Supporting Information for

"Single-Single" Amphiphilic Janus Dendrimers Self-Assemble into Uniform Dendrimersomes with Predictable Size

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1 Materials

4-(Dimethylamino)pyridinium 4-toluenesulfonate (DPTS) was prepared according to a literature procedure.[1] All other reagents were obtained from commercial sources and used without purification unless otherwise stated. CH_2Cl_2 was dried over CaH_2 and freshly distilled before use. DMF was dried from CaH_2 or ninhydrin, distilled, and kept over molecular sieves prior to use. THF was distilled over Na/benzophenone immediately before use. Solvents and reagents were deoxygenated when necessary by purging with nitrogen. Milli-Q water obtained by Milli-Q UV plus with the resistivity 18.2 MΩcm was used for vesicle preparation.

2 Techniques

^{1}H NMR and ^{13}C NMR spectra were recorded at 500 MHz and 126 MHz, respectively, on a Bruker DRX (500 MHz) NMR spectrometer. All NMR spectra were measured at 25°C in the indicated deuterated solvents. Proton and carbon chemical shifts (δ) are reported in ppm and coupling constants (J) are reported in Hertz (Hz). The resonance multiplicity in the ^{1}H NMR spectra are described as "s" (singlet), "d" (doublet), "t" (triplet), "quint" (quintet) and "m" (multiplet) and broad resonances are indicated by "br". Residual protic solvent of $CDCl_3$ (^{1}H, δ 7.27 ppm; ^{13}C, δ 77.0 ppm (central resonance of the triplet)), and D_2O (^{1}H, δ 4.67 ppm and 29.8 ppm for CH_3 of acetone for ^{13}C spectra of de-*O*-

acetylated compounds) and tetramethylsilane (TMS) were used as the internal reference in the ^{1}H- and ^{13}C-NMR spectra. The absorptions are given in wavenumbers (cm^{-1}). Evolution of the reaction was monitored by thin-layer chromatography using silica gel 60 F_{254} precoated plates (E. Merck) and compounds were visualized by 254 nm light. Purifications by flash column chromatography were performed using flash silica gel from Silicycle (60 Å, 40-63 μm) with the indicated eluent. The purity of the products was determined by a combination of thin-layer chromatography (TLC) on silica gel coated aluminium plates (with F253 indicator; layer thickness, 200 μm; particle size, 2-25 μm; pore size 60 Å) and high pressure liquid chromatography (HPLC) using Perkin-Elmer Series 10 high pressure liquid chromatograph equipped with an LC-100 column oven, Nelson Analytical 900 Series integrator data station and two Perkin-Elmer PL gel columns of 5x10-2 and 1x104 Å. THF was used as solvent at the oven temperature of 40 °C. Detection was done by UV absorbance at 254 nm.

2.1 Matrix-Assisted Laser Desorption/Ionization Time of Flight (MALDI-TOF)

MALDI-TOF mass spectrometry was performed on a PerSeptive Biosystem-Voyager-DE (Framingham, MA) mass spectrometer equipped with nitrogen laser (337 μm) and operating in linear mode. Internal calibration was performed using Angiotensin II and Bombesin as standards. The analytical sample was obtained by mixing the THF solution of the sample (5-10 mg/mL) and THF solution of the matrix (2,5-dihydroxybenzoic acid, 10 mg/mL) in a 1/5 v/v ratio. The prepared solution of the sample and the matrix (0.5 μm) was loaded on the MALDI plate and allowed to dry at 23 °C before the plate was inserted into the vacuum chamber of the MALDI instrument. The laser steps and voltages applied were adjusted depending on both the molecular weight and the nature of each analyzed compound.

2.2 Dynamic Light Scattering (DLS)

DLS was performed with a Malvern Instruments particle sizer (Zetasizer® Nano S, Malvern Instruments, UK) equipped with 4mW He-Ne laser 633 nm and avalanche photodiode positioned at 175° to the beam and temperature controlled cuvette holder. Instrument parameters were determined automatically along with measurement times. Experiments were performed in triplicate.

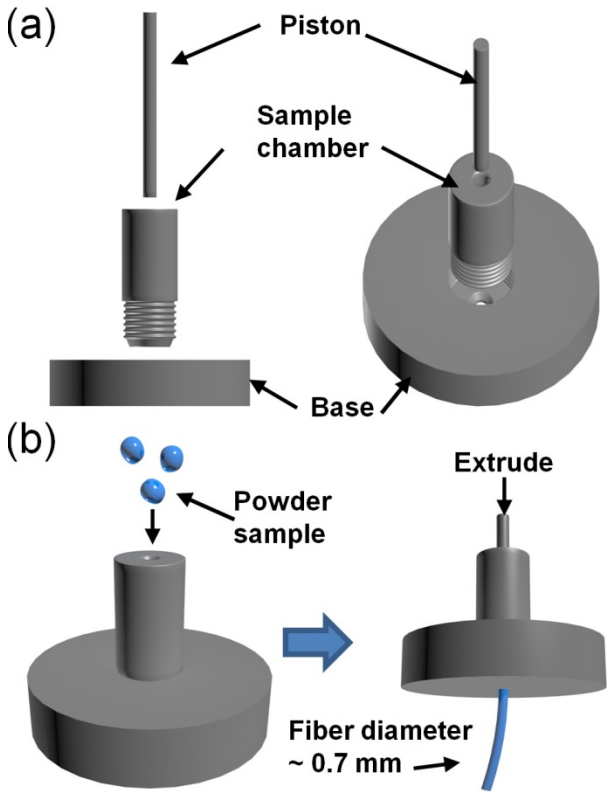
2.3 Cryogenic Transmission Electron Microscopy (Cryo-TEM)

Cryo-TEM was performed on a FEI Technai G2 12 microscope (Hillsboro, Oregon) at voltage of 120 kV. Briefly, a droplet of 1.2 μL dendrimersome solution was pipetted onto a lacey carbon film coated on a copper grid loaded into an FEI Vitrobot apparatus. For some samples the droplet placement and blotting process was repeated in order to obtain suitable specimens for imaging. The sample was allowed to relax for approximately 10 seconds to remove any residual stresses imparted by blotting, then quickly plunged into liquefied ethane (~90 K) cooled by a reservoir of liquid nitrogen to ensure the

vitrification of water. The vitrified samples were transferred to a Gatan 626 cryoholder in a cryo-transfer stage immersed in liquid nitrogen. During the imaging, the cryo-holder was kept below -170 °C to prevent sublimation of vitreous solvent. The digital images were recorded by a Gatan low-dose CCD camera. Image processing and analysis were completed with ImageJ 1.41 software. 3D surface plots of the intensity were created with ImageJ 1.41 for cryo-TEM.

2.4 X-ray Diffraction (XRD) Measurements

X-ray diffraction (XRD) measurements were performed using Cu-K_{α} radiation (λ=1.54178 Å) from a Bruker-Nonius FR-591 rotating anode X-ray source equipped with a 0.2 x 0.2 mm^2 filament operated at 3.4 kW. The radiation from Cu target was collimated and focused with Osmic™ confocal optics followed by circular pinholes, and a Bruker Hi-Star™ multiwire (area) detector was used to detect the scattered radiation. To minimize attenuation and background scattering, an integral vacuum was maintained along the length of the flight tube and within the sample chamber. Samples were held in thin glass capillaries (1.0 mm in diameter), mounted in a temperature-controlled oven (temperature precision: ± 0.1 °C, temperature range from -120 °C to 270 °C). The sample-to-detector distance was kept at 54.0 cm with a q-range of 0.02-0.38 $Å^{-1}$. Fiber samples were prepared for easy loading into capillaries. To prepared the fibers, about 10 mg sample was placed in a temperature controllable custom made extrusion device (see Figure SF1) and extruded at RT into fiber without prior heat treatment. Typically, the fibers have a thickness of ~ 0.3-0.7 mm and a length of ~ 3-7 mm. All XRD measurements were done with the fiber axis perpendicular to the beam direction. XRD peak positions and inter-planar *d*-spacing analysis were performed using Datasqueeze Software (version 3.0) that allows background elimination and Gaussian, Lorentzian, Lorentzian squared, or Voigt peak-shape fitting.



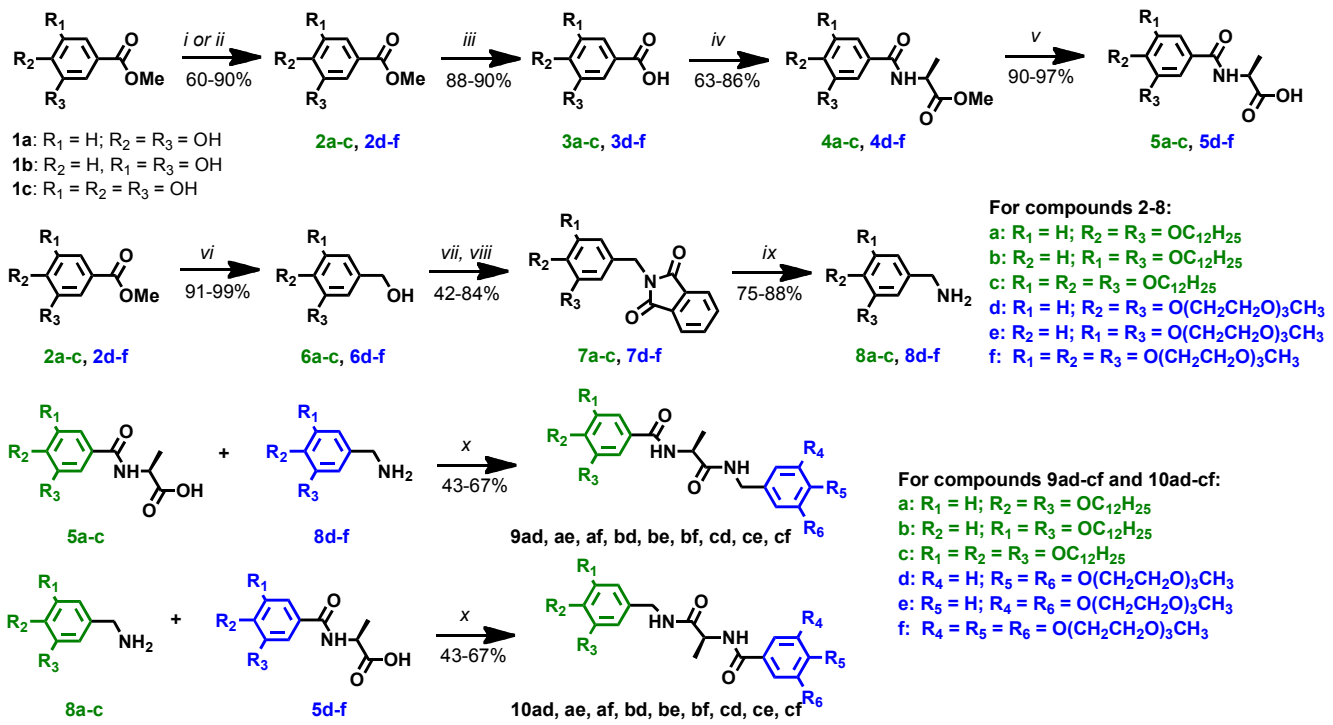
Supporting Figure SF1. The detailed design and parts of the sample extruder (a), and the process of making fiber sample from powder (b).

3 Synthesis

3.1 Modular Synthesis of L-Alanine Amide Containing "Single-Single" Amphiphilic Janus Dendrimers

3,4-Bis(dodecyloxy)benzoic acid (**3a**), 3,5-bis(dodecyloxy)benzoic acid (**3b**), 3,4,5-tris(dodecyloxy)benzoic acid (**3c**), 3,4-bis(methyl triethylene glycol) benzoic acid (**3d**), 3,5-bis(methyl triethylene glycol)benzoic acid (**3e**), 3,4,5-tris(methyl triethylene glycol)benzoic acid (**3f**) 3,4-bis(dodecyloxy)benzenemethanol (**6a**), 3,5-bis(dodecyloxy)benzenemethanol (**6b**), and 3,4,5-tris(dodecyloxy)benzenemethanol (**6c**) were prepared according to literature procedures.[2,3,4]

Supporting Scheme S1. Synthesis of L-Alanine Amide Containing Amphiphilic Janus Dendrimers[a]



[a]Reagents and conditions: *(i)* $C_{12}H_{25}Br$, K_2CO_3, DMF, KI, 80 °C, 8 h; *(ii)* $TsO(CH_2CH_2O)_3CH_3$, K_2CO_3, DMF, KI, 80 °C, 8 h; *(iii)* KOH, EtOH:H_2O, reflux, 1-4 h; *(iv)* $CH_3CH(NH_2)COOCH_3 \cdot HCl$, CDMT, NMM, THF, 23 °C, 6-8 h; *(v)* KOH, EtOH:H_2O, reflux, 1-4 h; *(vi)* $LiAlH_4$, THF, 0 °C to 23 °C, 4-6 h; *(vii)* $SOCl_2$, DCM, 0 °C to 23 °C, 2 h; *(viii)* Potassium phthalimide, THF/DMF, 0 °C, 4 h; *(ix)* $NH_2NH_2 \cdot H_2O$, EtOH:THF = 2:1, reflux, 8 h; *(x)* CDMT, NMM, THF, 23 °C, 8 h.

3.1.1 Synthesis of the First Generation L-Ala Containing Dendritic Acids 5a-f

General Synthetic Procedure for Compounds 4a-f. Compounds 3a-f (1eq), HCl•L-AlaOMe (1eq) and CDMT (1eq) were dissolved in DCM or THF and cooled to 0 °C. NMM (2.5 eq) was added dropwise. The ice bath was then removed and the reaction was maintained at 23 °C during 6-8 h. The reaction mixture was filtered through Celite and the solvent was distilled. The crude product was purified by column chromatography (SiO2) with MeOH/DCM = 1: 9.

(3,4)12G1-L-Ala-OMe (4a). From **3,4-12G1-COOH (3a)** (0.35 g, 0.713 mmol, 1 eq) and HCl•L-AlaOMe (0.10 g, 0.713 mmol, 1 eq), 0.32 g (78 %) of the **(3,4)12G1-L-AlaOMe** were obtained as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 2.0 Hz, 1H), 7.30 (m, J = 8.3, 2.0 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 6.61 (d, J = 7.1 Hz, 1H), 4.79 (quint, J = 7.1 Hz, 1H), 4.05-4.02 (m, 4H), 3.79 (s, 3H), 1.90-1.75 (m, 4H), 1.51 (d, J = 7.1 Hz, 3H), 1.48-1.44 (m, 4H), 1.35-1.26 (m, 32H), 0.88 (t, J = 6.9

Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.88, 166.55, 152.13, 148.92, 126.22, 119.87, 112.82, 112.17, 77.41, 77.16, 76.91, 69.24, 69.06, 52.39, 48.46, 31.94, 29.71, 29.67, 29.65, 29.63, 29.60, 29.59, 29.57, 29.43, 29.38, 29.24, 29.16, 26.02, 22.69, 18.39, 14.09. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{35}H_{61}NO_5Na$, 598.86, found 599.21

(3,5)12G1-L-Ala-OMe (**4b**). From **3,5-12G1-COOH** (**3b**) (0.44 g, 0.897 mmol, 1 eq) and HCl•L-AlaOMe (0.13 g, 0.897 mmol, 1 eq), 0.42 g (81 %) of the **(3,5)12G1-L-AlaOMe** were obtained. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 2.0 Hz, 1H), 7.29 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 4.77 (quint, *J* = 7.2 Hz, 1H), 4.01 (dt, *J* = 6.7, 2.4 Hz, 4H), 3.77 (s, 4H), 1.82 (m, 4H), 1.51 (d, *J* = 7.1, 3H), 1.45 (m, 4H), 1.34-1.25 (m, 36H), 0.87 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.00, 166.61, 152.29, 149.09, 126.42, 119.84, 112.94, 112.35, 69.45, 69.24, 52.62, 48.58, 32.65, 29.82, 29.78, 29.75, 29.53, 29.49, 29.34, 29.25, 26.11, 22.81, 18.77, 14.22. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{35}H_{61}NO_5Na$, 598.86, found 598.33

(3,4,5)12G1-L-Ala-OMe (**4c**). From **3,4,5-12G1-COOH** (**3a**) (0.53 g, 0.785 mmol, 1 eq) and HCl•L-AlaOMe (0.11 g, 0.785 mmol, 1 eq), 0.46 g (76 %) of the **(3,4,5)12G1-L-AlaOMe** were obtained as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (s, 2H), 6.83 (d, *J* = 7.23 Hz, 1H), 4.74 (quint, *J* = 7.27 Hz, 1H), 3.96 (s, 3H), 1.76-1.71 (m, 6H), 1.48 (d, *J* = 7.21, 3H), 1.44 (quint, *J* = 7.42, 4H), 1.34-1.24 (m, 48H), 0.87 (t, *J* = 6.56, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.91, 166.77, 153.13, 141.46, 128.73, 105.90, 77.42, 77.16, 76.91, 73.50, 69.36, 52.52, 48.60, 32.01, 30.40, 29.81, 29.78, 29.73, 29.66, 29.45, 26.16, 22.76, 16.49, 14.15. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{47}H_{85}NO_6Na$, 783.18, found 783.24.

(3,4)-3EOMe$_2$-G1-L-AlaOMe (**4d**). From 3,4-bis(methyl triethylene glycol)benzoate (**3d**) (1.04 g, 1.96 mmol, 1 eq), 0.77 g (76%) of the **(3,4)-3EOMe$_2$-G1-L-AlaOMe** (**4d**) were obtained as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.39 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.13 (d, *J* = 6.8 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 4.72 (p, *J* = 6.9 Hz, 1H), 4.19 (t, *J* = 4.7 Hz, 4H), 3.88-3.84 (m, 4H), 3.77-3.70 (m, 4H), 3.69-3.60 (m, 8H), 3.56-3.53 (m, 4H), 3.37 (s, 1H), 3.36 (s, 1H), 1.52 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.23, 167.13, 152.07, 148.54, 126.42, 120.95, 113.77, 113.09, 77.41, 77.41, 77.16, 77.16, 76.91, 76.91, 71.88, 70.85, 70.73, 70.64, 70.59, 70.46, 70.38, 69.69, 69.55, 68.93, 68.63, 58.96, 58.91, 48.70, 18.07. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{25}H_{41}NO_{11}Na$, 554.59, found 554.45.

(3,5)-3EOMe$_2$-G1-L-AlaOMe (**4e**). From 3,5-bis(methyl triethylene glycol)benzoate (**3e**) (0.55 g, 1.23 mmol, 1 eq), HCl•L-AlaOMe (0.17 g, 1.23 mmol, 1 eq), CDMT (0.22 g, 1.23 mmol, 1 eq), NMM (0.31 g, 3.08 mmol, 2,5 mmol) in THF (12 mL), 0.41 g (63 %) of the **(3,5)-3EOMe$_2$-G1-L-AlaOMe** were obtained. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (d, *J* = 7.2 Hz, 1H), 6.86 (d, *J* = 2.1 Hz, 2H), 6.50 (t, *J* =

2.0, 1H), 4.61 (p, J = 7.2 Hz, 1H), 4.06-3.96 (m, 4H), 3.79-3.69 (m, 4H), 3.65 (s, 3H), 3.61 (dd, J = 5.9, 3.6 Hz, 4H), 3.56-3.52 (m, 8H), 3.43 (dd, J = 5.7, 3.7 Hz, 4H), 3.25 (s, 6H), 1.39 (d, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.98, 167.10, 159.81, 135.58, 105.93, 105.13, 77.42, 77.42, 77.16, 77.16, 76.91, 76.91, 71.77, 70.64, 70.47, 70.34, 69.51, 67.57, 58.84, 48.54, 17.90. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{25}H_{41}NO_{11}Na$, 554.59, found 554.65.

(3,4,5)-3EOMe$_3$-G1-L-AlaOMe (**4f**). From 3,4,5-tris(methyl triethylene glycol)benzoate (**3f**) (1.06 g, 1.74 mmol, 1 eq), HCl•L-AlaOMe (0.24 g, 1.74 mmol, 1 eq), CDMT (0.31 g, 1.74, 1 eq), NMM (0.44 g, 4.35 mmol, 2.5 eq) in THF (17 mL), 1.04 g (86 %) of the **(3,4,5)-3EOMe$_3$-G1-L-AlaOMe** were obtained. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, J = 7.1 Hz, 1H), 6.93 (s, 2H), 4.46 (p, J = 7.2 Hz, 1H), 4.00-3.90 (m, 6H), 3.60 (t, J = 4.8 Hz, 4H), 3.58-3.54 (m, 2H), 3.52 (s, 3H), 3.49 (m, 6H), 3.44-3.30 (m, 12H), 3.32-3.29 (m, 6H), 3.14 (s, 3H), 3.12 (s, 6H), 1.26 (d, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.13, 166.03, 151.86, 140.92, 128.23, 106.63, 77.42, 77.16, 76.90, 71.82, 71.39, 71.37, 70.16, 70.13, 70.09, 70.03, 69.96, 69.94, 69.91, 69.16, 68.41, 58.35, 58.32, 51.76, 48.19, 17.10. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{32}H_{55}NO_{15}Na$, 716.78, found 717.50

General Synthetic Procedure of Compounds 5a-f. Compounds **4a-f** were dissolved in EtOH, and KOH pellet (5 eq) was dissolved in 2 mL of water and added. The resulting solution was stirred under reflux at 85 °C for 4 h. The solution was cooled to 23 °C and 200 mL of DCM was added and washed with 200 mL of HCl (1N), then 200 mL of water and finally 200 mL of brine. The organic phase was dried over $MgSO_4$, filtered and concentrated to dryness.

(3,4)12G1-L-Ala-OH (**5a**). From **(3,4)12G1-L-AlaOMe** (**4a**) (0.32 g, 0.557 mmol, 1 eq) and KOH (0.16 g, 2.78 mmol. 5 eq), 0.30 g (96%) of the **(3,4)12G1-L-AlaOH** were obtained. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.30 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 8.4 Hz, 1H), 6.71 (d, J = 6.7 Hz, 1H), 4.77 (quint, J = 7.0 Hz, 1H), 4.02 (dd, J = 6.7, 2.5 Hz, 4H), 1.82 (m, 4H), 1.57 (d, J = 7.1 Hz, 3H), 1.46 (m, 4H), 1.20 (m, 32H), 0.88 (t, J = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.54, 167.71, 152.67, 149.17, 125.69, 120.12, 112.97, 112.37, 69.55, 69.28, 48.98, 29.78, 29.57, 29.51, 29.25, 26.13, 22.83, 18.25, 14.25. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{34}H_{59}NO_5Na$, 584.84, found 585.11

(3,5)12G1-L-Ala-OH (**5b**). From **(3,5)12G1-L-Ala-OMe** (**4b**) (0.42 g, 0.729 mmol, 1 eq) and KOH (0.20 g, 3.647 mmol. 5 eq), 0.40 g (98%) of the **(3,5)12G1-L-AlaOH** were obtained. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (s, 2H), 6.83(d, J = 7.02 Hz, 1H), 6.57 (s, 1H), 4.77 (quint, J = 6.70 Hz, 1H), 3.99-3.94 (m, 4H), 1.75 (m, 4H), 1.56 (d, J = 6.87, 3H), 1.43 (m, 4H), 1.34-1.26 (m, 32H), 0.88 (t, J = 7.02 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.49, 167.83, 160.51, 153.20, 135.45, 106.05, 105.63,

105.00, 73.64, 69.47, 68.44, 32.03, 31.98, 30.42, 29.85, 29.83, 29.78, 29.76, 29.73, 29.70, 29.55, 29.51, 29.49, 29.47, 29.20, 26.22, 26.19, 26.13, 22.79, 18.23, 14.21. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{34}H_{59}NO_5Na$, 584.84, found 584.52

(3,4,5)12G1-L-Ala-OH (**5c**). From **(3,4,5)12G1-L-Ala-OMe** (**4c**) (0.46 g, 0.605 mmol 1 eq) and KOH (0.17 g, 3.03 mmol. 5 eq), 0.42 g (92%) of the **(3,4,5)12G1-L-AlaOH** were obtained. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.98 (s, 2H), 6.71 (d, *J* = 6.72 Hz, 1H), 4.72 (quint, *J* = 6.55 Hz, 1H), 3.98 (t, 6.23 Hz, 6H), 1.79-1.73 (m, 6H), 1.56 (d, *J* = 7.03 Hz, 3H), 1.54 (m, 6H), 1.36-1.26 (m, 48H), 0.88 (t, *J* = 6.50 Hz, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.81, 153.30, 141.86, 128.31, 106.09, 73.69, 69.58, 32.09, 20.48, 29.87, 29.81, 29.75, 29.59, 29.53, 26.26, 22.84, 18.19, 14.26. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{46}H_{83}NO_6Na$, 769.16, found 768.45.

(3,4)-3EOMe$_2$-G1-L-AlaOH (**5d**). From **(3,4)-3EOMe$_2$-G1-L-AlaOMe (4d)** (1.04 g, 1.96 mmol, 1 eq), KOH (0.55 g, 9.78 mmol. 5 eq), 0.97 g (96%) of the **(3,4)-3EOMe$_2$-G1-L-AlaOH** were obtained as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.39 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.13 (d, *J* = 6.8 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 4.72 (p, *J* = 6.9 Hz, 1H), 4.19 (t, *J* = 4.7 Hz, 4H), 3.88-3.84 (m, 4H), 3.77-3.70 (m, 4H), 3.69-3.60 (m, 8H), 3.56-3.53 (m, 4H), 3.37 (s, 1H), 3.36 (s, 1H), 1.52 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.23, 167.13, 152.07, 148.54, 126.42, 120.95, 113.77, 113.09, 77.41, 77.41, 77.16, 77.16, 76.91, 76.91, 71.88, 70.85, 70.73, 70.64, 70.59, 70.46, 70.38, 69.69, 69.55, 68.93, 68.63, 58.96, 58.91, 48.70, 18.07. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{24}H_{39}NO_{11}Na$, 540.56, found 541.09.

(3,5)-3EOMe$_2$-G1-L-AlaOH (**5e**). From **(3,5)-3EOMe$_2$-G1-L-AlaOMe** (**4e**) (0.41 g, 0.77, 1 eq), KOH (0.16 g, 2.82 mmol, 5 eq) in 15 mL EtOH/water, 0.36 g (90 %) of the **(3,5)-3EOMe$_2$-G1-L-AlaOH** were obtained as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 7.0 Hz, 1H), 6.97 (d, *J* = 1.9 Hz, 2H), 6.60 (s, 1H), 4.71 (p, *J* = 7.0 Hz, 1H), 4.18-4.04 (m, 4H), 3.92-3.80 (m, 4H), 3.72 (dd, *J* = 5.7, 3.4, 4H), 3.69-3.60 (m, 8H), 3.60-3.52 (m, 4H), 3.37 (s, 6H), 1.51 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.50, 166.30, 152.34, 141.53, 128.79, 107.13, 77.42, 77.42, 77.16, 77.16, 76.90, 76.90, 72.22, 71.79, 71.76, 70.58, 70.52, 70.49, 70.40, 70.35, 70.33, 69.56, 68.93, 58.81, 58.79, 52.29, 48.46, 17.98. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{24}H_{39}NO_{11}Na$, 540.56, found 540.23.

(3,4,5)-3EOMe$_3$-G1-L-AlaOH (**5f**). From **(3,4,5)-3EOMe$_3$-G1-L-AlaOMe** (**4f**) (1.04 g, 1.5 mmol, 1 eq), KOH (0.42 g, 7.5 mmol, 5 eq) in 50 mL EtOH/water, 0.99 g (97 %) of the **(3,4,5)-3EOMe$_3$-G1-L-AlaOH** were obtained as clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (s, 2H), 4.72-4.63 (m, 1H), 4.17 (t, *J* = 4.8 Hz, 6H), 3.85-3.80 (m, 4H), 3.77 (t, *J* = 4.9 Hz, 2H), 3.70 (m, 6H), 3.63 (m, 14H), 3.55-3.51 (m, 6H), 3.36 (s, 3H), 3.35 (s, 6H), 1.50 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.89, 167.07, 152.28, 141.52, 128.25, 107.17, 77.30, 77.10, 77.05, 76.79, 72.20, 71.75, 71.72, 70.51, 70.47,

70.43, 70.33, 70.29, 70.21, 69.56, 68.81, 58.81, 58.76, 48.67, 17.66. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{31}H_{53}NO_{15}Na$, 702.75, found 702.67.

3.1.2 Synthesis of the First Generation Dendritic Amines 8a-f

General Synthetic Procedure for Compounds 7a-f. Compounds **6a-f** were dissolved in DCM, and thionyl chloride was added dropwise at 0 °C. The reaction mixture was stirred at 23 °C during 3 h, and the solvent was removed under vacuum. The crude product was dissolved in THF (1g crude/10 mL), and potassium phtalimide (1 eq) was dissolved in DMF and added to the reaction mixture. The reaction was heated to 70 °C for 4 h. The reaction mixture was concentrated and purified by column chromatography on silica gel with a mobile phase of EtOAc/Hexanes = 1/9 for **7a-c** or EtOAc/MeOH = 97/3 for **7d-f**.

(3,4)12G1-CH_2-N(CO)$_2$C$_6$H$_5$ (**7a**). From **(3,4)12G1-CH_2-OH** (**6a**) (0.48 g, 1.01 mmol, 1 eq), thionyl chloride (0.13 g, 1,11 mmol, 1.1 eq) in 5 mL of DCM to yield **(3,4)12G1-CH_2-Cl**. **(3,4)12G1-CH_2-Cl** reacted with potassium phthalimide (0.21 g, 1.11 mmol, 1.1 eq) in 10 mL of DMF. The product was purified by column chromatography (EtOAc/Hexane = 1/9) to yield 0.43 g (70%) product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.00 (d, *J* = 2.0 Hz, 1H), 6.97 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 4.75 (s, 2H), 3.99-3.93 (m, 4H), 1.89-1.69 (m, 4H), 1.50-1.16 (m, 38H), 0.88 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.32, 149.34, 149.00, 134.04, 132.36, 129.25, 123.43, 121.56, 114.78, 113.95, 69.47, 69.39, 41.60, 29.82, 29.56, 29.41, 26.16, 22.84, 14.26. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{39}H_{59}NO_4Na$, 628.89, found 629.10.

(3,5)12G1-CH_2-N(CO)$_2$C$_6$H$_4$ (**7b**). From **(3,5)12G1-CH_2-OH** (**6b**) (2 g, 4.19 mmol, 1 eq), thionyl chloride (0.55 g, 4.61 mmol, 1.1 eq) in DCM (20 mL) to yield **(3,5)12G1-CH_2-Cl**. **(3,5)12G1-CH_2-Cl** reacted with potassium phthalimide (0.78 g, 4.19 mmol, 1 eq) in DMF (40 mL). The product was purified by column chromatography (EtOAc/Hexane = 1/9) to yield 2.0 g (79 %) product. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.54 (d, *J* = 2.1 Hz, 2H), 6.34 (t, *J* = 2.2 Hz, 1H), 4.76 (s, 2H), 3.90 (t, *J* = 6.6 Hz, 4H), 1.82-1.66 (m, 4H), 1.47-1.36 (m, 4H), 1.36-1.18 (m, 32H), 0.88 (t, *J* = 7.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.02, 160.58, 138.42, 134.00, 132.26, 123.39, 106.94, 100.71, 77.41, 77.16, 76.91, 68.09, 41.77, 32.02, 29.51, 29.35, 26.15, 22.79, 14.24. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{39}H_{59}NO_4Na$, 628.89, found 628.56.

(3,4,5)G1-CH_2-N(CO)$_2$C$_6$H$_4$ (**7c**). From **(3,4,5)12G1-CH_2-OH** (**6c**) (2.00 g, 3.03 mmol, 1 eq) and thionyl chloride (0.40 g, 3.33 mmol, 1.1 eq) in DCM (20 mL) to yield **(3,5)12G1-CH_2-Cl**. **(3,5)12G1-CH_2-Cl** reacted with potassium phthalimide (0.56 g, 3.03 mmol, 1 eq) in DMF (40 mL). The product was purified by column chromatography (EtOAc/Hexane = 1/9) to yield 2.0 g (84%) product. ^{1}H NMR

(500 MHz, $CDCl_3$) δ 7.84 (dd, J = 5.3, 3.1 Hz, 2H), 7.70 (dd, J = 5.3, 3.0 Hz, 2H), 6.66 (s, 2H), 4.72 (s, 2H), 3.95 (t, J = 6.4 Hz, 4H), 3.89 (t, J = 6.6 Hz, 2H), 1.75-1.66 (m, 8H), 1.44 (d, J = 6.2 Hz, 8H), 1.27 - 1.25 (m, 72H), 0.88 (dd, J = 8.8, 4.7 Hz, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.21, 153.28, 137.97, 134.07, 132.31, 131.51, 123.46, 107.57, 73.52, 69.22, 42.08, 32.07, 30.45, 29.88, 29.87, 29.85, 29.83, 29.81, 29.79, 29.75, 29.70, 29.66, 29.63, 29.58, 29.53, 29.51, 26.24, 22.83, 14.25. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{51}H_{83}NO_5Na$, 813.21, found 813.10.

(3,4)-3EOMe$_2$-G1-CH$_2$-N(CO)$_2$C$_6$H$_4$ (**7d**). From **(3,4)-3EOMe$_2$-G1-CH$_2$-OH (6d)** (3 g, 6.94 mmol, 1 eq), thionyl chloride (0.93 g, 8.33 mmol, 1.2 eq) in DCM (30 mL), 3.1 g of **(3,4)-3EOMe$_2$-G1-CH$_2$-Cl** were obtained as yellow oil. From **(3,4)-3EOMe$_2$-G1-CH$_2$-Cl** (3.1 g, 6.94 mmol, 1 eq), potassium phthalimide (1.41 g, 7,63 mmol, 1.1 eq) in DMF (40 mL), 2.96 g (76%) of the **(3,4)-3EOMe$_2$-G1-CH$_2$-N(CO)$_2$C$_6$H$_4$** were obtained as yellowish oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 3.5, 2H), 7.91 (m, 2H), 7.21 (d, J = 1.6, 2H), 7.20 (d, J = 8.2, 1H), 7.08 (d, J = 8.2, 1H), 4.96 (s, 2H), 4.39-4.36 (m, 4H), 4.09-4.07 (m, 4H), 3.97 (m, 4H), 3.89-3.86 (m, 8H), 3.77 (m, 4H), 3.59 (m, 6H). ^{13}C NMR ($CDCl_3$) δ 174.46, 155.40, 155.05, 140.57, 138.58, 136.37, 129.80, 129.69, 128.39, 121.67, 121.08, 84.41, 84.16, 83.90, 78.45, 76.21, 75.40, 75.33, 65.45, 47.79. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{29}H_{39}NO_{10}Na$, 584.62 found 584.66.

(3,5)-3EOMe$_2$-G1-CH$_2$-N(CO)$_2$C$_6$H$_4$ (**7e**). **(3,5)-3EOMe$_2$-G1-CH$_2$-OH (6e)** (3 g, 6.94 mmol, 1 eq) reacted with thionyl chloride (0.93 g, 8.33 mmol, 1.2 eq) in DCM (30 mL) to yield **(3,5)-3EOMe$_2$-G1-CH$_2$-Cl** as yellow oil. **(3,5)-3EOMe$_2$-G1-CH$_2$-Cl** reacted with potassium phthalimide (1.41 g, 7.63 mmol, 1.1 eq) was dissolved in 40 mL of DMF to yield 1.64 g (42 %) of **(3,5)-3EOMe$_2$-G1-CH$_2$-N(CO)$_2$C$_6$H$_4$** as yellowish oil. ^{1}H NMR ($CDCl_3$) δ 7.83 (m, 2H), 7.71 (m, 2H), 6.57 (s, 2H), 6.39 (s, 1H), 4.75 (s, 2H), 4.07 (m, 4H), 3.53-3.86 (m, 20H), 3.37 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 167.81, 159.94, 138.31, 133.89, 131.98, 123.25, 107.09, 100.81, 70.67, 70.43, 67.33, 58.90, 41.65. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{29}H_{39}NO_{10}Na$, 584.62 found 584.77.

(3,4,5)-3EOMe$_3$-G1-CH$_2$-N(CO)$_2$C$_6$H$_4$ (**7f**). **(3,4,5)-3EO-G1-(OCH$_3$)$_2$-CH$_2$-OH (6f)** (1.5 g, 2.52 mmol, 1 eq) reacted with thionyl chloride (0.36 g, 3.02 mmol, 1.2 eq) in DCM (17 mL) to yield **(3,4,5)-3EO-G1-(OCH$_3$)$_2$-CH$_2$-Cl**. **(3,4,5)-3EO-G1-(OCH$_3$)$_2$-CH$_2$-Cl** reacted with potassium phthalimide (0.51 g, 2.77 mmol, 1.1 eq.) in DMF (20 mL) to yield 1.5 g (82%) of **(3,4,5)-3EO-G1-(OCH$_3$)$_2$-CH$_2$-N(CO)$_2$C$_6$H$_5$** as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, J = 5.4, 3.0, 1H), 7.68 (dd, J = 5.5, 3.0, 1H), 4.16-4.08 (m, 3H), 4.08-4.04 (m, 1H), 3.86-3.65 (m, 8H), 3.64-3.56 (m, 7H), 3.54-3.45 (m, 4H), 3.34 (t, J = 3.4, 6H). ^{13}C NMR ($CDCl_3$) δ 168.06, 152.74, 138.18, 134.09, 132.21, 131.89, 123.48,

108.49, 72.35, 72.04, 70.90, 70.78, 70.65, 70.69, 69.79, 68.94, 59.11, 41.81. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{36}H_{53}NO_{14}Na$, 746.80, found 747.10.

General Synthetic Procedure for Compounds 8a-f. Compounds **7a-f** were dissolved in a mixture of THF and ethanol (THF/ethanol = 1:2, concentration of 7a-f = 0.025 g/mL). NH_2NH_2•H_2O (5 eq) was added to the solution. The reaction was maintained under reflux during 8 h. The solvent was evaporated and THF was added again. The crude product was filtered through Celite and concentrated to dryness. The residue was dissolved in DCM and extracted with HCl. The acidic phase was extracted two times with DCM and neutralized with KOH (pellets). DCM was then evaporated to yield the product.

(3,4)12G1-CH_2-NH_2 (**8a**). From **(3,4)12G1-CH_2-$N(CO)_2C_6H_4$** (**7a**) (1g, 1.65 mmol, 1 eq), NH_2NH_2•H_2O (0.41 g, 8.25 mmol, 5 eq) in THF/EtOH (1/2), 0.6 g (77 %) of **(3,4)12G1-CH_2-NH_2** were obtained as a yellowish solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90-6.75 (m, 2H), 4.01-3.96 (m, 4H), 3.77 (s, 2H), 1.89-1.73 (m, 4H), 1.46 (d, *J* = 3.3 Hz, 4H), 1.26 (m, 32H), 0.88 (t. *J* = 6.9 Hz, 6H), ^{13}C NMR ($CDCl_3$) δ 149.44, 148.12, 136.34, 125.53, 119.29, 114.27, 113.16, 69.56, 69.30, 67.96, 46.31, 31.98, 29.70, 29.55, 29.50, 29.43, 25.64, 22.74, 21.22, 14.15. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{31}H_{57}NO_2Na$, 498.79, found 499.12.

(3,5)12G1-CH_2-NH_2 (**8b**). From **(3,5)12G1-CH_2-$N(CO)_2C_6H_4$** (**7b**) (0.51 g, 0.842 mmol, 1 eq), NH_2NH_2•H_2O (0.21 g, 4.21 mmol, 5 eq) in a mixture of EtOH (20 mL) and THF (10 mL), 0.36 g (90%) of **(3,5)12G1-CH_2-NH_2** were obtained as a yellowish solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.44 (d, *J* = 2.1 Hz, 2H), 6.34 (t, *J* = 2.2 Hz, 1H), 3.93 (t, *J* = 6.6 Hz, 4H), 3.79 (t, *J* = 7.6 Hz, 2H), 1.84-1.68 (m, 4H), 1.54-1.39 (m, 4H), 1.39-1.18 (m, 32H), 0.88 (t, *J* = 7.0 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ 160.63, 145.87, 105.43, 99.71, 68.09, 46.83, 29.78, 29.72, 29.51, 29.41, 26.17, 22.79. 14.24. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{31}H_{57}NO_2Na$, 498.79, found 498.32.

(3,4,5)12G1-CH_2-NH_2 (**8c**). From **(3,5)12G1-CH_2-$N(CO)_2C_6H_4$ (7c)** (0.31 g, 0.42 mmol, 1 eq), NH_2NH_2•H_2O (1 mL) in a mixture of EtOH (20 mL) and THF (10 mL), 0.24 g (83%) of (**3,4,5)12G1-CH_2-NH_2** were obtained as a yellowish solid. ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 6.50 (s, 2H), 3.95 (dt, *J* = 21.9, 6.6, 6H), 3.77 (s, 2H), 1.77 (ddd, *J* = 20.7, 14.4, 7.3, 6H), 1.53-1.41 (m, 6H), 1.39-1.21 (m, 50H), 0.88 (t, *J* = 6.9, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 153.37, 138.53, 137.20, 105.64, 73.55, 69.27, 46.86, 32.08, 32.06, 30.48, 29.89, 29.88, 29.84, 29.80, 29.78, 29.77, 29.71, 29.67, 29.61, 29.56, 29.53, 29.50, 26.29, 26.25, 22.83, 14.24. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{43}H_{81}NNaO_3$, 682.62, found 683.58.

(3,4)-3EOMe$_2$-G1-CH$_2$-NH$_2$ (**8d**). From **(3,4)-3EOMe$_3$-G1-CH$_2$-N(CO)$_2$C$_6$H$_4$** (**7d**) (1.63 g, 2.90 mmol, 1 eq), NH_2NH_2•H_2O (0.73 g, 14.5 mmol, 5 eq) in a mixture of THF (15 mL) and EtOH (30 mL), 0.85 (68 %) of **(3,4)-3EOMe$_3$-G1-CH$_2$-NH$_2$** were obtained as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (d, *J* = 1.8 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 1H), 6.83 (dd, *J* = 8.2, 1.9 Hz, 1H), 4.23-4.09 (m, 4H), 3.85 (dd, *J* = 10.4, 5.9 Hz, 4H), 3.78 (s, 2H), 3.74-3.73 (m, 4H), 3.65-3.64 (m, 8H), 3.54 (dd, J = 5.7, 3.8 Hz, 4H), 3.37 (s, 6H), 1.78 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.03, 147.74, 136.82, 119.88, 115.07, 113.92, 77.41, 77.16, 76.90, 71.87, 70.73, 70.62, 70.61, 70.47, 69.74, 69.04, 68.84, 58.93, 46.03, 30.27. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{21}H_{37}NO_8Na$, 454.52, found 453.11.

(3,5)-3EOMe$_2$-G1-CH$_2$-NH$_2$ (**8e**). From **(3,5)-3EOMe$_3$-G1-CH$_2$-N(CO)$_2$C$_6$H$_4$** (**7e**) (0.7 g, 1.25 mmol, 1 eq), NH_2NH_2•H_2O (0.31 g, 6.25 mmol, 5 eq) in EtOH/THF (30 mL/15 mL), 0.50 g (93 %) of **(3,5)-3EOMe$_2$-G1-CH$_2$-NH$_2$** were obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.48 (d, *J* = 2.1 Hz, 2H), 6.38 (t, *J* = 2.2 Hz, 1H), 4.16-4.07 (m, 4H), 3.89-3.81 (m, 4H), 3.79 (s, 2H), 3.76-3.71 (m, 4H), 3.71-3.60 (m, 10H), 3.56 (dd, J = 5.6, 3.7 Hz, 4H), 3.38 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.22, 146.00, 105.93, 100.10, 72.08, 70.96, 70.81, 70.72, 69.86, 67.60, 59.18, 46.80/ MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{21}H_{37}NO_8Na$, 454.52, found 455.08

(3,4,5)-3EOMe$_3$-G1-CH$_2$-NH$_2$ (**8f**). From **(3,4,5)-3EOMe$_3$-G1-CH$_2$-N(CO)$_2$C$_6$H$_4$** (**7f**) (1.5 g, 1.90 mmol, 1 eq), NH_2NH_2•H_2O (0.48 g, 9.49 mmol, 5 eq) in EtOH/THF (30 mL/15 mL), 1.15 g (92 %) of **(3,4,5)-3EOMe$_2$-G1-CH$_2$-NH$_2$** were obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65 (d, *J* = 7.34 Hz, 2H), 4.16 (t, *J* = 4.78 Hz, 2H), 4.12 (t, *J* = 5.02 Hz, 1H), 4.08 (t, *J* = 4.30 Hz, 2H), 4.04 (t, *J* = 4.30 Hz, 2H), 3.93 (s, 1H), 3.86-3.82 (m, 4H), 3.79-3.58 (m, 21H), 3.53 (m, 5H), 3.38-3.34 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.80, 152.78, 152.17, 107.99, 107.91, 72.39, 72.33, 72.02, 72.00, 71.98, 71.89, 70.89, 70.77, 70.71, 70.68, 70.65, 70.62, 70.56, 70.53, 70.50, 70.38, 69.86, 69.83, 69.78, 69.07, 69.01, 68.97, 68.57, 59.10, 59.06.

3.1.3 Synthesis of "Single-Single" L-Ala Containing Amphiphilic Janus Dendrimers 9ad-10cf.

General Synthetic Procedure for Compounds 9ad-10cf. First generation dendritic acids **5a-c** were respectively mixed with first generation dendritic amines **8d-f** or **5d-f** with **8a-c** in dry THF (0.05 g mixture/mL). CDMT (1-2 eq) was added and the mixture was cooled to 0 °C. NMM (1-2 eq) was introduced dropwise in the mixture during 5 min. The reaction was maintained at 23 °C. for 8 h. The reaction mixture was filtered through Celite, washed with THF, and then concentrated to dryness. The crude product was purified column chromatography on silica gel with a mobile with DCM/MeOH (19:1).

(3,4)12G1-L-Ala-CH_2-(3,4)-3EO-G1-$(OCH_3)_2$ (9ad). From first generation dendritic acid **5a** (0.26 g, 0.46 mmol, 1 eq), first generation dendritic amine **8d** (0.2 g, 0.46 mmol, 1 eq), CDMT (0.08 g, 0.46 mmol, 1 eq), CDMT (0.081 g, 0.46 mmol, 1 eq), NMM (0.09 g. 0.91 mmol. 2 eq) in dry THF (3 mL), 0.3 g (67 %) of the title compound were obtained as a solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.33 (d, *J* = 7.4 Hz, 2H), 7.16 (d, *J* = 7.3 Hz, 1H), 6.79 (dd, *J* = 14.6, 9.2 Hz, 4H,), 4.75 (p, J = 6.9 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.37-4.27 (qd, *J* = 14.8, 5.8 Hz, 2H, 1×-NH_2-*CH_2*-), 4.10 (t, *J* = 5.0 Hz, 2H, 1×Ar-O-*CH_2*-), 4.06 (t, *J* = 4.8 Hz, 2H, 1×Ar-O-*CH_2*-), 4.01-3.96 (m, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.81 (t, *J* = 5.0 Hz, 2H, 1×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.77 (t, *J* = 4.8 Hz, 2H, 1×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.70-3.68 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.63(m, 8H, 2×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.53 (dd, *J* = 9.5, 5.0 Hz, 4H, 2×-*CH_2*O-CH_3), 3.36 (d, *J* = 7.1 Hz, 6H, 2×-O*CH_3*), 1.80 (m, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.57-1.40 (m, 7H, 1×-NHCH*(CH_3)*CO- and 2×-O$(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.40-1.17 (m, 32H, 2×-O$(CH_2)_3$*$(CH_2)_8$*CH_3), 0.88 (t, *J* = 6.8 Hz, 6H, 2×-O$(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.56, 166.81, 152.23, 149.01, 148.85, 148.18, 131.64, 126.06, 120.55, 120.27, 114.80, 114.19, 112.72, 112.19, 71.92, 70.77, 70.71, 70.65, 70.52, 70.44, 69.72, 69.36, 69.07, 68.93, 68.74, 58.97, 58.92, 49.33, 31.92, 29.70, 29.64, 29.63, 29.43, 29.36, 29.28, 29.16, 26.04, 26.02, 22.68, 18.68, 14.11. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{55}H_{94}N_2O_{12}Na$, 998.34, found 998.66.

(3,4)12G1-L-Ala-CH_2-(3,5)-3EO-G1-$(OCH_3)_2$ (9ae). From first generation dendritic acid **5a** (0.46 g, 0.811, 1eq), first generation dendritic amine **8e** (0.35 g, 0.811 mmol, 1 eq), NMM (0.16 g, 1.62 mmol, 2 eq), CDMT (0.28 g, 1.62 mmol, 2 eq) in THF (12.5 mL), 0.46 g (58 %) of the title compound were obtained as a slightly yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 2.1 Hz, 1H), 7.31 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.78 (d, *J* = 7.3 Hz, 1H), 6.64 (t, *J* = 5.8 Hz, 1H), 6.42 (d, *J* = 2.1 Hz, 2H), 6.38 (t, *J* = 2.2 Hz, 1H), 4.68 (p, *J* = 7.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.38 (qd, *J* = 15.0, 5.8 Hz, 2H, 1×-NH_2-*CH_2*-), 4.07-3.99 (m, 8H, 2×Ar-O-*CH_2*- and 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.81-3.77 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.73-3.70 (m, 4H, 1×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.67 (m, 8H, 2×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.54 (dd, *J* = 5.7, 3.7 Hz, 4H, 2×-*CH_2*O-CH_3), 3.37 (d, *J* = 2.9 Hz, 6H, 2×-O*CH_3*), 1.82 (dq, *J* = 12.9, 6.6 Hz, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.51-1.46 (m, 7H, 1×-NHCH*(CH_3)*CO- and 2×-O$(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.35-1.26 (m, 32H, 2×-O$(CH_2)_3$*$(CH_2)_8$*CH_3), 0.88 (t, J = 6.9 Hz, 6H, 2×-O$(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.39, 167.04, 160.32, 152.45, 149.14, 140.29, 126.20, 120.10, 112.87, 112.43, 106.45, 100.96, 72.08, 70.93, 70.80, 70.68, 69.82, 69.55, 69.30, 67.64, 59.15, 56.04, 49.38, 43.73, 32.07, 29.84, 29.81, 29.79, 29.77, 29.58, 29.56, 29.51, 29.41, 29.28, 26.18, 26.14, 22.83, 18.52, 14.25. MALDI-TOF MS (m/z): $[M+Na]^+$ calcd for $C_{55}H_{94}NaN_2O_{12}$, 997.7; found 997.0

(3,4)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$ (9af). From first generation dendritic acid **5a** (0.22 g, 0.387 mmol. 1 eq) and first generation dendritic amine **8f** (0.23 g, 0.387 mmol, 1 eq), 4-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMTMM, 0.12 g, 0.426 mmol, 1 eq) in THF (10 mL), 0.14 g (32 %) of the title compond were obtained as a yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 2.0 Hz, 1H), 7.35 (dd, *J* = 8.4 Hz, 1.9, 1H), 7.09 (d, *J* = 7.2 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 1H, 1×Ar*H*), 4.66 (p, *J* = 7.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.35 (d, J = 5.9, 2H, 1×-NH_2-*CH_2*-), 4.10 (t, *J* = 4.9 Hz, 6H, 3×Ar-O-*CH_2*-), 3.95 (t, *J* = 6.5 Hz, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.78 (dt, *J* = 5.3, 4.9 Hz, 6H, 3×Ar-O-CH_2-*CH_2*-), 3.69 (m, 6H, 3×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.66-3.62 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.55-3.52 (m, 6H, 3×-*CH_2*O-CH_3), 3.37 (s, 3H, 1×-O*CH_3*), 3.36 (s, 6H, 2×-O*CH_3*), 1.76 (p, *J* = 7.1 Hz, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.50 (d, *J* = 6.9 Hz, 3H, -NHCH*(CH_3)*CO-), 1.46 (p, *J* = 7.2 Hz, 4H, 2×-$O(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.26 (m, 32H, 2×-$O(CH_2)_3$*$(CH_2)_8$*CH_3), 0.88 (t, *J* = 7.0 Hz, 6H, 2×-$O(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.48, 167.01, 153.35, 152.90, 152.53, 149.12, 137.99, 133.62, 126.18, 120.18, 112.88, 112.41, 107.44, 77.42, 76.91, 72.40, 72.07, 70.93, 70.86, 70.82, 70.66, 70.62, 69.93, 69.87, 69.57, 69.30, 69.17, 69.01, 59.15, 59.12, 56.19, 49.40, 43.64, 32.07, 29.85, 29.81, 29.79, 29.77, 29.59, 29.56, 29.51, 29.42, 29.29, 26.19, 26.14, 22.83, 18.47, 14.26. MALDI-TOF MS (m/z): $[M+Na]^+$ calcd for $C_{62}H_{108}NaN_2O_{16}$, 1159.76; found 1159.05

(3,5)12G1-L-Ala-CH_2-(3,4)-3EO-G1-$(OCH_3)_2$ (9bd). From compound **5b** (0.1 g, 0.178, 1 eq), compound **8d** (0.077 g, 0.178 mmol, 1 eq), CDMT (0.031 g, 0.178 mmol, 1 eq), NMM (0.036, 0.356 mmol, 2 eq) in THF (3 mL), 0.09 g (53%) of the title compound were obtained as a yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 2.2 Hz, 3H), 6.81 (ddd, *J* = 9.8, 7.0 Hz, 1.6 Hz, 3H), 6.56 (t, *J* = 2.1 Hz, 1H), 4.66 (p, *J* = 6.9 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.34 (qd, J = 14.8, 5.8 Hz, 2H, 1×-NH_2-*CH_2*-), 4.12-4.08 (m, 4H, 1×Ar-O-*CH_2*-), 3.94-3.91 (m, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.84-3.77 (m, 4H, 2×Ar-O-CH_2-*CH_2*-,), 3.71-3.68 (m, 4H, 2×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.65-3.60 (m, 8H, 2×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.52 (m, 4H, 2×-*CH_2*O-CH_3), 3.35 (d, *J* = 6.5 Hz, 6H, 2×-O*CH_3*), 1.74 (m, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.48 (d, *J* = 7.0 Hz, 3H, 1×-NHCH*(CH_3)*CO-), 1.42 (m, 4H, 2×-$O(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.37-1.25 (m, 32H, 2×-$O(CH_2)_3$*$(CH_2)_8$*CH_3), 0.86 (t, *J* = 6.9 Hz, 7H, 2×-$O(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.27, 167.17, 160.50, 149.15, 148.38, 135.78, 131.49, 120.76, 114.93, 114.48, 105.53, 104.99, 72.02, 72.00, 70.88, 70.79, 70.75, 70.73, 70.61, 70.52, 69.86, 69.83, 69.01, 68.92, 68.41, 66.71, 59.09, 59.03, 54.63, 49.42, 44.08, 43.29, 32.00, 29.76, 29.72, 29.70, 29.67, 29.48, 29.44, 29.31, 26.11, 22.77, 18.56, 14.20. MALDI-TOF MS (m/z): $[M+Na]^+$ calcd for $C_{55}H_{94}NaN_2O_{12}$, 997.2; found 996.8.

(3,5)12G1-L-Ala-CH_2-(3,5)-3EO-G1-$(OCH_3)_2$ (9be). From compound **5b** (0.1 g, 0.178 mmol, 1 eq), compound **8e** (0.077 g, 0.178 mmol, 1 eq), CDMT (0.034 g, 0.196, 1.1 eq), NMM (0.045, 0.445 mmol, 2.5 eq) in dry THF (2mL), 0.04 g (24 %) of the title compound were obtained as a slightly yellowish oil. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88 (d, *J* = 2.0 Hz, 2H), 6.79 (d, *J* = 7.2 Hz, 1H), 6.57 (s, 1H), 6.54 (t, *J* = 5.5 Hz, 1H), 6.42 (s, 2H), 6.38 (s, 1H), 4.66 (m, 1H, 1×-NH*CH*(CH_3)NH-), 4.38 (qd, *J* = 14.9, 5.7 Hz, 2H, 1×-NH_2-*CH_2*-), 4.09-4.04 (m, 4H, 2×Ar-O-*CH_2*-), 3.95 (t, *J* = 6.4 Hz, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.83-3.80 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.73-3.70 (m, 4H, 2×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.68-3.64 (m, 8H, 2×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.54 (dd, *J* = 5.4, 3.9 Hz, 4H, 2×-*CH_2*O-CH_3), 3.37 (s, 6H, 2×-O*CH_3*), 1.77 (m, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.50 (d, *J* = 7.0 Hz, 3H, 1×-NHCH*(CH_3)*CO-), 1.44 (m, 4H, 2×-O$(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.27 (m, 32H, 2×-O$(CH_2)_3$*$(CH_2)_8$*CH_3), 0.88 (t, *J* = 6.9 Hz, 6H, 2×-O$(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.83, 167.20, 160.65, 160.34, 140.21, 135.86, 106.46, 105.60, 104.96, 100.94, 72.08, 70.93, 70.80, 70.69, 69.83, 68.51, 67.65, 59.16, 49.45, 43.81, 32.07, 29.82, 29.79, 29.76, 29.73, 29.54, 29.50, 29.37, 26.18, 22.84, 18.44, 14.27. MALDI-TOF MS (m/z): $[M+Na]^+$ calcd for$C_{55}H_{94}N_2NaO_{12}$, 998.33; found 998.67.

(3,5)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$ (9bf). From first generation dendritic acid **5b** (0.19 g, 0.338 mmol, 1.05 eq), first generation dendritic amine **8f** (0.19 g, 0.32 mmol, 1eq), CDMT (0.056 g, 0.32 mmol, 1eq) and NMM (0.081 g, 0.800 mmol, 2.5 eq) in 2.5 mL THF, 0.27 g (75%) of the title compound were obtained as colorless oil. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (ds, 3H), 6.77(b, 1H), 6.57 (t, *J* = 2.2 Hz, 1H), 6.51 (s, 2H), 4.66 (p, *J* = 7.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.35 (d, *J* = 5.9, 2H, 1×-NH_2-*CH_2*-), 4.11 (t, *J* = 4.9, 6H, 3×Ar-O-*CH_2*-), 3.96 (t, *J* = 6.5, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.78 (dt, *J* = 5.3, 4.9 Hz, 6H, 3×Ar-O-CH_2-*CH_2*-), 3.69 (m, 6H, 3×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.66-3.62 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.55-3.52 (m, 6H, 3×-*CH_2*O-CH_3), 3.37 (s, 3H, 1×-O*CH_3*), 3.36 (s, 6H, 2×-O*CH_3*), 1.77 (p, *J* = 7.1 Hz, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.50 (d, *J* = 6.9 Hz, 2H, -NHCH*(CH_3)*CO-), 1.44 (p, *J* = 7.2 Hz, 4H, 2×-O$(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.27 (m, 32H, 2×-O$(CH_2)_3$*$(CH_2)_8$*CH_3), 0.88 (t, *J* = 7.0 Hz, 6H, 2×-O$(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.20, 167.22, 160.60, 155.17, 152.91, 137.97, 135.78, 133.58, 107.49, 105.59, 104.91, 72.45, 72.40, 72.09, 72.07, 70.85, 70.66, 70.60, 70.00, 69.11, 69.03, 68.51, 59.15, 54.82, 54.73, 49.46, 45.25, 43.66, 32.06, 29.81, 29.78, 29.75, 29.73, 29.53, 29.49, 29.37, 26.24, 22.83, 18.39, 14.25. MALDI-TOF MS (m/z): $[M+Na]^+$ calcd for $C_{62}H_{108}N_2O_{16}Na$, 1160.53; found 1160.05.

(3,4,5)12G1-L-Ala-CH_2-(3,4)-3EO-G1-$(OCH_3)_2$ (9cd). From compound **5c** (0.2 g, 0.268 mmol, 1 eq), compound **8d** (0.14, 0.322 mmol, 1.2 eq), CDMT (0.047 g, 0.268 mmol, 1 eq), NMM (0.033 g, 0.322 mmol, 1.2 eq) in dry THF (3 mL), 0.19 g (61%) of the title compound were obtained as a slightly yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (s, 2H), 6.86 (m, 3H), 6.81

(dd, J = 8.2, 1.7 Hz, 1H), 6.59 (s, 1H), 4.66 (p, J = 7.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.41 (dd, J = 14.6, 5.8 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4.34 (dd, J = 14.7, 5.5 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4.15-4.10 (m, 4H, 2×Ar-O-*CH_2*-), 4.02-3.97 (m, 6H, 3×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.85-3.79 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.73-3.69 (m, 4H, 2×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.63-3.61 (m, 8H, 2×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.54-3.53 (m, 4H, 2×-*CH_2*O-CH_3), 3.37 (d, J = 3.4 Hz, 6H, 2×-O*CH_3*), 1.82-1.73 (m, 6H, 3×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.50 (d, J = 7.0 Hz, 3H, 1×-NHCH*(CH_3)*CO-), 1.48-1.44 (m, 6H, 3×-$O(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.39-1.19 (m, 48H, 3×-$O(CH_2)_3$*$(CH_2)_8$*CH_3), 0.88 (t, J = 6.9, 9H, 3×-$O(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.30, 167.10, 153.18, 149.12, 148.40, 141.36, 131.48, 128.64, 120.72, 114.89, 114.50, 105.85, 73.57, 71.99, 70.86, 70.78, 70.74, 70.61, 70.51, 69.86, 69.81, 69.42, 69.00, 68.92, 59.07, 59.01, 49.44, 32.01, 30.42, 29.83, 29.79, 29.73, 29.68, 29.51, 29.47, 29.45, 26.19, 22.77, 18.71, 14.19. MALDI-TOF MS (m/z): $[M+K]^+$ calcd for $C_{67}H_{118}KN_2O_{13}$, 1197.96; found 1197.59

(3,4,5)12G1-L-Ala-CH_2-(3,5)-3EO-G1-$(OCH_3)_2$ (9ce). From compound **5c** (0.1 g, 0.134 mmol, 1 eq), compound **8e** (0.058 g, 0.134 mmol, 1 eq), CDMT (0.026 g, 0.147 mmol, 1.1 eq), NMM (0.034 g, 0.335 mmol, 2.5 eq), in THF (3 mL), 0.05 g (30 %) of the title compound were obtained as a yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.98 (s, 2H), 6.78 (d, J = 7.2 Hz, 1H), 6.52 (d, J = 5.9 Hz, 1H), 6.42 (d, J = 2.1 Hz, 2H), 6.39 (s, 1H), 4.66 (dd, J = 14.0, 7.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.43 (dd, J = 14.8, 6.0 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4.34 (dd, J = 15.0, 5.5 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4.06 (m, 4H, 2×Ar-O-*CH_2*-), 4.00-3.98 (m, 6H, 3×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.80 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.71-3.70 (m, 4H, 2×Ar-O-$(CH_2)_2$-O-*CH_2*-) 3.67-3.63 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.54 (m, 4H, 2×-*CH_2*O-CH_3), 3.37 (d, J = 8.0 Hz, 6H, 2×-O*CH_3*), 1.80-1.73 (m, 6H, 3×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.50-1.47 (m, 9H, 1×-NHCH*(CH_3)*CO- and 3×-$O(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.26 (br, 48H, 3×-$O(CH_2)_3$*$(CH_2)_8$*CH_3), 0.88 (t, J = 6.9 Hz, 9H, 3×-$O(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.31, 167.08, 160.34, 153.28, 141.54, 140.23, 128.69, 106.48, 105.89, 100.94, 73.63, 72.07, 70.93, 70.79, 70.67, 69.82, 69.52, 67.64, 59.15, 49.45, 43.77, 32.07, 30.48, 29.90, 29.89, 29.85, 29.84, 29.81, 29.79, 29.74, 29.57, 29.54, 29.51, 26.25, 22.84, 18.59, 14.25. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{67}H_{118}N_2O_{13}Na$, 1182.67; found 1183.01

(3,4,5)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$ (9cf). From compound **5c** (0.14 g, 0.188 mmol, 1 eq), compound **8f** (0.111 g, 0.188 mmol, 1 eq), CDMT (0.036 g, 0.206 mmol, 1.1 eq), NMM (0.028 g, 0.281 mmol, 1.5 eq), in THF (3 mL), 0.14 g (56 %) of the title compound were obtained as a yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 7.2 Hz, 1H), 7.03 (s, 2H), 6.50 (s, 2H, 2×Ar*H*), 4.71 (p, J = 6.9 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.34 (qd, J = 15.0, 5.8 Hz, 2H, 1×-NH_2-*CH_2*-), 4.10 (dd, J = 8.9, 4.3 Hz, 6H, 3×Ar-O-*CH_2*-), 3.99 (dd, J = 12.2, 6.2 Hz, 6H, 3×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.77 (dd, J = 10.3, 5.7 Hz, 6H, 3×Ar-O-CH_2-*CH_2*-), 3.73-3.67 (m, 6H, 3×Ar-O-

$(CH_2)_2$-O-*CH_2*-), 3.66-3.61 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.50 (m, 6H, 3×-*CH_2*O-CH_3), 3.33 (d, *J* = 6.6 Hz, 9H, 3×-O*CH_3*), 1.77-1.71 (m, 6H, 3×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.55-1.41 (m, 9H, 3×-$O(CH_2)_2$*CH_2*$(CH_2)_8CH_3$ and 1×-NHCH*(CH_3)*CO-), 1.24 (m, 48H, 3×-$O(CH_2)_3$*$(CH_2)_8$*CH_3), 0.85 (t, *J* = 6.9 Hz, 9H, 3×-$O(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.58, 167.14, 153.18, 152.78, 141.43, 137.74, 133.54, 128.59, 107.19, 105.86, 73.54, 72.31, 72.00, 71.97, 70.77, 70.72, 70.57, 70.53, 70.51, 69.84, 69.39, 68.90, 59.04, 59.00, 55.98, 49.45, 43.50, 31.98, 30.40, 29.81, 29.79, 29.77, 29.75, 29.71, 29.66, 29.50, 29.47, 29.45, 29.42, 26.18, 22.74, 18.45, 14.17. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{74}H_{132}N_2O_{17}Na$, 1343.95, found 1341.02.

(3,4)12G1-CH_2-L-Ala-(3,4)-3EO-G1-$(OCH_3)_3$ (10ad). From compound **5d** (0.24 g, 0.46 mmol, 1 eq), compound **8a** (0.22 g, 0.46 mmol, 1 eq), CDMT (0.081 g, 0.46 mmol, 1 eq), NMM (0.09 g, 0.91 mmol, 1 eq) in THF, 0.37 g (82 %) of the title compound were obtained as a yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 1.5 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.27-7.18 (m, 2H), 6.83 (d, *J* = 8.5 Hz, 1H), 6.75 (dd, *J* = 12.4, 9.3 Hz, 3H), 4.74 (p, *J* = 6.9 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.36 (dd, *J* = 14.7, 5.9 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4.26 (dd, *J* = 14.7, 5.5 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4.14-4.11 (dt, *J* = 15.4, 4.9 Hz, 4H, 2×Ar-O-*CH_2*-CH_2-O-), 3.89-3.86 (ddd, *J* = 13.8, 11.8, 5.7 Hz, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.83-3.79 (dt, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.71-3.64 (m, 4H, 2×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.63-3.58 (m, 8H, 2×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.51-3.47 (ddd, *J* = 9.6, 5.7, 3.7 Hz, 4H, 2×-*CH_2*O-CH_3), 3.33 (t, *J* = 10.1 Hz, 6H, 2×-O*CH_3*), 1.84- 1.72(m, 4H, 3×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.42 (m, 7H, 2×-$O(CH_2)_2$*CH_2*$(CH_2)_8CH_3$ and 1×-NHCH*(CH_3)*CO-), 1.23 (br, 32H, 2×-$O(CH_2)_3$*$(CH_2)_8$*CH_3), 0.85 (t, J = 6.9 Hz, 6H, 2×-$O(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.44, 166.63, 151.95, 149.38, 148.55, 148.48, 130.87, 126.67, 120.96, 119.95, 114.05, 113.58, 113.43, 113.03, 71.93, 70.91, 70.78, 70.69, 70.65, 70.55, 70.47, 69.69, 69.57, 69.43, 69.21, 69.02, 68.66, 59.00, 58.94, 49.33, 43.23, 31.93, 29.73, 29.71, 29.67, 29.49, 29.48, 29.37, 26.09, 26.07, 22.69, 18.48, 14.12. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{55}H_{94}N_2O_{12}Na$, 998.35, found 998.58.

(3,4)12G1-CH_2-L-Ala-(3,5)-3EO-G1-$(OCH_3)_2$ (10ae). From compound **5e** (0.13 g, 0.251 mmol, 1eq), compound **8a** (0.12 g, 0.251 mmol, 1 eq), CDMT (0.048 g, 0.276 mmol. 1.1 eq), NMM (0.064 g, 0.628 mmol, 2.5 eq), THF (3 mL), 0.05 g (21 %) of the title compound were obtained as a white solid. (Purity HPLC 99%+) ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.99 (s, 1H), 6.95 (d, *J* = 2.2 Hz, 2H), 6.86-6.72 (m, 3H), 6.63 (t, *J* = 2.1 Hz, 1H), 6.56 (s, 1H), 4.69 (p, *J* = 7.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.40 (dd, *J* = 14.6, 5.8 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4.31 (dd, *J* = 14.6, 5.5 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4,10 (m, 4H, 2×Ar-O-*CH_2*-), 3.96 (m, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.82 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.71 (m, 4H, 2×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.67-3.62 (m, 8H, 2×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.53 (dd, *J* = 5.6, 3.6 Hz, 4H, 2×-*CH_2*O-CH_3), 3.35 (s, 6H, 2×-O*CH_3*), 1.76 (m, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.48 (d, *J* = 7.0 Hz, 3H,

1×-NHCH*(CH$_3$)*CO-), 1.41 (m, 4H, 2×-O(CH$_2$)$_2$*CH$_2$*(CH$_2$)$_8$CH$_3$), 1.24 (m, 32H, 2×-O(CH$_2$)$_3$*(CH$_2$)$_8$*CH$_3$), 0.86 (t, *J* = 6.7 Hz, 6H, 2×-O(CH$_2$)$_{11}$*CH$_3$*). ^{13}C NMR (126 MHz, CDCl$_3$) δ 172.37, 167.03, 160.05, 159.56, 149.45, 148.57, 135.74, 130.60, 119.98, 113.86, 113.39, 105.99, 105.32, 71.99, 70.87, 70.71, 70.61, 69.69, 69.46, 69.27, 67.82, 59.09, 56.09, 49.53, 43.40, 32.01, 29.79, 29.75, 29.55, 29.46, 29.41, 26.16, 26.14, 22.78, 18.37, 14.21. MALDI-TOF MS: (m/z): [M+Na]$^+$ calcd for $C_{55}H_{94}NaN_2O_{12}$ 997.67; found 997.16

(3,4)12G1-CH$_2$-L-Ala-(3,4,5)-3EO-G1-(OCH$_3$)$_3$ (10af). From compound **5f** (0.24 g, 0.35 mmol, 1eq), compound **8a** (0.17 g, 0.35 mmol, 1 eq), CDMT (0.062 g, 0.35 mmol. 1 eq), NMM (0.07 g, 0.71 mmol, 2 eq), THF (5 mL), 0.26 g (65 %) of the title compound were obtained as a white solid. (Purity HPLC 99%+) (Purity HPLC 99%+) ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.31 (s, 2H), 7.04 (d, *J* = 7.11 Hz, 2H), 6.78 (m, 3H), 6.74 (t, *J* = 5.8, 1H), 4.69 (p, *J* = 7.1 Hz, 1H, 1×-NH*CH*(CH$_3$)NH-), 4.44 (dd, J = 14.8, 6.0 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-) and 4.31 (dd, *J* = 14.6, 5.5 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.16 (m, 6H, 3×Ar-O-*CH$_2$*-), 3.95 (dt, *J* = 6.6, 6.5 Hz, 4H, 2×Ar-O-*CH$_2$*(CH$_2$)$_{10}$CH$_3$), 3.83 (m, 6H, 3×Ar-O-CH$_2$-*CH$_2$*-), 3.70 (m, 6H, 3×Ar-O-(CH$_2$)$_2$-O-*CH$_2$*-), 3.64 (ddd, *J* = 9.6, 6.5, 2.8 Hz, 12H, 3×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.55-3.51 (m, 6H, 3×-*CH$_2$*O-CH$_3$), 3.37 (s, 3H, 1×-O*CH$_3$*), 3.34 (s, 6H, 2×-O*CH$_3$*), 1.78-1.76 (p, *J* = 7.1 Hz, 4H, 2×-OCH$_2$*CH$_2$*(CH$_2$)$_9$CH$_3$), 1.50 (d, *J* = 6.9 Hz, 2H, -NHCH*(CH$_3$)*CO-), 1.44 (p, *J* = 7.2 Hz, 4H, 2×-O(CH$_2$)$_2$*CH$_2$*(CH$_2$)$_8$CH$_3$),1.26 (m, 32H, 2×-O(CH$_2$)$_3$*(CH$_2$)$_8$*CH$_3$), 0.88 (t, *J* = 7.0 Hz, 6H, 2×-O(CH$_2$)$_{11}$*CH$_3$*). ^{13}C NMR (126 MHz, CDCl$_3$) δ 172.17, 166.85, 152.70, 149.60, 148.80, 142.03, 130.74, 129.01, 120.20, 114.26, 113.75, 107.59, 72.55, 72.09, 72.07, 70.86, 70.82, 70.78, 70.67, 70.59, 69.88, 69.61, 69.47, 69.34, 59.13, 59.08, 49.61, 43.56, 32.06, 29.84, 29.80, 29.79, 29.60, 29.59, 29.50, 26.22, 26.19, 22.82, 18.40, 14.24. MALDI-TOF (m/z) calcd. [M+Na]$^+$ for $C_{62}H_{108}N_2O_{16}Na$, 1160.53, found 1160.79.

(3,5)12G1-CH$_2$-L-Ala-(3,4)-3EO-G1-(OCH$_3$)$_2$ (10bd). From compound **5d** (0.36 g, 0.754 mmol, 1 eq), compound **8b** (0.39 g, 0.754 mmol, 1 eq), CDMT (0.15 g, 0.829 mmol, 1.1 eq), NMM (0.19 g, 1.89 mmol, 2.5 eq) in dry THF (8 mL), 0.15 g (21 %) of the title compound were obtained as a slightly yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (360 MHz, CDCl$_3$) δ 7.43 (d, *J* = 2.1Hz, 1H), 7.37-7.35 (dd, *J* = 8.3, 1.9 Hz,1H), 7.02(d, *J* = 7.7 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.76 (d, *J* = 6.8 Hz, 1H), 6.37 (d, *J* = 2.1 Hz, 2H), 6.32 (t, *J* = 2.3Hz, 1H), 4.70 (m, 1H, 1×-NH*CH*(CH$_3$)NH-), 4,44 (dd, *J* = 14.8, 6.1 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.31 (dd, *J* = 14.9, 5.6 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.18 (dd, *J* = 10.7, 5.7 Hz, 4H, 2×Ar-O-*CH$_2$*-), 3.86 (m, 8H, 2×Ar-O-*CH$_2$*(CH$_2$)$_{10}$CH$_3$ and 2×Ar-O-CH$_2$-*CH$_2$*-), 3.71-3.67 (m, 4H, 2×Ar-O-(CH$_2$)$_2$-O-*CH$_2$*-), 3.62-3.55 (m, 8H, 2×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.51 (dd, *J* = 9.3, 6.2 Hz, 4H, 2×-*CH$_2$*O-CH$_3$), 3.36 (d, *J* = 8.7 Hz, 6H, 2×-O*CH$_3$*), 1.70 (m, 4H, 2×-OCH$_2$*CH$_2$*(CH$_2$)$_9$CH$_3$), 1.49 (d, *J* = 7.0 Hz, 3H, 1×-NHCH*(CH$_3$)*CO-), 1.40 (m, 4H, 2×-O(CH$_2$)$_2$*CH$_2$*(CH$_2$)$_8$CH$_3$), 1.38-1.25 (br, 32H, 2×-

O(CH_2)$_3$*(CH_2)$_8$*CH_3), 0.87 (t, *J* = 6.9 Hz, 6H, 2×-O(CH_2)$_{11}$*CH_3*). ^{13}C NMR (91 MHz, $CDCl_3$) δ 172.47, 166.86, 160.68, 152.27, 148.55, 140.19, 126.69, 120.87, 113.73, 113.21, 105.95, 100.53, 72.05, 71.02, 70.88, 70.80, 70.76, 70.67, 70.57, 69.81, 69.67, 69.12, 68.74, 68.14, 59.15, 59.08, 49.43, 43.82, 32.04, 29.80, 29.76, 29.74, 29.72, 29.54, 29.48, 29.38, 26.18, 22.81, 18.46, 14.25. MALDI-TOF MS (m/z): $[M+Na]^+$ calcd for $C_{55}H_{94}N_2O_{12}$ 997.67; found 997.15

(3,5)12G1-CH$_2$-L-Ala-(3,5)-3EO-G1-(OCH$_3$)$_2$ (10be). From compound **5e** (0.21 g, 0.41 mmol, 1 eq), compound **8b** (0.19 g, 0.41 mmol, 1 eq), CDMT (0.071 g, 0.41 mmol, 1 eq) and NMM (0.10 g, 1.03 mmol, 2.5 eq) in dry THF (5 mL), 0.37 g (93 %) of the title compound were obtained as a yellow oil. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 2.3 Hz, 1H), 6.95 (d, *J* = 7.3, 1H), 6.90 (t, *J* = 2.2 Hz, 2H), 6.58 (t, *J* = 6.0 Hz, 1H), 6.34 (d, *J* = 2.1 Hz, 2H), 6.29 (d, *J* = 2.2 Hz, 1H), 4.67 (p, *J* = 7.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4,41 (dd, *J* = 14.8, 6.1 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.28 (dd, *J* = 14.9, 5.6 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.06 (t, *J* = 9.6 Hz, 4H, 2×Ar-O-*CH$_2$*-), 3.84 (t, *J* = 13.1 Hz, 4H, 2×Ar-O-*CH$_2$*(CH_2)$_{10}$$CH_3$), 3.79 (t, *J* = 9.5 Hz, 4H, 2×Ar-O-CH$_2$-*CH$_2$*-), 3.69-3.68 (m, 4H, 2×Ar-O-(CH_2)$_2$-O-*CH$_2$*-), 3.65-3.61 (m, 8H, 2×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.51 (m, 4H, 2×-*CH$_2$*O-CH$_3$), 3.33 (s, 6H, 2×-O*CH$_3$*), 1.68 (p, *J* = 7.1 Hz, 4H, 2×-OCH$_2$*CH$_2$*(CH_2)$_9$$CH_3$), 1.48 (d, *J* = 7.0 Hz, 3H, 1×-NHCH*(CH$_3$)*CO-), 1.37 (p, *J* = 7.3 Hz, 4H, 2×-O(CH_2)$_2$*CH$_2$*(CH_2)$_8$$CH_3$), 1.29-1.24 (m, 32H, 2×-O(CH_2)$_3$*(CH_2)$_8$*CH_3), 0.85 (t, *J* = 6.9 Hz, 6H, 2×-O(CH_2)$_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.51, 166.81, 160.68, 152.14, 148.69, 140.09, 126.65, 120.87, 113.63, 113.10, 105.95, 100.47, 72.05, 71.02, 70.88, 70.80, 70.76, 70.67, 70.57, 69.81, 69.67, 69.12, 68.74, 68.14, 59.15, 59.08, 49.43, 32.04, 29.80, 29.76, 29.74, 29.72, 29.54, 29.48, 29.38, 26.18, 22.81, 18.50, 14.25. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{55}H_{94}N_2O_{12}Na$, 998.35, found 998.90.

(3,5)12G1-CH$_2$-L-Ala-(3,4,5)-3EO-G1-(OCH$_3$)$_3$ (10bf). From compound **5f** (0.18 g, 0.26 mmol, 1 eq), compound **8b** (0.13 g, 0.26 mmol, 1 eq), CDMT (0.05 g, 0.29 mmol, 1.1 eq) and NMM (0.08 g, 0.78 mmol, 3 eq) in dry THF (5 mL), 0.25 g (83 %) of the title compound were obtained as a yellow oil. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, CDCl3) δ 7.09 (s, 3H), 6.64 (t, *J* = 5.8 Hz, 1H), 6.37 (d, *J* = 2.1 Hz, 2H), 6.32 (t, *J* = 2.2 Hz, 1H), 4.67 (p, *J* = 2.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.44 (dd, *J* = 14.7, 6.2 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.28 (dd, J = 14.6, 5.5 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.18 (m, 6H, 3×Ar-O-*CH$_2$*-), 3.87 (t, *J* = 6.5 Hz, 4H, 2×Ar-O-*CH$_2$*(CH_2)$_{10}$$CH_3$), 3.83 (t, *J* = 4.8, 4H, 2×Ar-O-CH$_2$-*CH$_2$*-), 3.78 (t, *J* = 5.0 Hz, 2H, 1×Ar-O-CH$_2$-*CH$_2$*-), 3.71-3.69 (m, 6H, 3×Ar-O-(CH_2)$_2$-O-*CH$_2$*-), 3.65-3.61 (m, 12H, 3×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.54-3.51 (m, 6H, 3×-*CH$_2$*O-CH$_3$), 3.36 (s, 3H, 1×-O*CH$_3$*), 3.34 (s, 6H, 2×-O*CH$_3$*), 1.72 (p, *J* = 7.1 Hz, 4H, 2×-OCH$_2$*CH$_2$*(CH_2)$_9$$CH_3$), 1.49 (d, *J* = 7.1 Hz, 3H, -NHCH*(CH$_3$)*CO-), 1.41 (p, *J* = 7.0 Hz, 4H, 2×-O(CH_2)$_2$*CH$_2$*(CH_2)$_8$$CH_3$), 1.30-1.25 (m, 32H, 2×-O(CH_2)$_3$*(CH_2)$_8$*CH_3), 0.87 (t, *J* = 6.9, 6H, 2×-O(CH_2)$_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.34,

166.85, 160.70, 152.65, 141.94, 140.17, 128.96, 107.51, 106.04, 100.45, 72.52, 72.07, 72.04, 70.83, 70.80, 70.75, 70.67, 70.65, 70.64, 70.56, 69.85, 69.27, 68.18, 59.11, 59.06, 56.08, 49.60, 43.80, 32.03, 29.79, 29.75, 29.73, 29.71, 29.53, 29.46, 29.38, 26.18, 22.80, 18.35, 14.23. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{62}H_{108}N_2O_{16}Na$, 1160.53, found 1159.91.

(3,4,5)12G1-CH$_2$-L-Ala-(3,4)-3EO-G1-(OCH$_3$)$_2$ (10cd). From compound **5d** (0.064 g, 0.097 mmol, 1 eq), compound **8c** (0.05 g, 0.097 mmol, 1 eq), NMM (0.024 g, 0.243 mmol, 2.5 eq), CDMT (0.019 g, 0.107 mmol, 1.1 eq) in dry THF (2 mL), 0.06 g (55 %) of the title compound were obtained as a slightly yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 2.0, 1H), 7.39 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.93 (br, 1H, -*NH*-), 6.87 (d, *J* = 8.4 Hz, 1H), 6.41 (s, 2H), 4.72 (p, *J* = 7.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.35 (dd, J = 14.8, 5.9 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.32 (dd, J = 14.8, 5.6 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.21 (dd, J = 9.6, 4.4 Hz, 4H, 2×Ar-O-*CH$_2$*-), 3.89-3.84 (m, 10H, 3×Ar-O-*CH$_2$*(CH_2)$_{10}$CH$_3$ and 2×Ar-O-CH$_2$-*CH$_2$*-), 3.73-3.71 (m, 4H, 2×Ar-O-(CH_2)$_2$-O-*CH$_2$*-), 3.63-3.61 (m, 8H, 2×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.54-3.50 (m, 4H, 2×-*CH$_2$*O-CH$_3$), 3.36 (s, 3H, 1×-O*CH$_3$*), 3.33 (s, 3H,), 1.75-1.69 (m, 6H, 3×-OCH$_2$*CH$_2$*(CH_2)$_9$CH$_3$), 1.49 (d, *J* = 7.0 Hz, 3H, 1×-NHCH*(CH$_3$)*CO-), 1.41(m, 6H, 3×-O(CH_2)$_2$*CH$_2$*(CH_2)$_8$CH$_3$), 1.24 (m, 48H, 3×-O(CH_2)$_3$*(CH$_2$)$_8$*CH$_3$), 0.86 (t, *J* = 6.9 Hz, 9H, 3×-O(CH_2)$_{11}$*CH$_3$*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.86, 159.75, 153.44, 152.23, 148.66, 137.59, 133.02, 126.72, 121.03, 113.82, 113.21, 106.07, 72.07, 71.03, 70.89, 70.81, 70.68, 70.57, 69.84, 69.21, 59.15, 59.08, 56.18, 49.43, 43.95, 32.06, 30.53, 29.89, 29.85, 29.80, 29.59, 29.50, 26.27, 22.82, 18.27, 14.24. MALDI-TOF MS (m/z): $[M+Na]^+$ calcd for $C_{67}H_{118}NaN_2O_{13}$, 1182.65; found 1182.42.

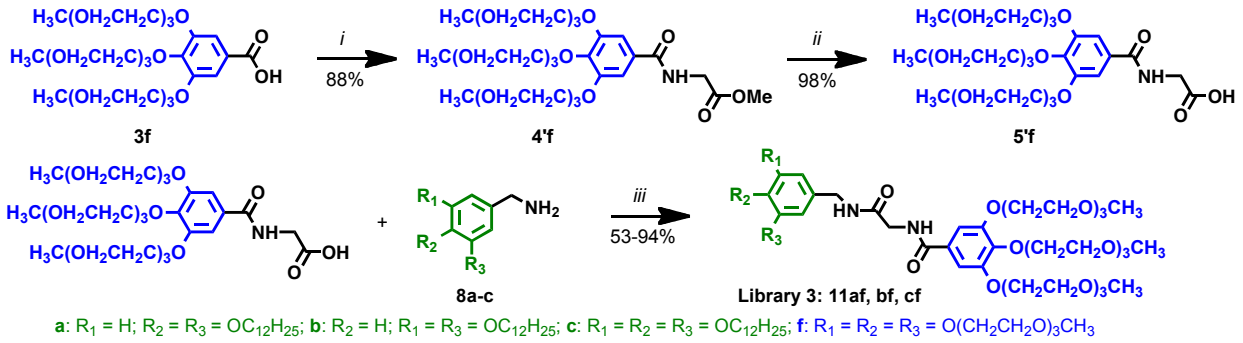
(3,4,5)12G1-CH$_2$-L-Ala-(3,5)-3EO-G1-(OCH$_3$)$_2$ (10ce). From compound **5e** (0.24 g, 0.35 mmol, 1 eq), compound **8c** (0.17 g, 0.35 mmol, 1 eq), CDMT (0.062 g, 0.35 mmol), NMM (0.07 g, 0.71 mmol, 2 eq), in dry THF (5 mL), 0.26 g (65%) of the title compound were obtained. From (3,5)-3EO-G1-(OCH$_3$)$_3$-L-Ala-OH (0.160 g, 0.31 mmol), (3,4,5)12-CH2-NH2 (0.205g, 0.31 mmol), CDMT (0.063g, 0.35 mmol), NMM (0.035g, 0.35 mmol) in dry THF (5mL), 0.29 g (97%) of the title compound was obtained. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.07 (d, *J* = 7.2 Hz, 1H), 6.91 (d, *J* = 2.1 Hz, 2H), 6.87 (t, *J* = 5.7 Hz, 1H), 6.58 (t, *J* = 2.0 Hz, 1H), 6.40 (s, 2H), 4.66 (dd, *J* = 14.0, 7.0 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.36 (dd, *J* = 14.8, 6.0 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.26 (dd, *J* = 14.8, 5.5 Hz, 1H, 0.5×-NH$_2$-*CH$_2$*-), 4.11-4.03 (m, 4H, 2×Ar-O-*CH$_2$*-), 3.86 (dt, *J* = 10.3, 5.3 Hz, 6H, 3×Ar-O-*CH$_2$*(CH_2)$_{10}$CH$_3$), 3.84-3.79 (m, 4H, 2×Ar-O-CH$_2$-*CH$_2$*-), 3.70 (dd, *J* = 5.7, 3.5 Hz, 4H, 2×Ar-O-(CH_2)$_2$-O-*CH$_2$*-), 3.68-3.65 (ddd, *J* = 9.3, 5.1, 3.0 Hz, 8H, 2×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.51 (dd, *J* = 5.7, 3.7 Hz, 4H, 2×-*CH$_2$*O-CH$_3$), 3.33 (d, *J* = 7.7 Hz, 6H, 2×-O*CH$_3$*), 1.70 (m, 6H, 3×-OCH$_2$*CH$_2$*(CH_2)$_9$CH$_3$), 1.48-1.40 (m, 9H, 1×-NHCH*(CH$_3$)*CO- and 3×-O(CH_2)$_2$*CH$_2$*(CH_2)$_8$CH$_3$), 1.24 (m, 48H, 3×-O(CH_2)$_3$*(CH$_2$)$_8$*CH$_3$), 0.85 (t, *J* = 6.8, 9H, 3×-O(CH_2)$_{11}$*CH$_3$*). ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 172.16,

166.96, 160.06, 153.32, 137.40, 135.83, 133.18, 105.98, 105.89, 105.17, 77.41, 77.16, 77.16, 76.91, 73.44, 71.97, 70.85, 70.69, 70.58, 69.65, 69.09, 67.79, 59.02, 49.55, 43.70, 31.98, 30.41, 29.81, 29.78, 29.72, 29.52, 29.49, 29.42, 26.20, 22.74, 18.43, 14.16. MALDI-TOF (m/z) calcd. $[M+K]^+$ for $C_{67}H_{118}N_2KO_{13}$, 1188.86, found 1182.21.

(3,4,5)12G1-CH_2-L-Ala-(3,4,5)-3EO-G1-$(OCH_3)_3$ (10cf). From compound **5f** (0.22 g, 0.32 mmol, 1 eq), compound **8c** (0.22 g, 0.32 mmol, 1 eq), CDMT (0.056 g, 0.32 g, 1 eq), NMM (0.065 g, 0.64 mmol, 2 eq) in dry THF (8 mL), 0.24 g (57 %) of the title compound were obtained as a yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, *J* = 7.2 Hz, 2H), 7.10 (s, 2H), 6.80 (t, *J* = 5.6 Hz, 1H), 6.44 (s, 2H), 4.67 (p, *J* = 6.9 Hz, 1H, 1×-NH*CH*(CH_3)NH-), 4.42 (dd, *J* = 14.8, 6.1 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4.26 (dd, *J* = 14.8, 5.3 Hz, 1H, 0.5×-NH_2-*CH_2*-), 4.18 (dt, *J* = 9.9, 4.9 Hz, 6H, 3×Ar-O-*CH_2*-), 3.83(m, 6H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.84-3.77 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.77-3.72 (m, 2H, 1×Ar-O-CH_2-*CH_2*-), 3.68 (m, 6H, 3×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.60 (ddd, *J* = 9.3, 5.1, 2.7 Hz, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.48 (m, 6H, 3×-*CH_2*O-CH_3), 3.35 (s, 3H, 1×-O*CH_3*) 3.31 (s, 6H, 2×-O*CH_3*), 1.72 (m, 6H, 3×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.50 (d, *J* = 7.0 Hz, 3H, 1×-NHCH*(CH_3)*CO-), 1.41 (m, 6H, 3×-$O(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.23 (m, 48H, 3×-$O(CH_2)_3$*$(CH_2)_8$*CH_3), 0.85 (t, J = 6.9, 9H, 3×-$O(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.76, 153.34, 152.60, 141.91, 137.47, 133.16, 128.84, 107.43, 105.98, 73.46, 72.47, 72.00, 71.97, 70.75, 70.69, 70.59, 70.49, 69.78, 69.21, 69.13, 59.04, 58.98, 49.61, 43.74, 31.98, 30.40, 29.81, 29.77, 29.75, 29.72, 29.51, 29.44, 29.42, 26.20, 22.74, 18.33, 14.16. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{74}H_{132}N_2O_{17}Na$, 1343.95, found 1343.72.

3.2 Modular Synthesis of Glycine Amide Containing "Single-Single" Amphiphilic Janus Dendrimers

Supporting Scheme S2. Synthesis of Glycine Amide Containing "Single-Single" Amphiphilic Janus Dendrimers[a]



[a]Reagents and conditions: *(i)* $NH_2CH_2COOCH_3{\cdot}HCl$, CDMT, NMM, THF, 23 °C, 8 h; *(ii)* KOH, EtOH:H_2O, reflux, 4 h; *(iii)* CDMT, NMM, THF, 23 °C, 8 h.

(3,4,5)-3EOMe$_3$-G1-Gly-OMe (**4'f**). 3,4,5-tris(methyl triethylene glycol)benzoate (**3f**) (1.2 g, 1.98 mmol, 1 eq) was dissolved in 20 mL of THF, and HCl•GlyOMe (0.24 g, 1.98 mmol, 1 eq) were added to form a suspension. The mixture was cooled to 0 °C, and CDMT (0.34 g, 1.98 mmol, 1 eq). NMM (0.50 g, 5.00 mmol, 2.5 eq) was then added dropwise during 4 min. The reaction was maintained at 23 °C for 8 h. The reaction mixture was dissolved in 100 mL of EtOAc and washed with 2×100 mL HCl (1N). The aqueous phase was further extracted with 3×100 mL of DCM. The combined organic phase was dried over $MgSO_4$, filtered and concentrated to yield 1.26 g (94 %) of **(3,4,5)-3EOMe$_3$-G1-Gly-OMe** as a yellowish oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (t, J = 5.4 Hz, 1H), 7.04 (s, 2H), 4.14–4.00 (m, 8H), 3.76–3.66 (m, 6H), 3.62–3.57 (m, 6H), 3.58–3.49 (m, 12H), 3.43 (dt, J = 6.6, 3.3, 6H), 3.25 (d, J = 7.7 Hz, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.37, 166.98, 152.25, 141.46, 128.57, 107.19, 72.18, 71.75, 71.70, 70.49, 70.45, 70.36, 70.32, 70.27, 69.51, 68.84, 58.78, 58.75, 52.06, 41.54. MALDI-TOF (m/z) calcd. $[M]^+$ for $C_{32}H_{55}NO_{15}Na$, 702.75, found 702.33.

(3,4,5)-3EOMe$_3$-G1-Gly-OH (**5'f**). **(3,4,5)-3EOMe$_3$-G1-Gly-OMe** (**4'f**) (1.26 g, 1.86 mmol, 1 eq) was dissolved in 60 mL of absolute EtOH (99%), and KOH (0.52 g, 9.3 mmol, 5eq) were added as an aqueous solution with 5.2 mL of water. The mixture was heated under reflux during 2 h, and then cooled to 23°C. The solution was evaporated to an aqueous phase that was acidified with HCl (2N) until pH = 1-2. The aqueous solution was extracted with 2×200 mL of EtOAc. The combined organic phase was dried over $MgSO_4$, filtered and concentrated to yield 1.06 g (86 %) of the title compound as a clear oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 5.3 Hz, 1H), 7.11 (s, 2H), 4.16 (dd, *J* = 9.5 Hz, 4.1, 6H), 4.11 (d, *J* = 5.3 Hz, 2H), 3.83-3.78 (m, 4H), 3.78-3.73 (m, 2H), 3.71-3.65 (m, 6H), 3.61 (ddd, *J* = 8.8, 5.4, 2.7 Hz, 12H), 3.51 (dt, *J* = 6.2, 3.2 Hz, 6H), 3.35-3.30 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.88, 167.61, 152.48, 141.74, 128.63, 107.50, 72.42, 71.97, 71.93, 70.70, 70.65, 70.52, 70.43, 69.78, 69.03, 59.02, 58.97, 41.92. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{32}H_{55}NO_{15}Na$, 688.72, found 688.32.

(3,4)12G1-CH$_2$-Gly-(3,4,5)-3EO-G1-(OCH$_3$)$_3$ (11af). From compound **5'f** (0.2 g, 0.3 mmol. 1 eq), compound **8a** (0.14 g, 0.3 mmol, 1eq), CDMT (0.053 g, 0.3 mmol, 1 eq), NMM (0.06 g, 0.6 mmol, 2 eq) in dry THF (5 mL), 0.18 g (53 %) of the title compound were obtained. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (t, *J* = 5.3 Hz, 1H, 1×-Ar-CO-*NH*-), 7.14 (s, 2H, 2×ArH), 6.78 (dd, *J* = 13.2, 10.3 Hz, 4H, 3×ArH and Ar-CH$_2$-*NH*-), 4.34 (d, *J* = 5.7 Hz, 2H, 1×Ar-*CH$_2$*-NH-), 4.23-4.13 (m, 6H, 3×Ar-O-*CH$_2$*-), 4.09 (d, *J* = 5.3 Hz, 2H, 1×-CO-*CH$_2$*-NH-), 3.94 (t, *J* = 6.6 Hz, 4H, 2×Ar-O-*CH$_2$*(CH$_2$)$_{10}$CH$_3$), 3.79 (dt, *J* = 15.4 Hz, 5.4, 6H, 1×Ar-O-CH$_2$-*CH$_2$*-), 3.73-3.66 (m, 6H, 3×Ar-O-(CH$_2$)$_2$-O-*CH$_2$*-), 3.62 (ddd, *J* = 9.1 Hz, 6.0, 3.9, 12H, 3×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.52 (ddd, *J* = 9.4, 5.8, 3.6 Hz, 6H, 3×-*CH$_2$*-O-CH$_3$), 3.35 (d, *J* = 16.3 Hz, 9H, 3×-O*CH$_3$*), 1.76 (m, 4H, 2×-OCH$_2$*CH$_2$*(CH$_2$)$_9$CH$_3$), 1.43 (m, 4H, 2×-O(CH$_2$)$_2$*CH$_2$*(CH$_2$)$_8$CH$_3$), 1.21 (m, 32H, 2×-O(CH$_2$)$_3$*(CH$_2$)$_8$*CH$_3$), 0.86 (t, *J* = 6.9, 6H, 2×-O(CH$_2$)$_{11}$*CH$_3$*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.20, 167.37, 152.47, 149.39, 148.61, 141.84, 130.81, 128.60, 120.18, 114.08, 113.79, 107.60, 100.08, 72.44, 71.98, 71.94, 70.71, 70.68, 70.64, 70.60, 70.55, 70.43, 69.76, 69.49, 69.38, 69.12, 59.02, 58.95, 43.99, 43.30, 31.97, 29.76, 29.75, 29.70, 29.53, 29.51, 29.41, 26.14, 22.79, 14.16. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{61}H_{106}N_2O_{16}Na$; 1146.50, found 1146.98.

(3,5)12G1-CH$_2$-Gly-(3,4,5)-3EO-G1-(OCH$_3$)$_3$ (11bf). From compound **5'f** (0.14 g, 0.21 mmol, 1 eq), compound **8b** (0.1 g, 0.21 mmol. 1 eq), CDMT (0.037 g, 0.21 mmol, 1 eq), NMM (0.043g, 0.42 mmol, 2 eq) in dry THF (5 mL), 0.11 g (47 %) of the title compound were obtained. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (s, 1H, 1×-Ar-CO-*NH*-), 7.14 (s, 2H, 2×ArH), 6.86 (s, 1H, Ar-CH$_2$-*NH*-), 6.37 (s, 2H, 2×ArH), 6.30 (s, 1H, 1×ArH), 4.34 (d, *J* = 5.4 Hz, 2H, 1×Ar-*CH$_2$*-NH-), 4.18 (dd, *J* = 11.5, 4.4 Hz, 6H, 1×Ar-O-*CH$_2$*-CH$_2$-), 4.10 (d, *J* = 4.8 Hz, 2H, 1×-CO-*CH$_2$*-NH-), 3.88 (t, *J* = 6.4 Hz, 4H, 2×Ar-O-*CH$_2$*(CH$_2$)$_{10}$CH$_3$), 3.78 (dd, *J* = 9.7 Hz, 4.8, 6H, 3×Ar-O-CH$_2$-*CH$_2$*-O-), 3,65 (m, 6H, 3×Ar-O-(CH$_2$)$_2$-O-*CH$_2$*-), 3.61 (ddd, *J* = 13.2, 8.9, 5.6 Hz, 12H, 3×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.50 (m, 6H, 3×-*CH$_2$*-O-CH$_3$), 3.35 (d, *J* = 15.5 Hz, 9H, 3×-O*CH$_3$*), 1.70 (m, 4H, 2×-OCH$_2$*CH$_2$*(CH$_2$)$_9$CH$_3$), 1.39 (m, 4H, 2×-O(CH$_2$)$_2$*CH$_2$*(CH$_2$)$_8$CH$_3$), 1.24 (br, 32H, 2×-O(CH$_2$)$_3$*(CH$_2$)$_8$*CH$_3$), 0.86 (t, *J* = 6.8 Hz, 6H, 2×-O(CH$_2$)$_{11}$*CH$_3$*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.30, 167.49, 160.55, 152.51, 141.81, 140.22, 128.59, 107.64, 106.09, 100.25, 72.47, 72.01, 71.97, 70.74, 70.70, 70.68, 70.62, 70.58, 70.46, 69.79, 69.16,

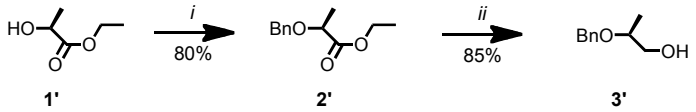
68.11, 59.06, 58.99, 44.12, 43.64, 31.98, 29.74, 29.71, 29.67, 29.49, 29.42, 29.35, 26.14, 22.75, 14.19. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{61}H_{106}N_2O_{16}Na$; 1146.50, found 1147.11.

(3,4,5)12G1-CH$_2$-Gly-(3,4,5)-3EO-G1-(OCH$_3$)$_3$ (11cf). From compound **5'f** (0.19 g, 0.29 mmol, 1 eq), compound **8c** (0.19 g, 0.29 mmol, 1 eq), CDMT (0.05 g, 0.29 mmol, 1 eq), NMM (0.058 g, 0.57 mmol, 2eq), 0.28 g (74 %) of the title compound were obtained as a yellowish solid. (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 5.2 Hz, 1H, 1×-Ar-CO-*NH*-), 7.17 (s, 2H, 2×ArH), 6.52 (t, *J* = 5.7 Hz, 1H, Ar-CH$_2$-*NH*-), 6.45 (s, 2H, 2×ArH), 4.36 (d, *J* = 5.7 Hz, 2H, 1×Ar-*CH$_2$*-NH-), 4.20 (dd, J = 9.5, 4.3 Hz, 6H, 1×Ar-O-*CH$_2$*-CH$_2$-), 4.10 (d, *J* = 5.3 Hz, 2H, 1×-CO-*CH$_2$*-NH-), 3.92 (dt, *J* = 10.5, 6.5 Hz, 6H, 2×Ar-O-*CH$_2$*(CH$_2$)$_{10}$CH$_3$), 3.78-3.71 (m, 6H, 3×Ar-O-CH$_2$-*CH$_2$*-O-), 3.68–3.65 (m, 6H, 3×Ar-O-(CH$_2$)$_2$-O-*CH$_2$*-), 3.61–3.54 (m, 12H, 3×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.50 (ddd, *J* = 9.4, 5.8, 3.7 Hz, 6H, 3×-*CH$_2$*-O-CH$_3$), 3.37 (s, 3H, 1×-O*CH$_3$*), 3.33 (s, 6H, 2×-O*CH$_3$*), 1.79-1.68 (m, 6H, 3×-OCH$_2$*CH$_2$*(CH$_2$)$_9$CH$_3$), 1.44 (p, *J* = 6.4 Hz, 6H, 3×-O(CH$_2$)$_2$*CH$_2$*(CH$_2$)$_8$CH$_3$), 1.26 (m 48H, 3×-O(CH$_2$)$_3$*(CH$_2$)$_8$*CH$_3$), 0.88 (t, *J* = 6.9 Hz, 9H, 3×-O(CH$_2$)$_{11}$*CH$_3$*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.07, 167.48, 153.48, 152.65, 142.23, 137.74, 133.04, 128.70, 108.01, 106.41, 73.57, 72.55, 72.08, 72.05, 70.82, 70.75, 70.74, 70.67, 70.50, 69.89, 69.40, 69.31, 59.14, 59.06, 44.21, 43.98, 32.08, 32.07, 30.49, 29.90, 29.88, 29.86, 29.84, 29.80, 29.78, 29.60, 29.53, 29.51, 26.28, 22.83, 14.25. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{73}H_{130}N_2O_{17}Na$; 1330.83, found 1329.35.

3.3 Modular Synthesis of L-PPD-Ester Containing "Single-Single" Amphiphilic Janus Dendrimers

3.3.1 Synthetic Procedure of (*S*)-2-(Benzyloxy)-1-Propanol.

Supporting Scheme S3. Synthesis of (*S*)-2-(Benzyloxy)-1-Propanol (3')[a]



[a]Reagents and conditions: (i) Benzyl bromide, NaH, THF, 23 °C, 8 h; (ii) $LiAlH_4$, THF, 23 °C, 4 h

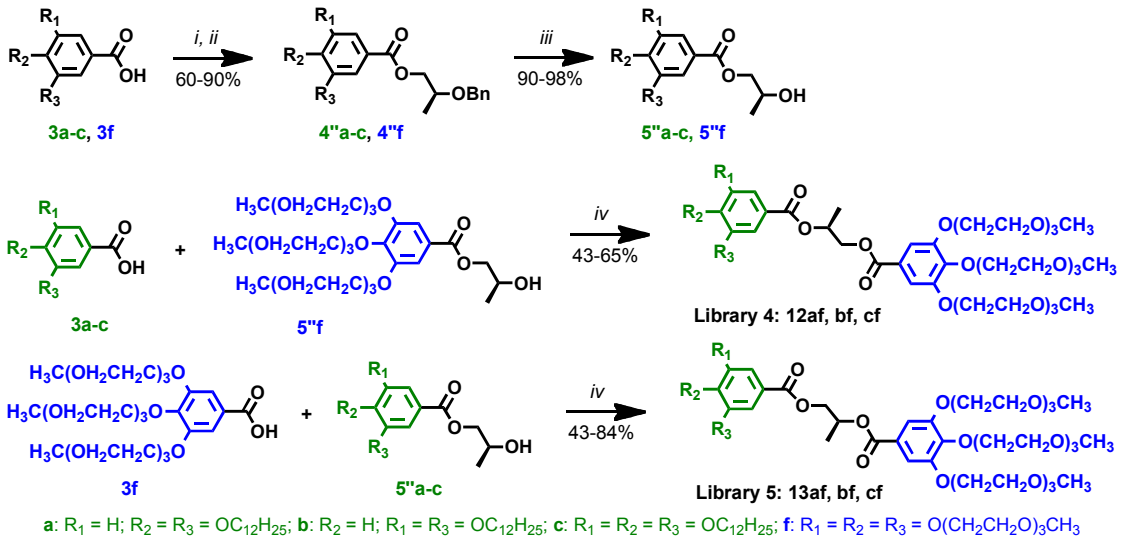
Bn-Lac-OEt (2'). Ethyl-(*S*)-Lactate (1') (40.0 mmol, 6.84 g) was dissolved in 30 mL THF. The reaction mixture was cooled at -78 °C, then NaH (1.77 g, 60% suspension in mineral oil) was added in small portions. The reaction mixture was stirred under Argon for 15 min then benzyl bromide (4.83 mL) was added dropwise. The reaction was stirred for additional 8 h at 23 °C. The precipitate was filtered off and the solution was concentrated under reduced pressure. Product was purified by column chromatography (SiO_2, EtOAc:Hexane 1/3) to give the product as a yellow oil (7.60 g, 80%). ^{1}H NMR (360 MHz,

$CDCl_3$) δ 7.34-7.25 (m, 5H), 4.69 (d, J = 11.5 Hz, 1H), 4.45 (d, J = 11.9 Hz, 1H), 4.43-4.4.17 (m, 2H), 4.05 (q, J = 6.8 Hz, 1H), 1.43 (d, J = 6.8 Hz, 3H), 1.29 (t, J = 6.8 Hz, 3H). ^{13}C NMR (90 MHz, $CDCl_3$) δ 173.4, 137.8, 128.5, 128.1, 127.9, 74.2, 72.1, 60.9, 18.8, 14.3.

(*S*)-2-(Benzyloxy)-1-Propanol (3'). Bn-Lac-OEt (**2'**) (20.6 mmol, 4.28 g) was dissolved in 25 mL THF, and the mixture was cooled to 0 °C. $LiAlH_4$ (20.6 mmol, 0.80 g) was added in the mixture. The reaction was maintained at 23 °C during 4 h. The reaction mixture was filtered through Celite and concentrated. The product was purified by column chromatography (SiO_2, EtOAc:Hexane 1/3) to give a yellow oil (2.5 g, 85% yield). ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.34-7.24 (m, 5H), 4.64 (d, J = 11.5 Hz, 1H), 4.48 (d J = 11.5 Hz, 1H), 3.67-3.57 (m, 2H), 3.50 (dd, J = 11.5, 6.8 Hz, 1H), 2.21 (br s, 1H), 1.17 (d, J= 6.1 Hz, 3H). ^{13}C NMR (90 MHz, $CDCl_3$) δ 138.6, 128.6, 127.8, 127.8, 75.7, 70.9, 66.5, 16.0.

3.3.2 Synthesis of the First Generation Dendritic Alcohol 5''a-c and 5''f

Supporting Scheme SF4. Synthesis of 1,2-Propanediol Ester Containing Amphiphilic Janus Dendrimers[a]



[a]Reagents and conditions: *(i)* $SOCl_2$, CH_2Cl_2, 0-60 °C, 2h; *(ii)* DCC, DPTS, CH_2Cl_2, 23 °C, 8 h; *(iii)* Pd/C, H_2, MeOH: CH_2Cl_2 = 1: 2, 23 °C, 4 h; *(iv)* DCC, DPTS, CH_2Cl_2, 23 °C, 8 h.

General Synthesis of Hydrophilic Dendritic Carboxylic Acid Chlorides. Thionyl chloride (2 eq) was added dropwise to a stirred solution of dendritic carboxylic acid (1 eq) in 20 mL CH_2Cl_2 under N_2 positive pressure at 0 °C. The resulting reaction mixture was stirred for additional 2 h at 23 °C then solvent was removed in vacuo, to give the product as a pale yellow oil.

General Synthesis of Hydrophobic Dendritic Carboxylic Acid Chlorides. Thionyl chloride (2 eq) was added dropwise to the corresponding dendritic carboxylic acid (1 eq) at 0 °C, and then the reaction mixture was stirred at 60 °C under N_2 positive pressure for 2h. The excess of thionyl chloride was removed in vacuo to give the product as a pale yellow solid.

(3,4)12G1-L-PPD-OBn (4''a). A solution of (3,4)12G1-COCl (3.93 g, 7.7 mmol), was added dropwise to a stirred solution of **(*S*)-2-(benzyloxy)-1-propanol (3')** (1.28 g, 7.7 mmol) in CH_2Cl_2 (20 mL), NEt_3 (1.13 mL, 8.0 mmol) and DMAP (cat.) under N_2 atmosphere. The title compound was isolated after column chromatography SiO_2, (EtOAc:hexane 1:2) as a white solid (3.40 g, 77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.5 Hz, 1H), 7.56 (s, 1H), 7.35-7.23 (m, 5H), 6.86 (d, J = 8.5 Hz, 1H), 4.66 (d, J = 12.6 Hz, 1H), 4.63 (d, J = 13.2 Hz, 1H), 4.34 (dd, J = 11.4, 4.3 Hz, 1H), 4.30 (dd, J = 11.6, 6.4 Hz, 1H), 4.07-4.00 (m, 5H), 3.91-3.87 (m, 1H), 1.85-1.79 (m, 5H), 1.47-1.46 (m, 6H), 1.29-1.28 (m, 45H), 0.88 (t, J = 6.5 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 153.5, 148.7, 138.7, 128.5, 127.7, 127.7, 123.8, 122.5, 114.6, 112.1, 72.9, 71.3, 69.4, 69.1, 67.8, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.3, 29.3, 29.2, 29.1, 26.1, 26.1, 22.8, 17.2,14.2. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{41}H_{66}NaO_5$ 661.49; found 662.58.

(3,5)12G1-L-PPD-OBn (4''b). A solution of (3,5)12G1-COCl (2.55 g 5.00 mmol), was added dropwise to a stirred solution of **(*S*)-2-(benzyloxy)-1-propanol (3')** (0.83 g, 5.00 mmol) in CH_2Cl_2 (30 mL), NEt_3 (0.77 mL, 5.5 mmol) and DMAP (cat.) under N_2 atmosphere. The title compound was isolated as a white solid (2.50 g, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.27 (m, 5H), 7.21 (d, J = 2.3 Hz, 2H), 6.68 (t, J = 2.3 Hz, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 4.39-4.32 (m, 2H), 3.98 (t, J = 6.5 Hz, 4H), 3.93-3.91 (m, 1H), 1.82-1.77 (m, 6H), 1.50-1.47 (m, 5H), 1.37-1.23 (m, 44H), 0.91 (t, J = 7.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 160.3, 138.6, 131.9, 128.4, 127.6, 127.6, 107.8, 106.5, 72.8, 71.2, 68.4, 68.1, 55.8, 35.0, 32.0, 29.8, 29.7, 29.7, 29.7, 29.5, 29.5, 29.3, 26.1, 25.6, 24.8, 22.8, 17.2, 14.2. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{41}H_{66}NaO_5$ 661.49; found 662.33.

(3,4,5)12G1-L-PPD-OBn (4''c). A solution of (3,4,5)12G1-COCl (0.624 g, 0.90 mmol), was added dropwise to a stirred solution of **(*S*)-2-(benzyloxy)-1-propanol (3')** (0.17 g, 1.00 mmol) in CH_2Cl_2 (20 mL), NEt_3 and DMAP (cat.) under N_2 atmosphere. The title compound was purified by column chromatography (SiO_2, EtOAc:Hexane 1:3). The product was obtained as a white solid (0.61 g, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.23 (m, 5H), 4.66 (d, J = 12.0 Hz, 1H), 4.63 (d, J = 12.0 Hz, 1H), 4.37 (dd, J = 11.4, 4.1 Hz, 1H), 4.29 (dd, J = 11.5, 6.6 Hz, 1H), 4.04-3.98 (m, 6H), 3.96-3.88 (m, 1H), 1.83-1.72 (m, 8H), 1.50-1.44 (m, 7H), 1.33-1.20 (m, 62 H), 0.88 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.3, 152.9, 142.7, 138.6, 128.5, 127.7, 127.6, 124.8, 108.3, 73.6, 72.9, 71.3, 69.3,

68.0, 55.8, 35.0, 32.0, 30.5, 29.9, 29.9, 29.8, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.4, 26.2, 26.2, 25.6, 24.8, 22.8, 17.2, 14.2. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{53}H_{90}NaO_6$ 845.67; found 845.50.

(3,4)-3EO-G1-$(OCH_3)_2$-L-PPD-OBn (4''d). A solution of (3,4)-3EO-G1-COCl (0.893 g, 1.92 mmol), was added dropwise to a stirred solution of **(*S*)-2-(benzyloxy)-1-propanol (3')** (0.32 g, 1.92 mmol) in CH_2Cl_2 (20 mL), NEt_3 (2.20 mmol) and DMAP (cat.) under N_2 atmosphere. The title compound was purified by column chromatography (SiO_2, EtOAc:Hexane 1:2 to yield the tile compound (1.00 g, 89 %) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (dd, J = 8.5, 2.0 Hz, 1H), 7.58 (d, J = 1.5 Hz, 1H), 7.36-7.24 (m, 5H), 6.96 (d, J = 8.5 Hz, 0.2H), 6.91 (d, J = 8.5 Hz, 0.8H), 4.66 (d J = 12.0 Hz, 1H), 4.62 (d, J = 12.0 Hz, 1H), 4.35-4.25 (m, 2H), 4.20-4.18 (m, 4H), 3.92-3.86 (m, 4H), 3.75-3.72 (m, 4H), 3.68-3.61 (m, 8H), 3.55-3.51 (m, 4H), 3.37 (s, 6H), 1.29 (d, J = 6.0 Hz, 2.5H), 1.19 (d, J = 6.5 Hz, 0.5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ166.3, 153.2, 148.5, 138.7, 128.6, 127.9, 127.7, 124.2, 123.1, 115.3, 112.9, 72.9, 72.1, 71.3, 71.1, 71.0, 70.8, 70.7, 69.8, 69.7, 69.0, 68.7, 67.8, 59.2, 17.3. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{31}H_{46}NaO_{11}$ 617.30, found 618.23.

(3,5)-3EO-G1-$(OCH_3)_2$-L-PPD-OBn (4''e). A solution of (3,5)-3EO-G1-COCl (0.893 g, 1.92 mmol), was added dropwise to a stirred solution of **(*S*)-2-(benzyloxy)-1-propanol (3')** (0.32 g, 1.92 mmol) in CH_2Cl_2 (20 mL), NEt_3 (2.27 mmol) and DMAP (cat.) under N_2 atmosphere. The title compound was purified by column chromatography (SiO_2, EtOAc:Hexane 1:2 to yield the tile compound (1.04 g, 90 %) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 7.20 (d, J = 2.5 Hz, 2H), 6.70 (d, J = 2.0 Hz, 1), 4.66 (d, J = 12.0 Hz, 1H), 4.62 (12.0 Hz, 1H), 4.33-4.32 (m, 2H), 4.15-4.12 (m, 4H), 3.91-3.82 (m, 5H), 3.75-3.69 (m, 4H), 3.69-3.64 (m, 9H),3.56-3.54 (m, 4H), 3.38 (s, 6H), 1.29 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 166.2, 159.9, 138.6, 132.0, 128.5, 127.7, 108.3, 106.9, 72.7, 72.0, 71.2, 71.0, 70.8, 70.7, 69.7, 68.1, 67.8, 59.1, 17.2. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{31}H_{46}NaO_{11}$ 617.30; found 618.32.

(3,4,5)-3EO-G1-$(OCH_3)_3$-L-PPD-OBn (4''f). A solution of (3,4,5)-3EO-G1-COCl (0.658 g, 1.05 mmol), was added dropwise to a stirred solution of **(*S*)-2-(benzyloxy)-1-propanol (3')** (0.175g, 1.05 mmol) in CH_2Cl_2 (20 mL), NEt_3 (0.11 mL) and DMAP (5mg) under N_2 atmosphere. The title compound was purified by column chromatography (SiO_2, EtOAc:MeOH 99/1 to yield the tile compound (0.70 g, 86 %) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.24 (m, 7H), 4.37-4.62 (m, 2H), 4.33-4.31 (m, 2H), 4.30-4.22 (m, 2H), 4.21-4.15 (m, 4H), 3.88-3.78 (m, 7H), 3.73-3.69 (m, 6H), 3.67-3.60 (m, 12H), 3.54-3.51 (m, 6H), 3.37 (s, 3H), 3.36 (s, 6H), 1.28 (d, J = 8.5 Hz, 2.8H), 1.17 (d, J = 8.5 Hz, 0.2H). MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{37}H_{58}O_{15}Na$ 780.38; found 780.12.

General Procedure for the Synthesis of HO-(*S*)-1,2-Propanediol Dendritic Acids 5''a-f. To a stirred solution of BnO-(*S*)-1,2-propanediol dendritic fragments 7a-g in CH_2Cl_2: MeOH (20 mL, 1:1 vol), Pd/C 100 mg (10% wt.) were added. The resulting reaction mixture was stirred under a positive atmosphere of H_2 at 23 °C for 3 h and then the catalyst was filtered off over Celite the organic layer was diluted with CH_2Cl_2 (40 mL), washed with water (20 mL), then with brine (20 mL) and dried over $MgSO_4$. The solvent was removed in vacuo to give the corresponding HO-(*S*)-1,2-propanediol dendritic building block**.**

(3,4)12G1-L-PPD-OH (5'a). (1.33 g, 90%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, J = 8.5, 2.0 Hz, 1H), 7.54 (d, J = 2Hz, 1H), 6.85 (d, J = 8.5 Hz, 1H), 4.33-4.28 (m, 1H), 4.20 -4.15 (m, 2H), 4.03 (q, J = 6.5 Hz, 5H), 1.86-1.79 (m, 4H), 1.50-1.44 (m, 5H), 1.36-1.27 (m, 45H), 0.88 (t, J = 6.75 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 153.6, 148.7, 123.8, 122.2, 114.6, 112.1, 70.1, 69.5, 69.1, 66.4, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.5, 29.3, 29.2, 26.1, 26.1, 22.8, 19.4, 14.2. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{34}H_{60}NaO_5$ 571.44; found 572.22.

(3,5)12G1-L-PPD-OH (5'b). (1.12 g, 94%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 2.3 Hz, 2H), 6.64 (2.3 Hz, 1H), 4.31-4.28 (m, 1H), 4.19-4.15 (m, 2H), 3.95 (t, J = 6.5 Hz, 4H), 1.76 (qui, J = 6.6 Hz, 5H), 1.44 (qui, J = 6.6 Hz, 5H), 1.38 -1.27 (m, 44H), 0.89-0.83 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 160.3, 131.6, 107.9, 106.6, 70.3, 68.5, 66.3, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.3, 29.2, 26.1, 22.8, 19.4, 14.2. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{34}H_{60}NaO_5$. 571.44; found 573.23.

(3,4,5)12G1-L-PPD-OH (5'c). (0.55 g, 95%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (s, 2H), 4.21-4.18 (m, 1H), 4.18-4.15 (m, 2H), 4.01 (qui, J = 6.8 Hz, 6H), 1.81 (qui J = 6.6 Hz, 5H), 1.74 (qui, J = 7.2 Hz, 2H), 1.47 (qui, J = 7.0 Hz, 7H), 1.41-1.27 (m, 59H), 0.89-0.84 (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 153.0, 142.9, 124.4, 108.3, 73.6, 70.3, 69.4, 66.5, 32.0, 30.5, 29.9, 29.8, 29.8, 29.8, 29.8, 29.7, 29.5, 29.5, 29.5, 29.4, 26.2, 26.2, 22.8, 19.4, 14.2. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{46}H_{84}O_6Na$ 732.63; found 734.52.

(3,4)-3EO-$(OCH_3)_3$-L-PPD-OH (5'd). (0.80 g, 95%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68-7.65 (m, 2H), 7.60-7.58 (m, 1H), 6.92-6.90 (m, 1H), 4.31-4.28 (m, 1H), 4.23-4.14 (m, 6H), 3.90-3.84 (m, 4H), 3.75-3.72 (m, 5H), 3.68-3.54 (m, 9H), 3.53-3.52 (m, 4H), 3.36 (s, 6H), 1.35 (d, J = 6.5 Hz, 0.5H), 1.27 (d, J = 6.5 Hz, 2.5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 166.4, 153.4, 153.3, 148.4, 148.4, 129.8, 124.3, 123.2, 122.8, 115.5, 112.9, 72.7, 72.0, 71.0, 71.0, 70.8, 70.7, 70.2, 70.0, 69.9, 69.8, 69.6, 69.4, 69.1, 69.0, 68.7, 66.4, 66.2, 59.1, 21.0, 19.4, 16.5. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{24}H_{40}NaO_{11}$527.26; found 527.01.

(3,5)-3EO-(OCH_3)$_3$-L-PPD-OH (5'e). (0.66 g, 92%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, J = 2.3 Hz, 2H), 6.71 (t, J = 2.3 Hz, 1H), 4.32-4.31 (m, 1H), 4.19-4.14 (m, 6H), 3.87 (t, J = 4.9 Hz, 4H), 3.75-3.73 (m, 4H), 3.70 -3.64 (m, 8H), 3.56-3.54 (m, 4H), 3.38 (m, 6H), 1.28 (d, J = 6.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 160.0, 131.8, 108.4, 107.0, 72.1, 71.0, 70.8, 70.7, 70.4, 69.7, 67.9, 66.3, 59.2, 19.4. MALDI-TOF *(m/z)* calcd. $[M+Na]^+$ for $C_{24}H_{40}NaO_{11}$ 527.26; found 526.62.

(3,4,5)-3EO-(OCH_3)$_3$-L-PPD-OH (5'f). (1.01 g, 98%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (s, 2H), 4.32-4.31 (m, 1H), 4.30 -4.15 (m, 9H), 3.88-3.85 (m, 4H), 3.81-3.79 (m, 2H), 3.74-3.70 (m, 7H), 3.69-3.62 (m, 13H), 3.55-3.80 (m, 6H), 3.36 (s, 3H), 3.37 (s, 6H), 1.28 (t, J = 6.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 152.5, 143.2, 124.8, 109.7, 72.6, 72.1, 71.0, 70.8, 70.7, 70.7, 70.7, 70.4, 69.8, 69.2, 66.3, 59.1, 19.5. MALDI-TOF *(m/z)* calcd. $[M+K]^+$ for $C_{30}H_{53}KO_{15}$ 691.33; found 690.30.

3.3.3 Synthesis of "Single-Single" L-PPD Ester Containing Amphiphilic Janus Dendrimers 12af-13cf.

(3,4)12G1-CH_2-I-PPD-(3,4,5)-3EO-G1-(OCH_3)$_3$ (12af). Compound **3a** (0.32 g, 0.66 mmol, 1.05 eq) and compound **5''f** (0.42 g, 0.63 mmol, 1eq) were dissolved in 10 mL DCM, then DCC (0.13 g, 0.63 mmol, 1eq) was added followed by DPTS (0.24, 0.82 mmol, 1.3 eq). The resulting reaction mixture was stirred at 23 °C for 8 h under N_2. Purification by column chromatography (SiO_2, EtOAc/MeOH (9:1)) yielded the title compound as a colorless solid (0.47 g, 65%). (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dd, J = 8.4, 1.9 Hz, 1H, Ar), 7.51 (d, J = 1.9 Hz, 1H, Ar), 7.24 (s, 2H, Ar), 6.84 (d, J = 8.6 Hz, 1H, Ar), 5.51-5.45 (m, 1H, -O-*CH*(CH_3)CH_2-O-), 4.47-4.37 (qd, J = 7.0, 6.8, 4.0, 4.0 Hz, 2H, 1×-CH(CH_3)*CH_2*-O-), 4.19 (t, J = 5.0 Hz, 2H, 1×Ar-O-*CH_2*-), 4.14-4.06 (m, 4H, 2×Ar-O-*CH_2*-), 4.03-3.98 (dt, J = 6.7, 6.4 Hz, 4H, 2×Ar-O-*CH_2*(CH_2)$_{10}$$CH_3$), 3.81 (t, J = 4.9 Hz, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.77 (t, J = 5.0 Hz, 2H, 1×Ar-O-CH_2-*CH_2*-), 3.71-3.68 (m, 6H, 3×Ar-O-(CH_2)$_2$-O-*CH_2*-), 3.64-3.60 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.51 (t, J = 4.7 Hz, 6H, 3×-*CH_2*O-CH_3), 3.35 (s, 9H, 3×-CH_2O-*CH_3*), 1.81 (sext, J = 6.1 Hz, 4H, 2×-OCH_2*CH_2*(CH_2)$_9$$CH_3$), 1.45 (quint, J = 6.6 Hz, 4H, 2×-O(CH_2)$_2$*CH_2*(CH_2)$_8$$CH_3$), 1.43 (d, J = 6.5 Hz, 3H, 1×-OCH(*CH_3*)CH_2O-), 1.38-1.18 (m, 32H, 2×-O(CH_2)$_3$*(CH_2)$_8$*CH_3), 0.86 (t, J = 6.9 Hz, 6H, 2×-O(CH_2)$_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.89, 165.83, 153.49, 152.38, 148.66, 142.83, 124.70, 123.73, 122.48, 114.51, 112.03, 109.14, 72.49, 72.02, 70.90, 70.77, 70.65, 70.62, 70.61, 69.68, 69.43, 69.12, 68.90, 68.60, 66.90, 59.08, 32.00, 29.79, 29.77, 29.74, 29.73, 29.69, 29.53, 29.48, 29.44, 29.32, 29.18, 26.13, 26.07, 22.77, 16.89, 14.19. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{62}H_{106}NaO_{18}$ 1162.50; found 1163.44.

(3,5)12G1-CH_2-I-PPD-(3,4,5)-3EO-G1-(OCH_3)$_3$ (12bf). Compound **3b** (0.16 g, 0.33 mmol, 1.05 eq) and **5''f** (0.21 g, 0.32 mmol, 1eq) were dissolved in 10 mL DCM, then DCC (0.07 g, 0.32 mmol, 1eq)

was added followed by DPTS (0.12 g, 0.41 mmol, 1.3 eq). The resulting reaction mixture was stirred at 23 °C for 8 h under N_2. Purification by column chromatography (SiO_2, EtOAc) yielded the title compound as a colorless oil (0.16 g, 43%). (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (s, 2H, Ar), 7.15 (s, 2H, Ar), 6.62 (s, 1H, Ar), 5.52 (dd, J = 10.4, 6.3 Hz, 1H, -O-*CH*(CH_3)CH_2-O-), 4.48 (dd, J = 11.4, 3.4 Hz, 1H, 1×-CH(CH_3)*CH_2*-O-), 4.39 (dd, J = 11.6, 7.4 Hz, 1H, 1×-CH(CH_3)*CH_2*-O-), 4.21 (t, J = 4.6 Hz, 2H, 1×Ar-O-*CH_2*-), 4.15-4.08 (m, 4H, 2×Ar-O-*CH_2*-), 3.95 (t, J = 6.4 Hz, 4H, 2×Ar-O-*CH_2*(CH_2)$_{10}$$CH_3$), 3.81 (dt, J = 19.5, 4.7 Hz, 6H, 3×Ar-O-CH_2-*CH_2*-), 3.75-3.68 (m, 6H, 3×Ar-O-(CH_2)$_2$-O-*CH_2*-), 3.68-3.60 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.51 (dd, J = 5.2, 4.0 Hz, 6H, 3×-*CH_2*O-CH_3), 3.35 (s, 9H, 3×-CH_2O-*CH_3*), 1.82-1.72 (m, 4H, 2×-OCH_2*CH_2*(CH_2)$_9$$CH_3$), 1.43 (t, J = 8.4 Hz, 7H, 1×-OCH(*CH_3*)CH_2O- and 2×-O(CH_2)$_2$*CH_2*(CH_2)$_8$$CH_3$), 1.39-1.20 (m, 32H, 2×-O(CH_2)$_3$*(CH_2)$_8$*CH_3), 0.88 (t, J = 6.6 Hz, 6H, 2×-O(CH_2)$_{11}$*CH_3*).^{13}C NMR (126 MHz, $CDCl_3$) δ 165.89, 165.80, 160.26, 152.38, 142.82, 131.98, 124.63, 109.10, 107.87, 106.38, 72.49, 72.02, 70.89, 70.77, 70.65, 70.62, 70.61, 69.68, 69.00, 68.89, 68.42, 66.82, 59.09, 49.15, 34.05, 32.00, 29.75, 29.72, 29.69, 29.66, 29.63, 29.48, 29.43, 29.29, 26.12, 25.72, 25.04, 22.77, 16.83, 14.20. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{62}H_{106}NaO_{18}$, 1161.74, found. 1161.76.

(3,5)12G1-CH_2-I-PPD-(3,4,5)-3EO-G1-(OCH_3)$_3$ (12cf). Compound **3c** (0.22 g, 0.32 mmol, 1. eq) and **5''f** (0.21 g, 0.32 mmol, 1eq) were dissolved in 10 mL DCM, then DCC (0.07 g, 0.32 mmol, 1eq) was added followed by DPTS (0.12, 0.41 mmol, 1.3 eq). The resulting reaction mixture was stirred at 23 °C for 8 h under N_2. Purification by column chromatography (SiO_2, EtOAc) yielded the title compound as a colorless solid (0.23 g, 53%). (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, J = 5.7 Hz, 2H, 2×Ar*H*), 7.22 (d, J = 5.7 Hz, 2H, 2×Ar*H*), 5.55-5.44 (m, 1H, 1×-O-*CH*(CH_3)CH_2-O-), 4.50-4.40 (m, 2H, 2×-CH(CH_3)*CH_2*-O-), 4.24-4.19 (m, 2H, 1×Ar-O-*CH_2*-CH_2-O-), 4.19-4.09 (m, 4H, 2×Ar-O-*CH_2*-CH_2-O-), 4.03-3.95 (m, 6H, 3×Ar-O-*CH_2*(CH_2)$_{10}$$CH_3$), 3.83 (dd, J = 9.5, 4.6, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.81-3.76 (m, 2H, 1×Ar-O-CH_2-*CH_2*-), 3.73-3.69 (m, 6H, 3×Ar-O-(CH_2)$_2$-O-*CH_2*-), 3.67-3.61 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.53 (dd, J = 5.5, 3.9 Hz, 6H, 3×-*CH_2*O-CH_3), 3.37 (s, 9H, 3×-CH_2O-*CH_3*), 1.84-1.70 (m, 6H, 3×-OCH_2*CH_2*(CH_2)$_9$$CH_3$), 1.50-1.43 (m, 9H, 1×-OCH(*CH_3*)CH_2O- and 3×-O(CH_2)$_2$*CH_2*(CH_2)$_8$$CH_3$), 1.37-1.22 (m, 48H, 3×-O(CH_2)$_3$*(CH_2)$_8$*CH_3), 0.88 (t, J = 6.9, 9H, 3×-O(CH_2)$_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.87, 165.86, 152.98, 152.45, 142.98, 142.73, 124.81, 124.69, 109.33, 109.26, 108.26, 73.64, 72.56, 72.07, 70.95, 70.86, 70.81, 70.77, 70.70, 70.66, 69.73, 69.38, 69.35, 69.27, 69.14, 69.04, 68.99, 66.82, 59.14, 32.05, 30.48, 29.88, 29.87, 29.86, 29.84, 29.82, 29.79, 29.78, 29.72, 29.68, 29.66, 29.57, 29.52, 29.49, 29.46, 29.42, 26.30, 26.26, 26.20, 22.82, 16.99, 14.23. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{74}H_{130}NaO_{19}$ 1345.92; found 1346.56.

(3,4)12G1-CH_2-II-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$ (13af). Compound **5''a** (0.22 g, 0.32 mmol, 1eq) and compound **3f** (0.16 g, 0.33 mmol, 1.05 eq) were dissolved in 10 mL DCM, then DCC (0.07 g, 0.32 mmol, 1eq) was added followed by DPTS (0.12 g, 0.41 mmol, 1.3 eq). The resulting reaction mixture was stirred at 23 °C for 8 h under N_2. Purification by column chromatography (SiO_2, EtOAc) yielded the title compound as a yellowish solid (0.16 g, 43%). (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (dd, J = 8.4, 2.0 Hz, 1H, 1×Ar*H*), 7.52 (d, J = 2.0 Hz, 1H, 1×Ar*H*), 7.29 (s, 2H, 2×Ar*H*), 6.84 (d, J = 8.5 Hz, 1H, 1×Ar*H*), 5.53-5.44 (m, 1H, 1×-O-CH_2*CH*(CH_3)-O-), 4.45 (qd, J = 11.7, 5.3 Hz, 2H, 2×-O-*CH_2*CH(CH_3)-O-), 4.24-4.19 (m, 6H, 3×Ar-O-*CH_2*-CH_2-O-), 4.19-4.13 (m, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 4.01 (dt, J = 18.3, 6.6 Hz, 4H), 3.88-3.82 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.82-3.76 (m, 2H, 1×Ar-O-CH_2-*CH_2*-), 3.72 (dt, J = 5.2, 3.8 Hz, 6H, 3×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.69-3.59 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.57-3.50 (m, 6H, 3×-*CH_2*O-CH_3), 3.39-3.35 (m, 9H, 3×-CH_2O-*CH_3*), 1.89-1.76 (m, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.51-1.41 (m, 7H, 1×-OCH(*CH_3*)CH_2O- and 2×-O$(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.31-1.24 (m, 32H, 2×-O$(CH_2)_3$*$(CH_2)_8$*CH_3), 0.88 (t, J = 6.9, 6H, 2×-O$(CH_2)_{11}$*CH_3*). ^{13}C NMR (126MHz, $CDCl_3$) δ 166.15, 165.51, 153.50, 152.36, 148.63, 142.82, 125.11, 123.71, 122.06, 114.43, 112.02, 109.22, 72.00, 70.88, 70.76, 70.63, 70.61, 70.60, 69.69, 69.32, 69.25, 69.08, 68.95, 66.39, 59.06, 31.98, 29.77, 29.74, 29.72, 29.70, 29.67, 29.50, 29.45, 29.42, 29.26, 29.15, 26.11, 26.04, 22.74, 16.86, 14.17. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{62}H_{106}NaO_{18}$ 1161.74; found 1161.68.

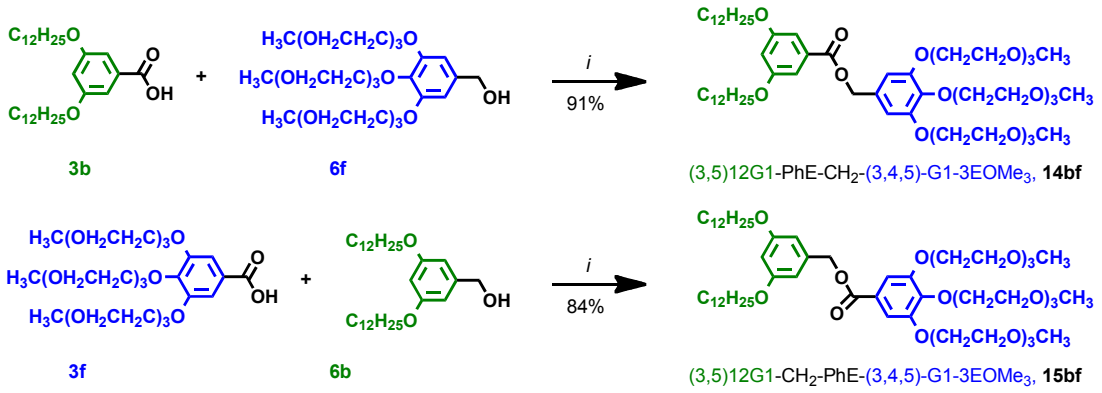
(3,5)12G1-CH_2-II-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$ (13bf). Compound **5''c** (0.1 g, 0.18 mmol, 1eq) and compound **3f** (0.1 g, 0.16 mmol, 1. eq) were dissolved in 10 mL DCM, then DCC (0.07 g, 0.32 mmol, 2 eq) was added followed by DPTS (0.05 g, 0.41 mmol, 1.3 eq). The resulting reaction mixture was stirred at 23 °C for 8 h under N_2. Purification by column chromatography (SiO_2 with EtOAc) yielded the title compound as a colorless oil (0.16 g, 84%). (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (s, 2H, 2×Ar*H*), 7.13 (d, J = 2.2 Hz, 2H, 2×Ar*H*), 6.62 (d, J = 2.0 Hz, 1H, 1×Ar*H*), 5.52-5.42 (m, 1H, 1×-O-CH_2*CH*(CH_3)-O-), 4.48 (m, 2H, 2×-O-*CH_2*CH(CH_3)-O-), 4.21 (t, J = 5.0 Hz, 2H, 1×Ar-O-*CH_2*-CH_2-O-), 4.18 (t, J = 4.9 Hz, 4H, 2×Ar-O-*CH_2*-CH_2-O-), 3.94 (t, J = 6.5 Hz, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.87-3.81 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.79 (t, J = 4.9 Hz, 2H, 1×Ar-O-CH_2-*CH_2*-), 3.74-3.69 (m, 6H, 3×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.67-3.61 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.55-3.51 (m, 6H, 3×-*CH_2*O-CH_3), 3.38 (s, 9H, 3×-CH_2O-*CH_3*), 1.79-1.71 (m, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.45-1.41 (m, 7H, 1×-OCH(*CH_3*)CH_2O- and 2×-O$(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.31-1.24 (m, 32H, 2×-O$(CH_2)_3$*$(CH_2)_8$*CH_3), 0.90 (t, J = 6.9, 6H, 2×-O$(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, CDCl3) δ 166.01, 165.32, 160.06, 152.20, 142.65, 131.38, 124.88, 109.02, 107.65, 106.45, 72.32, 71.84, 70.71, 70.58, 70.47, 70.45, 70.43,

69.51, 68.95, 68.76, 68.21, 66.47, 58.91, 31.81, 29.59, 29.56, 29.53, 29.50, 29.47, 29.29, 29.24, 29.07, 25.92, 22.58, 16.74, 14.01. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{62}H_{106}NaO_{18}$ 1161.74; found 1160.64.

(3,4,5)12G1-CH$_2$-II-PPD-(3,4,5)-3EO-G1-(OCH$_3$)$_3$ (**13cf**). Compound **5''c** (0.28 g, 0.23 mmol, 1eq), compound **3f** (0.23 g, 0.38 mmol, 1. eq) and DPTS (0.01 g, 0.04 mmol, 0.1 eq) were dissolved in 20 mL DCM, and DCC (0.08 g, 0.38 mmol, 1eq) was added. The resulting reaction mixture was stirred at 23 °C for 8 h under N_2. Purification by column chromatography (SiO_2, EtOAc) yielded the title compound as colorless solid (0.3 g, 53%). (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (s, 2H, 2×Ar*H*), 7.22 (s, 2H, 2×Ar*H*), 5.50-5.49 (m, 1H, 1×-O-CH$_2$*CH*(CH$_3$)-O-), 4.44-4.43 (m, 2H, 2×-O-*CH$_2$*CH(CH$_3$)-O-), 4.25-4.19 (m, 2H, 1×Ar-O-*CH$_2$*-CH$_2$-O-), 4.19-4.15 (m, 4H, 2×Ar-O-*CH$_2$*-CH$_2$-O-), 4.12 (d, *J* = 7.1 Hz, 2H, 1×Ar-O-*CH$_2$*(CH$_2$)$_{10}$CH$_3$), 4.00 (d, *J* = 6.6 Hz, 4H, 2×Ar-O-*CH$_2$*(CH$_2$)$_{10}$CH$_3$), 3.96 (dd, *J* = 14.0, 7.6 Hz, 4H, 2×Ar-O-*CH$_2$*(CH$_2$)$_{10}$CH$_3$), 3.88-3.83 (m, 4H, 2×Ar-O-CH$_2$-*CH$_2$*-), 3.83-3.77 (m, 2H, 1×Ar-O-CH$_2$-*CH$_2$*-), 3.72 (dt, *J* = 5.4, 3.9 Hz, 6H, 3×Ar-O-(CH$_2$)$_2$-O-*CH$_2$*-), 3.69-3.61 (m, 12H, 3×-*CH$_2$*-O-*CH$_2$*-CH$_2$-O-CH$_3$), 3.54 (dd, *J* = 5.7, 3.7 Hz, 6H, 3×-*CH$_2$*O-CH$_3$), 3.37 (d, *J* = 0.9 Hz, 9H, 3×-CH$_2$O-*CH$_3$*), 1.82-1.69 (m, 6H, 3×-OCH$_2$*CH$_2$*(CH$_2$)$_9$CH$_3$), 1.45 (d, *J* = 6.5 Hz, 9H, 1×-OCH(*CH$_3$*)CH$_2$O- and 3×-O(CH$_2$)$_2$*CH$_2$*(CH$_2$)$_8$CH$_3$), 1.32-1.24 (m, 48H, 3×-O(CH$_2$)$_3$*(CH$_2$)$_8$*CH$_3$), 0.88 (t, *J* = 7.0 Hz, 9H, 3×-O(CH$_2$)$_{11}$*CH$_3$*). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.11, 165.51, 152.91, 152.40, 142.91, 142.69, 125.07, 124.35, 109.28, 109.25, 108.23, 108.19, 73.57, 72.53, 72.02, 70.90, 70.77, 70.65, 70.64, 70.61, 69.70, 69.22, 69.10, 68.99, 60.44, 59.08, 32.01, 30.42, 29.83, 29.81, 29.80, 29.79, 29.77, 29.75, 29.73, 29.66, 29.51, 29.48, 29.46, 29.45, 29.41, 26.21, 26.14, 22.77, 16.93, 14.27, 14.18. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{74}H_{130}NaO_{19}$ 1345.92; found 1344.58.

3.4 Synthesis of Benzyl Ester "Single-Single" Amphiphilic Janus Dendrimers

Supporting Scheme S5. Synthesis of Benzyl Ester "Single-Single" Amphiphilic Janus Dendrimers[a]



[a]Reagents and conditions: *(i)* DCC, DPTS, CH_2Cl_2, 23 °C, 8 h.

(3,5)12G1-I-PhE-(3,4,5)-3EO-G1-$(OCH_3)_3$ (14bf). Compound **6f** (0.20 g, 0.33 mmol, 1eq), compound **3b** (0.16 g, 0.33 mmol, 1eq) and DPTS (0.1 g, 0.33 mmol, 1 eq) were dissolved in 16 mL of DCM. DCC (0.07 g, 0.33 mmol, 1 eq) was dissolved in 4 mL of DCM and added to the mixture. The reaction was maintained at 23 °C for 8 h. The reaction mixture was filtered over Celite and solvent was evaporated. The product was purified by column chromatography (SiO_2) with EtOAc/Hexane (2/1) to yield a colourless liquid (0.3 g, yield 91%). (Purity HPLC 99%+) (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 2.3, 2H, 2×Ar*H*), 6.66 (s, 2H, 2×Ar*H*), 6.63 (t, J = 2.3, 1H, 1×Ar*H*), 5,21 (s, 2H, 1×Ar*CH_2*-O-CO-), 4.15 (dd, J = 10.6, 5.4, 6H, 3×Ar-O-*CH_2*-CH_2-), 3.95 (t, J = 6.5, 4H, 2×Ar-O-*CH_2*$(CH_2)_{10}CH_3$), 3.88-3.81 (m, 4H, 2×Ar-O-CH_2-*CH_2*-), 3.81-3.77 (m, 2H, 1×Ar-O-CH_2-*CH_2*-), 3.72 (dd, J = 5.7, 3.2, 6H, 3×Ar-O-$(CH_2)_2$-O-*CH_2*-), 3.69-3.59 (m, 12H, 3×-*CH_2*-O-*CH_2*-CH_2-O-CH_3), 3.53 (dd, J = 5.5, 3.7, 6H, 3×-*CH_2*O-CH_3), 3.37 (d, J = 1.9, 9H, 3×-CH_2O-*CH_3*), 1.83–1.70 (m, 4H, 2×-OCH_2*CH_2*$(CH_2)_9CH_3$), 1.44 (s, 4H, 2×-O$(CH_2)_2$*CH_2*$(CH_2)_8CH_3$), 1.26 (s, 32H, 2×-O$(CH_2)_3$*$(CH_2)_8$*CH_3), 0.88 (t, J = 6.8, 6H, 2×-O$(CH_2)_{11}$*CH_3*). ^{13}C NMR (126 MHz, $CDCl_3$), δ 166.88, 159.20, 159.15, 152.81, 142.69, 130.38, 129.63, 129.41, 128.75, 125.16, 114.63, 114.26, 109.40, 74.84, 71.27, 68.23, 68.14, 52.30, 32.08, 29.80, 29.77, 29.75, 29.61, 29.59, 29.51, 29.47, 29.46, 26.23, 22.84, 14.26. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{59}H_{102}NaO_{16}$, 1090.44; found 1089.34.

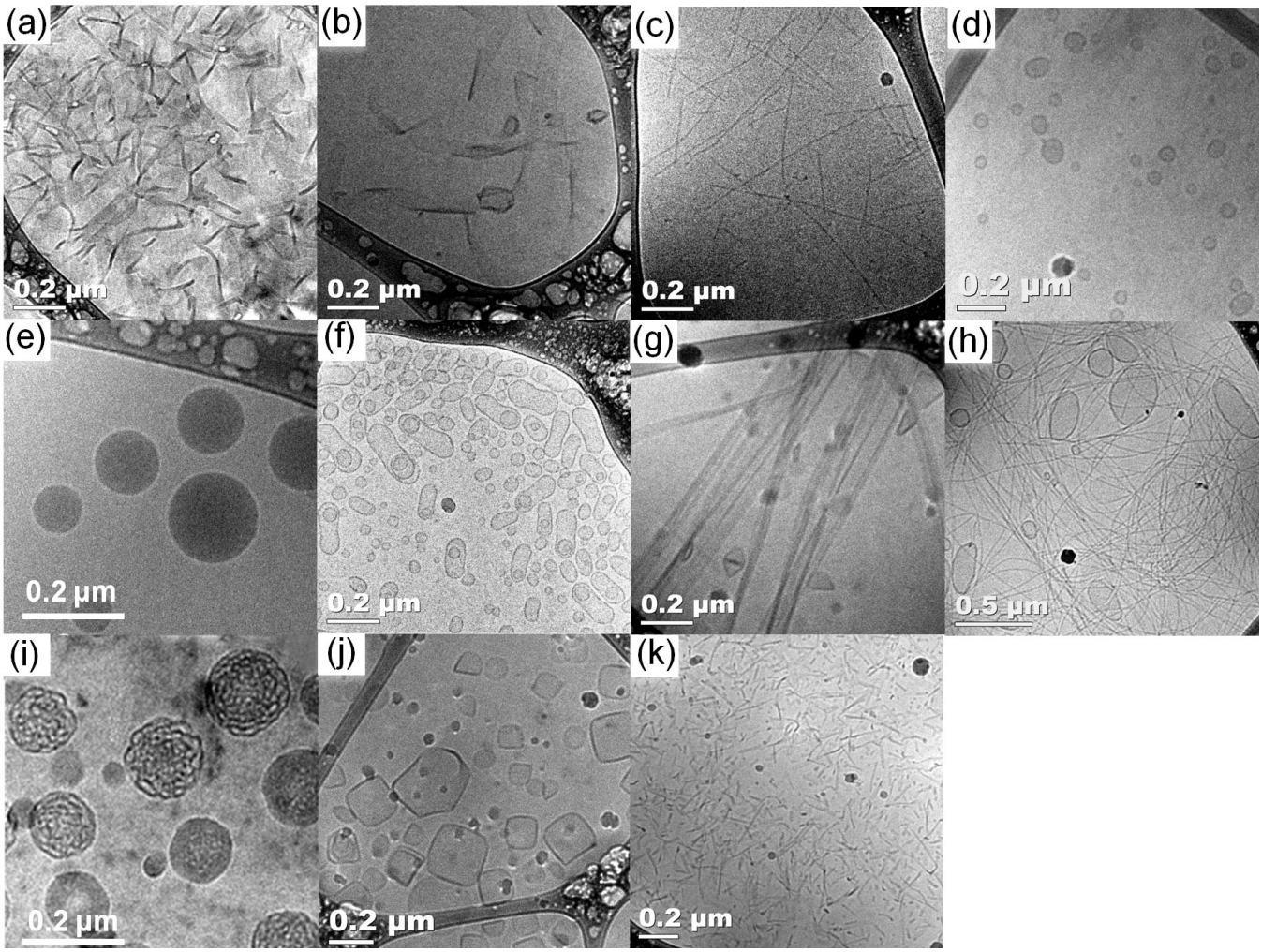
(3,5)12G1-II-PhE-(3,4,5)-3EO-G1-$(OCH_3)_3$ (15bf) Compound **6b** (0.49 g, 1.03 mmol, 1eq), compound **3f** (0.63 g, 1.03 mmol, 1eq) and DPTS (0.31 g, 1.03 mmol, 1 eq) were dissolved in 8 mL of DCM. DCC (0.28 g, 1.34 mmol, 1.3 eq) was dissolved in 2 mL of DCM and added to the mixture. The reaction was maintained at 23 °C for 8 h. The reaction mixture was filtered over Celite and solvent was evaporated. The product was purified by column chromatography (SiO_2) with EtOAc/MeOH (MeOH = 1-3%) to

yield a colourless liquid (0.94 g, yield 84%). (Purity HPLC 99%+) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (s, 2H, 2×Ar*H*), 6.53 (d, *J* = 2.3 Hz, 2H, 2×Ar*H*), 6.41 (t, *J* = 4.5 Hz, 1H, 1×Ar*H*), 5.21 (s, 2H, 1×Ar*CH*$_2$-O-CO-) 4.22 (t, *J* = 5.0 Hz, 2H, 1×Ar-O-*CH*$_2$-CH$_2$-), 4.18 (t, *J* = 5.0 Hz, 4H, 2×Ar-O-*CH*$_2$-CH$_2$-), 3.93 (t, *J* = 6.6 Hz, 4H, 2×Ar-O-*CH*$_2$(CH$_2$)$_{10}$CH$_3$), 3.85 (t, *J* = 5.0 Hz, 4H, 2×Ar-O-CH$_2$-*CH*$_2$-), 3.79 (t, *J* = 5.1 Hz, 2H, 1×Ar-O-CH$_2$-*CH*$_2$-), 3.73-3.70 (m, 6H, 3×Ar-O-(CH$_2$)$_2$-O-*CH*$_2$-), 3.66-3.61 (m, 12H, 3×-*CH*$_2$-O-*CH*$_2$-CH$_2$-O-CH$_3$), 3.54-3.52 (m, 6H, 3×-*CH*$_2$O-CH$_3$), 3.36 (s, 9H, 3×-CH$_2$O-*CH*$_3$), 1.76 (quint, *J* = 7.1 Hz, 4H, 2×-OCH$_2$*CH*$_2$(CH$_2$)$_9$CH$_3$), 1.44 (quint, *J* = 7.4 Hz, 4H, 2×-O(CH$_2$)$_2$*CH*$_2$(CH$_2$)$_8$CH$_3$), 1.35-1.26 (m, 32H, 2×-O(CH$_2$)$_3$*(CH*$_2$*)*$_8$CH$_3$), 0.88 (t, *J* = 6.9 Hz, 6H, 2×-O(CH$_2$)$_{11}$*CH*$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.52, 160.32, 160.32, 152.86, 138.67, 131.91, 131.57, 108.41, 108.41, 107.97, 106.62, 72.08, 70.97, 70.85, 70.71, 69.89, 69.10, 68.49, 67.02, 59.16, 32.06, 29.80, 29.78, 29.75, 29.72, 29.53, 29.49, 29.34, 26.17, 22.83, 14.26. MALDI-TOF (m/z) calcd. $[M+Na]^+$ for $C_{59}H_{102}NaO_{16}$, 1090.44; found 1090.05.

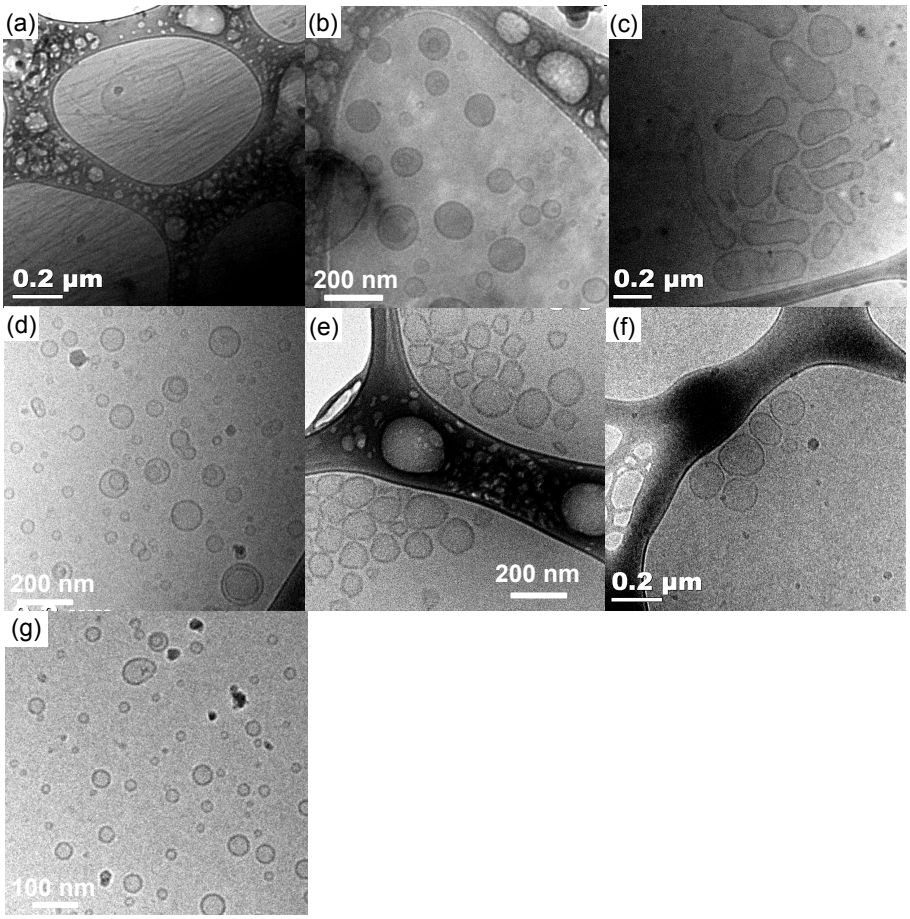
4 Preparation of Dendrimersomes.

A stock solution was prepared by dissolving the required amount of "single-single" amphiphilic Janus dendrimers in pure ethanol. Dendrimersomes were then generated by injection of 100 mL of the ethanol solution into 2 mL Milli-Q water followed by 5 sec vortexing to give the final dendrimer concentration of 0.5-4 mg/mL in water. Any exceptions to this protocol are noted in the figure captions of the experiment in question.

5 Cryo-TEM Images of the Assemblies Generated by "Single-Single" Amphiphilic Janus Dendrimers

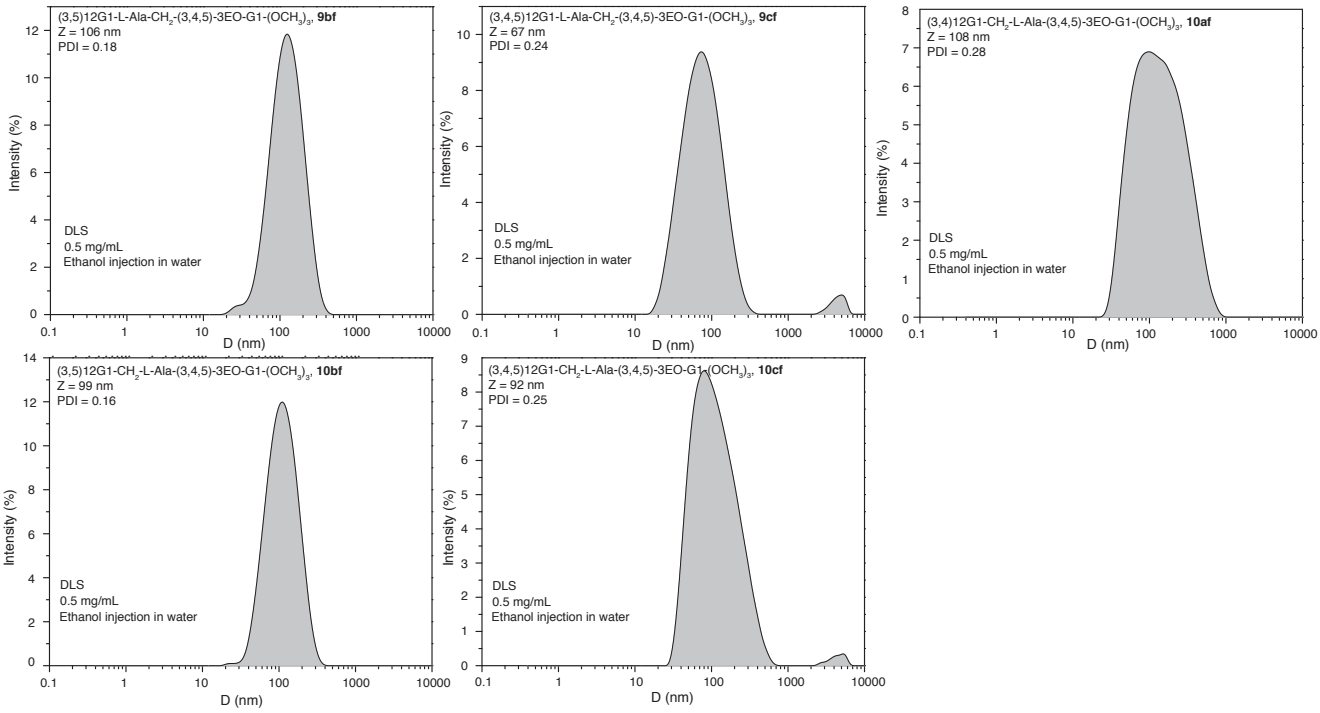


Supporting Figure SF2. Selected Cryo-TEM images of assemblies generated by (a) (3,4)12G1-L-Ala-CH_2-(3,4)-3EO-G1-$(OCH_3)_2$ **9ad**, (b) (3,4)12G1-L-Ala-CH_2-(3,5)-3EO-G1-$(OCH_3)_2$ **9ae**, (c) (3,4)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$ **9af**, (d) (3,5)12G1-L-Ala-CH_2-(3,4)-3EO-G1-$(OCH_3)_2$ **9bd**, (e) (3,5)12G1-L-Ala-CH_2-(3,5)-3EO-G1-$(OCH_3)_2$ **9be**, (f) (3,5)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_2$ **9bf**, (g) (3,4,5)12G1-L-Ala-CH_2-(3,4)-3EO-G1-$(OCH_3)_2$ **9cd**, (h) (3,4)12G1-CH_2-L-Ala-(3,4,5)-3EO-G1-$(OCH_3)_3$ **10af**, (i) (3,4,5)12G1-CH_2-L-Ala-(3,4)-3EO-G1-$(OCH_3)_2$ **10cd**, (k) (3,4,5)12G1-CH_2-L-Ala-(3,5)-3EO-G1-$(OCH_3)_2$ **10ce.**

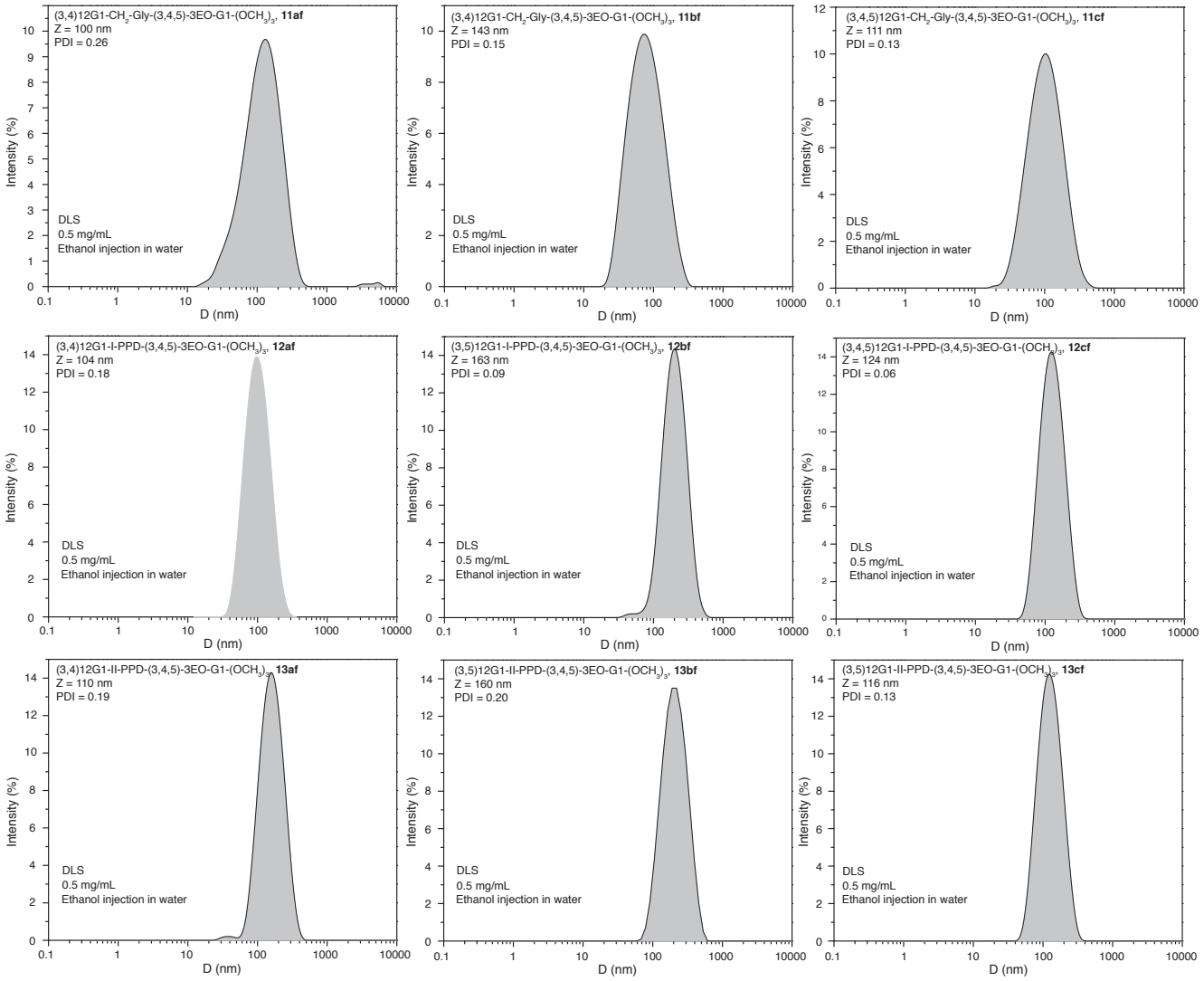


Supporting Figure SF3. Selected Cryo-TEM images of assemblies generated by (a) (3,4)12G1-CH_2-Gly-(3,4,5)G1-3EOMe$_3$ **11af**, (b) (3,5)12G1-CH_2-Gly-(3,4,5)G1-3EOMe$_3$ **11bf,** (c) (3,5)12G1-I-PPD-(3,4,5)G1-3EOMe$_2$ **12bf**, (d) (3,4,5)12G1-I-PPD-(3,4,5)G1-3EOMe$_2$ **12cf**, (e) (3,4)12G1-II-PPD-(3,4,5)G1-3EOMe$_2$ **13af,** (f) (3,5)12G1-II-PPD-(3,4,5)G1-3EOMe$_2$ **13bf,** (g) (3,4,5)12G1-II-PPD-(3,4,5)G1-3EOMe$_2$ **13cf.**

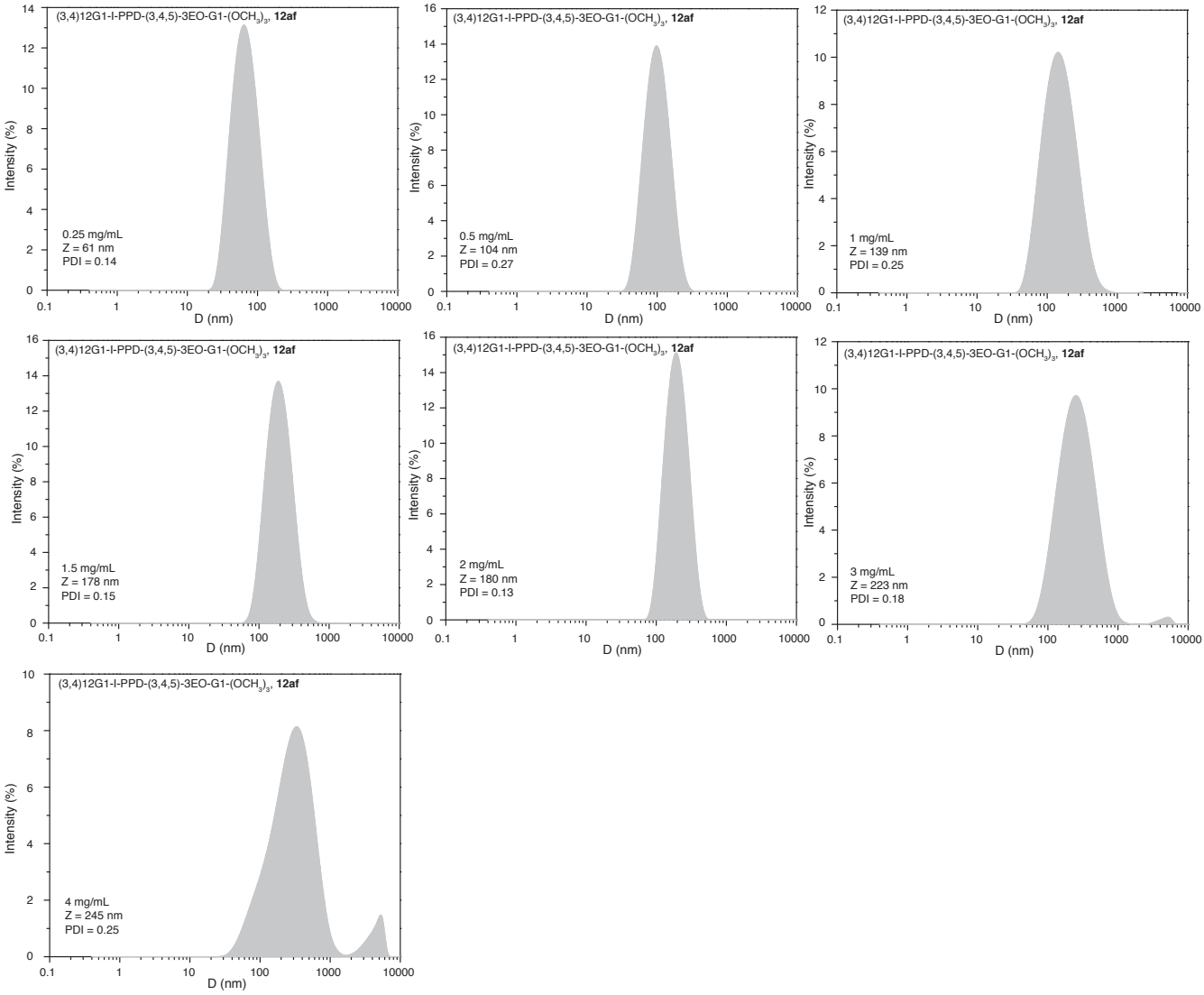
6 Spectra of Dynamic Light Scattering of the Assemblies Generated by "Single-Single" Amphiphilic Janus Dendrimers



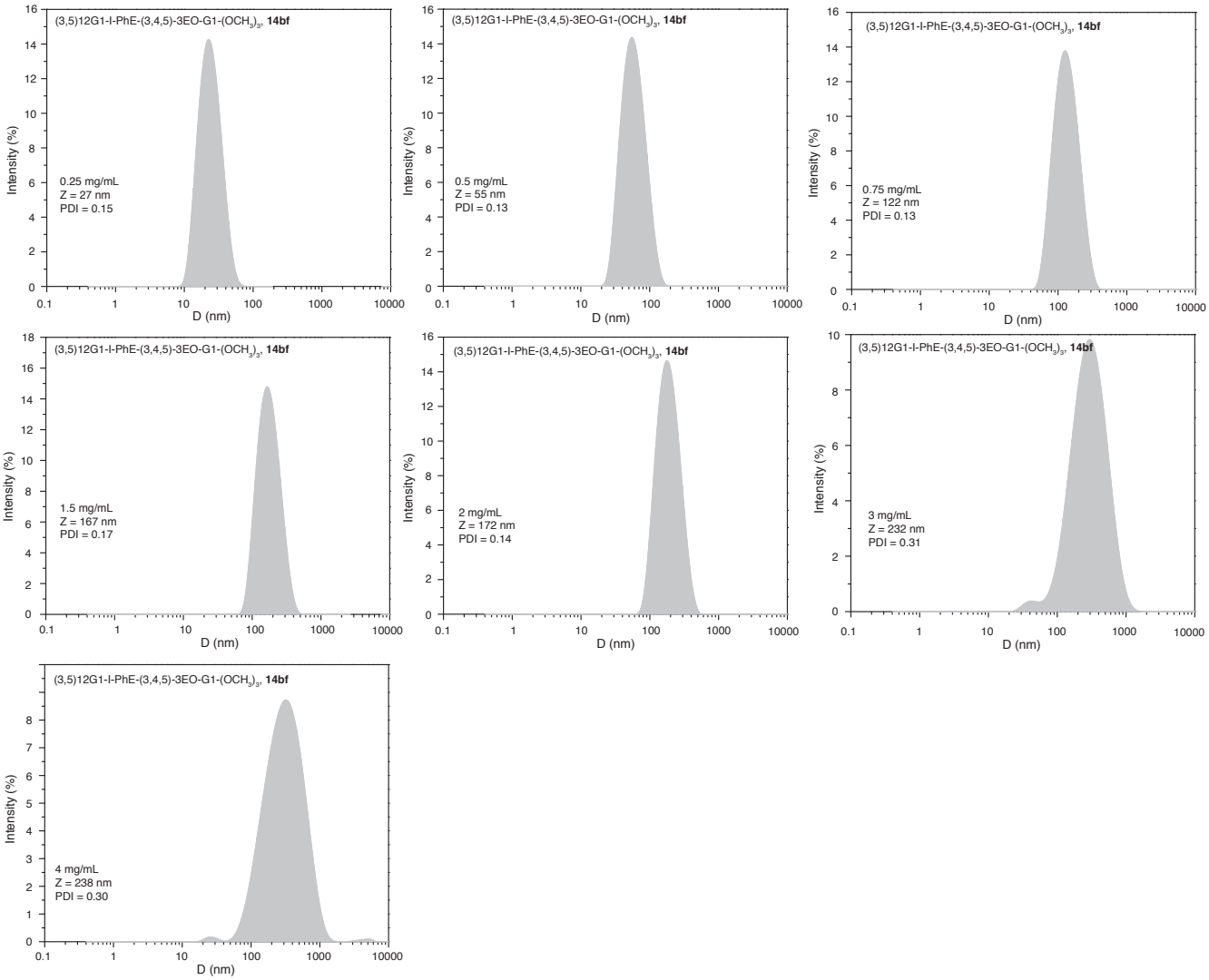
Supporting Figure SF4. DLS data of dendrimersomes generated by "single-single" amphiphilic Janus dendrimers in libraries 1 and 2 in water.



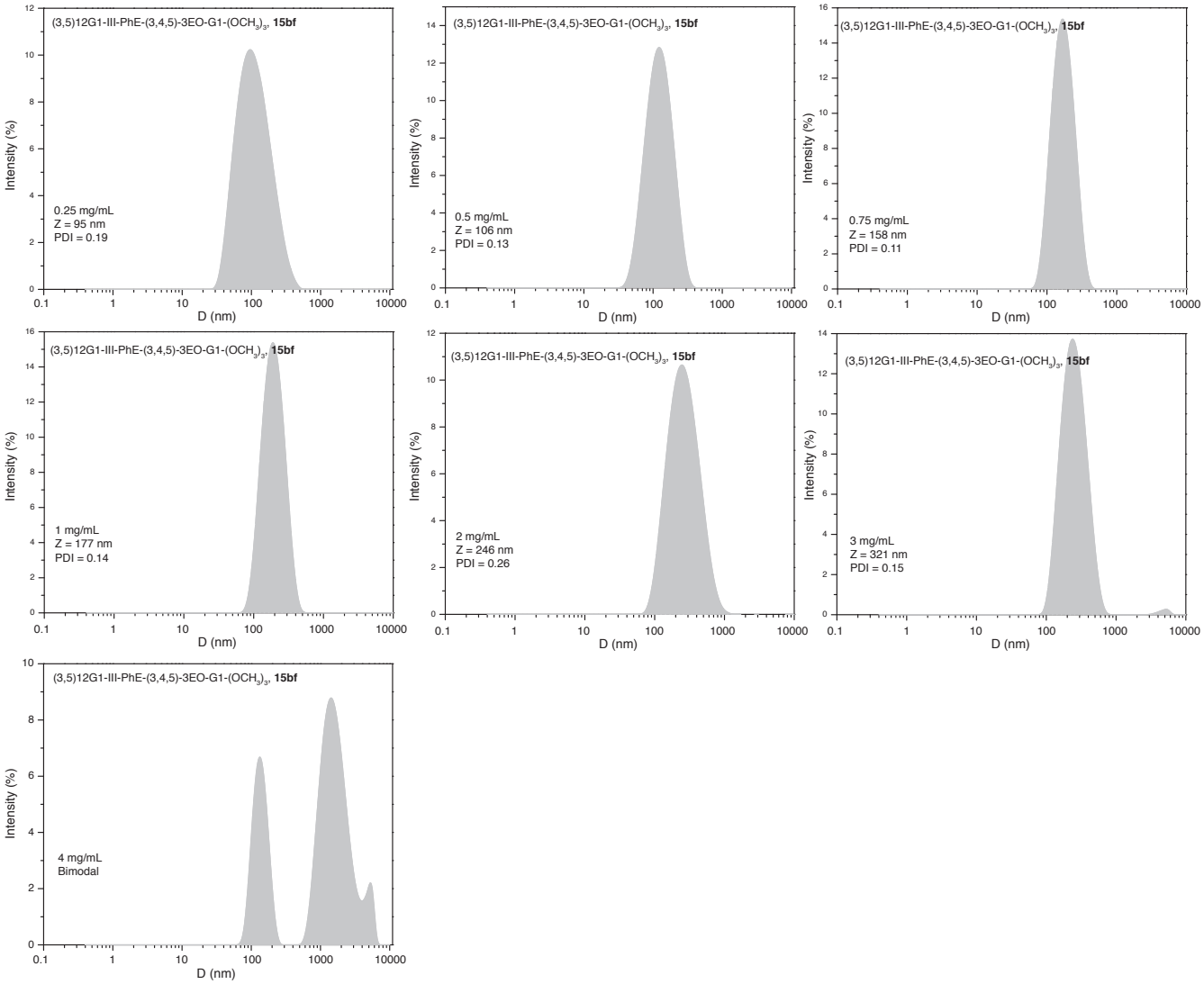
Supporting Figure SF5. DLS data of dendrimersomes generated by "single-single" amphiphilic Janus dendrimers in libraries 3, 4 and 5 in water.



Supporting Figure SF6. DLS data of dendrimersomes generated by (3,5)12G1-I-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$, **12bf** in water at different concentration.

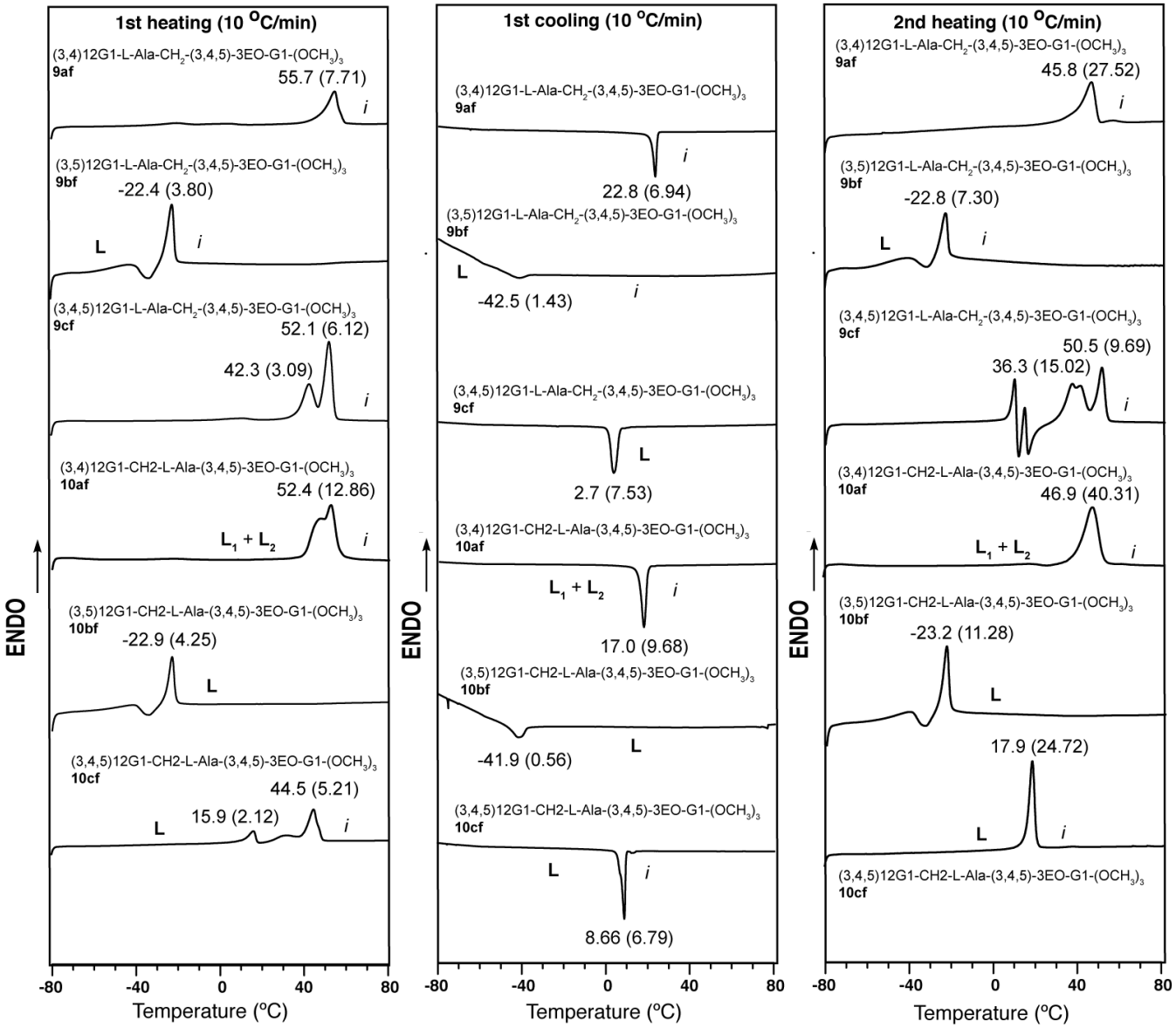


Supporting Figure SF7. DLS data of dendrimersomes generated by (3,5)12G1-I-PhE-(3,4,5)-3EO-G1-$(OCH_3)_3$, **14bf** in water at different concentration.

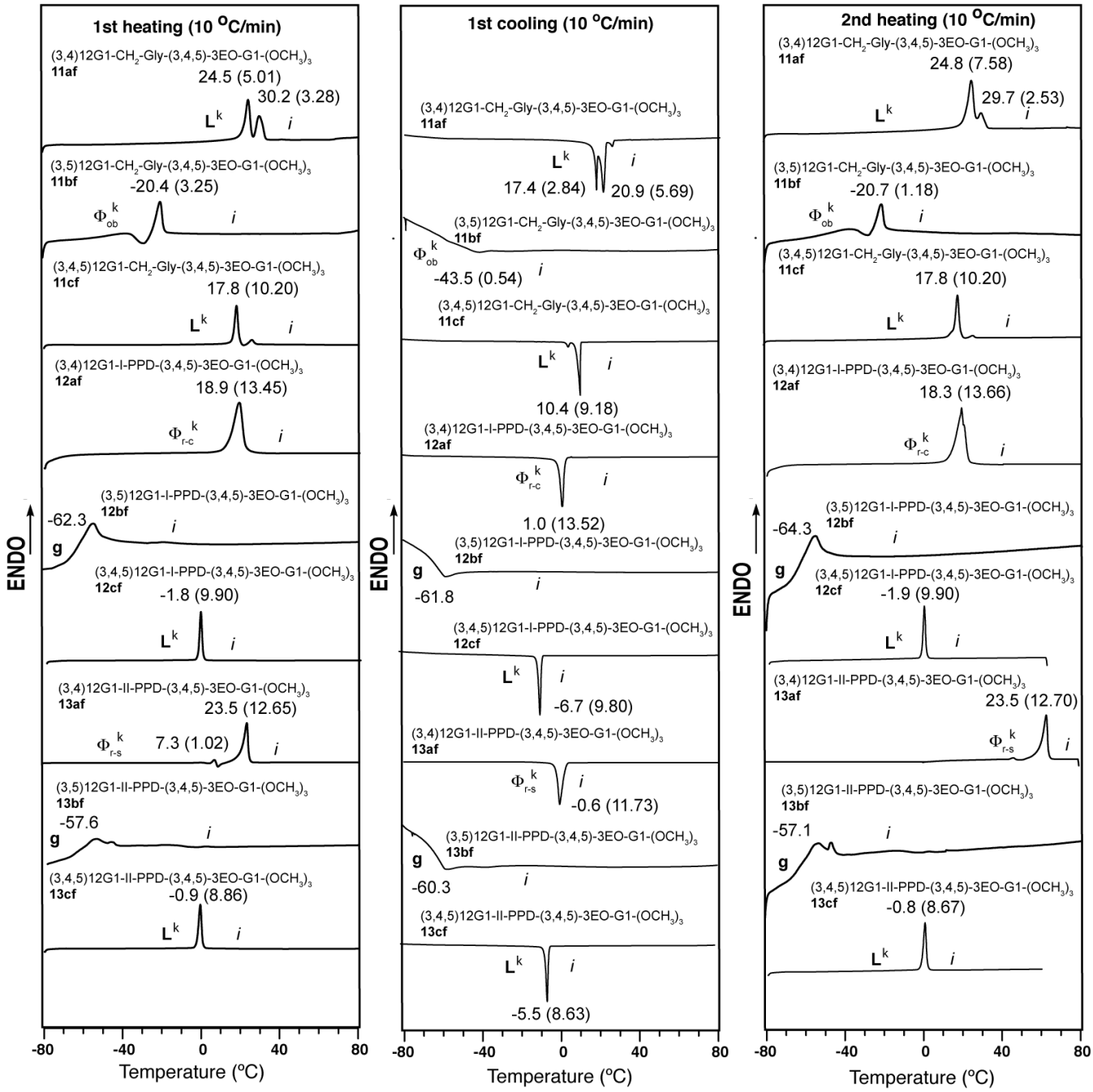


Supporting Figure SF8. DLS data of dendrimersomes generated by (3,5)12G1-III-PhE-(3,4,5)-3EO-G1-$(OCH_3)_3$, **15bf** in water at different concentration.

7 DSC Traces of the Assemblies Generated by "Single-Single" Amphiphilic Janus Dendrimers



Supporting Figure SF9. DSC traces of the "single-single" amphiphilic Janus dendrimers with 3,4,5-hydrophilic pattern from Library 1 and 2 at heating and cooling rate of 10 °C/min. Phases, transition temperatures, associated enthalpy changes (in between brackets, in kcal/mol) are indicated. Notation of the structure assembled in bulk: L as lamellar phase, $\Phi_{r\text{-}c}$ as columnar centered rectangular phase and Φ_h as columnar hexagonal phase.



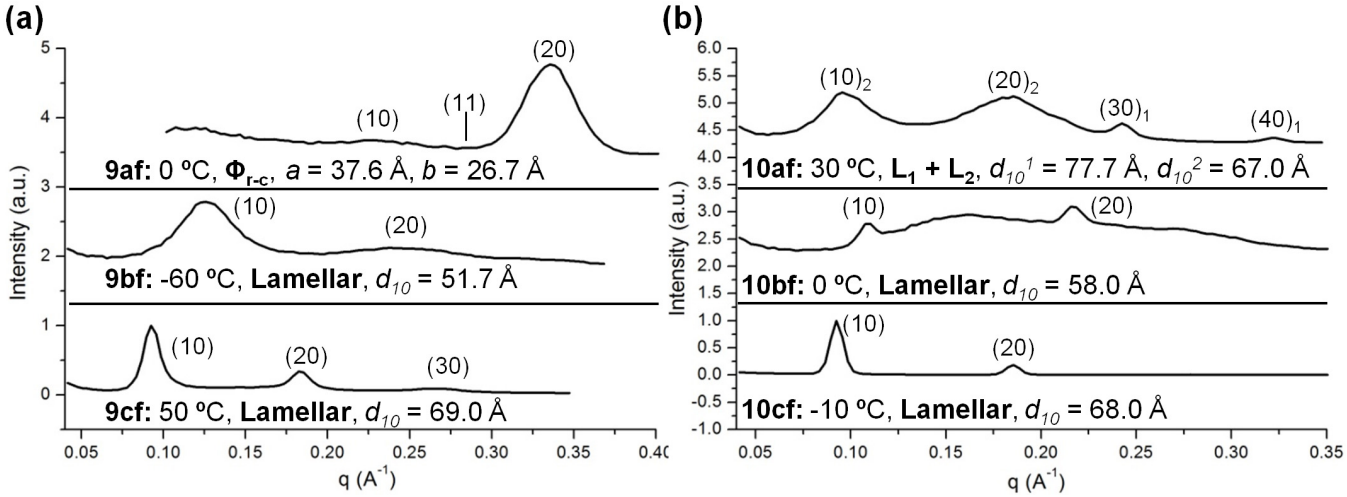
Supporting Figure SF10. DSC traces of the "single-single" amphiphilic Janus dendrimers with 3,4,5-hydrophilic pattern from Library 3, 4 and 5 at heating and cooling rate of 10 °C/min. Phases, transition temperatures, associated enthalpy changes (in between brackets, in kcal/mol) are indicated. Notation of the structure assembled in bulk: L as lamellar phase, $\Phi_{r\text{-}c}$ as columnar centered rectangular phase and Φ_h as columnar hexagonal phase.

Table ST1. Transition Temperature and Associated Enthalpy Changes of "Single-Single" Amphiphilic Janus Dendrimers with (3,4,5)-Hydrophilic Pattern[a]

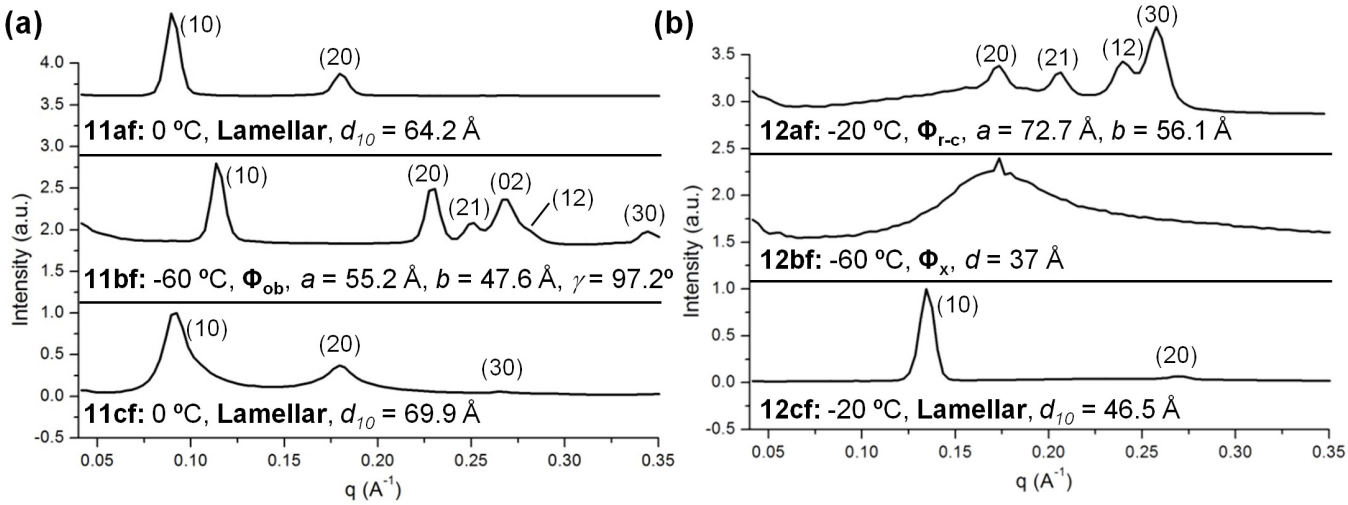
"Single-single" Amphiphilic Janus Dendrimer	Thermal Transition (°C) and Corresponding Enthalpy Changes (kcal/mol)	
	Heating[b]	Cooling
(3,4)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$, **9af**	$\Phi_{r\text{-}c}^k$ 55.7 (7.71) i $\Phi_{r\text{-}c}^k$ 45.8 (7.48) i	i 22.8 (6.94) $\Phi_{r\text{-}c}^k$
(3,5)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$, **9bf**	L^k -22.4 (3.80) i L^k -22.8 (1.96) i	i -42.5 (0.39) L^k
(3,4,5)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$, **9cf**	$\Phi_{r\text{-}c}^k$ 42.3 (3.09) L^k 52.1 (6.12) i $\Phi_{r\text{-}c}^k$ 36.3 (4.74) L^k 50.5 (3.06) i	i 2.7 (7.53) $\Phi_{r\text{-}c}^k$
(3,4)12G1-CH_2-L-Ala-(3,4,5)-3EO-G1-$(OCH_3)_3$, **10af**	L_1^k+L_2^k 52.4 (12.86) i L_1^k+L_2^k 46.9 (10.96) i	i 17.0 (9.68) L_1^k+L_2^k
(3,5)12G1-CH_2-L-Ala-(3,4,5)-3EO-G1-$(OCH_3)_3$, **10bf**	L^k -22.9 (4.25) i L^k -23.2 (3.07) i	i -41.9 (0.56) L^k
(3,4,5)12G1-CH_2-L-Ala-(3,4,5)-3EO-G1-$(OCH_3)_3$, **10cf**	L^k 15.9 (2.12) Φ_x 44.5 (5.21) i L^k 17.9 (7.81) i	i 8.7 (6.79) L^k
(3,4)12G1-CH_2-Gly-(3,4,5)-3EO-G1-$(OCH_3)_3$, **11af**	L^k 24.5 (5.01) Φ_x 30.2 (3.28) i L^k 24.8 (7.58) Φ_x 29.7 (2.53) i	i 24.8 (7.58) Φ_x 20.9 (8.53) L^k
(3,5)12G1-CH_2-Gly-(3,4,5)-3EO-G1-$(OCH_3)_3$, **11bf**	Φ_{ob}^k -20.4 (3.25) i Φ_{ob}^k -20.7 (1.18) i	i -43.5 (0.54) Φ_{ob}^k
(3,4,5)12G1-CH_2-Gly-(3,4,5)-3EO-G1-$(OCH_3)_3$, **11cf**	L^k 17.8 (10.20) i L^k 17.8 (10.20) i	i 10.4 (9.18) L^k
(3,4)12G1-I-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$, **12af**	$\Phi_{r\text{-}c}^k$ 18.9 (13.45) i $\Phi_{r\text{-}c}^k$ 18.3 (13.66) i	i 1.0 (13.52) $\Phi_{r\text{-}c}^k$
(3,5)12G1-I-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$, **12bf**	g -62.3 i g -64.3 i	i -61.8 g
(3,4,5)12G1-I-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$, **12cf**	L^k -1.8 (9.90) i L^k -1.9 (9.90) i	i -6.7 (9.80) L^k
(3,4)12G1-II-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$, **13af**	$\Phi_{r\text{-}s}^k$ 23.5 (12.65) i $\Phi_{r\text{-}s}^k$ 23.5 (12.70) i	i -0.6 (11.73) $\Phi_{r\text{-}s}^k$
(3,5)12G1-II-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$, **13bf**	g -57.6 i g -57.1 i	i -60.3 g
(3,4,5)12G1-II-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$, **13cf**	L^k -0.9 (8.86) i L^k -0.8 (8.67) i	i -5.5 (8.63) L^k

[a]Data were determined by DSC (10 °C/min) and XRD. [b]Data from the first heating and cooling scans are on the first line, and data from the second heating are on the second line. Phase notation: $\Phi_{r\text{-}c}^k$ as columnar centered rectangular crystalline phase; Φ_h^k as columnar hexagonal crystalline phase, Φ_{ob}^k as columnar oblique crystalline phase, $\Phi_{r\text{-}s}^k$ as columnar simple rectangular crystalline phase, Φ_x as unknown columnar phase, L^k as lamellar crystalline phase, g as amorphous glassy phase and i as isotropic.

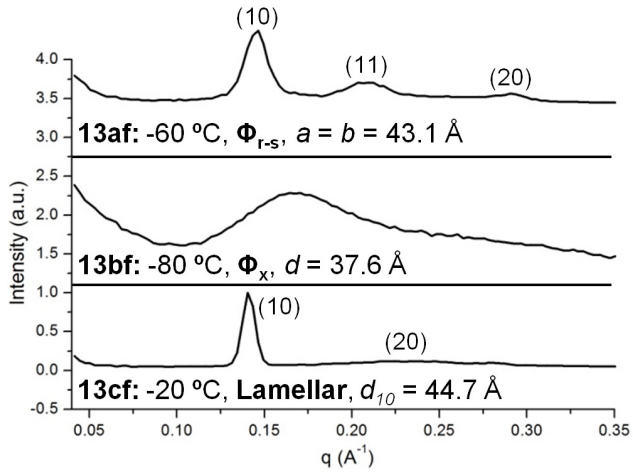
8 Powder XRD Diffraction Data of the Assemblies Generated by "Single-Single" Amphiphilic Janus Dendrimers



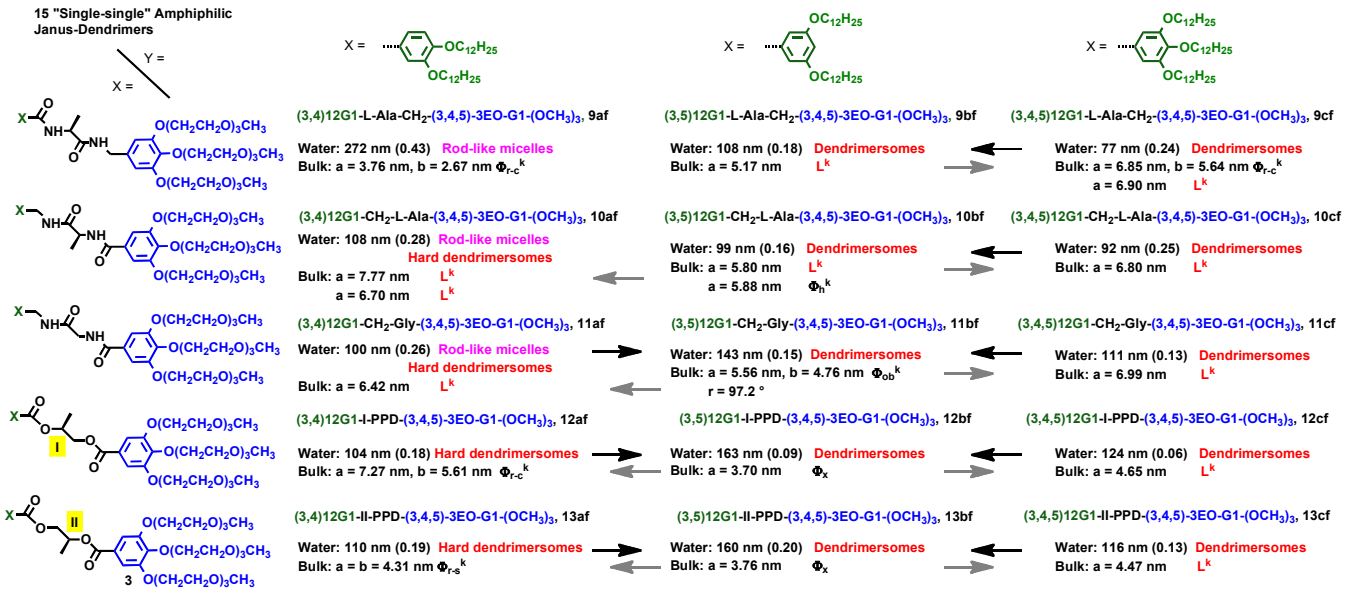
Supporting Figure SF11. Powder XRD diffraction data collected from (a) 9af, 9bf, and 9cf, and (b) 10af, 10bf, and 10cf in the first cooling cycle. Temperature, phase, lattice parameter, and indexing of the diffraction peaks are indicated. Phase notation: $\Phi_{r\text{-}c}$: 2D columnar centered rectangular phase; L : lamellar phase.



Supporting Figure SF12. Powder XRD diffraction data collected from (a) 11af, 11bf, and 11cf, and (b) 12af, 12bf, and 12cf in the first cooling cycle. Temperature, phase, lattice parameter, and indexing of the diffraction peaks are indicated. Phase notation: Φ_{ob} : 2D columnar oblique phase; $\Phi_{r\text{-}c}$: 2D columnar centered rectangular phase; Φ_x : unknown columnar phase.



Supporting Figure SF13. Powder XRD diffraction data collected from 13af, 13bf, and 13cf in the first cooling cycle. Temperature, phase, lattice parameter, and indexing of the diffraction peaks are indicated. Phase notation: $\Phi_{r\text{-}s}$: 2D columnar simple rectangular phase; Φ_x : unknown columnar phase.



Supporting Figure SF14. Structures of the amphiphilic Janus dendrimers from Libraries 3, 4 and 5, their short notations and the summary of their self-assembly in water at 23 °C and in bulk. The size (in nm), polydispersity (in between brackets) and the supramolecular structures self-assembled in water and in bulk, and d-spacing *d* from bulk (nm) are indicated. The black arrows illustrate the increase of the size of the structures assembled in water. The grey arrows indicate the increase of the d-spacing *d* in bulk. Phase notation in bulk: $\Phi_{r\text{-}c}^{k}$ as columnar centered rectangular crystalline phase; Φ_h^k as columnar hexagonal crystalline phase, Φ_{ob}^k as columnar oblique crystalline phase, $\Phi_{r\text{-}s}^{k}$ as columnar simple rectangular crystalline phase, Φ_x as unknown columnar phase, L^k as lamellar crystalline phase.

9 ^{1}H and ^{13}C NMR Spectra of "Single-Single"Amphiphilic Janus Dendrimers

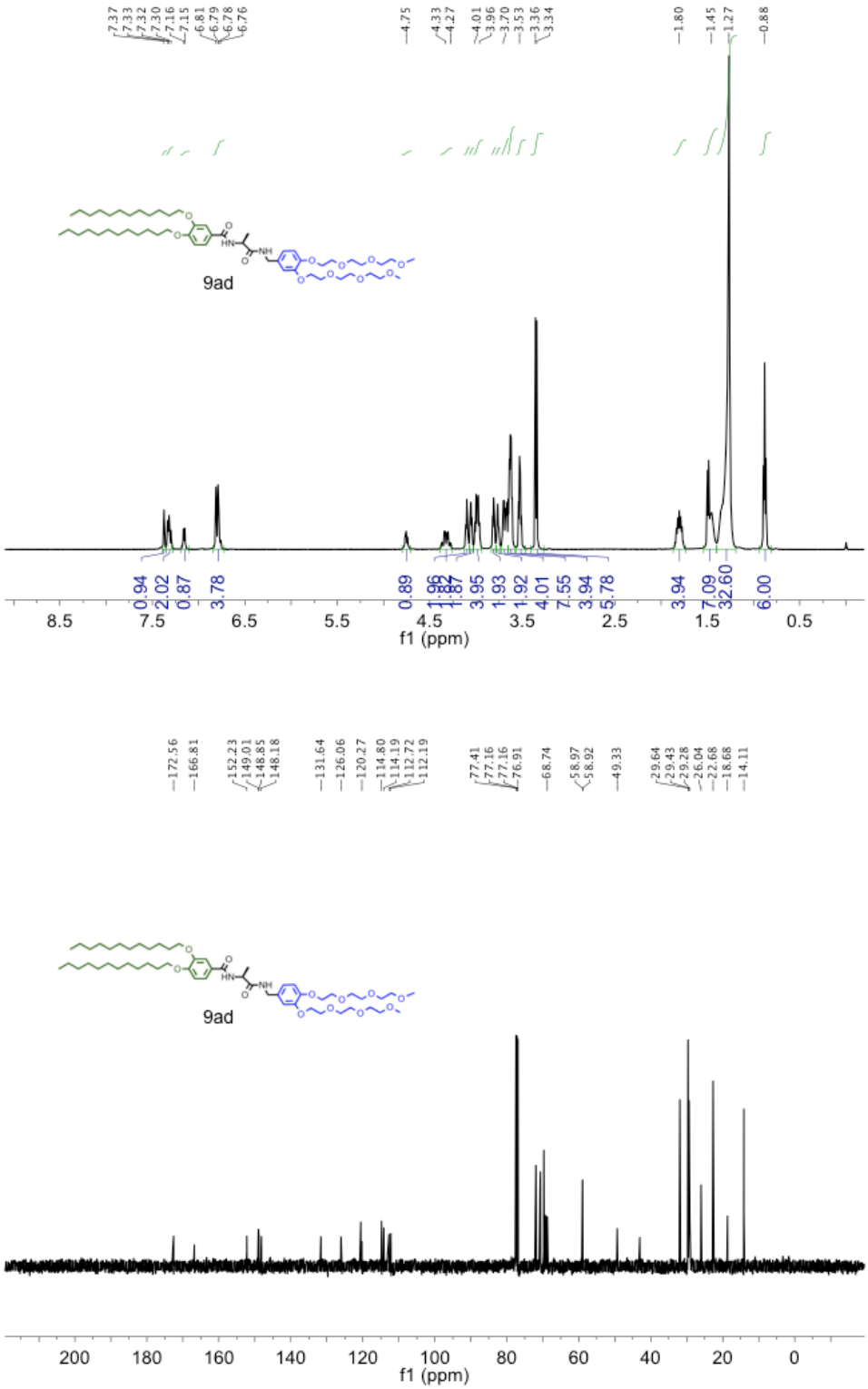


Figure SF15. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4)12G1-L-Ala-CH_2-(3,4)-3EO-G1-$(OCH_3)_2$ **9ad** in $CDCl_3$

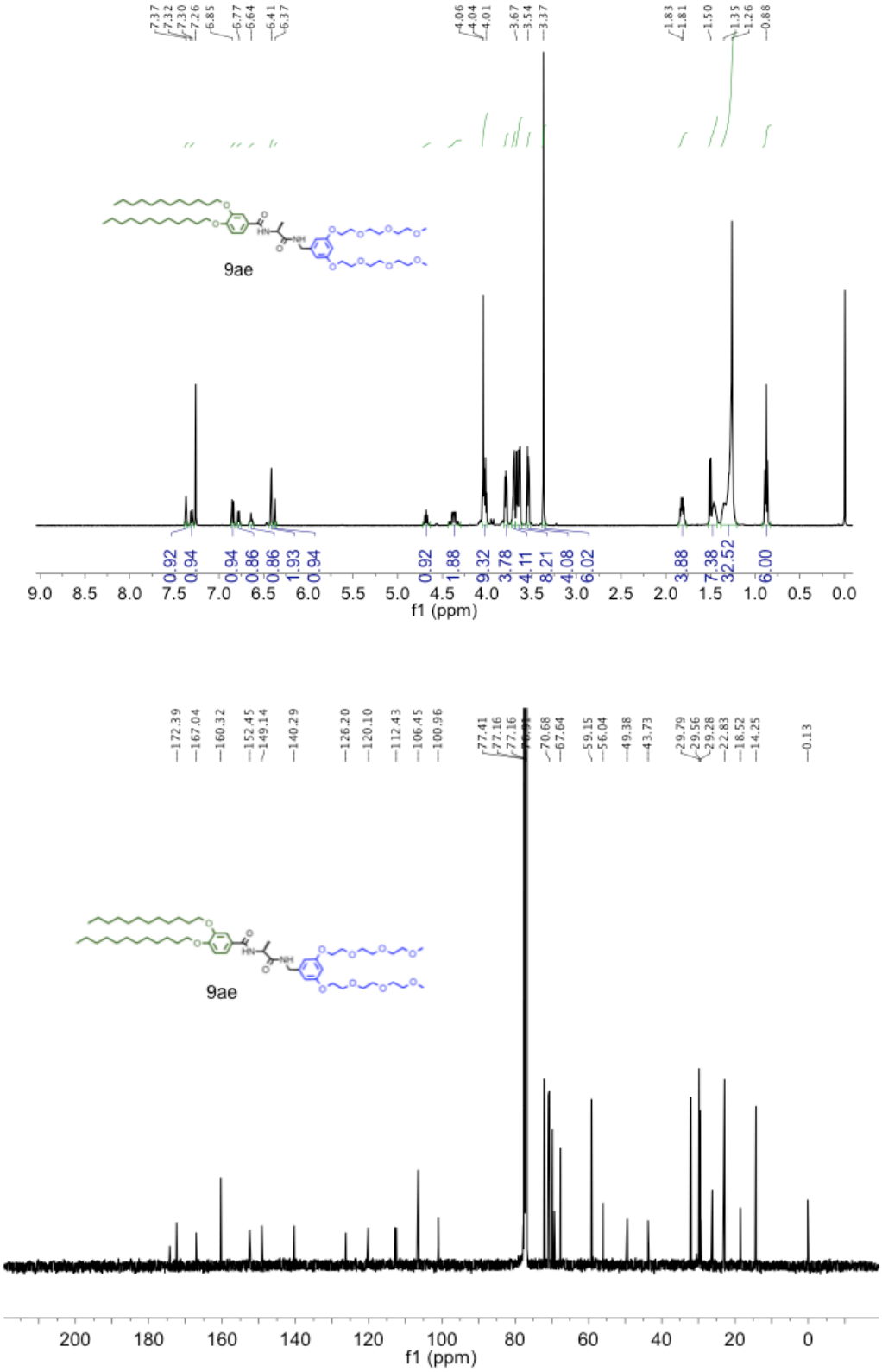


Figure SF16. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4)12G1-L-Ala-CH_2-(3,5)-3EO-G1-$(OCH_3)_2$ **9ae** in $CDCl_3$

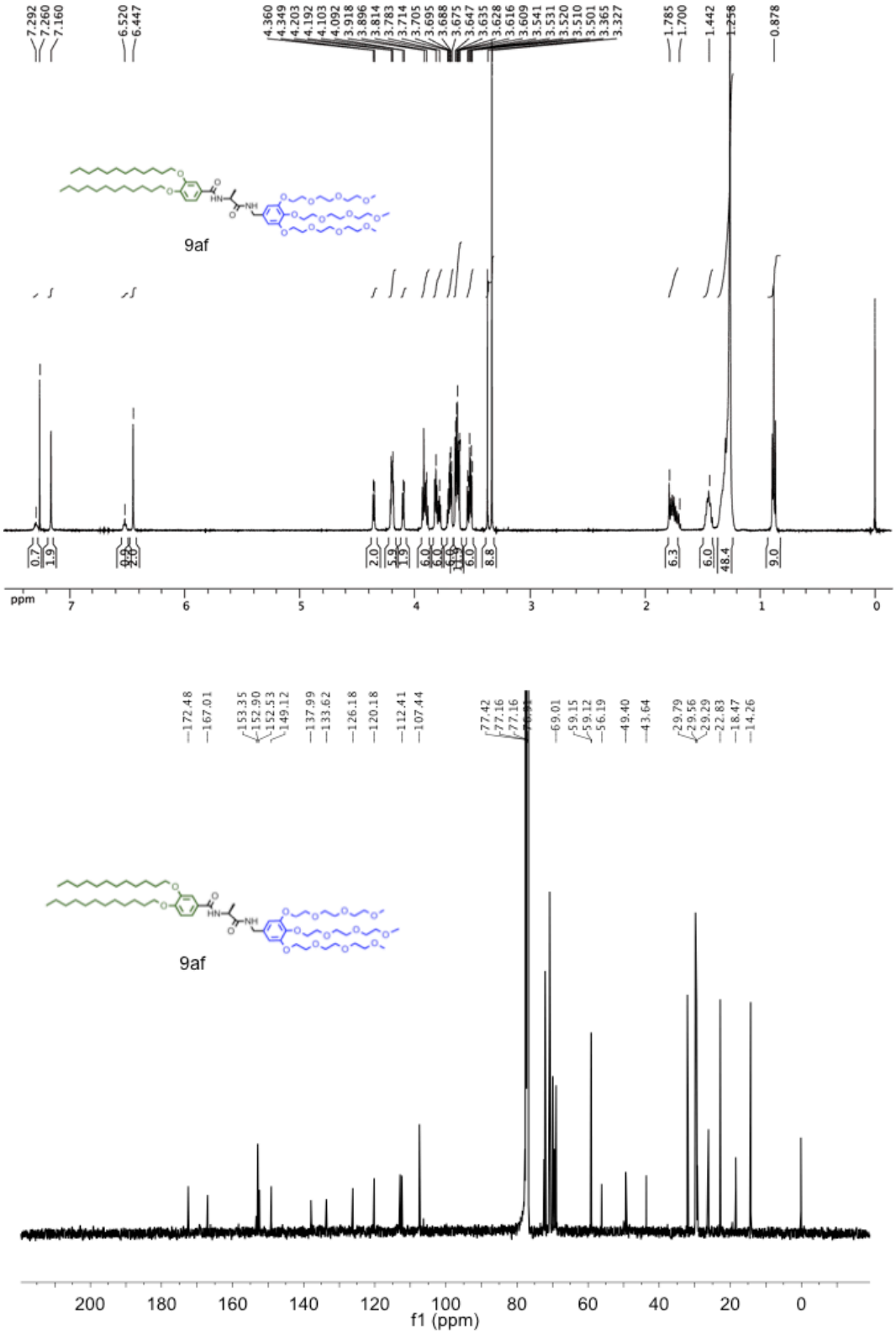


Figure SF17. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$ **9af** in $CDCl_3$

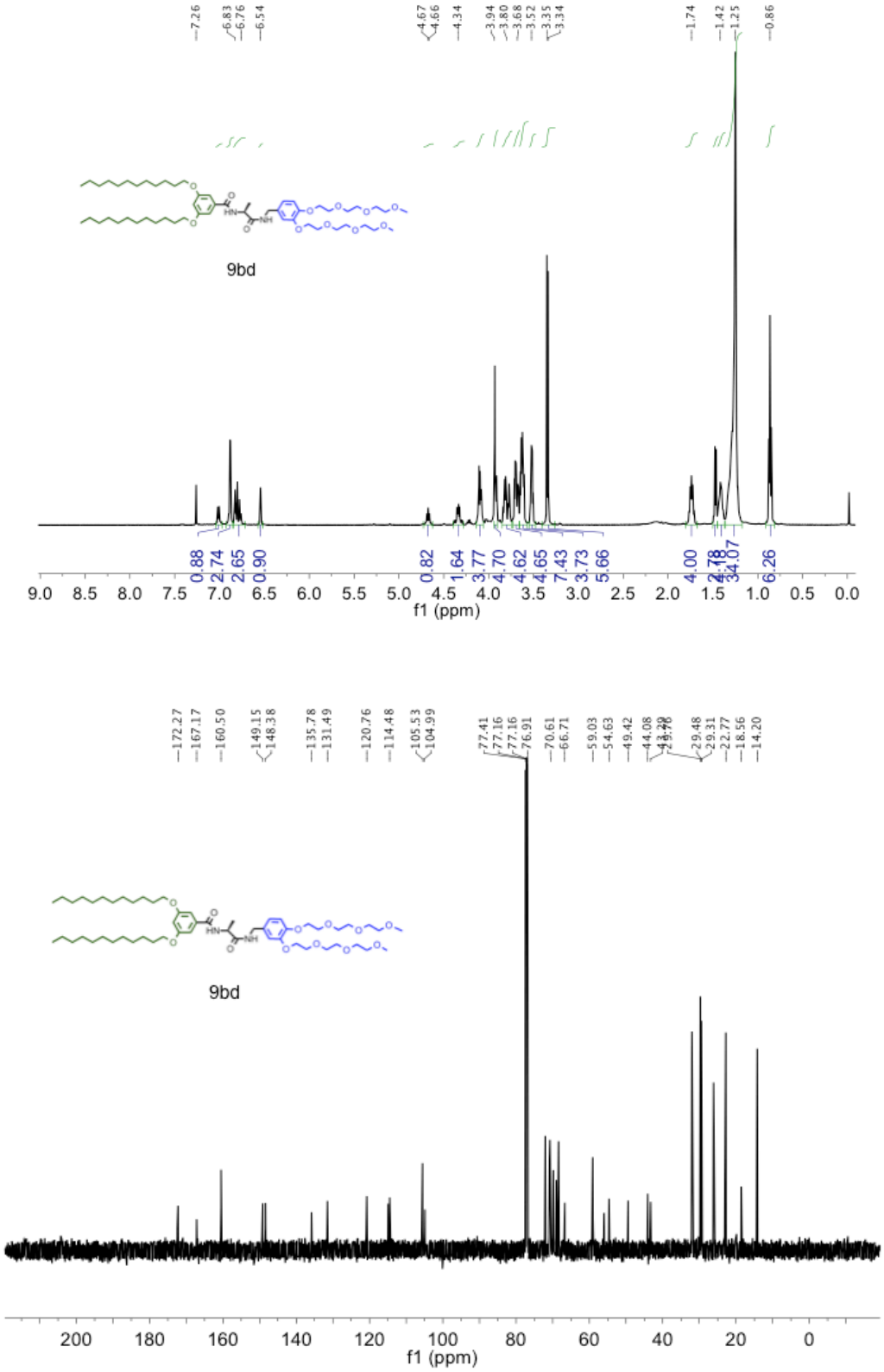


Figure SF18. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-L-Ala-CH_2-(3,4)-3EO-G1-$(OCH_3)_2$ **9bd** in $CDCl_3$

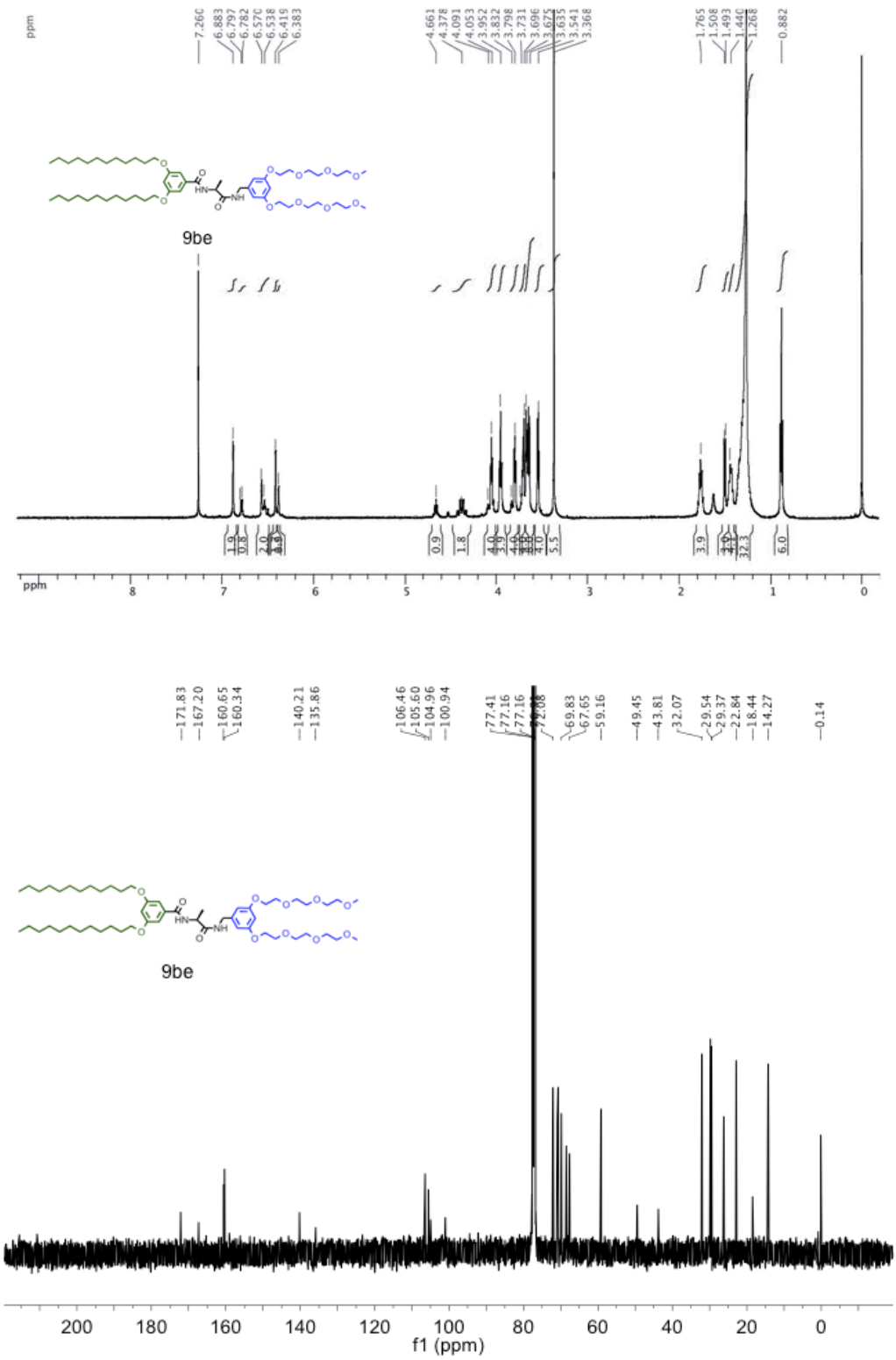


Figure SF19. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-L-Ala-CH_2-(3,5)-3EO-G1-$(OCH_3)_2$ **9be** in $CDCl_3$

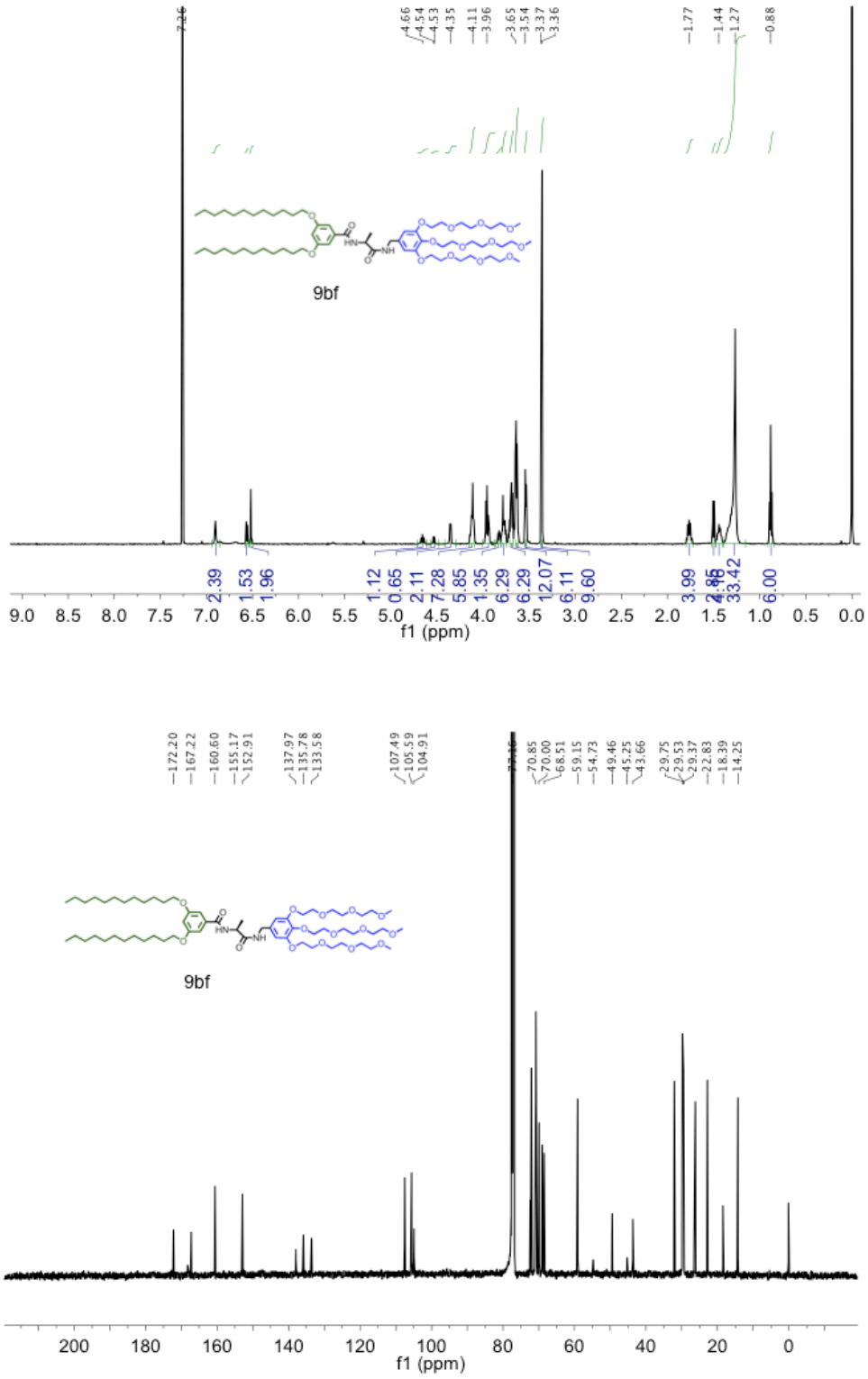


Figure SF20. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$ **9bf** in $CDCl_3$

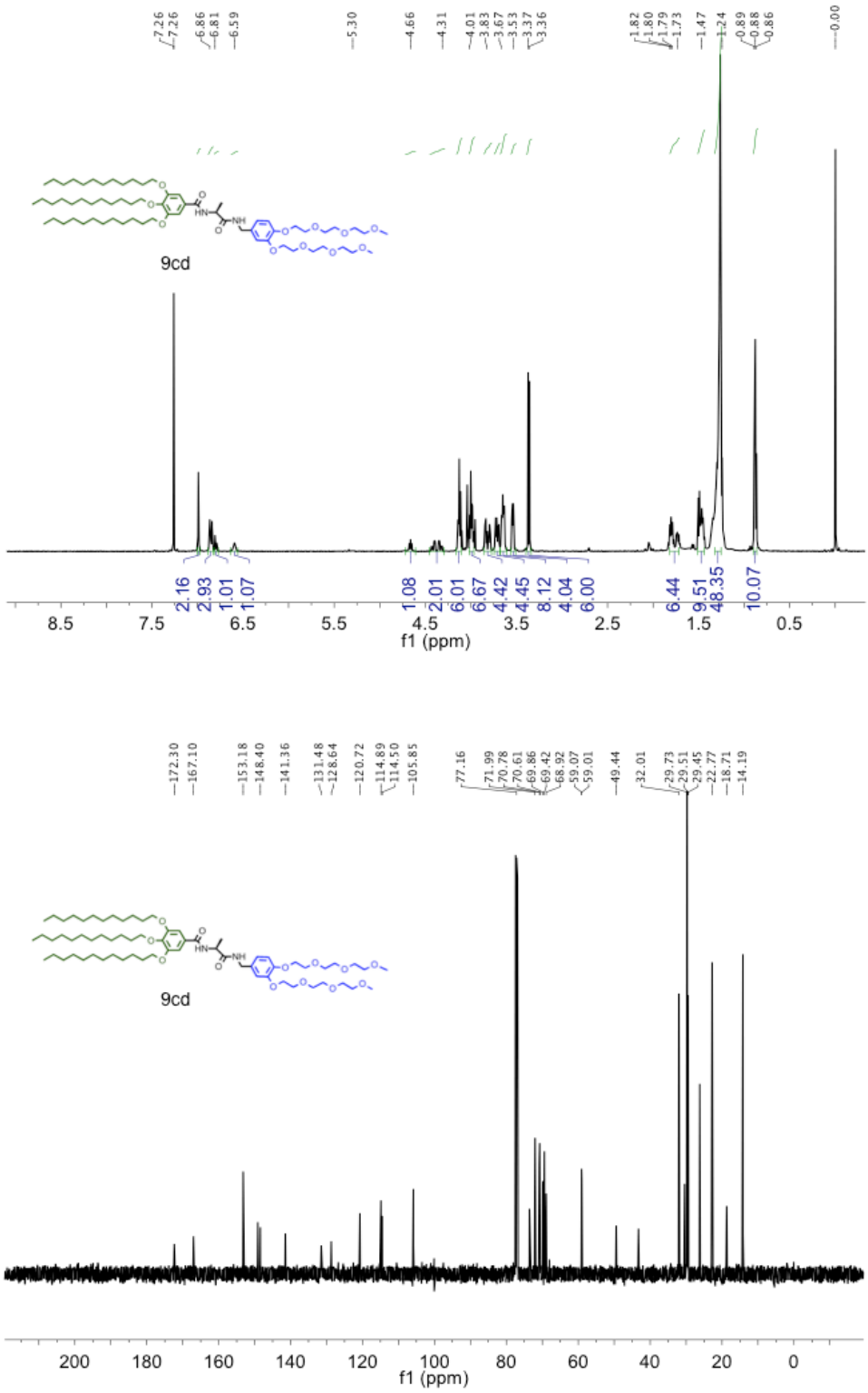


Figure SF21. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4,5)12G1-L-Ala-CH_2-(3,4) -3EO-G1-$(OCH_3)_2$ **9cd** in $CDCl_3$

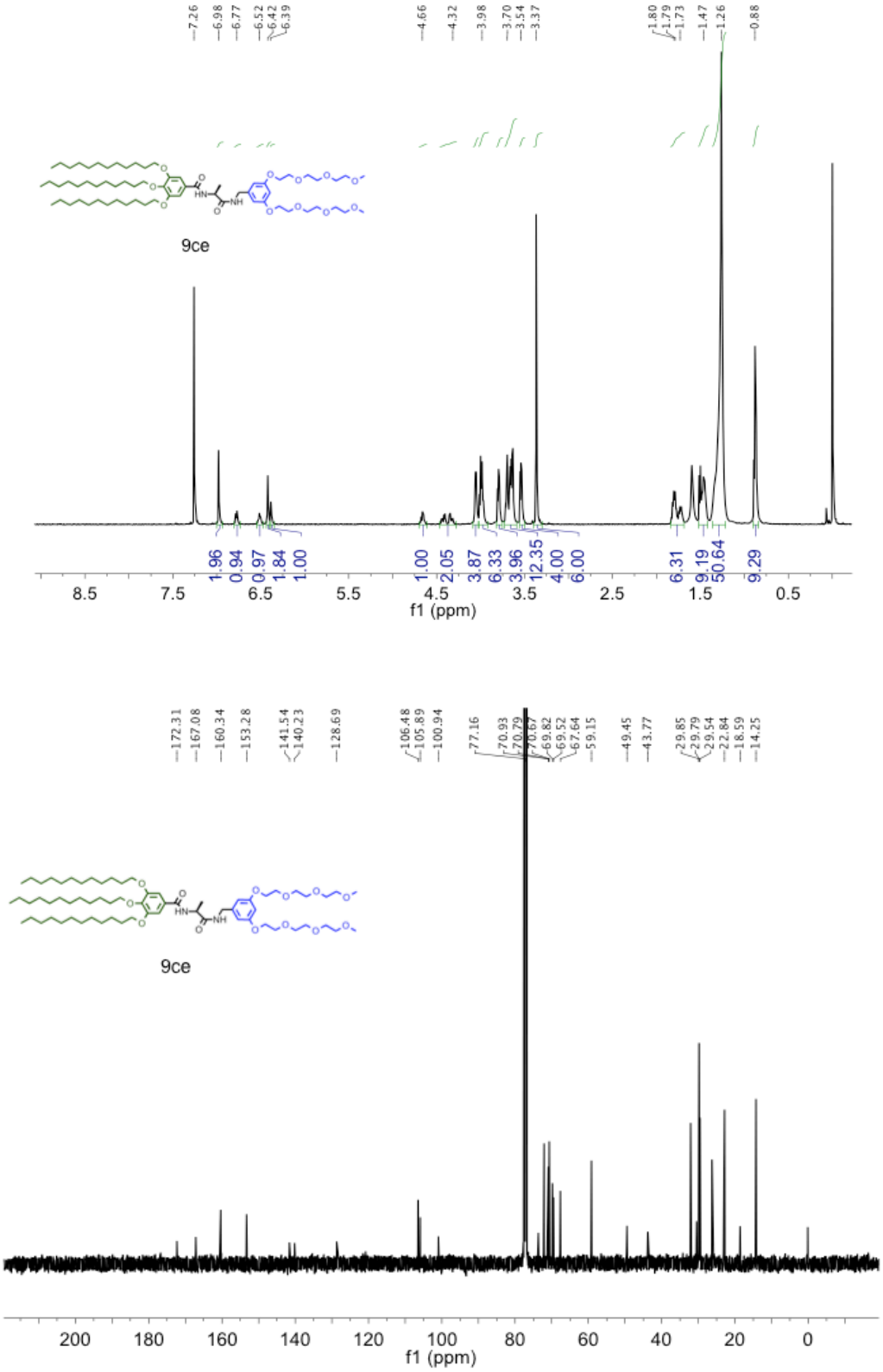


Figure SF22. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4,5)12G1-L-Ala-CH_2-(3,5)-3EO-G1-$(OCH_3)_2$ **9ce** in $CDCl_3$

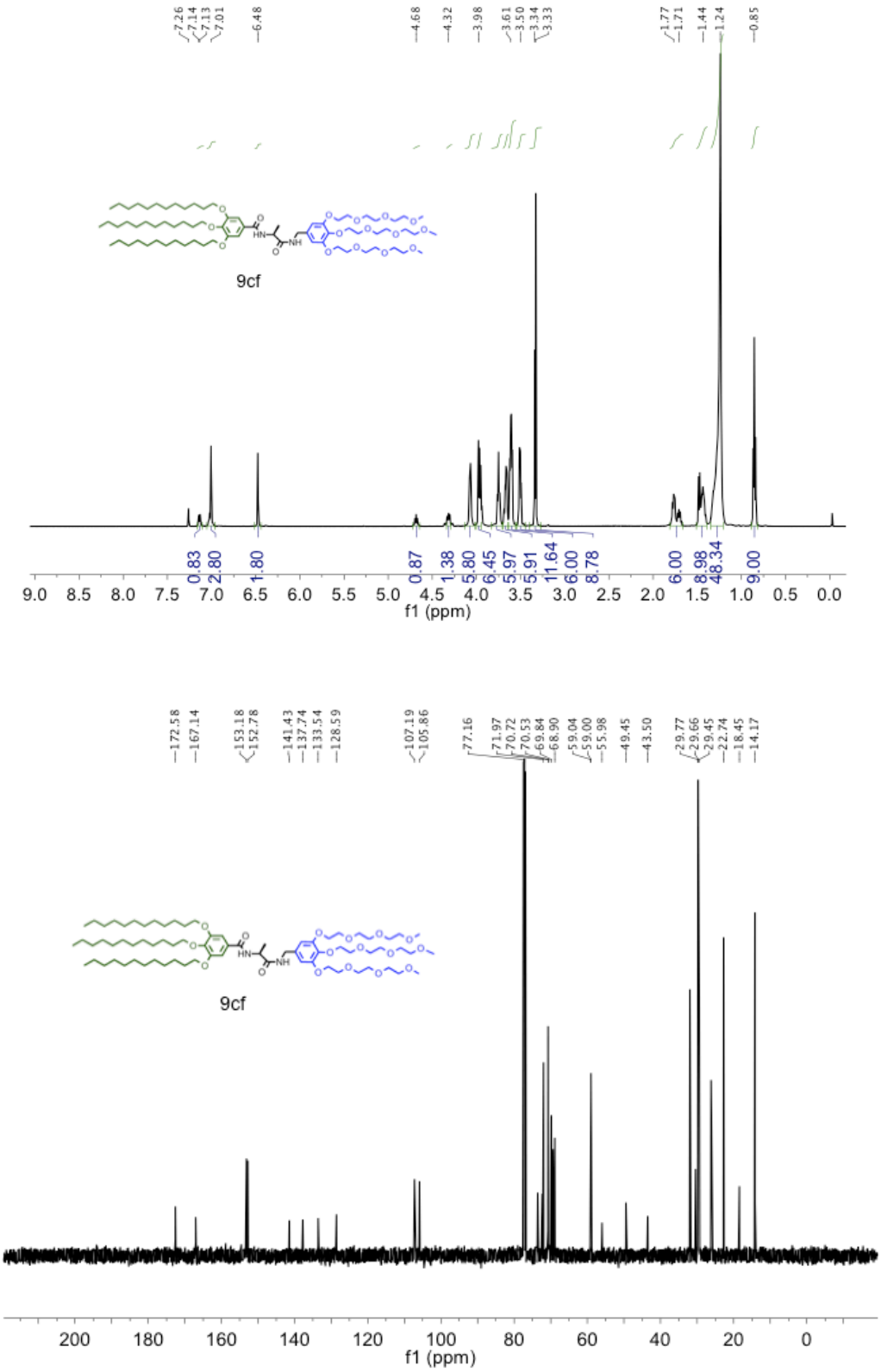


Figure SF23. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4,5)12G1-L-Ala-CH_2-(3,4,5)-3EO-G1-$(OCH_3)_3$ **9cf** in $CDCl_3$

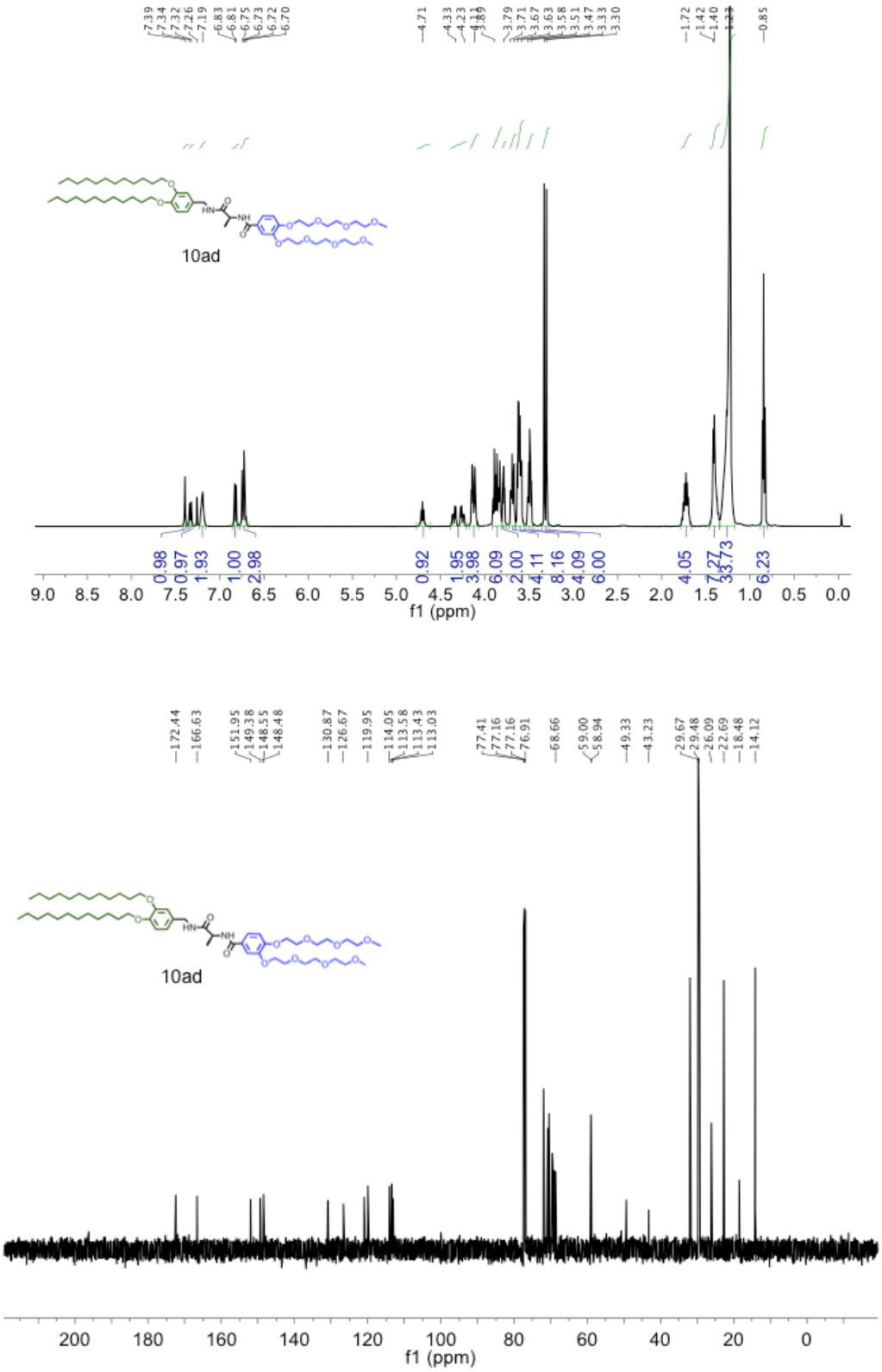


Figure SF24. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4)12G1-CH_2-L-Ala-(3,4) -3EO-G1-$(OCH_3)_2$ **10ad** in $CDCl_3$

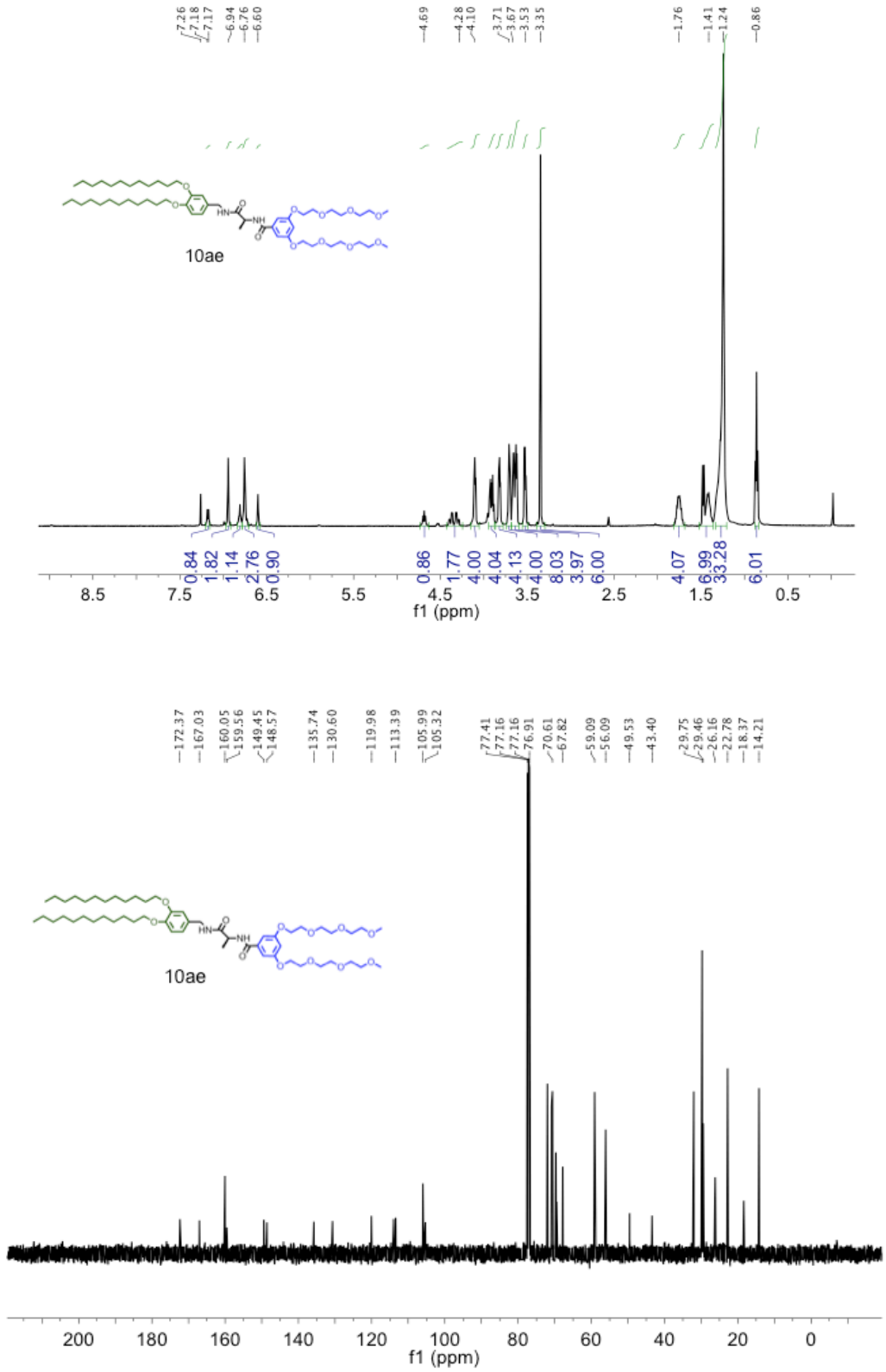


Figure SF25. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4)12G1-CH_2-L-Ala-(3,5)-3EO-G1-$(OCH_3)_2$ **10ae** in $CDCl_3$

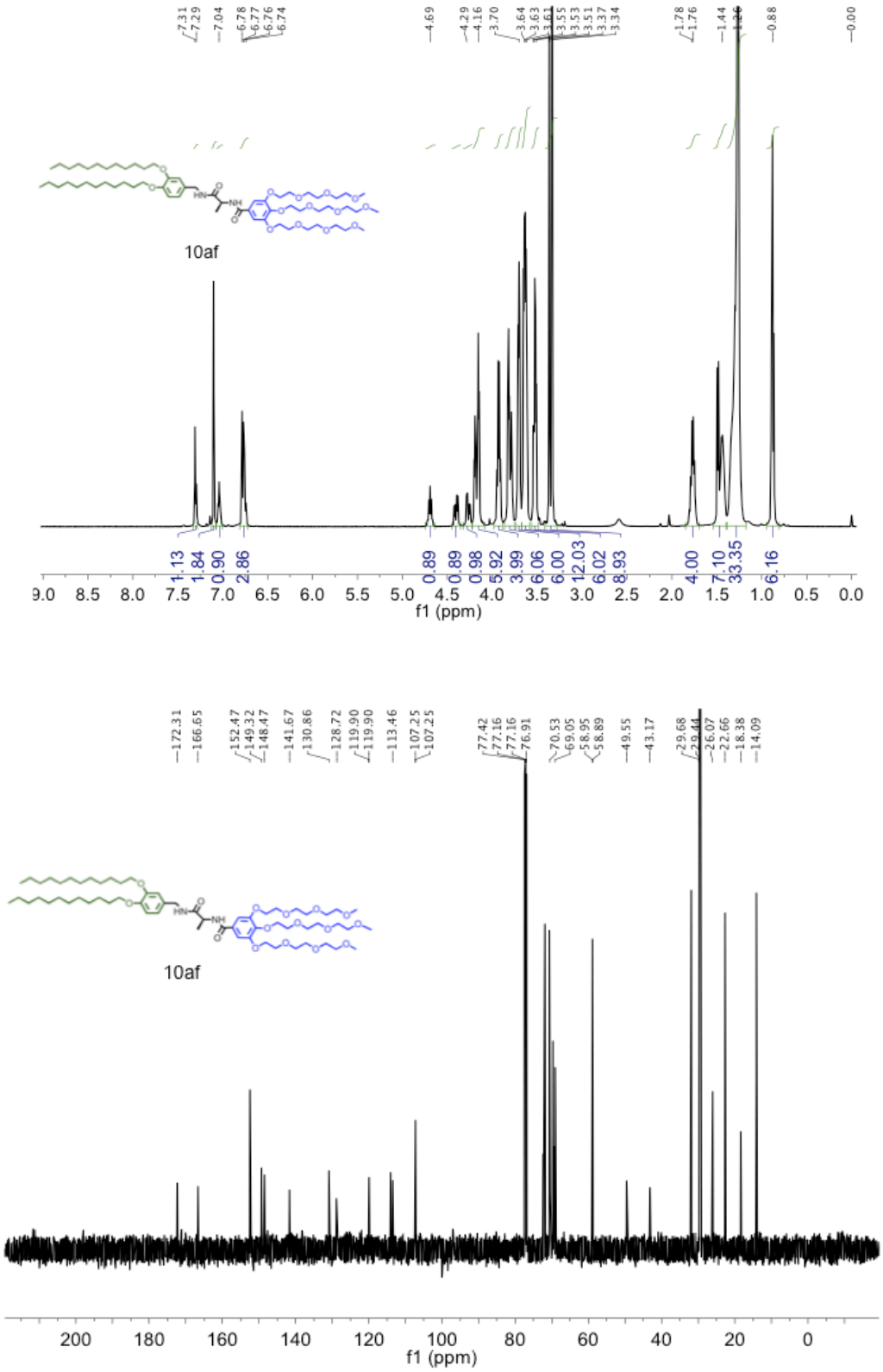


Figure SF26. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4)12G1-CH_2-L-Ala-(3,4,5)-3EO-G1-$(OCH_3)_3$ **10af** in $CDCl_3$

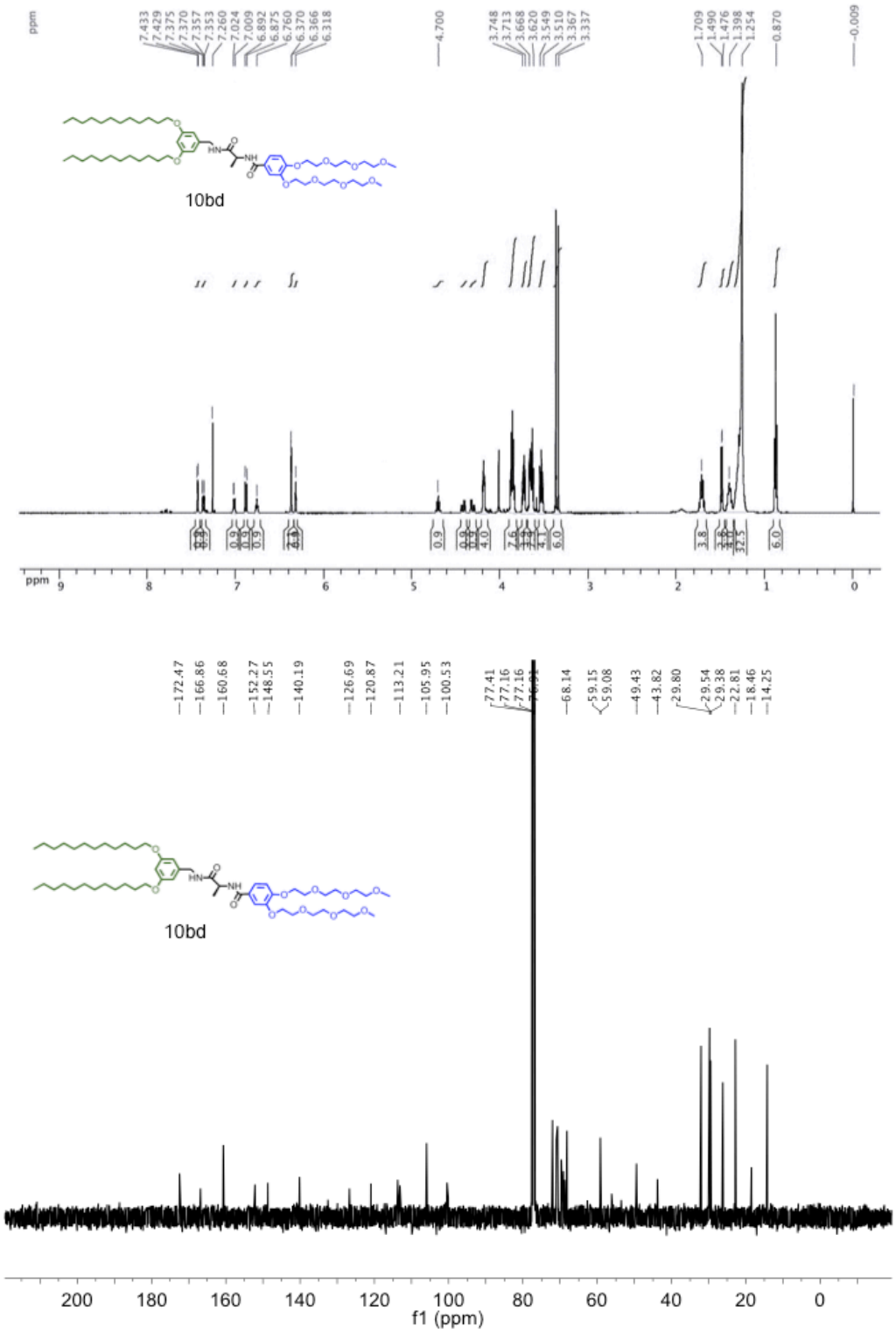
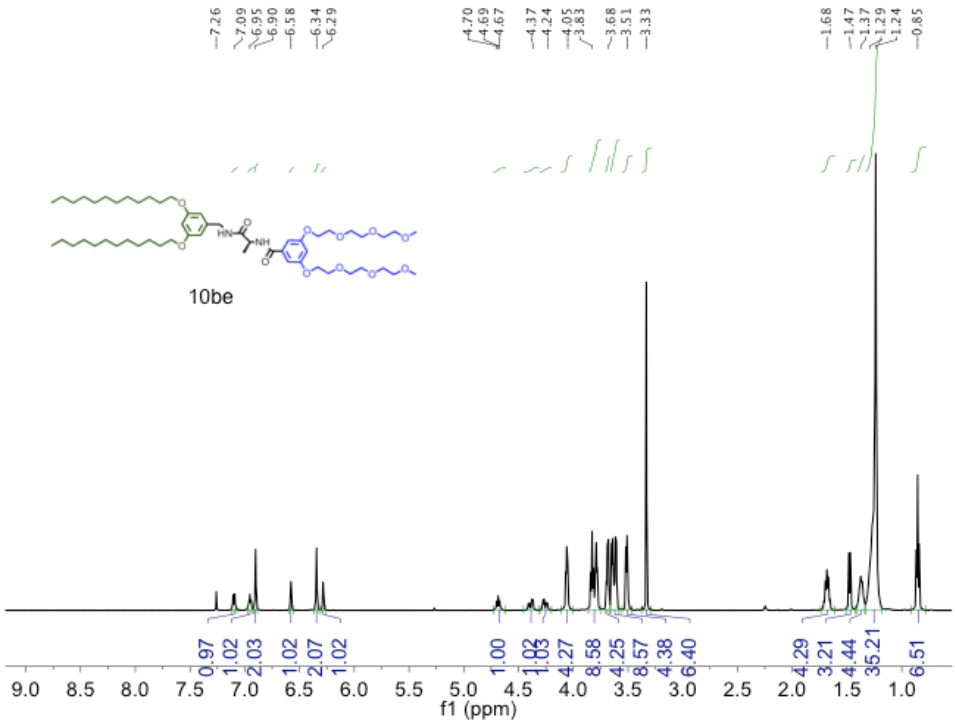


Figure SF27. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-CH_2-L-Ala-(3,4)-3EO-G1-$(OCH_3)_2$ **10bd** in $CDCl_3$



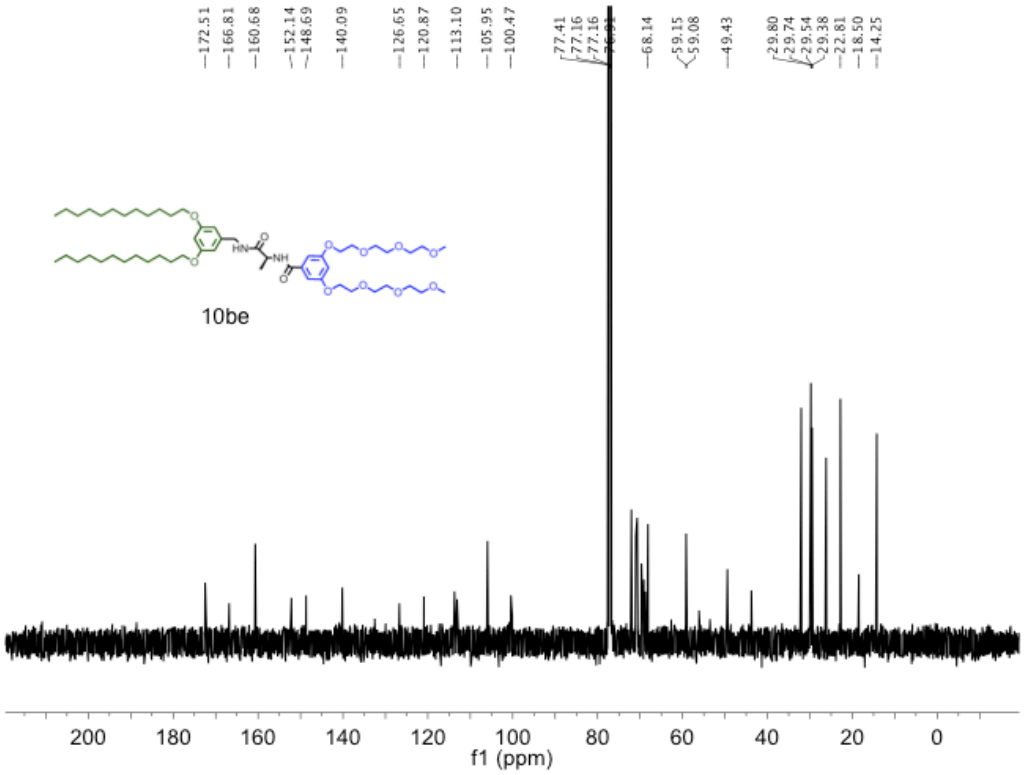
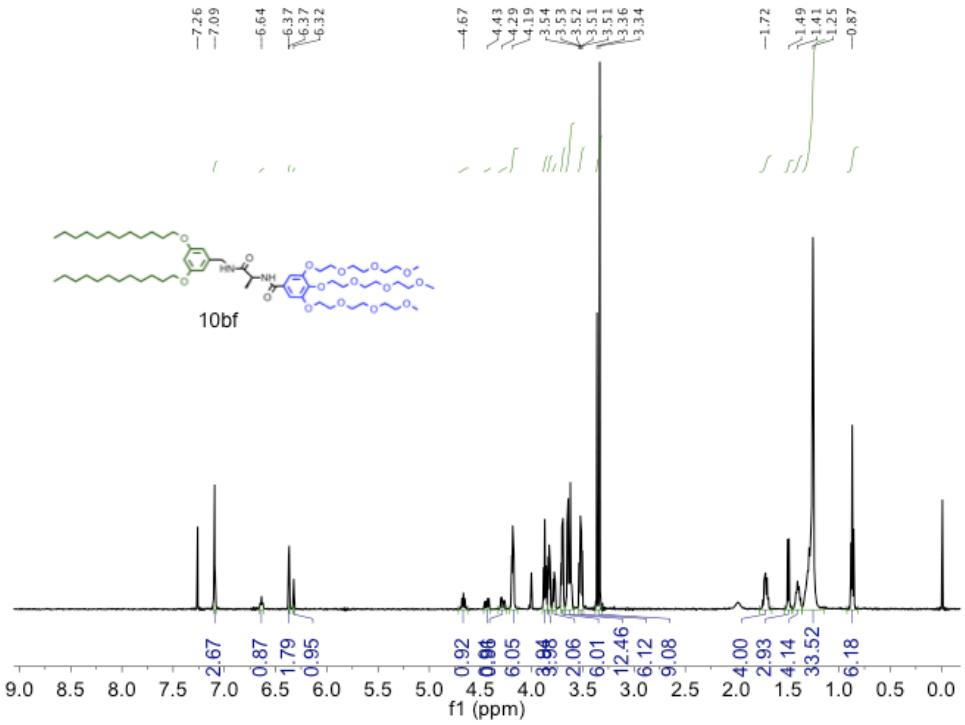


Figure SF28. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-CH_2-L-Ala-(3,5)-3EO-G1-$(OCH_3)_2$ **10be** in $CDCl_3$



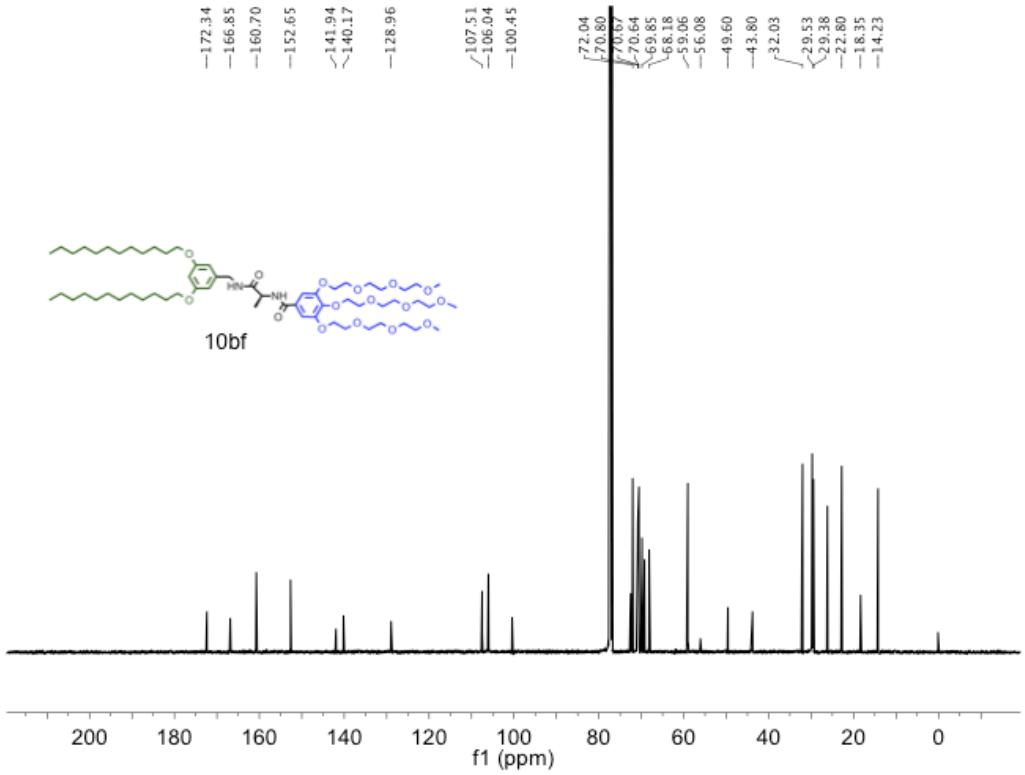


Figure SF29. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-CH_2-L-Ala-(3,4,5)-3EO-G1-$(OCH_3)_3$ **10bf** in $CDCl_3$

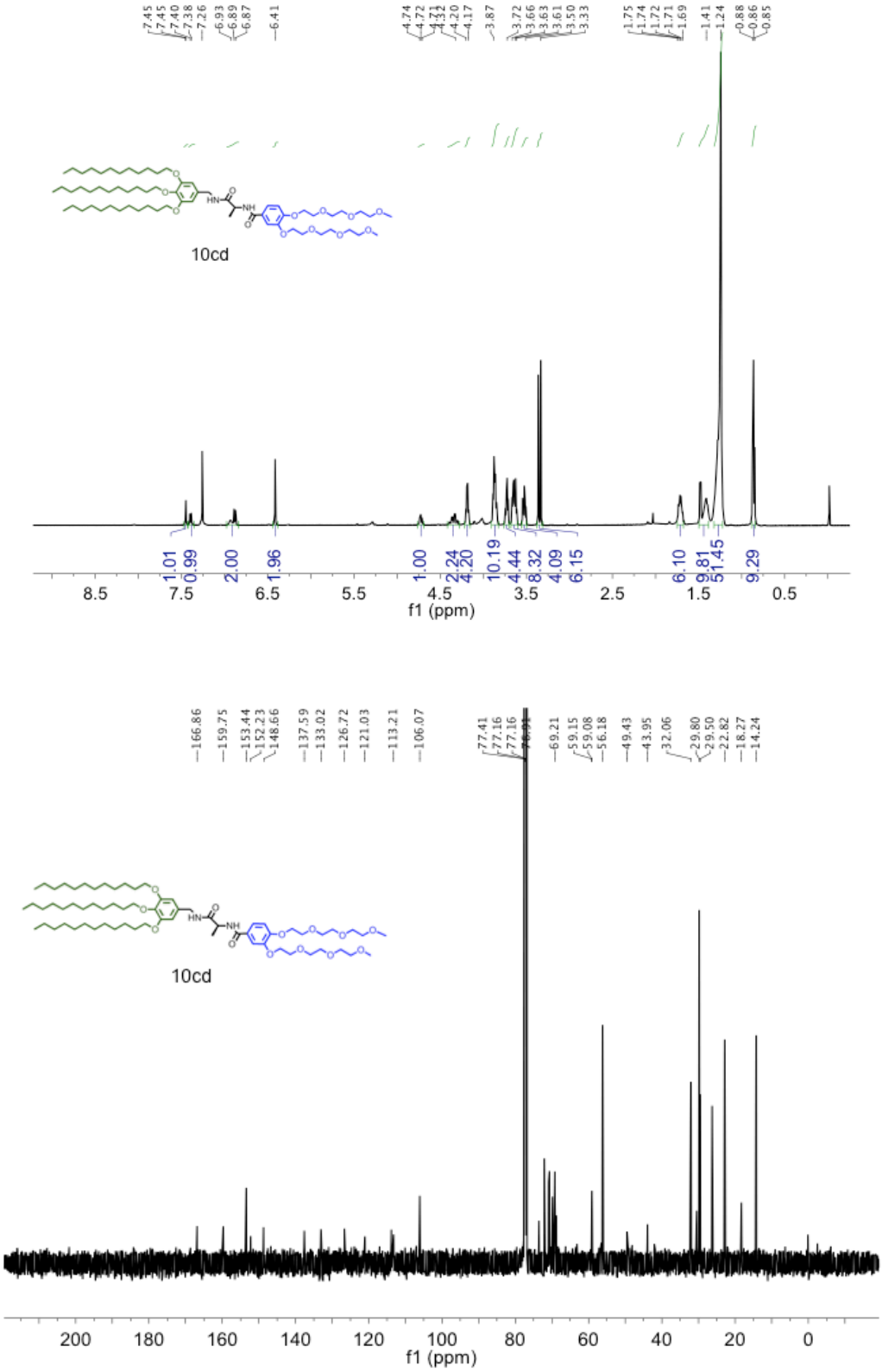


Figure SF30. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4,5)12G1-CH_2-L-Ala-(3,4)-3EO-G1-$(OCH_3)_2$ **10cd** in $CDCl_3$

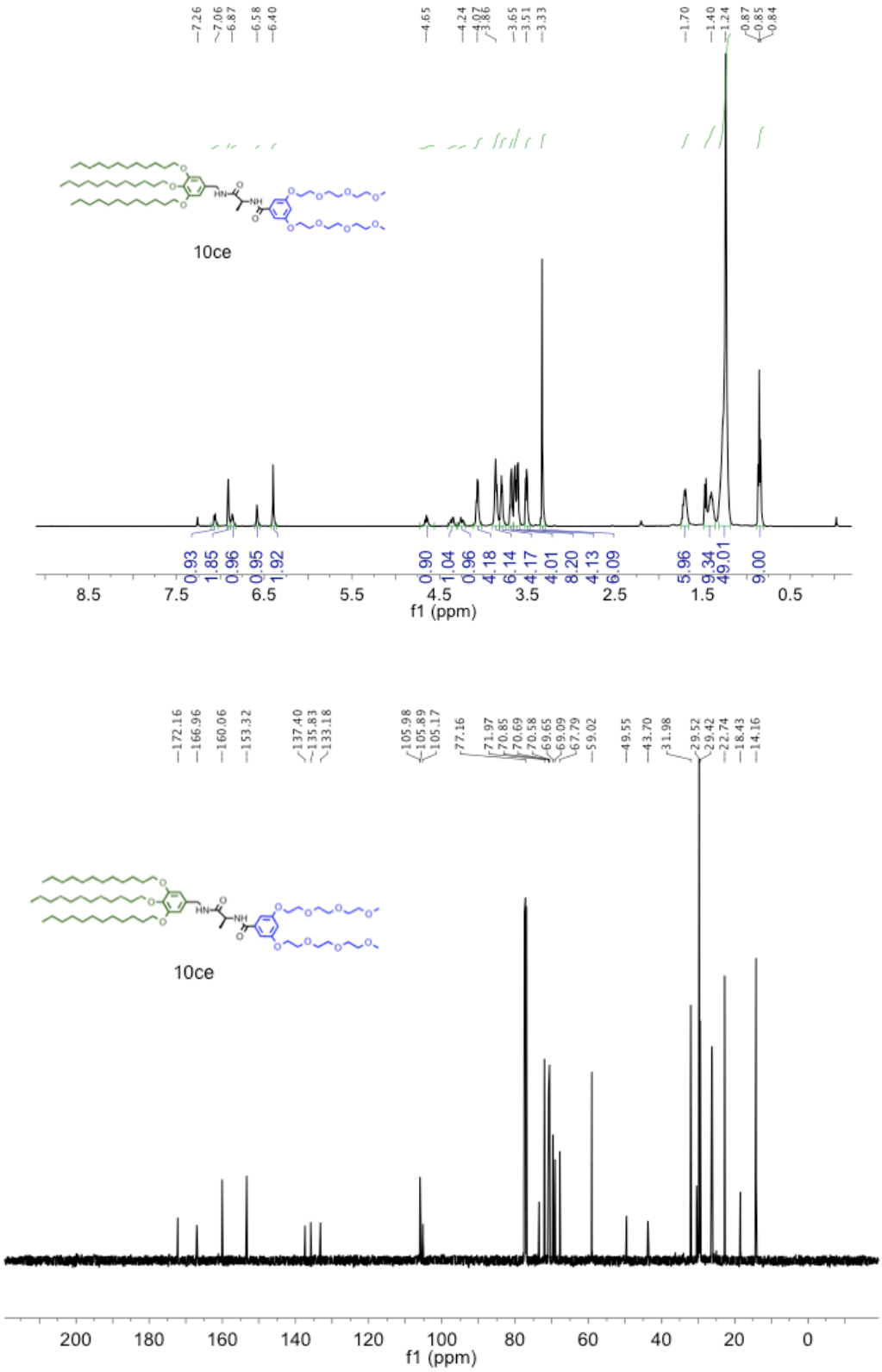


Figure SF31. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4,5)12G1-CH_2-L-Ala-(3,5)-3EO-G1-$(OCH_3)_2$ **10ce** in $CDCl_3$

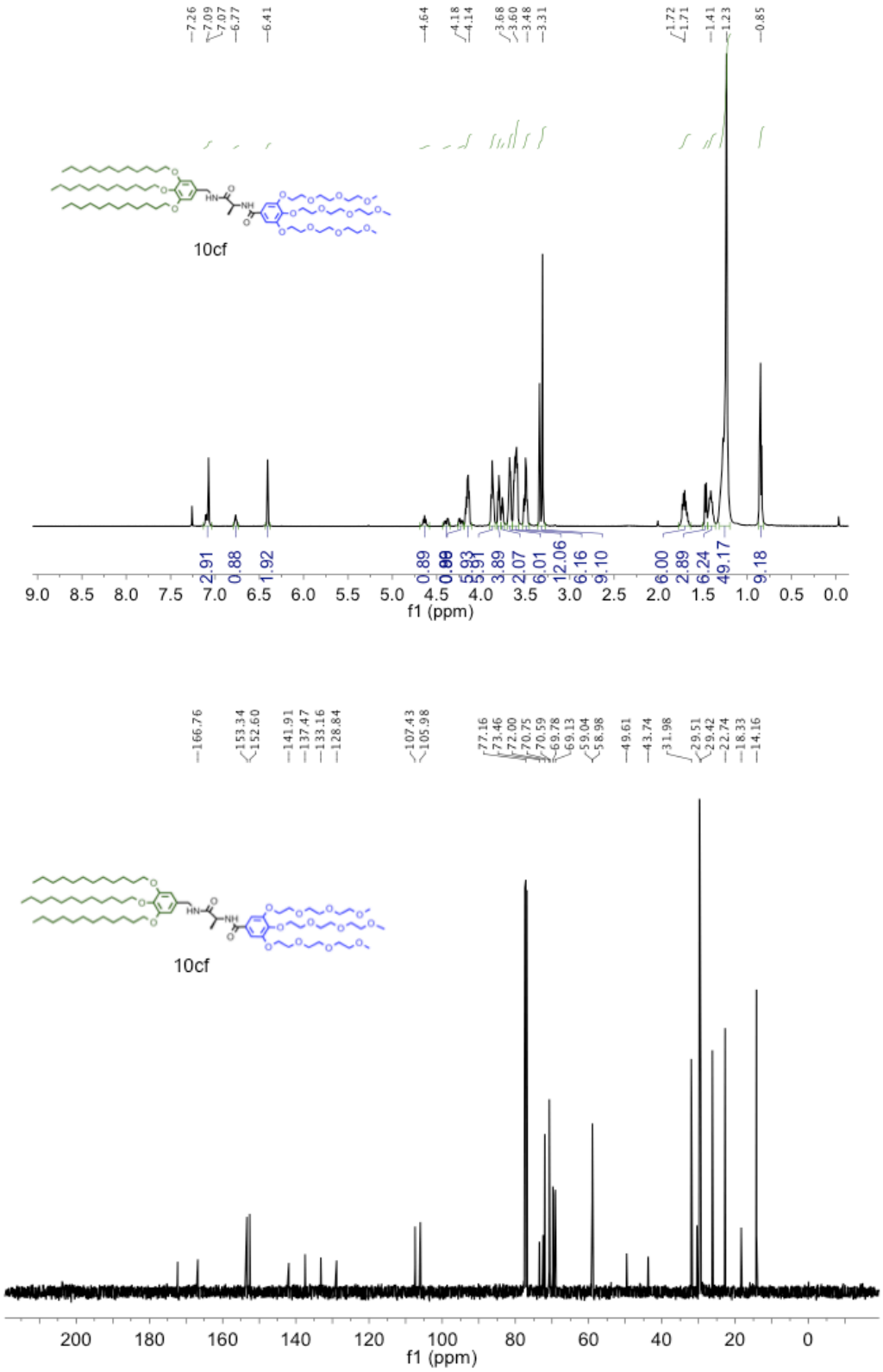


Figure SF32. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4,5)12G1-CH_2-L-Ala-(3,4,5)-3EO-G1-$(OCH_3)_3$ **10cf** in $CDCl_3$

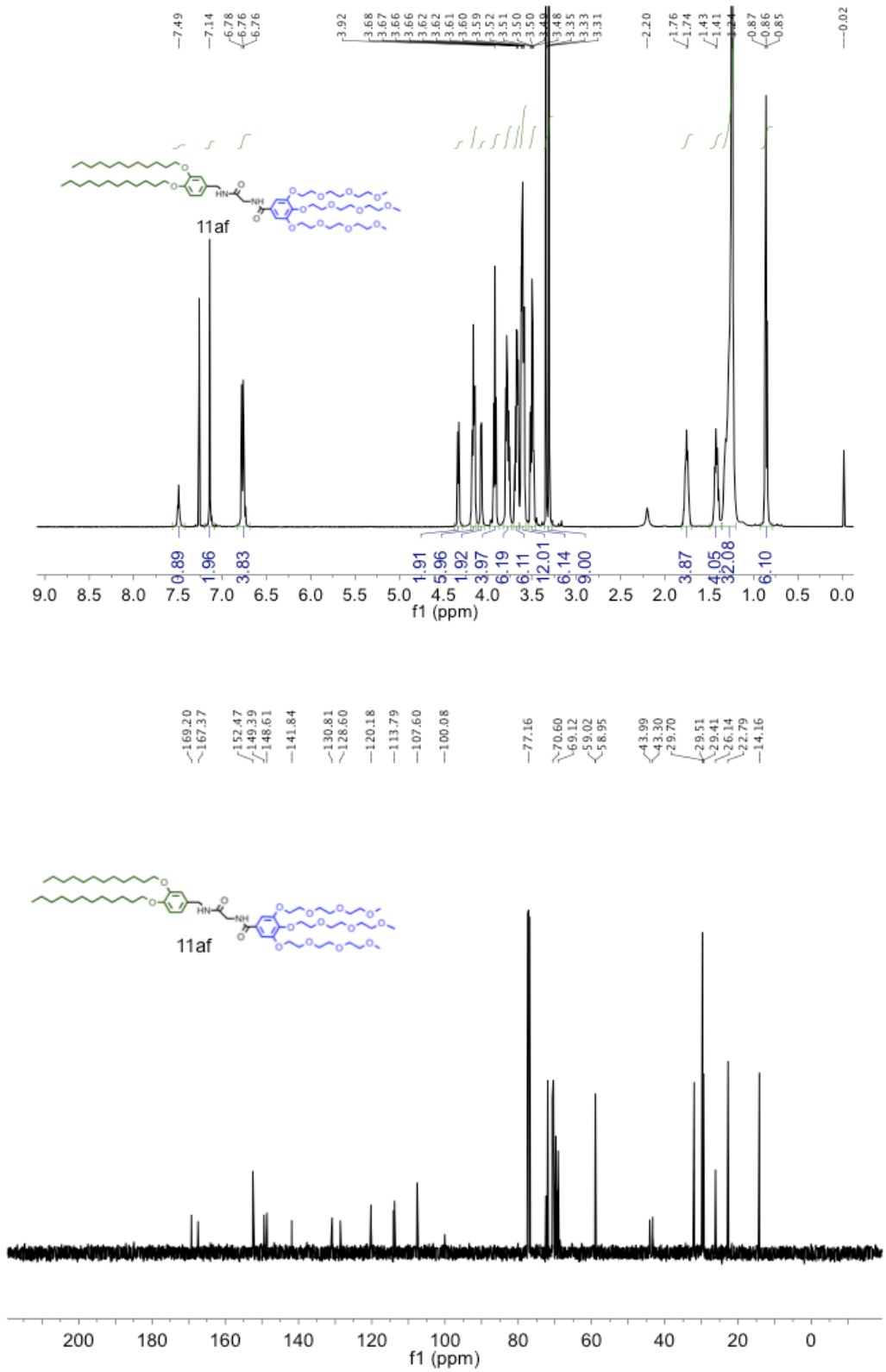
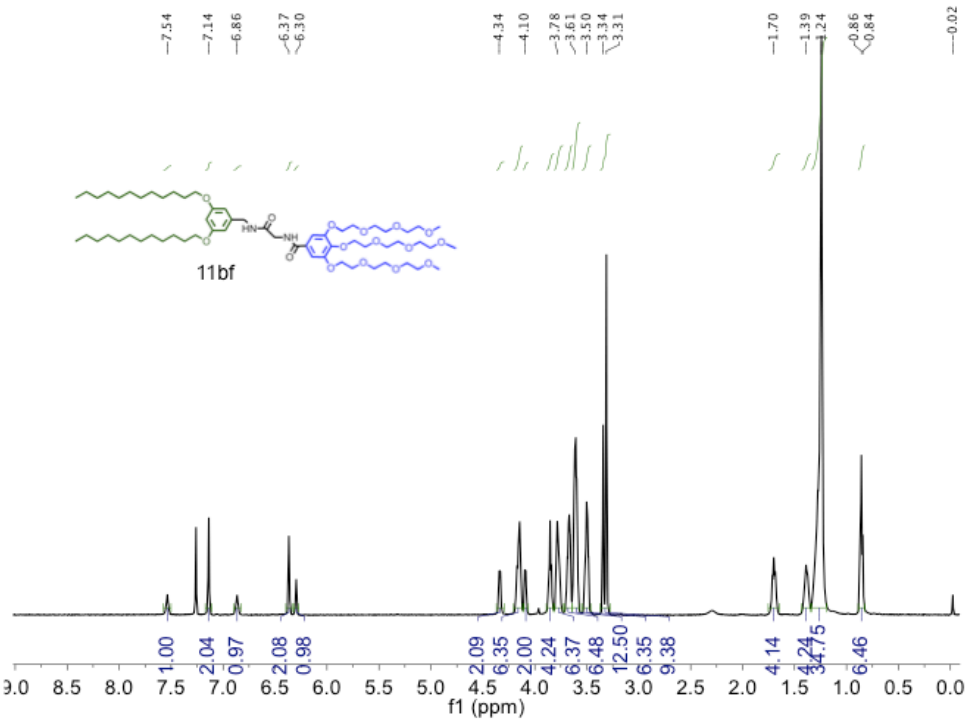


Figure SF33. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4)12G1-CH_2-Gly-(3,4,5)-3EO-G1-$(OCH_3)_3$ **11af** in $CDCl_3$



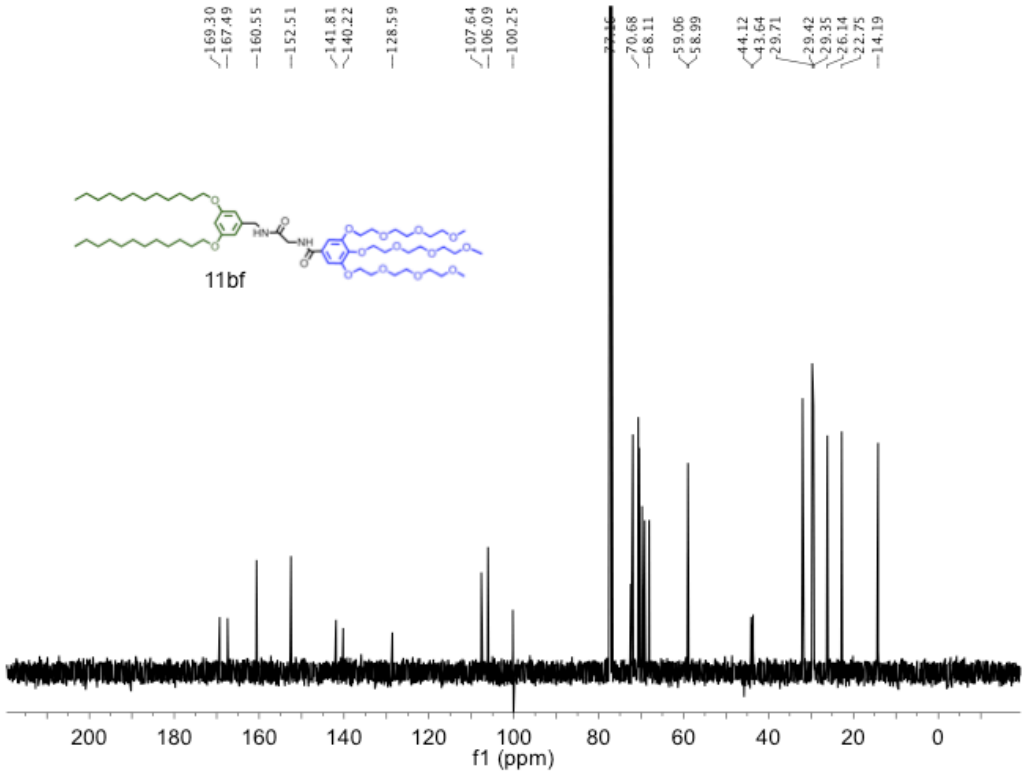


Figure SF34. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-CH_2-Gly-(3,4,5)-3EO-G1-$(OCH_3)_3$ **11bf** in $CDCl_3$

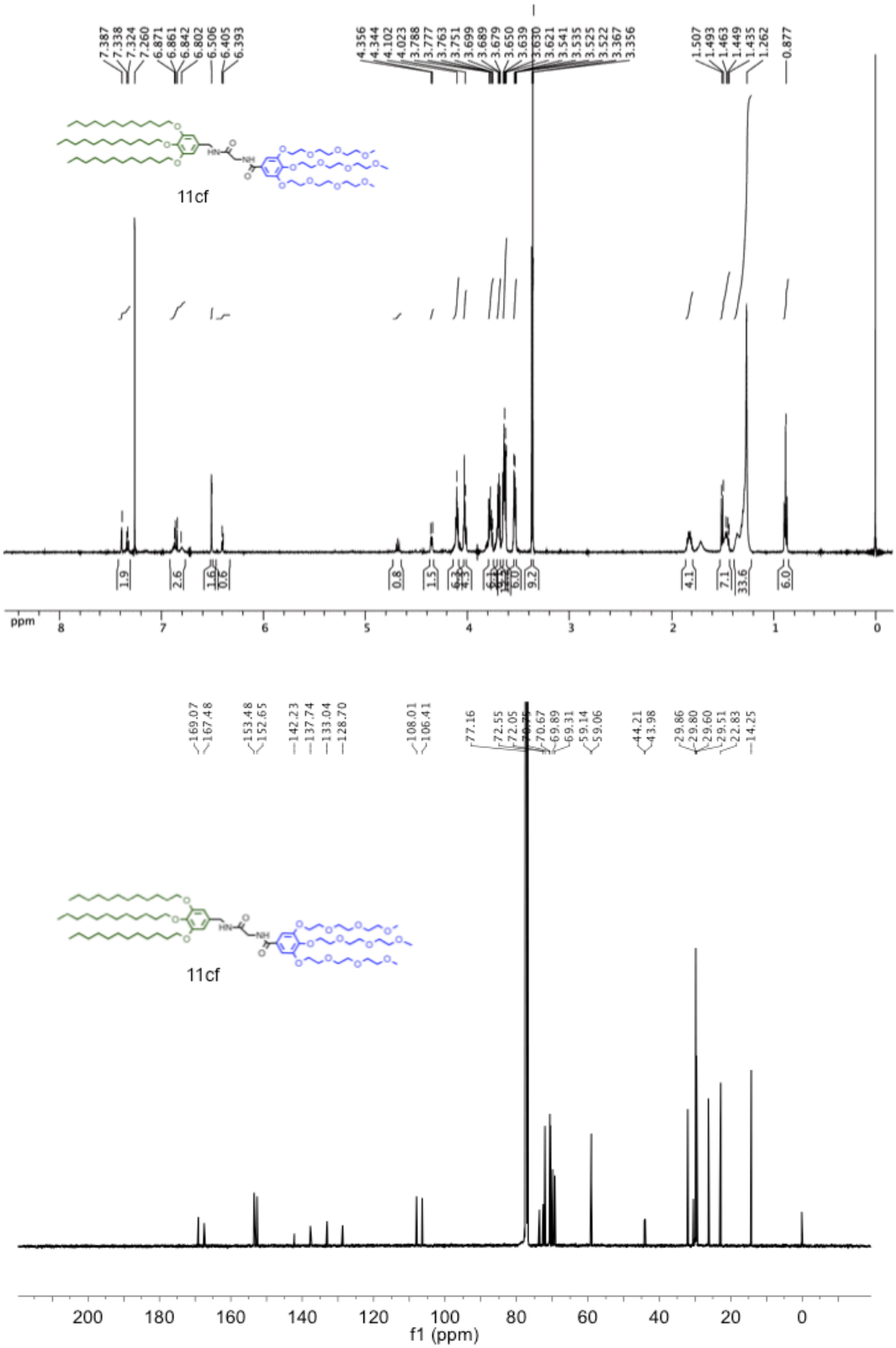
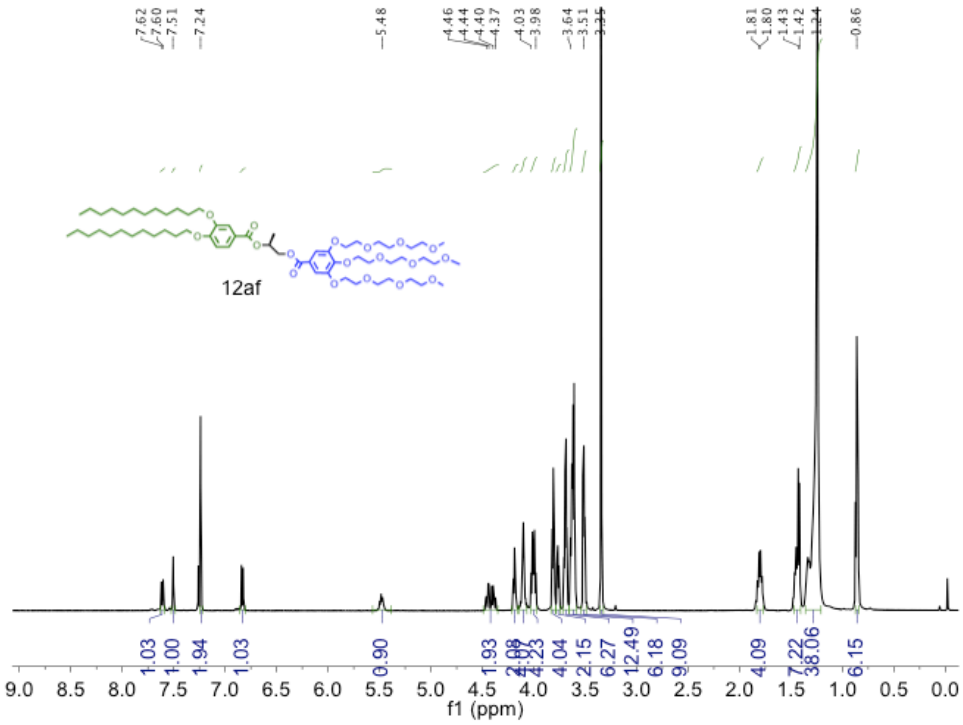


Figure SF35. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4,5)12G1-CH_2-Gly-(3,4,5)-3EO-G1-$(OCH_3)_3$ **11cf** in $CDCl_3$



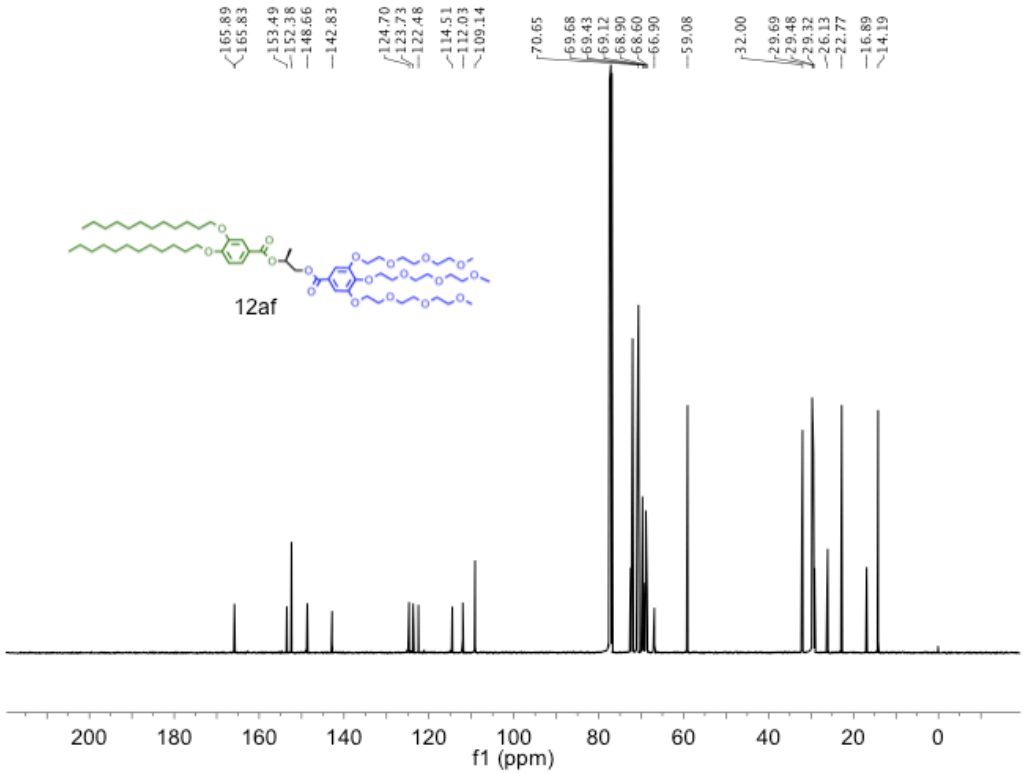


Figure SF36. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4)12G1-I-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$ **12af** in $CDCl_3$

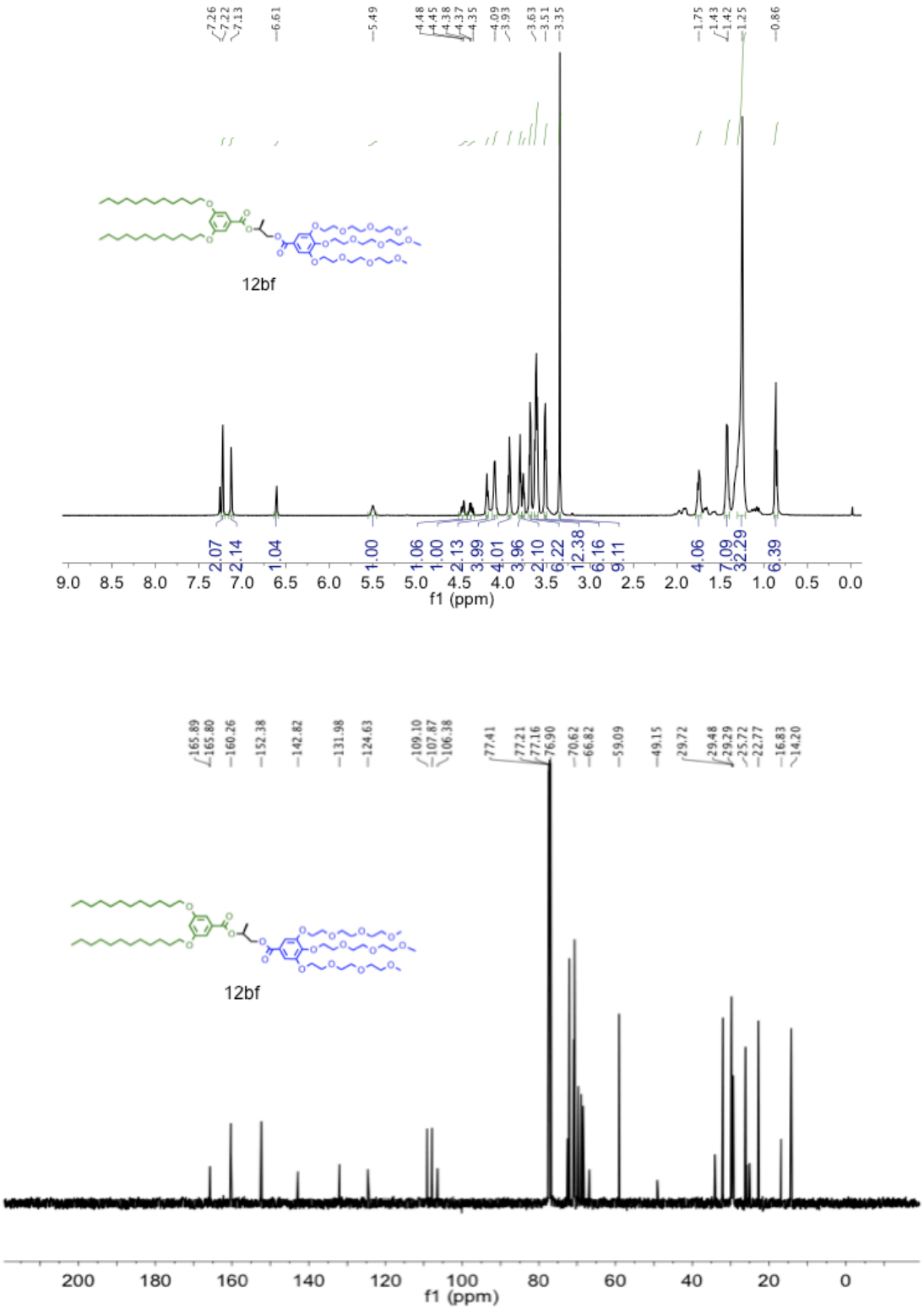


Figure SF37. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-I-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$ **12bf** in $CDCl_3$

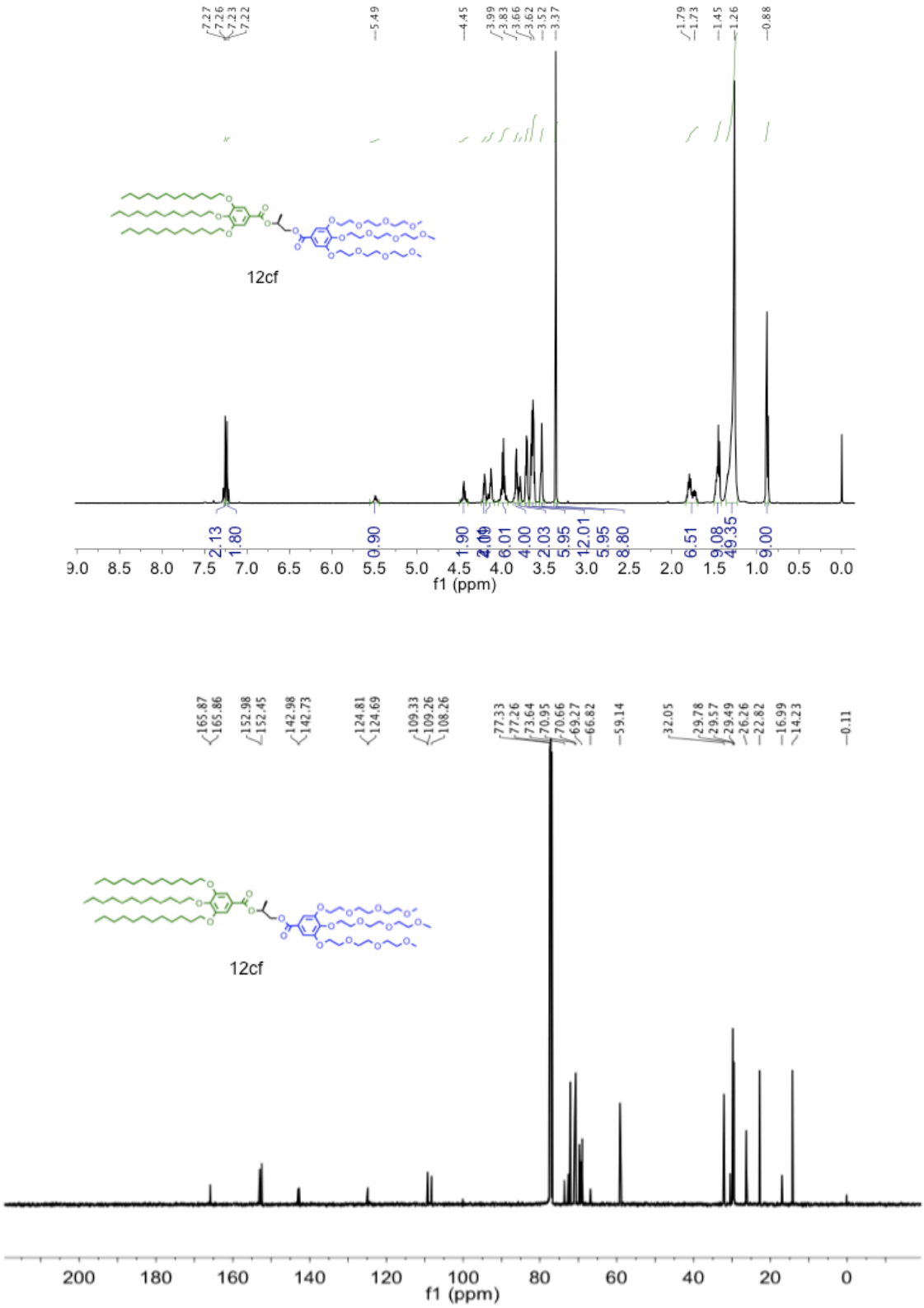
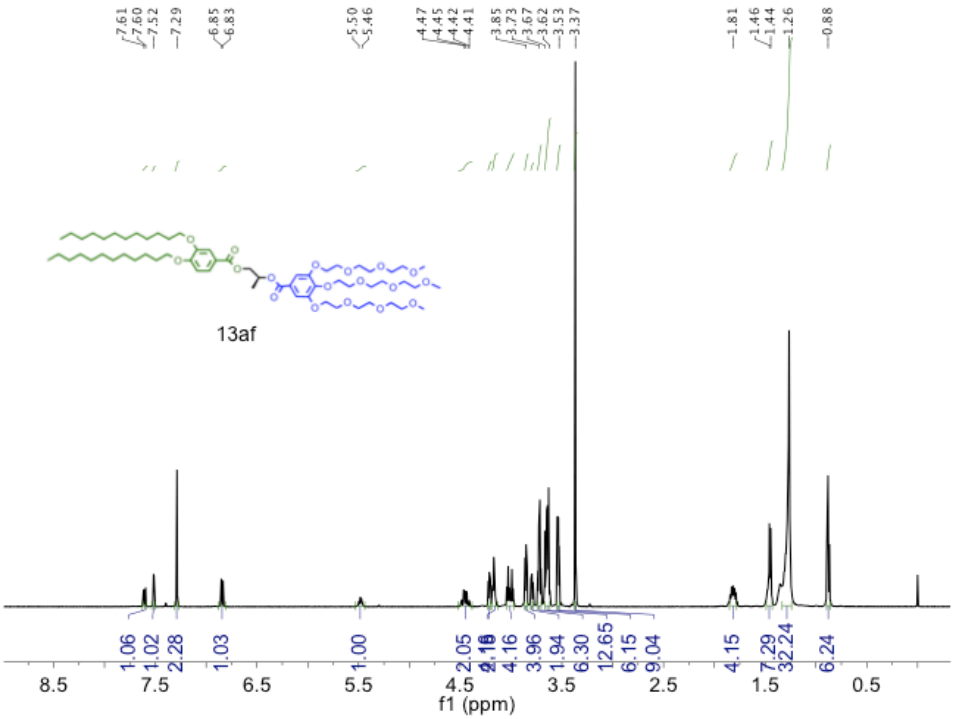


Figure SF38. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4,5)12G1-I-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$ **12cf** in $CDCl_3$



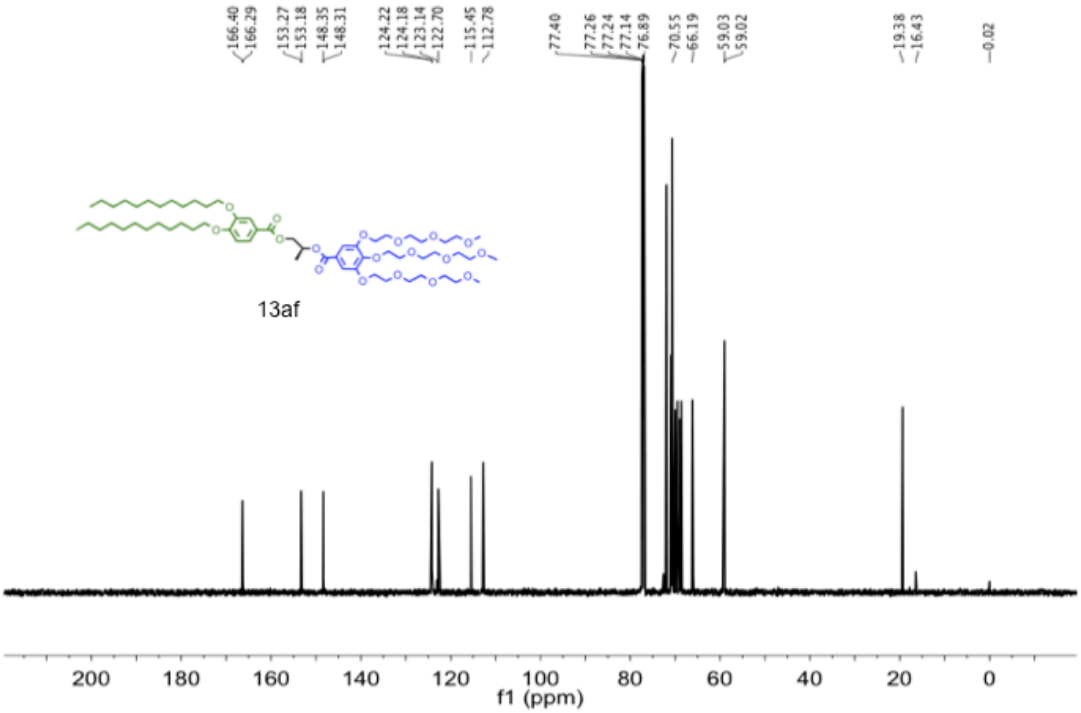
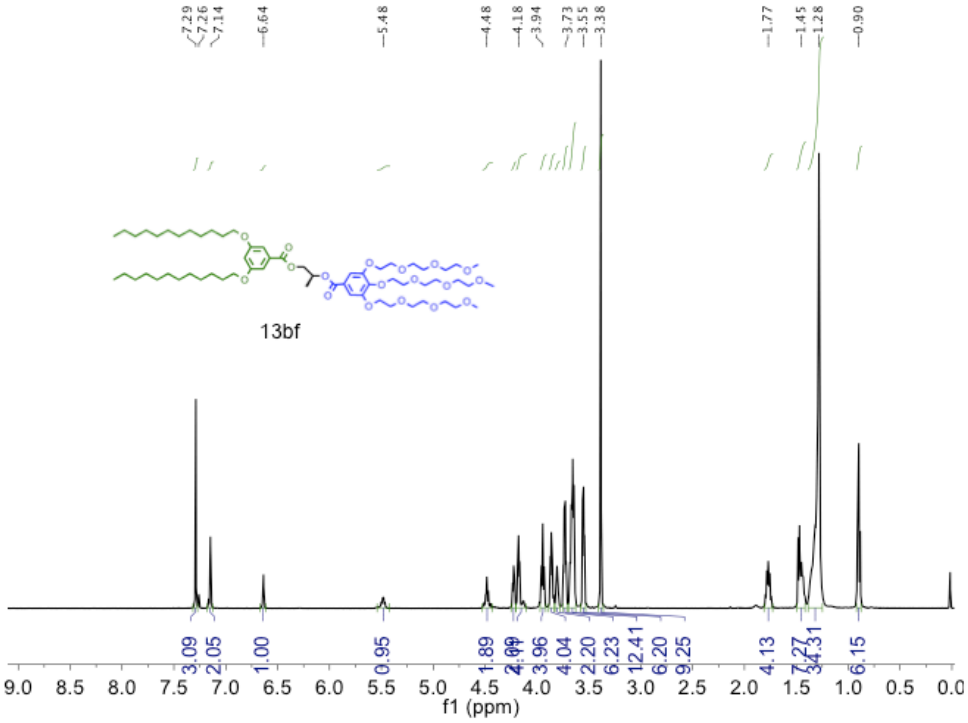


Figure SF39. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4)12G1-II-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$ **13af** in $CDCl_3$



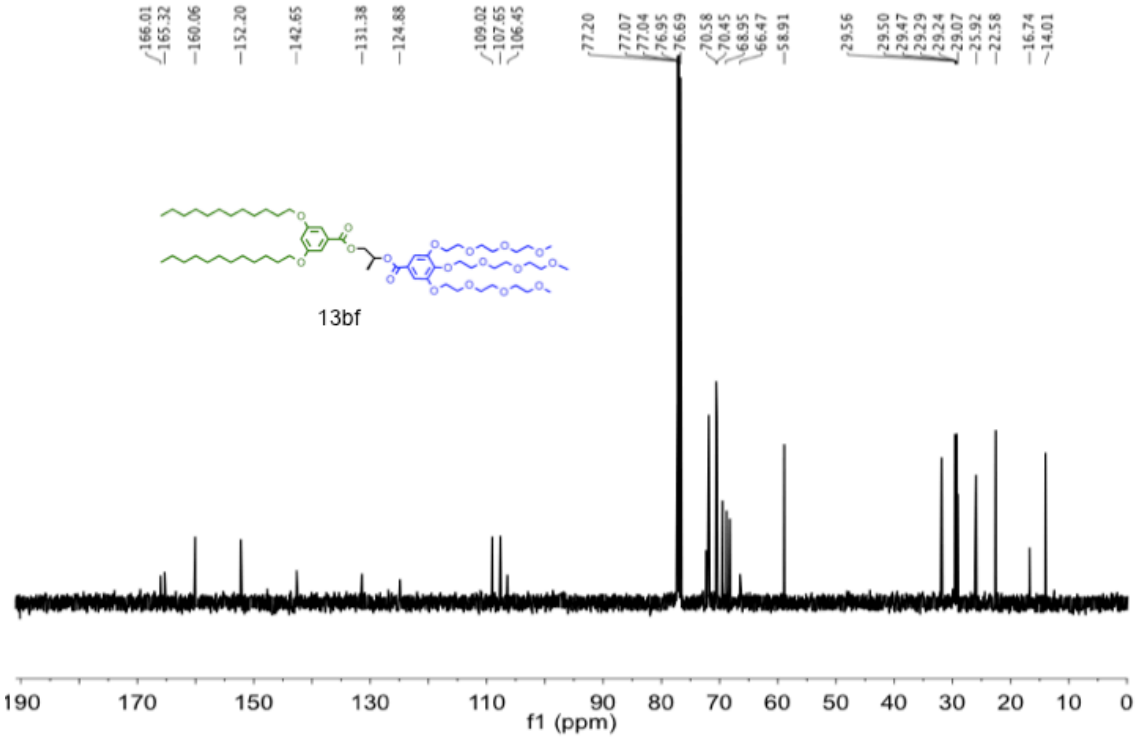
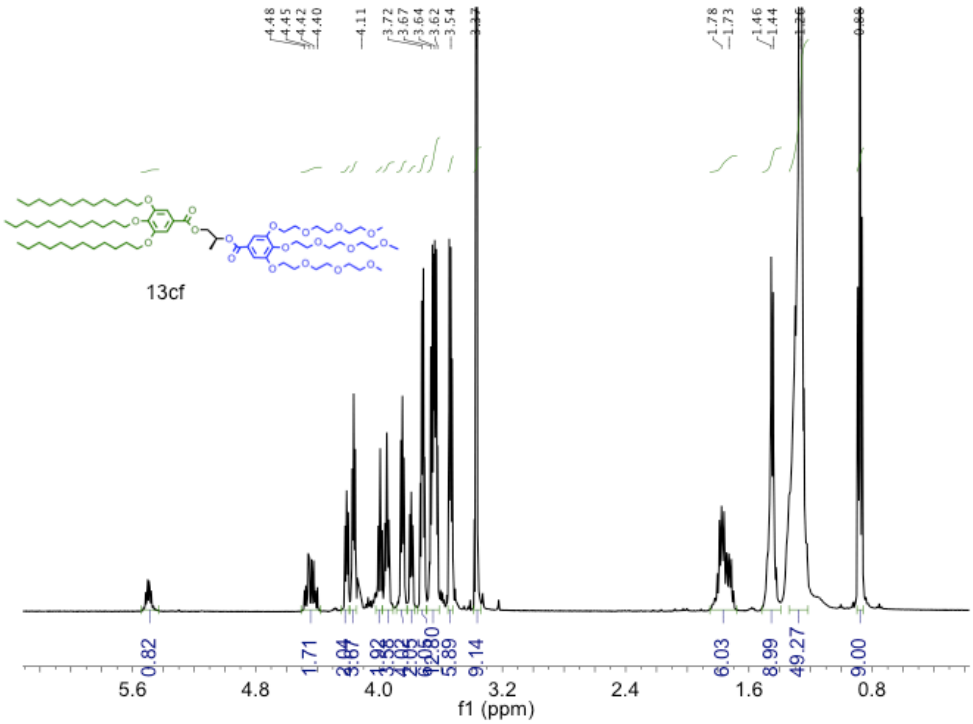


Figure SF40. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-II-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$ **13bf** in $CDCl_3$



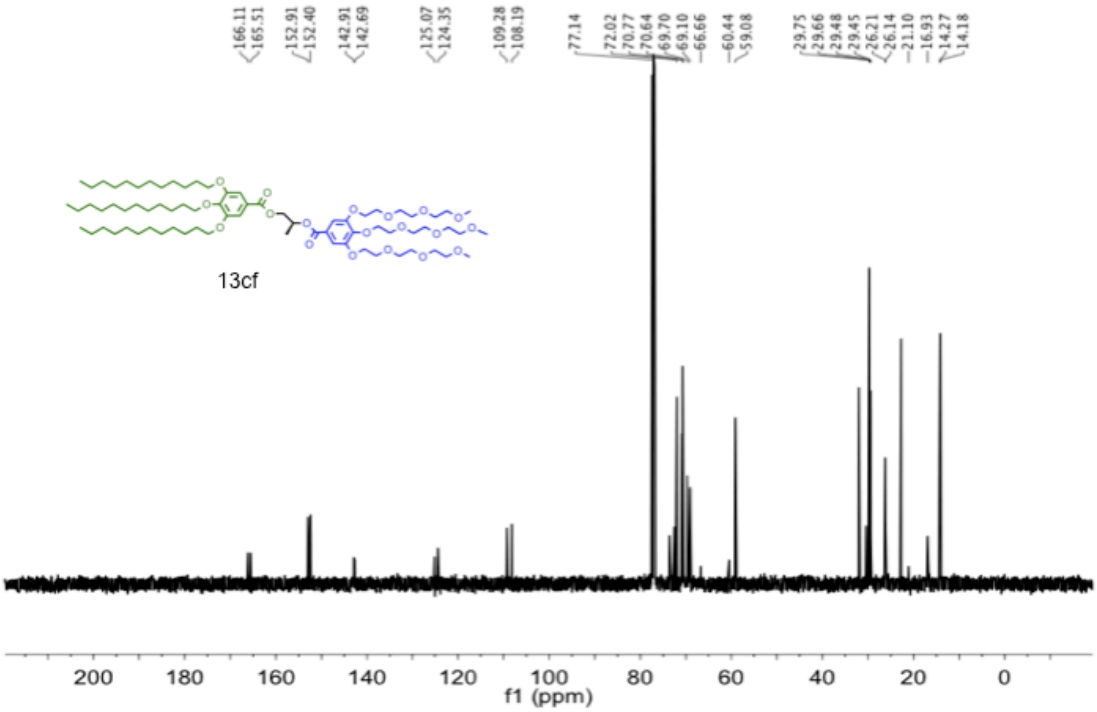
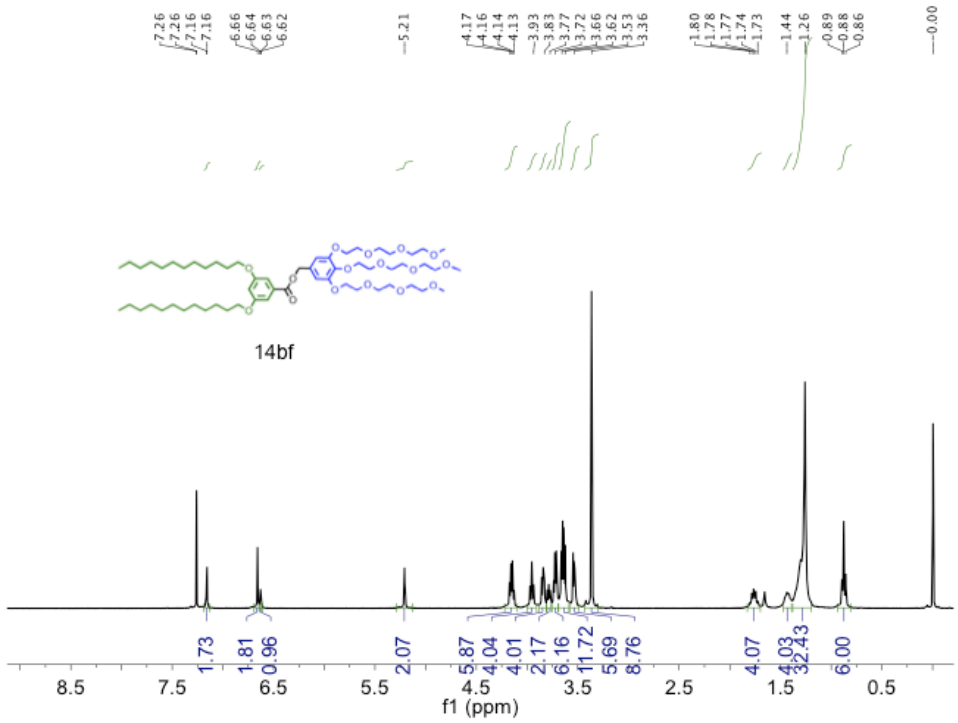


Figure SF41. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,4,5)12G1-II-PPD-(3,4,5)-3EO-G1-$(OCH_3)_3$ **13cf** in $CDCl_3$



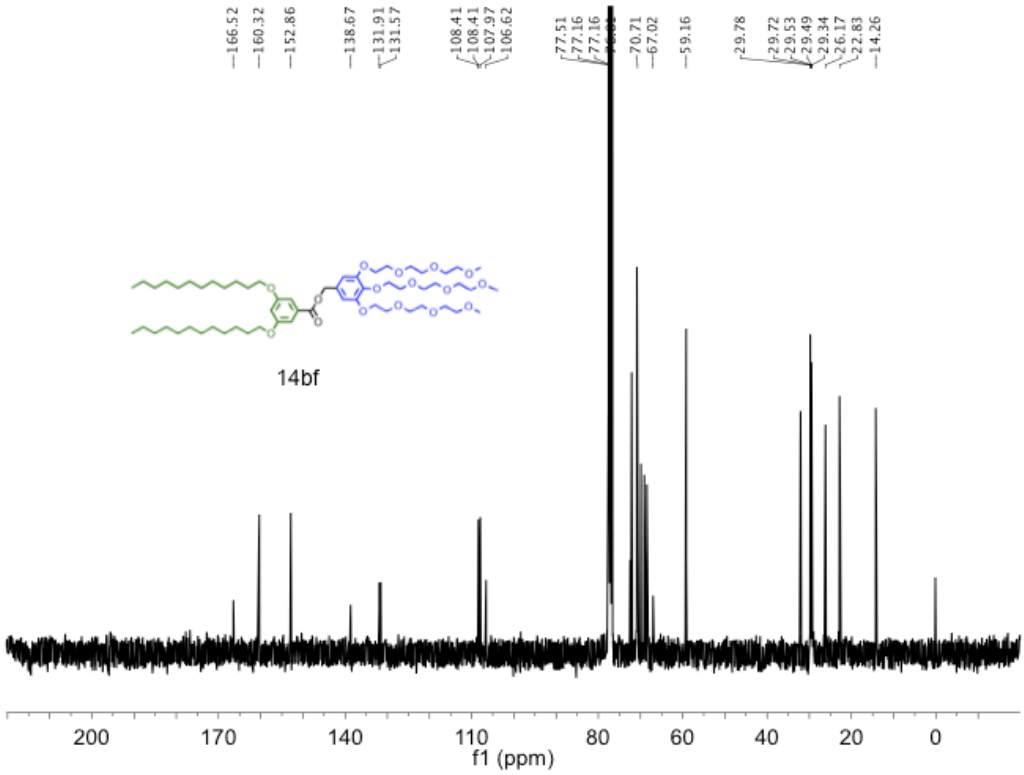
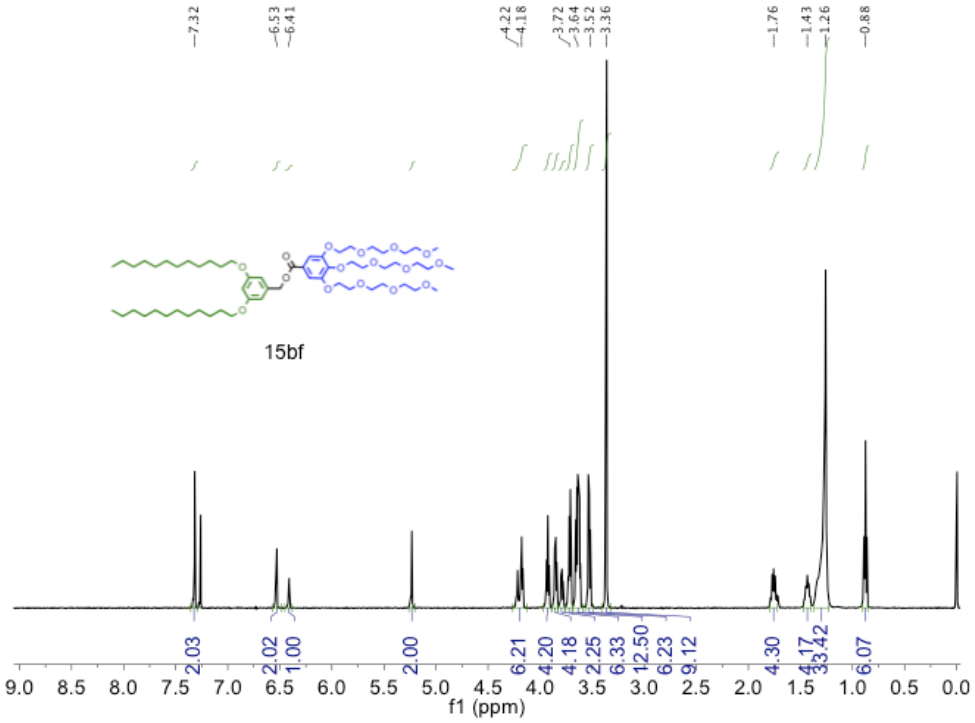


Figure SF42. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-III-Phe-(3,4,5)-3EO-G1-$(OCH_3)_3$ **14bf** in $CDCl_3$



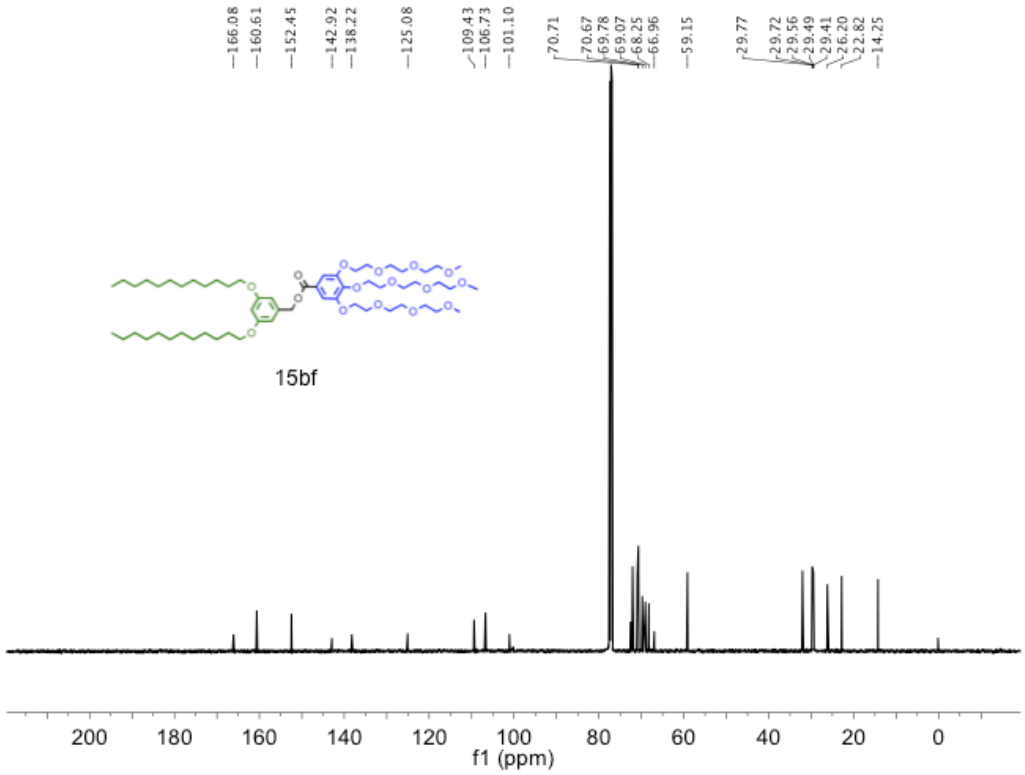


Figure S43. ^{1}H NMR (top, 500 MHz) and ^{13}C NMR (bottom, 126 MHz) spectra of (3,5)12G1-III-Phe-(3,4,5)-3EO-G1-$(OCH_3)_3$ **15bc** in $CDCl_3$

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