

Supplementary Information for:

The aromatic ene reaction

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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 ; to $\text{CD}_3\text{SOCHD}_2$ (δ 2.50 ppm) for $\text{DMSO}-d_6$; and to CHD_2OD (δ 3.31 ppm) for $\text{MeOH}-d_4$. 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 ; to $(\text{CD}_3)_2\text{SO}$ (δ 39.50 ppm) for $\text{DMSO}-d_6$; and to CD_3OD (δ 49.00 ppm) for $\text{MeOH}-d_4$. TMS is present in some of the ^{13}C NMR samples (δ ca. 0.0 ppm). HSQC refers to heteronuclear single quantum correlation. The acquired HSQC spectra are phase-sensitive: dots of blue color correspond to CH/CH_3 , dots of red to CH_2 .

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.

GCMS data (electron impact at 70 eV) were collected on an Agilent 5975 MSD instrument. The temperature ramp profile used was i) 2 min initial hold time at 50 °C, ii) a linear ramp to 310 °C at a rate of 20 °C min^{-1} , and iii) a final hold time of 7 min (for a total run time of 22 min). An HP-5 capillary GC column (30 m \times 0.32 mm \times 0.25 μm film thickness) was used.

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. Dichloroethane used for HDDA//Aromatic Ene//Ene cascade reaction experiments was dried with 4 Å molecular sieves for 24 h prior to use. Reported (external) reaction temperatures are the temperature of the heating bath. HDDA initiated cascade 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. Those carried out in deuterated solvents were typically performed in a capped NMR sample tube (5 mm diameter).

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 Supplementary 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.

Most reactions have been done more than once. The yields observed from each attempt were comparable. The reported yield for each reaction was the one conducted on the largest scale. The reported product ratios for instances where more than one product was identified are the average of however many runs were performed.

General Procedures A-E.

A. General Procedure A: Terminal Alkyne Bromination

Solid AgNO₃ (0.1 equiv) was added to a solution of *N*-bromosuccinimide (NBS, 1.05–1.1 equiv) and the terminal alkyne substrate (1.0 equiv) and in acetone (0.1 M) at rt. The resulting slurry was stirred for one hour and then either i) partitioned between water and Et₂O, and washed with brine, dried (Na₂SO₄) or ii) filtered (Celite[®] using acetone eluent) and then concentrated. The crude material was used either directly or after being purified by flash chromatography.

B. General Procedure 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 NH₄Cl was added and the resulting mixture was extracted with EtOAc or Et₂O. The combined extracts were washed (brine), dried (Na₂SO₄), and concentrated. The crude material was then purified using flash chromatography.

C. General Procedure C: Alkyne Cross-Coupling using Cadiot–Chodkiewicz in Et₂O/*n*-BuNH₂/water.

To a solution of CuCl (0.05 equiv) in 30:70 (v:v) *n*-BuNH₂:H₂O (0.01 M) in a capped reaction vessel was added an excess of NH₂OH•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 Et₂O (0.25 M) was added dropwise. The reaction mixture was stirred for 1 h, during which time a few crystals of NH₂OH•HCl were periodically added whenever the solution became blue. The reaction mixture was diluted with saturated aqueous NH₄Cl and extracted with EtOAc or Et₂O. The combined organic extracts were washed with brine, dried (Na₂SO₄), and concentrated. The crude material was typically purified by flash chromatography.

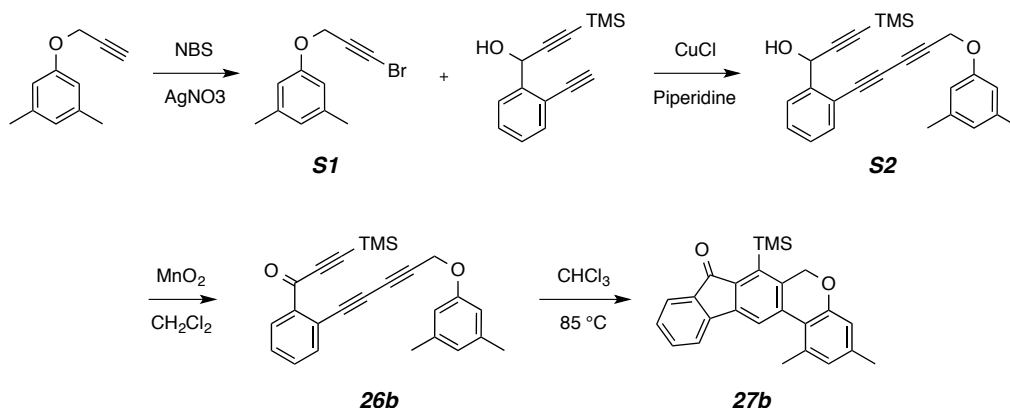
D. General Procedure D: Dicyclohexylcarbodiimide (DCC) Coupling

DCC (1.1 equiv) and DMAP (0.1 equiv) were added in one portion to a stirred solution of secondary amine or primary alcohol (1.0 equiv) and propiolic acid (1.2–1.5 equiv) in dry dichloromethane (0.15 M) at 0 °C. A large amount of precipitate was formed immediately. After 30 min, the reaction mixture was filtered through a pad of Celite[®], and the filter cake was carefully washed with a 3:1 mixture of hexanes and EtOAc. The filtrate was concentrated and the residue subjected to flash chromatography to provide the purified ester or amide.

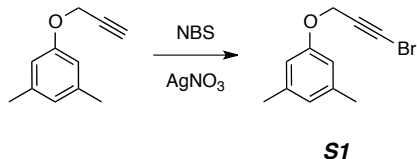
E. General Procedure E: HDDA / aromatic ene / Alder ene cascade reaction

A solution of a triyne (1 equiv) and an enophile (1.2–2 equiv) in CHCl₃, dichloroethane, or 1,2-dichlorobenzene (0.2–0.3 M) was heated for the indicated time. Unless otherwise noted, the resulting solution was concentrated and subjected to column chromatography for purification of the product.

Synthesis of fluorenone 27b (Figure 3c of manuscript)



1-((3-Bromoprop-2-yn-1-yl)oxy)-3,5-dimethylbenzene (S1)



Bromoalkyne **S1** was prepared following General Procedure A from 1,3-dimethyl-5-(prop-2-yn-1-yloxy)benzene³ (400 mg, 2.5 mmol), *N*-bromosuccinimide (NBS, 460 mg, 2.6 mmol), AgNO₃ (34 mg, 0.2 mmol), and acetone (25 mL). Purification by flash chromatography (hexanes:EtOAc 19:1) gave the bromoalkyne **S1** (500 mg, 2.1 mmol, 84%) as a clear yellow oil.

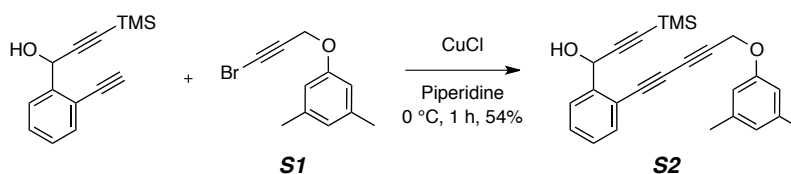
¹H NMR (500 MHz, CDCl₃): δ 6.65 (s, 1H, ArH₄), 6.58 (s, 2H, ArH₂H₆), 4.67 (s, 2H, CH₂O), and 2.30 [s, 6H, Ar(CH₃)₂].

¹³C NMR (125 MHz, CDCl₃): δ 157.8, 139.5, 123.6, 112.7, 75.5, 56.8, 47.5, and 21.7.

IR: 2919, 2862, 2219, 1615, 1594, 1470, 1451, 1373, 1318, 1293, 1168, 1151, 1070, and 829 cm⁻¹.

GC-LRMS: t_R = 7.37 min. *m/z*: 240 (M⁺, 50), 238 (M⁺, 50), 225 (M⁺-CH₃, 25), 223 (M⁺-CH₃, 25), 159 (M⁺-Br, 70), 131 (70), 116 (70), 91 (C₇H₇⁺, 100), and 77 (C₆H₅⁺, 50).

1-(2-(5-(3,5-Dimethylphenoxy)penta-1,3-diyn-1-yl)phenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (S2)



Triyne **S2** was prepared following General Procedure B from 1-(2-ethynylphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol⁴ (160 mg, 0.7 mmol), **S1** (237 mg, 1 mmol), CuCl (7 mg, 0.07 mmol), and piperidine (2 mL). Purification by MPLC (hexanes:EtOAc 5:1) gave the diyne **S2** (90 mg, 0.23 mmol, 33%) as a yellow oil.

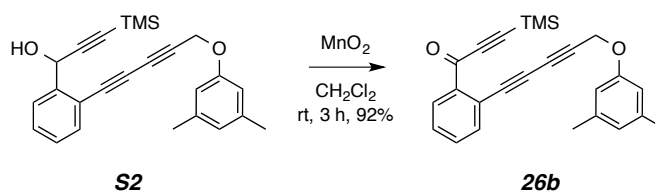
¹H NMR (500 MHz, CDCl₃): δ 7.69 (d, *J* = 7.8 Hz, 1H, *H6*), 7.49 (d, *J* = 7.7 Hz, 1H, *H3*), 7.40 (dd, *J* = 7.7, 7.7 Hz, 1H, *H4*), 7.27 (dd, *J* = 7.6, 7.6 Hz, 1H, *H5*), 6.65 (br s, 1H, *H4'*), 6.60 (br s, 2H, *H2'*/*H6'*), 5.78 (br s, 1H, *CHOH*), 4.79 (s, 2H, *CH₂O*), 2.52 (br s, 1H, *CHOH*), 2.30 [br s, 6H, Ar(*CH₃*)₂], and 0.19 [s, 9H, Si(*CH₃*)₃].

¹³C NMR (125 MHz, CDCl₃): δ 157.7, 143.7, 139.5, 133.9, 130.1, 128.5, 127.1, 123.7, 120.0, 112.7, 104.2, 92.0, 79.2, 78.5, 75.9, 71.5, 63.4, 56.4, 21.6, and 0.0.

IR: 3420, 2959, 2240, 2174, 1614, 1594, 1473, 1449, 1372, 1318, 1291, 1250, 1169, 1150, 1059, and 985 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₅H₂₆NaO₂Si⁺ [M+Na]⁺ requires 409.1594; found 409.1633.

1-(2-(5-(3,5-Dimethylphenoxy)penta-1,3-diyn-1-yl)phenyl)-3-(trimethylsilyl)prop-2-yn-1-one (**26b**)



Activated MnO₂ (300 mg, 3.44 mmol) was added to a solution of triyne **S2** (90 mg, 0.23 mmol) in CH₂Cl₂ (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 copious amount of CH₂Cl₂. The filtrate was concentrated and the residue subjected to column chromatography (hexanes:EtOAc = 12:1) to yield ketone **26b** as a pale yellow oil (83 mg, 0.22 mmol, 93%).

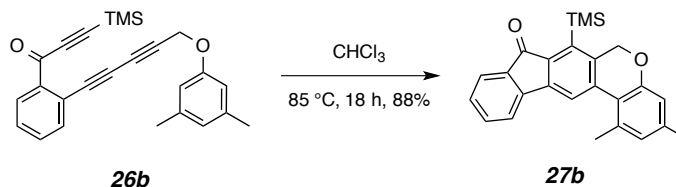
¹H NMR (500 MHz, CDCl₃): δ 8.11 (dd, *J* = 7.7, 1.4 Hz, 1H, *H3*), 7.61 (dd, *J* = 7.5, 1.4 Hz, 1H, *H6*), 7.51 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H, *H5*), 7.47 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H, *H4*), 6.65 (t of septets, *J* = 0.7, 0.7 Hz, 1H, *H4'*), 6.65 (dq, *J* = 0.7, 0.7 Hz, 2H, *H2'*/*H6'*), 4.81 (s, 2H, *CH₂O*), 2.30 [dt, *J* = 0.6, 0.6 Hz, 6H, Ar(*CH₃*)₂], and 0.29 [s, 9H, Si(*CH₃*)₃].

¹³C NMR (125 MHz, CDCl₃): δ 176.5, 157.8, 139.5, 139.2, 136.0, 132.8, 132.1, 129.1, 123.7, 121.4, 112.8, 101.8, 101.4, 79.9, 79.3, 76.8, 72.0, 56.5, 21.7, and -0.5.

IR: 2960, 2922, 2153, 1648, 1614, 1592, 1562, 1481, 1373, 1319, 1291, 1251, 1237, 1150, 1060, 1015, and 847 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₅H₂₄NaO₂Si⁺ [M+Na]⁺ requires 407.1438; found 407.1437.

1,3-Dimethyl-7-(trimethylsilyl)fluoreno[2,3-c]chromen-8(6H)-one (**27b**)



A solution of **26b** (16 mg, 0.042 mmol) in CHCl₃ (1.4 mL) was heated at 85 °C for 18 h. The resulting mixture was directly subjected to MPLC (SiO₂, hexanes:EtOAc = 9:1) to yield **27b** as a golden oil (14 mg, 0.036 mmol, 88%).

¹H NMR (500 MHz, CDCl₃): δ 7.80 (s, 1H, *H13*), 7.61 (ddd, *J* = 7.3, 1.0, 1.0 Hz, 1H, *H9*), 7.50 (ddd, *J* = 7.3, 1.0, 1.0 Hz, 1H, *H12*), 7.47 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H, *H11*), 7.29 (ddd, *J* = 7.2, 7.2, 1.4 Hz,

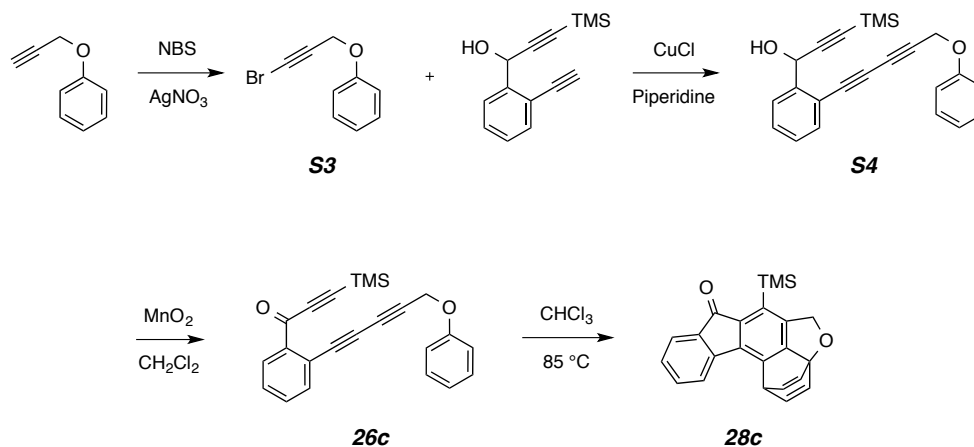
1H, *H10*), 6.82 (d, *J* = 1.7 Hz, 1H, *H2*), 6.73 (d, *J* = 1.8 Hz, 1H, *H4*), 5.05 (s, 2H, *CH*₂*O*), 2.69 (s, 3H, *C1-CH*₃), 2.34 (s, 3H, *C3-CH*₃), and 0.46 [s, 9H, *Si(CH*₃*)*₃].

¹³C NMR (125 MHz, CDCl₃): δ 194.8, 157.1, 144.2, 144.0, 141.6, 140.2, 139.0, 137.9, 136.0, 135.7, 134.6, 134.5, 129.2, 127.1, 124.1, 121.3, 119.7, 119.1, 115.2, 70.0, 22.4, 21.6, and 2.3.

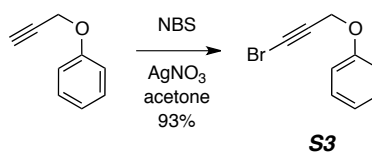
IR: 2949, 2921, 2855, 1709, 1606, 1588, 1463, 1300, 1294, 1248, 1181, 1135, 1071, 974, 961, 867, and 846 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₅H₂₄NaO₂Si⁺ [M+Na]⁺ requires 407.1438; found 407.1435.

Synthesis of fluorenone 28c (Figure 3c of manuscript)



((3-Bromoprop-2-yn-1-yl)oxy)benzene (S3)



Bromoalkyne **S3** was prepared following General Procedure A from (prop-2-yn-1-yloxy)benzene (396 mg, 3 mmol, 1 equiv), NBS (558 mg, 3.15 mmol, 1.05 equiv), AgNO₃ (51 mg, 0.3 mmol, 0.1 equiv), and acetone (20 mL). **S3** was obtained after flash chromatography (hexanes:EtOAc = 19:1) as a light yellow oil (587 mg, 2.89 mmol, 93%).

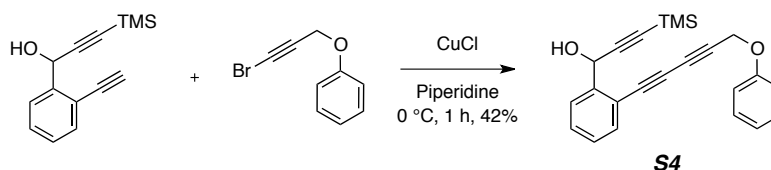
¹H NMR (500 MHz, CDCl₃): δ 7.31 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.00 (tt, *J* = 7.4, 1.2 Hz, 1H, *Hp*), 6.96 (dd, *J* = 8.9, 1.2 Hz, 2H, *Ho*), and 4.71 (s, 2H, CH₂O).

¹³C NMR (125 MHz, CDCl₃): δ 157.7, 129.7, 121.8, 115.0, 75.3, 56.8, and 47.7.

IR: 2915, 2860, 2219, 1598, 1588, 1494, 1456, 1374, 1304, 1262, 1232, 1212, 1174, 1080, 1051, 1031, and 990 cm⁻¹.

GC-LRMS: *t*_R = 6.19 min. *m/z*: 212 (M⁺, 25), 210 (M⁺, 25), 131 (M⁺-Br, 70), 119 (M⁺-PhO, 40), 117 (M⁺-PhO, 40), 103 (PhO⁺, 100), 77 (C₆H₅⁺, 50), and 65 (30).

1-(2-(5-Phenoxy)pent-1,3-diyne-1-yl)phenyl-3-(trimethylsilyl)prop-2-yn-1-ol (S4)



Triyne **S4** was prepared following General Procedure B from 1-(2-ethynylphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol⁴ (160 mg, 0.7 mmol), ((3-bromoprop-2-yn-1-yl)oxy)benzene (209 mg, 1 mmol), CuCl (7 mg, 0.07 mmol), and piperidine (2 mL). Purification by MPLC (hexanes:EtOAc 5:1) gave the diyne **S4** (95 mg, 0.27 mmol, 38%) as a yellow oil.

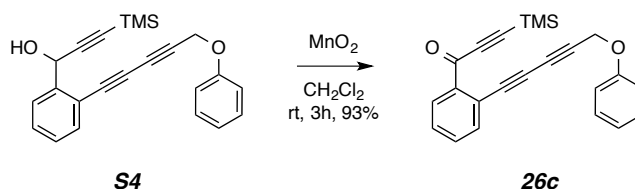
¹H NMR (500 MHz, CDCl₃): δ 7.71 (d, *J* = 7.8 Hz, 1H, *H3*), 7.51 (dd, *J* = 7.6, 1.0 Hz, 1H, *H6*), 7.42 (ddd, *J* = 7.6, 7.6, 1.2 Hz, *H5*), 7.33 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.30 (ddd, *J* = 7.6, 7.6, 1.1 Hz, 1H, *H4*), 7.03 (tt, *J* = 7.4, 1.1 Hz, 1H, *Hp*), 7.00 (dd, *J* = 8.8, 1.0 Hz, 2H, *Ho*), 5.80 (d, *J* = 4.7 Hz, 1H, *CHOH*), 4.86 (s, 2H, *CH₂O*), 2.49 (d, *J* = 4.7 Hz, 1H, *OH*), and 0.20 [s, 9H, Si(CH₃)₃].

¹³C NMR (125 MHz, CDCl₃): δ 157.6, 143.7, 133.9, 130.1, 129.8, 128.5, 127.1, 121.9, 120.0, 115.0, 104.2, 92.1, 78.9, 78.4, 76.1, 71.7, 63.4, 56.6, and 0.0.

IR: 3445, 3066, 2959, 2898, 2239, 2173, 1598, 1588, 1494, 1374, 1365, 1250, 1211, 1033, 1015, 986, 846, and 759 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₃H₂₂NaO₂Si⁺ [M+Na]⁺ requires 381.1281; found 381.1278.

1-(2-(5-Phenoxy-penta-1,3-diyne-1-yl)phenyl)-3-(trimethylsilyl)prop-2-yn-1-one (**26c**)



Activated MnO₂ (250 mg, 2.87 mmol) was added to a solution of triyne **S4** (85 mg, 0.24 mmol) in CH₂Cl₂ (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 copious amount of CH₂Cl₂. The filtrate was concentrated and the residue subjected to column chromatography (hexanes:EtOAc = 12:1) to yield ketone **26c** as a pale yellow oil (83 mg, 0.23 mmol, 98%).

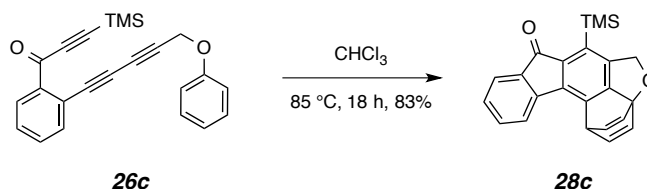
¹H NMR (500 MHz, CDCl₃): δ 8.10 (dd, *J* = 7.6, 1.6 Hz, 1H, *H6*), 7.60 (dd, *J* = 7.6, 1.5 Hz, 1H, *H3*), 7.50 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H, *H4*), 7.47 (ddd, *J* = 7.5, 7.5, 1.6 Hz, 1H, *H5*), 7.31 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.00 (tt, *J* = 7.3, 1.0 Hz, 1H, *Hp*), 6.98 (dd, *J* = 8.7, 1.0 Hz, 2H, *Ho*), 4.85 (s, 2H, *CH₂O*), and 0.29 [s, 9H, Si(CH₃)₃].

¹³C NMR (125 MHz, CDCl₃): δ 157.7, 139.2, 136.0, 132.8, 132.1, 129.7, 129.1, 121.9, 121.3, 115.0, 101.8, 101.4, 79.6, 79.2, 76.9, 72.2, 56.6, and -0.5.

IR: 3063, 2962, 2900, 2152, 1647, 1598, 1588, 1561, 1494, 1482, 1375, 1365, 1292, 1274, 1237, 1211, 1015, and 849 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₃H₂₀NaO₂Si⁺ [M+Na]⁺ requires 379.1125; found 379.1109.

6-(Trimethylsilyl)-1H-1,3a-ethenoindeno[1',2':5,6]naphtho[1,8-bc]furan-7(5H)-one (**28c**)



A solution of **26c** (35 mg, 0.98 mmol) in CHCl₃ (3 mL) was heated to 85 °C for 18 h. The resulting solution was then concentrated and the residue purified with MPLC (hexanes:EtOAc = 6:1) to give **28c** as a yellow solid (29 mg, 0.081 mmol, 83%).

¹H NMR (500 MHz, CDCl₃): δ 7.75 (ddd, *J* = 7.5, 0.9, 0.9 Hz, 1H, *H8*), 7.60 (ddd, *J* = 7.3, 1.0, 0.9 Hz, 1H, *H11*), 7.49 (ddd, *J* = 7.4, 7.4, 1.2 Hz, 1H, *H10*), 7.26 (dd, *J* = 7.5, 7.5, 1.0 Hz, 1H, *H9*), 7.07 (dd,

$J = 6.6, 1.3$ Hz, 2H, HC(HC=CH)₂), 6.71 (dd, $J = 5.6, 6.7$ Hz, 2H, HC(HC=CH)₂), 5.53 (s, 2H, CH₂O), 5.45 (tt, $J = 5.6, 1.3$ Hz, 1H, HC(HC=CH)₂), and 0.33 (s, 9H).

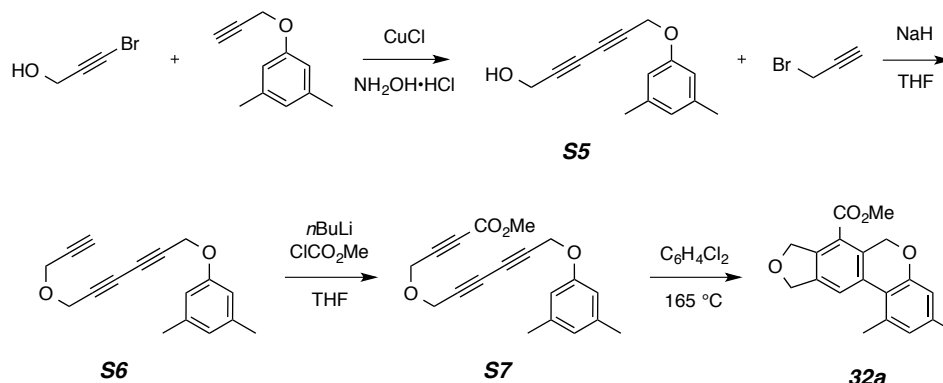
¹³C NMR (125 MHz, CDCl₃): δ 194.1, 156.2, 144.0, 143.7, 138.8, 137.5, 135.9, 135.5, 135.2, 135.0, 134.4, 133.7, 128.7, 124.2, 122.2, 95.5, 79.7, 45.9, and 0.4.

IR: 3063, 2948, 1705, 1606, 1588, 1468, 1338, 1245, 1165, 1082, 997, 901, 859, and 844 cm⁻¹.

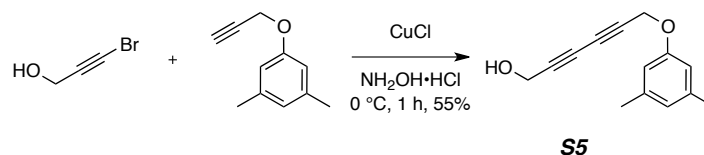
HRMS (ESI-TOF): Calcd for C₂₃H₂₀NaO₂Si⁺ [M+Na]⁺ requires 379.1125; found 379.1145.

mp: 227-228 °C.

Synthesis of isobenzofuran 32a (Figure 4b of manuscript)



6-(3,5-Dimethylphenoxy)hexa-2,4-diyne-1-ol (S5)



Diynol **S5** was prepared following General Procedure C from 3-bromoprop-2-yn-1-ol⁵ (520 mg, 3.9 mmol, 1.3 equiv), 1,3-dimethyl-5-(prop-2-yn-1-yloxy)benzene (480 mg, 3 mmol, 1 equiv), CuCl (30 mg, 0.3 mmol, 0.1 equiv), 30% aqueous BuNH₂ (12 mL), and Et₂O (12 mL). Diynol **S5** was obtained as a yellow oil (350 mg, 1.64 mmol, 55%) following purification by flash chromatography (hexanes:EtOAc = 5:1).

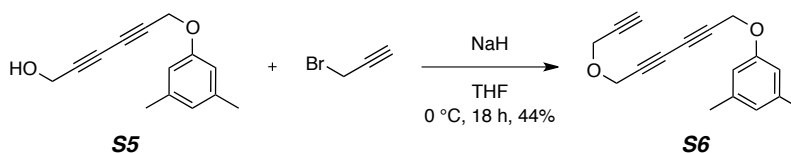
¹H NMR (500 MHz, CDCl₃): δ 6.64 (s, 1H, ArH₄), 6.57 (s, 2H, ArH₂H₆), 4.71 (br s, 2H), 4.32 (br s, 2H), and 2.29 (s, 6H, ArCH₃).

¹³C NMR (125 MHz, CDCl₃): δ 157.6, 139.5, 123.7, 112.8, 77.9, 74.8, 71.1, 70.0, 56.3, 51.6, and 21.6.

IR: 3600-3100, 2919, 2860, 2258, 2185, 1614, 1594, 1472, 1447, 1372, 1318, 1293, 1168, 1150, 1062, 1022, and 829 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₄H₁₄NaO₂⁺ [M+Na]⁺ requires 237.0886; found 237.0884.

3,5-Dimethyl-1-((6-(prop-2-yn-1-yloxy)hexa-2,4-diyne-1-yl)oxy)benzene (S6)



A solution of diynol **S5** (214 mg, 1 mmol) in THF (2 mL) was added to a stirred suspension of NaH (80 mg, 60% suspension in mineral oil, 2 mmol) in THF (10 mL) at 0 °C. The reaction mixture was allowed to warm to rt over 1 h and propargyl bromide (0.24 mL, 80 wt. % in toluene, 2.2 mmol) was added. After 18 h the mixture was cooled to 0 °C, water was added, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with brine, dried (Na₂SO₄), and

concentrated. Purification by flash chromatography (hexanes:EtOAc = 20:1) gave the triyne **S6** (110 mg, 0.44 mmol, 44%) as a colorless oil.

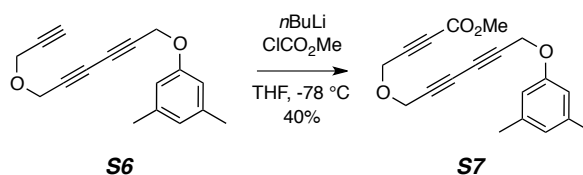
¹H NMR (500 MHz, CDCl₃): δ 6.65 (tq, *J* = 0.7, 0.7, 0.7 Hz, 1H, Ar*H*4), 6.57 (dq, *J* = 0.7, 0.7 Hz, 2H, Ar*H*2*H*6), 4.73 (t, *J* = 0.9 Hz, 2H), 4.33 (t, *J* = 0.9 Hz, 2H), 4.25 (d, *J* = 2.4 Hz, 2H), 2.46 (t, *J* = 2.4 Hz, 1H, HC≡), and 2.30 [dt, *J* = 0.7, 0.7 Hz, 6H, Ar(CH₃)₂]

¹³C NMR (125 MHz, CDCl₃): δ 157.7, 139.6, 123.8, 112.8, 78.7, 75.6, 75.1, 74.7, 71.11, 71.06, 57.1, 56.9, 56.3, and 21.7.

IR: 3295, 2965, 2918, 2855, 2119, 1614, 1594, 1472, 1443, 1344, 1318, 1293, 1168, 1150, 1081, 1065, and 830 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₇H₁₆AgO₂⁺ [M+Ag]⁺ requires 359.0196; found 359.0204 [the sample solution in MeOH was doped with AgNO₃ (ca. 10-100 μM) prior to introduction into the ionizing chamber].

Methyl 4-((6-(3,5-Dimethylphenoxy)hexa-2,4-diyn-1-yl)oxy)but-2-ynoate (**S7**)



n-BuLi (0.072 mL, 2.5 M in hexanes, 0.18 mmol) was added to a stirred solution of triyne **S6** (40 mg, 0.16 mmol) in THF (1 mL) at -78 °C. The reaction mixture turned dark green immediately. After 20 min methyl chloroformate (0.17 mL, 1.8 mmol) was added. After 30 min saturated aqueous NH₄Cl was added and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried (Na₂SO₄), and concentrated. Purification by flash chromatography (hexanes:EtOAc = 20:1) yielded, in order of elution, recovered **S6** (15 mg, 0.06 mmol, 37%) and the triyne **S7** (20 mg, 0.064 mmol, 40%) as a clear amber oil.

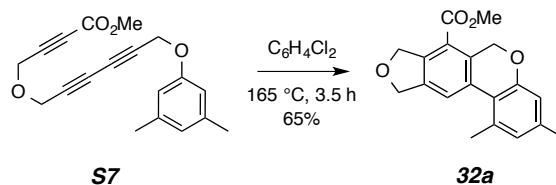
¹H NMR (500 MHz, CDCl₃): δ 6.65 (tq, *J* = 0.7, 0.7, 0.7 Hz, 1H, Ar*H*4), 6.57 (dq, *J* = 0.7, 0.7 Hz, 2H, Ar*H*2*H*6), 4.73 (t, *J* = 0.9 Hz, 2H), 4.38 (s, 2H, OCH₂CCO₂Me), 4.34 (t, *J* = 0.9 Hz, 2H), 3.79 (s, 3H, OMe), and 2.30 [dt, *J* = 0.7, 0.7 Hz, 6H, Ar(CH₃)₂]

¹³C NMR (125 MHz, CDCl₃): δ 157.7, 153.6, 139.6, 123.8, 112.8, 82.5, 78.7, 75.0, 74.4, 71.7, 70.9, 57.6, 56.5, 56.3, 53.1, and 21.7.

IR: 2954, 2919, 2853, 2239, 1718, 1614, 1594, 1535, 1345, 1318, 1293, 1255, 1169, 1151, 1089, 1062, and 830 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₉H₁₈NaO₄⁺ [M+Na]⁺ requires 333.1097; found 333.1055.

Methyl 1,3-Dimethyl-8,10-dihydro-6*H*-isobenzofuro[5,6-*c*]chromene-7-carboxylate (**32a**)



A solution of triyne **S7** (17 mg, 0.055 mmol) in dichlorobenzene (1.8 mL) was heated at 165 °C for 4.5 h. The resulting solution was cooled to rt and directly subjected to MPLC (hexanes:EtOAc = 5:1) to yield **32a** as a pale yellow oil (11 mg, 0.035 mmol, 65%), which solidified upon standing.

¹H NMR (500 MHz, CDCl₃): δ 7.70 (t, *J* = 1.0 Hz, 1H, ArH11), 6.79 (s, 1H, ArH), 6.76 (s, 1H, ArH), 5.34 (t, *J* = 2.0 Hz, 2H), 5.31 (s, 2H), 5.18 (td, *J* = 2.0, 1.0 Hz), 3.93 (s, 3H, OCH₃), 2.59 (s, 3H, C1-CH₃), and 2.33 (s, 3H, C3-CH₃).

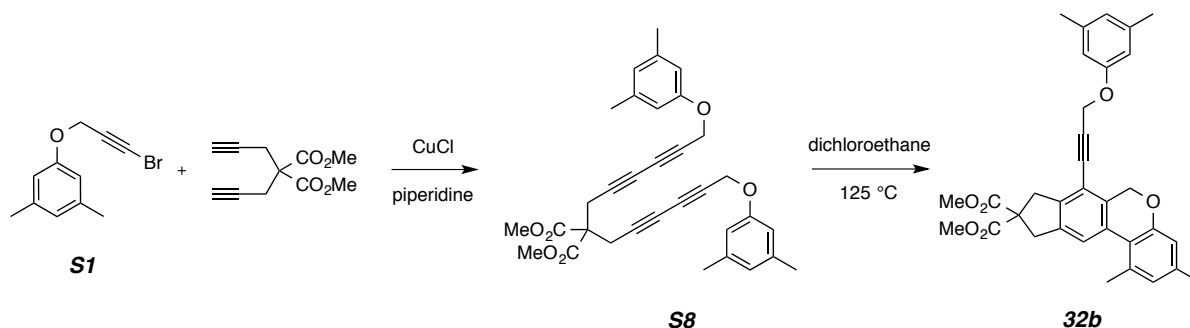
¹³C NMR (125 MHz, CDCl₃): δ 166.8, 156.7, 139.8, 139.37, 139.36, 136.2, 135.0, 132.0, 127.0, 122.4, 122.0, 120.4, 115.4, 75.3, 73.6, 66.9, 52.4, 22.6, and 21.4.

IR: 2951, 2920, 2854, 1717, 1616, 1563, 1462, 1434, 1362, 1321, 1294, 1260, 1240, 1222, 1195, 1177, 1114, 1057, 1025, 994, 911, and 846 cm⁻¹.

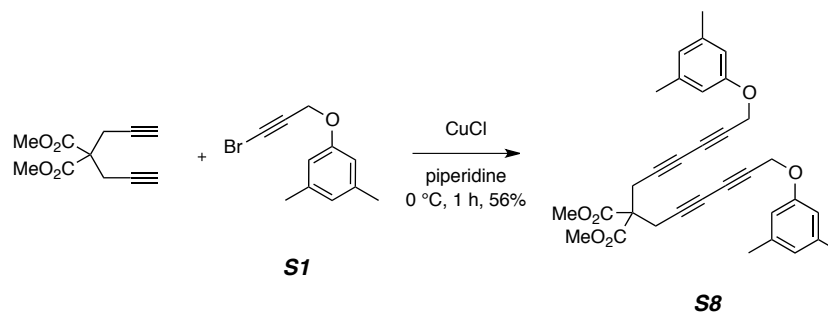
HRMS (ESI-TOF): Calcd for C₁₉H₁₈NaO₄⁺ [M+Na]⁺ requires 333.1097; found 333.1131.

mp: 115-119 °C.

Synthesis of isobenzofuran **32b** (Figure 4b of manuscript)



Dimethyl 2,2-Bis(6-(3,5-dimethylphenoxy)hexa-2,4-diyne-1-yl)malonate (**S8**)



Compound **S8** was prepared following General Procedure B from dimethyl 2,2-di(prop-2-yn-1-yl)malonate⁶ (176 mg, 0.85 mmol, 1 equiv), **S1** (480 mg, 2.01 mmol, 2.4 equiv), piperidine (2 mL), and CuCl (17 mg, 0.2 equiv). Tetrayne **S8** was isolated as a colorless solid (250 mg, 56%) following flash chromatography (hexanes:EtOAc = 6:1).

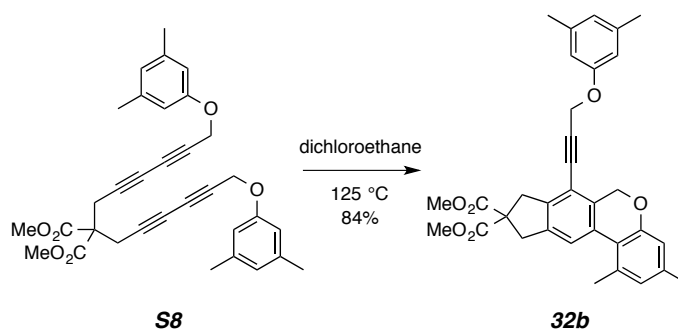
¹H NMR (500 MHz, CDCl₃): δ 6.64 (s, 2H, ArH4), 6.56 (s, 4H, ArH2H6), 4.69 (s, 4H, OCH₂), 3.76 (s, 6H, OCH₃), 3.07 (s, 4H, CCH₂C), and 2.29 [s, 12H, Ar(CH₃)₂].

¹³C NMR (125 MHz, CDCl₃): δ 168.6, 157.7, 139.5, 123.7, 112.7, 75.0, 72.3, 71.5, 68.0, 56.7, 56.3, 53.6, 24.1, and 21.7.

IR: 2954, 2920, 2861, 2260, 1742, 1614, 1594, 1470, 1436, 1373, 1318, 1293, 1255, 1212, 1169, 1151, 1062, and 830 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₃₃H₃₂NaO₆⁺ [M+Na]⁺ requires 547.2091; found 547.2097.

mp: 148-150 °C.

Dimethyl 7-(3-(3,5-Dimethylphenoxy)prop-1-yn-1-yl)-1,3-dimethyl-8,10-dihydroindeno[5,6-c]chromene-9,9(6H)-dicarboxylate (32b)

A solution of tetrayne **S8** (26 mg, 0.05 mmol) in dichloroethane (1.7 mL) was heated at 125 °C for 20 h. The resulting solution was concentrated and purified by MPLC (hexanes:EtOAc = 5:1) to yield **32b** as a colorless oil (22 mg, 0.042 mmol, 84%).

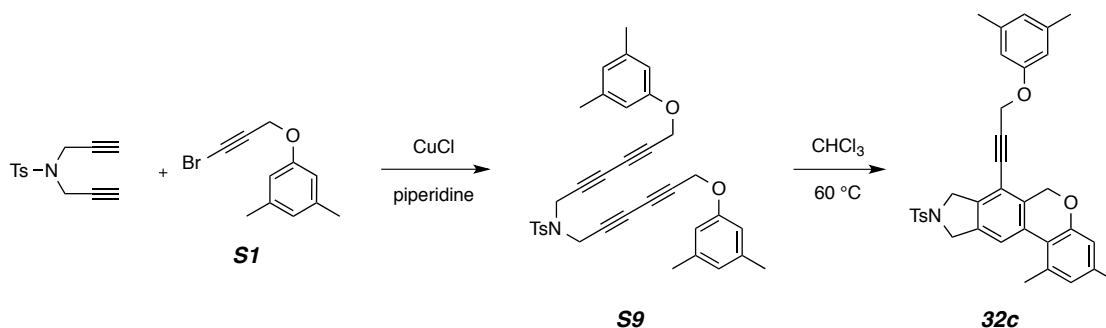
¹H NMR (500 MHz, CDCl₃): δ 7.49 (s, 1H, ArH11), 6.73 (s, 1H, ArH), 6.71 (s, 1H, ArH), 6.68 (s, 1H, ArH), 6.66 (s, 2H, ArH), 5.00 (s, 2H, OCH₂), 4.96 (s, 2H, OCH₂), 3.76 (s, 6H, OCH₃), 3.65 (s, 2H, CCH₂Ar), 3.64 (s, 2H, CCH₂Ar), 2.58 (s, 3H, C1-CH₃), 2.32 [s, 6H, Ar(CH₃)₂], and 2.30 (s, 3H, C3-CH₃).

¹³C NMR (125 MHz, CDCl₃): δ 172.1, 157.8, 156.5, 141.3, 139.4, 139.2, 138.9, 135.2, 134.7, 130.1, 126.8, 123.6, 122.2, 120.5, 115.6, 115.3, 113.1, 92.4, 82.4, 67.2, 59.8, 56.6, 53.3, 41.2, 40.6, 22.8, 21.7, and 21.4.

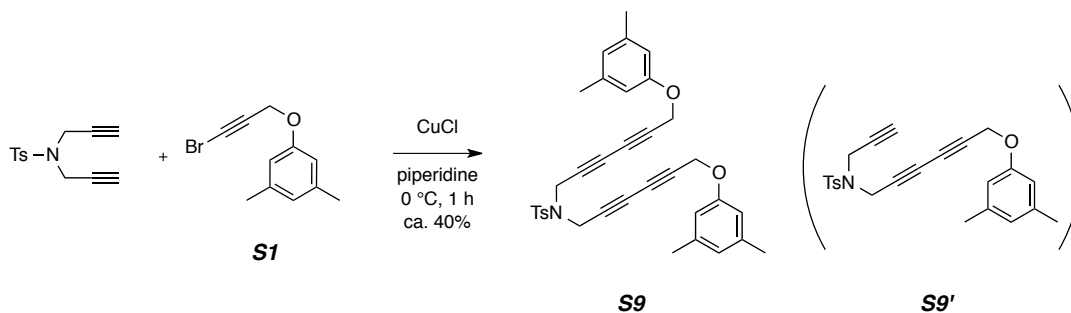
IR: 3005, 2988, 2953, 2854, 2260, 1737, 1615, 1594, 1455, 1435, 1318, 1291, 1277, 1260, 1246, 1199, 1166, and 764 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₃₃H₃₂NaO₆⁺ [M+Na]⁺ requires 547.2091; found 547.2123.

Synthesis of isoindoline 32c (Figure 4b of manuscript)



N,N-Bis(6-(3,5-dimethylphenoxy)hexa-2,4-diyne-1-yl)-4-methylbenzenesulfonamide (**S9**)



Compound **S9** was prepared following General Procedure B from *N,N*-di(prop-2-yn-1-yl) toluenesulfonamide⁷ (176 mg, 0.71 mmol, 1 equiv), bromoalkyne **S1** (370 mg, 1.78 mmol, 2.5 equiv), piperidine (1.5 mL), and CuCl (14 mg, 0.2 equiv). Tetrayne **S9** and triyne **S9'** were isolated by flash chromatography (5:1 hexanes:EtOAc) as a coeluting mixture [pale yellow oil, 220 mg, **S9** (ca. 40%) and **S9'** (ca. 20%)]. Data for **S9** are taken from spectra of the mixture in which it was the major component.

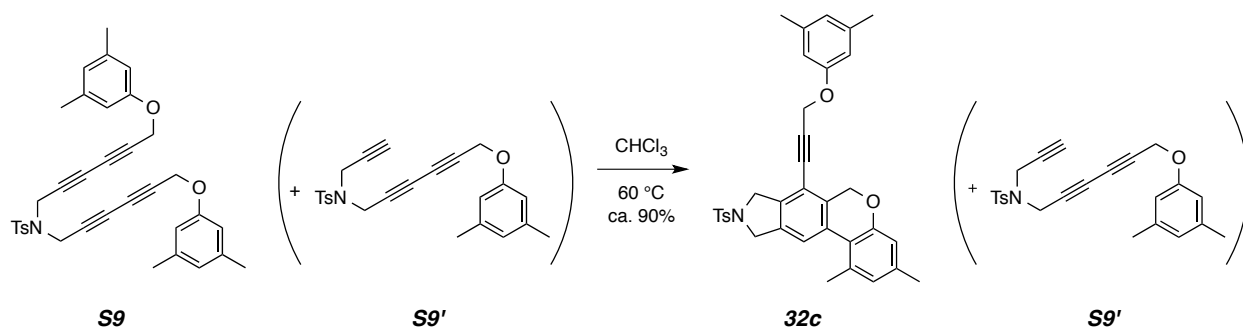
¹H NMR (500 MHz, CDCl₃): δ 7.65 (d, *J* = 8.3, 2H, *o*-SO₂ArH), 7.26 (d, *J* = 7.9 Hz, 2H, *m*-SO₂ArH), 6.65 (s, 2H, ArHp), 6.54 (s, 4H, ArHo), 4.66 (s, 4H, CH₂O), 4.18 (s, 4H, CH₂N), 2.35 (s, 3H, SO₂ArCH₃), and 2.29 [s, 12H, Ar(CH₃)₂].

¹³C NMR (125 MHz, HSQC, CDCl₃): δ 129.8, 127.7, 123.6, 112.5, 56.0, 37.4, 21.5, 21.5 (CH-containing carbons only, from the HSQC spectrum).

IR: 2919, 2855, 2258, 1614, 1594, 1471, 1447, 1353, 1319, 1293, 1164, 1152, 1093, 1064, and 892 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₃₂H₃₃NNaO₄S⁺ [M+Na]⁺ requires 586.2023; found 586.1998.

7-(3-(3,5-Dimethylphenoxy)prop-1-yn-1-yl)-1,3-dimethyl-9-tosyl-6,8,9,10-tetrahydrochromeno[3,4-f]isoindole (32c)



A solution of **S9** (50 mg, containing ca. 50 mol% of **S9'**, ca. 0.065 mmol) in CHCl_3 (2 mL) was heated at 65 °C for 20 h. The reaction mixture was concentrated to dryness. The resulting oil was initially triturated with ethanol, and the resulting slurry was dissolved in additional dichloromethane. The resulting solution was allowed to evaporate slowly. Compound **32c** precipitated as a light yellow solid. The yield of **32c** was determined by ^1H NMR analysis of the crude oil (using **S9'** as the internal standard) to be ($\geq 90\%$).

^1H NMR (500 MHz, CDCl_3): δ 7.74 (d, $J = 8.3$ Hz, 2H, *o*- SO_2ArH), 7.43 (s, 1H, *ArHI*), 7.30 (d, $J = 8.4$ Hz, 2H, *m*- SO_2ArH), 6.74 (s, 1H, *ArH*), 6.71 (s, 1H, *ArH*), 6.70 (s, 1H, *ArH*), 6.66 (s, 2H, *ArHo*), 4.96 (s, 2H, CH_2O), 4.95 (s, 2H, CH_2O), 4.66 (s, 2H, CH_2N), 4.62 (s, 2H, CH_2N), 2.54 (s, 3H, *ArCH}_3*), 2.40 (s, 3H, *ArCH}_3*), 2.35 [s, 6H, *Ar(CH}_3)_2*], and 2.29 (s, 3H, *ArCH}_3*).

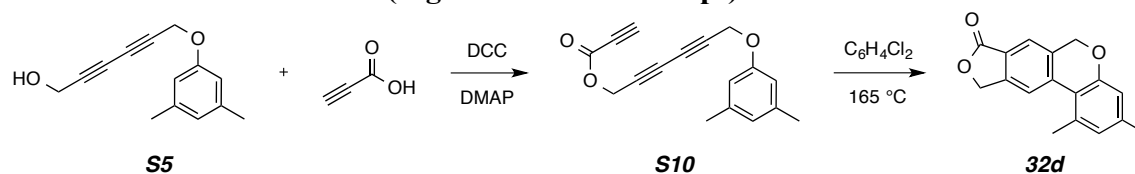
^{13}C NMR (125 MHz, CDCl_3): δ 157.6, 156.6, 144.0, 139.58, 139.55, 137.3, 135.53, 135.48, 135.2, 133.9, 131.5, 130.1, 127.8, 127.0, 123.8, 120.3, 120.0, 115.7, 114.1, 113.0, 93.4, 81.2, 66.9, 56.4, 54.6, 53.9, 22.8, 21.7/21.7 (2 unresolved resonances, as confirmed by HSQC), and 21.4.

IR: 2953, 2919, 2854, 2254, 1615, 1594, 1457, 1349, 1292, 1164, 1098, 1066, and 910 cm^{-1} .

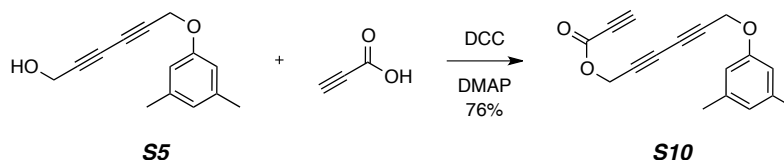
HRMS (ESI-TOF): Calcd for $\text{C}_{32}\text{H}_{33}\text{NNaO}_4\text{S}^+ [\text{M}+\text{Na}]^+$ requires 586.2023; found 586.2019.

mp: 150-153 °C.

Synthesis of isobenzofuran **32d** (Figure 4b of manuscript)



6-(3,5-Dimethylphenoxy)hexa-2,4-diyne-1-yl Propiolate (**S10**)



Triyne **S10** was prepared following General Procedure D from **S5** (214 mg, 1 mmol), propiolic acid (84 mg, 1.2 mmol), DCC (227 mg, 1.1 mmol), DMAP (12 mg, 0.1 mmol), and CH₂Cl₂ (10 mL). **S10** was obtained following flash chromatography (hexanes:EtOAc = 12:1) as a light yellow oil (222 mg, 0.76 mmol, 76%).

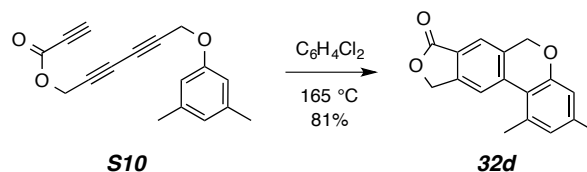
¹H NMR (500 MHz, CDCl₃): δ 6.65 (s, 1H, ArH₄), 6.56 (s, 2H, ArH₂H₆), 4.84 (t, *J* = 1.0 Hz, 2H), 4.73 (t, *J* = 1.0 Hz, 2H), 2.96 (s, 1H, CCH), and 2.30 (s, 6H, ArCH₃).

¹³C NMR (125 MHz, CDCl₃): δ 157.6, 151.8, 139.6, 123.8, 112.7, 76.4, 75.8, 73.9, 72.0, 71.8, 70.7, 56.2, 54.0, and 21.7.

IR: 3280, 2920, 2124, 1723, 1615, 1594, 1472, 1445, 1363, 1318, 1293, 1206, 1169, 1151, 1064, 980, and 830 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₇H₁₄NaO₃⁺ [M+Na]⁺ requires 289.0835; found 289.0849.

1,3-Dimethyl-6*H*-isobenzofuro[5,6-*c*]chromen-8(10*H*)-one (**32d**)



A solution of **S10** (21 mg, 0.072 mmol) in dichlorobenzene (2.4 mL) was heated at 165 °C for 4 h. The resulting solution was directly subjected to MPLC (hexanes:EtOAc = 3:1) to give isobenzofuran **32d** as a colorless solid (17 mg, 0.058 mmol, 81%).

¹H NMR (500 MHz, CDCl₃): δ 7.77 (d, *J* = 1.0 Hz, 1H), 7.76 (d, *J* = 1.0 Hz, 1H), 6.82 (br s, 1H), 6.80 (br s, 1H), 5.36 (br s, 2H), 4.99 (br s, 2H), 2.66 (br s, 3H, C1-CH₃), and 2.34 (br s, 3H, C3-CH₃).

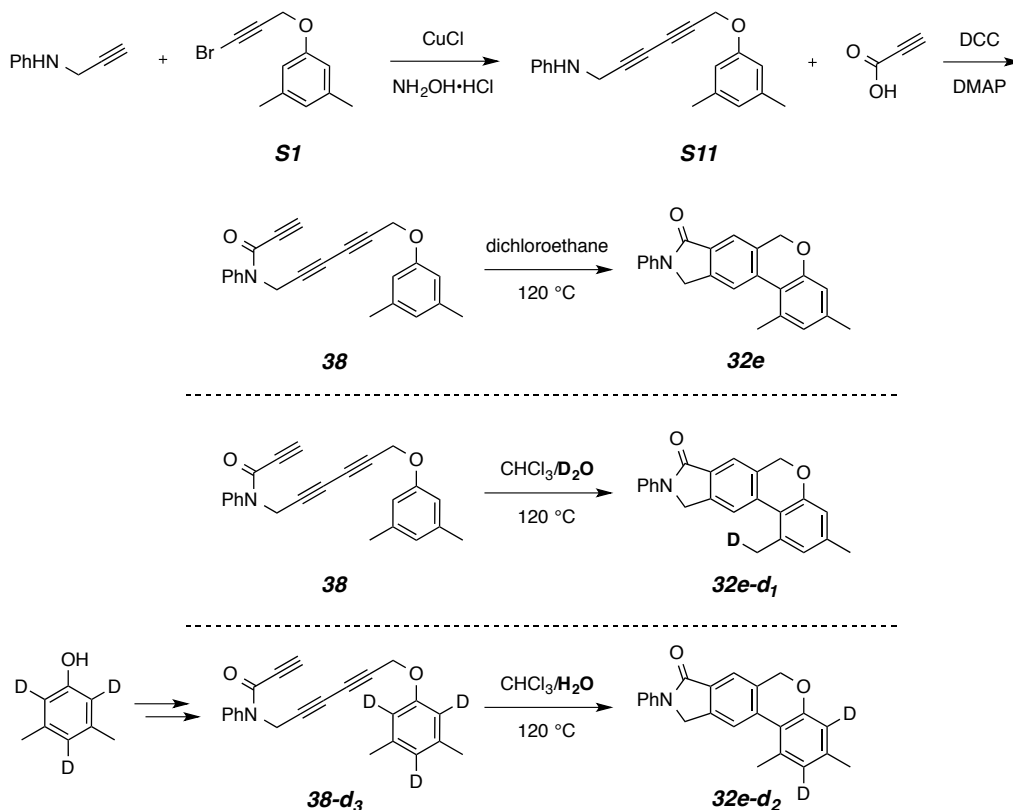
¹³C NMR (125 MHz, CDCl₃): δ 171.0, 157.4, 146.7, 141.0, 137.4, 136.0, 135.1, 127.3, 123.6, 122.0, 119.9, 119.2, 116.0, 70.0, 69.2, 22.9, and 21.5.

IR: 2959, 2917, 2857, 1757, 1615, 1593, 1451, 1355, 1355, 1315, 1287, 1195, 1180, 1154, 1138, 1067, 1046, 1015, 1006, 908, 847, 776, and 755 cm⁻¹.

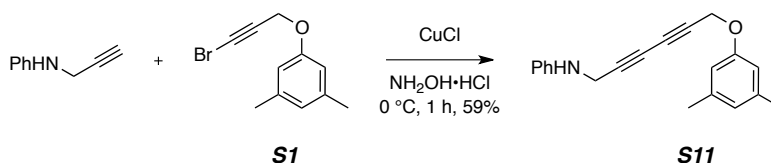
HRMS (ESI-TOF): Calcd for C₁₇H₁₄NaO₃⁺ [M+Na]⁺ requires 289.0835; found 289.0849.

mp: 154-156 °C.

Synthesis of isoindolones **32e**, **32e-d₁**, and **32e-d₂** (Figure 4b and 4d of manuscript)



N-(6-(3,5-Dimethylphenoxy)hexa-2,4-diyne-1-yl)aniline (**S11**)



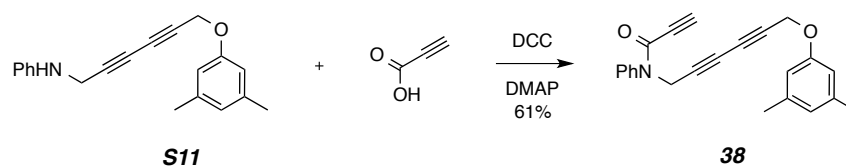
Diene **S11** was prepared following General Procedure C from *N*-(prop-2-yn-1-yl)aniline (131 mg, 1 mmol), **S1** (287 mg, 1.2 mmol), CuCl (5 mg, 0.05 mmol), 30% aqueous BuNH₂ (4 mL), and Et₂O (4 mL). Compound **S11** was isolated as a clear yellow oil (170 mg, 0.059 mmol, 59%) after purification by flash chromatography (hexanes:EtOAc 12:1 then 5:1).

¹H NMR (500 MHz, CDCl₃): δ 7.21 (dd, *J* = 8.6, 7.4 Hz, 2H, NArHm), 6.80 (tt, *J* = 7.4, 1.0 Hz, 1H, NArHp), 6.66 (dd, *J* = 8.6, 1.0 Hz, 1H, NArHo), 6.64 (s, 1H, OArHp), 6.55 (s, 2H, OArHo), 4.68 (s, 2H, CH₂O), 4.01 (s, 2H, CH₂N), 3.86 (s, 1H, NH), and 2.28 [s, 6H, Ar(CH₃)₂].

¹³C NMR (125 MHz, CDCl₃): δ 157.7, 146.7, 139.5, 129.5, 123.7, 119.1, 113.8, 112.7, 77.6, 73.2, 71.5, 67.4, 56.3, 34.5, and 21.7

IR: 3052, 3020, 2918, 2860, 2255, 1602, 1596, 1504, 1472, 1439, 1374, 1350, 1316, 1293, 1258, 1168, 1150, 1062, and 830 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₀H₁₉NNaO⁺ [M+Na]⁺ requires 312.1359; found 312.1371.

N-(6-(3,5-Dimethylphenoxy)hexa-2,4-diyne-1-yl)-N-phenylpropiolamide (38)

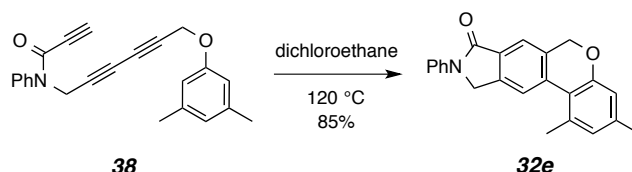
Amide **38** was prepared following General Procedure D from **S11** (289 mg, 1 mmol), propiolic acid (84 mg, 1.2 mmol), DCC (227 mg, 1.1 mmol), DMAP (12 mg, 0.1 mmol), and CH_2Cl_2 (10 mL). Compound **38** was isolated using MPLC (hexanes:EtOAc = 3:1) as a clear yellow oil (208 mg, 0.61 mmol, 61%).

^1H NMR (500 MHz, CDCl_3 , as a 8:1 ratio of two rotamers): Major rotamer δ 7.46-7.40 (m, 3H, NArHmHp), 7.35-7.31 (m, 2H, NArHo), 6.65 (s, 1H, OArHp), 6.56 (s, 2H, OArHo), 4.70 (s, 2H, CH_2O), 4.60 (s, 2H, CH_2N), 2.84 (s, 1H, $\text{C}\equiv\text{CH}$), and 2.29 [s, 6H, $\text{Ar}(\text{CH}_3)_2$]. Minor rotamer δ 4.80 (s, 2H, CH_2O), 4.75 (s, 2H, CH_2N), 3.32 (s, 1H, $\text{C}\equiv\text{CH}$), and 2.42 [s, 6H, $\text{Ar}(\text{CH}_3)_2$].

^{13}C NMR (125 MHz, CDCl_3): δ 157.7, 152.8, 140.4, 139.5, 129.7, 129.2, 128.4, 123.7, 112.7, 80.7, 75.8, 74.2, 73.8, 71.2, 68.7, 56.3, 38.8, and 21.7 (only resonances for the major rotamer are reported).

IR: 3287, 2919, 2859, 2111, 1644, 1614, 1594, 1493, 1383, 1318, 1292, 1276, 1220, 1168, 1151, 1063, 831, 765, and 750 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{23}\text{H}_{19}\text{NNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$ requires 364.1308; found 364.1311.

1,3-Dimethyl-9-phenyl-9,10-dihydrochromeno[3,4-f]isoindol-8(6H)-one (32e)

A solution of **38** (20 mg, 0.059 mmol) in dichloroethane (2 mL) was heated at $120\text{ }^\circ\text{C}$ for 18 h. The resulting solution was concentrated and subjected to MPLC (hexanes:EtOAc = 3:1) to give **32e** as a colorless solid (17 mg, 0.05 mmol, 85%).

^1H NMR (500 MHz, CDCl_3): δ 7.89 (dd, $J = 8.9, 1.3\text{ Hz}$, 2H, Ho), 7.83 (br s, 1H, H7), 7.77 (br s, 1H, H11), 7.44 (dd, $J = 8.7, 7.4\text{ Hz}$, 2H, Hm), 7.19 (tt, $J = 7.4, 1.2\text{ Hz}$, 1H, Hp), 6.82 (d, $J = 1.6\text{ Hz}$, 1H, H2 or H4), 6.78 (d, $J = 1.7\text{ Hz}$, 1H, H4 or H2), 5.01 (s, 2H, H6 or H10), 4.92 (s, 2H, H6 or H10), 2.69 (s, 3H, C1- CH_3), 2.34 (s, 3H, C3- CH_3).

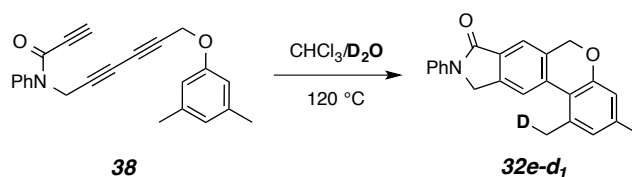
^{13}C NMR (125 MHz, CDCl_3): δ 167.4, 157.2, 140.3, 140.1, 139.8, 135.7, 135.3, 134.3, 131.3, 129.4, 127.2, 124.6, 120.5, 120.3, 120.0, 119.5, 116.0, 69.3, 51.1, 23.0, and 21.4.

IR: 2981, 2916, 2856, 1682, 1616, 1597, 1502, 1448, 1387, 1287, 1180, 1130, 1061, 1011, 891, and 857 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{23}\text{H}_{19}\text{NNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$ requires 364.1308; found 364.1298.

mp: $235\text{-}239\text{ }^\circ\text{C}$.

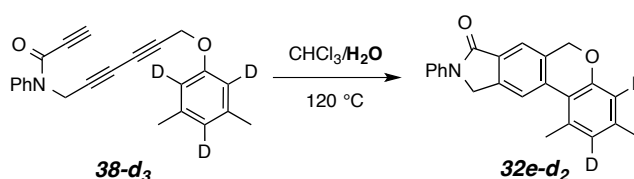
1-Deuteromethyl-3-methyl-9-phenyl-9,10-dihydrochromeno[3,4-f]isoindol-8(6H)-one (**32e-d₁**)



To a solution of **38** (4 mg, 0.012 mmol) in chloroform (1 mL), D₂O (0.05 mL) was added, and the resulting mixture was heated at 120 °C for 18 h. The resulting solution was concentrated. Analysis by integration of the C1-methyl resonances (δ 2.68 for **32e-d₁** vs. 2.69 for **32e**) in the ¹H NMR spectrum of this material suggested that it comprised ca. 93% of **32e-d₁** and 7% of **32e**.

¹H NMR (500 MHz, CDCl₃): δ 7.89 (dd, J = 8.9, 1.3 Hz, 2H, *Ho*), 7.83 (br s, 1H, *H7*), 7.77 (br s, 1H, *H11*), 7.44 (dd, J = 8.7, 7.4 Hz, 2H, *Hm*), 7.19 (tt, J = 7.4, 1.2 Hz, 1H, *Hp*), 6.82 (d, J = 1.6 Hz, 1H, *H2* or *H4*), 6.78 (d, J = 1.7 Hz, 1H, *H4* or *H2*), 5.01 (s, 2H, *H6* or *H10*), 4.92 (s, 2H, *H6* or *H10*), 2.68 (t, J_{HD} = 2.0 Hz, 2H, C1-CH₂D), and 2.34 (s, 3H, C3-CH₃).

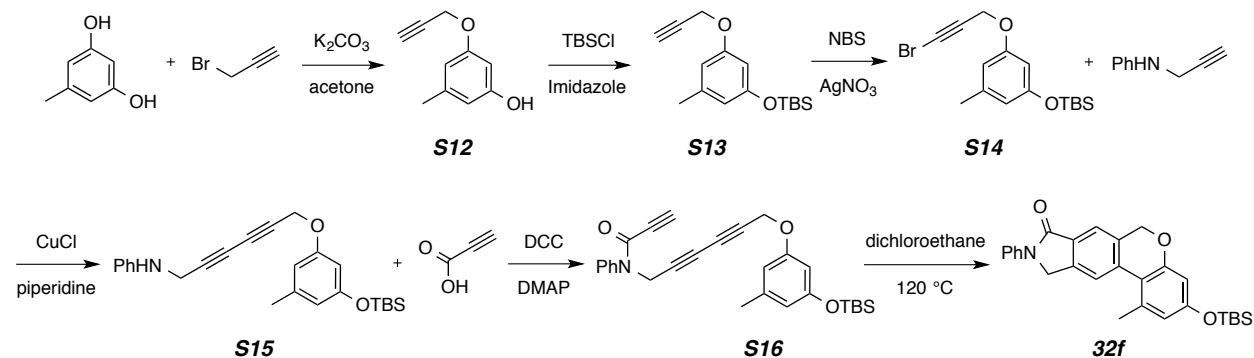
1,3-Dimethyl-2,4-dideutero-9-phenyl-9,10-dihydrochromeno[3,4-f]isoindol-8(6H)-one (**32e-d₂**)



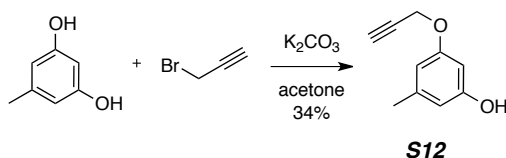
Substrate **38-d₃** was prepared by an analogous sequence to that described above to prepare **38**, starting with 2,4,6-trideutero-3,5-dimethylphenol.⁸ That phenol was judged to be ca. 98% deuterated by ¹H NMR analysis. To a solution of **38-d₃** (4 mg, 0.012 mmol) in chloroform (1 mL) was added H₂O (0.05 mL), and the resulting mixture was heated at 120 °C for 18 h. The resulting solution was concentrated to give **32e-d₂**. ¹H NMR analysis of (i) the region of the C1-methyl resonance showed no detectable amount of a CH₂D moiety (i.e., at δ 2.68, cf. **32e-d₁**) and (ii) the presence of only ca. 2% of a resonance of each of the C2-H and C4-H protons.

¹H NMR (500 MHz, CDCl₃): δ 7.89 (dd, J = 8.9, 1.3 Hz, 2H, *Ho*), 7.83 (br s, 1H, *H7*), 7.77 (br s, 1H, *H11*), 7.44 (dd, J = 8.7, 7.4 Hz, 2H, *Hm*), 7.19 (tt, J = 7.4, 1.2 Hz, 1H, *Hp*), 5.01 (s, 2H, *H6* or *H10*), 4.92 (s, 2H, *H6* or *H10*), 2.69 (s, 3H, C1-CH₃), and 2.34 (s, 3H, C3-CH₃).

Synthesis of isoindolone **32f** (Figure 4b of manuscript)



3-Methyl-5-(prop-2-yn-1-yloxy)phenol (**S12**)



K_2CO_3 (2.76 g, 20 mmol, 2 equiv) was added to a solution of orcinol (1.24 g, 10 mmol, 1 equiv) and 3-bromoprop-1-yne (1.77 g, 15 mmol, 1.5 equiv) in acetone (50 mL). The resulting mixture was heated at $50\text{ }^\circ\text{C}$ with stirring overnight. The resulting slurry was partitioned between EtOAc and H_2O . The aqueous layer was washed with EtOAc (30 mL x 3). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. The resulting oil was subjected to flash chromatography (hexanes:EtOAc = 19:1 then 5:1 then 3:1) to give **S12** as a light yellow oil (550 mg, 3.4 mmol, 34%).

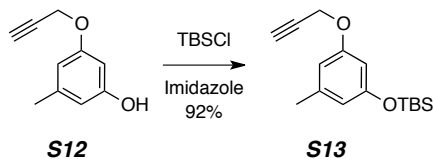
1H NMR (500 MHz, $CDCl_3$): δ 6.38 (br dd, $J = 1.8, 1.8$ Hz, 1H), 6.30 (overlapping d, $J = 1.8$ Hz, 2H), 4.65 (s, 1H, OH), 4.64 (d, $J = 2.4$ Hz, 2H, CH_2O), 2.52 (t, $J = 2.4$ Hz, 1H, $C\equiv CH$), and 2.28 (br s, 3H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 156.6, 140.9, 109.7, 108.4, 99.8, 78.8, 75.7, 56.0, and 21.8.

IR: 3390, 3290, 2923, 2867, 2123, 1596, 1496, 1467, 1372, 1327, 1305, 1146, 1056, 1023, and 832 cm^{-1} .

HRMS (ESI-TOF): Calcd for $C_{10}H_9O_2^- [M-H]^-$ requires 161.0608; found 161.0606.

tert-Butyldimethyl(3-methyl-5-(prop-2-yn-1-yloxy)phenoxy)silane (**S13**)



TBSCl (360 mg, 2.4 mmol, 1.2 equiv) and imidazole (272 mg, 4 mmol, 2 equiv) were sequentially added to a solution of **S12** (324 mg, 2 mmol, 1 equiv) in CH_2Cl_2 (10 mL) at $0\text{ }^\circ\text{C}$. The reaction mixture was allowed to warm to rt. After 3 h the reaction mixture was partitioned between CH_2Cl_2 (20 mL) and saturated aqueous NH_4Cl (20 mL). The aqueous layer was washed with CH_2Cl_2 (10 mL x 2). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. The resulting oil was

purified by flash chromatography (hexanes:EtOAc = 19:1) to give **S13** as a clear colorless oil (510 mg, 1.84 mmol, 92%).

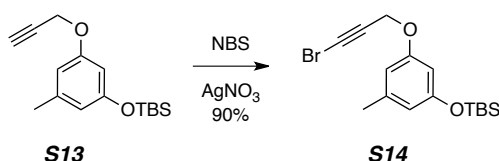
¹H NMR (500 MHz, CDCl₃): δ 6.40 (s, 1H, ArH), 6.32 (s, 1H, ArH), 6.30 (dd, *J* = 2.1, 2.1 Hz, 1H, ArH), 4.63 (d, *J* = 2.4 Hz, 2H, CH₂O), 2.51 (t, *J* = 2.4 Hz, 1H, C≡CH), 2.27 (s, 3H, ArCH₃), 0.98 [s, 9H, C(CH₃)₃], and 0.19 [s, 6H, Si(CH₃)₂].

¹³C NMR (125 MHz, CDCl₃): δ 158.6, 156.7, 140.3, 114.6, 108.9, 104.4, 78.9, 75.6, 56.0, 25.9, 21.9, 18.4 and -4.2.

IR: 3307, 2957, 2930, 2859, 2124, 1590, 1471, 1463, 1370, 1324, 1254, 1154, 1061, 1038, and 839 cm⁻¹.

GC-LRMS: t_R = 8.29 min. *m/z*: 276 (M⁺, 100), 261 (M⁺-CH₃, 20), 248 (M⁺-C₂H₄, 20), 219 [M⁺-C(CH₃)₃, 90], 203 (45), 189 (65), and 145 (70).

(3-((3-Bromoprop-2-yn-1-yl)oxy)-5-methylphenoxy)(*tert*-butyl)dimethylsilane (**S14**)



Bromoalkyne **S14** was prepared following General Procedure A from **S13** (276 mg, 1 mmol, 1 equiv), NBS (186 mg, 1.05 mmol, 1.05 equiv), AgNO₃ (16 mg, 0.1 mmol, 0.1 equiv), and acetone (10 mL). The reaction was closely monitored (GC analysis) to minimize over-bromination on the aromatic ring. **S14** was obtained as a clear yellow oil (320 mg, 0.90 mmol, 90%) following flash chromatography (hexanes:EtOAc = 19:1).

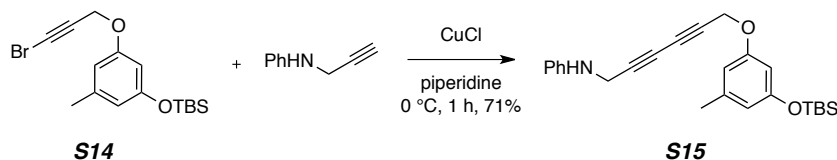
¹H NMR (500 MHz, CDCl₃): δ 6.38 (s, 1H, ArH), 6.32 (s, 1H, ArH), 6.28 (dd, *J* = 2.1, 2.1 Hz, 1H, ArH), 4.65 (s, 2H, CH₂O), 2.27 (s, 3H, ArCH₃), 0.98 [s, 9H, C(CH₃)₃], and 0.20 [s, 6H, Si(CH₃)₂].

¹³C NMR (125 MHz, CDCl₃): δ 158.5, 156.7, 140.4, 114.7, 109.0, 104.3, 75.4, 56.9, 47.6, 25.9, 21.8, 18.4, and -4.2.

IR: 2956, 2930, 2859, 2219, 1590, 1471, 1463, 1371, 1323, 1300, 1254, 1153, 1067, 1042, and 839 cm⁻¹.

GC-LRMS: t_R = 9.71 min. *m/z*: 356 (M⁺, 70), 354 (M⁺, 70), 299 [M⁺-C(CH₃)₃, 20], 297 [M⁺-C(CH₃)₃, 20], 284 (15), 282 (15), 269 (20), 267 (20), 217(50), 203 (100), 189 (40), and 73 (45).

N-(6-(3-((*tert*-Butyldimethylsilyl)oxy)-5-methylphenoxy)hexa-2,4-diyn-1-yl)aniline (**S15**)



Diyne **S15** was prepared following General Procedure B from **S14** (316 mg, 0.89 mmol, 1.2 equiv), *N*-(prop-2-yn-1-yl)aniline (100 mg, 0.76 mmol, 1 equiv), CuCl (8 mg, 0.08 mmol, 0.1 equiv), and piperidine (2 mL). **S15** was obtained following flash chromatography (hexanes:EtOAc = 5:1) as a clear yellow oil (220 mg, 0.54 mmol, 71%).

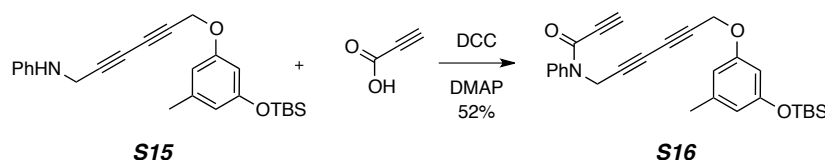
¹H NMR (500 MHz, CDCl₃): δ 7.21 (dd, *J* = 8.6, 7.4 Hz, 2H, ArH_m), 6.80 (tt, *J* = 7.3, 1.0 Hz, 1H, ArH_p), 6.67 (dd, *J* = 8.6, 1.0 Hz, 2H, ArH_o), 6.35 (m, 1H, ArH), 6.31 (m, 1H, ArH), 6.25 (m, 1H, ArH), 4.66 (s, 2H, CH₂O), 4.01 (d, *J* = 6.1 Hz, 2H, NHCH₂), 3.86 (br t, *J* = 5.6 Hz, 1H, NHCH₂), 2.26 (s, 3H, ArCH₃), 0.97 [s, 9H, C(CH₃)₃], and 0.18 [s, 6H, Si(CH₃)₂].

^{13}C NMR (125 MHz, CDCl_3): δ 158.5, 156.7, 146.7, 140.4, 129.5, 119.1, 114.7, 113.8, 108.9, 104.3, 77.7, 73.0, 71.6, 67.3, 56.4, 34.4, 25.9, 21.9, 18.4, and -4.2.

IR: 3400, 2955, 2930, 2886, 2858, 2258, 1603, 1591, 1505, 1471, 1463, 1321, 1254, 1152, 1058, 1035, and 840 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{25}\text{H}_{31}\text{NNaO}_2\text{Si}^+ [\text{M}+\text{Na}]^+$ requires 428.2016; found 428.2011.

***N*-(6-(3-((*tert*-Butyldimethylsilyl)oxy)-5-methylphenoxy)hexa-2,4-diyn-1-yl)-*N*-phenylpropiolamide (**S16**)**



Amide **S16** was prepared following General Procedure D from **S15** (202 mg, 0.5 mmol), propiolic acid (42 mg, 0.6 mmol), DCC (125 mg, 0.6 mmol), DMAP (6 mg, 0.05 mmol), and CH_2Cl_2 (4 mL). Amide **S16** was obtained following flash chromatography (hexanes:EtOAc = 3:1) as a clear yellow oil (119 mg, 0.26 mmol, 52%).

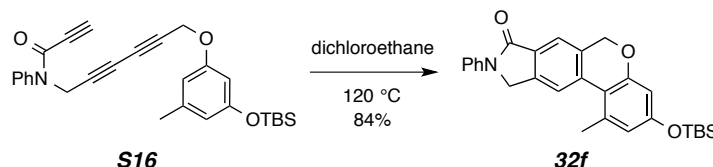
^1H NMR (500 MHz, CDCl_3 , as a 6.5:1 ratio of two rotamers): Major rotamer δ 7.47-7.40 (m, 3H, Ar*HoHp*), 7.36-7.31 (m, 2H, Ar*Hm*), 6.36 (s, 1H, Ar*H*), 6.32 (s, 1H, Ar*H*), 6.25 (s, 1H, Ar*H*), 4.67 (s, 2H, CH_2), 4.60 (s, 2H, CH_2), 2.83 (s, 1H, $\text{C}\equiv\text{CH}$), 2.27 (s, 3H, Ar*CH}_3*), 0.97 [s, 9H, $\text{C}(\text{CH}_3)_3$], and 0.19 [s, 6H, $\text{Si}(\text{CH}_3)_2$]. Minor rotamer δ 4.78 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), and 3.29 (s, 1H, $\text{C}\equiv\text{CH}$).

^{13}C NMR (125 MHz, CDCl_3): δ 158.4, 156.7, 152.7, 140.4, 140.3, 129.6, 129.2, 128.4, 114.7, 108.8, 104.3, 80.7, 75.8, 74.2, 73.6, 71.3, 68.6, 56.3, 38.8, 25.9, 21.8, 18.4, and -4.2. (only resonances for the major rotamer are reported).

IR: 3286, 2955, 2930, 2858, 2112, 1648, 1644, 1591, 1493, 1469, 1463, 1382, 1323, 1294, 1271, 1253, 1220, 1151, 1058, 1034, and 840 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{28}\text{H}_{31}\text{NNaO}_3\text{Si}^+ [\text{M}+\text{Na}]^+$ requires 480.1965; found 480.1950.

3-((*tert*-Butyldimethylsilyl)oxy)-1-methyl-9-phenyl-9,10-dihydrochromeno[3,4-*f*]isoindol-8(*6H*)-one (32f**)**



A solution of **S16** (25 mg, 0.055 mmol) in dichloroethane (1.8 mL) was heated to $120\text{ }^\circ\text{C}$ for 18 h. The resulting solution was concentrated and subjected to MPLC (hexanes:EtOAc = 3:1) to give **32f** as a colorless solid (21 mg, 0.046 mmol, 84%).

^1H NMR (500 MHz, CDCl_3): δ 7.88 (dd, $J = 8.7, 1.1$ Hz, 2H, *Ho*), 7.77 (s, 1H, *H7* or *H11*), 7.74 (s, 1H, *H7* or *H11*), 7.43 (dd, $J = 8.8, 7.4$ Hz, 2H, *Hm*), 7.18 (tt, $J = 7.4, 1.0$ Hz, 1H, *Hp*), 6.50 (d, $J = 2.5$ Hz, 1H, *H2*), 6.44 (d, $J = 2.5$ Hz, 1H, *H4*), 4.99 (s, 2H, *H6* or *H10*), 4.90 (s, 2H, *H6* or *H10*), 2.66 (s, 3H, Ar*CH}_3*), 1.00 [s, 9H, $\text{C}(\text{CH}_3)_3$], and 0.25 [s, 6H, $\text{Si}(\text{CH}_3)_2$].

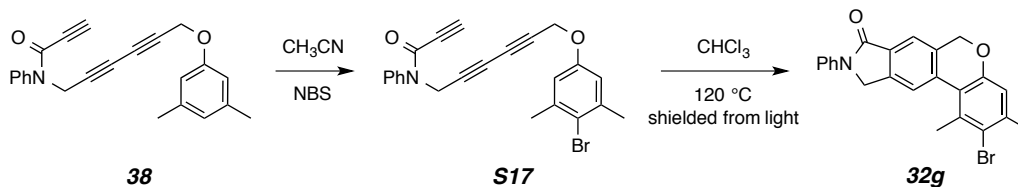
^{13}C NMR (125 MHz, CDCl_3): δ 167.4, 158.3, 156.9, 140.2, 139.8, 137.2, 135.4, 133.6, 130.9, 129.4, 124.6, 120.5, 119.6, 119.5, 118.4, 116.9, 106.8, 69.5, 51.1, 25.9, 23.1, 18.4, and -4.1.

IR: 2956, 2931, 2859, 1700, 1689, 1681, 1608, 1596, 1563, 1501, 1494, 1473, 1456, 1441, 1405, 1380, 1316, 1254, 1175, 1154, 1067, 853, and 836 cm^{-1} .

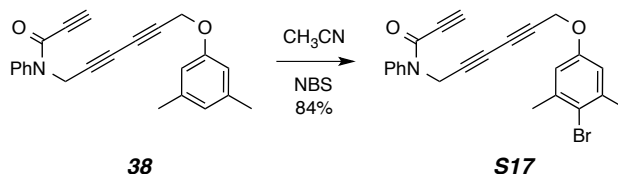
HRMS (ESI-TOF): Calcd for $\text{C}_{28}\text{H}_{31}\text{NNaO}_3\text{Si}^+$ $[\text{M}+\text{Na}]^+$ requires 480.1965; found 480.1955.

mp: 188-193 °C.

Synthesis of isoindolone **32g** (Figure 4b of manuscript)



N-(6-(4-Bromo-3,5-dimethylphenoxy)hexa-2,4-diyne-1-yl)-*N*-phenylpropiolamide (**S17**)



NBS (15 mg, 0.085 mmol) was added to a solution of **38** (28 mg, 0.082 mmol) in CH₃CN (0.27 mL)⁹. The reaction mixture was stirred for 1 h at rt and partitioned between H₂O and EtOAc. The aqueous layer was washed with EtOAc (10 mL x 3). The combined organic layers were washed with brine, dried (Na₂SO₄), and concentrated. The resulting oil was purified by flash chromatography (hexanes:EtOAc = 3:1) to give **S17** as a clear brown oil (29 mg, 0.069 mmol, 84%).

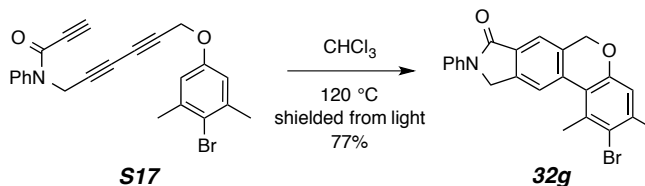
¹H NMR (500 MHz, CDCl₃, as a 9:1 ratio of two rotamers): Major rotamer δ 7.46-7.39 (m, 3H, ArH_mH_p), 7.33 (dd, *J* = 8.0, 2.1 Hz, 2H, ArH_o), 6.67 (br s, 2H, ArH₂/H₆), 4.68 (t, *J* = 0.9 Hz, 2H, OCH₂ or NCH₂), 4.59 (t, *J* = 0.9 Hz, 2H, OCH₂ or NCH₂), 2.84 (s, 1H, C≡CH), and 2.39 [br s, 6H, Ar(CH₃)₂]. Minor rotamer δ 4.78 (br s, 2H, OCH₂), 4.71 (br s, 2H, NCH₂), and 3.30 (s, 1H, C≡CH).

¹³C NMR (125 MHz, CDCl₃): δ 156.0, 152.7, 140.4, 139.5, 129.7, 129.2, 128.4, 119.6, 114.9, 80.8, 75.8, 74.4, 73.3, 71.5, 68.5, 56.5, 38.8, and 24.3. (only resonances for the major rotamer are reported)

IR: 2922, 2857, 2111, 1644, 1593, 1585, 1494, 1468, 1384, 1310, 1293, 1276, 1220, 1160, 1067, 1031, and 1017 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₃H₁₈BrNNaO₂⁺ [M+Na]⁺ requires 442.0413; found 442.0420.

2-Bromo-1,3-dimethyl-9-phenyl-9,10-dihydrochromeno[3,4-*f*]isoindol-8(6*H*)-one (**32g**)



A solution of **S17** (15 mg, 0.036 mmol) in CHCl₃ (1 mL) was heated to 120 °C for 18 h shielded from light. The resulting solution was concentrated and subjected to MPLC (hexanes:EtOAc = 3:1) to give **32g** as a colorless solid (11.5 mg, 0.028 mmol, 77%).

¹H NMR (500 MHz, CDCl₃): δ 7.88 (dd, *J* = 8.8, 1.1 Hz, 2H, H_o), 7.79 (s, 1H, H₇ or H₁₁), 7.73 (s, 1H, H₇ or H₁₁), 7.44 (dd, *J* = 8.7, 7.4 Hz, 2H, H_m), 7.20 (tt, *J* = 7.4, 1.0 Hz, 1H, H_p), 6.90 (br s, 1H, H₄), 5.00 (s, 2H, OCH₂ or NCH₂), 4.92 (s, 2H, OCH₂ or NCH₂), 2.79 (s, 3H, C1-CH₃), and 2.45 (br s, 3H, C3-CH₃).

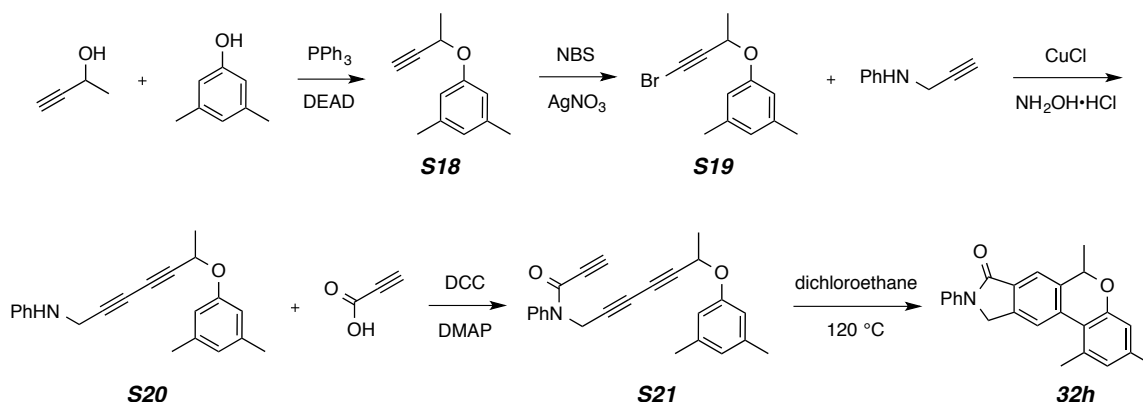
^{13}C NMR (125 MHz, CDCl_3): δ 167.2, 155.7, 140.6, 140.1, 139.7, 135.5, 134.9, 134.3, 131.9, 129.4, 124.8, 123.0, 122.8, 120.9, 120.8, 119.6, 117.2, 69.5, 51.1, 24.7, and 24.1.

IR: 2918, 2854, 1686, 1625, 1596, 1502, 1444, 1377, 1289, 1179, 1169, 1132, 1069, 957, 895, and 857 cm^{-1} .

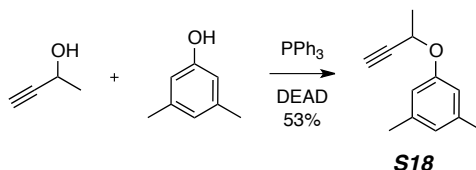
HRMS (ESI-TOF): Calcd for $\text{C}_{23}\text{H}_{18}\text{BrNNaO}_2^+$ $[\text{M}+\text{Na}]^+$ requires 442.0413; found 442.0434.

mp: 272-274 $^\circ\text{C}$.

Synthesis of isoindolone 32h (Figure 4b of manuscript)



1-(But-3-yn-2-yloxy)-3,5-dimethylbenzene (S18)



To a solution of but-3-yn-2-ol (560 mg, 8 mmol), 3,5-dimethylphenol (976 mg, 8 mmol), and PPh₃ (2.1 g, 8 mmol) in THF cooled at 0 °C was added diisopropyl azodicarboxylate (1.94 g, 9.6 mmol) dropwise. The resulting solution was stirred at this temperature for an additional 3 h. The resulting mixture was partitioned between H₂O and EtOAc. The aqueous layer was washed with EtOAc (20 mL x 2). The combined organic layers were washed with brine, dried (Na₂SO₄), and concentrated. The resulting slurry was purified by flash chromatography (hexanes:EtOAc = 25:1) to give **S18** as a light yellow oil (730 mg, 4.2 mmol, 53%), which solidified upon standing.

¹H NMR (500 MHz, CDCl₃): δ 6.63 (overlapping s, 3H, ArH), 4.85 (qd, *J* = 6.5, 2.0 Hz, 1H, CHOAr), 2.45 (d, *J* = 2.0 Hz, 1H, C≡CH), 2.29 [dt, *J* = 0.7, 0.7 Hz, 6H, Ar(CH₃)₂], and 1.64 (d, *J* = 6.5 Hz, 3H, CH₃CH).

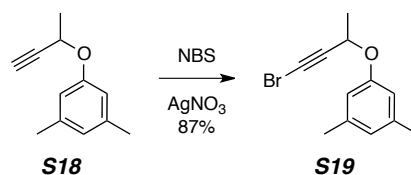
¹³C NMR (125 MHz, CDCl₃): δ 157.5, 139.3, 123.5, 113.6, 83.4, 73.8, 63.5, 22.4, and 21.7.

IR: 3293, 2990, 2938, 2920, 2115, 1613, 1594, 1470, 1447, 1375, 1317, 1291, 1169, 1154, 1127, 1091, 1054, and 830 cm⁻¹.

GC-LRMS: *t*_R = 5.59 min. *m/z*: 174 (M⁺, 70), 159 (M⁺-CH₃, 95), 122 (M⁺-C₄H₄, 100), 107 (M⁺-C₅H₇, 80), 91 (C₇H₇⁺, 30), 77 (C₆H₅⁺, 28), and 53 (20).

mp: 46-48 °C.

1-((4-Bromobut-3-yn-2-yl)oxy)-3,5-dimethylbenzene (S19)



Bromoalkyne **S19** was prepared following General Procedure A from **S18** (530 mg, 3.05 mmol), NBS (563 mg, 3.20 mmol), AgNO₃ (50 mg, 0.3 mmol), and acetone (20 mL). **S19** was obtained as a yellow oil (670 mg, 2.65 mmol, 87%), which solidified upon standing, following flash chromatography (Hexanes:EtOAc = 20:1).

¹H NMR (500 MHz, CDCl₃): δ 6.63 (s, 1H, ArHp), 6.61 (s, 2H, ArHo), 4.84 (q, *J* = 6.6 Hz, 1H, CHOAr), 2.29 [s, 6H, Ar(CH₃)₂], and 1.62 (d, *J* = 6.6 Hz, 3H, CH₃CH).

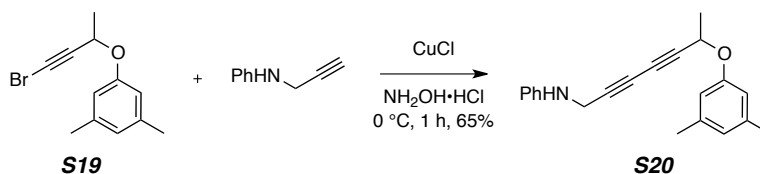
¹³C NMR (125 MHz, CDCl₃): δ 157.5, 139.4, 123.5, 113.6, 79.8, 64.5, 46.0, 22.4, and 21.7.

IR: 2989, 2936, 2920, 2209, 1613, 1594, 1471, 1450, 1374, 1316, 1291, 1169, 1154, 1131, 1093, 1060, and 829 cm⁻¹.

GC-LRMS: t_R = 7.23 min. *m/z*: 254 (M⁺, 15), 252 (M⁺, 15), 239 (M⁺-CH₃, 10), 237 (M⁺-CH₃, 10), 173 (M⁺-Br, 40), 145 (30), 122 (M⁺-BrC₄H₃, 100), 107 (M⁺-BrC₄H₃-CH₃, 70), 91 (C₇H₇⁺, 25), and 77 (C₆H₅⁺, 25).

mp: 41-51 °C.

N-(6-(3,5-Dimethylphenoxy)hepta-2,4-diyne-1-yl)aniline (**S20**)



Diyne **S20** was prepared following General Procedure C from **S19** (625 mg, 2.48 mmol, 1.24 equiv), *N*-(prop-2-yn-1-yl)aniline (262 mg, 2 mmol, 1 equiv), CuCl (10 mg, 0.1 mmol, 0.05 equiv), 30% aqueous BuNH₂ (8 mL), and Et₂O (8 mL). **S20** was obtained as a clear yellow oil (394 mg, 1.3 mmol, 65%) following flash chromatography (hexanes:EtOAc = 5:1).

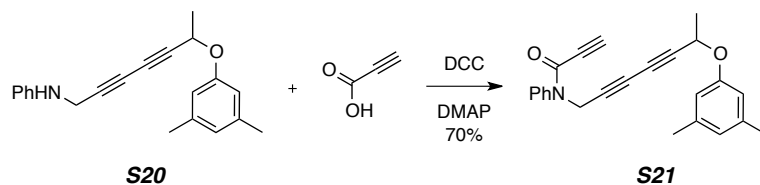
¹H NMR (500 MHz, CDCl₃): δ 7.21 (t, *J* = 7.5 Hz, 2H, NArHm), 6.79 (t, *J* = 7.5 Hz, 1H, NArHp), 6.65 (d, *J* = 7.5 Hz, 2H, NArHo), 6.63 (s, 1H, OArHp), 6.58 (s, 1H, OArHo), 4.84 (q, *J* = 6.6 Hz, 1H, CH₃CH), 3.99 (s, 2H, NCH₂), 3.85 (br s, 1H, NH), 2.28 [s, 6H, Ar(CH₃)₂], and 1.61 (d, *J* = 6.6 Hz, CH₃CH).

¹³C NMR (125 MHz, CDCl₃): δ 157.4, 146.7, 139.4, 129.5, 123.6, 119.0, 113.7, 113.5, 77.6, 77.4, 70.0, 67.3, 63.9, 34.4, 22.3, and 21.7

IR: 3470-3330, 3051, 2988, 2919, 2870, 2250, 2165, 1602, 1594, 1504, 1472, 1439, 1314, 1290, 1260, 1168, 1153, 1081, 1048, 964, and 830 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₁H₂₁NNaO⁺ [M+Na]⁺ requires 326.1515; found 326.1521.

N-(6-(3,5-Dimethylphenoxy)hepta-2,4-diyne-1-yl)-*N*-phenylpropiolamide (**S21**)



Amide **S21** was prepared following General Procedure D from **S20** (303 mg, 1 mmol, 1 equiv), propiolic acid (84 mg, 1.2 mmol, 1.2 equiv), DCC (237 mg, 1.15 mmol, 1.15 equiv), DMAP (6 mg, 0.05

mmol, 0.05 equiv), and CH_2Cl_2 (8 mL). Amide **S21** was obtained following flash chromatography (hexanes:EtOAc = 3:1) as a clear brown oil (249 mg, 0.7 mmol, 70%).

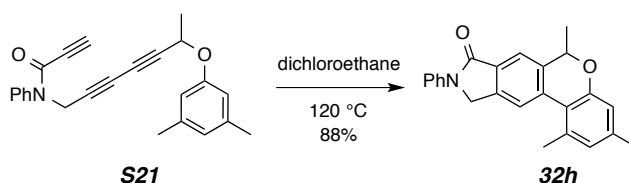
^1H NMR (500 MHz, CDCl_3 , as a 8.5:1 ratio of two rotamers): Major rotamer δ 7.46-7.30 (m, 5H, NArH), 6.64 (s, 1H, OArHp), 6.58 (s, 1H, OArHo), 4.86 (q, J = 6.6 Hz, 1H, CH_3CH), 4.57 (s, 2H, NCH_2), 2.83 (s, 1H, CCH), 2.29 [s, 6H, $\text{Ar}(\text{CH}_3)_2$], and 1.62 (d, J = 6.6 Hz, CH_3CH). Minor rotamer δ 6.59 (s, 1H, OArHp), 4.59 (s, 2H, NCH_2), 4.88 (q, J = 6.6 Hz, 1H, CH_3CH), 4.76 (s, 2H, NCH_2), 3.28 (s, 1H, CCH), and 1.64 (d, J = 6.7 Hz, CH_3CH).

^{13}C NMR (125 MHz, CDCl_3): δ 157.4, 152.7, 140.5, 139.4, 129.6, 129.2, 128.4, 123.6, 113.5, 80.7, 78.0, 75.8, 74.1, 69.8, 68.7, 63.9, 38.9, 22.2, and 21.7 (only resonances for the major rotamer are reported).

IR: 3282, 2917, 2849, 2111, 1644, 1613, 1594, 1493, 1383, 1315, 1290, 1278, 1220, 1168, 1153, 1116, 1082, 1052, 1016, and 830 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{24}\text{H}_{21}\text{NNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$ requires 378.1465; found 378.1455.

1,3,6-Trimethyl-9-phenyl-9,10-dihydrochromeno[3,4-*f*]isoindol-8(6*H*)-one (**32h**)



A solution of **S21** (17 mg, 0.048 mmol) in dichloroethane (1.6 mL) was heated to 120 °C for 18 h. The resulting solution was concentrated and subjected to MPLC (hexanes:EtOAc = 3:1) to give **32h** as a colorless solid (15 mg, 0.042 mmol, 88%).

^1H NMR (500 MHz, CDCl_3): 7.88 (dd, J = 8.8, 1.1 Hz, 2H, *Ho*), 7.80 (br s, 1H, *H7* or *H11*), 7.78 (br s, 1H, *H7* or *H11*), 7.43 (dd, J = 8.6, 7.4 Hz, 2H, *Hm*), 7.18 (tt, J = 7.4, 1.0 Hz, 1H, *Hp*), 6.79 (br d, J = 1.7 Hz, 1H, *H2*), 6.76 (br d, J = 1.7 Hz, 1H, *H4*), 5.02 (q, J = 6.5 Hz, 1H, CHCH_3), 4.91 (d, J = 16.1 Hz, 1H, *H10a*), 4.86 (d, J = 16.1 Hz, 1H, *H10b*), 2.68 (s, 3H, C1- CH_3), 2.33 (s, 3H, C3- CH_3), and 1.73 (d, J = 6.5 Hz, 3H, CHCH_3).

^{13}C NMR (125 MHz, CDCl_3): δ 167.6, 156.2, 140.2, 139.8, 139.6, 138.5, 135.4, 135.1, 131.4, 129.4, 127.0, 124.6, 120.3, 120.1, 119.6, 119.3, 116.2, 73.9, 51.1, 23.0, 21.5, and 18.8.

IR: 2978, 2917, 2849, 1693, 1615, 1598, 1501, 1449, 1379, 1293, 1267, 1179, 1135, 1086, 1059, 898, 846, and 767 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{24}\text{H}_{21}\text{NNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$ requires 378.1465; found 378.1455.

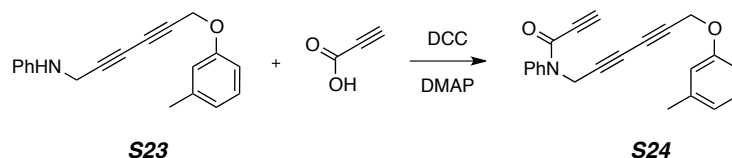
mp: 171-173 °C.

^{13}C NMR (125 MHz, CDCl_3): δ 157.6, 146.7, 139.8, 129.5, 129.4, 122.7, 119.0, 115.9, 113.7, 111.8, 77.7, 73.0, 71.6, 67.3, 56.3, 34.4, and 21.7.

IR: 3400, 3053, 2917, 2255, 1602, 1585, 1504, 1489, 1438, 1375, 1350, 1313, 1291, 1257, 1152, 1095, 1041, 924, 875, and 771 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{19}\text{H}_{17}\text{NNaO}^+$ $[\text{M}+\text{Na}]^+$ requires 298.1202; found 298.1205.

N-Phenyl-N-(6-(*m*-tolylloxy)hexa-2,4-diyne-1-yl)propiolamide (**S24**)



Amide **S24** was prepared following General Procedure D from **S23** (113 mg, 0.4 mmol, 1 equiv), propiolic acid (42 mg, 0.6 mmol, 1.5 equiv), DCC (124 mg, 0.6 mmol, 1.5 equiv), DMAP (6 mg, 0.05 mmol, 0.05 equiv), and CH_2Cl_2 (2 mL). Amide **S24** was obtained following flash chromatography (hexanes:EtOAc = 3:1) as a clear brown oil (84 mg, 0.26 mmol, 64%).

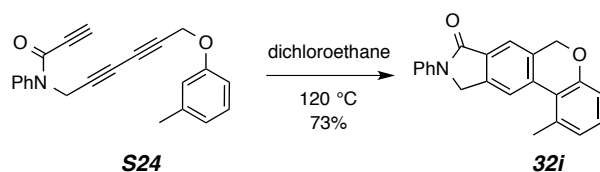
^1H NMR (500 MHz, CDCl_3 , as a 7:1 ratio of two rotamers): Major rotamer δ 7.46-7.38 (m, 3H, ArH), 7.33 (dd, $J = 8.1, 2.0$ Hz, 2H, ArHo), 7.18 (t, $J = 7.5$ Hz, 1H, ArH5), 6.81 (d, $J = 7.3$ Hz, 1H, ArH4), 6.76-6.72 (m, 2H, ArH), 4.71 (s, 2H, OCH_2), 4.59 (d, $J = 5.7$ Hz, 2H, NCH_2), 2.83 (s, 1H, CCH), and 2.34 (s, 3H, ArMe). Minor rotamer δ 4.78 (s, 2H), 4.75 (s, 2H), and 3.30 (s, 1H).

^{13}C NMR (125 MHz, CDCl_3): δ 157.6, 152.7, 140.4, 139.9, 129.7, 129.4, 129.2, 128.4, 122.8, 115.9, 111.8, 80.7, 75.8, 74.2, 73.7, 71.3, 68.6, 56.3, 38.8, and 21.7 (only resonances for the major rotamer are reported).

IR: 3280, 2930, 2856, 2111, 1642, 1593, 1587, 1491, 1382, 1290, 1277, 1259, 1244, 1220, 1152, 1035, 1061, 935, and 772 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{22}\text{H}_{17}\text{NNaO}_2^+$ $[\text{M}+\text{Na}]^+$ requires 350.1151; found 350.1167.

1-Methyl-9-phenyl-9,10-dihydrochromeno[3,4-*f*]isoindol-8(6*H*)-one (**32i**)



A solution of **S24** (22 mg, 0.067 mmol) in dichloroethane (2.2 mL) was heated to $120\text{ }^\circ\text{C}$ for 18 h. The resulting solution was concentrated and subjected to MPLC (hexanes:EtOAc = 3:1) to give **32i** as a colorless solid (16 mg, 0.049 mmol, 73%).

^1H NMR (500 MHz, CDCl_3): δ 7.88 (dd, $J = 8.7, 1.1$ Hz, 2H, Ho), 7.84 (s, 1H, H7 or H11), 7.77 (s, 1H, H7 or H11), 7.43 (dd, $J = 8.9, 7.4$ Hz, 2H, Hm), 7.20 (dd, $J = 7.9, 7.3$ Hz, 1H, H3), 7.18 (tt, $J = 7.4, 1.1$ Hz, 1H, Hp), 6.98 (ddq, $J = 7.6, 1.4, 0.7$ Hz, 1H, H2), 6.95 (ddq, $J = 8.0, 1.3, 0.6$ Hz, 1H, H4), 5.02 (s, 2H, H6 or H10), 4.90 (s, 2H, H6 or H10), and 2.72 (br s, 3H, ArCH_3).

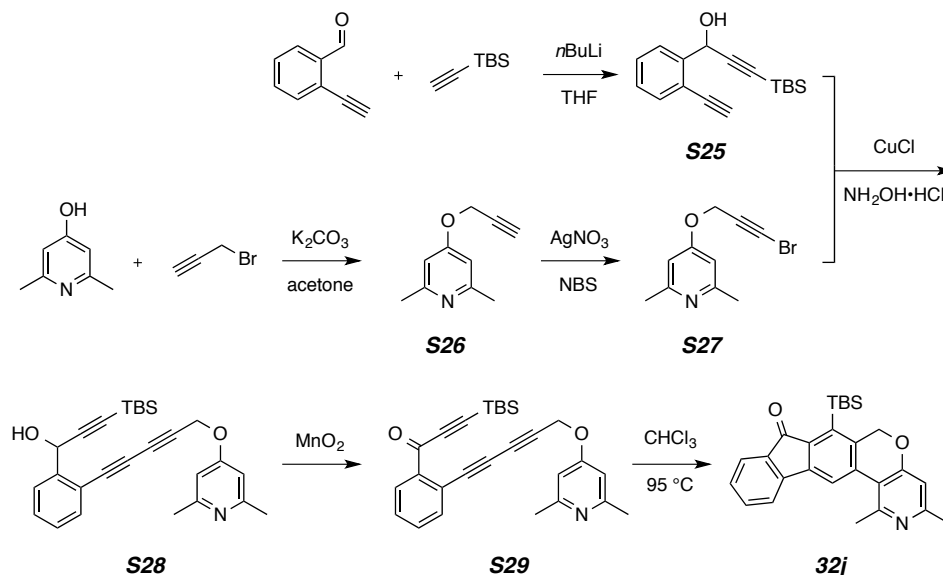
^{13}C NMR (125 MHz, CDCl_3): δ 167.3, 157.2, 140.0, 139.7, 136.0, 135.0, 134.7, 131.7, 129.8, 129.4, 126.1, 124.7, 123.1, 120.6, 120.4, 119.6, 115.5, 69.3, 51.1, and 23.0.

IR: 2917, 2857, 1683, 1596, 1503, 1449, 1417, 1385, 1328, 1293, 1272, 1260, 1241, 1203, 1179, 1158, 1133, 1039, 1009, and 892 cm^{-1} .

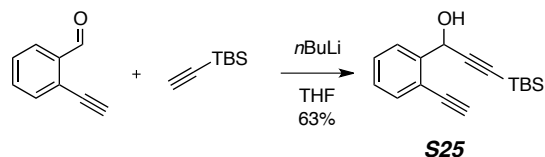
HRMS (ESI-TOF): Calcd for $C_{22}H_{17}NNaO_2^+$ $[M+Na]^+$ requires 350.1151; found 350.1159.

mp: 252-254 °C.

Synthesis of fluorenone 32j (Figure 4b of manuscript)



3-(*tert*-Butyldimethylsilyl)-1-(2-ethynylphenyl)prop-2-yn-1-ol (S25)



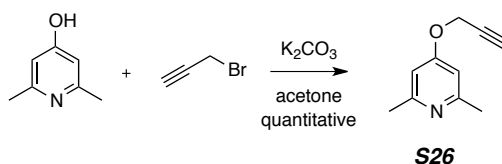
*n*BuLi (2.4 mL, 2.5 M solution in hexanes, 6 mmol, 1.2 equiv) was added to a solution of *tert*-butyl(ethynyl)dimethylsilane (6 mmol, 1.2 equiv) in THF (30 mL) cooled at $-78\text{ }^{\circ}\text{C}$. The solution was allowed to stir for 1 h at this temperature. A solution of 2-ethynylbenzaldehyde (650 mg, 5 mmol, 1.0 equiv) in THF (10 mL) was added dropwise. The resulting mixture was stirred for additional 2 h, after which saturated aqueous NH_4Cl was added. The resulting slurry was partitioned between EtOAc and H_2O . The aqueous layer was washed with EtOAc (15 mL x 3). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. The crude oil was subjected to flash chromatography (Hexanes:EtOAc = 5:1) to give **S25** as a light yellow oil (850 mg, 3.15 mmol, 63%).

$^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.73 (dd, $J = 7.8, 1.3$ Hz, 1H, ArH), 7.51 (dd, $J = 7.6, 1.2$ Hz, 1H, ArH), 7.40 (ddd, $J = 7.6, 7.6, 1.4$ Hz, 1H, ArH), 7.30 (ddd, $J = 7.6, 7.6, 1.3$ Hz, 1H, ArH), 5.88 (d, $J = 5.9$, 1H, CHO), 3.36 (s, 1H, CCH), 2.56 (d, $J = 5.9$ Hz, 1H, OH), 0.94 [s, 9H, $\text{C}(\text{CH}_3)_3$], and 0.13 [s, 6H, $\text{Si}(\text{CH}_3)_2$].

$^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 142.9, 133.4, 129.6, 128.5, 127.0, 121.0, 105.0, 90.3, 82.8, 81.2, 63.6, 26.3, 16.8, and -4.5 .

IR: 3500, 3300, 2954, 2929, 2885, 2857, 2173, 1471, 1463, 1449, 1250, 1037, 980, and 840 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{17}\text{H}_{22}\text{NaOSi}^+ [\text{M}+\text{Na}]^+$ requires 293.1332; found 293.1337.

2,6-Dimethyl-4-(prop-2-yn-1-yloxy)pyridine (S26)

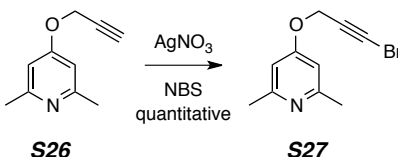
K_2CO_3 (3.36 g, 24.4 mmol, 2 equiv), 2,6-dimethylpyridin-4-ol (1.5 g, 12.2 mmol, 1 equiv), and 3-bromoprop-1-yne (2.37 g, 15.8 mmol, 1.3 equiv) in acetone (25 mL) were heated with stirring at 50 °C overnight. The resulting slurry was partitioned between EtOAc and H_2O . The aqueous layer was extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. The resulting dark oil (**S26**, 2.01 g, 102%) was used without further purification for the next step. A small aliquot was passed through a pad of silica gel (EtOAc) for characterization.

1H NMR (500 MHz, $CDCl_3$): δ 6.57 (s, 2H, ArH), 4.70 (d, $J = 2.4$ Hz, 2H, CH_2), 2.56 (t, $J = 2.4$ Hz, 1H, CH), and 2.49 (s, 6H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 164.6, 159.6, 107.1, 77.8, 76.4, 55.5, and 24.9.

IR: 3293, 2957, 2922, 2852, 2120, 1599, 1579, 1455, 1329, 1319, 1152, and 1060 cm^{-1} .

GC-LRMS: $t_R = 5.67$ min. m/z : 161 (M^+ , 100), 146 ($M^+ - CH_3$, 40), 132 (50), 118 (55), and 91 (70).

4-((3-Bromoprop-2-yn-1-yl)oxy)-2,6-dimethylpyridine (S27)

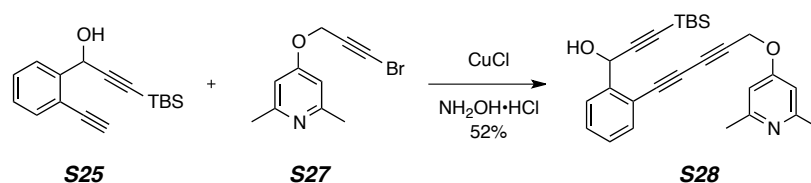
Bromide **S27** was prepared following General Procedure A from **S26** (480 mg, 3 mmol, 1 equiv), NBS (580 mg, 3.3 mmol, 1.1 equiv), $AgNO_3$ (51 mg, 0.3 mmol, 1 equiv), and acetone (20 mL). Compound **S27** was obtained and used for the next step without column chromatography. A small aliquot was passed through a pad of silica gel (EtOAc) for characterization.

1H NMR (500 MHz, $CDCl_3$): δ 6.55 (s, 2H, ArH), 4.72 (s, 2H, CH_2), and 2.49 (s, 6H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 164.6, 159.6, 107.0, 74.3, 56.3, 48.8, and 24.9.

IR: 3083, 2962, 2921, 2865, 2225, 1600, 1579, 1465, 1452, 1372, 1327, 1217, 1158, 993, 956, 849, and 823 cm^{-1} .

HRMS (ESI-TOF): Calcd for $C_{10}H_{11}BrNO^+$ [$M+H$] $^+$ requires 240.0019; found 240.0027.

3-(tert-Butyldimethylsilyl)-1-(2-(5-((2,6-dimethylpyridin-4-yl)oxy)penta-1,3-diyn-1-yl)phenyl)prop-2-yn-1-ol (S28)

Triyne **S28** was prepared following General Procedure C from **S25** (95 mg, 0.35 mmol, 1.2 equiv), **S27** (70 mg, 0.29 mmol, 1.0 equiv), $CuCl$ (3 mg, 0.03 mmol, 0.1 equiv), 30% aqueous $BuNH_2$ (1.5 mL),

and Et₂O (1.5 mL). Compound **S28** was obtained following flash chromatography (hexanes:EtOAc = 1:1, then pure EtOAc) as a brown oil (65 mg, 0.15 mmol, 52%).

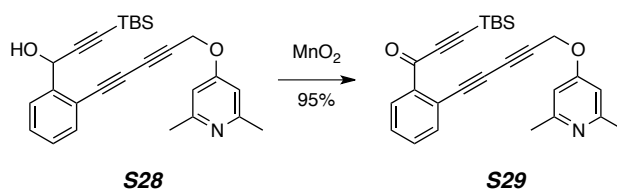
¹H NMR (500 MHz, CDCl₃): δ 7.75 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.50 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.42 (dd, *J* = 6.9, 6.9 Hz, 1H, Ar*H*), 7.30 (dd, *J* = 7.6, 7.6 Hz, 1H, Ar*H*), 6.56 (s, 2H, HetAr*H*), 5.81 (s, 1H, CHOH), 4.84 (s, 2H, CH₂O), 2.49 [s, 6H, HetAr(CH₃)₂], 0.91 [s, 9H, SiC(CH₃)₃], and 0.10 [s, 6H, Si(CH₃)₂].

¹³C NMR (125 MHz, CDCl₃): δ 164.6, 159.6, 144.3, 133.9, 130.2, 128.4, 127.1, 119.8, 107.1, 105.3, 90.0, 77.9, 77.4, 76.8, 72.5, 63.1, 56.1, 26.2, 24.8, 16.7, and -4.5.

IR: 2954, 2928, 2857, 2240, 2172, 1601, 1580, 1469, 1364, 1322, 1275, 1259, 1154, 1056, 988, 909, and 840 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₇H₃₂NO₂Si⁺ [M+H]⁺ requires 430.2197; found 430.2199.

3-(*tert*-Butyldimethylsilyl)-1-(2-(5-((2,6-dimethylpyridin-4-yl)oxy)penta-1,3-diyn-1-yl)phenyl)prop-2-yn-1-one (**S29**)



A mixture of **S28** (50 mg, 0.12 mmol) and MnO₂ (265 mg, 3.04 mmol) in CH₂Cl₂ (3 mL) was stirred at room temperature for 3 h. The resulting solution was filtered through a pad of Celite[®] and silica gel and concentrated to give **S29** as a clear yellow oil (48 mg, 0.11 mmol, 95%).

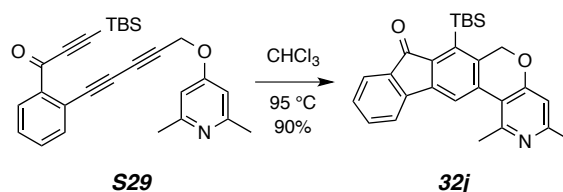
¹H NMR (500 MHz, CDCl₃): δ 8.15 (dd, *J* = 7.4, 1.6 Hz, 1H, Ar*H*), 7.62 (dd, *J* = 7.4, 1.4 Hz, 1H, Ar*H*), 7.52 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H, Ar*H*), 7.49 (ddd, *J* = 7.5, 7.5, 1.4 Hz, 1H, Ar*H*), 6.57 (s, 2H, HetAr*H*), 4.86 (s, 2H, CH₂O), 2.50 [s, 6H, HetAr(CH₃)₂], 1.00 [s, 9H, SiC(CH₃)₃], and 0.23 [s, 6H, Si(CH₃)₂].

¹³C NMR (125 MHz, CDCl₃): δ 176.2, 164.5, 159.6, 139.3, 136.0, 132.8, 132.4, 129.3, 121.1, 107.0, 102.1, 100.5, 78.6, 78.2, 77.6, 72.9, 56.1, 26.3, 24.9, 16.9, and -4.9.

IR: 2997, 2953, 2928, 2857, 2150, 1648, 1596, 1580, 1563, 1470, 1322, 1270, 1265, 1237, 1151, 1055, 1017, and 843 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₇H₃₀NO₂Si⁺ [M+H]⁺ requires 428.2040; found 428.2040.

7-(*tert*-Butyldimethylsilyl)-1,3-dimethylindeno[1',2':6,7]isochromeno[4,3-*c*]pyridin-8(6*H*)-one (**32j**)



A solution of **S29** (20 mg, 0.046 mmol) in CHCl₃ (1.4 mL) was heated at 95 °C for 36 h. The resulting solution was concentrated and subjected to flash chromatography (hexanes:EtOAc = 1:1) to give **32j** as a yellow oil (18 mg, 0.042 mmol, 90%).

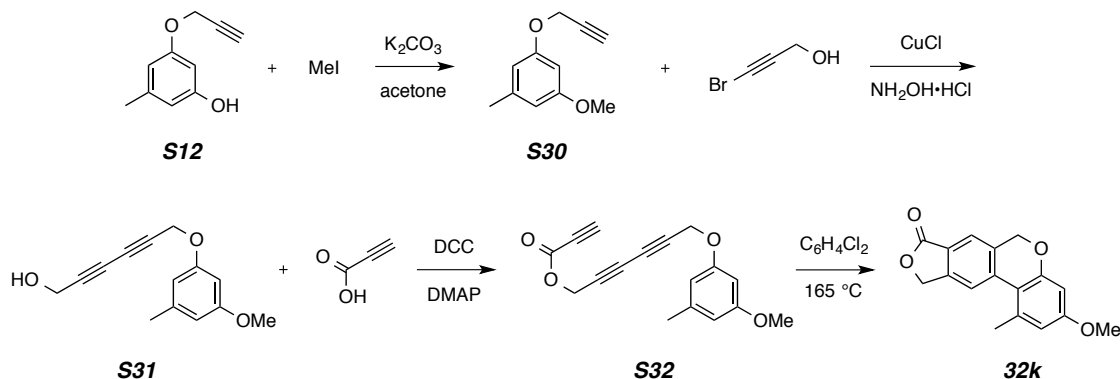
¹H NMR (500 MHz, CDCl₃): δ 7.84 (s, 1H, ArH), 7.62 (d, *J* = 7.3 Hz, 1H, ArH), 7.55 (d, *J* = 7.4 Hz, 1H, ArH), 7.50 (dd, *J* = 7.4, 7.4 Hz, 1H, ArH), 7.31 (dd, *J* = 7.4, 7.4 Hz, 1H, ArH), 6.69 (s, 1H, HetArH), 5.08 (s, 2H, CH₂O), 2.90 (s, 3H, C1CH₃), 2.53 (s, 3H, C3CH₃), 1.14 [s, 9H, SiC(CH₃)₃], and 0.43 [s, 6H, Si(CH₃)₂].

¹³C NMR (125 MHz, CDCl₃): δ 193.7, 163.8, 159.1, 155.6, 145.0, 143.2, 141.1, 139.6, 138.3, 134.7, 134.34, 134.32, 129.5, 124.2, 119.7, 118.7, 117.7, 109.0, 70.9, 28.4, 25.5, 24.8, 19.8, and 0.8.

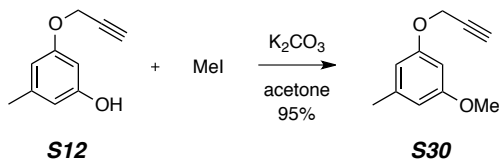
IR: 2952, 2928, 2855, 1715, 1590, 1567, 1467, 1434, 1383, 1298, 1250, 1181, 1165, 1136, 1072, and 828 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₇H₃₀NO₂Si⁺ [M+H]⁺ requires 428.2040; found 428.2068.

Synthesis of isobenzofuranone **32k** (Figure 4b of manuscript)



1-Methoxy-3-methyl-5-(prop-2-yn-1-yloxy)benzene (**S30**)



K_2CO_3 (828 mg, 6 mmol, 3 equiv), **S12** (324 mg, 2 mmol, 1 equiv), and MeI (568 mg, 4 mmol, 2 equiv) in acetone (10 mL) are heated with stirring at 50 °C overnight. The resulting slurry was partitioned between EtOAc and H_2O . The aqueous layer was washed with EtOAc (10 mL x 3). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. The resulting oil was subjected to flash chromatography (hexanes:EtOAc = 19 :1) to give **S30** as a light yellow oil (338 mg, 1.9 mmol, 95%).

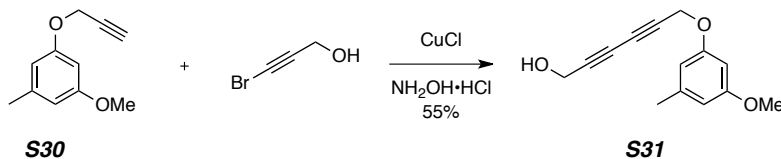
1H NMR (500 MHz, $CDCl_3$): δ 6.39 (br s, 1H, ArH), 6.38 (br s, 1H, ArH), 6.36 (br dd, $J = 2.3, 2.3$ Hz, 1H, ArH), 4.65 (d, $J = 2.4$ Hz, 2H, CH_2O), 3.77 (s, 3H, CH_3O), 2.52 (t, $J = 2.4$ Hz, 1H, $C\equiv CH$), and 2.31 (s, 3H, $ArCH_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ 160.8, 158.8, 140.5, 108.3, 108.0, 98.7, 78.8, 75.6, 56.0, 55.5, and 22.0.

IR: 3286, 3000, 2955, 2922, 2840, 2122, 1596, 1470, 1372, 1337, 1311, 1293, 1196, 1148, 1068, 1054, and 829 cm^{-1} .

GC-LRMS: $t_R = 6.52$ min m/z : 176 (M^+ , 100), 161 ($M^+ - CH_3$, 90), 145 ($M^+ - CH_3O$, 25), 133 (40), 105 (30), and 77 ($C_6H_5^+$, 30).

6-(3-Methoxy-5-methylphenoxy)hexa-2,4-diyne-1-ol (**S31**)



Diyne **S31** was prepared following General Procedure C from **S30** (150 mg, 0.85 mmol, 1 equiv), 3-bromoprop-2-yn-1-ol (126 mg, 0.94 mmol, 1.1 equiv), CuCl (4 mg, 0.04 mmol, 0.05 equiv), 30% aqueous

BuNH₂ (4 mL) and Et₂O (4 mL). **S31** was obtained following flash chromatography (hexanes:EtOAc = 3:1) as a clear colorless oil (108 mg, 0.47 mmol, 55%).

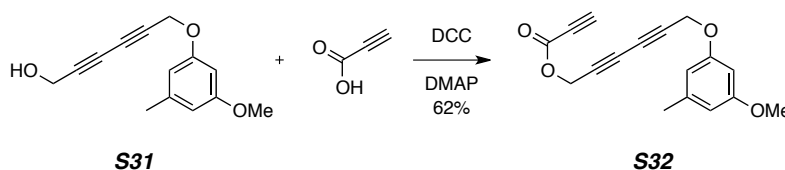
¹H NMR (500 MHz, CDCl₃): δ 6.39 (br d, *J* = 3.0 Hz, 1H, ArH), 6.37 (br d, *J* = 2.0 Hz, 1H, ArH), 6.33 (dd, *J* = 2.5, 2.5 Hz, 1H, ArH), 4.72 (t, *J* = 1.0 Hz, 2H, CH₂O), 4.33 (br d, *J* = 4.5 Hz, 2H, CH₂OH), 3.77 (s, 3H, CH₃O), 2.31 (br s, 3H, ArCH₃), and 1.75 (t, *J* = 5.5 Hz, 1H, OH).

¹³C NMR (125 MHz, CDCl₃): δ 160.8, 158.7, 140.6, 108.4, 108.0, 98.7, 77.9, 74.6, 71.2, 70.0, 56.4, 55.5, 51.6, and 22.0.

IR: 3406, 3000, 2920, 2841, 2258, 1595, 1471, 1371, 1336, 1310, 1293, 1195, 1148, 1068, 1048, 1023, and 828 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₄H₁₄NaO₃⁺ [M+Na]⁺ requires 253.0835; found 253.0855.

6-(3-Methoxy-5-methylphenoxy)hexa-2,4-diyne-1-yl Propiolate (**S32**)



Ester **S32** was prepared following General Procedure D from **S31** (54 mg, 0.23 mmol, 1.0 equiv), propiolic acid (18 mg, 0.26 mmol, 1.1 equiv), DCC (54 mg, 0.026 mmol, 1.1 equiv), DMAP (2 mg, 0.016 mmol, 0.07 equiv), and CH₂Cl₂ (2 mL). **S32** was obtained following flash chromatography (hexanes:EtOAc = 12:1 then 5:1 then 3:1) as a clear colorless oil (40 mg, 0.14 mmol, 62%).

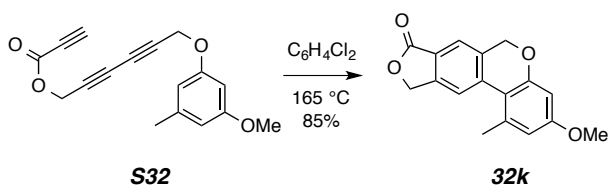
¹H NMR (500 MHz, CDCl₃): δ 6.39 (s, 1H, ArH), 6.37 (s, 1H, ArH), 6.32 (s, 1H, ArH), 4.83 (s, 2H, CH₂), 4.72 (s, 2H, CH₂), 3.77 (s, 3H, CH₃O), 2.96 (s, 1H, CCH), and 2.31 (s, 3H, ArCH₃).

¹³C NMR (125 MHz, CDCl₃): δ 160.9, 158.6, 151.8, 140.6, 108.5, 108.0, 98.7, 76.4, 75.6, 73.9, 72.1, 71.7, 70.8, 56.3, 55.5, 53.9, and 22.0.

IR: 3271, 3005, 2990, 2923, 2850, 2123, 1722, 1595, 1471, 1364, 1275, 1262, 1206, 1148, 1069, and 1051 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₇H₁₄NaO₄⁺ [M+Na]⁺ requires 305.0784; found 305.0767.

3-Methoxy-1-methyl-6*H*-isobenzofuro[5,6-*c*]chromen-8(10*H*)-one (**32k**)



A solution of **S32** (13 mg, 0.046 mmol) in 1,2-dichlorobenzene (1.5 mL) was heated at 165 °C for 3.5 h. The resulting solution was directly subjected to MPLC (hexanes:EtOAc = 3:1) to yield **32k** as a clear colorless oil (11 mg, 0.039 mmol, 85%).

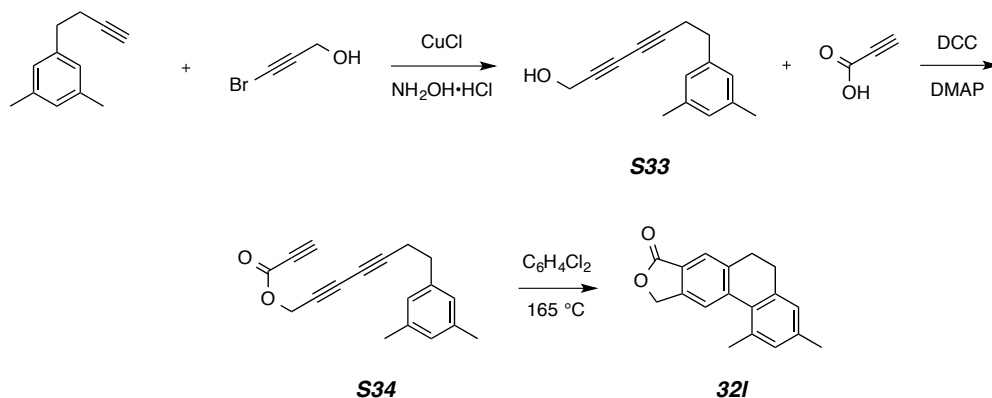
¹H NMR (500 MHz, CDCl₃): δ 7.74 (br s, 1H, *H*7), 7.72 (br s, 1H, *H*11), 6.56 (dq, *J* = 2.7, 0.7 Hz, 1H, *H*2), 6.50 (d, *J* = 2.7 Hz, 1H, *H*4), 5.35 (s, 2H, *H*10), 4.99 (s, 2H, *H*6), 3.83 (s, 3H, OCH₃), and 2.67 (br s, 3H, ArCH₃).

^{13}C NMR (125 MHz, CDCl_3): δ 171.1, 161.1, 158.9, 146.8, 137.7, 137.4, 134.2, 123.0, 121.9, 118.6, 115.7, 113.2, 100.3, 69.9, 69.3, 55.6, and 23.2.

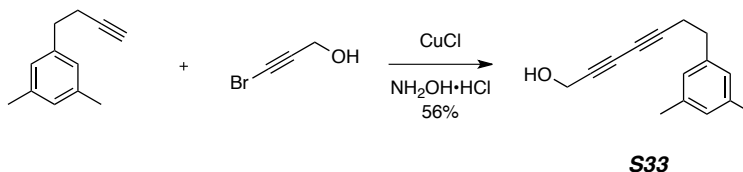
IR: 2958, 2925, 2850, 1756, 1716, 1609, 1592, 1570, 1453, 1412, 1356, 1320, 1295, 1195, 1149, 1142, 1070, 1040, and 1014 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{17}\text{H}_{14}\text{NaO}_4^+ [\text{M}+\text{Na}]^+$ requires 305.0784; found 305.0810.

Synthesis of isobenzofuranone **32I** (Figure 4b of manuscript)



7-(3,5-Dimethylphenyl)hepta-2,4-diyn-1-ol (**S33**)



Diynol **S33** was prepared following General Procedure C from 1-(but-3-yn-1-yl)-3,5-dimethylbenzene¹⁰ (100 mg, 0.63 mmol, 1 equiv), 3-bromoprop-2-yn-1-ol (101 mg, 0.76 mmol, 1.2 equiv), CuCl (6 mg, 0.06 mmol, 0.1 equiv), 30% aqueous BuNH₂ (2.4 mL) and Et₂O (2.4 mL). **S33** was obtained following flash chromatography (hexanes:EtOAc = 3:1) as a clear colorless oil (75 mg, 0.35 mmol, 56%).

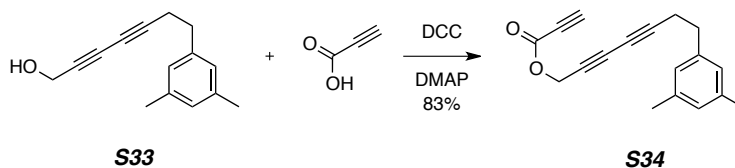
¹H NMR (500 MHz, CDCl₃): δ 6.86 (s, 1H, ArH₄), 6.81 (s, 2H, ArH₂H₆), 4.32 (d, *J* = 5.5 Hz, 2H, CH₂OH), 2.77 (t, *J* = 7.5 Hz, 2H, CH₂CH₂), 2.55 (t, *J* = 7.5 Hz, 2H, CH₂CH₂), 2.29 [s, 6H, Ar(CH₃)₂], and 1.55 (t, *J* = 6.0 Hz, OH).

¹³C NMR (125 MHz, CDCl₃): δ 140.1, 138.2, 128.3, 126.4, 81.2, 74.0, 71.1, 65.1, 51.8, 34.6, 21.7, and 21.5.

IR: 3340, 3015, 2944, 2918, 2857, 2257, 1606, 1464, 1447, 1424, 1376, 1350, 1231, 1017, and 846 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₅H₁₆NaO⁺ [M+Na]⁺ requires 235.1093; found 235.1092.

7-(3,5-Dimethylphenyl)hepta-2,4-diyn-1-yl Propiolate (**S34**)



Ester **S34** was prepared following General Procedure D from **S33** (32 mg, 0.15 mmol, 1.0 equiv), propiolic acid (11.5 mg, 0.165 mmol, 1.1 equiv), DCC (34 mg, 0.165 mmol, 1.1 equiv), DMAP (2 mg, 0.016 mmol, 0.1 equiv), and CH₂Cl₂ (1 mL). **S34** was obtained following flash chromatography (hexanes:EtOAc = 12:1) as a clear colorless oil (33 mg, 0.13 mmol, 83%).

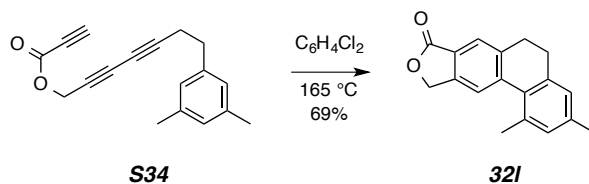
¹H NMR (500 MHz, CDCl₃): δ 6.86 (s, 1H, ArH₄), 6.81 (s, 2H, ArH₂H₆), 4.82 (s, 2H, OCH₂), 2.93 (s, 1H, CCH), 2.77 (t, *J* = 7.6 Hz, 2H, CH₂), 2.55 (t, *J* = 7.6 Hz, 2H, CH₂), and 2.29 [s, 6H, Ar(CH₃)₂].

¹³C NMR (125 MHz, CDCl₃): δ 151.9, 139.9, 138.2, 128.4, 126.3, 82.1, 76.2, 74.0, 72.9, 68.2, 64.9, 54.3, 34.4, 21.7, and 21.5.

IR: 3283, 3015, 2920, 2861, 2260, 2123, 1722, 1606, 1469, 1443, 1368, 1206, 979, 958, and 843 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₈H₁₆NaO₂⁺ [M+Na]⁺ requires 287.1043; found 287.1058.

1,3-Dimethyl-5,6-dihydrophenanthro[2,3-*c*]furan-8(10*H*)-one (32I)



A solution of **S34** (18 mg, 0.068 mmol) in 1,2-dichlorobenzene (2.2 mL) was heated at 165 °C for 3.5 h. The resulting solution was directly subjected to MPLC (hexanes:EtOAc = 3:1) to yield **32I** as a colorless solid (12.5 mg, 0.047 mmol, 69%).

¹H NMR (500 MHz, CDCl₃): δ 7.79 (br s, 1H, H₇), 7.67 (br s, 1H, H₁₁), 7.05 (br s, 1H, H₄), 6.99 (br s, 1H, H₂), 5.34 (s, 2H, OCH₂), 2.83 (dd, *J* = 9.4, 5.7 Hz, 2H, H₅ or H₆), 2.75 (dd, *J* = 9.4, 5.7 Hz, 2H, H₆ or H₅), 2.60 (s, 3H, C1CH₃), and 2.35 (s, 3H, C3CH₃).

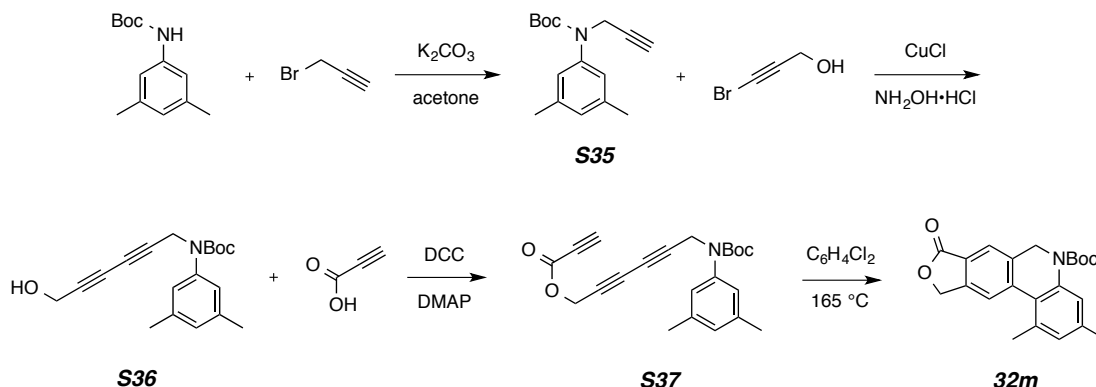
¹³C NMR (125 MHz, CDCl₃): δ 171.5, 144.8, 141.4, 141.3, 140.8, 138.4, 135.2, 131.8, 130.8, 126.8, 124.2, 123.4, 121.1, 69.9, 30.6, 30.4, 23.1, and 21.3.

IR: 2942, 1756, 1622, 1611, 1449, 1353, 1304, 1274, 1132, 1043, and 1009 cm⁻¹.

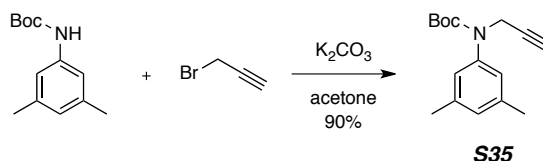
HRMS (ESI-TOF): Calcd for C₁₈H₁₆NaO₂⁺ [M+Na]⁺ requires 287.1043; found 287.1051.

mp: 129-133 °C.

Synthesis of isobenzofuranone **32m** (Figure 4b of manuscript)



tert-Butyl (3,5-dimethylphenyl)(prop-2-yn-1-yl)carbamate (**S35**)



A solution of *tert*-butyl (3,5-dimethylphenyl)carbamate¹¹ (880 mg, 4 mmol, 1 equiv) in 12 mL of a 1:1 mixture of DMF/THF was treated with NaH (60% dispersion in mineral oil, 320 mg, 8 mmol, 2 equiv) at 0 °C. This resulting solution was stirred for an additional 30 min at rt. The mixture was allowed to react with 3-bromoprop-1-yne (566 mg, 4.8 mmol, 1.2 equiv) and the mixture was stirred at rt for 8 h. The excess NaH was quenched with saturated aqueous NH₄Cl solution. The mixture was partitioned between EtOAc and H₂O. The aqueous layer was extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine, dried (Na₂SO₄), and concentrated. The resulting crude oil was subjected to flash chromatography (hexanes:EtOAc = 3:1) to yield **S35** as a yellow oil (930 mg, 3.59 mmol, 90%).

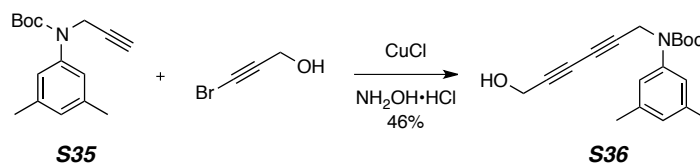
¹H NMR (500 MHz, CDCl₃): δ 6.93 (br s, 2H, ArH₂H₆), 6.85 (br s, 1H, ArH₄), 4.32 (d, *J* = 2.5 Hz, 2H, CH₂), 2.30 [br s, 6H, Ar(CH₃)₂], 2.24 (t, *J* = 2.5 Hz, 1H, CCH), and 1.47 [br s, 9H, C(CH₃)₃].

¹³C NMR (125 MHz, CDCl₃): δ 154.3, 142.2, 138.5, 128.2, 124.1, 81.0, 80.4, 71.7, 40.1 (br), 28.5, and 21.5

IR: 3293, 2976, 2923, 2866, 2121, 1700, 1610, 1598, 1473, 1455, 1433, 1422, 1376, 1367, 1316, 1245, 1168, 1143, 1083, 878, 851, and 769 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₆H₂₁NNaO₂⁺ [M+Na]⁺ requires 282.1465; found 282.1453.

tert-Butyl (3,5-dimethylphenyl)(6-hydroxyhexa-2,4-diyn-1-yl)carbamate (**S36**)



Diynol **S36** was prepared following General Procedure C from **S35** (300 mg, 1.15 mmol, 1 equiv), 3-bromoprop-2-yn-1-ol (190 mg, 1.40 mmol, 1.2 equiv), CuCl (6 mg, 0.06 mmol, 0.05 equiv), 30% aqueous

BuNH₂ (4 mL), and Et₂O (4 mL). **S36** was obtained following flash chromatography (hexanes:EtOAc = 3:1 then 1:1) as a clear colorless oil (165 mg, 0.53 mmol, 46%).

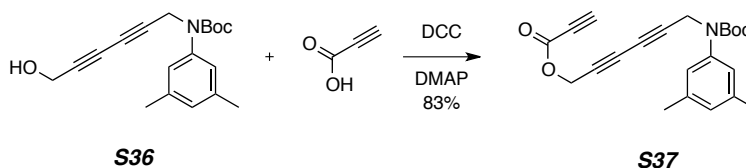
¹H NMR (500 MHz, CDCl₃): δ 6.89 (br s, 2H, ArH₂H₆), 6.86 (br s, 1H, ArH₄), 4.39 (br s, 2H, CH₂), 4.31 (br s, 2H, CH₂), 2.31 [br s, 6H, Ar(CH₃)₂], and 1.47 (s, 9H, *t*Bu).

¹³C NMR (125 MHz, CDCl₃): δ 154.3, 142.0, 138.6, 128.4, 124.1, 81.4, 76.6, 76.2, 70.5, 67.5, 51.7, 40.9 (br), 28.5, and 21.5.

IR: 3428, 2977, 2923, 2255, 1698, 1683, 1610, 1597, 1472, 1455, 1430, 1390, 1368, 1315, 1248, 1164, 1145, 1081, 1031, and 879 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₁₉H₂₃NNaO₃⁺ [M+Na]⁺ requires 336.1570; found 336.1568.

6-((*tert*-Butoxycarbonyl)(3,5-dimethylphenyl)amino)hexa-2,4-diyne-1-yl Propiolate (**S37**)



Ester **S37** was prepared following General Procedure D from **S36** (80 mg, 0.26 mmol, 1.0 equiv), propiolic acid (21 mg, 0.3 mmol, 1.15 equiv), DCC (60 mg, 0.29 mmol, 1.1 equiv), DMAP (2 mg, 0.016 mmol, 0.06 equiv), and CH₂Cl₂ (2 mL). **S37** was obtained following flash chromatography (hexanes:EtOAc = 12:1 then 5:1) as a clear colorless oil (49 mg, 0.134 mmol, 83%). This material contained ca. 10% of an unidentified impurity, perhaps originating from propiolic acid as judged from analysis of the ¹H and ¹³C NMR data, but was of sufficient quality to be used as the substrate in the subsequent HDDA/ene reaction.

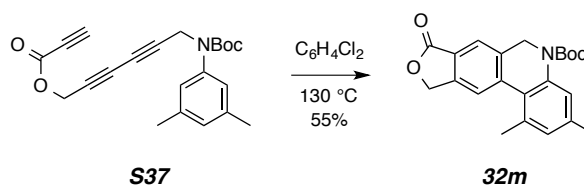
¹H NMR (500 MHz, CDCl₃): δ 6.88 (br s, 2H, ArH₂H₆), 6.86 (br s, 1H, ArH₄), 4.84 (br s, 2H, CH₂OCO), 4.40 (br s, 2H, CH₂N), 2.97 (s, 1H, HCC), 2.31 [br s, 6H, Ar(CH₃)₂], and 1.47 [s, 9H, C(CH₃)₃].

¹³C NMR (125 MHz, CDCl₃): δ 154.2, 151.9, 141.9, 138.7, 128.5, 124.1, 81.4, 77.6, 76.3, 74.0, 72.3, 70.3, 67.2, 54.1, 40.9 (br), 28.5, and 21.5.

IR: 3221, 2977, 2933, 2857, 2121, 1723, 1698, 1659, 1609, 1598, 1475, 1458, 1429, 1368, 1315, 1243, 1207, 1165, 1144, and 978 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₂H₂₃NNaO₄⁺ [M+Na]⁺ requires 388.1519; found 388.1525.

tert-Butyl 1,3-dimethyl-8-oxo-8,10-dihydrofuro[3,4-*j*]phenanthridine-5(6*H*)-carboxylate (**32m**)



A solution of **S37** (20 mg, 0.055 mmol) in 1,2-dichlorobenzene (1.8 mL) was heated at 130 °C for 16 h. The resulting solution was directly subjected to MPLC (hexanes:EtOAc = 3:1) to give **32m** as a colorless solid (11 mg, 0.03 mmol, 55%).

¹H NMR (500 MHz, CDCl₃): δ 7.83 (s, 1H, ArH), 7.77, (s, 1H, ArH), 7.43-7.32 (br s, 1H, ArH), 6.98 (s, 1H, ArH), 5.36 (s, 2H, ArCH₂O), 4.71-4.64 (br s, 2H, ArCH₂N), 2.63 (s, 3H, C1CH₃), 2.38 (s, 3H, C3CH₃), and 1.48 [br s, 9H, C(CH₃)₃].

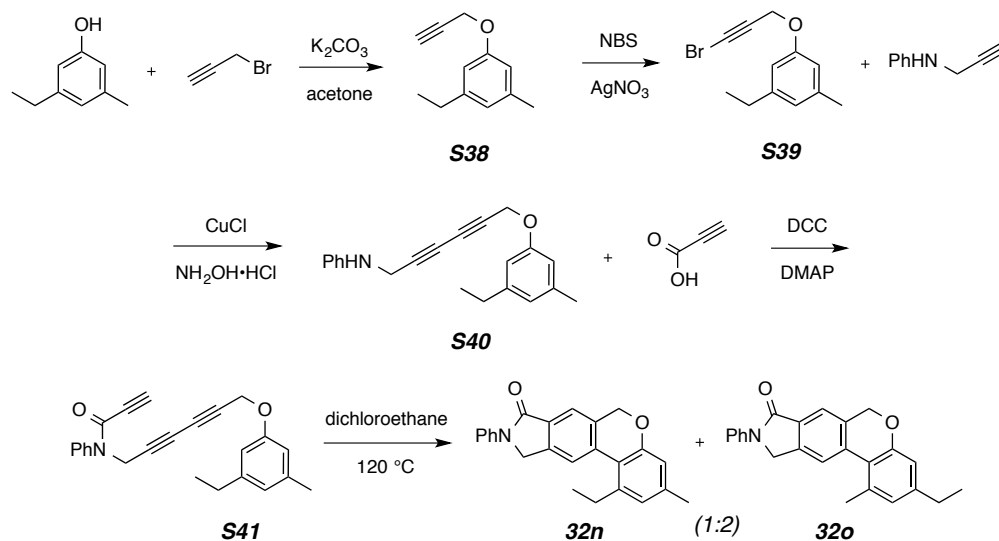
¹³C NMR (125 MHz, CDCl₃): δ 171.2, 152.6, 145.8, 140.2, 139.0 (br), 138.8, 137.7 (br), 135.3, 129.7, 125.1, 123.7, 123.5, 122.3 (br), 120.8, 81.7, 69.9, 48.0 (br), 28.5, 23.0, and 21.6.

IR: 2975, 2919, 1762, 1698, 1613, 1590, 1451, 1412, 1370, 1346, 1284, 1229, 1155, 1132, 1044, 1009, 890, 855, and 761 cm⁻¹.

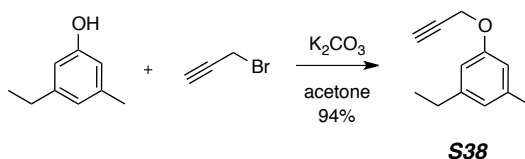
HRMS (ESI-TOF): Calcd for C₂₂H₂₃NNaO₄⁺ [M+Na]⁺ requires 388.1519; found 388.1530.

mp: 201-204 °C.

Synthesis of isoindolone 32n and 32o (Figure 4b of manuscript)



1-Ethyl-3-methyl-5-(prop-2-yn-1-yloxy)benzene (S38)



A mixture of K_2CO_3 (2.76 g, 20 mmol, 2 equiv), 3-ethyl-5-methylphenol (1.36 g, 10 mmol, 1 equiv), and 3-bromoprop-1-yne (1.77 g, 15 mmol, 1.5 equiv) were heated with stirring at 50 °C in acetone (50 mL) overnight. The resulting slurry was partitioned between EtOAc and H_2O . The aqueous layer was washed with EtOAc (30 mL x 3). The combined layers were washed with brine, dried (Na_2SO_4), and concentrated. The crude oil was subjected to flash chromatography (hexanes:EtOAc = 19:1) to give **S38** as a light yellow oil (1.64 g, 9.4 mmol, 94%).

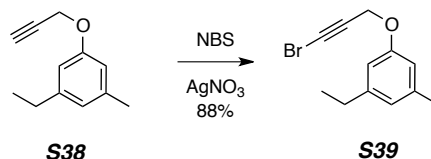
^1H NMR (500 MHz, CDCl_3): δ 6.66 (br s, 1H), 6.63 (br s, 1H), 6.61 (br s, 1H), 4.66 (d, $J = 2.4$ Hz, 2H, CH_2O), 2.59 (q, $J = 7.6$ Hz, CH_2CH_3), 2.50 (t, $J = 2.4$ Hz, 1H, $\text{HC}\equiv\text{C}$), 2.31 (s, 3H, ArCH_3), and 1.22 (t, $J = 7.6$ Hz, 3H, CH_2CH_3).

^{13}C NMR (125 MHz, CDCl_3): δ 157.9, 145.9, 139.5, 122.3, 112.9, 111.8, 79.1, 75.4, 55.9, 29.1, 21.7, and 15.7.

IR: 3288, 2965, 2921, 2872, 2122, 1611, 1594, 1457, 1330, 1288, 1168, 1151, 1078, 1049, 1012, 941, and 844 cm^{-1} .

GC-LRMS: $t_{\text{R}} = 6.09$ min. m/z : 174 (M^+ , 50), 159 ($\text{M}^+ - \text{CH}_3$, 70), 145 ($\text{M}^+ - \text{CH}_2\text{CH}_3$, 100), 131 ($\text{M}^+ - \text{C}_3\text{H}_7$, 40), 91 (C_7H_7^+ , 70), and 77 (C_6H_5^+ , 20).

1-((3-Bromoprop-2-yn-1-yl)oxy)-3-ethyl-5-methylbenzene (S39)



Bromoalkyne **S39** was prepared following General Procedure A from **S38** (865 mg, 5 mmol, 1 equiv), NBS (929 mg, 5.25 mmol, 1.05 equiv), AgNO₃ (42 mg, 0.25 mmol, 0.05 equiv), and acetone (40 mL). **S39** was isolated following flash chromatography (hexanes:EtOAc = 19:1) as a clear yellow oil (1.10 g, 0.44 mmol, 88%).

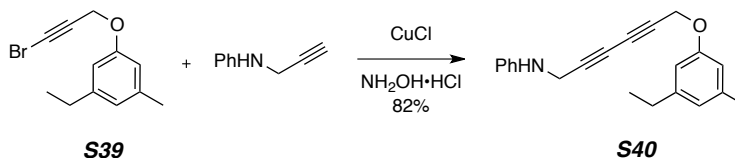
¹H NMR (500 MHz, CDCl₃): δ 6.67 (br s, 1H, *H4*), 6.60 (br s, 1H, *H6*), 6.59 (br s, 1H, *H2*), 4.67 (br s, 2H, CH₂O), 2.59 (br q, *J* = 7.6 Hz, 2H, CH₂CH₃), 2.31 (br s, 3H, ArCH₃), and 1.22 (t, *J* = 7.6 Hz, 3H, CH₂CH₃).

¹³C NMR (125 MHz, CDCl₃): δ 157.8, 146.0, 139.6, 122.4, 112.8, 111.7, 75.5, 56.8, 47.5, 29.1, 21.7, and 15.7.

IR: 2965, 2931, 2872, 2218, 1611, 1593, 1461, 1453, 1371, 1330, 1287, 1167, 1150, 1079, 1054, and 843 cm⁻¹.

GC-LRMS: *t*_R = 7.82 min. *m/z*: 254 (M⁺, 40), 252 (M⁺, 40), 239 (M⁺-CH₃, 20), 237 (M⁺-CH₃, 20), 225 (M⁺-CH₂CH₃, 30), 223 (M⁺-CH₂CH₃, 30), 173 (M⁺-Br, 60), 158 (50), 145 (80), 130 (50), 117 (70), 91 (C₇H₇⁺, 100), and 77 (C₆H₅⁺, 25).

N-(6-(3-Ethyl-5-methylphenoxy)hexa-2,4-diyn-1-yl)aniline (S40)



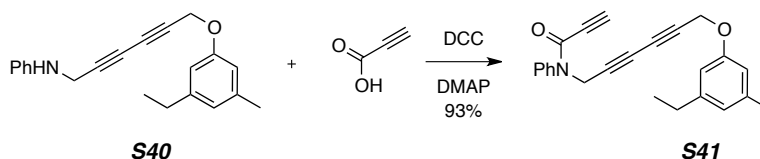
Diynol **S40** was prepared following General Procedure C from **S39** (506 mg, 2 mmol, 1.3 equiv), *N*-(prop-2-yn-1-yl)aniline (201 mg, 1.53 mmol, 1.0 equiv), CuCl (7 mg, 0.07 mmol, 0.05 equiv), 30% aqueous BuNH₂ (7 mL), and Et₂O (7 mL). **S40** was obtained following flash chromatography (hexanes:EtOAc = 5:1) as a clear yellow oil (381 mg, 1.26 mmol, 82%).

¹H NMR (500 MHz, CDCl₃): δ 7.20 (dd, *J* = 8.2, 7.7 Hz, 2H, *Hm*), 6.79 (t, *J* = 7.4 Hz, 1H, *Hp*), 6.66 (d, *J* = 7.9 Hz, 2H, *Ho*), 6.65 (br s, 1H, *H4*), 6.58 (br s, 1H, *H6*), 6.56 (br s, 1H, *H2*), 4.68 (br s, 2H, CH₂O), 4.00 (br s, 2H, NCH₂), 3.85 (br s, 1H, *NH*), 2.57 (br q, *J* = 7.6 Hz, 2H, CH₂CH₃), 2.30 (br s, 3H, ArCH₃), and 1.20 (t, *J* = 7.6 Hz, 3H, CH₂CH₃).

¹³C NMR (125 MHz, CDCl₃): δ 157.8, 146.7, 146.0, 139.6, 129.5, 122.4, 119.1, 113.8, 112.8, 111.7, 77.7, 73.2, 71.5, 67.3, 56.3, 34.4, 29.0, 21.7, and 15.7.

IR: 3405, 2965, 2931, 2869, 2255, 1602, 1593, 1505, 1456, 1437, 1314, 1287, 1258, 1167, 1150, 1075, 1046, and 752 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₁H₂₁NNaO⁺ [M+Na]⁺ requires 326.1515; found 326.1519.

***N*-(6-(3-Ethyl-5-methylphenoxy)hexa-2,4-diyn-1-yl)-*N*-phenylpropiolamide (**S41**)**

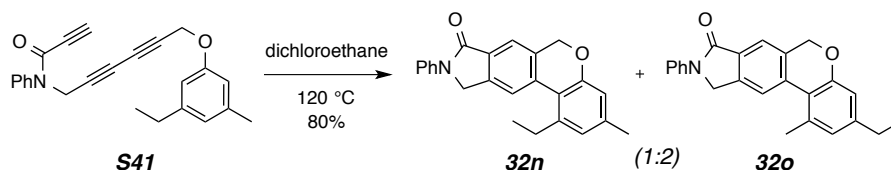
Amide **S41** was prepared following General Procedure D from **S40** (303 mg, 1 mmol, 1.0 equiv), propiolic acid (91 mg, 1.3 mmol, 1.3 equiv), DCC (236 mg, 1.15 mmol, 1.15 equiv), DMAP (6 mg, 0.05 mmol, 0.05 equiv), and CH_2Cl_2 (10 mL). **S41** was obtained following flash chromatography (hexanes:EtOAc = 3:1) as a clear brown oil (355 mg, 0.93 mmol, 93%).

^1H NMR (500 MHz, CDCl_3 , as a 7:1 ratio of two amide rotamers): Major isomer δ 7.45-7.40 (m, 3H, *HmHp*), 7.33 (dd, $J = 7.9, 2.0$ Hz, 2H, *Ho*), 6.67 (br s, 1H, *H4*), 6.58 (br s, 1H, *H6*), 6.57 (br s, 1H, *H2*), 4.70 (br s, 2H, CH_2O), 4.59 (br s, 2H, NCH_2), 2.83 (s, 1H, $\text{C}\equiv\text{CH}$), 2.59 (br q, $J = 7.6$ Hz, 2H, CH_2CH_3), 2.31 (br s, 3H, ArCH_3), and 1.21 (t, $J = 7.6$ Hz, 3H, CH_2CH_3). Minor isomer δ 4.77 (br s, 2H, CH_2O), 4.72 (br s, 2H, NCH_2), and 3.29 (s, 1H, CCH).

^{13}C NMR (125 MHz, CDCl_3): δ 157.7, 152.7, 146.0, 140.4, 139.6, 129.6, 129.2, 128.4, 122.5, 112.8, 111.7, 80.7, 75.8, 74.2, 73.8, 71.2, 68.7, 56.3, 38.8, 29.0, 21.7, and 15.7 (only resonances for the major rotamer are reported).

IR: 3283, 2965, 2923, 2873, 2111, 1643, 1611, 1593, 1492, 1456, 1414, 1383, 1330, 1287, 1220, 1168, 1150, 1076, 1048, 1015, and 842 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{24}\text{H}_{21}\text{NNaO}_2^+ [\text{M}+\text{Na}]^+$ requires 378.1465; found 378.1455.

1-Ethyl-3-methyl-9-phenyl-9,10-dihydrochromeno[3,4-*f*]isoindol-8(6*H*)-one (32n**) and****1-Methyl-3-ethyl-9-phenyl-9,10-dihydrochromeno[3,4-*f*]isoindol-8(6*H*)-one (**32o**)**

A solution of **S41** (25 mg, 0.07 mmol) in dichloroethane (2.3 mL) was heated at $120\text{ }^\circ\text{C}$ for 18 h. The resulting solution was concentrated and subjected to MPLC (hexanes:EtOAc = 3:1) to yield **32n** and **32o** as a coeluting 1:2 mixture (20 mg, 0.056 mmol, 80% combined yield).

Characterization data for 32n

^1H NMR (500 MHz, CDCl_3): δ 7.88 (dd, $J = 8.8, 1.0$ Hz, 1H, *Ho*), 7.74 (br s, 1H, *H7*), 7.73 (br s, 1H, *H11*), 7.42 (overlapping dd, $J = 8.5, 7.5$ Hz, 2H, *Hm*), 7.17 (overlapping tt, $J = 7.4, 1.0$ Hz, 1H, *Hp*), 6.87 (br d, $J = 1.8$ Hz, 1H, *H2*), 6.77 (br d, $J = 1.8$ Hz, 1H, *H4*), 4.97 (br s, 2H, OCH_2), 4.89 (br s, 2H, NCH_2), 3.02 (q, $J = 7.6$ Hz, 3H, CH_2CH_3), 2.35 (br s, 3H, C_3CH_3), and 1.40 (t, $J = 7.6$ Hz, 3H, CH_2CH_3).

^{13}C NMR (125 MHz, CDCl_3 , shifts deduced from HSQC): δ 128.8, 124.6, 124.0, 119.5, 119.5, 118.9, 115.1, 68.8, 50.6, 27.1, 21.3, and 15.3 (several of the cross peaks overlapping with major product).

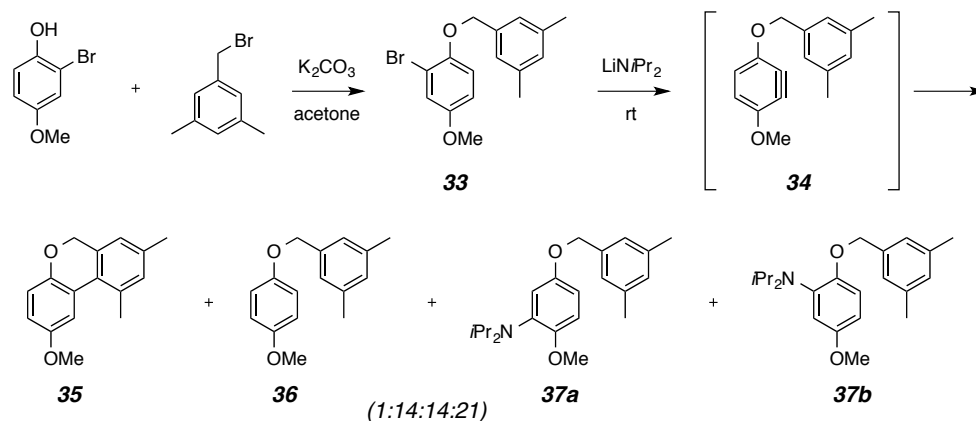
Characterization data for 32o

¹H NMR (500 MHz, CDCl₃): δ 7.87 (dd, $J = 8.8, 1.0$ Hz, 1H, *Ho*), 7.81 (br s, 1H, *H7*), 7.74 (br s, 1H, *H11*), 7.42 (overlapping dd, $J = 8.5, 7.5$ Hz, 2H, *Hm*), 7.17 (overlapping tt, $J = 7.4, 1.0$ Hz, 1H, *Hp*), 6.83 (br d, $J = 1.8$ Hz, 1H, *H2*), 6.79 (br d, $J = 1.8$ Hz, 1H, *H4*), 5.00 (br s, 2H, OCH₂), 4.88 (br s, 2H, NCH₂), 2.69 (br s, 3H, C1CH₃), 2.63 (q, $J = 7.6$ Hz, 3H, CH₂CH₃), and 1.26 (t, $J = 7.6$ Hz, 3H, CH₂CH₃).

¹³C NMR (125 MHz, CDCl₃, shifts deduced from HSQC): δ 128.8, 125.4, 124.0, 120.0, 119.5, 118.9, 114.0, 68.9, 50.6, 28.2, 22.8, and 15.0 (several of the cross peaks overlapping with major product).

IR: 2966, 2928, 2863, 1693, 1625, 1614, 1598, 1501, 1459, 1449, 1407, 1380, 1328, 1293, 1270, 1175, 1130, 1077, 1057, 1015, 908, and 859 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₄H₂₁NNaO₂⁺ [M+Na]⁺ requires 378.1465; found 378.1439.

Synthesis of 35, 36, 37a, and 37b (Figure 4c of manuscript, cf. Lautens^{12,13}).

2-Bromo-1-((3,5-dimethylbenzyl)oxy)-4-methoxybenzene (33)

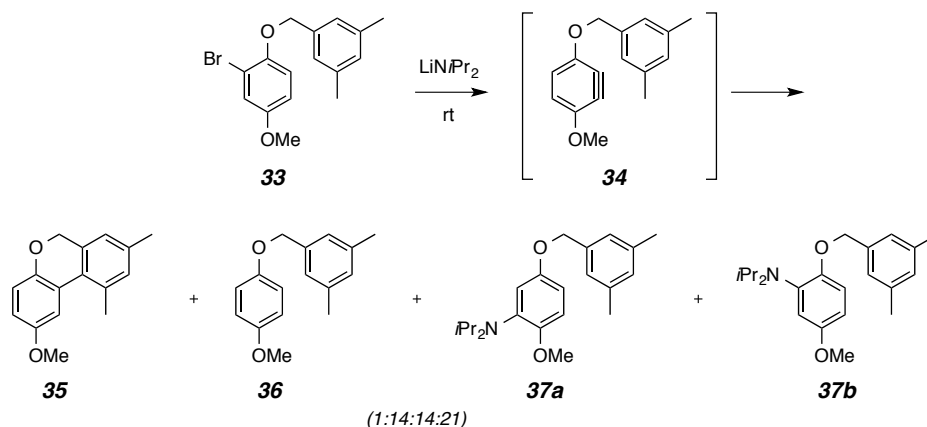
K_2CO_3 (924 mg, 6.7 mmol, 2 equiv), 2-bromo-4-methoxyphenol (800 mg, 4 mmol, 1.2 mmol), and 1-(bromomethyl)-3,5-dimethylbenzene (670 mg, 3.35 mmol, 1 equiv) in acetone (5 mL) was stirred at 50 °C overnight. The resulting slurry was partitioned between EtOAc and saturated aqueous NH_4Cl . The organic layer was washed with brine, dried (Na_2SO_4), and concentrated. The resulting crude oil was subjected to MPLC (hexanes:EtOAc = 20:1) to give **33** (612 mg, 57%) as a yellow oil.

1H NMR (500 MHz, $CDCl_3$): δ 7.13 (d, $J = 3.0$ Hz, 1H, $H3$), 7.07 (br s, 2H, $H2'$ / $H6'$), 6.95 (br s, 1H, $H4'$), 6.87 (d, $J = 9.0$ Hz, 1H, $H6$), 6.77 (dd, $J = 9.0, 3.0$ Hz, 1H, $H5$), 5.01 (s, 2H, CH_2O), 3.76 (s, 3H, CH_3O), and 2.33 [br s, 6H, $Ar(CH_3)_2$].

^{13}C NMR (125 MHz, $CDCl_3$): δ 154.6, 149.8, 138.3, 136.9, 129.7, 125.2, 119.0, 115.9, 113.9, 113.4, 72.4, 56.1, and 21.5.

IR: 3005, 2940, 2916, 2834, 1609, 1576, 1492, 1459, 1440, 1297, 1272, 1212, 1040, 844, and 786 cm^{-1} .

GC-LRMS: $t_R = 10.79$ min. m/z : 322 (M^+ , 10), 320 (M^+ , 10), 119 ($C_9H_{11}^+$, 100), 91 ($C_7H_7^+$, 8), and 77 ($C_6H_5^+$, 4).

2-Methoxy-8,10-dimethyl-6*H*-benzo[*c*]chromene (35)**1-((4-Methoxyphenoxy)methyl)-3,5-dimethylbenzene (36)****5-((3,5-Dimethylbenzyl)oxy)-*N,N*-diisopropyl-2-methoxyaniline (37a)** and**2-((3,5-Dimethylbenzyl)oxy)-*N,N*-diisopropyl-5-methoxyaniline (37b)**

A THF solution of LDA was freshly prepared at $-10\text{ }^{\circ}\text{C}$ from *n*BuLi (2.5 M solution in hexanes, 0.4 mL, 1 mmol), HNiPr_2 (101 mg, 1 mmol), and THF (2 mL). To a solution of **33** (80 mg, 0.25 mmol) in THF (5 mL) was added the freshly prepared LDA (ca. 0.4 M, 0.7 mL, 0.28 mmol, 1.1 equiv) at rt. The reaction was monitored by TLC and GCMS. An additional amount of LDA (0.8 mL, 0.32 mmol, 1.3 equiv) was added 1 h later to drive the reaction to completion. The resulting solution was stirred for 30 min and quenched by addition of saturated aqueous NH_4Cl solution. The mixture was partitioned between EtOAc and aqueous NaHCO_3 . The organic layer was washed with brine, dried (Na_2SO_4), and concentrated. The ratio of products (i.e., 1:14:14:21) was determined by analysis of the ^1H NMR spectrum of this crude oil. This ratio was qualitatively consistent with that observed by GC-MS analysis of the sample of crude products. This oil was then subjected to flash chromatography (hexanes:EtOAc = 16:1 then 5:1) to give, in order of elution, **35** and **36** as a co-eluting mixture, followed by **37a** as colorless oil, and finally **37b** as colorless oil. The overall mass recovery was ca. 85% (70 mg isolated).

Characterization data for 36 (containing ca. 5 mol% of 35)

^1H NMR (500 MHz, CDCl_3): δ 7.07 (br s, 2H, H_{2H6}), 6.99 (br s, 1H, H_4), 6.95 (d, $J = 9.0$ Hz, 2H, $H_{2'H6'}$), 6.86 (d, $J = 9.1$ Hz, 2H, $H_{3'H5'}$), 4.96 (s, 2H, CH_2O), 3.80 (s, 3H, CH_3O), and 2.36 (br s, 6H, $\text{Ar}(\text{CH}_3)_2$).

^{13}C NMR (125 MHz, CDCl_3): δ 154.1, 153.3, 138.6, 137.3, 129.8, 125.6, 116.0, 114.8, 71.1, 55.9, and 21.5.

IR: 3002, 2948, 2917, 2865, 2833, 1610, 1592, 1507, 1463, 1442, 1228, 1040, and 825 cm^{-1} .

GC-LRMS: $t_R = 9.69$ min. m/z : 242 (M^+ , 30), 119 ($\text{C}_9\text{H}_{11}^+$, 100), 91 (C_7H_7^+ , 10), and 77 (C_6H_5^+ , 4).

Characteristic ^1H NMR peaks of **35**

^1H NMR (500 MHz, CDCl_3): δ 4.92 (s, CH_2O), 3.86 (s, CH_3O), 2.66 (s, C_{10}CH_3), and 2.37 (s, C_8CH_3).

GC-LRMS: $t_R = 10.40$ min. m/z : 240 (M^+ , 100), 225 ($M^+ - CH_3$, 50), 197 (20), 182 (10), 165 (12), 153 (12), 128 (10), and 115 (8).

Characterization data for 37a

1H NMR (500 MHz, $CDCl_3$): δ 7.05 (br s, 2H, $H2'H6'$), 6.92 (br s, 1H, $H4'$), 6.78 (d, $J = 8.9$ Hz, 1H, $H3$), 6.75 (d, $J = 3.1$ Hz, 1H, $H6$), 6.59 (dd, $J = 8.9, 3.1$ Hz, 1H, $H4$), 4.98 (s, 2H, CH_2O), 3.75 (s, 3H, CH_3O), 3.60 {septet, $J = 6.4$ Hz, 2H, $N[CH(CH_3)_2]_2$ }, 2.31 [br s, 6H, $Ar(CH_3)_2$], and 1.04 {d, $J = 6.4$ Hz, 12H, $N[CH(CH_3)_2]_2$ }.

^{13}C NMR (125 MHz, $CDCl_3$): δ 153.5, 152.4, 138.31, 138.26, 138.1, 129.2, 125.1, 118.0, 114.8, 109.6, 71.4, 55.8, 49.6, 22.0, and 21.5.

IR: 2967, 2928, 2870, 2832, 1609, 1581, 1494, 1463, 1379, 1208, 1179, 1046, and 845 cm^{-1} .

HRMS (ESI-TOF): Calcd for $C_{22}H_{32}NO_2^+ [M+H]^+$ requires 342.2428; found 342.2448.

Characterization data for 37b

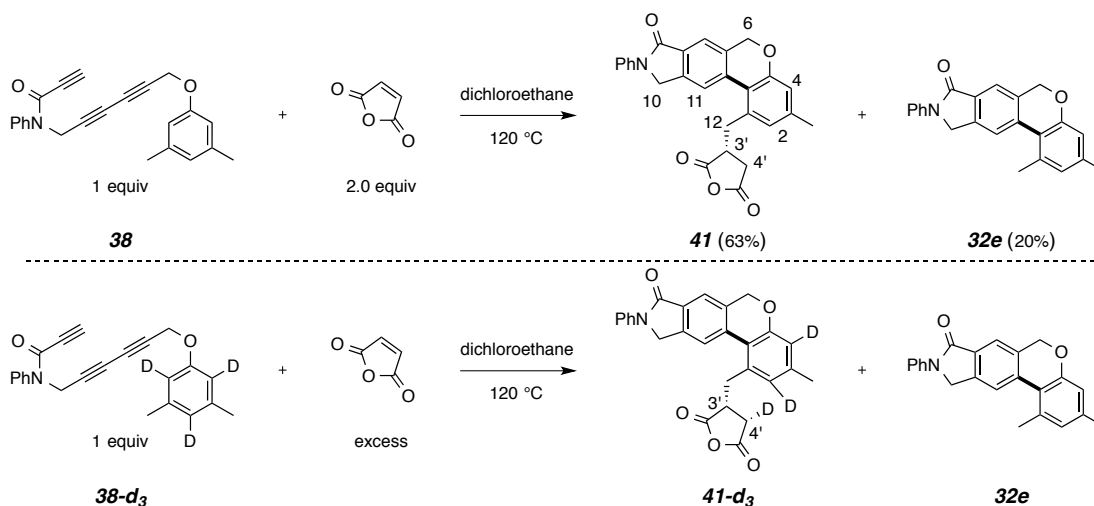
1H NMR (500 MHz, $CDCl_3$): δ 7.05 (br s, 2H, $H2'H6'$), 6.95 (br s, 1H, $H4'$), 6.82 (d, $J = 3.1$ Hz, 1H, $H6$), 6.78 (d, $J = 8.9$ Hz, 1H, $H3$), 6.73 (dd, $J = 8.9, 3.1$ Hz, 1H, $H4$), 4.91 (s, 2H, CH_2O), 3.76 (s, 3H, CH_3O), 3.52 {septet, $J = 6.4$ Hz, 2H, $N[CH(CH_3)_2]_2$ }, 2.32 [br s, 6H, $Ar(CH_3)_2$], and 0.99 {d, $J = 6.4$ Hz, 12H, $N[CH(CH_3)_2]_2$ }.

^{13}C NMR (125 MHz, $CDCl_3$): δ 153.3, 152.6, 138.3, 137.5, 137.4, 129.7, 125.8, 118.6, 112.1, 111.1, 71.0, 56.1, 49.7, 21.49, and 21.46.

IR: 2967, 2929, 2869, 2832, 1609, 1580, 1494, 1463, 1378, 1275, 1257, 1224, 1200, 1179, 1038, and 846 cm^{-1} .

HRMS (ESI-TOF): Calcd for $C_{22}H_{32}NO_2^+ [M+H]^+$ requires 342.2428; found 342.2437.

3-((3-Methyl-8-oxo-9-phenyl-6,8,9,10-tetrahydrochromeno[3,4-f]isoindol-1-yl)methyl)dihydrofuran-2,5-dione (**41** and **41-d₃**)



Compound **41** was prepared following General Procedure E from amide **38** (22 mg, 0.065 mmol, 1 equiv) and maleic anhydride (13 mg, 0.13 mmol, 2 equiv) in dichloroethane (0.25 mL). The reaction solution was stirred at 120 °C for 18 h. Compound **41** was isolated following flash chromatography (hexanes:EtOAc = 5:1 then 3:1 then 1:1) as a light yellow oil (18 mg, 0.04 mmol, 63%). The previously described rearomatized product **32e** was observed in the ¹H NMR spectrum of the crude reaction mixture (ca. 20%).

Compound **41-d₃** was obtained from the corresponding reaction using **38-d₃**. Only a single diastereomer (>98:2) was observed, as judged by scrutiny of the ¹H NMR spectrum of the crude product mixture. The relative configuration (i.e., *cis*) of **41-d₃** was determined by coupling constant analysis. Namely, the vicinal coupling constant of the remaining H4' proton in **41-d₃** (³J_{H3'H4'}) is 9.8 Hz; in the all protio compound **41**, the two vicinal ³J_{H3'H4'} values are 9.8 and 6.6 Hz.¹⁴ Also, the proton that is absent in **41-d₃** appeared more upfield (i.e., δ = 2.56) in **41**, consistent with its residing in a more highly shielded environment.

Characterization data for **41**

¹H NMR (500 MHz, CDCl₃): 7.84 (dd, *J* = 8.8, 1.2 Hz, 2H, *Ho*), 7.78 (s, 1H, *H7*), 7.73 (s, 1H, *H11*), 7.42 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.18 (tt, *J* = 7.4, 1.2 Hz, 1H, *Hp*), 6.86 (br d, *J* = 1.8 Hz, 1H, *H2*), 6.76 (br d, *J* = 1.7 Hz, 1H, *H4*), 4.97 (d, *J* = 12.7 Hz, *H6a*), 4.94 (d, *J* = 12.7 Hz, *H6b*), 4.89 (d, *J* = 16.5 Hz, *H10a*), 4.85 (d, *J* = 16.5 Hz, *H10b*), 4.08 (dd, *J* = 15.0, 4.0 Hz, 1H, *H12a*), 3.52 (dddd, *J* = 10.7, 9.8, 6.6, 4.0 Hz, 1H, *H3'*), 3.16 (dd, *J* = 15.0, 11.0 Hz, 1H, *H12b*), 2.88 (dd, *J* = 18.9, 9.8 Hz, 1H, *H4'a*), 2.56 (dd, *J* = 19.0, 6.6 Hz, 1H, *H4'b*), and 2.35 (dd, *J* = 0.6, 0.6 Hz, 3H, ArCH₃).

¹³C NMR (125 MHz, CDCl₃): δ 173.6, 169.5, 166.9, 158.0, 141.3, 140.7, 139.5, 134.44, 134.42, 133.8, 132.1, 129.4, 125.6, 124.8, 121.0, 120.2, 119.7, 119.6, 117.8, 69.3, 51.0, 41.3, 36.0, 34.1, and 21.6.

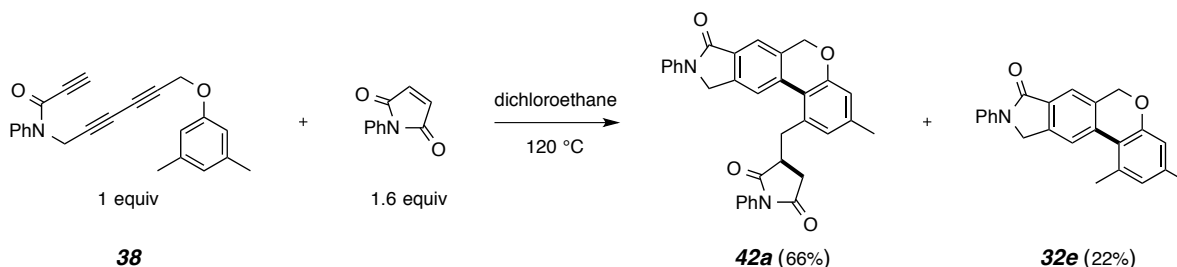
IR: 2919, 2859, 1862, 1780, 1690, 1615, 1598, 1501, 1459, 1448, 1383, 1293, 1268, 1227, 1177, 1129, 1071, 1023, 922, and 760 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₇H₂₁NNaO₅⁺ [M+Na]⁺ requires 462.1312; found 462.1319.

¹H NMR data for **41-d₃** (contaminated with excess maleic anhydride and **32e-d₂**)

¹H NMR (500 MHz, CDCl₃): 7.87 (dd, *J* = 8.8, 1.2 Hz, 2H, *Ho*), 7.83 (s, 1H, *H7*), 7.78 (s, 1H, *H11*), 7.44 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.20 (tt, *J* = 7.4, 1.2 Hz, 1H, *Hp*), 5.01 (d, *J* = 12.7 Hz, *H6a*), 4.98 (d, *J* = 12.7 Hz, *H6b*), 4.97 (d, *J* = 16.5 Hz, *H10a*), 4.92 (d, *J* = 16.5 Hz, *H10b*), 4.09 (dd, *J* = 15.0, 4.0 Hz, 1H, *H12a*), 3.54 (ddd, *J* = 10.7, 9.7, 4.0 Hz, 1H, *H3'*), 3.19 (dd, *J* = 15.0, 10.9 Hz, 1H, *H12b*), 2.88 (br d, *J* = 9.8 Hz, 1H, *H4'a*), and 2.35 (br s, 3H, ArCH₃).

3-((3-Methyl-8-oxo-9-phenyl-6,8,9,10-tetrahydrochromeno[3,4-f]isoindol-1-yl)methyl)-1-phenylpyrrolidine-2,5-dione (**42a**)



Compound **42a** was prepared following General Procedure E from amide **38** (25 mg, 0.073 mmol, 1 equiv) and *N*-phenyl maleimide (20 mg, 0.12 mmol, 1.6 equiv) in dichloroethane (0.25 mL). The reaction solution was stirred at 120 °C for 18 h. Compound **42a** was isolated following flash chromatography (hexanes:EtOAc = 5:1 then 3:1 then 1:1) as a clear yellow oil (25 mg, 0.049 mmol, 66%). The previously described rearomatized product **32e** was observed in the ¹H NMR spectrum of the crude reaction mixture (ca. 22%).

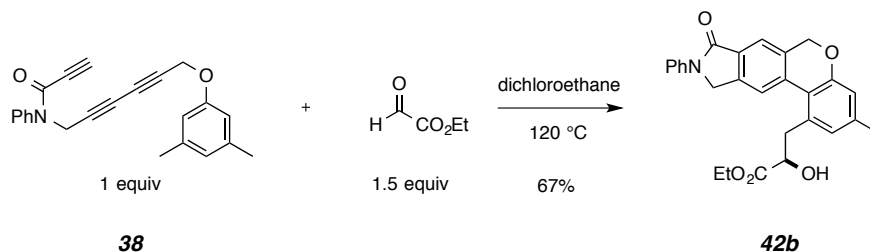
¹H NMR (500 MHz, CDCl₃): 7.93 (s, 1H, *H7*), 7.86 (dd, *J* = 8.8, 1.1 Hz, 2H, *Ho*), 7.78 (s, 1H, *H11*), 7.46 (dd, *J* = 8.7, 7.3 Hz, 2H, *Hm*), 7.42 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm'*), 7.39 (tt, *J* = 7.4, 1.3 Hz, 1H, *Hp'*), 7.23 (dd, *J* = 8.7, 1.5 Hz, 2H, *Ho'*), 7.18 (tt, *J* = 7.4, 1.1 Hz, 1H, *Hp*), 6.87 (br d, *J* = 1.7 Hz, 1H, *H2*), 6.83 (br d, *J* = 1.7 Hz, 1H, *H4*), 5.01 (d, *J* = 12.5 Hz, *H6a*), 4.98 (d, *J* = 13.0 Hz, *H6b*), 4.93 (d, *J* = 16.7 Hz, *H10a*), 4.89 (d, *J* = 16.6 Hz, *H10b*), 4.19 (dd, *J* = 15.0, 3.6 Hz, 1H, *H4'a*), 3.36 (dddd, *J* = 10.5, 8.6, 4.8, 3.6 Hz, 1H, *H3'*), 3.11 (dd, *J* = 14.9, 10.7 Hz, 1H, *H4'b*), 2.80 (dd, *J* = 18.5, 9.2 Hz, 1H, *H12a*), 2.47 (dd, *J* = 18.5, 5.0 Hz, 1H, *H12b*), and 2.36 (dd, *J* = 0.6, 0.6 Hz, 3H, ArCH₃).

¹³C NMR (125 MHz, CDCl₃): δ 178.5, 175.2, 167.1, 157.9, 141.0, 140.7, 139.6, 135.6, 134.5, 134.2, 132.0, 131.9, 129.40, 129.38, 128.9, 126.5, 125.9, 124.8, 120.9, 120.3, 120.1, 119.6, 117.5, 69.4, 51.1, 40.6, 36.6, 34.6, and 21.6.

IR: 2983, 2916, 1709, 1695, 1615, 1598, 1501, 1457, 1449, 1382, 1292, 1268, 1178, 1129, 1062, 909, and 759 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₃₃H₂₆N₂NaO₄⁺ [M+Na]⁺ requires 537.1785; found 537.1790.

Ethyl 2-Hydroxy-3-(3-methyl-8-oxo-9-phenyl-6,8,9,10-tetrahydrochromeno[3,4-f]isoindol-1-yl)propanoate (**42b**)



Compound **42b** was prepared following General Procedure E from amide **38** (22 mg, 0.064 mmol, 1 equiv) and ethyl glyoxalate (20 mg, 50 wt.% in toluene, 0.098 mmol, 1.5 equiv) in dichloroethane (0.3 mL). The reaction solution was stirred at 120 °C for 18 h. Compound **42b** was isolated following flash chromatography (hexanes:EtOAc = 5:1 then 1:1) as a colorless solid (19 mg, 0.043 mmol, 67%).

¹H NMR (500 MHz, CDCl₃): δ 7.98 (s, 1H, *H7'*), 7.86 (dd, *J* = 8.4, 1.0 Hz, 2H, *Ho*), 7.75 (s, 1H, *H11'*), 7.43 (dd, *J* = 8.3, 7.4 Hz, 2H, *Hm*), 7.18 (tt, *J* = 7.4, 1.1 Hz, 1H, *Hp*), 6.94 (br d, *J* = 1.8 Hz, 1H, *H2'*), 6.82 (br d, *J* = 1.8 Hz, 1H, *H4'*), 4.97 (d, *J* = 12.5 Hz, 1H, *H6a'*), 4.94 (d, *J* = 12.6 Hz, 1H, *H6b'*), 4.90 (d, *J* = 17.5 Hz, 1H, *H10a'*), 4.86 (d, *J* = 18.0 Hz, 1H, *H10b'*), 4.58 (ddd, *J* = 8.1, 5.5, 4.4 Hz, 1H, *H2*), 4.22 (dq, *J* = 10.8, 7.2 Hz, 1H, CH₃CHa), 4.14 (dq, *J* = 10.8, 7.2 Hz, 1H, CH₃CHb), 3.54 (dd, *J* = 14.7, 4.4 Hz, 1H, *H3a*), 3.43 (dd, *J* = 14.7, 8.2 Hz, 1H, *H3b*), 2.94 [dd, *J* = 8.6 (to H₂O in the NMR sample), 5.6 Hz, 1H, *OH*], 2.34 (br s, 3H, ArCH₃), and 1.24 (t, *J* = 7.1 Hz, 3H, CH₃CH₂).

¹H NMR (500 MHz, DMSO): δ 8.12 (s, 1H, *H7'*), 7.94 (dd, *J* = 8.8, 1.1 Hz, 2H, *Ho*), 7.80 (s, 1H, *H11'*), 7.45 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.18 (tt, *J* = 7.4, 1.1 Hz, 1H, *Hp*), 6.99 (br d, *J* = 1.8 Hz, 1H, *H2'*), 6.80 (br d, *J* = 1.8 Hz, 1H, *H4'*), 5.74 (d, *J* = 5.8 Hz, 1H, *OH*), 5.07 (d, *J* = 17.0 Hz, 1H, *H6a'*), 5.03 (d, *J* = 17.1 Hz, 1H, *H6b'*), 5.01 (d, *J* = 13.0 Hz, 1H, *H10a'*), 4.98 (d, *J* = 13.1 Hz, 1H, *H10b'*), 4.43 (ddd, *J* = 8.4, 5.8, 5.1 Hz, 1H, *H2*), 4.06 (q, *J* = 6.9 Hz, 1H, CH₃CH₂), 3.39 (dd, *J* = 14.6, 5.0 Hz, 1H, *H3a*), 3.32 (dd, *J* = 14.6, 8.4 Hz, 1H, *H3b*), 2.29 (br s, 3H, ArCH₃), and 1.13 (t, *J* = 7.1 Hz, 3H, CH₃CH₂).

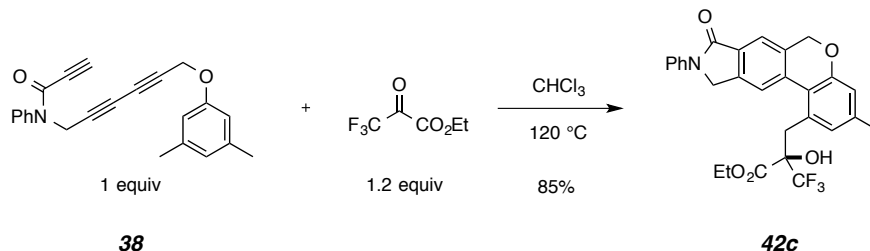
¹³C NMR (125 MHz, DMSO): δ 173.5, 166.3, 156.6, 140.8, 139.5, 139.4, 135.9, 134.1, 133.8, 130.6, 129.0, 126.0, 124.0, 120.6, 120.5, 120.0, 119.2, 115.7, 70.9, 68.2, 60.2, 50.6, 37.8, 20.9, and 14.0.

IR: 3420, 2980, 2917, 2859, 1736, 1694, 1615, 1598, 1501, 1459, 1448, 1381, 1292, 1269, 1178, 1129, 1096, 1062, 1031, 1017, 897, 852, 774, and 761 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₇H₂₅NNaO₅⁺ [*M*+Na]⁺ requires 466.1625; found 466.1629.

mp: 180-184 °C.

Ethyl 3,3,3-trifluoro-2-hydroxy-2-((3-methyl-8-oxo-9-phenyl-6,8,9,10-tetrahydrochromeno[3,4-f]isoindol-1-yl)methyl)propanoate (42c)



Compound **42c** was prepared following General Procedure E from amide **38** (11 mg, 0.032 mmol, 1 equiv) and ethyl trifluoropyruvate (6.4 mg, 0.038 mmol, 1.2 equiv) in chloroform (0.1 mL). The reaction solution was stirred at $120\text{ }^\circ\text{C}$ for 18 h. Compound **42c** was isolated following flash chromatography (hexanes:EtOAc = 5:1 then 3:1) as a clear colorless oil (14.2 mg, 0.028 mmol, 85%).

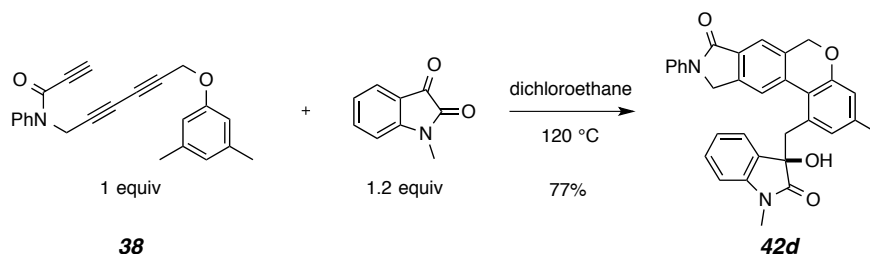
^1H NMR (500 MHz, CDCl_3): δ 8.03 (s, 1H, $H7'$), 7.89 (dd, $J = 8.8, 1.1$ Hz, 2H, H_o), 7.78 (s, 1H, $H11'$), 7.44 (dd, $J = 8.7, 7.4$ Hz, 2H, H_m), 7.19 (tt, $J = 7.4, 1.1$ Hz, 1H, H_p), 6.85 (br d, $J = 1.8$ Hz, 1H, $H2'$), 6.84 (br d, $J = 1.8$ Hz, 1H, $H4'$), 5.05 (d, $J = 12.5$ Hz, 1H, $H6a'$), 4.94 (d, $J = 16.5$ Hz, 1H, $H10a'$), 4.90 (d, $J = 16.2$ Hz, 1H, $H10b'$), 4.81 (d, $J = 12.4$ Hz, 1H, $H6b'$), 4.27 (dq, $J = 10.7, 7.1$ Hz, 1H, CH_3CHa), 4.04 (dq, $J = 10.7, 7.2$ Hz, 1H, CH_3CHb), 3.96 (s, 1H, OH), 3.85 (d, $J = 14.5$ Hz, 1H, ArCHa), 3.73 (d, $J = 14.4$ Hz, 1H, ArCHb), 2.34 (s, 3H, ArCH₃), and 1.19 (t, $J = 7.1$ Hz, 3H, CH_3CH_2).

^{13}C NMR (125 MHz, CDCl_3): δ 169.3, 167.3, 157.6, 140.4, 140.3, 139.7, 134.7, 134.4, 131.7, 130.9, 129.4, 126.4, 124.7, 123.7 (q, $^1J_{\text{FC}} = 286$ Hz), 122.0, 120.8, 120.7, 119.6, 117.5, 78.5 (q, $^2J_{\text{FC}} = 28.3$ Hz), 69.5, 64.1, 51.0, 34.3, 21.6, and 13.9.

IR: 2983, 2916, 2860, 1744, 1693, 1626, 1615, 1598, 1502, 1460, 1449, 1382, 1309, 1293, 1270, 1233, 1213, 1179, 1125, 1063, 1019, 953, 909, 858, and 758 cm^{-1} .

HRMS (ESI-TOF): Calcd for $\text{C}_{28}\text{H}_{24}\text{F}_3\text{NNaO}_5^+ [\text{M}+\text{Na}]^+$ requires 534.1499; found 534.1503.

1-((3-Hydroxy-1-methyl-2-oxoindolin-3-yl)methyl)-3-methyl-9-phenyl-9,10-dihydrochromeno[3,4-f]isoindol-8(6H)-one (42d)



Compound **42d** was prepared following General Procedure E from amide **38** (12.5 mg, 0.037 mmol, 1 equiv) and *N*-methyl isatin (6.9 mg, 0.043 mmol, 1.2 equiv) in dichloroethane (0.17 mL). The reaction solution was stirred at 120 °C for 18 h. The reaction mixture became a slurry as **42d** precipitated. The reaction mixture was cooled to -20 °C and filtered while cold. The filter cake (mostly **42d**) was carefully washed with a 3:1 mixture of hexanes and EtOAc to provide **42d** as a colorless solid (14 mg, 0.028 mmol, 77%).

¹H NMR (500 MHz, DMSO): δ 7.94 (dd, *J* = 8.8, 1.2 Hz, 2H, *Ho*), 7.74 (s, 1H, *H7*), 7.68 (s, 1H, *H11*), 7.46 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.19 (tt, *J* = 7.4, 1.1 Hz, 1H, *Hp*), 7.10 (ddd, *J* = 7.8, 6.9, 2.0 Hz, 1H, *H6'*), 6.73 (d, *J* = 1.9 Hz, 1H, *H2*), 6.69 (ddd, *J* = 7.8, 0.8, 0.8 Hz, 1H, *H7'*), 6.63 (d, *J* = 1.8 Hz, 1H, *H4*), 6.54 (ddd, *J* = 7.3, 7.3, 1.0 Hz, 1H, *H5'*), 6.52 (ddd, *J* = 7.3, 2.1, 0.6 Hz, 1H, *H4'*), 6.22 (s, 1H, *OH*), 5.15 (d, *J* = 17.1 Hz, 1H, *H10a*), 4.95 (d, *J* = 17.2 Hz, 1H, *H10b*), 4.90 (d, *J* = 12.5 Hz, 1H, *H6a*), 4.14 (d, *J* = 12.6 Hz, 1H, *H6b*), 4.01 (d, *J* = 13.2 Hz, 1H, *ArCHaHb*), 3.43 (d, *J* = 13.1 Hz, 1H, *ArCHaHb*), 2.85 (s, 3H, *NCH₃*), and 2.19 (dd, *J* = 0.7, 0.7 Hz, 3H, *ArCH₃*).

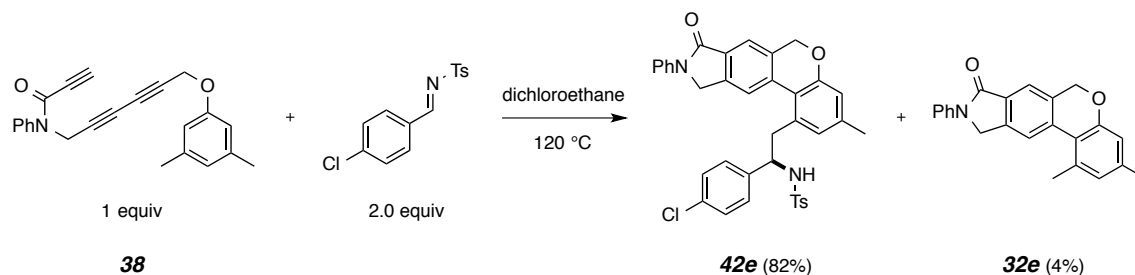
¹³C NMR (125 MHz, DMSO): δ 177.0, 166.4, 156.0, 142.9, 140.7, 139.6, 138.6, 134.2, 134.0, 132.6, 130.3, 129.9, 129.0, 128.7, 126.5, 124.1, 123.6, 121.5, 121.0, 120.6, 119.8, 119.2, 115.5, 107.6, 77.3, 68.2, 50.5, 40.5, 25.5, and 20.8.

IR: 3390, 2917, 2850, 1716, 1694, 1673, 1613, 1599, 1501, 1494, 1470, 1449, 1380, 1292, 1270, 1175, 1129, 1089, 1057, 1016, 908, and 759 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₃₂H₂₆N₂NaO₄⁺ [M+Na]⁺ requires 525.1785; found 525.1775.

mp: 273-276 °C.

***N*-(1-(4-Chlorophenyl)-2-(3-methyl-8-oxo-9-phenyl-6,8,9,10-tetrahydrochromeno[3,4-*f*]isoindol-1-yl)ethyl)-4-methylbenzenesulfonamide (42e)**



Compound **42e** was prepared following General Procedure E from amide **38** (35 mg, 0.103 mmol, 1 equiv) and *N*-(4-chlorobenzylidene)-4-methylbenzenesulfonamide¹⁵ (58 mg, 0.2 mmol, 2 equiv) in dichloroethane (0.35 mL). The reaction solution was stirred at 120 °C for 18 h. Compound **42e** was isolated following flash chromatography (hexanes:EtOAc = 5:1 then 1:1) as a colorless solid (53 mg, 0.083 mmol, 82%). The previously described rearomatized product **32e** was observed in the ¹H NMR spectrum of the crude reaction mixture (ca. 4%).

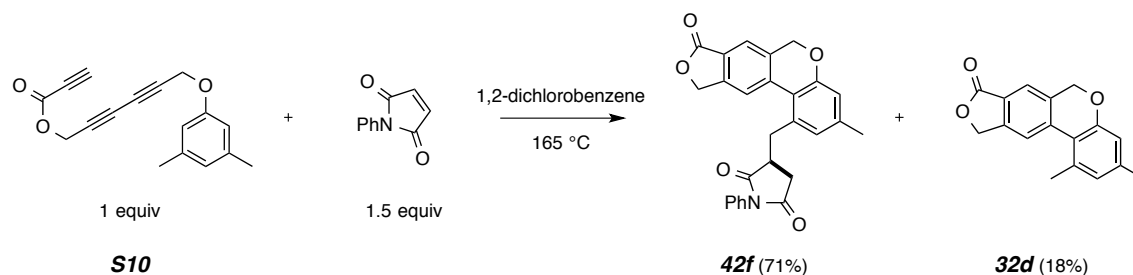
¹H NMR (500 MHz, CDCl₃): δ 7.86 (dd, *J* = 8.8, 1.1 Hz, 2H, *Ho*), 7.73 (s, 1H, *H7*), 7.72 (s, 1H, *H11*), 7.42 (dd, *J* = 8.6, 7.4 Hz, 2H, *Hm*), 7.32 (d, *J* = 8.3 Hz, 2H, ClAr*H3*), 7.19 (tt, *J* = 7.4, 1.1 Hz, 1H, *Hp*), 7.03 (d, *J* = 8.6 Hz, 2H, ClAr*H2*), 7.01 (d, *J* = 8.4 Hz, O₂SAr*H2*), 6.77 (d, *J* = 8.4 Hz, O₂SAr*H3*), 6.71 (br d, *J* = 1.8 Hz, 1H, *H2*), 6.53 (d, *J* = 1.8 Hz, 1H, *H4*), 5.08 (d, *J* = 6.4 Hz, 1H, *NH*), 4.89 (d, *J* = 16.4 Hz, *H10a*), 4.83 (d, *J* = 17.0 Hz, *H10b*), 4.82 (d, *J* = 12.2 Hz, *H6a*), 4.72 (d, *J* = 12.4 Hz, *H6b*), 4.51 (ddd, *J* = 7, 7, 7 Hz, 1H, CHNH), 3.65 (dd, *J* = 14.3, 7.0 Hz, ArHa*Hb*), 3.43 (dd, *J* = 14.3, 7.0 Hz, ArHa*Hb*), 2.33 (br s, 3H, CH₃-C₆H₄SO₂), and 2.22 (s, 3H, C3CH₃).

¹³C NMR (125 MHz, CDCl₃): δ 167.2, 157.5, 143.6, 140.6, 140.5, 139.6, 138.8, 137.2, 134.48, 134.45, 134.2, 133.5, 131.5, 129.5, 129.4, 128.6, 128.2, 127.0, 126.6, 124.7, 120.8, 120.6, 120.0, 119.4, 116.9, 69.2, 58.7, 51.0, 42.4, 21.6, and 21.5.

IR: 3250, 2925, 2863, 1679, 1615, 1598, 1501, 1493, 1449, 1384, 1326, 1292, 1269, 1158, 1129, 1092, 1062, 1014, 812, and 760 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₃₇H₃₁ClINNaO₄SSi⁺ [M+Na]⁺ requires 657.1585; found 657.1562.

mp: 140-143 °C.

3-((3-Methyl-8-oxo-8,10-dihydro-6H-isobenzofuro[5,6-c]chromen-1-yl)methyl)-1-phenylpyrrolidine-2,5-dione (42f)

Compound **42f** was prepared following General Procedure E from amide **S10** (30.8 mg, 0.12 mmol, 1 equiv) and *N*-phenyl maleimide (31 mg, 0.18 mmol, 1.5 equiv) in 1,2-dichlorobenzene (0.6 mL). The reaction solution was stirred at 165 °C for 4 h. Compound **42f** was isolated following flash chromatography (hexanes:EtOAc = 5:1 then 1:1) as a clear light yellow oil (36 mg, 0.082 mmol, 71%).

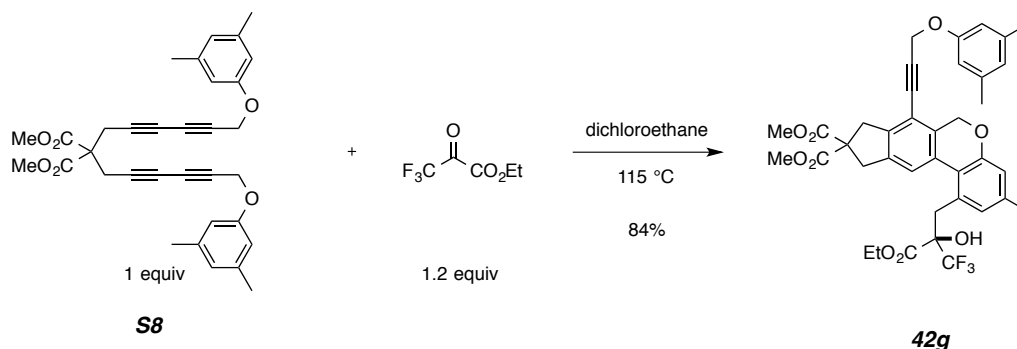
¹H NMR (500 MHz, CDCl₃): δ 7.85 (s, 1H, *H7*), 7.76 (s, 1H, *H11*), 7.46 (dd, *J* = 8.7, 7.3 Hz, 2H, *Hm*), 7.39 (tt, *J* = 7.4, 1.3 Hz, 1H, *Hp*), 7.22 (dd, *J* = 8.7, 1.5 Hz, 2H, *Ho*), 6.87 (br d, *J* = 1.7 Hz, 1H, *H2*), 6.85 (br d, *J* = 1.7 Hz, 1H, *H4*), 5.36 (d, *J* = 15.5 Hz, *H10a*), 5.32 (d, *J* = 15.7 Hz, *H10b*), 4.97 (s, 2H, *H6*), 4.10 (dd, *J* = 14.7, 3.7 Hz, 1H, *H4'a*), 3.36 (dddd, *J* = 10.5, 8.9, 5.0, 3.8 Hz, 1H, *H3'*), 3.13 (dd, *J* = 14.8, 10.5 Hz, 1H, *H4'b*), 2.81 (dd, *J* = 18.4, 9.2 Hz, 1H, ArCHaHb), 2.44 (dd, *J* = 18.5, 5.0 Hz, 1H, ArCHaHb), and 2.36 (dd, *J* = 0.6, 0.6 Hz, 3H, ArCH₃).

¹³C NMR (125 MHz, CDCl₃): 178.3, 175.1, 170.7, 158.1, 147.1, 141.7, 136.2, 135.9, 135.1, 131.8, 129.4, 128.9, 126.4, 125.8, 124.1, 122.3, 120.0, 119.4, 117.4, 69.9, 69.2, 40.7, 36.2, 34.5, and 21.7.

IR: 2916, 2849, 1757, 1708, 1615, 1594, 1500, 1454, 1384, 1355, 1315, 1294, 1181, 1155, 1138, 1047, 1007, 909, and 759 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₂₇H₂₁NNaO₅⁺ [M+Na]⁺ requires 462.1312; found 462.1343.

Dimethyl 7-(3-(3,5-Dimethylphenoxy)prop-1-yn-1-yl)-1-(2-(ethoxycarbonyl)-3,3,3-trifluoro-2-hydroxypropyl)-3-methyl-8,10-dihydroindeno[5,6-*c*]chromene-9,9(6*H*)-dicarboxylate (42g)



Compound **42g** was prepared following General Procedure E from amide **S8** (30 mg, 0.057 mmol, 1 equiv) and ethyl trifluoropyruvate (11.5 mg, 0.068 mmol, 1.2 equiv) in 1,2-dichlorobenzene (0.2 mL). The reaction solution was stirred at 115 °C for 24 h. Compound **42g** was isolated following flash chromatography (hexanes:EtOAc = 5:1 then 2:1) as a clear colorless oil (33.5 mg, 0.048 mmol, 84%).

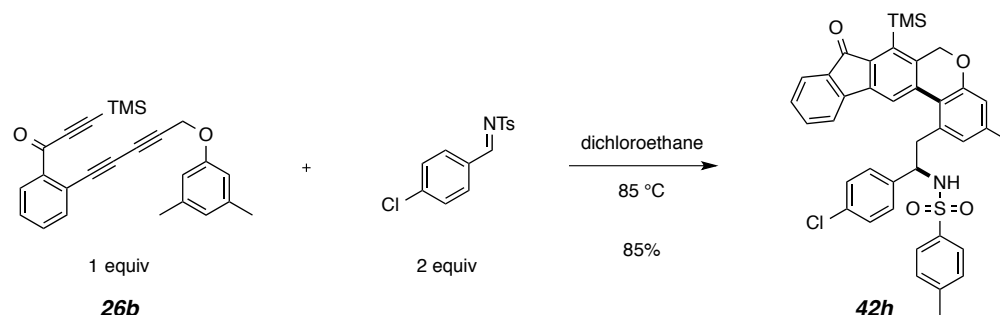
¹H NMR (500 MHz, CDCl₃): 7.65 (s, 1H, *H11*), 6.80 (br d, *J* = 1.8 Hz, 1H, *H2*), 6.78 (br d, *J* = 1.8 Hz, 1H, *H4*), 6.68 (br s, 2H, *Ho*), 6.66 (br s, 1H, *Hp*), 5.21 (d, *J* = 13.0 Hz, 1H, *H6a*), 4.96 (s, 2H, C≡CCH₂), 4.64 (d, *J* = 13.0 Hz, 1H, *H6b*), 4.19 (dq, *J* = 10.6, 7.1 Hz, 1H, CH₃CHaHb), 3.91 (dq, *J* = 10.6, 7.1 Hz, 1H, CH₃CHaHb), 3.81 (s, 1H, OH), 3.79 (d, *J* = 14.7 Hz, 1H, ArCHaHb), 3.77 (s, 3H, CO₂CH₃), 3.75 (s, 3H, CO₂CH₃), 3.65 [br s, 4H, CH₂C(CO₂Me)CH₂], 3.56 (d, *J* = 14.4 Hz, 1H, ArCHaHb), 2.32 (dt, *J* = 0.6, 0.6 Hz, 6H, Ar(CH₃)₂), and 2.28 (dd, *J* = 0.6, 0.6 Hz, 3H, ArCH₃).

¹³C NMR (125 MHz, CDCl₃): δ 172.0, 171.9, 169.4, 157.7, 156.9, 141.7, 139.8, 139.5, 139.0, 135.0, 130.4, 129.9, 126.1, 123.7 (q, ¹*J*_{FC} = 286 Hz), 123.6, 122.8, 122.1, 117.1, 115.5, 113.1, 92.5, 82.3, 78.5 (q, ²*J*_{FC} = 28.4 Hz), 67.2, 63.9, 59.8, 56.6, 53.27, 53.26, 41.1, 40.5, 34.2, 21.6, 21.5, and 13.8.

IR: 3474, 2955, 2918, 2849, 1737, 1615, 1594, 1436, 1370, 1315, 1291, 1258, 1239, 1202, 1179, 1168, 1152, 1138, 1121, 1064, 1017, 956, 856, and 832 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₃₈H₃₇F₃NaO₉⁺ [M+Na]⁺ requires 717.2282; found 717.2277.

***N*-(1-(4-Chlorophenyl)-2-(3-methyl-8-oxo-7-(trimethylsilyl)-6,8-dihydrofluoreno[2,3-*c*]chromen-1-yl)ethyl)-4-methylbenzenesulfonamide (42h)**



Compound **42h** was prepared following General Procedure E from ketone **26b** (21 mg, 0.054 mmol, 1 equiv) and *N*-(4-chlorobenzylidene)-4-methylbenzenesulfonamide¹⁵ (32 mg, 0.109 mmol, 2.0 equiv) in 1,2-dichloroethane (0.2 mL). The reaction solution was stirred at 85 °C for 18 h. Compound **42h** was isolated following flash chromatography (hexanes:EtOAc = 5:1 then 2:1) as a bright yellow oil (32 mg, 0.047 mmol, 85%).

¹H NMR (500 MHz, CDCl₃): δ 7.62 (d, *J* = 7.3 Hz, 1H, *H9*), 7.59 (s, 1H, *H13*), 7.47-7.44 (nfom, 2H, *H11* and *H12*), 7.32 (d, *J* = 8.2 Hz, 2H, ClAr*H3*), 7.32-7.28 (nfom, 1H, *H10*), 7.01 (d, *J* = 8.1 Hz, 2H, ClAr*H2*), 6.88 (d, *J* = 8.3 Hz, 2H, O₂SAr*H2*), 6.69 (br s, 1H, *H2*), 6.66 (br s, 1H, *H4*), 6.64 (d, *J* = 8.4 Hz, 2H, O₂SAr*H3*), 4.98 (d, *J* = 6.2 Hz, 1H, *NH*), 4.88 (d, *J* = 12.8 Hz, 1H, *H6a*), 4.44 (d, *J* = 12.8 Hz, 1H, *H6b*), 4.41 (ddd, *J* = 7, 7, 7 Hz, 1H, *CHNH*), 3.55 (dd, *J* = 13.9, 7.8 Hz, 1H, Ar*CHaHb*), 3.50 (dd, *J* = 13.9, 7.1 Hz, 1H, Ar*CHaHb*), 2.32 (s, 3H, *CH*₃-C₆H₄SO₂), 2.28 (s, 3H, C3*CH*₃), and 0.46 [s, 9H, Si(*CH*₃)₃].

¹³C NMR (125 MHz, CDCl₃): 194.6, 157.4, 144.4, 143.61, 143.55, 141.9, 140.7, 139.5, 138.3, 138.0, 137.1, 135.2, 134.8, 134.4, 134.0, 133.4, 129.5, 129.4, 128.4, 128.2, 127.1, 126.4, 124.1, 122.0, 120.0, 119.0, 116.2, 69.8, 59.2, 41.6, 21.63, 21.60 and 2.2.

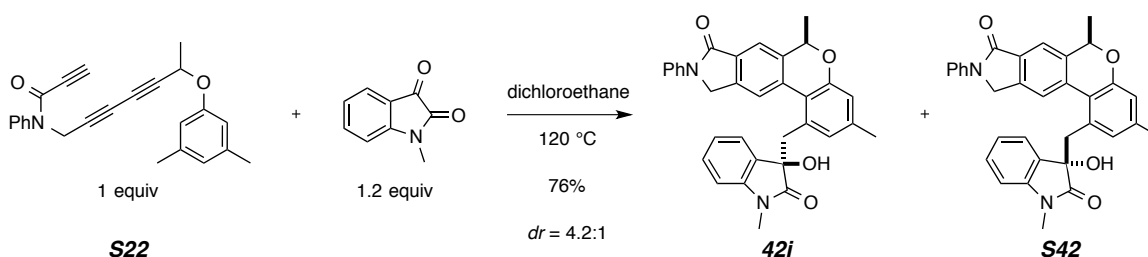
IR: 3258, 3055, 2997, 2948, 2900, 1709, 1606, 1588, 1492, 1463, 1322, 1303, 1248, 1183, 1158, 1091, 1063, 1014, 966, 901, and 859 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₃₉H₃₆ClNNaO₄SSi⁺ [M+Na]⁺ requires 700.1715; found 700.1760.

(±)-(R)-1-(((R)-3-Hydroxy-1-methyl-2-oxoindolin-3-yl)methyl)-3,6-dimethyl-9-phenyl-9,10-dihydrochromeno[3,4-f]isoindol-8(6H)-one (**42i**)

and

(±)-(R)-1-(((S)-3-Hydroxy-1-methyl-2-oxoindolin-3-yl)methyl)-3,6-dimethyl-9-phenyl-9,10-dihydrochromeno[3,4-f]isoindol-8(6H)-one (**S42**)



Compound **42i** was prepared following General Procedure E from amide **S22** (19 mg, 0.054 mmol, 1 equiv) and *N*-methyl isatin (10.5 mg, 0.065 mmol, 1.2 equiv) in 1,2-dichloroethane (0.25 mL). The reaction solution was stirred at 120 °C for 18 h. The reaction mixture became a slurry as **42i** precipitated. The reaction mixture was cooled to -20 °C and filtered while cold. The filter cake (mostly **42i**) was carefully washed with a 3:1 mixture of hexanes and EtOAc to give compound **42i** as a colorless solid (16.8 mg, 0.033 mmol, 60%). The filtrate was concentrated, and subjected to column chromatography (hexanes:EtOAc = 3:1 then 1:1) to give a coeluting mixture of the minor epimer **S42** as a pale yellow oil (4.6 mg, 0.0089 mmol, 16%, containing ca. 20 mol% of **42i**, as judged from the ¹H NMR data).

Characterization data for **42i**

¹H NMR (500 MHz, CDCl₃): δ 7.89 (dd, *J* = 8.8, 1.2 Hz, 2H, *Ho*), 7.75 (s, 1H, *H7*), 7.65 (s, 1H, *H11*), 7.47 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.22 (tt, *J* = 7.4, 1.1 Hz, 1H, *Hp*), 7.12 (ddd, *J* = 7.7, 7.2, 1.9 Hz, 1H, *H6'*), 6.85 (d, *J* = 1.7 Hz, 1H, *H2*), 6.64 (dd, *J* = 1.8, 0.8 Hz, 1H, *H4*), 6.58 (ddd, *J* = 7.3, 7.3, 0.9 Hz, 1H, *H5'*), 6.544 (dd, *J* = 7.3, 1.7 Hz, 1H, *H4'*), 6.536 (d, *J* = 7.8 Hz, 1H, *H7'*), 5.02 (d, *J* = 16.2 Hz, 1H, *H10a*), 4.84 (d, *J* = 16.3 Hz, 1H, *H10b*), 4.32 (d, *J* = 13.0 Hz, ArCHaHb), 4.02 (q, *J* = 6.5 Hz, 1H, *H6*), 3.47 (d, *J* = 13.0 Hz, 1H, ArCHaHb), 2.95 (s, 3H, NCH₃), 2.88 (s, 1H, OH), 2.27 (br s, 3H, ArCH₃), and 1.70 (d, *J* = 6.5 Hz, 3H, CHCH₃).

¹H NMR (500 MHz, DMSO): δ 7.95 (dd, *J* = 8.8, 1.1 Hz, 2H, *Ho*), 7.73 (s, 1H, *H7*), 7.60 (s, 1H, *H11*), 7.47 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.20 (tt, *J* = 7.4, 1.1 Hz, 1H, *Hp*), 7.09 (nfom, 1H, *H6'*), 6.73 (d, *J* = 1.8 Hz, 1H, *H2*), 6.69 (ddd, *J* = 7.8, 0.8, 0.8 Hz, 1H, *H7'*), 6.60 (d, *J* = 1.8 Hz, 1H, *H4*), 6.52-6.48 (nfom, 2H, *H4'H5'*), 6.21 (s, 1H, OH), 5.18 (d, *J* = 17.0 Hz, 1H, *H10a*), 4.94 (d, *J* = 17.0 Hz, 1H, *H10b*), 4.09 (d, *J* = 12.9 Hz, 1H, ArCHaHb), 4.08 (q, *J* = 6.5 Hz, 1H, CHCH₃), 3.39 (d, *J* = 13.0 Hz, 1H, ArCHaHb), 2.85 (s, 3H, NCH₃), 2.18 (dd, *J* = 0.7, 0.7 Hz, 3H, ArCH₃), and 1.60 (d, *J* = 6.5 Hz, 3H, CHCH₃).

¹³C NMR (125 MHz, DMSO): δ 176.9, 166.5, 155.5, 142.9, 140.4, 139.6, 138.5, 138.0, 134.4, 132.4, 130.6, 129.9, 129.0, 128.7, 126.1, 124.1, 123.5, 121.5, 121.0, 120.8, 119.2, 117.9, 115.4, 107.7, 77.4, 73.2, 50.5, 40.4, 25.5, 20.8, and 17.3.

IR: 3350, 1697, 1615, 1599, 1561, 1502, 1492, 1380, 1094, and 767 cm⁻¹.

HRMS (ESI-TOF): Calcd for C₃₃H₂₈N₂NaO₄⁺ [M+Na]⁺ requires 539.1941; found 539.1928.

mp: 297-299 °C.

Characterization data for **S42**

¹H NMR (500 MHz, CDCl₃): δ 7.86 (dd, *J* = 8.8, 1.2 Hz, 2H, *Ho*), 7.70 (s, 1H, *H7*), 7.65 (s, 1H, *H11*), 7.44 (dd, *J* = 8.7, 7.4 Hz, 2H, *Hm*), 7.19 (tt, *J* = 7.4, 1.2 Hz, 1H, *Hp*), 7.16 (ddd, *J* = 7.7, 7.7, 1.4 Hz, 1H, *H6'*), 6.85 (d, *J* = 1.7 Hz, 1H, *H2*), 6.81 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H, *H5'*), 6.74 (dd, *J* = 7.4, 1.4 Hz, 1H, *H4'*), 6.72 (br d, *J* = 1.7 Hz, 1H, *H4*), 6.64 (d, *J* = 6.7 Hz, 1H, *H7'*), 4.88 (d, *J* = 16.5 Hz, 1H *H10a*), 4.86 (q, *J* = 6.7 Hz, 1H, *H6*), 4.85 (d, *J* = 16.5 Hz, 1H, *H10b*), 3.87 (d, *J* = 13.0 Hz, ArCHaHb), 3.71 (d, *J* = 13.0 Hz, 1H, ArCHaHb), 3.00 (s, 3H, NCH₃), 2.85 (s, 1H, OH), 2.25 (br s, 3H, ArCH₃), and 1.49 (d, *J* = 6.5 Hz, 3H, CHCH₃).

¹³C NMR (125 MHz, CDCl₃, shifts determined from HSQC data): δ 130.0, 129.3, 127.1, 124.6, 124.6, 122.9, 120.6, 119.6, 119.5, 116.7, 108.3, 74.0, 50.8, 40.9, 26.1, 21.4, and 18.2.

III. Computational details

DFT calculations were carried out in Gaussian 09¹⁶ using the M06-2X/6-31G(d) functional¹⁷/basis set for geometry optimizations and frequency calculations. To identify starting geometries for the DFT calculations, Monte Carlo conformational searches were carried out in MacroModel version 9.9¹⁸. All of the identified lowest energy conformers were subjected to geometry optimization using the above DFT method. The optimized reactant and product geometries were found to have no imaginary frequencies, and the optimized transition structure geometries were found to have only one imaginary frequency. The values for the “Sum of electronic and thermal Free Energies=” were used to determine the free energy (G) of the reactant(s) (G_{reactant}), the transition structure (G_{TS}), and the product (G_{product}) for each reaction. The ΔG^\ddagger and ΔG values for the reaction were determined using the following equations respectively:

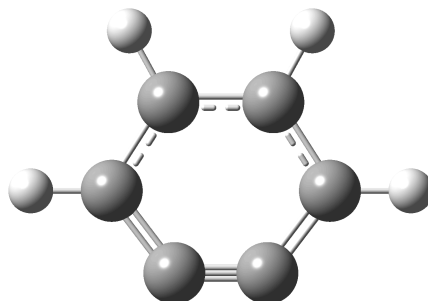
$$\Delta G^\ddagger = G_{\text{TS}} - \sum G_{\text{reactant}}$$

$$\Delta G = G_{\text{product}} - \sum G_{\text{reactant}}$$

where the G values were those of the lowest energy conformer(s) of the reactant(s), transition state, and product. Use of other functionals/basis set combinations gave, qualitatively, the same results and conclusions.

Energies and geometries for all of the entries in Figures 3a and 3b

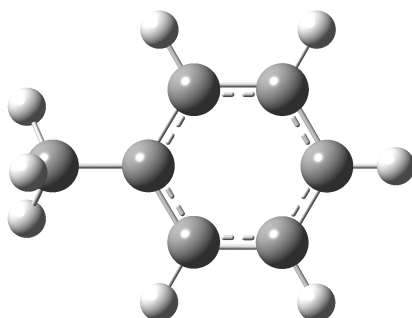
Computed energy and geometry of *o*-benzyne (**3**)



Sum of electronic and thermal Free Energies = -230.756334 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-0.702817	1.052804	-0.000026
2	6	0	-1.460783	-0.132358	0.000112
3	6	0	-0.622548	-1.232617	-0.000072
4	6	0	0.622556	-1.232618	-0.000071
5	6	0	1.460783	-0.132351	0.000114
6	6	0	0.702812	1.052807	-0.000025
7	1	0	-1.224960	2.006005	-0.000133
8	1	0	-2.544826	-0.133016	0.000043
9	1	0	2.544826	-0.133002	0.000037
10	1	0	1.224949	2.006012	-0.000138

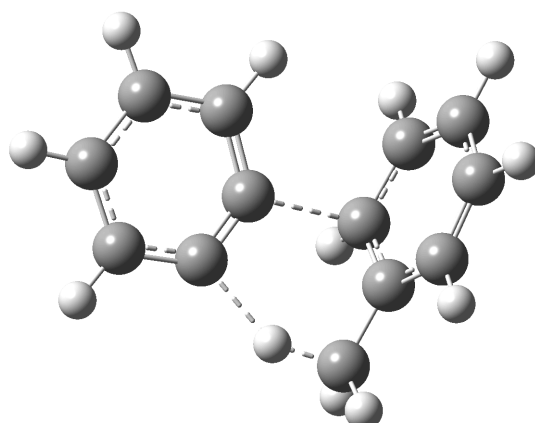
^a Atomic Units = Hartrees

Computed energy and geometry of toluene (**1**)Sum of electronic and thermal Free Energies = -271.333929 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	1.195457	-1.203789	0.002033
2	6	0	1.898569	-0.001602	0.007684
3	6	0	1.199175	1.201721	0.002019
4	6	0	-0.193180	1.200413	-0.008189
5	6	0	-0.909783	0.002213	-0.010638
6	6	0	-0.195958	-1.198760	-0.008224
7	1	0	1.732066	-2.148002	0.001584
8	1	0	2.984203	-0.003232	0.012614
9	1	0	1.738000	2.144656	0.001541
10	1	0	-0.734579	2.143463	-0.016433
11	1	0	-0.740162	-2.140355	-0.016513
12	6	0	-2.417723	0.000809	0.008761
13	1	0	-2.821361	-0.829789	-0.577500
14	1	0	-2.796615	-0.105129	1.031532
15	1	0	-2.820898	0.932354	-0.397502

^a Atomic Units = Hartrees

Computed energy and geometry of TS-4

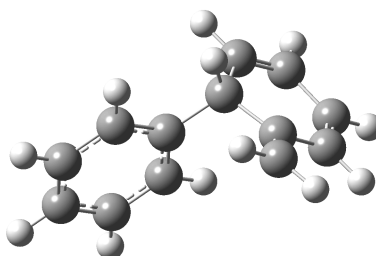


Sum of electronic and thermal Free Energies = -502.060678 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-1.342995	-1.356535	0.197892
2	6	0	-0.839637	-0.077016	0.353345
3	6	0	-2.672181	-1.386861	-0.235921
4	6	0	-3.386182	-0.204184	-0.470670
5	6	0	-1.466089	1.034128	0.138532
6	1	0	-3.157418	-2.345949	-0.394373
7	1	0	-4.416559	-0.264283	-0.812273
8	6	0	1.050444	0.054304	1.073487
9	1	0	0.687067	0.368417	2.049343
10	6	0	0.955057	2.402647	0.331203
11	1	0	0.990184	2.793361	1.350513
12	1	0	-0.204196	2.210932	0.157099
13	1	0	1.316309	3.134865	-0.391702
14	6	0	1.601217	-1.262679	0.964728
15	6	0	1.502779	1.069191	0.178038
16	6	0	2.350741	-1.606321	-0.128940
17	1	0	2.736606	-2.615341	-0.236387
18	6	0	2.648639	-0.634591	-1.112939
19	1	0	3.236691	-0.915842	-1.981277
20	6	0	2.234903	0.670224	-0.958832
21	1	0	2.501110	1.419731	-1.699523
22	6	0	-2.793438	1.049354	-0.279751
23	1	0	-3.356354	1.960586	-0.466379
24	1	0	-0.773376	-2.262838	0.386579
25	1	0	1.380392	-1.993622	1.737355

^a Atomic Units = Hartrees

Computed energy and geometry of 4

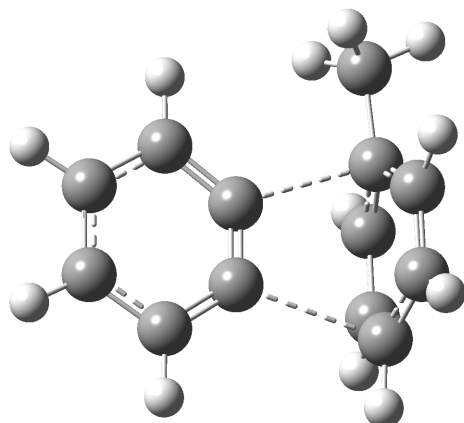


Sum of electronic and thermal Free Energies = -502.159136 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	0.816980	-0.110298	0.310416
2	6	0	1.203139	-0.564578	-0.954026
3	6	0	2.545817	-0.609509	-1.310555
4	6	0	3.523876	-0.195348	-0.407045
5	6	0	3.148913	0.261712	0.851920
6	6	0	1.801303	0.301939	1.206854
7	1	0	0.436723	-0.881753	-1.657497
8	1	0	2.832203	-0.966772	-2.295240
9	1	0	4.572823	-0.228864	-0.685304
10	1	0	3.903704	0.587923	1.561286
11	1	0	1.509686	0.658585	2.192013
12	6	0	-3.396040	-0.367598	-0.204886
13	6	0	-2.834651	0.849710	-0.289021
14	6	0	-1.405070	1.059838	-0.042401
15	6	0	-0.653327	-0.061523	0.677901
16	6	0	-1.313698	-1.413096	0.509121
17	6	0	-2.589699	-1.542013	0.131348
18	1	0	-4.449784	-0.503987	-0.428729
19	1	0	-3.418010	1.710771	-0.605940
20	6	0	-0.811254	2.204509	-0.402917
21	1	0	-0.711946	-2.282605	0.761020
22	1	0	-3.046899	-2.524878	0.063258
23	1	0	-0.712069	0.171225	1.755458
24	1	0	0.253070	2.368772	-0.269157
25	1	0	-1.387232	3.009113	-0.851422

^a Atomic Units = Hartrees

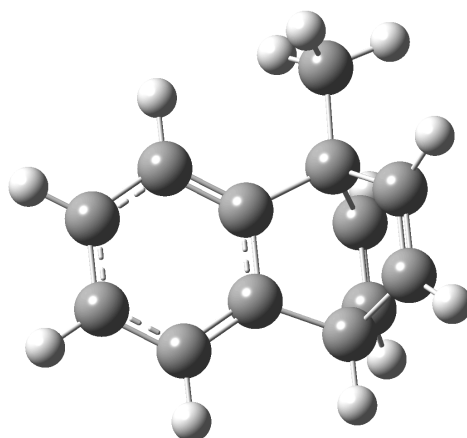
Computed energy and geometry of TS-21a



Sum of electronic and thermal Free Energies = -502.062192 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	1.623267	1.474051	0.000000
2	6	0	0.687909	0.459343	0.000088
3	6	0	2.946334	0.995625	-0.000165
4	6	0	3.229687	-0.375381	-0.000225
5	6	0	0.939460	-0.791799	0.000001
6	1	0	3.768722	1.706317	-0.000245
7	1	0	4.266896	-0.700571	-0.000349
8	6	0	-1.780056	0.096674	1.215381
9	1	0	-1.917065	0.643850	2.144423
10	6	0	-1.657573	0.817774	0.000046
11	6	0	-1.780048	0.096666	-1.215281
12	1	0	-1.917053	0.643813	-2.144342
13	6	0	-1.571941	-1.258466	-1.217920
14	1	0	-1.539854	-1.816933	-2.147916
15	6	0	-1.248023	-1.896029	0.000118
16	1	0	-1.006432	-2.954784	0.000182
17	6	0	2.206916	-1.341582	-0.000148
18	1	0	2.435623	-2.403964	-0.000218
19	1	0	1.405180	2.539352	0.000068
20	6	0	-1.571955	-1.258433	1.218088
21	1	0	-1.539886	-1.816859	2.148109
22	6	0	-1.777637	2.320542	0.000047
23	1	0	-1.301606	2.749471	-0.886036
24	1	0	-2.829824	2.627000	-0.000633
25	1	0	-1.302747	2.749401	0.886772

^a Atomic Units = Hartrees

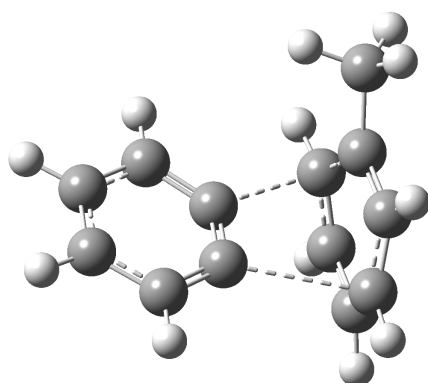
Computed energy and geometry of **21a**

Sum of electronic and thermal Free Energies = -502.162693 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-0.642923	-0.845956	-0.000108
2	6	0	-1.348137	1.463236	-0.000032
3	6	0	-2.682826	1.034333	-0.000004
4	6	0	-2.985012	-0.319776	-0.000010
5	1	0	-1.119212	2.525417	-0.000031
6	1	0	-3.482933	1.768522	0.000032
7	1	0	-4.020870	-0.645345	0.000027
8	6	0	1.407866	-1.274105	-1.228365
9	6	0	1.178919	0.788745	-0.000114
10	6	0	1.697014	0.022165	-1.225169
11	1	0	1.670855	-1.974375	-2.013049
12	1	0	2.234272	0.548861	-2.008058
13	6	0	1.407658	-1.274056	1.228566
14	1	0	1.669961	-1.974358	2.013445
15	6	0	-0.335730	0.521386	-0.000079
16	6	0	-1.957199	-1.272574	-0.000071
17	1	0	-2.190780	-2.334294	-0.000075
18	6	0	0.611600	-1.722392	-0.000104
19	1	0	0.376462	-2.787640	-0.000047
20	6	0	1.559798	2.260214	-0.000009
21	1	0	1.166284	2.767024	0.887046
22	1	0	2.648757	2.369685	0.000077
23	1	0	1.166421	2.767119	-0.887077
24	6	0	1.696831	0.022157	1.225385
25	1	0	2.233635	0.549122	2.008398

^a Atomic Units = Hartrees

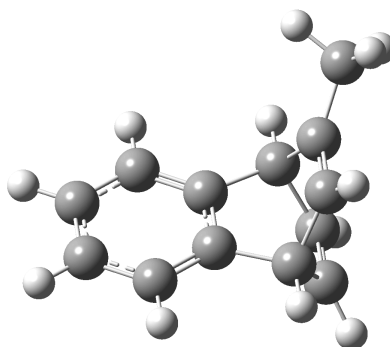
Computed energy and geometry of TS-21b



Sum of electronic and thermal Free Energies = -502.062471 A.U.^a

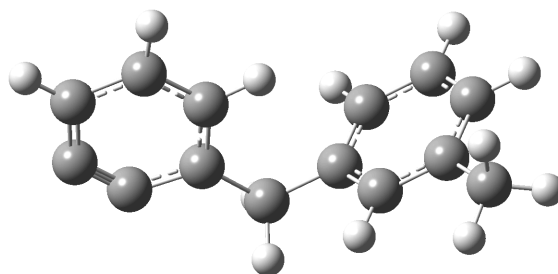
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	2.151579	-1.143119	-0.854442
2	6	0	0.914304	-0.770874	-0.354939
3	6	0	3.209247	-0.302092	-0.465300
4	6	0	2.998773	0.807956	0.360619
5	6	0	0.751934	0.251042	0.396959
6	1	0	4.216691	-0.518996	-0.811631
7	1	0	3.843850	1.431109	0.640602
8	6	0	-1.846854	-0.297254	-1.163524
9	1	0	-2.021393	-0.194162	-2.230910
10	6	0	-1.858040	2.214779	-0.904484
11	1	0	-0.871411	2.694429	-0.877635
12	1	0	-2.540652	2.830622	-0.310499
13	1	0	-2.205601	2.215806	-1.940380
14	6	0	-1.558103	-1.564958	-0.619654
15	6	0	-1.758106	0.816758	-0.363462
16	6	0	-1.591126	-1.760674	0.776077
17	1	0	-1.579004	-2.765757	1.184592
18	6	0	-1.519817	-0.659061	1.590710
19	1	0	-1.443121	-0.757956	2.668703
20	6	0	-1.360994	0.611589	0.987195
21	1	0	-1.245307	1.485364	1.626461
22	6	0	1.717144	1.132927	0.837199
23	1	0	1.546929	1.990457	1.483043
24	1	0	-1.533969	-2.429044	-1.276921
25	1	0	2.333342	-2.003988	-1.493150

^a Atomic Units = Hartrees

Computed energy and geometry of **21b**Sum of electronic and thermal Free Energies = -502.165950 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-0.726896	0.686613	-0.288217
2	6	0	-1.505816	-1.402785	0.643365
3	6	0	-2.794263	-1.106974	0.178479
4	6	0	-3.036978	0.073391	-0.510540
5	1	0	-1.314213	-2.325988	1.184464
6	1	0	-3.605037	-1.806180	0.359261
7	1	0	-4.037690	0.296335	-0.868251
8	6	0	1.788591	-0.523577	-0.477067
9	6	0	1.049009	1.753375	0.985300
10	6	0	0.981579	-0.633904	0.827200
11	6	0	1.281424	0.623885	1.646081
12	1	0	1.174900	2.751973	1.387969
13	1	0	1.180197	-1.561990	1.368389
14	1	0	1.625989	0.556192	2.671646
15	6	0	1.551414	0.610793	-1.131055
16	1	0	1.999493	0.881166	-2.081471
17	6	0	2.689635	-1.643919	-0.887246
18	1	0	3.464364	-1.820082	-0.131304
19	1	0	2.124127	-2.577997	-0.990964
20	1	0	3.180556	-1.432304	-1.840669
21	6	0	-0.482217	-0.504281	0.406196
22	6	0	-1.996561	0.982022	-0.748156
23	1	0	-2.186207	1.906833	-1.287110
24	6	0	0.540070	1.530925	-0.441879
25	1	0	0.359582	2.458669	-0.986733

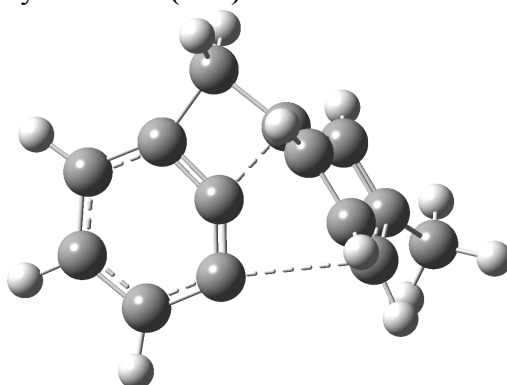
^a Atomic Units = Hartrees

Computed energy and geometry of **22** (n=1)Sum of electronic and thermal Free Energies = -540.180166 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-1.672217	-0.387724	0.546763
2	6	0	-1.633601	0.348947	-0.654452
3	6	0	-2.775780	0.920802	-1.243510
4	6	0	-4.059643	0.807878	-0.683673
5	6	0	-3.993563	0.072226	0.487167
6	6	0	-2.982813	-0.433556	1.006750
7	6	0	-0.473717	-1.027791	1.213718
8	1	0	-0.672630	0.479417	-1.145486
9	1	0	-2.658199	1.472481	-2.172826
10	1	0	-4.940143	1.247884	-1.137142
11	6	0	3.224125	-0.196349	-0.820725
12	6	0	2.776283	0.677780	0.173962
13	6	0	1.582739	0.380164	0.830608
14	6	0	0.837010	-0.758334	0.516710
15	6	0	1.300928	-1.612742	-0.482597
16	6	0	2.492059	-1.332324	-1.147617
17	1	0	4.156389	0.016107	-1.338573
18	6	0	3.560548	1.920448	0.512762
19	1	0	1.220352	1.052047	1.607039
20	1	0	0.727037	-2.499780	-0.739091
21	1	0	2.852488	-2.005604	-1.919650
22	1	0	-0.426887	-0.671064	2.249361
23	1	0	-0.649938	-2.108751	1.271139
24	1	0	3.220933	2.359084	1.454541
25	1	0	4.628715	1.701651	0.604110
26	1	0	3.447736	2.679985	-0.268608

^a Atomic Units = Hartrees

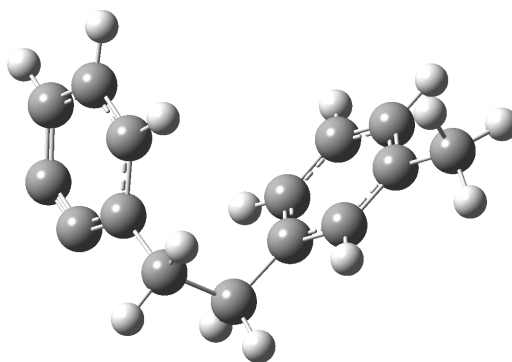
Computed energy and geometry of TS-24 (n=1)



Sum of electronic and thermal Free Energies = -540.107446 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-1.699651	0.785143	-0.422490
2	6	0	-0.696233	0.011235	0.102975
3	6	0	-2.936202	0.138634	-0.478830
4	6	0	-2.976678	-1.184136	-0.000057
5	6	0	-0.613153	-1.209358	0.563628
6	1	0	-3.834929	0.607772	-0.868486
7	1	0	-3.927183	-1.711870	-0.031468
8	6	0	1.327410	0.623349	-1.026473
9	1	0	1.250439	0.766424	-2.101970
10	6	0	-0.870503	2.035326	-0.706067
11	1	0	-1.145469	2.925275	-0.131582
12	1	0	-0.778791	2.312054	-1.760924
13	6	0	2.872544	-1.344567	-1.339844
14	1	0	3.916170	-1.403556	-1.015098
15	1	0	2.858089	-1.049259	-2.391922
16	1	0	2.442832	-2.349977	-1.262538
17	6	0	0.388238	1.301323	-0.146658
18	6	0	2.079219	-0.386161	-0.495431
19	6	0	0.837880	1.481715	1.221058
20	1	0	0.402941	2.265200	1.835252
21	6	0	1.598127	0.479364	1.752996
22	1	0	1.821201	0.444394	2.813954
23	6	0	1.962296	-0.604075	0.911307
24	1	0	2.455708	-1.469158	1.345480
25	6	0	-1.852426	-1.868515	0.515693
26	1	0	-1.986209	-2.892970	0.858461

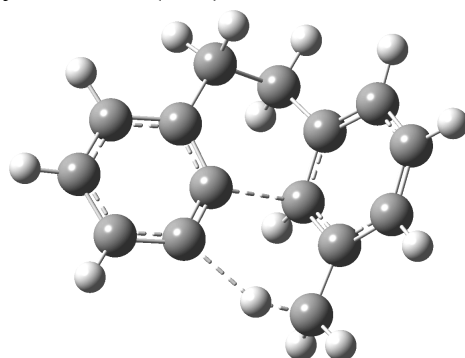
^a Atomic Units = Hartrees

Computed energy and geometry of **22** (n=2)Sum of electronic and thermal Free Energies = -579.449673 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-1.852780	0.872304	-0.402483
2	6	0	-1.726439	-0.293935	-1.184712
3	6	0	-2.565337	-1.412395	-1.046741
4	6	0	-3.607458	-1.467405	-0.104342
5	6	0	-3.651747	-0.283052	0.609482
6	6	0	-2.906203	0.706689	0.489975
7	6	0	-0.905292	2.033687	-0.478365
8	1	0	-0.924373	-0.328878	-1.919311
9	1	0	-2.397170	-2.271324	-1.691337
10	1	0	-4.253750	-2.330165	0.007841
11	6	0	2.631474	-1.471613	0.416059
12	6	0	3.017560	-0.293392	-0.225332
13	6	0	2.193271	0.827053	-0.107370
14	6	0	1.005717	0.793426	0.625388
15	6	0	0.637359	-0.399730	1.251495
16	6	0	1.448008	-1.524936	1.147067
17	1	0	3.265604	-2.351975	0.344646
18	6	0	4.282818	-0.234515	-1.044368
19	1	0	2.488607	1.755949	-0.594978
20	1	0	-0.291385	-0.443133	1.815463
21	1	0	1.158672	-2.447313	1.641957
22	1	0	-0.363278	2.004655	-1.430090
23	1	0	-1.467794	2.972555	-0.443422
24	1	0	5.016846	-0.964837	-0.693116
25	1	0	4.078617	-0.452819	-2.098728
26	1	0	4.740289	0.757869	-0.997371
27	6	0	0.111537	2.007267	0.684686
28	1	0	0.715905	2.920138	0.644926
29	1	0	-0.441720	2.022568	1.630872

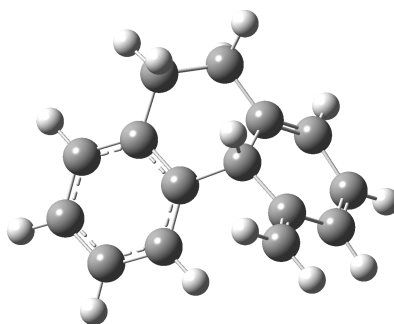
^a Atomic Units = Hartrees

Computed energy and geometry of TS-23 (n=2)

Sum of electronic and thermal Free Energies = -579.428661 A.U.^a

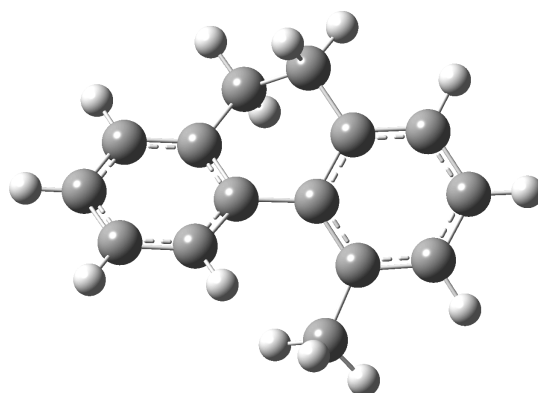
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-1.474196	-0.920320	-0.043682
2	6	0	-0.844560	0.309580	0.133312
3	6	0	-2.831966	-0.768694	-0.362564
4	6	0	-3.428380	0.490934	-0.491042
5	6	0	-1.348287	1.498156	0.020519
6	1	0	-3.432554	-1.661935	-0.521313
7	1	0	-4.484255	0.549444	-0.744202
8	6	0	0.980454	0.151916	0.870760
9	1	0	0.561224	0.240632	1.872418
10	6	0	-0.823465	-2.278822	0.043254
11	1	0	-0.561452	-2.614901	-0.968390
12	1	0	-1.540946	-3.003906	0.441806
13	6	0	0.464463	-2.288747	0.896902
14	1	0	0.964403	-3.256107	0.789465
15	1	0	0.203346	-2.156396	1.952936
16	6	0	1.181337	2.603227	0.749801
17	1	0	1.068945	2.726116	1.830106
18	1	0	0.079033	2.586938	0.361440
19	1	0	1.725951	3.441546	0.313041
20	6	0	1.336060	-1.164668	0.426814
21	6	0	1.662639	1.289405	0.345261
22	6	0	2.261014	-1.309783	-0.579559
23	1	0	2.499758	-2.302024	-0.954566
24	6	0	2.887122	-0.178260	-1.140397
25	1	0	3.622368	-0.312260	-1.928321
26	6	0	2.571693	1.094874	-0.706717
27	1	0	3.051323	1.960404	-1.155254
28	6	0	-2.692354	1.665449	-0.306953
29	1	0	-3.166580	2.636962	-0.423416

^a Atomic Units = Hartrees

Computed energy and geometry of **23** (n=2)Sum of electronic and thermal Free Energies = -579.524049 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-0.664377	-0.358822	0.236850
2	6	0	-0.978453	-1.616367	-0.266749
3	6	0	-2.271259	-1.888396	-0.714049
4	6	0	-3.250627	-0.902991	-0.664629
5	6	0	-2.936139	0.360204	-0.166641
6	6	0	-1.650800	0.641094	0.284564
7	1	0	-0.213793	-2.385615	-0.306085
8	1	0	-2.507880	-2.872831	-1.106691
9	1	0	-4.256354	-1.112761	-1.016077
10	1	0	-3.696378	1.136908	-0.127898
11	6	0	-1.252645	1.982055	0.846084
12	6	0	2.827714	0.217839	-1.248740
13	6	0	2.734317	-0.908452	-0.521272
14	6	0	1.790425	-1.020172	0.588963
15	6	0	0.728287	0.055765	0.722760
16	6	0	1.023155	1.337182	-0.039289
17	6	0	1.975483	1.372594	-0.980247
18	1	0	3.555826	0.290285	-2.051374
19	1	0	3.391611	-1.752974	-0.711589
20	6	0	1.845577	-2.043195	1.452994
21	6	0	0.076901	2.480103	0.238106
22	1	0	2.115744	2.271364	-1.576412
23	1	0	0.633100	0.305417	1.791134
24	1	0	1.158085	-2.118388	2.291102
25	1	0	2.582571	-2.833646	1.343165
26	1	0	-2.044043	2.720932	0.690435
27	1	0	-1.129225	1.884252	1.933507
28	1	0	0.541321	3.195832	0.928863
29	1	0	-0.115938	3.020582	-0.694312

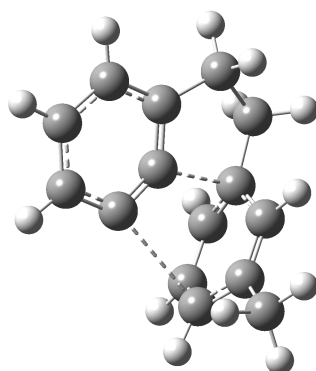
^a Atomic Units = Hartrees

Computed energy and geometry of **25** (n=2)Sum of electronic and thermal Free Energies = -579.583138 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-0.790167	0.260660	-0.072132
2	6	0	-1.468640	1.401076	-0.516982
3	6	0	-2.858798	1.462257	-0.511620
4	6	0	-3.600913	0.372250	-0.071095
5	6	0	-2.941077	-0.787903	0.324944
6	6	0	-1.551496	-0.860426	0.316213
7	1	0	-0.907349	2.244562	-0.901127
8	1	0	-3.358606	2.360160	-0.862112
9	1	0	-4.685778	0.413319	-0.060598
10	1	0	-3.512593	-1.660664	0.631441
11	6	0	1.251064	-1.125898	-0.256298
12	6	0	1.556779	1.248912	0.174554
13	6	0	2.629064	-1.295101	-0.321915
14	6	0	2.937943	1.043012	0.107005
15	6	0	3.478530	-0.206486	-0.160917
16	1	0	3.036009	-2.289943	-0.484380
17	1	0	3.598846	1.887185	0.287725
18	1	0	4.555269	-0.337834	-0.209158
19	6	0	0.695180	0.156371	-0.055239
20	6	0	1.081198	2.632427	0.556424
21	1	0	1.851516	3.133631	1.148799
22	1	0	0.890261	3.262245	-0.319916
23	1	0	0.162030	2.600520	1.146333
24	6	0	0.322818	-2.313813	-0.350153
25	1	0	-0.096525	-2.392798	-1.362747
26	1	0	0.878670	-3.235801	-0.153421
27	6	0	-0.823148	-2.138293	0.647755
28	1	0	-0.408482	-2.091991	1.664127
29	1	0	-1.513278	-2.986855	0.611771

^a Atomic Units = Hartrees

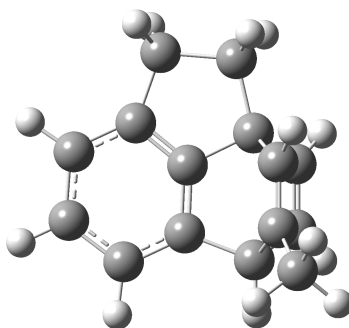
Computed energy and geometry of TS-24 (n=2)



Sum of electronic and thermal Free Energies = -579.420570 A.U.^a

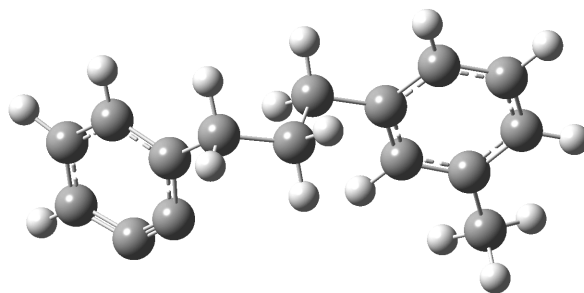
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	1.828380	0.509657	-0.259983
2	6	0	0.710283	-0.136756	0.212303
3	6	0	2.936340	-0.348507	-0.329183
4	6	0	2.806652	-1.694572	0.037538
5	6	0	0.490436	-1.372708	0.515704
6	1	0	3.894800	0.026011	-0.680510
7	1	0	3.678968	-2.340615	-0.029003
8	6	0	-1.140013	1.105833	1.511207
9	1	0	-0.781742	1.733726	2.322093
10	6	0	1.664100	1.939946	-0.700452
11	1	0	1.597814	1.976136	-1.795524
12	1	0	2.510688	2.573951	-0.418893
13	6	0	0.347066	2.457206	-0.066136
14	1	0	-0.117559	3.217387	-0.701995
15	1	0	0.573388	2.932491	0.893532
16	6	0	-0.623049	1.308415	0.193780
17	6	0	-1.356262	0.712541	-0.885714
18	1	0	-1.154185	1.043157	-1.903316
19	6	0	-2.122786	-0.402363	-0.655214
20	6	0	-2.211438	-0.861308	0.680548
21	1	0	-2.726476	-1.798064	0.877680
22	6	0	1.580464	-2.241633	0.459724
23	1	0	1.520403	-3.300658	0.702399
24	6	0	-2.708939	-1.219389	-1.774199
25	1	0	-3.762896	-1.453792	-1.595807
26	1	0	-2.631843	-0.694881	-2.729936
27	1	0	-2.167662	-2.168572	-1.864624
28	6	0	-1.907977	-0.001773	1.753349
29	1	0	-2.193226	-0.273805	2.764260

^a Atomic Units = Hartrees

Computed energy and geometry of **24** (n=2)Sum of electronic and thermal Free Energies = -579.514834 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	0.608837	0.038694	0.052818
2	6	0	-0.008303	-1.168949	0.308060
3	6	0	0.777112	-2.308690	0.235609
4	6	0	2.140810	-2.164283	-0.088175
5	6	0	2.725853	-0.921620	-0.337624
6	6	0	1.926850	0.227286	-0.264088
7	1	0	0.365575	-3.296877	0.423164
8	1	0	2.759149	-3.055590	-0.143230
9	1	0	3.782772	-0.862207	-0.583006
10	6	0	2.184973	1.709561	-0.459687
11	6	0	-1.485217	0.099846	1.784797
12	6	0	-1.487523	-0.907089	0.623739
13	6	0	-2.034036	-0.140765	-0.600886
14	6	0	-1.386156	0.998388	-0.846919
15	6	0	-0.230394	1.287035	0.120093
16	6	0	-0.843854	1.237563	1.524936
17	1	0	-1.969524	-0.138647	2.724964
18	1	0	-2.057336	-1.813441	0.839942
19	6	0	-3.174291	-0.718702	-1.377426
20	6	0	0.790963	2.397776	-0.228712
21	1	0	-0.719999	2.059522	2.223293
22	1	0	-3.448873	-0.077572	-2.219079
23	1	0	-4.057920	-0.848731	-0.740808
24	1	0	2.932856	2.082224	0.248680
25	1	0	2.571792	1.922460	-1.462161
26	1	0	0.476909	2.938347	-1.126475
27	1	0	0.853310	3.134150	0.577923
28	1	0	-2.913440	-1.709072	-1.770287
29	1	0	-1.609005	1.669128	-1.672128

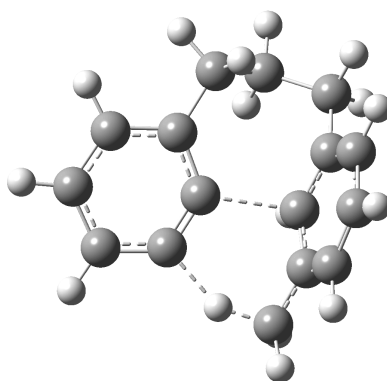
^a Atomic Units = Hartrees

Computed energy and geometry of **22** (n=3)Sum of electronic and thermal Free Energies = -618.715412 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	2.676209	-0.580628	0.443074
2	6	0	3.671866	-0.686363	-0.549343
3	6	0	4.453959	0.399252	-0.981143
4	6	0	4.302294	1.696670	-0.462147
5	6	0	3.304183	1.699096	0.495930
6	6	0	2.611995	0.739105	0.880402
7	6	0	1.822380	-1.723598	0.916496
8	1	0	3.838328	-1.660981	-1.003390
9	1	0	5.202479	0.228869	-1.750664
10	1	0	4.900212	2.537376	-0.793867
11	6	0	-4.350152	0.171280	-0.135687
12	6	0	-3.337078	1.122634	0.006384
13	6	0	-2.011283	0.704920	-0.113653
14	6	0	-1.680396	-0.627923	-0.365845
15	6	0	-2.710343	-1.560302	-0.498357
16	6	0	-4.038824	-1.161568	-0.384441
17	1	0	-5.389260	0.481006	-0.054981
18	6	0	-3.666875	2.563767	0.304352
19	1	0	-1.210164	1.436688	-0.011545
20	1	0	-2.468200	-2.601220	-0.700440
21	1	0	-4.834905	-1.891502	-0.498800
22	1	0	1.982271	-2.589522	0.262855
23	1	0	2.146203	-2.020215	1.921905
24	1	0	-4.636309	2.844154	-0.117055
25	1	0	-3.714439	2.739062	1.385096
26	1	0	-2.908870	3.237546	-0.104479
27	6	0	-0.234116	-1.050422	-0.437067
28	1	0	0.362532	-0.257331	-0.903608
29	1	0	-0.133853	-1.940903	-1.070750
30	6	0	0.335990	-1.355380	0.953194
31	1	0	0.202071	-0.475756	1.596503
32	1	0	-0.236946	-2.170518	1.410312

^a Atomic Units = Hartrees

Computed energy and geometry of TS-23 (n=3)

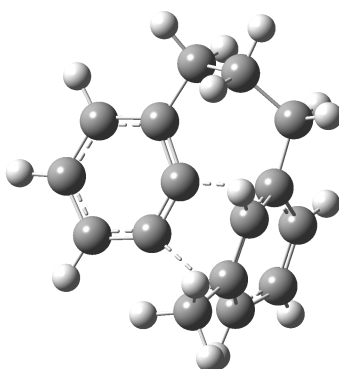


Sum of electronic and thermal Free Energies = -618.692443 A.U.^a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-1.498121	0.865106	0.283183
2	6	0	-0.905991	-0.311371	-0.170917
3	6	0	-2.839826	0.666518	0.646011
4	6	0	-3.478153	-0.575063	0.534907
5	6	0	-1.471190	-1.464527	-0.294247
6	1	0	-3.405584	1.520161	1.013710
7	1	0	-4.520546	-0.661575	0.831330
8	1	0	-0.302851	-2.513850	-0.768572
9	6	0	1.476360	-1.561224	-0.446641
10	6	0	2.400549	0.693926	0.955321
11	1	0	2.809260	1.551830	1.483616
12	6	0	2.648535	-0.608380	1.445000
13	1	0	3.221443	-0.734425	2.359000
14	6	0	2.197239	-1.710336	0.757921
15	1	0	2.412226	-2.712027	1.120179
16	6	0	-2.802886	-1.691406	0.035400
17	1	0	-3.303076	-2.649871	-0.073066
18	6	0	1.675440	0.889231	-0.194462
19	6	0	-0.871780	2.238646	0.352822
20	1	0	-1.676653	2.965182	0.501947
21	1	0	-0.223619	2.310001	1.237178
22	6	0	-0.058425	2.600671	-0.901613
23	1	0	-0.478465	2.071555	-1.764942
24	1	0	-0.153468	3.670075	-1.117425
25	6	0	1.433411	2.268147	-0.750479
26	1	0	1.930024	2.371575	-1.724076
27	1	0	1.897288	3.001062	-0.079873
28	6	0	0.846885	-2.682265	-1.104153
29	1	0	0.787151	-2.615422	-2.192147
30	1	0	1.171880	-3.667574	-0.769634
31	6	0	1.098044	-0.249559	-0.846828
32	1	0	0.734442	-0.115388	-1.864580

^a Atomic Units = Hartrees

Computed energy and geometry of TS-24 (n=3)

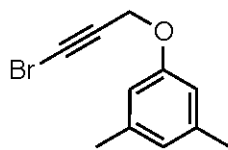
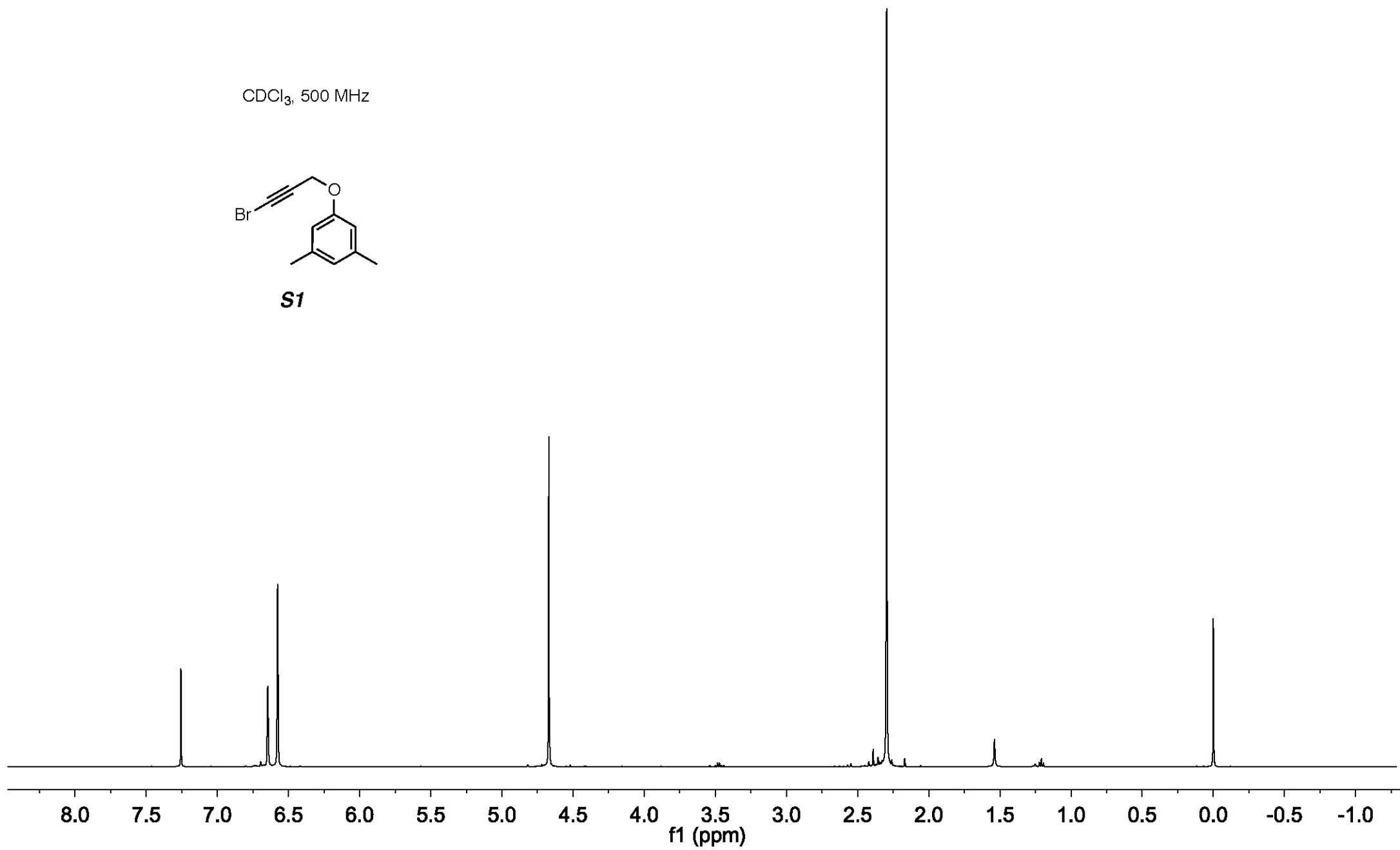


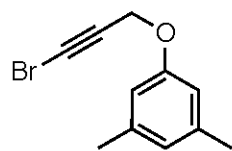
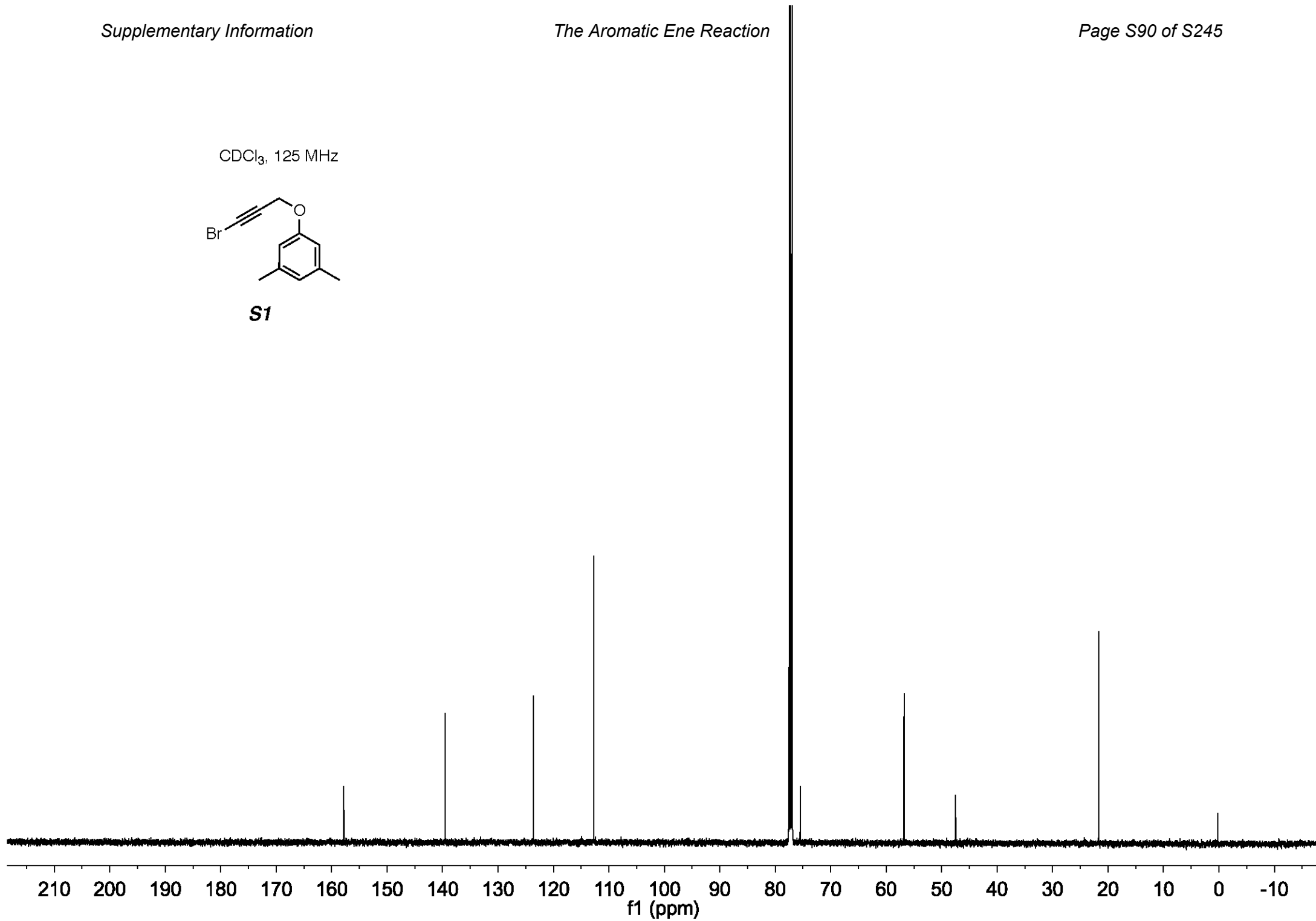
Sum of electronic and thermal Free Energies = -618.694744 A.U.^a

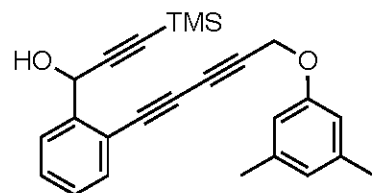
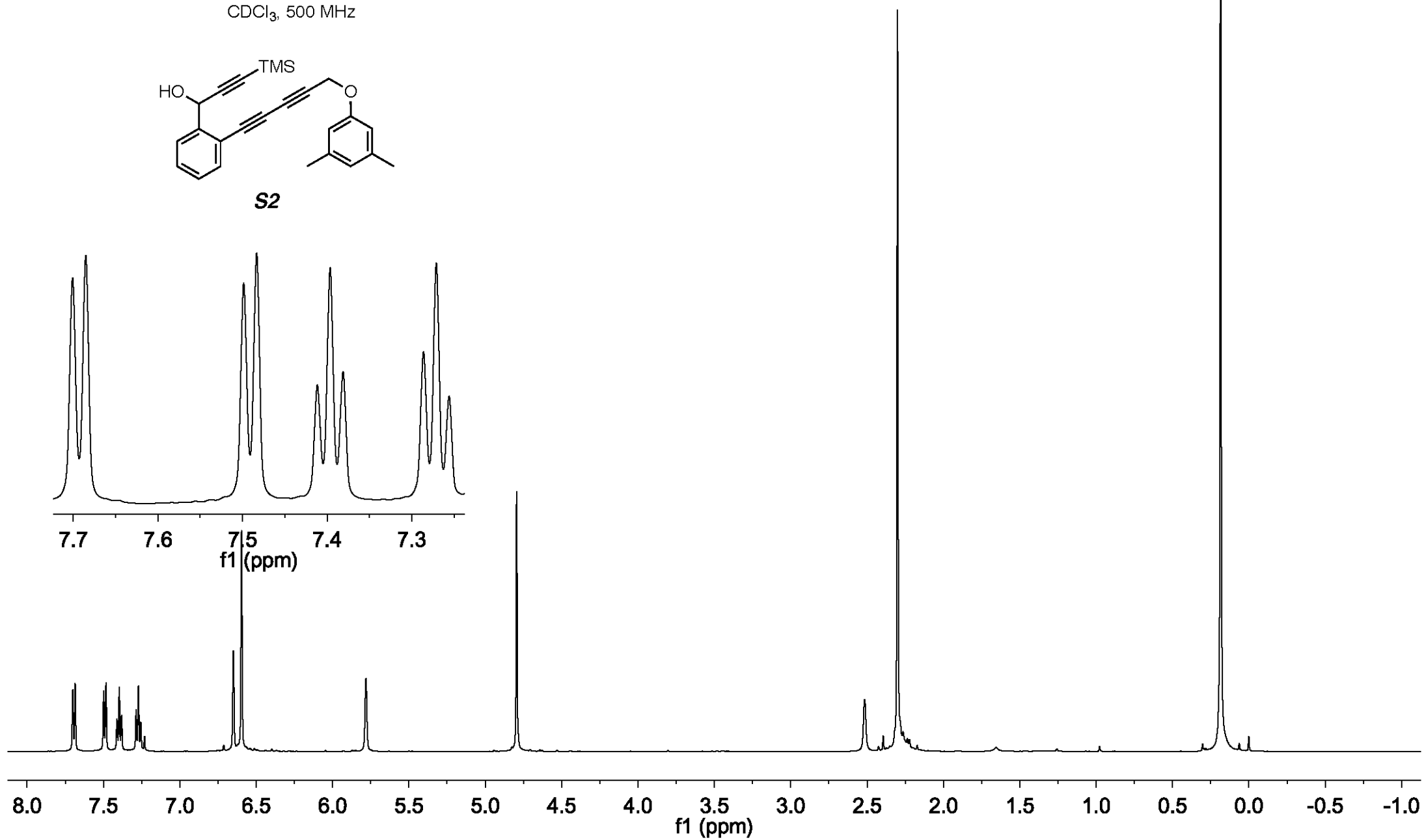
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	0.664883	-0.362527	0.199163
2	6	0	2.791633	-1.141610	-0.173361
3	6	0	2.281984	-2.437742	-0.037427
4	6	0	0.149192	-1.526290	0.317170
5	1	0	3.850998	-1.004649	-0.382540
6	1	0	2.959799	-3.281736	-0.140100
7	6	0	-1.162327	0.987301	1.631129
8	1	0	-0.758127	1.506139	2.496112
9	6	0	-0.729941	1.364708	0.332663
10	6	0	-1.484327	0.889012	-0.777314
11	1	0	-1.328125	1.340809	-1.755430
12	6	0	-2.265659	-0.232031	-0.650690
13	6	0	-2.326615	-0.842378	0.625952
14	1	0	-2.878398	-1.773252	0.733205
15	6	0	0.917973	-2.675816	0.213280
16	1	0	0.538437	-3.690340	0.304902
17	6	0	1.970096	-0.002357	-0.057733
18	6	0	2.458682	1.414363	-0.217248
19	1	0	2.793066	1.805616	0.754549
20	1	0	3.338854	1.421513	-0.870234
21	6	0	1.382989	2.346567	-0.782709
22	1	0	1.030574	1.951250	-1.743763
23	1	0	1.834352	3.323390	-0.987956
24	6	0	0.188413	2.560988	0.159250
25	1	0	0.564586	2.867753	1.143182
26	1	0	-0.411195	3.398725	-0.219257
27	6	0	-2.904080	-0.903435	-1.835559
28	1	0	-3.952312	-1.152719	-1.644051
29	1	0	-2.859452	-0.267832	-2.723563
30	1	0	-2.376598	-1.837876	-2.061756
31	6	0	-1.956762	-0.122042	1.776147
32	1	0	-2.203266	-0.507059	2.760423

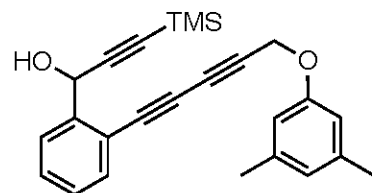
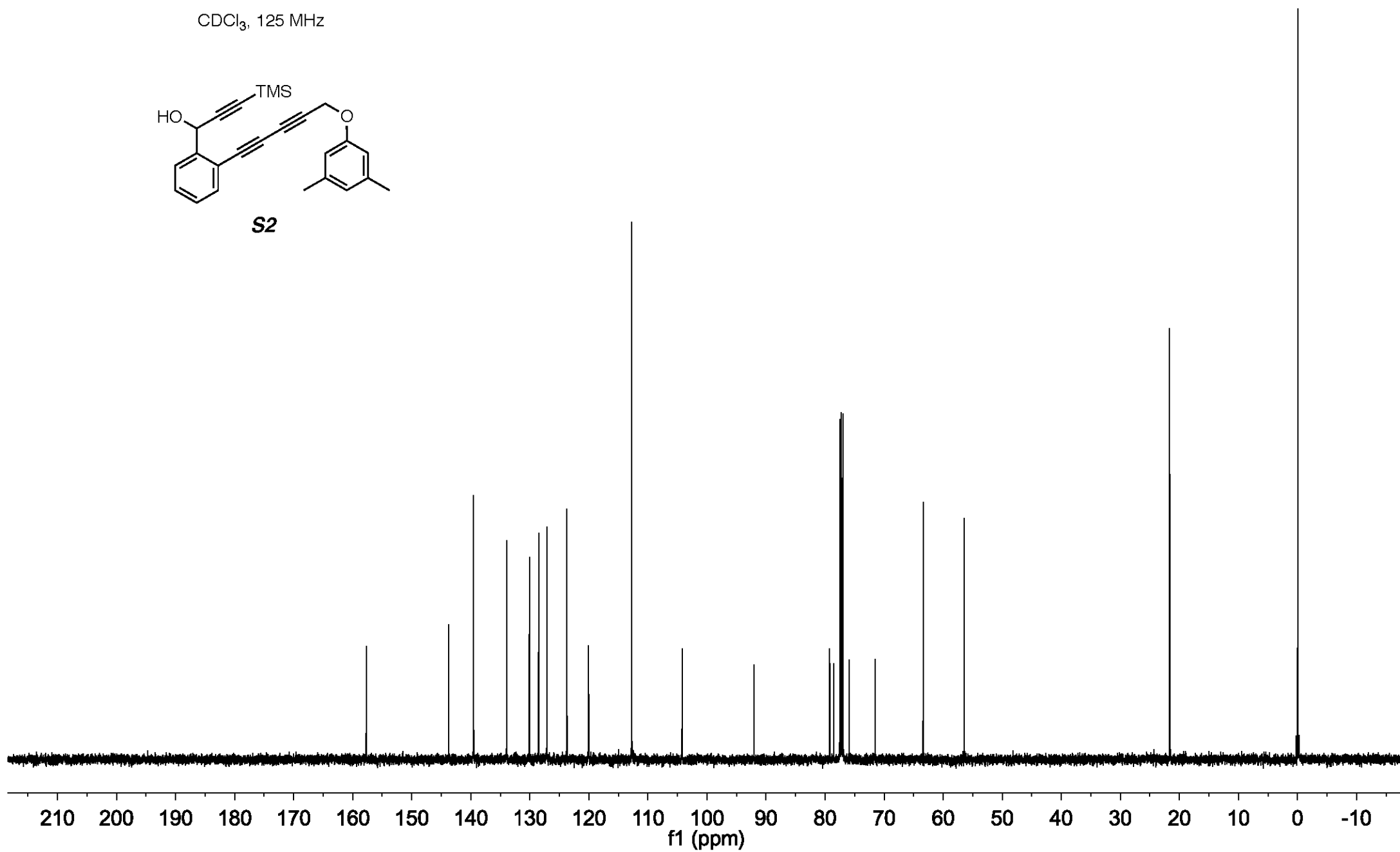
^a Atomic Units = Hartrees

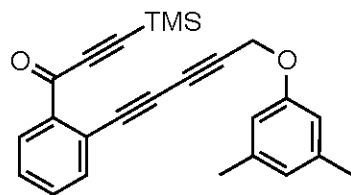
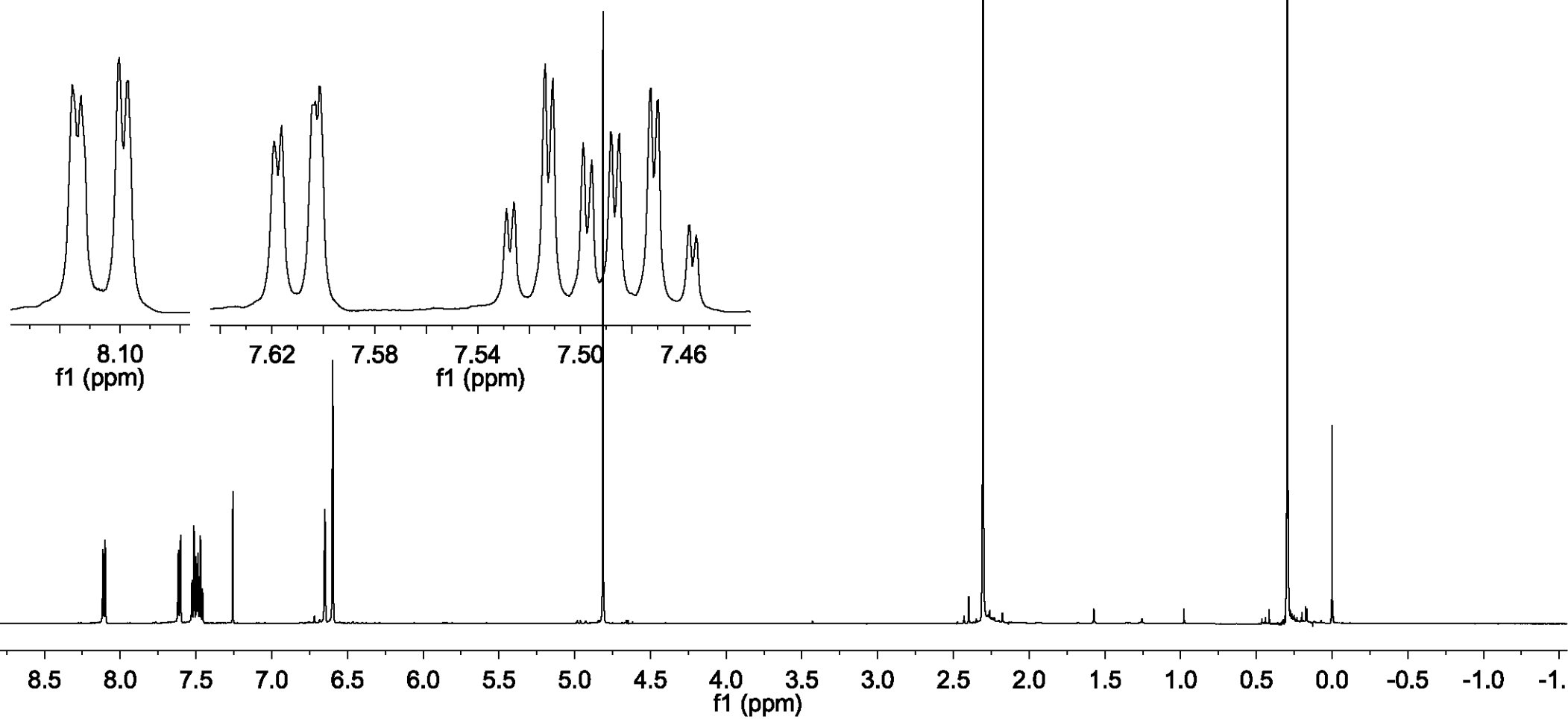
VI. Copies of ^1H and ^{13}C NMR spectra for each isolated compound

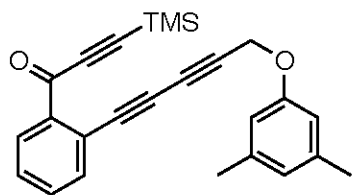
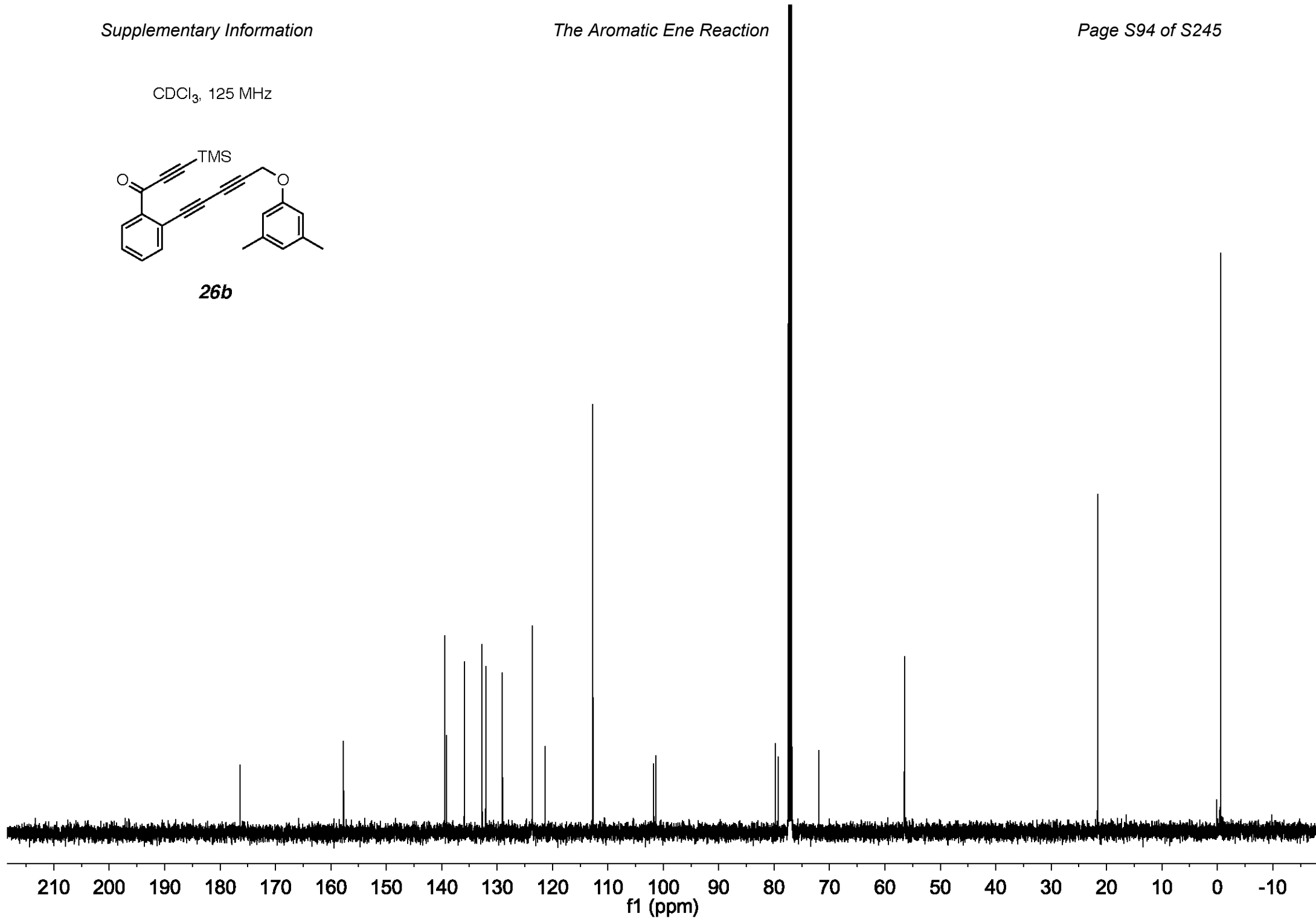
CDCl₃, 500 MHz**S1**

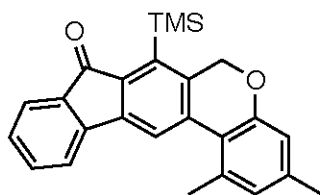
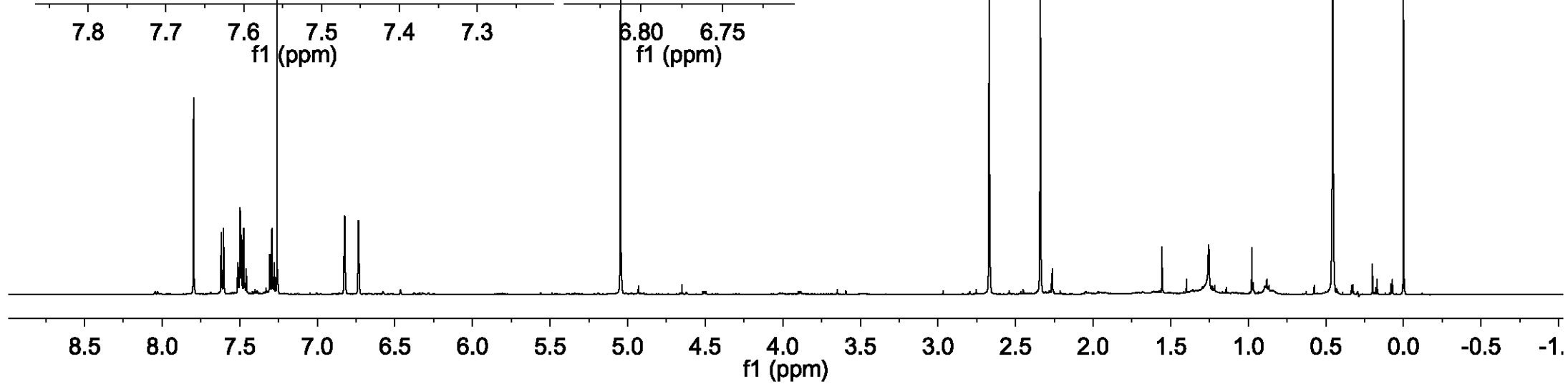
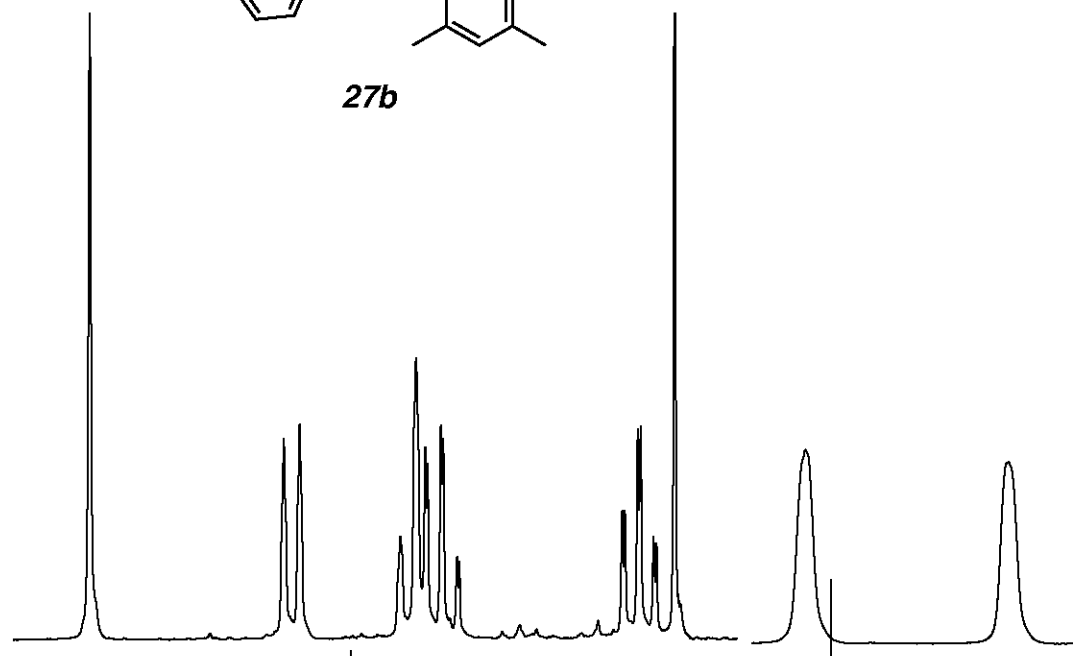
CDCl₃, 125 MHz**S1**

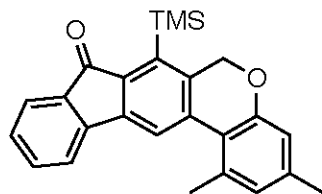
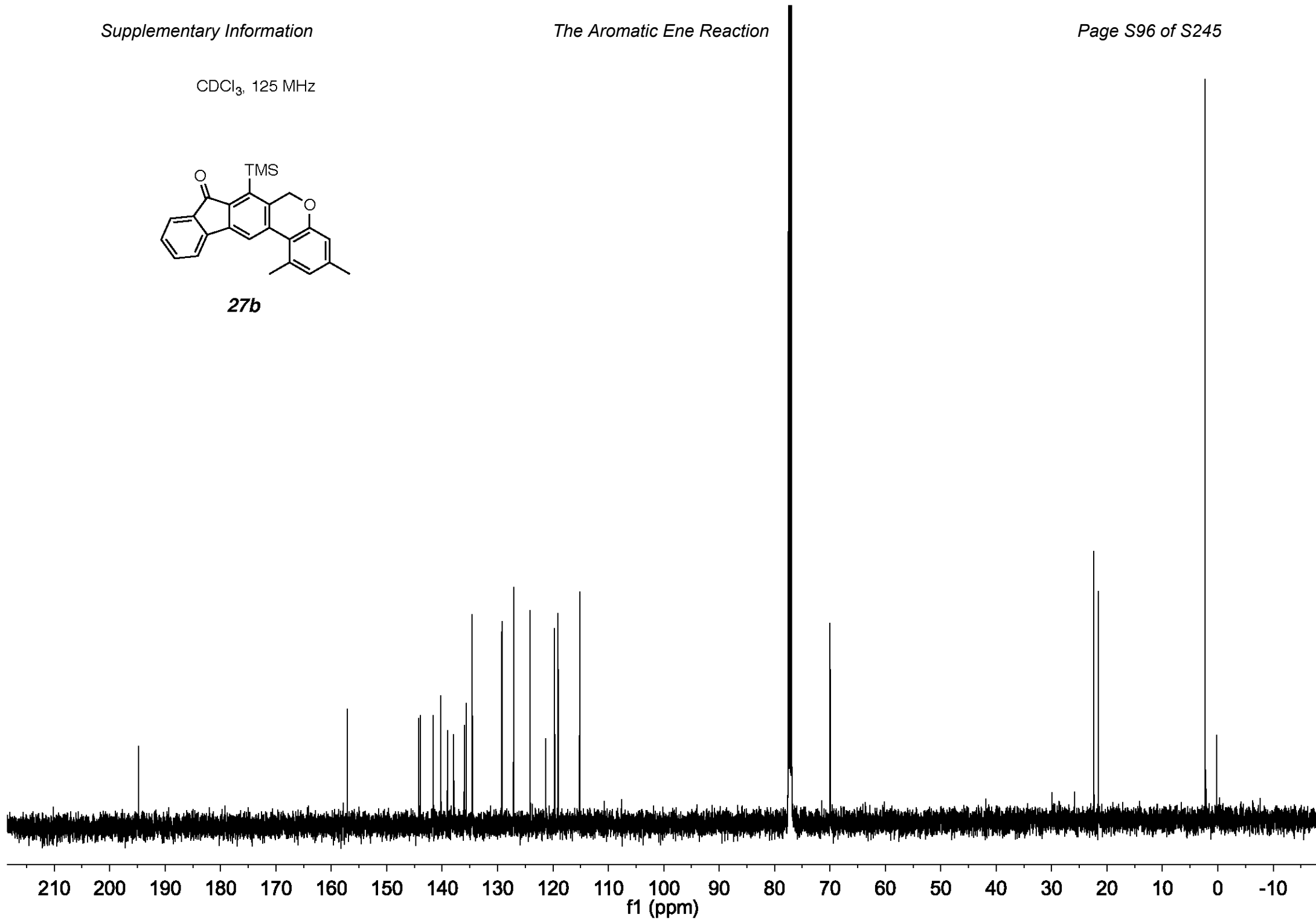
CDCl₃, 500 MHz**S2**

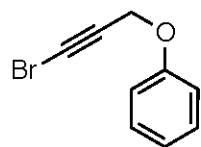
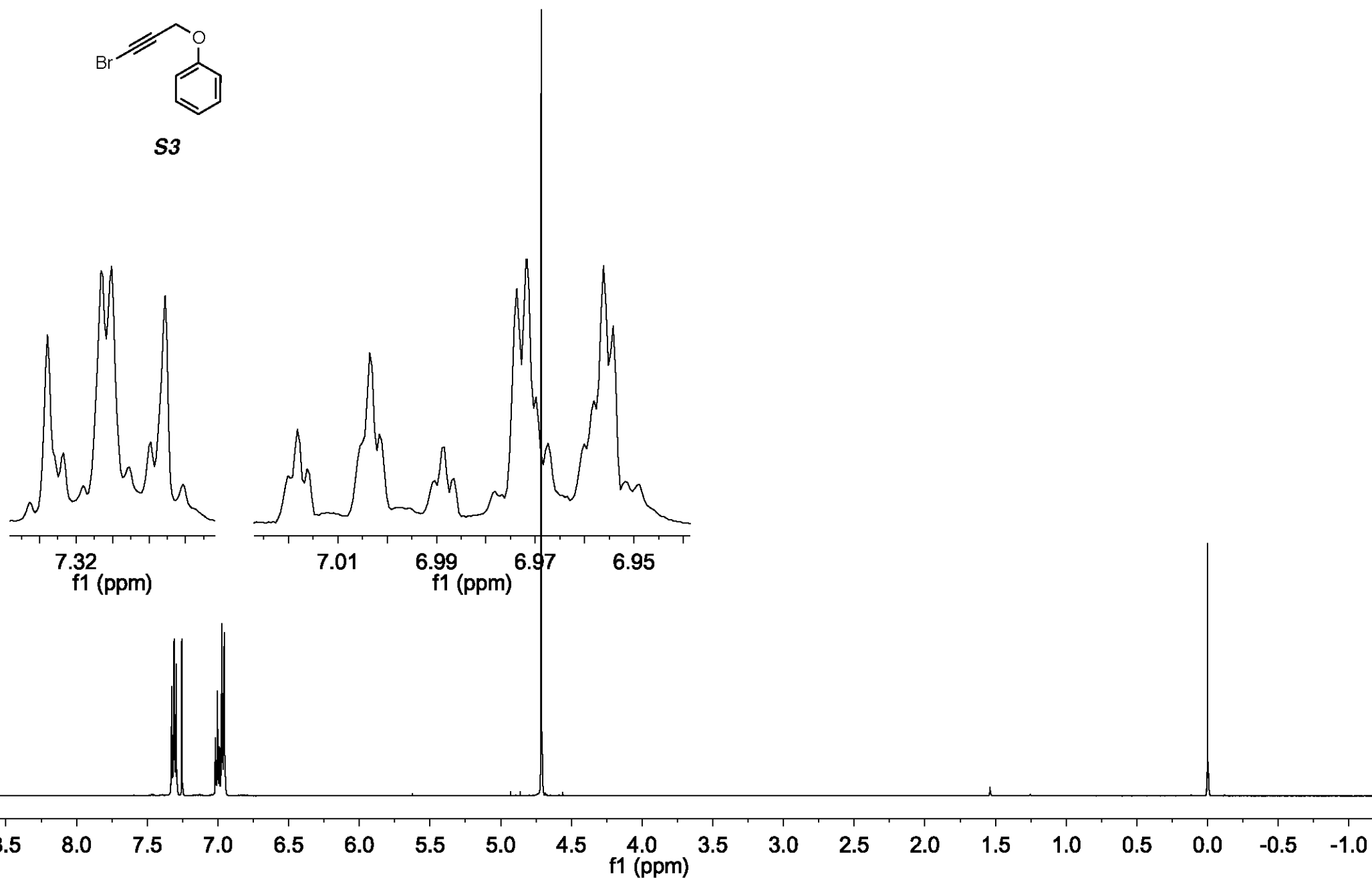
CDCl₃, 125 MHz**S2**

CDCl₃, 500 MHz**26b**

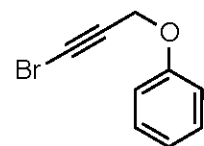
CDCl₃, 125 MHz**26b**

CDCl₃, 500 MHz**27b**

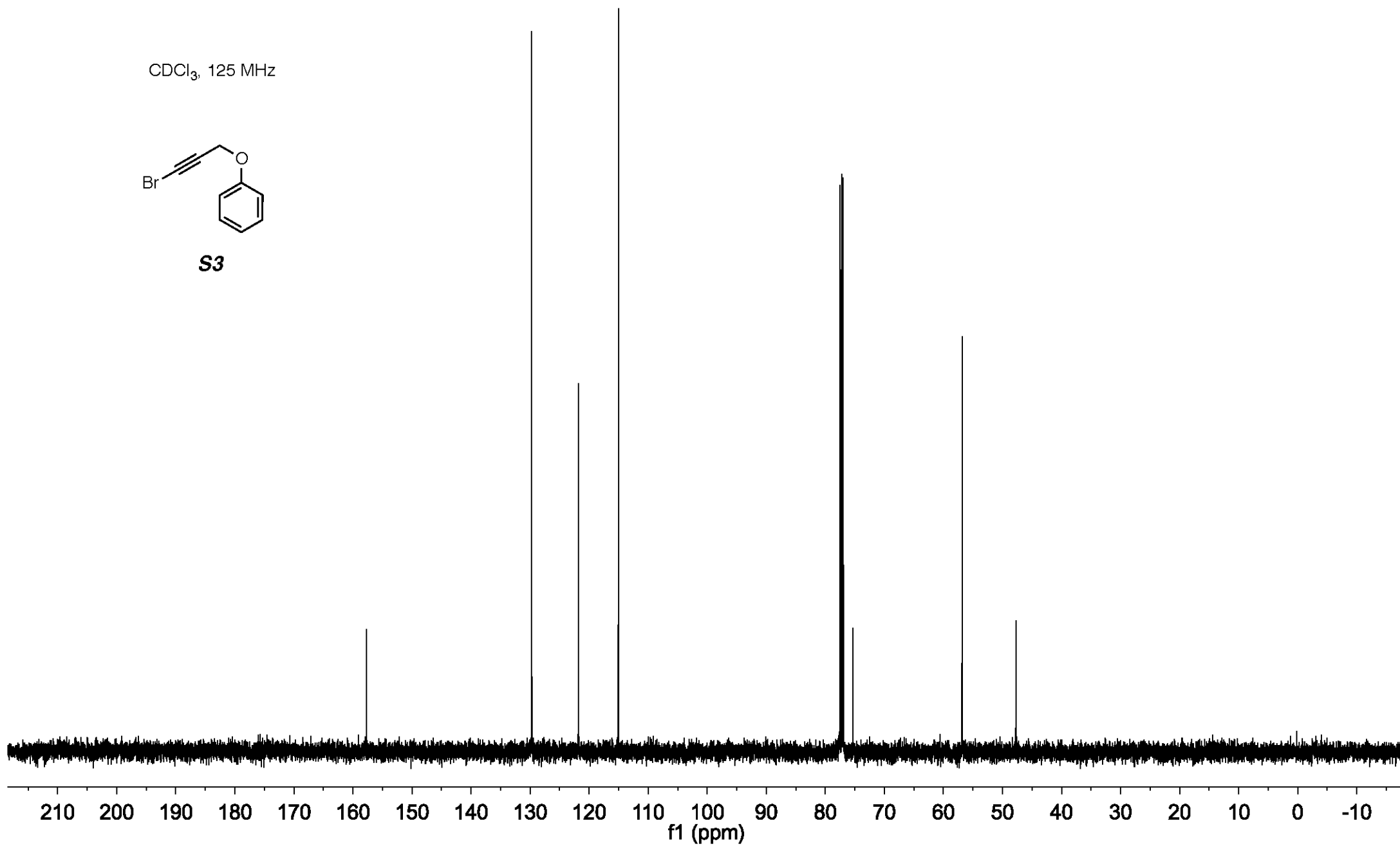
CDCl₃, 125 MHz**27b**

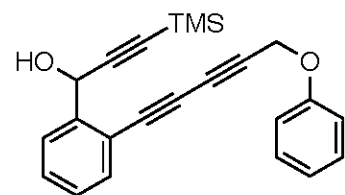
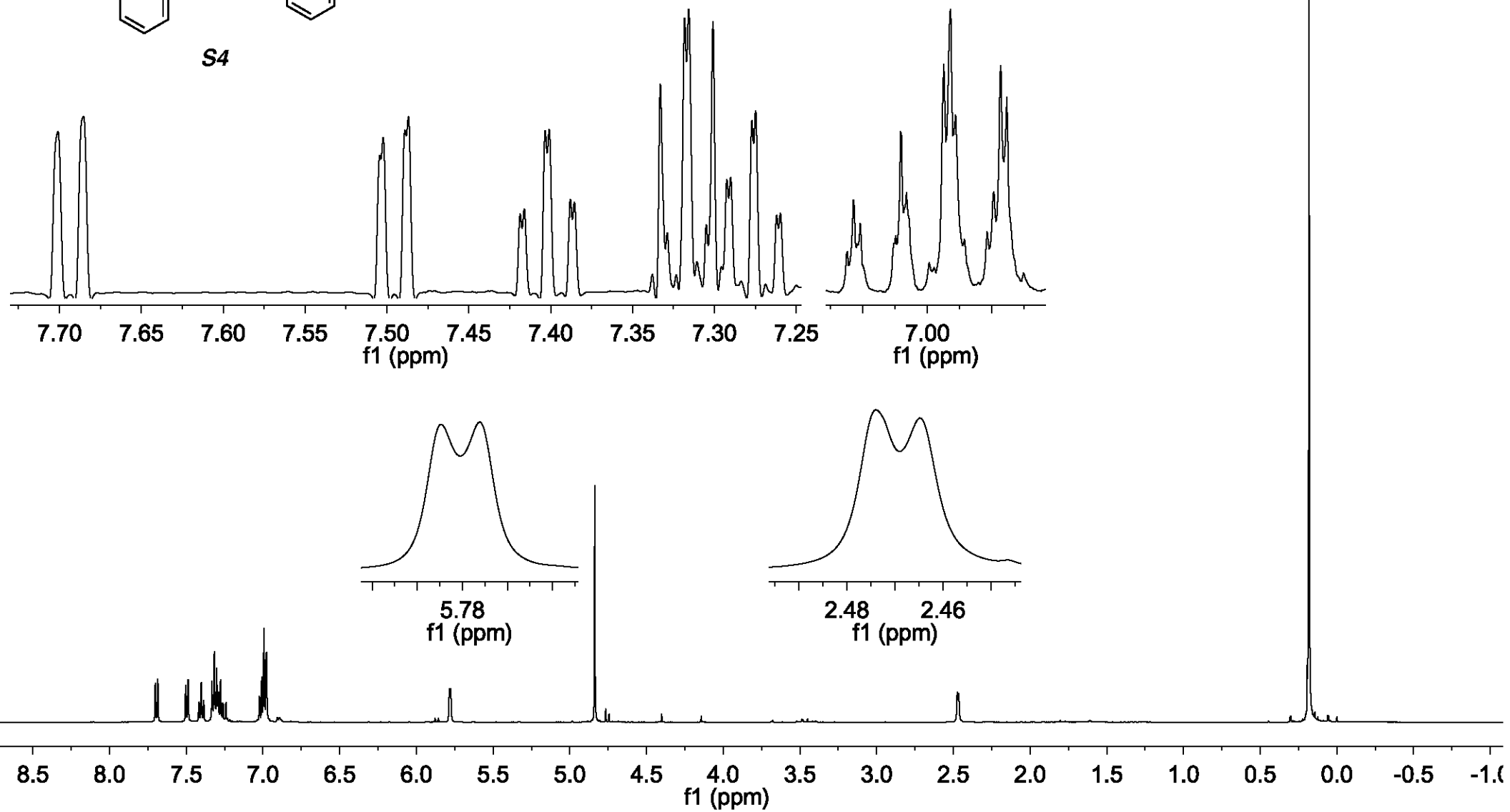
CDCl₃, 500 MHz**S3**

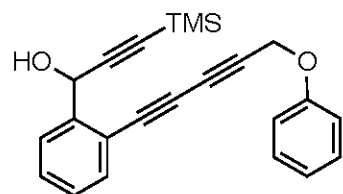
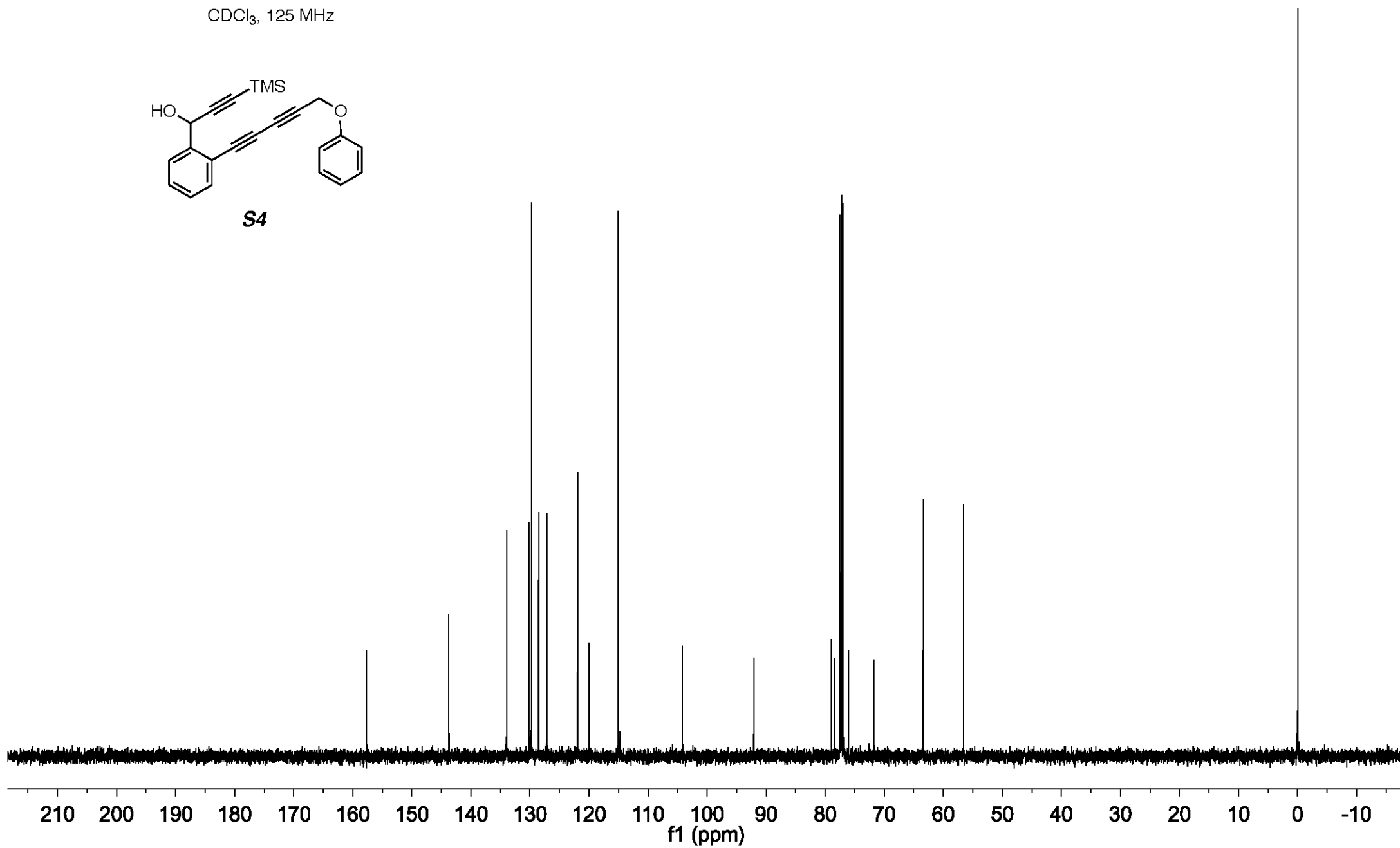
CDCl₃, 125 MHz

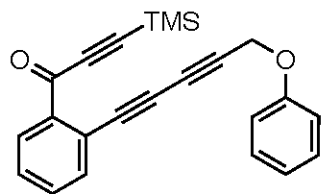


S3

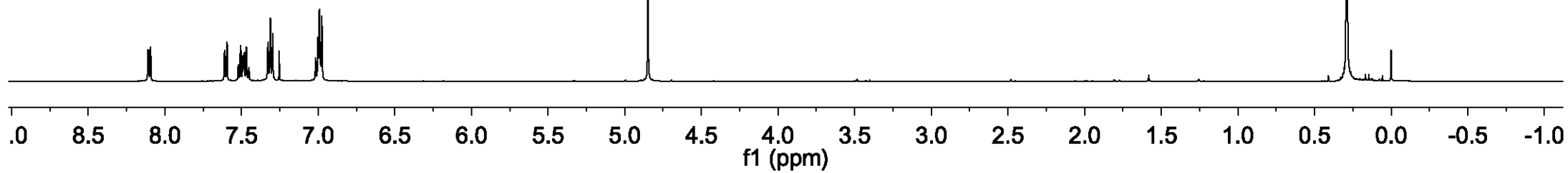
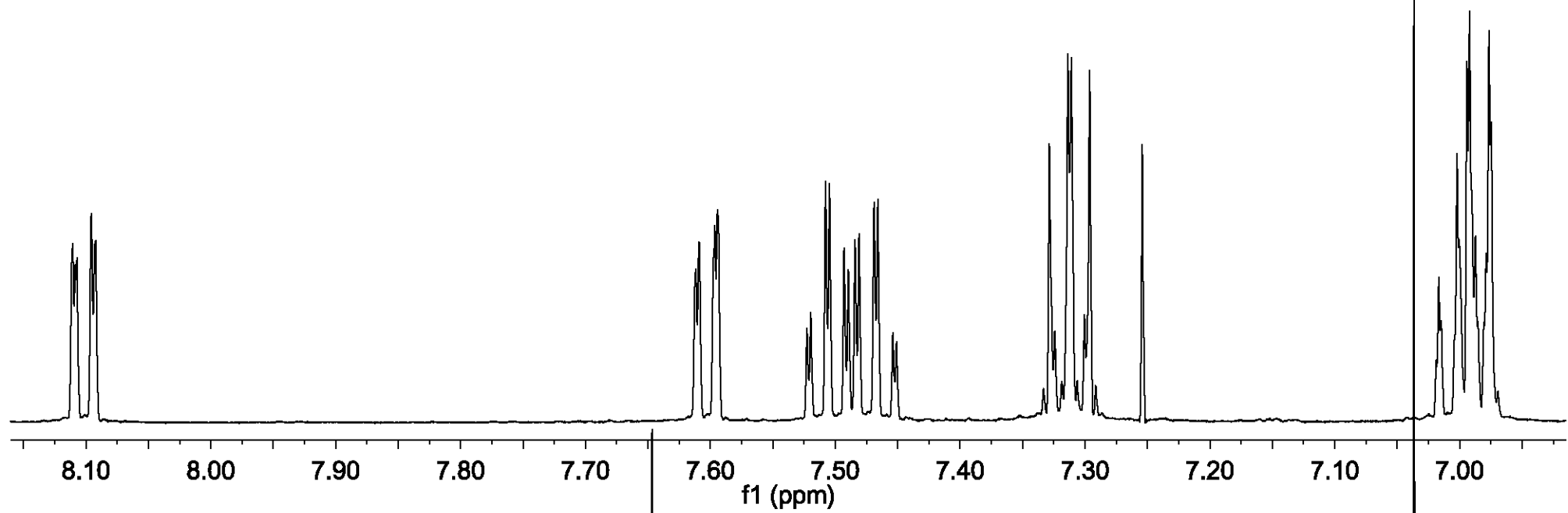


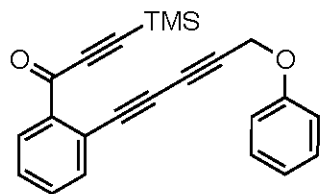
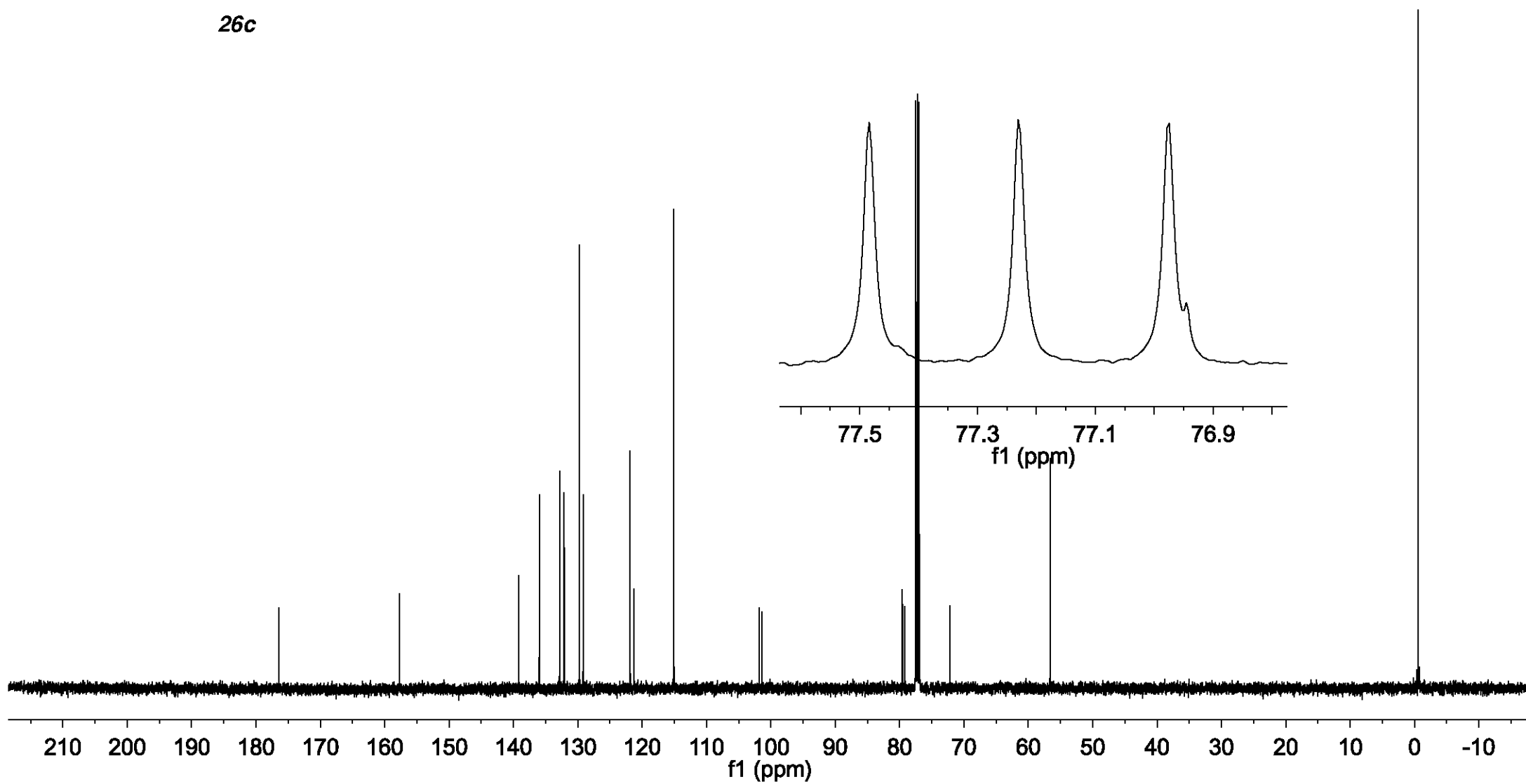
CDCl₃, 500 MHz**S4**

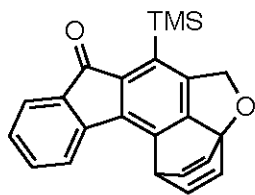
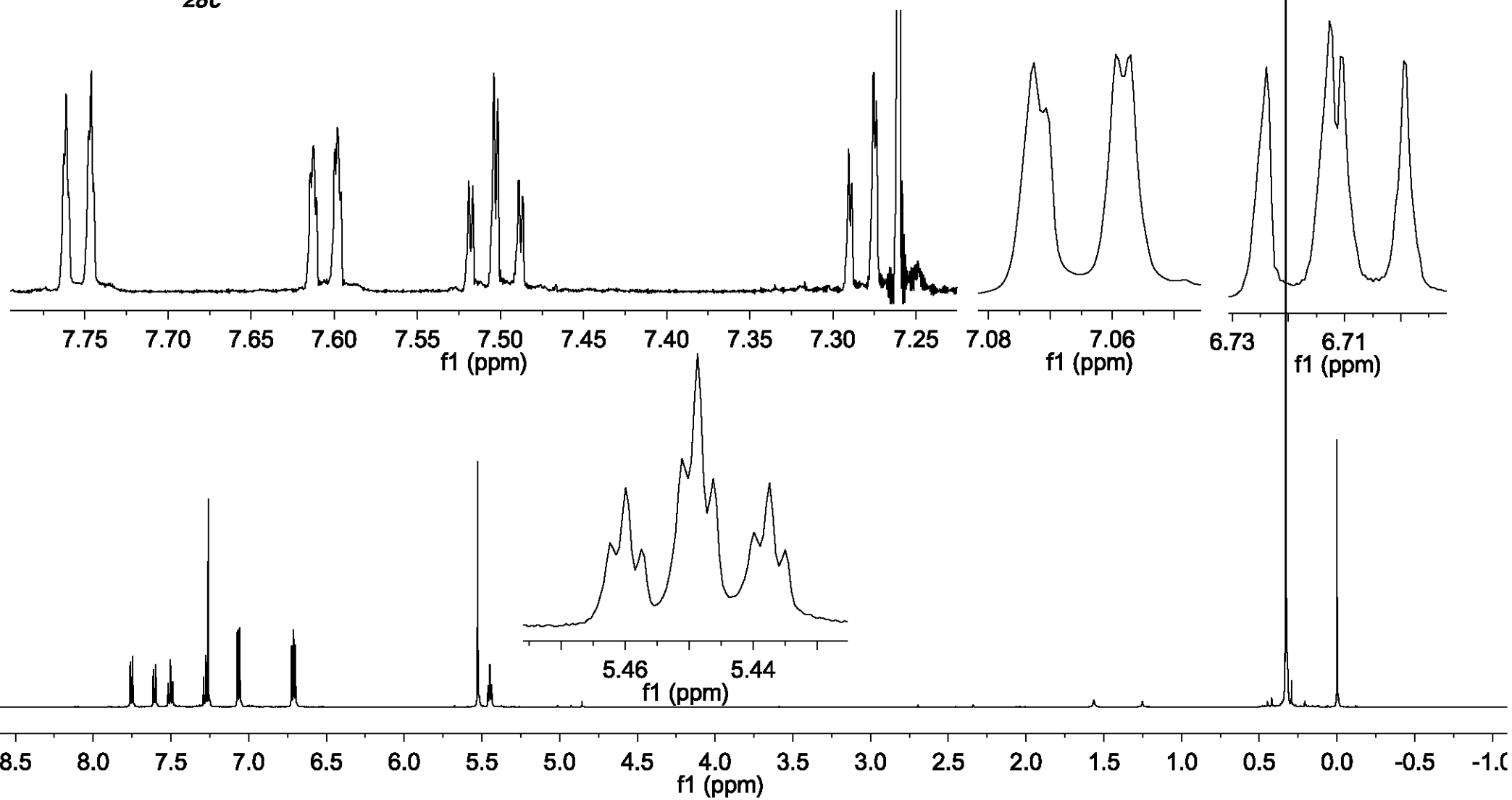
CDCl₃, 125 MHz**S4**

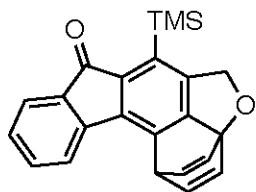
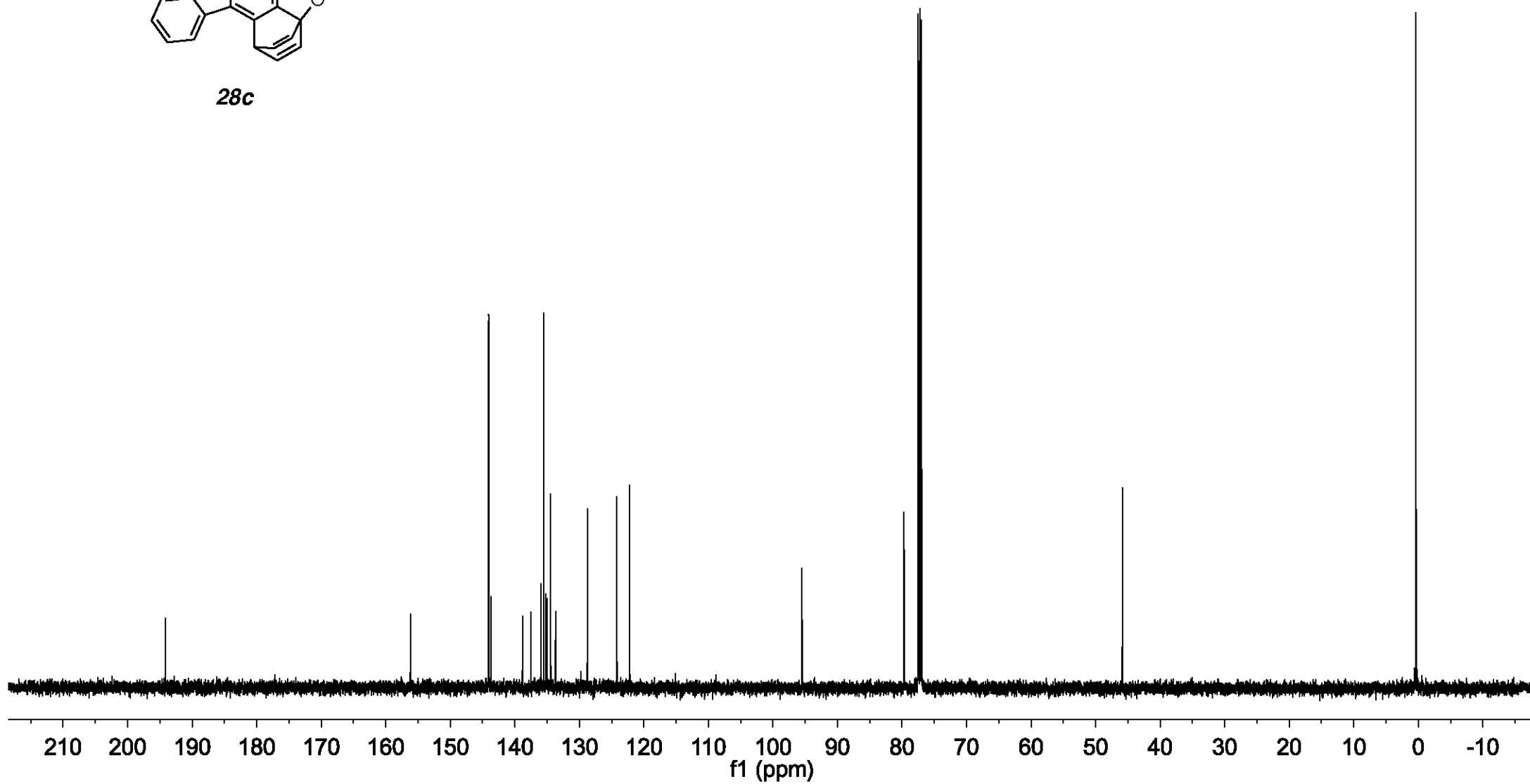


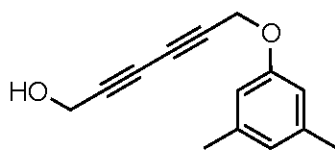
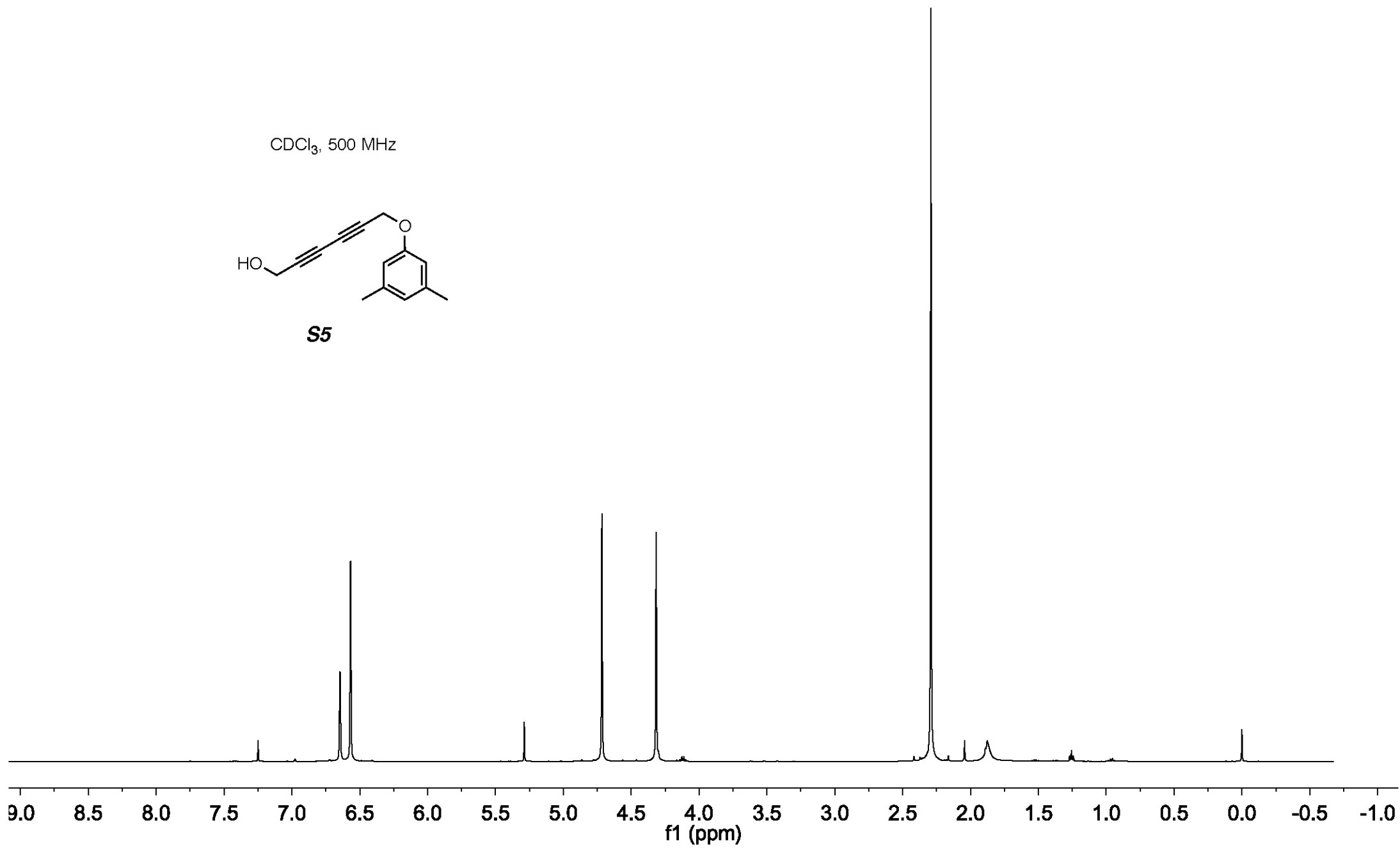
26c

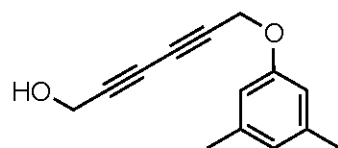
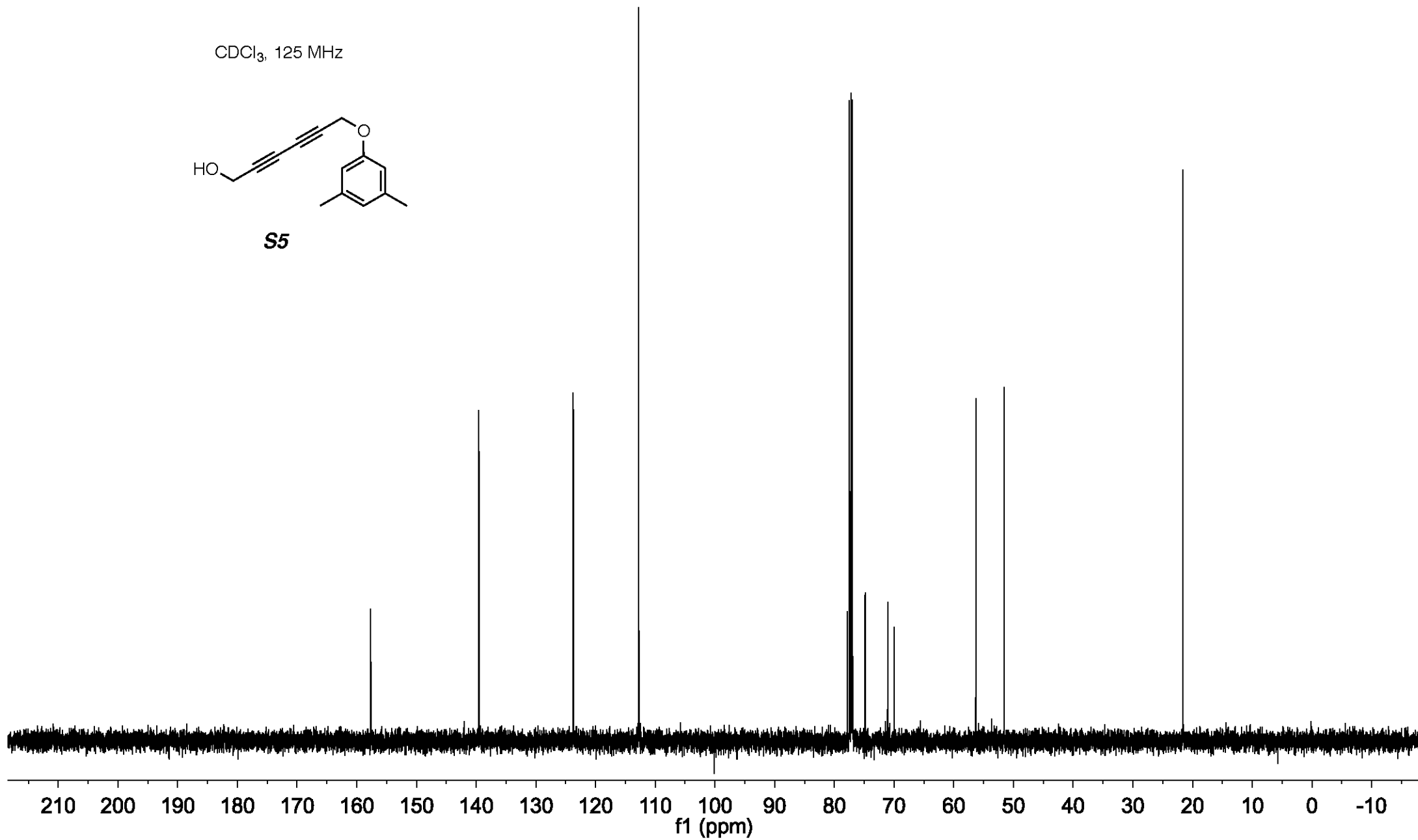


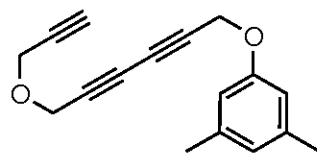
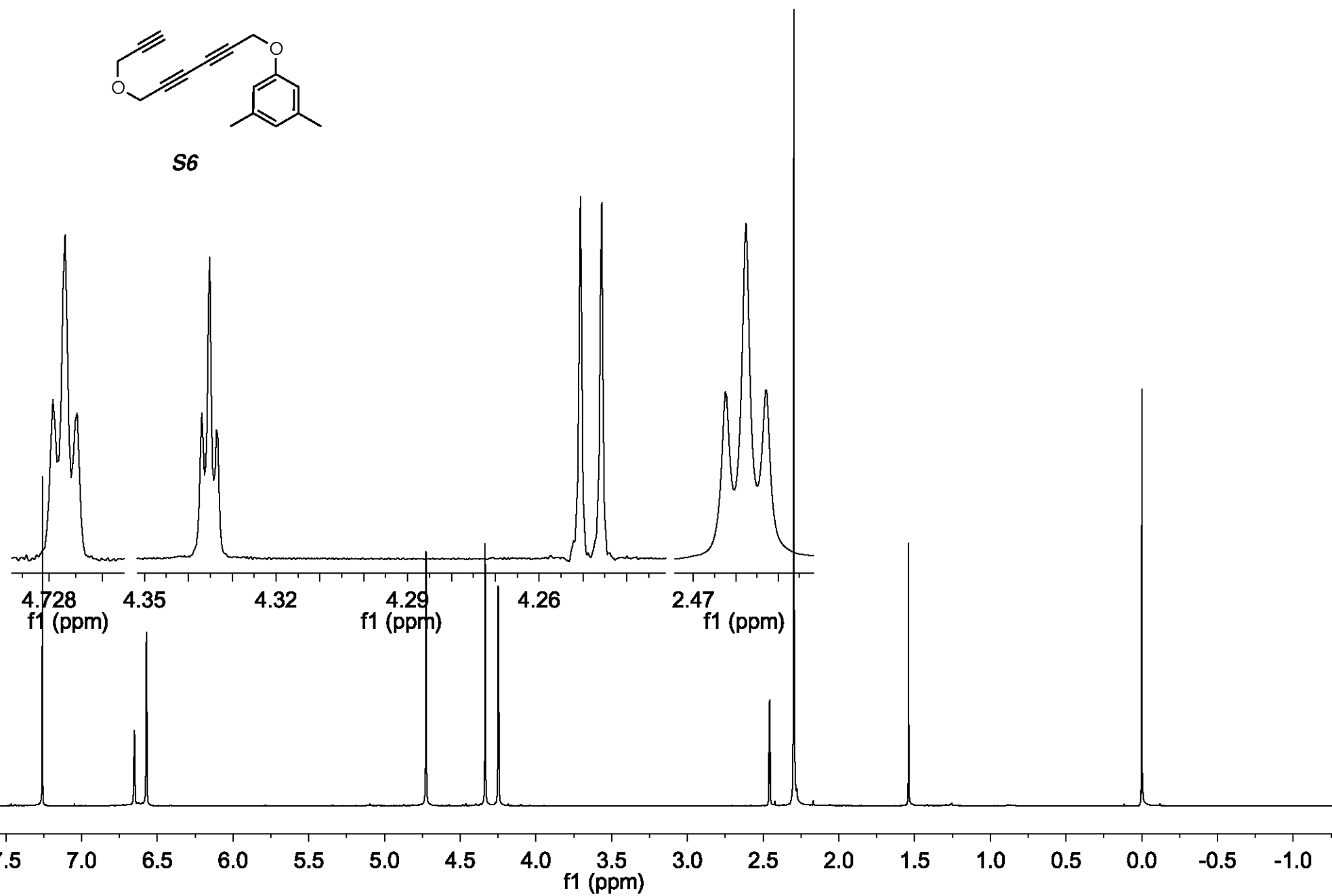
CDCl₃, 125 MHz**26c**

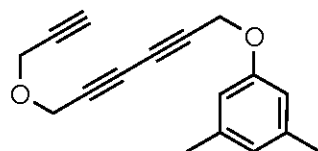
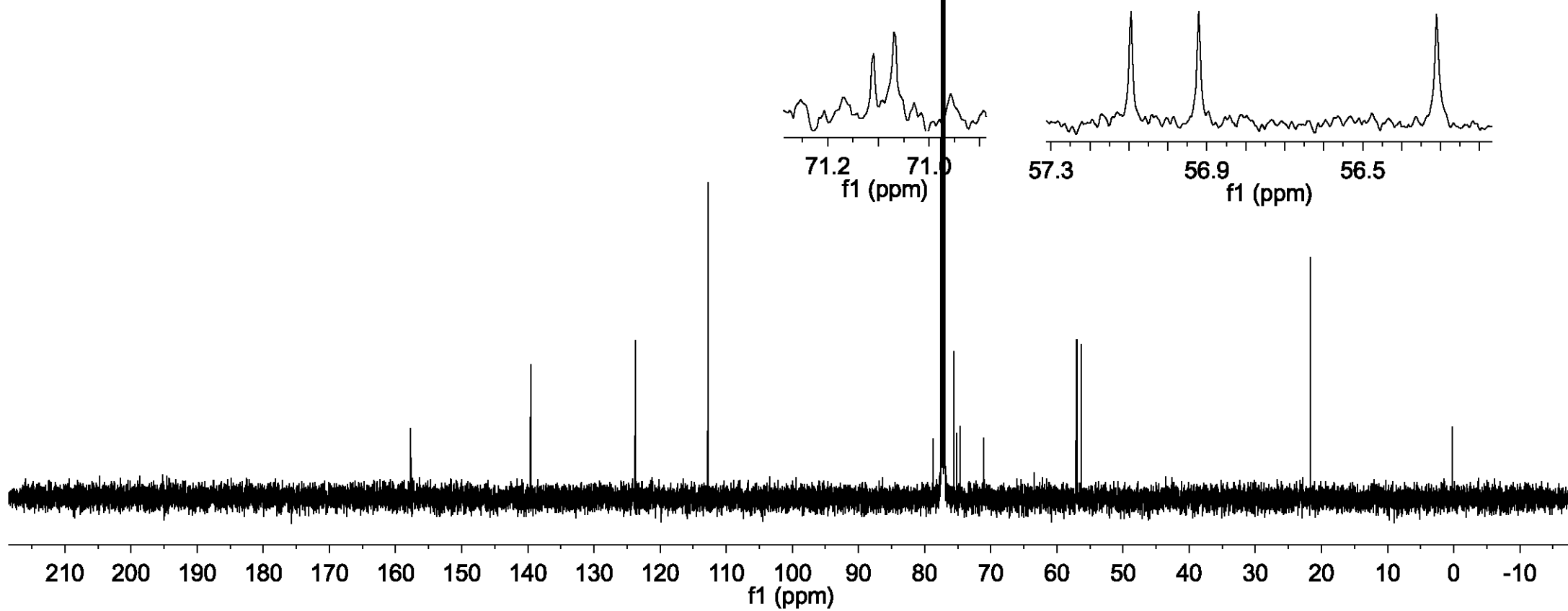
CDCl₃, 500 MHz**28c**

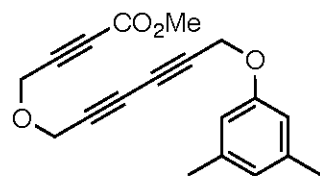
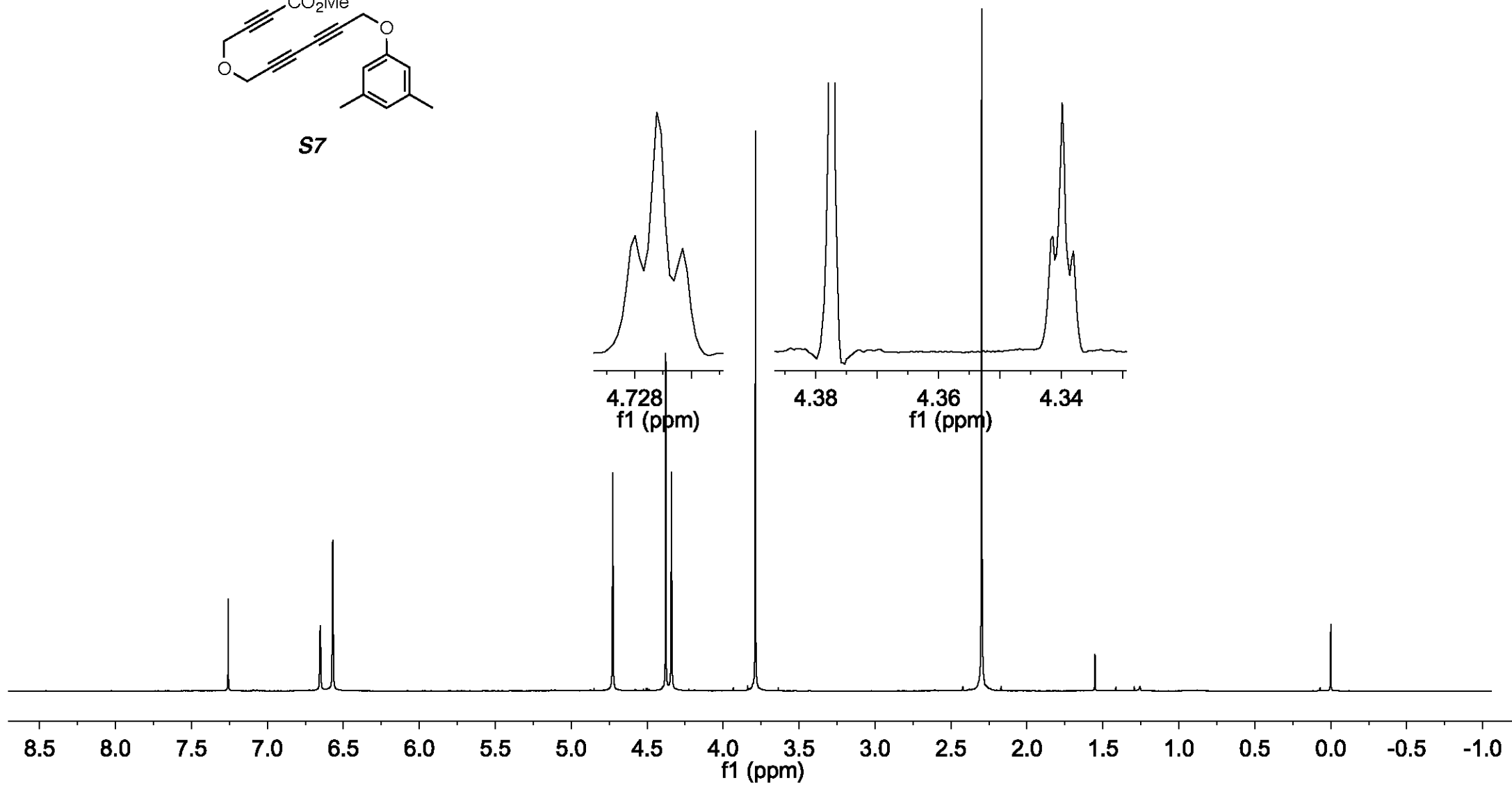
CDCl₃, 125 MHz**28c**

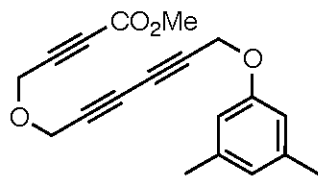
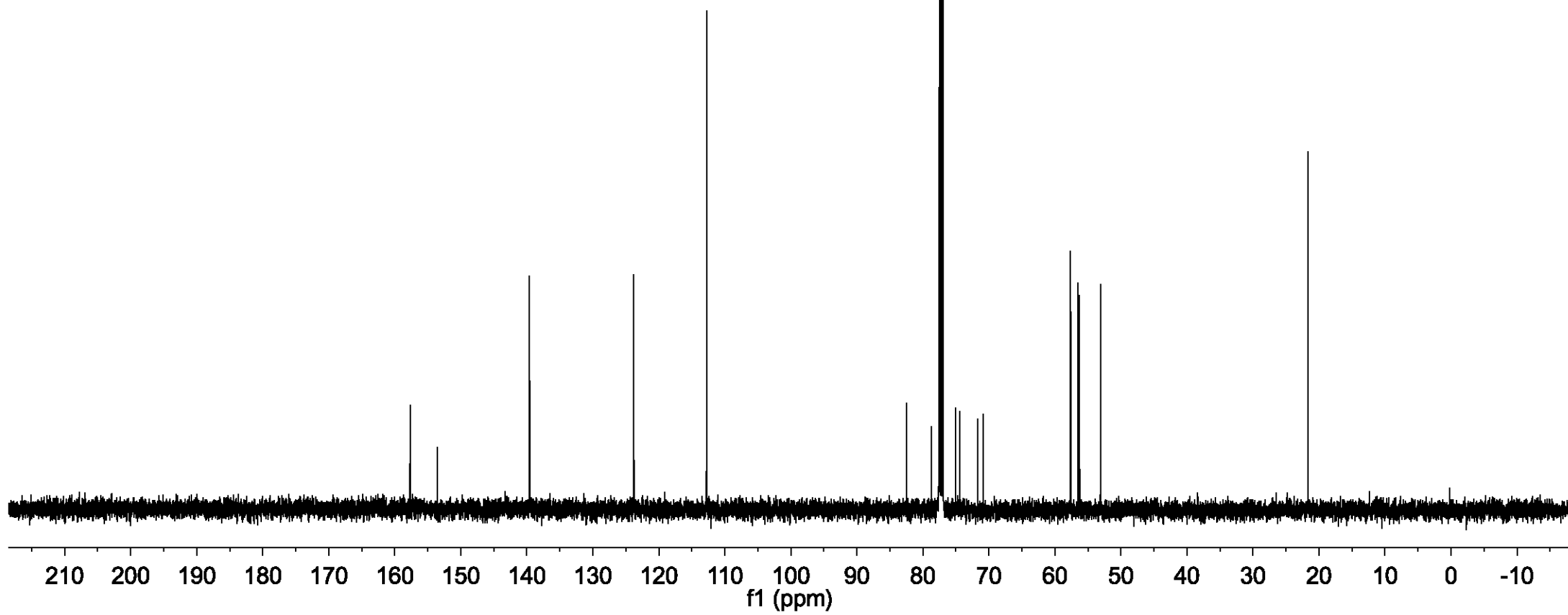
CDCl₃, 500 MHz**S5**

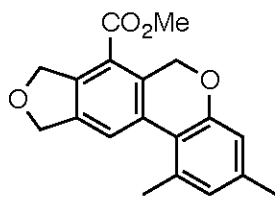
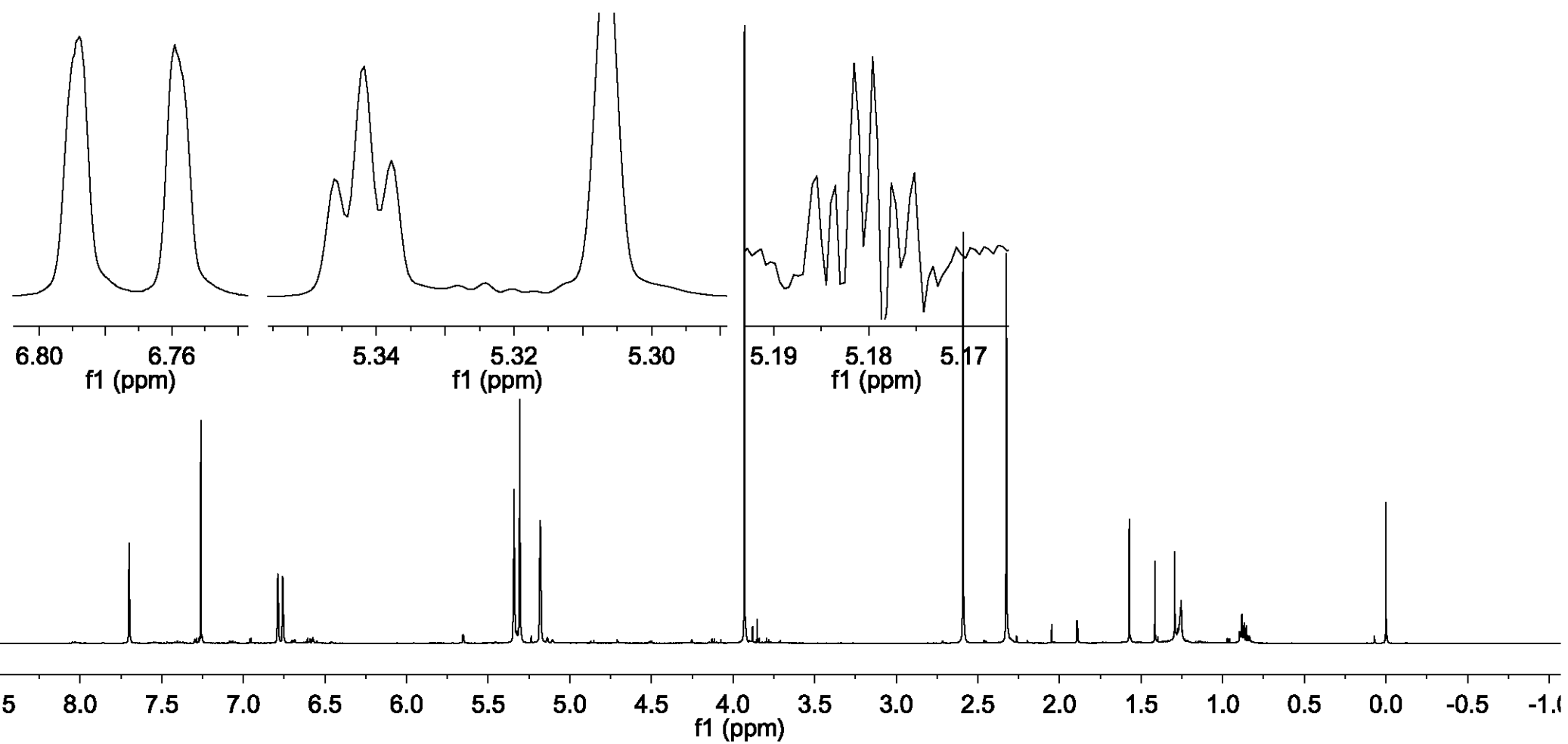
CDCl₃, 125 MHz**S5**

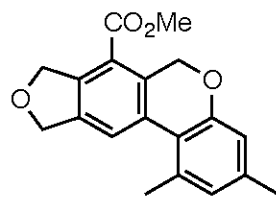
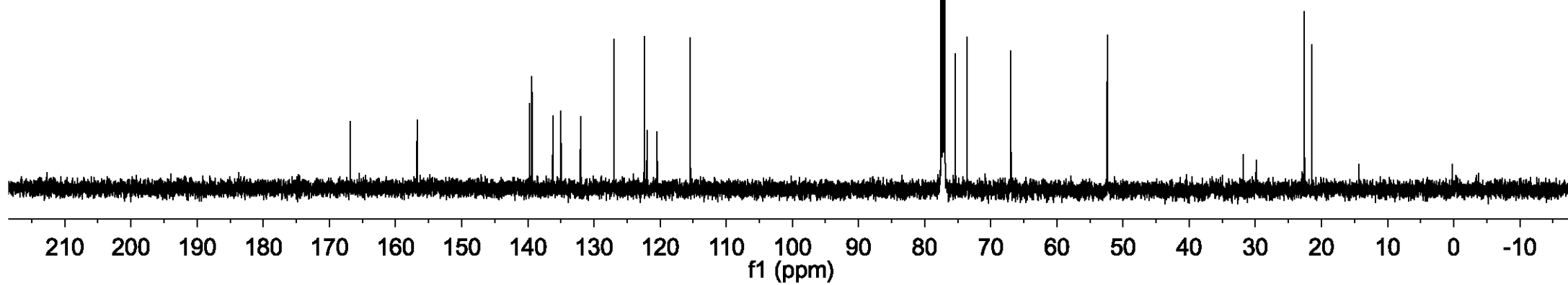
CDCl₃, 500 MHz**S6**

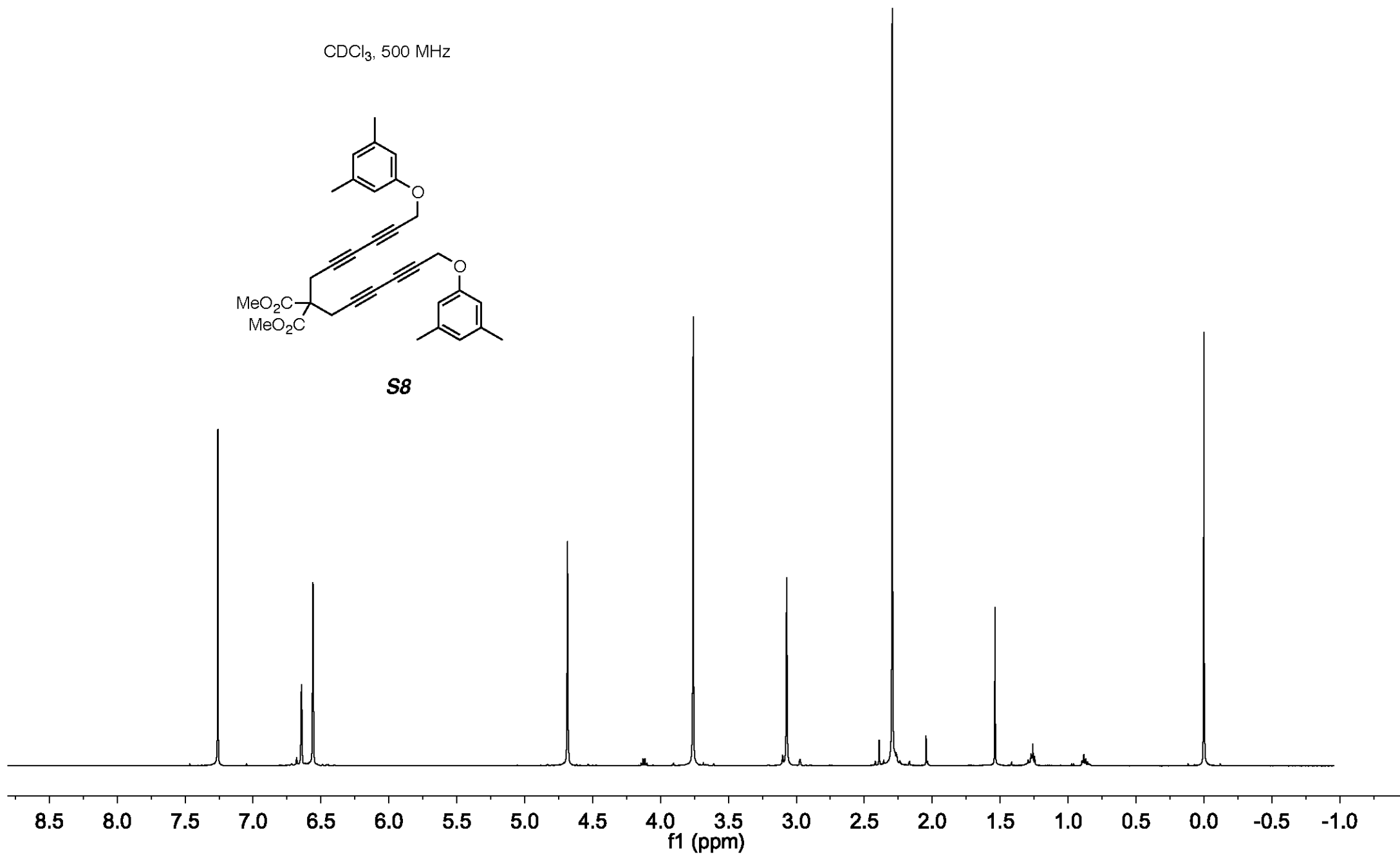
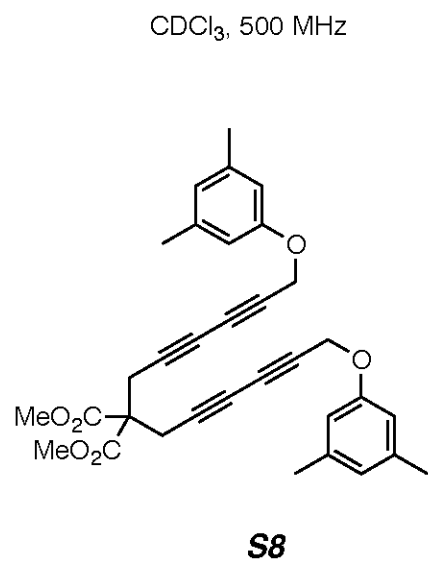
CDCl₃, 125 MHz**S6**

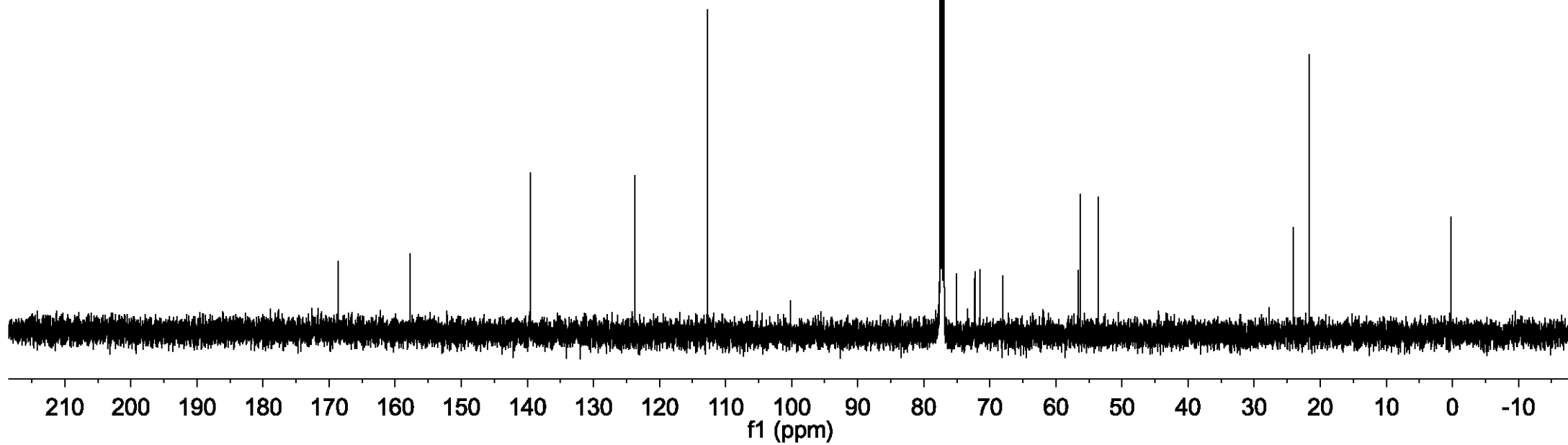
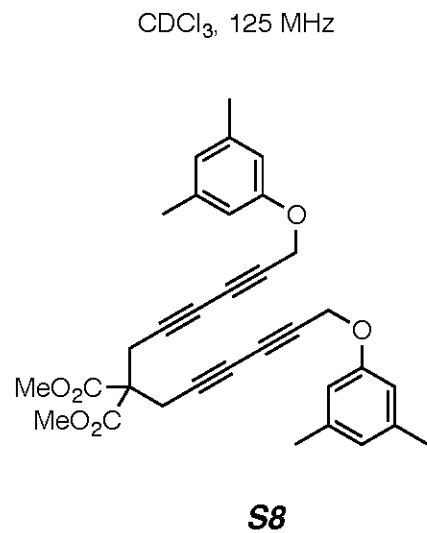
CDCl₃, 500 MHz**S7**

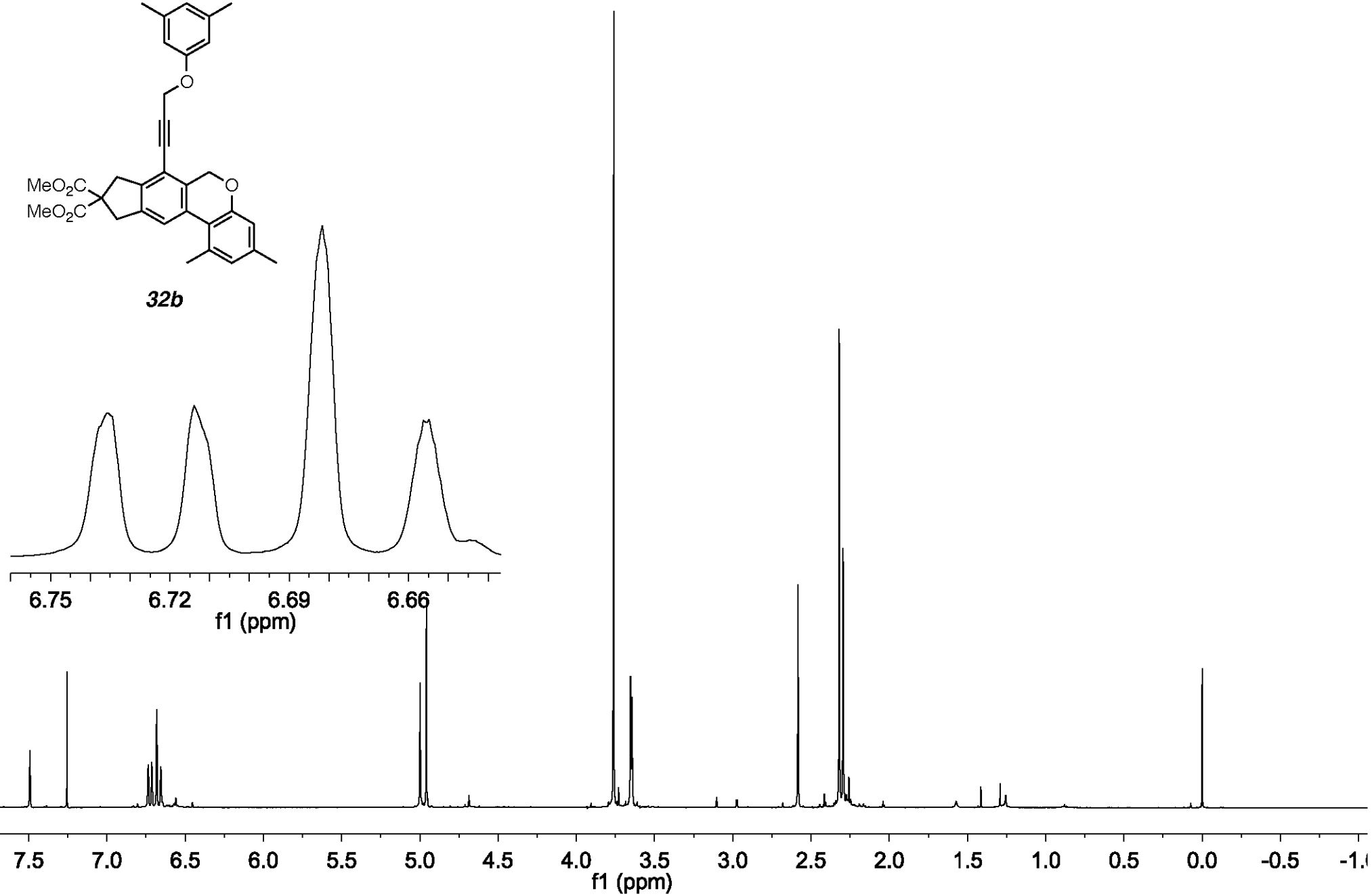
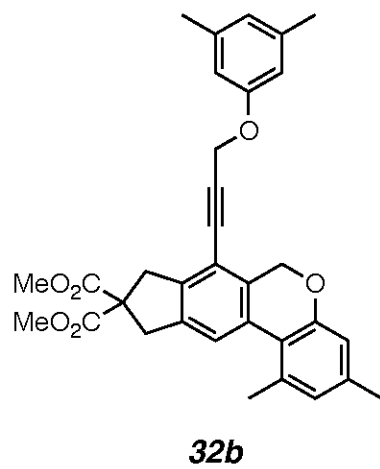
CDCl₃, 125 MHz**S7**

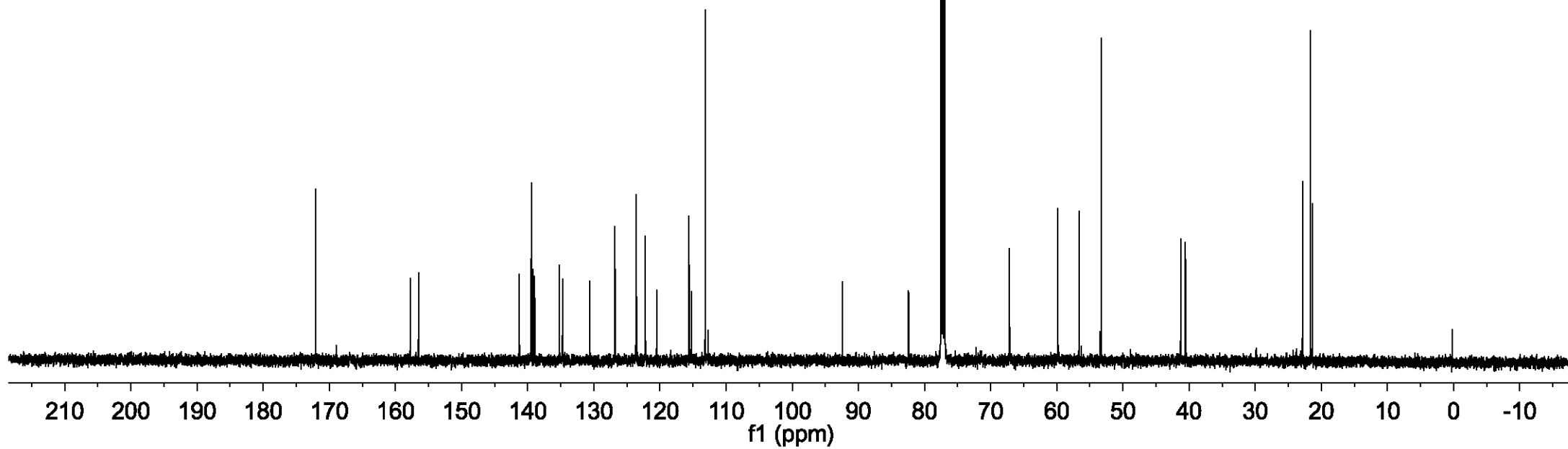
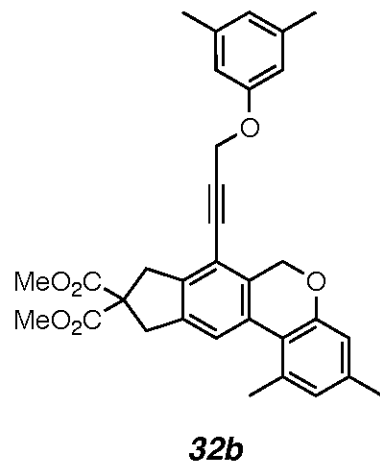
CDCl₃, 500 MHz**32a**

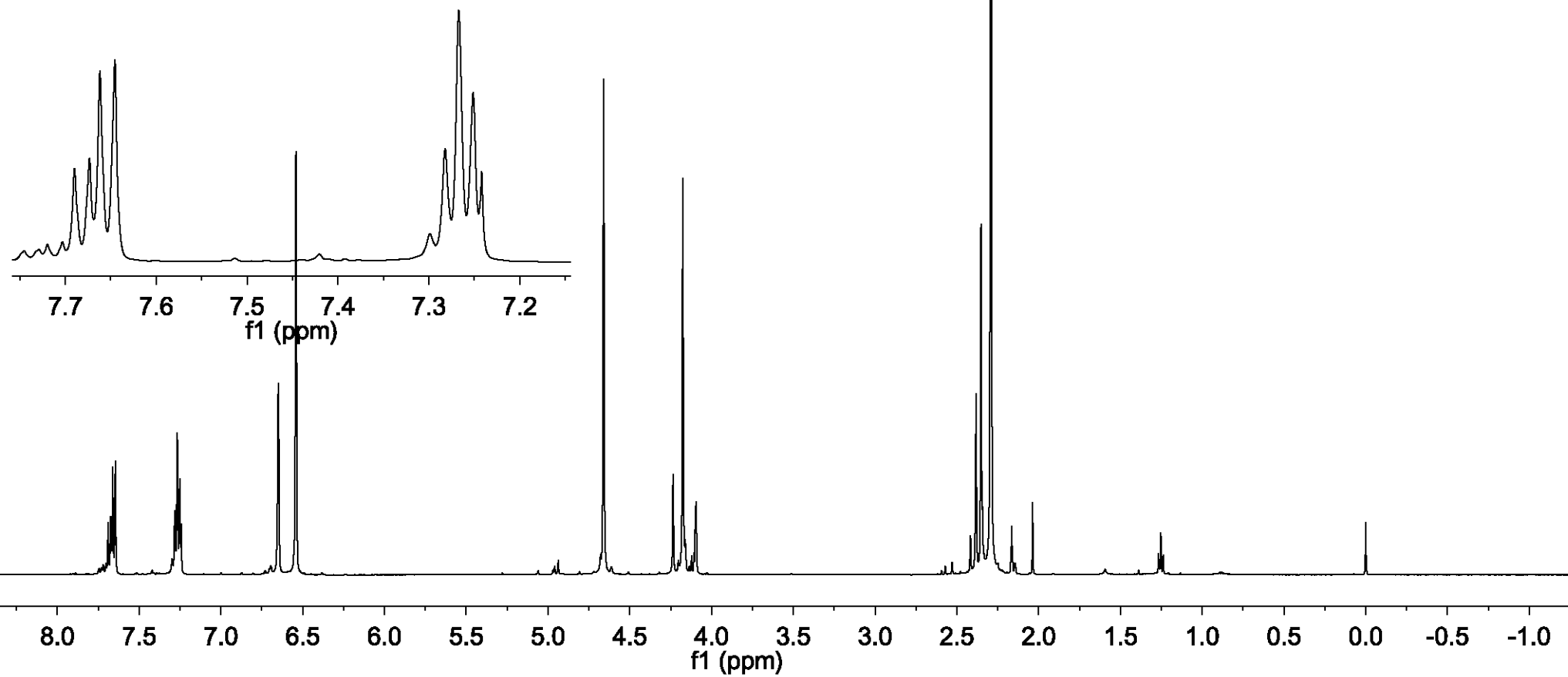
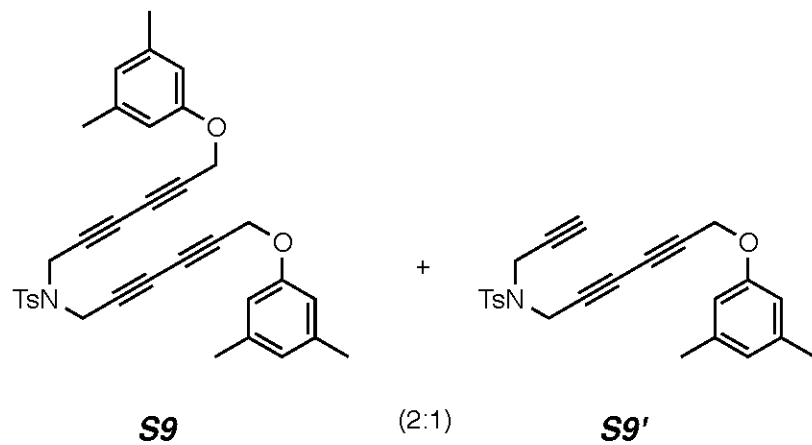
CDCl₃, 125 MHz**32a**

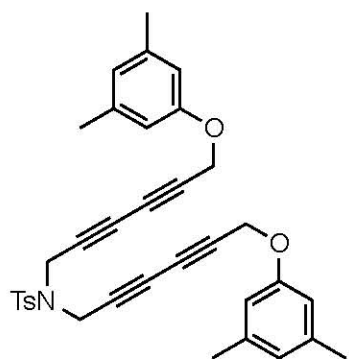




CDCl₃, 500 MHz

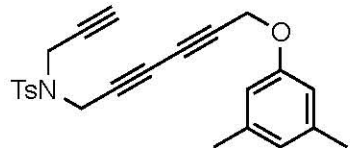
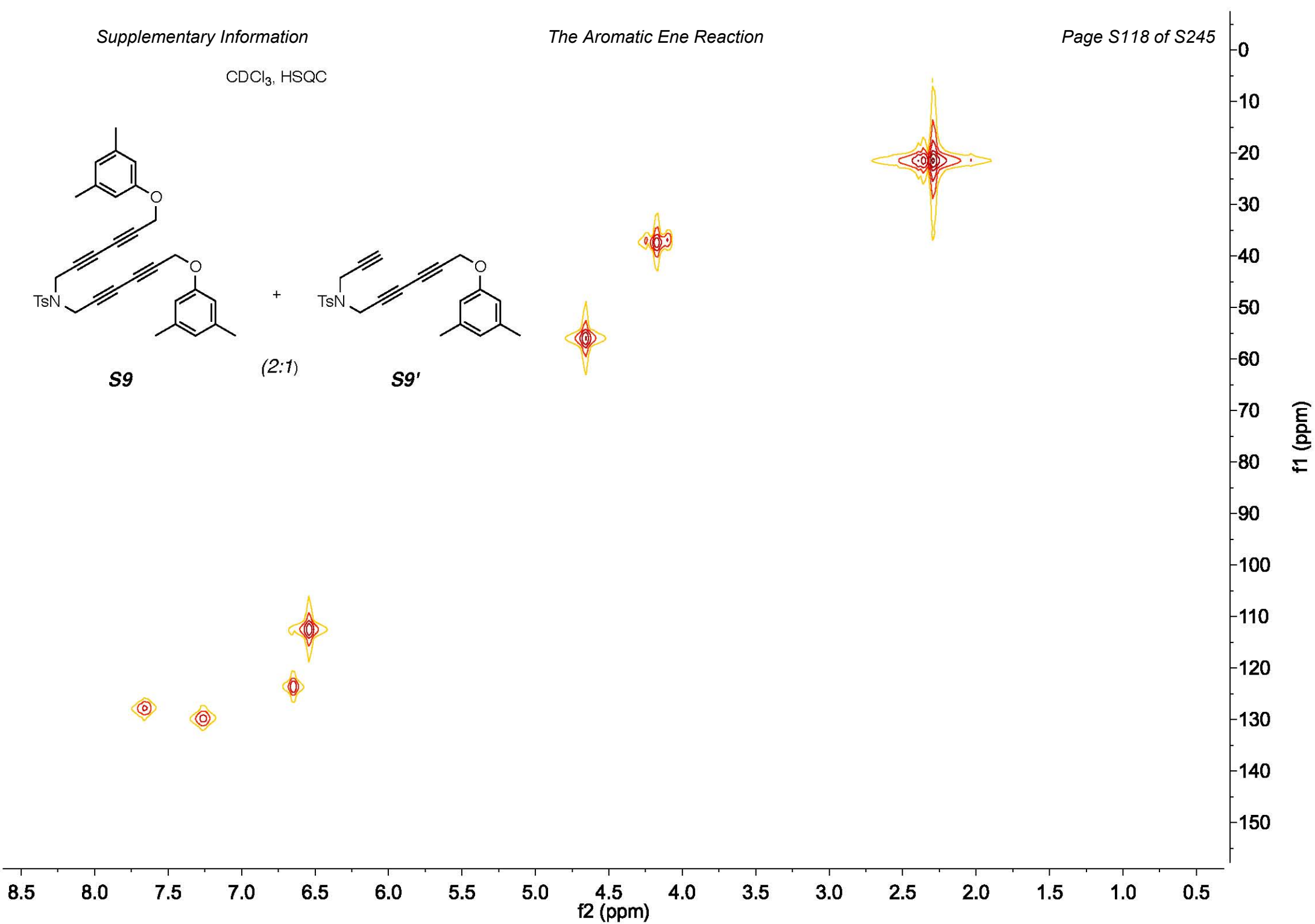
CDCl₃, 125 MHz

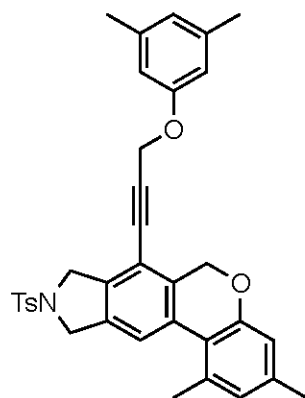
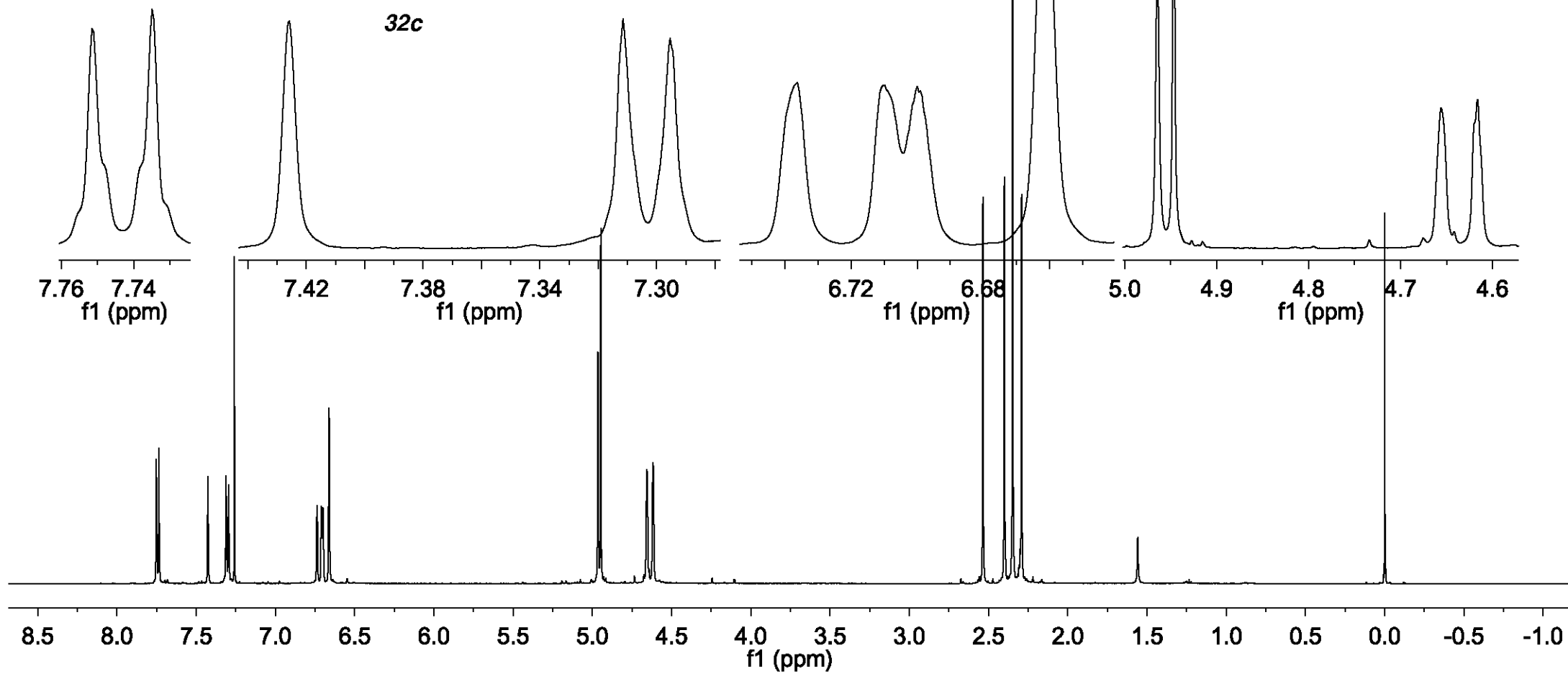
CDCl₃, 500 MHz

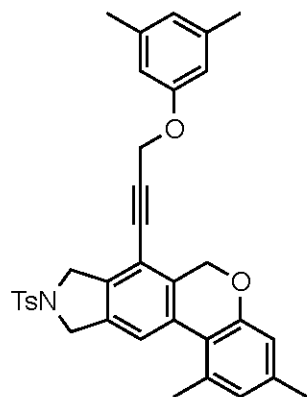
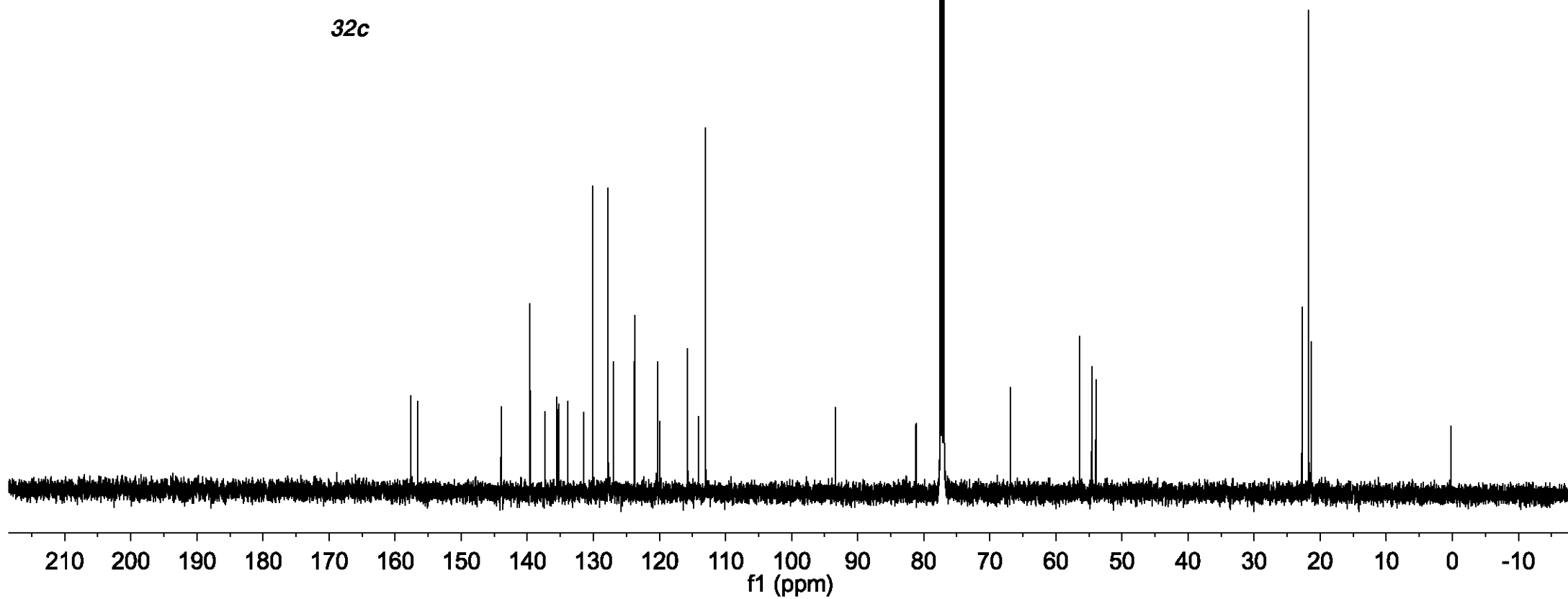
CDCl₃, HSQC**S9**

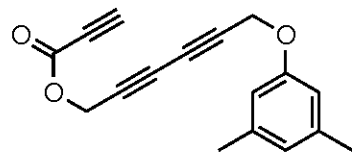
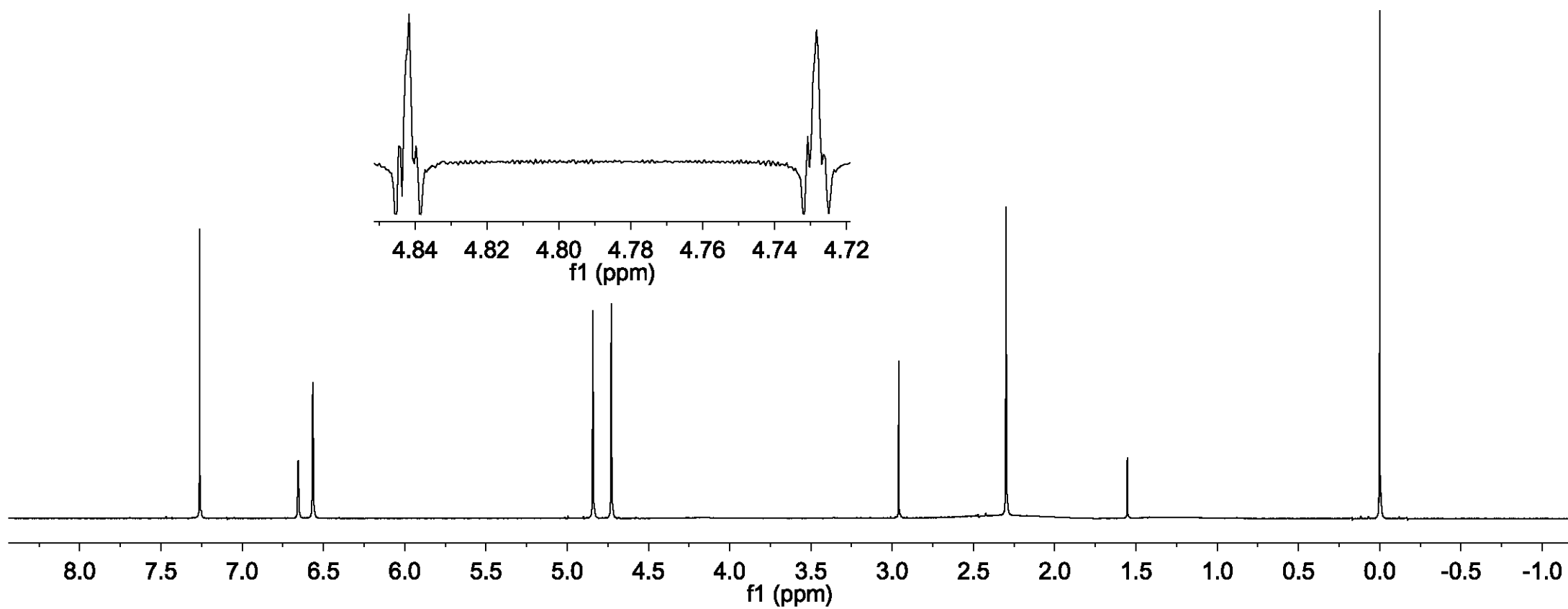
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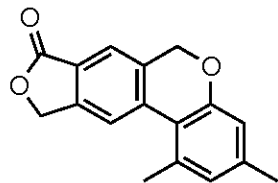
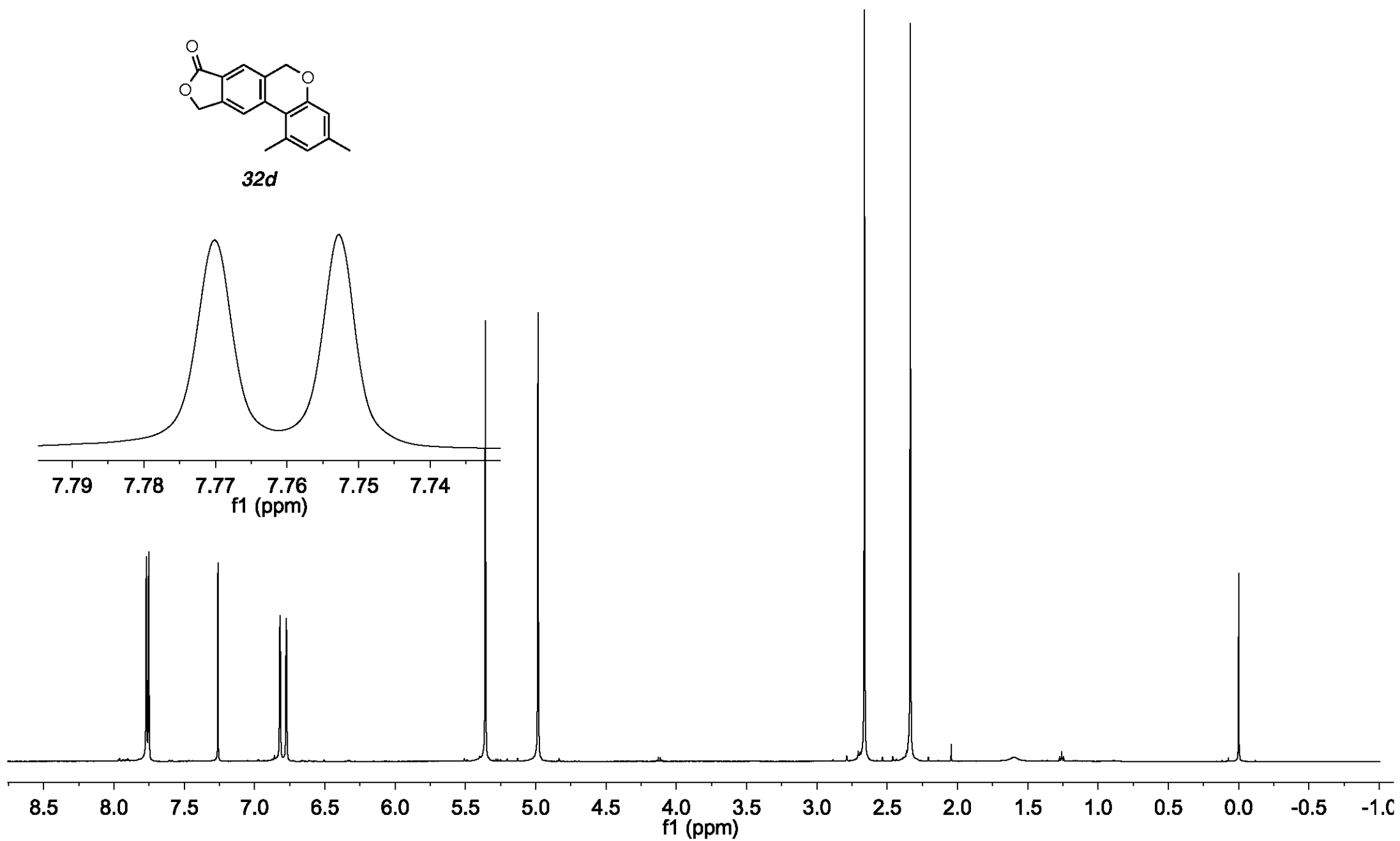
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**S9'**

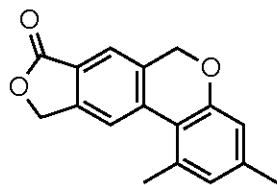
CDCl₃, 500 MHz**32c**

CDCl₃, 125 MHz**32c**

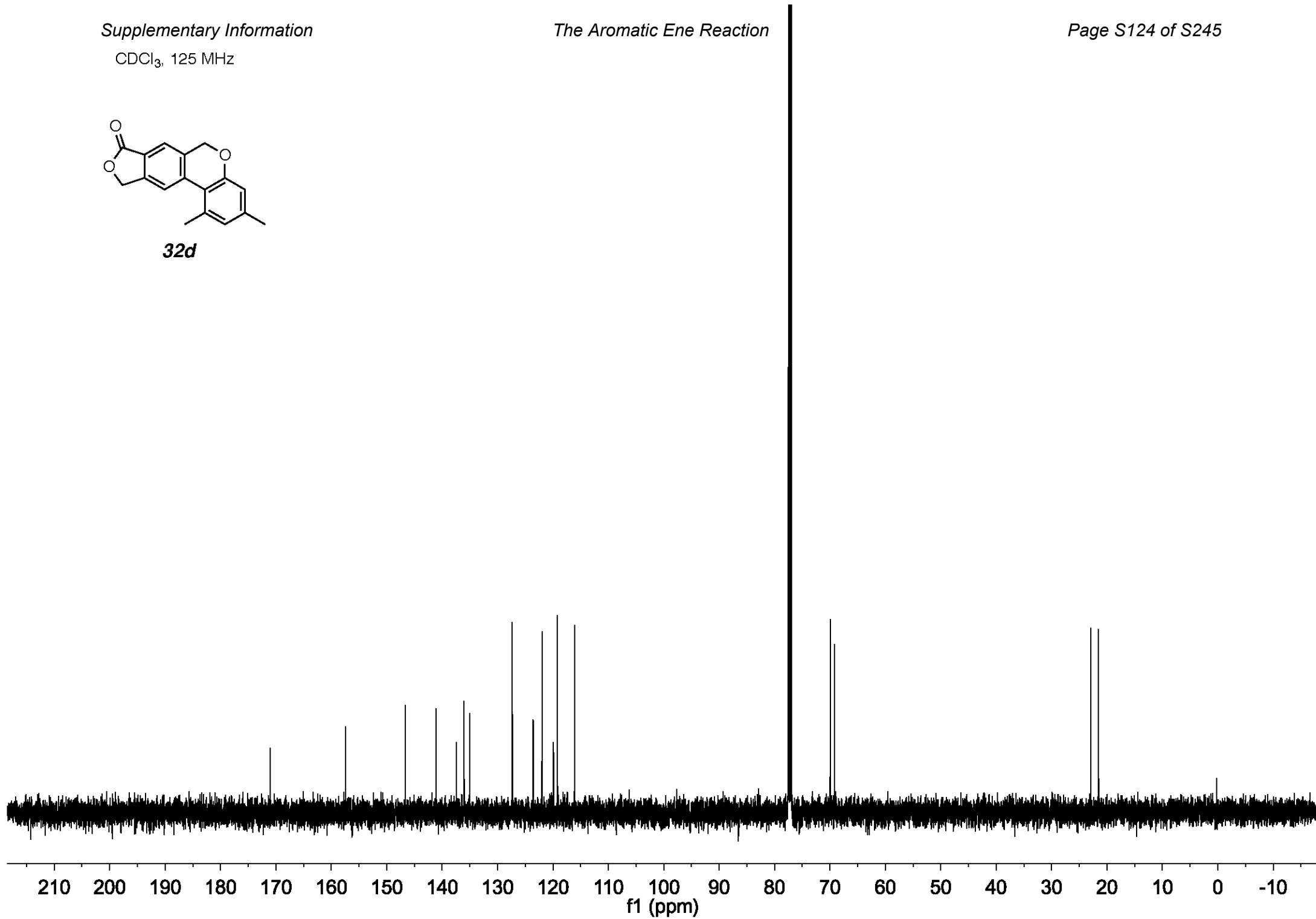
CDCl₃, 500 MHz**S10**

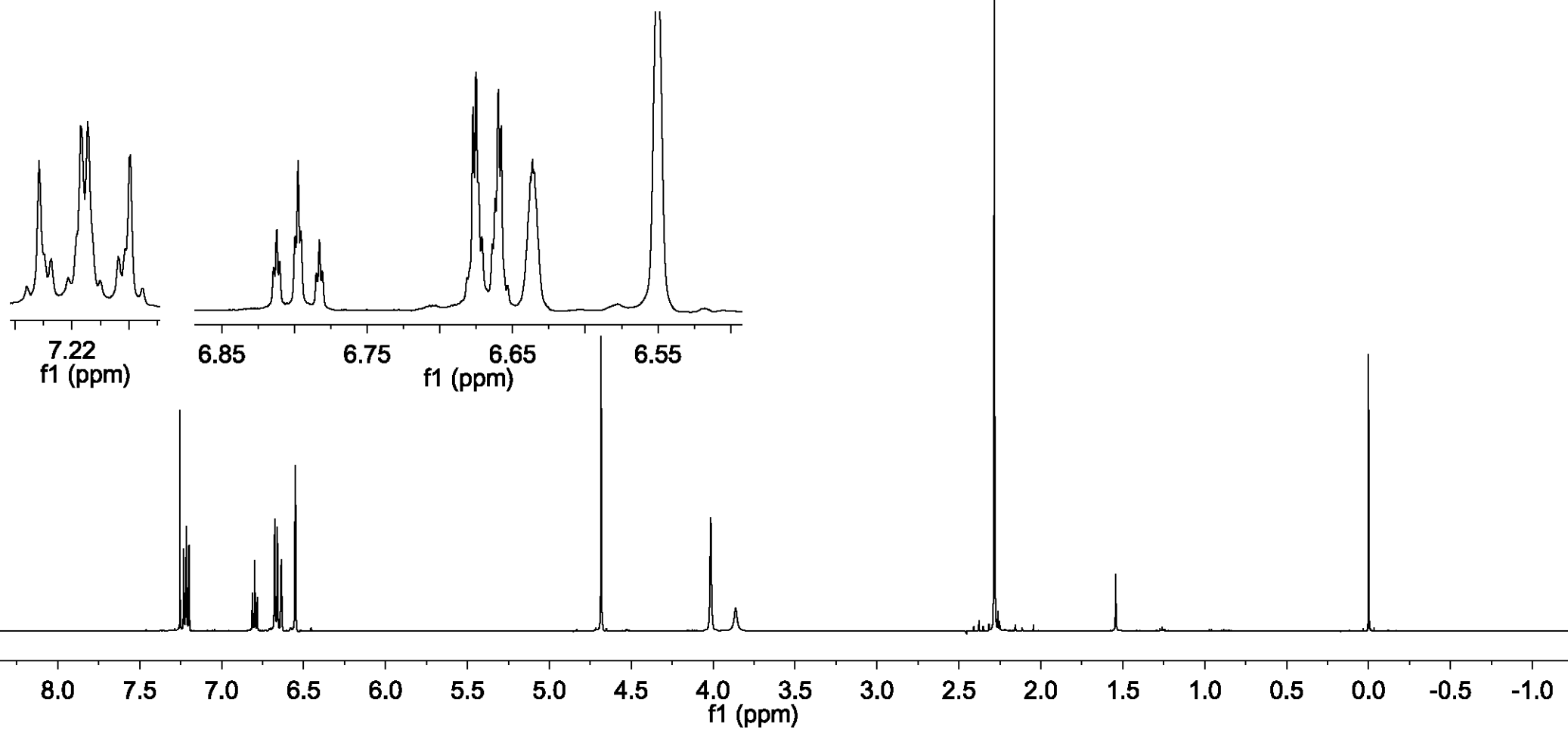
CDCl₃, 500 MHz**32d**

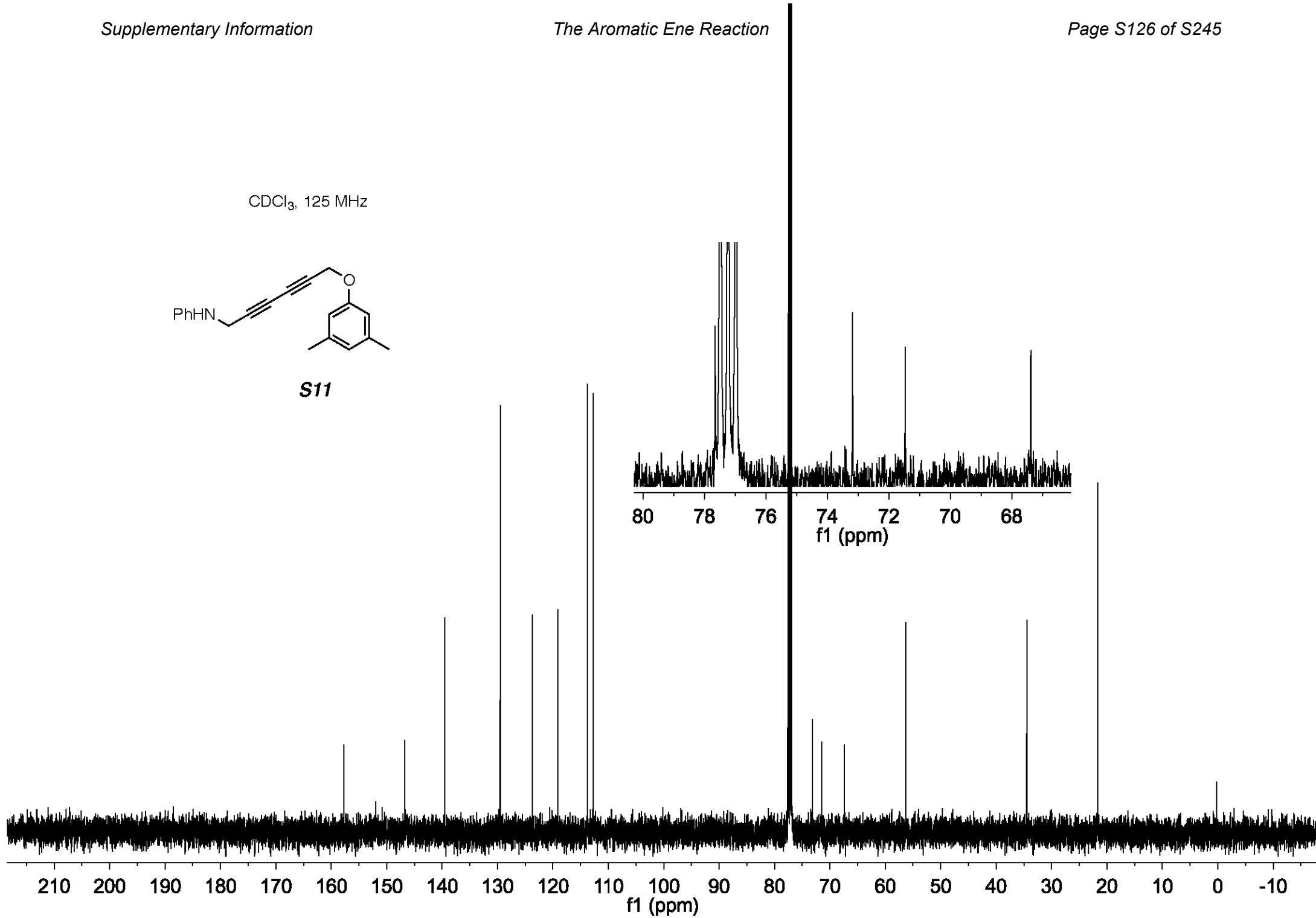
CDCl₃, 125 MHz

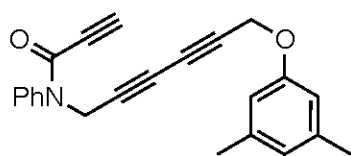
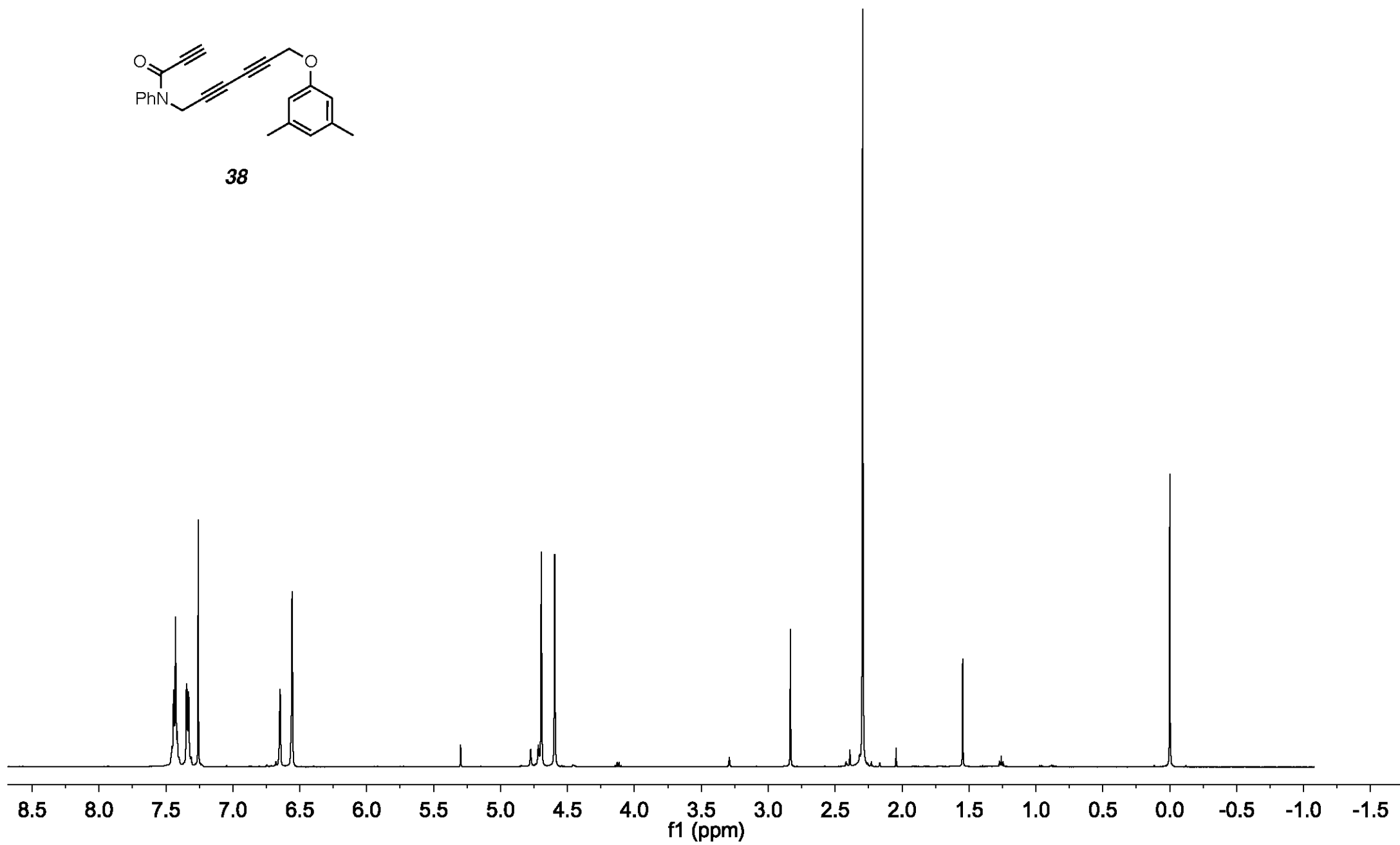


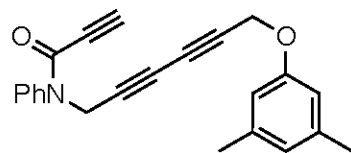
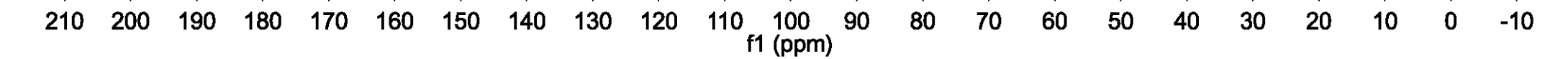
32d

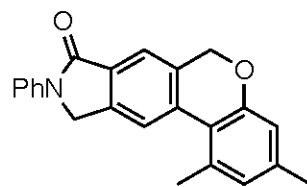
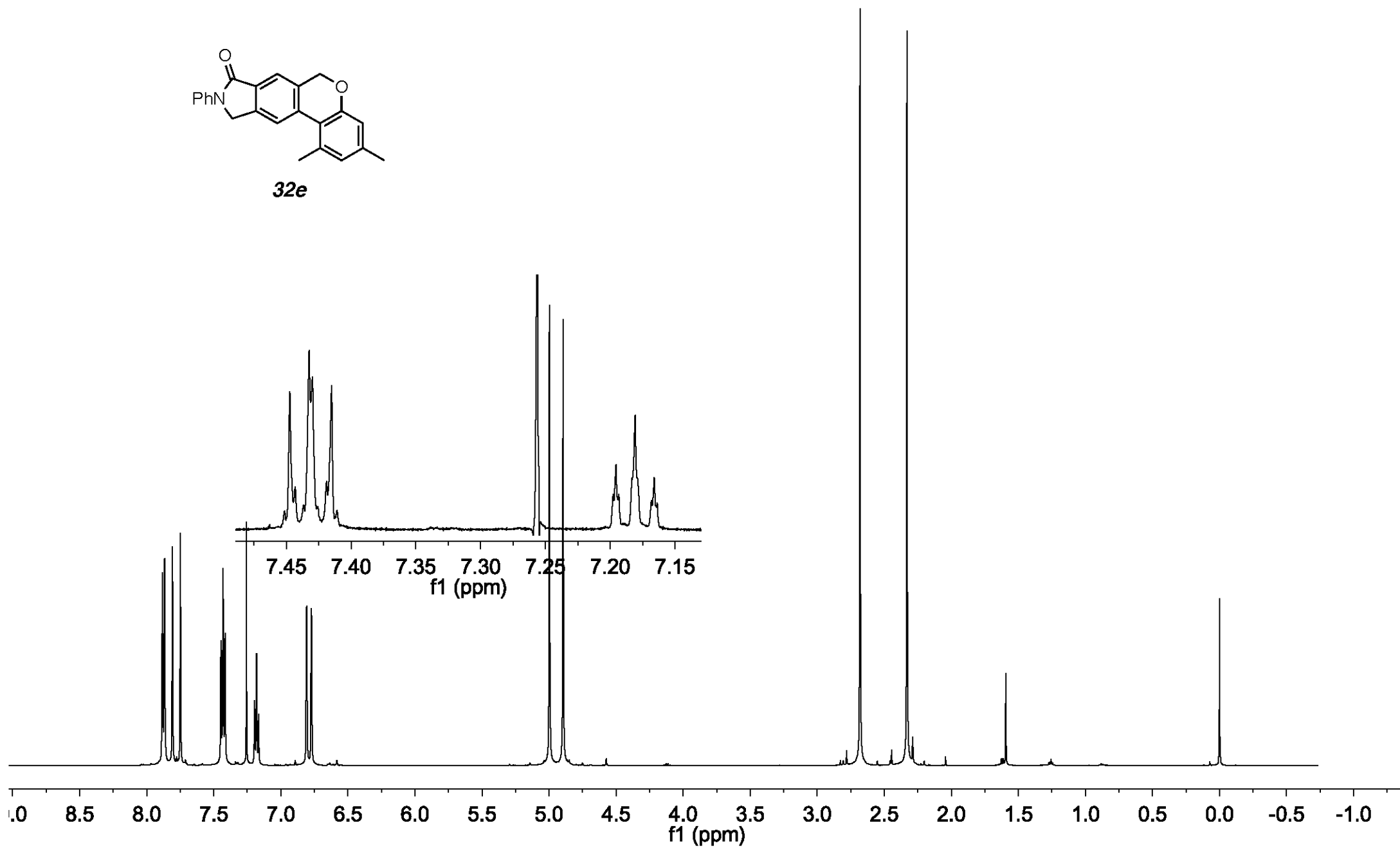


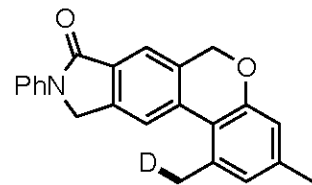
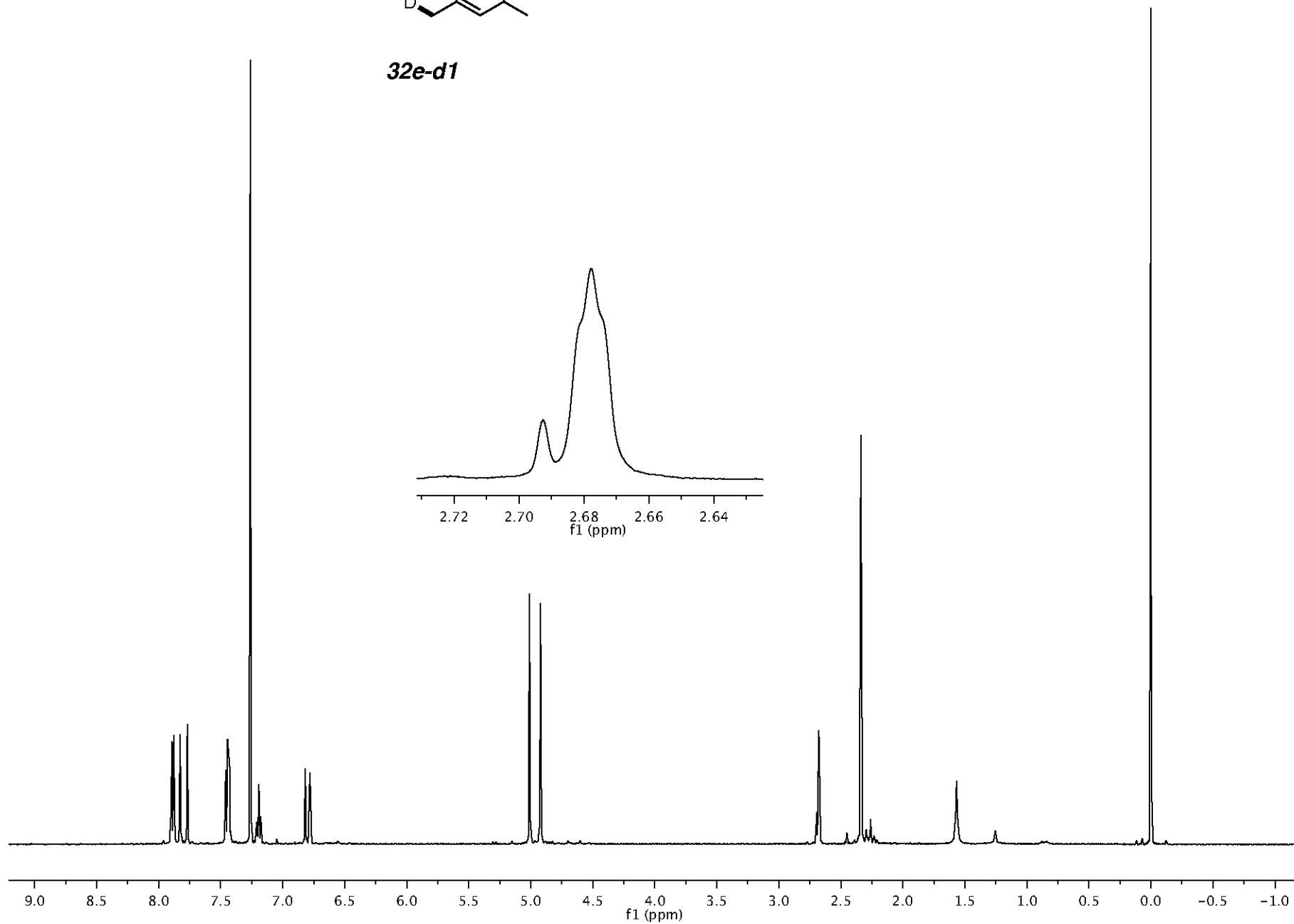
CDCl₃, 500 MHz**S11**

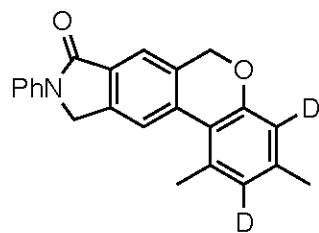
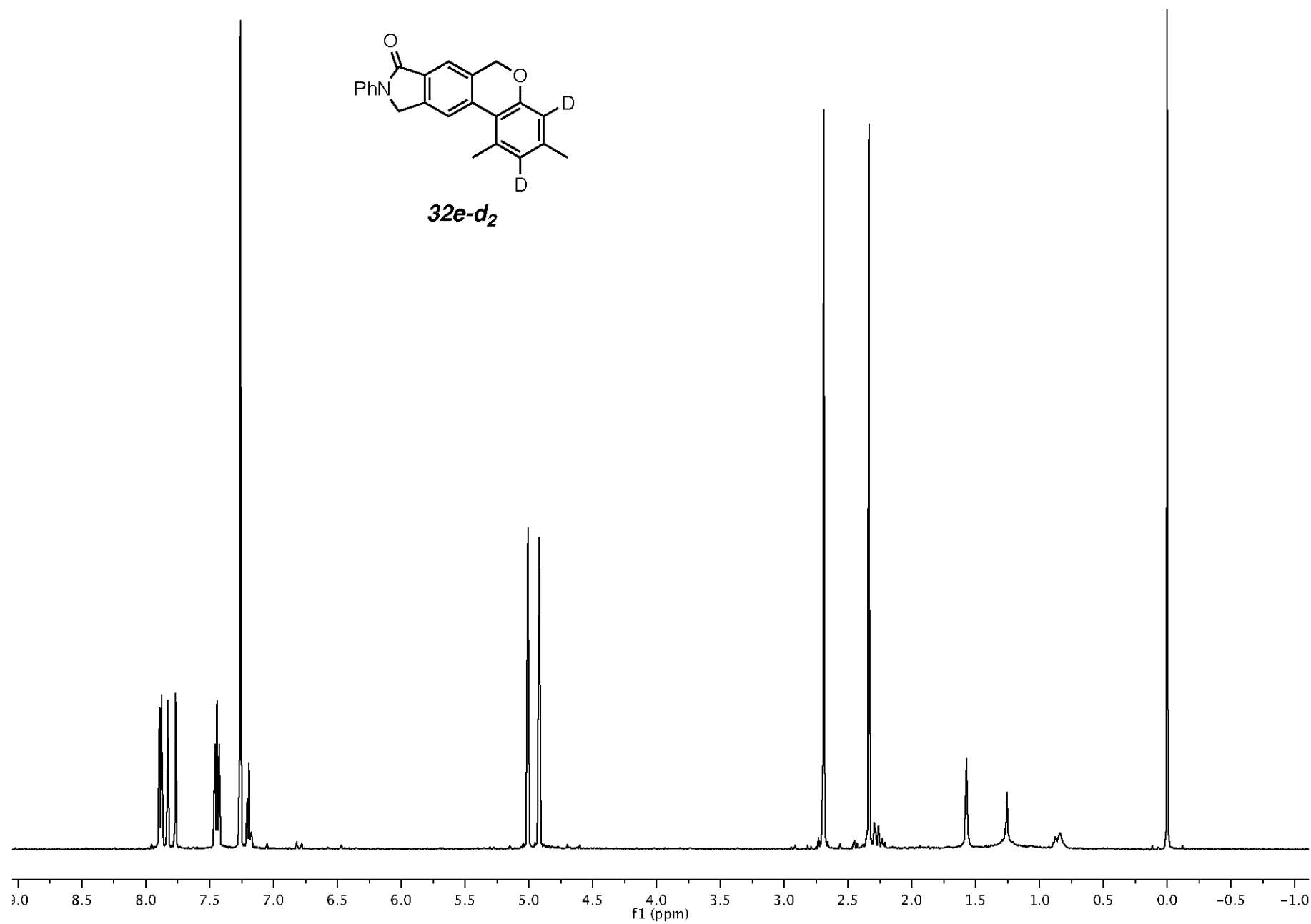
CDCl₃, 125 MHz**S11**

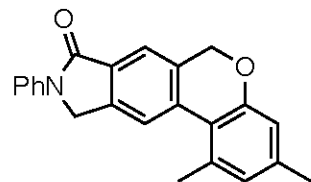
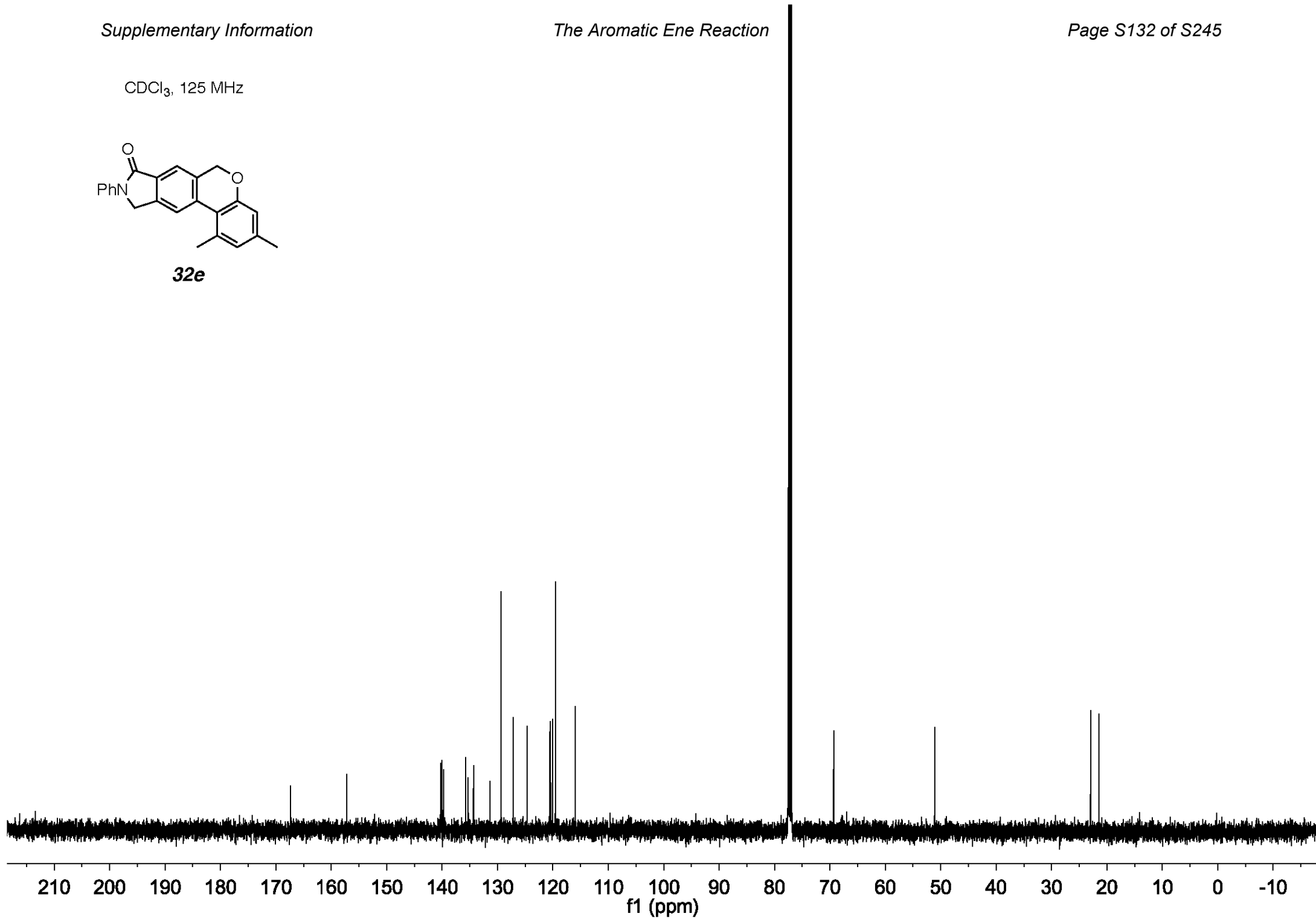
CDCl₃, 500 MHz**38**

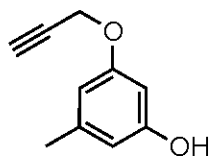
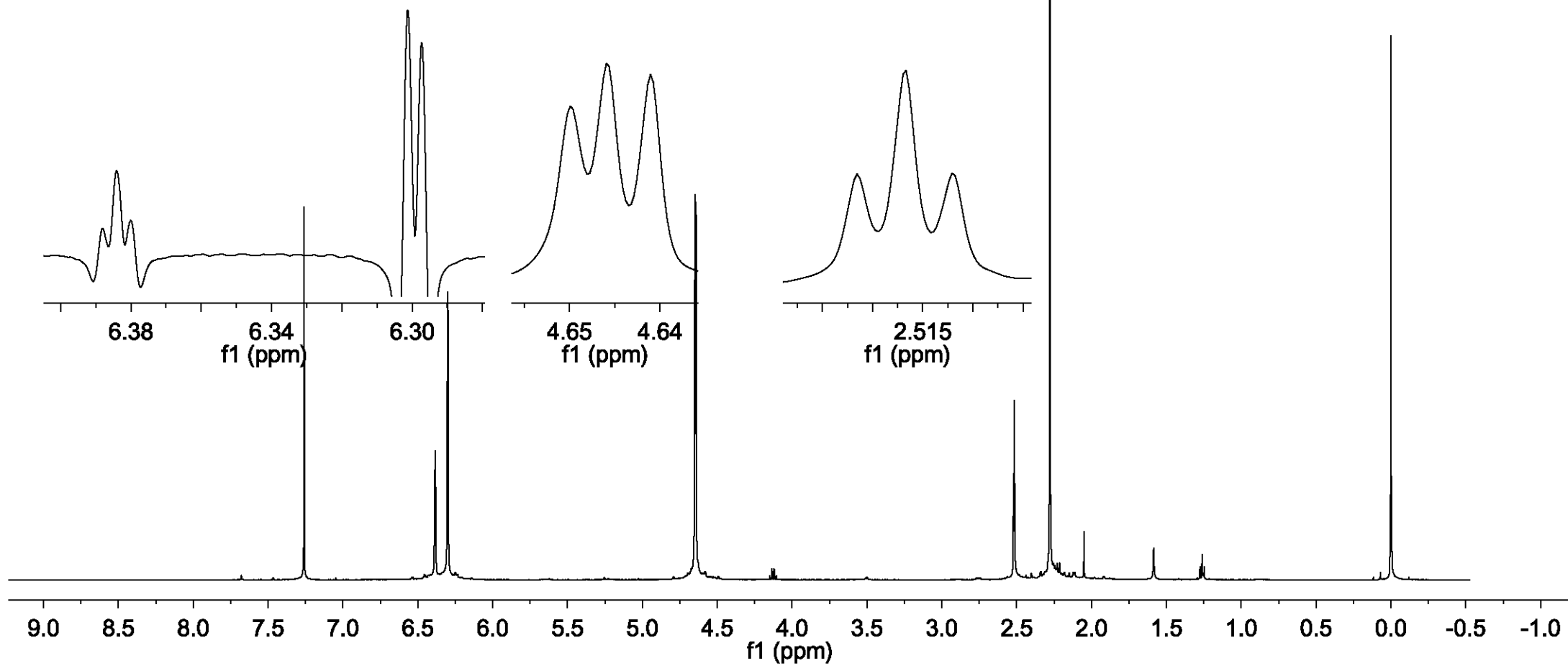
CDCl₃, 125 MHz**38**

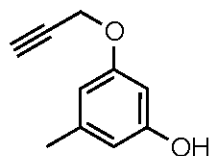
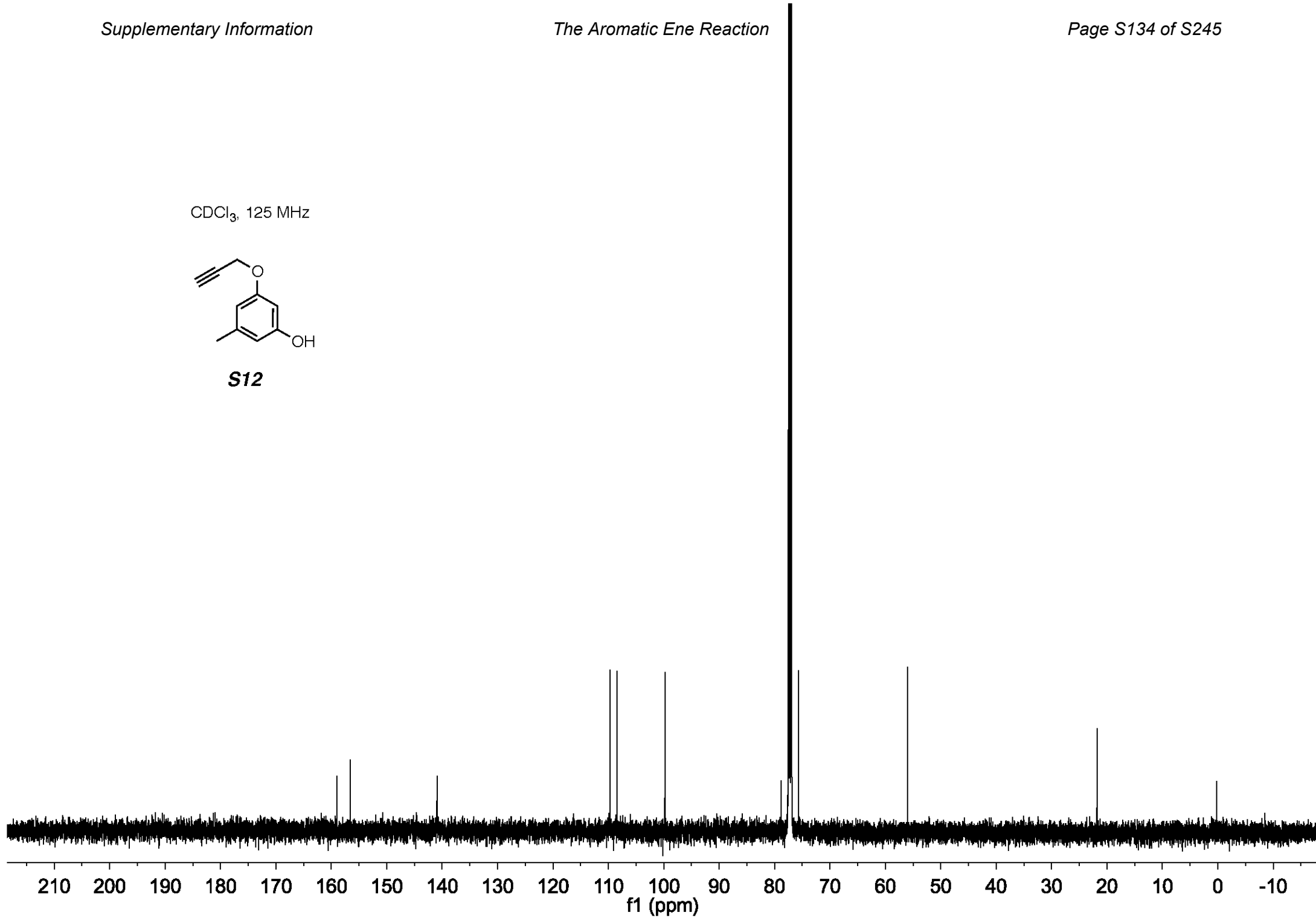
CDCl₃, 500 MHz**32e**

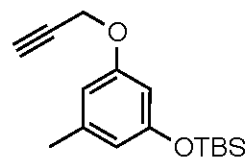
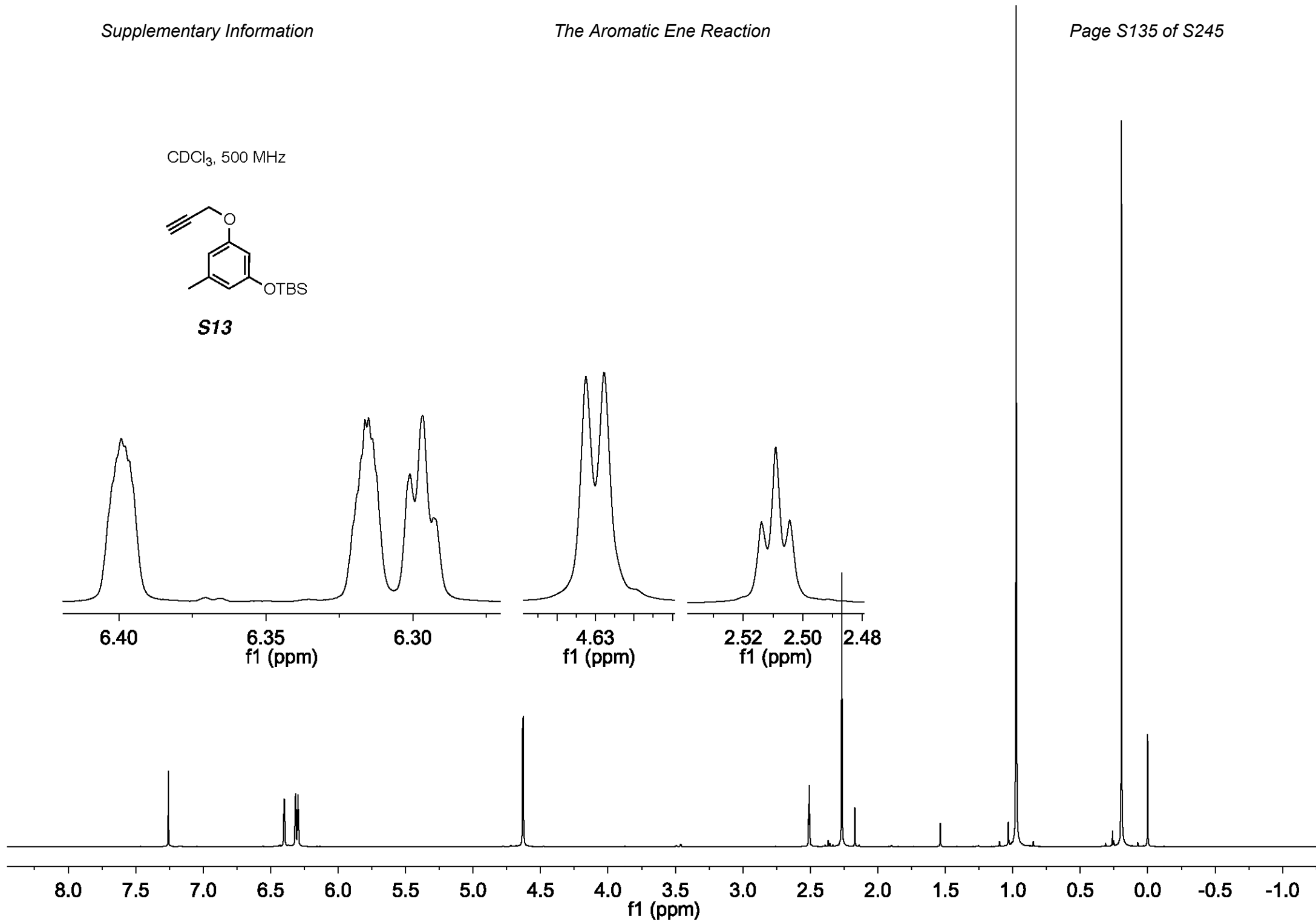
**32e-d1**

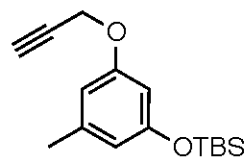
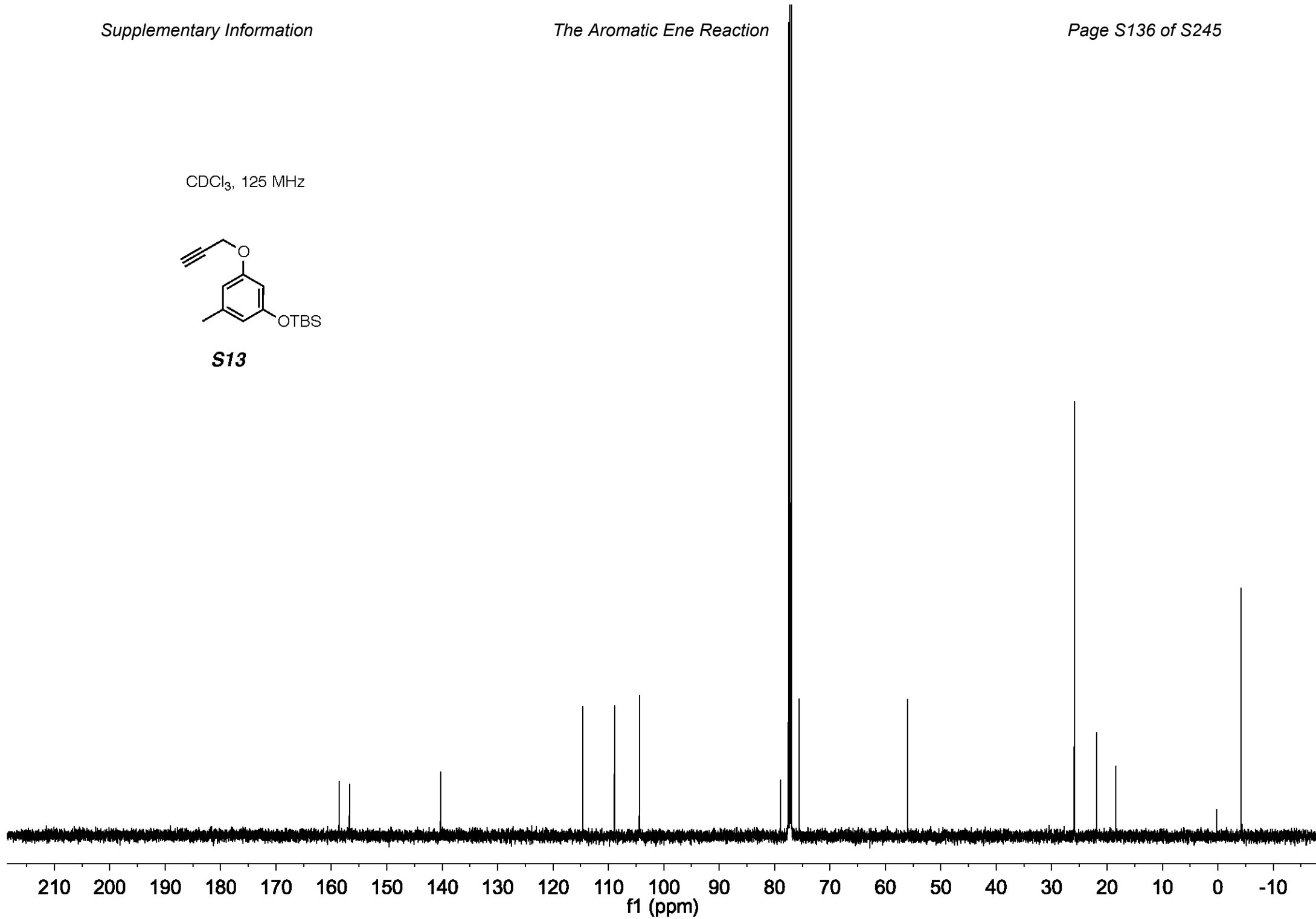
CDCl₃, 500 MHz**32e-d₂**

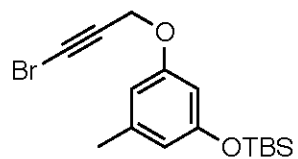
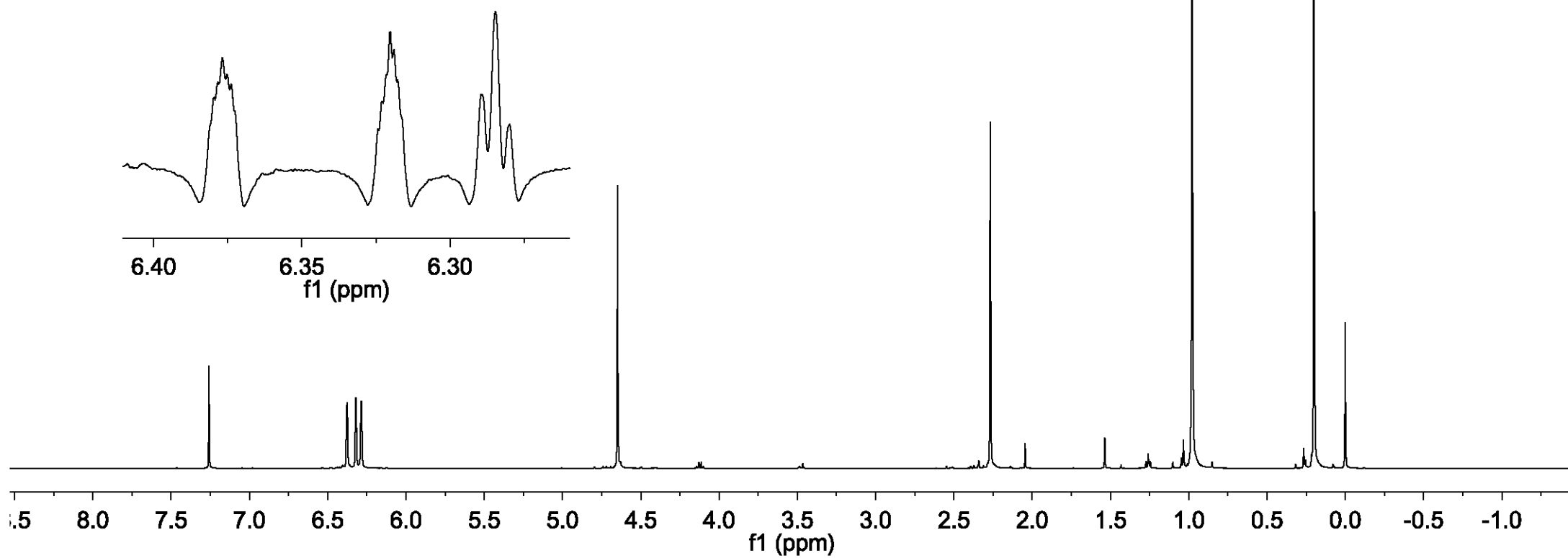
CDCl₃, 125 MHz**32e**

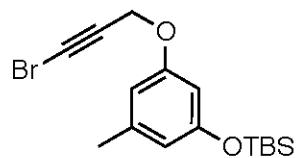
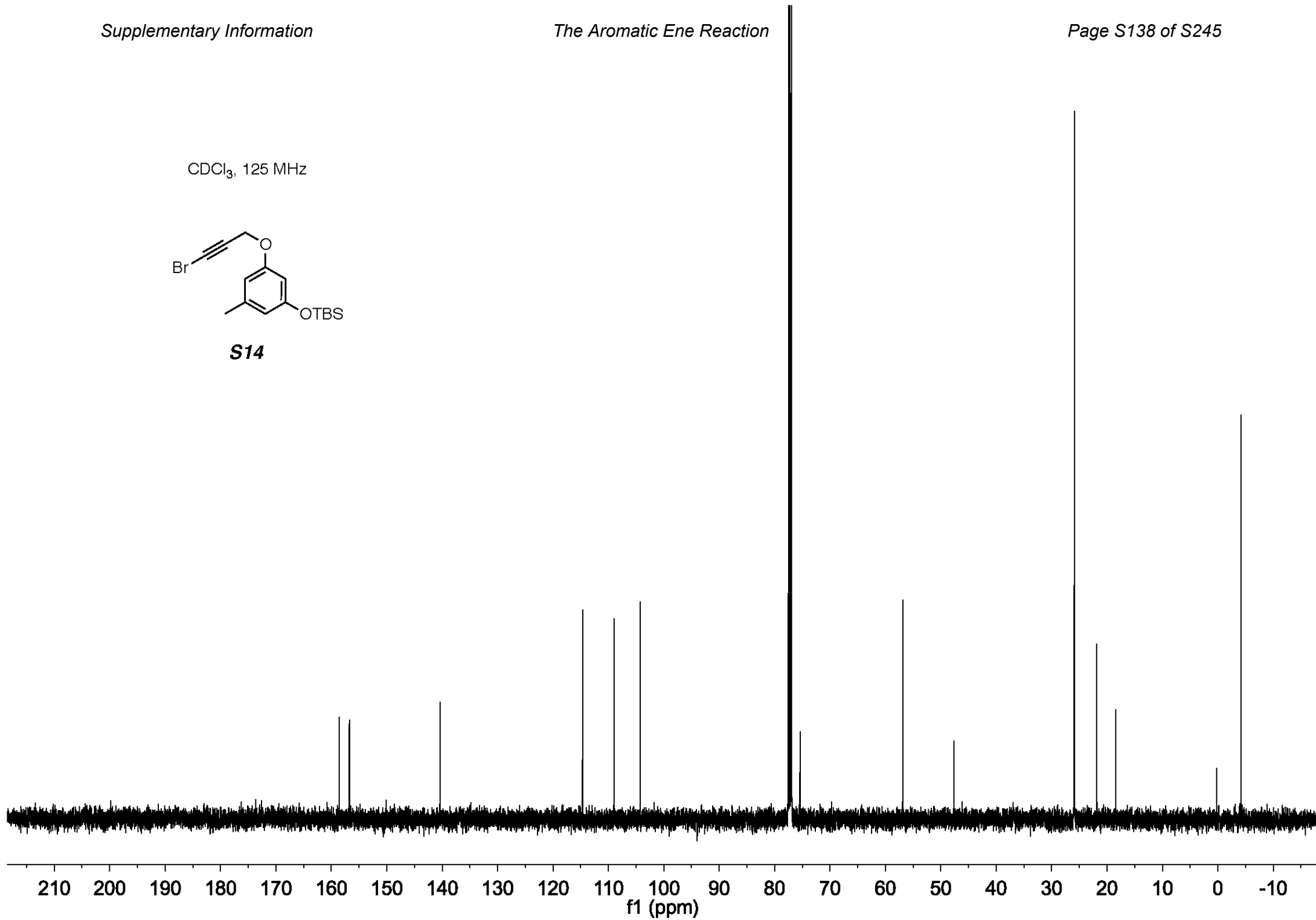
CDCl₃, 500 MHz**S12**

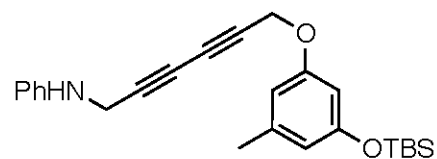
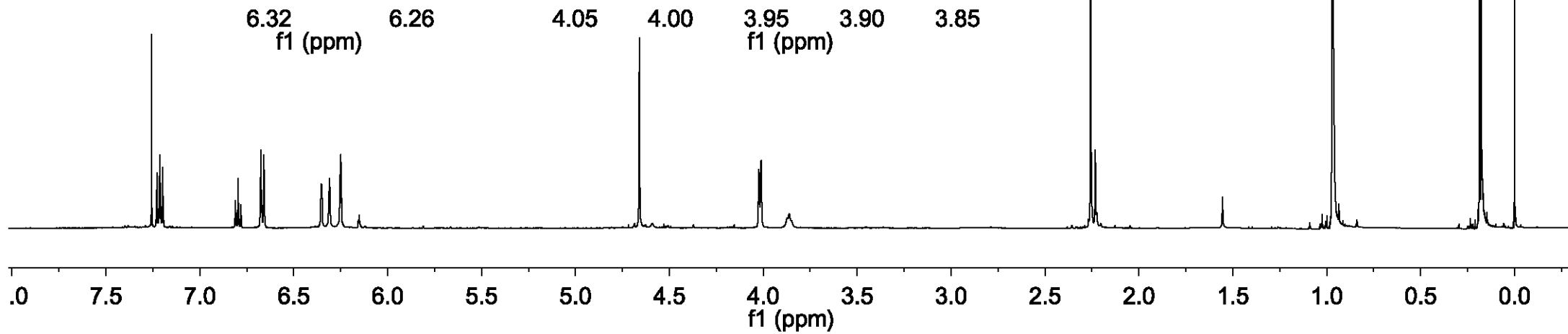
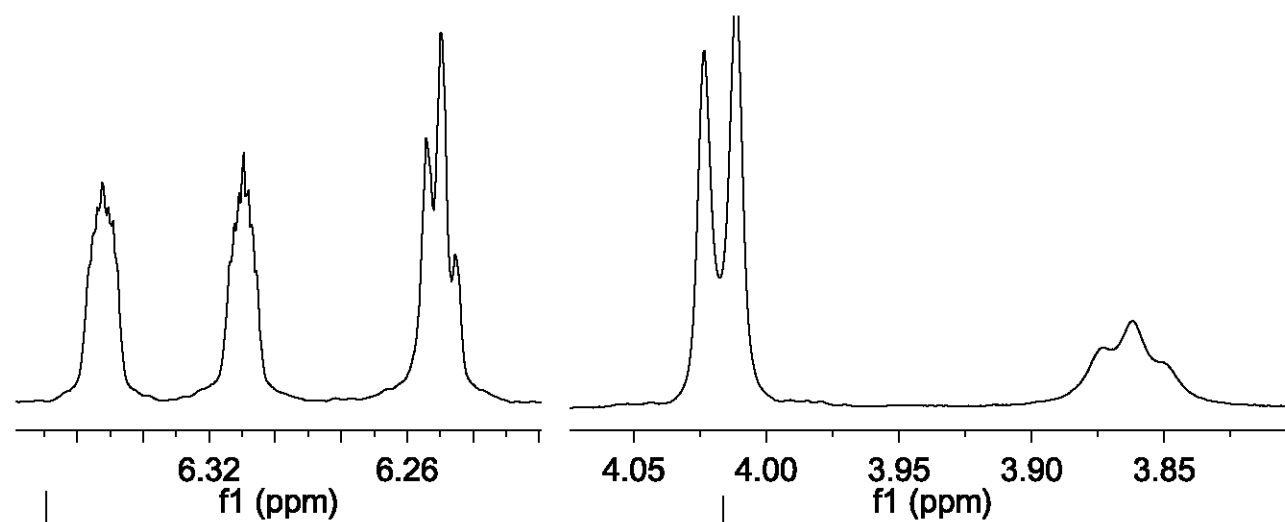
CDCl₃, 125 MHz**S12**

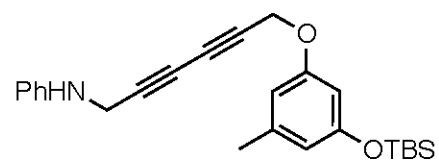
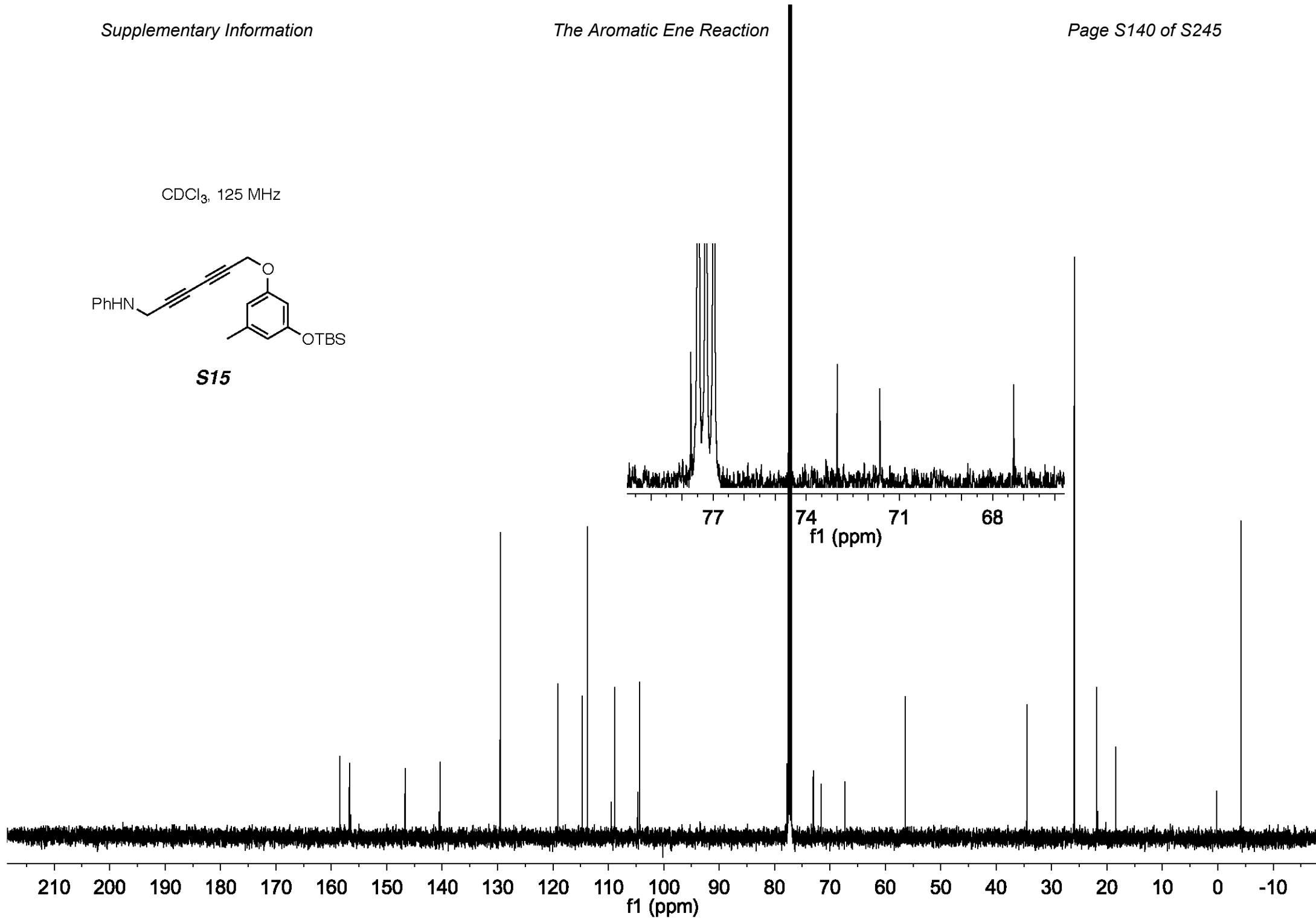
CDCl₃, 500 MHz**S13**

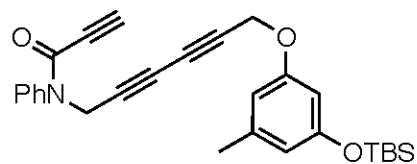
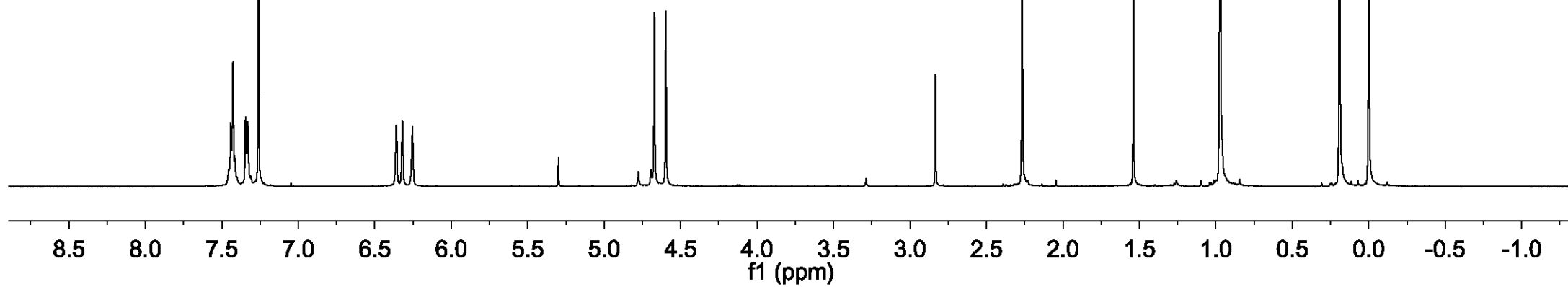
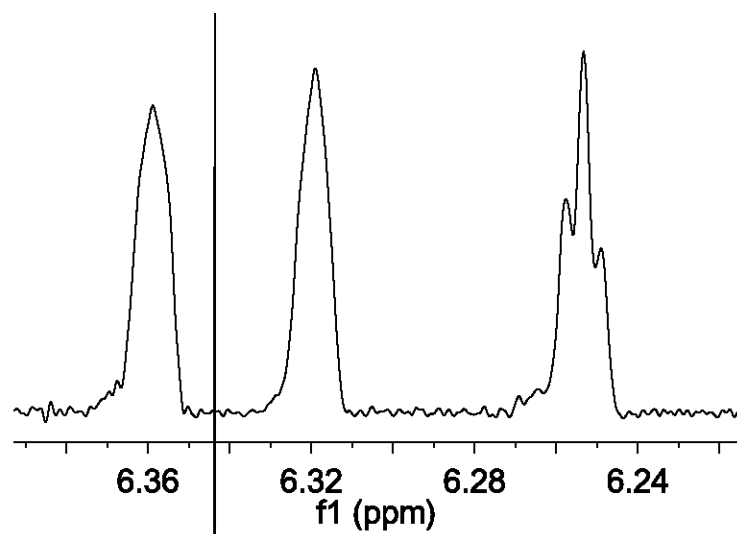
CDCl₃, 125 MHz**S13**

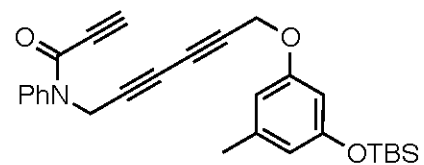
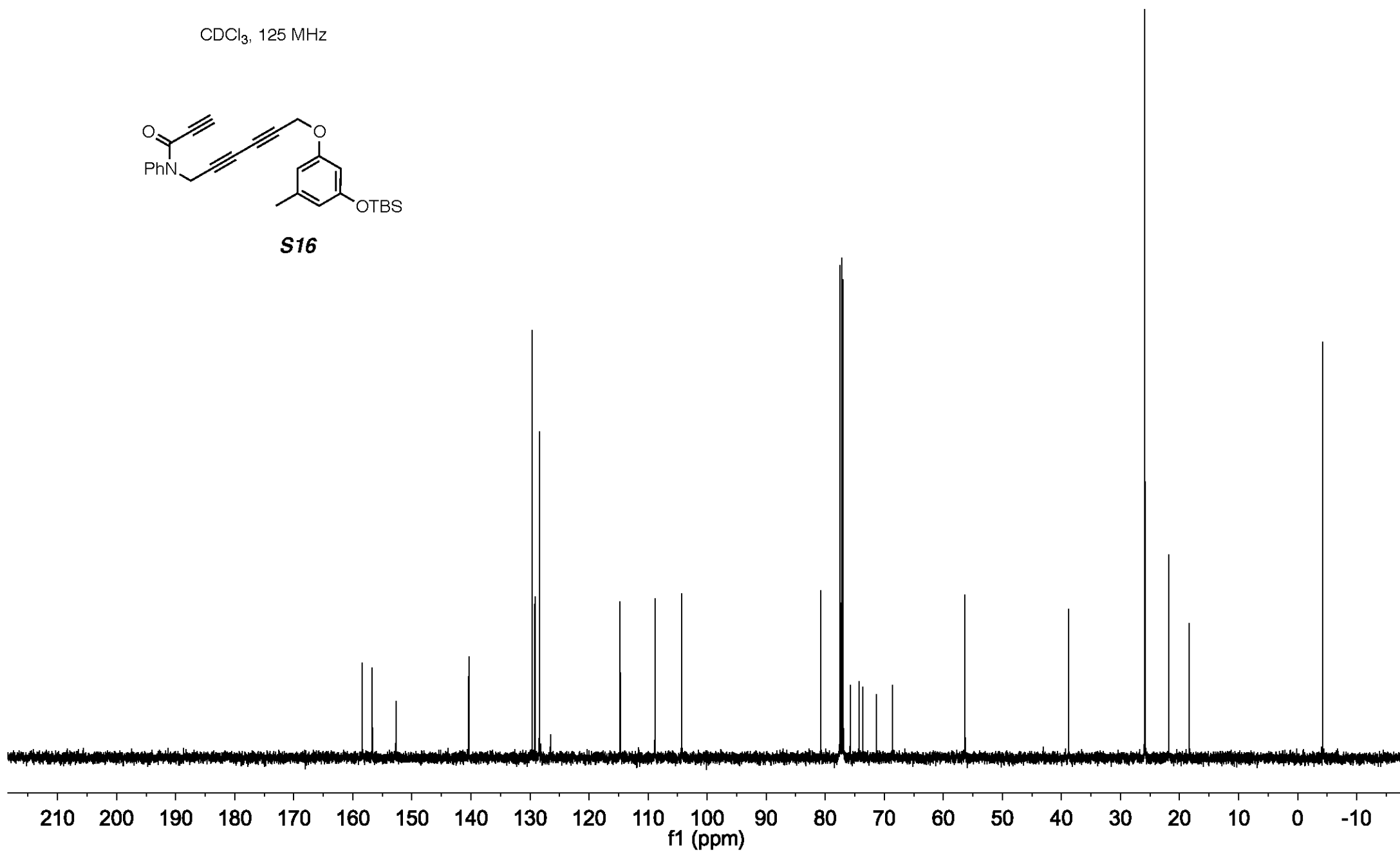
CDCl₃, 500 MHz**S14**

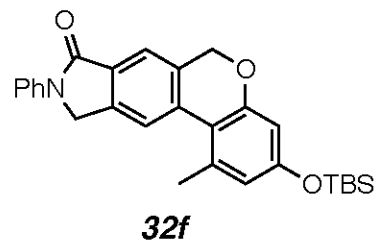
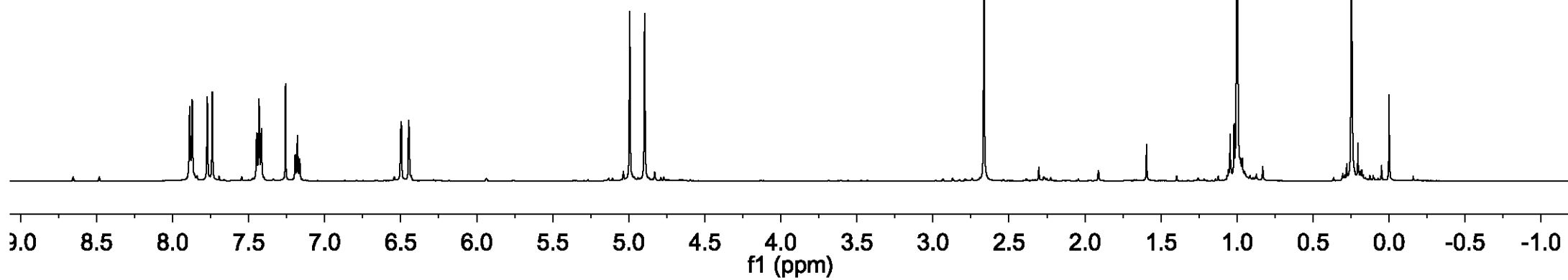
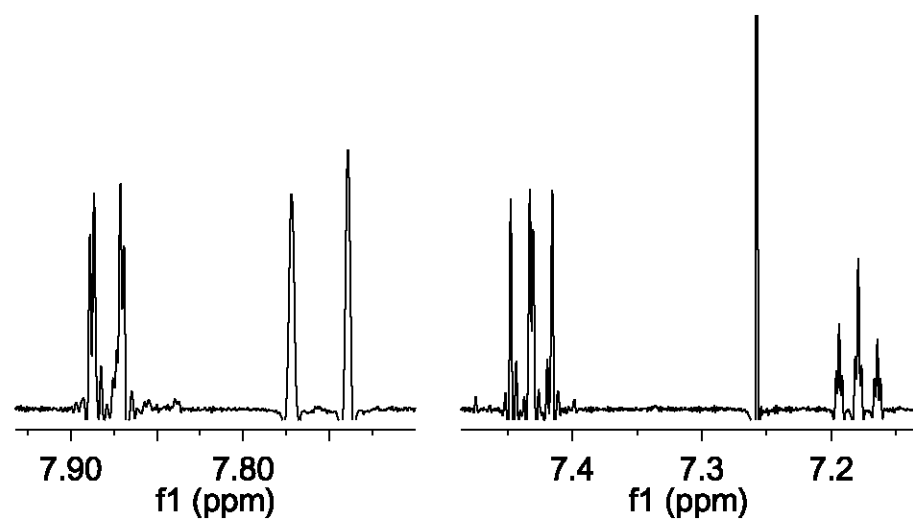
CDCl₃, 125 MHz**S14**

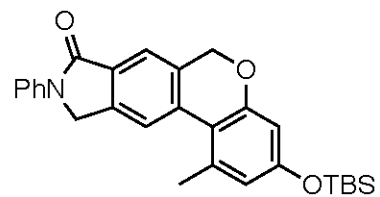
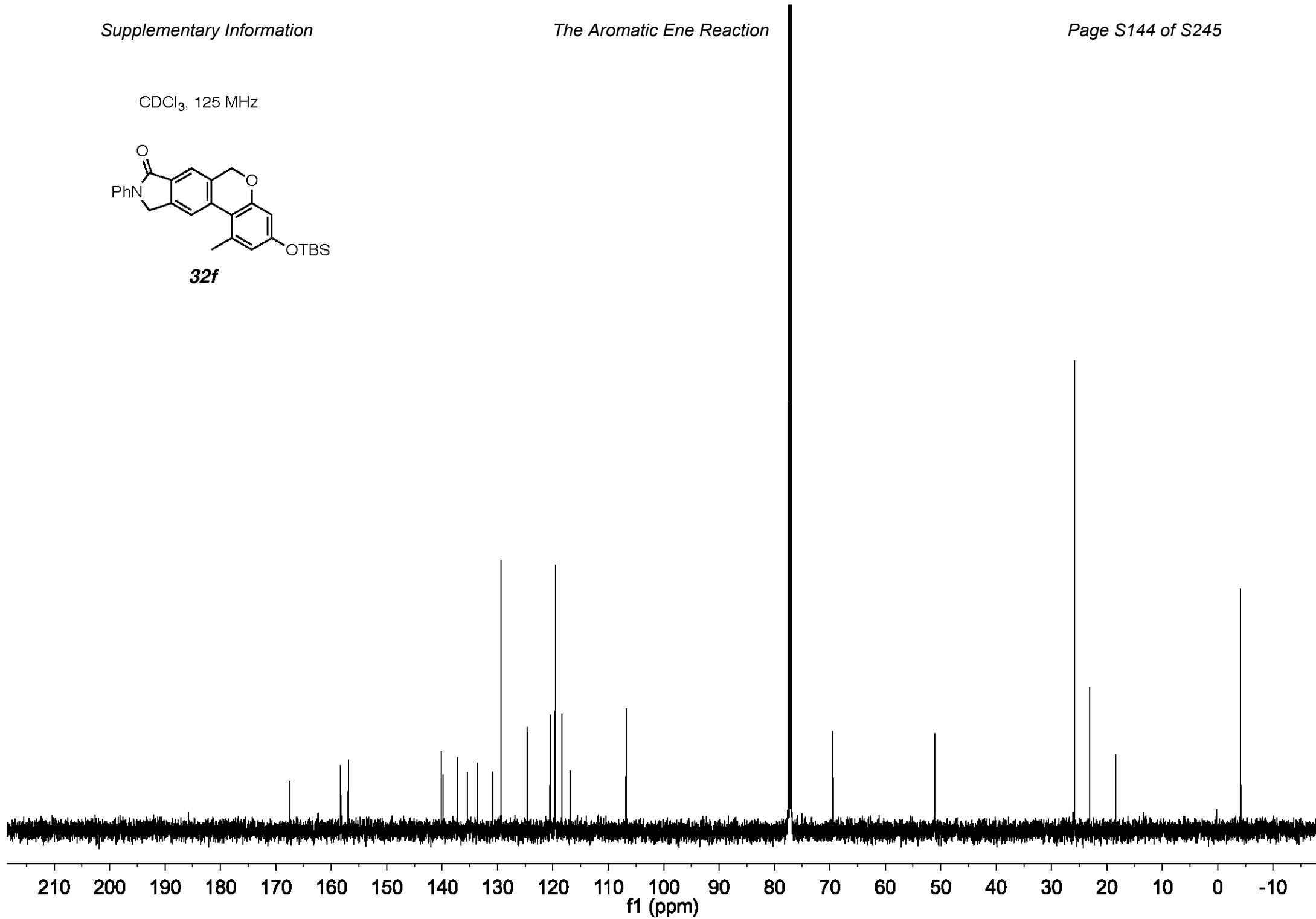
CDCl₃, 500 MHz**S15**

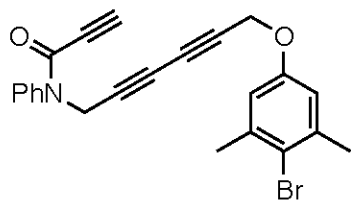
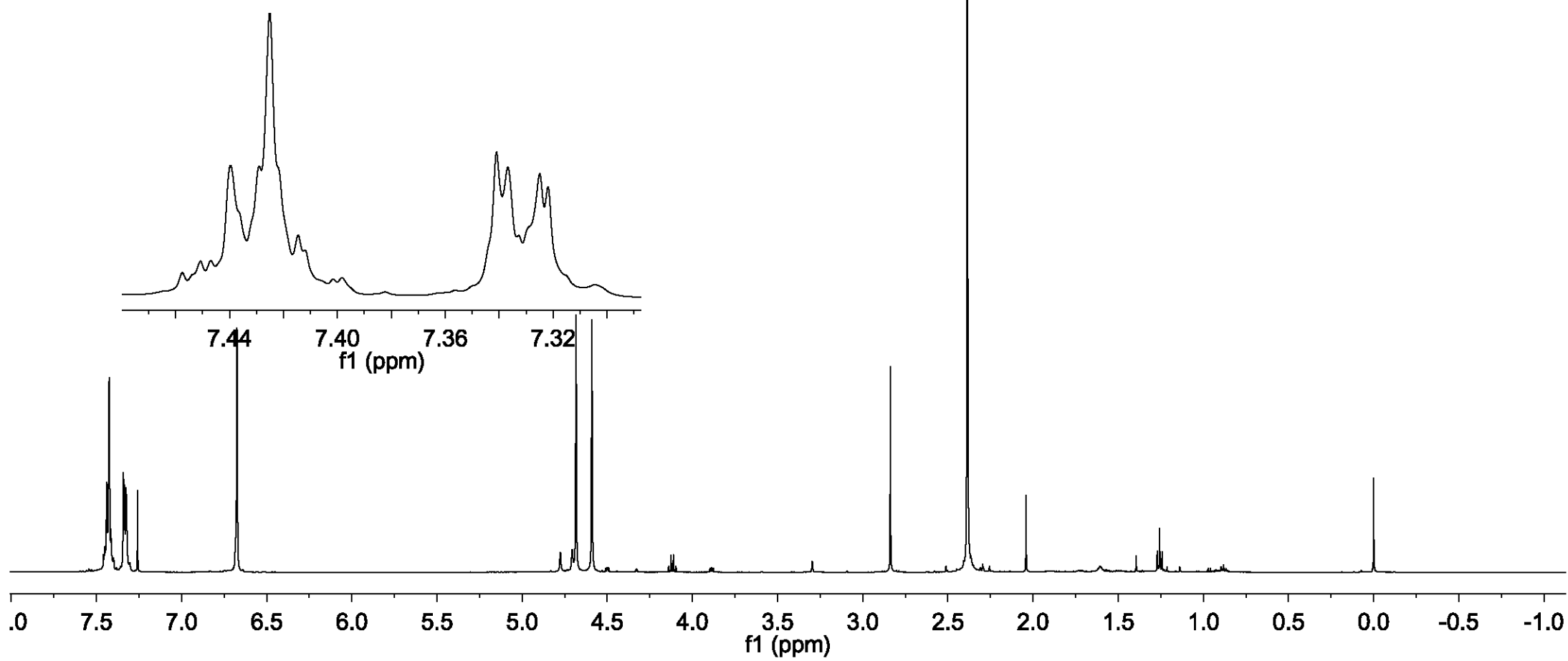
CDCl₃, 125 MHz**S15**

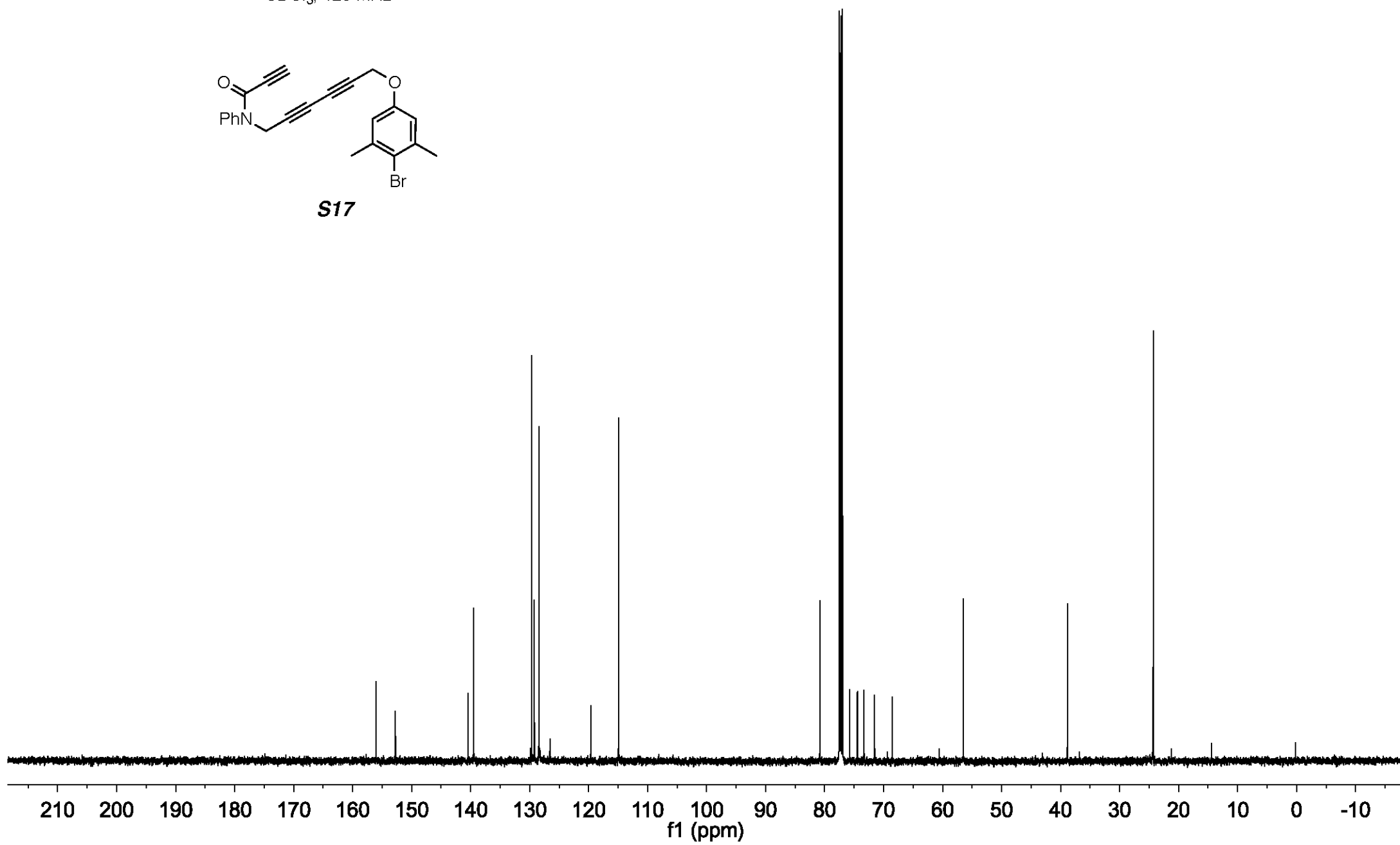
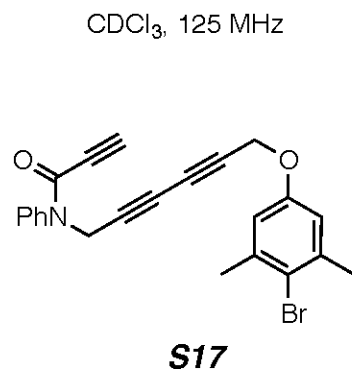
CDCl₃, 500 MHz**S16**

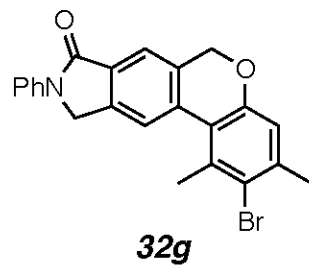
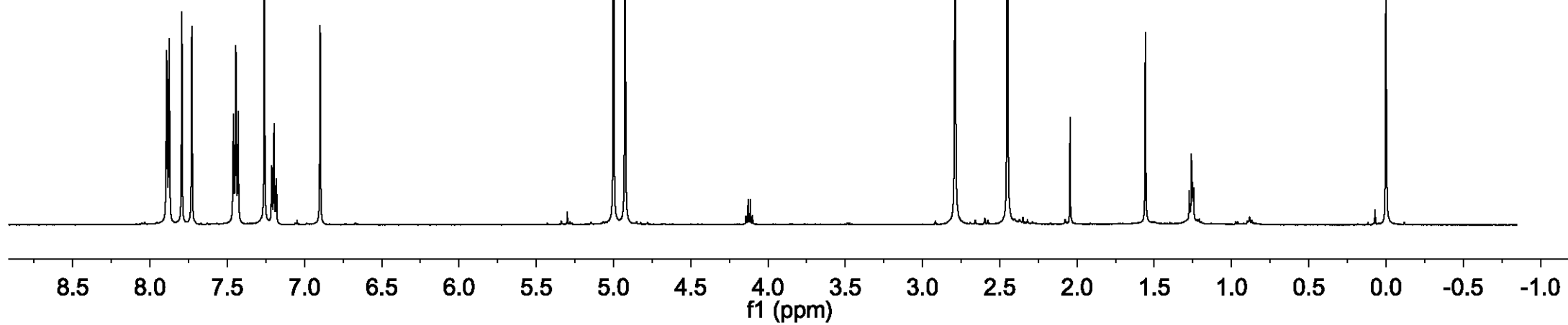
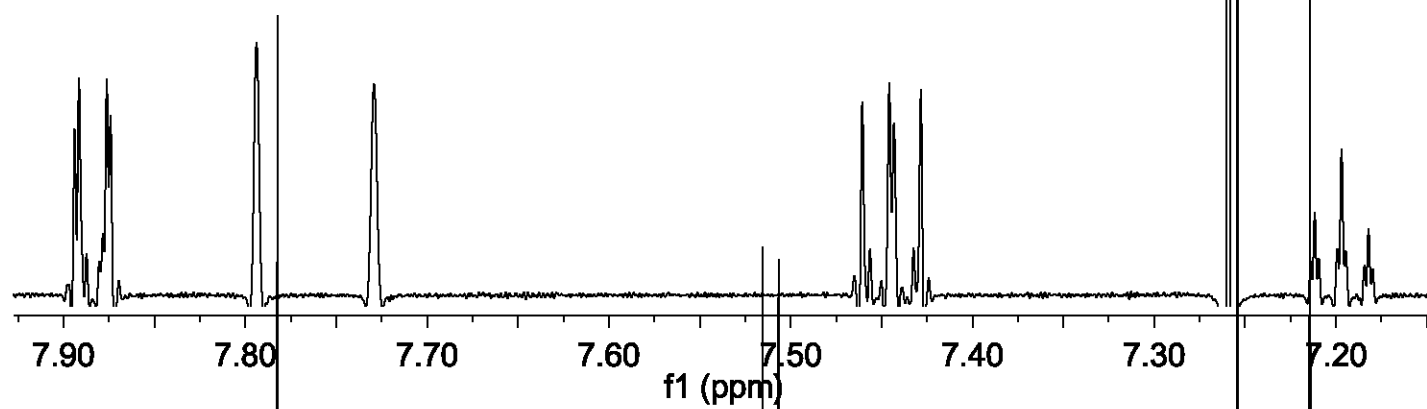
CDCl₃, 125 MHz**S16**

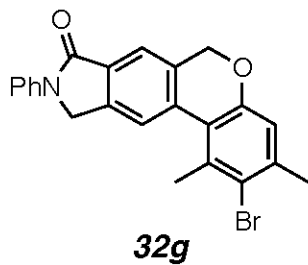
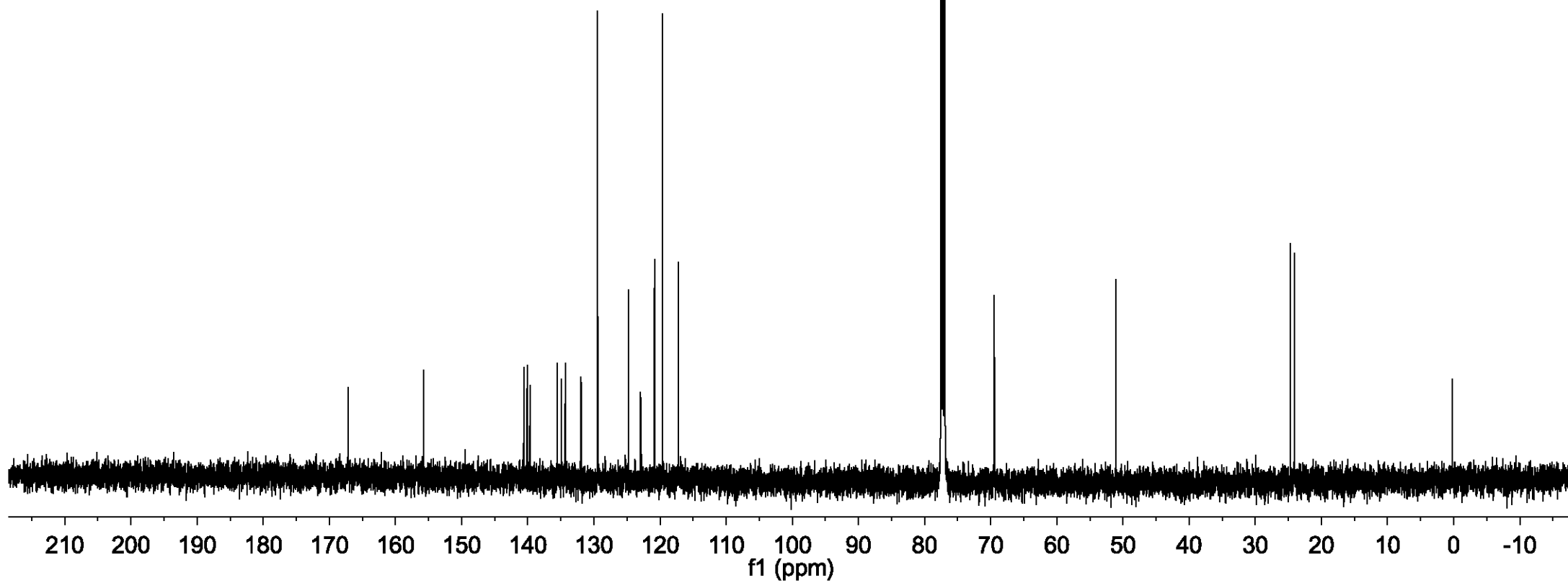
CDCl₃, 500 MHz**32f**

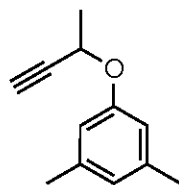
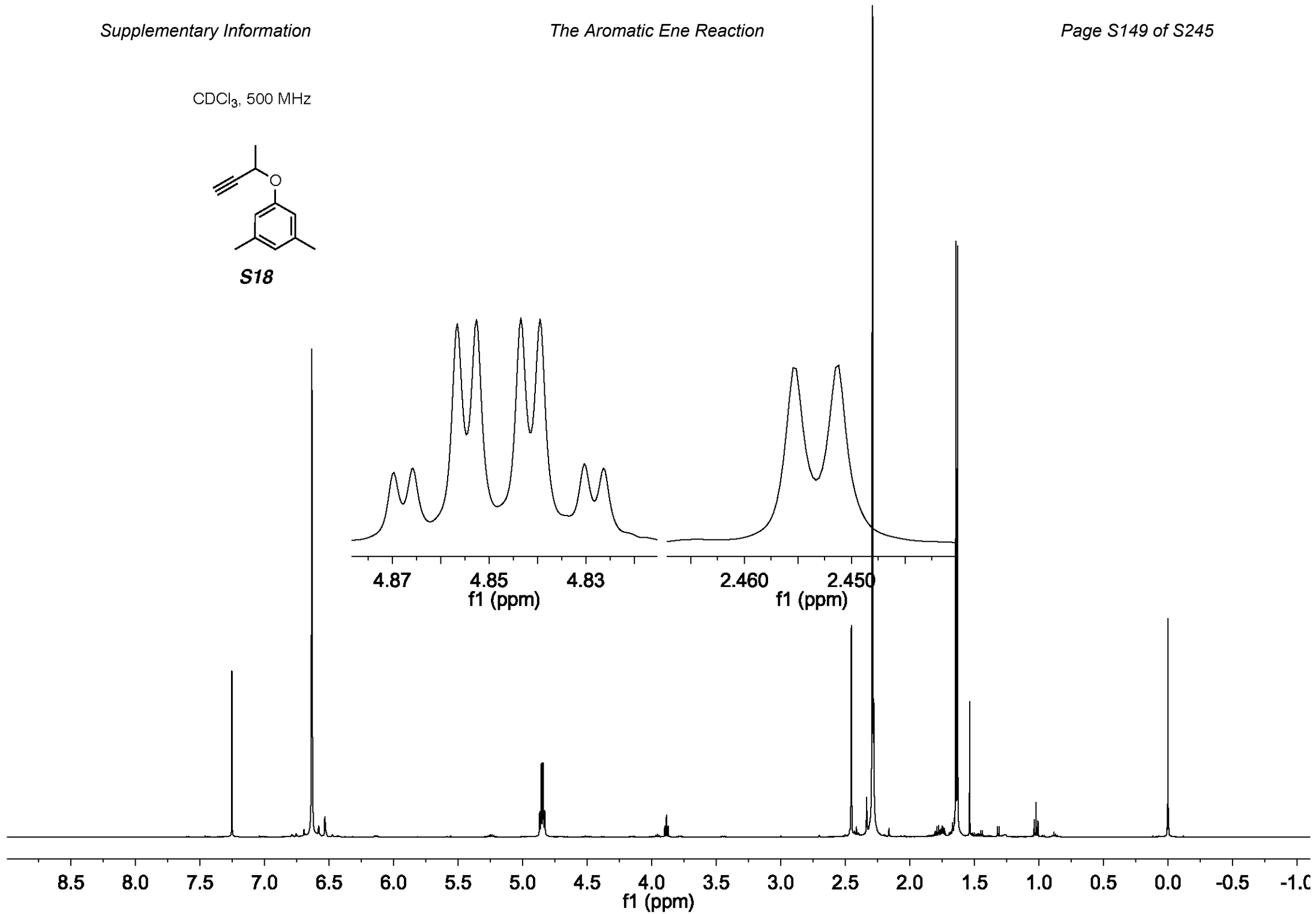
CDCl₃, 125 MHz**32f**

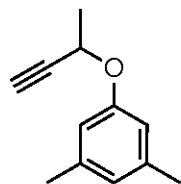
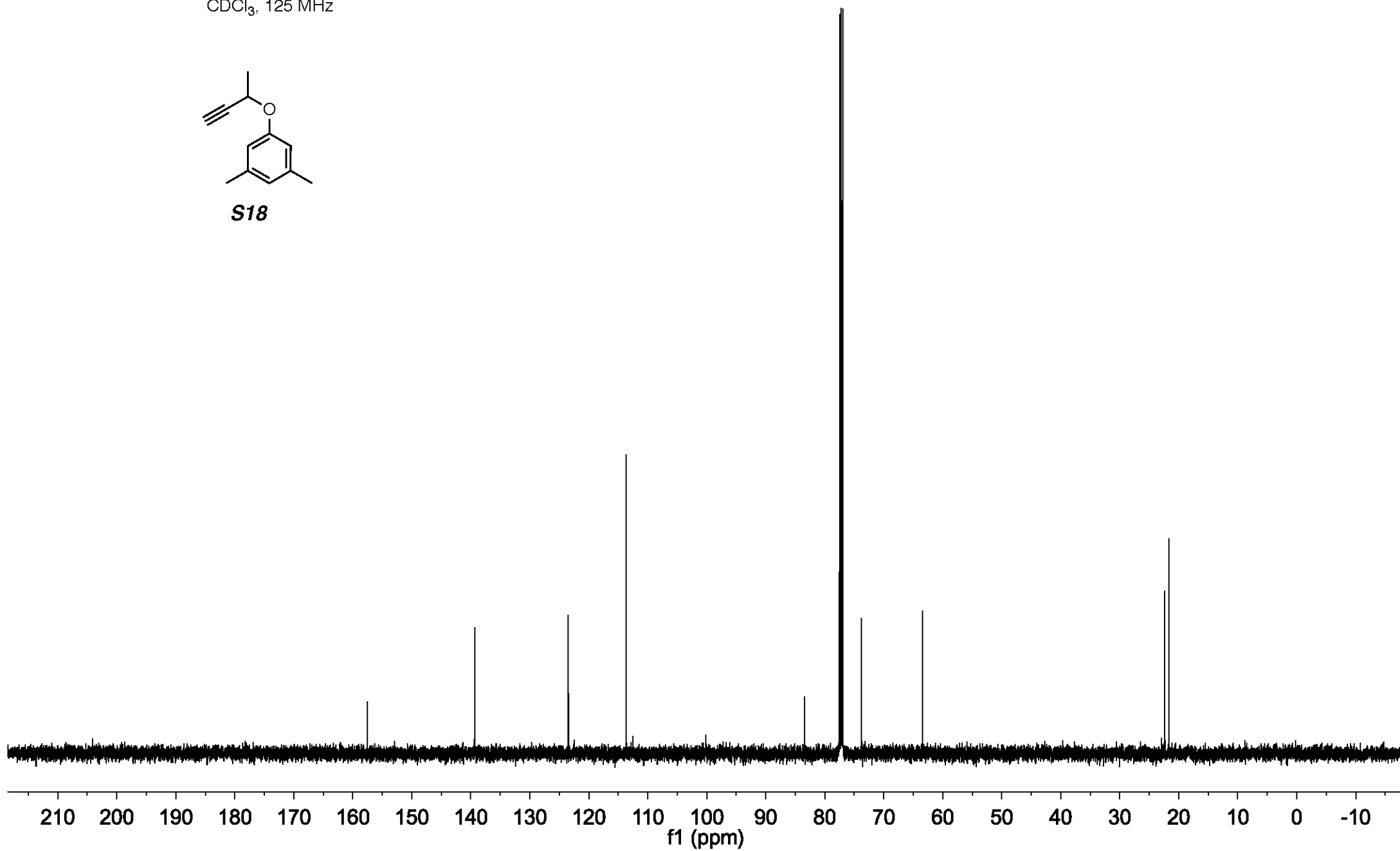
CDCl₃, 500 MHz**S17**

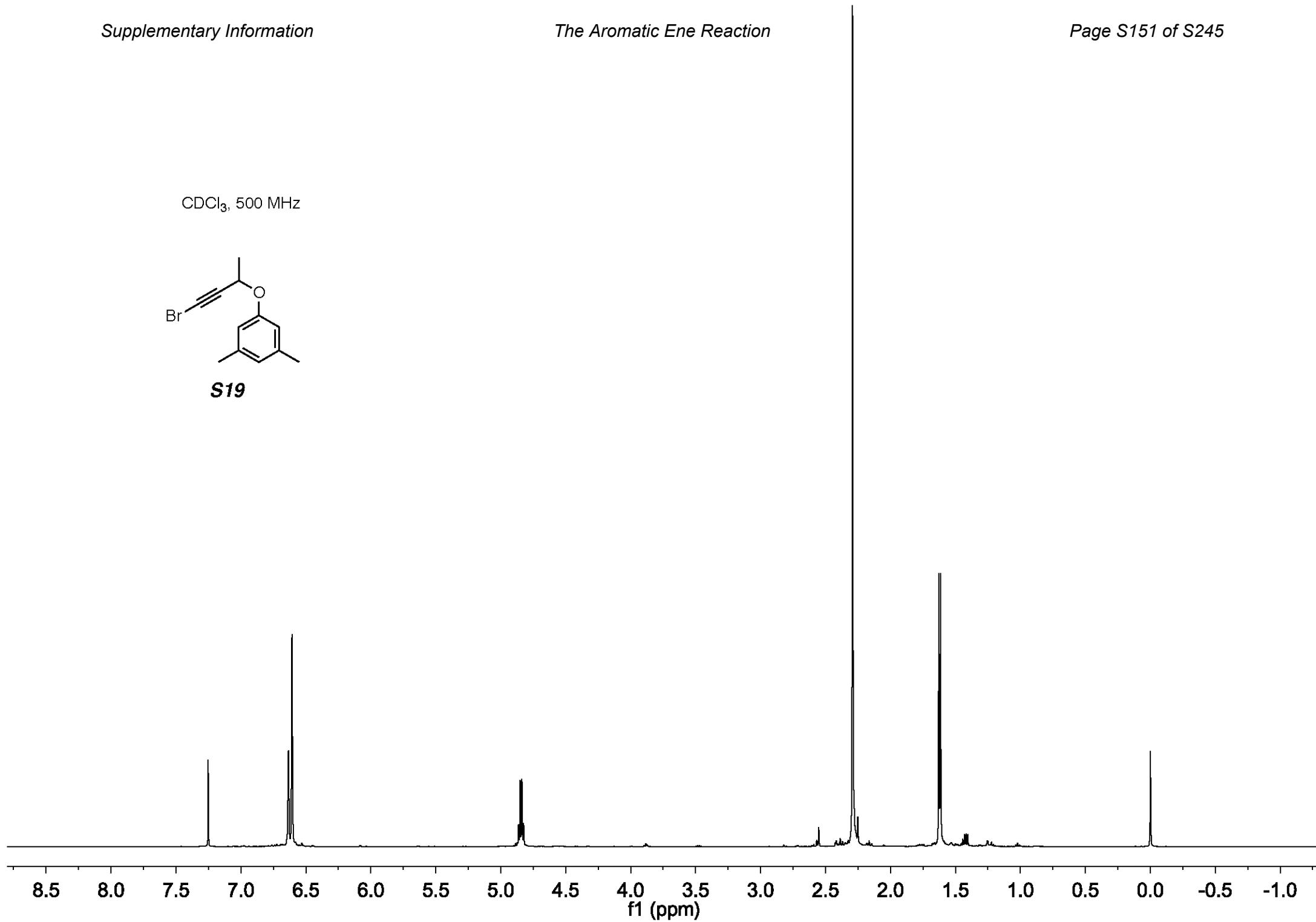
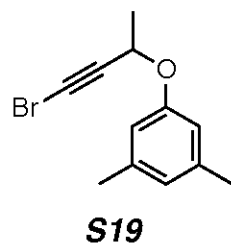


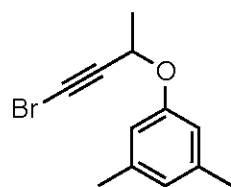
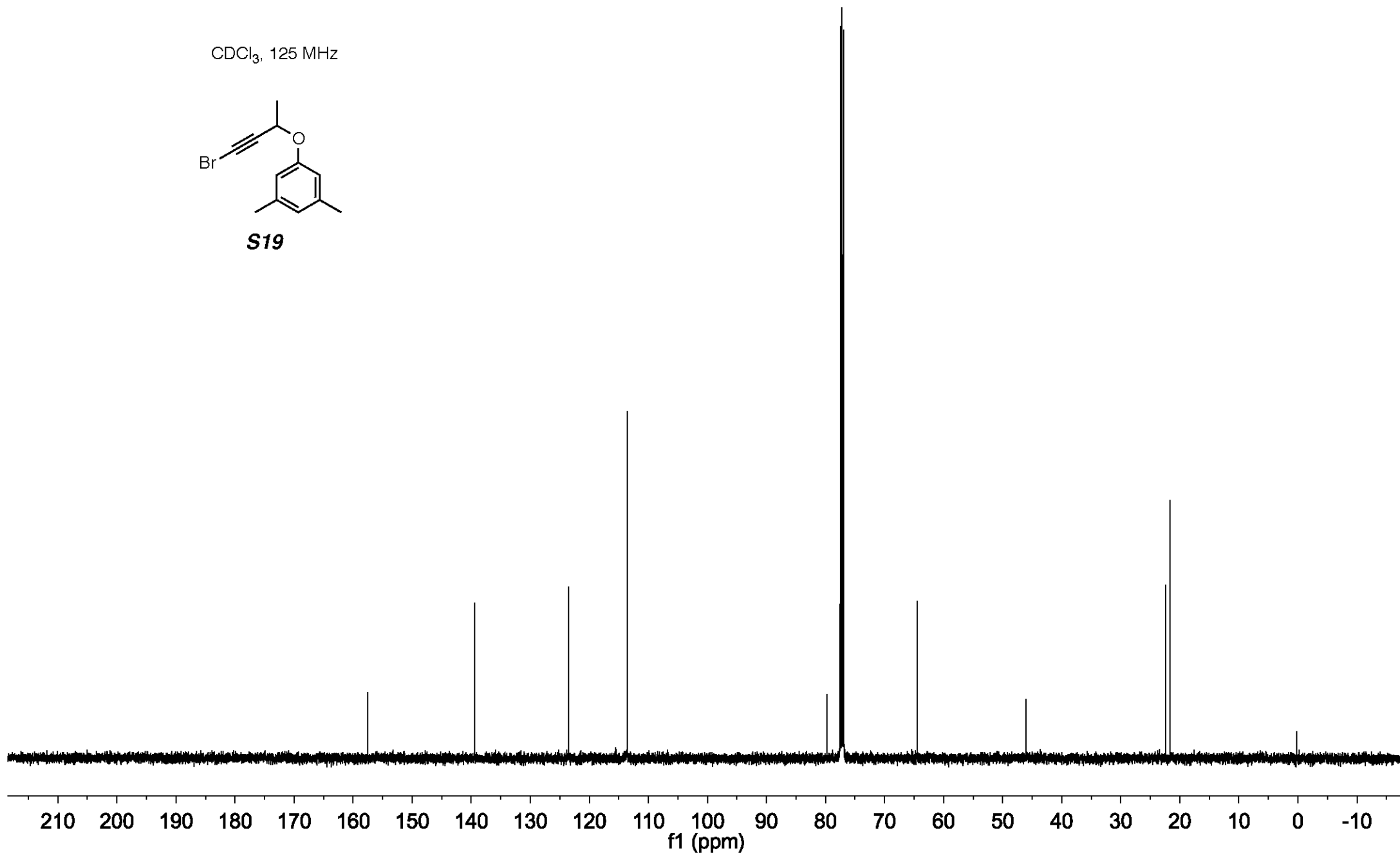
CDCl₃, 500 MHz**32g**

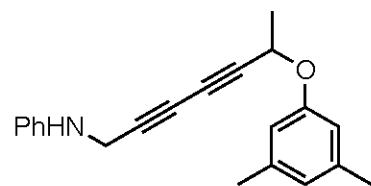
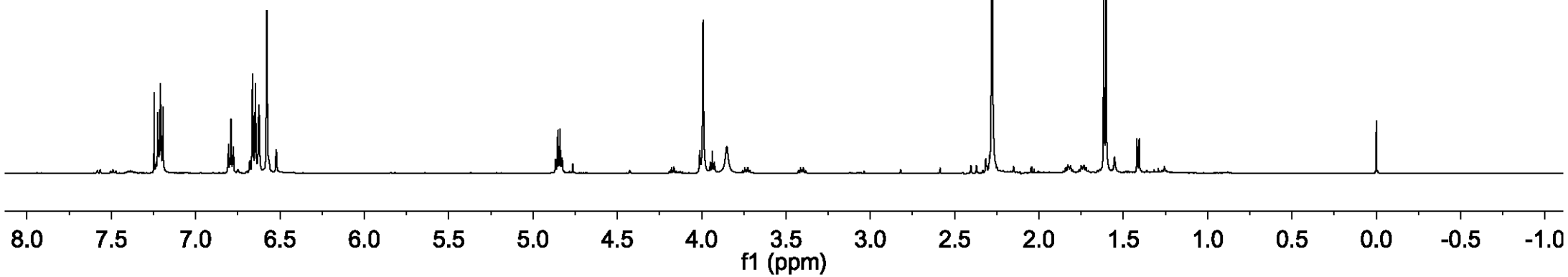
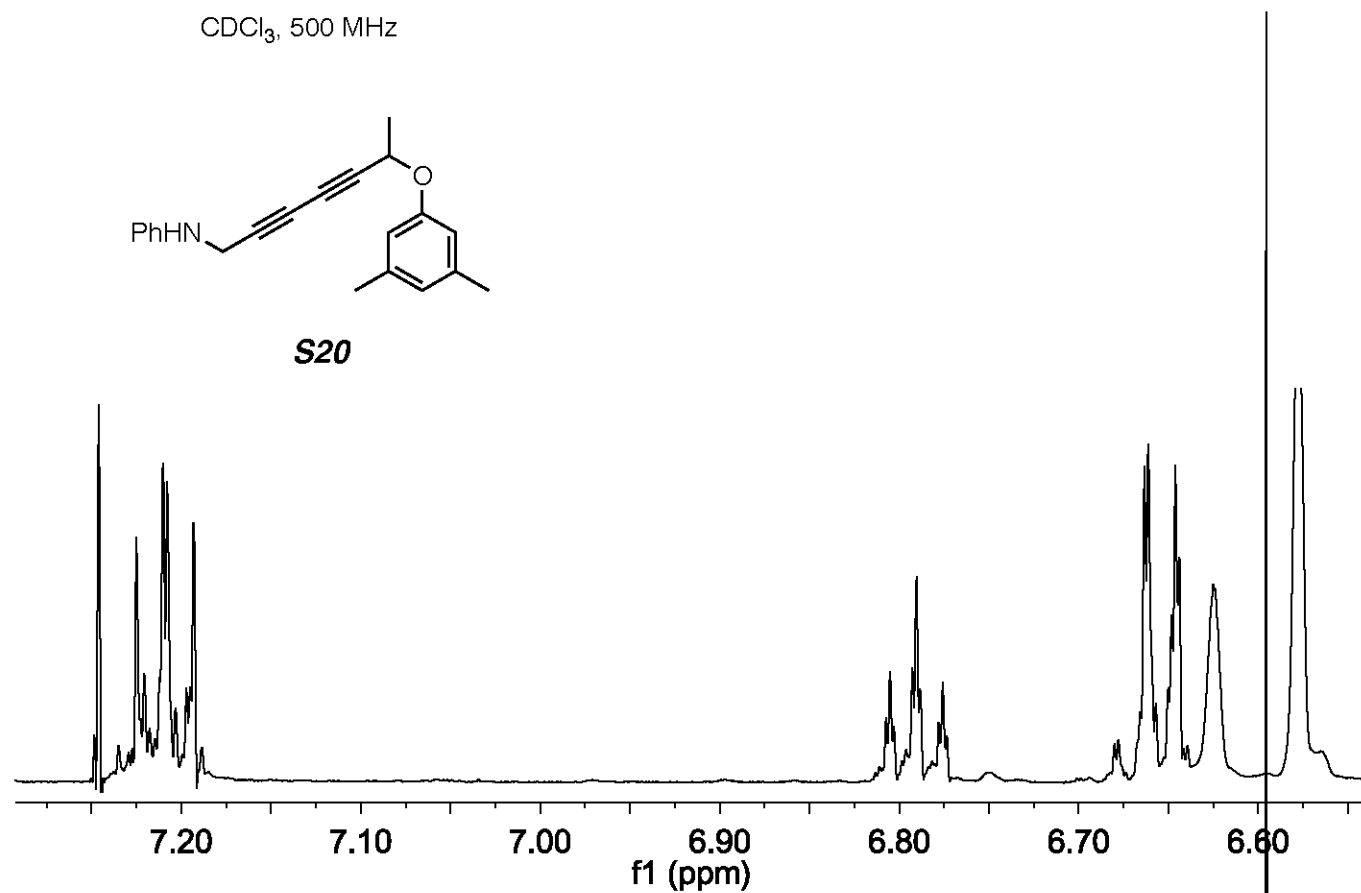
CDCl₃, 125 MHz**32g**

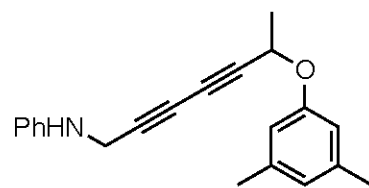
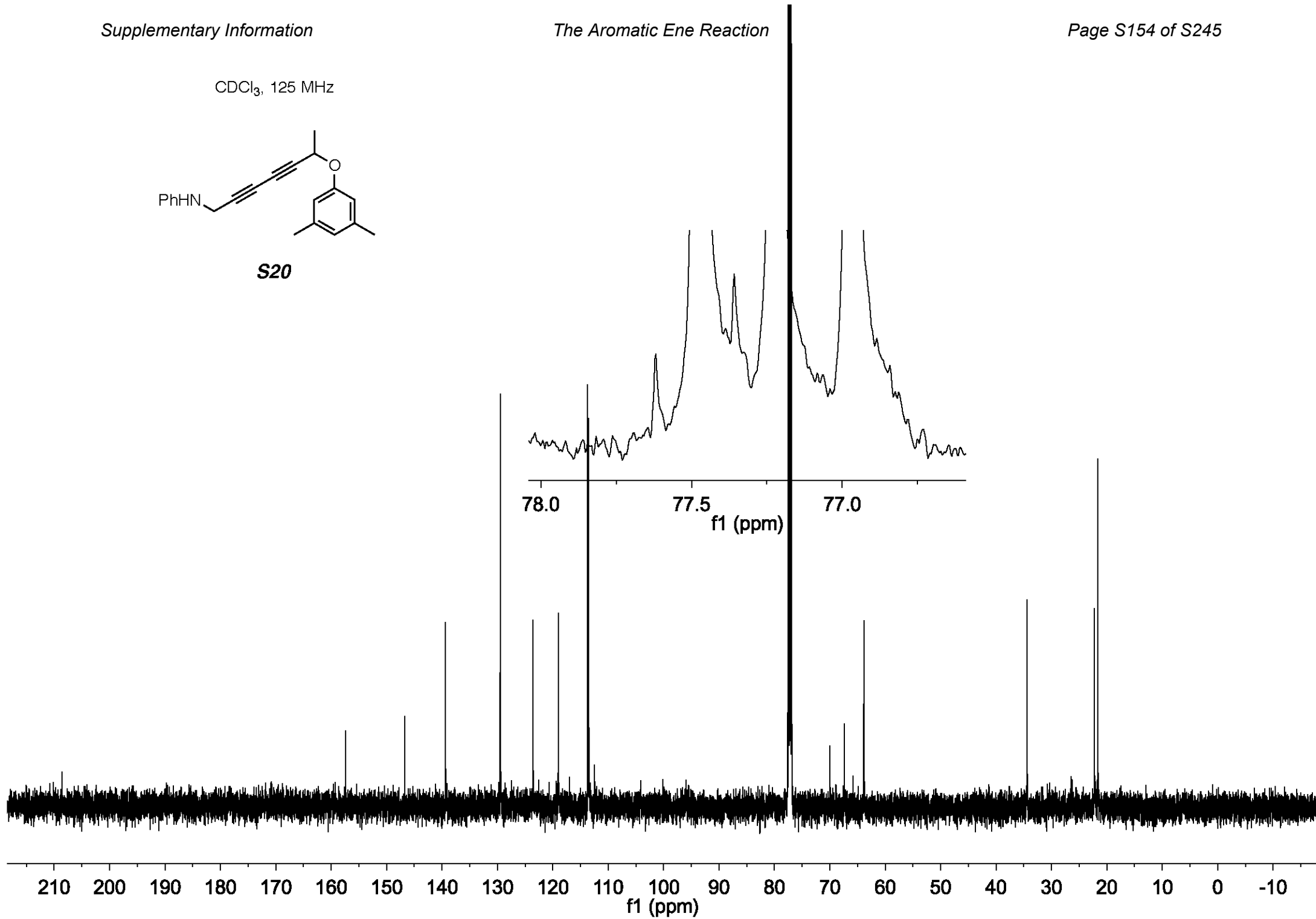
CDCl₃, 500 MHz**S18**

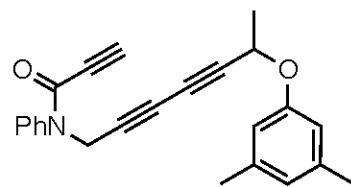
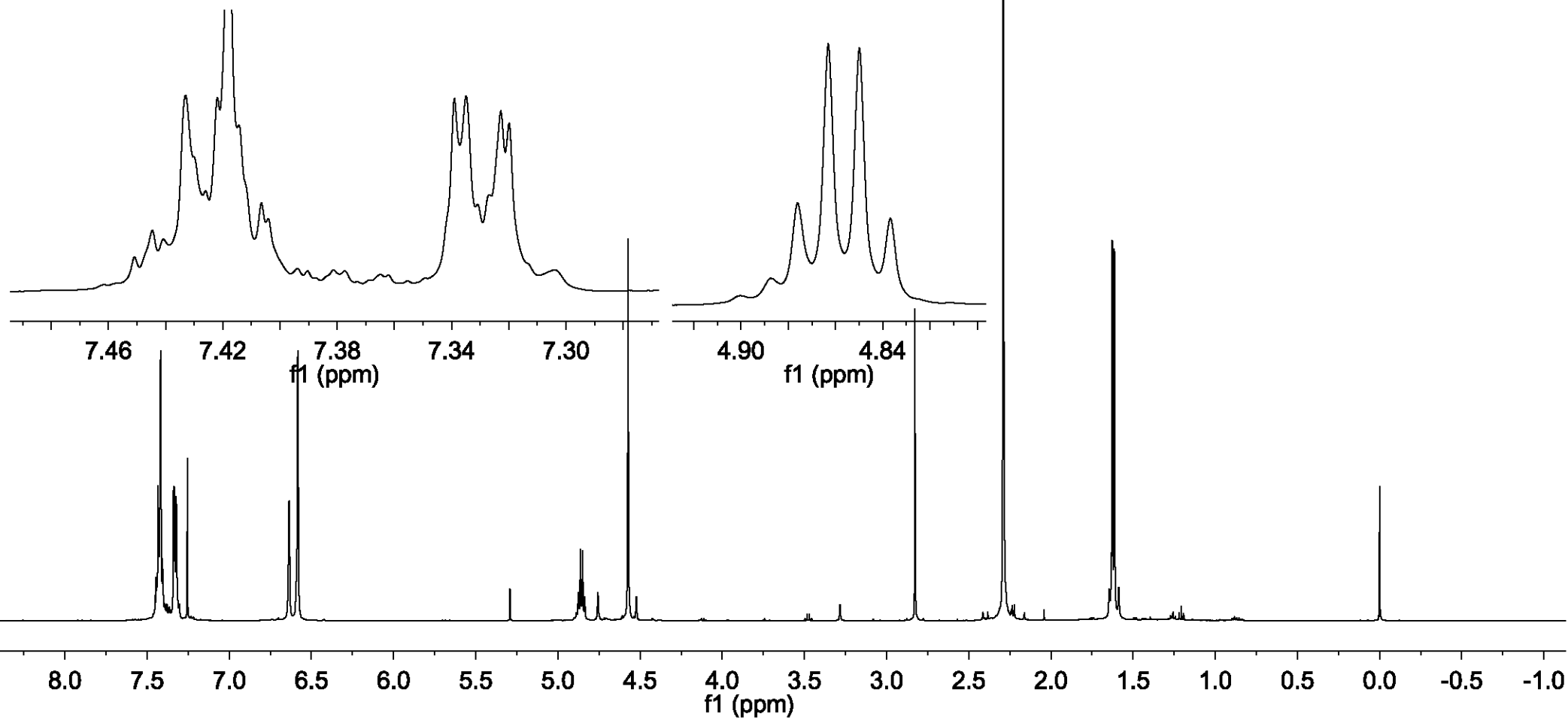
CDCl₃, 125 MHz**S18**

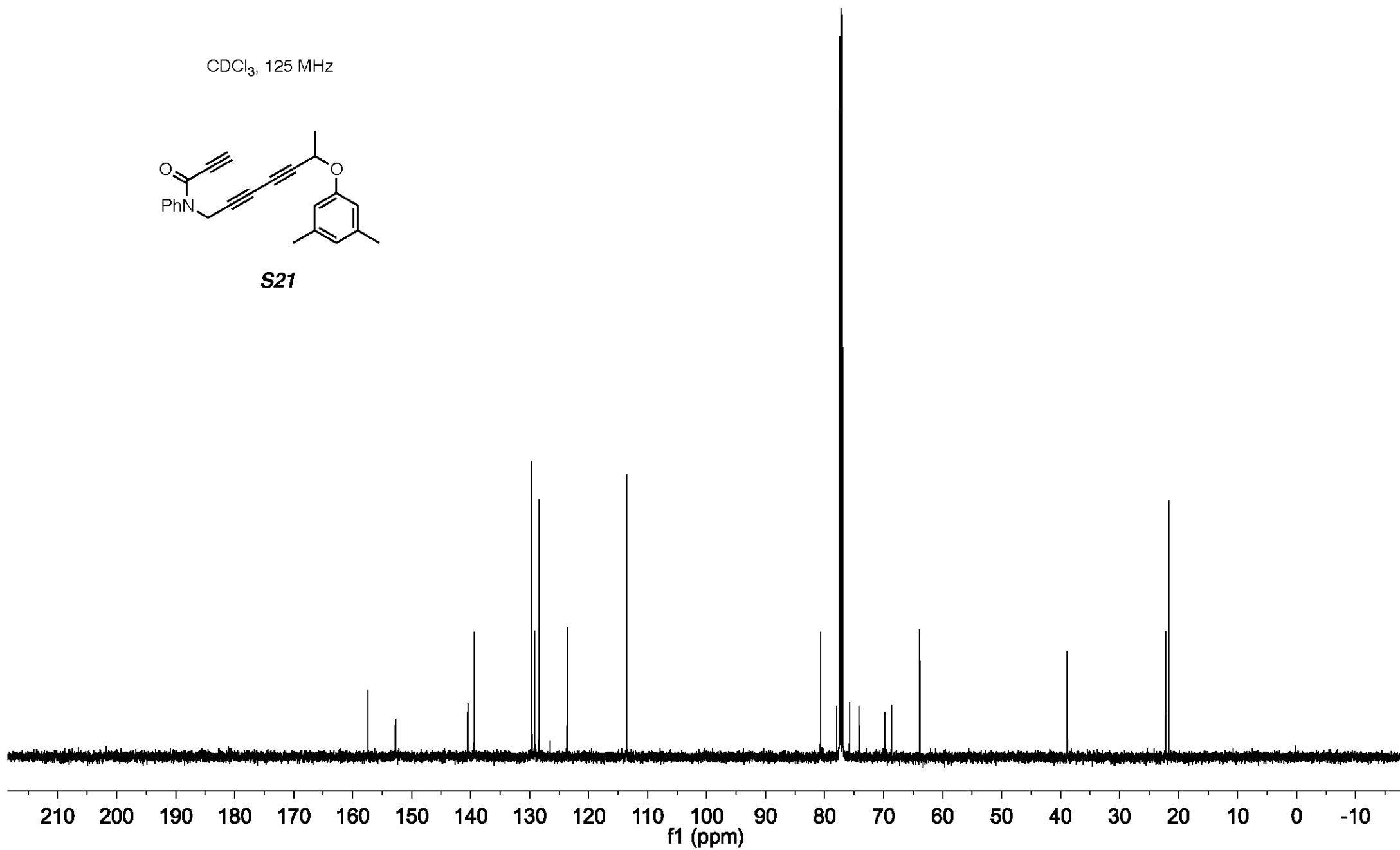
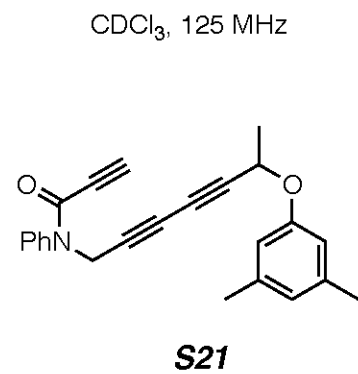
CDCl₃, 500 MHz

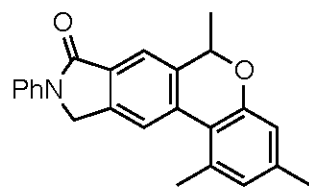
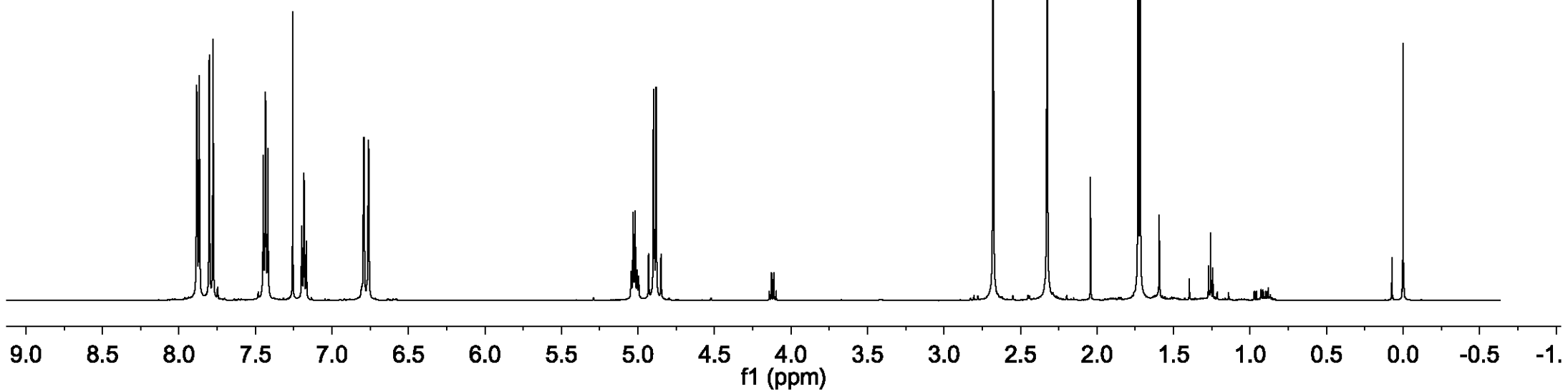
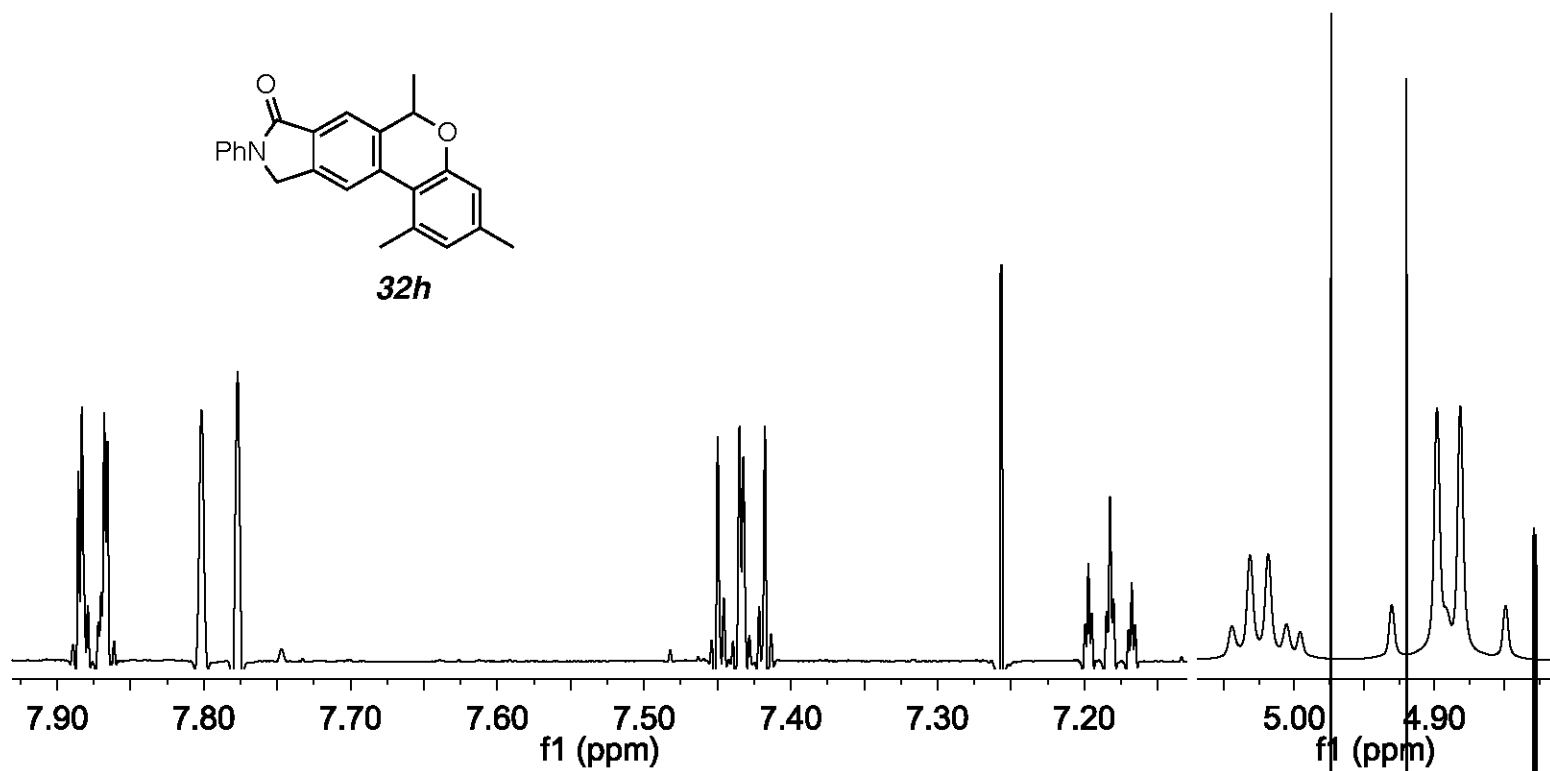
CDCl₃, 125 MHz**S19**

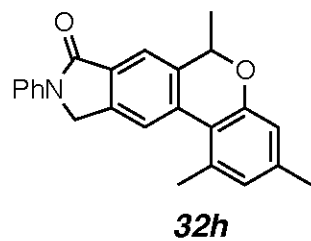
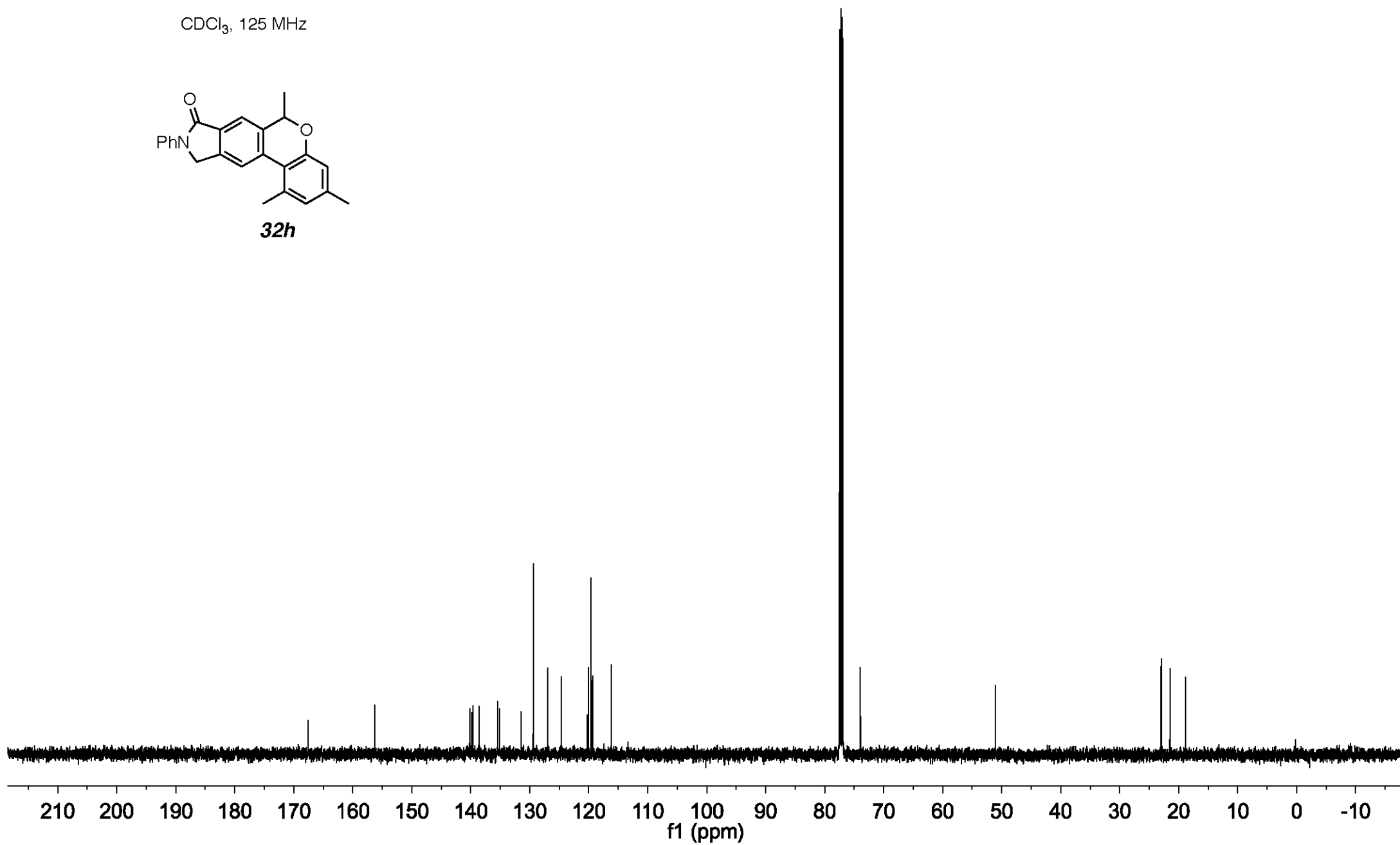
CDCl₃, 500 MHz**S20**

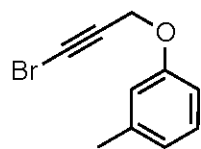
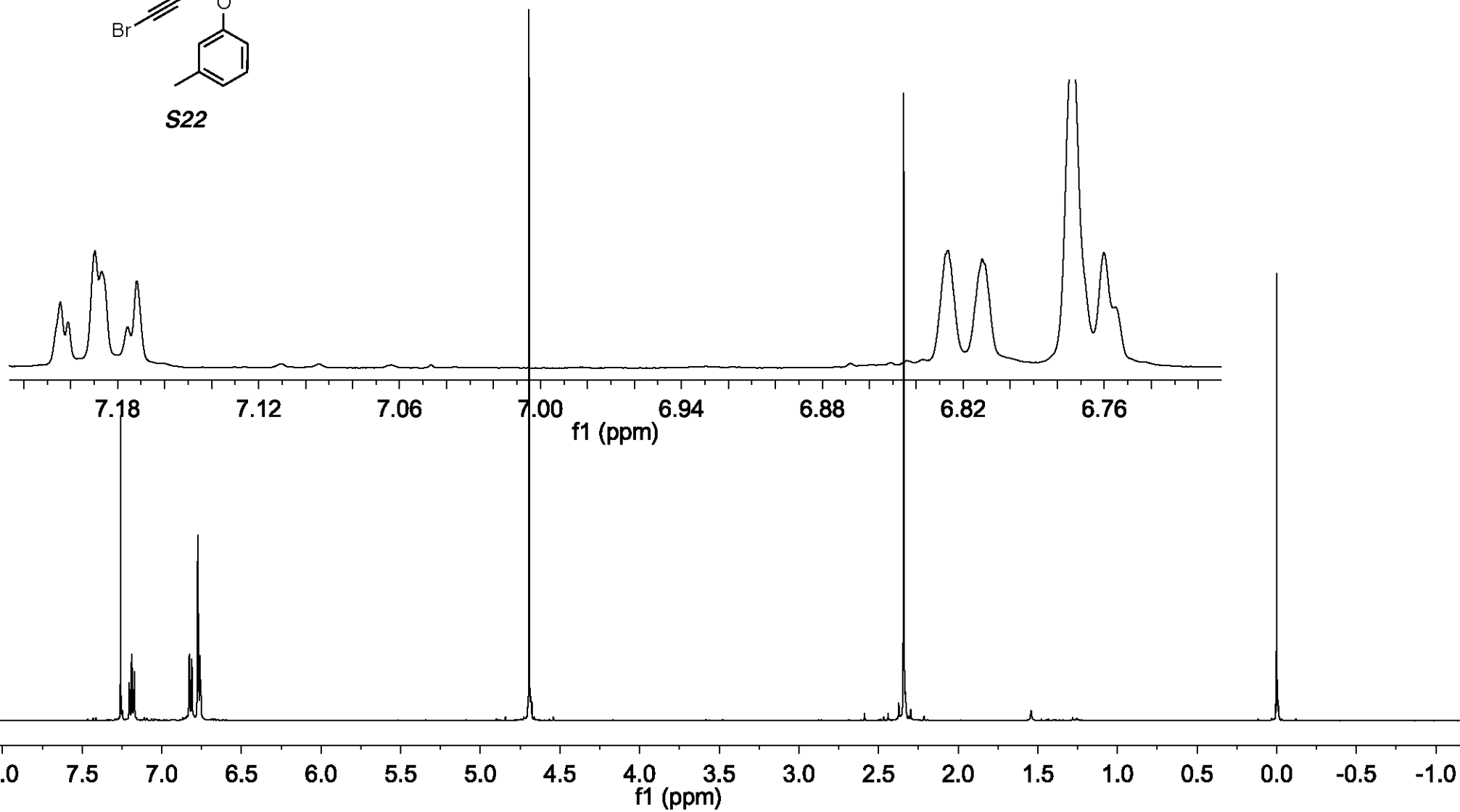
CDCl₃, 125 MHz**S20**

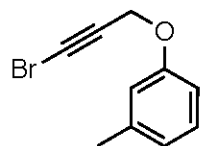
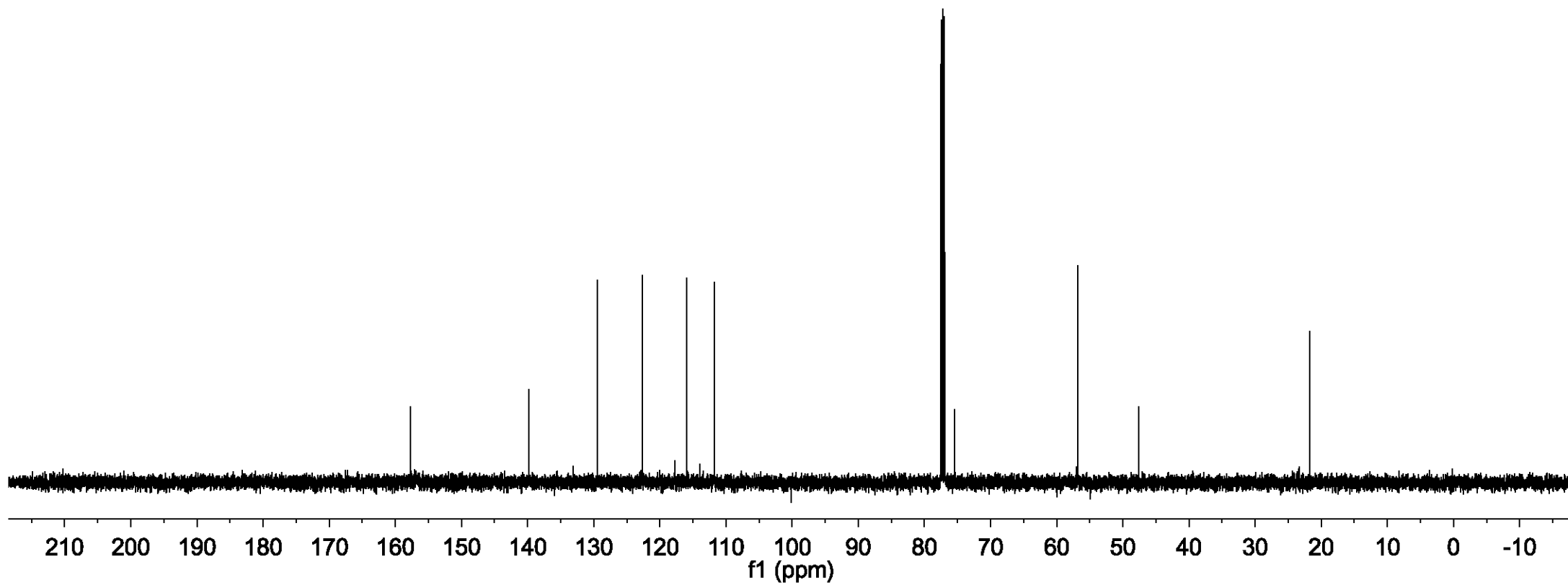
CDCl₃, 500 MHz**S21**

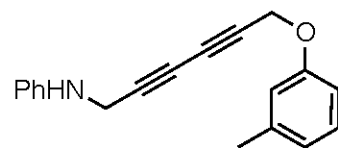
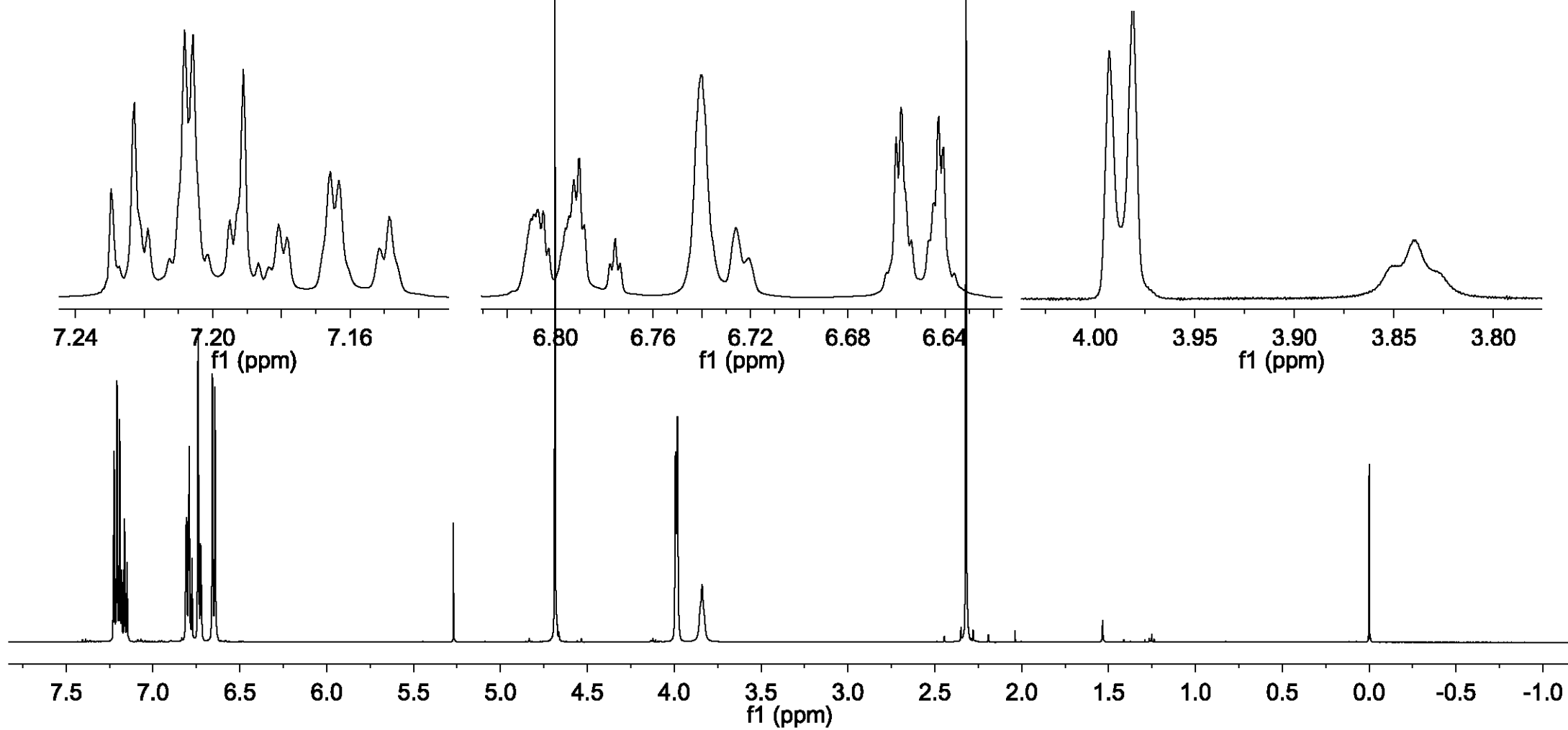


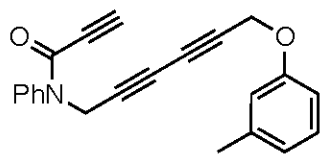
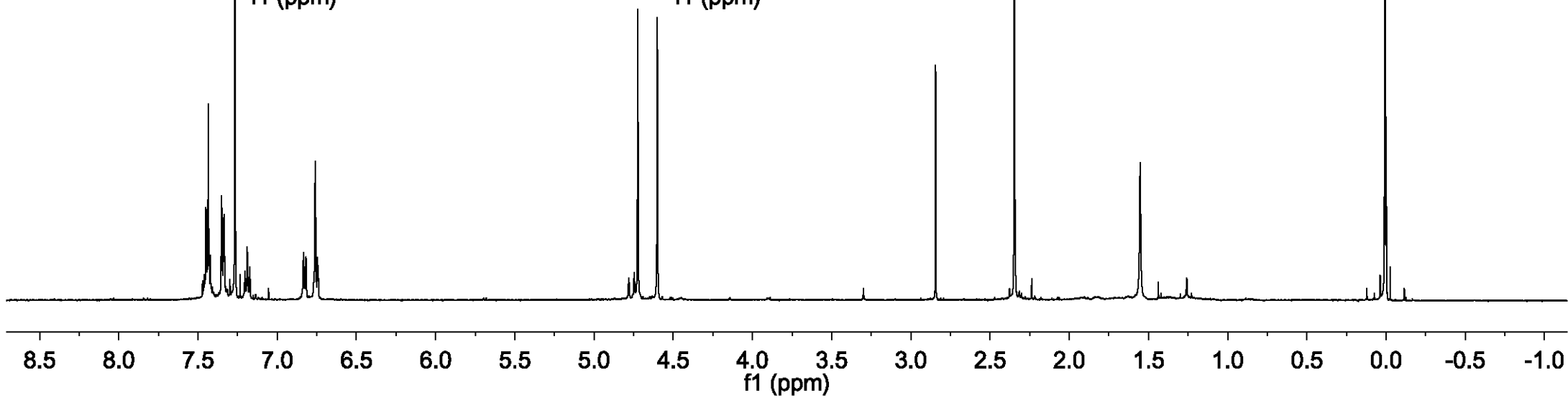
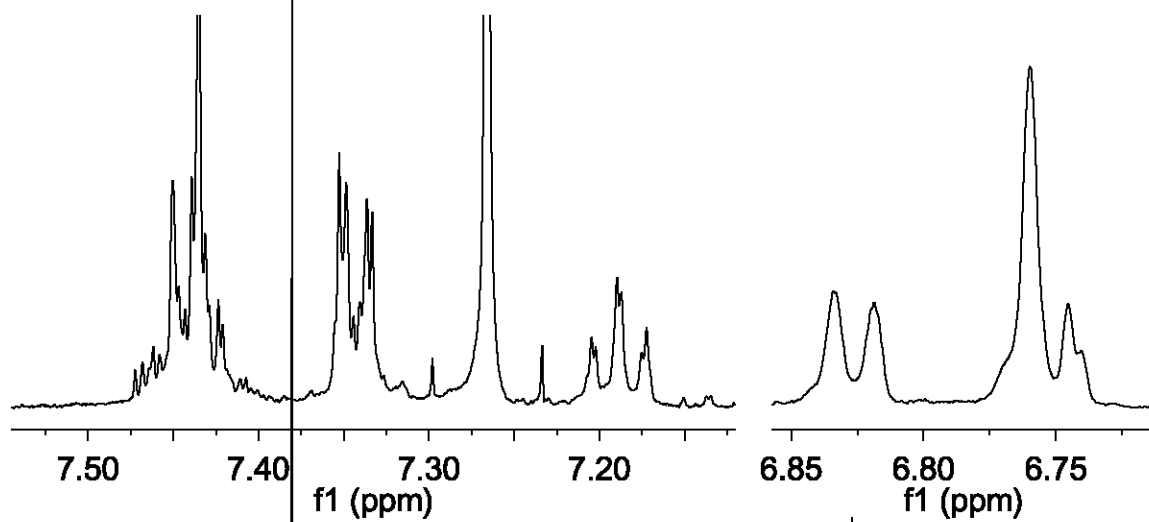
CDCl₃, 500 MHz**32h**

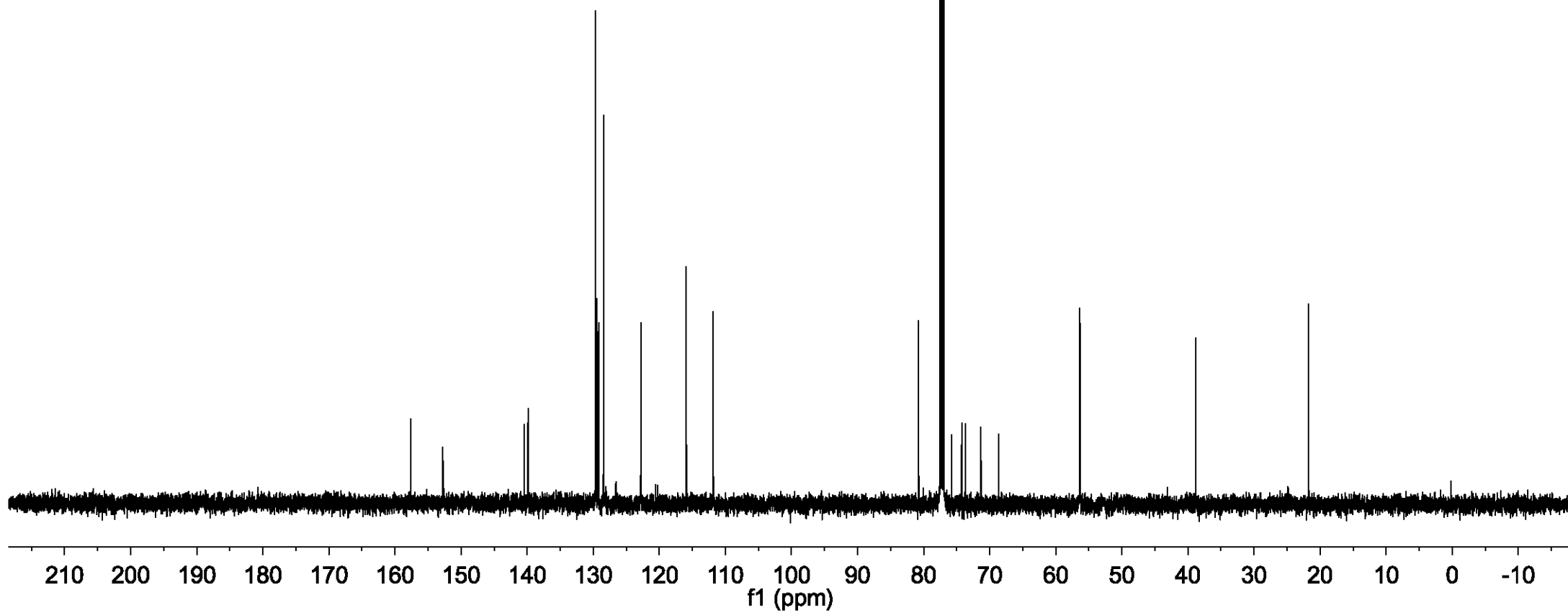
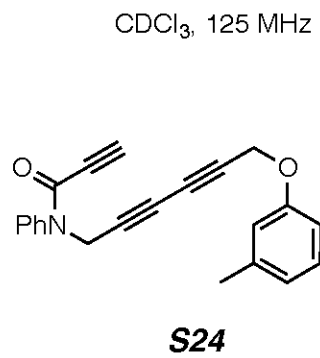
CDCl₃, 125 MHz**32h**

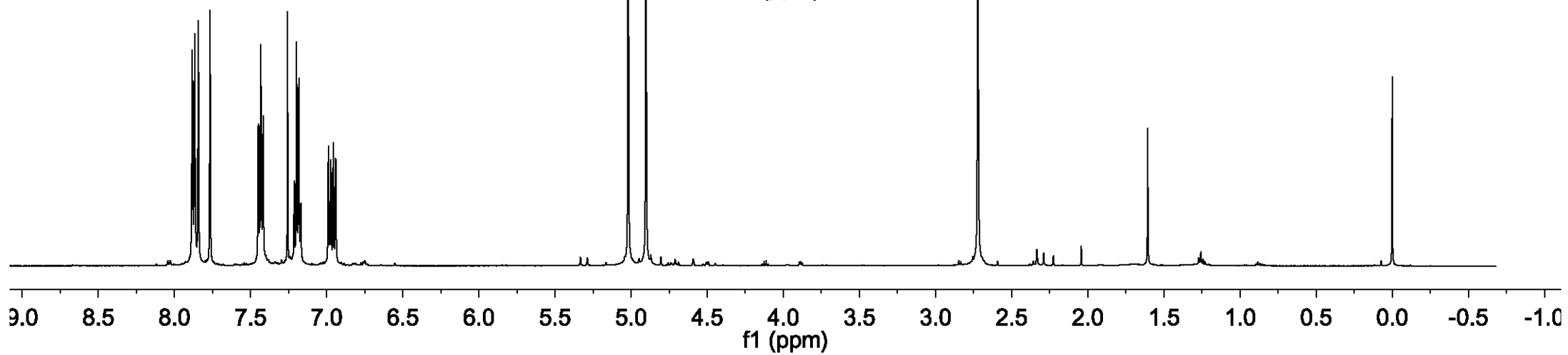
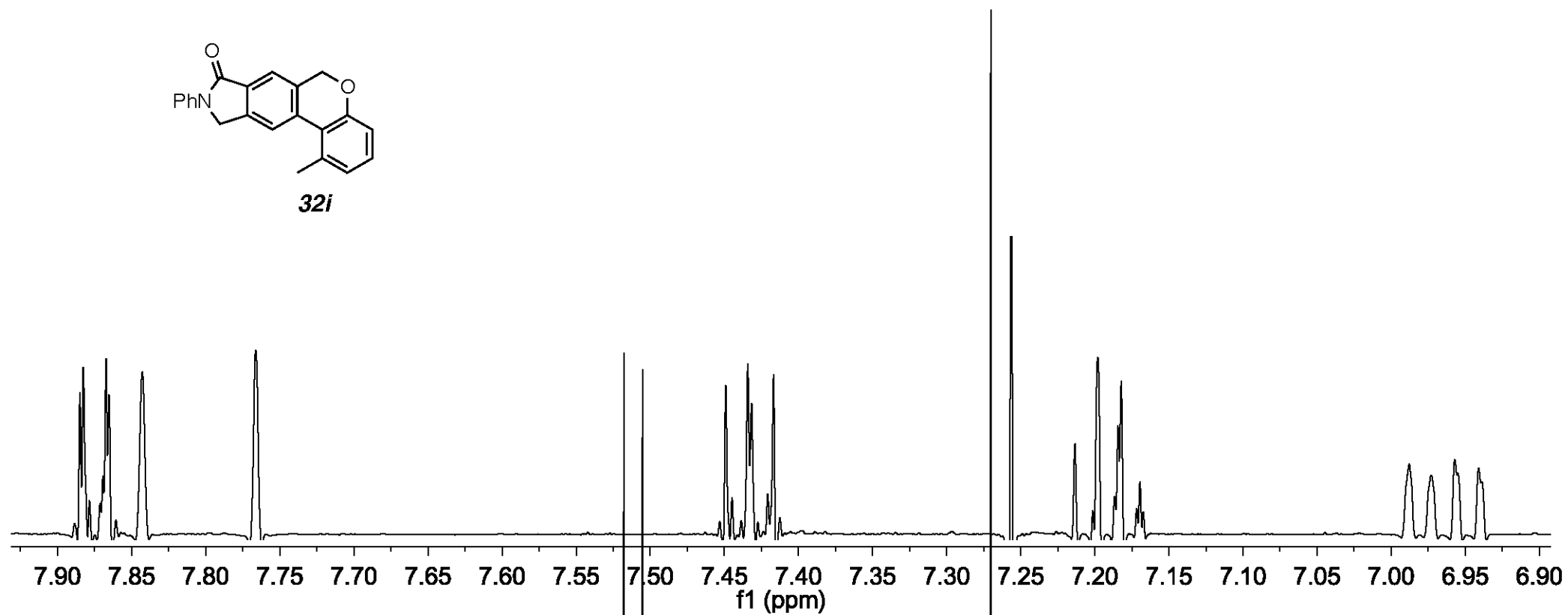
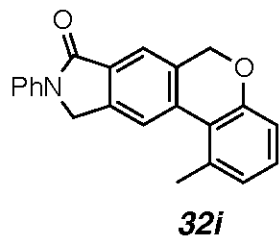
CDCl₃, 500 MHz**S22**

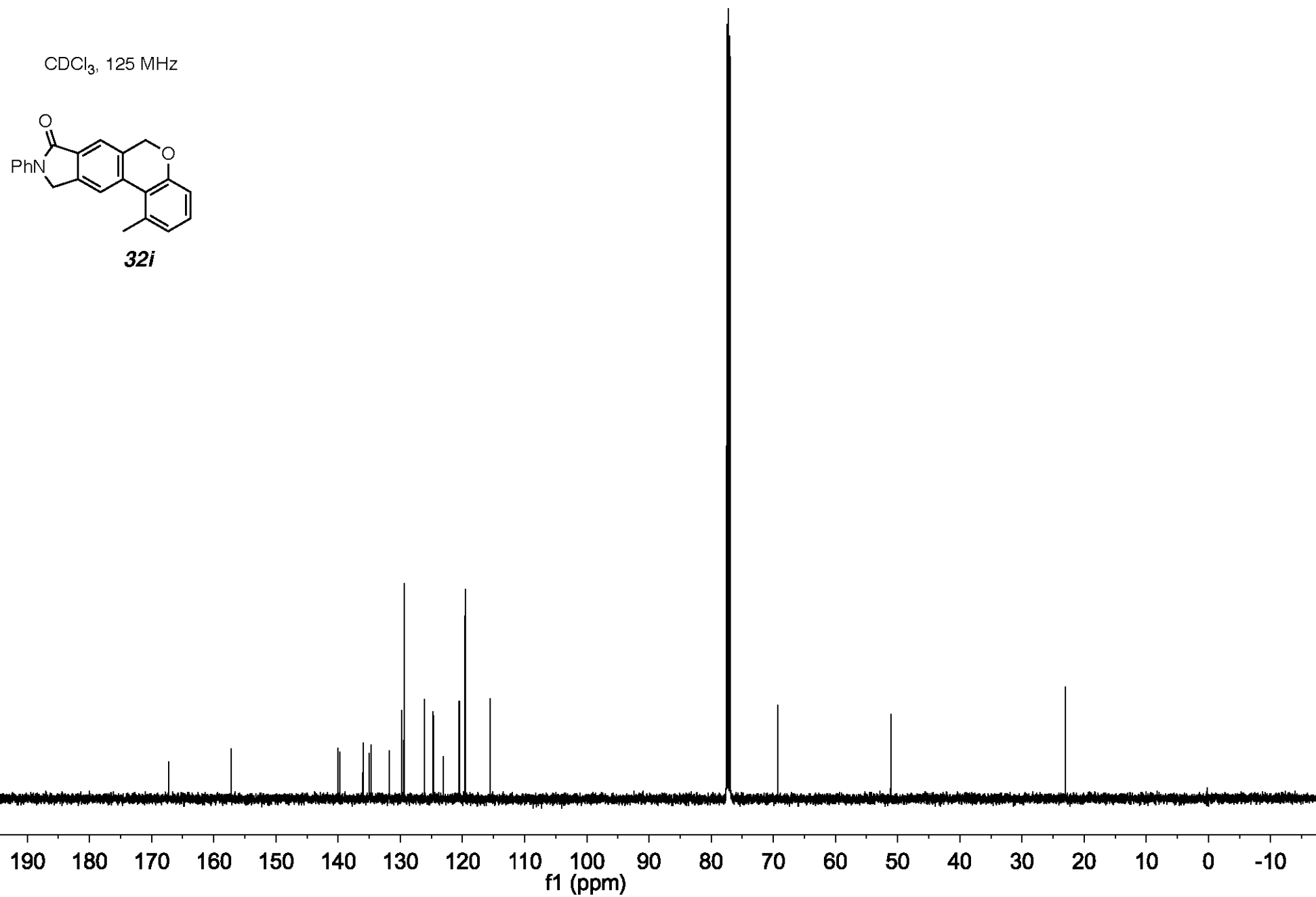
CDCl₃, 125 MHz**S22**

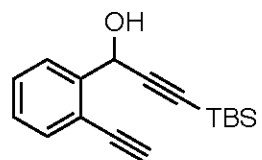
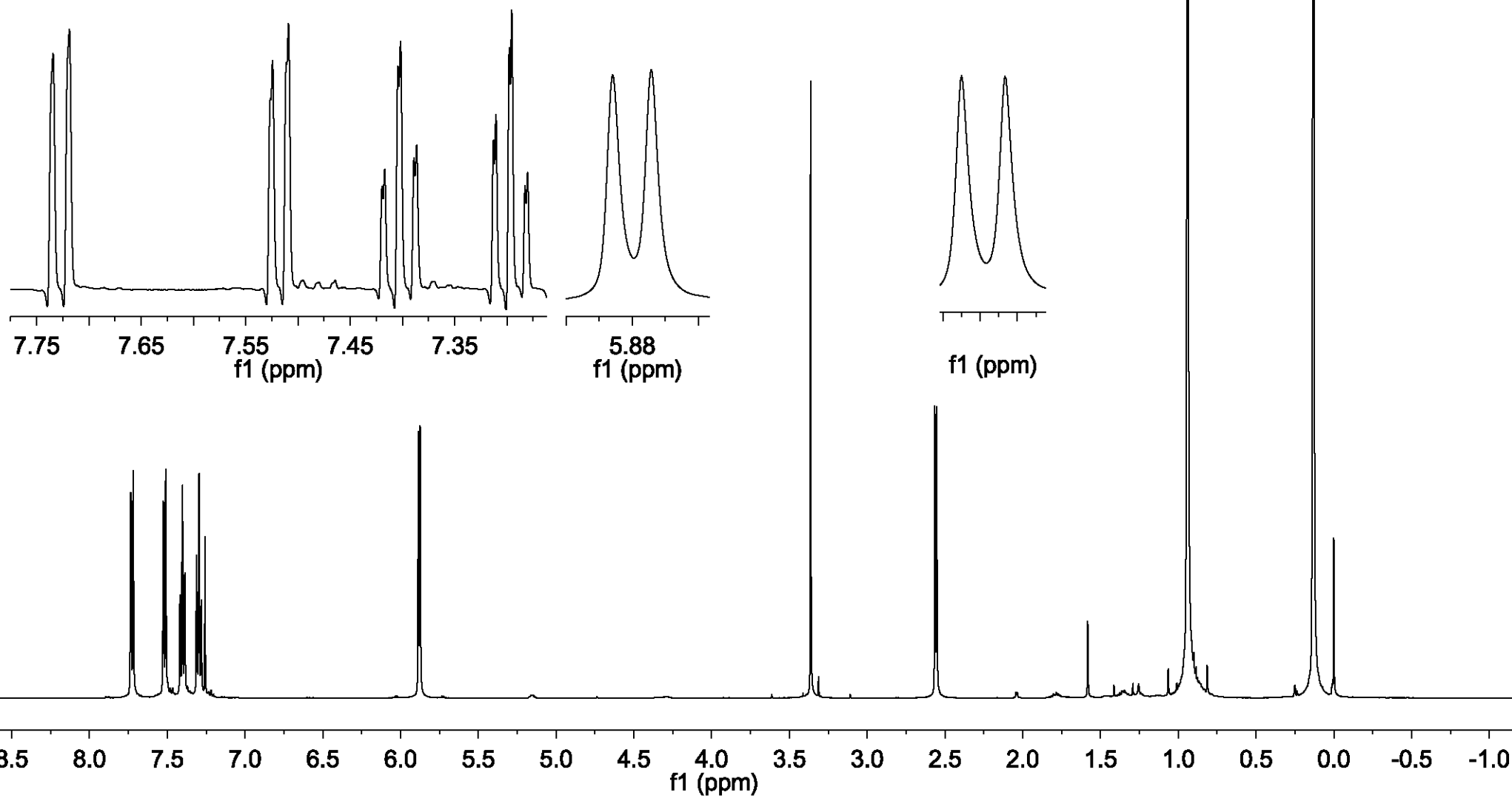
CDCl₃, 500 MHz**S23**

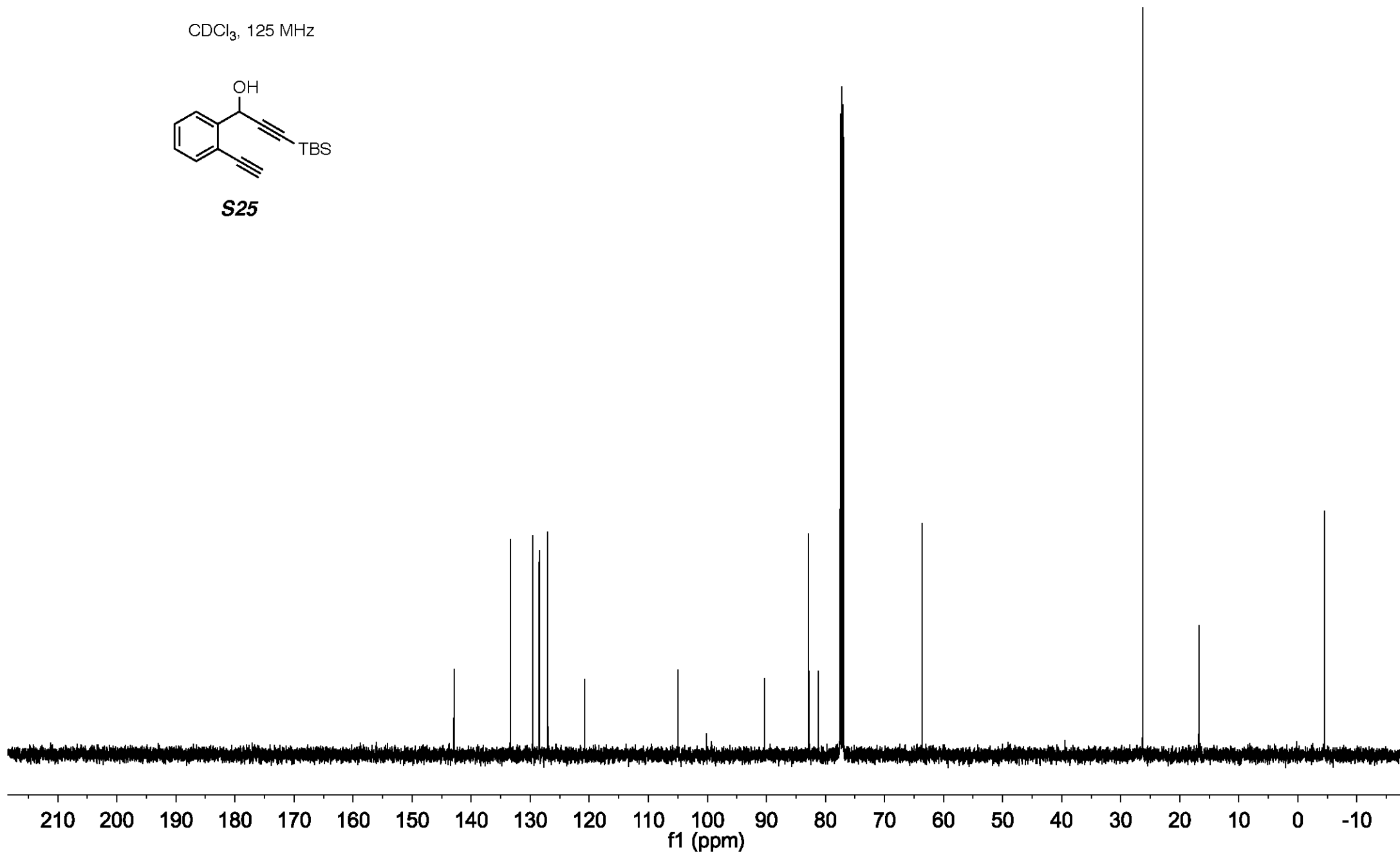
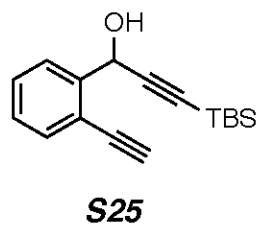
CDCl₃, 500 MHz**S24**

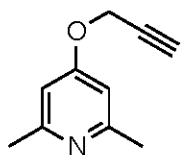
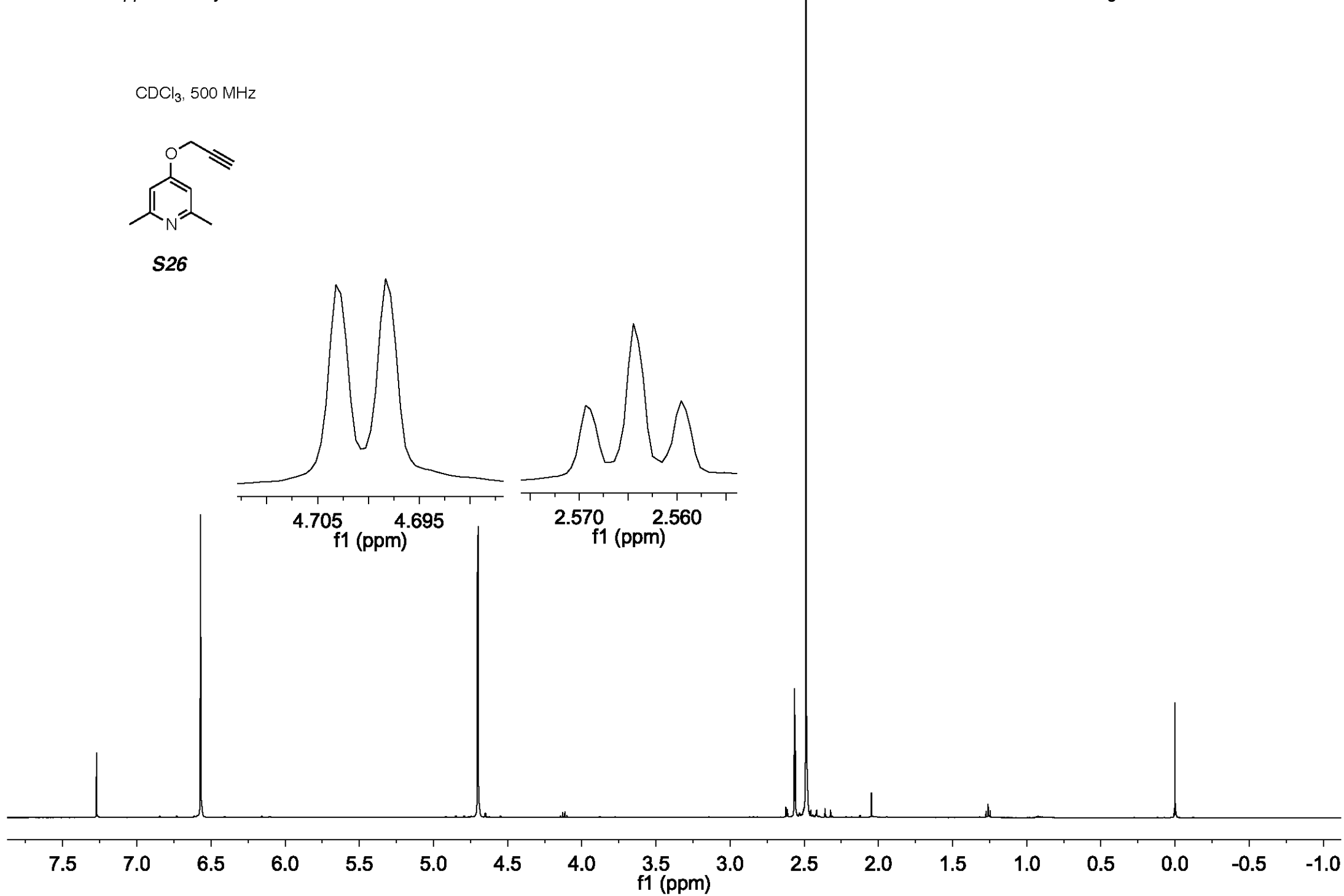
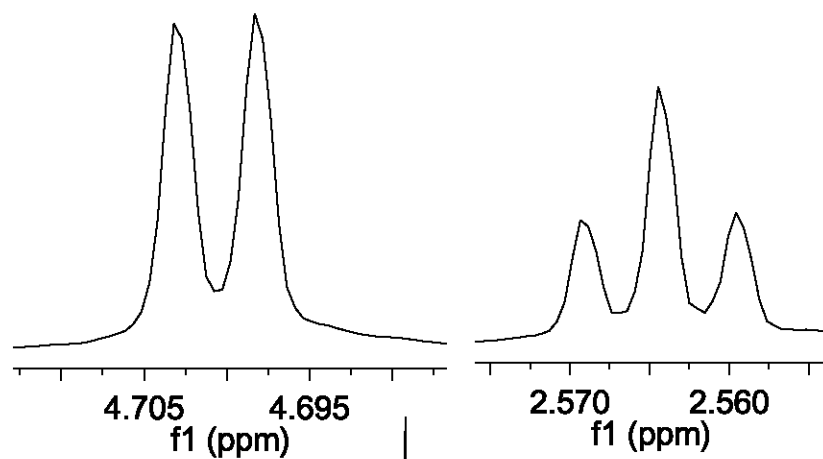


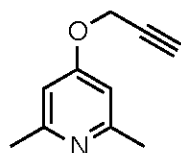
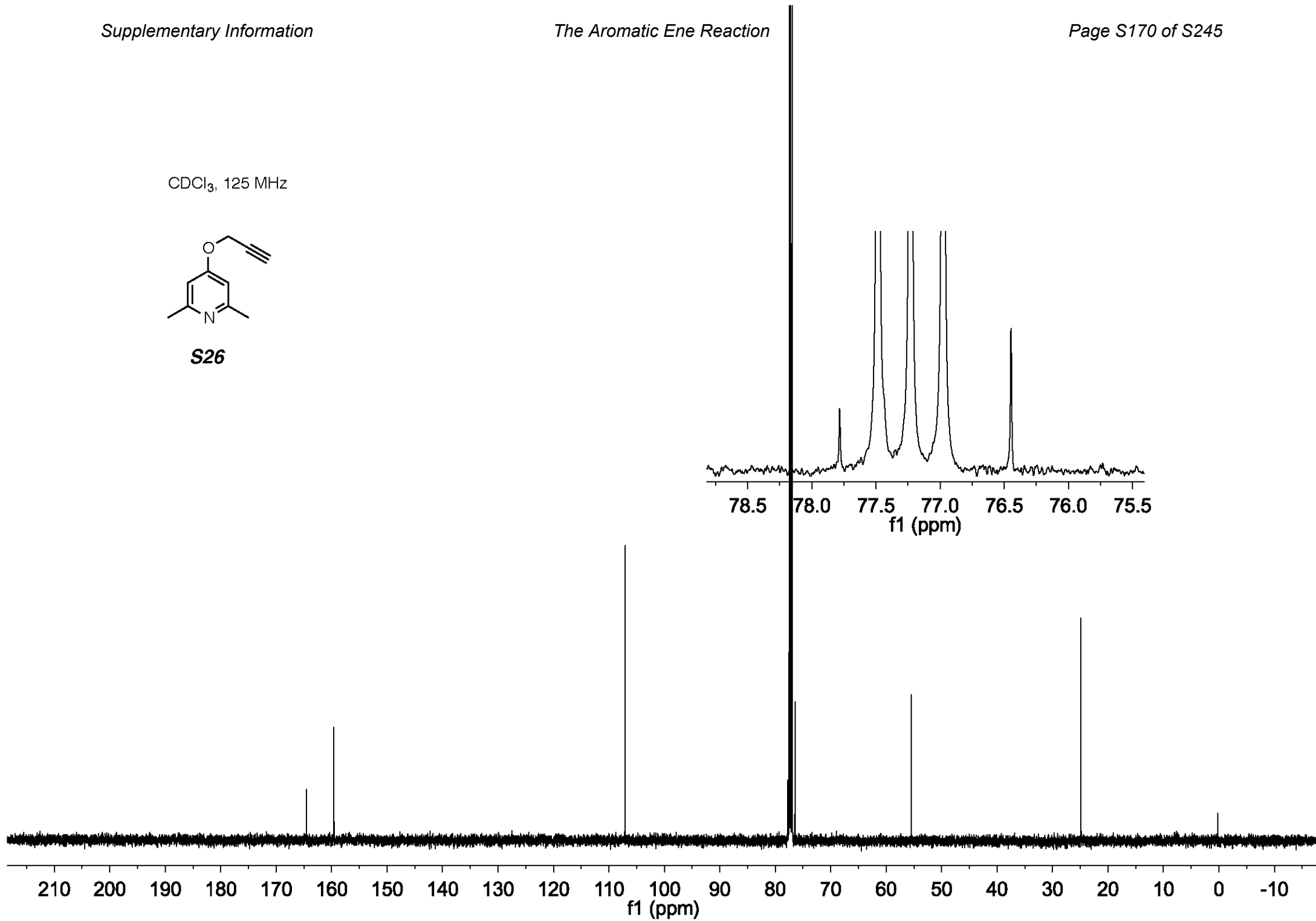
CDCl₃, 500 MHz

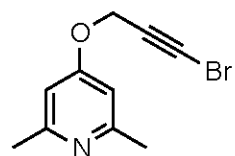
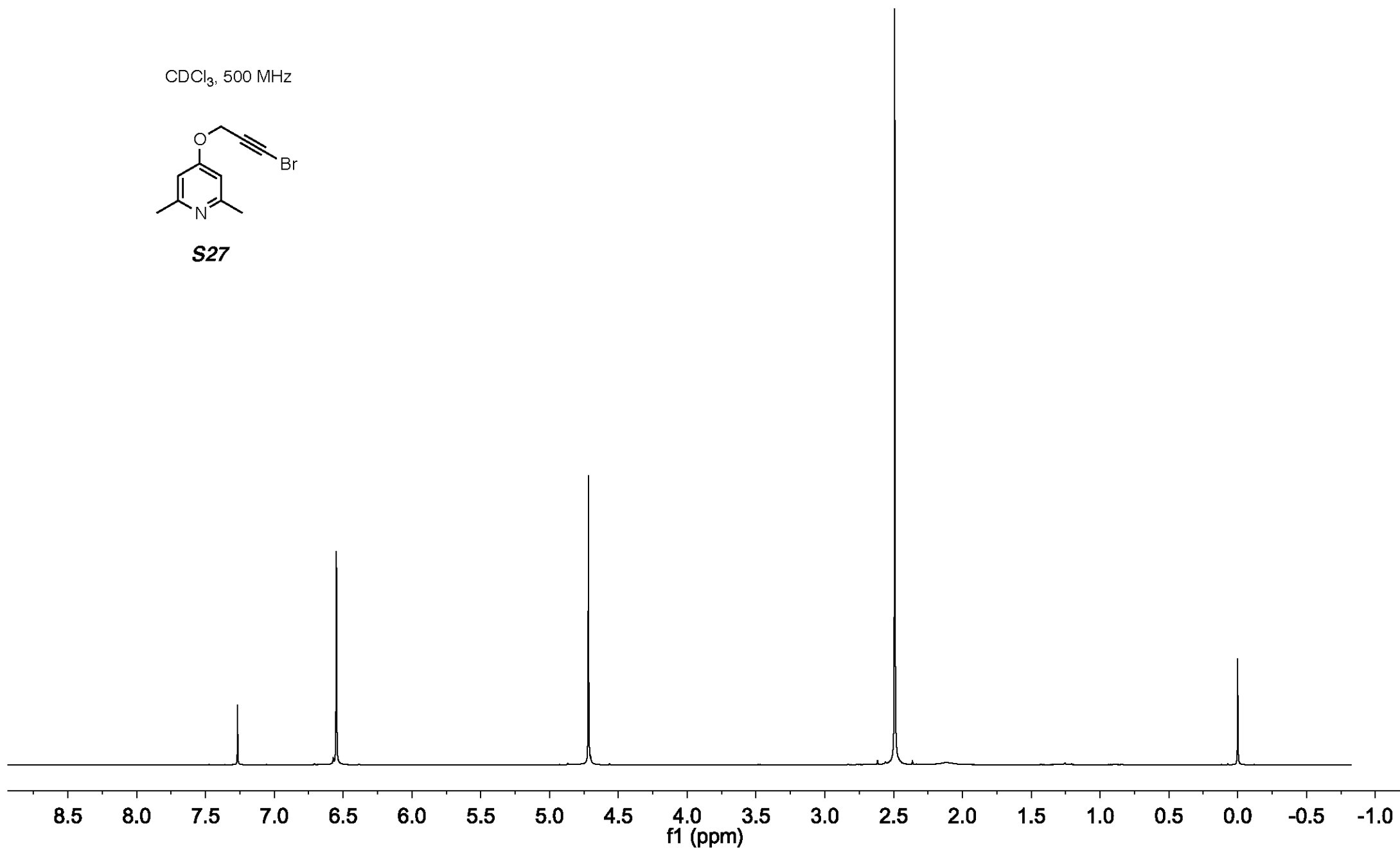


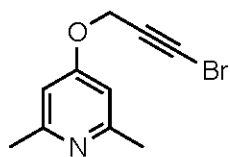
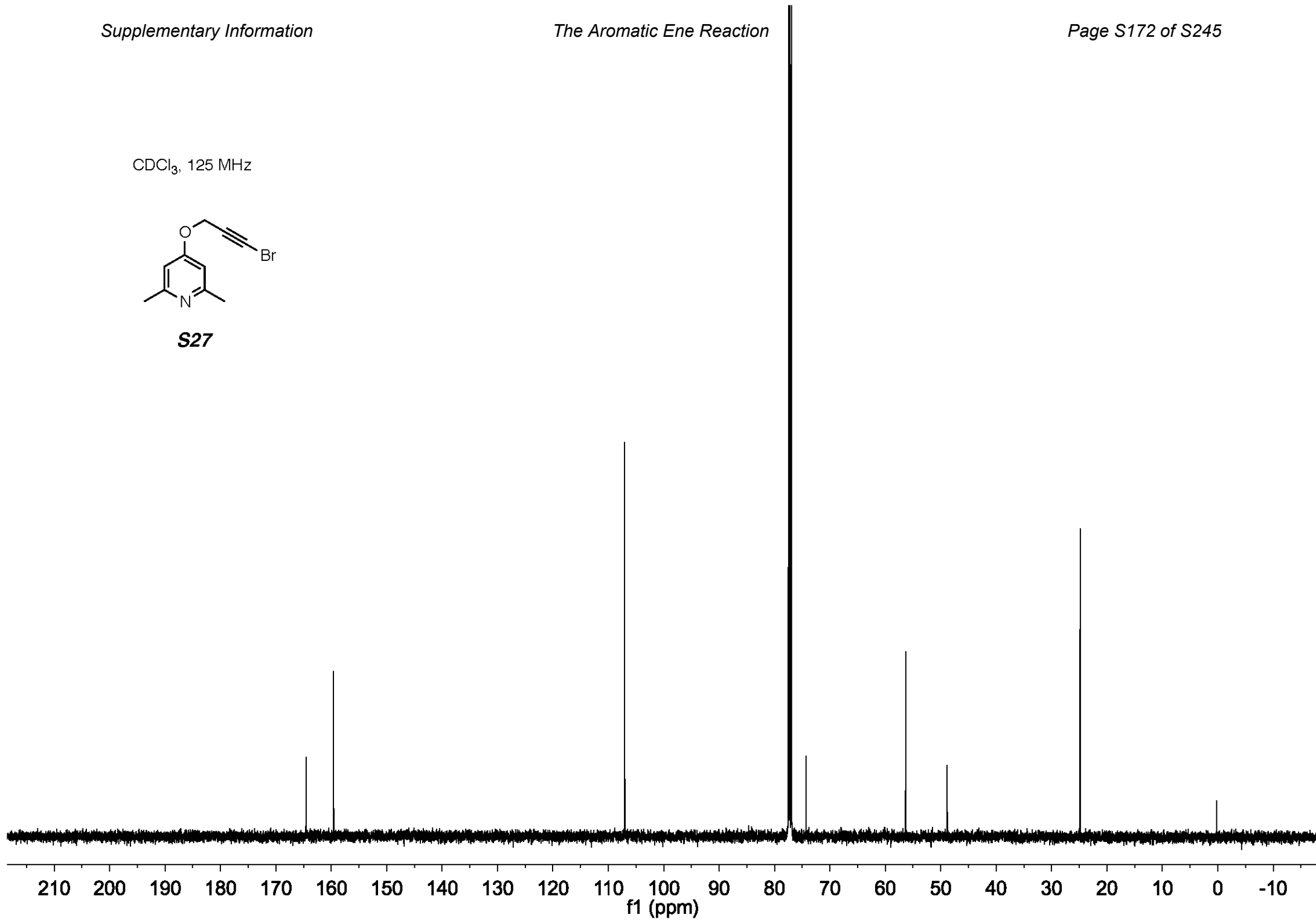
CDCl₃, 500 MHz**S25**

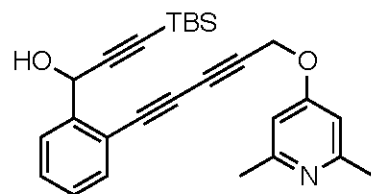
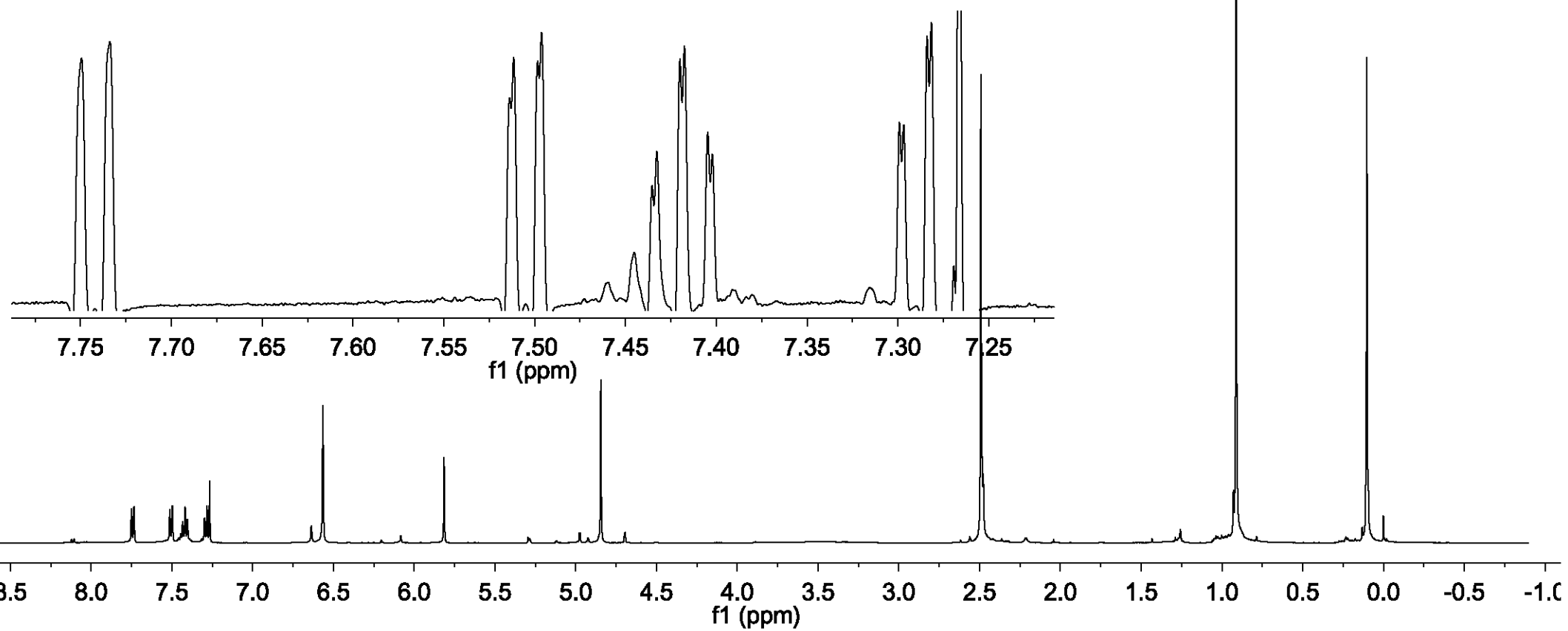
CDCl₃, 125 MHz

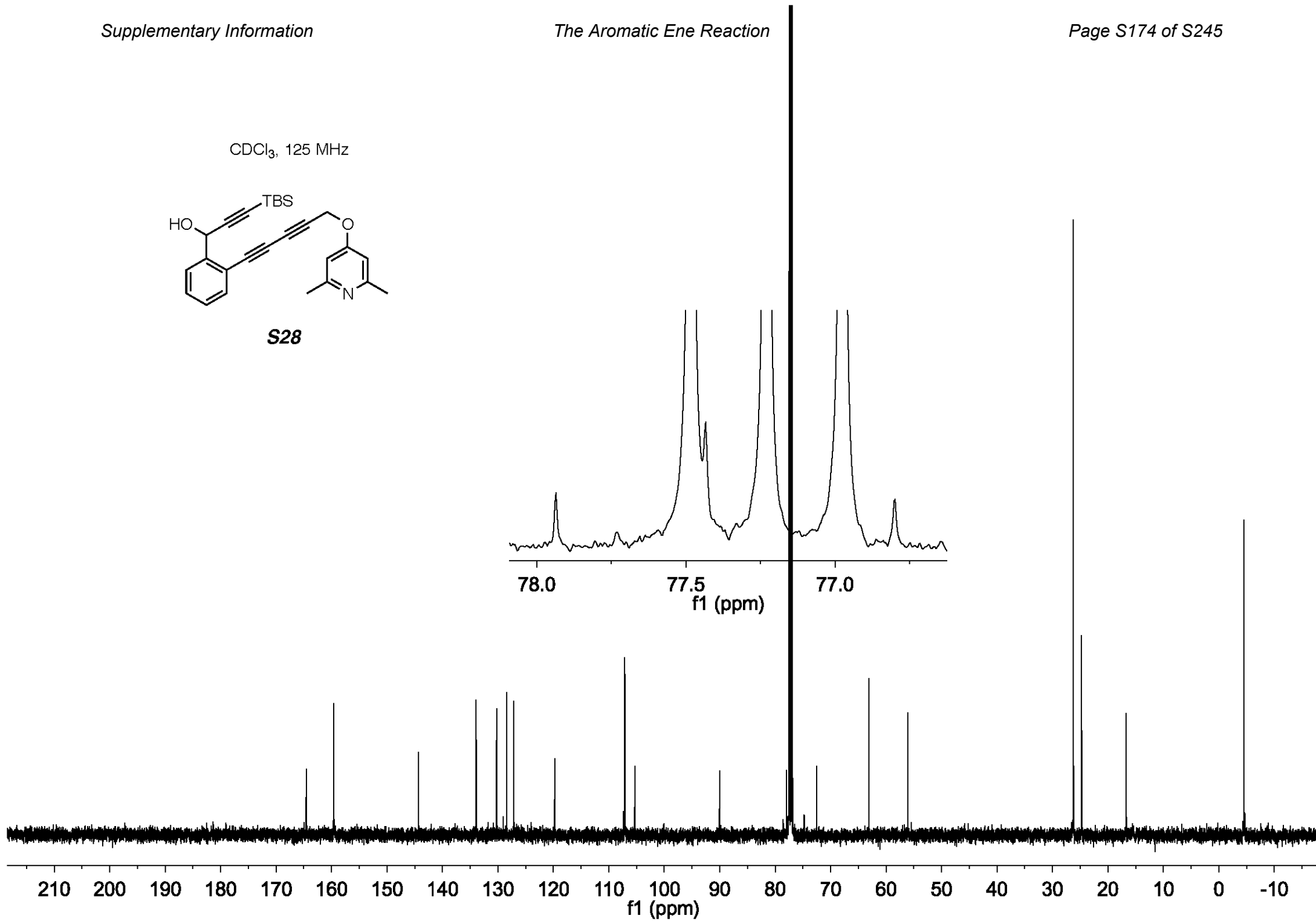
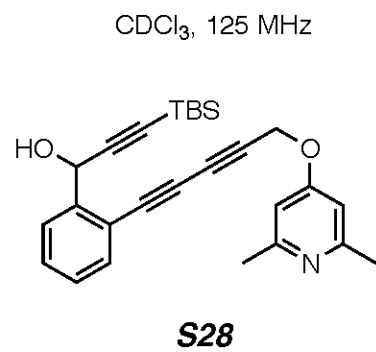
CDCl₃, 500 MHz**S26**

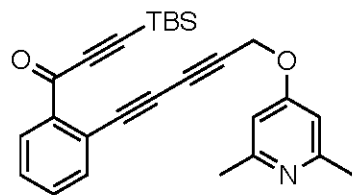
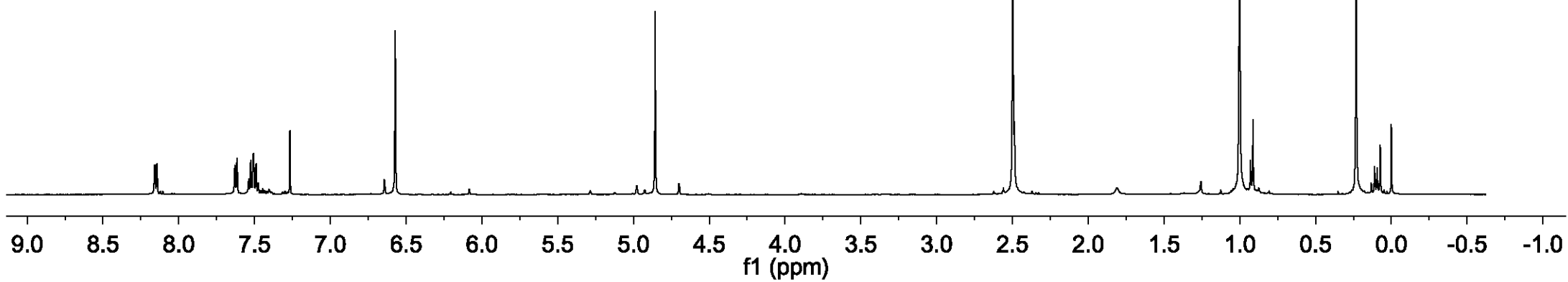
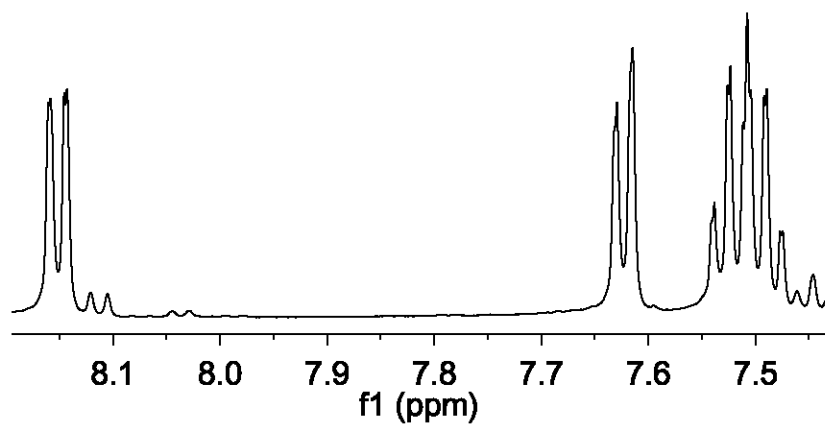
CDCl₃, 125 MHz**S26**

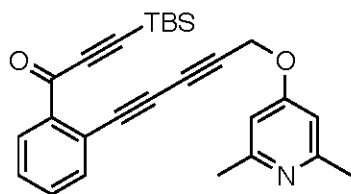
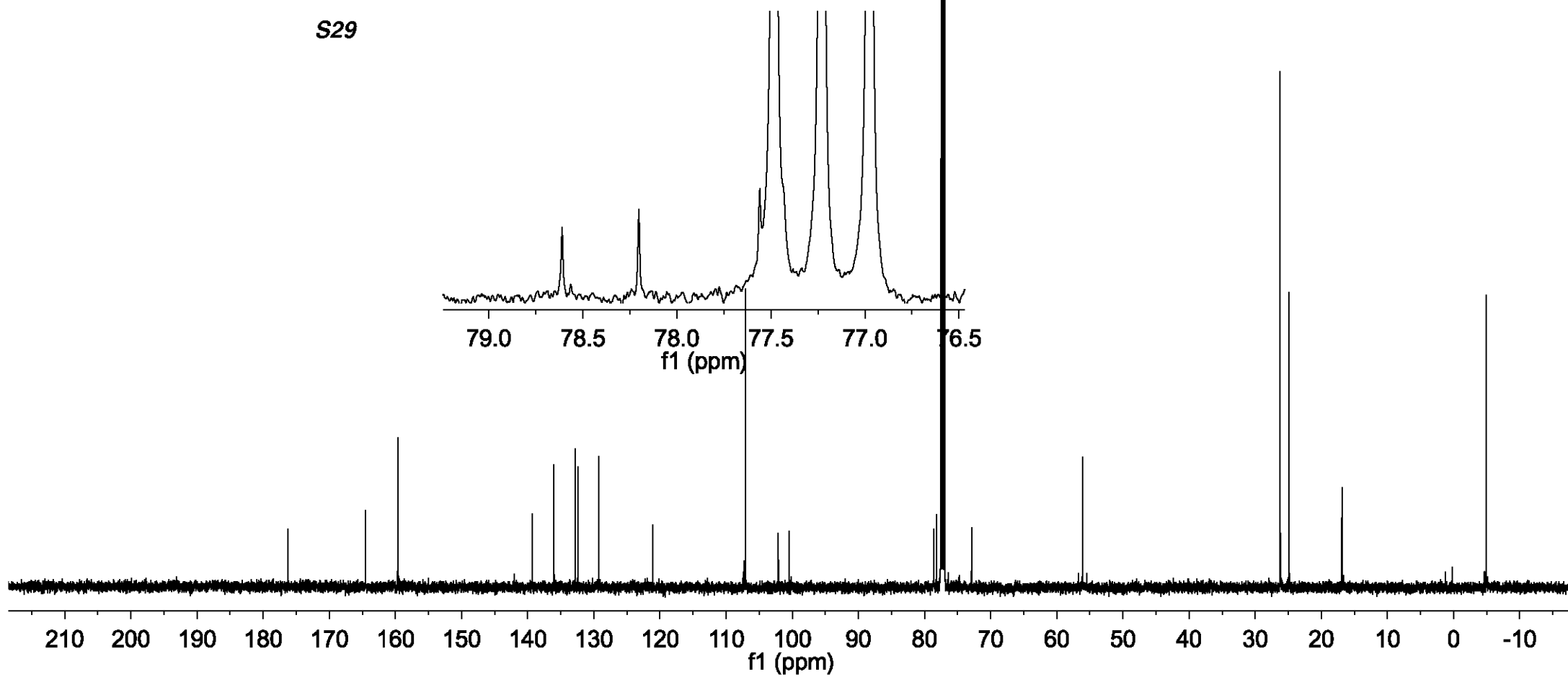
CDCl₃, 500 MHz**S27**

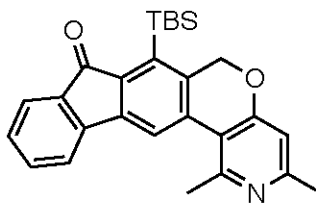
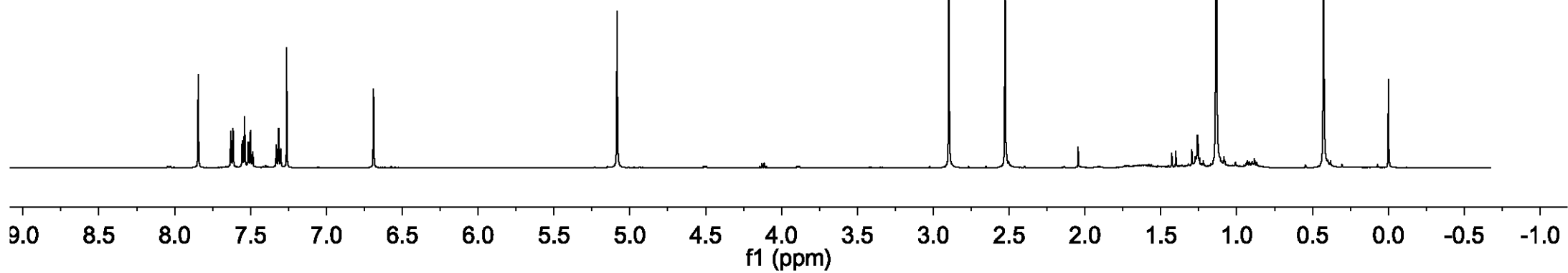
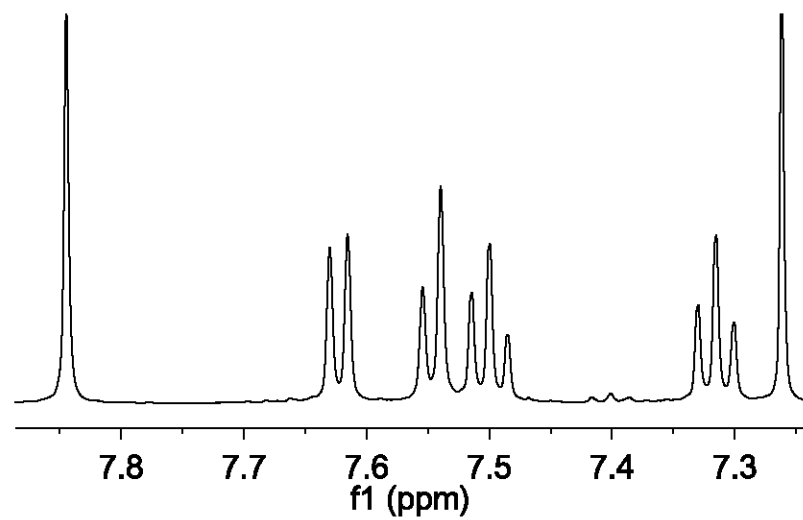
CDCl₃, 125 MHz**S27**

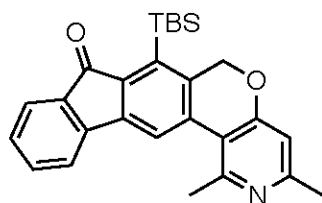
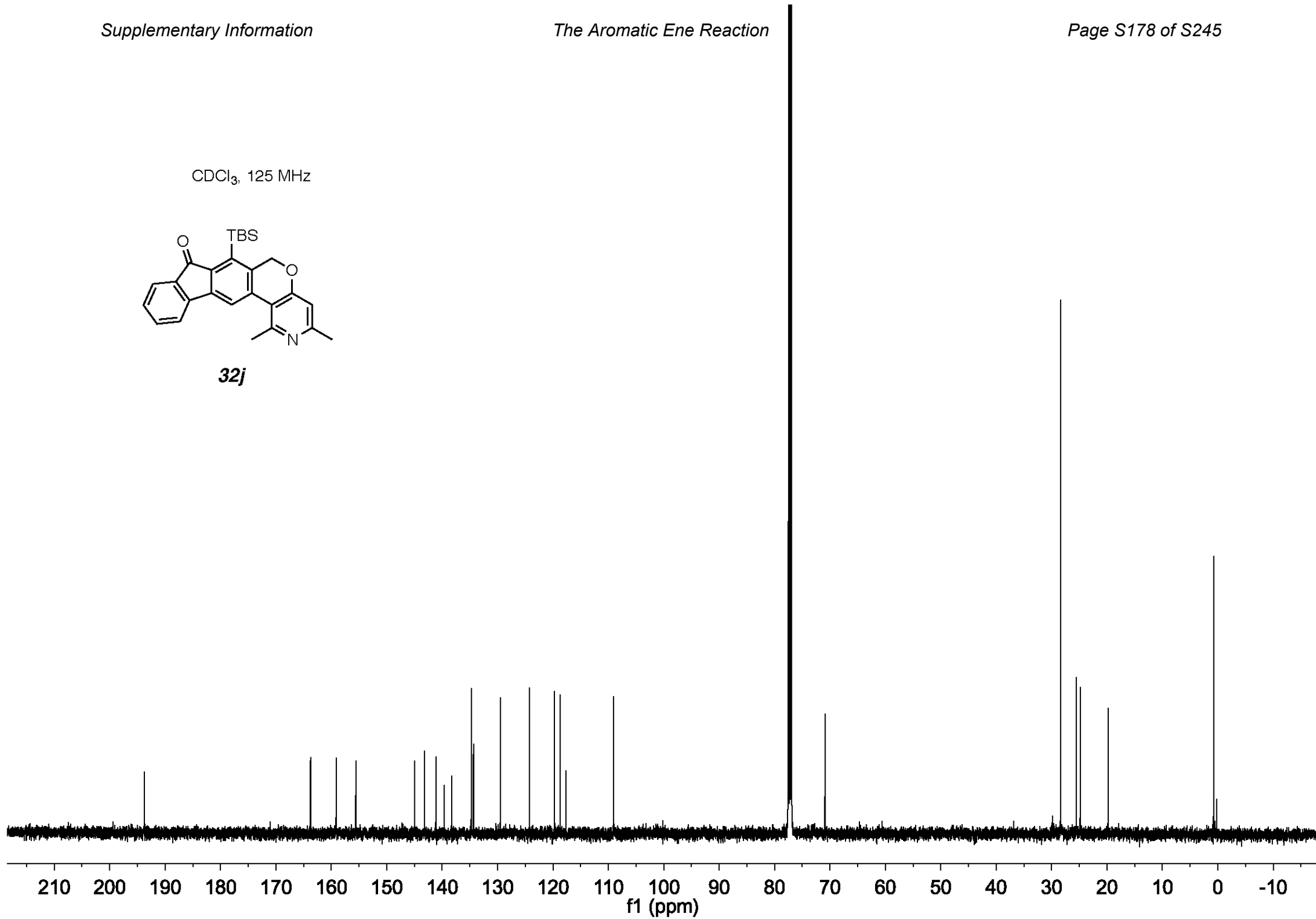
CDCl₃, 500 MHz**S28**

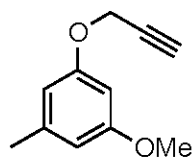
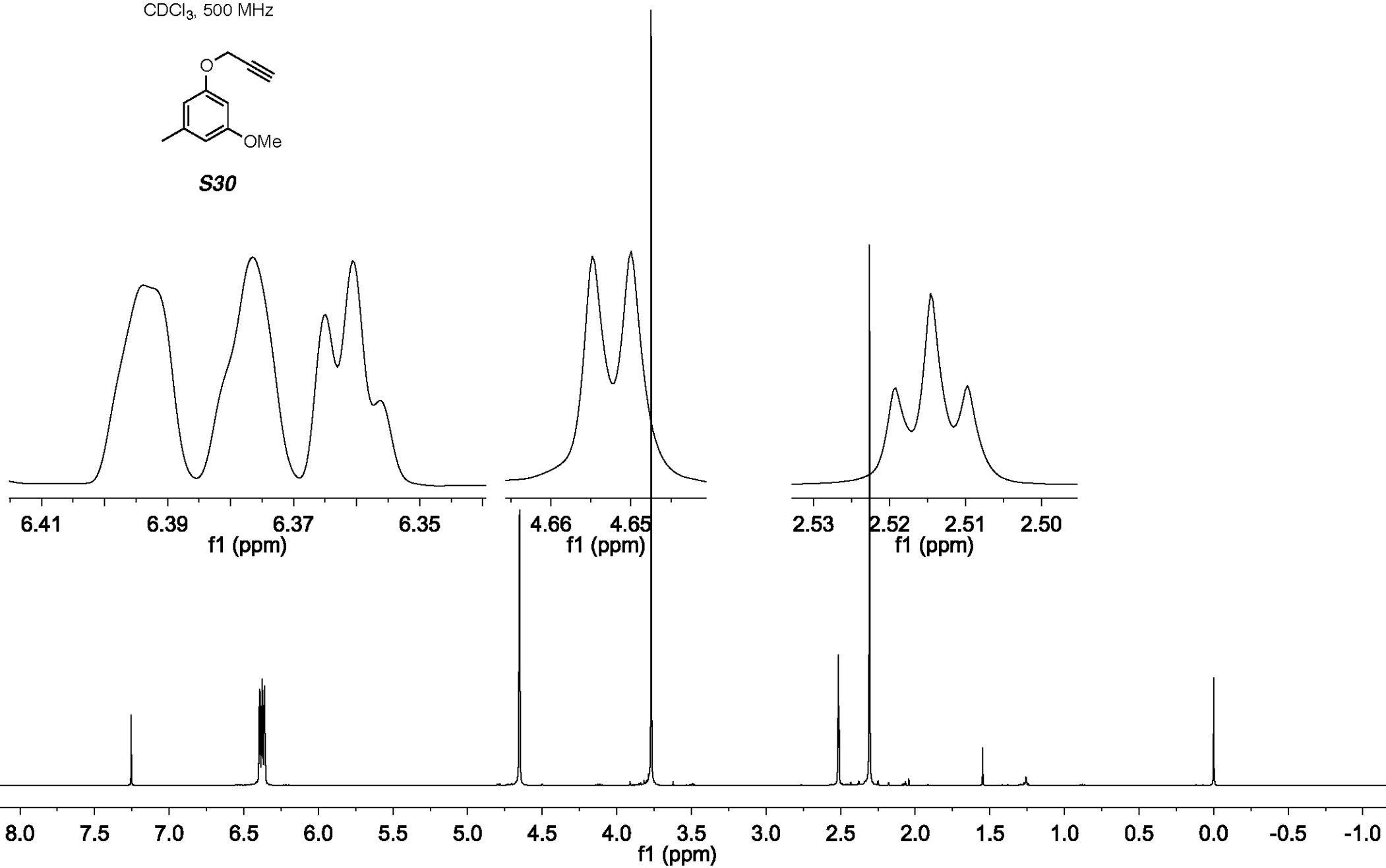


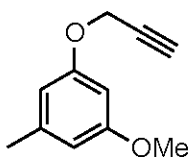
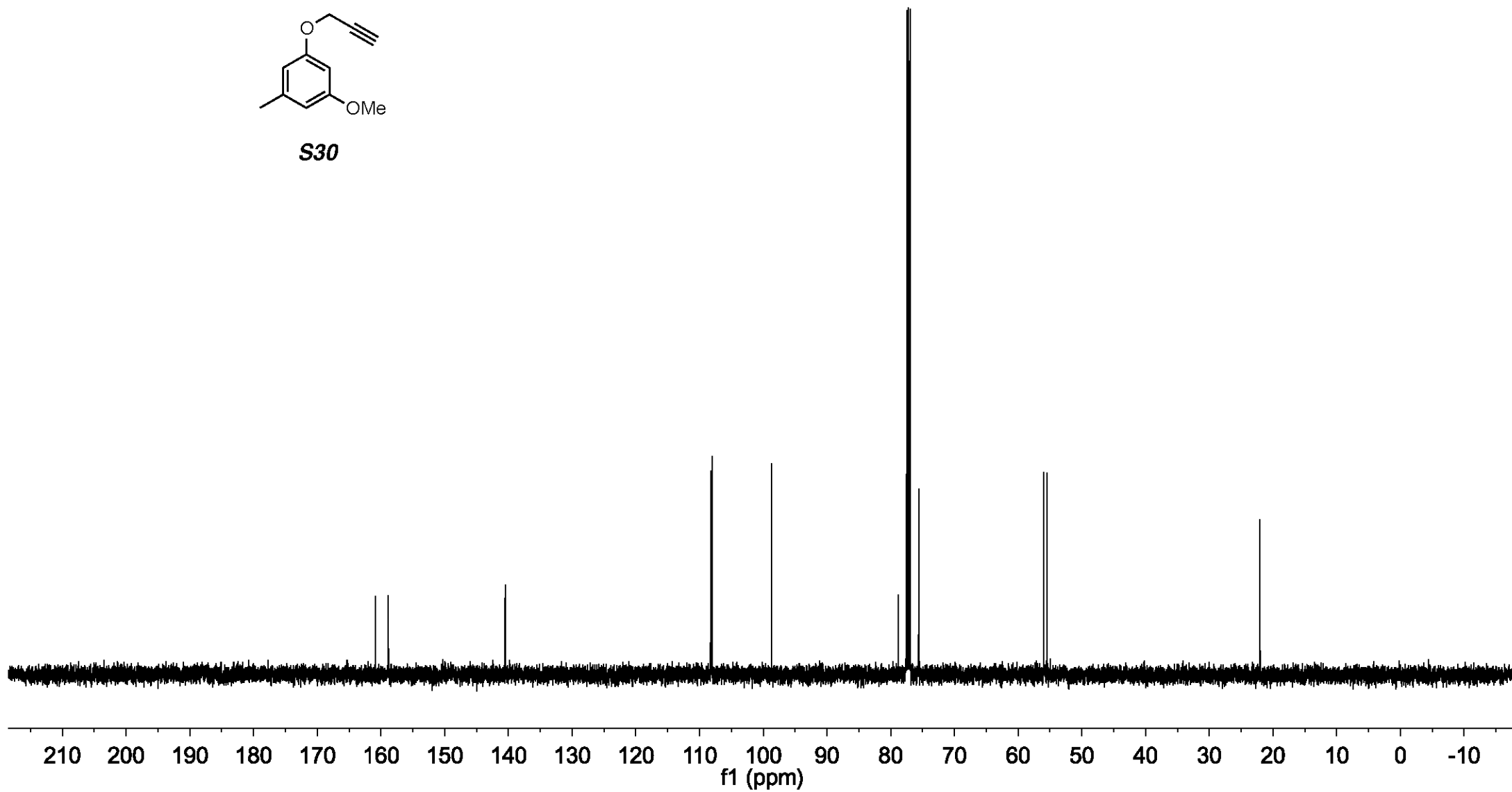
CDCl₃, 500 MHz**S29**

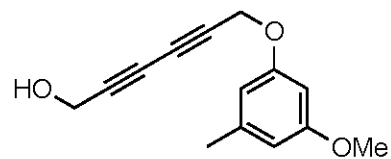
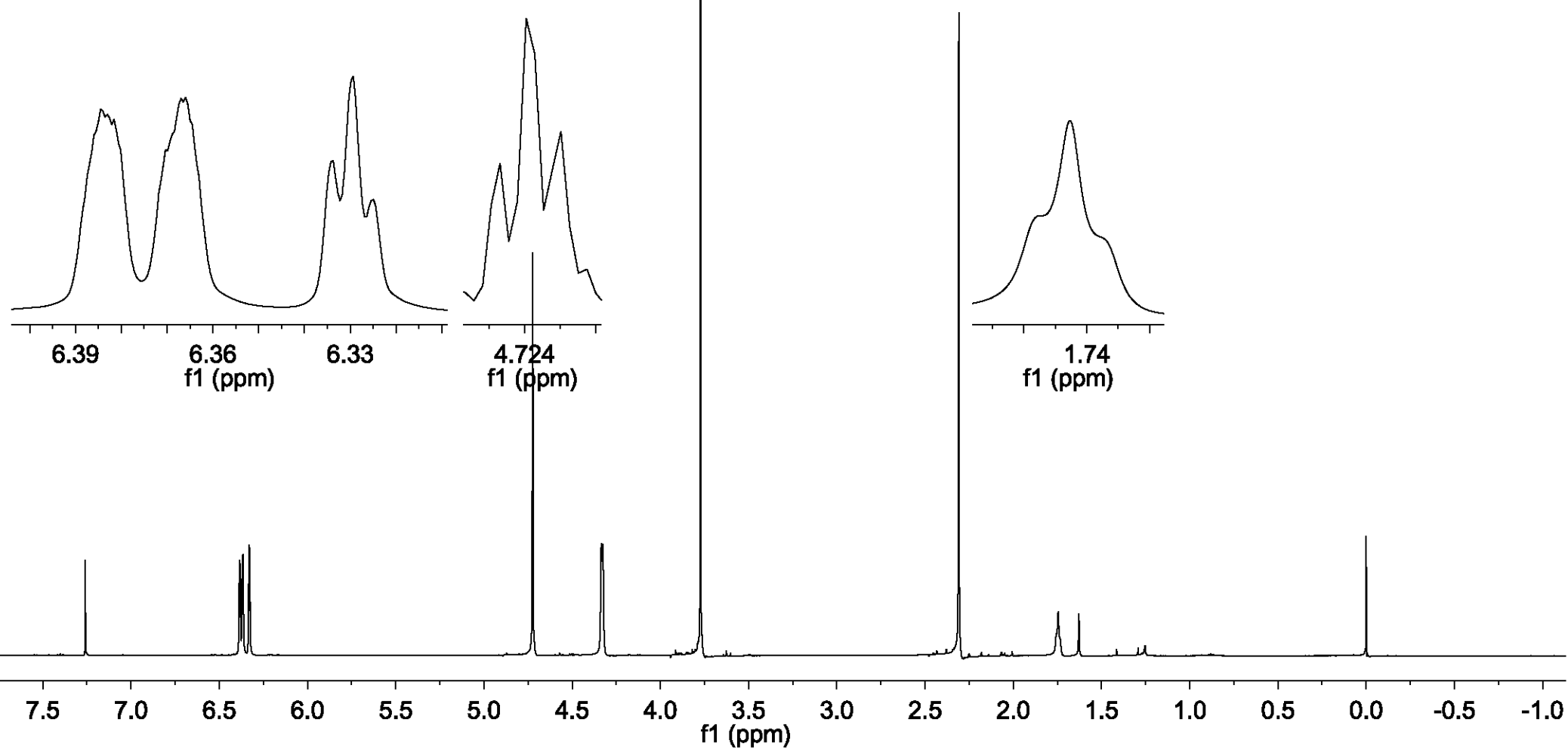
CDCl₃, 125 MHz**S29**

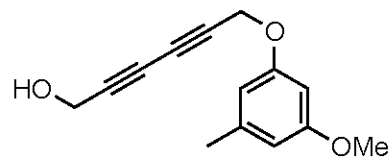
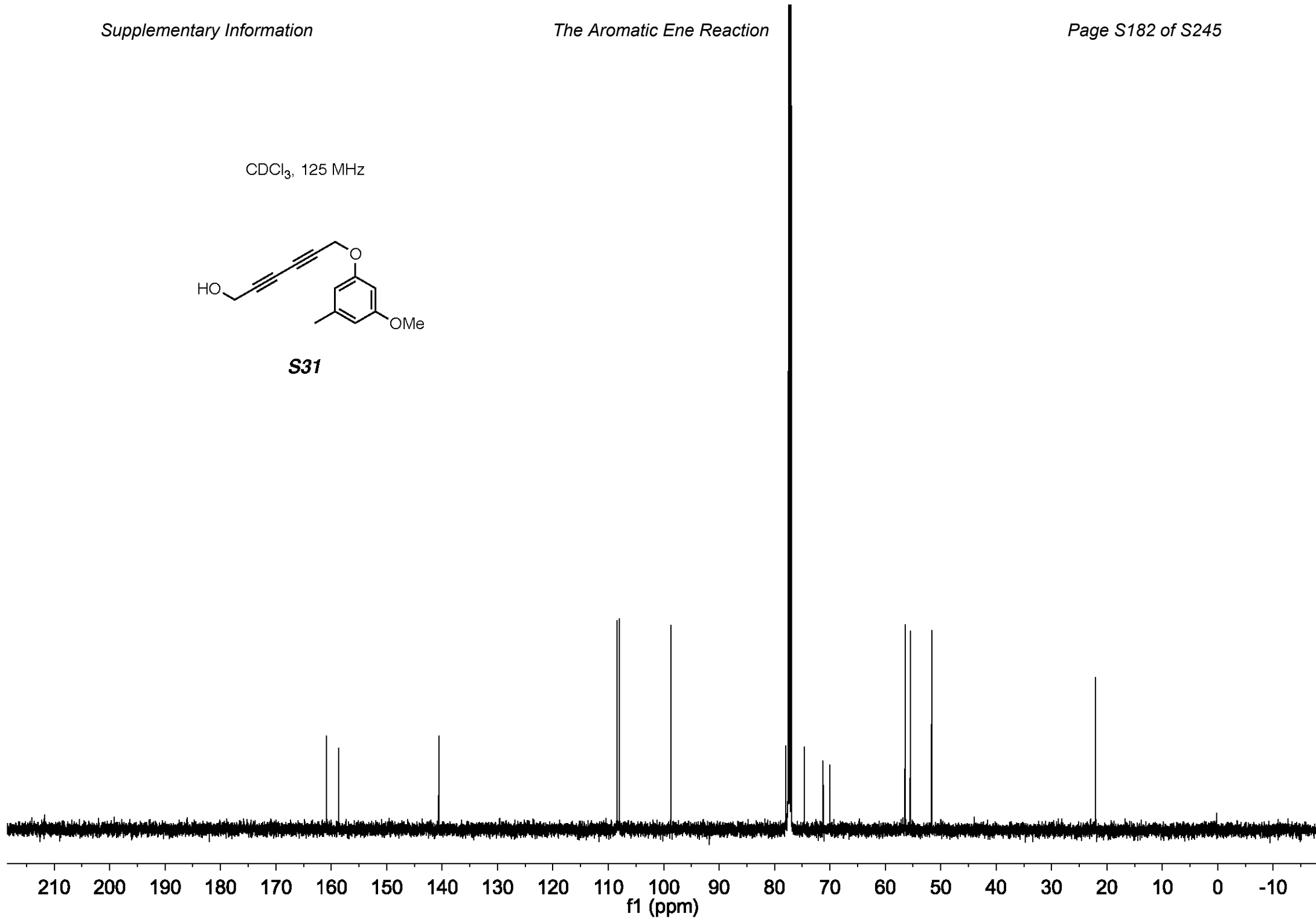
CDCl₃, 500 MHz**32j**

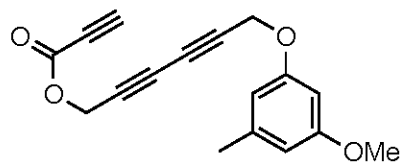
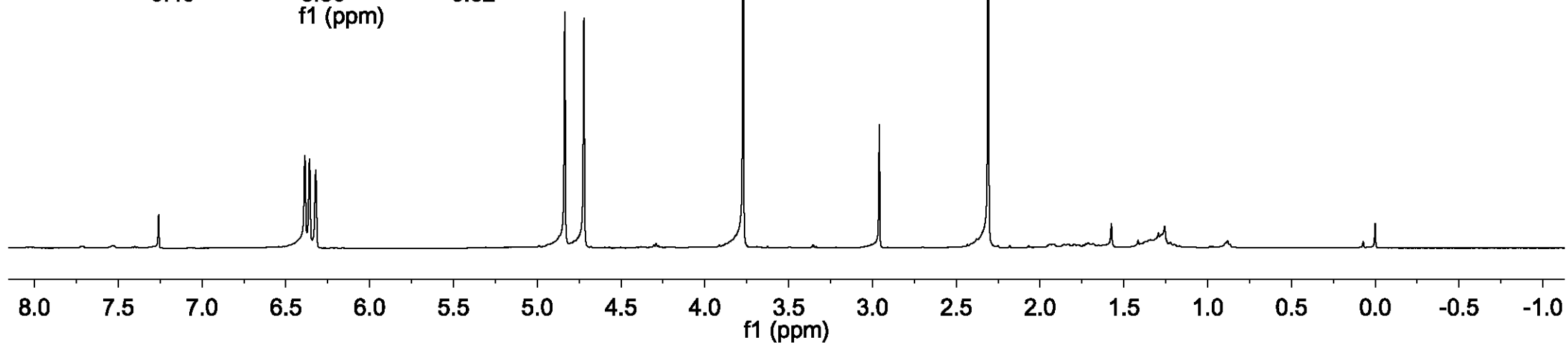
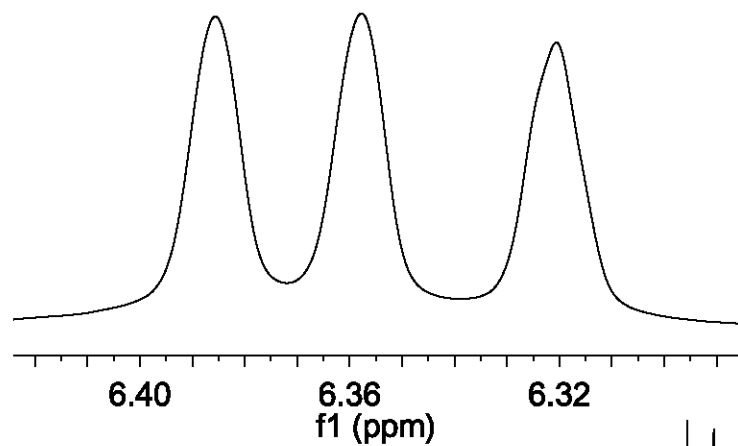
CDCl₃, 125 MHz**32j**

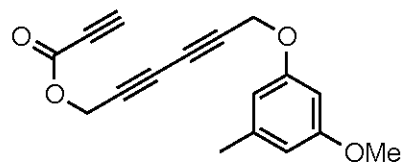
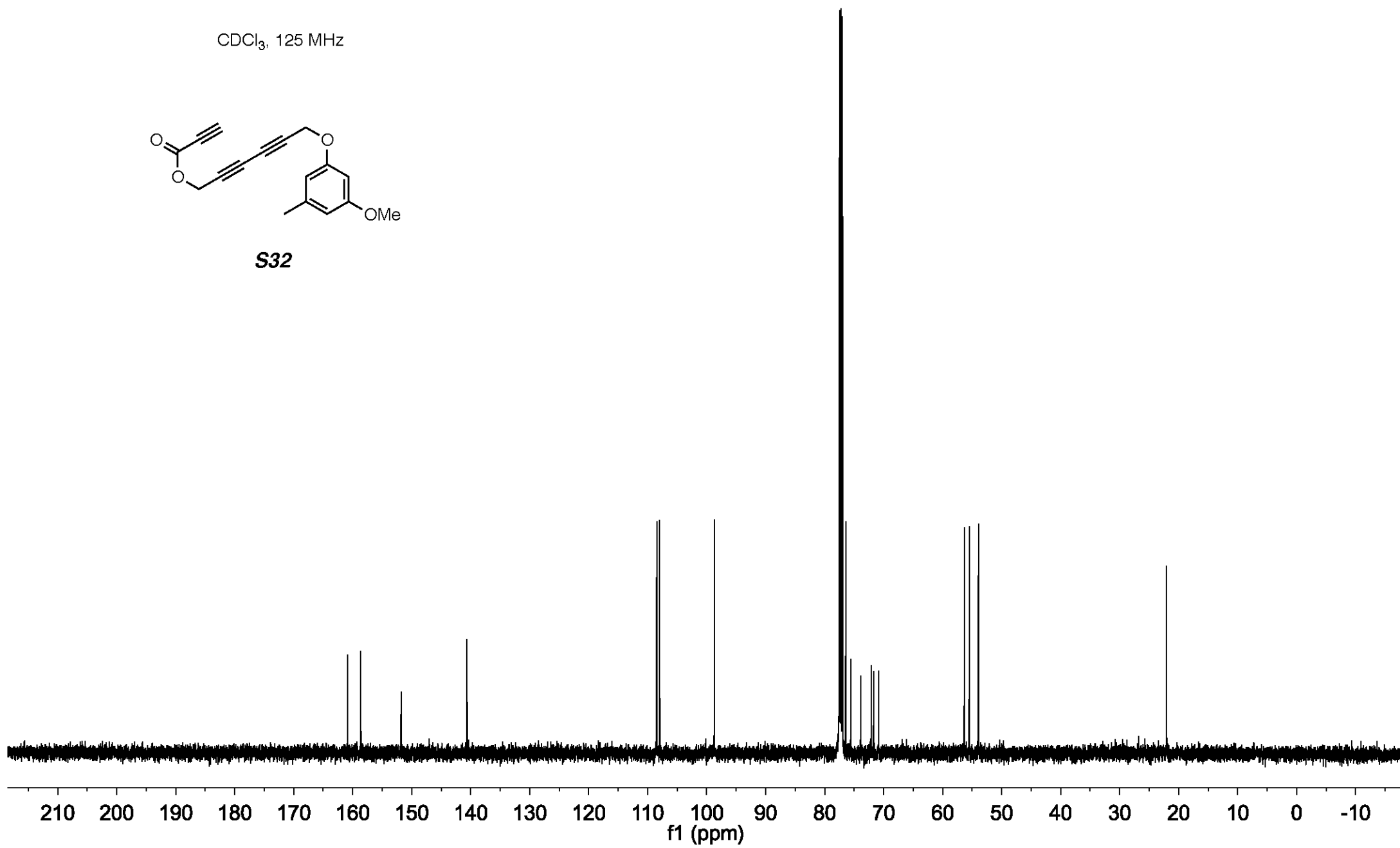
CDCl₃, 500 MHz**S30**

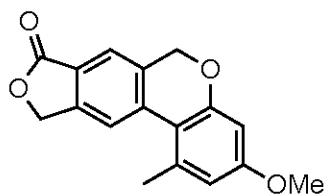
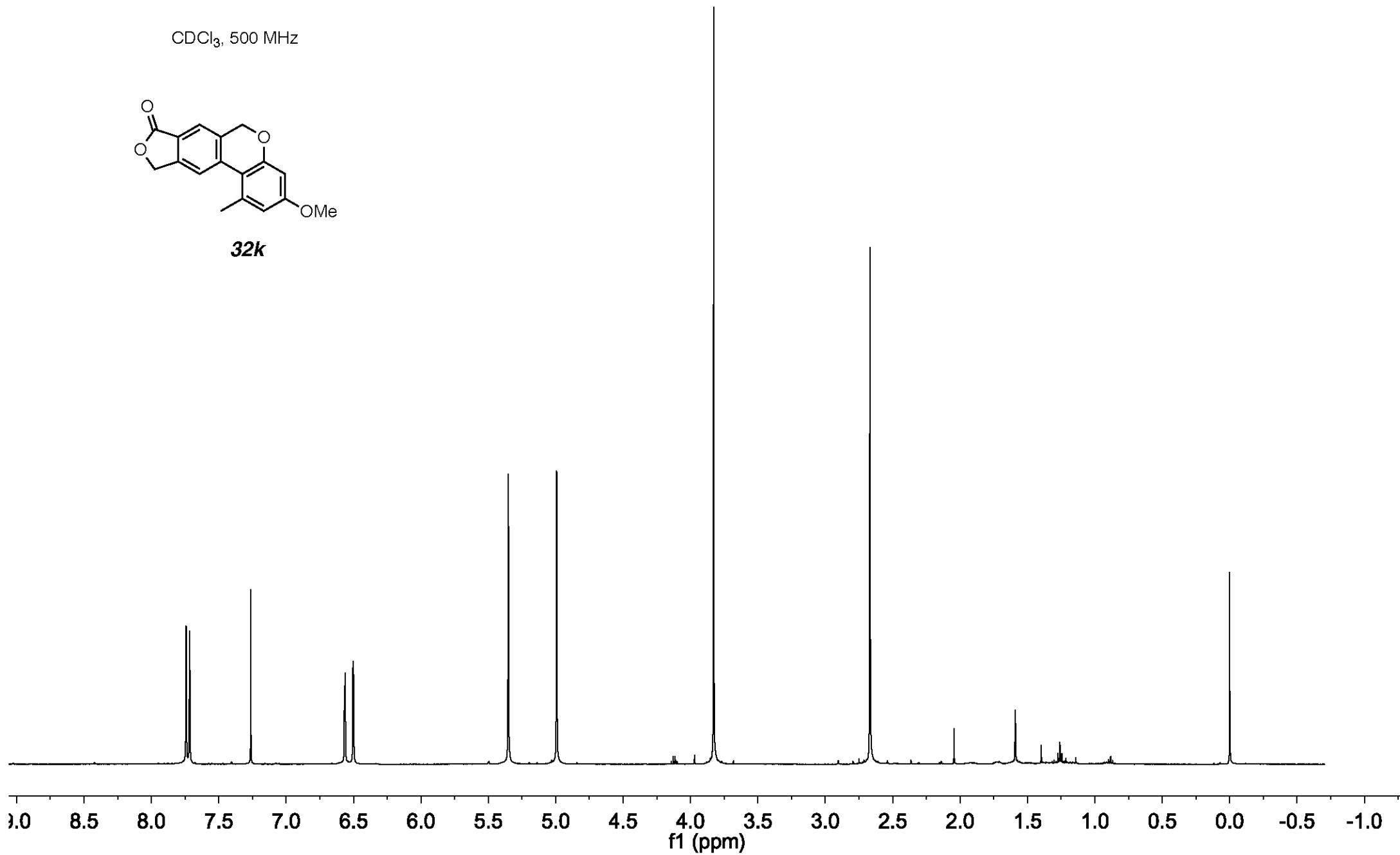
CDCl₃, 125 MHz**S30**

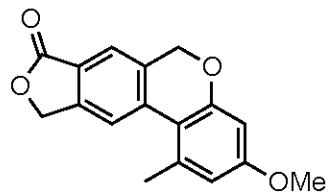
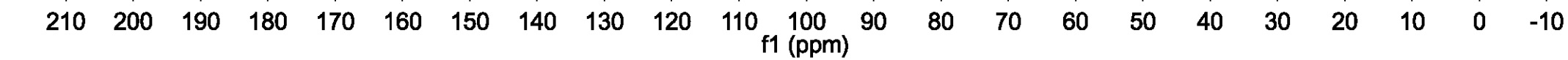
CDCl₃, 500 MHz**S31**

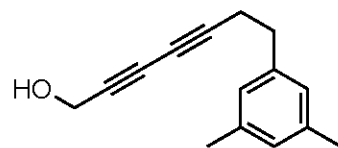
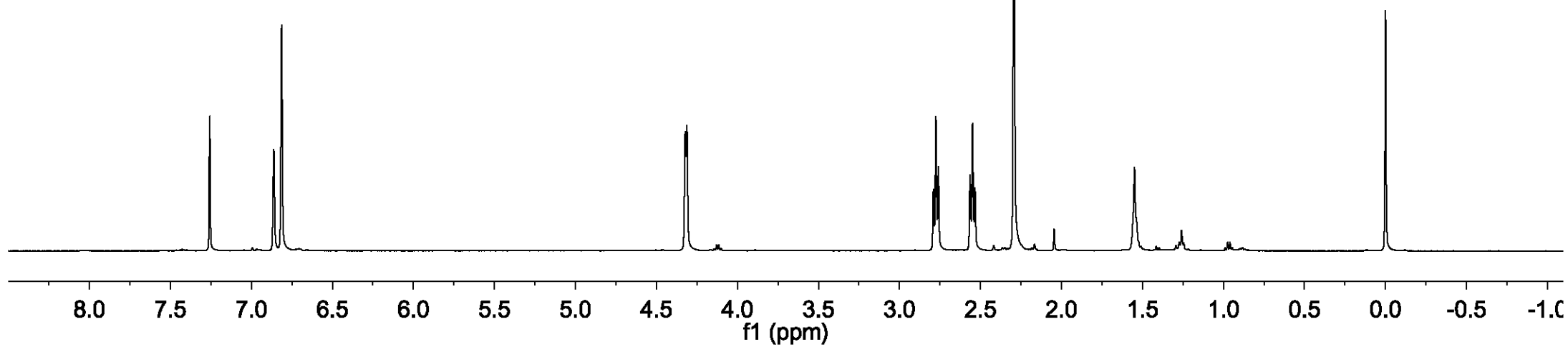
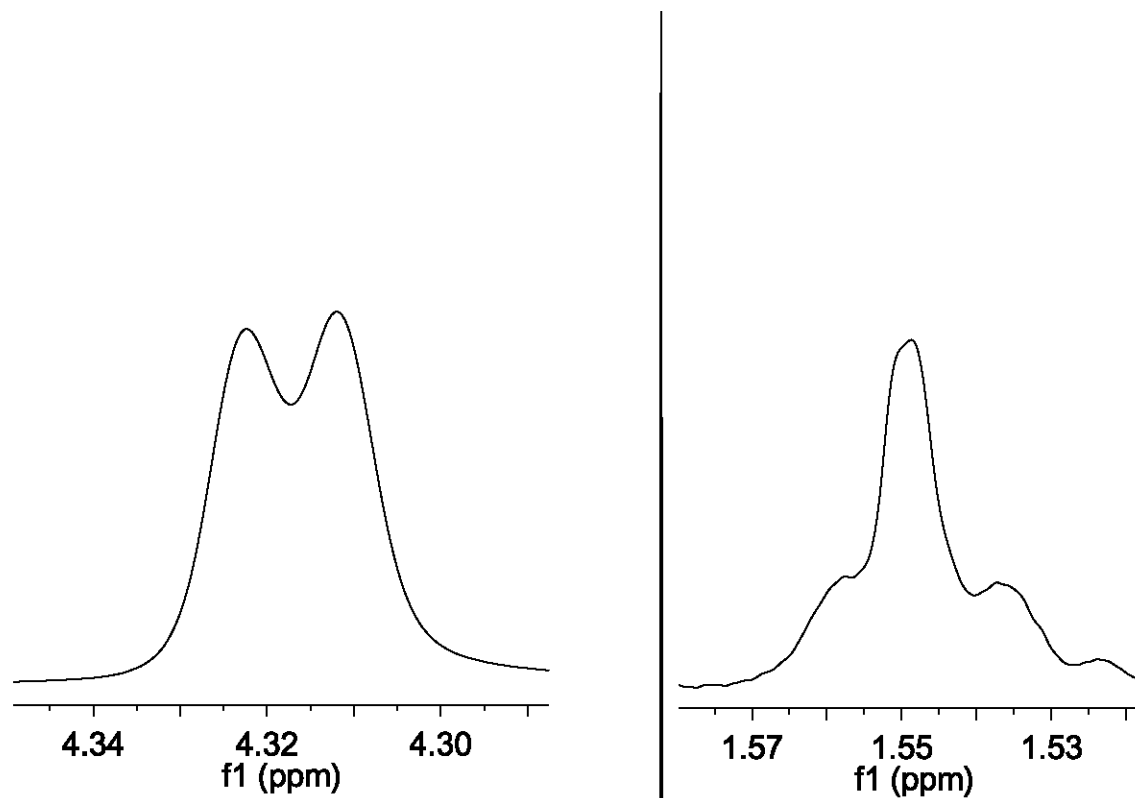
CDCl₃, 125 MHz**S31**

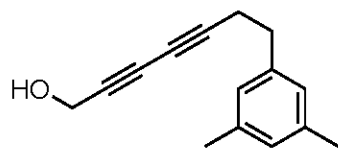
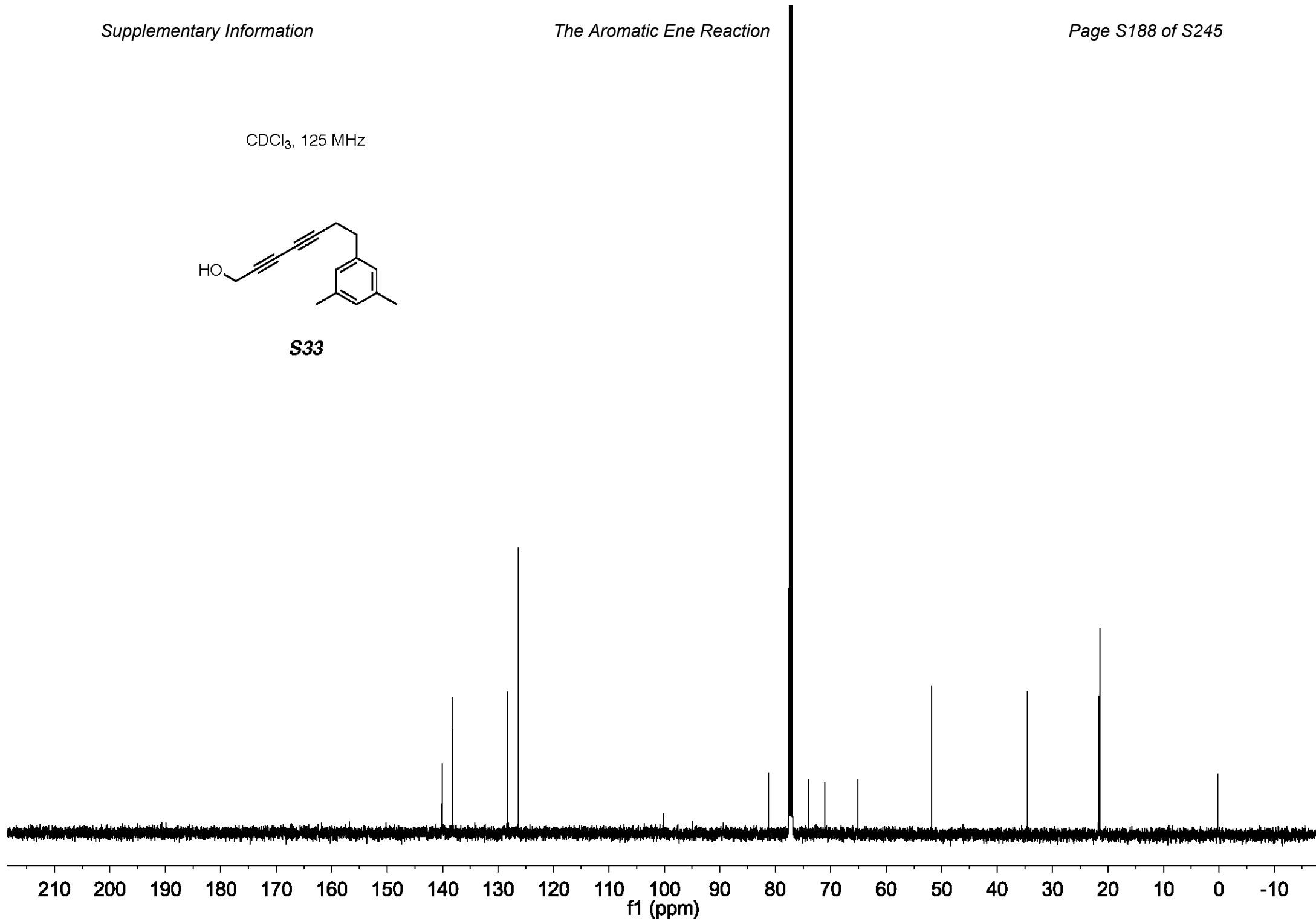
CDCl₃, 500 MHz**S32**

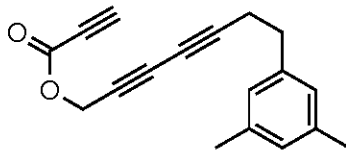
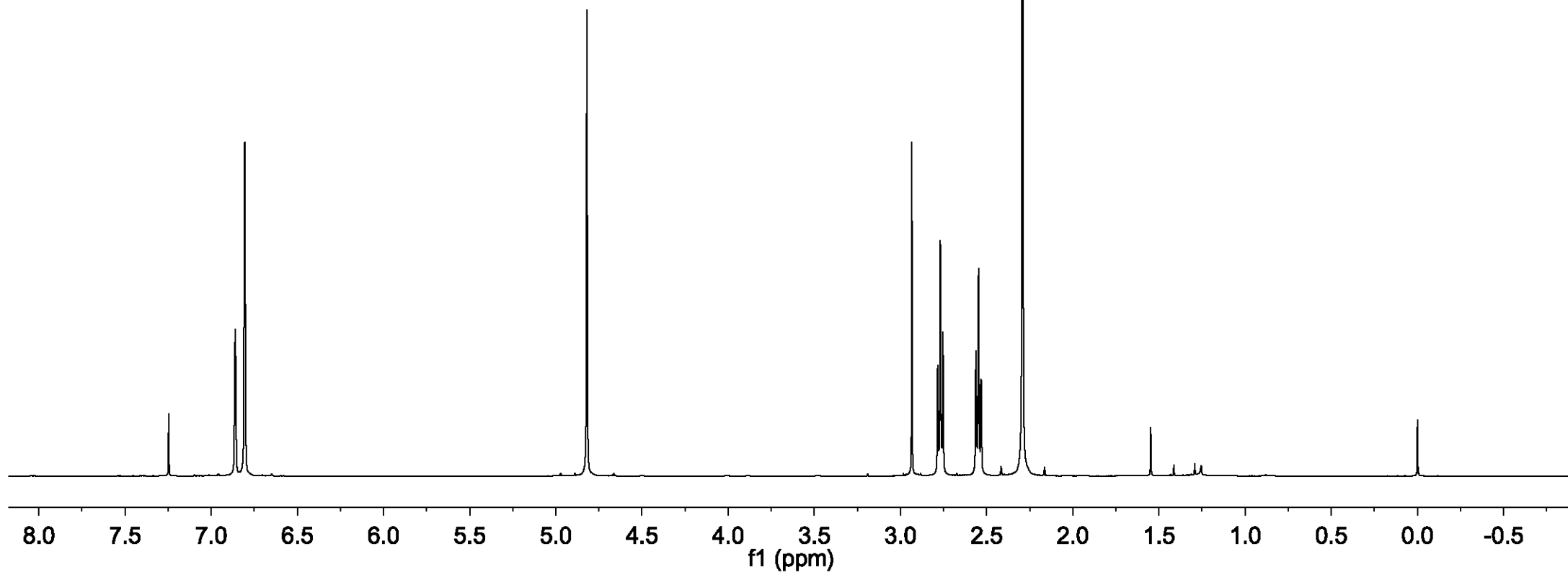
CDCl₃, 125 MHz**S32**

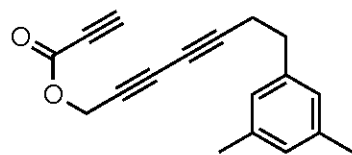
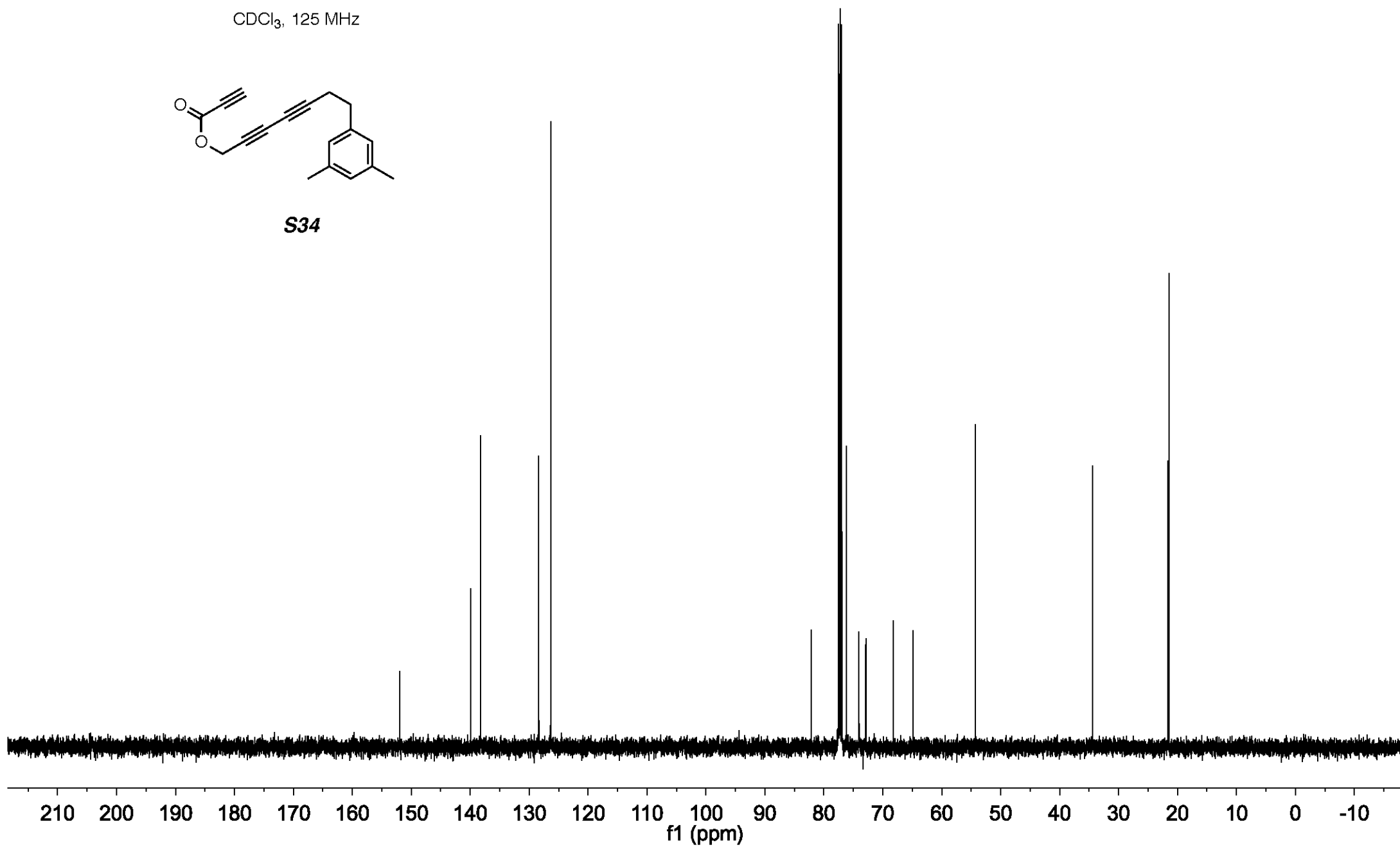
CDCl₃, 500 MHz**32k**

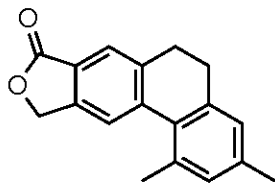
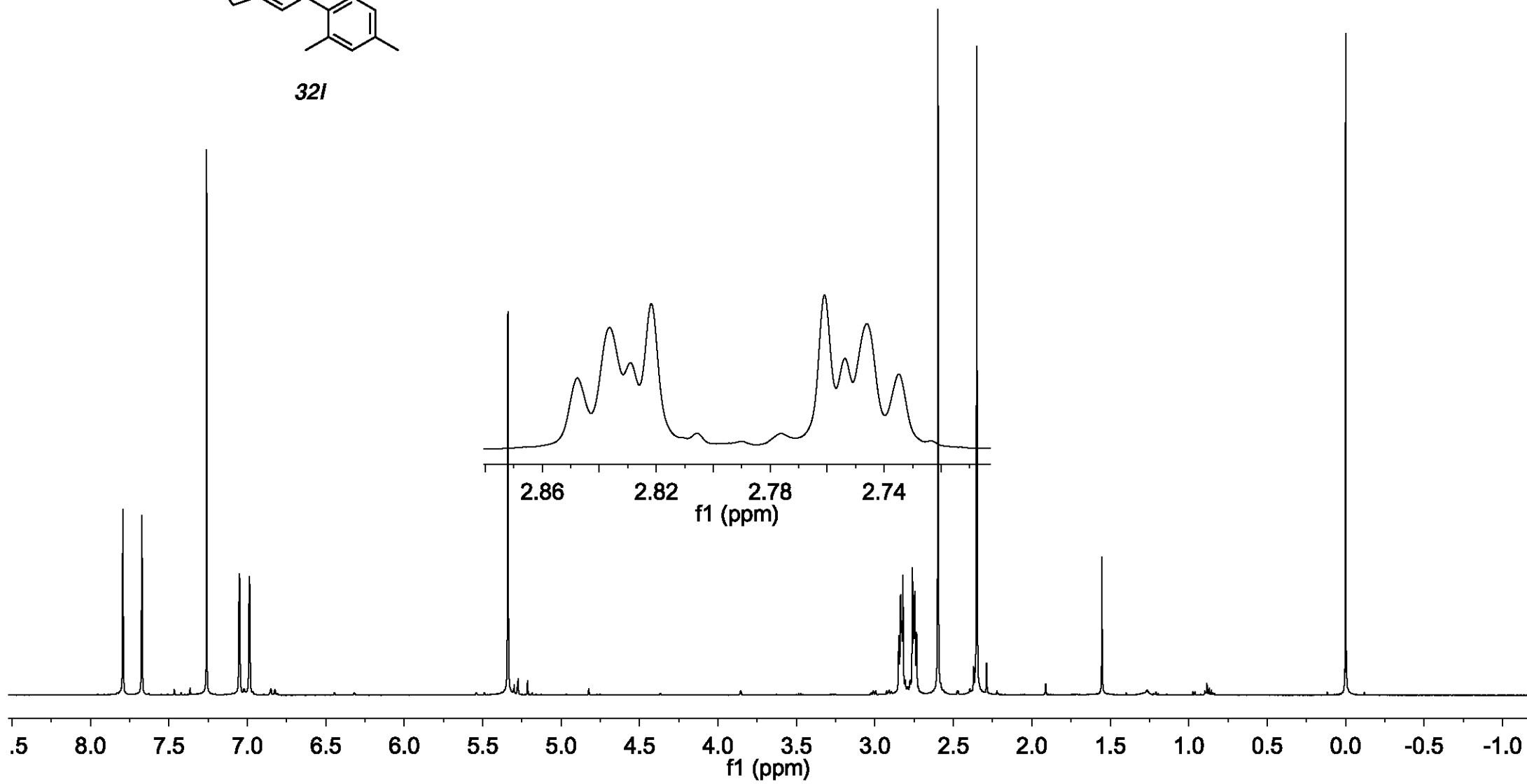
CDCl₃, 125 MHz**32k**

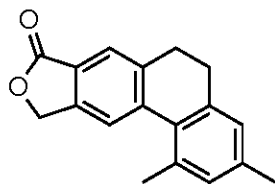
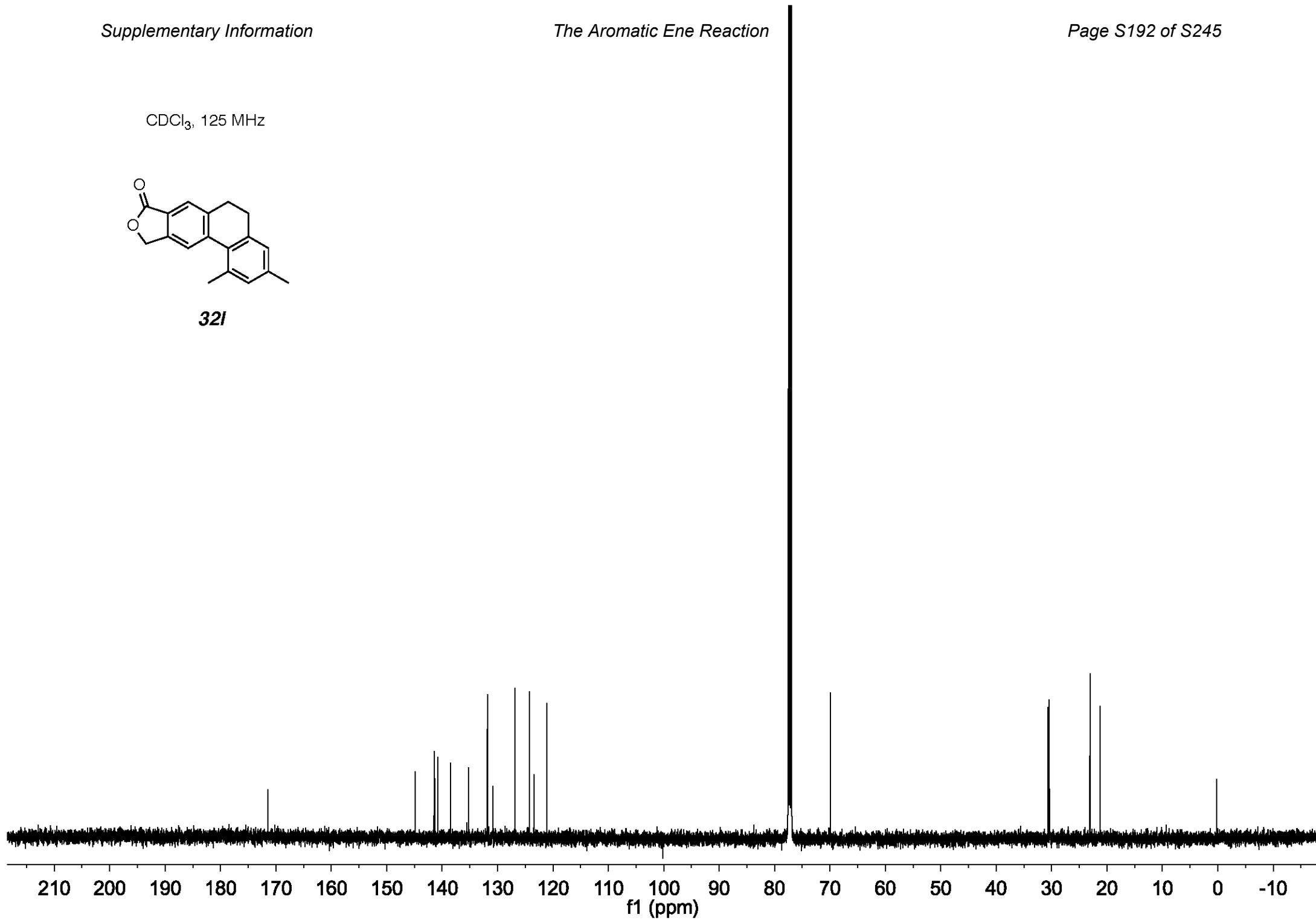
CDCl₃, 500 MHz**S33**

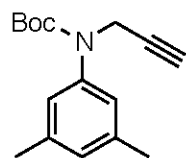
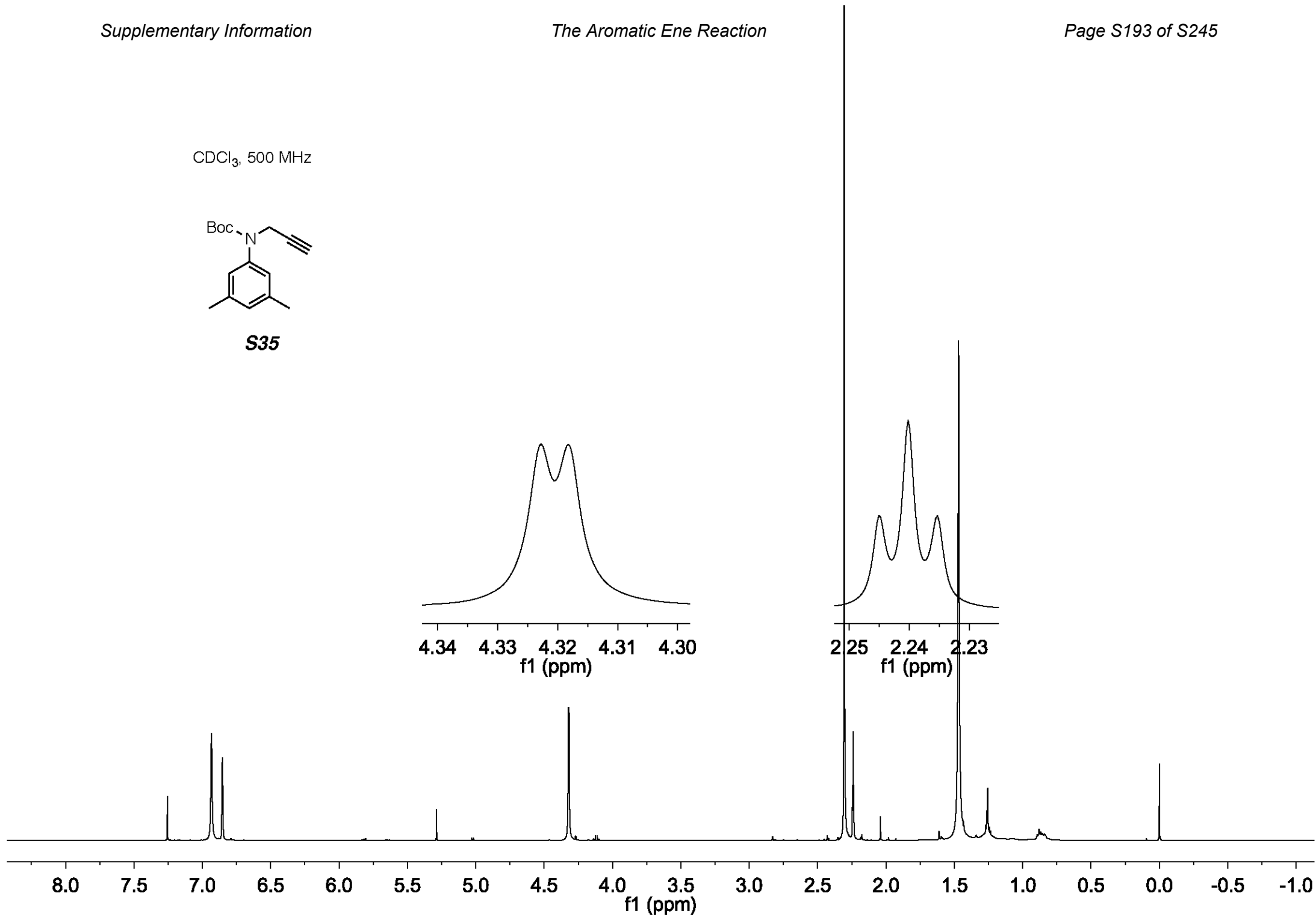
CDCl₃, 125 MHz**S33**

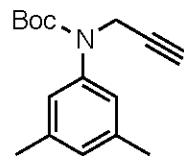
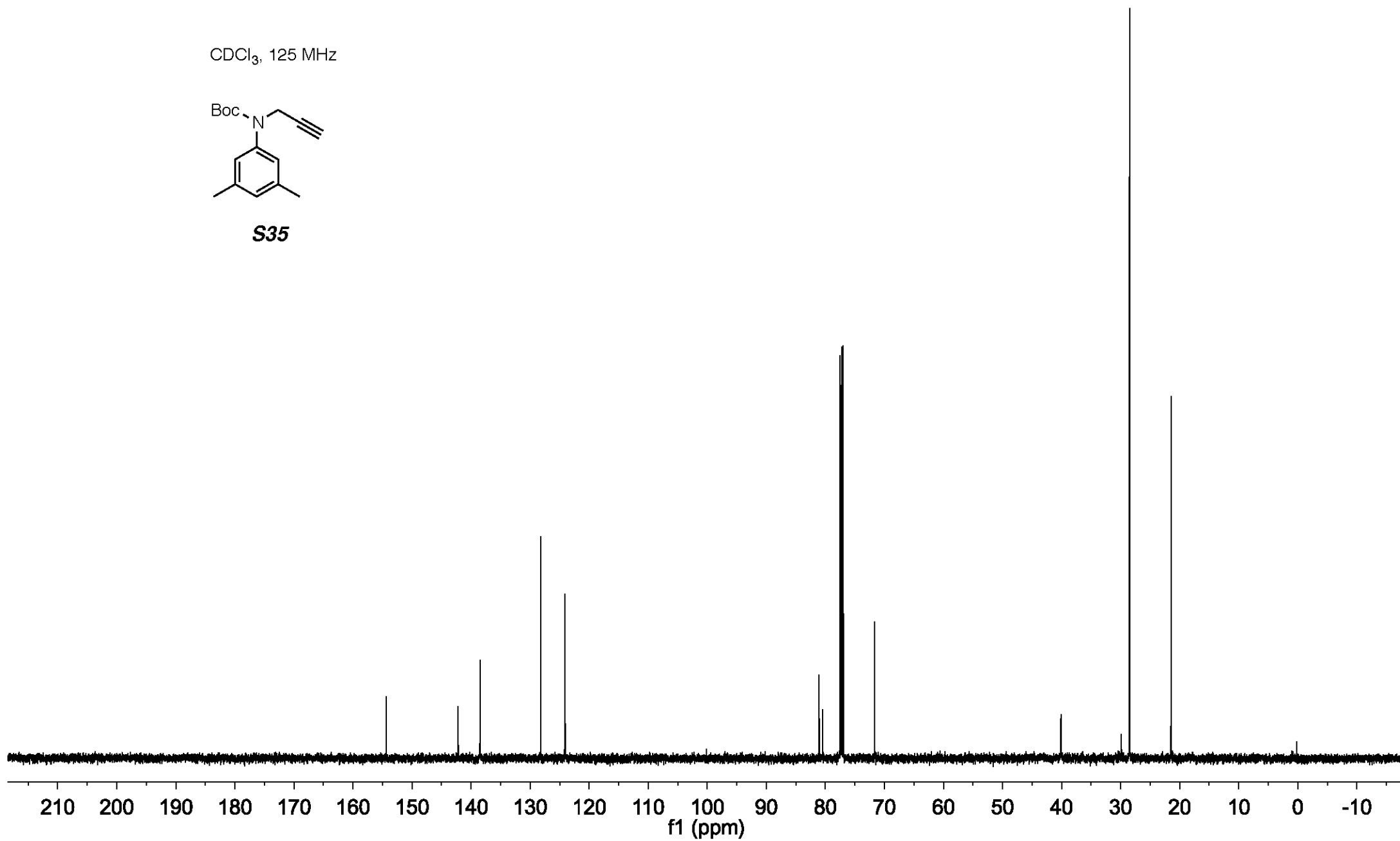
CDCl₃, 500 MHz**S34**

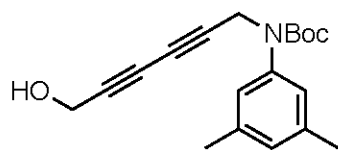
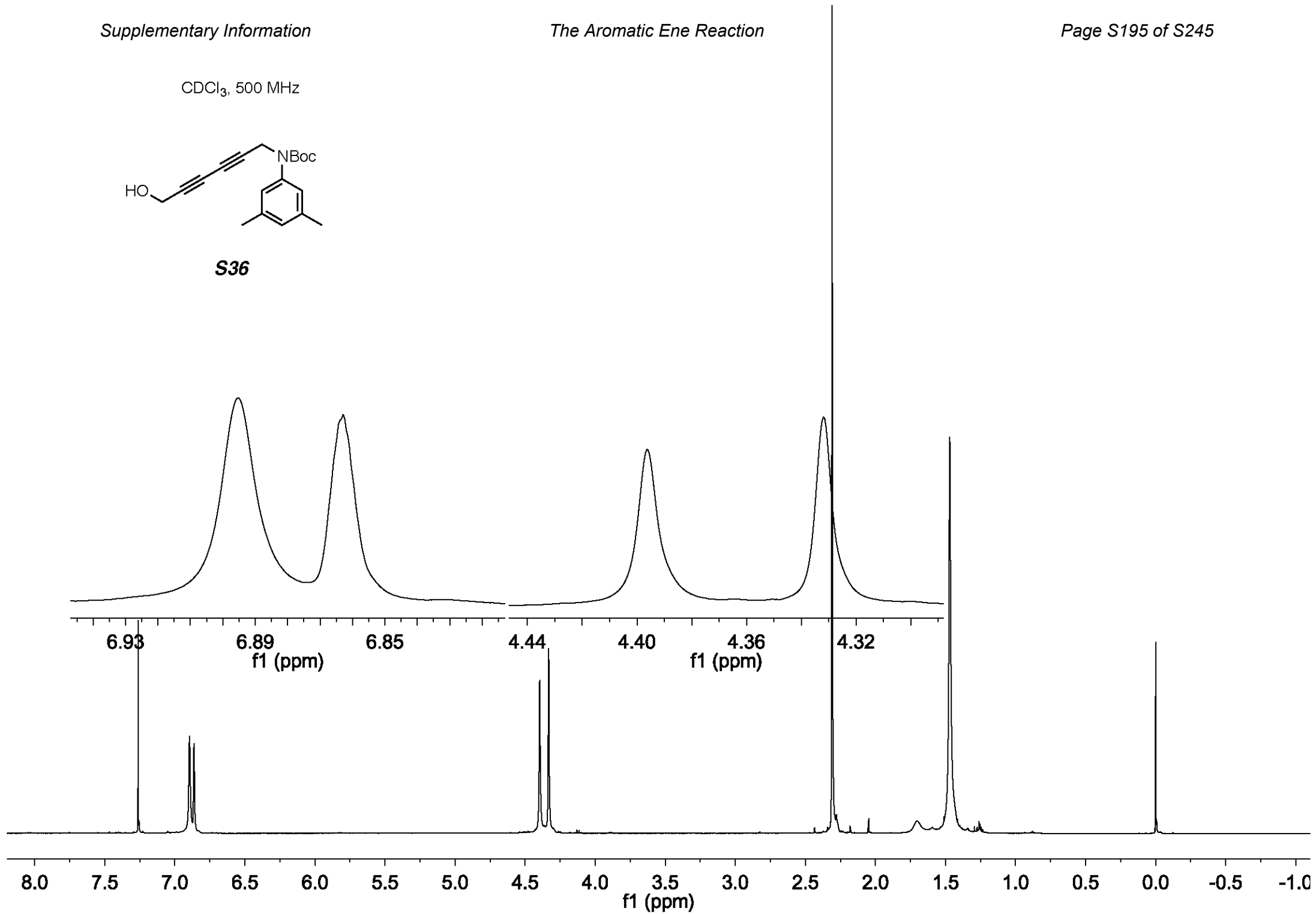
CDCl₃, 125 MHz**S34**

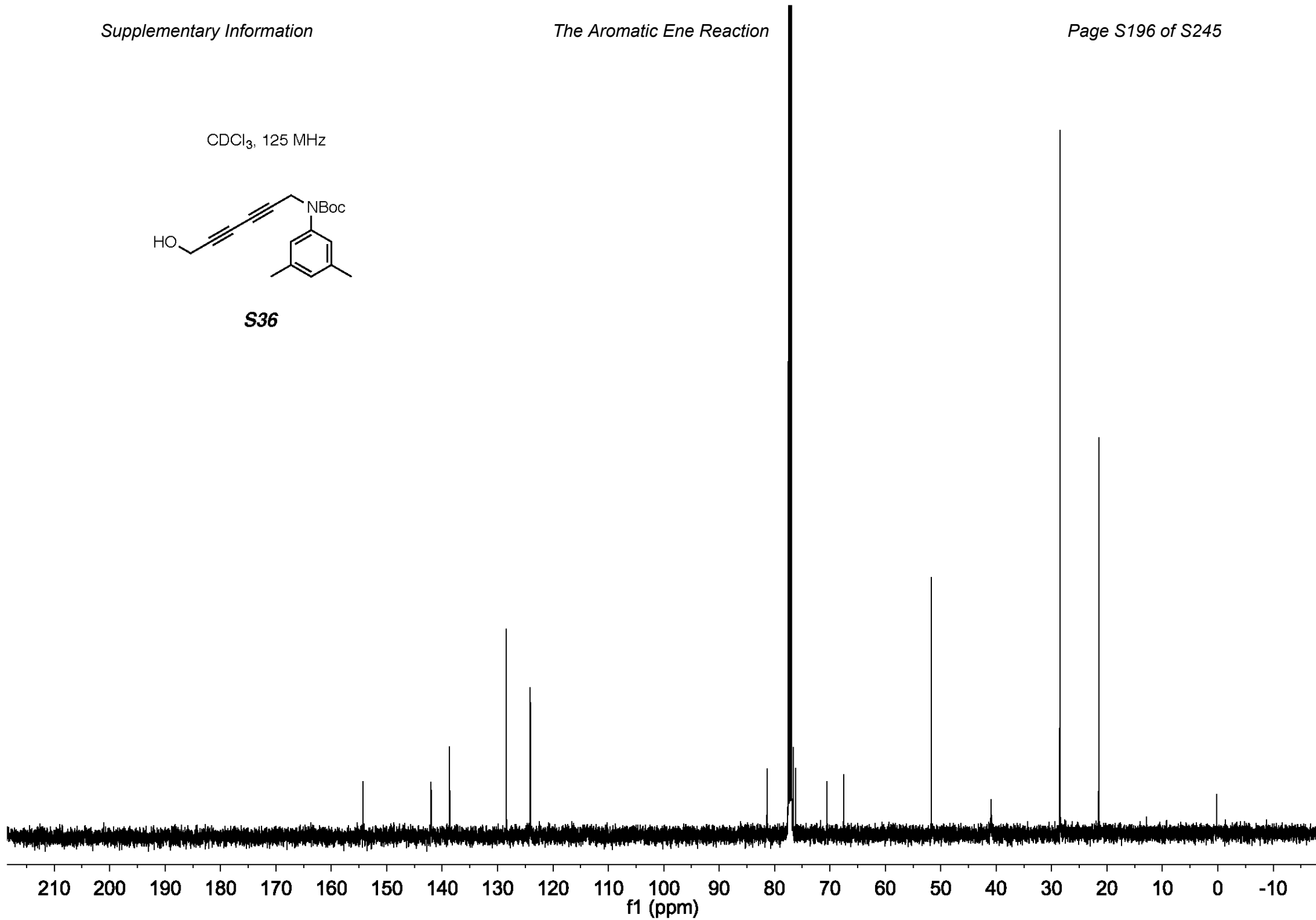
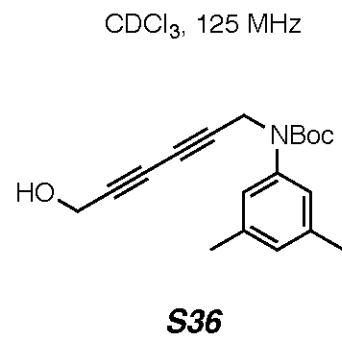
CDCl₃, 500 MHz**32I**

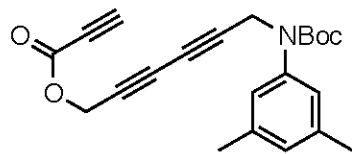
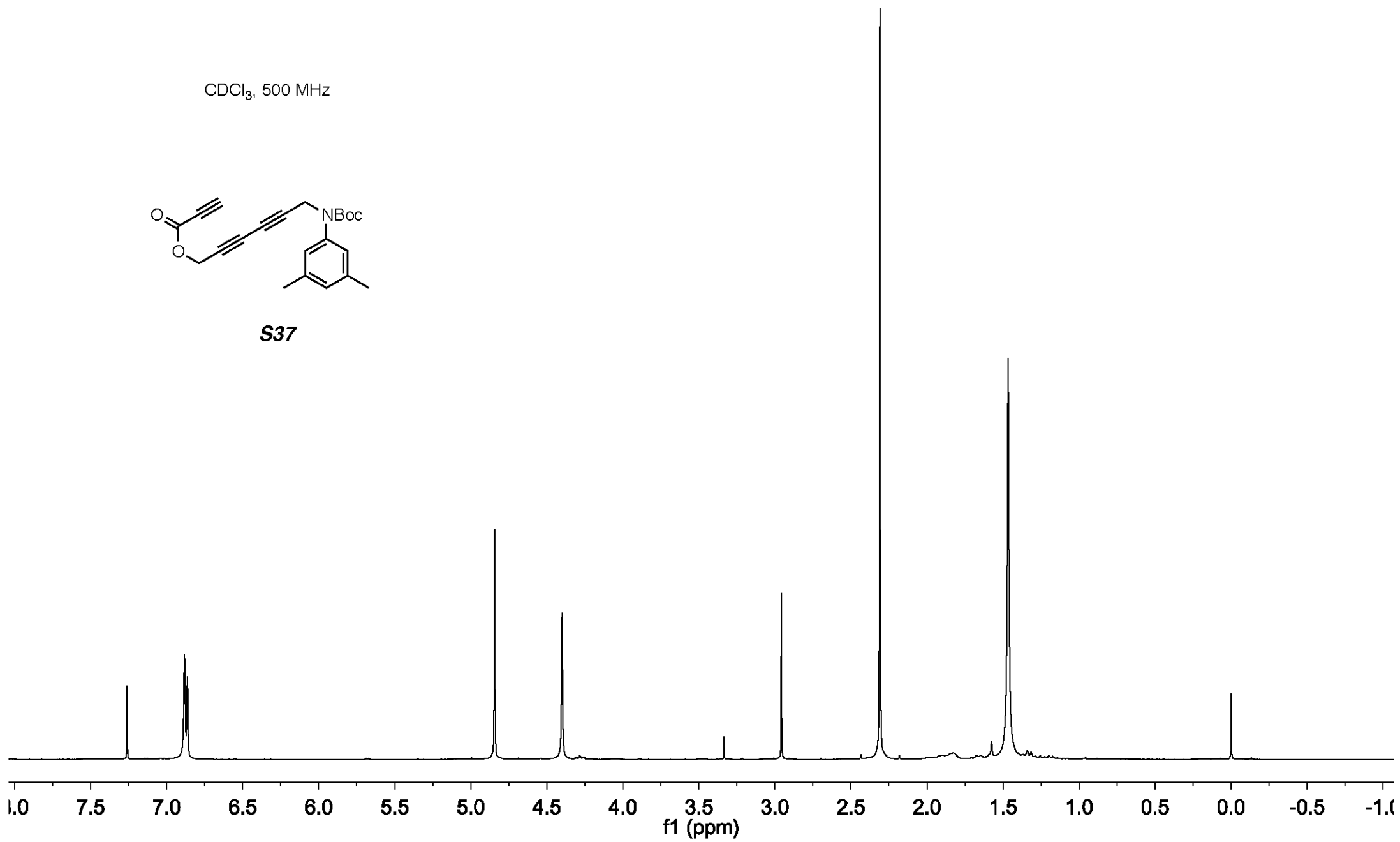
CDCl₃, 125 MHz**321**

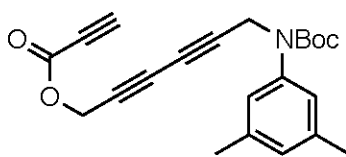
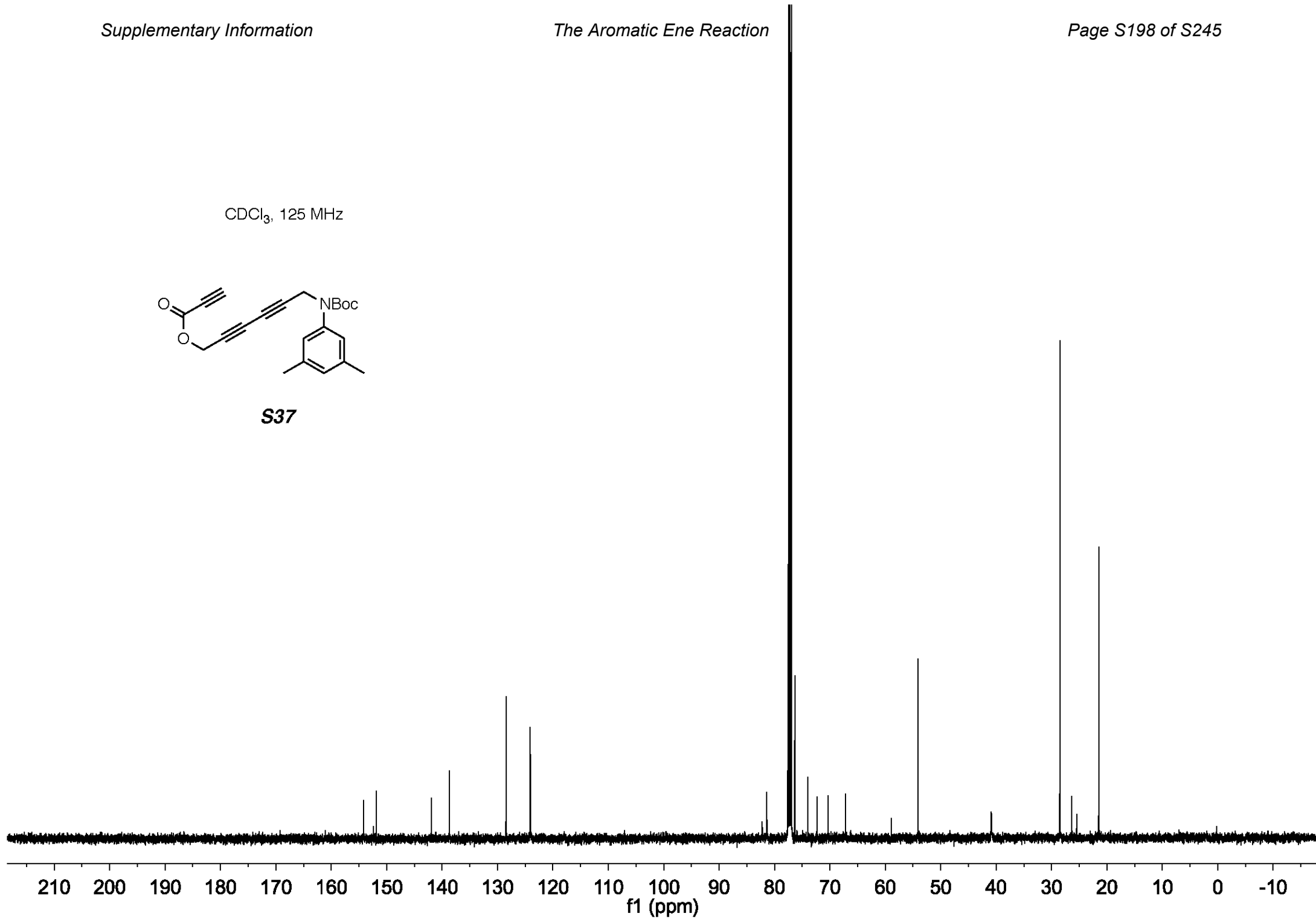
CDCl₃, 500 MHz**S35**

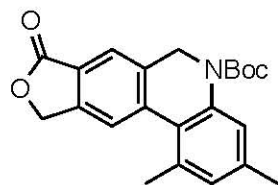
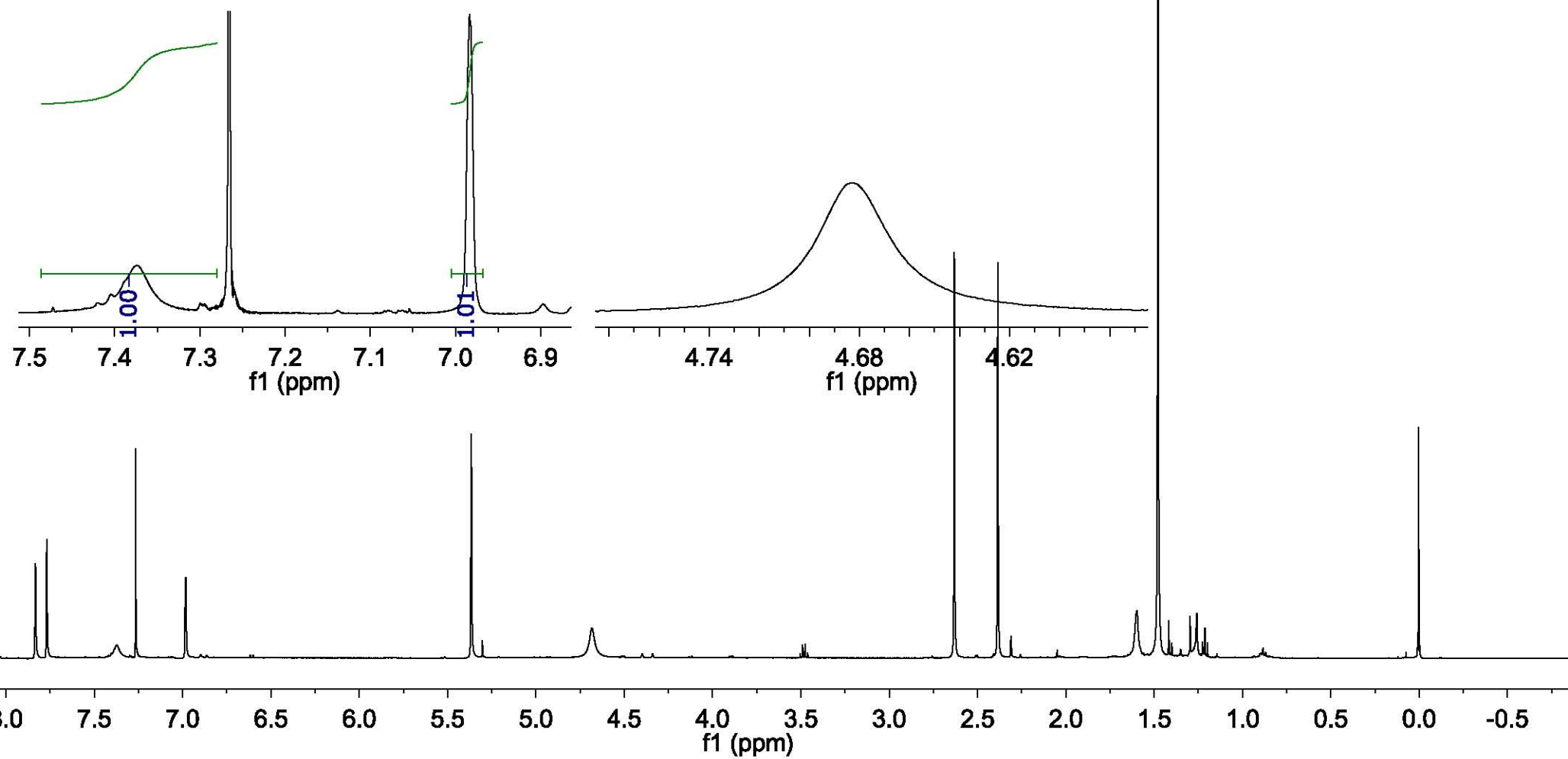
CDCl₃, 125 MHz**S35**

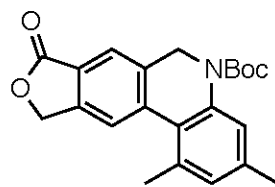
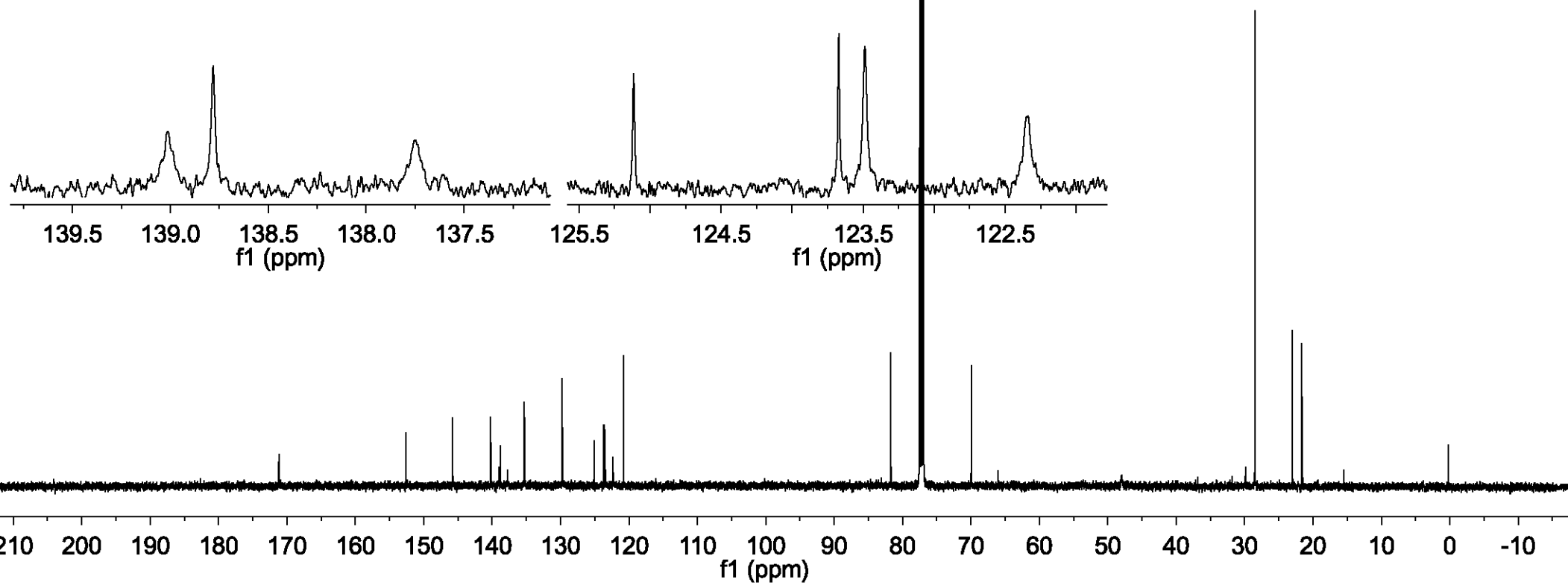
CDCl₃, 500 MHz**S36**

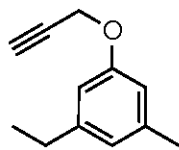
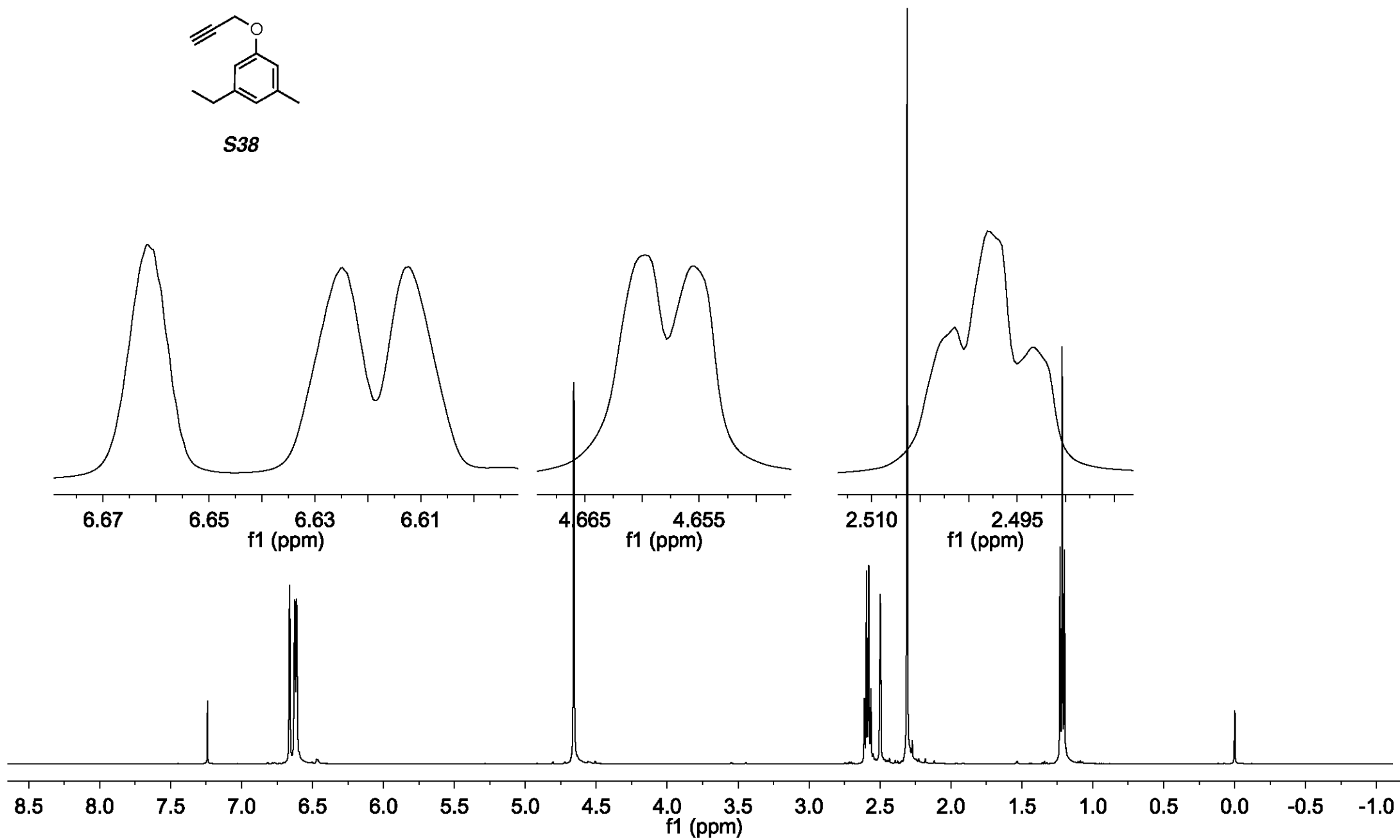


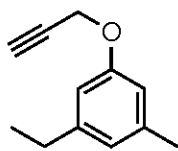
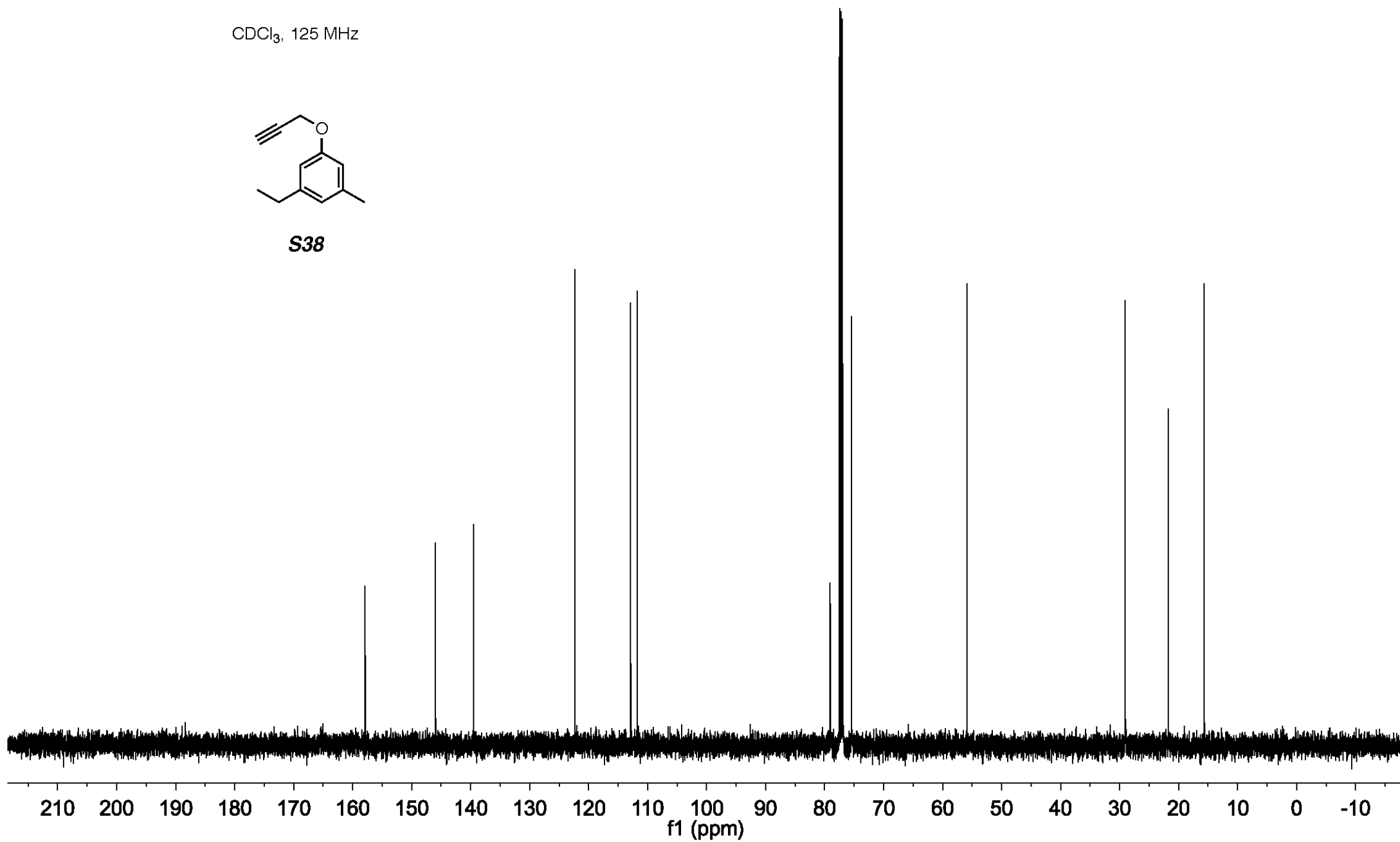
CDCl₃, 500 MHz**S37**

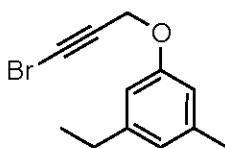
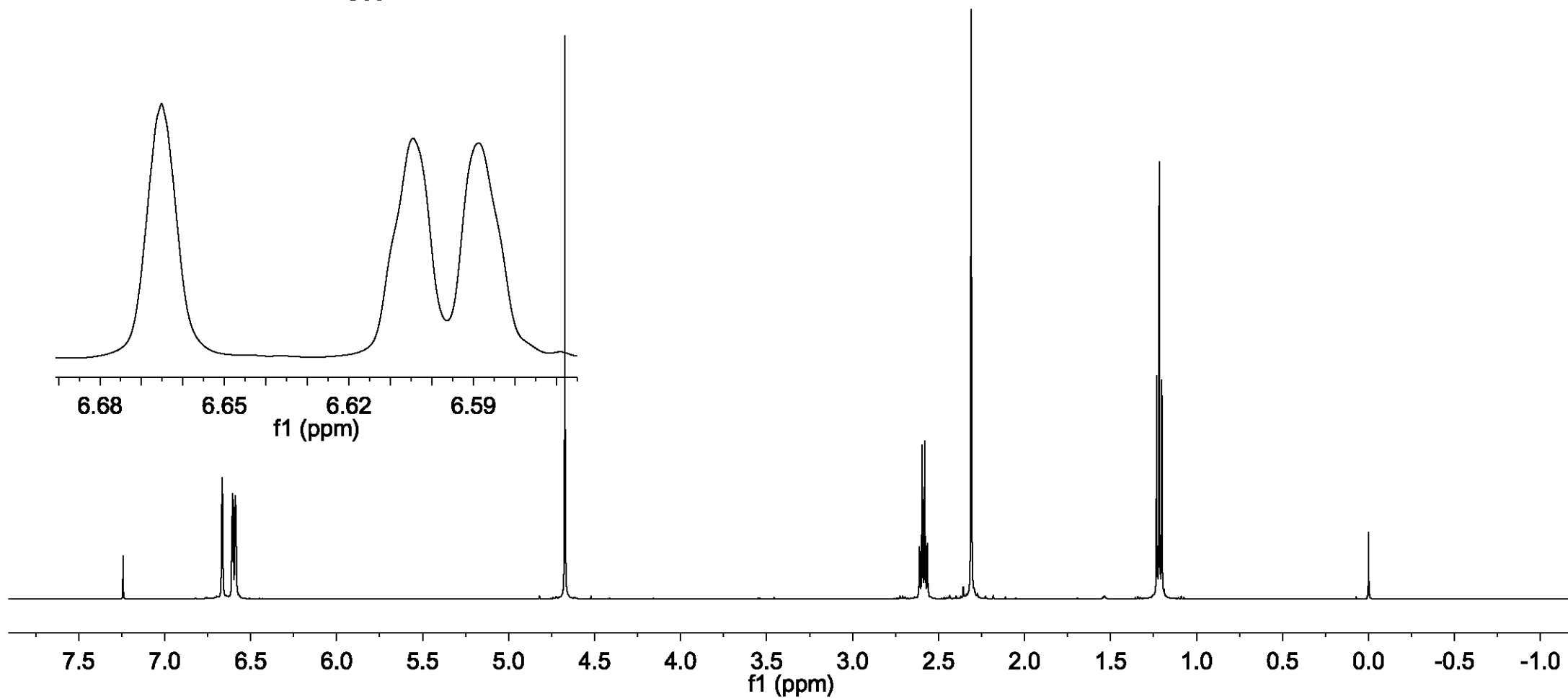
CDCl₃, 125 MHz**S37**

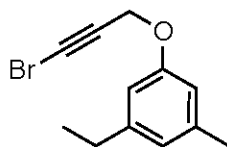
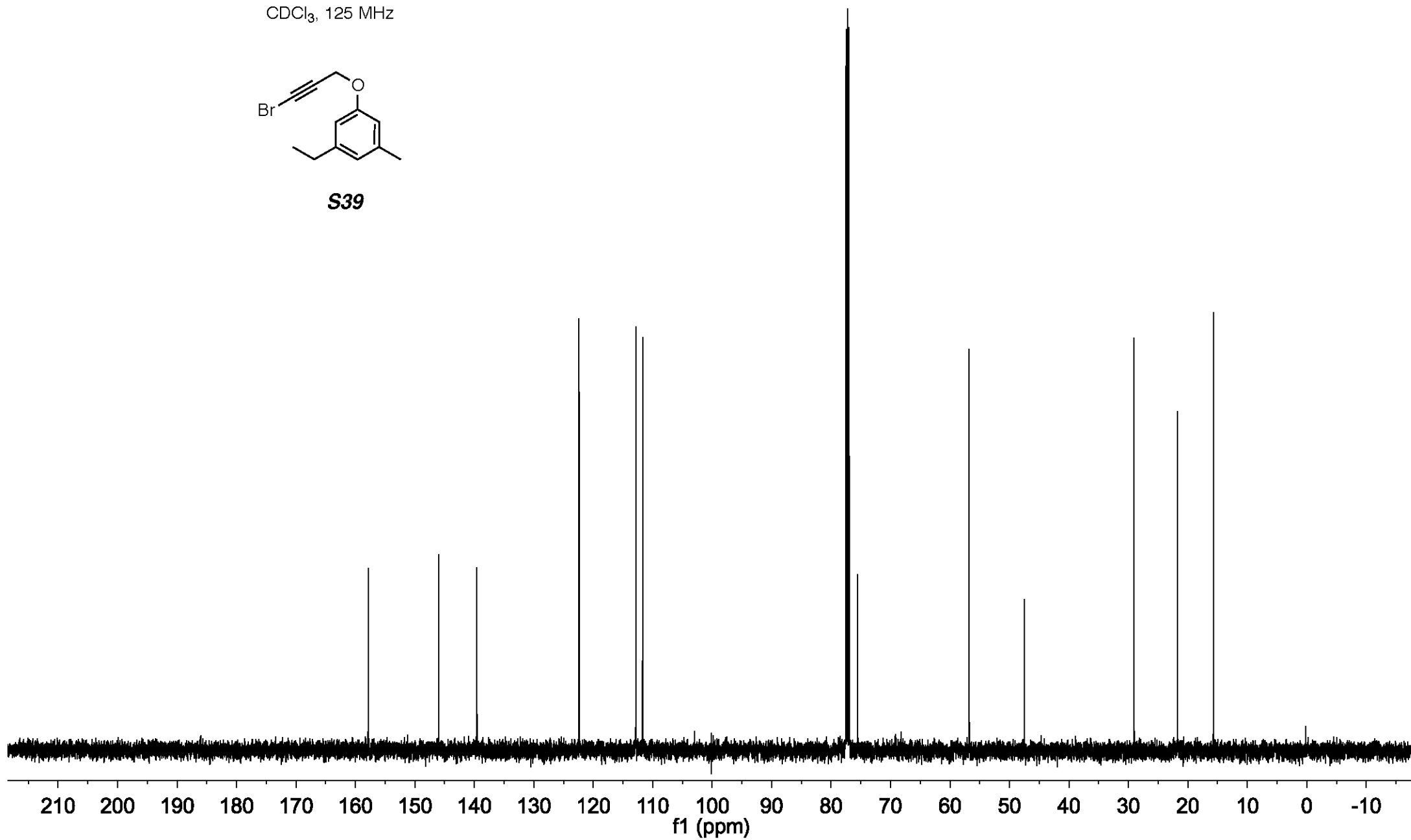
CDCl₃, 500 MHz**32m**

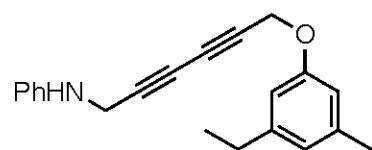
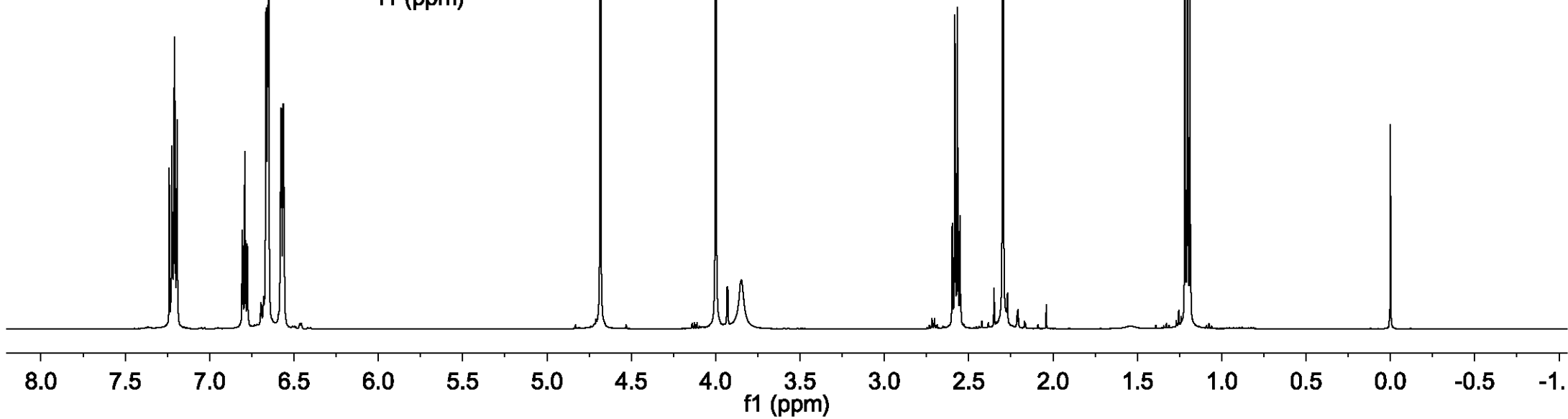
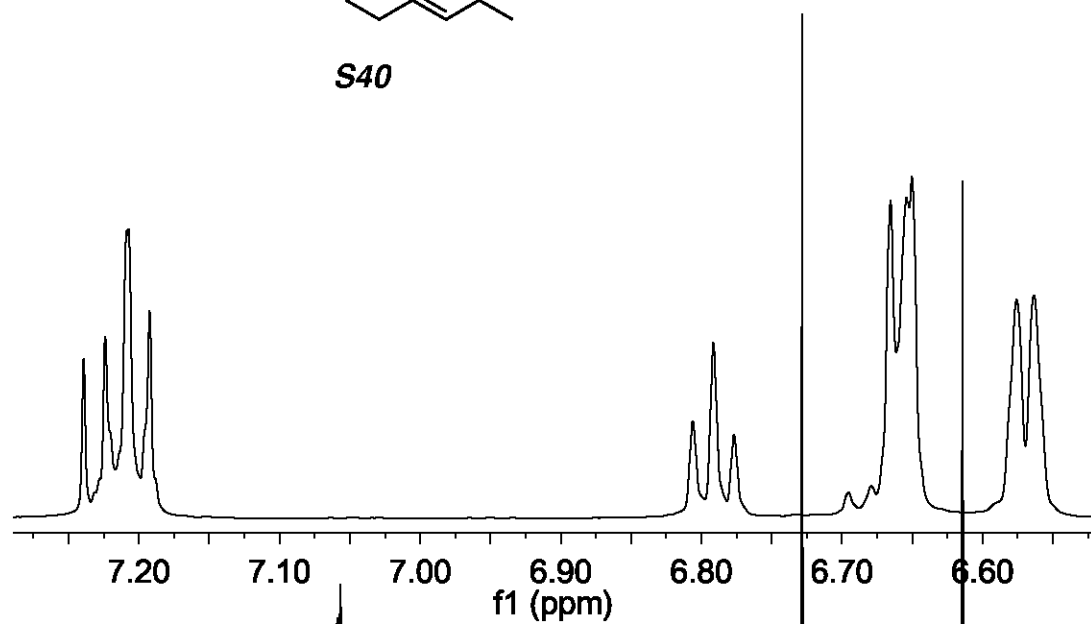
CDCl₃, 125 MHz**32m**

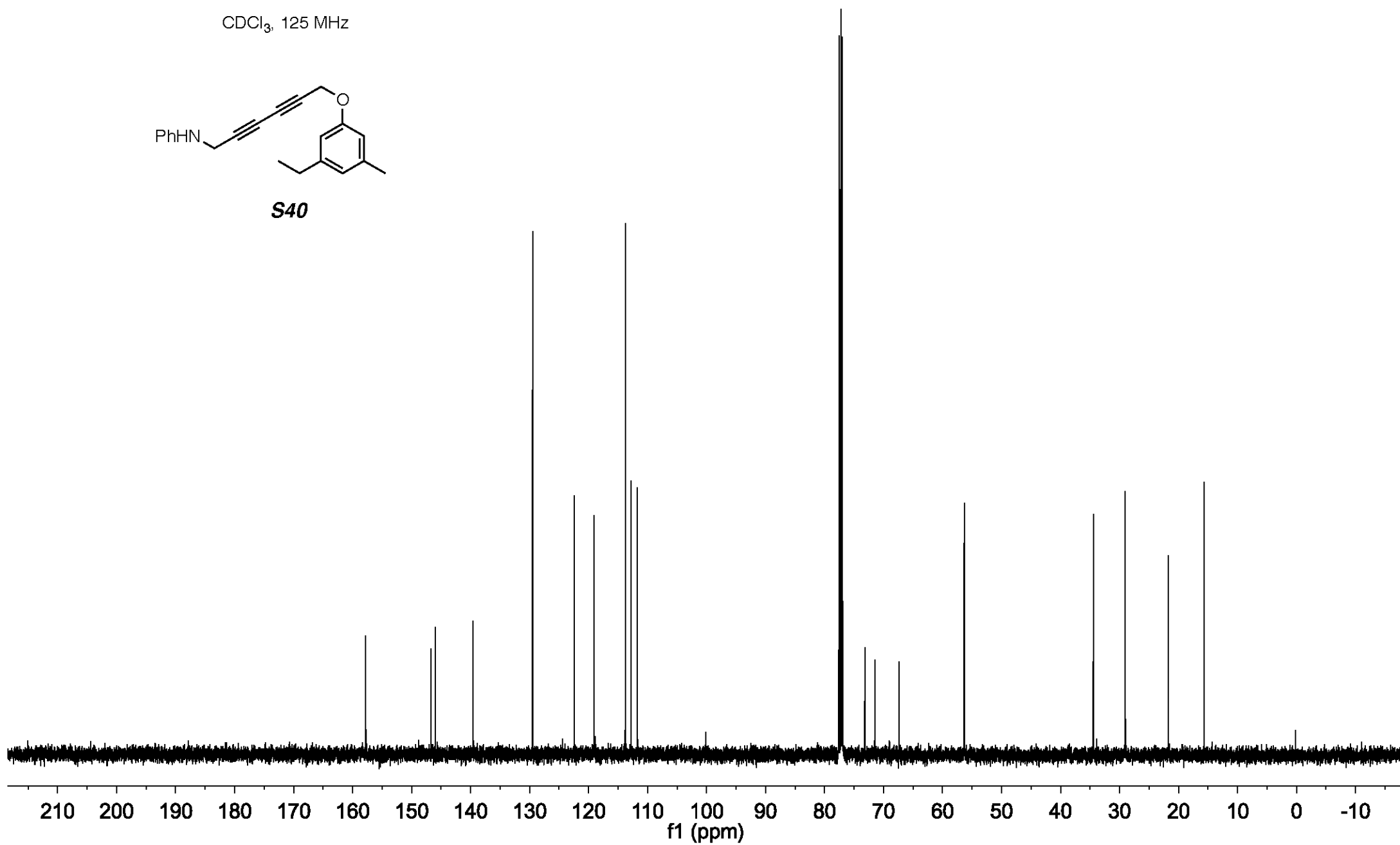
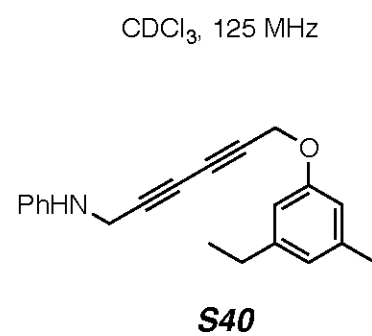
CDCl₃, 500 MHz**S38**

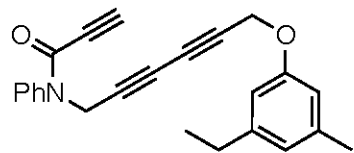
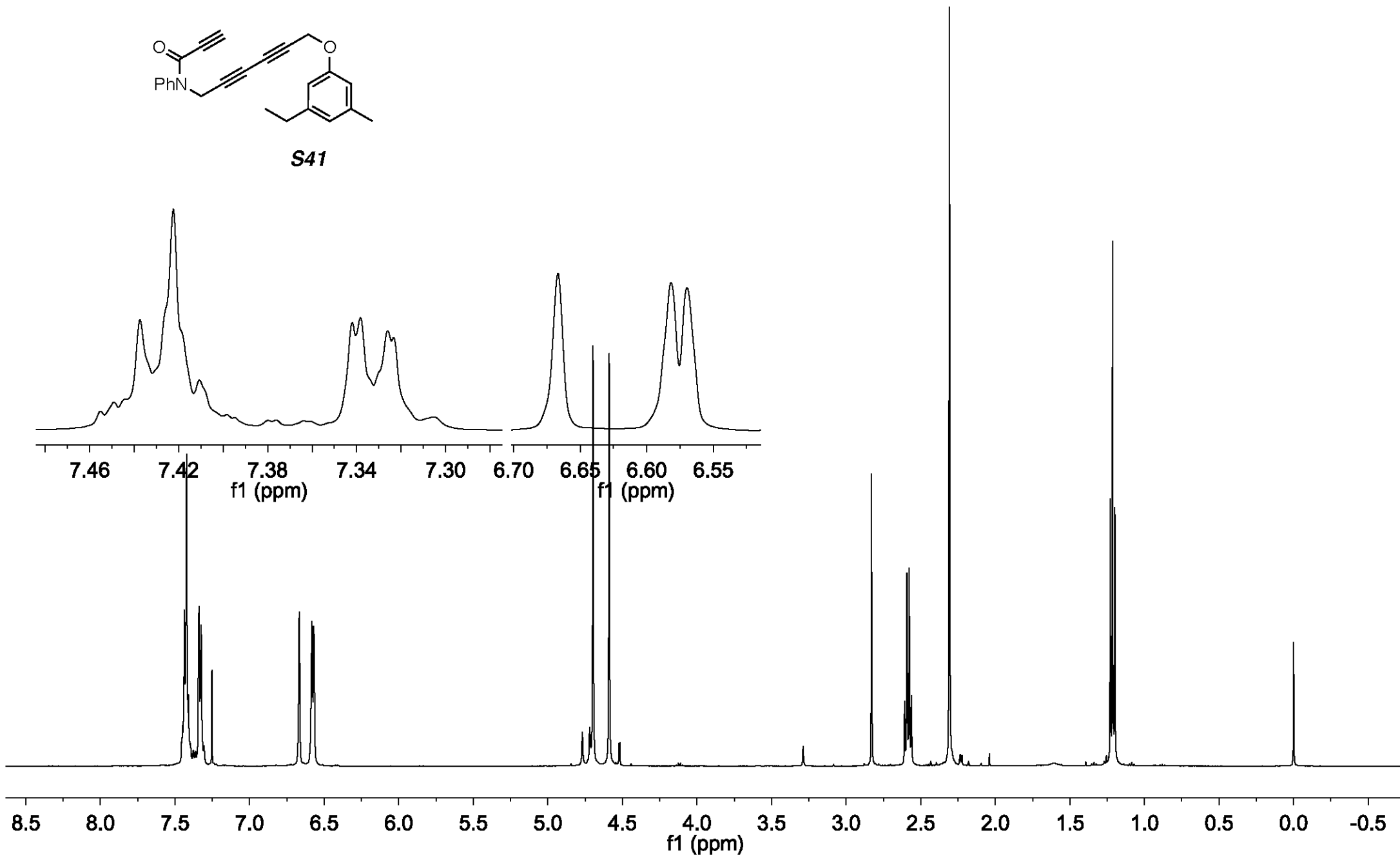
CDCl₃, 125 MHz**S38**

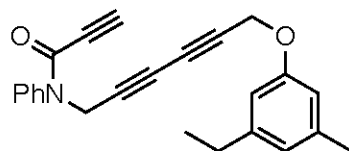
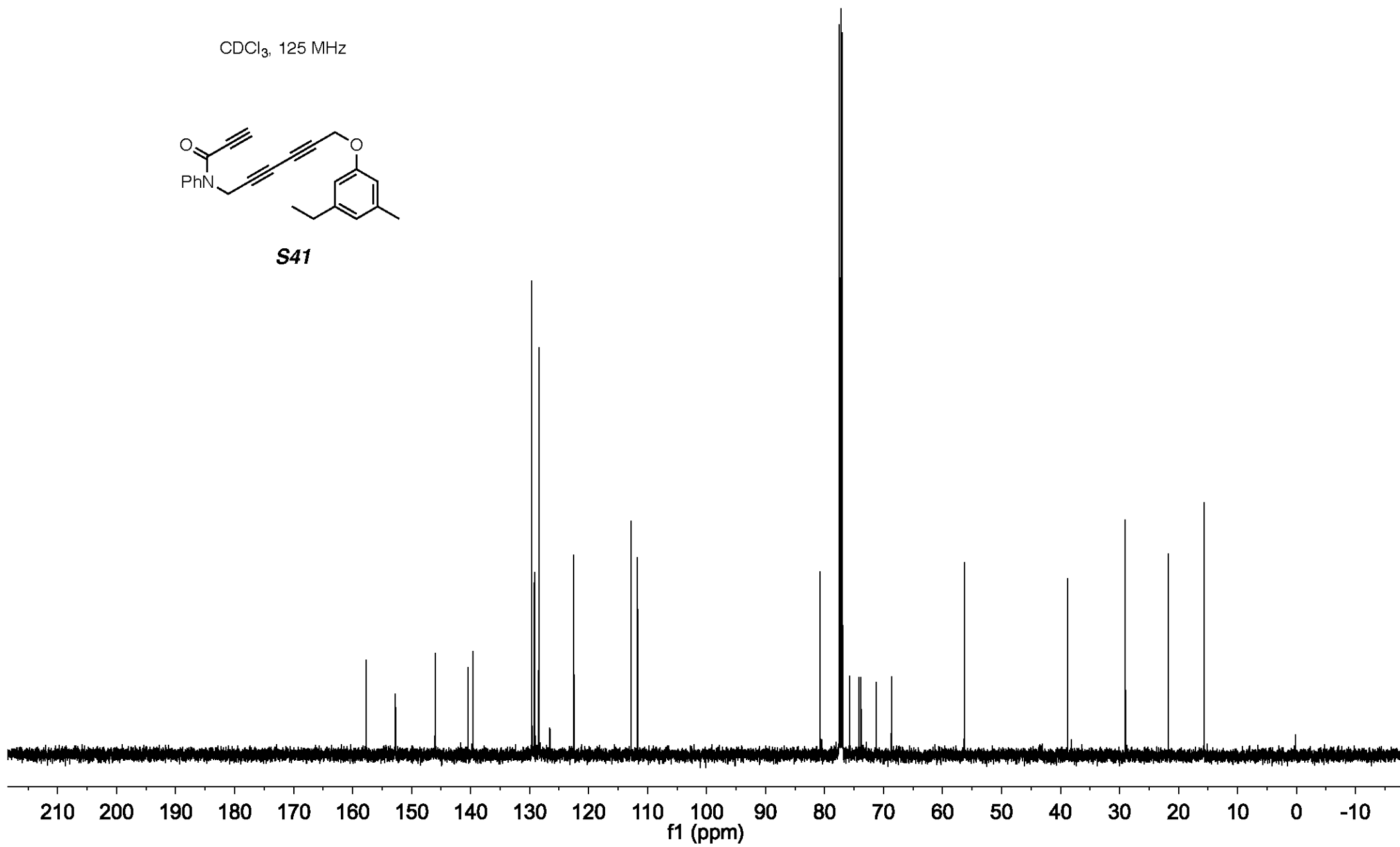
CDCl₃, 500 MHz**S39**

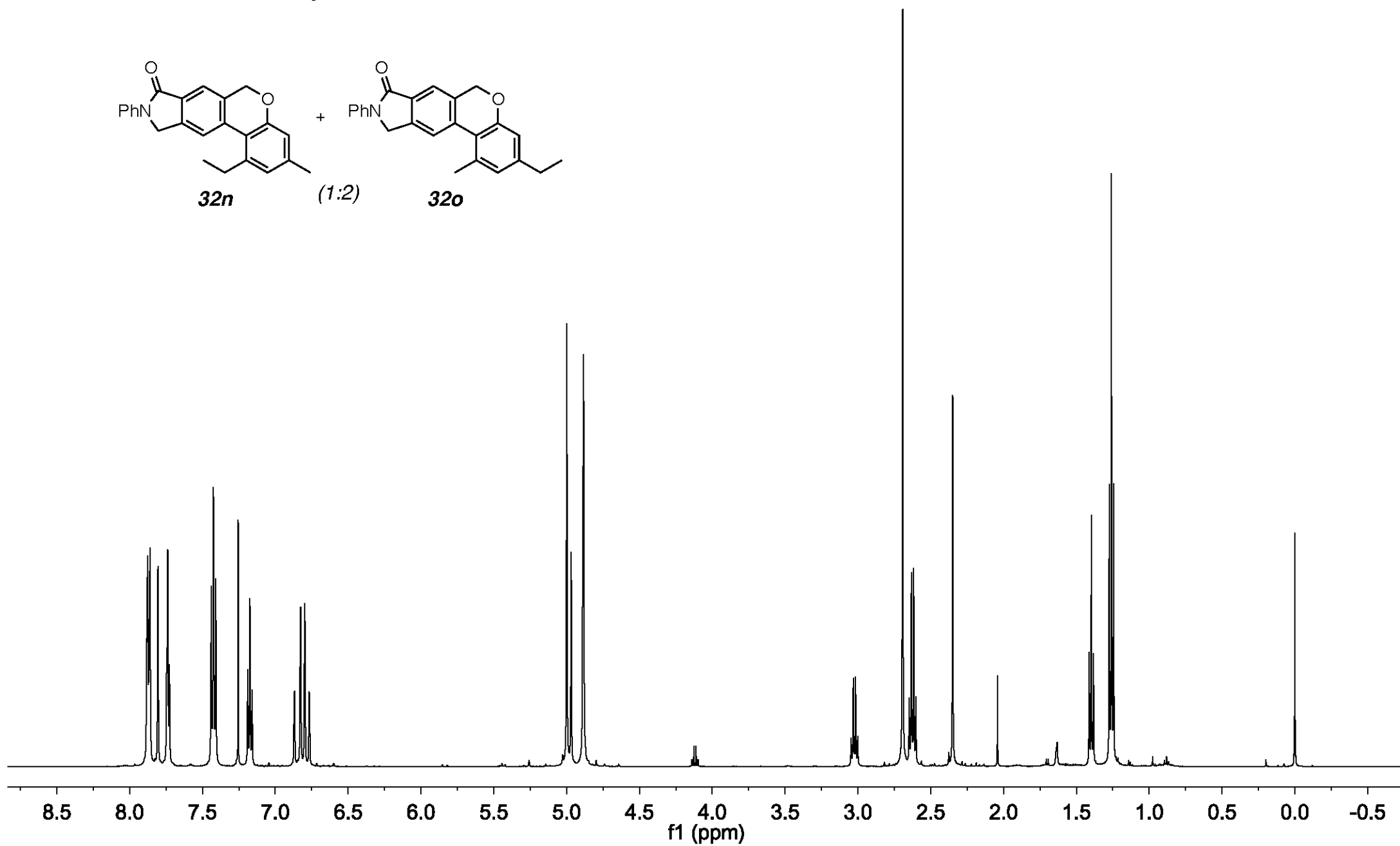
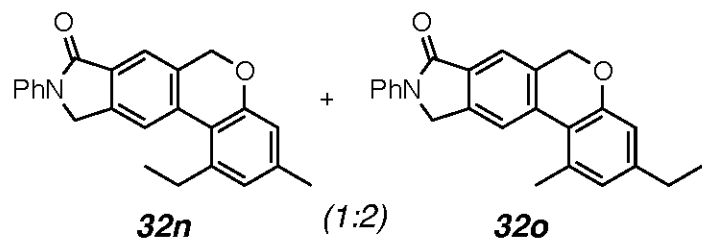
CDCl₃, 125 MHz**S39**

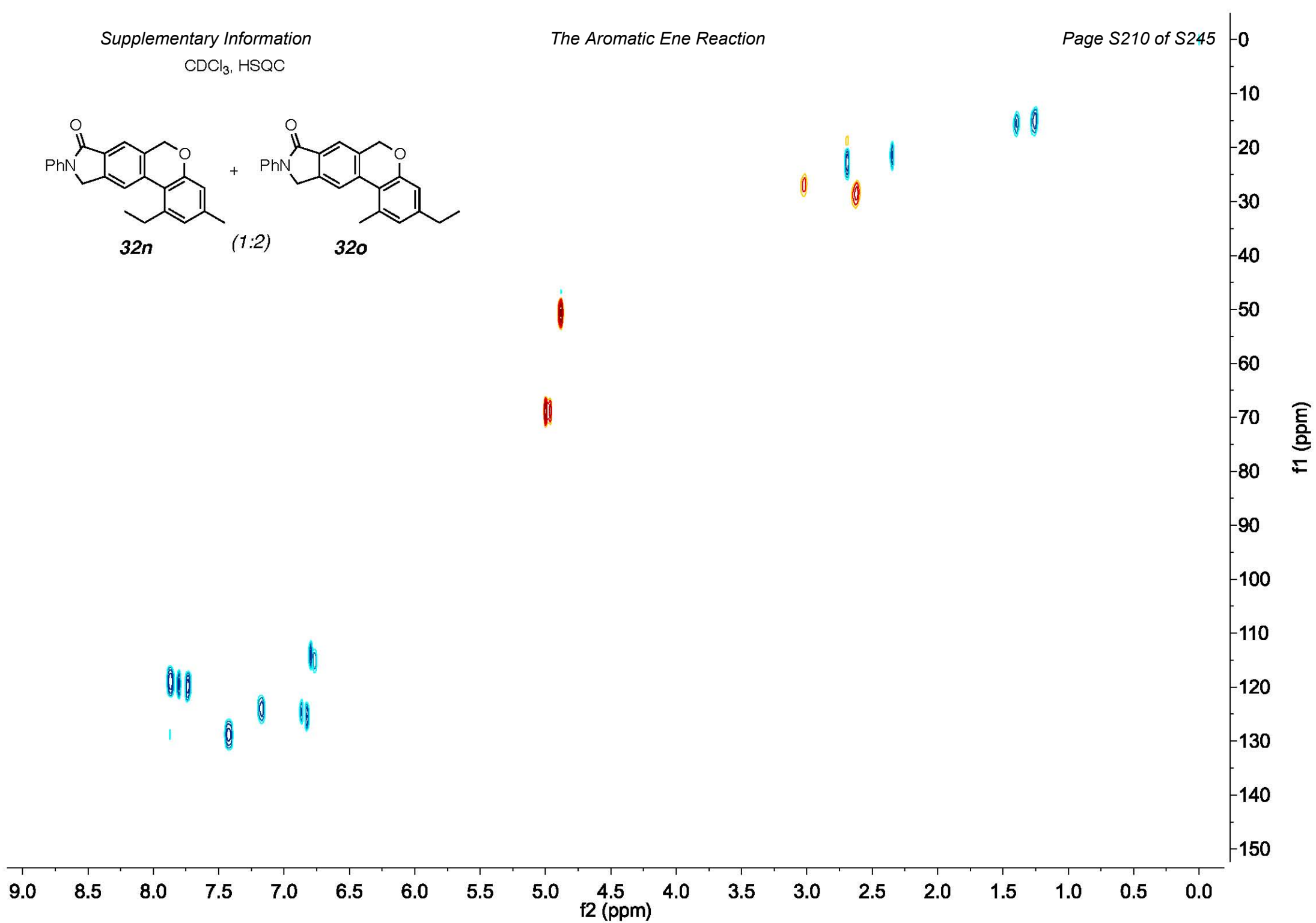
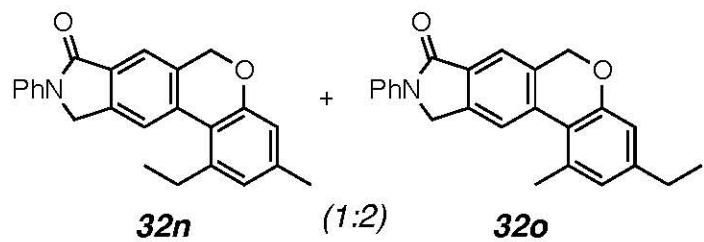
CDCl₃, 500 MHz**S40**

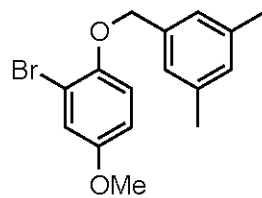
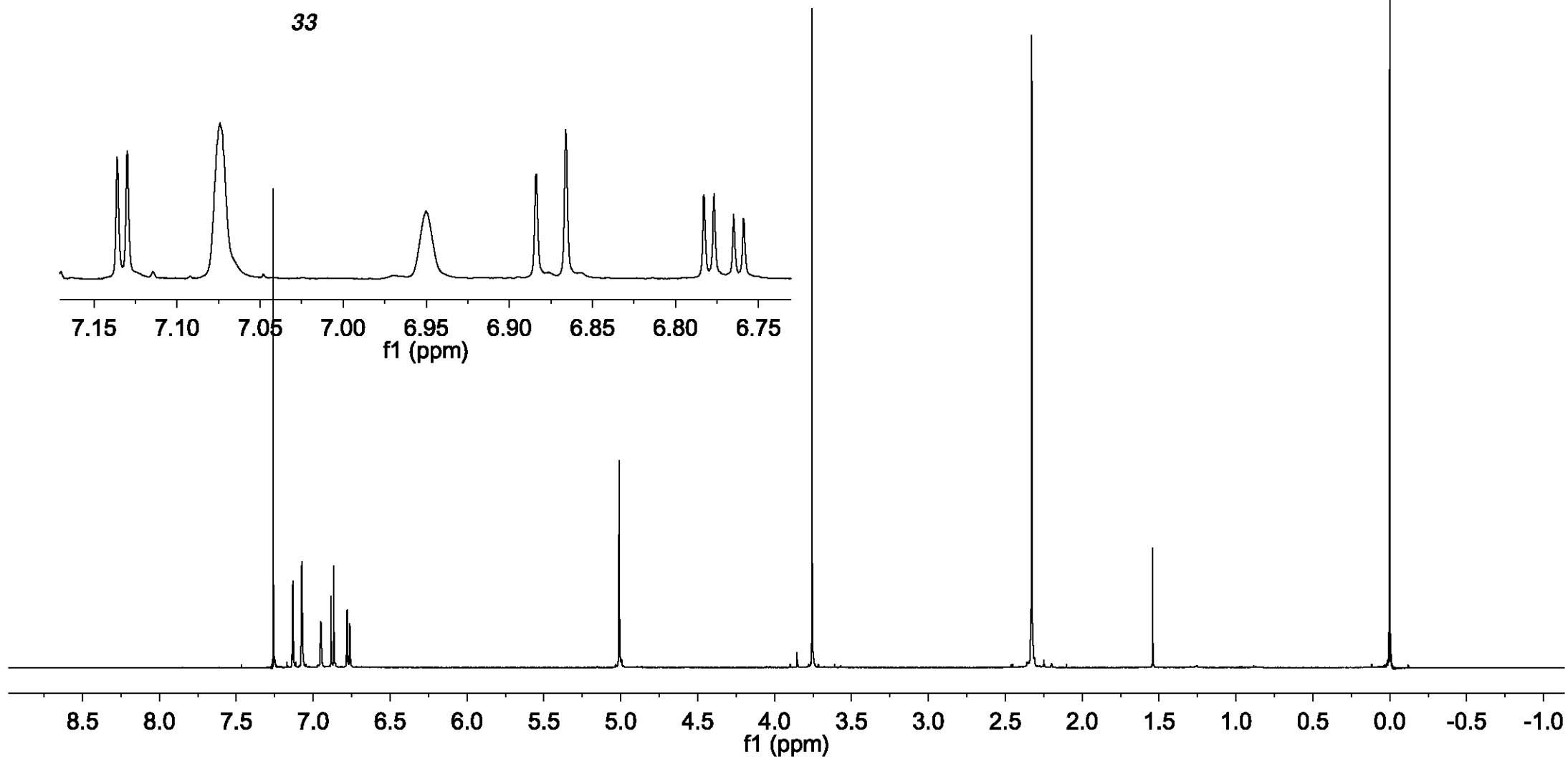
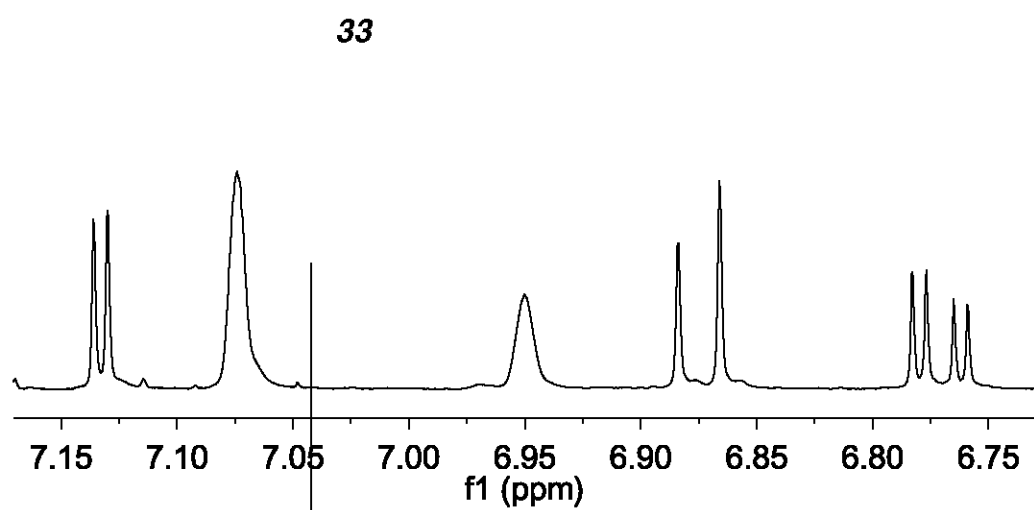


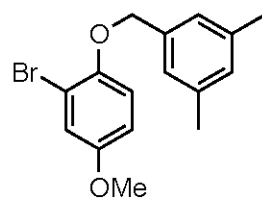
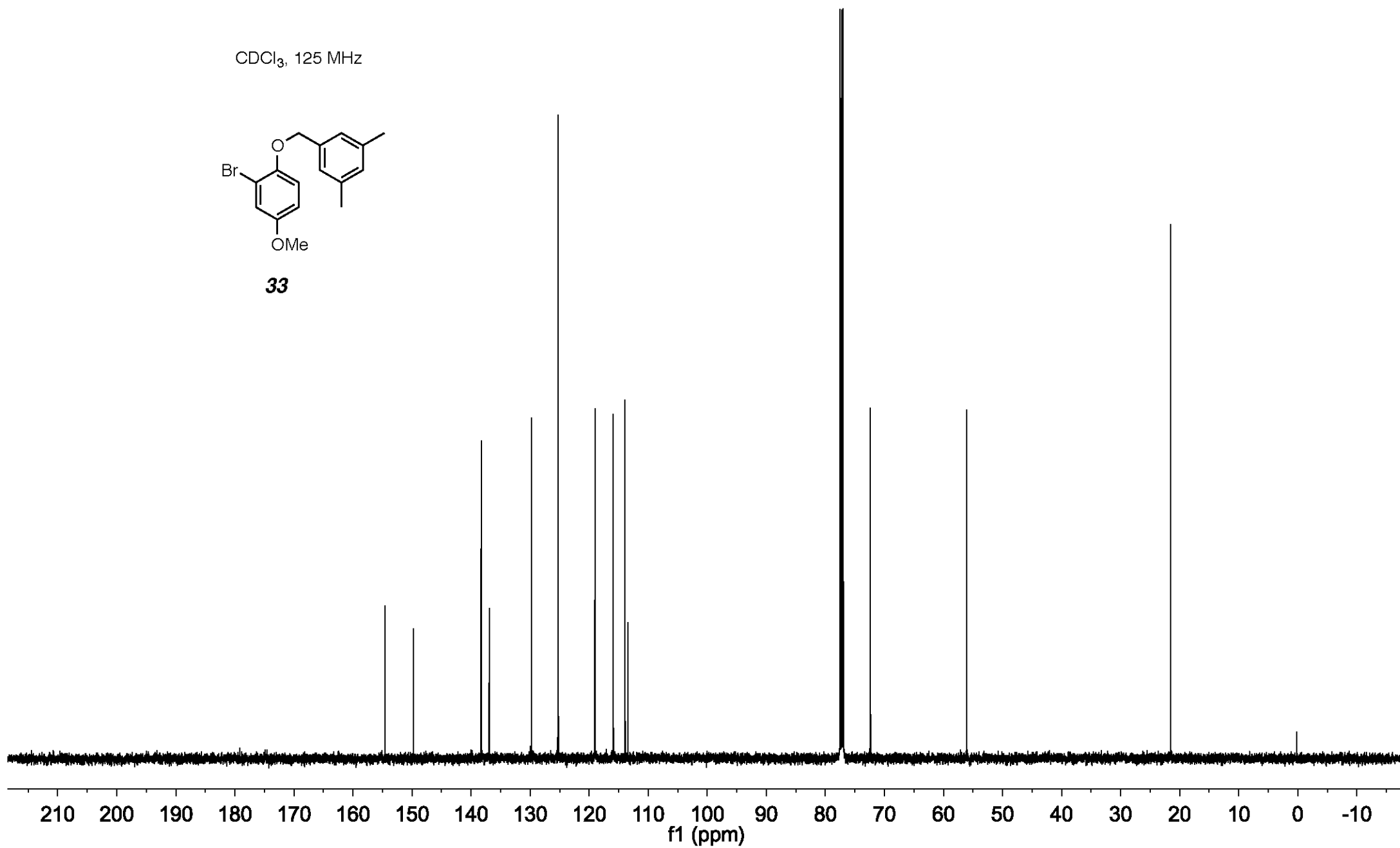
CDCl₃, 500 MHz**S41**

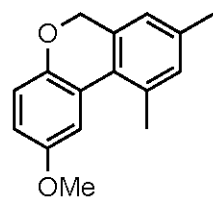
CDCl₃, 125 MHz**S41**

CDCl₃, 500 MHz



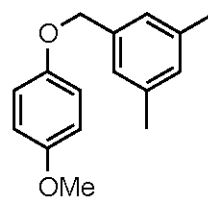
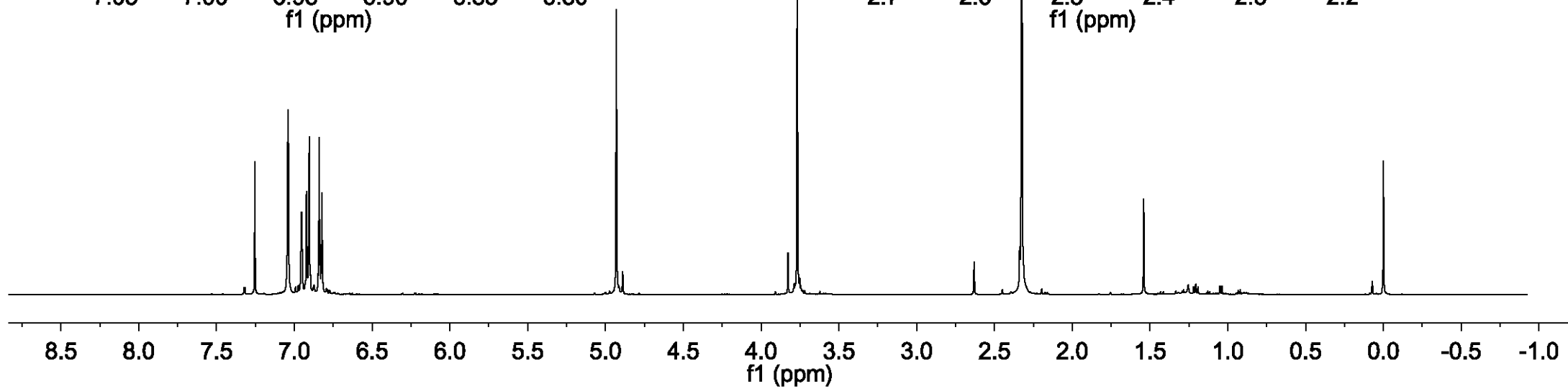
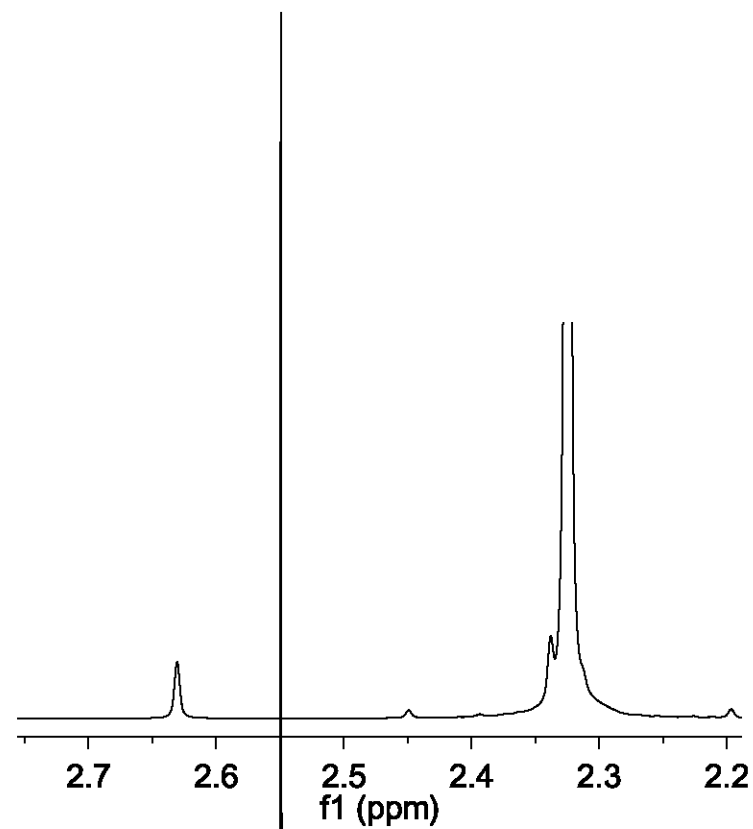
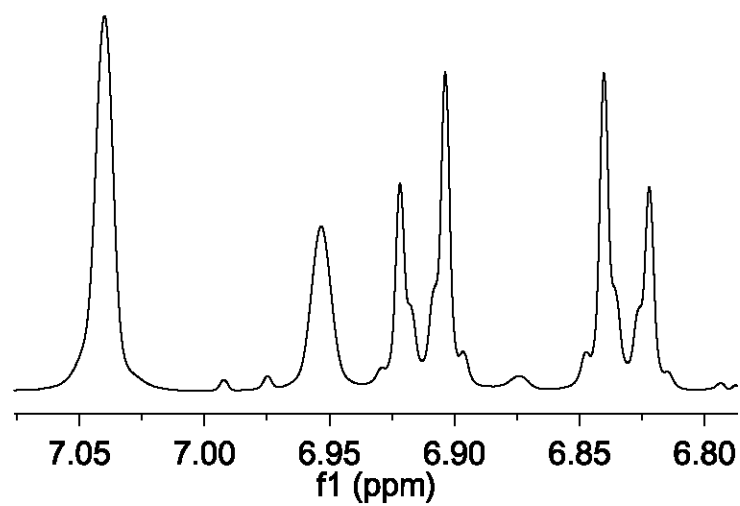
CDCl₃, 500 MHz**33**

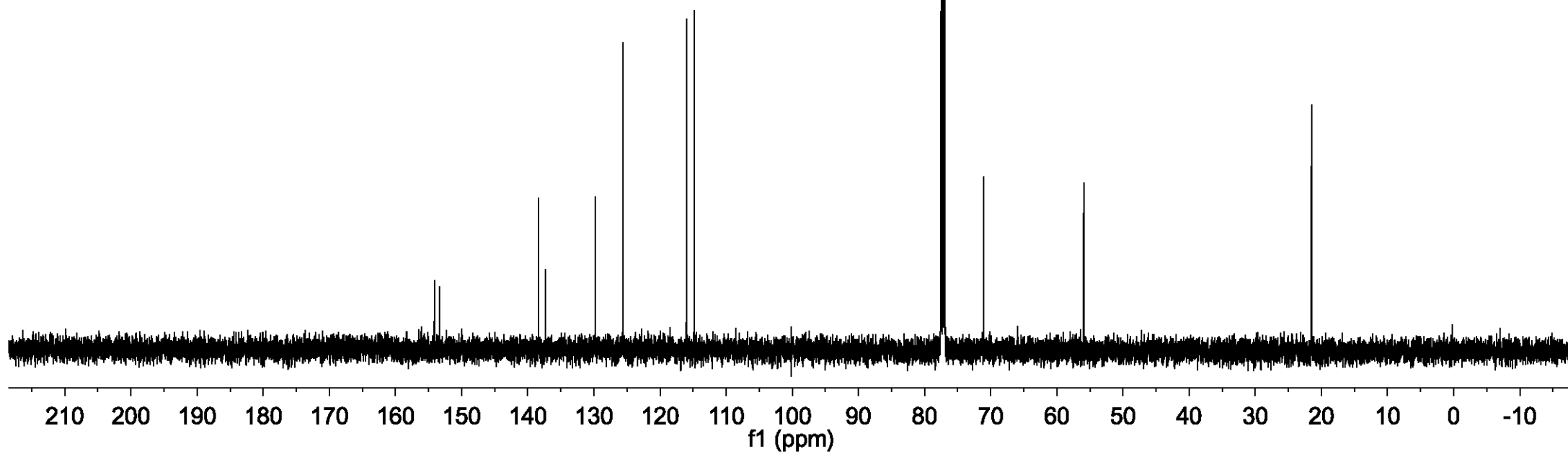
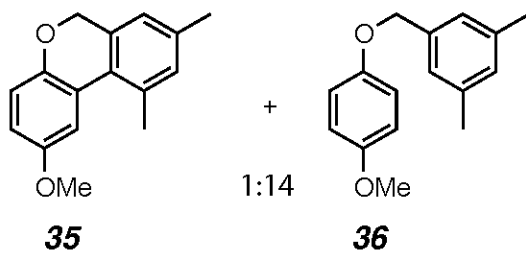
CDCl₃, 125 MHz**33**

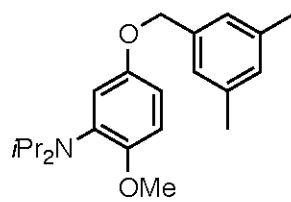
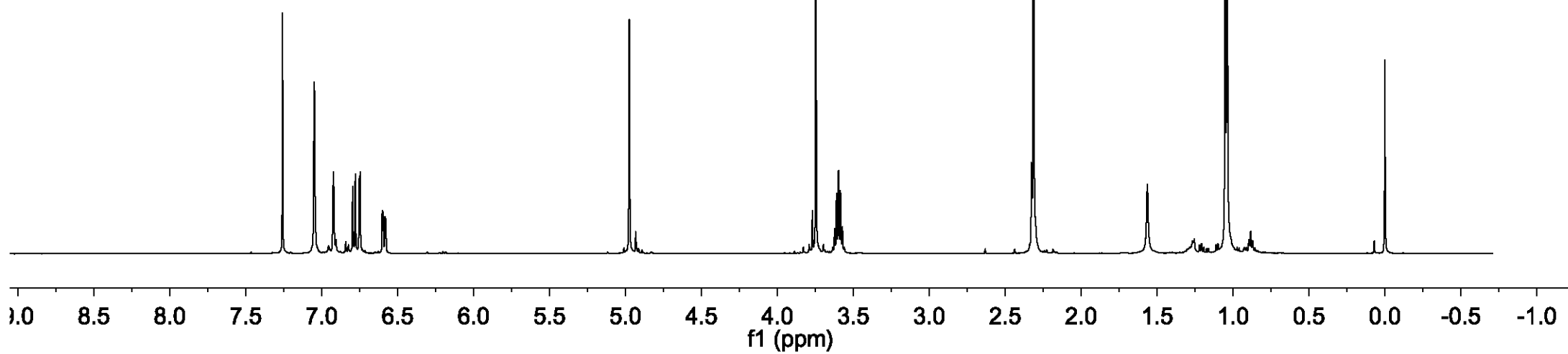
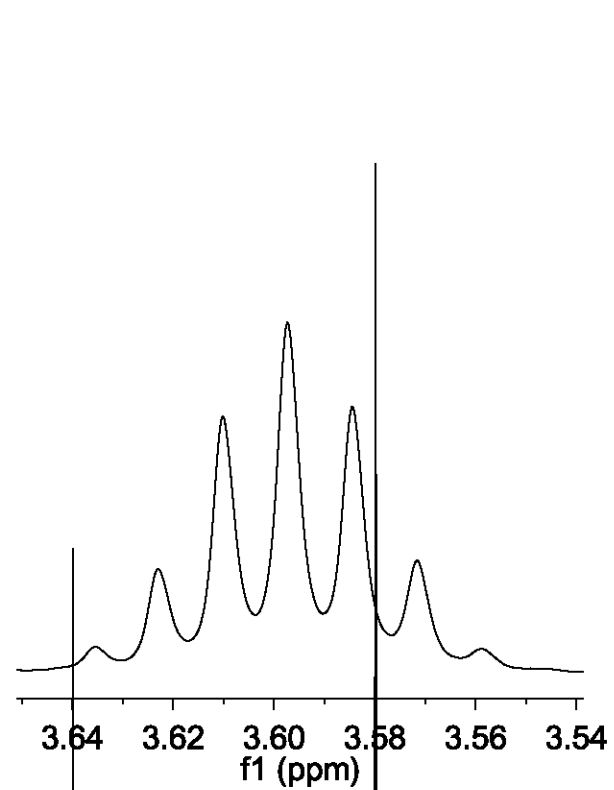
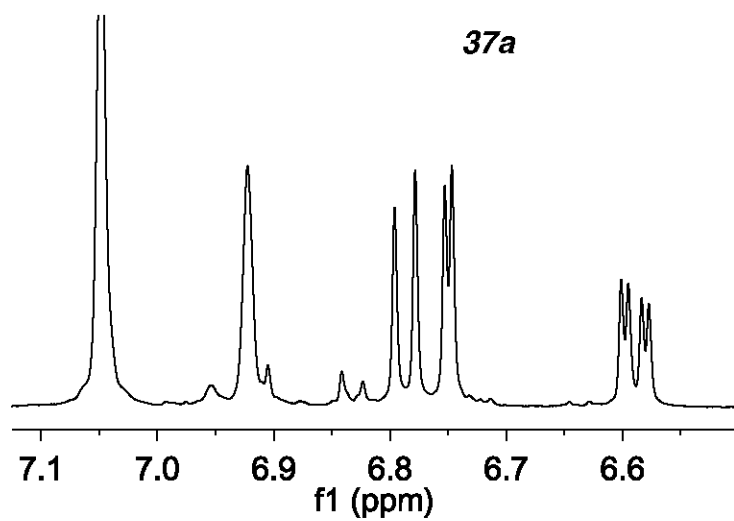
CDCl₃, 500 MHz**35**

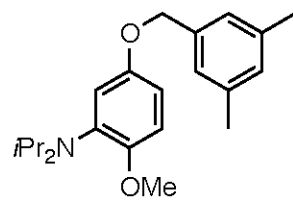
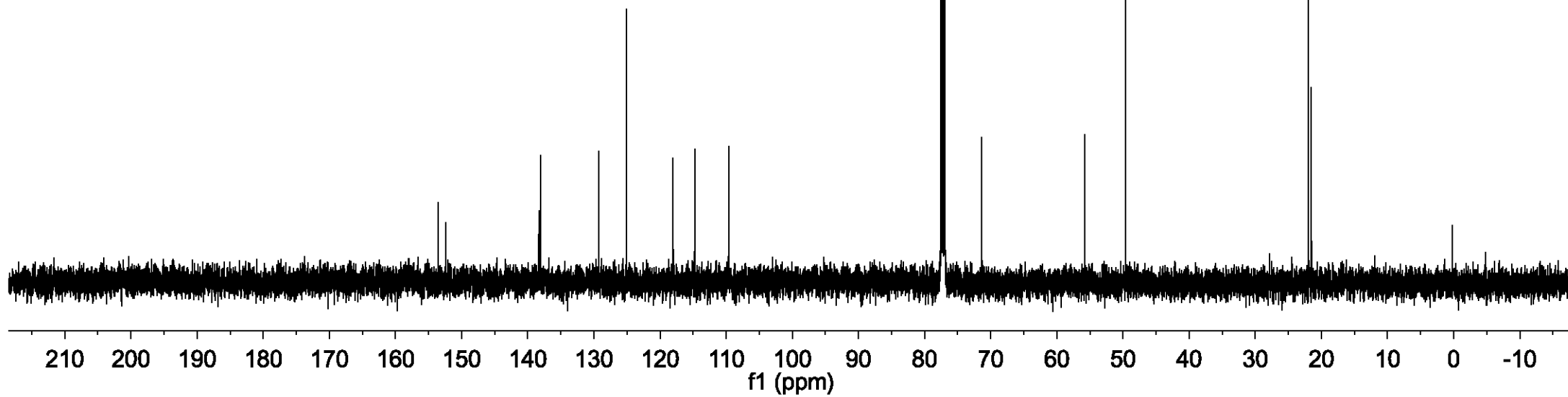
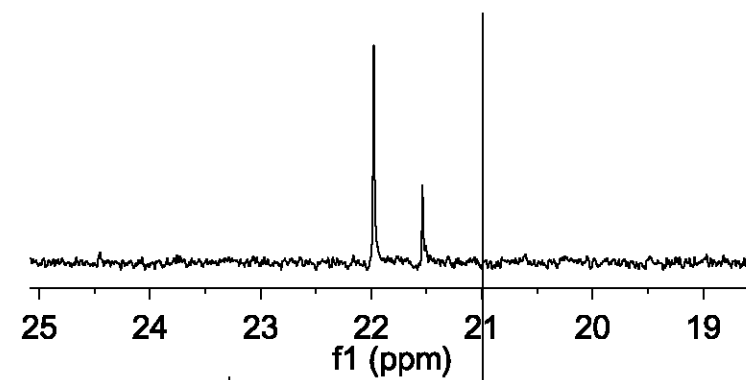
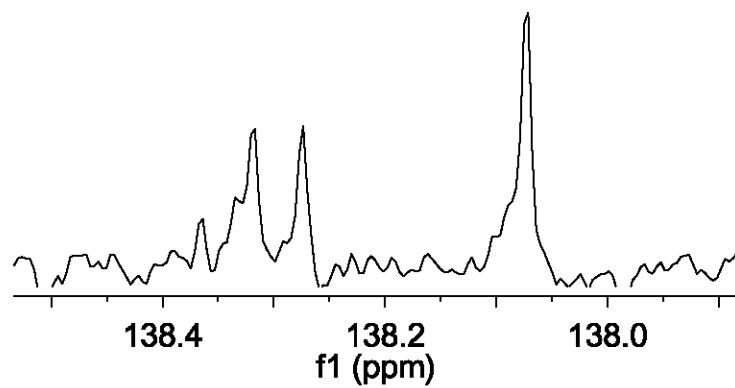
+

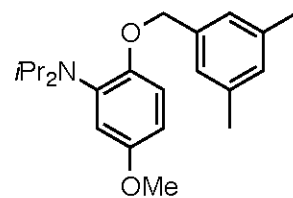
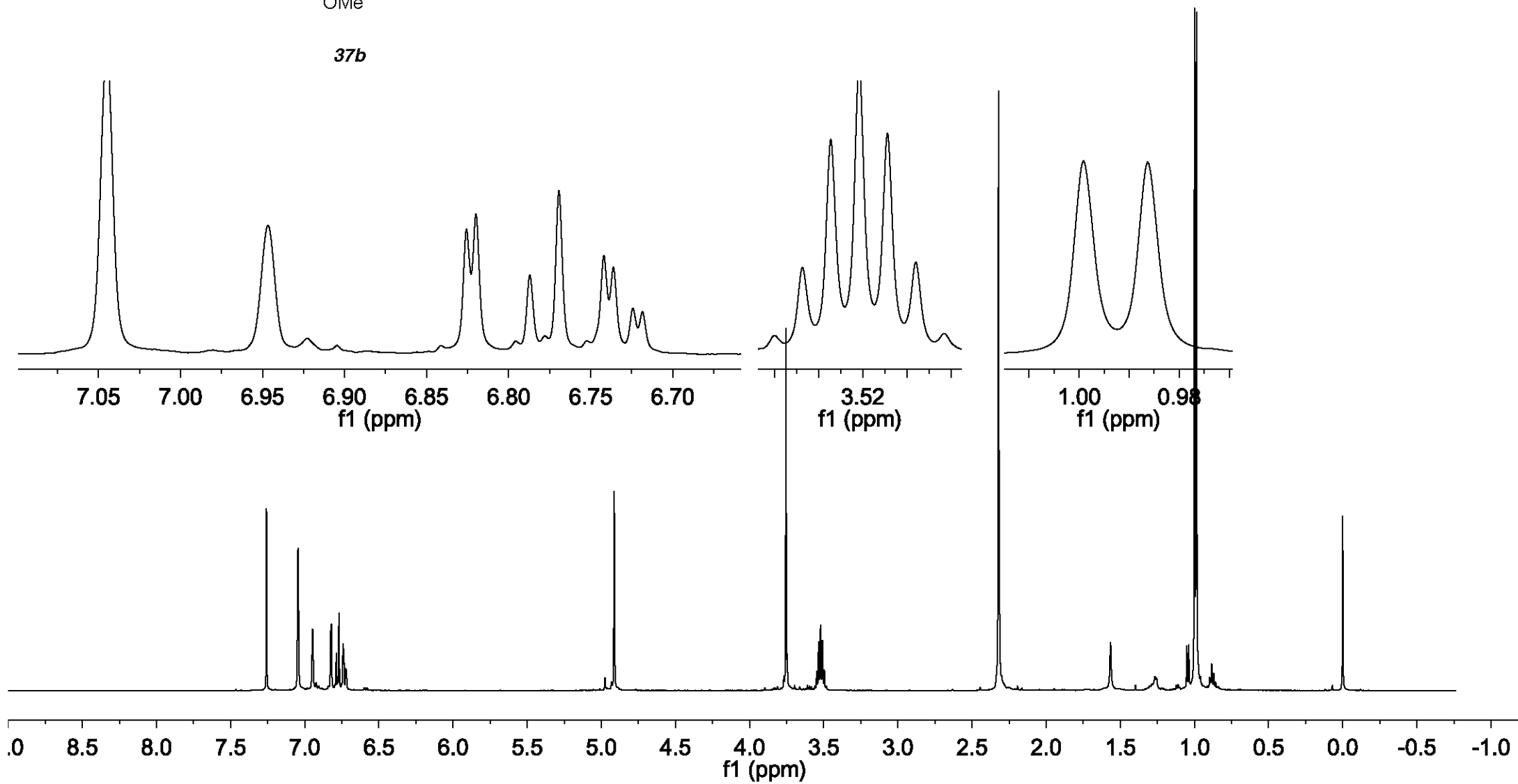
1:14

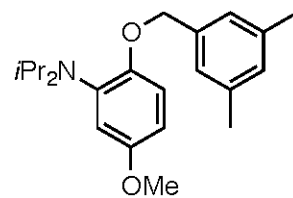
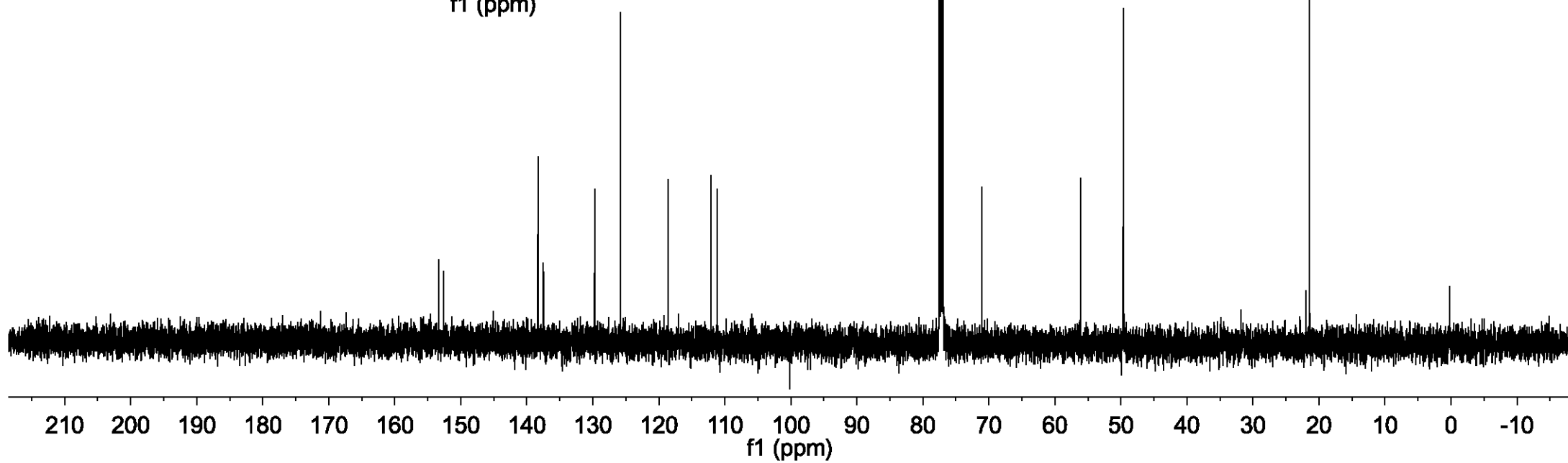
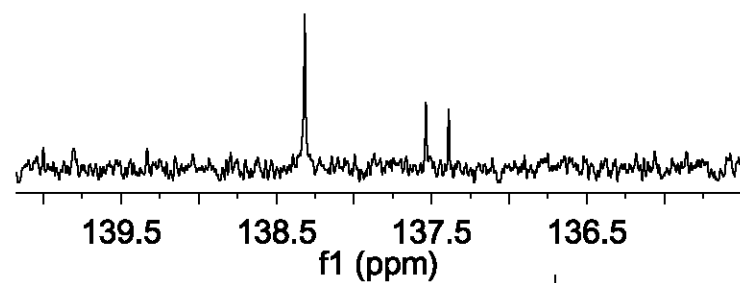
**36**

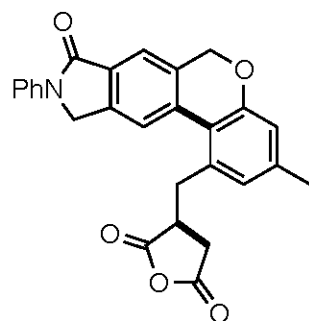
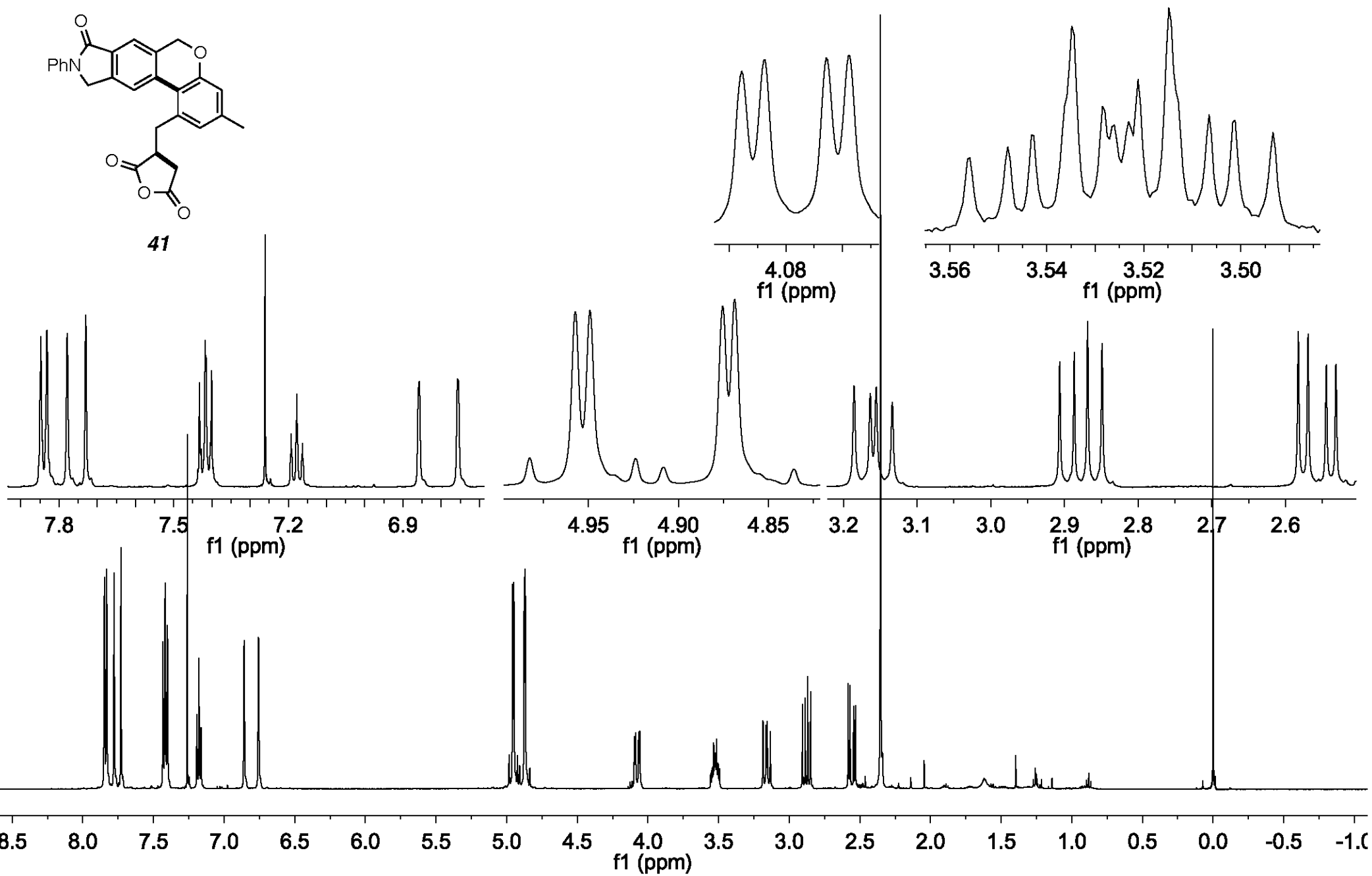
CDCl₃, 125 MHz

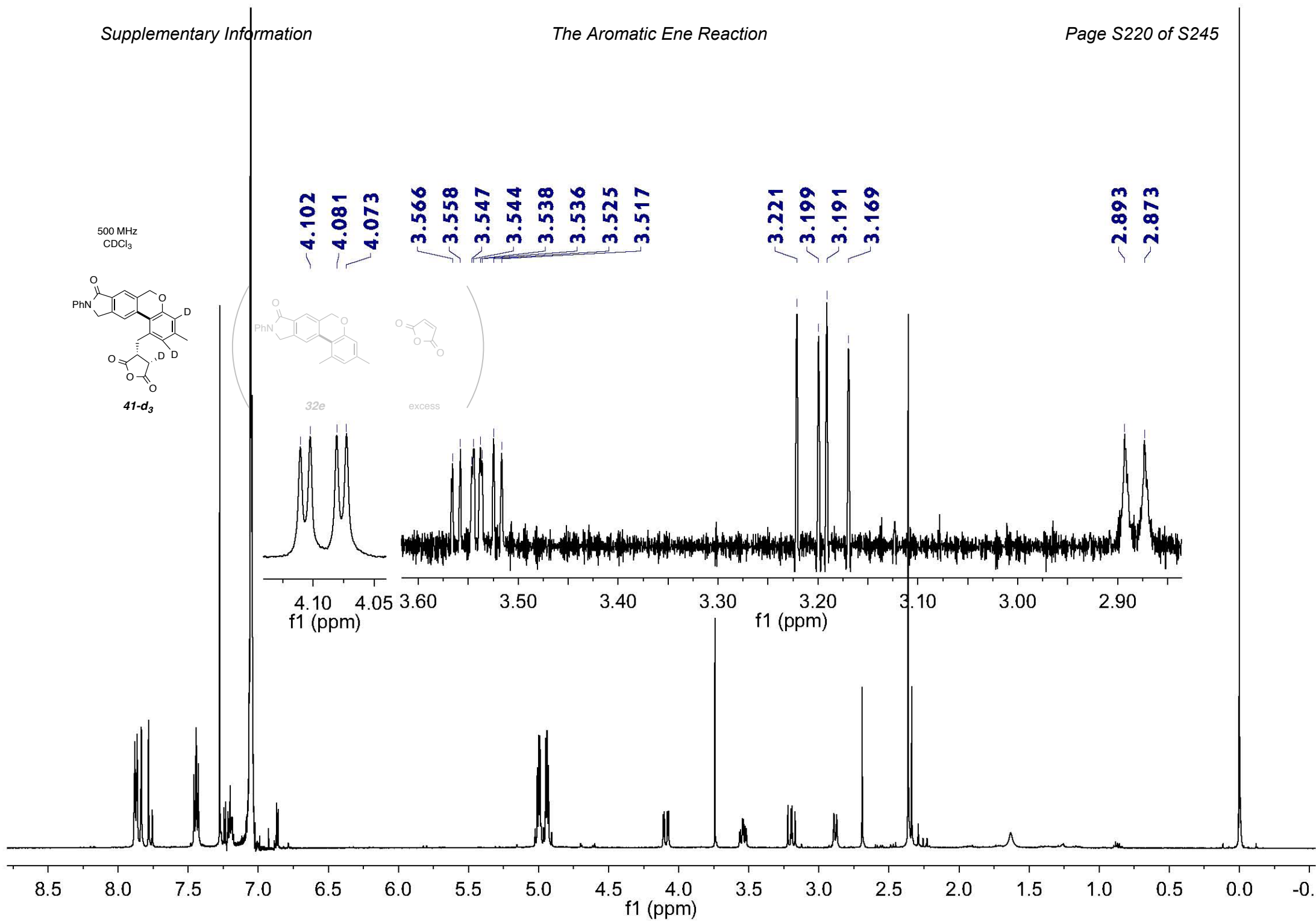
CDCl₃, 500 MHz**37a**

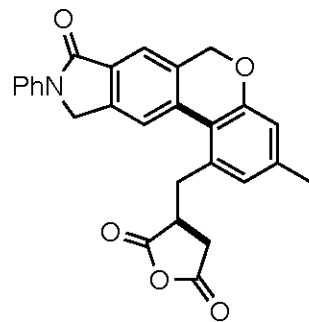
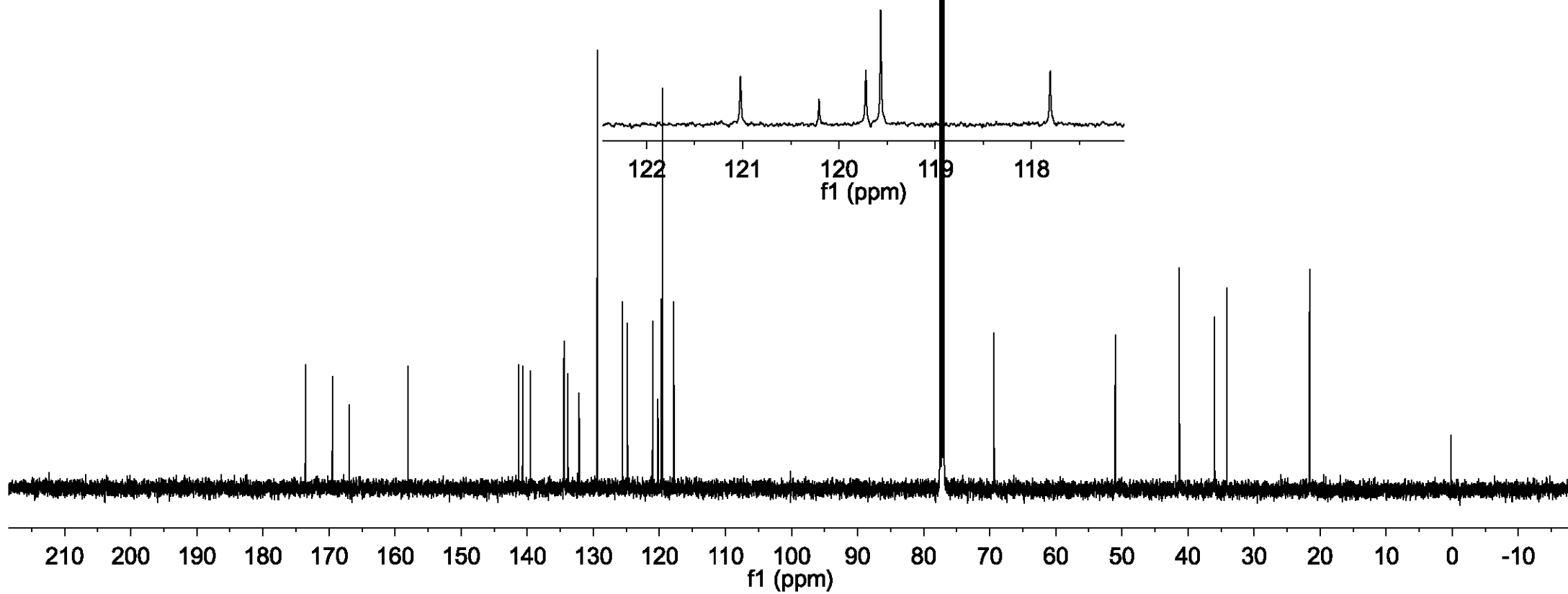
CDCl₃, 125 MHz**37a**

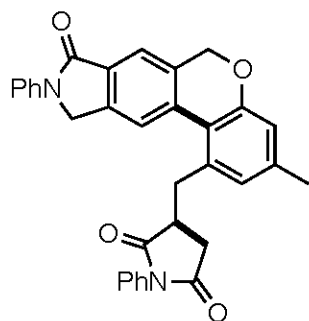
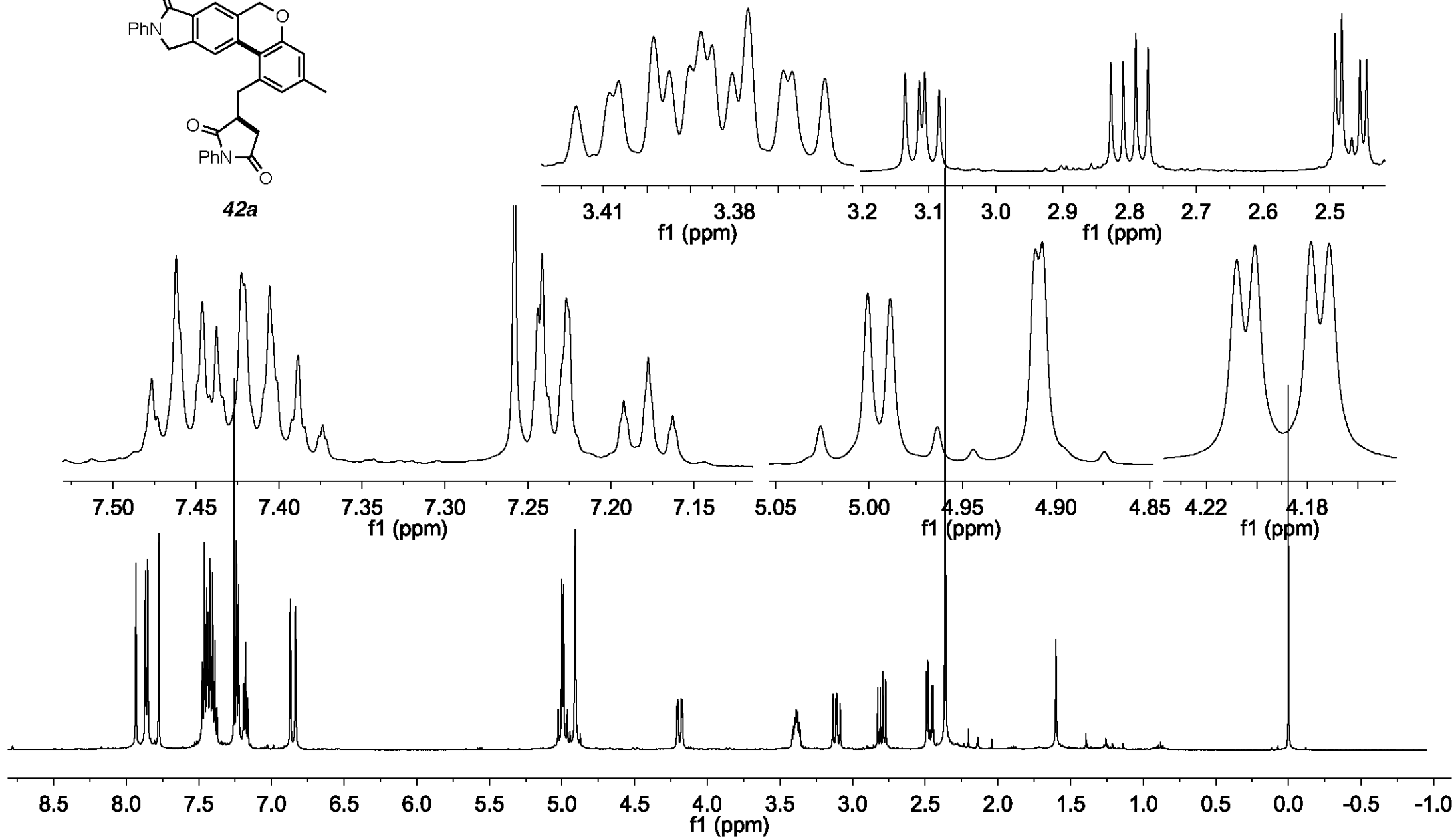
CDCl₃, 500 MHz**37b**

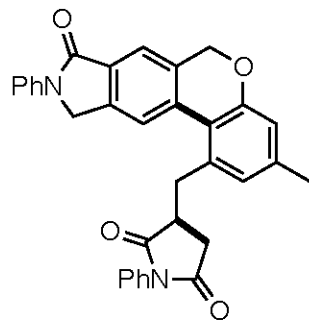
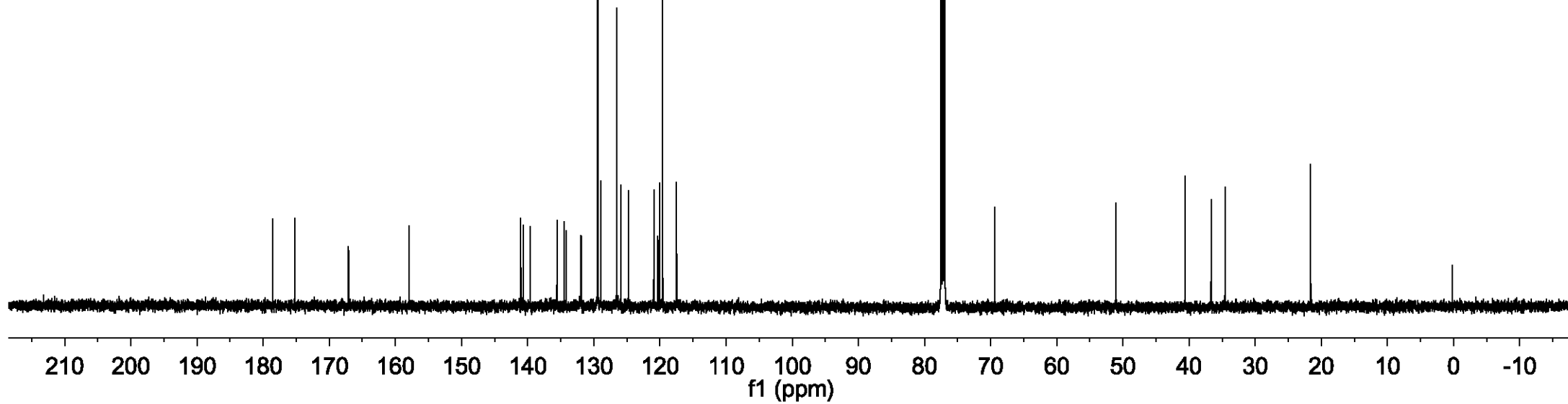
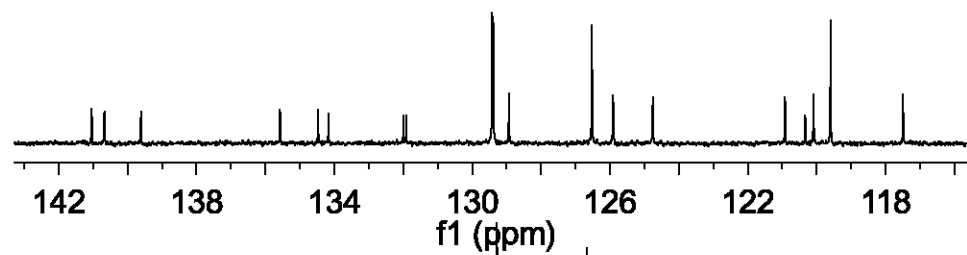
CDCl₃, 125 MHz**37b**

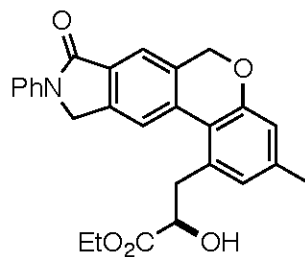
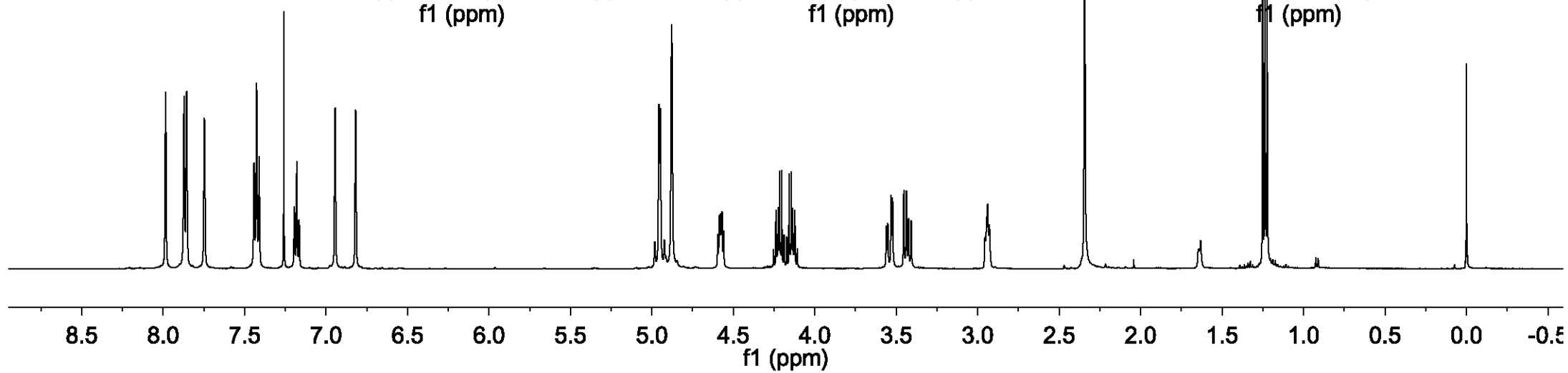
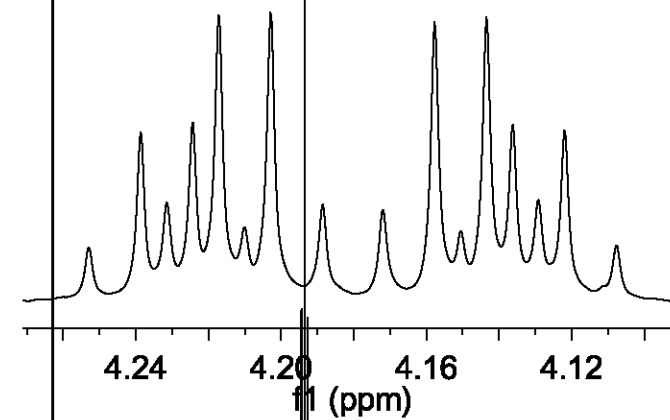
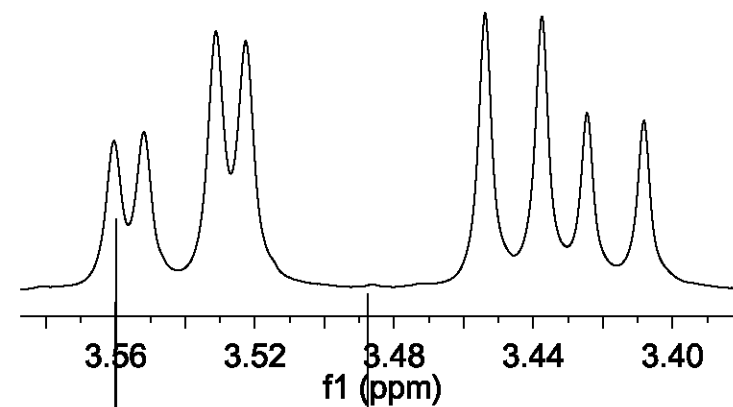
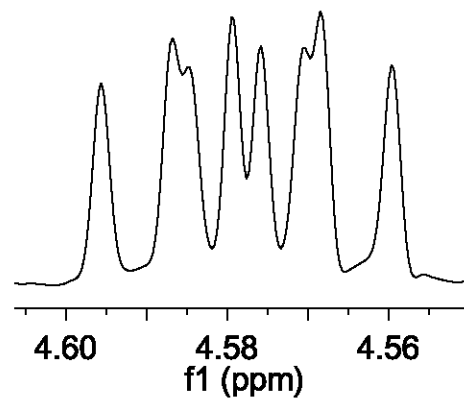
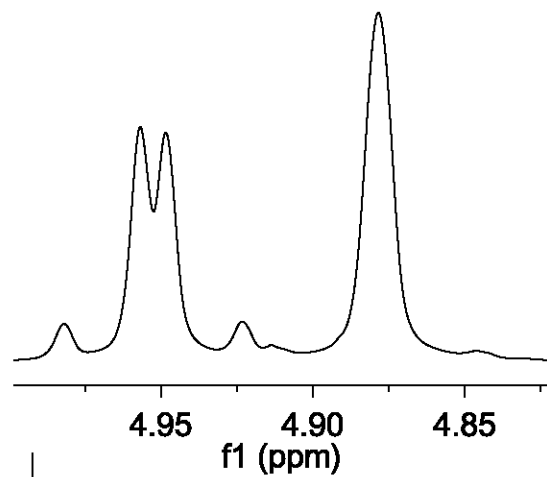
CDCl₃, 500 MHz**41**



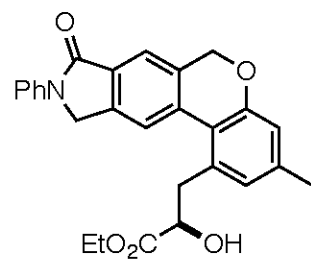
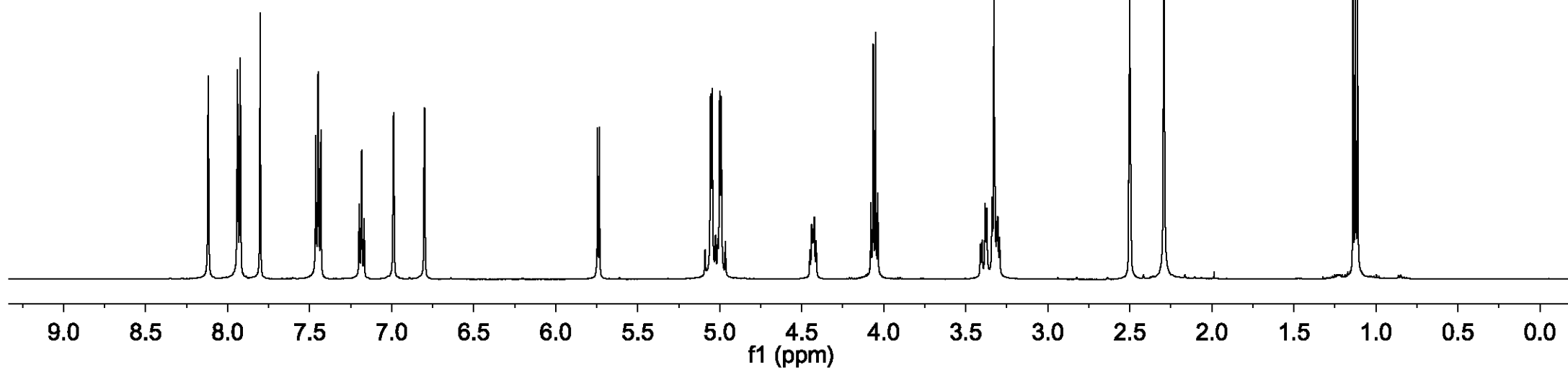
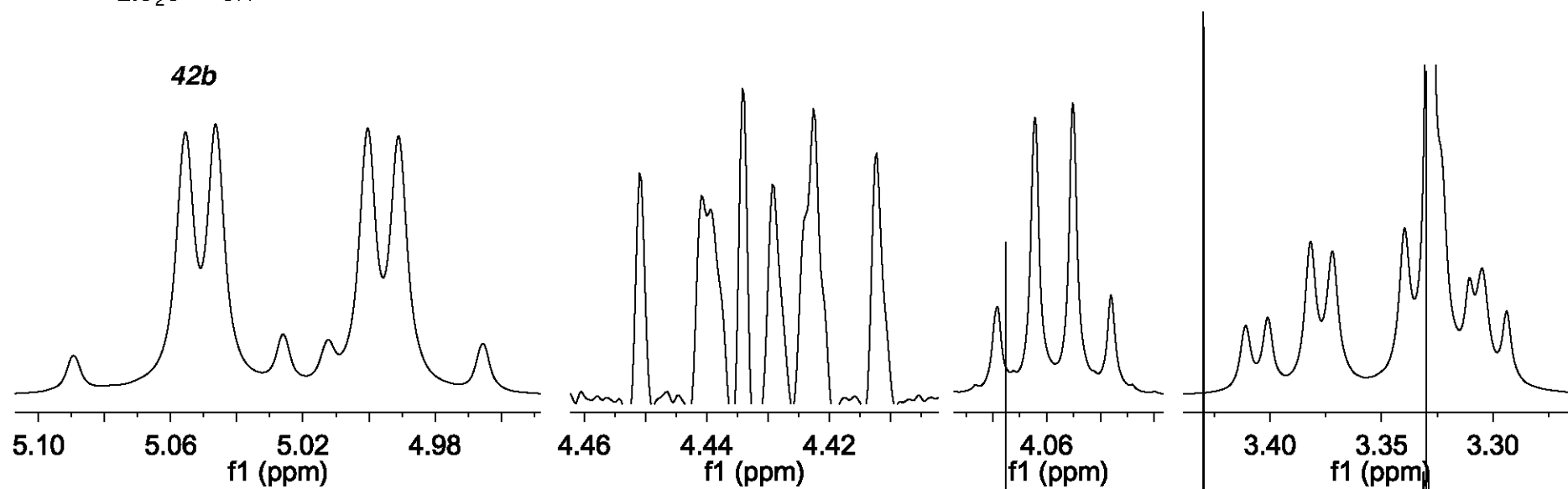
CDCl₃, 125 MHz**41**

CDCl₃, 500 MHz**42a**

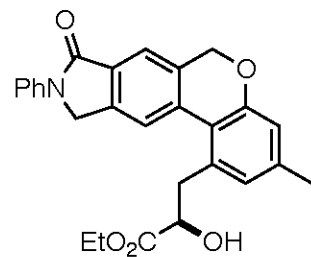
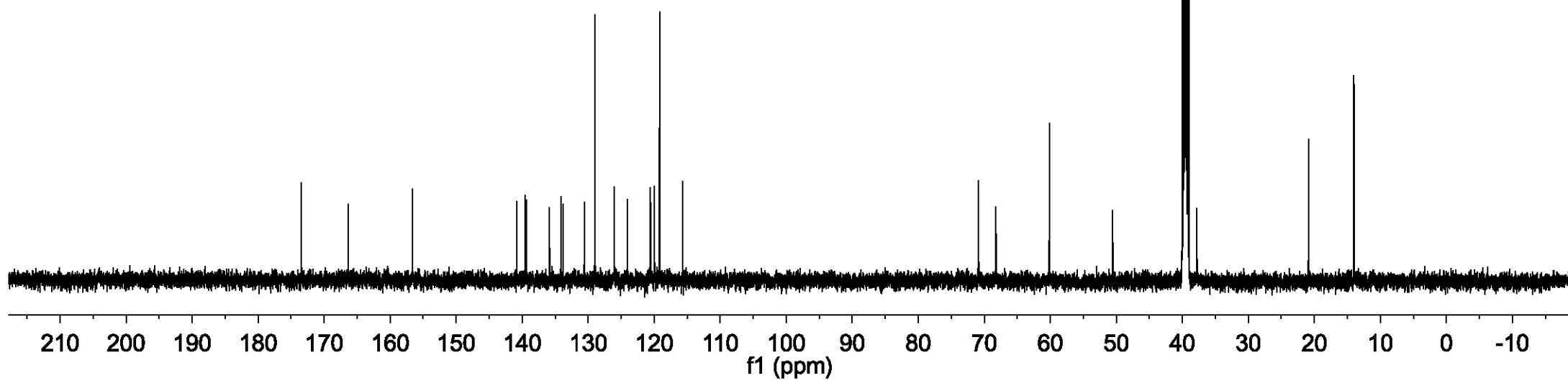
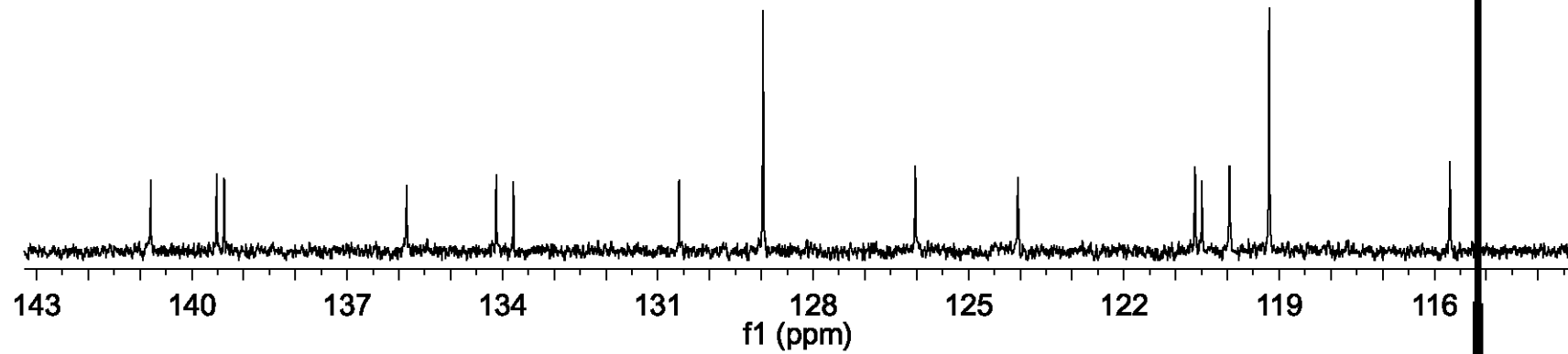
CDCl₃, 125 MHz**42a**

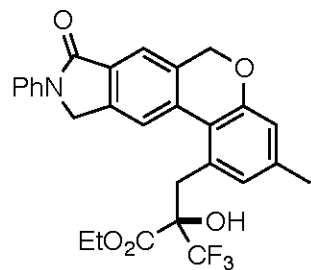
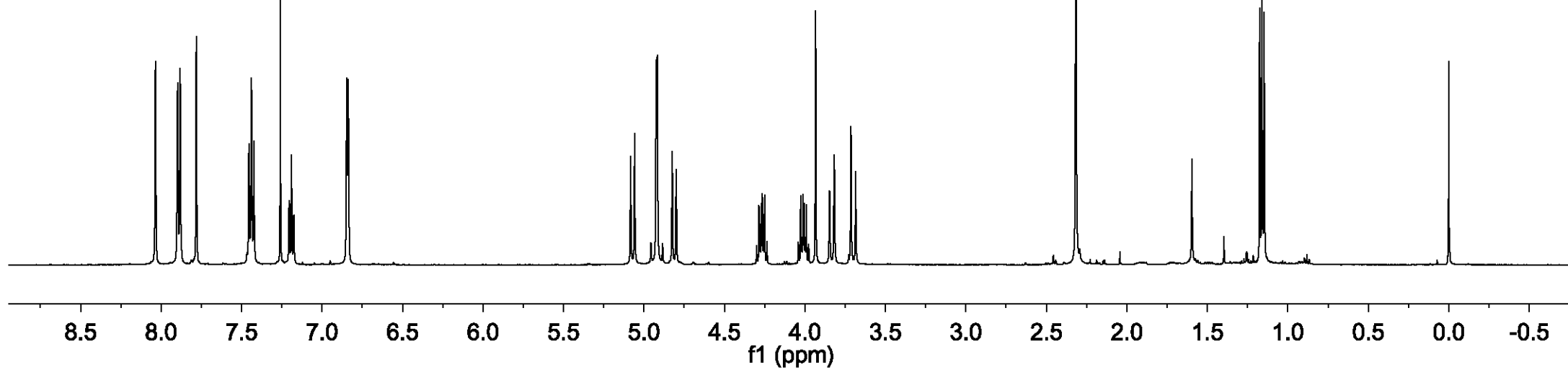
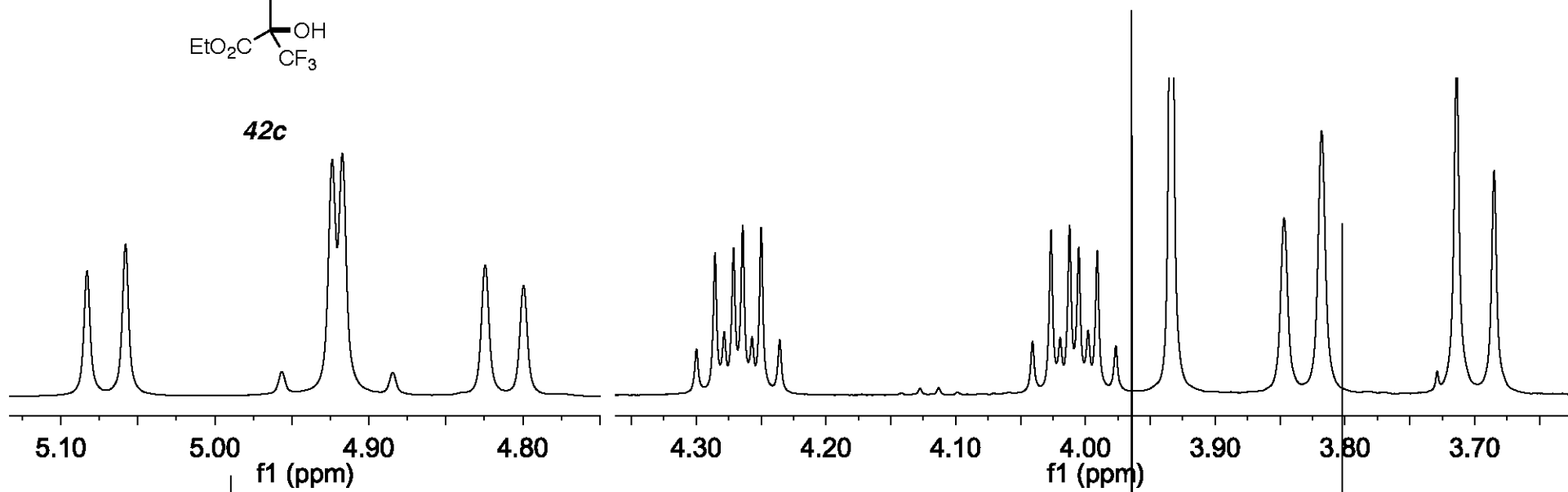
CDCl₃, 500 MHz**42b**

DMSO, 500 MHz

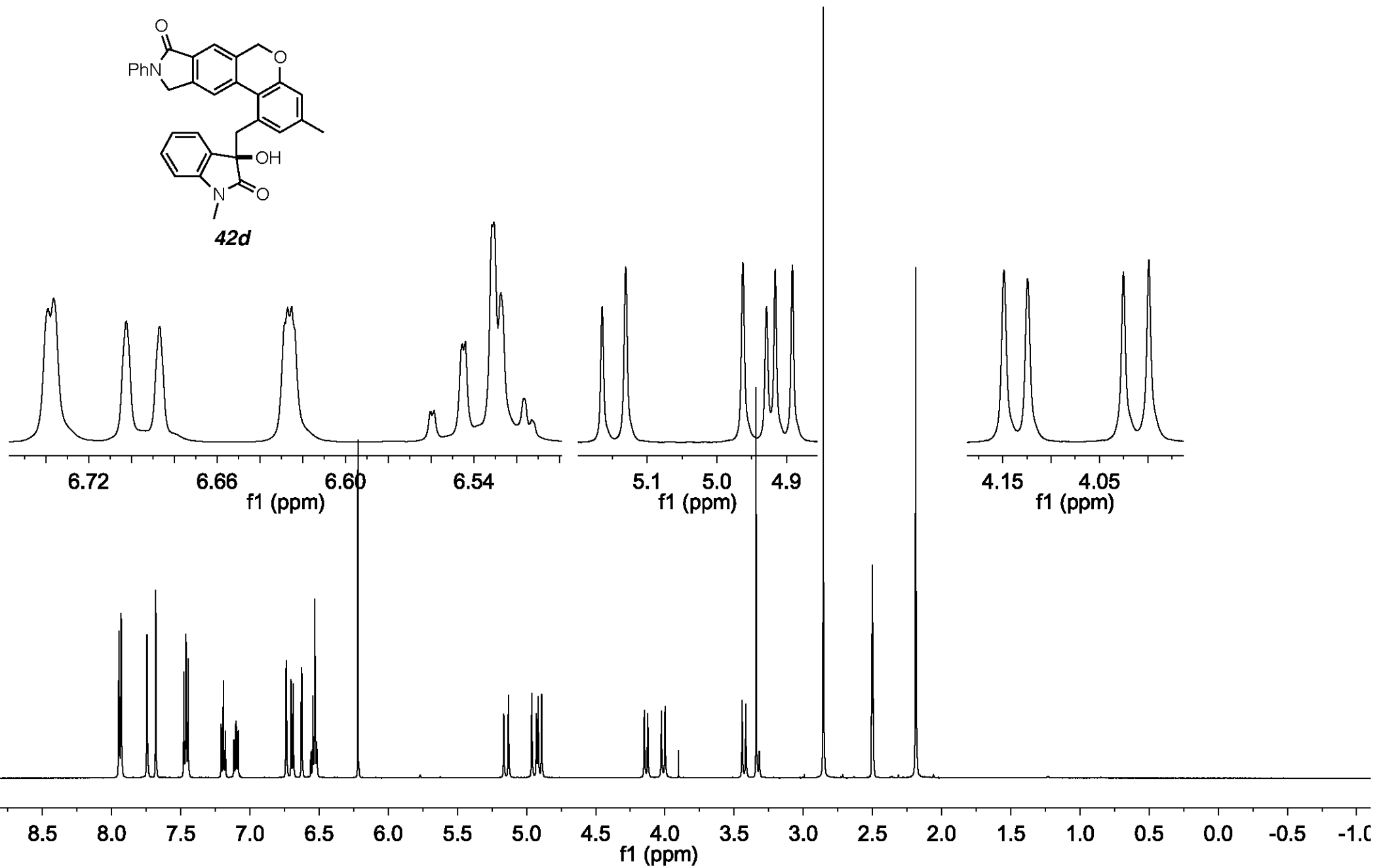
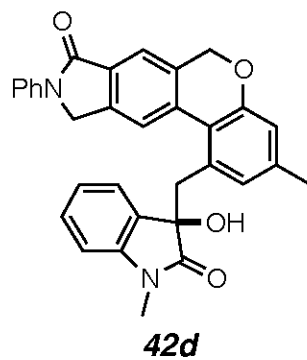
**42b**

DMSO, 125 MHz

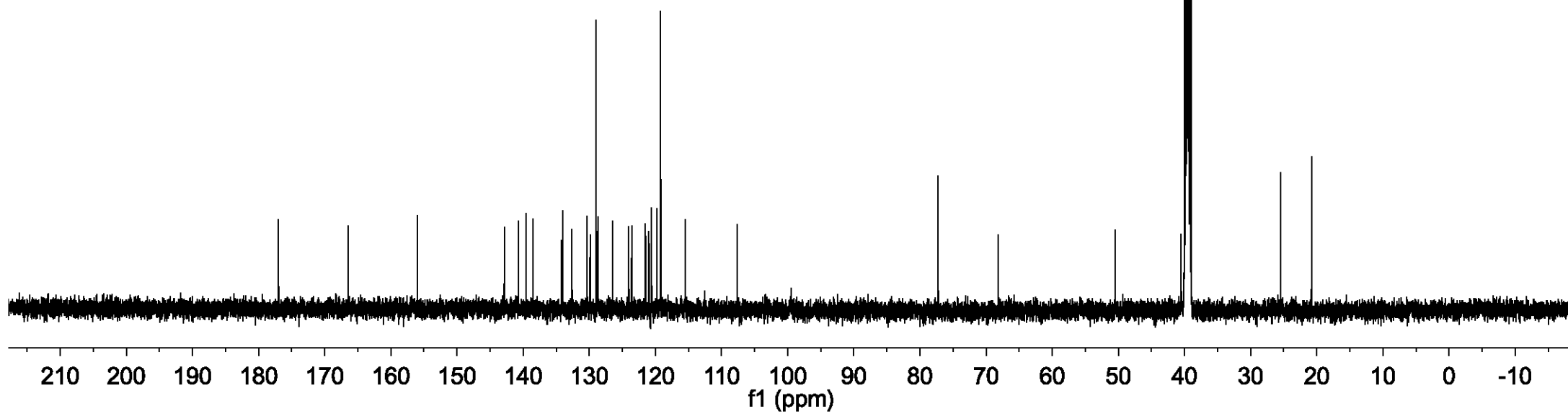
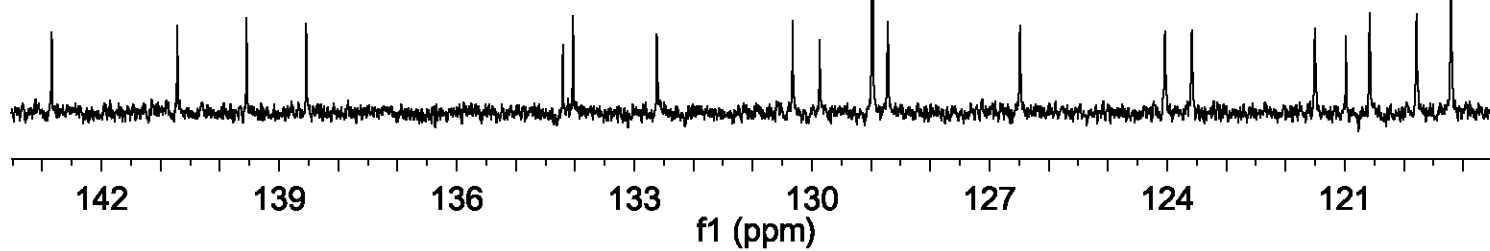
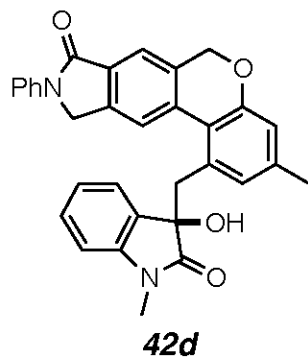
**42b**

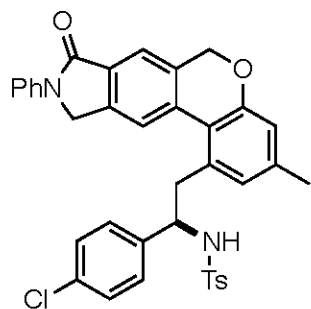
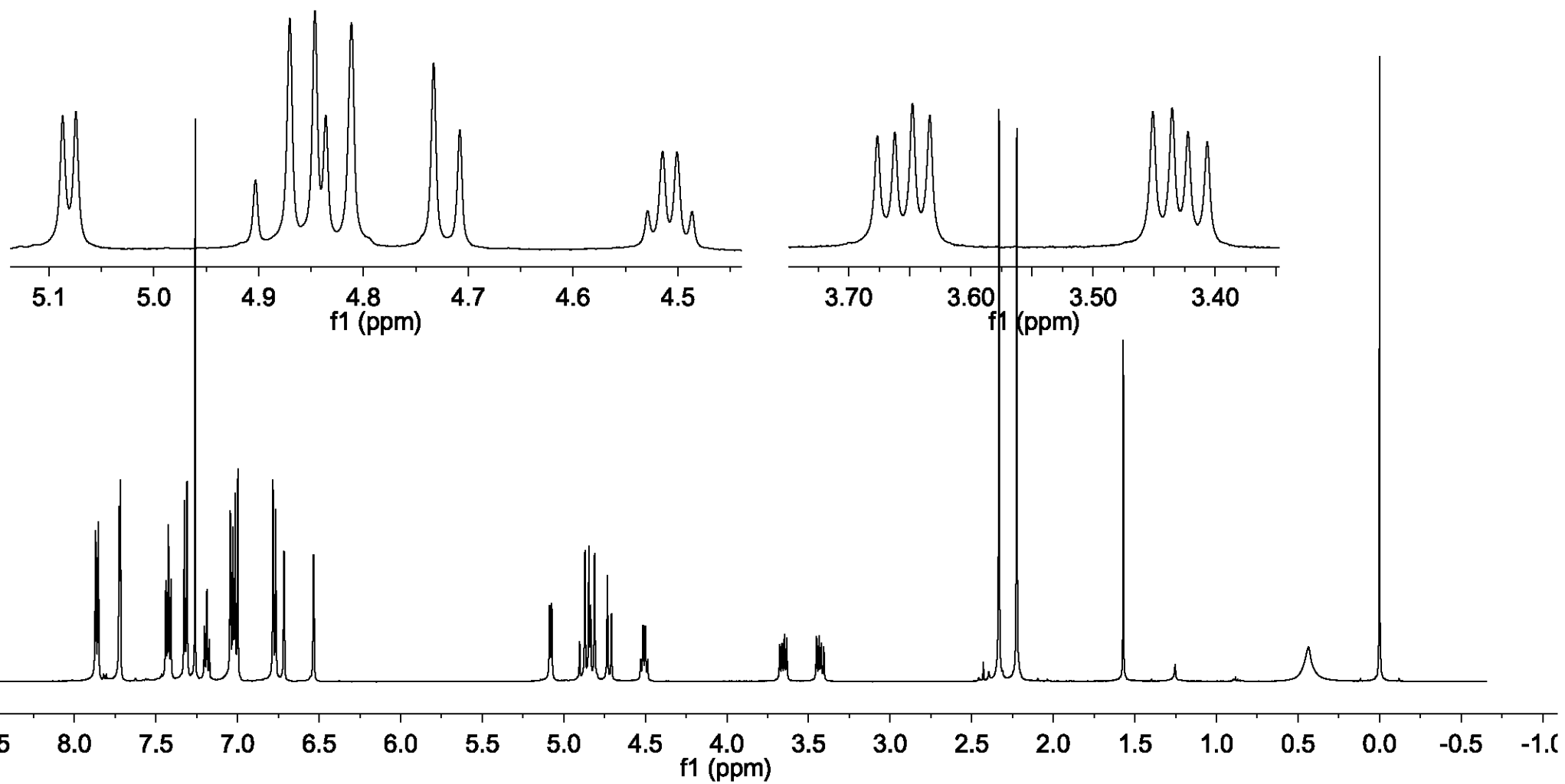
CDCl₃, 500 MHz**42c**

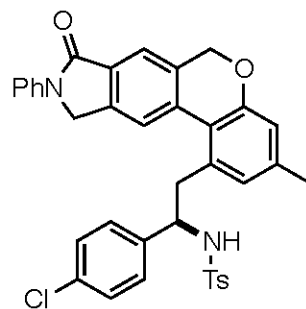
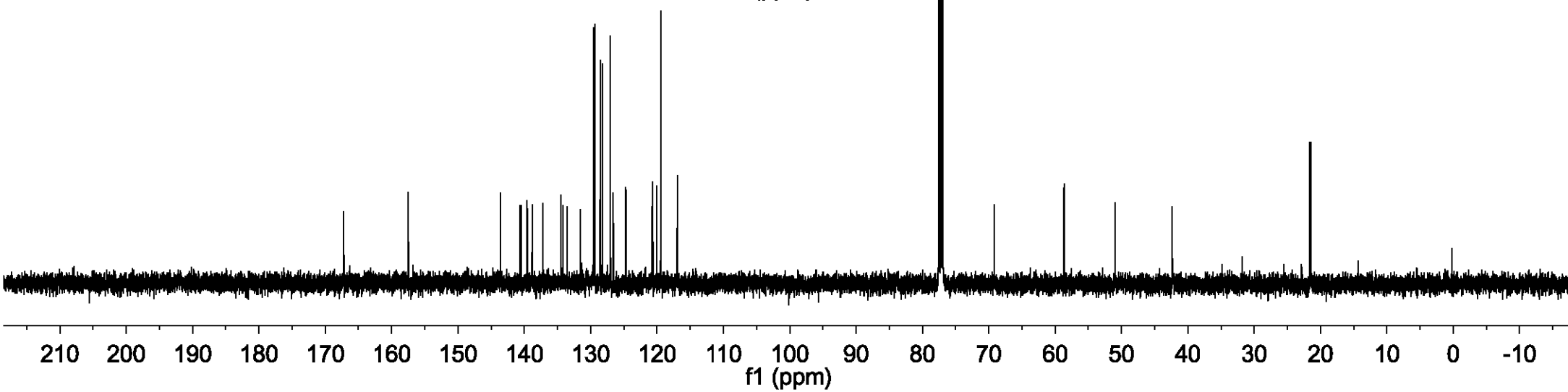
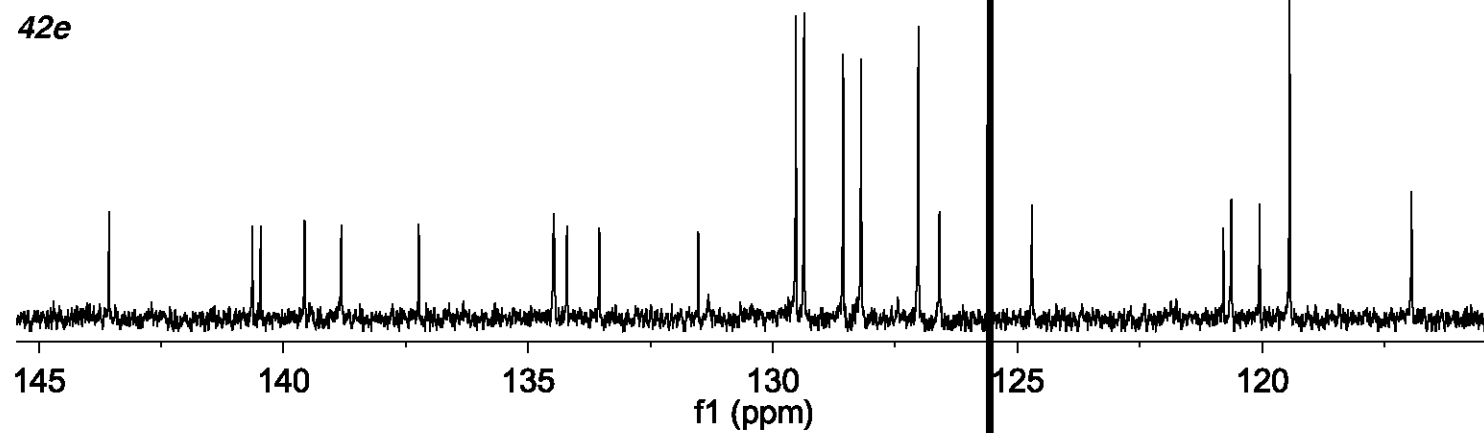
DMSO, 500 MHz

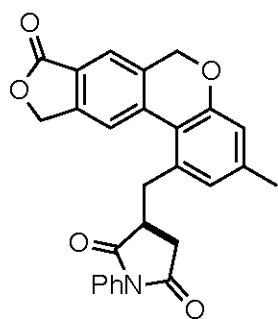
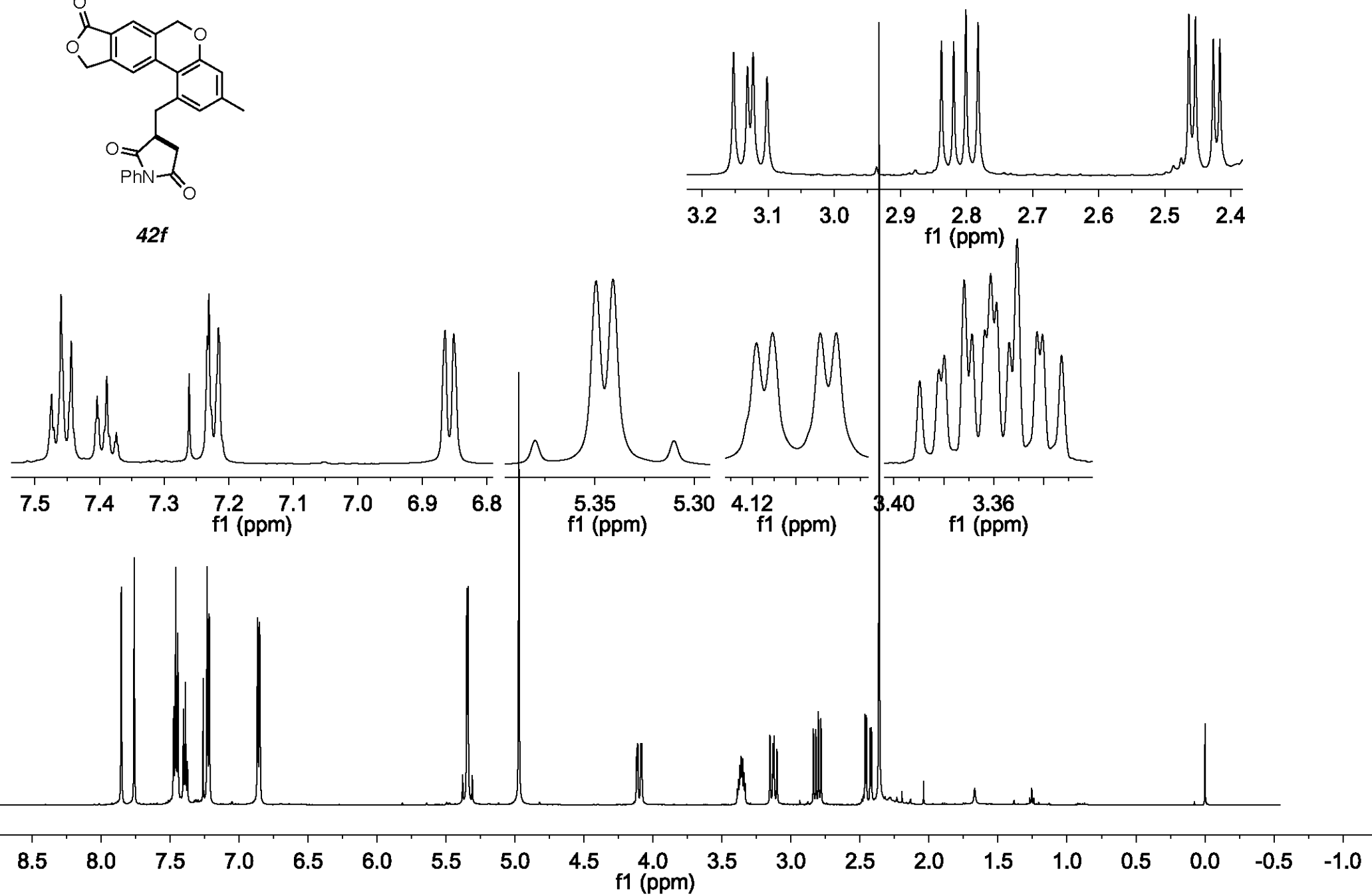


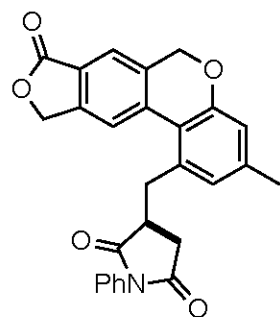
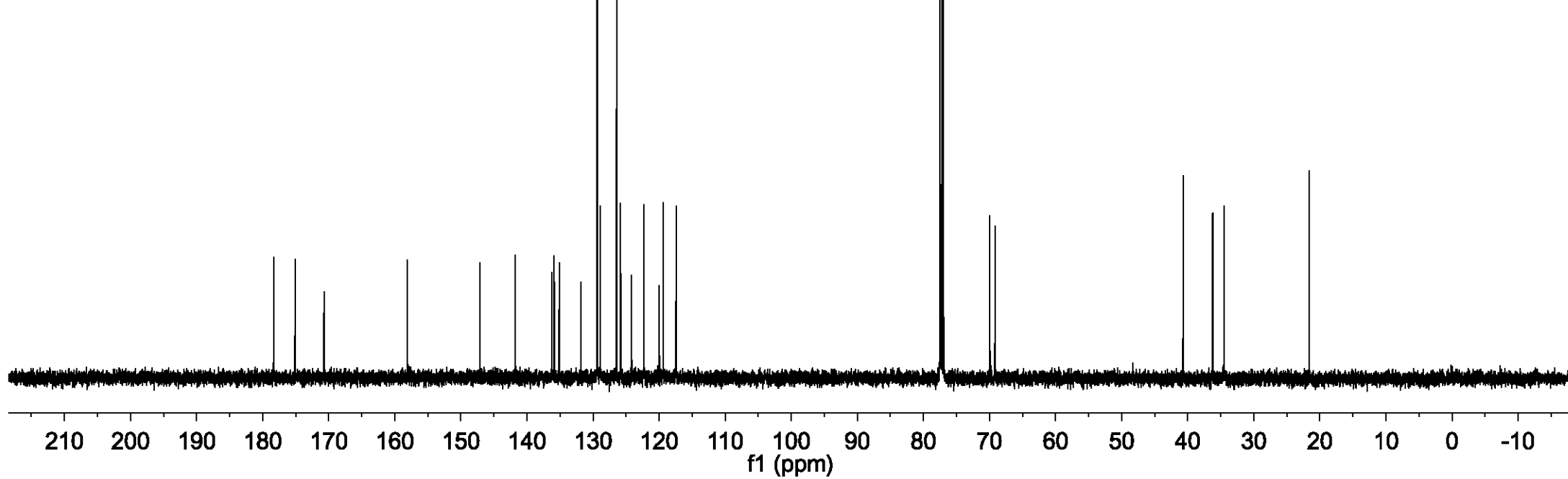
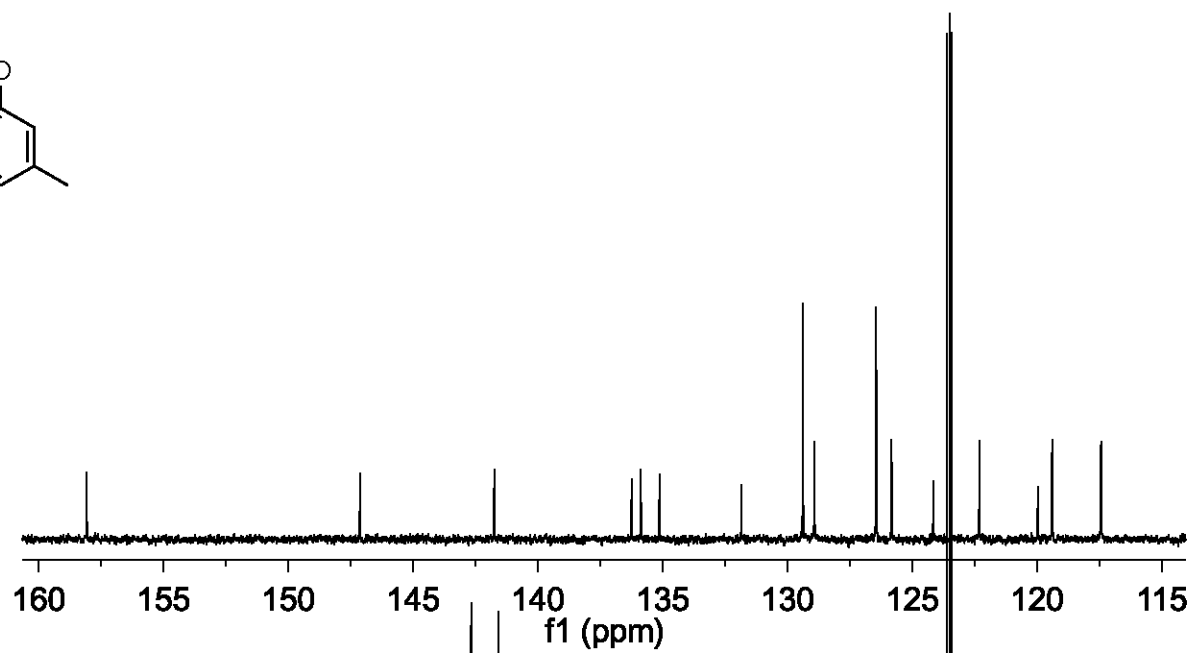
DMSO, 125 MHz

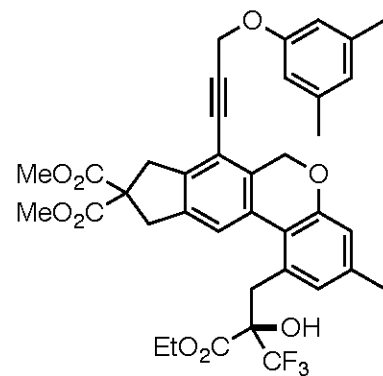
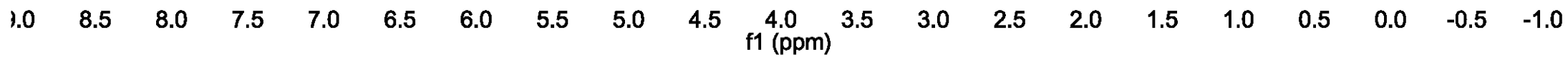
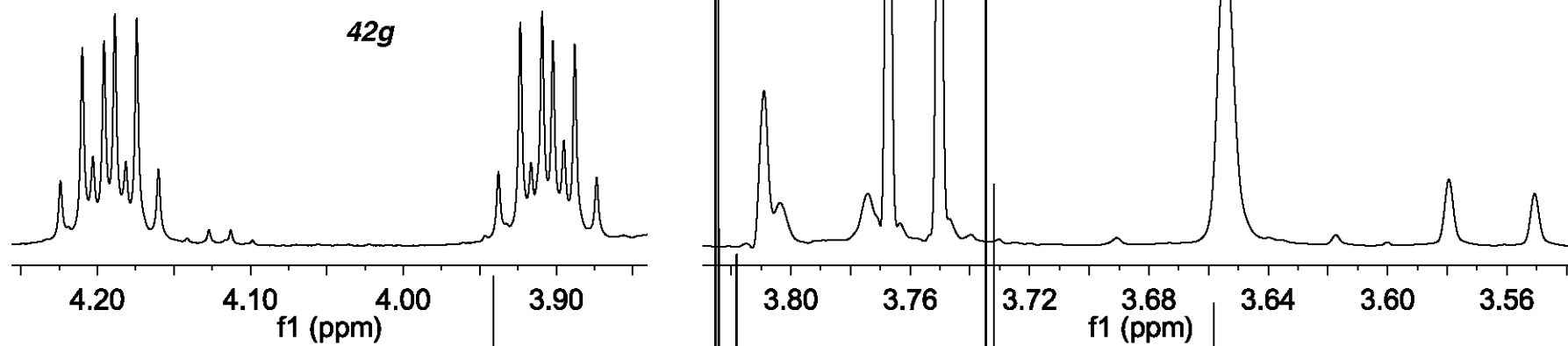


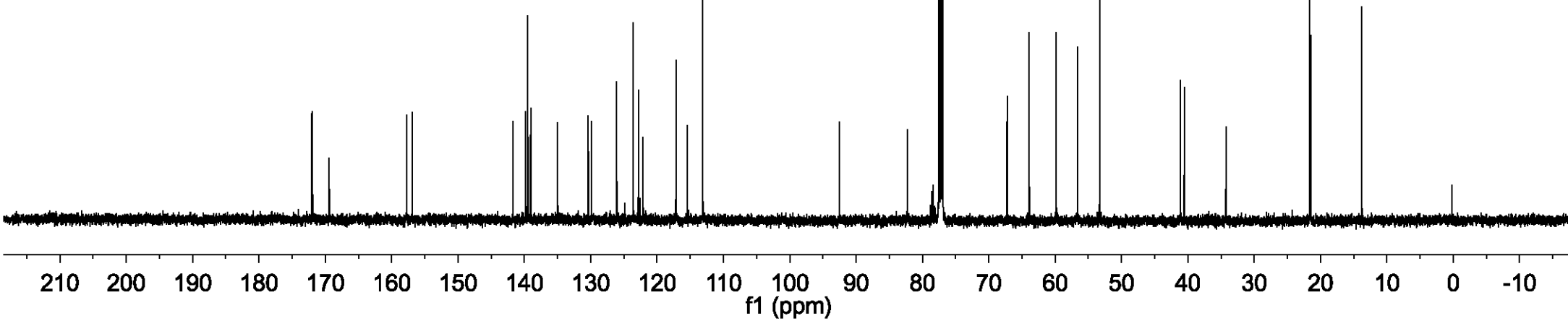
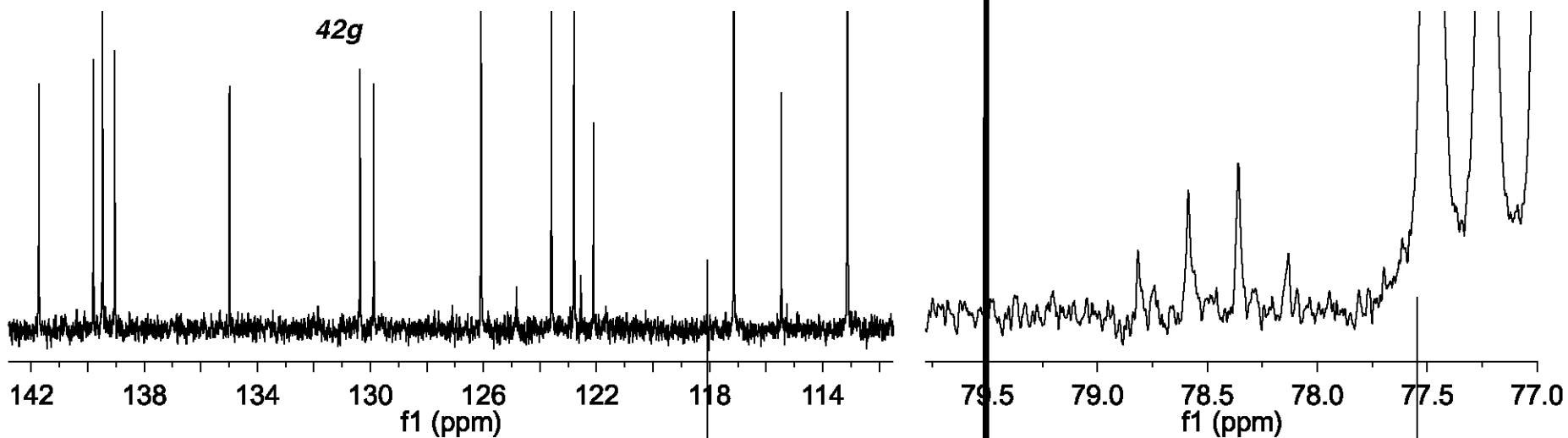
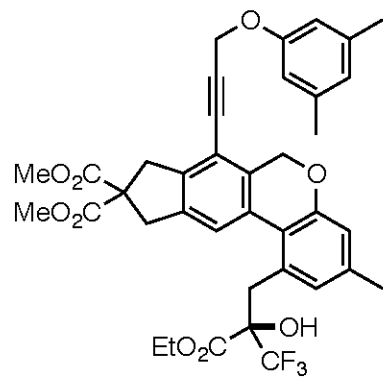
**42e**

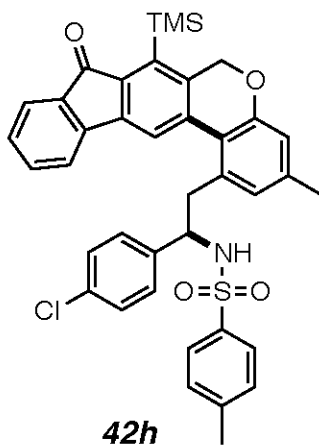
CDCl₃, 125 MHz**42e**

CDCl₃, 500 MHz**42f**

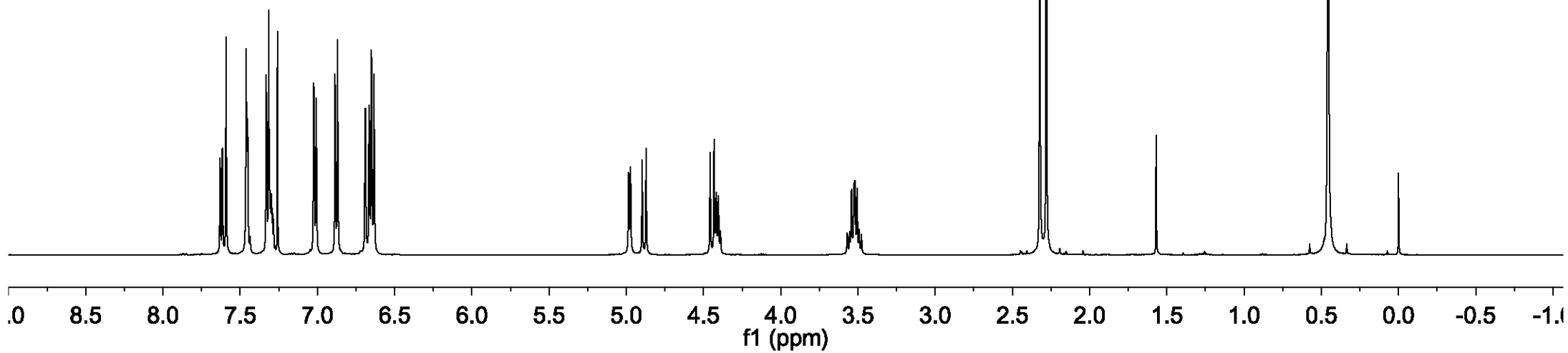
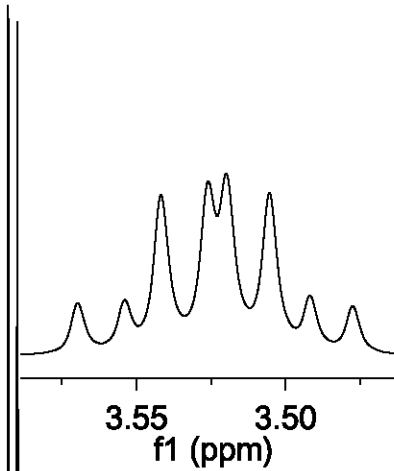
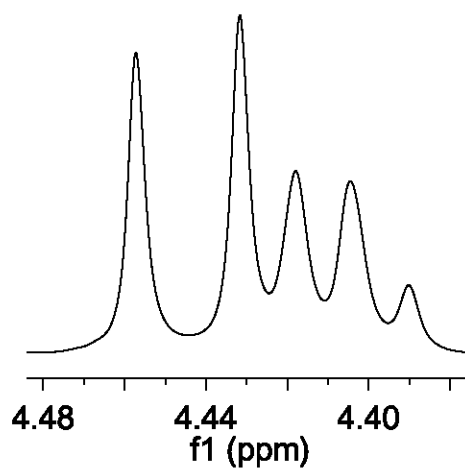
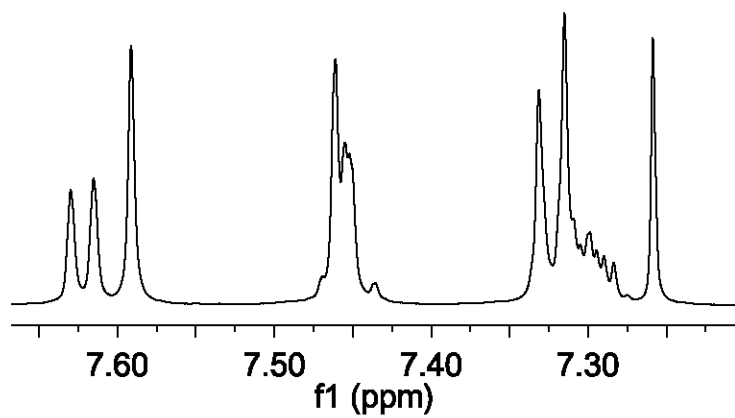
CDCl₃, 125 MHz**42f**

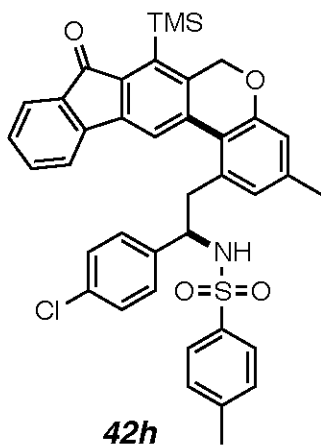
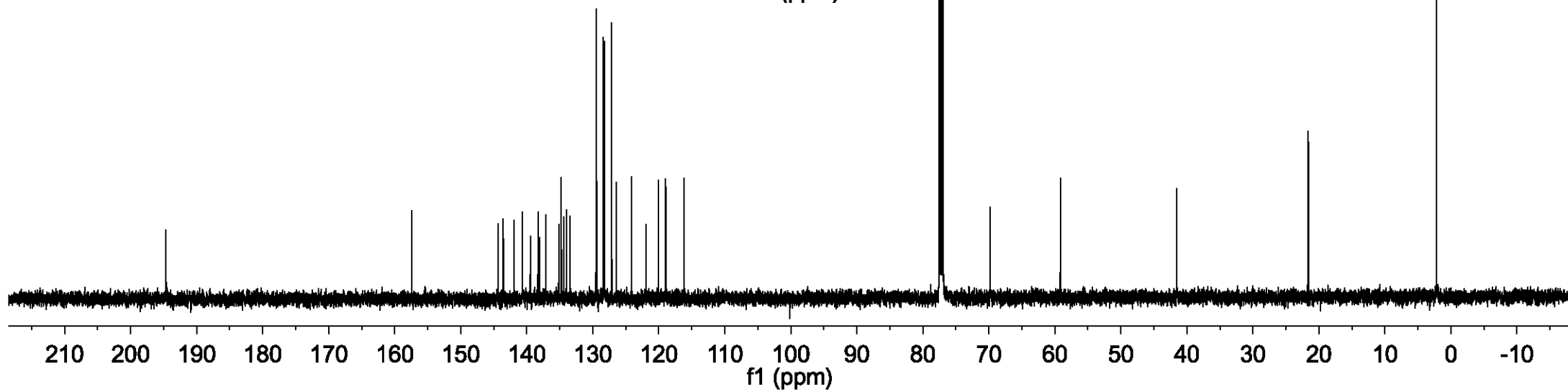
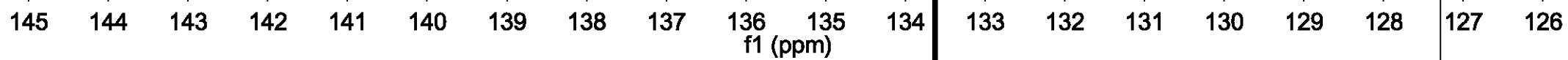
CDCl₃, 500 MHz**42g**

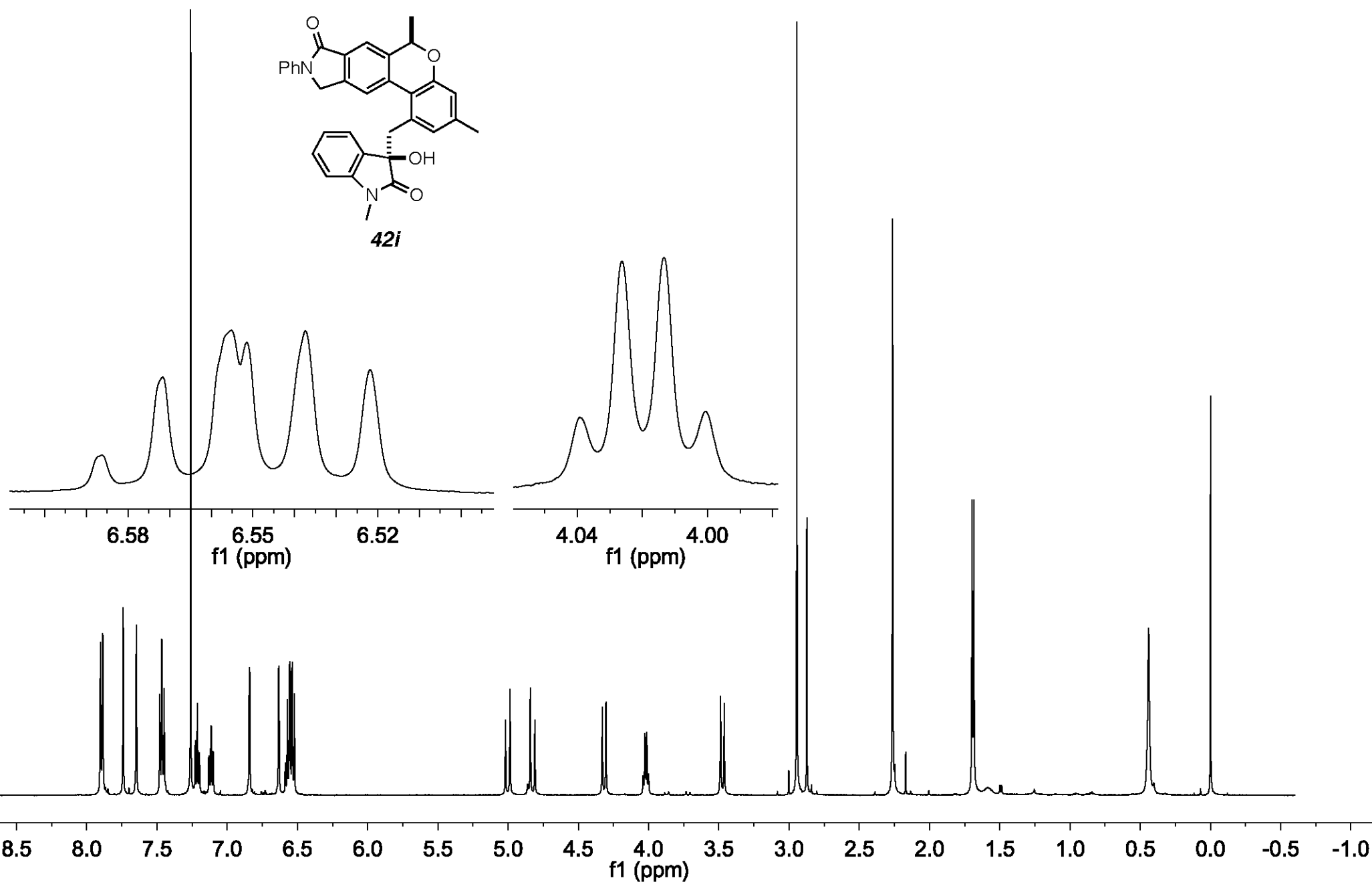
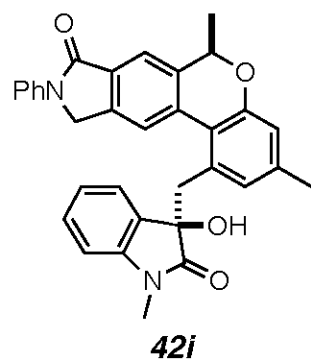




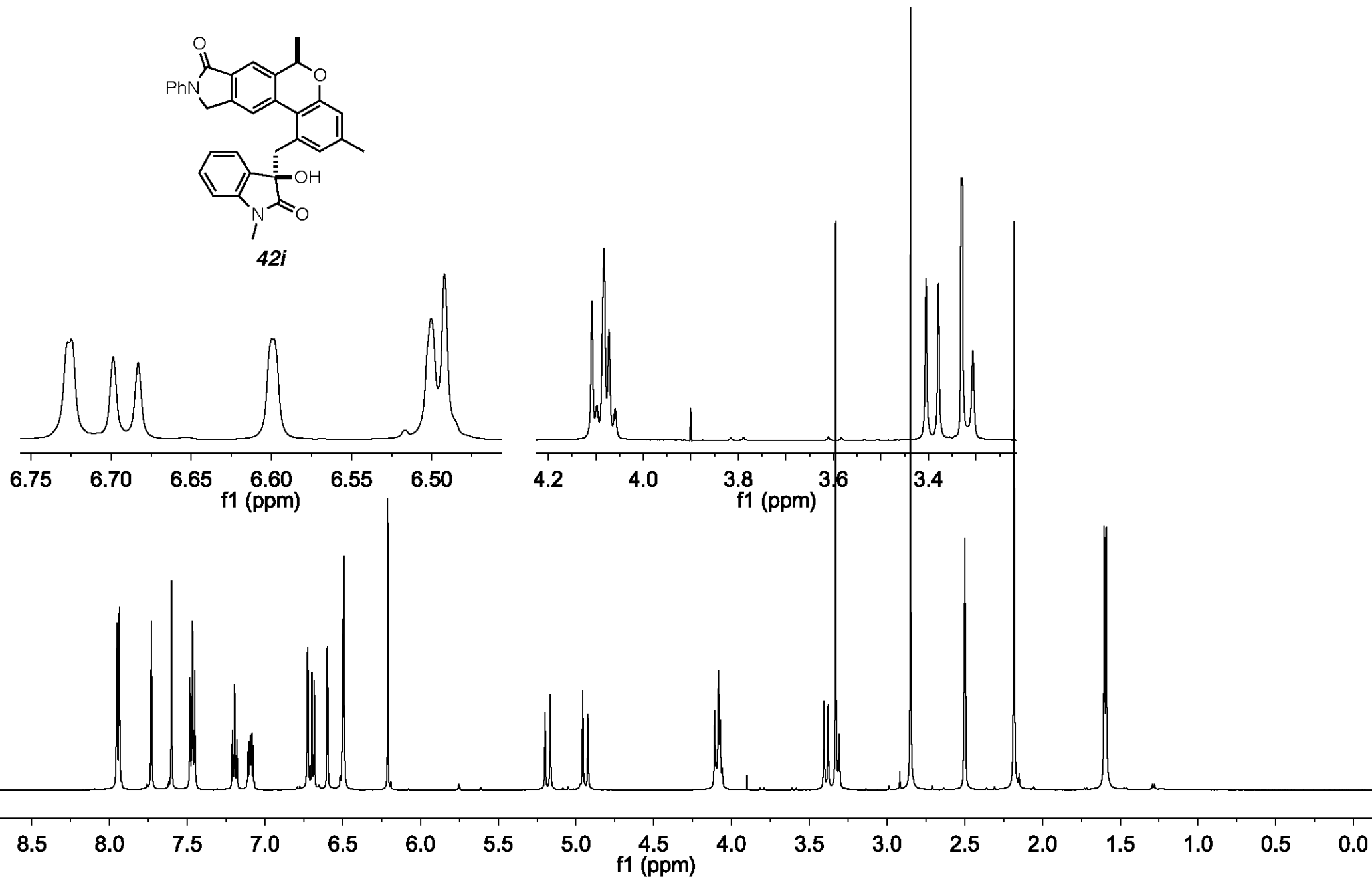
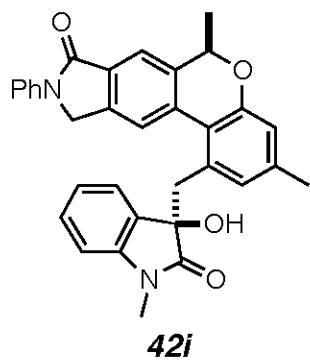
42h



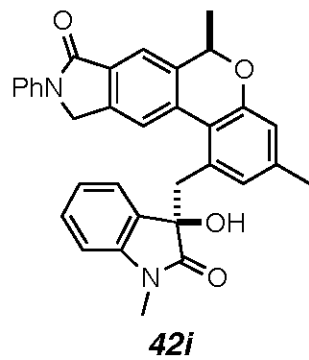
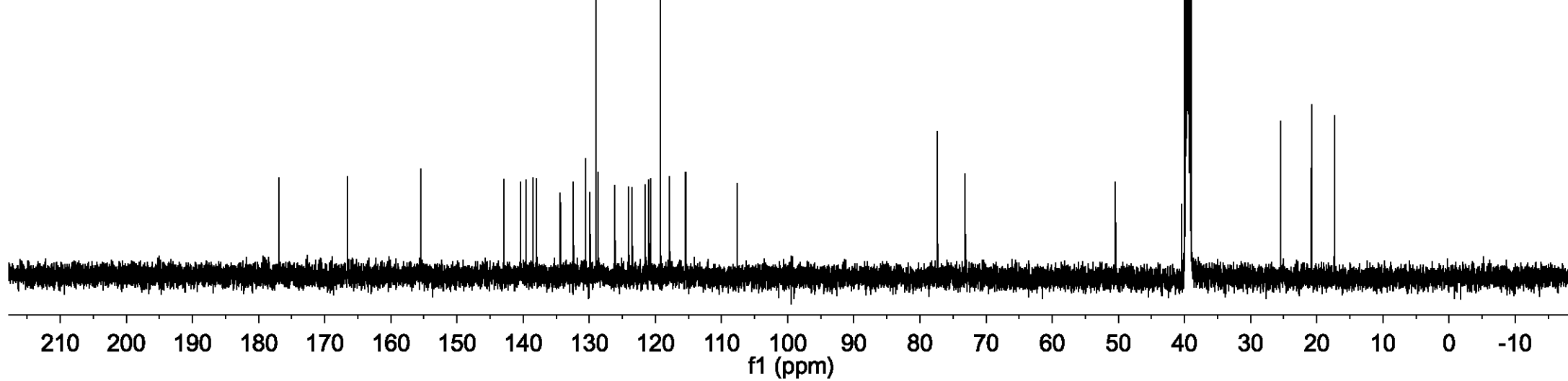
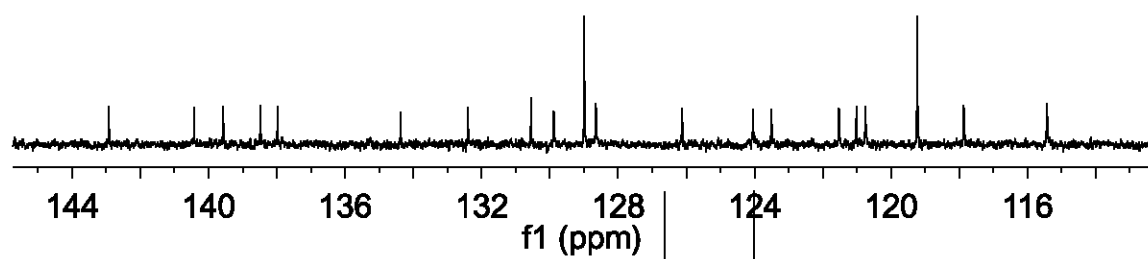
CDCl₃, 125 MHz**42h**

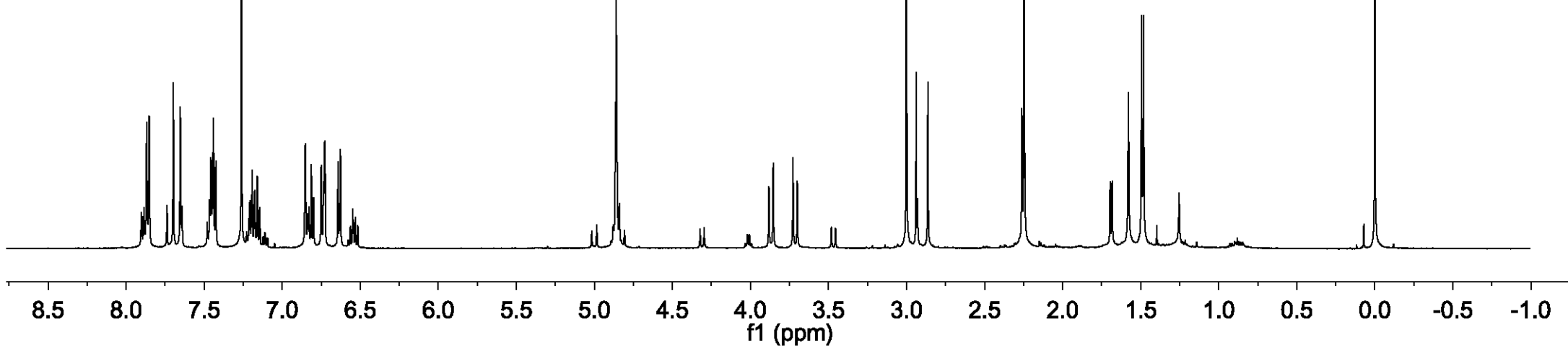
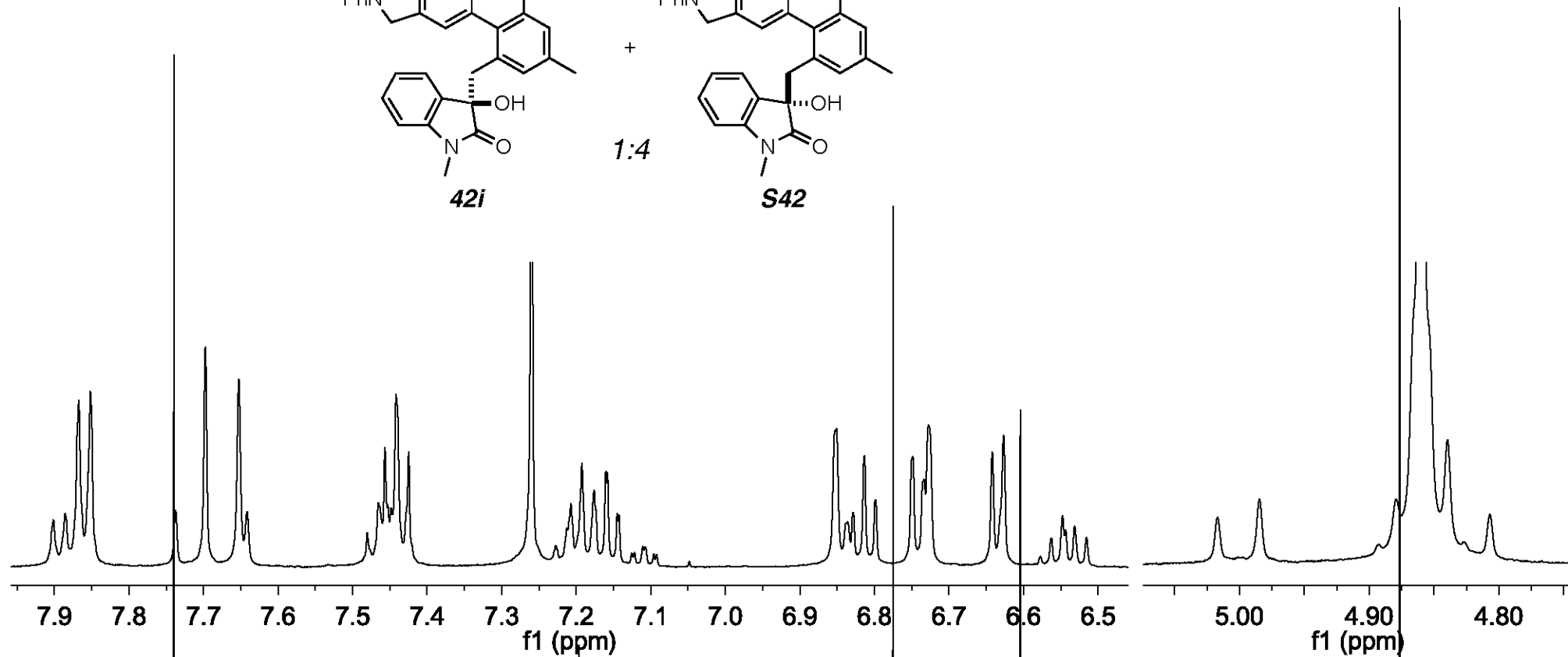
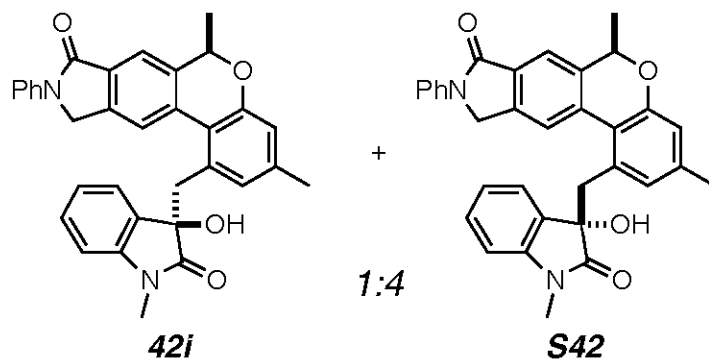
CDCl₃, 500 MHz

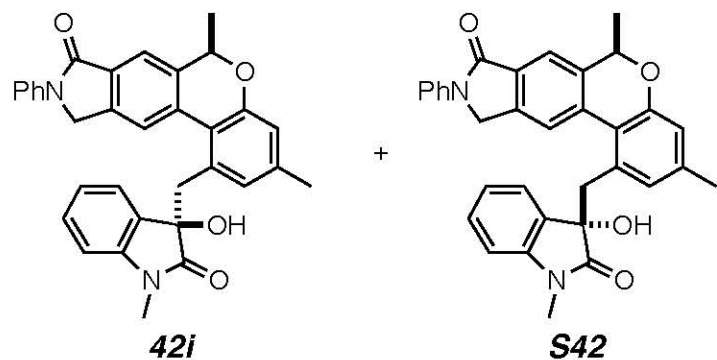
DMSO, 500 MHz



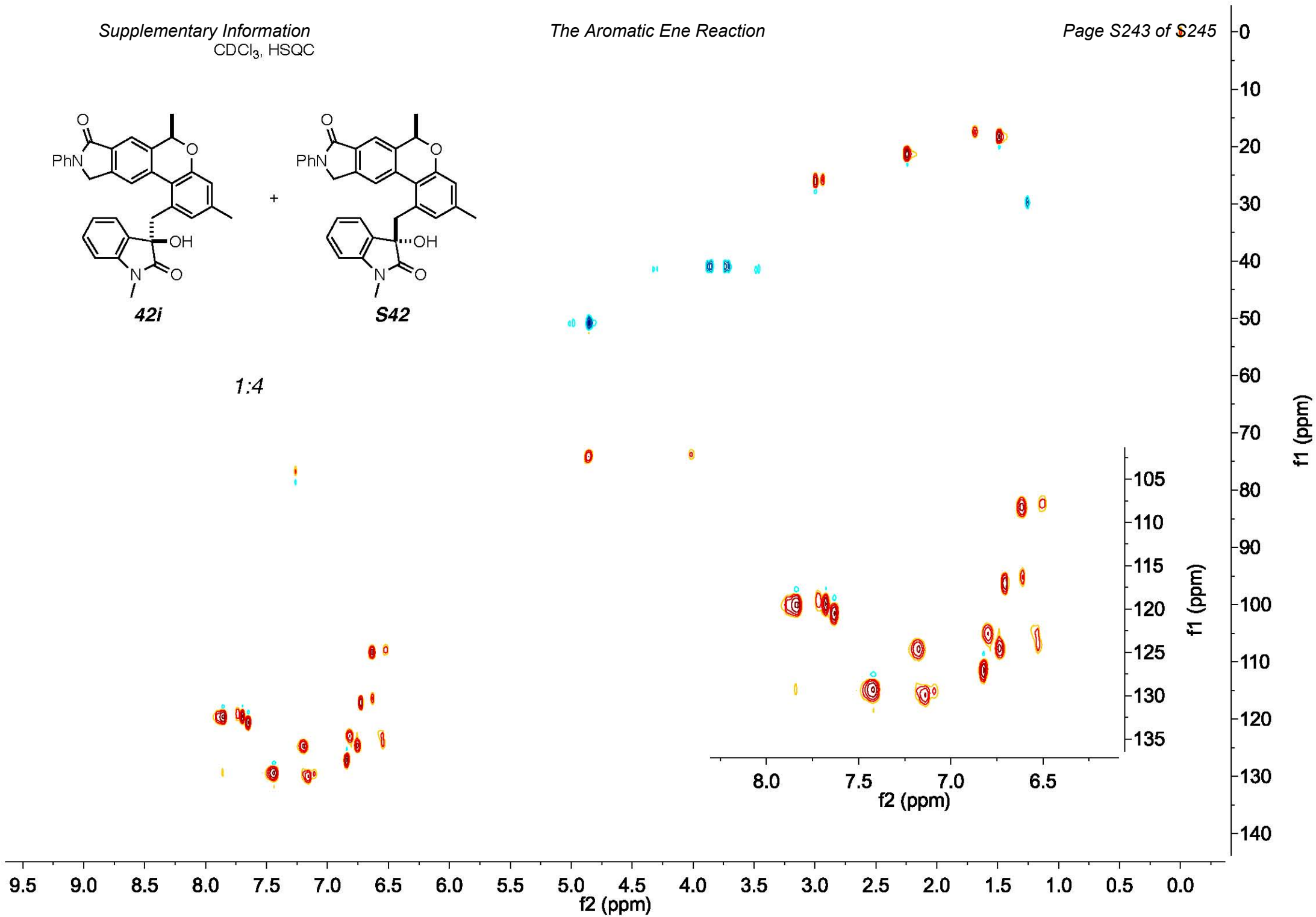
DMSO, 125 MHz

**42i**





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VI. References for the Supplementary Information

- ¹ Hoye, T. R., Hanson, P. R. & Vyvyan, J. R. A practical guide to first-order multiplet analysis in ¹H NMR spectroscopy. *J. Org. Chem.* **59**, 4096–4103 (1994).
- ² Hoye, T. R. & Zhao, H. A method for easily determining coupling constant values: An addendum to “A practical guide to first-order multiplet analysis in ¹H NMR spectroscopy”. *J. Org. Chem.* **67**, 4014–4016 (2002).
- ³ Wang, Y., Ji, K., Lan, S. & Zhang, L. Rapid access to chroman-3-ones through gold-catalyzed oxidation of propargyl aryl ethers. *Angew. Chem. Int. Ed.* **51**, 1915–1918 (2012).
- ⁴ Hoye, T. R., Baire, B., Niu, D., Willoughby, P. H. & Woods, B. P. The hexadehydro-Diels–Alder reaction. *Nature* **490**, 208–212 (2012).
- ⁵ Ouyang, X., Fowler, F. W. & Lauher, J. W. Single-Crystal-to-Single-Crystal topochemical polymerizations of a terminal diacetylene: two remarkable transformations give the same conjugated polymer. *J. Am. Chem. Soc.* **125**, 12400–12401 (2003).
- ⁶ Severa, L., Vávra, J., Kohoutová, A., Čížková, M., Šálová, T., Hývl, J., Saman, D., Pohl, R., Adriaenssens, L. & Teplý, F. Air-tolerant C–C bond formation via organometallic ruthenium catalysis: Diverse catalytic pathways involving (C₅Me₅)Ru or (C₅H₅)Ru are robust to molecular oxygen. *Tetrahedron Lett.* **50**, 4526–4528 (2009).
- ⁷ Oppolzer, W., Pimm, A., Stammen, B. & Hume, W. E. Palladium-catalysed intramolecular cyclisations of olefinic propargylic carbonates and application to the diastereoselective synthesis of enantiomerically pure (–)- α -thujone. *Helv. Chim. Acta.* **80**, 623–639 (1997).
- ⁸ Hayama, T., Baldridge, K. K., Wu, Y-T., Linden, A., & Siegel, J. S. Steric isotope effects gauged by the bowl-inversion barrier in selectively deuterated pentaarylcorannulenes. *J. Am. Chem. Soc.* **130**, 1583–1591 (2008).
- ⁹ Eli, Z-C., Karla, A., & Siegel, J. S. Synthesis of arylbromides from arenes and *N*-bromosuccinimide (NBS) in acetonitrile—A convenient method for aromatic bromination. *Can. J. Chem.* **87**, 440–447 (2009).
- ¹⁰ Zhang, L. & Kozmin, S. A. Brønsted acid-promoted cyclizations of siloxyalkynes with arenes and alkenes. *J. Am. Chem. Soc.* **126**, 10204–10205 (2004).
- ¹¹ Brucelle, F. & Renaud, P. Synthesis of indolines, indoles, and benzopyrrolizidinones from simple aryl azides. *Org. Lett.* **14**, 3048–3051 (2012).
- ¹² Candito, D. A., Pantelev, J. & Lautens, M. Intramolecular aryne–ene reaction: synthetic and mechanistic studies. *J. Am. Chem. Soc.* **133**, 14200–14203 (2011).
- ¹³ Candito, D. A., Dobrovolsky, D. & Lautens, M. Development of an intramolecular aryne ene reaction and application to the formal synthesis of (\pm)-crinine. *J. Am. Chem. Soc.* **134**, 15572–15580 (2012).
- ¹⁴ Qiao, C. & Marsh, E. N. G. Mechanism of benzyl succinate synthase: Stereochemistry of toluene addition to fumarate and maleate. *J. Am. Chem. Soc.* **127**, 8608–8609 (2005).
- ¹⁵ McNulty, J. & McLeod, D. Amine- and sulfonamide-promoted Wittig olefination reactions in water. *Chem. Eur. J.* **17**, 8794–8798 (2011).

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- ¹⁶ Frisch, M. J. *et al.* *Gaussian 09*, revision A.2; Gaussian, Inc.: Wallingform, CT, 2009.
- ¹⁷ Zhao, Y. & Truhlar, D. G. The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: Two new functionals and systematic testing of four M06-class functionals and 12 other functionals. *Theor. Chem. Acc.* **120**, 215–241 (2008).
- ¹⁸ MacroModel, version 9.9, Schrödinger, LLC, New York, NY, 2011.