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Tris(pyrazolyl)borate Copper Hydroxide Complexes Featuring **Tunable Intramolecular H-Bonding**

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Supporting Information

ABSTRACT: A modular synthesis provides access to a series of new tris(pyrazolyl)borate ligands XpyMeTpK that possess a single functionalized pendant pyridyl (py) or pyrimidyl (pyd) arm designed to engage in tunable intramolecular H-bonding to metal-bound functionalities. To illustrate such H-bonding interactions, a series of $[^{XpyMe}TpCu]_2(\mu$ -OH), (6a-6e) complexes were synthesized from the corresponding XpyMeTp-Cu–OAc (5a–5e) complexes. Single crystal X-ray structures of three new dinuclear $[^{XpyMe}TpCu]_2(\mu$ -OH)₂ complexes reveal H-bonding between the pendant heterocycle and bridging hydroxide ligands while the donor arm engages the copper center in an unusual monomeric DMAPMeTpCu-OH



complex. Vibrational studies (IR) of each bridging hydroxide complex reveal reduced $\nu_{\rm OH}$ frequencies that tracks with the Hbond accepting ability of the pendant arm. Reversible protonation studies that interconvert $[^{XpyMe}TpCu]_2(\mu$ -OH)_2 and [^{XpyMe}TpCu(OH₂)]OTf species indicate that the acidity of the corresponding aquo ligand decreases with increasing H-bond accepting ability of the pendant arm.

INTRODUCTION

In metalloenzymes, hydrogen bonding (H-bonding) interactions prevalent in the tightly regulated microenvironment of metal ions are closely tied to functionality.¹⁻³ When applied in synthetic systems, arrays of rigid H-bonding frameworks have had notable effects on chemical reactivity.^{4–8} The number and diversity of new synthetic systems featuring secondary coordination sphere H-bonding are expanding as efforts to better understand these phenomena continue.

Secondary sphere H-bond donor and/or acceptor groups are featured especially often in tripodal systems (Figure 1).9-15 For instance, several synthetic systems showcase the utility of H-bonding interactions with oxygen-containing small molecules. The stabilization of the peroxide anion (O_2^{2-}) via interactions with H-bond donors, first observed in Cummins¹⁶ metal-free cryptand, is underscored by Szymczak's¹⁷ tripodal Zn(II) complex, where secondary coordination sphere Hbonding governs O22- binding at Zn (Figure 1a). Fewer systems possessing H-bond acceptors have been re-ported^{14,18,19} but include Fout's¹⁰ tripodal scaffold with pyrrole-imine H-bond acceptors that H-bond to coordinated water (Figure 1b). In addition, this ligand can undergo redox tautomerization to form a "hybrid" H-bond donor/acceptor system as well as an all H-bond donor variant. Borovik's²⁰ recent example of this hybrid class is a tripodal scaffold containing a mix of two amine H-bond donors and one phosphinic amide H-bond acceptor (Figure 1c).

Since it can be difficult to directly examine the nature of the hydrogen bonding with highly reactive intermediates, more



Figure 1. Examples of systems incorporating second sphere H-bond donor and/or acceptor groups.

stable hydroxide complexes possessing secondary sphere Hbonding serve useful roles to survey H-bond contribu-tions.²¹⁻²³ Such hydroxide species have been important for revealing the influence of the number of H-bonding groups as well as the type of H-bonding groups on the properties of the complex.^{11,14,21,24}

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In a landmark report, Kitajima and Fujisawa established TpCu scaffolds (Tp = tris(pyrazolyl)borate) as important biorelevant models for O₂ reactivity at copper-based hemocyanin with [^{iPr2}TpCu]₂(μ -O₂) and the related [^{iPr2}TpCu]₂(μ -OH)₂.²⁵ Molecular copper–oxygen complexes attract interest as intermediates in chemical transformations mediated by hemocyanin,^{25–27} copper oxidases,^{28–30} and other copper-based enzymes.^{31,32}

We set out to construct a new family of Tp ligands with tunable secondary sphere H-bonding through only a single heterocyclic pyridyl (py) or pyrimidyl group (pyd). While examples of Tp scaffolds bearing pendant H-bonding groups^{33–37} or ancillary ligands capable of H-bonding have been reported,^{38–40} particularly inspiring is a ^{py3}TpK ligand^{35,37,41} that bears three pendant pyridyl groups that engages in secondary sphere H-bonding with an aqua ligand at Cu^{II} (Figure 2a).^{35,37} The targeted Tp ligand, however, bears



Figure 2. Intramolecular H-bonding in TpCu complexes featuring pendant H-bond acceptor groups.

only a single pendant base, since Tp systems with three pyridyl groups—one pyridyl arm per pyrazole—lead to an array of Cu coordination motifs involving Cu–py interactions (Figure 2).^{35,37,41} We report herein a new, modular synthesis for singly functionalized ^{XpyMe}TpK heteroscorpionates along with crystallographic and spectroscopic characterization of corresponding [^{XpyMe}TpCu]₂(μ -OH)₂ complexes that demonstrate tunable secondary coordination sphere H-bonding.

RESULTS AND DISCUSSION

A series of substituted pyrazoles was prepared starting with the Claisen condensation of a series of commercially available py or pyd (pyrimidine) ester derivatives with acetone to give the corresponding diketone (Scheme 1). This reaction most reliably proceeds with a non-nucleophilic base such as KH in Et₂O. Condensation of respective diketones 2a-2d with anhydrous hydrazine in methanol affords the py and pyd functionalized pyrazoles (^{XpyMe}PzH) 3a-3d in high yields (Scheme 2). This approach was not successful, however, in the synthesis of 3e that possesses a dimethylamino-pyridine

Scheme 1. Synthesis of Diketones (2a-2d)



Scheme 2. Synthesis of ^{XpyMe}PzH (3a-3d)



(DMAP) functionality. Instead, nucleophilic aromatic substitution of chloropyridine-pyrazole 3d with neat 40% aqueous dimethyl amine under reflux gives 3e in 73% yield (Scheme S4). Single crystal X-ray diffraction structures obtained for 3c and 3e illustrate intermolecular x py…H–Pz H-bonding interactions (Figures S10 and S11).

A pyrazole exchange reaction starting from the symmetric iPr2 TpK ligand⁴² conveniently leads to singly substituted XpyMe TpK heteroscorpionates (4a–4e) (Scheme 3). Unlike



other heteroscorpionates that bear nonsymmetric functionalities,43-46 parallel efforts to generate the monosubstituted XpyMeTpK from a molten reaction of KBH₄ 2:1 ratio of the corresponding pyrazoles or postmetalation modifications to the ligand were unsuccessful. Instead, XpyMeTpK can be synthesized by combining equimolar amounts of ^{1Pr2}TpK and ^{XpyMe}PzH (**3a-3e**) at 160 °C under a dynamic vacuum. These conditions facilitate both pyrazole exchange and removal of ^{iPr2}PzH via sublimation onto a coldfinger, recycled for future use (Figure S1). Crystallization from minimal dichloromethane (DCM) with several drops of acetonitrile provide ^{XpyMe}TpK ligands 4a-4e as acetonitrile adducts, which can be dried in vacuo to provide solvent-free species in 46-60% yields. X-ray crystallography of acetonitrile adducts reveals either mono- or dinuclear structures (Figure 3). For instance, 4a crystallizes as monomeric $^{CF3pyMe}TpK(NCMe)_2$ whereas 4c is isolated as a dimer bridged by three MeCN molecules (Figure 3).

Transmetalation of ligands **4a**–**4e** occurs smoothly with anhydrous Cu(OAc)₂ in DCM to afford ^{XpyMe}TpCu–OAc complexes **5a**–**5e** in 72–88% yield (Scheme 4). Single crystal structures of **5b** and **5c** reveal coordination of the py and pyd donor arms with the respective Cu centers. A τ_5 analysis⁴⁷ (τ_5 = 0, square pyramidal; τ_5 = 1, trigonal bipyramidal) reveals a slight distortion toward trigonal bipyramidal geometries (τ_5 = 0.56 and 0.62) for **5b** and **5c** respectively (Figure 4). Both feature monodentate acetate coordination, unlike in a simple ^{Tn}TpCu–OAc⁴⁸ complex that possesses a bidentate acetate ligand. Related TpCu–OAc complexes with an extra copper donor such as [^{PhMe}TpCu(^{PhMe}PzH)]OAc⁴⁹ and [^{Ph}TpCu-(^{Ph}PzH)]OAc⁵⁰ also feature monodentate acetate ligands,



Figure 3. X-ray structures of $^{CF3pyMe}TpK(NCMe)_2$ (4a) and $[^{pyMe}TpK]_2(\mu$ -NCMe)_3 (4c). In structure 4a the CF₃ group is disordered over two positions and is represented by sites of highest occupancy. Isopropyl groups on the pyrazoles, MeCN solvate molecules, and most hydrogen atoms are omitted for clarity.



indicating that the presence of an additional ligand disfavors bidentate acetate coordination. Coordination of the pendant py and pyd groups in **5b** and **5c** leads to C1–C4–N3 bond angles of 112.81(19)° and 113.22(15)° (Figure 4), respectively. While these angles are below the idealized 120° for sp² carbon centers, other Cu centers coordinated to bidentate ^{py}Pz ligands similarly show modest strain.^{51,52} We hypothesized that the presence of a H-bond donor at copper would turn on intramolecular H-bonding that then would compete with the py-Cu or pyd-Cu interaction.



 $[^{XpyMe}TpCu]_2(\mu$ -OH)_2 complexes (6) result from stirring $_{XpyMe}TpCuOAc$ (5) in a biphasic DCM/aqueous NaOH mixture (Scheme 5), similar to that used to prepare $[^{iPr2}TpCu]_2(\mu$ -OH)_2 (7).²⁵ Crystallization from DCM solutions layered with MeCN allows for isolation of $[^{XpyMe}TpCu]_2(\mu$ -OH)_2 (6a-6e) in 75–95% yields. Single crystal X-ray structures of $[^{XpyMe}TpCu]_2(\mu$ -OH)_2 species 6a-6c reveal intramolecular H-bonding between the respective pendant py and pyd arms with the bridging hydroxo groups (Figure 5). The Cu^{II} centers in 6a-6c adopt a more square pyramidal geometry ($\tau_5 = 0.22$ (6a), 0.19 (6b), and 0.27 (6c) similar to $[^{iPr2}TpCu]_2(\mu$ -OH)_2 ($\tau_5 = 0.31$) that does not have



Figure 4. X-ray structures of ^{pymMe}TpCu–OAc (5b) and ^{pyMe}TpCu–OAc (5c), respectively. Isopropyl groups on the pyrazoles, solvate molecules, and most hydrogen atoms are omitted for clarity.



Figure 5. X-ray structures of $[^{CF3pyMe}TpCu]_2(\mu$ -OH)_2 (**6a**), $[^{pymMe}TpCu]_2(\mu$ -OH)_2 (**6b**), $[^{pyMe}TpCu]_2(\mu$ -OH)_2 (**6c**), and $^{DMAPMe}TpCu$ -OH (**6e**), respectively. In structure **6a**, the CF₃ groups are disordered and are represented by sites of highest occupancy. Isopropyl groups on the pyrazoles and hydrogen atoms are omitted for clarity.

an additional donor arm.²⁵ The distance between Cu centers for **6a–6c** (2.9384(7) to 2.9457(11) Å) are also nearly identical to unmodified 7 (2.937(2) Å).²⁵ As a measure of the H-bonding interaction, the py–N···O(H) and pyd–N···O(H) distance decreases with increasing basicity of the N-based H-bond acceptor.^{53–55}

Curiously, the crystal X-ray structure of the copper(II) hydroxide with the most electron-rich donor arm corresponds to a mononuclear ^{DMAPMe}TpCu-OH (**6e**) complex (Figure 5). Instead of H-bonding with the hydroxide group, the pendant DMAP binds the Cu^{II} center (Figure 5). Close inspection reveals no H-bonding interactions with the terminal OH⁻ ligand. The five-coordinate environment is between square pyramidal and trigonal bipyramidal ($\tau_5 = 0.51$). This mononuclear copper hydroxide, however, is somewhat surprising due to the enhanced H-bond accepting ability of its DMAP arm as well as the scarcity of structurally characterized mononuclear Cu^{II}-OH species.⁵⁶⁻⁵⁹

To probe the influence of H-bonding on the hydroxide ligand, **6a–6e** as well as 7 were characterized via IR spectroscopy (Figure 6 and S10). Species **6a–6c** and 7 were analyzed as KBr pellets whereas **6e** was analyzed as a thin film evaporated from DCM on a KBr window. The variant lacking any H-bonding, 7, features a high energy ν_{OH} stretch at 3660 cm⁻¹. In contrast, dinuclear and H-bonded **6a–6c** exhibit broad ν_{OH} bands centered at ever decreasing energy as the H-



Figure 6. H-bonding in dinuclear copper(II) hydroxides as revealed through IR spectra. The ν_{OH} stretching region of IR spectra of **6a**-**6e** and **7**.

bond accepting ability of the donor arm increases (Table 1). Interestingly, the IR spectrum of complex **6e** features a broad $\nu_{\rm OH}$ band lower in energy than observed for **6a**–**6c** consistent with the greatest H-bond accepting ability of the DMAP arm despite the mononuclear structure indicated in crystals from DCM by X-ray crystallography (Figure 5). The IR spectra were taken as films that result from solvent evaporation of DCM solutions of **6**, and therefore this suggests a dinuclear species $[^{\rm DMAPMe}TpCu]_2(\mu-OH)_2$ that features intramolecular H-

Table 1. H-Bonding: Comparison of 6a-6e and 7

complex	$\nu_{\rm O-H}~({\rm cm^{-1}})$	$O(H) \cdots N$ (Å)
$[^{iPr2}TpCu]_{2}(\mu$ -OH)_{2} (7)	3660	
$[^{CF3pyMe}TpCu]_2(\mu\text{-}OH)_2 (\mathbf{6a})$	3340	2.901(4)
$[^{pymMe}TpCu]_2(\mu-OH)_2 (6b)$	3331	2.864(4)
$[^{pyMe}TpCu]_2(\mu\text{-}OH)_2 (\mathbf{6c})$	3267	2.849(3)
$[^{DMAPMe}TpCu]_2(\mu\text{-}OH)_2 (\mathbf{6e})$	3223, 3647	

bonding is accessible in solution. Nonetheless, the IR spectrum of **6e** also possesses a sharp ν_{OH} at 3647 cm⁻¹ consistent with the mononuclear ^{DMAPMe}TpCu–OH that lacks H-bonding.

We hypothesize that intramolecular H-bonding between the pendant base and the bridging hydroxyl ligands in 6a-6e influences the basicity of the Cu–OH moiety. As an indirect measure, we sought to assess the relative acidity of the corresponding aquo moiety $[Cu-OH_2]^+$ formed upon protonation (Figure 7). Titrating dinuclear hydroxide com-



Figure 7. Reversible protonation of 6a-6e and 7. The pendant groups of each respective [^XTpCu(OH₂)]OTf species (8) is illustrated next to the weakest base (collidine, Et₃N, DBU) required for deprotonation to the corresponding [^XTpCu]₂(OH)₂ species in DCM.

plexes [^{XpyMe}TpCu]₂(μ -OH₂)₂ (**6a**-**6d**) with HOTf in CH₂Cl₂ at -10 °C results in the loss of the band near 600 nm corresponding to **6** with concomitant growth of a lower energy band near 800 nm (Figures 8, S19, and S23). Since titration end points for **6a**-**6d** occur with 2 equiv of HOTf, it suggests the conversion of dinuclear [^{XpyMe}TpCu]₂(μ -OH)₂ (**6a**-**6d**) to 2 equiv of mononuclear [^{XpyMe}TpCu(OH₂)]OTf (**8a**-**8d**). Although DMAP substituted **6e** may exist in both mononuclear and dinuclear forms, titration with HOTf reaches an end point at 1:1 ratio of Cu: HOTf suggesting similar formation of [^{DMAPMe}TpCu(OH₂)]OTf (**8e**). While attempts to structurally characterize **8a**-**8e** via X-ray diffraction were unsuccessful, characterization of **8a** and **8e** by IR show the formation of two new broad ν_{HO-H} bands centered around



Figure 8. Stepwise protonation of $[^{CF3pyMe}TpCu]_2(\mu$ -OH)₂ (6a) with HOTf in DCM at -10 °C.

3262 and 3176 cm⁻¹ respectively (Figures S31 and S32). These new bands occur at similar energies as other reported $[Cu]-OH_2^+$ species.^{60,61} In contrast, protonation of $[^{iPr2}TpCu]_2(\mu$ -OH)_2 (7) without the pendant arm reaches completion after addition of 0.5 equiv HOTF/Cu. This result reveals the decisive role played by the pendant arm in modifying the basicity of the bridging hydroxide ligands in $[^{XpyMe}TpCu]_2(\mu$ -OH_2)_2 (6a-6d).

Backtitration of these cationic aquo species 8 to return the dinuclear hydroxo species 6 exhibits a dependency on the added base used. In this study, we examined three different bases of increasing strength: 2,4,6-collidine (col) < triethylamine (Et₃N) < DBU. Aquo complex 9 that lacks any pendant donor is most acidic, amenable to deprotonation back to 7 with the least basic collidine. Deprotonation of complexes 8 that possess pendant arms require stronger bases with the base required correlating with the basicity of the pendant arm. While CF₃-pyridine 8a and pyrimidine 8b undergo deprotonation with Et₃N, the more basic pyridine 8c and DMAP 8e species require DBU to affect deprotonation.

CONCLUSIONS

The modular synthesis of a Tp scaffold possessing a single pyridine or pyrimidine donor arm allows ready access to a new class of heteroscorpionate ligands capable of H-bonding in the second coordination sphere. While a series of XpyMeTpCu-OAc complexes reveal that the respective py and pyd arms can coordinate to the copper center, this coordination is absent when intramolecular H-bonding occurs between the pendant arm and the hydroxide O-H moiety in corresponding $[^{XpyMe}TpCu]_2(\mu \cdot OH)_2$ complexes. Single crystal X-ray structures and IR spectroscopy of these copper-hydroxide species reveal a direct correlation between the N…O(H) bond distance and $\nu_{\rm OH}$ stretching frequency with the electronic nature of the H-bond acceptor arm. This family of Tp ligands features highly tunable pendant arms that participate in Hbonding interactions illustrated through copper(II) hydroxides $[^{XpyMe}TpCu]_2(\mu$ -OH)₂. For instance, the corresponding cationic aquo complexes {[$^{XpyMe}TpCu$](OH₂)}⁺ (8) formed upon protonation of [$^{XpyMe}TpCu$]₂(μ -OH)₂ (6) require added bases that correlate with the basicity of the pendant arm. The synthetic accessibility and tunability of these ^{py}Tp ligands suggest that they may enable H-bonding interactions with other functionalities bridged between two TpM centers. One such target is diazene, an important intermediate in dinitrogen

Inorganic Chemistry

reduction^{62,63} that is foreshadowed by the isolation of $[{}^{iPr2}TpCu]_2(\mu-N_2H_2)$.⁶⁴

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorg-chem.9b01991.

Experimental and X-ray structure details (PDF)

Accession Codes

CCDC 1890609–1890618 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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