

Synthesis and Properties of New, Spatially Relaxed Dendrons Containing Internal Carboxyl Groups

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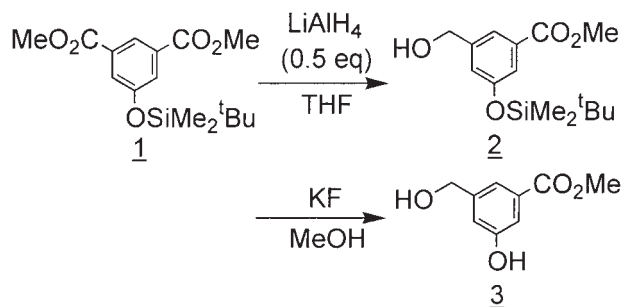
We synthesized a series of new dendrons with up to fourteen internal carboxyl groups. These dendrons are made from a branching unit and a spacer unit with a carboxyl group. The growth reactions (formation of the benzylic ether bonds) are completed within a few hours, which suggests high reactivity at the “focal” point of the dendritic framework. The final deprotection of the internal ester groups also proceeded smoothly. These high reactivities were attributed to the presence of spacer units, which caused spatially relaxed conformations of these molecules. The carboxylate salt form of the dendron produced both normal and reverse micelles in a THF/water mixed solvent according to the fraction.

Dendrimers containing carboxyl functional groups are well-studied as pH-controllable unimolecular micelles,¹ shape-persistent amphiphiles,² polyionic materials,³ potential metal-complexing agents,⁴ and multiply modifiable materials.⁵ They are also utilized for solubilizing highly hydrophobic materials, such as fullerenes⁶ and porphyrins.^{1c–g} Most of these dendrimers have carboxyl groups in the periphery with internal frameworks of polyimines,^{1c,4a} polyamides,^{1a,b,d,3b,5b,6,7} benzyl ethers,^{1e–g,3a,c,d,5a} and phenylacetylenes.² Some dendrimers have carboxyl groups at the core that participate in self-assembly through hydrogen bonds⁸ and metal-ligating interactions.^{4b} On the other hand, Fréchet reported on dendrimers⁹ with “internal” functional groups, and examined their catalytic activity as unimolecular reverse micelles. Such dendrimers with internal functional groups will also be useful for multiple functionalization and as metal-complexing agents. However, Fréchet’s dendrimers are based on 3,5-dialkoxybenzyl ether frameworks that lead to densely packed materials, which will make further derivatization of the carboxyl groups rather difficult.

Herein we report on a new series of dendrons with internal carboxyl groups. These dendrons are built from a spacer unit containing a carboxyl group (methyl 3-hydroxy-5-(hydroxymethyl)benzoate, **3**) and a branching unit (3,5-dihydroxybenzyl alcohol, **4**). The introduction of spacer units makes room around the carboxyl groups, so that these groups maintain reactivity even after the construction of a high generation of dendrons. The growth reactions are also easier because of the high reactivity at the focal point. Molecular dynamics (MD) simulations have shown that these dendrons have void space inside, where the carboxylate groups are accessible by the solvent molecules. An interesting micelle-forming behavior of the carboxylate salt form of the dendron is also reported.

Results and Discussion

Synthesis. The spacer unit **3** was synthesized according to Scheme 1. The silyl-protected diester **1**¹⁰ was partially reduced by 0.5 molar equivalents of LiAlH₄, and the monoalcohol **2** was isolated by column chromatography.

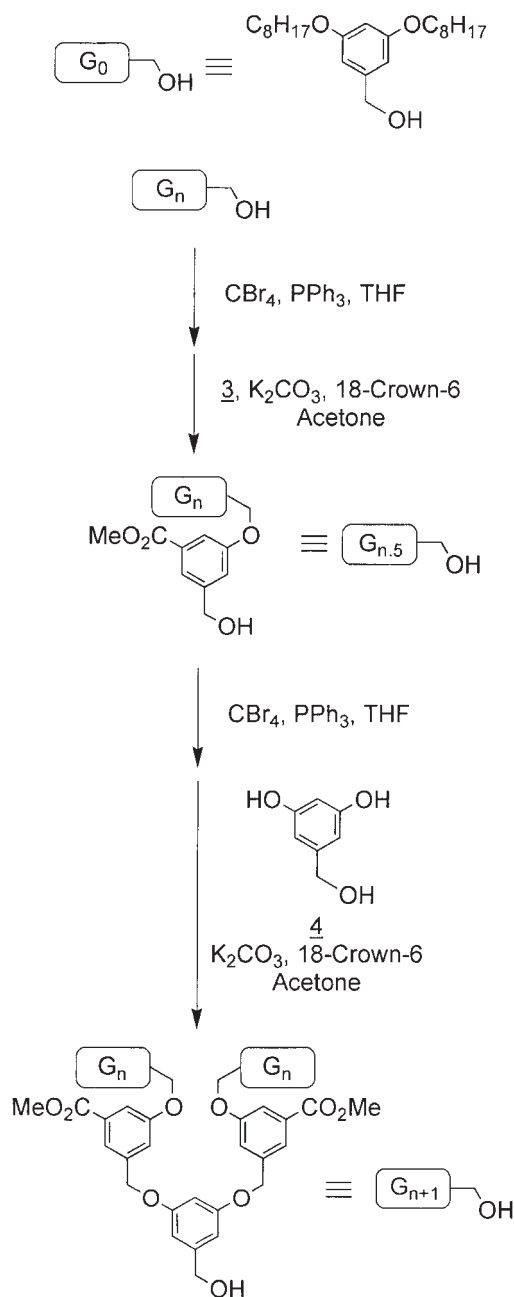


Scheme 1. Synthesis of the spacer unit **3**.

Compound **3** is crucial in the synthesis of this series of dendrimers. Therefore, for these dendrimers to be useful, compound **3** needs to be prepared in large quantities. The *t*-butyldimethylsilyl-protected compound **2** is useful because it is easily handled in column chromatography. However, the usual deprotection with Bu₄NF led to a mixture of **3** with tetrabutylammonium salts, which could not be easily separated out. We used KF instead, so that the by-products could be separated by utilizing differences in the solubility. A similar compound (an ethyl ester) was recently prepared via a direct partial reduction of diethyl 5-hydroxyisophthalate,¹² but our three-steps procedure gave higher overall yield (53% vs 30%).

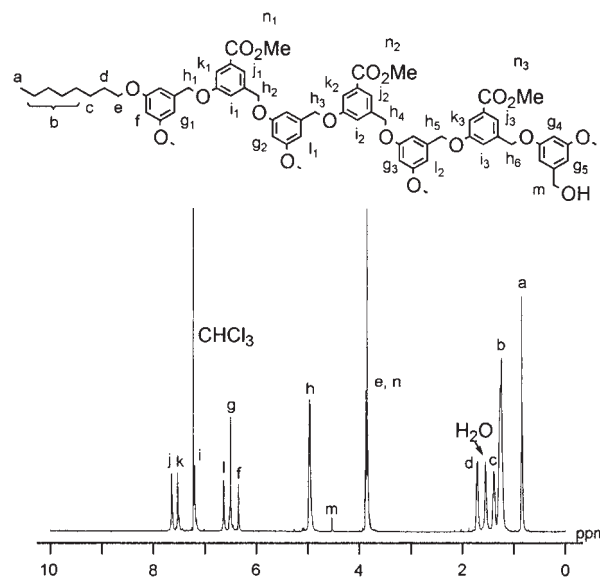
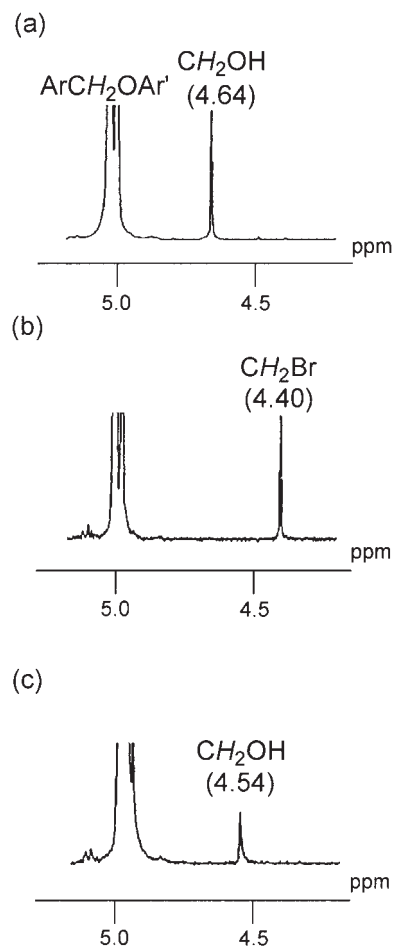
The general synthetic procedures for the dendrons are shown in Scheme 2. The terminal unit, **G**₀, was synthesized from **4** and 1-bromooctane.¹¹ The dendrons **G**_{1–3} were prepared by the convergent method,¹³ by an alternating treatment with the spacer unit **3** and the branching unit **4**. Specifically, compound **G**_{*n*} was converted to the bromide by CBr₄/PPh₃, and the bromide was allowed to react with **3** in the presence of K₂CO₃ and 18-crown-6 to give the spacer-connected compound **G**_{*n*+1}. This compound **G**_{*n*+1} was similarly converted to **G**_{*n*+2} by a treatment with CBr₄/PPh₃, followed by a reaction with **4**. Finally, the ester groups in the dendron **G**₃ were hydrolyzed by excess KOH in THF/MeOH, and **G**₃(CO₂H) was obtained.

The formation of the ether linkage and hydrolysis of the ester

Scheme 2. Synthesis of the dendrons G_{1-3} .

groups proceeded smoothly in short periods (2 to 3 h). This is in contrast with other benzyl-ether-based dendrons that often require several days for the reaction to complete,^{3a,3d,5a} and is a useful feature for synthesizing higher generations of this series of dendrons. The high reactivity of the ester groups will also be useful for preparing functionalized derivatives via ester/amide linkages.

Characterization. The 1H NMR spectrum of G_3 is shown in Fig. 1. All signals were assigned to the corresponding kinds of protons with the expected integral values: aromatic (with and without ester groups), benzylic, methyl ester, and octyloxy groups. Each synthetic step was monitored by the 1H NMR signals of the focal benzylic protons (i.e., the ones at the core benzene ring). The typical spectral change is shown in Fig. 2. The CH_2OH signal at 4.64 ppm (a) moved to 4.40 ppm after conver-

Fig. 1. 1H NMR spectrum of the dendron G_3 in $CDCl_3$.Fig. 2. 1H NMR spectra of the focal benzylic protons in $CDCl_3$. (a) $G_{2.5}$, (b) the bromide, and (c) G_3 .

sion to CH_2Br (b); after ether formation, a new CH_2OH signal appears at 4.54 ppm (c). The hydrolysis of the methyl ester was also monitored by 1H NMR (Fig. 3).

The MALDI-TOF spectra of the dendrons are shown in

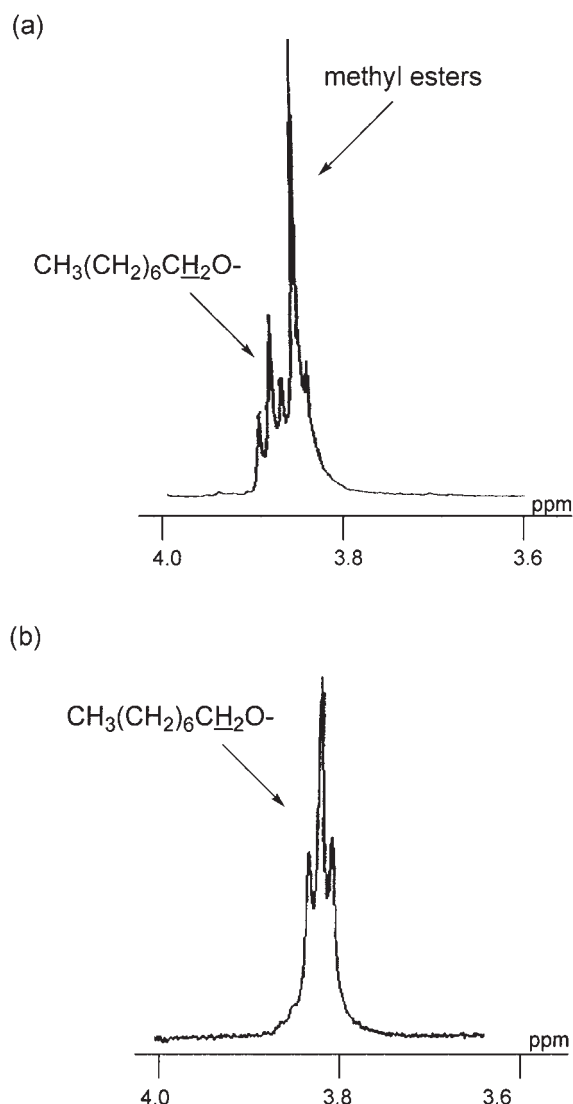


Fig. 3. ¹H NMR spectra of methyl ester groups of **G**₃ in CDCl₃ (a), and **G**₃(CO₂H) in DMSO-*d*₆ after hydrolysis (b).

Fig. 4. In all of the spectra, the peaks of the highest intensities were assigned as $M + Na^+$. In addition, the peaks assigned as $M + K^+$ were observed for **G**₂ and **G**₃. In all cases, no peaks with a lower m/z than these peaks were observed, except for those from the matrix, which indicate the purity of these compounds.

The analytical gel-permeation chromatograms of these compounds (Fig. 5) revealed a change of the retention times corresponding to the molecular sizes. The symmetric peaks also indicate the purity of these compounds.

Molecular Dynamics (MD) Simulations. In order to visualize the molecular shape of these dendrons, we performed MD simulations on the **G**₃ dendron using the AMBER7 program package.¹⁴ Such simulations will also aid us to design functional molecules based on these dendrons. Two types of simulations were examined, one without a solvent (i.e., in vacuo simulation) and the other in an explicit solvent box of chloroform.

Figure 6 shows the resultant three conformers of the **G**₃ dendron: (a) the initial, energy-minimized conformation, (b) after a

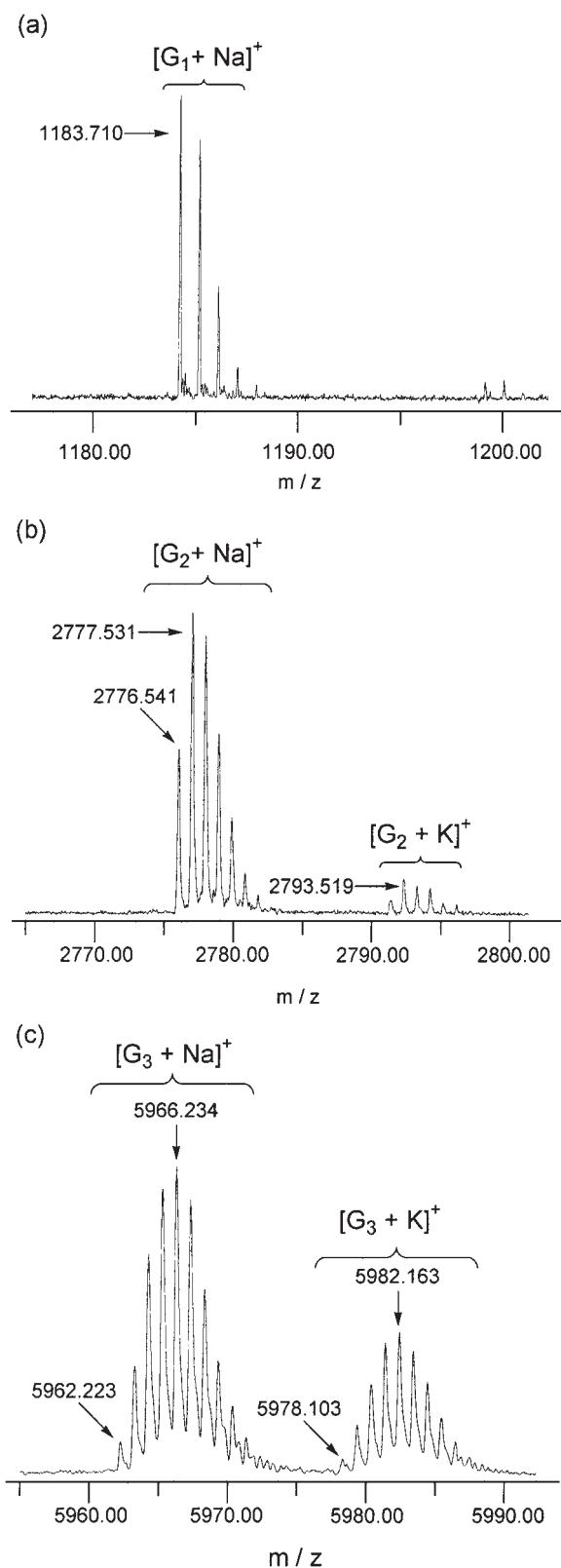


Fig. 4. MALDI-TOF mass spectra of the dendrons **G**₁₋₃.

100-ps run of molecular dynamics at 300 K without solvent, and (c) after a 100-ps run of molecular dynamics at 300 K, 1 atm with an explicit solvent. In the absence of a solvent the dendron collapsed completely within 100 ps, whereas in the pres-

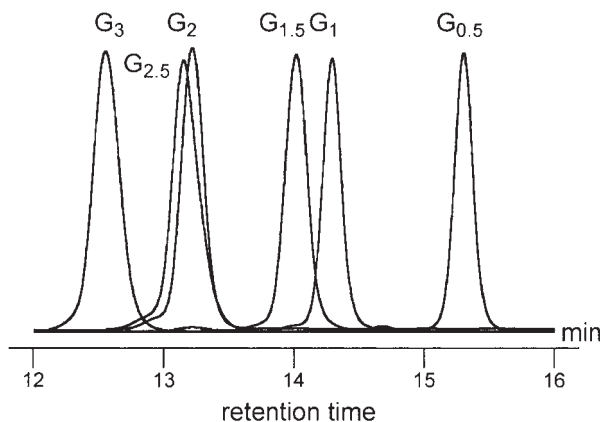


Fig. 5. Analytical gel-permeation chromatograms of the dendrons of $G_{0.5-3}$.

ence of a solvent the dendron retained its extended conformation during the same time period. These results reveal the presence of spatial “voids” in this molecule, which can only be maintained by solvation. They also emphasize the importance of including explicit solvent molecules in a simulation of this type of dendrons.

The microscopic structure around the innermost (i.e., closest to the core) carboxylate functional groups are further pictured by calculating the radial distribution functions of both the solvent and dendron atoms (Fig. 7). With explicit solvents (part (a)), no dendron atoms, but the solvent atoms, are found at distances less than 5 Å. On the other hand, the results without explicit solvents (part (b)) show the presence of dendron atoms at distances as short as 3 Å. These results suggest high accessibility of the ester functional groups from the solution phase.

Formation of Micelles by the Carboxylate Salt Form of the G_3 Dendron. In order to examine the micelle-forming properties of these dendrons, the carboxylate salt form of the G_3 dendron, $G_3(\text{CO}_2\text{Na})$, was prepared by neutralization of $G_3(\text{CO}_2\text{H})$ with an equivalent amount of aqueous sodium hydroxide. After 5 min of sonication, the following solvents gave uniform emulsions: THF, CH_2Cl_2 , CHCl_3 , and CH_3CN . On the other hand, MeOH, EtOH, acetone, hexane, EtOAc, and water did not give emulsions, but suspensions of amorphous solid materials. Among the examined solvents, only a THF/water mixture gave a colorless transparent solution with the $G_3(\text{CO}_2\text{Na})$ when the water fraction was 2–45% by volume. When the water fraction was less than 2%, part of $G_3(\text{CO}_2\text{Na})$ precipitated. As the water fraction increased from 45%, the solution turned white and turbid, and became opaque when the water fraction was more than 60%, suggesting the formation of micelles.

The average diameters of micellar particles were estimated by dynamic light scattering (DLS) measurements. Figure 8 shows the results, together with the intensities of the scattered light. From 90% to 60% of water fraction, the intensities were slightly diminished, and the estimated diameters increased from 100 to 400 nm. From 60% to 45%, the diameters changed irregularly between 200–700 nm, and intensities were drastically diminished. From 45% to 0%, the intensities were constantly low, suggesting that very small amount of large micellar particles were present; the estimated diameters were almost constant at around 400 nm.

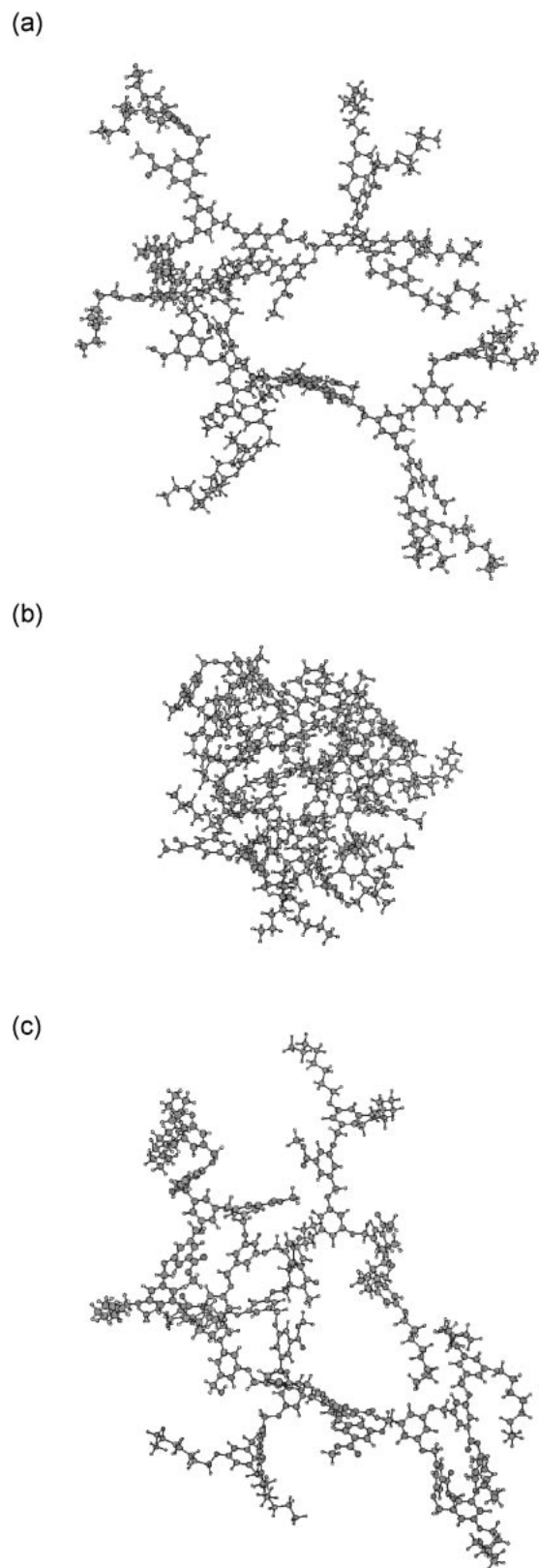


Fig. 6. Ball-and-stick representations of the G_3 dendron, (a) before the MD run, (b) after 100-ps MD without solvent, and (c) after 100-ps MD with explicit solvent.

Figure 9 shows a model to account for these results. From 90–60% of water, the dendron molecules form normal micelles

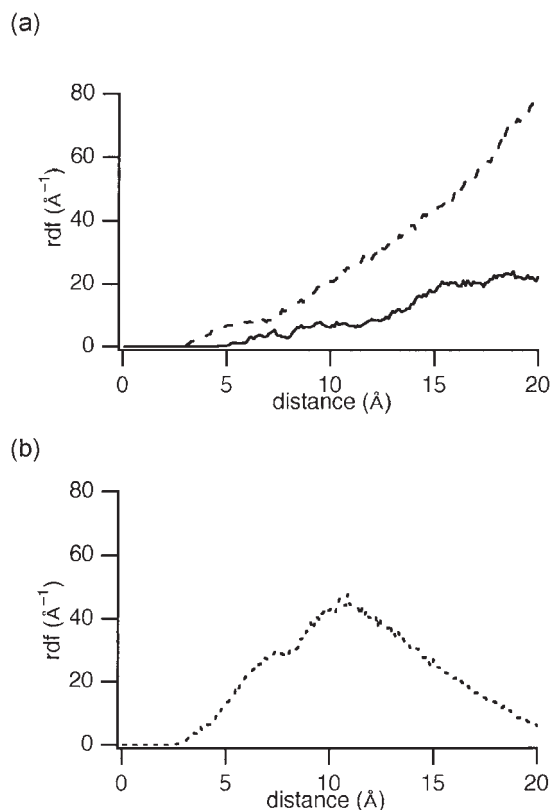


Fig. 7. The radial distribution functions from the innermost ester carbonyl atoms. (a) Calculated from the MD results with explicit solvents; the dendron atoms (solid line) and the solvent atoms (dotted line). (b) Calculated for the dendron atoms from the MD results without solvent. For the dendron atoms, those atoms are omitted that are included in or directly connected to the aromatic ring to which the ester carbonyl atom in question is attached.

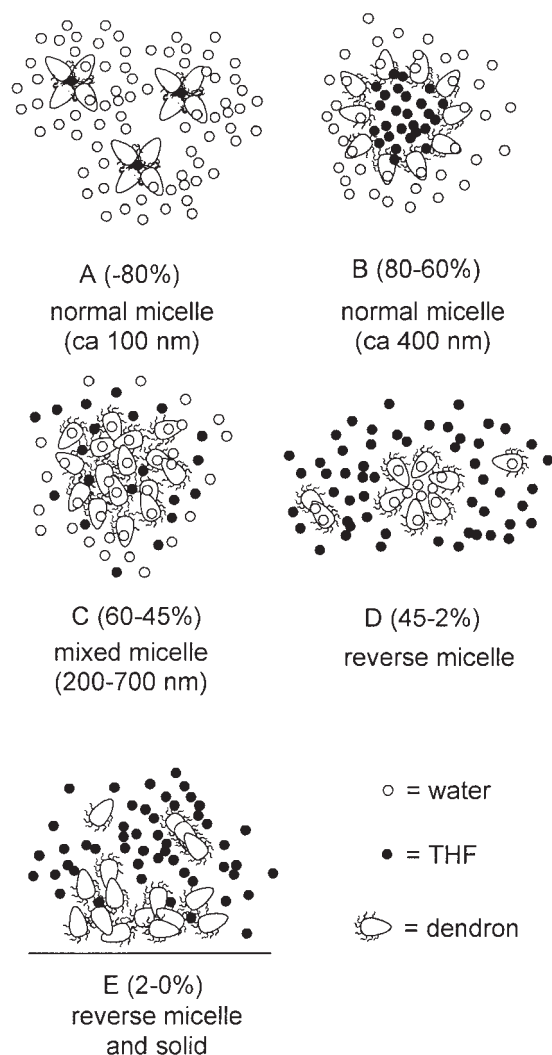


Fig. 9. A proposed model of switching between normal and reverse micelles in a mixed solvent of THF/water.

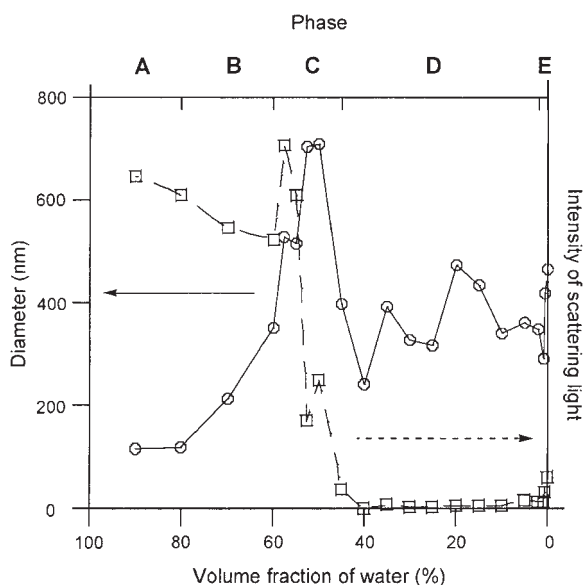


Fig. 8. Estimated average diameters of micelles (solid line, circle) and intensities of the scattered light (broken line, square) at various volume fractions of water.

with hydrophobic octyloxy groups and THF inside (phase A). As the fraction of THF in solution increases, the micellar particles continue to swell by uptaking more THF molecules (phase B). However, between 60–45% of water, these micellar particles become unstable, and break down to form smaller particles of reverse micelle (phase C). Note that these dendrons, which have hydrophilic groups inside and hydrophobic groups outside, can form reverse-micelles structurally more easily than normal micelles. Consequently, the reverse-micelle particles in this phase may consist of a smaller number of dendrons, or may even be unimolecular. From 45% to 2% of water, these small reverse-micelle particles are mainly present together with a small number of large (ca. 400 nm) particles (phase D). When the water fraction is less than 2%, the dendrons are no longer capable to form reverse micelles and begin to precipitate as solid (phase E).

In summary, we developed new dendrons with internal carboxyl groups. The introduction of a spacer group made these dendrons spatially relaxed, which caused high reactivity both in the growth process of the dendritic framework and in the final manipulation of the internal carboxyl groups. The structural feature led to interesting reverse/normal switching of micelle

formation. The utilization of these dendrons for the development of new materials is currently underway.

Experimental

THF and CH_2Cl_2 were distilled from sodium diphenylketyl and CaH_2 , respectively. Other reagents were obtained commercially and used as received. ^1H NMR spectra (500 MHz) were measured on a JEOL LAMBDA-500 spectrometer and chemical shifts were reported in the δ scale relative to CHCl_3 (7.24) and $\text{DMSO}-d_6$ (2.49) in ppm. MALDI-TOF-MS was performed on an Applied Biosystems Voyager System DE-DTR using 2-(4-hydroxyphenyl)-azo)benzoic acid as a matrix. GPC experiments were performed on a Japan Analytical Industry Co. model LC-908 with JAIGEL 2H/2.5H (preparative) and TOSOH model GPC-8020 (analytical). The analytical chromatograms were obtained under the following conditions; columns, TSKgel super HM-H/HM-M/H3000; solvent, CHCl_3 ; flow rate, 0.6 mL/min; column temperature, 30 °C. Medium-pressure preparative column chromatography was performed with Yamazen PUMP540-2CSC and Wakogel C-200 silica gel. DLS was performed on an Otsuka Electronics model DLS-6000. The intensity of scattering light was analyzed on a Shimadzu RF-5300PC spectrofluorometer.

Methyl 3-(*t*-Butyldimethylsilyloxy)-5-(hydroxymethyl)benzoate (2). LiAlH_4 (1.90 g, 50.0 mmol) was added in portions to a solution of **1** (32.5 g, 100 mmol) in THF (100 mL) at 0 °C. The mixture was stirred vigorously for 30 min, then quenched slowly with water (3.60 mL). The solid was filtered and washed with CH_2Cl_2 (500 mL). The combined filtrate was concentrated and purified by column chromatography (silica gel, hexane/AcOEt). Colorless oil. Yield 16.3 g (55%). ^1H NMR (500 MHz, CDCl_3) δ 7.59 (s, 1H, 6- C_6H_3), 7.37 (s, 1H, 2- C_6H_3), 7.03 (s, 1H, 4- C_6H_3), 4.66 (s, 2H, CH_2), 3.87 (s, 3H, $-\text{CO}_2\text{Me}$), 1.94 (s, 1H, $-\text{OH}$), 0.97 (s, 9H, *t*-Bu), and 0.19 (s, 6H, Me).

Methyl 3-Hydroxy-5-(hydroxymethyl)benzoate (3). A solution of KF (5.81 g, 100 mmol) in MeOH (150 mL) was added to **2** (14.7 g, 50.0 mmol) at room temperature, and then the solution was stirred for 10 min, followed by the addition of 4 M HCl aq. (12.5 mL). After removal of the solvent, MeOH (20 mL), CHCl_3 (400 mL), and anhydrous Na_2SO_4 were added. The solid was filtered and washed with CHCl_3 (200 mL), and the combined filtrate was evaporated. The residue was recrystallized with hot CHCl_3 (50 mL). Yield 8.70 g (96%). ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 9.74 (s, 1H, OH), 7.36 (s, 1H, 6- C_6H_3), 7.19 (s, 1H, 2- C_6H_3), 6.97 (s, 1H, 4- C_6H_3), 5.25 (t, 1H, $J = 6$ Hz, CH_2OH), 4.46 (d, 2H, $J = 6$ Hz, CH_2), and 3.81 (s, 3H, CO_2Me).

General Procedure for the Synthesis of the Benzylic Bromide from the Alcohol (Procedure A). CBr_4 was dissolved in a solution of benzylic alcohol in THF at 0 °C for 1–2 min. PPh_3 was added, and when all solids were dissolved (1–2 min), the solution was stirred under N_2 at room temperature. A white precipitate appeared after 5–8 min. Before the color turned yellowish, the resulting mixture was cooled to 0 °C and monitored by ^1H NMR and TLC. CBr_4 and PPh_3 were added if necessary, until NMR and TLC showed no starting benzylic alcohol. After the usual workup, the product was purified by two consecutive column chromatography (silica gel, CH_2Cl_2 , then hexane/EtOAc).

General Procedure for Formation of the Ether Linkage (Procedure B). The bromide, the phenolic compound (**3** or **4**), 18-crown-6, and K_2CO_3 were suspended in acetone, and the suspension was purged with Ar. The resulting suspension was stirred vigorously and heated at 80 °C. The usual workup and purification

by column chromatography (silica gel hexane/EtOAc, and/or preparative GPC) gave the product.

Compound G₁. 3,5-Bis(octyloxy)benzyl bromide¹¹ (15.1 g, 35.4 mmol), **3** (10.7 g, 58.9 mmol), K_2CO_3 (6.1 g, 44 mmol), and 18-crown-6 ether (0.703 g, 2.66 mmol) in acetone 350 mL were allowed to react according to Procedure B to give **G_{0.5}** (12.8 g, 69%). **G_{0.5}** (5.29 g, 10.0 mmol) was converted to the bromide (5.70 g, 9.60 mmol, 96%) according to Procedure A (CBr_4 , 4.97 g, 15.0 mmol; PPh_3 , 3.94 g, 15.0 mmol; THF, 40 mL). This bromide (4.97 g, 8.40 mmol) was allowed to react with **4** (0.561 g, 4.00 mmol) in the presence of K_2CO_3 (2.76 g, 20.0 mmol) and 18-crown-6 (0.317 g, 1.20 mmol) in acetone (50 mL) for 30 min according to Procedure B, to give **G₁** (4.34 g, 93%). ^1H NMR (CDCl_3) δ 7.68 (s, 2H, Ar), 7.57 (s, 2H, Ar), 7.23 (s, 2H, Ar), 6.59 (d, 2H, $J = 2$ Hz, Ar), 6.54 (d, 4H, $J = 2$ Hz, Ar), 6.50 (t, 1H, $J = 2$ Hz, Ar), 6.39 (t, 2H, $J = 2$ Hz, Ar), 5.02, 5.01 (2s, 4H + 4H, $\text{ArOCH}_2\text{Ar}'$), 4.62 (s, 2H, CH_2OH), 3.92 (t, 8H, $J = 7$ Hz, OCH_2CH_2), 3.89 (s, 6H, CO_2Me), 1.74 (m, 8H, OCH_2CH_2), 1.41 (m, 8H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.22–1.30 (m, 32H, CH_2), and 0.86 (m, 12H, CH_3). HRMS (MALDI-TOF). Found: m/z 1183.710. Calcd for $[\text{M} + \text{Na}]^+$ 1183.706.

Compound G₂. **G₁** (3.72 g, 3.20 mmol) was converted to the bromide (3.85 g, 3.14 mmol, 98%) according to Procedure A (CBr_4 , 2.65 g, 8.00 mmol; PPh_3 , 2.10 g, 8.00 mmol; THF 24 mL). This bromide (3.67 g, 3.00 mmol) was allowed to react with **3** (0.574 g, 3.15 mmol) in the presence of K_2CO_3 (0.518 g, 3.75 mmol) and 18-crown-6 ether (0.0596 g, 0.225 mmol) in acetone (64 mL) for 2 h according to Procedure B, to give **G_{1.5}** (4.34 g, 93%). **G_{1.5}** (3.98 g, 3.00 mmol) was converted to the bromide (3.75 g, 90%) according to Procedure A (CBr_4 , 5.97 g, 18.0 mmol; PPh_3 , 4.72 g, 18.0 mmol; THF, 40 mL). This bromide (2.63 g, 1.89 mmol) was allowed to react with **4** (0.126 g, 0.900 mmol) in the presence of K_2CO_3 (0.622 g, 4.50 mmol) and 18-crown-6 (0.0713 g, 0.270 mmol) in acetone (36 mL) for 2 h according to Procedure B to give **G₂** (2.28 g, 91%). ^1H NMR (500 MHz, CDCl_3) δ 7.69 (s, 4H, Ar), 7.68 (s, 2H, Ar), 7.57 (m, 4H, Ar), 7.56 (m, 2H, Ar), 7.24 (s, 4H, Ar), 7.21 (s, 2H, Ar), 6.67 (d, 4H, $J = 2$ Hz, Ar), 6.59 (d, 2H, $J = 2$ Hz, Ar), 6.55 (m, 10H, Ar), 6.49 (t, 1H, $J = 2$ Hz, Ar), 6.39 (t, 4H, $J = 2$ Hz, Ar), 4.99–5.02 (4s, 24H, $\text{ArOCH}_2\text{Ar}'$), 4.59 (d, 2H, $J = 6$ Hz, CH_2OH), 3.91 (t, 16H, $J = 7$ Hz, OCH_2CH_2), 3.88 (s, 18H, CO_2Me), 1.99 (t, 1H, $J = 7$ Hz, OH), 1.74 (m, 16H, OCH_2CH_2), 1.41 (m, 16H, $\text{OCH}_2\text{CH}_2\text{CH}_2$), 1.26–1.31 (m, 64H, CH_2), and 0.86 (t, 24H, $J = 7$ Hz, CH_3). HRMS (MALDI-TOF). Found: m/z 2776.541, 2792.536. Calcd for $[\text{M} + \text{Na}]^+$ 2776.543, $[\text{M} + \text{K}]^+$ 2792.517.

Compound G₃. **G₂** (1.76 g, 0.640 mmol) was converted to the bromide (1.73 g, 96%) according to Procedure A (CBr_4 , 1.27 g, 3.84 mmol; PPh_3 , 1.01 g, 3.84 mmol; THF 20 mL). This bromide (1.58 g, 0.560 mmol) was allowed to react with **3** (0.107 g, 0.588 mmol) in the presence of K_2CO_3 (97 mg, 0.70 mmol) and 18-crown-6 (11 mg, 0.042 mmol) in acetone (30 mL) for 2 h according to Procedure A, to give **G_{2.5}** (1.22 g, 75%). **G_{2.5}** was converted to the bromide (0.897 g, 91%) according to Procedure A (CBr_4 , 0.657 g, 1.98 mmol; PPh_3 , 0.519 g, 1.98 mmol; THF, 40 mL). This bromide (0.815 g, 0.273 mmol) was allowed to react with **4** (18.2 mg, 0.130 mmol) in the presence of K_2CO_3 (90 mg, 0.65 mmol) and 18-crown-6 (10 mg, 0.039 mmol) in acetone (16 mL) for 2 h according to Procedure B, to give **G₃** (0.422 g, 55%). ^1H NMR (500 MHz, CDCl_3) δ 7.64–7.68 (m, 14H, Ar), 7.51–7.57 (m, 14H, Ar), 7.17–7.24 (m, 14H, Ar), 6.65–6.68 (m, 12H, Ar), 6.47–6.55 (m, 25H, Ar), 6.37 (m, 8H, Ar), 4.94–4.99 (m, 56H, $\text{ArOCH}_2\text{Ar}'$), 4.54 (s, 2H, CH_2OH), 3.84–3.90 (m, 74H, OCH_2CH_2 , CO_2Me),

1.70 (m, 32H, OCH₂CH₂), 1.38 (m, 32H, OCH₂CH₂CH₂), 1.23–1.26 (m, 128H, CH₂), and 0.84 (t, 48H, *J* = 7 Hz, CH₃). HRMS (MALDI-TOF). Found: *m/z* 5962.223, 5978.103. Calcd for [M + Na]⁺ 5962.218, [M + K]⁺ 5978.191.

G₃(CO₂H). To a solution of G₃ (96 mg, 0.016 mmol) in THF (5 mL) was added KOH (0.39 g, 6.95 mmol) in water (0.6 mL). MeOH (2 mL) was added to the two-phase mixture to afford a homogeneous solution. The reaction mixture was heated at 80 °C for 3 h and monitored by ¹H NMR. The solution was quenched by HCl aq. and worked up usually, to give the product (86 mg, 94%). ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.57–7.60 (m, 14H, Ar), 7.41–7.45 (m, 14H, Ar), 7.26–7.27 (m, 14H, Ar), 6.69–6.71 (m, 12H, Ar), 6.60–6.63 (m, 4H, Ar), 6.50–6.55 (m, 21H, Ar), 6.32 (m, 8H, Ar), 5.00–5.08 (m, 56H, ArOCH₂Ar'), 4.38 (s, 2H, CH₂OH), 3.82 (t, 32H, *J* = 6 Hz, OCH₂CH₂), 1.58 (m, 32H, OCH₂CH₂), 1.27 (m, 32H, OCH₂CH₂CH₂), 1.16–1.22 (m, 128H, CH₂), and 0.78 (t, 48H, *J* = 7 Hz, CH₃).

Molecular Dynamics Calculations. The initial geometry of the G₃ dendron was obtained by building a molecular model with the Chem 3D program package. The atom types and force field parameters were taken from general Amber force field (GAFF). The RESP (restrained ElectroStatic Potential fit) atomic charge¹⁵ were obtained by a quantum mechanical calculation (HF/6-31G*) with the Gaussian 98,¹⁶ followed by a treatment with the ANTECHAMBER module of AMBER 7. Since the G₃ dendron was too large to calculate, the G₁ and G_{1.5} dendron were calculated, and the RESP charges were transferred to the G₃ dendron for atoms with similar topology and offset by a constant value to maintain the neutrality of the whole molecule. The Amber topology and parameter files were generated by the tLeap module of AMBER 7. For a simulation with an explicit solvent, a rectangular box was added, providing at least 10 Å of CHCl₃ around any atom. Molecular-dynamics calculations were carried out by using the SANDER module of Amber 7.0 with SHAKE¹⁷ applied to all hydrogen atoms and 2-fs time steps. Berendsen temperature coupling¹⁸ was used with a time constant of 0.5 ps. The in-vacuo simulation protocol involved three sequential phases: energy minimization for 500 steps, slow heating from 0 to 300 K over 10 ps, and production run at 300 K for 100 ps. Generalized Born model¹⁹ with dielectric constant of 1.0 was used, and a 20-Å cutoff was applied. The simulation with a solvent box involved seven sequential phases: energy minimization for 500 steps with constraints of 500 kcal/mol/Å² on the solute atoms, two-stage initial equilibration of the solvent with constraints of 10 kcal/mol/Å² on the solute atoms (stage 1: constant volume, heating from 100 to 300 K over 1 ps and keeping at 300 K for 24 ps; stage 2: 24 ps at 300 K, constant pressure at 1 atm), two successive minimizations for 600 steps with constraints of 50 kcal/mol/Å² and 0 on the solute atoms, pre-equilibration of the whole system at constant volume (heating from 100 to 300 K over 1 ps and keeping at 300 K for 24 ps), and production run at 300 K, 1 atm for 100 ps. Long-range electrostatic forces were evaluated using the particle mesh Ewald method.²⁰ A 9-Å cutoff was applied. A constant procedure was maintained with isotropic molecule based scaling. All calculations were performed on an NEC SX-7 computer.

Micellization Experiments. Aqueous NaOH (10 mg, 0.25 mmol in 0.3 mL) was added to a solution of G₃(CO₂H) (101 mg, 0.018 mmol) in CHCl₃ (30 mL). The turbid mixture was stirred for 10 min. After removal of the solvent, G₃(CO₂Na) was dried in vacuo. For DLS measurements, *x* mL of THF and (2 – *x*) mL of water was added to 2.0 mg of G₃(CO₂Na) (0.33 μmol), and the mixture was sonicated for 5 min. In order to calculate diameters,

the viscosities and refractive indices of aqueous mixtures of THF were taken from the literature.²¹ The intensities of the scattered light were measured with light of 530 nm wavelength as incident light, and the value of the peaktop intensity was adopted.

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