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Architectural Spiroligomers Designed for Binuclear Metal Complex Templating

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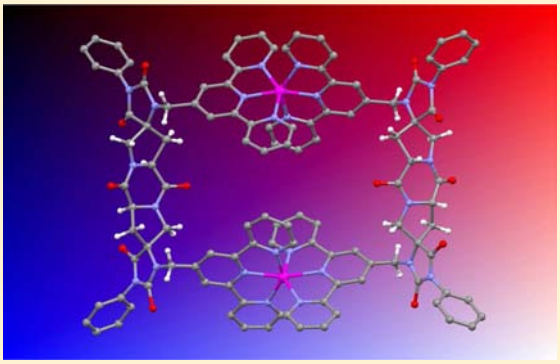
Supporting Information

ABSTRACT: The first structurally, spectroscopically, and electronically characterized metal-spiroligomer complexes are reported. The binuclear $[M_2L_2]^{4+}$ ions (M = Mn, Zn) are macrocyclic "squares" and are characterized by X-ray diffraction, ^{1}H and ^{13}C NMR, electronic absorption, emission, and mass spectroscopies. The manganese complex contains two spin-independent Mn^{II} ions and is additionally characterized using EPR and CD spectroscopies and CV.



INTRODUCTION

The development of rationally designed transition metal complexes depends upon strict control of the coordination geometry about the metal. As a result of this requirement, ligand design has become a major thrust in the development of inorganic materials.[1] In particular, development of chiral coordination environments[2] and multi-metal[3] geometries has become increasingly important. Despite the clear benefits of ligand design, a major drawback is that each new desired coordination environment demands a reinvention of the ligand synthesis, involving new starting materials, catalysts, coupling agents, and purification techniques. For instance, the preparation of an achiral hangman porphyrin designed to model the sophisticated cytochrome C oxidase active sites requires a 13 step synthesis from commercially available starting materials.[4] A geometrically and functionally versatile ligand synthesis template for rapid generation of new coordination geometries is thus an important goal for increasing throughput in the field of ligand design.

The Schafmeister group has developed a new class of spiroligomer macromolecules ideally suited for this purpose. Spiroligomers are shape-programmable ladder-oligomers that display a large variety of functional groups with control over their relative three-dimensional presentation. We have developed spiroligomers that bind and stabilize the protein HDM2 in cell culture[5] and another that mimics the active site of serine esterases and catalyzes a trans-esterification reaction.[6] The preparation of these materials is achieved by solution-phase or solid-phase synthesis via the modular assembly of stereochemically pure protected bis-amino acids (from an ever-growing library of ca. 24 monomers) through pairs of amide bonds to create ladder oligomers with programmable shapes and functional group display.[7] The three-dimensional structure of spiroligomers is controlled by the stereochemistry of the monomers, structure of the monomer rings, and regiochemistry of the functional groups that they display. The control that they permit over their three-dimensional structure suggest that spiroligomers could serve as excellent scaffolds for the display of chiral multi-metal active sites to explore sophisticated multi-functional catalysis and other metal-based applications.

While spiroligomers have demonstrated their utility in the rational design of functional molecules, they have only begun to be applied to the construction of controlled transition metal ligation environments.[8] Inherently chiral and enantiomerically pure, spiroligomers offer an excellent opportunity for controlled geometric metal complex templating and for imparting chiral character onto metal centers. We report here the first fully characterized metal−spiroligomer complexes: binuclear dimers of manganese and zinc using a simple spiroligomer with terpyridine side chains. We also demonstrate the first X-ray crystal structures of spiroligomers with or without bound metals and the formation of the first metal-templated supramolecular complex of two spiroligomers.

RESULTS AND DISCUSSION

The spiroligomer **L** possesses two terpyridyl side chains on a four-"*S*" stereocenter nucleus designed so that the side chains are oriented on the same side of the 5−6−5 fused ring system (Figure 1, top). Synthesis of the *S*,*S* configured bis-amino acid **1a** (Scheme 1) has been previously reported.[7] The terpyridyl group was then attached to the primary amine by utilizing the

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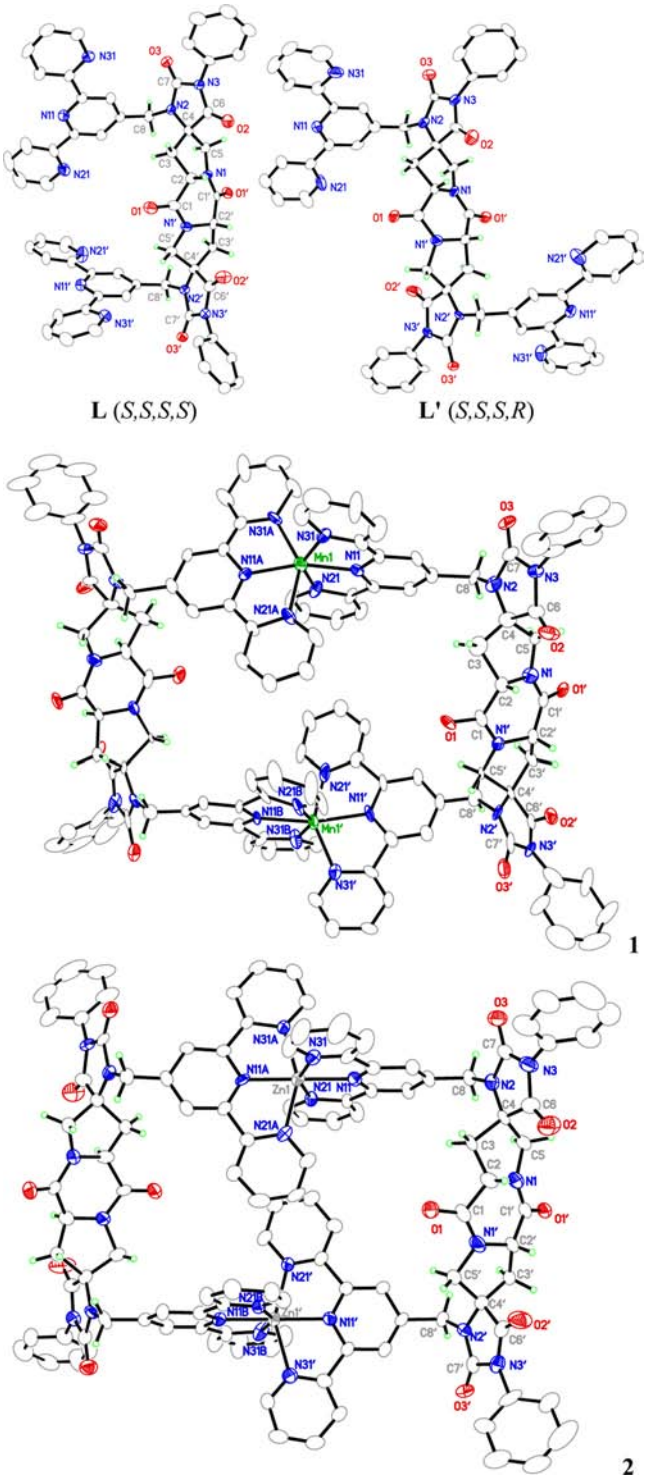
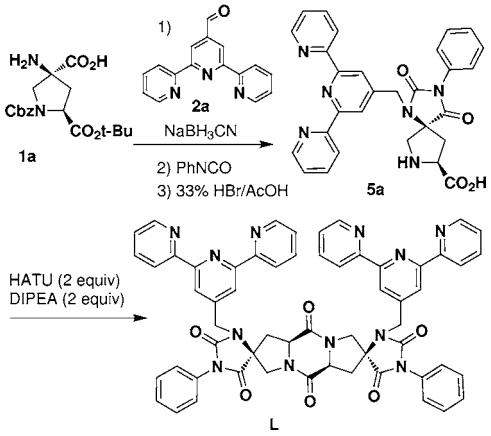


Figure 1. X-ray crystallographic structures of unmetalated ligand **L** (*S,S,S,S*, top left, 50% probability ellipsoids), diastereoisomer **L′** (*S,S,S,R*, top right, 50% probability ellipsoids), dimeric manganese–spiroligomer complex cation $\mathbf{1}^{4+}$ (middle, 30% probability ellipsoids), and dimeric zinc–spiroligomer complex cation $\mathbf{2}^{4+}$ (bottom, 50% probability ellipsoids). Carbon atoms displayed as open ellipses, and aryl-hydrogen atoms are omitted for clarity. Anions in **1** and **2** are not shown.

reductive alkylation method between **1a** and aldehyde **2a** (4′-formyl-2,2′:6′2″-terpyridine).[9] The resulting functionalized bis-amino acid was combined with phenyl isocyanate and

Scheme 1. Synthesis and Structure of *S,S,S,S* Bis(terpyridyl)spiroligomer Ligand L



triethylamine to form phenyl hydantoin, which was treated with 33% HBr in acetic acid to remove carboxybenzyl and tert-butyl protecting groups to yield amino acid **5a**. Finally, HATU and DIPEA were applied with **5a** to produce our desired symmetric bifunctionalized spiroligomer **L** with a diketopiperazine structure and *S,S,S,S* stereochemistry shown in Figure 1. For comparison, the *S,S,S,R* diastereoisomer is shown alongside **L**, illustrating that by selection of precursor stereochemistry the display of functional groups is controlled in the resulting spiroligomers. **L′** was prepared via an identical procedure to that of **L** except that for the last step an asymmetrical coupling method was used.

The manganese–ligand complex may be prepared by two methods (identical but for the presence or absence of acetic acid), resulting in two crystalline polymorphs of the product. Both methods involve the addition of spiroligomer ligand to a solution of manganese(II) in dichoromethane:acetonitrile (1:1). Filtration and concentration of the reaction mixture results in small colorless crystals of **1**. The zinc complex is prepared in 1:1 dichloromethane:acetonitrile by addition of $Zn(ClO_4)_2$ to the ligand. The dried mixture is extracted into hot DMF, and cooling gives colorless crystals of **2**.

Table 1. Selected Distances (Å) and Angles (deg) with Standard Deviations for Dimeric Complexes 1 and 2

	1 (M = Mn)	**2** (M = Zn)
N(11)–M(1)	2.104(3)	2.091(4)
N(21)–M(1)	2.258(3)	2.115(5)
N(31)–M(1)	2.214(5)	2.194(4)
M(1)···M(1′)	10.463(2)	9.0058(8)
N(11)–M(1)–N(11A)	163.2(2)	176.99(18)
N(21)–M(1)–N(31)	142.74(19)	152.21(15)
N(11)–M(1)–N(21/31)	73.07(17)	77.63(17)
N(11)–M(1)–N(21/31)	70.51(17)	74.58(16)

Single crystal X-ray analysis reveals the structures as dimeric complexes with the formula $[M_2L_2]^{4+}$ (Table 1). A metal atom is ligated to a terpyridine group of a spiroligomer, and the remaining metal coordination sites are filled by the terpyridine of a second spiroligomer ligand resulting in a linkage "square" topologically related to a number of previously reported complexes.[10] In the manganese complex (**1**), the manganese atoms are bowed outward, with the central bpy pyridine–pyridine axial bond angle compressed to 163°, resulting in a

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significant cavity of ca. 136 Å^3 at the center of the molecule that contains disordered solvent or anions.[11] This cavity is smaller in **2** due to the analogous axial ligands on zinc being nearly linear at 177° (Figure 1) and a π-stacking interaction (3.7 Å) between pyridyl groups through the central cavity.[12]

The crystal structure of complex **2** exhibits four clearly resolved perchlorate counterions, consistent with the assignment of a dizinc(II) complex. In the structure of **1**, the manganese charge is balanced by perchlorate and possibly acetate ions, though the protonation state of the latter cannot be determined, and solvent flattening (SQUEEZE)[11] may have corrected for additional electron density from disordered perchlorate or acetate ions. Thus, the oxidation state of Mn is not assigned based on charge counting in the structure but upon electronic structure analysis by spectroscopic techniques.

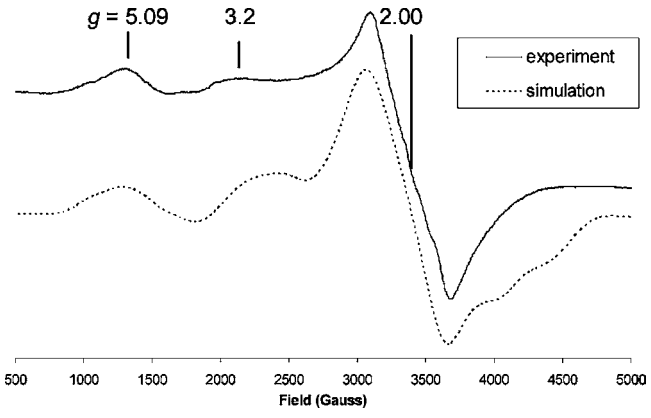

Figure 2. Top: EPR spectrum of **1**. MW Freq: 9.476 GHz. MW Power: 2.0 mW. Mod Freq: 100 kHz. Mod Amp: 10 G. Bottom: Simulation of EPR spectrum of **1** with hyperfine from a single $I = 5/2$ Mn nucleus. $g_x = g_y = g_z = 2.03$, $a_x = a_y = a_z = 90$ G, $D = 470$ G, $E = 190$ G.

The X-band EPR spectrum of **1** is given and simulated in Figure 2. The signature is characteristic of a high-spin $S = 5/2$ Mn(II) system, with the anisotropy attributed to second-order zero-field splitting.[13] The similarity of the spectrum in Figure 2 to reported spectra of Mn-terpyridine ions suggests that the d^5 high-spin Mn atoms are not only uncoupled from one another but that the signal symmetry is not significantly distorted by the nearby (~10 Å) second magnetic ion. The isotropic g values obtained from simulation are similar to those previously reported.[13]

The electronic absorption spectrum of **1** (Figure 3, top) exhibits similarities to that of the unmetalated ligand (**L**) but with the appearance of two charge transfer bands appearing in the region of 280−290 and 320−350 nm. No d−d transitions are observed, consistent with the assignment of $S = 5/2$ Mn(II). These are also highly analogous to the spectra of bis-(terpyridyl)manganese(II) ions.[14]

The charge transfer features are exaggerated in the CD spectrum (Figure 3, bottom). The CD signal at 290 nm is a strong positive peak, while that at 340 nm is a moderate negative peak. The CD results imply that despite the distance between the metal ions and the stereocenters the chiral backbone of the ligand is able to impart chiral character to the metal-tpy coordination environment, as evidenced by the observable Cotton effect in the charge transfer bands of the CD spectrum.

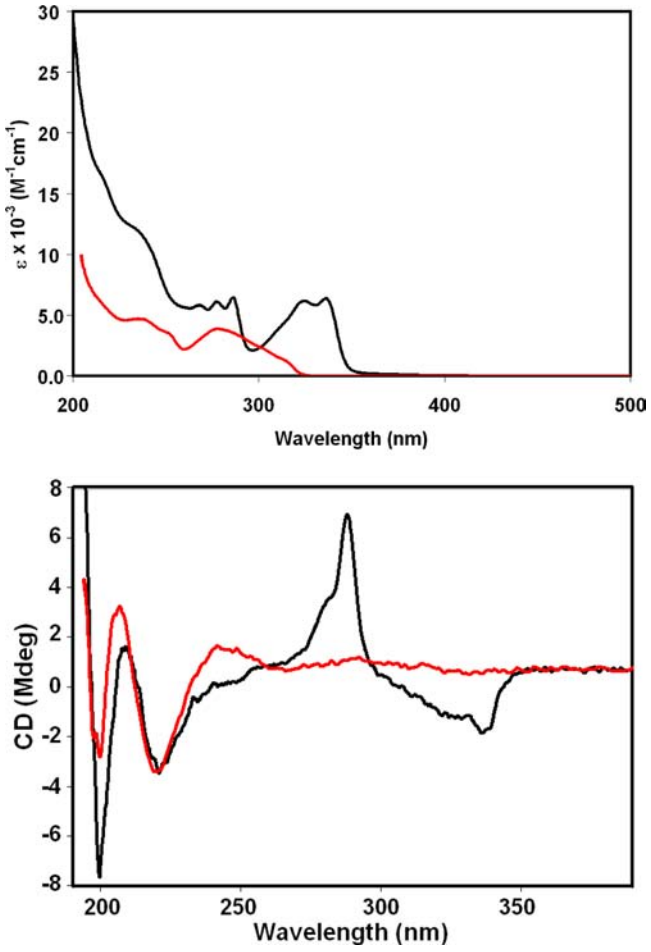

Figure 3. Electronic absorption (top) and circular dichroism (bottom) spectra of **L** (red) and **1** (black) taken in acetonitrile solvent. CD spectra collected on 2×10^{-5} M and 1.32×10^{-4} M samples of **L** and **1**, respectively.

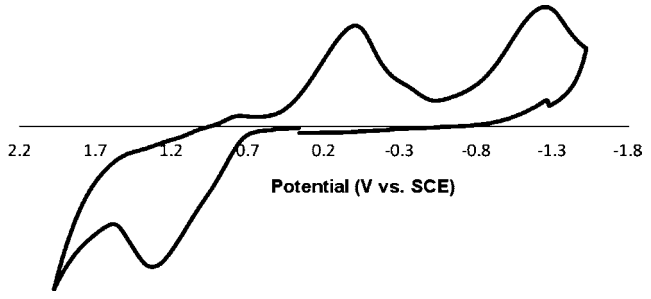

Figure 4. Cyclic voltammagram of complex **1** vs SCE. Potential sweep from +0.38 V to +2.0 V to −1.5 V and back to +0.38 V.

Cyclic voltammetry on the complex **1** (Figure 4) shows an oxidation wave at a potential of 1.2 V vs SCE similar to that reported for the parent $Mn^{II}(tpy)_2^{2+}$ ion,[14] except that in the case of the spiroligomer, this oxidation is irreversible. In Mn-terpyridine chemistry, oxidation of a Mn^{2+} terpyridine mixture results in the formation of a mixed-valent Mn(III/IV)-oxo dimer,[15] though we have not isolated the spiroligomer analogue of this product, and the methylene bridges to the terpyridine ligands may not provide flexibility enough for the Mn atoms to become sufficiently close for intramolecular oxo-dimer formation. On the reduction end, the CV of **1** exhibits an irreversible wave corresponding to reduction of the terpyridine

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ligand at −1.2 V vs SCE. Thus, ligand reduction triggers complex decomposition as evidenced by the irreversibility of the reduction wave.

In summary, we have reported the first structurally and electronically characterized metal−spiroligomer complexes. This is also the first crystallographic characterization of any spiroligomer, and the three-dimensional structures of the metal free and metal bound spiroligomers are consistent with the designed stereochemistry and the predicted structures from molecular mechanics calculations and nuclear magnetic resonance determined solution structures that we have determined in the past. The complex demonstrates that spiroligomers are well suited for accessing stereochemical control, multi-metal binding, and imposition of chiral character to the metal center, and most importantly, versatility of design and ease of preparation of the ligand itself. The next stage is to design spiroligomer-based scaffolds that bring the metal centers in close proximity with each other to encourage electronic communication and cooperative catalysis.

EXPERIMENTAL SECTION

Instrumentation. HPLC-MS analysis was performed on an Agilent Technologies Series 1200 with a Waters Xterra MS C18 column (3.5 mm packing, 4.6 mm × 150 mm) with a solvent system of H_2O/acetonitrile with 0.1% formic acid at a flow rate of 0.8 mL/min. NMR experiments were performed on a Bruker Advance 500 MHz NMR. NMR chemical shifts (δ) are reported relative to DMSO-d_6, benzene-d_6, or $CDCl_3$ residual solvent peaks. When possible, rotamers were resolved by performing the analysis at 350 K. Crystal diffraction data for all compounds were collected using a Bruker APEX II DUO diffractometer using Mo Kα radiation (λ = 0.71073) from a fine-focused sealed tube. Data was collected at 173 K, and structures were solved using direct methods and refined by full-matrix least-squares refinement.

Optical rotation was determined on a PERKIN ELMER Polarimeter 341 (20 °C, 589 nm). Circular dichroism spectra were obtained on a JASCO instruments model J-815 CD spectrometer.

Mass spectra were performed on an Agilent G6520 Q-TOF by Dr. Cliff Soll at HunterCollege, CUNY, a Waters/micromass LC-TOF mass spectrometer, LCT-Premier-XE at Boston College, MA, or a 6520 Accurate Mass Q-TOF-LC/MS at Temple University. UV−visible spectra were recorded on a Shimadzu UV-1800 UV spectrophotometer in the range of 200−900 nm. Fluorescence spectra were obtained on a PTI Photon Technology International Fluorometer with slit width set to 3.0 nm. All reported fluorescence intensities are reported as relative values with relative intensities consistent across all samples (**L**, **1**, and **2**). EPR spectra were acquired on a Bruker EMX EPR spectrometer equipped with a liquid He cryostat.

Cyclic voltammagrams were obtained using a CHI-630D electrochemical analyzer/workstation with PIcoamp booster. Electrochemical studies were performed under anaerobic conditions using a standard three-electrode assembly; glassy Pt working, Pt wire auxiliary, and Ag/$AgNO_3$ (10 mM Ag^+) reference were employed. Cyclic voltammogram of compound **1** (1 mM) was acquired in acetonitrile (1 mM TBAP) with a scan rate of 50 mV/s at room temperature. The open circuit potential was determined at around 0.38 V, and positive and negative sweeps were examined. Ferrocene was used as a standard (0.16 V vs SCE), and potentials were corrected to SCE.

General Methods for Spiroligomer Synthesis. Anhydrous dichloromethane (DCM), hexanes, ethyl acetate (EtOAc), anhydrous dimethylformamide (DMF), acetonitrile (MeCN), HBr (33% in glacial AcOH), phenyl isocyanate, triethylamine, and redistilled diisopropylethylamine(DIPEA) were obtained from Sigma-Aldrich and used without purification. Sodium cyanoborohydride ($NaBH_3CN$), allyl chloroformate, borane dimethyl amine complex ($HNMe_2{\cdot}BH_3$), and tetrakis(triphenylphosphine) palladium(0) ($Pd(PPh_3)_4$) was obtained from Aldrich. Anhydrous tetrahydrofuran (THF) was obtained from EMD. *O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HATU) and HOAt were obtained from Genscript. Ammonium hydroxide (NH_4OH) was obtained from Fisher Chemicals. All other reagents such as NMR solvent were obtained from Sigma-Aldrich and used without further purification. The starting material, the pro4 amino acids (compound **1a, 1b**), was synthesized according to a published procedure,[7] as well as the synthesis of 4′-formyl-2,2′:6′2″-terpyridine **2a**.[9]

Compound 3a: (3S,5S)-1-[(Benzyloxy)carbonyl]-3-({[2,6-bis(pyridin-2-yl)pyridin-4-yl]methyl}amino)-5-[(tert-butoxy)carbonyl]pyrrolidine-3-carboxylic Acid. **1a** (2.09g, 5.74 mmol) and **2a** (1.50g, 5.74 mmol) were dissolved in 60 mL MeOH, and the reaction mixture was stirred at room temperature for 1 h. A solution of $NaBH_3CN$ (433 mg, 6.89 mmol) in 5 mL MeOH was added, and the solution was stirred overnight. The reaction mixture was concentrated and purified by flash chromatography (Al_2O_3, EtOAc/MeCN/MeOH/NH_4OH: 7/1/0.5/0.5 to 6/1/1/1) to afford **3a** as a pale yellow solid (1.80g, 2.95 mmol, 51.5%). ^{1}H NMR (500 MHz, 350 K, DMSO-d_6): δ (ppm) 8.73 (2H, d, J = 4.0 Hz), 8.61 (2H, d, J = 7.9 Hz), 8.50 (2H, s), 8.02 (2H, t, J = 7.7 Hz), 7.50 (2H, t, J = 5.9 Hz), 7.38−7.28 (5H, m), 5.10 (2H, s), 4.32 (1H, t, J = 7.6), 4.19−4.06 (3H, m), 3.61 (1H, d, J = 11.2 Hz), 2.87 (1H, dd, J = 12.7, 8.8 Hz), 2.25 (1H, dd, J = 13.1, 7.2 Hz), 1.35 (9H, s). ^{13}C NMR (125 MHz, 350 K, DMSO-d_6): δ (ppm) 172.13, 169.84, 154.72, 154.64, 153.25, 148.64, 137.05, 136.22, 127.86, 127.34, 126.90, 123.92, 120.60, 120.32, 120.03, 80.72, 66.01, 58.54, 53.40, 47.54, 41.48, 37.18, 27.18. $[\alpha]_D^{20}$ = −13.2°(MeOH). HPLC analysis (30 min, 5−95% MeCN/H_2O with 0.1% formic acid): T_r = 16.9 min. ESI HR-MS $[M+H]^+$ Calculated: 610.2666. Found: 610.2660.

Compound 3b: (*3R,5S*)-1-[(Benzyloxy)carbonyl]-3-({[2,6-bis(pyridin-2-yl)pyridin-4-yl]methyl}amino)-5-[(tert-butoxy)carbonyl]pyrrolidine-3-carboxylic Acid. **1b** (2.09g, 5.74 mmol) and **2a** (1.50g, 5.74 mmol) were dissolved in 60 mL MeOH, and the reaction mixture was stirred at room temperature for 1 h. A solution of $NaBH_3CN$ (433 mg, 6.89 mmol) in 5 mL MeOH was added, and the solution was stirred overnight. The reaction mixture was concentrated and purified by flash chromatography (Al_2O_3, EtOAc/MeCN/MeOH/NH_4OH: 7/1/0.5/0.5 to 6/1/1/1) to afford **3b** as a pale yellow solid (1.53g, 2.51 mmol, 43.7%). ^{1}H NMR (500 MHz, 350 K, DMSO-d_6): δ (ppm) 8.75 (2H, d, J = 4.0 Hz), 8.64 (2H, d, J = 8.0 Hz), 8.60 (2H, s), 8.06 (2H, dt, J = 7.8 Hz), 7.55 (2H, m), 7.32 (5H, m), 5.08 (2H, broad), 4.56 (1H, broad), 4.37 (2H, dd, J = 30.2, 13.6 Hz), 4.12 (1H, d, J = 12.4 Hz), 3.88 (1H, d, J = 12.5 Hz), 2.94 (1H, m), 2.59 (1H, m), 1.38 (9H, J = 12.5 Hz). ^{13}C NMR (125 MHz, 350 K, DMSO-d_6): δ (ppm) 173.1, 171.2, 155.3, 155.1, 154.6, 148.8, 136.7, 136.6, 127.7, 127.0, 126.6, 123.7, 123.5, 120.4, 119.6, 118.9, 85.8, 79.6, 68.8, 66.0, 59.3, 55.3, 47.9, 27.0. $[\alpha]_D^{20}$ = −71.8°(sodium salt in MeOH). HPLC analysis (30 min, 5−95% MeCN/H_2O with 0.1% formic acid): T_r = 15.8 min. ESI HR-MS $[M+H]^+$ Calculated: 610.2666. Found: 610.2896.

Compound 4a: 7-Benzyl 8-Tert-butyl (5S,8S)-1-{[2,6-bis(pyridin-2-yl)pyridin-4-yl]methyl}-2,4-dioxo-3-phenyl-1,3,7-triazaspiro[4.4]nonane-7,8-dicarboxylate. To the solution of **3a** (1.80g, 2.95 mmol) in 90 mL THF was added Et_3N (1.03 mL, 7.39 mmol), and then phenyl isocyanate (805 μL, 7.39 mmol) was added. The resulted reaction mixture was stirred overnight at room temperature. The reaction mixture was concentrated and purified by flash chromatography (SiO_2, EtOAc/hexanes: 3/7 to 1/1) to afford **4a** as a white solid (1.60g, 2.25 mmol, 76.4%). ^{1}H NMR (500 MHz, 350 K, DMSO-d_6): δ (ppm) 8.72 (2H, d, J = 4.2 Hz), 8.59 (2H, d, J = 8.0 Hz), 8.48 (2H, s), 8.00 (2H, dt, J = 7.7, 1.8 Hz), 7.54−7.40 (7H, m), 7.36−7.25 (5H, m), 5.06 (2H, s), 4.92 (2H, d, J = 7.7 Hz), 4.40 (1H, t, J = 8.4 Hz), 4.07 (1H, d, J = 11.7 Hz), 3.75 (1H, d, J = 11.8 Hz), 2.81 (1H, dd, J = 13.6, 8.6 Hz), 2.31 (1H, dd, J = 13.7, 8.3 Hz), 1.26 (9H, s). ^{13}C NMR (125 MHz, 350K, DMSO-d_6): δ (ppm) 172.6, 169.5, 155.2, 154.7, 154.4, 153.3, 148.8, 148.7, 136.8, 136.0, 131.5, 128.2, 127.8, 127.6, 127.3, 126.9, 126.2, 123.8, 120.5, 119.0, 80.9, 66.1, 57.9, 49.5, 42.1, 35.0, 27.0. $[\alpha]_D^{20}$ = −16.5°($CHCl_3$). HPLC analysis (30

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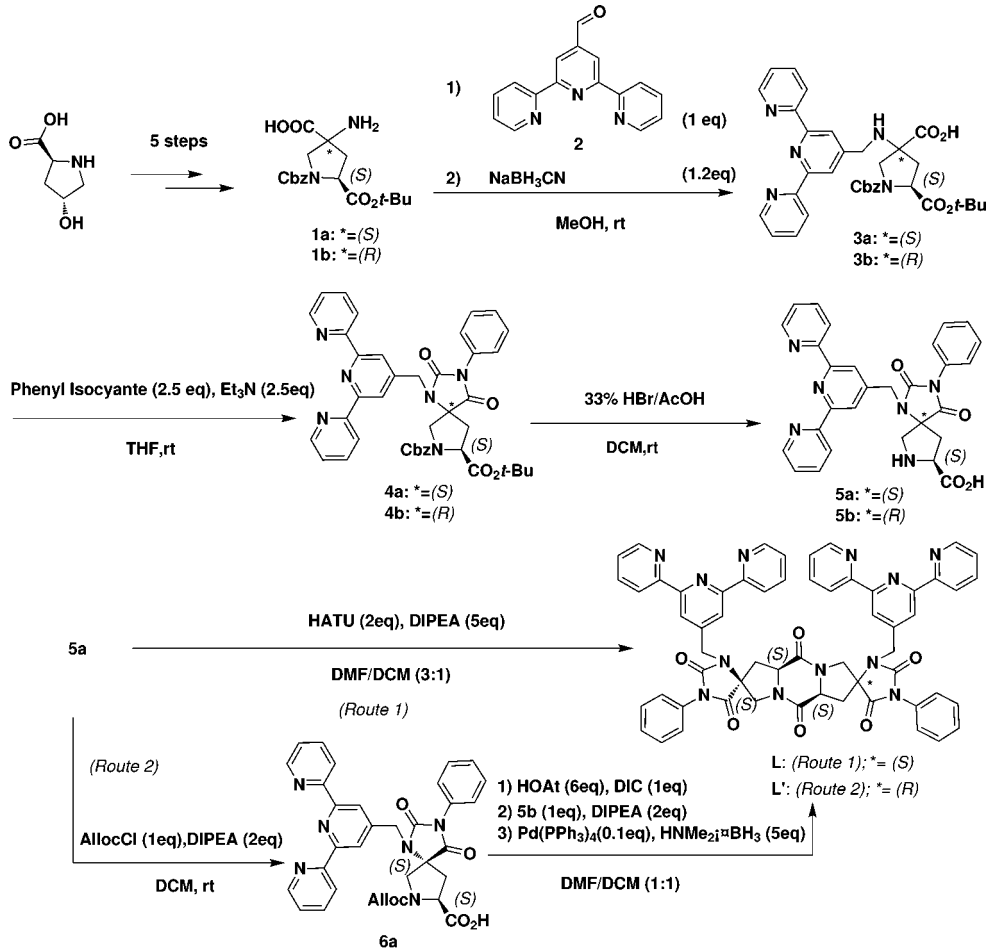
Scheme 2. Full Synthetic Scheme for Preparation of Spiroligomer Ligand L



min, 5−95% MeCN/H_2O with 0.1% formic acid): T_r = 23.8 min. ESI HR-MS $[M+H]^+$ Calculated: 711.2926. Found: 711.2924.

Compound 4b: 7-Benzyl 8-Tert-butyl (5R,8S)-1-{[2,6-bis(pyridin-2-yl)pyridin-4-yl]methyl}-2,4-dioxo-3-phenyl-1,3,7-triazaspiro[4.4]nonane-7,8-dicarboxylate. To the solution of **3b** (1.53 g, 2.51 mmol) in 80 mL THF was added Et_3N (0.88 mL, 6.28 mmol), and then phenyl isocyante (700 μL, 6.28 mmol) was added. The resulted reaction mixture was stirred overnight at room temperature. The reaction mixture was concentrated and purified by flash chromatography (SiO_2, EtOAc/hexanes: 3/7 to 1/1) to afford **4b** as a white solid (1.28 g, 1.80 mmol, 71.8%). ^1H NMR (500 MHz, 350 K, DMSO-d_6): δ (ppm) 8.69 (2H, broad), 8.58 (2H, d, J = 7.4 Hz), 8.45 (2H, s), 7.97 (2H, dt, J = 7.7, 1.8 Hz), 7.48 (7H, m), 7.21 (3H, broad), 7.05 (2H, broad), 5.00 (1H, broad), 4.76 (2H, broad), 4.48 (2H, broad), 3.84 (1H, d, J = 11.8 Hz), 3.62 (1H, d, J = 12.0 Hz), 2.95 (1H, m), 2.44 (1H, m), 1.30 (9H, broad). ^{13}C NMR (125 MHz, 350K, DMSO-d_6): δ (ppm) 170.9, 169.6, 155.1, 154.9, 154.5, 152.4, 148.8, 148.3, 136.8, 135.6, 131.6, 128.2, 127.6, 127.5, 127.2, 126.7, 126.2, 123.8, 120.5, 118.8, 81.1, 78.4, 68.5, 66.1, 58.2, 54.3, 42.8, 27.2. $[\alpha]_D^{20}$ = −38.1°($CHCl_3$). HPLC analysis (30 min, 5−95% MeCN/H_2O with 0.1% formic acid): T_r = 22.6 min. ESI HR-MS $[M+H]^+$ Calculated: 711.2926. Found: 711.3322.

Spiroligomer Ligand L (SSSS): 7-Benzyl 8-Tert-butyl (5R,8S)-1-{[2,6-bis(pyridin-2-yl)pyridin-4-yl]methyl}-2,4-dioxo-3-phenyl-1,3,7-triazaspiro[4.4]nonane-7,8-dicarboxylate. An amount of 4.5 mL of 33% HBr/AcOH was added to the solution of **4a** (1.60g, 2.25 mmol) in 80 mL DCM. Then the solution was stirred at room temperature for 3 h. The reaction mixture was then concentrated and transferred with DCM to a falcon tube and centrifuged to afford **5a** as a yellow solid (1.30 g, 2.16 mmol, 96.1%). Then it was used without further purification. Compund **5a** (400 mg, 0.665 mmol) and HATU (505 mg, 1.33 mmol) were dissolved in 24 mL DMF and 8 mL DCM followed by addition of DIPEA (575 μL). The solution was stirred overnight at room temperature. An amount of 20 mL of water and saturated NH_4Cl (aq) was added to the reaction mixture followed by the extraction of EtOAc (60 mL) three times, and the combined organic layer was washed with 40 mL brine/water: 1/1 and then 40 mL brine and dried over Na_2SO_4. Then the organic layer was concentrated and purified by flash chromatography (SiO_2, toluene/EtOAc: 1/1 to toluene/EtOAc/water: 1/4/0.04) to afford **L** (104 mg, 0.10 mmol, 31.0%) (Scheme 2). ^1H NMR (500 MHz, rt, $CDCl_3$): δ (ppm) 8.65 (4H, d, J = 4.2 Hz), 8.60 (4H, d, J = 8.1 Hz), 8.36 (4H, s), 7.84 (4H, dt, J = 7.7, 1.7 Hz), 7.56−7.47 (8H, m), 7.44−7.39 (2H, m), 7.32 (4H, ddd, J = 8.65, 4.8, 1.2 Hz), 4.91 (2H, dd, J = 10.1, 7.1 Hz), 4.77 (4H, dd, J = 33.0, 17.0 Hz), 3.93 (2H, d, J = 12.9 Hz), 3.73 (2H, d, J = 12.9 Hz), 2.66−2.53 (4H, m). ^{13}C NMR (125 MHz, rt, $CDCl_3$): δ (ppm) 173.4, 165.1, 156.4, 155.6, 155.0, 149.3, 147.3, 137.0, 131.1, 129.4, 128.7, 126.1, 124.2, 121.6, 118.5, 66.5, 58.8, 48.7, 42.8, 34.1. $[\alpha]_D^{20}$ = −11.4°($CHCl_3$). HPLC analysis (30 min, 5−95% MeCN/H_2O with 0.1% formic acid): T_r = 19.3 min. UV−vis (acetonitrile) λ (ε × 10^{-3}): 236 (4.68), 252 (3.43), 278 (3.85), 302 (2.23), 314 (1.24). Emission (λ_{excit} = 278 nm). λ (relative intensity): 326 (25.9), 342 (3.57), 357 (3.24), 652 (0.252), 667 (0.265). ESI HR-MS $[M+H]^+$ Calculated: 1005.3580. Found: 1005.3571.

Compound 6a: (5S,8S)-1-{[2,6-Bis(pyridin-2-yl)pyridin-4-yl]methyl}-2,4-dioxo-3-phenyl-7-[(prop-2-en-1-yloxy)carbonyl]-1,3,7-triazaspiro[4.4]nonane-8-carboxylic acid. Compound **5a** (600 mg, 1.00 mmol) was suspended in 30 mL DCM and allyl chloroformate (116 μL, 1.10 mmol) was added, followed by addition of DIPEA (517 μL, 2.99 mmol). The resultant mixture was stirred overnight at room temperature. To work up the reaction, another 30 mL of DCM was added, and the mixture was then washed with 20 mL

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brine/water: 1/1, 20 mL saturated NH_4Cl (aq), and 20 mL brine. The organic layer was dried over Na_2SO_4 and then concentrated to afford **6a** (422 mg, 0.70 mmol, 70%) as a white solid. ^1H NMR (500 MHz, rt, DMSO-d_6): δ (ppm) 8.74 (2H, d, J = 4.2 Hz), 8.63 (2H, d, J = 8.0 Hz), 8.46 (2H, s), 8.02 (2H, dt, J = 7.8, 1.6 Hz), 7.52 (6H, m), 7.4 (1H, m), 5.82 (1H, m), 5.23 (1H, t, J = 17.0 Hz), 5.11 (1H, d, J = 10.5 Hz), 4.93 (2H, dd, J = 33.2, 17.0 Hz), 4.44 (3H, m), 4.04 (1H, t, J = 13.1 Hz), 3.63 (1H, dd, J = 46.0, 14.4 Hz), 2.81 (1H, m), 2.39 (1H, m). ^{13}C NMR (125 MHz, 350 K, DMSO-d_6): δ (ppm) 172.8, 171.7, 155.2, 154.9, 153.2, 148.9, 148.7, 136.8, 132.5, 131.5, 128.3, 127.6, 126.2, 123.8, 120.6, 118.7, 116.3, 66.3, 65.0, 57.5, 49.8, 42.1, 35.2. $[\alpha]_D^{20}$ = +9.44°(MeOH). HPLC analysis (30 min, 5−95% MeCN/H_2O with 0.1% formic acid): T_r = 15.5 min. ESI HR-MS $[M+H]^+$ Calculated: 605.2143. Found: 605.2447.

Spiroligomer Ligand L′ (SSSR): (3′S,4R,9′S,11′S)-3,3″-Bis-({[2,6-bis(pyridin-2-yl)pyridin-4-yl]methyl})-1,1″-diphenyl-dispiro[imidazolidine-4,5′-[1,7]diazatricyclo[7.3.0.03,7]-dodecane-11′,4″-imidazolidine]-2,2′,2″,5,5″,8′-hexone. Compound **6a** (273 mg, 0.45 mmol) and HOAt (369.1 mg, 2.71 mmol) were dissolved in 12 mL DCM and 6 mL DMF, and then DIC (77.8 μL, 0.50 mmol) was added. The resultant mixture was stirred at room temperature for 2 h, **5b** (218 mg, 0.362 mmol). Compound **5b** is prepared by the same method as the preparation for **5a**, except that the precursor is the *R* stereoisomer. Compound **4b** was dissolved in 6 mL DMF, followed by addition of DIPEA (125 μL, 0.72 mmol). Then the prementioned mixture of **6a** was added dropwise to the mixture of **5b**. The resultant was stirred overnight. $HNMe_2{\cdot}BH_3$ (159.8 mg, 2.71 mmol) and $Pd(PPh_3)_4$ (52.23 mg, 0.05 mmol) were dissolved in 3 mL DCM and added to the reaction mixture. The resultant mixture was stirred at room temperature overnight. An amount of 20 mL water and saturated NH_4Cl (aq) was added to the reaction mixture followed by the extraction of EtOAc (60 mL) three times, and the combined organic layer was washed with 40 mL brine/water: 1/1 and then 40 mL brine and dried over Na_2SO_4. Then the organic layer was concentrated and purified by flash chromatography (SiO_2, toluene/EtOAc: 1/1 to toluene/EtOAc/water: 1/4/0.04) to afford **L′** (163 mg, 0.16 mmol, 44.7%). ^1H NMR (500 MHz, rt, $CDCl_3$): δ (ppm) 8.68 (2H, d, J = 3.8 Hz), 8.59 (6H, m), 8.44 (2H, s), 8.33 (2H, s), 7.81 (4H, m), 7.52 (6H, m), 7.41 (3H, m), 7.32 (3H, m), 7.24 (2H, m), 4.97 (1H, d, J = 16.3 Hz), 4.76 (4H, m), 4.51 (1H, t, J = 7.4 Hz), 4.20 (1H, d, J = 12.7 Hz), 3.88 (2H, m), 3.38 (1H, d, J = 12.7 Hz), 3.03 (1H, dd, J = 14.0, 6.2 Hz), 2.63 (1H, m), 2.55 (2H, dd, J = 12.8, 8.4 Hz). ^{13}C NMR (125 MHz, rt, $CDCl_3$): δ (ppm) 172.2, 171.2, 163.9, 163.6, 155.6, 155.1, 154.8, 154.5, 154.2, 153.9, 148.4, 148.2, 146.5, 146.5, 136.1, 135.9, 130.4, 130.4, 128.3, 128.2, 127.6, 127.6, 125.2, 125.1, 123.3, 123.1, 120.6, 120.5, 118.4, 118.0, 65.9, 65.3, 58.1, 57.6, 49.8, 49.4, 42.5, 41.8, 33.4, 33.4. $[\alpha]_D^{20}$ = −12.33°($CHCl_3$). HPLC analysis (30 min, 5−95% MeCN/H_2O with 0.1% formic acid): T_r = 18.3 min. ESI HR-MS $[M+H]^+$ Calculated: 1005.3580. Found: 1005.3907.

General Methods for Metal Complex Preparation. All reagents were purchased from commercial sources (Aldrich, Strem Chemicals). Anhydrous solvents such as benzene, dichloromethane, and toulene were purified using an Innovative Technology, Inc. Pure Solv. system. Diethyl ether was distilled from sodium benzophenone-ketyl under a nitrogen atmosphere. $Mn(ClO_4)_2{\cdot}H_2O$ and $Zn(ClO_4)_2.6H_2O$ were purchased from Strem Chemicals or Aldrich. Anhydrous solvents were used throughout all experiments.

Synthesis of $[Mn_2L_2]{\cdot}(ClO_4)_4$ (1). Manganese perchlorate, $Mn(ClO_4)_2{\cdot}H_2O$ (0.005 g, 0.02 mmol) was added to a slurry of *S,S,S,S* bis(terpyridyl)spiroligomer ligand **L** (tt-Terpy-SSSS) (0.01g, 0.01 mmol) in 10 mL 1:1 acetonitrile:dichloromethane. The resultant yellow mixture was then stirred at room temperature for 24 h. The reaction mixture was filtered, and the filtrate dried under vacuum. The dried residue was extracted with acetonitrile, resulting in a yellow solution, onto which was layered toluene in a 0.5 mm diameter vial. Light yellow crystals of **1** were obtained at room temperature after three weeks of diffusion in the closed vial. X-ray quality crystals were grown by addition of 1 mL glacial acetic acid in the reaction mixture and slow evaporation at room temperature. Yield 0.013 g of $[1][ClO_4]_4{\cdot}1.5$ (C_7H_8), 98% based on L. UV−Vis (acetonitrile) $\lambda(\varepsilon \times 10^{-3})$: 215 (16.5), 235 (11.8), 269 (58.1), 278 (6.06), 286 (64.3)325 (6.16). Emission (λ_{excit} = 333 nm). λ(relative intensity): 357 (6.31), 408 (3.24), 432 (2.66), 682 (0.471), 708 (0.417). ESI MS $[m/z]$ (m/z theory): $[Mn_2(tt\text{-}Terpy\text{-}SSSS)_2{\cdot}2ClO_4]^{2+}$ 1159.7 (1159.4), $[Mn_2(tt\text{-}Terpy\text{-}SSSS)_2{\cdot}ClO_4]^{3+}$ 739.9 (739.5).

Synthesis of $[Zn_2L_2]{\cdot}(ClO_4)_4$ (2). Zinc perchlorate, $Zn(ClO_4)_2{\cdot}6H_2O$ (0.00784 g, 0.02 mmol) was added to a slurry of *S,S,S,S* bis(terpyridyl)spiroligomer ligand (**L**) (0.01g, 0.01 mmol) in 10 mL 1:1 acetonitrile:dichloromethane. The resultant mixture was then stirred at room temperature for 24 h. The reaction mixture was filtered, and the filtrate was dried under vacuum. The dried residue was extracted with dimethylformamide and the solution heated to 80−90 °C for 5 min. Next, the solution was filtered, and the filtrate kept at room temperature, while crystals grew by slow evaporation. White rectangular crystals were obtained after two weeks. Yield 0.01 g of $[2][ClO_4]_4$, 79% based on **L**. ^1H NMR (500 MHz, rt, DMSO-d_6): δ (ppm) 8.83 (8H, s), 8.66 (8H, d, J = 7.3 Hz), 7.89 (8H, broad), 7.68 (8H, broad), 7.62 (8H, d, J = 7.7 Hz), 7.56 (8H, t, J = 7.8 Hz), 7.47−7.43 (4H, m), 7.88 (8H, broad), 5.32 (4H, d, J = 17.6 Hz), 4.92 (8H, t, J = 8.4 Hz), 4.15 (4H, d, J = 11.6), 3.91 (4H, broad), 2.95−2.91 (4H, m), 2.68−2.64 (4H, m). ^{13}C NMR (125 MHz, rt, DMSO-d_6): δ (ppm) 173.0, 164.4, 157.0, 155.0, 148.7, 147.6, 147.2, 141.0, 131.7, 128.7, 127.7, 126.5, 123.0, 121.1, 66.8, 58.3, 48.8, 42.9, 33.2. Emission (λ_{excit} = 333 nm. λ(relative intensity): 354 (100), 378 (61.6), 403 (33.0), 688 (7.51), 713 (5.50), 797 (0.580). LC-MS $[m/z]$ (m/z theory): $[Zn_2(tt\text{-}Terpy\text{-}SSSS)_2]^{4+}$535.14, (535.14).

■ ASSOCIATED CONTENT

Supporting Information

Crystallographic tables, NMR, fluorescence, and MS figures, and crystallographic data in cif format. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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