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Coordination-Driven Self-Assembly of Three-Dimensional Supramolecular Dendrimers

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Abstract

The design and synthesis of novel 3-D supramolecular dendrimers is described. Coordination-driven self-assembly of a 120° diplatinum acceptor and tritopic pyridyl donors bearing [G-0]–[G-3] Fréchet-type dendrons results in a series of supramolecular dendrimers under mild conditions, possessing a robust adamantanoid core of well-defined shape and size. The assemblies were identified using multinuclear (³¹P and ¹H) NMR spectroscopy and electrospray ionization (ESI) mass spectrometry, as well as pulsed field gradient spin-echo (PGSE) NMR measurement together with computational simulations. Isotopically resolved mass spectral data support the existence of the [6 + 4] assembly of adamantanoid dendrimers, and the NMR results are consistent with the formation of these symmetrical assemblies. PGSE NMR measurements together with MMFF force-field modeling clearly reveal the structural feature of the 3-D supramolecular dendrimers with varying sizes.

Dendrimers of high structural complexity have emerged as one of the most important structures of significant interest in chemistry, biology, and medical research.^{1,2} While merging with self-assembly, complicated dendritic structures can be synthesized in a simple manner. One-dimensional (1-D) helical supramolecular dendrimers, for example, that vividly mimic natural pore-forming proteins can be efficiently self-assembled by a library of amphiphilic dendritic peptides.^{2a–c} Recently, via coordination-driven self-assembly, a variety of two-dimensional (2-D), such as rhomboid, square, and hexagon, supramolecular dendrimers have been prepared.^{3,4} Most reported systems are limited to utilizing helical and 2-D structures. As compared with 1-D and 2-D structures, three-dimensional (3-D) assemblies exhibit a finite cavity of well-defined shape and size, and can be valuable in applications such as guest encapsulation, gas storage, catalysis, and drug delivery.⁵ However, 3-D supramolecular dendrimers are still rare,^{2d} mainly because of the design constraint of rigid well-defined 3-D structures.

Coordination-driven self-assembly represents a successful methodology for constructing 3-D supramolecules, as indicated by a variety of elaborate supramolecular cages, prisms, and polyhedra of well-defined shape and size.⁶ The self-assembled 3-D supramolecules have proven useful for capturing guest molecules, in supramolecular catalysis, and opening access to unusual reactions by virtue of 3-D nano-cavities.⁷ Covalent modifications of molecular subunits can endow assemblies with a wide variety of fascinating structural and functional properties.⁸ Recent examples reported by Fujita et al. demonstrated that functionalization of

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Supporting Information Available: General detailed experimental procedures for synthesis and characterization of dendritic tripyridyl donors **2a–d** and supramolecular dendrimers **3a–d**. (<http://pubs.acs.org/paragonplus/submission/jacsat/>).

the interior and/or exterior of a $M_{12}L_{24}$ Pd-based supramolecular sphere can result in saccharide clusters, nanoscale fluoro-droplets, and confined polymerization.⁹ Because of the robust structure, unique confined space, and designable framework, the coordination-driven self-assembled 3-D metallocupramolecule is a promising candidate for constructing 3-D supramolecular dendrimers.

We have recently prepared 2-D hexagonal and 3-D cuboctahedral multifunctional scaffolds with a precise number, position, and orientation of functional groups by chemical tailoring of molecular subunits.¹⁰ Encouraged by the power and versatility of this methodology, we extend it to the construction of 3-D supramolecular dendrimers, and hereby present the self-assembly of 120° diplatinum acceptors **1** with tritopic donors **2a–d**, substituted with Fréchet-type dendrons from [G-0] to [G-3].¹⁰ As shown in Scheme 1, coordination-driven self-assembly allows for quantitative generation of a series of supramolecular dendrimers **3a–d** possessing a rigid 3-D adamantanoid core. These structures have been identified by multinuclear (³¹P and ¹H) NMR spectroscopy and electrospray ionization (ESI) mass spectrometry, as well as pulsed field gradient spin-echo (PGSE) NMR measurement together with computational simulations.

[G-0]–[G-3] tripyridyl donors **2a–d** were prepared by substituting the tripyridin-4-yl methanol with Fréchet-type dendrons. The CD₂Cl₂ solution of tripyridyl donors **2** was slowly added into an acetone-*d*₆ solution of 120° organoplatinum acceptor **1** in a 2:3 ratio, and after stirring for 15 min at R.T., [6 + 4] self-assembly of adamantanoid dendrimers **3** of different sizes was quantitatively obtained. In the ³¹P{¹H} NMR spectra (Figure 1a and b and Supporting Information) of these mixtures, only a sharp singlet (**3a**: 14.06 ppm; **3b**: 14.06 ppm; **3c**: 14.05 ppm; **3d**: 14.01 ppm) with concomitant ¹⁹⁵Pt satellites can be found. Due to the formation of the Pt–N coordination bond, the signals are shifted upfield from that of the organoplatinum acceptor **1** by approximately 9.0 ppm. Likewise, the ¹H NMR spectra (see Supporting Information) exhibit sharp signals for the pyridyl protons with small shifts downfield ($\Delta\delta_{\text{Py}\alpha\text{-H}}$: 0.30 ppm; $\Delta\delta_{\text{Py}\beta\text{-H}}$: 0.75 ppm) due to the loss of electron density that occurs upon coordination. The well assigned sharp NMR signals in both the ³¹P and ¹H NMR agree with the high symmetry of **3** and rule out the formation of oligomers.

ESI mass spectrometry further confirmed the [6 + 4] structures (Supporting Information). In the ESI mass spectrum of the [G-0] adamantanoid dendrimer **3a**, peaks corresponding to [M – 4OTf]⁴⁺ and [M – 5OTf]⁵⁺ can be found at $m/z = 1742.4$ and $m/z = 1427.3$. The ESI mass peak for loss of triflate anions from [G-1] adamantanoid dendrimer **3b** at $m/z = 1912.2$ [M – 5OTf]⁵⁺ is observed, likewise for the [G-2] adamantanoid dendrimer **3c** at $m/z = 2251.6$ [M – 5OTf]⁵⁺ (Figure 2). All ESI mass peaks are isotopically resolved and agree with their theoretical distributions. However, for the [G-3] adamantanoid dendrimer **3d**, because of its high molecular weight, an isotopically resolved ESI mass signal was not obtained.

As suitable X-ray quality crystals could not be obtained, a computational study was carried out to gain insight into the structural characteristics of these assemblies. A 1.0 ns molecular dynamics simulation (MMFF force field, 300K, gas phase) was used to equilibrate each supramolecule, and the output of the simulation was then minimized to full convergence. As shown in Figure 3, each assembly has a 3.0 nm adamantanoid core with *T_d* symmetry, and the size of the overall structure is increased from 3.0 nm (for [G-0] **3a**) to 4.6 nm (for [G-3] **3d**). In **3d**, the adamantanoid core is partially covered by a dendritic shell.

PGSE NMR measurements were used to characterize these structures by determination of the translational self-diffusion coefficient, and in conjunction with the Stokes-Einstein equation, the “effective size” of the overall assembly in solution was obtained.¹¹ The ¹H PGSE for all assemblies in acetone-*d*₆ (see Supporting Information) were determined: **3a**: 3.0 ± 0.1 nm;

3b: 4.0 ± 0.12 nm; **3c**: 4.5 ± 0.1 nm; **3d**: 4.5 ± 0.15 nm. As indicated in Figure 3, they are in good agreement with the computational values (**3a**: 3.0 nm; **3b**: 3.8 nm; **3c**: 4.3 nm; **3d**: 4.6 nm) from the molecular force field modeling. Since the dendrons on the exterior are spreading around the adamantanoid core instead of spreading out, the size increase from **3c** to **3d** is minor resulting in a similar size in the PGSE NMR measurement.

In conclusion, we have developed a convergent synthesis of 3-D metallocsupramolecular dendrimers via coordination-driven self-assembly, where the exterior dendrons were introduced by pre-modification of the molecular subunits. These supramolecular dendrimers show a unique 3-D adamantanoid core, which is partially covered by the dendritic exterior, and exploration of the interior environment would be interesting and valuable. Furthermore, functionalization of dendrons and/or the supramolecular core should allow access to 3-D hollow supramolecular functional systems with potential applications such as guest encapsulation, nanoreactor, and drug delivery.¹

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
 $^{31}\text{P}\{^1\text{H}\}$ NMR (300 MHz, Acetone- d_6 /CD $_2$ Cl $_2$: 1/1) Spectra of (a) 120° Organoplatinum Acceptor **1** and (b) [G-3] Supramolecular Dendrimer **3d**.

Figure 2. Calculated (blue, top) and Experimental (red, bottom) ESI Mass Spectra of [G-2] Supramolecular Dendrimer **3c**.

Figure 3.

Computational simulations (MMFF force field) of 3-D dendrimers **3a–d** (protons and triethyl phosphorous moieties of adamantanoid core omitted for clarity) and their calculated (blue) sizes as well as experimental (red) values from PGSE NMR measurements.

Scheme 1.
Representation of the [6 + 4] Self-Assembly of Adamantanoid Supramolecular [G-0]–[G-3] Dendrimers **3a–d**.