Organic & Biomolecular Chemistry

Dendritic Architectures by Orthogonal Thiol-Maleimide "Click" and Furan-Maleimide Dynamic Covalent Chemistries.

Stephen H. Frayne, Robert M. Stolz, Brian H. Northrop*
Wesleyan University, Department of Chemistry
Hall-Atwater Laboratories, 52 Lawn Ave., Middletown, CT 06459, USA.
Email: bnorthrop@wesleyan.edu, phone: 860-685-3987

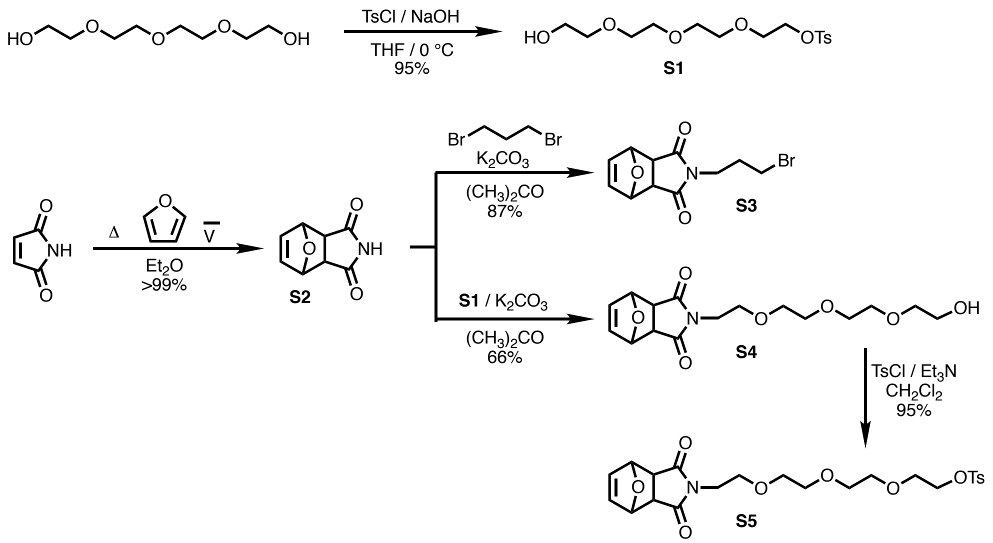
SUPPORTING INFORMATION

(52 pages)

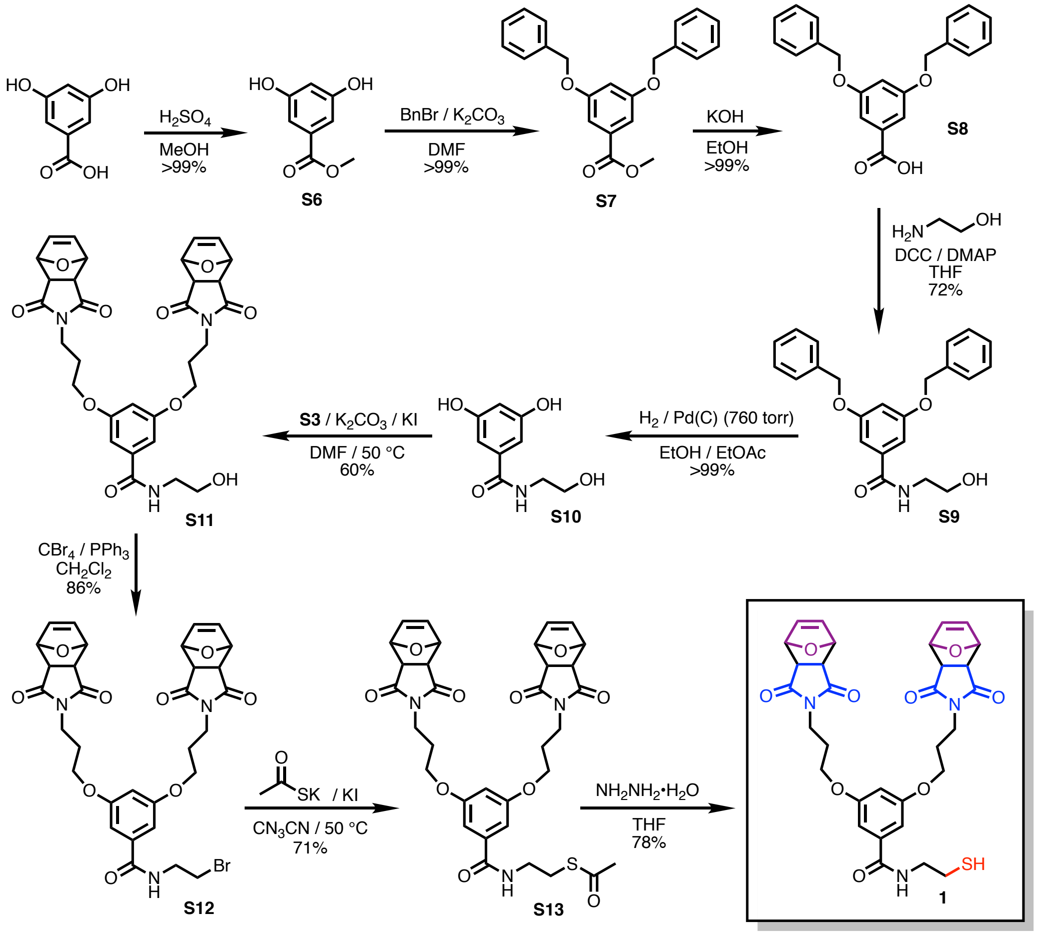
I. Materials and Methods.

Unless otherwise stated chemicals were purchased from commercial suppliers and used as received. The syntheses of compounds **S1**,[1] **S2**,[2] **S3**,[3] **S4**,[4] **S5**,[5] **S6**,[6] **S7**,[7] **S8**,[8] **S10**,[9] **S17**,[10] **S18**,[11] and **tris–M**[11] were carried out according to modified literature procedures. Solvents were dried using an Innovative Technologies SPS-400-5 solvent purification system. All reactions were carried out under an anhydrous N_2 atmosphere unless otherwise noted. Thin layer chromatography (TLC) was performed on alumina-backed sheets coated with silica gel 60 F254. TLC plates were visualized using a UV/Vis lamp and/or by staining with iodine or *p*-anisaldehyde solution. Column chromatography was performed using glass columns over 60 Å, 32–63 µm silica gel. Melting points were determined on a Mettler Toledo Mel-Temp II melting point apparatus and are uncorrected. Melting points for compounds containing a furan-protected maleimide are not reported due to complications arising from the thermally promoted loss of furan upon heating. All ^1H and ^{13}C NMR spectra were recorded on with a Varian Mercury (300 and 75 MHz, respectively) or Varian Unity Inova (500 and 125 MHz, respectively) spectrometer using residual solvent as the internal standard. All chemical shifts are quoted using the δ scale and all coupling constants are expressed in Hertz (Hz). Gel permeation chromatography (GPC) of THF-soluble dendrons and dendrimers was performed on a Viscotek TDA 305 eluting with THF at 35 °C at 1.0 mL min^{-1}. The Viscotek TDA 305 was arranged with one guard column (particle size 8 micron, dimensions 10x4.6 mm) and a series of two identical SEC columns (particle size 10 micron, max pore size 5,000 Å, dimensions 300x7.8 mm). The number average molecular weight (M_n), molecular weight (M_W), and polydispersity index (PDI) were determined using the Viscotek RI detector and OmniSEC software, and calculated relative to linear poly(methyl methacrylate) (PMMA) standards in the range of Mp 1,960-903,000 purchased from Polymer Standards Service. Dendrons above generation 3 were not soluble enough in THF to allow for GPC analysis using the instrument at Wesleyan University, therefore samples were analyzed at the University of Massachusetts, Amherst, using an Agilent GPC eluting with DMF. Samples were analyzed using Agilent GPC/SEC Software Version 1.2.3182.29519 and calibrated against polystyrene standards. ESI, APCI, and MALDI high-resolution mass spectrometric analysis was performed at the University of Illinois, Urbana-Champaign, the University of California, Riverside, or the University of Massachusetts, Amherst, Mass Spec facilities.

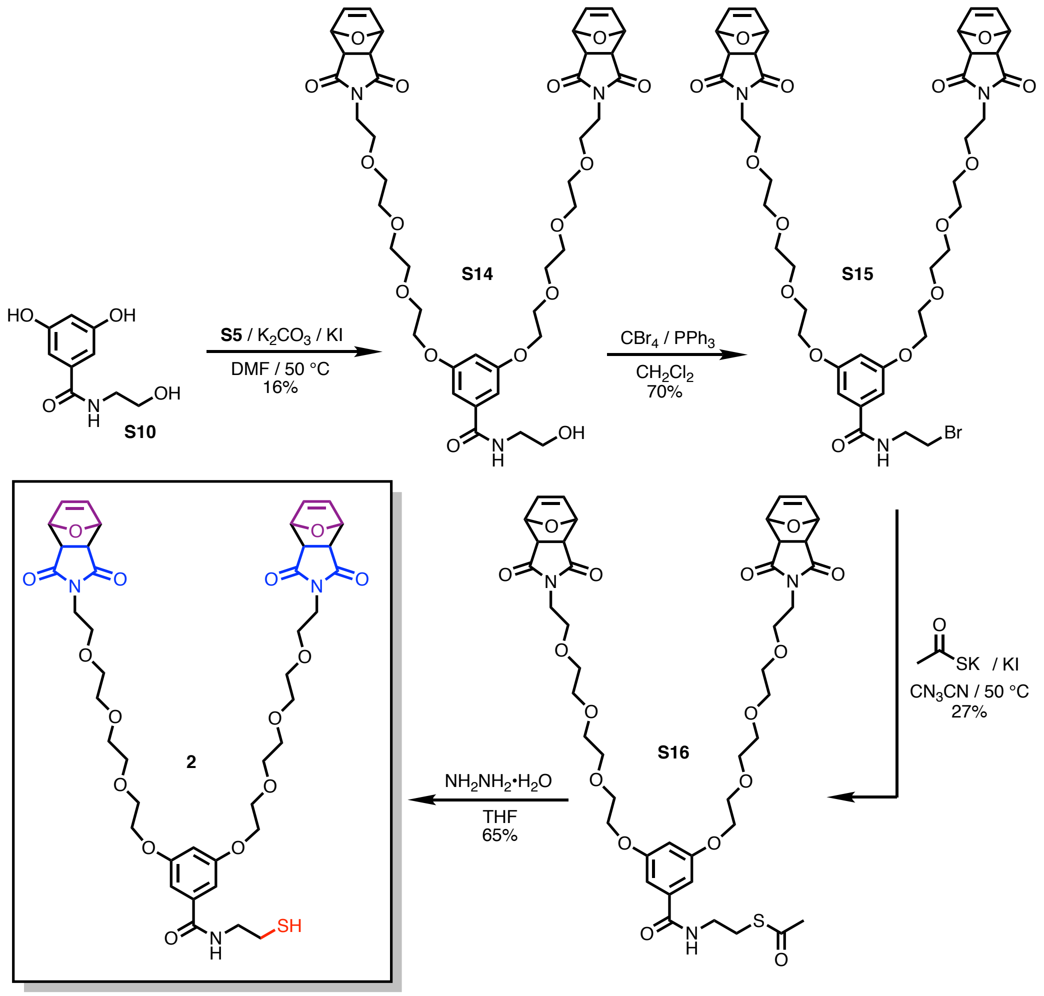
II. Synthetic Schemes.



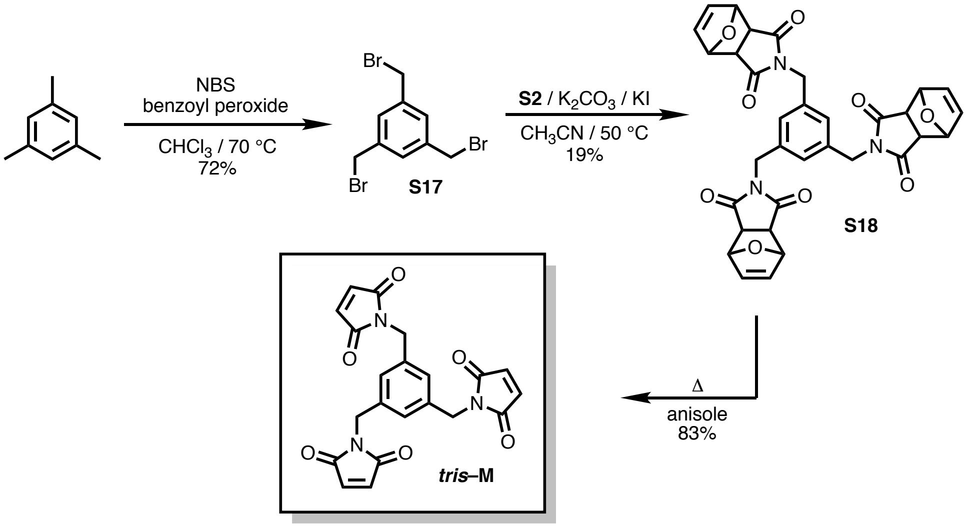
Scheme S1: Synthesis of furan-protected maleimide linkers **S3** and S**5**.



Scheme S2: Synthesis of propyl-linked branched monomer **1**.



Scheme S3: Synthesis of tetra(ethylene glycol)-linked branched monomer **2**.



Scheme S4: Synthesis of maleimide-functionalized core ***tris*–M**.

III. Experimental Procedures.

Compound S1: Tetraethylene glycol (100.9 g, 520.0 mmol) was added to a round-bottom flask, dissolved in 100 mL of tetrahydrofuran, and cooled to 0 °C. Separately, sodium hydroxide (3.32 g, 83.0 mmol) was dissolved in 30 mL of water. The sodium hydroxide/water solution was added to the tetraethylene glycol solution at 0 °C, and the resulting mixture was stirred for 30 minutes at 0 °C. A solution of *p*-toluenesulfonyl chloride (9.90 g, 52.0 mmol) in tetrahydrofuran (30 mL) was added dropwise to the solution of tetraethylene glycol solution at 0 °C over the course of 1 hour. The resulting mixture was warmed slowly to room temperature and stirred overnight at room temperature. The mixture was concentrated under reduced pressure, diluted with dichloromethane, and extracted three times with dichloromethane. The combined organic layers were washed three times with water, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford 18.0 g (99%) of compound **S1** as a viscous oil. Characterization matched literature values.[1]

Compound S2: Maleimide (20.0 g, 0.21 mol) was added to a round-bottom heavy wall pressure vessel, and suspended in diethyl ether (100 mL, 2.1 M). Furan (28.1 g, 0.41 mol) was added and the pressure vessel was immediately sealed with the threaded Teflon cap. The reaction was heated at 100 °C overnight, and then allowed to cool down to room temperature. After cooling down to room temperature the reaction mixture was filtered through a fritted glass funnel and washed with excess diethyl ether. The solid was collected and dried under high vacuum to afford 33.7 g (99%) of compound **S2** as a white solid. The product was used without further purification. Characterization matched literature values.[2]

Compound S3: A three-neck round-bottom flask was charged with 1,3-dibromopropane (61.1 g, 0.30 mol), potassium carbonate (41.0 g, 0.29 mol), potassium iodide (0.51 g, 31.0 mmol), and acetone (305 mL) under an atmosphere of dry N_2(g). Compound **S2** (10.0 g, 0.061 mol) was added and the solution was stirred at 50 °C for 8 hours. The solution was filtered through a fritted glass funnel and the filtrate was concentrated under reduced pressure. The resulting residue was purified on a short pad of silica using a mixture of EtOAc:Hex (1:1) to yield 15.4 g (89%) of compound 2 as a white solid. Characterization matched literature values.[3]

Compound S4: Compound **S2** (8.5 g, 51.0 mmol) and potassium carbonate (9.4 g, 68.0 mmol) were added to a three-neck round-bottom flask, placed under an inert N_2 atmosphere, and dissolved in acetone (34 mL, 1.0 M). In a separate round-bottom flask, compound **S1** (11.9 g, 34.0 mmol) was dissolved in acetone (34 mL, 1.0 M) under an N_2 atmosphere. The solution containing compound **S1** was added to the three-neck round-bottom, and the resulting mixture was heated at 50 °C for 60 hours. Solids were removed by filtration through a fritted glass funnel, and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography DCM:MeOH (98:2) to afford 11.1 g (95%) compound S**4** as a viscous oil. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{16}H_{24}NO_7$, 342.1541, found 342.1553. ^1H and ^{13}C NMR spectroscopic characterization matched literature values.[4]

Compound S5: Triethylamine (13.2 g, 130.0 mmol) was added to a solution of compound S**4** (11.1 g, 33.0 mmol) and *p*-toluenesulfonyl chloride (7.7 g, 41.0 mmol) in dichloromethane (66 mL, 0.5 M), and the resulting solution was stirred overnight at room temperature. The solution was diluted with water and extracted three times with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was purified by column chromatography using a mixture of DCM:Hex (80:20) to afford 10.7 g (66%) compound **S5**[5] as a viscous oil. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.82 (d, 2H, J = 8.0 Hz), 7.37 (d, 2H, J = 8.5 Hz), 6.53 (s, 2H), 5.28 (s, 2H), 4.18 (t, 2H, J = 4.5 Hz), 3.70 (t, 4H, J = 5.0 Hz), 3.64 (t, 2H, J = 5.0 Hz), 3.62-3.57 (m, 8H), 2.88 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 176.1, 144.8, 136.5, 132.9, 129.8, 128.0, 80.9, 80.8, 70.7, 70.6, 70.5, 69.3, 68.6, 67.1, 47.5, 38.2, 21.6 ppm.

Compound S6: A catalytic amount of concentrated sulfuric acid (95-98%, 1 mL) was added to a solution of 3,5-dihydroxybenzoic acid (65.0 mmol, 10.0 g) in methanol (80 mL, 0.81 M). The solution was refluxed for 5 hours, concentrated under reduced pressure and diluted with ethyl acetate. The resulting solution was washed once each with saturated sodium bicarbonate, water, and brine. The organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield 9.9 g (91%) of compound **S6** as a white solid. Characterization matched literature values.[6]

Compound S7: Compound S**6** (9.9 g, 59.0 mmol) and potassium carbonate (37.0 g, 267.6 mmol) were added to a two-neck flask and placed under an inert N$_2$ atmosphere. Acetone (100 mL, 0.89 M) and benzyl bromide (45.8 g, 267.6 mmol) were added and the resulting solution was stirred overnight at room temperature. The solution was diluted with ethyl acetate and water, and extracted four time with ethyl acetate. The combined organic layer were washed once with brine, dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was recrystallized three times from ether to afford 21.0 g (67%) of compound **S7**[7] as a white solid. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.46-7.35 (m, 10H), 7.32 (d, 2H, J = 2.0 Hz), 6.83 (t, 1H, J = 2.5 Hz), 5.10 (s, 4H), 3.93 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 166.8, 159.9, 136.6, 132.2, 128.7, 128.2, 127.6, 108.5, 107.3, 70.3, 52.3 ppm.

Compound S8: A mixture of compound **S7** (21.0 g, 60.0 mmol), powdered potassium hydroxide (8.5 g, 151.0 mmol), and ethanol (200 mL, 0.3 M) were refluxed for two hours. The resulting mixture was diluted with ethyl acetate and acidified to pH 1 with 1N HCl. The organic layer was washed twice with water, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield 18.7 g (93%) of compound **S8**[8] as a white solid. ^{1}H NMR (DMSO-d$_6$, 500 MHz): δ 7.46-7.33 (m, 10H), 7.15 (d, 2H, J = 2.5 Hz), 6.92 (t, 1H, J = 2.5 Hz), 5.15 (s, 4H). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ 167.5, 159.9, 137.2, 133.7, 128.9, 128.3, 128.1, 108.6, 106.9, 70.0 ppm.

Compound S9: Compound **S8** (18.0 g, 54.0 mmol), ethanolamine (4.0 g, 65.0 mmol), and triethylamine (13.6 g, 135.0 mmol) were added to a three-neck flask and placed under an inert N$_2$ atmosphere. Anhydrous dimethylformamide (54.0 mL, 0.5 M) and anhydrous dichloromethane

(54.0 mL, 0.5 M) were added and the solution was cooled down to 0 °C. N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (12.4 g, 65.0 mmol) was added portion-wise to the solution at 0 °C and the cooled solution was then slowly warmed to room temperature and stirred further at room temperature for 24 hours. The resulting mixture was filtered, diluted with water, and extracted five times with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was purified over a short pad of silica eluting with a mixture of DCM:MeOH (97:3) and the residue was purified further by recrystallization from dichloromethane to yield 11.5 g (57%) of compound **S9** as a white solid. Mp 148-150 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.45-7.29 (m, 10H), 7.03 (d, 2H, J = 2.5 Hz), 6.76 (t, 1H, J = 2.5 Hz), 6.57 (s, 1H), 5.08 (s, 4H), 3.85 (q, 2H, J = 5.0 Hz), 3.64 (q, 2H, J = 5.0 Hz), 2.48 (t, 1H, 5.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.3, 160.0, 136.4, 128.6, 128.2, 127.6, 106.2, 105.3, 70.3, 62.0, 42.9 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{23}H_{24}NO_4$, 378.1697, found 378.1705.

Compound S10: 10 wt % Palladium on carbon (1.15 g) was added to a solution of compound **S9** (11.5 g, 30.0 mmol) in ethanol (60 mL) and ethyl acetate (40 mL) under a hydrogen atmosphere (1.0 atm). The suspension was stirred at room temperature for 16 hours and then filtered through celite while washing with excess ethyl acetate. The filtrate was concentrated under reduced pressure and recrystallized from warm methanol to afford 5.3 g (88%) of compound **S10**[9] as a brown solid. ^{1}H NMR (CD_3OD, 500 MHz): δ 6.73 (d, 2H, J = 1.5 Hz), 6.42 (t, 1H, J = 2.0 Hz), 3.70 (t, 2H, J = 6.0 Hz), 3.48 (t, 2H, J = 6.0 Hz). ^{13}C NMR (125 MHz, CD_3OD): δ 169.5, 158.4, 136.4, 105.4, 105.3, 60.3, 42.1 ppm. TOF MS ESI (m/z) $[M+H]^-$ Calculated for $C_9H_{10}NO_4$, 196.0604, found 196.0610.

Compound S11: A three-neck round-bottom flask was charged with compound **S3** (7.02 g, 0.025 mol), potassium carbonate (3.4 g, 0.025 mol), potassium iodide (91 mg, 0.55 mmol), and acetone (22 mL) under an inert N_2 atmosphere. After stirring for 10 minutes at room temperature, compound **S10** (2.2 g, 0.011 mol) was added and the resulting mixture was heated overnight at 50 °C. The mixture was filtered through a fritted funnel and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography using a mixture of EtOAc:MeOH (96:4) to yield 4.2 g (62%) of **S11** as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.88 (d, 2H, J = 2.4 Hz), 6.72 (s, 1H), 6.54 (t, 1H, J = 2.4 Hz), 6.51 (s, 4H), 5.25 (s, 4H), 3.96 (t, 4H, J = 6.8 Hz), 3.81 (q, 2H, J = 5.4 Hz), 3.69 (t, 4H, J = 6.8 Hz), 3.58 (q, 2H, J = 5.4 Hz), 2.85 (s, 4H), 2.75 (t, 1H, J = 5.7 Hz), 2.05 (p, 4H, J = 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.2, 168.3, 159.9, 136.5, 136.2, 105.9, 105.4, 80.9, 65.6, 62.6, 47.4, 43.0, 36.1, 27.1 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{31}H_{34}N_3O_{10}$, 608.2244, found 608.2250.

Compound S12: A three-neck round-bottom flask was charged with compound **S11** (3.2 g, 0.0053 mol) and dry dichloromethane (27 mL) under an inert N_2 atmosphere. The three-neck round-bottom flask was charged with carbon tetrabromide (2.1 g, 0.0063 mol) and triphenylphosphine (1.7 g, 0.0063 mol) and stirred at room temperature overnight. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of EtOAc:Hex (3:1) to yield 3.0g (86%) of **S12** as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.87 (d, 2H, J = 1.8 Hz), 6.63 (s, 1H), 6.54 (s, 1H), 6.51 (s, 4H), 5.25 (s, 4H), 3.96 (t, 4H, J = 6.0 Hz), 3.81 (q, 2H, J = 6.0 Hz), 3.69 (t, 4H, J = 6.0 Hz), 3.57 (t, 2H, J = 6.0 Hz), 2.85 (s, 4H), 2.06 (p, 4H, J = 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.1, 167.2, 159.9, 136.5, 136.1, 105.8, 105.0, 80.9, 65.5, 47.4, 41.6, 36.1, 32.2, 27.1 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{31}H_{33}N_3O_9$, 670.1400, found 670.1410.

Compound S13: A three-neck round-bottom flask was charged with compound **S12** (2.0 g, 0.003 mol), potassium thioacetate (0.68 g, 0.006 mol), potassium iodide (25 mg, 0.15 mmol), and acetonitrile (15 mL) under an inert N_2 atmosphere. The solution was stirred at room temperature for 5 hours before it was filtered through a fritted glass funnel. The filtrate was concentrated under reduced pressure and purified by column chromatography using a mixture EtOAc:Hex (2:1) to yield 1.4 g (71%) of **S13** as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.84 (d, 2H, J = 1.8 Hz), 6.61 (s, 1H), 6.53 (s, 1H), 6.51 (s, 4H), 5.26 (s, 4H), 3.96 (t, 4H, J = 5.9 Hz), 3.69 (t, 4H, J = 6.8 Hz), 3.59 (q, 2H, J = 6.5 Hz), 3.11 (t, 2H, J = 6.5 Hz), 2.85 (s, 4H), 2.37 (s, 3H), 2.06 (p, 4H, J = 6.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.4, 176.1, 167.2, 159.8, 136.5, 136.2, 105.7, 105.1, 80.9, 65.5, 47.4, 40.0, 36.1, 30.7, 28.7, 27.2 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{33}H_{36}N_3O_{10}S$, 666.2121, found 666.2124.

Compound 1: A three-neck round-bottom flask was charged with compound **S9** (1.0 g, 0.0015 mol) and tetrahydrofuran under an inert N_2 atmosphere. Hydrazine monohydrate (0.14 g, 0.0045 mol) was added and the reaction was stirred at room temperature for 4 hours and quenched with acetic acid (0.27 g, 0.0045 mol). The solution was concentrated under reduced pressure, and extracted three times from water using dichloromethane. The organic layers were collected and concentrated under reduced pressure, and the residue was purified by column chromatography using a mixture of DCM/MeOH (99:1) to yield 0.7 g (78%) of **1** as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.87 (d, 2H, J = 2.4 Hz), 6.63 (s, 1H), 6.54 (s, 1H), 6.51 (s, 4H), 5.25 (s, 4H), 3.96 (t, 4H, J = 6.2 Hz), 3.69 (t, 4H, J = 7.1 Hz), 3.59 (q, 2H, J = 6.3 Hz), 2.84 (s, 4H), 2.76 (q, 2H, J = 6.3 Hz), 2.06 (p, 4H, J = 6.3 Hz), 1.41 (t, 1H, J = 8.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.2, 167.3, 159.8, 136.5, 105.8, 104.8, 80.9, 65.5, 47.4, 43.0, 36.0, 27.1, 24.4. ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{31}H_{34}N_3O_9S$, 624.2012, found 624.2016.

Compound S14: A three-neck round-bottom flask was charged with compound **S5** (9.9 g, 0.02 mol), potassium carbonate (2.8 g, 0.02 mol), and acetone (45 mL) under an inert N_2 atmosphere. After stirring for 10 minutes at room temperature, compound **S10** (1.8 g, 0.009 mol) was added and heated overnight at 50 °C. The mixture was filtered through a fritted glass funnel and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography using a mixture of EtOAc:MeOH (96:4) to yield 1.2 g (16%) of **S14** as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.02 (t, 1H, J = 5.5 Hz), 6.99 (d, 2H, J = 2.5 Hz), 6.63 (t, 1H, J = 2.5 Hz), 6.50 (s, 4H), 5.25 (s, 4H), 4.15 (t, 4H, J = 4.5 Hz), 3.85 (t, 4H, J = 4.5 Hz), 3.82 (t, 2H, J = 5.0 Hz), 3.72-3.60 (m, 26H), 3.09 (t, 1H, J = 5.5 Hz), 2.86 (s, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.2, 168.0, 159.8, 136.5, 106.0, 104.6, 80.9, 80.8, 70.6, 70.5, 70.4, 70.0, 69.5, 67.6, 67.0, 61.8, 47.4, 43.0, 38.1 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{41}H_{54}N_3O_{16}$, 844.3499, found 844.3504.

Compound S15: A three-neck round-bottom flask was charged with compound **S14** (1.2 g, 0.0014 mol) and dry dichloromethane (14 mL) under an inert N_2 atmosphere. The three-neck round-bottom flask was charged with carbon tetrabromide (0.57 g, 0.0017 mol) and triphenylphosphine (0.45 g, 0.0017 mol) and stirred at room temperature overnight. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of EtOAc:Hex (3:1) to yield 0.9g (70%, crude yield) of **S15** as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.12 (d, 2H, J = 2.0 Hz), 6.64 (s, 1H), 6.51 (s, 4H), 5.27 (s, 4H), 4.44 (t, 2H, J = 9.5 Hz), 4.15 (t, 4H, J = 5.0 Hz), 4.07 (t, 2H, J = 9.5 Hz), 3.86 (t, 4H, J = 5.0 Hz), 3.73-3.63 (m, 26H), 2.87 (s, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.0, 164.2, 159.6, 136.5, 106.5, 105.3, 80.8, 80.7, 70.6, 70.5, 70.4, 70.0, 69.4, 67.6, 67.0, 54.7, 47.3, 38.1 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{41}H_{52}N_3O_{15}$, 826.3392, found 826.3398.

Compound S16: A three-neck round-bottom flask was charged with compound **S15** (3.0 g, 0.0033 mol), potassium thioacetate (0.76 g, 0.0066 mol), potassium iodide (55 mg, 0.33 mmol), and acetonitrile (16.5 mL) under an inert N_2 atmosphere. The solution was stirred at room temperature for 5 hours before it was filtered through a fritted glass funnel. The filtrate was concentrated under reduced pressure and purified by column chromatography using a mixture EtOAc:Hex (2:1) to yield 0.8 g (27%) of **S16** as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.98 (d, 2H, J = 2.0 Hz), 6.80 (s, 1H), 6.65 (t, 1H, J = 2.0 Hz), 6.50 (s, 4H), 5.26 (s, 4H), 4.16 (t, 4H, J = 5.0 Hz), 3.86 (t, 4H, J = 5.0 Hz), 3.73-3.61 (m, 28H), 2.87 (s, 4H), 1.45 (t, 1H, J = 8.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.2, 167.2, 160.0, 136.5, 136.4, 106.0, 104.7, 80.6, 70.7, 70.6, 70.5, 70.1, 69.6, 67.7, 67.1, 47.4, 43.0, 38.2, 25.4 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{43}H_{56}N_3O_{16}S$, 902.3373, found 902.3381.

Compound 2: A three-neck round-bottom flask was charged with compound **S16** (0.8 g, 0.88 mmol) and tetrahydrofuran under an inert N_2 atmosphere. Hydrazine monohydrate (138.8 mg, 1.77 mmol) was added, and the reaction was stirred at room temperature for 4 hours and quenched with acetic acid (106.3 mg, 1.77 mmol). The solution was concentrated under reduced pressure, and extracted three times from water using dichloromethane. The organic layers were collected and concentrated under reduced pressure, and the residue was purified by column chromatography eluting with a mixture of DCM/MeOH (99:1) to yield 0.6 g (65%) of **2** as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.95 (d, 2H, J = 2.5 Hz), 6.79 (t, 1H, J = 5.5 Hz), 6.64 (t, 1H, J = 2.5 Hz), 6.50 (s, 4H), 5.26 (s, 4H), 4.16 (t, 2H, J = 5.0 Hz), 3.86 (t, 4H, J = 4.5 Hz), 3.73-3.62 (m, 28H), 3.15 (t, 2H, J = 6.0 Hz), 2.87 (s, 4H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.6, 176.2, 167.2, 160.0, 136.7, 136.3, 105.8, 105.0, 80.9, 80.8, 70.6, 70.1, 69.6, 67.7, 67.1, 47.5, 40.1, 38.2, 30.7, 28.8 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{41}H_{54}N_3O_{15}S$, 860.3256, found 860.3276.

Compound S17: N-bromosuccinimide (NBS) was dissolved in near-boiling (~90 °C) water, gravity filtered into a round-bottom flask that was preemptively cooled down to 0 °C, and allowed to recrystallize at 0 °C for 2 hours. The crystals were filtered through a Buchner funnel and washed with ca 100 mL of ice water before drying under high vacuum. The freshly recrystallized NBS (6.7 g, 0.038 mol), mesitylene (1.3 g, 0.011 mol), and benzoyl peroxide (0.78 g, 0.003 mol) were dissolved in chloroform (16 mL, 0.7 M) and refluxed at 70 °C for 6 hours. The crude reaction mixture was filtered, washed with water, and extracted 3 times with DCM. The combined organic layers were washed once with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography using mixture of Hexanes:EtOAc (98:2) to afford 2.8 g (72%) of **S17** as a light yellow solid. Characterization matched literature values.[10]

Compound S18: **S2** (4.3 g, 0.026 mol) and potassium carbonate (4.3 g, 0.031 mol) were added to a 3-arm flask and placed under an inert N_2 atmosphere and dissolved in anhydrous acetonitrile (9 mL, 0.87 M). Compound **S17** (2.8 g, 0.0078 mol) was dissolved in anhydrous acetonitrile (9 mL, 0.87 M) under N_2, and added to the 3-arm flask. The reaction mixture was heated at 50 °C for 48 hours, and the completion of the reaction was monitored by TLC. The reaction mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography eluting with a mixture of EtOAc:MeOH (98:2) to afford 0.9 g (19%) of S**18**[11] as a white solid. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.13 (s, 3H), 6.53 (s, 6H), 5.32 (s, 6H), 4.60 (s, 6H), 2.87 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.8, 136.6, 136.3, 126.5, 80.9, 47.5, 42.0 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{33}H_{28}N_3O_9$, 610.1825, found 610.1826.

Compound *tris*–M: **S18** (0.9 g, 0.0015 mol) was added to a round-bottom flask and suspended in anisole (5 mL). The reaction mixture was heated at 140 °C for 1 hour, and then allowed to cool down to room temperature. The crude reaction was added directly to a silica gel column. Excess anisole was removed by eluting with hexanes. The remaining residue was purified in an elution mixture to DCM:MeOH (99:1) to afford 0.5 g (83%) of ***tris*–M** as a white solid. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.19 (s, 3H), 6.73 (s, 6H), 4.63 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 137.2, 134.2, 127.4, 41.0 ppm. TOF MS ESI (m/z) $[M+H]^+$ Calculated for $C_{21}H_{16}N_3O_6$, 406.1029, found 406.1039.

General Procedure for Dendron Synthesis: Growth step: *N*-methylmaleimide (1.0 equiv) and either **1** or **2** (1.05 equivs) were added to a 3 dram vial and dissolved in 1.0 M deuterated chloroform. A catalytic amount of Et_3N was added and the reaction mixture was stirred under ambient atmosphere for 2-16 hours as monitored by TLC. The crude reaction mixture was added directly to a short pad of silica and eluted using a mixture of CH_2Cl_2/MeOH. Activation step: The dendron sample (1 equiv) was added to a 10 mL round-bottom flask and suspended in 3 mL of anisole or toluene. The reaction mixture was heated at 140 °C for 1-8 hours. After cooling down to room temperature the crude reaction mixture was added directly to a short pad of silica. Ansiole or toluene was removed by eluting with hexanes and the activated dendron was obtained by eluting with a mixture of CH_2Cl_2/MeOH. The above growth and activation steps were repeated sequentially, doubling the molar equivalents of **1** or **2** at each growth step, up to the synthesis of a $G4_F$ dendron.

General Procedure for Dendrimer Synthesis: Dendrimer synthesis followed the same steps as dendron synthesis with the key difference being that tris-maleimide ***tris*–M** is used as a core molecule in place of *N*-methylmaleimide. Growth step: Compound **S19** (1.0 equiv) and either **1** or **2** (3.15 equivs) was added to a 3 dram vial and dissolved in 1.0 M deuterated chloroform. A catalytic amount of Et_3N was added and the reaction mixture was stirred under ambient atmosphere for 2-16 hours as monitored by TLC. The crude reaction mixture was added directly to a short pad of silica and purified with a mixture of CH_2Cl_2/MeOH. Activation step: The dendrimer sample (1 equiv) was added to 10 mL round-bottom flask and suspended in 3 mL of anisole. The reaction mixture was heated at 140 °C for 1-8 hours. After cooling down to room temperature the crude reaction mixture was added directly to a short pad of silica. Ansiole was removed by eluting with hexanes and the activated dendrimer was obtained by eluting with a mixture of CH_2Cl_2/MeOH. The above growth and activation steps were repeated sequentially using a 1.05:1 molar equivalent of **1** or **2** to maleimide at each growth step, up to the synthesis of a $G3_F$ dendrimer.

$G1_F$ Dendron: *N*-methylmaleimide (28.9 mg, 0.26 mmol) and **1** (170.0 mg, 0.27 mmol) were added to a 3 dram vial and dissolved in $CDCl_3$ (0.5 mL). Et_3N (12.5 mg, 0.124 mmol) was added, the vial was capped, and the reaction was allowed to stir at room temperature for 2 hours. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (99:1) to afford 160.0 mg (80%) of **$G1_F$** dendron as a white solid. ESI-TOF MS (*m/z*) $[M+H]^+$ calculated for $C_{36}H_{39}N_4O_{11}S$, 735.2331, found, 735.2359.

$G1_M$ Dendron: $G1_F$ dendron (140.0 mg, 0.19 mmol) was added to a 100 mL round-bottom flask and suspended in toluene (30 mL). The reaction mixture was heated at 100 °C for 8 hours, and it should be noted that **$G1_F$** dendron is only soluble in toluene at higher temperatures. The reaction mixture was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (99:1) to afford 110.0 mg (96%) of **$G1_M$** dendron as a white solid. ESI-TOF MS (*m/z*) $[M+H]^+$ calculated for $C_{28}H_{31}N_4O_9S$, 599.1812, found, 599.1813.

$G2_F$ Dendron: $G1_M$ dendron (84.0 mg, 0.140 mmol) and **1** (184.0 mg, 0.295 mmol) were added to a 3 dram vial and dissolved in $CDCl_3$ (0.5 mL). Et_3N (29.8 mg, 0.295 mmol) was added, the vial was capped, and the reaction was allowed to stir overnight at room temperature. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (97:3) to afford 189.0 mg (73%) of **$G2_F$** dendron as a white solid. ESI-TOF MS (*m/z*) $[M+H]^+$ calculated for $C_{90}H_{97}N_{10}O_{27}S_3$, 1845.5681, found, 1845.5676.

$G2_M$ Dendron: $G2_F$ dendron (170.0 mg, 0.092 mmol) was added to a 100 mL round-bottom flask and suspended in toluene (30 mL). The reaction mixture was heated at 100 °C for 8 hours, and it should be noted that **$G2_F$** dendron is only soluble in toluene at higher temperatures. The reaction mixture was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (97:3) to afford 50.0 mg (34%) of **$G2_M$** dendron as a white solid. ESI-TOF MS (*m/z*) $[M+H]^+$ calculated for $C_{74}H_{81}N_{10}O_{23}S_3$, 1573.4638, found, 1573.4619.

G3$_F$ Dendron: **G2$_M$** dendron (40.0 mg, 0.023 mmol) and **1** (61.3 mg, 0.098 mmol) were added to a 3 dram vial and dissolved in $CDCl_3$ (0.5 mL). Et_3N (1.2 mg, 0.012 mmol) was added, the vial was capped, and the reaction was allowed to stir overnight at room temperature. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (95:5) to afford 40.0 mg (39%) of **G3$_F$** dendron as a white solid. The parent ion of the **G3$_F$** dendron could not be observed under MALDI ionization conditions, however the parent ion of the fully deprotected **G3$_M$** dendron was found. As discussed in the text, it is believed that all eight peripheral furan protecting groups are removed by a thermal retro-Diels-Alder reaction during ionization under vacuum. MALDI-TOF MS (*m/z*) $[M+Na]^+$ calculated for the deprotected **G3$_M$** dendron $C_{166}H_{180}N_{22}NaO_{51}S_7$ (observed during measurement of the **G3$_F$** dendron), 3544.01, found, 3543.9.

G3$_M$ Dendron: **G3$_F$** dendron (80.0 mg, 0.019 mmol) was added to a 50 mL round-bottom flask and suspended in toluene (20 mL). The reaction mixture was heated at 100 °C for 8 hours, and it should be noted that **G3$_F$** dendron is only soluble in toluene at higher temperatures. The reaction mixture was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (97:3) to afford 33.0 mg (48%) of **G3$_M$** dendron as a white solid. MALDI-TOF MS (*m/z*) $[M+Na]^+$ calculated for $C_{166}H_{180}N_{22}NaO_{51}S_7$, 3544.01, found, 3546.0.

G4$_F$ Dendron (compound designated as **3** in the main text)**:** **G3$_M$** dendron (25.0 mg, 0.007 mmol) and **1** (37.2 mg, 0.060 mmol) were added to a 3 dram vial and dissolved in $CDCl_3$ (0.5 mL). Et_3N (0.9 mg, 0.009 mmol) was added, the vial was capped, and the reaction was allowed to stir overnight at room temperature. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (95:5) to afford 33.8 mg (56%) of **G4$_F$** dendron as a white solid. As with the **G3$_F$** dendron, the parent ion of the **G4$_F$** dendron could not be observed under MALDI ionization conditions. The parent ion of the fully deprotected **G4$_M$** dendron, however, was found during MALDI analysis of the intended **G4$_F$** dendron. MALDI-TOF MS (*m/z*) $[M+Na]^+$ calculated for the deprotected **G4$_M$** dendron $C_{350}H_{380}N_{46}NaO_{107}S_{15}$ (observed during measurement of the **G4$_F$** dendron), 7441.14, found, 7443.5.

G1$_F$ Dendrimer: ***Tris*–M** (50.0 mg, 0.124 mmol) and **2** (243.0 mg, 0.389 mmol) were added to a 3 dram vial and dissolved in $CDCl_3$ (0.5 mL). Et_3N (12.5 mg, 0.124 mmol) was added, the vial was capped, and the reaction was allowed to stir at room temperature overnight. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (97:3) to afford 238.0 mg (85%) of **G1$_F$** as a white solid. Analysis by MALDI-TOF MS resulted in thermal deprotection of the three peripheral furan groups of dendrimer **G1$_F$**, revealing the parent ion corresponding to its deprotected analogue **G1$_M$**. MALDI-TOF MS (*m/z*) $[M+Na]^+$ calculated for $C_{90}H_{90}N_{12}NaO_{27}S_3$, 1889.51, found, 1889.7.

G1$_M$ Dendrimer: **G1$_F$** (93.0 mg, 0.041 mmol) was added to a 10 mL round-bottom flask and suspended in anisole (3 mL). The reaction mixture was heated at 145 °C for 1 hour, and it should be noted that **G1$_F$** is only soluble in anisole at higher temperatures. The reaction mixture was cooled to room temperature and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (97:3) to afford 69.0 mg (91%) of **G1$_M$** as a white solid. MALDI-TOF MS (*m/z*) $[M+Na]^+$ calculated for $C_{90}H_{90}N_{12}NaO_{27}S_3$, 1889.51, found, 1890.9.

G2$_F$ Dendrimer: **G1$_M$** (100.0 mg, 0.054 mmol) and **1** (210.0 mg, 0.337 mmol) were added to a 3 dram vial and dissolved in $CDCl_3$ (0.5 mL). Et_3N (5.4 mg, 0.054 mmol) was added, the vial was capped, and the reaction was allowed to stir at room temperature overnight. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (95:5) to afford 180.0 mg (60%) of **G2$_F$** as a white solid.

G2$_M$ Dendrimer: **G2$_F$** (150.0 mg, 0.027 mmol) was added to a 10 mL round-bottom flask and suspended in anisole (3 mL). The reaction mixture was heated at 145 °C for 1 hour, and it should be noted that **G2$_F$** is only soluble in anisole at higher temperatures. The reaction mixture was cooled to room temperature and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (95:5) to afford 58.0 mg (45%) of **G2$_M$** as a white solid.

G3$_F$ Dendrimer (compound designated as **4** in the main text): **G2$_M$** (44.0 mg, 0.009 mmol) and **1** (72.1 mg, 0.116 mmol) were added to a 3 dram vial and dissolved in $CDCl_3$ (0.5 mL). Et_3N (0.93 mg, 0.009 mmol) was added, the vial was capped, and the reaction was allowed to stir at room temperature overnight. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (93:7) to afford 86.0 mg (76%) of **G3$_F$** as a white solid. MALDI-TOF MS positively identified the parent $[M+Na]^+$ ion of the **G3$_M$** ion arising from thermal deprotection of peripheral furan groups under ionization conditions. $[M+Na]^+$ (*m/z*) calculated for $C_{504}H_{540}N_{66}NaO_{153}S_{21}$, 10658.05, found, 10662.4.

G3$_F$ Dendrimer (compound designated as **5** in the main text): **G2$_M$** (37.0 mg, 0.008 mmol) and **2** (83.6 mg, 0.097 mmol) were added to a 3 dram vial and dissolved in $CDCl_3$ (0.5 mL). Et_3N (0.78 mg, 0.008 mmol) was added, the vial was capped, and the reaction was allowed to stir at room temperature overnight. The solution was concentrated under reduced pressure and purified by column chromatography using a mixture of CH_2Cl_2:MeOH (93:7) to afford 72.0 mg (62%) of **G3$_F$** as a white solid.

IV. NMR and Mass Spectra.

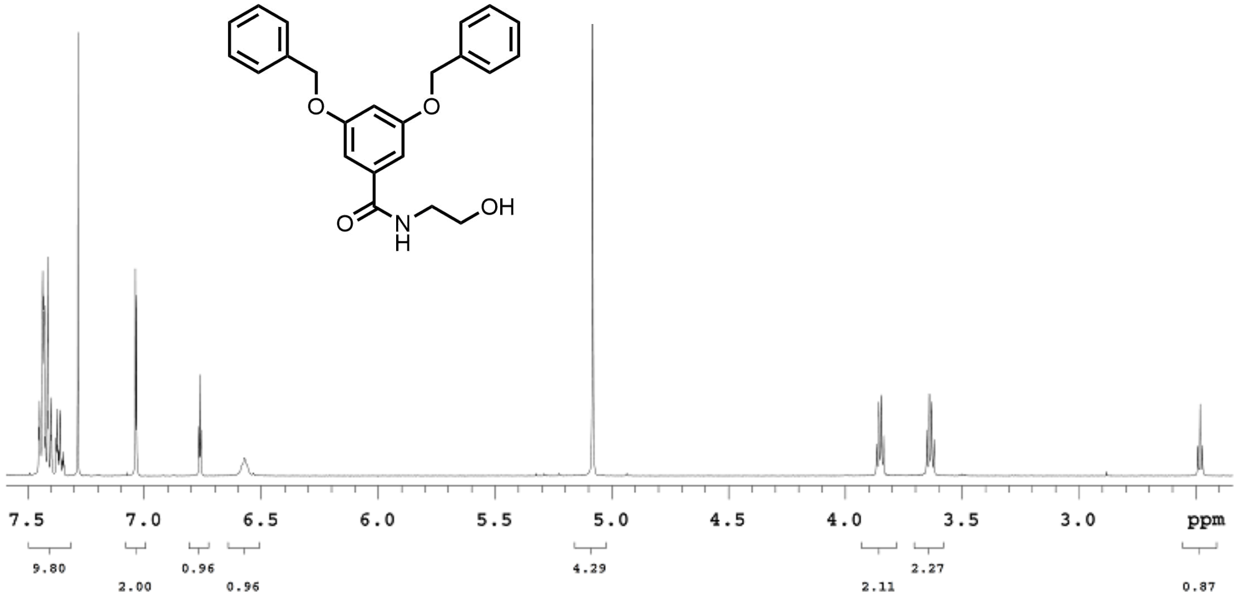


Figure S1. ^{1}H NMR spectrum (500 MHz) of compound **S9**.

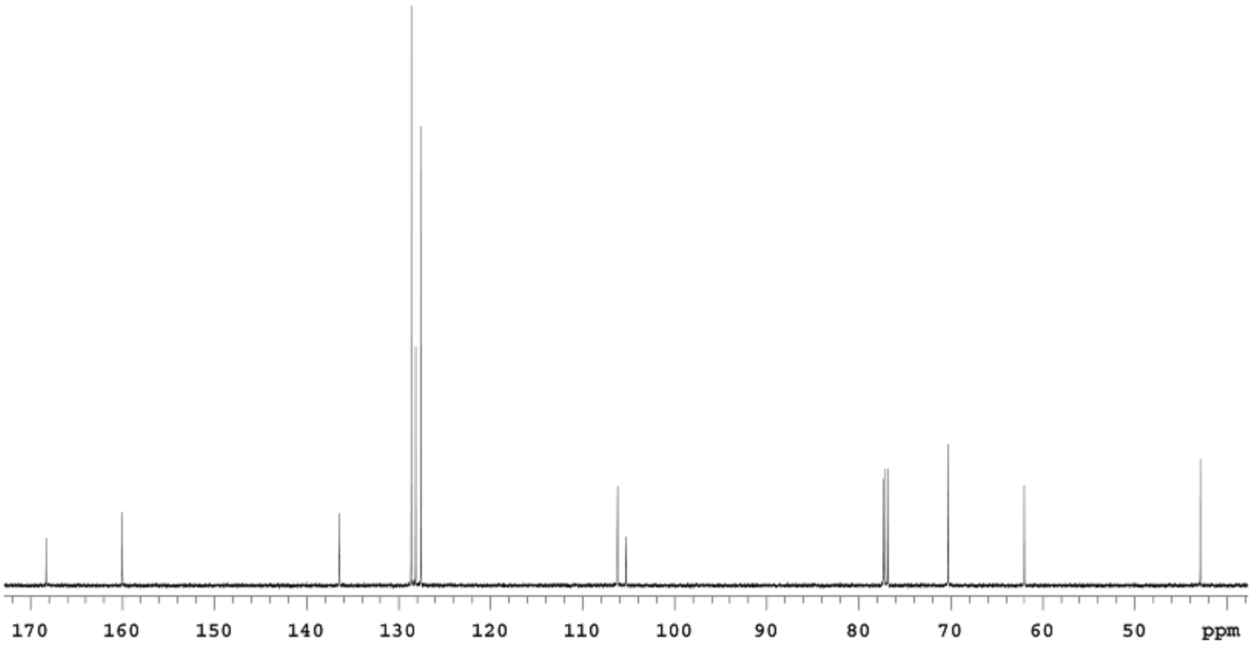
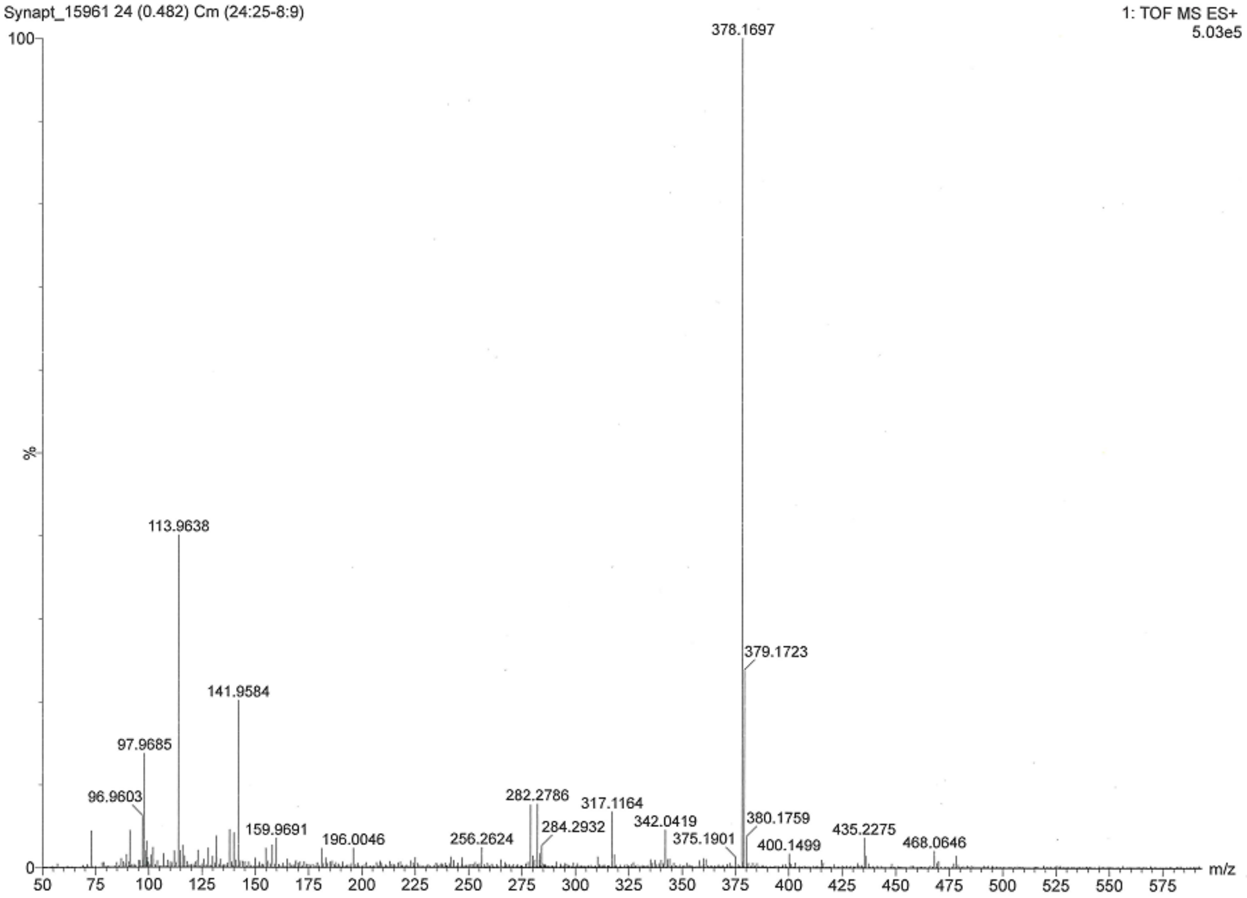


Figure S2. ^{13}C NMR spectrum (125MHz) of compound **S9**.



```
Monoisotopic Mass, Even Electron Ions
74 formula(e) evaluated with 1 results within limits (up to 10 closest results for each mass)
Elements Used:
C: 0-50    H: 0-80    N: 0-1    O: 0-5



Minimum:                                 -10.0
Maximum:                5.0     5.0      100.0

Mass        Calc. Mass  mDa     PPM      DBE      i-FIT    Norm     Conf(%) Formula

378.1697    378.1705    -0.8    -2.1     12.5     1671.6   n/a      n/a     C23 H24 N O4
```

Figure S3. TOF ESI MS of compound **S9**.

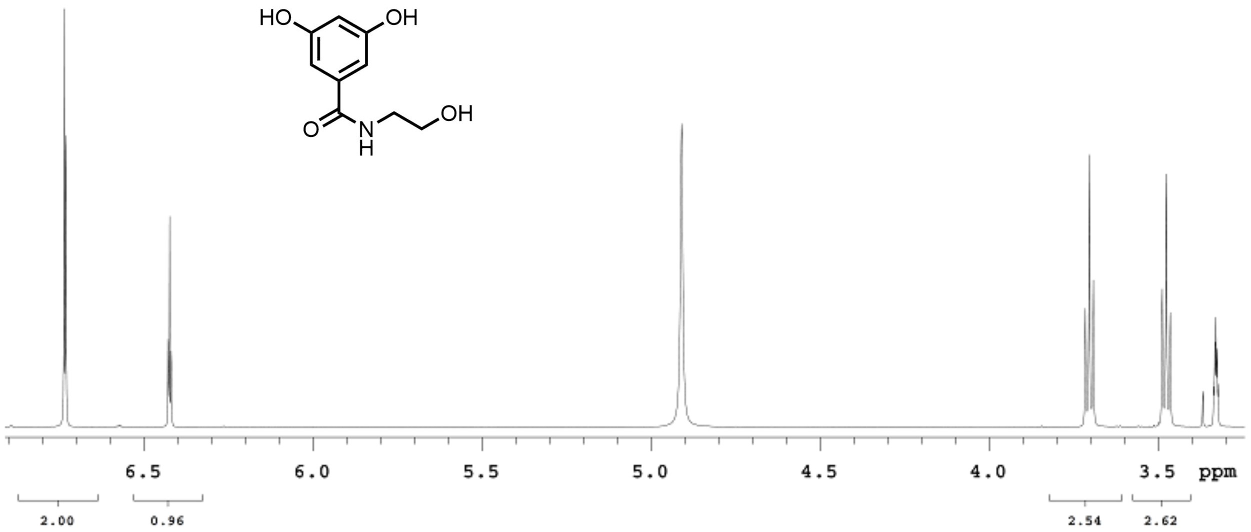


Figure S4. ^{1}H NMR spectrum (500 MHz) of compound **S10**.

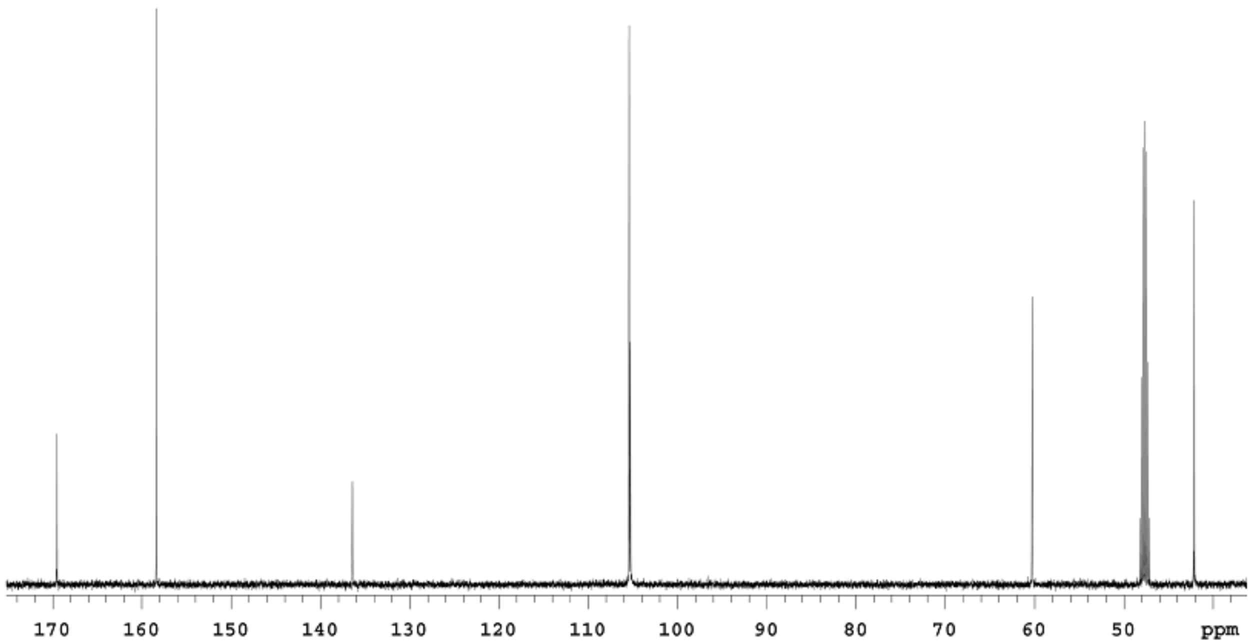
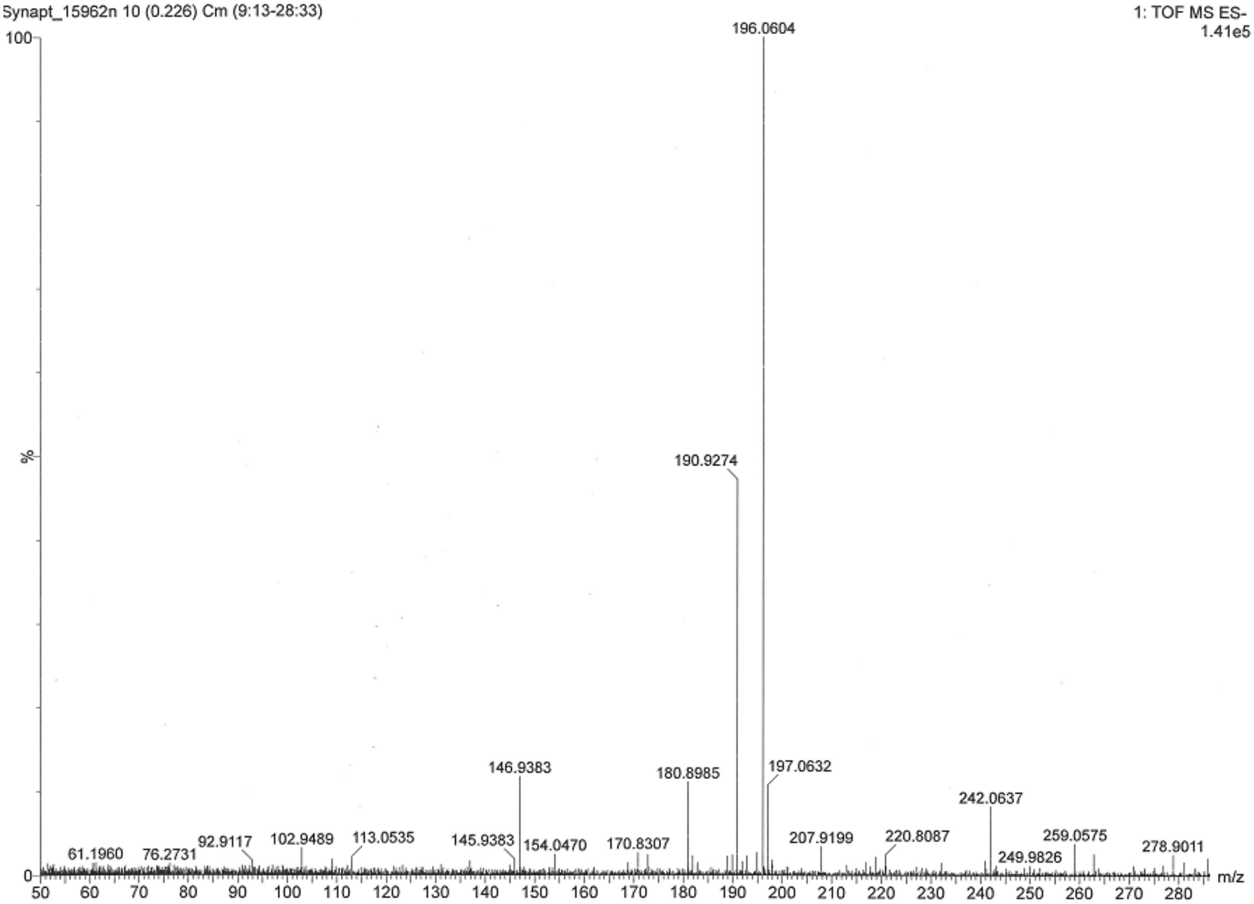


Figure S5. ^{13}C NMR spectrum (125 MHz) of compound **S10**.



Monoisotopic Mass, Even Electron Ions
93 formula(e) evaluated with 1 results within limits (up to 10 closest results for each mass)
Elements Used:
C: 0-50   H: 0-80   N: 0-3   O: 0-5

```
Minimum:                             -10.0
Maximum:                 5.0    5.0  100.0

Mass      Calc. Mass  mDa    PPM    DBE    i-FIT   Norm   Conf(%) Formula

196.0604  196.0610    -0.6   -3.1   5.5    1489.2  n/a    n/a     C9 H10 N O4
```

Figure S6. TOF ESI MS of compound **S10**.

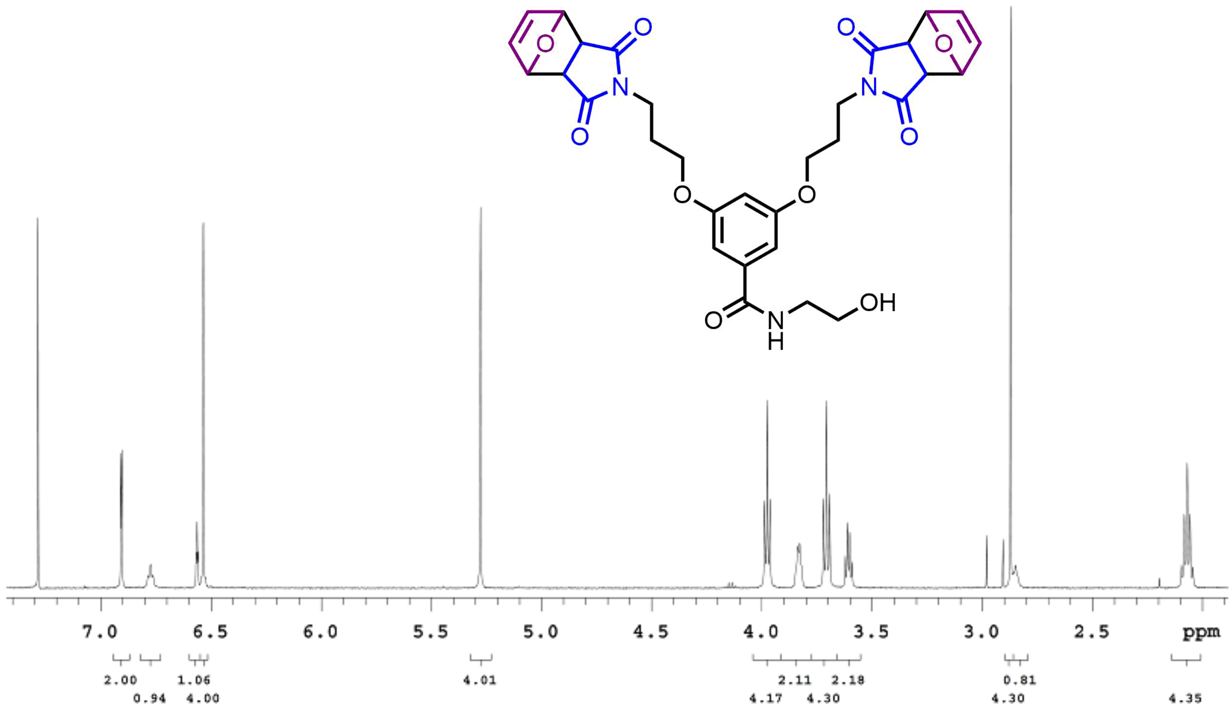


Figure S7. ^{1}H NMR spectrum (300 MHz) of compound **S11**.

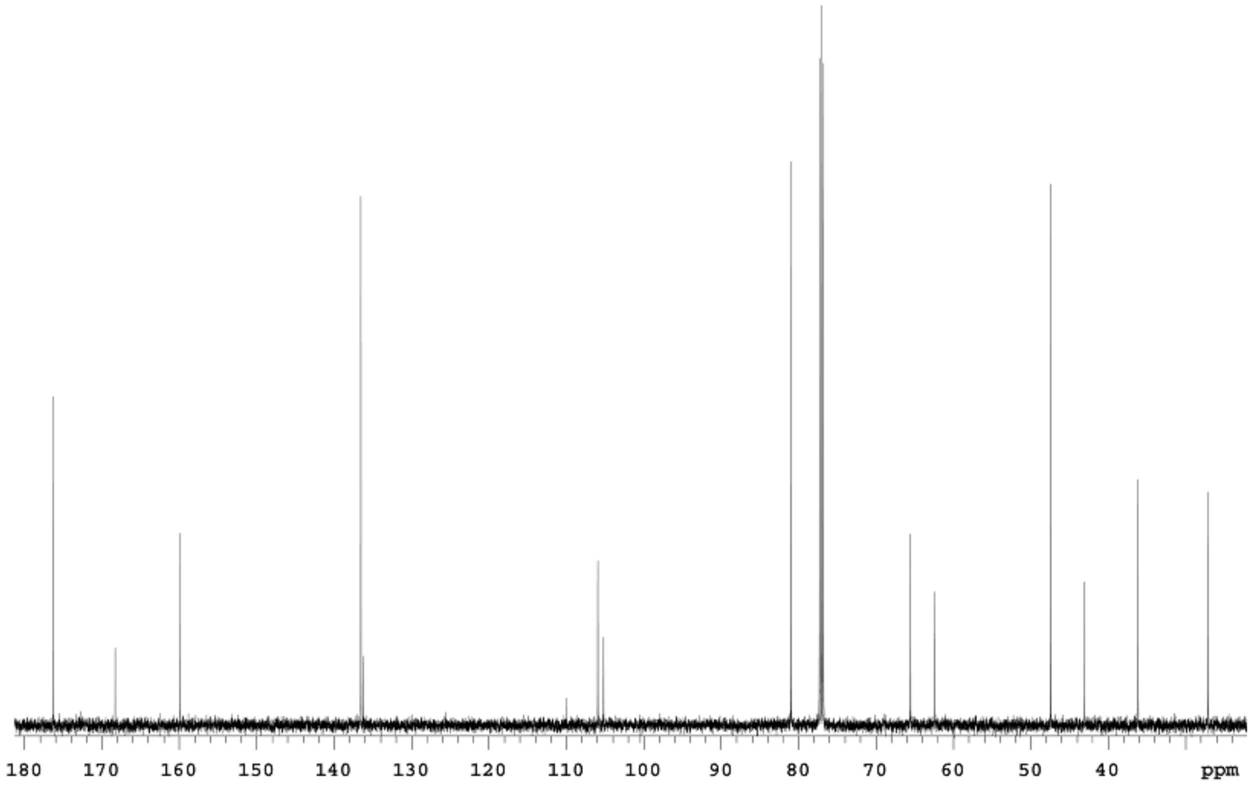


Figure S8. ^{13}C NMR spectrum (75 MHz) of compound **S11**.

Monoisotopic Mass, Even Electron Ions
148 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-120   H: 0-180   N: 0-5   O: 8-11

```
Minimum:                                   -1.5
Maximum:                 5.0      20.0     600.0

Mass       Calc. Mass    mDa      PPM      DBE      i-FIT      Formula

608.2250   608.2244      0.6      1.0      16.5     2.4        C31  H34  N3  O10
           608.2284      -3.4     -5.6     20.5     11.1       C36  H34  N  O8
           608.2357      -10.7    -17.6    16.5     7.7        C30  H34  N5  O9
           608.2132      11.8     19.4     16.5     6.9        C32  H34  N  O11
```

Figure S9. TOF ESI MS of compound **S11**.

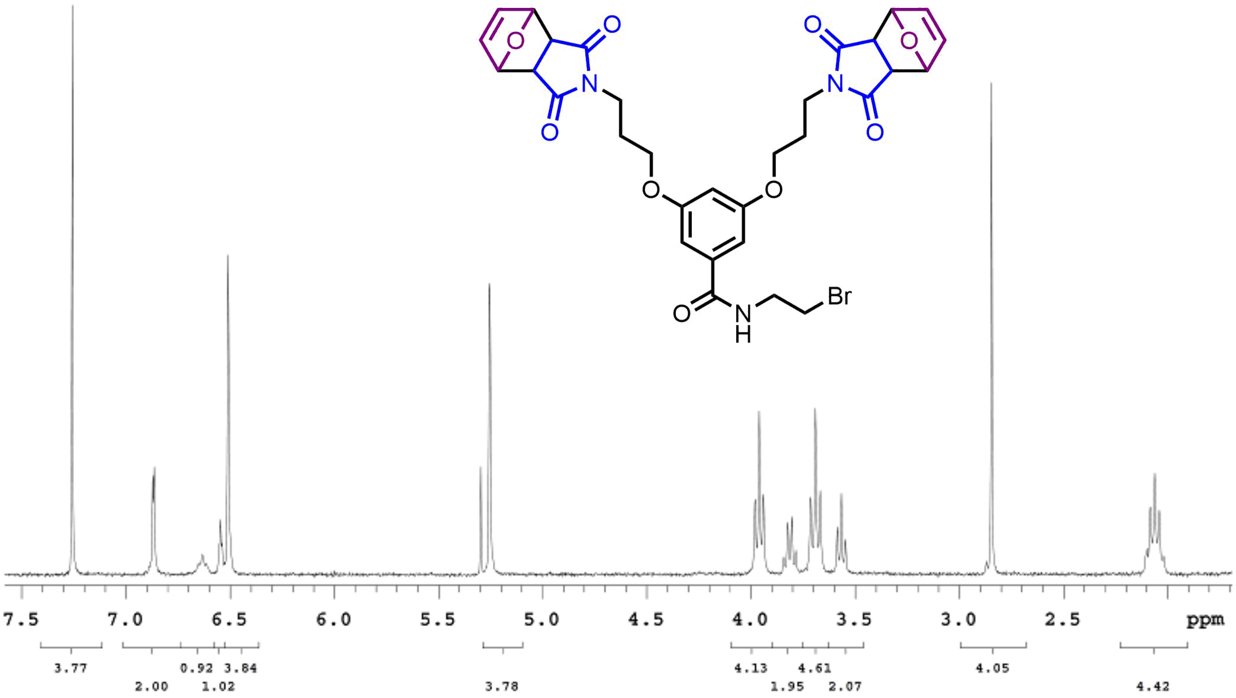


Figure S10. ^{1}H NMR spectrum (300 MHz) of compound **S12**.

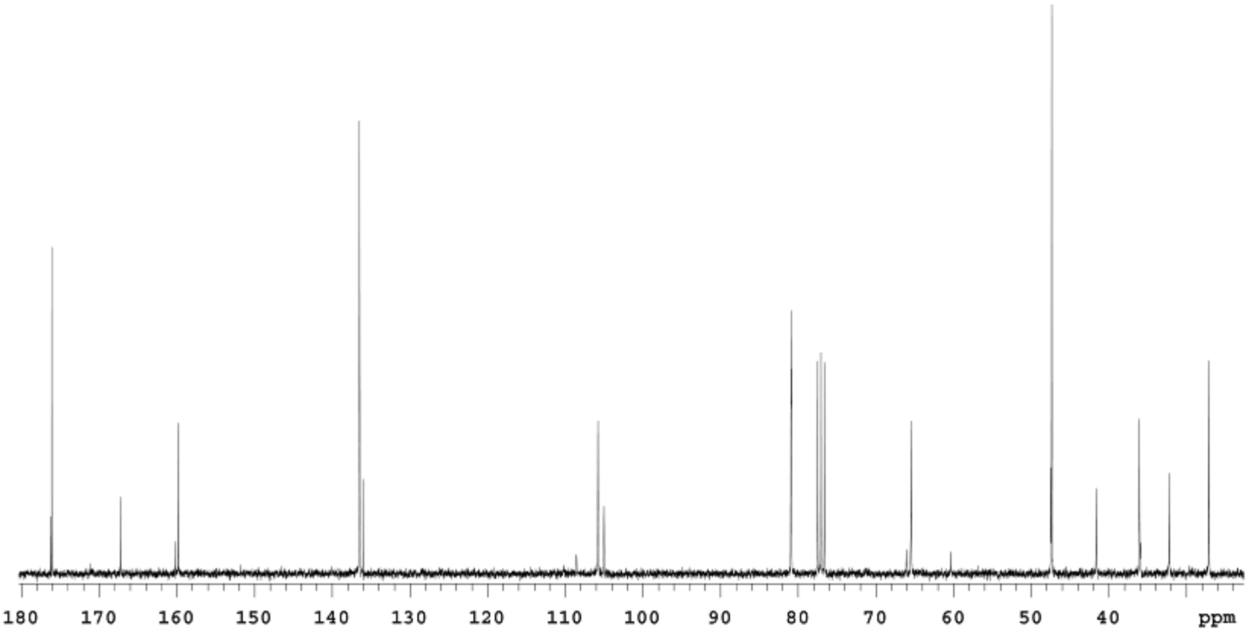
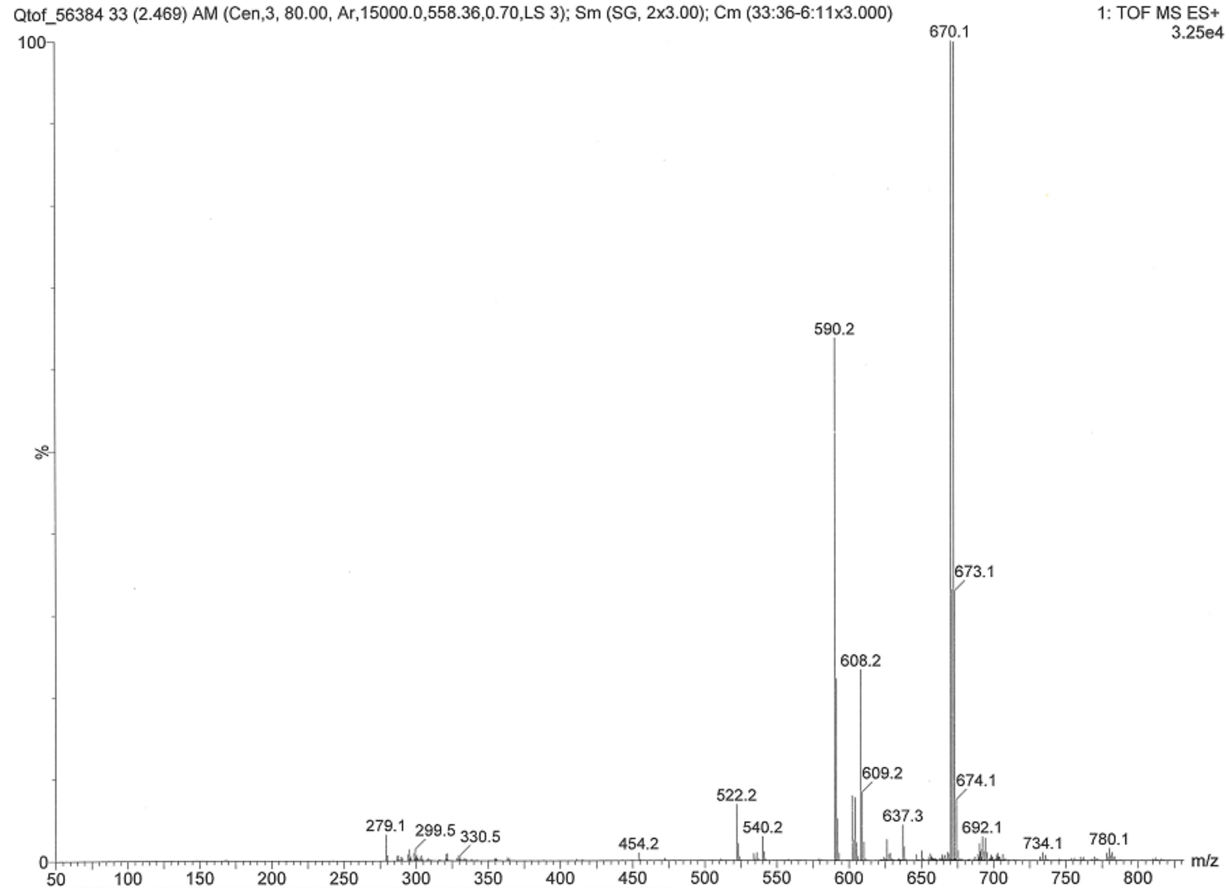


Figure S11. ^{13}C NMR spectrum (75 MHz) of compound **S12**.



Monoisotopic Mass, Even Electron Ions
146 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-120 H: 0-180 N: 0-5 O: 8-11 Br: 1-1

```
Minimum:                                  -1.5
Maximum:                  5.0      20.0    600.0

Mass        Calc. Mass    mDa      PPM      DBE      i-FIT     Formula

670.1410    670.1400      1.0      1.5      16.5     0.8       C31  H33  N3  O9  Br
            670.1360      5.0      7.5      12.5     4.5       C26  H33  N5  O11  Br
            670.1512      -10.2    -15.2    16.5     4.3       C30  H33  N5  O8  Br
            670.1288      12.2     18.2     16.5     5.6       C32  H33  N  O10  Br
```

Figure S12. TOF ESI MS of compound **S12**.

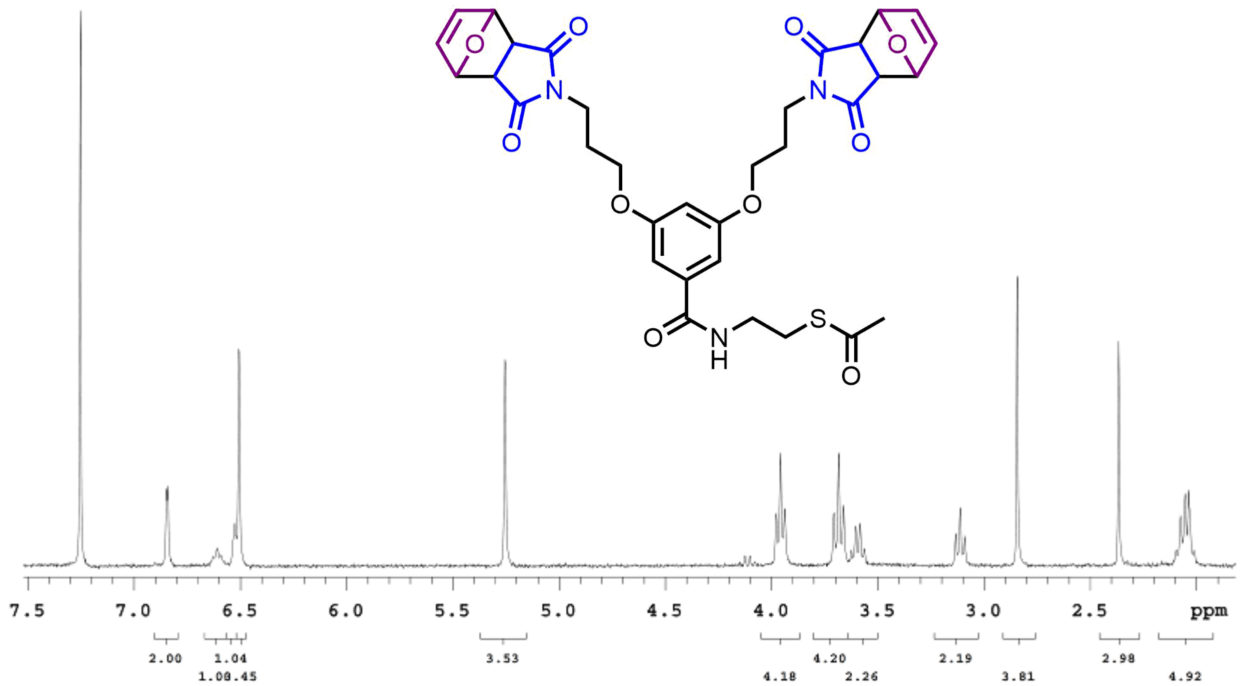


Figure S13. ^{1}H NMR spectrum (300 MHz) of compound **S13**.

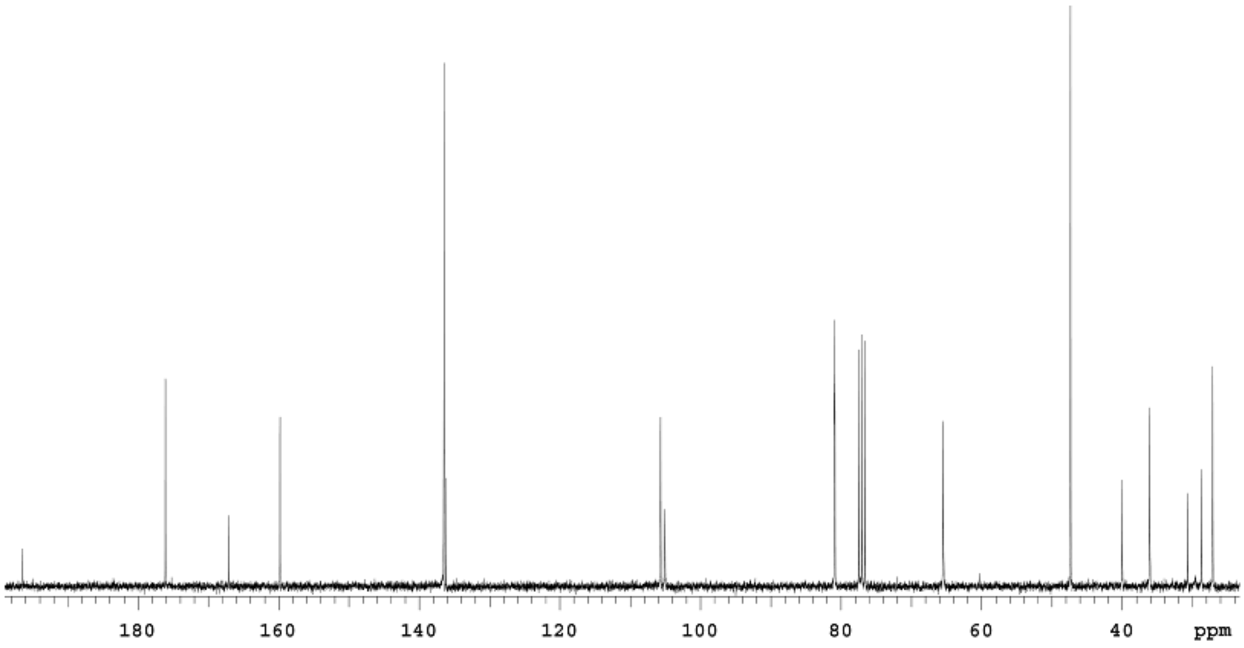


Figure S14. ^{13}C NMR spectrum (75 MHz) of compound **S13**.

```
Monoisotopic Mass, Even Electron Ions
225 formula(e) evaluated with 5 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-120    H: 0-180    N: 0-5    O: 9-11    Na: 0-1    S: 1-1



Minimum:                                    -1.5
Maximum:                   5.0      20.0    600.0

Mass        Calc. Mass     mDa      PPM     DBE      i-FIT      Formula

666.2124    666.2121       0.3      0.5     17.5     0.1        C33  H36  N3  O10  S
            666.2097       2.7      4.1     14.5     1.1        C31  H37  N3  O10  Na  S
            666.2210       -8.6     -12.9   14.5     2.0        C30  H37  N5  O9  Na  S
            666.2234       -11.0    -16.5   17.5     1.2        C32  H36  N5  O9  S
            666.2009       11.5     17.3    17.5     1.3        C34  H36  N  O11  S
```

Figure S15. TOF ESI MS of compound **S13**.

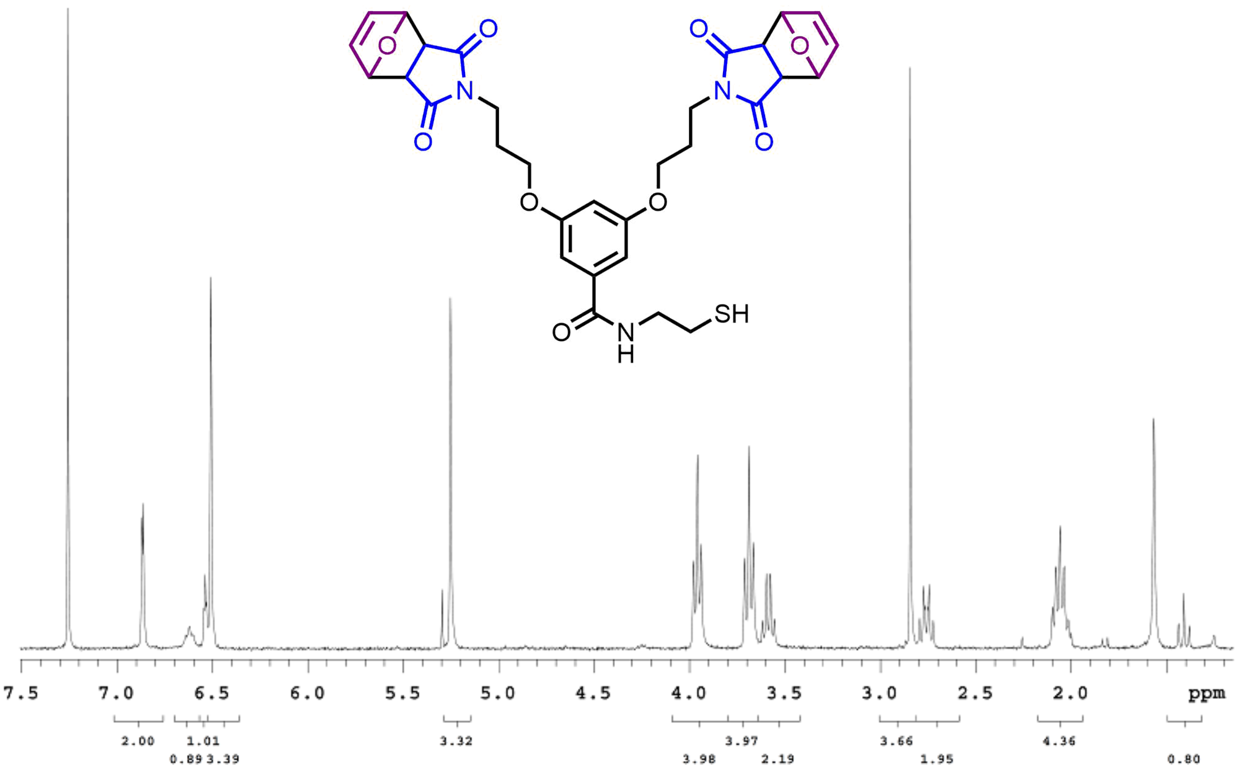


Figure S16. ^{1}H NMR spectrum (300 MHz) of compound **1**.

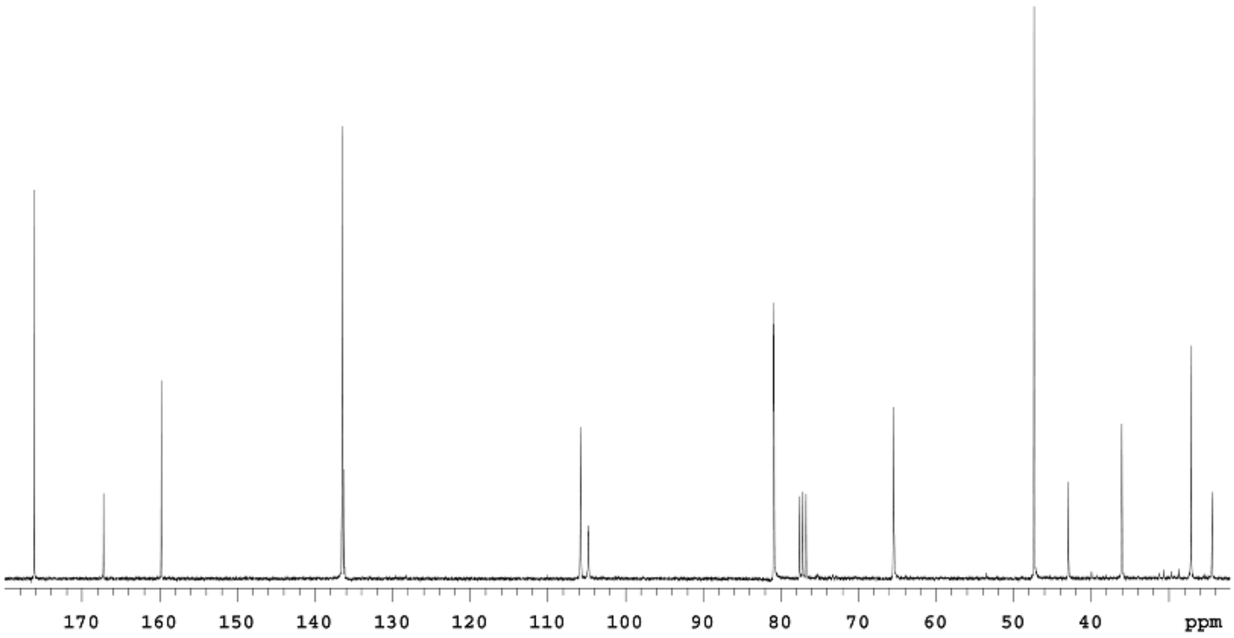


Figure S17. ^{13}C NMR spectrum (75 MHz) of compound **1**.

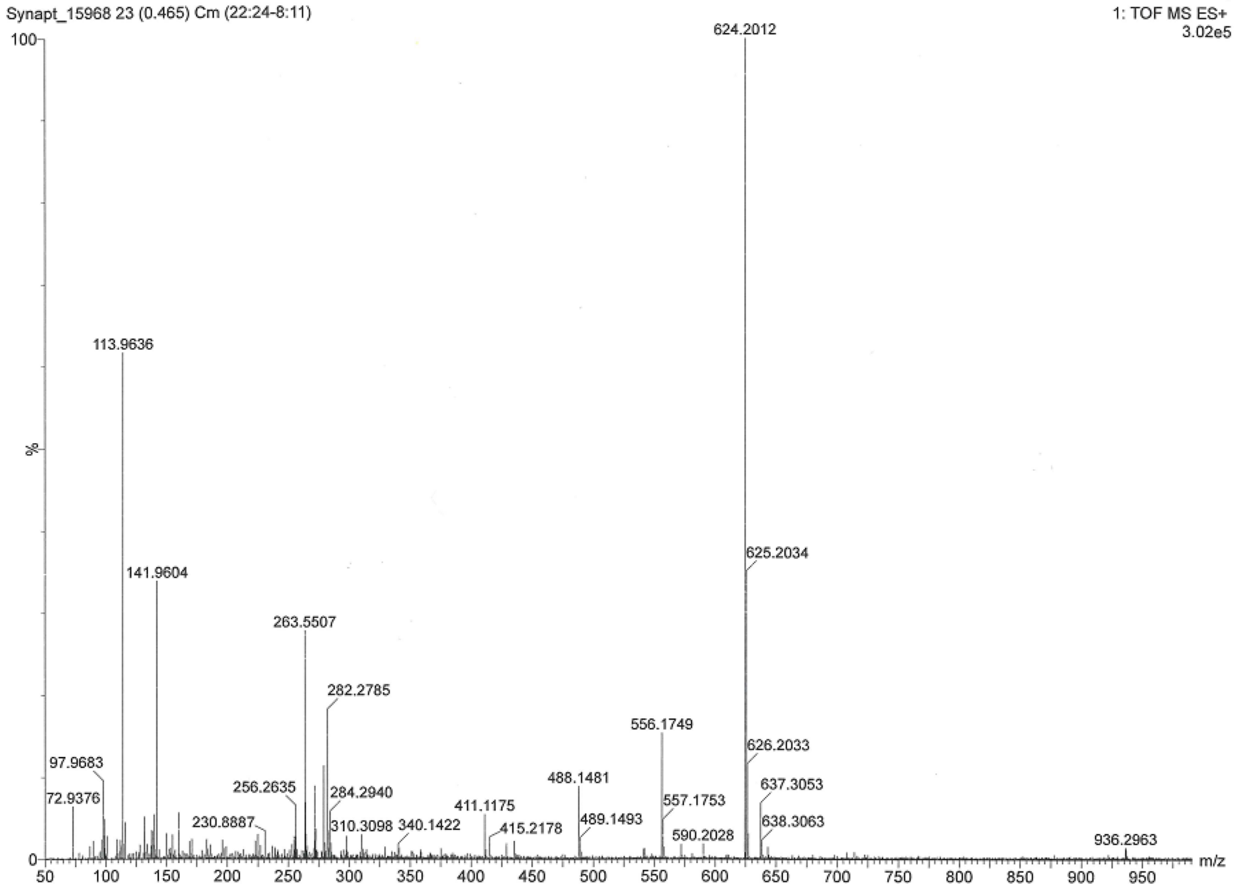


Figure S18. TOF ESI MS of compound **1**.

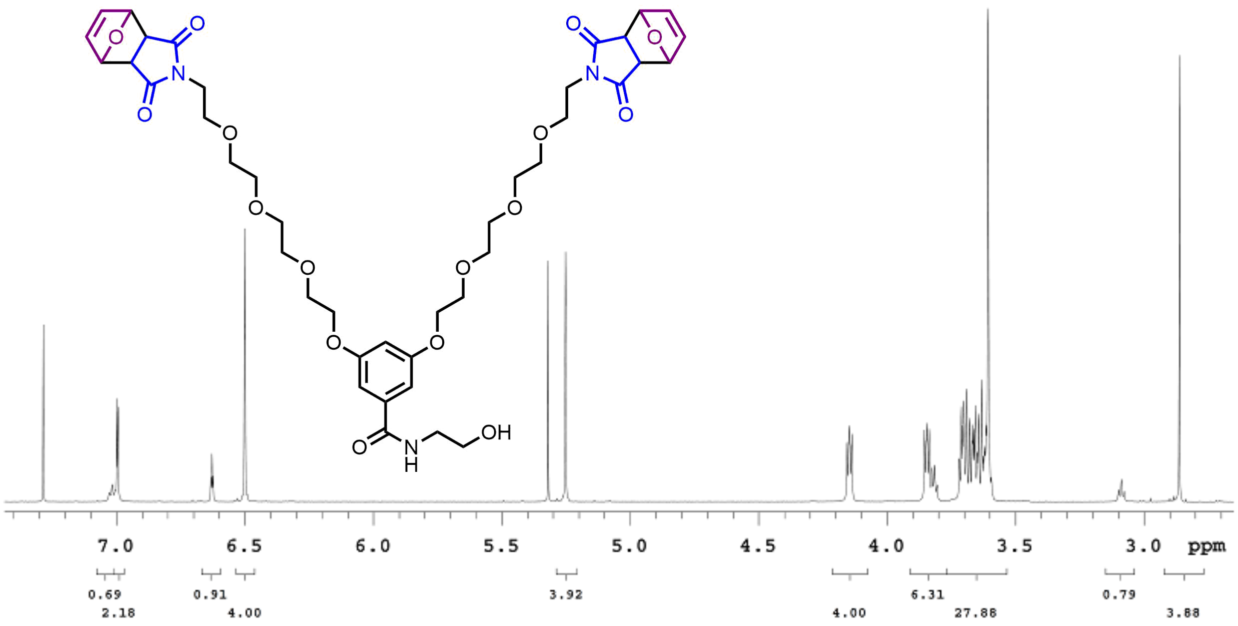


Figure S19. ^{1}H NMR spectrum (500 MHz) of compound **S14**.

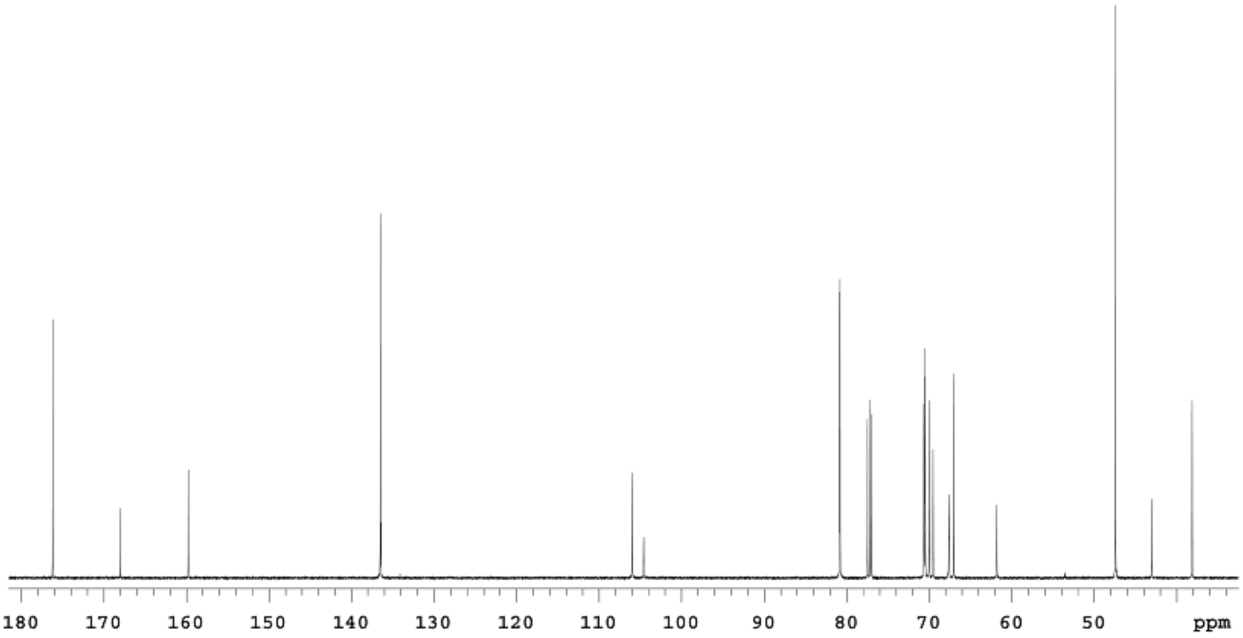
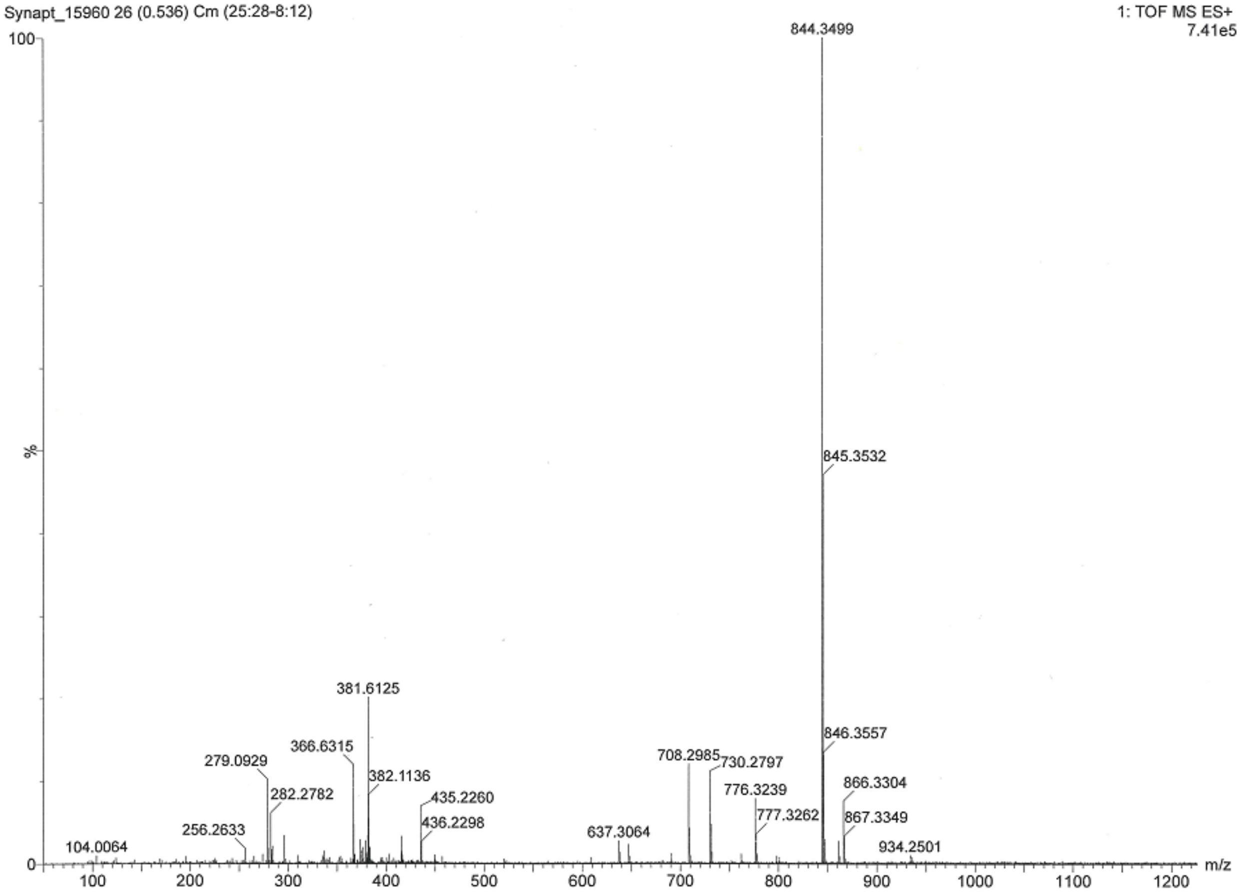


Figure S20. ^{13}C NMR spectrum (125 MHz) of compound **S14**.



Monoisotopic Mass, Even Electron Ions
82 formula(e) evaluated with 1 results within limits (up to 10 closest results for each mass)
Elements Used:
C: 0-50   H: 0-80   N: 0-3   O: 8-10   S: 1-1

```
Minimum:                             -10.0
Maximum:                 5.0    5.0   100.0

Mass        Calc. Mass   mDa    PPM    DBE     i-FIT    Norm    Conf(%)  Formula

624.2012    624.2016     -0.4   -0.6   16.5    948.0    n/a     n/a      C31 H34 N3 O9 S
```

Figure S21. TOF ESI MS of compound **S14**.

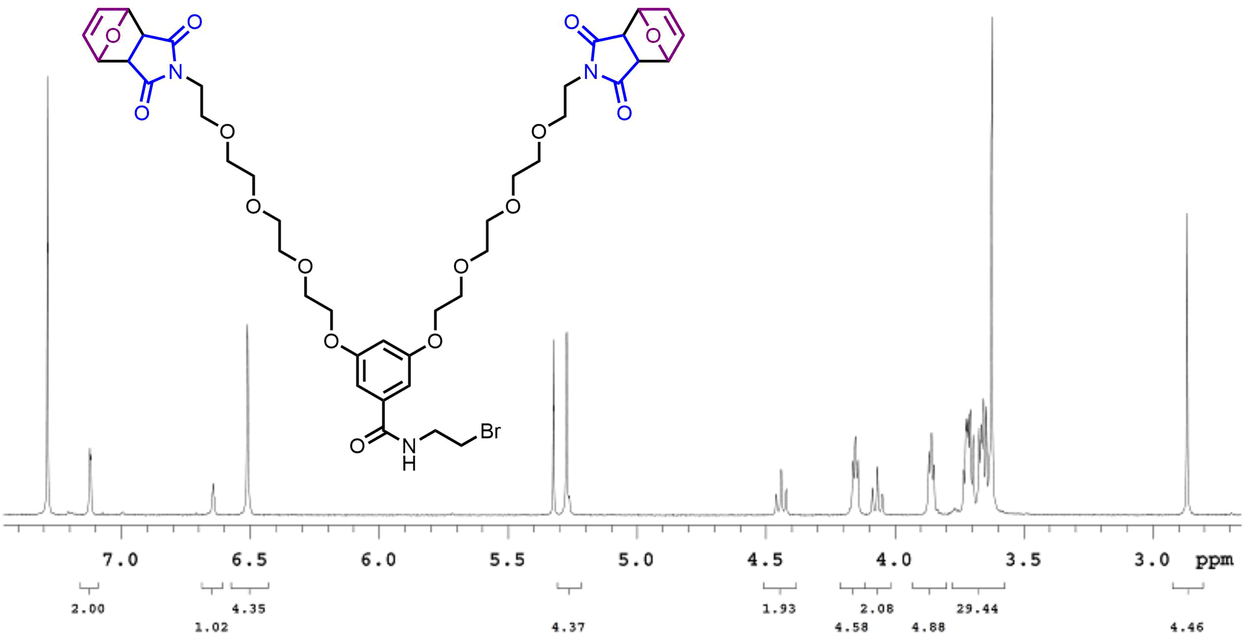


Figure S22. ^{1}H NMR spectrum (500 MHz) of compound **S15**.

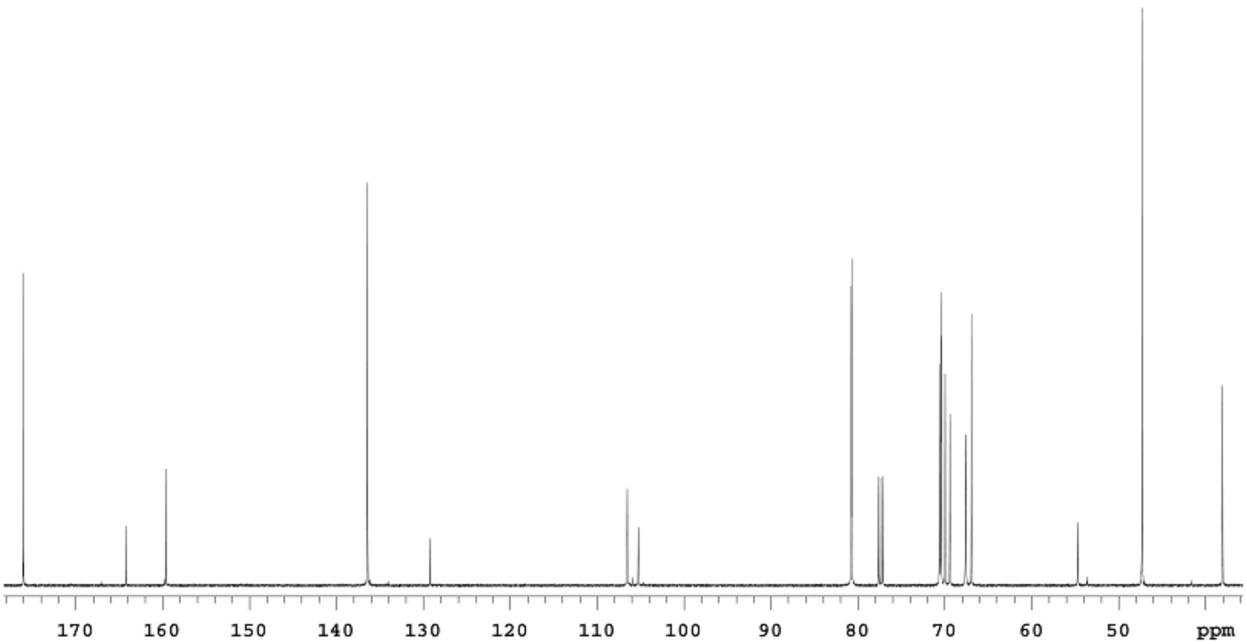
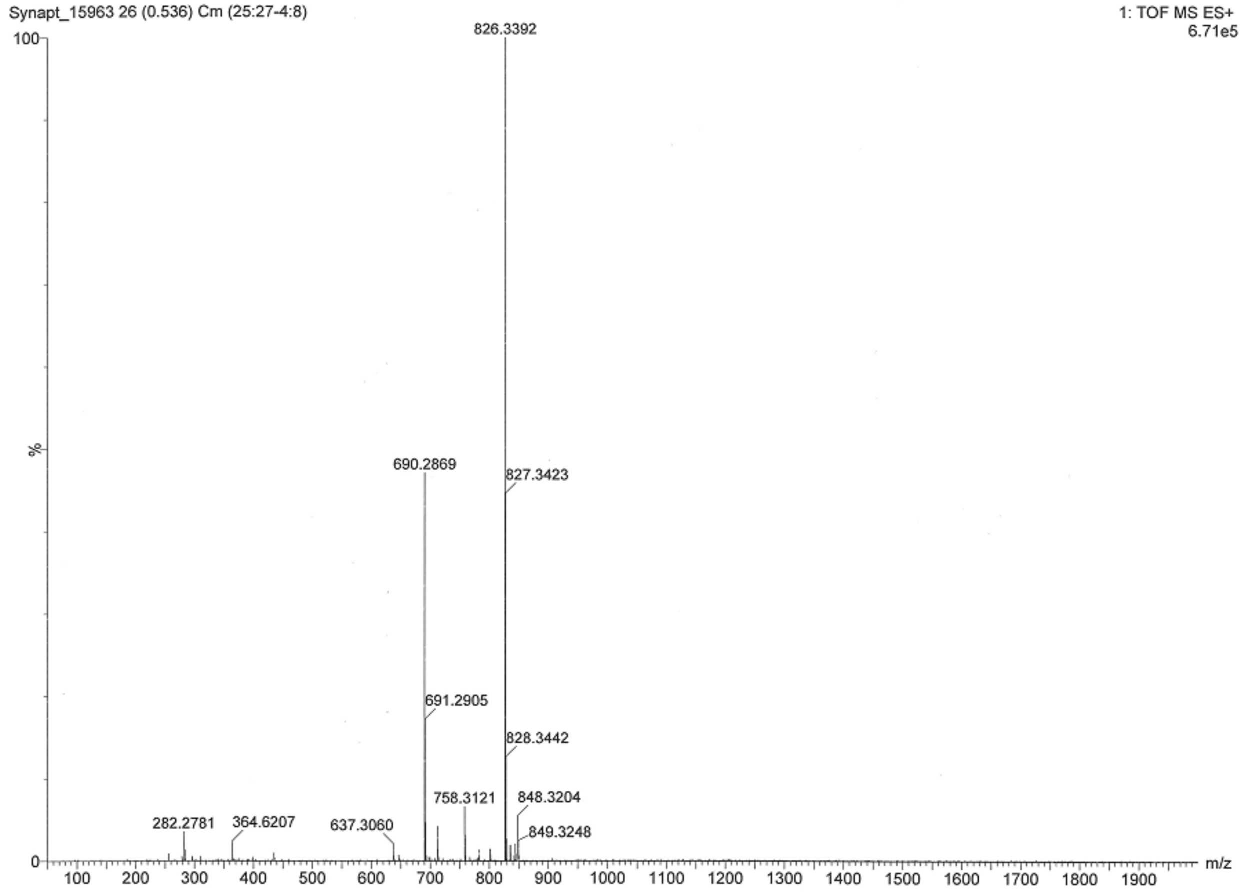


Figure S23. ^{13}C NMR spectrum (125 MHz) of compound **S15**.



Monoisotopic Mass, Even Electron Ions
62 formula(e) evaluated with 1 results within limits (up to 10 closest results for each mass)
Elements Used:
C: 0-50   H: 0-80   N: 2-4   O: 15-17

```
Minimum:                                -10.0
Maximum:               5.0      5.0     100.0

Mass        Calc. Mass  mDa      PPM      DBE      i-FIT    Norm     Conf(%)  Formula

844.3499    844.3504    -0.5     -0.6     16.5     1224.7   n/a      n/a      C41 H54 N3 O16
```

Figure S24. TOF ESI MS of compound **S15**.

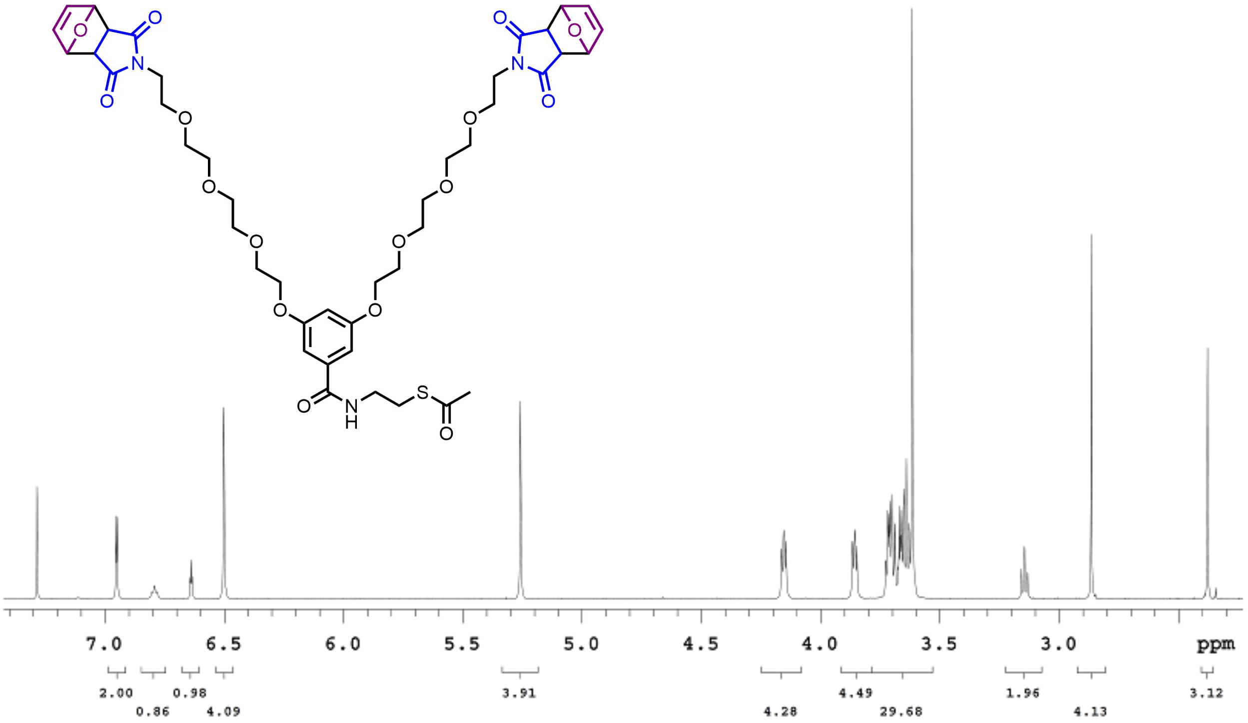


Figure S25. ^{1}H NMR spectrum (500 MHz) of compound **S16**.

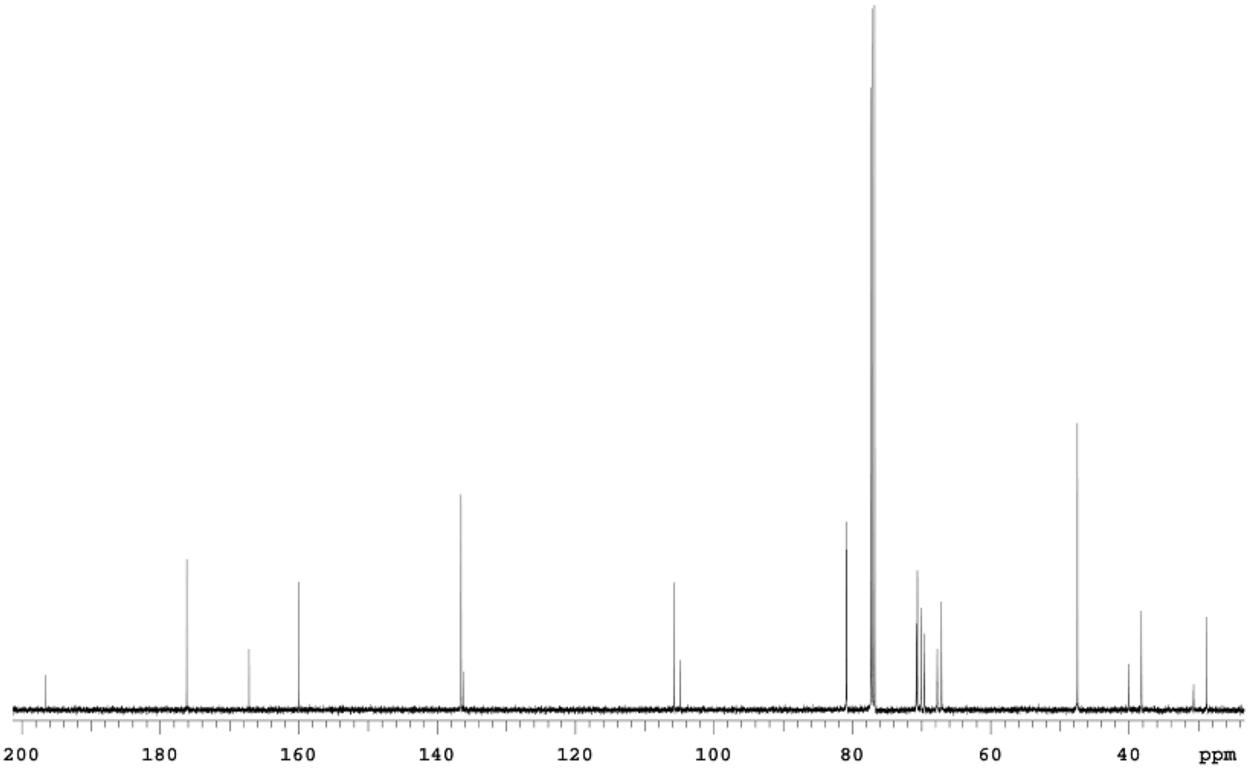
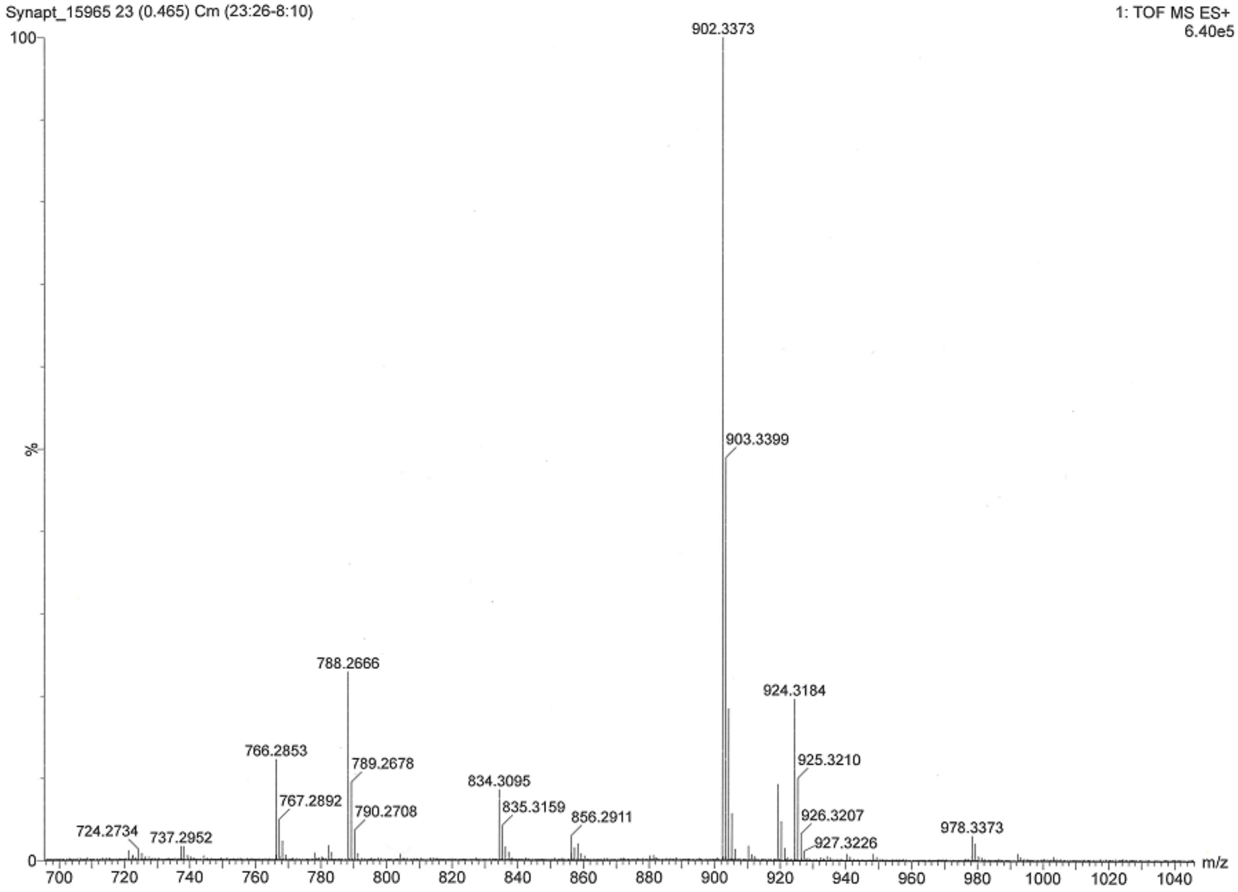


Figure S26. ^{13}C NMR spectrum (125 MHz) of compound **S16**.



Monoisotopic Mass, Even Electron Ions
51 formula(e) evaluated with 1 results within limits (up to 10 closest results for each mass)
Elements Used:
C: 0-50   H: 0-80   N: 0-3   O: 15-16   S: 1-1

```
Minimum:                            -10.0
Maximum:                5.0    5.0   100.0

Mass       Calc. Mass  mDa    PPM    DBE    i-FIT   Norm   Conf(%) Formula

902.3373   902.3381    -0.8   -0.9   17.5   1992.7  n/a    n/a     C43 H56 N3 O16 S
```

Figure S27. TOF ESI MS of compound **S16**.

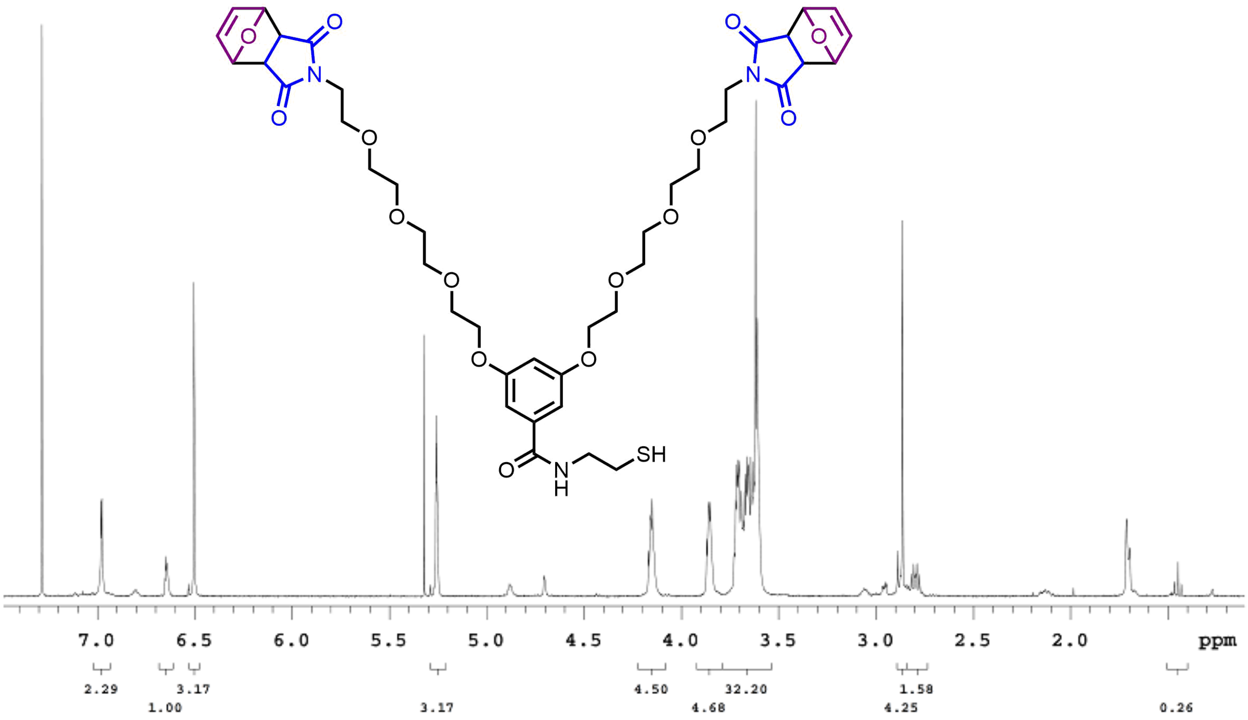


Figure S28. ^{1}H NMR spectrum (500 MHz) of compound **2**.

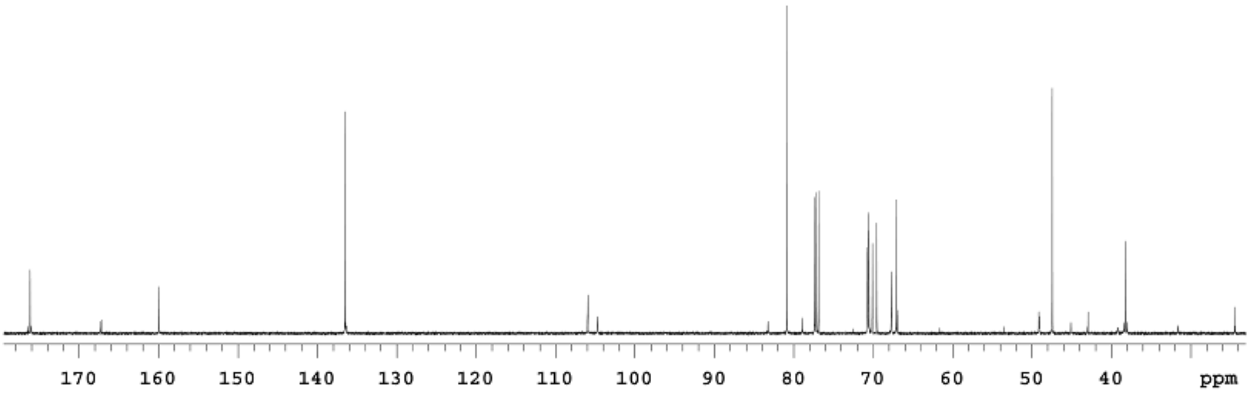
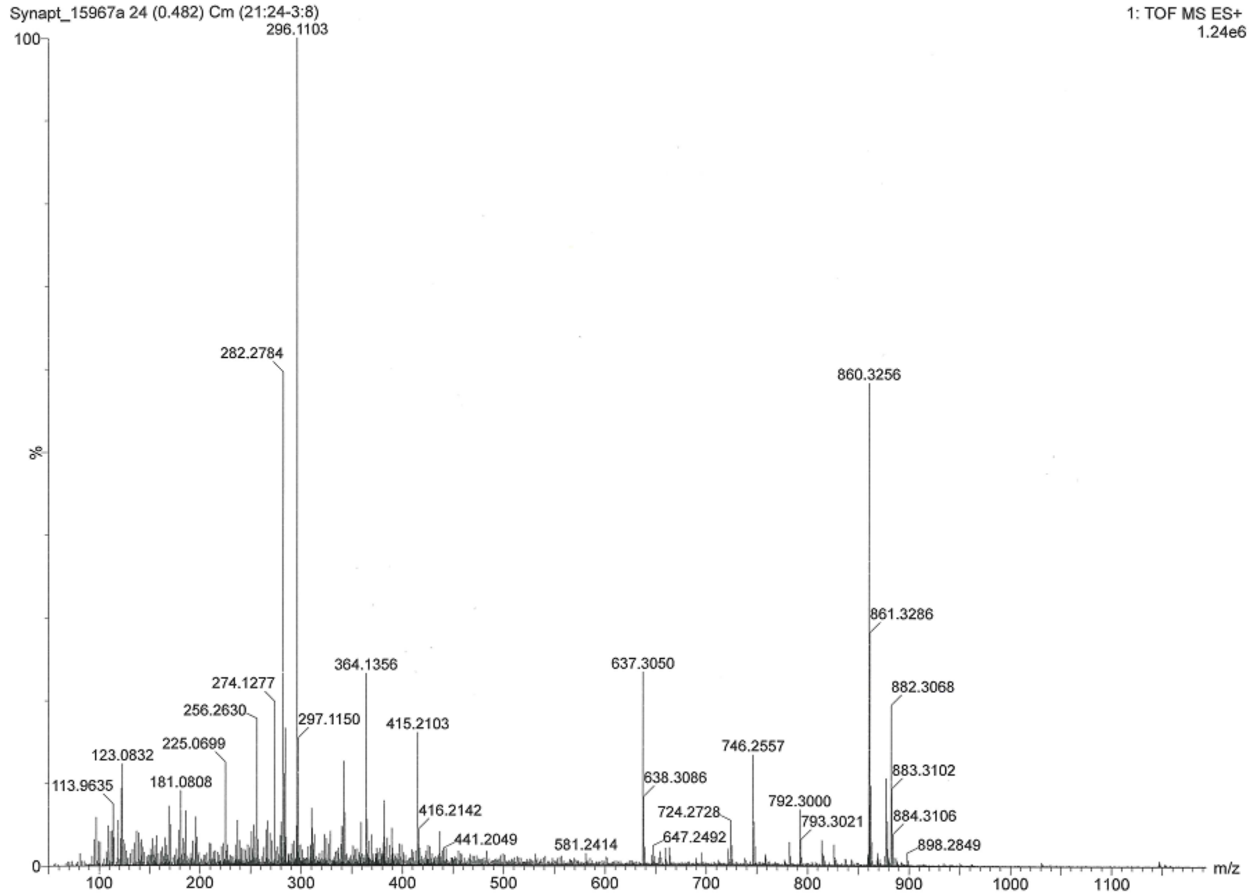


Figure S29. ^{13}C NMR spectrum (125 MHz) of compound **2**.



Monoisotopic Mass, Even Electron Ions
82 formula(e) evaluated with 1 results within limits (up to 10 closest results for each mass)
Elements Used:
C: 0-50 H: 0-80 N: 0-3 O: 14-16 S: 1-1

```
Minimum:                             -10.0
Maximum:               5.0    5.0    100.0

Mass       Calc. Mass  mDa    PPM    DBE    i-FIT   Norm   Conf(%) Formula

860.3256   860.3276    -2.0   -2.3   16.5   1665.6  n/a    n/a     C41 H54 N3 O15 S
```

Figure S30. TOF ESI MS of compound **2**.

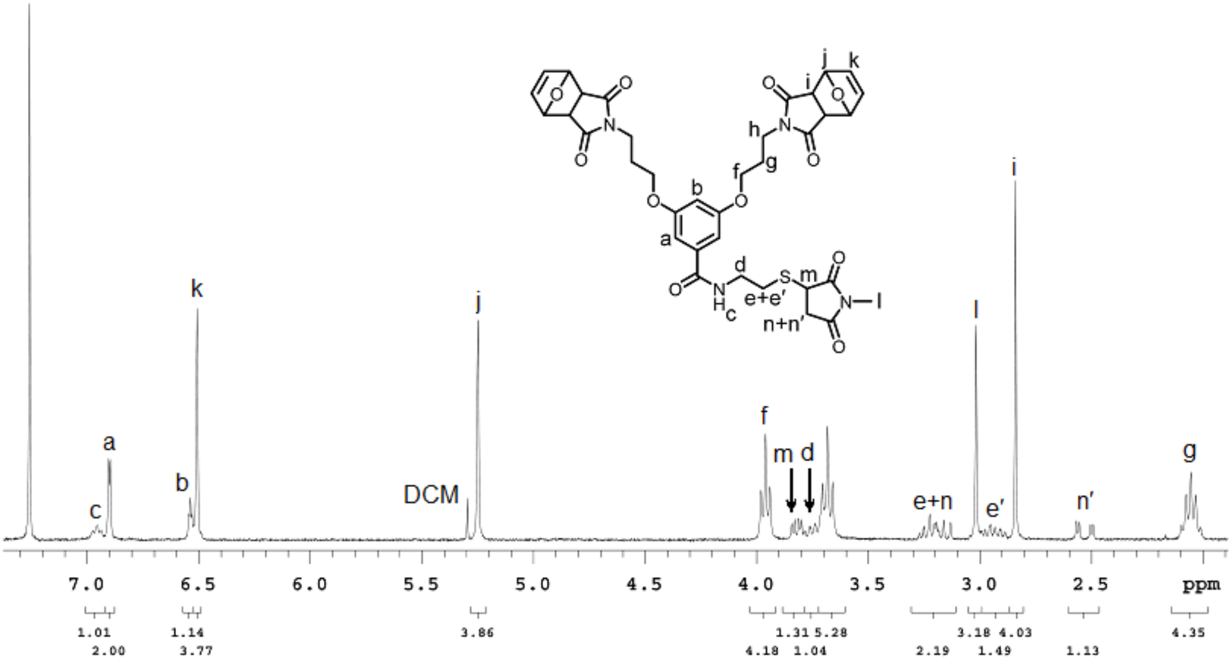


Figure S31. ^{1}H NMR spectrum (300 MHz) of the G1$_{F}$ dendron.

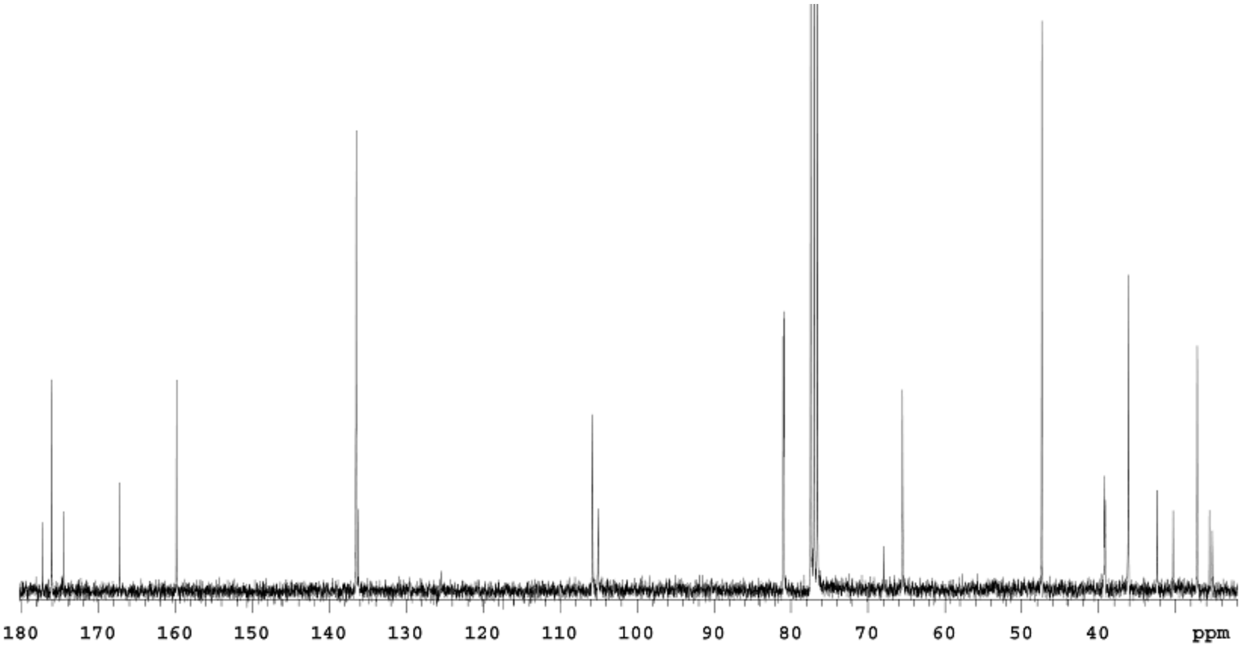
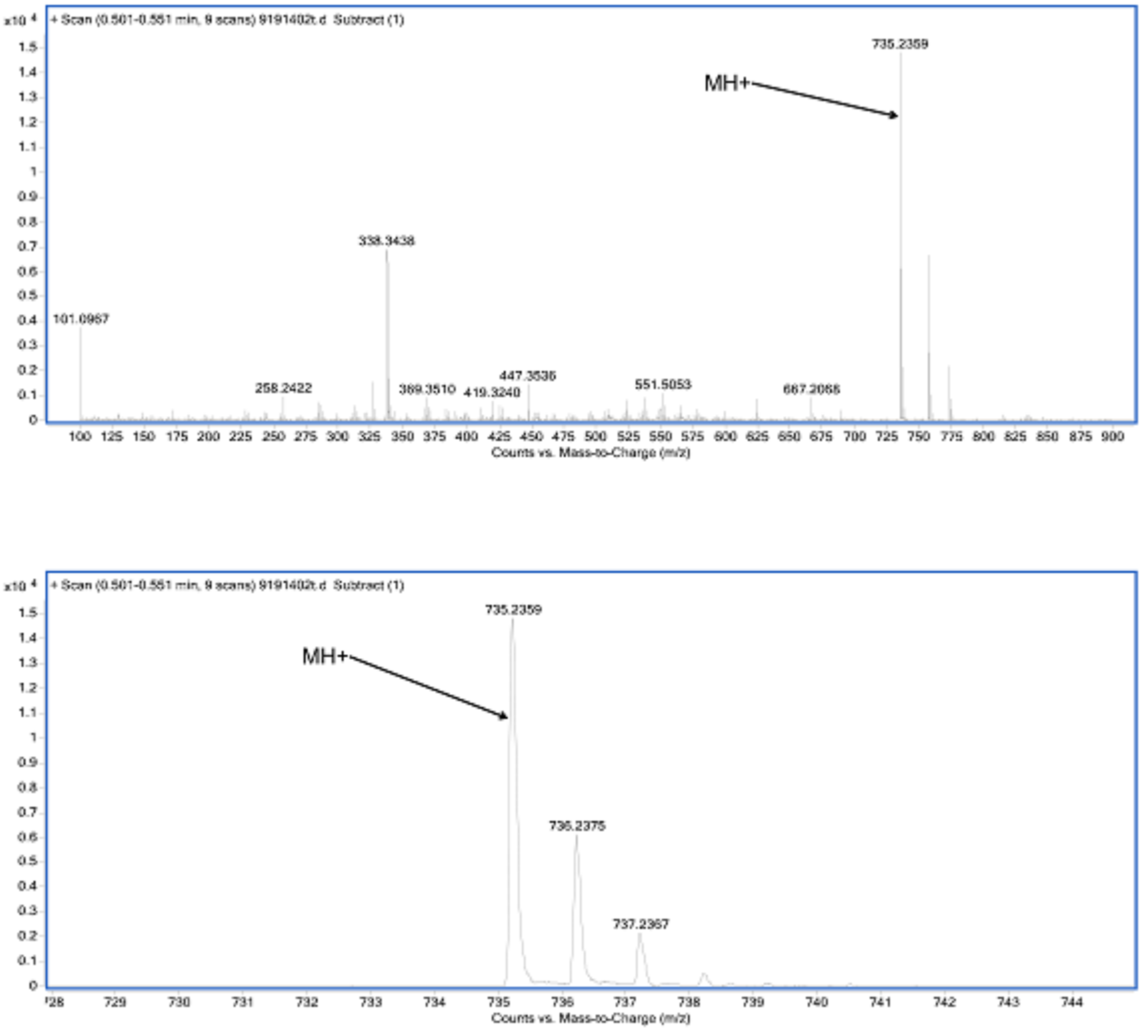


Figure S32. ^{13}C NMR spectrum (75 MHz) of the G1$_{F}$ dendron.



Measured Mass	735.2359

Element	Low Limit	High Limit
C	28	38
H	25	45
N	2	4
O	8	12
S	0	1

Formula	Calculated Mass	mDaError	ppmError	RDB
C36 H39 N4 O11 S	735.2331	2.8	3.9	19.5

Figure S33. TOF ESI MS of the $G1_F$ dendron.

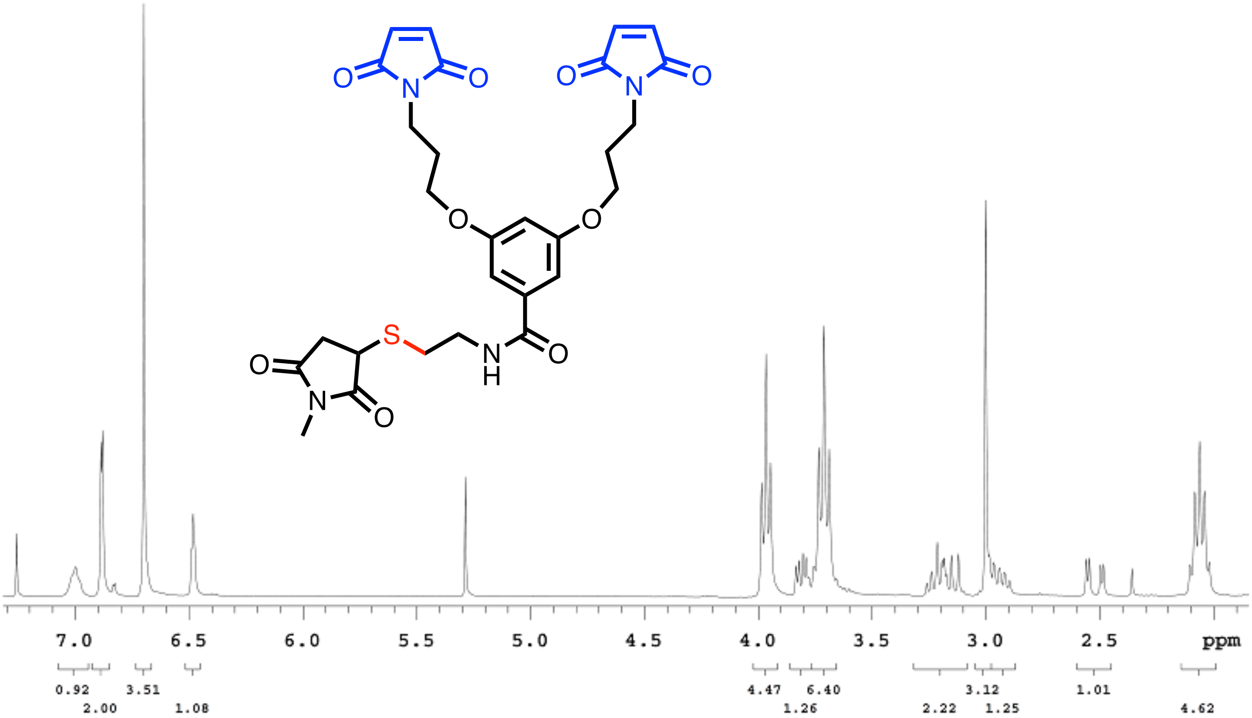


Figure S34. ^{1}H NMR spectrum (300 MHz) of the G1$_M$ dendron.

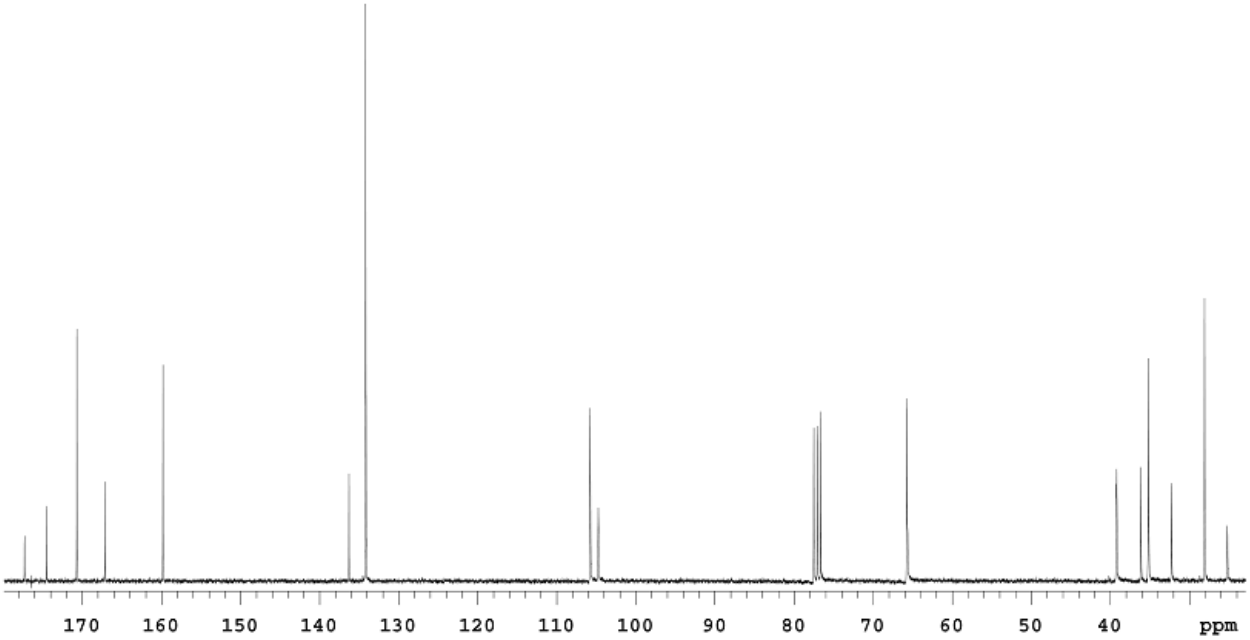
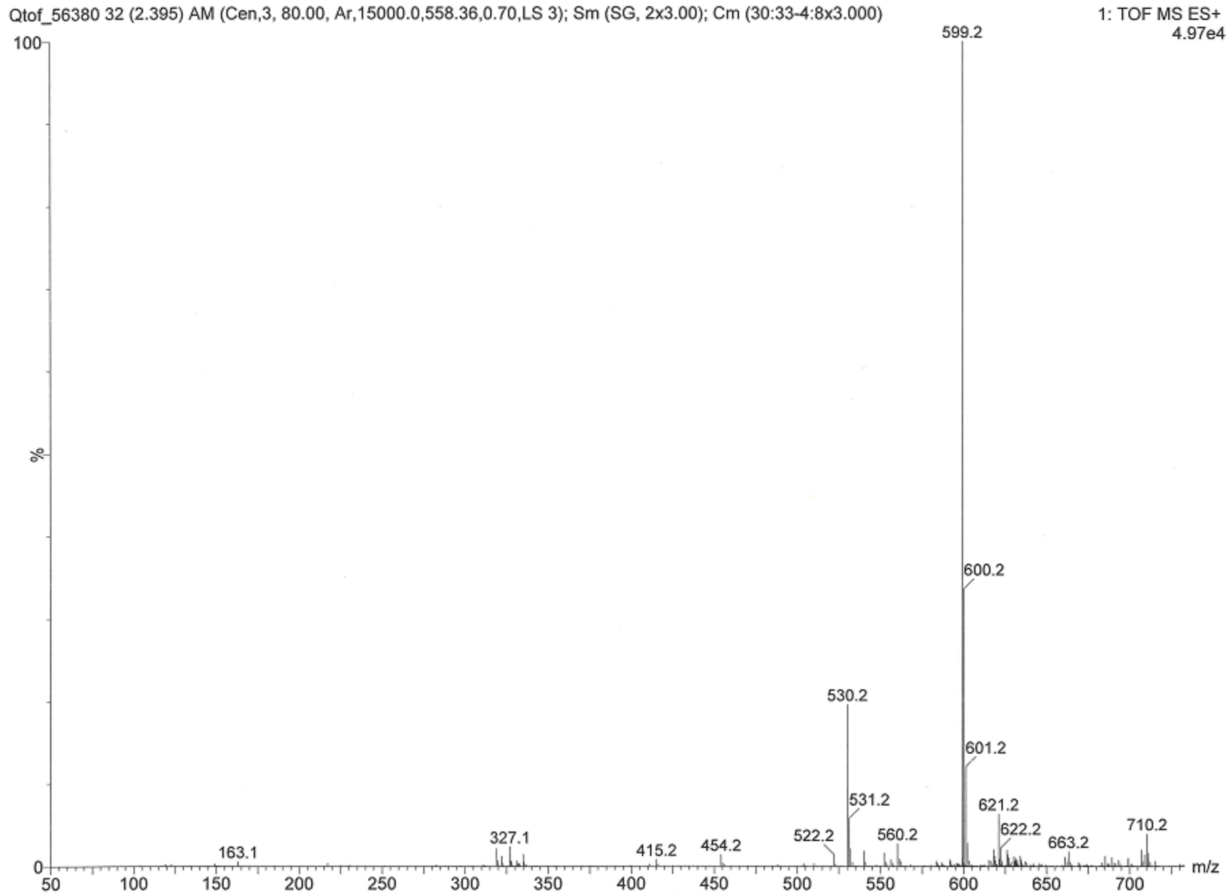


Figure S35. ^{13}C NMR spectrum (75 MHz) of the G1$_M$ dendron.



Monoisotopic Mass, Even Electron Ions
195 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-120   H: 0-180   N: 0-5   O: 9-11   Na: 0-1   S: 1-1

```
Minimum:                                    -1.5
Maximum:                5.0       20.0      600.0

Mass        Calc. Mass  mDa       PPM       DBE       i-FIT     Formula

599.1813    599.1812    0.1       0.2       15.5      1.7       C28  H31  N4  O9  S
            599.1788    2.5       4.2       12.5      7.7       C26  H32  N4  O9  Na  S
            599.1927    -11.4     -19.0     11.5      6.7       C29  H36  O10  Na  S
            599.1699    11.4      19.0      15.5      5.5       C29  H31  N2  O10  S
```

Figure S36. TOF ESI MS of compound the $G1_M$ dendron.

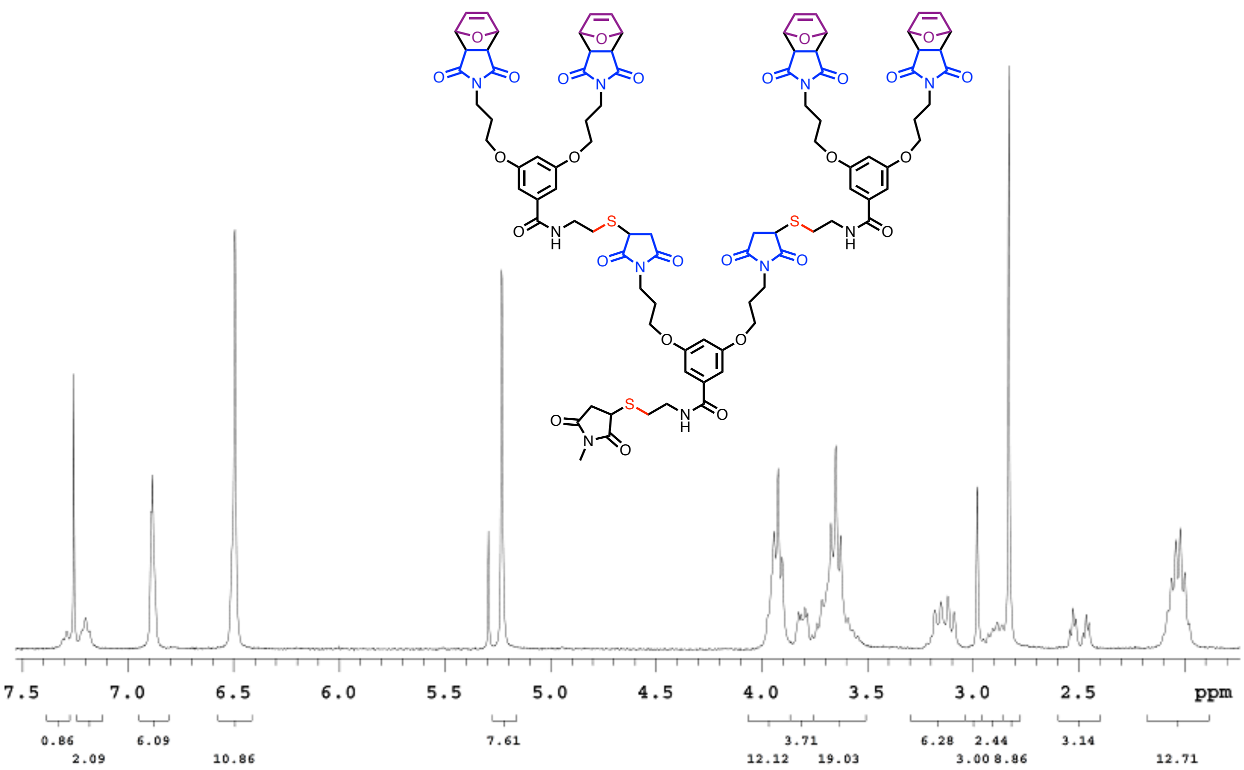


Figure S37. ^{1}H NMR spectrum (300 MHz) of the G2$_{F}$ dendron.

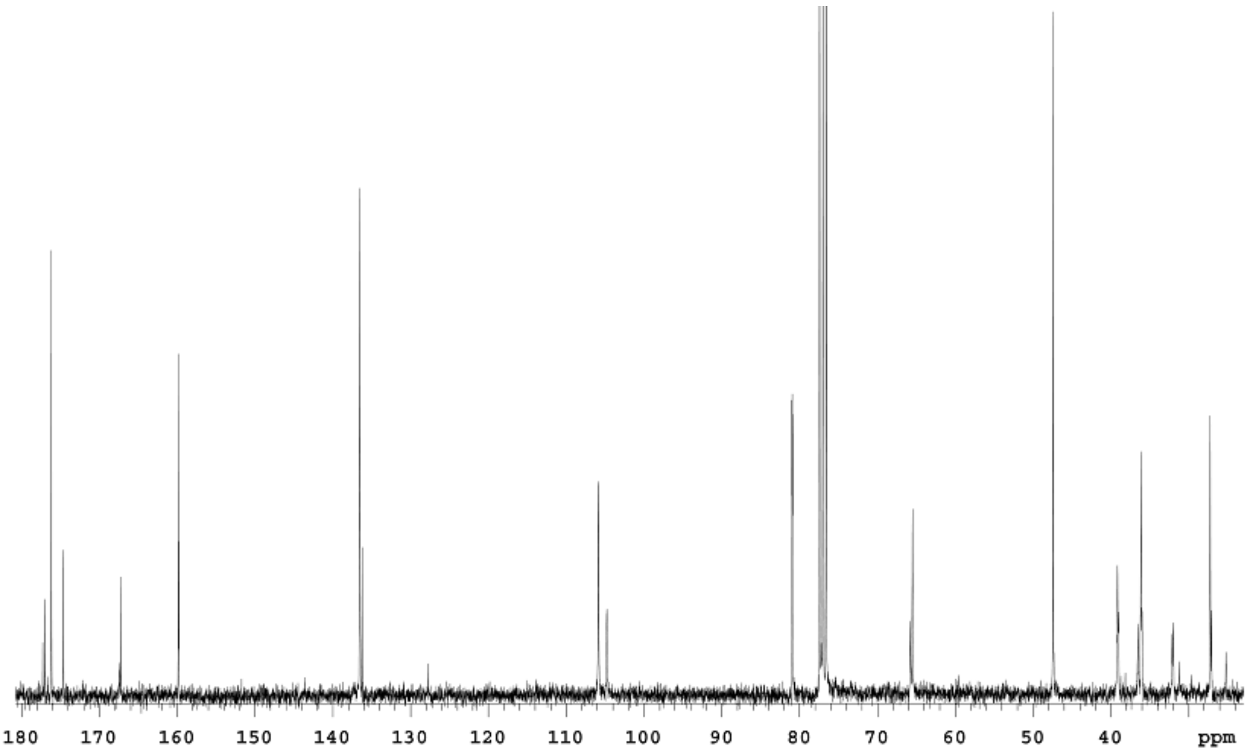
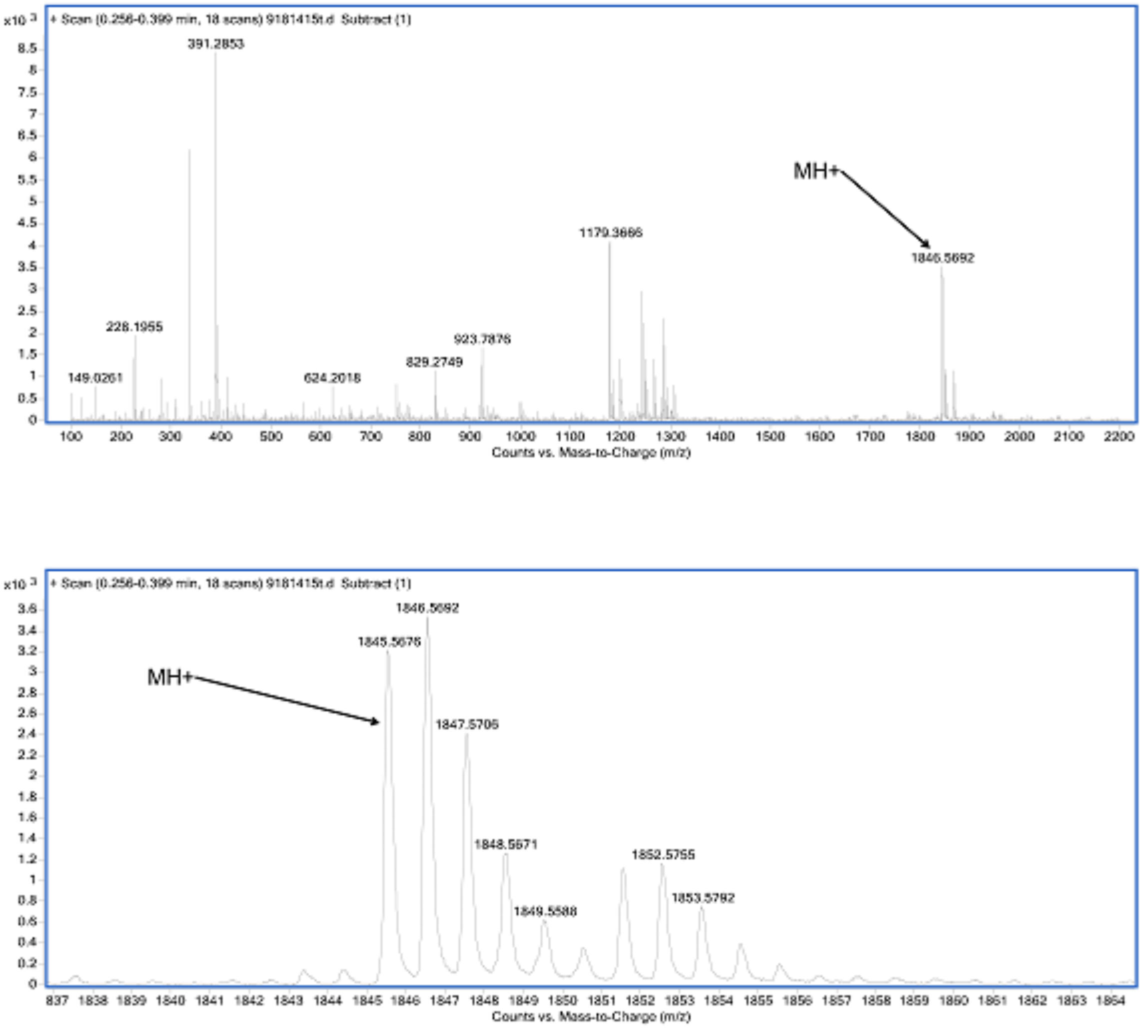


Figure S38. ^{13}C NMR spectrum (75 MHz) of the G2$_{F}$ dendron.



Measured Mass 1845.5676

Element	Low Limit	High Limit
C	85	95
H	85	105
N	9	11
O	26	28
S	2	4

Formula	Calculated Mass	mDaError	ppmError	RDB
C90 H97 N10 O27 S3	1845.5681	-0.5	-0.3	47.5
C93 H93 N10 O27 S2	1845.5648	2.8	1.5	52.5
C87 H101 N10 O27 S4	1845.5715	-3.9	-2.1	42.5
C86 H99 N11 O27 S4	1845.5589	8.7	4.7	43

Figure S39. TOF ESI MS of compound the G2$_F$ dendron.

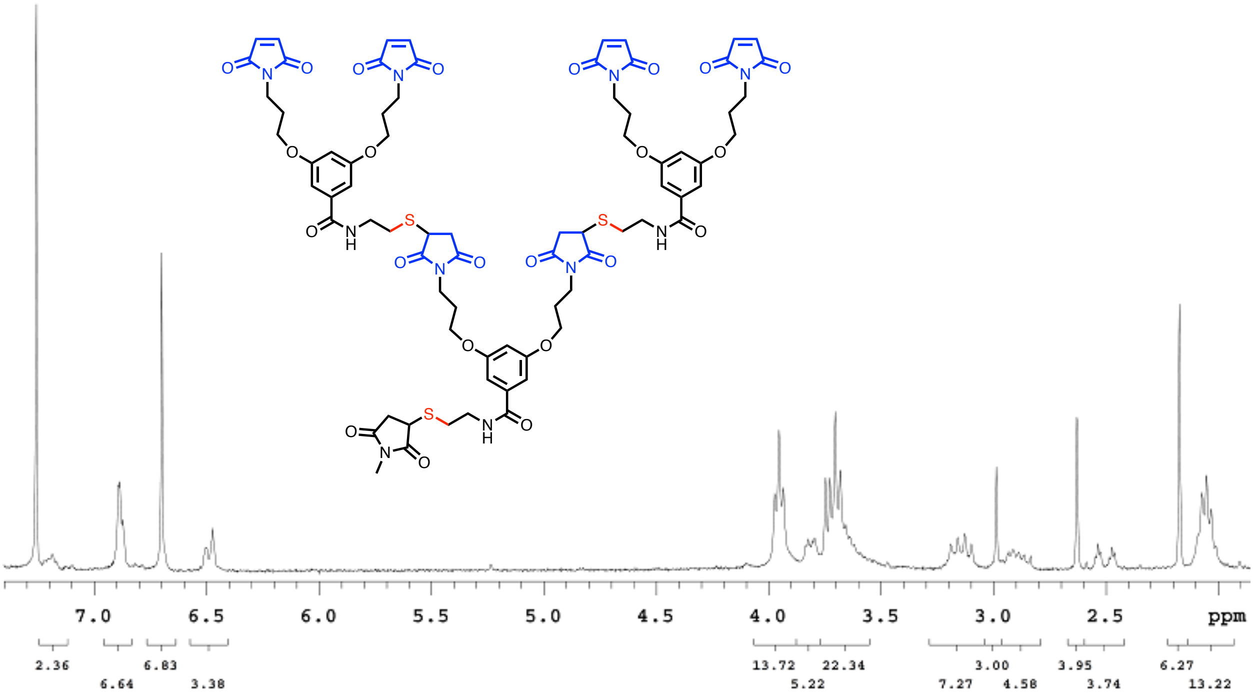


Figure S40. ^{1}H NMR spectrum (300 MHz) of the G2$_M$ dendron.

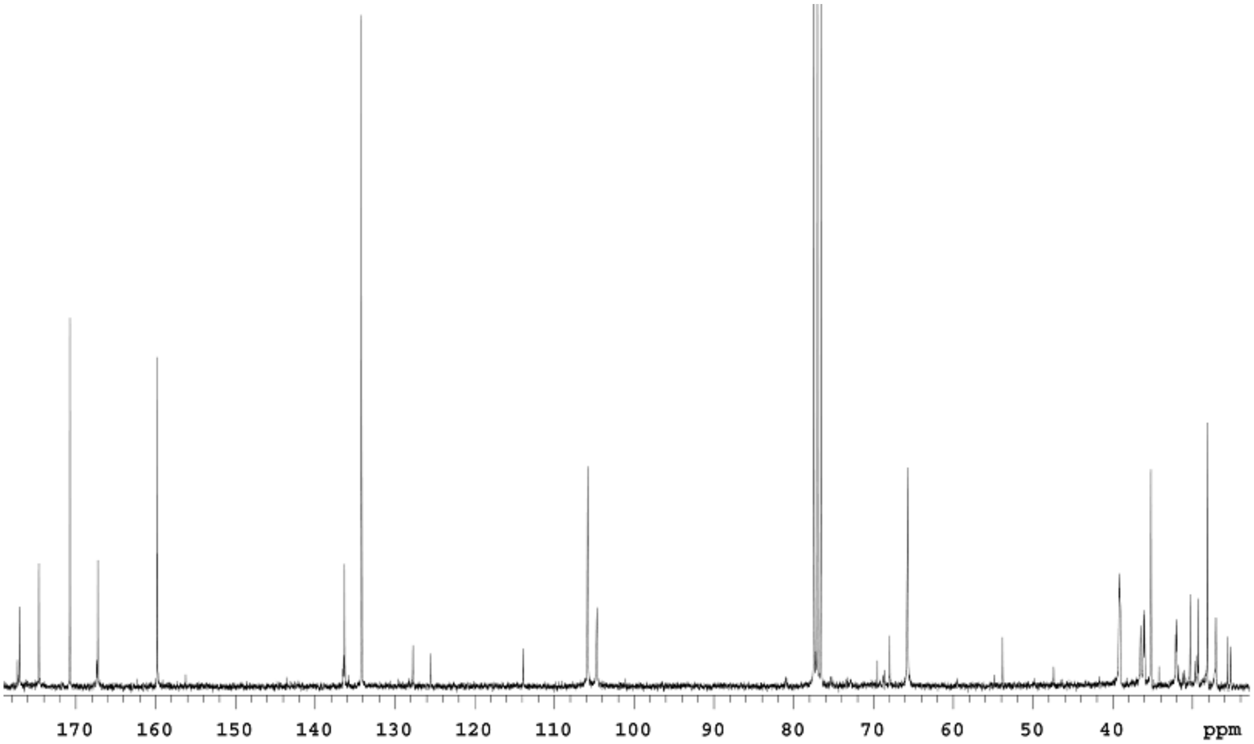
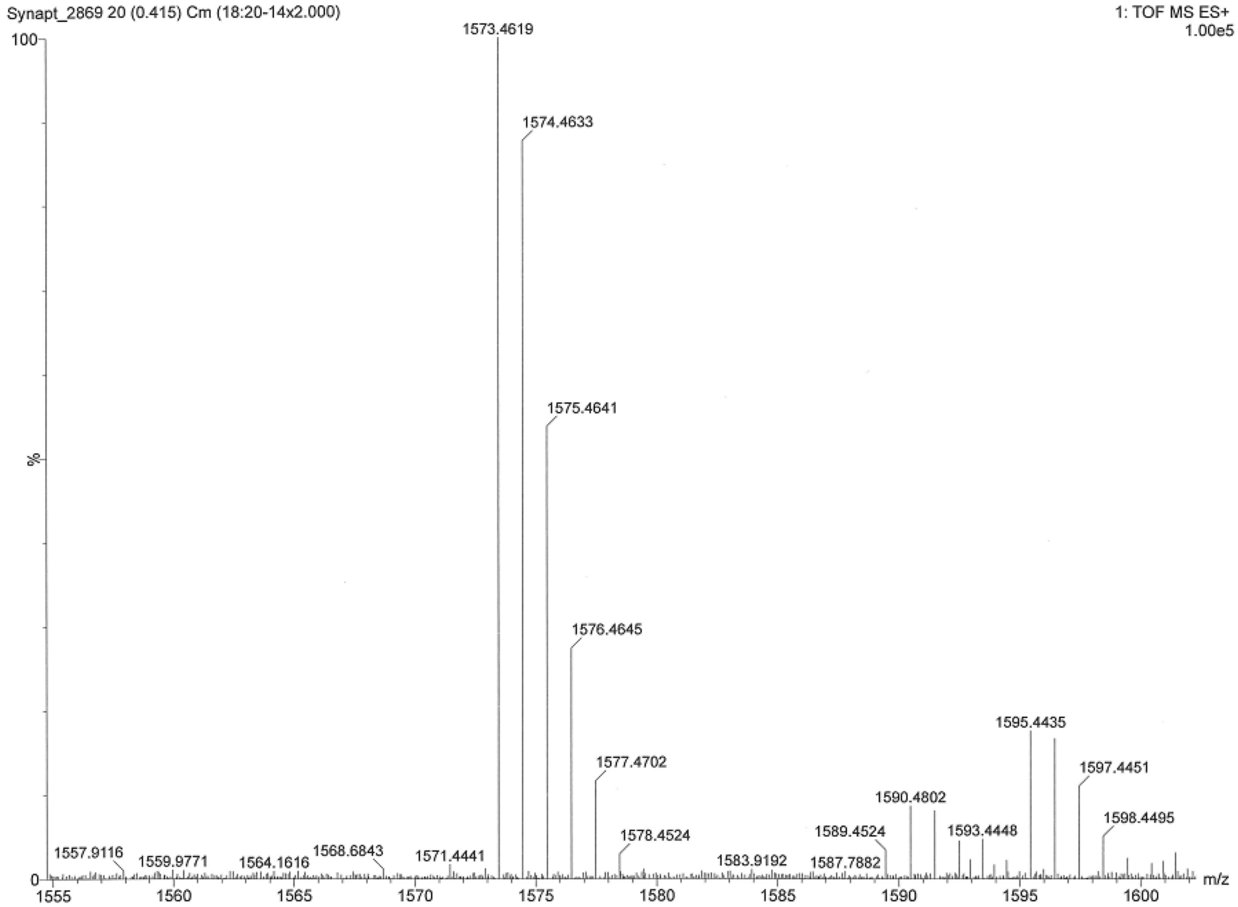


Figure S41. ^{13}C NMR spectrum (75 MHz) of the G2$_M$ (A-R-B$_2$/A-R-B$_2$) dendron.



```
Monoisotopic Mass, Even Electron Ions
206 formula(e) evaluated with 2 results within limits (up to 10 best isotopic matches for each mass)
Elements Used:
C: 0-100    H: 0-150    N: 8-11    O: 22-25    S: 3-3


Minimum:                                 -1.5
Maximum:                5.0     10.0     150.0

Mass         Calc. Mass  mDa     PPM     DBE     i-FIT    Norm    Conf(%)  Formula

1573.4619    1573.4638   -1.9    -1.2    39.5    211.1    0.216   80.60    C74 H81 N10 O23 S3
             1573.4526   9.3     5.9     39.5    212.5    1.640   19.40    C75 H81 N8 O24 S3
```

Figure S42. TOF ESI MS of compound the G2$_M$ dendron.

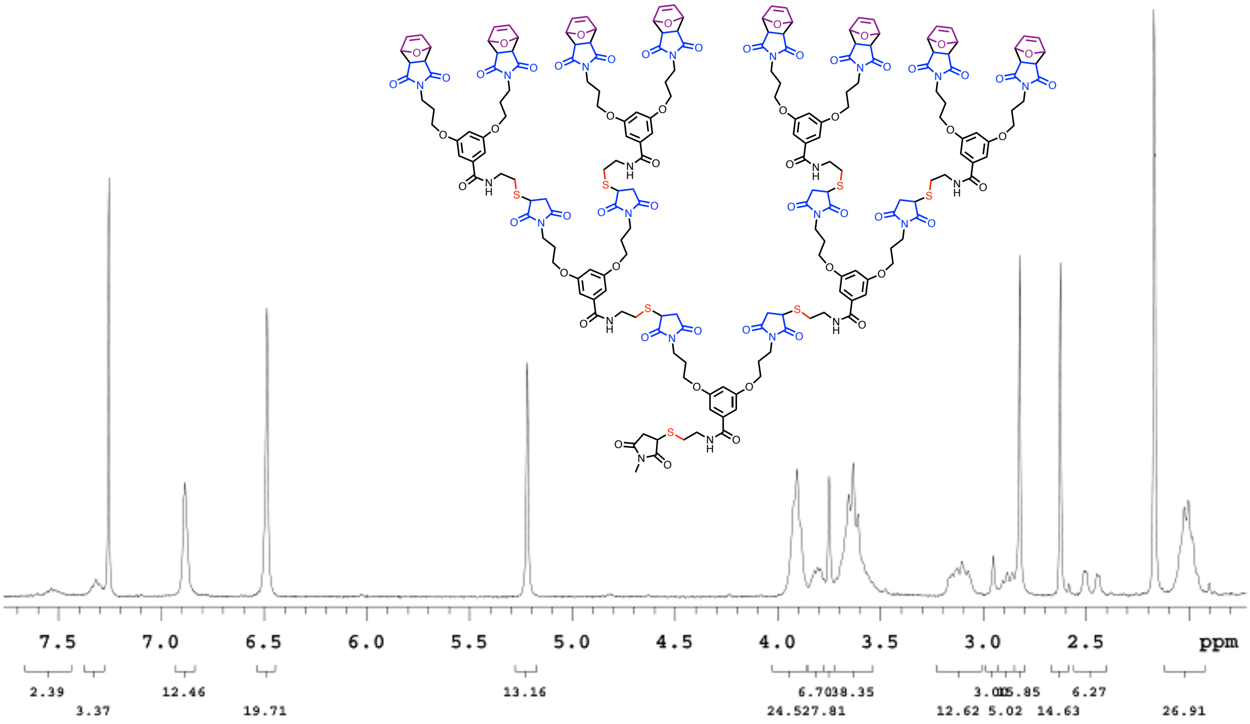


Figure S43. ^{1}H NMR spectrum (300 MHz) of the G3$_F$ dendron.

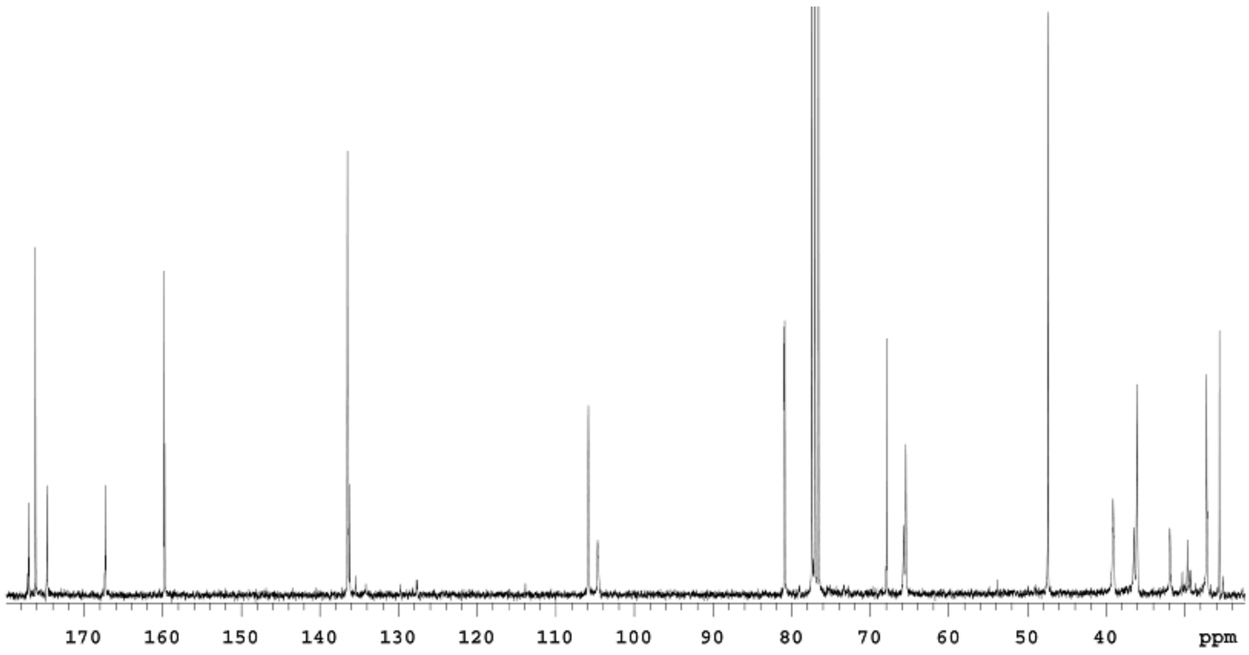


Figure S44. ^{13}C NMR spectrum (75 MHz) of the G3$_F$ dendron.

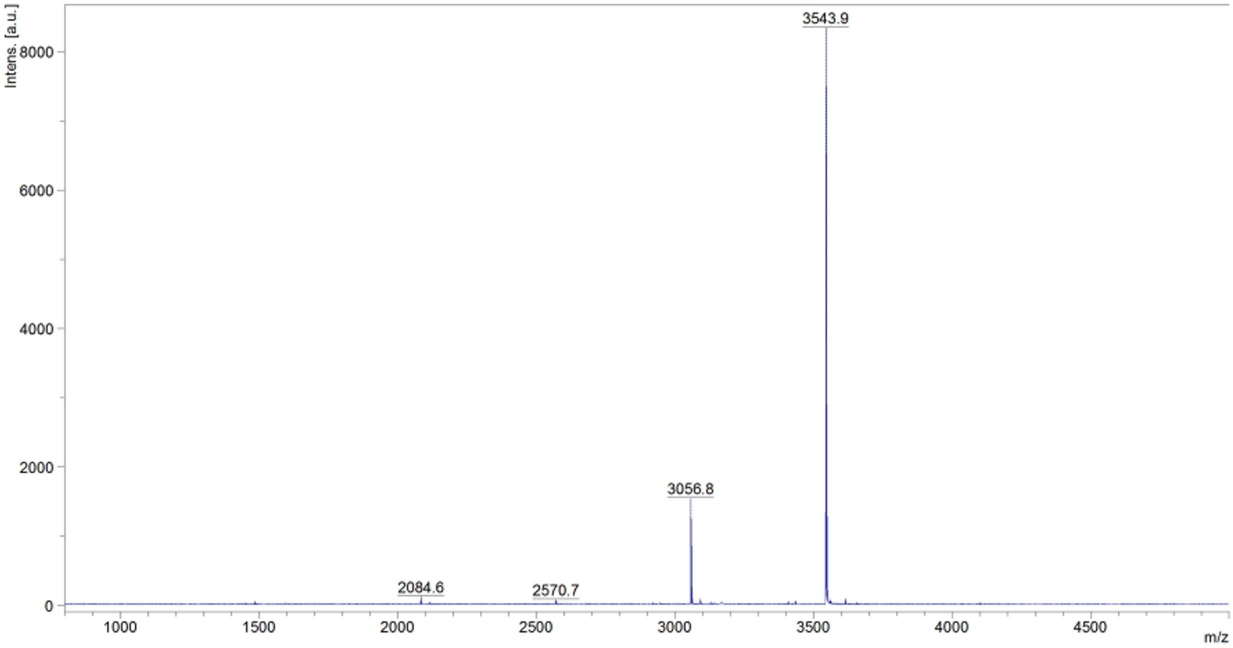


Figure S45. MALDI MS of $G3_F$ dendron results in the observation of the parent $[M+Na]^+$ ion of the fully deprotected dendron $G3_M$. Minor peaks can be observed below that of the parent ion, and the spacing between these peaks is approximately equal to the mass of thermally deprotected branched monomer **1** (*m/z* calculated for $C_{23}H_{25}N_3O_7S$ is 487.14). Konkolewicz and co workers have observed thermally promoted retro-thiol-Michael reactions.[12-13] It is possible that such retro-thiol-maleimide reactions could occur under MALDI conditions, which would explain the agreement between the regular spacing of minor peaks observed in several MALDI MS results.

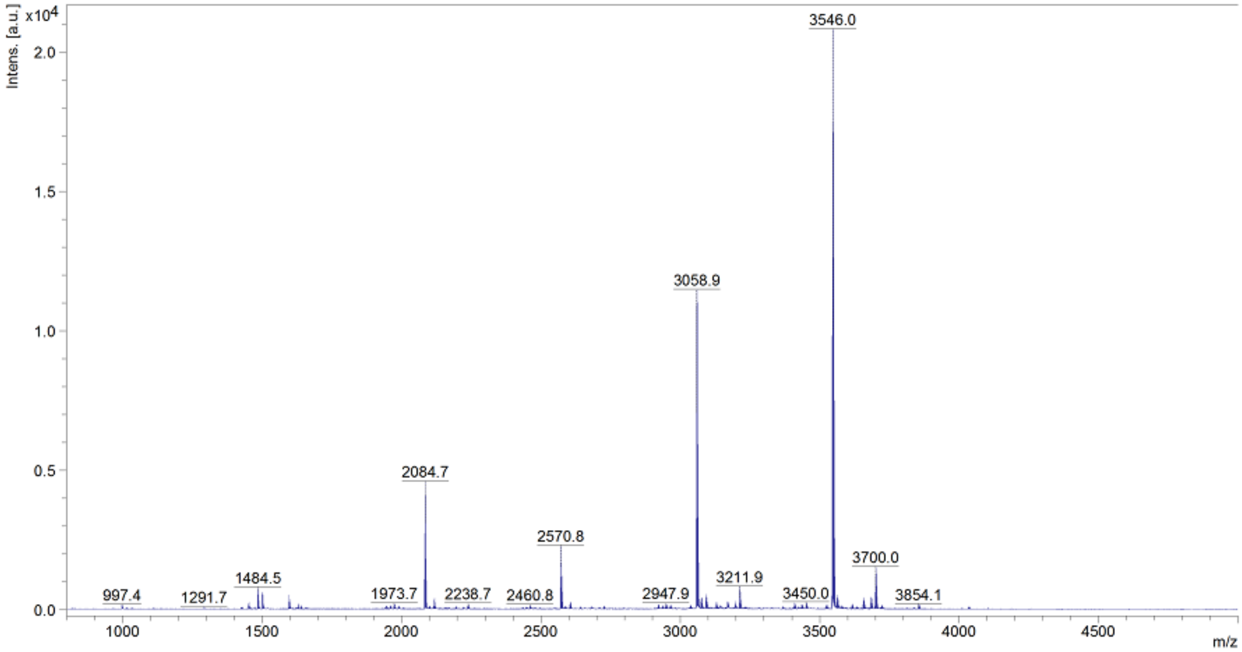


Figure S46. MALDI MS of $G3_M$ dendron. Minor peaks with approximate *m/z* spacing of 487 are observed.

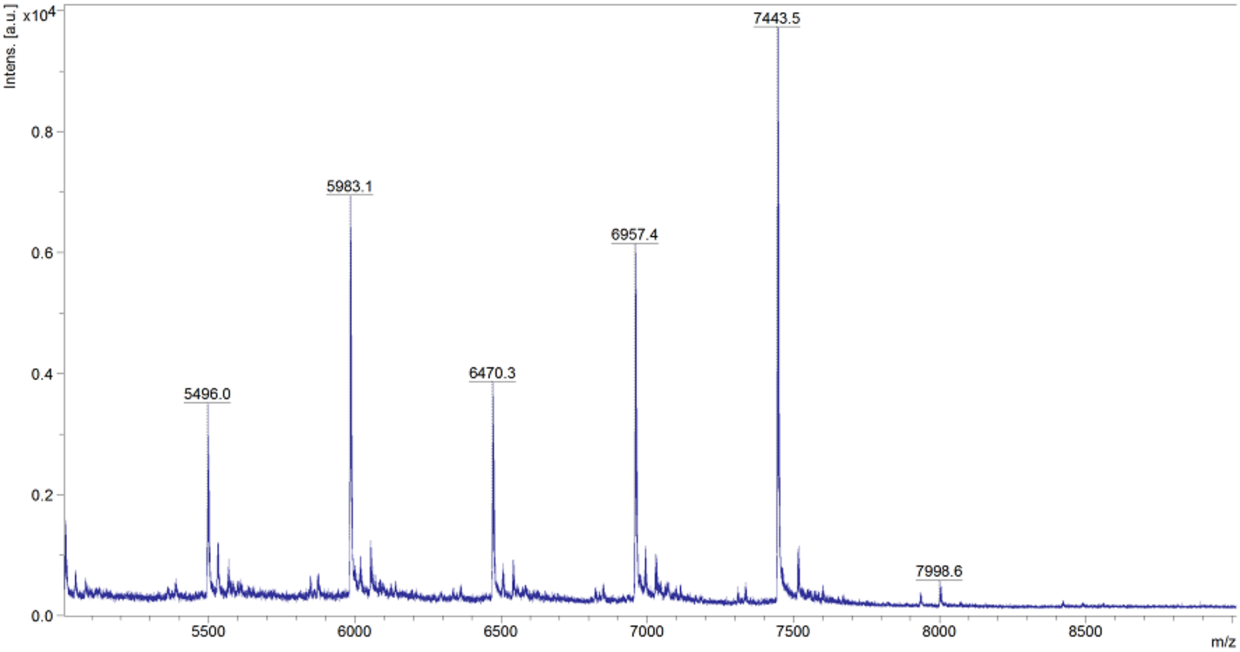


Figure S47. MALDI MS of G4$_F$ dendron results in the observation of the parent $[M+Na]^+$ ion of the fully deprotected dendron G4$_M$. Minor peaks with approximate *m/z* spacing of 487 are observed.

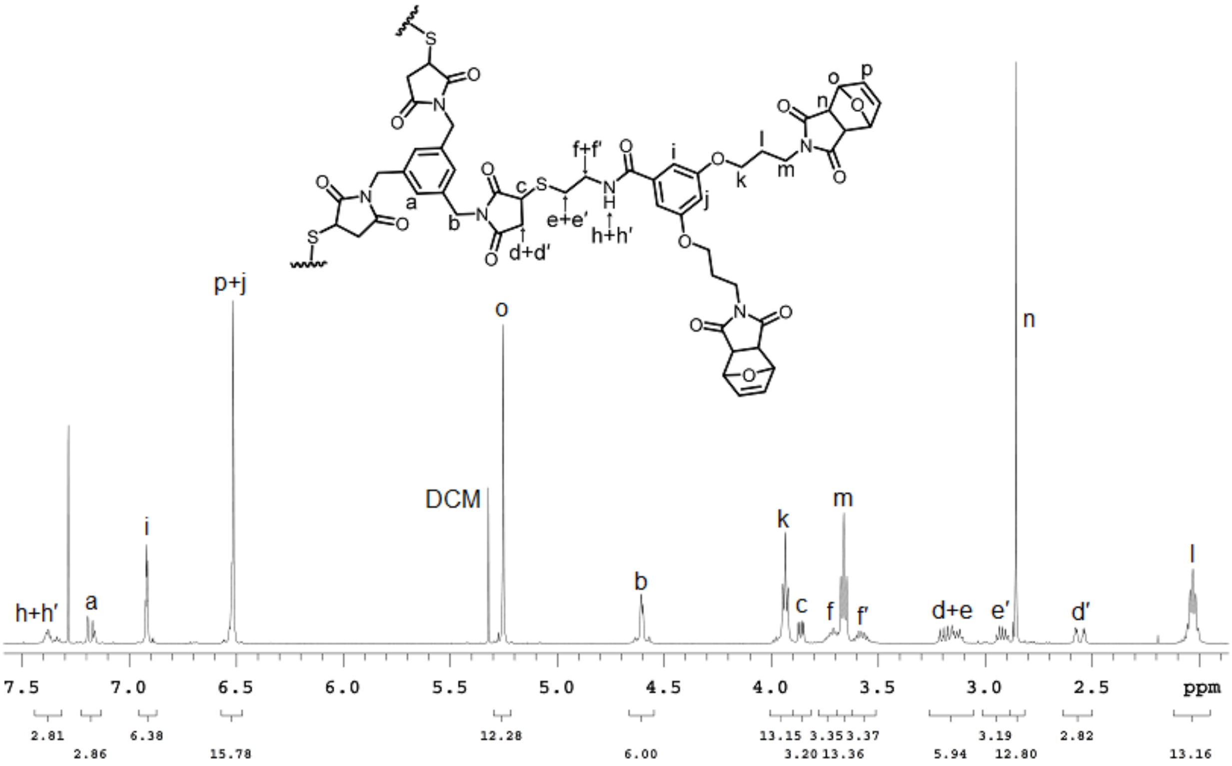


Figure S48. ^1H NMR spectrum (500 MHz) of G1$_F$ (A-R-B$_2$) dendrimer.

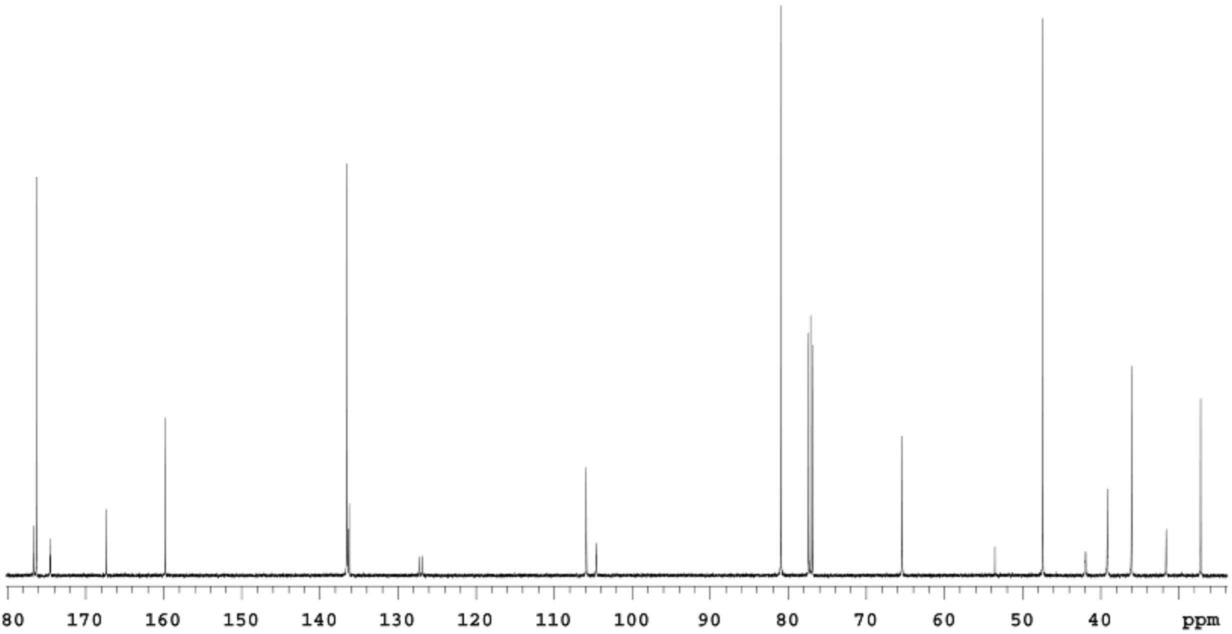


Figure S49. ^{13}C NMR spectrum (125 MHz) of $G1_F$ dendrimer.

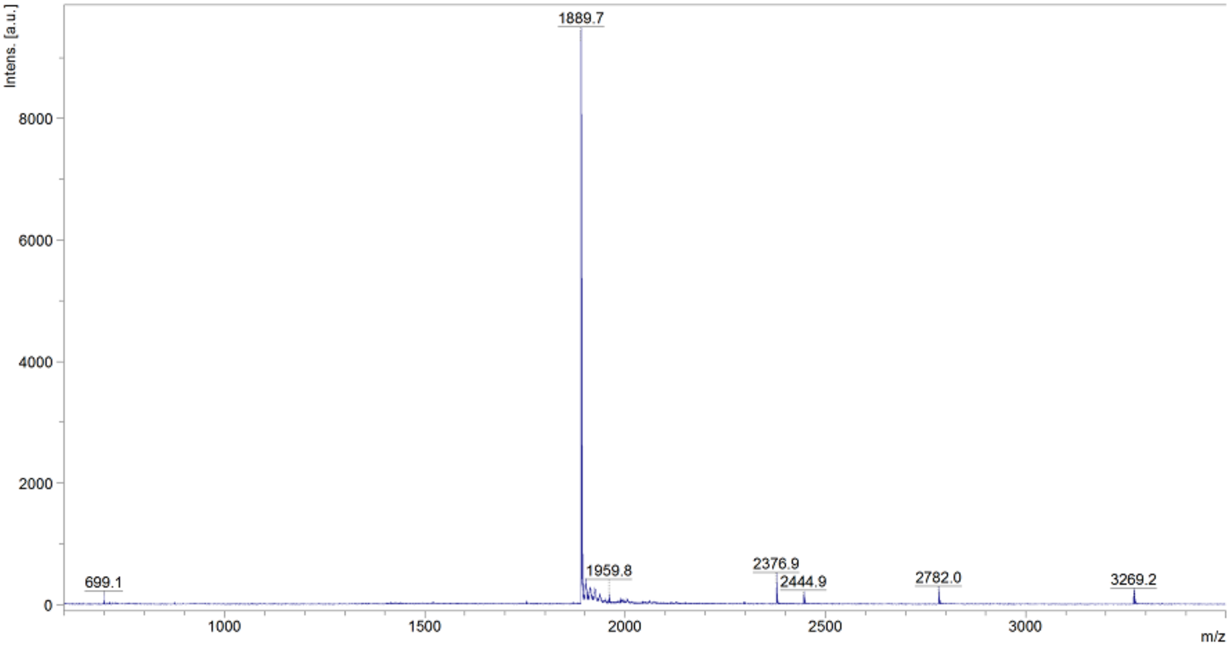


Figure S50. MALDI MS of $G1_F$ dendrimer results in the observation of the fully thermally deprotected $G1_M$ dendrimer.

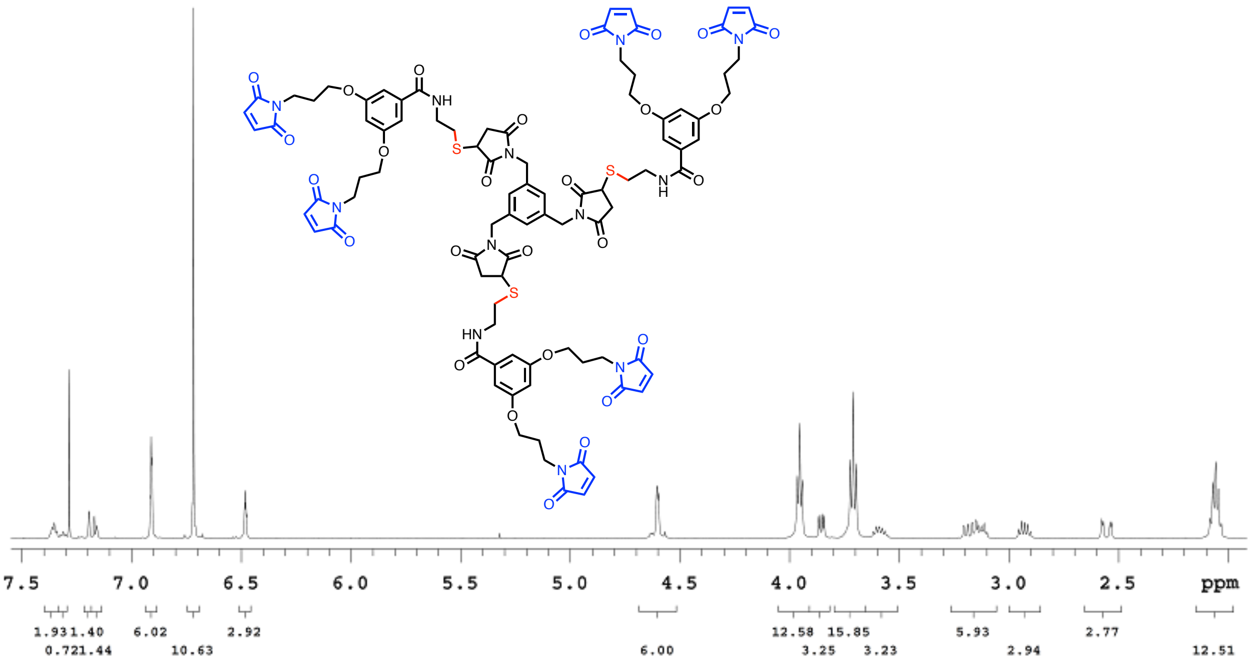


Figure S51. ^{1}H NMR spectrum (500 MHz) of G1$_{M}$ dendrimer.

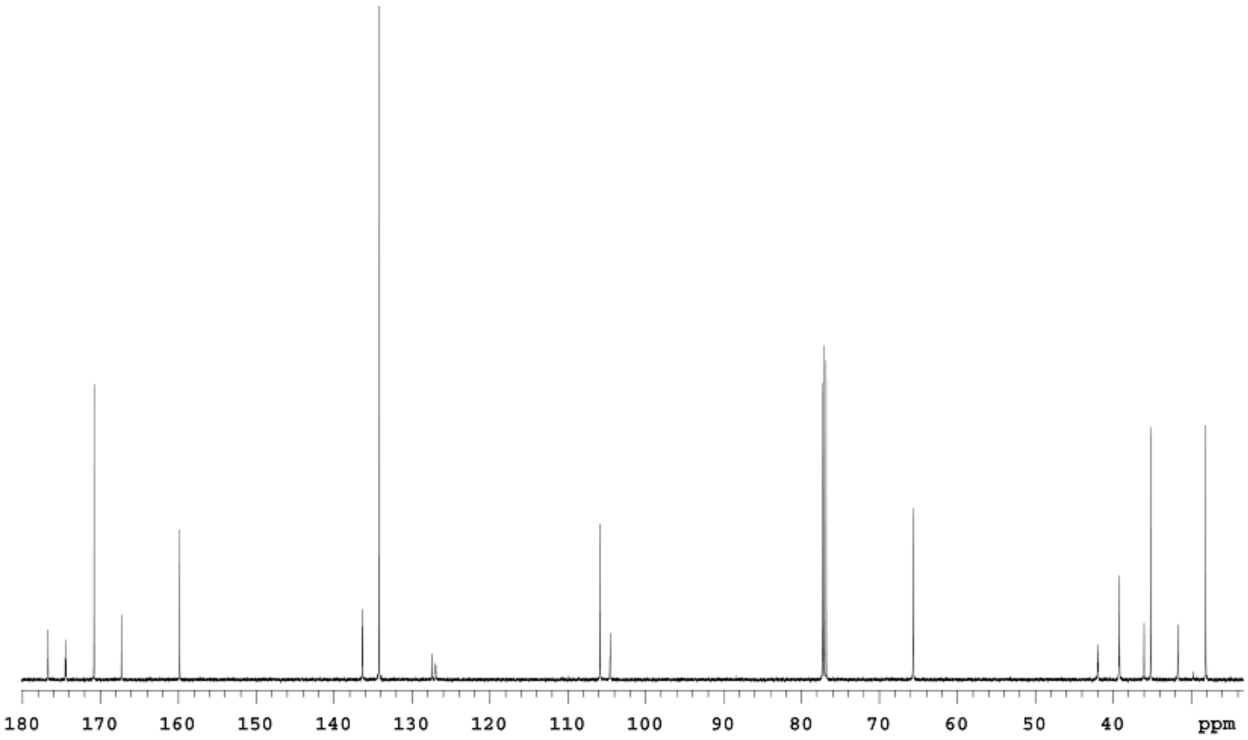


Figure S52. ^{13}C NMR spectrum (125 MHz) of G1$_{M}$ dendrimer.

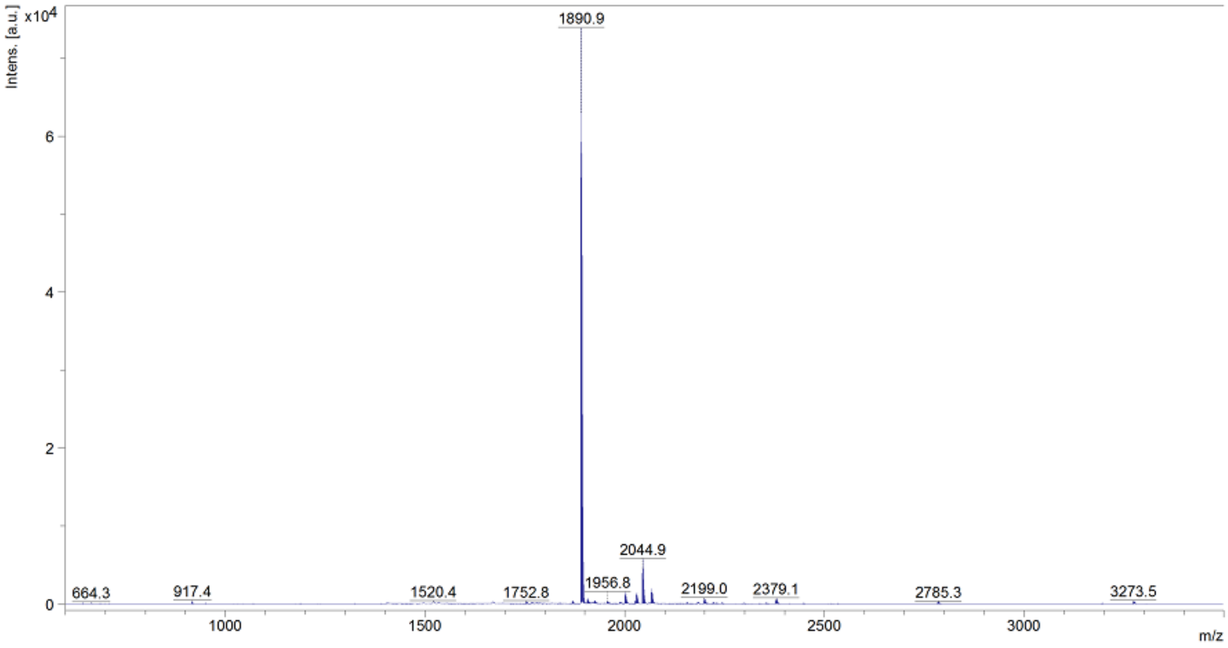


Figure S53. MALDI MS of G1$_M$ dendrimer.

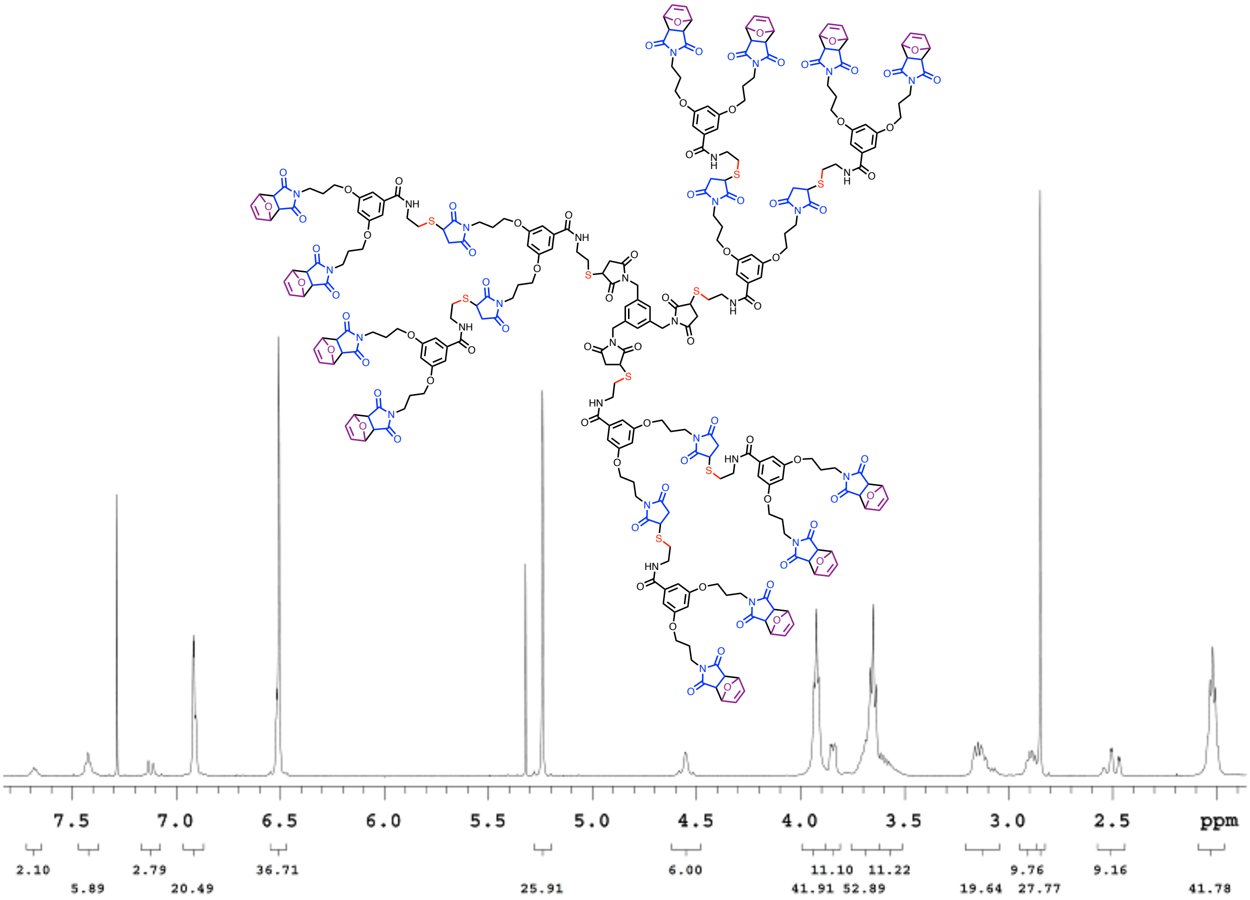


Figure S54. ^{1}H NMR spectrum (500 MHz) of G2$_F$ dendrimer.

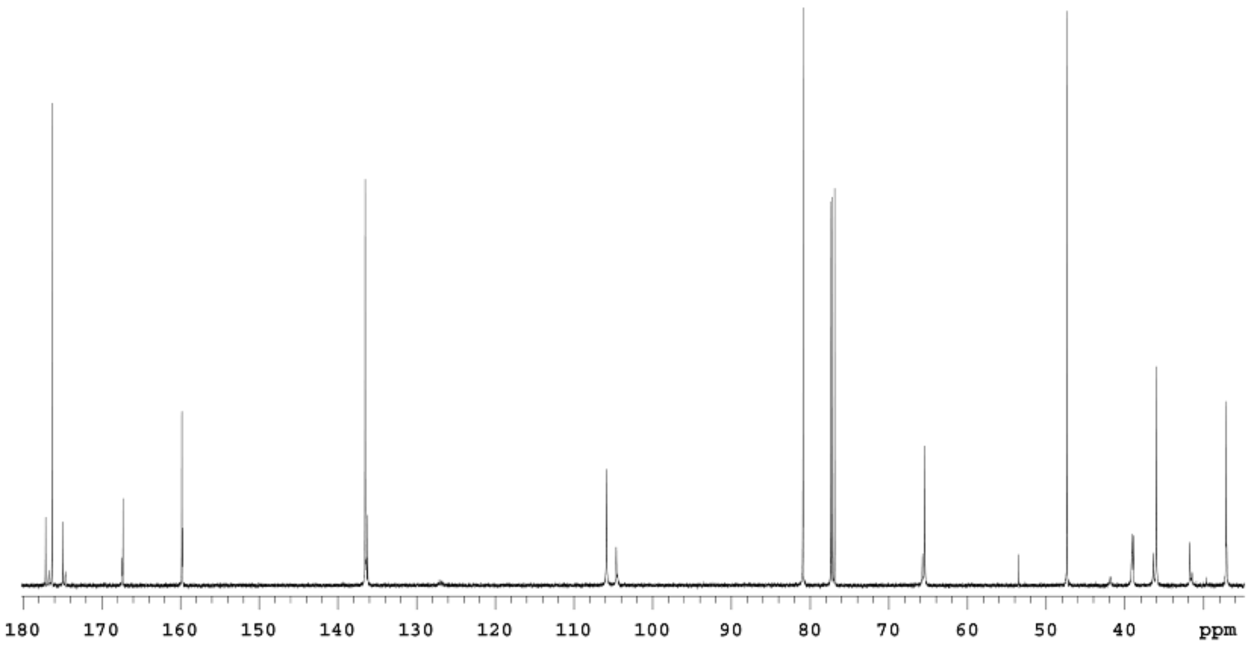


Figure S55. ^{13}C NMR spectrum (125 MHz) of G2$_F$ dendrimer.

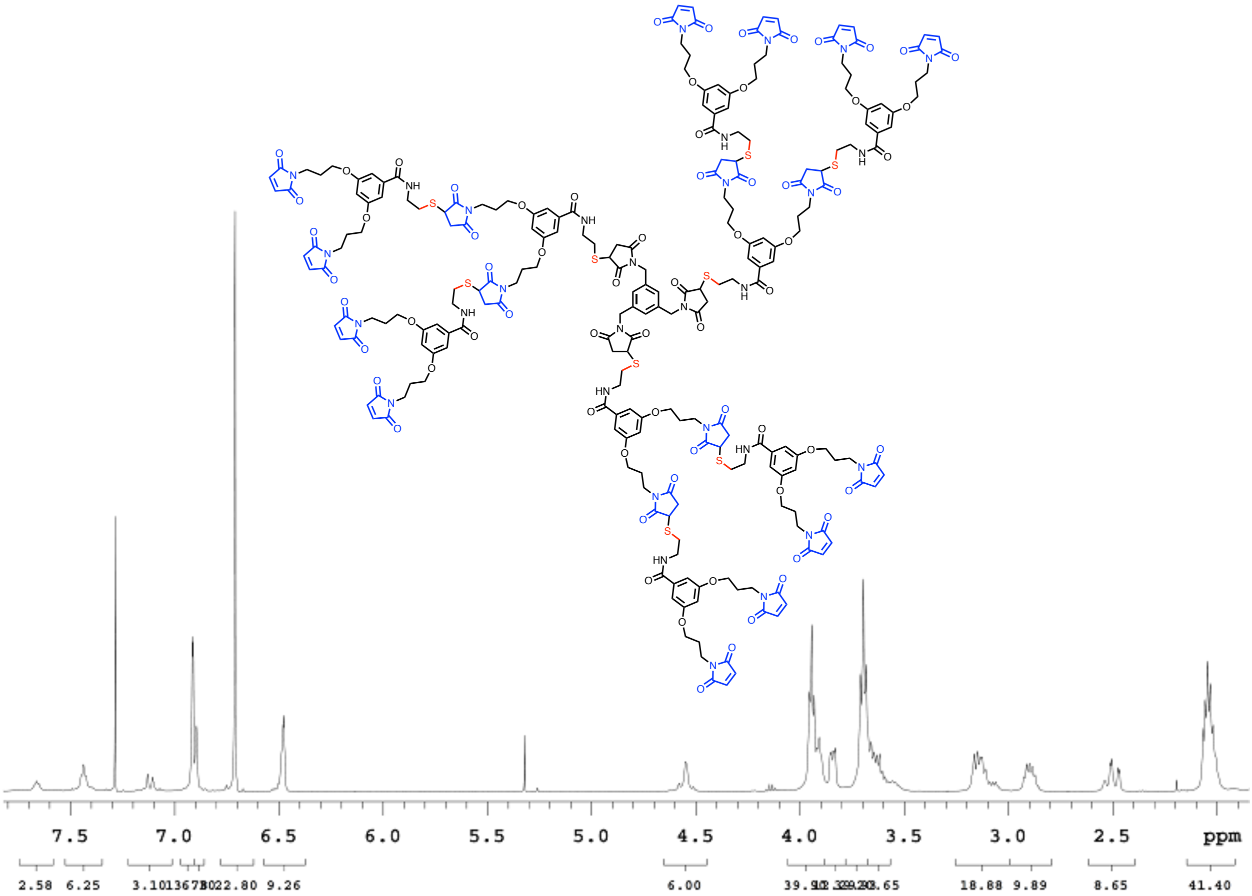


Figure S56. ^{1}H NMR spectrum (500 MHz) of G2$_M$ dendrimer.

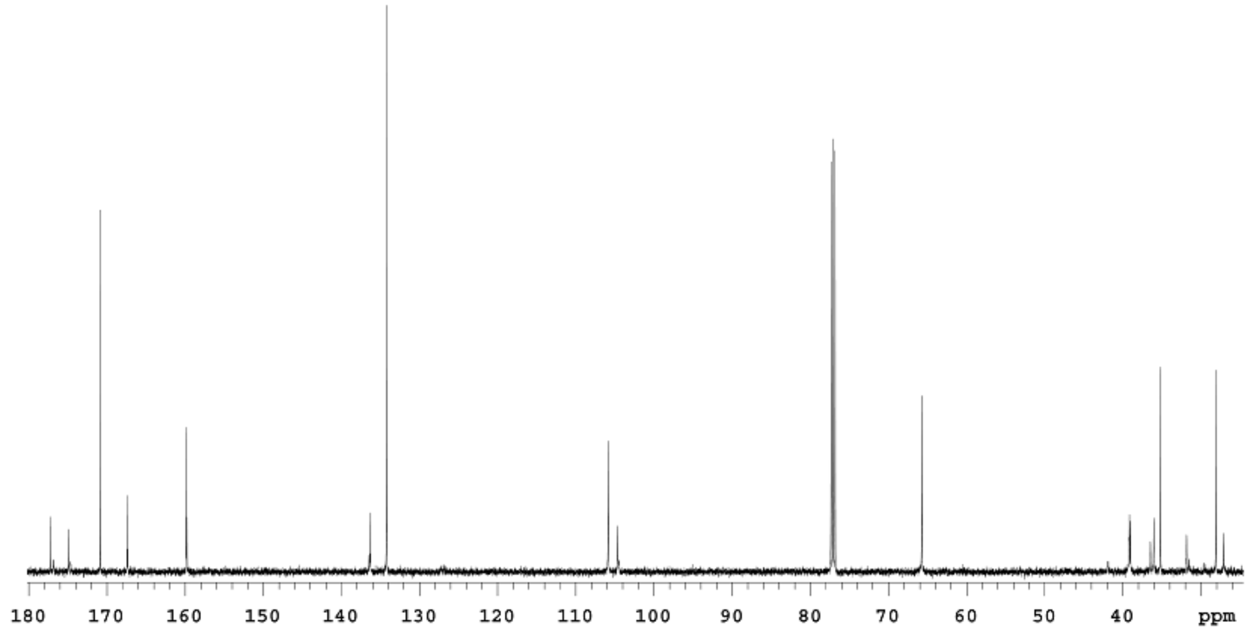


Figure S57. ^{13}C NMR spectrum (125 MHz) of G2$_M$ dendrimer.

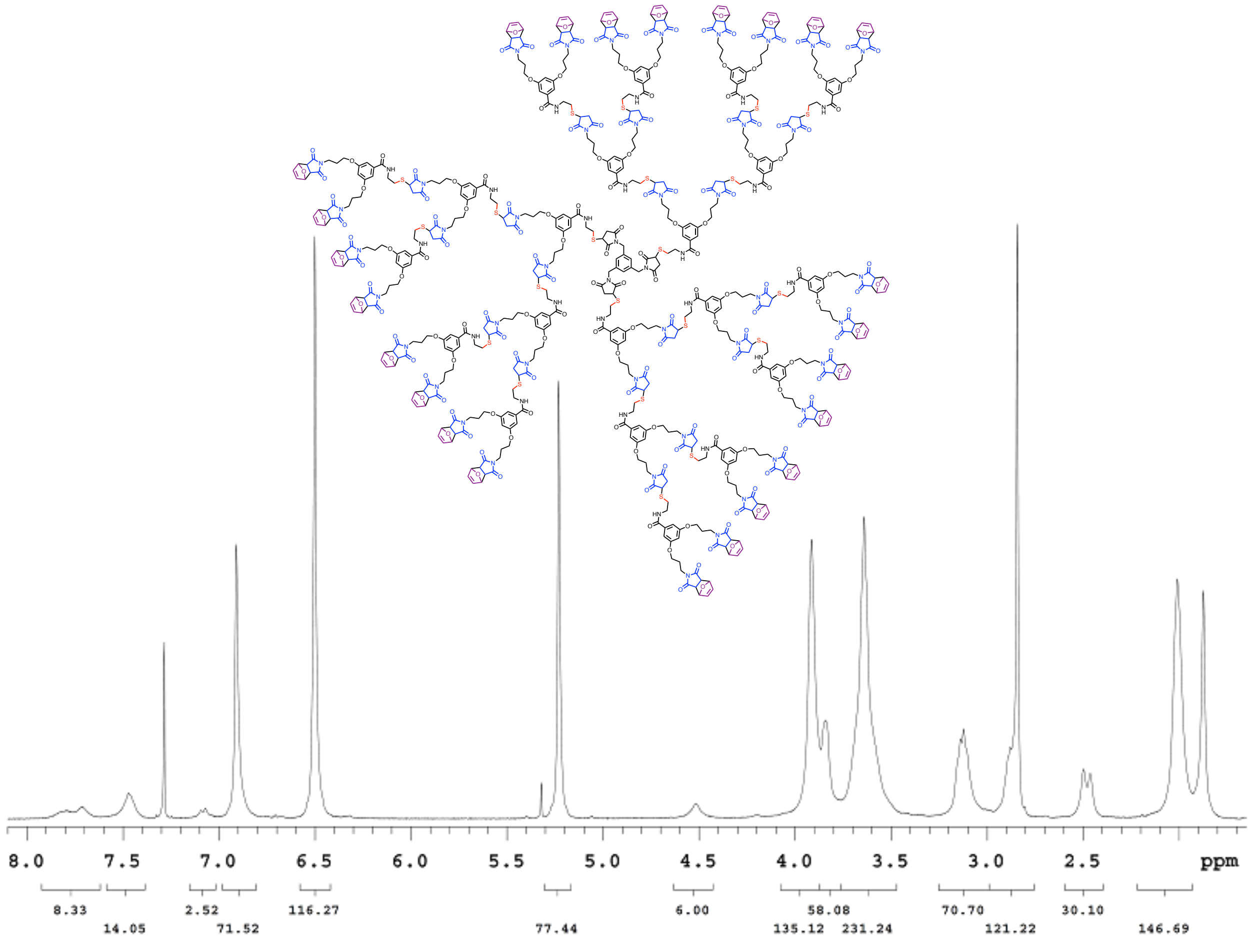


Figure S58. ^{1}H NMR spectrum (500 MHz) of G3$_F$ dendrimer **4**.

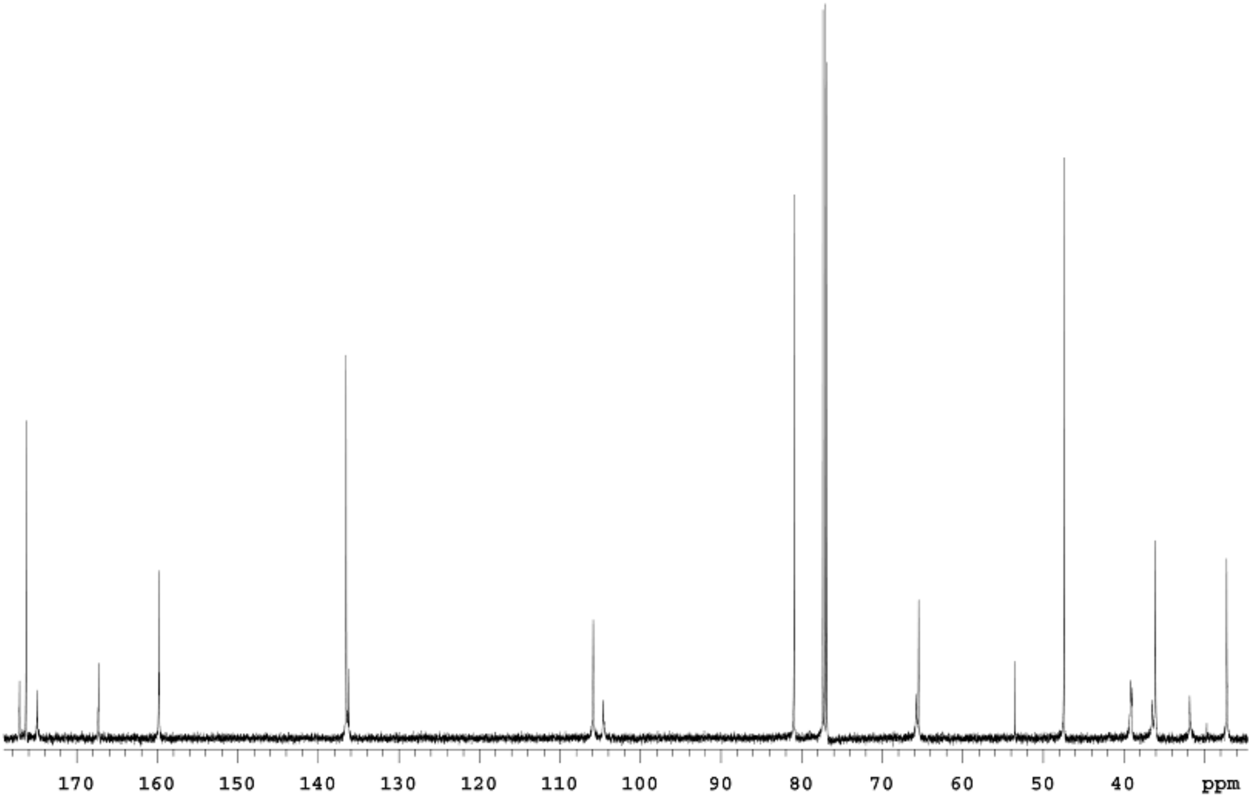


Figure S59. ^{13}C NMR spectrum (125 MHz) of G3$_F$ (A-R-B$_2$/A-R-B$_2$/A-R-B$_2$) dendrimer.

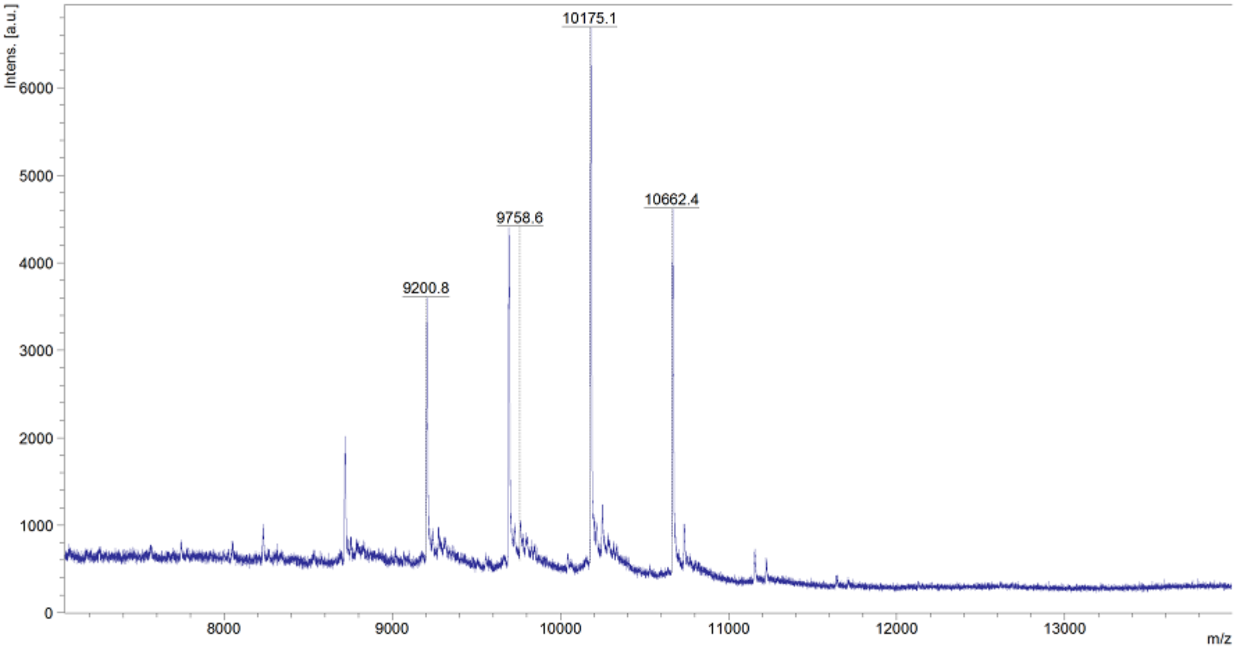


Figure S60. MALDI MS of G3$_F$ results in the observation of the thermally deprotected G3$_M$ dendrimer. Minor peaks with approximate *m/z* spacing of 487 are observed.

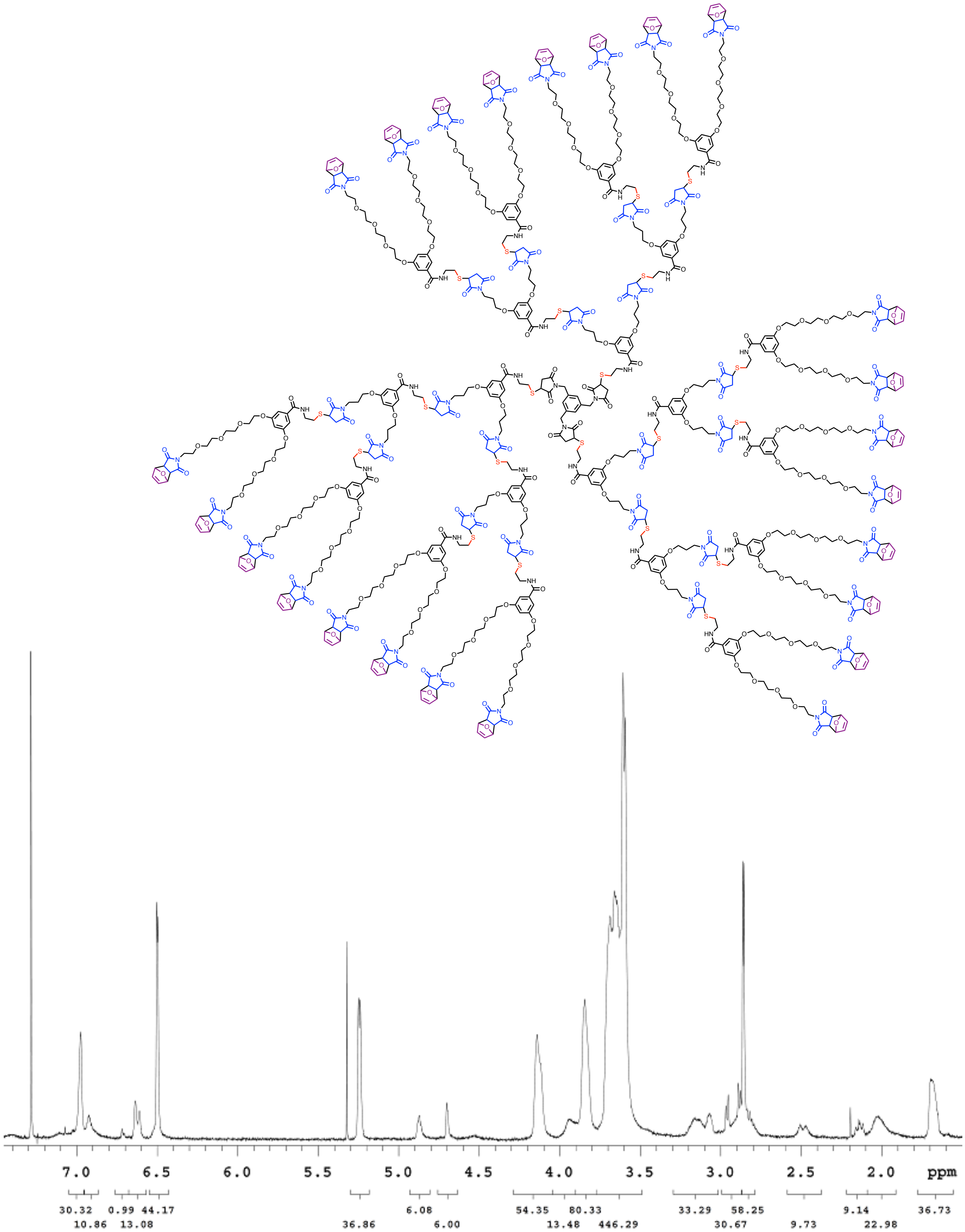


Figure S61. ^{1}H NMR spectrum (500 MHz) of G3$_F$ dendrimer **5**.

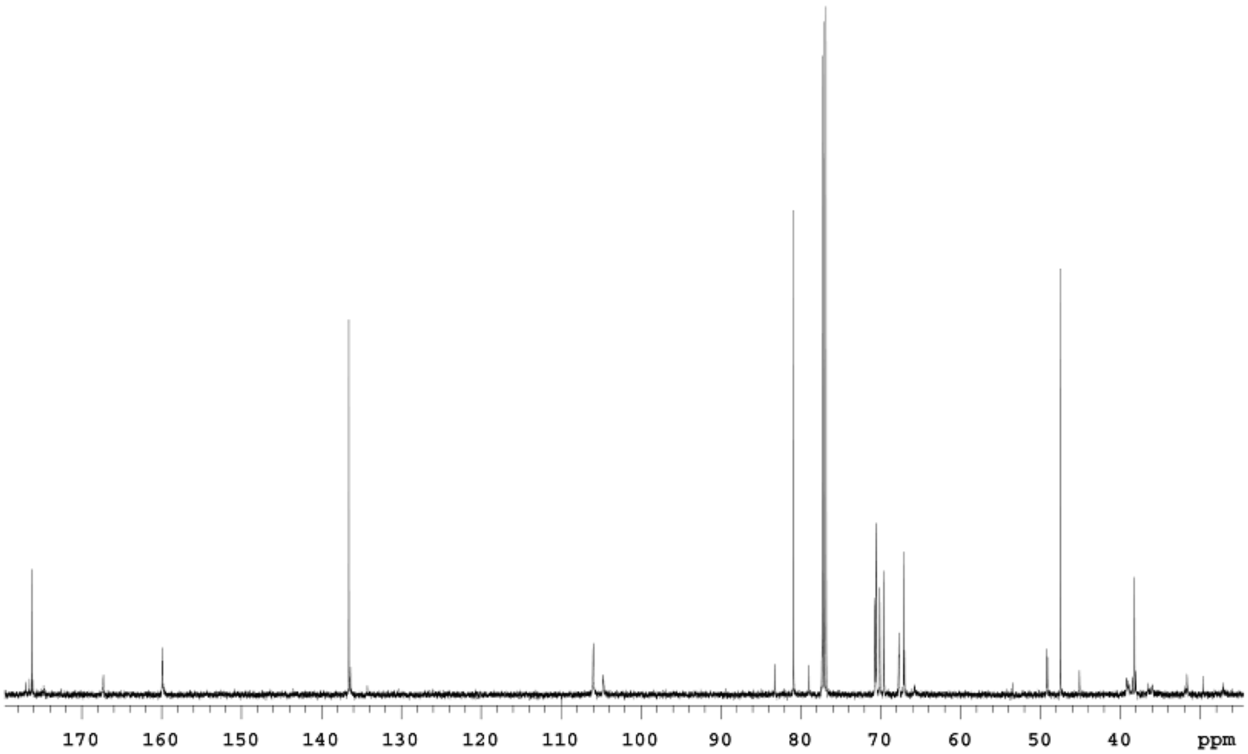


Figure S62. ^{13}C NMR spectrum (125 MHz) of G3$_F$ (A-R-B$_2$/A-R-B$_2$/A-R′-B$_2$) dendrimer.

V. Supporting References

1. Bruns, C. J.; Basu, S.; Stoddart, J. F. *Tetrahedron Lett*. **2010**, *51*, 983–986.

2. Zhu, J.; Ganton, M. D.; Kerr, M. A.; Workentin, M. S. *J. Am. Chem. Soc*. **2007**, *129*, 4904-4905.

3. Gobbo, P.; Gunawardene, P.; Luo, W.; Workentin, M. S. Synthesis of a Toolbox of Clickable Rhodamine B Derivatives. *Synlett*. **2015**, *26*, 1169-1174.

4. Emrick, T. S. PEG-Substituted Pyridine Ligand and Related Water-Soluble Catalysts. U.S. Patent 7,960,555 B2, June 14, 2011.

5. Gobbo, P.; Workentin, M. S. *Langmuir*. **2012**, *28*, 12357–12363.

6. Chakraborty, T. K.; Reddy, G. V. *J. Org. Chem*. B, *57*, 5462–5469.

7. van Nunen, J. L. M.; Folmer, B. F. B.; Nolte, R. J. M. *J. Am. Chem. Soc*. **1997**, *119*, 283–291.

8. Hawker, C. J.; Lee, R.; Fréchet, J. M. J. *J. Am. Chem. Soc*. **1991**, *113*, 4588-4595.

9. Kalle, A. G. Diazotype Process and Materials. GB 1152920 A, May 21, 1969.

10. Siva, A.; Murugan, E. *Synthesis*. **2005**, *17*, 2927-2933.

11. Farha, O. K.; Julius, R. L.; Hawthorne, M. F. *Tetrahedron Letters*. 2006, *47*, 2619–2622.

12. Zhang, B.; Digby, Z. A.; Flum, J. A.; Chakma, P.; Saul, J. M.; Sparks, J. L.; Konkolewicz, D. *Macromolecules* **2016**, *49*, 6871-6878.

13. Ahang, B.; Chakma, P.; Shulman, M. P.; Ke, J.; Digby, Z. A.; Konkolewicz, D. *Org. Biomol. Chem*. **2018**, *16*, 2725-2734.