

Synthesis and Stabilization of a Monomeric Iron(II) Hydroxo Complex via Intramolecular Hydrogen Bonding in the Secondary Coordination Sphere

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Utilizing the pyridinediimine ligand [(2,6-ⁱPrC₆H₃)N=CMe](N(ⁱPr)₂C₂H₄)N=CMe)C₅H₃N (didpa), the iron(II) complexes Fe(didpa)Br₂ (**1**), [Fe(Hdidpa)Br₂][PF₆] (**2**), and [Fe(Hdidpa)CH₃CN(OH)][2PF₆] (**3**) were synthesized and characterized by X-ray diffraction and spectroscopic methods. The X-ray data show that the didpa scaffold is capable of forming intramolecular hydrogen bonds in the solid state located within the secondary coordination sphere of complexes **2** and **3**. These hydrogen bonds are responsible for stabilizing the iron(II) hydroxo ligand in **3**, which originates from H₂O.

Iron centers with terminal hydroxo ligands are proposed to be the active species in the catalytic cycles of many metalloenzymes¹ including lipoxigenases,^{2,3} nitrile hydratases,^{4,5} acid phosphatases,^{6,7} and dioxygenases.^{8,9} The Fe–OH moieties in these active sites originate from water and are typically stabilized by neighboring amino acid residues within the secondary coordination sphere. These residues serve as endogenous bases during formation of the Fe–OH moieties and/or provide hydrogen bonds to the terminal hydroxo ligand. These interactions add structural stability to the active site and play a key role in regulating the activity.^{10,11}

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Developing synthetic systems that mimic these structural properties has been challenging because of the propensity for the monomeric Fe–OH moiety to form multinuclear hydroxo- or oxo-bridged complexes. For this reason, mononuclear nonheme Fe–OH (Fe^{II}/Fe^{III}) complexes are exceedingly rare.^{12–20} To the best of our knowledge, only four X-ray structures with a terminally bound Fe^{II}–OH have been reported to date. Moro-oka et al. reported the first Fe^{II}–OH complex, [(Tpz^{bu,ipr})Fe–OH], which was isolated utilizing a sterically hindered tris(pyrazolyl)borate ligand, making formation of the monomeric complex possible.¹² Li et al. have shown that intermolecular hydrogen bonds can be utilized to stabilize monomeric Fe^{II}–OH complexes.¹⁵ Borovik et al.¹⁴ have reported the bulky tripodal urea-based ligand H₃buea, which places hydrogen-bond-directing groups in a cavity capable of stabilizing the Fe^{II}–OH derived from water through intramolecular hydrogen bonds. Chang et al.¹⁶ have recently shown that the N4Py^{2PhNH} polypyridine backbone functionalized with amines can also stabilize the Fe^{II}–OH moiety through intramolecular hydrogen bonds.

Of the systems described above, those employing sterically hindered ligands (Tpz^{bu,ipr}) and/or placing hydrogen-bond directors inside a tripodal cavity located in the secondary coordination sphere (H₃buea and N4Py^{2PhNH}) are successful in stabilizing terminal Fe^{II}–OH complexes (with the exception of Me₂Imz^{MeSOH}, which is a histidine residue mimic¹⁵). Structures based on those types of geometries mimic biological

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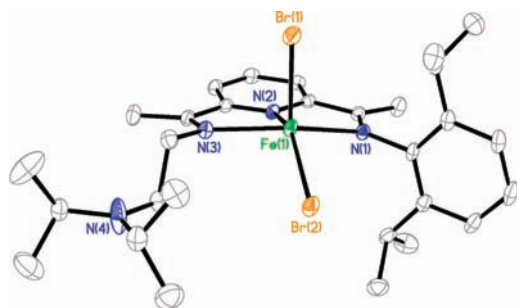
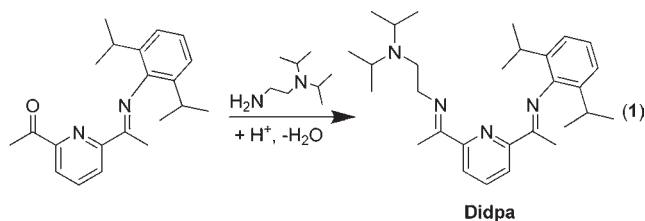


Figure 1. Solid-state structure (30% probability) of **1**. The hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Fe(1)–Br(1) 2.4519(4), Fe(1)–Br(2) 2.4252(4), Fe(1)–N(1) 2.2604(16), Fe(1)–N(2) 2.0745(15), Fe(1)–N(3) 2.1801(17), C(2)–N(1) 1.288(2), C(8)–N(3) 1.290(3); Br(1)–Fe(1)–Br(2) 120.021(14), N(2)–Fe(1)–Br(2) 140.30(5), N(1)–Fe(1)–N(3) 145.79(6).

iron-based metalloenzyme systems quite well. However, we envisioned that exploring other ligand geometries could allow us to access biologically relevant iron complexes that are also synthetically rare.

Herein we report a new class of ligands based on the pyridinediimine²¹ (PDI) core, which is able to stabilize a terminally bound monomeric Fe^{II}–OH complex through the use of an *intramolecular* hydrogen-bonding group. This new scaffold is able to mimic the secondary coordination sphere through the proper placement of a pendant base²² (diisopropylamine) capable of deprotonating water to produce a terminal hydroxo ligand and subsequently stabilizing the hydroxo ligand through formation of an intramolecular hydrogen bond.

The ligand [(2,6-ⁱPrC₆H₃)N=CMe)(N(ⁱPr)₂C₂H₄)N=CMe)C₅H₃N] (didpa; eq 1) was synthesized via the Schiff base condensation of [(2,6-ⁱPrC₆H₃)N=CMe)(O=CMe)C₅H₃N] with an excess of *N,N*-diisopropylethylenediamine (see the Supporting Information for details). Inspection of the IR spectrum of the product reveals that the C=O stretch at 1698 cm⁻¹ from the monoimine starting material disappears, leaving only a C=N stretch at 1640 cm⁻¹, and an absence of the primary amine (–NH₂) at 3420 cm⁻¹. ¹³C NMR also confirms the presence of the two C=N groups at 167.74 and 166.58 ppm, respectively, with the concomitant disappearance of C=O at 200.42 ppm.



The reaction of the didpa ligand with 1 equiv of FeBr₂ in tetrahydrofuran (THF) resulted in the formation of a blue solution of Fe(didpa)Br₂ (**1**), which was precipitated with diethyl ether. Purple single crystals of **1** were obtained from the vapor diffusion of diethyl ether into a solution of the product in methanol at –10 °C over a period of 1 week.

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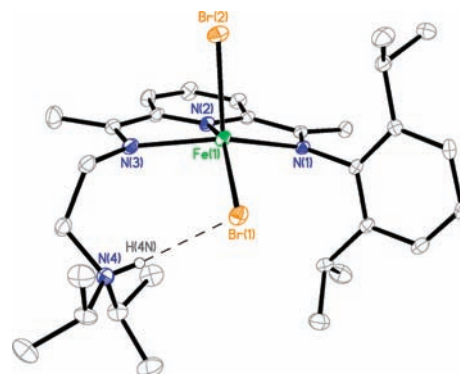


Figure 2. Solid-state structure (30% probability) of **2**. Only the hydrogen atom involved in hydrogen bonding is shown, and the PF₆⁻ counterion has been omitted for clarity. Selected bond lengths (Å) and angles (deg): Fe(1)–Br(1) 2.4439(6), Fe(1)–Br(2) 2.4661(6), Fe(1)–N(1) 2.200(2), Fe(1)–N(2) 2.065(3), Fe(1)–N(3) 2.189(3), N(4)–H(4N) 0.84(3), Br(1)···H(4N) 2.56(3), N(4)···Br(1) 3.392(3), C(2)–N(1) 1.283(4), C(8)–N(3) 1.284(4); Br(1)–Fe(1)–Br(2) 117.63(2), N(2)–Fe(1)–Br(1) 146.89(7), N(1)–Fe(1)–N(3) 143.90(10), N(4)–H(4N)···Br(1) 170(3).

An ORTEP view of **1** is shown in Figure 1. The iron center is five-coordinate with a square-pyramidal geometry ($\tau = 0.09$).²³ The nitrogen atoms of the PDI ring along with one bromine atom make up the basal plane, with the other bromine atom occupying the apical position. The bond lengths and angles (see the Supporting Information) are similar to those of other structurally characterized iron complexes containing an ⁱPrPDI ligand.^{24–26} The measured μ_{eff} of **1** yielded a value of 5.66 μ_{B} in the solid state and 5.17 μ_{B} in solution, consistent with a high-spin ($S = 2$) square-pyramidal Fe^{II} center.²⁴

The reaction of a blue solution of **1** in THF with the weak acid NH₄PF₆ in MeOH resulted in the formation of a purple solution. Slow evaporation of the resultant filtered solution yielded the purple crystalline solid [Fe(Hdidpa)Br₂][PF₆] (**2**) in quantitative yield. An ORTEP of **2**, the protonated form of **1**, is shown in Figure 2. The iron center retains the five-coordinate square-pyramidal geometry ($\tau = 0.05$). The measured μ_{eff} of **2** yielded a value of 5.22 μ_{B} in the solid state and 4.93 μ_{B} in solution, consistent with a high-spin ($S = 2$) square-pyramidal Fe^{II} center. The solid-state structure of **2** contains an intramolecular hydrogen bond between the protonated diisopropylamine group and the basal bromine atom. The hydrogen atom was located and refined, yielding a N–H···Br distance of 2.56(3) Å and a N···Br distance of 3.392(3) Å, consistent with an intramolecular hydrogen bond.²⁷ The N(4)–H(4N) group is directed toward the bromine atom, which is also indicative of intramolecular hydrogen bonding;²⁸ the N–H···Br angle is 170(3)°. The $\nu_{\text{N–H}}$ peak in the solid-state IR spectrum is obscured by hydrogen bonding.²⁹

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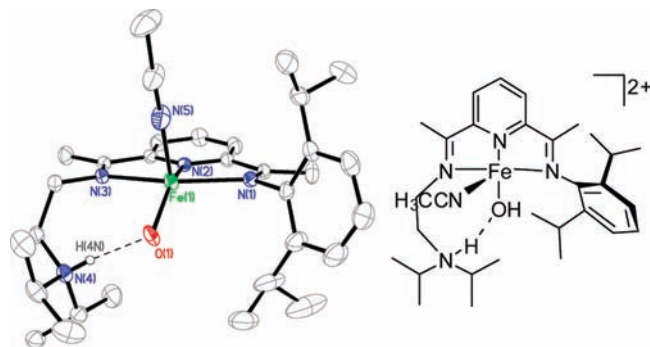


Figure 3. Solid-state structure (left, 30% probability) and molecular structure (right) of **3**. Only the hydrogen atom involved in hydrogen bonding is shown, and the PF_6^- counterions have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Fe(1)–O(1) 1.883(3), Fe(1)–N(1) 2.207(3), Fe(1)–N(2) 2.076(3), Fe(1)–N(3) 2.202(3), Fe(1)–N(5) 2.063(4), N(4)–H(4N) 0.80(5), H(4N)···O(1) 2.695(4), N(4)···O(1) 2.695(4), C(2)–N(1) 1.276(5), C(8)–N(3) 1.276(5); O(1)–Fe(1)–N(5) 104.99(17), N(2)–Fe(1)–O(1) 142.62(13), N(1)–Fe(1)–N(3) 148.80(12), N(4)–H(4N)···O(1) 171(5).

The reaction of **1** with 2 equiv of the halide abstractor, TIPF_6 , in wet acetonitrile results in an immediate color change from blue to red. Evaporation of acetonitrile and dissolution of the resultant red oil with CH_2Cl_2 , followed by slow evaporation of the filtered solution, resulted in the formation of deep-red crystals of the monomeric Fe–OH complex $[\text{Fe}(\text{Hdidpa})(\text{CH}_3\text{CN})(\text{OH})][2\text{PF}_6]$ (**3**). An ORTEP of **3** is shown in Figure 3. The iron center is five-coordinate with a square-pyramidal geometry ($\tau = 0.10$). The nitrogen atoms of the PDI ring along with the oxygen atom of the hydroxide ligand of **3** make up the basal plane, with a coordinated acetonitrile molecule occupying the apical position. The solid-state attenuated total reflectance Fourier transform IR spectrum reveals a $\nu_{\text{O-H}}$ peak at 3618 cm^{-1} and a $\nu_{\text{N-H}}$ peak at 3193 cm^{-1} . The measured μ_{eff} value of $5.11\ \mu_{\text{B}}$ (consistent with a high-spin ($S = 2$) square-pyramidal Fe^{II} center), coupled with the presence of two PF_6^- counterions per iron center, indicates that the iron is in a $\text{II}+$ oxidation state.³¹

It is noteworthy that the Fe–OH ligand in **3** is stable within the didpa scaffold, despite the presence of a tripodal cavity,³² given the tendency of mononuclear Fe–OH species to dimerize. The pendant base likely plays a key role as the

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Table 1. Fe–O Bond Lengths in Selected Fe^{II} –OH Complexes

complex	$d(\text{Fe}-\text{O})$ (Å)	ref
$[\text{Fe}(\text{Tp}^{\text{tBu,Pr}})(\text{OH})]^a$	1.830(8)	12
$[\text{Fe}(\text{H}_3\text{urea})(\text{OH})]^{2-}$ ^b	2.048(3)	14
$[\text{Fe}(\text{Me}_2\text{Imz}^{\text{MeSOH}})_2(\text{OH})]^{+c}$	1.938(3)	15
$\text{Fe}(\text{N}4\text{Py}^{2\text{PhNH}})(\text{OH})^d$	1.9153	16
$[\text{Fe}(\text{Hdidpa})(\text{CH}_3\text{CN})(\text{OH})]^{2+}$	1.883(3)	this work

^a $\text{Tp}^{\text{tBu,Pr}}$ = hydrotris(3-*tert*-butyl-5-isopropylpyrazol-1-yl)borate. ^b H_3urea = tris[(*N'* = *tert*-butylureayl)-*N*-ethylene]amine. ^c $\text{Me}_2\text{Imz}^{\text{MeSOH}}$ = bis(*N*-methylimidazol-2-yl)-3-methylthiopropanol. ^d $\text{N}4\text{Py}^{2\text{PhNH}}$ = *N,N*-bis(2-phenyl-NH-6-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine.

hydroxide ligand of **3** is stabilized through an intramolecular hydrogen bond formed with the protonated diisopropylamine of the didpa ligand. In the crystal structure, the hydrogen atom was located and refined, yielding a N–H···O distance of 1.90(6) Å and a N···O distance of 2.695(4) Å, consistent with an intramolecular hydrogen bond.³³ The N(4)–H(4N) group is directed toward the oxygen atom, which is also indicative of intramolecular hydrogen bonding; the N–H···O angle is 171(5)°. The Fe–O distance of 1.883(3) Å falls within the range of previously published synthetic (Table 1) and biological³⁴ complexes.

The hydroxide ligand and protonated amine in **3** originate from the deprotonation of water via the pendant diisopropylamine base. Attempts to synthesize an Fe^{II} –OH complex via the addition of stoichiometric amounts of different OH^- sources to **1** resulted in complete decomposition of the starting material (likely to insoluble $\text{Fe}(\text{OH})_x$ species). This illustrates the importance of the pendant diisopropylamine base in the deprotonation of water and stabilization of the iron(II) hydroxo ligand.

In conclusion, we have synthesized a new ligand scaffold (didpa) based on the PDI core. This ligand is capable of regulating the secondary coordination sphere by utilizing intramolecular hydrogen bonds. Fe^{II} complexes of the didpa ligand (**1–3**) were synthesized and structurally characterized to be square-pyramidal, high-spin Fe^{II} complexes. Complexes **2** and **3** were shown to possess intramolecular hydrogen bonds from the protonated diisopropylamine of the didpa scaffold. These hydrogen bonds are responsible for stabilizing the iron(II) hydroxo ligand in **3**, which originates from H_2O . Reactions in our laboratory are currently underway to investigate Fe^{III} and other biologically relevant metal ions with the didpa scaffold, as well as the redox activity of **3**.

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Supporting Information Available: Experimental procedures, spectroscopic data, more detailed ORTEPs, and X-ray crystallographic data in table and CIF format. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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