

Dendrimer with Rotaxane-Like Mechanical Branching

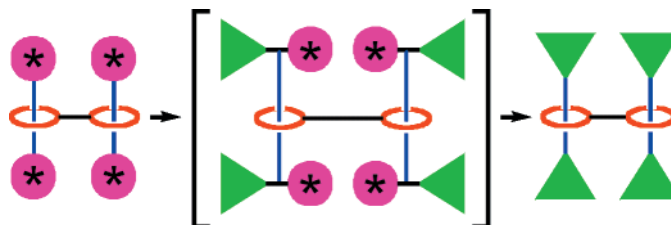
Arkadij M. Elizarov, Sheng-Hsien Chiu, Peter T. Glink, and J. Fraser Stoddart*

Department of Chemistry and Biochemistry, University of California, Los Angeles,
405 Hilgard Avenue, Los Angeles, California 90095-1569

stoddart@chem.ucla.edu

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ABSTRACT



A dendrimer wherein the branching points are mechanical in nature has been synthesized. It contains two identical covalently linked bis-dendrons and a core unit fused to two rings that encircle the two bis-dendrons. A “threading-followed-by-stoppering” approach is used in the template-directed synthesis of a precursor bis[2]rotaxane, which undergoes stopper exchange four times to yield the dendrimer in which the two bis-dendrons act as stoppers within the two [2]rotaxane subunits.

Dendrimers¹ that incorporate noncovalently linked and mechanically interlocked components at their branching points are compounds that hold great promise for potential applications in materials science as well as in macro- and supramolecular chemistry. Most dendrimers reported to date are covalent molecules,^{2–6} i.e., all the atoms are linked to the core by a series of covalent bonds. There are, however, examples of dendrimers that have components that are mechanically interlocked. In such assemblies, the dendrons have been covalently attached to one or more of the components that are involved in the mechanical bond, i.e.,

to the different ring components (Figure 1a) of a [2]catenane,⁷ to the dumbbell component (Figure 1b) of a [2]rotaxane,⁸ or to both the dumbbell and ring components of a [2]rotaxane⁷ (Figure 1c). Examples have also been reported of dendrimers that have their components intertwined with the aid of reversible noncovalent bonds in pseudorotaxane-like motifs, either at their cores⁹ (Figure 1d) or on their peripheries¹⁰ (Figure 1e).

Dendrimers (e.g., Figure 1f) in which each branching unit occurs at a mechanically bonded junction, not covalently bonded as usual, are molecules that had not been reported when we began this program of research.¹¹ We have begun our investigations toward constructing such entities by

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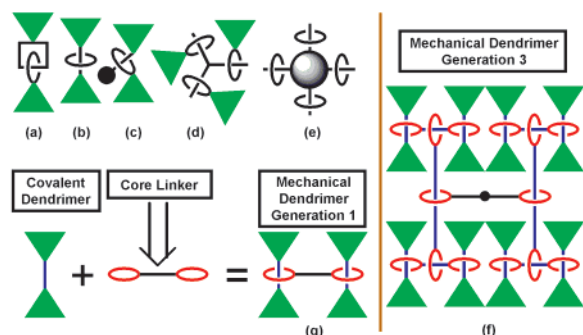
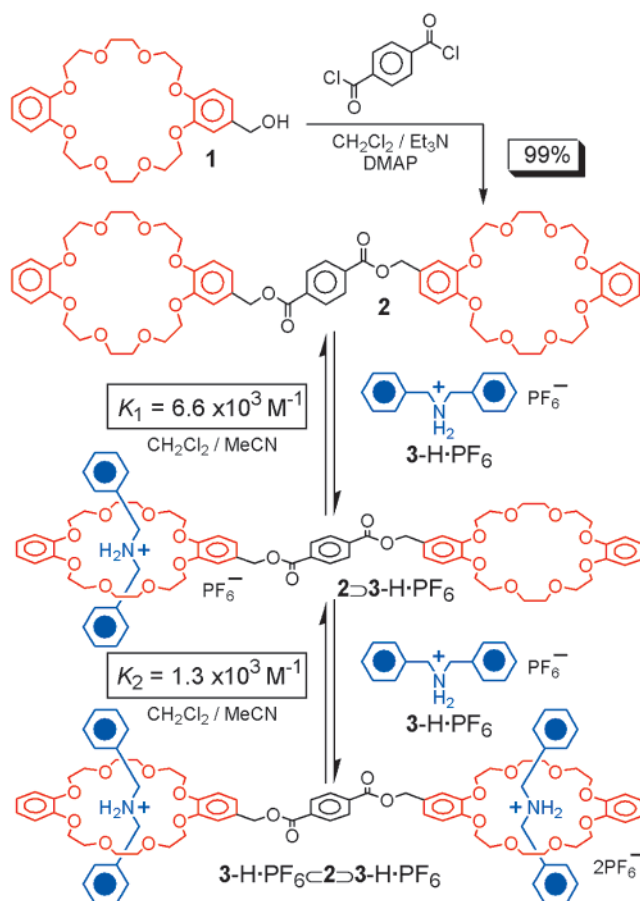


Figure 1. Graphical representations of dendrimers with mechanically interlocked or intertwined components.

preparing a dendrimer $8\text{-}2\text{H}\cdot 2\text{PF}_6$ (shown graphically in Figure 1g) containing a combination of mechanical (first generation) and covalent (second and third generations) bonds at its branching points. The mechanical bonds utilized at the branching points are associated with two [2]rotaxanes wherein the *dumbbell* components provide the branching and two ring components link the two dumbbell components to the core. In dendrimer $8\text{-}2\text{H}\cdot 2\text{PF}_6$, the stoppers on the dumbbell-shaped components are composed of Fréchet-type wedges that have two covalent branching points. To prepare a dendrimer with mechanical bonds at all its branching points, such as that represented graphically by (f) in Figure 1, the stoppers of the dumbbell-shaped component of every rotaxane-like subunit would need to be ring-shaped.¹² Thus, each repeating unit in the mechanical dendrimer would have the characteristics of a conventional dendrimer repeat unit¹³ in that it contains two reactive sites (rings) at the branches and one complementary reactive site (rod) at the pivotal point.

The synthesis of the dendrimer $8\text{-}2\text{H}\cdot 2\text{PF}_6$ starts with the preparation of the bis-dibenzo[24]crown-8 core **2** by subjecting the hydroxymethyl-functionalized¹⁴ macrocyclic dibenzo[24]crown-8 **1** to a high-yielding esterification with terephthaloyl chloride (Scheme 1). To confirm that **2** can act as a suitable host for secondary dialkylammonium ions, we investigated the binding of **2** and its parent, dibenzo[24]crown-8 (DB24C8),¹⁵ with dibenzylammonium hexafluorophosphate ($3\text{-H}\cdot \text{PF}_6$) in a mixture of CD_3CN and CD_2Cl_2 (1:2). The binding of both **2** and DB24C8 with this salt

Scheme 1. Synthesis of the Bis-crown Ether **2** and Its Complexation with Dibenzylammonium Hexafluorophosphate $3\text{-H}\cdot \text{PF}_6$



occurs under the expected^{15b} slow exchange regime in their respective ^1H NMR spectra (400 MHz, 25°C) in this solvent mixture.

The association constant (K_a) for the $[\text{DB24C8}\cdot 3\text{-H}\cdot \text{PF}_6]$ complex was determined¹⁶ by the single-point method¹⁷ to be 5300 M^{-1} . K_a values for the complexes $[\text{2}\cdot 3\text{-H}\cdot \text{PF}_6]$ and $[\text{3-H}\cdot \text{PF}_6\cdot \text{2}\cdot 3\text{-H}\cdot \text{PF}_6]$ could not be calculated so easily since we could not determine by integration the concentrations of these *doubly* and *singly* threaded complexes. Since we were able to integrate the signals for the uncomplexed (i.e., $[\text{3-H}\cdot \text{PF}_6]$) and “total complexed” (i.e., $[\text{2}\cdot 3\text{-H}\cdot \text{PF}_6]$ plus $[\text{3-H}\cdot \text{PF}_6\cdot \text{2}\cdot 3\text{-H}\cdot \text{PF}_6]$) dibenzylammonium ions, we derived¹⁸ eq 1, which relates these two concentrations to the values of the association constants, K_1 and K_2 , for the first and second binding events, respectively.

These association constants were determined from a dilution experiment, in which ^1H NMR spectra of a 1:2

(16) The binding constant was determined by a single-point method at 1.00 mM concentration in a 1:2 $\text{MeCN}/\text{CH}_2\text{Cl}_2$ mixture.

(17) For examples of the use of the single-point method for determining the values of K_a by ^1H NMR for systems in slow kinetic exchange, see: (a) Ashton, P. R.; Chrystal, E. J. T.; Glink, P. T.; Menzer, S.; Schiavo, C.; Spencer, N.; Stoddart, J. F.; Tasker, P. A.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1996**, *2*, 709–728. (b) Ashton, P. R.; Fyfe, M. C. T.; Hickingbottom, S. K.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2117–2128.

(18) The derivation of eq 1 is available in Supporting Information.

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molar ratio mixture of **2** and **3-H**·PF₆ were obtained at different concentrations in a CD₃CN/CD₂Cl₂ (1:2) solvent mixture. From each spectrum, the concentration of complexed dibenzylammonium salt (i.e., [2·3-H·PF₆] plus [3-H·PF₆·2·3-H·PF₆]) was plotted (Figure 2) against the

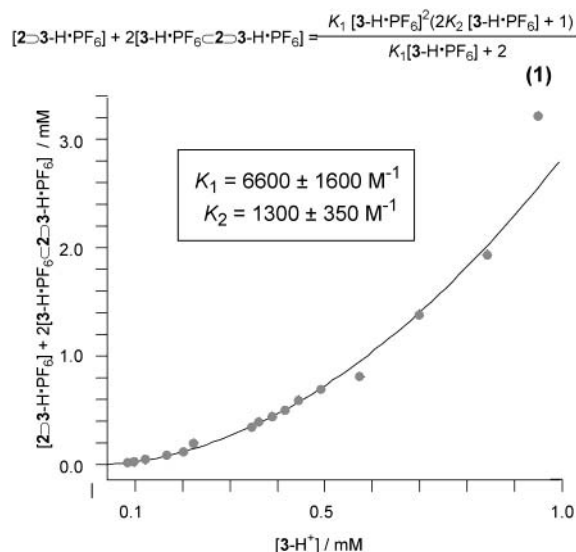


Figure 2. Plot of the total concentration of the complexed dibenzylammonium ions (y-axis) against the concentration of the uncomplexed dibenzylammonium ions (x-axis) in the dilution of a 1:2 molar mixture of **2** and **3-H**·PF₆ in CD₃CN/CD₂Cl₂ (1:2). The solid line represents the line of best fit as defined by eq 1.

concentration of free salt (i.e., [3-H⁺]) and the data points were fitted to eq 1 by a nonlinear, least-squares, iterative procedure. The values of the equilibrium constants, *K*₁ and *K*₂, for the first and second binding events were calculated to be 6600 ± 1600 and 1300 ± 350 M^{−1}, respectively.¹⁹ Gratifyingly, these values suggest that **2** binds to dialkylammonium ions with a similar strength as does DB24C8 itself.

The synthesis of the dendritic bis[2]rotaxane **8-2H**·2PF₆ is outlined in Scheme 2. We chose to use the approach of “threading-followed-by-stoppering”²⁰ and then “stopper exchange”.²¹ The latter, a recently reported,²² high-yielding method, is a valuable technique for preparing dialkylammonium ion/crown ether-based rotaxanes bearing benzylic triphenylphosphonium ion stoppers, which can be exchanged, subsequently, for other stoppers — via Wittig reactions with bulky aldehydes — without occurrence of disassembly.^{21,22}

(19) The ratio *K*₁/*K*₂ is ca. 5, suggesting that a weak negative cooperativity is operative in the second binding event. See: Connors, K. A. *Binding Constants*; John Wiley: New York, 1987.

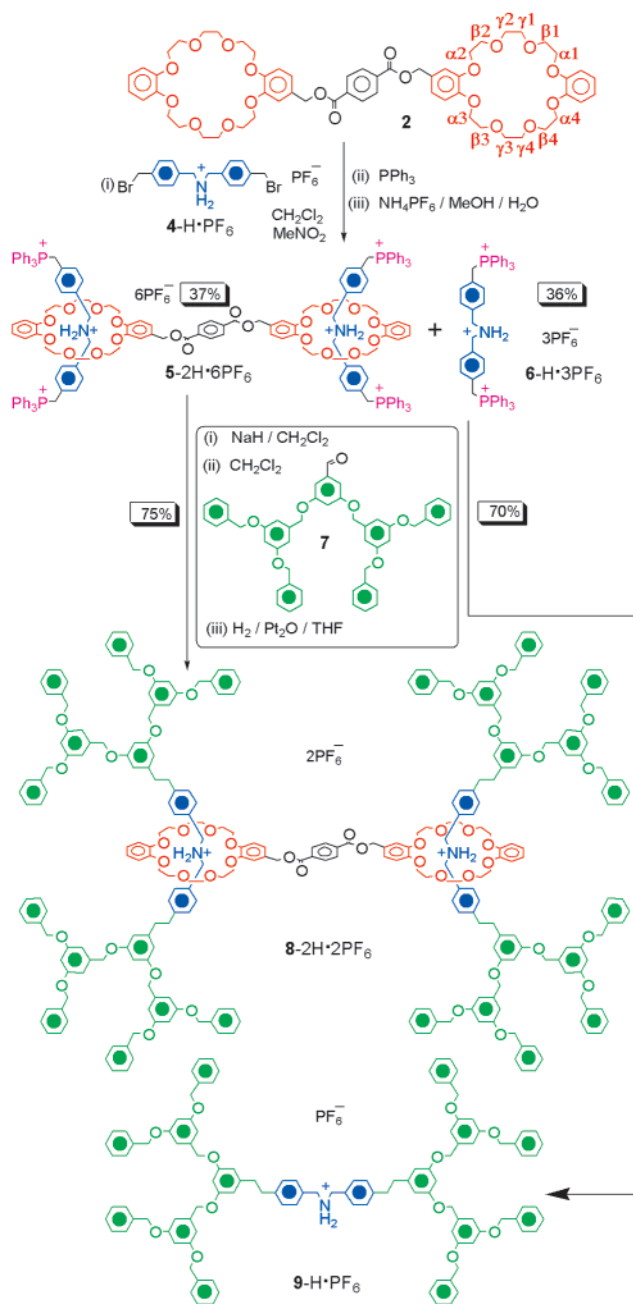
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Scheme 2. Synthesis of the Mechanically Interlocked Dendrimer **8-2H**·2PF₆ and the Dumbbell-Shaped Covalent Dendrimer **9-H**·PF₆



Thus, once a benzylic triphenylphosphonium ion-stoppered rotaxane is prepared, that core structure can be used, for instance, in a dendrimer synthesis, without the risk of forming unthreaded products.

The bis[2]rotaxane **5-2H**·6PF₆, carrying four benzylic triphenylphosphonium stoppers, was prepared by first dissolving the pseudorotaxane components (**2** and the bis-(bromomethyl)-substituted dibenzylammonium derivative²¹ **4-H**·PF₆) in a mixture of CH₂Cl₂ and MeNO₂ (threading), and then treating this solution with a 3-fold excess of triphenylphosphine (stoppering). The bis[2]rotaxane **5-2H**·6PF₆ (37%) was obtained, along with the mono[2]rotaxane

(28%) in which one of the crown ether rings is unoccupied, as well as the dumbbell²¹ **6-H**·3PF₆, following counterion exchange (NH₄PF₆/H₂O) and thorough drying. The bis[2]-rotaxane **5-2H**·6PF₆ was subjected to a Wittig reaction by treatment with NaH and the wedge-shaped aldehyde²³ **7** (stopper exchange). This reaction resulted in a mixture of isomeric (*E/Z*)-olefinic products that could not be separated from each other. Reduction of their olefinic bonds²⁴ by catalytic hydrogenation (H₂/PtO₂, 30 min) gave the bis[2]-rotaxane **8-2H**·2PF₆ in good yield. The benzylic triphenylphosphonium-stoppered dumbbell **6-H**·3PF₆ was subjected to the same reaction conditions. Thus, after Wittig reaction and catalytic hydrogenation, a symmetric covalent dendrimer **9-H**·PF₆ was isolated in good yield.

The structures of the mechanical dendrimer **8-2H**·2PF₆ and the covalent dendrimer **9-H**·PF₆ were confirmed spectroscopically and by elemental analysis. Signals were observed by FABMS at *m/z* 4446 and 2223, corresponding to [**8-H**]⁺ and [**8-2H**]²⁺, respectively. A peak was observed in the ESMS of **9-H**·PF₆ at *m/z* 1860 corresponding to [**9-H**]⁺. Partial ¹H NMR spectra of the mechanical dendrimer **8-2H**·2PF₆, and its components **2** and **9-H**·PF₆, are shown in Figure 3. The signal of the protons of the CH₂N⁺ groups in **8-2H**·2PF₆ is shifted downfield by 0.93 ppm relative to the corresponding signal in the covalent dendrimer **9-H**·PF₆. This change is characteristic of the binding of dibenzylammonium ions with DB24C8. The polyether signals of the α-, β-, and γ-OCH₂ groups of the crown ether moieties are shifted upfield in **8-2H**·2PF₆ between 0.07 and 0.36 ppm relative to the corresponding signals in **2**, an observation which is consistent with the shifts registered by DB24C8 and its derivatives upon complexation with dibenzylammonium ions.¹⁵ In addition, the signals of the α-, β-, and γ-OCH₂ groups are more complicated in **8-2H**·2PF₆ than in **2**, reflecting the enhanced asymmetry of crown ether moieties in **8-2H**·2PF₆ (e.g., the difference between the chemical environments of the four different α-OCH₂ groups increases) brought about by the presence of the dendritic wedge-stoppered dumbbells.

We have demonstrated that Wittig-style stopper exchange can be used effectively to construct a dendrimer with rotaxane-like mechanical bonds at its branching points. This research opens the way to the construction of dendrimers

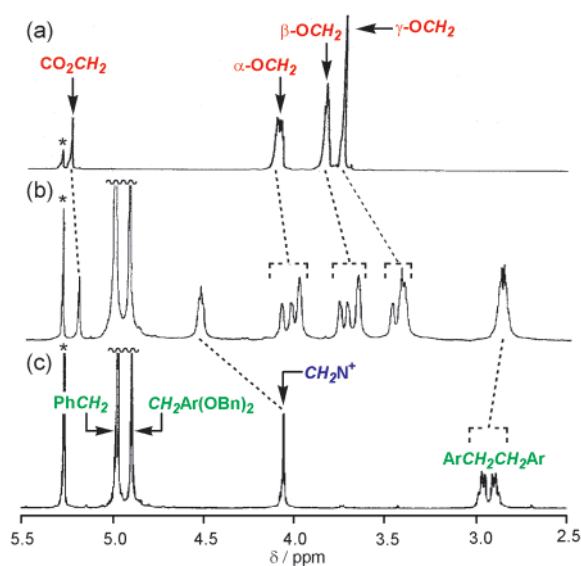


Figure 3. Partial ¹H NMR (500 MHz, CD₂Cl₂) spectra of (a) the bis-crown ether **2**, (b) the mechanical dendrimer **8-2H**·2PF₆, and (c) the covalent dendrimer **9-H**·PF₆. (* = CH₂Cl₂).

with mechanical branching points at more than one generation such as that depicted graphically in Figure 1f.

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Supporting Information Available: ¹H and ¹³C NMR spectra and mass spectra of compounds **2**, **5-2H**·6PF₆, **6-H**·3PF₆, **8-2H**·2PF₆, and **9-H**·PF₆, experimental procedures for their preparation, and the derivation of eq 1. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(24) Since it is very difficult to separate under-reduced species from the product, it is important to allow this reduction to reach completion. However, over-reduction of the product, e.g., by cleavage of benzylic bonds, occurs when reaction times are longer than 30 min.