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Communications to the Editor

Toward Chiral Dendrimers with Highly Functionalized Interiors. Dendrons from Synthetic AB$_2$ Monomers

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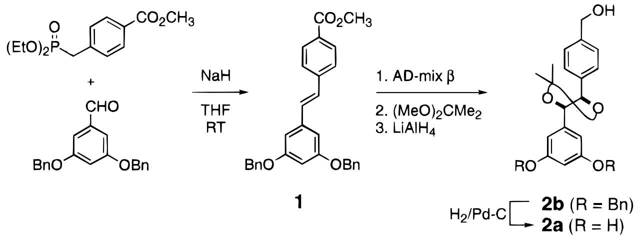
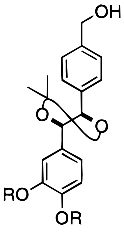
With their potential for enantioselective clathration of small chiral molecules, dendrimers with chiral surfaces[1] or interiors[2] have attracted much recent interest. Possible applications for these materials include chemical separations, sensor technology, and asymmetric catalysis. For selectivity with regard to shape and functionality of small molecules, we anticipate that a dendrimer must possess both structural subunits with well-defined topology and interior moieties capable of interacting strongly with encapsulated guests. While several workers have introduced chirality into the interior of dendritic structures, only those structures reported by Mitchell[2d] and Chapman[3] possess moieties (amide linkages) capable of providing strong enthalpic contributions to guest binding. In addition, few dendrimers have appropriate functionality to anchor well-defined transition-metal moieties for asymmetric catalysis.[4,5] We have designed a family of dendritic materials which consist of (1) chiral, nonracemic subunits in the interior for shape selectivity and (2) functionality suitable for hydrogen bonding with guest molecules. We report here our approach to these materials with highly functionalized interior cavities as constructed from chiral, nonracemic 1,2-diol-containing AB$_2$ monomers[6] prepared by catalytic asymmetric synthesis.[7]

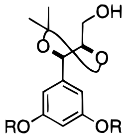
Previous syntheses of chiral dendrimers have relied in large part on building blocks from natural sources. To increase the structural diversity of chiral dendrimers, we have prepared a series of monomers for dendrimer construction through asymmetric synthesis.[6] A prototypical monomer synthesis, which employs osmium-catalyzed asymmetric dihydroxylation (AD),[8] is shown in Scheme 1. Stilbene derivative **1**, prepared by a Horner−Emmons modified Wittig reaction in 95% yield, is an excellent substrate for the AD reaction, which proceeded in very good yield and enantioselectivity (>97% ee by chiral HPLC). The diol moiety was masked as the cyclic acetonide derivative, and LiAlH$_4$ reduction of the benzoate ester followed by hydrogenolysis of the benzyl groups yielded hydrobenzoin derivative **2a** in 62% overall yield (five steps). Monomers **3a**−**5a** were prepared by analogous routes in 57, 64, and 67% overall yields, respectively. The 1,2-diol units in **2a**−**5a** were protected as their acetonide derivatives to avoid complications during dendrimer construction. The intention is to unmask these diols in the final dendrimers (infra vide).

Scheme 1

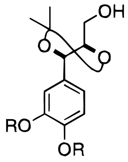




3a (R = H)
3b (R = Bn)



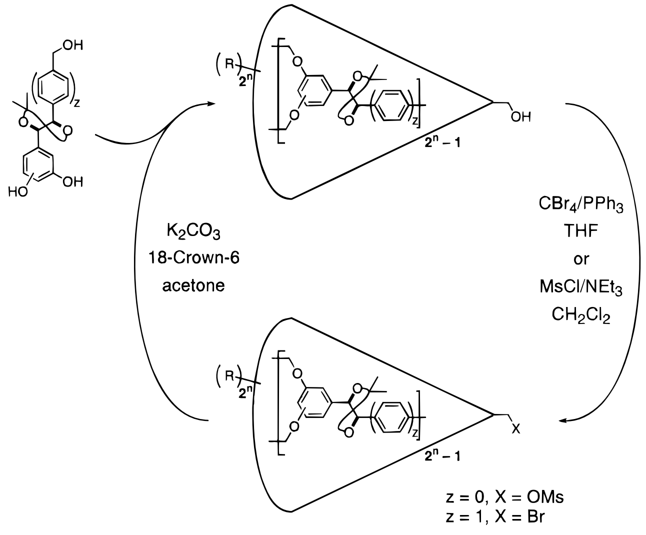
4a (R = H)
4b (R = Bn)



5a (R = H)
5b (R = Bn)

Monomers **2a**−**5a** are primed for dendrimer construction by the convergent method developed by Hawker and Fréchet.[9] Accordingly (Scheme 2), zeroth generation monodendrons **2b** and **3b** were converted to their corresponding bromides (>85% yields), which were then allowed to react with 0.5 equiv of monomers **2a** and **3a**, respectively, in a slurry of K$_2$CO$_3$ and 18-crown-6 in acetone. First generation monodendrons **2c** and **3c** were obtained in yields typically ranging from 60 to 85%. In the case of **4b** and **5b**, the corresponding bromides did not couple efficiently to **4a** and **5a** under these conditions. Use of a mesylate leaving group in place of the bromide,[10] however, yielded first generation

Scheme 2



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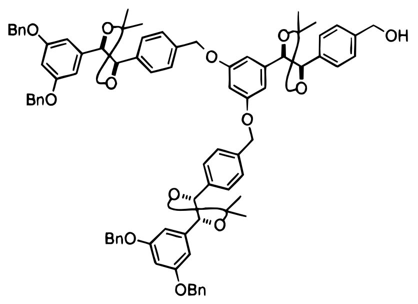
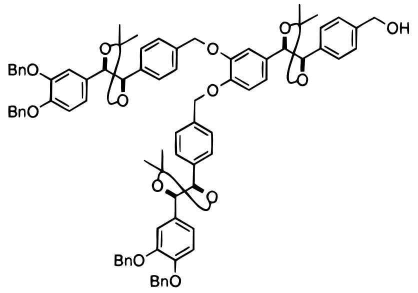
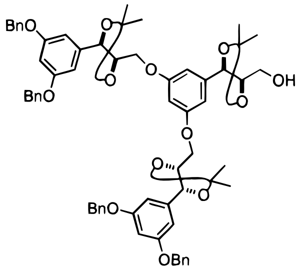


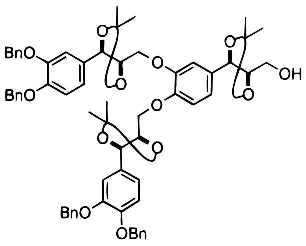
2c



3c



4c



5c

monodendrons **4c** and **5c** in typically 50–60% yields. Second generation dendrons **2d**–**5d** have been obtained in essentially the same yields.

Principal characterization was carried out by 400 MHz ^{1}H NMR. For symmetrically branched monodendrons (**2b**–**d** and **4b**–**d**) the 6.3–6.7 ppm region of the ^{1}H NMR spectra contained the characteristic resonances of the three protons on the trisubstituted aryl rings (Figure 1) and proved most diagnostic of generational growth.[11] In the spectra of zeroth generation dendrons **2b** and **4b** the three protons on the 1,3,5-substituted aromatic ring appeared as a doublet (2H) and a triplet (1H) (Figure 1a,b). Albeit with some overlap, the first generation dendrons **2c** and **4c** clearly exhibited two sets of doublet/triplet patterns in a 1:2 ratio (Figure 1c,d), and the second generation dendrons **2d** and **4d** exhibited three sets of doublet/triplet patterns in a 1:2:4 ratio (Figure 1e,f). For nonsymmetrically branched monodendrons,[12] ^{13}C NMR proved a more useful characterization technique. Although the nonsymmetrical branching geometry of monodendrons **3b**–**d** and **5b**–**d** renders most of the carbons in the structures unique, the 100 MHz ^{13}C NMR spectrum showed certain classes of carbon atoms resolved rather well. For example, in the spectrum of **3c** (Figure 2), the six benzyloxy carbons (A), six carbinol carbons (B), and three quaternary carbons on the oxygen-substituted aryl rings (C) appeared at approximately 71, 85, and 130 ppm, respectively, with only slight overlap evident in region B.

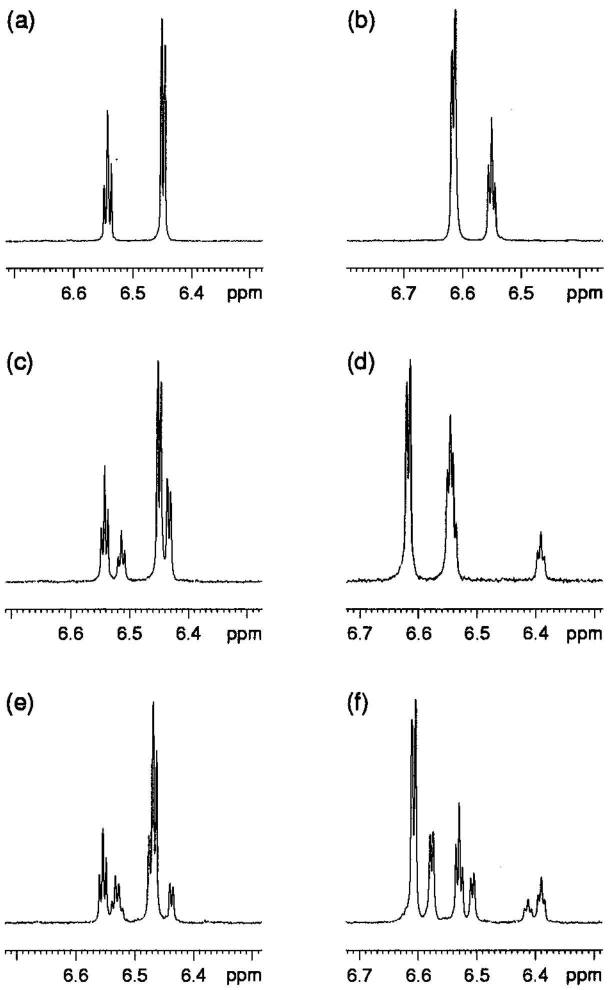


Figure 1. ^{1}H NMR spectra (ca. 6.3–6.7 ppm) of symmetrically branched monodendrons (a) **2b**, (b) **4b**, (c) **2c**, (d) **4c**, (e) **2d**, and (f) **4d**.

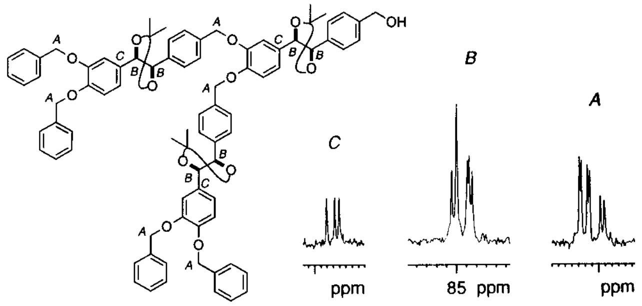
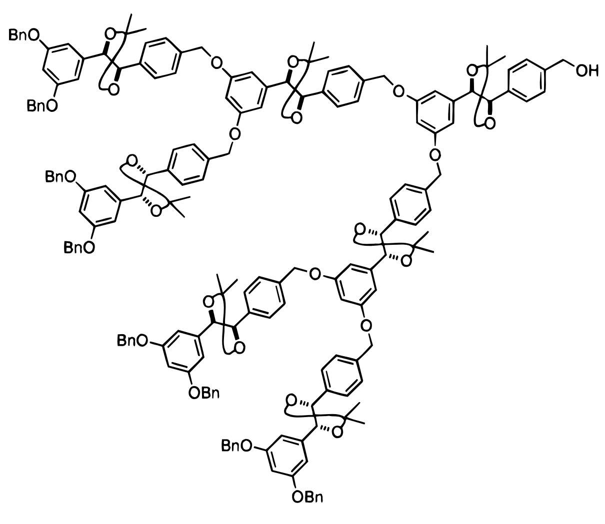
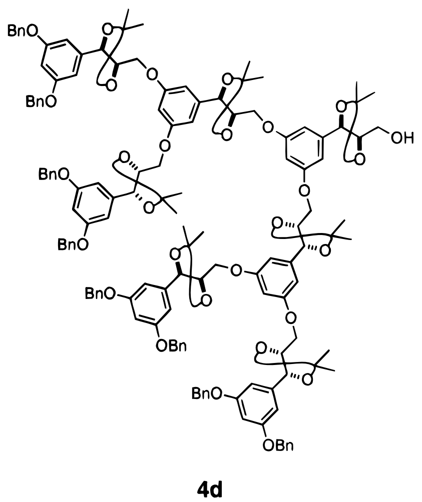


Figure 2. ^{13}C NMR (100 MHz) characterization of first generation monodendron **3c**: region A, approximately 71 ppm; region B, approximately 85 ppm; region C, approximately 130 ppm.

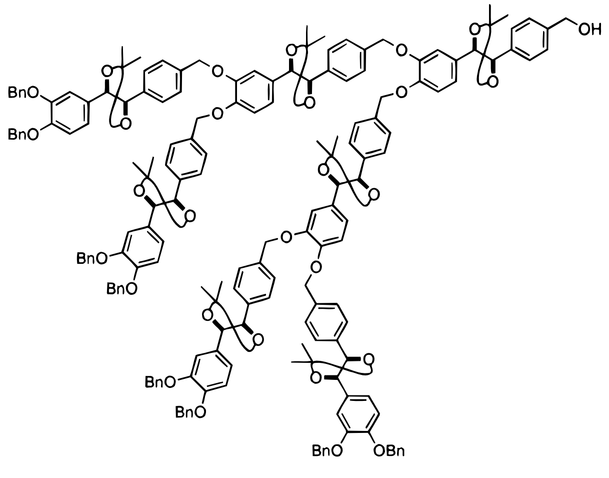
Our investigation of the chiroptical properties of these monodendrons is summarized in Figure 3. For the monodendrons derived from monomers **2a** (**2b**–**d**), **3a** (**3b**–**d**), **4a** (**4b**–**d**), and **5a** (**5b**–**d**), we found little to no contribution to the molar rotation from molecular conformation. This was indicated by the small change in molar rotation per chiral unit on going from zeroth to first to second generation. There appeared to be a significant difference in molar rotation between zeroth generation monodendrons **4b** and **5b** and respective first generation monodendrons **4c** and **5c**. We believe this is not an indication of chiral conformation, but merely a result of **4b** and **5b** being poor model compounds for **4c** and **5c**. In other words, the chiral units in **4c** and **5c** are not all identical to those in **4b** and **5b**. A more



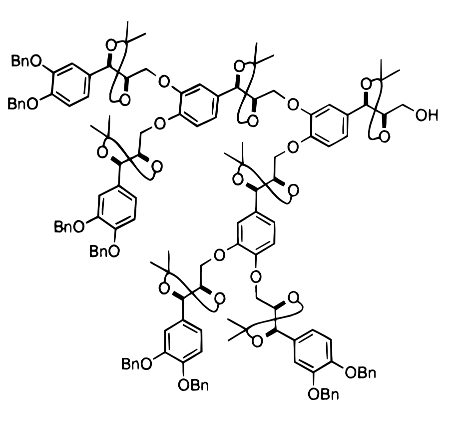
2d



4d



3d



5d

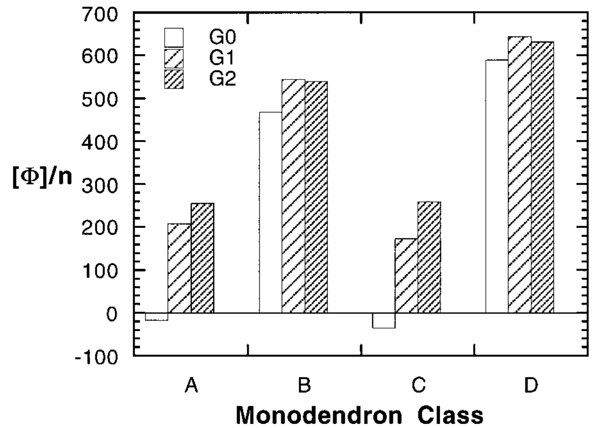
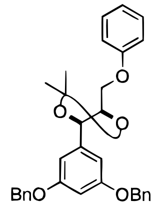


Figure 3. Molar optical rotations (Φ) per chiral unit (*n*) for zeroth ($n = 1$), first ($n = 3$), and second ($n = 7$) generation monodendrons: A (**4b**−**d**), B (**2b**−**2d**), C (**5a**−**5d**), and D (**3b**−**3d**).

appropriate model compound, **6**, was prepared, and its rotation measured as $[\alpha]_D = +52.7$ ($c = 2.36$, CH_2Cl_2). When the corresponding molar rotation ($[\Phi]_D = +262$) is used to calculate the expected rotation for the first and second generation monodendrons **4c** and **4d**, values of +507 and +1555 are obtained, much closer to the observed values of +625 and +1786. The circular dichroism spectra (not shown) of these monodendrons all exhibit positive Cotton effects throughout the absorption range. No exciton coupling is observed.



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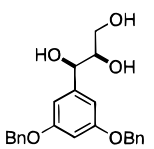
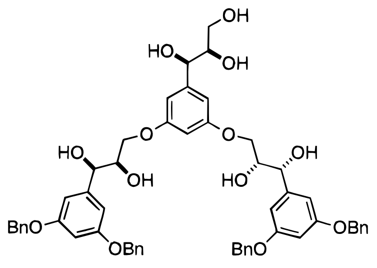
We have carried out a preliminary investigation of the deprotection of the 1,2-diol units in these materials. Liberation of the protected 1,2-diols can be achieved by treatment with 3 N HCl in acetonitrile. Monodendrons **7** and **8** are obtained in quantitative yield from **4b** and



7



8

4c, respectively. Polyols **7** and **8** are only soluble in polar solvents such as acetone and DMSO.

In summary, we have prepared a new series of chiral, nonracemic AB_2 monomers and have demonstrated their efficacy in the synthesis of dendritic structures using convergent techniques. Synthesis and investigation of the chiroptical properties of higher generation materials continue.

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Supporting Information Available: Spectroscopic, analytical, and polarimetry data for monodendrons **2c**−**5c** and **2d**−**5d** (2 pages). Ordering information is given on any current masthead page.

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(7) To our knowledge, our preliminary report of this work (Polym. Prepr. (*Am. Chem. Soc., Div. Polym. Chem.*) **1996**, *37*(2), 495) is only the second example of chiral dendrimer synthesis from building blocks not derived from natural sources. See ref 2a.

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(11) Spectral data (400 MHz ^1H and 100 MHz^{13}C NMR) was in accord with the assigned structures. All compounds except **2d**−**5d** gave acceptable combustion analyses. Compounds **2d**−**5d** were >95% pure based on normal phase HPLC.

(12) For another example of a nonsymmetric branching structure see: Percec, V.; Chu, P.; Unger, G.; Zhou, J. *J. Am. Chem. Soc.* **1995**, *117*, 11441.

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