Supporting Information for:

Accelerated Synthesis of Dendrimers by Thermal Azide-Alkyne Cycloaddition with Internal Alkynes

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1. Materials

All chemicals were purchased from Sigma-Aldrich or Acros Organics and were used without further purification. All solvents were HPLC grade, purchased from Scharlab and Fisher Chemical and used as received. DMSO was dried under 4Å molecular sieves. NaN₃ was dried under vacuum at 60 °C for 12 h in the presence of P₂O₅. H₂O was Milli-Q grade obtained using a Millipore water purification system. Thin-layer chromatography (TLC) was done on silica aluminum-backed plates. Merrifield’s peptide resin (200-400 mesh, 1.04×10⁻³ equiv Cl per g) was purchased from Sigma-Aldrich.

2. Instrumentation

**Microwave Synthesis.** Microwave (MW) assisted reactions were performed in a Discover SP microwave synthesizer (CEM, USA), using a fixed power method with simultaneous external cooling with compressed air. The reaction temperature was controlled with the infrared (IR) sensor integrated in the apparatus that had previously been calibrated with an internal probe provided with a fiber-optic sensor (Thermowell Kit-541165, CEM, USA).

**Column Chromatography.** Automated column chromatography was performed on a MPLC Teledyne ISCO CombiFlash RF 200 psi. Samples were adsorbed onto silica 40-63 µm from VWR Chemicals and loaded into solid cartridges. When required, RediSep Rf columns refilled with silica 40-63 µm from VWR Chemicals were used.
**Ultrafiltration.** Purifications by ultrafiltration were performed on Millipore Amicon stirred cells fitted with an Amicon YM5 membrane and applying a 5 psi N₂ pressure.

**NMR Spectroscopy.** NMR spectra were recorded on Varian Inova 400 MHz, Varian Mercury 300 MHz, or Bruker DPX 250 MHz spectrometers. Chemical shifts are reported in ppm (δ units) downfield from internal tetramethylsilane (TMS, in CDCl₃) or residual solvent peak.

**Infrared Spectroscopy.** FT-IR spectra were recorded on a Bruker IFS-66v or a Perkin-Elmer Spectrum Two spectrometer.

**Mass Spectrometry.** Mass spectra were collected on a Thermo Finnigan TRACE-DSQ quadrupole/electronic impact spectrometer (EI-MS). MALDI-TOF mass spectra were performed on a 4800 MALDI-TOF/TOF analyzer (Applied Biosystems, Foster City, CA, USA). The dried-droplet method was used to deposit 1 μL of a dendrimer and matrix mixture onto a 384 Opti-TOF MALDI plate (Applied Biosystems, Foster City, CA, USA). Dendrimer samples were lyophilized and dissolved (8-10 mg/mL) in 500 μL of MeOH (Pr[G1]-Br) or CHCl₃ (Pr[G2]-Br, Pr[G3]-Br, Pr[G4]-Br, Pr[G5]-Br, Het[G1]-Br, Het[G2]-Cl, and Het[G3]-Ar).

In the case of Pr[G1]-Br and Pr[G2]-Br, 5 μL of dendrimer solutions were mixed with 20 μL of a dithranol solution (10 mg/mL in CHCl₃). For Het[G1]-Br and Het[G2]-Cl, 1 μL of dendrimer solution was mixed with 20 μL of 2,5-dihydroxybenzoic acid (DHB) solution (10 mg/mL in MeOH). MS spectra were acquired in reflectron positive-ion mode with a ND:YAG, 355 nm wavelength laser, and averaging 100 laser shots. The mass of the dendrimers was determined by reference to a peptide Standard II (Bruker-Daltonics).
composed of angiotensin II \((m/z = 1046.5418)\), angiotensin I \((m/z = 1296.6848)\), substance P \((m/z = 1347.7354)\), bombesin \((m/z = 1619.8223)\), ACTH clip 1-17 \((m/z = 2093.0862)\), ACTH clip 18-39 \((m/z = 2465.1983)\) and somatostatin 28 \((m/z = 3147.4710)\) as internal standards.

For \(\text{Pr}[G3]-\text{Br}\) and \(\text{Pr}[G4]-\text{Br}\), 5 μL of dendrimer solution was mixed with 20 μL of 2-(4-hydroxyphenylazo)benzoic acid (HABA) solution (0.05 M in dioxane). For \(\text{Pr}[G5]-\text{Br}\), 1 μL of dendrimer solution was mixed with 40 μL of HABA solution (0.05 M in dioxane). For \(\text{Het}[G3]-\text{Ar}\), 1 μL of dendrimer solution was mixed with 20 μL of HABA solution (0.05 M in dioxane). MS spectra were acquired in linear mode (20 kV source) with a Nd:YAG, 355 nm laser and averaging 1000 laser shots. The mass of these dendrimers was determined by reference to insulin \((m/z = 5733)\), ribonuclease A \((m/z = 13682)\) and lysozyme \((m/z = 14305)\) (Sigma-Aldrich, St. Louis, MO) as internal standards.

**Elemental Analysis.** Samples were analyzed in a Thermo Finnigan Flash 1112 elemental analyzer.

**Gel Permeation Chromatography (GPC).** GPC experiments were performed on an Agilent 1100 series separation module using a PSS SDV pre-column (5 mm, 8 x 50 mm), a PSS SDV Linear S column (5 mm, 8 x 300 mm), and a PSS SDV Lux Linear M column (5 mm, 8 x 300 mm) connected to an Agilent 1100 series ultraviolet detector at 254 nm. THF was used as eluent at 1 mL/min. Samples at 1 mg/mL were filtered through 0.45 μm PTFE filters before injection.
**Dynamic Light Scattering (DLS).** DLS measurements were carried out on a Malvern Nano ZS (Malvern Instruments, U.K.) operating at 633 nm with a 173° scattering angle at 25 °C. Dendrimer hydrodynamic diameters were measured in THF at 1 mg/mL. Mean diameters were obtained from the volume particle size distribution provided by Malvern Zetasizer Software.
3. Synthesis and Characterization of New Compounds

1,3,5-Tris(3-bromopropoxy)benzene (Pr[G0]-Br). Phloroglucinol (1.3 g, 10.4 mmol) and dry K2CO3 (5.7 g, 41.6 mmol) were added to a solution of 1,3-dibromopropane (12.7 mL, 0.12 mol) in dry DMSO (10 mL). The resulting mixture was stirred at rt under Ar for 24 h. Then, H2O (50 mL) was added and the mixture was lyophilized to remove DMSO. The crude product was distributed between EtOAc (50 mL) and H2O (50 mL). The aqueous phase was extracted with EtOAc (50 mL), and the combined organic phase was washed with H2O (4 x 50 mL), NaHCO3 (50 mL) and brine (30 mL). The organic layer was dried (MgSO4) and concentrated to give a crude product that was purified by automated MPLC (gradient from heptane to 5:95 acetone:heptane, 25 min) to yield Pr[G0]-Br as a white solid (2.1 g, 42%; unoptimized). 1H NMR (400 MHz, CDCl3, TMS) δ: 6.10 (s, 3H), 4.07 (t, \( J = 5.8 \) Hz, 6H), 3.59 (t, \( J = 6.4 \) Hz, 6H), 2.30 (quint, \( J = 6.1 \) Hz, 6H). 13C NMR (100 MHz, CDCl3) δ: 160.5, 94.2, 65.4, 32.3, 29.9. Elem. Anal. Calcd. for C15H21Br3O3: C, 36.84; H, 4.33. Found: C, 37.18; H, 4.44. IR (neat, CsI window): 2932, 1604, 1170, 556 cm\(^{-1}\).

1,3,5-Tris(3-azidopropoxy)benzene (Pr[G0]-N3). In a microwave tube fitted with a magnetic bar, NaN3 (356 mg, 5.48 mmol) was added to a solution of 1,3,5-tris(3-bromopropoxy)benzene (Pr[G0]-Br) (446 mg, 0.91 mmol) in 20:80 acetone:H₂O (3.4 mL). The mixture was stirred for 15 min at 125 °C under microwave irradiation (200 W) and then was distributed between EtOAc (30 mL) and H₂O (30 mL). The aqueous phase was extracted with EtOAc (30 mL), and the combined organic phase was washed with H₂O (3 x 30 mL) and brine (30 mL). The organic layer was dried (MgSO4) and concentrated to yield Pr[G0]-N3 as a pale yellow oil (338 mg, 99%). 1H NMR (400 MHz, CDCl3, TMS) δ: 6.08 (s, 3H), 4.01 (t, \( J = 5.9 \) Hz, 6H), 3.50 (t, \( J = 6.6 \) Hz, 6H),
2.03 (quint, $J = 6.2$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 160.5, 94.1, 64.6, 48.2, 28.7. Elem. Anal. Calcd. for C$_{15}$H$_{21}$N$_9$O$_3$: C, 47.99; H, 5.64; N, 33.33. Found: C, 48.16; H, 5.77; N, 33.63. IR (neat, CsI window): 2937, 2098, 1601, 1164 cm$^{-1}$. EI-HRMS Calcd. for C$_{15}$H$_{22}$N$_9$O$_3$+: 376.1846; Found [M+H]$^+$: 376.1857.

**Bis(3-bromopropyl) but-2-ynedioate (1).** Acetylenedicarboxylic acid (1.6 g, 14.0 mmol), 3-bromo-1-propanol (5.8 g, 42.1 mmol), and $p$-TsOH (227 mg, 1.2 mmol) were added to a round-bottomed flask fitted with a Dean-Stark and a reflux condenser. Toluene (24 mL) was added and the reaction mixture was refluxed for 2 h. Then, the reaction was allowed to reach rt and was distributed between EtOAc (30 mL) and H$_2$O (30 mL). The aqueous phase was extracted with EtOAc (30 mL), and the combined organic phase was washed with NaHCO$_3$ (2 x 30 mL), H$_2$O (3 x 30 mL), and brine (30 mL). The organic layer was dried (MgSO$_4$) and concentrated. The crude product was purified by automated MPLC (gradient from heptane to 85:15 heptane:EtOAc, silica refilled column, crude product adsorbed onto silica and loaded into a solid cartridge, 30 min) to yield 1 as a colourless oil (4.5 g, 90%). $^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 4.40 (t, $J = 6.0$ Hz, 4H), 3.48 (t, $J = 6.4$ Hz, 4H), 2.24 (quint, $J = 6.2$ Hz, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 151.4, 74.7, 64.6, 31.1, 28.7. Elem. Anal. Calcd. for C$_{10}$H$_{12}$Br$_2$O$_4$: C, 33.74; H, 3.40. Found: C, 33.90; H, 3.40. IR (neat, CsI window): 2969, 1725, 1250, 563 cm$^{-1}$.

**Pr[G1]-Br.** Pr[G0]-N$_3$ (70 mg, 0.19 mmol) and 1 (398 mg, 1.12 mmol) were dissolved in EtOAc (280 µL) in a microwave tube. The mixture was stirred at 70 °C under microwave irradiation (100 W, air flow 14 psi) for 40 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to EtOAc, silica refilled
column, crude product adsorbed onto silica and loaded into a solid cartridge, 12 min) to afford \( ^{\text{Pr}}[\text{G1}]\)-Br as a pale yellow oil (267 mg, 99% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\): 5.98 (s, 3H), 4.84 (t, \(J = 6.8\) Hz, 6H), 4.52 (t, \(J = 6.1\) Hz, 6H), 4.47 (t, \(J = 6.0\) Hz, 6H), 3.95 (t, \(J = 5.6\) Hz, 6H), 3.54 (t, \(J = 6.4\) Hz, 6H), 3.52 (t, \(J = 6.4\) Hz, 6H), 2.41 (quint, \(J = 6.2\) Hz, 6H), 2.32 (quint, \(J = 6.3\) Hz, 6H), 2.26 (quint, \(J = 6.2\) Hz, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 160.2, 160.0, 158.2, 139.9, 129.9, 94.2, 77.4, 77.1, 76.9, 64.6, 64.3, 63.6, 47.8, 31.5, 31.1, 29.8, 29.3, 29.2. Elem. Anal. Calcd. for C\(_{45}\)H\(_{57}\)Br\(_6\)N\(_9\)O\(_{15}\): C, 37.44; H, 3.98; N, 8.73. Found: C, 37.82; H, 4.18; N, 8.89. IR (neat, CsI window): 2965, 1735, 1166, 566 cm\(^{-1}\). MALDI-TOF MS (dithranol, reflected mode, \(m/z\)): 1444.03. Calcd. for [M+H]+, C\(_{45}\)H\(_{58}\)Br\(_6\)N\(_9\)O\(_{15}\): 1443.91.

\(^{\text{Pr}}[\text{G1}]-\text{N}_3\). In a microwave tube fitted with a magnetic bar, NaN\(_3\) (63 mg, 0.96 mmol) was added to a solution of \(^{\text{Pr}}[\text{G1}]-\text{Br} \) (116 mg, 80.4 \(\mu\)mol) in dry DMSO (603 \(\mu\)L). The mixture was stirred for 2 min at 100 °C under microwave irradiation (25 W) and then was distributed between EtOAc (15 mL) and H\(_2\)O (15 mL). The aqueous phase was extracted with EtOAc (15 mL), and the combined organic phase was washed with H\(_2\)O (3 x 15 mL) and brine (15 mL). The organic layer was dried (MgSO\(_4\)) and concentrated to give \(^{\text{Pr}}[\text{G1}]-\text{N}_3\) as a pale yellow oil (97 mg, 99%). \(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\): 5.98 (s, 3H), 4.83 (t, \(J = 6.8\) Hz, 6H), 4.46 (t, \(J = 6.2\) Hz, 6H), 4.40 (t, \(J = 6.1\) Hz, 6H), 3.94 (t, \(J = 5.6\) Hz, 6H), 3.49 (t, \(J = 6.6\) Hz, 6H), 3.46 (t, \(J = 6.6\) Hz, 6H), 2.39 (quint, \(J = 6.2\) Hz, 6H), 2.06 (quint, \(J = 6.4\) Hz, 6H), 1.97 (quint, \(J = 6.3\) Hz, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 160.2, 159.9, 158.3, 139.9, 130.0, 94.1, 64.2, 63.7, 62.7, 47.9, 47.7, 29.7, 28.0, 27.8. IR (neat, ATR): 2922, 2094, 1729, 1162 cm\(^{-1}\).
**Pr[G2]-Br.** Pr[G1]-N3 (89 mg, 73.2 μmol) and 1 (469 mg, 1.32 mmol) were dissolved in EtOAc (220 μL) in a microwave tube. The mixture was stirred at 60 ºC under microwave irradiation (100 W, air flow 14 psi) for 40 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to EtOAc, crude product adsorbed onto silica and loaded into a solid cartridge, no column, 12 min) to afford Pr[G2]-Br as a pale yellow oil (234 mg, 95%). 1H NMR (400 MHz, CDCl3, TMS) δ: 6.00 (s, 3H), 4.87 - 4.76 (m, 18H), 4.53 - 4.49 (m, 36H), 3.97 (t, J = 5.5 Hz, 6H), 3.56 - 3.52 (m, 24H), 2.47 - 2.25 (m, 42H). 13C NMR (100 MHz, CDCl3) δ: 160.2, 159.9, 159.8, 158.2, 158.0, 140.0, 139.7, 129.7, 129.7, 94.21, 64.6, 64.5, 64.4, 63.6, 63.5, 63.3, 62.3, 47.9, 47.7, 47.5, 31.5, 31.4, 31.1, 31.0, 29.3, 29.2, 29.0, 28.7. Elem. Anal. Calcd. for C105H129Br12N27O39: C, 37.62; H, 3.88; N, 11.28. Found: C, 37.85; H, 4.09; N, 11.42. IR (neat, ATR): 2974, 1732, 1203, 574 cm⁻¹. MALDI-TOF MS (dithranol, reflected mode, m/z): 3352.22. Calcd. for [M+H]+, C105H130Br12N27O39: 3352.91.

**Pr[G2]-N3.** In a microwave tube fitted with a magnetic bar, NaN3 (79 mg, 1.22 mmol) was added to a solution of Pr[G2]-Br (170 mg, 50.7 μmol) in dry DMSO (760 μL). The mixture was stirred for 2 min at 100 ºC under microwave irradiation (25 W) and then was distributed between EtOAc (15 mL) and H2O (15 mL). The aqueous phase was extracted with EtOAc (15 mL), and the combined organic phase was washed with H2O (3 x 15 mL) and brine (15 mL). The organic layer was dried (MgSO4) and concentrated to give Pr[G2]-N3 as a pale yellow oil (146 mg, 99%). 1H NMR (400 MHz, CDCl3, TMS) δ: 6.00 (s, 3H), 4.86 - 4.76 (m, 18H), 4.48 - 4.38 (m, 36H), 3.97 (t, J = 5.6 Hz, 6H), 3.51 - 3.46 (m, 24H), 2.47 - 2.37 (m, 18H), 2.08 - 1.96 (m, 24H). 13C NMR (100 MHz, CDCl3) δ: 160.3, 159.9, 158.2, 158.1, 140.0, 139.8, 129.9, 94.3, 64.4, 63.8, 63.4,
62.8, 62.7, 62.4, 48.0, 47.8, 47.6, 29.8, 29.1, 28.8, 28.1, 27.9. IR (neat, ATR): 2918, 2096, 1729, 1198 cm⁻¹.

**Pr[G3]-Br.** Pr[G2]-N₃ (120 mg, 41.4 µmol) and 1 (354 mg, 0.99 mmol) were dissolved in EtOAc (248 µL) in a microwave tube. The mixture was stirred at 60 °C under microwave irradiation (50 W, air flow 14 psi) for 40 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to EtOAc, crude product adsorbed onto silica and loaded into a solid cartridge, no column, 12 min) to afford Pr[G3]-Br as a pale yellow oil (282 mg, 95%). ¹H NMR (400 MHz, CDCl₃, TMS) δ: 6.00 (s, 3H), 4.84 - 4.78 (m, 42H), 4.52 - 4.42 (m, 84H), 3.98 (bs, 6H), 3.56 - 3.48 (m, 48H), 2.47 - 2.24 (m, 90H). ¹³C NMR (100 MHz, CDCl₃) δ: 159.9, 159.8, 159.7, 158.2, 158.1, 158.0, 140.0, 139.7, 129.7, 64.6, 63.6, 63.4, 62.4, 47.7, 47.6, 31.5, 31.1, 29.8, 29.4, 29.0, 28.7. Elem. Anal. Calcd. for C₂₂₅H₂₇₃Br₂₄N₆₃O₈₇: C, 37.69; H, 3.84; N, 12.31. Found: C, 37.67; H, 3.84; N, 11.99. IR (neat, ATR): 2967, 1735, 1203, 565 cm⁻¹. MALDI-TOF MS (HABA, linear mode, m/z): 7225.55. Calcd. for [M+K]⁺, C₂₂₅H₂₇₃Br₂₄N₆₃O₈₇K: 7207.83.

**Pr[G3]-N₃.** In a microwave tube fitted with a magnetic bar, NaN₃ (65 mg, 1.00 mmol) was added to a solution of Pr[G3]-Br (150 mg, 20.9 µmol) in dry DMSO (628 µL). The mixture was stirred for 2 min at 100 °C under microwave irradiation (25 W) and then was distributed between EtOAc (15 mL) and H₂O (15 mL). The aqueous phase was extracted with EtOAc (15 mL), and the combined organic phase was washed with H₂O (3 x 15 mL) and brine (15 mL). The organic layer was dried (MgSO₄) and concentrated to give Pr[G3]-N₃ as a pale yellow oil (126 mg, 96%). ¹H NMR (400 MHz, CDCl₃, TMS) δ: 6.01 (s, 3H), 4.82 - 4.77 (m, 42H), 4.47 - 4.41 (m, 84H), 3.98 (bs, 6H), 3.50 -
3.46 (m, 48H), 2.48 - 2.41 (m, 42H), 2.06 - 2.00 (m, 48H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 160.2, 159.8, 159.7, 159.6, 158.2, 158.1, 158.0, 157.9, 140.0, 139.9, 139.7, 129.8, 129.7, 129.6, 94.1, 64.4, 63.8, 63.4, 62.7, 62.6, 62.3, 47.9, 47.7, 47.6, 47.5, 29.7, 29.0, 28.7, 28.6, 28.0, 27.8, 27.7. IR (neat, ATR): 2922, 2099, 1729, 1195 cm$^{-1}$.

$^{p}$[G4]-Br. $^{p}$[G3]-N$_3$ (147 mg, 23.5 μmol) and 1 (401 mg, 1.12 mmol) were dissolved in EtOAc (282 μL) in a microwave tube. The mixture was stirred at 60 ºC under microwave irradiation (50 W, air flow 14 psi) for 40 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to EtOAc, crude product adsorbed onto silica and loaded into a solid cartridge, no column, 12 min) to afford $^{p}$[G4]-Br as a pale yellow oil (315 mg, 91%). $^1$H NMR (400 MHz, CDCl$_3$, TMS) δ: 6.04 (bs, 3H), 3.81 - 4.79 (m, 90H), 4.51 - 4.43 (m, 180H), 4.01 (bs, 6H), 3.55 - 3.51 (m, 96H), 2.45 - 2.23 (m, 186H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 160.0, 159.9, 159.8, 158.3, 158.1, 140.2, 140.1, 139.9, 129.8, 94.4, 64.7, 63.7, 63.6, 62.5, 47.8, 47.7, 31.6, 31.3, 31.2, 29.5, 29.4, 29.1, 28.5, 28.8. Elem. Anal. Calcd. for C$_{464}$H$_{559}$Br$_{48}$N$_{135}$O$_{183}$: C, 37.68; H, 3.81; N, 12.78. Found: C, 38.08; H, 4.09; N, 12.73. IR (neat, ATR): 2972, 1731, 1202, 581 cm$^{-1}$. MALDI-TOF MS (HABA, linear mode, m/z): 14803.37. Calcd. for [M+H]$^{+}$, C$_{465}$H$_{562}$Br$_{48}$N$_{135}$O$_{183}$: 14800.29.

$^{p}$[G4]-N$_3$. In a microwave tube fitted with a magnetic bar, NaN$_3$ (63 mg, 0.97 mmol) was added to a solution of $^{p}$[G4]-Br (150 mg, 10.1 μmol) in dry DMSO (608 μL). The mixture was stirred for 2 min at 100 ºC under microwave irradiation (25 W) and then was distributed between EtOAc (15 mL) and H$_2$O (15 mL). The aqueous phase was extracted with EtOAc (15 mL), and the combined organic phase was washed with H$_2$O (3 x 15 mL) and brine (15 mL). The organic layer was dried (MgSO$_4$) and concentrated.
to give $^{13}$[G4]-N$_3$ as a pale yellow oil (127 mg, 97%). $^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 6.04 (bs, 3H), 4.80 - 4.79 (m, 90H), 4.47 - 4.42 (m, 180H), 4.00 (bs, 6H), 3.49 - 3.45 (m, 96H), 2.44 - 2.42 (m, 90H), 2.05 - 1.97 (m, 96H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 160.2, 159.8, 159.7, 158.1, 157.9, 139.9, 139.7, 129.7, 129.6, 94.2, 63.7, 63.4, 62.6, 62.3, 47.8, 47.7, 47.6, 47.5, 29.7, 29.5, 29.1, 28.9, 28.6, 28.5, 27.9, 27.7. IR (neat, ATR): 2922, 2099, 1729, 1204 cm$^{-1}$.

$^{13}$[G5]-Br. $^{13}$[G4]-N$_3$ (100 mg, 7.7 $\mu$mol) and 1 (264 mg, 0.74 mmol) were dissolved in EtOAc (185 $\mu$L) in a microwave tube. The mixture was stirred at 60 °C under microwave irradiation (50 W, air flow 14 psi) for 40 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to EtOAc, crude product adsorbed onto silica and loaded into a solid cartridge, no column, 12 min) to afford $^{13}$[G5]-Br as a pale yellow oil (211 mg, 91%). $^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 6.09 (bs, 3H), 4.80 - 4.78 (m, 186H), 4.50 - 4.47 (m, 372H), 4.04 (bs, 6H), 3.53 - 3.51 (m, 192H), 2.43 - 2.24 (m, 378H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 159.9, 159.8, 159.7, 158.2, 158.0, 140.0, 139.8, 139.7, 129.7, 94.3, 69.5, 64.6, 63.6, 62.4, 53.8, 47.7, 47.6, 31.8, 31.5, 31.2, 31.1, 29.4, 29.3, 29.0, 28.7. Elem. Anal. Calcd. for C$_{944}$H$_{1139}$Br$_{96}$N$_{279}$O$_{375}$: C, 37.70; H, 3.81; N, 13.00. Found: C, 37.93; H, 4.05; N, 13.17. IR (neat, ATR): 2971, 1727, 1198, 572 cm$^{-1}$. MALDI-TOF MS (HABA, linear mode, m/z): 30011.72. Calcd. for [M+H]$^+$, C$_{944}$H$_{1139}$Br$_{96}$N$_{279}$O$_{375}$: 30058.50.

$^{13}$[G5]-N$_3$. In a microwave tube fitted with a magnetic bar, NaN$_3$ (73 mg, 1.12 mmol) was added to a solution of $^{13}$[G5]-Br (176 mg, 5.8 $\mu$mol) in dry DMSO (703 $\mu$L). The mixture was stirred for 2 min at 100 °C under microwave irradiation (25 W) and then was distributed between EtOAc (15 mL) and H$_2$O (15 mL). The aqueous phase was
extracted with EtOAc (15 mL), and the combined organic phase was washed with H₂O (3 x 15 mL) and brine (15 mL). The organic layer was dried (MgSO₄) and concentrated to give Pr[G5]-N₃ as a pale yellow oil (150 mg, 97%). ¹H NMR (400 MHz, CDCl₃, TMS) δ: 6.10 (bs, 3H), 4.78 (bs, 186H), 4.43 - 4.41 (m, 372H), 4.05 (bs, 6H), 3.47 - 3.46 (m, 192H), 2.42 (bs, 186H), 2.04 - 1.97 (m, 192H). ¹³C NMR (100 MHz, CDCl₃) δ: 160.0, 159.9, 159.8, 158.3, 158.1, 140.1, 140.0, 139.9, 139.8, 129.9, 129.8, 94.31, 63.9, 63.7, 63.6, 62.8, 62.7, 62.4, 48.0, 47.8, 47.7, 47.6. IR (neat, ATR): 2921, 2098, 1729, 1202 cm⁻¹.

**Bis(2-(2-(2-chloroethoxy)ethoxy)ethyl) but-2-ynedioate (2).** Acetylenedicarboxylic acid (2.0 g, 17.5 mmol), 2-(2-(2-chloroethoxy)ethoxy) ethanol (6.5 g, 38.6 mmol), and conc. H₂SO₄ (80 μL, 1.5 mmol) were added to a round-bottomed flask fitted with a Dean-Stark and a reflux condenser. Toluene (30 mL) was added and the reaction mixture was refluxed for 3 h. Then, the reaction was allowed to reach rt and was distributed between Et₂O (150 mL) and sat NaHCO₃ (75 mL). The organic phase was washed with H₂O (4 x 75 mL), dried (MgSO₄) and concentrated to yield 2 as a colourless oil (6.7 g, 91%). ¹H NMR (400 MHz, CDCl₃, TMS) δ: 4.40 – 4.36 (m, 4H), 3.79 – 3.72 (m, 8H), 3.70 – 3.66 (m, 8H), 3.64 (t, J = 5.8 Hz, 4H). ¹³C NMR (100 MHz, CDCl₃) δ: 151.7, 74.9, 71.4, 70.7, 70.6, 68.5, 65.8, 42.7. Elem. Anal. Calcd. for C₁₆H₂₄Cl₂O₈: C, 46.28; H, 5.83. Found: C, 46.05; H, 5.79. IR (neat, CsI window): 2959, 2873, 1725, 1257 cm⁻¹.

Extraction of the combined aqueous layer with EtOAc (3 x 100 mL) allowed, after drying (MgSO₄) and concentration, to recover 65% of the excess of 2-(2-(2-chloroethoxy)ethoxy) ethanol added to the reaction mixture.
**TEG[G1]-Cl.** TEG[G0]-N₃² (110 mg, 0.185 mmol) and 2 (460 mg, 1.11 mmol) were dissolved in EtOAc (277 µL) in a microwave tube. The mixture was stirred at 60 °C under microwave irradiation (20 W, air flow 14 psi) for 30 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to acetone, silica refilled column, crude product adsorbed onto silica and loaded into a solid cartridge, 12 min) to afford TEG[G1]-Cl as a pale yellow oil (332 mg, 99%). ¹H NMR (400 MHz, CDCl₃, TMS) δ: 6.07 (s, 3H), 4.81 (t, J = 5.2 Hz, 6H), 4.53 – 4.47 (m, 12H), 4.04 – 3.99 (m, 6H), 3.88 - 3.51 (m, 84H). ¹³C NMR (100 MHz, CDCl₃) δ: 160.4, 159.9, 158.2, 139.5, 131.6, 94.2, 71.4, 71.3, 70.9, 70.7, 70.6, 70.5, 70.3, 69.5, 69.3, 68.7, 68.4, 67.3, 65.4, 64.6, 50.1, 42.8. Elem. Anal. Calcd. for C₇₂H₁₁₁Cl₆N₉O₈: C, 46.91; H, 6.07; N, 6.84. Found: C, 46.81; H, 6.12; N, 6.84. IR (neat, CsI window): 2874, 1733, 1120 cm⁻¹.

**TEG[G1]-N₃.** In a microwave tube fitted with a magnetic bar, NaN₃ (41 mg, 0.63 mmol) and 15-crown-5 (6.7 mg, 31.5 µmol) were added to a solution of TEG[G1]-Cl (97 mg, 52.6 µmol) in dry DMSO (158 µL). The mixture was stirred for 25 min at 100 °C under microwave irradiation (20 W, air flow 20 psi) and then was distributed between EtOAc (15 mL) and H₂O (15 mL). The aqueous phase was extracted with EtOAc (3 x 15 mL), and the combined organic phase was washed with brine (5 x 15 mL). The organic layer was dried (MgSO₄) and concentrated to give TEG[G1]-N₃ as a pale yellow oil (98 mg, 99%). ¹H NMR (250 MHz, CDCl₃, TMS) δ: 6.08 (s, 3H), 4.81 (t, J = 5.1 Hz, 6H), 4.52 (t, J = 5.0 Hz, 6H), 4.50 (t, J = 5.0 Hz, 6H), 4.07-3.99 (m, 6H), 3.86 - 3.56 (m, 72 H), 3.42 - 3.30 (m, 12H). IR (neat, ATR): 2872, 2103, 1729, 1111 cm⁻¹.

**TEG[G2]-Cl.** TEG[G1]-N₃ (226 mg, 120 mmol) and 2 (598 mg, 1.44 mmol) were dissolved in EtOAc (360 µL) in a microwave tube. The mixture was stirred at 60 °C
under microwave irradiation (20 W, air flow 14 psi) for 30 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to acetone, silica refilled column, crude product adsorbed onto silica and loaded into a solid cartridge, 12 min) to afford $\text{TEG}[G2]-\text{Cl}$ as a pale yellow oil (332 mg, 99%). $^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 6.07 (s, 3H), 4.82 - 4.78 (m, 18H), 4.53 - 4.44 (m, 36H), 4.04 - 3.99 (m, 6H), 3.86 - 3.51 (m, 192H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 160.5, 159.9, 158.2, 139.7, 139.5, 131.6, 131.3, 94.3, 71.3, 70.6, 70.5, 70.4, 70.2, 69.6, 69.4, 69.3, 69.2, 68.8, 68.6, 68.5, 68.4, 67.4, 65.5, 65.4, 64.7, 64.6, 50.1, 42.8. Elem. Anal. Calcd. for C$_{168}$H$_{255}$Cl$_{12}$N$_{27}$O$_{81}$: C, 46.13; H, 5.88; N, 8.65. Found: C, 46.03; H, 5.74; N, 8.45. IR (neat, CsI window): 2952, 2874, 1734, 1120 cm$^{-1}$.

$\text{TEG}[G2]-\text{N}_3$. In a microwave tube fitted with a magnetic bar, NaN$_3$ (45 mg, 0.69 mmol) and 15-crown-5 (7.6 mg, 33.6 µmol) were added to a solution of $\text{TEG}[G2]-\text{Cl}$ (126 mg, 28.8 µmol) in dry DMSO (691 µL). The mixture was stirred for 25 min at 100 ºC under microwave irradiation (20 W, air flow 20 psi) and then was distributed between EtOAc (15 mL) and H$_2$O (15 mL). The aqueous phase was extracted with EtOAc (3 x 15 mL), and the combined organic phase was washed with brine (5 x 15 mL). The organic layer was dried (MgSO$_4$) and concentrated to give $\text{TEG}[G2]-\text{N}_3$ as a pale yellow oil (119 mg, 93%). $^1$H NMR (300 MHz, CDCl$_3$, TMS) $\delta$: 6.07 (s, 3H), 4.82-4.75 (m, 18H), 4.54 - 4.40 (m, 36H), 4.06 - 3.98 (m, 6H), 3.90 - 3.48 (m, 168H), 3.42 - 3.31 (m, 24H). IR (neat, ATR): 2876, 2103, 1730, 1115 cm$^{-1}$.

$\text{TEG}[G3]-\text{Cl}$. $\text{TEG}[G2]-\text{N}_3$ (133 mg, 29.9 µmol) and 2 (297 mg, 0.72 mmol) were dissolved in EtOAc (179 µL) in a microwave tube. The mixture was stirred at 60 ºC under microwave irradiation (20 W, air flow 14 psi) for 30 min. Then, it was
concentrated and purified by automated MPLC (gradient from heptane to acetone, silica refilled column, crude product adsorbed onto silica and loaded into a solid cartridge, 12 min) to afford TEG\textsuperscript{[G3]}-Cl as a pale yellow oil (270 mg, 97%). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, TMS) \(\delta\): 6.05 (s, 3H), 4.82 - 4.74 (m, 42H), 4.52 - 4.41 (m, 84H), 4.02 - 3.97 (m, 6H), 3.86 - 3.48 (m, 408H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\): 160.4, 159.9, 158.2, 158.1, 139.6, 139.4, 131.5, 94.2, 71.3, 71.2, 70.5, 70.4, 68.7, 65.4, 50.1, 42.8. Elem. Anal. Calcd. for C\textsubscript{360}H\textsubscript{243}Cl\textsubscript{24}N\textsubscript{63}O\textsubscript{177}: C, 45.82; H, 5.80; N, 9.35. Found: C, 46.21; H, 5.55; N, 9.03. IR (neat, CsI window): 2953, 2874, 1734, 1169 cm\textsuperscript{-1}.

TEG\textsuperscript{[G3]}-N\textsubscript{3}. In a microwave tube fitted with a magnetic bar, NaN\textsubscript{3} (21 mg, 0.33 mmol) and 15-crown-5 (3.6 mg, 16.6 \(\mu\)mol) were added to a solution of TEG\textsuperscript{[G3]}-Cl (65 mg, 68.9 \(\mu\)mol) in dry DMSO (331 \(\mu\)L). The mixture was stirred for 25 min at 100 °C under microwave irradiation (20 W, air flow 20 psi) and then was distributed between EtOAc (15 mL) and H\(_2\)O (15 mL). The aqueous phase was extracted with EtOAc (3 x 15 mL), and the combined organic phase was washed with brine (5 x 15 mL). The organic layer was dried (MgSO\textsubscript{4}) and concentrated to give TEG\textsuperscript{[G3]}-N\textsubscript{3} as a pale yellow oil (65 mg, 98%). \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}, TMS) \(\delta\): 6.07 (s, 3H), 4.85 - 4.75 (m, 42H), 4.55 - 4.42 (m, 84H), 4.05 - 3.99 (m, 6H), 3.93 - 3.47 (m, 360H), 3.43 - 3.33 (m, 48H). IR (neat, ATR): 2922, 2857, 2107, 1731, 1119 cm\textsuperscript{-1}.

TEG\textsuperscript{[G4]}-Cl. TEG\textsuperscript{[G3]}-N\textsubscript{3} (69 mg, 7.2 \(\mu\)mol) and 2 (143 mg, 0.35 mmol) were dissolved in EtOAc (86 \(\mu\)L) in a microwave tube. The mixture was stirred at 60 °C under microwave irradiation (20 W, air flow 14 psi) for 30 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to acetone, crude product adsorbed onto silica and loaded into a solid cartridge, no column, 12 min) to afford
**TEG\[G4\]-Cl** as a pale yellow oil (122 mg, 87%). $^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 6.07 (bs, 3H), 4.76 - 4.58 (m, 90H), 4.56 - 4.40 (m, 180H), 4.06 - 3.98 (m, 6H), 3.92 - 3.46 (m, 840H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 160.5, 159.9, 158.2, 139.6, 139.4, 131.6, 131.5, 131.4, 131.3, 131.2, 94.2, 71.3, 71.2, 70.5, 70.4, 70.2, 69.4, 69.3, 69.2, 68.7, 68.6, 68.4, 68.3, 65.5, 64.7, 64.6, 50.2, 42.9. Elem. Anal. Calcd. for C$_{744}$H$_{1119}$Cl$_4$N$_{135}$O$_{369}$: C, 45.57; H, 5.78; N, 9.67. Found: C, 45.17; H, 5.58; N, 9.48. IR (neat, CsI window): 2954, 2874, 1733, 1168 cm$^{-1}$.

**TEG\[G4\]-N$_3$**. In a microwave tube fitted with a magnetic bar, NaN$_3$ (14 mg, 0.22 mmol) and 15-crown-5 (2.3 mg, 10.6 $\mu$mol) were added to a solution of TEG\[G4\]-Cl (44 mg, 2.2 $\mu$mol) in dry DMSO (216 $\mu$L). The mixture was stirred for 25 min at 100 °C under microwave irradiation (20 W, air flow 20 psi) and then was distributed between EtOAc (15 mL) and H$_2$O (15 mL). The aqueous phase was extracted with EtOAc (3 x 15 mL), and the combined organic phase was washed with brine (5 x 15 mL). The organic layer was dried (MgSO$_4$) and concentrated to give TEG\[G4\]-N$_3$ as a pale yellow oil (41 mg, 92%). $^1$H NMR (250 MHz, CDCl$_3$, TMS) $\delta$: 6.07 (s, 3H), 4.86 - 4.74 (m, 90H), 4.56 - 4.40 (m, 180H), 4.05 - 3.99 (m, 6H), 3.91 - 3.46 (m, 744H), 3.43 - 3.31 (m, 96H). IR (neat, ATR): 2922, 2855, 2107, 1731, 1121 cm$^{-1}$.

**TEG\[G5\]-Cl**. TEG\[G4\]-N$_3$ (55 mg, 2.8 $\mu$mol) and 2 (110 mg, 0.27 mmol) were dissolved in EtOAc (66 $\mu$L) in a microwave tube. The mixture was stirred at 60 °C under microwave irradiation (20 W, air flow 14 psi) for 30 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to acetone, crude product adsorbed onto silica and loaded into a solid cartridge, no column, 12 min) to afford TEG\[G5\]-Cl as a pale yellow oil (88 mg, 80%). $^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 6.07 (b, 3H), 4.76 - 4.58 (m, 90H), 4.56 - 4.40 (m, 180H), 4.06 - 3.98 (m, 6H), 3.92 - 3.46 (m, 840H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 160.5, 159.9, 158.2, 139.6, 139.4, 131.6, 131.5, 131.4, 131.3, 131.2, 94.2, 71.3, 71.2, 70.5, 70.4, 70.2, 69.4, 69.3, 69.2, 68.7, 68.6, 68.4, 68.3, 65.5, 64.7, 64.6, 50.2, 42.9. Elem. Anal. Calcd. for C$_{744}$H$_{1119}$Cl$_4$N$_{135}$O$_{369}$: C, 45.57; H, 5.78; N, 9.67. Found: C, 45.17; H, 5.58; N, 9.48. IR (neat, CsI window): 2954, 2874, 1733, 1168 cm$^{-1}$.
6.03 (bs, 3H), 4.82 - 4.69 (m, 186H), 4.53 - 4.36 (m, 372H), 4.02 - 3.96 (m, 6H), 3.90 - 3.42 (m, 1800H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 160.3, 159.8, 158.1, 139.5, 139.3, 131.6, 131.5, 131.4, 131.2, 131.1, 94.5, 71.2, 71.1, 70.5, 70.4, 70.3 70.2, 70.1, 69.3, 69.2, 69.1, 68.6, 68.5, 68.3, 68.2, 65.4, 64.6, 64.5, 50.0, 42.8. Elem. Anal. Calcd. for C$_{15}$H$_{21}$Cl$_6$N$_{27}$O$_{75}$: C, 45.59; H, 5.76; N, 9.82. Found: C, 45.85; H, 5.64; N, 9.68. IR (neat, CsI window): 2953, 2874, 1733, 1167 cm$^{-1}$.

Pr$^{[G5]}$-Fc. Pr$^{[G4]}$-N$_3$ (30 mg, 2.3 µmol) and 1,4-bis(ferrocenyl)but-2-yn-1,4-dione (3) (127 mg, 0.22 mmol) were dissolved in EtOAc (444 µL) in a microwave tube. The mixture was stirred at 120 $^\circ$C under microwave irradiation (100 W, air flow 14 psi) for 5 h. Then, the solvent was evaporated and the mixture was dissolved in CH$_2$Cl$_2$ and precipitated with acetone. The resulting purple crystals were filtered to afford Pr$^{[G5]}$-Fc (89 mg, 94%). $^1$H NMR (400 MHz, CDCl$_3$, TMS) $\delta$: 6.10 (bs, 3H), 5.30 (s, 192H), 4.79 (bs, 90H), 4.65 - 4.44 (m, 468H), 4.21 - 4.18 (m, 480H), 4.00 (bs, 6H), 2.53 - 2.42 (m, 192H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 190.8, 188.9, 160.2, 158.5, 146.8, 146.7, 140.4, 140.2, 138.0, 137.9, 130.3, 79.6, 79.5, 78.3, 73.9, 73.4, 72.0, 70.7, 64.0, 63.9, 63.0, 62.9, 53.8, 48.2, 47.0, 46.6, 29.8, 29.5, 29.2. Elem. Anal. Calcd. for C$_{16}$H$_{14}$Fe$_6$N$_{27}$O$_{27}$: C, 56.13; H, 4.15; N, 11.30. Found: C, 55.98; H, 4.44; N, 10.99. IR (neat, ATR): 3107, 3052, 2972, 1730, 1630 cm$^{-1}$.

$^{1,7}$-Diazido-3,6,9,12,15-pentaoxaheptadecane. A mixture of hexaethylene glycol (0.5 g, 1.77 mmol) and benzyltrimethylammonium chloride (0.2 mg 1.062 µmol) was heated at 65 $^\circ$C in a two-necked round-bottom flask under Ar. Thionyl chloride (0.51 mL, 7.08 mmol) was added dropwise and then the reaction was stirred at 65 $^\circ$C for 3 h while maintaining a continuous positive Ar flow. After cooling at rt, the excess of
thionyl chloride was removed at reduced pressure. The resulting crude product was suspended in phosphate buffer (50 mM, pH 7.0, 20 mL) and extracted with CH₂Cl₂ (2 x 15 mL). The combined organic layer was washed with phosphate buffer (50 mM, pH 7.0, 20 mL), dried (Na₂SO₄), and concentrated to give 1,17-dichloro-3,6,9,12,15-pentaoxaheptadecane as a pale yellow oil (0.51 g, 91%).

In a microwave tube fitted with a magnetic bar, NaN₃ (275 mg, 4.23 mmol) and 15-crown-5 (47 mg, 0.22 mmol) were added to a solution of 1,17-dichloro-3,6,9,12,15-pentaoxaheptadecane (337 mg, 1.06 mmol) in dry DMSO (4.2 mL). The mixture was stirred for 25 min at 100 ºC under microwave irradiation (20 W, air flow 20 psi) and then was distributed between EtOAc (15 mL) and H₂O (15 mL). The aqueous phase was extracted with EtOAc (3 x 15 mL), and the combined organic phase was washed with brine (5 x 15 mL), dried (Na₂SO₄) and concentrated. The crude product was purified by automated MPLC (gradient from heptane to acetone, silica refilled column, crude product adsorbed onto silica and loaded into a solid cartridge, 25 min) to afford 1,17-diazido-3,6,9,12,15-pentaoxaheptadecane as a yellow oil (315 mg, 90%). ¹H NMR (400 MHz, CDCl₃, TMS) δ: 3.76 - 3.60 (m, 20H), 3.42 - 3.35 (m, 4H). IR (neat, ATR): 2872, 2094, 1100 cm⁻¹.

Polystyrene-supported azide (PS-N₃). Merrifield resin (3 g, 1.04 mmol/g) in DMF (50 mL) was shaken at 60 ºC in the presence of NaN₃ (0.81 g, 4.16 mmol) for 24 h. After being cooled to rt, the resin was sequentially filtered and washed with H₂O (5 x 50 mL), MeOH (5 x 50 mL) and DCM (5 x 50 mL). The azidomethyl polystyrene resin (PS-N₃) was dried under vacuum (2.9 g, 97%). Estimated azide loading by elemental analysis: 1.01 mmol N₃/g. Before use, PS-N₃ resin was swollen in DMF (5 mL) for 3 h and washed with CH₂Cl₂ (5 x 5 mL) and EtOAc (5 x 5 mL).
**Bis(4-phenylbutyl) but-2-ynedioate (4).** Acetylenedicarboxylic acid (329 mg, 2.88 mmol), 4-phenylbutan-1-ol (1.30 g, 8.64 mmol), and \( p \)-TsOH (46 mg, 0.24 mmol) were added to a round-bottomed flask fitted with a Dean-Stark trap and a reflux condenser. Toluene (4 mL) was added and the reaction mixture was refluxed for 4 h. Then, the reaction was allowed to reach rt and was distributed between Et<sub>2</sub>O (15 mL) and sat NaHCO<sub>3</sub> (25 mL). The organic phase was washed with H<sub>2</sub>O (4 x 25 mL), dried (MgSO<sub>4</sub>) and concentrated. The crude product was purified by automated MPLC (gradient from heptane to EtOAc, silica refilled column, crude product adsorbed onto silica and loaded into a solid cartridge, 25 min) to yield 4 as a colourless oil (1.00 g, 92%).

1H NMR (400 MHz, CDCl<sub>3</sub>, TMS) \( \delta \): 7.33 - 7.25 (m, 4H), 7.24 – 7.15 (m, 6H), 4.29 - 4.22 (m, 4H), 2.70 - 2.61 (m, 4H), 1.79 - 1.66 (m, 8H). 13C NMR (100 MHz, CDCl<sub>3</sub>) \( \delta \): 151.8, 141.7, 128.4, 125.9, 74.7, 69.8, 35.3, 27.8, 27.5. Elem. Anal. Calcd. for C<sub>24</sub>H<sub>26</sub>O<sub>4</sub>: C, 76.17; H, 6.92. Found: C, 75.84; H, 7.06. IR (neat, ATR): 3086, 3065, 3025, 2939, 2861, 1720, 1186 cm<sup>-1</sup>.

**Het[G1]-Br.** 1,17-Diazido-3,6,9,12,15-pentaoxaheptadecane (32 mg, 96 \( \mu \)mol) and 1 (82 mg, 0.23 mmol) were dissolved in EtOAc (97 \( \mu \)L) in a microwave tube. The mixture was stirred at 60 °C under microwave irradiation (20 W, air flow 14 psi) for 90 min. Then, PS-N<sub>3</sub> resin (226 mg, 0.228 mmol) and EtOAc (140 \( \mu \)L) were added, and the mixture was heated at 60 °C under microwave irradiation (20 W, air flow 14 psi) for 3 h without stirring. After removal of the resin by filtration, the filtrate was concentrated to give Het[G1]-Br as a yellow oil (99 mg, 99%). 1H NMR (400 MHz, CDCl<sub>3</sub>, TMS) \( \delta \): 4.81 (t, \( J = 5.2 \) Hz, 4H), 4.53 (t, \( J = 5.2 \) Hz, 4H), 4.50 (t, \( J = 5.3 \) Hz, 4H), 3.86 (t, \( J = 5.2 \), 4H), 3.59 - 3.50 (m, 24H), 2.32 (quint, \( J = 6.5 \) Hz, 4H), 2.31 (quint, \( J = 6.5 \) Hz,
Het[G1]-N₃. In a microwave tube fitted with a magnetic bar, NaN₃ (42 mg, 0.65 mmol) was added to a solution of Het[G1]-Br (85 mg, 81.6 µmol) in dry DMSO (653 µL). The mixture was stirred for 2 min at 100 ºC under microwave irradiation (25 W) and then was distributed between EtOAc (15 mL) and H₂O (15 mL). The aqueous phase was extracted with EtOAc (3 x 15 mL), and the combined organic phase was washed with brine (5 x 15 mL). The organic layer was dried (MgSO₄) and concentrated to give Het[G1]-N₃ as a pale yellow oil (67 mg, 92%). ¹H NMR (300 MHz, CDCl₃, TMS) δ: 4.81 (t, J = 5.2 Hz, 4H), 4.47 (t, J = 6.0 Hz, 4H), 4.45 (t, J = 6.0 Hz, 4H), 3.87 (t, J = 5.2 Hz, 4H), 3.61 - 3.46 (m, 24H), 2.06 (quint, J = 6.6 Hz, 4H), 2.03 (quint, J = 6.6 Hz, 4H). IR (neat, ATR): 2877, 2098, 1731, 1204 cm⁻¹.

Het[G2]-Cl. Het[G1]-N₃ (29 mg, 32 µmol) and 2 (106 mg, 0.26 mmol) were dissolved in EtOAc (64 µL) in a microwave tube. The mixture was stirred at 60 ºC under microwave irradiation (20 W, air flow 14 psi) for 30 min. Then, it was concentrated and purified by automated MPLC (gradient from heptane to acetone, silica refilled column, crude product adsorbed onto silica and loaded into a solid cartridge, 14 min) to afford Het[G2]-Cl as a yellow oil (76 mg, 92%). ¹H NMR (400 MHz, CDCl₃, TMS) δ: 4.85 - 4.72 (m, 12H), 4.55 - 4.37 (m, 24H), 3.89 - 3.55 (m, 100H), 2.34 (quint, J = 6.7 Hz, 8H). ¹³C NMR (100 MHz, CDCl₃) δ: 159.9, 159.7, 158.1, 158.0, 140.1, 139.3, 131.2, 130.0,
129.9, 71.3, 71.2, 70.5, 70.4, 70.3, 68.7, 68.4, 68.3, 65.6, 47.6, 47.5, 42.8, 42.7, 29.1, 28.8. Elem. Anal. Calcd. for C_{96}H_{144}Cl_{8}N_{18}O_{45}: C, 45.15; H, 5.68; N, 9.87. Found: C, 44.82; H, 6.11; N, 9.87. IR (neat, ATR): 2957, 2876, 1728, 1112 cm\(^{-1}\). MALDI-TOF MS (DHB, reflected mode, \(m/z\)): 2575.19. Calcd. for [M+Na]\(^{+}\), C\(_{96}H_{144}Cl_{8}N_{18}O_{45}Na\): 2576.69.

\(\text{Het[G2]-N}_3\). In a microwave tube fitted with a magnetic bar, \(\text{NaN}_3\) (42 mg, 0.65 mmol) and 15-crown-5 (7.2 mg, 32.6 \(\mu\)mol) were added to a solution of \(\text{Het[G2]-Cl}\) (103 mg, 40.8 \(\mu\)mol) in dry DMSO (653 \(\mu\)L). The mixture was stirred for 25 min at 100 °C under microwave irradiation (20 W, air flow 20 psi) and then was distributed between EtOAc (15 mL) and H\(_2\)O (15 mL). The aqueous phase was washed with EtOAc (3 x 15 mL), and the combined organic phase was washed with brine (5 x 15 mL). The organic layer was dried (MgSO\(_4\)) and concentrated to give \(\text{Het[G2]-N}_3\) as a pale yellow oil (98 mg, 93%). \(^1\)H NMR (300 MHz, CDCl\(_3\), TMS) \(\delta\): 4.89 - 4.73 (m, 12H), 4.59 - 4.36 (m, 24H), 3.94 - 3.47 (m, 84H), 3.44 - 3.33 (m, 16H), 2.43 (quint, \(J = 7.2\) Hz, 8H). IR (neat, ATR): 2877, 2105, 1729, 1111 cm\(^{-1}\).

\(\text{Het[G3]-Ar}\). \(\text{Het[G2]-N}_3\) (38 mg, 14.8 \(\mu\)mol) and 4 (89 mg, 0.24 mmol) were dissolved in EtOAc (59 \(\mu\)L) in a microwave tube. The mixture was stirred at 70 °C under microwave irradiation (30 W, air flow 14 psi) for 45 min. Then, it was concentrated and purified by ultrafiltration (Amicon YM5, acetone, 6 x 15 mL) to give \(\text{Het[G3]-Ar}\) as a yellow oil (77 mg, 93%). \(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\): 7.21 - 7.04 (m, 80H), 4.76 - 4.63 (m, 28H), 4.43 - 4.20 (m, 56H), 3.82 - 3.70 (m, 20H), 3.68 - 3.39 (m, 64H), 2.56 (t, \(J = 7.2\) Hz, 32H), 2.33 (quint, \(J = 6.4\) Hz, 8H), 1.72 - 1.56 (m, 64H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 160.1, 159.9, 159.8, 158.5, 158.1, 158.0, 141.8, 141.6, 131.1, 130.9, 129.9,
128.3, 128.2, 125.9, 125.8, 70.5, 70.4, 70.3, 69.3, 69.2, 68.6, 66.5, 65.6, 65.5, 49.9, 47.6, 35.3, 35.2, 29.1, 28.8, 28.0, 27.8, 27.5. Elem. Anal. Calcd. for C\textsubscript{288}H\textsubscript{352}N\textsubscript{42}O\textsubscript{77}: C, 61.40; H, 6.30; N, 10.44. Found: C, 61.38; H, 6.70; N, 10.81. IR (neat, ATR): 3086, 3061, 3023, 2942, 2860, 1726, 1200 cm\textsuperscript{-1}. MALDI-TOF MS (HABA, linear mode, m/z): 5652.36. Calcd. for [M+Na]\textsuperscript{+}, C\textsubscript{288}H\textsubscript{352}N\textsubscript{42}O\textsubscript{77}Na: 5656.49.
4. Spectra of New Compounds

$^1$H NMR spectrum of $^{Pr}[G0]-Br$ (CDCl$_3$)

$^{13}$C NMR spectrum of $^{Pr}[G0]-Br$ (CDCl$_3$)
$^1$H NMR spectrum of $^{Pr}[G0]-N_3$ (CDCl$_3$)

$^{13}$C NMR spectrum of $^{Pr}[G0]-N_3$ (CDCl$_3$)
IR spectrum of $^{Pr}[G0]-N_3$
The image contains two sets of spectra:

1. **$^1$H NMR spectrum of 1 (CDCl$_3$)**

2. **$^{13}$C NMR spectrum of 1 (CDCl$_3$)**

The spectra show distinct peaks at specific chemical shifts, corresponding to the protons and carbon atoms labeled in the molecular structures.
IR spectrum of 1
$^1$H NMR spectrum of $^{Pr}[G1]$-Br (CDCl$_3$)

$^{13}$C NMR spectrum of $^{Pr}[G1]$-Br (CDCl$_3$)
IR spectrum of $^{Pr}[G1]-Br$

MALDI-TOF MS of $^{Pr}[G1]-Br$
$^1$H NMR spectrum of $^{Pr[G1]}$-N$_3$ (CDCl$_3$)

$^{13}$C NMR spectrum of $^{Pr[G1]}$-N$_3$ (CDCl$_3$)
IR spectrum of $^{Pr}[G1]-N_3$
$^1$H NMR spectrum of $^{Pr}[G2]-Br$ (CDCl$_3$)

$^{13}$C NMR spectrum of $^{Pr}[G2]-Br$ (CDCl$_3$)
IR spectrum of $^{Pr}[G2]-Br$

MALDI-TOF MS of $^{Pr}[G2]-Br$
$^1$H NMR spectrum of Pr$[G2]\text{-N}_3$ (CDCl$_3$)

$^{13}$C NMR spectrum of Pr$[G2]\text{-N}_3$ (CDCl$_3$)
IR spectrum of $^{Pr}[G2]-N_3$
$^1$H NMR spectrum of Pr$^\text{[G3]}$-Br (CDCl$_3$)

$^{13}$C NMR spectrum of Pr$^\text{[G3]}$-Br (CDCl$_3$)
IR spectrum of $^{3}$Pr[G3]-Br

MALDI-TOF MS of $^{3}$Pr[G3]-Br
$^1$H NMR spectrum of $^{Pr}[G3]-N_3$ (CDCl$_3$)

$^{13}$C NMR spectrum of $^{Pr}[G3]-N_3$ (CDCl$_3$)
IR spectrum of Pr[G3]-N₃
$^1$H NMR spectrum of Pr[G4]-Br (CDCl$_3$)

$^{13}$C NMR spectrum of Pr[G4]-Br (CDCl$_3$)
IR spectrum of Pr[G4]-Br

MALDI-TOF MS of Pr[G4]-Br
$^1$H NMR spectrum of Pr$_4$[G4]-N$_3$ (CDCl$_3$)

$^{13}$C NMR spectrum of Pr$_4$[G4]-N$_3$ (CDCl$_3$)
IR spectrum of $^{Pr}[G4]\cdot N_3$
$^1$H NMR spectrum of $\text{Pr}[\text{G5}]-\text{Br}$ (CDCl$_3$)

$^{13}$C NMR spectrum of $\text{Pr}[\text{G5}]-\text{Br}$ (CDCl$_3$)
IR spectrum of $^{39}$Pr[G5]-Br

MALDI-TOF MS of $^{39}$Pr[G5]-Br
$^1$H NMR spectrum of Pr[G5]-N3 (CDCl₃)

$^{13}$C NMR spectrum of Pr[G5]-N3 (CDCl₃)
$^1$H NMR spectrum of 2 (CDCl$_3$)

$^{13}$C NMR spectrum of 2 (CDCl$_3$)
$^1$H NMR spectrum of $^{\text{TEG}[G1]}$-Cl (CDCl$_3$)

$^{13}$C NMR spectrum of $^{\text{TEG}[G1]}$-Cl (CDCl$_3$)
$^1$H NMR spectrum of $^{^3}$TEG[6-G1]-N$_3$ (CDCl$_3$)
$^1$H NMR spectrum of $^{\text{TEG}[G2]-\text{Cl}}$ (CDCl$_3$)

$^{13}$C NMR spectrum of $^{\text{TEG}[G2]-\text{Cl}}$ (CDCl$_3$)

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\(^1\)H NMR spectrum of TEG\(^{\text{G3}}\)-Cl (CDCl\(_3\))

\(^{13}\)C NMR spectrum of TEG\(^{\text{G3}}\)-Cl (CDCl\(_3\))
$^1$H NMR spectrum of $^{\text{TEG}[G4]}$-Cl (CDCl$_3$)

$^{13}$C NMR spectrum of $^{\text{TEG}[G4]}$-Cl (CDCl$_3$)
$^1$H NMR spectrum of $^{\text{TEG}}[\text{G5}]-\text{Cl (CDCl}_3\text{)}$ 

$^{13}$C NMR spectrum of $^{\text{TEG}}[\text{G5}]-\text{Cl (CDCl}_3\text{)}$
$^1$H NMR spectrum of $^{Pr}[G5]$-Fc (CDCl$_3$)

$^{13}$C NMR spectrum of $^{Pr}[G5]$-Fc (CDCl$_3$)
IR spectrum of Pr[G5]-Fc
\(^1\)H NMR spectrum of 4 (CDCl\textsubscript{3})

\(^{13}\)C NMR spectrum of 4 (CDCl\textsubscript{3})
$^1$H NMR spectrum of $^{\text{Het}[G1]}$-Br (CDCl$_3$)

$^{13}$C NMR spectrum of $^{\text{Het}[G1]}$-Br (CDCl$_3$)
IR spectrum of $^{\text{Het[G1]}}$-Br

MALDI-TOF MS of $^{\text{Het[G1]}}$-Br
$^1$H NMR spectrum of $^{\text{Het}[G1]}$-N$_3$ (CDCl$_3$)

IR spectrum of $^{\text{Het}[G1]}$-N$_3$. 
$^1$H NMR spectrum of $^\text{Het}[G2]-\text{Cl} (\text{CDCl}_3)$

$^{13}$C NMR spectrum of $^\text{Het}[G2]-\text{Cl} (\text{CDCl}_3)$
IR spectrum of $^{\text{Het}}[G2]$-Cl.

MALDI-TOF MS of $^{\text{Het}}[G2]$-Cl.
$^1$H NMR spectrum of $^{\text{Hetero}}$[G2]-N$_3$ (CDCl$_3$)

IR spectrum of $^{\text{Hetero}}$[G2]-N$_3$
$^1$H NMR spectrum of $^{\text{Het}[G3]}$-Ar (CDCl$_3$)

$^{13}$C NMR spectrum of $^{\text{Het}[G3]}$-Ar (CDCl$_3$)
IR spectrum of $^{\text{Het}}[\text{G3}]$-Ar

MALDI-TOF MS of $^{\text{Het}}[\text{G3}]$-Ar
5. References


