Inorganic Chemistry
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Structural Diversity in Metal Complexes with a Dinucleating Ligand Containing Carboxyamidopyridyl Groups

Gary K.-Y. Ng, Joseph W. Ziller, and A. S. Borovik*

Department of Chemistry, University of California—Irvine, 1102 Natural Science II, Irvine, California 92697, United States

S *Supporting Information*

ABSTRACT: The synthesis of a (carboxyamido)pyridinepyrazolate (H_5bppap) dinucleating ligand is described. Bimetallic iron and cobalt complexes of H_5bppap ($[M^{II}{}_2H_2\text{bppap}]^+$) showed structural differences in both their primary and secondary coordination spheres. The binding of small molecules into the preorganized ligand cavity is verified by the hydration of $[Fe^{II}{}_2H_2\text{bppap}]^+$ and $[Co^{II}{}_2H_2\text{bppap}]^+$, leading to the formation of complexes $[\{Co^{II}(OH)\}Co^{II}H_3\text{bppap}]^+$ and $[\{Fe^{II}(OH)\}Fe^{II}H_3\text{bppap}]^+$, in which one of the metal centers has a terminal hydroxo ligand.

Hydrogen bonds (H-bonds) within the secondary coordination sphere of metalloprotein active sites are effective at regulating metal-mediated processes.[1] In many cases, these intramolecular H-bonds are formed between amino residues and external ligands, which are often derived from water molecules. A key feature of biological H-bonding networks is their ability to change structure during a chemical transformation to aid in the transfer of protons and electrons or in the orientation of substrates.[2] There have been numerous efforts to incorporate these properties in synthetic systems, and notable advancements have been made.[3] One approach is to place basic functional groups proximal to metal centers that upon protonation can serve as H-bond donors.[4] Following this concept, we have developed a new dinucleating ligand, 3,5-bis[bis(*N*-6-pivalamido-2-pyridylmethyl)aminomethyl]-1*H*-pyrazole (H_5bppap), that when bonded to metal ions, adopted a variety of structures depending on its protonation state.[5] This report illustrates that H_5bppap can produce dinuclear species, in which each metal ion can have a different primary coordination sphere. Furthermore, we show that the ligand can aid in forming varied intramolecular H-bonding networks.

Nearly all of the binucleating ligands that have appeared in the literature provide symmetrical primary coordination spheres around each metal ion.[6] However, there are several situations in which differing metal coordination geometries would be beneficial for function.[6b,7] For example, the reduced form of the respiratory protein hemerthyrin contains one six-coordinate and one five-coordinate ferrous center: dioxygen binding occurs at the coordinately unsaturated site.[8] Our group[9] and others[10] have been utilizing (carboxyamido)pyridyl units in the design of multidentate ligands because they potentially coordinate to metal ions in two distinct modes. In one case, the carboxyamido group is deprotonated and functions as a bidentate ligand through coordination of the pyridyl nitrogen and carbonyl oxygen atoms (Figure 1A). Alternatively, the protonated form of the carboxyamido group assumes a conformation such that it is an intramolecular H-bond donor (Figure 1B). We have found that coupling these units to a pyrazolate ring led to H_5bppap, a dinucleating ligand whose complexes can have metal centers with differing primary and secondary coordination spheres.

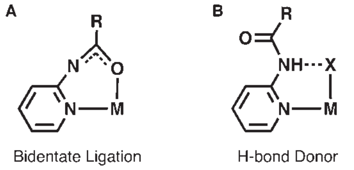
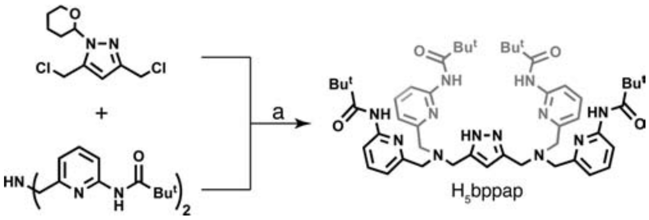


Figure 1. Possible binding modes of the carboxyamido unit.

Scheme 1. Synthesis of H_5bppap[a]



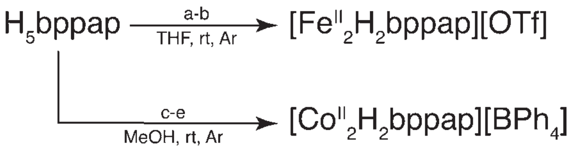
[a] Conditions: (a) Na_2CO_3, MeCN, Δ, 24 h; then HCl(aq)/EtOH, rt, 21 h, 80%.

H_5bppap was synthesized in multigram quantities via a convergent synthetic route, as outlined in Scheme 1. The protected bridging unit, 3,5-bis(chloromethyl)tetrahydropyran-2-yl-1*H*-pyrazole,[5,11a,12] and bis[*N*-(6-pivalamido-2-pyridylmethyl)]-amine[1] were coupled to afford a protected form of the ligand, which was subsequently deprotected to afford H_5bppap as a white powder in good yield (84%).

To evaluate the structural properties of metal complexes with H_5bppap, $[Fe^{II}{}_2H_2\text{bppap}]^+$ and $[Co^{II}{}_2H_2\text{bppap}]^+$ were prepared (Scheme 2) and crystallized.[12] Treating H_5bppap with 3 equiv of KH in anhydrous tetrahydrofuran gave the $[H_2\text{bppap}]^{3-}$ anion, which was allowed to react with 2 equiv of $Fe(OTf)_2$. The salt $[Fe^{II}{}_2H_2\text{bppap}](OTf)$ was isolated in almost quantitative yields via separation of the product from insoluble KCl. $[Co^{II}{}_2H_2\text{bppap}](BPh_4)$ was prepared by treating a methanolic solution of H_5bppap with NaOMe, $Co(OAc)_2$, and $NaBPh_4$; the salt was isolated as a

Received: April 27, 2011
Published: July 27, 2011

Scheme 2. Synthesis of Bimetallic Complexes of H_5bppap[a]



[a] Conditions: (a) 3 equiv of KH; (b) 2 equiv of $Fe(OTf)_2$; (c) 3 equiv of NaOMe; (d) 2 equiv of $Co(OAc)_2$; (e) 1 equiv of $NaBPh_4$.

lime green solid in high yield (86%). Both complexes were stable in a dry, anaerobic environment for several weeks.

The molecular structures for $[Fe^{II}_2H_2bppap]^+$ and $[Co^{II}_2H_2bppap]^+$ were determined by X-ray diffraction methods (Figure 2) and illustrate the versatility of the $[H_2bppap]^{3-}$ ligand in regulating the primary and secondary coordination spheres. The structure $[Co^{II}_2H_2bppap]^+$ shows that both Co^{II} centers have nearly identical distorted trigonal-bipyramidal coordination geometries ($\tau_{Co1} = 0.74$; $\tau_{Co2} = 0.76$).[13] The pyridyl and pyrazolate nitrogen atoms define the trigonal planes: for pyrazolate nitrogen atoms, the Co1−N4 and Co2−N10 bond distances are equivalent within experimental error. However, each cobalt center has two distinct $Co-N_{py}$ bond lengths: for example, the Co1−N2 and Co1−N3 bond distances are 2.028(2) and 2.135(2) Å, respectively. This difference in bond lengths reflects the fact that N2 is contained within two chelating rings, while N3 is only involved in a single chelating ring. The apical nitrogen atoms N1 and N9 bind to one of the axial coordination sites on each metal ion [avg. $Co-N_{axial} = 2.171(2)$ Å]. The other axial positions around each cobalt center are occupied by atoms O1 and O3 from the deprotonated carboxyamido groups, which coordinate in an identical manner (Table S2 in the Supporting Information). The remaining carboxyamido groups are protonated and form intramolecular H-bonds with O1 and O3, in which N6···O1 and N12···O3 distances of less than 3 Å are observed. A Co1···Co2 separation of 4.513 (1) Å was observed in $[Co^{II}_2H_2bppap]^+$.

The structural analysis of $[Fe^{II}_2H_2bppap]^+$ revealed that each iron center has different primary and secondary coordination spheres (Figure 2B). Fe1 has a distorted trigonal-bipyramidal geometry ($\tau_{Fe1} = 0.68$), containing an N_4O donor set that is similar to what was observed for the cobalt centers in $[Co^{II}_2H_2bppap]^+$. In contrast, Fe2 is six-coordinate, having an N_4O_2 arrangement of donor atoms, in which both oxygen atoms of the carboxyamido groups are bonded to the iron center. The significant difference in the Fe2−O3 and Fe2−O4 bond lengths of 1.957(2) and 2.267(2) Å reflects the protonation states of the carboxyamido groups. The shorter Fe2−O3 bond length agrees with the carboxyamido group containing O3 being deprotonated and serving as an anionic ligand. The carboxyamido group that includes O4 is protonated and thus is a neutral donor. Differences in the ligand N−C(O) bond lengths support this assignment: for the neutral group, N12−C45 is 1.358(3) Å, whereas for the anionic group, N11−C34 is 1.307(4) Å, indicating increased double-bond character. Furthermore, this type of coordination prevents the formation of intramolecular H-bonds around Fe2. It is not clear why there is a difference in the coordination spheres for the two iron centers in $[Fe^{II}_2H_2bppap]^+$.

The synthetic and structural results with the $[M^{II}_2H_2bppap]^+$ (M^{II} = Fe, Co) complexes suggested that the appended carboxyamido groups of $[H_2bppap]^{3-}$ are flexible and could readily adopt different conformations that may be useful in controlling the binding of exogenous ligands. To examine this possibility and evaluate the accessibility of the metal centers, we studied the binding of water molecules to $[M^{II}_2H_2bppap]^+$ complexes (Scheme 3). Treating either complex with 1 equiv of water produced the monohydroxide complexes $[\{M^{II}(OH)\}M^{II}H_3bppap]^+$.[12,14] Our analytical and spectroscopic studies suggested that water addition caused protonation of the dinucleating ligand with concomitant binding of a hydroxide ion to one of the metal centers. Note that additional amounts of water, up to 40 equiv, afford only the monohydroxo complexes.

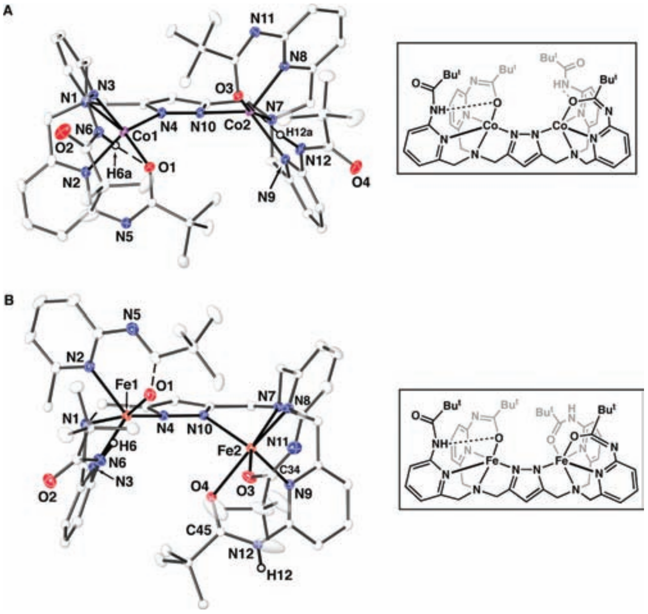
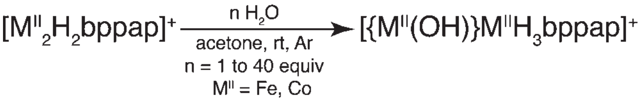


Figure 2. Thermal ellipsoid plots and schematic drawings for $[Co^{II}_2H_2bppap]^+$ (A) and $[Fe^{II}_2H_2bppap]^+$ (B). Only carboxyamido hydrogen atoms are shown for clarity. Selected metrical parameters are given in the Supporting Information.[12]

Scheme 3. Synthesis of Dimetallic $[\{M^{II}(OH)\}M^{II}H_3bppap]^+$ Complexes[12]



X-ray diffraction studies revealed that the cobalt ions in $[\{Co^{II}(OH)\}Co^{II}H_3bppap]^+$ (Figure 3A) have dissimilar trigonal-bipyramidal coordination geometries ($\tau_{Co1} = 0.88$; $\tau_{Co2} = 0.74$). For Co2, the metrical parameters and overall structures of the primary and secondary coordination spheres are nearly identical with those found for the cobalt centers in $[Co^{II}_2H_2bppap]^+$. For Co1, the hydroxo ligand is terminally bonded at one of the axial sites with a Co1−O5 bond length of 1.931(2) Å and a N1−Co1−O5 bond angle of 176.154°. This binding caused a major structural change in the dinucleating ligand: O1 is not bonded to Co1 (as in $[Co^{II}_2H_2bppap]^+$) but is positioned outside the cavity surrounding the metal ions. Moreover, the appended carboxyamido group containing O1 is now protonated, with the N5−H5B vector placed within the cavity. The structural rearrangement resulted in two intramolecular H-bonds forming between the hydroxo ligand and the carboxyamido groups (N5···O5, 2.773 Å; N3···O5,

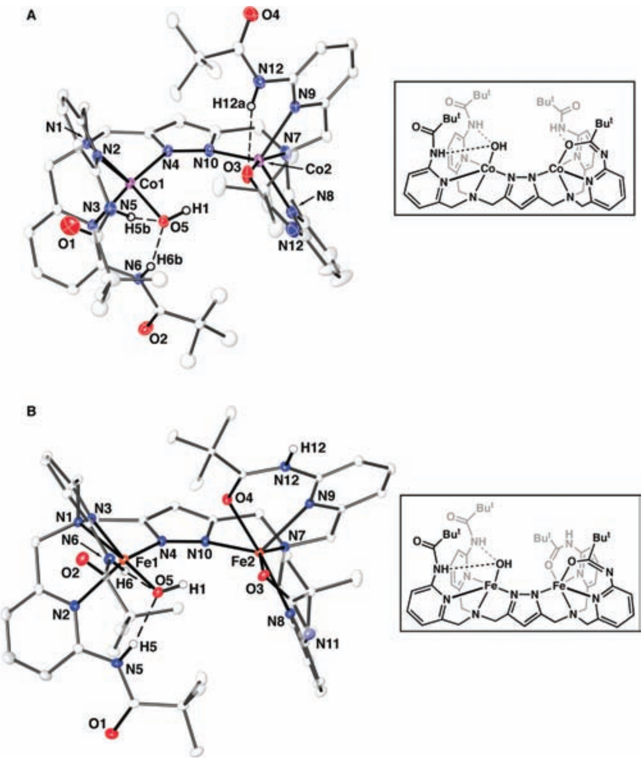


Figure 3. Thermal ellipsoid plots and schematic drawings for $[\{Co^{II}(OH)\}Co^{II}H_3bppap]^+$ (A) and $[\{Fe^{II}(OH)\}Fe^{II}H_3bppap]^+$ (B). Only carboxyamido hydrogen atoms are shown for clarity. Selected metrical parameters are given in the Supporting Information.[12]

2.773 Å). The Fourier transform IR spectrum supports this premise by having a single $\nu(O-H)$ peak at 3613 cm^{-1} and several broad $\nu(N-H)$ signals between 3400 and 3200 cm^{-1}, consistent with H-bonds involving the carboxyamido units.[14e]

The structural analysis on $[\{Fe^{II}(OH)\}Fe^{II}H_3bppap]^+$ showed that again one five-coordinate and one six-coordinate iron center exist, yet now an endogenous hydroxo ligand is terminally bonded to one of the iron sites. The hydroxo ligand is bonded to the five-coordinate iron site ($\tau_{Fe1} = 0.68$), with a Fe1−O5 bond length of 1.938(2) Å and a N1−Fe1−O5 bond angle of 172.62(9)° (Figure 3B). Both carboxyamido groups are protonated around Fe1 and form intramolecular H-bonds to the Fe1−O5 unit in a manner similar to that observed in $[\{Co^{II}(OH)\}Co^{II}H_3bppap]^+$. The Fe2 site remained six-coordinate, with both O3 and O4 of the appended carboxyamido groups bonded to the iron center.

In summary, we have developed a new dinucleating ligand that utilizes a pyrazolate bridge and (carboxyamido)pyridyl groups. The structures of $[M^{II}{}_2H_2bppap]^+$ and their hydrated products $[\{M^{II}(OH)\}M^{II}H_3bppap]^+$ showed the versatility of this design to produce complexes with varied coordination chemistry. The formation of a single metal ion site with a terminal hydroxo ligand is rare because of the propensity of this ligand to bridge between metal ions. The formation of only one M−OH site in each complex is attributed to several factors, including the spacing provided by the pyrazolate unit,[11b] the intramolecular H-bonds, and the bidentate binding mode of the carboxyamido groups. Our findings illustrate the utility of this design in preparing new classes of unsymmetrical dinuclear complexes.

ASSOCIATED CONTENT

Supporting Information. Details for all experiments, spectra, and crystallographic details (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: aborovik@uci.edu.

ACKNOWLEDGMENT

Acknowledgment is made to the NIH (Grant GM50781 to A. S.B.) for financial support.

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