An Electrochemical Study of Thiohydroxamate and Hydroxamate Complexes of Iron(III)

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Direct-current polarographic, cyclic voltammetric, and constant-potential coulometric measurements have been made on acetone solutions of tris(thiohydroxamato)- and tris(hydroxamato)-complexes of iron(III), [Fe{ONR'-CR(=X)}$_3$] (X = S or O; R = H, Ph, C_6H_4Me-*p*, or CH_2Ph; R' = H, Me, Ph, or cyclohexyl). In all cases rapid one-electron reductions to Fe^{II} are observed with the reduction potential for the thiohydroxamate chelates being less cathodic than those of the hydroxamates, consistent with the softer S-donor ligand stabilizing the iron(II) state. A notable feature is the reversible electron transfer which occurs when the ligand nitrogen is substituted with an alkyl or aryl group. In contrast, when N is bonded to an hydrogen atom an irreversible Fe^{III}–Fe^{II} electron transfer is observed, probably because of decomposition of the iron(II) complex. The relation of the present results to iron-release mechanisms in microbial iron-transport compounds (siderophores) is briefly discussed.

WE have recently described the structural and electronic features of a range of iron(III) thiohydroxamate chelates of the type [Fe{ONR'CR(=S)}$_3$].[1-3] Our interest in compounds of this type stemmed from a general interest in iron compounds involved in biological transport.[4] One such thiohydroxamate complex, with R = H, R' = Me (termed Thioformin [5] or Fluopsin F [6]), can be obtained from cultures of *Pseudomonas Fluorescens.* It displays potent antibiotic properties and may be involved in bacterial iron transport.[7] The structure of the chemically synthesized tris(*N*-methylthioformohydroxamato)iron(III) chelate displays a *facial* arrangement of the S,O donor groups (Figure 1). The thiohydroxamate chelates, like their hydroxamate analogues (and siderophores in general), display high-spin $S = \frac{5}{2}$ electronic behaviour, except for some preparations of the benzothiohydroxamate derivative which show spin-equilibrium features.[3]

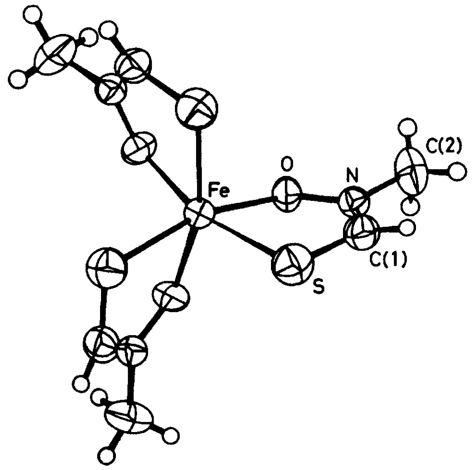


FIGURE 1 Crystal structure of tris(*N*-methylformothiohydroxamato)iron(III) viewed down the *C*3 axis (see ref. 1 for details)

In probing the features of chelating ligands such as hydroxamates, thiohydroxamates, and catecholates which render them appropriate for iron transport, it seemed important to gain an understanding of the redox properties of their chelates. Siderophores are certainly not implicated in electron-transfer processes as are cytochromes and ferredoxins, but changes in valency state of the metal ion have been postulated in their transport mechanisms.[7] It is only since completion of the present work that the reduction potentials of Fe^{III}–Fe^{II} in ferrichrome and ferrioxamine have been shown by Raymond and co-workers [8,9] to occur within the range of physiological reducing agents.

In this paper we describe polarographic, cyclic voltammetric, and electrolysis studies on acetone solutions of tris(thiohydroxamato)- and tris(hydroxamato)-iron(III) complexes.

EXPERIMENTAL

The thiohydroxamatoiron(III) complexes were prepared as described earlier.[1,3] Tris(pyridine-2-thionato *N*-oxide)iron(III), [Fe(pyot)$_3$], was prepared by the method of Robinson [10] or by treating the ligand with [Fe(acac)$_3$] (acac = pentane-2,4-dionate) in ethanol. Tris(5,5-dimethyl-4-phenylpyrrolidine-2-thionato 1-oxide)iron(III), [Fe(dpyrot)$_3$], was obtained as black crystals from [Fe(acac)$_3$]. The ligand was supplied by Dr. D. St. C. Black. The hydroxamate complexes were synthesized by published methods.[11]

In the electrochemical measurements May and Baker ' Pronalysis ' acetone was employed. The supporting electrolyte tetraethylammonium hexafluorophosphate was obtained as white needles by the reaction of tetraethylammonium bromide (B.D.H. Chemicals) and K[PF$_6$] (PCR Chemicals) in water and recrystallizing the product from methanol–light petroleum. The supporting electrolyte gave no electrochemical response in the accessible range.

A PAR 170 instrument with IR compensation was used for electrochemical measurements in conjunction with a Tektronix storage oscilloscope. Direct-current (d.c.) polarography involved the use of a three-electrode system incorporating the dropping-mercury working electrode (d.m.e.), Ag/AgCl (0.1 mol dm^{-3} LiCl) reference electrode (Metrohm EA 427), and platinum-wire auxiliary electrode. The concentrations of supporting electrolyte and electroactive species were 0.1 and 1 × 10^{-3} mol dm^{-3} respectively. Solutions were degassed with high-purity nitrogen. The solutions were thermostatted at 25 ± 1 °C.

Cyclic voltammetry was conducted at mercury or platinum working electrodes. A single drop of mercury at the d.m.e. was employed. Attempts to use the hanging-mercury-drop electrode were unsuccessful; the mercury drop fell away prematurely due to the low surface tension of the solvent. Fast scans were required at the d.m.e. to eliminate the effect of size increase of the drop.[12]

The platinum wire used in cyclic voltammetry had to be pre-treated in the same way before each experiment in order to obtain reproducible data, because of surface contamination. This treatment was carried out using the method of Adams [13] and repeated whenever the electrode became contaminated.

Constant-potential coulometry was carried out in a conventional H-cell where the auxiliary electrode was separated from the working electrode by two sintered-glass frits. Reductions were performed either on a mercury-pool working electrode of area 11.3 cm^2 or on platinum gauze (6.3 cm^2).

RESULTS

The electrochemical behaviour of some of the free ligands, in the form of their sodium or potassium salts, was initially investigated to see if they were electroactive in the range of the appropriate working electrode in acetone. The d.c. polarograms of the following salts showed no reduction wave in the range +0.2 to −1.7 V *vs.* Ag/AgCl: K[ONHCPh(=O)], Na[ONHCPh(=S)], Na[ONPhCPh(=S)], and Na[ONMeCH(=S)]. Cyclic voltammetry at a stationary platinum electrode revealed that the free ligands were oxidized at quite positive potentials, 1.0—1.4 V *vs.* Ag/AgCl (Table 1). In most cases the electrode process was irreversible; however, in the case of Na[ONPhCPh(=S)] the process was quasi-reversible with a peak separation of 200 mV at a voltage scan rate of 200 mV s^{-1} and increased with increasing scan rate. Chemical oxidation of the sodium salts of thiohydroxamic acids is known to occur with oxidizing agents such as hydrogen peroxide or iodine to yield the corresponding disulphides, RC(NR′OH)SSC(NR′OH)R.

TABLE 1

Parameters for oxidation of Na[ONR′CR(=X)] and [Fe{ONR′CR(=X)}$_3$] *

			Na[ONR′CR(=X)]			[Fe{ONR′CR(=X)}$_3$]		
R	R′	X	$E_p{}^a$/ V	$i_p{}^a$/ $i_p{}^c$	ΔE_p/ mV	$E_p{}^a$/ V	$i_p{}^a$/ $i_p{}^c$	ΔE_p/ mV
Ph	H	O	1.30			1.36		
Ph	Ph	O	1.32			1.34		
Ph	H	S	1.12			1.13		
Ph	Ph	S	1.12	1.4	200	1.16	1.46	210
Ph	Me	S	1.03	1.3	210	1.06	1.32	205
H	Me	S	1.02			1.13		

* Potentials relative to Ag/AgCl at 25 °C. [a] All measurements at 200 mV s^{-1}.

A great deal of difficulty was experienced in selecting a supporting electrolyte which did not react with iron(III) complexes of the type [Fe{ONHCR(=S)}$_3$], *i.e.* complexes with non-N-substituted thiohydroxamic acids. The supporting electrolyte tetraethylammonium perchlorate reacted rapidly with acetone solutions of the iron(III) complexes and the deep violet solutions began to decolourize. In some cases a small quantity of unidentified black solid was precipitated from solution. Some of the complexes were found to be stable in acetone–tetraethylammonium hexafluorophosphate solution for a period of *ca.* 2 h. The stability of the solutions was monitored by changes in the visible spectrum.[3] The three complexes of moderate stability were [Fe{ONHCPh(=S)}$_3$], [Fe{ONHCC$_6$H$_4$Me-*p*-(=S)}$_3$], and [Fe{ONHCCH$_2$Ph(=S)}$_3$]. In contrast, iron(III) complexes of the N-substituted thiohydroxamic acids and two cyclic thiohydroxamic acids were stable in [NEt$_4$][ClO$_4$] and [NEt$_4$][PF$_6$] for long periods of time.

Iron(III) *Thiohydroxamates and Hydroxamates,* [Fe{ONHCR(=X)}$_3$] (X = O *or* S).—The d.c. polarogram of tris(benzohydroxamato)iron(III) which has R = Ph and X = O showed only one drawn-out wave in the region −0.6 to −1.2 V [Figure 2(*a*)]. In view of the large potential range over which this wave occurred, it would appear that several processes are occurring upon reduction. The value of the limiting current divided by the concentration (i_l/c) was found to be much higher than that expected for a one-electron reduction of Fe^{III} to Fe^{II}. The cyclic voltammogram of this complex on a platinum wire showed only one cathodic peak over the same voltage range with $E_p{}^c = -0.84$ V, no anodic peak being observed in the reverse cycle at fast scan rates. This behaviour is consistent with an irreversible Fe^{III}–Fe^{II} couple complicated by other electrochemical processes.

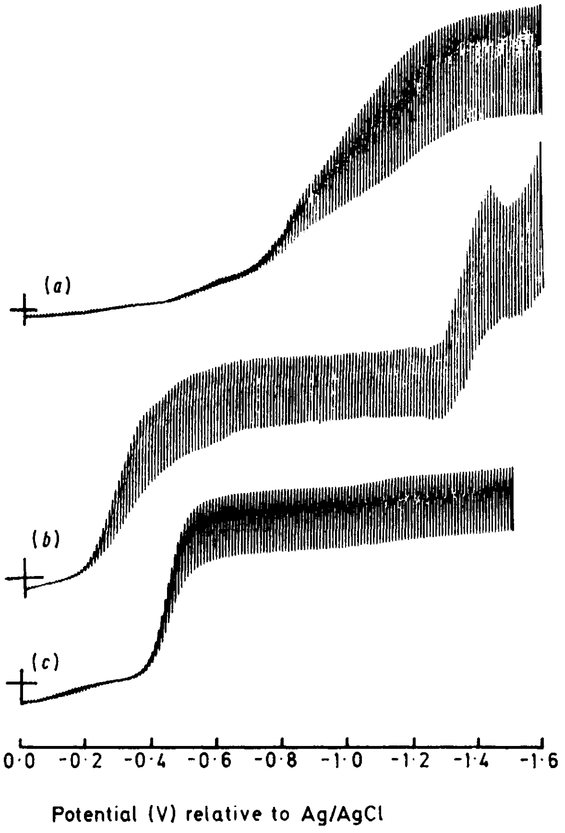


FIGURE 2 D.c. polarograms of (*a*) [Fe{ONHCPh(=O)}$_3$], (*b*) [Fe{ONHCPh(=S)}$_3$], and (*c*) [Fe{ONPhCPh(=S)}$_3$], in acetone. Scan rate 2 mV s^{-1}

Direct-current polarography of the three thiohydroxamate chelates which were reasonably stable in acetone–[NEt$_4$][PF$_6$] were unfortunately complicated by reaction with the mercury electrode. Thus, the complexes with R = Ph, C$_6$H$_4$Me-*p*, or CH$_2$Ph all showed two waves in the cathodic sweep range, the first at *ca.* −0.3 V and the second at −1.4 V [Figure 2(*b*)]. The wave at −1.4 V is present only when mercury is used as the working electrode. Close examination of the wave at −0.3 V revealed that it in fact consisted of two: a major wave and a minor wave at a slightly more negative potential. The mercury pool forming at the bottom of the cell consisted of tiny spheres which showed no tendency to recombine, suggesting that some interaction of the iron complex with the mercury surface was occurring.

TABLE 2

Parameters for first reduction of [Fe{ONR′CR(=X)}$_3$] complexes *

			D.c. polarography (Hg)			Cyclic voltammetry (Hg)			Cyclic voltammetry (Pt)		
R	R′	X	$E_{\frac{1}{2}}$/V	Slope †/ mV	i_d/c ‡	E_p^c/V	i_p^c/i_p^a §	ΔE_p/ mV	E_p^c/V	i_p^c/i_p^a ¶	ΔE_p ¶/ mV
Ph	H	O	‖		2.23				-0.84_2		
Ph	Me	O	-0.88_9	64	1.27	-0.91_5	1.0	60	-0.93_3	1.07	80
Ph	Ph	O	-0.70_7	63	1.39	-0.73_4	1.0	61	-0.76_1	1.08	73
Ph	H	S	-0.21_3	108	1.19				-0.38_2		
C_6H_4Me-*p*	H	S	-0.27_9	94	1.23				-0.44_5		
CH_2Ph	H	S	-0.27_2	82	1.27				-0.47_5		
Ph	Me	S	-0.54_8	63	1.21	-0.57_5	1.0	60	-0.59_8	1.10	75
Ph	Ph	S	-0.42_6	62	1.14	-0.54_4	1.0	61	-0.46_1	1.02	68
H	Me	S	-0.51_6	63	1.60	-0.54_4	1.0	60	-0.55_2	1.01	62
H	Ph	S	-0.31_8	62	1.64	-0.34_6	1.0	62	-0.34_7	1.08	72
H	C_6H_{11}	S	-0.61_6	63	1.61	-0.64_5	1.0	61	-0.65_8	1.05	74
pyot			-0.41_1	60	1.48	-0.44_0	1.0	63	-0.46_2	1.04	82
dpyrot			-0.54_5	62	1.31	-0.57_5	1.0	60	-0.59_2	1.05	68

* Potentials relative to Ag/AgCl at 25 °C. † Determined from slope of *E vs.* log[$i/(i_d - i)$]. ‡ Units mA dm^3 mol^{-1}. § Scan rate 5 V s^{-1}. ¶ Scan rate 200 mV s^{-1}. ‖ Too drawn-out for reliable data.

Independent tests of a solution of the iron(III) complex with mercury showed similar fragmentation. The minor component at −0.3 V and the wave at −1.4 V are therefore spurious and associated with interaction with or adsorption onto the mercury surface. Other sulphur-containing metal chelate complexes have displayed similar behaviour on mercury electrodes.[14-16] Despite this effect the diffusion current for the major wave at *ca.* −0.3 V varied linearly with the square root of the height of the mercury column for each compound, suggesting that the electrode process is diffusion controlled. A log plot analysis of *E* against log [$i/(i_d - i)$] was linear for each compound; however, the slopes were much higher than predicted for one-electron reversible reduction (Table 2). The i_d/c value was similar to that of the chelates with N-substituted ligands described below. The results suggest that the electrode process is an irreversible metal-based reduction. Cyclic voltammetry on these three complexes was carried out on a platinum-wire electrode and irreversible behaviour was observed as in the case of the tris(benzohydroxamato)-complex, only one cathodic peak being observed in the voltage range used (Figure 3) and at scan rates up to 200 V s^{-1}. This peak corresponds to an irreversible Fe^{III}–Fe^{II} electron transfer. The peak positions shifted to more negative potentials with increasing scan rate (Table 3). On scanning to positive potentials the thiohydroxamate and hydroxamate complexes all showed a single irreversible oxidation peak at approximately the same potential as recorded for the sodium salts of the ligands.

TABLE 3

Effect of scan rate on cyclic voltammogram of [Fe{ONHCR(=S)}$_3$] complexes *

Scan rate/ V s^{-1}	E_p^c/V		
	R = Ph	R = C_6H_4Me-*p*	R = CH_2Ph
0.05	-0.35_7	-0.40_1	-0.41_3
0.10	-0.36_6	-0.42_4	-0.42_5
0.20	-0.38_2	-0.45_1	-0.44_8
0.50	-0.40_4	-0.47_2	-0.46_6
1.0	−0.42	−0.48	−0.47
2.0	−0.42	−0.50	−0.49
5.0	−0.44	−0.53	−0.52
10.0	−0.45	−0.55	−0.53
20.0	−0.47		
50.0	−0.47		
100.0	−0.48		
200.0	−0.51		

* Potentials relative to Ag/AgCl at 25 °C.

The Complexes [Fe{ONR′CR(=X)}$_3$] *and Two Cyclic Thiohydroxamates,* [Fe(pyot)$_3$] *and* [Fe(dpyrot)$_3$].—These complexes, which contain N-substituted ligand groupings, all exhibited only one well defined polarographic reduction wave at a potential near −0.8 V for the hydroxamates and −0.5 V for the thiohydroxamates (Table 2). One such polarogram is shown in Figure 2(*c*) for tris(*N*-phenylbenzothiohydroxamato)iron(III); those for the other com-

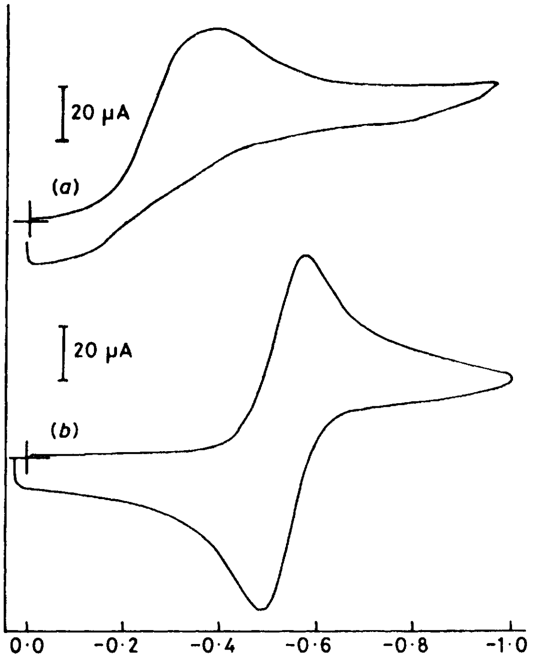
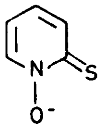


FIGURE 3 Cyclic voltammograms of (*a*) [Fe{ONHCR(=S)}$_3$] and (*b*) [Fe{ONMeCPh(=S)}$_3$] in acetone at a platinum electrode. Scan rate 200 mV s^{-1}

plexes had similar characteristics. Plots of i_d *versus* $h_{Hg}^{\frac{1}{2}}$ were linear as were plots of E against log $[i/(i_d - i)]$, the slope of the latter being 60 ± 3 mV. The criteria for a reversible one-electron electrode process are therefore satisfied. There was no observed reaction with mercury as occurred with the non-N-substituted derivatives. Controlled-potential reduction on a mercury pool led to discharge of the purple colour of the thiohydroxamate complexes and an n value of 1 was deduced from integrating i *vs.* t plots. On reoxidation the purple colour was restored.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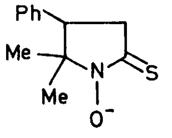
dpyrot

Cyclic voltammetry was performed on a single drop at the d.m.e. The voltammograms display characteristics typical of a reversible one-electron electrochemical reduction. The peak separation between cathodic and anodic peaks was equal to 60 ± 2 mV for all compounds and was independent of scan rate over the range 500 mV s^{-1} to 20 V s^{-1}. The quotient i_p^c/i_p^a was equal to 1 at high scan rates. At scan rates lower than 5 V s^{-1}, i_p^c/i_p^a was slightly less than 1 due to the mercury drop expanding in size during the measurement.[12] Cyclic voltammetry at a platinum electrode gave peak separation of *ca.* 60—80 mV indicative of a reversible one-electron process. Although a peak separation greater than 60 mV is not theoretically predictable, it is felt that surface effects cause the greater peak separation.

All of the complexes displayed an irreversible or quasi-reversible oxidation wave at *ca.* 1.0 V probably due to a ligand-based oxidation process.

DISCUSSION

Several interesting features have emerged from this study. In the iron(III) thiohydroxamate series rapid one-electron reduction (Fe^{III}–Fe^{II}) occurs both at the d.m.e. and at a stationary platinum electrode. The ease of reduction is observed experimentally to decrease in the order R = H > Ph > Me > cyclohexyl. This behaviour may be rationalized in terms of the electron-releasing or -withdrawing characteristics of the substituent groups on nitrogen and carbon. Martin and co-workers[17] observed a similar order in reduction for a large range of tris(dithiocarbamato)iron(III) chelates of the type $[Fe(S_2CNR_2)_3]$.

Changing the donor atoms from S,O to O,O, *i.e.* thiohydroxamate to hydroxamate, leads to a cathodic shift (*ca.* 0.3 V) in the reduction potential, that is the thiochelate is more easily reduced to the iron(II) state. A similar effect has been observed in comparative studies on tris(dithio-β-diketonato)iron(III) complexes, with S,S donor atoms, and the β-diketonato-analogues which have O,O donor atoms.[17] This effect is compatible with the softer sulphur donor stabilizing the lower oxidation state of the metal.

The magnitudes of the Fe^{III}–Fe^{II} reduction potentials in the hydroxamato-chelates are quite similar to those observed in other O,O chelates such as [Fe(acac)$_3$], $E_{\frac{1}{2}} = -0.58$ V (Hg) under similar conditions.[17] The recent study on the natural products ferrichrome A and ferrioxamine B likewise showed $E_{\frac{1}{2}}$ values similar in magnitude to those of the present model complexes, *viz.* −0.69 and −0.698 V (in water, *vs.* s.c.e.; 1 mol dm^{-3} KCl supporting electrolyte).[8] The magnitude of $E_{\frac{1}{2}}$ in the thiohydroxamate series is likewise similar to that observed in other sulphur ligand derivatives such as dithiocarbamates and dithio-β-diketonates.[15,17]

The most significant feature to emerge is the marked difference in the electrochemical behaviour displayed by the N-substituted and non-N-substituted chelates of both hydroxamate and thiohydroxamate ligands. On reduction the [Fe{ONR'CR(=X)}$_3$] chelates (X = O or S; R = Ph or H; R' = Me, Ph, or C_6H_{11}) and the two cyclic thiohydroxamate complexes, [Fe(pyot)$_3$] and [Fe(dpyrot)$_3$], show reversible one-electron transfer at the mercury and platinum electrodes. The electrode reaction is as in (1) where L = N-substituted hydroxamate or thiohydroxamate.

$$[Fe^{III}L_3] + e^- \rightleftharpoons [Fe^{II}L_3]^- \qquad (1)$$

The iron(II) species $[FeL_3]^-$ can be generated as a colourless complex in acetone by prolonged reduction on a mercury pool, but no crystalline derivatives have yet been obtained. Reversible Fe^{III}–Fe^{II} couples of this kind are now known for a number of sulphur-containing chelate complexes.[15-18]

In contrast, the complexes with R' = H, where the ligands are formed by acylation or thioacylation of NH_2OH, all show totally irreversible Fe^{III}–Fe^{II} couples. Two explanations may be generally considered to account for this electrochemical irreversibility.[19] First, if the charge-transfer rate constants (k_f,k_b) are small, the reaction will be irreversible [equation (2)]. The potential

$$\text{Ox} + ne^- \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \text{Red} \ (k_f,k_b \text{ small}) \qquad (2)$$

will be shifted cathodically and there is usually no current observed on the return potential sweep of a cyclic voltammogram. A similar response occurs if the product of the reduction undergoes a rapid irreversible chemical reaction such that no reverse electrochemical reaction can occur [equation (3)].

$$\text{Ox} + ne^- \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \text{Red} \xrightarrow{k_d} \text{Products} \ (k_d \text{ large}) \qquad (3)$$

These possibilities can sometimes be distinguished. In the first case, with k_f small, the potential should shift cathodically as the scan rate is increased. In the second, the cathodic shift is much less apparent at high scan rates. Depending on the value of k_d, as the scan rate is increased, i_p^a/i_p^c increases towards unity until the response for a reversible system is eventually obtained. If, however, k_d is very large, the response will be similar to that for an irreversible electron transfer, and it is difficult to distinguish the two mechanisms. Cyclic voltammetric measurements on the present [Fe{ONHCR(=S)}$_3$] complexes (R = Ph, C_6H_4Me-*p*, or CH_2Ph) as a function of increasing scan rate showed that the cathodic scan potential did increase. In the case of tris(benzothiohydroxamato)iron(III) no discernible anodic response was observed even at 200 V s^{-1}. The results suggest that either the reduction is occurring by an irreversible electron-transfer process or that the reduced species is rapidly decomposing. If rapid decomposition can be eliminated, the electrochemical process, *per se*, must be irreversible. In order to further study the process for $[Fe\{ONHCPh(=S)\}_3]$, constant-potential coulometry was carried out at a platinum-gauze electrode and an *n* value of *ca.* 0.85 was obtained. This number is consistent with a one-electron process where a small amount of the starting material has been removed by prior reaction with the supporting electrolyte as discussed above. Cyclic voltammetric measurements made before and after electrolysis showed that the reduced product undergoes an irreversible chemical reaction to give a new electroactive species. Thus, after complete reduction, the initial peak at —0.35 V [Figure 3(*a*)] was no longer evident and another irreversible process was observed with $E_p^c = -0.55$ V. This confirms that the complex undergoes complete chemical reaction or decomposition in the time scale of the electrolysis. It is important to note, however, that the chemical reaction is not rapid since the peak at —0.55 V does not appear in the cyclic voltammogram even at scan rates less than 0.1 V s^{-1}. It is thus apparent that the electrochemical reaction is actually irreversible and is followed by a chemical reaction giving an electroactive product in the classical ECE mechanism.[19,*]

Since the fundamental chemical difference between the two classes of compounds is the presence of or lack of an NH-O- group in the ligand it is tempting to look here for an explanation of the electrochemical differences. Under strongly alkaline aqueous conditions it is known [11] that this proton can be dissociated from tris(hydroxamato)- and tris(thiohydroxamato)-iron(III) complexes to yield hydroximato-anionic species, $[Fe\{ON=CR(X)\}_3]^{3-}$. The present solutions in acetone certainly give no evidence for such dissociation occurring in the iron(III) species, although it is possible that the reduced species $[Fe^{II}\{ONHRC(=X)\}_3]^-$ may lose protons more readily. We feel that this is not occurring since qualitative variations in effective ' pH ' by adding $[NEt_4][OH]$ did not show any shift in the Fe^{III}–Fe^{II} reduction potential which would be expected.

Relation to Intracellular Iron-release Mechanism in Siderophores.—The mechanism for the release of iron from hydroxamate siderophores is thought to occur *via* reduction of Fe^{III} to the weakly bound iron(II) state.[7,20] The dissociated metal-free siderophore can then be recycled to bind to free trivalent iron. The best known examples are ferrichrome A and ferrioxamine B shown in Figure 4, which are produced, for example, by *Ustilago sphaerogena* and *Streptomyces pilosus*, respectively. Both these compounds contain secondary nitrogen atoms substituted by CH_2 groups. As stated earlier the naturally occurring tris(*N*-methylformothiohydroxamato)iron(III) chelate may also be involved in microbial iron transport.

Although the present study on model hydroxamate and thiohydroxamate complexes can in no way give direct evidence on *in vivo* iron-release mechanisms, it does give information which may indirectly aid such investigation. First, it, and the recent study on ferrichrome A and ferrioxamine B, show that the iron(II) state is readily accessible with $E_{\frac{1}{2}}$ values in the range of physiological reductants such as NADH.[8,†] Further, the iron(II) state is more readily attained in the sulphur-containing chelates. The subsequent mechanism of dissociation or removal of the ligand grouping away from the iron(II) ion, implicit in the previously proposed mechanism, is not as clear cut as was perhaps thought. In the present N-substituted derivatives it was observed that the $[Fe^{II}L_3]^-$ species were stable for long periods as evidenced by the subsequent reoxidation to $[Fe^{III}L_3]$. It is possible, therefore, that the iron(II) siderophore has a finite lifetime in the cell and some other binding site might be required to displace the hydroxamic acid moiety. This is in qualitative agreement with the recent work of Ratledge and co-workers [21] on mycobacteria in which it is suggested that a binding group with preference for Fe^{II}, *e.g.* salicylate in *Mycobacterium smegmatis*, might displace the siderophore group from the metal.

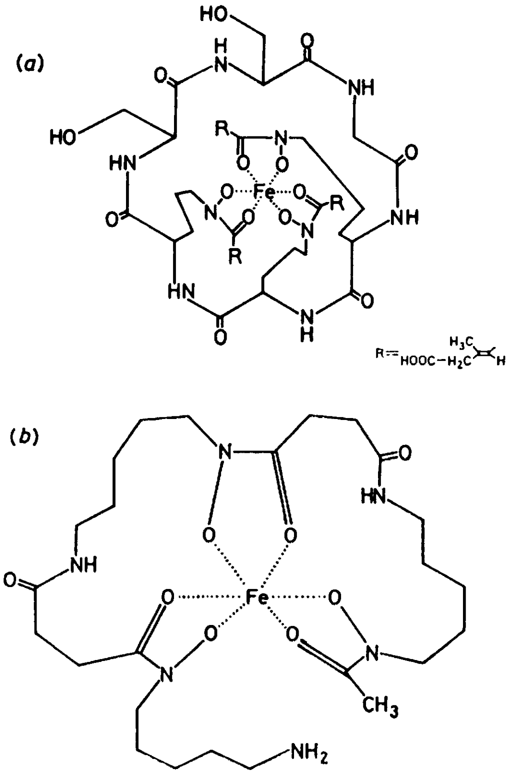

FIGURE 4 Structures of (*a*) ferrichrome A and (*b*) ferrioxamine B (see ref. 7)

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[*] Electron transfer followed by chemical reaction followed by electron transfer.

[†] NADH = Nicotinamide–adenine dinucleotide (reduced).

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