JOC*Article*

Design, Synthesis, and Photochemical Behavior of Poly(benzyl ester) Dendrimers with Azobenzene Groups throughout Their Architecture

Shuangxi Wang*,† Ximeng Wang,‡ Lijuan Li,‡ and Rigoberto C. Advincula*,†,‖

Department of Chemistry, University of Alabama at Birmingham, Birmingham, Alabama 35294, Department of Chemistry and Biochemistry, California State University, Long Beach, California 90840, and Department of Chemistry, University of Houston, Houston, Texas 77204

wangsx99@yahoo.com; radvincula@uh.edu

Received January 2, 2004

A new class of dendrons and dendrimers containing azobenzene units (bearing up to 29 azobenzene groups for four generations) were designed and synthesized with the convergent method, which uses azobenzene derivatives as monomers and benzyl ester groups as linkages leading to photoresponsive dendrons and dendrimers with azobenzene units *throughout* their architecture. Photochemical isomerization experiments revealed that all of the dendrons and dendrimers undergo *trans*−*cis* isomerization by irradiation and *cis*−*trans* isomerization by either irradiation or heating.

Introduction

Dendrimers have been the subject of intense investigation due to both interesting structural properties and promising applications in the areas of biological and material sciences.[1] Their highly branched structure, monodispersed molecular weight, and the large number of functional groups in the periphery as well as internal cavities are important characteristics which make dendrimers excellent candidates for evaluation as drug deliverers.[2] In fact, biologically active molecules can be conjugated to a dendrimer surface or loaded into the interior of the dendrimer. Several examples include antibodies,[3] carbohydrate moieties,[4] and anti-cancer drugs[5] that have been conjugated to poly(amidoamine)dendrimers. These dendrimeric drug conjugates have improved solubility, reduced toxicity, and increased circulation time of the dendrimer−drug conjugates in the blood plasma and have allowed the well-defined dendrimer to carry drugs at high density.[6] Moreover, Gd^{III} chelates conjugated to poly(amidoamine)dendrimers were found to show excellent MRI images of blood vessels and have long blood circulation times (>100 min).[7] The interiors of dendrimers have also been shown to be capable of encapsulating guest molecules.[8] For example, a restricted number of guests, such as Rose Bengal, can be encapsulated in the dentritic box of the poly(propylene imine) dendrimer, modified with a dense shell of aminocation of the acids,[9a] and released by simple chemical modification of the shell.[9b] Dendrimers with a hydrophobic interior and hydrophilic chain ends were shown to behave as unimolecular micelles capable of solubilizing various compounds in aqueous solution.[10] Furthermore, dendritic unimolecular micelles have been used to encapsulate drugs inside their hydrophobic interiors and release them slowly into solution.[11]

* Addresses for correspondence: (S.W.) LA Tech Center, Inc., 6140 Bristol Parkway, Culver City, CA 90230. Fax: 310-670-0348. (R.A.) Department of Chemistry, University of Houston, 136 Fleming Bldg, Houston, TX 77204-5003. Fax/Lab Tel: 713-743-1760.

† University of Alabama at Birmingham.

‡ California State University at Long Beach.

‖ University of Houston.

(1) (a) Tomalia, D. A.; Naylor, A. M.; Goddard, W. A., III. *Angew. Chem., Int. Ed. Engl*. **1990**, *29*, 138. (b) Fréchet, J. M. J. *Science* **1994**, *263*, 1710. (c) Zeng, F.; Zimmerman, S. C. *Chem. Rev*. **1997**, *97*, 1681. (d) Bosman, A. W.; Janssen H. M.; Weijer, E. W. *Chem. Rev*. **1999**, *99*, 1665. (e) Fisher, M.; Vogtle, F. *Angew. Chem., Int. Ed*. **1999**, *38*, 884. (f) Stiriba, S.-E.; Frey, H.; Haag, R. *Angew. Chem., Int. Ed*. **2002**, *41*, 1329.

(2) Liu, M.; Fréchet, J. M. J. *Pharm. Sci. Technol. Today* **1999**, *2*, 393.

(3) (a) Roberts, J.; Adams, Y. E.; Tomalia, D.; Mercer-Smith, J. A.; Lavallee, D. K. *Bioconjugate Chem*. **1990**, *1*, 305. (b) Singh, P.; Moll, F., III, Lin, S. H.; Ferzli, C.; Kwok, S. Y.; Koski, R. K.; Saul, R. G.; Gronin, P. *Clin. Chem*. **1994**, *40*, 1845. (c) Barth, R. F.; Adams, D. M.; Soloway, A H.; Alam, F.; Darby, M. V. *Bioconjugate Chem*. **1994**, *5*, 58.

(4) (a) Aoi, K.; Itoh, K.; Okada, M. *Macromolecules* **1995**, *28*, 5391. (b) Zanini, D.; Roy, R. *J. Am. Chem. Soc*. **1997**, *119*, 2088.

(5) (a) Zhuo, R. X.; Du, B.; Lu, Z. R. *J. Controlled Release* **1999**, *57*, 249. (b) Kono, K.; Liu, M.; Fréchet, J. M. J. *Bioconjugate Chem*. **1999**, *10*, 1115. (b) Kojima, C.; Kono, K.; Maruyama, K.; Takagishi, T. *Biocojugate Chem*. **2000**, *11*, 910.

(6) (a) Wiwattanapatapee, N. M. R.; Klopsch, R.; Lorenz, K.; Frey, H.; Weener, J. W.; Meijer, E. W.; Paulus, W.; Duncan, R. *J. Controlled Release* **2000**, *65*, 133. (b) Davis, B. G. *J. Chem. Soc., Perkin Trans*. **1999**, *1*, 3215.

(7) (a) Wiener, E. C.; Brechbiel, M. W.; Brothers, H.; Magin, R. L.; Gansov, O. A.; Domalia, D. A.; Lauterbur, P. C. *Magn. Reson. Med*. **1994**, *31*, 1. (b) Wiener, E. C.; Auteri, F. P.; Chen, J. W.; Brechbiel, M. W.; Gansov, O. A.; Schneider, D. S.; Belford, R. L.; Clarkson, R. B.; Lauterbur, P. C. *J. Am. Chem. Soc*. **1996**, *118*, 7774. (c) Bryant, L. H., Jr.; Brechbiel, M. W.; Wu, C.; Bulte, J. W. M.; Herynek, V.; Frank, J. A. *J. Magn. Reson. Imaging* **1999**, *9*, 348.

(8) (a) Baars, M. W. P. L.; Meijer, E. W. *Top. Curr. Chem*. **2001**, *210*, 131 and references therein. (b) Hecht, S.; Fréchet, J. M. J. *Angew. Chem., Int. Ed*. **2001**, *40*, 75.

(9) (a) Jansen, J. F. G. A.; de Brababder-van den Berg, E. M. M.; Meijer, E. W. *Science* **1994**, *266*, 1226. (b) Jansen, J. F. G. A.; Weijer, E. W. *J. Am. Chem. Soc*. **1995**, *117*, 4417.

(10) (a) Newkome, G. R.; Moorefield, C. N.; Baker, G. R.; Johnson, A. W.; Behera, R. K., *Angew. Chem., Int. Ed. Engl*. **1991**, *30*, 1176. (b) Newkome, G. R., Moorefield, C. N., Baker, G. R.; Saunders: M. J.; Grossman, S. H. *Angew. Chem., Int. Ed. Engl*. **1991**, *30*, 1178.

(11) (a) Liu, M.; Fréchet, J. M. J. *Polym. Mater. Sci. Eng*. **1999**, *80*, 167. (b) Liu, M.; Kono, K.; Fréchet, J. M. J. *J. Controlled Release* **2000**, *65*, 121.

10.1021/jo0499773 CCC: $27.50
Published on Web 12/01/2004

Dendrimers with highly branched and structurally regular architecture, which are prepared step by step either divergently or convergently, allow precise placement of functional groups within their structural interior or at their periphery, providing new opportunities for creating new functional materials.[12−15] For example, incorporation of azobenzene groups into the skeleton of dendritic macromolecules either in the exterior,[16] at the core,[17] or throughout the dendritic architecture[18] offers wide range of potential functional materials including optical switching,[16f,g] holographic storage,[16e] light harvesting,[17b,c] long-term energy storage,[17f] and nonlinear optical materials.[18a]

In this paper, we describe the design, synthesis,[19] and photochemical properties of new photoresponsive dendrons and dendrimers with orthogonal photosensitive azobenzene groups placed throughout their architecture. Figure 1 illustrates the three generations of dendrimers. Whole dendrimers are only constructed with photosensitive azobenzene units that are linked together through degradable benzyl ester bonds. It is our long-term aim to create "intelligent" macromolecules whose molecular shapes and sizes can be altered simply by UV irradiation or can be used as carriers of smaller guest molecules or small molecule drugs that can be locked up and released by means of a light beam.

Results and Discussion

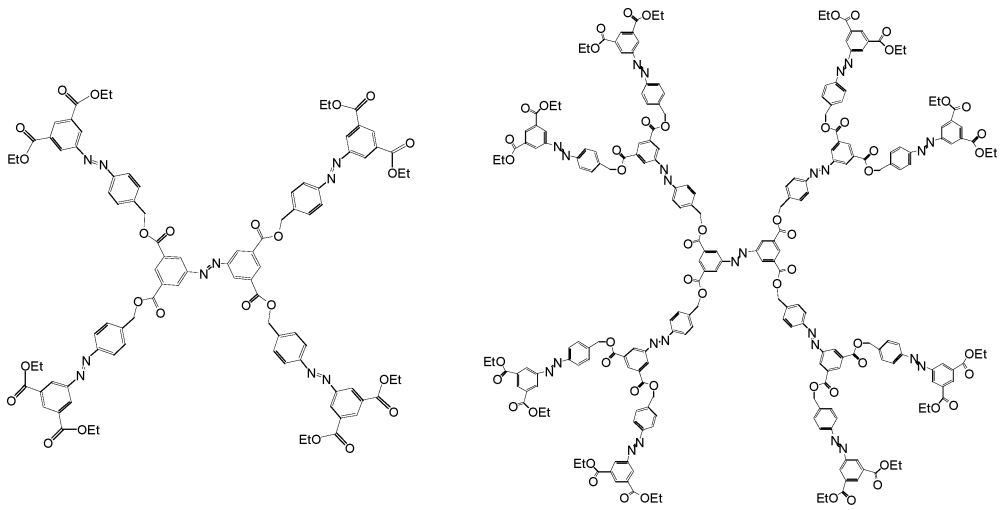
The synthesis of dendrimers **G-1**−**4**, **G-2**−**4**, and **G-3**−**4** involves separate preparation of three building blocks: the orthogonal AB_2 monomer **4** contains active carboxylic groups for generation growth and hydroxymethyl groups as linkages for next generation growth, the central linkage **AB_4** with four branches, and the peripheral **G-1-OH** monomer which is put on the surface of the target dendrimers **G-n-4** (n = 1−3). Dendrimer **G-n-4** can be prepared with a convergent approach using these three building blocks through esterification of the carboxylic groups and the hydroxymethyl groups (Scheme 1).

Synthesis of Building Blocks G-1-OH, 4, and AB_4. Several synthetic methods for the preparation of azobenzene compounds are available, such as (a) coupling of aromatic diazonium compounds with electron-rich aromatic phenol or aniline compounds; (b) condensation of nitroso with amino compounds, which is suitable for various starting materials, but it is usually not easy to get nitroso compounds due to their instability; and (c) reductive coupling of nitro compounds for the preparation of symmetric azo-benzene compounds. Method b was chosen for the preparation of **G-1-OH** and **4** because of their electron-deficient aromatic and asymmetric structures, while method c is employed to prepare the symmetric four-branched core linker **AB_4**. Scheme 2 shows the synthetic route for **G-1-OH**, **4**, and **5**. The **G-1-OH** is derived from the nitroso compound **3,** which was made from the diethyl ester nitro compound **2,** prepared by the esterification of 5-nitroisophthalic acid, **1**. The esterification of **1** with ethanol in the presence of catalytic concentrated H_2SO_4 under reflux produced the diethyl ester **2** in 88% yield. Compound **3** was prepared according to a modified literature method[20] by reduction of **2** using Zn dust at 33−35 °C in 2-methyloxyethanol to the hydroxylamine intermediate. This was followed by the oxidation of the hydroxylamine intermediate with $FeCl_3$ at about 0−5 °C to get nitroso compound **3** with an overall 47% yield. Condensation of **3** with commercially available 4-aminobezyl alcohol in CH_2Cl_2 catalyzed by acetic acid gave the first-generation azo-dendron **G-1-OH** with a good yield (86%). Saponification of the **G-1-OH** with aqueous KOH in a refluxing mixture of EtOH and H_2O resulted in the AB_2 monomer **4** in 84% yield. Bromination of the **G-1-OH** with CBr_4 and PPh_3 yielded the bromomethyl compound, **5**.

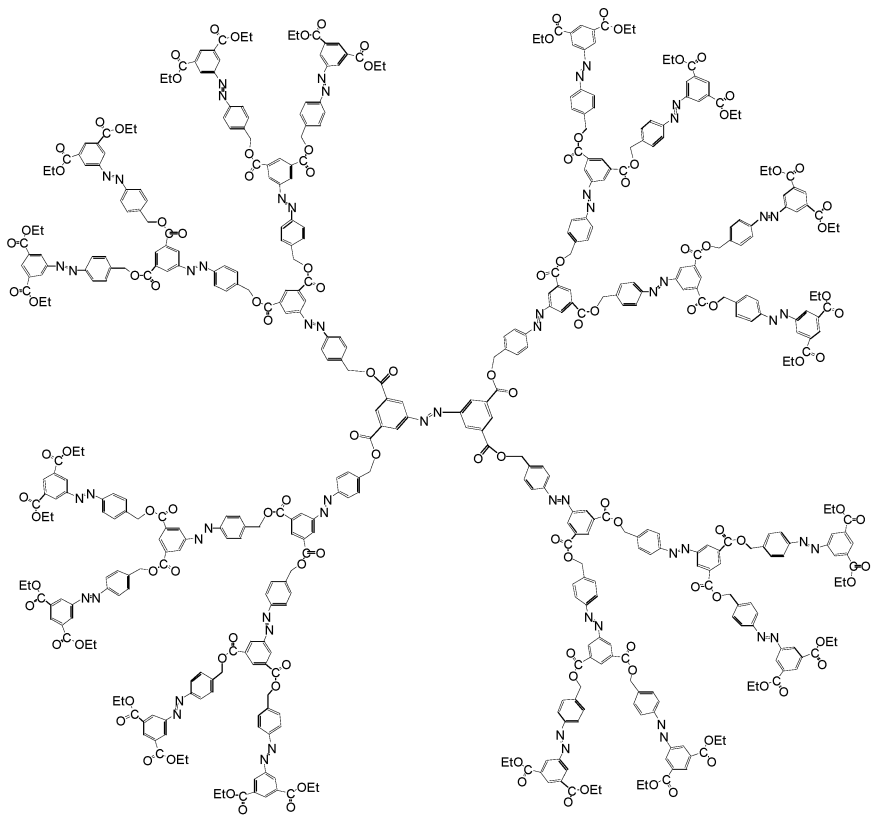
The symmetric four-branched central linker **AB_4** was prepared by reductive coupling of 5-nitroisophthalic acid with Zn/NaOH in a refluxing mixture of EtOH and water for 12 h, followed by acidification using 1 M HCl (aq) in 78% yield. The crystal structure of **G-1-OH** in a solid state was revealed by X-ray diffraction analysis. Crystal data and collection parameters are presented in the Supporting Information.

Synthesis of Dendron (G-2-OH). The **G-2-OH** was prepared by refluxing the AB_2 monomer **4** with the benzyl

(12) (a) Balazani, V.; Campagna, S.; Denti, G.; Juris, A.; Serroni, S.; Venturi, M. *Acc Chem. Res*. **1998**, *31*, 26. (b) Wang, P.-W.; Liu, Y.-J.; Devadoss, C.; Bharathi, P.; Moor, J. S. *Adv. Mater*. **1996**, *8*, 237.
(13) (a) Miller, L. L.; Duan, R. G.; Tully, D. C.; Tomalia, D. A. *J. Am. Chem. Soc*. **1997**, *119*, 1005. (b) Tanaka, S.; Iso, T.; Doke, Y. *Chem. Commun*. **1997**, 2603. (c) Wang, C.; Bryce, M. R.; Batsanov, A. S.; Goldenberg, L. M.; Howard, J. A. K. *J. Mater. Chem*. **1997**, *7*, 118. (d) Gorman, C. B.; Parkhurst, B. L.; Su, W. Y.; Chen, K.-Y. *J. Am. Chem. Soc*. **1997**, *119*, 1141. (f) Newkome, G. R.; Narayanan, V. V.; Echegoyen, L.; Pérez-Cordero, E.; Luftmann, H. *Macromolecules* **1997**, *30*, 5187. (g) Cardona, C. M.; Kaifer, A. E. *J. Am. Chem. Soc*. **1998**, *120*, 4023.
(14) (a) Zimmerman, S. C.; Wang, Y.; Bharathi, P.; Moore, J. S. *J. Am. Chem. Soc*. **1998**, *120*, 2172 and references therein. (b) Newkome, G. R.; He, E.; Godínez, L. A. *Macromolecules* **1998**, *31*, 4382.
(15) (a) Stewart, G. M.; Fox, M. A. *J. Am. Chem. Soc*. **1996**, *118*, 4354. (b) Adronov, A.; Gilat, S. L.; Fréchet, J. M. J.; Ohta, K.; Neuwahl, F. V. R.; Fleming, G. R. *J. Am. Chem. Soc*. **2000**, *122*, 1175. (c) Gilat, S. L.; Adronov, A.; Fréchet, J. M. J. *Angew. Chem., Int. Ed*. **1999**, *38*, 1422. (d) Adronov, A.; Malenfant, P. R. L.; Fréchet, J. M. *J. Chem. Mater*. **2000**, *12*, 1463. (e) Heinen, S.; Walder, L. *Angew. Chem*., *Int. Ed*. **2000**, *39*, 806. (f) Chrisstoffels, L. A. J.; Adronov, A.; Fréchet, J. M. J. *Angew. Chem*., *Int. Ed*. **2000**, *39*, 2163. (g) Kawa, M.; Fréchet, J. M. J. *Thin Solid Films* **1998**, *331*, 259. (h) Gilat, S. L.; Adronov, A.; Fréchet, J. M. J. *J. Org. Chem*. **1999**, *64*, 7474. (i) Sato, T.; Jiang, D.-L.; Aida, T. *J. Am. Chem. Soc*. **1999**, *121*, 10658. (j) Schenning, A. P. H. J.; Peeters, E.; Meijer, E. W. *J. Am. Chem. Soc*. **2000**, *122*, 4489. (k) Pollak, K. W.; Leon, J. W.; Fréchet, J. M. J.; Maskus, M.; Abruña, H. D. *Chem. Mater*. **1998**, *10*, 30 (l) Adronov, A.; Fréchet, J. M. J. *Chem. Commun*. **2000**, 1701. (m) Hecht, S.; Fréchet, J. M. J. *Angew. Chem*., *Int. Ed*. **2001**, *40*, 74. (n) Hecht, S.; Vladimirov, N.; Fréchet, J. M. J. *J. Am. Chem. Soc*. **2001**, *123*, 18.
(16) (a) Archut, A.; Azzellini, G. C.; Balzani, V.; Cola, L. D.; Vögtle, F. *J. Am. Chem. Soc*. **1998**, *120*, 12187 and references therein. (b) Archut, A.; Vögtle, F.; Cola, L. D.; Azzellini, G. C.; Balzani, V.; Ramanujam, P. S.; Berg, R. H. *Chem. Eur. J*. **1998**, *4*, 699. (c) Schenning, A. P. H. J.; Elissen-Román, C.; Weener, J.-W.; Baars, M. W. P. L.; van der Gaast, S. J.; Meijer, E. W. *J. Am. Chem. Soc*. **1998**, *120*, 8199. (c) Tsuda, K.; Dol, G. C.; Gensch, T.; Hofkens, J.; Latterini, L.; Weener, J. W.; Meijer, E. W.; Schryver, F. C. *J. Am. Chem. Soc*. **2000**, *122*, 3445. (e) Mekelburger, H. B.; Rissanen, K.; Vögtle, F. *Chem. Ber*. **1993**, *126*, 1161. (f) Li, S.; McGrath, D. V. *J. Am. Chem. Soc*. **2000**, *122*, 6795. (g) Archut, A.; Vögtle, F. *Chem. Soc. Rev*. **1998**, *27*, 233. (f) Moors, R.; Vögtle, F. *Adv. Dendritic Macromol*. **1995**, *2*, 41.
(17) (a) Junge, D. M.; McGrath, D. V. *Chem. Commun*. **1997**, 857. (b) Jiang, D.-L.; Aida, T. *Nature* **1997**, *388*, 454. (c) Aida, T.; Jiang, D.-L.; Yashima, E.; Okamoto, Y. *Thin Solid Films* **1998**, *331*, 254. (d) Junge, D. M.; McGrath, D. V. *J. Am. Chem. Soc*. **1999**, *121*, 4912. (e) Wakabayashi, E.; Tokeshi, M.; Jiang, D.-L.; Aida, T. *J. Lumin*. **1999**, *83*−*84*, 313. (f) Grebel-Koehler, D.; Liu, D.; Feyter, S. D.; Enkelmann, V.; Weil, T.; Engels, C.; Samyn, C.; Müllen, K.; Schryver, F. C. D. *Macromolecules* **2003**, *36*, 578.
(18) (a) Yokoyama, S.; Nakahama, T.; Otomo, A.; Mashiko, S. *Chem. Lett*. **1997**, 1137; *J. Am. Chem. Soc*. **2000**, *122*, 3174. (b) Sebastián, R.-M.; Blais, J.-M.; Caminade, A.-M.; Majoral, J.-P. *Chem. Eur. J*. **2002**, *8*, 2172. (c) Liao, L.; Junge, D. M.; McGrath, D. V. *Macromolecules* **2002**, *35*, 319.
(19) Wang, S.; Advincula, G. R. *Org. Lett*. **2001**, *3*, 3831.



G-1-4 **G-2-4**



G-3-4

FIGURE 1. Three generations of azobenzene dendrimers **G-1−4**, **G-2−4**, and **G-3−4**.

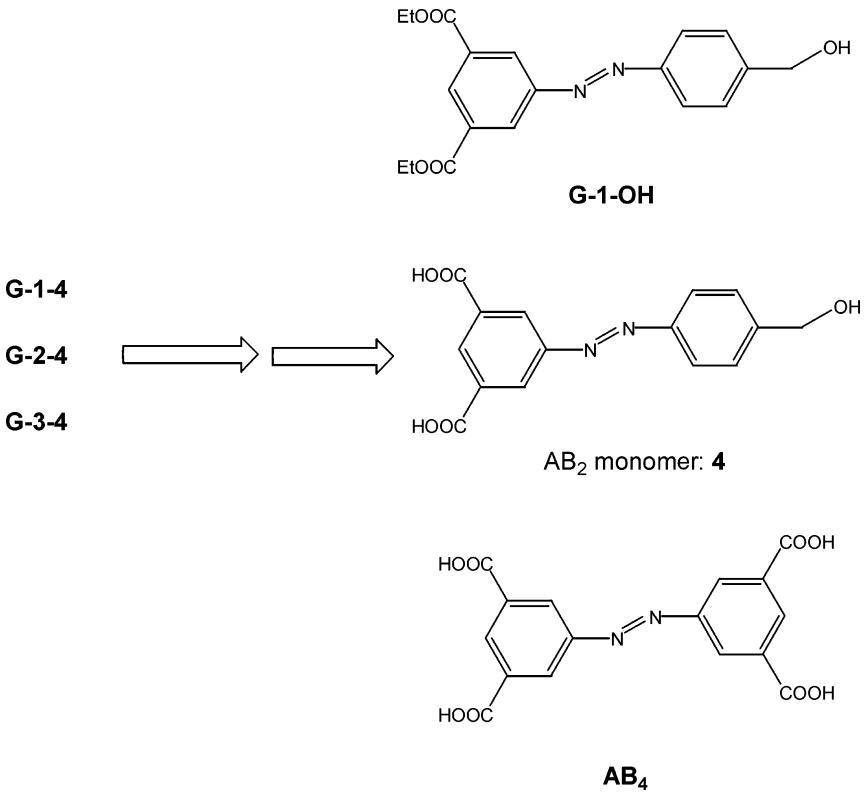
bromide **5** in the presence of potassium carbonate and 18-crown-6 in dried acetone in 74% yield as an orange solid (Scheme 3).

Unfortunately, there is a problem with the bromination of **G-2-OH** for next generation growth. The **G-2-OH** could not be brominated by CBr_4/PPh_3, even with excess reagents and an elevated temperature. In addition, an array of brominating agents[21] (PBr_3;[21a] PPh_3/NBS;[21b] NBS/Me_2S;[21c] Me_3SiBr;[21d] and Me_3SiBr/2.6-di-*tert*-butylpyridine) gave uniformly unsatisfactory results. It is unclear why these reactions did not work. Thus, we turned to design and synthesis of the AB_2 monomer **10**, which contains two activated carboxylic groups for generation growth and one hydroxymethyl group protected by *tert*-butyldiphenylsilane chloride (TBDPSCl) for subsequent generation growth as outlined in Scheme 4.

(20) Hutting, W. H.; Jewell, R. A.; Rapoport, H. *J. Org. Chem*. **1970**, *35*, 505.

(21) (a) Taschner, M. J. In *Encyclopedia of Reagents For Organic Synthesis*; Paquette, L. A., Ed.; John Wiley & Sons, Ltd.: New York, 1995; Vol. 8, pp 5364−5366. (b) Bose, A. K.; Lal, B. *Tetrahedron Lett*. **1972**, 3937. (c) Firouzabadi, H.; Ghaderi, E. *Tetrahedron Lett*. **1978**, 839. (d) Jung, M. E.; Hatfield, G. L. *Tetrahedron Lett*. **1978**, 4483.

SCHEME 1



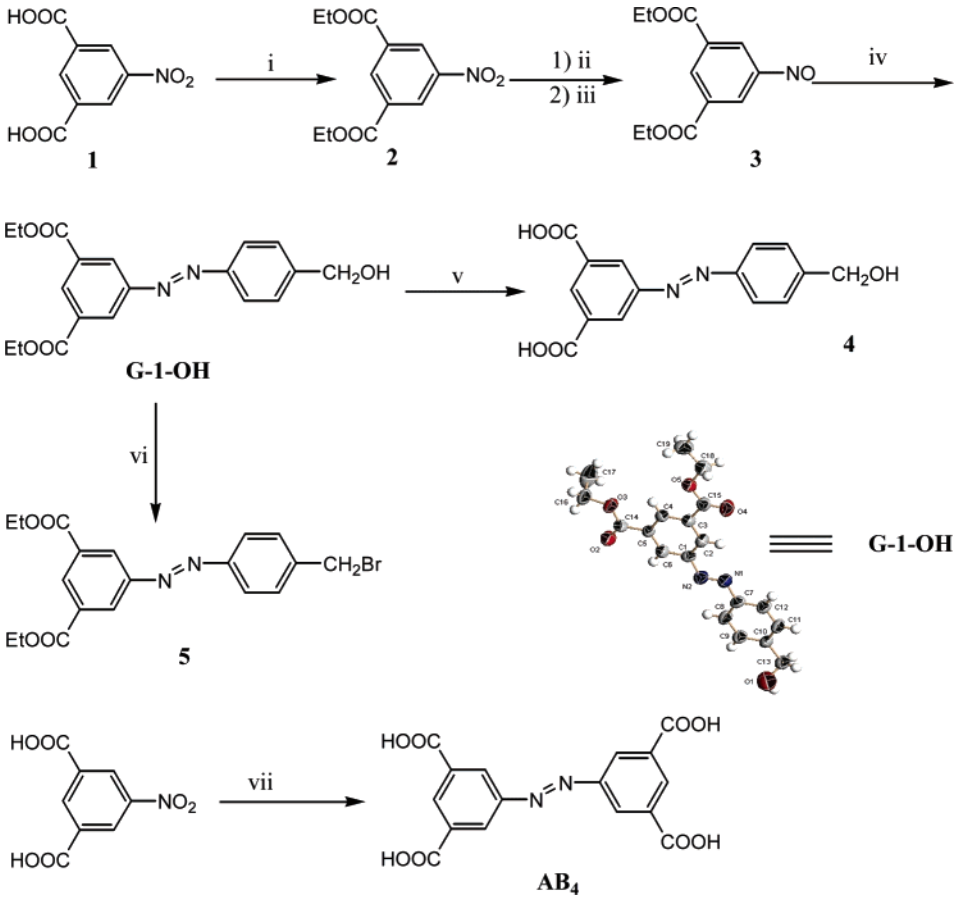
4-Nitrobenzyl alcohol (**7)** was treated with TBDPSCl in the presence of imidazole in DMF to yield the protected compound **8** with in 96% yield. Reduction of **8** using Zn dust at 33−35 °C in 2-methyloxyethanol**,** as in the preparation of nitroso compound **3**, followed by oxidation using $FeCl_3$ yielded nitroso compound **9** in 82% yield as an off-white solid. Condensation of the nitroso compound **9** with 5-aminoisophthalic acid using acetic acid as a solvent produced the new crude AB_2 monomer **10** as an orange solid, which was recrystallized from diethyl ether to afford **10** in 90% yield.

Synthesis of G-3-OH and G-4-OH. With AB_2 monomer **10**, the third dendron (**G-3-OH**) based on **G-2-OH** was smoothly obtained following the convergent synthetic approach developed by Fréchet.[22] This involved an iterative and alternating sequence of DCC (dicyclohexylcarboxycardodiimide)/DPTS 4-(dimethylamino)pyridinium 4-toluenesulfonate-mediated esterifications[23] and deprotection by HF−pyridine as shown in Scheme 5. These reactions were selected because they are known to be extremely mild and fast and can afford high conversions. Thus, the coupling of the **G-2-OH** alcohol with the AB_2 monomer **10** in the presence of DCC and catalytic amount of DPTS followed by deprotection with HF−pyridine proceeded cleanly and efficiently. These reactions gave the **G-3-OH** dendron in 86% yield after purification. For deprotection of the alcohol group, the initial attempt to desilylate using TBAF (tetrabutylammonium fluoride) to remove the protected TBDPS group was unsuccessful. Under this reaction condition, complicated mixtures were obtained because of cleavage of ester linkages. We also tried other numerous reaction conditions containing more or less water, counterions other than tetrabutylammonium, and adding water buffered to different pHs to effect a clean reaction. All reactions containing the fluoride ion gave complicated mixtures because the F^- anion is a Lewis base that is strong enough to cleave the benzyl ester bonds. We also tried to use the THF−HCl (aq) system to desilylate. It was found that the protection group could not be completely removed at room temperature and the product decomposes at higher temperatures. Finally, after many failures, we found that the mild HF−pyridine reagent efficiently and cleanly removes the protected group. The coupling and deprotected steps were then repeated to convert the **G-3-OH** to **G-4-OH** in overall 65% yield. However, extending the synthesis to the pure **G-5-OH** dendron does not seem to be possible.

Synthesis of Perfect Dendrimers. Perfect dendrimers based on poly(benzyl ester) monodendrons were prepared by coupling different generation monodendrons with the four-branched azobenzene core $\mathbf{AB_4}$ using the same coupling conditions DCC/DPTS at room temperature. Therefore, coupling of **G-1-OH**, **G-2-OH**, and **G-3-OH** with the four-branched core $\mathbf{AB_4}$ in the presence of DCC/DPTS afforded the all azobenzene dendrimers **G-1**−**4, G-2**−**4**, and **G-3**−**4** in 82%, 54%, and 38% yields, respectively (Scheme 6a−c). It is worth pointing out that the synthesis and purification of dendrons and dendrimers becomes progressively more challenging from one generation to the next. For example, **G-3**−**4** was only synthesized in a small quantity (less than 500 mg) and it took 6 days. A yield of 82% was obtained for **G-1**−**4**, with a decrease to 54% for **G-2**−**4**, and a decrease to 38% for **G-3**−**4**. An apparent limitation of the convergent

(22) Hawker, C. J.; Fréchet, J. M J. *J. Am. Chem. Soc*. **1990**, *112*, 7638.
(23) (a) Moore, J. S.; Stupp, S. I. *Macromolecules* **1990**, *23*, 65. (b) Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc*. **1992**, *114*, 8405.

SCHEME 2[a]



[a] Reagents and conditions: (i) H_2SO_4/EtOH, reflux; (ii) Zn/33−35 °C/N_2, 2-methoxyethanol; (iii) $FeCl_3$/0−5 °C/N_2, EtOH/H_2O; (iv) 4-aminobenzyl alcohol/acetic acid/N_2/rt, CH_2Cl_2; (v) KOH/EtOH/H_2, reflux; (vi) CBr_4/PPh_3/THF/N_2, 0 °C to rt; (vii) Zn/NaOH/EtOH/H_2O, reflux.

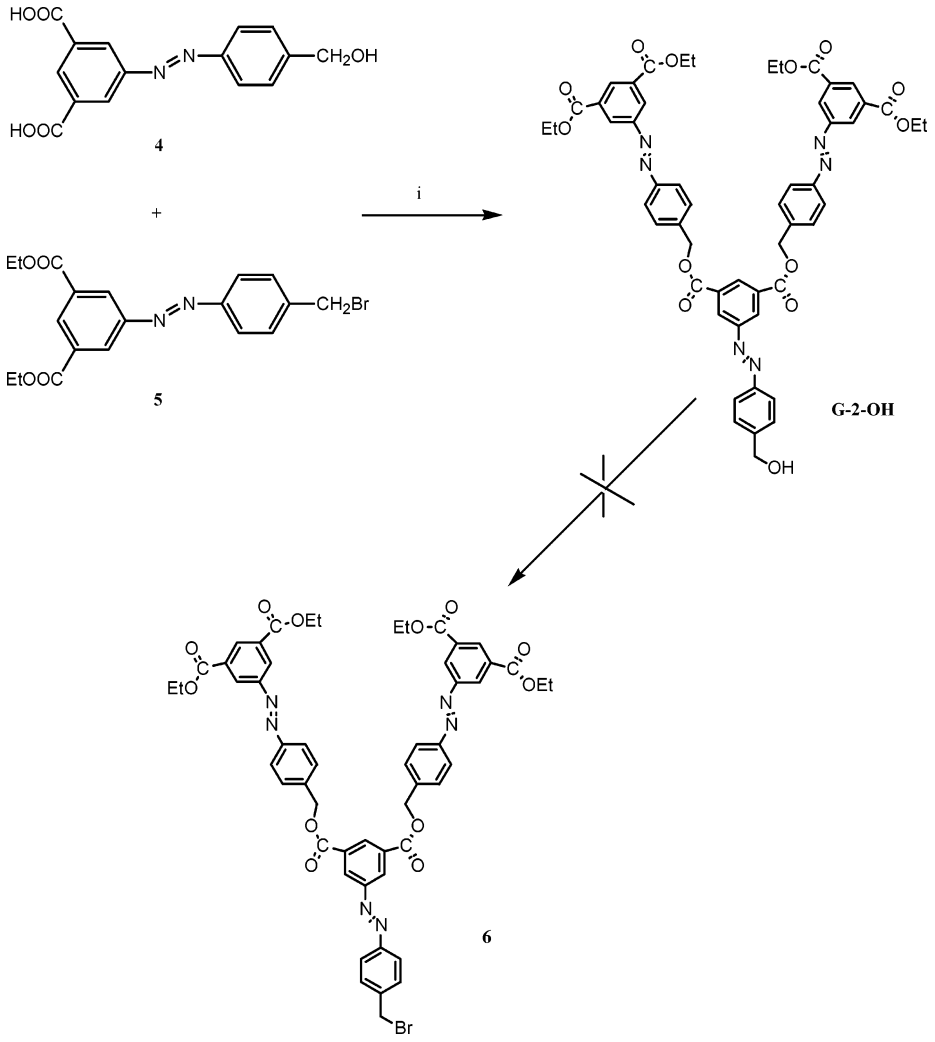
approach is its susceptibility to steric inhibition as the macromolecules become larger, the functional group at the focal point becomes "masked" by the growing macromolecule and its reactivity is lessened. With the tetrafunctionalized core **AB$_4$** linkage, which leads to greater steric congestion, this limit appears to be reached before **G-4-OH**, and no **G-4**−**4** dendrimer could be produced from **G-4-OH** and **AB$_4$** despite repeated attempts under a variety of conditions.

Characterization. The techniques used for the characterization of dendrons **G-2-OH**, **G-3-OH**, and **G-4-OH** and dendrimers **G-1**−**4**, **G-2**−**4**, and **G-3**−**4** were ^{1}H NMR, ^{13}C NMR, LC−MS, and MALDI-TOF mass spectra. In the ^{1}H NMR spectra of the dendrons and dendrimers the resonances for the isophthalate aromatic protons occur at 8.90−8.60 ppm and the resonances for the protons of exterior benzylic groups occur at ∼7.93 and ∼7.60 ppm as two doublets. The chemical shift of exterior benzyl methyl groups stayed consistently at ∼5.50 ppm, while that of benzyl methyl group at the focal point was at ∼4.80 ppm as single peaks. The chemical shifts of $-OCH_2-$ and $-CH_3$ of ethyl groups at the periphery were around 4.45 and 1.46 ppm, respectively. However, the single peak at ∼4.8 ppm for the protons of the benzyl methyl group at the focal point in the dendrons disappeared in the spectra of the dendrimers, which is fully consistent with the molecular structures of the dendrimers. The relative integration ratios of benzyl methyl groups at the exterior (∼5.5 ppm) vs benzyl methyl at the focal point (∼4.8 ppm) were a useful diagnostic tool for characterizing the generation progression of the dendrons. The ratios increase as the generation of the dendrons grow, such as with 4:2 for **G-1-OH**, 12:2 for **G-3-OH**, and 28:2 for **G-4-OH** as shown in Figure 2. The structures of the dendrons and dendrimers were also confirmed by MALDI-TOF-MS. Figures 3, 4 and 5 show representative MALDI-TOF spectra of **G-1**−**4**, **G-3-OH**, and **G-3**−**4**.

All the dendrons and dendrimers were obtained as orange red solids or glasses that were soluble in aprotic solvents such as CH_2Cl_2, ethyl acetate, and THF but were insoluble in methanol and acetone except for **G-1-OH**.

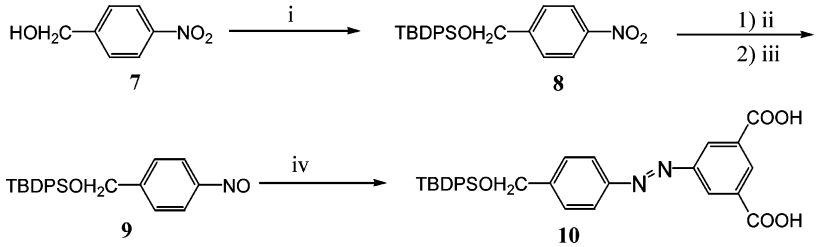
Absorption Spectra. The absorption spectra of the dendrons and dendrimers were carried out in dichloromethane at 298 K. The wavelengths of the maxima of the absorption bands and the values of the molar absorption coefficients were collected in Table 1. All absorption spectra of the dendrons and dendrimers show the same absorption bands with a high-intensity band at about 335 nm assigned to $\pi \rightarrow \pi^*$ transitions and a low intensity band at 440 nm assigned to the n $\rightarrow \pi^*$ transition, indicating the independence of the generation number. However, the molar absorption coefficient increases linearly with an increasing number of azobenzene groups

SCHEME 3[a]



[a] Reagents and conditions: (i) K_2CO_3/18-crown-6/acetone, reflux.

SCHEME 4[a]

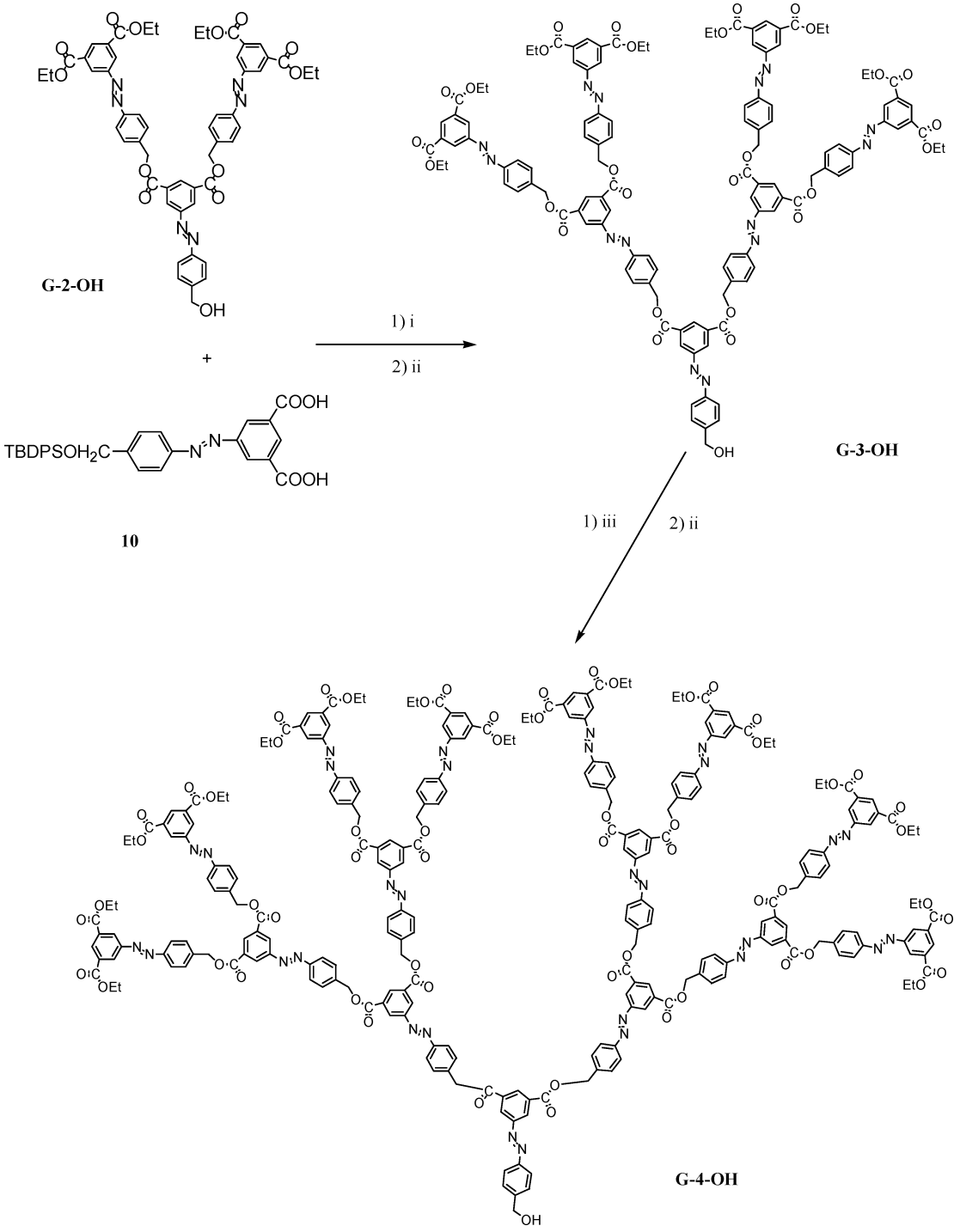


[a] Reagents and conditions: (i) TBDPSCl/imidazole/DMF, 0 °C to rt; (ii)) Zn/33−35 °C/N_2, 2-methoxyethanol; (iii) $FeCl_3$/0−5 °C/N_2, EtOH/H_2O; (iv) 5-aminoisophthalic acid/acetic acid/N_2/rt, CH_2Cl_2.

present in the dendrons and dendrimers. The number of azobenzene groups present is 1, 3, 7, and 15 for dendrons **G-1-OH**, **G-2-OH**, **G-3-OH**, and **G-4-OH** and 5, 13, and 29 for dendrimers **G-1**−**4**, **G-2**−**4**, and **G-3**−**4**, respectively. Accordingly, the molar absorption coefficients are 15800, 42200, 105600, and 196200 (M^{-1} cm^{-1}) for dendrons and 72000, 179400, and 334800 (M^{-1} cm^{-1}) for dendrimers.

Photoisomerization. All the azobenzene-type dendrons and dendrimers in this work are found to undergo the *trans* → *cis* and *cis* → *trans* photoisomerizations as well as the *cis* → *trans* thermal isomerization. Figure 6 shows the spectroscopic changes observed for the isomerization of **G-3-OH**. Qualitatively, similar results have been obtained for all the dendrons and dendrimers examined. Irradiation of a dendron or dendrimer in CH_2Cl_2 solution at 310 nm results in photoisomerization from the *trans*- to the *cis*-isomer, as indicated by a decrease of the absorption in the region of $\pi \rightarrow \pi^*$ electron transition at $\lambda_{max} = \sim 335$ nm and an increase of the

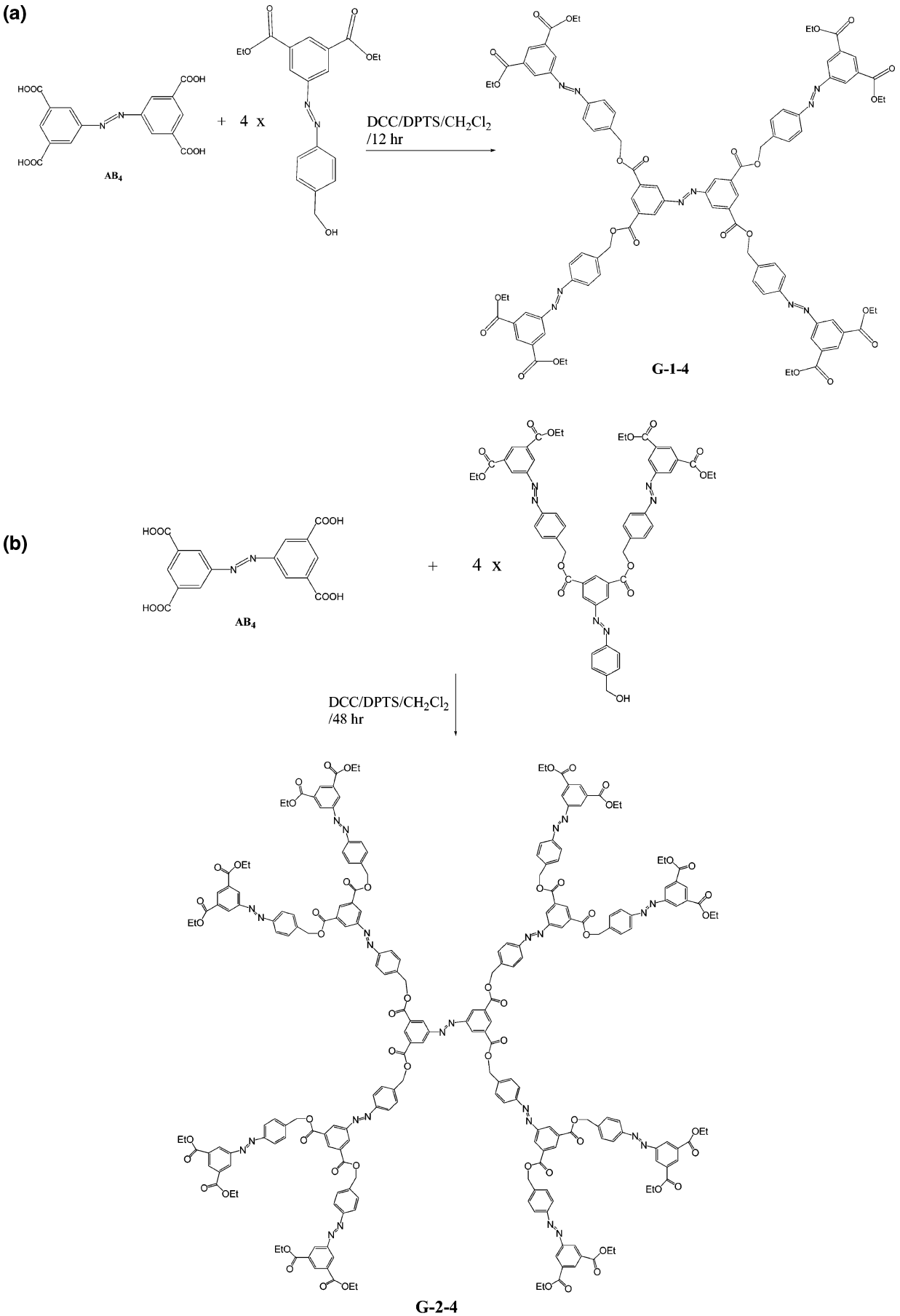
SCHEME 5[a]



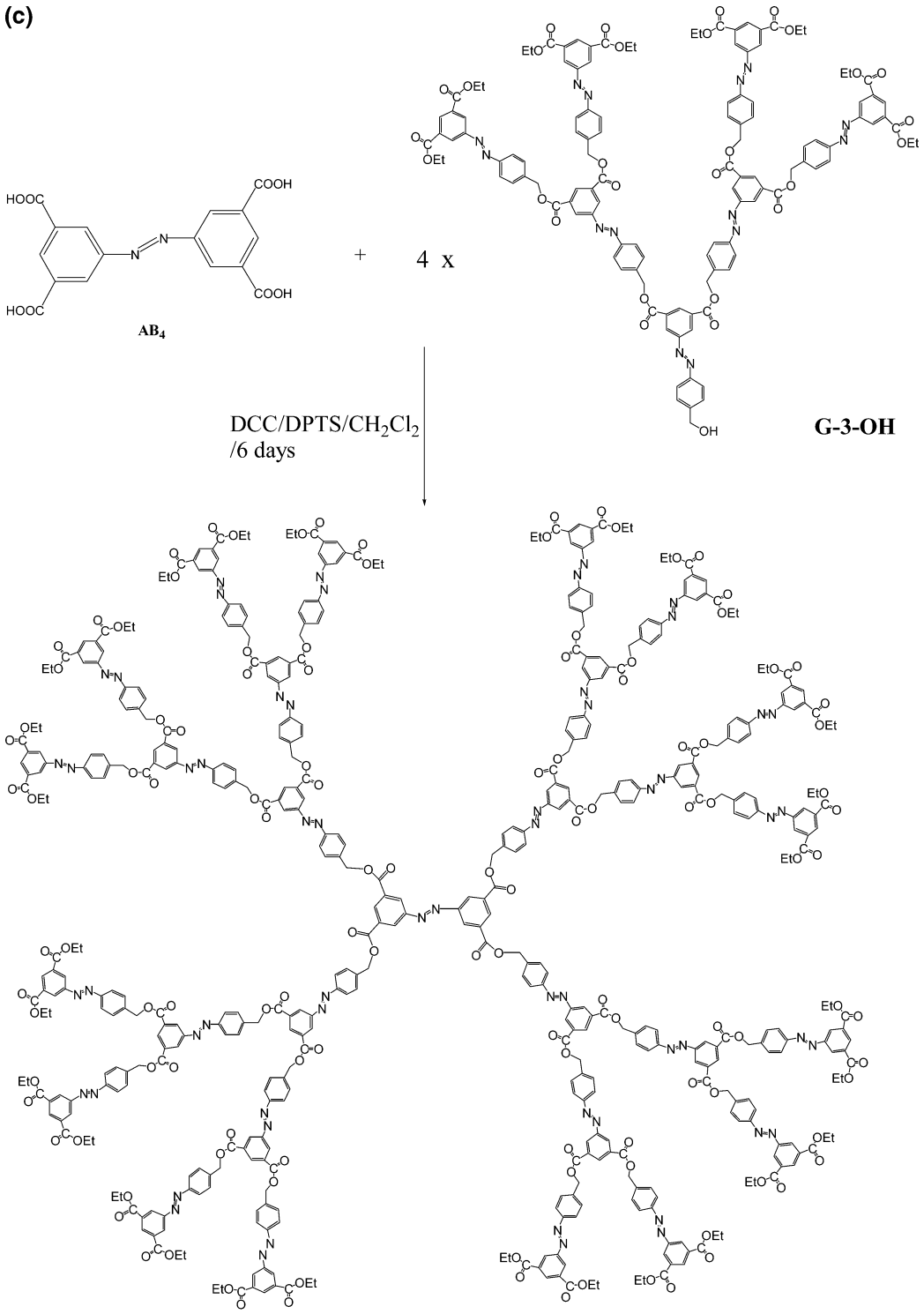
[a] Reagents and conditions: (i) DCC/DPTS/CH_2Cl_2, rt; (ii) HF−pyridine/CH_2Cl_2, rt; (iii) 10/DCC/DPTS/CH_2Cl_2, rt.

absorption in the region of n → π^* transition of azobenzene chromophores at $\lambda_{max} = \sim 440$ nm, with maintenance of a clear isosbestic point (Figure 6). After a suitable irradiation period, a photostationary state (PSS) was reached. The *cis*-isomer content at PSS was calculated by $(A_0 - A_{PSS\ (330\ nm)})/A_0$, where A_0 and $A_{PSS(330\ nm)}$ are the absorbance at 335 nm of the unirradiated solution and of the solution at PSS under 310 nm irradiation. The calculation is based on the assumption that the *cis*-isomer has negligible absorbance at 335 nm. The *cis*-isomer content at PSS under 310 nm irradiation for all dendrons and dendrimers studied is listed in Table 1. From Table 1, it can be seen that the *cis*-isomer content from **G-1-OH** to **G-4-OH** decreases to 61% from 87%, while *cis*-isomer content from **G-1**−**4** to **G-3**−**4** decreases to 36% from 77%. This indicates that the *cis*-isomer content decreases with increasing dendron and dendrimer generation, the effect of the latter being more profound than

SCHEME 6


(a)
HOOC
COOH
HOOC
COOH
AB4
+ 4 x
EtO
OEt
OH
DCC/DPTS/CH2Cl2
/12 hr
G-1-4
(b)
AB4
+ 4 x
DCC/DPTS/CH2Cl2
/48 hr
G-2-4

SCHEME 6 (Continued)



the former, as observed in the literature.[17f,18b] In contrast, the incorporation of azobenzene cores within dendrimers or polymers has no influence on their *trans*−*cis* thermal isomerization.[24] This may be explained as the effect of steric hindrance and lower flexibility of the dendrons and dendrimers studied in this work.

The reverse *cis* → *trans* isomerization of the dendrons and dendrimers from PSS obtained upon 310 nm irradiation can be induced either thermally in the dark or by visible irradiation at 449 nm. Visible irradiation leads to a photostationary state that is very rich in the *trans*-isomer, while the thermal isomerization leads to only pure *trans*-isomer. It is worth noting that the reaction rate of thermal isomerization is much slower under visible irradiation; in fact, it took about 2 weeks to recover

(24) (a) Junge, D. M.; McGrath, D. V. *J. Am. Chem. Soc*. **1999**, *121*, 4912. (b) Tabak, D.; Morawetz, H. *Macromolecules* **1970**, *3*, 403. (c) Chen, D. T.-L.; Morawetz, H. *Macromolecules* **1976**, *9*, 463.

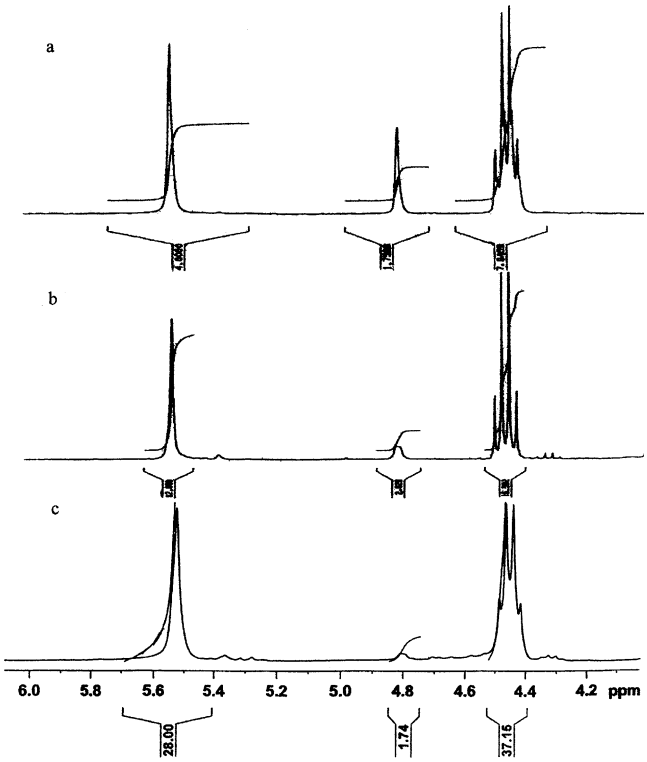


FIGURE 2. Comparison of ^{1}H NMR spectra of (a) **G-2-OH**, (b) **G-3-OH**, and (c) **G-4-OH**.

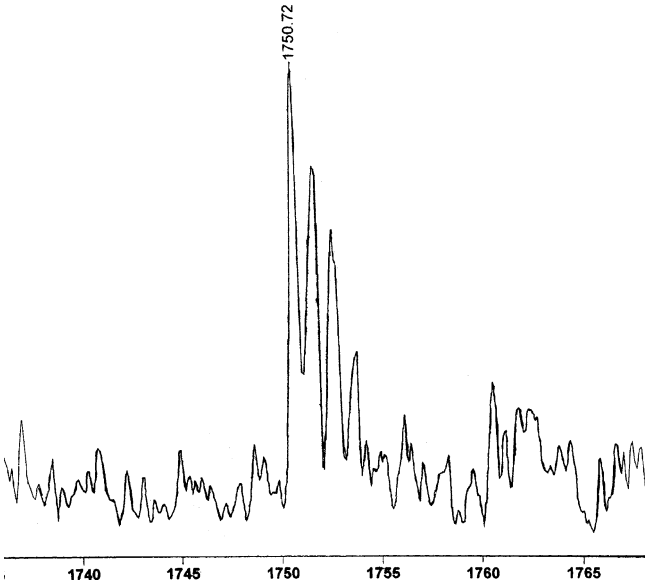


FIGURE 3. MALDI-TOF MS spectrum of **G-1−4**.

all of the *trans* dendrimer **G-3−4** when a solution of **G-3−4** in CH_2Cl_2 that had reached the photostationary state under excitation with 310 nm was placed in the dark.

Conclusions

In conclusion, four generations of dendrons and three generations of dendrimers with up to 29 photoresponsive azobenzene groups throughout their structures have been designed and successfully synthesized by the convergent approach. The photochemical isomerization experiments reveal that the synthetic azobenzene dendrons and

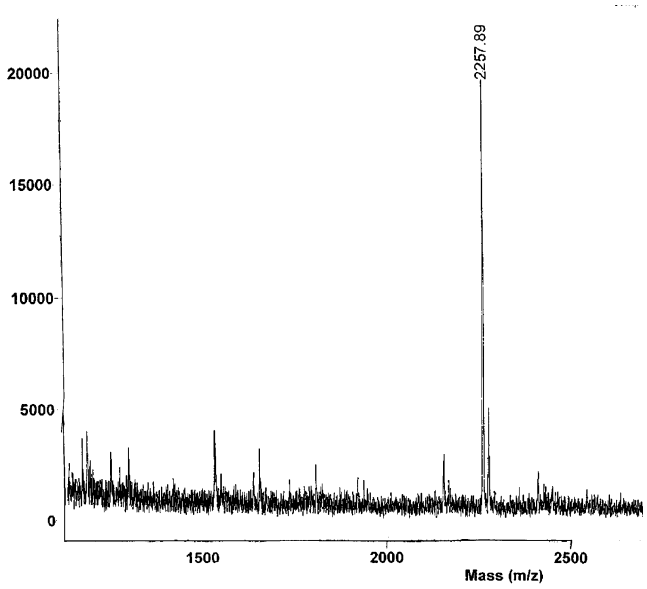


FIGURE 4. MALDI-TOF MS spectrum of **G-3-OH**.

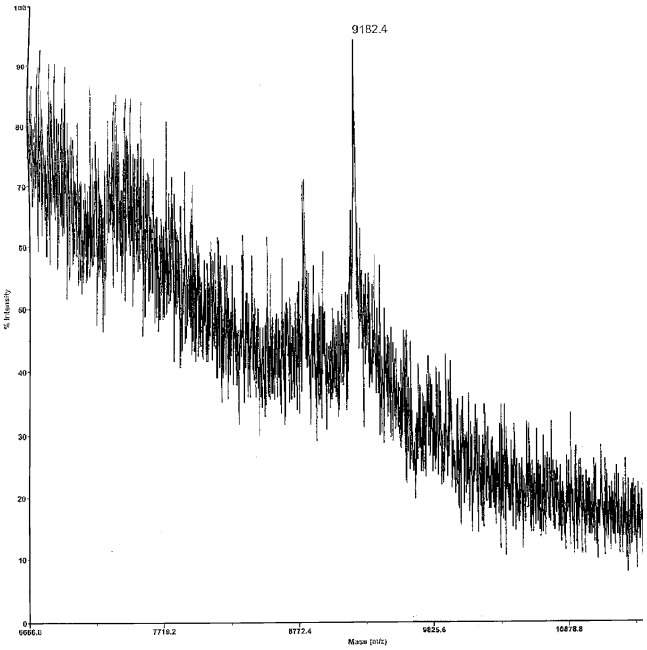


FIGURE 5. MALDI-TOF MS spectrum of **G-3−4**.

TABLE 1. Absorption Data and *Cis* Isomer Content at PPS[a] under 310 nm Irradiation

	absorption λ_{max}/nm (ϵ, $M^{-1}cm^{-1}$)		*cis*-isomer content[b] (%)
	$\pi \rightarrow \pi^*$	$n \rightarrow \pi^*$	
G-1-OH	334 (15800)	too flat	87
G-2-OH	337 (42200)	440 (1200)	81
G-3-OH	335 (105600)	441 (2100)	78
G-4-OH	339 (196200)	442 (4800)	61
G-1−4	336 (72200)	440 (1900)	77
G-2−4	338 (179400)	441 (4300)	55
G-3−4	340 (334800)	443 (8900)	36

[a] Photostationary state. [b] *Cis* isomer content at PPS under 310 nm irradiation.

dendrimers exhibit effective and reversible photoresponsive properties upon UV and visible irradiation. The dendrons and dendrimers are only constructed from

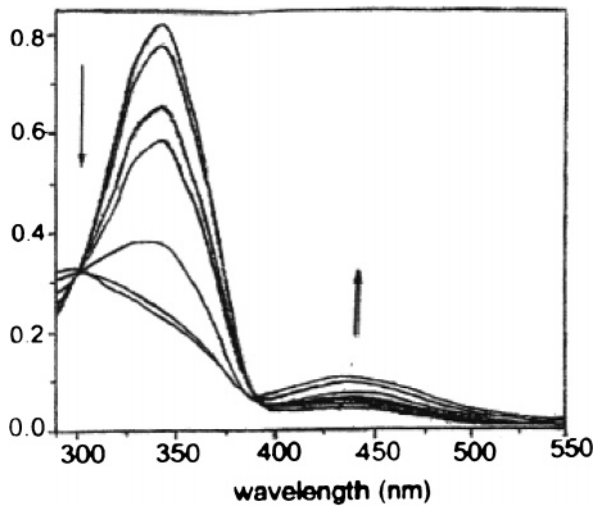


FIGURE 6. Changes in the absorption spectrum of **G-3-OH** upon irradiation at 310 nm

azobenzene groups using degradable benzyl ester bonds as linkages. Their photoresponsive and interior encapsulation (dendritic box) behaviors may allow them to become promising candidates for drug delivery systems that can be manipulated by a light stimulus.

Experimental Selection

General Methods. ^{1}H and ^{13}C NMR spectra were collected on a Bruker ARX 300 spectrometer with $CDCl_3$ or acetone-d_6 as the solvent and TMS as the internal standard. EI-MS spectra were recorded on a Finnigan MATMS 70 with EI ionization, while LC−MS spectra were recorded on an Agilent 1100 series LC/MSD. MALDI-TOF data were collected on a PerSpective Biosystems Voyager-DE instrument using a 9-nitroanthracene as matrix with K^+ as the modifier in THF for **G-3-OTBDPS**, **G-3-OH**, **G-4-OTPDBS**, **G-4-OH**, **G-1**−**4**, and **G-2**−**4** and α-cyano-4-hydroxylcinnamic acid as a matrix with Ag^+ as the modifier in THF for **G-2**−**4**. All starting materials were from commerical suppliers and were used as received unless otherwise stated. THF was distilled from sodium/benzophenone, CH_2Cl_2 was distilled from calcium hydrogen, and the acetone was distilled.

Diethyl 5-Nitroso-isophthalate (3).[20] Diethyl 5-nitroisophthalate (21.4 g, 80 mmol) was dissolved in 400 mL of 2-methoxyethanol. A solution of NH_4Cl (6.8 g, 112 mmol) in 50 mL of water was then added, and the mixed solution was warmed to 30 °C in N_2 atmosphere. With vigorous stirring, 14.4 g (220 mmol) of finely powered zinc dust was added in small portions over 30 min. The temperature was held at 33−35 °C by cooling it in an ice bath. After the addition was completed, the stirring was continued until the reaction temperature decreased. The reaction mixture was suction-filtered and the filtered cake was washed with 2-methoxyethanol (2 × 20 mL). The combined filtrate and washing was then added dropwise, with rapid stirring over a period of 90 min, to a solution of 25.2 g (456 mmol) of ferric chloride dissolved in 300 mL of water and 120 mL of ethanol maintained at −5 °C in an ice−methanol bath. After an additional 2 h of stirring, the reaction mixture was poured into 800 mL of water. The precipitate was obtained and collected by filtration. It was purified by chromatography on silica gel using hexane/ethyl acetate (5/1, v/v) to give 9.6 g of the desired product (**3**), as a light yellow solid, in 47% of yield. EI-MS: *m/z* [M + H] 252.4 (calcd for $C_{12}H_{13}NO_5$, 251.6). ^{1}H NMR (300 MHz, $CDCl_3$): 9.02 (s, 1H), 8.70 (m, 2H), 4.27 (q, 4H, J = 7.0 Hz), 1.46 (t, 6H, J = 8.7 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): 165.1, 163.7,148.4, 134.8, 132.8, 126.1, 62.3, 14.3. Anal. Calcd for $C_{12}H_{13}N_1O_5$: C, 57.37; H, 5.22; N, 5.58 Found: C, 53.45; H, 5.12; N, 5.71.

4-(Diethyl 5′-azo-isophthalate)benzyl Alcohol (G-1-OH). A mixture of diethyl 5-nitrosoisophthalate (**3**) (508 mg, 2.0 mmol), 4-aminobenzyl alcohol (249 mg, 2.0 mmol), and two drops of acetic acid in 15 mL of dichloromethane was stirred at room temperature under a nitrogen atmosphere. After being stirred for 12 h, the resultant dark red solution was filtered to remove insoluble solids. The solvent was removed by rotary evaporation to afford the crude product, which was purified by chromatography on silica gel using ethyl acetate/*n*-hexane (1:1, v/v) as the eluent to give 521 mg of 4-(diethyl 5′-azoisophthalate)benzyl alcohol (**G-1-OH**) as orange crystals in 86% of yield. Single crystals suitable for the X-ray diffraction study were obtained by slow evaporation of the mixture of **G-1-OH** in dichloromethane/*n*-hexane. EI-MS: *m/z* [M + H] 357.2 (calcd for $C_{19}H_{20}N_2O_5$, 356.8). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.00 (s, 1H), 8.79 (s, 2H), 7.97 (d, 2H, J = 8.1 Hz), 7.55 (d, 2H, J = 8.0 Hz), 4.82 (s, H), 4.48 (q, 4H, J = 7.0 Hz), 1.46 (t, 6H, J = 7.0 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): δ 165.8, 153.1,152.1, 145.3, 132.6, 132.4, 128.0, 127.8, 123.8, 65.2, 62.1, 14.8. Anal. Calcd for $C_{19}H_{20}N_2O_5$: C, 64.04; H, 5.66; N, 7.86. Found: C, 64.31; H, 5.72; N, 7.71.

4-(5′-Azoisophthalate acid)benzyl Alcohol (4). A solution of 4-(diethyl 5′-azoisophthalate)benzyl alcohol (**G-1-OH**) (3.0 g, 8.4 mmol) in ethanol (20 mL) was mixed with a solution of KOH (1.9 g, 33.6 mmol) in water (20 mL). After the mixture was refluxed overnight, a yellow solid formed. Water was added to the reaction mixture until all of the yellow solid was dissolved. The resultant solution was filtered and acidified to pH = 3−4 with 1 M HCl (aq) to give a yellow solid, which was recrystallized from acetone, yielding 2.1 g of pure 4-(5′-azoisophthalate acid)benzyl alcohol (**4**) in 84% yield as needle-like orange crystals. EI-MS: *m/z* [M − H] 299.3 (calcd for $C_{15}H_{12}N_2O_5$, 300.4). ^{1}H NMR (300 MHz, acetone-d_6): δ 13.60 (br, s, 2H), 8.60 (s, 1H), 8.58 (s, 2H), 7.97(d, 2H, J = 8.2 Hz), 7.57 (d, 2H, J = 8.2 Hz), 5.43 (br, s, 1H), 4.64(s, 2H), 4.50 (q, 4H, J = 7.0 Hz), 1.46 (t, 6H, J = 7.0 Hz). ^{13}C NMR (300 MHz, acetone-d_6): δ 155.2, 155.1, 145.3, 132.6, 132.4, 128.0, 127.8, 123.8, 65.2. Anal. Calcd for $C_{15}H_{12}N_2O_5$: C, 60.00; H, 4.03; N, 9.33 Found: C, 59.78; H, 4.16; N, 9.38.

G-1-Br (**5**)**.** To a solution of 4-(diethyl 5′-azoisophthalate)-benzyl alcohol (**G-1-OH**) (2.00 g, 5.63 mmol) in 50 mL of dry THF was added CBr_4 (3.00 g, 9.1 mmol) under Ar, followed by PPh_3 (2.37 g, 9.1 mmol) in four equal-sized portions spaced over 20 min with stirring. After the mixture was stirred for 10 min, a white precipitate formed and the reaction mixture turned dark red. The reaction was stirred for another 30 min at room temperature and was quenched with 50 mL of water, followed by addition of dichloromethane. (100 mL). The organic layer was washed twice with equal volumes of water and dried over magnesium sulfate. The solvent was removed on a rotary evaporator to yield the organic solid. The crude product was recrystallized from CH_2Cl_2 (20 mL)/*n*-hexane (80 mL) to afford 2.1 g of the desired product, as orange crystals, in 88% yield. EI-MS: *m/z* [M + H] 419.1 (calcd for $C_{19}H_{19}BrN_2O_4$, 418.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.80 (1H, s, Ar−H), 8.79 (s, 2H), 7.95 (d, 2H, J = 8.1 Hz), 7.56 (d, 2H, J = 8.0 Hz), 4.67 (s, 2H), 4.48 (q, 4H, J = 7.0, Hz), 1.46 (t, 6H, J = 7.1 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): δ 153.2, 152.1, 145.3, 132.6, 132.4, 128.0, 127.8, 123.8, 65.2, 59.1, 14.8. Anal. Calcd for $C_{19}H_{19}BrN_2O_4$: C, 54.43; H, 4.57; N, 6.68. Found: C, 54.31; H, 4.72; N, 6.54.

3,5-Dicarboxyl-(3′,5′-dicarboxylazophenyl)benzene (AB_4). A mixture of 5-nitroisophthalic acid (2.1 g, 10 mmol), Zn (1.3 g, 20 mmol), and NaOH (0.8 g, 20 mmol) in a mixture of ethanol (50 mL) and water (20 mL) was heated under reflux. After the mixture was refluxed for 12 h, a yellow solid was obtained and collected by filtration. The resultant solid was dissolved in 50 mL of NaOH (aq, 1 M) and filtered to remove any insoluble solids. The filtrate was acidified to pH = 3 with 3 M HCl (aq) to afford 2.8 g of 3,5-dicarboxyl (3′, 5′-dicarboxylazophenyl)benzene (**AB_4**) as an orange precipitate (yield: 78%). LC−MS: [M − H] 357.1 (calcd for $C_{16}H_{10}N_2O_8$, 358.2). ^{1}H NMR (300 MHz, acetone-d_6): δ 8.51 (s, 2H), 8.50 (s, 4H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 192.1, 191.8 191.6, 151.8, 151.0,

138.9, 119.6, 119.2, 119.1, 118.9, 114.2, 113.8. Anal. Calcd for $C_{16}H_{10}N_2O_8$: C, 53.64; H, 2.81; N, 7.82. Found: C53.26; H, 2.92; N, 7.98.

G-2-OH. G-1-Br (**5**) (1.12 g, 2.67 mmol) was combined with pure 4-(5′-azoisophthalate acid)benzyl alcohol (**4**) (390 mg, 1.30 mmol), K_2CO_3 (369 mg, 2.67 mmol), 18-crown-6 (2 mg), and acetone (50 mL) in a 100 mL three-necked round-bottomed flask equipped with a magnetic stirrer, reflux condenser, and N_2 inlet. After the mixture was refluxed for 48 h, a large amount of organic precipitate was observed. The reaction mixture was cooled to room temperature, and the orange precipitate was collected by suction filtration. The crude product was recrystallized from THF/acetone and dried overnight in a vacuum oven, yielding 968 mg of **G-2-OH** in 74% yield. LC−MS: *m/z* [M + H] 977.3 (calcd for $C_{53}H_{48}N_6O_{13}$, 976.4). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.90 (s, 1H), 8.80 (d, 4H, J = 2.4 Hz), 8.77(s, 4H), 8.02 (d, 4H, J = 8.5 Hz), 7.97 (d, 2H, J = 8.5 Hz), 7.96 (d, 4H, J = 8.3 Hz), 7.66 (d, 2H, J = 8.4 Hz), 5.54 (s, 4H), 4.82(s, 2H), 4.46 (q, 8H, J = 7.0 Hz), 1.44 (t, 12H, J = 7.0 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): δ 164.3, 163.9, 151.8, 151.6, 151.2, 150.7, 144.0, 138.3, 131.5, 131.3, 131.1, 130.6, 127.9, 127.1, 126.7, 126.4, 122.5, 122.4, 65.7, 63.7, 60.6, 13.3. Anal. Calcd for $C_{53}H_{48}N_6O_{13}$: C, 65.16; H, 4.95; N, 8.60. Found: C, 65.15; H, 4.99; N, 8.45.

1-Nitro-4-(*tert*-butyldiphenylsiloxymethyl)benzene (8). To a solution of 4-nitrobenzyl alcohol (15.3 g, 100 mmol) and imidazole (13.4 g, 200 mmol) in DMF (50 mL) was added dropwise a solution of *tert*-butyldiphenylsilyl chloride (41.1 g, 150 mmol) in DMF (50 mL) at 0 °C under nitrogen. The mixture was stirred at room temperature for 12 h, and then water was added to give a white precipitate. The precipitate was collected by filtration and recrystallized from CH_2Cl_2/hexane (20/100) to afford 37.6 g of 1-nitro-4-(*tert*-butyldiphenylsiloxymethyl)benzene (**8**) as a colorless crystal in 96% yield. EI-MS: *m/z* [M + H] 392.2 (calcd for $C_{23}H_{25}NO_3Si$, 391.1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (d, 2H, J = 8.2 Hz), 7.67 (m, 4H), 7.49 (d, 2H, J = 8.4 Hz), 7.49−7.37 (m, 6H), 4.84 (s, 2H), 1.12 (s, 9H,). ^{13}C NMR (300 MHz, $CDCl_3$): δ 145.2, 145.0, 133.8, 131.2, 127.1, 127.0, 126.9, 126.5, 126.1, 126.2, 121.8, 66.3, 27.4, 20.1. Anal. Calcd for $C_{23}H_{25}NO_3Si$: C, 70.55; H, 6.44; N, 3.58. Found: C, 70.24; H, 6.62; N, 3.45.

1-Nitroso-4-(*tert*-butyldiphenylsiloxymethyl)benzene (9). This was prepared from compound **8** using the procedure described above for diethyl 5-nitrosoisophthalate **(3)** and purified by flash chromatography using ethyl acetate/hexane (1:5) as an eluent to give 1-nitroso-4-(*tert*-butyldiphenylsiloxymethyl)benzene (**9**) as a white solid. Yield: 82%. EI-MS: *m/z* [M + H] 376.1 (calcd for $C_{23}H_{25}NO_2Si$, 375.2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (d, 2H, J = 8.2 Hz), 7.67 (m, 4H), 7.45 (d, 2H, J = 8.4 Hz), 7.49−7.37 (m, 6H), 4.84 (s, 2H), 1.12 (s, 9H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 162.8, 145.9, 133.8, 131.2, 127.1, 126.1, 121.8, 66.3, 27.5, 20.1. Anal. Calcd for $C_{23}H_{25}NO_2Si$: C, 73.56; H, 6.74; N, 3.73. Found: C, 73.28; H, 6.82; N, 3.78.

AB_2 Monomer 10. A mixture of 5-aminoisophthalic acid (484 mg, 2.67 mmol) in 50 mL of acetic acid and 1-nitroso-4-(*tert*-butyldiphenylsiloxymethyl)benzene (**9**) (1000 mg, 2.67 mmol) in 10 mL of CH_2Cl_2 was stirred at room temperature under nitrogen. After the mixture was stirred for 24 h, an orange solid was obtained, collected by filtration, and washed with water. The crude product was recrystallized from diethyl ether/hexane to give 1.2 g (yield: 91%) of pure AB_2 monomer **10** as an orange solid. EI-MS: *m/z* [M + H] 539.1 (calcd for $C_{31}H_{30}N_2O_5Si$, 538.2). ^{1}H NMR (300 MHz, acetone-d_6): δ 8.83 (s, 1H), 8.77 (s, 2H), 8.67 (d, 2H, J = 8.2 Hz), 7.79−7.77 (m, 4H), 7.69 (d, 2H, J = 8.4 Hz), 7.49−7.37 (m, 6H), 4.92 (s, 2H), 1.15 (s, 9H). ^{13}C NMR (300 MHz, acetone-d_6): δ 206.8, 166.7, 154.0, 152.7, 146.9, 136.7, 134.4, 133.7, 133.5, 131.3, 129.2, 128.6, 128.1, 125.9, 124.5, 66.3, 27.6, 20.8. Anal. Calcd for $C_{31}H_{30}N_2O_5Si$: C, 69.12; H, 5.61; N, 5.20. Found: C, 69.08; H, 5.67; N, 5.41.

Dendron G-3-OTBDPS and General Procedure for Ester Formation. To a solution of **G-2-OH** (2.1 mmol) in dry dichloromethane (15 mL) was added the AB_2 monomer (**10**) (1 mmol), followed by 4-dimethylaminopyridinum toluene-4-sulfonate (DPTS) (1 mg). The mixture was stirred at room temperature under nitrogen for 15 min. Dicyclohexylcarbodiimide (DCC) (2.2 mmol) was then added and stirring continued at room temperature until the reaction was complete. The reaction mixture was filtered to remove the precipitate dicyclohexylurea and evaporated to dryness under reduced pressure. The crude product was purified by silica gel chromatography using dichloromethane/ethyl acetate (30/1) as an eluent to give **G-3-OTBDPS** (yield: 91%). MALDI-TOF-MS: [M + H] 2307.9 (calcd for $C_{137}H_{122}N_{14}O_{29}Si$, 2454.83). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.89−8.88 (m, 3H), 8.80−8.77 (m, 9H), 8.73−8.68 (m, 9H), 8.01 (d, 12H, J = 8.8 Hz), 7.95 (d, 2H, J = 8.5 Hz), 7.71−7.68 (m, 4H), 7.66 (d, 12H, J = 8.2 Hz), 7.52 (d, 2H, J = 8.1 Hz), 7.44−7.36 (m, 6H), 5.44 (s, 12H), 4.85 (s, 2H), 4.46 (q, 6H, J = 7.0 Hz), 1.44 (t, 24H, J = 7.0 Hz), 1.10 (s, 9H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 165.3, 165.0, 164.9, 152.7, 152.6, 152.2, 139.5, 139.2, 135.5, 133.2, 132.4, 132.0, 131.6, 131.5, 129.8, 128.9, 128.2, 127.8, 127.7, 126.6, 123.6, 123.5, 123.3, 66.7, 61.7, 14.3.

Dendron G-3-OH and General Procedure for Desilylation. To a solution of **G-3-OTBDPS** (1 equiv) in CH_2Cl_2 in a polyethylene bottle was added HF−pyridine (2 equiv), and the mixture was vigorously stirred at room temperature. After being stirred overnight, the mixture was diluted with twice the volume of water, CH_2Cl_2 was added, and the solution was washed with saturated $NaHCO_3$ (aq). After the solvent was dried ($MgSO_4$) and evaporated, an orange solid was obtained, which was washed with methanol and purified by silica gel chromatography using a mixture of CH_2Cl_2/EtOAc from 100:1 to 10:1 (v/v) (yield 86%). MALDI-TOF: [M + K] 2257.4 (calcd for $C_{121}H_{104}N_{14}O_{29}$, 2218.2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.89−8.88 (m, 3H), 8.80−8.77 (m, 9H), 8.72−8.65 (m, 9H), 8.01 (d, 12H, J = 8.8 Hz), 7.87 (d, 2H, J = 8.4 Hz), 7.55 (d, 12H, J = 8.4 Hz), 7.53 (d, 2H, J = 8.7 Hz), 5.44 (s, 12H), 4.81 (s, 2H), 4.44 (q, 16H, J = 7.0 Hz), 1.44 (t, 24H, J = 7.0 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): δ 165.3, 164.9, 152.8, 152.7, 152.6, 152.2, 152.1, 145.1, 139.4, 139.2, 132.4, 132.0, 131.6, 131.5, 129.0, 128.9, 128.2, 127.7, 127.4, 123.6, 123.5, 123.4, 66.7, 64.7, 61.7, 14.3. Anal. Calcd for $C_{121}H_{104}N_{14}O_{29}$: C, 65.52; H, 4.73; N, 8.84 Found: C, 65.38; H, 4.92; N, 8.96.

Dendrimer G-1−4. This compound was prepared by coupling 5-dicarboxyl-(3′,5′-dicarboxylazophenyl)benzene (**AB_4**) (1 equiv) with **G-1-OH** (4.2 equiv) for 6 h using the same coupling conditions described above for dendron **G-3-OSPDBT** and purified by chromatography eluted with dichloromethane/ethyl acetate (25/1). Yield: 82%. MALDI-TOF-MS: [M + K] 1750.7 (calcd for $C_{92}H_{82}N_{10}O_{24}$, 1711.7). ^{1}H NMR (300 MHz, acetone-d_6): δ 8.95 (m, 2H), 8.87 (m, 3H), 8.77 (m, 3H), 8.71 (m, 4H), 8.02 (d, 8H, J = 8.3 Hz), 7.67 (d, 8H, J = 8.3 Hz), 5.55 (s, 8H), 4.44 (q, 16H, J = 7.0 Hz), 1.46 (t, 24H, J = 7.0 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): δ 165.3, 164.8, 152.5, 152.4, 152.2, 139.1, 133.4, 132.4, 132.0, 131.8, 129.1, 128.4, 127.7, 123.6, 66.8, 61.7, 14.3. Anal. Calcd for $C_{92}H_{82}N_{10}O_{24}$: C, 64.56; H, 4.83; N, 8.18. Found: C, 64.26; H, 4.92; N, 8.38.

Acknowledgment. This work was supported in part by the National Institute of Health (NIH) MBRS SCORE (No. 1 S06 GM 63119-01), the Petroleum Research Fund administrated by the American Chemical Society (No. 35036-G7) and the Robert A. Welch Foundation (E-1551). Mr. Tony Gies (UAB) is gratefully acknowledged for assistance with MALDI-TOF experiment. We also thank Professor Henry Po (CSULB) and Ms. Jacaqueline Corbeil (UCSD) for their comments.

Supporting Information Available: Additional copies of ^{1}H NMR and ^{13}C NMR for new compounds and the X-ray crystal data of G-1-OH. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0499773