Pagani, *Biochim. Biophys. Acta, 994* (1989) 180.
3 S. Pagani, F. Bonomi, P. Caracino, A. Pozzi and F. Cariati, *Inorg. Biochem., 190* (1989) 3.
4 F. Bonomi and S. Pagani, *Eur. J. Biochem., 199* (1991) 181.
5 F. Bonomi, S. Pagani and D. M. Kurtz, *Eur. J. Biochem., 148* (1985) 67.
6 S. Pagani, S. Iametti, G. Cervato and B. Cestaro, *Biochem. Int., 18* (1989) 923.
7 F. Bonomi, F. Cariati, G. Crisponi, F. Cristiani, A. Diaz, A. Pozzi and R. Zanoni, *Inorg. Chim. Acta, 192* (1992) 237.
8 F. Cariati, F. Bonomi, S. Iametti, D. M. Kurtz, S. Pagani, A. Pozzi, U. Russo and R. Zanoni, *Recl. Trav. Chim. Pays-Bas, 106* (1987) 425.
9 E. Rizzarelli, personal communication.
10 P. M. May and D. R. Williams, in D. J. Legget (ed.), *Computational Methods for Determination of Formation Constant,* Plenum, New York, 1985, Ch. 3.
11 L. Zekany and I. Najypat, in D. J. Legget (ed.), *Computational Methods for Determination of Formation Constant,* Plenum, New York, 1985, Ch. 8.
12 J. A. McCleverty, *Prog. Inorg. Chem., 10* (1968) 49.
13 Y. Nishida, S. Oshio, S. Kida and Y. Maeda, *Inorg. Chim. Acta, 26* (1987) 207.
14 R. E. Richards and H. W. Thompson, *J. Chem. Soc.,* (1947) 1248; N. B. Colthup, L. H. Daly and S. E. Wiberly, *Introduction to Infrared and Raman Spectroscopy,* Academic Press, New York, 1964.
15 G. B. Deacon and R. J. Phillips, *Coord. Chem. Rev., 33* (1980) 227.
16 E. König, G. Ritter and B. Kanellakopulos, *J. Chem. Phys., 58* (1973) 3001; E. König and K. Madeja, *Inorg. Chem., 7* (1968) 1848; E. König and R. Schnakig, *Inorg. Chim. Acta, 7* (1973) 383.
17 R. Aasa, *J. Chem. Phys., 52* (1970) 3919.
18 G. Harris, *Theor. Chim. Acta, 5* (1966) 379; T. L. Bohan, *J. Magn. Reson., 26* (1977) 109; M. Weissbluth, *Struct. Bonding (Berlin), 2* (1967) 2.
19 J. S. Griffith, *The Theory of Transition Metal Ions,* Cambridge University Press, Cambridge, UK, 1964.
20 A. Hudson and M. J. Kennedy, *J. Chem. Soc. A,* (1969) 1116.
21 D. W. Stephan, G. C. Papaefthymiou, R. B. Frankel and R. H. Holm, *Inorg. Chem., 22* (1983) 1550.
22 E. König and K. Madeja, *J. Am. Chem. Soc., 88* (1966) 4528.
23 V. Valenti, P. Fantucci, F. Cariati, G. Micera, M. Petrera and N. Burriesci, *Inorg. Chim. Acta, 148* (1988) 191.