

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

Shuangxi Wang^{*,†} Ximent 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

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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 drugs⁵ that have been conjugated to poly(amidoamine) dendrimers. These dendrimeric drug conjugates have improved solubility, reduced toxicity, and increased circula-

tion 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 dendritic 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.

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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 architecture¹⁸ 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 AB₂ monomer **4** contains active carboxylic groups for generation growth and hydroxymethyl groups as linkages for next generation growth, the central linkage AB₄ 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 AB₄. 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 AB₄. 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-nitrosophthalic acid, **1**. The esterification of **1** with ethanol in the presence of catalytic concentrated H₂SO₄ under reflux produced the diethyl ester **2** in 88% yield. Compound **3** was prepared according to a modified literature method²⁰ by reduction of **2** using Zn dust at 33–35 °C in 2-methoxyethanol to the hydroxylamine intermediate. This was followed by the oxidation of the hydroxylamine intermediate with FeCl₃ at about 0–5 °C to get nitroso compound **3** with an overall 47% yield. Condensation of **3** with commercially available 4-aminobenzyl alcohol in CH₂Cl₂ 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 H₂O resulted in the AB₂ monomer **4** in 84% yield. Bromination of the **G-1-OH** with CBr₄ and PPh₃ yielded the bromomethyl compound, **5**.

The symmetric four-branched central linker AB₄ was prepared by reductive coupling of 5-nitrosophthalic 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 AB₂ monomer **4** with the benzyl

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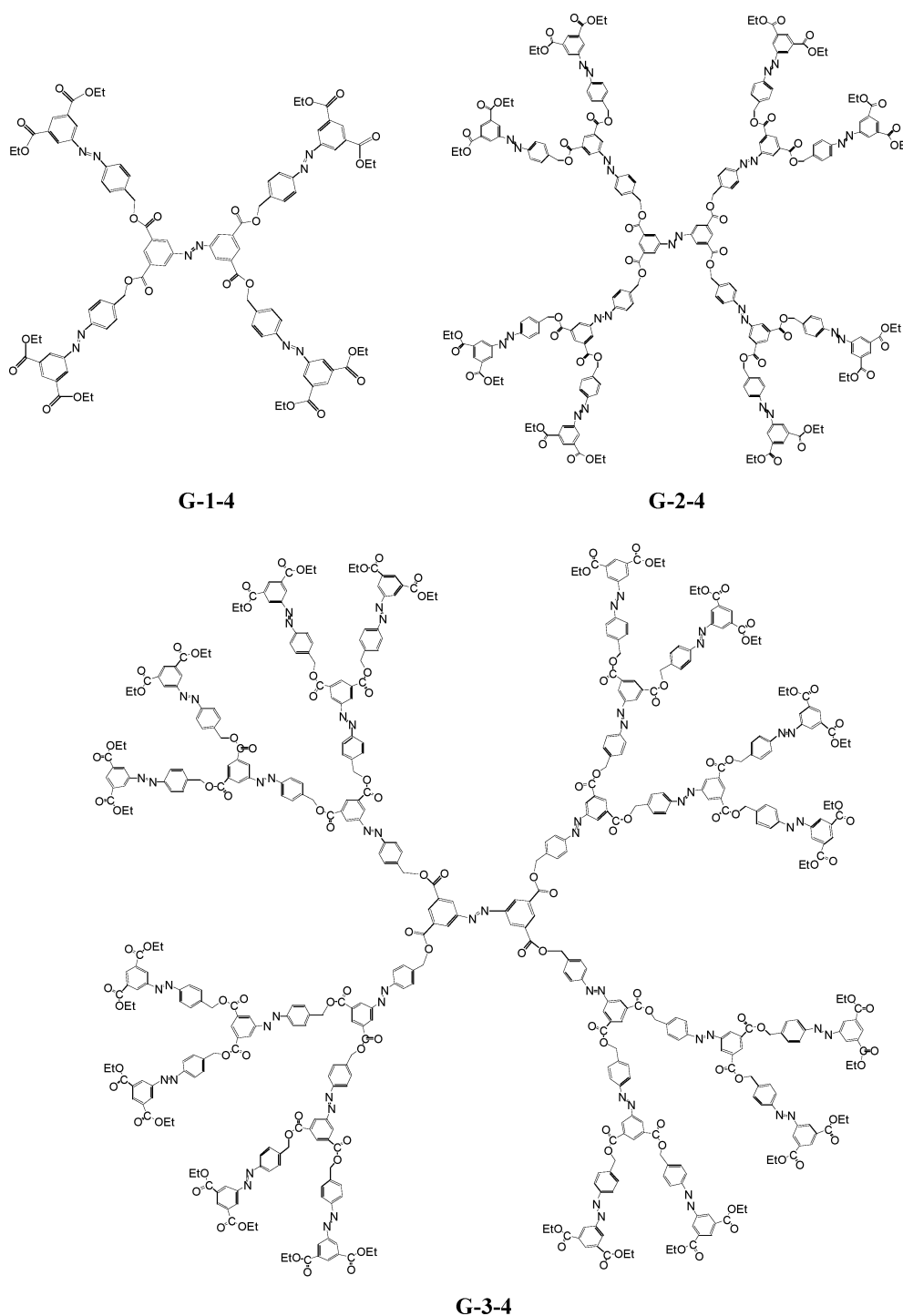


FIGURE 1. Three generations of azobenzene dendrimers **G-1-4**, **G-2-4**, and **G-3-4**.

134 bromide **5** in the presence of potassium carbonate and
 135 18-crown-6 in dried acetone in 74% yield as an orange
 136 solid (Scheme 3).

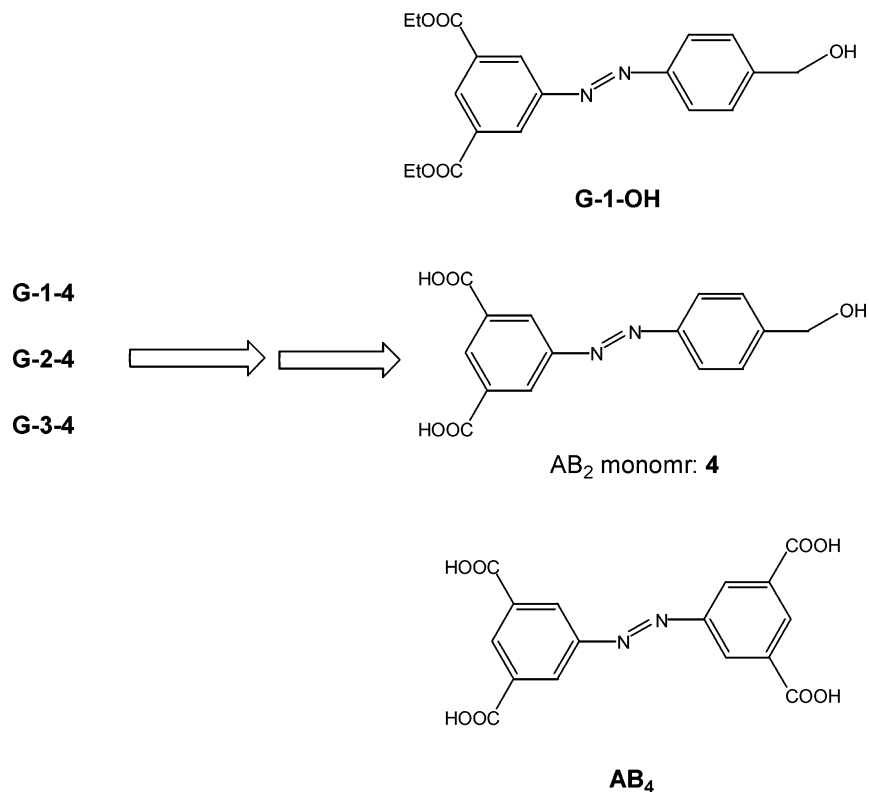
137 Unfortunately, there is a problem with the bromination
 138 of **G-2-OH** for next generation growth. The **G-2-OH** could
 139 not be brominated by $\text{CBr}_4/\text{PPh}_3$, even with excess
 140 reagents and an elevated temperature. In addition, an
 141 array of brominating agents²¹ (PBr_3 ,^{21a} PPh_3/NBS ,^{21b}
 142 $\text{NBS}/\text{Me}_2\text{S}$,^{21c} Me_3SiBr ,^{21d} and $\text{Me}_3\text{SiBr}/2.6\text{-di-}t\text{-bu-}$

134 tyropyridine) gave uniformly unsatisfactory results. It is
 135 unclear why these reactions did not work. Thus, we
 136 turned to design and synthesis of the AB_2 monomer **10**,
 137 which contains two activated carboxylic groups for gen-
 138 eration growth and one hydroxymethyl group protected
 139 by *tert*-butyldiphenylsilane chloride (TBDPSCl) for sub-
 140 sequent generation growth as outlined in Scheme 4. 149

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SCHEME 1



150 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-methoxyethanol, as in the preparation of nitroso compound **3**, followed by oxidation using FeCl₃ 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 AB₂ monomer **10** as an orange solid, which was recrystallized from diethyl ether to afford **10** in 90% yield.

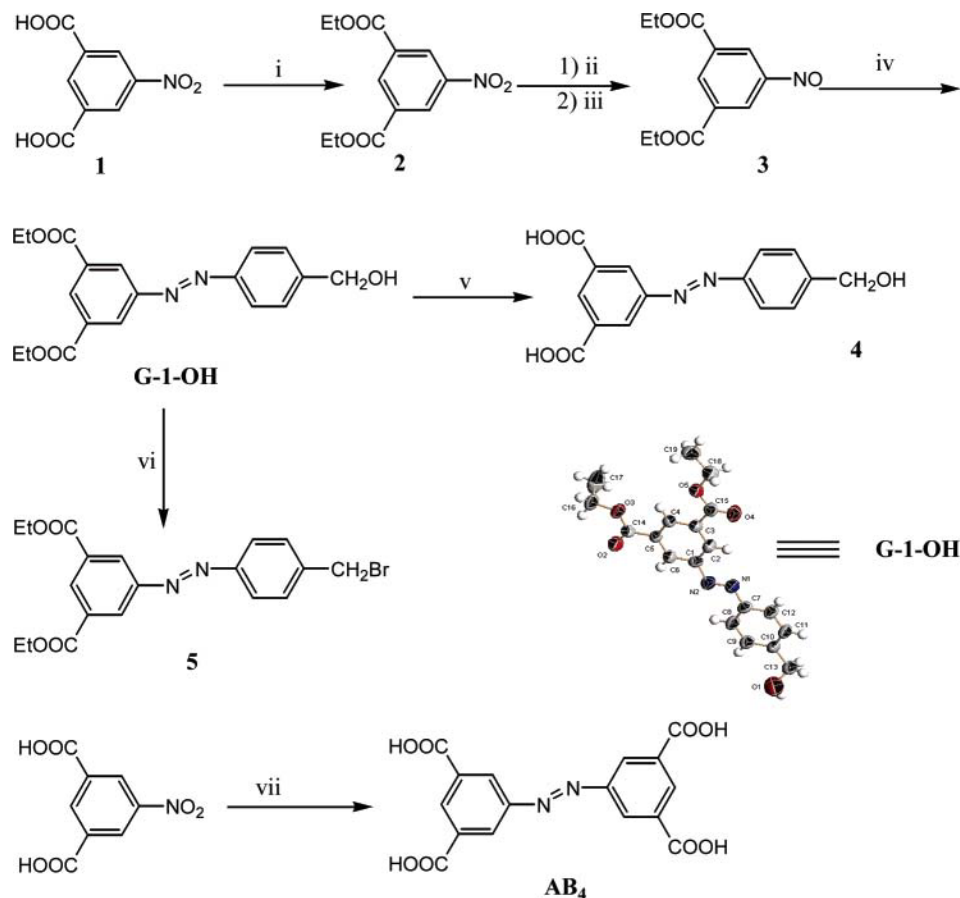
161 **Synthesis of G-3-OH and G-4-OH.** With AB₂ monomer **10**, the third dendron (**G-3-OH**) based on **G-2-OH** was smoothly obtained following the convergent synthetic approach developed by Fréchet.²² This involved an iterative and alternating sequence of DCC (dicyclohexylcarbodiimide)/DPTS 4-(dimethylamino)pyridinium 4-toluenesulfonate-mediated esterifications²³ 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 AB₂ 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

180 obtained because of cleavage of ester linkages. We also 180
 181 tried other numerous reaction conditions containing more 181
 182 or less water, counterions other than tetrabutylammo- 182
 183 nium, and adding water buffered to different pHs to effect 183
 184 a clean reaction. All reactions containing the fluoride ion 184
 185 gave complicated mixtures because the F[−] anion is a 185
 186 Lewis base that is strong enough to cleave the benzyl 186
 187 ester bonds. We also tried to use the THF–HCl (aq) 187
 188 system to desilylate. It was found that the protection 188
 189 group could not be completely removed at room temper- 189
 190 ature and the product decomposes at higher tempera- 190
 191 tures. Finally, after many failures, we found that the mild 191
 192 HF–pyridine reagent efficiently and cleanly removes the 192
 193 protected group. The coupling and deprotected steps were 193
 194 then repeated to convert the **G-3-OH** to **G-4-OH** in 194
 195 overall 65% yield. However, extending the synthesis to 195
 196 the pure **G-5-OH** dendron does not seem to be possible. 196

197 **Synthesis of Perfect Dendrimers.** Perfect den- 197
 198 drimers based on poly(benzyl ester) monodendrons were 198
 199 prepared by coupling different generation monodendrons 199
 200 with the four-branched azobenzene core **AB₄** using the 200
 201 same coupling conditions DCC/DPTS at room tempera- 201
 202 ture. Therefore, coupling of **G-1-OH**, **G-2-OH**, and **G-3-** 202
 203 **O-H** with the four-branched core **AB₄** in the presence of 203
 204 DCC/DPTS afforded the all azobenzene dendrimers **G-1-** 204
 205 **4**, **G-2-4**, and **G-3-4** in 82%, 54%, and 38% yields, 205
 206 respectively (Scheme 6a–c). It is worth pointing out that 206
 207 the synthesis and purification of dendrons and den- 207
 208 drimers becomes progressively more challenging from one 208
 209 generation to the next. For example, **G-3-4** was only 209
 210 synthesized in a small quantity (less than 500 mg) and 210
 211 it took 6 days. A yield of 82% was obtained for **G-1-4**, 211
 212 with a decrease to 54% for **G-2-4**, and a decrease to 38% 212
 213 for **G-3-4**. An apparent limitation of the convergent 213

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SCHEME 2^a

^a Reagents and conditions: (i) H₂SO₄/EtOH, reflux; (ii) Zn/33–35 °C/N₂, 2-methoxyethanol; (iii) FeCl₃/0–5 °C/N₂, EtOH/H₂O; (iv) 4-aminobenzyl alcohol/acetic acid/N₂/rt, CH₂Cl₂; (v) KOH/EtOH/H₂, reflux; (vi) CBr₄/PPh₃/THF/N₂, 0 °C to rt; (vii) Zn/NaOH/EtOH/H₂O, reflux.

214 approach is its susceptibility to steric inhibition as the
215 macromolecules become larger, the functional group at
216 the focal point becomes “masked” by the growing mac-
217 romolecule and its reactivity is lessened. With the tetra-
218 rfunctionalized core **AB**₄ linkage, which leads to greater
219 steric congestion, this limit appears to be reached before
220 **G-4-OH**, and no **G-4-4** dendrimer could be produced
221 from **G-4-OH** and **AB**₄ despite repeated attempts under
222 a variety of conditions.

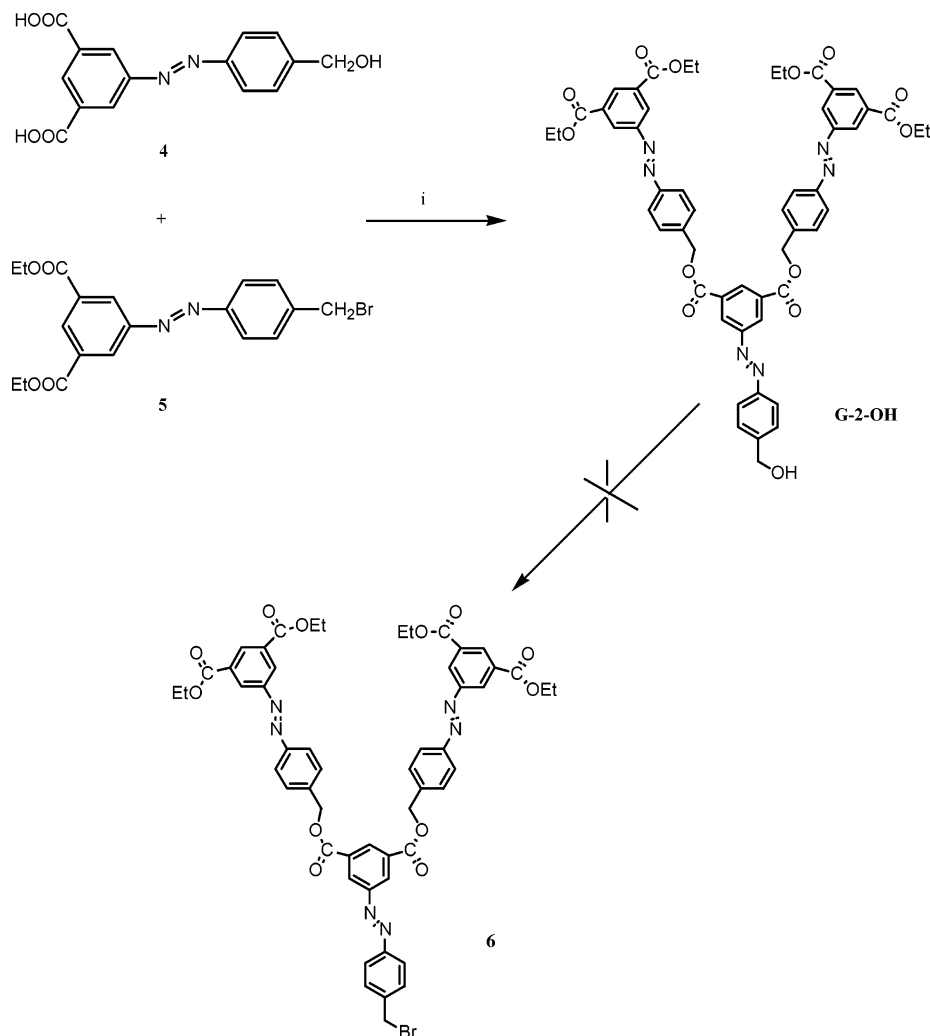
223 **Characterization.** The techniques used for the char-
224 acterization of dendrons **G-2-OH**, **G-3-OH**, and **G-4-OH**
225 and dendrimers **G-1-4**, **G-2-4**, and **G-3-4** were ¹H
226 NMR, ¹³C NMR, LC-MS, and MALDI-TOF mass spectra.
227 In the ¹H NMR spectra of the dendrons and dendrimers
228 the resonances for the isophthalate aromatic protons
229 occur at 8.90–8.60 ppm and the resonances for the
230 protons of exterior benzylic groups occur at ~7.93 and
231 ~7.60 ppm as two doublets. The chemical shift of exterior
232 benzyl methyl groups stayed consistently at ~5.50 ppm,
233 while that of benzyl methyl group at the focal point was
234 at ~4.80 ppm as single peaks. The chemical shifts of
235 –OCH₂– and –CH₃ of ethyl groups at the periphery were
236 around 4.45 and 1.46 ppm, respectively. However, the
237 single peak at ~4.8 ppm for the protons of the benzyl
238 methyl group at the focal point in the dendrons disap-
239 peared in the spectra of the dendrimers, which is fully
240 consistent with the molecular structures of the den-

241 drimers. The relative integration ratios of benzyl methyl
242 groups at the exterior (~5.5 ppm) vs benzyl methyl at
243 the focal point (~4.8 ppm) were a useful diagnostic tool
244 for characterizing the generation progression of the
245 dendrons. The ratios increase as the generation of the
246 dendrons grow, such as with 4:2 for **G-1-OH**, 12:2 for **G-3-**
247 **O-H**, and 28:2 for **G-4-OH** as shown in Figure 2. The
248 structures of the dendrons and dendrimers were also
249 confirmed by MALDI-TOF-MS. Figures 3, 4 and 5 show
250 representative MALDI-TOF spectra of **G-1-4**, **G-3-OH**,
251 and **G-3-4**.

252 All the dendrons and dendrimers were obtained as
253 orange red solids or glasses that were soluble in aprotic
254 solvents such as CH₂Cl₂, ethyl acetate, and THF but were
255 insoluble in methanol and acetone except for **G-1-OH**.

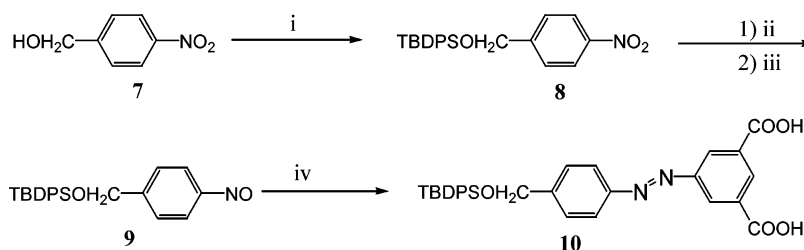
256 **Absorption Spectra.** The absorption spectra of the
257 dendrons and dendrimers were carried out in dichlo-
258 romethane at 298 K. The wavelengths of the maxima of
259 the absorption bands and the values of the molar absorp-
260 tion coefficients were collected in Table 1. All absorption
261 spectra of the dendrons and dendrimers show the same
262 absorption bands with a high-intensity band at about 335
263 nm assigned to π → π* transitions and a low intensity
264 band at 440 nm assigned to the n → π* transition,
265 indicating the independence of the generation number.
266 However, the molar absorption coefficient increases
267 linearly with an increasing number of azobenzene groups

SCHEME 3^a



^a Reagents and conditions: (i) $K_2CO_3/18\text{-crown-6/acetone}$, reflux.

SCHEME 4^a

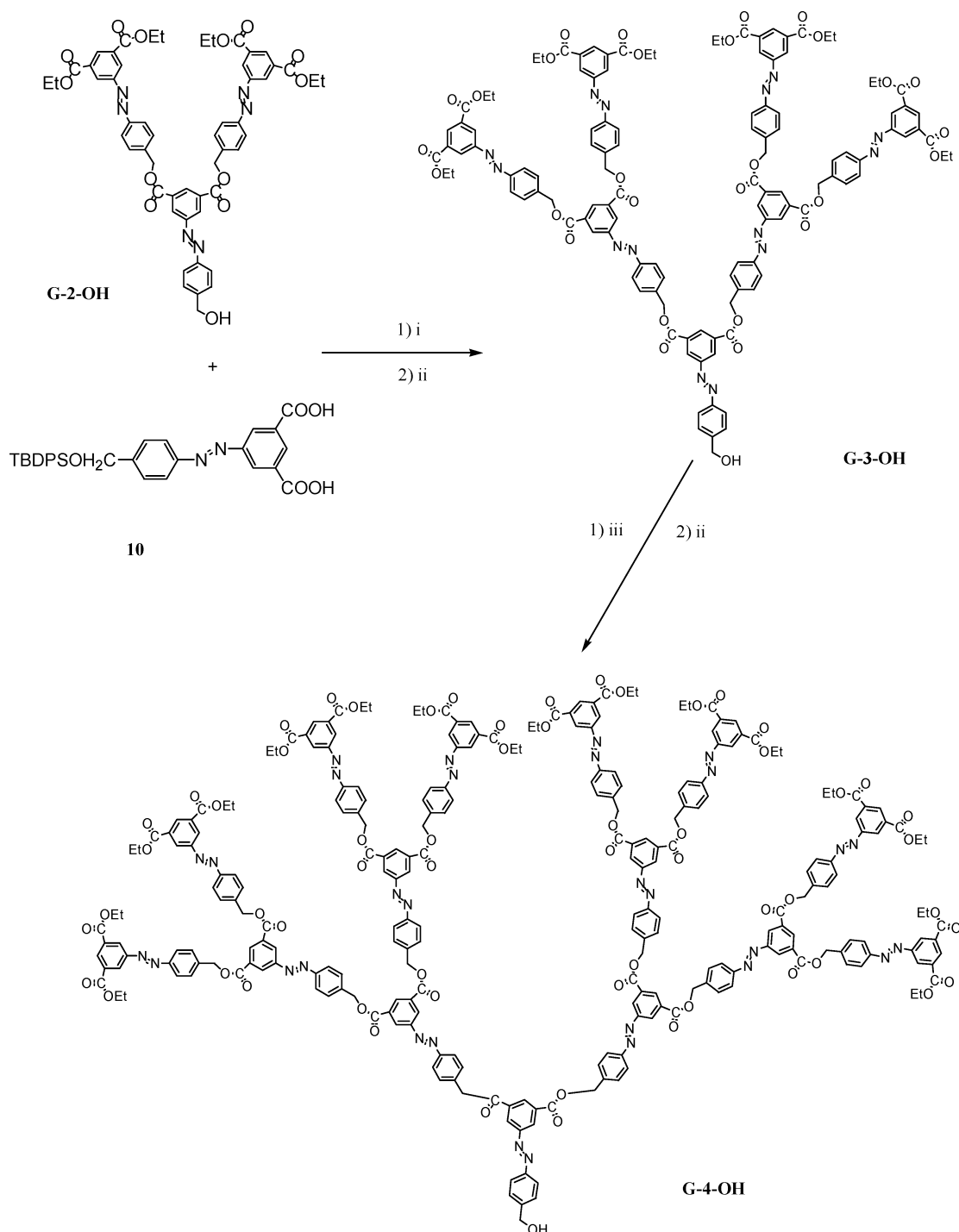


^a Reagents and conditions: (i) $TBDPSCl/imidazole/DMF$, 0 °C to rt; (ii) $Zn/33\text{--}35\text{ °C}/N_2$, 2-methoxyethanol; (iii) $FeCl_3/0\text{--}5\text{ °C}/N_2$, $EtOH/H_2O$; (iv) 5-aminoisophthalic acid/acetic acid/ N_2/rt , CH_2Cl_2 .

268 present in the dendrons and dendrimers. The number of
269 azobenzene groups present is 1, 3, 7, and 15 for dendrons
270 **G-1-OH**, **G-2-OH**, **G-3-OH**, and **G-4-OH** and 5, 13, and
271 29 for dendrimers **G-1-4**, **G-2-4**, and **G-3-4**, respec-
272 tively. Accordingly, the molar absorption coefficients are
273 15800, 42200, 105600, and 196200 ($M^{-1} cm^{-1}$) for den-
274 dendrons and 72000, 179400, and 334800 ($M^{-1} cm^{-1}$) for
275 dendrimers.

276 **Photoisomerization.** All the azobenzene-type den-
277 dendrons and dendrimers in this work are found to undergo

278 the *trans* \rightarrow *cis* and *cis* \rightarrow *trans* photoisomerizations as 278
279 well as the *cis* \rightarrow *trans* thermal isomerization. Figure 6 279
280 shows the spectroscopic changes observed for the isomer- 280
281 ization of **G-3-OH**. Qualitatively, similar results have 281
282 been obtained for all the dendrons and dendrimers 282
283 examined. Irradiation of a dendron or dendrimer in CH_2- 283
284 Cl_2 solution at 310 nm results in photoisomerization from 284
285 the *trans*- to the *cis*-isomer, as indicated by a decrease 285
286 of the absorption in the region of $\pi \rightarrow \pi^*$ electron 286
287 transition at $\lambda_{max} = \sim 335$ nm and an increase of the 287

SCHEME 5^a

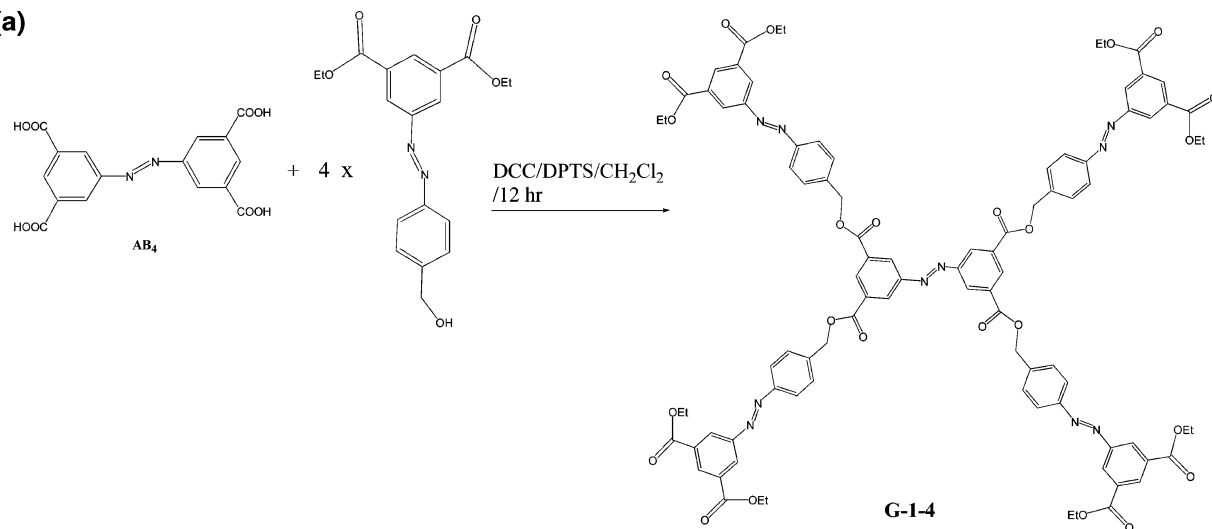
^a Reagents and conditions: (i) DCC/DPTS/CH₂Cl₂, rt; (ii) HF-pyridine/CH₂Cl₂, rt; (iii) 10/DCC/DPTS/CH₂Cl₂, rt.

288 absorption in the region of $n \rightarrow \pi^*$ 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 $(A_0 - A_{\text{PSS}(330 \text{ nm})})/A_0$, where A_0 and $A_{\text{PSS}(330 \text{ nm})}$ 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

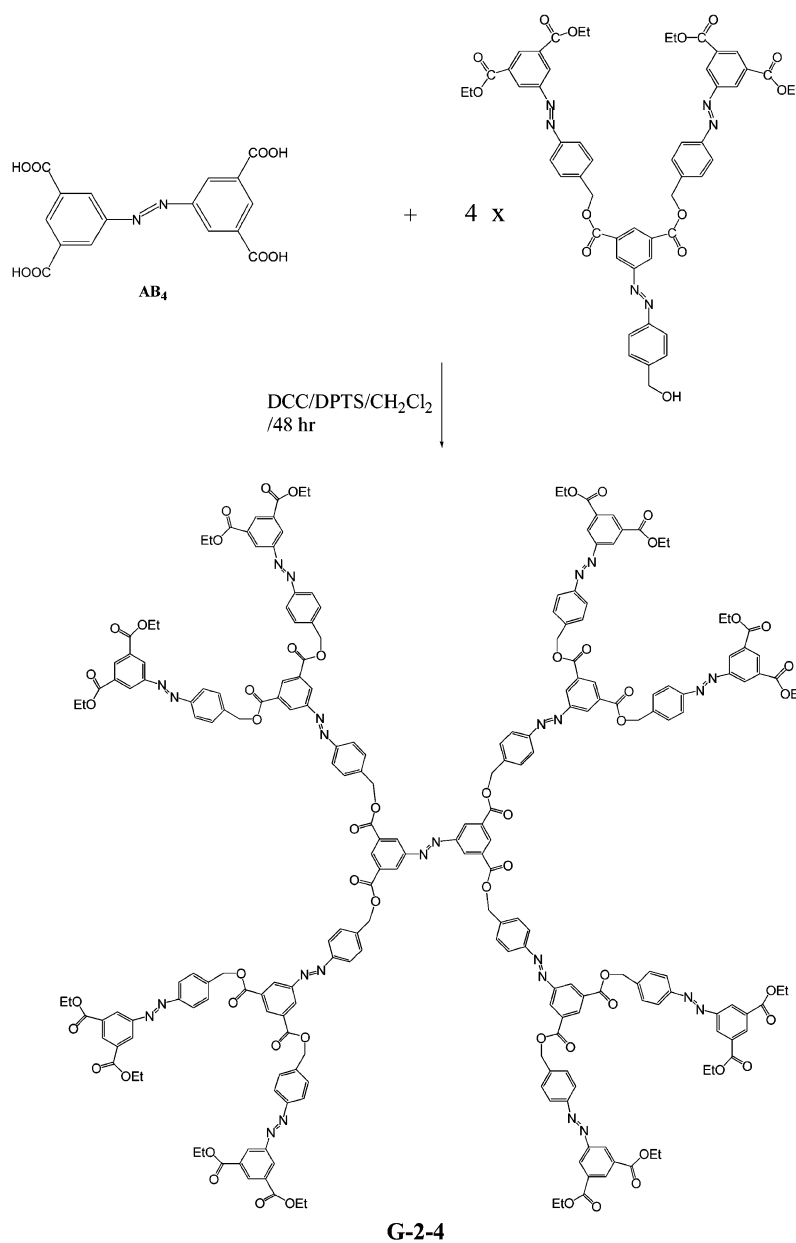
297 has negligible absorbance at 335 nm. The *cis*-isomer 298 content at PSS under 310 nm irradiation for all dendrons 299 and dendrimers studied is listed in Table 1. From Table 300 1, it can be seen that the *cis*-isomer content from G-1- 301 OH to G-4-OH decreases to 61% from 87%, while *cis*- 302 isomer content from G-1-4 to G-3-4 decreases to 36% 303 from 77%. This indicates that the *cis*-isomer content 304 decreases with increasing dendron and dendrimer gen- 305 eration, the effect of the latter being more profound than

SCHEME 6

(a)

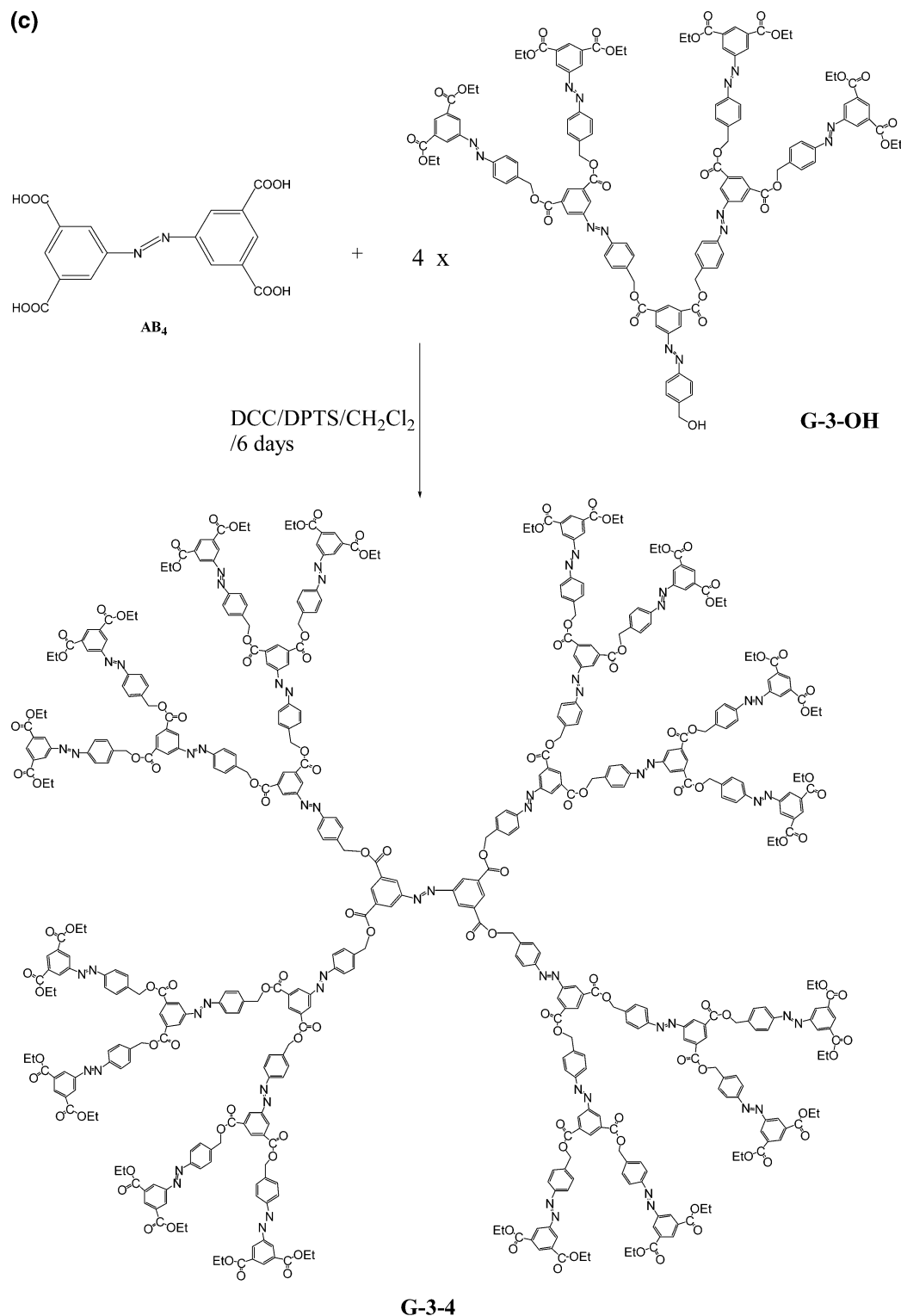


(b)



SCHEME 6 (Continued)

(c)



G-3-4

306 the former, as observed in the literature.^{17f,18b} In contrast, 312
 307 the incorporation of azobenzene cores within dendrimers 313
 308 or polymers has no influence on their *trans*–*cis* thermal 314
 309 isomerization.²⁴ This may be explained as the effect of 315
 310 steric hindrance and lower flexibility of the dendrons and 316
 311 dendrimers studied in this work. 317

The reverse *cis* → *trans* isomerization of the dendrons 312
 and dendrimers from PSS obtained upon 310 nm irradiation 313
 can be induced either thermally in the dark or by 314
 visible irradiation at 449 nm. Visible irradiation leads 315
 to a photostationary state that is very rich in the *trans*- 316
 isomer, while the thermal isomerization leads to only 317
 pure *trans*-isomer. It is worth noting that the reaction 318
 rate of thermal isomerization is much slower under 319
 visible irradiation; in fact, it took about 2 weeks to recover 320

(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.

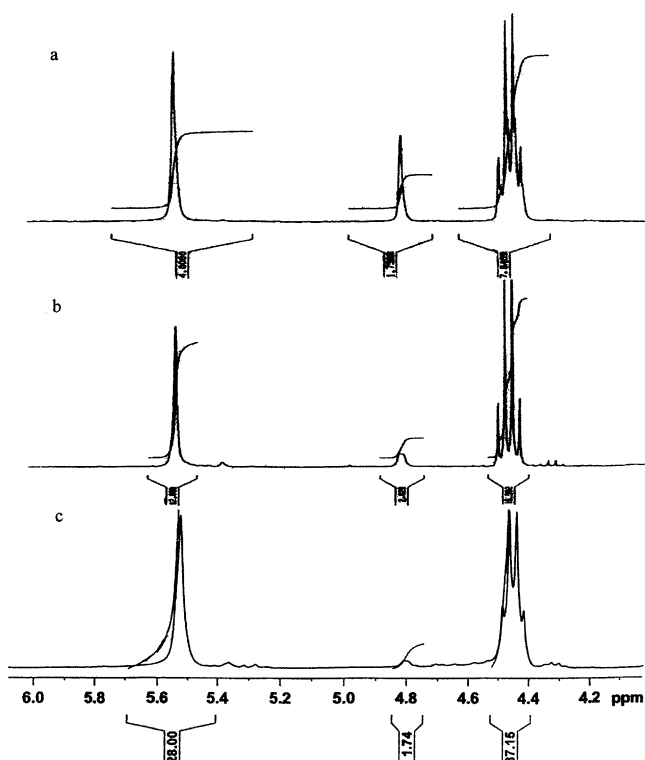


FIGURE 2. Comparison of ¹H NMR spectra of (a) G-2-OH, (b) G-3-OH, and (c) G-4-OH.

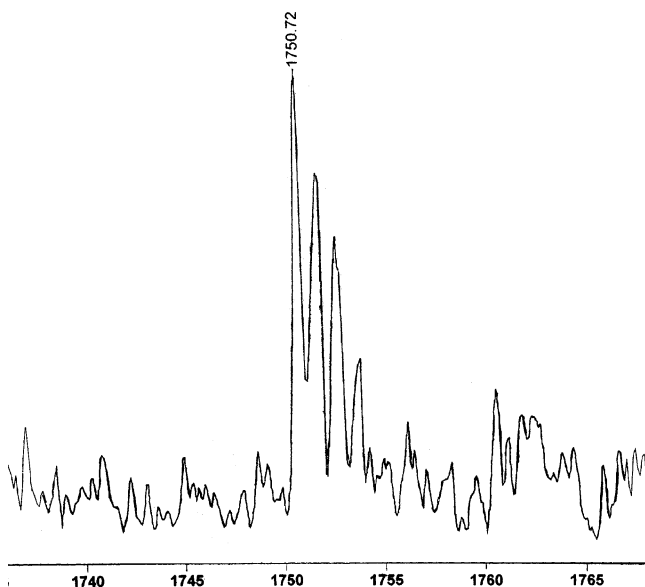


FIGURE 3. MALDI-TOF MS spectrum of G-1-4.

321 all of the *trans* dendrimer G-3-4 when a solution of
 322 G-3-4 in CH₂Cl₂ that had reached the photostationary
 323 state under excitation with 310 nm was placed in the
 324 dark.

325 Conclusions

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

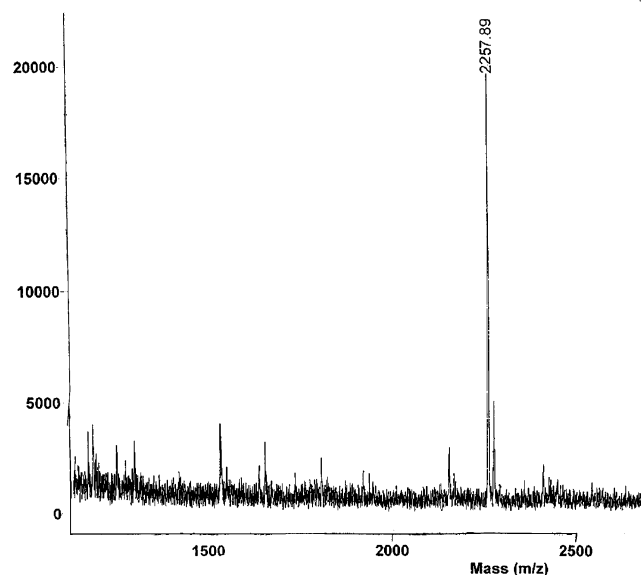


FIGURE 4. MALDI-TOF MS spectrum of G-3-OH.

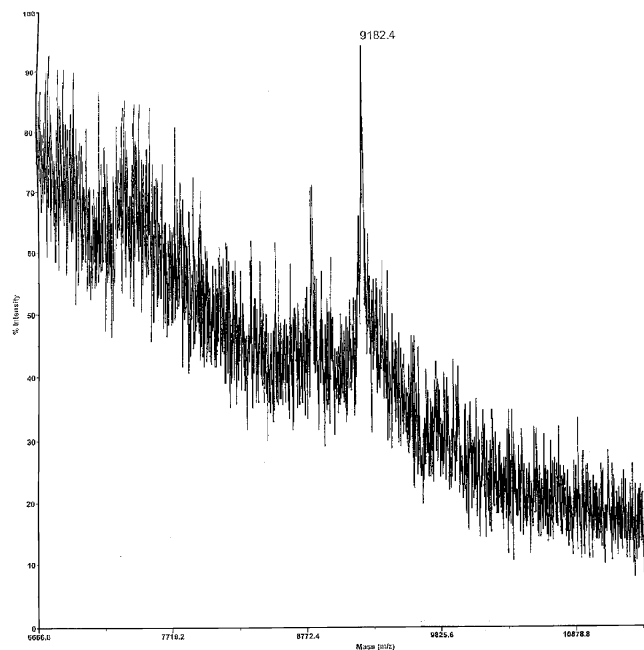


FIGURE 5. MALDI-TOF MS spectrum of G-3-4.

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

	absorption λ_{\max}/nm (ϵ , M ⁻¹ cm ⁻¹)		<i>cis</i> -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 photorespon- 332
 sive properties upon UV and visible irradiation. The 333
 dendrons and dendrimers are only constructed from 334

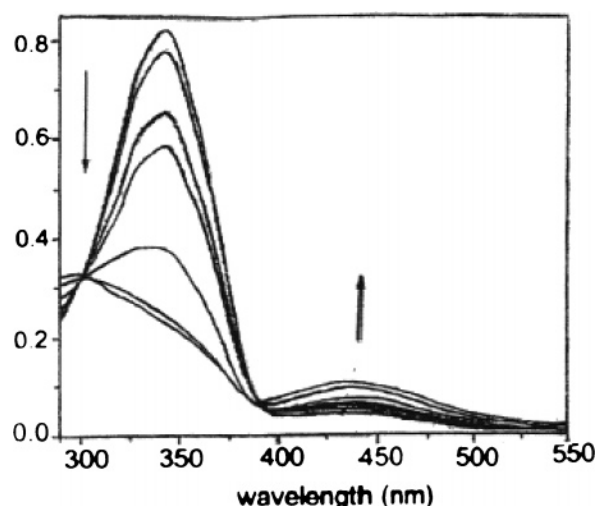


FIGURE 6. Changes in the absorption spectrum of **G-3-OH** upon irradiation at 310 nm

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. ^1H 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-hydroxycinnamic acid as a matrix with Ag^+ as the modifier in THF for **G-2-4**. All starting materials were from commercial 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-nitrosoisophthalate (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 \times 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 $\text{C}_{12}\text{H}_{13}\text{NO}_5$, 251.6). ^1H 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 $\text{C}_{12}\text{H}_{13}\text{NO}_5$: 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 $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_5$, 356.8). ^1H 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 $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_5$: 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 $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_5$, 300.4). ^1H 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 $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_5$: 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 $\text{C}_{19}\text{H}_{19}\text{BrN}_2\text{O}_4$, 418.5). ^1H 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 $\text{C}_{19}\text{H}_{19}\text{BrN}_2\text{O}_4$: 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 (AB₄). 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 (**AB₄**) as an orange precipitate (yield: 78%). LC-MS: [M – H] 357.1 (calcd for $\text{C}_{16}\text{H}_{10}\text{N}_2\text{O}_8$, 358.2). ^1H 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, 149.5

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: C 53.26; 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). 1H 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-butyl)diphenylsiloxymethyl)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). 1H 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-butyl)diphenylsiloxymethyl)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). 1H 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.

AB₂ 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 AB₂ 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). 1H 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 AB₂ monomer (10) (1 mmol), followed by 4-dimethylaminopyridinium 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). 1H 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). 1H 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 (AB₄) (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). 1H 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.

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Supporting Information Available: Additional copies of 1H 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>.

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