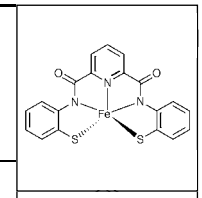
Coordination of carboxamido nitrogen to tervalent iron: insight into a new chapter of iron chemistry



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Although coordination of carboxamido nitrogen to Fe(III) center has been assumed to be improbable, research work during the past few years has demonstrated that Fe(III) complexes with ligated carboxamido nitrogens can be readily synthesized. The Fe(III)–N_{amido} bond distances lie in the range of 1.8–2.2 Å in the various low spin and high spin Fe(III) complexes. These complexes are stable in aqueous media and their redox parameters indicate that the carboxamido nitrogens provide significant stability to the Fe(III) center.

1 Introduction

In the excellent review by Sigel and Martin on the chemistry of metal–peptide complexes,[1] a problem with respect to the complexation of Fe(II) and Fe(III) by peptido nitrogen was discussed. Since the pH necessary for deprotonation of the peptide nitrogen is too high for Fe(II) and Fe(III) to exist in aqueous solution (both ions precipitate as hydroxides at pH $\geqslant$3),[2] it had generally been concluded that ligation of peptido nitrogen to iron was improbable. However, our research work in the area of iron bleomycin and related chemistry revealed that small ligands with peptide NH groups readily coordinate to both Fe(II) and Fe(III) centers in their deprotonated forms.[3–8] These findings along with reports from other groups[9–15] have provided some insight into the nature of the iron–peptide bond. In addition, the recent identification of coordination of peptido nitrogen from the peptide backbone to iron centers in the p-cluster of nitrogenase[16] and in the mononuclear non-heme iron center of nitrile hydratase[17,18] has raised more interest in this area. During the past few years, several complexes of tervalent iron with carboxamido nitrogen (peptido nitrogen is a subset of carboxamido nitrogen) donors have been structurally characterized. The majority of these complexes have two carboxamido nitrogens[3–6,8–10] and the rest have four such donors in the first coordination sphere.[7,11–14] In contrast, Fe(III) complexes with an odd number of coordinated carboxamido nitrogens have been limited[19,20] and no structural information is available so far. Collectively, the spectral and structural data for the Fe(III) complexes now indicate that coordination of carboxamido nitrogens to an Fe(III) center is *not unusual* and the coordination chemistry of Fe(III) complexes with peptides could be developed much like any other ligand. The purpose of this review is to highlight the synthetic routes to such complexes and to determine the effect(s) of the coordinated carboxamido group on their stability and redox properties.

2 Synthetic methods

To date, the ligands that have been employed to isolate Fe(III) complexes are cyclic or acyclic polydentate ligands with one,

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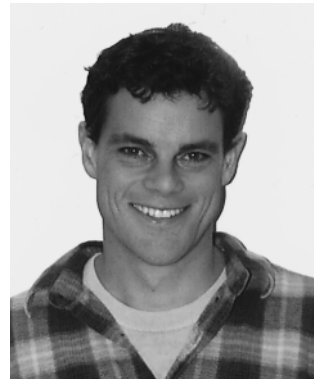

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two, or four carboxamide groups.† Since the focus of this review is on Fe(III) complexes for which the structures are known, the list of such ligands is limited to the ones shown in Fig. 1. These ligands were designed for various reasons in

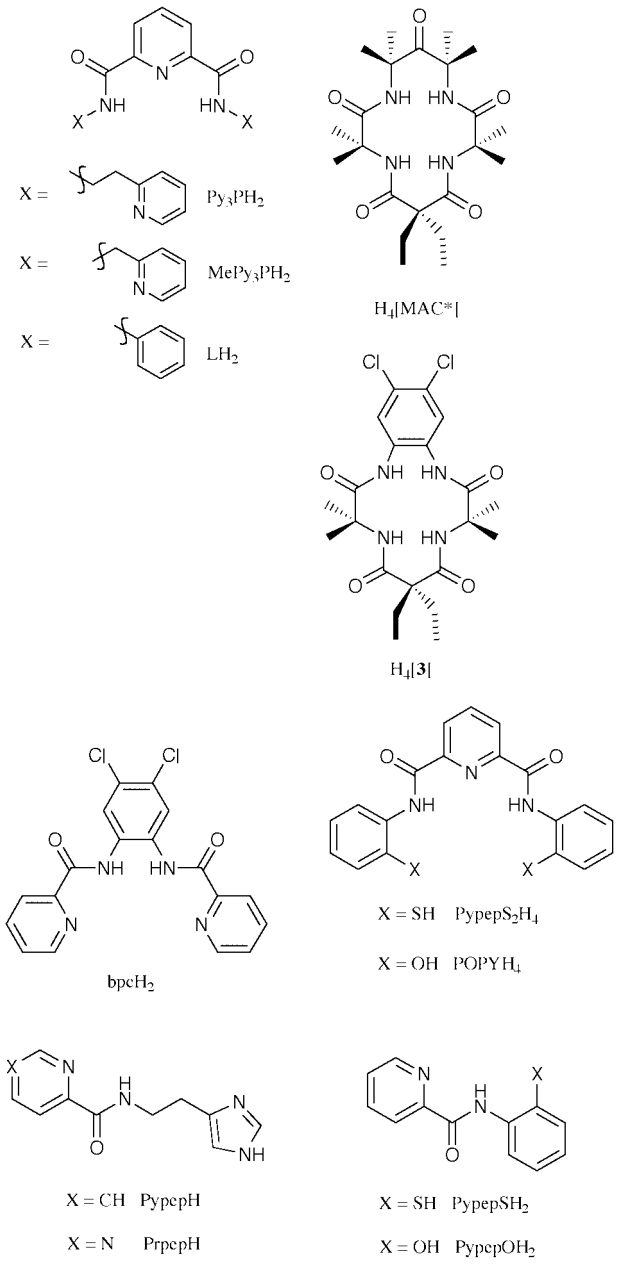


Fig. 1 Ligands used in the syntheses of Fe(III) complexes.

different laboratories. For example, the tridentate ligands PypepH and PrpepH were designed to establish the mode of binding of bleomycin to iron[3,4] while $bpcH_2$ was synthesized as part of studies on oxidation of hydrocarbons by metal complexes.[9,10] Along the same line, the S-containing ligands $PypepSH_2$[5] and $PypepS_2H_4$[6] were specially prepared to model the active site of the enzyme nitrile hydratase. The ligands Py_3PH_2, $MePy_3PH_2$,[7] LH_2,[11] $PypepOH_2$,[21] and $POPYH_4$[8] were however intended for the development of the coordination chemistry of Fe(III) complexes with carboxamido nitrogens as donors. And finally, the macrocyclic tetraamido ligands H_4[MAC*],[14] and H_4[**3**][12,13] were developed by Collins and coworkers to stabilize metal ions in high oxidation states.

Although the synthetic strategies for successful isolation of Fe(III) complexes with ligated carboxamido nitrogens have just begun to emerge, some common themes in their syntheses have already been recognized. The known Fe(III) complexes have been synthesized by either of the two following methods. The first one involves initial formation of the Fe(II) species under anaerobic conditions followed by oxidation to the Fe(III) complex. The second approach involves the synthesis of the Fe(III) complex directly from the reaction of a suitable Fe(III) salt with the deprotonated ligand. The correct choice of base and solvent, as well as the appropriate Fe(III) salt are the crucial factors for success with this method.

The choice of the Fe(III) source depends on the type of complex one decides to synthesize. For the bis complexes with two carboxamido nitrogens around Fe(III), $FeCl_3$[3] or $[Et_4N][FeCl_4]$[4–6] is preferred. However, attempts to prepare the bis complexes with four carboxamido nitrogens involving the ligands Py_3PH_2 and $MePy_3PH_2$ invariably failed.[7] We have recently discovered that $[Fe(DMF)_6](ClO_4)_3$ is a very convenient starting material for the syntheses of Fe(III) complexes with these multidentate ligands[7] and others like $PyPepS_2H_4$ and $POPYH_4$.[6,8] This Fe(III) starting material can be readily prepared and it is indefinitely stable and not very hygroscopic. One may also isolate the Fe(III) complex *via* oxidation of the corresponding Fe(II) species. The tetracarboxamido macrocyclic complexes $[Fe(\mathbf{3})(H_2O)]^-$ and $[Fe(\eta^4\text{-MAC*})(Cl)]^{2-}$ have been prepared from $FeCl_2$ followed by air oxidation.[12–14] $[Fe(CH_3CN)_4](ClO_4)_2$ is another Fe(II) starting material that has also been used in several cases.[9,11]

Both protic and aprotic solvents have been used in the syntheses of Fe(III) complexes with ligated carboxamido nitrogens. In our earlier work, protic solvents such as ethanol and methanol have been employed in the preparation of $[Fe(Pypep)_2]Cl$ and $[Fe(Prpep)_2]Cl$.[3,4] Che and coworkers have also used methanol in their synthesis of *trans*-$[Fe(bpc)(1\text{-}MeIm)_2]ClO_4$.[10] For the remaining complexes, the two aprotic solvents *N*,*N*′-dimethylformamide (DMF) and acetonitrile have been used. The need for these aprotic media arises from the strongly basic conditions necessary to deprotonate the carboxamide nitrogen.[1] Once the Fe(III)–N_{amido} bonds are formed, the complexes are often indefinitely stable in various protic solvents including water. Indeed, some of the reported complexes have been manipulated further in water. For example, $[Fe(\mathbf{3})H_2O]^-$ has been prepared from the $[Fe(\mathbf{3})Cl]^{2-}$ precursor *via* removal of the chloride anion with Ag^+ in water.[12,13] Also, the seven coordinate complexes $Na[Fe(POPY)(1\text{-}MeIm)_2]$ and $Na_3[Fe(POPY)(NCS)_2]$ are converted to the corresponding aquo species in water. This transformation is reversible since the original complexes are recovered from such solutions upon addition of excess 1-MeIm or NaSCN.[8] It is therefore evident that the inherent basicity of the carboxamido nitrogen is lowered considerably upon coordination to the Fe(III) center, a fact that prevents hydrolysis of these complexes in water.[7]

The choice of base is very crucial in all the syntheses mentioned above. The base must be sufficiently strong to deprotonate the peptide nitrogens, but must not react with the solvent. In protic solvents, one generally adds the metal source to the ligand prior to the addition of the base. It appears that initial coordination of the ligand to the Fe(III) center assists deprotonation of the carboxamide group. In such cases, amines like triethylamine or 1,8-bis(dimethylamino)naphthalene are good bases.[3,4] In acetonitrile, other bases like CH_3COONa have

† Ligand abbreviations used in this paper: H_2L = 2,6-bis(*N*-phenylcarbamoyl)pyridine; Py_3PH_2 = *N*,*N*′-bis[2-(pyridyl)ethyl]pyridine-2,6-dicarboxamide; $MePy_3PH_2$ = *N*,*N*′-bis[2-(2-pyridyl)methyl]pyridine-2,6-dicarboxamide; H_2bpc = 4,5-dichloro-1,2-bis(pyridine-2-carboxamido)-benzene; PypepH = *N*-[2-(4-imidazoyl)ethyl]pyridine-2-carboxamide; PrpepH = *N*-[2-(4-imidazolyl)ethyl]pyrimidine-4-carboxamide; $PypepSH_2$ = *N*-2-mercaptophenylpyridine-2′-carboxamide; $PypepOH_2$ = *N*-2-hydroxyphenylpyridine-2′-carboxamide; H_4[MAC*] = 1,4,8,11-tetraaza-13,13-diethyl-2,2,5,5,7,7,10,10-octamethyl-3,6,9,12,14-pentaoxocyclotetradecane; H_4[**3**] = 13,14-dichloro-6,6-diethyl-2,5,7,10(6*H*,11*H*)-tetraoxo-3,3,9,9-tetramethyl-1*H*-1,4,8,11-benzotetraazacyclotridecine; $PypepS_2H_4$ = *N*,*N*′-bis(2-mercaptophenyl)pyridine-2,6-dicarboxamide; $POPYH_4$ = *N*,*N*′-bis(2-hydroxyphenyl)pyridine-2,6-dicarboxamide.

also been used.[10] When the complexation reaction is performed in DMF, NaH is the base of choice. In such reactions, the base must be added to the ligand prior to the addition of the metal salt. The combination of NaH and DMF (or acetonitrile) is particularly favorable since coordination of solvent to the Na^+ ions in the crystal lattice often helps crystallization of the Na^+ salts of the anionic complexes. The strong base *tert*-butyllithium has been used to deprotonate the macrocyclic ligands H_4[**3**][12,13] and H_4[MAC*].[14]

Finally it is important to mention the need for anaerobic conditions while preparing the thiolato complexes $[Fe(PypepS)_2]^-$ and $[Fe(PypepS_2)]^-$. Upon subsequent exposure to oxygen, these complexes are converted to the sulfinato derivatives $[Fe(PypepSO_2)_2]^-$ and $[Fe(PypepS_2O_4)]^-$.[6,22] Fe(III) complexes with no thiolato sulfur(s) in the first coordination sphere are however synthesized under aerobic conditions and the complexes are stable in air.

3 Structures

Of the twelve ligands listed in Fig. 1, the majority form six coordinate octahedral complexes with Fe(III) although some form complexes with coordination numbers of five and seven. In addition, the complexes that have been structurally characterized so far have the Fe(III) center coordinated to either two or four carboxamido nitrogen donors. For the sake of comparison, the structural features of these Fe(III) complexes with two carboxamido nitrogens and four carboxamido nitrogens are treated separately in the following sections. The average Fe(III)–N_{amido} bond distances for these complexes are listed in Table 1. As expected, the average Fe(III)–N_{amido} bond lengths are longer for the high spin (HS) complexes compared to the low spin (LS) ones.

3.1 Complexes with two carboxamido nitrogens

The bis complexes of the tridentate ligands PypepH and PrpepH were the first examples of structurally characterized Fe(III) complexes that contain ligated carboxamido nitrogens.[3,4] The deprotonated ligands, $Pypep^-$ and $Prpep^-$, form octahedral Fe(III) complexes with the two carboxamido nitrogens *trans* to each other (Fig. 2a and 2b). The complexes are thus the *mer* isomers. The average Fe(III)–N_{amido} bond distances in $[Fe(Pypep)_2]Cl$ and $[Fe(Prpep)_2]ClO_4$ are 1.957(4) Å and 1.955(2) Å respectively.[3,4] Comparison of the Fe–N_{amido} distances in $[Fe(Prpep)_2]$ (1.984(6) Å) and $[Fe(Prpep)_2]ClO_4$ reveals that carboxamido nitrogen donors favor the Fe(III) center over Fe(II). This fact has been discussed in detail in our previous paper.[4] The average Fe(III)–N_{amido} bond distance in the two bis complexes $[Fe(PypepO)_2]^-$ and $[Fe(PypepS)_2]^-$ (Fig. 2c and 2d) differs by 0.11 Å (Table 1)[5,21] presumably due to a change in the spin state (HS to LS) upon replacement of the phenolato oxygen by thiolato sulfur around the Fe(III) center. In the Fe(III) complexes of the ligand $bpcH_2$ (Fig. 3), the carboxamido nitrogens are situated in a *cis* configuration. The average Fe(III)–N_{amido} bond distance in $[Fe(bpc)(MeCO_2)_2]^-$ (2.064(2) Å, Fig. 3a) is considerably longer than that in $[Fe(bpc)(1\text{-}MeIm)_2]^+$ (1.886(4) Å, Fig. 3b). This large difference in bond length could be related to different spin states (HS *vs.* LS respectively) in addition to the overall charge of the species.

Another interesting fact emerges upon comparison of the structural parameters of $[Fe(bpc)(1\text{-}MeIm)_2]^+$ (Fig. 3b) and $[Fe(Pypep)_2]^+$ (Fig. 2a). These two complexes have identical donor atoms around the Fe(III) center. However, the average Fe(III)–N_{amido} bond length in $[Fe(bpc)(1\text{-}MeIm)_2]^+$ is shorter than that in $[Fe(Pypep)_2]^+$ (1.886(4) Å *vs.* 1.957(4) Å). This difference clearly arises from a *trans*-effect since the carboxamido nitrogens are *cis* to each other in the former complex while the same nitrogens are in a *trans* configuration in the latter.

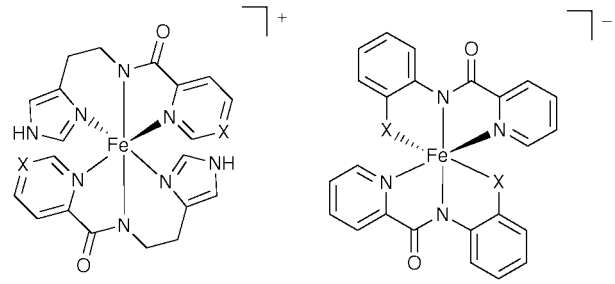


Fig. 2

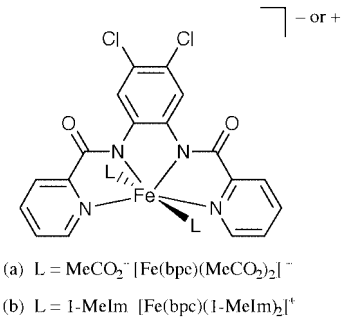
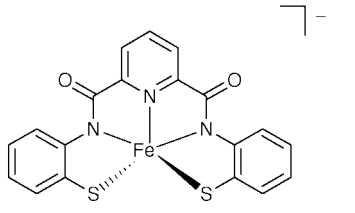


Fig. 3

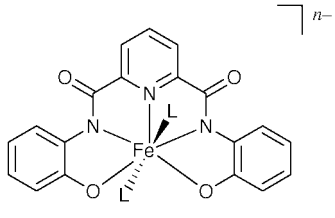
Table 1 Fe(III)–N_{amido} bond distances in structurally characterized complexes

Complex	Average Fe(III)–N_{amido} distance/Å	Number of Fe(III)–N_{amido} bonds	Spin state of iron(III)	Reference
$[Fe(Pypep)_2]^+$	1.957(4)	2	LS	3
$[Fe(Prpep)_2]^+$	1.955(2)	2	LS	4
$[Fe(PypepS)_2]^-$	1.954(2)	2	LS	5
$[Fe(PypepO)_2]^-$	2.064(4)	2	HS	21
$[Fe(bpc)(MeCO_2)_2]^-$	2.064(2)	2	HS	9
$[Fe(bpc)(1\text{-}MeIm)_2]^+$	1.886(4)	2	LS	10
$[Fe(PypepS_2)]^-$	2.040(3)	2	HS	6
$[Fe(POPY)(1\text{-}MeIm)_2]^-$	2.228(4)	2	HS	8
$[Fe(POPY)(NCS)_2]^{3-}$	2.224(6)	2	HS	8
$[Fe(L)_2]^-$	1.971(3)	4	LS	11
$[Fe(Py_3P)_2]^-$	1.962(2)	4	LS	7
$[Fe(MePy_3P)_2]^-$	1.955(3)	4	LS	7
$[Fe(H_2O)(\mathbf{3})]^-$	1.877(8)	4	IS	12
$[Fe(\eta^4\text{-}MAC^*)(Cl)]^{2-}$	1.927(16)	4	IS	14

The two pentadentate ligands $PypepS_2H_4$ and $POPYH_4$ afford Fe(III) complexes of different geometries. The fully deprotonated pentadentate $PypepS_2^{4-}$ ligand coordinates to Fe(III) in a helical geometry (Fig. 4a).[6] The average Fe(III)–



(a) [Fe(PypepS$_2$)]



(b) L = 1-MeIm, n = 1 [Fe(POPY)(1-MeIm)$_2$]

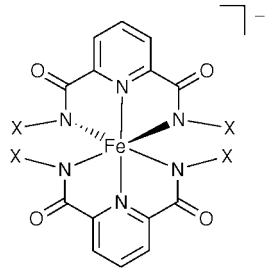
(c) L = NCS$^-$, n = 3 [Fe(POPY)(NCS)$_2$][3]

Fig. 4

N_{amido} distance noted with HS $[Fe(PypepS_2)]^-$ is 2.040(3) Å. Quite in contrast, the fully deprotonated $POPY^{4-}$ assumes a planar conformation and occupies the equatorial plane of seven coordinate pentagonal bipyramid geometry (Fig. 4b) in [Fe(POPY)(X)]$^{n-}$ (when X = 1-MeIm, n = 1; X = NCS^-, n = 3). In these two HS seven coordinate complexes, the average Fe(III)–N_{amido} distances are virtually identical (Table 1) despite very different overall charges.

3.2 Complexes with four carboxamido nitrogens

In all the structurally characterized Fe(III) complexes, the four carboxamido nitrogens are situated in the equatorial plane. In $[Fe(L)_2]^-$, the Fe(III) center is coordinated to the N_{amide}–$N_{pyridine}$–N_{amide} frame of the two ligands in *mer* fashion (Fig. 5a).[11] Similar coordination is observed in $[Fe(Py_3P)_2]^-$ and $[Fe(MePy_3P)_2]^-$ (Fig. 5b and 5c) despite the presence of two



(a) X = -C$_6$H$_5$ [Fe(L)$_2$]$^-$

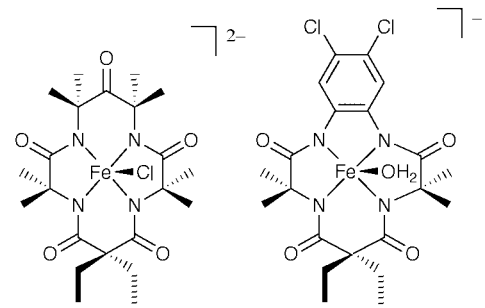
(b) X = -CH$_2$CH$_2$C$_5$H$_4$N [Fe(Py$_3$P)$_2$]$^-$

(c) X = -CH$_2$C$_5$H$_4$N [Fe(MePy$_3$P)$_2$]$^-$

Fig. 5

pendant pyridine arms in the ligand frames.[6] It thus becomes evident that in all three species, the N_{amide}–$N_{pyridine}$–N_{amide} portion of the ligands provide exceptional stability to the Fe(III) center. The enhanced stability is further supported by the fact that only the bis complexes $[Fe(Py_3P)_2]^-$ and $[Fe(MePy_3P)_2]^-$ are isolated even when the reaction mixtures contain 1 : 1 metal-to-ligand ratios. Clearly, enhanced stability provided by the carboxamido nitrogen donors outweighs the chelate effect of the pentadentate ligands in the latter two complexes. The average Fe(III)–N_{amido} bond distances in all three complexes are very similar to each other (Table 1).

There are two other examples of Fe(III) complexes with four carboxamido nitrogens. These are derived from the macrocyclic ligands H_4[MAC*] and H_4[**3**].[12–14] The fully deprotonated tetraanionic ligands occupy the equatorial plane in both complexes with distorted square pyramidal geometry (Fig. 6a and 6b). The Fe(III)–N_{amido} bond distances are shorter in these intermediate spin (IS) species (1.927(3) and 1.877(8) Å for and $[Fe(\eta^4\text{-MAC*})(Cl)]^{2-}$ and $[Fe(H_2O)[\mathbf{3}]]^-$ respectively) presumably due to the structural constraints of the macrocyclic ligand frames.

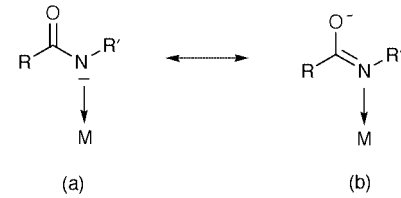


(a) [Fe(η^4-MAC*)(Cl)]$^{2-}$ (b) [Fe(H$_2$O)(**3**)]$^-$

Fig. 6

4 Spectroscopic and redox properties

Ligation of carboxamido nitrogen to Fe(III) centers can be conveniently followed by (a) disappearance of the N–H stretch(es) and (b) shift of the strong carbonyl stretching band (ν_{CO}) to lower frequencies. For example, the bis complex $[Fe(Py_3P)_2]^-$ exhibits its ν_{CO} at 1593 cm^{-1} while for the free ligand Py_3PH_2, ν_{CO} is noted at 1654 cm^{-1}. The position of ν_{CO} provides additional information in some cases. Comparison of the ν_{CO} of the two bis complexes $[Fe(Prpep)_2]$ and $[Fe(Prpep)_2]^+$ (1590 cm^{-1} and 1630 cm^{-1} respectively relative to 1665 cm^{-1} in the free ligand PrpepH) reveals that the carboxamido nitrogen binds to Fe(III) more strongly than Fe(II).[4] It is evident that between the two possible resonance structures shown below, the Fe(II) complex has a larger contribution of structure **b** while structure **a** contributes more to the Fe(III) complex.



(a) (b)

Most of the Fe(III) complexes included in this account are low spin (LS), although some high spin (HS) cases are noted (Table 1). The LS bis complexes with four carboxamido nitrogen donors in the equatorial plane (Fig. 5) exhibit sharp axial signals with $g_\perp$ = 2.18 and $g_\parallel$ = 1.94 (Table 2). Rhombic signals are usually observed for LS bis complexes with two carboxamido nitrogens like $[Fe(PypepS)_2]^-$ (g = 2.22, 2.14 and 1.98) due to the inequivalent electronic axes at the metal center. The LS nature of these Fe(III) complexes appears to be a result of the strong donor capacity of the carboxamido nitrogens.

The Fe(III) complexes of $PypepS_2H_4$ and $POPYH_4$ with coordination number 5 and 7 are HS despite the presence of

Table 2 EPR parameters, magnetic susceptibility (in Bohr magneton), and half-wave potentials (V *vs.* saturated calomel electrode, SCE)

Complex	*g* values	μ_B	$E_{1/2}$
$[Fe(Pypep)_2]^+$		2.22 (298K)	−0.31 (DMF)
$[Fe(Prpep)_2]^+$		2.24 (298K)	−0.10 (DMF)
$[Fe(PypepS)_2]^-$	2.22, 2.14, 1.98		−1.12 (DMF)
$[Fe(PypepO)_2]^-$	9.3, 4.2		−1.08 (DMF)
$[Fe(bpc)(MeCO_2)_2]^-$	5.22, 2.02	5.99 (300K)	−0.44 (CH_3CN)
$[Fe(bpc)(1\text{-MeIm})_2]^+$		1.79 (298K)	−0.54 (CH_3CN)
$[Fe(PypepS_2)]^-$	9.3, 4.2	6.13 (298K)	−0.65 (DMF)
$[Fe(POPY)(1\text{-MeIm})_2]^-$	6.43, 5.55, 1.99		−1.01 (DMF)
$[Fe(POPY)(NCS)_2]^{3-}$	6.74, 5.10, 2.00		
$[Fe(L)_2]^-$	2.160, 1.990	2.38 (300K)	−0.91 (CH_3CN)
$[Fe(Py_3P)_2]^-$	2.18, 1.94		−0.95 (DMF)
$[Fe(MePy_3P)_2]^-$	2.18, 1.94		−1.05 (DMF)
$[Fe(H_2O)[\mathbf{3}]]^-$	5.8, 5.0, 2.9, 1.8		
$[Fe(\eta^4\text{-MAC*})(Cl)]^{2-}$	4.38, 3.73, 2.06		

strong donors (Table 1). The unusual coordination geometries of these species (Fig. 4a–c) could be responsible for this behavior. Intermediate spin (3/2) states have also been noted with the 5 coordinate Fe(III) complexes with macrocyclic ligands (Fig. 1, Table 1). Collins and coworkers have studied the magnetic and Mössbauer properties of these species in detail.[12–14]

Changes in donor sets in structurally similar complexes also bring about changes in the spin state. Two interesting pairs of examples are given in Table 1. In the first case which involves the two bis complexes $[Fe(PypepS)_2]^-$ and $[Fe(PypepO)_2]^-$ (Fig. 2b and 2c), a change of thiolato sulfur to phenolato oxygen around Fe(III) causes a spin change from LS to HS. In the second example, a change of the neutral 1-MeIm axial donors of the LS complex $[Fe(bpc)(1\text{-MeIm})_2]^+$ to acetate results in the HS species $[Fe(bpc)(MeCO_2)_2]^-$. Clearly, several factors dictate the overall spin state of these Fe(III) complexes and more work is required to determine the contribution of the individual factors.

The half-wave potentials ($E_{1/2}$) for most of the complexes have been recorded and are listed in Table 2. That the carboxamido nitrogens provide extra stability to the +3 oxidation state of iron is readily noted in the highly negative reduction potentials (~ -1.0 V *vs.* SCE) for complexes like $[Fe(L)_2]^-$, $[Fe(Py_3P)_2]^-$, and $[Fe(MePy_3P)_2]^-$ (Table 2). These complexes comprise four carboxamido and two aromatic nitrogens around the Fe(III) center. The reduction potentials drop sharply when the number of carboxamido nitrogens (negatively-charged) is decreased. For example, the bis complexes $[Fe(Pypep)_2]^+$ and $[Fe(Prpep)_2]^+$ are reduced at −0.31 V and −0.10 V *vs.* SCE respectively. The major part of the stability of the Fe(III) center arises from electrostatic effects of the negatively-charged donors. This is further evidenced by the reduction potentials of the complexes $[Fe(PypepO)_2]^-$ and $[Fe(PypepS)_2]^-$ (−1.08 and −1.12 V *vs.* SCE respectively) compared to $[Fe(Pypep)_2]^+$. Collectively, the redox potentials now suggest that carboxamido nitrogen stabilizes the Fe(III) center to a great extent much like the carboxylates and phenolates.[23,24]

5 Stability

The topic of whether the Fe(III)–N_{amido} bond will survive in an aqueous medium has long been the subject of intense debate. Since the carboxamido nitrogen is highly basic, it was assumed to be susceptible to hydrolysis. However, the Fe(III) complexes with Fe(III)–N_{amido} bonds are often stable in water. For example, the bis complexes $[Fe(Py_3P)_2]^-$ and $[Fe(MePy_3P)_2]^-$ are very stable in water and undergo no further reaction in the presence of strong ligands such as CN^- and N_3^-.[7] Several complexes with Fe(III)–N_{amido} bonds have been synthesized in aqueous alcohol.[3,10] In aqueous solution, $[Fe(POPY)(1\text{-MeIm})_2]^-$ exchanges 1-MeIm ligands with water reversibly without any decomposition.[8] It is therefore clear that the Fe(III)–N_{amido} bond in such complexes remains intact even during substitution reactions in water. Results of extensive spectroscopic studies on $[Fe(bpc)(MeCO_2)_2]^-$ also indicate that substitution of the axial acetates with a wide variety of neutral or anionic ligands does not destroy the complexes.[9] In addition, the Fe(III) complexes derived from the macrocyclic ligands (Fig. 6a and 6b) have been oxidized to their Fe(IV) analogues in aqueous environments. The structurally characterized Fe(IV) species demonstrate that the Fe–N_{amido} bonds remain intact during oxidation of the iron center.[13,14] These results lend further support to our conclusion[7] that the Fe(III)–N_{amido} bond is quite stable toward hydrolytic decomposition and aqueous solutions of Fe(III) complexes with Fe(III)–N_{amido} bonds seldom afford oxo- or hydroxo-bridged dimeric (or polymeric) Fe(III) species which are often recognized as thermodynamically very stable entities.[2]

6 Summary

Over the past few years, a new area of coordination chemistry, namely, ligation of carboxamido nitrogen to Fe(III) has begun to unfold. Results from a few laboratories including ours have provided insight into the syntheses, structures, and properties of Fe(III) complexes with one or more Fe(III)–N_{amido} bond(s). In this account we demonstrate that these complexes are not anomalies but very stable entities in most cases. Also along this line, we emphasize that the carboxamido nitrogens are good donors for Fe(III) and impart significant stability to the Fe(III) center. We expect that this review will serve as a starting point for the preparation and characterization of additional complexes of this type in the future.

7 References

1 H. Sigel and R. B. Martin, *Chem. Rev.*, 1982, **82**, 385.
2 S. J. Lippard, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 344.
3 X. Tao, D. W. Stephan and P. K. Mascharak, *Inorg. Chem.*, 1987, **26**, 754.
4 S. J. Brown, M. M. Olmstead and P. K. Mascharak, *Inorg. Chem.*, 1990, **29**, 3229.
5 J. C. Noveron, M. M. Olmstead and P. K. Mascharak, *Inorg. Chem.*, 1998, **37**, 1138.
6 J. C. Noveron, M. M. Olmstead and P. K. Mascharak, *J. Am. Chem. Soc.*, submitted.
7 D. S. Marlin, M. M. Olmstead and P. K. Mascharak, *Inorg. Chem.*, 1999, **38**, 3258.
8 D. S. Marlin, M. M. Olmstead and P. K. Mascharak, *Inorg. Chim. Acta*, in the press.
9 M. Ray, R. Mukherjee, J. F. Richardson and R. M. Buchanan, *J. Chem. Soc., Dalton Trans.*, 1993, 2457.
10 C.-M. Che, W.-H. Leung, C.-K. Li, H.-Y. Cheng and S.-M. Peng, *Inorg. Chim. Acta*, 1992, **196**, 43.
11 M. Ray, D. Ghosh, Z. Shirin and R. Mukherjee, *Inorg. Chem.*, 1997, **36**, 3568.
12 M. J. Bartos, C. Kidwell, K. E. Kauffmann, S. W. Gordon-Wylie, T. J. Collins, G. C. Clark, E. Münck and S. T. Wientraub, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1216.
13 M. J. Bartos, S. W. Gordon-Wylie, B. G. Fox, L. J. Wright, S. T. Wientraub, K. E. Kauffmann, E. Münck, K. L. Kostka, E. S. Uffelman, C. E. F. Rickard, K. R. Noon and T. J. Collins, *J. Coord. Chem. Rev.*, 1998, **174**, 361.
14 K. L. Kostka, B. G. Fox, M. P. Hendrich, T. J. Collins, C. E. F. Rickard, L. J. Wright and E. Münck, *J. Am. Chem. Soc.*, 1993, **115**, 6746.
15 M. Ray, A. P. Golombek, M. P. Hendrich, V. G. Young, Jr. and A. S. Borovik, *J. Am. Chem. Soc.*, 1996, **118**, 6084.

16 J. W. Peters, M. H. Stowell, M. Soltis, M. G. Finnegan, M. K. Johnson and D. C. Rees, *Biochemistry*, 1997, **36**, 1181.
17 S. Nagashima, M. Nakasako, N. Dohmae, M. Tsujimura, K. Takio, M. Odaka, M. Yohda, N. Kamiya and I. Endo, *Nat. Struct. Biol.*, 1998, **5**, 347.
18 W. Huang, J. Jia, J. Cummings, M. Nelson, G. Schneider and Y. Lindqvist, *Structure*, 1997, **5**, 691.
19 R. J. Guajardo, S. E. Hudson, S. J. Brown and P. K. Mascharak, *J. Am. Chem. Soc.*, 1993, **115**, 7971.
20 Y. Sugiura, T. Takita and H. Umezawa, *Met. Ions Biol. Syst.*, 1985, **19**, 81.
21 D. S. Marlin, M. M. Olmstead and P. K. Mascharak, unpublished work.
22 L. A. Tyler, J. C. Noveron, M. M. Olmstead and P. K Mascharak, *Inorg. Chem.*, 1999, **38**, 616.
23 K. Ramesh and R. Mukherjee, *J. Chem. Soc., Dalton Trans.*, 1992, 83.
24 C. Stockheim, L. Hoster, T. Weyhermüller, K. Wieghardt and B. Nuber, *J. Chem. Soc., Dalton Trans.*, 1996, 4409.

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