Supporting Information for:

Dichlorination of (HDDA-Generated) Benzynes and a Protocol for Interrogating the Kinetic Order of Bimolecular Aryne Trapping Reactions

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Contents of Supporting Information

I. General Experimental Protocols

NMR spectra were recorded on Bruker Avance 500 (500 MHz) or Varian Inova 500 (500 MHz) spectrometers in the indicated solvent. The following format is used to report the proton NMR data: chemical shift in ppm [multiplicity, coupling constant(s) in Hz, integral, and assignment]. Coupling constant analysis was informed by methods we have previously reported[1,2]. Chemical shifts for proton spectra are referenced to TMS (δ 0.00 ppm) for spectra recorded in $CDCl_3$. Non-first order multiplets are identified as "nfom". Chemical shifts for carbon spectra are referenced to $CHCl_3$ (δ 77.23 ppm) for spectra recorded in $CDCl_3$ and to CHD_2CN (δ 1.32 ppm) for CD_3CN. TMS is present in some of the ^{13}C NMR samples (δ ca. 0.0 ppm).

Infrared spectral data were collected on an FT-IR spectrometer (Midac Corporation Prospect 4000). Spectra were collected as thin films in attenuated total reflectance (ATR) mode on a germanium window.

Electrospray ionization (ESI) mass spectrometry data were collected on a Bruker BioTOF II (ESI-TOF) instrument. Samples for high resolution mass spectral (HRMS) analysis were doped with PEG, PPG, or Agilent tune mix as an internal calibrant. Samples were introduced as solutions in acetonitrile or methanol.

MPLC (medium pressure liquid chromatography) was performed at 25-200 psi. Columns were hand-packed with Silasorb silica gel (18-32 μm, 60 Å pore size). A Waters HPLC pump and R401 differential refractive index detector were used. Flash chromatography was performed on E. Merck silica gel (230-400 mesh). Thin layer chromatography was carried out on glass or plastic backed plates of silica gel. Spots were visualized by UV irradiation and/or dipping in a solution of anisaldehyde, phosphomolybdic acid, potassium permanganate, or ceric ammonium molybdate followed by heat treatment.

Reactions requiring anhydrous conditions were performed in flame- or oven-dried glassware under an inert atmosphere (nitrogen or argon). Anhydrous diethyl ether, toluene, THF, and methylene chloride were passed through a column of activated alumina and tapped immediately prior to use. $CHCl_3$ used as a medium for the HDDA reaction was ethanol-free. Reported (external) reaction temperatures are the temperature of the heating bath. HDDA initiated reactions, including those that were carried out at temperatures above the boiling point of the solvent, were typically carried out in a screw-capped vial or culture tube fitted with an inert, Teflon®-lined cap.

Procedures for preparation and spectral data are provided for i) all new compounds in the manuscript and ii) all new intermediates used in the synthetic route by which the former were made. The latter are specified by **S#**, since they only appear here in the Supporting Information. A reference is provided for each non-commercially available compound that is used in the syntheses and these have not been given a structure number.

General Procedures A-C.

General procedures A. and B., used in the preparation of the HDDA substrates, are identical to those we have recently reported in the Supporting Information of a manuscript describing otherwise unrelated benzyne trapping reactions.[3]

A. Alkyne Cross-Coupling using Cadiot–Chodkiewicz in Et_2O/*n*-$BuNH_2$/water.

"To a solution of CuCl (0.05 equiv) in 30:70 (v:v) *n*-$BuNH_2$:H_2O (0.01 M) in a capped reaction vessel was added an excess of NH_2OH•HCl (typically a few crystals on a reaction scale ≤1 mmol). The color of the solution turned from deep blue to colorless within seconds, indicating full consumption of Cu(II). The resulting solution was then cooled at 0 °C. A solution of the terminal alkyne (1.0 equiv) and the 1-bromoalkyne (1.2–1.5 equiv) in Et_2O (0.25 M) was added dropwise. The reaction mixture was stirred for 1 h, during which time a few crystals of NH_2OH•HCl were periodically added whenever the solution became blue. The reaction mixture was diluted with saturated aqueous NH_4Cl and extracted with EtOAc or Et_2O. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The crude material was typically purified by flash chromatography."[3]

B. Alkyne Cross-Coupling using Cadiot–Chodkiewicz in piperidine

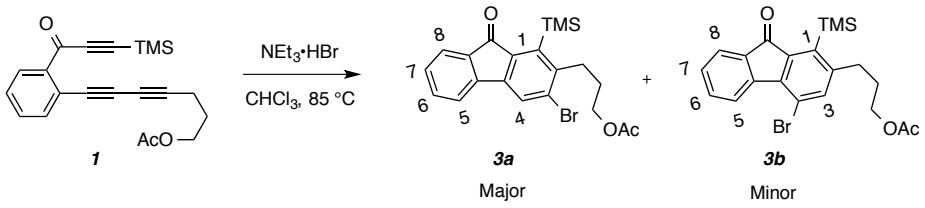
"A solution of a terminal alkyne (1.0 equiv) and a 1-bromoalkyne (1.2–1.5 equiv) in piperidine (0.3-0.8 M) was deoxygenated (three freeze-pump-thaw cycles). The solution was cooled to 0 °C and CuCl was added. After 1 h saturated aqueous NH_4Cl was added and the resulting mixture was extracted with EtOAc or Et_2O. The combined extracts were washed (brine), dried (Na_2SO_4), and concentrated. The crude material was then purified using flash chromatography."[3]

C. HDDA Reaction with *in situ* Dichlorination

Anhydrous lithium chloride and copper(II) chloride were combined in THF to arrive at a homogenous, red-orange stock solution of Li_2CuCl_4 (1.0 M). This was stored at room temperature in a tightly capped culture tube. Ten equivalents of this stock solution of Li_2CuCl_4 was added to the triyne substrate in a culture tube fitted with a teflon-lined cap. Additional THF was added to bring the final concentration of triyne to 0.03 M. The resulting solution was heated at the indicated temperature for the indicated time. Saturated aqueous NH_4Cl was added and the resulting mixture was extracted with EtOAc or Et_2O. The combined extracts were washed (brine), dried (Na_2SO_4), and concentrated. The crude material was purified using flash chromatography.

II. Preparation procedures and characterization data for all key compounds

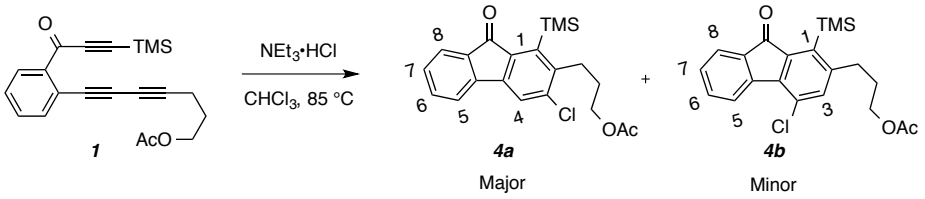
Synthesis of monobrominated fluorenones 3a and 3b (Scheme 1 of manuscript)



3-(3-Bromo-9-oxo-1-(trimethylsilyl)-9H-fluoren-2-yl)propyl acetate (3a) and 3-(4-Bromo-9-oxo-1-(trimethylsilyl)-9H-fluoren-2-yl)propyl acetate (3b)

A solution of known triyne acetate **1**[4] (27 mg, mmol, 1 equiv) and Et_3N•HBr (mg, mmol, 5 equiv) in $CHCl_3$ was heated at 85 °C for 18 h. The resulting solution was concentrated and subjected to flash chromatography (SiO_2, Hexanes:EtOAc = 5:1) to give a co-eluting mixture (13:1 ratio by ^{1}H NMR analysis, 25 mg, 75%) of the known bromides **3a** and **3b**.[4]

Synthesis of monochlorinated fluorenones 4a and 4b (Scheme 1 of manuscript)



3-(3-Chloro-9-oxo-1-(trimethylsilyl)-9H-fluoren-2-yl)propyl acetate (4a) and 3-(4-Chloro-9-oxo-1-(trimethylsilyl)-9H-fluoren-2-yl)propyl acetate (4b)

A solution of known triyne acetate **1**[4] (27 mg, 0.077 mmol, 1 equiv) and Et_3N•HCl (53 mg, 0.385 mmol, 5 equiv) in $CHCl_3$ was heated at 85 °C for 18 h. The resulting solution was concentrated and subjected to flash chromatography (SiO_2, Hexanes:EtOAc = 5:1) to give a co-eluting mixture (6:1 ratio by ^{1}H NMR analysis, 23 mg, 77%) of **4a** and **4b** from which the following spectral data were deduced.

Characteristic peaks for **4a:**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (ddd, *J* = 7.3, 1.0, 1.0 Hz, 1H, *H8*), 7.54 (s, 1H, *H4*), 7.47 (ddd, *J* = 7.4, 7.4, 1.3 Hz, 1H, *H6*), 7.44 (ddd, *J* = 7.3, 1.0, 1.0 Hz, 1H, *H5*), 7.29 (ddd, *J* = 7.3, 7.3, 1.3 Hz, 1H, *H7*), 4.16 (t, *J* = 6.4 Hz, AcOCH_2), 3.05 (br t, *J* = 8.3 Hz, 2H, ArCH_2), 2.08 (s, 3H, CH_3C=O), 1.88-1.82 (m, 2H, $CH_2CH_2CH_2$), and 0.47 [s, 9H, Si(CH_3)$_3$].

^{13}C NMR (125 MHz, $CDCl_3$): δ 194.3, 171.3, 145.6, 144.7, 144.2, 142.9, 140.9, 138.8, 134.8, 134.1, 129.5, 124.3, 122.8, 119.9, 64.2, 30.4, 29.8, 21.2, and 3.0 ppm.

Characteristic peaks for **4b:**

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (ddd, *J* = 7.6, 0.9, 0.9 Hz, 1H, *H5*), 7.62 (ddd, *J* = 7.3, 1.0, 1.0 Hz, 1H, *H8*), 7.50 (ddd, *J* = 7.6, 7.6, 1.3 Hz, 1H, *H6*), 7.31 (ddd, *J* = 7.3, 7.3, 1.0 Hz, 1H, *H7*), 7.20 (s, 1H, *H3*), 4.12 (t, *J* = 6.5 Hz, AcOCH_2), 2.84 (br t, *J* = 8.0 Hz, 2H, ArCH_2), 1.90-1.83 (m, 2H, $CH_2CH_2CH_2$), and 0.43 [s, 9H, Si(CH_3)$_3$].

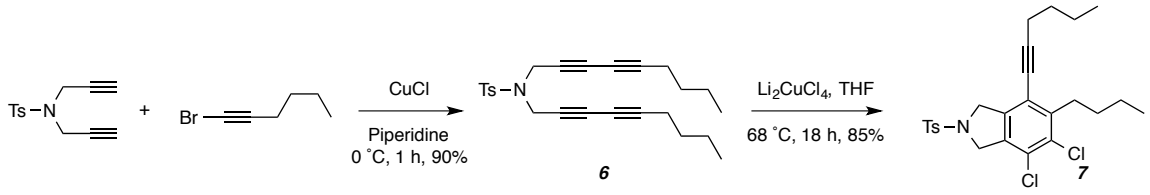
^{13}C NMR (125 MHz, $CDCl_3$, not all resonances were discernable for the minor isomer): δ 136.3, 135.0, 129.2, 124.2, 123.8, 63.8, 33.0, 32.2, and 2.7 ppm.

IR (neat): 2951, 2896, 1740, 1714, 1606, 1582, 1469, 1386, 1365, 1247, 1233, and 851cm^{-1}.

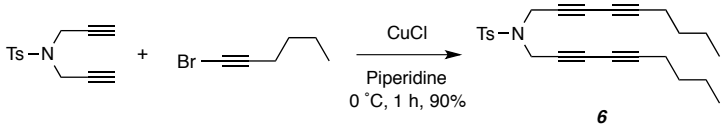
HRMS (ESI-TOF): Calcd for $C_{21}H_{23}ClNaO_3Si^+$ $[M+Na]^+$ requires 409.0997; found 409.1050.

mp: 57–64 °C.

Synthesis of isoindoline 7 (Figure 3 of manuscript)



4-Methyl-*N*,*N*-di(nona-2,4-diyn-1-yl)benzenesulfonamide (6)



Tetrayne **6** was prepared following General Procedure B from 4-methyl-*N,N*-di(prop-2-yn-1-yl)benzenesulfonamide[5] (500 mg, 2.0 mmol), 1-bromohex-1-yne[6] (ca. 3 g, 40 wt% in pentane, 1.2 g, 7.5 mmol), CuCl (60 mg, 0.6 mmol), and piperidine (5 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the tetrayne **6** (733 mg, 1.8 mmol, 90%) as a clear yellow oil.

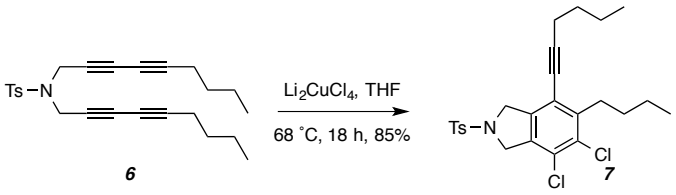
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.3 Hz, 2H, SO_2ArHo), 7.32 (d, *J* = 8.2 Hz, 2H, SO_2ArHm), 4.18 (s, 4H, NCH_2), 2.43 (s, 3H, $ArCH_3$), 2.24 (t, *J* = 6.9 Hz, 4H, $C{\equiv}CCH_2$), 1.53-1.45 (m, 4H, $C{\equiv}CCH_2CH_2$), 1.44-1.35 [m, 4H, CH_2CH_3], and 0.91 (t, *J* s= 7.2 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.3, 134.9, 129.9, 128.1, 81.1, 71.2, 68.1, 64.4, 37.5, 30.3, 22.1, 21.8, 19.1 and 13.7.

IR: 2958, 2932, 2872, 2257, 1465, 1426, 1354, 1164, 1093, and 894 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{25}H_{29}NNaO_2S^+$ $[M+Na]^+$ requires 430.1811; found 430.1813.

5-Butyl-6,7-dichloro-4-(hex-1-yn-1-yl)-2-tosylisoindoline (7)



Dichloride **7** was prepared following General Procedure C from tetrayne **6** (28 mg, 0.07 mmol), Li_2CuCl_4 (0.7 mL, 1M in THF, 0.7 mmol), and THF (1.4 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the dichloride **7** (28 mg, 0.059 mmol, 85%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 2H, SO_2ArH_o), 7.34 (d, *J* = 8.0 Hz, 2H, SO_2ArH_m), 4.66 (s, 2H, NCH_2), 4.61 (s, 2H, $NC'H_2$), 2.89 (nfom, 2H, $ArCH_2$), 2.47 (t, 2H, *J* = 6.9 Hz, $C{\equiv}CCH_2$), 2.42 (s, 3H, $ArCH_3$), 1.60 (m, 2H,$CH_2CH_2CH_3$), 1.49 (m, 4H, CH_2CH_3 and $C'H_2C'H_2C'H_3$), 1.39 (tq, *J* = 7.3, 7.3 Hz, 2H, CH_2CH_3), 0.97 (t, *J* = 7.3 Hz, 3H, CH_2CH_3), and 0.93 (t, *J* =7.3 Hz, 3H, $C'H_2C'H_3$).

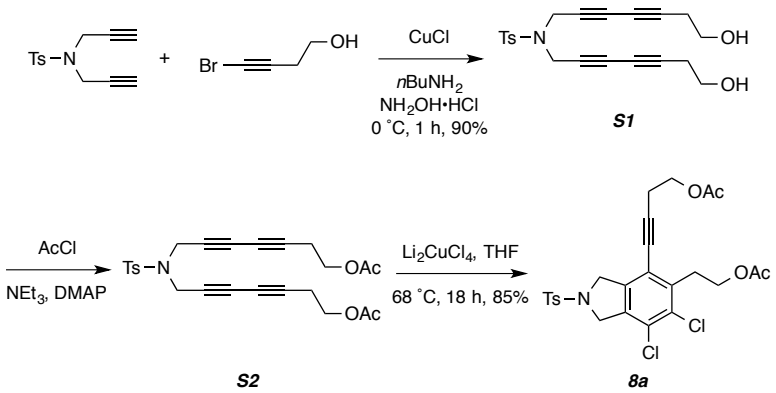
^{13}C NMR (125 MHz, $CDCl_3$): δ 144.3, 144.1, 138.3, 133.8, 133.7, 131.7, 130.2, 127.7, 126.8, 118.6, 100.3, 75.5, 55.1, 54.6, 33.1, 31.2, 30.9, 23.0, 22.2, 21.7, 19.5, 14.1, and 13.8.

IR (neat): 2955, 2933, 2861, 2226, 1346, 1153, 1098, 764, and 751 cm^{-1}.

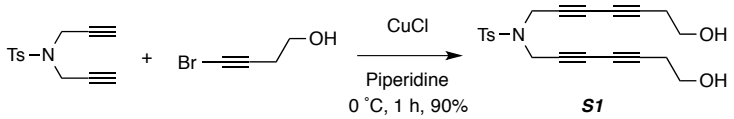
HRMS (ESI-TOF): Calcd for $C_{23}H_{25}Cl_2NNaO_2S^+$ $[M+Na^+]$ requires 500.1188; found 500.1204.

mp: 132–134 °C.

Synthesis of isoindoline 8a (Figure 3a of manuscript)



N,*N*-Bis(7-hydroxyhepta-2,4-diyn-1-yl)-4-methylbenzenesulfonamide (S1)



Diol **S1** was prepared following General Procedure A from 4-methyl-*N,N*-di(prop-2-yn-1-yl)benzenesulfonamide (412 mg, 1.67 mmol), 4-bromobut-3-yn-1-ol (740 mg, 5 mmol), CuCl (33 mg, 0.33 mmol), 30% aq. *n*$BuNH_2$ (4 mL), and CH_2Cl_2 (4 mL). Purification by flash chromatography (hexanes:EtOAc = 1:1) gave the diol **S1** (575 mg, 1.5 mmol, 90%) as a light yellow oil.

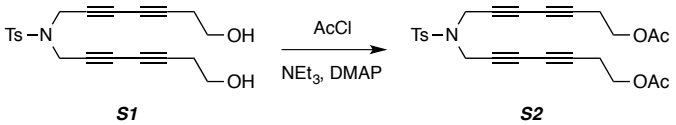
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.3 Hz, 2H, $SO_2Ar\mathit{H_o}$), 7.33 (d, *J* = 8.2 Hz, 2H, $SO_2Ar\mathit{H_m}$), 4.18 (s, 4H, $NC\mathit{H_2}$), 3.73 (br dt, *J* = 5.3, 5.3 Hz, 4H, $OC\mathit{H_2}$), 2.52 (t, *J* = 6.3 Hz, 4H, $C{\equiv}CC\mathit{H_2}$), 2.44 (s, 3H, $ArC\mathit{H_3}$), and 2.17 (t, *J* = 5.7 Hz, 2H, O*H*).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.5, 134.7, 129.9, 128.0, 77.7, 70.9, 68.8, 66.0, 60.7, 37.5, 23.7, and 21.8 ppm.

IR (neat): 3374, 2943, 2888, 2258, 1597, 1420, 1348, 1329, 1160, 1092, 1045, and 750 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{21}H_{21}NNaO_4S^+$ $[M+Na]^+$ requires 406.1083; found 406.1072.

N,*N*-Bis(7-acetoxyhepta-2,4-diyn-1-yl)-4-methylbenzenesulfonamide (S2)



To a solution of diol **S1** (80 mg, 0.21 mmol) in DCM (1 mL) cooled at 0 °C was sequentially added NEt_3 (80 mg, 0.8 mmol), DMAP (a few crystals), and AcCl (47 mg, 0.6 mmol). The reaction mixture was allowed to stir at this temperature for an additional 2 h. The resulting solution was partitioned between water and EtOAc. The organic layer was washed (satd. NH_4Cl and brine), dried (Na_2SO_4), and concentrated. The resulting crude oil was purified by flash chromatography (hexanes:EtOAc = 1:1) to give the diacetate **S2** (70 mg, 0.15 mmol, 71%) as a light yellow oil.

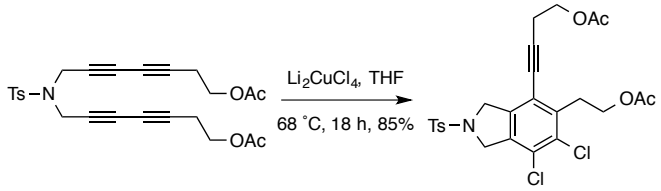
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.3 Hz, 2H, $SO_2Ar\mathit{H_o}$), 7.33 (d, *J* = 8.1 Hz, 2H, $SO_2Ar\mathit{H_m}$), 4.18 (s, 4H, $NC\mathit{H_2}$), 4.14 (t, *J* = 6.7 Hz, 4H, $OC\mathit{H_2}$), 2.60 (t, *J* = 6.7 Hz, 4H, $C{\equiv}CC\mathit{H_2}$), 2.44 (s, 3H, $ArC\mathit{H_3}$), and 2.08 (s, 6H, $C\mathit{H_3}C{=}O$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 144.4, 134.8, 129.9, 128.0, 76.3, 70.8, 69.0, 65.9, 61.7, 37.4, 21.8, 21.1, and 19.9 ppm.

IR (neat): 2966, 2918, 2261, 1739, 1598, 1494, 1452, 1353, 1232, 1163, 1093, 1043, and 903 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{25}H_{25}NNaO_6S^+$ $[M+Na]^+$ requires 490.1295; found 490.1311.

2-[4-(4-Acetoxybut-1-yn-1-yl)-6,7-dichloro-2-tosylisoindolin-5-yl]ethyl acetate (8a)



S2 ***8a***

Dichloride **8a** was prepared following General Procedure C from tetrayne **S2** (21 mg, 0.045 mmol), Li_2CuCl_4 (0.45 mL, 1M in THF, 0.45 mmol), and THF (1 mL). Purification by flash chromatography (hexanes:EtOAc 5:1 to 2:1) gave the dichloride **8a** (22 mg, 0.041 mmol, 91%) as a colorless oil.

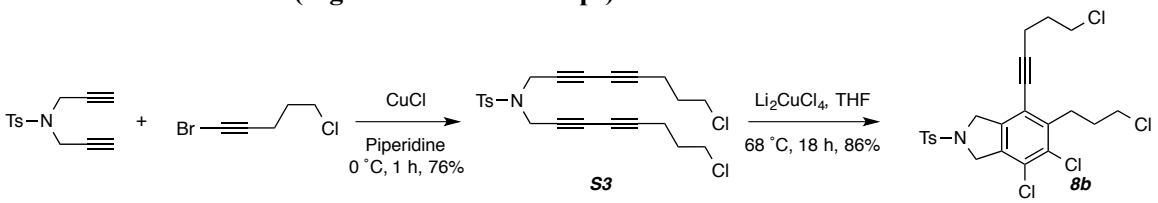
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 8.2 Hz, 2H, $SO_2Ar\mathit{H}_o$), 7.35 (d, J = 8.0 Hz, 2H, $SO_2Ar\mathit{H}_m$), 4.67 (br s, 2H), 4.63 (br s, 2H), 4.27 (t, J = 6.6 Hz, 2H, $AcOC\mathit{H}_2$), 4.25 (t, J = 6.6 Hz, 2H, $AcOC'\mathit{H}_2$), 3.28 (t, J = 6.9 Hz, 2H, $ArC\mathit{H}_2CH_2$), 2.82 (t, J = 6.5 Hz, 2H, $\equiv CC\mathit{H}_2CH_2$), 2.43 (s, 3H, $ArC\mathit{H}_3$), 2.13 (s, 3H, $C\mathit{H}_3C{=}O$), and 2.01 (s, 3H, $C'\mathit{H}_3C{=}O$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.01, 171.00, 144.3, 139.3, 138.7, 135.1, 133.8, 132.5, 130.2, 127.74, 127.72, 118.7, 96.2, 76.4, 62.3, 62.1, 55.0, 54.6, 32.5, 21.8, 21.2, 21.0, and 20.4 ppm.

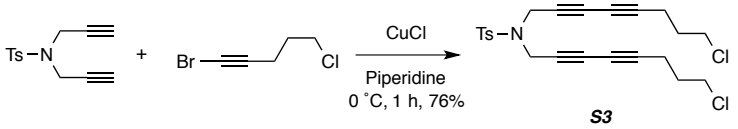
IR (neat): 2960, 2925, 2856, 1739, 1351, 1234, 1165, 1098, 1042, and 816 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{25}H_{25}Cl_2NNaO_6S^+$ $[M+Na]^+$ requires 560.0672; found 560.0677.

Synthesis of isoindoline 8b (Figure 3a of manuscript)



***N,N*-Bis(8-chloroocta-2,4-diyn-1-yl)-4-methylbenzenesulfonamide (S3)**



Tetrayne **S3** was prepared following General Procedure A from 4-methyl-*N,N*-di(prop-2-yn-1-yl)benzenesulfonamide (124 mg, 0.5 mmol), 1-bromo-5-chloropent-1-yne[7] (305 mg, 1.69 mmol), CuCl (15 mg, 0.15 mmol), NH_2OH•HCl (a few crystals), CH_2Cl_2 (2 mL), and 30 wt% aqueous $BuNH_2$ (1.5 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the tetrayne **S3** (170 mg, 0.38 mmol, 76%) as a clear yellow oil.

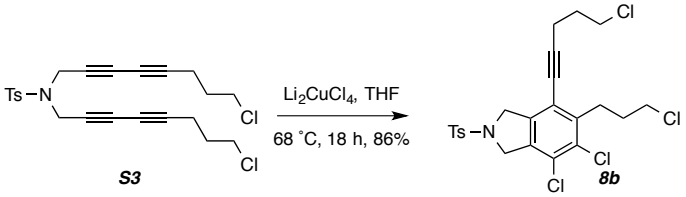
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 8.3 Hz, 2H, SO_2ArH_o), 7.33 (d, J = 8.5 Hz, 2H, SO_2ArH_m), 4.18 (s, 4H, CH_2N), 3.62 (t, J = 6.3 Hz, 4H, CH_2Cl), 2.46 (t, J = 6.8 Hz, 4H, ≡CCH_2), 2.44 (s, 3H, CH_3), and 1.97 (tt, J = 6.8, 6.8 Hz, 4H, $CH_2CH_2CH_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.4, 134.8, 129.9, 128.0, 78.9, 70.9, 68.6, 65.4, 43.5, 37.4, 30.9, 21.8, and 16.8 ppm.

IR (neat): 2961, 2258, 1597, 1494, 1440, 1351, 1162, 1092, 891, and 815 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{23}H_{23}Cl_2NNaO_2S^+$ $[M+Na]^+$ requires 470.0719; found 470.0751.

4,5-Dichloro-7-(5-chloropent-1-yn-1-yl)-6-(3-chloropropyl)-2-tosylisoindoline (8b)



Dichloride **8b** was prepared following General Procedure C from tetrayne **S3** (50 mg, 0.12 mmol), Li_2CuCl_4 (1.2 mL, 1M in THF, 1.2 mmol), and THF (2.8 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the dichloride **8b** (50 mg, 0.097 mmol, 86%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 8.0 Hz, 2H, SO_2ArH_o), 7.35 (d, J = 8.0 Hz, 2H, SO_2ArH_m), 4.66 (s, 2H, NCH_2), 4.62 (s, 2H, $NC'H_2$), 3.69 (t, 2H, J = 6.2 Hz, CH_2Cl), 3.59 (t, 2H, J = 6.3 Hz, $C'H_2Cl$), 3.07 (nfom, 2H, $ArCH_2$), 2.70 (t, J = 6.9 Hz, 2H, C≡CCH_2), 2.42 (s, 3H, $ArCH_3$), 2.09 (tt, J = 6.5, 6.5 Hz, 2H, C≡CCH_2CH_2), and 1.99 (nfom, 2H, $ArCH_2CH_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.2, 142.5, 138.5, 134.5, 133.7, 131.9, 130.2, 127.7, 127.4, 118.3, 98.7, 76.0, 55.0, 54.6, 44., 43.8, 31.7, 31.2, 30.9, 21.7, and 17.3.

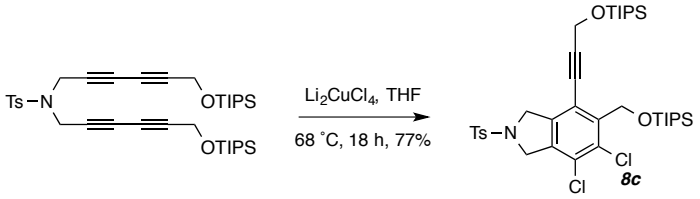
IR (neat): 2960, 2861, 2230, 1349, 1164, 1098, 1069, 764, and 751 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{23}H_{23}Cl_4NNaO_2S^+$ $[M+Na^+]$ requires 540.0096; found 540.0087.

mp: 138–144 °C.

Synthesis of isoindoline 8c (Figure 3a of manuscript)

4,5-Dichloro-2-tosyl-6-{[(triisopropylsilyl)oxy]methyl}-7-{3-[(triisopropylsilyl)oxy]prop-1-yn-1-yl}isoindoline (8c)



Dichloride **8c** was prepared following General Procedure C from known tetrayne[8] (20 mg, 0.03 mmol), Li_2CuCl_4 (0.3 mL, 1M in THF, 0.3 mmol), and THF (0.7 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the dichloride **8c** (17 mg, 0.023 mmol, 77%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, J = 8.0 Hz, 2H, $SO_2Ar\mathit{H}_o$), 7.33 (d, J = 8.0 Hz, 2H, $SO_2Ar\mathit{H}_M$), 4.97 (s, 2H, $C\mathit{H}_2$), 4.68 (s, 2H, $C\mathit{H}_2$), 4.65 (s, 2H, $C\mathit{H}_2$), 4.61 (s, 2H, $C\mathit{H}_2$), 2.42 (s, 3H, $ArC\mathit{H}_3$), 1.20-1.08 (m, 2H, $SiC\mathit{H}(CH_3)_2$], 1.12 [d, J = 5.9 Hz, 6H, $SiCH(C\mathit{H}_3)_2$], and 1.07 [d, J = 6.5 Hz, 6H, $SiCH(C\mathit{H}_3)_2$].

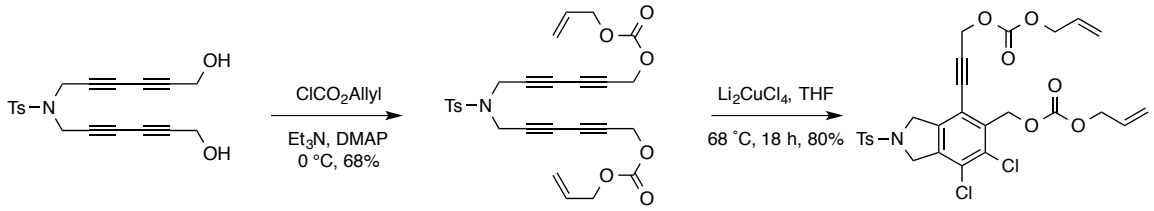
^{13}C NMR (125 MHz, $CDCl_3$): δ 144.2, 141.3, 138.9, 136.0, 133.7, 133.5, 130.2, 128.2, 127.8, 118.2, 97.6, 78.8, 62.5, 55.1, 54.7, 52.7, 21.8, 18.2, 12.3, and 12.2.

IR (neat): 2944, 2891, 2863, 2362, 2343, 1463, 1356, 1167, 1100, 1068, 883, and 813 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{37}H_{57}Cl_2NNaO_4SSi_2^+$ [M+Na^+] requires 760.2816; found 760.2839.

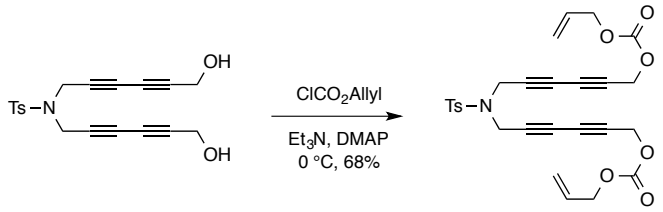
mp: 122–126 °C.

Synthesis of isoindoline 8d (Figure 3a of manuscript)



S4 ***8d***

Diallyl [(tosylazanediyl)bis(hexa-2,4-diyne-6,1-diyl)] bis(carbonate) (S4)



S4

To a solution of *N*,*N*-bis(6-hydroxyhexa-2,4-diyn-1-yl)-4-methylbenzenesulfonamide[8] (90 mg, 0.25 mmol) in CH_2Cl_2 cooled at 0 °C was sequentially added allyl chloroformate (90 mg, 0.75 mmol), NEt_3 (100 mg, 1 mmol), and DMAP (5 mg, 0.04 mmol). The reaction mixture was stirred at this temperature for 2 h. The resulting solution was partitioned between EtOAc and aq. NH_4Cl. The aqueous layer was washed with EtOAc two times. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. The resulting oil was subjected to flash chromatography (SiO_2, hexanes:EtOAc = 12:1 to 5:1) to give carbonate **S4** (90 mg, 0.17 mmol, 68%) as a clear yellow oil.

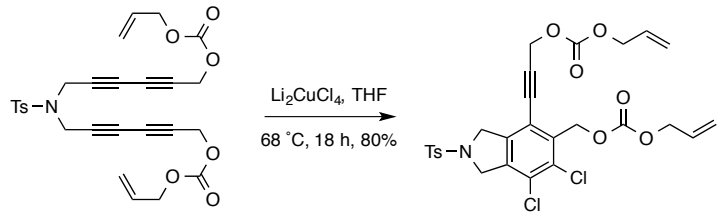
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, J = 8.3 Hz, 2H, $SO_2Ar\mathit{H}_o$), 7.33 (d, J = 8.0 Hz, 2H, $SO_2Ar\mathit{H}_m$), 5.94 (ddt, J = 17.1, 10.5, 5.8 Hz, 2H, $CH_2C\mathit{H}$=C), 5.38 (ddt, J = 17.2, 1.4, 1.4 Hz, 2H, CH=CH_ZH$_E$), 5.30 (ddt, J = 10.4, 1.2, 1.2 Hz, 2H, CH=CH$_Z\mathit{H}_E$), 4.77 (s, 4H, OCH_2), 4.66 (ddd, J = 5.8, 1.3, 1.3 Hz, 4H, CH_2C=), 4.20 (s, 4H, NCH_2), and 2.44 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 154.4, 144.8, 134.4, 131.2, 130.0, 127.9, 119.5, 72.8, 72.1, 71.1, 69.9, 69.2, 55.6, 37.5, and 21.7 ppm.

IR: 3005, 2989, 2918, 2261, 1752, 1649, 1597, 1449, 1382, 1353, 1274, 1164, 1092, 968, and 893 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{27}H_{25}NNaO_8S^+$ $[M+Na]^+$ requires 546.1193; found 546.1201.

Allyl {[4-(3-(((allyloxy)carbonyl)oxy)prop-1-yn-1-yl)-6,7-dichloro-2-tosylisoindolin-5-yl]methyl} carbonate (8d)



S4 ***8d***

Dichloride **8d** was prepared following General Procedure C from tetrayne **S4** (23 mg, 0.04 mmol), Li_2CuCl_4 (0.4 mL, 1M in THF, 0.4 mmol), and THF (1.2 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the dichloride **8d** (20 mg, 0.034 mmol, 80%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H, $SO_2Ar\mathit{H}_o$), 7.35 (d, *J* = 8.1 Hz, 2H, $SO_2Ar\mathit{H}_m$), 5.97 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H, $CH_2{=}C\mathit{H}$), 5.92 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1H, $C'H_2{=}C'\mathit{H}$), 5.41 (ddt, *J* = 17.2, 1.4, 1.4 Hz, 1H, $CH\mathit{H}_Z H_E{=}CH$), 5.41 (s, 2H, $ArC\mathit{H}_2O$), 5.35 (ddt, *J* = 17.2, 1.4, 1.4 Hz, 1H, $C'\mathit{H}_Z H_E{=}C'H$), 5.32 (ddt, *J* = 10.5, 1.2, 1.2 Hz, 1H, $CH_Z\mathit{H}_E{=}CH$), 5.26 (ddt, *J* = 10.4, 1.2, 1.2 Hz, 1H, $C'H_Z\mathit{H}_E{=}C'H$), 4.98 (s, 2H, $OC\mathit{H}_2C{\equiv}$), 4.71 (ddd, *J* = 5.8, 1.3, 1.3 Hz, 2H, $CO_2C\mathit{H}_2$), 4.69 (nfom, 2H, $C\mathit{H}_2N$), 4.65 (nfom, 2H, $C'\mathit{H}_2N$), 4.64 (ddd, *J* = 5.8, 1.3, 1.3 Hz, 2H, $C'O_2C'\mathit{H}_2$), and 2.43 (s, 3H, $ArC\mathit{H}_3$).

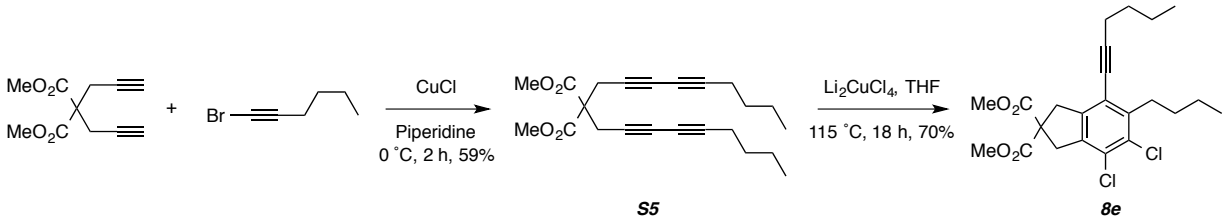
^{13}C NMR (125 MHz, $CDCl_3$): δ 154.7, 154.5, 144.4, 139.3, 137.8, 136.0, 134.1, 133.5, 131.6, 131.4, 130.3, 129.1, 127.7, 119.7, 119.2, 118.4, 93.1, 80.4, 69.4, 69.0, 65.6, 55.8, 54.8, 54.7, and 21.8 ppm

IR (neat): 2954, 2853, 1750, 1438, 1383, 1353, 1256, 1165, 1098, and 958 cm^{-1}.

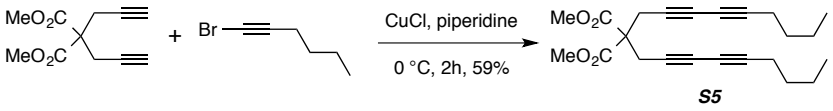
HRMS (ESI-TOF): Calcd for $C_{27}H_{25}Cl_2NNaO_8S^+$ $[M+Na]^+$ requires 616.0570; found 616.0589.

mp: 112–116 °C.

Synthesis of indane 8e (Figure 3a of manuscript)



Dimethyl 2,2-di(nona-2,4-diyn-1-yl)malonate (S5)



Tetrayne **S5** was prepared following the General Procedure B from bromoalkyne (480 mg, 3.0 mmol), diyne[9] (208 mg, 1.0 mmol), CuCl (20 mg, 0.20 mmol), and piperidine (5 mL). Purification by flash chromatography (hexanes:EtOAc 3:1) gave tetrayne **S5** (216 mg, 0.59 mmol, 59%) as a yellow oil.

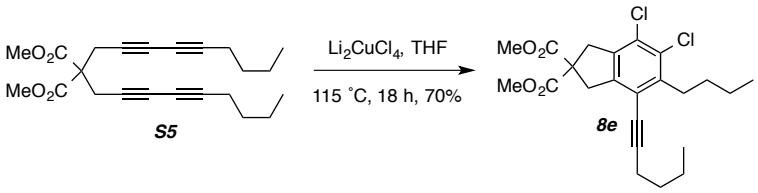
^{1}H NMR (500 MHz, $CDCl_3$): δ 3.77 (s, 6H, CO_2CH_3), 3.06 [s, 4H, $CH_2C(CO_2Me)_2$], 2.24 (t, J = 6.9 Hz, 4H, $CH_2C{\equiv}C$), 1.50 (br tt, J = 7.0, 7.0 Hz, 4H, $C{\equiv}CCH_2CH_2$), 1.40 (br tq, J = 7.0, 7.0 Hz, 4H, CH_2CH_3), and 0.91 (t, J = 7.3 Hz, 6H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.0, 79.2, 70.7, 68.9, 65.0, 56.9, 53.5, 30.4, 24.0, 22.1, 19.1, and 13.7.

IR (neat): 2957, 2934, 2873, 2259, 1744, 1435, 1320, 1292, 1210, 1184, 1072, and 1054 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{23}H_{28}NaO_4^+$ [M+Na^+] requires 391.1880; found 391.1885.

Dimethyl 5-butyl-6,7-dichloro-4-(hex-1-yn-1-yl)-1,3-dihydro-2H-indene-2,2-dicarboxylate (8e)



Dichloride **8e** was prepared following General Procedure C from tetrayne **S5** (30 mg, 0.08 mmol), Li_2CuCl_4 (0.8 mL, 1M in THF, 0.8 mmol), and THF (1.9 mL). Purification by MPLC (hexanes:EtOAc 8:1) gave the dichloride **8e** (25 mg, 0.057 mmol, 70%) as a colorless solid.

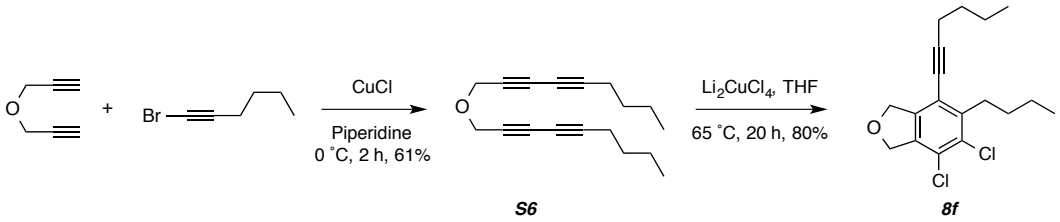
^{1}H NMR (500 MHz, $CDCl_3$): δ 3.77 (s, 6H, CO_2CH_3), 3.67 [s, 2H, $CH_2C(CO_2Me)_2$], 3.65 [s, 2H, $C'H_2C(CO_2Me)_2$], 2.92 (nfom, 2H, $ArCH_2$), 2.47 (t, J = 7.0 Hz, 2H, $C{\equiv}CCH_2$), 1.61 (m, 2H, CH_2CH_2Ar), 1.52 (m, 4H, $\equiv CCH_2CH_2$, $CH_2CH_2CH_3$), 1.41 (tq, J = 7, 7 Hz, 2H, CH_2CH_3), 0.96 (t, J = 7.3 Hz, 3H, CH_3), and 0.95 (t, J = 7.3 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.8, 143.3, 141.9, 137.0, 130.7, 128.2, 119.7, 99.1, 76.5, 58.8, 53.3, 41.7, 41.3, 33.2, 31.2, 30.9, 23.0, 22.1, 19.5, 14.0, and 13.7.

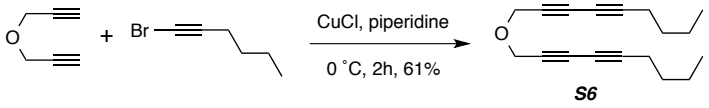
IR (neat): 2957, 2933, 2872, 2245, 1740, 1434, 1276, 1249, 1199, and 1074 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{23}H_{28}NaO_4^+$ [M+Na^+] requires 461.1257; found 461.1331.

Synthesis of isobenzofuran 8f (Figure 3a of manuscript)



1-(Nona-2,4-diyn-1-yloxy)nona-2,4-diyne (S6)



Tetrayne **S6** was prepared following the General Procedure B from 1-bromohexyne (400 mg, 2.5 mmol), dipropargyl ether (94 mg, 1.0 mmol), CuCl (20 mg, 0.20 mmol), and piperidine (5 mL). Purification by flash chromatography (hexanes:EtOAc 20:1) gave tetrayne **S6** (156 mg, 0.61 mmol, 61%) as a yellow oil.

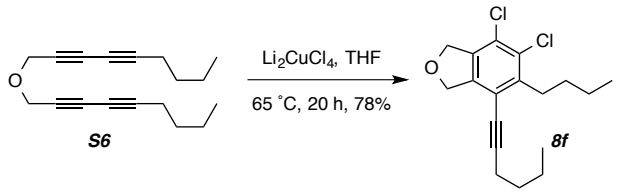
^{1}H NMR (500 MHz, $CDCl_3$): δ 4.31 (s, 4H, OC*H*$_2$), 2.29 (t, *J* = 6.9 Hz, 4H, C≡CC*H*$_2$), 1.52 (tt, *J* = 7,7 Hz, 4H, C≡CCH$_2$C*H*$_2$), 1.42 (tq, *J* = 7, 7 Hz, 4H, C*H*$_2$CH$_3$), and 0.91 (t, *J* = 7.3 Hz, 6H, CH$_2$C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 81.8, 72.3, 70.8, 64.6, 57.3, 30.3, 22.1, 19.2, and 13.7.

IR (neat): 2959, 2934, 2873, 2363, 2342, 2255, 1345, and 1077 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{18}H_{22}NaO^+$ [M+Na$^+$] requires 277.1563; found 277.1532.

5-Butyl-6,7-dichloro-4-(hex-1-yn-1-yl)-1,3-dihydroisobenzofuran (8f)



Dichloride **8f** was prepared following General Procedure C from tetrayne **S6** (20 mg, 0.079 mmol), Li_2CuCl_4 (0.8 mL, 1M in THF, 0.8 mmol), and THF (1.9 mL). Purification by MPLC (hexanes:EtOAc 20:1) gave the dichloride **8f** (20 mg, 0.062 mmol, 78%) as a colorless solid.

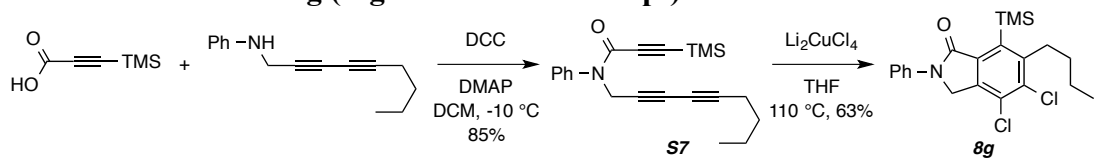
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.17 (s, 2H, OC*H*$_2$), 5.14 (s, 2H, OC*H*$_2$), 2.97 (nfom, 2H, ArC*H*$_2$), 2.48 (t, *J* = 6.8 Hz, 2H, C≡CC*H*$_2$), 1.60 (m, 2H, C*H*$_2$CH$_2$Ar), 1.51 (m, 4H, ≡CCH$_2$C*H*$_2$, CH$_2$C*H*$_2$CH$_3$), 1.45 (tq, *J* = 7, 7 Hz, 2H, C*H*$_2$CH$_3$), 0.98 (t, *J* = 7.3 Hz, 3H, C*H*$_3$), and 0.98 (t, *J* = 7.3 Hz, 3H, C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 143.9, 141.5, 136.5, 131.1, 125.7, 117.1, 99.2, 76.0, 75.3, 74.6, 33.0, 31.3, 30.9, 23.1, 22.2, 19.5, 14.1, and 13.8.

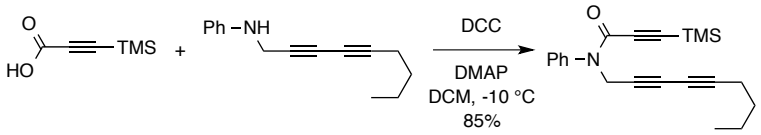
IR (neat): 2958, 2932, 2861, 2227, 1781, 1465, 1457, 1420, 1360, 1082, 1061, 904, 764, and 757 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{18}H_{22}Cl_2NaO^+$ [M+Na$^+$] requires 347.0940; found 347.0925.

Synthesis of isoindolinone 8g (Figure 3a of manuscript)



N-(Nona-2,4-diyn-1-yl)-*N*-phenyl-3-(trimethylsilyl)propiolamide (S7)



To a solution of 3-(trimethylsilyl)propiolic acid (180 mg, 1.27 mmol) and *N*-(nona-2,4-diyn-1-yl)-*N*-phenyl-3-(trimethylsilyl)propiolamide[10] (210 mg, 1 mmol) in CH_2Cl_2 cooled to -10 °C was sequentially added DMAP (17 mg, 0.13 mmol) and DCC (235 mg, 1.15 mmol). The reaction flask was allowed to warm to room temperature for 3 h. The resulting slurry was filtered through Celite® (EtOAc) and concentrated. The oil obtained was subjected to flash chromatography (SiO_2, hexanes:EtOAc = 12:1 to 5:1) to give amide **S7** (286 mg, 0.85 mmol, 85%) as a yellow oil.

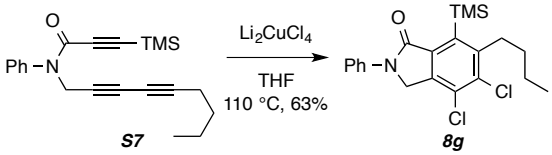
^{1}H NMR (500 MHz, $CDCl_3$, as a 9:1 ratio of two rotamers): Major rotamer δ 7.44-7.37 (m, 3H, NAr*H*m*H*p), 7.35 (dd, *J* = 7.7, 1.4 Hz, 2H, NAr*H*o), 4.57 (s, 2H, CH_2N), 2.25 (t, *J* = 7.1 Hz, 2H, C≡CCH_2), 1.50 (tt, *J* = 7.1, 7.1 Hz, 2H, C≡CCH$_2$CH_2), 1.39 (tq, *J* = 7.1, 7.1 Hz, 2H, CH_2CH$_3$), 0.90 (t, *J* = 7.1 Hz, 3H, CH_3), and -0.04 [s, 9H, Si(CH_3)$_3$]. Minor rotamer δ 4.74 (s, 2H, CH_2N), 2.28 (t, *J* = 7.0 Hz, 2H, C≡CCH_2), 0.89 (t, *J* = 7.2 Hz, 3H, CH_3), and 0.30 [s, 9H, Si(CH_3)$_3$].

^{13}C NMR (125 MHz, $CDCl_3$): δ 153.3, 141.1, 129.3, 128.8, 128.7, 99.6, 96.2, 80.7, 70.2, 69.6, 64.8, 38.6, 30.4, 22.1, 19.1, 13.8, and -0.9 (only resonances for the major rotamer are reported).

IR: 2958, 2932, 2862, 2257, 2118, 1644, 1593, 1493, 1377, 1275, 1252, 1219, and 848 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{21}H_{25}NNaOSi^+$ $[M+Na]^+$ requires 358.1598; found 358.1604.

6-Butyl-4,5-dichloro-2-phenyl-7-(trimethylsilyl)isoindolin-1-one (8g)



Dichloride **8g** was prepared following General Procedure C from amide **S7** (20 mg, 0.059 mmol), Li_2CuCl_4 (0.6 mL, 1M in THF, 0.6 mmol), and THF (1.4 mL). Purification by MPLC (hexanes:EtOAc = 5:1) gave the dichloride **8g** (15 mg, 0.036 mmol, 63%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (m, 2H, NPh*Ho*), 7.43 (m, 2H, NPh*Hm*), 7.19 (tt, *J* = 7.4, 1.1 Hz, 1H, NPh*Hp*), 4.76 (s, 2H, CONPhCH_2), 3.12-3.06 (nfom, 2H, ArCH_2), 1.53-1.41 (m, 4H, ArCH$_2$CH_2CH_2), 0.97 [t, *J* = 7.1 Hz, 3H, CH$_2$CH_3], and 0.52 (s, 9H, Si(CH_3)$_3$).

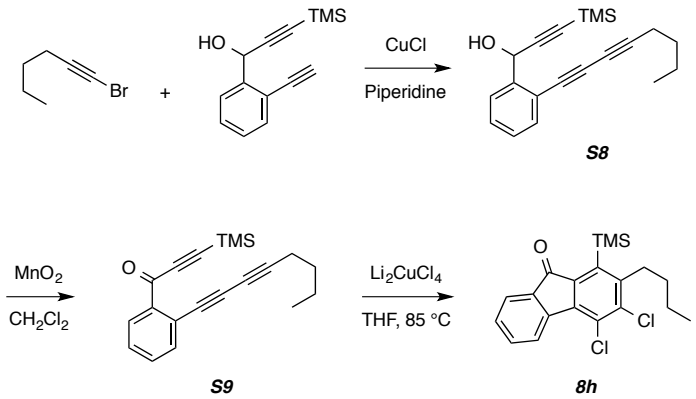
^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 149.6, 139.7, 139.3, 138.2, 137.9, 136.6, 129.4, 129.1, 125.0, 120.0, 49.7, 34.2, 34.1, 22.9, 14.2, and 3.7.

IR: 2959, 2928, 2865, 1705, 1599, 1501, 1381, 1246, 1099, 920, and 848 cm^{-1}.

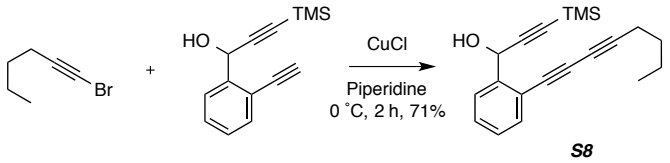
HRMS (ESI-TOF): Calcd for $C_{21}H_{25}Cl_2NNaOSi^+$ $[M+Na]^+$ requires 428.0975; found 428.0976.

mp: 127–132 °C.

Synthesis of fluorenone 8h (Figure 3a of manuscript)



1-(2-(Octa-1,3-diyn-1-yl)phenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (S8)



Triyne **S8** was prepared following General Procedure B from 1-(2-ethynylphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol[4] (160 mg, 0.7 mmol), 1-bromohex-1-yne (500 mg, ca. 40 wt% in pentane, 1.25 mmol), CuCl (7 mg, 0.07 mmol), and piperidine (2 mL). Purification by MPLC (hexanes:EtOAc 7:1) gave the diyne **S8** (153 mg, 0.5 mmol, 71%) as a yellow oil. This sample contained ca. 10 mol% of the starting diyne, with which it coeluted.

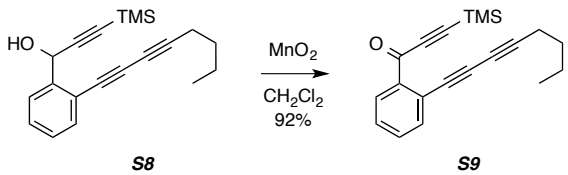
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.0 Hz, 1H, H3), 7.50 (d, *J* = 7.5 Hz, 1H, H6), 7.38 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.28 (dd, *J* = 8.0, 8.0 Hz, 1H), 5.83 (d, *J* = 5.5 Hz, 1H, C*H*OH), 2.38 (t, *J* = 7.0 Hz, 2H, C≡CC*H*$_2$), 1.57 (tt, *J* = 7, 7 Hz, 2H, C≡CCH$_2$C*H*$_2$), 1.46 (tq, *J* = 7, 7 Hz, 2H, CH$_2$C*H*$_2$CH$_3$), and 0.94 (t, *J* = 7.0 Hz, 3H, C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 143.5, 133.8, 129.5, 128.5, 127.1, 121.0, 104.3, 92.0, 86.7, 80.0, 71.9, 65.1, 63.7, 30.4, 22.2, 19.5, 13.7, and 0.02.

IR: 3364, 2959, 2934, 2872, 2238, 2174, 1482, 1466, 1449, 1249, 1037, 983, and 845 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{20}H_{24}NaOSi^+$ $[M+Na]^+$ requires 331.1489; found 331.1496.

1-(2-(Octa-1,3-diyn-1-yl)phenyl)-3-(trimethylsilyl)prop-2-yn-1-one (S9)



Activated MnO_2 (300 mg, 3.44 mmol) was added to a solution of triyne **S9** (150 mg, 0.49 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at rt until full conversion (within 2 h) was indicated by TLC analysis. The mixture was then filtered through Celite® and the filter cake was washed with a copious amount of CH_2Cl_2. The filtrate was concentrated and the residue subjected to column

chromatography (hexanes:EtOAc = 12:1) to yield ketone **S9** as a pale yellow oil (138 mg, 0.45 mmol, 92%).

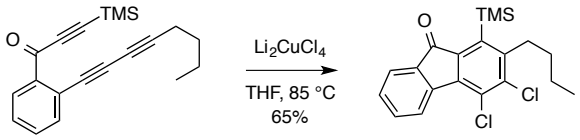
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar*H6*), 7.61 (dd, *J* = 7.5, 1.0 Hz, 1H, Ar*H3*), 7.50 (ddd, *J* = 7.5, 7.5, and 1.5 Hz, 1H, Ar*H4*), 7.40 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H, Ar*H5*), 2.39 (t, *J* = 7.0 Hz, 2H, CCCH_2), 1.56 (app p, *J* = 7.0 Hz, 2H, $CH_2CH_2CH_2$), 1.45 (app sextet, *J* = 7.5 Hz, 2H, $CH_2CH_2CH_3$), and 0.93 (t, *J* = 7.5 Hz, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 176.8, 139.1, 135.8, 132.7, 131.9, 128.5, 122.3, 101.62, 101.58, 87.5, 80.9, 72.8, 65.7, 30.4, 22.2, 19.6, 13.8, and -0.5 ppm

IR: 2959, 2933, 2873, 2239, 2153, 1649, 1589, 1561, 1480, 1274, 1251, 1234, 1014, 848, and 755 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{20}H_{22}NaOSi^+$ $[M+Na]^+$ requires 329.1332; found 329.1329.

2-Butyl-3,4-dichloro-1-(trimethylsilyl)-9H-fluoren-9-one (8h)



S9 ***8h***

Dichloride **8h** was prepared following General Procedure C from triyne **S9** (15 mg, 0.049 mmol) and Li_2CuCl_4 (0.2 mmol) in THF (2 mL). Purification by MPLC (hexanes:EtOAc = 5:1) gave the dichloride **8h** (12 mg, 0.032 mmol, 65%) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (ddd, *J* = 7.7, 0.9, 0.9 Hz, 1H, *H5*), 7.64 (ddd, *J* = 7.3, 0.9, and 0.9 Hz, 1H, *H8*), 7.52 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H, *H6*), 7.34 (ddd, *J* = 7.4, 7.4, 1.0 Hz, 1H, *H7*), 3.02 (br t, *J* = 8.0 Hz, 2H, ArCH_2), 1.52-1.40 (m, 4H, $CH_2CH_2CH_3$), 0.97 (t, *J* = 7.2 Hz, 3H, CH_3), and 0.45 [s, 9H, $Si(CH_3)_3$].

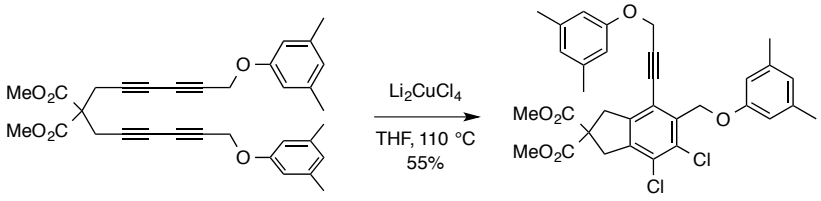
^{13}C NMR (125 MHz, $CDCl_3$): δ 193.7, 149.4, 142.7, 141.6, 141.0, 139.8, 139.5, 134.9, 134.1, 129.9, 129.5, 124.2, 124.1, 34.4, 33.6, 22.9, 14.2, and 3.2 ppm.

IR: 2958, 2931, 2871, 1719, 1601, 1466, 1249, 1093, and 849 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{20}H_{24}Cl_2NaOSi^+$ $[M+Na]^+$ requires 399.0709; found 399.0713.

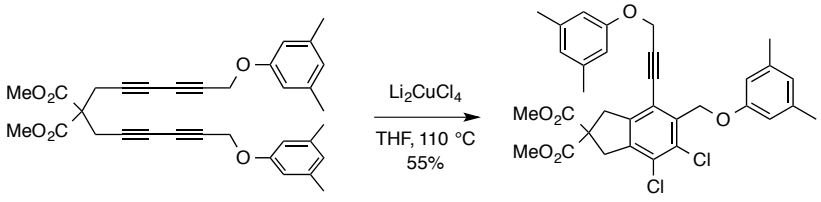
mp: 110–111 °C.

Synthesis of indane 8i (Figure 3b of manuscript)



S10 ***8i***

Dimethyl 4,5-dichloro-6-[(3,5-dimethylphenoxy)methyl]-7-[3-(3,5-dimethylphenoxy)prop-1-yn-1-yl]-1,3-dihydro-2H-indene-2,2-dicarboxylate (8i)



S10 ***8i***

Dichloride **8i** was prepared following General Procedure C from the dimethyl tetraynylmalonate **S10**[3] (14 mg, 0.027 mmol) and Li_2CuCl_4 (4 mL, 0.1 M in THF). The reaction flask was heated at 110 °C for 24 h. Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the dichloride **8i** (9 mg, 0.015 mmol, 55%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.64 (t of sextet, J = 0.7, 0.7 Hz, 1H, OAr_p), 6.61 (overlapping br s, 3H), 6.59 (dq, J = 0.7, 0.7 Hz, 2H, OAr_o), 5.18 (s, 2H, $ArCH_2O$), 4.85 (s, 2H, $\equiv CCH_2O$), 3.77 (s, 6H, CO_2CH_3), 3.69 (s, 2H, CH_2CCH_2), 3.66 (s, 2H, CH_2CCH_2), 2.29 (ddd, J = 0.7, 0.7, 0.7 Hz, 6H, $ArCH_3$), and 2.25 (ddd, J = 0.7, 0.7, 0.7 Hz, 6H, $ArCH_3$).

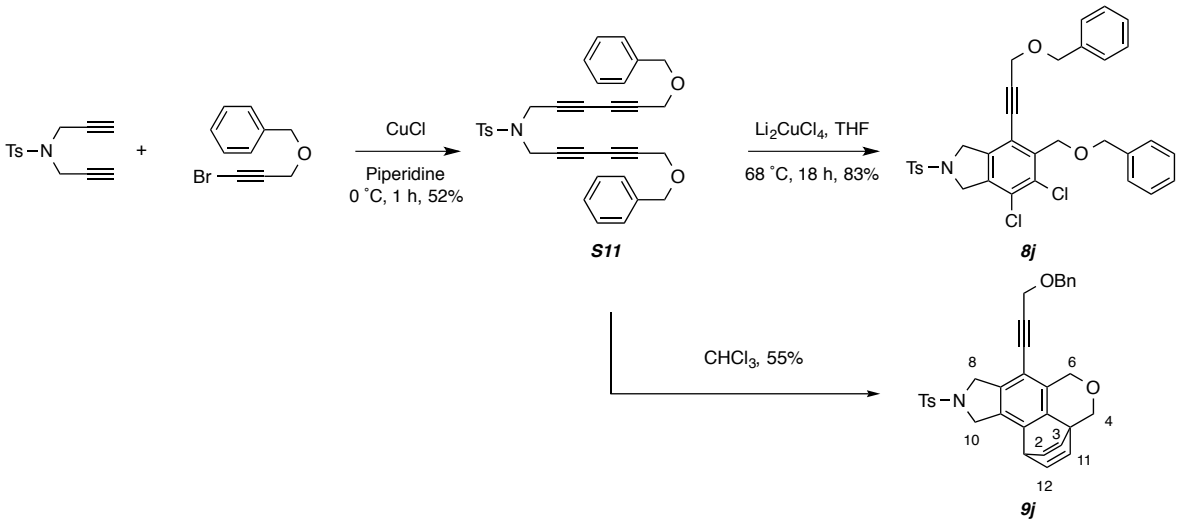
^{13}C NMR (125 MHz, $CDCl_3$): δ 171.5, 159.2, 157.7, 143.0, 140.7, 139.44, 139.37, 136.8, 133.2, 130.3, 123.6, 123.2, 119.7, 112.9, 112.8, 93.6, 81.9, 66.8, 58.9, 56.4, 53.5, 41.53, 41.50, 21.7, and 21.6 ppm.

IR: 2954, 2920, 1738, 1593, 1434, 1293, 1256, 1167, 1153, and 1061cm^{-1}.

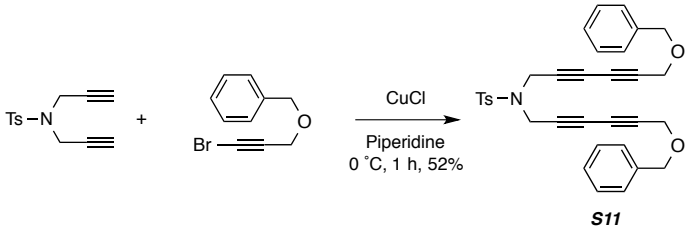
HRMS (ESI-TOF): Calcd for $C_{33}H_{32}Cl_2NaO_6^+$ $[M+Na]^+$ requires 617.1468; found 617.1487.

mp: 140–143 °C.

Synthesis of isoindolines 8j and 9j (Figure 3b of manuscript)



N,N-Bis[6-(benzyloxy)hexa-2,4-diyn-1-yl]-4-methylbenzenesulfonamide (S11)



Tetrayne **S11** was prepared following General Procedure B from 4-methyl-*N,N*-di(prop-2-yn-1-yl)benzenesulfonamide (198 mg, 0.8 mmol), {[(3-bromoprop-2-yn-1-yl)oxy]methyl}benzene[11] (540 mg, 2.4 mmol), CuCl (24 mg, 0.24 mmol), and piperidine (2.5 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the tetrayne **S11** (223 mg, 0.41 mmol, 52%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 8.4 Hz, 2H, SO_2Ar*Ho*), 7.38-7.29 (m, 12H, Ar*H*), 4.57 (s, 4H, OCH_2Ar), 4.23 (s, 4H, OCH_2C≡C), 4.19 (s, 4H, NCH_2), and 2.39 (s, 3H, ArCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.6, 137.1, 134.7, 130.0, 128.7, 128.30, 128.27, 128.0, 75.4, 72.0, 71.7, 70.4, 70.3, 57.6, 37.5, and 21.8 ppm.

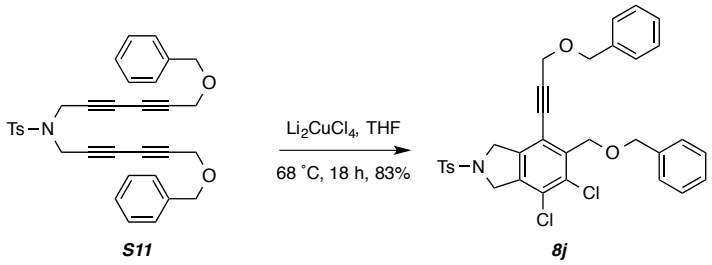
IR: 3031, 2865, 2255, 1597, 1495, 1454, 1351, 1164, 1091, 1073, 1027, 945, and 892 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{33}H_{29}NNaO_4S^+$ $[M+Na]^+$ requires 558.1710; found 558.1713.

mp: 64–66 °C.

[cont.]

5-((Benzyloxy)methyl)-4-(3-(benzyloxy)prop-1-yn-1-yl)-6,7-dichloro-2-tosylisoindoline (8j)



S11 *8j*

Dichloride **8j** was prepared following General Procedure C from tetrayne **S11** (50 mg, 0.093 mmol) and Li_2CuCl_4 (0.9 mL, 1M in THF, 0.9 mmol) in THF (2.1 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the dichloride **8j** (48 mg, 0.079 mmol, 83%) as a colorless solid.

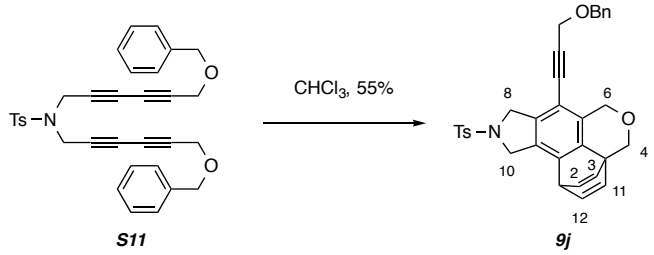
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 2H, SO_2ArH_O), 7.31 (m, 12H), 4.77 (s, 2H, $ArCH_2OBn$), 4.71 (br s, 2H, CH_2N), 4.65 (br s, 2H, $C'H_2N$), 4.63 (s, 2H, $PhCH_2O$), 4.57 (s, 2H, $PhCH_2O$), 4.38 (s, 2H, $\equiv CCH_2OBn$), and 2.41 (s, 3H, $ArCH_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 144.4, 138.82, 138.80, 138.0, 137.2, 136.7, 133.9, 133.5, 130.3, 128.8, 128.53, 128.51, 128.34, 128.31, 128.00, 127.95, 127.7, 118.7, 95.2, 80.4, 73.2, 72.1, 68.4, 57.9, 55.0, 54.7, and 21.8.

IR (neat): 3064, 3033, 2855, 1454, 1351, 1166, 1096, 1071, 857, 827, and 817 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{33}H_{29}Cl_2NNaO_4S^+$ $[M+Na^+]$ requires 628.1087; found 628.1204.

7-[3-(Benzyloxy)prop-1-yn-1-yl]-9-tosyl-6,8,9,10-tetrahydro-1*H*,4*H*-1,3a-ethenoisochromeno[5,4-ef]isoindole (9j)



S11 *9j*

A solution of tetrayne **S11** (22 mg, 0.041 mmol) in $CHCl_3$ (2 mL) was heated at 68 °C for 18 h. The resulting solution was concentrated and subjected to flash chromatography (SiO_2, hexanes:EtOAc = 5:1) to give isoindoline **9j** (12 mg, 0.022 mmol, 55%) as a colorless solid.

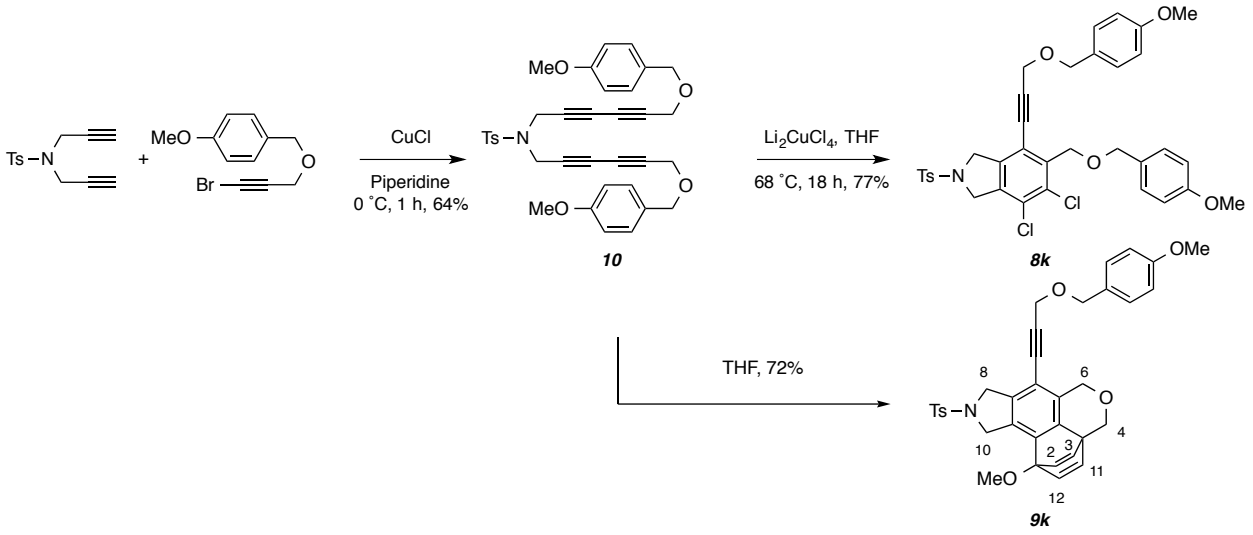
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H, SO_2ArH_o), 7.40-7.32 (m, 5H, C_6H_5), 7.31 (d, *J* = 8.0 Hz, 2H, SO_2ArH_m), 6.85 (dd, *J* = 6.4, 5.8 Hz, 2H, *H*2 and *H*12), 6.68 (d, *J* = 6.5, 1.5 Hz, 2H, *H*3 and *H*11), 4.81 (tt, *J* = 5.8, 1.5 Hz, 1H, *H1*), 4.73 (br s, 2H, CH_2), 4.66 (br s, 2H, CH_2), 4.63 (br s, 2H, CH_2), 4.58 (br s, 2H, CH_2), 4.53 (br s, 2H, CH_2), 4.40 (br s, 2H, CH_2), and 2.40 (s, 3H, $ArCH_3$).

^{13}C NMR (125 MHz, CD_3CN): δ 145.1, 144.0, 143.8, 142.9, 141.1, 138.9, 135.3, 134.3, 132.7, 130.8, 129.3, 129.0, 128.8, 128.7, 128.5, 108.5, 93.8, 80.8, 72.1, 71.5, 66.5, 58.5, 54.5, 53.3, 51.8, 46.8, and 21.4.

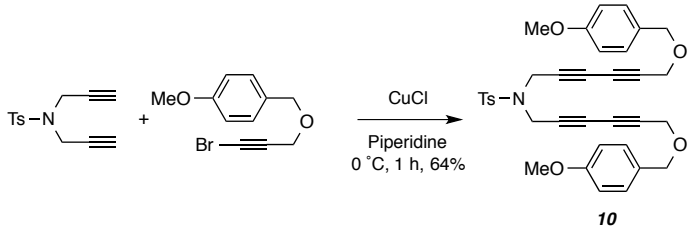
IR (neat): 3062, 2945, 2918, 1597, 1495, 1454, 1348, 1163, 1096, 1073, 920, and 816 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{33}H_{29}NNaO_4S^+$ $[M+Na]^+$ requires 558.1710; found 558.1695.

Synthesis of isoindoline 8k and 9k (Figure 4a of manuscript)



N,N-Bis{6-[(4-methoxybenzyl)oxy]hexa-2,4-diyn-1-yl}-4-methylbenzenesulfonamide (10)



Tetrayne **10** was prepared following General Procedure B from 4-methyl-*N,N*-di(prop-2-yn-1-yl)benzenesulfonamide (150 mg, 0.6 mmol), 1-{[(3-bromoprop-2-yn-1-yl)oxy]methyl}-4-methoxybenzene (512 mg, 2.0 mmol), CuCl (24 mg, 0.24 mmol), and piperidine (2 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the tetrayne **10** (230 mg, 0.39 mmol, 64%) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.3 Hz, 2H, SO_2ArHo), 7.32 (d, *J* = 8.4 Hz, 2H, SO_2ArHm), 7.26 (d, *J* = 8.6 Hz, 4H, $MeOAr H_m$), 6.88 (d, *J* = 8.8 Hz, 4H, $MeOAr H_o$), 4.50 (s, 4H, OCH_2Ar), 4.23 (s, 4H, $OCH_2C{\equiv}C$), 4.15 (s, 4H, NCH_2), 3.80 (s, 6H, OCH_3), and 2.39 (s, 3H, $ArCH_3$).

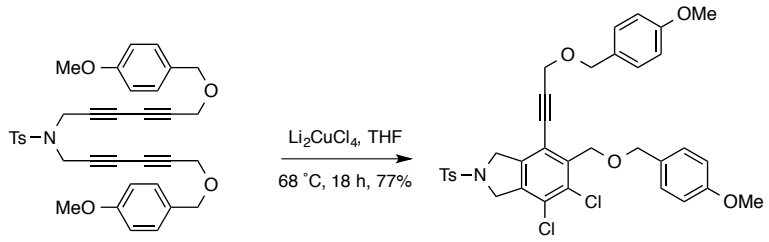
^{13}C NMR (125 MHz, $CDCl_3$): δ 159.7, 144.6, 134.6, 129.99, 129.94, 129.1, 128.0, 114.0, 75.5, 71.6, 70.3, 70.2, 57.2, 55.4, 37.5, and 21.8 ppm.

IR: 3010, 2838, 2365, 1612, 1586, 1513, 1350, 1303, 1249, 1163, 1071, 1033, 891, and 817 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{35}H_{33}NNaO_6S^+$ $[M+Na]^+$ requires 618.1921; found 618.1978.

[cont.]

4,5-Dichloro-6-{[(3-methoxybenzyl)oxy]methyl}-7-{3-[(4-methoxybenzyl)oxy]prop-1-yn-1-yl}-2-tosylisoindoline (8k)



10 ***8k***

Dichloride **8k** was prepared following General Procedure C from tetrayne **10** (24 mg, 0.04 mmol), Li_2CuCl_4 (0.4 mL, 1M in THF, 0.4 mmol), and THF (1 mL). Purification by flash chromatography (hexanes:EtOAc 12:1 to 5:1) gave the dichloride **8k** (21 mg, 0.032 mmol, 77%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H, SO_2ArH_o), 7.30 (d, *J* = 8.5 Hz, 2H, SO_2ArH_m), 7.29 (d, *J* = 8.6 Hz, 2H, MeOArH_m), 6.98 (d, *J* = 7.0 Hz, 2H, MeOAr'H_m), 6.91 (d, *J* = 8.6 Hz, 2H, MeOArH_o), 6.83 (d, *J* = 7.0 Hz, 2H, MeOAr'H_o), 4.74 (s, 2H), 4.71 (br s, 2H), 4.65 (br s, 2H), 4.56 (s, 2H), 4.51 (s, 2H), 4.35 (s, 2H), 3.82 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), and 2.41 (s, 3H, ArCH_3).

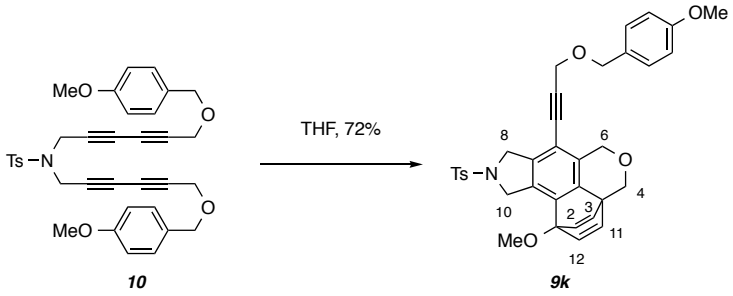
^{13}C NMR (125 MHz, $CDCl_3$): δ 159.8, 159.5, 144.3, 138.9, 138.8, 136.6, 133.9, 133.6, 130.3, 130.2, 130.0, 129.7, 129.3, 128.5, 127.7, 118.8, 114.2, 113.9, 95.3, 80.4, 73.0, 71.8, 68.2, 57.6, 55.52, 55.46, 55.0, 54.7, and 21.8 ppm.

IR (neat): 2932, 2838, 1612, 1513, 1350, 1249, 1164, 1096, 1071, and 1034cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{35}H_{33}Cl_2NNaO_6S^+$ $[M+Na]^+$ requires 688.1298; found 688.1315.

mp: 132–137 °C.

1-Methoxy-7-{3-[(4-methoxybenzyl)oxy]prop-1-yn-1-yl}-9-tosyl-6,8,9,10-tetrahydro-1*H*,4*H*-1,3a-ethenoisochromeno[5,4-*ef*]isoindole (9k)



10 ***9k***

A solution of tetrayne **10** (22 mg, 0.037 mmol) in THF (2 mL) was heated at 68 °C for 18 h. The resulting solution was concentrated and subjected to flash chromatography (SiO_2, hexanes:EtOAc = 5:1) to give isoindoline **9k** (16 mg, 0.027 mmol, 72%) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H, SO_2ArH_o), 7.30 (d, *J* = 8.6 Hz, 2H, MeOArH_m), 7.29 (d, *J* = 8.7 Hz, 2H, SO_2ArH_m), 6.98 (d, *J* = 6.9 Hz, 2H, *H*2 and *H*12), 6.91 (d, *J* = 8.7 Hz, 2H, MeOArH_o), 6.63 (d, *J* = 6.9 Hz, 2H, *H*3 and *H*11), 4.83 (br s, 2H, CH_2), 4.71 (br s, 2H, CH_2), 4.56 (br s, 2H, CH_2), 4.52 (br s, 2H, CH_2), 4.48 (br s, 2H, CH_2), 4.35 (br s, 2H, CH_2), 3.82 (s, 3H, ArOCH_3), 3.73 (s, 3H, C1OCH_3), and 2.40 (s, 3H, ArCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 159.7, 143.7, 143.0, 141.5, 141.3, 140.7, 136.0, 134.0, 131.5, 130.1, 130.0, 129.4, 127.8, 127.7, 114.1, 108.8, 93.1, 90.9, 80.4, 71.4, 71.1, 66.5, 57.6, 55.5, 54.6, 53.5, 53.0, 50.2, and 21.7 ppm.

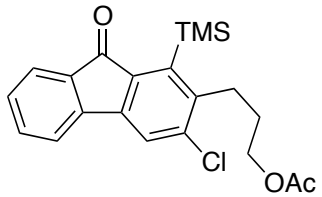
IR: 2946, 2837, 1612, 1513, 1459, 1440, 1344, 1249, 1163, 1097, 1068, 1036, 909, and 817 cm^{-1}.

HRMS (ESI-TOF): Calcd for $C_{35}H_{33}NNaO_6S^+$ $[M+Na]^+$ requires 618.1921; found 618.1915.

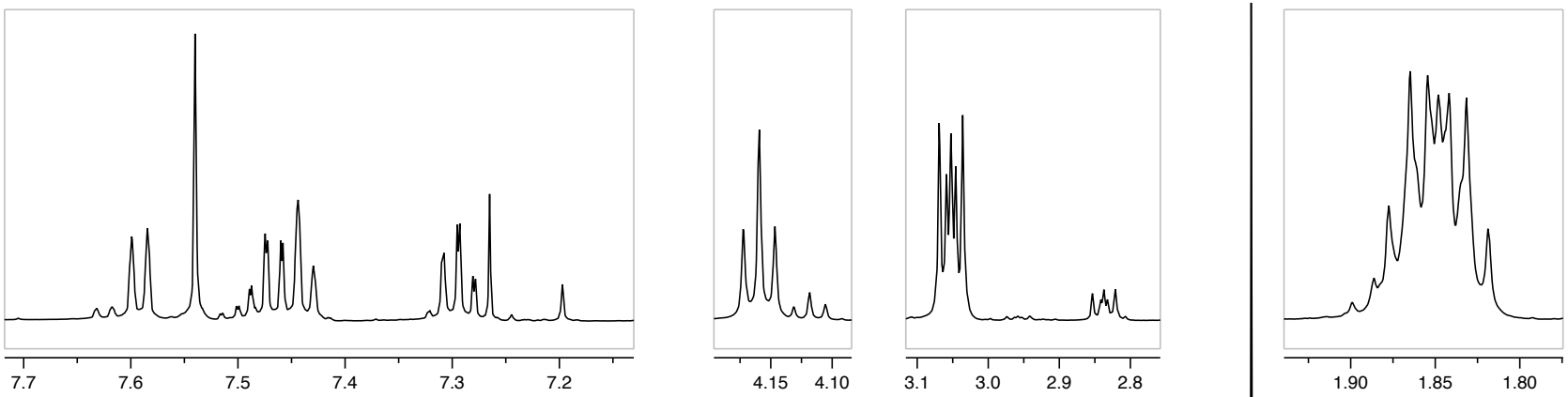
mp: 185–191 °C.

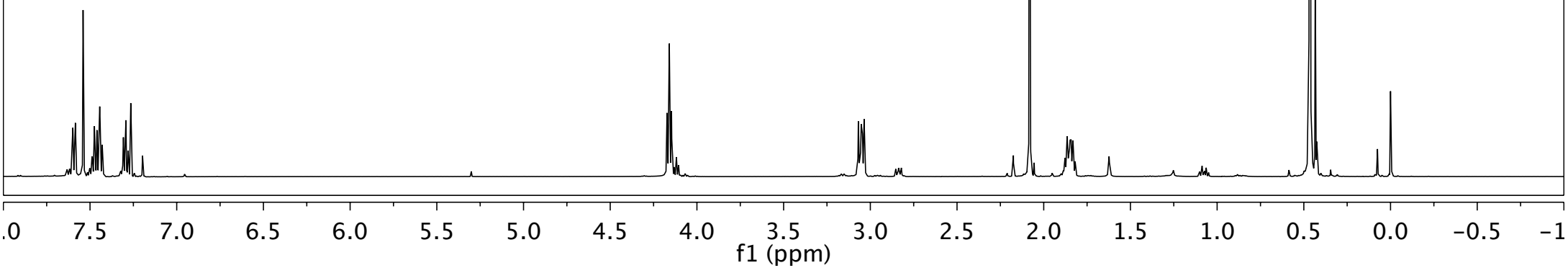
III. Copies of ^{1}H and ^{13}C NMR spectra for each isolated compound

CDCl3, 500 MHz

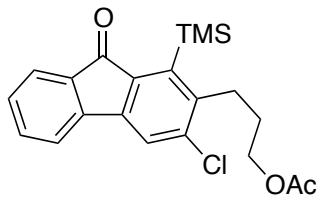


4a



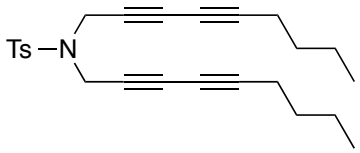


CDCl3, 125 MHz

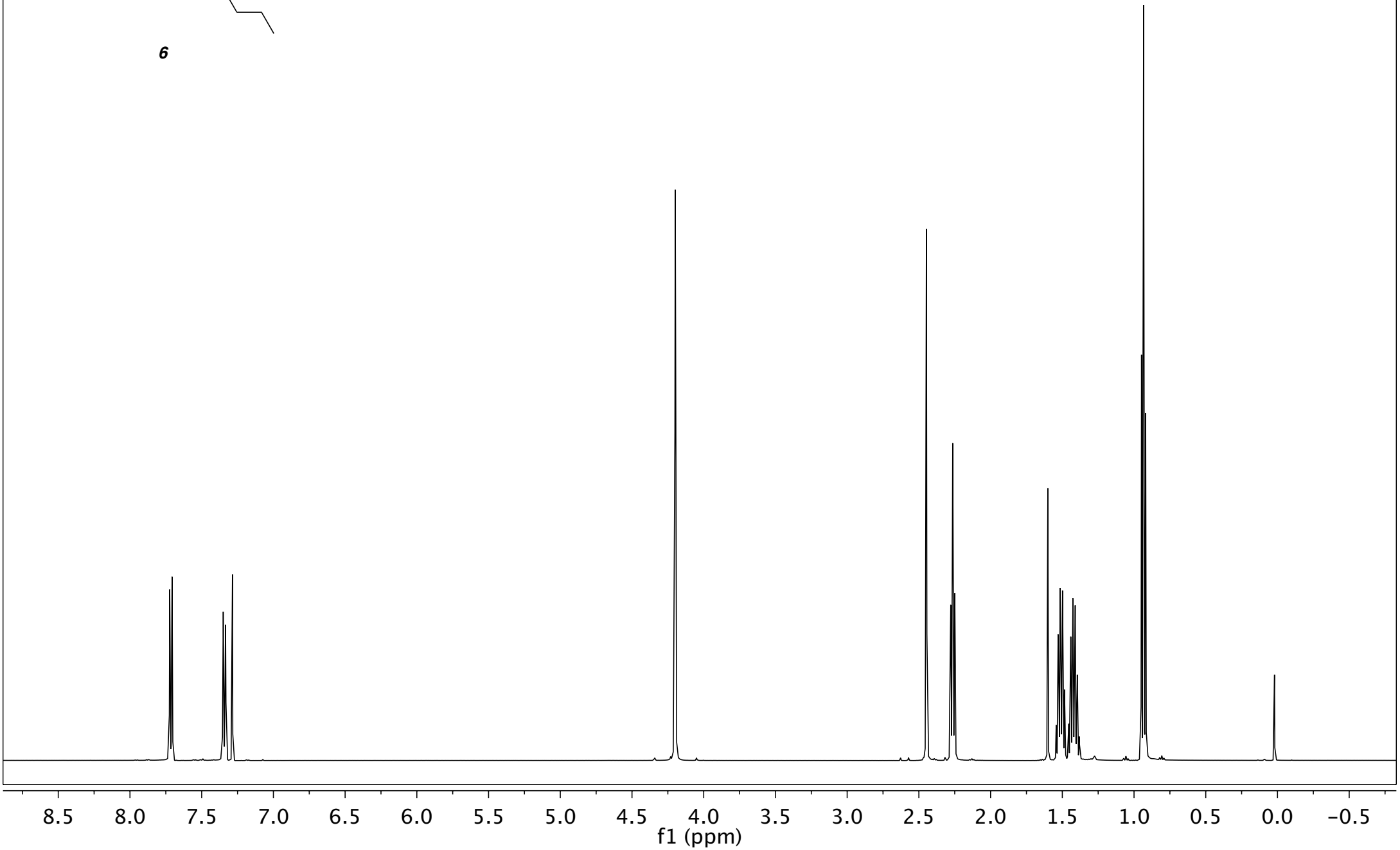


4a

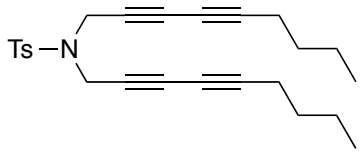
CDCl3, 500 MHz



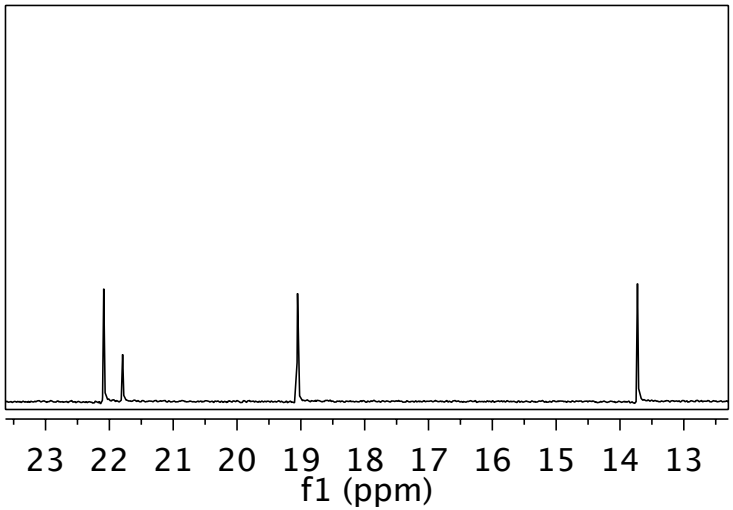
6

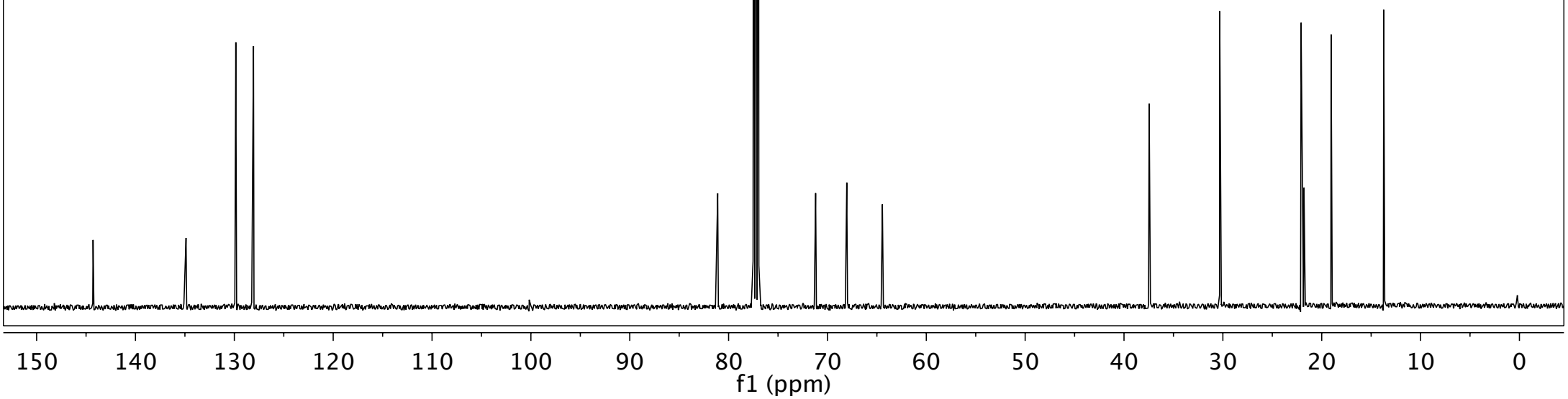


CDCl3, 125 MHz

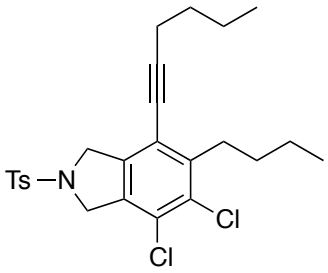


6

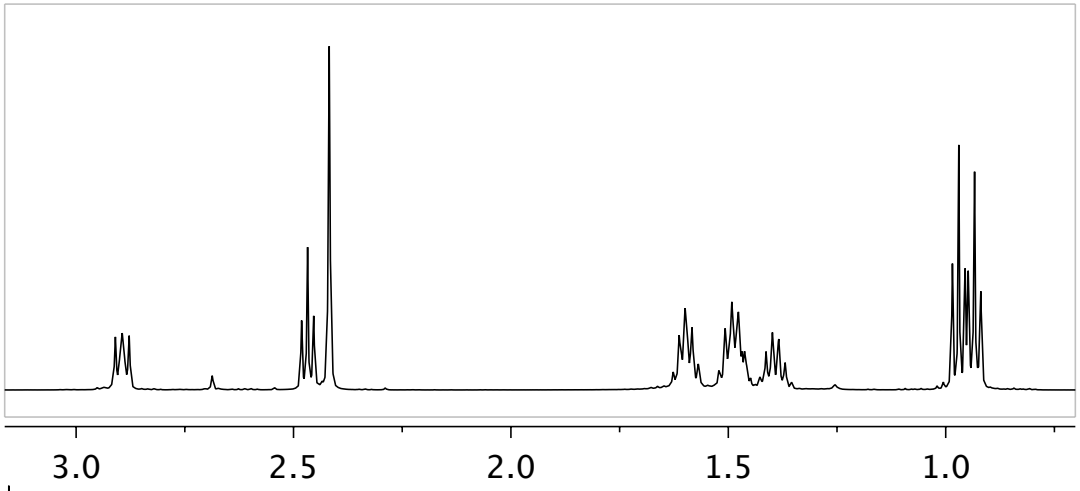




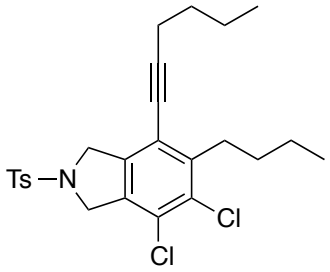
CDCl3, 500 MHz



7

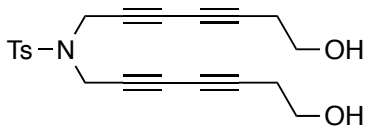


CDCl3, 500 MHz

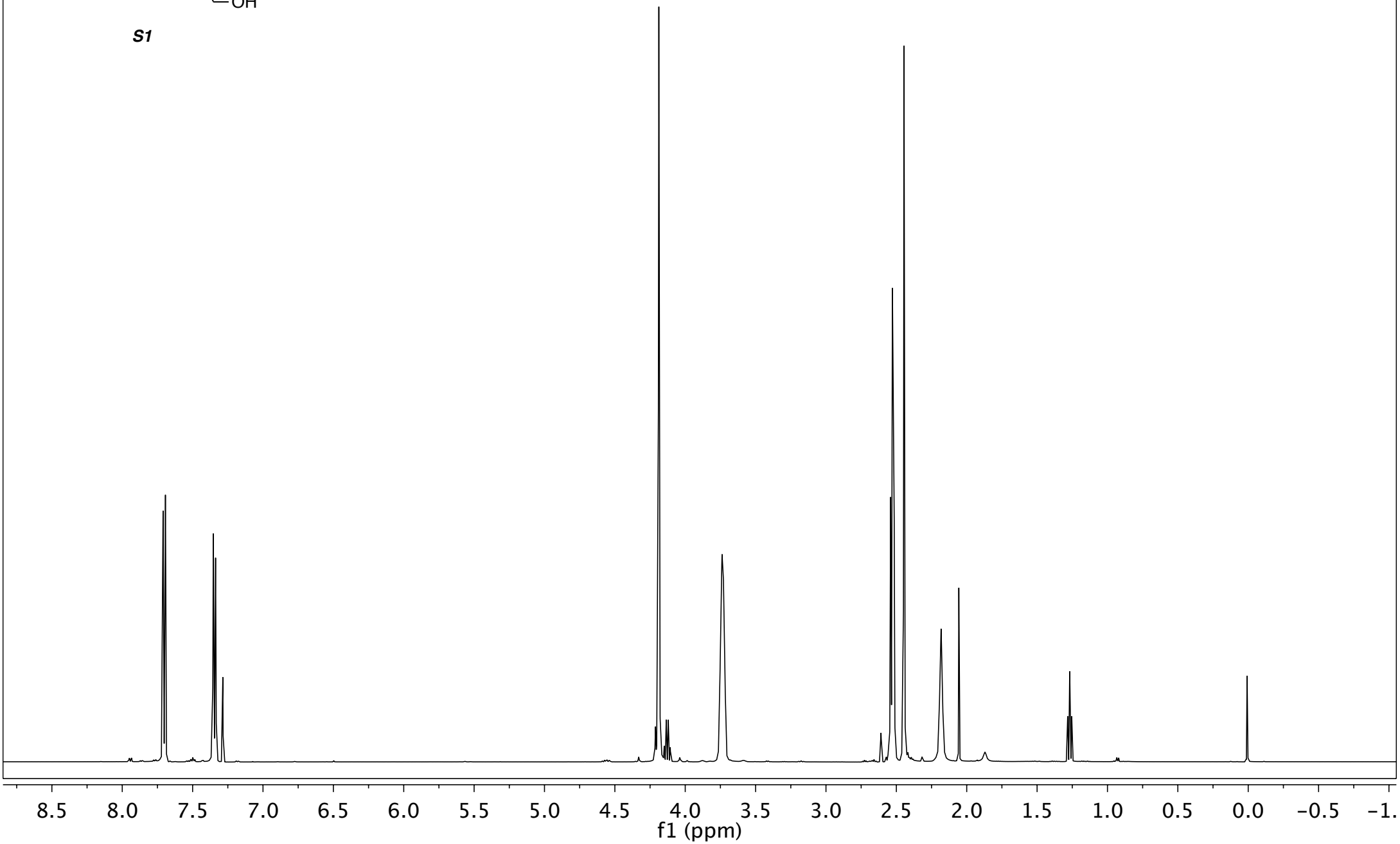


7

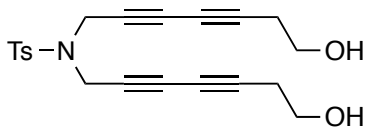
CDCl3, 500 MHz



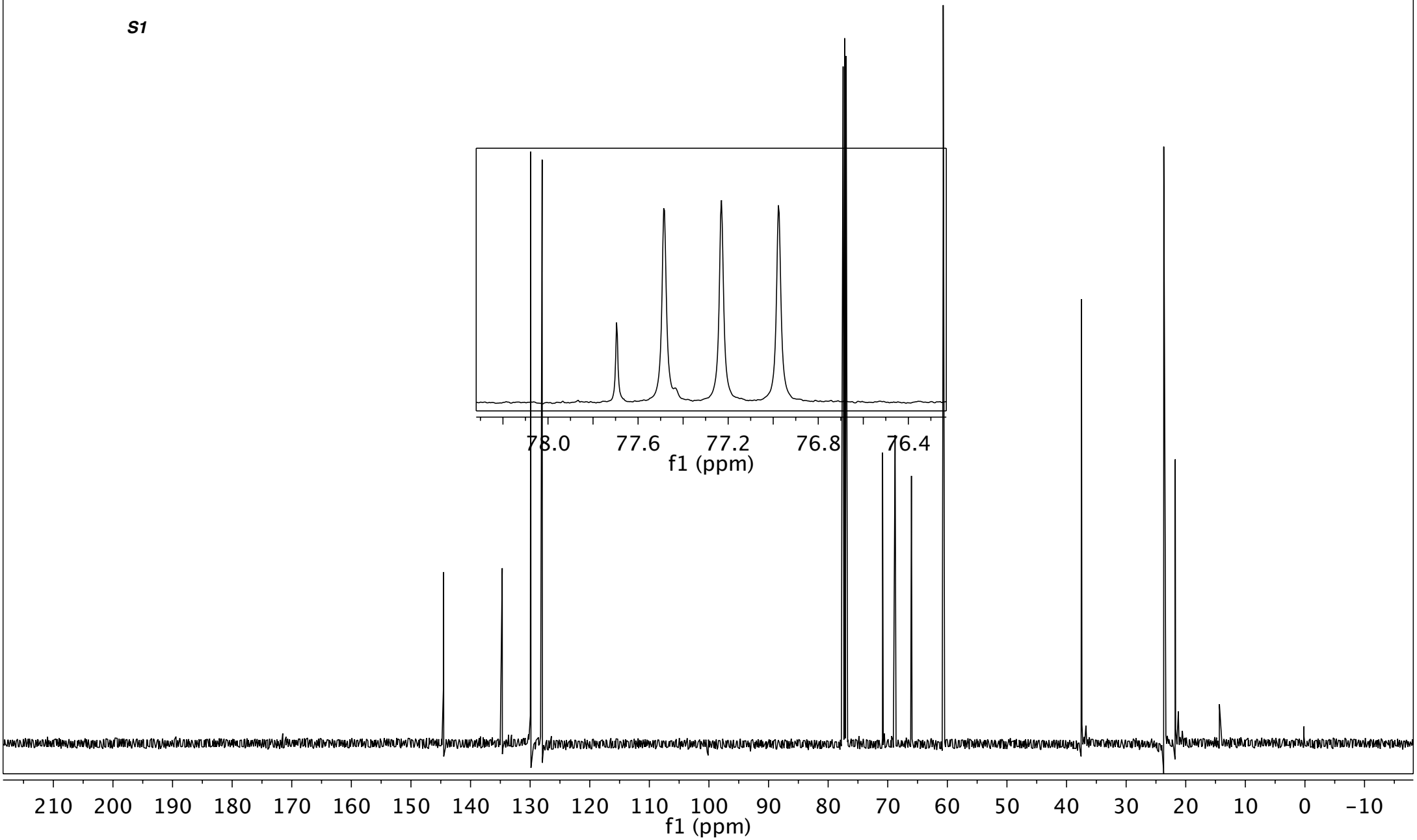
S1



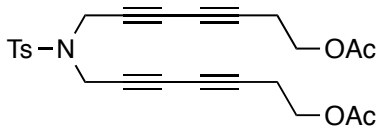
CDCl3, 125 MHz



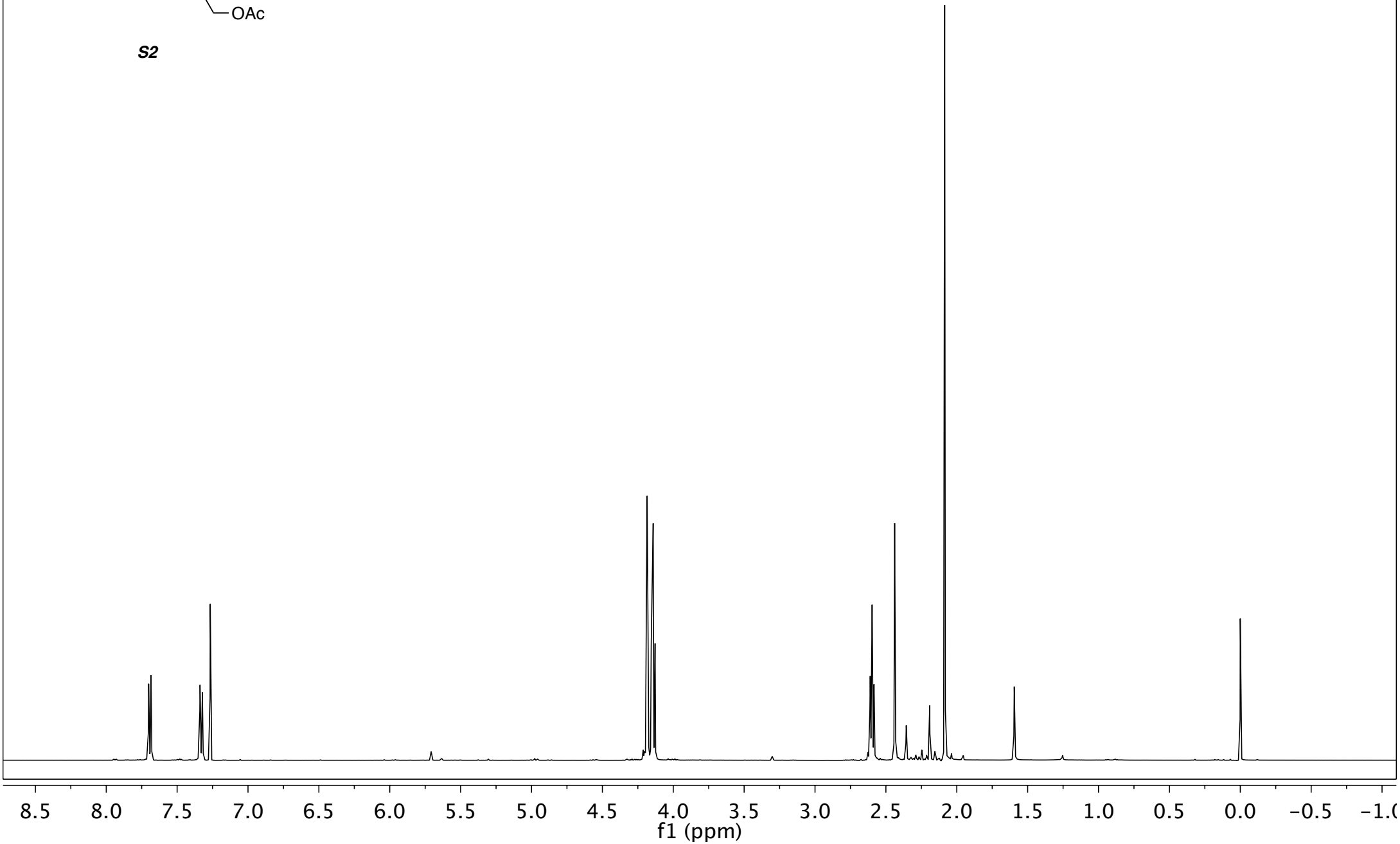
S1



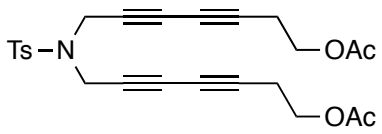
CDCl3, 500 MHz



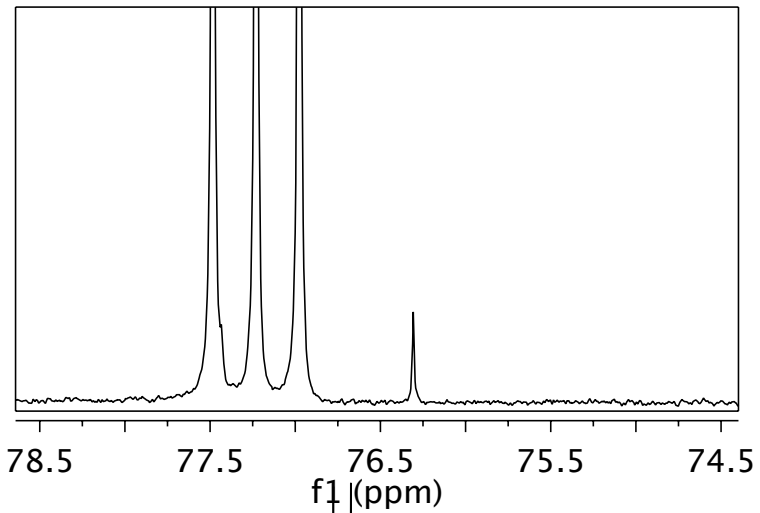
S2



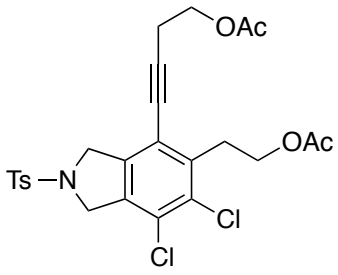
CDCl3, 125 MHz



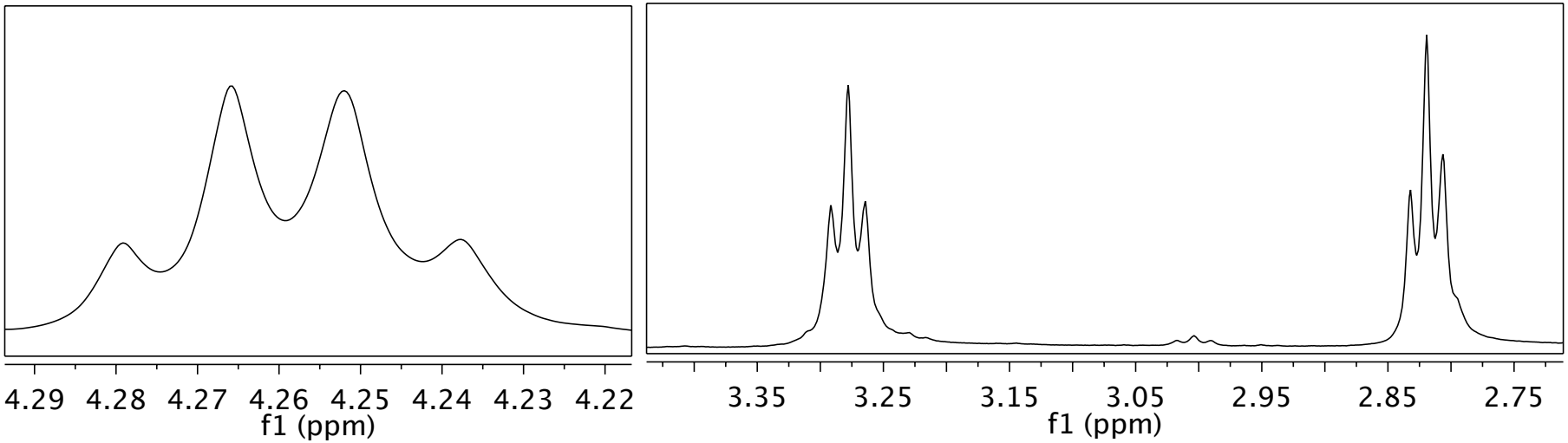
S2

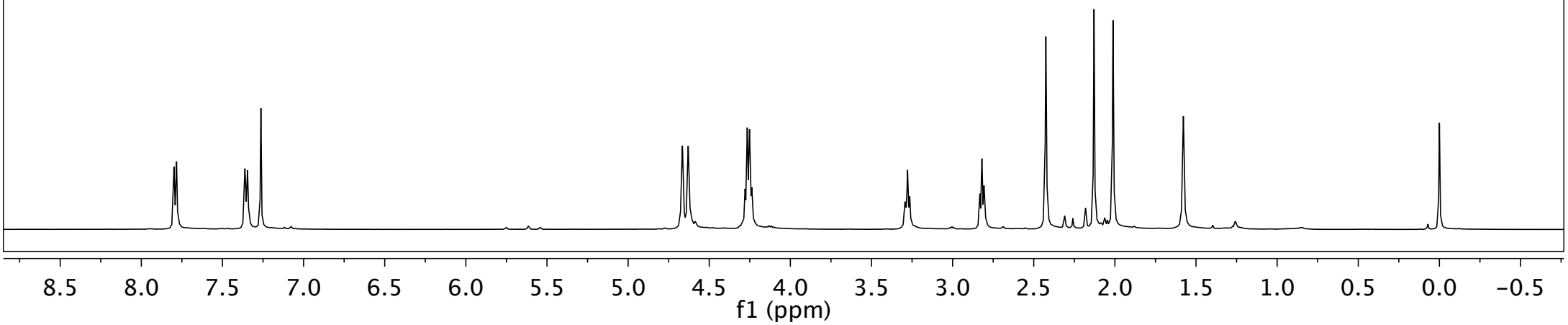


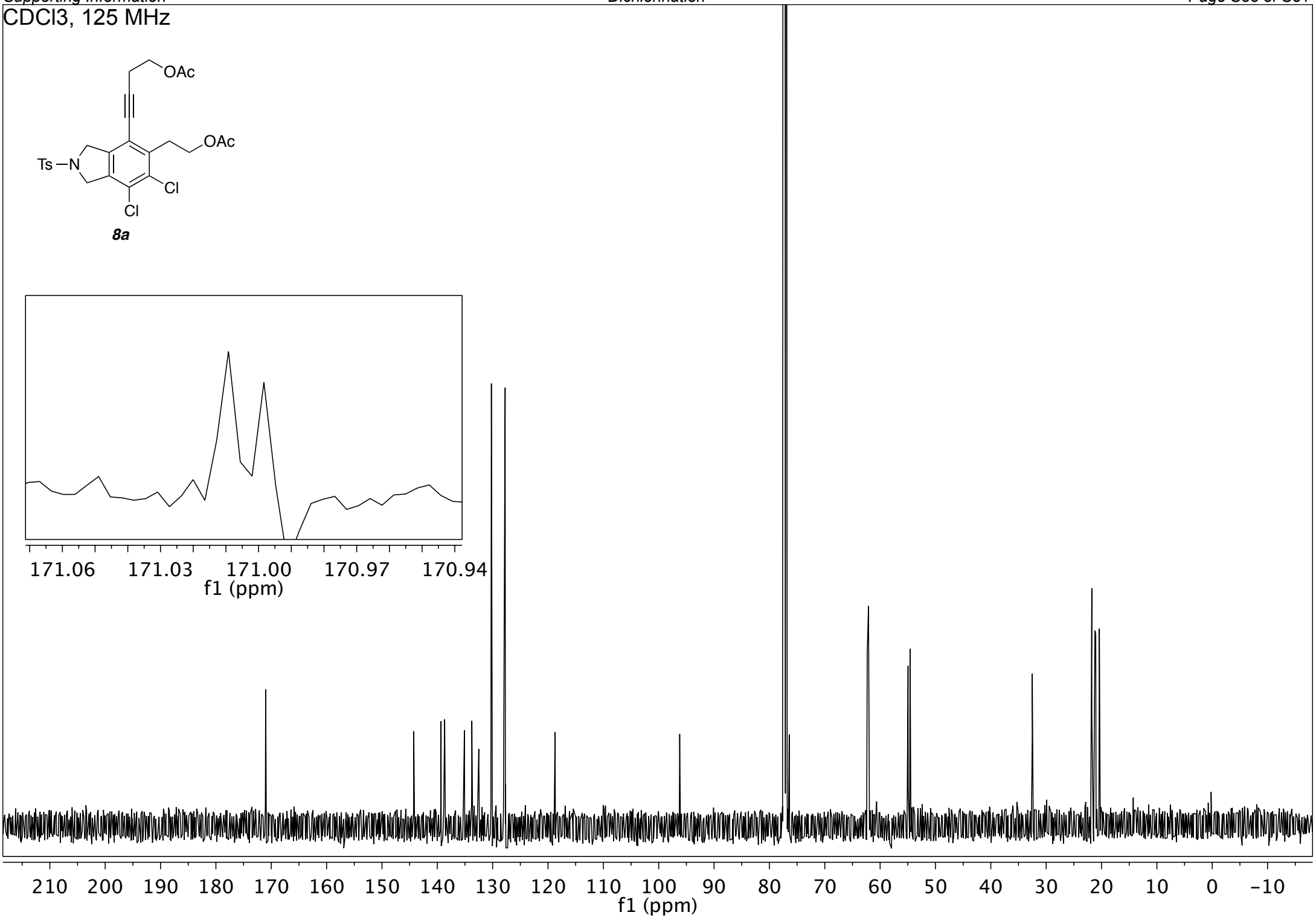
CDCl3, 500 MHz



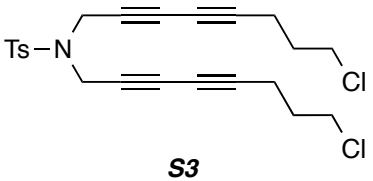
8a



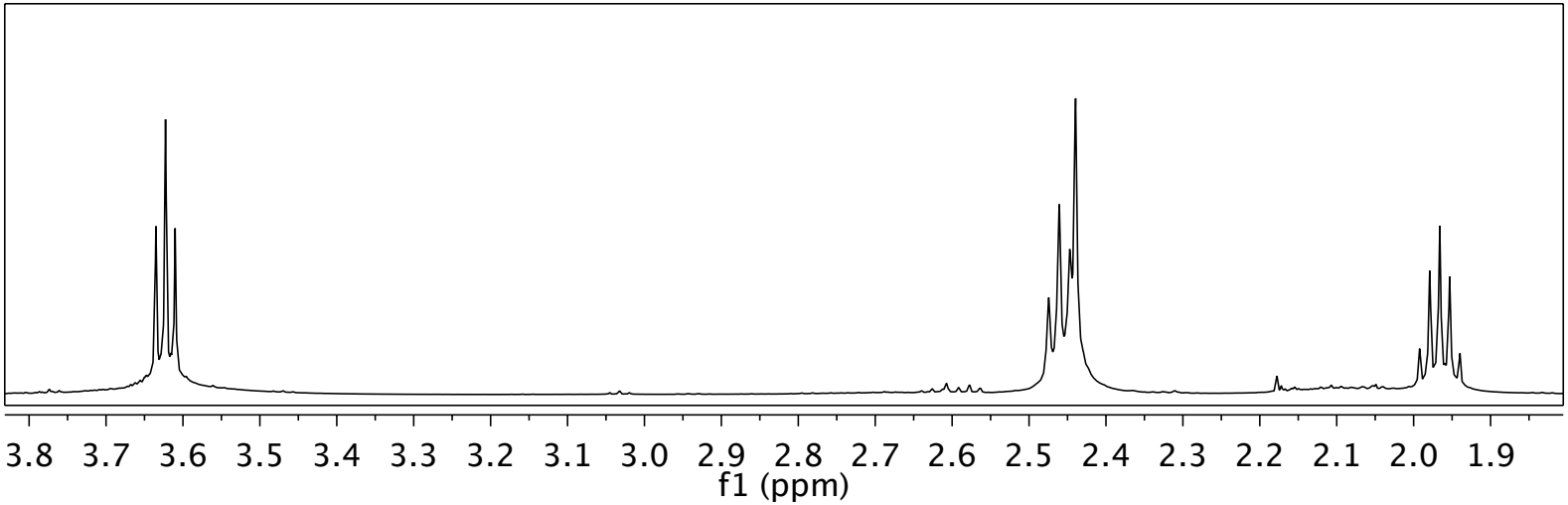


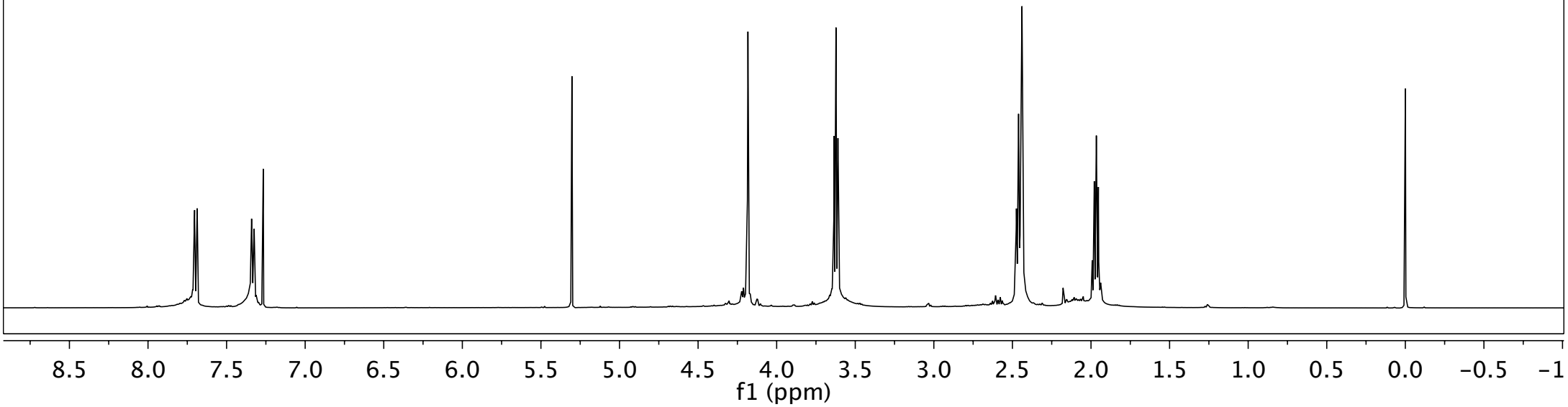

CDCl3, 125 MHz
OAc
OAc
Ts—N
Cl
Cl
8a
171.06
171.03
171.00
170.97
170.94
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

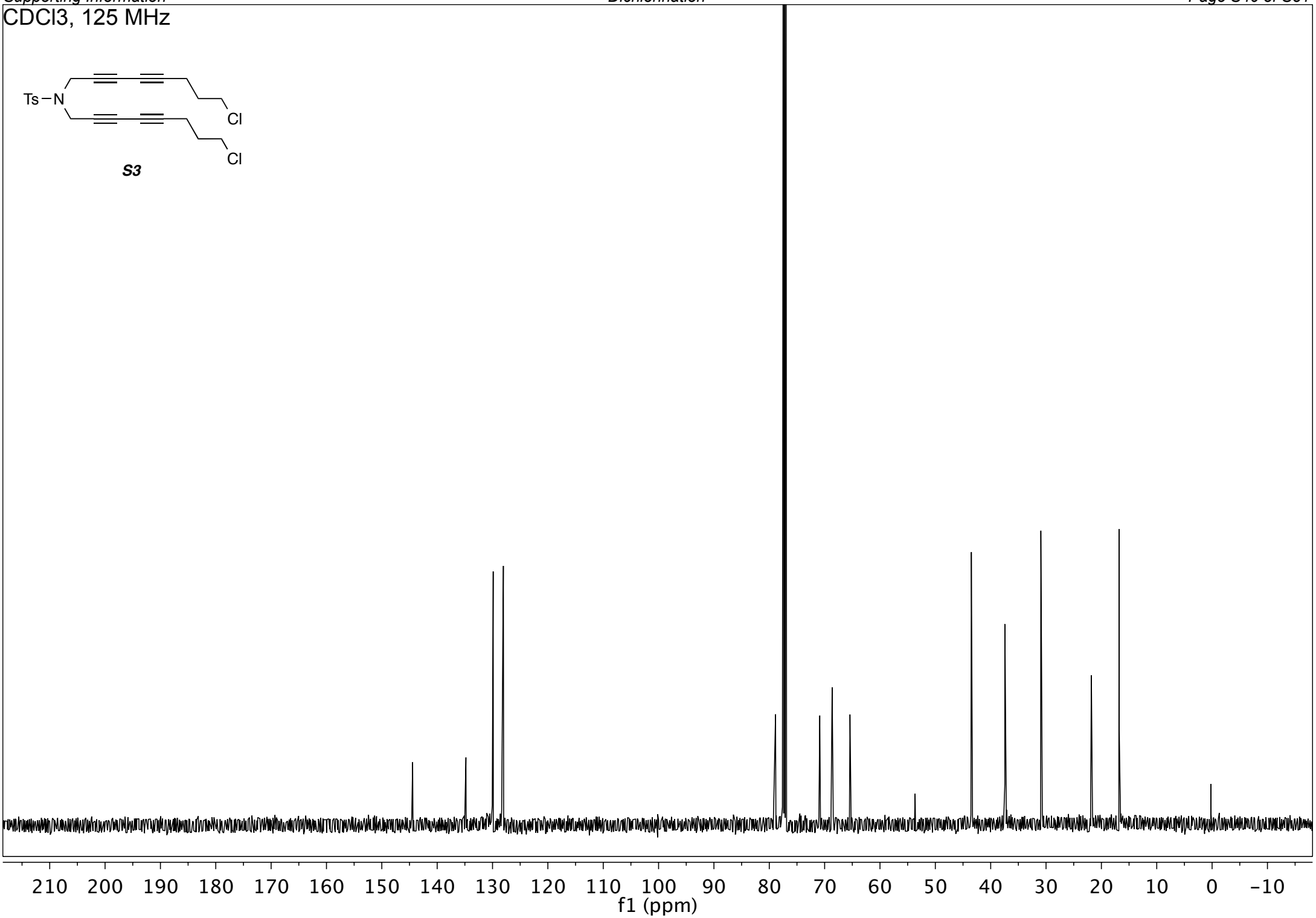
CDCl3, 500 MHz



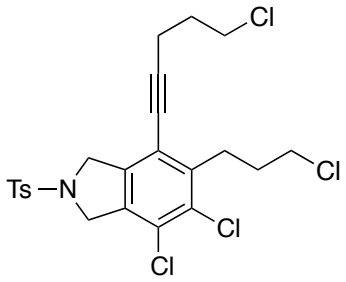
S3



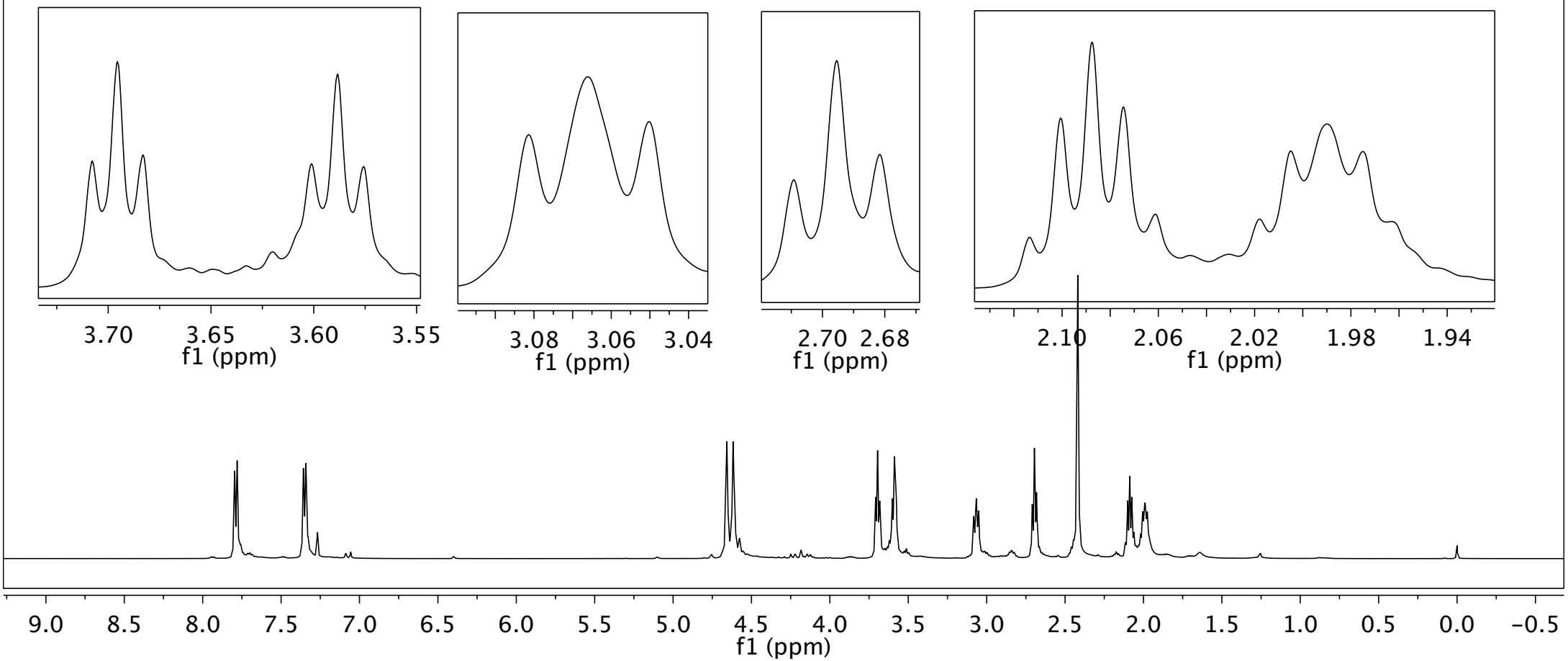



CDCl3, 125 MHz
Ts−N
Cl
Cl
S3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

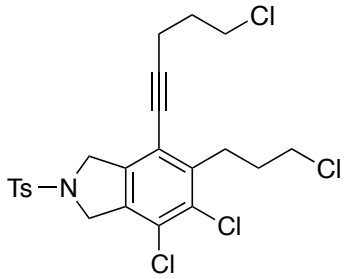
CDCl3, 500 MHz



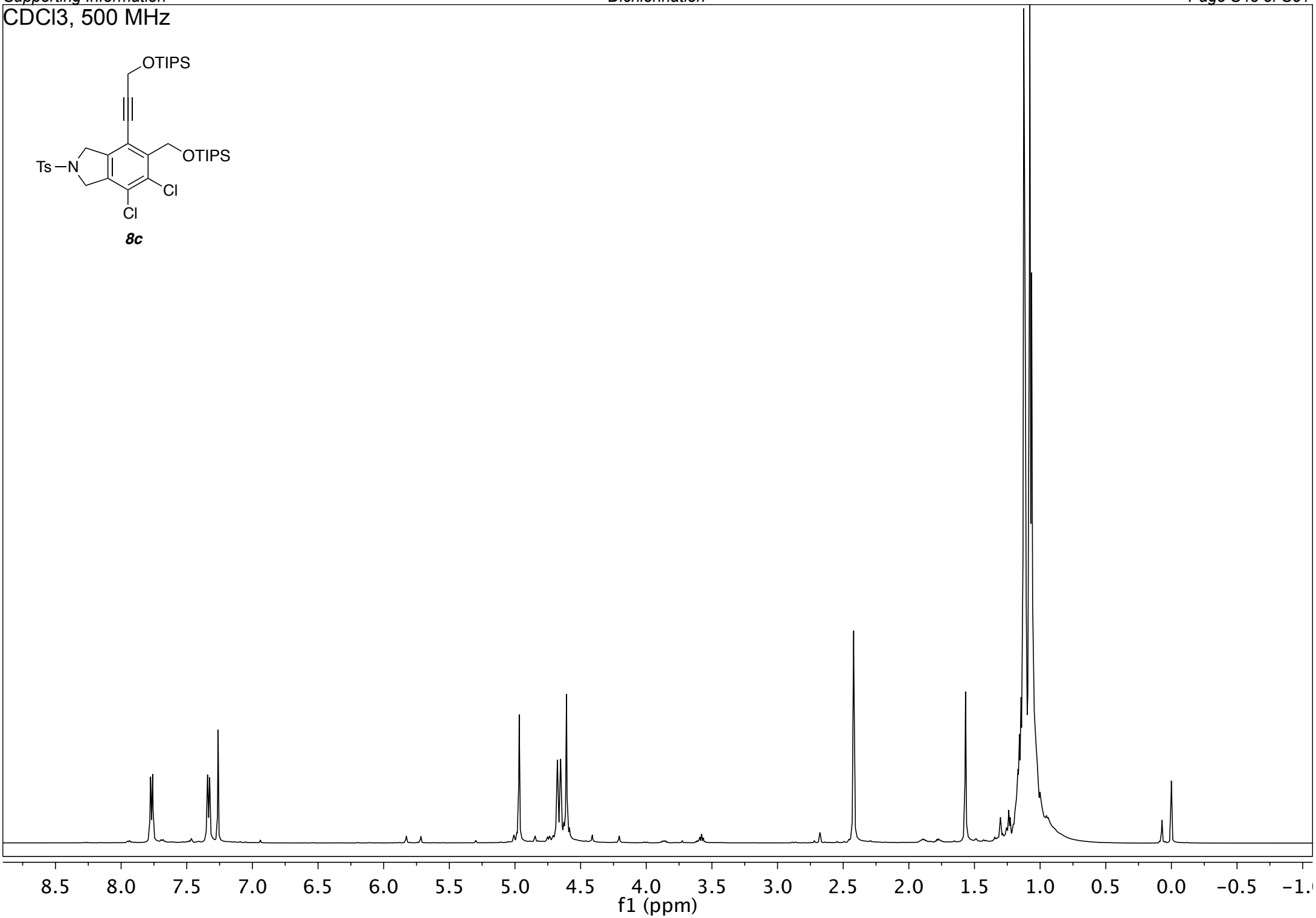
8b



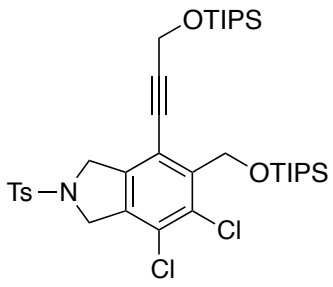
CDCl3, 125 MHz



8b

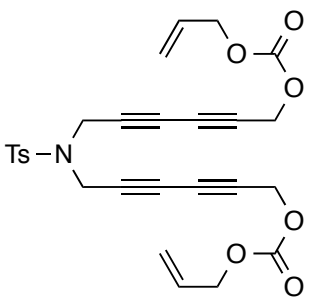

CDCl3, 500 MHz
OTIPS
OTIPS
Ts—N
Cl
Cl
8c
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

CDCl3, 125 MHz

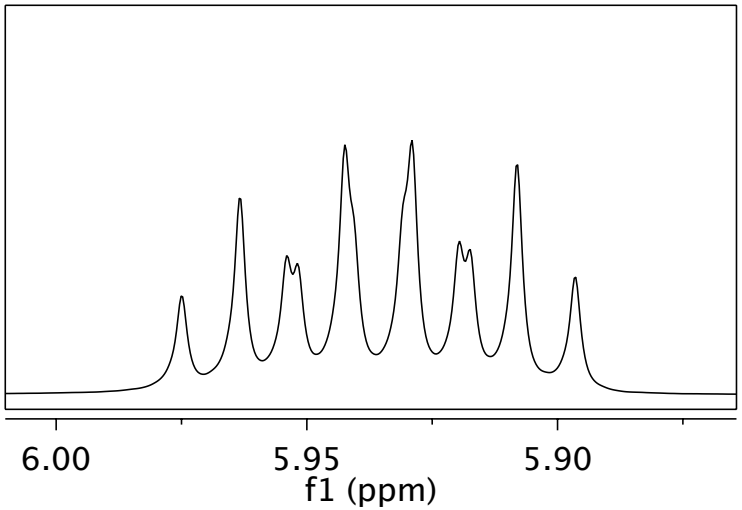


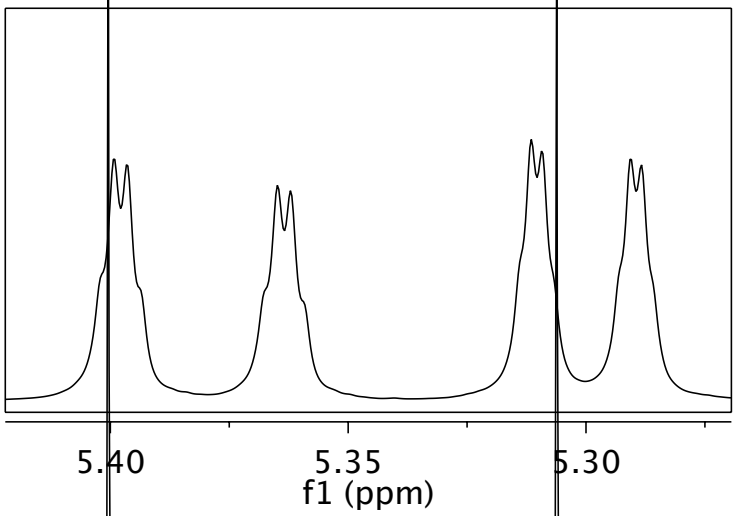
8c

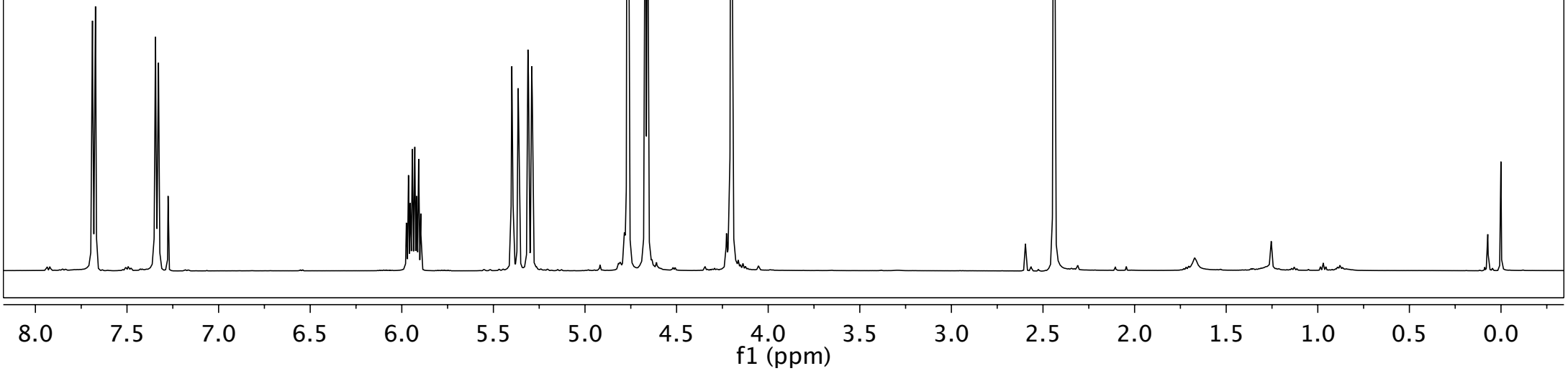
CDCl3, 500 MHz



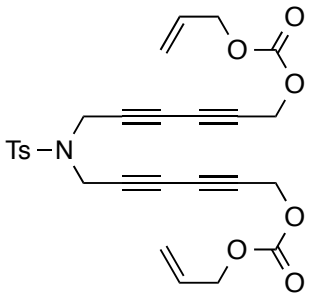
S4



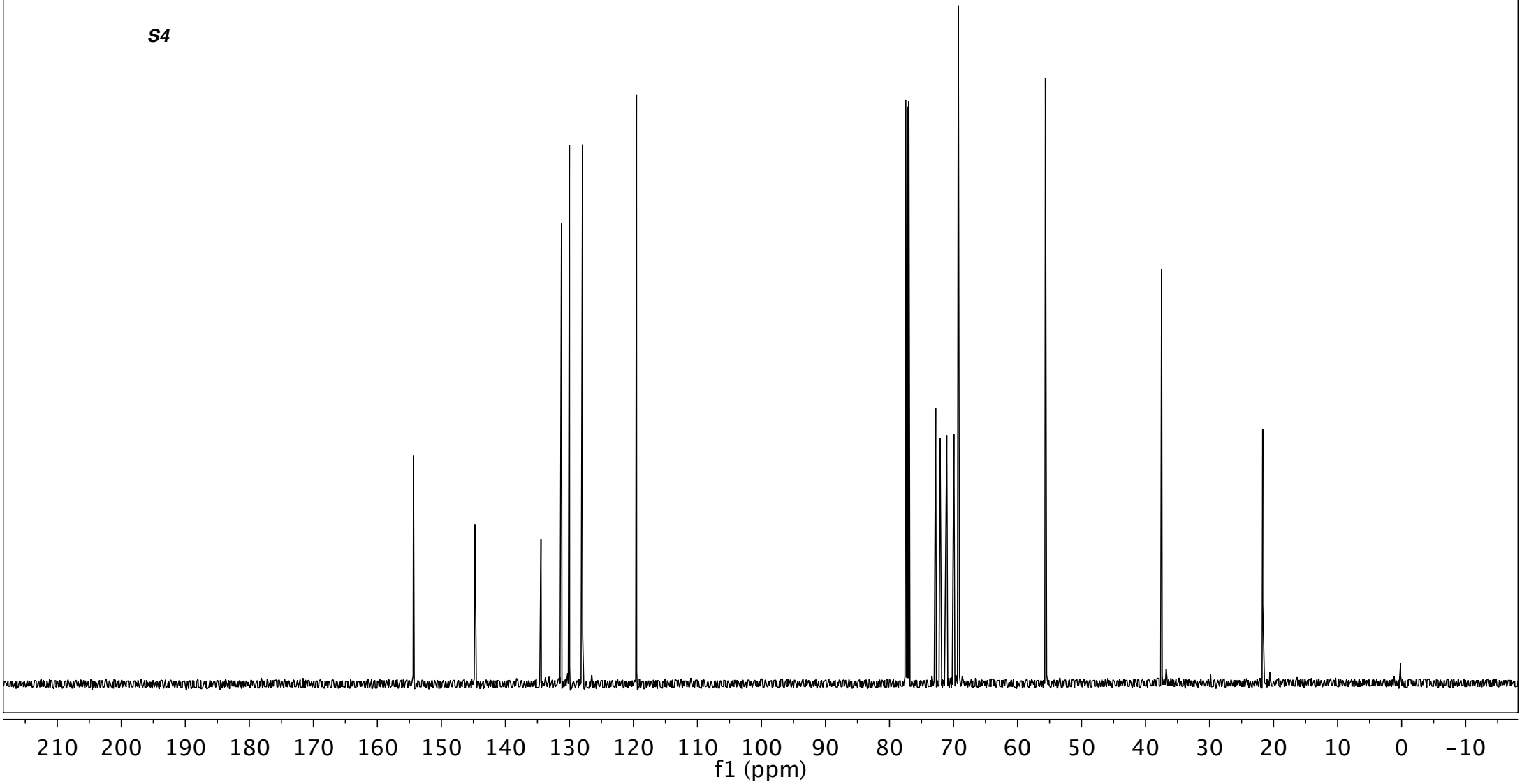


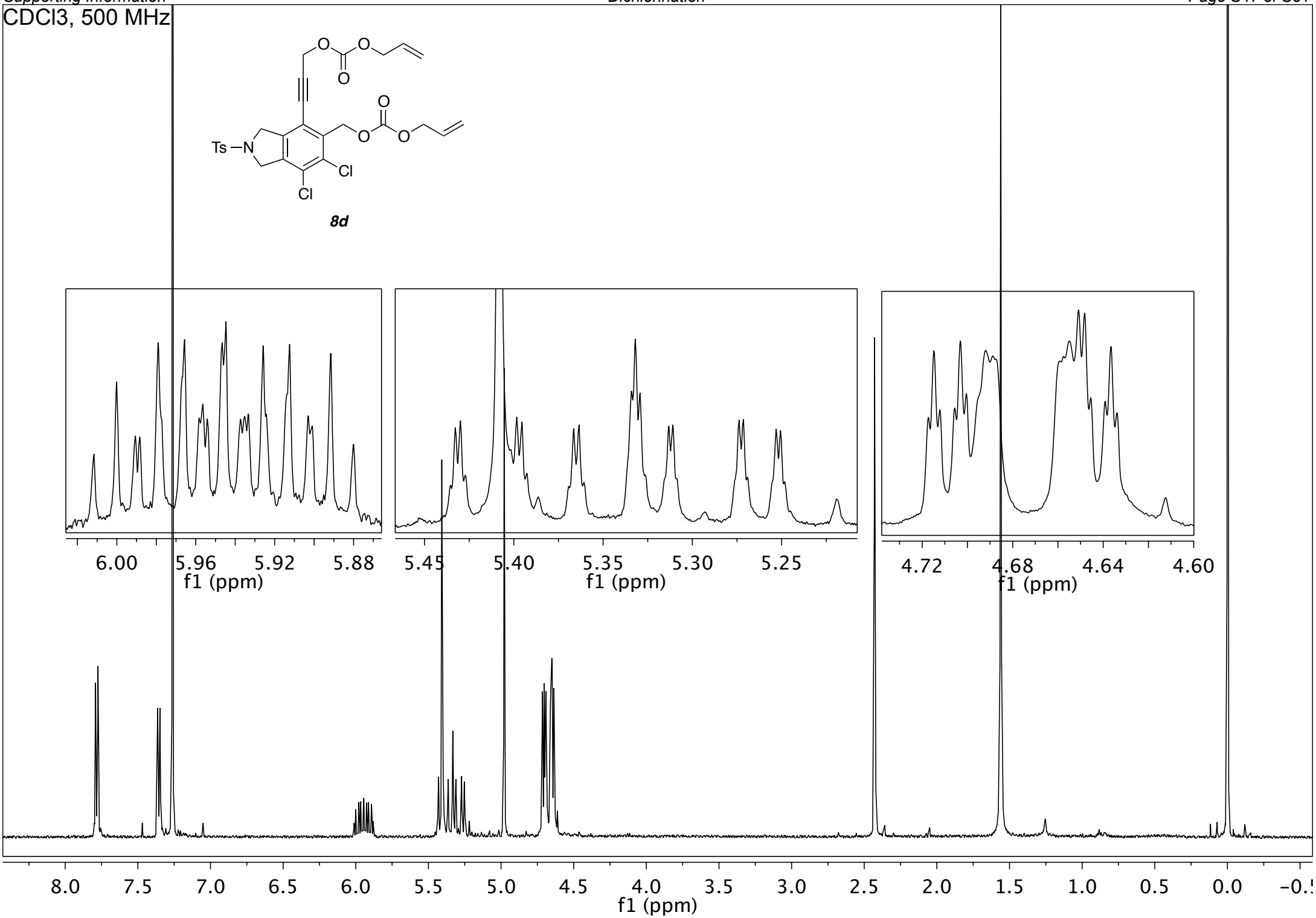


CDCl3, 125 MHz

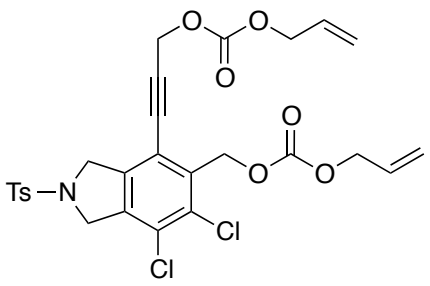


S4

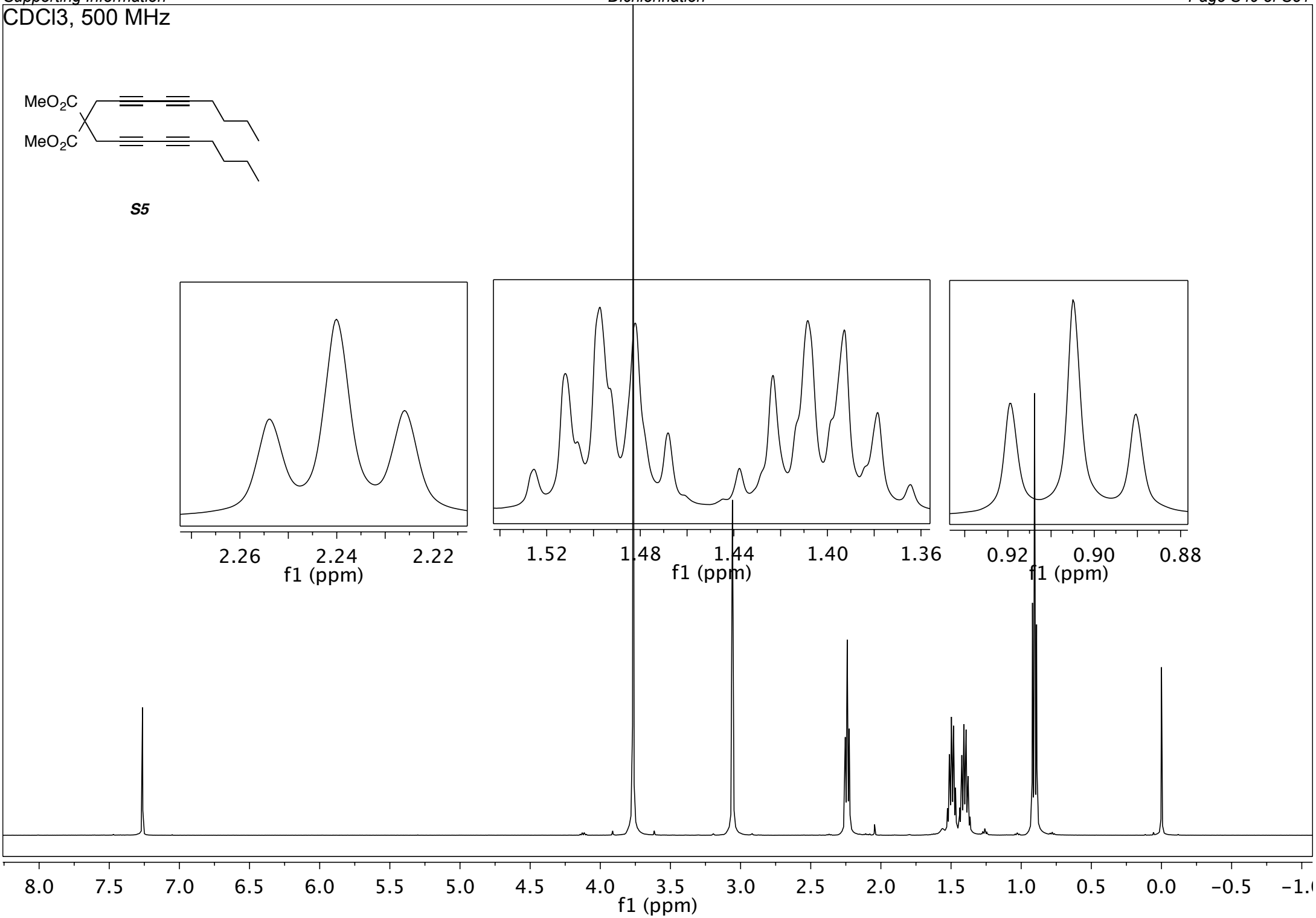



CDCl3, 500 MHz
Ts
N
Cl
Cl
8d
6.00
5.96
5.92
5.88
f1 (ppm)
5.45
5.40
5.35
5.30
5.25
f1 (ppm)
4.72
4.68
4.64
4.60
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

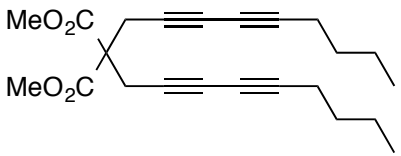
CDCl3, 125 MHz



8d

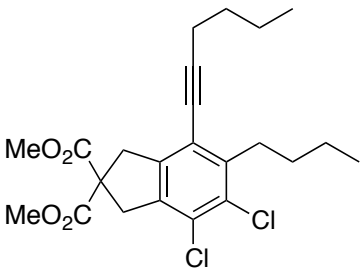

CDCl3, 500 MHz
MeO2C
MeO2C
S5
2.26
2.24
2.22
f1 (ppm)
1.52
1.48
1.44
1.40
1.36
f1 (ppm)
0.92
0.90
0.88
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

CDCl3, 125 MHz



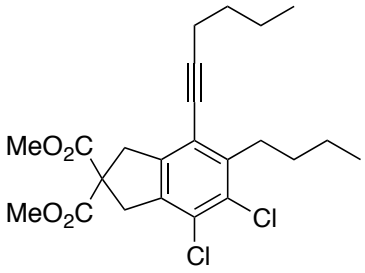
S5

CDCl3, 500 MHz

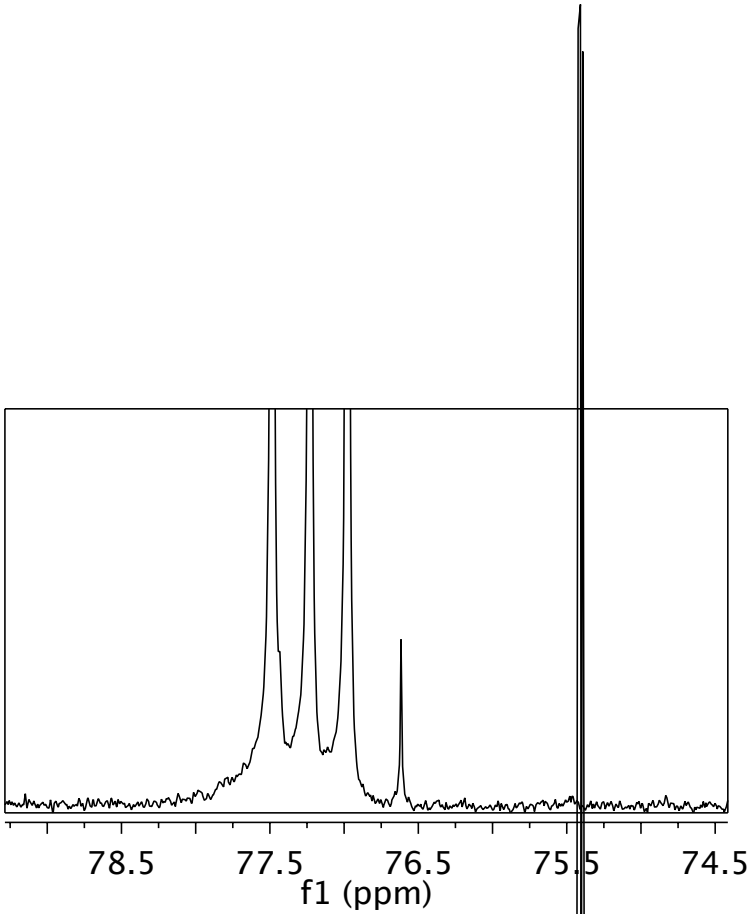


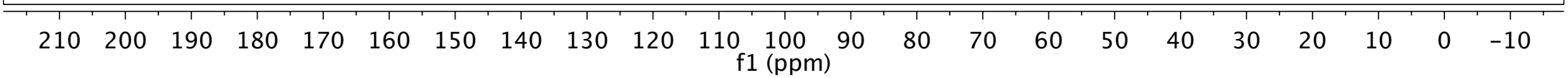
8e

CDCl3, 125 MHz

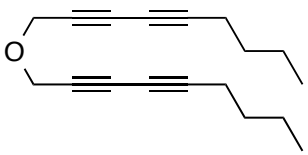


8e

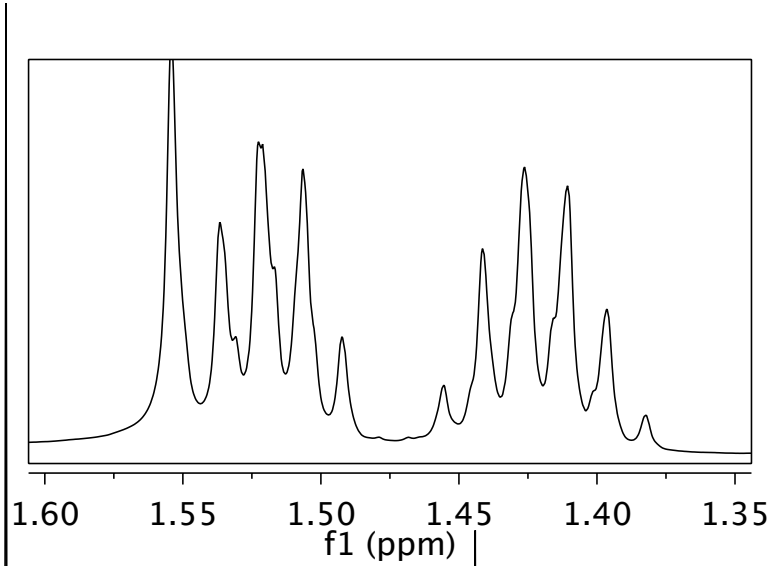




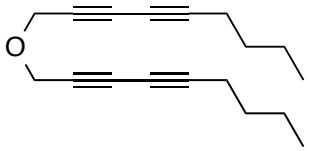
CDCl3, 500 MHz



S6

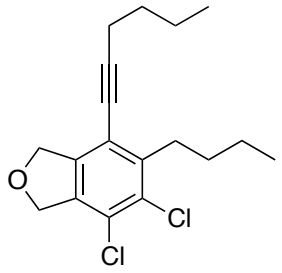


CDCl3, 125 MHz



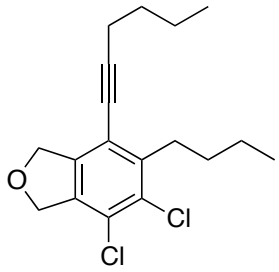
S6

CDCl3, 500 MHz

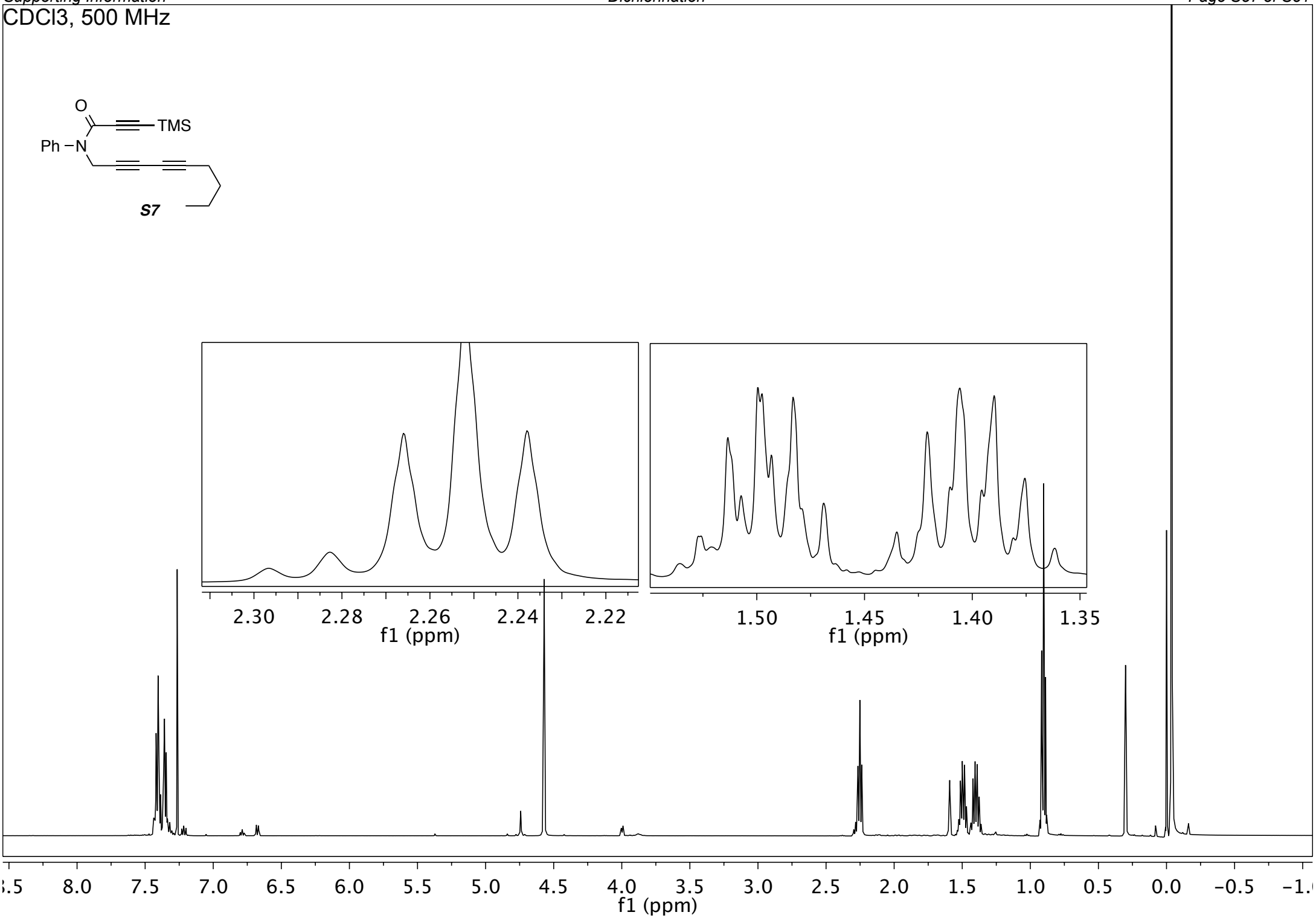


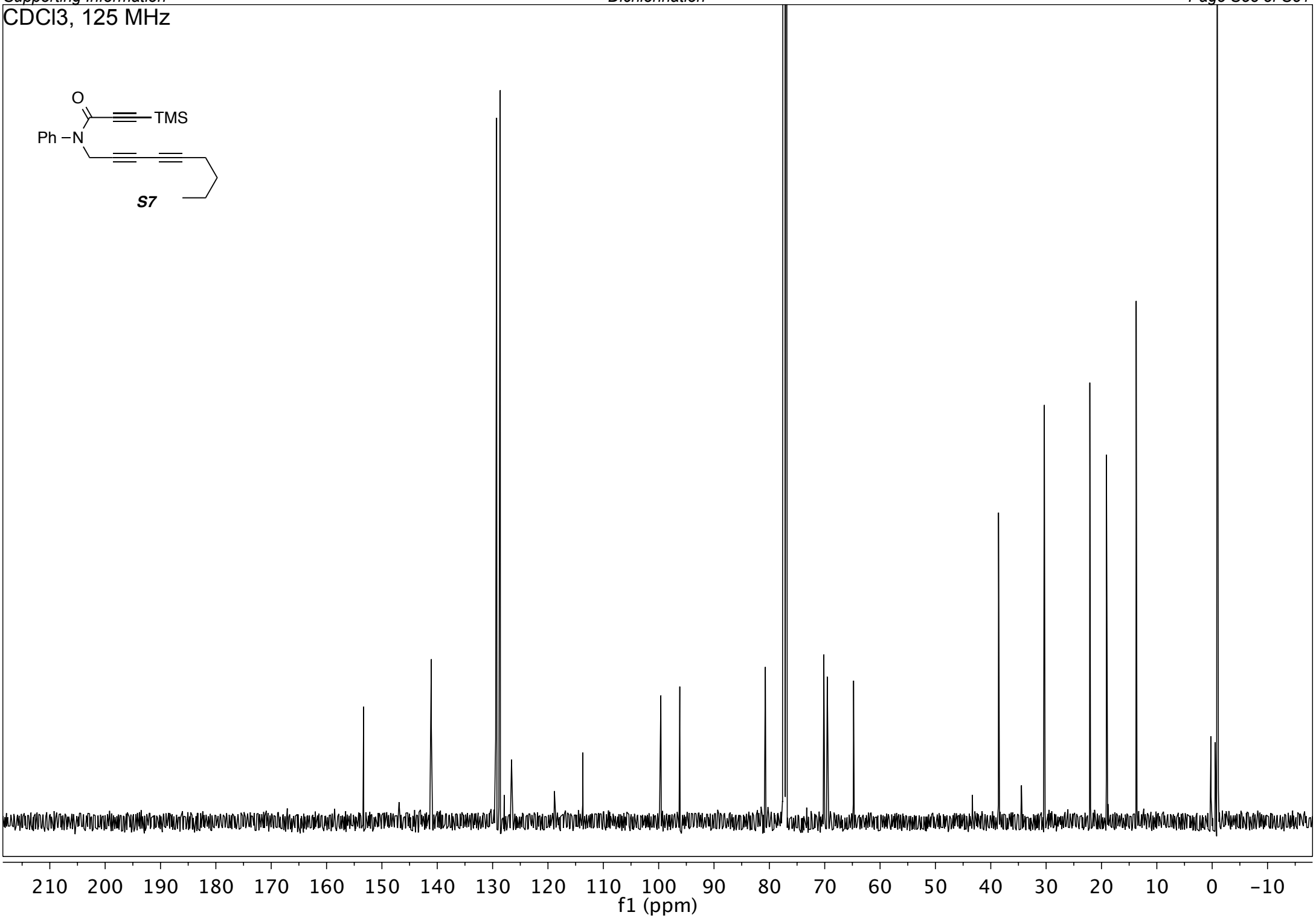
8f

CDCl3, 125 MHz

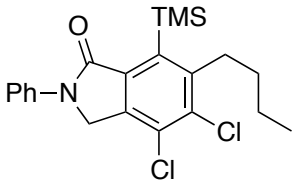


8f

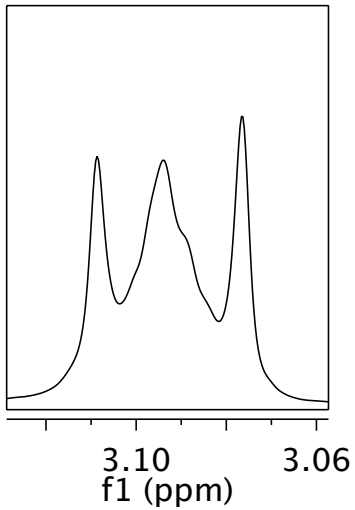

CDCl3, 500 MHz
O
TMS
Ph –N
S7
2.30
2.28
2.26
2.24
2.22
f1 (ppm)
1.50
1.45
1.40
1.35
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)


CDCl3, 125 MHz
O
TMS
Ph –N
S7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

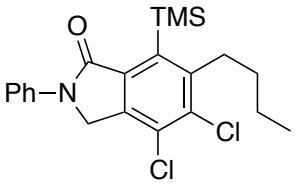
CDCl3, 500 MHz



8g

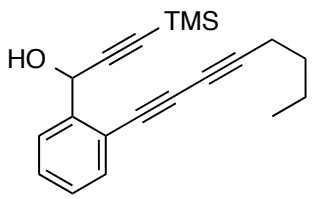


CDCl3, 125 MHz

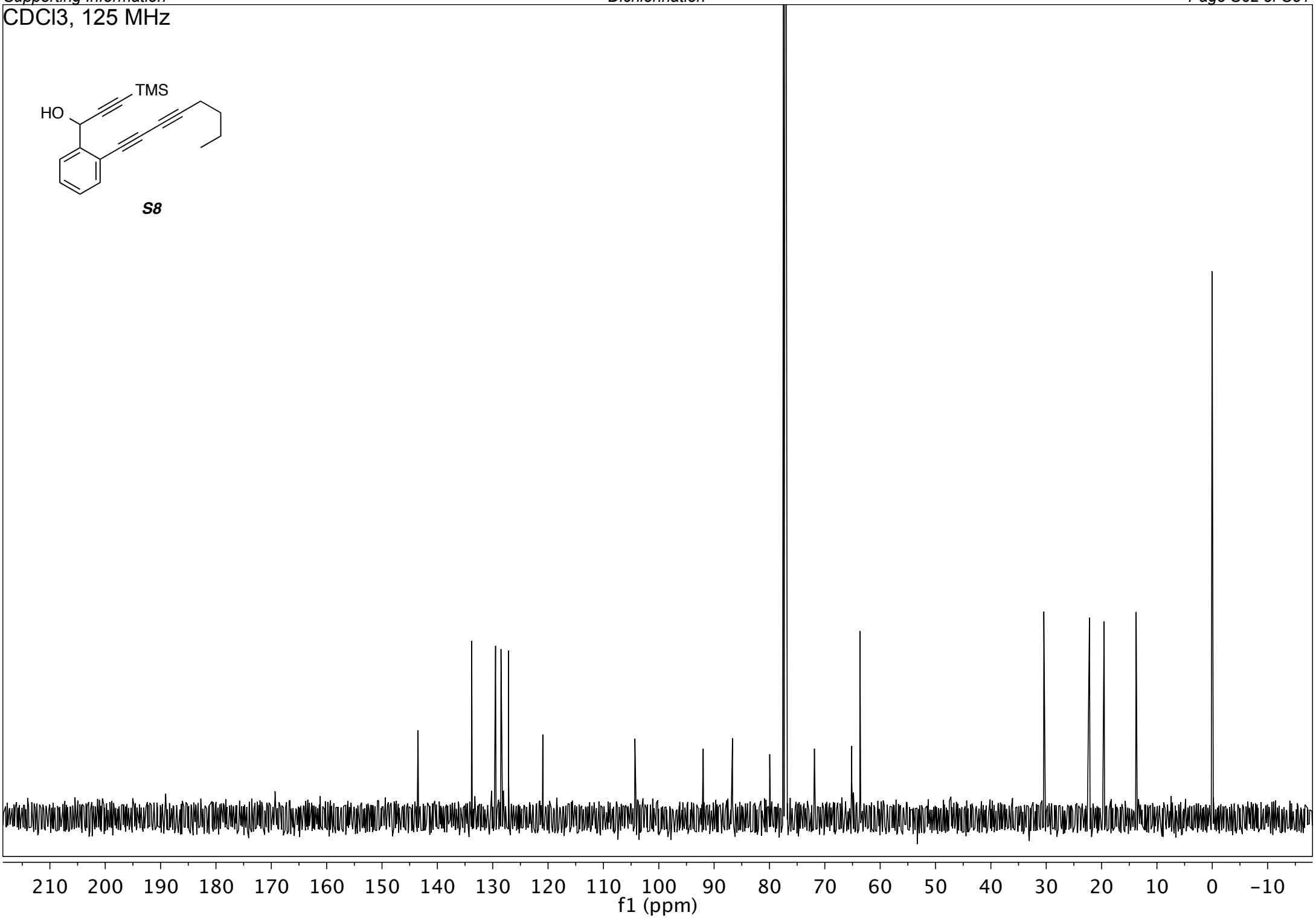


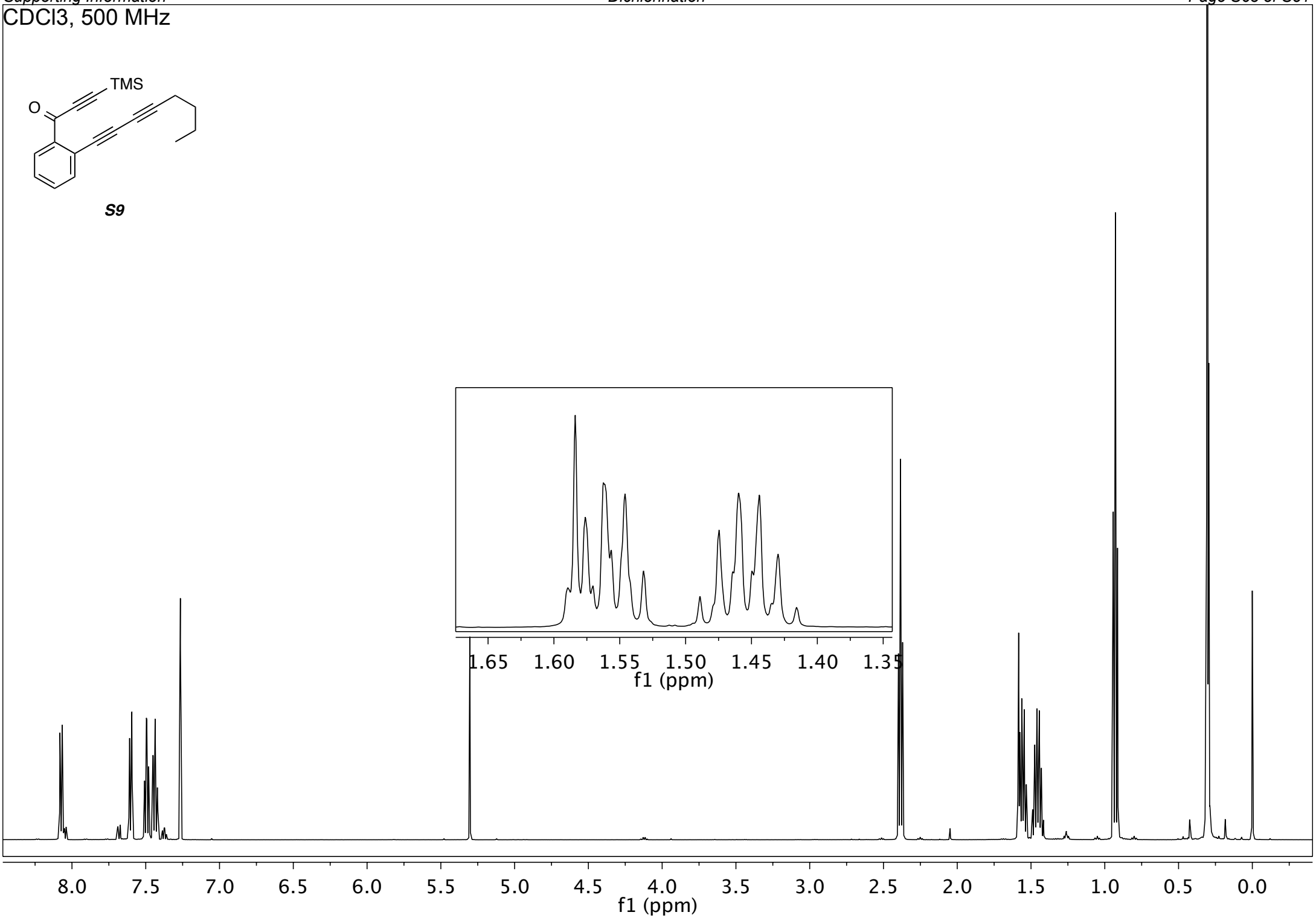
8g

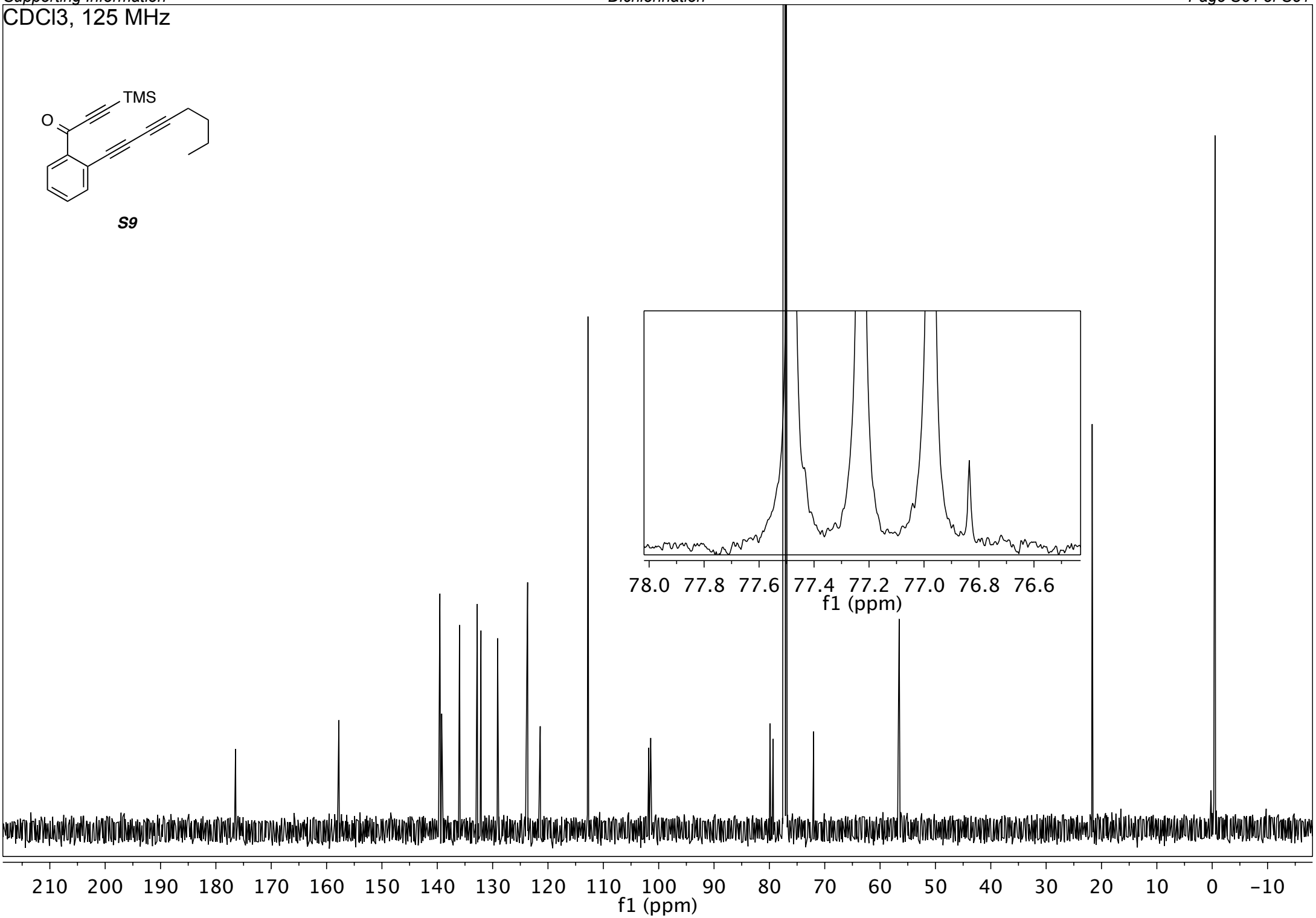
CDCl3, 500 MHz



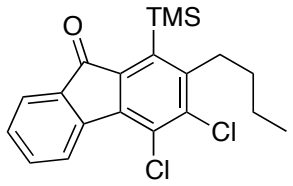
S8


CDCl3, 125 MHz
TMS
HO
S8
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

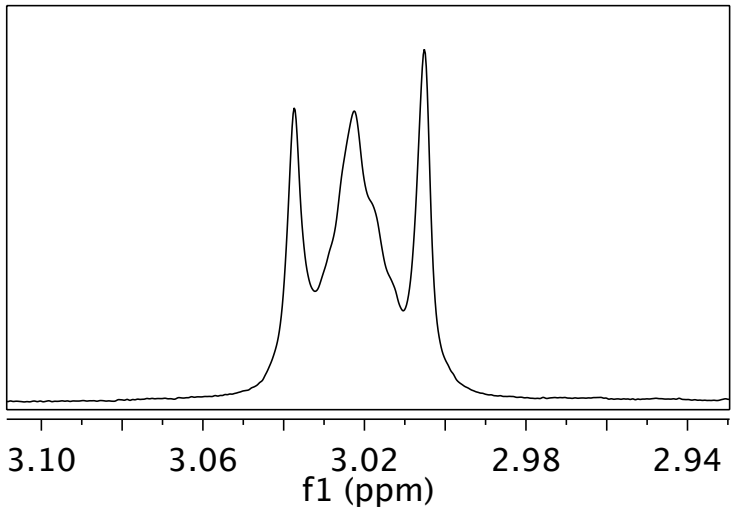

CDCl3, 500 MHz
TMS
O
S9
1.65 1.60 1.55 1.50 1.45 1.40 1.35
f1 (ppm)
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


CDCl3, 125 MHz
TMS
O
S9
78.0 77.8 77.6 77.4 77.2 77.0 76.8 76.6
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

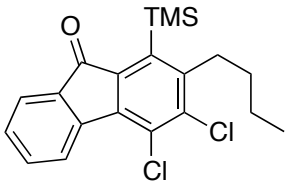
CDCl3, 500 MHz



8h



CDCl3, 125 MHz



8h

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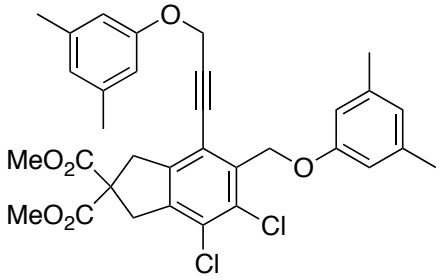
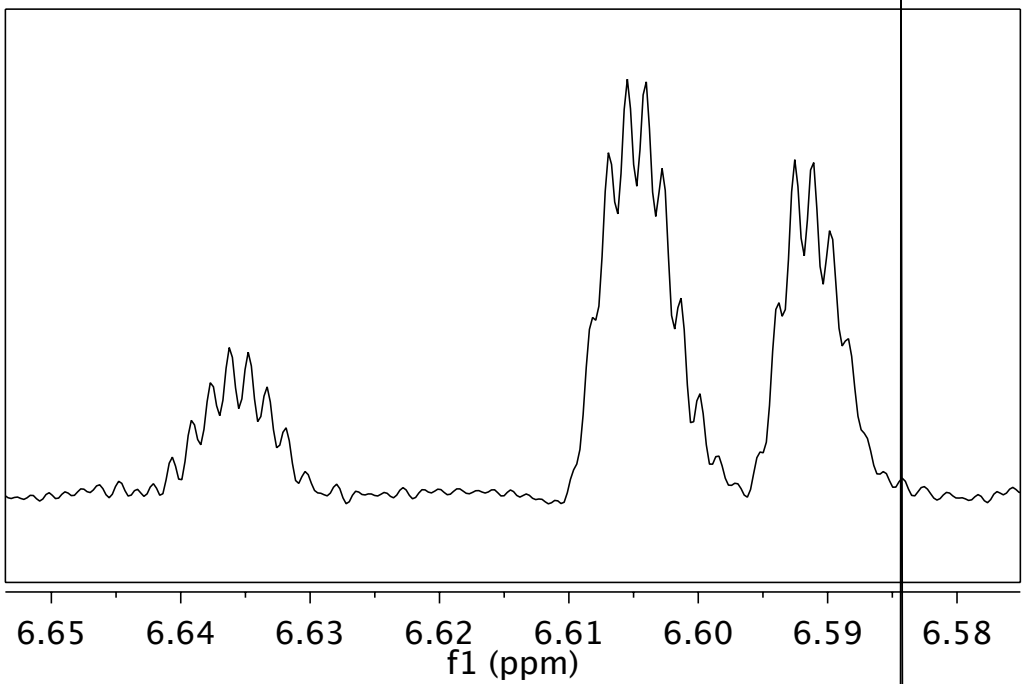
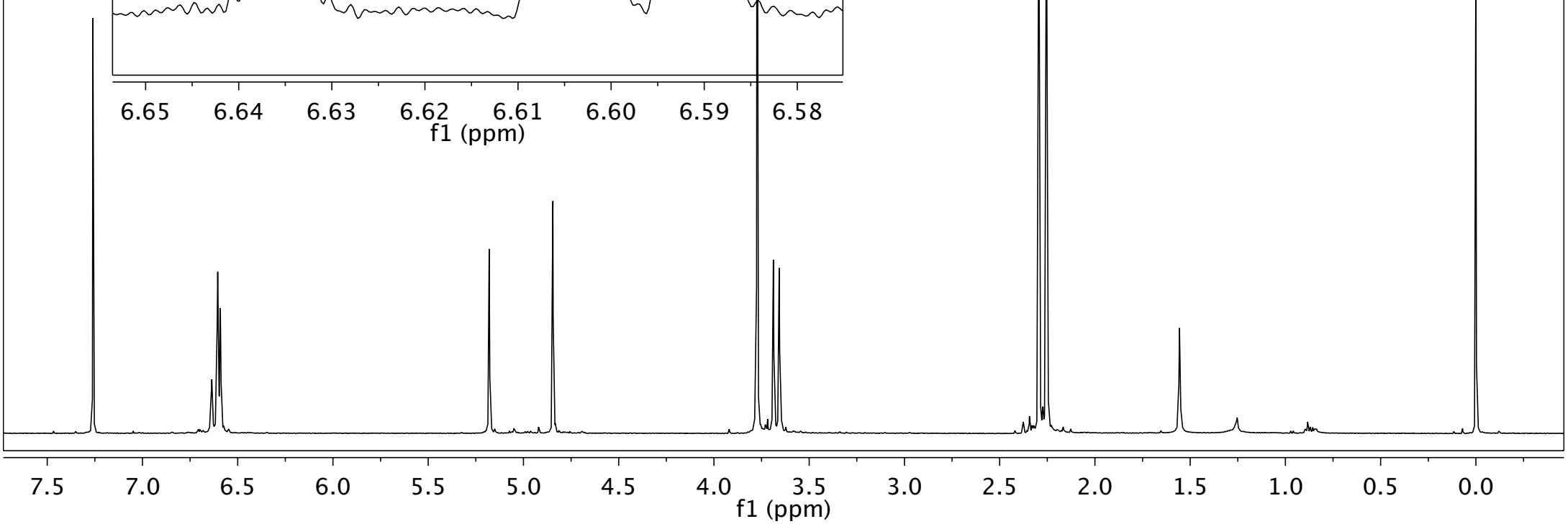
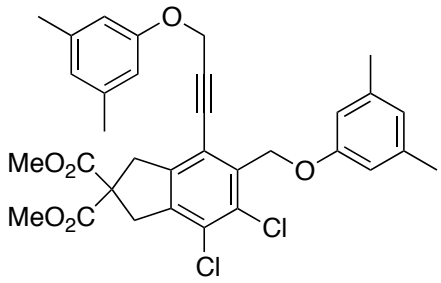


8i



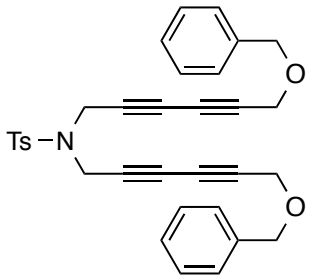


CDCl3, 125 MHz



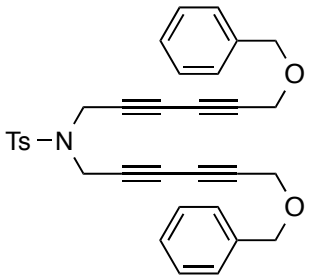
8i

CDCl3, 500 MHz



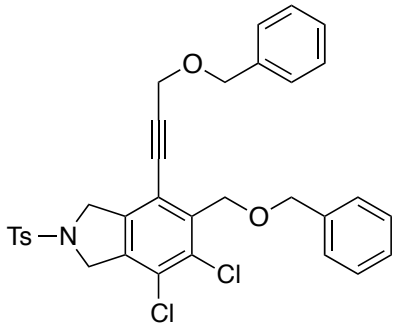
S11

CDCl3, 125 MHz

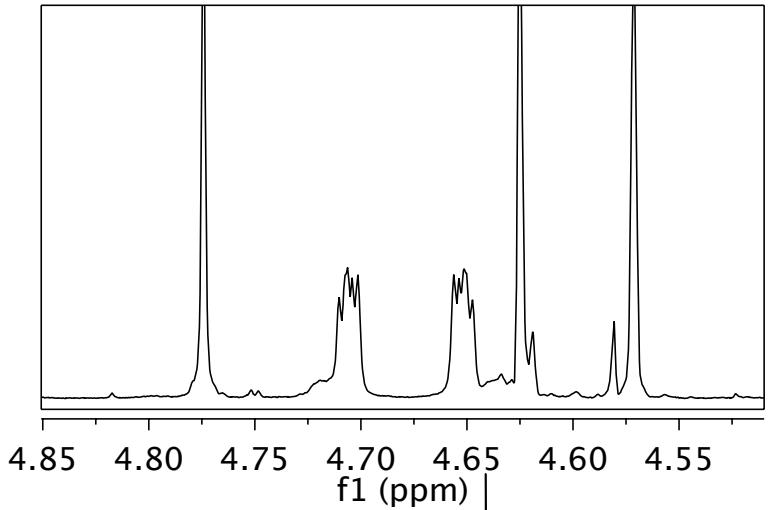


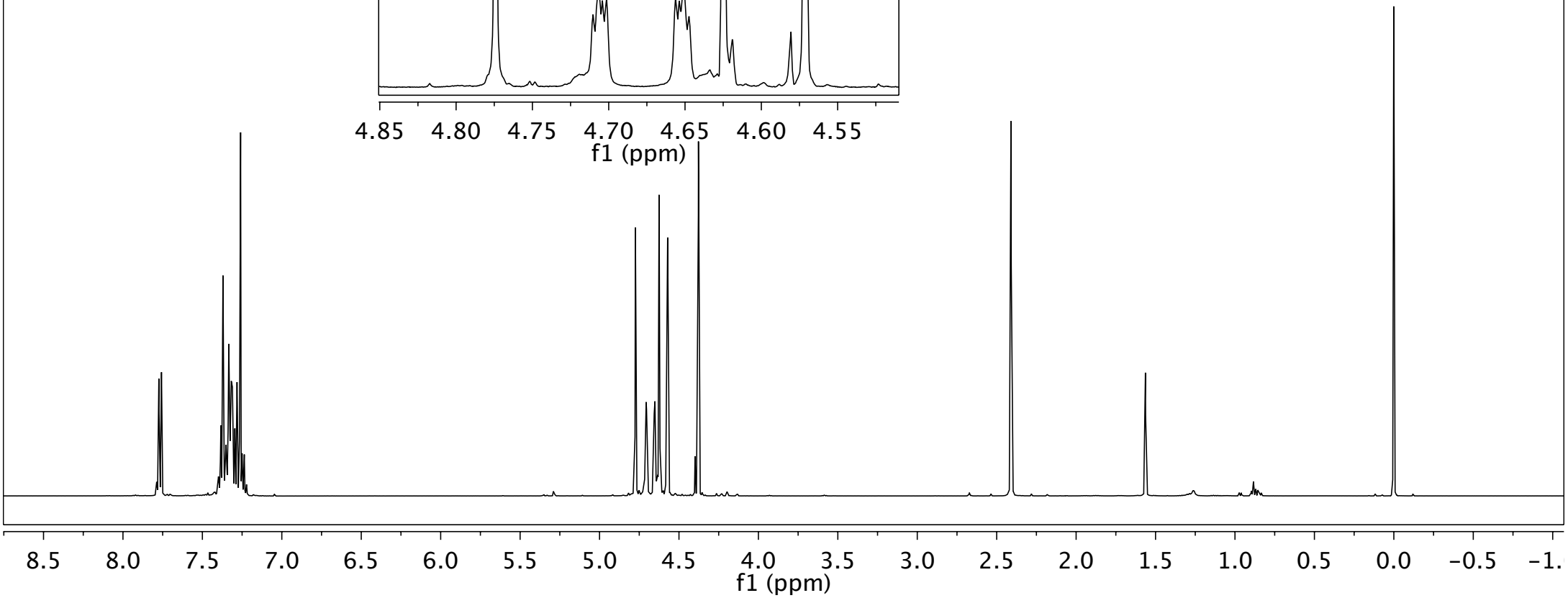
S11

CDCl3, 500 MHz

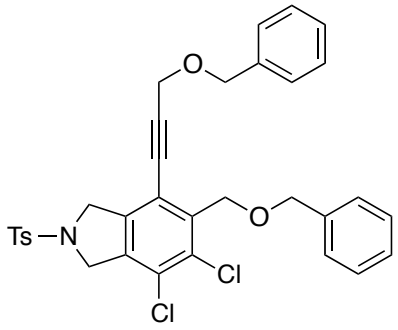


8j

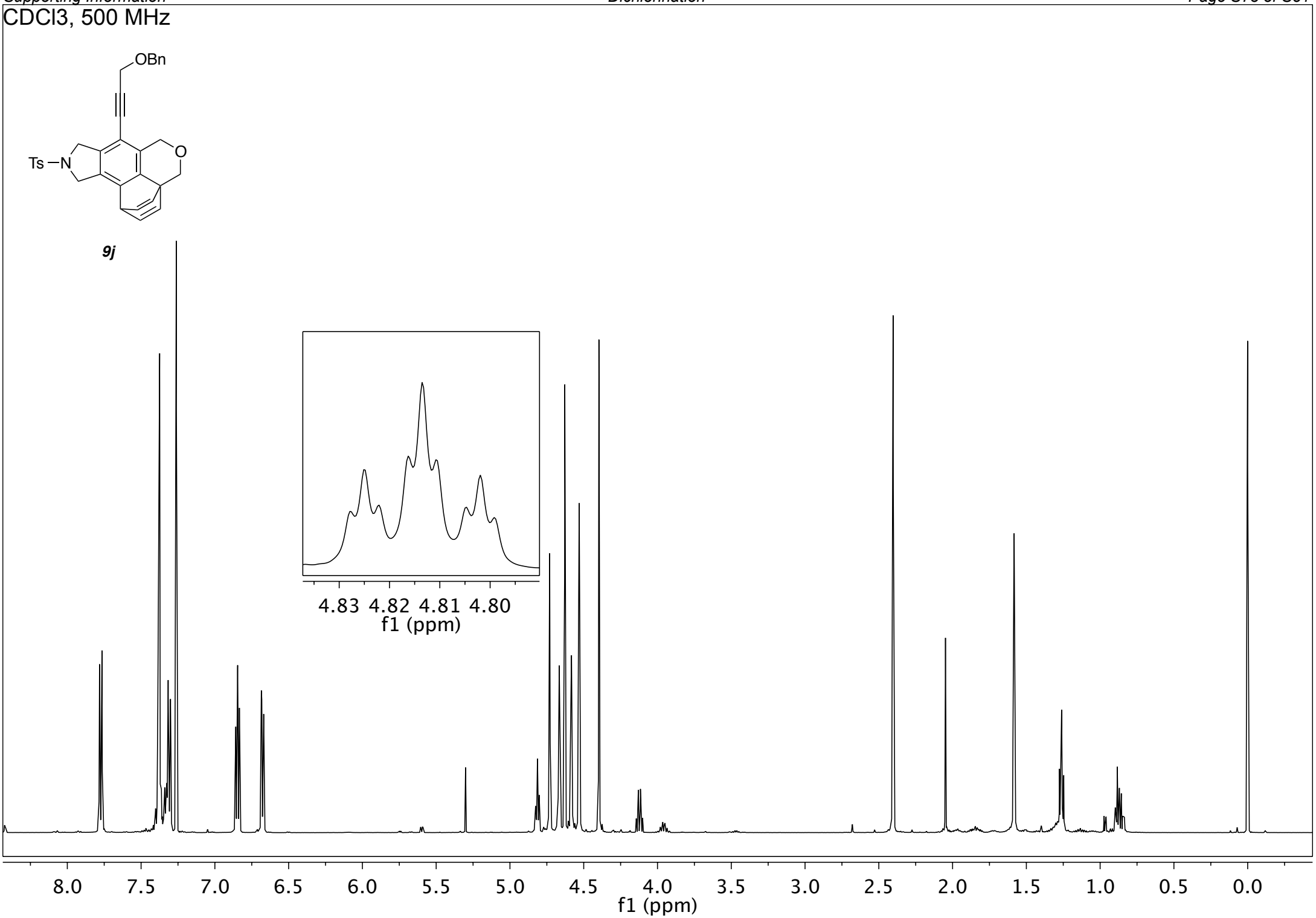


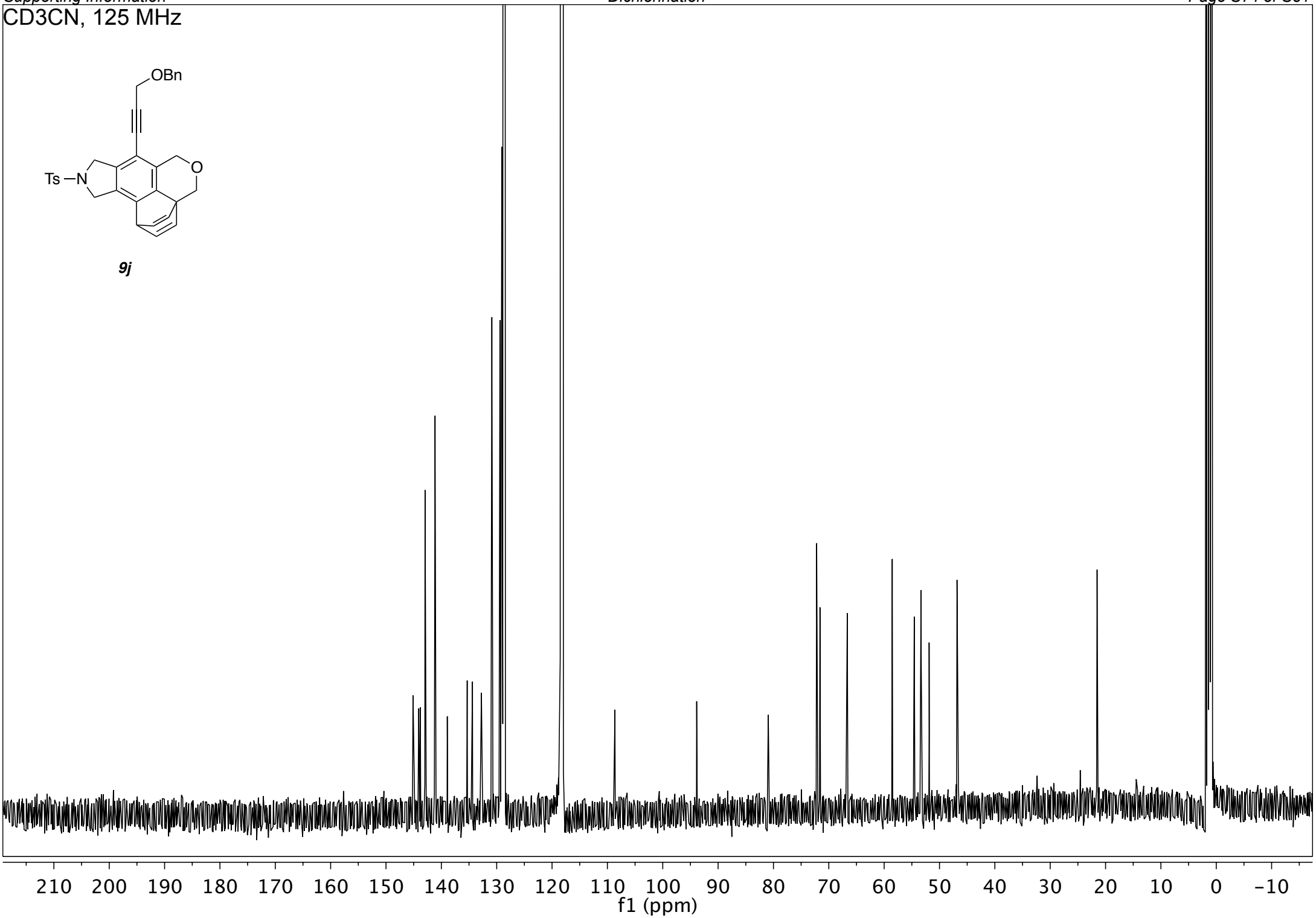


CDCl3, 125 MHz

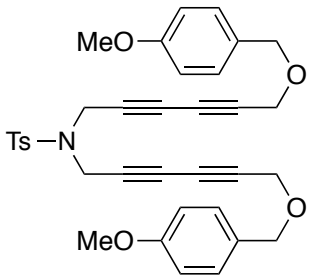


8j


CDCl3, 500 MHz
OBn
Ts
N
O
9j
4.83 4.82 4.81 4.80
f1 (ppm)
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
f1 (ppm)


CD3CN, 125 MHz
OBn
Ts
N
O
9j
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

CDCl3, 500 MHz



10

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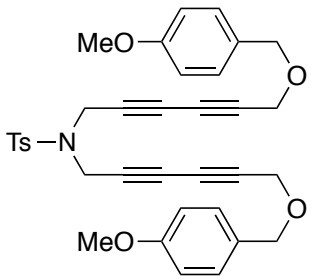

10

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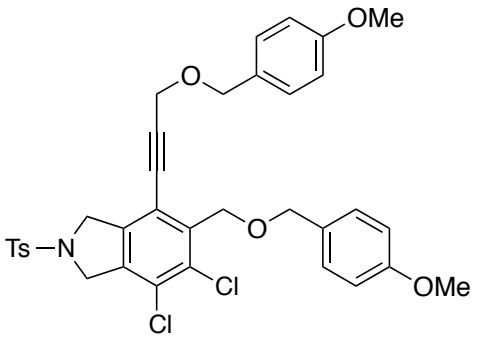
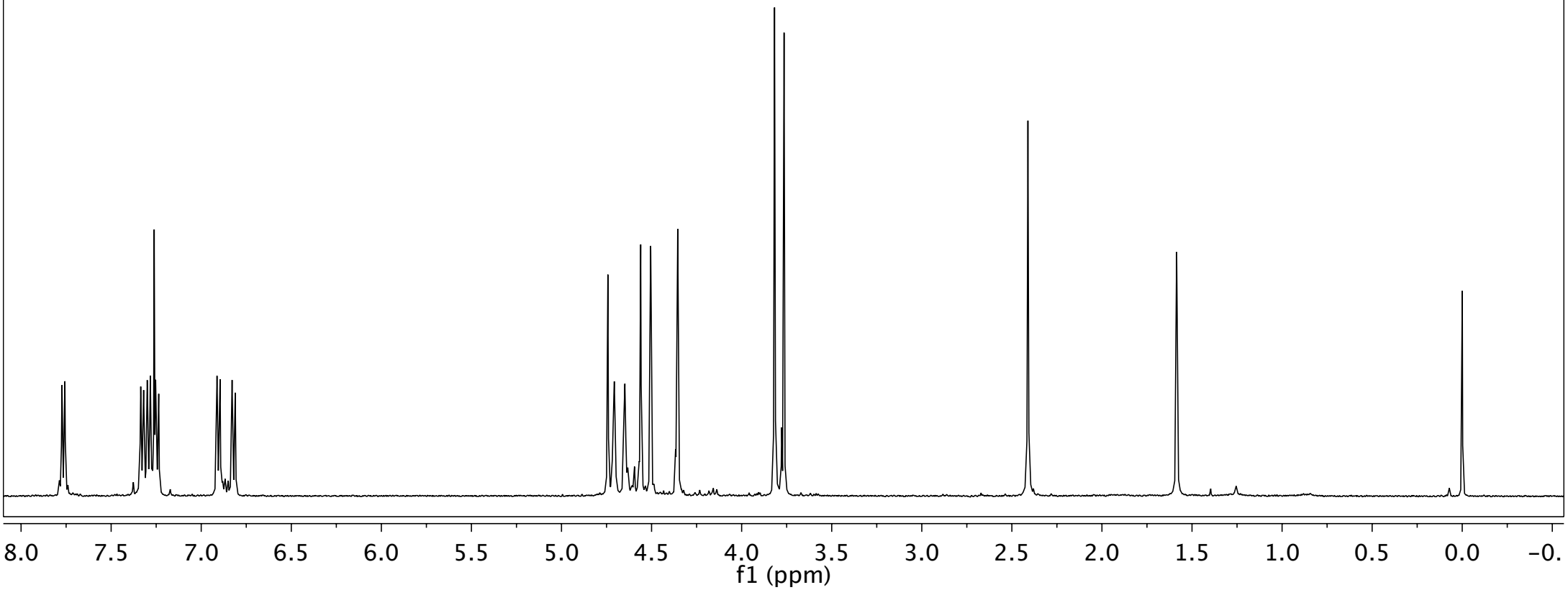
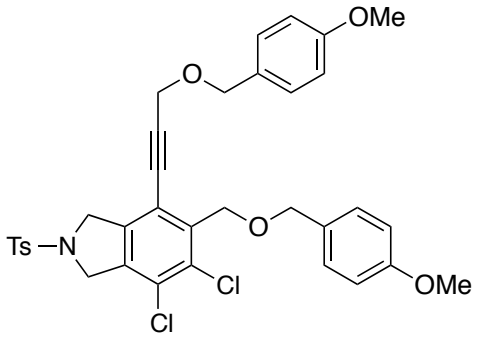


8k



CDCl3, 125 MHz



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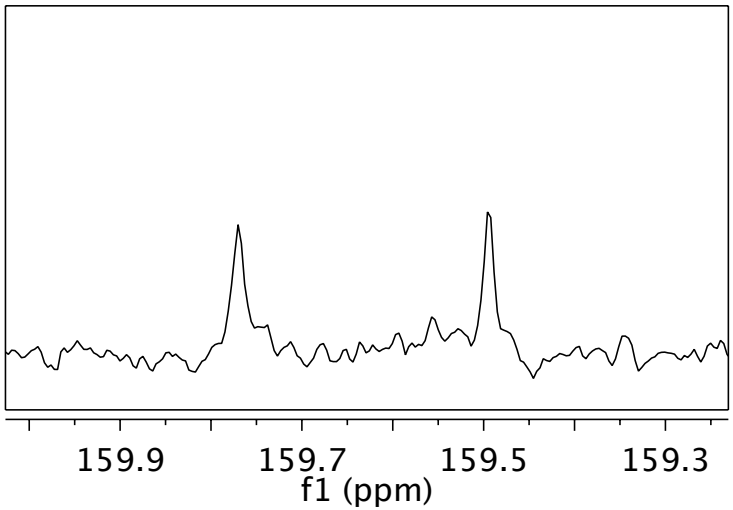

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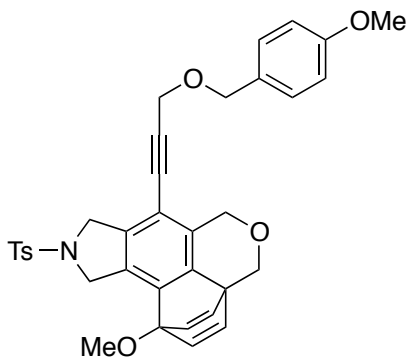

9k

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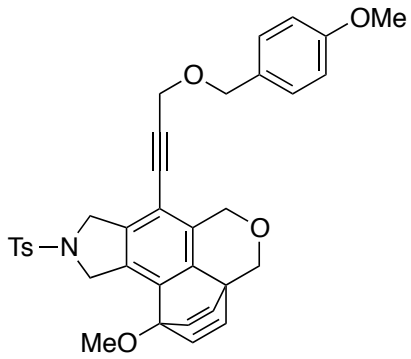

9k

IV. References for the Supporting Information

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