Supplementary Information

Synthesis of Non-ionic Bolaamphiphiles and Study of their Self-assembly and Transport Behaviour for Drug Delivery Applications

Rashmi,[a] Abhishek K. Singh,[a] Katharina Achazi,[b] Boris Schade,[c] Christoph Böttcher,[c] Rainer Haag,[b] Sunil K. Sharma[a]*

[a]*Department of Chemistry, University of Delhi, Delhi 110 007, India*

[b]*Institut für Chemie und Biochemie, Freie Universität Berlin, Takustraße 3, 14195 Berlin, Germany*

[c]*Forschungszentrum für Elektronenmikroskopie, Institut für Chemie und Biochemie, Freie Universität Berlin, Fabeckstraße 36a, 14195 Berlin, Germany*

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1. Experimental Section

1.1 Material

All the chemicals and solvents used were purchased from Spectrochem Pvt. Ltd., India and Sigma-Aldrich Chemicals, USA. Immobilized *Candida antarctica* lipase (Novozym 435) was obtained from Novo Nordisk A/S Denmark. All the dyes/drugs used for encapsulation studies were purchased from Fluka Chemie GmbH, (Buchs, Switzerland) and Sigma-Aldrich Chemicals, USA with maximum purity. The solvents used in the reactions were dried and distilled prior to use. Pre-coated TLC plate (Merck silica gel 60F254) was used to monitor the progress of the react with visualization of the spots on TLC using cerric solution. Silica gel (100-200 mesh) was used for column chromatography. Millipore water was used for preparing samples for physico-chemical characterization and transport analysis.

1.2. Instrumentation and Methods

1.2.1 NMR, IR Spectroscopy, and GPC Analysis

The ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on JEOL 400 MHz, Bruker DRX 400, and Bruker AMX 500 MHz spectrometers with the residual solvent peak used as a reference. Infrared spectra (IR) of the samples were recorded using a Perkin-Elmer FT-IR model 9 spectrometer. The chemical shift values are on a δ scale and the coupling constant values (*J*) are in Hertz. High-resolution mass spectrometry (HRMS) data were recorded on Q-

TOF LCMS-Agilent Technology-6530 and HPLC/MS-Agilent 6210 (Agilent Technologies). To determine the molecular weight M_w, M_n and M_z of amphiphiles, an Agilent GPC system equipped with an Agilent 1100 pump, refractive index detector, and PLgel columns, was used using tetrahydrofuran (THF) as an eluent at a flow rate of 1.0 mL min^{-1} and molecular weight calibration carried using polystyrene standards.

1.2.2 Critical aggregation concentration (CAC) measurements

The CAC of the synthesized amphiphiles was determined by fluorescence technique using 'Nile red' as a model dye. A stock solution of the dye at a concentration of 1 mg mL^{-1} (3.14 x 10^{-3} M) was prepared in THF. 10 µL of 3.14 x 10^{-4} M Nile red solution was added in each empty vial followed by complete evaporation of THF. The stock solutions of bolaamphiphiles were prepared at a concentration of 1 mM using Milli-Q water, and allowed to stir for 1 h. Twofold serial dilution of the stock solutions was done to achieve different concentrations of the amphiphiles, which were then transferred to the vials having thin film of the dye followed by overnight stirring. The non-encapsulated dye in all the solutions was removed by filtration through 0.45 µm polytetrafluoroethylene (PTFE) filter with subsequent fluorescence measurements using Cary Eclipse fluorescence spectrophotometer. The plot of fluorescence intensity maxima values against log [amphiphile concentration] for different samples afforded the CAC value.

1.2.3 Dynamic Light Scattering (DLS)

Malvern Zetasizer Nano ZS analyzer integrated with 4 mW He–Ne laser, λ= 633 nm, using backscattering detection (scattering angle θ = 173°) with an avalanche photodiode detector, was used for determining the size of nanostructures (micelles/aggregates) formed by the supramolecular organization of bolaamphiphiles in the aqueous solution (Milli-Q water) at a concentration of 5 mg mL^{-1}. The samples were then further allowed to mix at 25 °C for 20 h with vigorous stirring. The obtained solutions were then filtered through 0.22 µm PTFE filters and equilibrated for 1h at room temperature, then transferred to disposable micro BRAND ultraviolet (UV) cuvettes, and used for DLS measurements.

1.2.4 Cryogenic transmission electron microscopy (cryo-TEM)

Perforated carbon film-covered microscopical 200 mesh grids (R1/4 batch of Quantifoil, MicroTools GmbH, Jena, Germany) were cleaned with chloroform and hydrophilised by 60 s glow discharging at 8 W in a BAL-TEC MED 020 device (Leica Microsystems, Wetzlar, Germany) before 5 µl aliquots of the sample solution (5 mg ml^{-1}) were applied to the grids. The samples were automatically blotted and vitrified with a FEI Vitrobot Mark IV and (Thermo Fisher Scientific Inc., Waltham, Massachusetts, USA) using liquid ethane as cryogen. Cryo-TEM measurements were carried out on a Tecnai F20 TEM (FEI Company, Oregon) equipped with a field emission gun (FEG) at an acceleration voltage of 160kV using a Gatan cryo holder at 94 K sample temperature. By using the microscope's low-dose protocol, the micrographs were recorded with a FEI Eagle 4k × 4k CCD camera in twofold binning mode.

1.2.3 Cytotoxicity study

The cytotoxicity of bolaamphiphiles in A549 lung cancer cells (ATCC CCL-185) was analysed by the One Solution Cell Proliferation Assay (MTS) from Promega (Mannheim Germany). The cells were routinely propagated in DMEM medium supplemented with 2% glutamine, 100 U/mL penicillin, 100 µg/mL streptomycin (all from Gibco BRL, Eggenstein, Germany), and 10% fetal calf serum (Biochrom AG, Berlin, Germany) at 37 °C with 5% CO2, and passaged twice a week. For the MTS assay, A549 cells were seeded in a 96-well plate (4.000 cells/well) and cultured over night at 37 °C before adding the amphiphiles in serial dilutions. Cells treated with 0.01% SDS and non-treated cells served as controls. For background subtraction, also wells containing no cells but only sample were used. Cells were incubated for another day at 37 °C before the MTS solution was added. After 2 hours of incubation, absorbance was measured at a measurement wavelength of 490 nm and a reference wavelength of 630 nm with a Tecan plate reader (Infinite pro200, TECAN-reader Tecan Group Ltd., Männedorf, Switzerland). Measurements were done in triplicates. The cell viability was calculated by setting the non-treated control to 100% and the non-cell control to 0% after subtracting the background using the GraphPad Prism 5.01 software.

1.2.4 Nile red and nimodipine encapsulation and quantification

Nile red and nimpdipine encapsulation studies were performed by following the film method using ultraviolet-visible (UV-Vis) spectral measurement. The dye/drug was solubilized at a concentration of 5 mg ml^{-1} for all the bolaamphiphiles using 0.12 mg of Nile red and 1mg of

nimodipine. The required amount of the dye/drug was dissolved in THF and the solvent was allowed to evaporate to form a uniform thin film at the bottom of vial, followed by the addition of 1mL of aqueous amphiphilic solution. After stirring for 20 h at room temperature. The non-encapsulated dye/drug was removed by filtering it (twice), slowly through 0.45 μm pore size PTFE filter. For the quantification of encapsulated dye/drug, the encapsulated samples were lyophilized and re-dissolved in anhydrous methanol for Nile red, and in ethanol for nimodipine. The absorbance (220–800 nm) spectra were recorded on a Perkin Elmer LAMBDA 950 UV/Vis/near-infrared (NIR) spectrophotometer using standard disposable poly(methyl methacrylate) (PMMA) UV/Vis cuvettes with a path length of 1 cm from PLASTIBRAND.

1.2.5 Cellular uptake study

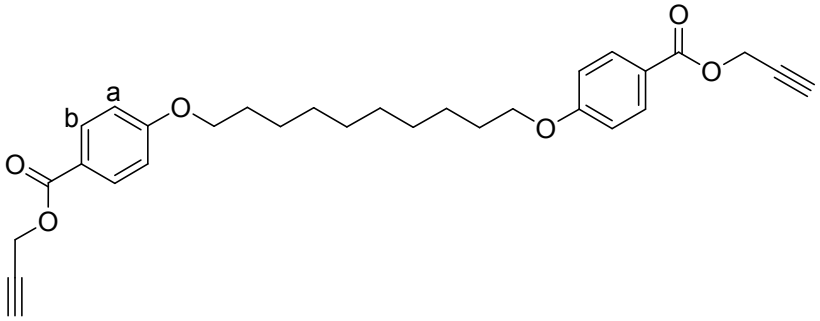
The cellular uptake of bolaamphiphiles in A549 lung cancer cells (ATCC CCL-185) was analysed by confocal laser scanning microscopy (cLSM). The cells were routinely propagated as described above. For cLSM, cells were seeded in 8-well ibidi μ-slides (15.000 cells/well) in colourless cell culture medium. After 1 day, the Nile red loaded amphiphiles were added at a final test concentration of 0.01 mg ml^{-1}, and the cells were grown for another day. Cell nuclei were stained with 1μg/ml Hoechst 33342 (Life Technologies GmbH, Darmstadt, Germany). Confocal images were taken with an inverted confocal laser scanning microscope Leica DMI6000CSB SP8 (Leica, Wetzlar, Germany) with a 63x/1.4 HC PL APO CS2 oil immersion objective using the LAS X software.

1.2.6 Enzyme-triggered release study

For the time-dependent enzymatic release study, Nile red was used as a model dye and encapsulated in the amphiphilic solution following the same protocol used for quantification. After removing the non-encapsulated dye through 0.45 μm PTFE filter, a few drops of *n*-butanol and 200 wt % of the enzyme were added. The final solutions were incubated at 37 ^{o}C and stirred at 200 rpm and time dependent fluorescence measurement was made after every 1 h. The time-dependent release was studied using fluorescence spectroscopy (Cary Eclipse fluorescence spectrophotometer, Agilent Technologies) by measuring the emission maxima.

1.3 Experimental

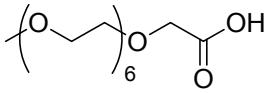
*1.3.1 Synthesis of di(prop-2-yn-1-yl) 4,4'-(decane-1,10-diylbis(oxy))dibenzoate (**9**)*



To a stirred solution of prop-2-yn-1-yl 4-hydroxybenzoate (5g, 28.4 mmol) and K_2CO_3 (11.7g 85.2 mmol) in DMF (50 ml) 1,10-dibromodecane (25.5 g, 85.2 mmol) was added at room temperature and the reaction mixture was stirred at 35 ^oC for 15 h. The progress of the reaction was monitored by TLC using ethyl acetate/petroleum ether (1:9), after completion of the reaction DMF was evaporated under reduced pressure and the crude product was suspended in water (150 mL) and the solution extracted with ethyl acetate (3 x 30 mL). The combined organic layer was dried over sodium sulphate and concentered under reduced pressure, the obtained residue was subjected to purification through column chromatography to get the desired product as a white solid in 91% yield.

^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8 Hz, 4H, **H-b**), 6.91-6.89 (d, *J* = 8 Hz, 4H, **H-a**), 4.89 (d, *J* = 4 Hz, 4H, -COOC**H$_2$**-), 4.01 – 3.97 (t, 4H, *J* = 8 Hz, Ph-O-C**H$_2$**-), 2.52 – 2.50 (d, *J* = 4 Hz, 2H, C**H**≡C-), 1.82-1.77 (q, *J* = 8 Hz, 4H, Ph-O-CH$_2$**CH$_2$**-), 1.46 – 1.25 (m, 12H, **alkyl protons**) ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 165.80, 163.39, 131.98, 121.44, 115.45, 114.23, 76.84, 74.98, 68.29, 52.30, 29.53, 29.40, 29.15, 26.04; IR (Neat) ν_{max}: 3267, 2933, 2854, 2125, 1707, 1606 cm^{-1}.

*1.3.2 Synthesis of methoxypolyethylene glycol (mPEG 350) carboxymethyl ether (**3**)*

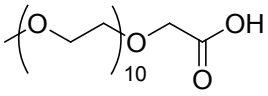


Monomethoxy polyethylene glycol (M_w: 350) (5 g, 10 mmol) was dissolved in distilled water (50 mL) in a 250 mL round-bottom flask and (2.2 g, 40 mmol) of sodium hydroxide was added. The reaction mixture was stirred in an ice bath to allow the temperature to reach at 0 ^oC, then (13.5 g, 60 mmol) of potassium permanganate was added in small amounts in approximately 2-3 h. The reaction mixture was allowed to warm at room temperature and left for stirring at 80 ^oC for 24 h. Progress of the reaction was monitored by TLC using methanol/chloroform (1:9). On

completion of the reaction, black residue was filtered off. The filtrate was acidified using 2 M hydrochloric acid to pH 2 and the solution was extracted with chloroform (4 x 50 mL). The organic layer was dried over anhydrous sodium sulphate, and concentrated under reduced pressure to get the desired product as a viscous liquid in 90% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.12 (s, 2H, -OOCCH_2O-mPEG), 3.71-3.50 (m, 24H, **mPEG** region), 3.34 (s, 3H, CH_3O-mPEG). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 172.21, 71.80, 71.66, 70.33, 68.89, 58.93; IR (Neat) ν_{max} : 2868, 1741, 1455 cm^{-1}.

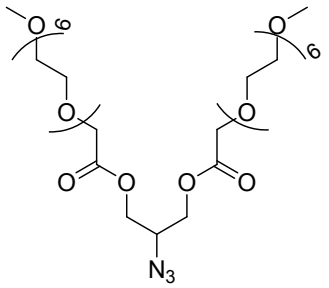
*1.3.3 Synthesis of methoxy polyethylene glycol (mPEG-550) carboxymethyl ether (**4**)*



Monomethoxy polyethylene glycol (M_w: 550) (5 g, 10 mmol) was dissolved in distilled water (50 mL) in a 250 mL round-bottom flask and (0.8 g, 40 mmol) of sodium hydroxide was added. The reaction mixture was stirred in ice bath to allow the temperature to reach at 0 ^{o}C, then (4.7 g, 60 mmol) of potassium permanganate was added in small amounts in approx. 1-2 h. The reaction mixture was allowed to warm at room temperature and then heated to 80 ^{o}C for 24 h. Progress of the reaction was monitored by TLC using methanol/chloroform (1:9). On completion of the reaction, black residue was filtered off. The filtrate was acidified using 2 M hydrochloric acid solution to pH 2 and the solution was extracted with chloroform (6 x 50 mL). The organic layer was dried over anhydrous sodium sulphate, and concentrated under reduced pressure to get the desired product as a viscous liquid, in 90 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.10 (s, 2H, -OOC**CH_2**O-mPEG), 3.70-3.53 (m, 83H, **mPEG**, region), 3.37 (s, 3H, **CH_3**O-mPEG). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 172.0, 71.88, 70.95, 70.51, 68.80, 58.98. IR (Film) ν_{max} : 2865, 1743, 1465 cm^{-1}.

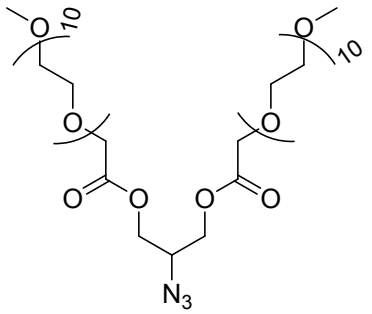
*1.3.4 Synthesis of 2-azidopropane-1,3-diyl bis(methoxypoly(oxyethylene)oate) (mPEG-350) (**6**)*



To a solution of azido glycerol (0.5 g, 4.2 mmol) and mPEG-350 acid (5.17 g, 9.4 mmol) in DCM (25 mL), EDC.HCL (1.8 g, 9.4 mmol) and DMAP (0.62g, 5.1 mmol) were added and the reaction mixture was stirred at 35 ^{o}C for 12 h. The progress of the reaction was monitored by TLC using methanol/chloroform (1:9), after completion of the reaction DMF was evaporated under reduced pressure and the crude product was suspended in water (150 mL) and extracted with $CHCl_3$ (3 x 30 mL). The organic layer was dried over sodium sulphate and concentered under reduced pressure, the obtained residue was subjected to purification through column chromatography to get the desired product as a viscous liquid in 91% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.31-4.12 (m, 8H, N_3CH-(**CH_2**)$_2$-, -OOC**CH_2**-O-mPEG) 3.95-3.89 (m, 1H, N_3C**H**(CH_2), 3.73-3.52 (m, 52H, **m-PEG region**), 3.36 (s, 6H, C**H_3**O-PEG);^{13}C NMR (100.5 MHz, $CDCl_3$): δ 169.92, 71.87, 71.05, 70.51, 68.28, 63.19, 58.96, 58.43.; IR (Neat) ν_{max}: 2867, 2110, 1745, 1440 cm^{-1}.

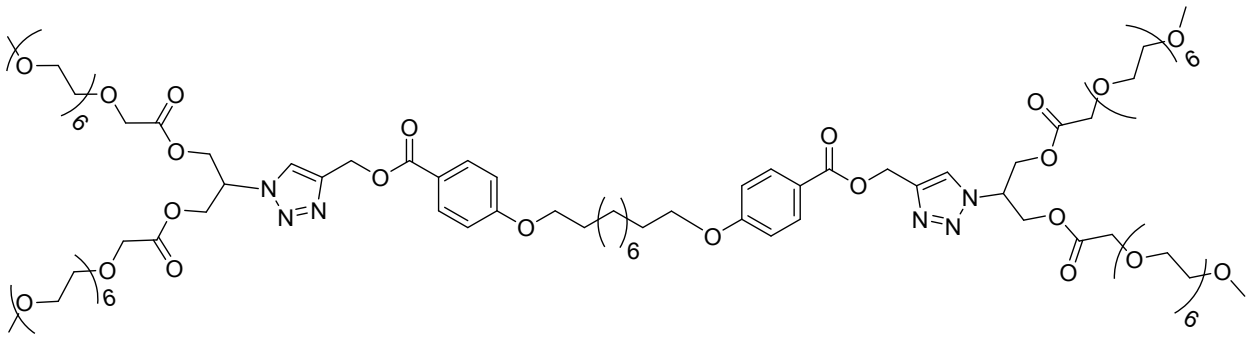
1.3.5 Synthesis of 2-azidopropane-1,3-diyl bis(methoxypoly(oxyethylene)oate) (mPEG-550) (7)



To a solution of azido glycerol (0.5 g, 4.2 mmol) and mPEG-550 acid (5.17 g, 9.4 mmol) in DCM (25 mL), EDC.HCL (1.8 g, 9.4 mmol) and DMAP (0.62 g, 5.1 mmol) were added and the reaction mixture was stirred at 35^{o}C for 12 h. The progress of the reaction was monitored by TLC using methanol/chloroform (1:9), after completion of the reaction DMF was evaporated under reduced pressure and the crude product was suspended in water (150 mL) and extracted with $CHCl_3$ (3 x 30 mL). The organic layer was dried over sodium sulphate and concentered under reduced pressure, the obtained residue was subjected to purification through column chromatography to get the desired product as a viscous liquid in 91% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.38-4.13 (m, 8H, N_3CH-(**CH_2**)$_2$-, -OOC**H_2**-O-mPEG), 3.91-3.90 (m, 1H, N_3C**H**(CH_2), 3.88-3.49(m, 91H, **m-PEG region**), 3.30 (s, 6H, C**H_3**O-PEG); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 169.87, 71.84, 70.95, 70.47, 70.41, 68.24, 63.14, 58.93, 58.39. IR(Neat) ν_{max} : 2871, 2102, 1755, 1457 cm^{-1}.

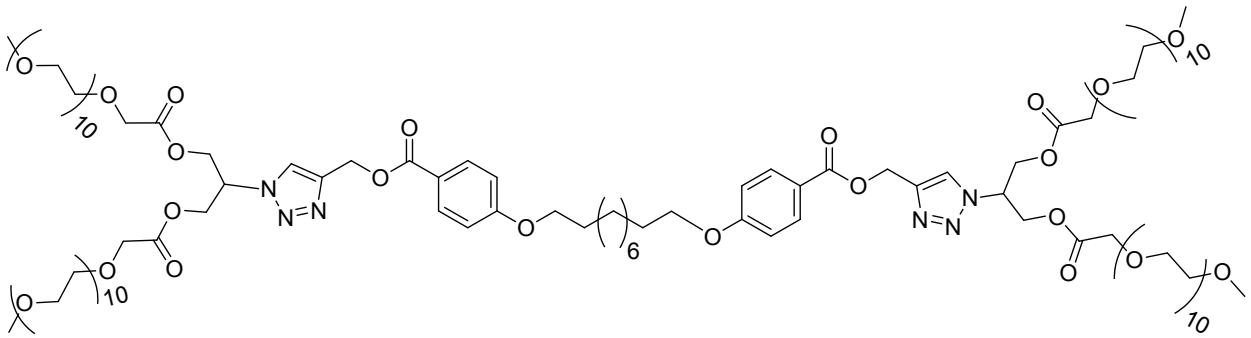
*1.3.6 Synthesis of bolaamphiphile Bola-PEG$_6$ (**10**)*



To a solution of 2-azidopropane-1,3-diyl bis(methoxypoly(oxyethylene)oate) (1.9 g, 2.55 mmol) and di(prop-2-yn-1-yl) 4,4'-(decane-1,10-diylbis(oxy))dibenzoate (0.5 mg, 1.01mmol) in 2:1 THF :water mixture (20 mL), $CuSO_4.5H_2O$ (0.10 g, 0.4 mmol) and sodium ascorbate (0.16 g, 0.6 mmol) were added and the reaction mixture was stirred at 50 ^{o}C for 24 h. The progress of the reaction was monitored by TLC using methanol/chloroform (1:9), after completion of the reaction as indicated by TLC, THF and water were evaporated under reduced pressure and the crude product so obtained was suspended in water (150 mL) and extracted with $CHCl_3$ (3 x 30 ml). The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The obtained residue was subjected to purification through column chromatography to give the desired product as a viscous liquid in 95% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8 Hz, 4H, aromatic **CH**), 7.87 (s, 1H, triazole ring **CH**), 7.81(s, 1H, triazole ring **CH**), 6.85 (d, *J* = 8 Hz, 4H, aromatic **CH**), 5.40 (s, 4H, -OC**H_2**-triazole), 5.12-5.09 (m, 1H, N-**CH**(CH_2)$_2$, 4.90-4.89 (m, 1H, N-**CH**(CH_2)$_2$), 4.65-4.29 (m, 8H, N-CH(**CH_2**)$_2$), 4.18-4.11 (m, 8H, -OOCC**H_2**-O-mPEG), 3.96 (t, 4H, Ph-O-**CH_2**-) 3.72-3.51 (m, 90H, **PEG region**), 3.34 (s, 12H, C**H_3**O-mPEG), 1.77-1.74 (m, 4H, Ph-O-CH_2-**CH_2**-) , 1.42-1.22 (m, 12H, **alkyl protons**); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 169.87, 166.22, 163.24 131.84, 124.27, 121.80, 114.16, 71.94, 71.04, 70.56, 68.29, 62.64, 61.32, 59.07, 57.68, 29.49, 29.13, 26.01; IR(Neat) ν_{max} : 3662, 2872, 1714, 1604 cm^{-1}.

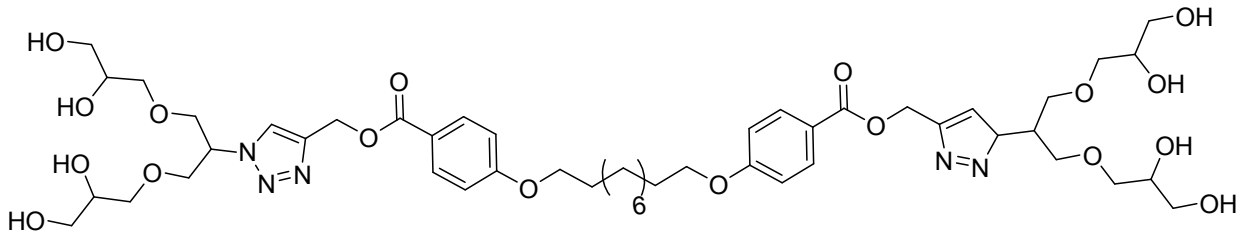
*1.3.7 Synthesis of bolaamphiphile Bola-PEG$_{10}$ (**11**)*



To a solution of 2-azidopropane-1,3-diyl bis(methoxypoly(oxyethylene)oate) (3.01 g, 2.55 mmol) and di(prop-2-yn-1-yl) 4,4'-(decane-1,10-diylbis(oxy))dibenzoate (0.5 g, 1.02 mmol) in 2:1 THF:water mixture (20 mL) $CuSO_4.5H_2O$ (0.10g, 0.4 mmol) and sodium ascorbate (0.16 g, 0.6 mmol) were added, and the reaction mixture was stirred at 50 ^oC for 24 h. The progress of the reaction was monitored by TLC using methanol/chloroform (1:9), after completion of the reaction as indicated by TLC, THF and water were evaporated under reduced pressure and the crude product was suspended in water (150 mL) and extracted with $CHCl_3$ (3 x 30 ml). The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The obtained residue was subjected to purification through column chromatography to get the desired product as a viscous liquid in 95% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8 Hz, 4H, aromatic **CH**), 7.86 (s, 1H, triazole ring **CH**), 7.80 (s, 1H, triazole ring **CH**) , 6.85 (d, *J* = 8 Hz, 4H, aromatic **CH**), 5.39 (s, 4H, -OC**H$_2$**-triazole), 5.11-5.08 (m, 1H, N-C**H**$(CH_2)_2$), 5.07- 4.87 (m, 1H, N-C**H**$(CH_2)_2$), 4.63-4.40 (m, 8H, N-CH(C**H$_2$**)$_2$), 4.18-4.10 (m, 8H, -OOCC**H$_2$**-O-mPEG), 3.95(t, 4H, Ph-O-**CH$_2$**-), 3.69-3.50 (m, 172H, **PEG region**), 3.34 (s, 12H, s, 12H, **CH$_3$**O-mPEG), 1.79- 1.72 (m, 4H, Ph-O-CH_2-C**H$_2$**), 1.43-1.29(m, 12H, **alkyl protons**); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 169.84, 169.33, 166.33, 163.09, 131.81, 121.80, 113.73, 71.84, 71.04, 70.51, 68.26, 62.61, 59.03, 58.40, 57.69, 29.52, 29.13, 28.94, 25.99; IR(Neat) ν_{max} :3786, 2868, 1714, 1604 cm^{-1}.

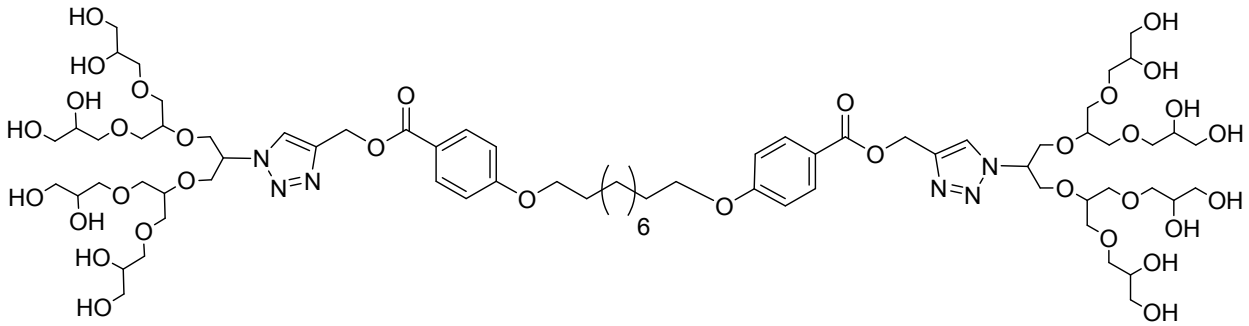
*1.3.8 Synthesis of bolaamphiphile Bola-[G1.0](**12**)*



To a solution of polyglycerol azide (G-1) (1.35g, 2.55 mmol) and di(prop-2-yn-1-yl)4,4'-(decane-1,10-diylbis(oxy))dibenzoate (0.5g, 1.02 mmol) in 2:1 THF:water mixture (20 ml) $CuSO_4.5H_2O$ (0.10g, 0.4 mmol) and sodium ascorbate (0.16g, 0.6 mmol) were added and the reaction mixture was stirred at room temperature for 24 h. The progress of the reaction was monitored by TLC using methanol/chloroform (1:4), after completion of the reaction as indicated by TLC, THF and water were evaporated under reduced pressure and the crude product was suspended in water (150 mL) and extracted with $CHCl_3$ (3 x 30 ml). The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The obtained residue was subjected to purification through column chromatography to get the desired product as a viscous liquid in 95% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H, triazole ring **CH**), 8.18 (s, 1H, triazole ring **CH**), 7.96 (d, *J* = 8 Hz ,4H, aromatic **CH**), 6.94(d, *J* = 8 Hz , 4H, aromatic **CH**), 5.40 (s, 4H, -OC**H$_2$**-N), 5.04–5.03 (m, 2H, N-**CH**$(CH_2)_2$), 4.70-4.55 (m, 4H, **dendron protons**), 4.03-4.01 (t, 4H, Ph-O-C**H$_2$**-), 3.99 – 3.41(m, 20H, **dendron protons**), 1.79– 1.75 (m, 4H, Ph-O-CH_2-C**H$_2$**), 1.48-1.36 (m, 12H, **alkyl protons**); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 167.52, 164.82, 144.07, 143.81, 132.77, 127.40, 126.06, 122.94, 115.32, 78.79, 73.95, 73.67, 72.59, 72.27, 72.10, 71.10, 69.31, 69.25, 64. 15, 62.50, 58.53, 52.28, 52.18, 30.51, 30.34, 30.17, 27.02; IR (Neat) ν_{max}: 3662, 3340, 2924, 1707, 1604 cm^{-1}.

*1.3.9 Synthesis of bolaamphiphile Bola-[G2.0] (**13**)*



To a solution of polyglycerol azide (G-2) (2.86 g, 2.55mmol) and di(prop-2-yn-1-yl)4,4'-(decane-1,10-diylbis(oxy))dibenzoate (0.5 g, 1.01mmol) in 2:1 THF:water mixture (20 ml), $CuSO_4.5H_2O$ (0.1 g, 0.4 mmol) and sodium ascorbate (0.16 g, 0.6 mmol) were added and the reaction mixture was stirred at room temperature for 12 h. The progress of the reaction was monitored by TLC, after completion of the reaction as indicated by TLC using methanol/chloroform (1:4), THF and water was evaporated under reduced pressure and the crude product was suspended in water (150 mL) and extracted with $CHCl_3$ (3 x 30 ml). The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The obtained residue was subjected to purification through column chromatography to get the desired product as a viscous liquid in 95% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (s, 1H, , triazole ring **CH**), 8.24 (s, 1H, , triazole ring **CH**), 7.98-7.96 (d, *J* = 8.8 Hz, 4H, aromatic **CH**), 6.97-6.96 (d, *J* = 8.8 Hz, 4H, aromatic **CH**), 5.42 (s, 4H, -OC**H$_2$**-N), 5.03-4.98 (m, 2H, N-C**H**$(CH_2)_2$), 4.15-3.39 (m, 68H, **dendron protons**), 1.79-1.76 (m, 4H, Ph-O-CH_2-C**H$_2$**), 1.49-1.35 (m, 12H, **alkyl protons**); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 167.52, 164.84, 143.79, 132.81, 126.14, 122.99, 115.37, 80.01, 79.68, 73.91, 73.62, 72.47, 72.41, 72.19, 71.99, 71.28, 70.40, 69.35, 64.44, 63.15, 62.85, 62.49, 58.57, 30.55, 30.39, 30.21, 27.05.; IR(Neat) ν_{max}: 3662, 3381, 2926, 2858, 1712, 1604 cm^{-1}.

NMR and GPC data

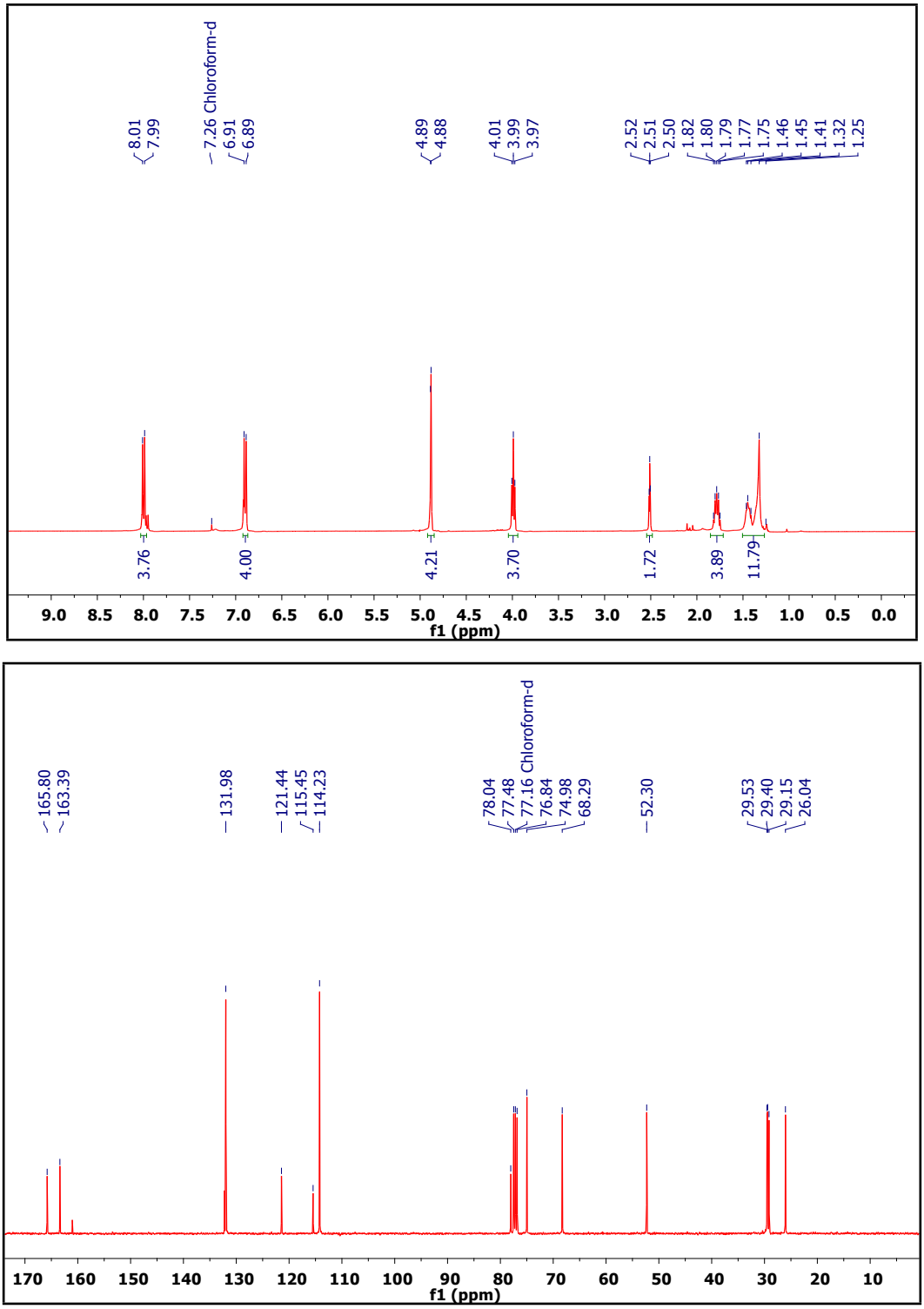


Figure S1. ^{1}H and ^{13}C NMR spectra of di(prop-2-yn-1-yl) 4,4'-(decane-1,10-diylbis(oxy))dibenzoate.

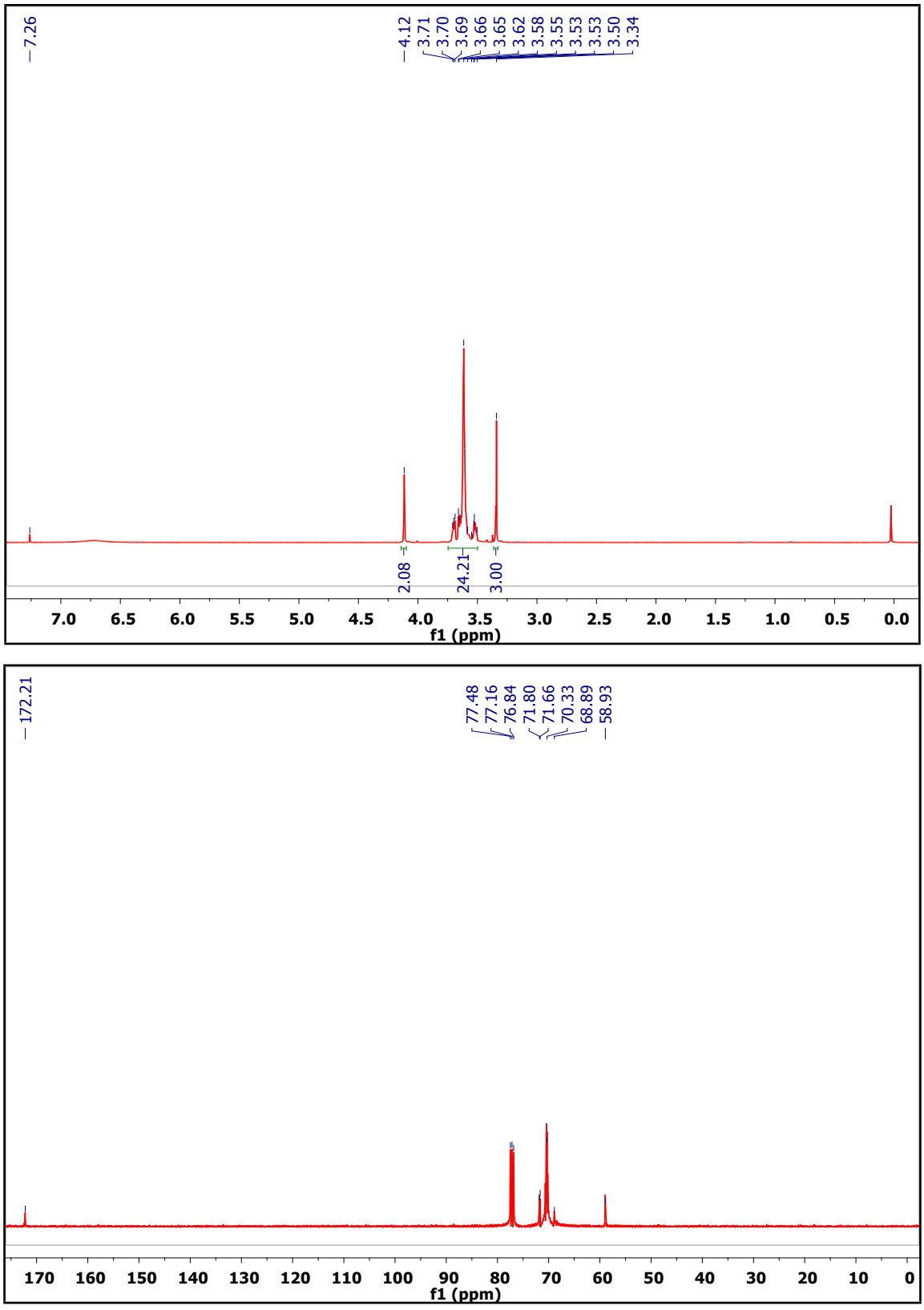


Figure S2. ^{1}H and ^{13}C NMR spectra of methoxypolyethylene glycol carboxymethyl ether.

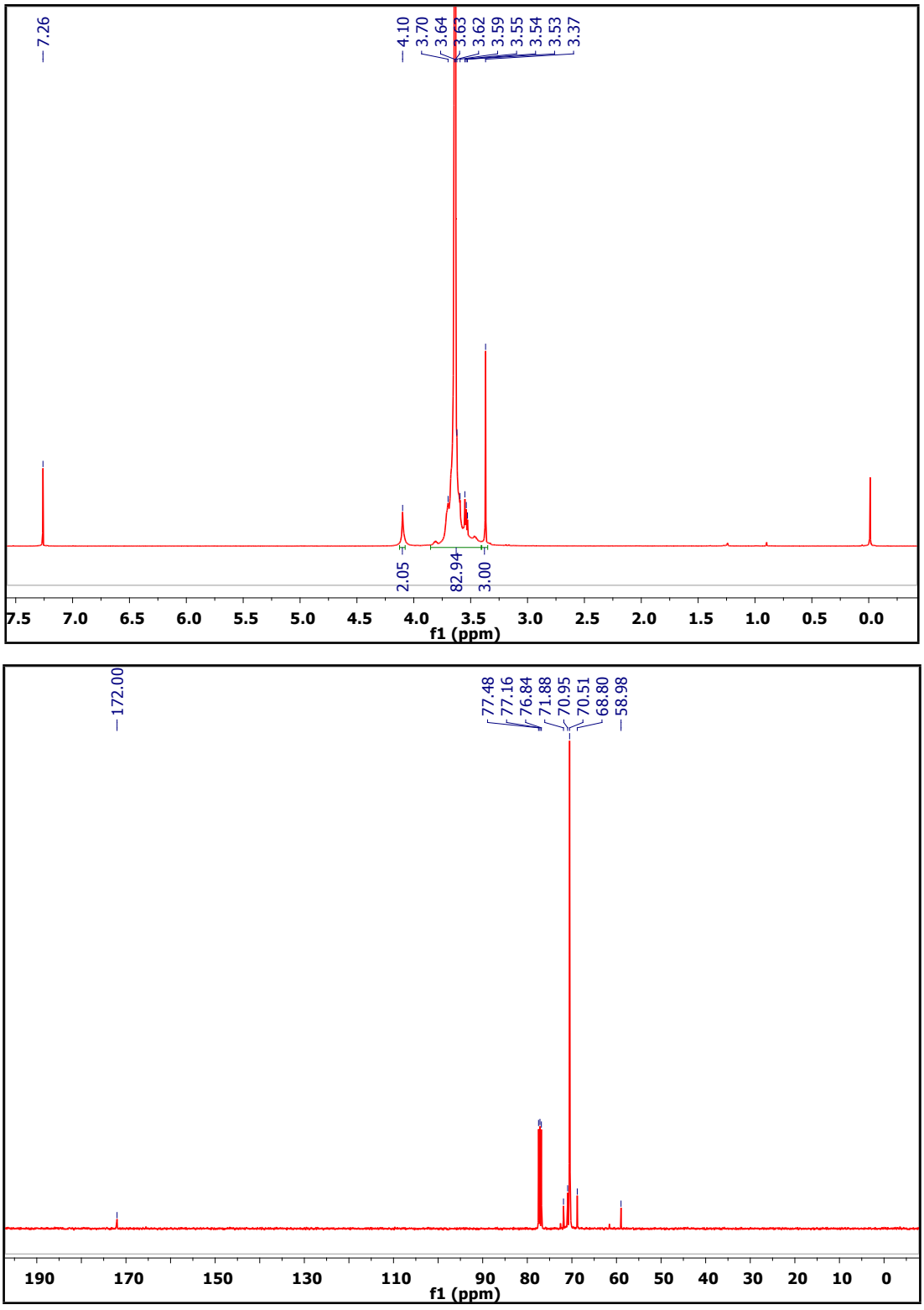


Figure S3. ^{1}H and ^{13}C NMR spectra of methoxypolyethylene glycol carboxymethyl ether.

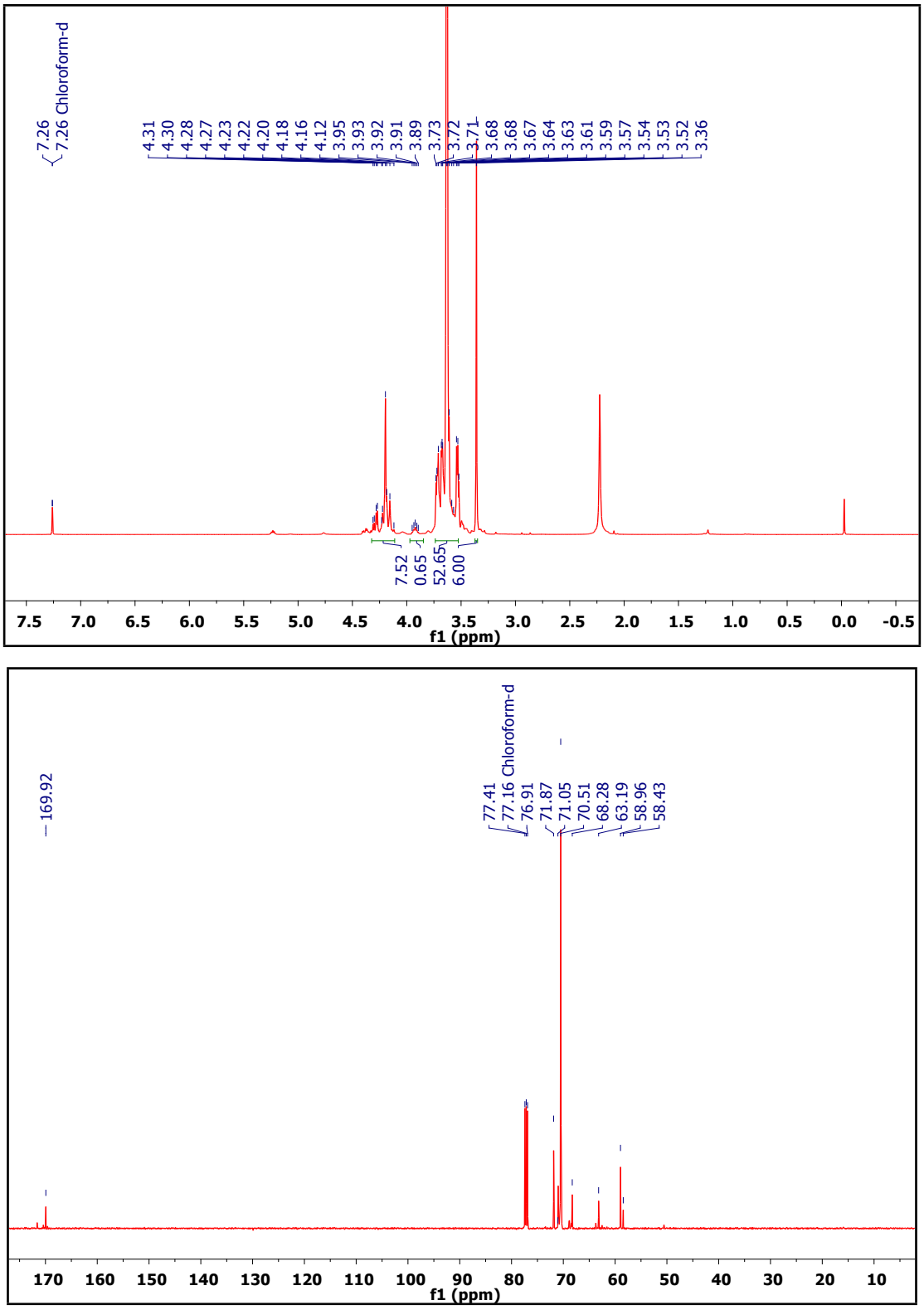


Figure S4. ^{1}H and ^{13}C NMR spectra of 2-azidopropane-1,3-diyl bis(methoxypoly(oxyethylene)oate).

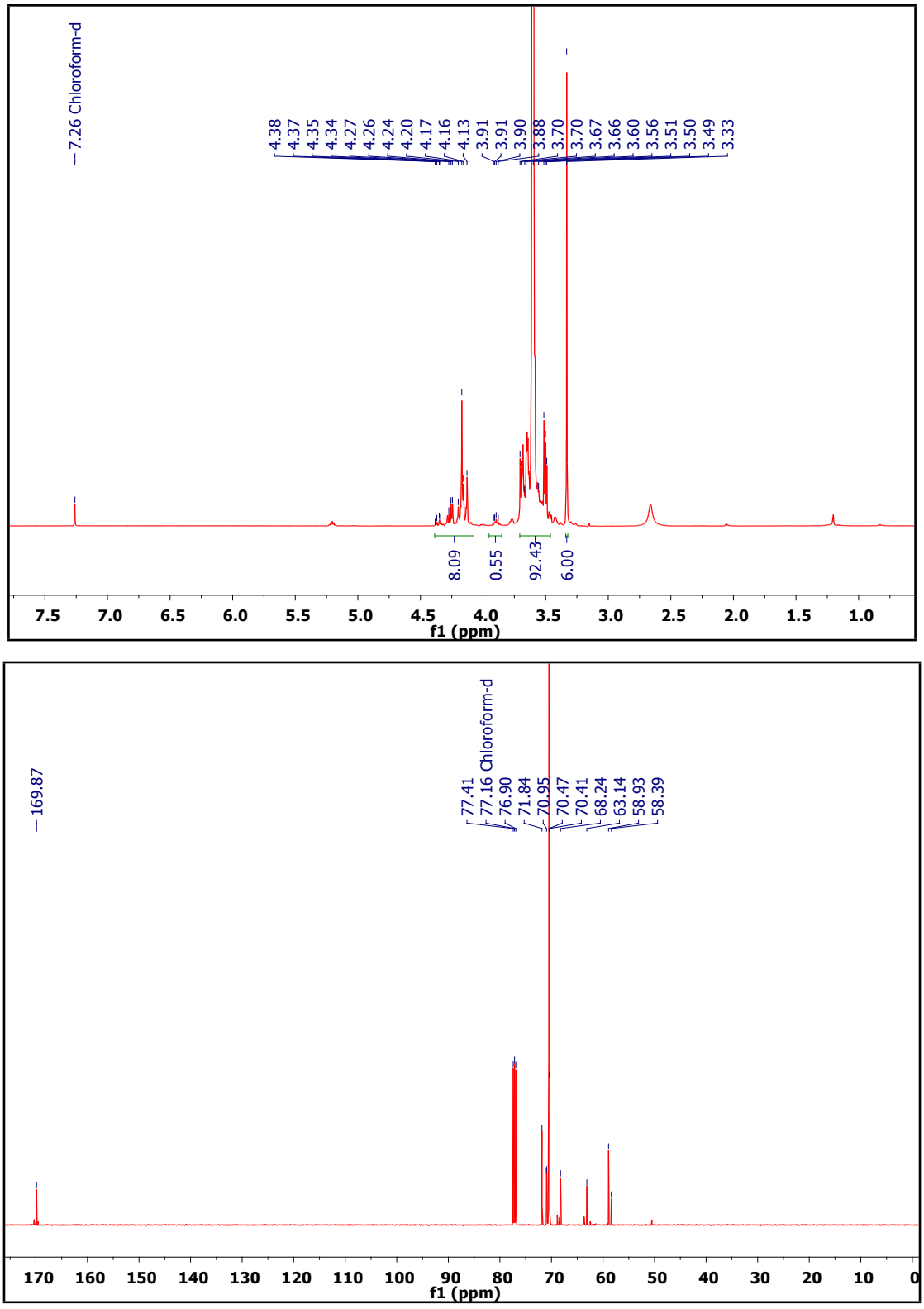


Figure S5. ^{1}H and ^{13}C NMR spectra of 2-azidopropane-1,3-diyl bis(methoxypoly(oxyethylene)oate)

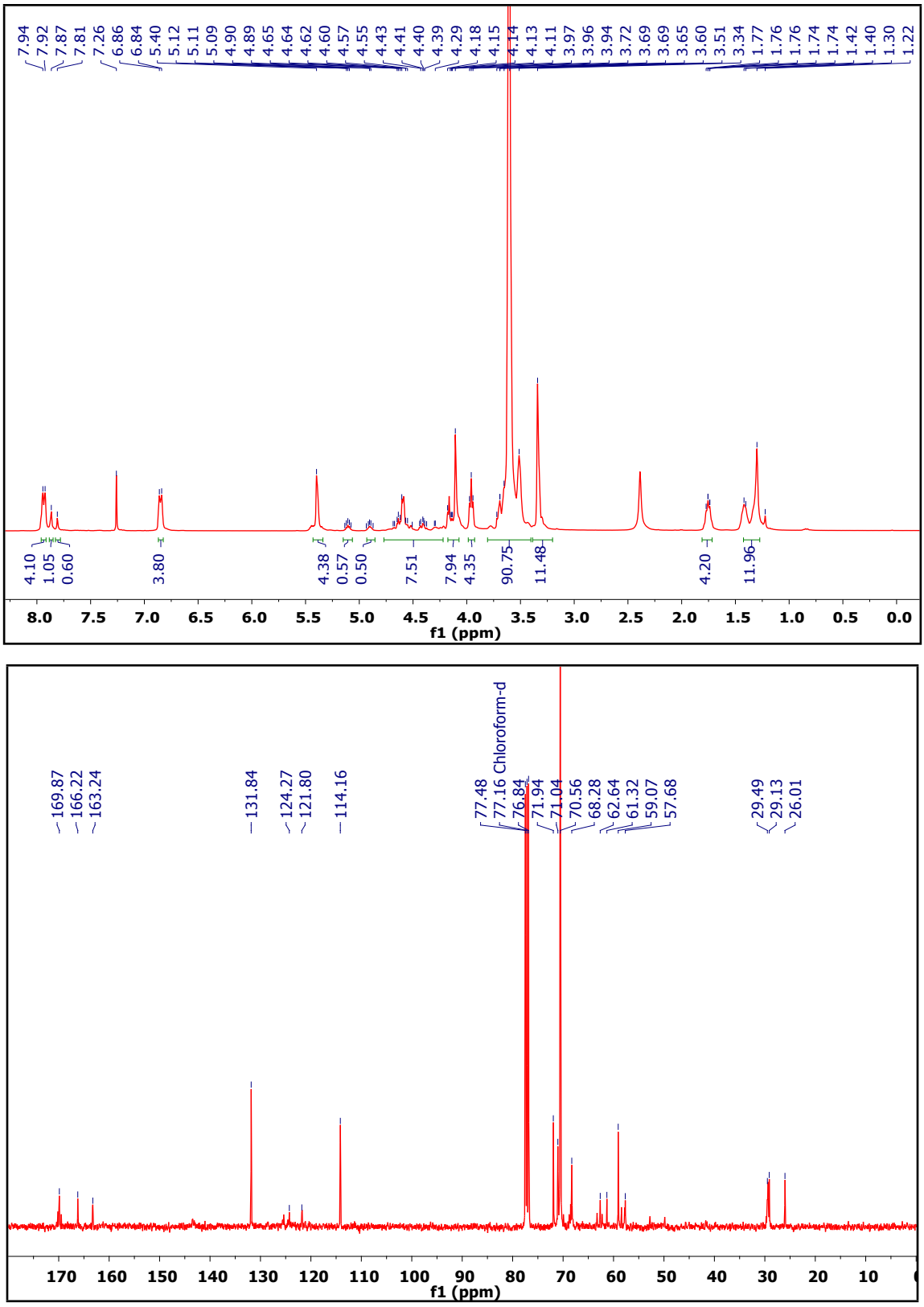


Figure S6. ^{1}H and ^{13}C NMR spectra of Bola-PEG_6.

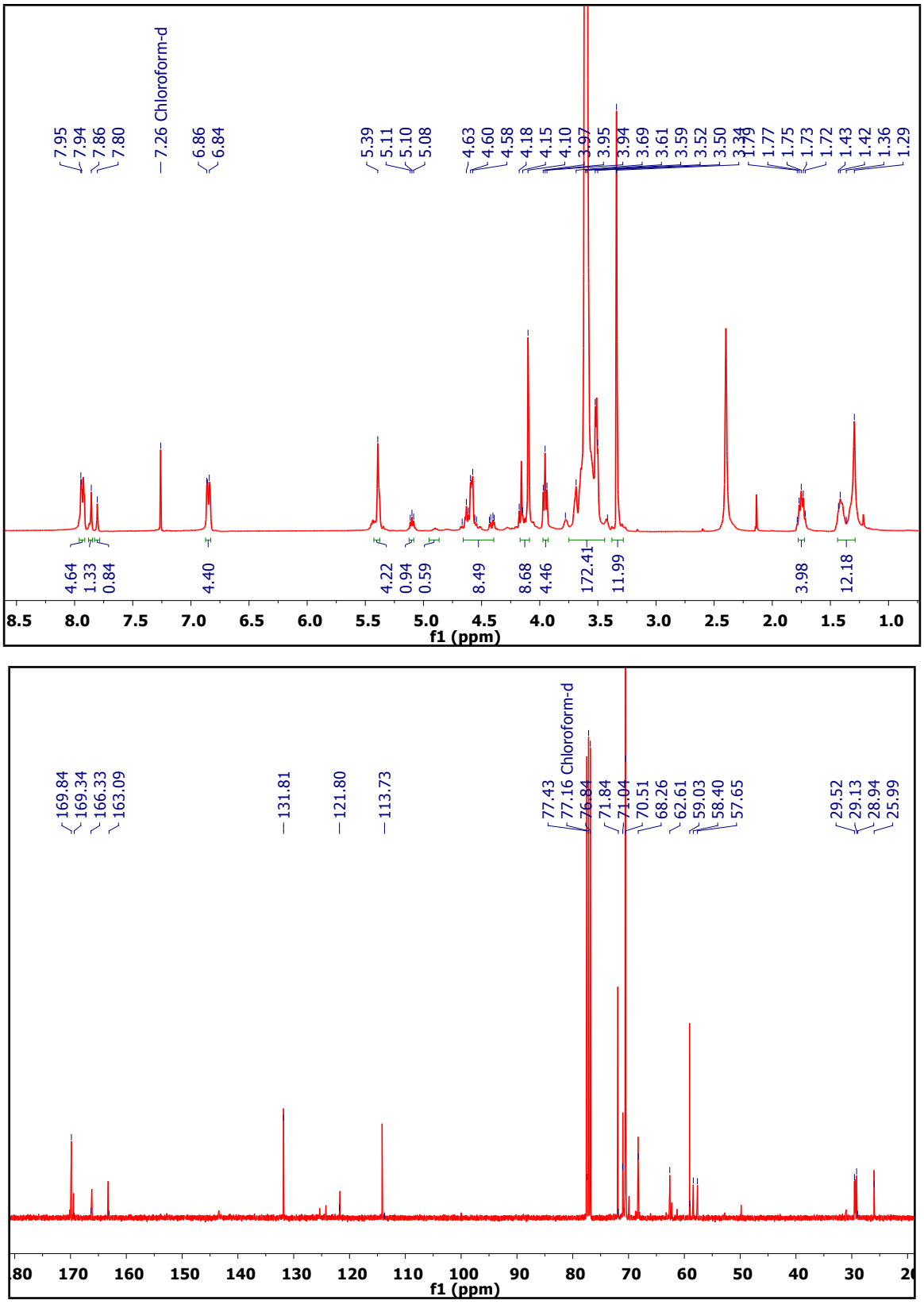


Figure S7. ^{1}H and ^{13}C NMR spectra of Bola-PEG_{10}**.**

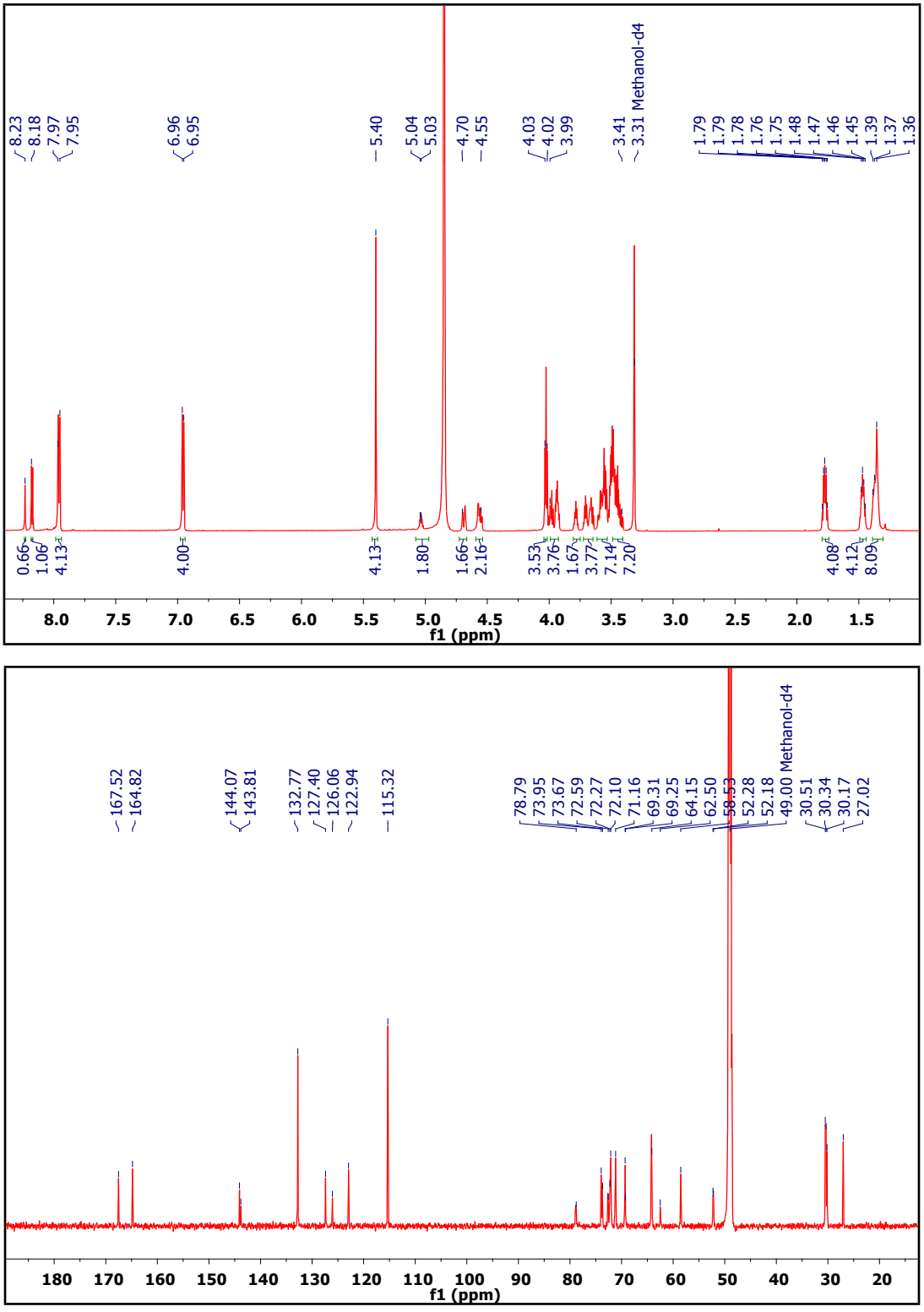


Figure S8. ^{1}H and ^{13}C NMR spectra of Bola-[G1.0]**.**

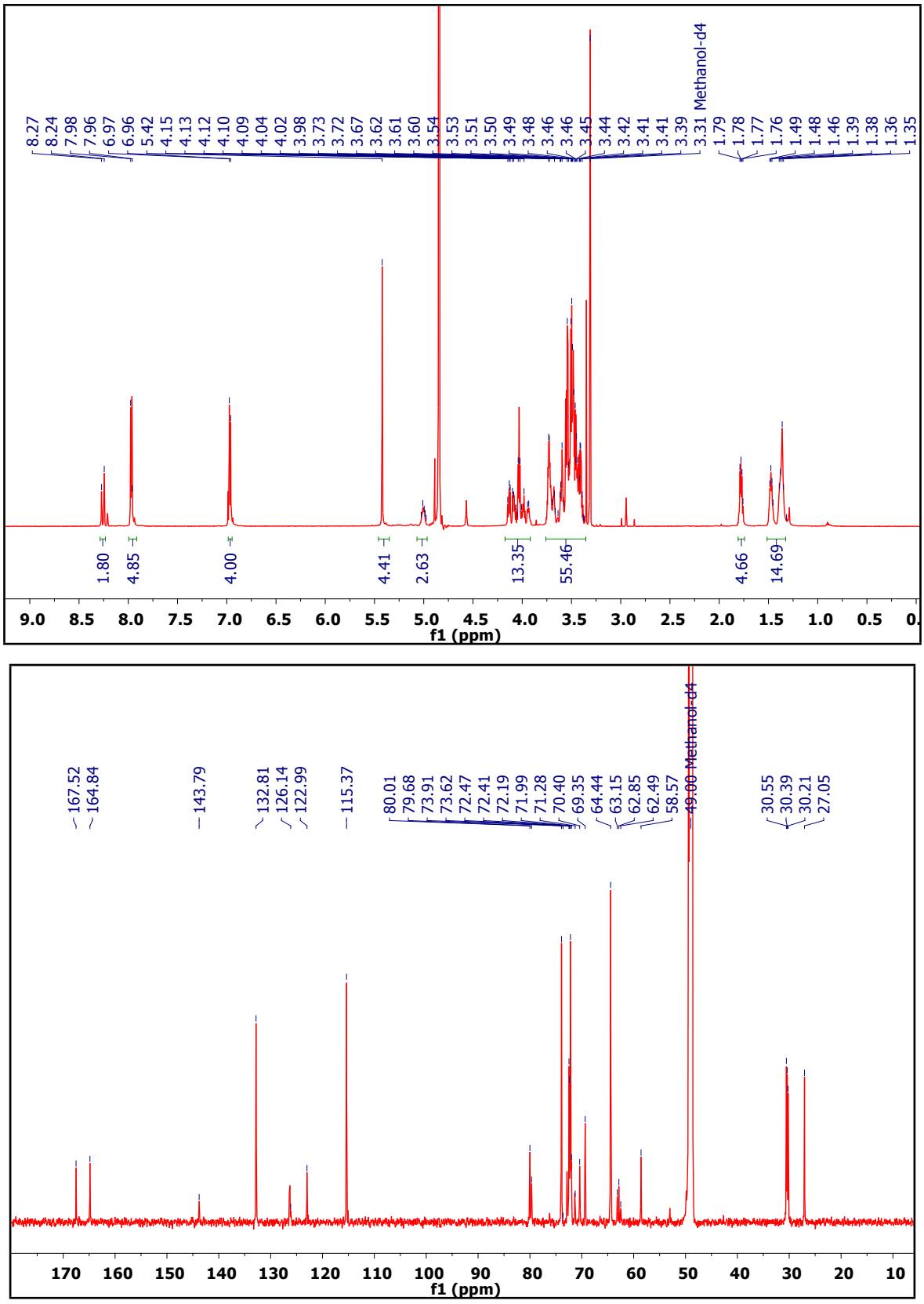


Figure S9. ^{1}H and ^{13}C NMR spectra of Bola-[G2.0]

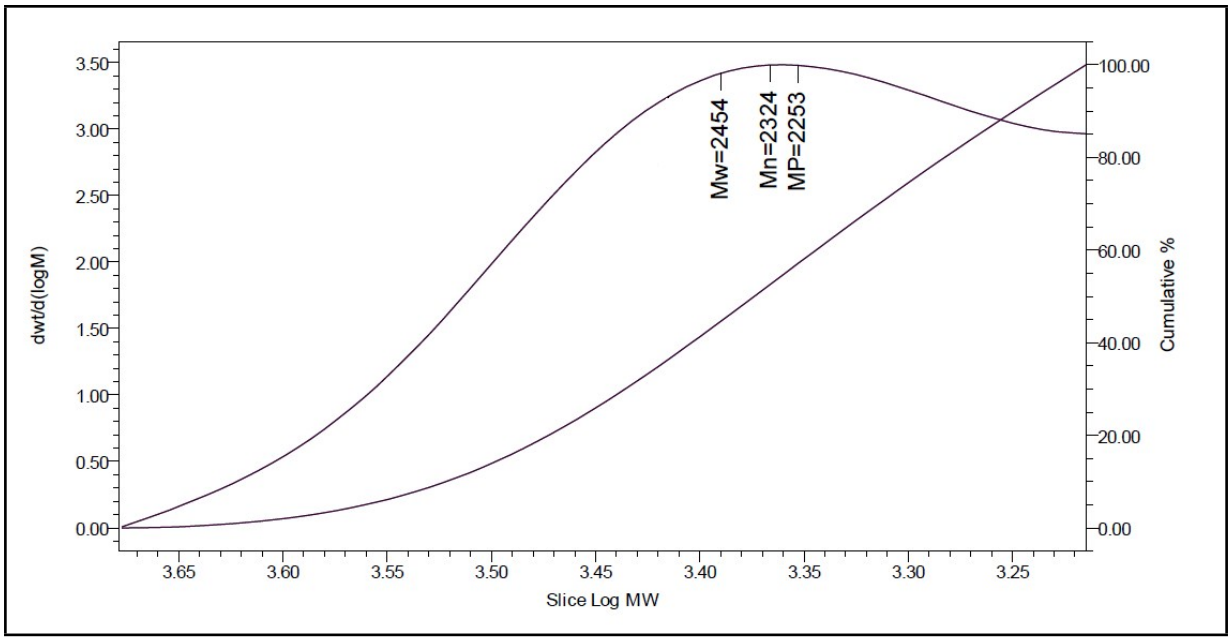


Figure S10. Gel permeation chromatography of Bola-PEG$_6$.

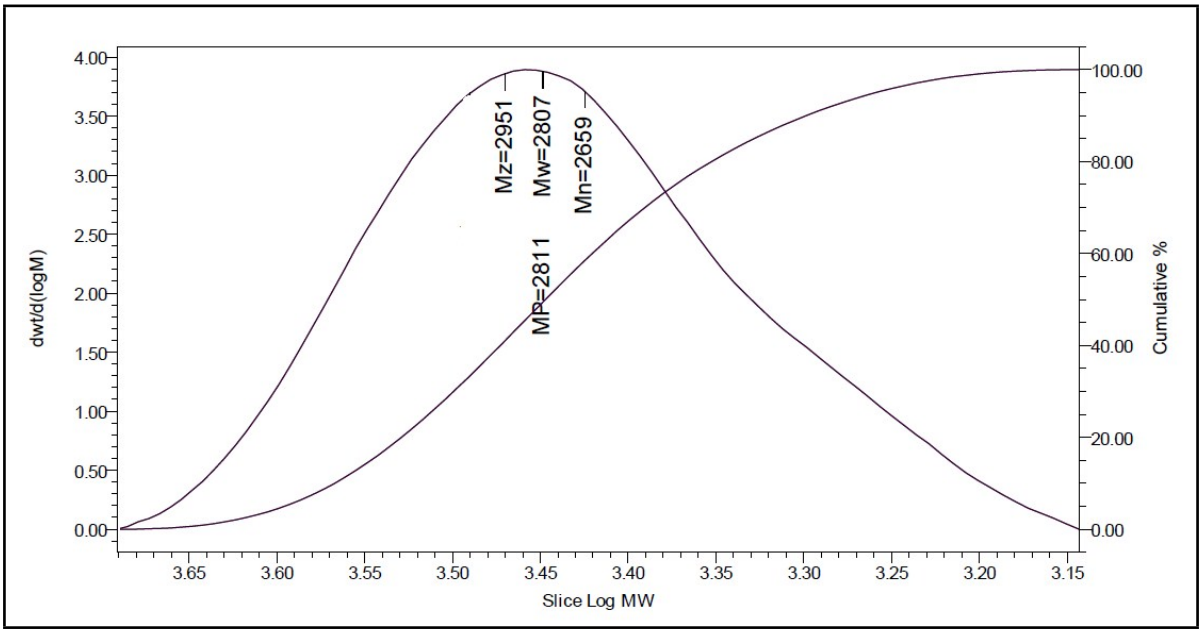


Figure S11. Gel permeation chromatography of Bola-PEG$_{10}$.

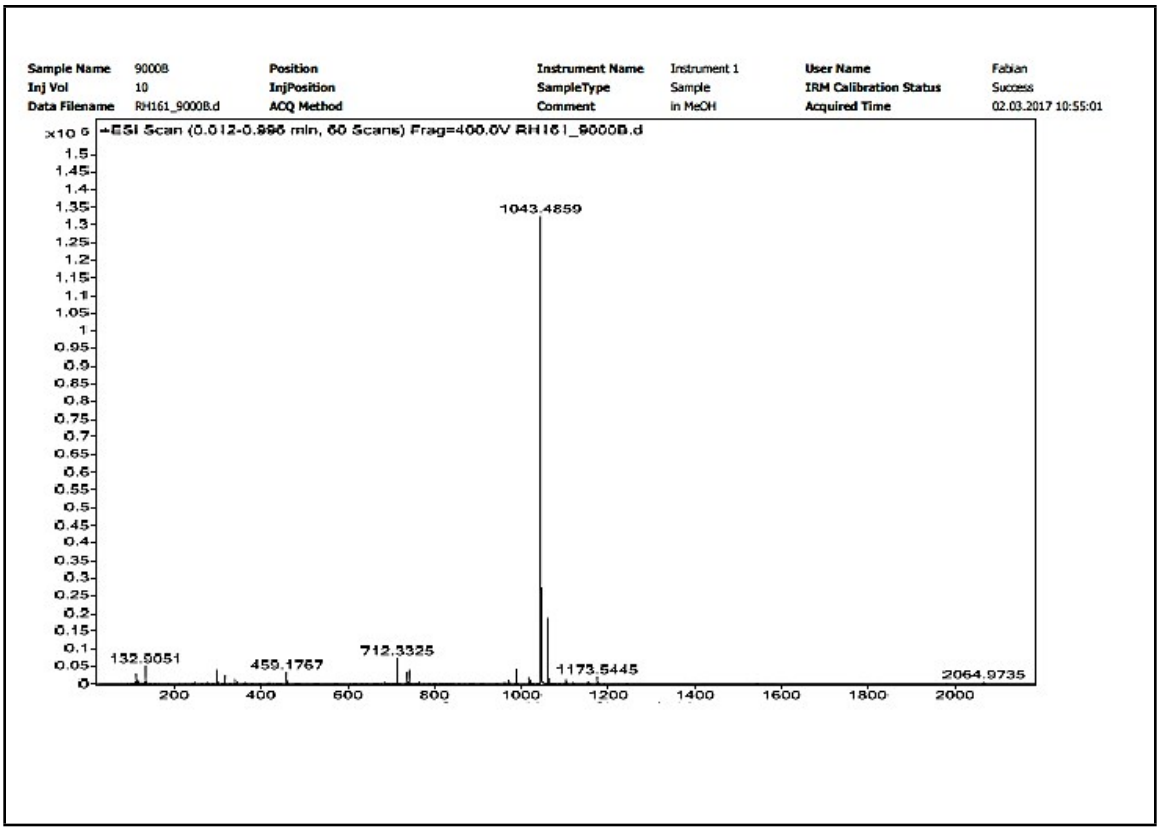


Figure S12: HRMS of Bola-[G1.0].

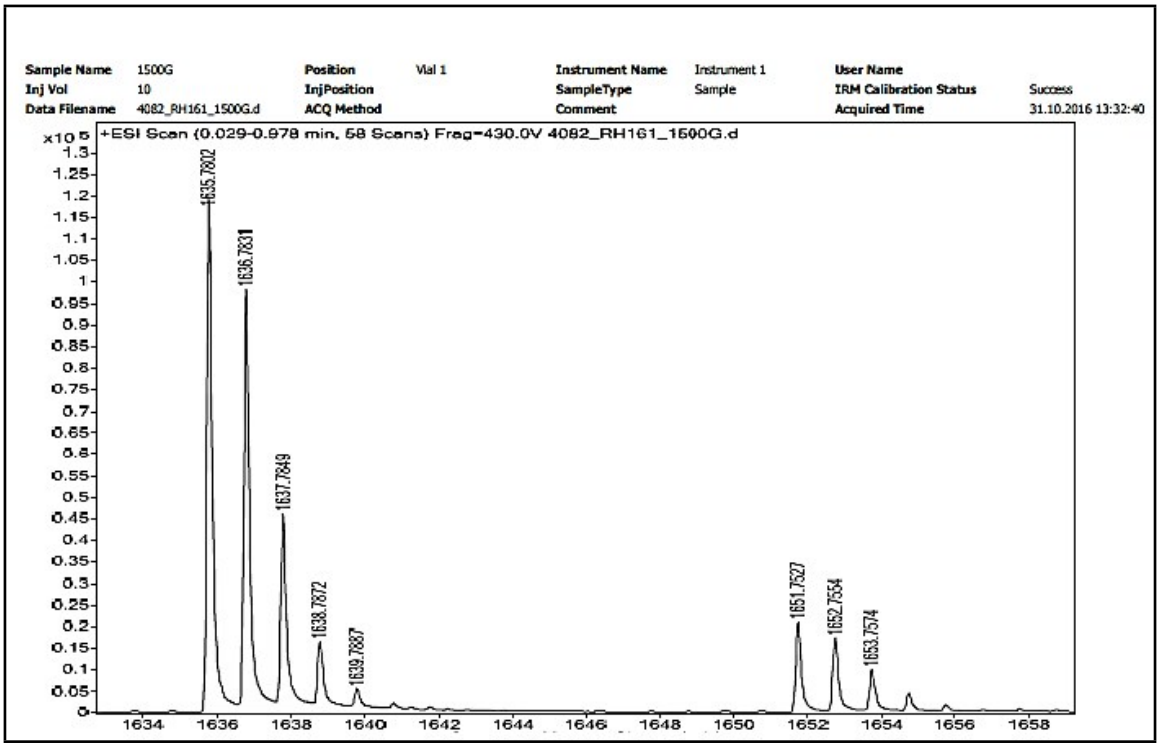


Figure S13: HRMS of Bola-[G2.0].

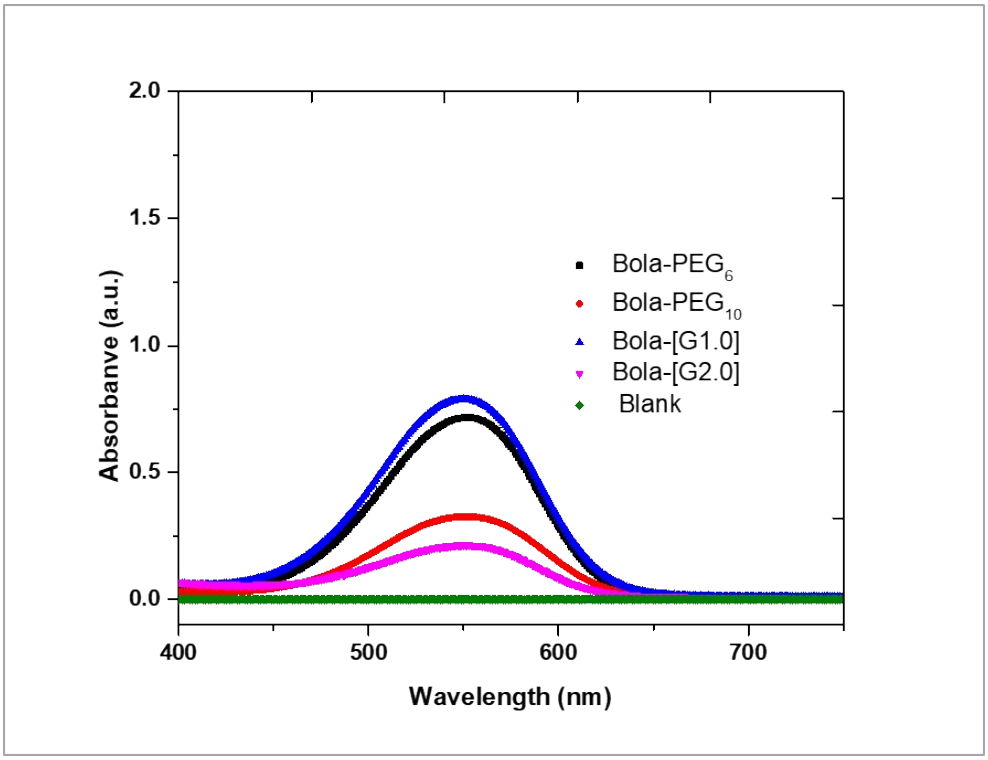


Figure S14. UV Absorbance spectra of Nile red in methanol.

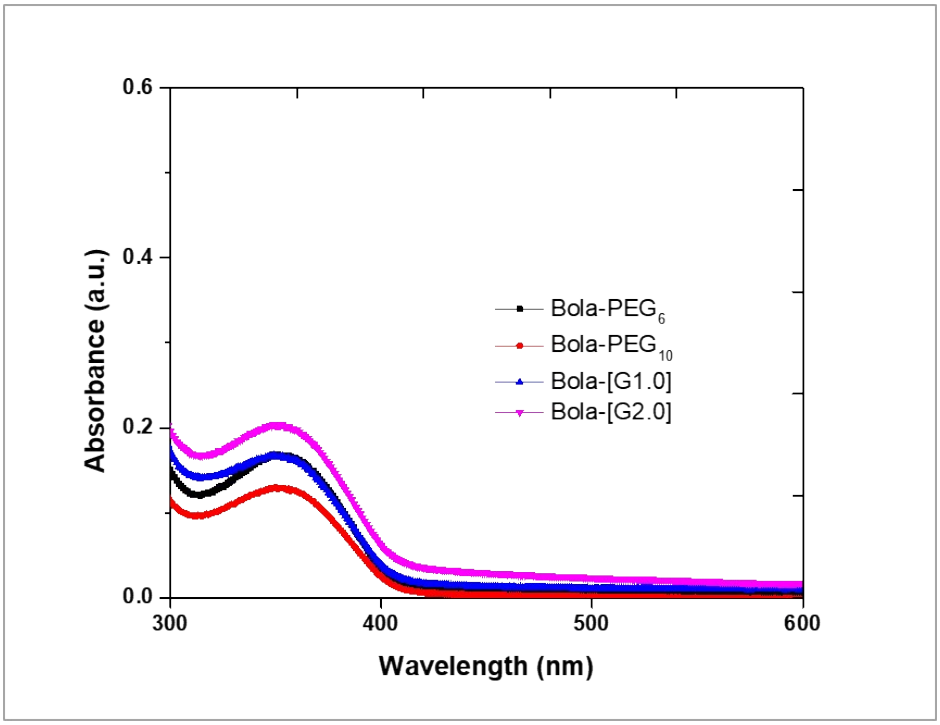


Figure S15. UV Absorbance spectra of Nimodipine in ethanol.

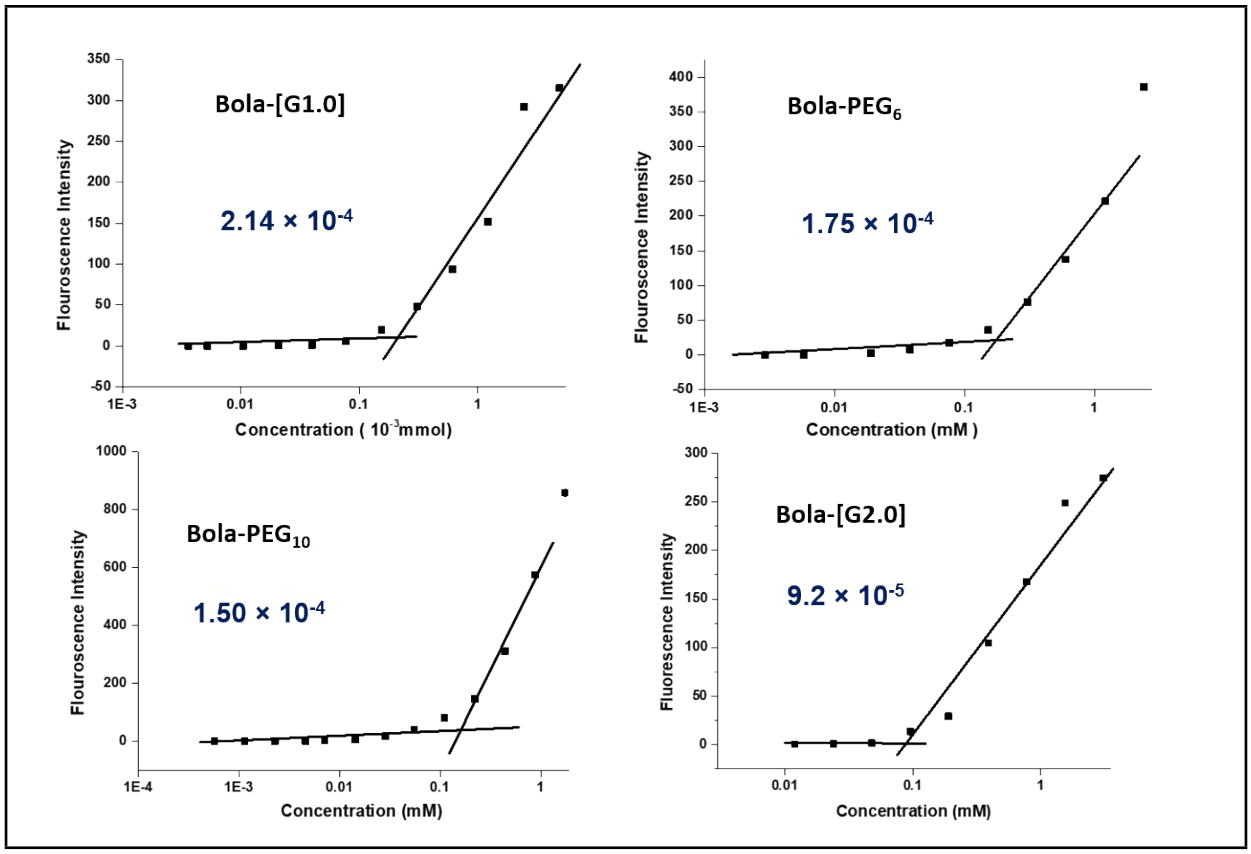


Figure S16, Plot of fluorescence intensity *versus* concentration for calculating critical aggregation concentration.