A Programmable "Build - Couple" Approach to the Synthesis of Heterofunctionalized Polyvalent Molecules

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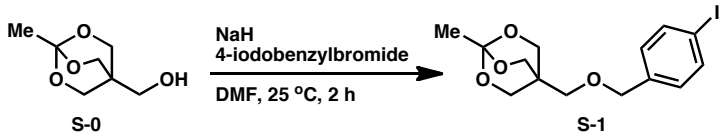
Materials and Methods

All non-protic reactions were run under an inert atmosphere (nitrogen) and all glassware was stored in an oven and/or was flame-dried prior to use under an inert atmosphere of nitrogen. Anhydrous solvents were obtained from a Glass Contour Seca Solvent System by SG Water USA, LLC. Commercially available reagents were used without further purification. Thin layer chromatography (TLC) was performed using 0.25 mm silica gel 60F plates with fluorescent indicator (Silicycle). Flash chromatography was performed on silica gel 60, 230-400 mesh, using a forced flow of eluent at 0.3-0.5 bar pressure.[1] Concentration under reduced pressure was performed by rotary evaporation at 35 °C. Purified compounds were further dried under high cavuum (0.02-0.10 Torr). Yields refer to purified and spectroscopically pure compounds. ^{1}H NMR spectra were recorded on a Varian spectrometer operating at 300 MHz. ^{13}C NMR spectra were recorded on a Varian spectrometer operating at 300 or 400 MHz. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad), coupling constant in Hz, integration and assignment. High-resolution mass spectra were obtained at the Colorado State University Central Instrument Facility on an Agilent 6210 TOF LC/MS. MALDI-TOF spectra were obtained at the Colorado State University Proteomics and Metabolomics Center, using the following protocol: 1 µl of purified sample was mixed with 1 µl of 2,5-dihydroxy benzoic acid (DHB, 10 mg/ml in 50% ACN, 0.1% TFA). The mixture was spotted on the MALDI target and allowed to air dry. The sample was analyzed by an Ultraflex-TOF/TOF mass spectrometer (Bruker Daltonics, Billerica, MA) in positive ion, reflector mode using a 25 kV accelerating voltage. External calibration was done using a peptide calibration mixture (4 to 6 peptides) on a spot adjacent to the sample. The raw data was processed using FlexAnalysis software (version 2.4, BrukerDaltonics). All IR spectra were obtained on NaCl plates (film) with a Nicolet Magna -760 FTIR Spectrometer.

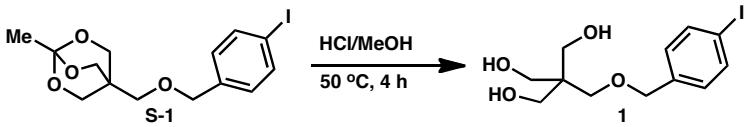
(1) Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

Experimental Data



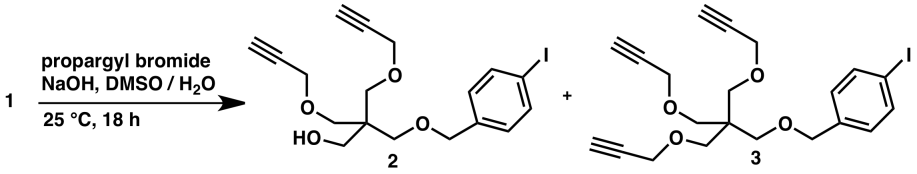
Compound S-1: S0[2] (0.160 g, 1.0 mmol, 1.0 equiv.) was dissolved in anhydrous dimethylformamide (2 mL) and cooled to 0 °C under argon atmosphere. Sodium hydride (0.040 g, 60% wt, 1.0 mmol, 1.0 equiv.) was added to the cooled solution and stirred for 20 min. 4-iodobenzylbromide (0.296 g, 1.0 mmol, 1.0 equiv.) was added and the solution was stirred for 2 hours, ultimately reaching room temperature. Brine (30 mL) was added to the reaction mixture and extracted with ethyl acetate (30 mL). The organic layer was dried over Na_2SO_4 and concentrated under vacuum to provide a white solid (0.357 g, 98%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.68 (d, *J* = 9.0 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 2H), 4.38 (s, 2H), 4.00 (s, 6H), 3.19 (s, 2H), 1.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, δ): 137.8, 137.3, 129.4, 108.7, 93.6, 73.0, 69.6, 68.7, 35.1, 23.6; FT-IR (NaCl plate): 3078, 3002, 2845, 2822, 1617, 1362 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{14}H_{18}IO_4^+$ $[M+H]^+$, 377.0250; Found 377.0233.



Compound 1: S-1 (0.376 g, 1.0 mmol) was dissolved in methanol (10 mL) and concentrated hydrochloric acid (0.14 mL) was added. This solution was heated at 50 °C for 4 h. The reaction mixture was concentrated, washed with $NaHCO_3$, extracted with ethyl acetate and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure to provide a white solid (0.344 g, 98%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, DMSO-d_6, δ): 7.67 (d, *J* = 9.0 Hz, 2H), 7.12 (d, *J* = 9.0 Hz, 2H), 4.38 (s, 2H), 4.22 (t, *J* = 6.0 Hz, 3H), 3.36 (d, *J* = 6.0 Hz, 6H), 3.31 (s, 2H). FT-IR (NaCl plate): 3478, 3062, 3042, 2805, 1645, 1358 cm^{-1}. ^{13}C NMR: (100 MHz, DMSO-d_6, δ): 138.8, 136.9, 129.4, 93.0, 71.7, 69.3, 60.7, 45.7. HRMS-ESI (*m/z*): Calcd for $C_{14}H_{18}IO_4^+$ $[M+H]^+$, 353.0224; Found 353.0218.



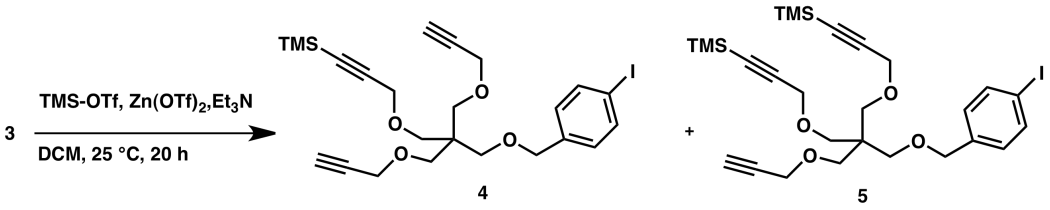
Compounds 2 and 3: Triol **1** (0.704 g, 2.0 mmol, 1 equiv.) was dissolved in dimethylsulfoxide (4.0 mL). NaOH (0.700 g, 17.5 mmol) was dissolved in water (2 mL), added to the dimethylsulfoxide solution and stirred for 30 min at room temperature. Propargyl bromide (80%

(2) For a procedure for the synthesis of **S-0**, see: Gorodetskaya, I. A.; Choi, T.-A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2007**, *129*, 12672.

wt in toluene, 1.78 mL, 12.0 mmol, 6.0 equiv) was added slowly and this solution was stirred for 18 hours. Brine (50 ml) was added and extracted with ethyl acetate (50 mL). Ethyl acetate was dried over Na_2SO_4 and concentrated under reduced pressure. The product was purified by flash column chromatography using ethyl acetate:hexanes (6:94) to provide trialkyne **3** (0.326 g, 35%) as colorless oil. Subsequent elution with dichloromethane:methanol (97:3) provided dialkyne **2** (0.470 g, 55%) as colorless oil.

Compound 2: NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.65 (d, *J* = 9.0 Hz, 2H), 7.06 (d, *J* = 9.0 Hz, 2H), 4.45 (s, 2H), 4.12 (d, *J* = 2.5 Hz, 4H), 3.71 (d, *J* = 5.5. Hz, 2H), 3.58 (s, 4H), 3.51(s, 2H), 2.50 (t, *J* = 6.0 Hz, 1H), 2.42 (t, *J* = 2.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 138.2, 137.6, 129.5, 93.2, 79.8, 74.7, 73.0, 70.7, 70.4, 65.5, 58.9, 45.0. FT-IR (NaCl plate): 3498, 3293, 2980, 2872, 2116, 1483, 1360 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{18}H_{22}IO_4^+$ $[M+H]^+$, 429.0563; Found 429.0566.

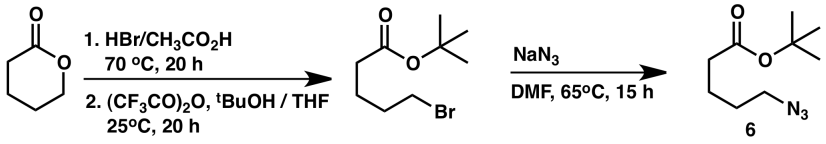
Compound 3: NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.65 (d, *J* = 9.0 Hz, 2H), 7.06 (d, *J* = 9.0 Hz, 2H), 4.44 (s, 2H), 4.11(d, *J* = 3.0 Hz, 2H), 3.54 (s, 6H), 3.47 (s, 2H), 2.39 (t, *J* = 3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 138.7, 137.5, 129.4, 92.9, 80.2, 74.3, 72.8, 69.4, 69.2, 58.9, 45.2. FT-IR (NaCl plate): 3303, 2958, 2876, 2174, 1589, 1483, 1302 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{21}H_{24}IO_4^+$ $[M+H]^+$, 467.0719; Found 467.0659.



Compounds 4 and 5: Zinc triflate (0.03 g, 0.086 mmol, 10.0 mol %) was added to anhydrous dichloromethane (10 mL) under argon atmosphere. Anhydrous triethyl amine (0.156 g, 1.54 mmol, 1.8 equiv.) was added to the solution. Trialkyne **3** was dissolved in dichloromethane (5 mL) and slowly added to the reaction mixture followed by the addition of TMS-triflate (0.343 g, 1.54 mmol, 1.8 equiv). The reaction was stirred for 20 hours under nitrogen atmosphere. The reaction mixture was diluted with dichloromethane (50 mL) and washed with a saturated aqueous ammonium chloride solution. The dichloromethane layer was dried over Na_2SO_4 and concentrated. The crude reaction mixture was purified by flash column chromatography using ethyl acetate:hexanes (2:98) to provide tri-TMS-alkyne (0.088 g, 15%), di-TMS-alkyne **5** (0.273 g, 52%), mono-TMS-alkyne **4** (0.132, 29%).

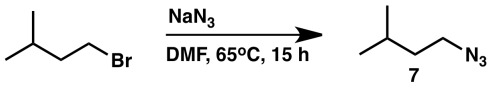
Compound 4: NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.65 (d, *J* = 9.0 Hz, 2H), 7.07 (d, *J* = 9.0 Hz, 2H), 4.44 (s, 2H), 4.11 (s, 2H), 4.10 (s, 4H), 3.54 (s, 4H), 3.53 (s, 2H), 3.46 (s, 2H), 2.39 (t, *J* = 2.5 Hz, 2H), 0.17 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 138.8, 137.5, 129.4, 102.2, 92.8, 91.2, 80.2, 74.3, 72.7, 69.4, 69.3, 69.2, 59.7, 58.9, 45.2, 0.10. FT-IR (NaCl plate): 3273, 2985, 2802, 2174, 1535, 1322 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{24}H_{35}INO_4Si^+$ $[M+NH_4]^+$, 556.1380; Found 556.1367.

Compound 5: NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.65 (d, *J* = 9.0 Hz, 2H), 7.07 (d, *J* = 9.0 Hz, 2H), 4.45 (s, 2H), 4.11 (s, 2H), 4.10 (s, 4H), 3.54 (s, 2H), 3.53 (s, 4H), 3.47 (s, 2H), 2.39 (t, *J* = 2.5 Hz, 2H), 0.17 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 138.8, 137.5, 129.3, 102.2, 92.8, 91.1, 80.3, 74.3, 72.7, 69.5, 69.4, 69.2, 59.7, 58.9, 45.2, 0.12. FT-IR (NaCl plate): 3298, 2947, 2845, 2168, 1574, 1375 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{47}H_{43}INO_4Si_2^+$ $[M+NH_4]^+$, 628.1775; Found 628.1772.



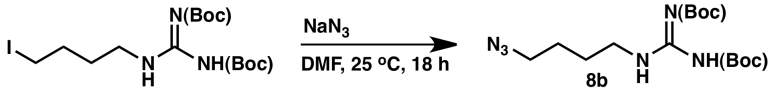
Compound 6: NaN_3 (0.260 g, 4.0 mmol, 2.0 equiv) was added to *t*-butyl 5-bromopentanoate (0.474 g, 2.0 mmol, 1.0 equiv) in anhydrous dimethylformamide (2.0 mL) and heated at 65 °C for 15 hours. The reaction mixture was diluted with brine (30 mL) and extracted with diethyl ether (30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to afford a colorless liquid (0.360 g, 90%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 3.28 (t, *J* = 6.0 Hz, 2H), 2.24 (t, *J* = 6.0 Hz, 2H), 1.64 (m, 4H), 1.44 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 172.3, 80.1, 51.0, 34.8, 28.2, 28.0, 22.2. FT-IR (NaCl plate): 2978, 2840, 2097, 1729, 1367 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_9H_{18}NO_2^+$ $[MH-N_2]^+$,172.1338; Found 172.1334.



Compound 7: NaN_3 (0.130 g, 2.0 mmol, 2.0 equiv) was added to 1-bromo-3-methylbutane (0.151g, 1.0 mmol, 1.0 equiv) in anhydrous DMF (2.0 mL) and heated at 65 °C for 15 hours. The reaction mixture was filtered to get remove solid NaN_3 and the azide was stored as a DMF solution for subsequent reactions.

Compound 8a: was prepared using a previously described method.[3]

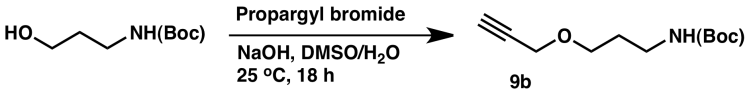


Compound 8b: The di-Boc-iodo precursor was synthesized using a previously reported method.[4] NaN_3 (0.97 g, 15.0 mmol, 10.0 equiv) was added to the di-Boc-iodo compound (0.66 g, 1.5 mmol, 1.0 equiv) in anhydrous dimethylformamide (5.0 mL) and stirred at 25 °C for 18 hours. The reaction mixture was diluted with brine (50.0 mL) and extracted with ethyl acetate (30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to afford a colorless liquid (0.51 g, 95%).

(3) Michael, S.; Michael, E. D.; Michael, J. D. PCT Int. Appl., 9507291, 16 Mar **1995**
(4) Neubert, B. J.; Snider, B. B. *Org. Lett.* **2003**. *5*(5), 765.

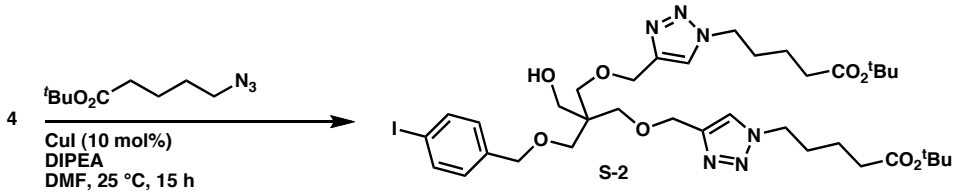
NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, d): 11.42 (s, 1H), 8.25 (s, 1H), 3.34 (q, *J* = 6.0 Hz, 2H), 3.22 (t, *J* = 6.0 Hz, 2H) 1.55 (m, 4H), 1.39 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, d): 163.6, 156.2, 153.3, 83.1, 79.2, 51.0, 40.2, 28.3, 28.0, 26.4, 26.3. FT-IR (NaCl plate): 3054, 2986, 2101, 1721, 1614, 1421, 1265 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{15}H_{29}N_6O_4^+$ $[M+H]^+$, 357.2250; Found 357.2248.

Compound 9a: This compound is commercially available.



Compound 9b: Boc-protected amino alcohol was prepared using a previously reported method.[5] NaOH (2.0 equiv. 10 M aqueous solution) was added slowly to the Boc-protected amino alcohol (1.0 equiv.) in dimethylsulfoxide. The reaction mixture was stirred at 25 °C for 18 hours, then diluted with brine and extracted with ethyl acetate to provide the Boc-protected amino alkyne **9** (~ 62%).

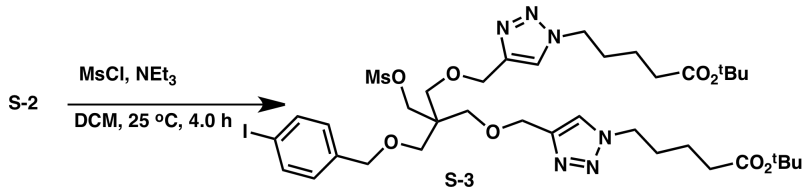
NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.57 (bs, 1H), 4.13 (d, *J* = 3.0 Hz, 2H), 3.57 (t, *J* = 6.0 Hz, 2H), 3.22 (q, *J* = 6.0 Hz, 2H), 2.42 (t, *J* = 3.0 Hz, 2H), 1.77 (t, *J* = 6.0 Hz, 2H), 1.43 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 156.0, 79.7, 78.9, 74.5, 68.0, 58.1, 38.2, 29.7, 28.4. FT-IR (NaCl plate): 3265, 2920, 2210, 1704, 1462 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{11}H_{19}NNaO_3^+$ $[M+Na]^+$, 236.1263; Found 236.1260.



Compound S-2: The *t*-butyl ester azide (0.800 g, 4.0 mmol, 2.0 equiv.) and dialkyne **4** (0.856 g, 2.0 mmol, 1.0 equiv.) were taken up in tetrahydrofuran (15 mL). To this solution was added CuI (0.038 g, 10 mol%) and Hünig's base (0.5 mL), and the solution was stirred at room temperature for 15 hours. The reaction mixture was concentrated, diluted with water (50 mL) and extracted with dichloromethane (80 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography using methanol:dichloromethane (2:98) as an eluent to provide yellow thick liquid **S-2** (1.42 g, 86%).

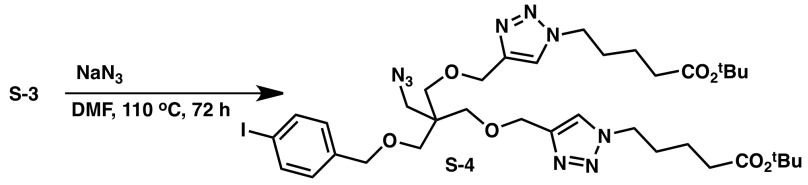
NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.52 (d, *J* = 9.0 Hz, 2H), 7.45 (s, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 4.50 (s, 4H), 4.30 (s, 2H), 4.22 (t, *J* = 6.0 Hz, 4H), 3.56 (s, 2H), 3.45 (s, 4H), 3.37 (s, 2H), 3.14 (bs, 1H), 2.15 (t, *J* = 6.0 Hz, 4H), 1.84-1.79 (m, 4H), 1.51-1.48 (m, 4H), 1.42 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.4, 145.1, 138.2, 137.4, 129.3, 122.3, 92.9, 80.5, 72.7, 70.3, 65.0, 64.6, 50.0, 45.2, 34.6, 29.6, 28.1, 21.9. FT-IR (NaCl plate): 3417, 2977, 2870, 1725, 1588, 1482, 1366 cm^{-1}.

(5) Kane, B. E.; Grant, M. K. O.; El-Fakahany, E. E.; Ferguson, D. M. Bioorg. Med. Chem. **2008**, *16*(3), 1376.



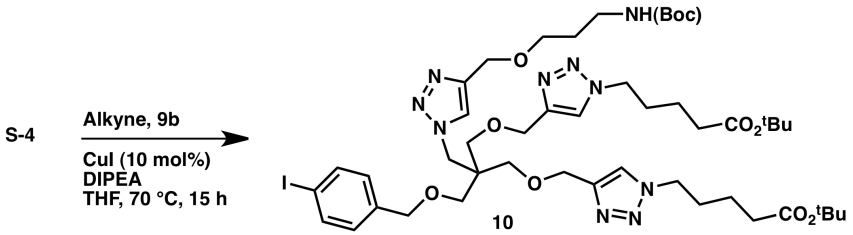
Compound S-3: Alcohol **S-2** (0.826 g, 1.0 mmol, 1.0 equiv.) and triethylamine (0.288 mL, 2.0 mmol) were dissolved in anhydrous dichloromethane (10 mL). Methyl sulfonyl chloride (0.115 mL, 1.5 mmol, 1.5 equiv.) was added to the reaction mixture and the solution was stirred at room temperature for 4 hours. The reaction mixture was diluted with water (40 mL) and e(xtracted with dichloromethane (40 mL). The organic layer was dried over Na_2SO_4 and then concentrated under reduced pressure to provide a red thick oil **S-3** (0.905 g, 100 %).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.53 (d, *J* = 9.0 Hz, 2H), 7.48 (s, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 4.48 (s, 4H), 4.29 (s, 2H), 4.23 (t, *J* = 6.0 Hz, 4H), 4.11 (s, 2H), 3.41 (s, 4H), 3.34 (s, 2H), 2.85 (s, 3H), 2.16 (t, *J* = 6.0 Hz, 4H), 1.85-1.70 (m, 4H), 1.52-1.47 (m, 4H), 1.32 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.3, 144.6, 137.8, 137.2, 129.2, 122.6, 92.9, 80.3, 77.2, 72.4, 67.9, 64.7, 49.8, 46.0, 44.7, 36.6, 34.5, 29.4, 28.0, 21.8.



Compound S-4: Mesolate **S-3** (0.905 g, 1.0 mmol, 1.0 equiv) was dissolved in anhydrous dimethylformamide (10 mL). NaN_3 (0.650 g, 10.0 mmol) was added and the solution was stirred for 72 hours at 110 °C. The reaction mixture was cooled to room temperature, diluted with brine (50 mL) and extracted with ethyl acetate (50 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to provide a yellow oil **S-4** (0.851 g, 100%)

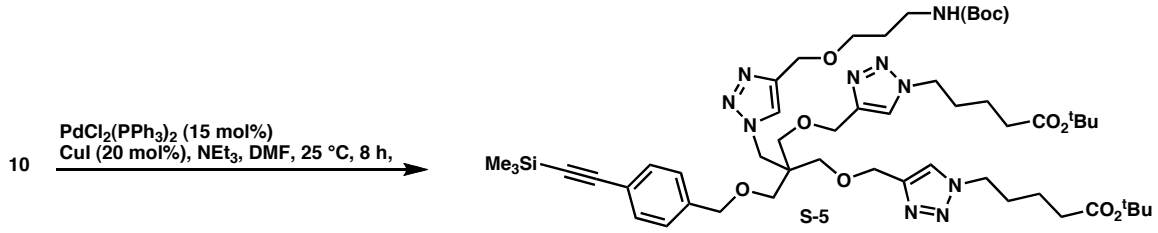
NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.64 (d, *J* = 9.0 Hz, 2H), 7.48 (s, 2H), 7.01 (d, *J* = 9.0 Hz, 2H), 4.57 (s, 4H), 4.38 (s, 2H), 4.32 (t, *J* = 6.0 Hz, 4H), 3.44 (s, 4H), 3.37 (s, 2H), 3.35 (s, 2H), 2.25 (t, *J* = 7.5 Hz, 4H), 1.94-1.89 (m, 4H), 1.62-1.59 (m, 4H), 1.42 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.5, 145.1, 138.3, 137.5, 129.5, 122.6, 93.0, 80.6, 72.7, 69.2, 65.1, 51.9, 50.1, 45.5, 34.8, 30.0, 28.3, 22.1. FT-IR (NaCl plate): 2956, 2889, 2097, 1720, 1578, 1387 cm^{-1}.



Compound 10: S-4 (0.550 g, 0.64 mmol, 1.0 equiv) and alkyne **9b** (0.164 g, 0.76 mmol, 1.2 equiv) were dissolved in anhydrous tetrahydrofuran (15 mL). To this solution was added CuI (0.012 g, 10 mol %) and Hünig's base (0.2 mL) and the solution was stirred at 70 °C for 15

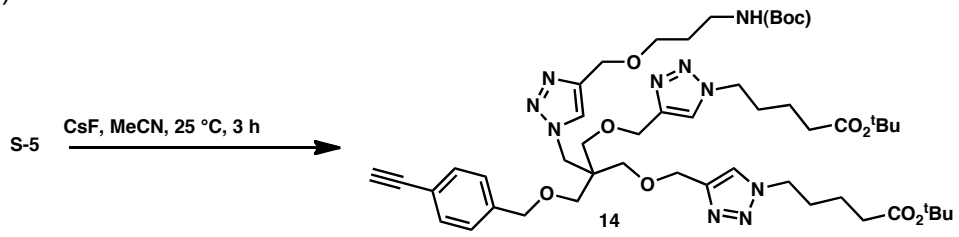
hours. The reaction mixture was concentrated, diluted with water (30 mL) and extracted with dichloromethane (60 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography using methanol:dichloromethane (2:98) as an eluent to provide pure product **10** (0.531 g, 78%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.63 (d, *J* = 9.0 Hz, 2H), 7.55 (s, 1H), 7.53 (s, 2H), 6.99 (d, *J* = 9.0 Hz, 2H), 5.11(bs, 1H), 4.54 (s, 2H), 4.53 (s, 4H), 4.37 (s, 2H), 4.36 (s, 2H), 4.30 (t, *J* = 6.0 Hz, 4H), 3.54 (t, *J* = 6.0 Hz, 4H), 3.35 (s, 4H), 3.31 (s, 2H), 3.27 (m, 2H), 2.22 (t, *J* = 6.0 Hz, 4H), 1.92-1.87 (m, 4H), 1.59-1.56 (m, 4H) 1.37 (s, 27H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.3, 156.0, 144.6, 144.4, 137.9, 137.4, 129.5, 124.8, 122.6, 93.0, 80.5, 79.1, 77.4, 72.6, 69.9, 68.8, 64.8, 64.3, 50.0, 49.8, 45.3, 40.4, 34.6, 29.6, 28.4, 28.1, 21.9. FT-IR (NaCl plate): 3054, 2979, 2869, 1721, 1508, 1367 cm^{-1}. Mass Spectrometry: HRMS-ESI (*m/z*): Calcd for $C_{47}H_{74}IN_{10}O_{10}^+$ $[M+H]^+$, 1065.4634; Found 1065.4620.



Compound S-5: Iodide, **10** (0.270 g, 0.253 mmol, 1.0 equiv.), ethylnyltrimethylsilane (0.071 g, 0.72 mmol, 2.84 equiv.), $PdCl_2(PPh_3)_2$ (0.026 g, 15 mol%) and copper iodide (0.010 g, 20 mol%) were placed into a 25 mL round bottomed flask. Degassed and anhydrous dimethylformamide (2 mL) and triethylamide (2 mL) were added, allowed to stir the reaction mixture at room temperature under nitrogen for 8 h. The reaction mixture was cooled, brine (20.0 mL) was added and the product was extracted with ethyl acetate (40 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography using methanol/dichloromethane (2:98) to provide yellowish liquid **S-5** (0.244 g, 92%).

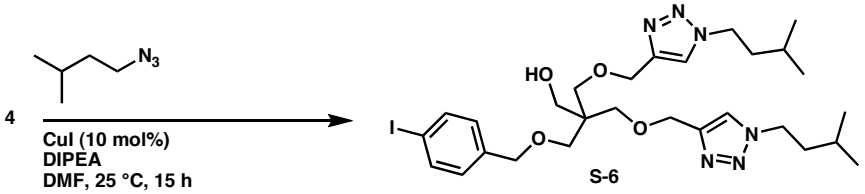
NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.55 (s, 1H), 7.52 (s, 2H), 7.40 (d, *J* = 9.0 Hz, 2H), 7.20 (d, *J* = 9.0 Hz, 2H), 4.94 (bs, 1H), 4.55 (s, 4H), 4.54 (s, 2H), 4.42 (s, 2H), 4.40 (s, 2H), 4.32 (t, *J* = 6.0 Hz, 4H), 3.55 (t, *J* = 6.0 Hz, 2H), 3.38 (s, 4H), 3.33 (s, 2H), 3.18 (m, 2H), 2.24 (t, *J* = 6.0 Hz, 4H), 1.94-1.89 (m, 4H), 1.77-1.73 (m, 2H), 1.61-1.56 (m, 4H), 1.40 (s, 27H), 0.24 (s, 9H).



Compound 14: **S-5** (0.240 g, 0.23 mmol, 1.0 equiv.) was dissolved in acetonitrile (2.0 mL) and CsF (0.051 g, 0.34 mmol, 1.50 equiv.) was added. The reaction mixture was stirred at room temperature for 3 hours. Saturated aqueous ammonium chloride solution was added to the organic layer and extracted using dichloromethane (30 mL). Organic layer was concentrated under reduced pressure to give crude product which was purified by flash column

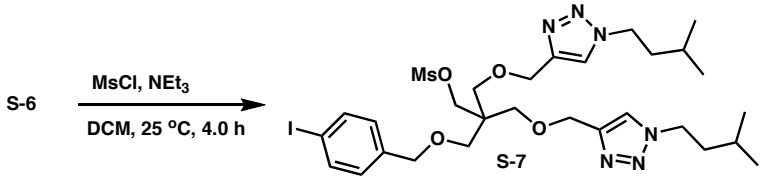
chromatography using methanol:dichloromethane (4:96) to provide colorless liquid (0.159 g, 72%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.53 (s, 1H), 7.50 (s, 2H), 7.39 (d, *J* = 9.0 Hz, 2H), 7.19 (d, *J* = 9.0 Hz, 2H), 4.96 (bs, 1H), 4.51 (m, 6H), 4.40 (s, 2H), 4.37 (s, 2H), 4.28 (t, *J* = 6.0 Hz, 4H), 3.51 (t, *J* = 6.0 Hz, 2H), 3.34 (s, 4H), 3.31 (s, 2H), 3.13 (m, 2H), 3.05 (s, 1H) 2.22 (t, *J* = 6.0 Hz, 4H), 1.89-1.84 (m, 4H), 1.73-1.70 (m, 2H), 1.56-1.51 (m, 4H) 1.37 (s, 27H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.3, 156.0, 144.6, 139.0, 132.1, 127.5, 124.7, 122.6, 121.4, 83.4, 80.4, 78.9, 72.8, 68.8, 68.7, 68.5, 64.8, 64.3, 53.5, 49.9, 49.8, 45.3, 38.2, 34.6, 29.9, 29.6, 28.5, 28.1, 21.9. FT-IR (NaCl plate): 3406, 3140, 2976, 2868, 2200, 1722, 1590, 1417 cm^{-1}. Mass Spectrometry: HRMS-ESI (*m/z*): Calcd for $C_{49}H_{76}N_{10}O_{10}^{+}$ $[M-H]^{+}$, 963.5668; Found 963.5509.



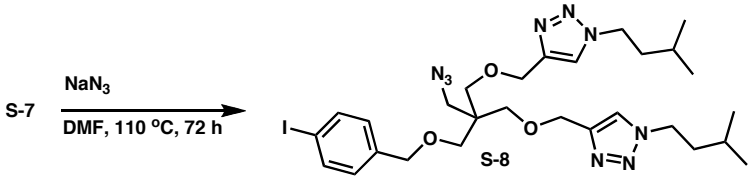
Compound S-6: The azide **7** (1.31 g, 11.65 mmol, 5.0 equiv. in DMF, 4 mL) was added to dialkyne **4** (1.0 g, 2.33 mmol, 1.0 equiv.) in dimethylformamide (5 mL). CuI (0.038 g, 10 mol%) and Hünig's base (0.5 mL) were added and stirred at room temperature for 15 hours. The reaction mixture was diluted with brine (50 mL) and extracted with dichloromethane (50 mL), The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography using methanol:dichloromethane (3:97) as the eluent to provide a yellow liquid **S-6** (1.25 g, 82%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.54 (d, *J* = 9.0 Hz, 2H), 7.44 (s, 2H), 6.95 (d, *J* = 9.0 Hz, 2H), 4.53 (s, 4H), 4.34 (s, 2H), 4.26 (t, *J* = 6.0 Hz, 4H), 3.62 (s, 2H), 3.49 (s, 4H), 3.41 (s, 2H), 3.14 (bs, 1H), 1.72 (q, *J* = 6.0 Hz, 4H), 1.52 (sept, *J* = 6.0, 2H), 0.88 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 144.9, 138.1, 137.3, 129.2, 122.0, 92.8, 72.61, 70.34, 70.29, 64.9, 65.6, 48.6, 45.1, 38.9, 25.5, 22.2.



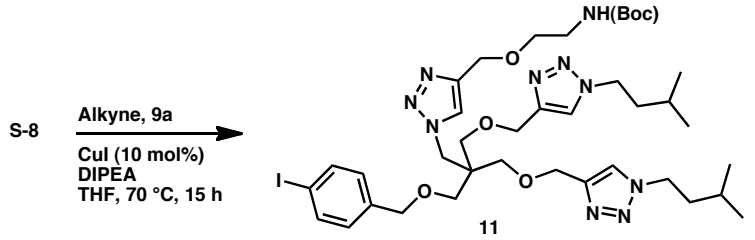
Compound S-7: **S-6** (1.25 g, 1.91 mmol, 1.0 equiv.) and triethylamine (0.53 mL, 3.82 mmol, 2.0 equiv.) were dissolved in anhydrous dichloromethane (25.0 mL). Methyl sulfonyl chloride (0.220 mL, 2.86 mmol, 1.5 equiv.) was added to the reaction mixture and stirred at room temperature for 4 hours. The reaction mixture was diluted with water (60.0 mL) and extracted with dichloromethane (50 mL). The dichloromethane layer was dried over Na_2SO_4 and concentrated under vacuum to provide a slightly red thick oil **S-7** (1.39 g, 100 %).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.62 (d, *J* = 9.0 Hz, 2H), 7.49 (s, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 4.55 (s, 4H), 4.17 (s, 2H), 4.30 (t, *J* = 6.0 Hz, 4H), 4.18 (s, 2H), 3.47 (s, 4H), 3.42 (s, 2H), 2.93 (s, 3H), 1.76 (q, *J* = 6.0 Hz, 4H), 1.57 (sept, *J* = 6.0, 2H), 0.93 (d, *J* = 6.0 Hz, 6H).



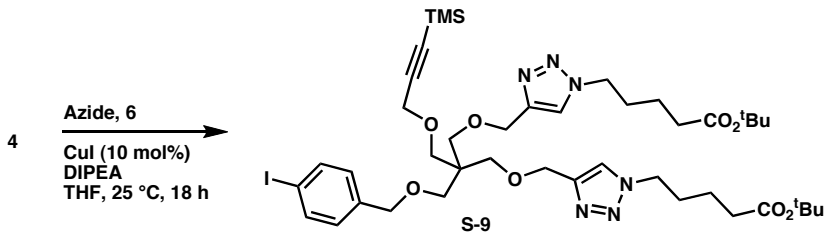
Compound S-8: **S-7** (0.890 g, 1.22 mmol, 1.0 equiv) was dissolved in anhydrous dimethylformamide (10.0 mL). NaN_3 (0.793 g, 12.2 mmol, 10.0 equiv.) was added to this solution and stirred for 72 hours at 110 °C. The reaction mixture was cooled to room temperature, diluted with brine (60 mL) and extracted with ethyl acetate (50 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to provide yellow oil (0.830 g, 100%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.57 (d, *J* = 9.0 Hz, 2H), 7.45 (s, 2H), 6.95 (d, *J* = 9.0 Hz, 2H), 4.52 (s, 4H), 4.33 (s, 2H), 4.27 (t, *J* = 6.0 Hz, 4H), 3.39 (s, 4H), 3.32 (s, 2H), 3.30 (s, 2H), 1.72 (q, *J* = 6.0 Hz, 4H), 1.53 (sept, *J* = 6.0, 2H), 0.89 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 144.9, 138.1, 137.3, 129.2, 122.2, 92.8, 72.5, 68.9, 64.9, 51.6, 48.6, 45.3, 38.99, 25.5, 22.2. FT-IR (NaCl plate): 3136, 2957, 2869, 2101, 1616, 1467, 1367 cm^{-1}.



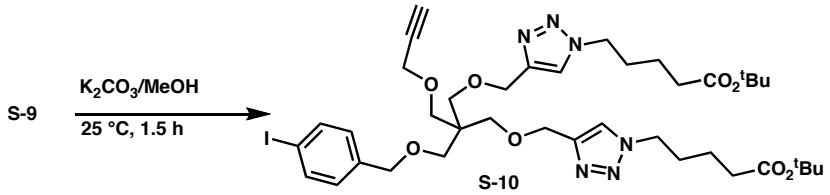
Compound 11: The azide **S-8** (1.10 g, 1.61 mmol, 1.0 equiv) and alkyne **9a** (0.386 g, 1.93 mmol, 1.2 equiv) were dissolved in tetrahydrofuran (20 mL). CuI (0.031 g, 10 mol %) and Hünig's base (1.0 mL) were added and the solution was stirred at 70 °C for 15 hours. The reaction mixture was concentrated, diluted with water (30 mL) and extracted with dichloromethane (60 mL), The organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by flash column chromatography using methanol:dichloromethane (3:97) as an eluent to provide pure product (1.2 g, 85%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.65 (d, *J* = 9.0 Hz, 2H), 7.59 (s, 1H), 7.51 (s, 2H), 7.02 (d, *J* = 9.0 Hz, 2H), 5.08 (bs, 1H), 4.58 (s, 2H), 4.56 (s, 4H), 4.41 (s, 2H), 4.38 (s, 2H), 4.34 (t, *J* = 6.0 Hz, 4H), 3.57 (t, *J* = 6.0 Hz, 2H), 3.38 (s, 4H), 3.35 (s, 4H), 1.77 (q, *J* = 6.0 Hz, 4H), 1.60 (sept, *J* = 6.0, 2H), 1.41 (s, 9H), 0.95 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 155.9,144.5, 144.37, 137.8, 137.4, 129.4, 124.8, 122.4, 93.0, 79.0, 72.5, 69.5, 68.7, 64.7, 64.3, 53.5, 49.8, 48.7, 45.3, 40.4, 39.0, 28.4, 25.5, 22.2. FT-IR (NaCl plate): 3442, 2959, 2870, 1707, 1507, 1366 cm^{-1}. Mass Spectrometry: HRMS-ESI (*m/z*): Calcd. for $C_{38}H_{60}IN_{10}O_6$ $[M+H]^+$, 879.3742. Found 879.3735.



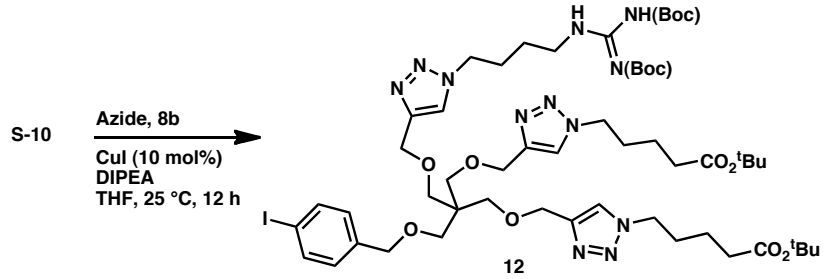
Compound S-9: Azide **6** (0.34 g, 1.712 mmol, 2.0 equiv.) was added to the stirred solution of alkyne **4** (0.461 g, 0.856 mmol, 1.0 equiv.) in anhydrous tetrahydrofuran (4 mL). CuI (0.016 g, 10 mol %) and Hünig's base (0.2 mL) was added to the reaction mixture and stirred at 25 °C for 18 hours. The reaction mixture was concentrated, diluted with water (30 mL) and extracted with dichloromethane (30 mL). The organic layer was dried over Na_2SO_4 and purified by flash column chromatography using methanol:dichloromethane (2:98) as an eluent to provide pure product (0.560 g, 70%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.64 (d, *J* = 9.0 Hz, 2H), 7.49 (s, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 4.59 (s, 4H), 4.41 (s, 2H), 4.31 (t, *J* = 6.0 Hz, 4H), 4.08 (s, 2H), 3.56 (s, 2H), 3.51(s, 6H), 3.45 (s, 2H), 2.26 (t, *J* = 6.0 Hz, 4H), 1.95-1.90 (m, 4H), 1.63-1.57 (m, 4H), 1.41 (s, 18H), 0.16 (s, 9H).



Compound S-10: TMS- alkyne **S-9** (0.41 g, 0.43 mmol, 1.0 equiv.) was dissolved in methanol (5 mL). K_2CO_3 (0.118 g, 0.86 mmol, 2.0 equiv.) was added to this solution and stirred at room temperature for 1.5 hours. The reaction mixture was concentrated, diluted with water (20 mL) and extracted with dichloromethane (30 mL), The organic layer was dried over Na_2SO_4 and purified by flash column chromatography using methanol:dichloromethane (3:97) as an eluent to provide pure product **S-10** (0.334 g, 90%).

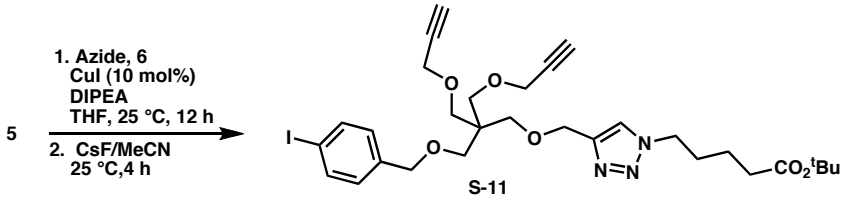
NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.64 (d, *J* = 9.0 Hz, 2H), 7.49 (s, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 4.59 (s, 4H), 4.41 (s, 2H), 4.32 (t, *J* = 6.0 Hz, 4H), 4.08 (d, *J* = 3.0 Hz, 2H), 3.52 (s, 2H), 3.51(s, 4H), 3.44 (s, 2H), 2.41 (t, J = 3.0 Hz, 1H), 2.26 (t, *J* = 6.0 Hz, 4H), 1.92-1.88 (m, 4H), 1.65-1.58 (m, 4H), 1.41 (s, 18H).



Compound 12: **S-10** (0.385 g, 0.45 mmol, 1.0 equiv.) was dissolved in anhydrous tetrahydrofuran (4 mL). Azide **8b** (0.160 g, 0.45 mmol, 1.0 equiv.) was added to this solution

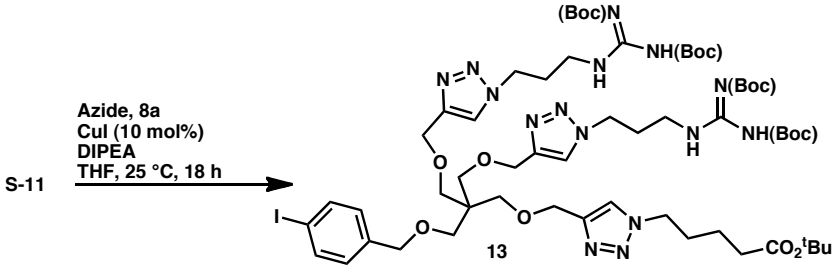
and CuI (0.009 g, 10 mol %) and Hünig's base (0.3 mL) were added. The reaction mixture and stirred at 25 °C for 12 hours. The reaction mixture was concentrated, diluted with water (30.0 mL) and extracted with dichloromethane (30 mL), The organic layer was dried over Na_2SO_4 and purified by flash column chromatography using methanol:dichloromethane (2:98) as an eluent to provide pure product **13** (0.417 g, 76%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 11.43 (s, 1H), 8.28 (t, *J* = 6.0 Hz, 1H), 7.54 (d, *J* = 9.0 Hz, 2H), 7.50 (s, 1H), 7.50 (s, 2H), 6.95 (d, *J* = 9.0 Hz, 2H), 4.50 (s, 6H), 4.32 (s, 2H, 4.27 (t, *J* = 6.0 Hz, 6H), 3.43 (s, 6H), 3.39-3.35 (m, 4H), 2.19 (t, *J* = 6.0 Hz, 4H), 1.87-1.82 (m, 6H), 1.55-1.42 (m, 6H), 1.42 (s, 9H), 1.41 (s, 9H), 1.35 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.3, 163.5, 156.3, 153.2, 145.3, 138.5, 137.3, 129.2, 122.5, 122.4, 92.7, 83.2, 80.4, 79.3, 77.4, 72.4, 69.2, 69.01, 65.07, 49.9, 49.7, 45.3, 39.9, 34.6, 29.7, 28.3, 28.13, 28.1, 27.6, 26.2, 22.0. FT-IR (NaCl plate): 3331, 2980, 2870, 1722, 1620, 1392 cm^{-1}. Mass Spectrometry: HRMS-ESI (*m/z*): Calcd for $C_{54}H_{86}IN_{12}O_{12}^+$ $[M+H]^+$, 1221.5455. Found 1221.5523.



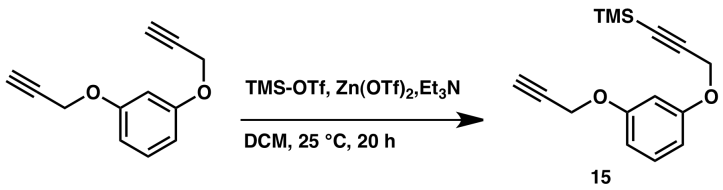
Compound S-11: Azide **6** (0.20 g, 1.0 mmol, 1.0 equiv.) was added to the stirred solution of alkyne **5** (0.61 g, 1.0 mmol, 1.0 equiv.) in anhydrous tetrahydrofuran (5 mL). CuI (0.019 g, 10 mol %) and Hünig's base (0.5 mL) were added to the reaction mixture and stirred at 25 °C for 12 hours. The reaction mixture was concentrated, diluted with water (30 mL) and extracted with dichloromethane (30 mL), The organic layer was dried over Na_2SO_4 and purified by flash column chromatography using methanol:dichloromethane (1:99) as an eluent to provide pure TMS-alkyne product (0.525 g, 65%). TMS- alkyne (0.390 g, 0.47 mmol, 1.0 equiv.) was dissolved in acetonitrile (3 mL) and CsF (0.105 g, 0.70 mmol, 1.50 equiv.) was added. This solution was stirred at room temperature for 4 hours. The reaction mixture was concentrated, diluted with saturated ammonium chloride solution (20 mL) and extracted with ethyl acetate (30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by flash column chromatography using methanol:dichloromethane (2:98) as an eluent to provide pure product (0.240 g, 75%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.63 (d, *J* = 9.0 Hz, 2H), 7.47 (s, 1H), 7.04 (d, *J* = 9.0 Hz, 2H), 4.61 (s, 2H), 4.41 (s, 2H), 4.29 (t, *J* = 6.0 Hz, 6H), 4.08 (s, 4H), 3.52 (s, 4H), 3.50 (s, 4H), 3.44 (s, 4H), 2.40 (t, *J* = 3.0 Hz, 2H), 2.23 (t, *J* = 6.0 Hz, 2H), 1.94-1.89 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.4, 145.8, 138.6, 137.4, 129.3, 122.2, 92.8, 80.6, 80.2, 74.3, 72.6, 69.3, 69.2, 69.1, 65.4, 58.8, 50.1, 45.2, 34.7, 29.8, 28.2, 21.1.



Compound 13: Azide **8a** (0.23 g, 0.66 mmol, 2.0 equiv.) was added to a solution of alkyne **S-11** (0.220 g, 0.33 mmol, 1.0 equiv.) in anhydrous tetrahydrofuran (3 mL). CuI (0.006 g, 10 mol %) and Hünig's base (0.3 mL) were added and this mixture was stirred at room temperature for 18 hours. The reaction mixture was concentrated, diluted with water (20 mL) and extracted with dichloromethane (30 mL), The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure and purified by flash column chromatography using methanol:dichloromethane (2:98) as an eluent to provide pure product (0.433 g, 95%).

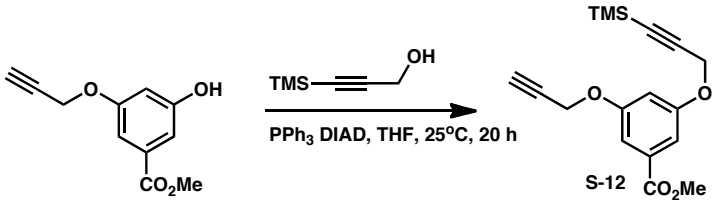
NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$ δ): 11.36 (s, 2H), 8.33 (t, *J* = 3.0 Hz, 1H), 7.73 (s, 2H), 7.48 (d, *J* = 9.0 Hz, 2H), 7.43 (s, 1H), 6.88 (d, *J* = 9.0 Hz, 2H), 4.43 (s, 6H), 4.29-4.25 (m, 6H), 4.20 (t, *J* = 3.0 Hz, 2H), 3.37 (s, 4H), 3.33-3.30 (m, 8H), 3.15 (t, *J* = 3.0 Hz, 6H), 2.12-2.04 (m, 8H), 1.80-1.76 (m, 2H), 1.51-1.47 (m, 6H), 1.36 (s, 9H), 1.41 (s, 9H), 1.39-1.32 (m, 45H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.3, 163.3, 156.4, 153.0, 145.2, 145.0, 138.5, 137.1, 129.1, 123.2, 122.3, 92.5, 83.2, 90.2, 79.2, 72.2, 69.0, 65.0, 64.8, 51.0, 49.8, 47.4, 45.2, 37.4, 34.7, 34.5, 30.3, 29.5, 28.2, 28.6, 22.1, 21.8. FT-IR (NaCl plate): 3328, 2978, 2870, 1723, 1640, 1391 cm^{-1}. Mass Spectrometry: HRMS-ESI (m/z): Calcd for $C_{58}H_{92}IN_{15}O_{14}$ $[M+2H]^{2+}$, 675.8069. Found 675.8088.



Compound 15: The di-propargyl ether precursor was prepared using a previously reported method.[6] Zinc triflate (0.363 g, 1.0 mmol, 10.0 mol %) was dissolved in anhydrous dichloromethane (60.0 mL) under argon atmosphere. Anhydrous triethylamine (2.08 mL, 15.0 mmol, 1.5 equiv.) was added to the solution. 1,3-dipropargylic ether (1.86 g, 10.0 mmol, 1.0 equiv.) was dissolved in dichloromethane (20 mL) and slowly added to the reaction mixture followed by the addition of TMS-triflate (0.2.70 mL, 15.0 mmol, 1.5 equiv). The reaction was stirred for 20 hours under nitrogen atmosphere. The reaction mixture was then diluted with dichloromethane (50.0 mL) and washed with saturated aqueous ammonium chloride solution. The dichloromethane layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography using hexanes (100%) to provide **15** (1.16 g, 45%).

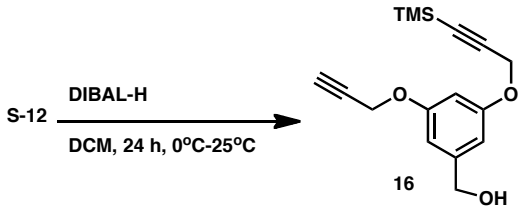
(6) Srinivasan, M.; Sankararaman, S.; Hopf, H.; Dix, I.; Jones, P. G. *J. Org. Chem*. **2001**, *66*, 4299.

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.23-7.18 (m, 1H), 6.62 (d, *J* = 6.0 Hz, 2H), 4.67-4.66 (m, 4H), 2.53 (t, *J* = 3.0 Hz, 1H), 0.20 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 159.2, 158.9, 130.0, 108.0, 102.6, 100.1, 93.0, 78.7, 75.8, 57.0, 55.9, -0.36. FT-IR (NaCl plates): 3252, 2958, 2822, 2122, 1641, 1390 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{15}H_{19}O_2Si^+$ $[M+H]^+$, 259.1154; Found 259.1155.



Compound S-12: Methyl-3-hydroxy-5-(prop-2-yn-1-yloxy)benzoate (0.516 g, 2.5 mmol, 1.0 equiv), which was prepared using a previously reported method[7], was dissolved in 10 mL of tetrahydrofuran, followed by the addition of PPh_3 (0.790 g, 3.0 mmol, 1.2 equiv.), DIAD (0.607 g, 3.0 mmol, 1.2 equiv.) and 3-(Trimethylsilyl)propargyl alcohol (0.385 g, 3.0 mmol, 1.2 equiv.) . This solution was stirred at 0 °C, and stirred for 20 hours, ultimately reaching room temperature. The reaction mixture was evaporated and the residue was extracted with ethyl acetate (50 mL). The organic extract was washed with water (3 x 50 mL) and brine solution (50 mL). The organic phase was dried over Na_2SO_4, filtered off from an insoluble fraction, and solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography using with CH_2Cl_2 as an eluent to allow isolation of a yellow oil in quantitative yield.

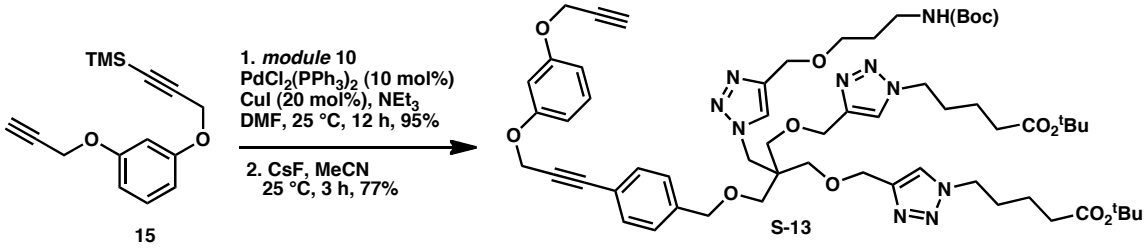
NMR spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.30 (m, 2H), 6.80 (t, *J* = 3.0 Hz, 1H), 4.71 (d, *J* = 3.0 Hz, 2H), 4.69 (s, 2H), 3.91 (s, 3H), 2.54 (t, *J* = 2.5 Hz, 1H), 0.17 (s, 9H).



Compound 16: The methyl ester **S-12** (1.0 g, 3.0 mmol, 1.0 equiv.) was dissolved in anhydrous dichloromethane (20 mL) and cooled to 0 °C. DIBAL-H (11.918 g, 84.0 mmol) was added over a period of 5 min. After stirring for 3 hours at 0 °C, the reaction mixture was allowed to warm to room temperature and stirred for an additional 24 hours. Saturated aqueous ammonium chloride (20 mL) was added and this solution was stirred for 10 minutes. The resulting gel was passed through a short column (~ 3 cm) of Celite. The layer was washed with dichloromethane (50 mL), the filtrate was dried by addition of Na_2SO_4 and solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography using methanol:dichloromethane (2:98) as an eluent to give a yellow oil (0.802 g, 88%).

(7) Zou, Y.; Yin, J. *ChemBioChem* **2008**, *9*, 2804.

NMR spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 6.60 (d, *J* = 3.0 Hz, 2H), 6.52 (t, *J* = 3.0 Hz 1H), 4.67 (d, *J* = 2.5 Hz, 2H), 4.65 (s, 2H), 4.60 (s, 2H), 2.52 (t, *J* = 2.5 Hz 1H), 2.06 (bs, 1H), 0.17 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 159.1, 158.8, 143.8, 106.3, 106.2, 101.4, 100.1, 93.0, 78.6, 75.9, 64.9, 57.0, 56.0, 0.07. FT-IR (NaCl plate): 3290, 2959, 2868, 2180, 1717, 1597, 1251 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{16}H_{21}O_3Si^+$ $[M+H]^+$, 289.1260; Found 289.1257.



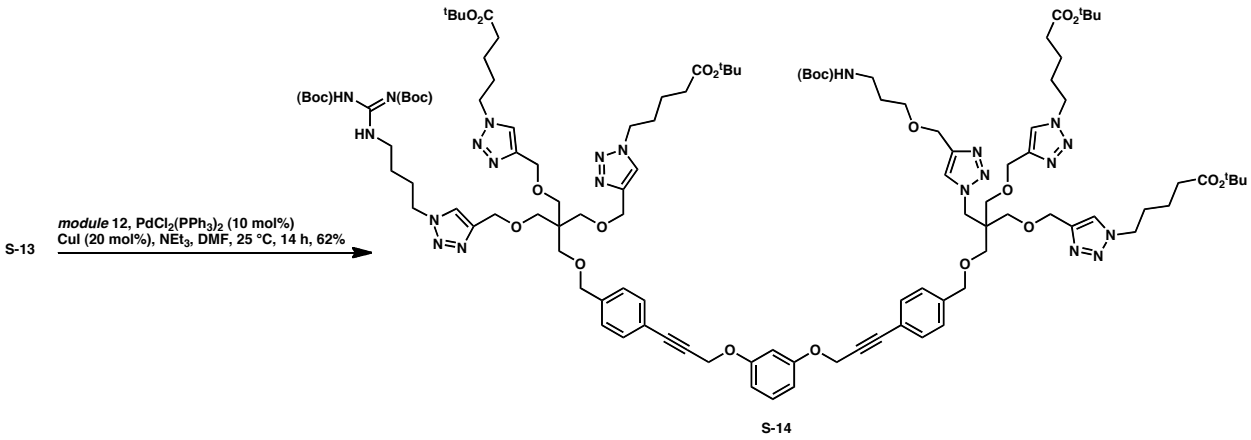
15 S-13

Compound S-13: Compound **10** (0.106 g, 0.10 mmol, 1.0 equiv.), mono-TMS protected dialkyne, **15** (0.36 g, 0.14 mmol, 1.4 equiv.), $PdCl_2(PPh_3)_2$ (0.007 g, 15 mol%) and copper iodide (0.004 g, 20 mol%) were placed into a 25 mL round bottomed flask and dissolved in degassed anhydrous dimethylformamide (1.5 mL) and triethylamine (1.5 mL). This solution was stirred at room temperature under nitrogen for 12 hours. The reaction mixture was cooled, brine (20 mL) was added and the product was extracted with ethyl acetate (30 mL). The organic layer was dried over Na_2SO_4 and solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography using methanol:dichloromethane (3: 97) eluent to provide a light yellow solid (0.114 g, 95%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.55 (s, 1H), 7.52 (s, 2H), 7.38 (d, *J* = 9.0 Hz, 2H), 7.22-7.16 (m, 3H), 6.65-6.58 (m, 3H), 4.94 (bs, 1H), 4.86 (s, 2H), 4.63 (s, 2H), 4.55 (s, 6H), 4.42 (s, 2H), 4.40 (s, 2H), 4.30 (t, *J* = 6.0 Hz, 4H), 3.53 (t, *J* = 6.0 Hz, 4H), 3.53 (s, 4H), 3.51 (s, 2H), 3.19-3.16 (m, 2H), 2.23 (t, *J* = 6.0 Hz, 4H), 1.95-1.85 (m, 4H), 1.76-1.72 (m, 4H), 1.62-1.55 (m, 4H), 1.40-1.40 (m, 27H), 0.14 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 172.5, 159.2, 159.1, 156.2, 144.8, 139.1, 132.0, 130.0, 127.6, 124.9, 122.8, 121.7, 108.0, 107.9, 102.7, 100.2, 100.0, 93.0, 87.1, 84.2, 80.6, 77.3, 73.0, 69.0, 68.7, 65.0, 64.5, 57.1, 56.9, 50.1, 49.9, 45.5, 38.4, 34.8, 30.0, 29.8, 28.6, 28.3, 22.1, 0.07.

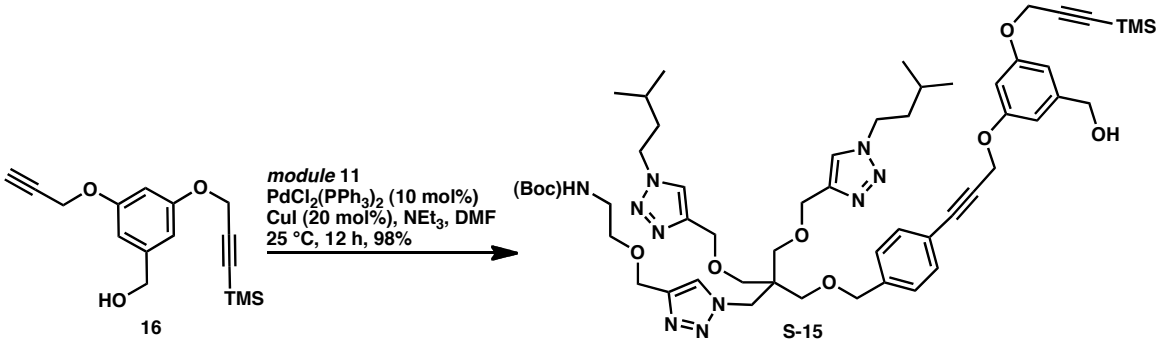
CsF (0.022 g, 0.15 mmol) was added to a solution of the purified product (0.114 g, 0.1 mmol) in acetonitrile (4 mL) and stirred at room temperature for 3 hours. Saturated aqueous ammonium chloride was added to the organic layer and extracted using dichloromethane (30 mL). Organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography using methanol:dichloromethane (5:95) to provide a sticky solid **S-13** (0.082 g, 77%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.55 (s, 1H), 7.52 (s, 2H), 7.38 (d, *J* = 9.0 Hz, 2H), 7.23-7.19 (m, 3H), 6.62-6.59 (m, 3H), 4.94 (bs, 1H), 4.87 (s, 2H), 4.66 (d, *J* = 3.0 Hz, 2H), 4.55 (s, 4H), 4.54 (s, 2H), 4.42 (s, 2H), 4.40 (s, 2H), 4.30 (t, *J* = 6.0 Hz, 4H), 3.54 (t, *J* = 6.0 Hz, 2H), 3.38 (s, 4H), 3.34 (s, 2H), 3.21-3.15 (m, 2H), 2.51 (t, *J* = 3.0 Hz, 1H), 2.23 (t, *J* = 6.0 Hz, 4H), 1.95-1.85 (m, 4H), 1.76-1.72 (m, 2H), 1.63-1.53 (m, 4H), 1.40-1.39 (m, 27H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.4, 159.1, 158.9, 156.1, 144.8, 139.0, 131.9, 130.1, 127.5, 124.8, 122.7, 121.6, 108.0, 107.9, 102.6, 87.0, 84.1, 80.6, 79.0, 78.6, 77.4, 75.8, 72.9, 68.9, 68.6, 64.9, 64.4, 56.8, 56.0, 50.0, 49.9, 45.4, 38.4, 34.7, 29.9, 29.7, 28.6, 28.4, 22.0. FT-IR (NaCl plate): 3403, 3294, 2976, 2869, 1721, 1592, 1490 cm^{-1}.



Compound S-14: Compound **12** (0.240 g, 0.196 mmol, 1.0 equiv.), **S-13** (0.223 g, 0.196 mmol, 1.0 equiv.), $PdCl_2(PPh_3)_2$ (0.014 g, 10 mol%) and CuI (0.008 g, 20 mol%) were placed into a 25 mL round bottom flask. Degassed anhydrous dimethylformamide (2 mL) and triethylamine (2 mL) was added and allowed to stir at room temperature under nitrogen for 14 hours. The reaction mixture was cooled and brine (20 mL) was added. Product was extracted with ethyl acetate (30 mL). The organic layer was dried over Na_2SO_4 and solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography using methanol:dichloromethane (4:96) to provide a light yellow solid (0.270 g, 62%).

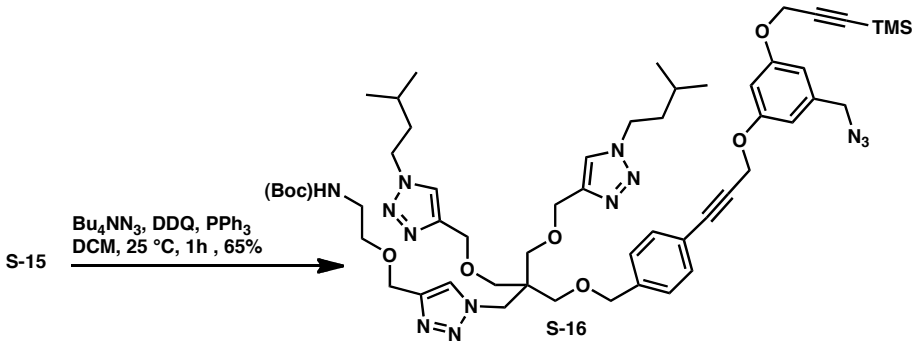
NMR Spectroscopy: ^{1}H NMR (400 MHz, $CDCl_3$, δ): 11.48 (s, 1H), 8.32 (s, 1H), 7.57-7.50 (m, 6H), 7.39-7.37 (m, 4H), 7.23-7.18 (m, 5H), 6.69-6.66 (m, 3H), 4.94 (bs, 1H), 4.89 (s, 4H), 4.72 (s, 12H), 4.44-4.42 (m, 6H), 4.34-4.27 (m, 10H), 3.55 (t, *J* = 6.0 Hz, 2H), 3.50-3.36 (m, 14H), 3.20 (q, *J* = 6.0 Hz, 2H), 2.27-2.22 (m, 8H), 1.95-1.87 (m, 10H), 1.76 (t, J = 6.0 Hz, 2H), 1.61-1.54 (m, 8H), 1.49 (s, 9H), 1.47 (s, 9H), 1.41 (s, 45H), ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.3, 163.5, 159.0, 156.3, 156.0, 153.3, 145.3, 144.6, 139.7, 138.9, 131.9, 131.8, 130.1, 130.0, 127.4, 127.1, 124.7, 122.6, 122.5, 122.4, 121.5, 121.1, 107.7, 102.5, 87.0, 86.9, 84.0, 83.8, 83.2, 80.4, 80.3, 79.3, 78.9, 72.8, 72.7, 69.2, 68.8, 68.5, 65.1, 64.8, 64.3, 58.8, 56.3, 53.7, 50.0, 49.8, 49.7, 45.3, 39.9, 38.2, 34.6, 29.8, 29.6, 28.5, 28.3, 28.1, 27.6, 26.2, 21.9. FT-IR (NaCl plate): 3332, 2976, 2869, 2361, 1718, 1686, 1539, 1436 cm^{-1}. Mass Spectrometry: HRMS-ESI (m/z): Calcd for $C_{113}H_{168}IN_{22}O_{24}$ $[M+2H]^{2+}$, 1108.6295. Found 1108.6330.



Compound S-15: Module **11** (0.250 g, 0.284 mmol, 1.0 equiv.), core **16** (0.120 g, 0.420 mmol, 1.5 equiv.), $PdCl_2(PPh_3)_2$ (0.020 g, 10 mol%) and CuI (0.010 g, 20 mol%) were placed into a 25 mL round bottomed flask. Degassed, anhydrous dimethyl formamide (1.5 mL) and triethylamine (1.5 mL) were added and this solution stirred at room temperature under nitrogen for 12 hours. The reaction mixture was cooled and brine (20 mL) was added. The product was extracted with

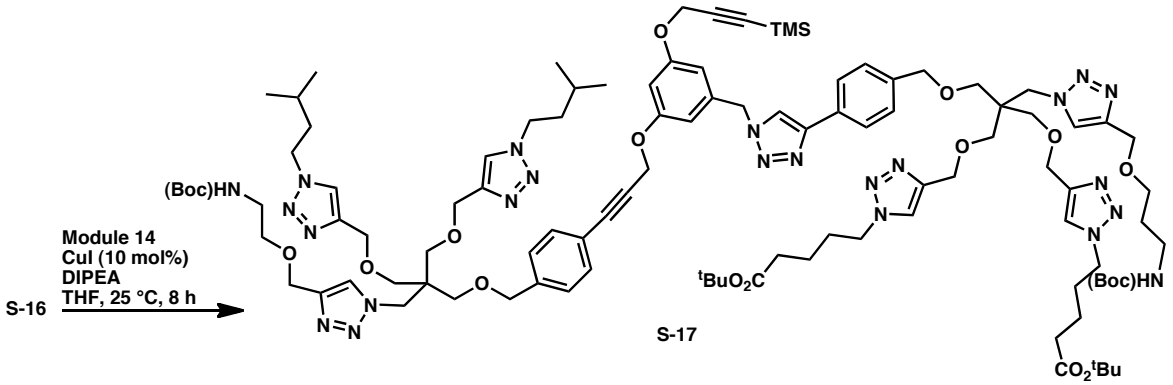
ethyl acetate (30 mL). The organic layer was dried over Na_2SO_4 and solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography using methanol:dichloromethane (5:95) to provide light yellow solid (0.290 g, 98%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.51 (s, 1H), 7.47 (s, 2H), 7.31 (d, *J* = 9.0 Hz, 2H), 7.12 (d, *J* = 9.0 Hz, 2H), 6.63 (s, 1H), 6.55 (s, 1H), 6.46 (s, 1H), 5.23 (bs, 1H), 4.79 (s, 2H), 4.57 (s, 2H), 4.56 (s, 4H), 4.47 (s, 6H), 4.35 (s, 2H), 4.33 (s, 2H), 4.24 (t, *J* = 6.0 Hz, 4H), 3.82 (bs, 1H), 3.46 (t, *J* = 3.0 Hz, 2H), 3.30 (s, 4H), 3.27 (s, 2H), 3.22 (m, 2H), 1.68 (q, *J* = 6.0 Hz, 4H), 1.49 (m, 2H), 1.33 (s, 9H), 0.86 (d, *J* = 3.0 Hz, 12H), 0.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 158.9, 158.8, 156.0, 144.4, 144.2, 138.8, 131.7, 127.3, 124.8, 122.5, 121.4, 106.0, 105.9, 101.1, 99.9, 92.6, 86.8, 84.0, 79.0, 77.4, 72.7, 69.5, 68.6, 64.6, 64.4, 64.1, 56.8, 56.6, 49.7, 48.6, 45.2, 40.3, 38.9, 28.3, 25.4, 22.1, 22.1, -0.32. FT-IR (NaCl plate): 3349, 3141, 2958, 2870, 2180, 1708, 1596, 1411, 1387 cm^{-1}.



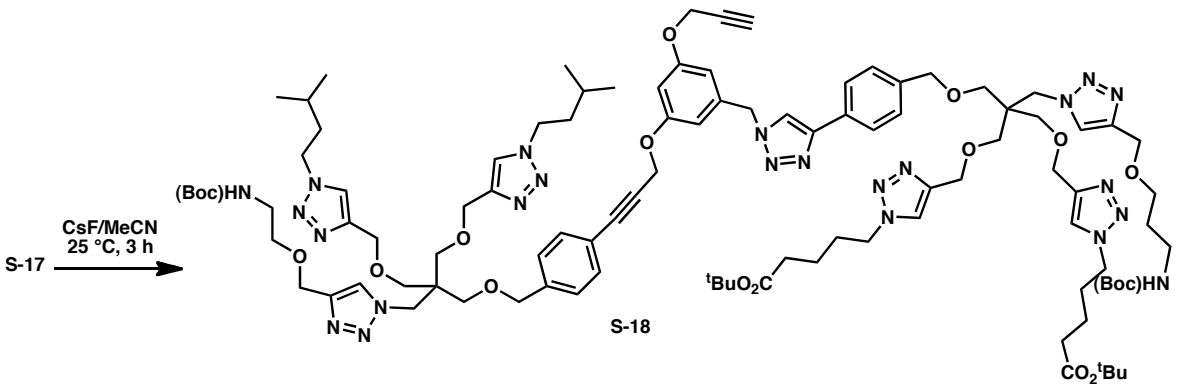
Compound S-16: Tetrabutylammonium azide (0.128 g, 0.45 mmol, 2.0 equiv) was added to a mixture of PPh_3 (0.088 g, 0.337 mmol, 1.5 equiv.) and DDQ (0.102 g, 0.45 mmol, 2.0 equiv.) in anhydrous dichloromethane (3 mL) at room temperature. Benzyl alcohol **S-15** (0.233 g, 0.225 mmol, 1.0 equiv.) was then added the reaction mixture and stirred for 1 h. The reaction mixture was diluted with dichloromethane (20 mL) and washed with 10% Na_2CO_3 (20 ml X 3). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography using methanol:dichloromethane (2:98) as an eluent to provide pure product (0.155 g, 65%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.60 (s, 3H), 7.41 (d, *J* = 9.0 Hz, 2H), 7.23 (d, *J* = 9.0 Hz, 2H), 6.62-6.58 (m, 3H), 5.10 (bs, 1H), 4.89 (s, 2H), 4.67 (s, 2H), 4.57 (s, 2H), 4.56 (s, 4H), 4.44 (s, 2H), 4.42 (s, 2H), 4.33 (t, *J* = 6.0 Hz, 4H), 4.29 (s, 2H), 3.57 (t, *J* = 3.0 Hz, 2H), 3.39 (s, 4H), 3.37 (s, 2H), 3.32 (m, 2H), 1.78 (q, *J* = 6.0 Hz, 4H), 1.55 (m, 2H), 1.41 (s, 9H), 0.95 (d, *J* = 3.0 Hz, 12H), 0.17 (s, 9H). Mass Spectrometry: HRMS-ESI (m/z): Calcd for $C_{54}H_{78}N_{23}O_8Si^+$ $[M+H]^+$, 1064.5886. Found 1064.5854.



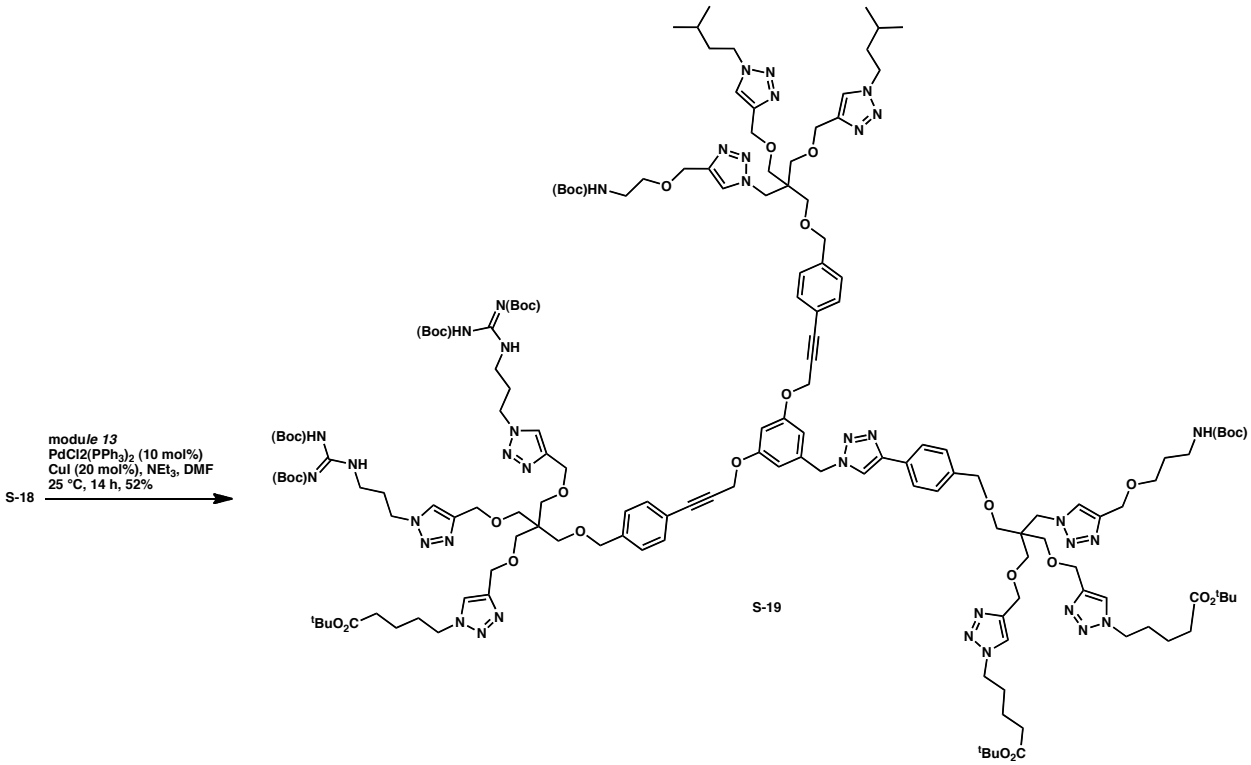
Compound S-17: The azide **S-16** (0.125 g, 0.117 mmol, 1.0 equiv) and alkyne **14** (0.112 g, 0.117 mmol, 1.0 equiv) were dissolved in tetrahydrofuran (5.0 mL). To this solution CuI (0.004 g, 10 mol %) and Hünig's base (0.2 mL) were added and stirred at room temperature for 8 hours. The reaction mixture was concentrated, diluted with water (20 mL) and extracted with dichloromethane (30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography using methanol /dichloromethane (4: 96) as an eluent to provide pure product (0.175 g, 74%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.74-7.70 (m, 3H), 7.56-7.50 (m, 5H), 7.33 (d, *J* = 9.0 Hz, 2H), 7.28-2.26 (m, 2H), 7.14 (d, *J* = 9.0 Hz, 2H), 6.60 (s, 1H), 6.56 (s, 1H), 6.52 (s, 1H), 5.47 (s, 2H), 5.02 (bs, 1H), 4.83(bs, 1H), 4.59 (s, 2H), 4.52 (s, 12H), 4.42 (s, 2H), 4.37 (s, 6H), 4.25 (m, 10H), 3.49 (m, 4H), 3.32 (m, 14H), 3.13 (m, 2H), 2.21 (t, *J* = 6.0 Hz, 4H), 1.85-1.83 (m, 4H), 1.76-1.69 (m, 6H), 1.57-1.50 (m, 6H), 1.36 (s, 36H), 0.89 (d, *J* = 3.0 Hz, 12H), 0.10 (s, 9H). FT-IR (NaCl plate): 3396, 3140, 2959, 2869, 1710, 1652, 1419, 1292 cm^{-1}.



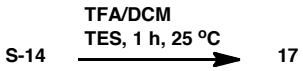
Compound S-18: CsF (0.017 g, 0.12 mmol) was added to the solution of **S-17** (0.150 g, 0.074 mmol) in acetonitrile (2.0 mL) and stirred at room temperature for 3 h. Saturated ammonium chloride solution was added to the organic layer and extracted using dichloromethane (20.0 mL). Organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to provide pure product **S-18** (0.142 g, 99%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.72-7.67 (m, 3H), 7.52-7.46 (m, 5H), 7.30 (d, *J* = 9.0 Hz, 2H), 7.25-2.23 (m, 2H), 7.11 (d, *J* = 9.0 Hz, 2H), 6.57 (s, 1H), 6.54 (s, 1H), 6.45 (s, 1H), 5.45 (s, 2H), 5.10 (bs, 1H), 4.95 (bs, 1H), 4.79 (s, 2H), 4.59 (s, 2H), 4.48 (s, 8H), 4.46 (s, 4H), 4.39 (s, 2H), 4.34 (s, 6H), 4.24 (m, 10H), 3.47 (m, 4H), 3.32-3.24 (m, 14H), 3.11 (m, 2H), 2.44 9m, 1H), 2.16 (t, *J* = 6.0 Hz, 4H), 1.85-1.79 (m, 4H), 1.72-1.67 (m, 6H), 1.53-1.48 (m, 6H), 1.33 (s, 36H), 0.86 (d, *J* = 3.0 Hz, 12H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.3, 159.4, 159.1, 156.0, 147.8, 144.6, 144.5, 144.3, 139.0, 138.1, 137.0, 132.5, 131.8, 129.9, 128.1, 127.3, 125.6, 124.8, 124.7, 122.6, 122.5, 121.2, 198.0, 107.8, 107.6, 102.2, 87.3, 83.4, 80.4, 79.1, 78.8, 78.0, 76.1, 72.9, 72.7, 69.5, 68.8, 68.7, 68.5, 64.7, 64.3, 64.2, 56.8, 56.0, 54.1, 49.9, 49.8, 48.7, 45.3, 40.4, 39.0, 38.2, 34.2, 29.8, 29.6, 28.46, 28.43, 25.522.2, 21.9. Mass Spectrometry: HRMS-ESI (*m/z*): Calcd for $C_{100}H_{143}N_{23}O_{18}$ $[M+H]^+$, 1956.1088. Found 1956.1096.



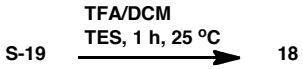
Compound S-18: Module **14** (0.49 g, 0.072 mmol, 1.0 equiv.), alkyne **S-18** (0.142 g, 0.072 mmol, 1.0 equiv.), $PdCl_2(PPh_3)_2$ (0.005 g, 10 mol%) and copper iodide (0.002 g, 20 mol%) were added to a 25 mL round bottomed flask. Degassed anhydrous dimethylformamide (1.5 mL) and triethylamine (1.5 mL) were added, and the solution was stirred at room temperature under nitrogen for 14 hours. The reaction mixture was cooled, brine (20 mL) was added and the product was extracted with ethyl acetate (20 mL). Solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography using methanol:dichloromethane (5:95) to provide light yellow solid (0.118 g, 52%).

NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, δ): 11.47 (s, 2H), 8.45 (m, 2H), 7.80-7.74 (m, 4H), 7.60-7.52 (m, 7H), 7.40-7.30 (m, 7H), 7.21-7.17 (m, 3H), 6.68-6.67 (m, 3H), 5.54 (s, 2H), 5.15 (bs, 1H), 4.99 (bs, 1H), 4.88 (s, 4H), 4.57-4.54 (m, 18H), 4.47-4.28 (m, 26H), 3.59-3.32 (m, 28H), 3.19 (m, 2H), 2.27-2.13 (m, 12H), 1.96-1.86 (m, 8H), 1.81-1.74 (m, 8H), 1.62-1.55 (m, 8H), 1.48 (s, 36H), 1.42 (s, 45H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 172.4, 163.5, 159.6, 153.3, 147.9, 145.5, 145.3, 144.8, 144.7, 144.7, 144.6, 144.5, 139.9, 139.1, 138.2, 137.1, 132.6, 131.99, 131.89, 131.0, 130.1, 128.9, 127.5, 127.4, 127.1, 125.8, 124.9, 124.8, 123.3, 122.7, 122.5, 122.4, 121.38, 120.9, 119.9, 107.7, 102.3, 94.5, 87.6, 87.3, 83.4, 80.5, 79.4, 79.2, 79.1, 73.0, 72.9, 72.6, 69.7, 69.4, 69.3, 69.1, 68.6, 65.26, 65.06, 65.0, 64.9, 64.44, 64.42, 57.0, 54.3, 50.06, 50.02, 48.8, 47.6, 45.5, 45.4, 40.5, 39.1, 38.3, 34.7, 30.5, 29.9, 29.8, 29.78, 29.73, 28.5, 28.4, 28.2, 25.7, 22.3, 22.0. FT-IR (NaCl plate): 3324, 2959, 2869, 1721, 1613, 1415, 1330 cm^{-1}. Mass Spectrometry: HRMS-ESI (*m/z*): Calcd for $C_{158}H_{234}N_{38}O_{32}$ $[M+2H]^{2+}$, 1588.8998. Found 1588.9016.



Compound 17: To a stirred solution of compound **S-14** (0.036 g, 0.016 mmol, 1.0 equivalent) in DCM (2.40 mL) was added triethylsilane (30 mL) and trifluoroacetic acid (0.6 ml) and the resulting reaction mixture was stirred at room temperature for 1hour, then concentrated under reduced pressure. Cooled diethyl ether (10 mL) was added and the product was precipitated. The product was filtered and washed with more with cooled ether to provide the desired compound (0.032 g, 95%) as a TFA salt.

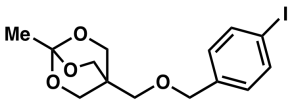
NMR Spectroscopy: ^{1}H NMR (300 MHz, CD_3OD, δ): 7.94-7.80 (m, 5H), 7.40-7.35 (m, 4H), 7.26-7.20 (m, 5H), 6.78-6.70 (m, 3H), 4.56-4.36 (m, 30H), 3.52 (m, 2H), 3.50-3.32 (m, 12H), 3.25-3.20 (m, 2H), 3.09-3.05 (m, 2H), 3.33 (t, *J* = 3.0 Hz, 8H), 1.96-1.92 (m, 12H), 1.62-1.54 (m, 12H). Mass Spectrometry: MALDI-TOF (*m/z*): Calcd. for $C_{82}H_{111}N_{22}O_{18}^+$ $[M+H]^+$, 1691.844; Found 1692.473.



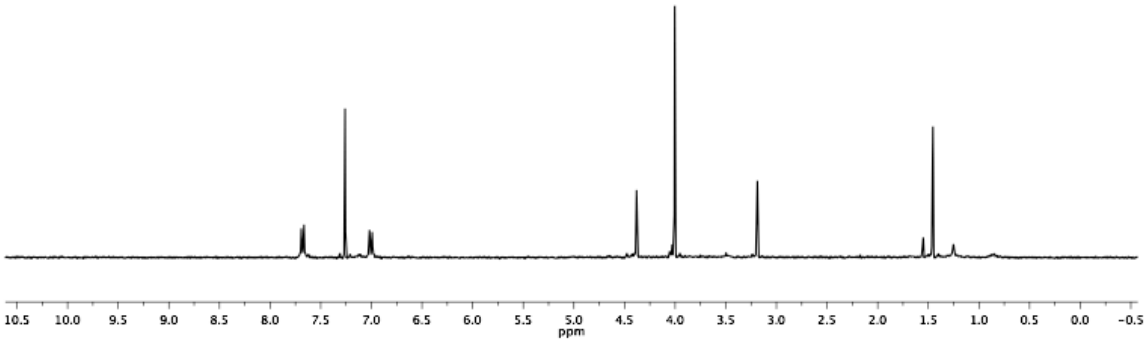
Compound 18: To a stirred solution of compound **S-19** (0.032 g, 0.01 mmol, 1.0 equivalent) in dichloromethane (4 mL) was added triethylsilane (50 mL) and trifluoroacetic acid (1.00 ml) and the resulting reaction mixture was stirred at room temperature for 1 hour. The solvent was removed under reduced pressure. Cooled diethyl ether (10 mL) was added and the product was precipitated. The product was filtered and washed with more cooled ether to provide the desired compound (0.030 g, 95%) as a TFA salt.

NMR Spectroscopy: ^{1}H NMR (300 MHz, CD_3OD, δ): 8.40 (s, 2H), 7.94-7.74 (m, 10H), 7.34-7.29 (m, 6H), 7.18-7.15 (m, 5H), 6.80-6.76 (m, 3H), 5.67 (s, 2H), 5.51 (s, 2H), 5.00 (s, 6H), 4.63-4.34 (m, 40H), 3.73-3.38 (m, 21H), 3.25-3.07 (m, 9H), 2.34-2.16 (m, 12H), 1.94-1.89 (m, 8H), 1.76-1.74 (m, 4H), 1.61-1.35 (m, 12H). Mass Spectrometry: MALDI-TOF (*m/z*): Calcd. for $C_{116}H_{163}N_{38}O_{20}^+$ $[M+H]^+$, 2408.290; Found 2408.754.

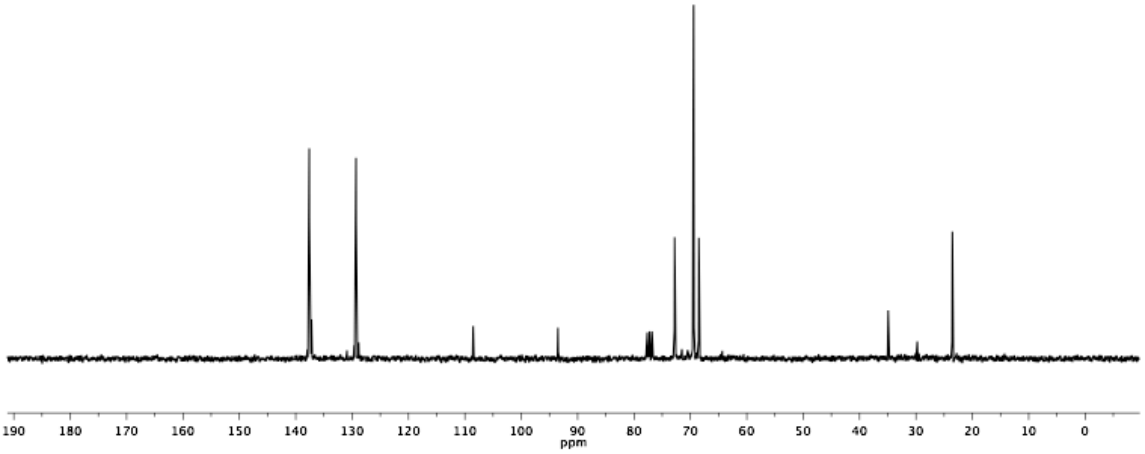
Spectroscopic Data



S-1



^{1}H NMR



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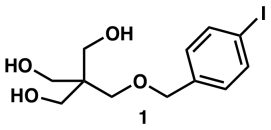

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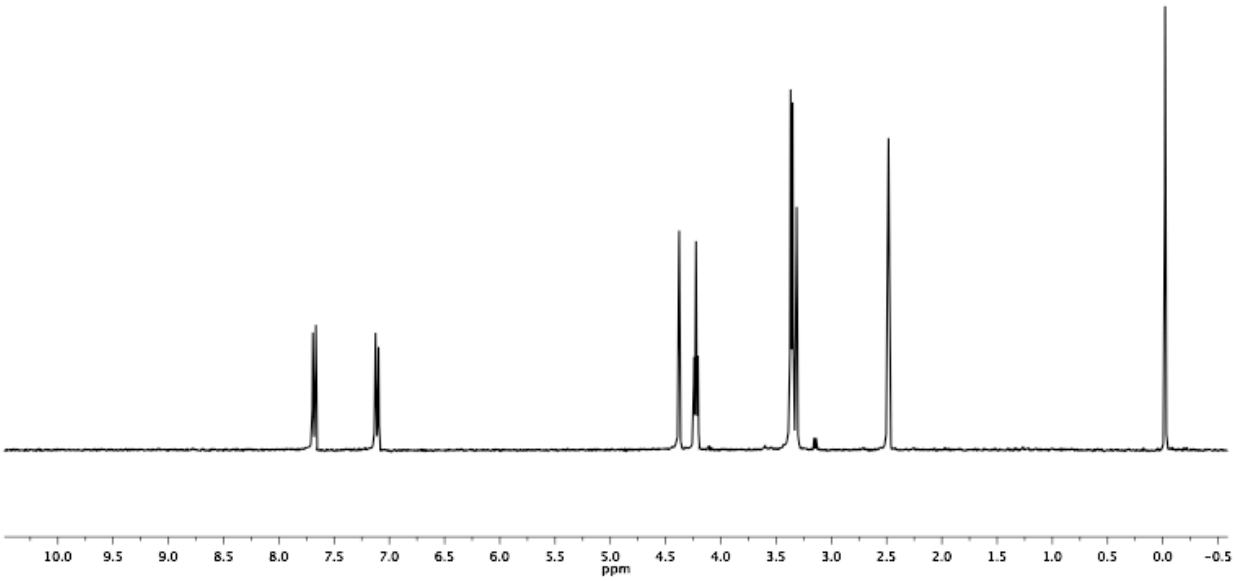

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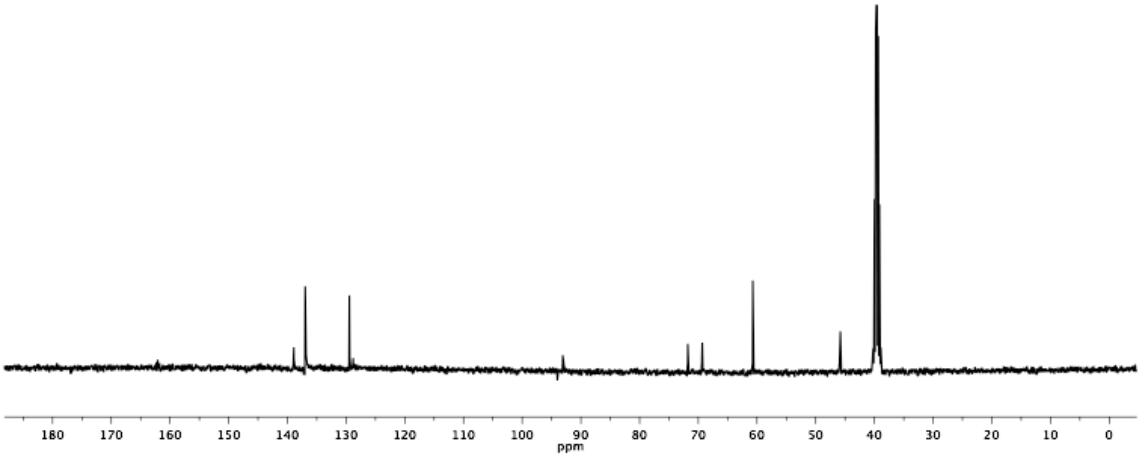

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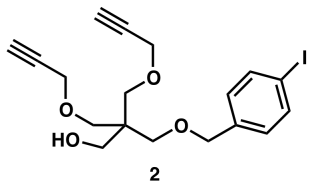

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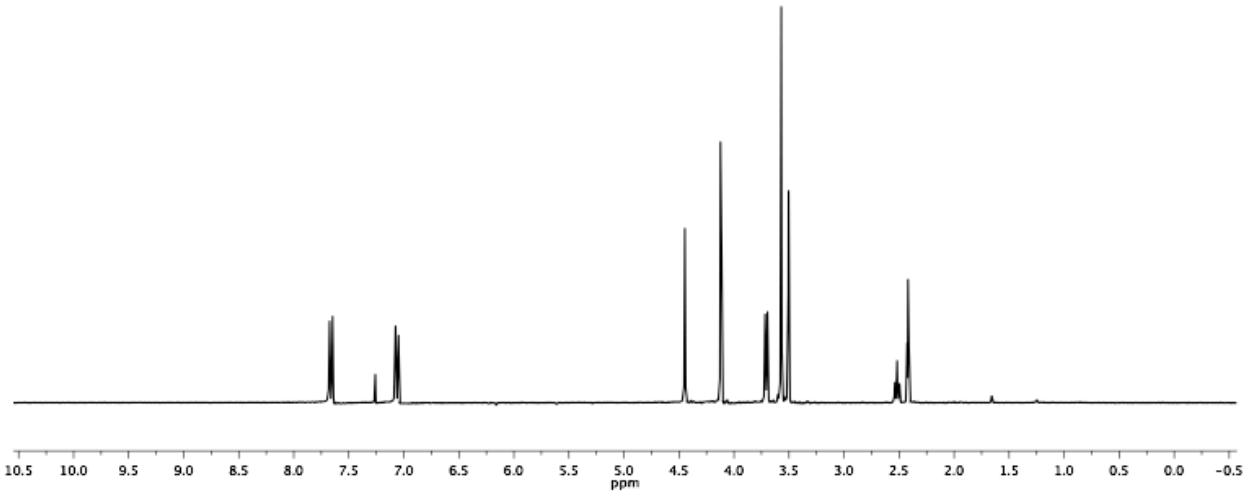

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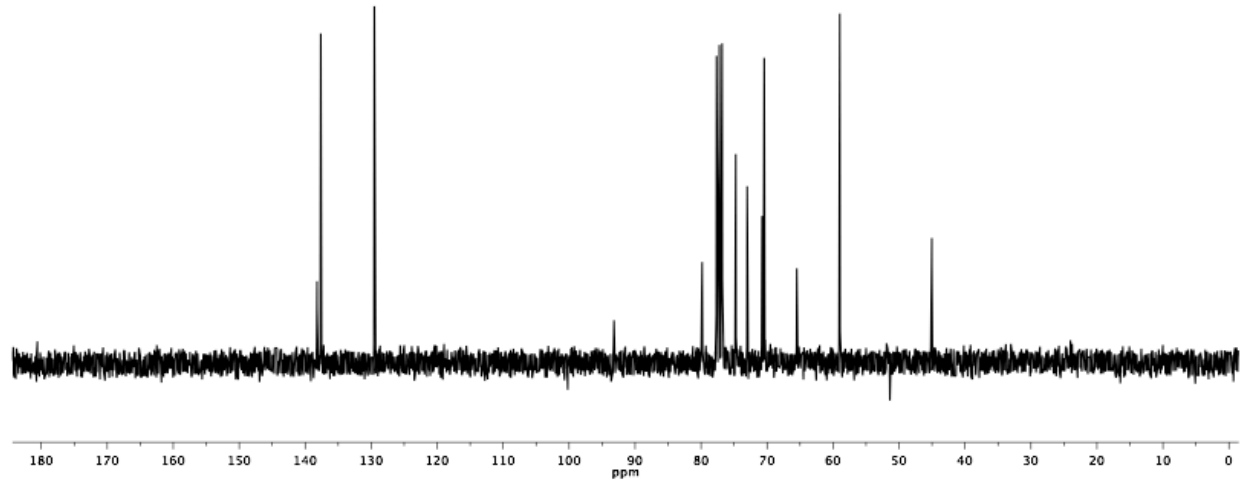

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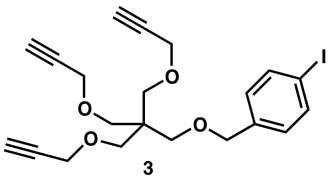

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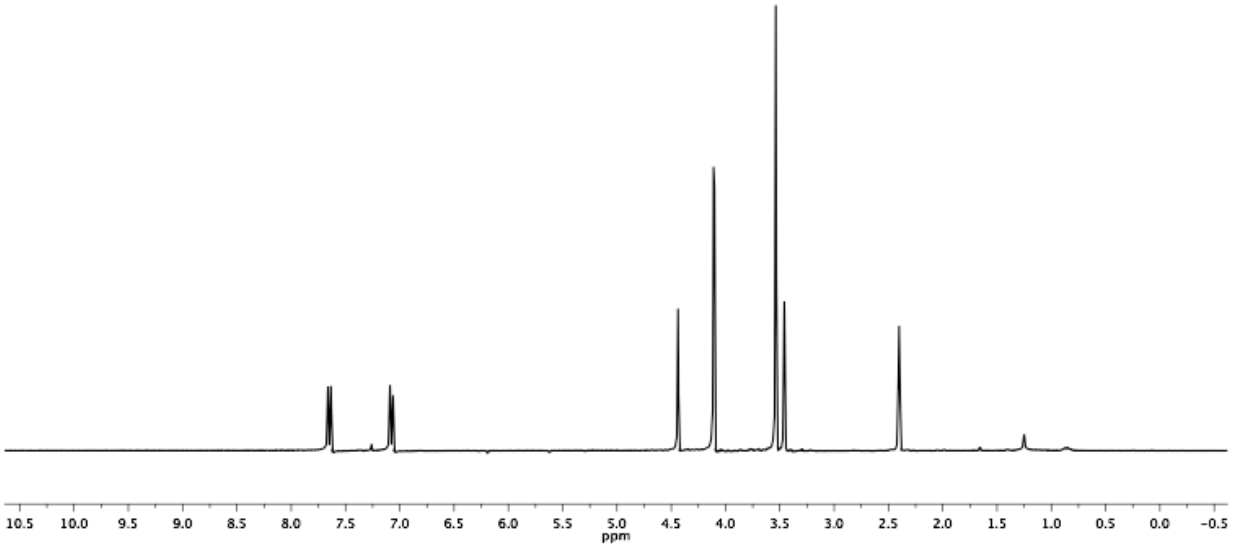

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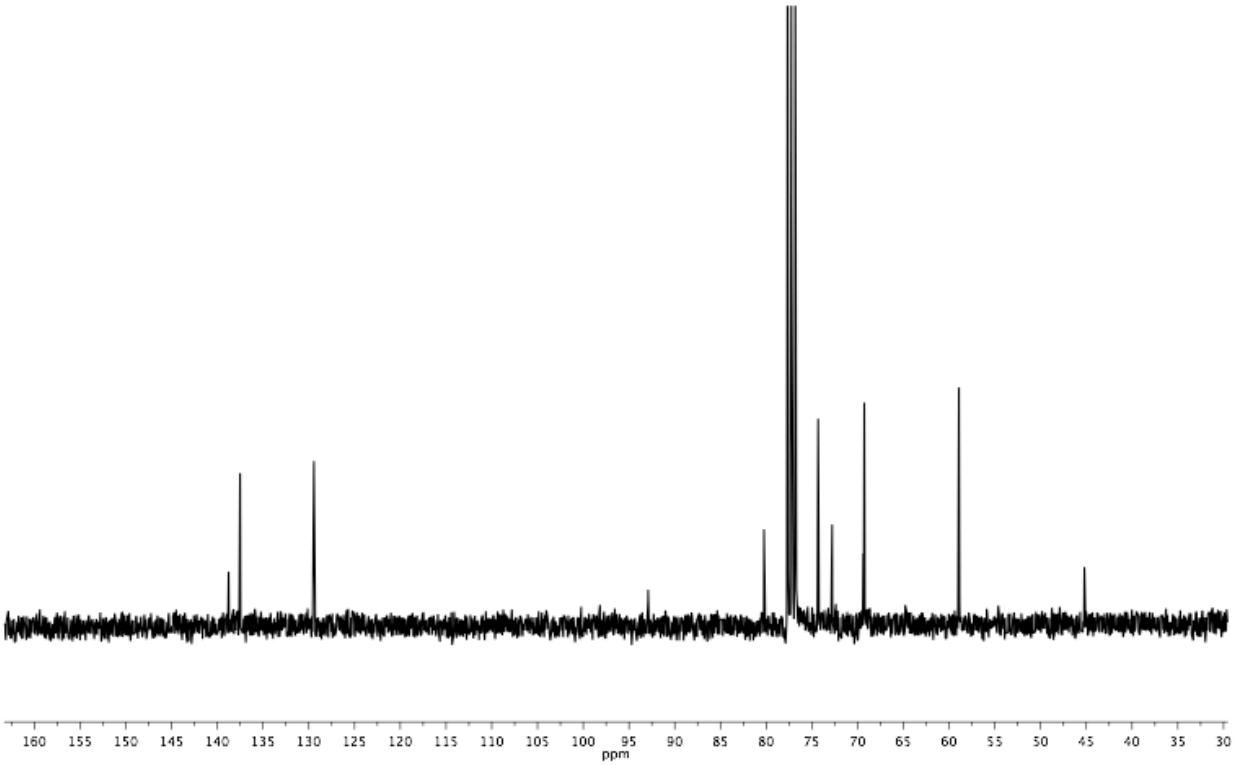

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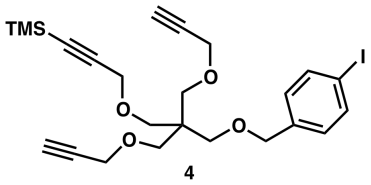

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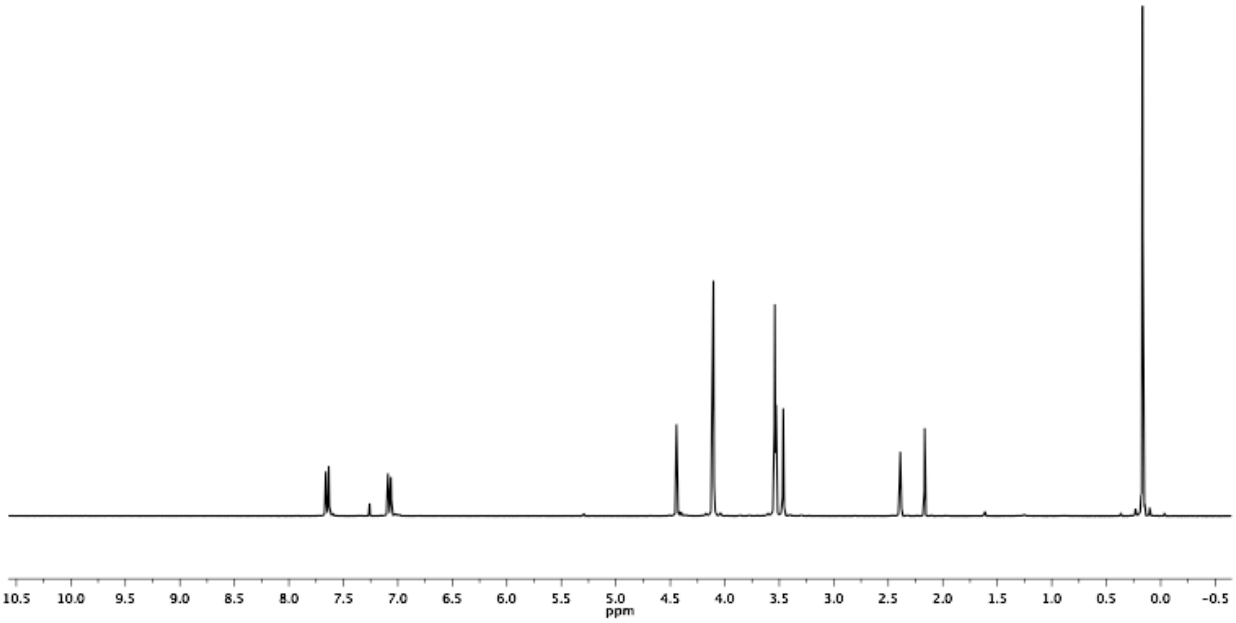

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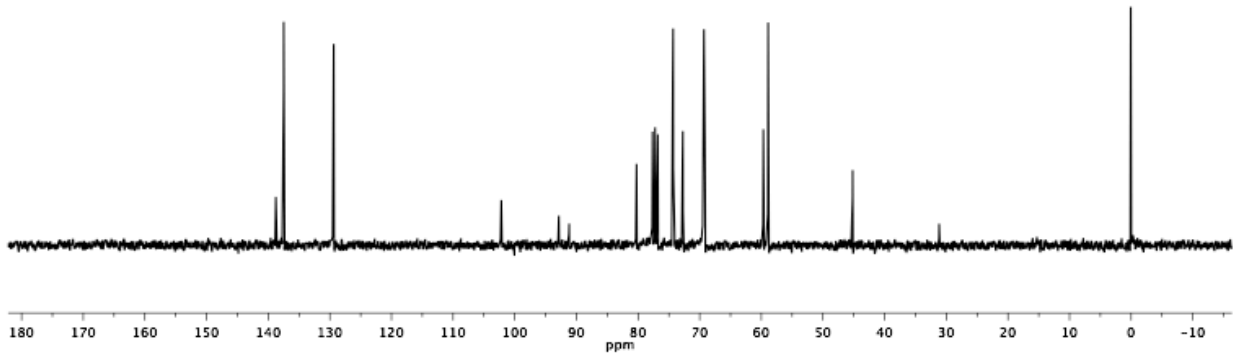

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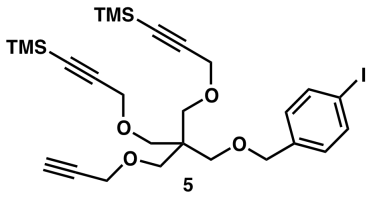

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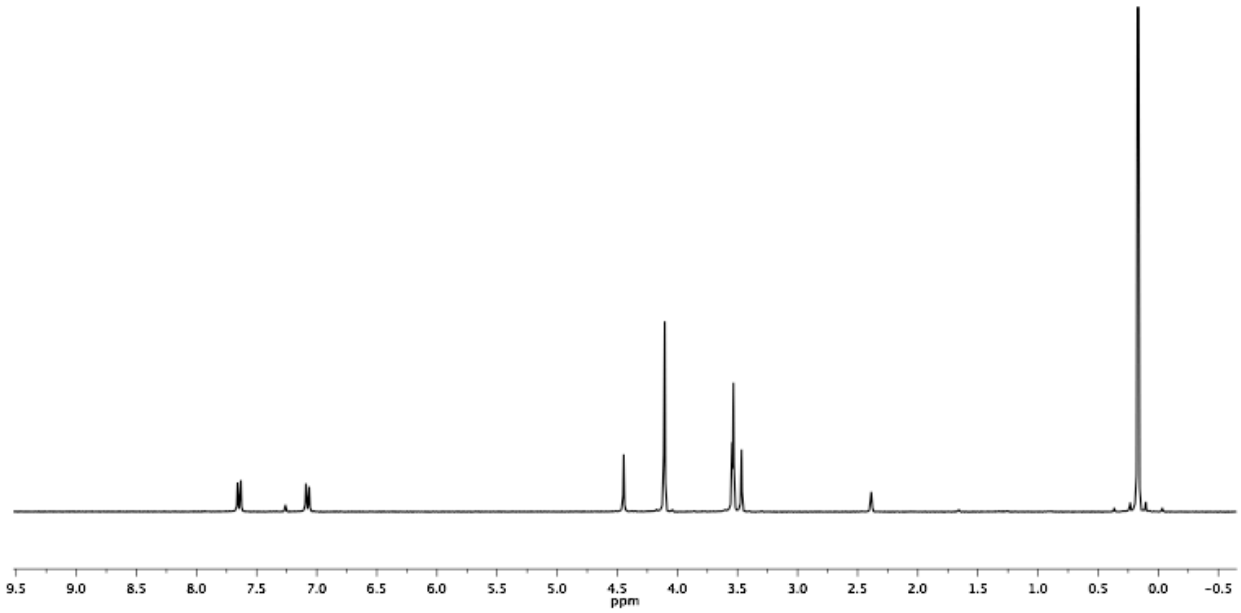

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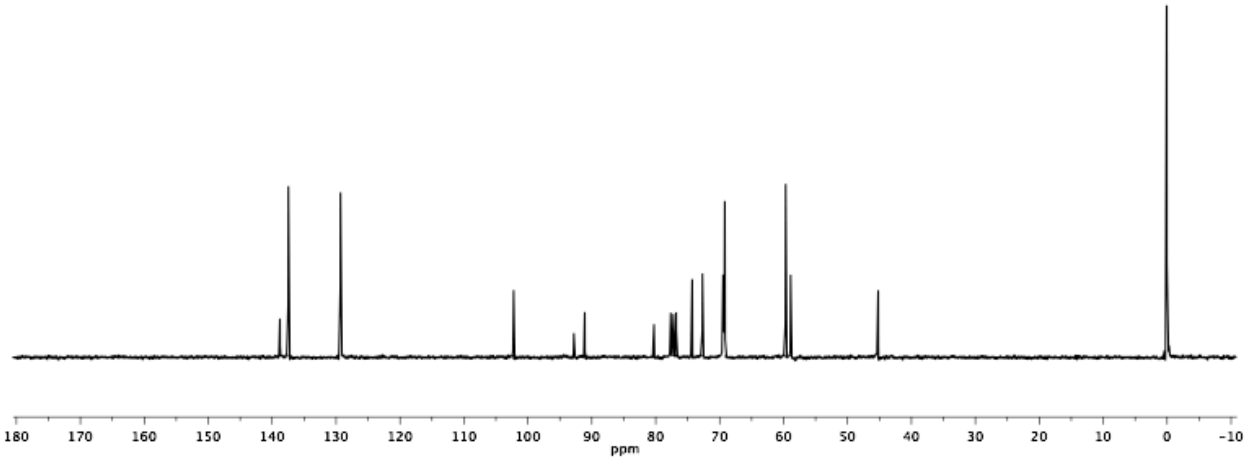

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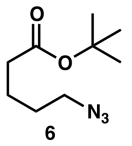

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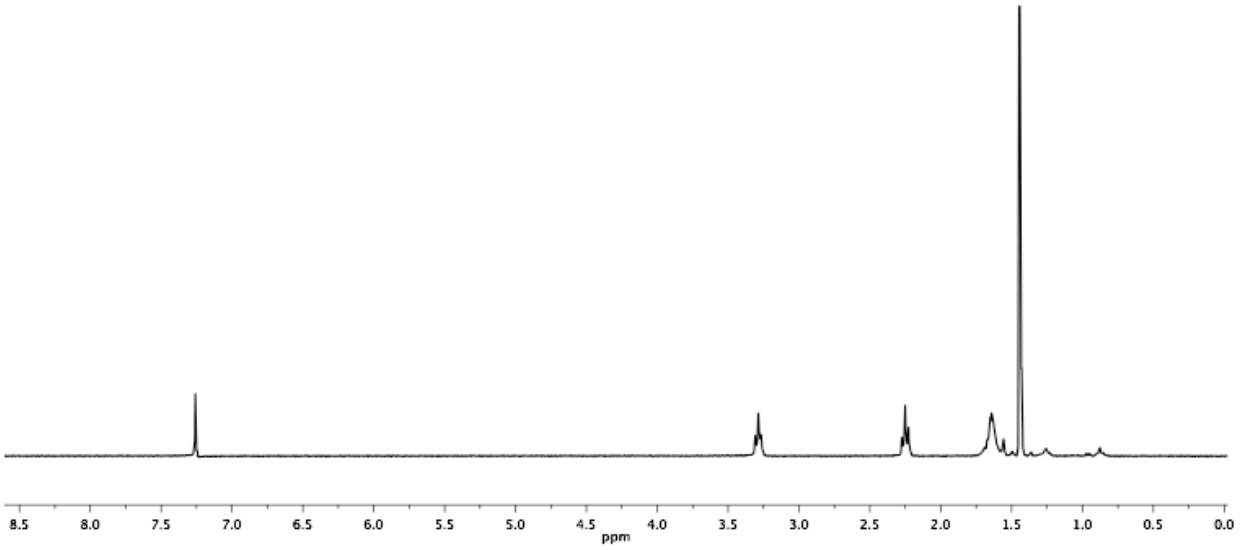

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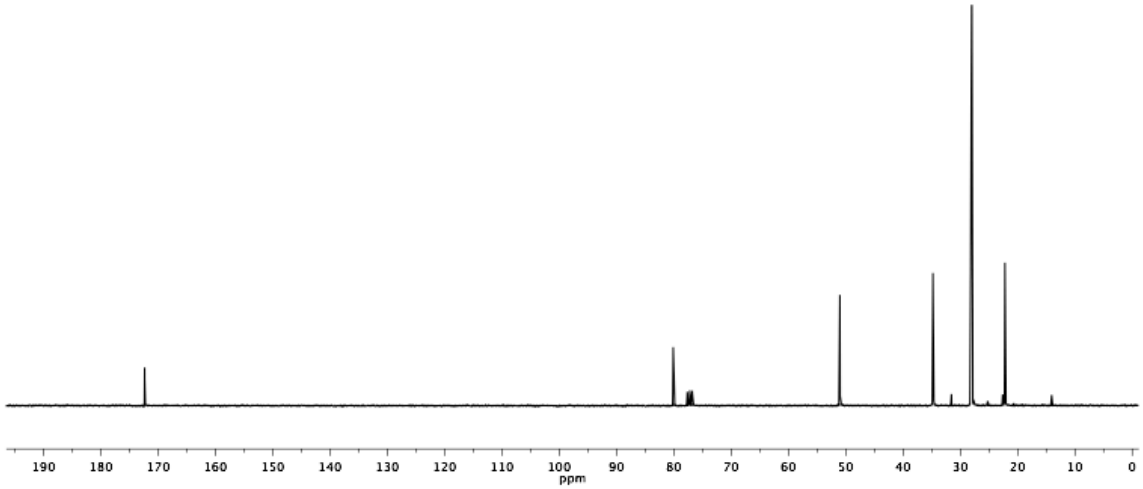

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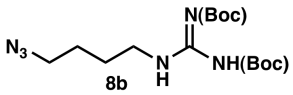

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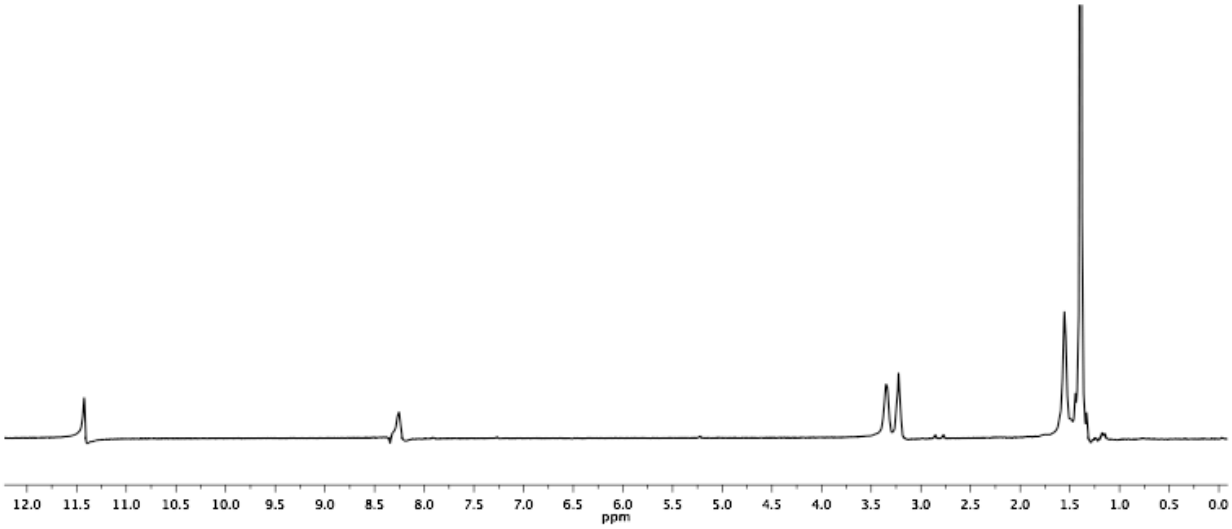

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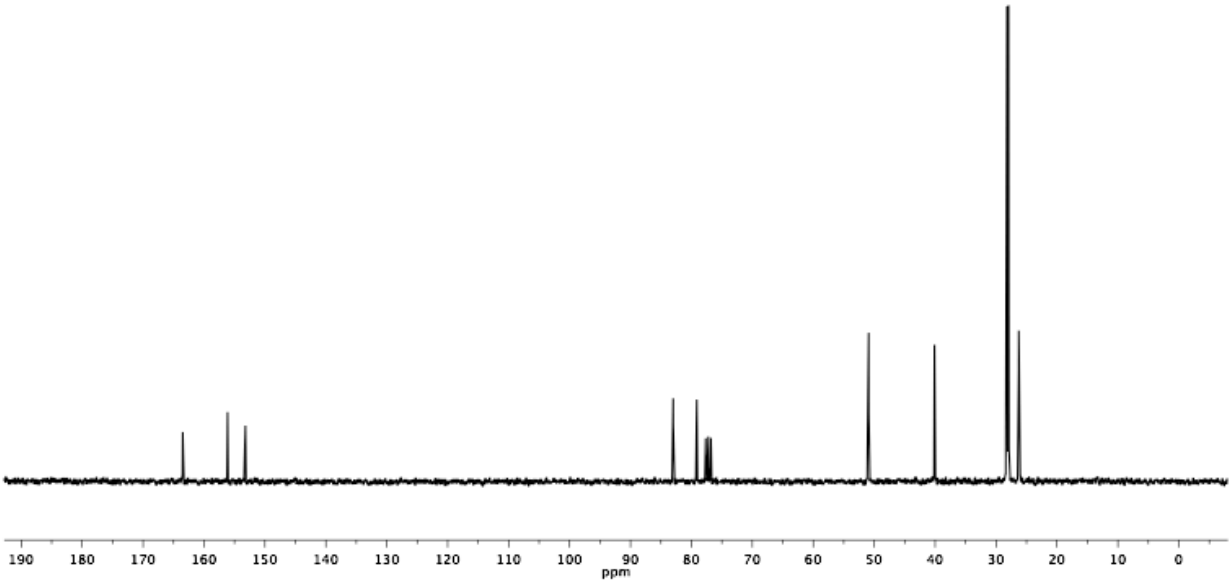

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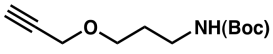

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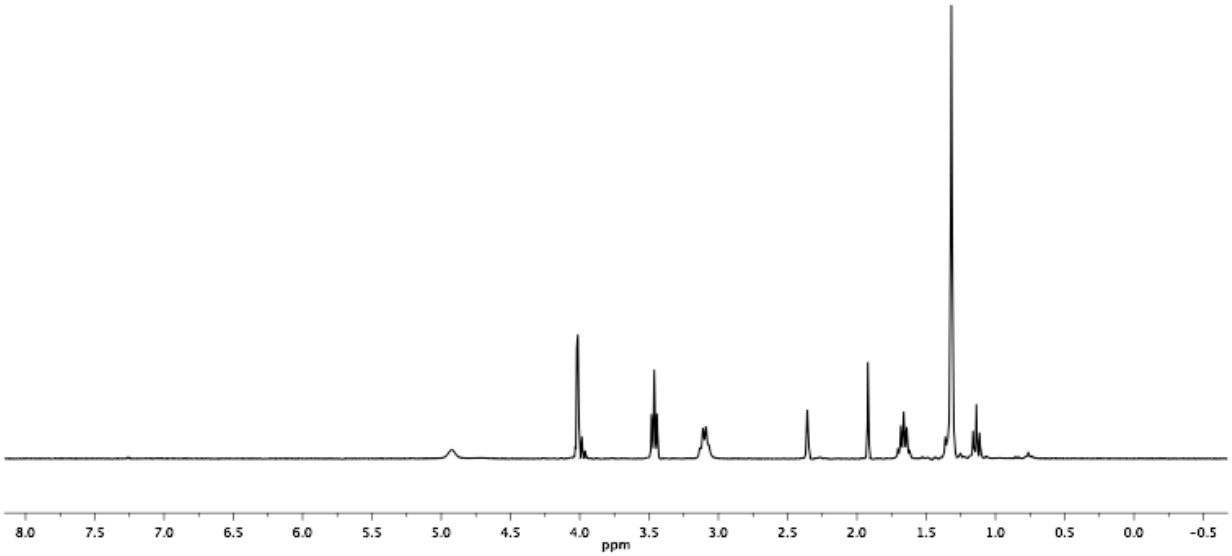

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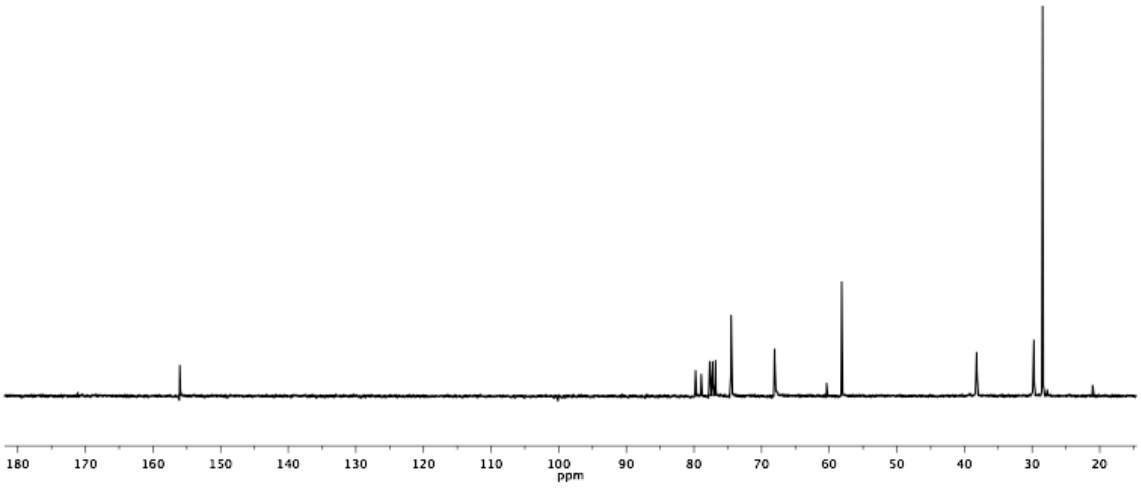

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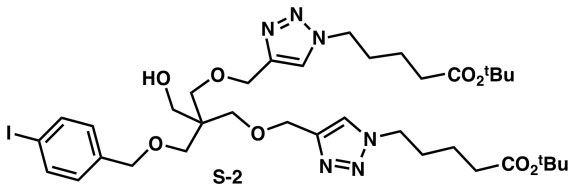
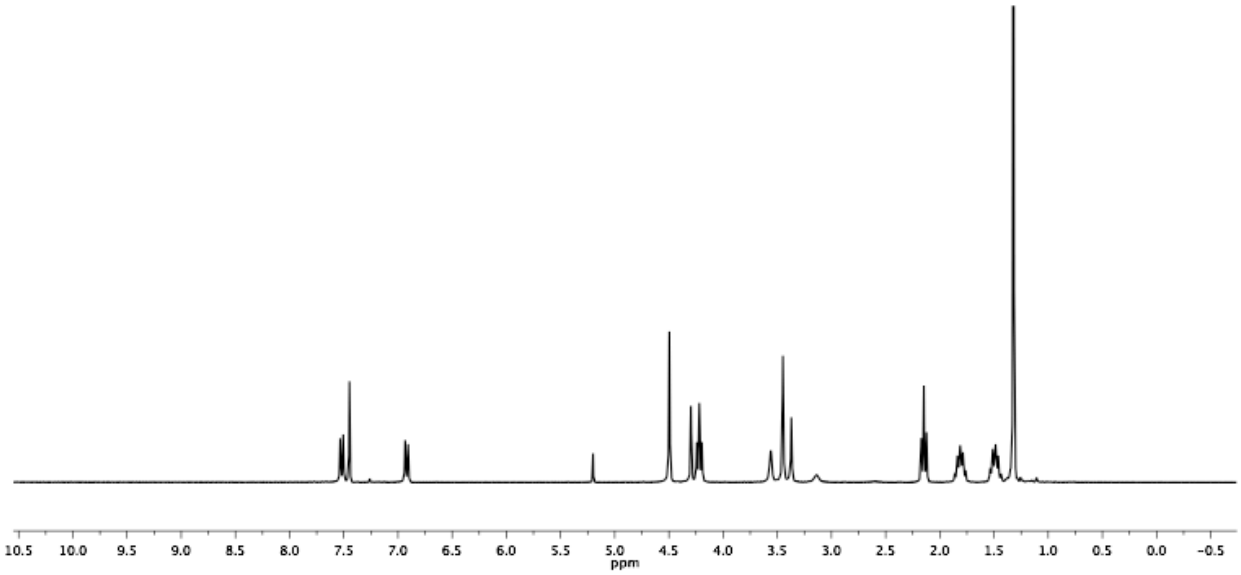


S-2



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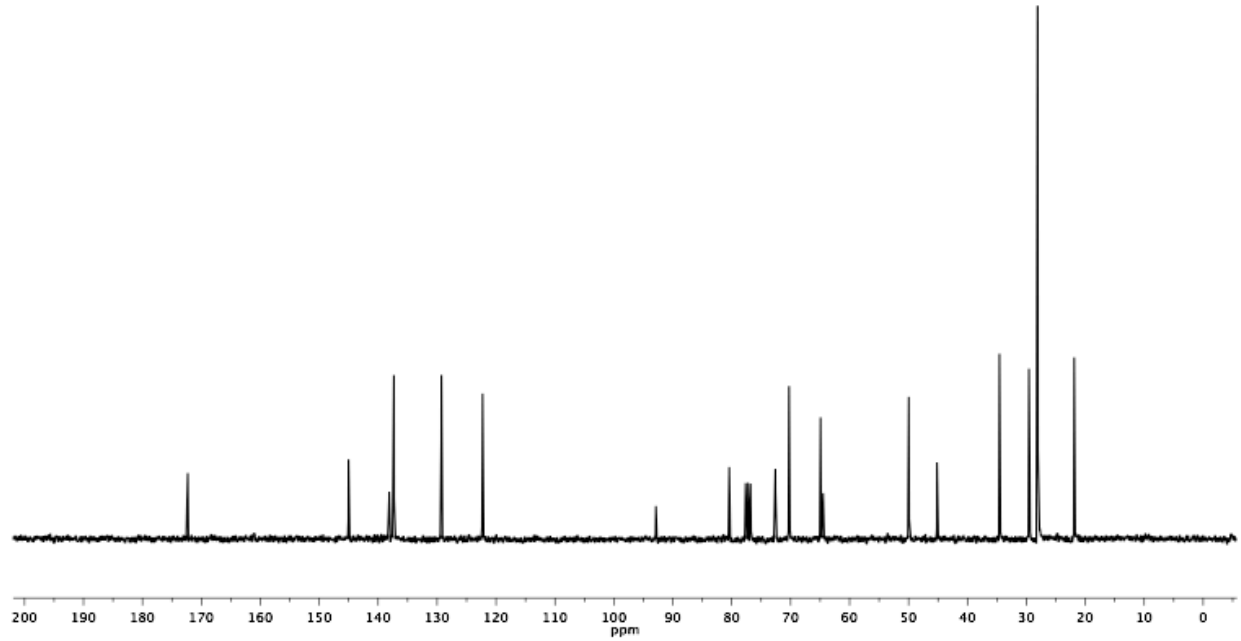

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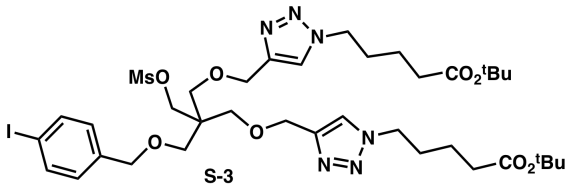

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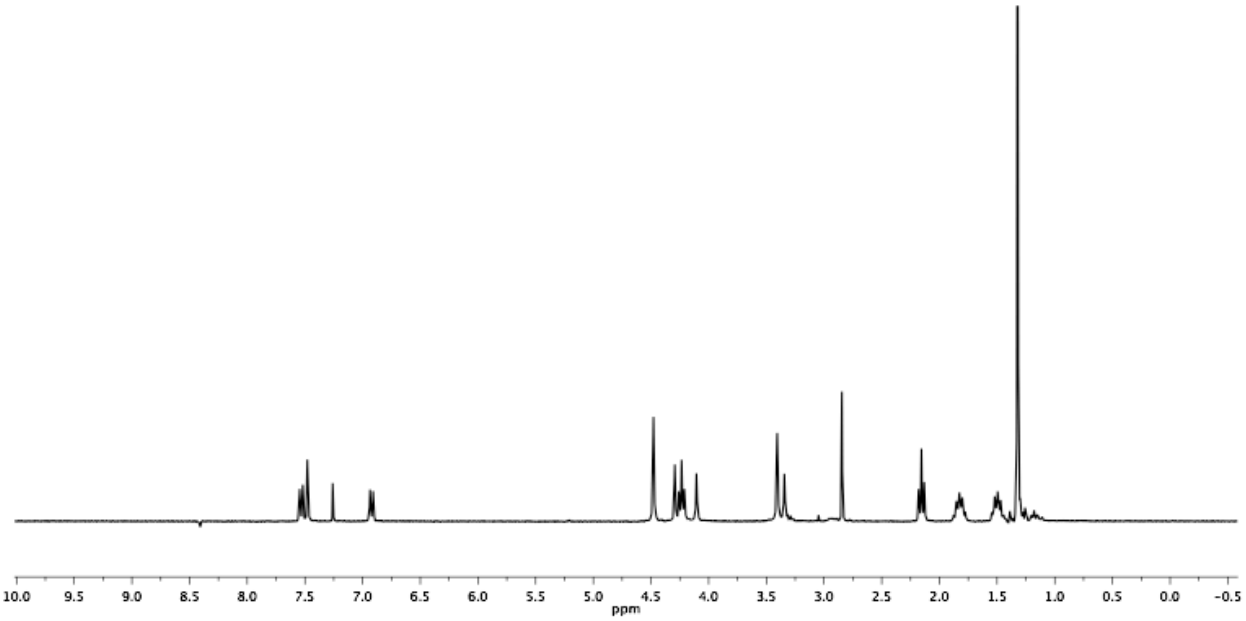

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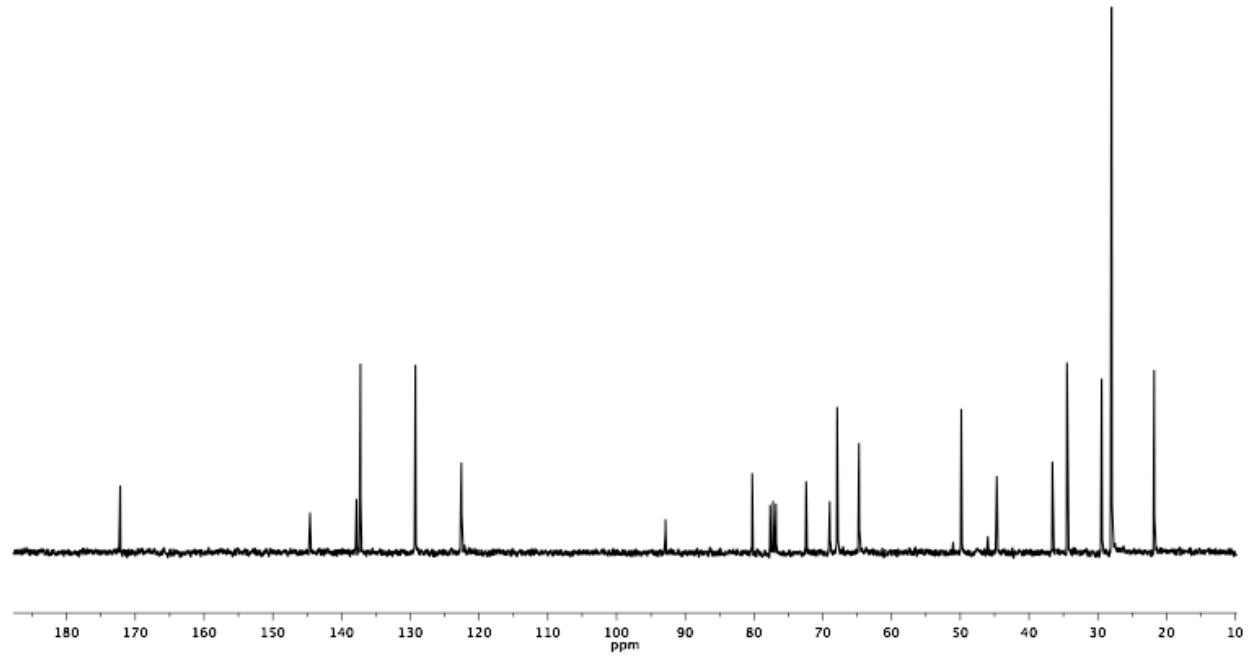

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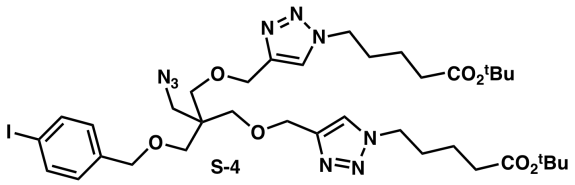

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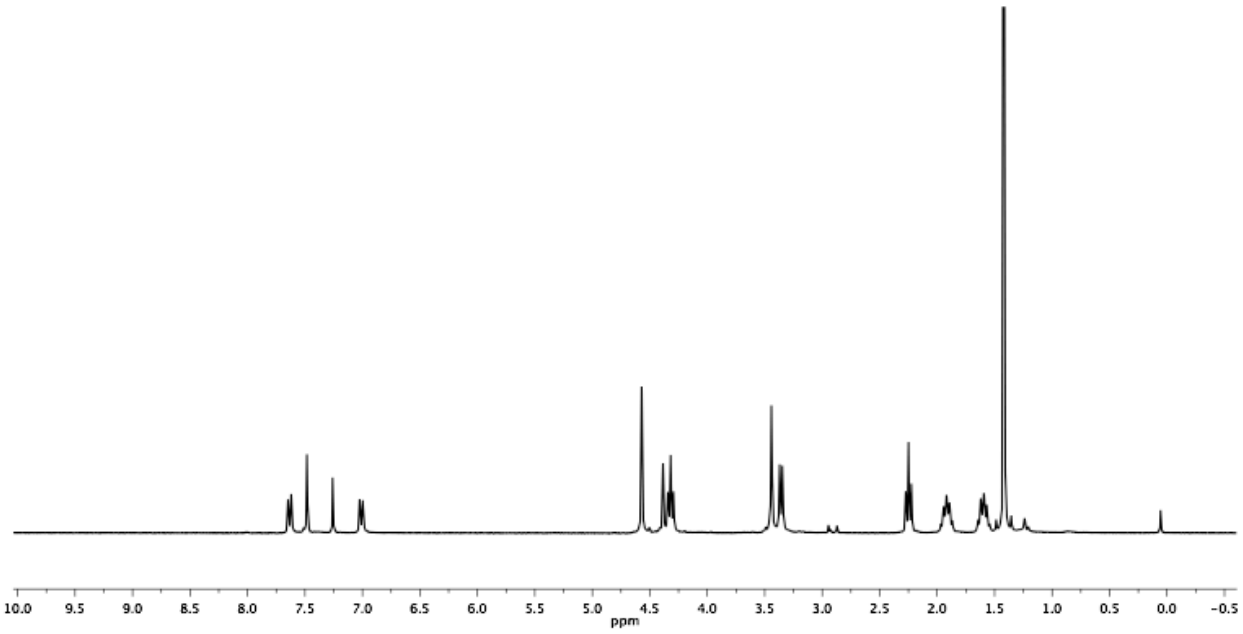

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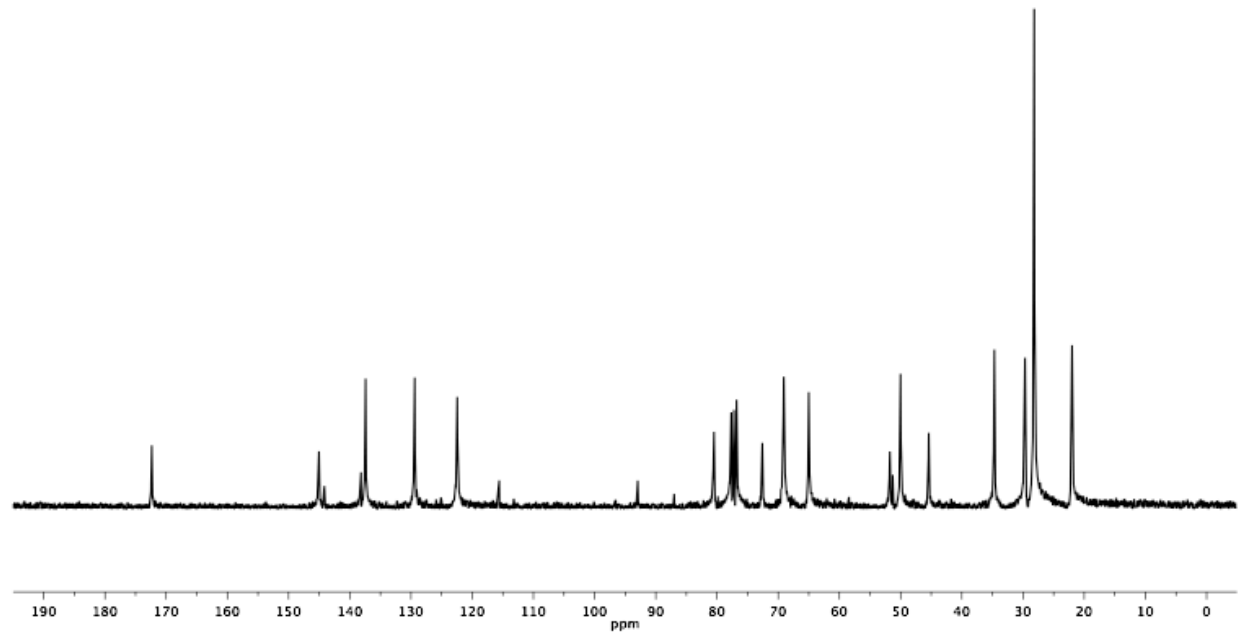

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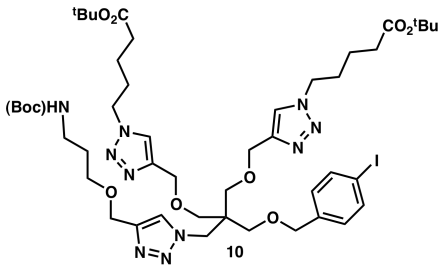

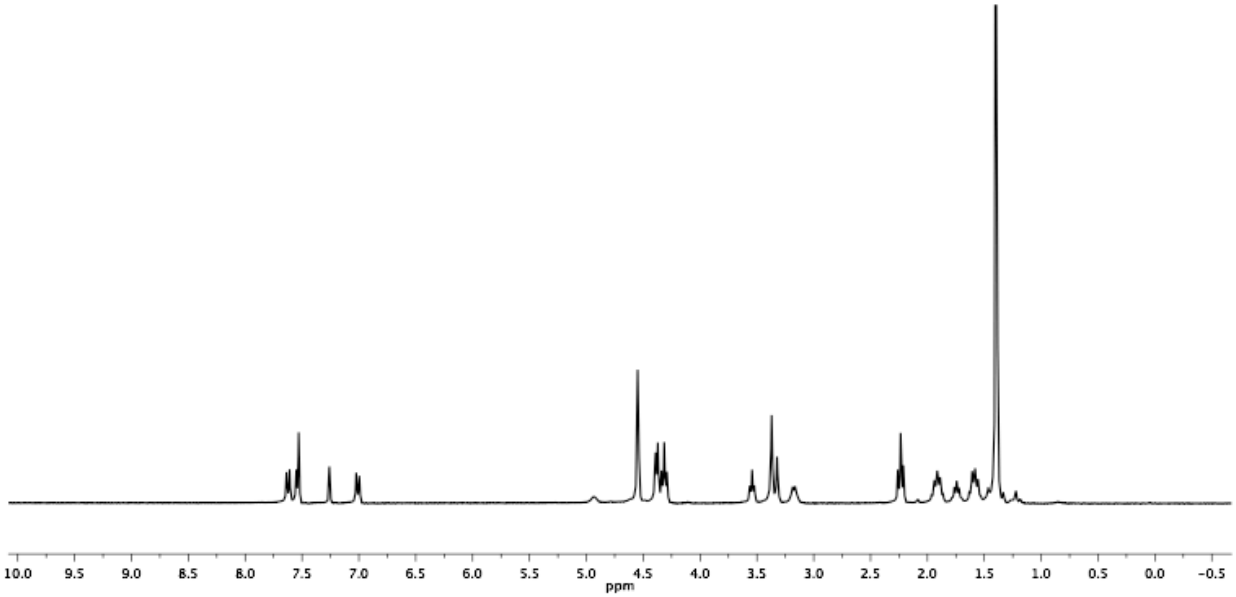

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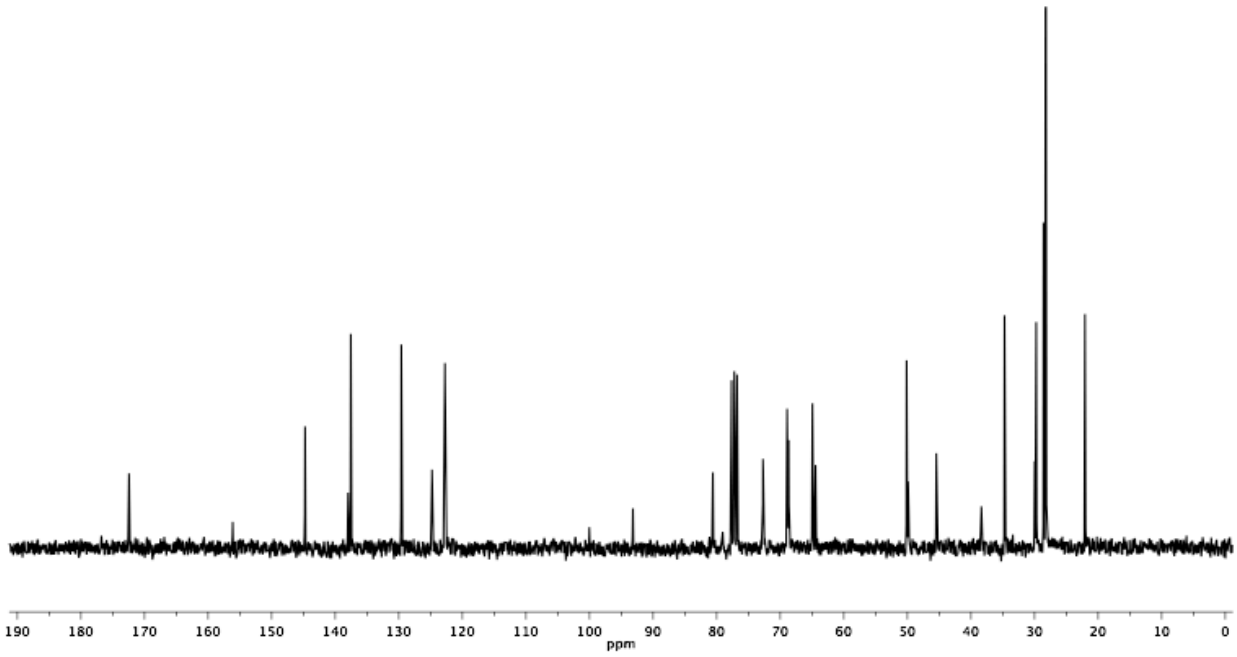

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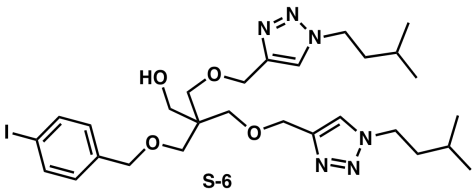
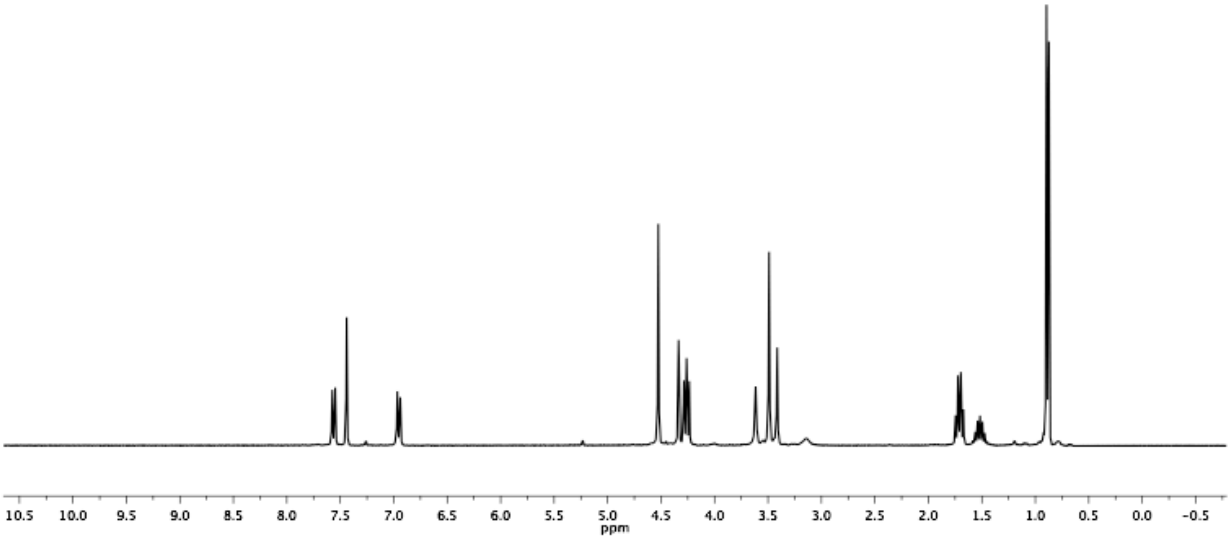


S-6



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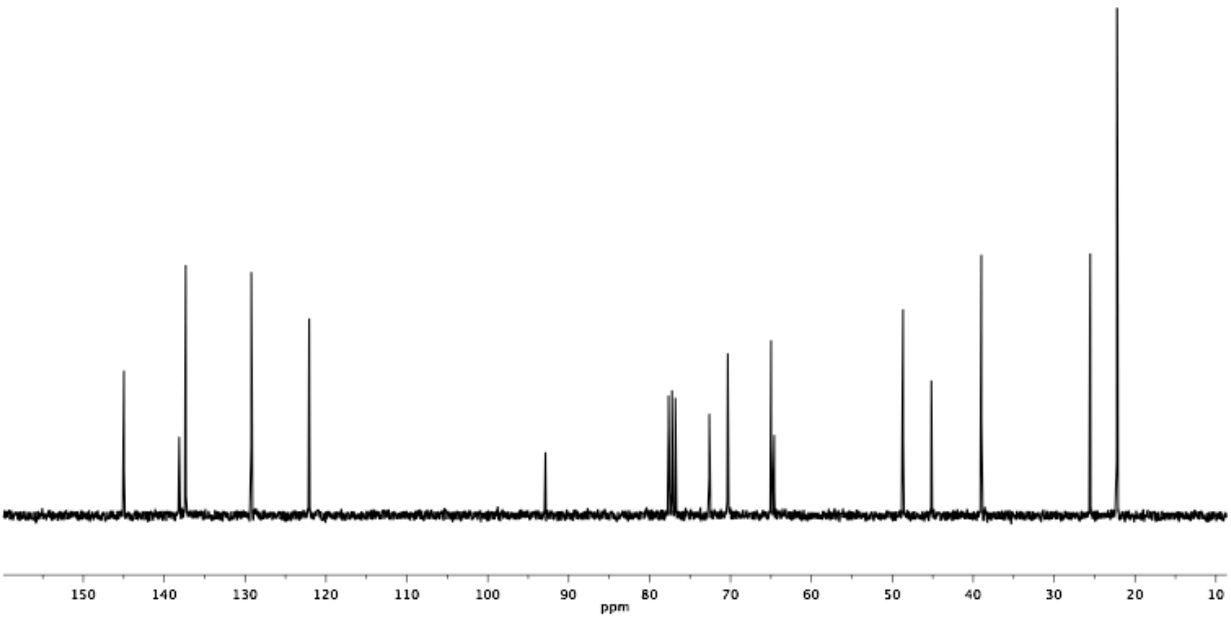

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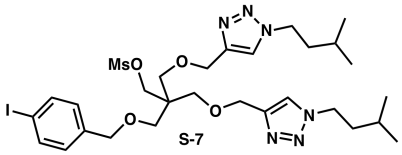
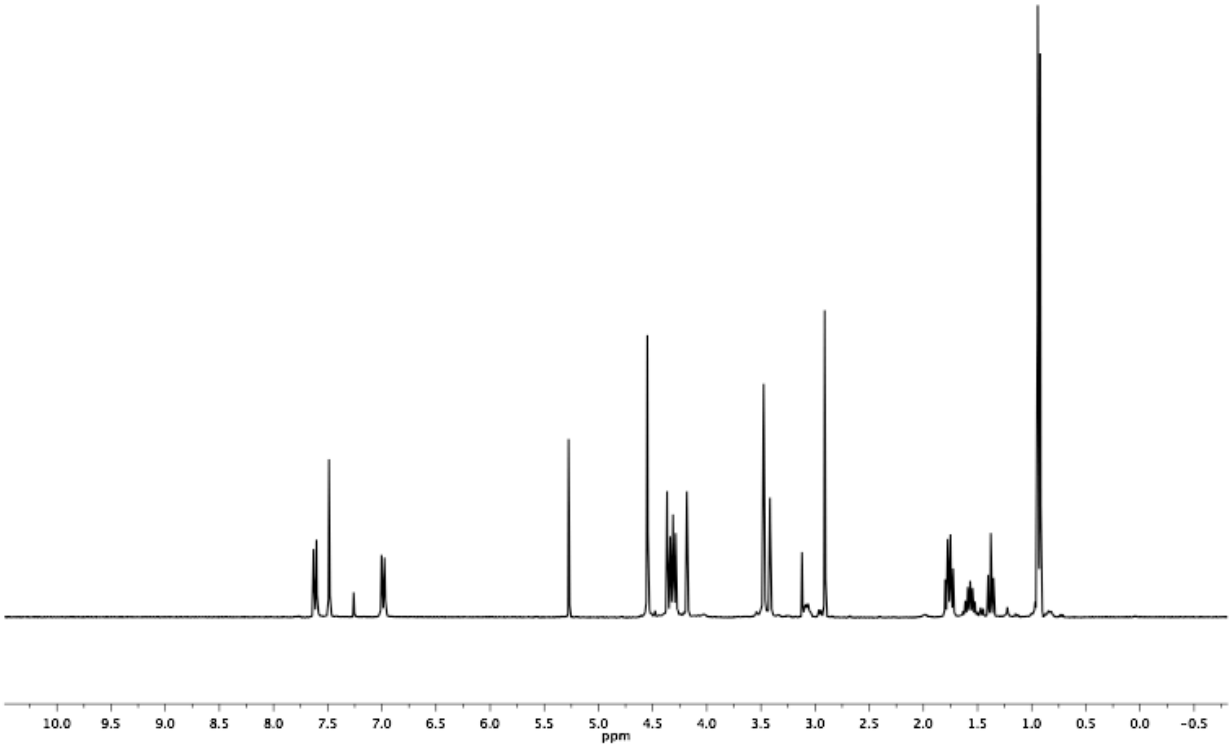
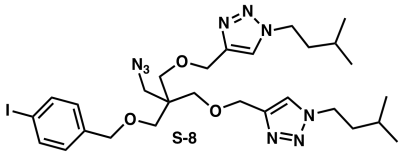
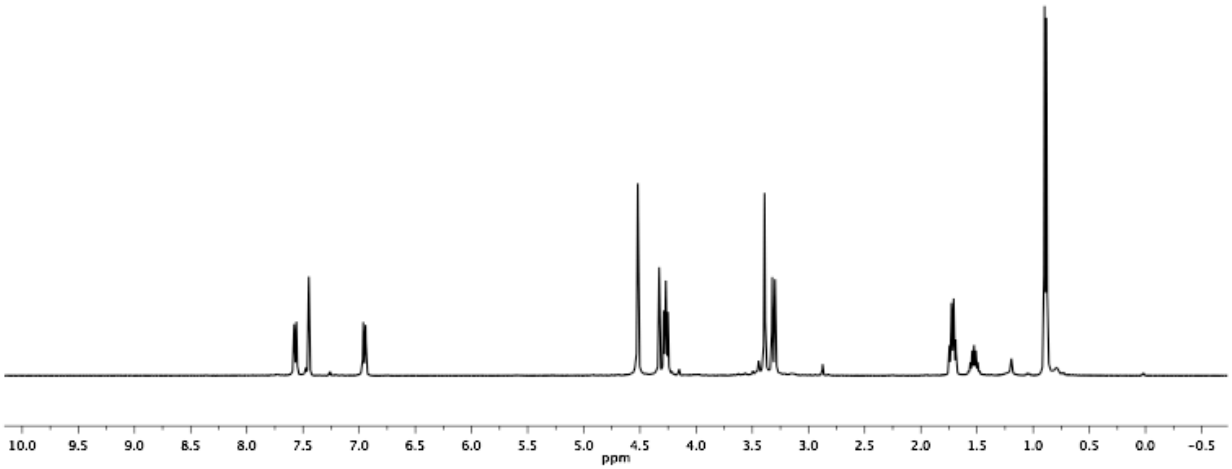




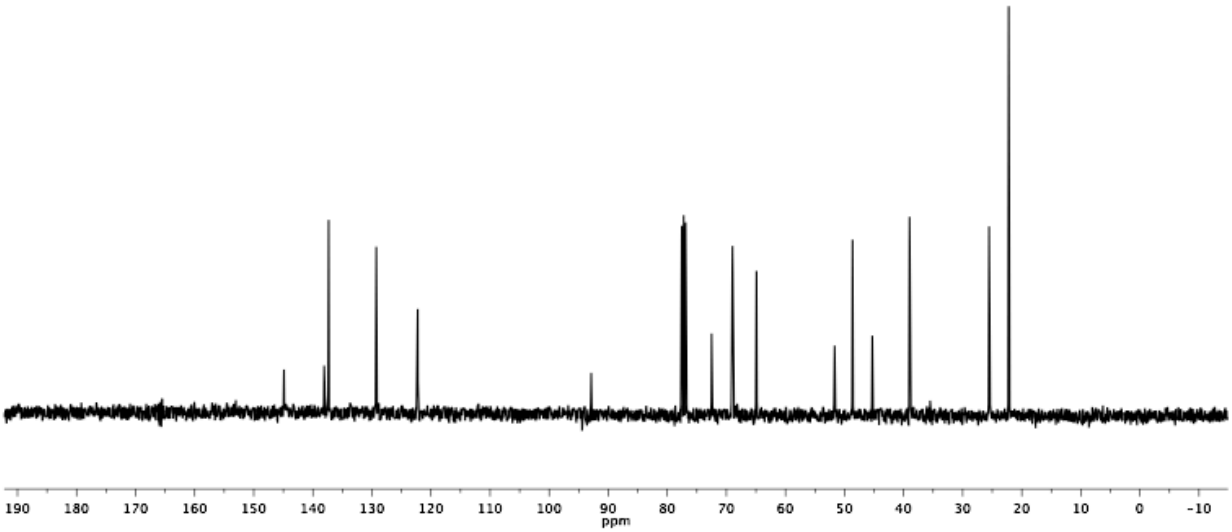
^{1}H NMR



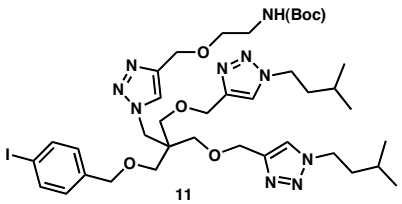
S-8



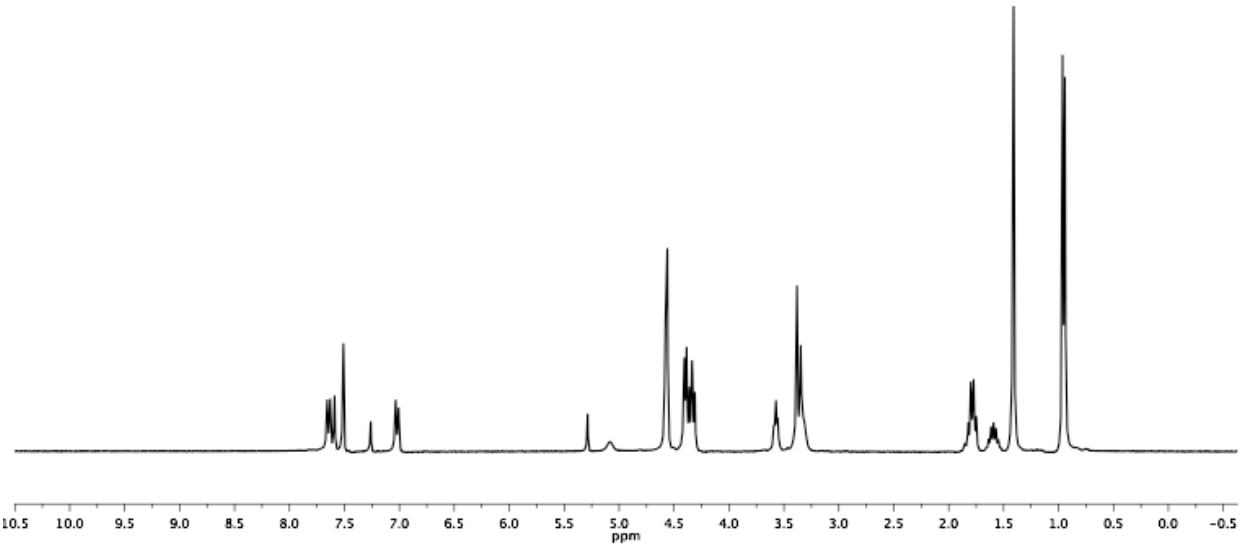
^{1}H NMR



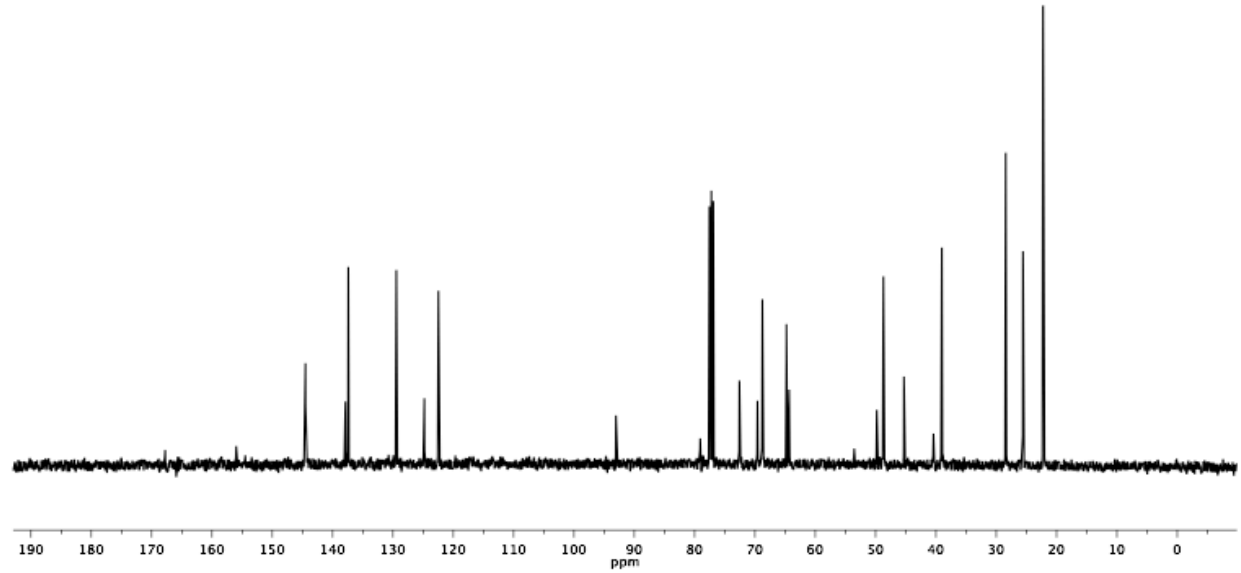
^{13}C NMR



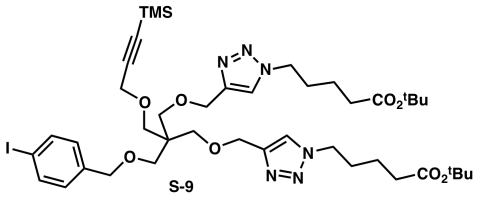
11

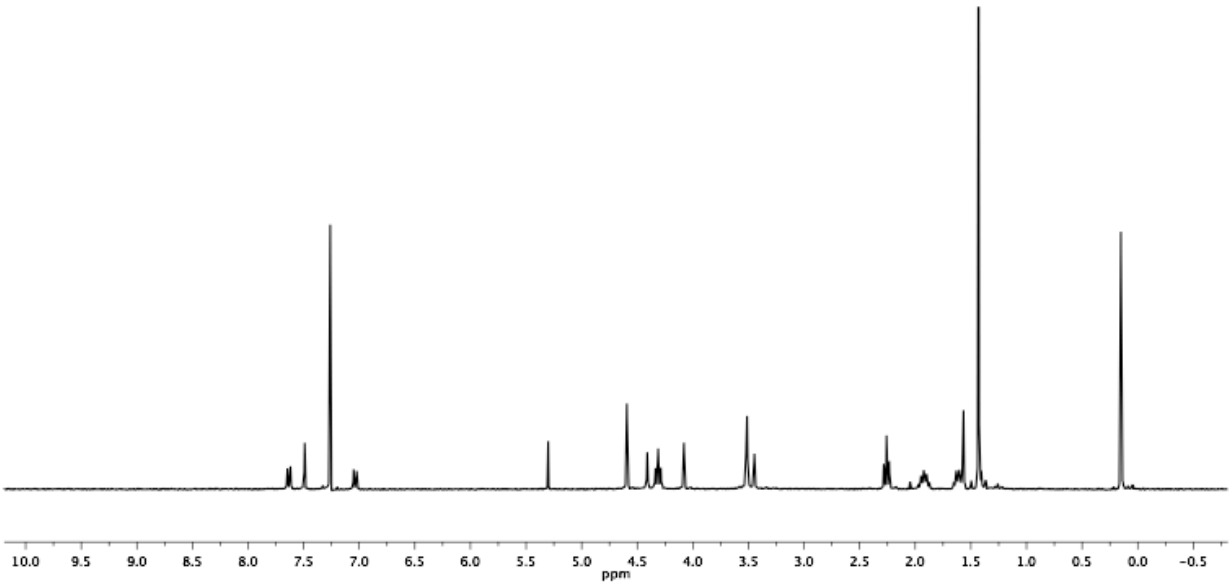


^{1}H NMR

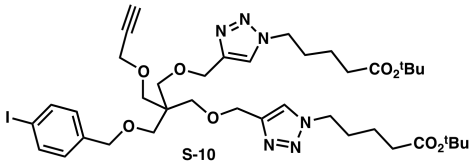


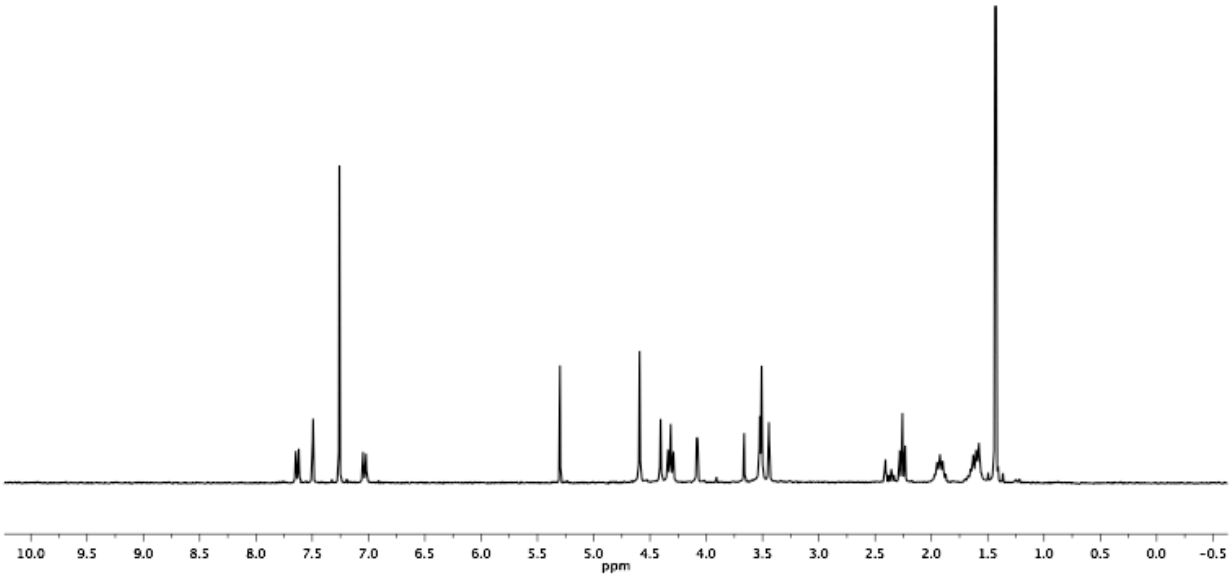
^{13}C NMR


TMS
I
O
N
N
N
CO2tBu
S-9

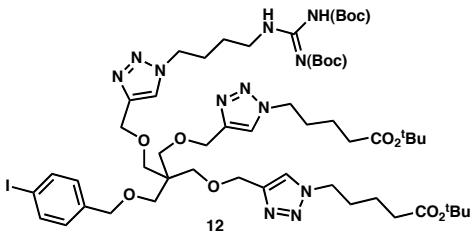

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

^{1}H NMR

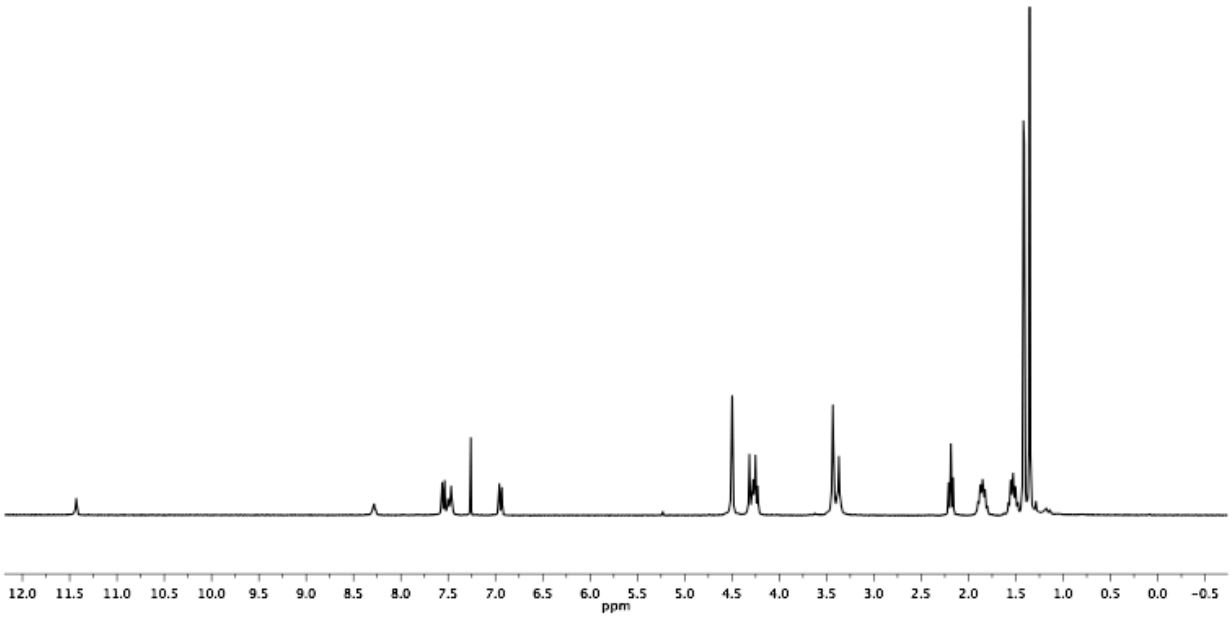

I
O
N
N
N
CO2tBu
S-10


10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

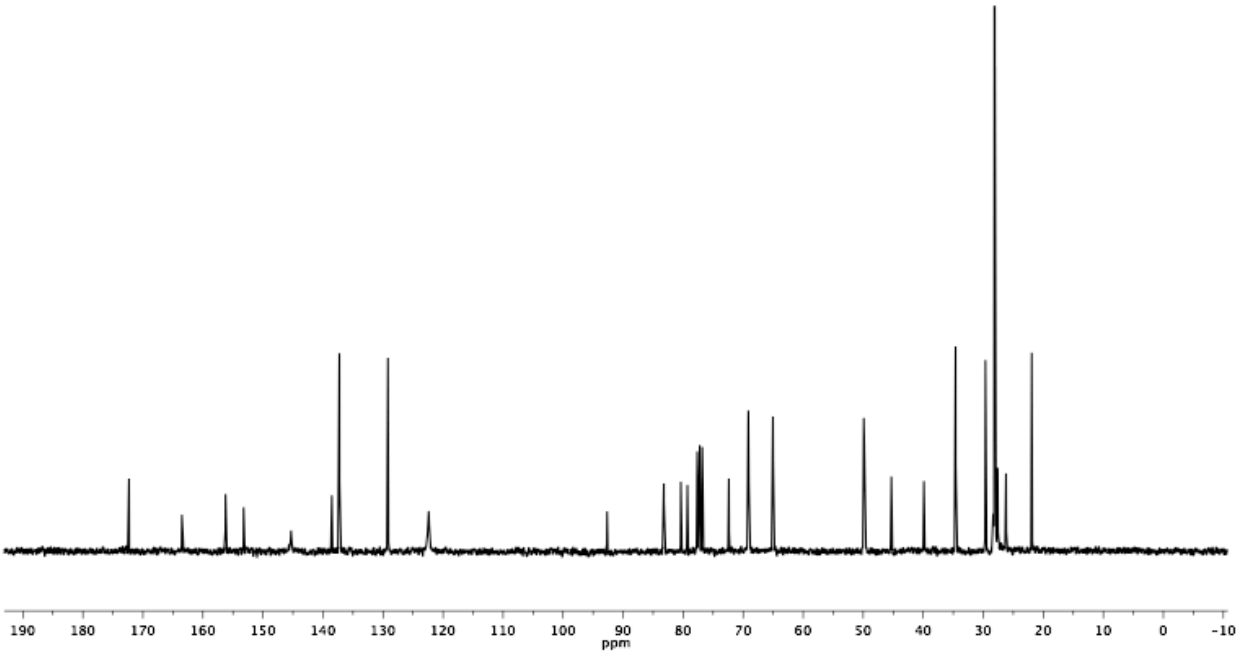
^{1}H NMR



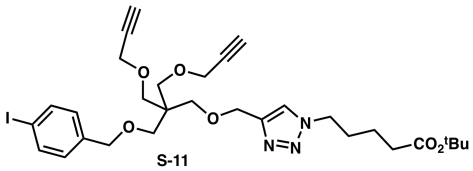
12



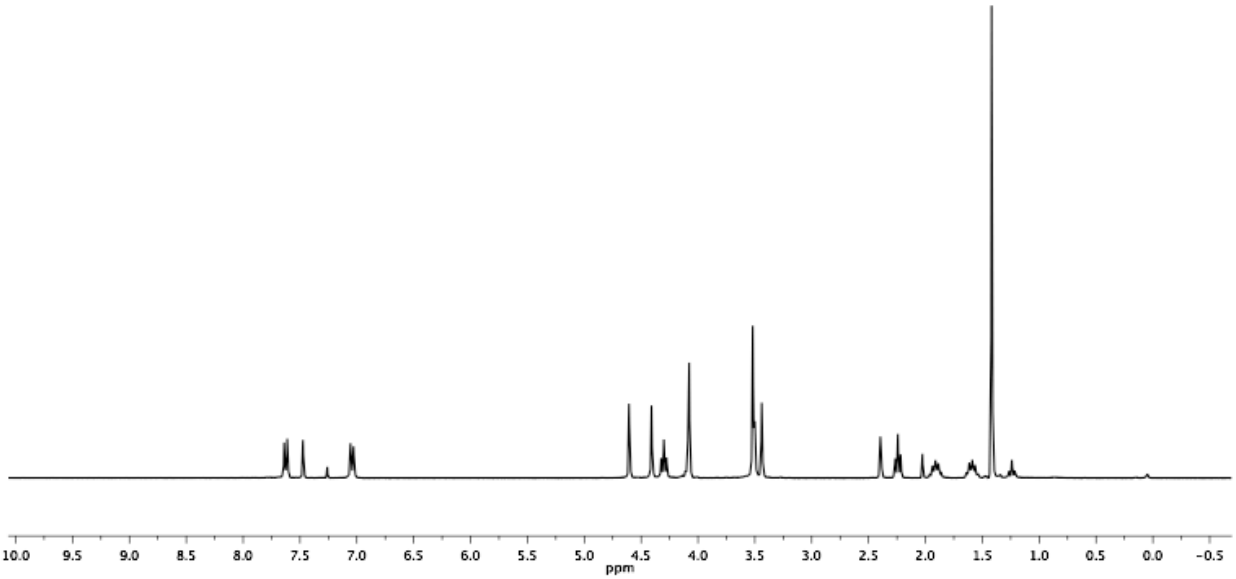
^{1}H NMR



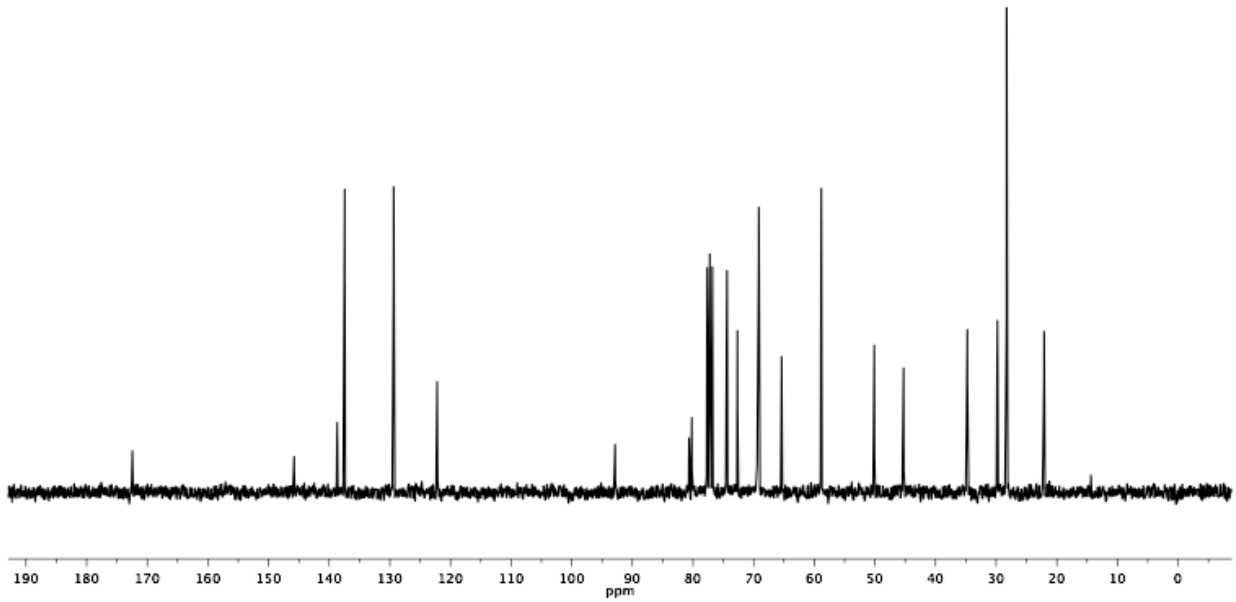
^{13}C NMR



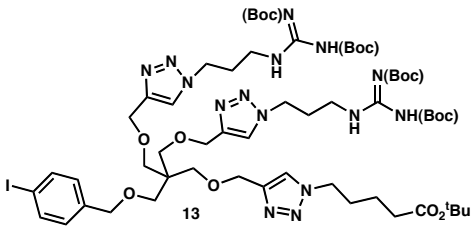
S-11



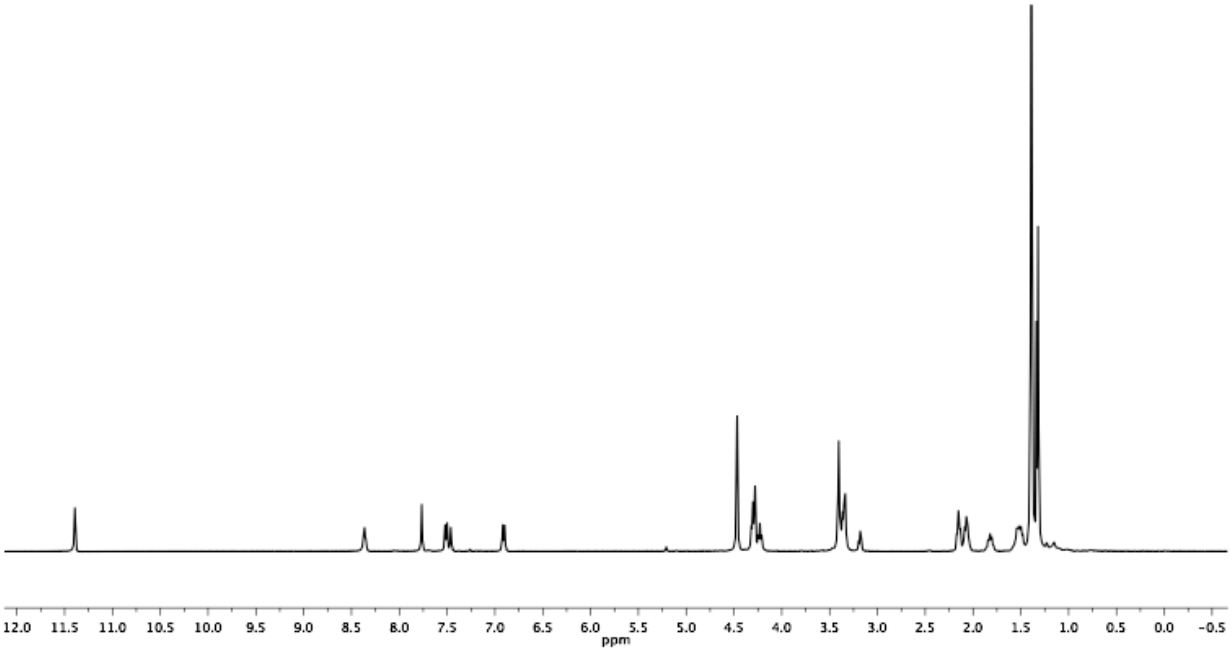
^{1}H NMR



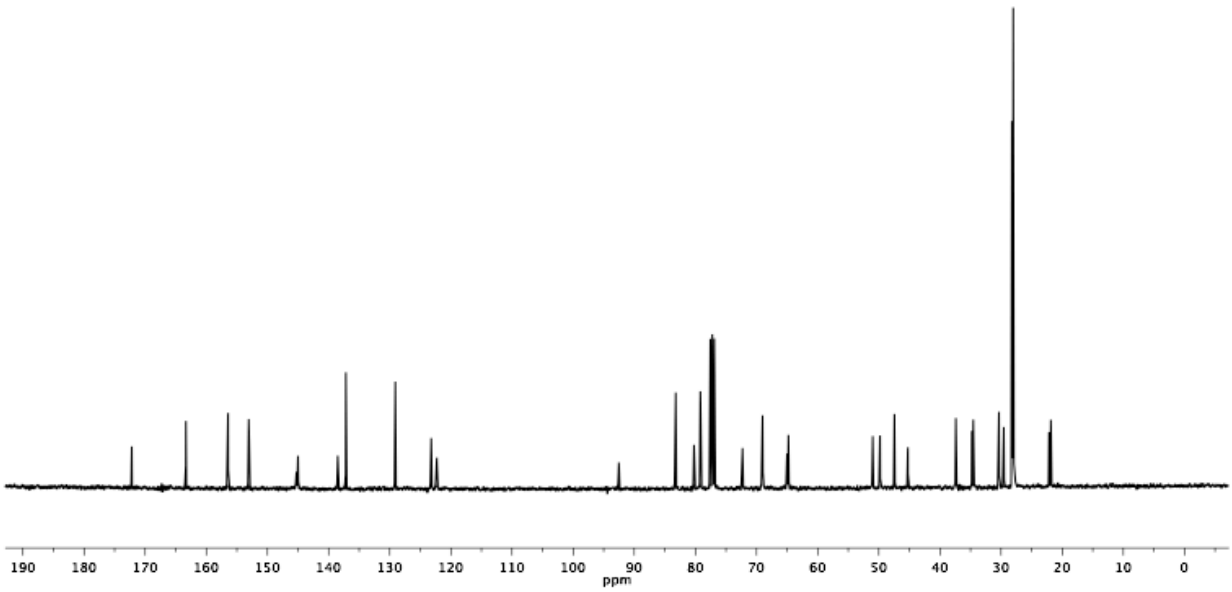
^{13}C NMR



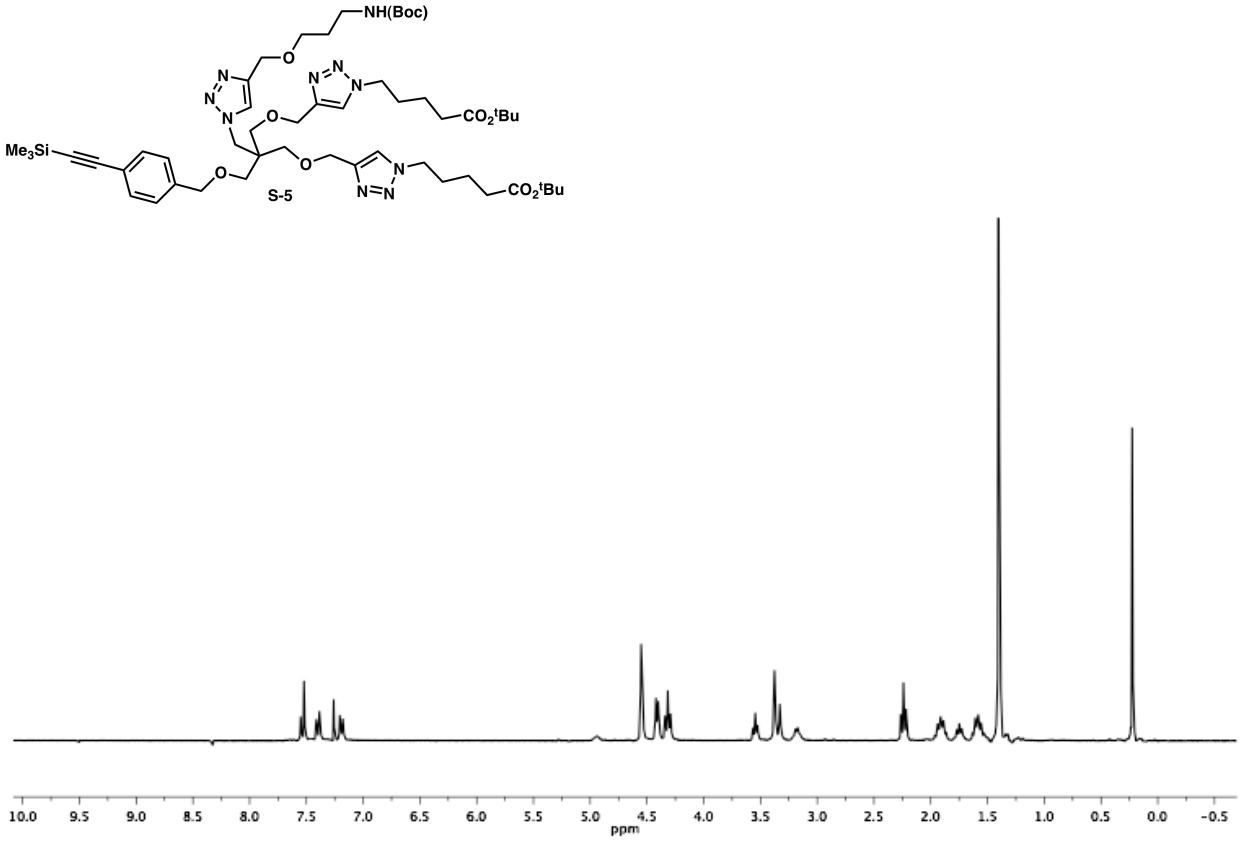
13



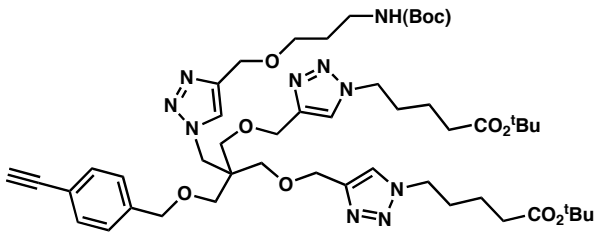
^{1}H NMR



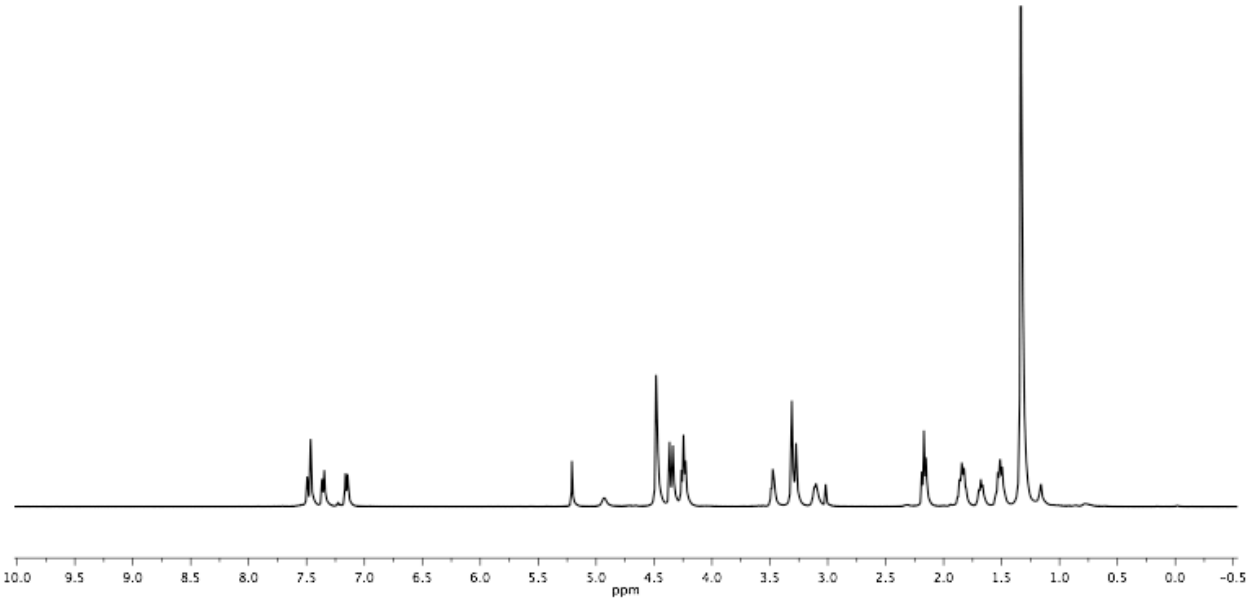
^{13}C NMR


NH(Boc)
Me3Si
CO2tBu
CO2tBu
S-5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

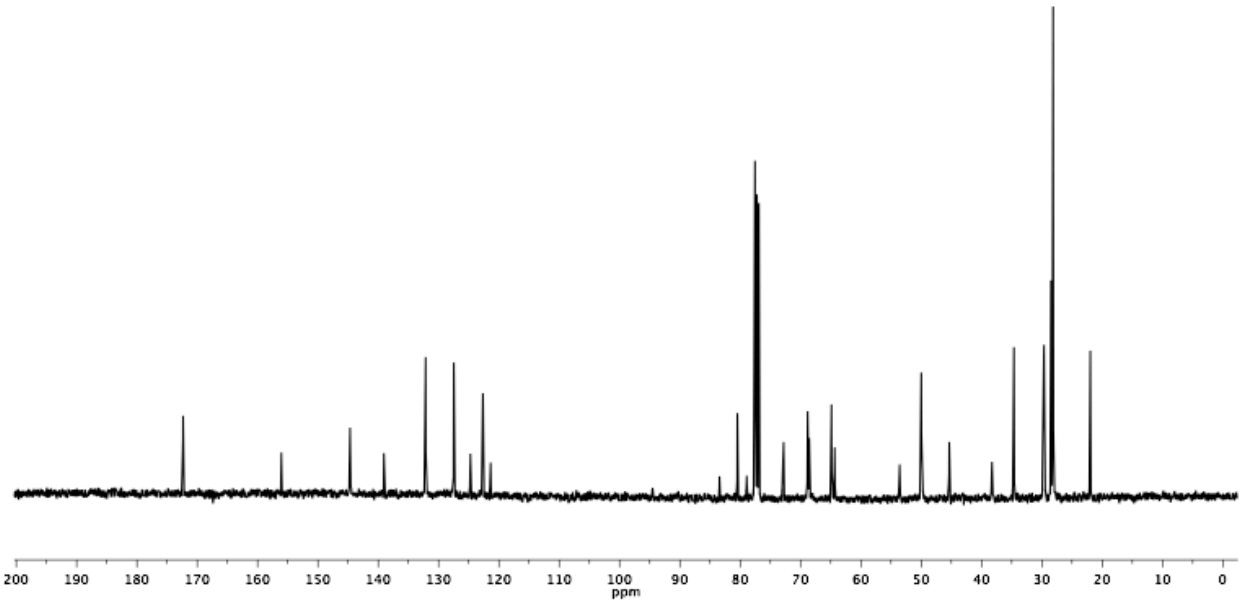
^{1}H NMR



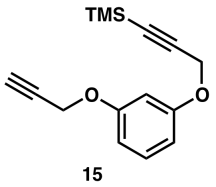
14



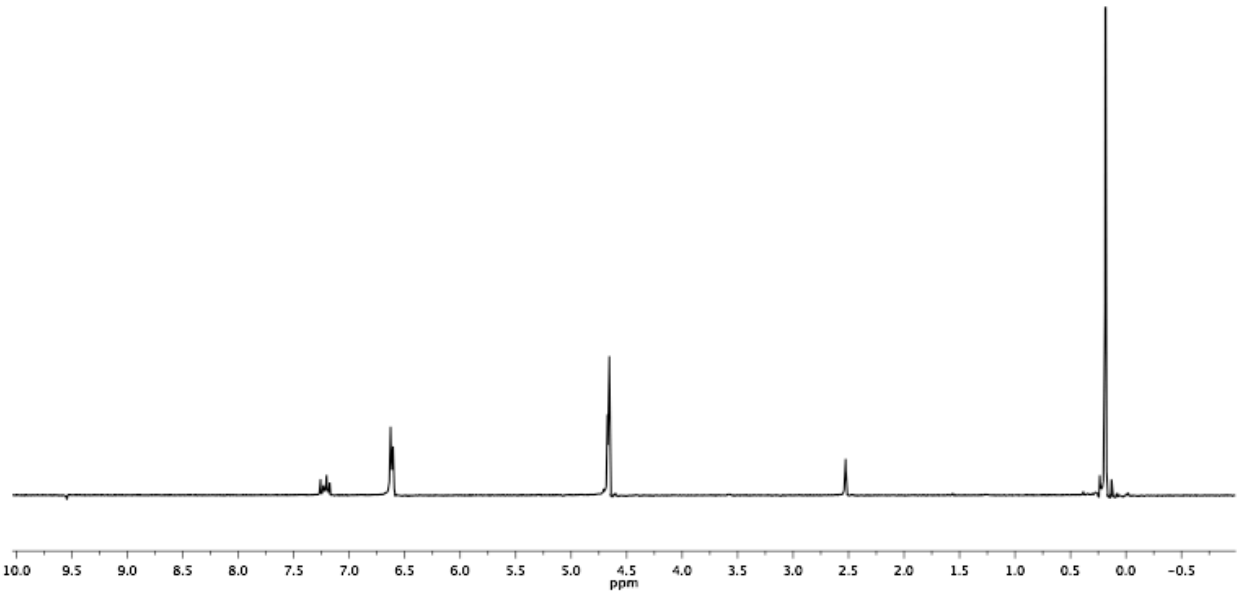
^{1}H NMR



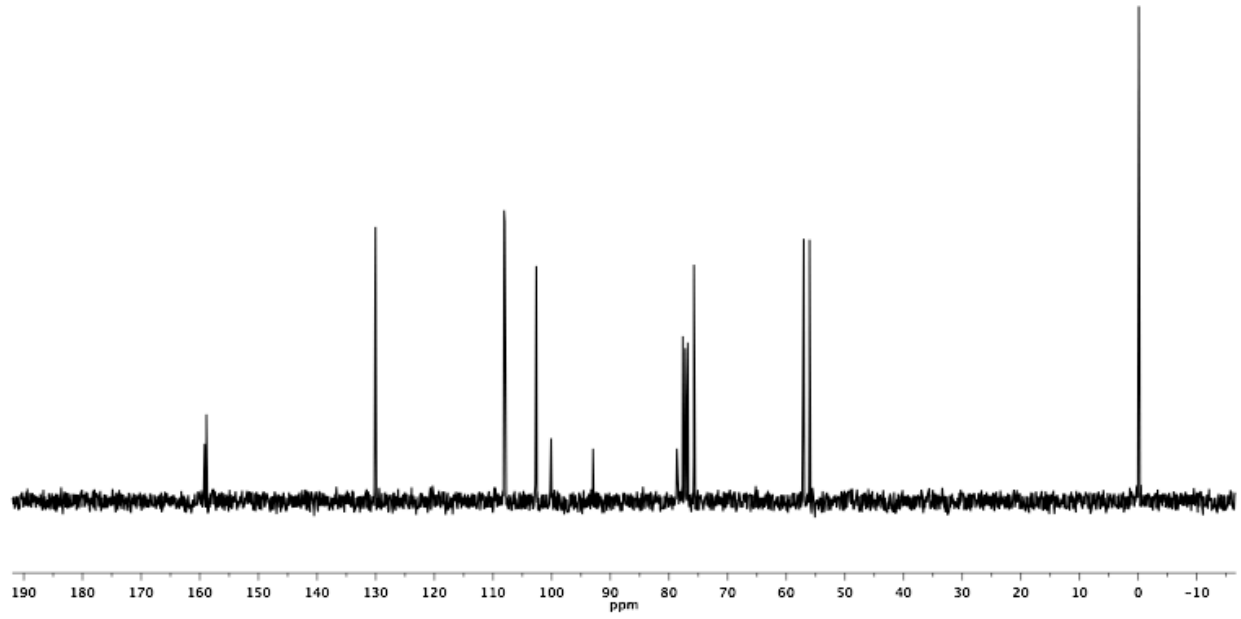
^{13}C NMR



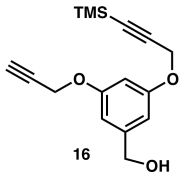
15

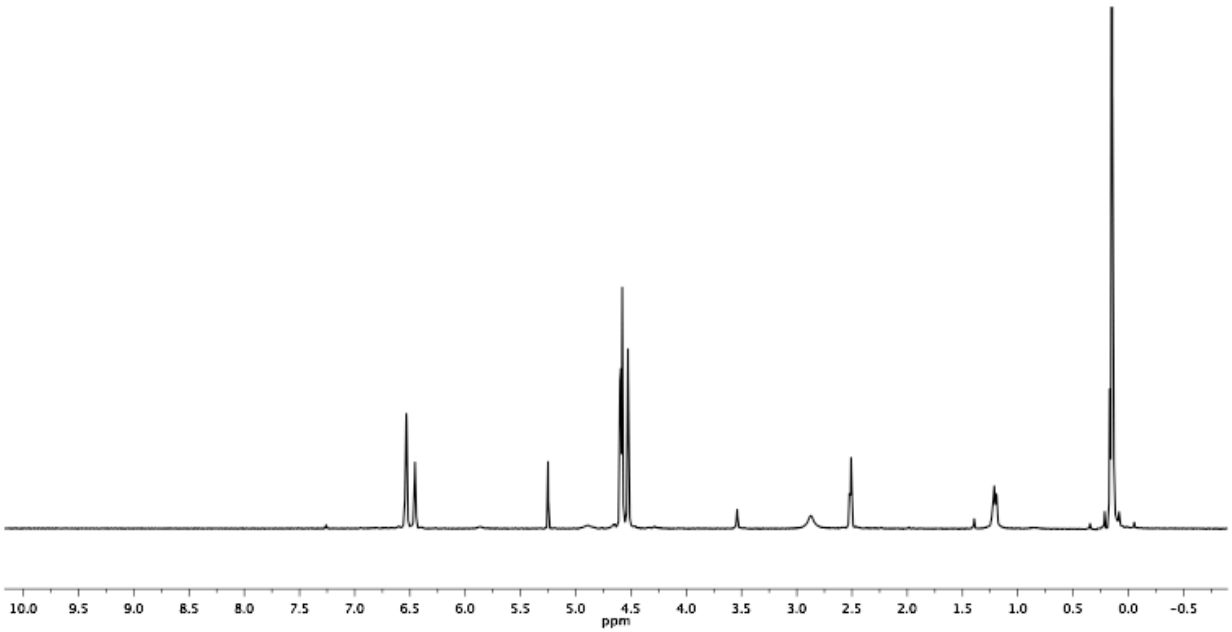


^{1}H NMR

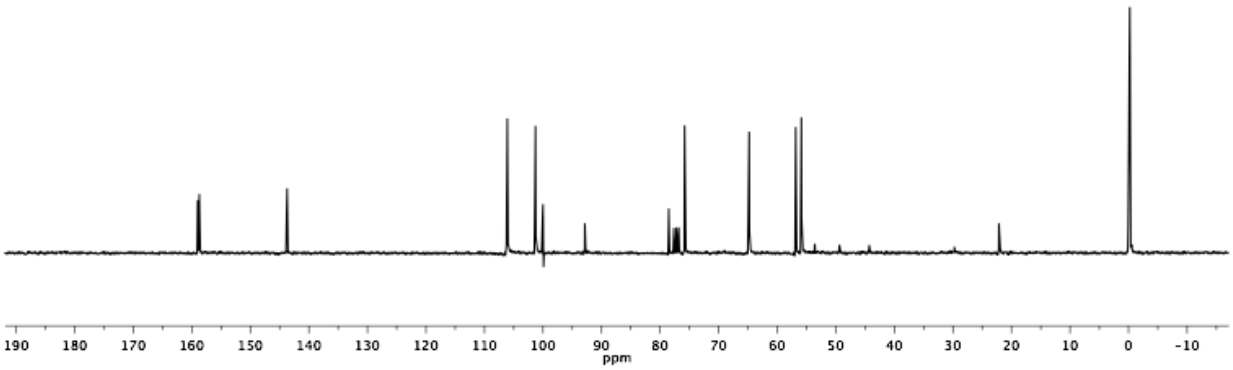


^{13}C NMR

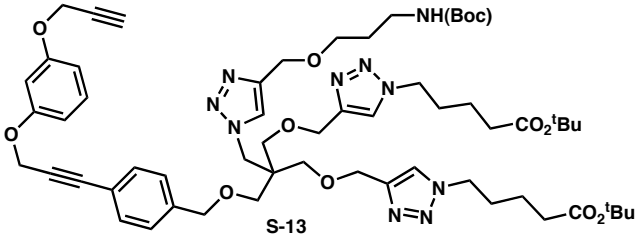




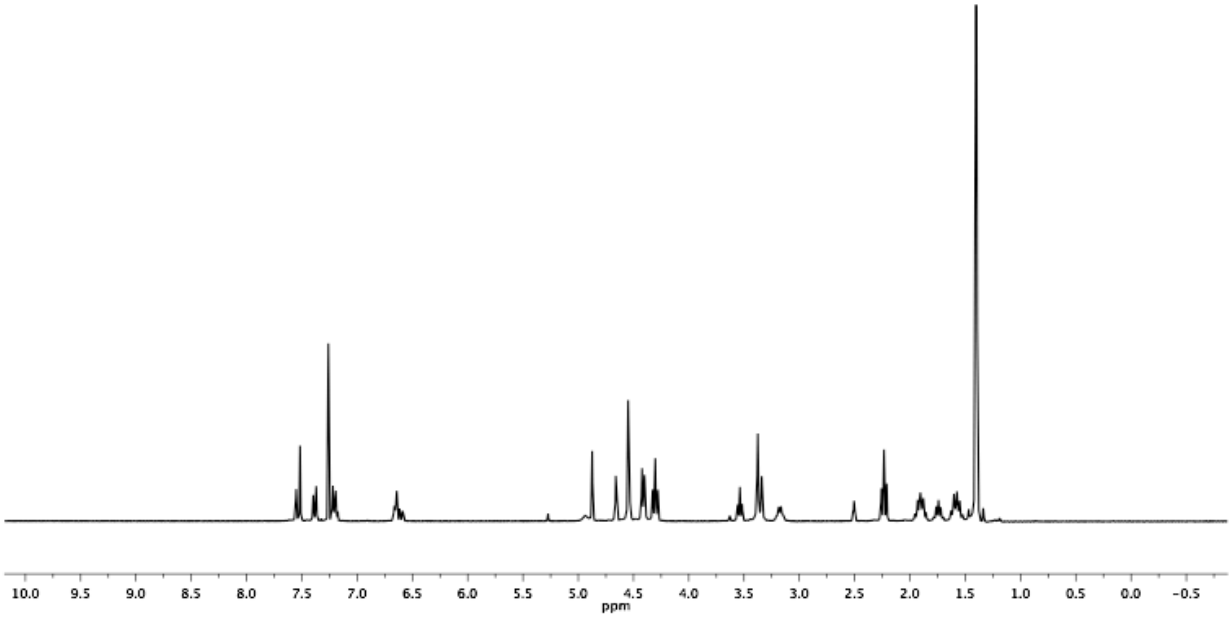
^{1}H NMR



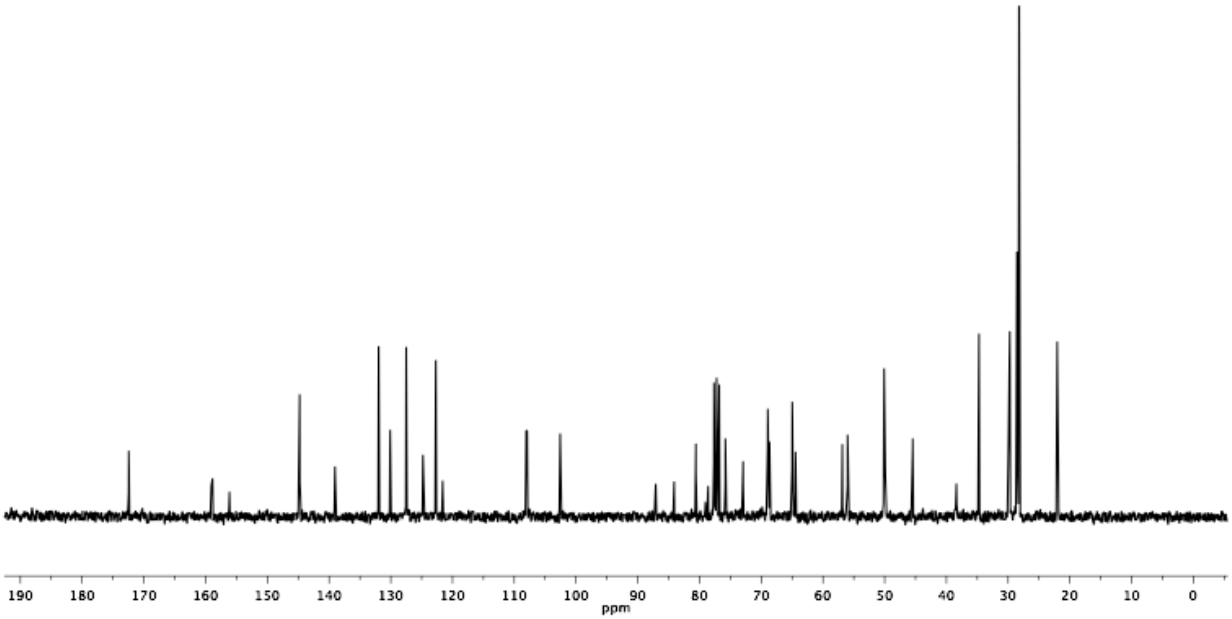
^{13}C NMR



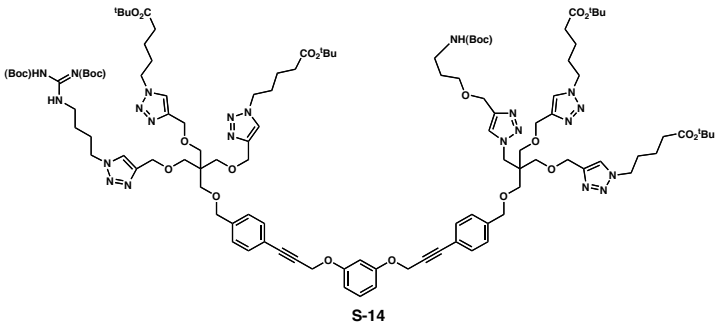
S-13



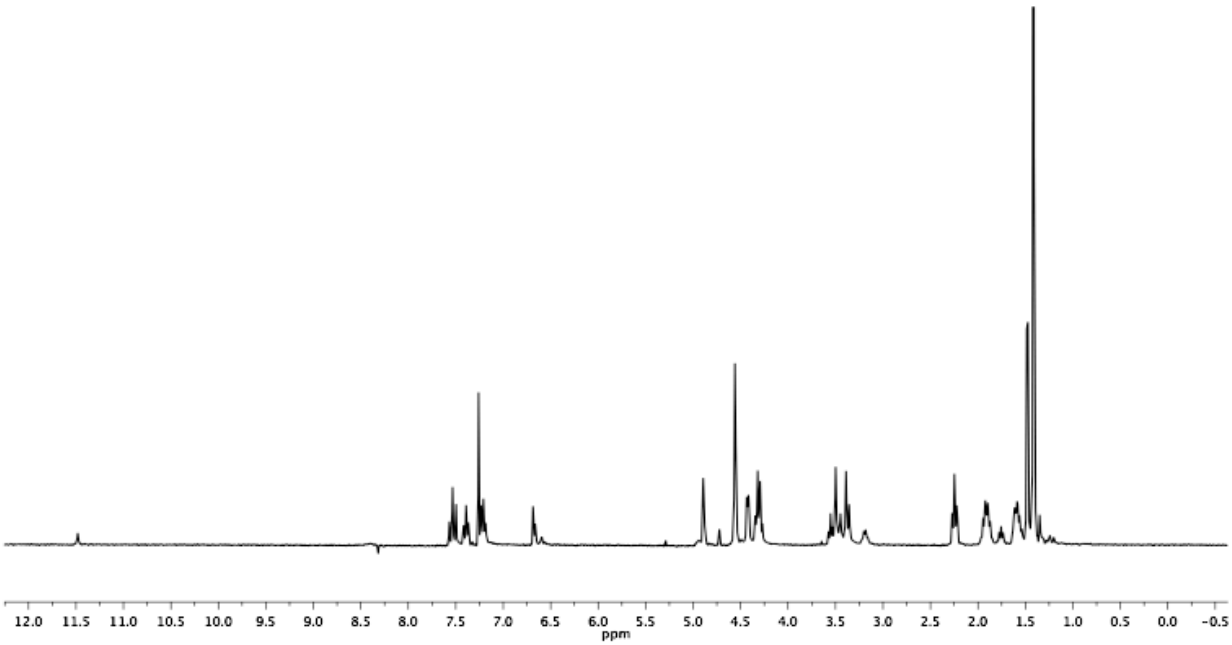
^{1}H NMR



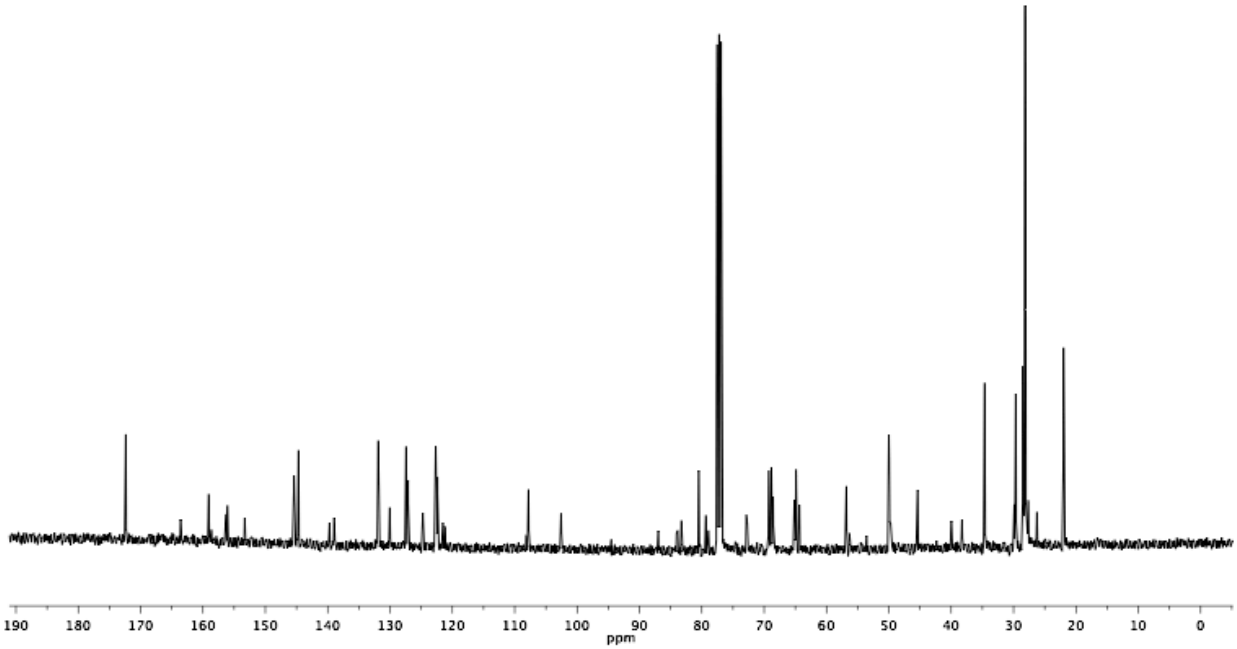
^{13}C NMR



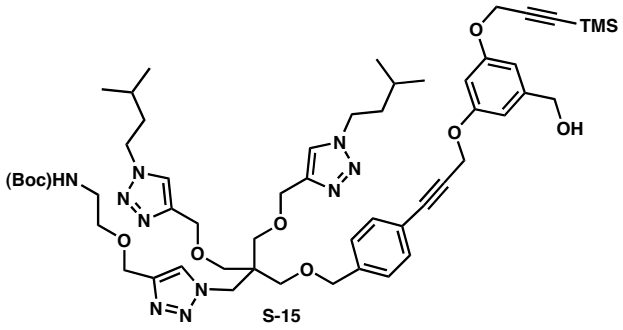
S-14



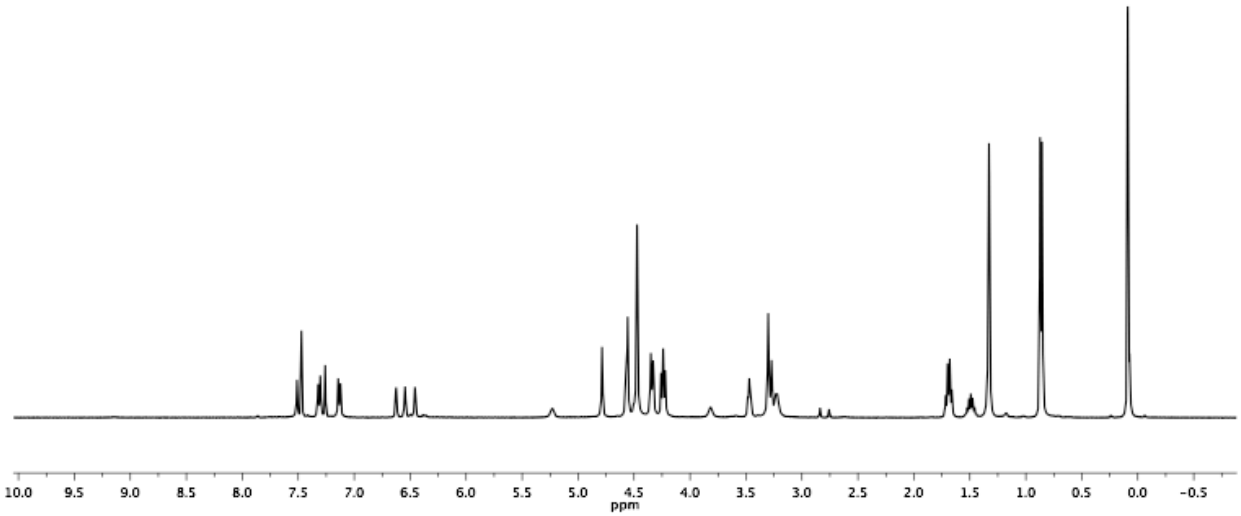
^{1}H NMR



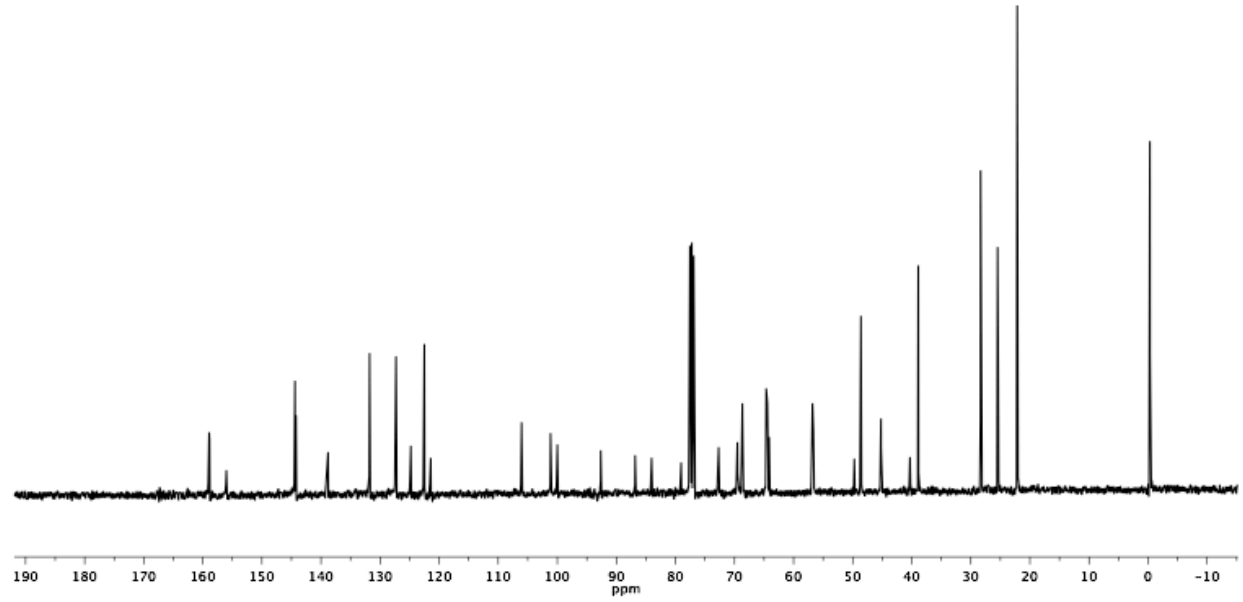
^{13}C NMR



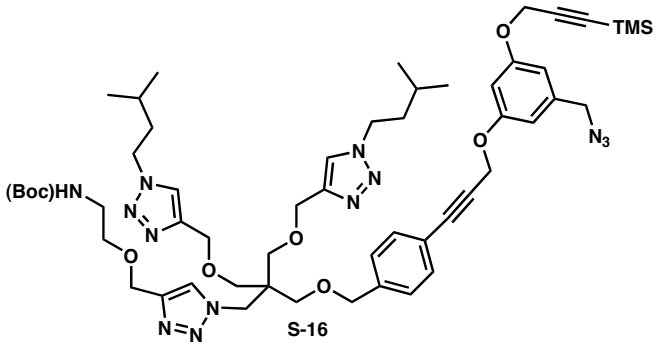
S-15

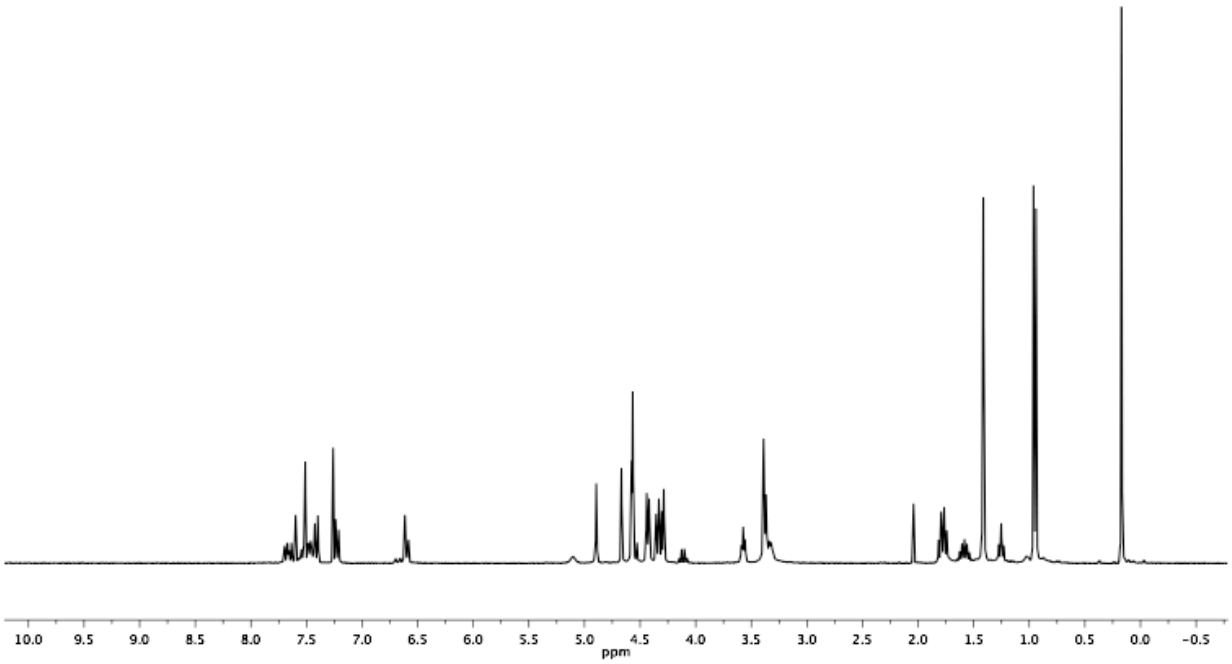


^{1}H NMR

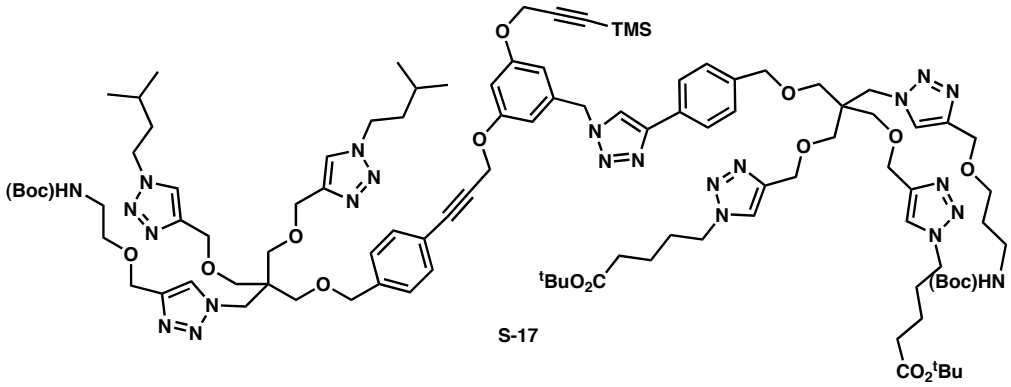


^{13}C NMR

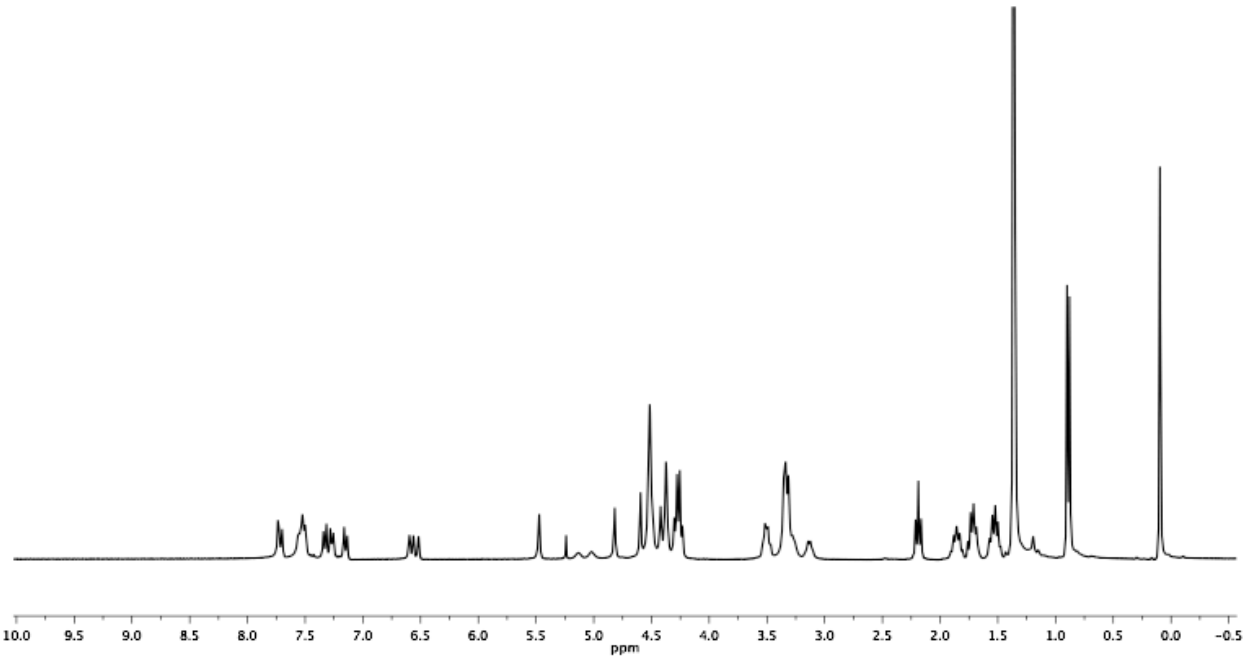




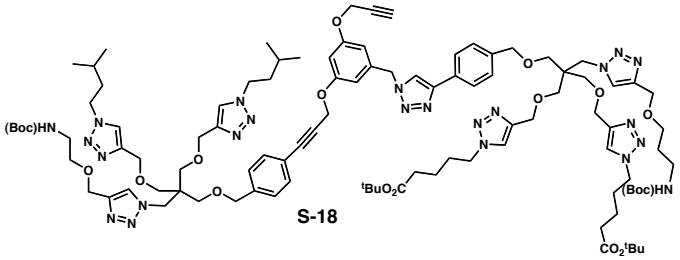
^{1}H NMR


TMS
(Boc)HN
^{t}BuO$_2$C
(Boc)HN
CO$_2$^{t}Bu

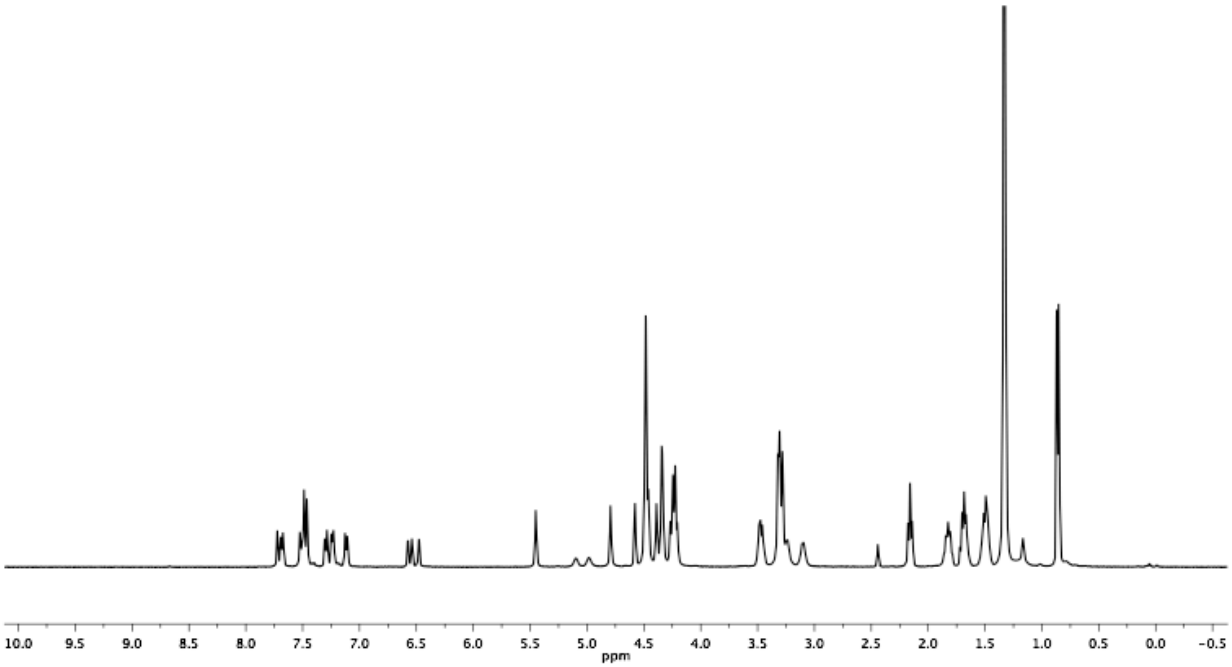
S-17


10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

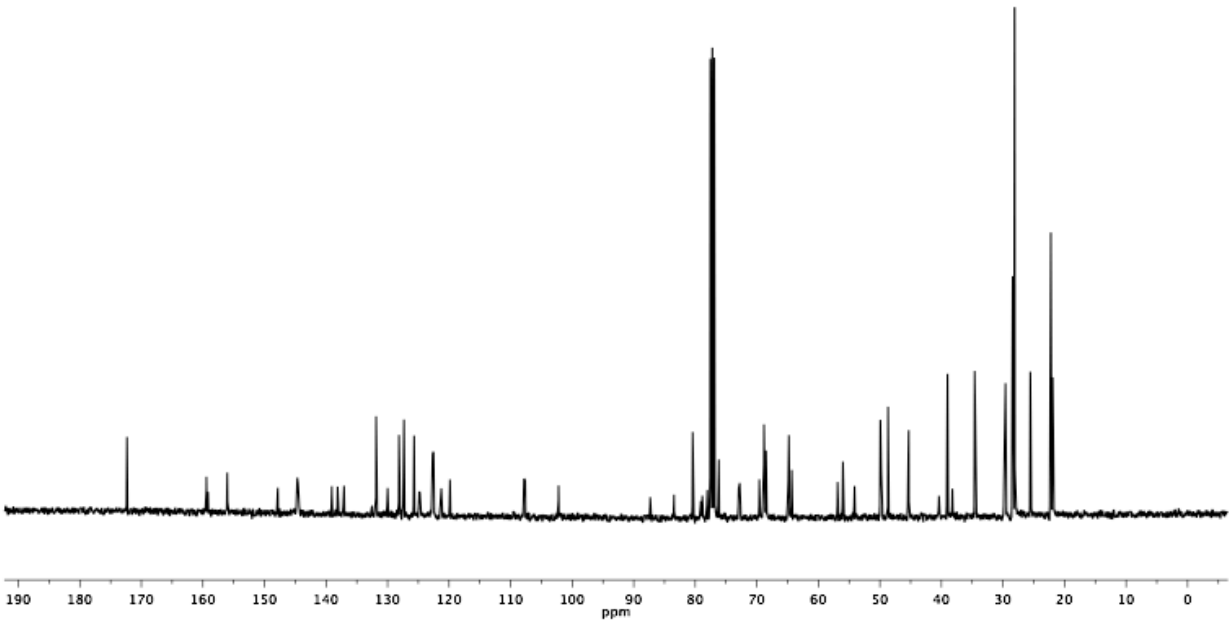
^{1}H NMR



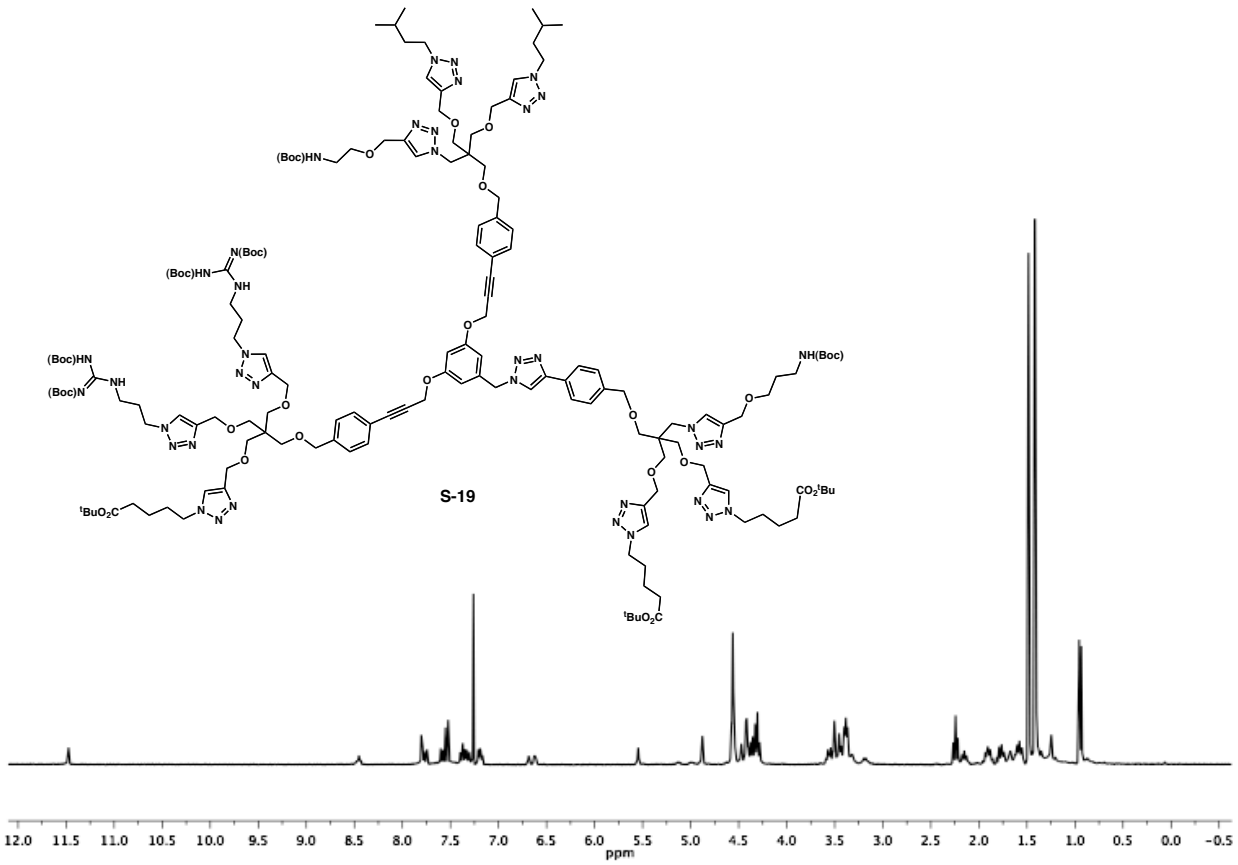
S-18



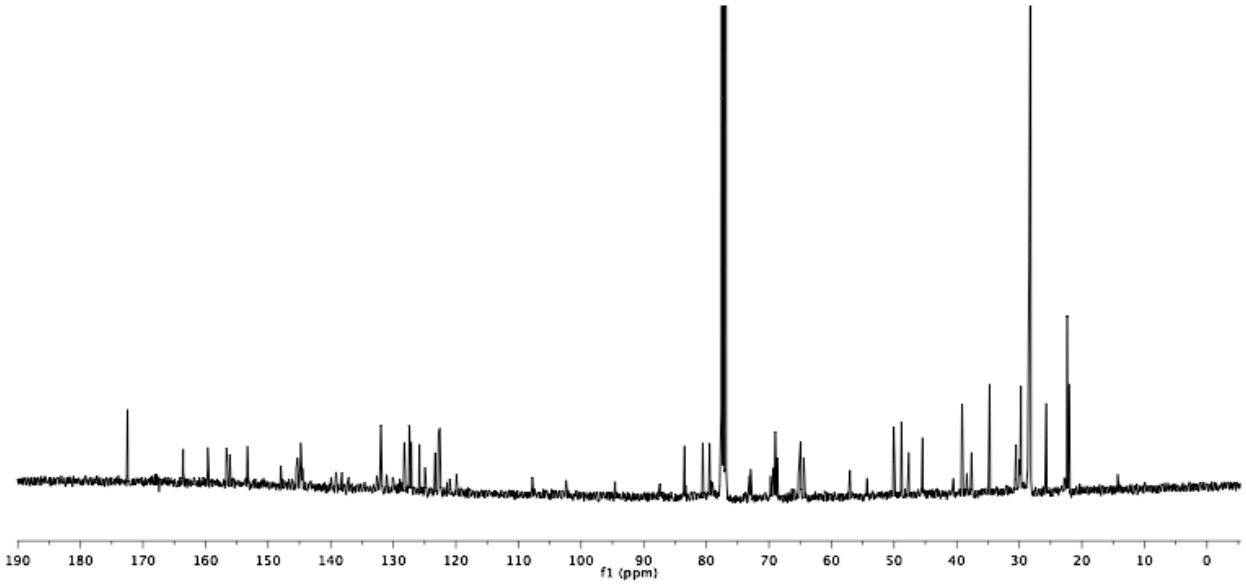
^{1}H NMR



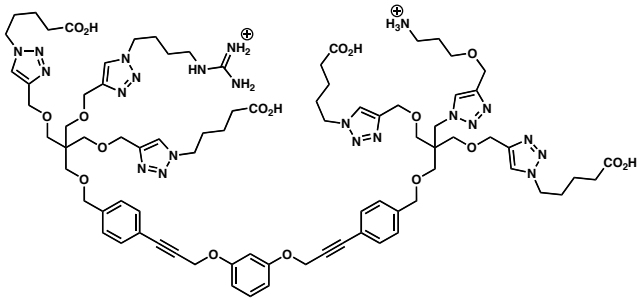
^{13}C NMR



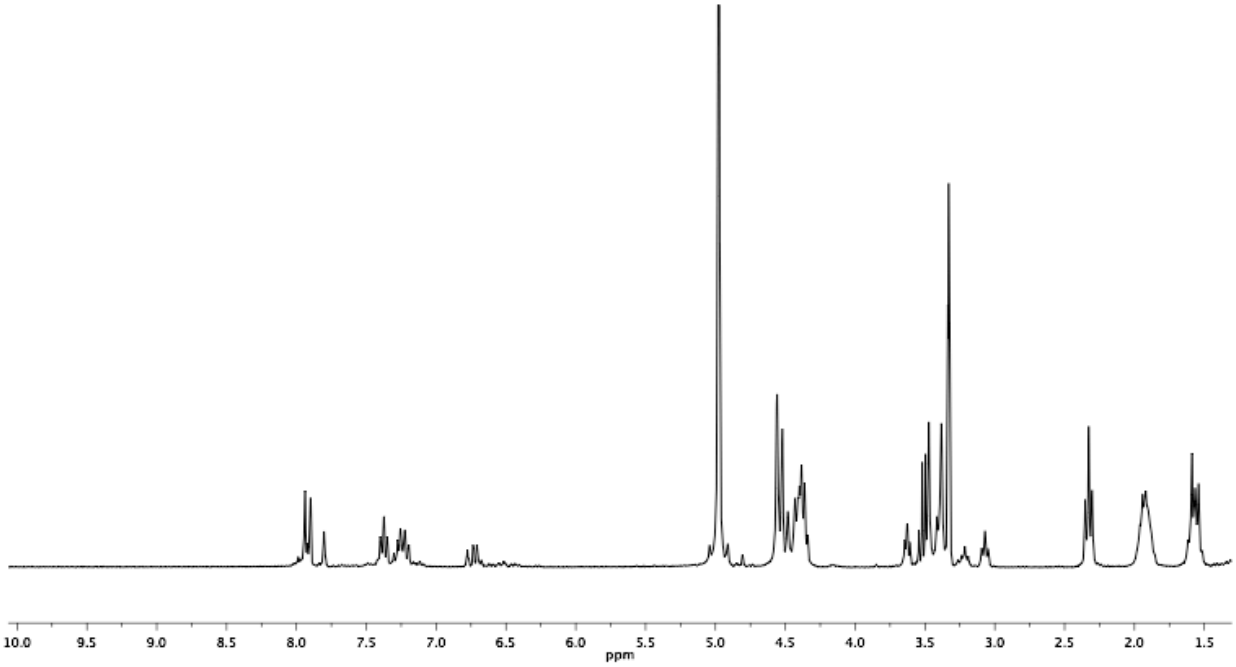
^{1}H NMR



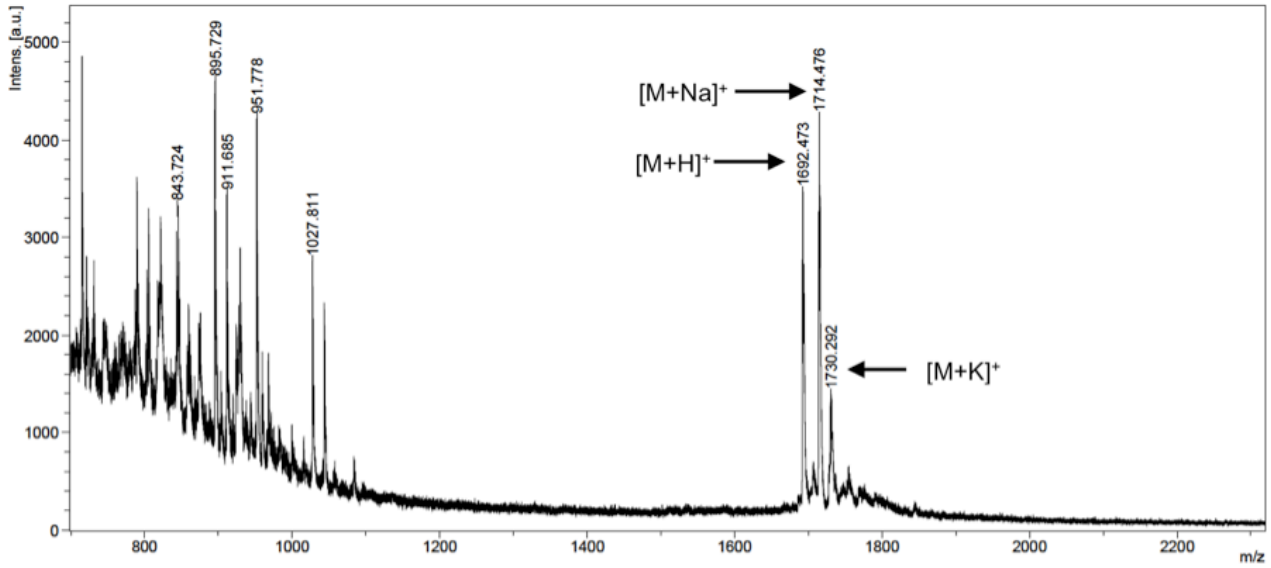
^{13}C NMR



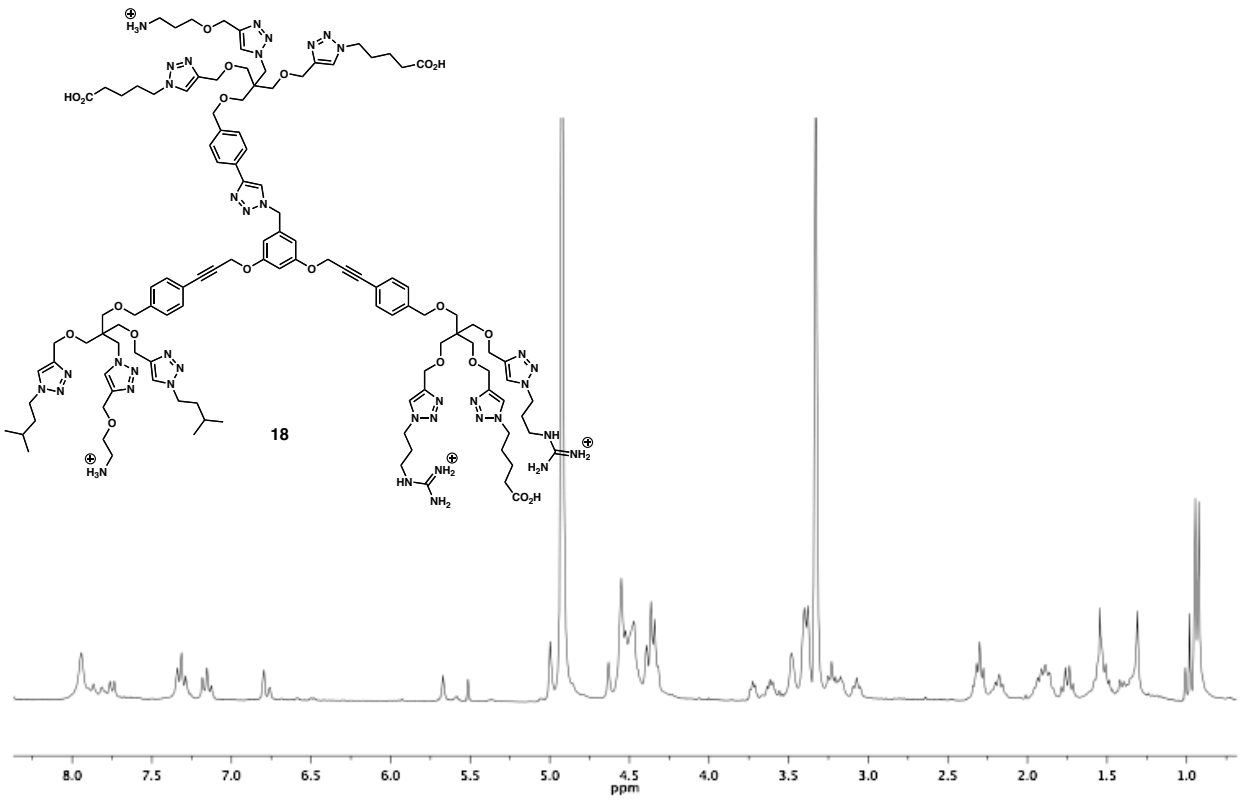
17



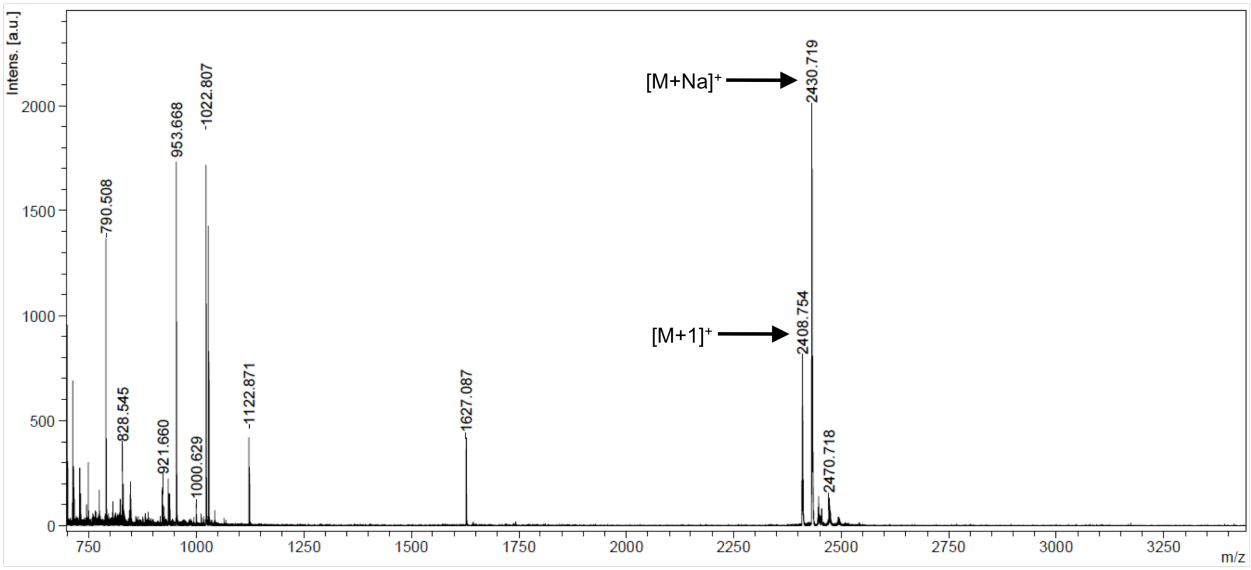
^{1}H NMR



MALDI-TOF



^{1}H NMR



MALDI-TOF