Supplementary Information Section: Part 1

Synthesis, transport activity, membrane localization, and dynamics of oligoester ion channels containing diphenylacetylene units.

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GENERAL METHODS:

Most chemicals and solvents were used as received from known suppliers, except THF and DMF which were dried and distilled before use. NMR spectra were collected on a 300 MHz Bruker or 500 MHz Varian instrument. HPLC was performed using an HP Series 1100 instrument, with either a Macherey-Nagel "Nucleosil" RP C_{18} analytical (4 mm x 250 mm) or a Grace Davison "Alltima" RP C_{18} semi-prep (10 mm x 150 mm) column. Solvents used (ACN, CH_3OH; HPLC-grade, H_2O; Milipore) were filtered through a Milipore sub-micrometer filter before use. HPLC elution was monitored at various UV wavelengths (typically 254, 280 and 220 nm) and fluorometrically (λex = 310, λem = 330 nm). All samples used in transport experiments were HPLC-purified. UV was run on a Cary 5 UV-VIS spectrometer in a 10 x 10 mm quartz cell. Fluorescence was run on a PTI QM-2 instrument at T= 20^0C, slit width = 3 nm in 10 x 10 mm quartz cells equipped with a micro stir rod. The HPTS transport assay: done as previously reported[1]; minor changes to the published procedure include the use of a different buffer (100mM NaCl, 10mM $Na_3PO_4 \cdot 5H_2O$, pH ~6.4) and the injection of compound through a specially-designed injection port, which allows constant monitoring without the need for opening the instrument. Vesicles were made as reported, and sized on a Brookhaven Instruments ZetaPALS instrument. Average vesicle size was found to be ~180 – 220 μm. The experimental and data analysis systems for the voltage clamp experiments has been previously decsribed.[2,3] All data were hardware filtered (8-pole Bessel filter, 1 kHz) and in a survey mode were filtered during acquisition at 1 kHz. The rapid spike and the flicker behaviors are near the 1 kHz limit and data for more detailed examination did not use the digital acquisition filter.

SYNTHETIC PROCEDURES

Sonogashira coupling (***i***): To a round bottomed flask equipped with a septum, 1.2 – 1.5 equivalents (in relation to the alkyne starting material) of the iodo-containing reactant and 6 – 10% CuI were dissolved in dry DMF, which was then deoxygenated under vacuum. The alkyne reactant was then added to the flask, which was kept in the dark. $Pd(PPh_3)_4$ (3 – 5%) was then added, followed by 2 – 5 equivalents of NEt_3. The reaction was then stirred under N_2 at temperatures ranging from rt to 50^0C, for 10 – 24 hrs, depending on the reagents used. Reactions were monitored by TLC (silica gel, EtOAc/hexanes as eluent, visualized by UV, p-anisaldehyde and/or vanillin stain). Once complete, reactions were cooled if necessary, diluted with EtOAc and washed with saturated EDTA (2-3 times), H_2O (once), saturated NaCl (once), dried over sodium sulfate, and concentrated under vacuum. Unless noted otherwise, the crude products were purified by column chromatography on silica gel, typically using EtOAc/hexanes as eluent.

Ester coupling (***ii***): To a solution of 1.3 – 2 equivalents of either the alcohol or acid building block in relation to 1 equivalent of the other (excess reagent choice determined by ease of synthesis or availability) in THF or DMF (depending on substrate) were added 1.3 – 2 eq. of DIC, HOBt and 2.6 – 4 eq. of DIPEA. The reaction was sealed under an atmosphere of N_2, and stirred for 16 – 24 hr at temperatures varying between rt and 50^0C. Reaction completion was monitored by TLC. Once complete, the reaction was cooled (if necessary), filtered to remove DIU, and diluted with DCM or EtOAc. The organic phase was extracted with H_2O (twice), saturated $NaHCO_3$ (twice), rinsed with sat NaCl (once), dried with anhydrous sodium sulfate, and concentrated under vacuum. Unless noted otherwise, the crude product was purified by column chromatography on silica gel, typically using EtOAc/hexanes as eluent.

THP removal (***iii***): pTsOH (5-25%) was added to a solution of compound in ~10 – 30% CH_3OH: DCM, which was stirred at rt for 1-3 hr, as monitored by TLC. Once complete, the reaction was diluted with DCM, washed with H_2O (once), saturated $NaHCO_3$ (twice), and saturated NaCl (once), then dried over sodium sulfate and concentrated under vacuum. If necessary, further purification was carried out as noted.

Fluoride deprotection (***iv***): ~5 - 10 equivalents of 1.0M TBAF in THF were added to a solution of compound in THF, which was then stirred at rt for 1 – 3 hr, as monitored by TLC. Once complete, the reaction was quenched by the addition of H_2O, diluted into EtOAc, washed with 10% aqueous HCl, (once), then H_2O (until neutral) and saturated NaCl (once), then dried over sodium sulfate and concentrated under vacuum. Further purification was carried out as noted.

Prenyl deprotection (***v***) (adapted[4]): 0.025 – 0.1 equivalents TMSOTf were added to the compound dissolved in DCM, which was stirred at rt. Once complete (as monitored by TLC, generally < 1hr), the reaction mixture was diluted further into DCM, washed with H_2O, saturated $NaHCO_3$ and saturated NaCl, then dried over sodium sulfate and concentrated under vacuum. Further purification was carried out as noted.

2: Previously synthesized[5] but no spectral data reported. 1.0 equivalent of 4-ethynylbenzyl alcohol (**16**), 1.2 equivalents DHP, 0.10 equivalents TsOH, stirred in DCM at 0^0C – rt for 0.5 – 2hr. Once complete, the reaction was diluted with DCM, extracted against saturated $NaHCO_3$ (twice), washed with H_2O and saturated NaCl (until neutral), then dried over sodium sulfate and concentrated under vacuum. Purification by silica gel column (elution at ~5% EtOAc/hexanes). Yields average ~90% (multiple preparations) of a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 7.46 (d, 2H, *J*= 8Hz), 7.31 (d, 2H, *J*= 8Hz), 4.77 (d, 1H, *J*= 13Hz), 4.68, (t, 1H, *J*= 4Hz), 4.49 (d, 1H, *J*= 13Hz), 3.89 (m, 1H), 3.53 (m, 1H), 3.06 (s, 1H), 1.85-1.55 (m, 6H). ^{13}C: 139.2, 132.1, 127.5, 121.1, 97.8, 83.6, 77.1, 68.3, 62.1, 30.5, 25.4, 19.3.

3: Sonogashira coupling (***i***); 1.2 – 1.5 equivalents **1**, 1.0 equivalent **2**, 5% $Pd(PPh_3)_4$, 10% CuI, DMF, 2-5 eq. NEt_3, Stir at 40 – 50^0C for 16 – 24 hr. Standard workup, purification by silica gel column; (elution at ~15% EtOAc/hexanes, 1% AcOH added to all eluting solvents). Yields **3** (74 – 90%, multiple preparations) of clear, colourless crystals, which can be re-crystallized from slow evaporation of THF/pentane. MP: 151 – 153^0C. NMR ($CDCl_3$): ^{1}H : 7.49 (m, 4H), 7.34, (d, 2H, *J*= 8Hz), 7.27 (d, 2H, *J*= 8 Hz), 4.78 (d, 1H, *J*= 13Hz), 4.71 (t, 1H, *J*= 1Hz), 4.50 (d, 1H, *J*= 13Hz),

3.91 (m, 1H), 3.66 (s, 2H), 3.55 (m, 1H), 1.89 – 1.52 (m, 6H). ^{13}C: 176.6, 138.6, 133.3, 131.8, 131.6, 129.4, 127.6, 122.4, 122.3, 97.8, 89.6, 88.9, 68.5, 62.1, 40.8, 30.5, 25.4, 19.3.

4: Ester coupling (***ii***): 1.0 equivalent (1.5g, 4.23mmol) of **3**, 3 equivalents TES-OH, DIC, HOBt, 5 equivalents DIPEA in THF. Stirred at 40^{0}C for 16 hr. Standard workup, purification by silica gel column (elution at ~5% EtOAc/hexanes). Yields 1.81g (90%) of a white, waxy solid. MP: 46 – 48^{0}C. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.32 (d, 2H, *J*= 8Hz), 7.26 (d, 2H, *J*= 8Hz), 4.78 (d, 1H, *J*= 13Hz), 4.69 (t, 1H, *J*= 4Hz), 4.50 (d, 1H, *J*= 13Hz), 4.15 (m, 2H), 3.91 (m, 1H), 3.59 (s, 2H), 3.54 (m, 1H), 1.86-1.53 (m, 6H), 0.95 (m_c, 2H), 0.00 (s, 9H). ^{13}C: 171.3, 138.6, 134.3, 131.7, 131.6, 129.3, 127.6, 122.3, 122.0, 97.8, 89.4, 89.1, 68.4, 63.3, 62.2, 41.5, 30.5, 25.5, 19.3, 17.2, -1.5.

5: THP removal conditions (***iii***); 1.0 equivalent (1.4g, 2.99mmol) of **4**, 0.3 equivalents TsOH in 10% CH_3OH/DCM. Stirred for 3 hr at rt. Standard workup, used without further purification. Yields 1.05g (95%) of a white solid. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.32 (d, 2H, *J*= 8Hz), 7.26 (d, 2H, *J*= 8Hz), 4.69 (d, 2H, *J*= 4Hz), 4.16 (m_c, 2H), 3.58 (s, 2H), 1.85 (t, 1H, *J*= 4Hz), 0.95 (m_c, 2H), 0.0 (s, 9H). ^{13}C: 171.4, 140.9, 134.9, 131.7, 129.3, 126.8, 122.4, 121.9, 89.3, 89.2, 64.9, 63.3, 41.5, 17.2, -1.6.

7: Ester coupling conditions (***ii***); 1.0 equivalent (1 g, 2.73 mmol) of **5**, 2 equivalents **6a**[6], DIC, HOBt, 4 equivalents DIPEA in DMF. Stirred at 40^{0}C for 24 hr. Standard workup, purification by silica gel column (elution at ~10% EtOAc/hexanes). Yields 1.23g (79%) of pale yellow crystals, MP < rt. NMR ($CDCl_3$): ^{1}H: 7.47 (m, 4H), 7.30 (d, 2H, *J*= 8Hz), 7.25 (d, 2H, *J*= 8Hz), 5.09 (s, 2H), 4.54 (t, 1H, *J*= 4Hz), 4.17 (m_c, 2H), 3.83 (m, 1H), 3.71 (m, 1H), 3.58 (s, 2H), 3.47 (m, 1H), 3.35 (m, 1H), 2.36 (t, 2H, *J*= 7Hz), 1.68-1.36 (m, 12H), 0.95 (m_c, 2H), 0.00 (s, 9H). ^{13}C: 173.4, 171.2, 136.1, 134.4, 131.7, 131.6, 129.3, 127.9, 123.1, 121.8, 98.8, 89.5, 89.0, 67.2, 65.6, 63.2, 62.3, 41.4, 34.2, 30.7, 29.3, 25.8, 25.4, 24.8, 19.6, 17.2, -1.6.

8: THP removal conditions (***iii***); 1.0 equivalent (1.2g, 2.12mmol) of **7**, 0.2 equivalents TsOH in 25% CH_3OH/DCM. Stirred for 2.5 hr at rt. Standard workup, used without further purification. Yields 0.99g, (97%) of a white solid. MP = 48 – 50^{0}C. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.30 (d, 2H, *J*= 8Hz), 7.25 (d, 2H, *J*= 8Hz), 5.09 (s, 2H), 4.16 (m_c, 2H), 3.61 (m, 4H), 2.37 (t, 2H, *J* = 7Hz), 1.66 (m, 2H), 1.56 (m, 2H), 1.45 (s, br, 1H), 1.38 (m, 2H), 0.95 (m_c, 2H), 0.00 (s, 9H). ^{13}C: 173.4, 171.3, 136.1, 134.5, 131.7, 131.6, 129.3, 128.0, 123.1, 121.8, 89.5, 89.0, 65.6, 63.3, 62.6, 41.5, 34.1, 32.2, 25.2, 24.6, 17.2, -1.6.

9: Ester coupling conditions (***ii***): 1.0 equivalent (0.63g, 1.31mmol) of **8**, 2 equivalents **6a**, DIC, HOBt, 4 equivalents DIPEA in THF. Stirred at 40^{0}C for 24hr. Standard workup, purification by silica gel column (1:1 EtOAc/hexanes). Yields 0.68g (76%) of a clear, colourless, viscous oil. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.30 (d, 2H, *J*= 8Hz), 7.24 (d, 2H, *J*= 8Hz), 5.09 (s, 2H), 4.54 (t, 1H, *J*= 4Hz), 4.16 (m_c, 2H), 4.03 (t, 2H, *J*= 7Hz), 3.83 (m, 1H), 3.69 (m, 1H), 3.58 (s, 2H), 3.46 (m, 1H), 3.36 (m, 1H), 2.36 (t, 2H, *J*= 7Hz), 2.28 (t, 2H, *J*= 7Hz), 1.75-1.32 (m, 18H), 0.95 (m_c, 2H), 0.00 (s, 9H). ^{13}C: 173.7, 173.2, 171.2, 136.1, 134.4, 131.7, 131.6, 129.3, 128.1, 123.1, 121.8, 98.8, 89.6, 89.0, 67.3, 65.7, 63.9, 63.3, 62.3, 41.5, 34.2, 34.0, 30.7, 29.4, 28.3, 25.8, 25.5, 25.4, 24.8, 24.5, 19.6, 17.2, -1.6.

10: THP removal conditions (***iii***): 1.0 equivalent of **9**, 0.25 equivalents TsOH in 20% CH_3OH/DCM. Stirred for 3 hr at rt. Standard workup, used without further purification. Yields 0.42g (96%) of a clear, pale yellow oil. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.30 (d, 2H, *J*= 8Hz), 7.26 (d, 2H, *J*= 8Hz), 5.10 (s, 2H), 4.17 (m_c, 2H), 4.04 (t, 2H, *J*= 7Hz), 3.65 (m, 3H), 3.59 (s, 2H), 2.36 (t, 2H, *J*= 7Hz), 2.29 (t, 2H, *J*= 7Hz), 1.69 – 1.53 (m, 7H), 1.43 – 1.34 (m, 5H), 0.96 (m_c, 2H), 0.0 (s, 9H). ^{13}C: 173.8, 173.4, 171.4, 136.2, 134.6, 131.8, 129.4, 128.1, 123.3, 121.9, 89.1, 65.8, 64.1, 63.4, 62.7, 41.6, 34.3, 34.2, 32.4, 28.4, 25.6, 25.3, 24.7, 24.6, 17.4, -1.5.

12: Ester coupling conditions (***ii***); 1.0 equivalent **10** (0.336g, 0.56mmol), 2 equivalents **11**[7], DIC, HOBt, 4 equivalents DIPEA in DMF. Stirred at 40^{0}C for 24 hr. Standard workup, purification by silica gel column (elution at ~5% EtOAc/hexanes). Yields 0.341g (60%) of a clear, pale yellow oil. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.30 (d, 2H, *J*= 8Hz), 7.26 (d, 2H, *J*= 8Hz), 5.09 (s, 2H), 4.51

(quintet, 1H, *J*= 6Hz), 4.17 (m_c, 2H), 4.03 (m, 6H), 3.59 (s, 2H), 2.52 (m, 4H), 2.36 (t, 2H, *J*= 7Hz), 2.27 (t, 2H, *J*= 7Hz), 1.69 – 1.57 (m, 10H), 1.37 (m, 4H), 1.23 (s, 18H), 0.96 (m_c, 2H), 0.86 (t, 3H, *J*= 7Hz), 0.82 (s, 9H), 0.04 (s, 6H), 0.00 (s, 9H). ^{13}C: 173.5, 173.1, 171.2, 171.0, 136.1, 134.5, 131.7, 129.3, 128.0, 123.2, 121.8, 89.6, 89.0, 66.3, 65.6, 64.7, 64.3, 64.0, 63.2, 42.5, 42.4, 41.5, 34.0, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 28.5, 28.3, 28.2, 25.9, 25.6, 25.5, 24.6, 24.5, 22.6, 17.9, 17.3, 14.1, -1.6, -4.9.

HO_2C-Dip-Hex-Hex-G(12)OH: Fluoride deprotection conditions (***iv***): 6 equivalents of 1.0M TBAF in THF was added to **12** in THF. Stirred for 3hr at rt. Standard workup. The crude residue was purified on Florisil (EtOAc/hexanes, 1% AcOH added to all eluting solvents). While the reaction appeared quantitative by TLC, the purification was problematic, leading to a 59% yield (0.121g) of a pale blue solid, which was further purified by RP-HPLC (1:1ACN: CH_3OH as eluting solvents) to yield a crystalline white solid. UV: λ_{max} (CH_3OH) = 305 nm. Fluorescence: λ_{max}Ex (CH_3OH) = 305 nm, λ_{max}Em (CH_3OH) = 322 nm. NMR (1:1 $CDCl_3$: CD_3OD, 500MHz): ^{1}H: 7.48 (d, 2H, *J*= 8Hz), 7.40 (d, 2H, *J*= 8Hz), 7.34 (d, 2H, *J*= 8Hz), 7.30 (d, 2H, *J*= 8Hz), 5.12 (s, 2H), 4.42 (m, 1H), 4.07 (m, 6H), 3.61 (s, br, 2H), 2.53 (m, 4H), 2.40 (t, 2H, *J*= 7Hz), 2.31 (t, 2H, *J*= 7Hz), 1.70 – 1.59 (m, 10H), 1.39 (m, 4H), 1.26 (s, 18H), 0.88 (t, 3H, *J*= 7Hz). ^{13}C: 175.4, 174.9, 172.9, 172.8, 139.9, 137.4, 132.6, 132.3, 130.4, 129.1, 124.6, 121.8, 90.9, 89.2, 66.7, 66.0, 65.8, 65.5, 65.3, 42.7, 42.6, 35.0, 34.9, 32.9, 30.7, 30.7, 30.6, 30.5, 30.4, 30.3, 29.6, 29.3, 29.2, 26.9, 26.5, 26.4, 25.6, 23.6, 14.5. HR-MS (-ve ESI): Calc'd for $C_{46}H_{63}O_{11}$; 791.4376 amu, obtained; 791.4550 amu. Overall yield over 8 steps from **3** = 17%

6b: Ester coupling conditions (***ii)***: 1.0 equivalent (0.5g, 2.32mmol) of **6a**, 1.2 equivalents PRE-OH, DIC, HOBt, 2.4 equivalents DiPEA in THF as solvent. Stirred at rt for 18 hr. Yields 0.49g (74 %) of clear colourless oil. NMR ($CDCl_3$): ^{1}H: 5.31 (m, 1H), 4.53 (m, 3H), 3.83 (m, 1H), 3.70 (m, 1H), 3.46 (m, 1H), 3.35 (m, 1H), 2.28 (t 2H, *J*= 7Hz), 1.79 (m, 1H), 1.73 (s, 3H), 1.68 (s, 3H), 1.66 – 1.49 (m, 9H), 1.36 (m, 2H). ^{13}C: 173.7, 138.9, 118.7, 98.8, 67.3, 65.8, 62.3, 61.2, 34.3, 30.7, 29.4, 25.8, 25.7, 25.5, 24.8, 19.6, 17.9.

6c: THP removal conditions (***iii***): 1.0 equivalent (0.45g, 1.59mmol) of **6b**, 0.1equivalent TsOH in 10% CH_3OH/DCM. Stirred at rt for 2 hr. Standard workup, purification by silica gel column (elution at ~15% EtOAc/hexanes) yields 0.32g (86 %) of a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 5.26 (m, 1H), 4.49 (d, 2H, *J*= 7Hz), 3.54 (t, 2H, *J*= 7Hz), 2.33 (s, br, 1H), 2.24 (t, 2H, *J*= 7Hz), 1.68 (s, 3H), 1.63 (s, 3H), 1.58 (m, 2H), 1.50 (m, 2H), 1.31 (m, 2H).^{13}C: 173.8, 138.9, 118.6, 62.3, 61.2, 34.2, 32.2, 25.7, 25.2, 24.6, 17.9.

13: Ester coupling conditions (***ii***): 1.0 equivalent (1.4g, 6.0mmol) of **1**, 1.5 equivalents of **6c**, DIC, HOBt, 3 equivalents DiPEA in THF. Stirred at 40^{0}C for 16hr. Standard workup, purification by silica gel column (elution at ~7% EtOAc/hexanes). Yields 1.76g (73%) of a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 7.61 (dt, 2H, *J*= 8, 2Hz), 7.00 (d, 2H, *J*= 8Hz), 5.31 (m, 1H), 4.54 (d, 2H, *J*= 7Hz), 4.05 (t, 2H, *J*= 7Hz), 3.51 (s, 2H), 2.26 (t, 2H, *J*= 7Hz), 1.73 (s, 3H), 1.68 (s, 3H), 1.60 (m, 4H), 1.31 (m, 2H).^{13}C: 173.5, 171.0, 139.0, 137.6, 133.7, 131.3, 118.6, 92.6, 64.8, 61.3, 40.9, 34.1, 28.2, 25.8, 25.4, 24.5, 18.0.

14: Prenyl deprotection conditions (***v***): 1.0 equivalent (0.5g, 1.16mmol) **13**, 0.05 equivalents TMSOTf in DCM, stirred at rt for 1 hr. During this time, the reaction turned dark brown/purple. Standard workup yielded a brown oil, from which a white solid precipitated with the addition of hexanes, yielding 0.359g (83%) of **14**, which was used without further purification. NMR ($CDCl_3$): ^{1}H: 11.38 (s, br, 1H), 7.61 (d, 2H, *J*= 8Hz), 6.99 (d, 2H, *J*= 8Hz), 4.05 (t, 2H, *J*= 7Hz), 3.52 (s, 2H), 2.31 (t, 2H, *J*= 7Hz), 1.60 (m, 4H), 1.33 (m, 2H). ^{13}C: 179.7, 171.2, 137.6, 133.7, 131.3, 92.7, 64.9, 40.9, 33.9, 28.2, 25.3, 24.2.

6d: Ester coupling conditions (***ii***): 1.0 equivalent (1.43g, 6.62mmol) of **6a**, 1.5 equivalents TES-OH, DIC, HOBt, 3 equivalents DiPEA in THF. Stirred at rt for 16 hr. Standard workup, purification by silica gel column (elution at ~4% EtOAc/hexanes) yields 1.71g, (82 %) as a clear colourless oil. NMR ($CDCl_3$): ^{1}H: 4.54 (m, 1H), 4.12 (m_c, 2H), 3.83 (m, 1H), 3.69 (m, 1H), 3.46 (m, 1H), 3.34 (m,

1H), 2.26 (t, 2H, *J*= 7Hz), 1.81-1.34 (m, 12H), 0.94 (m_c, 2H), 0.01 (s, 9H).^{13}C: 173.5, 98.5, 67.0, 62.1, 61.9, 34.2, 30.5, 29.2, 25.7, 25.3, 24.6, 19.4, 17.1, -1.7.

6e: THP deprotection conditions (***iii***): 1.0 equivalent (0.4g, 1.26mmol) of **6d**, 0.1equivalent TsOH in 10% CH_3OH/DCM. Stirred at rt for 2.5 hr. Standard workup, purification by silica gel column (elution at ~20% EtOAc/hexanes) yields 0.272g, (93%) as a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 4.12 (m_c, 2H), 3.60 (t, 2H, *J*= 6Hz), 2.26 (t, 2H, *J*= 7Hz), 1.90 (s, br, 1H), 1.66 – 1.49 (m, 4H), 1.35 (m, 2H), 0.94 (m_c, 2H), 0.00 (s, 9H).^{13}C: 173.9, 62.5, 62.4, 34.3, 32.2, 25.2, 24.6, 17.2, -1.6.

15: Ester coupling conditions (***ii***): 1.0 equivalent (0.359g, 0.965mmol) of **14**, 1.4 equivalents of **6e**, DIC, HOBt, 2.8 equivalents DiPEA in THF. Stirred at rt for 16hr. Standard workup, purification by silica gel column (elution at ~10% EtOAc/hexanes) yields 0.520g (92%) as a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 7.62 (d, 2H, *J*= 8Hz), 7.01 (d, 2H, *J*= 8Hz), 4.14 (m_c, 2H), 4.05 (m, 4H), 3.52 (s, 2H), 2.26 (m, 4H), 1.69-1.55 (m, 8H), 1.41-1.26 (m, 4H), 0.96 (m_c, 2H), 0.02 (s, 9H).^{13}C: 173.6, 173.4, 170.9, 137.6, 133.6, 131.2, 92.5, 64.8, 64.1, 62.4, 40.8, 34.3, 34.0, 28.3, 28.2, 25.5, 25.4, 24.5, 24.4, 17.3, -1.5.

17: Sonogashira coupling conditions (***i***); 1.0 equivalent (0.348g, 0.591mmol) of **15**, 1.5 equivalents **16**, 5% $Pd(PPh_3)_4$, 10% CuI, 3 equivalents NEt_3 in deoxygenated DMF. Stirred in the dark under N_2 at rt for 16hr. Standard workup, purification by silica gel column (elution at ~35% EtOAc/hexanes), yields 0.299g, (85%) as a pale yellow semi-solid. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.33 (d, 2H, *J*= 8Hz), 7.25 (d, 2H, *J*= 8Hz), 4.69 (d, 2H, *J*= 1Hz), 4.14 (m_c, 2H), 4.06 (m, 4H), 3.61 (s, 2H), 2.26 (m, 4H), 1.91 (s, br, 1H), 1.67 – 1.56 (m, 8H), 1.35 (m, 4H), 0.96 (m_c, 2H), 0.03 (s, 9H).^{13}C: 173.7, 173.5, 171.2, 141.1, 134.3, 131.7, 129.3, 126.8, 122.4, 122.0, 89.3, 89.1, 64.9, 64.8, 64.2, 62.5, 41.3, 34.3, 34.1, 28.4, 28.2, 25.6, 25.5, 24.6, 24.5, 17.3, -1.5.

18: Ester coupling conditions (***ii***): 1.0 equivalent (0.25g, 0.42mmol) of **17**, 1.3 equivalents **11**, DIC, HOBt, 2.6 equivalents DIPEA in DMF. Stirred at 50^{0}C for 24hr. Standard workup, purification by silica gel column (elution at ~15% EtOAc/hexanes) yields 0.26g (61%) as a pale yellow oil. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.30 (d, 2H, *J*= 8Hz), 7.25 (d, 2H, *J*= 8Hz), 5.09 (m, 2H), 4.56 (quintet, 1H, *J*= 6Hz), 4.14 (m_c, 2H), 4.10 – 4.00 (m, 6H), 3.61 (s, 2H), 2.61 (d, 2H, *J*= 6Hz), 2.54 (d, 2H, *J*= 6Hz), 2.27 (t, 4H, *J*= 7Hz), 1.67 – 1.56 (m, 10H), 1.38 (m, 4H), 1.24 (s, br, 18H), 0.96 (m_c, 2H), 0.86 (t, 3H, *J*= 7Hz), 0.82 (s, 9H), 0.03 (m, 6H), 0.02 (s, 9H).^{13}C: 173.6, 173.4, 171.1, 170.9, 170.7, 135.8, 134.4, 131.7, 131.6, 129.3, 128.0, 123.1, 121.9, 89.6, 89.2, 66.2, 65.8, 64.7, 64.6, 64.1, 62.4, 42.4, 42.3, 41.3, 34.2, 34.0, 31.8, 29.6, 29.5, 29.4, 29.3, 29.2, 28.5, 28.3, 28.2, 25.9, 25.6, 25.5, 25.4, 24.5, 24.4, 22.6, 17.8, 17.3, 14.1, -1.6, -4.9.

HO_2C-Hex-Hex-Dip-G(12)-OH: Fluoride deprotection conditions (***v***): 1.0 equivalent (0.2g, 0.198mmol) of **18**, 10 equivalents of 1.0M TBAF in THF, stirred at rt for 3 hours. Standard workup, purification by silica gel chromatography (elution at ~30% EtOAc/hexanes, 1% AcOH added to all eluting solvents) yields the desired oligomer (0.115g, 73%) as an off-white solid. The compound was further purified by RP-HPLC (1: 1 ACN: CH_3OH as eluting solvents) to yield a white powder. UV: λ_{max} (CH_3OH) = 305 nm. Fluorescence: λ_{max}Ex (CH_3OH) = 305nm, λ_{max}Em (CH_3OH) = 322nm. NMR (1:1 $CDCl_3$: CD_3OD, 500MHz): ^{1}H: 7.47 (m, 4H), 7.33 (d, 2H, *J*= 8Hz), 7.25 (d, 2H, *J*= 8Hz), 5.13 (s, 2H), 4.46 (m, 1H), 4.09 – 4.01 (m, 6H), 3.63 (s, 2H), 2.60 (m, 2H), 2.53 (m, 2H), 2.28 (t, 4H, *J*= 7Hz), 1.66 – 1.58 (m, 10H), 1.40 – 1.23 (m, 23H), 0.85 (t, 3H, *J*= 7Hz).^{13}C: 175.0, 172.7, 172.6, 172.2, 136.7, 135.2, 132.4, 132.3, 130.1, 128.8, 123.9, 122.7, 90.1, 89.7, 66.7, 65.7, 65.6, 65.5, 65.1, 42.1, 41.9, 34.7, 32.6, 30.3, 30.3, 30.2, 30.1, 30.0, 29.9, 29.2, 28.9, 28.8, 26.6, 26.2, 26.0, 25.3, 25.1, 23.3, 14.5. HR-MS (-ve ESI): Calc'd for $C_{46}H_{63}O_{11}$; 791.4379 amu, obtained; 791.4780 amu. HR-MS (+ve ESI): Calc'd for $C_{46}H_{64}O_{11}Na$; 815.4357 amu, obtained; 815.4356 amu. Overall yield over 6 steps from **1**: 21%

19: Ester coupling conditions (***ii***): 1.0 equivalent (1.18g, 8.92mmol) of **16**, 1.5 equivalents of **6a**, DIC, HOBt, 3 equivalents DIPEA in THF. Stir at rt for 16 hr. Standard workup, purification by silica gel column (elution at ~5% EtOAc/hexanes), yields 2.41g (82%) of a clear, pale yellow oil. NMR ($CDCl_3$): ^{1}H: 7.43 (d, 2H, *J*= 7Hz), 7.26 (d, 2H, *J*= 7Hz), 5.05 (s, 2H), 4.50 (m, 1H), 3.81 (m,

1H), 3.67 (m, 1H), 3.44 (m, 1H), 3.34 (m, 1H), 3.06 (s, 1H), 2.33 (t, 2H, *J*= 7Hz), 1.77 – 1.34 (m, 12H).^{13}C: 173.3, 136.8, 132.2, 127.9, 121.9, 98.8, 83.2, 77.6, 67.2, 65.4, 62.3, 34.1, 30.7, 29.3, 25.8, 25.4, 24.7, 19.6.

20: Sonogashira coupling conditions (***i***); 1.0 equivalent of **19**, 1.3 equivalents **1**, 4% $Pd(PPh_3)_4$, 8% CuI, 2 equivalents NEt_3, in DMF. Stir at rt for 16hr. After standard workup, the crude residue (a brown oil) was treated with diethyl ether, from which a white precipitate was isolated by filtration. This procedure lead to a suitably pure compound in ~80% yield (78 – 83, three separate preparations), which could be further purified by column chromatography on silica gel (EtOAc/hexanes, 1% AcOH added to all eluting solvents). NMR (d_6-acetone): ^{1}H: 7.53 (m, 4H), 7.43 (d, 2H, *J*= 8Hz), 7.37 (d, 2H, *J*= 8Hz), 5.15 (s, 2H), 4.55 (m, 1H), 3.78 (m, 1H), 3.67 (m, 3H), 3.43 (m, 1H), 3.35 (m, 1H), 2.40 (t, 2H, *J*= 7Hz), 1.81 – 1.39 (m, 12H). ^{13}C: 173.5, 172.4, 138.2, 136.7, 132.4, 132.3, 130.6, 129.0, 123.7, 122.4, 99.2, 90.2, 89.6, 67.6, 65.8, 62.2, 41.1, 34.5, 31.5, 30.1, 26.6, 26.4, 25.5, 20.2.

21: Ester coupling conditions (***ii***): 1.0 equivalent (0.25g, 0.756mmol) of **6c**, 1.2 equivalents of **20**, DIC, HOBt, 2.4 equivalents DIPEA in THF. Stirred at 40^{0}C for 24 hr. Standard workup, purification by silica gel column (elution at ~20% EtOAc/hexanes) yields 0.32g (55%) of a pale yellow, clear oil. NMR ($CDCl_3$): ^{1}H: 7.47 (m, 4H), 7.29 (d, 2H, *J*= 8Hz), 7.24 (d, 2H, *J*= 8Hz), 5.31 (m, 1H), 5.09 (s, 2H), 4.54 (m, 3H), 4.06 (t, 2H, *J*= 7Hz), 3.83 (m, 1H), 3.71 (m, 1H), 3.59 (s, 2H), 3.47 (m, 1H), 3.35 (m, 1H), 2.36 (t, 2H, *J*= 7Hz), 2.27 (t, 2H, *J*= 7Hz), 1.78 (m, 1H), 1.73 (s, 3H), 1.68 (s, 3H), 1.67 – 1.29 (m, 17H). ^{13}C: 173.4, 173.3, 171.1, 138.9, 136.1, 134.3, 131.7, 131.6, 129.3, 127.9, 123.1, 121.8, 118.5, 98.8, 89.5, 89.0, 67.2, 65.5, 64.7, 62.3, 61.2, 41.2, 34.1, 34.0, 30.7, 29.3, 28.2, 25.8, 25.7, 25.4, 25.3, 24.7, 24.4, 19.6, 17.9.

22: THP deprotection conditions (***iii***); 1.0 equivalent (0.32g, 0.419mmol) of **21**, 0.20 equivalents TsOH in 20% CH_3OH/DCM, stirred at rt for 3 hr. Standard workup yields 0.28g (>95%, quantitative conversion by TLC) of a clear, pale yellow oil, which was used directly without further purification to synthesize **23**.

23: Ester coupling conditions (***ii***); 1.0 equivalent (0.28g, 0.411mmol) of **22**, 1.5 equivalents **11**, DIC, HOBt, 3 equivalents DIPEA in THF. Stirred at rt for 30hr (sluggish coupling, poor conversion by TLC). Standard workup, purification by silica gel column (elution at ~10% EtOAc/hexanes) yields 0.21g (53%) of a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 7.44 (m, 4H), 7.25 (d, 2H, *J*= 8Hz), 7.20 (d, 2H, *J*= 8Hz), 5.27 (m, 1H), 5.05 (s, 2H), 4.50 (m, 3H), 4.07 – 3.96 (m, 6H), 3.56 (s, 2H), 2.48 (m, 4H), 2.32 (t, 2H, *J*= 7Hz), 2.23 (t, 2H, *J*= 7Hz), 1.69 (s, 3H), 1.64 (s, 3H), 1.57 (m, 10H), 1.38 – 1.19 (m, 22H), 0.82 (t, 3H, *J*= 7Hz), 0.77 (s, 9H), 0.00 (m, 6H). ^{13}C: 173.5, 173.2, 171.1, 171.0, 171.0, 138.9, 136.1, 134.4, 131.7, 129.3, 128.0, 123.2, 121.9, 118.6, 89.6, 89.0, 66.3, 65.7, 64.8, 64.7, 64.2, 61.2, 42.5, 42.4, 41.3, 34.1, 34.0, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 28.5, 28.3, 28.2, 25.9, 25.7, 25.6, 25.5, 25.4, 24.5, 22.6, 17.9, 17.8, 14.1, -4.9.

HO_2C-Hex-Dip-Hex-G(12)-OH: Prenyl deprotection conditions (***v***); 1.0 equivalent (0.115g, 0.197mmol) of **23**, 0.05 equivalents TMSOTf in DCM, stirred at rt for 1 hr. Standard workup yields a yellow oil, from which an off-white solid precipitated upon hexanes addition. Further purification by silica gel column (elution at ~20% EtOAc/hexanes, 1% AcOH added to all eluting solvents) yields 0.073g (76%) of a pale blue powder, which was further purified by RP-HPLC (1: 1 ACN/CH_3OH as eluting solvents) to afford a white crystalline solid. UV: λ_{max} (CH_3OH) = 305 nm. Fluorescence: λ_{max}Ex (CH_3OH) = 305 nm, λ_{max}Em (CH_3OH) = 322 nm. NMR ($CDCl_3$): ^{1}H: 7.49 (m, 4H), 7.31 (d, 2H, *J*= 8Hz), 7.25 (d, 2H, *J*= 8Hz), 5.11 (s, 2H), 4.44 (quintet, 1H, *J*= 6Hz), 4.12 – 4.06 (m, 6H), 3.61 (s, 2H), 2.59 (m, 1H), 2.53 (m, 4H), 2.35 (m, 4H), 1.69 – 1.52 (m, 10H), 1.41 – 1.32 (m, 4H), 1.25 (s, br, 18H), 0.86 (t, 3H, *J*= 7Hz). ^{13}C: 173.2, 171.9, 171.8, 171.2, 136.1, 134.4, 131.8, 131.7, 129.3, 128.1, 123.2, 121.9, 89.6, 89.1, 65.7, 65.0, 64.8, 64.7, 64.6, 41.3, 40.6, 34.0, 33.6, 31.9, 29.6, 29.5, 29.5, 29.3, 29.2, 28.5, 28.2, 25.9, 25.4, 25.3, 24.5, 24.2, 22.7, 14.1. HR-MS (-ve ESI): Calc'd for $C_{46}H_{63}O_{11}$; 791.4376 amu, obtained; 791.4670 amu. HR-MS (+ve ESI): Calc'd for $C_{46}H_{64}O_{11}Na$; 815.4346 amu, obtained; 815.4316 amu. Overall yield in 6 steps from **16**: 14%

24b: Ester coupling conditions (***ii***): 1.0 equivalent (2g, 7.35mmol) of **24a**[6], 2 equivalents PRE-OH, 0.5 DiPEA in THF. Stirred for 24 hr at 40^0C. Standard workup, purification by silica gel (elution at ~ 3% EtOAc/hexanes, 1% AcOH added to all eluting solvents). Sluggish coupling and a seemingly unstable starting material lead to a poor (1.10 g, 44%) yield of a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 5.31 (t7, 1H, *J*= 6, 1Hz), 4.53 (m, 3H), 3.58 (m, 1H), 3.70 (m, 1H), 3.47 (m, 1H), 3.35 (m, 1H), 2.26 (t, 2H, *J*= 7Hz), 1.73 (s, 3H), 1.68 (s, 3H), 1.67 – 1.50 (m, 10H), 1.27 (s, 10H).^{13}C: 173.8, 138.8, 118.8, 98.9, 67.7, 62.3, 61.1, 34.4, 30.8, 29.7, 29.3, 29.2, 29.1, 26.2, 25.7, 25.5, 24.9, 19.7, 17.9.

24c: THP removal conditions (***iii***): 1.0 equivalent (0.85g, 2.5mmol) **24b**, 0.2 equivalents TsOH in 20% CH_3OH/DCM. Stirred for 1 hour at rt. Standard work up, purification by silica gel plug, (15% EtOAc/hexanes) yields 0.64g (75%) of a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 5.32 (t7, 1H, *J*= 7, 1Hz), 4.55 (d, 2H, *J*= 7Hz), 3.61 (t, 2H, *J*= 7Hz), 2.27 (t, 2H, *J*= 7Hz), 1.74 (s, 3H), 1.69 (s, 3H), 1.62 – 1.49 (m, 4H), 1.35 – 1.27 (m, 11H). ^{13}C: 173.9, 138.9, 118.7, 62.9, 61.2, 34.3, 32.7, 29.4, 29.3, 29.1, 29.0, 25.7, 25.6, 24.9, 17.9.

25: Ester coupling conditions (***ii***): 1.0 equivalent (0.45g, 1.75mmol) of **24c,** 1.5 equivalents of **1**, DIC, HOBt, and 3 equivalents DIPEA in DMF. Stirred for 16 hr at rt. Standard work up, purification by silica gel plug (15% EtOAc/hexanes) yields 0.709g (83%) of a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 7.62 (d, 2H, *J*= 8Hz), 7.01 (d, 2H, *J*= 8Hz), 5.32 (m, 1H), 4.55 (d, 2H, *J*= 7Hz), 4.05 (t, 2H, *J*= 7Hz), 3.53 (s, 2H), 2.28 (t, 2H, *J*= 7Hz), 1.74 (s, 3H), 1.69 (s, 3H), 1.62 – 1.53 (m, 4H), 1.25 (s, br, 10H).^{13}C: 173.8, 170.9, 138.9, 137.5, 133.8, 131.2, 118.7, 92.5, 65.1, 61.2, 40.9, 34.3, 29.2, 29.1, 29.0, 28.5, 25.7, 24.9, 17.9.

26: Sonogashira coupling conditions (***i***): 1.6 equivalents of **19**, 5% $Pd(PPh_3)_4$, 10% CuI, and 3 equivalents NEt_3 were added to a solution of 1.0 equivalent (0.409g, 0.84mmol) of **25** in deoxygenated THF. Reaction was stirred under N_2 at rt for 10 hrs. Standard work up, purification by silica gel column (elution at ~10% EtOAc/hexanes) yields 0.495g (85%) of a pale yellow oil. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.31 (d, 2H, *J*= 8Hz), 7.26 (d, 2H, *J*= 8Hz), 5.32 (t7, 1H, *J*= 6, 1Hz), 5.10 (s, 2H), 4.55 (m, 3H), 4.07 (t, 2H, *J*= 7Hz), 3.84 (m, 1H), 3.72 (m, 1H), 3.61 (s, 2H), 3.48 (m, 1H), 3.36 (m, 1H), 2.37 (t, 2H, *J*= 7Hz), 2.27 (t, 2H, *J*= 7Hz), 1.75 (s, 3H), 1.69 (s, 3H), 1.65 – 1.50 (m, 14H), 1.45 -1.35 (m, 2H), 1.26 (s, 10H).^{13}C: 173.9, 173.4, 171.2, 138.9, 136.2, 134.5, 131.7, 129.3, 128.0, 123.1, 121.9, 118.7, 98.9, 89.5, 89.0, 67.3, 65.6, 65.1, 62.4, 61.2, 41.3, 34.3, 34.2, 30.7, 29.4, 29.3, 29.1, 29.0, 28.5, 25.8, 25.8, 25.7, 25.5, 24.9, 24.8, 19.7, 17.9.

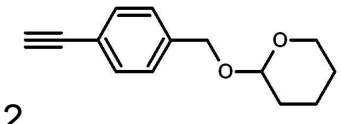
27: THP removal conditions (***iii***): 1.0 equivalent (0.48g, 0.69mmol) of **26,** 0.3 equivalents TsOH in 20% CH_3OH/DCM. Stirred for 1 hr at rt. Standard work up, purification by silica gel column (elution ~ 30% EtOAc/hexanes) yields 0.373g (89%) of a white solid. MP = 63 – 65^0C. NMR ($CDCl_3$): ^{1}H: 7.49 (m, 4H), 7.31 (d, 2H, *J*= 8Hz), 7.26 (d, 2H, *J*= 8Hz), 5.32 (t7, 1H, *J*= 6, 1Hz), 5.10 (s, 2H), 4.55 (d, 2H, *J*= 7Hz), 4.07 (t, 2H, *J*= 7Hz), 3.63 (m, 4H), 2.38 (t, 2H, *J*= 7Hz), 2.27 (t, 2H, *J*= 7Hz), 1.74 (s, 3H), 1.69 (s, 3H), 1.65 – 1.55 (m, 8H), 1.44 – 1.34 (m, 3H), 1.26 (s, 10H). ^{13}C: 173.9, 173.4, 171.2, 138.9, 136.1, 134.5, 131.7, 131.7, 129.3, 128.0, 123.2, 121.9, 118.7, 89.6, 89.0, 65.7, 65.1, 62.6, 61.2, 41.4, 34.3, 34.2, 32.3, 29.3, 29.1, 29.1, 28.5, 25.8, 25.7, 25.3, 24.9, 24.6, 17.9.

28: Ester coupling conditions (***ii***): 1.0 equivalent (0.25g, 0.413mmol) of **27**, 1.5 equivalents **11**, DIC, HOBt, 3 equivalents DIPEA. Stirred in THF for 16 hr at rt. Standard work up, purification by silica gel column (elution at ~15% EtOAc/hexanes) yields 0.316g (75%) of a clear, colourless oil. NMR ($CDCl_3$): ^{1}H: 7.48 (m, 4H), 7.31 (d, 2H, *J*= 8Hz), 7.25 (d, 2H, *J*= 8Hz), 5.32 (m, 1H), 5.10 (s, 2H), 4.53 (m, 3H), 4.09 – 4.00 (m, 6H), 3.60 (s, 2H), 2.52 (m, 4H), 2.36 (t, 2H, *J*= 7Hz), 2.27 (t, 2H, *J*= 7Hz), 1.74 (s, 3H), 1.69 (s, 3H), 1.67 – 1.56 (m, 9H), 1.43 – 1.20 (m, 32H), 0.86 (t, 3H, *J*= 7Hz), 0.82 (s, 9H), 0.04 (s, 6H). ^{13}C: 173.8, 173.1, 171.1, 171.0, 170.9, 138.8, 136.0, 134.5, 131.7, 129.3, 128.0, 123.2, 121.9, 118.7, 89.6, 89.0, 66.3, 65.6, 65.1, 64.6, 64.2, 61.1, 42.5, 42.5, 41.3, 34.3, 34.0, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 29.2, 29.1, 29.0, 28.5, 28.4, 28.2, 25.9, 25.7, 25.7, 25.6, 25.5, 24.9, 24.5, 22.6, 17.9, 17.8, 14.1, -4.9.

HO_2C-Dec-Dip-Hex-G(12)-OH: Prenyl deprotection (***v***):, 0.1 equivalents TMSOTf was added to a

solution of 1.0 equivalent (0.180g, 0.177mmol) of **28** in DCM. The reaction turned greenish brown immediately. Reaction was complete after 20 mins. After standard workup, hexanes was added to the crude residue (a greenish oil), from which a white solid immediately precipitated. This was then filtered, rinsed with hexanes and dried to yield 0.133 g (87%) of the desired compound. The product was further purified by RP-HPLC (1:1 ACN/CH_3OH as eluting solvents) to yield a white powder. UV: λ_{max} (CH_3OH) = 305 nm. Fluorescence: λ_{max}Ex (CH_3OH) = 305 nm, λ_{max}Em (CH_3OH) = 322 nm. NMR ($CDCl_3$, 500 MHz): ^{1}H: 7.50 (d, 2H, *J*= 8Hz), 7.46 (d, 2H, *J*= 8Hz), 7.31 (d, 2H, *J*= 8Hz), 7.26 (d, 2H, *J*= 8Hz), 5.10 (s, 2H), 4.45 (m, 1H), 4.10 – 4.05 (m, 6H), 3.61 (s, 2H), 2.53 (m, 4H), 2.37 (t, 2H, *J*= 7Hz), 2.31 (t, 2H, *J*= 7Hz), 1.68 – 1.57 (m, 10H), 1.41 – 1.36 (m, 2H), 1.25 (m, 29H), 0.86 (t, 3H, *J*= 7Hz). ^{13}C: 178.9, 173.2, 171.9, 171.2, 136.1, 134.5, 131.7, 131.7, 129.3, 128.0, 123.2, 121.9, 89.6, 89.0, 65.7, 65.1, 65.0, 64.7, 64.5, 41.3, 40.7, 34.0, 33.9, 31.9, 29.6, 29.5, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 29.0, 28.9, 28.5, 28.4, 28.2, 25.8, 25.7, 25.4, 24.6, 24.4, 22.6, 14.1. HR-MS (-ve ESI): Calc'd for $C_{50}H_{71}O_{11}$; 847.4996 amu, obtained; 847.5021 amu. Overall yield in 5steps from **24c**: 41%

[1]H. Luong and T. M. Fyles, *Org. Biomol. Chem.*, 2008, **7**, 725-732.
[2]M. B. Buchmann, T. M. Fyles and T. Sutherland, *Bioorg. Med. Chem.*, 2004, **12**, 1315-1324.
[3]P. K. Eggers, T. M. Fyles, K. D. D. Mitchell and T. Sutherland, *J. Org. Chem.*, 2003, **68**, 1050-1058.
[4]M. Nishizawa, H. Yamamoto, K. Seo, H. Imagawa and T. Sugihara, *Org. Lett.*, 2002, **4**, 1947-1949.
[5]R. R. Fraser, P. Hanbury and C. Reyes-Zamora, *Can. J. Chem.*, 1967, **45**, 2481-2487.
[6]H. Luong and T. M. Fyles, *Org. Biomol. Chem.*, 2008, **7**, 725-732.
[7]T. M. Fyles, C. Hu and H. Luong, *J. Org. Chem.*, 2006, **71**, 8545-8551.



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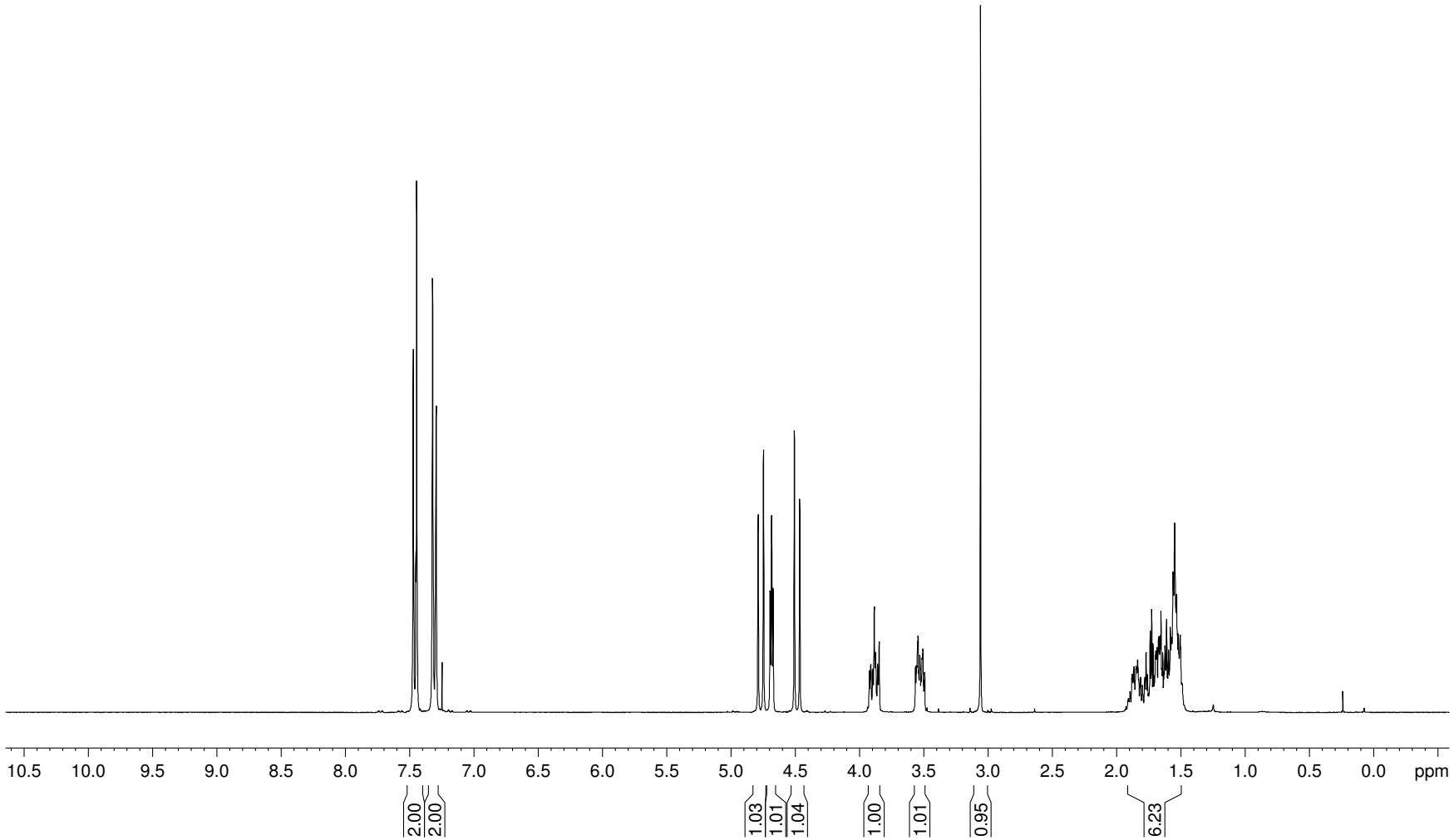
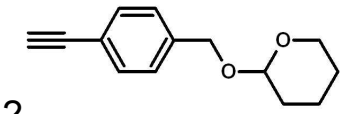
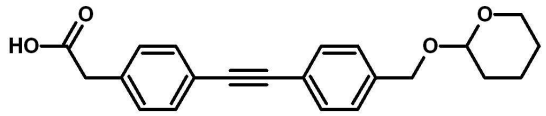
^{1}H NMR ($CDCl_3$) 300 MHz





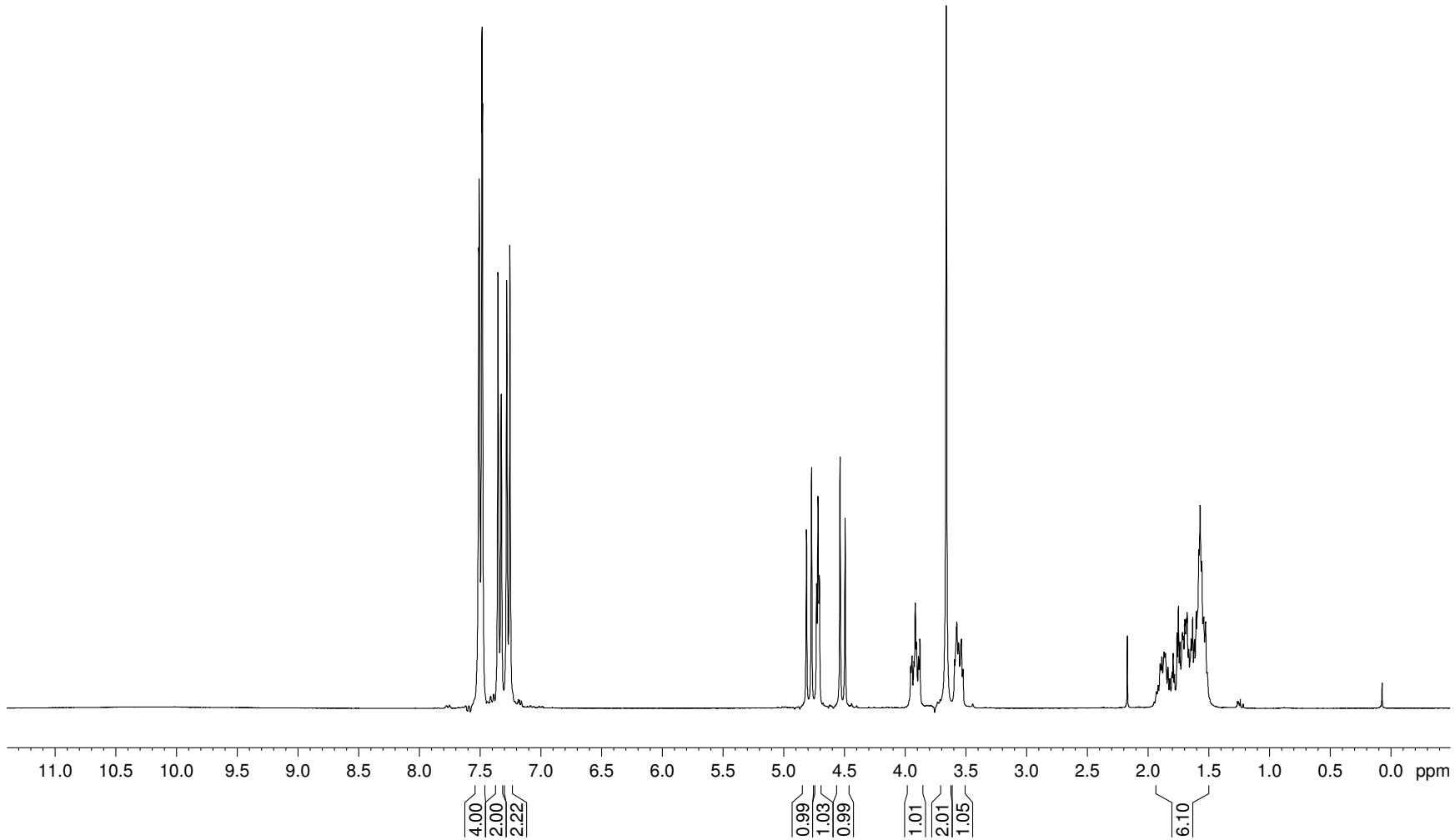
2

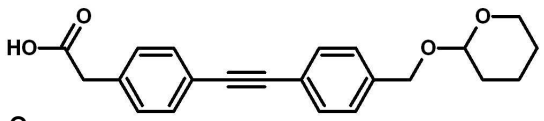
^{13}C NMR ($CDCl_3$) 75 MHz



3

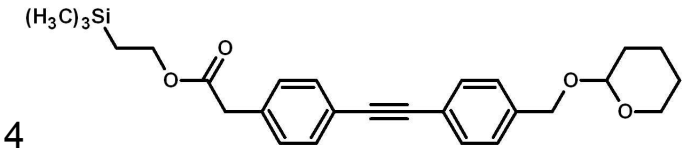
^{1}H NMR ($CDCl_3$) 300 MHz





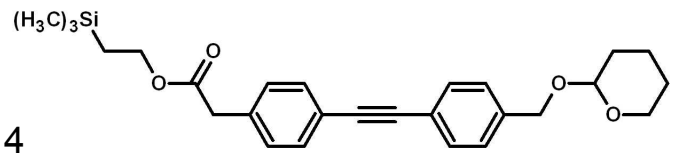
3

^{13}C NMR ($CDCl_3$) 75 MHz



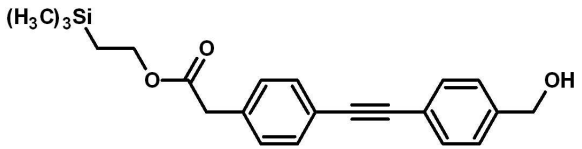
4

^{1}H NMR ($CDCl_3$) 300 MHz



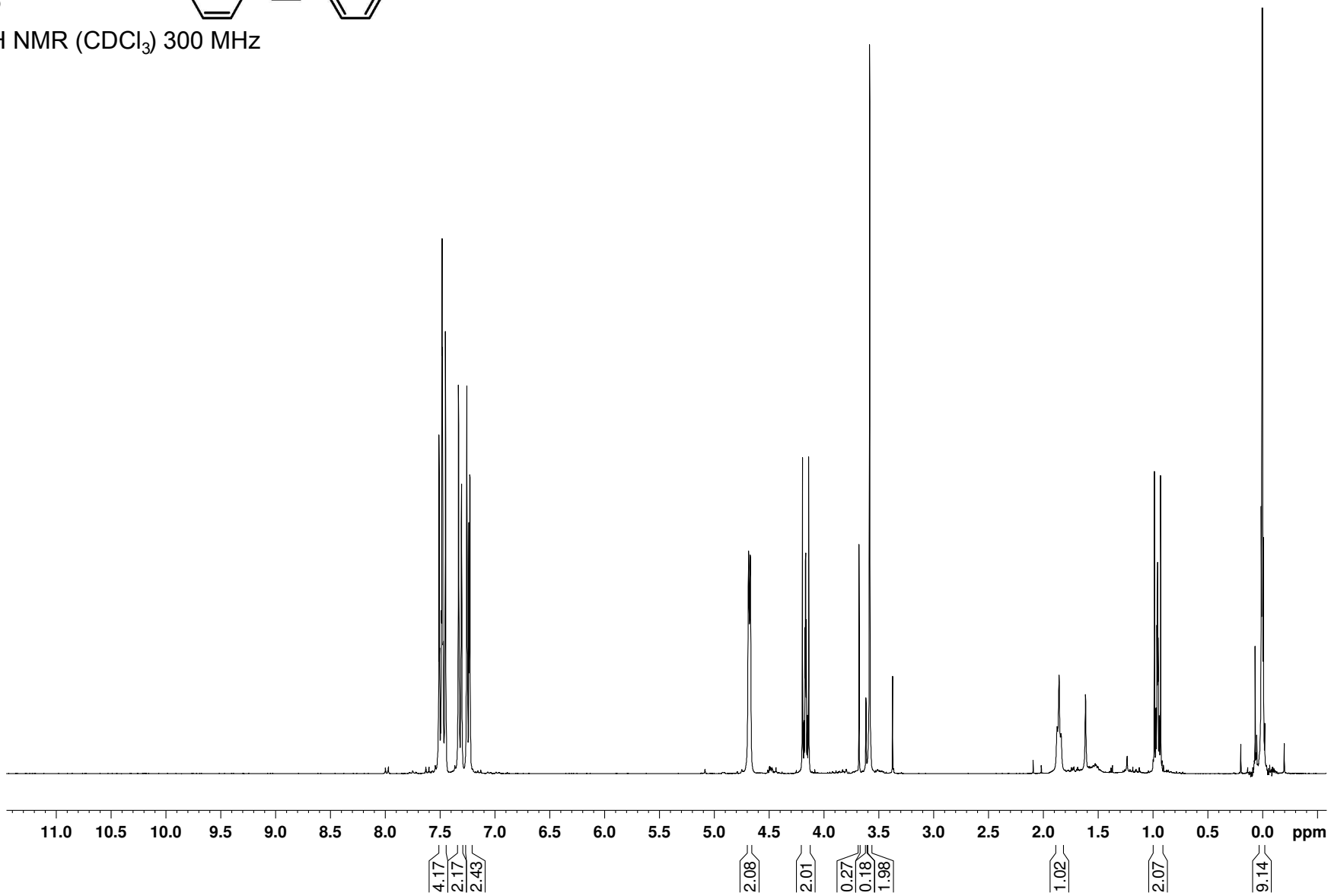
4

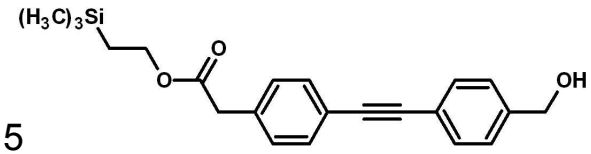
^{13}C NMR ($CDCl_3$) 75 MHz



5

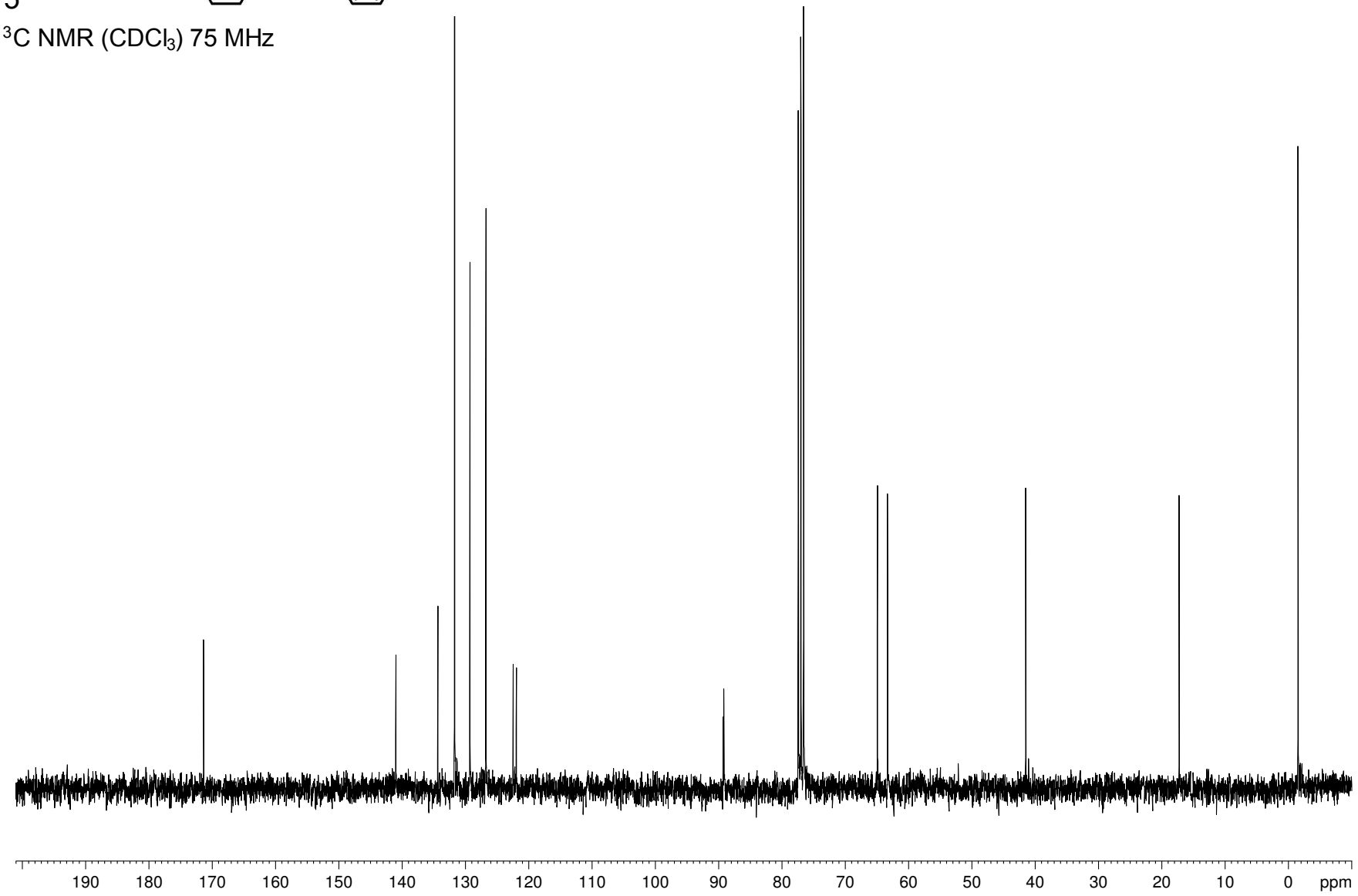
^{1}H NMR ($CDCl_3$) 300 MHz

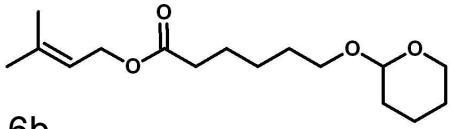




5

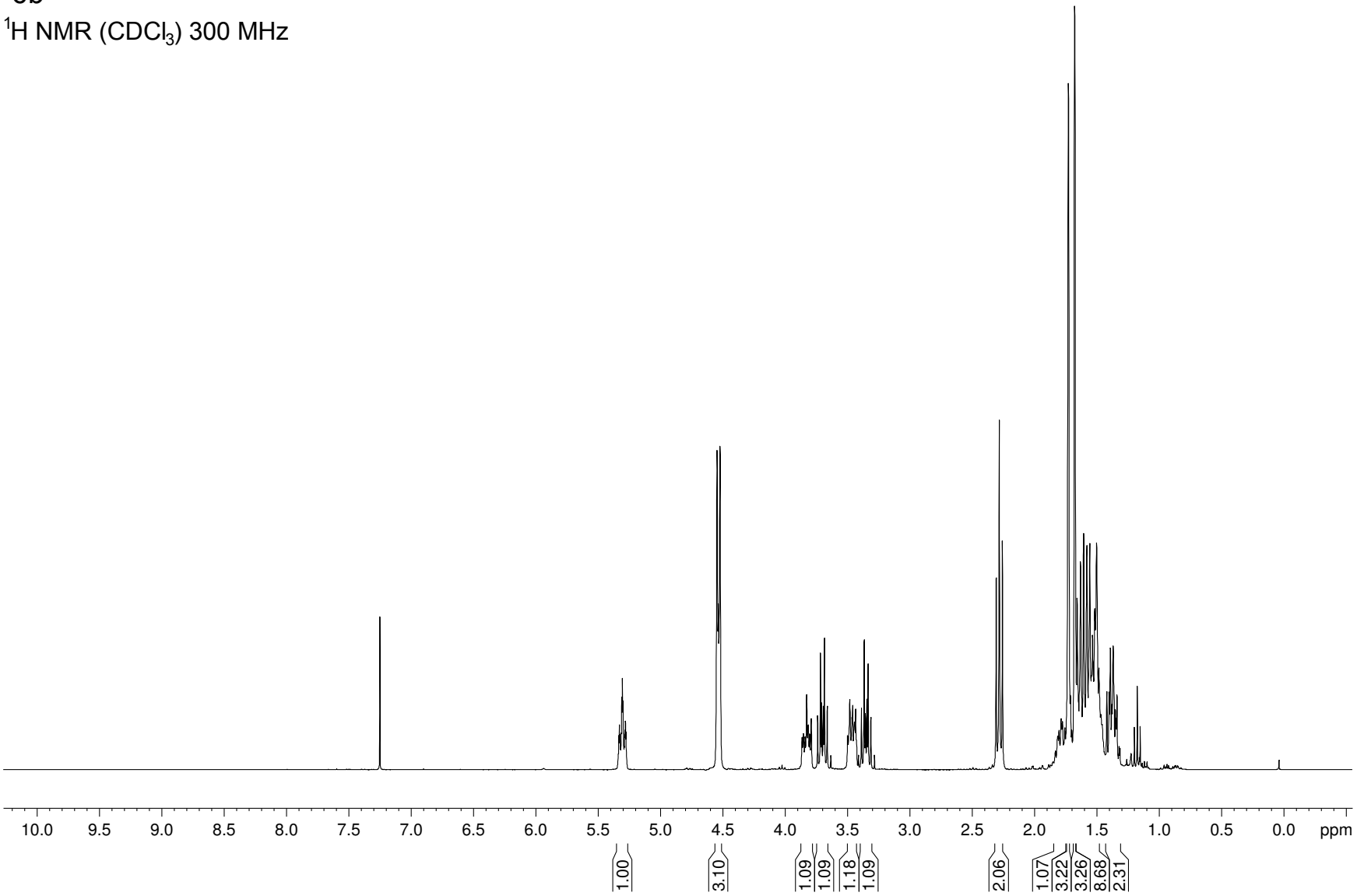
^{13}C NMR ($CDCl_3$) 75 MHz

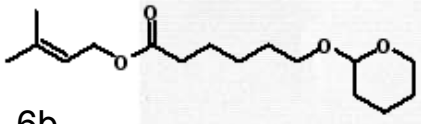




6b

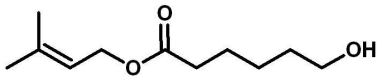
^{1}H NMR ($CDCl_3$) 300 MHz





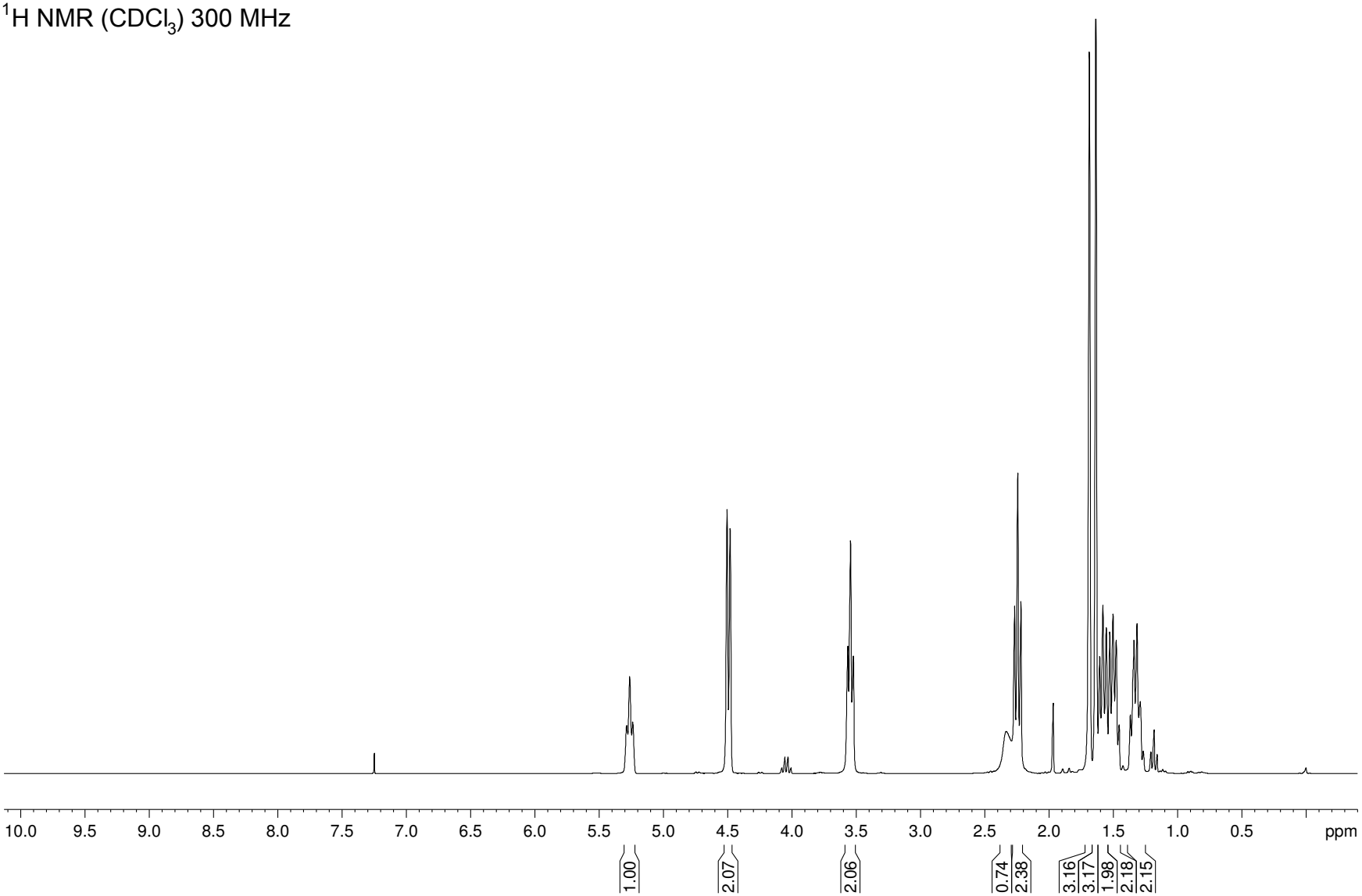
6b

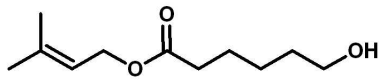
^{13}C NMR ($CDCl_3$) 75 MHz



6c

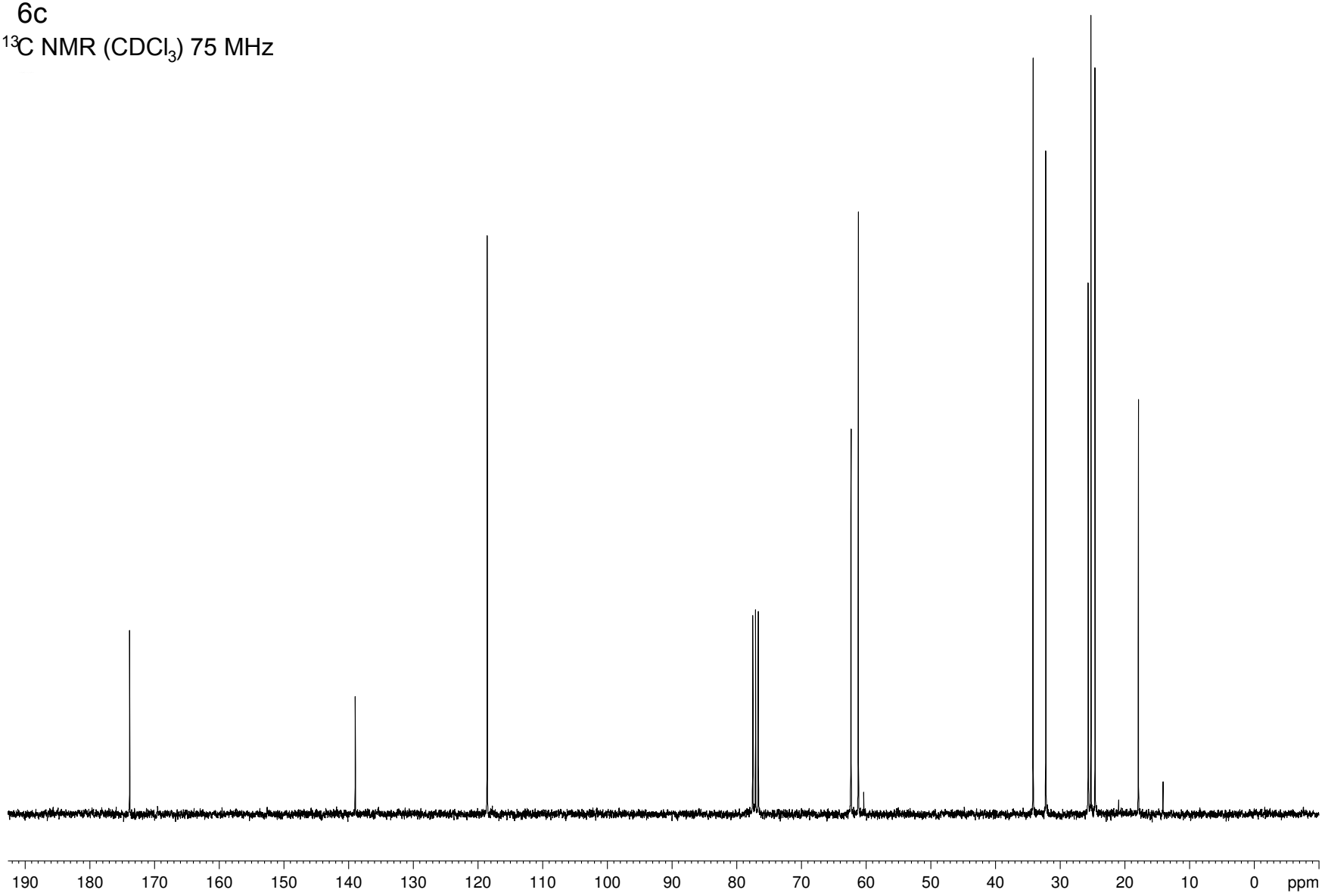
^{1}H NMR ($CDCl_3$) 300 MHz

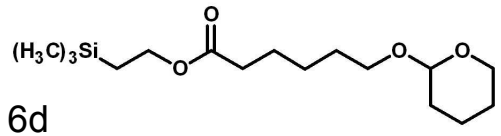




6c

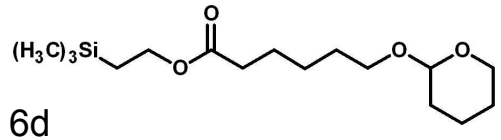
^{13}C NMR ($CDCl_3$) 75 MHz





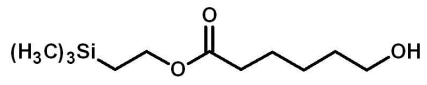
6d

^{1}H NMR ($CDCl_3$) 300 MHz



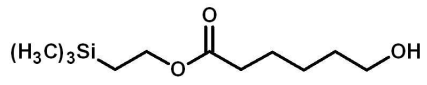
6d

^{13}C NMR ($CDCl_3$) 75 MHz



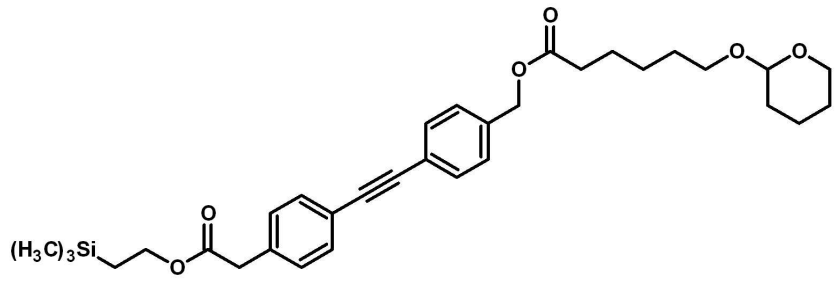
6e

^{1}H NMR ($CDCl_3$) 300 MHz



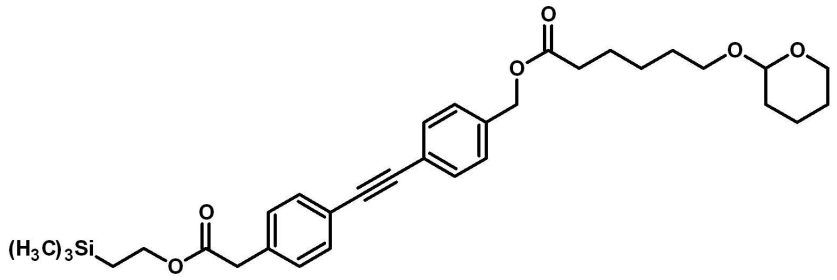
6e

^{13}C NMR ($CDCl_3$) 75 MHz



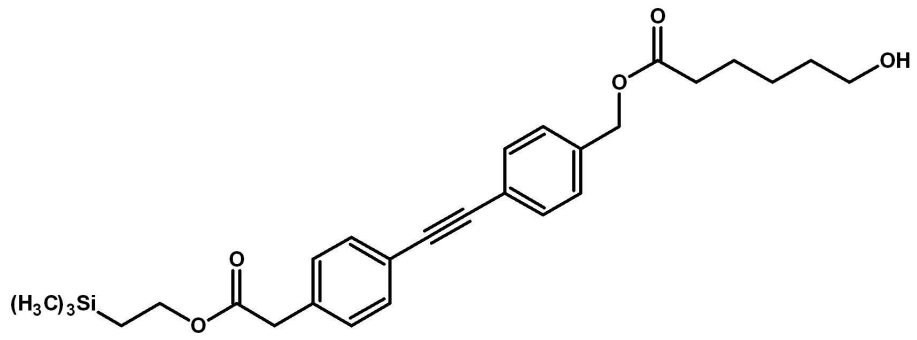
7

^{1}H NMR ($CDCl_3$) 300 MHz



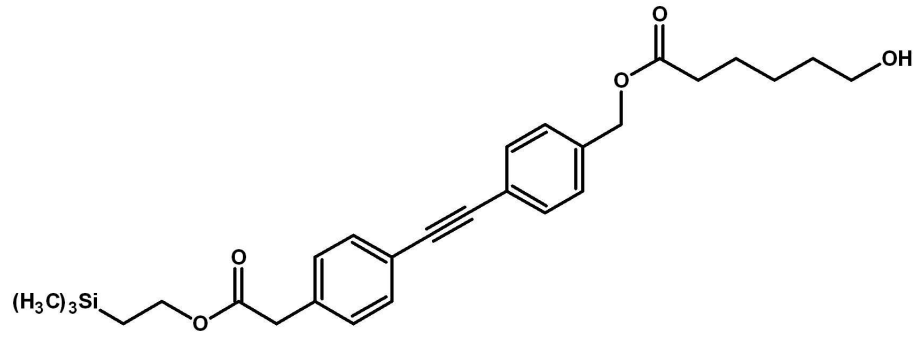
7

^{13}C NMR ($CDCl_3$) 75 MHz



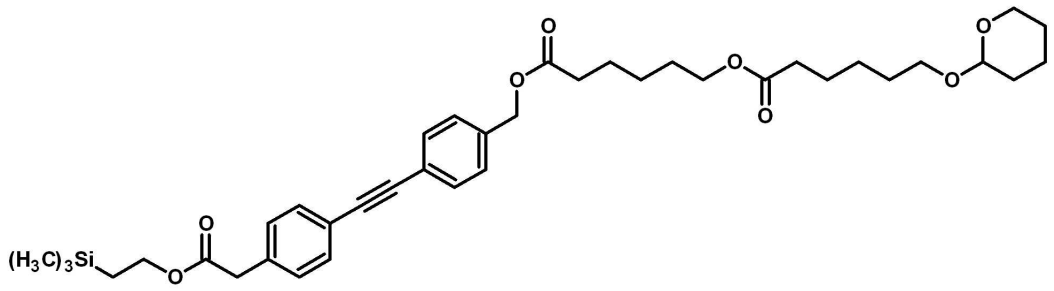
8

^{1}H NMR ($CDCl_3$) 300 MHz



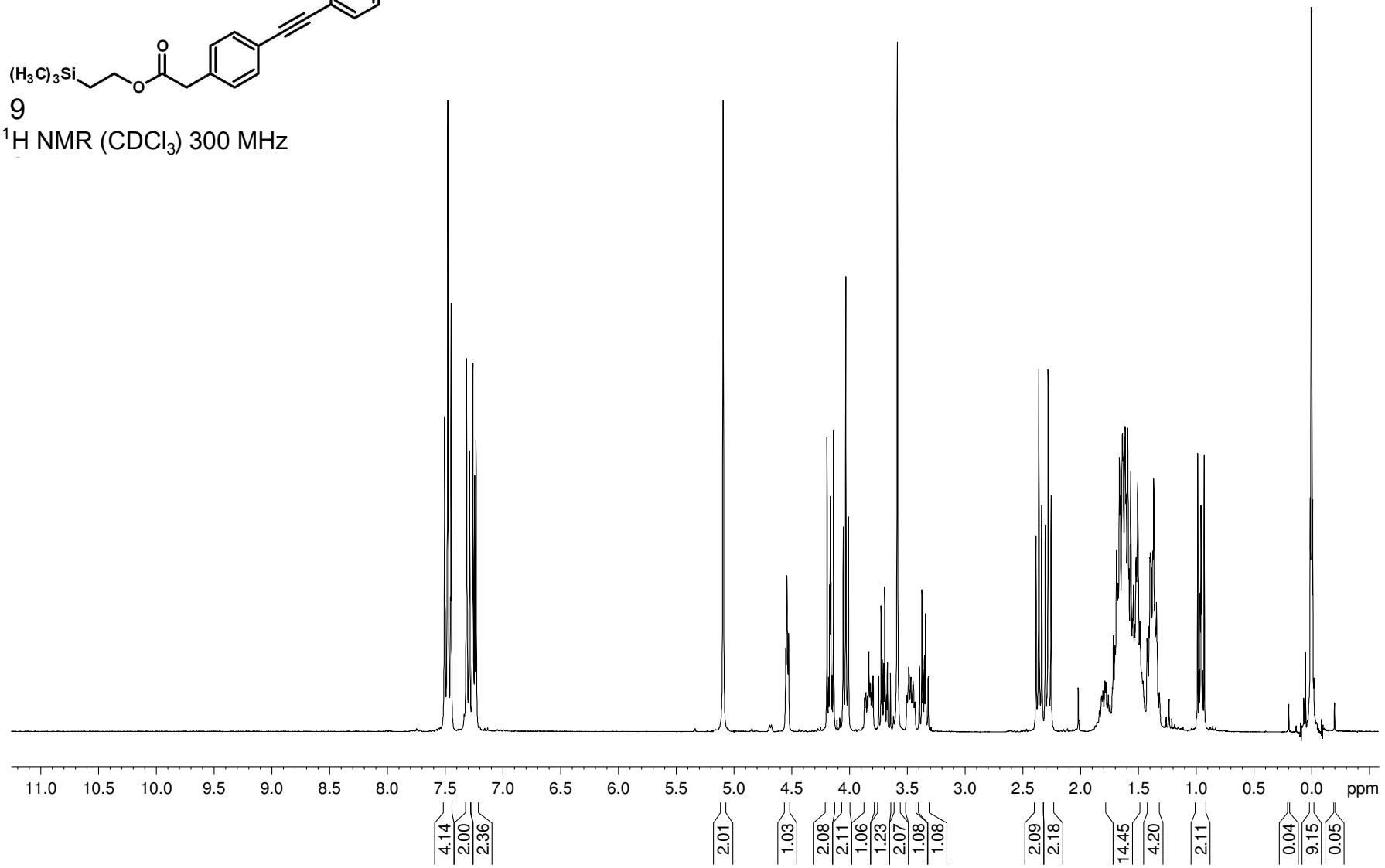
8

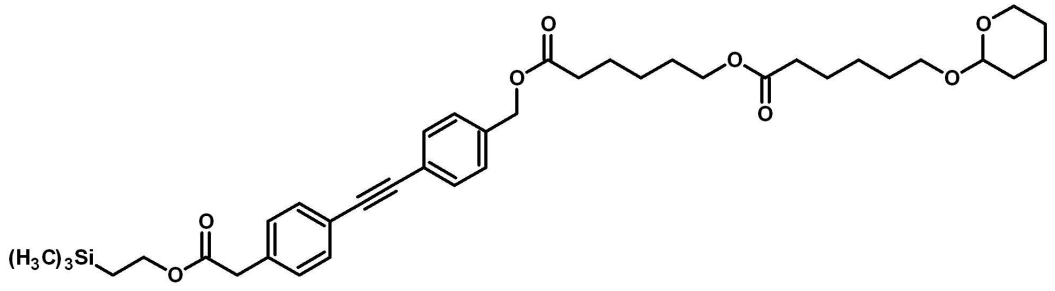
^{13}C NMR ($CDCl_3$) 75 MHz



9

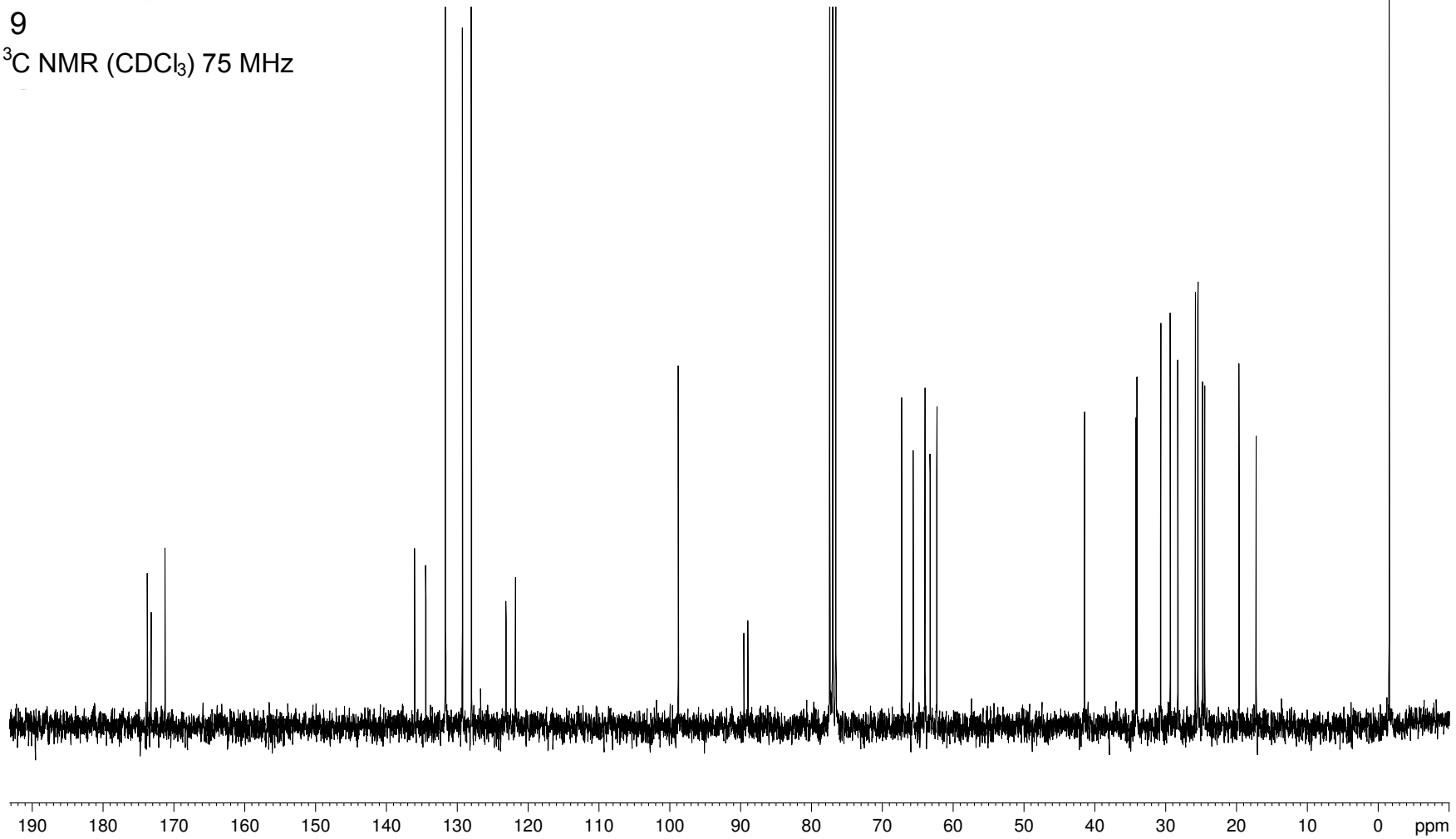
^{1}H NMR ($CDCl_3$) 300 MHz

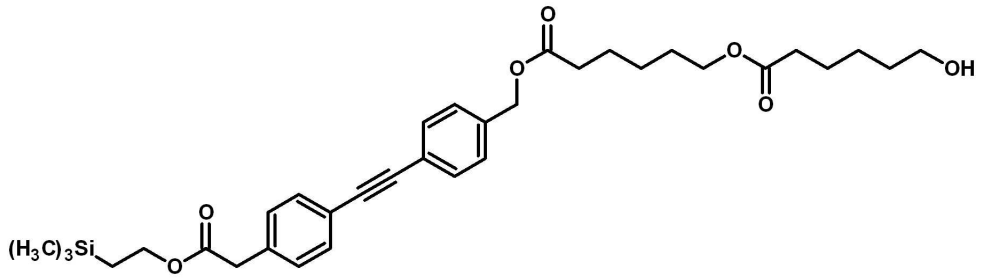




9

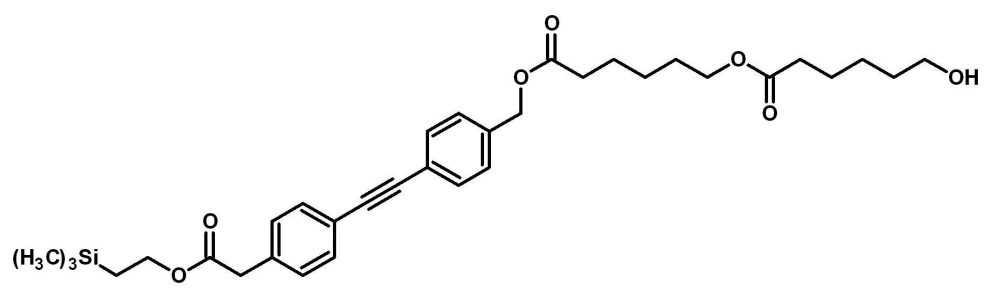
^{13}C NMR ($CDCl_3$) 75 MHz





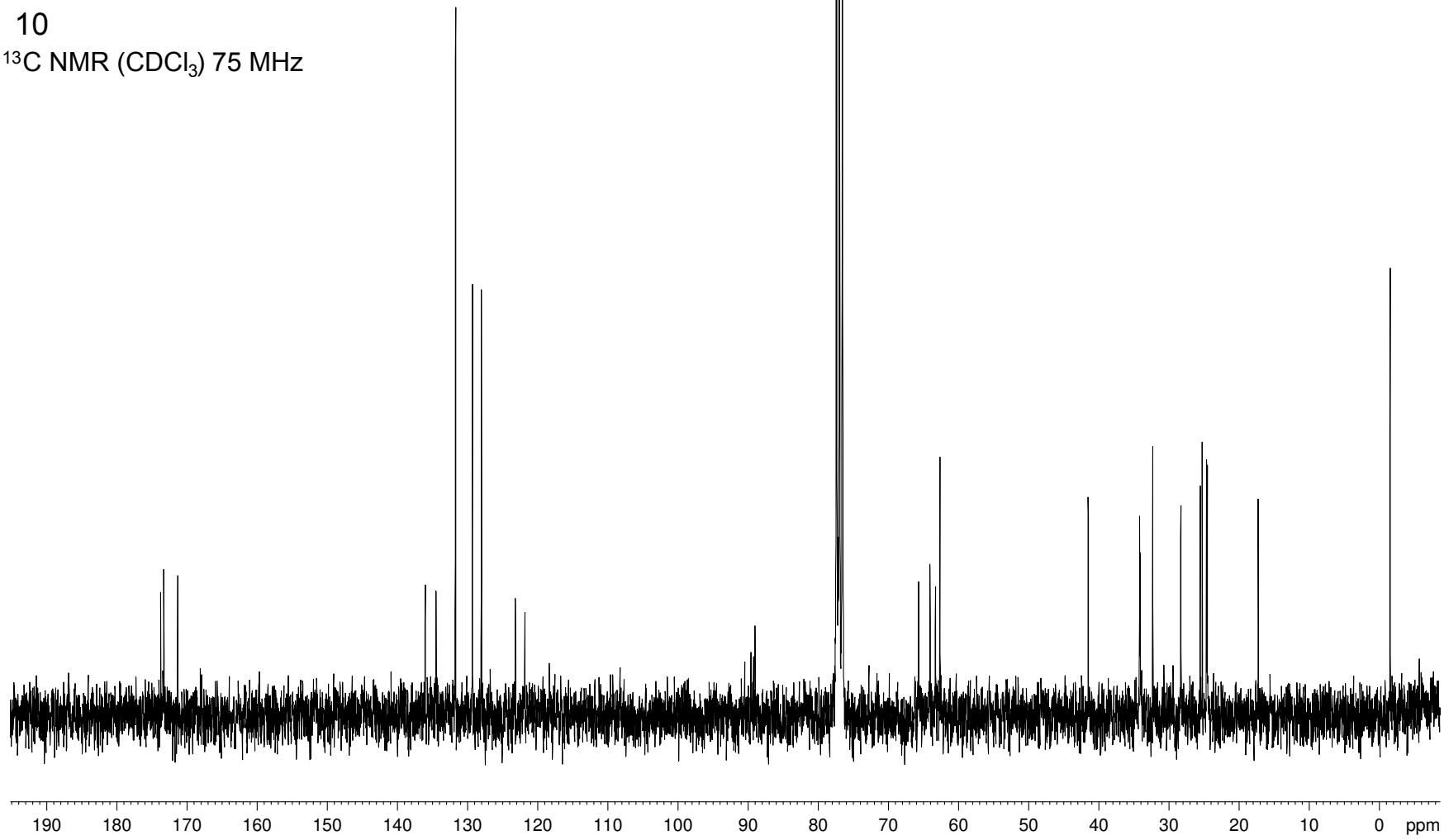
10

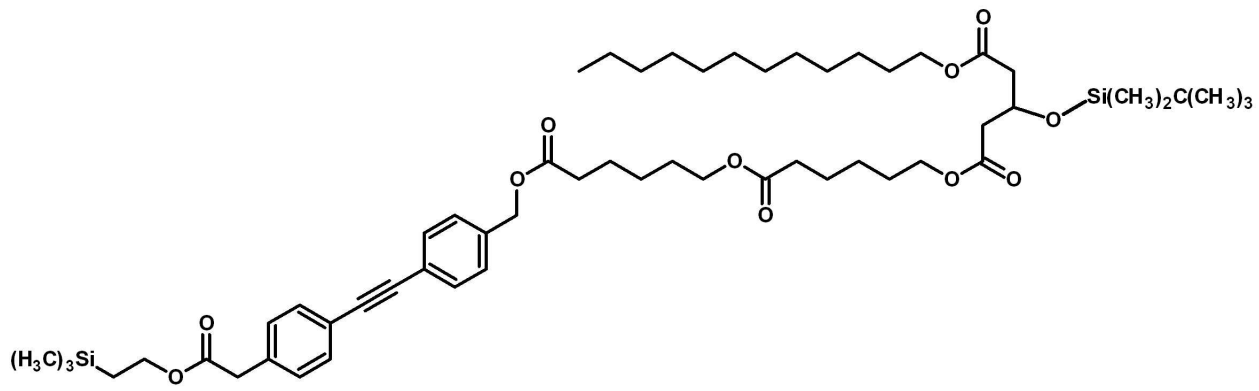
^{1}H NMR ($CDCl_3$) 300 MHz



10

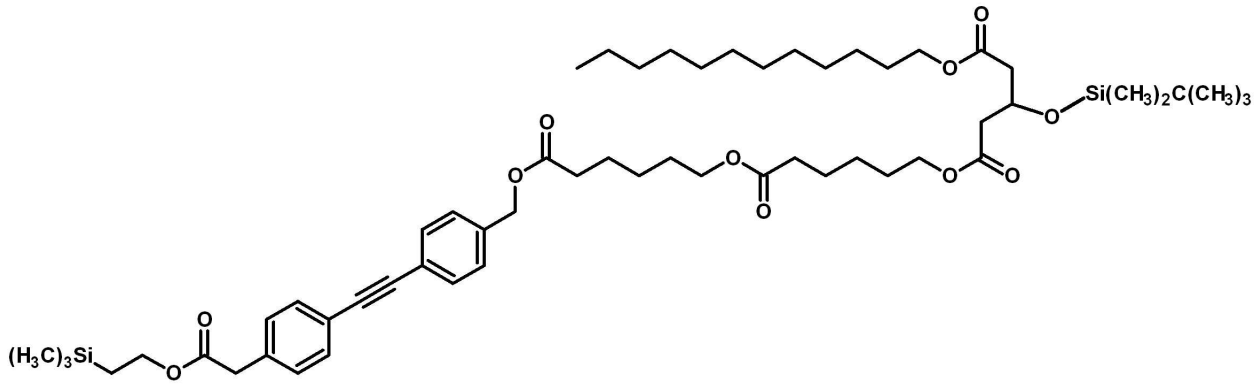
^{13}C NMR ($CDCl_3$) 75 MHz





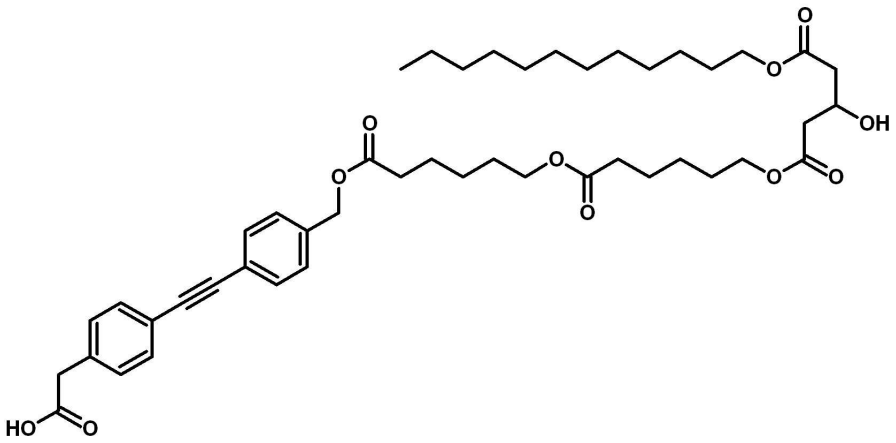
12

^{1}H NMR ($CDCl_3$) 300 MHz



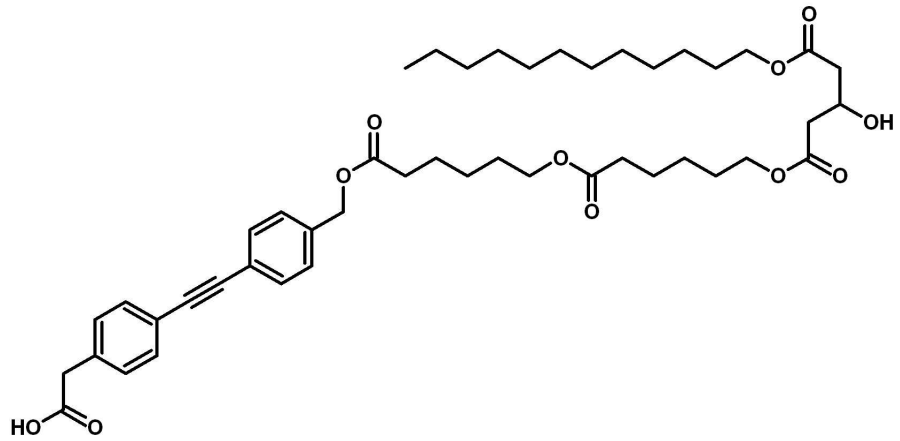
12

^{13}C NMR ($CDCl_3$) 75 MHz



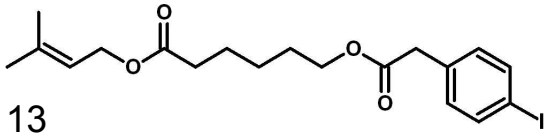
HO_2C-**Dip-Hex-Hex-G(12)**-OH

^1H NMR (1:1 $CDCl_3$: CD_3OD) 500 MHz



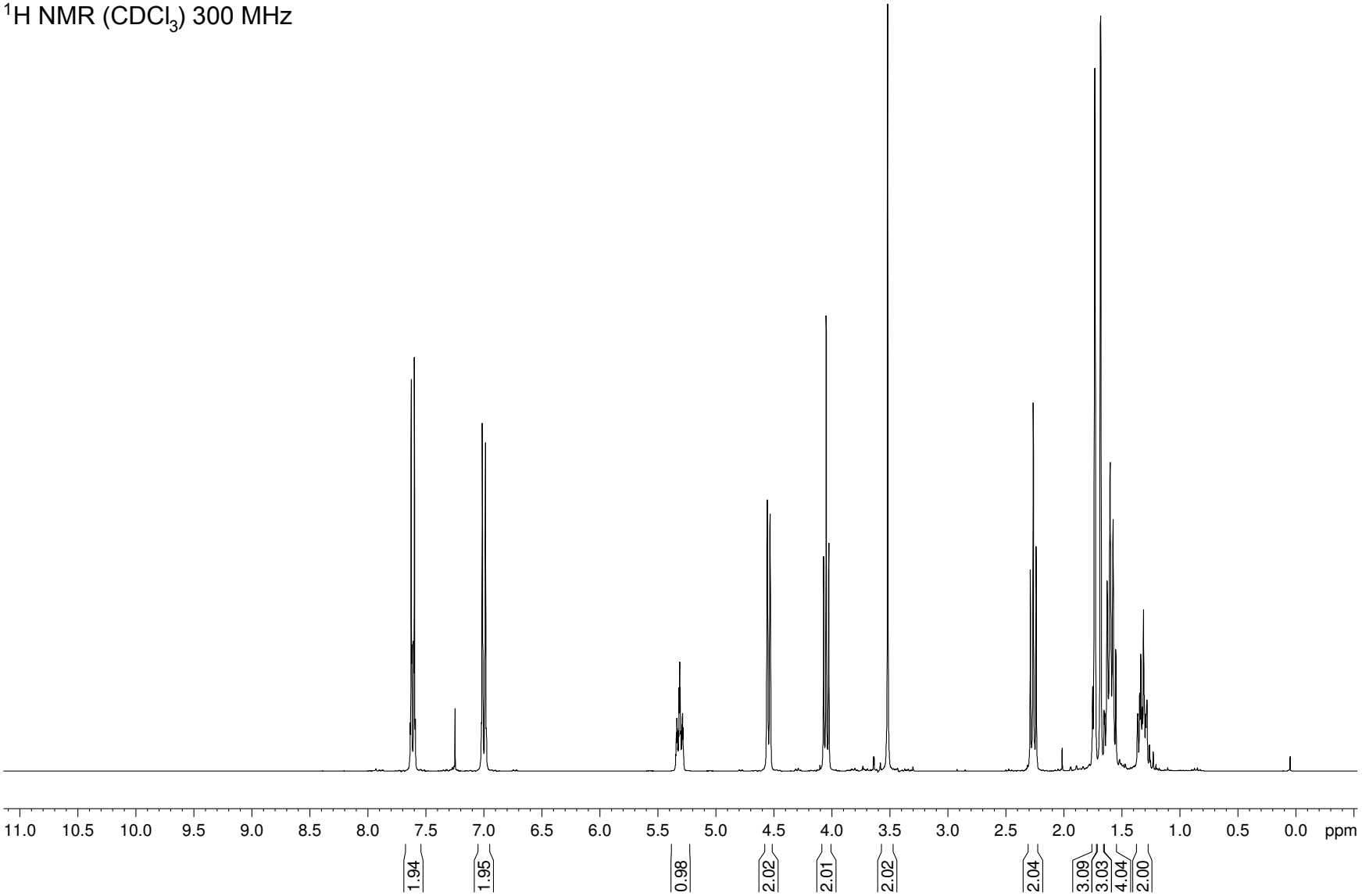
HO_2C-**Dip-Hex-Hex-G(12)**-OH

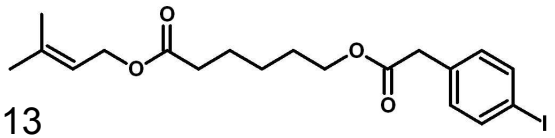
^{13}C NMR (1:1 $CDCl_3$: CD_3OD) 125 MHz



13

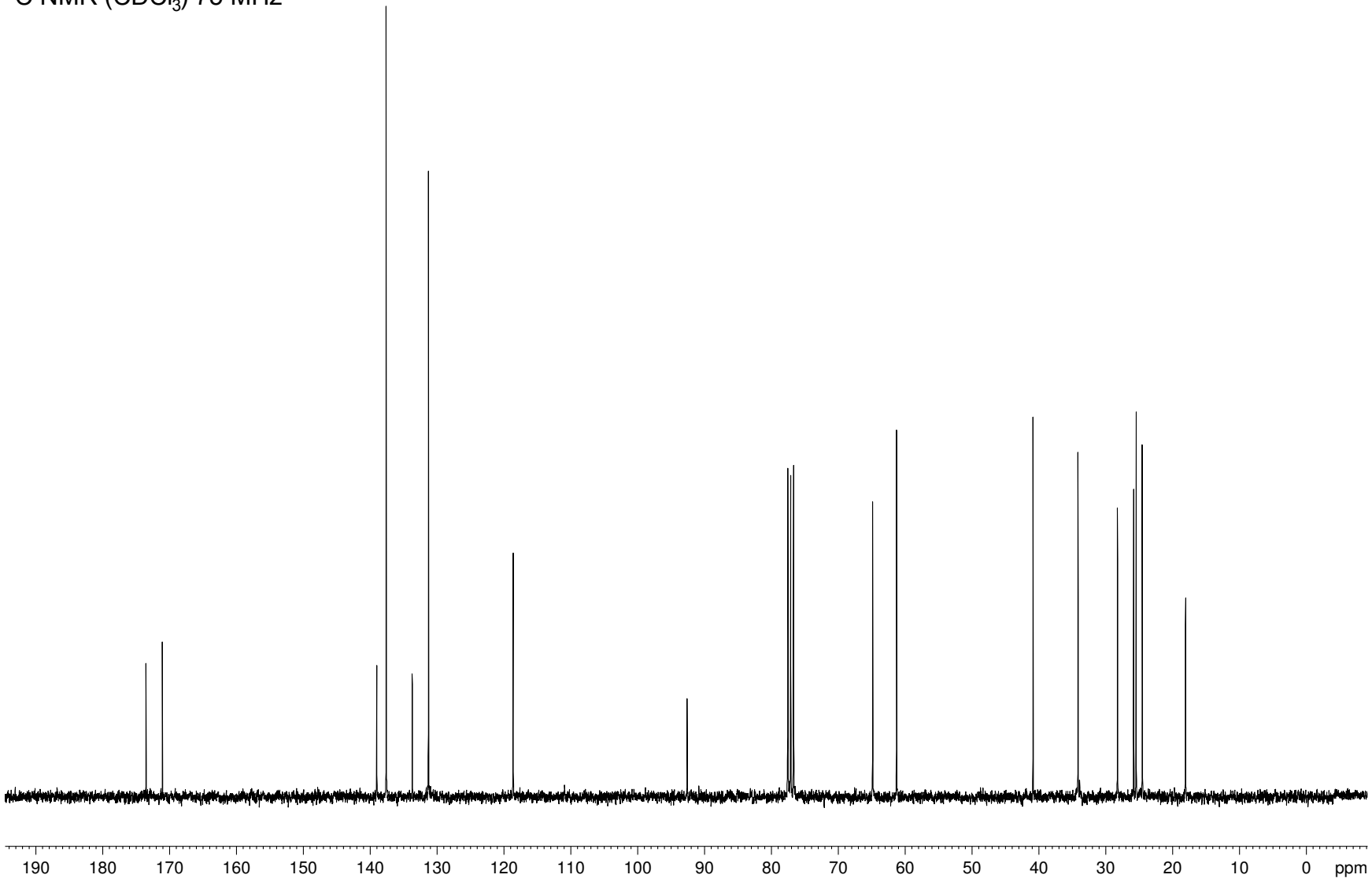
^{1}H NMR ($CDCl_3$) 300 MHz

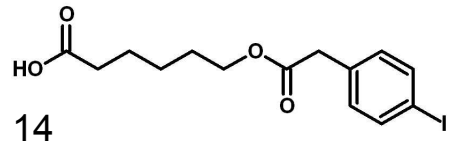




13

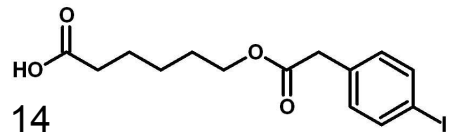
^{13}C NMR ($CDCl_3$) 75 MHz





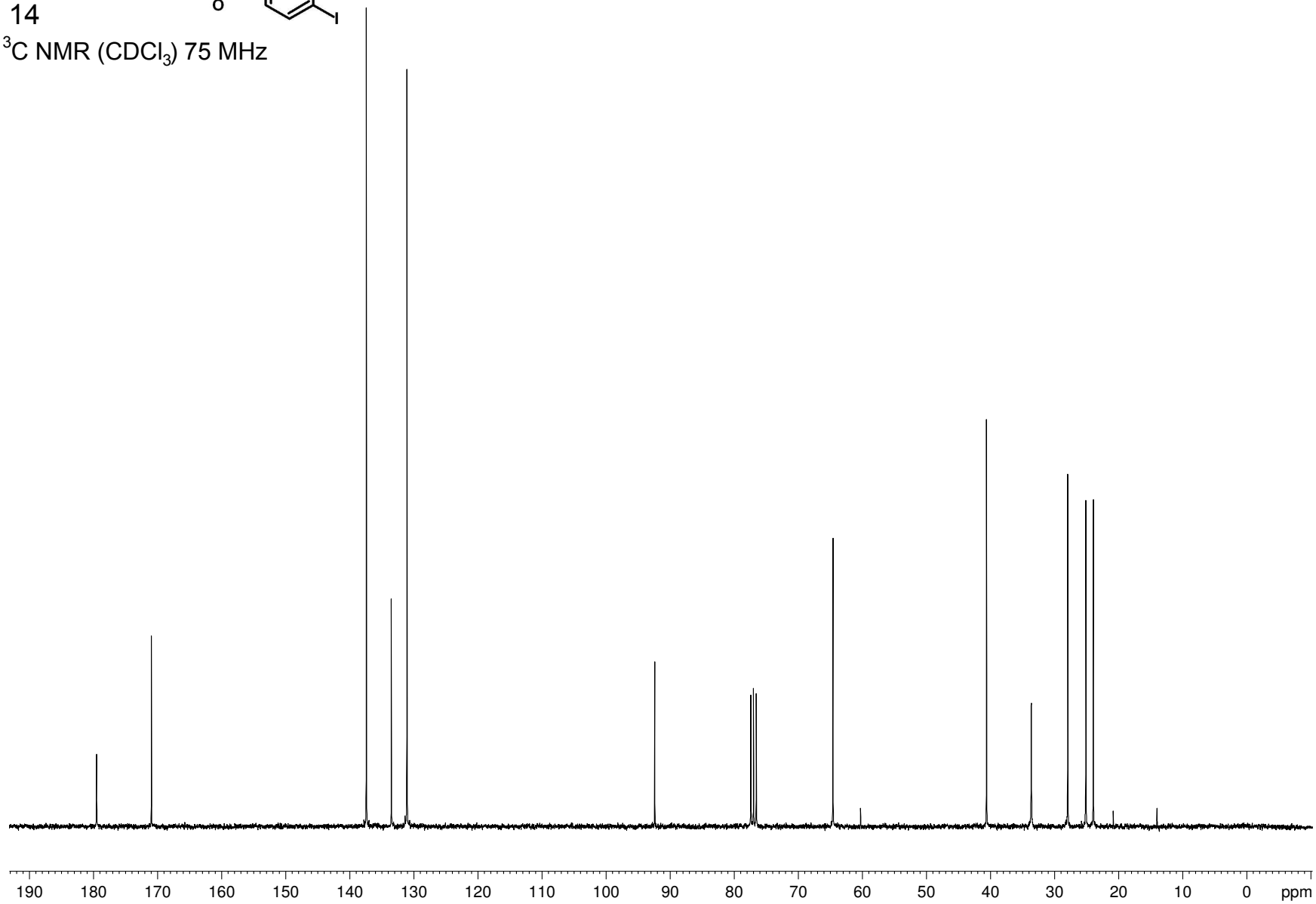
14

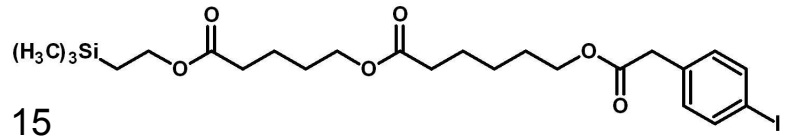
^{1}H NMR ($CDCl_3$) 300 MHz



14

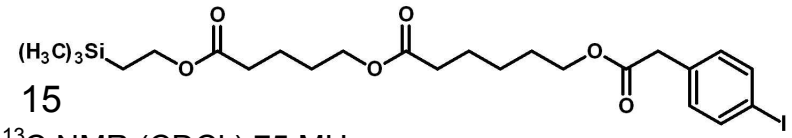
^{13}C NMR ($CDCl_3$) 75 MHz





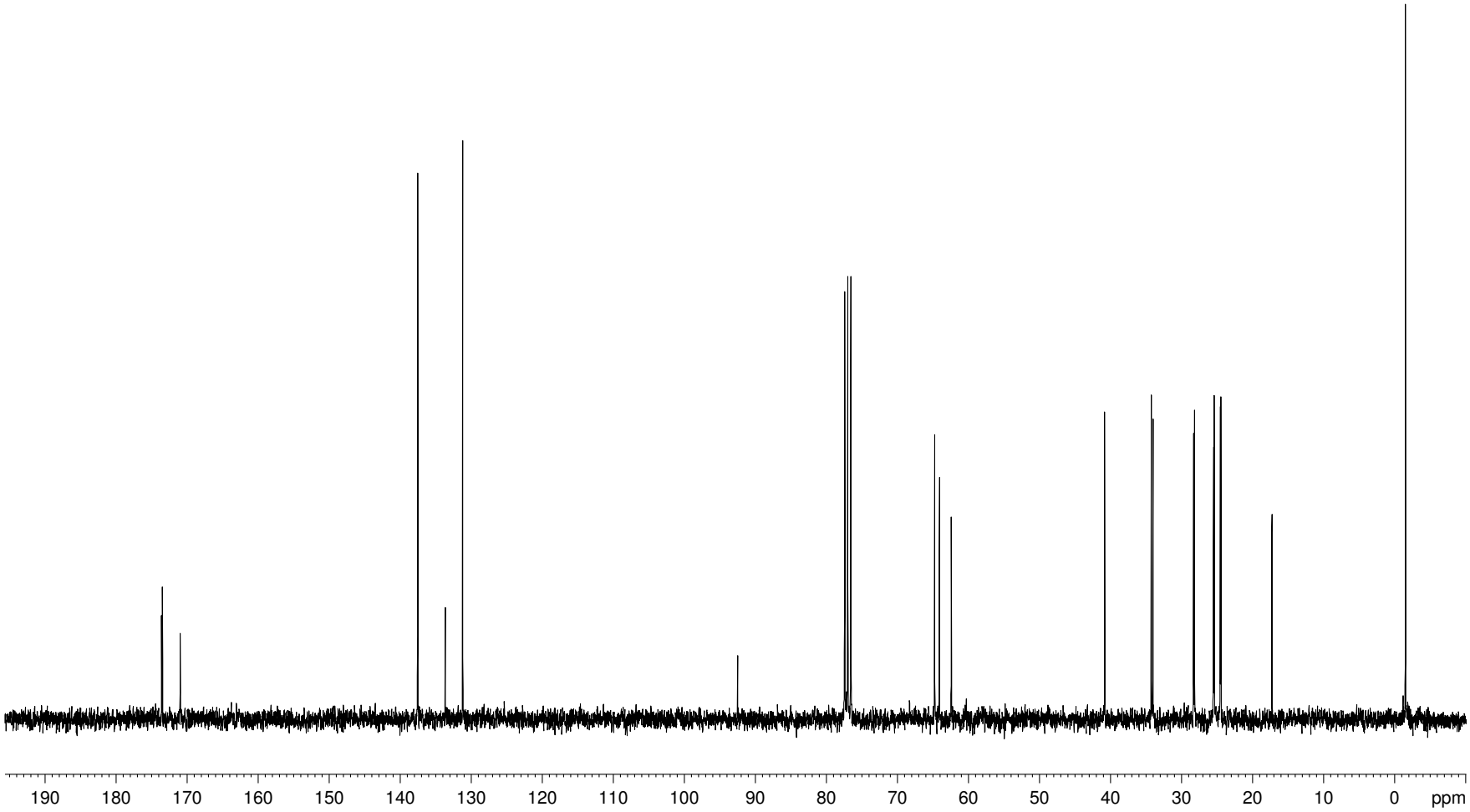
15

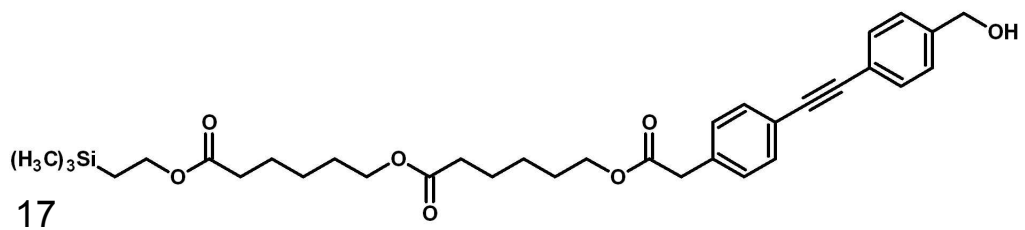
^{1}H NMR ($CDCl_3$) 300 MHz



15

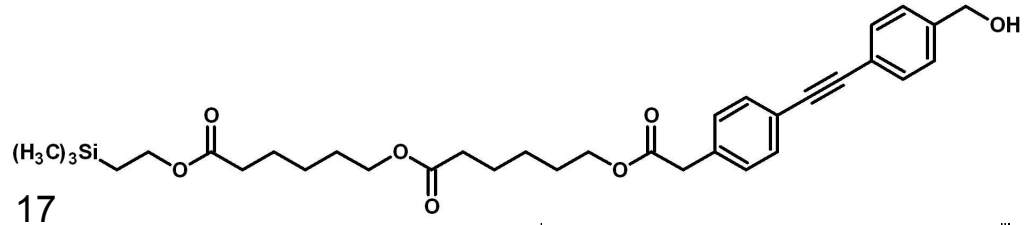
^{13}C NMR ($CDCl_3$) 75 MHz





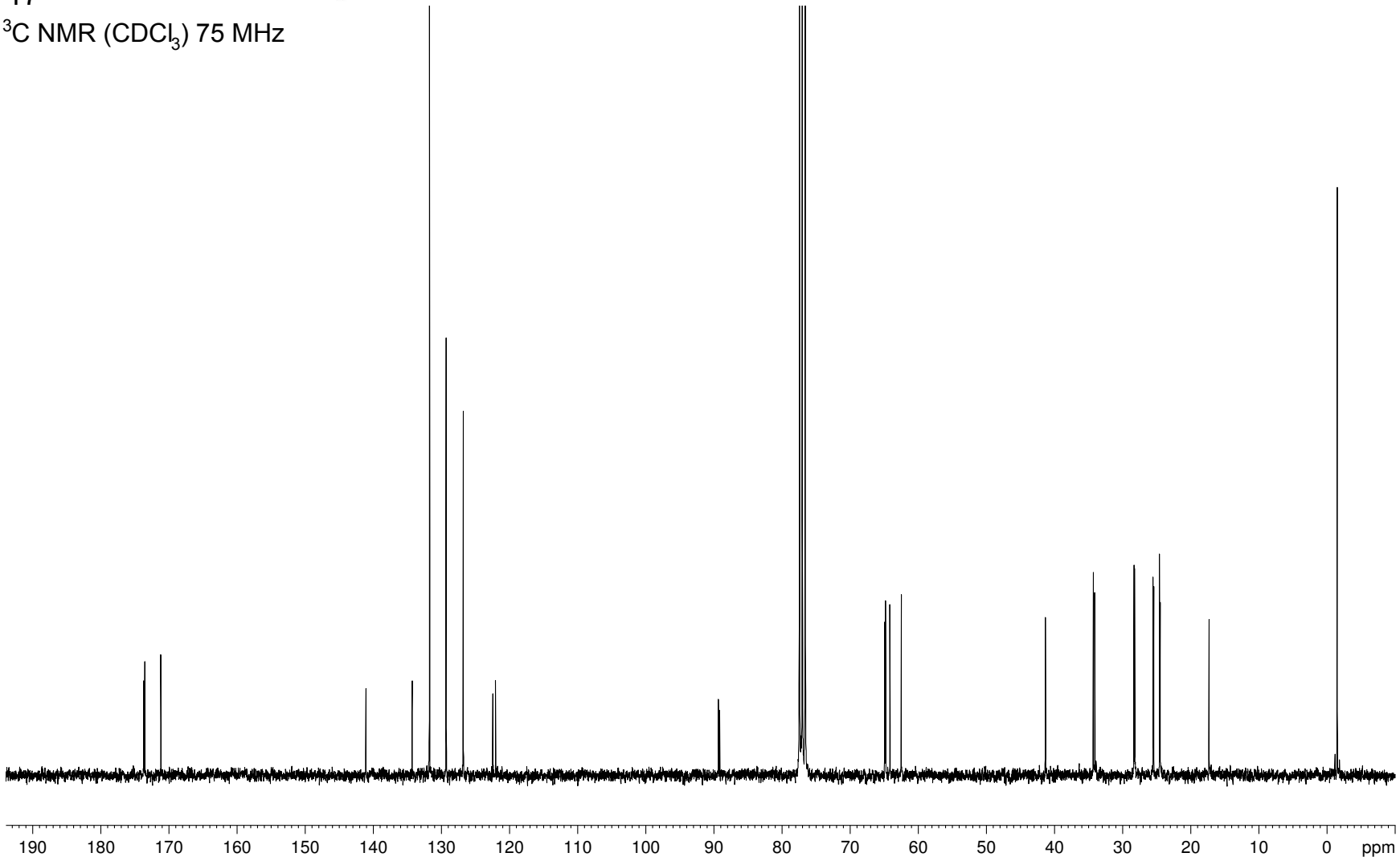
17

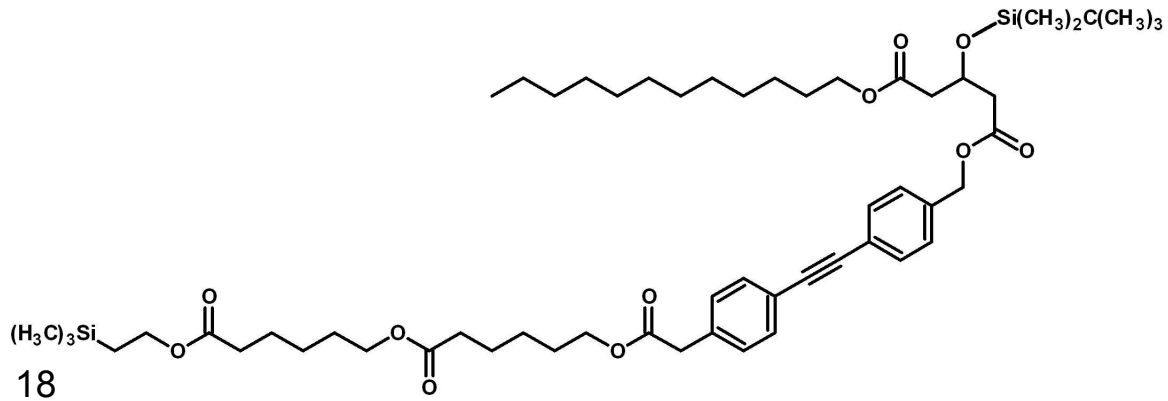
^{1}H NMR ($CDCl_3$) 300 MHz



17

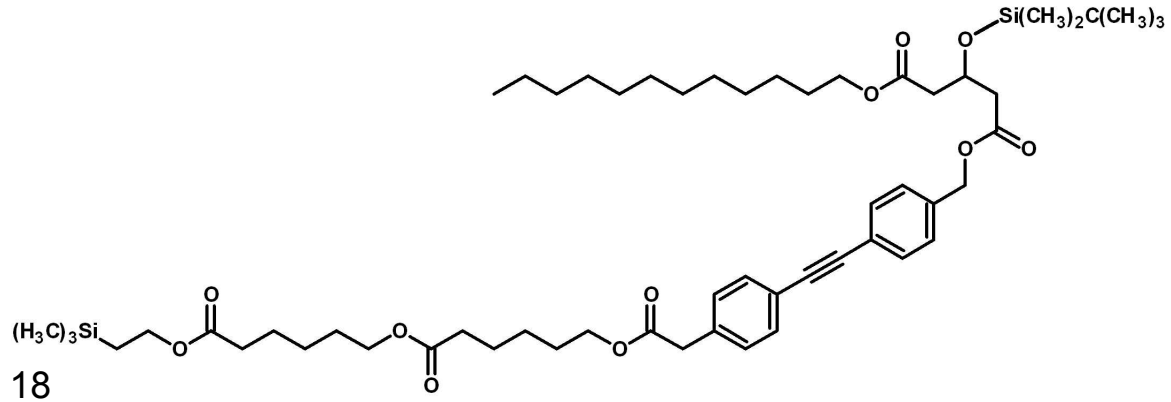
^{13}C NMR ($CDCl_3$) 75 MHz





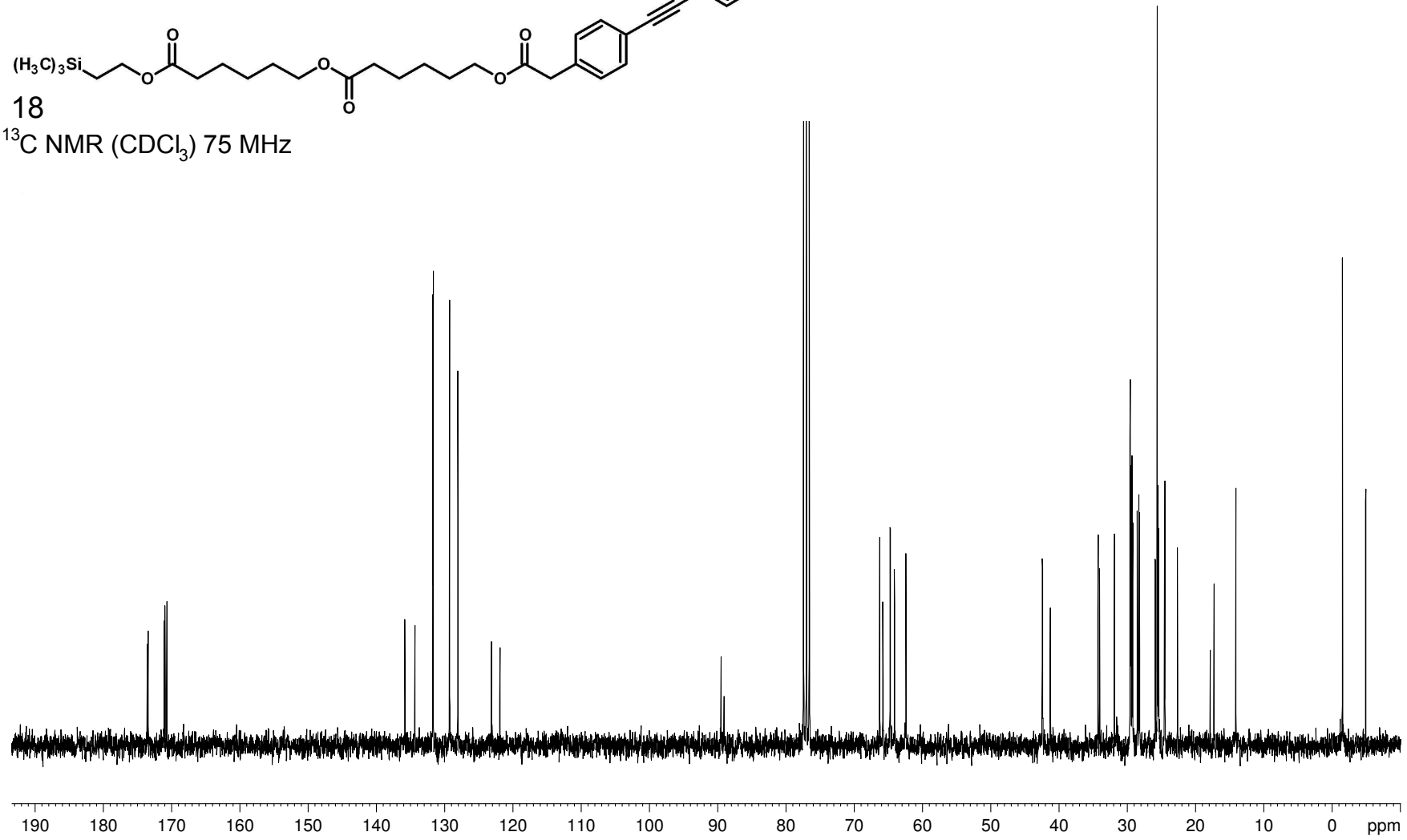
18

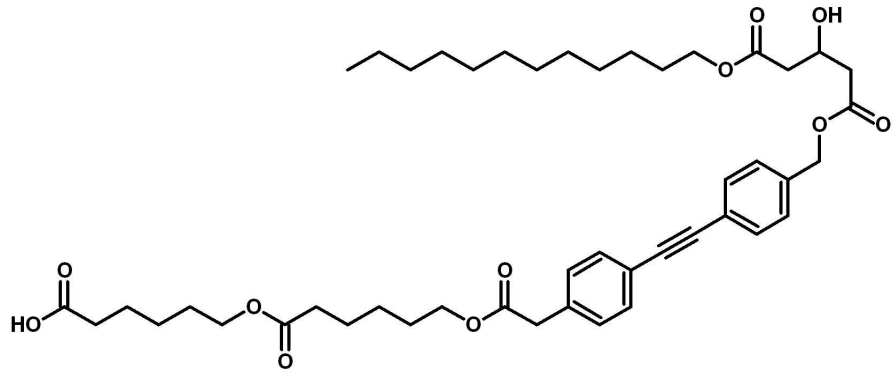
^{1}H NMR ($CDCl_3$) 300 MHz



18

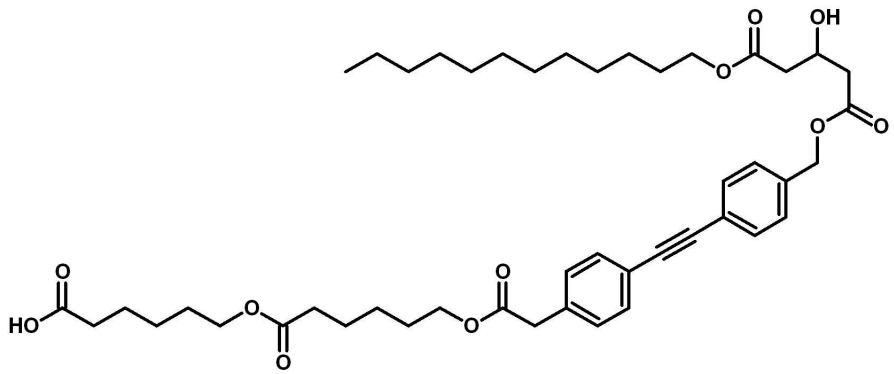
^{13}C NMR ($CDCl_3$) 75 MHz





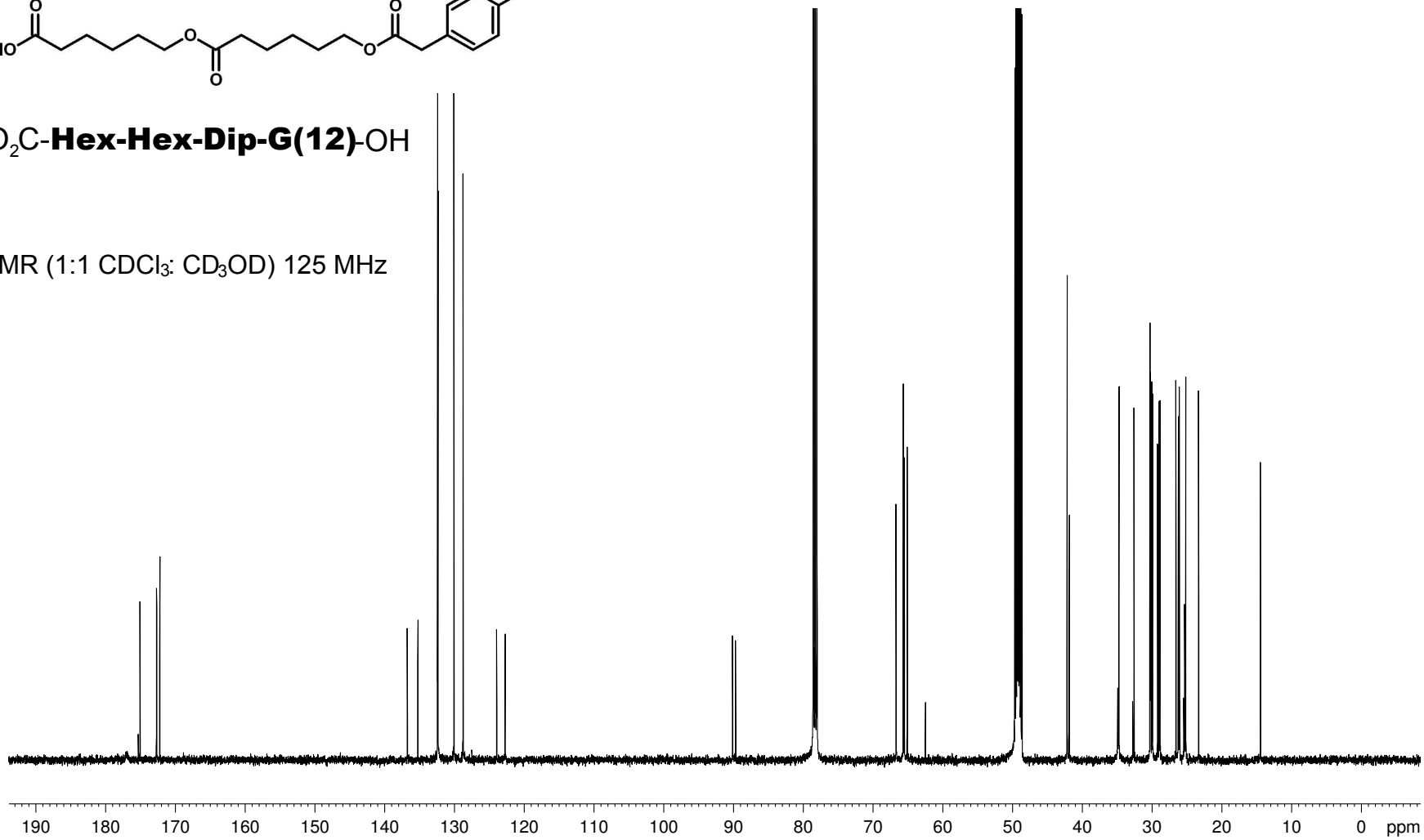
HO_2C-**Hex-Hex-Dip-G(12)**-OH

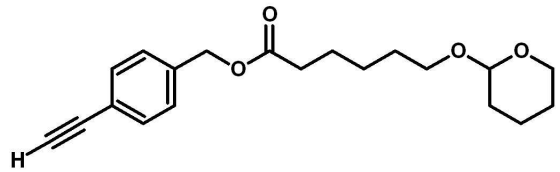
^1H NMR (1:1 $CDCl_3$: CD_3OD) 500 MHz



HO_2C-**Hex-Hex-Dip-G(12)**-OH

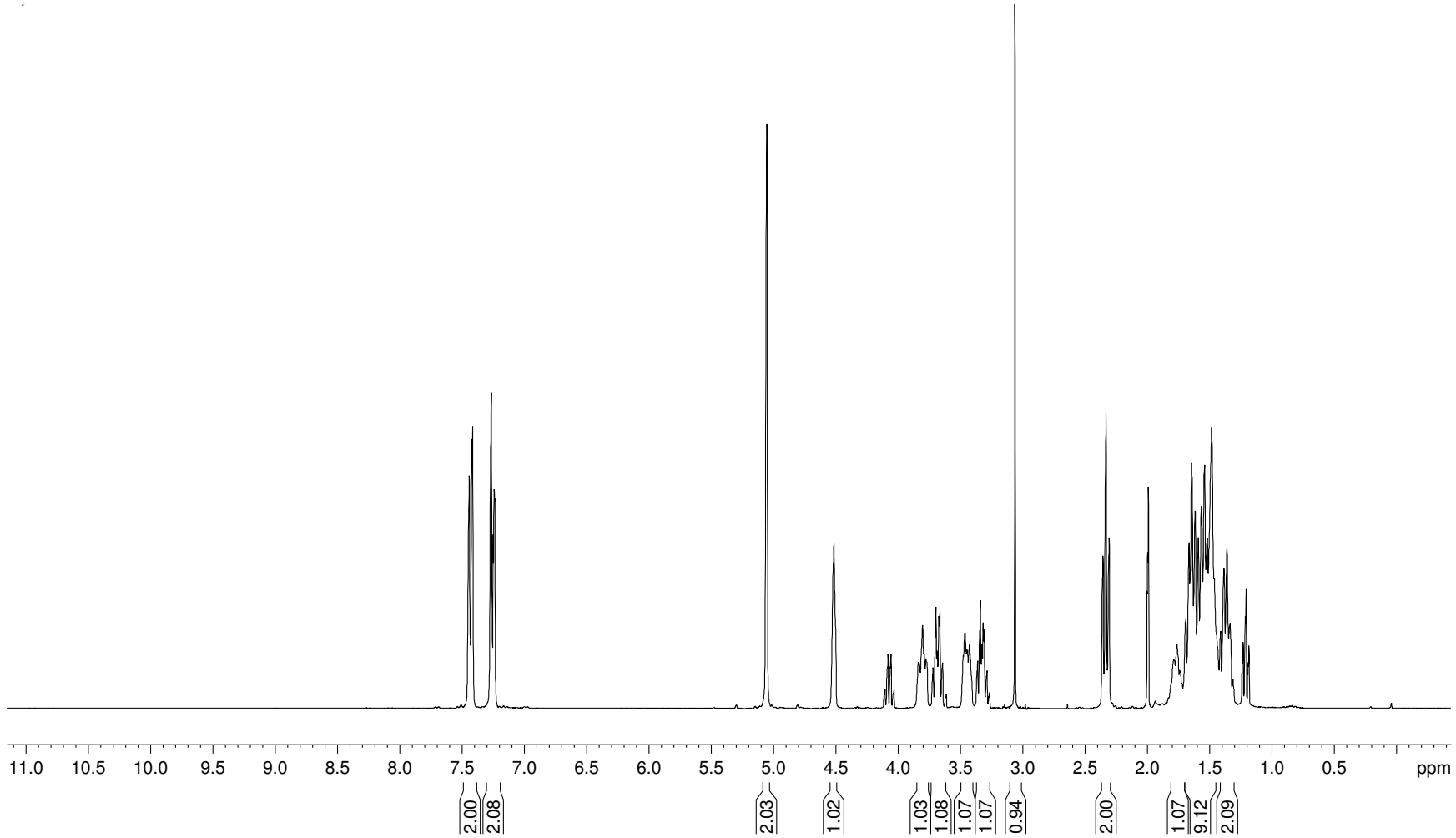
^{13}C NMR (1:1 $CDCl_3$: CD_3OD) 125 MHz

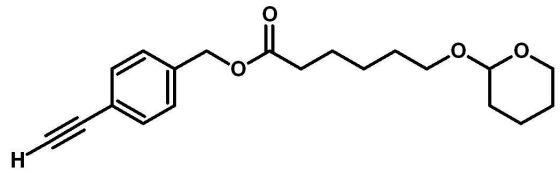




19

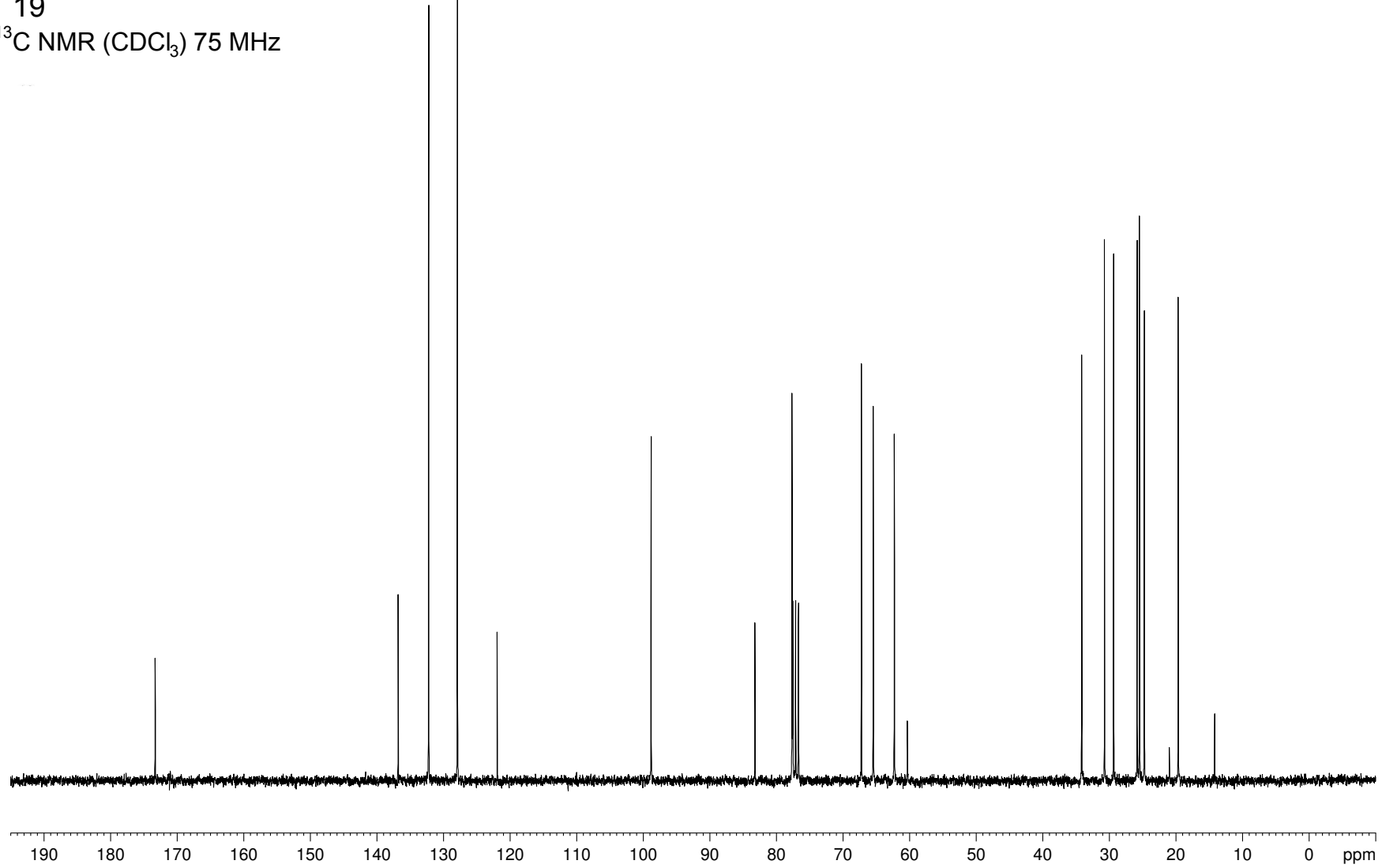
^{1}H NMR ($CDCl_3$) 300 MHz

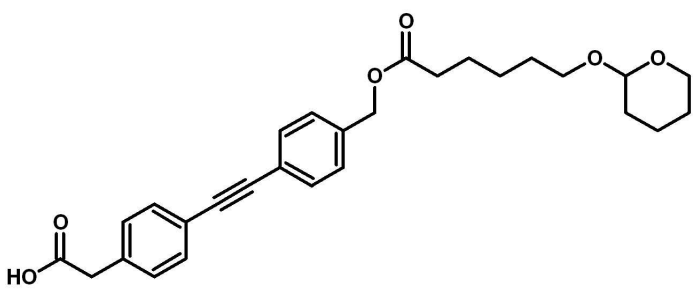




19

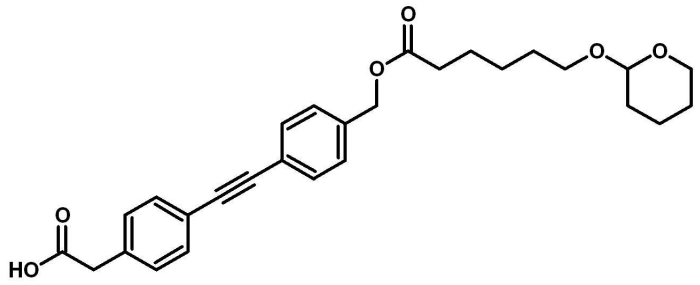
^{13}C NMR ($CDCl_3$) 75 MHz





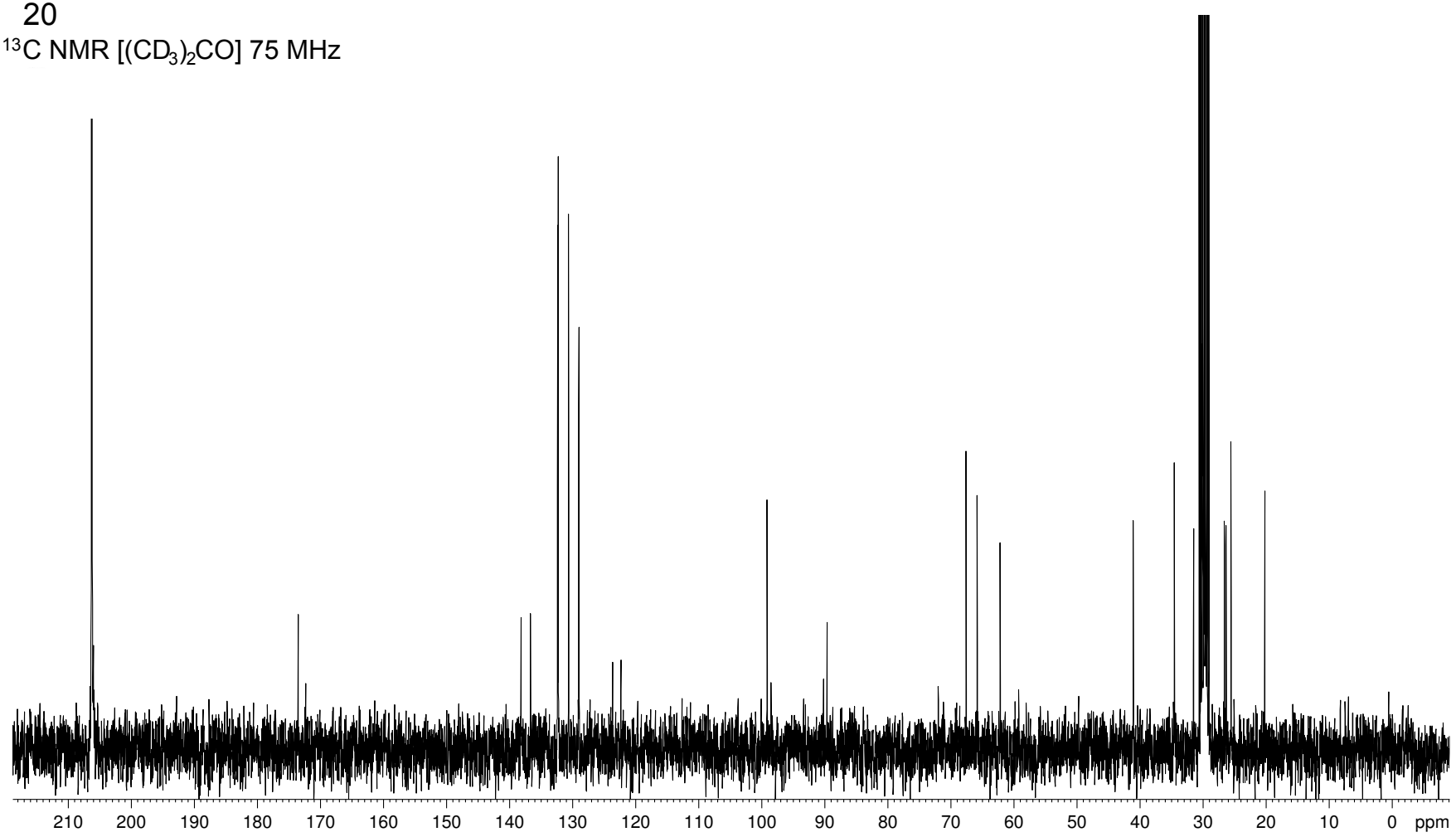
20

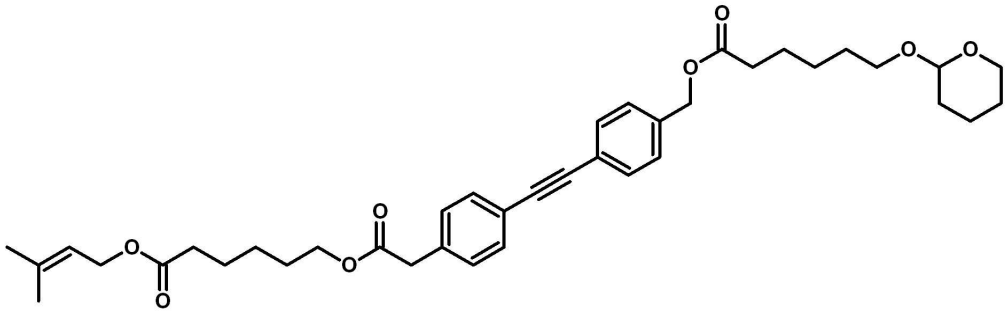
^{1}H NMR [$(CD_3)_2CO$] 300 MHz



20

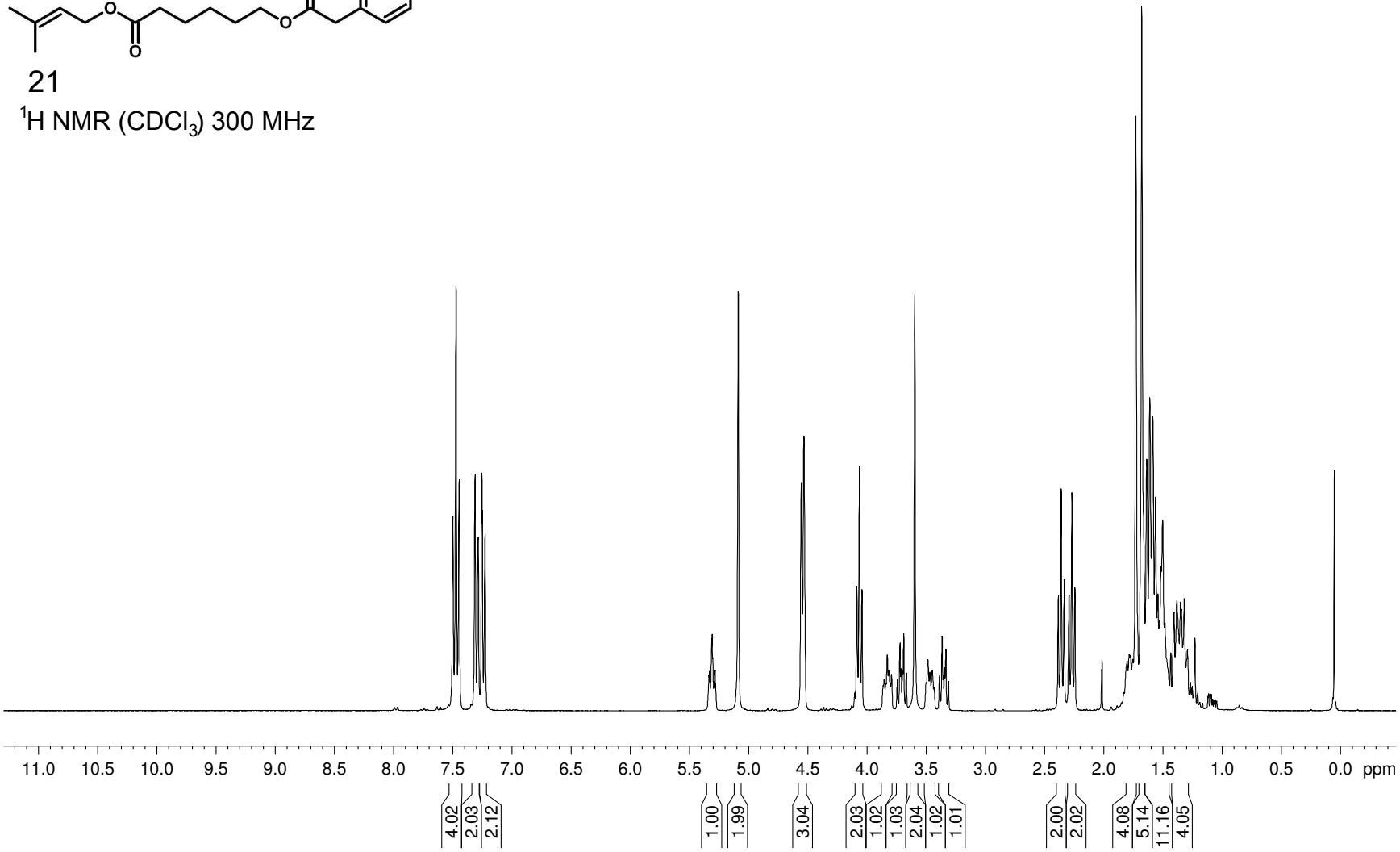
^{13}C NMR [$(CD_3)_2CO$] 75 MHz

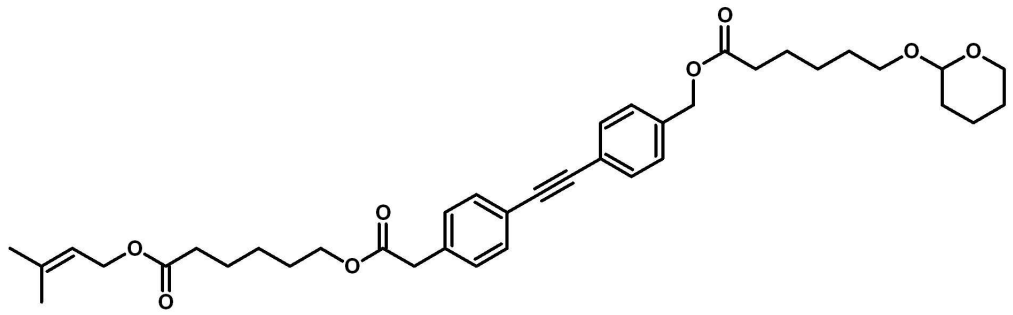




21

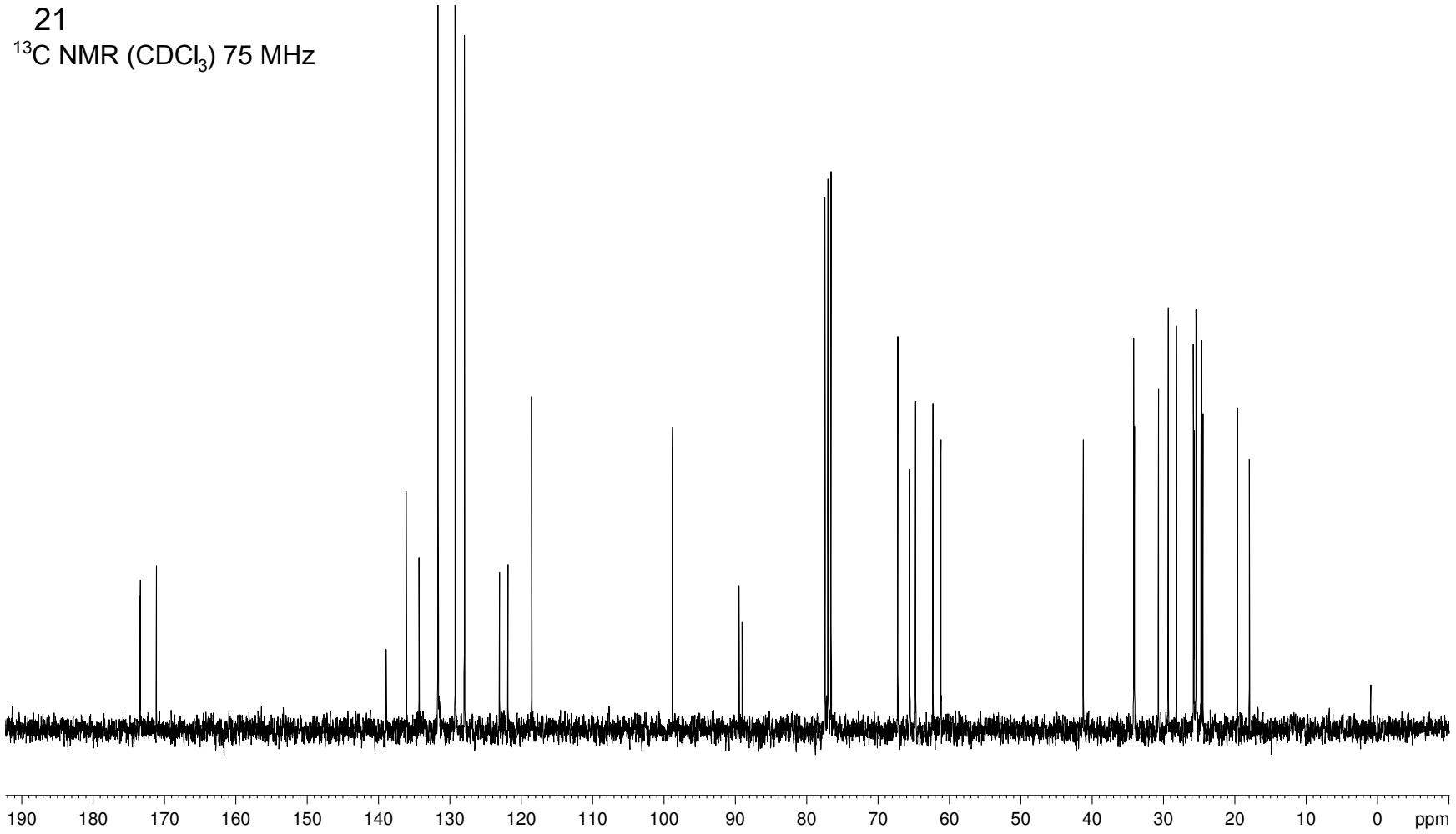
^{1}H NMR ($CDCl_3$) 300 MHz

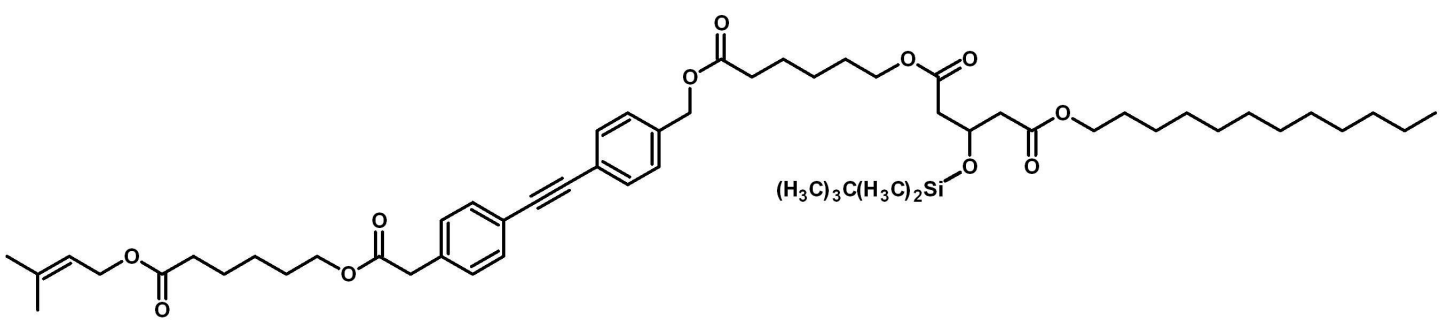




21

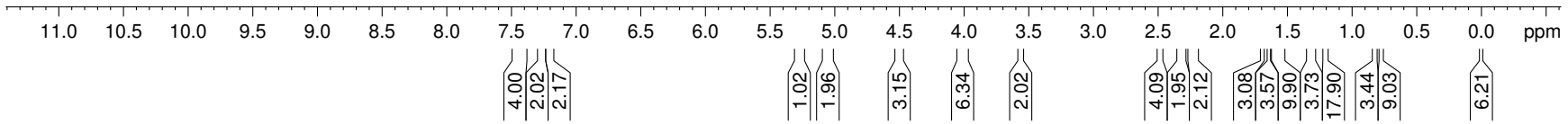
^{13}C NMR ($CDCl_3$) 75 MHz

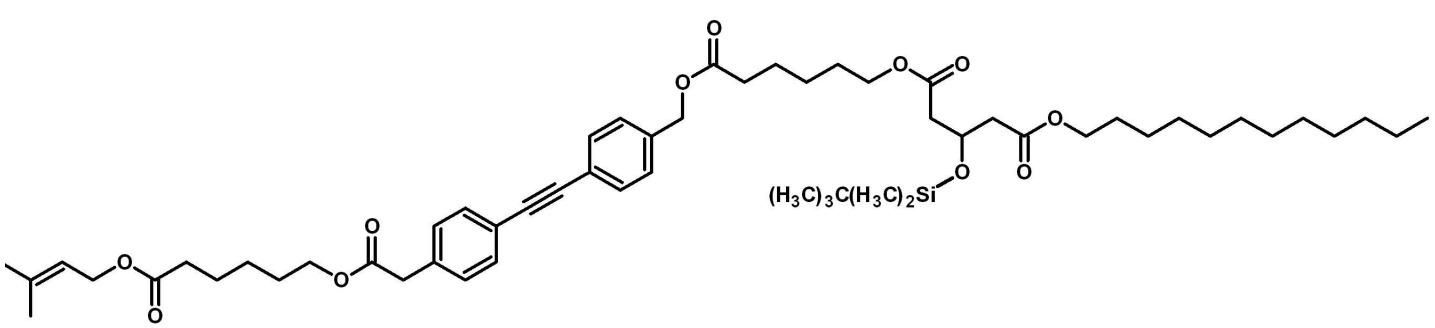




23

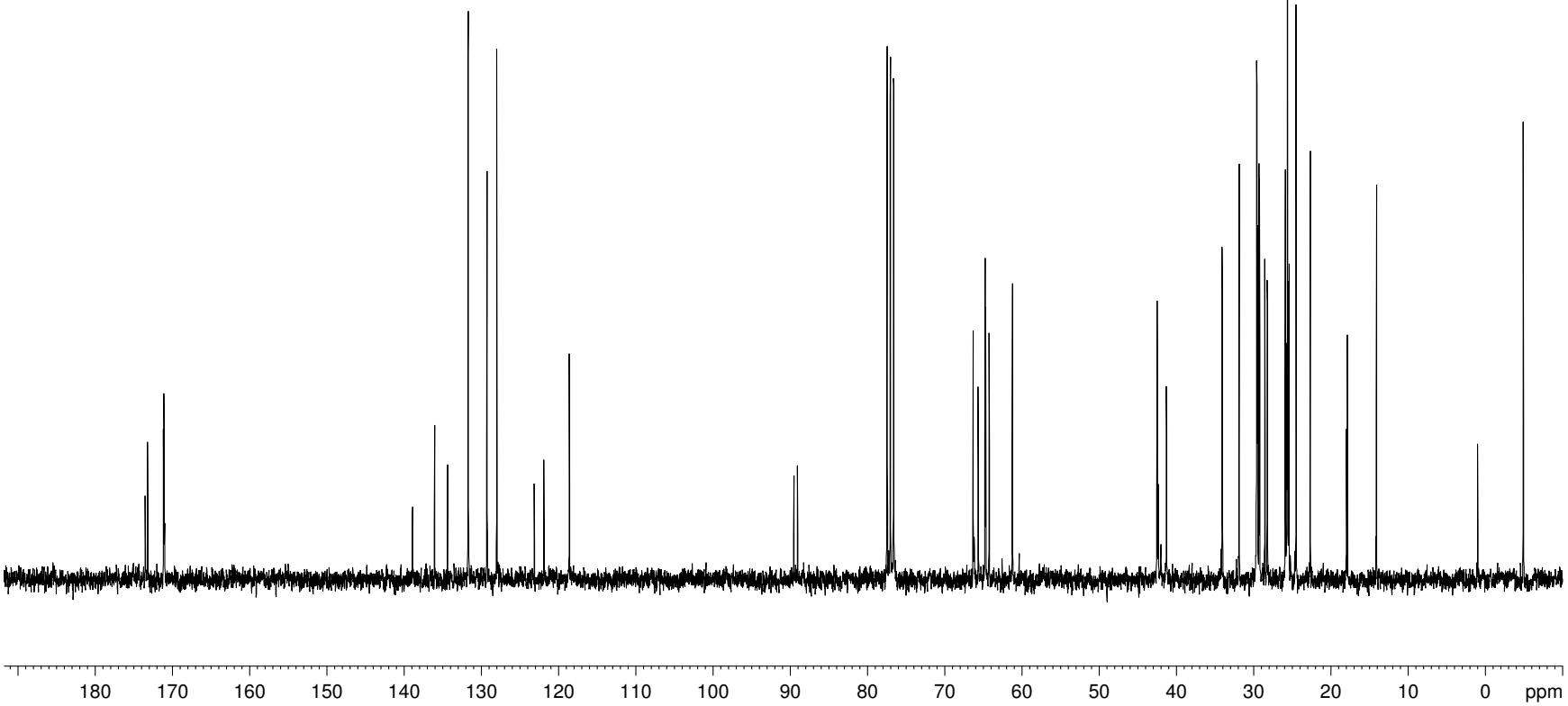
^{1}H NMR ($CDCl_3$) 300 MHz

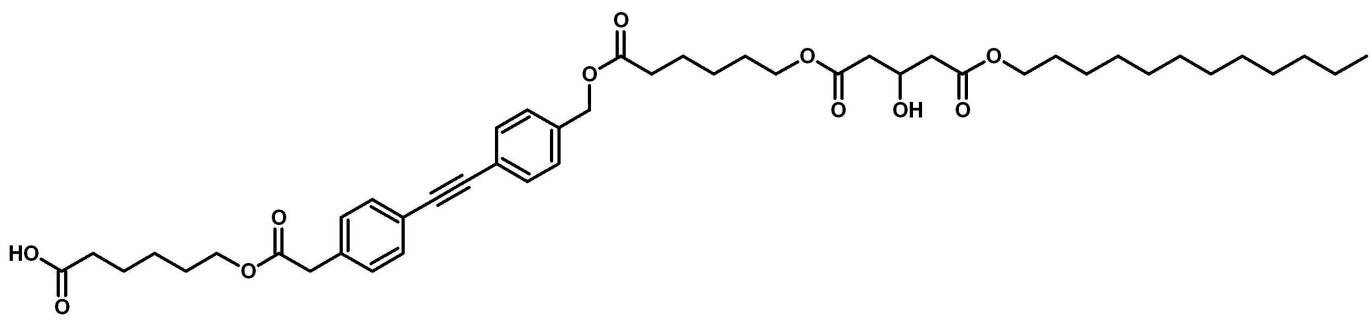




23

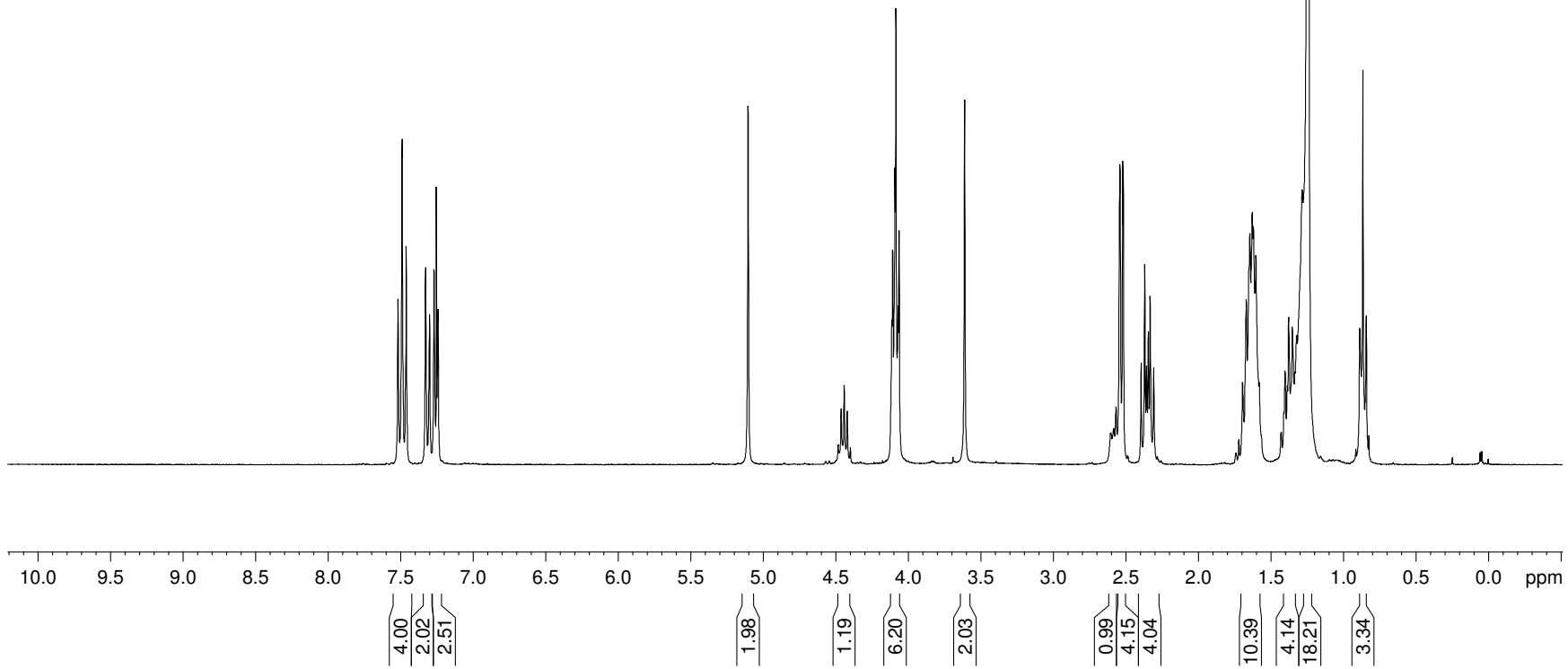
^{13}C NMR ($CDCl_3$) 75 MHz

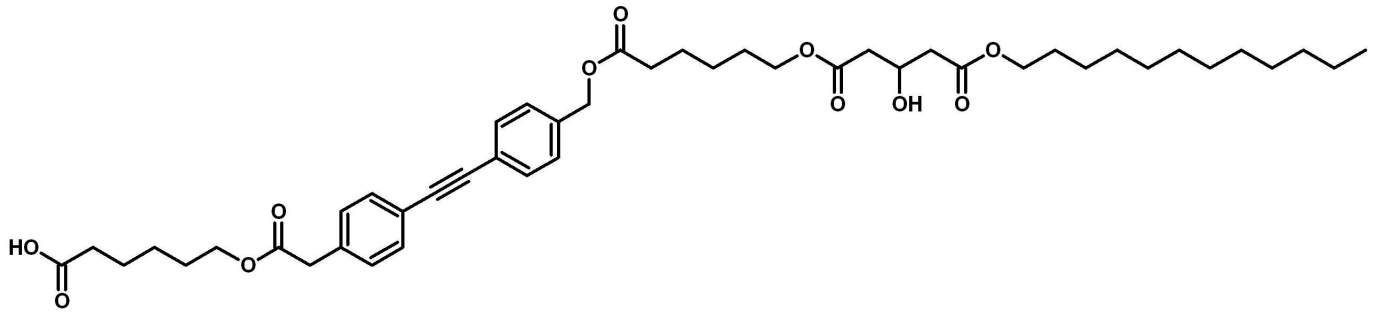




HO_2C-**Hex-Dip-Hex-G(12)**-OH

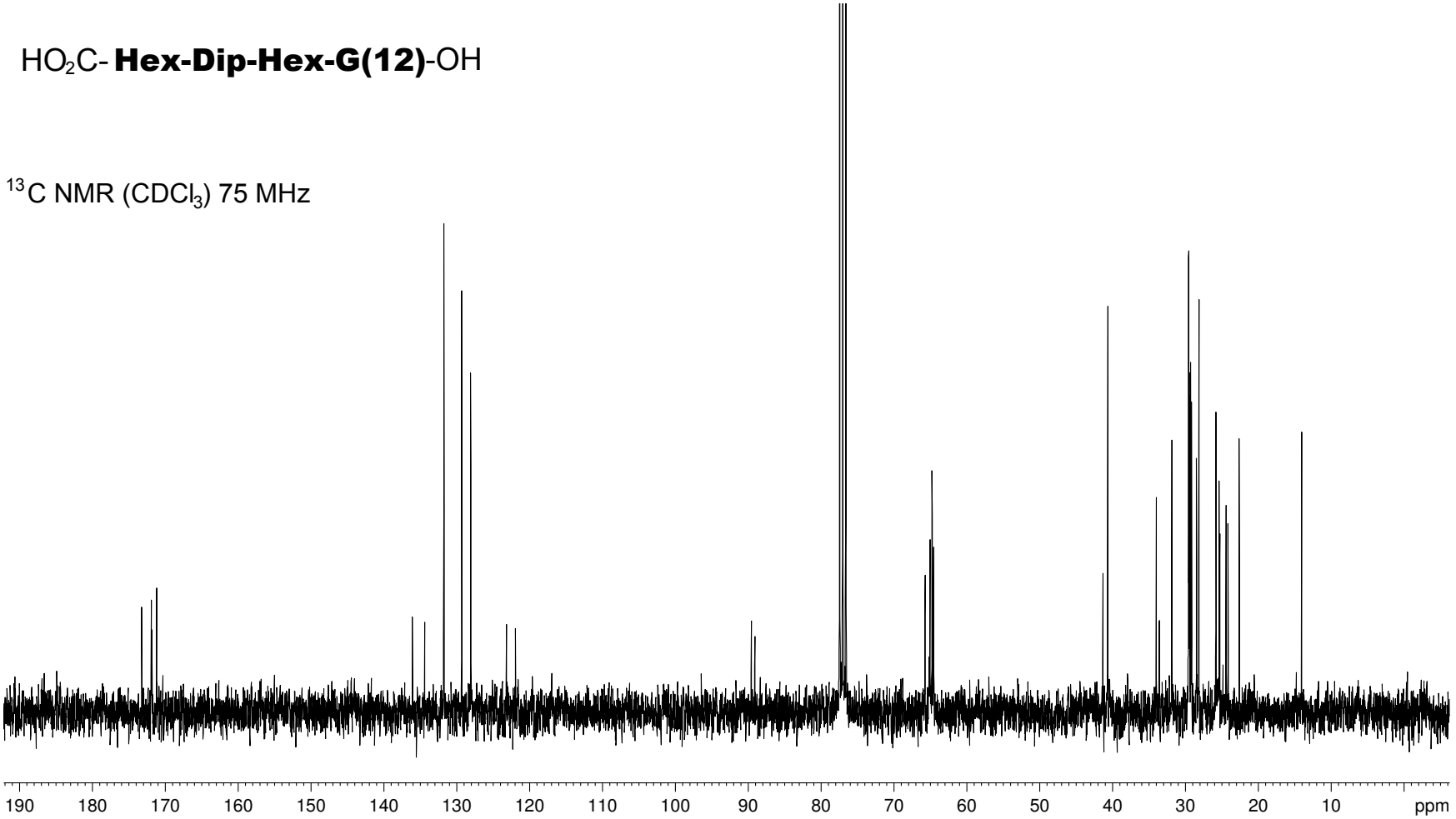
^1H NMR ($CDCl_3$) 300 MHz

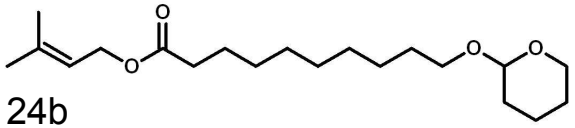




HO_2C-**Hex-Dip-Hex-G(12)**-OH

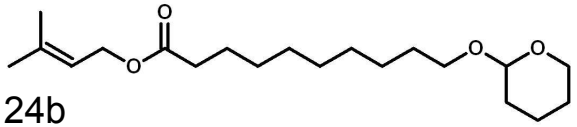
^{13}C NMR ($CDCl_3$) 75 MHz





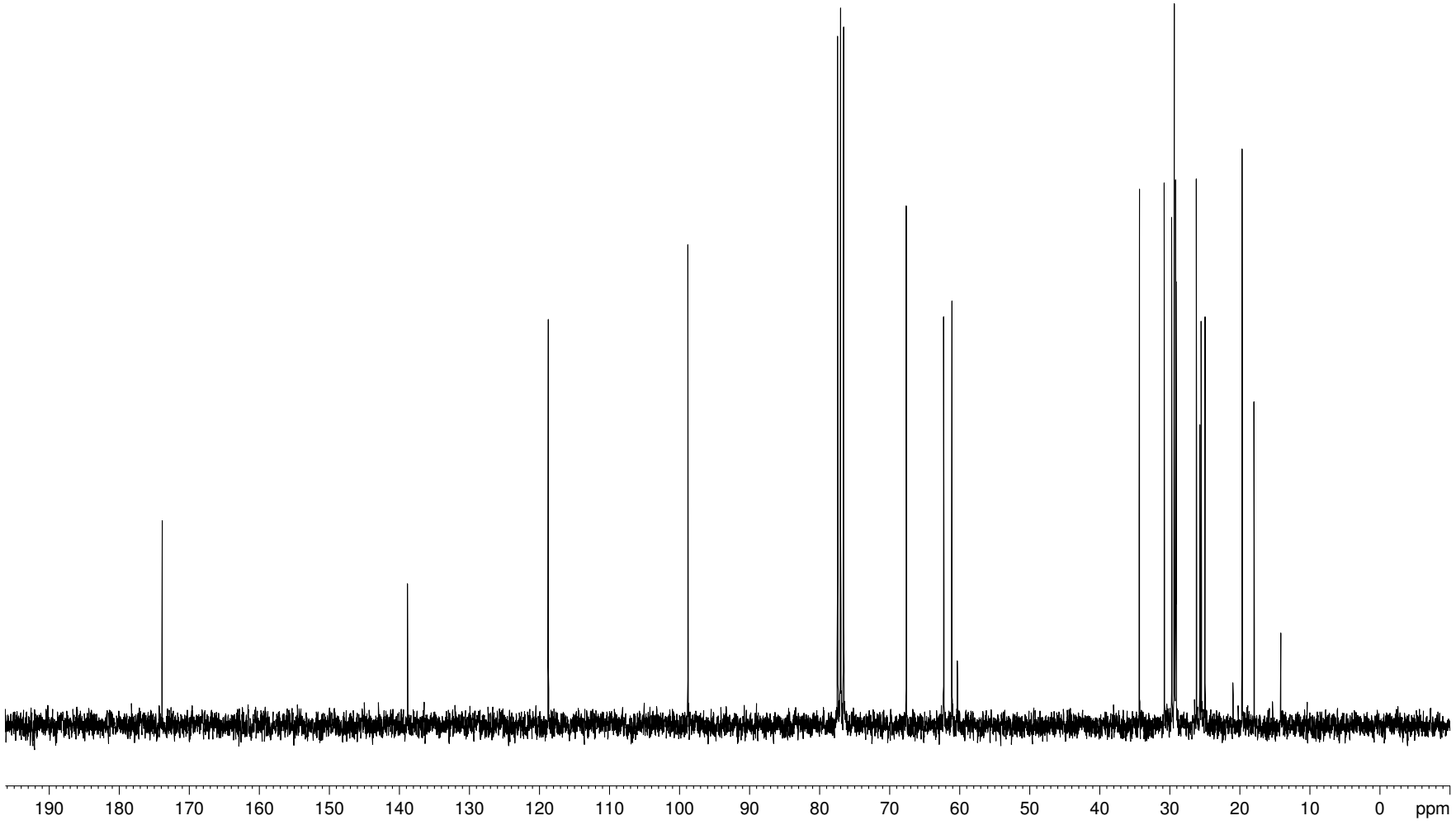
24b

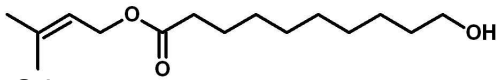
^{1}H NMR ($CDCl_3$) 300 MHz



24b

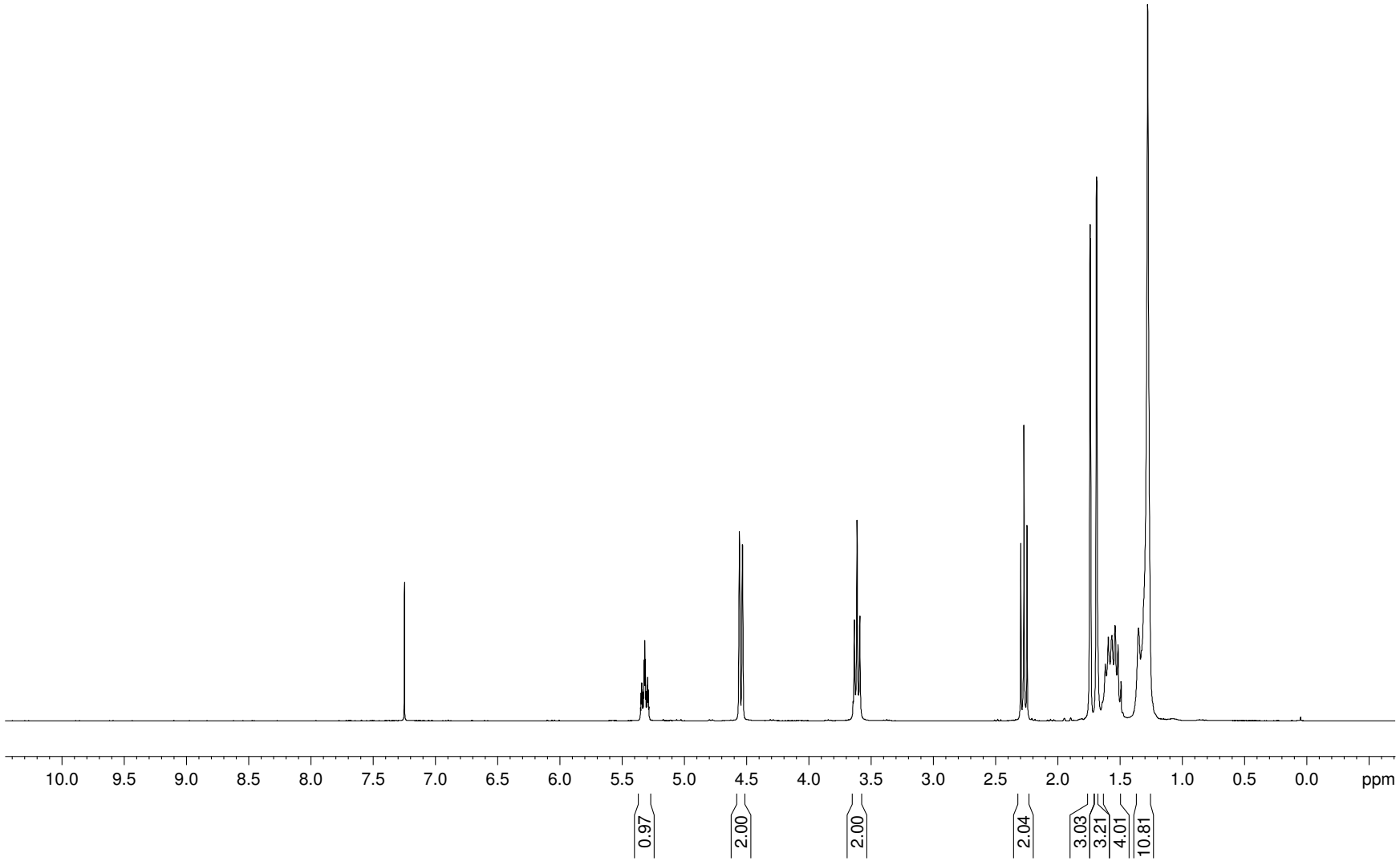
^{13}C NMR ($CDCl_3$) 75 MHz

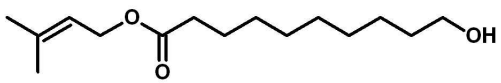




24c

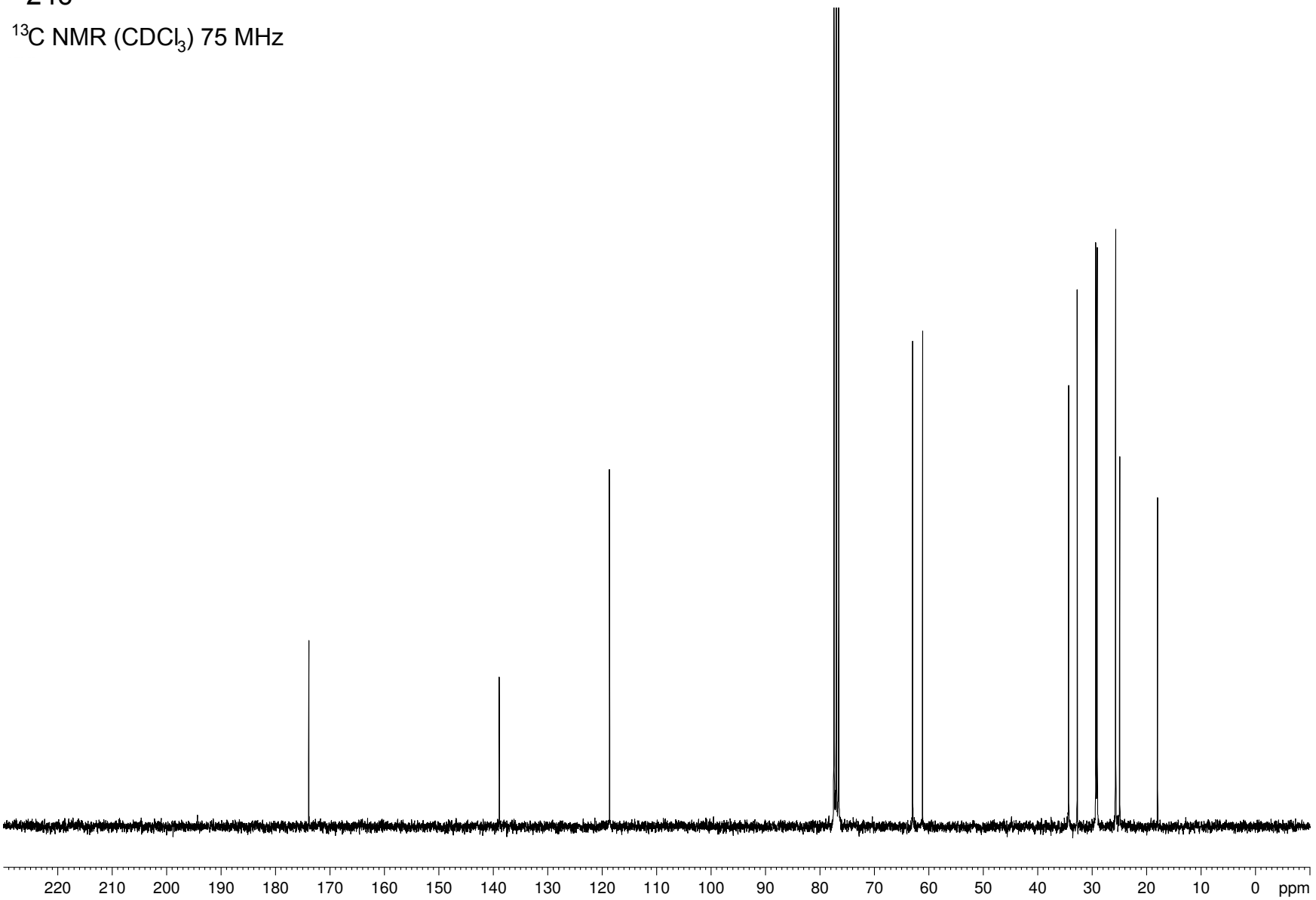
^{1}H NMR ($CDCl_3$) 300 MHz

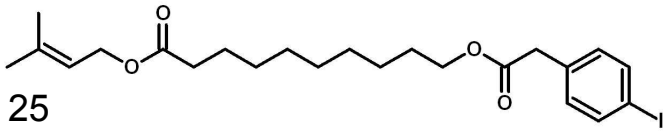




24c

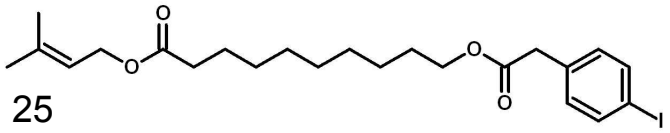
^{13}C NMR ($CDCl_3$) 75 MHz





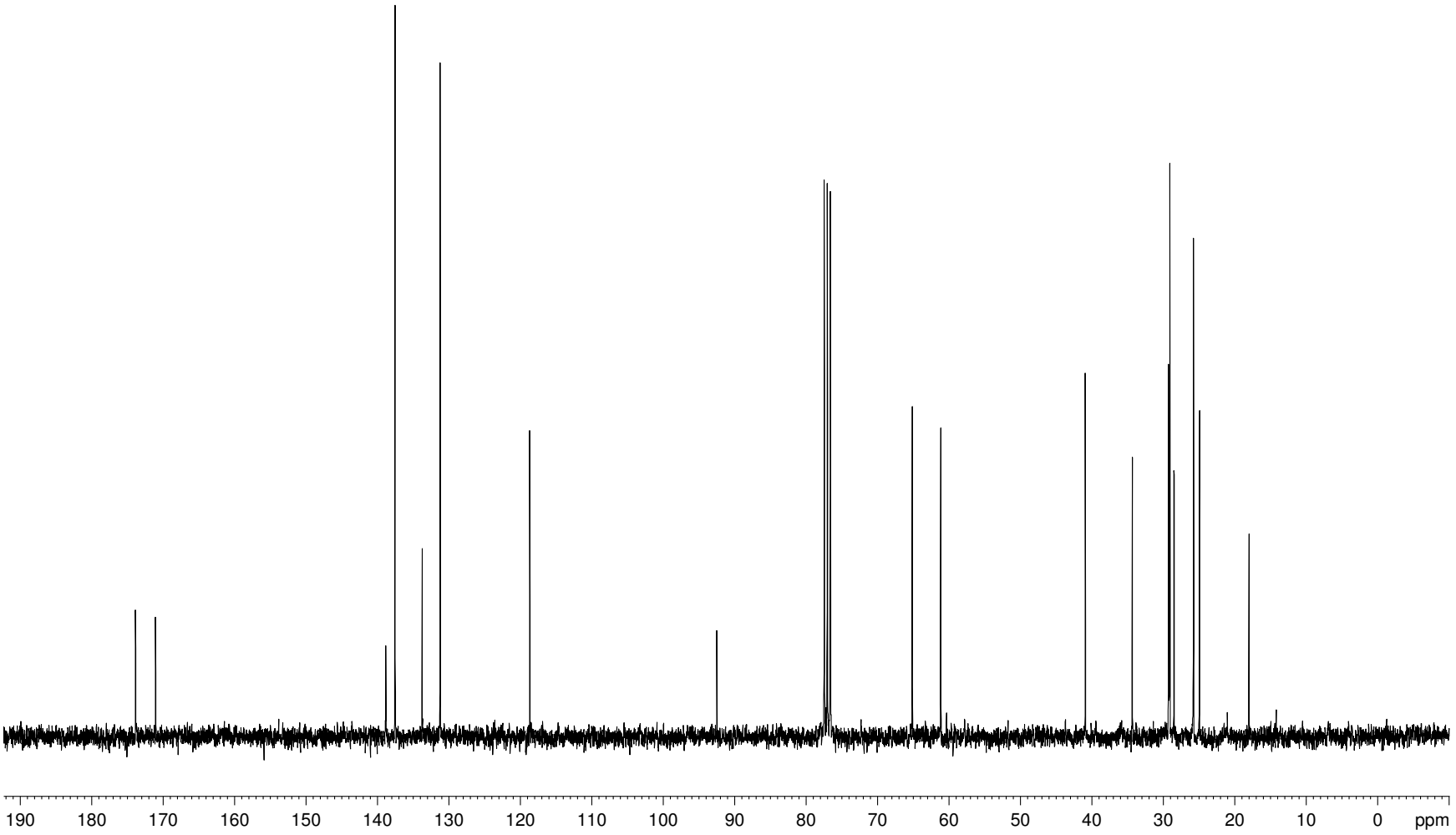
25

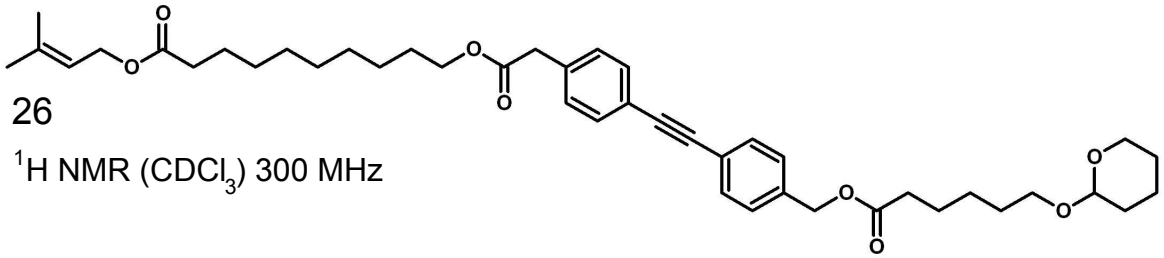
^{1}H NMR ($CDCl_3$) 300 MHz



25

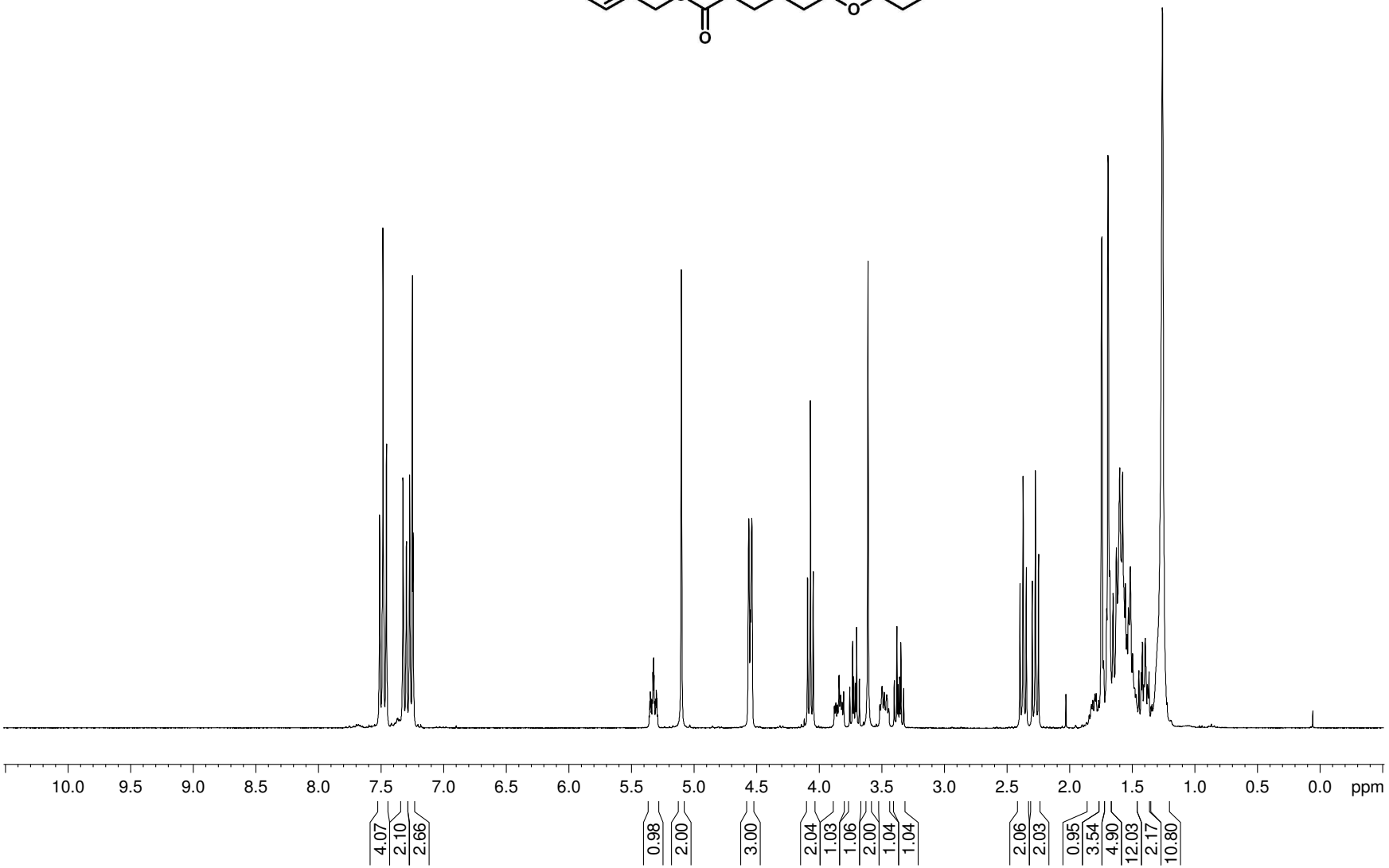
^{13}C NMR ($CDCl_3$) 75 MHz

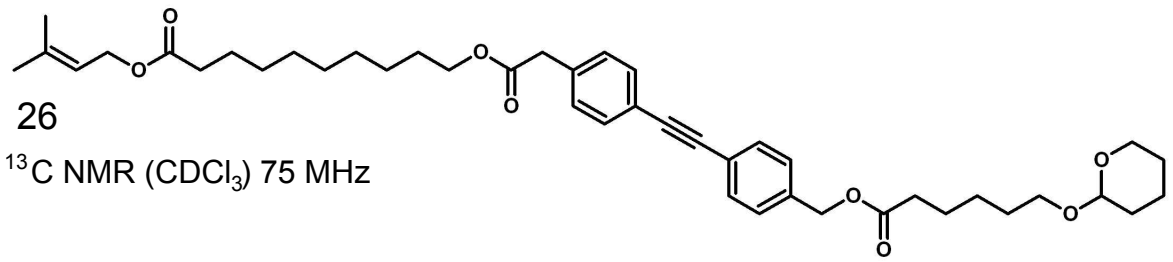




26

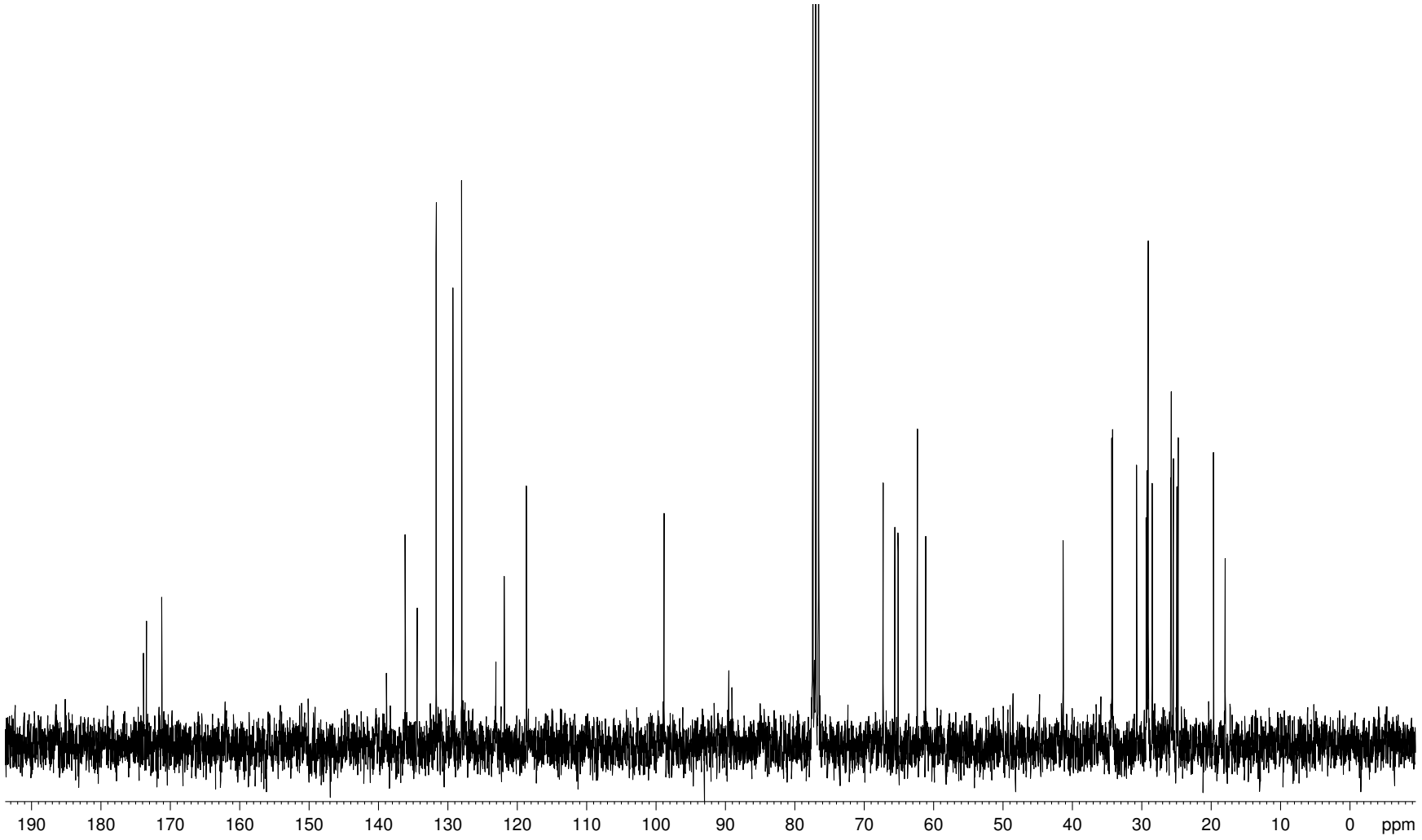
^{1}H NMR ($CDCl_3$) 300 MHz

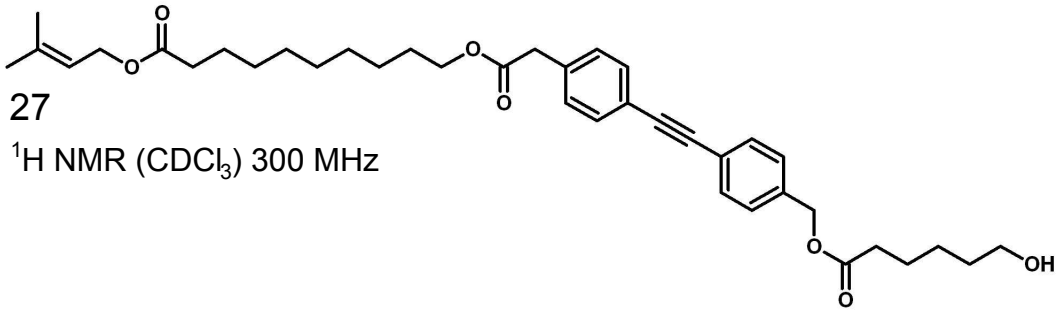




26

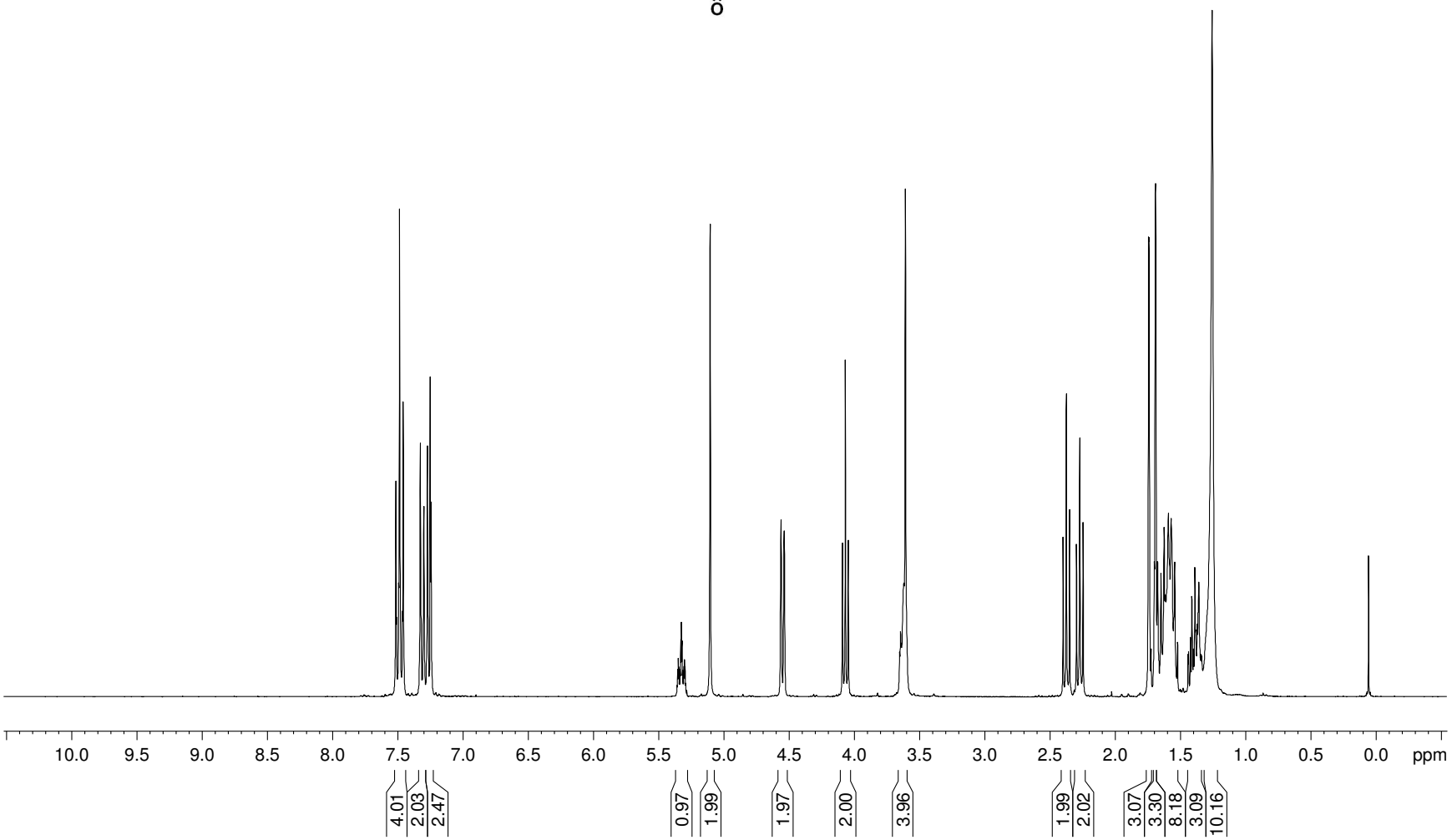
^{13}C NMR ($CDCl_3$) 75 MHz

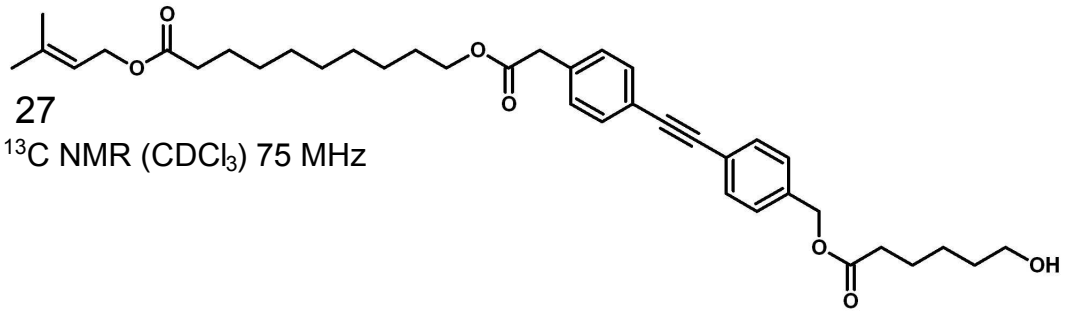




27

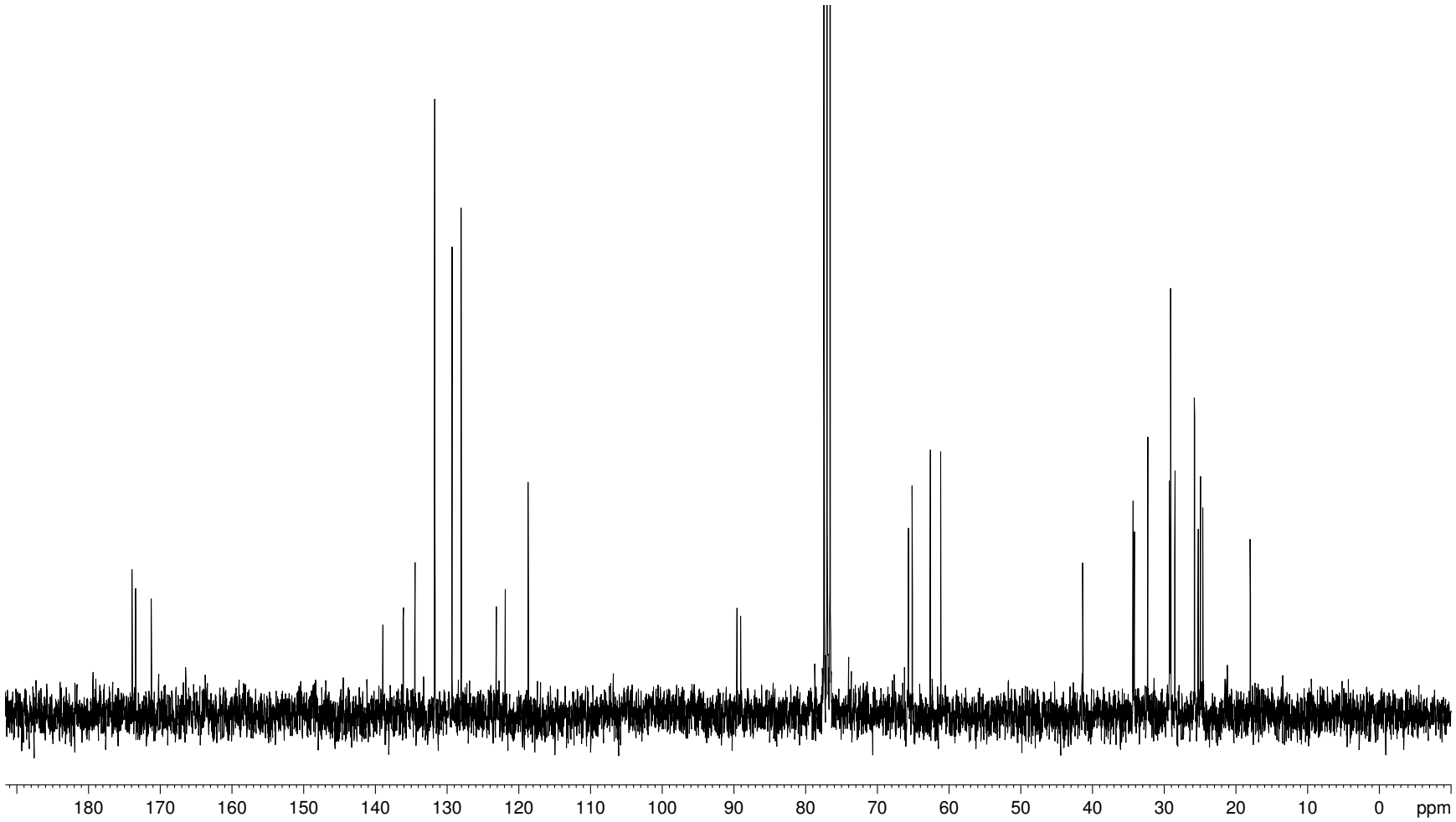
^{1}H NMR ($CDCl_3$) 300 MHz

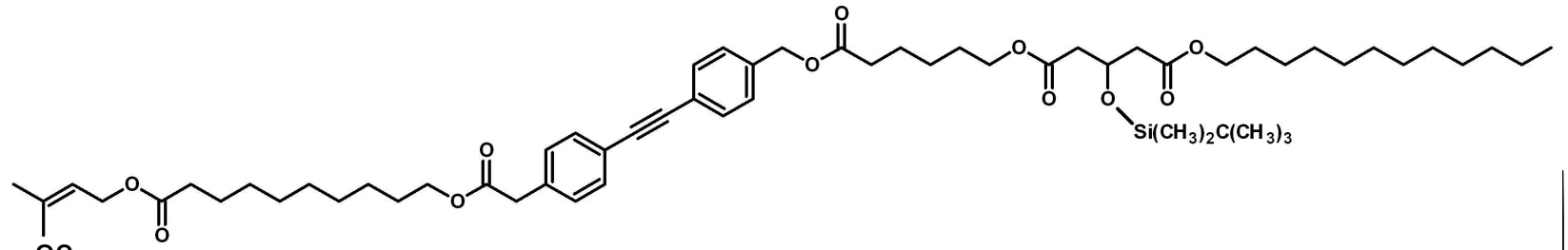




27

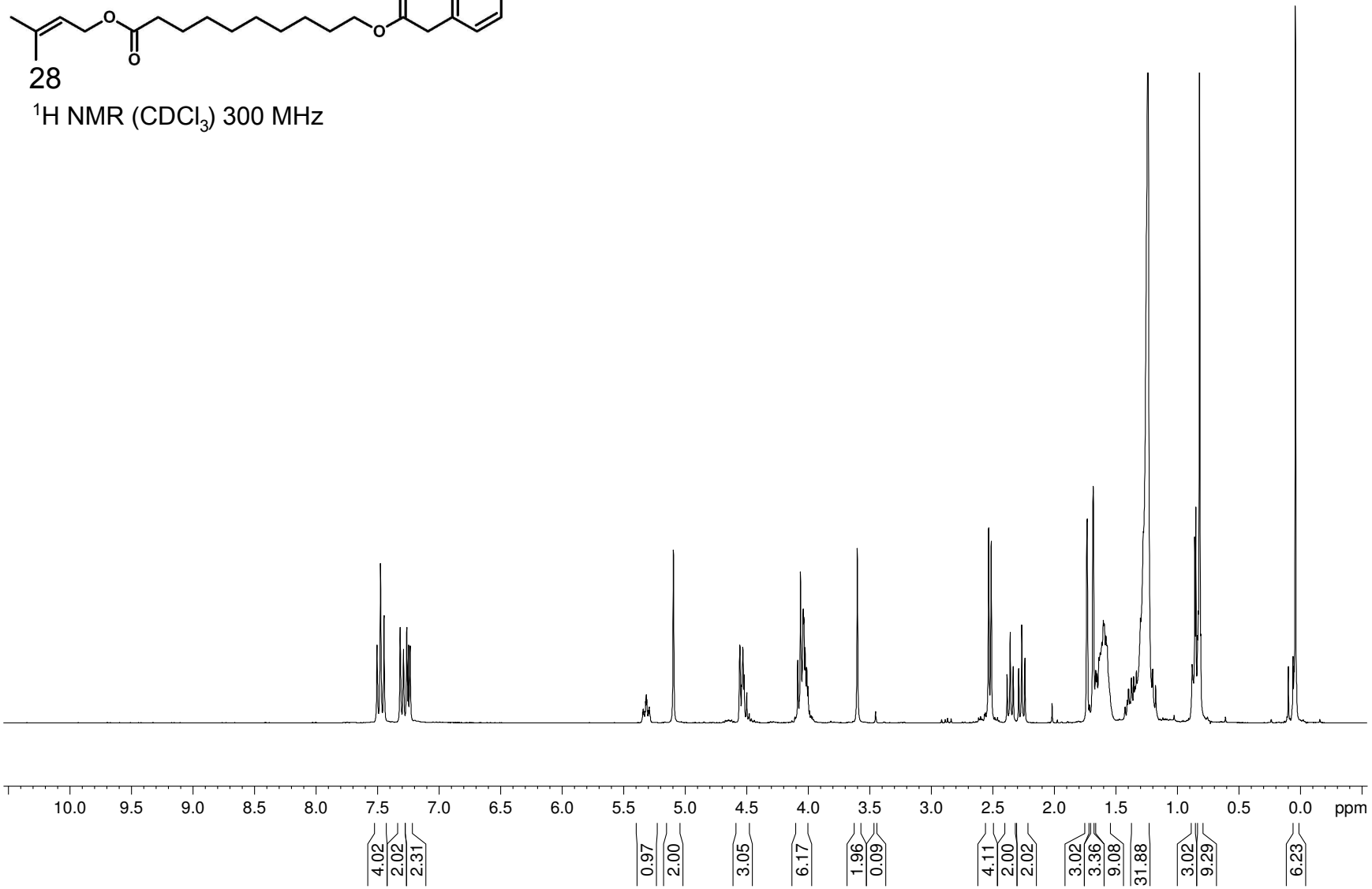
^{13}C NMR ($CDCl_3$) 75 MHz

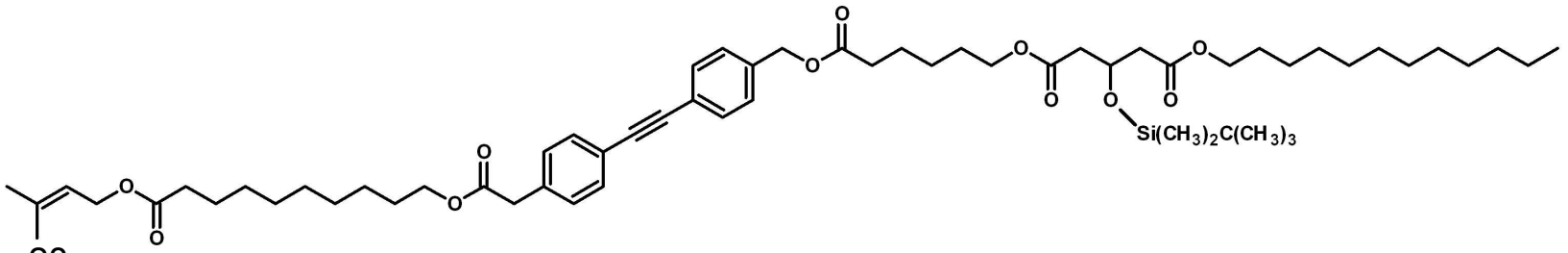




28

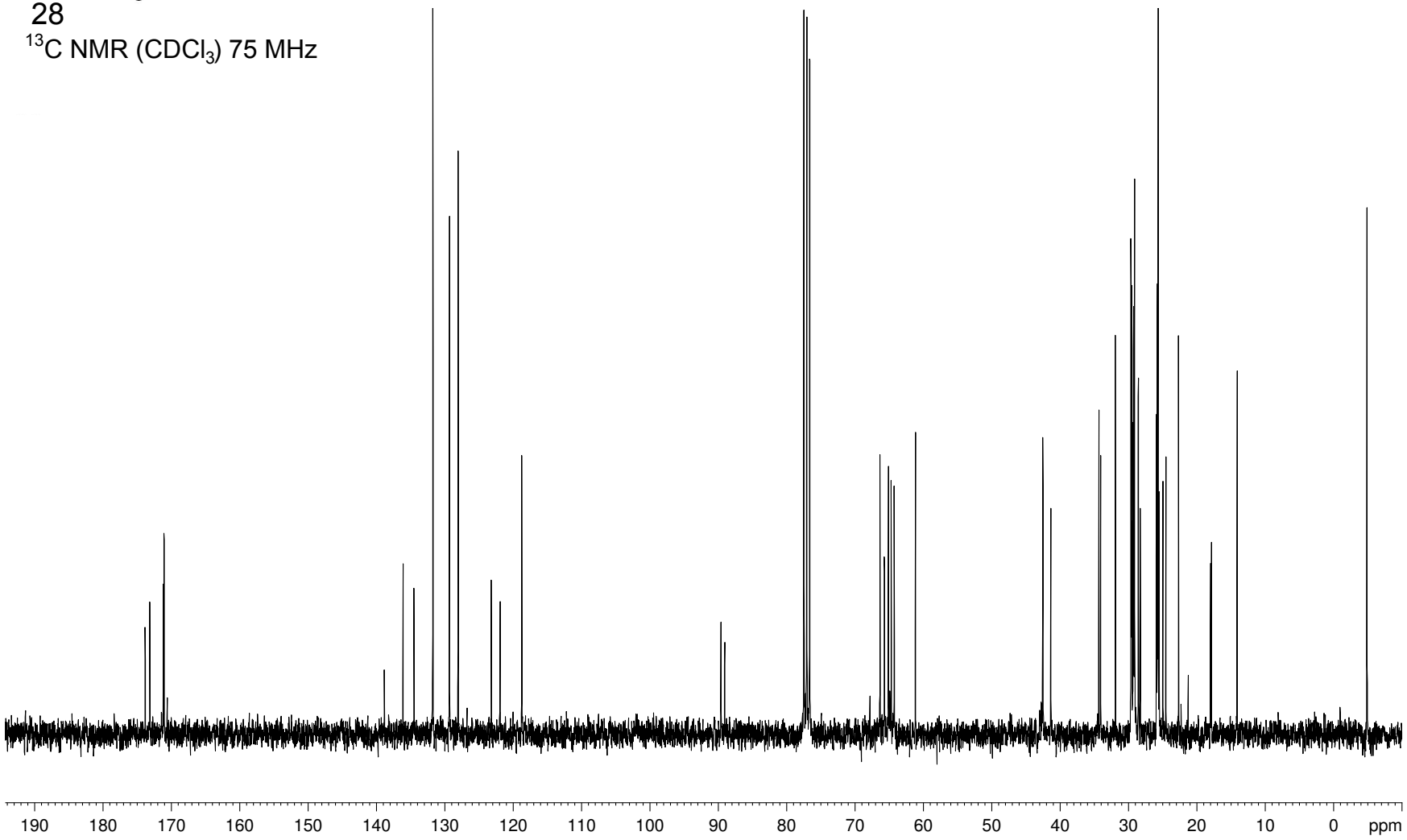
^{1}H NMR ($CDCl_3$) 300 MHz

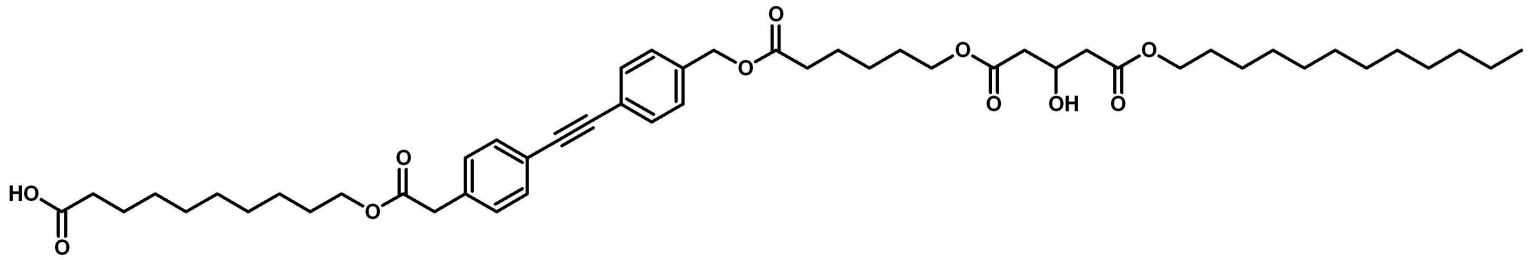




28

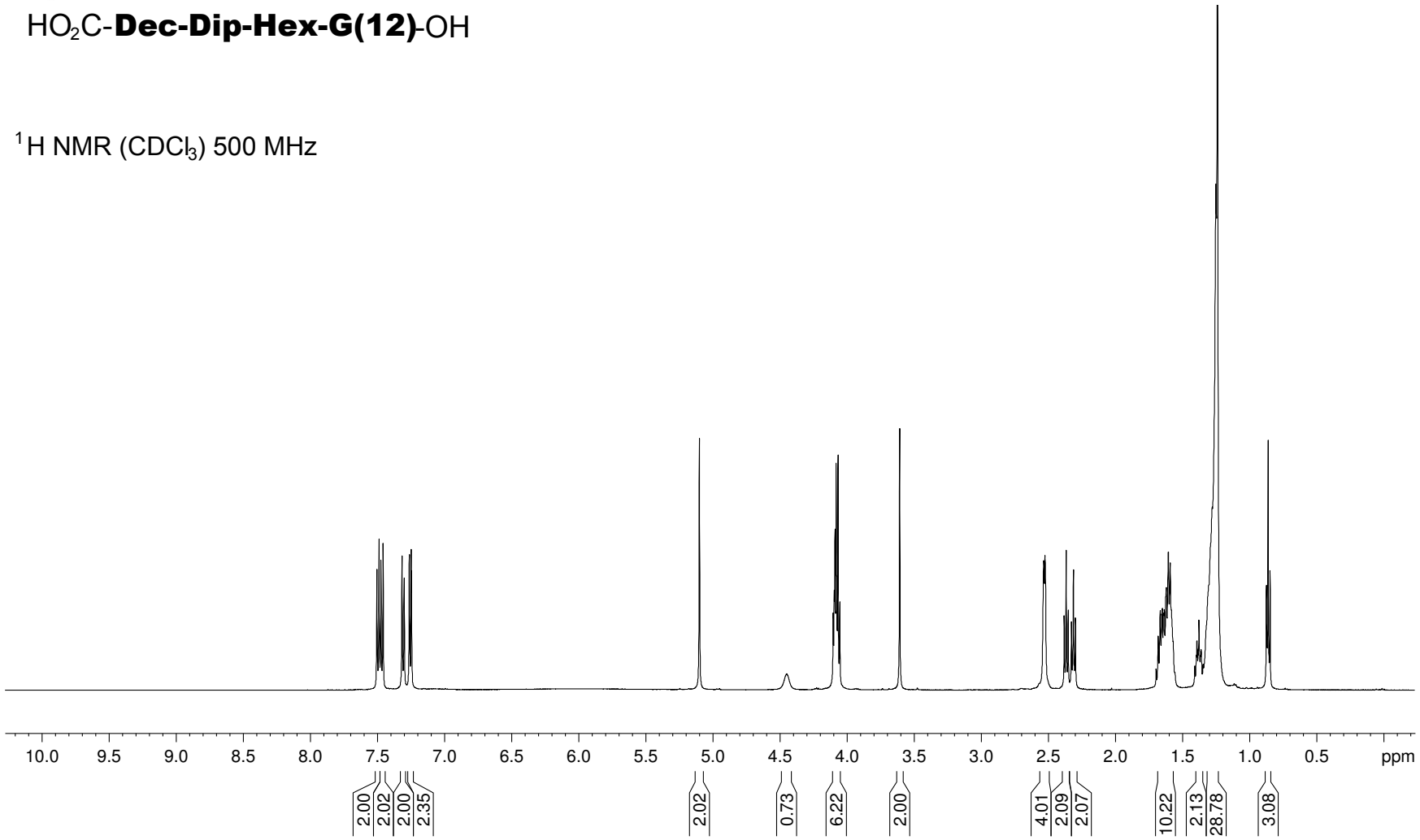
^{13}C NMR ($CDCl_3$) 75 MHz

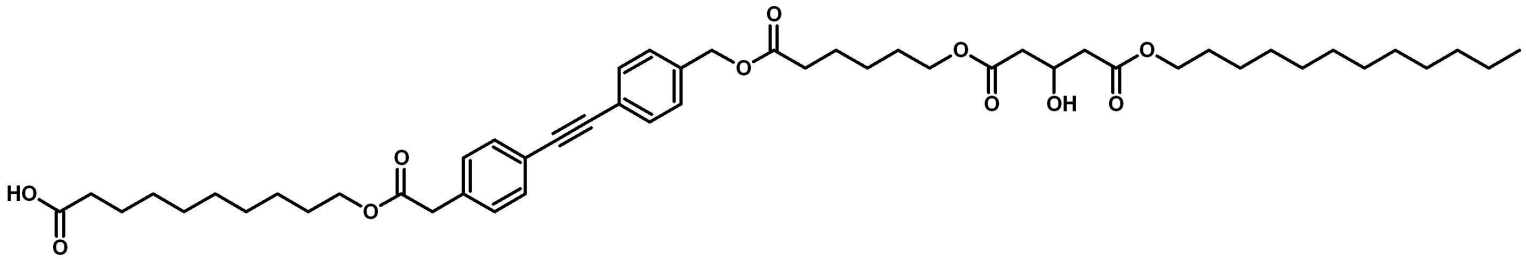




HO_2C-**Dec-Dip-Hex-G(12)**-OH

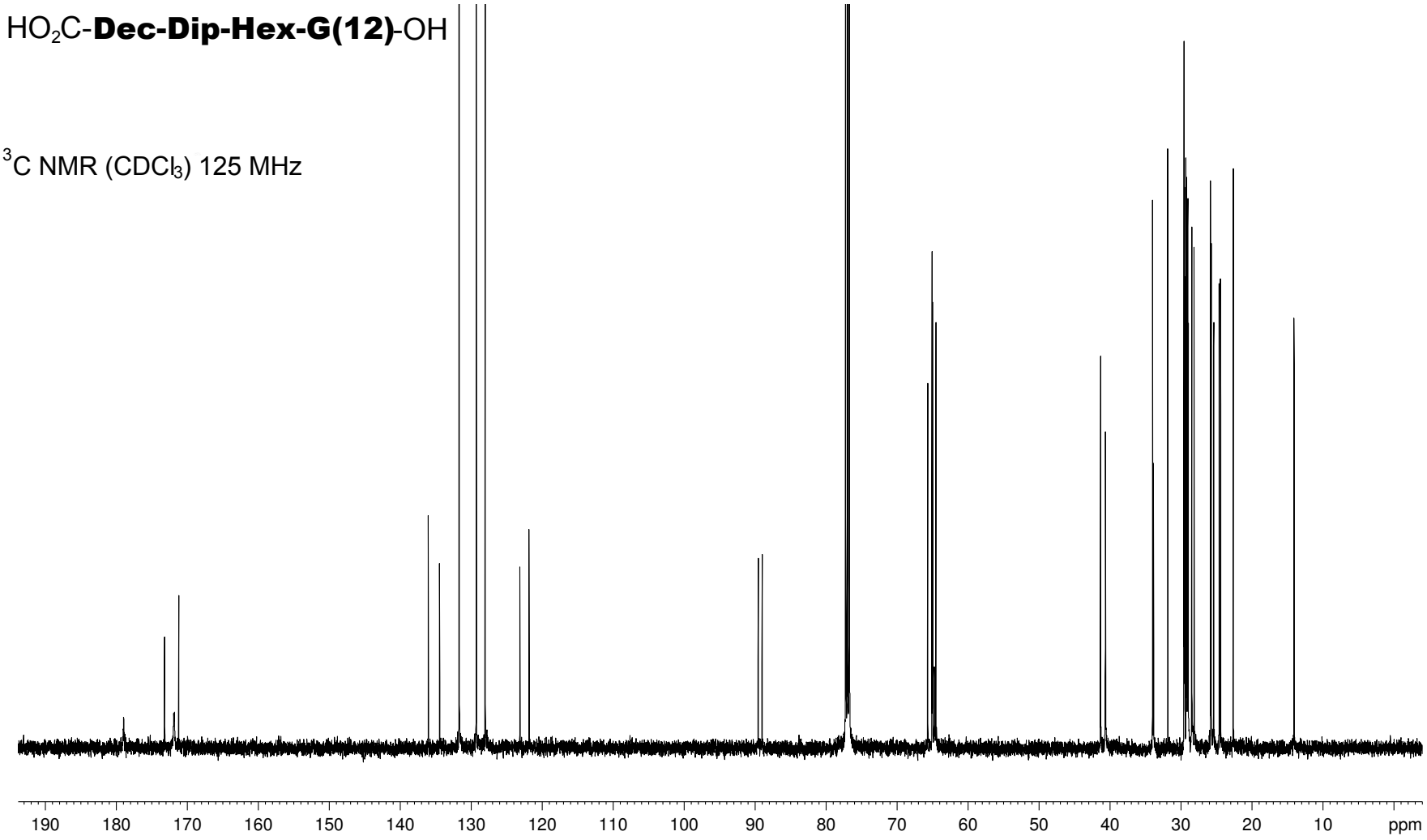
^1H NMR ($CDCl_3$) 500 MHz



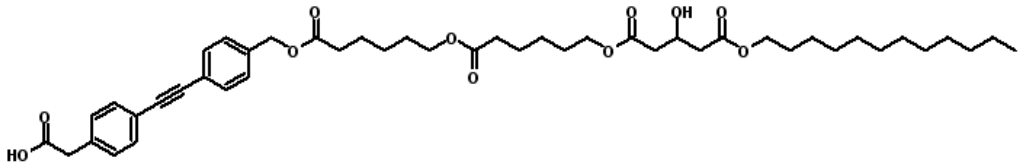


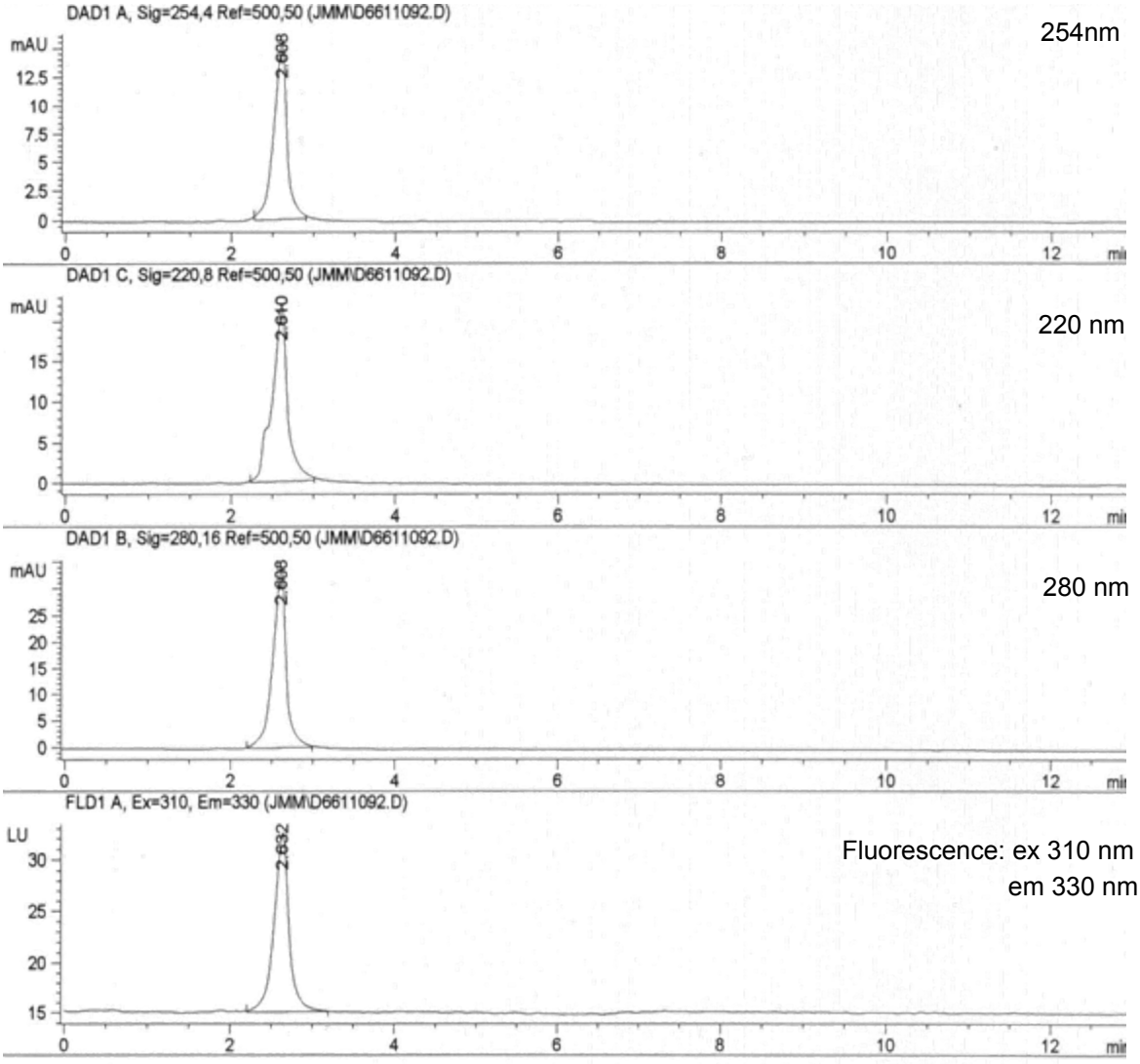
HO_2C-**Dec-Dip-Hex-G(12)**-OH

^{13}C NMR ($CDCl_3$) 125 MHz

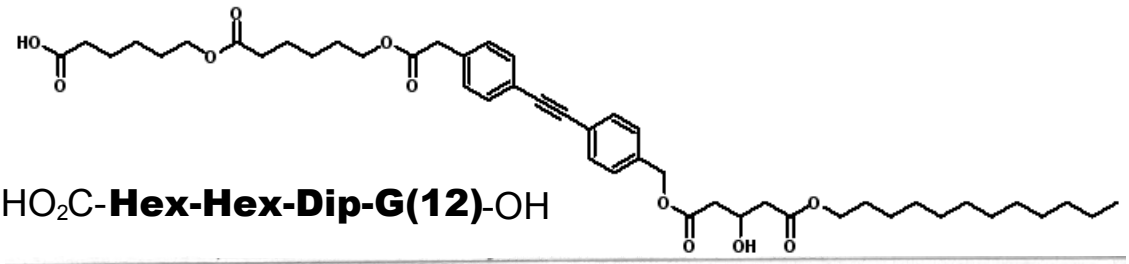


HO_2C-**Dip-Hex-Hex-G(12)**-OH

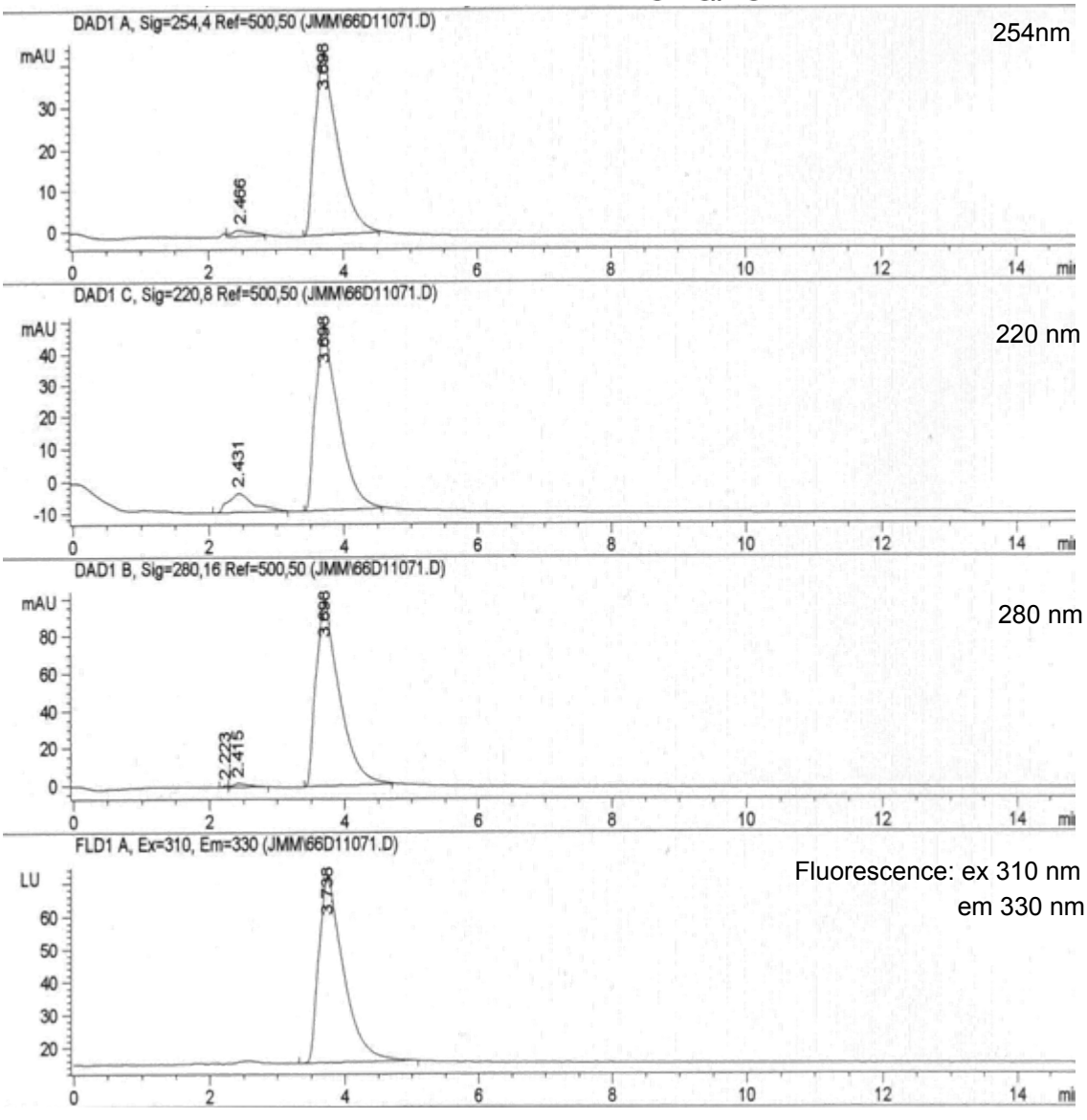




-HPLC trace of purified sample (used for transport and fluorescence studies)
-CONDITIONS: HP series 1100 HPLC
-Macherey-Nagel RP C^{18} "Nucleosil" analytical column (4 mm x 250 mm)
-1:1 CH_3OH: ACN as eluting solvents, flow 1mL/min



HO_2C-**Hex-Hex-Dip-G(12)**-OH



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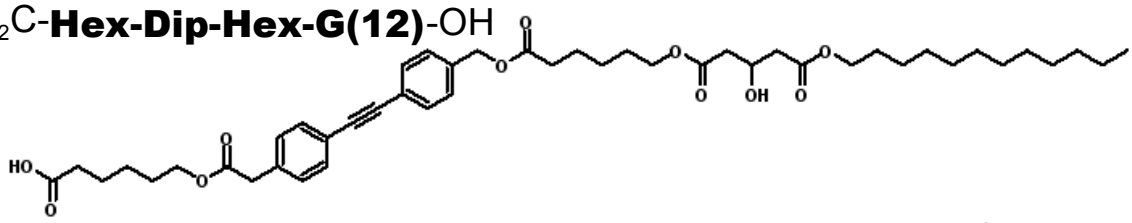
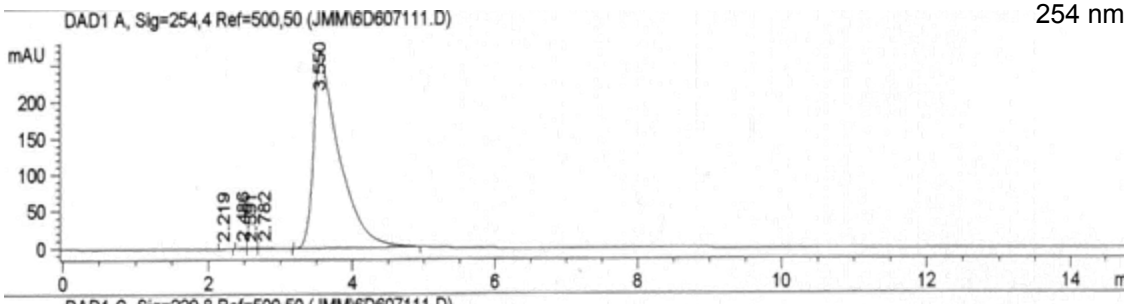
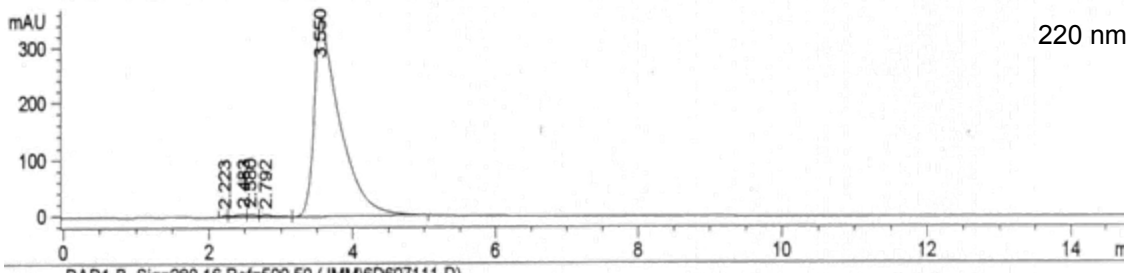
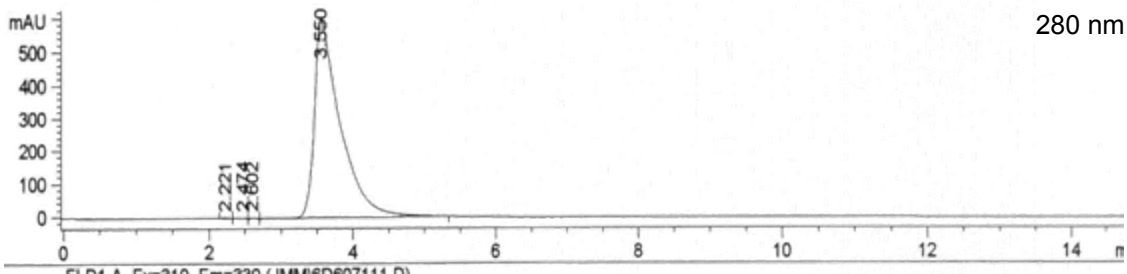
-1:1 CH_3OH: ACN as eluting solvents, flow 1mL/min

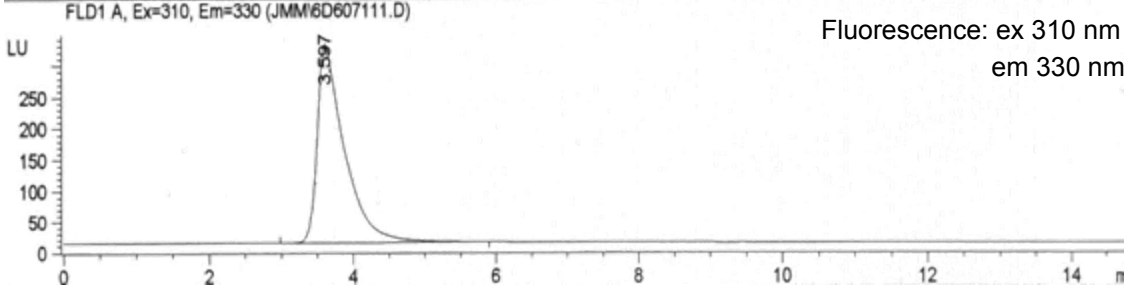
HO_2C-**Hex-Dip-Hex-G(12)**-OH





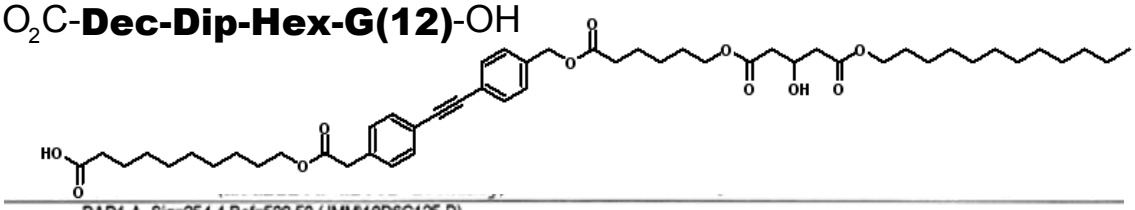


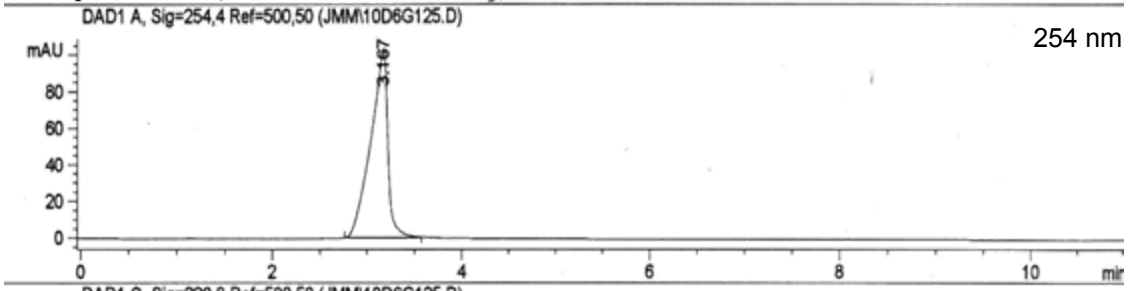




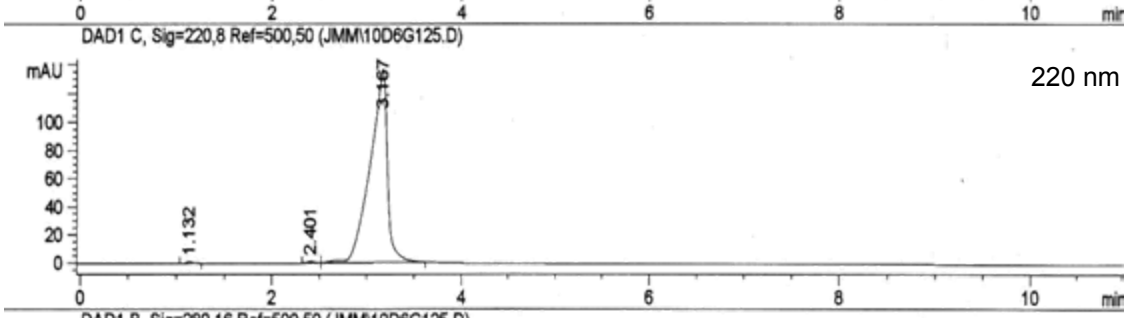
-HPLC trace of purified sample (used for transport and fluorescence studies)
-CONDITIONS: HP series 1100 HPLC
-Macherey-Nagel RP C^{18} "Nucleosil" analytical column (4 mm x 250 mm)
-1:1 CH_3OH: ACN as eluting solvents, flow 1mL/min

HO_2C-**Dec-Dip-Hex-G(12)**-OH





254 nm



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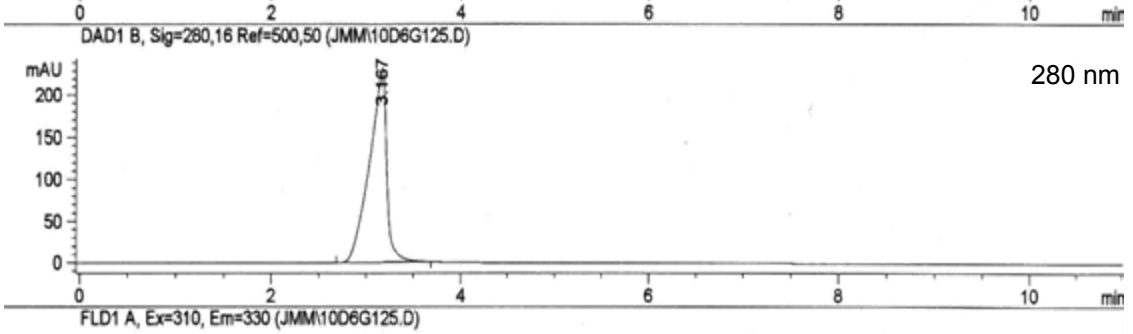
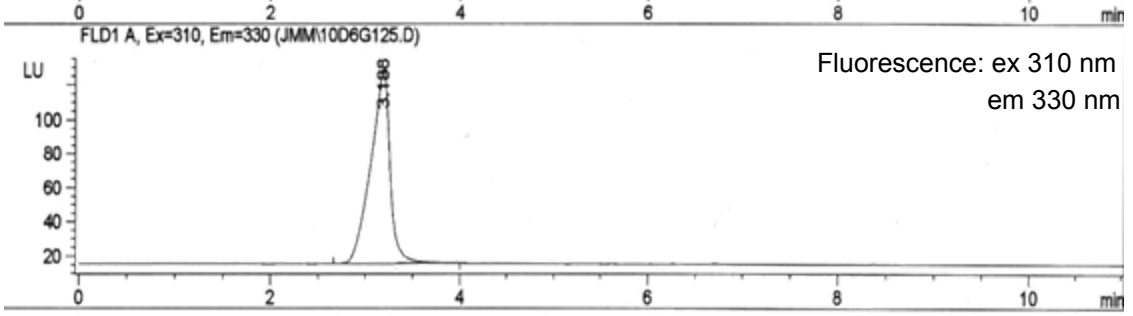


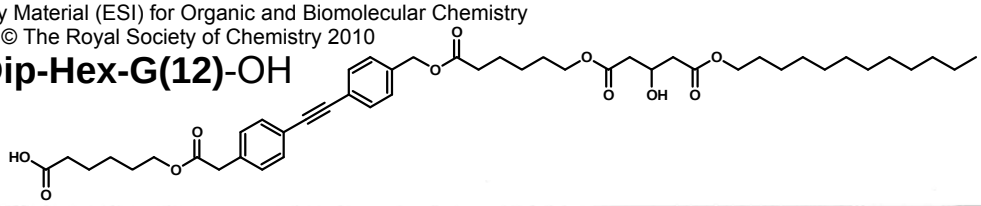
280 nm

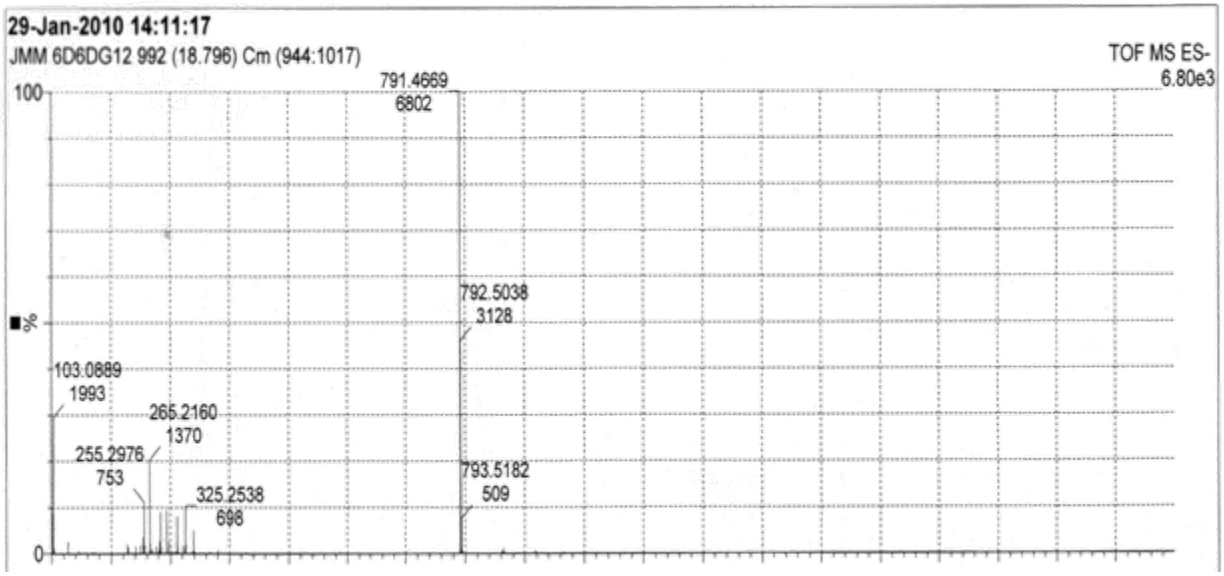


Fluorescence: ex 310 nm
em 330 nm

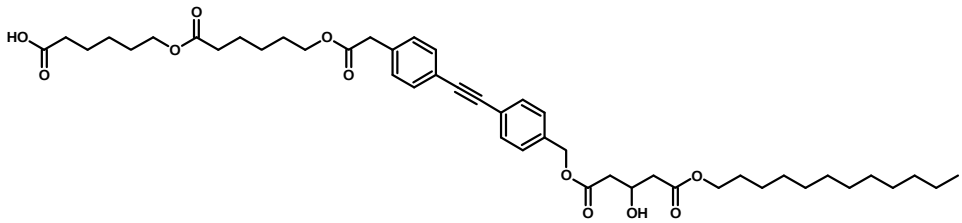
-HPLC trace of purified sample (used for transport and fluorescence studies)
-CONDITIONS: HP series 1100 HPLC
-Macherey-Nagel RP C^{18}"Nucleosil" analytical column (4 mm x 250 mm)
-1:1 CH_3OH: ACN as eluting solvents, flow 1mL/min

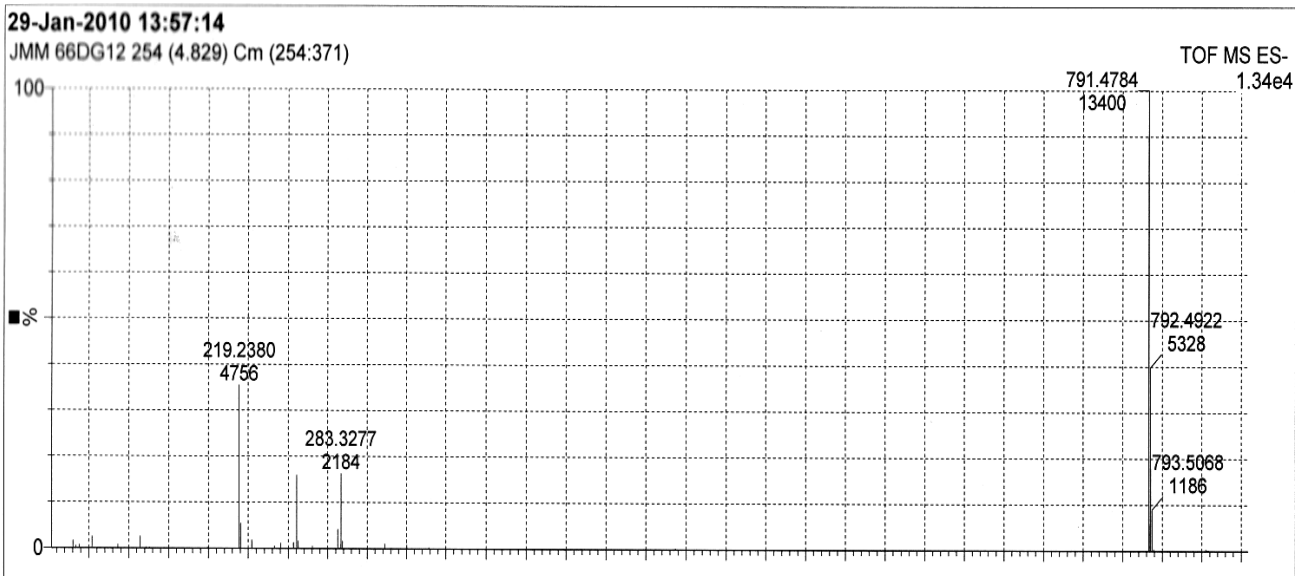
HO_2C-**Hex-Dip-Hex-G(12)**-OH



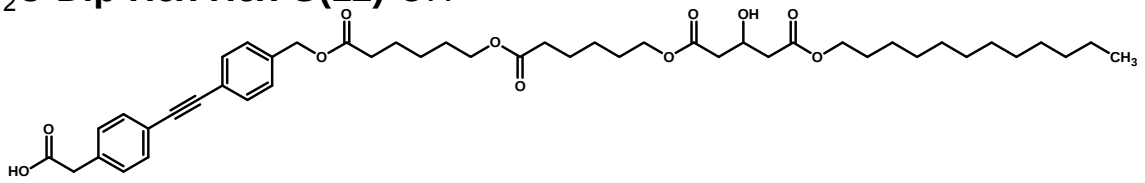


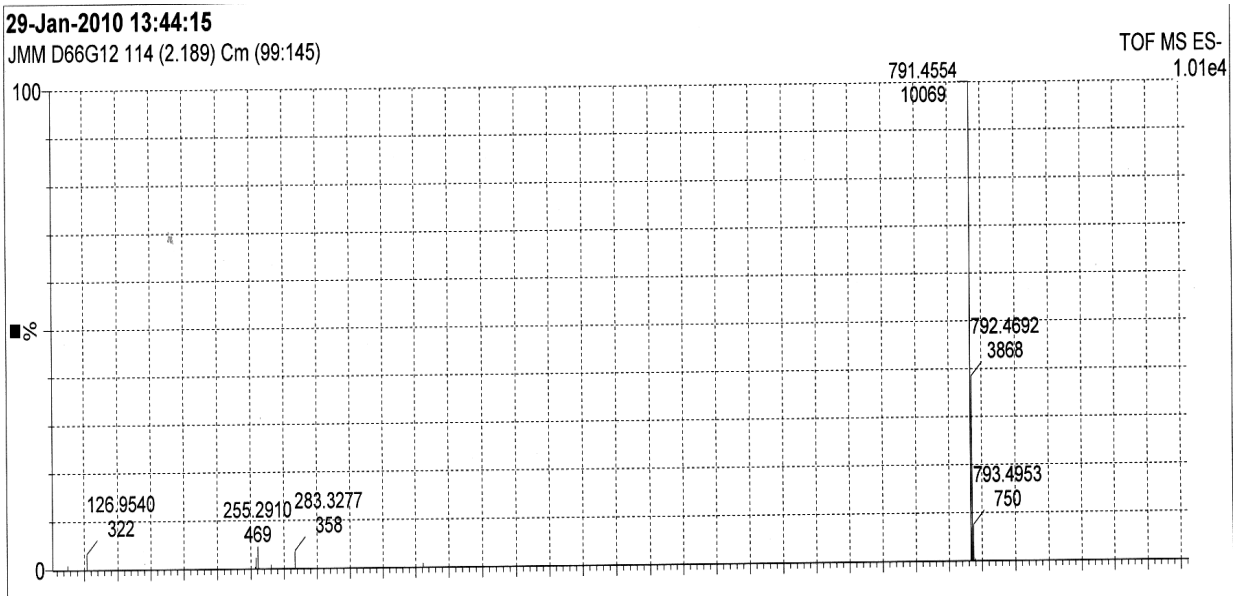
HO_2C-**Hex-Hex-Dip-G(12)**-OH



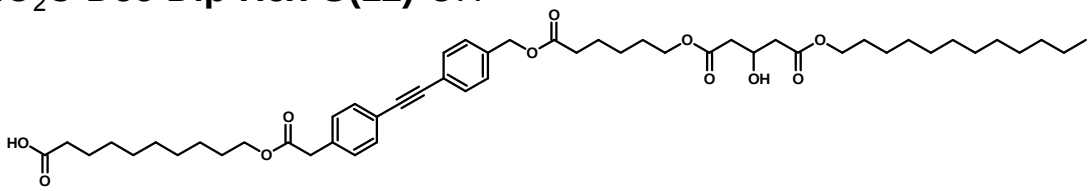


HO_2C-**Dip-Hex-Hex-G(12)**-OH





HO_2C-**Dec-Dip-Hex-G(12)**-OH



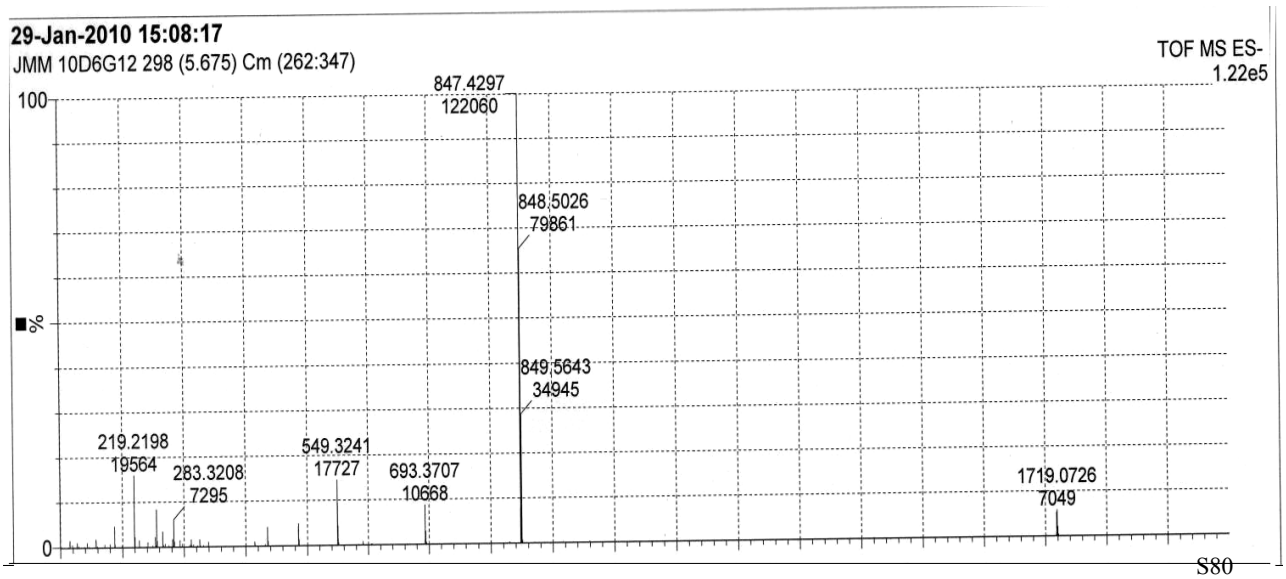


Table S1: Graphing parameters and rate data for HPTS transport assay

Compound	Curve	Conc. μM	k0[a] Frac/sec	Int0[a] Frac.	k1[b] Sec^{-1}	Int1[b] Frac	initial rate[c] Frac/sec
HO_2C-**Hex-Dip-Hex-G(12)**-OH	GLGM	23.2			2.49E-01	-7.57E-01	4.16E-03
	GTGU	23.2			2.68E-01	-9.08E-01	4.48E-03
	HBHC	16.7			1.92E-01	-6.63E-01	3.21E-03
	HJHK	16.7			1.97E-01	-6.87E-01	3.29E-03
	HRHS	8.3	7.71E-04	1.58E-01			7.71E-04
	HZIA	8.3	6.72E-04	1.59E-01			6.72E-04
	IHII	3.3	5.80E-04	1.49E-01			5.80E-04
HO_2C-**Hex-Hex-Dip-G(12)**-OH	CTCU	24.1			2.38E-01	-6.64E-01	3.98E-03
	DBDC	24.1			2.36E-01	-7.02E-01	3.94E-03
	DRDS	16.9			1.86E-01	-5.82E-01	3.11E-03
	DJDK	16.9			1.74E-01	-5.31E-01	2.91E-03
	CLCM	12.2	5.78E-04	1.52E-01			5.78E-04
	CDCE	12.2	5.80E-04	1.61E-01			5.80E-04
HO_2C-**Dip-Hex-Hex-G(12)**-OH	EHEI	20.2			2.27E-01	-6.36E-01	3.79E-03
	DZEA	20.2			2.23E-01	-6.20E-01	3.73E-03
	EXEY	12.6			2.10E-01	-5.91E-01	3.51E-03
	EPEQ	12.6			2.03E-01	-5.71E-01	3.39E-03
	FNFO	6.3	7.17E-04	1.99E-01			7.17E-04
	FFFG	6.3	6.51E-04	2.06E-01			6.51E-04
	FVFW	3.1	4.97E-04	1.57E-01			4.97E-04
	GDGE	3.1	4.64E-04	1.74E-01			4.64E-04
HO_2C-**Dec-Dip-Hex-G(12)**-OH	AXAW	30.2	3.32E-04	1.68E-01			3.32E-04
	BEBF	30.2	3.27E-04	1.78E-01			3.27E-04
	AHAG	15.3	2.12E-04	1.33E-01			2.12E-04
	APAO	15.3	2.53E-04	1.30E-01			2.53E-04
	BNBM	7.7	1.99E-04	1.36E-01			1.99E-04
	BVBU	7.7	2.18E-04	9.63E-02			2.18E-04
none	HI	0	2.27E-04	8.49E-02			2.27E-04
HO_2C-**Oct-Dod-Oct-G(10)**-OH		60	1.43E-03				1.43E-03
		60	1.38E-03				1.38E-03
		60	1.48E-03				1.48E-03
		45.1	1.15E-03				1.15E-03
		45.1	1.26E-03				1.26E-03
		45.1	1.25E-03				1.25E-03
		30	8.56E-04				8.56E-04
		30	8.43E-04				8.43E-04
		30	8.71E-04				8.71E-04
		15	5.30E-04				5.30E-04

15	5.26E-04	5.26E-04
15	5.43E-04	5.43E-04
7.5	3.53E-04	3.53E-04
7.5	3.04E-04	3.04E-04
7.5	3.40E-04	3.40E-04
0	1.98E-04	1.98E-04
0	1.74E-04	1.74E-04
0	2.25E-04	2.25E-04

a) Fraction of transport as a function of time fit to: frac = k0*time + int0. All fits $R^2 > 0.97$.

b) Fraction of transport as a function of time fit to: frac = k1*ln(time) + int1. All fits $R^2 > 0.99$.

c) Initial rate = zeroth order rate when available otherwise calculated from the first order fit at time = 60 seconds (approximately 5 seconds after transport initiated).

Supplementary Information Section: Part 2

Synthesis, transport activity, membrane localization, and dynamics of oligoester ion channels containing diphenylacetylene units.

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Table of Contents:

GENERAL METHODS:

The compounds were synthesized and characterized as described in the report.[1] All oligomers studied were purified by HPLC prior to use. Stock concentrations of approximately 1 – 6mM in THF were stored under N_2 in the freezer when not in use, and periodically re-checked by HPLC. Volumes of compound in THF used in each experiment did not exceed 25μL added into typically 2 mL of aqueous solution. UV spectra were collected on a Cary 5 UV-VIS spectrometer in a 10 x 10 mm quartz cell. Fluorescence spectra were collected on a PTI QM instrument at T=20^0C, with slits open to 3nm in 10 x 10 mm quartz cells equipped with a stir rod. The volume of solutions was kept approximately at 2mL for all experiments. For studies in organic solvents, the solvents used were of spectral or higher quality, and were purged with N_2. For all aqueous studies except those involving $CuSO_4$, the aqueous buffer consisted of 10mM $Na_3PO_4 \cdot 12H_2O$, 100mM NaCl, pH=6.4. For quenching studies with $CuSO_4$ in aqueous solution, either 100mM unbuffered NaCl or 10mM Bis-Tris, 100mM NaCl, pH=6.4 were used (as noted). Vesicles were prepared and sized as reported previously[2], however, rather than always containing the HPTS dye, in certain cases, the vesicles were made with the same buffer both internal and external to the vesicle. Alternatively, for certain experiments, the compound was pre-incorporated into the vesicle bilayer by adding a solution of the compound of interest to the lipid mix before continuing the preparation as usual. Regardless of the identity of the vesicles, the volume of vesicle stock solution added to the cell was kept constant at 100uL for each experiment.

[1] See experimental section and SI part 1 of current report (J. M.Moszynski and T. M. Fyles, 2010.)
[2] H. Luong and T. M. Fyles, Org. Biomol. Chem., 2008, **7**, 733-738.

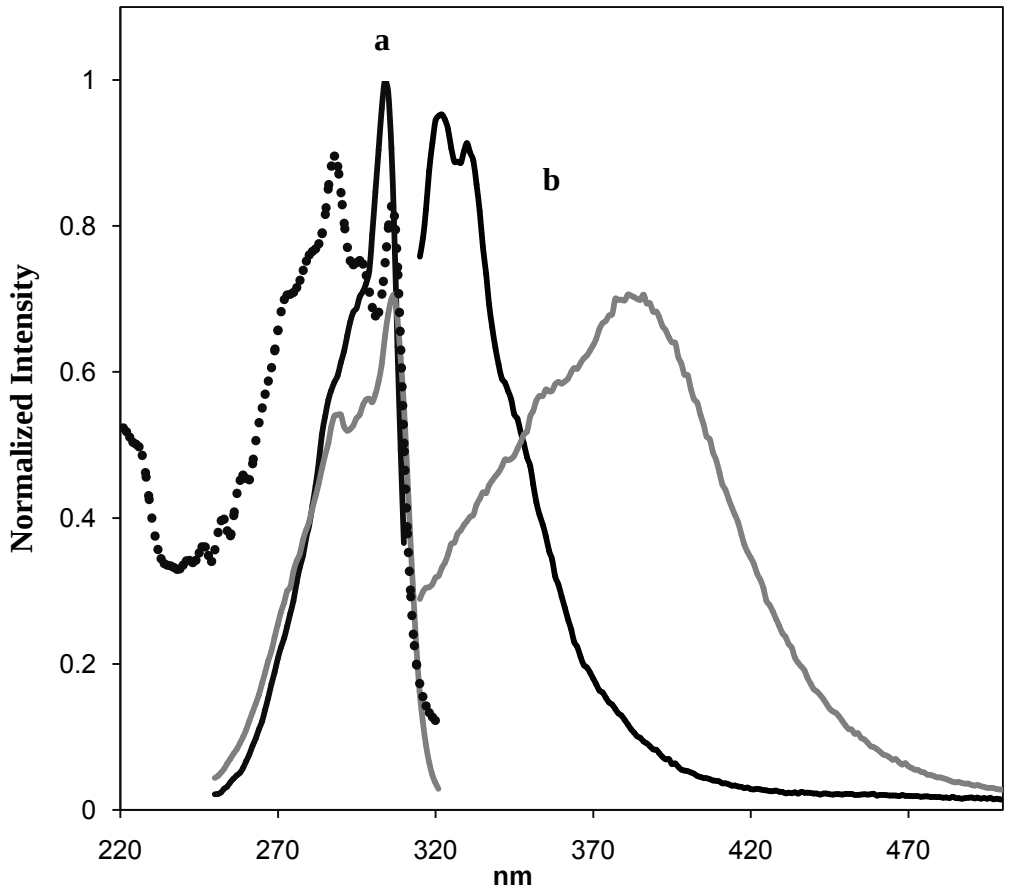

Fig. S1: Normalized UV (dotted line), excitation (**a**) and emission (**b**) scans of 20μM HO_2C-**Dip-Hex-Hex-G(12)-**OH in THF (black) and aqueous phosphate buffer (grey). For fluorescence, scans shown are for 1 minute after mixing, in aqueous solution, fluorescence intensity decreases over time. Other **Dip** isomers exhibit identical behavior in both solvents.

PYRENE AGGREGATION ASSAY

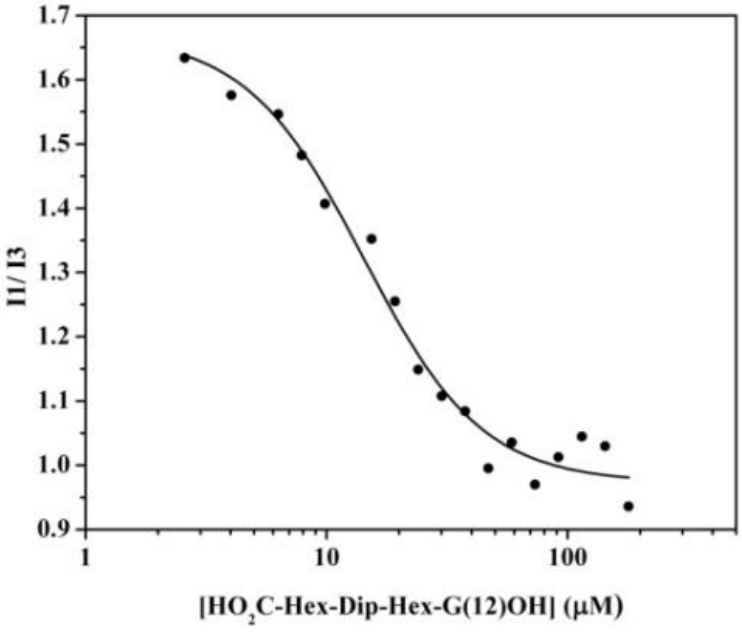

Fig. S2: Ratio of pyrene vibronic band intensities (I_1/I_3) as a function of the concentration of HO_2C-***Hex-Dip-Hex-G(12)***-OH (10mM phosphate buffer, pH 6.4, 100mM NaCl, 2 μM pyrene).

QUENCHING WITH $CuSO_4$ IN AQUEOUS SOLUTION FOR DIP ISOMERS

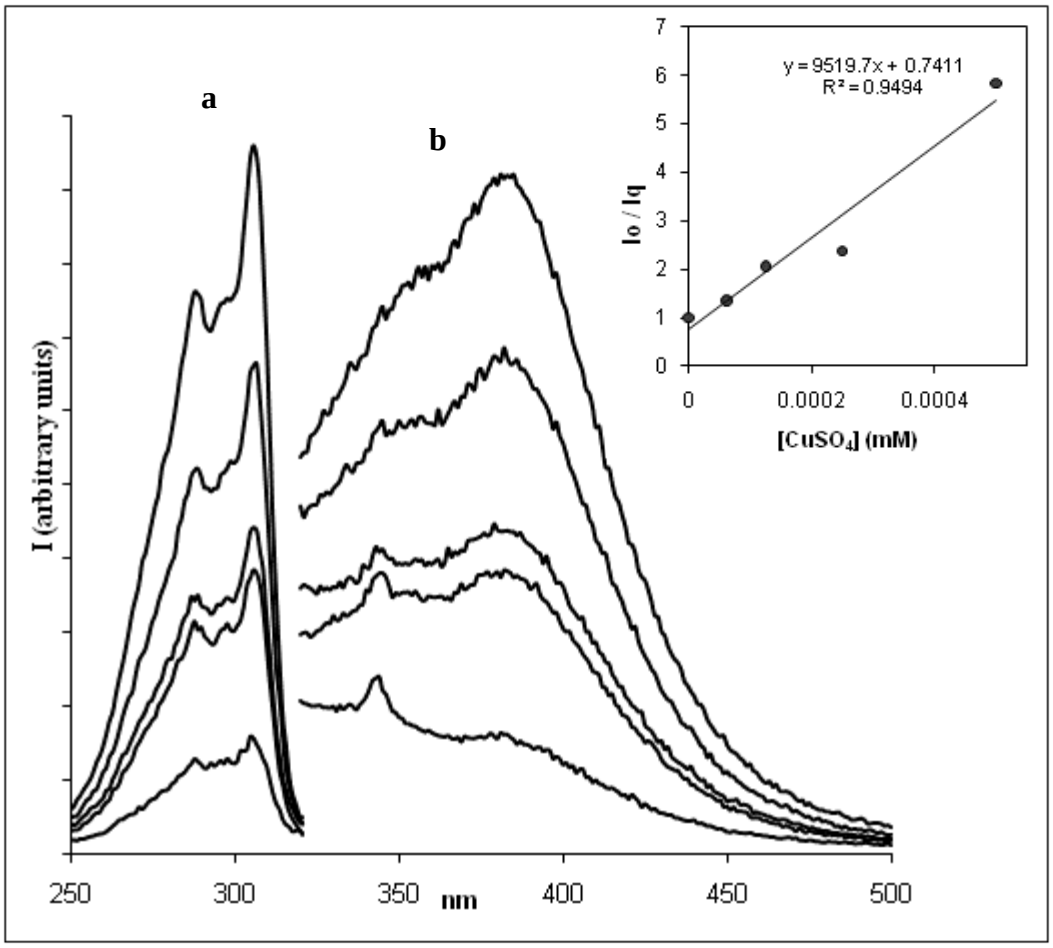

Fig. S3: Fluorescence excitation (**a**) and emission (**b**) spectra of 16 μM HO_2C-**Dip-Hex-Hex-G(12)-**OH in 100mM unbuffered aqueous NaCl with the addition of increasing concentrations of $CuSO_4$ (stock solution made in unbuffered aqueous NaCl). From top to bottom, [$CuSO_4$] = 0, 0.0625, 0.125, 0.25 and 0.5 μM. Solutions of compound and quencher were made, and scans taken immediately. Although fluorescence intensity in aqueous solution has been observed to decrease over time with these compounds, the intensity of the quenched solution was always much decreased over that of the unquenched solution. **Inset:** Stern-Volmer analysis of quenching data.

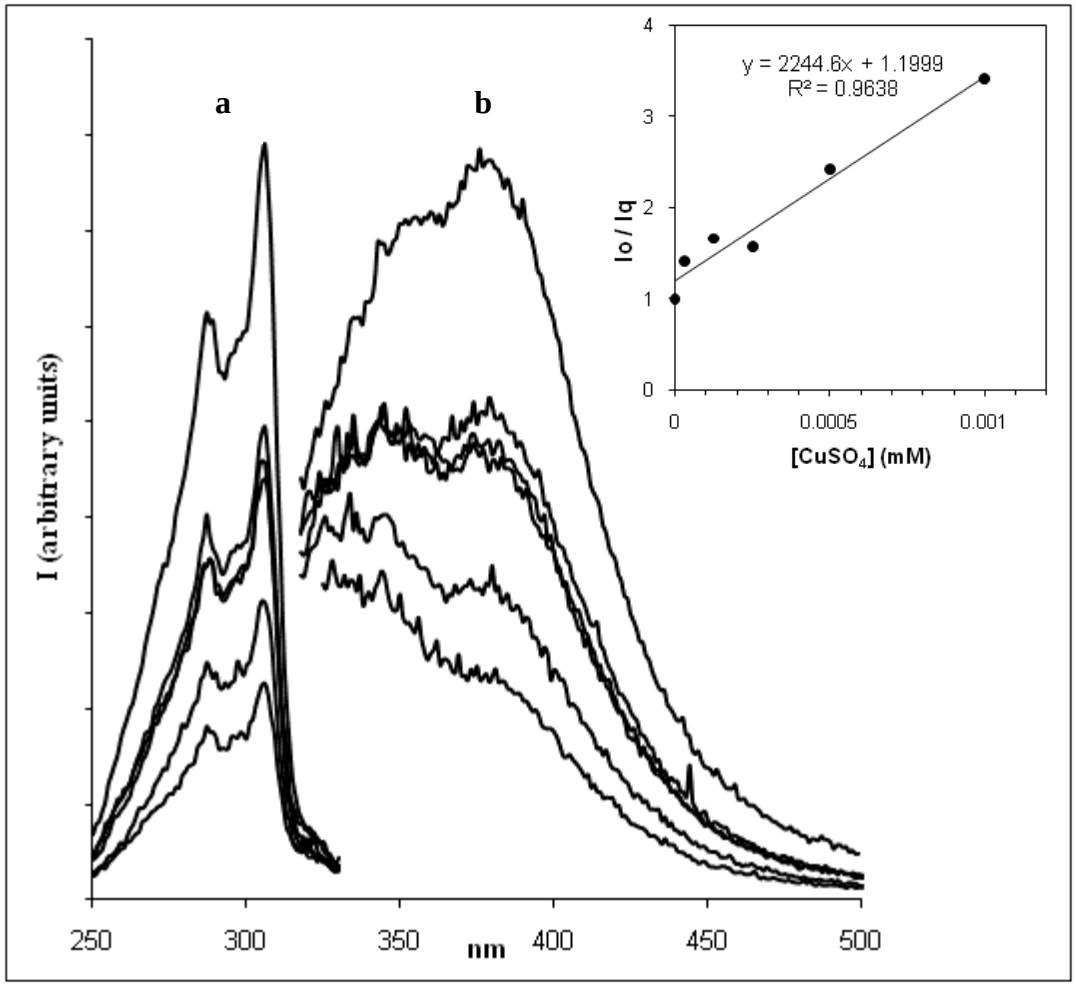

Fig. S4: Fluorescence excitation (**a**) and emission (**b**) spectra of 17 μM HO_2C-**Hex-Hex-Dip-G(12)**-OH in aqueous NaCl with the addition of increasing concentrations of $CuSO_4$ (stock solution made in aqueous NaCl). From top to bottom, [$CuSO_4$] = 0, 0.0625, 0.125, 0.5 and 1.0 μM. Experimental conditions are same as those for Fig. S3. **Inset:** Stern-Volmer analysis of quenching data.

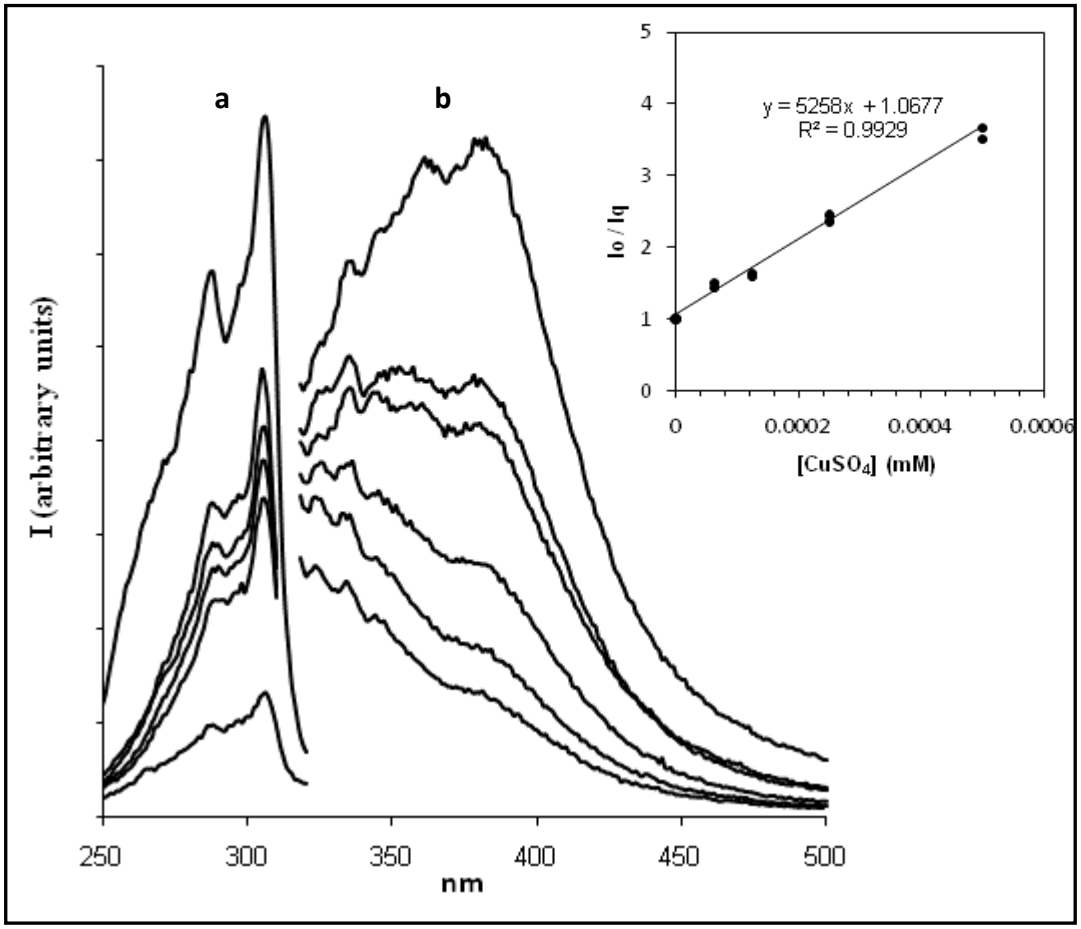

Fig S5: Fluorescence excitation (**a**) and emission (**b**) spectra of 25 μM CO_2H-**Dec-Dip-Hex-G(12)**-OH in aqueous NaCl with the addition of increasing concentrations of $CuSO_4$ (stock solution made in aqueous NaCl). From top to bottom, [$CuSO_4$] = 0, 0.0625, 0.125, 0.5 and 1.0 μM. Experimental conditions are same as those for Fig. S3. **Inset:** Stern-Volmer analysis of quenching data.

QUENCHING WITH $CuSO_4$ IN CH_3OH FOR DIP ISOMERS

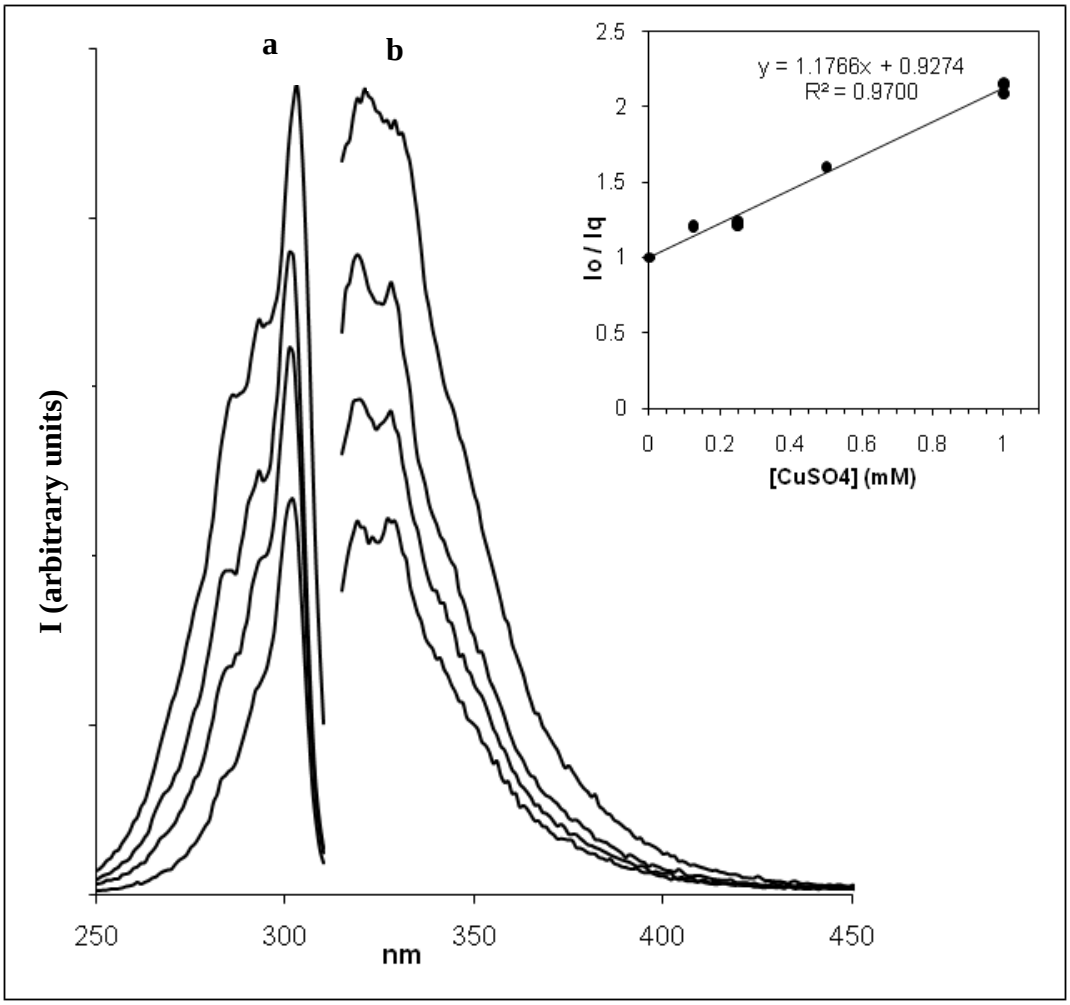

Fig. S6. Fluorescence excitation (**a**) and emission (**b**) spectra of 16 μM HO_2C-**Dip-Hex-Hex-G(12)**-OH in CH_3OH with the addition of increasing concentrations of $CuSO_4$ (stock solution made in CH_3OH). From top to bottom, [$CuSO_4$] = 0, 0.25, 0.5 and 1mM. Solutions of compound and quencher were made, and scans taken immediately. Fluorescence intensity remained stable over time. **Inset**: Stern-Volmer analysis of quenching data.

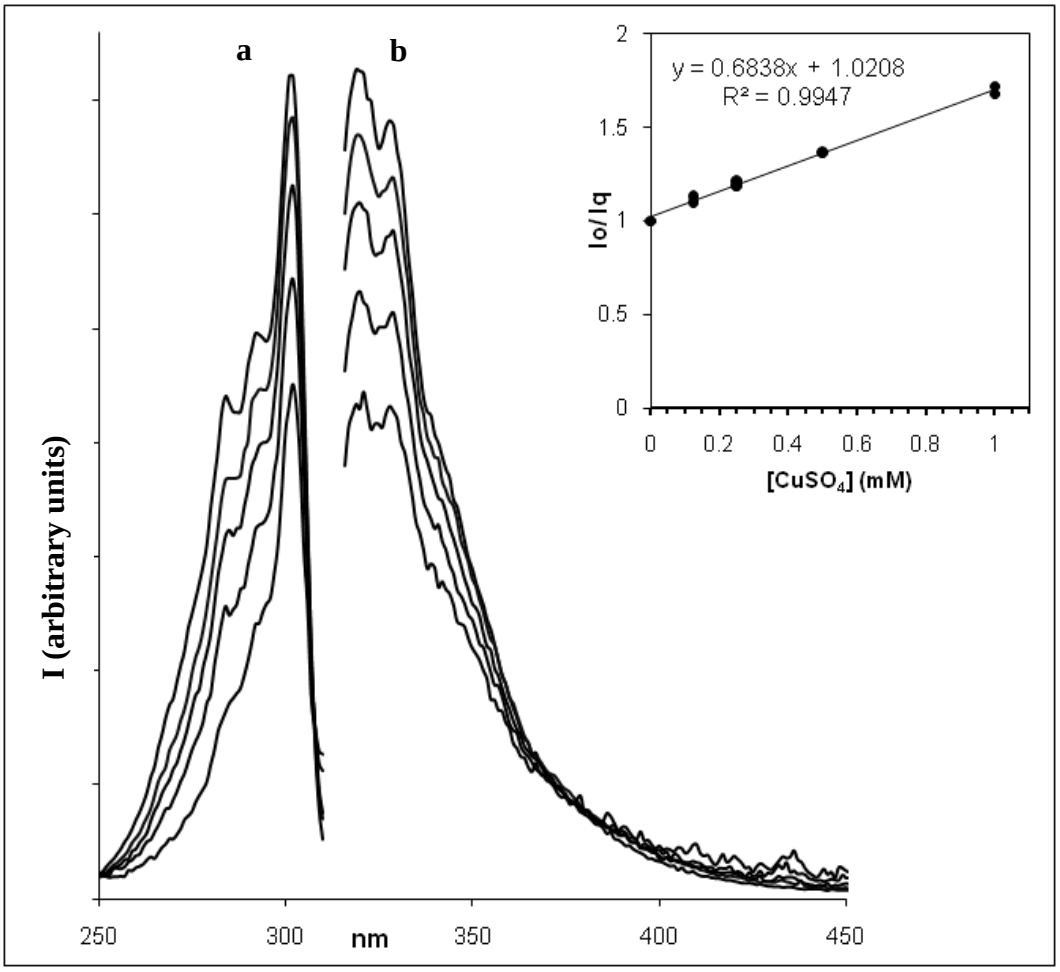

Fig. S7. Fluorescence excitation (**a**) and emission (**b**) spectra of 25μM HO_2C-**Hex-Hex-Dip-G(12)**-OH in CH_3OH with the addition of increasing concentrations of $CuSO_4$. From top to bottom, [$CuSO_4$] = 0, 0.125, 0.25, 0.5 and 1mM. Experimental conditions as Fig. S6. **Inset**: Stern-Volmer analysis of quenching data.

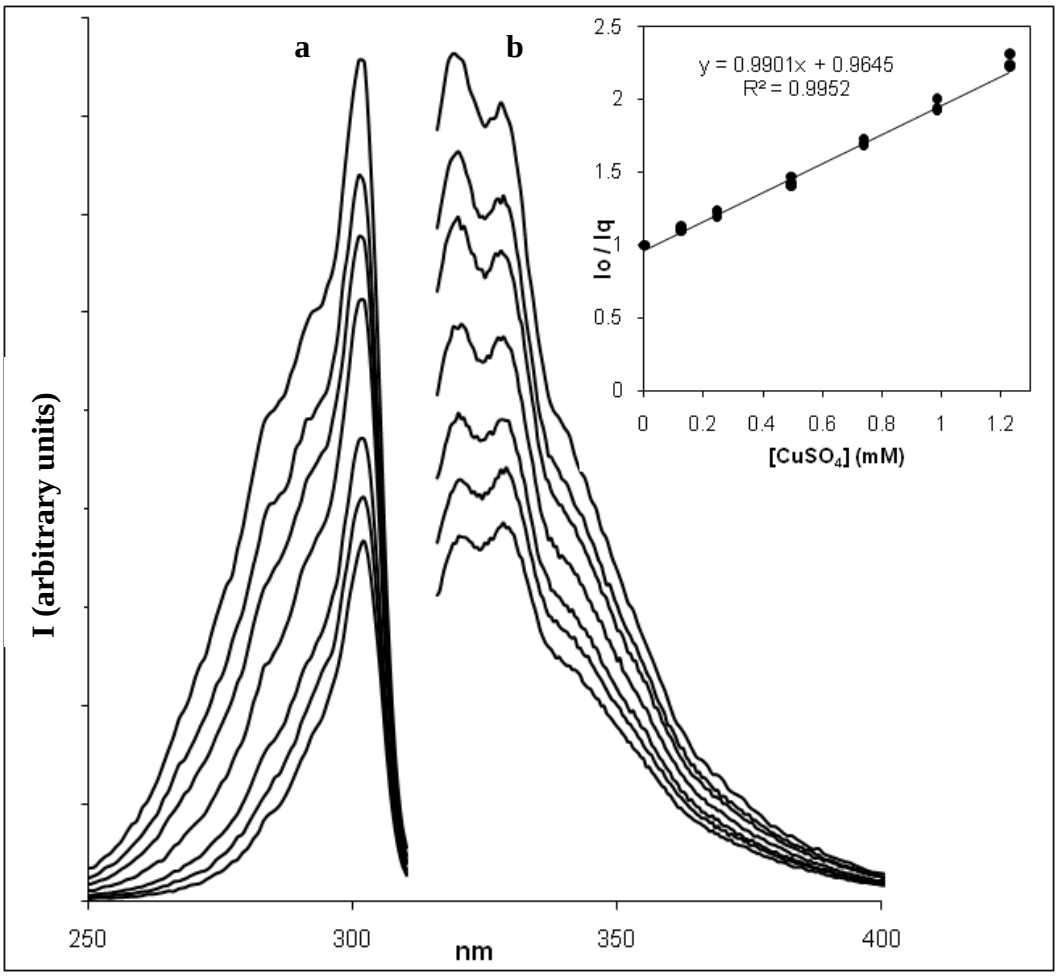

Fig. S8. Fluorescence excitation (**a**) and emission (**b**) spectra of 30 μM HO_2C-**Dec-Dip-Hex-G(12)**-OH in CH_3OH with the addition of increasing concentrations of $CuSO_4$. From top to bottom, [$CuSO_4$] = 0, 0.125, 0.25, 0.49, 0.74, 0.98 and 1.23mM. Experimental conditions as Fig. S6. **Inset:** Stern-Volmer analysis of quenching data.

	STERN-VOLMER CONSTANT(K_{sv}) (M^{-1})	
	Aqueous Solution	Methanol Solution
HO_2C-**Dip-Hex-Hex-G(12)**-OH	9.52×10^6	1.17×10^3
HO_2C-**Hex-Hex-Dip-G(12)**-OH	2.24×10^6	0.684×10^3
HO_2C-**Dec-Dip-Hex-G(12)**-OH	5.26×10^6	0.990×10^3

Table S1: All experimentally-derived Stern-Volmer constants for the compounds studied.

PARTITIONING INTO BILAYER: TIMEBASED EMISSION RATIOS

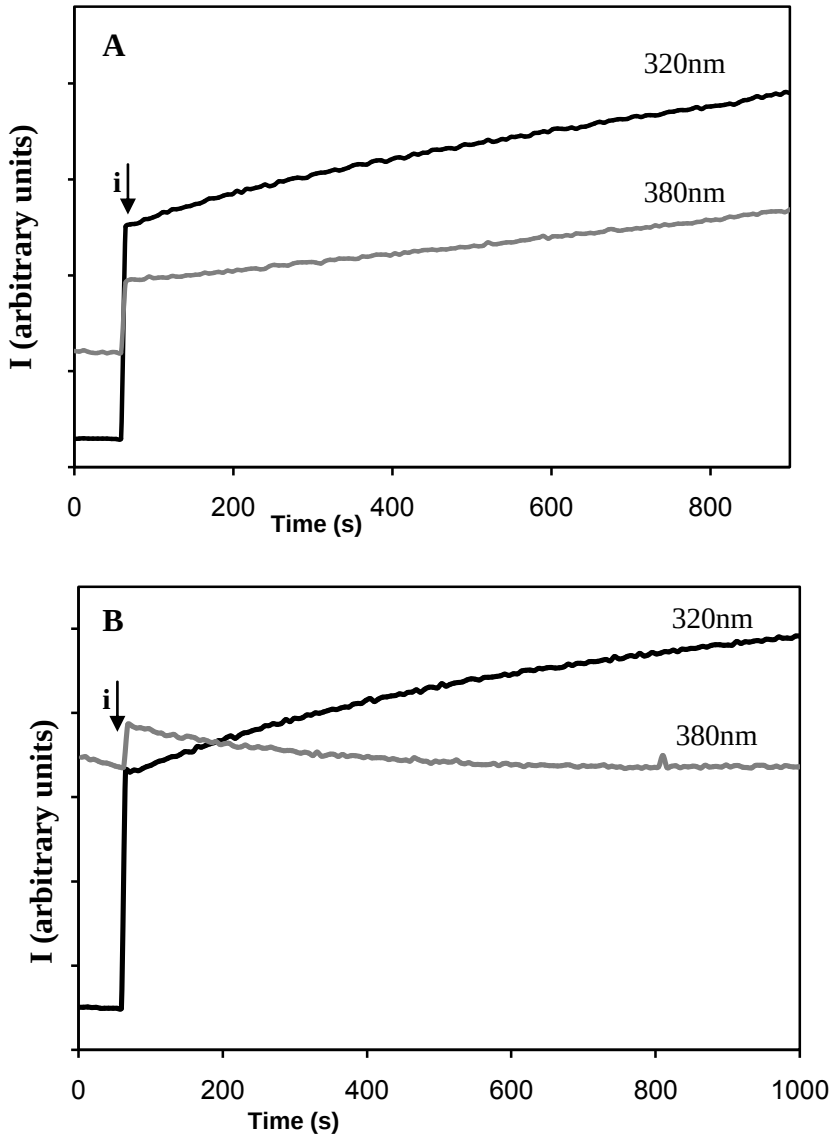

Fig S9: Time-based fluorescence emission ratio at 320 nm (black lines) versus 380 nm (grey lines), (λ_{Ex} = 305 nm) for 20μM HO_2C-**Hex-Hex-Dip-G(12)**-OH (**A**) and 22μM HO_2C-**Hex-Dip-Hex-G(12)**-OH (**B**) indicating the evolution of the 320 nm signal upon the addition of vesicles. The compounds were initially in aqueous phosphate buffer, to which 100μL of lipid vesicles were injected into the solution (at time i). Compare with Fig. 4C, D in the report.

CONCURRENT HPTS ASSAY & EMISSION RATIOS

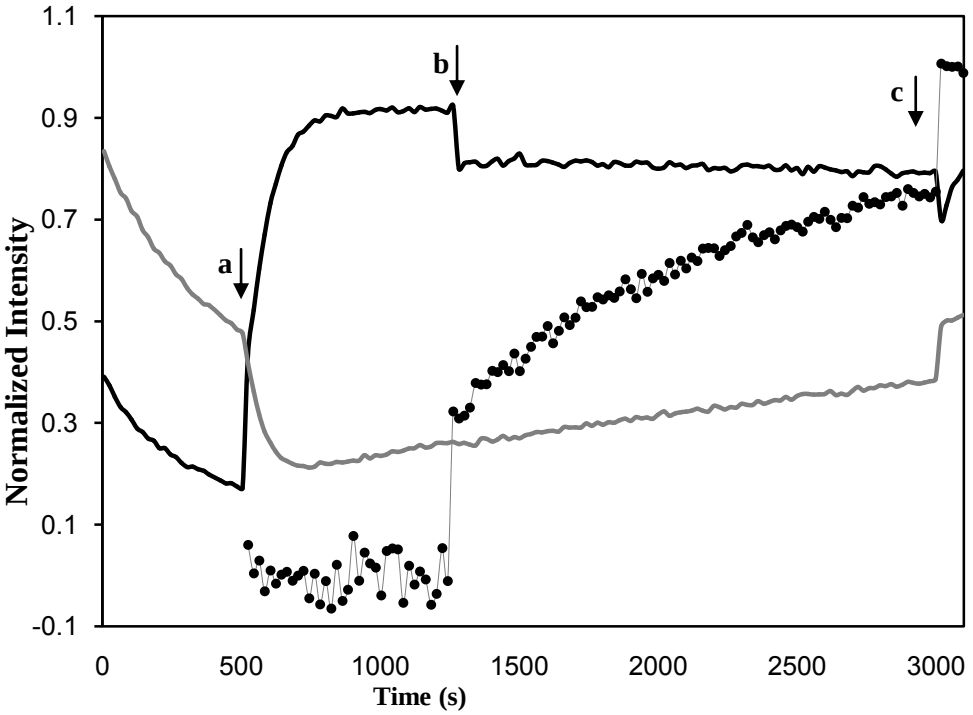

Fig S10: Simultaneous monitoring of HPTS transport activity [3](black circles) and emission ratio between 320nm (black line) and 380 nm (grey line) (λ_{ex}= 305nm) for 16μM HO_2C-**Dip-Hex-Hex-G(12)**-OH. The compound is initially in aqueous phosphate buffer. At t=500s (**a**), 100uL of lipid vesicles containing the HPTS dye entrapped within were injected. After an equilibration period, 50uL of 0.5M NaOH was injected (**b**) to initiate the transport assay. After a suitable data collection period, the experiment was concluded by the addition of the surfactant Triton-X 100 (**c**), which lyses the vesicles. The data for the HPTS assay was analyzed by methods described previously.[3] Compare with Fig S11.

[3] H. Luong and T. M. Fyles, Org. Biomol. Chem., 2008, **7**, 733-738.

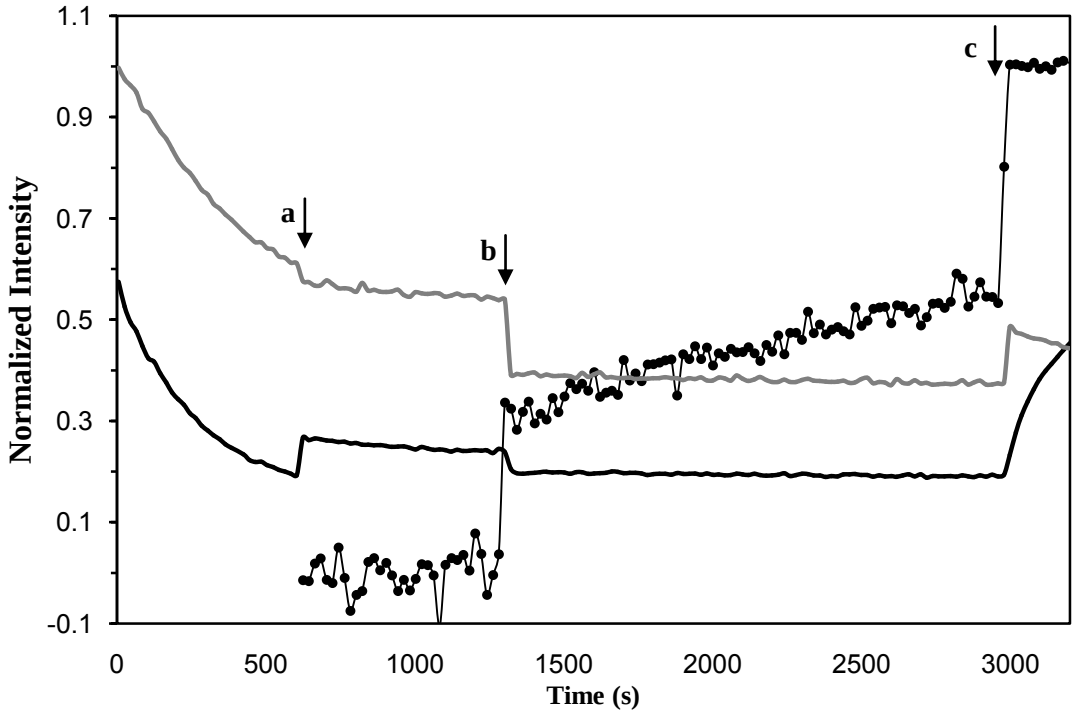

Fig. S11: Simultaneous monitoring of HPTS transport activity (black circles) and emission ratio between 320nm (black line) and 380 nm (grey line) (λ_{ex}= 305nm) for 15uM HO_2C-**Dec-Dip-Hex-G(12)**-OH. The compound is initially in aqueous phosphate buffer. At t=800s (**a**), 100uL of lipid vesicles containing the HPTS dye entrapped within were injected. After an equilibration period, 50uL of 0.5M NaOH was injected (**b**) to initiate the transport assay. After a suitable data collection period, the experiment was concluded by the addition of the surfactant Triton-X 100 (**c**), which lyses the vesicles. The data for the HPTS assay was analyzed by methods described previously.[3] Activity is comparable to that of a THF blank control.

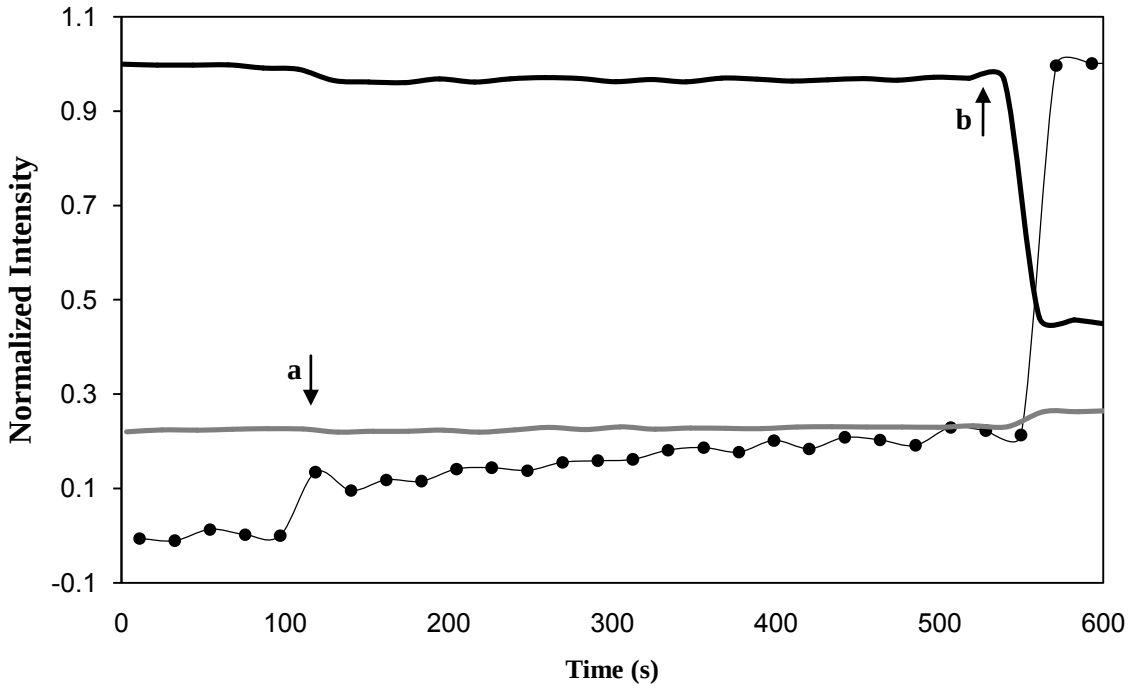

Fig. S12: Simultaneous monitoring of HPTS transport activity (black circles) and emission ratio between 320nm (black line) and 380 nm (grey line) (λ_{ex}= 305nm) for 0.1% HO_2C-**Dec-Dip-Hex-G(12)-**OH pre-incorporated into lipid vesicles containing the HPTS dye. The vesicles were prepared in the manner previously reported, with the addition of a solution of the compound in THF to the lipid mix, which was then sonicated with an aqueous solution of HPTS in the usual way. The compound-containing vesicles are initially in aqueous phosphate buffer. After an equilibration period, 50uL of 0.5M NaOH was injected (**a**) to initiate the transport assay. After a suitable data collection period, the experiment was concluded by the addition of the surfactant Triton-X 100 (**b**), which lyses the vesicles. The data for the HPTS assay was analyzed by methods described previously[3]. Activity is comparable to that of a THF blank control, and to that of Fig. S11.

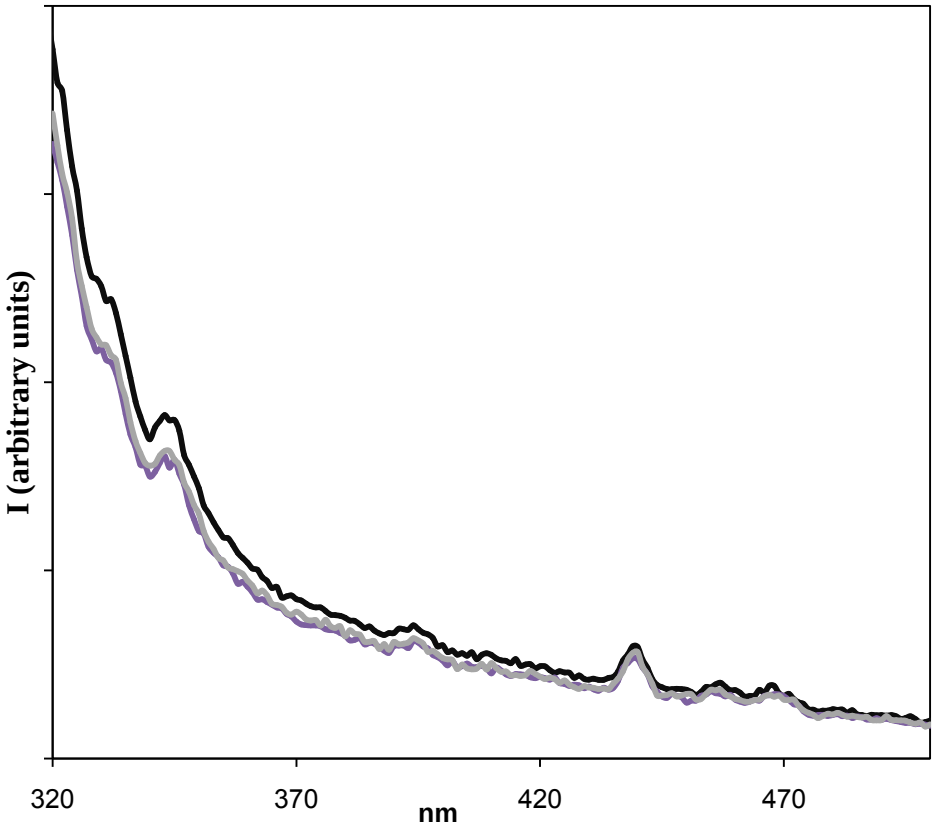

Fig. S13: Fluorescence emission spectra for 0.1% HO_2C-**Dec-Dip-Hex-G(12)**-OH pre-incorporated into lipid vesicles (black line)(λex=305) with the addition of 0.076mM (dark grey) and 1mM (light grey) $CuSO_4$ (solution in aq. NaCl). Vesicles were prepared in the usual manner, with a solution of compound in THF added to the lipid mix. However, vesicles contain only 100mM aq. NaCl within and without and the entire experiment was done in this solution. Scans shown were taken immediately after mixing; however, the emission was not seen to vary significantly over time.

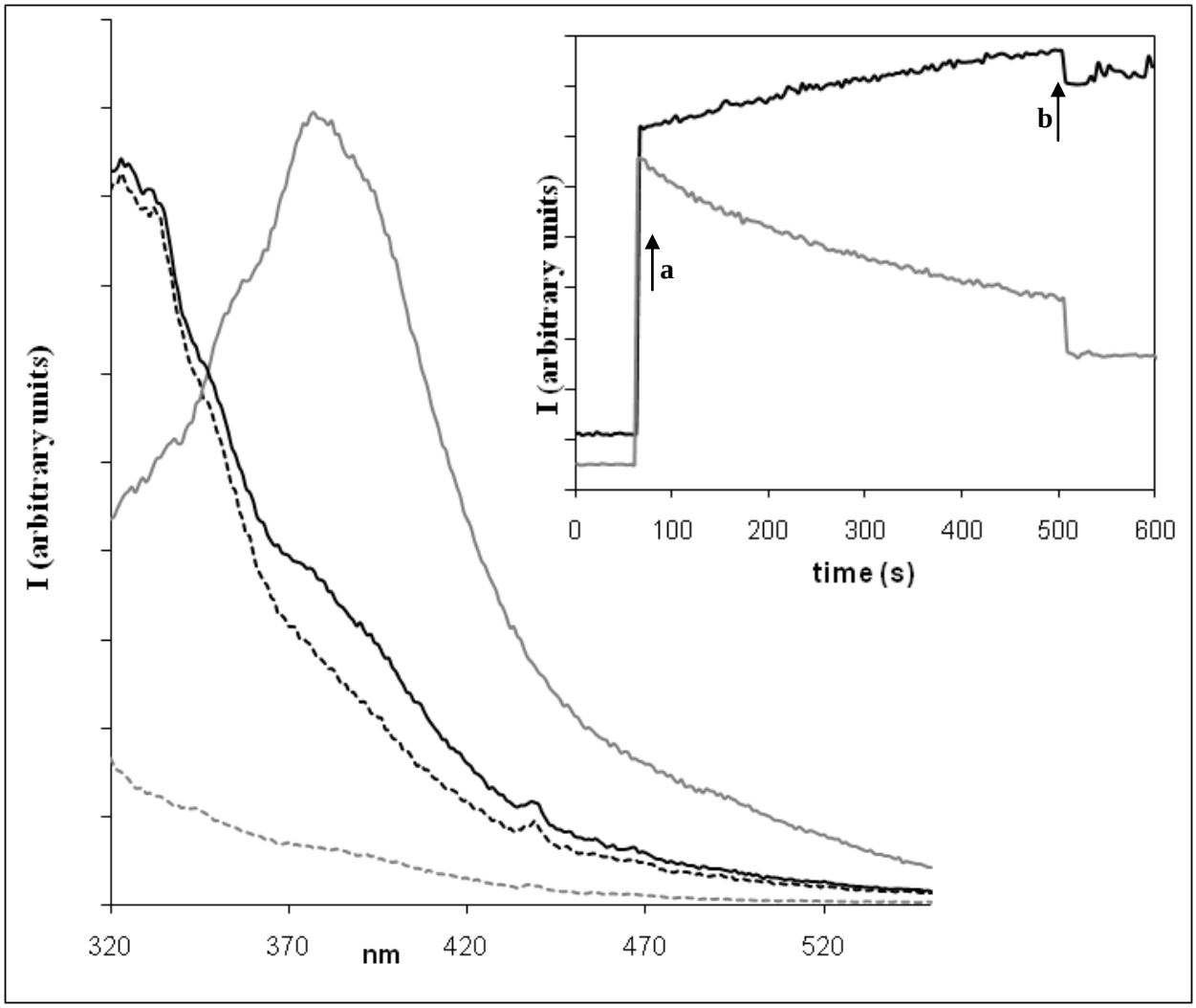

Fig. S14: Fluorescence emission spectra of 22μM HO_2C-**Dip-Hex-Hex-G(12)**-OH in aqueous Bis-Tris buffer (10mM Bis-Tris, 100mM NaCl, pH=6.4) (λex= 305nm) in the presence (black) and absence (grey) of lipid vesicles (vesicles contain Bis-Tris buffer within and without) with the addition of 100μM $CuSO_4$ (dashed lines, solution in aqueous Bis-Tris). In the absence of vesicles, the fluorescence at 380nm is quenched by ~90%, while in the presence of vesicles, the extent of quenching is reduced to ~20%. Scans were taken after a 5 minute period for aqueous only solutions, after 10 minutes for vesicle-containing solutions. **Inset**: timebased emission ratio (λex= 305nm) between 320nm (black) and 380nm (grey). Initially, the vesicles are in aqueous Bis-Tris solution; **a**: addition of compound, **b**: addition of 100μM $CuSO_4$. While the fluorescence intensity is seen to depend on the buffer used (compare **Fig. 5A,C** in the report), the general trends (Emission at 320nm > 380nm, decreased quenching in the presence of vesicles) remain the same.

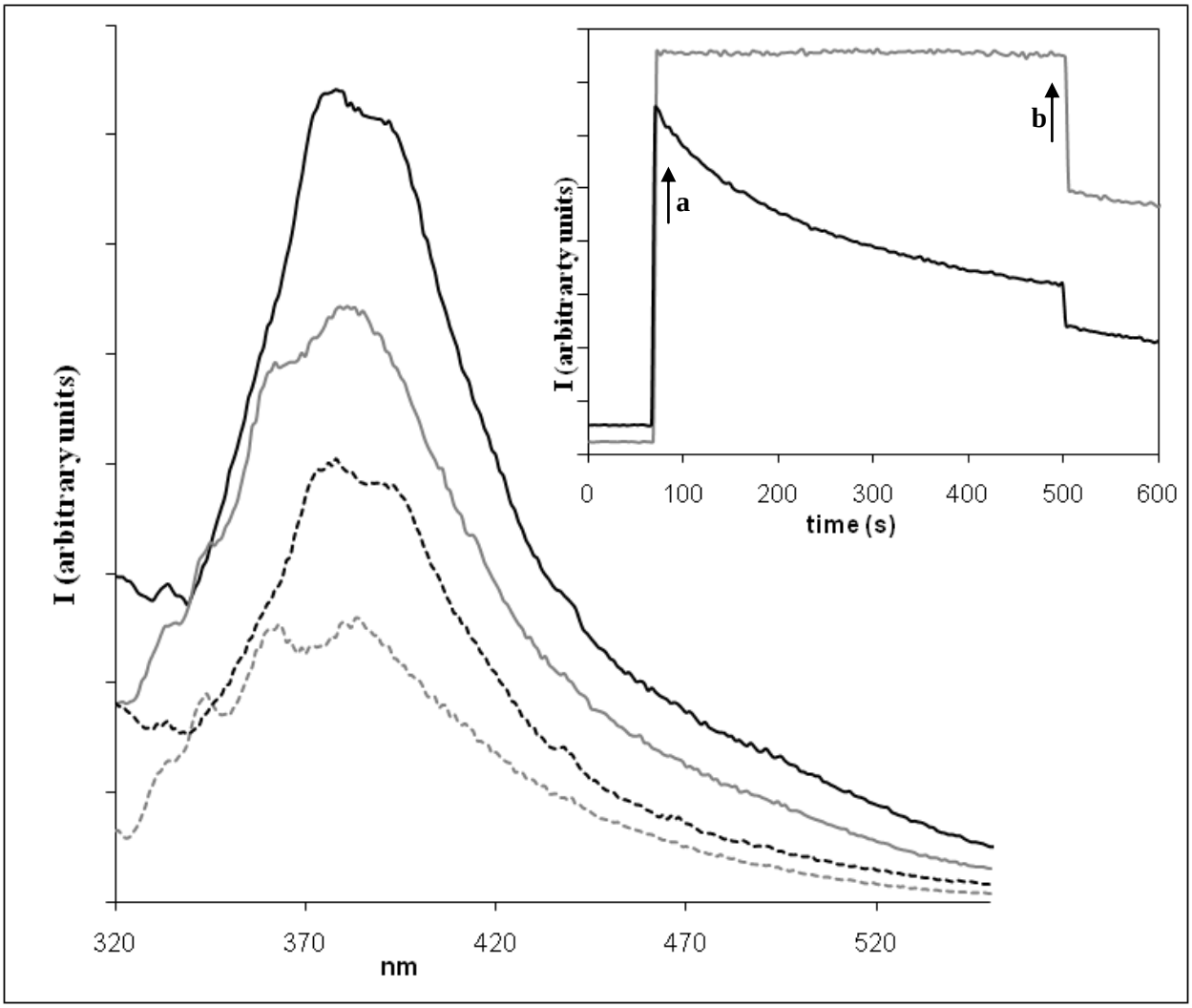

Fig. S15: Fluorescence emission spectra of 25μM HO_2C-**Dec-Dip-Hex-G(12)**-OH in aqueous Bis-Tris buffer (10mM Bis-Tris, 100mM NaCl, pH=6.4) (λex= 305nm) in the presence (black) and absence (grey) of lipid vesicles (vesicles contain Bis-Tris buffer within and without) with the addition of 100μM $CuSO_4$ (dashed lines, solution in aqueous Bis-Tris). In the absence of vesicles, the fluorescence at 380nm is quenched by ~50%, while in the presence of vesicles, the extent of quenching remains very similar (~45%). Scans were taken after a 5 minute period for aqueous only solutions, after 10 minutes for vesicle-containing solutions. **Inset**: time-based emission ratio (λex= 305nm) between 320nm (black) and 380nm (grey). Initially, the vesicles are in aqueous Bis-Tris solution; **a**: addition of compound, **b**: addition of 100μM $CuSO_4$. While the fluorescence intensity is seen to depend on the buffer used (compare **Fig. 5B, D** in the report), the general trends (Emission at 380nm > 320nm, unchanged quenching in the presence of vesicles) remain the same.