

Folded Metallodendrons: Shell-Selective Metal Coordination and Conformational Properties

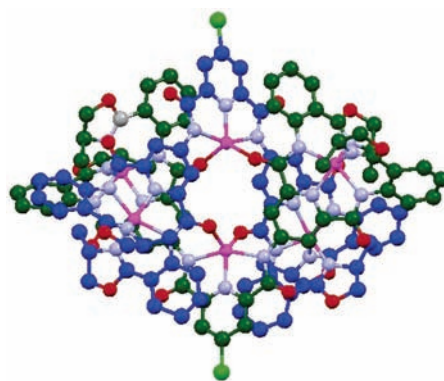
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ABSTRACT



The synthesis, structure, and conformational properties of folded metallodendrons are described. The enhanced coordination ability of oxazoline-functionalized pyridyl-2,6-dicarboxamides, compared with pyridyl-2,6-diarylamides, permits unique metals to be installed at the peripheral and focal shells of the dendron. Circular dichroism (CD) studies and X-ray crystallography indicate that the intrinsic helical preference of the parent dendron is not perturbed by coordination. However, the CD spectra become insensitive to temperature due to an increase in structural rigidity that occurs upon metal coordination.

The dynamic interplay of structure and function in natural systems¹ underscores the importance of controlling the structure of synthetic molecules.² Many proteins derive their functional capabilities via the presence of internally coordinated metal ions, which play critical roles in catalysis, electron transfer, and ligand binding.³ Precise control of the number, type, and radial location of metal ions coordinated within a dendrimer structure will be crucial to realize the

full functional capabilities of dendrimers.⁴ The shell-selective assembly of dendrimers containing more than one type of metal center has been achieved by employing generational growth steps based on sequential coordination events.⁵ Such high levels of post-synthetic coordination selectivity have only been reported for the complexation of SnCl₂ to polyphenylazomethine dendrimers.⁶ In this paper, we report a synthetic

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approach to incorporate two different metals within a folded dendritic structure.

A strategy to discriminate the internal and peripheral sites was devised on the basis of the differential coordinating ability of pyridyl-2,6-dicarboxamides **A/C** and **B** (Figure 1).

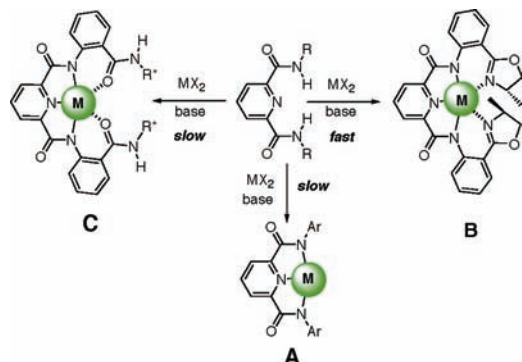


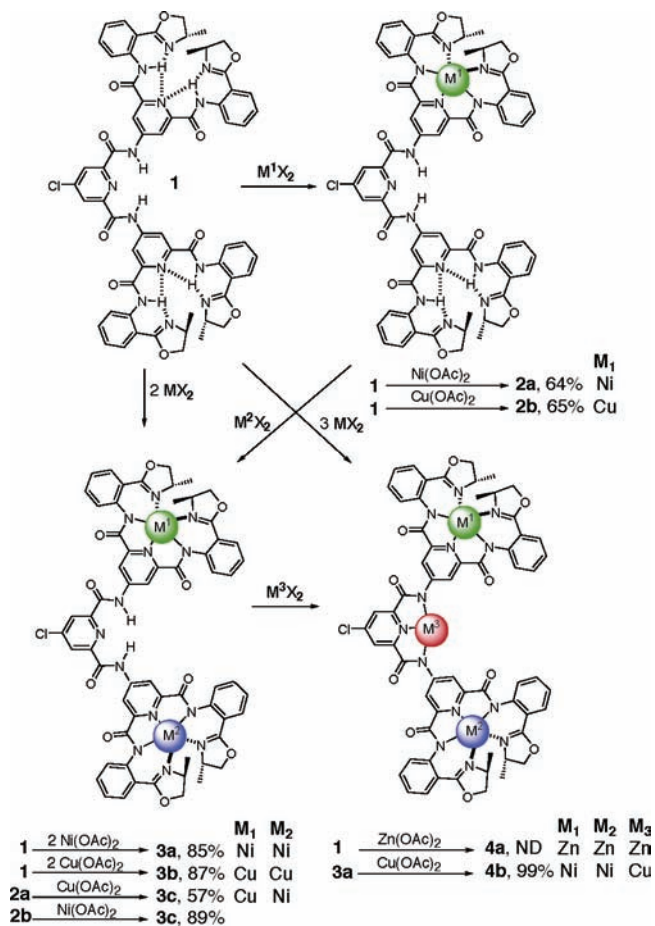
Figure 1. Differential coordinating ability of type A/C and B pyridyl-2,6-dicarboxamides.

Coordinating type A or C ligands to divalent metals requires full amide deprotonation with KH or extended reaction times (6 h) with weak bases such as Et₃N.⁷ In contrast, oxazoline-functionalized pyridyl-2,6-diarylamides **B** rapidly form complexes within minutes upon exposure to divalent metal salts in the presence of triethylamine.⁸ On this basis, we reasoned that type B sites would selectively coordinate metals within dendrimers also containing ligands of type A or C, a ubiquitous repeat unit in this dendrimer system.^{10,12}

To investigate this potential selectivity, a second-generation dendron (**1**) was constructed that displayed two peripheral type B and one focal type A sites (Scheme 1 and Supporting Information). Exposure of **1** to 2 equiv of Cu(OAc)₂ or Ni(OAc)₂ in the presence of triethylamine in CH₂-Cl₂-MeOH afforded metallodendrons **3a** and **3b** displaying two Ni or Cu atoms selectively coordinated at the peripheral sites. The paramagnetic nature of the complexes precluded characterization by ¹H NMR spectroscopy. Accordingly, the metal/dendrion stoichiometry of **3a/3b** was determined by high-resolution electrospray mass spectrometry, which revealed experimental isotopic distributions identical to calculated patterns (Supporting Information).

Further structural verification was obtained for nickel complex **3a** by X-ray crystallography. Slow evaporation of a CH₂Cl₂/EtOAc solution of **3a** afforded brown crystals of either space group *P*3₁ or *P*3₁21. The probable occurrence of twinning in the crystal hampered determination of the space group and full refinement of the structure. However,

Scheme 1. Shell-Selective Metalation of Type I Dendrons Using MX₂ and (C₂H₅)₃N in CH₃OH–CH₂Cl₂



several important structural features were unambiguously elucidated (Supporting Information). (1) Two nickel atoms were selectively coordinated at the peripheral type B positions. (2) Coordination maintained the *P* helical conformational preference exhibited by the uncomplexed dendron.⁹ (3) The asymmetric unit was composed of two virtually identical, intertwined monodendrons. We have previously observed similarly intertwined dimers in the crystal structures of related second-generation dendrons lacking metal atoms.¹⁰

The formation of **3a** and **3b** was accompanied by the formation of trace amounts of the corresponding monometallic complex. The significantly lower polarity of the monometallic species permitted chromatographic separation from the bimetallic compounds. The facile isolation of the monometallic complexes suggested the possibility of installing two different metals on the periphery. Accordingly, exposure to 1 equiv of Cu(OAc)₂ or Ni(OAc)₂ afforded brown mononickel complex **2a** or green monocopper complex **2b** in 64% and 65% yields, respectively. Subsequent exposure of **2a** or **2b** to another equivalent of Cu(OAc)₂ or Ni(OAc)₂ afforded identical bimetallic complexes (**3c**)

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containing both copper and nickel atoms in 57% and 89% yields, respectively. Conversion of **2a** or **2b** to the mixed metal complex **3c** was accompanied by a color change from brown (for **2a**) or green (for **2b**) to green–brown. Similarly, the UV–vis spectra of **3c** exhibited a broad $\pi \rightarrow \pi^*$ transition associated with the 2-acylaminophenyl oxazoline chromophore in the range of 340–350 nm due to the superposition of the corresponding Cu and Ni transitions that occur at 343 and 350 nm, respectively (Figure 3).

These observations also suggested the possibility of installing unique metals at the peripheral and internal shells. Accordingly, exposure of bisnickel complex **3a** to $\text{Cu}(\text{OAc})_2/\text{Et}_3\text{N}$ provided trimetallic complex **4b** displaying two nickel atoms in the outer shell and one copper atom in the inner shell in 99% yield, as evidenced by high-resolution QTOF mass spectrometry and comparison to the calculated isotopic distribution pattern (Supporting Information). Attempts to place nickel at the focal point by reacting biscopper complex **3b** with $\text{Ni}(\text{OAc})_2/\text{Et}_3\text{N}$ were unsuccessful, returning starting **3b**, even when stronger bases such as NaH or DBU were employed. Although HRMS confirms the expected stoichiometry of the mixed metal complex, **4b**, potential scrambling of the positions of the metals cannot be unambiguously ruled out. However, treating the nickel complex of 4-chloro-2,6-bis[2-((4*S*)-4-methyl-4,5-dihydro-1,3-oxazol-2-yl)phenyl]carbamoyl-pyridine (**5**)⁸ with $\text{Cu}(\text{OAc})_2/\text{Et}_3\text{N}$ or the corresponding copper complex with $\text{Ni}(\text{OAc})_2/\text{Et}_3\text{N}$ did not interconvert the two complexes, suggesting that metal exchange is not facile under these conditions.

Attempts to obtain X-ray quality crystals of the copper and mixed metal complexes were not successful. However, treatment of **1** with 3 equiv of $\text{Zn}(\text{OAc})_2/\text{Et}_3\text{N}$ for 6 h provided a highly crystalline yellow complex (**4a**).¹¹ Although the hydrolytic instability of the zinc complex prevented chromatographic isolation, slow evaporation of the crude reaction mixture produced pale yellow crystals of space group *P*3₁. An X-ray crystal structure revealed a dimeric structure composed of two interdigitated dendrons containing six coordinated zinc atoms (Figure 2). Similar to bisnickel complex **3a**, intertwining of two metallodendrons induces face-to-face π stacking interactions that sandwich the focal pyridine-2,6-dicarboxamide ring of one dendron between two adjacent terminal rings of the other dendron. The dimer is further stabilized by coordination of two amide carbonyls of one dendron with the focal zinc atom of the other dendron with an average $\text{Zn} \cdots \text{O}=\text{C}$ distance of 2.150 Å. However, the focal coordination sites were not fully occupied by zinc atoms throughout the crystal lattice. This leads to an average interdendron distance between the focal pyridine and Ns of 9.557 Å. The average $\text{Zn} \cdots \text{N}_{\text{amide}}$, $\text{Zn} \cdots \text{N}_{\text{pyridine}}$, and $\text{Zn} \cdots \text{N}_{\text{oxazoline}}$ distances of the peripheral shell were 2.116, 2.023, 2.031 Å. The focal shell zinc complexes display average $\text{Zn} \cdots \text{N}_{\text{amide}}$ and $\text{Zn} \cdots \text{N}_{\text{pyridine}}$ distances of 2.165 and 1.956 Å. Similar to **3a**, a *P* helical conformational orientation relates the terminal aryloxazoline groups of each terminal zinc complex.

The selectivity in metalation of the peripheral type B pyridyl-2,6-diarylamides in the presence of the focal type A

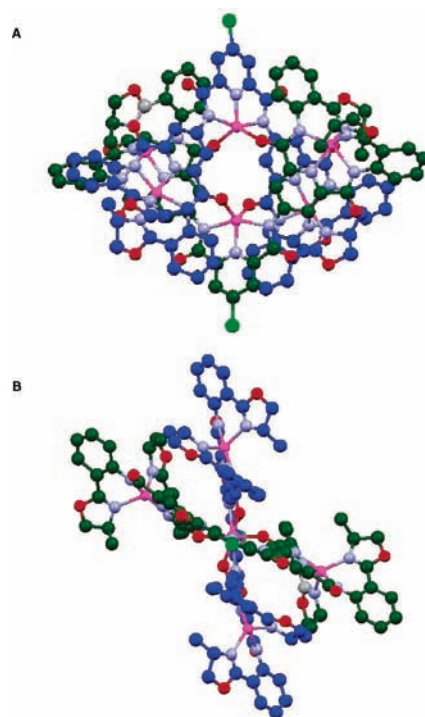
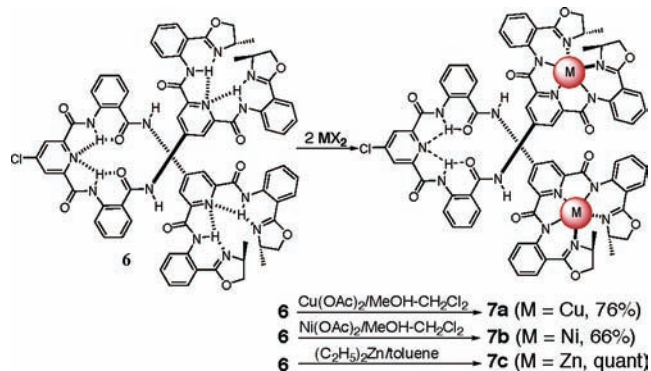


Figure 2. X-ray structure of trizinc complex **4a**. (A) Side-on view showing focal zinc atoms coordinated by the 2,6-pyridyl diamide of one dendron and the amide carbonyls of the other dendron. (B) Top-on view showing intertwined dimer structure. Hydrogens omitted for clarity.

ligand in **1** indicated that the aryloxazoline groups significantly accelerate complexation. Accordingly, the proximity of the amide groups (type C ligand)¹² at the focal position of type II dendron **6** could be expected to decrease the selectivity in peripheral metalation. Nonetheless, exposing **6** to 2 equiv of $\text{Cu}(\text{OAc})_2$, $\text{Ni}(\text{OAc})_2$, or $(\text{C}_2\text{H}_5)_2\text{Zn}$ provided bismetallodendrons **7a–c** in good yields without any evidence of focal complexation (Scheme 2).

Scheme 2. Selective Coordination of Type II Dendron



The UV–vis and CD spectra of the parent and metallodendrons are depicted in Figures 3 and 4. Complexation of

1 by Cu(II) or Ni(II) is accompanied by a red shift of the $\pi \rightarrow \pi^*$ transition associated with the 2-acylaminophenyl oxazoline chromophore from 309 (**1**) to 343 nm (**3b** (Cu₂)), 350 nm (**3a** (Ni₂)), and a broad peak over 340–350 nm (**4b** (Ni₂Cu)) in the UV–vis spectrum. CD spectra of **1**, **3a**, **3b**, and **4b** exhibited positive excitonic couplets with zero crossings near these transitions (Figure 3). Similar UV and

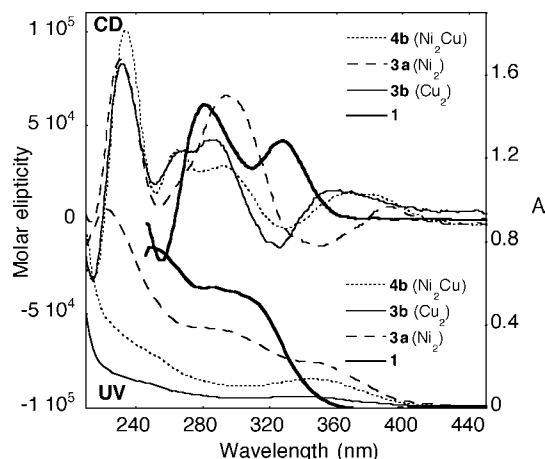


Figure 3. CD and UV spectra of **3a**, **3b**, **4b** (CH₃CN), and **1** (CH₂Cl₂) at 25 °C. UV–vis spectral scale adjusted for clarity.

CD spectral features occur in the type II dendrons **6** and **7a–c** (Figure 4).

These spectroscopic properties are also present in complexes of the first-generation ligand (**5**).⁸ On the basis of the calculated (TDDFT-B3LYP) direction of the electronic transition moment for this ligand (**5**), the positive excitonic couplets of **1**, **3a**, **3b**, **4b**, **6**, and **7a–c** correspond to a *P* helical conformational preference in solution, identical to the helical bias exhibited by **3a**, **4a**, and **5** in the solid state.

NMR line-shape analysis of the Zn complex of **5** indicated that coordination significantly increases the helical interconversion barrier.⁸ It is noteworthy that the amplitude of the CD transitions of metal complexes **3a**, **3b** and **4b** exhibited

(11) Zn (**4c**): (C₆₁H_{47.24}Cl₁N₁₃O₁₀Zn_{2.38}) and (C₆₁H_{47.77}Cl₁N₁₃O₁₀Zn_{2.11}) plus disordered solvent, Mo K α radiation, *T* = 150 K, trigonal, *P*3₁, *a* = 32.195(2) Å, *c* = 12.584(1) Å, *V* = 11296.2(13) Å³, *Z* = 326 254 unique reflections, *R*1(*F*) = 0.088, *wR*2(*F*²) = 0.219 (all data). A merohedral twin law (TWIN 010/100/00-1) was used in the final refinement cycles, and the fraction of this twin component was refined to 0.082(1).

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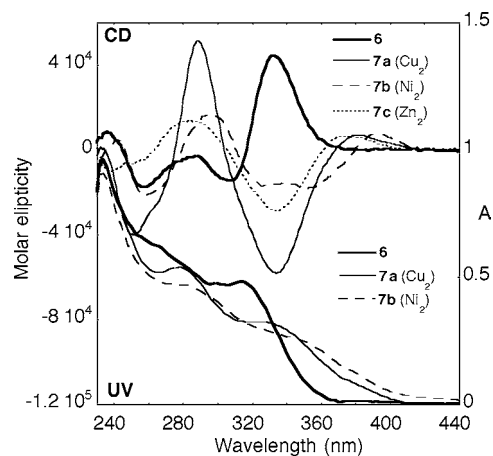


Figure 4. CD and UV spectra of **6** and **7a–c** in CH₂Cl₂ at 25 °C.

no temperature sensitivity up to 60 °C in CH₃CN, whereas the CD spectra of uncomplexed dendron, **1**, decreased in amplitude upon heating (Supporting Information). The increased conformational stability of the metalated dendrons likely emerges via the increase in the helical interconversion barrier that occurs upon metal coordination.

In conclusion, these studies have demonstrated the potential of selectively installing unique metals at each generational shell of dendrons. Whereas metal coordination increases the stability of the dendron secondary structure in solution, the intrinsic helical bias of the uncomplexed dendron is maintained.

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Supporting Information Available: Experimental procedures and compound characterization for **1–4** and **6–7**; ¹H and ¹³C NMR spectra for **1**, **6**, and **7c**; partially refined X-ray structure of **3a**; temperature-dependent CD spectra of **3a–c** and **4b**; and high-resolution mass spectra and calculated isotopic patterns for **3a–c**, **4b**, and **7a–c**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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