

Self-Assembly of a Supramolecular, Three-Dimensional, Spoked, Bicycle-like Wheel**

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The function and properties of materials and biological organisms are not only related to the chemical structure and connectivity, but also through higher-order domain structure, such as in the magnetic domain of magnetic materials^[1] as well as the secondary and tertiary structures of proteins and DNA.^[2] Weak interactions such as hydrogen bonding and coordination exist widely in biological systems and are vital for biological metabolism and many other essential functions.^[3] These supramolecular interactions^[4] have attracted attention both in biology^[5] as well as in numerous other fields,^[6] such as supramolecular catalysis, chemical sensing, and molecular electronics.^[7]

2,2':6',2''-Terpyridine (tpy) has been a widely used ligand for the creation of such motifs, partly because of its ability to coordinate diverse metals. There are numerous examples of tpy-based supramolecular systems, from 2D-based macrocycles and grids^[8] to 3D arrangements, such as cages and prisms.^[9]

A two-dimensional, tpy-based supramolecular spoked wheel was previously reported.^[10] In this three-component ensemble, two different terpyridine ligands and one type of metal were self-assembled. This 2D wheel structure is more rigid than macrocyclic hexagons because of its fixed space-filling centerpiece, which also serves as a template for the outer ligands. Notably, very few supramolecular spoked-wheel systems have been reported,^[10,11] since the self-assembly of multiple components can be a synthetic challenge that

requires more precise control over the geometry and connectivity.^[12]

To further functionalize the well-established tpy-based spoked-wheel assembly, the backbone and connectivity components of its original structure were redesigned. The framework, in this case, includes two parts: the spokes (**S3**) and rims (**R3**; core and outer ligands, respectively; numbers equate to the available tpy units). The core that originally consisted of the single, hexakis(terpyridine) **S6** was replaced by two aromatic cores functionalized with three terpyridine ligands at 120° that adopt a staggered conformation (Scheme 1). Thus, the new construct involves the two tris(terpyridine)s **S3**, six rim units **R3** in which the three tris(terpyridine)s are separated by angles of 60°, and twelve metals in a precise 2:6:12 ratio, respectively. The two central tris-tpy ligands are stacked with a common perpendicular axis to impart the 3D bicycle-wheel motif. β -Glucose moieties were attached to the tris-tpy rim component **R3** to increase the solubility of the desired complex.

The synthesis of rim ligand **R3** (Scheme 2) started with bromination of 2,6-dimethoxyphenol to afford **1**, followed by etherification with benzyl bromide to give **2**. Next, **3** was prepared (67%) through a Suzuki cross-coupling reaction between **2** and 4'-boronatephenyl-2,2':6',2''-terpyridine^[13] by utilizing [PdCl₂(PPh₃)₂] as a catalyst. The benzyl group in **3** was removed with ammonium formate in the presence of a Pd/C catalyst to afford **4**, which underwent alkylation with *N*-(6-bromohexyl)phthalimide^[14] to give the imide **5**. Deprotection of the phthalimide with hydrazine then gave the free amine **6**. Subsequent treatment with 2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl isocyanate^[15] afforded (66%) the desired tris-tpy ligand **R3**, which was fully characterized by NMR spectroscopy and MS. Its ¹H NMR spectrum exhibited signals for two sets of protons in the aromatic region with an integration ratio of 2:1 for the tpy units, as well as one set of signals corresponding to protons of the alkyl linker and glucose. The full assignment of the signals was confirmed by 2D COSY and ROESY NMR spectroscopy.

The core **S3**, prepared by a similar Suzuki cross-coupling reaction^[13] with 2,4,6-tribromomesitylene^[16] (Scheme 2), exhibited signals for only one set of tpy-based protons in the aromatic region of the ¹H NMR spectrum and its identity was confirmed by the single charged signal at *m/z* 1042.49 in the MALDI-TOF mass spectrum.

The 3D wheel **C1** (Scheme 3) was synthesized by mixing a precise stoichiometric ratio (6:2:12) of ligands **R3**, **S3**, and Zn(NO₃)₂·6H₂O in MeOH and stirring at 70°C for 1 h (Scheme 1). After cooling the mixture to 25°C, excess NH₄PF₆ was added to afford a light-yellow precipitate,

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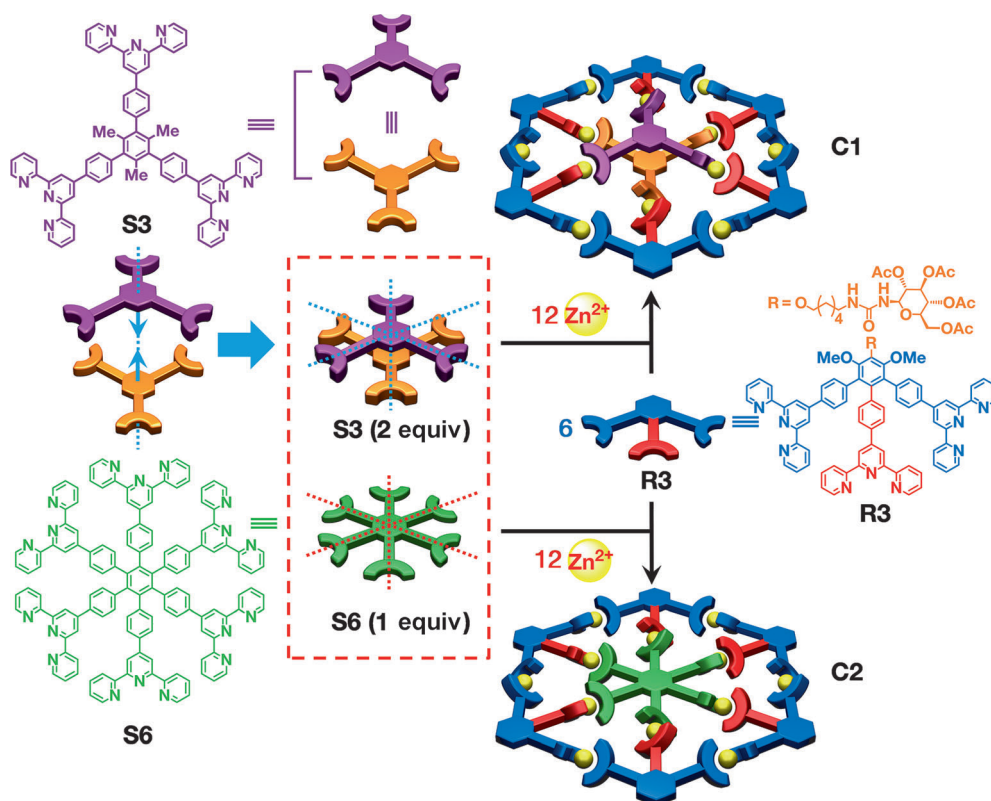
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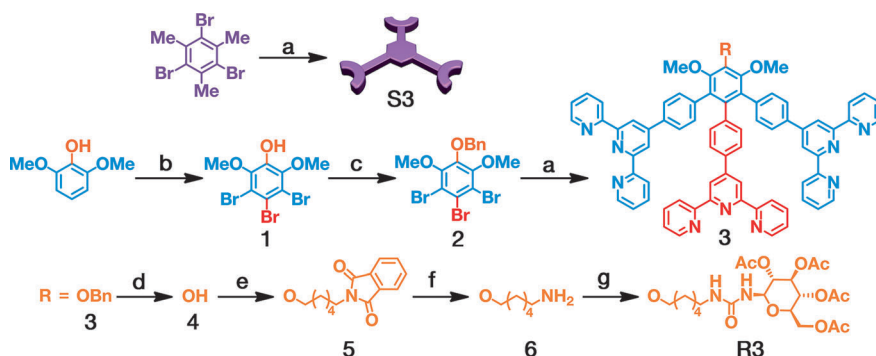
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Scheme 1. Synthesis of the supramolecular 3D bicycle wheel **C1** and 2D spoked wheel **C2**.



Scheme 2. Synthetic route to ligands **S3** and **R3**; reagents and conditions: a) 4'-boronatophenyl-2,2':6',2''-terpyridine,^[13] Na₂CO₃, toluene/H₂O/*t*BuOH (3:3:1), 90 °C, 48 h; b) Br₂, CH₂Cl₂, 0 °C, 12 h; c) C₆H₅CH₂Br, K₂CO₃, MeCN, 70 °C, 18 h; d) HCO₂NH₄, Pd/C, DMF, 90 °C, 3 h; e) K₂CO₃, *N*-(6-bromohexyl)phthalimide,^[14] DMF, 80 °C, 24 h; f) hydrazine hydrate, EtOH, 70 °C, 12 h; g) 2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl isocyanate,^[15] CH₂Cl₂, 25 °C, 24 h.

which was washed thoroughly with water. Complex **C1** was isolated (91 %) as a light-yellow powder with PF₆[−] as the counterion after drying in vacuo at 50 °C.

The ¹H NMR spectrum (Figure 1) of the 3D wheel **C1** exhibited three sets of signals for tpy units in the aromatic region with an integration ratio of 2:1:1, which was consistent with the subunit of the desired structure bound by the dotted lines in Scheme 3. All of the signals for the 6,6''-protons of the tpy units were shifted upfield because of the electron-shielding effect, which is typical for pseudooctahedral terpyridine–metal complexes.^[17] There are two singlets at 3.85 and

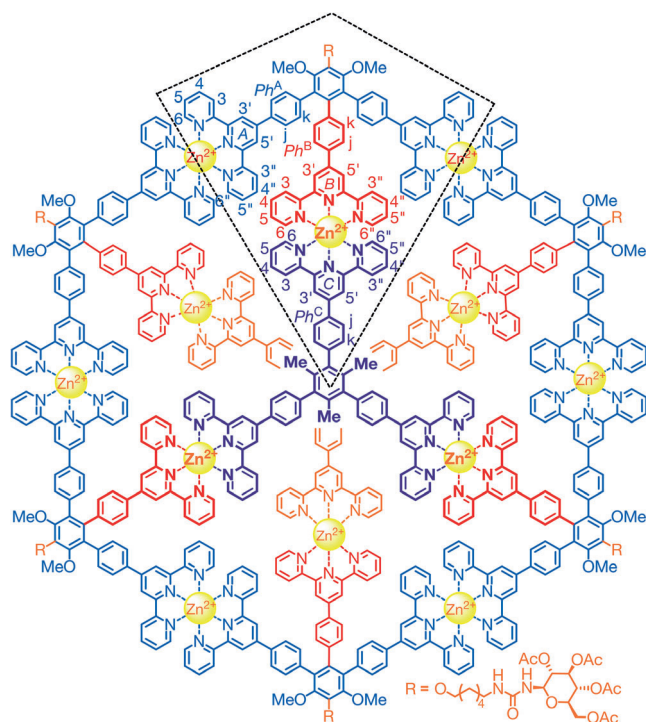
2.00 ppm, which were assigned to the rim methoxy groups of **R3** and the methyl groups from internal ligand **S3**, respectively. The integration ratio of these two signals is 2:1, thus indicating that the ratio of **R3** to **S3** is 3:1, which is also consistent with the desired structure. Only one set of signals were seen for the alkyl linker and glucose protons, which further confirmed that only one self-assembled structure is formed. The 2D NOESY NMR spectrum (see the Supporting Information) showed typical cross-peaks for all of the adjacent protons in the tpy units. The cross-peak between the protons at 7.60 and 7.40 ppm arises from the NOE effect between Ph^A-H^k and Ph^B-H^k from different branches in ligand **R3**; this cross-peak was used to distinguish the tpy^B and tpy^C units, both of which have equal integration.

The full assignment of the ¹H NMR spectrum was confirmed by 2D COSY and 2D NOESY NMR spectroscopy.

Complex **C1** was also characterized by ESI-MS coupled with traveling-wave ion mobility (TWIM) mass spectrometry (Figure 2).^[8b,10,18] The ESI mass spectrum of **C1** showed a series of signals with charge states from 8 + to 17 +. Each charge state was derived by the loss of a different number of PF₆[−] units. The isotope patterns of each charge state agree well with the corresponding simulated isotope pattern. No other structures or aggregates were detected in the ESI mass spectrum, thus showing that the 3D bicycle-like

wheel **C1** is the only product. ESI-TWIM-MS further confirmed the structural assignment, and each charge state showed a narrow drift time distribution, thus indicating that no structural conformer or isomer was present.

Collision cross-sections (CCSs)^[10,18c,19] of the ions separated by TWIM can also be derived. To compare the structure size, the Zn²⁺-based 2D spoked wheel **C2** (Scheme 1), an analogue of complex **C1**, was also synthesized and fully characterized by NMR spectroscopy and ESI-MS (see the Supporting Information). The CCSs for both **C1** and **C2** are listed in Table 1. For all the charge states probed, the CCSs of



Scheme 3. Structure of the supramolecular 3D bicycle wheel **C1**.

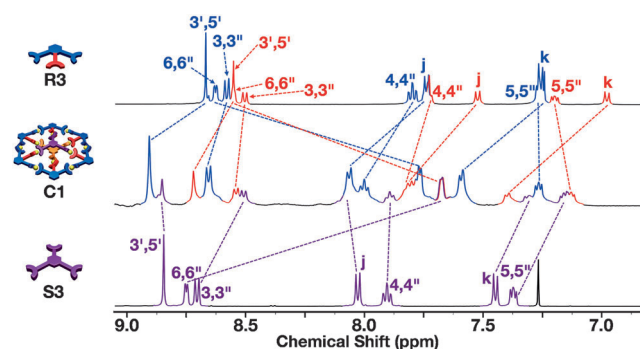


Figure 1. ^1H NMR spectra (500 MHz) of ligands **S3** and **R3** in CDCl_3 and bicycle wheel **C1** in CD_3CN (see Scheme 3 for proton assignments).

C1 are consistently smaller than those of **C2** despite the slightly higher mass of **C1**. This trend provides evidence that **C1** has a somewhat more compact architecture, consistent with its more globular 3D shape compared with the flat (and more extended) shape of **C2**. Transmission electron microscopy (TEM) images were also acquired (see the Supporting Information) by casting a dilute solution of either complex (ca. 10^{-7} M) in MeCN on carbon-coated Cu grids (200 mesh). The average diameters for both structures are about (6.0 ± 1.0) nm, consistent with the optimized molecular model (Figure 2); the TEM resolution is evidently too low to detect the small size/shape differences between **C1** and **C2**, as revealed by TWIM-MS.

Thus, the first supramolecular, 3D, bicycle-like wheel **C1**, was successfully synthesized in near quantitative yield through a simple self-assembly procedure by utilizing {tpy-

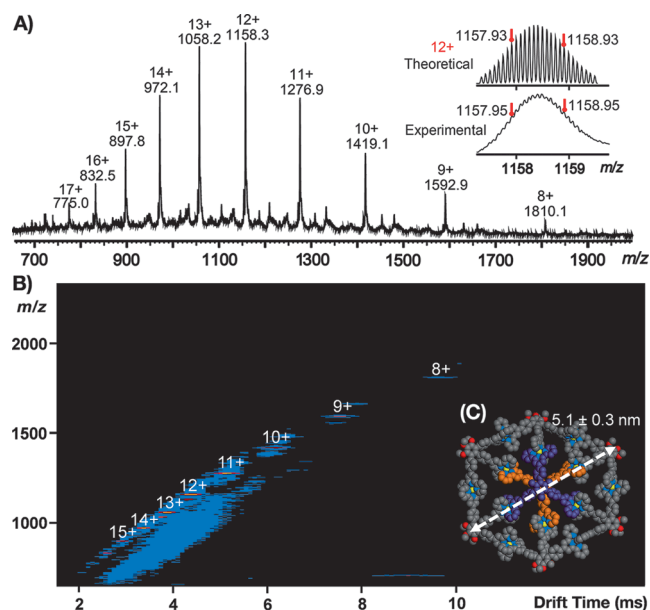


Figure 2. A) ESI mass spectra for complex **C1**; B) 2D ESI-TWIM-MS plots (m/z versus drift time) for complex **C1**. The charge states of intact assemblies are marked; C) representative energy-minimized structure of the 3D bicycle wheel **C1** (protons and glucose moieties were omitted for clarity).

Table 1: Experimental collision cross-sections (CCSs) of supramolecular architectures **C1** and **C2**.

Z	CCSs [\AA^2]	
	3D wheel C1	2D wheel C2
8 +	1815.6	1841.0
9 +	1824.2	1861.5
10 +	1760.8	1819.4
11 +	1570.7	1679.0
average	1742.8 ± 118.1	1800.2 ± 82.6

Zn^{II}-tpy} connectivity. Its 2D analogue spoked wheel **C2** was also synthesized for comparison. These two new supramolecular structures open the door to more complex, three-dimensional, one-step, self-assembly of different macromolecular architectures.

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