Notes

Exploring the Reversibility of the Ring-Closing Metathesis Mediated Cross-linking of Dendrimers

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Received June 3, 2007
Revised Manuscript Received July 16, 2007

Introduction

The ring closing metathesis reaction has become a powerful and, thus, ubiquitous method for preparing medium and large ring systems.[1] Ruthenium-based catalysts such as **1** and **2** (Figure 1) have been employed to produce a diversity of compounds including natural products,[2] artificial polymers,[3] and mechanically interlocked compounds.[4] Macrocyclic systems using the ring-closing metathesis (RCM) reaction such as metallomacrocycles,[5] nanotubes,[6] monomolecularly imprinted dendrimers (MIDs),[7] and a triply threaded molecular bundle[8] have been described. A monometallic complex has been used as a template to ensure the desired geometry in the synthesis of metallomacrocycles,[5] catenanes,[9] molecular knots,[10] and molecular wires.[11] Stoddart and Grubbs reported the template-directed olefin metathesis using metal ion templation under thermodynamic control to prepare a rotaxane.[4b−d] Here, we analyze the reversibility of the RCM process in a complex macromolecular system related to MIDs.

It was suggested previously that the RCM-mediated cross-linking of dendrimers is an excellent approach to MIDs because the reversibility of the ruthenium catalyst allows dynamic molding of the dendritic framework around the template.[7] In prior studies, the rate of cross-linking[12] and the extent of inter-dendron vs intra-dendron cross-linking was investigated, but definitive evidence for reversibility in the RCM was not obtained.[13,14] Herein, we describe a simple test of whether metathesized end groups of a dendrimer are able to open and close again. As shown in Scheme 1 the strategy involves examining whether Grubbs catalyst **1** or **2** is capable of fully cross-linking dendrimer **7** in which two of the three dendrons have already undergone the RCM reaction. If all three dendrons become interconnected, hydrolysis will afford **8**; otherwise, **9** and **10** will result. Our previous work used **1** nearly exclusively,[6,7,12,13] but we chose additionally to examine **2** because it is more reactive[15] and displays greater functional group tolerance.[1b]

Results and Discussion

The synthesis of **7** began by coupling mono-TBDMS-protected 1,1,1-tris(hydroxymethyl)ethane[16] and [G-3] acid chloride dendron **3**[17] to produce dendrimer **4** (Scheme 1). Deprotection of the silyl group followed by cross-linking with first generation Grubbs catalyst **1** at high dilution produced didendron **6**, which was fully cross-linked. The RCM product was carefully purified by preparative size exclusion chromatography (SEC) and characterized by both ^{1}H NMR and MALDI−TOF−MS, both techniques indicating complete metathesis. Subsequent coupling with excess **3** provided key dendrimer **7** in which two of the three dendritic wedges are fully cross-linked.

Using standard conditions,[17] portions of dendrimer **7** were treated in separate reactions with 1.0 equiv (6 mol % per alkene) of Grubbs catalyst **1** and **2** in benzene at a concentration of 10^{-5} M at room temperature. An additional 1.0 equiv of catalyst was added on day 2 and 3 for a total of 3.0 equiv. Nearly complete cross-linking was observed by MALDI−TOF−MS

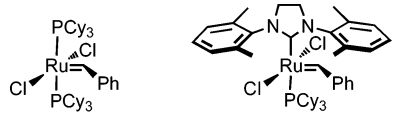
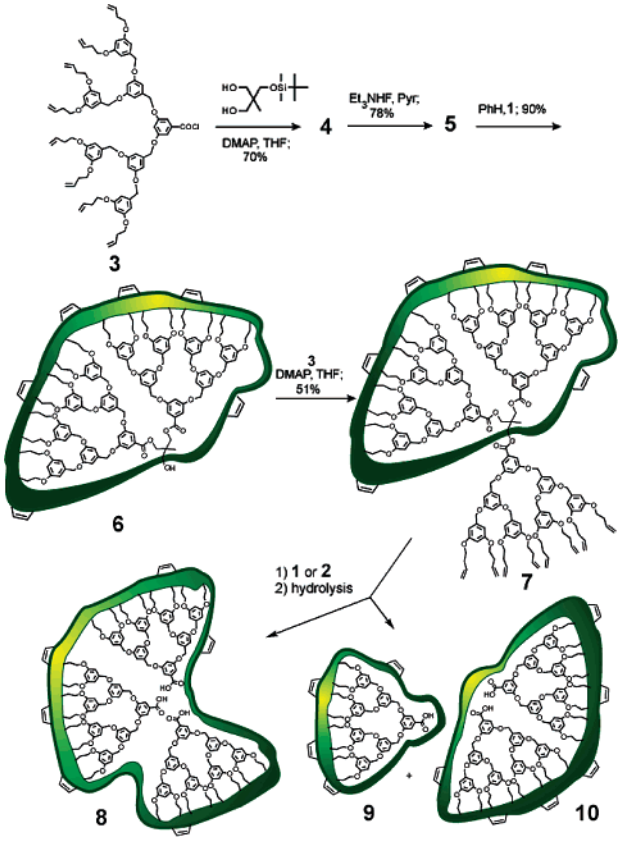


Figure 1. Catalysts used for RCM reaction.

Scheme 1. Synthesis of Dendrimer 7 and Test for Dynamic Cross-Linking



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10.1021/ma071233e CCC: $37.00
Published on Web 09/29/2007

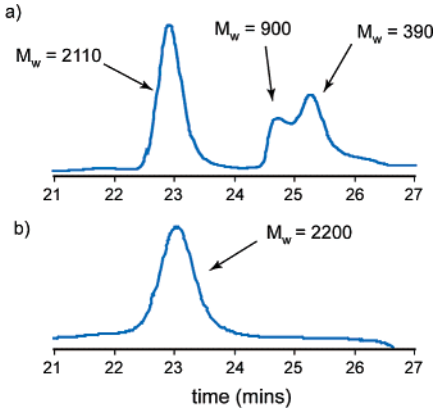


Figure 2. Analytical SEC spectra of dendrimer **7** after cross-linking and hydrolysis using (a) catalyst **1** and (b) catalyst **2**.

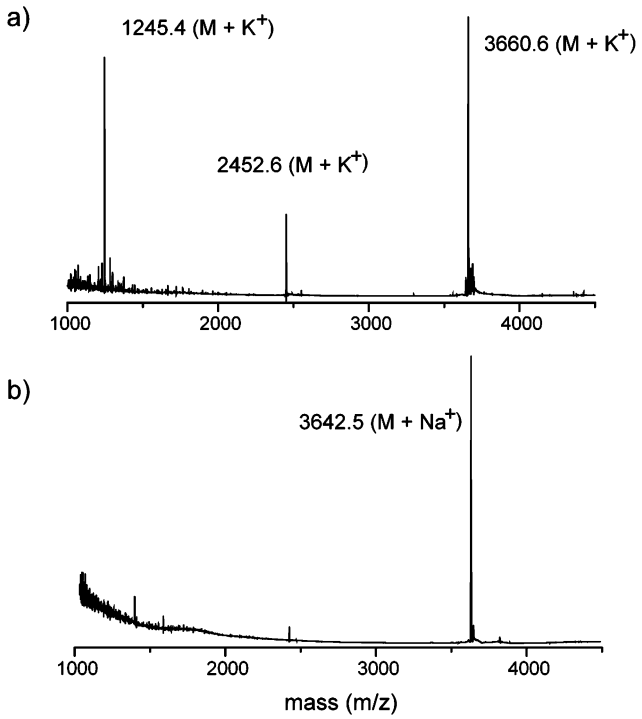


Figure 3. MALDI−TOF−MS spectra of dendrimer **7** after cross-linking and hydrolysis using (a) catalyst **1** and (b) catalyst **2**.

after 3 days, however, the reactions proceeded for 7 days to ensure complete cross-linking. As usual, oligomerization was not observed for any of the RCM reactions under these conditions.

The product of the RCM reaction was hydrolyzed by treatment with 2 M aqueous KOH in ethanol-THF at reflux for 12 h. The product was characterized by analytical SEC and MALDI−TOF−MS. As seen in Figure 2a, the RCM reaction of dendrimer **7** using catalyst **1** underwent significant hydrolytic fragmentation. Separation of the products by preparative SEC indicated a ca. 60:40 ratio of **8** to **9** + **10**, consistent with the SEC integration. The MALDI−TOF mass spectra also revealed fragmentation (Figure 3a), and further showed that **8** was fully cross-linked so **1** was active and undergoing the RCM reaction.

In contrast to the results with **1**, treatment of dendrimer **7** with catalyst **2** followed by hydrolysis produced **8** exclusively. Thus, as seen in the analytical SEC (Figure 2b) and MALDI−TOF mass spectra (Figure 3b), only tridendron **8** is observed, and within the limits of detection of the SEC and MALDI−TOF methods, no **9** or **10** are seen. Although these data can be

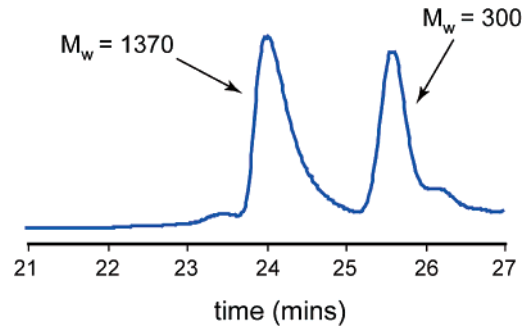


Figure 4. Analytical SEC spectrum of dendrimer **12** after cross-linking and hydrolysis.

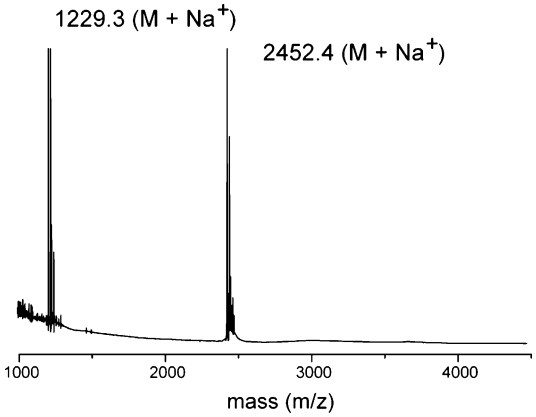
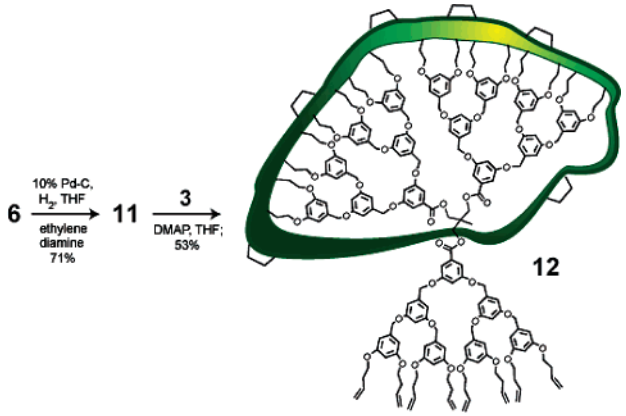


Figure 5. MALDI−TOF−MS of dendrimer **12** after cross-linking and hydrolysis.

Scheme 2. Synthesis of Dendrimer 12, an Analog of 7 with Alkenes Reduced to Prevent RCM Reaction



interpreted in terms of reversible cross-linking leading all three dendrons to become linked, it is also possible that the connection to the third dendron is mechanical.

To exclude the possibility that the third dendron undergoes an RCM reaction that links it to the other dendrons (e.g., catenation), an analog of **7** was prepared with the disubstituted alkenes fully reduced (see **12**). Thus, as outlined in Scheme 2, **6** was hydrogenated with 10 mol % Pd−C deactivated with ethylene diamine to avoid hydrogenolysis of the benzyl ether groups. Coupling dendrimer **11** with acid chloride **3** produced **12**. Cross-linking dendrimer **12** with **1** using standard conditions followed by hydrolysis exclusively produced fragmented products corresponding to **9** and **10** with reduced alkene groups. Thus, only peaks corresponding to fully cross-linked **9** and reduced **10** were observed by analytical SEC (Figure 4) and MALDI−TOF−MS (Figure 5). Therefore, it was concluded that the formation of **8** was indeed through the formation of cross-

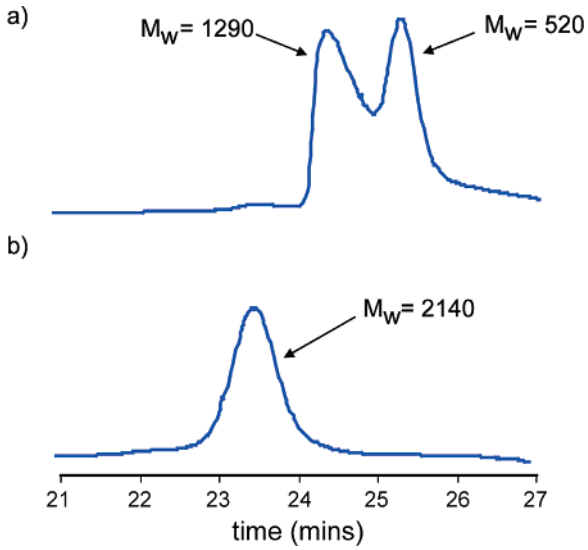


Figure 6. Analytical SEC spectra of dendrimer **14** after cross-linking and hydrolysis using (a) catalyst **1** and (b) catalyst **2**.

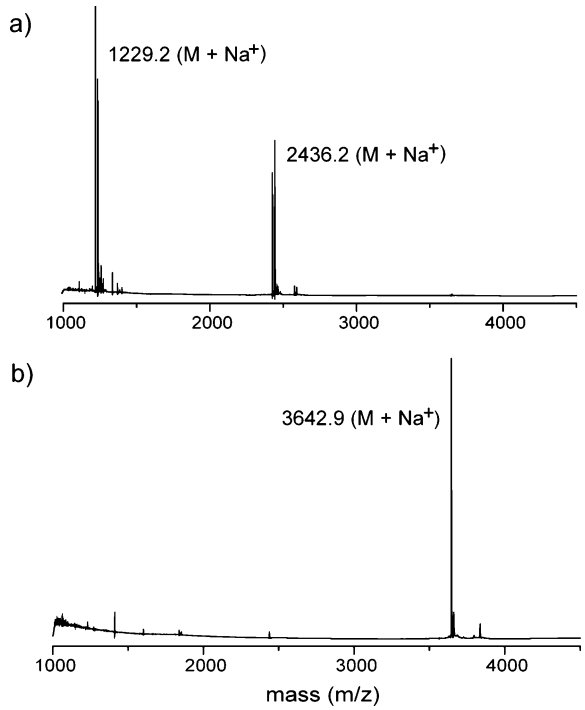
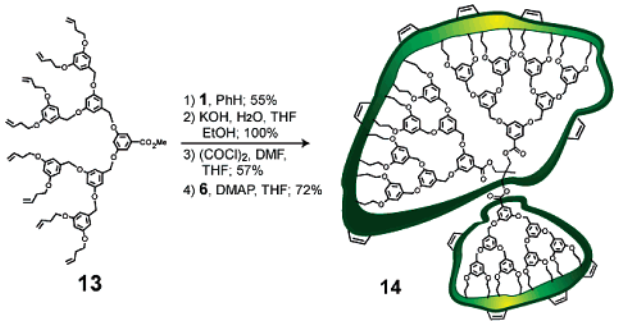


Figure 7. MALDI−TOF−MS of dendrimer **14** after cross-linking and hydrolysis using (a) catalyst **1** and (b) catalyst **2**.

links between the three dendrons.

It was previously shown that in a related system, inter-dendron cross-linking is favored.[13] What was not known in that case was whether kinetic or thermodynamic products were produced. The finding that preformed cross-links in two of the three dendrons of **7** are opened and linked to the third dendron provides evidence that longer range RCM products are preferred thermodynamically in these kinds of dendrimers. However, one question remaining is whether catalyst **1** or **2** can rearrange the cross-links in a fully cross-linked dendrimer. In partially cross-linked **7**, the reaction with **1** and **2** presumably involves initial metathesis with a terminal alkene producing a new ruthenium carbene covalently connected to the uncross-linked dendron. This carbene may react with a disubstituted alkene in the precross-linked dendrons through an intramolecular metathesis reaction. To answer this question, dendrimer **14** was synthesized as outlined in Scheme 3.

Scheme 3. Synthesis of 14, an Analog of 7 with the Third Dendron Intramolecularly Cross-Linked



Cross-linking the [G-3] methyl ester **13** with **1** using standard conditions followed by hydrolysis and reaction with oxalyl chloride produced the [G-3] acid chloride dendron. The cross-linked acid chloride was coupled to dendron **6** to afford dendrimer **14**. Two portions of dendrimer **14** were cross-linked independently using 1.0 equiv (6 mol % per alkene) of **1** and **2** using standard conditions. An additional 1.0 equiv of catalyst was added on day 2 and day 3. Fully cross-linked dendrimers were hydrolyzed to afford cored dendrimers. After hydrolysis, the dendrimer cross-linked using **1** fragmented into two dendrons (**9** and **10**) with no **8** observed by analytical SEC (Figure 6a) or MALDI−TOF−MS (Figure 7a). In contrast, the dendrimer treated with **2** formed **8** exclusively as evidenced by the analytical SEC (Figure 6b) and MALDI−TOF mass spectrum (Figure 7b). These results clearly indicate that catalyst **2** allows for rearrangement of fully cross-linked dendrimers, whereas catalyst **1** does not alter the inter-dendron connections.

Conclusion

Previously reported studies of molecularly imprinted dendrimers (MIDs)[7] and dendritic nanoparticles[12] utilized catalyst **1**. This work shows that the rearrangement of cross-links in those systems is possible provided at least one terminal alkene is present. However, to achieve more extensive dynamic molding, and presumably, structures that better represent thermodynamic products, the second generation catalyst **2** is preferred. This catalyst was avoided primarily because its higher activity made it more difficult to fully quench making some inter-dendrimer reaction possible during workup. It is likely that the results reported here can be extended to other systems where the opening and closing of rings made by metathesis is desired.

Experimental Section

Materials and Methods. All reactions were carried out under a nitrogen atmosphere. All solvents were of reagent grade and purchased commercially. THF was distilled over sodium and benzophenone. All NMR spectra were collected on a Varian Unity 400 or 500 MHz spectrometer and $CDCl_3$ was used as the solvent. The ^1H NMR chemical shifts were reported in parts per million (ppm) and were referenced to the residual protio-solvent peak at 7.26 ppm in chloroform-*d*. The ^{13}C NMR chemical shifts were reported in parts per million (ppm) and were referenced to the solvent peak at 77.0 ppm in chloroform-*d*.

Preparative SEC was performed using a 5.25 ft × 50 mm or 1.5 ft × 30 mm column of Bio-Beads S-X1 beads 200−400 mesh (Bio-Rad) using reagent grade toluene as eluent. Analytical SEC was performed using a 2 × Styragel HR3, 1 × Styragel HR4E column in THF with a 1.0 mL/min flow rate. Detection of peaks was achieved using a Viscotek triple array 300 refractive index detector with SEC-derived molecular weights based on conventional calibration with linear polystyrene. High-resolution MALDI−TOF mass

spectra were recorded on a PerSeptive Biosystems Voyager DE-STR spectrometer using *trans*-3-indoleacrylic acid (IAA) as matrix.

Commercially available first generation Grubbs catalyst **1** and second generation Grubbs catalyst **2** were purchased from Aldrich and used without additional purification. The [G-3] acid chloride **3**,[17] the [G-3] methyl ester **13**,[7] and 1,1,1-tris(hydroxymethyl)-ethane[16] were prepared according to previously published procedures.

2-(*tert*-Butyldimethylsilanyloxymethyl)-2-methyl-1,3-bis{3,5-bis[3,5-bis(3,5-bis(3-buten-1-oxy)benzyloxy)benzyloxy]benzyloxy}-propane (4). To 0.033 g (0.14 mmol) of 2-(*tert*-butyl-dimethyl-silanyloxymethyl)-2-methylpropane-1,3-diol in 8 mL of THF were added 0.55 g (0.41 mmol) of acid chloride dendron **3** and 0.10 g (0.085 mmol) of DMAP. The reaction mixture was heated to 60 °C. After 24 h, the solid was filtered and the solvent was removed in vacuo. The resulting brown oil was purified using column chromatography (silica gel, 4:1 PE/EtOAc) followed by a SEC column (toluene) to obtain 0.28 g (70%) of a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, 4H, J = 2.4), 6.77 (t, 2H, J = 2.4), 6.66 (d, 8H, J = 2.4), 6.55 (d, 16H, J = 2.4), 6.53 (t, 4H, J = 2.4), 6.39 (t, 8H, J = 2.4), 5.87 (ddt, 16H, J = 17.2, 10.4, 6.4), 5.14 (ddt, 16H, J = 17.2, 1.6, 1.6), 5.08 (ddt, 16H, J = 10.4, 1.6, 1.6), 4.94 (s, 8H), 4.92 (s, 16H), 4.31 (s, 4H), 3.97 (t, 32H, J = 6.8), 3.61 (s, 2H), 2.50 (dt, 32H, J = 6.8, 6.4, 1.6), 1.10 (s, 3H), 0.86 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 160.5, 160.4, 160.0, 139.2, 139.0, 134.6, 132.3, 117.3, 108.5, 106.6, 106.2, 105.5, 101.9, 101.2, 70.4, 70.3, 67.4, 40.8, 33.8, 29.9, 26.0, 18.4, 8.7, −5.4; MS (MALDI−TOF) m/z 2859.1 (M + Na^+), 2875.0 (M + K^+).

2-Hydroxymethyl-2-methyl-1,3-bis{3,5-bis[3,5-bis(3,5-bis(3-buten-1-oxy)benzyloxy)benzyloxy]benzyloxy}propane (5). A solution of 0.17 g (0.060 mmol) of dendrimer **4**, 0.080 mL (0.49 mmol) of triethylaminetrihydrofluoride, and 5 mL of pyridine was stirred for 20 h. The reaction was quenched by adding 20 mL of H_2O and 1 M HCl until pH < 5 and the solvent was removed under reduced pressure. The resultant solution was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with H_2O, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting yellow oil was purified by silica gel chromatography (9:1 PE/EtOAc to 7:3 PE/EtOAc) to afford 0.13 g (78%) of a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, 4H, J = 2.4), 6.77 (t, 2H, J = 2.4), 6.65 (d, 8H, J = 2.4), 6.55 (d, 16H, J = 2.0), 6.53 (t, 4H, J = 2.4), 6.39 (t, 8H, J = 2.0), 5.87 (ddt, 16H, J = 17.2, 10.4, 6.4), 5.14 (ddt, 16H, J = 17.2, 1.6, 1.6), 5.08 (ddt, 16H, J = 10.4, 1.6, 1.6), 4.94 (s, 8H), 4.92 (s, 16H), 4.32 (s, 4H), 3.97 (t, 32H, J = 6.8), 3.53 (s, 2H), 2.5 (dt, 32H, J = 6.8, 6.4, 1.6), 1.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 160.5, 160.4, 160.0, 139.2, 139.0, 134.6, 117.3, 108.6, 106.1, 105.5, 101.8, 101.2, 73.7, 70.4, 70.3, 67.4, 67.0, 40.6, 33.8, 8.7; MS (MALDI−TOF) m/z 2747.7 (M + Na^+). Anal. Calcd for $C_{167}H_{188}O_{33}$: C, 73.65; H, 6.96. Found: C, 73.74; H, 7.06.

[G-3]-Tris(hydroxymethyl)ethane Cross-Linked Dendrimer (6). A solution of 0.10 g (0.037 mmol) dendrimer **5**, 0.015 g (0.019 mmol) first generation Grubbs catalyst **1**, and 1.0 L of benzene was stirred for 24 h. After 24 h, an additional 0.019 g of (0.023 mmol) of **1** was added. After an additional 24 h, 0.017 g (0.020 mmol) of catalyst **1** was added. After 7 days, added 1 mL of ethyl vinyl ether to quench reaction. The mixture was eluted using a silica gel plug to remove the benzene followed by eluting with 0.5 L of EtOAc. The solvent was evaporated off and the brownish solid purified using preparative SEC (toluene) to obtain 0.083 g (90%) of a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−6.97 (bm, 4H), 6.80−6.08 (bm, 38H), 5.73−5.42 (bs, 16H), 5.08−4.25 (bm, 30H), 4.11−3.65 (bs, 32H), 2.67−2.21 (bs, 32H), 1.18−1.02 (bs, 3H); MS (MALDI−TOF) m/z 2499.2 (MH^+), 2519.6 (M + Na^+); SEC (THF) calcd M_w = 1450, PDI = 1.02.

[G-3]-Tris(hydroxymethyl)ethane Partially Cross-Linked Dendrimer (7). A solution of 0.083 g (0.033 mmol) of dendrimer **6**, 0.11 g (0.084 mmol) of acid chloride dendron **3**, and 0.026 g (0.21 mmol) of DMAP in 10 mL of THF was stirred for 24 h. After removal of the solvent in vacuo, the mixture was extracted with CH_2Cl_2 (2 × 50 mL) and washed with 50 mL of H_2O and 50 mL of brine. The crude mixture was purified by column chromatography (silica gel, 4:1 PE/EtOAc) followed by preparative SEC (toluene) to obtain 0.064 g (51%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.22−6.97 (bm, 6H), 6.84−6.78 (bm, 3H), 6.72−6.61 (bs, 12H), 6.61−6.52 (bs, 24H), 6.52−6.43 (bs, 6H), 6.43−6.37 (bs, 8H), 6.37−6.22 (bs, 4H), 5.91 (m, 8H), 5.74−5.40 (bs, 16H), 5.14 (m, 8H), 5.07 (m, 8H), 5.00−4.56 (bm, 36H), 4.44−4.22 (bs, 6H), 4.16−3.70 (bs, 48H), 2.60−2.22 (bs, 48H), 1.18−1.02 (bs, 3H); MS (MALDI−TOF) m/z 3824.0 (M + Na^+), 3839.9 (M + K^+); SEC (THF) calcd M_w = 2390, PDI = 1.01.

Palladium/C(ethylene diamine). To 0.50 g of 10% palladium on carbon was added 1.1 mL of ethylene diamine and 10 mL of methanol. The reaction mixture was stirred for 48 h, filtered, washed with methanol (3 × 20 mL) and Et_2O (3 × 20 mL), and dried under N_2 overnight. The black powder was used without purification.

Hydrogenated, [G-3]-Tris(hydroxymethyl)ethane Cross-Linked Dendrimer (11). To 59 mg (0.024 mmol) of dendrimer **6** in 5 mL of THF was added 0.10 g (0.063 mmol) of Pd (ethylene diamine)/C. After evacuation of the reaction vessel, the mixture was stirred under 1 atm of hydrogen gas. After 18 h, this was filtered using Celite and washed with EtOAc, dried over sodium sulfate, filtered, and the solvent evaporated. Purification of the crude material using preparative SEC (toluene) afforded 46 mg (71%) of dendrimer **11** as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.22−6.97 (bm, 4H), 6.67−6.20 (bm, 38H), 5.09−4.63 (bm, 24H), 4.42−4.18 (bm, 6H), 4.09−3.78 (bs, 32H), 1.89−1.67 (bs, 32H), 1.62−1.39 (bs, 32H), 1.36−1.28 (bs, 3H); MS (MALDI−TOF) m/z 2537.4 (M + Na^+), 2552.4 (M + K^+); SEC (THF) calcd M_w = 1630, PDI = 1.03.

Hydrogenated, [G-3]-Tris(hydroxymethyl)ethane Partially Cross-Linked Dendrimer (12). A solution of 15 mg (0.0061 mmol) of dendrimer **11**, 30 mg (0.023 mmol) of acid chloride dendron **3**, and 6.4 mg (0.052 mmol) of DMAP in 4 mL of THF was stirred for 24 h. After removal of the solvent in vacuo, the mixture was extracted with EtOAc (3 × 50 mL) and washed with 50 mL of H_2O and 50 mL of brine. The mixture was dried over sodium sulfate, filtered, and evaporated. The crude mixture was purified by preparative SEC (toluene) to obtain 12 mg (53%) of **12** as a white powder: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.22−6.97 (bm, 6H), 6.84−6.20 (bm, 57H), 5.91 (m, 8H), 5.14 (m, 8H), 5.07 (m, 8H), 5.07−4.63 (bm, 36H), 4.42−4.18 (bm, 6H), 4.09−3.78 (bs, 48H), 2.41 (m, 16H), 1.89−1.67 (bs, 32H), 1.62−1.39 (bs, 32H), 1.36−1.28 (bs, 3H); MS (MALDI−TOF) m/z 3837.3 (M + Na^+), 3853.3 (M + K^+); SEC (THF) calcd M_w = 2420, PDI = 1.01.

Cross-Linked [G-3]-Benzoic Acid Methyl Ester. To a solution of 100 mg (0.076 mmol) of methyl ester dendron **13** in 2.0 L of benzene was added 25 mg (0.030 mmol) of first generation Grubbs catalyst **1**. After 16 h, an additional 24 mg (0.029 mmol) of catalyst **1** was added. After an additional 24 h, 23 mg (0.028 mmol) of catalyst **1** was added. After 7 days, 2 mL of ethyl vinyl ether was added and the mixture stirred for 1 h to quench the reaction. The mixture was eluted using a silica gel plug to remove the benzene followed by eluting with 0.5 L of EtOAc. Evaporated off solvent and purified using preparative SEC (toluene) to obtain 51 mg (55%) of a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.30 (m, 2H), 6.57 (m, 5H), 6.44 (m, 10H), 6.30 (m, 4H), 5.62 (m, 8H), 5.00 (m, 8H), 4.81 (m, 4H), 3.91 (m, 16H), 3.83 (m, 3H), 2.47 (m, 16H); MS (MALDI−TOF) m/z 1243.3 (M + Na^+), 1259.3 (M + K^+).

Cross-Linked [G-3]-Benzoic Acid. To 0.10 g (0.083 mmol) of cross-linked [G-3]-benzoic acid methyl ester was added 4 mL of ethanol, 7 mL of THF and 47 mg (0.83 mmol) of KOH dissolved in 2 mL of H_2O. The reaction mixture was heated to 80 °C for 20 h. After the mixture was cooled to room temperature, 5 mL of H_2O and 1 M HCl were added until pH < 5.0. The solvents were evaporated in vacuo, and the remaining product was extracted with EtOAc (3 × 50 mL). The organic layers were washed with 50 mL of H_2O, dried over sodium sulfate, filtered, and evaporated to afford 0.11 g (100%) of a white powder: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32 (m, 2H), 6.57 (m, 5H), 6.44 (m, 10H), 6.30 (m, 4H), 5.62 (m,

8H), 5.00 (m, 8H), 4.81 (m, 4H), 3.91 (m, 16H); MS (MALDI−TOF) *m*/*z* 1230.2 ($M + Na^+$), 1246.1 ($M + K^+$).

Cross-Linked [G-3]-Benzoic Acid Chloride. To 0.10 g (0.083 mmol) of cross-linked [G-3]-benzoic acid in 6 mL of THF was added 0.030 mL (0.32 mmol) of oxalyl chloride and 2 drops of DMF. After 16 h, the solvent was removed in vacuo. The crude mixture was purified using a silica gel plug (CH_2Cl_2) to obtain 0.059 g (57%) of a yellow oil that was used without further purification.

Cross-Linked [G-3]-Tris(hydroxymethyl)ethane Dendrimer (14). A solution of 35 mg (0.014 mmol) of dendrimer **6**, 59 mg (0.048 mmol) of cross-linked [G-3]-benzoic acid chloride and 12 mg (0.097 mmol) of DMAP in 7 mL of THF was stirred for 24 h. After removal of the solvent in vacuo, the mixture was extracted with CH_2Cl_2 (2 × 50 mL) and washed with 50 mL of H_2O and 50 mL of brine. The crude mixture was purified by column chromatography (silica gel, 4:1 PE/EtOAc) followed by preparative SEC (toluene) to afford 38 mg (72%) of **14** as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36−7.27 (bm, 6H), 6.70−6.16 (bm, 57H), 5.70−5.44 (bs, 24H), 5.08−4.55 (bm, 36H), 4.55−4.21 (bs, 6H), 4.11−3.60 (bs, 48H), 2.65−2.18 (bs, 48H), 1.17−1.03 (bs, 3H); MS (MALDI−TOF) *m*/*z* 3709.3 ($M + Na^+$), 3725.4 ($M + K^+$); SEC (THF) calcd $M_w = 1960$, PDI = 1.01.

General Procedure for Cross-Linking of Dendrimers. To a 10^{-5} M solution of the dendrimer in benzene was added 6 mol % per alkene of catalyst **1** or **2**. After 16 h, an additional 6 mol % per alkene of catalyst was added. After an additional 24 h, an additional 6 mol % per alkene of catalyst was added. After 7 days, 1 mL of ethyl vinyl ether was added to quench the reaction. The mixture was eluted using a silica gel plug to remove the benzene followed by eluting with 0.5 L of EtOAc. Solvent was removed and the residue purified using a preparative SEC (toluene) column.

General Procedure for Coring of Dendrimers. To the dendrimer was added ethanol, THF, and 2 M aqueous KOH. The reaction mixture was heated to 80 °C for 20 h. After the mixture was cooled to room temperature, 2 mL of H_2O and 1 M HCl were added until pH < 5.0. The solvents were evaporated off in vacuo, and the resulting product extracted with EtOAc (3 × 50 mL). The organic layers were washed with 50 mL of H_2O, dried over sodium sulfate, filtered, and the solvent evaporated.

Acknowledgment. Funding of this work by the National Institutes of Health (GM61067) is gratefully acknowledged.

Supporting Information Available: Figures showing MALDI−TOF−MS and analytical SEC spectra for dendrimers **7**, **12** and **14**, text dicussing the detailed characterization of the products obtained after cross-linking and coring dendrimers **7**, **12**, and **14**, schemes showing these reactions, and figures showing MALDI−TOF−MS and analytical SEC spectra for these products. This material is available free of charge via the Internet at http://pubs.acs.org.

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MA071233E