Supporting information for:

Comparison of Facially Amphiphilic Biaryl Dendrimers with Classical Amphiphilic Ones for Biomolecular Recognition

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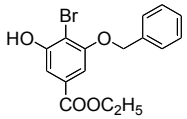
Experiment Section:

^{1}H-NMR spectra were recorded on a 400 MHz or 300 MHz NMR spectrometer (Bruker AVANCE 400 MHz, and Bruker AVANCE 300 MHz spectrometer, respectively) using the residual proton resonance of the solvent as the internal standard. Chemical shifts are reported in parts per million (ppm). When peak multiplicities are given, the following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; d of d, doublet of a doublet; m, multiplet; br, broad. ^{13}C-NMR spectra were proton decoupled and recorded on a 100 MHz or 75 MHz NMR spectrometer using the carbon signal of the deuterated solvent as the internal standard. Flash chromatography was performed with 40-63 μm silica gel. Analytical thin layer chromatography was performed on silica plates with F-254 indicator and the visualization was accomplished by UV lamp or using an iodine chamber. THF was distilled over Na/ Ph2CO ketyl. All other chemicals were obtained from commercial sources and used as received.

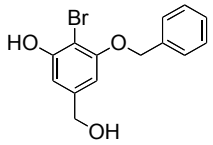
Synthesis of compound BD1



Ethyl-4-bromo-3,5-dihydroxybenzoate (49.4 g, 190 mmol), potassium carbonate (27.6 g, 200 mmol), 18-Crown-6 (2.64 g, 10 mmol) and benzyl bromide (19.2 mL, 160 mmol) were taken in 1000 mL of acetone and refluxed for 8 h under argon atmosphere. The reaction mixture was allowed to cool and solvent was evaporated to dryness. The residue was partitioned between water and ethyl acetate. The organic layer was separated, the aqueous layer extracted with ethyl acetate. The combined organic layer was washed with brine and dried with anhydrous Na_2SO_4 and evaporated to dryness. The residue was purified by silica gel column by eluting with CH_2Cl_2 to afford 25.0 g (37%) of **BD1.** The major by-product of this reaction is the compound, where two

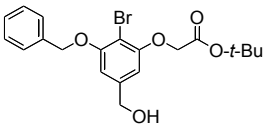
benzyl groups are added to the two phenolic groups of compound ethyl-4-bromo-3,5-dihydroxybenzoate**.** ^{1}H NMR (400MHz, $CDCl_3$) δ 7.51-7.32 (m, 5H), 7.23 (d, *J* = 2.0 Hz, 2H), 5.20 (s, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz , $CDCl_3$) δ 165.8, 155.4, 153.4, 135.9, 130.9, 128.5, 128.0, 127.1, 109.8, 105.79, 105.70, 71.0, 61.4, 14.2; EI/MS (*m*/*z*, r.i): 352 (M+2, 25), 350 (M^+, 25), 304 (12), 214 (3), 174 (2), 91 (100), 65 (16), 51 (5).

Synthesis of compound BD2:



The bromo ester **BD1** (25.0 g, 71.5 mmol) was taken in dry THF (125 mL) and cooled to 0 ºC. To this 2.0 M solution of $(CH_3)_2S.BH_3$ (143 mL, 286.0 mmol) was added under argon atmosphere dropwise for 15 min. The reaction mixture was allowed to stir at room temperature and further refluxed for 36 h. The reaction mixture was slowly added to a cold solution of 2N HCl and extracted with ethyl acetate. The organic layer was washed with brine solution and concentrated under reduced pressure to afford the crude mixture, which was purified by column chromatography (SiO_2, 2% EtOAc in dichloromethane) to afford 19.7 g (90%) of product **BD2**. ^{1}H NMR (400MHz, CD_3COCD_3) δ 8.79 (bs, 1H), 7.53-7.29 (m, 5H), 6.69 (s, 2H), 5.15 (s, 2H), 4.53 (s, 2H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 156.8, 155.8, 144.3, 137.9, 129.1, 128.4, 127.9, 107.6, 103.5, 71.0, 64.0; EI/MS (*m*/*z*, r.i): 310 (M^++2, 20), 308 (M^+, 20), 276 (2), 229 (2), 110 (2), 91 (100), 65 (12).

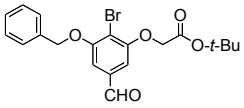
Synthesis of compound BD3:



Compound **BD2** (21.0 g, 67 mmol) was dissolved in acetone (250 mL). To this solution were added, K_2CO_3 (37.0 g, 268 mmol), NaI (12.5 g, 81 mmol) and 18-Crown-6 (3.6 g, 13.5 mmol) followed by *tert*-butyl bromoacetate (12 mL, 81 mmol). The reaction mixture was refluxed for 24 h. It was then cooled to room temperature and solvent was evaporated to dryness. The residue was partitioned between water and CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and evaporated to dryness. The crude product was purified by silica gel column chromatography

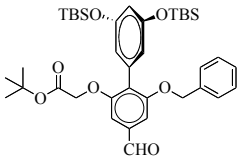
by elution with EtOAc/CH_2Cl_2 (5:95) to afford 29 g (89% yield) of compound **BD3**. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.49-7.31 (m, 5H), 6.65 (s, 1H), 6.47 (s, 1H), 5.16 (s, 2H), 4.61 (s, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 156.2, 155.5, 141.7, 136.3, 128.4, 127.7, 126.8, 105.1, 104.0, 100.8, 82.5, 70.7, 66.4, 64.6, 27.9; EI/MS (*m/z*, r.i): 424 (M+2, 8), 422 (M^+, 8), 366 (12), 287 (10), 196 (8), 140 (10), 91 (100), 57 (28).

Synthesis of compound BD4:



To a stirred solution of compound **BD3** (29.0 g, 69 mmol) in dry dichloromethane (470 mL) was added pyridinium chlorochromate (17.8 g, 82.5 mmol). It was stirred at room temperature for 3 h. The reaction mixture was filtered over alumina and the filtrate was evaporated and purified by silica gel chromatography (20% EtOAc in hexanes) to afford 26.8 g (93% yield) of **BD4**. ^{1}H NMR (400MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.49-7.33 (m, 5H), 7.12 (s, 1H), 6.92 (s, 1H), 5.22 (s, 2H), 4.66 (s, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.6, 166.8, 156.9, 156.2, 135.9, 135.7, 128.6, 128.0, 126.9, 109.9, 107.3, 105.8, 82.8, 71.0, 66.3, 27.9; EI/MS (*m/z*, r.i): 422 (M+2, 5), 420 (M^+, 5), 366 (12), 364 (12), 319 (5), 285 (6), 107 (3), 91 (100), 57 (15).

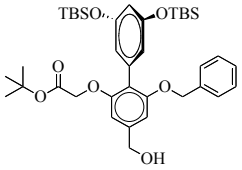
Synthesis of compound BD5:



Compound Aryl tin (2.0 g, 3.3 mmol) and bromo aldehyde **BD4** (1.29 g, 3.0 mmol) were dissolved in deoxygenated DMF (7 mL) under argon atmosphere. To this 1 mol% $Pd(PPh_3)_2Cl_2$ (0.021 g, 0.03 mmol) was added and the reaction mixture heated at 110-120 ºC for 2 days. It was then cooled to room temperature and residue was partitioned between water and CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and evaporated to dryness. The crude product was purified by silica gel chromatography by elution with EtOAc/hexane (8:92) to afford 1.38 g of compound **BD5** (67% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.11-7.03 (m, 6H), 6.84 (s, 1H), 6.43 (d, J = 2.0 Hz, 2H), 6.19 (t, J = 2.2 Hz, 1H), 4.91 (s, 2H), 4.34 (s, 2H), 1.28 (s, 9H), 0.80 (s, 18H), 0.00 (s, 12H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 191.2, 167.5, 157.2, 156.5, 155.7, 136.4,

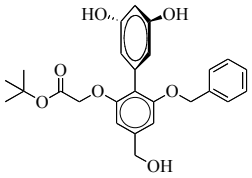
136.2, 134.1, 128.3, 127.6, 126.9, 126.7, 115.7, 111.4, 107.8, 106.2, 82.3, 70.5, 65.7, 27.9, 25.6, 18.1, -4.5; EI/MS (*m*/*z*, r.i): 678 (M^+, 55), 621 (24), 565 (15), 531 (12), 487 (8), 457 (6), 258 (5), 201 (30), 91 (100), 57 (28).

Synthesis of compound BD6:



The biaryl aldehyde **BD5** (13.56 g, 20 mmol) was dissolved in anhydrous CH_2Cl_2 (200 mL) under argon atmosphere. To this tetrabutylammonium borohydride (5.2 g, 20 mmol) was added and stirred at room temperature for 12 h. The reaction mixture was quenched with water and extracted with dichloromethane. The organic layer was washed with brine solution and evaporated to dryness. The crude product was purified by silica gel column chromatography by elution with EtOAc/hexane (20:80) to afford 12.0 g (88% yield) of compound **BD6**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.13-7.03 (m, 5H), 6.55 (s, 1H), 6.42 (d, J = 2.4 Hz, 2H), 6.36 (s, 1H), 6.17 (t, J = 2.0 Hz, 1H), 4.84 (s, 2H), 4.47 (s, 2H), 4.25 (s, 2H), 1.28 9s, 9H), 0.80 (s, 18H), 0.00 (s, 12H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.1, 156.9, 156.1, 155.6, 141.5, 137.1, 135.1, 128.2, 127.4, 126.7, 120.0, 116.2, 110.9, 105.3, 104.2, 82.0, 70.4, 66.1, 65.3, 27.9, 25.6, 18.1, -4.5; EI/MS (*m*/*z*, r.i): 680.2 (M^+, 100), 623 (42), 567 (18), 549 (18), 459 (20), 431 (10), 91 (69), 73 (23).

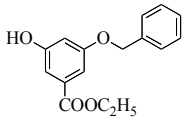
Synthesis of monomer BD7 (monomer)



The biaryl alcohol **BD6** (6.85 g, 10 mmol) was dissolved in anhydrous THF (50 mL) under argon atmosphere. To this TBAF (80 mL of 1.0 M THF solution, 80 mmol) was added and stirred at room temperature for 12 h. Saturated NH_4Cl was added to the reaction mixture. The aqueous layer was extracted with EtOAc, and the organic layer was concentrated under reduced pressure to afford the crude product, which was purified by column chromatography (SiO_2, 40% ethyl acetate in hexanes) to afford 3.93 g (87% yield) of **BD7**. ^{1}H-NMR (400 MHz, CD_3COCD_3) δ 8.03 (s, 2H), 7.34-7.22 (m, 5H), 6.81 (s, 1H), 6.61 (s, 1H), 6.42 (d, J = 2.4 Hz, 2H), 6.31 (t, J =

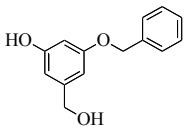
2.0 Hz, 1H), 5.05 (s, 2H), 4.59 (s, 2H), 4.47 (s, 2H), 1.45 (s, 9H); ^{13}C-NMR (100 MHz, CD_3COCD_3) δ 168.7, 158.4, 157.6, 157.0, 143.9, 138.6, 137.1, 129.0, 128.1, 127.6, 120.2, 110.6, 105.6, 104.3, 101.9, 81.9, 70.8, 66.5, 64.7, 28.1; *EI/MS (m/z, r.i)* : 452 (M^+, 10), 410 (6), 396 (22), 341 (7), 308 (16), 256 (22), 196 (20), 142 (20), 129 (20), 91 (82), 69 (100), 57 (82).

Synthesis of compound BD8:



Ethyl-3,5-dihydroxybenzoate (27.3 g, 150 mmol), potassium carbonate (20.7 g, 150 mmol), 18-Crown-6 (2.0 g, 7.5 mmol) and benzyl bromide (14.3 mL, 120 mmol) were taken in 750 mL of acetone and refluxed for 12 h under argon atmosphere. The reaction mixture was allowed to cool and solvent was evaporated to dryness. The residue was partitioned between water and ethyl acetate. The organic layer was separated, the aqueous layer extracted with ethyl acetate. The combined organic layer was washed with brine and dried with anhydrous Na_2SO_4 and evaporated to dryness. The residue was purified by silica gel column, eluting with EtOAc/hexane (5:95) to afford 14.5 g (36%) of **BD8** as a colorless solid. ^{1}H NMR (400 MHz , $CDCl_3$) δ 7.43-7.25 (m, 6H), 7.16 (s, 1H), 6.67 (t, J = 2.4 Hz, 1H), 5.07 (s, 2H), 4.35 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 159.9,157.0, 136.4, 132.2, 128.6, 128.1, 127.5, 109.5, 108.1, 107.3, 70.2, 61.4, 14.1; EI/MS (m/z, r.i): 272 (M^+, 35), 227 (15), 199 (2), 153 (2), 108 (2), 91 (100), 83 (10), 65 (8).

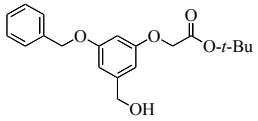
Synthesis of compound BD9:



$LiAlH_4$ (3.0 g, 79 mmol) was taken in dry THF (200 mL) under argon atmosphere and cooled to 0 ºC. Compound **BD8** (14.3 g, 53 mmol) dissolved in dry THF (200 mL) was added drop wise to the above solution for 30 min. It was allowed to stir at room temperature for 12 h. The reaction mixture was quenched with ethyl acetate followed by water. The precipitated material was filtered and washed with ethyl acetate. The filtrate was then taken in a separating funnel. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with water, followed by brine solution. The organic layer was evaporated and purified by silica gel chromatography by elution with 25-30% ethyl

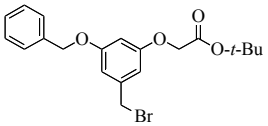
acetate in dichloromethane as eluent to afford 10.8 g (89% yield) of **BD9**. ^{1}H NMR (400MHz, CD_3COCD_3) δ 8.28 (s, 1H), 7.47-7.29 (m, 5H), 6.53 (s, 1H), 6.47 (s, 1H), 6.36 (s, 1H), 5.05 (s, 2H), 4.52 (s, 2H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 160.8, 159.1, 145.8, 138.4, 129.0, 128.3, 128.1, 106.8, 104.7, 101.2, 70.1, 64.5; EI/MS (m/z, r.i): 230 (M^+, 100), 211 (10), 199 (15), 91 (100), 65 (32), 63 (6).

Synthesis of compound BD10:



Compound **BD9** (4.8 g, 21 mmol) was dissolved in acetonitrile (60 mL). To this solution were added, K_2CO_3 (3.5 g, 25.2 mmol), NaI (3.2 g, 21 mmol) and 18-Crown-6 (0.33 g, 1.25 mmol) followed by *tert*-butyl bromoacetate (3.1 mL, 21 mmol). The reaction mixture was refluxed for 36 h. It was then cooled to room temperature and solvent was evaporated to dryness. The residue was partitioned between water and CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and evaporated to dryness. The crude product was purified by silica gel chromatography by elution with EtOAc/hexane (25:75) to afford 7.0 g (97% yield) of compound **BD10**. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.41-7.38 (m, 5H), 6.64 (s, 1H), 6.52 (s, 1H), 6.49 (t, J = 2.4 Hz, 1H), 5.04 (s, 2H), 4.63 (s, 2H), 4.50 (s, 2H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 160.0, 159.1, 143.4, 136.7, 128.5, 127.9, 127.4, 106.3, 105.1, 101.1, 82.3, 70.0, 65.6, 65.1, 28.0; EI/MS (m/z, r.i): 344 (M^+, 35), 288 (14), 257 (6), 137 (3), 91 (100), 69 (16), 57 (18).

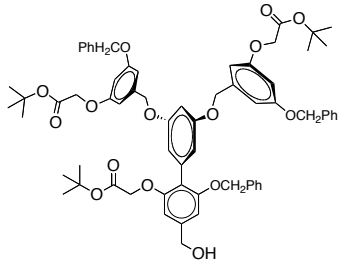
Synthesis of compound BD11:



The alcohol **BD10** (1.72 g, 5 mmol) was dissolved in dry THF (20 mL) under argon atmosphere. To this PPh_3 (1.44 g, 5.5 mmol) was added. After 5 min *N*-bromosuccinimide (0.98 g, 5.5 mmol) was added in one portion. After stirring for 4 min, it was quenched with water and extracted with dichloromethane. The organic layer was evaporated to dryness and the residue purified by column chromatography (SiO_2, 10% ethyl acetate in hexanes) to afford the product **BD11**, 1.80 g (90% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.43-7.33 (m, 5H), 6.65 (s, 1H), 6.52

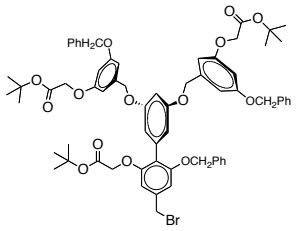
(s, 1H), 6.49 (t, J = 2.0 Hz, 1H), 5.09 (s, 2H), 4.49 (s, 2H), 4.39 (s, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 159.8, 158.9, 139.6, 136.3, 128.4, 127.9, 127.4, 108.7, 107.4, 101.9, 82.3, 69.9, 65.5, 33.2, 27.9; EI/MS (m/z, r.i): 408 (M+2, 18), 406 (M^+, 18), 350 (8), 271 (22), 137 (2), 91 (100), 57 (18).

Synthesis of compound BD12:



The monomer **BD7** (2.54 g, 5.4 mmol), potassium carbonate (3.0 g, 22 mmol), 18-Crown-6 (0.33 g, 1.25 mmol) and bromomethyl compound **BD11** (4.46 g, 11 mmol) in dry acetone (125 mL) were heated at reflux and stirred vigorously under argon atmosphere for 16 h. The mixture was allowed to cool and evaporated to dryness under reduced pressure. The residue was partitioned between water and dichloromethane. The organic layer was separated and the aqueous layer extracted with dichloromethane. The combined organic layers were dried and evaporated to dryness. The residue was purified by silica gel column chromatography by elution with EtOAc/hexane (40:60) to afford 5.24 g (94% yield) of the product **BD12**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41-7.25 (m, 15H), 6.75-6.49 (m, 11H), 5.01 (s, 6H), 4.92 (s, 4H), 4.65 (s, 2H), 4.47-4.45 (m, 6H), 1.47-1.43 (m, 27H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.9, 167.7, 159.9, 159.03, 159.00, 156.8, 156.0, 141.9, 139.6, 137.0, 136.6, 135.4, 128.4, 128.2, 127.8, 127.4, 126.6, 119.4, 110.2, 107.0, 105.7, 105.2, 103.8, 101.2, 82.2, 81.9, 70.4, 69.9, 69.7, 66.0, 65.5, 65.0, 27.9; MALDI-ToF: Calcd for $C_{66}H_{72}O_{15}$: 1104.49; Found: 1127.13 (M+, 23).

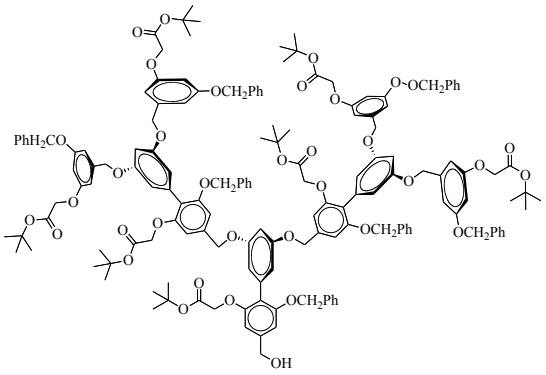
Synthesis of compound BD13:



The alcohol **BD12** (5.24 g, 4.75 mmol) and PPh_3 (1.86 g, 7.2 mmol) were dissolved in dry THF (20 mL) under argon atmosphere. *N*-Bromosuccinimide (1.26 g, 7.2 mmol) was added in one portion. After stirring for 2 min, it was quenched with water and extracted with

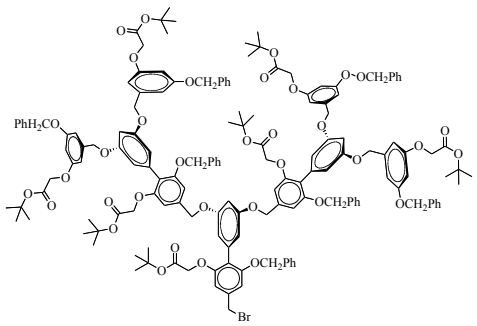
dichloromethane. The solvent was removed under reduced pressure and the residue was purified by silica gel column by elution with ethyl acetate/hexane (25:75) to afford 4.64 g (83% yield) of the product **BD13**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44-7.25 (m, 15H), 6.76-6.52 (m, 11H), 5.04 (s, 6H), 4.95 (s, 4H), 4.50-4.46 (m, 8H), 1.50-1.56 (m, 27H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.6, 159.8, 158.97, 158.94, 156.6, 155.8, 139.5, 138.0, 136.6, 136.5, 134.9, 128.3, 128.2, 127.8, 127.4, 127.3, 126.6, 110.0, 107.6, 106.9, 106.1, 105.6, 101.4, 101.2, 82.1, 82.03, 70.4, 69.8, 69.6, 65.9, 65.4, 33.5, 27.8; MALDI-ToF: Calcd for $C_{66}H_{71}BrO_{14}$: 1166.40; Found: 1188.98 (M+, 23).

Synthesis of compound BD14:



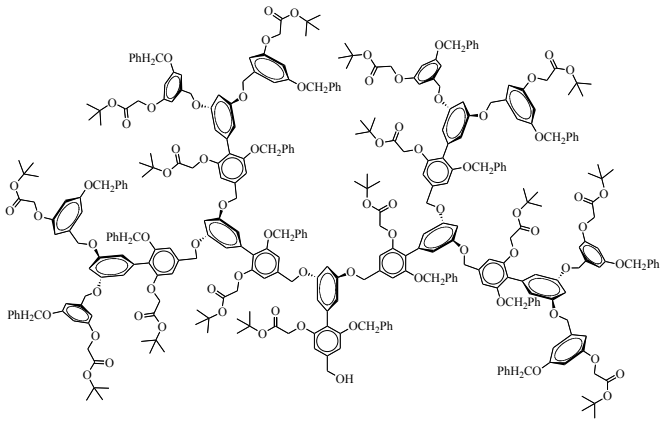
The monomer **BD7** (0.67 g, 1.47 mmol), potassium carbonate (1.0 g, 7.4 mmol), 18-Crown-6 (0.1 g, 0.37 mmol) and bromomethyl compound **BD13** (3.80 g, 3.25 mmol) in dry acetone (50 mL) were heated at reflux and stirred vigorously under argon atmosphere for 15 h. The work-up procedure used in the synthesis of **BD12** was followed. The residue was purified by silica gel column by elution with EtOAc/hexane (40:60) to afford 3.67 g (94%) of the product **BD14**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41-7.35 (m, 35H), 6.80-6.50 (m, 27H), 5.05-4.92 (m, 26H), 4.67 (s, 2H), 4.48-4.45 (m, 14H), 1.47-1.41 (m, 63H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.8, 167.7, 159.9, 159.06, 159.03, 156.8, 156.0, 142.0, 139.6, 137.8, 137.08, 137.00, 136.6, 135.6, 135.4, 128.4, 128.2, 127.9, 127.4, 126.7, 126.6, 119.9, 119.4, 110.1, 107.0, 106.3, 105.7, 105.2, 104.8, 103.7, 101.3, 82.2, 82.04, 82.0, 70.5,70.4, 69.9, 69.7, 66.14, 66.10, 65.6, 65.1, 27.9; MALDI-ToF: Calcd for $C_{158}H_{168}O_{35}$: 2625.14; Found: 2648.65 (M+, 23).

Synthesis of compound BD15:



The G-2 alcohol **BD14** (1.14 g, 0.43 mmol) and PPh_3 (0.15 g, 0.57 mmol) were dissolved in dry THF (15 mL) under argon atmosphere. *N*-Bromosuccinimide (0.10 g, 0.57 mmol) was added in one portion. After stirring for 5 min, it was quenched with water and extracted with dichloromethane. The work-up procedure used in the synthesis of **BD13** was followed. The residue was purified by silica gel column using EtOAc/hexane (40:60) eluent to afford 0.91 g (79%) of the product **BD15**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44-7.24 (m, 35H), 6.82-6.53 (m, 27H), 5.07-4.95 (m, 26H), 4.51-4.48 (m, 16H), 1.50-1.43 (m, 63); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.7, 167.6, 159.8, 159.01, 158.98, 158.95, 156.7, 155.9, 139.5, 137.9, 137.7, 136.9, 136.7, 136.5, 135.3, 135.1, 128.3, 128.25, 128.20, 127.8, 127.3, 126.6, 120.3, 119.8, 110.1, 109.9, 107.7, 106.9, 106.2, 105.6, 104.6, 101.2, 82.1, 82.08, 81.90, 70.4, 69.8, 69.6, 66.0, 65.9, 65.5, 33.5, 27.8; MALDI-ToF: Calcd for $C_{158}H_{167}BrO_{34}$: 2687.05; Found: 2710.87 (M+, 23).

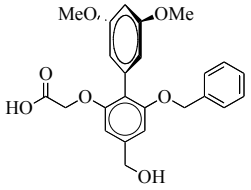
Synthesis of compound BD16



The monomer **BD7** (0.066 g, 0.14 mmol), potassium carbonate (0.24 g, 1.76 mmol), 18-Crown-6 (0.011g, 0.04 mmol) and bromomethyl compound **BD15** (0.85 g, 0.28 mmol) in dry acetone (5 mL) were heated at reflux and stirred vigorously under argon atmosphere for 24 h. The work-up procedure used in the synthesis of **BD12** was followed. The residue was purified by silica gel column by elution with EtOAc/hexane (50:50) to afford 0.79 g (95%) of the product **BD16**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42-7.20 (m, 75H), 6.83-6.49 (m, 59H), 5.05-4.92 (m, 58H), 4.67 (s, 2H), 4.490-4.45 (m, 30H), 1.56-1.41 (m, 135H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ

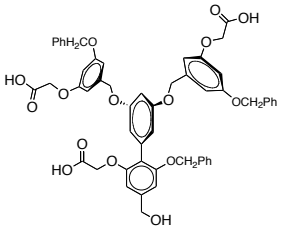
167.85, 167.80, 167.74, 159.9, 159.06, 159.03, 159.0, 156.8, 156.0, 142.0, 139.5, 138.0, 137.8, 137.1, 136.9, 136.6, 135.7, 135.5, 135.3, 128.4, 128.2, 127.8, 127.4, 126.7, 126.6, 119.9, 119.4, 110.1, 107.0, 106.3, 105.7, 105.2, 104.8, 103.7, 101.2, 82.2, 82.0, 81.9, 70.5, 69.9, 69.7, 66.10, 65.9, 65.58, 65.1, 27.9; MALDI-ToF: Calcd for $C_{342}H_{360}O_{75}$: 5670.47; Found: 5695.26 (M+, 23).

Synthesis of compound 1 (G0-OH)



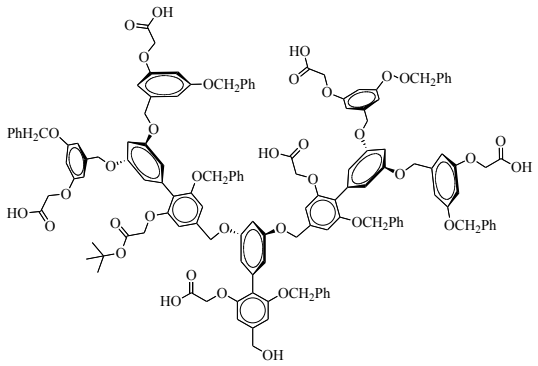
The monomer **BD7** (0.50 g g, 1.1 mmol), potassium carbonate (0.45 g, 3.3 mmol) and methyl iodide (0.27 mL, 4.4 mmol) in dry acetone (10 mL) were heated at reflux and stirred vigorously under argon atmosphere for 16 h. The mixture was allowed to cool and evaporated to dryness under reduced pressure. The residue was partitioned between water and dichloromethane. The organic layer was separated and the aqueous layer extracted with dichloromethane. The combined organic layers were dried and evaporated to dryness. This crude mixture was dissolved in tetrahydrofuran (10 mL) and aqueous potassium hydroxide (0.56 g, 10 mmol) dissolved in water (1.8 mL) was added. Methanol (5 mL) was then added to this two-phase system to give homogeneous solution. This mixture was then heated at reflux for 12 h. The reaction mixture was evaporated to dryness and the residue dissolved in water (20 mL) and the mixture heated at reflux for 24 h. After cooling to room temperature, the reaction mixture was acidified with 2N HCl. The precipitate formed was collected by vacuum filtration and dried to afford **1.** Yield: 0.38 g (82%). ^{1}H-NMR (400 MHz, CD_2Cl_2) δ 7.36-7.30 (m, 5H), 6.81 (s, 1H), 6.36-6.47 (m, 4H), 5.08 (s, 2H), 4.68 (s, 2H), 4.63 (s, 2H), 3.79 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ ; 172.2, 160.0, 156.8, 155.5, 141.8, 136.9, 135.2, 128.3, 127.5, 126.7, 119.7, 109.0, 105.7, 104.1, 99.6, 70.4, 65.4, 64.7, 55.2; FAB (m/z, r.i): 424 (M+, 15), 399 (5), 390 (5), 327 (18), 325 (12), 281 (14), 206 (20), 190 (12), 136 (32), 91 (65), 73 (100), 55 (70).

Synthesis of compound 2 (G1-OH):



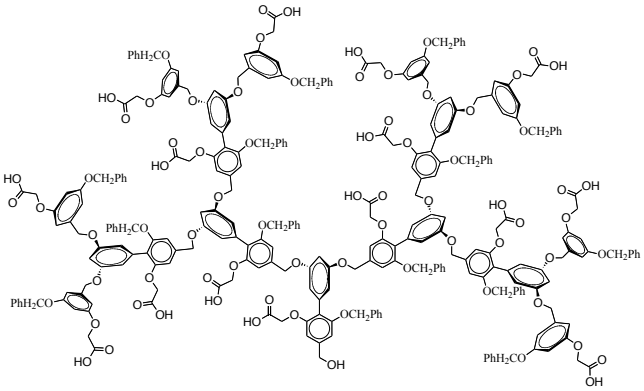
To a solution of alcohol **BD12** (0.12 g, 0.115 mmol) in tetrahydrofuran (4 mL) was added aqueous potassium hydroxide (0.19 g, 3.4 mmol) dissolved in water (1.0 mL). Methanol (2 mL) was then added to this two-phase system to give homogeneous solution. This mixture was then heated at reflux for 12 h. The reaction mixture was evaporated to dryness and the residue dissolved in water (20 mL) and the mixture heated at reflux for 24 h. After cooling to room temperature, the reaction mixture was acidified with 2N HCl. The precipitate formed was collected by vacuum filtration and dried to afford **2**. Yield: 0.080 g (90%). ^{1}H-NMR (400 MHz, $(CD_3)_2SO$) δ 7.44-7.22 (m, 15H), 6.79-6.51 (m, 11H), 5.07-4.96 (m, 10H), 4.60-4.47 (8H); ^{13}C-NMR (75 MHz, $(CD_3)_2SO$) δ 170.6, 170.4, 159.5, 159.2, 158.5, 156.0, 155.8, 143.8, 139.6, 137.3, 136.9, 135.9, 128.4, 128.3, 127.9, 127.8, 127.6, 127.1, 117.4, 110.5, 106.5, 106.0, 104.1, 103.2, 100.8, 100.3, 69.6, 69.4, 69.2, 65.1, 63.0; MALDI-ToF: Calcd for $C_{54}H_{48}O_{15}$: 936.30; Found: 959.30 (M^+ +23).

Synthesis of compound 3 (G2-OH):



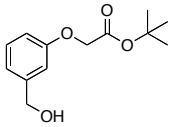
To a solution of alcohol **BD14** (0.32 g, 0.12 mmol) in tetrahydrofuran (18 mL) was added aqueous potassium hydroxide (0.49 g, 8.6 mmol) dissolved in water (5 mL). Methanol (6 mL) was then added to this two-phase system to give homogeneous solution. This mixture was then heated at reflux for 12 h. The reaction mixture was evaporated to dryness and the residue dissolved in water (25 mL) and the mixture heated at reflux for 24 h. After cooling to room temperature, the reaction mixture was acidified with 2N HCl. The precipitate formed was collected by vacuum filtration and dried to afford **2**. Yield: 0.25 g (85%). ^{1}H-NMR (400 MHz, CD_3COCD_3) δ 7.47-6.55 (m, 62H), 5.09-5.06 (m, 26H), 4.69-4.63 (m, 16H); ^{13}C-NMR (100 MHz, $(CD_3)_2SO$) δ 170.5, 170.4, 170.2, 159.7, 159.1, 158.89, 158.80, 156.4, 156.3, 155.8, 155.7, 144.0, 139.7, 138.2, 137.4, 137.2, 137.0, 136.2, 135.7, 128.6, 128.4, 128.0, 127.9, 127.7, 127.38, 127.32, 118.8, 117.6, 110.4, 106.9, 106.4, 106.0, 104.8, 104.4, 103.1, 100.9, 69.9, 69.8, 69.5, 69.3, 64.9, 64.7, 63.1; MALDI-ToF: Calcd for $C_{130}H_{112}O_{35}$: 2232.70; Found: 2272.75 (M+39).

Synthesis of compound 4 (G3-OH):



To a solution of alcohol **BD16** (0.33 g, 0.58 mmol) in tetrahydrofuran (18 mL) was added aqueous potassium hydroxide (0.50 g, 8.8 mmol) dissolved in water (5.0 mL). Methanol (6 mL) was then added to this two-phase system to give homogeneous solution. This mixture was then heated at reflux for 12 h. The reaction mixture was evaporated to dryness and the residue dissolved in water (25 mL) and the mixture heated at reflux for another 24 h. After cooling to room temperature, the reaction mixture was acidified with 2N HCl. The precipitate formed was collected by vacuum filtration and dried to afford **4**. Yield: 0.29 g (90%). ^{1}H-NMR (400 MHz, CD_3COCD_3) δ 7.45-6.54 (m, 134H), 5.09-4.98 (m, 58H), 4.69-4.62 (m, 32H); ^{13}C-NMR (75 MHz, $(CD_3)_2SO$) δ 170.6, 170.5, 170.3, 159.7, 159.1, 158.9, 158.8, 156.4, 155.9, 144.0, 139.7, 138.2, 137.4, 137.3, 137.2, 137.0, 136.3, 135.9, 135.7, 128.6, 128.4, 128.0, 127.9, 127.8, 127.46, 127.41, 118.9, 118.8, 117.6, 110.4, 106.9, 106.4, 106.1, 104.8, 103.2, 100.9, 100.6, 70.0, 69.5, 69.3, 64.9, 64.7, 63.1; MALDI-ToF: Calcd for $C_{282}H_{240}O_{75}$: 4825.50; Found: 4851.95 (M^++23).

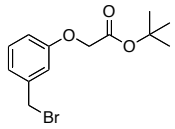
Synthesis of compound CD1 (periphery):



3-hydroxybenzyl alcohol (10.0 g, 80.1 mmol), potassium carbonate (33.4 g, 241.7 mmol), 18-Crown-6 (2.5 g, 24.2 mmol), sodium iodide (18.0 g, 120.2 mmol) and *t*-butylbromoacetate (17.75 mL, 120.2 mmol) were taken in 300 mL of acetone and refluxed for 12 hrs under argon atmosphere. The reaction mixture was allowed to cool and solvent was evaporated to dryness. The residue was partitioned between water and dichloromethane. The organic layer was separated, the aqueous layer extracted with dichloromethane. The combined organic layer was washed with brine and dried with anhydrous Na2SO4 and evaporated to dryness. The residue was purified by silica gel column by eluting with ethyl acetate/hexane (20:80) to afford 16.0 g (82%) of **CD1** as a colorless viscous liquid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34 (t, J = 2.8 Hz, 1H),

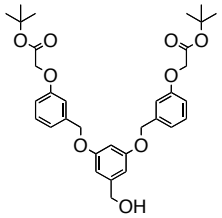
6.98-6.82 (m, 3H), 4.51 (s, 2H), 4.42 (s, 2H) 1.47 (s, 9H); ^{13}C-NMR (100 MHz, CDCl^3) δ 168.03, 158.10, 142.66, 129.57, 119.85, 113.74, 112.93, 82.35, 65.61, 65.01, 27.99.

Synthesis of compound CD2:



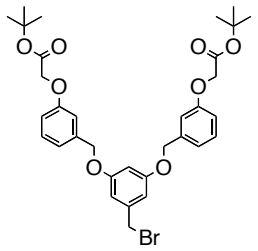
The alcohol **CD1** (11.31 g, 4.75 mmol) was dissolved in dry THF (10 mL) under argon atmosphere. To this PPh3 (13.7 g, 5.23 mmol) was added. After 5 min *N*-bromosuccinimide (9.30 g, 5.23 mmol) was added in one portion. After stirring for 15 mins, it was quenched with water and extracted with dichloromethane. The organic layer was evaporated to dryness and the residue purified by column chromatography (SiO2, 5% ethyl acetate in hexanes) to afford the product **CD2**, 12.4 g (88% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 1H), 7.01-6.84 (m, 3H), 4.52 (s, 2H), 4.45 (s, 2H) 1.48 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.61, 157.73, 138.93, 129.55, 121.83, 114.91, 114.44, 82.14, 65.34, 33.02, 27.74.

Synthesis of compound CD3 (G1-OH):



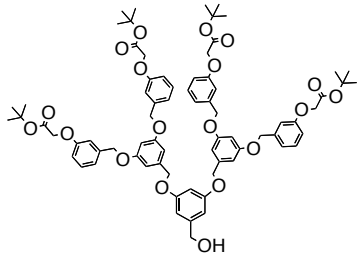
CD2 (10 g, 34.1 mmol), 3, 5-dihydroxybenzylalcohol (2.3 g, 16.5 mmol), potassium carbonate (13.46 g, 97 mmol), 18-Crown-6 (2.4 g, 9.7 mmol), were taken in 200 mL of acetone and refluxed for 12 hrs under argon atmosphere. The reaction mixture was allowed to cool and solvent was evaporated to dryness. The residue was partitioned between water and dichloromethane. The organic layer was separated, the aqueous layer extracted with dichloromethane. The combined organic layer was washed with brine and dried with anhydrous Na2SO4 and evaporated to dryness. The residue was purified by silica gel column by eluting with ethyl acetate/hexane (20:80) to afford 11.3 g (98%) of **CD3** as a light yellow liquid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.27 (m, 2H), 7.02-6.97 (m, 4H), 6.84 (s, 2H), 6.59 (s, 2H), 6.50 (s, 1H), 4.99 (s, 4H), 4.60-4.51 (m, 6H), 1.47 (s, 18H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.87, 159.80, 157.95 143.58, 138.47, 129.48, 120.26, 113.91, 113.40, 105.50, 101.01, 82.23, 69.53, 65.50, 64.81, 27.86.; MALDI-ToF: Calculated for C33H40O9: 580.67; Found: 602.80 (M+, 23).

Synthesis of compound (CD4, G1-Br):



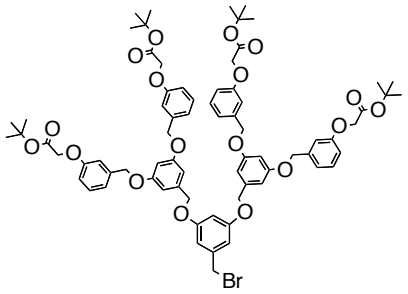
The alcohol **CD3** (10.0 g, 34.4 mmol) was dissolved in dry THF (10 mL) under argon atmosphere. To this PPh3 (13.6 g, 52 mmol) was added. After 5 min carbontetrabromide (17.2 g, 52 mmol) was added in one portion. After stirring for 15 min, it was quenched with water and extracted with dichloromethane. The organic layer was evaporated to dryness and the residue purified by column chromatography (SiO2, ethyl acetate/hexane (20:80)) to afford the product **CD4**, 9.66 g (85% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31-7.26 (m, 3H), 7.02-6.84 (m, 5H), 6.66-6.60 (m, 3H), 4.98-4.93 (m, 4H), 4.57-4.36 (m, 6H), 1.50 (s, 18H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.46, 159.22, 157.45, 157.19, 139.21, 137.80, 129.00, 119.98, 119.75, 113.40, 113.13, 112.94, 107.54, 101.41, 81.58, 68.97, 64.91, 64.04, 27.34.

Synthesis of compound (CD5, G2-OH):



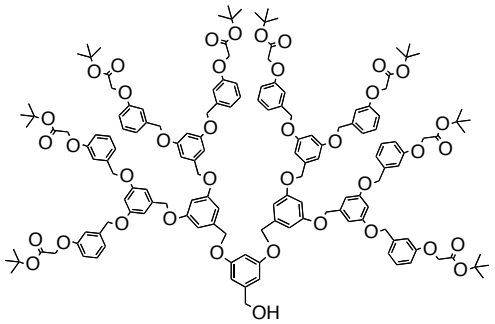
CD4 (9.17 g, 14 mmol), 3, 5-dihydroxybenzylalcohol (0.95 g, 6.5 mmol), potassium carbonate (5.4 g, 36 mmol), 18-Crown-6 (1 g, 3.6 mmol), were taken in 200 mL of acetone and refluxed for 12 hrs under argon atmosphere. The reaction mixture was allowed to cool and solvent was evaporated to dryness. The residue was partitioned between water and dichloromethane. The organic layer was separated, the aqueous layer extracted with dichloromethane. The combined organic layer was washed with brine and dried with anhydrous Na2SO4 and evaporated to dryness. The residue was purified by silica gel column by eluting with ethyl acetate/hexane (25:75) to afford 6.0 g (80%) of **CD5** as a light yellow liquid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28-7.26 (m, 5H), 7.02-6.97 (m, 8H), 6.86-6.69 (m, 4H), 6.65-6.50 (m, 8H), 5.0-4.97 (m, 12H), 4.60 (s, 2H), 4.52 (s, 8H) 1.48 (s, 36H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.08, 160.12, 160.05, 158.23, 143.95, 139.50, 138.64, 129.76, 120.55, 114.21, 113.67, 106.43, 105.70, 101.60, 101.19, 82.44, 69.85, 65.76, 28.12.; MALDI-ToF: Calculated for C73H84O19: 1265.44; Found: 1287.91 (M+, 23).

Synthesis of compound (CD6, G2-Br):



The alcohol **CD5** (4.4 g, 3.5 mmol) was dissolved in dry THF (10 mL) under argon atmosphere. To this PPh3 (1.82 g, 7.0 mmol) was added. After 5 min carbontetrabromide (2.3 g, 7.0 mmol) was added in one portion. After stirring for 15 min, it was quenched with water and extracted with dichloromethane. The organic layer was evaporated to dryness and the residue purified by column chromatography (SiO2, 20% ethyl acetate in hexanes) to afford the product **CD6**, 3.3 g (72.4% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28-7.26 (m, 4H), 7.02-6.84 (m, 12H), 6.64-6.35 (m, 9H), 5.0-4.81 (m, 12H), 4.62-4.40 (m, 10H), 1.47 (s, 36H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.14, 160.18, 160.06, 158.28, 139.91, 139.20, 138.63, 129.79, 120.56, 114.25, 113.70, 108.31, 106.52, 102.26, 101.71, 82.43, 70.07, 69.90, 65.80, 28.16.

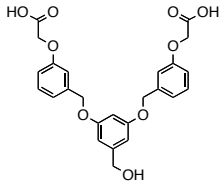
Synthesis of compound CD7 (G3-OH):



CD6 (3.25 g, 2.5 mmol), 3, 5-dihydroxybenzylalcohol (0.15 g, 1.7 mmol), potassium carbonate (1.0 g, 7.0 mmol), 18-Crown-6 (0.25 g, 0.7 mmol), were taken in 80 mL of acetone and refluxed for 12 hrs under argon atmosphere. The reaction mixture was allowed to cool and solvent was evaporated to dryness. The residue was partitioned between water and dichloromethane. The organic layer was separated, the aqueous layer extracted with dichloromethane. The combined organic layer was washed with brine and dried with anhydrous Na2SO4 and evaporated to dryness. The residue was purified by silica gel column by eluting with ethyl acetate/hexane (30:70) to afford 1.9 g (70%) of **CD7** as a light yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (m, 38H), 6.86-6.28 (m, 15H), 5.20-4.85 (m, 36H), 4.53-4.27 (m, 10H),

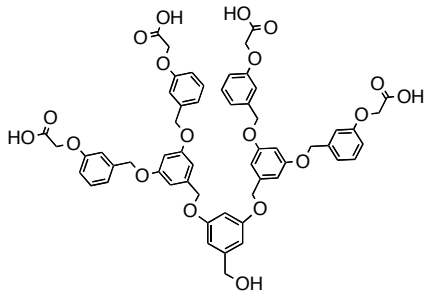
1.47 (s, 72H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.03, 159.76, 158.22, 143.98, 139.48, 139.36, 138.60, 129.73, 120.53, 114.18, 113.67, 106.47, 105.72, 101.62, 101.11, 82.18, 69.98, 69.83, 65.73, 29.46.; MALDI-ToF: Calculated for C153H172O39: 2634.98; Found: 267.401 (M+, 39).

Synthesis of compound 5 (G1-OH):



To a solution of compound **CD3** (1.2 g, 2.1 mmol) in tetrahydrofuran (6 mL) was added aqueous potassium hydroxide (0.46 g, 8.2 mmol) dissolved in water (2 mL). Methanol (4 mL) was then added to this two-phase system to give homogeneous solution. This mixture was then heated at reflux for 12 h. The reaction mixture was evaporated to dryness and the residue dissolved in water (25 mL) and the mixture heated at reflux for another 12 h. After cooling to room temperature, the reaction mixture was acidified with 2N HCl. The precipitate formed was collected by vacuum filtration and dried to afford **5**. Yield: 1.1 g (97%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32-7.30 (m, 2H), 7.12-6.97 (m, 4H), 6.84 (s, 2H), 6.59 (s, 2H), 6.50 (s, 1H), 4.91 (s, 4H), 4.64-4.52 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.83, 159.96, 158.45, 145.85, 139.36, 130.13, 120.92, 114.38, 105.82, 100.76, 69.56, 65.22, 63.45.; MALDI-ToF: Calculated for C25H24O9: 468.45; Found: 490.89 (M+, 23).

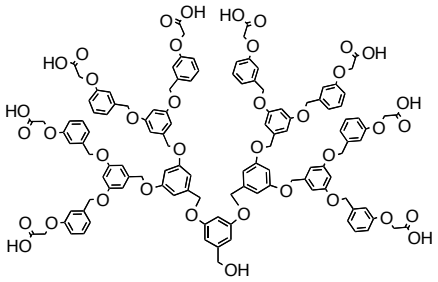
Synthesis of compound 6 (G2OH):



To a solution of compound **CD5** (1.0 g, 0.87 mmol) in tetrahydrofuran (10 mL) was added aqueous potassium hydroxide (0.40 g, 7.0 mmol) dissolved in water (2 mL). Methanol (5 mL) was then added to this two-phase system to give homogeneous solution. This mixture was then heated at reflux for 12 h. The reaction mixture was evaporated to dryness and the residue dissolved in water (25 mL) and the mixture heated at reflux for another 12 h. After cooling to room temperature, the reaction mixture was acidified with 2N HCl. The precipitate formed was collected by vacuum filtration and dried to afford **5**. Yield: 0.80 g (95%).^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37-7.10 (m, 13H), 6.96-6.76 (m, 4H), 6.71-6.50 (m, 8H), 5.10-4.97 (m, 12H), 4.71

(m, 10H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.79, 160.14, 159.94, 158.43, 140.18, 139.14, 130.14, 120.91, 114.49, 114.18, 107.18, 107.05, 101.62, 69.71, 65.03.; MALDI-ToF: Calculated for C57H52O19: 1041.01; Found: 1063.05 (M+, 23), 1079.04 (M+, 39).

Synthesis of compound 7 (G3-OH):



To a solution of compound **CD7** (1.5 g, 0.57mmol) in tetrahydrofuran (20 mL) was added aqueous potassium hydroxide (0.51 g, 9.12 mmol) dissolved in water (3 mL). Methanol (6mL) was then added to this two-phase system to give homogeneous solution. This mixture was then heated at reflux for 12 h. The reaction mixture was evaporated to dryness and the residue dissolved in water (25 mL) and the mixture heated at reflux for another 24 h. After cooling to room temperature, the reaction mixture was acidified with 2N HCl. The precipitate formed was collected by vacuum filtration and dried to afford compound **7**. Yield: 1.25 g (90%).^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 38H), 7.15-7.09 (m, 15H), 5.10-5.03(m, 36H), 4.49-4.47 (m, 10H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.67, 160.00, 158.31, 139.00, 129.99, 120.75, 114.35, 114.05, 107.03, 69.58, 68.93.; MALDI-ToF: Calculated for C121H108O39: 2186.13; Found: 2207.90 (M+, 23), 2224.83 (M+, 39).

Estimation of the Binding Constants from Activity Assay:

Assuming that one dendron has *n* identical and independent binding sites that are able to bind one ChT molecule each, the complexation of ChT with dendron could be expressed by equation S1.

Site + ChT $\rightleftharpoons$ **Site-ChT** **(S1)**

Where *K*S denotes the microscopic binding constant. Because the activity decrease of ChT is attributed to the complexation with dendron, the activity difference (ΔZ) is assumed to be proportional to the concentration of complexed ChT, i.e. $\Delta Z = \alpha \cdot$[Site-ChT]. The proportionality coefficient α reflects the activity difference of unit ChT before and after complexation. Then *K*S could be defined as:

$$Ks = \frac{[\text{Site-ChT}]}{[\text{Site}][\text{ChT}]} = \frac{\Delta Z/\alpha}{([\text{Site}]_0 - \Delta Z/\alpha)([\text{ChT}]_0 - \Delta Z/\alpha)} \qquad \textbf{(S2)}$$

Where [Site]0 and [ChT]0 denote the initial concentrations of binding sites and ChT, repectively. The relationship between the concentrations of binding sites and dendron is describable by [Site]0=*n*[dend]0. After a few manipulation, equation S2 is solved for Δ*Z* to give equation S3:

$$\Delta Z = \frac{\alpha}{2} \cdot \{([\text{ChT}]_0 + n[\text{dend}]_0 + 1/Ks) - \sqrt{([\text{ChT}]_0 + n[\text{dend}]_0 + 1/Ks)^2 - 4n[\text{ChT}]_0[\text{dend}]_0}\} \qquad \textbf{(S3)}$$

On the basic of Equation S3, microscopic binding constants (*K*S) could be readily determined by using the nonlinear least-squares curve-fitting analysis. The binding ratio (i.e. the number of polymer nanoparticles' binding sites) of each dendron was obtained from gel study. The curve-fitting analysis was done on PC using Origin 7.0 program (OriginLab Co., Northampton, USA).

Dynamic Light Scattering (DLS):

Dendron solutions (**5-7**) were prepared in 5mM sodiumphosphate buffer pH 7.4 to make 10^{-4} M concentration. A digital correlator and a goniometer were used for the DLS measurements. The light source was a solid-state laser system, operating at 514 nm. The temperature was kept constant at 25^0 C. The solutions were filtered by 0.22mm pore size for aqueous solutions filters to eliminate dust particle. All the measurements were done at a correlation time of 1.30 minutes. The particle sizes taken are average of at least five readings. In all cases, no evidence of aggregation was found.