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Iron catalysed assembly of an asymmetric mixed-ligand triple helicate†

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The 2-pyridinecarbaldehyde isonicotinoyl hydrazone (**H**PCIH) family of ligands are typically tridentate *N*,*N*,*O* chelators that exhibit very high *in vitro* activity in mobilizing intracellular Fe and are promising candidates for the treatment of Fe overload diseases. Complexation of ferrous perchlorate with **H**PCIH in MeCN solution gives the expected six-coordinate complex $Fe^{II}(PCIH)_2$. However, complexation of Fe^{II} with 2-pyridinecarbaldehyde picolinoyl hydrazone (**H**PCPH, an isomer of **H**PCIH) under the same conditions leads to spontaneous assembly of an unprecedented asymmetric, mixed-ligand dinuclear triple helical complex $Fe^{II}_2(PCPH)_2(PPH)$, where PPH^{2-} is the dianion of bis(picolinoyl)hydrazine. The X-ray crystal structure of this complex shows that each ligand binds simultaneously to both metal centres in a bidentate fashion. The dinuclear complex exhibits two well separated and totally reversible $Fe^{III/II}$ redox couples as shown by cyclic voltammetry in MeCN solution.

Introduction

In our search for an orally active drug for the treatment of iron overload diseases, we have focused our attention on the Fe coordination chemistry of two series of ligands; the pyridylcarbaldehyde isonicotinoyl hydrazone (**H**PCIH) and isonicotinoyl picolinoyl hydrazine (**H_2**IPH) analogues (Chart 1). Several ligands from each of these families have shown high *in vitro* activity in mobilizing Fe from ^{59}Fe-loaded cells and also in preventing Fe uptake from ^{59}Fe-labeled transferrin.[1,2] Both series of ligands have been found to coordinate meridionally as tridentate chelators through the pyridyl (N), azomethine/amide (N) and carbonyl (O) groups. The **H**PCIH hydrazones are monobasic acids and coordinate typically in their monoanionic form,[3] while the **H_2**IPH hydrazines bear two weakly acidic N-atoms and can coordinate in either their mono- or dianionic forms.[2] These labile protons are highlighted in bold type in Chart 1.

In an earlier publication, we reported that complexation of Fe^{III} or Fe^{II} with **H**PCIH in aerated aqueous solution gave an unexpected and unprecedented Fe-catalysed oxidation of **H**PCIH to **H_2**IPH, which was identified by isolation and structural characterisation of the complex Fe^{III}(IPH)(**H**IPH).[2] This serendipitous observation initiated our interest in the **H_2**IPH series, which has now emerged as an equally effective series of Fe chelators. Furthermore, we have found that the isonicotinoyl (4-pyridyl) N-atom enables **H**PCIH to act as a bridging ligand, with oligonuclear **H**PCIH complexes of Mn^{II}, Co^{III} and Zn^{II} having been identified and characterised structurally.[3]

The picolinoyl hydrazone **H**PCPH is isomeric with **H**PCIH, but the N-atom on the pyridyl ring adjacent to the carbonyl group is in a position where it may coordinate in a chelating mode in partnership with either the adjacent N- or O-donor of the amide group. As we illustrate in this study, the coordination mode of **H**PCPH is unique amongst members of the **H**PCIH family, but its Fe^{II} complex is also susceptible to oxidation as seen for its isomer **H**PCIH.

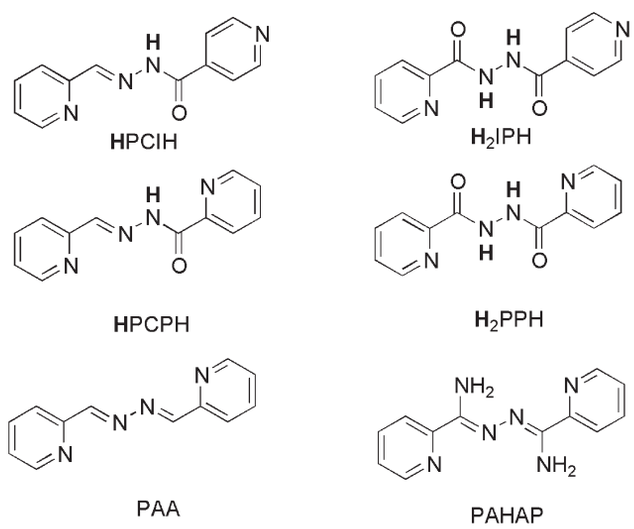

Chart 1

Experimental

Syntheses

HPCIH and **H**PCPH were prepared by Schiff base condensations between 2-pyridinecarbaldehyde and either isonicotinic and picolinic acid hydrazide, respectively, as described.[4]

General synthetic procedure for complexes

4 mmol of **H**PCIH (or **H**PCPH) was dissolved in 40 cm^3 of oxygen-free MeCN together with 32 mmol of triethylamine. 1.6 mmol of $Fe(ClO_4)_2{\cdot}6H_2O$, dissolved in 10 cm^3 of oxygen-free MeCN, was added dropwise to the basic ligand solution with stirring. The resulting mixture was gently refluxed under a nitrogen atmosphere for 3 h. In each case, the product precipitated during the course of the reaction, and was collected by filtration then washed with MeOH and Me_2CO.

$Fe^{II}(PCIH)_2{\cdot}½H_2O$. Dark green powder 89% yield. Microanalysis, found: C, 55.42; H, 3.44; N, 21.79%; calc. for $C_{24}H_{19}FeN_8O_{2.5}$: C, 55.94; H, 3.72; N, 21.74%. Electronic spectrum (MeOH): λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}) 649 (4000), 349 (39000), 268 (19500), 229 (35200). IR (KBr disk): $\bar{\nu}$ (strong and

† Electronic supplementary information (ESI) available: Fig. S1: C_2-symmetric and asymmetric isomers of $Fe^{II}_2(PCPH)_2(PPH)$. Fig. S2: 500 MHz ^{1}H NMR spectrum of $Fe^{II}_2(PCPH)_2(PPH)$. Fig. S3: Analysis of the possible isomeric forms of $[Fe^{II}_2(PCPH)_3]^+$ and $[Fe^{II}_2(PCPH)_2(PPH)]$ formed through ligand self assembly and ligand oxidation. See http://www.rsc.org/suppdata/dt/b4/b408781j/

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very strong peaks, cm^{-1}): 1498s, 1482s, 1456vs, 1362vs, 1344s, 1151s, 1063s, 754s, 700s. ESI-MS (MeOH soln.): m/z^+ 506 ($[Fe^{III}(PCIH)_2]^+$).

$[Fe^{II}_2(PCPH)_2(PPH)]\cdot 2MeCN\cdot 6H_2O$. Purple powder 60% yield. Recrystallisation from MeCN afforded crystals suitable for X-ray work. IR and UV-vis spectroscopic data for the bulk and crystalline samples were indistinguishable. Electronic spectrum (MeOH): λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1}): 571 (11600), 400 sh (~9000), 320 (19300), 284 (29100), 269 (29700). IR (KBr disk): $\bar{\nu}$ (strong and very strong peaks, cm^{-1}): 1616vs, 1591vs, 1560s, 1465s, 1361s, 1143s, 1114s, 1088s, 761s. ^{1}H NMR (DMSO-d_6): δ 2.06 (s, 3H, MeCN), 6.88 (d, 1H), 7.02 (d, 1H), 7.13 (s, 1H), 7.36 (d, 1H), 7.43 (t, 1H), 7.50 (s, 1H), 7.54 (t, 1H), 7.60 (t, 2H), 7.76 (s, 2H), 7.90 (t, 1H), 7.95 (d, 1H), 8.04 (m, 4H), 8.11 (t, 2H), 8.15 (s, 2H), 8.23 (d, 1H), 8.74 (s, 1H), 8.84 (s, 1H), 9.37 (s, 1H) and 9.66 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 1.09 (MeCN), 120.0 (MeCN), 122.8, 124.4, 124.5, 124.8, 125.6, 125.9, 126.0, 126.8, 127.5, 127.6, 128.5, 128.6, 135.5, 136.6, 136.7, 136.8, 137.4, 138.3, 148.5, 149.3, 149.5, 151.8, 152.2, 153.0, 153.6, 153.7, 154.7, 156.6, 158.1, 158.2, 159.1, 159.2, 160.3, 161.1, 163.5, 163.7. ESI-MS (MeOH soln.): m/z^+ 802 ($[Fe^{III}Fe^{II}(PCPH)_2(PPH)]^+$).

Physical methods

Electronic spectra were recorded on a Perkin-Elmer Lambda 40 spectrophotometer, and IR spectra were obtained on a Perkin-Elmer 1600 Series FTIR spectrometer, with samples dispersed in KBr disks. Nuclear magnetic resonance spectra were recorded at 500 (^{1}H) and 125.8 MHz (^{13}C) on a Bruker Avance spectrometer using DMSO-d_6 as the solvent and TMS as the reference. Cyclic voltammetry was performed with a BAS100B/W electrochemical workstation employing glassy-carbon working electrode, a Pt auxiliary electrode and a non-aqueous Ag/Ag^+ (MeCN) reference electrode. Bulk electrolysis was carried out with a BAS reticulated vitreous carbon electrode. All solutions for electrochemistry contained *ca.* 2 mmol dm^{-3} analyte and 0.1 mol dm^{-3} n-Bu_4NClO_4 in dry MeCN and were purged with nitrogen gas before measurement. Electron paramagnetic resonance spectra were recorded at 77 K on a Bruker ER200D spectrometer at X-band frequency (9.303 GHz). Samples were prepared as 1 mM solutions in MeCN. Spectra were simulated with the program EPR50F.[5]

Crystallography

Data were collected at 150 K with an Oxford 600 Series Cryostream Cooler attached to an Enraf Nonius CAD4 diffractometer. Cell constants were determined by a least-squares fits to the setting parameters of 25 independent reflections employing graphite-monochromated Mo-Kα radiation (0.71073 Å). Data reduction and empirical absorption correction (ψ-scans) were performed with the WinGX package.[6] The structure was solved by direct methods with SHELXS and refined by full-matrix least-squares analysis with SHELXL. The MeCN solvent molecule was severely disordered about a three-fold rotation axis. Three unique positions were identified for this solvent molecule. One position has the molecule (N3A, C7A and C8A) coincident with a three-fold axis; another (N3B, C7B and C8B) finds only the nitrile carbon (C7B) on the three-fold axis, while the third (N3C, C7C and C8C) finds that only the N-atom on the three-fold axis. The occupancies were restrained to sum to one-third comprising a 1 : 1 ratio of Fe : MeCN, which is consistent with the NMR data obtained from the crystals. Restraints to the C–C and C–N bond lengths were necessary to enable refinement. The unique water molecule was disordered over two sites and the occupancies were refined complementarily (O2A : O2B 87 : 13%).

Crystal data

$[Fe_2(PCPH)_2(PPH)]\cdot 6H_2O\cdot 2MeCN$: $C_{40}H_{44}Fe_2N_{14}O_{10}$, M = 992.59, trigonal, space group $R\bar{3}c$ (no. 167), a = 13.353(4), c = 43.288(7) Å, U = 6684(3) Å^3, T = 150 K, Z = 6, μ(Mo-Kα) = 7.61 cm^{-1}, 3862 reflections measured, 1324 unique (R_{int} = 0.1146) which were used in all calculations, R_1 = 0.0868 (for 756 obs. data, $I > 2\sigma(I)$), wR_2 = 0.2656 (all data). CCDC reference number 239850.

See http://www.rsc.org/suppdata/dt/b4/b408781j/ for crystallographic data in CIF or other electronic format.

Results and discussion

Reaction of $Fe(ClO_4)_2\cdot 6H_2O$ with 2.5 equivalents of **H**PCIH in anhydrous, deoxygenated MeCN gave the dark green bis-ligand complex $Fe^{II}(PCIH)_2$. Microanalytical, IR and ESI-MS data were consistent with this formulation. The complex is partially oxidised to $[Fe^{III}(PCIH)_2]^+$ in aerated solution, and the base peak of the electrospray mass spectrum (in MeOH) corresponded with this species. Furthermore, the formation of this paramagnetic ferric complex prevented acquisition of an NMR spectrum of the parent ferrous compound. The IR bands of $Fe^{II}(PCIH)_2$ were identical to those reported for other $M^{II}(PCIH)_2$ analogues (M = Ni, Cu) complexes that have been characterised structurally.[3] In non-aqueous solution, $[Fe^{III}(PCIH)_2]^+$ is quite stable and does not undergo any further oxidation. As reported previously,[2] reaction of Fe^{II} with **H**PCIH in aerated aqueous solution leads to spontaneous, rapid and quantitative oxidation of the hydrazone to give the ferric bis-hydrazine complex $Fe^{III}(IPH)(\mathbf{H}IPH)$.

By contrast, complexation of **H**PCPH with ferrous perchlorate in MeCN under the same conditions gave a purple product. The compound proved to be a complex of stoichiometry $Fe^{II}_2L_3$, but structural elucidation required a combination of crystallographic and spectroscopic methods. Despite using pure **H**PCPH as the starting material and conducting the reaction and recrystallisation in MeCN, one of the three ligands was converted into the symmetrical hydrazine, PPH^{2-} in the unusual dinuclear complex $Fe^{II}_2(PCPH)_2(PPH)$ in good yield. No other products were obtained.

The crystal structure of $[Fe^{II}_2(PCPH)_2(PPH)]\cdot 6H_2O\cdot 2MeCN$ was determined (Fig. 1) revealing a dinuclear triple helical assembly, with each ligand coordinating in a bis-bidentate mode exclusively through its N-donors. The complex has crystallographic D_3 symmetry, but this is not an intrinsic property of the complex, which is in fact asymmetric (see below). The apparent symmetry is a consequence of disorder. The crystallographically unique carbonyl O-atom (O1) was refined at ⅔ occupancy *i.e.* it is present on but four of the six symmetry-related atoms (C6) adjacent to each pyridyl ring as illustrated in Fig. 1. H-atoms are attached to the two remaining symmetry-related C6 atoms.

The coordinate bond lengths are typical of those found in low-spin Fe^{II} complexes with pyridyl ligands *e.g.* $[Fe^{II}(bipy)_3](PF_6)_2$ 1.967 Å;[8] high-spin complexes exhibit Fe^{II}–N_{pyr} bond lengths in excess of 2.19 Å.[9,10] In order to attain this triple helical conformation each ligand is twisted about the N–N bond (C6–N2–N2′–C6′ torsion angle of 80.8°). The crystallographically unique Fe–N2 bond length is representative of both Fe–N=CH and Fe–N–CO groups due to the disorder found in the structure, and any differences in the actual N=CH and N–CO bond lengths were not resolved. The intramolecular Fe···Fe′ separation is 3.489(3) Å. Disordered water and MeCN molecules were also identified in the structure.

Asymmetry of the complex was established by NMR spectroscopy, where sharp signals were observed due to both metal centres existing in low-spin d^6 electronic ground states. There are two possible isomers of $Fe^{II}_2(PCPH)_2(PPH)$: one with C_2 symmetry, and one being asymmetric (ESI,† Fig. S1). Each of the 36 C-atoms in $Fe^{II}_2(PCPH)_2(PPH)$ gave a unique ^{13}C NMR resonance, thus the complex is asymmetric. Resonances from the co-crystallised MeCN molecule were also seen. Most telling was the appearance of two separate azomethine ^{1}H NMR resonances each integrating to a single

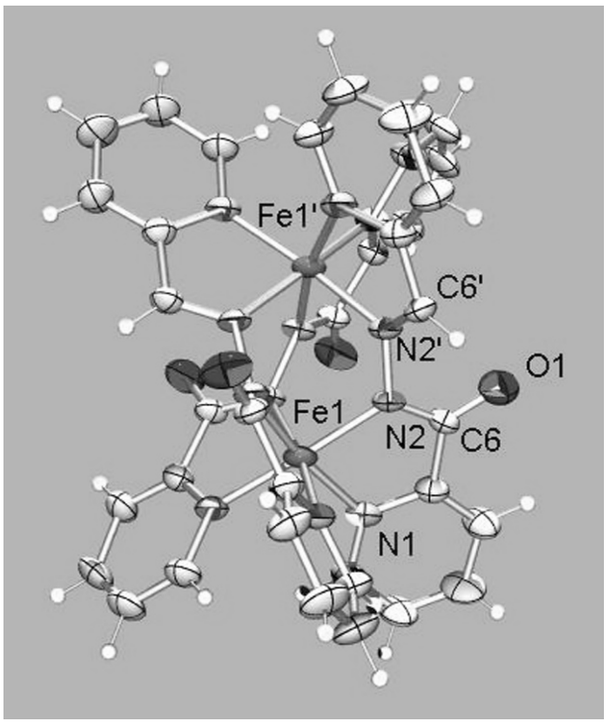


Fig. 1 View of the $Fe^{II}_2(PCPH)_2(PPH)$ helicate (30% probability ellipsoids, drawn with ORTEP[7] and rendered with PovRay V3.5): selected bond lengths (Å) and angles (°): Fe1–N1 1.962(5), Fe1–N2 1.920(5), C6–O1 1.199(10), C6–N2 1.272(8), N2–N2′ 1.404(8) (primed atom symmetry operation $x - y + 1/3, -y + 2/3, -z + 13/6$); N1–Fe1–N2 80.2(2).

proton (ESI,† Fig. S2). This observation reinforces the fact that only two of the three ligands bear azomethine H-atoms; the third (PPH^{2-}) has only pyridyl H-atoms, all of which give multiplet resonances. For comparison, the azomethine protons must be chemically equivalent in the C_2-symmetrical isomer. Finally, the existence of *exactly* 36 ^{13}C NMR resonances for $Fe^{II}_2(PCPH)_2(PPH)$ indicates that the sample is isomerically pure. A co-crystallised mixture of asymmetric and symmetric isomers would not be apparent from the disordered crystal structure, but would result in 54 (36 + 18) chemically inequivalent C-atoms in addition to three azomethine protons.

The electronic spectrum of $Fe^{II}_2(PCPH)_2(PPH)$, exhibits a hypsochromically shifted metal to ligand charge transfer band at 571 nm compared with the simple mononuclear $Fe(PCIH)_2$ analogue (649 nm). Given that the dinuclear complex bears two different $Fe^{II}N_6$ chromophores, this band represents two overlapping transitions. Although we have no crystallographic data, all spectroscopic (IR, ESI-MS) and analytical data for $Fe^{II}(PCIH)_2$ point to the complex having an $Fe^{II}N_4O_2$ coordination sphere such as that seen[3] in other divalent ML_2 analogues from this series.

Cyclic voltammetry of $Fe(PCIH)_2$ in MeCN solution gave a single reversible $Fe^{III/II}$ couple at +35 mV *vs* Ag/Ag^+. Bulk electrolysis of $Fe^{II}(PCIH)_2$ in MeCN at a potential of +400 mV *vs* Ag/Ag^+ enabled measurement of the EPR spectrum of the putative Fe^{III} complex $[Fe^{III}(PCIH)_2]^+$ at 77 K (Fig. 2(a)). An identical result was achieved by combining one equivalent of $FeCl_3$ and two equivalents of **H**PCIH in MeCN, with two equivalents of Et_3N added as base (Fig. 2(b)). The spectrum is typical of a low-spin, axially symmetric Fe^{III} complex[11] with $g_x = g_y = 2.255$ and $g_z = 1.935$. The parameter $g_x = 1.935$ is diagnostic of compounds with a d_{xy} ground state, which usually exhibit one g value below 2.[12] Coordinate bond lengths of low-spin Fe^{II} and low-spin Fe^{III} complexes are generally very similar, and it is assumed that oxidation of the parent Fe^{II} complex does not bring about a significant structural change.

Cyclic voltammetry of $Fe^{II}_2(PCPH)_2(PPH)$ in MeCN solution (Fig. 3) revealed two totally reversible $Fe^{III/II}$ couples at +28 mV

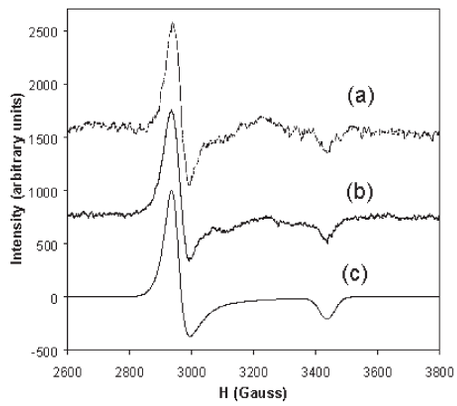


Fig. 2 X-Band ($\nu = 9.303$ GHz) EPR spectra of $[Fe^{III}(PCIH)_2]^+$ (77 K, MeCN): (a) from bulk electrolysis of $Fe^{II}(PCIH)_2$ complex in MeCN at a potential of +400 mV *vs*. Ag/Ag^+(MeCN) (b) from in situ complexation of $FeCl_3$ with **H**PCIH in MeCN/Et_3N and (c) EPR50F computer simulation with parameters $g_x = g_y = 2.255$, $g_z = 1.935$.

and +507 mV *vs* Ag/Ag^+. We propose that the lower potential couple of $Fe^{II}_2(PCPH)_2(PPH)$ corresponds to the Fe centre bearing the three coordinated amides, while the higher potential wave is due to the centre bearing two azomethine N-donors and only one amide. This assignment is based on the well-known ability of N-bound deprotonated amides to stabilise higher oxidation states.[13] The large separation (~500 mV) between the two $Fe^{III/II}$ couples is further evidence for the asymmetric structure deduced from the NMR data *i.e.* the two metals are in different FeN_6 coordination environments and moreover distinct from $Fe(PCIH)_2$ (FeN_4O_2).

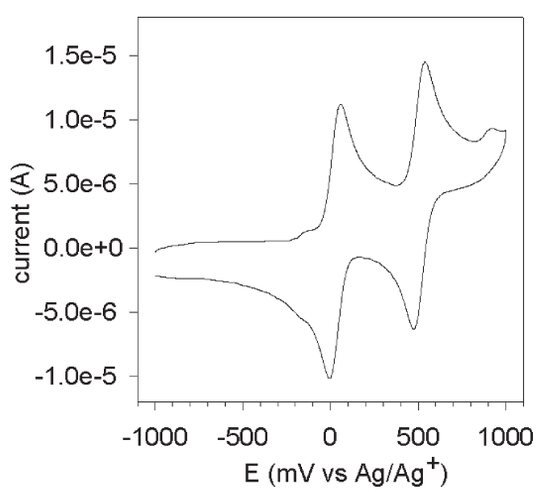
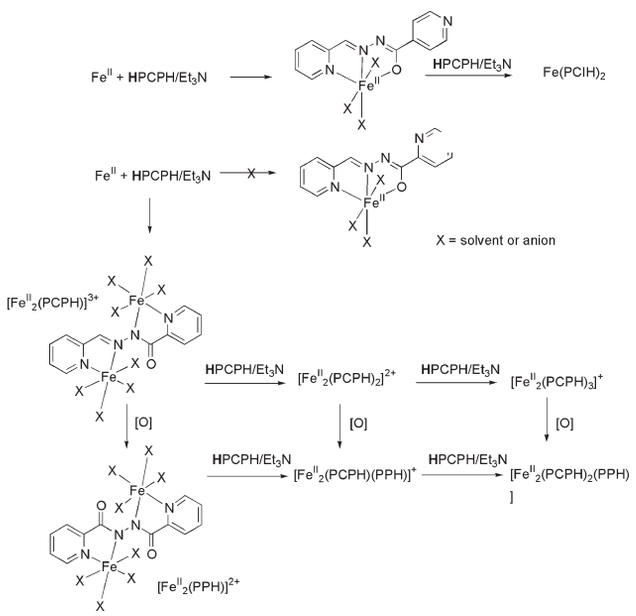


Fig. 3 Cyclic voltammogram of $Fe^{II}_2(PCPH)_2(PPH)$ in MeCN solution (0.1 M Bu_4NClO_4, glassy carbon working electrode, Pt counter and Ag/Ag^+(MeCN) reference electrodes. Scan rate 100 mV s^{-1}).

The unexpected and interesting product $Fe^{II}_2(PCPH)_2(PPH)$ reported here provides the first example to our knowledge of an asymmetric, mixed-ligand, triple helicate. Three-fold symmetric helicates bearing identical ligands are the norm.[14–16] Stratton and Busch[17–19] originally synthesised the dinuclear Fe^{II} complex $[Fe_2(PAA)_3]X_4$ (PAA = 2-pyridinealdazine, X = I^- or ClO_4^-) and proposed, in the absence of crystallographic data, a (D_3-symmetric) dinuclear triple helical structure. This is now credited as the first recognised example of a dinuclear triple helicate. This proposed structure was eventually confirmed by crystallographic work of Hannon and co-workers.[20] Other related systems that also form symmetrical triple helical di-Fe^{II} complexes include $[Fe_2(PAHAP)_3](NO_3)_4$ and its pyrazine analogue.[21]

We have seen no other helical compounds of this type in our investigations of the coordination chemistry of the **H**PCIH and $\mathbf{H_2}$IPH analogues.[2,3] In addition, none of the O-donors are coordinated in $Fe^{II}_2(PCPH)_2(PPH)$; a unique feature for both

the **H**PCIH and **H**$_2$IPH series. Instead, all other ligands we have studied bind as meridionally coordinating N,N,O ligands (Scheme 1).[2,3] In the present case, the all-N coordination mode of PCPH$^-$ appears to be driven by the preference of the Fe^{II} centres for the softer unsaturated N-donors. Once formed, the putative [Fe$_2$(PCPH)]$^{3+}$ (Scheme 1) acts as a template for the formation of the triple helicate. Ligand oxidation may take place at the stage of [Fe$_2$(PCPH)]$^{3+}$, the (presumed) double helicate [Fe$_2$(PCPH)$_2$]$^{2+}$ or after complete assembly of the triple helicate [Fe$_2$(PCPH)$_3$]$^+$ (Scheme 1). At present we have no way of discriminating between these three pathways, but we favour the fully formed helicate [Fe$_2$(PCPH)$_3$]$^+$ as the species which undergoes ligand oxidation.



Scheme 1

The fact that the oxidation of PCPH$^-$ to PPH^{2-} has occurred under the reactions conditions employed is remarkable. Previously, we reported that the reaction of **H**PCIH with Fe^{II} or Fe^{III} salts in aerated aqueous solution led to rapid and quantitative formation of the hydrazine complex Fe^{III}(IPH)(**H**IPH).[2] Therefore, we took great care to minimise exposure of the reaction mixture to oxygen or water, but it appears that the conversion of PCPH$^-$ to PPH^{2-} (catalysed by Fe) is facile, although incomplete in this case as two of the three coordinated ligands remain intact. The mechanism for this hydrazone-to-hydrazine transformation remains the subject of future investigations. Our current hypothesis is that in the presence of oxygen, the ferric oxidation state is reached, and the highly polarised azomethine C-atom is rapidly attacked by (trace amounts of) water. A complicated two-electron oxidative dehydrogenation then occurs by an unknown mechanism, but one in which redox cycling of the adjacent Fe ion is implicated. The identification of water in the crystal structure of [Fe$^{II}_2$(PCP-H)$_2$(PPH)]·6H$_2$O·2MeCN confirms its presence in the reaction medium, and complete exclusion, perhaps in a dry-box or using an anhydrous Fe^{II} salt, may lead to a different outcome. There is a related report of a Re and Ru-catalysed conversion of an imine to its amide,[22] but apart from our earlier paper,[2] the present example is only the second report of the direct conversion of an aroyl hydrazone to a diaroyl hydrazine.

The other remarkable feature of this chemistry is that we only observe the asymmetric isomer of [Fe$^{II}_2$(PCPH)$_2$(PPH)], isolated as a solid in ~60% yield. An analysis of the possible combinations of Fe^{II} and ligand is given in ESI,† Fig. S3, which shows that complexation of Fe^{II} with PCPH$^-$ in a 2 : 3 ratio should, on a purely statistical basis, result in a 3 : 1 ratio of asymmetric and C_3-symmetric helical [Fe$^{II}_2$(PCPH)$_3$]$^+$. If each of these four combinations can be oxidised at any one of its three azomethine C-atoms an equal distribution of asymmetric and C_2-symmetric isomers of [Fe$^{II}_2$(PCPH)$_2$(PPH)] should ensue. However, the reaction appears to be regioselective, so other factors must be at work. On the basis of our previous study[2] involving the Fe-catalysed oxidation of PCIH$^-$ to IPH^{2-}, oxidation of the azomethine C-atom is associated with oxidation of the Fe ion to which the adjacent N-donor is coordinated. As mentioned above in discussion of the cyclic voltammetry results, within either the asymmetric or C_3-symmetric [Fe$^{II}_2$(PCPH)$_3$]$^+$, the Fe atom bearing the greater number of picolinoyl (amide) chelates will be oxidized at lower potential. For the asymmetric isomer, this would favour oxidation of the sole azomethine C-atom adjacent to the two picolinoyl amide chelates (now coordinated to Fe^{III}) to give asymmetric [Fe$^{II}_2$(PCPH)$_2$(PPH)] (ESI,† Fig. S3). If C_3-symmetric [Fe$^{II}_2$(PCPH)$_3$]$^+$ is formed then one would expect the tris-picolinoyl (triamide) coordinated Fe atom to be oxidised preferentially; but this would not lead to any additional chemistry as the amide chelates cannot undergo further oxidation. In this case, both Fe atoms would need to be oxidised before ligand oxidation may commence.

Our continuing interest in the coordination chemistry of the **H**PCIH and **H**$_2$IPH analogues is driven by their high activity in mobilizing Fe from Fe-loaded cells and in preventing Fe-uptake from transferrin,[1,2] We have already shown[2] that an Fe-catalysed hydrazone-to-hydrazine transformation of **H**PCIH to **H**$_2$IPH occurs rapidly in aqueous solution, and the fact that a similar result occurs in deoxygenated dry MeCN raises the question of whether compounds such as Fe$^{II}_2$(PCPH)$_2$(PPH) may form *in vivo.* Evidently the ligands PCPH$^-$ and PPH^{2-} are predisposed to act as (hypodentate) bis-bidentate chelates like the azine analogues PAA and PAHAP, and no other products were observed in the present synthesis, so assembly of this complicated structure must be rapid and highly favorable. Further work is needed to address the question of whether ligands such as **H**PCPH and **H**$_2$PPH behave differently to the other related hydrazones and hydrazines of their respective families in the complexation and mobilisation of intracellular Fe.

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