Preparation of Poly[(ether)-(ether ether ketone)] Dendrimers by the Convergent Method

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ABSTRACT: New highly branched poly[(ether)-(ether ether ketone)] dendrimers were synthesized by the convergent approach using two building blocks, 3, 5-dihydroxybenzyl alcohol, **1**, and 3, 5-dihydroxy-4'-(4-fluorobenzoyl)diphenylether, **2**, alternatively. The reaction of *p*-fluorobenzonitrile and **1** gave 3, 5-di(4-cyanophenoxy)benzylalcohol (the first generation dendron, **G 1-OH**). After **G 1-OH** was converted to 3, 5-di(4-cyanophenoxy)benzylbromide (**G 1-Br**), the resultant benzylic bromide functionality was allowed to react with **2** to yield the second-generation dendron (**G 2-F**). The third-generation dendron (**G 3-OH**) was obtained by the reaction of **G 2-F** and **1**, and the fourth-generation dendron (**G 4-F**) was obtained by reaction of **G 3-Br** derived from **G 3-OH**, with **2**. Finally, dendrimers, **Den-(G 2)₃** and **Den-(G 4)₃** were synthesized by reaction of **G 2-F** and **G 4-F** with trifunctional core, respectively. Analysis was made of these structurally unambiguous dendrons and dendrimers by gel permeation chromatography (GPC) and matrix-assisted laser desorption ionization time of flight (MALDI-TOF) mass spectroscopy. ¹H and ¹³C NMR spectra were consistent with the structures of these dendrons and dendrimers.

KEY WORDS Poly[(ether)-(ether ether ketone)] Dendrimers / 3, 5-Dihydroxybenzyl alcohol / 3, 5-Dihydroxy-4'-(4-fluorobenzoyl)diphenylether / Two Building Blocks / Alternatively /

Dendrimers^{1–4} are molecules with highly branched structures, and have been prepared by a divergent^{5–8} or a convergent method,^{9–11} which consists of repeating stepwise reactions. In the divergent method, the preparation starts from a core molecule, which possesses two or more reactive groups. A building block contains one functional group to connect with reactive groups of the core and two or more protected reactive group, which are the same as those of the core. In the convergent method, a compound possessing only one reactive group is used as the starting molecule. The building block contains two or more connecting points and only one protected reactive group, and the preparation starts to the inside direction from peripheral molecule. In both cases, after the reactive points on the starting molecule and the building block are connected, the protected reactive points are released. Connection of building blocks followed by deprotection are repeated until the molecules have grown to the desired size.^{12, 13}

Recently, we reported the preparation of poly(ether ether ketone) dendrimers by the divergent method, using 3, 5-dimethoxy-4'-(4-fluorobenzoyl)diphenylether, **3** (eq 1), as the building block.¹⁴ The methoxy groups were the protective form for hydroxy groups, and the dendrimers were grown by a reaction between the hydroxy groups and aromatic fluorides activated by carbonyl

groups in the para position. To prepare dendritic molecules using this building block by the convergent method, the methoxy groups and 4-fluorobenzoyl group should be converted to reactive hydroxy groups and a protective form, respectively. However, there were no proper groups in the protective form for 4-fluorobenzoyl group.

Consequently, in this study, 3, 5-dihydroxybenzyl alcohol, **1**, used as the building block in the synthesis of polyether dendrimers,¹⁰ and 3, 5-dihydroxy-4'-(4-fluorobenzoyl)diphenylether, **2**, derived from **3**, were used as building blocks alternatively without protecting 4-fluorobenzoyl group. Generally, the shape of dendrimers, prepared from only one building block, are thought to be flexible and expanded structures in low generation and be more globular with increasing generation.¹⁵ However, in the case of the present dendrimers, such the transition to the globular structure is expected to be difficult due to the alternation of the lengths between the branching points. By such a method, wherein some different building blocks are used, arboral,¹⁶ poly(ether-urethane),¹⁷ poly(amine-ester),¹⁸ poly(arylacetylene),¹⁹ poly(ester-arylacetylene),²⁰ poly(phenylenevinylene),²¹ poly(ether ketone),²² and cyclodextrin-modified dendrimer,^{23–24} have been synthesized.

In our previous convergent synthesis of poly(ether ketone),²² it was thought to be impossible to introduce functional groups into the periphery because highly reactive aluminum chloride was used in the conversion of the protected methoxy group to the reactive hydroxy group. However, as the dendrimers could be prepared without such conversion in this convergent synthesis, cyano groups, which can be converted to other functional groups such as carboxylic acid and amine, could be introduced at the periphery using 4-fluorobenzonitrile as the starting molecule. Such a dendrimers, with hydrophilic outer surfaces, are expected to be applied as micelles.²⁵

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Scheme 1.

RESULTS AND DISCUSSION

As two the building blocks were used in the present synthesis of the dendritic molecules, the covalent bonds for extension to dendrimers were two ethers; aromatic benzyl ether formed by the reaction between phenolic groups and benzyl bromide derivative, and aromatic ether formed by reaction between phenolic group and aryl fluoride activated by electron withdrawing group. As the former reaction proceeded at lower temperatures than the later, 4-fluorobenzoyl group of **2** was expected to be inert under the conditions of the former reaction.

A general synthetic procedure for the poly[(ether)-(ether ether ketone)] dendrimers is shown in Scheme 1. First, reaction of *p*-fluorobenzonitrile and **1** gave 3, 5-di-(4-cyanophenoxy)benzylalcohol (the first generation dendron, **G1-OH**). After **G1-OH** was converted to 3, 5-di(4-cyanophenoxy)benzylbromide (**G1-Br**), the resultant benzylic bromide functionality was allowed to react with **2** to yield the second-generation dendron (**G2-F**). Further reaction of **G2-F** with **1** yielded the third-generation dendron (**G3-OH**), and the fourth-generation dendron (**G4-F**) was obtained by reaction of **G3-Br** derived from **G3-OH**, with **2**. The reaction for the preparation of **G-OH** proceeded at 150°C using a mixture of *N,N*-dimethylacetamide and toluene as solvent, and that of **G-F** proceeded at the reflux temperature (56°C) using acetone as a solvent. The method for the conversion of **G-OH** to **G-Br** was the same as that reported by Hawker

et al. for the preparation of polyether dendrimers.¹⁰ These dendrons, **G1-OH**, **G1-Br**, **G2-F**, **G3-OH**, **G3-Br**, and **G4-F**, were colorless powders purified by silica gel column chromatography with final isolated yields of 70, 95, 92, 65, 91, and 88%, respectively. The yield of **G3-OH** was slightly lower due to the presence of small amounts of impurities as shown in GPC curves (Figure 1). In the MALDI-TOF mass spectra (Figure 2) of the crude **G3-OH**, *m/z* of the signal for the lower molecular weight impurity corresponded to the molecular weight of **G2-F** and that for the higher molecular weight impurity corresponded to the molecular weight of the compound **5**, which was formed by reaction between benzylic alcohol group of **G3-OH** and **G2-F** (Scheme 2). The reaction between **1** and **G2-F** at higher than 150°C resulted in higher ratio of **5** to **G3-OH** and lower yield of **G3-OH**. The reaction at 155°C gave **G3-OH** in only 38%. Finally, dendrimers, **Den-(G2)₃** and **Den-(G4)₃** were synthesized by the reaction of **G2-F** and **G4-F** with trifunctional core **4**, respectively (Scheme 3).

The formation and purity of these dendrimers were confirmed by gel permeation chromatography (GPC) (Figure 1) and MALDI-TOF-MS (Figure 2). In the MALDI-TOF mass spectra of the purified dendritic molecules, molecular ion peaks occurred at *m/z* which agreed very closely with calculated values, and all spectra confirmed that the products were of very high purity and monodispersed.

Figure 3 shows the ¹H NMR spectra of **G4-F** and **Den-(G4)₃**. The resonance of **G4-F**, could be classified as that of the methylene protons (4.9–5.1 ppm), protons

on 1, 3, 5-trisubstituted aromatic rings with three oxygen atoms, ascribed to **2** (6.2–6.5 ppm), protons on the 1, 3, 5-trisubstituted aromatic rings with two oxygen atoms and methylene group, ascribed to **1** (6.6–7.0 ppm), protons on the meta-position of the carbonyl and cyano groups (7.0–7.2 ppm), and protons on the ortho-position of the carbonyl and cyano groups (7.5–7.9 ppm). In the ^1H NMR spectrum of **Den-(G4)₃**, the resonance of the protons on the fluorine substituted aromatic ring (7.13 and 7.76 ppm, Δ) of **G4-F** shifted, while that of the aromatic protons ascribed to **4** (7.17, 7.67, 7.71, and 7.88 ppm, $\circ$) appeared. The obtained ratios of these protons agreed with calculated values.

In the ^{13}C NMR spectra of these dendritic molecules, three methylene resonances; $-\text{CH}_2-\text{OH}$ (64–65 ppm), $-\text{CH}_2-\text{Br}$ (31–32 ppm), and $-\text{CH}_2-\text{O}-\text{Ar}$ (68–70 ppm), were easily distinguishable. However, aromatic reso-

nance was complicated due to the presence of many signals. Thus, only the region 96–116 ppm of these dendritic molecules, the most distinctive, are shown in Figure 4. Resonance for the carbons bonded to hydrogen atoms on the 1, 3, 5-trisubstituted aromatic rings was seen in this region; the resonance attributed to the trisubstituted aromatic rings with three oxygen atoms, at 98–100 ppm (a and b), and to the trisubstituted aromatic rings with two oxygen atoms and methylene group, at 110–116 ppm (c and d). The resonance was clearly separated, and chemical structures of these dendritic mole-

Figure 1. GPC curves of poly[(ether)-(ether ether ketone)] dendrimers.

Figure 2. MALDI-TOF mass spectra and the molecular mass data of poly[(ether)-(ether ether ketone)] dendrimers. ^a Measured mass. ^b Calculated mass.

Scheme 2.

Scheme 3.

cules were clearly as the expected structures.

The dendritic molecules were soluble in various organic solvents such as amide solvents, dimethyl sulfoxide, tetrahydrofuran, methylene chloride, chloroform and benzene as well as the poly(ether ether ketone) dendrimers with methoxy groups on the periphery, prepared using only **2** as the building block.¹⁴

Thermal behavior of these dendritic molecules was evaluated by differential scanning calorimetry (DSC), and appeared non-crystalline and only glass transition temperature (T_g) was observed. T_g s of the dendrons, **G2-F**, **G3-OH**, **G3-Br**, and **G4-F** were 58°C, 86°C, 84°C, and 95°C, respectively, and drastic increment of T_g between **G2-F** and **G3-OH** was seen. The T_g s of these dendrons were higher than dendrons,²⁶ which had the same cyano groups at the periphery and prepared by using only **1** as the building block. The presence of benzophenone unit in the present dendritic molecules may affect the structure and T_g s. However, T_g s of **Den-(G2)₃** and **Den-(G4)₃** were 95 and 96°C, respectively, and independent on the molecular size.

Thermal stability of the dendrimers was evaluated by thermogravimetry (TG) in air. **Den-(G2)₃** and **Den-(G4)₃**, initiated thermal decomposition at 330°C, and temperatures at which weight losses of 5% were observed were 390°C and 408°C, respectively.

Figure 3. ¹H NMR spectra of **G4-F** and **Den-(G4)₃** at room temperature in CDCl₃.

Figure 4. ^{13}C NMR spectra of G 2-F, G 3-OH, G 3-Br, G 4-F, and Den-(G 4)₃ at room temperature in CDCl_3 .

EXPERIMENTAL

Materials

p-Fluorobenzonitrile was purified by distillation under reduced pressure, and triphenylphosphine was recrystallized from toluene. 3, 5-dihydroxybenzyl alcohol, **1**, tetrabromomethane, and potassium carbonate were used as supplied. All solvents were purified by distillation before use.

Measurements

^1H and ^{13}C NMR spectra and IR spectra were recorded on a JNM-GSX-400 FT-NMR spectrometer and Shimadzu IR 435 spectro-photometer, respectively. The measurements of NMR were performed at room temperature using chloroform- d_1 as a solvent. GPC was performed using a Polymer Laboratories analytical column, PL gel 5 μ MIXED-C, and tetrahydrofuran (THF) as eluent at 35°C. DSC was performed with a Shimadzu DSC-60, and measurements were made at a heating rate of 10 $^\circ\text{C min}^{-1}$ in nitrogen. TG was performed with Rigaku Thermal Analysis Station TG 8110, and the measurements were made at a heating rate of 10 $^\circ\text{C min}^{-1}$ in air. MALDI-TOF-MS spectra were recorded on a Shimadzu/Kratos Kompact MALDI II equipped with a 337 nm ni-

trogen laser. Sample preparation was as follows. A solution of the analyte (5 mg), the matrix (20 mg), and trifluoroacetic acid (one drop) in THF (1 mL) was prepared and a 1 μL of this matrix / sample solution was transferred to a stainless steel sample plate *via* automatic pipette. Measurement was performed in positive ion mode using 2, 5-dihydroxybenzoic acid as the matrix.

Synthesis

3, 5-Dihydroxy-4'-(4-fluorobenzoyl)diphenylether, **2**, 3, 5-Dimethoxy-4'-(4-fluorobenzoyl)diphenylether,¹⁴ **3**, (10.57 g, 30 mmol) was heated together with pyridine hydrochloride (50 g) at reflux temperature (240°C) for about 30 min. After the reaction mixture was homogeneous, it was poured into water (1000 mL), and extracted twice with 100 mL of ethyl acetate. The combined extract was dried over anhydrous magnesium sulfate. After evaporation of the solvent, pure **2** was obtained by silica gel column eluted by methylene chloride and ethyl acetate (2 : 1). Mp: 137–138°C. Yield: 8.8 g (90%). IR (KBr): 3400–3000, 1640, 1590, 1500, 1240, 1160 cm^{-1} . ^1H NMR (CDCl_3 , ppm): δ 5.40 (s, 2H), 6.15 (d, 2H, $J=2.2$ Hz), 6.19 (t, 1H, $d=2.2$ Hz), 7.06 (d, 2H, $J=8.8$ Hz), 7.16 (m, 2H), 7.77 (d, 2H, $J=8.8$ Hz), 7.81 (m, 2H). ^{13}C NMR (CDCl_3 , ppm): δ 99.28, 99.88, 115.53 (d, $J=22.3$ Hz), 117.92, 132.09, 132.31, 132.55 (d, $J=9.5$ Hz),

133.89 (d, $J=3.2$ Hz), 157.66, 157.88, 160.99, 165.37 (d, $J=234.3$ Hz), 194.61. *Anal.* Calcd for $C_{19}H_{13}FO_4$: C, 70.37; H, 4.04. Found: C, 70.43; H, 4.09.

1, 3, 5-Tris(*p*-(*p*-hydroxyphenyl)phenyl)benzene, **4.** **4** was prepared from 1, 3, 5-tris(*p*-bromophenyl)benzene.²⁷ 1, 3, 5-Tris(*p*-bromophenyl)benzene (5.43 g, 10 mmol), (4-methoxyphenyl)boronic acid (6.08 g, 40 mmol), potassium carbonate (5.53 g, 40 mmol), and deoxygenated toluene (100 mL) were added to a flask equipped with a reflux condenser. The flask was flushed with nitrogen and tetrakis(triphenylphosphine)palladium (Pd(PPh₃)₄) (0.2 g) was added to the reaction mixture. After the mixture was stirred at 90°C for 8 h, salts were removed by filtration, and the solvent was evaporated. The residue was recrystallized twice from toluene to give pure 1, 3, 5-tris(*p*-(*p*-methoxyphenyl)phenyl)benzene. Yield: 3.93 g (63%). Mp: 201–202°C. IR (KBr): 2940, 1610, 1500, 1250 cm⁻¹. ¹H NMR (CDCl₃, ppm): δ 3.85 (s, 9H), 7.01 (d, 6H, $J=2.2$ Hz), 7.59 (d, 6H, $J=8.8$ Hz), 7.72 (d, 6H, $J=8.8$ Hz), 7.77 (d, 6H, $J=8.8$ Hz), 7.86 (s, 3H). ¹³C NMR (CDCl₃, ppm): δ 114.44, 124.85, 127.17, 127.71, 128.12, 133.35, 139.57, 140.18, 142.08, 159.49. *Anal.* Calcd for $C_{45}H_{36}O_3$: C, 86.51; H, 5.81. Found: C, 86.22; H, 5.60.

1, 3, 5-Tris(*p*-(*p*-methoxyphenyl)phenyl)benzene (3.12 g, 5 mmol) was heated together with pyridine hydrochloride (50 g) at reflux temperature (240°C) for about 30 min. After the reaction mixture was homogeneous, it was poured into water (500 mL), and extracted twice with 100 mL of ethyl acetate. The combined extracts were dried over anhydrous magnesium sulfate. After evaporation of the solvent, pure **4** was obtained by silica gel column eluted by methylene chloride and ethyl acetate (1 : 1). Yield: 2.56 g (87%). Mp: 198–200°C. IR (KBr): 3400–3000, 1590, 1500, 1300–1200 cm⁻¹. ¹H NMR (dimethyl sulfoxide (DMSO)-*d*₆, ppm): δ 6.89 (d, 6H, $J=2.2$ Hz), 7.56 (d, 6H, $J=8.8$ Hz), 7.72 (d, 6H, $J=8.8$ Hz), 7.92 (d, 6H, $J=8.8$ Hz), 7.95 (s, 3H), 9.87 (s, 3H). ¹³C NMR (DMSO-*d*₆, ppm): δ 116.61, 124.56, 127.17, 128.28, 128.44, 131.20, 138.86, 140.37, 142.06, 158.08. *Anal.* Calcd for $C_{42}H_{30}O_3$: C, 86.57; H, 5.19. Found: C, 86.52; H, 4.99.

General Procedure for the Synthesis of G-OH. In a flask, a mixture of **1** (1.00 equiv), *p*-fluorobenzonitrile (2.00 equiv), potassium carbonate (1.00 equiv), toluene, and *N,N*-dimethylacetamide was stirred at 130°C for 1 h. The temperature was raised to 150°C and water formed during the reaction was removed as an azeotrope with toluene. The reaction mixture was stirred at this temperature for 1.5 h. After the reaction was complete, the mixture was cooled to about 80°C, and the solvent was evaporated under a reduced pressure of 15–20 torr. The residue was washed with 300 mL of water and extracted twice with 200 mL of methylene chloride. After the combined extract was dried over anhydrous magnesium sulfate, the solvent was evaporated. The crude product was purified as outlined in the following.

General Procedure for the Synthesis of G-Br. In a flask, a mixture of **G-OH** (1.00 equiv), carbon tetrabromide (1.25 equiv), triphenylphosphine (1.25 equiv), and dry tetrahydrofuran was stirred under nitrogen at room temperature for 1 h. The reaction mixture was poured into water and extracted twice with 100 mL of methylene chloride. After the combined extract was dried over

anhydrous magnesium sulfate, the solvent was evaporated. The crude product was purified as outlined in the following.

General Procedure for the Synthesis of G-F. A mixture of **G-Br** (2.00 equiv), **2** (1.00 equiv), potassium carbonate (2.00 equiv), and a few drop of 18-crown-6 in acetone was heated at reflux and stirred vigorously under nitrogen for 24 h. The reaction mixture was poured into water and extracted twice with 100 mL of methylene chloride. After the combined extract was dried over anhydrous magnesium sulfate, the solvent was evaporated. The crude product was purified as outlined in the following.

General Procedure for the Synthesis of Den-(G)₃. In a flask, a mixture of **G-F** (3.33 equiv), **4** (1.00 equiv), potassium carbonate (1.00 equiv), toluene, and *N,N*-dimethylacetamide was stirred at 130°C for 1 h. The temperature was raised to 150°C and water formed during the reaction was removed as an azeotrope with toluene. The reaction mixture was stirred at this temperature for 1.5 h. After the reaction was complete, the mixture was cooled to about 80°C, and the solvent was evaporated under reduced pressure of 15–20 torr. The residue was washed with 300 mL of water and extracted twice with 200 mL of methylene chloride. After the combined extract was dried over anhydrous magnesium sulfate, the solvent was evaporated. The crude product was purified as outlined in the following text.

G1-OH. This compound was prepared from *p*-fluorobenzonitrile and **1**, and purified by silica gel column chromatography eluted by methylene chloride and ethyl acetate (15 : 1). Yield: 11.98 g (70 %). Mp: 103–104°C. IR (KBr): 3400–3000, 2940, 2230, 1600, 1500, 1230 cm⁻¹. ¹H NMR (CDCl₃, ppm): δ 1.95 (t, 1H, $J=5.5$ Hz), 4.72 (d, 2H, $J=5.5$ Hz), 6.70 (t, 1H, $J=2.2$ Hz), 6.94 (d, 2H, $J=2.2$ Hz), 7.07 (d, 4H, $J=8.8$ Hz), 7.64 (d, 4H, $J=8.8$ Hz). ¹³C NMR (CDCl₃, ppm): δ 64.07, 106.73, 110.77, 114.13, 118.49, 118.52, 134.27, 145.43, 156.66, 160.64. *Anal.* Calcd for $C_{21}H_{14}N_2O_3$: C, 73.68; H, 4.12. Found: C, 73.43; H, 4.06.

G1-Br. This compound was prepared from **G1-OH**, and purified by silica gel column chromatography eluted by methylene chloride, and pure **G1-Br** was obtained by recrystallization from toluene. Yield: 11.55 g (95%). Mp: 160–161°C. IR (KBr): 2940, 2230, 1600, 1500, 1230 cm⁻¹. ¹H NMR (CDCl₃, ppm): δ 4.41 (s, 2H), 6.70 (t, 1H, $J=2.2$ Hz), 6.93 (d, 2H, $J=2.2$ Hz), 7.07 (d, 4H, $J=8.8$ Hz), 7.66 (d, 4H, $J=8.8$ Hz). ¹³C NMR (CDCl₃, ppm): δ 31.53, 107.12, 111.41, 116.43, 118.43, 118.68, 134.35, 141.84, 156.75, 160.23. *Anal.* Calcd for $C_{21}H_{13}BrN_2O_2$: C, 62.24; H, 3.23. Found: C, 62.18; H, 3.27.

G2-F. This compound was prepared from **G1-Br**, and purified by silica gel column eluted by methylene chloride and ethyl acetate (30 : 1). Yield: 11.19 g (92%). IR (KBr): 2940, 2230, 1650, 1590, 1500, 1230 cm⁻¹. ¹H NMR (CDCl₃, ppm): δ 4.99 (s, 4H), 6.30 (d, 2H, $J=2.2$ Hz), 6.37 (t, 1H, $J=2.2$ Hz), 6.72 (t, 2H, $J=2.2$ Hz), 6.94 (d, 4H, $J=2.2$ Hz), 7.05 (m, 10H), 7.17 (m, 2H), 7.62 (d, 8H, $J=8.8$ Hz), 7.79 (d, 2H, $J=8.8$ Hz), 7.82 (m, 2H). ¹³C NMR (CDCl₃, ppm): δ 69.06, 98.58, 99.64, 106.99, 111.19, 114.65, 115.50 (d, $J=22.3$ Hz), 117.73, 118.43, 118.58, 132.26, 132.42 (d, $J=9.5$), 132.47, 133.83 (d, $J=3.2$ Hz), 134.30, 140.77, 156.83, 157.69, 160.28, 160.37,

160.61, 165.31 (d, $J=254.3$ Hz), 193.88. *Anal.* Calcd for $C_{61}H_{37}FN_4O_8$: C, 75.30; H, 3.83. Found: C, 75.20; H, 3.71.

G3-OH. This compound was prepared from **G2-F**, and purified by silica gel column chromatography beginning with methylene chloride and ethyl acetate (25 : 1) as eluent and gradually changing to methylene chloride and ethyl acetate (10 : 1). Yield: 7.32 g (65%). IR (KBr): 3400–3000, 2940, 2230, 1650, 1590, 1500, 1230 cm^{-1} . 1H NMR ($CDCl_3$, ppm): δ 4.71 (s, 2H), 5.00 (s, 8H), 6.29 (d, 4H, $J=2.2$ Hz), 6.37 (t, 2H, $J=2.2$ Hz), 6.72 (t, 4H, $J=2.2$ Hz), 6.74 (t, 4H, $J=2.2$ Hz), 6.93 (d, 2H, $J=2.2$ Hz), 6.94 (d, 8H, $J=2.2$ Hz), 7.02–7.07 (m, 20H), 7.08 (d, 4H, $J=8.8$ Hz), 7.62 (d, 16H, $J=8.8$ Hz), 7.75–7.83 (m, 8H). ^{13}C NMR ($CDCl_3$, ppm): δ 64.24, 69.02, 98.50, 99.55, 106.90, 110.25, 111.22, 113.45, 114.65, 117.73, 117.79, 118.46, 118.55, 132.21, 132.28, 132.58, 132.72, 134.30, 140.75, 144.32, 156.79, 157.28, 157.72, 160.23, 160.37, 160.38, 160.60, 194.07. *Anal.* Calcd for $C_{129}H_{80}N_8O_{19}$: C, 75.73; H, 3.94. Found: C, 75.52; H, 3.88.

G3-Br. This compound was prepared from **G3-OH**, and purified by silica gel column chromatography beginning with methylene chloride and ethyl acetate (40 : 1) as eluent and gradually changing to methylene chloride and ethyl acetate (20 : 1). Yield: 6.14 g (91%). IR (KBr): 2940, 2230, 1650, 1590, 1500, 1230 cm^{-1} . 1H NMR ($CDCl_3$, ppm): δ 4.43 (s, 2H), 5.00 (s, 8H), 6.30 (d, 4H, $J=2.2$ Hz), 6.36 (t, 2H, $J=2.2$ Hz), 6.73 (t, 4H, $J=2.2$ Hz), 6.75 (t, 4H, $J=2.2$ Hz), 6.93 (d, 2H, $J=2.2$ Hz), 6.94 (d, 8H, $J=2.2$ Hz), 7.02–7.07 (m, 20H), 7.10 (d, 4H, $J=8.8$ Hz), 7.62 (d, 16H, $J=8.8$ Hz), 7.81 (d, 4H, $J=8.8$ Hz), 7.83 (d, 4H, $J=8.8$ Hz). ^{13}C NMR ($CDCl_3$, ppm): δ 31.99, 69.00, 98.46, 99.53, 106.88, 110.82, 111.20, 114.65, 115.66, 117.72, 117.98, 118.44, 118.54, 132.23, 132.31, 132.63, 132.86, 134.29, 140.74, 141.35, 156.77, 157.35, 157.69, 160.14, 160.22, 160.36, 160.45, 194.02. *Anal.* Calcd for $C_{129}H_{79}BrN_8O_{18}$: C, 73.47; H, 3.78. Found: C, 73.29; H, 3.80.

G4-F. This compound was prepared from **G3-Br**, and purified by silica gel column chromatography beginning with methylene chloride and ethyl acetate (40 : 1) as eluent and gradually changing to methylene chloride and ethyl acetate (15 : 1). Yield: 4.82 g (88%). IR (KBr): 2940, 2230, 1650, 1590, 1500, 1230 cm^{-1} . 1H NMR ($CDCl_3$, ppm): δ 4.98 (s, 16H), 5.01 (s, 4H), 6.28 (d, 8H, $J=2.2$ Hz), 6.31 (d, 2H, $J=2.2$ Hz), 6.37 (t, 4H, $J=2.2$ Hz), 6.42 (t, 1H, $J=2.2$ Hz), 6.72 (t, 8H, $J=2.2$ Hz), 6.75 (t, 2H, $J=2.2$ Hz), 6.94 (d, 16H, $J=2.2$ Hz), 6.96 (d, 4H, $J=2.2$ Hz), 7.00–7.08 (m, 50H), 7.12 (m, 2H), 7.61 (d, 32H, $J=8.8$ Hz), 7.75–7.83 (m, 20H). ^{13}C NMR ($CDCl_3$, ppm): δ 69.07, 69.30, 98.51, 98.54, 99.61, 99.77, 106.93, 110.57, 111.23, 114.10, 114.70, 115.46 (d, $J=22.3$ Hz), 117.69, 117.76, 117.88, 118.48, 118.59, 132.25, 132.31, 132.33, 132.41 (d, $J=9.5$ Hz), 132.47, 132.66, 132.80, 133.92 (d, $J=3.2$ Hz), 134.32, 140.44, 140.79, 156.82, 157.44, 157.53, 157.72, 160.28, 160.36, 160.41, 160.42, 160.50, 160.80, 165.22 (d, $J=254.3$ Hz), 193.90, 194.01. *Anal.* Calcd for $C_{277}H_{169}FN_{16}O_{40}$: C, 75.95; H, 3.89. Found: C, 75.87; H, 3.87.

Den-(G2)₃. This compound was prepared from **G2-F**, and purified by silica gel column chromatography beginning with methylene chloride and ethyl acetate (40 : 1) as eluent and gradually changing to methylene chlo-

ride and ethyl acetate (20 : 1). Yield: 4.23 g (82%). IR (KBr): 2940, 2230, 1650, 1590, 1500, 1230 cm^{-1} . 1H NMR ($CDCl_3$, ppm): δ 4.99 (s, 12H), 6.28 (d, 6H, $J=2.2$ Hz), 6.36 (t, 3H, $J=2.2$ Hz), 6.72 (t, 6H, $J=2.2$ Hz), 6.93 (d, 12H, $J=2.2$ Hz), 7.05 (m, 30H), 7.12 (d, 6H, $J=8.8$ Hz), 7.22 (d, 6H, $J=8.8$ Hz), 7.62 (d, 24H, $J=8.8$ Hz), 7.72 (d, 6H, $J=8.8$ Hz), 7.76 (d, 6H, $J=8.8$ Hz), 7.80–7.87 (m, 18H). ^{13}C NMR ($CDCl_3$, ppm): δ 69.05, 98.49, 99.50, 106.96, 111.20, 114.66, 117.40, 117.78, 118.46, 118.57, 120.42, 125.02, 127.44, 127.82, 128.66, 132.12, 132.21, 132.31, 132.96, 134.32, 137.04, 139.55, 139.98, 140.77, 141.92, 155.22, 156.82, 157.83, 160.25, 160.31, 160.37, 161.42, 194.13. *Anal.* Calcd for $C_{225}H_{138}N_{12}O_{27}$: C, 78.52; H, 4.04. Found: C, 78.56; H, 4.01.

Den-(G4)₃. This compound was prepared from **G4-F**, and purified by the same by silica gel column chromatography beginning with methylene chloride and ethyl acetate (30 : 1) as eluent and gradually changing to methylene chloride and ethyl acetate (15 : 1). Yield: 4.61 g (75%). IR (KBr): 2940, 2230, 1650, 1590, 1500, 1230 cm^{-1} . 1H NMR ($CDCl_3$, ppm): δ 4.98 (s, 48H), 5.02 (s, 12H), 6.28 (d, 24H, $J=2.2$ Hz), 6.32 (d, 6H, $J=2.2$ Hz), 6.36 (t, 12H, $J=2.2$ Hz), 6.42 (t, 3H, $J=2.2$ Hz), 6.72 (t, 24H, $J=2.2$ Hz), 6.75 (t, 6H, $J=2.2$ Hz), 6.93 (d, 6H, $J=2.2$ Hz), 6.97 (d, 12H, $J=2.2$ Hz), 7.00–7.10 (m, 156H), 7.17 (d, 6H, $J=8.8$ Hz), 7.61 (d, 96H, $J=8.8$ Hz), 7.67 (d, 6H, $J=8.8$ Hz), 7.71 (d, 6H, $J=8.8$ Hz), 7.75–7.83 (m, 66H), 7.88 (s, 3H). ^{13}C NMR ($CDCl_3$, ppm): δ 69.05, 69.29, 98.44, 98.52, 99.60, 99.68, 106.90, 110.57, 111.23, 114.11, 114.70, 117.40, 117.75, 117.84, 117.86, 118.49, 118.57, 120.36, 124.94, 127.43, 127.79, 128.63, 132.22, 132.25, 132.31, 132.36, 132.64, 132.67, 132.79, 132.80, 134.32, 136.88, 139.51, 139.89, 140.45, 140.79, 141.88, 155.25, 156.80, 157.42, 157.66, 157.70, 160.27, 160.36, 160.39, 160.49, 160.53, 160.54, 161.21, 194.01, 194.10. *Anal.* Calcd for $C_{873}H_{534}N_{48}O_{123}$: C, 76.74; H, 3.94. Found: C, 76.58; H, 3.81.

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