Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

for

Bundle-Forming α-Helical Peptide-Dendron Hybrids

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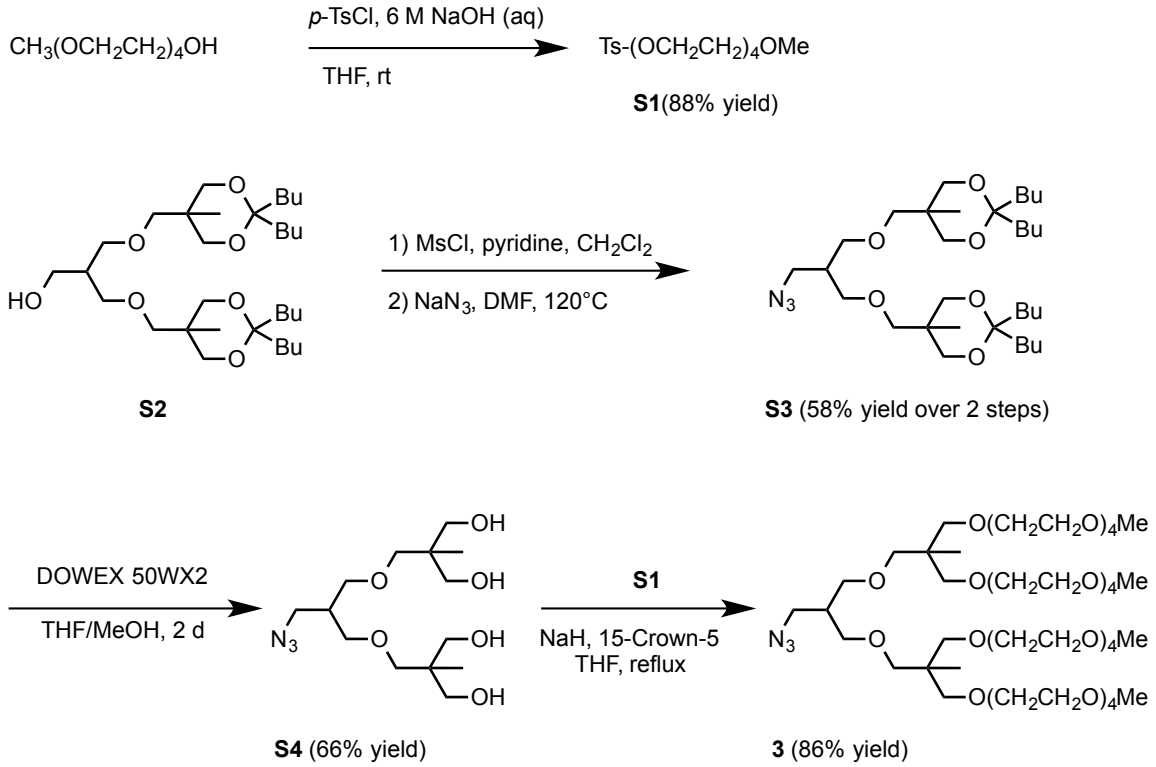
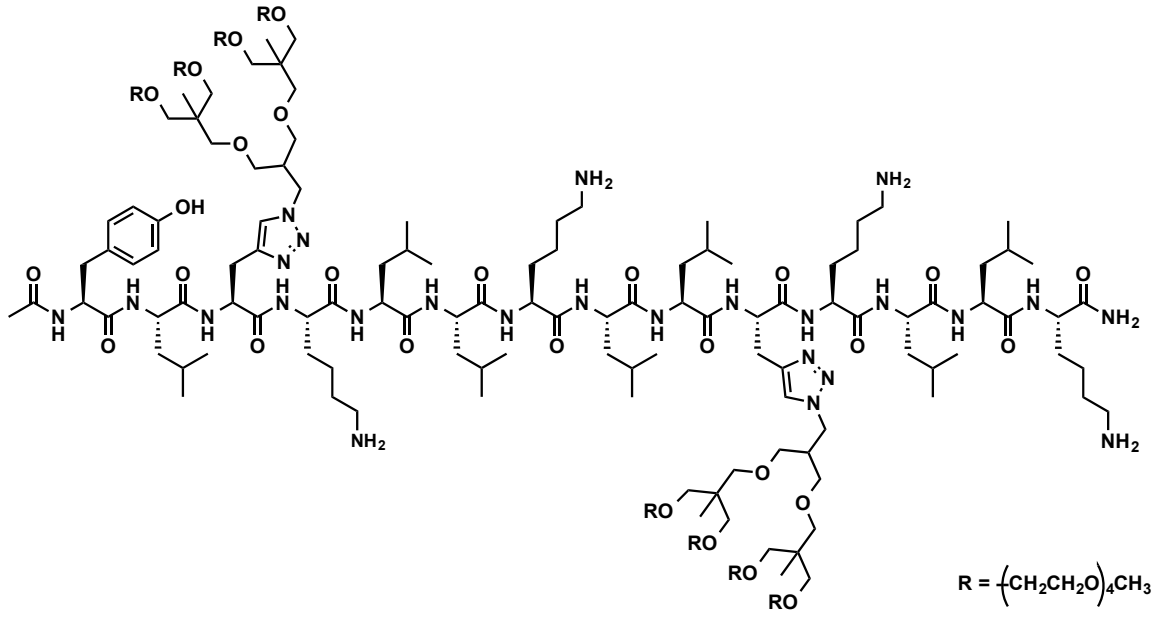
Additional Synthesis Schemes



Scheme S1. Synthesis of dendritic azide **3**.



Scheme S2. Chemical structure of dendron-peptide hybrid **1**.

Additional Discussion of Fig. 3

The MALDI-TOF mass spectrum shown in Fig. 3 supports that we have successfully isolated peptide-dendron hybrid 1 from any residual dendron, starting peptide, or singly dendronized intermediates. We observe three different ionized forms of the conjugate ($[M + X]^+$, X = H, Na, and K). The remaining low-intensity peaks could not be assigned to any reasonable side-reaction products or fragmentations of the conjugate. We see excellent agreement between the observed isotope pattern for the peak assigned as the $[M + H]^+$ ion to the expected isotope pattern for the same ion (Fig. 3 inset). The attributes of the MALDI-TOF mass spectrum emphasize that we have synthesized the desired peptide-dendron hybrid as a monodisperse macromolecule with a completely defined chemical structure.

Experimentals

Materials. Dowex-50W2X hydrogen form (50-100 mesh), sodium hydride, anhydrous dichloromethane, anhydrous tetrahydrofuran (THF), trifluoroacetic acid (TFA), and piperdine were used as received from Aldrich. Anhydrous dimethylformamide (DMF), sodium azide, and Fmoc-Tyr(*t*-Bu)-OH were used as received from EMD. Fmoc-Lys(Boc)-OH, Fmoc-Leu-OH, Fmoc-Pra-OH, *N*-methylmorpholine, and *O*-(benzotriazol-1-yl)-*N*,*N*,*N*',*N*'-tetramethyluroniumhexafluorophosphate (HBTU) were used as received from Chem-Impex International. Ethyl acetate (EtOAc), diethyl ether (Et_2O), sodium hydroxide, sodium bicarbonate, acetonitrile (MeCN), and pyridine were used as received from Fisher. Triisopropylsilane ($^iPr_3SiH$) and copper(II) sulfate pentahydrate ($CuSO_4 \bullet 5H_2O$) were used as received from Acros. Sodium chloride and anhydrous magnesium sulfate were used as received from J. T. Baker. Methanesulfonyl chloride (MsCl), tetraethyleneglycol monomethyl ether, *p*-toluenesulfonyl chloride (*p*-TsCl), L-ascorbic acid sodium salt, and acetic anhydride (Ac_2O) were used as received from Alfa-Aesar. Hexanes (hex), methanol (MeOH), dichloromethane, dimethylsulfoxide (DMSO), and silica gel 60 (60-200 microns) were used as received from BDH. Chloroform-*d* with 0.03% v/v tetramethylsilane ($CDCl_3$) and Dimethylsulfoxide-d_6 (DMSO-d_6) were used as received from Cambridge Isotope Laboratories. H-Rink amide-ChemMatrix resin (0.51 mmol/g) was used as received from PCAS BioMatrix Inc. Isopropyl alcohol was used as received from Pharmaco-Aaper. Potassium chloride was used as received from G-Biosciences. Tris-(hydroxymethyl) aminomethane hydrochloride (Tris HCl) and were 2-Amino-2-(hydroxymethyl)-1,3-propanediol were used as received from Ameresco. Compound **S2** and Ac-YLKKLLKLLKKLLK-NH_2 were prepared according to literature procedures.[1,2]

Techniques. ^1H NMR (400 MHz, 500 MHz, 700 MHz) and ^{13}C NMR (100 MHz, 125 MHz, 175 MHz) spectra were recorded on a Bruker Avance III (400, 500, and 700) NMR spectrometer. Peak multiplicities are denoted as follows: s = singlet, d = doublet, t = triplet, q = quartet, pent = pentet, hept = heptet, sept = septet, and m = multiplet. The MALDI-TOF data were recorded on a Bruker Autoflex II TOF/TOF workstation. MALDI-TOF samples (10 mg/mL) were prepared in MeCN/H_2O with α-cyano-4-hydroxycinnamic acid as the matrix. Equal volumes of the matrix and peptide solutions were mixed and 1 μL of the mixture was injected onto the target plate. Gel permeation chromatography (GPC) in THF (1 mL/min) was performed using a Shimadzu LC-20AD liquid chromatography pump equipped with a DGU-20A5 degasser, CBM-20A controller, RID-10A RI detector, CTO-20A column oven (all from Shimadzu), and three American Polymer Standards AM GPC gel columns of 100 Å (5 μm), 500 Å (5 μm), and 10,000 Å (5 μm). Relative molecular weights and molecular weight distributions were determined according to a calibration with narrow polydispersity polystyrene standards (American Polymer Standards). Thin layer chromatography (TLC) was performed using Whatman silica gel 60 Å plates (250 μm) with fluorescent indicator and visualized using a UV lamp (254 nm) or $KMnO_4$ stain. Flash column chromatography was performed on a Teledyne Isco CombiFlash Rf with RedSep Rf Normal Phase disposable silica columns. Low-resolution electrospray mass spectrometry (ESI–MS) were acquired in positive polarity mode on an Agilent LC-MSD with an 1100 HPLC and a G1956A single-quadrupole mass spectrometer (accuracy ±0.1 amu). High-resolution electrospray ionization mass spectra (HRMS–ESI) were acquired by the Mass Spectrometry Laboratory at the University of Illinois at Urbana-Champaign on a Micromass Q-Tof Ultima. Peptides were synthesized using 9-fluorenylmethoxycarbonyl (Fmoc) chemistry on a Protein Technologies PS3 peptide synthesizer. Peptides were cleaved from the resin using a TFA/$^iPr_3SiH$/H_2O (95:2.5:2.5 v/v/v; 10 mL). High-performance liquid chromatography (HPLC) was performed on a Waters 1525 Binary pump equipped with a Waters 2489 UV/Visible Detector set at 210 nm

and 280 nm. To determine the analytical purity of samples, the HPLC was equipped with a SunFire^{TM} C18 column (5 μm, 4.6 mm × 250 mm; Waters) operating at a flow rate of 1 mL/min and a solvent gradient of 1%/min. Purification of samples was done on the HPLC equipped with a SunFire^{TM} C18 (5 μm, 19 mm × 250 mm) column operating at a flow rate of 17 mL/min and a solvent gradient of 5%/min. Absorbance of peptide solutions in deionized water at 280 nm was recorded on an Evolution 201 spectrophotometer using a 1-cm quartz cuvette. The concentration of the peptide was calculated from the absorbance using Beer's Law and an extinction coefficient (e) for tyrosine of 1490 L mol^{-1} cm^{-1}.[3] Circular dichroism (CD) spectra were performed on an Applied Photophysics Chirascan instrument.

Peptide Concentration CD Experiments. The samples for the peptide concentration CD experiments were made by serial dilution of peptide-dendron hybrid **1** (500 μM) with 20 mM Tris buffer (pH 7.3) were vortexed to allow for mixing. The 500 μM, 250 μM, 125 μM were measured in a 10-mm quartz cuvette and the 50 μM, 25 μM, 10 μM, 5 μM, 2.5 μM were measured in a 1-mm quartz cuvette.

Salt Titration CD Experiments. The salt titration CD experiments were performed using a 1-mm quartz cuvette to aquire CD spectra with Cl^- concentrations of: 1 M, 0.75 M, 0.5 M, 0.3 M, 0.2 M, and 0.1 M solutions after they had been vortexed to allow appropriate mixing. Two equimolar (500 μM) peptide solutions with initial concentrations of 1M Cl^- and 0.015 M Cl^- were mixed together using a vortex to form solution with a final concentration of 0.75 M and 0.1 M Cl^-. The 0.75 M solution and 0.1 M solution were mixed together using a vortex to form solution with a final concentration of 0.50 M and 0.2 M. The 0.5 M and 0.2 M solutions were mixed together using a vortex to form a final concentration of 0.3M Cl^-.

General Solid-Phase Peptide Synthesis Procedures. Single Coupling Protocol. The resin was washed three times for 30 seconds with DMF (15 mL/g). The N-terminus was deprotected using a 8:2 DMF/piperdine solution (15 mL/g) two times for 5 minutes. The resin was then washed six times using DMF (15 mL/g) for 30 seconds each time. The Fmoc-protected amino acid and HBTU was dissolved in a 0.2 M NMM. The solution was then transferred to the peptide reaction vessel containing the swelled resin and was further diluted with DMF to a concentration achieve a final concentration of Fmoc-protected amino acid (0.22 M) and HBTU (0.21 M). The coupling was done for 20 minutes. The resin was then washed three times for 30 seconds each time

General Solid-Phase Peptide Synthesis Procedures. Double Coupling Protocol. The resin was washed three times for 30 seconds with DMF. The N-terminus was deprotected using a 8:2 DMF/piperdine solution two times for 5 minutes. The resin was then washed six times using DMF for 30 seconds each time. The Fmoc-protected amino acid (0.50 M) and HBTU (0.48 M) was dissolved in 0.2 M NMM. The solution was then transferred to the peptide reaction vessel containing the swelled resin and was further diluted with DMF to a concentration achieve a final concentration of Fmoc-protected amino acid (0.22 M) and HBTU (0.21 M). The coupling was done for 20 minutes. The resin was drained and Fmoc-protected amino acid (0.52 M) and HBTU (0.48 M) was dissolved in 0.2 M NMM. The solution was then transferred to the peptide reaction vessel and was further diluted with DMF to a concentration achieve a final concentration of Fmoc-protected amino acid (0.22 M) and HBTU (0.21 M). The coupling was done for 20 minutes after which the resin was then washed three times with DMF (3 mL) for 30 seconds each time.

***N*$^{\alpha}$-Fmoc Deprotection Protocol.** The resin was washed three times for 30 seconds using DMF (15 mL/g). The N-terminus was then deprotected using a stock solution of 20% (v/v) piperdine in DMF two times for five minutes each time. The resin was then washed six times for 30 seconds each time.

Protocol for Capping and Acetylation of the *N*-Terminus. The resin was washed six times for 30 seconds using DMF. A vial containing acetic anhydride (2 mL) was diluted with a 0.2 M NMM solution (2 mL) the solution was then transferred to the reaction vessel and further diluted with DMF (2.5 mL). The solution in the reaction vessel was mixed for 5 minutes. The resin was then washed three times with DMF (15 mL/g) for 30 seconds each time.

Cleavage and Side-Chain Deprotection. To the resin, a mixture of TFA/$^{i}Pr_3SiH/H_2O$ (95:2.5:2.5 v/v/v; 10 mL) was added. The reaction mixture was agitated for 1 h. The liquids were separated from the resin and collected by forcing the liquid phase through the peptide reaction vessel frit by positive pressure displacement with N_2. The resin was washed with TFA/$^{i}Pr_3SiH/H_2O$ (95:2.5:2.5 v/v/v; 2 mL) and the liquids were separated from the resin and collected by positive pressure displacement with N_2. The volume

of the collected liquids was reduced under a stream of N_2. The mixture was precipitated into cold Et_2O. The solids were separated from the liquids by centrifugation (Thermo Scientific CL10) at 3500 rpm for 5 min, and the solids were isolated by decanting the supernatant liquid. The crude peptide was precipitated from TFA into cold Et_2O two more times. The solid pellet was dissolved in H_2O and lyophilized. The peptide was purified by preparative HPLC on a C18 reversed-phase column.

Assembly of Ac-YLXKLLKLLXKLLK-NH_2 X = propargyl glycine (2). Peptide **2** was assembled on ChemMatrix Rink amide resin (0.10 mmol, 0.2288 g) in a glass-fritted peptide reaction vessel using a PS3 synthesizer and cleaved from the resin to yield peptide **1**. The sequence of operations is detailed in the table below: **Table S1**. Protocol for the synthesis of Ac-YLXKLLKLLXKLLK-NH_2 X = propargyl glycine(**2**).

		Mass of Reagents (g)	
Cycle		Fmoc-AA-OH	HBTU
1	Single Coupling: Fmoc-Lys(Boc)-OH	0.4714	0.3596
	Capping		
	N^{α}-Fmoc Deprotection		
2	Single Coupling: Fmoc-Leu-OH	0.3531	0.3543
	Capping		
	N^{α}-Fmoc Deprotection		
3	Single Coupling: Fmoc-Leu-OH	0.3531	0.3513
	Capping		
	N^{α}-Fmoc Deprotection		
4	Single Coupling: Fmoc-Lys(Boc)-OH	0.4634	0.3578
	Capping		
	N^{α}-Fmoc Deprotection		
5	Single Coupling: Fmoc-Pra-OH	0.3380	0.3556
	Capping		
	N^{α}-Fmoc Deprotection		
6	Singe Coupling: Fmoc-Leu-OH	0.3566	0.3543
	Capping		
	N^{α}-Fmoc Deprotection		
7	Single Coupling: Fmoc-Leu-OH	0.3542	0.3539
	Capping		
	N^{α}-Fmoc Deprotection		
8	Single Coupling: Fmoc-Lys(Boc)-OH	0.4735	0.3552
	Capping		
	N^{α}-Fmoc Deprotection		
9	Single Coupling: Fmoc-Leu-OH	0.3552	0.3545
	Capping		
	N^{α}-Fmoc Deprotection		
10	Double Coupling: Fmoc-Leu-OH	0.3526	0.3530
		0.3567	0.3518
	Capping		
	N^{α}-Fmoc Deprotection		
11	Single Coupling: Fmoc-Lys(Boc)-OH	0.4699	0.3538
	Capping		
	N^{α}-Fmoc Deprotection		
12	Single Coupling: Fmoc-Pra-OH	0.3394	0.3551
	Capping		
	N^{α}-Fmoc Deprotection		
13	Single Coupling: Fmoc-Leu-OH	0.3567	0.3508

	Capping		
	N^{α}-Fmoc Deprotection		
14	Single Coupling: Fmoc-Tyr(t-Bu)-OH	0.4598	0.3543
	N^{α}-Fmoc Deprotection		
	Acetylation of the *N*-terminus		
	Cleavage and Side-Chain Deprotection		

2,2-Bis[(2,2-dibutyl-5-methyl-1,3-dioxan-5-yl)methoxy]ethyl azide (S3)

A solution of **S2** (4.00 g, 7.16 mmol), MsCl (1.66 mL, 21.5 mmol), and pyridine (1.71 mL, 21.5 mmol) in anhydrous CH_2Cl_2 (29 mL) was stirred for 21 h at room temperature under a N_2 atmosphere. The reaction mixture was washed with saturated $NaHCO_3$ (aq) solution. The organic layer was washed once with saturated NaCl (aq) solution, and dried over $MgSO_4$. The solids were removed by filtration and the solvent was removed from the filtrate *in vacuo*. To a solution of crude oil in anhydrous DMF (28 mL), and NaN_3 (2.33 g, 35.8 mmol) were added to the mixture. The mixture was heated at 120 °C in an oil bath under N_2 atmosphere for 41 h. The mixture was cooled to room temperature. The solids were removed by filtration and the solvent was removed from the filtrate *in vacuo*. The resulting oil was purified by flash column chromatography (SiO_2, hex to 9:1 hex:EtOAc) to yield **S3** as a colorless oil (2.44 g, 58 %). TLC (SiO_2, hex/EtOAc = 9:1): R_f = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 3.63 (m, 4H; CH_3CCH_2O), 3.50 (d, J = 11.5 Hz, 4H; CCH_2OC), 3.45 (overlapping m, 4H; CCH_2OC), 3.39 (m, 6H; $CHCH_2O$, CH_2N_3), 2.14 (m, 1H; $CHCH_2O$), 1.73 (m, 4H; CCH_2), 1.62 (m, 4H; CCH_2), 1.33 (m, 16H; $CCH_2CH_2CH_2CH_3$), 0.93 (t, J = 3.4 Hz, 6H, $CCH_2CH_2CH_2CH_3$), 0.90 (t, J = 3.4 Hz, 6H, $CCH_2CH_2CH_2CH_3$), 0.88 (s, 6H; CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 100.8 (CO_2), 74.4 (CH_3CCH_2OC), 69.9 ($CHCH_2$), 66.1 ($CH_3CCH_2OCH_2$), 50.7 (CH_2N_3), 40.3 (CCH_3), 36.1 ($CHCH_2$), 34.5 ($CCH_2CH_2CH_2CH_3$), 31.1 ($CCH_2CH_2CH_2CH_3$), 25.9 ($CCH_2CH_2CH_2CH_3$), 25.3 ($CCH_2CH_2CH_2CH_3$), 23.3 ($CCH_2CH_2CH_2CH_3$), 23.3 ($CCH_2CH_2CH_2CH_3$), 18.6 (CCH_3), 14.3 (CH_2CH_3). HRMS–ESI (*m/z*): [M + H]+ calcd for $C_{32}H_{62}N_3O_6$, 584.4639; found, 584.4644. GPC: M_n = 570, M_w/M_n= 1.06.

2,2-Bis[2,2-di(hydroxymethyl)propyloxymethyl]ethyl azide (S4)

To a solution of **S3** (2.44 g, 4.18 mmol) in 1:1 (v/v) THF/MeOH (20 mL), Dowex-50W acidic resin beads (42.01 g) were added. The mixture was stirred at room temperature under a N_2 atmosphere for 3 days. The resin was removed by filtration and the solvent was removed from the filtrate *in vacuo*. The resulting product was purified by flash column chromatorgraphy (SiO_2, CH_2Cl_2 to 9:1 CH_2Cl_2/MeOH) to yield **S4** as a colorless soild (0.89 g, 66 %). TLC (SiO_2, CH_2Cl_2/MeOH = 9:1): R_f = 0.23. ^{1}H NMR (500 MHz, DMSO-d_6, δ): 4.28 (t, J = 5.3 Hz, 4H, CH_2CCH_3), 3.38 (d, J = 5.9 Hz, 2H; CH_2N_3), 3.32 (m, 4H; OH), 3.24 (d, 8H; CH_2OH), 3.18 (q, J = 8.1 Hz, 4H; $CHCH_2$), 2.05 (m, 1H; $CHCH_2O$), 0.76 (s, 6H; CCH_3). ^{13}C NMR (125 MHz, DMSO-d_6, δ): 73.4 ($CH_3CCH_2OCH_2$), 69.2 ($CHCH_2O$), 63.9 (CH_2OH), 50.0 (CH_2N_3), 41.5 (CCH_3), 16.8 (CCH_3). HRMS–ESI (*m/z*): [M + H]+ calcd for $C_{14}H_{30}N_3O_6$, 336.2135; found, 336.2131. GPC: M_n = 300, M_w/M_n = 1.08.

2-(2-[2-(2-Methoxyethoxy)ethoxy]ethoxy)ethyl tosylate (S1) [1, 2]

To an ice-water bath-cooled solution of tetraethylene glycol monomethyl ether (1.61 mL, 8.28 mmol) in THF (2.9 mL), 6 M NaOH (aq) solution (2.6 mL) was added dropwise. To this mixture *p*-TsCl (2.93 g, 15.4 mmol) was added. The mixture was stirred at room temperature under N_2 atmosphere for 20 h. The reaction mixture was diluted with H_2O (10 mL) and the product was extracted three times with CH_2Cl_2 (10 mL). The organic layer was washed once with saturated NaCl (aq) solution, and dried over $MgSO_4$. The solids were removed by filtration and the solvent was removed from the filtrate *in vacuo*. The resulting oil was purified by flash column chromatography (SiO_2, CH_2Cl_2 to 19:1 CH_2Cl_2/MeOH) to yield **S1** as a colorless oil (2.64 g, 88 %). TLC (SiO_2, hex/EtOAc = 9:1): R_f = 0.32. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.78 (d, J = 8.3 Hz, 2H; $SCCH$), 7.33 (d, J = 8.0 Hz, 2H; CH_3CCH), 4.15 (t, J = 5.0 Hz, 2H; $SOCH_2$), 3.68 (t, J = 4.9 Hz, 2H; $SOCH_2CH_2$), 3.63 (t, J = 4.6 Hz, 6H; $SOCH_2CH_2OCH_2$ CH_2OCH_2), 3.58 (apparent s, 4H; $CH_2OCH_2CH_2OCH_3$), 3.54 (m, 2H; CH_2OCH_3), 3.37 (s, 3H; CH_3CCH), 2.44 (s, 3H; CH_2OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 144.8 ($SCCH$), 133.0 (CH_3CCH), 129.8 ($SCCH$), 128.0 (CH_3CCH), 71.9 ($SOCH_2$), 70.7 ($SOCH_2CH_2$), 70.6 ($SOCH_2CH_2OCH_2$), 70.6 ($SOCH_2CH_2OCH_2CH_2$), 70.5 ($CH_2CH_2OCH_2CH_2OCH_3$), 70.5 ($CH_2CH_2OCH_2CH_2OCH_3$), 69.2 ($CH_2CH_2OCH_3$), 68.7 ($CH_2CH_2OCH_3$), 59.0 (OCH_3), 21.7 (CH_3CCH). ESI–MS (*m/z*): $[M + NH_4]^+$ calcd for $C_{16}H_{30}O_7NS$, 380.2; found, 380.1. Spectral data agree with those previously reported.[5, 6]

2,2-Bis(2,2-di[2-(2-[2-(2-methoxyethoxy)ethoxy]ethoxy)ethoxymethyl]propyloxymethyl)ethyl azide (3)

To an ice-water bath-cooled solution of **S4** (0.20 g, 0.60 mmol) in anhydrous THF (6 mL), NaH (0.10 g, 4.2 mmol) (Caution! The addition of NaH to solutions of alcohol is exothermic) and **S1** (1.09 g, 3.01 mmol) were added. The mixture was heated to reflux in an oil bath under N_2 atmosphere for 18 h. The mixture was cooled in an ice-water bath. The reaction mixture was quenched with deionized water. The product was extracted three times with CH_2Cl_2 (10 mL). The organic washings were combined, washed once with saturated NaCl (aq) solution and dried over anhydrous $MgSO_4$. The solid was removed by filtration and the solvent was removed from the filtrate *in vacuo*. The resulting oil was purified by flash chromatography (SiO_2, CH_2Cl_2 to 9:1 CH_2Cl_2/MeOH) to yield **3** as a colorless liquid (0.58 g, 86 %). TLC (SiO_2, CH_2Cl_2/MeOH = 9:1): R_f = 0.51. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 3.65-3.69 (m, 48H; $CH_2O(CH_2CH_2O)_3CH_2CH_2OCH_3$), 3.54 (m, 16H; $CH_2O(CH_2CH_2O)_3CH_2CH_2OCH_3$), 3.37 (s, 12H; $CH_2CH_2OCH_3$), 3.34-3.29 (m, 14H, CH_3CCH_2, CH_2N_3), 3.23 (t, J = 9.3 Hz, 4H; $CHCH_2$), 2.10 (m, 1H; $CHCH_2O$), 0.91 (s, 6H; CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 74.1 ($CH_3CCH_2OCH_2CH$), 72.1 ($CH_3CCH_2OCH_2CH_2$), 71.2 ($CCH_2O(CH_2CH_2O)_4CH_3$), 70.86 ($CCH_2O(CH_2CH_2O)_4CH_3$), 70.82 ($CCH_2O(CH_2CH_2O)_4CH_3$), 70.79 ($CCH_2O(CH_2CH_2O)_4CH_3$), 70.73 ($CCH_2O(CH_2CH_2O)_4CH_3$), 70.6 ($CCH_2O(CH_2CH_2O)_4CH_3$), 69.8 ($CHCH_2O$), 59.3 (OCH_3), 50.6 (CH_2N_3), 41.2 (CCH_3), 40.2 ($CHCH_2O$), 17.6 (CCH_3). HRMS–ESI (m/z): [M + H]+ calcd for $C_{50}H_{102}N_3O_{22}$, 1096.6955; found, 1096.6965. GPC: M_n =1,100, M_w/M_n=1.08.

Peptide-Dendron Hybrid (1)

Dendritic azide **3** (33.1 mg, 0.0302 mmol) was dissolved in 600 μL H_2O and transferred to a vial containing peptide **2** (20.0 mg, 0.012 mmol), $CuSO_4{\cdot}5H_2O$ (1.2 mg, 0.0048 mmol), sodium ascorbate (4.1 mg, 0.021 mmol) in 600 μL of DMSO. The reaction mixture was agitated at room temperature under a N_2 atmosphere for 22 h. The reaction mixture was purified by preparative HPLC on a C18 reversed-phase column by gradient elution using a H_2O/MeCN mobile phase containing 0.1% TFA. The resulting oil yielded peptide dendron hybrid **1** (12.5 mg, 27 %). ^{1}H NMR (700 MHz, DMSO-d_6, δ): 8.43 (s, 1H), 8.16 (s, 1 H), 8.09 (s, 1H), 7.98 (s, 1 H), 7.92 (s, 1H), 7.87 (s, 2H), 7.85 (s, 1H), 7.78 (s, 1H), 7.70 (s, 7H), 7.65 (s, 3H), 7.62 (s, 1H), 7.47 (m, 1 H), 7.38 (m, 1 H), 7.29 (m, 1 H), 7.21 (m, 1 H), 7.05 (s, 1 H), 6.99 (d, 2H), 6.65 (d, 2H), 4.34 (m, 2 H), 4.20 (s, 2 H), 4.10-3.87 (m, 6 H), 3.47-3.44 (m, 105 H), 3.39 (m, 15 H), 3.20 (m, 38 H), 3.15 (m, 9 H), 2.85 (m, 1 H), 2.73 (m, 6 H), 2.60 (m, 1 H), 2.34 (m, 1 H), 2.04 (m, 1 H), 1.94 (s, 2 H), 1.72-1.27 (m, 34 H), 0.83 (m, 48 H). ^{13}C NMR (175 MHz, $CDCl_3$, δ): 173.4, 173.0, 173.0, 172.6, 172.6, 172.5, 172.9, 172.2, 171.9, 171.8, 171.74, 171.74, 171.7, 171.2, 170.3, 158.3, 158.1, 157.9, 157.8, 155.9, 142.9, 130.0, 127.9, 125.4, 123.5, 118.2, 116.5, 114.9, 73.3, 73.1, 71.3, 70.5, 69.9, 69.85, 69.84, 69.82, 69.6, 68.7, 68.6, 58.1, 52.2, 48.3, 40.6, 36.2, 31.2, 30.6, 30.6, 26.8, 26.8, 26.72, 26.66, 24.1, 24.09, 24.1, 23.96, 23.19, 23.04, 23.02, 22.98, 22.9, 22.8, 22.7, 22.5, 22.3, 22.25, 22.2, 21.7, 21.6, 21.4, 21.3, 21.3, 21.2, 17.3.

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Chromatograms and Mass Spectra

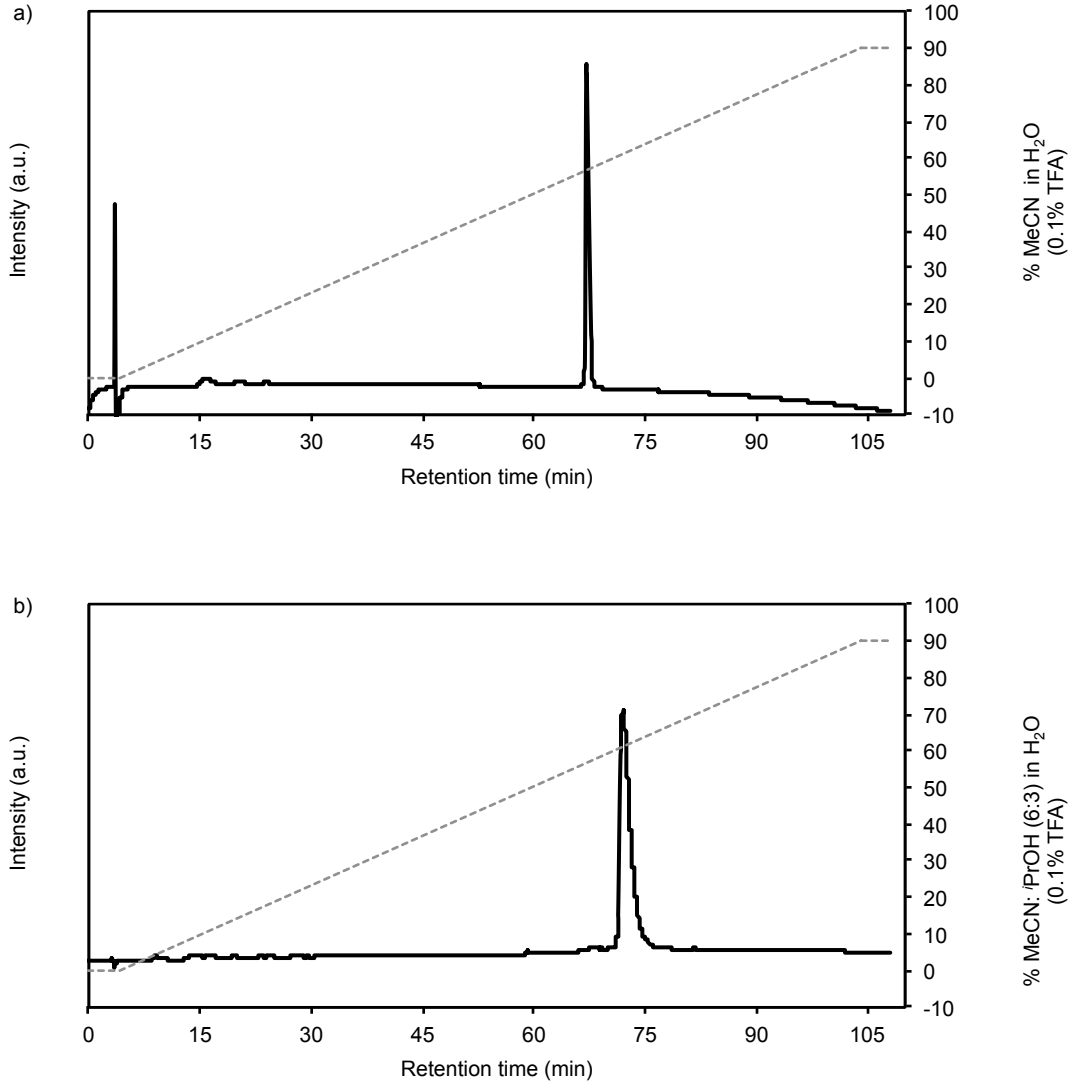


Figure S1. Chromatograms of peptide **2** (solid line) eluted with solvent A = H_2O + 0.1% TFA and a) solvent B = MeCN/H_2O (9:1 v/v) + 0.1% TFA and b) solvent B = MeCN/^{i}PrOH/H_2O (6:3:1 v/v/v) + 0.1% TFA). The dashed line indicates the solvent composition during elution of the peptide at 1 mL/min from a C18 column.

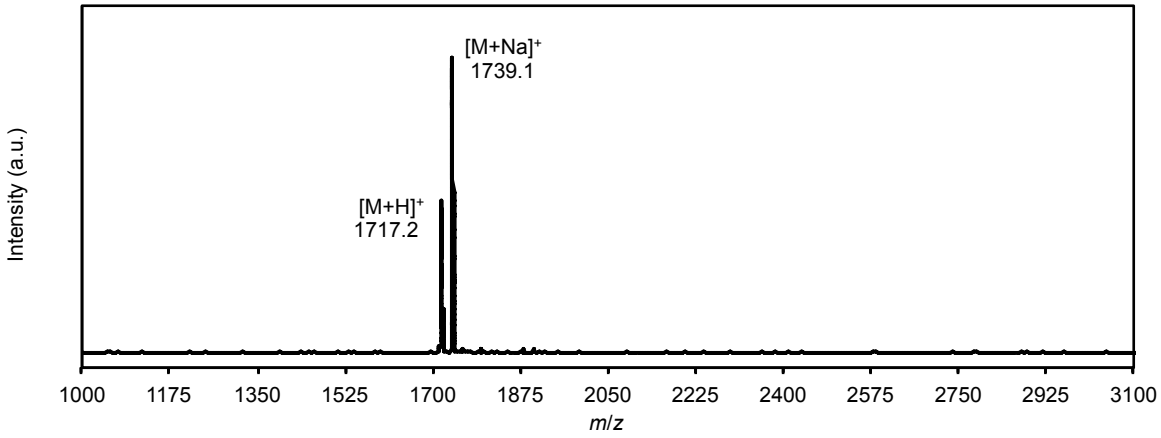


Figure S2. MALDI-TOF Mass spectrum of peptide **2**.

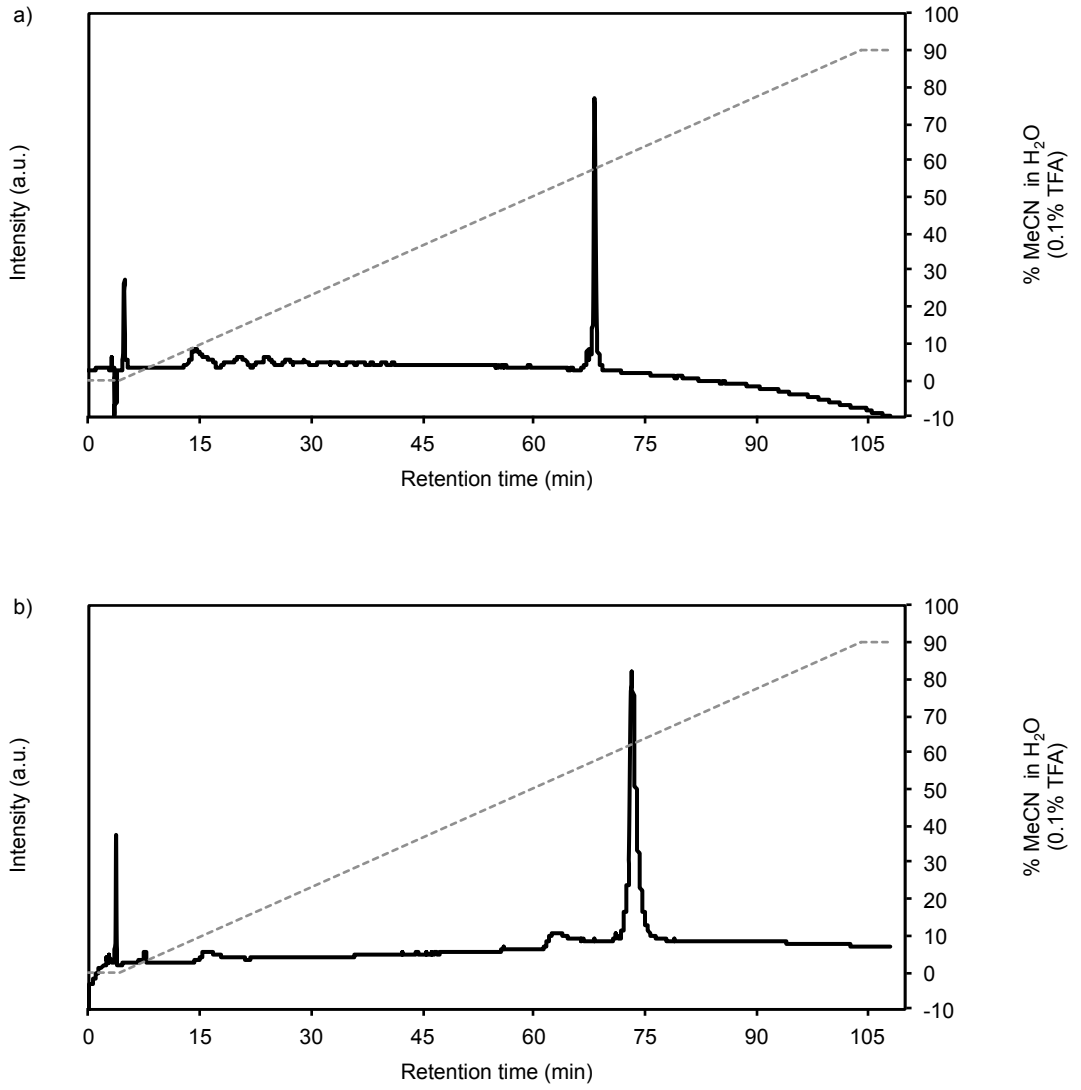
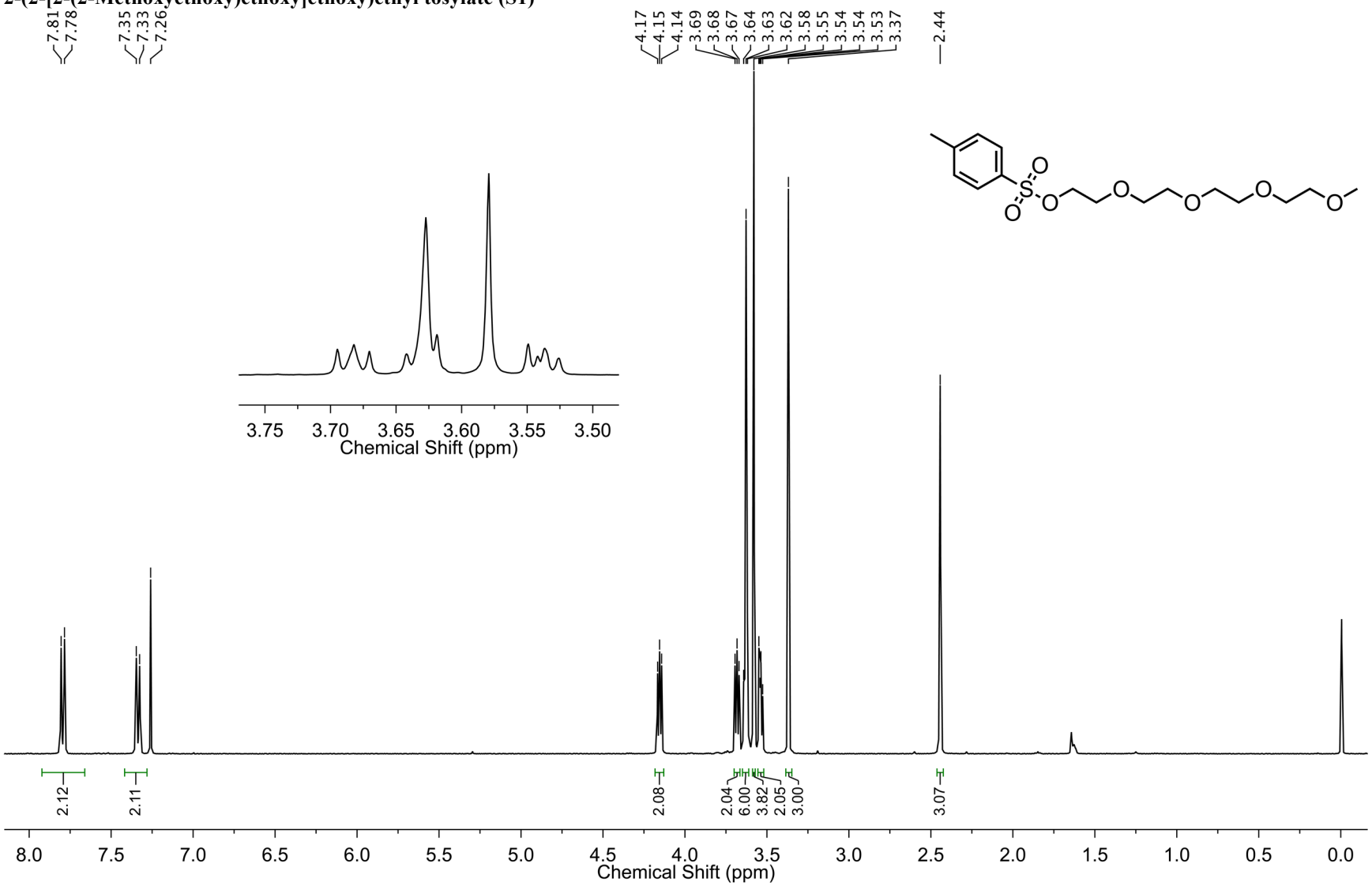
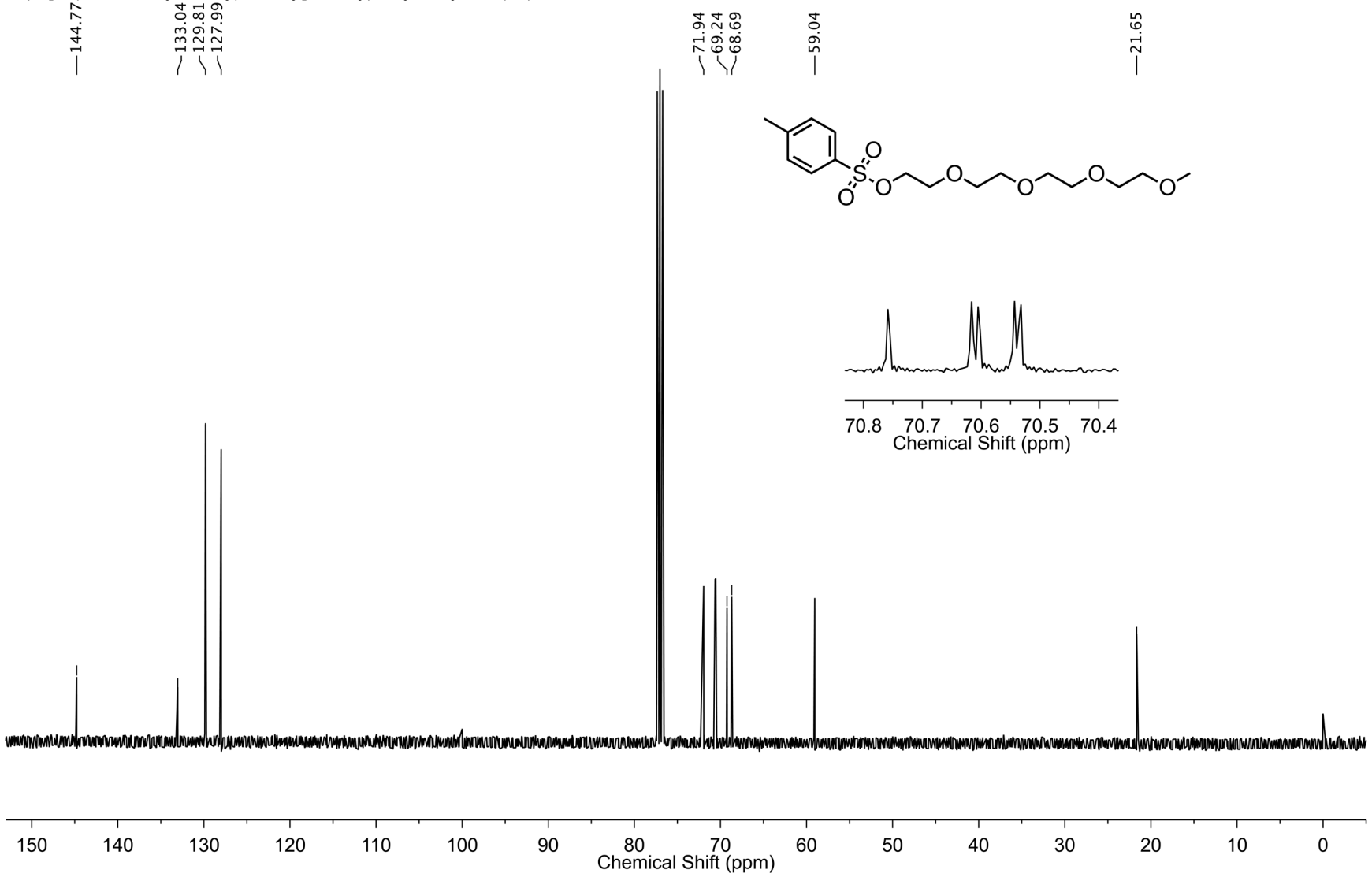


Figure S3. Chromatograms of dendron peptide conjugate **1** (solid line) eluted with solvent A = H_2O + 0.1% TFA and a) solvent B = MeCN/H_2O (9:1 v/v) + 0.1% TFA and b) solvent B = MeOH/H_2O (9:1 v/v) + 0.1% TFA. The dashed line indicates the solvent composition during elution of the peptide at 1 mL/min from a C18 column.

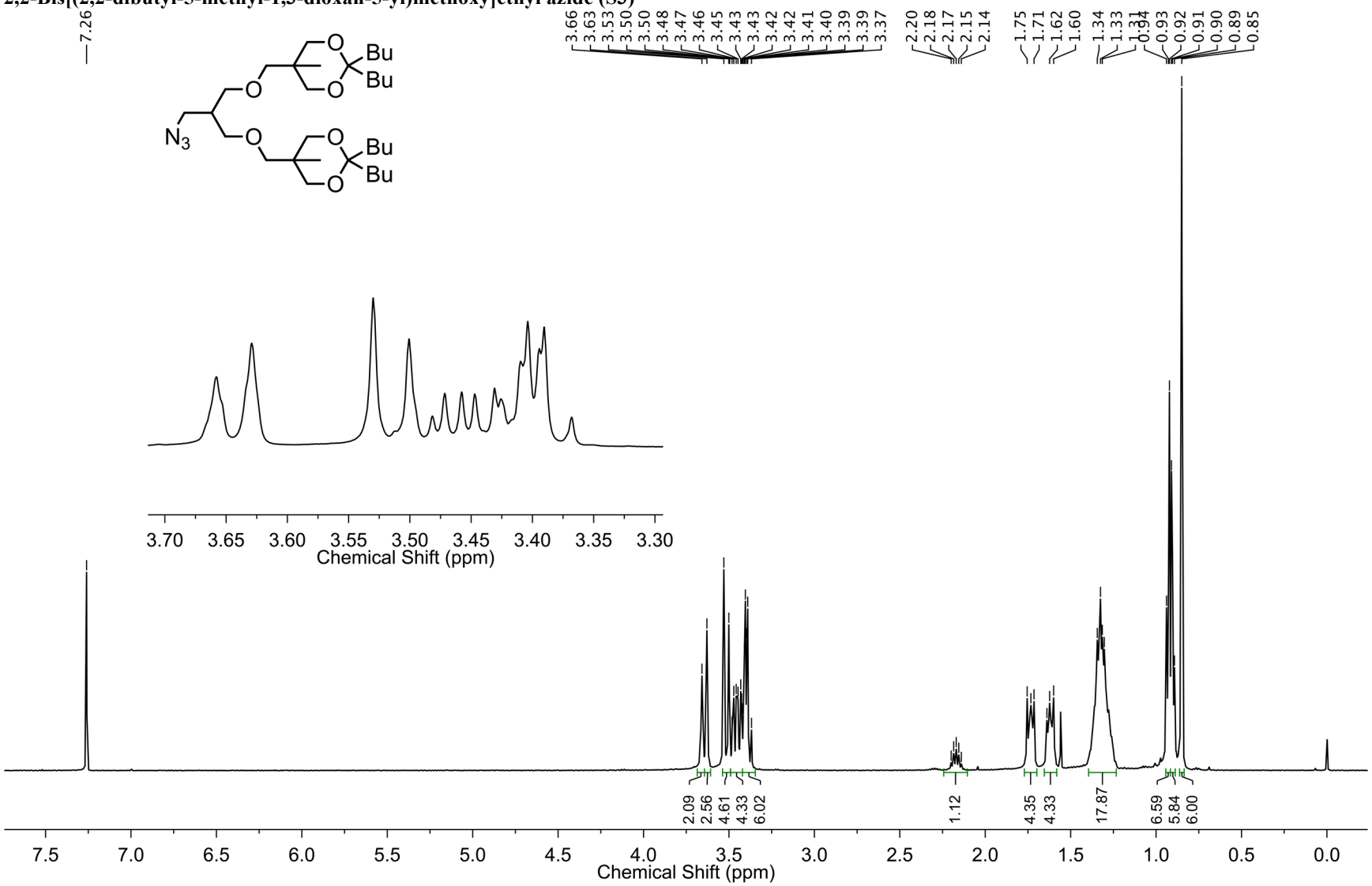
2-(2-[2-(2-Methoxyethoxy)ethoxy]ethoxy)ethyl tosylate (S1)



2-(2-[2-(2-Methoxyethoxy)ethoxy]ethoxy)ethyl tosylate (S1)



2,2-Bis[(2,2-dibutyl-5-methyl-1,3-dioxan-5-yl)methoxy]ethyl azide (S3)



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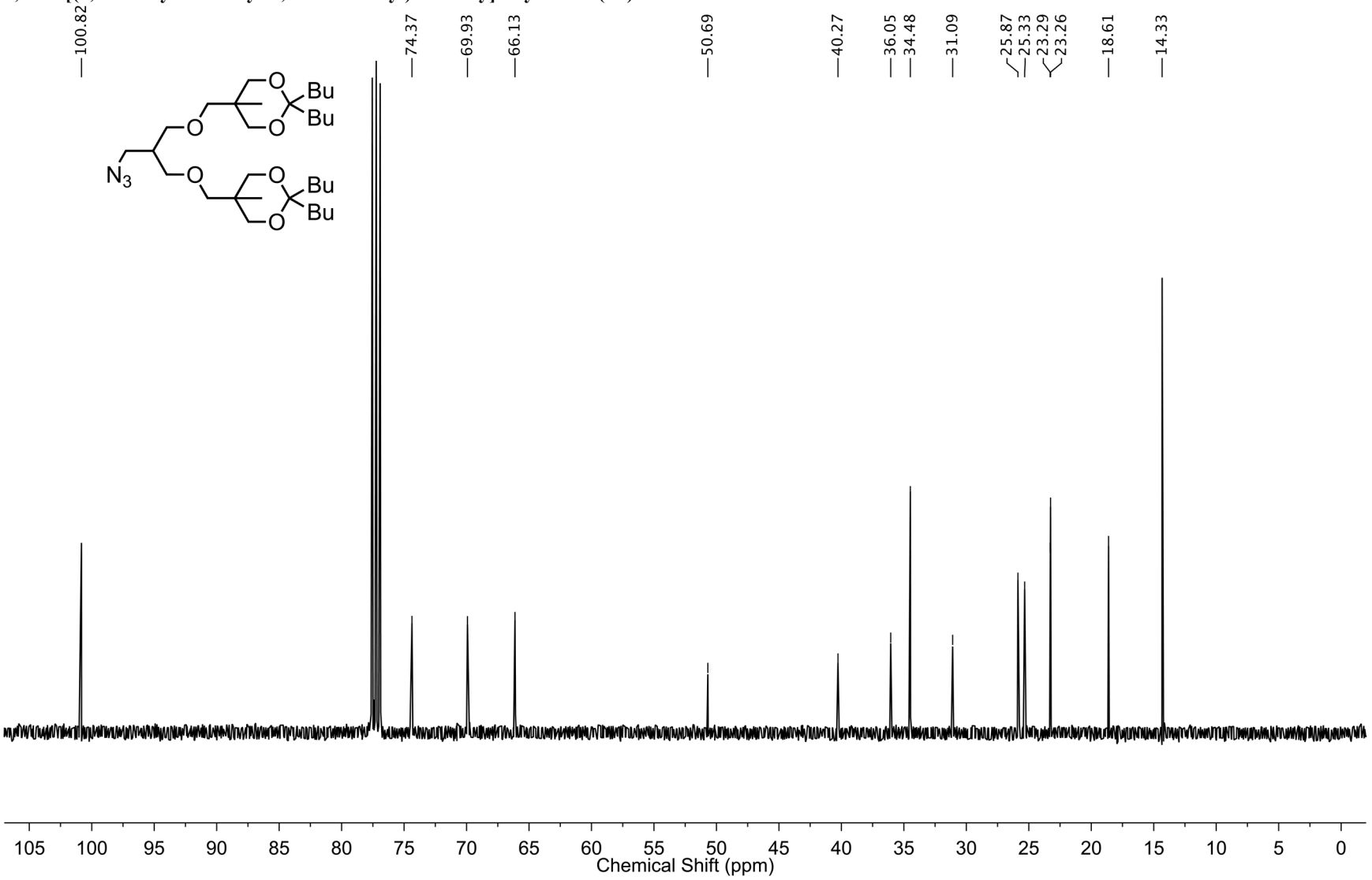
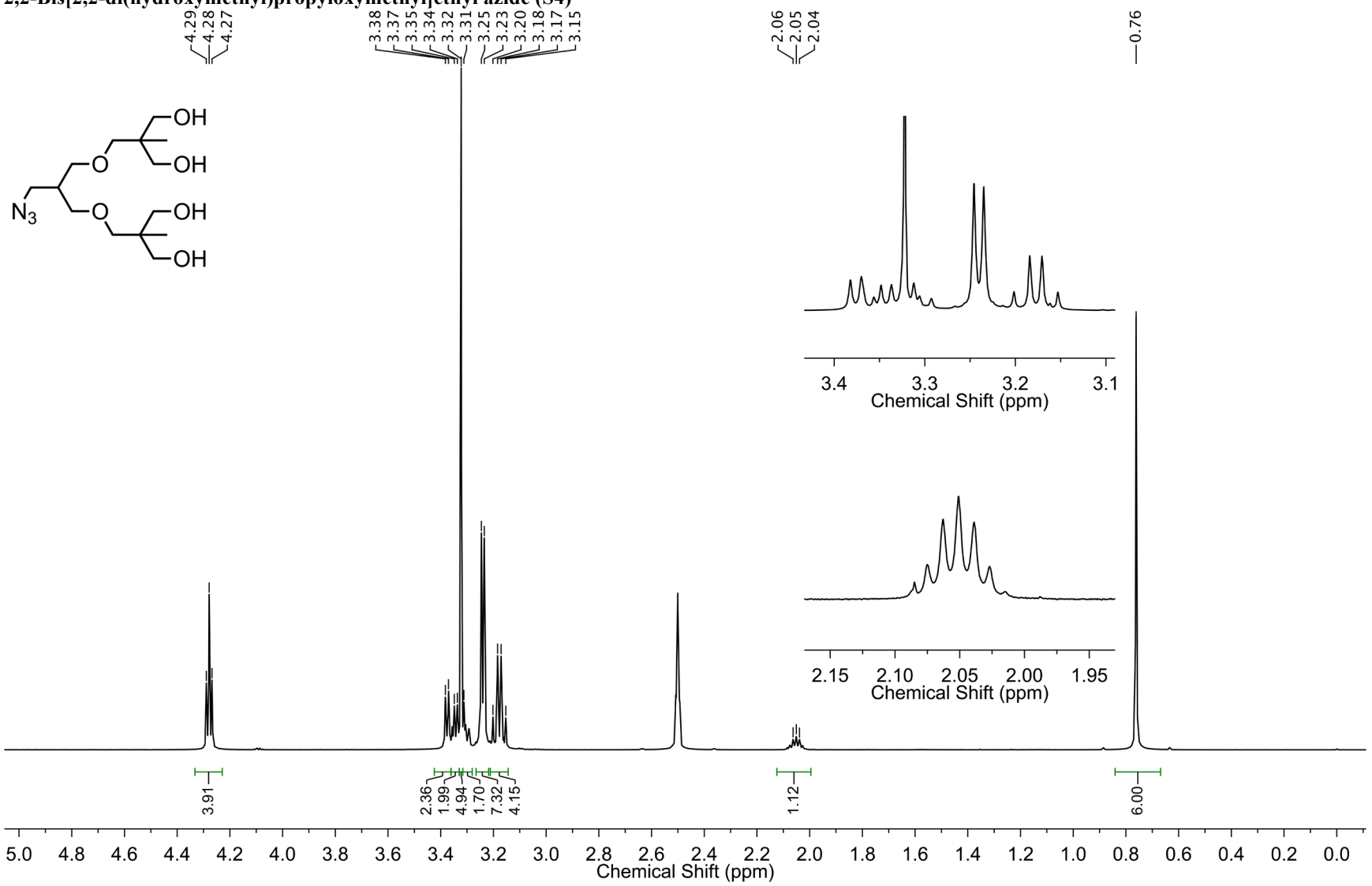
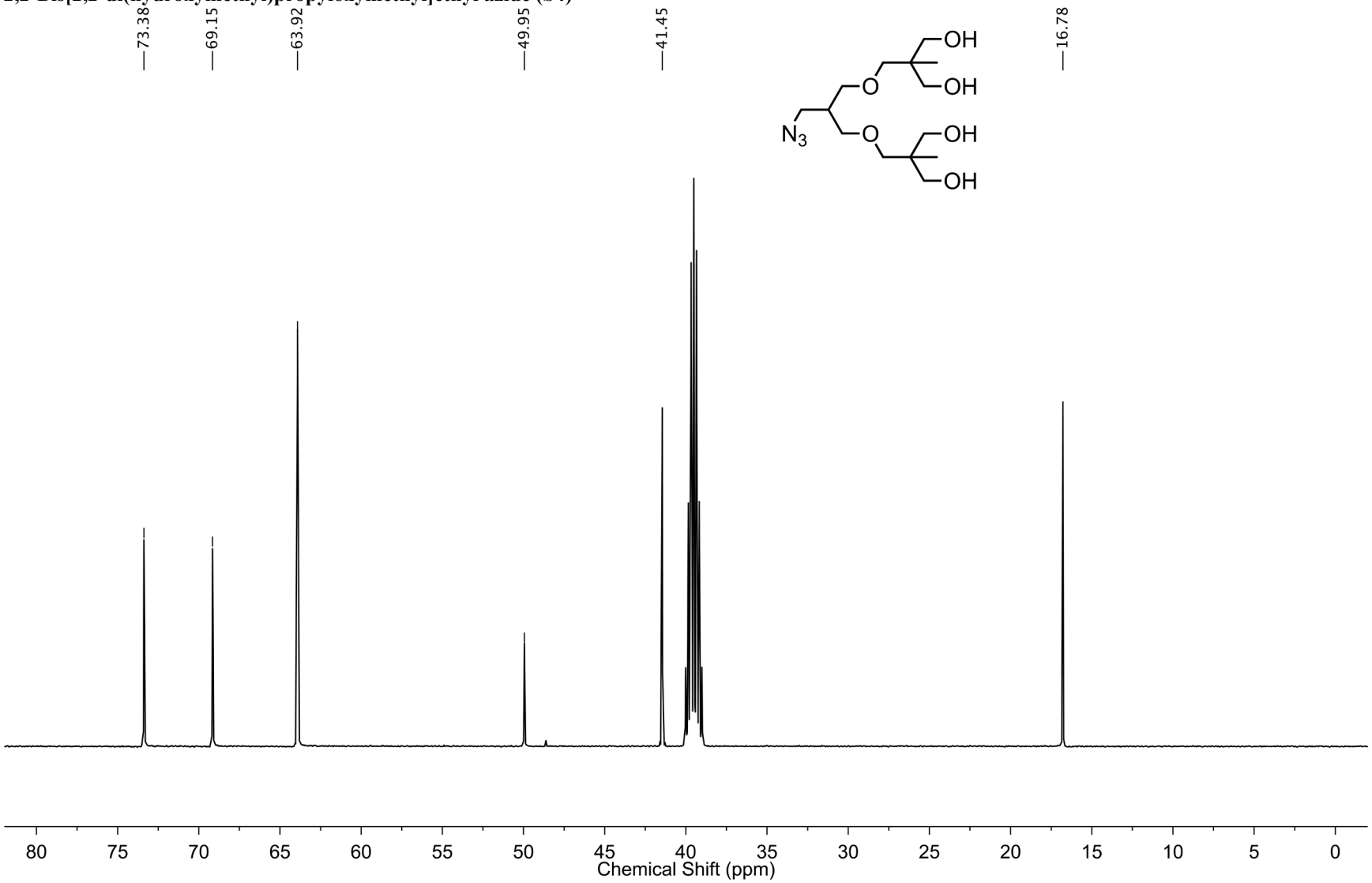


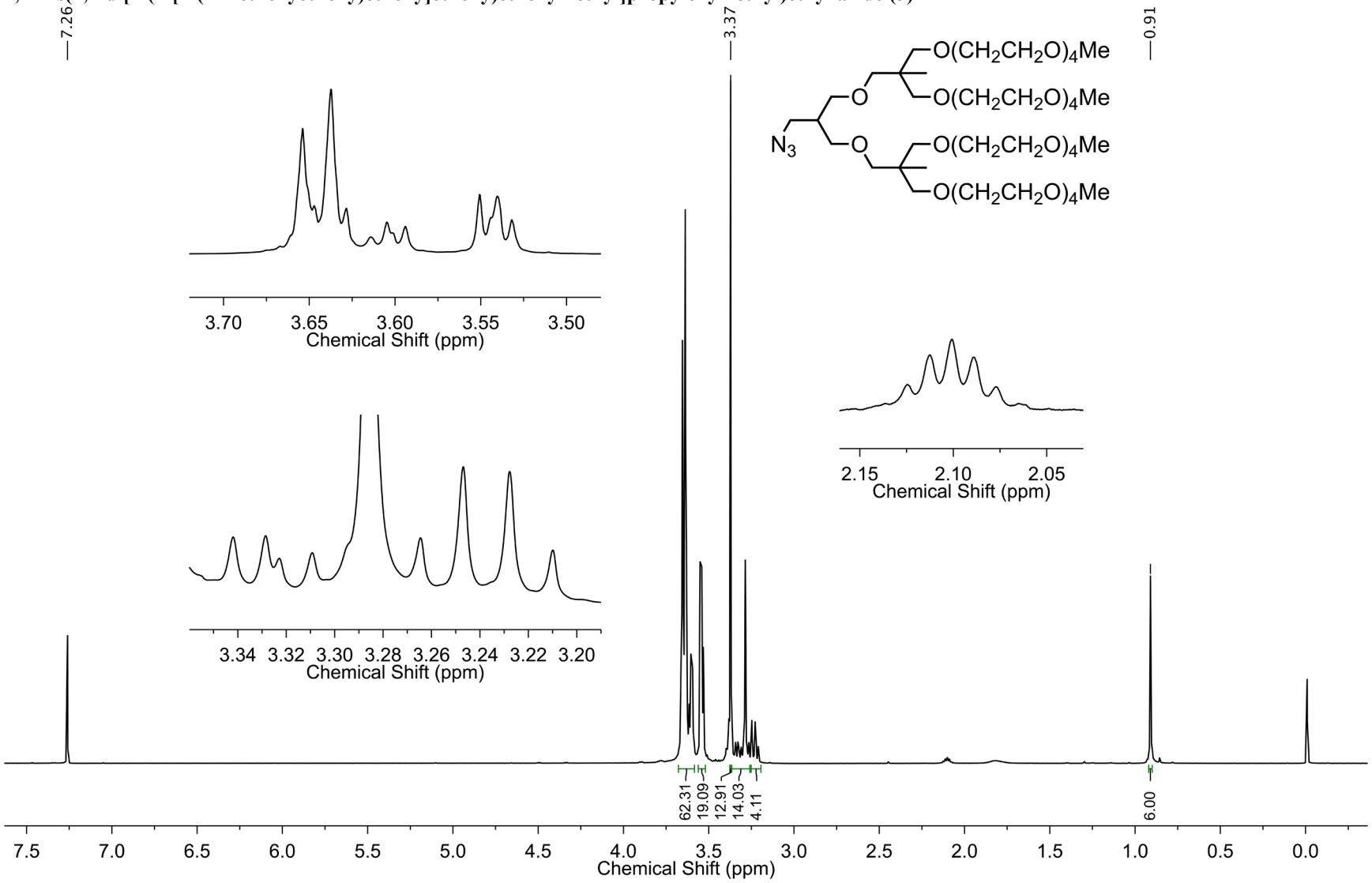
2,2-Bis[2,2-di(hydroxymethyl)propyloxymethyl]ethyl azide (S4)



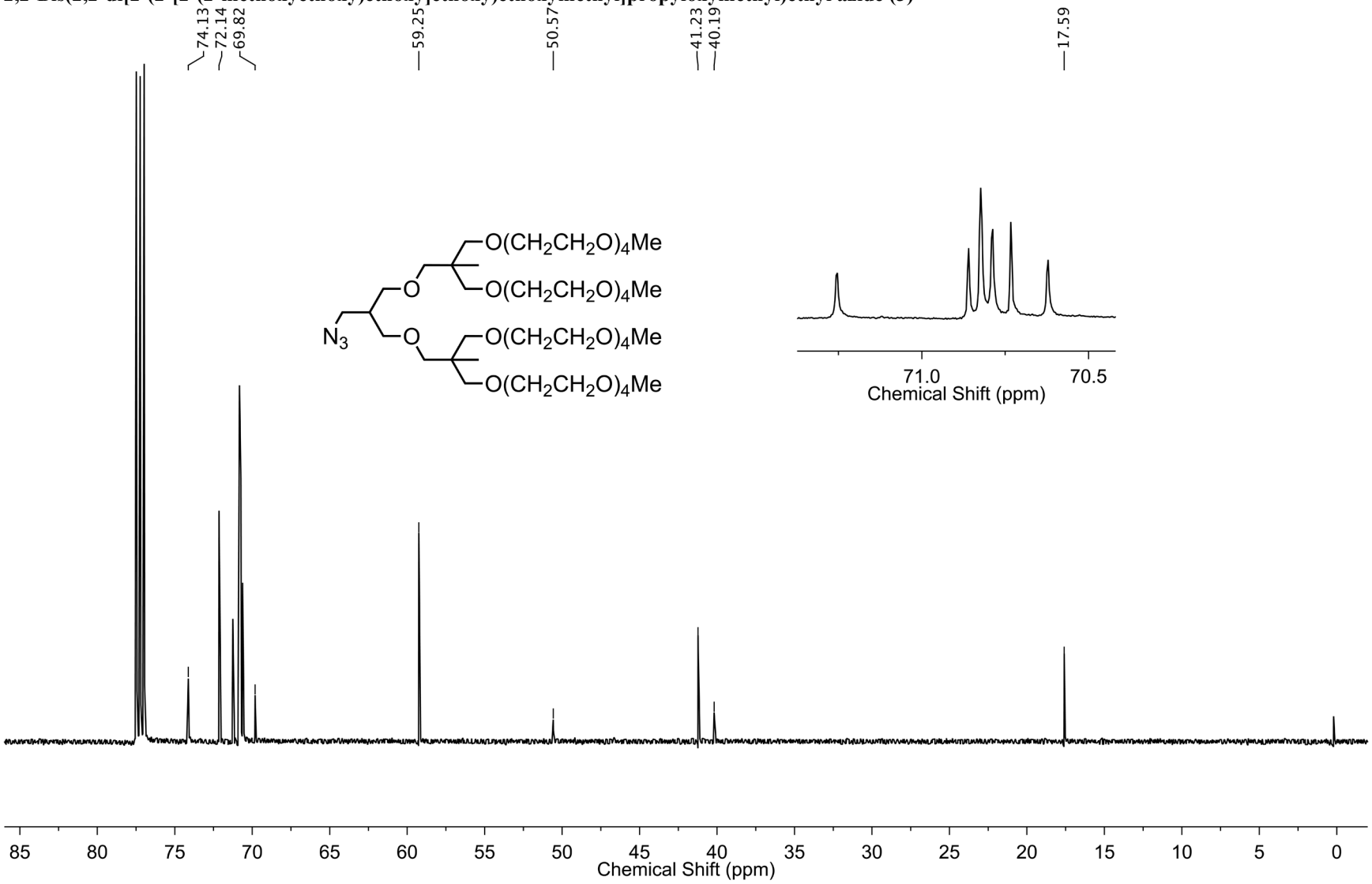
2,2-Bis[2,2-di(hydroxymethyl)propyloxymethyl]ethyl azide (S4)



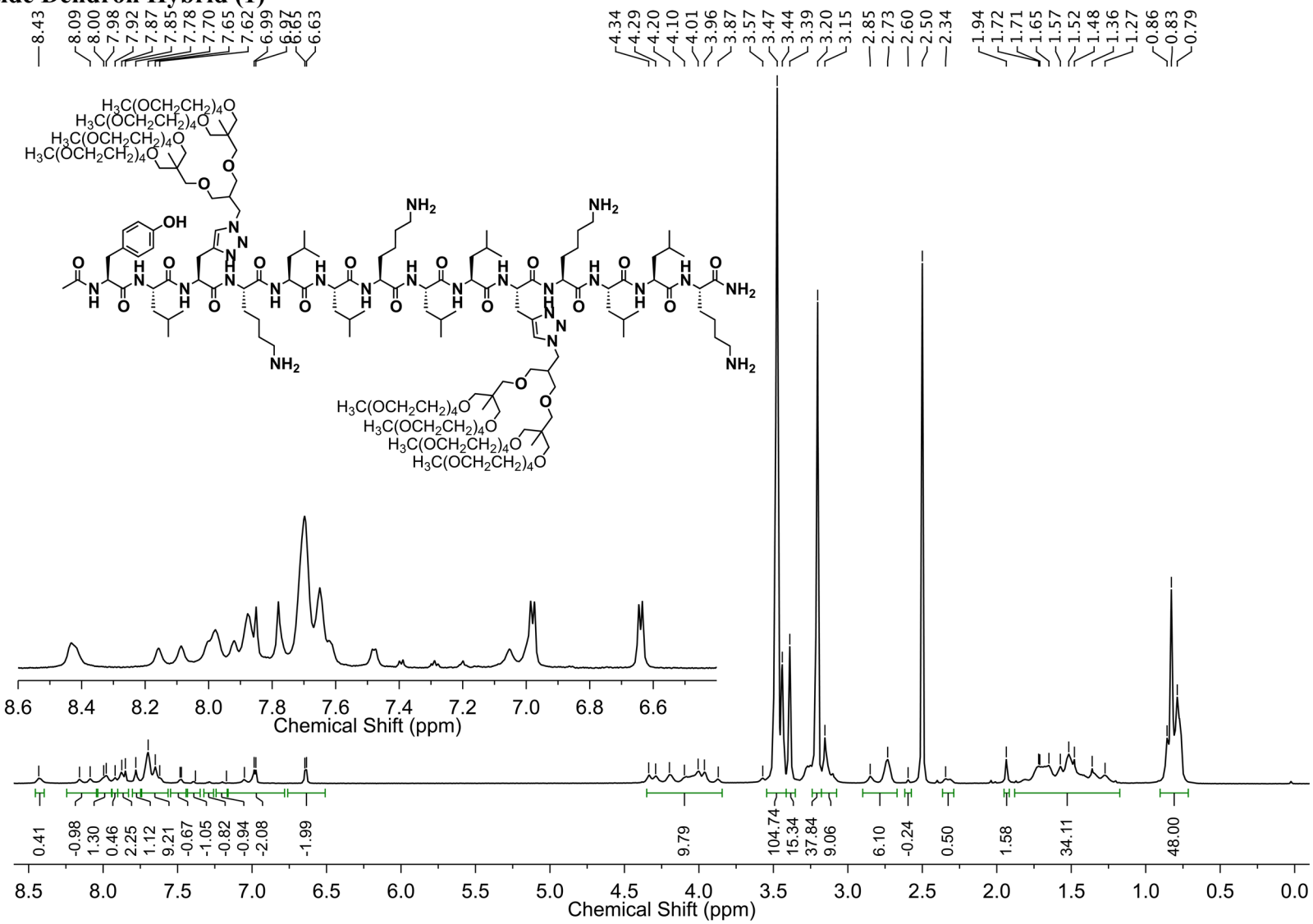
2,2-Bis(2,2-di[2-(2-[2-(2-methoxyethoxy)ethoxy]ethoxy)ethoxymethyl]propyloxymethyl)ethyl azide (3)



2,2-Bis(2,2-di[2-(2-[2-(2-methoxyethoxy)ethoxy]ethoxy)ethoxymethyl]propyloxymethyl)ethyl azide (3)



Peptide Dendron Hybrid (1)



Peptide Dendron Hybrid (1)