

8 Modelling Electrochemical Properties of Iron Containing Enzymes and Siderands

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Abstract

We describe the synthesis, structures and properties of novel mono- and tetranuclear iron(III) complexes.

The mononuclear iron(III) species is formed by a new type of siderand without any catechol or hydroxamate unit and characterized by X-ray structure determination, Mößbauer, SQUID, EPR and cyclovoltammetric measurements.

In order to get a better understanding of the redox activity of enzymes we studied the electrochemical behaviour of new tetranuclear iron complexes and proved two simple methods to adjust their redox potentials to a given value ("redox tuning"). X-ray structure determination, Mößbauer studies and electrochemical investigations are reported as well.

8.1 Introduction

Polynuclear metal clusters have attracted great interest during the past few years (Wieghardt 1989). There are many different reasons for researchers to work in this field of chemistry. On one hand these metal complexes could be used as models for the active sites in enzymes, for example the tetranuclear manganese cluster in the photosystem II (an apparatus for the water oxidation by light in green plants and algae) or the ubiquitous iron-sulfur clusters that play an outstanding role in many electron transport systems.

On the other hand these non-natural systems, formed in simple experiments with high yields, are very useful to study the process of self-organisation at a fundamental level. Subsequently it should be possible to use similar components to create

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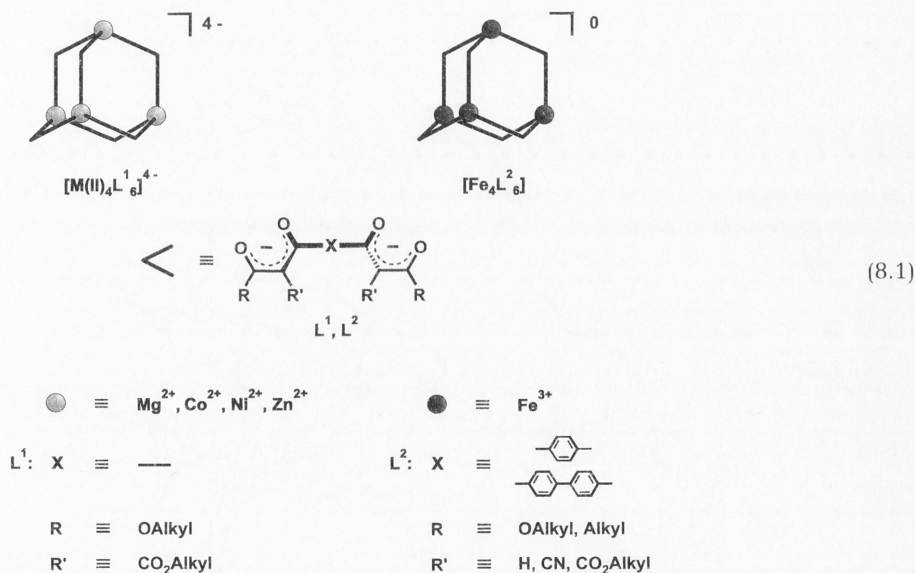
new materials with desired material properties, like magnetic, electric, optic or catalytic activities.

Furthermore compounds of this type containing cavities may be used to carry out basic studies in the field of host-guest chemistry. Hosts are the synthetic analogues of receptors and guests are the corresponding substrates, so that it should be possible to mimic the naturally occurring systems (Cram and Cram 1994; Vögtle 1989).

8.2 Tetranuclear iron chelate complexes

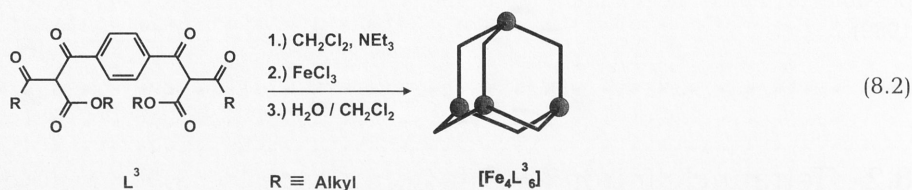
8.2.1 X-ray determination

While we were working in the field of multinuclear metal-chelate complexes we obtained tetranuclear adamantanoid $[M(II)_4L_6]^{4-}$ chelate complex anions (Saalfrank et al. 1990). By slight changes in the experimental conditions and the use of trivalent metals like Fe(III) and spacers ligands we also accomplished the synthesis of neutral tetranuclear chelate complexes $[Fe_4L_6^2]$ (Saalfrank et al. 1993) (see Formula 8.1).



This strategy allows us to build up systems with cavities of different shape and size (an important feature for applications in the field of host-guest chemistry where the cavities often have to be adjusted to the need of the guest) (Saalfrank et al. 1994a).

We have also been interested in the synthesis of novel ligands that enable different coordination modes in binding Fe(III) to learn more about the favoured coordination sites of iron in such complexes. We have found that the reaction of ligands of type L^3 with NEt_3 and $FeCl_3$ in CH_2Cl_2 and subsequent aqueous work up yields a dark red powder (Formula 8.2).



By recrystallizing the material from $CHCl_3/Et_2O$ we were able to obtain crystals suitable for X-ray analysis. This proves that we synthesized a neutral tetranuclear iron(III)-chelate complex. The core of the structure consists of a regular tetrahedron that is formed by the iron centers. The six edges of the tetrahedron are each bridged by the bis-(bidentate), doubly negatively charged ligands L^3 . Each of the four iron centers is octahedrally coordinated by six oxygen atoms (Figure 8.1).

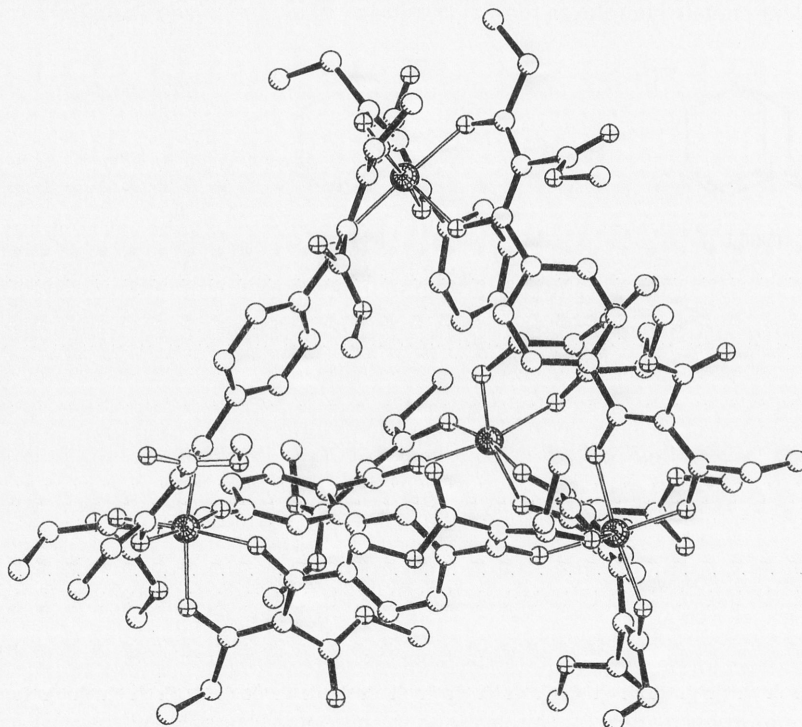


Figure 8.1: X-ray structure of $[Fe_4L^3_6]$, Fe(III) globular, O-crossed, C-shaded; H atoms and solvent molecules omitted for clarity.

Two pairs of enantiomers [(Δ) -fac, (Λ) -fac und (Δ) -mer, (Λ) -mer] are in principle possible for octahedral complexes of type MA_3B_3 [for bidentate ligands $M(AB)_3$]. The $Fe_4L_6^3$ complex shows in the solid state exact S_4 symmetry and is therefore achiral. This means, that the ligands are facially coordinated to the metal and that two of the four centers show identical configuration [(Λ, Λ) -/ (Δ, Δ) -fac]. This result is in concordance with recently investigated tetranuclear spacer complexes (Saalfrank et al. 1993; Raymond et al. 1996).

The space group determination is rather difficult because some of the systematic extinctions are falsified by reflex overlaps because of the extremely elongated c axis (82 Å). The extinctions suggest the space group $C222_1$. According to this result the asymmetric unit consists of 1.5 molecules [$Fe_4L_6^3$] as well as only partly localized diethyl ether and chloroform molecules. Two thirds of the [$Fe_4L_6^3$] tetrahedra could be refined without any problems whereas in the remaining molecules, situated on the diadic axis (parallel to b), the iron atoms are disordered. The ligands in this area are completely disordered. Despite these problems nearly all atomic layers could be localized (Figure 8.2). The O atoms of the keto functions coordinate to the metal whereas the O atoms of the ester residues stay uncoordinated (this was deduced from the temperature coefficients).

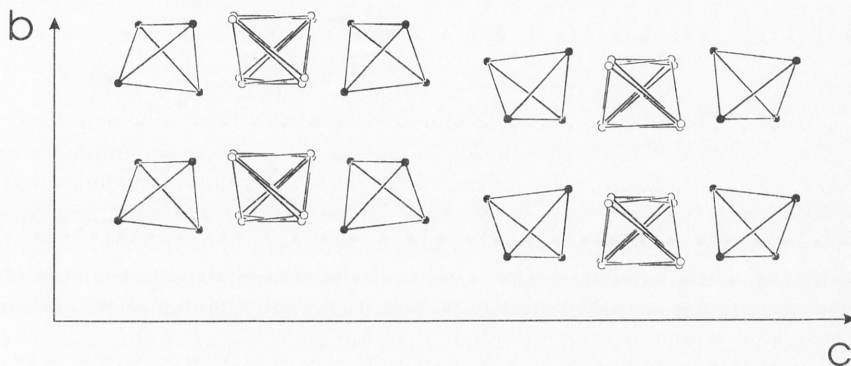


Figure 8.2: Alignment of the localized and disordered [$Fe_4L_6^3$] tetrahedra in [100].

8.2.2 Mößbauer studies

To come to a better understanding of the Fe coordination spheres we carried out further experiments. In a first step we looked at the Mößbauer spectra recorded at different temperatures (77 K and 4.2 K) (see Figure 8.3). The result of two nearly identical spectra excludes a high-spin/low-spin transition. Both measurements exhibit a signal broadened by relaxation phenomena caused by interactions between the metal centers with an isomeric shift of $\delta = 0.7 \text{ mms}^{-1}$. The value of the isomeric shift and the missing quadrupolar splitting suggest high-spin iron(III) centers in an octahedral coordination sphere. This is in agreement with the results of the X-ray analysis.

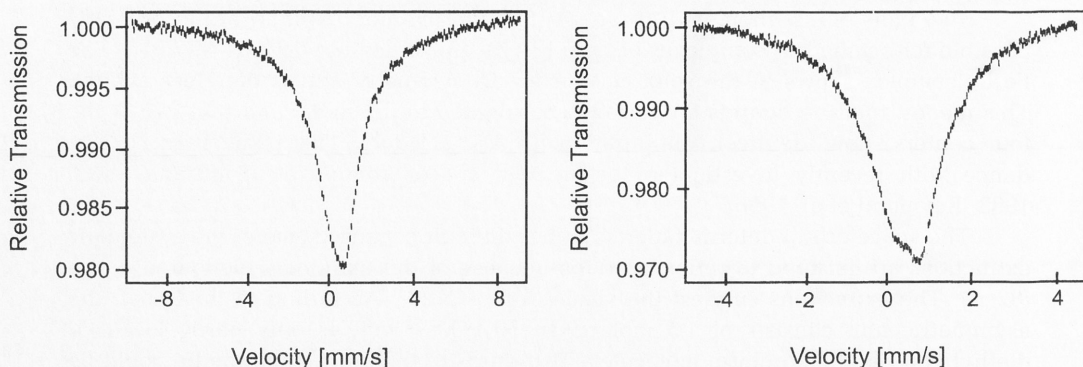


Figure 8.3: Mößbauer spectra of $[\text{Fe}_4\text{L}_6^3]$ at 4.2 K (left) and at 77 K (right).

8.2.3 Electrochemical investigations

The electrochemical behaviour of these complexes is of particular interest. By gaining deeper insight in this field the mode of action of redox active enzymes with multinuclear metal clusters in the active sites could be studied.

Electrochemical studies show the following results: cyclic voltammetric measurements at standard conditions (chart speed 250 mVs^{-1} and TBAHF as supporting electrolyte) exhibit a broad signal for reduction (this suggests a reorganization during the redox process) and a sharper one for back oxidation. The peak separation is rather large (250–340 mV). For this reason a half-wave potential could not be measured and so we carried out experiments under thin-layer conditions. No signal splitting could be observed in contrast to the unspaced systems (Saalfrank et al. 1994 b). This means there is no interaction between the iron centers. A multisweep experiment is mainly reversible. The calibration with ferrocene shows a one-potential-four-electron transfer with a half-wave potential of $E_{1/2}^{\text{Red}} = -720 \text{ mV}$ (vs Ag/AgCl) (Figure 8.4).

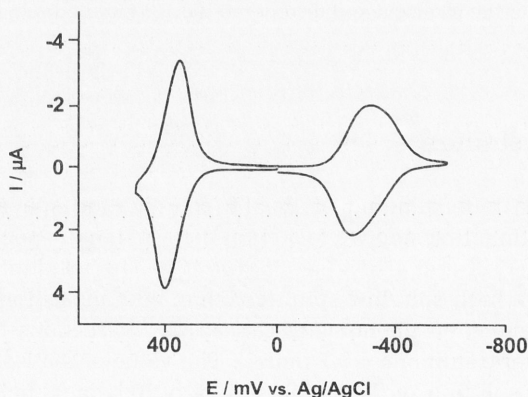


Figure 8.4: Cyclovoltammogramme of $[\text{Fe}_4\text{L}_6^3]$ vs Ag/AgCl.

The spectroelectrochemistry is completely reversible. In contrast to the unsparred iron complexes there is a continuous change of spectral behaviour during the decrease of the electrochemical potential. No partial processes could be detected. Only a slight shift of the isosbestic points was observed. The educt shows absorption at 242 nm, 300 nm and a shoulder at 428 nm, the peaks of the product occur at 250 nm, 315 nm and with a weaker extinction at 533 nm (Figure 8.5).

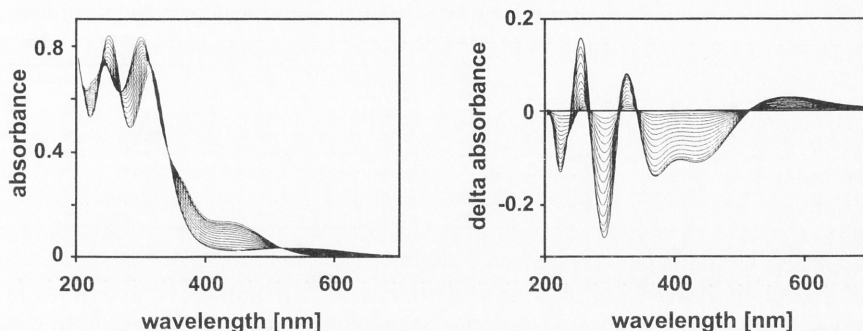
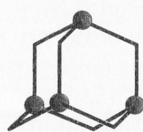
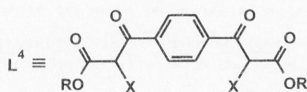


Figure 8.5: Spectroelectrogramme of $[\text{Fe}_4\text{L}_6^3]$.

In naturally occurring Fe/S clusters the stability and the redox potential is influenced by small changes in the protein skeleton (Stephenst et al. 1992). In general different factors like polarity of the direct environment of the active site (Sligar and Rodger 1991), the possibility to interact with solvent molecules (in vivo water) or specific electrostatic interactions are responsible for these changes (Diederich et al. 1994; Moore 1983). To get an idea of the mode of action of our metal complexes as models for the active sites in enzymes we carried out further electrochemical studies with $[\text{Fe}_4\text{L}_6^4]$ (Formula 8.3).



$[\text{Fe}_4\text{L}_6^4]$



(8.3)

Coarse adjustment of the redox potential is achieved by variation of the substituents X in α -position to the two coordinating oxygen atoms. Whereas the redox potential of $[\text{Fe}_4\text{L}_6^4]$ (X = H; R = Me) is $E_{1/2} = -985$ mV (all potentials vs ferrocen/ferrocenium) the complex $[\text{Fe}_4\text{L}_6^4]$ (X = CN; R = Me) shows a half-wave potential of -275 mV. This expected behaviour could be explained by the electron withdrawing effect of the cyano-function and the resulting reduced electron density at the iron centers. Fine tuning of the redox potential is achieved by variation of the ester residues R. The experiments show that there is a correlation between the residue R and the corresponding potential. By varying the residues from methyl, ethyl, i-propyl, i-amyl to cyclo-hexyl a change of

the redox potential could be observed. At this time we cannot decide whether the shift of the potential is due to the steric hindrance, the changed interaction with solvent molecules or the different inductive effects of the alkyl substituents (Table 8.1).

Table 8.1: Tetranuclear iron(III)-chelate complexes measured in dichloromethane, chart speed 50 mVs⁻¹.

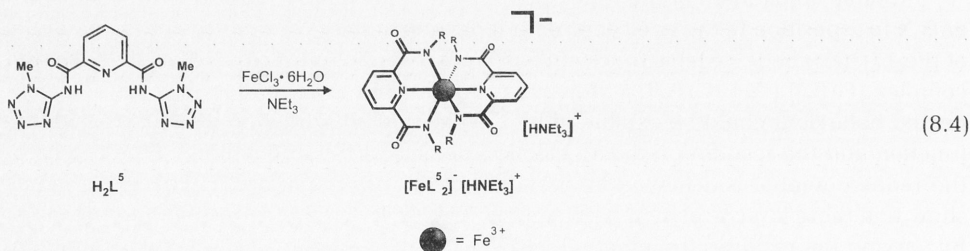
ester residue R	half wave potential $E_{1/2} = [\text{mV vs Fc/Fc}^+]$	peak potential separation $\Delta E = [\text{mV}]$
methyl	-275	180
ethyl	-365	115
isopropyl	-410	150
iso-amyl	-375	210
cyclohexyl	-430	260

All in all we proved that it is possible to change the half-wave potentials of the complexes by different methods (variation of the substituents X in α -position respectively changing the ester residues R) in such a way, that the redox potentials could be adjusted in a large scale. We call this process "redox tuning".

8.3 Siderands

To come to a better understanding of the extraordinary properties of naturally occurring siderophores, a wide range of analogous model compounds, so-called siderands has been synthesized recently and their ability of complex formation has been studied (Raymond et al. 1991; Vögtle and Seel 1992). In analogy to the natural systems these compounds contain catechol or hydroxamic acid ligands which show high affinity to di- or trivalent metal ions like iron(III). In contrast to these results our model complex $[\text{FeL}_2]^-$ comprises no catechol or hydroxamate units but is nevertheless soluble in water.

Reacting ligands of type H_2L^5 with NEt_3 and FeCl_3 in CH_2Cl_2 , filtering the solution free from the precipitating HNEt_3Cl yields a dark red powder. The anionic siderand $[\text{FeL}_2]^-$ is isolated as the triethylammonium salt (Formula 8.4).



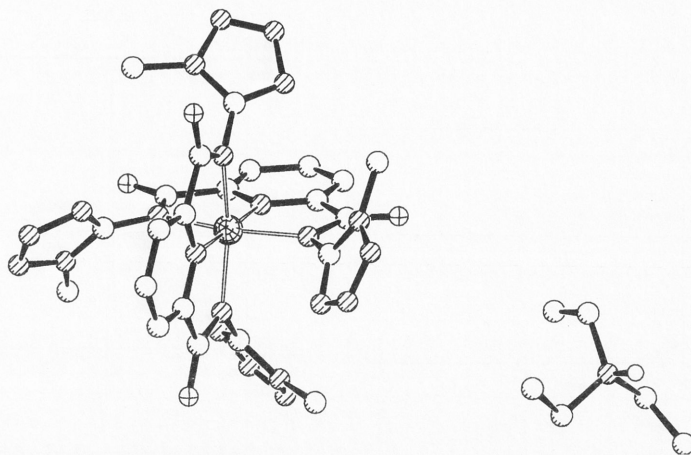


Figure 8.6: X-ray structure of $[\text{FeL}_5]^{2-}$, Fe(III) globular, O-crossed, C-shaded, N-hatched; H atoms omitted for clarity.

For an unambiguous characterization we carried out an X-ray crystallographic structure analysis (Figure 8.6).

To prove the oxidation state of the metal center several Mößbauer, EPR, magnetic and electrochemical studies were carried out. The Mößbauer spectrum (4.2 K) shows an asymmetric doublet that could be fitted (in first approximation) with two superimposed doublets. The isomer shifts $\delta = 0.03 \text{ mms}^{-1}$ and $\delta = 0.135 \text{ mms}^{-1}$ and the quadrupole splittings $\Delta E_Q = 3.55 \text{ mms}^{-1}$ and $\Delta E_Q = 3.35 \text{ mms}^{-1}$ are consistent with two slightly different iron(III) low-spin positions in the solid state. The inconsistency of the X-ray and the Mößbauer data with respect to the localization of the iron(III) centers is yet not fully understood and may be due to polymorphism (Figure 8.7).

The EPR spectra exhibit a low spin state ($S = \frac{1}{2}$) of the iron(III) center at $g = 2.2$.

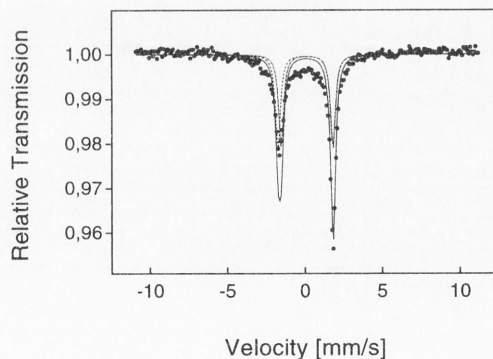


Figure 8.7: Mößbauer spectrum of $[\text{FeL}_5]^{2-}$ at 4.2 K.

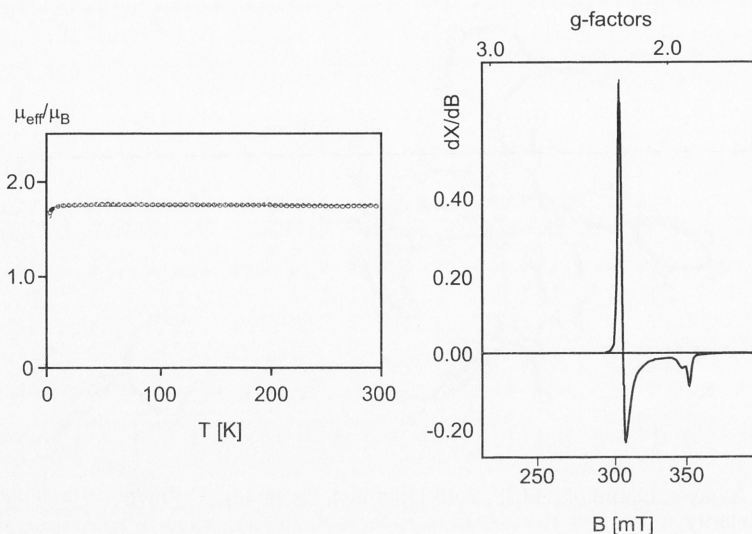


Figure 8.8: SQUID and EPR spectrum of $[\text{FeL}_2]^{5-3}$.

SQUID measurements show a temperature-independent paramagnetism of $150 \cdot 10^{-6} \text{ cm}^3 \text{ mol}^{-1}$ (Figure 8.8).

The cyclic voltammogramme of $[\text{FeL}_2]^{5-}$ in acetonitrile exhibits a reversible redox process for the reduction of the iron(III) center to iron(II) at chart speeds of $125\text{--}1000 \text{ mVs}^{-1}$. The relatively high value of the half wave potential of $E_{1/2} = -690 \text{ mV}$ proves the stability of the iron(III) state. We believe that the third peak at $E = +660 \text{ mV}$ is due to the oxidation of the metal center to Fe(IV). An exact localization of this potential is not possible because of a further oxidation of the ligand (Figure 8.9).

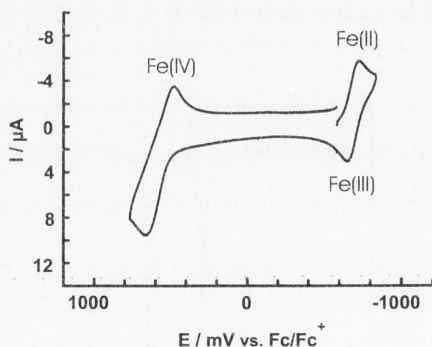


Figure 8.9: Cyclic voltammogramme of $[\text{FeL}_2]^{5-3}$ vs Fc/Fc^{3+} .

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