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Supporting Information

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Asymmetric Synthesis and Binding Study of Novel long-chain HPA-12 analogues as Potent Ligands of the Ceramide Transfer Protein CERT

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Experimental Section/Chemistry

General Remarks

Solvents were purified and dried by standard methods. Flash column chromatography was performed using silica gel (40 – 63 mm, Merck). TLC analyses were performed by means of Merck Kieselgel 60 F_{254} (0.25 mm) Plates. Visualization was accomplished with UV light (254 nm) and/or an aqueous alkaline $KMnO_4$ solution, followed by heating. Melting points are

uncorrected. NMR spectra were recorded in $CDCl_3$ on either a Varian Mercury Plus 300 (300 MHz for ^1H, 75 MHz for ^{13}C) or Varian Unity Inova 600 (600 MHz for ^1H, 151 MHz for ^{13}C) spectrometer. Chemical shifts (δ) are quoted in ppm and are referenced to TMS as internal standard. Elemental analyses were run with a FISONS EA1108 instrument. Optical rotations were measured with a JASCO P-1020 polarimeter with a water-jacketed 10.000 cm cell at a wavelength of the sodium D line (λ=589 nm), $[\alpha]_D$ values are given in 10^{-1} deg.cm^2.g^{-1}. FTIR spectra were obtained on a Nicolet 5700 spectrometer (Thermo Electron) equipped with a Smart Orbit (diamond crystal ATR) accessory, using the reflectance technique (4000–400 cm^{-1}). HPLC was carried out using a PU-4015/PU-4021 PYE UNICAM HPLC system, using C18 5 μm reverse phase column and a mixture acetonitrile/water/Et_3N from 400:600:15 to 100:900:15, pH adjusted to 2.9-3.5 by H_3PO_4. Detector PU-4021 was set in SUM ABS mode, λ = 210-310 nm. High-resolution mass spectra (HRMS) were recorded on a Thermo Scientific Orbitrap Velos mass spectrometer with a heated electrospray ionisation (HESI) source. The mass spectrometer was operated with full scan (50–2000 amu) in positive or negative FT mode (at a resolution of 100000). The analyte was dissolved in MeOH and infused via syringe pump at a rate of 5 mL/min. The heated capillary was maintained at 275 °C with a source heater temperature of 50 °C, and the sheath, auxiliary and sweep gases were at 10, 5 and 0 units, respectively. The source voltage was set to 3.5 kV. (*R*)-1-Phenylethylamine, ChiPros 99+%, ee 99+% from Alfa Aesar, was used for the preparation of oxoamino acids 16A-C using our previously published CIAT applications.

General procedure for (2*R*)-4-Aryl-4-oxo-2-{[(1*R*)-1-phenylethyl]amino}-butanoic acids 16A–C

To the solution of corresponding aroylacrylic acids in methanol, (*R*)-1-phenylethylamine was added under stirring. The mixture was stirred at 25 °C for 4 days in the dark. The course of the CIAT process was monitored by HPLC. HPLC conditions: Luna 5 μm, Phenyl-hexyl column 250x4.6 mm (Phenomenex), eluent: acetonitrile/water/TEA/phosphoric acid = 200:800:8:4, flow rate 1.2 mL/min, detection UV 210 nm, retention time: (1´*R*,2*R*)-**16A**, 27.5 min; (1´*R*,2*S*)-**16A**, 29.1 min; (1´*R*,2*R*)-**16B**, 26.8 min; (1´*R*,2*S*)-**16B**, 28.6 min; (1´*R*,2*R*)-**16C**, 23.3 min; (1´*R*,2*S*)-**16C**, 24.9 min. The precipitate was filtered off, washed with methanol and ether, and dried under reduced pressure to give the corresponding adduct as a white powder with d.r. >97:3. Small quantity of diastereommerically pure crystals has been obtained by crystallization from the acetonitrile–water mixture.

(2*R*)-4-(3-bromophenyl-4-oxo-2-{[(1*R*)-1-phenylethyl]amino}-butanoic acid (16A). This product was prepared according to the general procedure starting from the (*E*)-4-(3-bromophenyl)-4-oxobutenoic acid (20 g, 78.4 mmol) and (*R*)-1-phenylethanamine (10.5 g, 86.3 mmol) in methanol (500 mL); the compound **16A** (20.6 g, 70 %, dr 98 :2) was obtained as a white solid; mp 172-175 °C; $[\alpha]_D^{20}$ = –63.0 (c 0.10, MeOH:1M HCl = 3:1); ^1H NMR (300 MHz, acetone-d_6/DCl): δ = 7.86-8.03 (d, 2H, J = 8.6, H-Ar); 7.56-7.78 (m, 4H, H-Ar); 7.35-7.52 (m, 3H, H-Ar); 4.84 (q, 1H, J = 6.8, H-1´); 4.12 (t, 1H, J = 5.6 Hz, H-2); 3.93 (d, 2H, J = 5.5 Hz, H-3); 1.83 (d, 3H, J = 6.8 Hz, H-2´) ; ^{13}C NMR (75 MHz, acetone-d_6/DCl): δ = 196.4 (C-4); 170.6 (C-1); 137.5, 136.3, 131.9, 131.2, 131.0, 130.1, 129.9 (C-Ar); 60.5, 54.6 (C-2, C-1´); 40.6 (C-3); 21.7 (C-2´); IR (ATR): 2979, 2850,

1695, 1626, 1586, 1563, 1380, 1246, 1069, 987, 809, 698 cm^{-1}. Anal. calcd for $C_{18}H_{18}BrNO_3$: C 57.47, H 4.82, N 3.72; found C 57.61, H 4.83, N 3.64.

(2*R*)-4-(4-bromophenyl-4-oxo-2-{[(1*R*)-1-phenylethyl]amino}-butanoic acid (16B). Starting from the (*E*)-4-(4-bromophenyl)-4-oxobutenoic acid (4.7 g, 18.4 mmol) and (*R*)-1-phenylethanamine (2.7 g, 22.0 mmol) in methanol (100 mL); the compound **16A** (4.8 g, 69 %, dr 99 :1) was obtained as a white solid; mp 187-189 °C; $[\alpha]_D^{20}$ = - 42.1 (c 0.70, MeOH:1M HCl = 3:1); ^{1}H NMR (300 MHz, acetone-d_6/DCl): δ = 7.82-7.89 (m, 2H, H-Ar); 7.61-7.70 (m, 4H, H-Ar); 7.35-7.48 (m, 3H, H-Ar); 4.83 (q, 1H, J = 6.9 Hz, H-1´); 4.10 (t, 1H, J = 5.3 Hz, H-2); 3.89 (d, 2H, J = 5.4 Hz, H-3); 1.80 (d, 3H, J = 6.9 Hz, H-2´); ^{13}C NMR (75 MHz, acetone-d_6/DCl): δ = 196.3 (C-4); 170.3 (C-1); 137.1, 136.0, 133.4, 131.7, 131.1, 130.9, 129.9, 129.8 (C-Ar); 60.4, 54.4 (C-2, C-1´); 40.3 (C-3); 21.5 (C-2´); IR (KBr): 3027, 2983, 2851, 1697, 1631, 1606, 1587, 1478, 1383, 1354, 1275, 1248, 1207, 988, 760, 700 cm^{-1}. Anal. calcd for $C_{18}H_{18}BrNO_3$: C 57.47, H 4.82, N 3.72; found C 57.73 H 4.87, N 3.44.

(2*R*)-4-(5-bromothiophene-2-yl)-4-oxo-2-{[(1*R*)-1-phenylethyl]amino}-butanoic acid (16C). Starting from the (*E*)-4-(5-bromothiophene-2-yl)-4-oxobutenoic acid (1.84 g, 7.1 mmol) and (*R*)-1-phenylethanamine (1.03 g, 8.5 mmol) in methanol (20 mL); the compound **16C** (2.0 g, 74 %, dr 99:1) was obtained as a white solid; mp 175-178 °C; $[\alpha]_D^{20}$ = - 46.1 (c 0.80, MeOH:1M HCl = 3:1); ^{1}H NMR (300 MHz, acetone-d_6/DCl): δ = 7.80 (d, 1H, J = 4.1 Hz, H-Het); 7.64-7.68 (m, 1H, H-Ar, 1H, H-Het); 7.38-7.47 (m, 4H, H-Ar); 4.82 (q, 1H, J = 6.7 Hz, H-1´); 4.06 (t, 1H, J = 5.5 Hz, H-2); 3.85 (d, 2H, J = 5.5 Hz, H-3); 1.82 (d, 3H, J = 6.8 Hz, H-2´); ^{13}C NMR (75 MHz, acetone-d_6/DCl): δ = 188.8 (C-4); 170.0 (C-1); 137.1, 136.5, 134.0, 131.2, 130.9, 130.0, 124.4 (C-Ar, C-Het); 60.4, 54.3 (C-2, C-1´); 39.9 (C-3); 21.5 (C-2´); IR (KBr): 2988, 2840, 1696, 1623, 1588, 1559, 1320, 1296, 1069, 1033, 987, 700 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{17}BrNO_3S$: 382.01070; found: 382.01050.

General procedure for DCC-mediated lactonization

A suspension of γ-oxo-α-aminoacid **(16A-C**, 10 mmol) and $MnCl_2.4H_2O$ (2 mmol) in MeOH (120 mL) was cooled to 0 °C and $NaBH_4$ (40 mmol) was added in small portions. The mixture was stirred at 0 °C until HPLC analysis had shown complete consumption of starting materials (typical 3–4 hours). The solution was evaporated *in vacuo*. To a residue was added water (50 mL) and 10% K_2CO_3 (100 mL). The resulting mixture was stirred for 10 minutes and the insoluble solid was filtered off. The pH of the filtrate was adjusted to 6.5 using 4N HCl. The resulting *syn*-hydroxy acid was filtered off, washed with water (3 x 30 mL), diethyl ether (30 mL) and dried under the diminished pressure at 60 °C. To the well-homogenized (ultrasound) suspension of *syn*-hydroxy acid in dry dichloromethane (50 mL), DCC (11 mmol) was added in one portion. The mixture was stirred for 20 h. The suspension was concentrated to 1/3 of volume and insoluble solids were filtered off and filtrated was concentrated under reduced pressure. Filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography to yield the *trans*-lactone **17A-C**.

(3*R*,5*S*)-5-(3-Bromophenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-17A). This product was prepared according to the general procedure; compound ***trans*-17A** (2.413 g,

67%) was obtained as yellowish oil after purification by flash column chromatography, eluting with hexane/EtOAc (5:1 up to 3:1). TLC: R*f* = 0.25 (hexane/EtOAc 3:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +97 (*c* 0.21, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44-7.39 (m, 1H, H-Ar); 7.36-7.17 (m, 7H, H-Ar); 7.11-7.06 (m, 1H, H-Ar); 5.48 (dd, 1H, *J* = 4.0, 7.9 Hz, H-5); 4.03 (q, 1H, *J* = 6.6 Hz, H-1´); 3.46 (t, 1H, *J* = 8.1 Hz, H-3); 2.22 (td, 1H, *J* = 8.1, 13.1 Hz, H-4A); 2.01 (ddd, 1H, *J* = 4.0, 8.0, 13.1 Hz, H-4B); 1.39 (d, 3H, *J* = 6.6 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.9 (C-2); 144.7, 141.6, 131.3, 130.3, 128.5, 128.0, 127.4, 126.9, 123.5, 122.9 (C-Ar); 77.4 (C-5); 57.7, 54.5 (C-3, C-1´); 38.6 (C-4); 24.6 (C-2´); IR (ATR): 3355, 2977, 2853, 1771, 1448, 1255, 1135, 1019, 955, 732, 699, 500 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{19}BrNO_2$: 360.05992; found: 360.05920.

3*R*,5*S*)-5-(4-Bromophenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-17B). This product was prepared according to the general procedure; compound ***trans*-17B** (1.729 g, 48%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (3:1). TLC: R*f* = 0.26 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 90-92 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +114 (*c* 0.63, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48-7.43 (m, 2H, H-Ar); 7.36-7.23 (m, 5H, H-Ar); 7.04 (d, 2H, *J* = 8.4 Hz, H-Ar); 5.47 (dd, 1H, *J* = 4.0, 7.9 Hz, H-5); 4.03 (q, 1H, *J* = 6.6 Hz, H-1´); 3.43 (t, 1H, *J* = 8.1 Hz, H-3); 2.22 (td, 1H, *J* = 8.1, 13.1 Hz, H-4A); 1.99 (ddd, 1H, *J* = 4.0, 8.0, 13.0 Hz, H-4B); 1.38 (d, 3H, *J* = 6.6 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.0 (C-2); 144.7, 138.4, 131.9, 128.5, 127.4, 126.9, 126.6, 122.6 (C-Ar); 77.7 (C-5); 57.8, 54.6 (C-3, C-1´); 38.7 (C-4); 24.7 (C-2´); IR (ATR): 3346, 2970, 1774, 1489, 1448, 1254, 1139, 1009, 958, 764, 702, 497 cm^{-1}. Anal. Calcd. For $C_{18}H_{18}BrNO_2$: C 60.01, H 5.04, N 3.89. Found: C 60.21, H 5.08, N 3.92.

(3*R*,5*S*)-5-(5-Bromo-thiophen-2-yl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-17C). This product was prepared according to the general procedure; compound ***trans*-17C** (2.307 g, 63%) was obtained as pale brown oil after purification by flash column chromatography, eluting with hexane/EtOAc (5:1 up to 3:1). TLC: R*f* = 0.28 (hexane/EtOAc 3:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +115 (*c* 0.31, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38-7.23 (m, 5H, H-Ar); 6.89 (d, 1H, *J* = 3.8, H-Het); 6.65 (d, 1H, *J* = 3.8 Hz, H-Het); 5.57 (dd, 1H, *J* = 3.4, 7.7 Hz, H-5); 4.04 (q, 1H, *J* = 6.6 Hz, H-1´); 3.56 (t, 1H, *J* = 8.5 Hz, H-3); 2.18 (ddd, 1H, *J* = 7.8, 9.0, 13.2 Hz, H-4A); 2.07 (ddd, 1H, *J* = 3.4, 8.1, 13.2 Hz, H-4B); 1.41 (d, 3H, *J* = 6.6 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.4 (C-2); 144.7, 143.4, 129.8, 128.6, 127.5, 127.0, 125.7, 113.1 (C-Ar, C-Het); 74.5 (C-5); 58.1, 55.1 (C-3, C-1´); 38.3 (C-4); 24.5 (C-2´); IR (ATR): 3332, 2958, 1765, 1441, 1203, 1112, 965, 801, 760, 698, 550 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{16}H_{17}BrNO_2S$: 366.01634; found: 366.01709.

General procedure for acid catalyzed *cis*-lactonization

Sodium borohydride (40 mmol) was added in small portions to the finely homogenized suspension of the oxoamino acid **(16A-c**, 20 mmol) in MeOH (100 mL) over 1 hour. When the reduction was complete (3-5 hours, HPLC monitoring), MeOH was evaporated under reduced pressure. The remaining mixture fo the both diastereomers of hydroxyamino acids (d.r.~2:1) was triturated with 8 M hydrochlorid acid (100 mL) and treated with ultrasound bath (15 min). Thereafter the reaction mixture was stirred at 40 °C for additional 24 hours. The course of CIAT

process was monitored by HPLC. HPLC conditions: Luna 5 μm, Phenyl-hexyl column 250x4.6 mm (Phenomenex), eluent: acetonitrile/water/TEA/85 % phosphoric acid = 333:666:5:5, flow rate 1.2 mL/min, detection UV 210 nm, retention time: *cis*-**18A**, 11.3 min; *trans*-**18A**, 12.4 min; *cis*-**18B**, 10.7 min; *trans*-**18B**, 13.8 min; *cis*-**18C**, 12.2 min; *trans*-**18C**, 13.5 min. The crystalline solid was filtered off, washed with cold 1% hydrochloric acid and ether. The raw **(18A-C).HCl** was triturated with 200 mL of 5% potassium carbonate solution and extracted with Et_2O (3 × 100 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure and the crude product was purified by crystallization (hexane/Et_2O) to yield the desired *cis*-lactone **18A-C**.

(3*R*,5*R*)-5-(3-Bromophenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-18A). This product was prepared according to the general procedure; compound ***cis*-18A** (5.044 g, 70%) was obtained as a white solid after purification by crystallization. TLC: R*f* = 0.30 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 86-89 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -25 (*c* 0.35, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45-7.15 (m, 9H, H-Ar); 5.09 (dd, 1H, *J* = 5.3, 11.1 Hz, H-5); 4.13 (q, 1H, *J* = 6.5 Hz, H-1´); 3.59 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.28 (ddd, 1H, *J* = 5.3, 7.9, 13.0 Hz, H-4A); 1.80-1.68 (m, 1H, H-4B); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.0 (C-2); 144.7, 140.6, 131.7, 130.3, 128.7, 128.5, 127.4, 127.0, 124.1, 122.8 (C-Ar); 77.4 (C-5); 58.5, 57.6 (C-3, C-1´); 40.9 (C-4); 24.8 (C-2´); IR (ATR): 3325, 2965, 1777, 1499, 1312, 1247, 1168, 1008, 766, 700, 507 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{18}H_{19}BrNO_2$: 360.05937; found: 360.05927.

(3*R*,5*R*)-5-(4-Bromophenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-18B). This product was prepared according to the general procedure; compound ***cis*-18B** (4.755 g, 66%) was obtained as a white solid after purification by crystallization. TLC: R*f* = 0.30 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 107-109 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -34 (*c* 0.25, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47 (d, 2H, *J* = 8.2 Hz, H-Ar); 7.38-7.20 (m, 5H, H-Ar); 7.12 (d, 2H, *J* = 8.4 Hz, H-Ar); 5.09 (dd, 1H, *J* = 5.3, 11.1 Hz, H-5); 4.13 (q, 1H, *J* = 6.5 Hz, H-1´); 3.59 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.26 (ddd, 1H, *J* = 5.3, 7.8, 12.9 Hz, H-4A); 1.72 („dd“, 1H, *J* = 11.4, 12.0 Hz, H-4B); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.1 (C-2); 144.8, 137.3, 131.9, 128.5, 127.5, 127.3, 122.6 (C-Ar); 77.7 (C-5); 58.6, 57.7 (C-3, C-1´); 40.9 (C-4); 24.8 (C-2´); IR (ATR): 3321, 2968, 1780, 1491, 1314, 1170, 1001, 818, 764, 698, 505 cm^{-1}. Anal. Calcd. For $C_{18}H_{18}BrNO_2$: C 60.01, H 5.04, N 3.89. Found:C 60.20, H 5.24, N 3.81.

(3*R*,5*R*)-5-(5-Bromo-thiophen-2-yl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-18C). This product was prepared according to the general procedure; compound ***cis*-18C** (5.201 g, 71%) was obtained as a white solid after purification by crystallization. TLC: R*f* = 0.33 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 67-68 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -132 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40-7.22 (m, 5H, H-Ar); 6.91 (d, 1H, *J* = 3.8 Hz, H-Het); 6.77 (d, 1H, *J* = 3.8 Hz, H-Het); 5.24 (dd, 1H, *J* = 5.2, 11.1 Hz, H-5); 4.13 (q, 1H, *J* = 6.5 Hz, H-1´); 3.55 (dd, 1H, *J* = 7.9, 11.8 Hz, H-3); 2.28 (ddd, 1H, *J* = 5.3, 7.8, 12.9 Hz, H-4A); 1.89 („dd“, 1H, *J* = 11.8, 12.9 Hz, H-4B); 1.42 (d, 3H, *J* = 6.5 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.4 (C-2); 144.6, 141.9, 129.6, 128.6, 127.5, 127.1, 127.0, 113.8 (C-Ar, C-Het); 74.0 (C-5); 58.5, 57.5 (C-3, C-1´); 40.3 (C-

4); 24.7 (C-2′); IR (ATR): 3354, 2972, 1777, 1430, 1153, 1137, 912, 807, 697, 488 cm^{-1}. Anal. Calcd. For $C_{16}H_{16}BrNO_2S$: C 52.47, H 4.40, N 3.82. Found: C 52.13, H 4.39, N 3.69.

General procedure for Sonogashira coupling process

To a stirred mixture of lactone **(*trans*-17A-C** or ***cis*-17A-C)** (1 mmol) and corresponding alkyne (3 mmol) in Et_3N (12 mL) at room temperature were added CuI (19 mg, 0.1 mmol) and tetrakis(triphenylphosphine)palladium ($Pd(PPh_3)_4$, 57.8 mg, 0.05 mmol). The resulting mixture was stirred at indicated temperature until TLC analysis had shown complete consumption of starting material. The reaction mixture was concentrated and mixture of hexane/EtOAc = 1:1 (15 mL) was added. The brown solid was filtered off and washed with mixture of hexane/EtOAc = 1:1 (3 × 5 mL). Filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography to yield the desired product ***trans*-19A-C** or ***cis*-20A-C**.

(3*R*,5*S*)-5-(3-Dec-1-ynyl-phenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-19Aa). This product was prepared according to the general procedure; compound ***trans*-19Aa** (346 mg, 83%) was obtained as a pale brown oil after purification by flash column chromatography, eluting with hexane/EtOAc (7:1 up to 3:1). TLC: R*f* = 0.27 (hexane/EtOAc 3:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +85 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54-7.44 (m, 1H, H-Ar); 7.40-7.18 (m, 7H, H-Ar); 7.05 (d, 1H, *J* = 7.6 Hz, H-Ar); 5.48 (dd, 1H, *J* = 3.8, 7.9 Hz, H-5); 4.03 (q, 1H, *J* = 6.6 Hz, H-1′); 3.47 (t, 1H, *J* = 8.2 Hz, H-3); 2.38 (t, 2H, *J* = 7.0 Hz, H-3′′); 2.22 (td, 1H, *J* = 8.2, 13.0 Hz, H-4A); 2.03 (ddd, 1H, *J* = 4.0, 8.0, 12.6 Hz, H-4B); 1.64-1.55 (m, 2H, H-4′′); 1.48-1.41 (m, 2H, H-5′′); 1.39 (d, 3H, *J* = 6.5 Hz, H-2′); 1.38-1.22 (m, 8H, H-6′′-H-9′′); 0.88 (t, 3H, *J* = 6.7 Hz, H-10′′); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 144.8, 139.5, 131.3, 128.7, 128.0, 127.4, 126.9, 124.7, 123.9 (C-Ar); 91.4, 80.0 (C-1′′, C-2′′); 78.0 (C-5); 57.8, 54.6 (C-3, C-1′); 38.7 (C-4); 31.9 (C-3′′); 29.2 (C-4′′); 29.2 (C-5′′); 29.0 (C-6′′); 28.7 (C-7′′); 24.7 (C-2′); 22.7 (C-8′′); 19.4 (C-9′′); 14.1 (C-10′′); IR (ATR): 3322, 2926, 2841, 1769, 1611, 1469, 1191, 1115, 1041, 792, 700 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{28}H_{36}NO_2$: 418.27460; found: 418.27482.

(3*R*,5*S*)-5-(3-Hex-1-ynyl-phenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-19Ab). This product was prepared according to the general procedure; compound ***trans*-19Ab** (247 mg, 69%) was obtained as pale brown oil after purification by flash column chromatography, eluting with hexane/EtOAc (7:1 up to 3:1). TLC: R*f* = 0.27 (hexane/EtOAc 3:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +105 (*c* 0.29, $CHCl_3$) (hexane:EtOAc = 6:1 – 2:1, R_f = 0.24); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36-7.19 (m, 8H, H-Ar); 7.08-7.02 (m, 1H, H-Ar); 5.48 (dd, 1H, *J* = 3.8, 7.9 Hz, H-5); 4.04 (q, 1H, *J* = 6.6 Hz, H-1′); 3.47 (t, 1H, *J* = 8.2 Hz, H-3); 2.40 (t, 2H, *J* = 7.0 Hz, H-3′′); 2.22 (td, 1H, *J* = 8.1, 13.1 Hz, H-4A); 2.03 (ddd, 1H, *J* = 3.9, 8.1, 13.0 Hz, H-4B); 1.64-1.54 (m, 2H, H-4′′); 1.52-1.42 (m, 2H, H-5′′); 1.39 (d, 3H, *J* = 6.5 Hz, H-2′); 0.94 (t, 3H, *J* = 6.7 Hz, H-6′′); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 144.8, 139.5, 131.3, 128.7, 128.0, 127.4, 126.9, 124.7, 123.9 (C-Ar); 91.3, 80.0 (C-1′′, C-2′′); 78.0 (C-5); 57.8, 54.6 (C-3, C-1′); 38.7 (C-4); 30.8 (C-3′′); 24.7 (C-2′); 22.0 (C-4′′); 19.1 (C-5′′); 13.7 (C-6′′); IR (ATR): 3315, 2929, 2831, 1771, 1600, 1454, 1189, 1160, 1044, 795, 764, 698 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{28}NO_2$: 362.21200; found: 362.21147.

(3*R*,5*S*)-5-[(3-(3,3-Dimethyl-but-1-ynyl)-phenyl]-3-{[(1*R*)-1-phenylethyl]amino}dihydro-furan-2(3*H*)-one (*trans*-19Ac). This product was prepared according to the general procedure; compound ***trans*-19Ac** (217 mg, 60%) was obtained as pale yellow oil after purification by flash column chromatography, eluting with hexane/EtOAc (4:1 up to 2:1). TLC: R*f* = 0.28 (hexane/EtOAc 2:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +108 (*c* 0.27, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37-7.19 (m, 8H, H-Ar); 7.06-7.01 (m, 1H, H-Ar); 5.48 (dd, 1H, *J* = 3.8, 7.9 Hz, H-5); 4.04 (q, 1H, *J* = 6.6 Hz, H-1´); 3.47 (t, 1H, *J* = 8.2 Hz, H-3); 2.22 (td, 1H, *J* = 8.2, 13.4 Hz, H-4A); 2.03 (ddd, 1H, *J* = 3.8, 8.1, 13.0 Hz, H-4B); 1.39 (d, 3H, *J* = 6.6 Hz, H-2´); 1.31 (s, 3H, H-4´´, 6H, 2 × C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.34 (C-2); 144.8, 139.4, 131.2, 128.5, 128.5, 127.9, 127.3, 126.9, 124.6, 123.8 (C-Ar); 99.3, 78.4 (C-1´´, C-2´´); 77.9 (C-5); 57.7, 54.6 (C-3, C-1´); 38.7 (C-4); 30.9 (C-3´´); 27.9 (C-4´´, 2 × *C*H$_3$); 24.6 (C-2´); IR (ATR): 3323, 2967, 1771, 1452, 1299, 1176, 1155, 1043, 798, 762, 699, 541 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{28}NO_2$: 362.21200; found: 362.21095.

(3*R*,5*S*)-3-{[(1*R*)-1-Phenylethyl]amino}-5-(3-phenylethynyl-phenyl)dihydrofuran-2(3*H*)-one (*trans*-19Ad). This product was prepared according to the general procedure; compound ***trans*-19Ad** (313 mg, 82%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (8:1 up to 3:1). TLC: R*f* = 0.28 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 93-94 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +133 (*c* 0.63, $CHCl_3$);^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55-7.47 (m, 2H, H-Ar); 7.46-7.42 (m, 1H, H-Ar); 7.40-7.20 (m, 10H, H-Ar); 7.15-7.09 (m, 1H, H-Ar); 5.52 (dd, 1H, *J* = 3.9, 7.9 Hz, H-5); 4.05 (q, 1H, *J* = 6.6 Hz, H-1´); 3.49 (t, 1H, *J* = 8.2 Hz, H-3); 2.25 (td, 1H, *J* = 8.1, 13.1 Hz, H-4A); 2.06 (ddd, 1H, *J* = 3,9, 7.4, 8.0 Hz, H-4B); 1.39 (d, 3H, *J* = 6.6 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.2 (C-2); 144.8, 139.7, 131.6, 131.3, 128.8, 128.5, 128.4, 128.0, 127.4, 126.9, 124.7, 123.9, 122.9 (C-Ar); 90.1, 88.7 (C-1´´, C-2´´); 77.9 (C-5); 57.8, 54.6 (C-3, C-1´); 38.7 (C-4); 24.7 (C-2´); IR (ATR): 3322, 2927, 1786, 1611, 1455, 1174, 1122, 1054, 791, 764, 700 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{24}NO_2$: 382.18016; found: 382.18003.

(3*R*,5*S*)-5-[(3-(4-Methoxy-phenylethynyl)-phenyl]-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-19Ae). This product was prepared according to the general procedure; compound ***trans*-19Ae** (296 mg, 72%) was obtained as pale yellow oil after purification by flash column chromatography, eluting with hexane/EtOAc (4:1 up to 2:1). TLC: R*f* = 0.26 (hexane/EtOAc 2:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +131 (*c* 0.19, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50-7.20 (m, 10H, H-Ar); 7.12-7.05 (m, 1H, H-Ar); 6.87 (d, 2H, *J* = 8.5 Hz, H-Ar); 5.51 (dd, 1H, *J* = 3.8, 7.9 Hz, H-5); 4.05 (q, 1H, *J* = 6.6 Hz, H-1´); 3.82 (s, 3H, OC*H*$_3$); 3.49 (t, 1H, *J* = 8.2 Hz, H-3); 2.24 (td, 1H, *J* = 8.2, 13.1 Hz, H-4A); 2.06 (ddd, 1H, *J* = 3.9, 8.1, 13.0 Hz, H-4B); 1.40 (d, 3H, *J* = 6.6 Hz, H-2´). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.2 (C-2); 159.8, 144.8, 139.6, 133.1, 131.1, 128.8, 128.5, 127.8, 127.3, 126.9, 124.3. 143.2, 114.9, 114.0 (C-Ar); 90.1, 87.4 (C-1´´, C-2´´); 77.9 (C-5); 57.8, 55.3, 54.6 (C-3, C-1´, O*C*H$_3$); 38.7 (C-4); 24.7 (C-2´); IR (ATR): 3321, 2960, 2837, 2210, 1770, 1599, 1509, 1246, 1171, 1027, 830, 762, 700, 536 cm^{-1}.

(3*R*,5*S*)-5-(4-Dec-1-ynyl-phenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-19Ba). This product was prepared according to the general procedure; compound ***trans*-19Ba** (301 mg, 72%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.32 (hexane/EtOAc 2:1,

UV, $KMnO_4$); Mp = 50-51 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +126 (*c* 0.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36-7.22 (m, 7H, H-Ar); 7.07 (d, 2H, *J* = 8.1 Hz, H-Ar); 5.50 (dd, 1H, *J* = 3.8, 8.9 Hz, H-5); 4.04 (q, 1H, *J* = 6.6 Hz, H-1′); 3.45 (t, 1H, *J* = 8.2 Hz, H-3); 2.38 (t, 2H, *J* = 7.0 Hz, H-3′′); 2.27-2.16 (m, 1H, H-4A); 2.01 (ddd, 1H, *J* = 3.9, 8.1, 13.0 Hz, H-4B); 1.64-1.53 (m, 2H, H-4′′); 1.48-1.41 (m, 2H, H-5′′); 1.39 (d, 3H, *J* = 6.5 Hz, H-2′); 1.34-1.25 (m, 8H, H-6′′-H-9′′); 0.88 (t, 3H, *J* = 6.7 Hz, H-10′′); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.2 (C-2); 144.7, 138.4, 131.8, 128.5, 127.4, 126.9, 124.8, 124.2 (C-Ar); 91.4, 79.9 (C-1′′, C-2′′); 78.1 (C-5); 57.8, 54.6 (C-3, C-1′); 38.6 (C-4); 31.8 (C-3′′); 29.2 (C-4′′); 29.1 (C-5′′); 28.9 (C-6′′); 28.7 (C-7′′); 24.6 (C-2′); 22.7 (C-8′′); 19.4 (C-9′′); 14.1 (C-10′′); IR (ATR): 3550, 2910, 2837, 1722, 1644, 1539, 1467, 1098, 1026, 1011, 700 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{28}H_{36}NO_2$: 418.27406; found: 418.27370.

(3*R*,5*S*)-5-(4-Hex-1-ynyl-phenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-19Bb). This product was prepared according to the general procedure; compound ***trans*-19Bb** (152 mg, 42%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (7:1 up to 2:1). TLC: R*f* = 0.28 (hexane/EtOAc 2:1, UV, $KMnO_4$); Mp = 64-64 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +141 (*c* 0.25, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.24 (m, 7H, H-Ar); 7.07 (d, 2H, *J* = 8.2 Hz, H-Ar); 5.50 (dd, 1H, *J* = 3.8, 7.9 Hz, H-5); 4.04 (q, 1H, *J* = 6.6 Hz, H-1′); 3.45 (t, 1H, *J* = 8.2 Hz, H-3); 2.39 (t, 2H, *J* = 6.9 Hz, H-3′′); 2.22 (td, 1H, *J* = 8.2, 13.1 Hz, H-4A); 2.01 (ddd, 1H, *J* = 3.9, 8.1, 12.9 Hz, H-4B); 1.66-1.54 (m, 2H, H-4′′); 1.51-1.44 (m, 2H, H-5′′); 1.39 (d, 3H, *J* = 6.6 Hz, H-2′); 0.94 (t, 3H, *J* = 7.2 Hz, H-6′′); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.2 (C-2); 144.7, 138.4, 131.8, 128.5, 127.4, 126.9, 124.8, 124.1 (C-Ar); 91.3, 79.9 (C-1′′, C-2′′); 78.1 (C-5); 57.8, 54.6 (C-3, C-1′); 38.7 (C-4); 30.8 (C-3′′); 24.6 (C-2′); 22.0 (C-4′′); 19.1 (C-5′′); 13.6 (C-6′′); IR (ATR): 3332, 2922, 2855, 1769, 1620, 1455, 1188, 1115, 1046, 792, 699 cm^{-1}. Anal. Calcd. For $C_{24}H_{27}NO_2$: C 79.74, H 7.53, N 3.87. Found: C 79.51, H 7.65, N 3.77.

(3*R*,5*S*)-5-[(4-(3,3-Dimethyl-but-1-ynyl)-phenyl]-3-{[(1*R*)-1-phenylethyl]amino}dihydro-furan-2(3*H*)-one (*trans*-19Bc). This product was prepared according to the general procedure; compound ***trans*-19Bc** (184 mg, 51%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.28 (hexane/EtOAc 2:1, UV, $KMnO_4$); Mp = 98-100 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +135 (*c* 0.17, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38-7.20 (m, 7H, H-Ar); 7.06 (d, 2H, *J* = 8.1 Hz, H-Ar); 5.49 (dd, 1H, *J* = 3.7, 7.9 Hz, H-5); 4.02 (q, 1H, *J* = 6.6 Hz, H-1′); 3.43 (t, 1H, *J* = 8.3 Hz, H-3); 2.20 (td, 1H, *J* = 8.2, 13.0 Hz, H-4A); 1.99 (ddd, 1H, *J* = 3.8, 8.0, 12.9 Hz, H-4B); 1.38 (d, 3H, *J* = 6.6 Hz, H-2′); 1.29 (s, 3H, H-4′′, 6H, 2 × C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 144.7, 138.4, 131.9, 128.5, 127.4, 126.9, 124.7, 124.1 (C-Ar); 99.4, 78.4 (C-1′′, C-2′′); 78.1 (C-5); 57.8, 54.6 (C-3, C-1′); 38.8 (C-4); 31.0 (C-3′′); 28.0 (C-4′′, 2 × *C*H$_3$); 24.6 (C-2′); IR (ATR): 3320, 2931, 2825, 1771, 1602, 1433, 1175, 1091, 1033, 786, 702 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{28}NO_2$: 362.21200; found: 362.21134.

(3*R*,5*S*)-3-{[(1*R*)-1-Phenylethyl]amino}-5-(4-phenylethynylphenyl)dihydrofuran-2(3*H*)-one (*trans*-19Bd). This product was prepared according to the general procedure; compound ***trans*-19Bd** (271 mg, 71%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.32 (hexane/EtOAc 2:1,

UV, $KMnO_4$); Mp = 118-119 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +164 (*c* 0.13, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55-7.46 (m, 4H, H-Ar); 7.36-7.24 (m, 8H, H-Ar); 7.15 (d, 2H, *J* = 8.1 Hz, H-Ar); 5.53 (dd, 1H, *J* = 3.9, 7.9 Hz, H-5); 4.05 (q, 1H, *J* = 6.6 Hz, H-1´); 3.47 (t, 1H, *J* = 8.2 Hz, H-3); 2.24 (td, 1H, *J* = 8.1, 13.1 Hz, H-4A); 2.04 (ddd, 1H, *J* = 3.9, 8.0, 12.9 Hz, H-4B); 1.40 (d, 3H, *J* = 6.6 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.1 (C-2); 144.7, 139.3, 131.9, 131.6, 128.5, 128.5, 128.4, 127.4, 127.0, 124.9, 123.3, 123.0 (C-Ar); 90.1, 88.6 (C-1´´, C-2´´); 78.1 (C-5); 57.8, 54.6 (C-3, C-1´); 38.7 (C-4); 24.6 (C-2'); IR (ATR): 3315, 2922, 2833, 1769, 1605, 1455, 1175, 1156, 1036, 791, 698 cm^{-1}. Anal. Calcd. For $C_{26}H_{23}NO_2$: C 81.86, H 6.08, N 3.67. Found: C 81.53, H 6.19, N 3.51.

(3*R*,5*S*)-5-[(4-(4-Methoxy-phenylethynyl)-phenyl]-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-19Be). This product was prepared according to the general procedure; compound ***trans*-19Be** (354 mg, 86%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (8:1 up to 2:1). TLC: R*f* = 0.32 (hexane/EtOAc 2:1, UV, $KMnO_4$); Mp = 121-122 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +150 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50-7.42 (m, 4H, H-Ar); 7.36-7.24 (m, 5H, H-Ar); 7.13 (d, 2H, *J* = 8.3 Hz, H-Ar); 6.87 (d, 2H, *J* = 8.5 Hz, H-Ar); 5.53 (dd, 1H, *J* = 3.8, 7.8 Hz, H-5); 4.05 (q, 1H, *J* = 6.6 Hz, H-1´); 3.82 (s, 3H, OC*H*$_3$); 3.47 (t, 1H, *J* = 8.2 Hz, H-3); 2.24 (td, 1H, *J* = 8.1, 13.1 Hz, H-4A); 2.04 (ddd, 1H, *J* = 3.9, 8.0, 13.1 Hz, H-4B); 1.40 (d, 3H, *J* = 6.6 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.2 (C-2); 159.8, 144.7, 138.9, 133.1, 131.8, 128.5, 127.4, 127.0, 124.9, 123.6, 123.0, 115.1, 114.0 (C-Ar); 90.1, 87.4 (C-1´´, C-2´´); 78.1 (C-5); 57.8, 55.3, 54.6 (C-3, C-1´, O*C*H$_3$); 38.7 (C-4); 24.6 (C-2´); IR (ATR): 3319, 2923, 2828, 1772, 1602, 1454, 1178, 1145, 1029, 798, 767, 699 cm^{-1}. Anal. Calcd. For $C_{26}H_{23}NO_2$: C 78.81, H 6.12, N 3.40. Found: C 78.56, H 6.21, N 3.32.

(3*R*,5*S*)-5-(5-Dec-1-ynyl-thiophen-2-yl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-19Ca). This product was prepared according to the general procedure; compound ***trans*-19Ca** (305 mg, 72%) was obtained as colorless oil after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 3:1). TLC: R*f* = 0.30 (hexane/EtOAc 3:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +128 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40-7.27 (m, 5H, H-Ar); 6.92 (d, 1H, *J* = 3.7 Hz, H-Het); 6.72 (d, 1H, *J* = 3.7 Hz, H-Het); 5.61 (dd, 1H, *J* = 3.1, 7.7 Hz, H-5); 4.05 (q, 1H, *J* = 6.6 Hz, H-1´); 3.59 (t, 1H, *J* = 8.6 Hz, H-3); 2.41 (t, 2H, *J* = 7.1 Hz, H-3´´); 2.25-2.15 (m, 1H, H-4A); 2.14-2.05 (m, 1H, H-4B); 1.64-1.53 (m, 2H, H-4´´); 1.48-1.44 (m, 2H, H-5´´); 1.42 (d, 3H, *J* = 6.6 Hz, H-2´); 1.34-1.24 (m, 8H, H-6´´-H-9´´); 0.89 (t, 3H, *J* = 6.7 Hz, H-10´´). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.5 (C-2); 144.6, 141.8, 130.7, 128.5, 127.5, 127.0, 125.2, 125.1 (C-Ar, C-Het); 95.8, 73.1 (C-1´´, C-2´´); 74.7 (C-5); 58.2, 55.1 (C-3, C-1´); 38.5 (C-4); 31.8 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 28.9 (C-6´´); 28.4 (C-7´´); 24.5 (C-2´); 22.6 (C-8´´); 19.7 (C-9´´); 14.1 (C-10´´); IR (ATR): 3321, 2923, 2853, 1775, 1453, 1186, 1151, 803, 762, 700, 552 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{26}H_{34}NO_2S$: 424.23103; found: 424.23042.

(3*R*,5*S*)-5-(5-Hex-1-ynyl-thiophen-2-yl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*trans*-19Cb). This product was prepared according to the general procedure; compound ***trans*-19Cb** (305 mg, 83%) was obtained as colorless oil after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.31 (hexane/EtOAc 2:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +163 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38-7.23 (m, 5H, H-Ar); 6.92 (d, 1H, *J* = 3.7 Hz, H-Het); 6.71 (d, 1H, *J* = 3.7 Hz, H-Het); 5.59 (dd, 1H, *J* = 3.1, 7.5 Hz, H-5);

4.04 (q, 1H, *J* = 6.6 Hz, H-1´); 3.58 (t, 1H, *J* = 8.6 Hz, H-3); 2.40 (t, 2H, *J* = 7.0 Hz, H-3´´); 2.24-2.15 (m, 1H, H-4A); 2.14-2.04 (m, 1H, H-4B); 1.62-1.52 (m, 2H, H-4´´); 1.51-1.44 (m, 2H, H-5´´); 1.41 (d, 3H, *J* = 6.6 Hz, H-2´); 0.93 (t, 3H, *J* = 7.2 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6 (C-2); 144.7, 141.8, 130.7, 128.6, 127.5, 127.0, 125.2, 125.1 (C-Ar, C-Het); 95.8, 73.1 (C-1´´, C-2´´); 74.7 (C-5); 58.2, 55.1 (C-3, C-1´); 38.5 (C-4); 30.5 (C-3´´); 24.5 (C-2´); 22.0 (C-4´´); 19.4 (C-5´´); 13.6 (C-6´´); IR (ATR): 3322, 2927, 2863, 1769, 1444, 1184, 1135, 801, 761, 700, 555 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{26}NO_2S$: 368.16842; found: 368.16764.

(3*R*,5*S*)-5-[(5-(3,3-Dimethyl-but-1-ynyl)-thiophen-2-yl]-3-{[(1*R*)-1-phenylethyl]amino}dihydro-furan-2(3*H*)-one (*trans*-19Cc). This product was prepared according to the general procedure; compound ***trans*-19Cc** (254 mg, 69%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.30 (hexane/EtOAc 2:1, UV, $KMnO_4$); Mp = 108-110 °C; $[\alpha]_D^{20}$ = +177 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38-7.23 (m, 5H, H-Ar); 6.90 (d, 1H, *J* = 3.7 Hz, H-Het); 6.70 (d, 1H, *J* = 3.7 Hz, H-Het); 5.59 (dd, 1H, *J* = 3.1, 7.7 Hz, H-5); 4.03 (q, 1H, *J* = 6.6 Hz, H-1´); 3.57 (t, 1H, *J* = 8.6 Hz, H-3); 2.24-2.13 (m, 1H, H-4A); 2.08 (ddd, 1H, *J* = 3.3, 8.1, 13.1 Hz, H-4B); 1.41 (d, 3H, *J* = 6.6 Hz, H-2´); 1.28 (s, 3H, H-4´´, 6H, 2 × C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6 (C-2); 144.6, 141.9, 130.7, 128.6, 127.5, 127.0, 125.2, 125.1 (C-Ar, C-Het); 103.5, 71.7 (C-1´´, C-2´´); 74.7 (C-5); 58.2, 55.0 (C-3, C-1´); 38.5 (C-4); 30.7 (C-3´´); 28.2 (C-4´´, 2 × *C*H$_3$); 24.5 (C-2´); IR (ATR): 3321, 2923, 2853, 1775, 1453, 1186, 1151, 803, 762, 700, 552 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{26}NO_2S$: 368.16788; found: 368.16780.

(3*R*,5*S*)-3-{[(1*R*)-1-Phenylethyl]amino}-5-(5-phenylethynyl-thiophen-2-yl)-dihydrofuran-2(3*H*)-one (*trans*-19Cd). This product was prepared according to the general procedure; compound ***trans*-19Cd** (291 mg, 75%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.34 (hexane/EtOAc 2:1, UV, $KMnO_4$); Mp = 103-104 °C; $[\alpha]_D^{20}$ = +216 (*c* 0.24, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55-7.44 (m, 2H, H-Ar); 7.40-7.24 (m, 8H, H-Ar); 7.07 (d, 1H, *J* = 3.7 Hz, H-Het); 6.78 (d, 1H, *J* = 3.7 Hz, H-Het); 5.63 (dd, 1H, *J* = 3.1, 7.7 Hz, H-5); 4.04 (q, 1H, *J* = 6.6 Hz, H-1´); 3.59 (t, 1H, *J* = 8.6 Hz, H-3); 2.27-2.15 (m, 1H, H-4A); 2.14-2.04 (m, 1H, H-4B); 1.41 (d, 3H, *J* = 6.6 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6 (C-2); 144.7, 143.4, 131.8, 131.5, 128.7, 128.6, 128.6, 128.4, 127.5, 127.0, 125.3, 124.2, 122.5 (C-Ar, C-Het); 94.0, 81.9 (C-1´´, C-2´´); 74.6 (C-5); 58.2, 55.1 (C-3, C-1´); 38.6 (C-4); 24.5 (C-2´); IR (ATR): 3321, 2926, 2844, 1775, 1453, 1177, 800, 764, 698, 553 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{22}NO_2S$: 388.13658; found: 388.13640.

(3*R*,5*S*)-5-[(5-(4-Methoxy-phenylethynyl)-thiophen-2-yl]-3-{[(1*R*)-1-phenyl-ethyl]amino}-dihydrofuran-2(3*H*)-one (*trans*-19Ce). This product was prepared according to the general procedure; compound ***trans*-19Ce** (284 mg, 68%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (4:1 up to 2:1). TLC: R*f* = 0.33 (hexane/EtOAc 2:1, UV, $KMnO_4$); Mp = 98-100 °C; $[\alpha]_D^{20}$ = +159 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45-7.25 (m, 7H, H-Ar); 7.05 (d, 1H, *J* = 3.7 Hz, H-Het); 6.95-6.85 (m, 2H, H-Ar); 6.76 (dd, 1H, *J* = 0.9, 3.7 Hz, H-Het); 5.62 (dd, 1H, *J* = 3.1, 7.7 Hz, H-5); 4.04 (q, 1H, *J* = 6.6 Hz, H-1´); 3.82 (s, 3H, OC*H*$_3$); 3.59 (dd, 1H, *J* = 8.2, 8.9 Hz, H-3); 2.26-2.17 (m, 1H, H-4A); 2.15-2.04 (m, 1H, H-4B); 1.41 (d, 3H, *J* = 6.6 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.6 (C-2); 160.0, 144.7,

142.8, 133.0, 131.2, 128.6, 127.5, 127.0, 125.3, 124.7, 114.6, 114.1 (C-Ar, C-Het); 94.1, 80.6 (C-1´´, C-2´´); 74.6 (C-5); 58.2, 55.3, 55.1 (C-3, C-1´, O*C*H$_3$); 38.6 (C-4); 24.5 (C-2´); IR (ATR): 3322, 2921, 2845, 1768, 1455, 1187, 1122, 801, 760, 701, 555 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{25}H_{23}NO_3S$: 418.14714; found: 418.14719.

(3*R*,5*R*)-5-(3-Dec-1-ynyl-phenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-20Aa). This product was prepared according to the general procedure; compound ***cis*-20Aa** (355 mg, 85%) was obtained as pale brown oil after purification by flash column chromatography, eluting with hexane/EtOAc (8:1 up to 4:1). TLC: R*f* = 0.26 (hexane/EtOAc 4:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -28 (*c* 0.14, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.20 (m, 8H, H-Ar); 7.17-7.12 (m, 1H, H-Ar); 5.09 (dd, 1H, *J* = 5.2, 11.1 Hz, H-5); 4.14 (q, 1H, *J* = 6.5 Hz, H-1´); 3.59 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.38 (t, 2H, *J* = 7.0 Hz, H-3´´); 2.26 (ddd, 1H, *J* = 5.3, 7.9, 12.9 Hz, H-4A); 1.75 („dd", 1H, *J* = 12.1, 12.4 Hz, H-4B); 1.64-1.54 (m, 2H, H-4´´); 1.48-1.37 (m, 2H, H-5´´); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); 1.34-1.24 (m, 8H, H-6´´-H-9´´); 0.89 (t, 3H, *J* = 6.6 Hz, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 144.8, 138.4, 131.7, 128.7, 128.6, 128.5, 127.4, 127.0, 124.6 (C-Ar); 91.3, 79.9 (C-1´´, C-2´´); 78.0 (C-5); 58.5, 57.7 (C-3, C-1´); 40.9 (C-4); 31.8 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 28.9 (C-6´´); 28.7 (C-7´´); 24.8 (C-2´); 22.7 (C-8´´); 19.4 (C-9´´); 14.1 (C-10´´); IR (ATR): 3323, 2924, 1774, 1452, 1165, 1148, 1013, 795, 763, 699, 457 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{28}H_{36}NO_2$: 418.27460; found: 418.27542.

(3*R*,5*R*)-5-(3-Hex-1-ynyl-phenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-20Ab). This product was prepared according to the general procedure; compound ***cis*-20Ab** (242 mg, 67%) was obtained as pale brown oil after purification by flash column chromatography, eluting with hexane/EtOAc (7:1 up to 3:1). TLC: R*f* = 0.28 (hexane/EtOAc 3:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -18 (*c* 0.34, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38-7.20 (m, 8H, H-Ar); 7.16-7.11 (m, 1H, H-Ar); 5.09 (dd, 1H, *J* = 5.2, 11.1 Hz, H-5); 4.14 (q, 1H, *J* = 6.5 Hz, H-1´); 3.59 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.39 (t, 2H, *J* = 6.9 Hz, H-3´´); 2.26 (ddd, 1H, *J* = 5.3, 7.8, 12.9 Hz, H-4A); 1.75 („dd", 1H, *J* = 12.0, 12.6 Hz, H-4B); 1.62-1.44 (m, 2H, H-4´´, 2H, H-5´´); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); 0.94 (t, 3H, *J* = 6.6 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 144.8, 138.5, 131.7, 128.8, 128.6, 128.5, 127.4, 127.1, 124.7, 127.7 (C-Ar); 91.3, 80.0 (C-1´´, C-2´´); 78.0 (C-5); 58.5, 57.7 (C-3, C-1´); 40.9 (C-4); 30.8 (C-3´´); 24.8 (C-2´); 22.0 (C-4´´); 19.1 (C-5´´); 13.7 (C-6´´); IR (ATR): 3320, 2935, 1711, 1436, 1198, 1156, 1010, 796, 700, 452 cm^{-1}. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{24}H_{28}NO_2$: 362.21200; found: 362.21105.

(3*R*,5*R*)-5-[(3-(3,3-Dimethyl-but-1-ynyl)-phenyl]-3-{[(1*R*)-1-phenylethyl]amino}dihydro-furan-2(3*H*)-one (*cis*-20Ac). This product was prepared according to the general procedure; compound ***cis*-20Ac** (108 mg, 30%) was obtained as pale yellow oil after purification by flash column chromatography, eluting with hexane/EtOAc (5:1 up to 3:1). TLC: R*f* = 0.29 (hexane/EtOAc 3:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -14.2 (*c* 0.22, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38-7.20 (m, 8H, H-Ar); 7.14-7.09 (m, 1H, H-Ar); 5.09 (dd, 1H, *J* = 5.2, 11.1 Hz, H-5); 4.14 (q, 1H, *J* = 6.5 Hz, H-1´); 3.59 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.26 (ddd, 1H, *J* = 5.3, 7.9, 12.9 Hz, H-4A); 1.75 („dd", 1H, *J* = 11.9, 12.4 Hz, H-4B); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); 1.30 (s, 3H, H-4´´, 6H, 2 × C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.4 (C-2); 144.8, 138.4, 131.6, 128.7, 128.5, 128.5, 127.4, 127.0, 124.6 (C-Ar); 99.3, 78.4 (C-1´´, C-2´´); 78.1 (C-5); 58.5, 57.7 (C-3, C-1´); 41.0 (C-4); 31.0 (C-3´´); 27.9 (C-4´´, 2 ×

CH_3); 24.8 (C-2´); IR (ATR): 3325, 2932, 1773, 1569, 1500, 1233, 1173, 1022, 811, 697, 525 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{28}NO_2$: 362.21200; found: 362.21113.

(3*R*,5*R*)-3-{[(1*R*)-1-Phenylethyl]amino}-5-(3-phenylethynyl-phenyl)dihydrofuran-2(3*H*)-one (*cis*-20Ad). This product was prepared according to the general procedure; compound ***cis*-20Ad** (326 mg, 85%) was obtained as pale yellow oil after purification by flash column chromatography, eluting with hexane/EtOAc (8:1 up to 4:1). TLC: R*f* = 0.29 (hexane/EtOAc 4:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -23.4 (*c* 0.4, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55-7.17 (m, 14H, H-Ar); 5.13 (dd, 1H, *J* = 5.3, 11.1 Hz, H-5); 4.15 (q, 1H, *J* = 6.5 Hz, H-1´); 3.61 (dd, 1H, *J* =7.9, 11.9 Hz, H-3); 2.30 (ddd, 1H, *J* = 5.3, 7.9, 12.9 Hz, H-4A); 1.78 („dd“, 1H, *J* = 11.7, 12.3 Hz, H-4B); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 144.8, 138.7, 131.7, 131.6, 128.8, 128.6, 128.5, 128.4, 127.5, 127.1, 123.9, 122.9 (C-Ar); 90.0, 88.7 (C-1´´, C-2´´); 77.9 (C-5); 58.5, 57.7 (C-3, C-1´); 40.9 (C-4); 24.8 (C-2´); IR (ATR): 3343, 2935, 1777, 1448, 1136, 1112, 1025, 796, 745, 702, 469 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{24}NO_2$: 382.18070; found: 382.18007.

(3*R*,5*R*)-5-[(3-(4-Methoxy-phenylethynyl)-phenyl]-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-20Ae). This product was prepared according to the general procedure; compound ***cis*-20Ae** (325 mg, 79%) was obtained as pale brown oil after purification by flash column chromatography, eluting with hexane/EtOAc (5:1 up to 3:1). TLC: R*f* = 0.28 (hexane/EtOAc 3:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -7.5 (*c* 0.19, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48-7.20 (m, 10H, H-Ar); 7.20-7.16 (m, 1H, H-Ar); 6.88 (d, 2H, *J* = 8.5 Hz, H-Ar); 5.13 (dd, 1H, *J* = 5.3, 11.6 Hz, H-5); 4.15 (q, 1H, *J* = 6.5 Hz, H-1´); 3.83 (s, 3H, OC*H*$_3$); 3.60 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.29 (ddd, 1H, *J* = 5.3, 7.9, 13.0 Hz, H-4A); 1.78 („dd“, 1H, *J* = 11.8, 12.4 Hz, H-4B); 1.42 (d, 3H, *J* = 6.5 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 159.7, 144.8, 138.6, 133.1, 131.5, 128.7, 128.6, 128.5, 127.4, 127.0, 125.0, 124.1, 115.0, 114.0 (C-Ar); 90.1, 87.4 (C-1´´, C-2´´); 78.0 (C-5); 58.5, 57.7, 55.3 (C-3, C-1´, O*C*H_3); 40.9 (C-4); 24.8 (C-2´); IR (ATR): 3325, 2929, 1770, 1599, 1509, 1246, 1171, 1149, 1026, 830, 695, 536 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{27}H_{26}NO_3$: 412.19072; found: 412.19075.

(3*R*,5*R*)-5-(4-Dec-1-ynyl-phenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-20Ba). This product was prepared according to the general procedure; compound ***cis*-20Ba** (359 mg, 86%) was obtained as colorless oil after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.34 (hexane/EtOAc 2:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -45 (*c* 0.18, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.20 (m, 7H, H-Ar); 7.15 (d, 2H, *J* = 8.2 Hz, H-Ar); 5.10 (dd, 1H, *J* = 5.2, 11.1 Hz, H-5); 4.14 (q, 1H, *J* = 6.5 Hz, H-1´); 3.58 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.38 (t, 2H, *J* = 7.0 Hz, H-3´´); 2.26 (ddd, 1H, *J* = 5.3, 7.8, 12.9 Hz, H-4A); 1.74 („dd“, 1H, *J* = 12.0, 12.3 Hz, H-4B); 1.64-1.53 (m, 2H, H-4´´); 1.48-1.37 (m, 2H, H-5´´); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); 1.36-1.22 (m, 8H, H-6´´-H-9´´); 0.88 (t, 3H, *J* = 6.6 Hz, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 144.8, 137.4, 131.8, 128.5, 127.4, 127.0, 125.5, 124.6 (C-Ar); 91.4, 80.0 (C-1´´, C-2´´); 78.1 (C-5); 58.5, 57.7 (C-3, C-1´); 40.8 (C-4); 31.8 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 28.9 (C-6´´); 28.7 (C-7´´); 24.8 (C-2´); 22.7 (C-8´´); 19.4 (C-9´´); 14.1 (C-10´´); IR (ATR): 3322, 2922, 1759, 1445, 1126, 1102, 1025, 794, 755, 699, 456 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{28}H_{36}NO_2$: 418.27460; found: 418.27452.

(3*R*,5*R*)-5-(4-Hex-1-ynyl-phenyl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-20Bb). This product was prepared according to the general procedure; compound ***cis*-20Bb** (253 mg, 70%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (7:1 up to 3:1). TLC: R*f* = 0.30 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 63-64 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -33 (*c* 0.24, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.22 (m, 7H, H-Ar); 7.16 (d, 2H, *J* = 8.2 Hz, H-Ar); 5.11 (dd, 1H, *J* = 5.2, 11.1 Hz, H-5); 4.15 (q, 1H, *J* = 6.5 Hz, H-1´); 3.59 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.40 (t, 2H, *J* = 7.0 Hz, H-3´´); 2.26 (ddd, 1H, *J* = 5.3, 7.8, 12.9 Hz, H-4A); 1.75 („dd", 1H, *J* = 12.0, 12.3 Hz, H-4B); 1.64-1.52 (m, 2H, H-4´´); 1.51-1.43 (m, 2H, H-5´´); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); 0.95 (t, 3H, *J* = 7.2 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.2 (C-2); 144.7, 137.4, 131.8, 128.5, 127.5, 127.1, 125.5, 124.6 (C-Ar); 91.3, 80.0 (C-1´´, C-2´´); 78.1 (C-5); 58.5, 57.6 (C-3, C-1´); 40.8 (C-4); 30.8 (C-3´´); 24.7 (C-2´); 22.0 (C-4´´); 19.1 (C-5´´); 13.6 (C-6´´); IR (ATR): 3332, 2956, 1769, 1445, 1258, 1165, 1015, 794, 763, 701, 452 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{28}NO_2$: 362,21146; found: 362,21147.

(3*R*,5*R*)-5-[(4-(3,3-Dimethyl-but-1-ynyl)-phenyl]-3-{[(1*R*)-1-phenylethyl]amino}dihydro-furan-2(3*H*)-one (*cis*-20Bc). This product was prepared according to the general procedure; compound ***cis*-20Bc** (112 mg, 31%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.30 (hexane/EtOAc 2:1, UV, $KMnO_4$); Mp = 103-105 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -27.1 (*c* 0.25, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48-7.22 (m, 7H, H-Ar); 7.14 (d, 2H, *J* = 8.2 Hz, H-Ar); 5.10 (dd, 1H, *J* = 5.3, 11.0 Hz, H-5); 4.14 (q, 1H, *J* = 6.5 Hz, H-1´); 3.58 (dd, 1H, *J* = 7.9, 12.1 Hz, H-3); 2.25 (ddd, 1H, *J* = 5.1, 7.8, 12.8 Hz, H-4A); 1.73 (td, 1H, *J* = 11.3, 12.4 Hz, H-4B); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); 1.30 (s, 3H, H-4´´, 6H, 2 × C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 144.8, 137.3, 131.8, 128.5, 127.4, 127.0, 125.4, 124.5 (C-Ar); 99.4, 78.4 (C-1´´, C-2´´); 78.1 (C-5); 58.5, 57.6 (C-3, C-1´); 40.8 (C-4); 31.0 (C-3´´); 27.9 (C-4´´, 2 × *C*H_3); 24.8 (C-2´); IR (ATR): 3321, 2931, 1712, 1434, 1189, 1145, 1020, 789, 699, 451 cm^{-1}. Anal. Calcd. For $C_{24}H_{27}NO_2$: C 79.74, H 7.53, N 3.87. Found: C 79.45, H 7.59, N 3.77.

(3*R*,5*R*)-3-{[(1*R*)-1-Phenylethyl]amino}-5-(4-phenylethynyl-phenyl)dihydrofuran-2(3*H*)-one (*cis*-20Bd). This product was prepared according to the general procedure; compound ***cis*-20Bd** (267 mg, 70%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 3:1). TLC: R*f* = 0.28 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 119-121 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -37 (*c* 0.49, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55-7.47 (m, 4H, H-Ar); 7.40-7.20 (m, 10H, H-Ar); 5.14 (dd, 1H, *J* = 5.3, 11.1 Hz, H-5); 4.15 (q, 1H, *J* = 6.5 Hz, H-1´); 3.61 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.29 (ddd, 1H, *J* = 5.3, 7.8, 12.9 Hz, H-4A); 1.75 („dd", 1H, *J* = 11.6, 12.1 Hz, H-4B); 1.42 (d, 3H, *J* = 6.5 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C-2); 144.8, 138.3, 131.9, 131.6, 128.6, 128.5, 128.4, 127.5, 127.1, 125.7, 123.7, 123.0 (C-Ar); 90.1, 88.7 (C-1´´, C-2´´); 78.1 (C-5); 58.5, 57.7 (C-3, C-1´); 40.9 (C-4); 24.8 (C-2´); IR (ATR**):** 3320, 2935, 1711, 1433, 1198, 1156, 1015, 796, 701, 452 cm^{-1}. Anal. Calcd. For $C_{26}H_{23}NO_2$: C 81.86, H 6.08, N 3.67. Found: C 81.58, H 6.19, N 3.72.

(3*R*,5*R*)-5-[(4-(4-Methoxy-phenylethynyl)-phenyl]-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-20Be). This product was prepared according to the general procedure; compound ***cis*-20Be** (342 mg, 83%) was obtained as an off-white solid after purification by flash

column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.34 (hexane/EtOAc 2:1, UV, $KMnO_4$); Mp = 97-98 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -86 (*c* 0.21, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 7.50-7.45 (m, 4H, H-Ar); 7.40-7.22 (m, 7H, H-Ar); 6.92-6.87 (m, 2H, H-Ar); 5.15 (dd, 1H, *J* = 5.2, 11.1 Hz, H-5); 4.17 (q, 1H, *J* = 6.6 Hz, H-1´); 3.83 (s, 3H, OCH_3); 3.61 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.30 (ddd, 1H, *J* = 5.2, 7.9, 12.8 Hz, H-4A); 1.79 („dd", 1H, *J* = 12.0, 12.4 Hz, H-4B); 1.48 (d, 3H, *J* = 6.6 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.2 (C-2); 159.8, 144.8, 137.9, 133.1, 131.7, 128.6, 127.5, 127.1, 125.7, 124.1, 115.1, 114.1 (C-Ar); 90.2, 87.5 (C-1´´, C-2´´); 78.1 (C-5); 58.5, 57.7 (C-3, C-1´); 55.3 (OCH_3); 31.9 (C-4); 24.8 (C-2´); IR (ATR): 3326, 2922, 1725, 1445, 1189, 1155, 1016, 794, 701, 455 cm^{-1}. Anal. Calcd. For $C_{26}H_{23}NO_2$: C 78.81, H 6.12, N 3.40. Found: C 79.13, H 6.19, N 3.51.

(3*R*,5*R*)-5-(5-Dec-1-ynyl-thiophen-2-yl)-3-{[(1*R*)-1-phenylethyl]amino}dihydrofuran-2(3*H*)-one (*cis*-20Ca). This product was prepared according to the general procedure; compound ***cis*-20Ca** (326 mg, 77%) was obtained as colorless oil after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 2:1). TLC: R*f* = 0.36 (hexane/EtOAc 2:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -142 (*c* 0.39, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.24 (m, 5H, H-Ar); 6.95 (d, 1H, *J* = 3.7 Hz, H-Het); 6.84 (d, 1H, *J* = 3.7 Hz, H-Het); 5.27 (dd, 1H, *J* = 5.1, 10.9 Hz, H-5); 4.15 (q, 1H, *J* = 6.4 Hz, H-1´); 3.56 (dd, 1H, *J* = 7.8, 11.6 Hz, H-3); 2.40 (t, 2H, *J* = 7.1 Hz, H-3´´); 2.29 (ddd, 1H, *J* = 5.5, 7.6, 12.8 Hz, H-4A); 1.93 („dd", 1H, *J* = 11.9, 12.5 Hz, H-4B); 1.64-1.53 (m, 2H, H-4´´); 1.48-1.38 (m, 2H, H-5´´); 1.41 (d, 3H, *J* = 6.4 Hz, H-2´); 1.36-1.25 (m, 8H, H-6´´-H-9´´); 0.89 (t, 3H, *J* = 6.7 Hz, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.6 (C-2); 140.3, 130.6, 128.6, 127.5, 127.1, 126.2 125.8 (C-Ar, C-Het); 95.9, 73.2 (C-1´´, C-2´´); 74.2 (C-5); 58.7, 57.5 (C-3, C-1´); 40.5 (C-4); 31.8 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 28.9 (C-6´´); 28.4 (C-7´´); 24.7 (C-2´); 22.7 (C-8´´); 19.7 (C-9´´); 14.1 (C-10´´); IR (ATR): 3314, 2923, 2822, 1759, 1601, 1455, 1175, 1022, 791, 699 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{34}NO_2S$: 424.23103; found: 424.23041.

(3*R*,5*R*)-5-(5-Hex-1-ynyl-thiophen-2-yl)-3-{[(1*R*)-1-phenylethyl]amino}dihydro-furan-2(3*H*)-one (*cis*-20Cb). This product was prepared according to the general procedure; compound ***cis*-20Cb** (228 mg, 62%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 3:1). TLC: R*f* = 0.33 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 56-57 °C; $[\alpha]_D^{20}$ = -134 (*c* 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.25 (m, 5H, H-Ar); 6.95 (d, 1H, *J* = 3.7 Hz, H-Het); 6.83 (d, 1H, *J* = 3.7 Hz, H-Het); 5.27 (dd, 1H, *J* = 5.2, 11.1 Hz, H-5); 4.15 (q, 1H, *J* = 6.5 Hz, H-1´); 3.56 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.42 (t, 2H, *J* = 7.0 Hz, H-3´´); 2.30 (ddd, 1H, *J* = 5.3, 7.8, 12.9 Hz, H-4A); 1.93 („dd", 1H, *J* = 12.0, 12.4 Hz, H-4B); 1.64-1.53 (m, 2H, H-4´´); 1.52-1.45 (m, 2H, H-5´´); 1.43 (d, 3H, *J* = 6.5 Hz, H-2´); 0.94 (t, 3H, *J* = 7.2 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6 (C-2); 144.7, 140.3, 130.6, 128.6, 127.5, 127.1, 126.2, 125.8 (C-Ar, C-Het); 95.8, 73.3 (C-1´´, C-2´´); 74.2 (C-5); 58.5, 57.6 (C-3, C-1´); 40.5 (C-4); 30.5 (C-3´´); 24.8 (C-2´); 22.0 (C-4´´); 19.4 (C-5´´); 13.6 (C-6´´); IR (ATR): 3323, 2920, 1721, 1436, 1179, 1132, 1010, 795, 698, 459 cm^{-1}. Anal. Calcd. For $C_{22}H_{25}NO_2S$: C 71.90, H 6.86, N 3.81. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{26}NO_2S$: 368.16788; found: 368.16765.

(3*R*,5*R*)-5-[(5-(3,3-Dimethyl-but-1-ynyl)-thiophen-2-yl]-3-{[(1*R*)-1-phenylethyl]amino}dihydro-furan-2(3*H*)-one (*cis*-20Cc). This product was prepared according to the general procedure; compound ***cis*-20Cc** (202 mg, 55%) was obtained as a white solid after purification by flash

column chromatography, eluting with hexane/EtOAc (10:1 up to 3:1). TLC: R*f* = 0.32 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 102-103 °C; $[\alpha]_D^{20}$ = -130 (*c* 0.13, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42-7.28 (m, 5H, H-Ar); 6.98 (d, 1H, *J* = 3.7 Hz, H-Het); 6.88 (d, 1H, *J* = 3.7 Hz, H-Het); 5.31 (dd, 1H, *J* = 5.2, 11.1 Hz, H-5); 4.19 (q, 1H, *J* = 6.5 Hz, H-1´); 3.60 (dd, 1H, *J* = 7.9, 11.8 Hz, H-3); 2.33 (ddd, 1H, *J* = 5.2, 7.8, 12.9 Hz, H-4A); 1.97 („dd", 1H, *J* = 11.8, 12.3 Hz, H-4B); 1.47 (d, 3H, *J* = 6.5 Hz, H-2´); 1.36 (s, 3H, H-4´´, 6H, 2 × C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.6 (C-2); 144.7, 140.3, 130.5, 128.6, 127.5, 127.1, 126.2, 125.8 (C-Ar, C-Het); 103.5, 71.8 (C-1´´, C-2´´); 74.2 (C-5); 58.5, 57.6 (C-3, C-1´); 40.5 (C-4); 30.8 (C-3´´); 28.3 (C-4´´, 2 × *C*H$_3$); 24.8 (C-2´); IR (ATR): 3316, 2921, 2822, 1769, 1611, 1433, 1175, 1149, 1036, 785, 699 cm^{-1}. Anal. Calcd. For $C_{22}H_{25}NO_2S$: C 71.90, H 6.86, N 3.81. Found: C 72.21, H 6.94, N 3.72.

(3*R*,5*R*)-3-{[(1*R*)-1-Phenylethyl]amino}-5-(5-phenylethynyl-thiophen-2-yl)-dihydrofuran-2(3*H*)-one (*cis*-20Cd). This product was prepared according to the general procedure; compound ***cis*-20Cd** (263 mg, 68%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (10:1 up to 3:1). TLC: R*f* = 0.35 (hexane/EtOAc 3:1, UV, $KMnO_4$); Mp = 99-101 °C; $[\alpha]_D^{20}$ = -161 (*c* 0.15, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55-7.48 (m, 2H, H-Ar); 7.40-7.26 (m, 8H, H-Ar); 7.13 (d, 1H, *J* = 3.7 Hz, H-Het); 6.92 (d, 1H, *J* = 3.7 Hz, H-Het); 5.31 (dd, 1H, *J* = 5.2, 11.0 Hz, H-5); 4.17 (q, 1H, *J* = 6.5 Hz, H-1´); 3.58 (dd, 1H, *J* = 7.9, 11.8 Hz, H-3); 2.34 (ddd, 1H, *J* = 5.3, 7.7, 12.9 Hz, H-4A); 1.75 („dd", 1H, *J* = 11.9, 12.4Hz, H-4B); 1.44 (d, 3H, *J* = 6.5 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.4 (C-2); 144.6, 141.8, 131.6, 131.4, 128.7, 128.6, 128.4, 127.5, 127.1, 126.3, 124.7, 122.5 (C-Ar, C-Het); 94.0, 82.0 (C-1´´, C-2´´); 74.1 (C-5); 58.5, 57.5 (C-3, C-1´); 40.5 (C-4); 24.7 (C-2´); IR (ATR): 3321, 2931, 1710, 1434, 1152, 1133, 1020, 788, 699, 469 cm^{-1}. Anal. Calcd. For $C_{24}H_{21}NO_2S$: C 74.39, H 5.46, N 3.61. Found: C 74.79, H 5.55, N 3.55.

(3*R*,5*R*)-5-[(5-(4-Methoxy-phenylethynyl)-thiophen-2-yl]-3-{[(1*R*)-1-phenylethyl]amino}-dihydrofuran-2(3*H*)-one (*cis*-20Ce). This product was prepared according to the general procedure; compound ***cis*-20Ce** (234 mg, 56%) was obtained as colorless oil after purification by flash column chromatography, eluting with hexane/EtOAc (7:1 up to 2:1). TLC: R*f* = 0.34 (hexane/EtOAc 2:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -135 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45-7.24 (m, 7H, H-Ar); 7.07 (d, 1H, *J* = 3.7 Hz, H-Het); 6.92 (d, 1H, *J* = 3.7 Hz, H-Het); 6.90-6.84 (m, 2H, H-Ar); 5.29 (dd, 1H, *J* = 5.2, 11.0 Hz, H-5); 4.14 (q, 1H, *J* = 6.5 Hz, H-1´); 3.82 (s, 3H, OC*H*$_3$); 3.57 (dd, 1H, *J* = 7.9, 11.9 Hz, H-3); 2.31 (ddd, 1H, *J* = 5.3, 7.8, 12.9 Hz, H-4A); 1.94 (dd, 1H, *J* = 11.8, 12.4 Hz, H-4B); 1.42 (d, 3H, *J* = 6.5 Hz, H-2´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6 (C-2); 160.0, 144.7, 141.3, 133.0, 131.1, 128.6, 127.5, 127.1, 126.4, 125.2, 114.6, 114.1, 114.1 (C-Ar, C-Het); 94.1, 80.8 (C-1´´, C-2´´); 74.1 (C-5); 58.5, 57.6 (C-3, C-1´); 55.3 (O*C*H$_3$); 40.5 (C-4); 24.8 (C-2´); IR (ATR): 3322, 2932, 2829, 1760, 1600, 1441, 1259, 1132, 1036, 801, 702 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{25}H_{24}NO_3S$: 418.14714; found: 418.14718.

General procedure for reduction of lactones to aminodiols

Sodium borohydride (0.37 g, 10 mmol) was added to the suspension of the corresponding lactone **(*tans*-19A-C** or ***cis*-20A-C)** (1 mmol) in 96 % ethanol (15 mL) in one portion at room temperature. The reaction mixture was stirred for the indicated time at room temperature.

Then 5% potassium carbonate solution (20 mL) was added and the ethanol was evaporated under reduced pressure. The water phase was extracted with Et_2O (3 x 100 mL). Organic extracts were dried with Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography to yield the desired diaminoalcohol ***anti*-21A-C** or ***syn*-22A-C**.

(1*R*,3*R*)-1-(3-Dec-1-ynyl-phenyl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*anti*-21Aa). This product was prepared according to the general procedure; compound ***anti*-21Aa** (282 mg, 67%) was obtained as a pale yellow oil after purification by flash column chromatography, eluting with CH_2Cl_2/acetone (7:1 up to 5:1). TLC: R*f* = 0.29 (CH_2Cl_2/acetone 5:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +97 (*c* 0.14, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.15 (m, 7H, H-Ar); 7.08 (t, 1H, *J* = 7.6 Hz, H-Ar); 6.97-6.92 (m, 1H, H-Ar); 4.85 (dd, 1H, *J* = 4.1, 6.2 Hz, H-1); 3.89 (q, 1H, *J* = 6.6 Hz, H-1´); 3.76 (dd, 1H, *J* = 4.1, 10.9 Hz, H-4A); 3.40 (dd, 1H, *J* = 4.0, 10.9 Hz, H-4B); 2.64 (td, 1H, *J* = 3.8, 12.3 Hz, H-3); 2.39 (t, 2H, *J* = 7.0 Hz, H-3´´); 1.92 (ddd, 1H, *J* = 4.0, 8.6, 14.3 Hz, H-2A); 1.70-1.54 (m, 1H, H-2B, 2H, H-4´´); 1.48-1.42 (m, 2H, H-5´´); 1.38 (d, 3H, *J* = 6.6 Hz, H-2´); 1.35-1.22 (m, 8H, H-6´´-H-9´´); 0.88 (t, 3H, *J* = 6.6 Hz, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.9, 144.2, 129.9, 128.7, 128.6, 128.0, 127.4, 127.0, 124.8, 123.7 (C-Ar); 90.2, 80.7 (C-1´´, C-2´´); 71.9 (C-1); 62.8 (C-4); 55.1, 53.1 (C-3, C-1´); 39.5 (C-2); 31.8 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 29.0 (C-6´´); 28.8 (C-7´´); 24.3 (C-2´); 22.6 (C-8´´); 19.4 (C-9´´); 14.1 (C-10´´); IR (ATR): 3286, 2920, 2857, 1435, 1139, 1066, 1052, 795, 761, 698, 555 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{28}H_{40}NO_2$: 422.30536; found: 422.30508.

(1*R*,3*R*)-1-(3-Hex-1-ynyl-phenyl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*anti*-21Ab). This product was prepared according to the general procedure; compound ***anti*-21Ab** (212 mg, 58%) was obtained as a pale yellow oil after purification by flash column chromatography, eluting with CH_2Cl_2/acetone (10:1 up to 6:1). TLC: R*f* = 0.28 (CH_2Cl_2/acetone 6:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +63 (*c* 0.16, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.17 (m, 7H, H-Ar); 7.09 (t, 1H, *J* = 7.6 Hz, H-Ar); 6.99-6.94 (m, 1H, H-Ar); 4.88 (dd, 1H, *J* = 4.2, 6.1 Hz, H-1); 3.91 (q, 1H, *J* = 6.5 Hz, H-1´); 3.78 (dd, 1H, *J* = 4.1, 10.9 Hz, H-4A); 3.43 (dd, 1H, *J* = 4.0, 10.9 Hz, H-4B); 2.67 (td, 1H, *J* = 3.8, 12.1 Hz, H-3); 2.43 (t, 2H, *J* = 7.0 Hz, H-3´´); 1.95 (ddd, 1H, *J* = 4.0, 8.5, 14.3 Hz, H-2A); 1.73-1.65 (m, 1H, H-2B); 1.65-1.65 (m 2H, H-4´´); 1.55-1.45 (m, 2H, H-5´´); 1.41 (d, 3H, *J* = 6.6 Hz, H-2´); 0.97 (t, 3H, *J* = 6.6 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.9, 144.3, 130.0, 128.8, 128.7, 128.7, 128.0, 127.4, 127.1, 124.8, 123.8 (C-Ar); 90.2, 80.7 (C-1´´, C-2´´); 71.9 (C-1); 62.9 (C-4); 55.2, 53.1 (C-3, C-1´); 39.5 (C-2); 30.9 (C-3´´); 24.3 (C-2´); 22.1 (C-4´´); 19.1 (C-5´´); 13.7 (C-6´´); IR (ATR): 3276, 2922, 2850, 1451, 1122, 1080, 1059, 795, 763, 701, 544 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{24}H_{32}NO_2$: 366.24276; found: 366.24258.

(1*R*,3*R*)-1-(4-Dec-1-ynyl-phenyl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*anti*-21Ba). This product was prepared according to the general procedure; compound ***anti*-21Ba** (308 mg, 73%) was obtained as a pale yellow oil after purification by flash column chromatography, eluting with EtOAc/NH_3 (100:1). TLC: R*f* = 0.33 (EtOAc/NH_3 100:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +50 (*c* 0.27, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.27 (m, 5H, H-Ar); 7.20 (d, 2H, *J* = 8.2 Hz, H-Ar); 6.95 (d, 2H, *J* = 8.2 Hz, H-Ar); 4.90 (dd, 1H, *J* = 4.2, 5.8 Hz, H-1); 3.89 (q, 1H, *J* = 6.6 Hz, H-1´); 3.78 (dd, 1H, *J* = 4.1, 10.9 Hz, H-4A); 3.41 (dd, 1H, *J* = 3.8, 10.9 Hz, H-4B); 2.65 (td, 1H, *J* = 3.8, 12.4 Hz, H-3); 2.39 (t, 2H, *J* = 7.0 Hz, H-3´´); 1.96 (ddd, 1H, *J* = 4.1, 8.9, 14.3 Hz, H-2A); 1.68-1.54 (m, 1H, H-

2B, 2H, H-4´´); 1.48-1.37 (m, 2H, H-5´´); 1.42 (d, 3H, *J* = 6.6 Hz, H-2´); 1.40-1.20 (m, 8H, H-6´´-H-9´´); 0.90 (t, 3H, *J* = 6.6 Hz, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.2, 131.3, 128.7, 127.5, 127.2, 125.4, 122.3 (C-Ar); 90.0, 80.5 (C-1´´, C-2´´); 72.1 (C-1); 62.8 (C-4); 55.1, 53.0 (C-3, C-1´); 39.4 (C-2); 31.9 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 29.0 (C-6´´); 28.8 (C-7´´); 24.1 (C-2´); 22.7 (C-8´´); 19.4 (C-9´´); 14.1 (C-10´´); IR (ATR): 3288, 2923, 2854, 1453, 1059, 838, 760, 700, 553 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{28}H_{40}NO_2$: 422.30536; found: 422.30523.

(1*R*,3*R*)-1-(4-Hex-1-ynyl-phenyl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*anti*-21Bb). This product was prepared according to the general procedure; compound ***anti*-21Bb** (285 mg, 78%) was obtained as a pale yellow oil after purification by flash column chromatography, eluting with EtOAc/NH_3 (100:1). TLC: R*f* = 0.32 (EtOAc/NH_3 100:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +62 (*c* 0.32, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37-7.24 (m, 5H, H-Ar); 7.19 (d, 2H, *J* = 8.2 Hz, H-Ar); 6.92 (d, 2H, *J* = 8.2 Hz, H-Ar); 4.87 (dd, 1H, *J* = 3.8, 5.6 Hz, H-1); 3.87 (q, 1H, *J* = 6.6 Hz, H-1´); 3.76 (dd, 1H, *J* = 3.9, 10.8 Hz, H-4A); 3.39 (dd, 1H, *J* = 3.6, 10.8 Hz, H-4B); 2.63 (td, 1H, *J* = 3.7, 12.4 Hz, H-3); 2.38 (t, 2H, *J* = 7.0 Hz, H-3´´); 1.94 (ddd, 1H, *J* = 4.1, 8.8, 14.0 Hz, H-2A); 1.64-1.52 (m, 1H, H-2B, 2H, H-4´´); 1.50-1.42 (m, 2H, H-5´´); 1.40 (d, 3H, *J* = 6.6 Hz, H-2´); 0.94 (t, 3H, *J* = 6.6 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.2, 144.1, 131.3, 128.7, 127.5, 127.2, 125.4, 122.3 (C-Ar); 90.0, 80.5 (C-1´´, C-2´´); 72.1 (C-1); 62.7 (C-4); 55.1, 53.0 (C-3, C-1´); 39.4 (C-2); 30.9 (C-3´´); 24.1 (C-2´); 22.0 (C-4´´); 19.1 (C-5´´); 13.7 (C-6´´); IR (ATR): 3288, 2927, 2869, 1452, 1354, 1087, 1059, 1039, 838, 760, 700, 554 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{24}H_{32}NO_2$: 366.24276; found: 366.24202.

(1*R*,3*R*)-1-(5-Dec-1-ynyl-thiophen-2-yl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*anti*-21Ca). This product was prepared according to the general procedure; compound ***anti*-21Ca** (334 mg, 78%) was obtained as an yellowish oil after purification by flash column chromatography, eluting with EtOAc/NH_3 (100:1). TLC: R*f* = 0.45 (EtOAc/NH_3 100:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = + 27.1 (*c* 0.23, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35-7.21 (m, 5H, H-Ar); 6.82 (d, 1H, *J* = 3.6 Hz, H-Het); 6.46 (d, 1H, *J* = 3.6 Hz, H-Het); 5.10-5.05 (m, 1H, H-1); 3.91 (q, 1H, *J* = 6.4 Hz, H-1´); 3.80 (dd, 1H, *J* = 4.1, 10.9 Hz, H-4A); 3.44 (dd, 1H, *J* = 3.6, 11.0 Hz, H-4B); 2.79-2.74 (m, 1H, H-3); 2.41 (t, 2H, *J* = 7.1 Hz, H-3´´); 2.10-2.00 (m, 1H, H-2A); 1.74 (ddd, 1H, *J* = 3.5, 5.8, 14.7 Hz, H-2B); 1.64-1.54 (m, 2H, H-4´´); 1.50-1.41 (m, 2H, H-5´´); 1.38 (d, 3H, *J* = 6.5 Hz, H-2´); 1.34-1.24 (m, 8H, H-6´´-H-9´´); 0.89 (t, 3H, *J* = 6.7 Hz, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.9, 143.8, 130.6, 128.7, 127.4, 127.0, 122.6, 122.5 (C-Ar, C-Het); 94.2, 73.9 (C-1´´, C-2´´); 69.1 (C-1); 62.6 (C-4); 55.0, 53.0 (C-3, C-1´); 39.3 (C-2); 31.9 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 28.9 (C-6´´); 28.6 (C-7´´); 24.4 (C-2´); 22.7 (C-8´´); 19.7 (C-9´´); 14.1 (C-10´´); IR (ATR): 3290, 2933, 2843, 1451, 1055, 803, 755, 724, 701, 556 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{26}H_{38}NO_2S$: 428.26178; found: 428.26149.

(1*R*,3*R*)-1-(5-Hex-1-ynyl-thiophen-2-yl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*anti*-21Cb). This product was prepared according to the general procedure; compound ***anti*-21Cb** (279 mg, 75%) was obtained as an yellowish oil after purification by flash column chromatography, eluting with CH_2Cl_2/acetone/NH_3 (30:10:0.5). TLC: R*f* = 0.45 (CH_2Cl_2/acetone/NH_3 30:10:0.5, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +25.7 (*c* 0.26, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35-7.20 (m, 5H, H-Ar); 6.83 (d, 1H, *J* = 3.6 Hz, H-Het); 6.45 (d, 1H, *J* = 3.6 Hz, H-Het);

5.09-5.03 (m, 1H, H-1); 3.90 (q, 1H, *J* = 6.5 Hz, H-1´); 3.79 (dd, 1H, *J* = 4.1, 10.9 Hz, H-4A); 3.43 (dd, 1H, *J* = 3.5, 11.0 Hz, H-4B); 2.80-2.74 (m, 1H, H-3); 2.41 (t, 2H, *J* = 7.1 Hz, H-3´´); 2.04 (ddd, 1H, *J* = 4.1, 9.2, 14.2 Hz, H-2A); 1.74 (ddd, 1H, *J* = 3.4, 5.7, 14.5 Hz, H-2B); 1.64-1.50 (m, 2H, H-4´´); 1.50-1.41 (m, 2H, H-5´´); 1.36 (d, 3H, *J* = 6.5 Hz, H-2´); 0.94 (t, 3H, *J* = 6.7 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.9, 143.8, 130.6, 128.6, 127.4, 127.0, 122.6, 122.5 (C-Ar, C-Het); 94.1, 73.9 (C-1´´, C-2´´); 69.2 (C-1); 62.6 (C-4); 55.0, 52.9 (C-3, C-1´); 39.3 (C-2); 30.7 (C-3´´); 24.4 (C-2´); 22.0 (C-4´´); 19.4 (C-5´´); 13.6 (C-6´´); IR (ATR): 3277, 2935, 2844, 1450, 1151, 1098, 800, 760, 699, 555 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{22}H_{30}NO_2S$: 372.19918; found: 372.19862.

(1*S*,3*R*)-1-(3-Dec-1-ynyl-phenyl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*syn*-22Aa). This product was prepared according to the general procedure; compound ***syn*-22Aa** (278 mg, 66%) was obtained as a pale yellow oil after purification by flash column chromatography, eluting with CH_2Cl_2/acetone (7:1 up to 5:1). TLC: R*f* = 0.31 (CH_2Cl_2/acetone 5:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +10.5 (*c* 0.19, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43-7.17 (m, 9H, H-Ar); 4.64 (dd, 1H, *J* = 1.7, 10.3 Hz, H-1); 4.02 (q, 1H, *J* = 6.6 Hz, H-1´); 3.82 (dd, 1H, *J* = 3.9, 11.0 Hz, H-4A); 3.42 (dd, 1H, *J* = 2.2, 11.0 Hz, H-4B); 2.780-2.73 (m, 1H, H-3); 2.38 (t, 2H, *J* = 7.0 Hz, H-3´´); 1.74 (td, 1H, *J* = 10.7, 14.3 Hz, H-2A); 1.62-1.51 (m, 1H, H-2B, 2H, H-4´´); 1.50-1.36 (m, 2H, H-5´´); 1.39 (d, 3H, *J* = 6.6 Hz, H-2´); 1.34-1.22 (m, 8H, H-6´´-H-9´´); 0.87 (t, 3H, *J* = 6.6 Hz, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.0, 144.0, 130.2, 128.8, 128.8, 128.1, 127.4, 127.0, 124.7, 123.9 (C-Ar); 90.2, 80.6 (C-1´´, C-2´´); 74.1 (C-1); 62.2 (C-4); 55.9, 54.9 (C-3, C-1´); 41.3 (C-2); 31.8 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 28.9 (C-6´´); 28.8 (C-7´´); 25.2 (C-2´); 22.7 (C-8´´); 19.4 (C-9´´); 14.1 (C-10´´); IR (ATR): 3286, 2923, 2851, 1452, 1119, 1080, 1055, 795, 761, 698, 555 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{28}H_{40}NO_2$: 422.30536; found: 422.30531.

(1*S*,3*R*)-1-(3-Hex-1-ynyl-phenyl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*syn*-22Ab). This product was prepared according to the general procedure; compound ***syn*-22Ab** (281 mg, 77%) was obtained as a pale yellow oil after purification by flash column chromatography, eluting with CH_2Cl_2/acetone (8:1 up to 5:1). TLC: R*f* = 0.33 (CH_2Cl_2/acetone 5:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +12.1 (*c* 0.55, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43-7.16 (m, 9H, H-Ar); 4.66 (dd, 1H, *J* = 1.6, 10.4 Hz, H-1); 4.04 (q, 1H, *J* = 6.6 Hz, H-1´); 3.84 (dd, 1H, *J* = 3.9, 10.9 Hz, H-4A); 3.42 (dd, 1H, *J* = 2.2, 11.0 Hz, H-4B); 2.83-2.75 (m, 1H, H-3); 2.40 (t, 2H, *J* = 7.0 Hz, H-3´´); 1.76 (td, 1H, *J* = 10.7, 14.4 Hz, H-2A); 1.64-1.53 (m, 1H, H-2B, 2H, H-4´´); 1.53-1.44 (m, 2H, H-5´´); 1.42 (d, 3H, *J* = 6.6 Hz, H-2´); 0.95 (t, 3H, *J* = 6.6 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.0, 144.0, 130.2, 128.9, 128.8, 128.1, 127.5, 127.1, 124.8, 123.9 (C-Ar); 90.1, 80.7 (C-1´´, C-2´´); 74.1 (C-1); 62.3 (C-4); 56.0, 54.9 (C-3, C-1´); 41.3 (C-2); 30.9 (C-3´´); 25.3 (C-2´); 22.0 (C-4´´); 19.1 (C-5´´); 13.7 (C-6´´); IR (ATR): 3278, 2943, 2855, 1444, 1198, 1126, 1045, 788, 755, 699, 556 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{24}H_{32}NO_2$: 366.24276; found: 366.24275.

(1*S*,3*R*)-1-(4-Dec-1-ynyl-phenyl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*syn*-22Ba). This product was prepared according to the general procedure; compound ***syn*-22Ba** (337 mg, 80%) was obtained as a pale yellow oil after purification by flash column chromatography, eluting with EtOAc/NH_3 (100:1). TLC: R*f* = 0.31 (EtOAc/NH_3 100:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -7.6 (*c* 0.28, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42-7.19 (m, 9H, H-Ar); 4.65 (dd, 1H, *J* = 1.2, 9.9 Hz, H-1); 4.04 (q, 1H, *J* = 6.6 Hz, H-1´); 3.82 (dd, 1H, *J* = 3.7, 11.0 Hz, H-4A); 3.42 (dd, 1H, *J* = 2.1, 11.1 Hz,

H-4B); 2.82-2.73 (m, 1H, H-3); 2.38 (t, 2H, *J* = 7.0 Hz, H-3´´); 1.81-1.65 (m, 1H, H-2A); 1.62-1.51 (m, 1H, H-2B, 2H, H-4´´); 1.50-1.36 (m, 2H, H-5´´); 1.42 (d, 3H, *J* = 6.6 Hz, H-2´); 1.34-1.22 (m, 8H, H-6´´-H-9´´); 0.87 (t, 3H, *J* = 6.6 Hz, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.3, 143.8, 131.5, 128.8, 127.5, 127.1, 125.4, 122.8 (C-Ar); 90.1, 80.5 (C-1´´, C-2´´); 74.2 (C-1); 62.2 (C-4); 56.0, 55.0 (C-3, C-1´); 41.2 (C-2); 31.9 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 29.0 (C-6´´); 28.8 (C-7´´); 25.2 (C-2´); 22.7 (C-8´´); 19.4 (C-9´´); 14.1 (C-10´´); IR (ATR): 3268, 2935, 2844, 1441, 1188, 1135, 1040, 758, 702, 554 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{28}H_{40}NO_2$: 422.30536; found: 422.30531.

(1*S*,3*R*)-1-(4-Hex-1-ynyl-phenyl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*syn*-22Bb). This product was prepared according to the general procedure; compound ***syn*-22Bb** (219 mg, 60%) was obtained as a pale yellow oil after purification by flash column chromatography, eluting with EtOAc/NH_3 (100:1). TLC: R*f* = 0.30 (EtOAc/NH_3 100:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -9.3 (*c* 0.38, $CHCl_3$) (EtOAc:NH_3 = 100:1, R_f = 0.30); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42-7.19 (m, 9H, H-Ar); 4.66 (dd, 1H, *J* = 1.6, 10.4 Hz, H-1); 4.06 (q, 1H, *J* = 6.6 Hz, H-1´); 3.84 (dd, 1H, *J* = 3.9, 11.0 Hz, H-4A); 3.42 (dd, 1H, *J* = 2.3, 11.1Hz, H-4B); 2.79 (tdd, 1H, *J* = 3.5, 6.7, 10.4 Hz, H-3); 2.40 (t, 2H, *J* = 6.9 Hz, H-3´´); 1.84-1.73 (m, 1H, H-2A); 1.66-1.55 (m, 2H, H-4´´); 1.53-1.46 (m, 1H, H-2B); 1.42 (d, 3H, *J* = 6.6 Hz, H-2´); 1.45-1.25 (m, 2H, H-5´´); 0.95 (t, 3H, *J* = 6.6 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.0, 144.0, 130.2, 128.9, 128.8, 128.1, 127.5, 127.1, 124.8, 123.9 (C-Ar); 90.1, 80.7 (C-1´´, C-2´´); 74.1 (C-1); 62.3 (C-4); 56.0, 54.9 (C-3, C-1´); 41.3 (C-2); 30.9 (C-3´´); 25.3 (C-2´); 22.0 (C-4´´); 19.1 (C-5´´); 13.7 (C-6´´); IR (ATR): 3277, 2947, 2853, 1444, 1189, 1122, 1033, 787, 745, 698, 556 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{24}H_{32}NO_2$: 366.24276; found: 366.24273.

(1*S*,3*R*)-1-(5-Dec-1-ynyl-thiophen-2-yl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*syn*-22Ca). This product was prepared according to the general procedure; compound ***syn*-22Ca** (312 mg, 73%) was obtained as an yellowish oil after purification by flash column chromatography, eluting with EtOAc/NH_3 (100:1). TLC: R*f* = 0.38 (EtOAc/NH_3 100:1, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +7.8 (*c* 0.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44-7.28 (m, 5H, H-Ar); 6.92 (d, 1H, *J* = 3.6 Hz, H-Het); 6.66 (d, 1H, *J* = 3.6 Hz, H-Het); 4.87 (dd, 1H, *J* = 1.5, 10.4 Hz, H-1); 4.05 (q, 1H, *J* = 6.5 Hz, H-1´); 3.84 (dd, 1H, *J* = 3.9, 11.0 Hz, H-4A); 3.46 (dd, 1H, *J* = 2.1, 11.0 Hz, H-4B); 2.81-2.76 (m, 1H, H-3); 2.41 (t, 2H, *J* = 7.1 Hz, H-3´´); 1.89 (td, 1H, *J* = 10.8, 14.2 Hz, H-2A); 1.74-1.66 (m, 1H, H-2B); 1.64-1.54 (m, 2H, H-4´´); 1.47-1.37 (m, 2H, H-5´´); 1.41 (d, 3H, *J* = 6.5 Hz, H-2´); 1.34-1.25 (m, 8H, H-6´´-H-9´´); 0.89 (t, 3H, *J* = 6.7 Hz, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.7, 143.7, 130.6, 128.9, 127.6, 127.1, 122.6, 122.0 (C-Ar, C-Het); 94.2, 74.0 (C-1´´, C-2´´); 70.9 (C-1); 62.1 (C-4); 55.7, 55.0 (C-3, C-1´); 41.4 (C-2); 31.9 (C-3´´); 29.2 (C-4´´); 29.1 (C-5´´); 29.0 (C-6´´); 28.6 (C-7´´); 25.1 (C-2´); 22.7 (C-8´´); 19.7 (C-9´´); 14.1 (C-10´´); IR (ATR): 3284, 2923, 2853, 1451, 1087, 1053, 803, 761, 700, 557 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{26}H_{38}NO_2S$: 428.26178; found: 428.26162.

(1*S*,3*R*)-1-(5-Hex-1-ynyl-thiophen-2-yl)-3-((*R*)-1-phenylethylamino)-butane-1,4-diol (*syn*-22Cb). This product was prepared according to the general procedure; compound ***syn*-22Cb** (275 mg, 74%) was obtained as an yellowish oil after purification by flash column chromatography, eluting with CH_2Cl_2/acetone/NH_3 (50:10:0.5). TLC: R*f* = 0.44 (CH_2Cl_2/acetone/NH_3 50:10:0.5, UV, $KMnO_4$); $[\alpha]_D^{20}$ = +10.4 (*c* 0.37, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40-7.25 (m, 5H, H-Ar);

6.91 (d, 1H, *J* = 3.6 Hz, H-Het); 6.65 (d, 1H, *J* = 3.6 Hz, H-Het); 4.86 (dd, 1H, *J* = 1.6, 10.3 Hz, H-1); 4.02 (q, 1H, *J* = 6.5 Hz, H-1´); 3.82 (dd, 1H, *J* = 3.9, 11.0 Hz, H-4A); 3.44 (dd, 1H, *J* = 2.2, 11.0 Hz, H-4B); 2.80-2.71 (m, 1H, H-3); 2.41 (t, 2H, *J* = 7.1 Hz, H-3´´); 1.86 (td, 1H, *J* = 10.7, 14.2 Hz, H-2A); 1.72-1.65 (m, 1H, H-2B); 1.64-1.54 (m, 2H, H-4´´); 1.47-1.37 (m, 2H, H-5´´); 1.38 (d, 3H, *J* = 6.5 Hz, H-2´); 0.93 (t, 3H, *J* = 6.7 Hz, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.7, 143.8, 130.5, 128.8, 127.5, 127.0, 122.5, 121.9 (C-Ar, C-Het); 94.1, 74.0 (C-1´´, C-2´´); 70.9 (C-1); 62.0 (C-4); 55.6, 54.9 (C-3, C-1´); 41.5 (C-2); 30.7 (C-3´´); 25.2 (C-2´); 22.0 (C-4´´); 19.4 (C-5´´); 13.6 (C-6´´); IR (ATR): 3327, 3284, 2928, 1451, 1356, 1052, 803, 761, 700, 556, 542 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{22}H_{30}NO_2S$: 372.19918; found: 372.19814.

General procedure for the tandem/one-pot triple bond C≡C hydrogenation, *N*-debenzylation and *N*-acylation

The acetic acid (57 µL, 1 mmol) and subsequently 20 % $Pd(OH)_2/C$ (20 wt %) were added to the solution of ***anti*-21A-C** or ***syn*-22A-C** (0.5 mmol) in MeOH (25 mL). The reduction was carried out under 1.1 bar of H_2 pressure at 40 °C. When the reduction was completed (monitoring TLC), MeOH was evaporated under reduced pressure. The residue was dissolved in THF (15 mL) and dodecanoic acid *N*-hydroxysuccinimide ester (X=$C_{11}H_{23}CO_2Su$, 178 mg, 0.6 mmol) was added. The reaction mixture was stirred for the indicated time at room temperature. Solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography to yield the desired product **14**.

(1*R*,3*R*)-1-*N*-(3-(3-Decylphenyl)-3-hydroxy-1-hydroxymethyl)dodecanamide (*anti*-14Aa). This product was prepared according to the general procedure; compound ***anti*-14Aa** (212 mg, 84%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 up to 1:3). TLC: R*f* = 0.35 (hexane/EtOAc 1:3, UV, $KMnO_4$); Mp = 44-45 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +8.0 (*c* 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27-7.12 (m, 3H, H-Ar); 7.09-7.04 (m, 1H, H-Ar); 6.26 (d, 1H, *J* = 8.1 Hz, N*H*); 4.65 (dd, 1H, *J* = 2.7, 10.1 Hz, H-4´); 4.28-4.22 (m, 1H, H-2´); 3.76 (dd, 1H, *J* = 3.7, 11.0 Hz, H-1´A); 3.70 (dd, 1H, *J* = 4.4, 11.0 Hz, H-1´B); 2.58 (t, 2H, *J* = 7.5 Hz, H-1´´); 2.24 (t, 2H, *J* = 7.3 Hz, H-2); 1.95-1.55 (m, 2H, H-3´); 1.72-1.54 (m, H-3, 2H, H-2´´); 1.40-1.18 (m, 16H, H-4-H-11, 14H, H-3´´-H-9´´); 0.87 (t, 6H, *J* = 7.0 Hz, H-12, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.9 (C-1); 143.8, 143.2, 128.3, 127.4, 125.6, 122.8 (C-Ar); 70.6 (C-4´); 65.4 (C-1´); 48.9 (C-2´); 41.8 (C-3´); 36.8 (C-2); 36.1 (C-1´´); 31.9, 31.6, 29.7, 29.6, 29.5, 29.5, 29.4, 29.4, 29.0, 25.8, 22.7, 14.1 (C-3-C-12, C-2´´-C-10´´); IR (ATR): 3560, 2915, 2848, 1641, 1538, 1467, 1038, 1020, 705 cm^{-1}. Anal. Calcd. For $C_{32}H_{57}NO_3$: C 76.29, H 11.40, N 2.78. Found: C 76.54, H 11.53, N 2.80.

(1*R*,3*R*)-1-*N*-(3-(3-Hexylphenyl)-3-hydroxy-1-hydroxymethyl)dodecanamide (*anti*-14Ab). This product was prepared according to the general procedure; compound ***anti*-14Ab** (137 mg, 61%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 up to 2:3). TLC: R*f* = 0.28 (hexane/EtOAc 1:3, UV, $KMnO_4$); Mp = 42-43 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +10.5 (*c* 0.86, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27-7.12 (m, 3H, H-Ar); 7.09-7.04 (m, 1H, H-Ar); 6.28 (d, 1H, *J* = 8.1 Hz, N*H*); 4.65 (dd, 1H, *J* = 2.6, 10.1 Hz, H-4´); 4.27-4.19 (m, 1H, H-2´); 3.75 (dd, 1H, *J* = 3.6, 11.0 Hz, H-1´A); 3.69 (dd, 1H, *J* = 4.3, 11.0 Hz, H-1´B); 2.57 (t, 2H, *J* = 7.7 Hz, H-1´´); 2.23 (t, 2H, *J* = 7.3 Hz, H-2); 1.95-1.86 (m, 1H, H-3´A); 1.86-

1.75 (m, 1H, H-3´B); 1.70-1.54 (m, 2H, H-3, 2H, H-2´´); 1.39-1.22 (m, 16H, H-4-H-11, 6H, H-3´´-H-5´´); 0.88 (t, 6H, *J* = 7.0 Hz, H-12, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.9 (C-1); 143.8, 143.2, 128.3, 127.4, 125.6, 122.8 (C-Ar); 70.6 (C-4´); 65.3 (C-1´); 48.9 (C-2´); 41.8 (C-3´); 36.8 (C-2); 36.1 (C-1´´); 31.9, 31.7, 31.5, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1, 25.8, 22.7, 22.6, 14.1, 14.1 (C-3-C-12, C-2´´-C-6´´); IR (ATR): 3566, 3332, 2914, 2849, 1644, 1520, 1466, 1046, 1027, 720, 702 cm^{-1}. Anal. Calcd. For $C_{28}H_{49}NO_3$: C 75.12, H 11.03, N 3.13. Found: C 75.07, H 11.14, N 3.06.

(1*R*,3*R*)-1-*N*-(3-(4-Decylphenyl)-3-hydroxy-1-hydroxymethyl)dodecanamide (*anti*-14Ba). This product was prepared according to the general procedure; compound ***anti*-14Ba** (146 mg, 58%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 up to 1:3). TLC: R*f* = 0.37 (hexane/EtOAc 1:3, UV, $KMnO_4$); Mp = 88-89 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +11.9 (*c* 0.85, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, 2H, *J* = 8.0 Hz, H-Ar); 7.13 (d, 2H, *J* = 8.0 Hz, H-Ar); 6.27 (d, 1H, *J* = 8.0 Hz, N*H*); 4.65 (dd, 1H, *J* = 2.2, 10.3 Hz, H-4´); 4.26-4.20 (m, 1H, H-2´); 3.74 (dd, 1H, *J* = 3.4, 11.0 Hz, H-1´A); 3.69 (dd, 1H, *J* = 4.3, 11.0 Hz, H-1´B); 2.57 (t, 2H, *J* = 7.6 Hz, H-1´´); 2.22 (t, 2H, *J* = 7.5 Hz, H-2); 1.90 (ddd, 1H, *J* = 2.5, 10.1, 12.8 Hz, H-3´A); 1.82 (ddd, 1H, *J* = 3.8, 10.4, 14.1 Hz, H-3´B); 1.68-1.61 (m, 2H, H-3); 1.61-1.55 (m, 2H, H-2´´); 1.35-1.20 (m, 16H, H-4-H-11, 14H, H-3´´-H-9´´); 0.87 (t, 6H, *J* = 7.0 Hz, H-12, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.9 (C-1); 142.1, 141.1, 128.5, 125.5 (C-Ar); 70.4 (C-4´); 65.4 (C-1´); 49.0 (C-2´); 41.6 (C-3´); 36.8 (C-2); 35.6 (C-1´´); 31.9, 31.7, 31.4, 29.6, 29.5, 29.4, 29.3, 29.0, 25.9, 22.7, 14.1 (C-3-C-12, C-2´´-C-10´´); IR (ATR): 3560, 2911, 2848, 1645, 1538, 1467, 1038, 1020, 703 cm^{-1}. Anal. Calcd. For $C_{32}H_{57}NO_3$: C 76.29, H 11.40, N 2.78. Found: C 75.96, H 11.61, N 2.72.

(1*R*,3*R*)-1-*N*-(3-(4-Hexylphenyl)-3-hydroxy-1-hydroxymethyl)dodecanamide (*anti*-14Bb). This product was prepared according to the general procedure; compound ***anti*-14Bb** (148 mg, 66%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 up to 1:3). TLC: R*f* = 0.33 (hexane/EtOAc 1:3, UV, $KMnO_4$); Mp = 63-64 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = +8.1 (*c* 1,4, $CHCl_3$) (hexane/EtOAc = 1:1 – 1:3, R_f = 0.33); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.25 (d, 2H, *J* = 8.0 Hz, H-Ar); 7.13 (d, 2H, *J* = 8.0 Hz, H-Ar); 6.29 (d, 1H, *J* = 7.9 Hz, N*H*); 4.65 (dd, 1H, *J* = 2.3, 10.3 Hz, H-4´); 4.26-4.20 (m, 1H, H-2´); 3.74 (dd, 1H, *J* = 3.5, 11.0 Hz, H-1´A); 3.69 (dd, 1H, *J* = 4.3, 11.0 Hz, H-1´B); 2.57 (t, 2H, *J* = 7.7 Hz, H-1´´); 2.22 (t, 2H, *J* = 7.3 Hz, H-2); 1.89 (ddd, 1H, *J* = 2.6, 10.1, 12.9 Hz, H-3´A); 1.81 (ddd, 1H, *J* = 3.8, 10.4, 14.1 Hz, H-3´B); 1.68-1.61 (m, 2H, H-3); 1.61-1.55 (m, 2H, H-2´´); 1.35-1.24 (m, 16H, H-4-H-11, 6H, H-3´´-H-5´´); 0.88 (t, 6H, *J* = 7.0 Hz, H-12, H-6´´); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.8 (C-1); 142.1, 141.1, 128.4, 125.5 (C-Ar); 70.4 (C-4´); 65.4 (C-1´); 49.0 (C-2´); 41.6 (C-3´); 36.7 (C-2); 35.6 (C-1´´); 31.9, 31.7, 31.4, 29.6, 29.5, 29.3, 29.3, 29.3, 29.0, 25.8, 22.6, 22.6, 14.1, 14.0 (C-3-C-12, C-2´´-C-6´´); IR (ATR): 3558, 3292, 2919, 2851, 1640, 1615, 1517, 1044, 1027, 721, 580 cm^{-1}. Anal. Calcd. For $C_{28}H_{49}NO_3$: C 75.12, H 11.03, N 3.13. Found: C 74.69, H 11.33, N 3.26. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{28}H_{50}NO_3$: 448.37852; found: 448.37807.

(1*R*,3*S*)-1-*N*-(3-(3-Decylphenyl)-3-hydroxy-1-hydroxymethyl)dodecanamide (*syn*-14Aa). This product was prepared according to the general procedure; compound ***syn*-14Aa** (154 mg, 61%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 up to 1:2). TLC: R*f* = 0.30 (hexane/EtOAc 1:2, UV, $KMnO_4$); Mp = 50-52 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -22.3 (*c* 0.98, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28-7.21 (m, 1H,

H-Ar); 7.16-7.07 (m, 3H, H-Ar); 6.42 (d, 1H, *J* = 6.3 Hz, N*H*); 4.79 (dd, 1H, *J* = 2.7, 8.8 Hz, H-4´); 4.12-4.02 (m, 1H, H-2´); 3.74-3.60 (m, 2H, H-1´); 2.58 (t, 2H, *J* = 7.7 Hz, H-1´´); 2.17 (t, 2H, *J* = 7.5 Hz, H-2); 2.04 (ddd, 1H, *J* = 3.4, 5.3, 14.6 Hz, H-3´A); 1.94 (ddd, 1H, *J* = 7.1, 8.8, 14.7 Hz, H-3´B); 1.63-1.52 (m, 2H, H-3, 2H, H-2´´); 1.37-1.22 (m, 16H, H-4-H-11, 14H, H-3´´-H-9´´); 0.88 (t, 6H, *J* = 7.0 Hz, H-12, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.3 (C-1); 144.1, 143.5, 128.5, 127.9, 125.5, 122.8 (C-Ar); 72.2 (C-4´); 65.9 (C-1´); 50.9 (C-2´); 40.5 (C-3´); 36.8 (C-2); 36.0 (C-1´´); 31.9, 31.5, 29.6, 29.6, 29.5, 29.4, 29.3, 29.3, 29.3, 25.7, 22.7, 22.6, 14.1, (C-3-C-12, C-2´´-C-10´´); IR (ATR): 3332, 2913, 2849, 1638, 1528, 1470, 1271, 1010, 706 cm^{-1}. Anal. Calcd. For $C_{32}H_{57}NO_3$: C 76.29, H 11.40, N 2.78. Found: C 76.65, H 11.49, N 2.74.

(1*R*,3*S*)-1-*N*-(3-(3-Hexylphenyl)-3-hydroxy-1-hydroxymethyl)dodecanamide (*syn*-14Ab). This product was prepared according to the general procedure; compound ***syn*-14Ab** (135 mg, 60%) was obtained as a pale yellow oil after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 up to 1:3). TLC: R*f* = 0.33 (hexane/EtOAc 1:3, UV, $KMnO_4$); $[\alpha]_D^{20}$ = -27 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24-7.21 (m, 1H, H-Ar); 7.16-7.06 (m, 3H, H-Ar); 6.45 (d, 1H, *J* = 6.5 Hz, N*H*); 4.78 (dd, 1H, *J* = 3.2, 9.0 Hz, H-4´); 4.10-4.01 (m, 1H, H-2´); 3.69 (dd, 1H, *J* = 3.6, 10.6 Hz, H-1´A); 3.64 (dd, 1H, *J* = 2.9, 10.6 Hz, H-1´B); 2.58 (t, 2H, *J* = 7.7 Hz, H-1´´); 2.17 (t, 2H, *J* = 7.5 Hz, H-2); 2.04 (ddd, 1H, *J* = 3.4, 5.3, 14.6 Hz, H-3´A); 1.92 (ddd, 1H, *J* = 7.0, 8.9, 14.8 Hz, H-3´B); 1.63-1.55 (m, 2H, H-3, 2H, H-2´´); 1.37-1.22 (m, 16H, H-4-H-11, 6H, H-3´´-H-5´´); 0.88 (t, 6H, *J* = 7.0 Hz, H-12, H-6´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.3 (C-1); 144.1, 143.4, 128.5, 127.8, 125.5, 122.8 (C-Ar); 72.2 (C-4´); 65.9 (C-1´); 50.8 (C-2´); 40.6 (C-3´); 36.8 (C-2); 36.0 (C-1´´); 31.9, 31.7, 31.5, 29.6, 29.6, 29.5, 29.4, 29.3, 29.3, 29.1, 25.7, 22.7, 22.6, 14.1, 14.1 (C-3-C-12, C-2´´-C-6´´); IR (ATR): 3299, 2918, 2850, 1641, 1546, 1467, 1415, 1057, 702, 653 cm^{-1}. HRMS (ESI): m/z [M + H]+ calcd for $C_{28}H_{49}NO_3$: 447.37124; found: 448.37817.

(1*R*,3*S*)-1-*N*-(3-(4-Decylphenyl)-3-hydroxy-1-hydroxymethyl)dodecanamide (*syn*-14Ba). This product was prepared according to the general procedure; compound ***syn*-14Ba** (131 mg, 52%) was obtained as an off-white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 – 1:3). TLC: R*f* = 0.36 (hexane/EtOAc 1:3, UV, $KMnO_4$); Mp = 91-93 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -21.5 (*c* 0.76, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, 2H, *J* = 8.0 Hz, H-Ar); 7.13 (d, 2H, *J* = 8.0 Hz, H-Ar); 6.27 (d, 1H, *J* = 8.0 Hz, N*H*); 4.65 (dd, 1H, *J* = 2.5, 8.5 Hz, H-4´); 4.20-4.26 (m, 1H, H-2´); 3.74 (dd, 1H, *J* = 3.4, 11.0 Hz, H-1´A); 3.69 (dd, 1H, *J* = 4.3, 11.0 Hz, H-1´B); 2.57 (t, 2H, *J* = 7.6 Hz, H-1´´); 2.22 (t, 2H, *J* = 7.5 Hz, H-2); 1.90 (ddd, 1H, *J* = 2.5, 10.1, 12.8 Hz, H-3´A); 1.82 (ddd, 1H, *J* = 3.8, 10.4, 14.1 Hz, H-3´B); 1.61-1.61 (m, 2H, H-3); 1.61-1.55 (m, 2H, H-2´´); 1.35-1.20 (m, 16H, H-4-H-11, 14H, H-3´´-H-9´´); 0.87 (t, 6H, *J* = 7.0 Hz, H-12, H-10´´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.3 (C-1); 142.7, 141.4, 128.6, 125.5 (C-Ar); 72.0 (C-4´); 66.0 (C-1´); 50.8 (C-2´); 40.5 (C-3´); 36.9 (C-2); 35.6 (C-1´´); 31.9, 31.5, 31.4, 29.6, 29.6, 29.5, 29.5, 29.4, 29.4, 29.3, 25.7, 22.7, 14.1 (C-3-C-12, C-2´´-C-10´´); IR (ATR): 3292, 2916, 2848, 1642, 1548, 1468, 1057, 1039, 720, 654 cm^{-1}. Anal. Calcd. For $C_{32}H_{57}NO_3$: C 76.29, H 11.40, N 2.78. Found: C 76.35, H 11.55, N 2.72.

(1*R*,3*S*)-1-*N*-(3-(4-Hexylphenyl)-3-hydroxy-1-hydroxymethyl)dodecanamide (*syn*-14Bb). This product was prepared according to the general procedure; compound ***syn*-14Bb** (132 mg, 59%) was obtained as an off-white solid after purification by flash column chromatography, eluting

with hexane/EtOAc (1:1 – 1:3). TLC: R*f* = 0.31 (hexane/EtOAc 1:3, UV, $KMnO_4$); Mp = 91-93 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = -23.8 (*c* 0.59, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.23 (d, 2H, *J* = 8.0 Hz, H-Ar); 7.14 (d, 2H, *J* = 8.0 Hz, H-Ar); 6.46 (d, 1H, *J* = 5.6 Hz, N*H*); 4.78 (dd, 1H, *J* = 2.4, 8.6 Hz, H-4´); 4.03-4.08 (m, 1H, H-2´); 3.67 (dd, 1H, *J* = 4.5, 11.4 Hz, H-1´A); 3.64 (dd, 1H, *J* = 3.0, 11.3 Hz, H-1´B); 2.57 (t, 2H, *J* = 7.7 Hz, H-1´´); 2.16 (t, 2H, *J* = 7.5 Hz, H-2); 2.05-2.00 (m, 1H, H-3´A); 1.96-1.90 (m, 1H, H-3´B); 1.63-1.55 (m, 2H, H-3, 2H, H-2´´); 1.35-1.20 (m, 16H, H-4-H-11, 6H, H-3´´-H-5´´); 0.88 (t, 6H, *J* = 7.0 Hz, H-12, H-6´´); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.3 (C-1); 142.6, 141.4, 128.6, 125.5 (C-Ar); 72.0 (C-4´); 65.9 (C-1´); 50.8 (C-2´); 40.6 (C-3´); 36.9 (C-2); 35.6 (C-1´´); 31.9, 31.7, 31.5, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.0, 25.8, 22.7, 22.6, 14.1, 14.1 (C-3-C-12, C-2´´-C-6´´); IR (ATR): 3288, 2922, 2844, 1644, 1544, 1455, 1045, 1011, 721, 651 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{28}H_{50}NO_3$: 448.37852; found: 448.37837.

General procedure fot thiophene ring hydrodesulfurization (HDS)

A solution of ***anti*-21C** or ***syn*-22C** (1 mmol) in methanol (15 mL) was added to stirred suspension of activated Raney-Ni (5 wt eq.) in MeOH (4 mL). The catalyst was prepared from 2 g of commercial Raney-Ni suspension (Merck) by slow addition of solid NaOH (3.6 g) at 100 °C during 1 h with subsequent decantation with water (2 × 20 mL) and methanol (3 × 20 mL). The reaction mixture was stirred under atmosphere of hydrogen at room temperature for 24 h. After this time, the Raney-Ni was filtered off and washed with MeOH (3 × 10 mL). Solvent was removed under reduced pressure and the crude product was purified by flash column chromatography to yield the desired product ***anti*-23C** or ***syn*-24C**.

(2*R*,4*S*)-2-((*R*)-1-Phenylethylamino)-octadecane-1,4-diol (*anti*-23a). This product was prepared according to the general procedure; compound ***anti*-23a** (292 mg, 72%) was obtained as a white solid after purification by flash column chromatography, eluting with CH_2Cl_2/acetone/NH_3 (30:10:0.5). TLC: R*f* = 0.35 (CH_2Cl_2/acetone/NH_3 30:10:0.5, $KMnO_4$); Mp = 45-46 °C; $[\alpha]_D^{20}$ = +29 (*c* 0.18, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.36-7.31 (m, 4H, H-Ar); 7.28-7.24 (m, 1H, H-Ar); 3.93 (q, 1H, *J* = 6.5 Hz, H-1´); 3.76 (dd, 1H, *J* = 4.1, 10.8 Hz, H-1A); 3.73-3.67 (m, 1H, H-4); 3.47 (dd, 1H, *J* = 4.1, 10.8 Hz, H-1B); 2.80-2.75 (m, 1H, H-2); 1.66 (ddd, 1H, *J* = 2.8, 8.4, 14.1 Hz, H-3A); 1.41-1.36 (m, 1H, H-3B); 1.37 (d, 3H, *J* = 6.6 Hz, H-2´); 1.34-1.14 (m, 26H, H-5-H-17); 0.87 (t, 3H, *J* = 6.6 Hz, H-18); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 144.6, 128.6, 127.3, 127.0 (C-Ar); 69.9 (C-4); 63.1 (C-1); 55.3, 53.3 (C-2, C-1´); 37.7 (C-3); 37.2, 31.9, 29.7, 29.7, 29.7, 29.6, 29.4, 25.8, 22.7, 14.1 (C-5-C-18); 24.3 (C-2´); IR (ATR): 3278, 2922, 2856, 1461, 1453, 1256, 1110, 1060, 761, 702, 548 cm^{-1}. Anal. Calcd. For $C_{26}H_{47}NO_2$: C 76.98, H 11.68, N 3.45. Found: C 77.29, H 11.82, N 3.33.

(2*R*,4*S*)-2-((*R*)-1-Phenylethylamino)-tetradecane-1,4-diol (*anti*-23b). This product was prepared according to the general procedure; compound ***anti*-23b** (255 mg, 73%) was obtained as a colorless oil after purification by flash column chromatography, eluting with CH_2Cl_2/acetone/NH_3 (30:10:0.5). TLC: R*f* = 0.40 (CH_2Cl_2/acetone/NH_3 30:10:0.5, $KMnO_4$); $[\alpha]_D^{20}$ = +28 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36-7.22 (m, 5H, H-Ar); 3.92 (q, 1H, *J* = 6.6 Hz, H-1´); 3.76 (dd, 1H, *J* = 4.3, 10.8 Hz, H-1A); 3.73-3.65 (m, 1H, H-4); 3.46 (dd, 1H, *J* = 4.1, 10.8 Hz, H-1B); 2.79-2.75 (m, 1H, H-2); 1.66 (ddd, 1H, *J* = 3.1, 8.5, 14.4 Hz, H-3A); 1.41-1.35 (m, 1H, H-3B); 1.37 (d, 3H, *J* = 6.6 Hz, H-2´); 1.34-1.14 (m, 18H, H-5-H-13); 0.88 (t, 3H, *J* = 6.6 Hz, H-14); ^{13}C NMR

(75 MHz, $CDCl_3$): δ = 144.7, 128.6, 127.3, 127.0 (C-Ar); 69.9 (C-4); 63.2 (C-1); 55.3, 53.3 (C-2, C-1´); 37.9 (C-3); 37.2, 31.9, 29.7, 29.6, 29.4, 25.8, 22.7, 14.1 (C-5-C-14); 24.4 (C-2´); IR (ATR): 3288, 2921, 2852, 1466, 1453, 1113, 1061, 760, 700, 551 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{22}H_{40}NO_2$: 350.30536; found: 350.30485.

(2*R*,4*R*)-2-((*R*)-1-Phenylethylamino)-octadecane-1,4-diol (*syn*-24a). This product was prepared according to the general procedure; compound ***syn*-24a** (207 mg, 51%) was obtained as a white solid after purification by flash column chromatography, eluting with CH_2Cl_2/acetone/NH_3 (20:10:0.3). TLC: R*f* = 0.42 (CH_2Cl_2/acetone/NH_3 20:10:0.3, $KMnO_4$); Mp = 81-82 °C; $[\alpha]_D^{20}$ = +36.8 (*c* 0.75, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36-7.22 (m, 5H, H-Ar); 4.00 (q, 1H, *J* = 6.5 Hz, H-1´); 3.80 (dd, 1H, *J* = 4.0, 10.9 Hz, H-1A); 3.65-3.55 (m, 1H, H-4); 3.42 (dd, 1H, *J* = 2.3, 10.9 Hz, H-1B); 2.67-2.58 (m, 1H, H-2); 1.52-1.16 (m, 3H, H-2´, 2H, H-3, 26H, H-5-H-17); 0.87 (t, 3H, *J* = 6.6 Hz, H-18); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.3, 128.7, 127.3, 127.0 (C-Ar); 71.9 (C-4); 62.4 (C-1); 55.7, 54.8 (C-2, C-1´); 38.7 (C-3); 38.1, 31.9, 29.7, 29.4, 25.4, 22.7, 14.1 (C-5-C-18); 25.4 (C-2´); IR (ATR): 3226, 2911, 2844, 1456, 1322, 1189, 1111, 1035, 821, 761, 699, 556 cm^{-1}. Anal. Calcd. For $C_{26}H_{47}NO_2$: C 76.98, H 11.68, N 3.45. Found: C 77.35, H 11.85, N 3.29.

(2*R*,4*R*)-2-((*R*)-1-Phenylethylamino)-tetradecane-1,4-diol (*syn*-24b). This product was prepared according to the general procedure; compound ***syn*-24b** (217 mg, 62%) was obtained as a colorless oil after purification by flash column chromatography, eluting with CH_2Cl_2/acetone/NH_3 (30:10:0.5). TLC: R*f* = 0.38 (CH_2Cl_2/acetone/NH_3 30:10:0.5, $KMnO_4$); $[\alpha]_D^{20}$ = +37.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36-7.24 (m, 5H, H-Ar); 4.02 (q, 1H, *J* = 6.5 Hz, H-1´); 3.81 (dd, 1H, *J* = 4.0, 10.9 Hz, H-1A); 3.65-3.57 (m, 1H, H-4); 3.43 (dd, 1H, *J* = 2.2, 10.9 Hz, H-1B); 2.67-2.59 (m, 1H, H-2); 1.52-1.42 (m, 1H, H-3A, 2H, H-5); 1.37 (d, 3H, *J* = 6.5 Hz, H-2´); 1.34-1.22 (m, 1H, H-3B, 16H, H-6-H-13); 0.88 (t, 3H, *J* = 6.6 Hz, H-14); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.2, 128.7, 127.3, 127.0 (C-Ar); 72.0 (C-4); 62.4 (C-1); 55.8, 54.8 (C-2, C-1´); 38.7 (C-3); 38.1, 31.9, 29.8, 29.7, 29.4, 25.4, 22.7, 14.2 (C-5-C-14); 25.4 (C-2´); IR (ATR): 3236, 2917, 2899, 2847, 1469, 1371, 1116, 1044, 820, 766, 701, 549 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{22}H_{40}NO_2$: 350.30536; found: 350.30480.

General procedure for one-pot Pd-catalyzed *N*-debenzylation and acylation

The acetic acid (2 eq.) and subsequently 20% $Pd(OH)_2$/C (20 wt%) were added to the solution of aminodiols ***anti*-23a,b** or ***syn*-24a,b** (0.5 mmol) in methanol (50 mL). The reduction was carried out under 1.1 bar of H_2 pressure at 40 °C. When the reduction was completed (monitoring TLC), methanol was evaporated under reduced pressure. The residue was dissolved in dry THF (10 mL) and dodecanoic acid *N*-hydroxysuccinimide ester (**X=$C_{11}H_{23}CO_2$Su,** 1.2 eq.) was added. Reaction mixture was stirred 1-2 days and was monitored by TLC. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silicagel to give HPA-12 or its analogues.

(1*R*,3*S*)-1-*N*-(3-Hydroxy-1-hydroxymethyl-heptadecyl)dodecanamide (*anti*-15a). This product was prepared according to the general procedure; compound ***anti*-15a** (143 mg, 59%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 up to 1:3). TLC: R*f* = 0.32 (hexane/EtOAc 1:3, $KMnO_4$); Mp = 82-83 °C; $[\alpha]_D^{20}$ =

+5.7 (*c* 0.71, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$/DMSO-d_6 = 1/1): δ = 6.57 (d, 1H, *J* = 7.2 Hz, N*H*); 4.02-3.96 (m, 1H, H-2´); 3.56 (dd, 1H, *J* = 3.0, 11.1 Hz, H-1´A); 3.47 (dd, 1H, *J* = 4.0, 11.1 Hz, H-1´B); 3.34-3.39 (m, 1H, H-4´); 2.09 (t, 2H, *J* = 7.5 Hz, H-2); 1.56-1.47 (m, 1H, H-3´A, 2H, H-3); 1.40-1.33 (m, 1H, H-3´B); 1.31-1.10 (m, 16H, H-4-H-11, 26H, H-5´-H-17´); 0.75 (t, 6H, *J* = 6.6 Hz, H-12, H-18´); ^{13}C NMR (150 MHz, $CDCl_3$/DMSO-d_6 = 1/1): δ = 174.8 (C-1); 67.5 (C-4´); 64.9 (C-1´); 48.6 (C-2´); 40.0 (C-3´); 37.1, 36.6, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.3, 26.0, 25.9, 22.6, 14.1 (C-2-C-12, C-5´-C-18´); IR (ATR): 3287, 2922, 2849, 1645, 1543, 1455, 1044, 1022, 720, 651 cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{30}H_{62}NO_3$: 484.47242; found: 484.47233.

(1*R*,3*S*)-1-*N*-(3-Hydroxy-1-hydroxymethyl-tridecyl)dodecanamide (*anti*-15b). This product was prepared according to the general procedure; compound ***anti*-15b** (114 mg, 53%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 up to 1:4). TLC: R*f* = 0.35 (hexane/EtOAc 1:4, $KMnO_4$); Mp = 88-90 °C; $[\alpha]_D^{20}$ = +7.5 (*c* 0.67, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.20 (d, 1H, *J* = 8.3 Hz, N*H*); 4.23-4.11 (m, 1H, H-2´); 3.74 (dd, 1H, *J* = 3.6, 10.9 Hz, H-1´A); 3.66 (dd, 1H, *J* = 4.3. 10.9 Hz, H-1´B); 3.58-3.48 (m, 1H, H-4´); 2.22 (t, 2H, *J* = 7.6 Hz, H-2); 1.71-1.51 (m, 1H, H-3´A, 2H, H-4´); 1.52-1.38 (m, 1H, H-3´B, 2H, H-5´); 1.33-1.15 (m, 16H, H-4-H-11, 16H, H-6´-H-13´); 0.87 (t, 6H, *J* = 6.6 Hz, H-12, H-14´); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.8 (C-1); 67.9 (C-4´); 65.5 (C-1´); 48.5 (C-2´); 39.7 (C-3´); 37.2, 36.8, 31.9, 29.7, 29.7, 29.6, 29.4, 29.3, 26.0, 25.9, 22.7, 14.1 (C-2-C-12, C-5´-C-14´); IR (ATR): 3288, 2922, 2835, 1646, 1549, 1455, 1155, 1022, 1011, 718, 651 cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{54}NO_3$: 428.40982; found: 428.40941.

(1*R*,3*R*)-1-*N*-(3-Hydroxy-1-hydroxymethyl-heptadecyl)dodecanamide (*syn*-15a). This product was prepared according to the general procedure; compound ***syn*-15a** (145 mg, 60%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:1 up to 1:3). TLC: R*f* = 0.31 (hexane/EtOAc 1:3, $KMnO_4$); Mp = 85-86 °C; $[\alpha]_D^{20}$ = -3.9 (*c* 0.36, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.45 (d, 1H, *J* = 6.5 Hz, N*H*); 4.06-4.01 (m, 1H, H-2´); 3.75-3.70 (m, 1H, H-4´); 3.69-3.63 (m, 2H, H-1´); 2.19 (t, 2H, *J* = 7.3 Hz, H-2); 1.87 (ddd, 1H, *J* = 2.0, 5.8, 14.6 Hz, H-3´A); 1.64-1.59 (m, 2H, H-3); 1.53 (ddd, 1H, *J* = 6.6, 9.4, 15.0 Hz, H-3´B); 1.49-1.44 (m, 2H, H-5´); 1.41-1.35 (m, 2H, H-6´); 1.33-1.24 (m, 16H, H-4-H-11, 22H, H-7´-H-17´); 0.88 (t, 6H, *J* = 6.6 Hz, H-12, H-18´); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.2 (C-1); 69.7 (C-4´); 65.9 (C-1´); 50.7 (C-2´); 38.7 (C-3´); 38.2, 36.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.3, 29.3, 25.8, 25.5, 22.7, 14.1 (C-2-C-12, C-5´-C-18´); IR (ATR): 3287, 2922, 2844, 1652, 1548, 1455, 1131, 1061, 728, 600 cm^{-1}. Anal. Calcd. For $C_{30}H_{61}NO_3$: C 74.48, H 12.71, N 2.90. Found: C 74.15, H 12.59, N 2.95.

(1*R*,3*R*)-1-*N*-(3-Hydroxy-1-hydroxymethyl-tridecyl)dodecanamide (*syn*-15b). This product was prepared according to the general procedure; compound ***syn*-15b** (129 mg, 60%) was obtained as a white solid after purification by flash column chromatography, eluting with hexane/EtOAc (1:2 up to 1:4). TLC: R*f* = 0.34 (hexane/EtOAc 1:4, $KMnO_4$); 60%; Mp = 67-69 °C; $[\alpha]_D^{20}$ = -6.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.44 (d, 1H, *J* = 6.4 Hz, N*H*); 4.08-4.00 (m, 1H, H-2´); 3.79-3.69 (m, 1H, H-4´); 3.69-3.61 (m, 2H, H-1´); 2.20 (t, 2H, *J* = 7.2 Hz, H-2); 1.89 (ddd, 1H, *J* = 1.9, 5.7, 14.6 Hz, H-3´A); 1.70-1.40 (m, 1H, H-3´B, 2H, H-3, 2H, H-5´, 2H, H-6´); 1.39-1.20 (m, 16H, H-4-H-11, 14H, H-7´-H-13´); 0.88 (t, 6H, *J* = 6.6 Hz, H-12, H-14´); ^{13}C NMR (150 MHz, $CDCl_3$): δ =

174.1 (C-1); 69.8 (C-4´); 66.0 (C-1´); 50.8 (C-2´); 38.7 (C-3´); 38.2, 36.9, 31.9, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 25.8, 25.5, 22.7, 14.1 (C-2-C-12, C-5´-C-14´); IR (ATR): 3288, 2918, 2847, 1641, 1561, 1468, 1132, 1066, 720, 601 cm^{-1}. Anal. Calcd. For $C_{26}H_{53}NO_3$: C 73.01, H 12.49, N 3.27. Found: C 72.79, H 12.63, N 3.22.

General procedure for one-pot procedure exemplified by the preparation of the product *syn*-15a.

(1*R*,3*R*)-1-*N*-(3-Hydroxy-1-hydroxymethyl-heptadecyl)dodecanamide (*syn*-15a). A solution of **(**syn-**22Ca**, 0.491 mmol, 0.21 g) in methanol (8 mL) was added to stirred suspension of activated Raney-Ni (10 wt eq., 2.10 g) in MeOH (2 mL). The catalyst was prepared from 2 g of commercial Raney-Ni via the above described procedure. The reaction mixture was stirred under atmosphere of hydrogen at RT for 60 h. After this time, the Raney-Ni was filtered off and washed with MeOH (3 × 5 mL). Solvent was evaporated under reduced pressure. The residue was dissolved in THF (5 mL) and dodecanoic acid *N*-hydroxysuccinimide ester (**X**=$C_{11}H_{23}CO_2Su$, 0.588 mmol, 0.175 g, 1.2 eq.) was added. The reaction mixture was stirred at room temperature for 72 h. Solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography to yield the expected product syn-**15a** (0.086 g, 36%) as a white solid. Mp = 86-88 ºC; $[\alpha]_D^{20}$ = -3.9 (*c* 0.36, MeOH). All the other characteristics data are identical to those reported earlier.

Experimental Section/Biology

Binding assays

Materials.

Human COL4A3ABP recombinant histidine-tagged protein fragment (START) (Product #ab95897) was obtained from Abcam. TALON® metal affinity resin was from Clontech. Fluorescence spectra were recorded with a Carey Eclipse spectrofluorometer equipped with a xenon lamp source and a Hamamatsu R928 photomultiplier tube. Fluorescent ceramide probe (*N*-((2*S*,3*R*,*E*)-1,3-Dihydroxy-18-((7-nitrobenzo[*c*][1,2,5]oxadiazol-4-yl)amino)octadec-4-en-2-yl)palmitamide) was synthesized according to ref.[1]

Fluorescence binding assays [1]

The His-tagged recombinant START domain of CERT protein (200 pmol, 6.5 mg, 13 µL of 0.5mg/mL commercial solution) was dissolved in TBS (46 µL) in an Eppendorf tube. The HPA-12 stereoisomer (200 pmol, 2 µL of 0.1 mM ethanolic solution) and TBS (30µL) was added to the tube and the mixture was incubated at 37 °C for 30 minutes. An equimolar amount of fluorescent ceramide probe (200pmol, 2 µL of 0.1mM ethanolic solution) was then added and after 30 minutes of incubation, the resulting complex was retained on a TALON® metal affinity resin (40 µL of 50% (v/v) preequilibrated with wash buffer), and incubated for 10 min at room

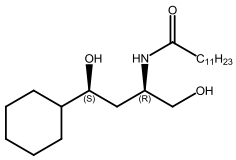
[1] S. Combemale, C. Santos, F. Rodriguez, V. Garcia, C. Galaup, C. Frongia, V. Lobjois, T. Levade, C. Baudoin-Dehoux, S. Ballereau, Y. Genisson, *RSC Advances*, **2013**, *3*, 18970-18984.

temperature with rotary shaking. After centrifugation (14000 rpm, 30 s), the supernatant was collected as the "free fraction". For washing, the resin was suspended in a 10mM imidazole solution in TBS (75 µL), and after centrifugation (14000 rpm, 30 s); the supernatant was collected as the "wash fraction 1". This washing step was repeated to give the "wash fraction 2". To liberate the protein bound fraction to the TALON® resin, the resin was suspended in a 250mM imidazole solution in TBS (75 µL) and incubated for 5 minutes at room temperature. After centrifugation (14000 rpm, 30 s), the supernatant was collected as the "bound fraction". A solution of chloroform/methanol (1:2 (v/v), 3.75-fold volume of each fraction) was then added to each collected fraction. Finally, to retrieve residual fluorophores non-specifically bound to the resin in the tube, TBS (85µL) and chloroform/methanol (1:2 (v/v), 375µL) were added to the resin in the tube, mixed, and centrifuged (14000rpm, 30s). The supernatant was collected as the "residual fraction". For each fraction, the fluorescence was quantified with a Cary Eclipse spectrofluorimeter (NBD: excitation at 465 nm, emission at 530 nm).

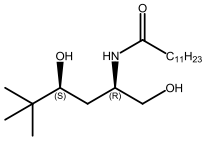
Ratio between the fluorescence intensity of this "bound fraction" and that of gathered washing fractions ("unbound fraction") allows quantification of the probe binding to the START domain of CERT. Probe shifting results in a reduction of fluorescence intensity in this "bound fraction" in comparison to a blank experiment without competitor and compound binding was quantified by this percentage of fluorescence diminution.

Results

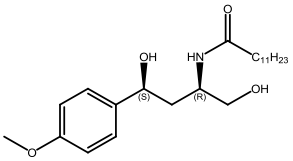
Binding assays of ceramide fluorescent probe to START domain in presence of ligand candidates **AD754, AD762** and **SynAnHPA-12**.



AD754



AD762



SynAnHPA-12

	Fluorescent probe	(1*R*,3*S*)-HPA12	AD754	AD762	SynAnHPA-12
% Unbound Fluo	55.8	87.4	85.8	75.9	90.9
% Bound Fluo	44.2	12.6	14.2	24.1	9.1
SD	0.9	4.5	2.8	3.1	0.6
Fluo probe bound (% of control)	-	28.5	32.2	54.6	20.6

Table 1: Binding assays of a Cer fluorescent probe to START domain in the presence of competitors.

The first line (% unbound Fluo) is the part of fluorescence in the "unbound fraction" in percentage, the second line (% bound fluo) is the part in percent of fluorescence in the "bound fraction". Results are means from triplicate experiments and standard deviation (SD) is indicated. The last line is the probe fluorescence in the bound fraction as a percentage of the maximum value recorded in a control experiment without competitor.

TR-FRET binding assay [2]

Materials

Streptavidin-d2 conjugate (Product #610SADLA) and Europium cryptate-labeled anti-Histidine monoclonal antibody (Product #61HISKLA) were obtained from Cisbio Bioassays® (Codolet, France). Human COL4A3ABP recombinant histidine-tagged protein fragment (START) (Product #ab95897) was obtained from Abcam. Biotinylated ceramide probe (BioCer, or *N*-((2*S*,3*R*,*E*)-1,3-dihydroxy-18-(5-(2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)pentanamido)octadec-4-en-2-yl)palmitamide) was synthesized according to ref.[1]

HTRF assay

8 µl of 5% of DMSO or compounds and a 1µM solution containing the START were incubated 30 minutes at 37 °C. 2 µL of 1 µM Biotinylated ceramide solution was added in 384 Well Low Volume White Round Bottom Polystyrene NBS™ Microplate (Product #*3673 from Corning*®). After 30 minutes to 37 °C streptavidin-d2 and monoclonal anti-hist antibody labelled with Europium cryptate were added in detection buffer as recommended by manufacturer. After 15 h of incubation at room temperature, the time-resolved fluorescence was measured using an Envision® plate reader (Perkin Elmer; λ_{ex} = 320 nm, λ_{em} = 590 and 665 nm; 60 µsec delay time). The donor fluorescence emission was measured at 590 nm instead of 620 nm in accordance with Envision apparatus and Cisbio recommendation. The HTRF readout was calculated as two wavelengths signal ratio: (665 nm/590 nm) x 10^4. FRET signal was defined as (HTRF compound ratio - HTRF negative ratio)/ HTRF blank ratio. HTRF negative ratio was (665 nm/590 nm) x 10^4 of well containing streptavidin-d2 and anti-Hist monoclonal antibody labelled with Europium cryptate. HTRF blank ratio was (665 nm/590 nm) x 10^4 of well containing anti-Hist monoclonal antibody labelled with Europium cryptate.

Data handling

Positive FRET signals were performed by dispensing DMSO 5%, so no inhibition of interaction was done. This maximal signal value obtained was set to 0 % inhibition.

Percentage of inhibition was calculated using ***eq. 1***:

% inhib. = 100-(100* FRET signal compound) x FRET signal without compound ratio.

The Z' factor was calculated according to Zhang *et al*.[3] with at least 32 assays for each control:

$$Z' = 1 - \frac{(3\,SD\ positive\ control + 3\,SD\ negative\ control)}{(mean\ positive\ control - mean\ negative\ control)} \qquad \textit{eq. 1}$$

All curves fits of sigmoïdal dose-response curves were performed with Prism 3.0 (Graphpad Software, San Diego, CA).

EC50 determination by TR-FRET

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[2] L. Fleury, C. Faux, C. Santos, S. Ballereau, Y. Génisson, F. Ausseil, *J. Biomol. Screen.*, **2015**, *20*, 779-787.

[3] Zhang, J. H.; Chung, T. D.; Oldenburg, K. R. *J. Biomol. Screen.* **1999,** *4*, 67-73.

The data obtained from the doses curve responses for HPA analogues were treated with Prism 3.0 (Graphpad Software, San Diego, CA). Curve fits of sigmoïdal dose-response curves allowed the determination of EC_{50} for each analog.

Compound	EC_{50} (M)	EC_{50} (nM)	R^2
***Syn*-HPA-12**	4.10E-06	4100	0.9897
***Anti*-HPA-12**	2.25E-05	22500	0.9899
***Syn*-14Aa**	3.24E-08	32.4	0.9571
***Anti*-14Aa**	6.74E-07	674	0.9607
***Syn*-14Ab**	1.49E-09	1.49	0.9868
***Anti*-14Ab**	1.23E-07	123	0.9773
***Syn*-14Ba**	4.18E-08	41.8	0.9175
***Anti*-14Ba**	7.28E-07	728	0.7654
***Syn*-14Bb**	8.49E-08	84.9	0.9334
***Anti*-14Bb**	3.17E-07	317	0.9426
***Syn*-15b**	6.32E-08	63.2	0.9825
***Anti*-15b**	1.18E-07	118	0.9874

Table-2: EC_{50} and R squared values for HPA analogs determined by TR-FRET.

Molecular graphics, molecular docking

Molecular graphics and structural studies

Protein molecular structures were generated using UCSF Chimera 1.8.1, UCSF Chimera is developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco (supported by the NIGMS P41-GM103311). Protein structure used in this paper (2E3P) was structurally aligned with structure 2E3N set as reference using UCSF Chimera/Matchmaker.

The protein structures in the reference space (2E3N) were prepared (structures check, rotamers, hydrogenation) using Accelrys Discovery Studio Visualizer (Accelrys Software Inc., Discovery Studio Modeling Environment, Release 4.0, San Diego: Accelrys Software Inc., 2013, http://accelrys.com/) and UCSF Chimera.

The new ligand structures were sketched using ChemAxon Marvin 5.3.2 (2010, ChemAxon, http://www.chemaxon.com). The co-crystallized ligand structures were extracted from protein structures using SciTE text editor and Accelrys Discovery Studio Visualizer. The ligands were prepared (hybridization, hydrogenation, some geometry optimizations, 3D sketching) and aligned (center of mass) with co-crystallized ligands in the previously defined reference space using Discovery Studio Visualizer (DSV). The ligands were merged in libraries encoded with various chemical or tabular formats using DSV or in-house software. The libraries were checked using ChemAxon Marvin and eventually corrected using previous cited software.

Docking protocols

Molecular modelling (docking, scoring) was carried with Molegro Virtual Docker 6 (MVD) software (http://www.clcbio.com).

The structure 2E3P (chain A: 2E3Pa) was chosen for molecular docking with a search space of 15 Å radius (centered in the CERT binding cavity).

Ligands and residues of binding pocket were set flexible. According to the structural study, 42 residues were defined for flexible docking: ALA 475, ALA 572, ALA 521, ALA 555, ALA 563, ARG 442, ARG 471, ARG 478, ARG 574, ASN 504, GLN 467, GLN 477, GLU 446, GLU 575, HIS 469, ILE 449, ILE 465, ILE 523, LEU 568, LYS 470, LYS 578, PHE 436, PHE 579, PRO 474, PRO 559, PRO 564, SER 476, THR 447, THR 448, THR 468, TRP 445, TRP 473, TRP 562, TYR 482, TYR 553, TYR 576, VAL 472, VAL 480, VAL 525, VAL 557, VAL 567, VAL 571. A tolerance of 0.99, a flexibility of 0.90 and softened potentials were used during docking. Values of 2000 steps (lateral chains of residues) and 2000 steps (backbone) were used for final minimization (default values).

No water molecules were taken in account in the paper.

Moldock[4]was used as search function with a grid resolution of 0.20 Å. Moldock SE was used as docking optimizer with a population size of 200 (other parameters set as default) and 5000 steps of calculation by run. Tabu clustering was used in order to rank the poses. For each ligand, a set of 20 poses per run was generated, using a RMSD threshold of 2.0 Å and Energy penalty of 100 (default values) as clustering parameters.

A template model was used[5] with a grid resolution of 0.20 Å and a strength of 500 (default value). This template model was derived from structural studies. Polar heads of ceramides/HPAs have very similar conformations and positions in CERT's binding pocket; this is also the case for the overall trajectory of hydrophobic chains (structural alignments of CERT's protein structures in the reference space).

Using these structural data, template centers were defined on a basis of structurally aligned atoms of same chemical features. Then, 3 similarity groups were defined: (i) a steric group of 19 atoms (1.8 Å radius, strength = 0.5); (ii) a hydrogen donor group of 3 atoms (1.8 Å radius, strength = 3) and (iii) a hydrogen acceptor group of 3 atoms (1.8 Å radius, strength = 3).

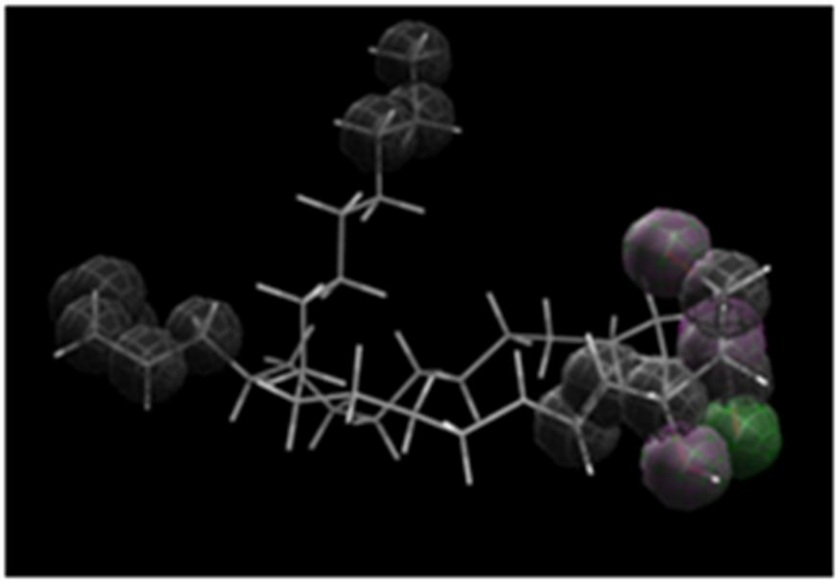


Figure 1 – Definition of docking templates

[4] R. Thomsen, M.H. Christensen. *J. Med. Chem.* **2006**, *49*, 3315-3321.

[5] C. Santos, F. Rogriguez, V. Garcia, D. Berkeš, A. Daïch, L. Levade, C. Baudoin-Dehoux, S. Ballereau, Y. Génisson, *ChemBioChem* **2014**, *15*, 2522-2528.

Docking results

Docking poses were analyzed using Molegro Virtual Docker and Molegro Data Modeler software (MDM).

After docking, the results issued from various protocols and docking templates were not merged and all poses were checked individually using MVD/MDM features.

A filter was then applied on these ensembles, using 3 rules: i) A set of descriptors (Moldock, Rerank) was chosen, and the poses corresponding to the 10 best values, for each descriptor, were retained, giving a 10 desc ensemble by descriptor. ii) In each 10 desc ensemble, the so called 'conform' poses were selected.

A 'conform' pose is defined by superposition of some ligands groups of polar head with their counterparts of ceramide/HPA-13. Ligand groups checked were: amide group, primary and secondary alcohols groups. iii) The pose which exhibits the maximum number of best values of descriptors, was retained for further analysis.

For the best poses of each compound, some descriptors issued from docking protocol are reported in following table.

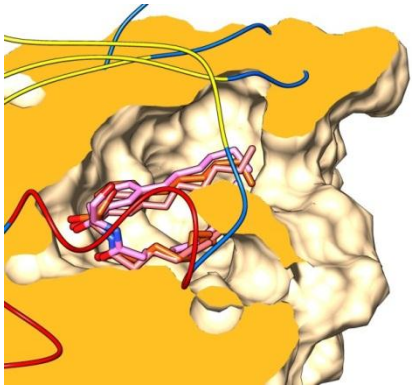
Name	Moldock Score	HBond	Rerank Score	LE1	LE3	MW	Heavy Atoms
Syn-HPA-12	-149.681	-15.1339	-115.417	-5.75695	-4.43913	363.534	26
Anti-HPA-12	-153.891	-10.3748	-121.602	-5.91887	-4.67702	363.534	26
Syn-**14Aa**	-190.276	-12.5	-132.213	-5.28544	-3.67257	503.8	36
Anti-**14Aa**	-199.257	-11.5942	-152.717	-5.5349	-4.24214	503.8	36
Syn-**14Ab**	-188.581	-14.6496	-141.576	-5.89317	-4.42425	447.694	32
Anti-**14Ab**	-170.583	-9,07174	-116.255	-5.33072	-3.63296	447.694	32
Syn-**14Ba**	-207.049	-10.1426	-156.418	-5.75135	-4.34493	503.8	36
Anti-**14Ba**	-188.569	-9.65318	-142.99	-5.23802	-3.97193	503.8	36
Syn-**14Bb**	-190.935	-15.7128	-139.07	-5.9667	-4.34593	447.694	32
Anti-**14Bb**	-164.538	-9.07403	-124.072	-5.14182	-3.87725	447.694	32
Syn-**15b**	-164.641	-18.4239	-122.279	-5.48803	-4.07597	427.704	30
Anti-**15b**	-180.658	-10.7279	-135.015	-6.02192	-4.5005	427.704	30

Table 3: ***Docking data***

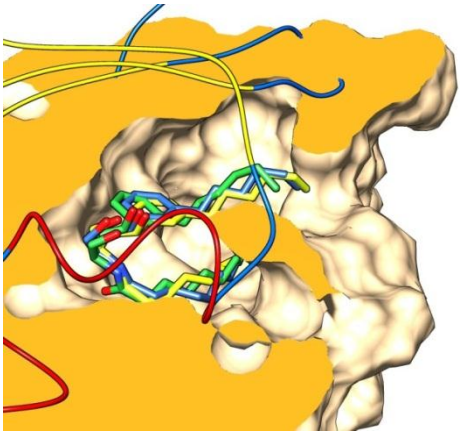
The values are given for best docking poses of compounds used in this study.

MW is the molecular weight and *Heavy atoms* count is the number of heavy atoms (C, N, O) of each ligand. The other scores (*Moldock*, *HBond*, *LE1*, *LE3*, *Rerank*) are values obtained after docking and final minimization. The *Moldock* score (arbitrary units) is a value related to the total Energy. The *Rerank* score (arbitrary units) is a different weighting of terms included Moldock equation. *HBond* (arbitrary units) is a value related Hydrogen bonding energy. The values of *LE1* and *LE3* are *Moldock* and *Rerank* scores values divided by the number of heavy atoms.

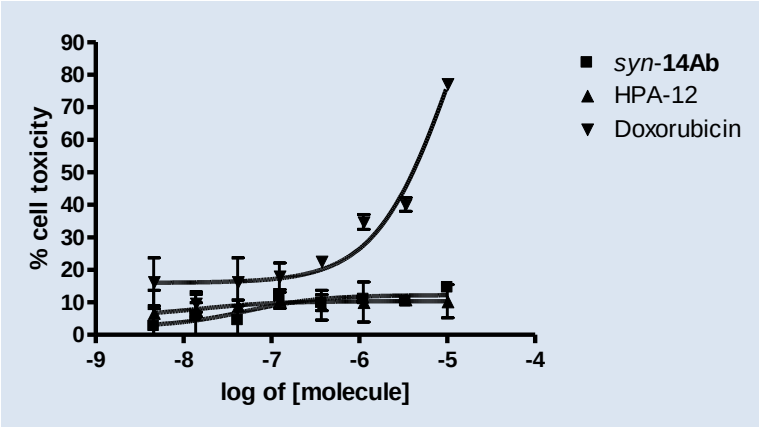
Superposition of the three calculated best poses of compound Anti-***14Ab***



Superposition of the three calculated best poses of compound Syn-***14Ab***

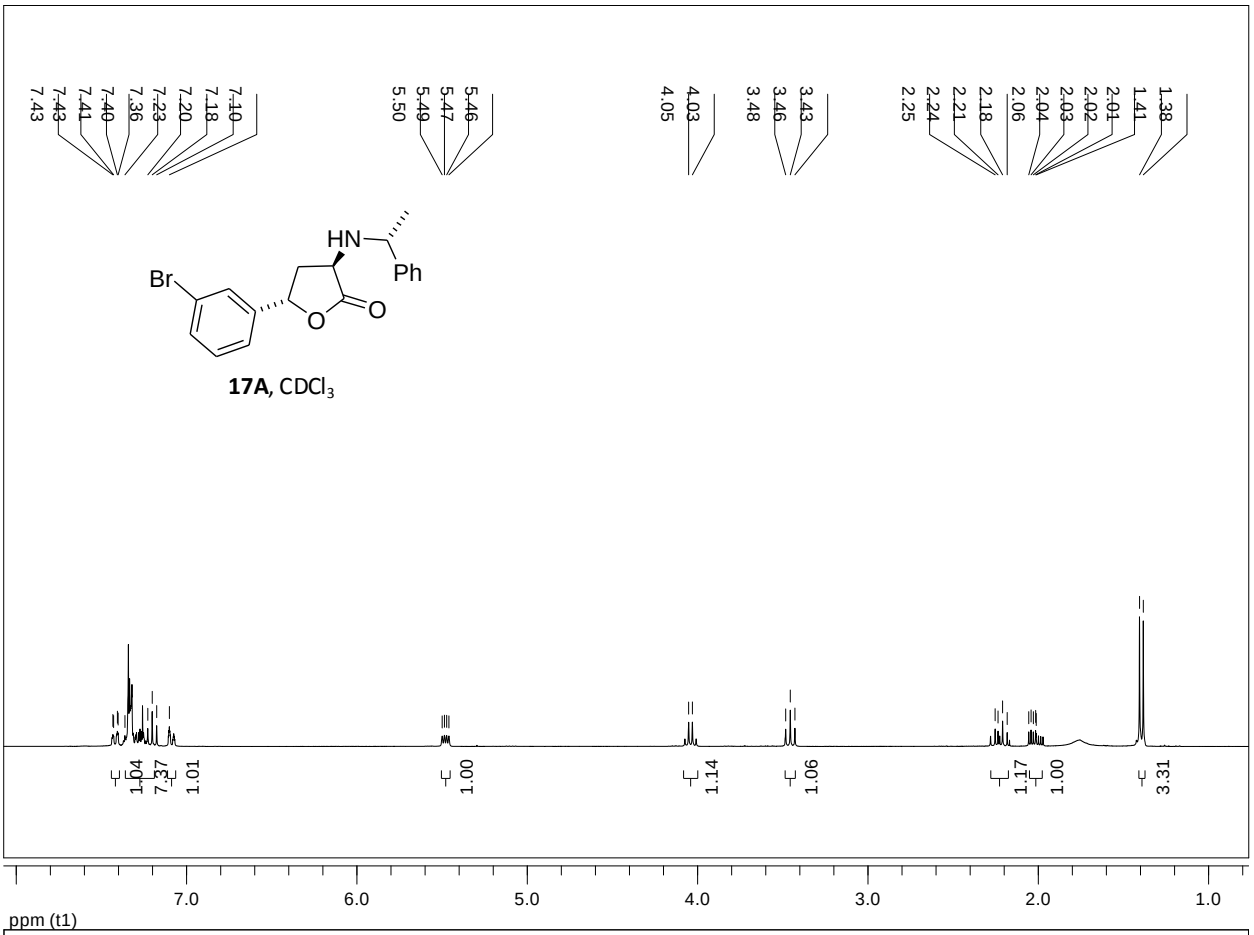


Primary cells cytotoxicity for compounds HPA-12 and *Syn*-14Ab

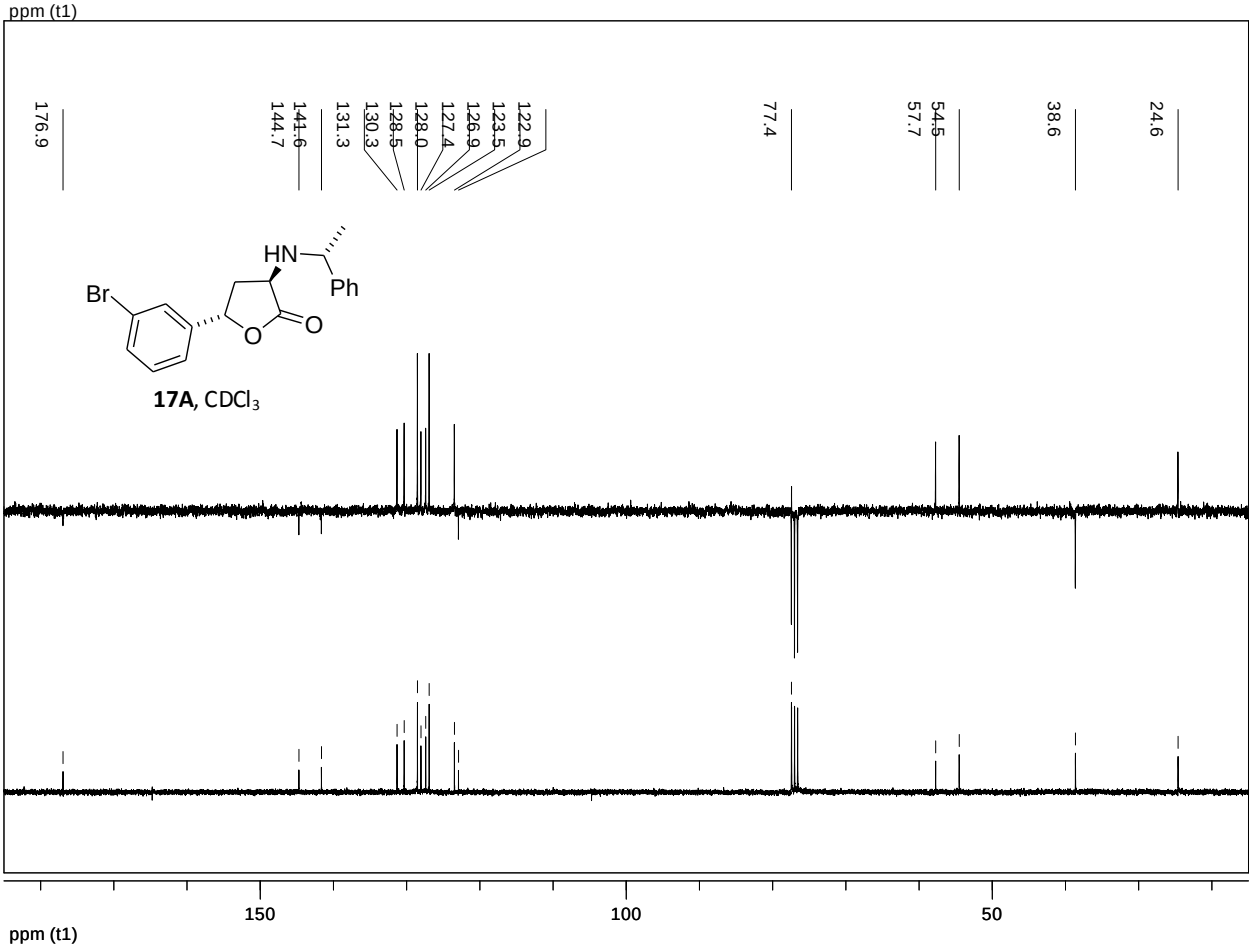


Legend : *Primary cells cytotoxicity:* human fibroblastes cells were obtained from donation of Thierry Levade's laboratory (CRCT, Toulouse, France) and cultivated in DMEM medium (Gibco® GlutaMAX™, ThermoFisher, France) containing l-D-glutamine and supplemented with 10 % of fetal calf serum (Lonza, France), at 37 °C and under 5 % CO_2. Cells (2×10^4) were seeded at day 0 in a 96-well plate. Solutions of test compound, stored at −20 °C as a 10^{-2} M stock solution in 100 % DMSO, were freshly prepared by dilution on day 1 in DMEM medium. Cells were treated in triplicate with test compound solutions at a dose range from 4.7 nM to 10 µM. Cell viability was assessed using the ATPLite kit (ATPlite 1step Luminescence Assay System, ref: 3016739, PerkinElmer), following the manufacturer's instructions at day 3. Raw data were analyzed with Prism 4.03.

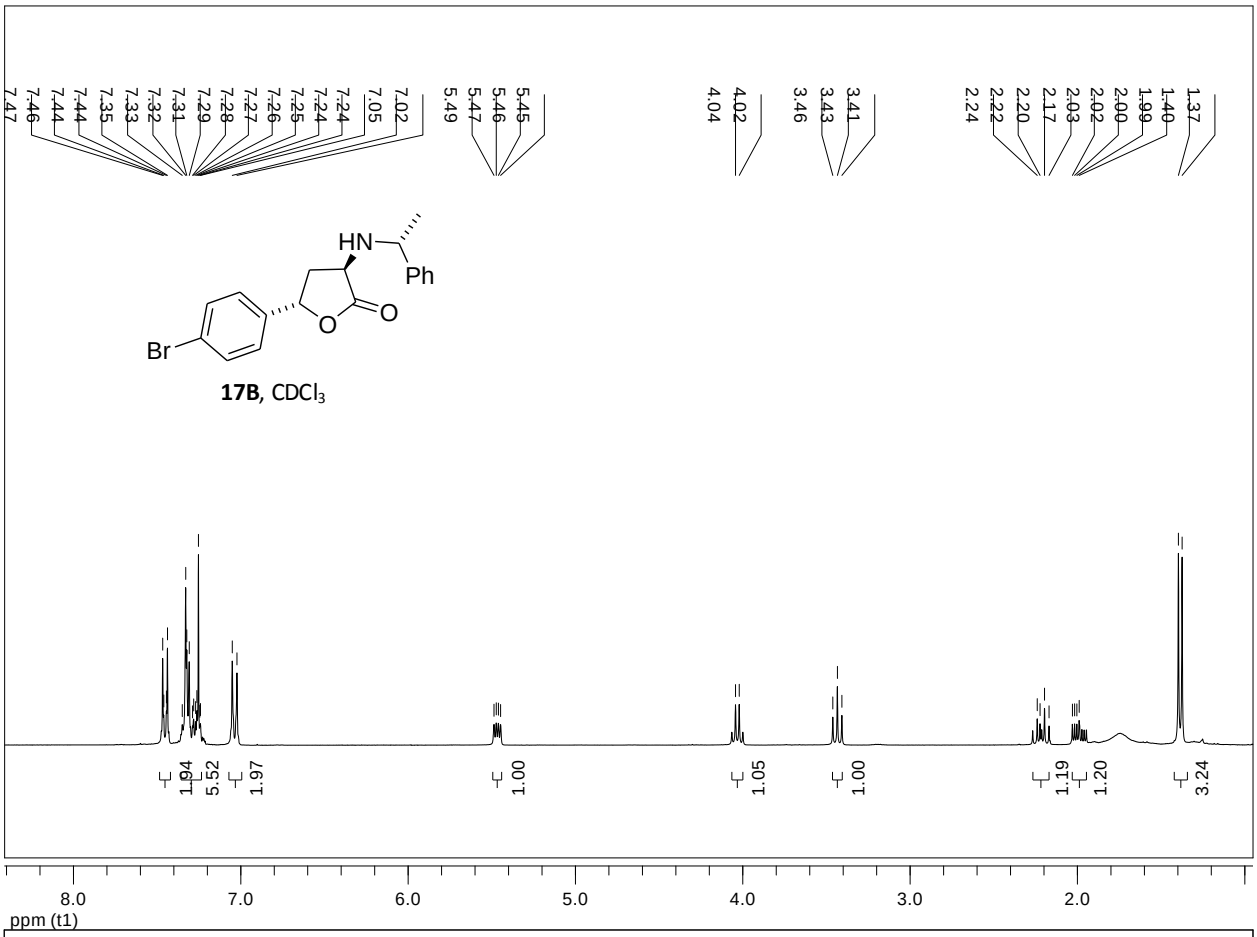
NMR Spectra of the all new compounds



17A, $CDCl_3$



17A, $CDCl_3$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7.27
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7.24
7.24
7.05
7.02
5.49
5.47
5.46
5.45
4.04
4.02
3.46
3.43
3.41
2.24
2.22
2.20
2.17
2.03
2.02
2.00
1.99
1.40
1.37
HN
Ph
O
O
Br
17B, CDCl3
1.94
2.52
1.97
1.00
1.05
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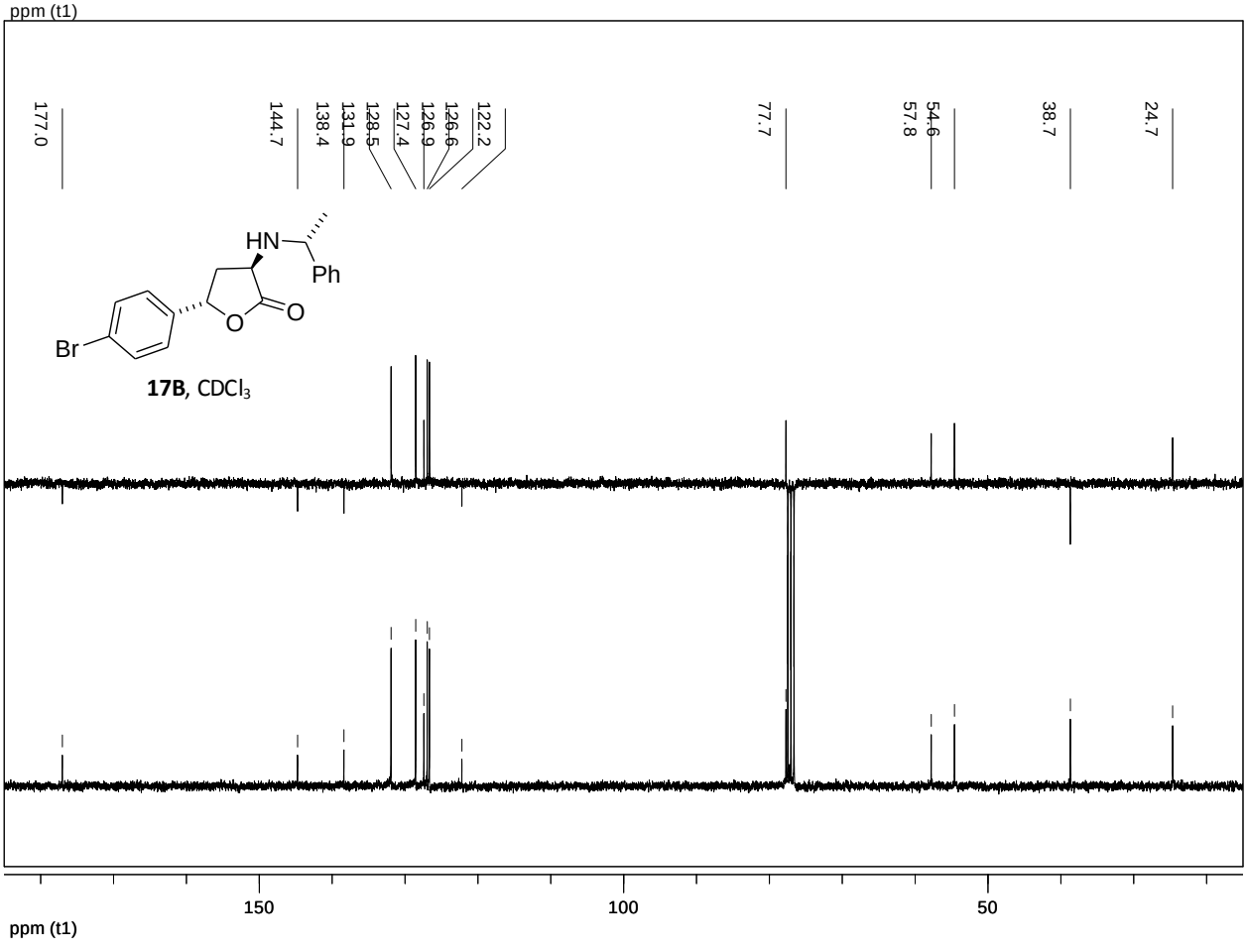
4.0
3.0
2.0
ppm (t1)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131.9
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127.4
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126.6
122.2
77.7
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24.7
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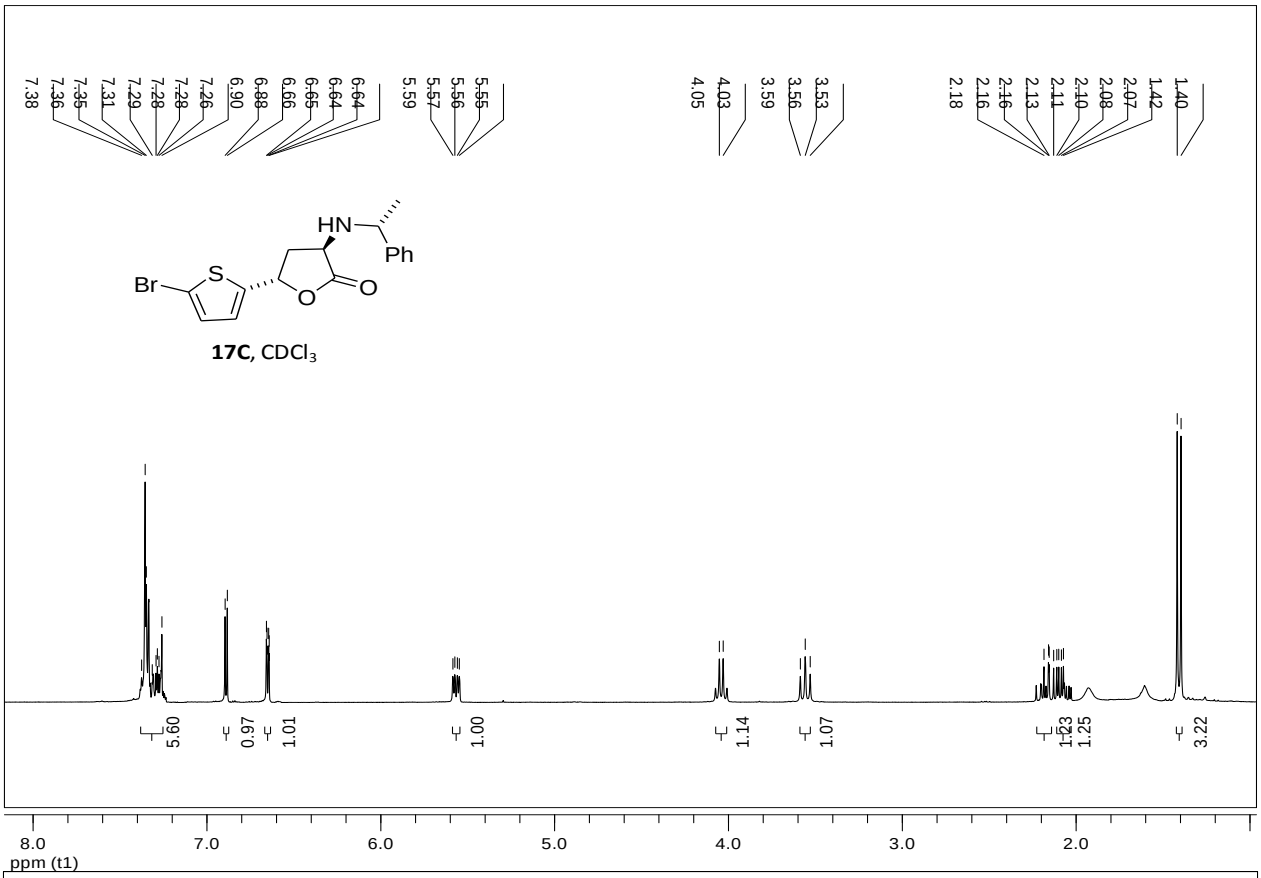
Ph
O
O
Br
17B, CDCl3
150
100
50
ppm (t1)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2.11
2.10
2.08
2.07
1.42
1.40
HN
Ph
Br
S
O
O
17C, CDCl3
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1.01
1.00
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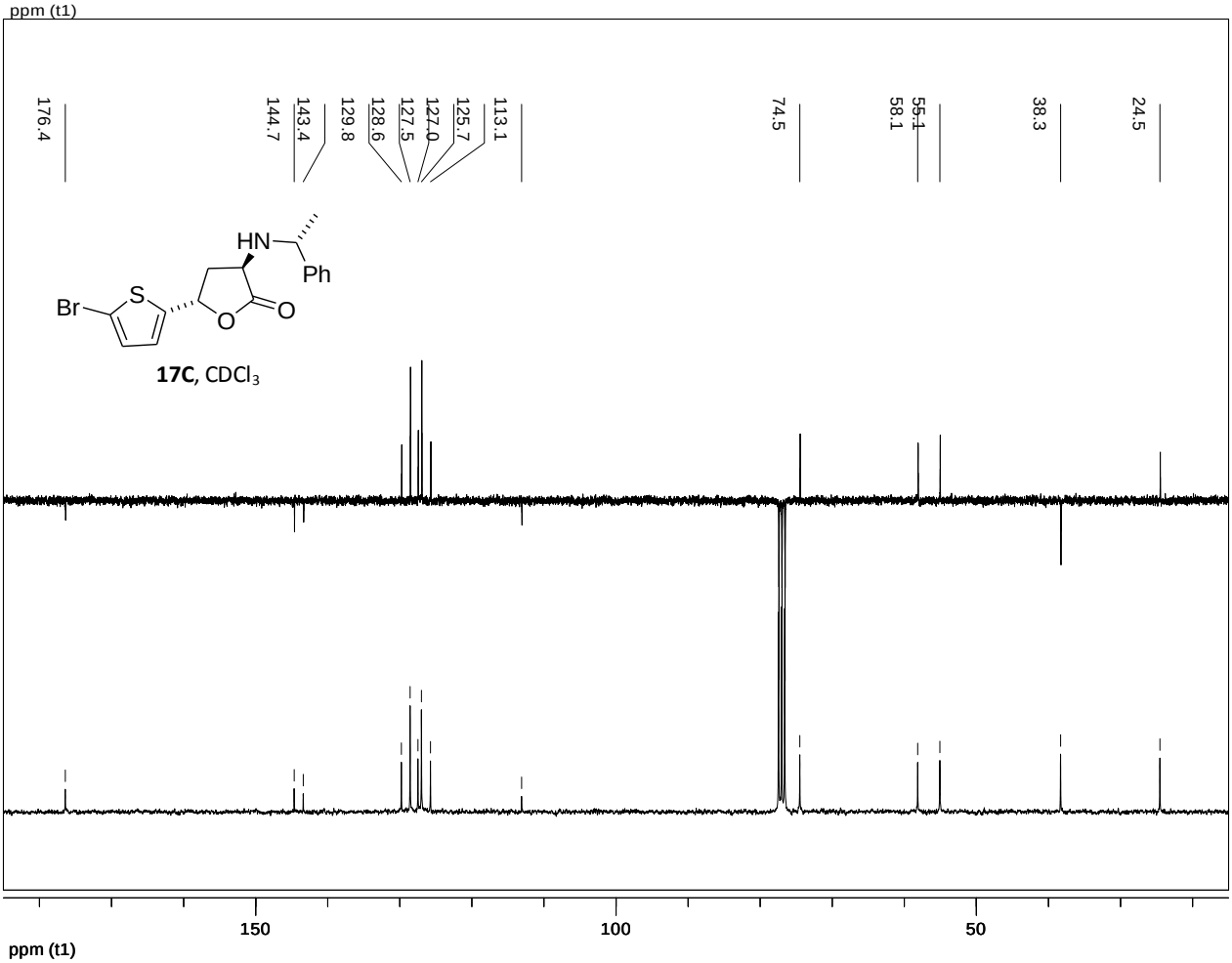
4.0
3.0
2.0
ppm (t1)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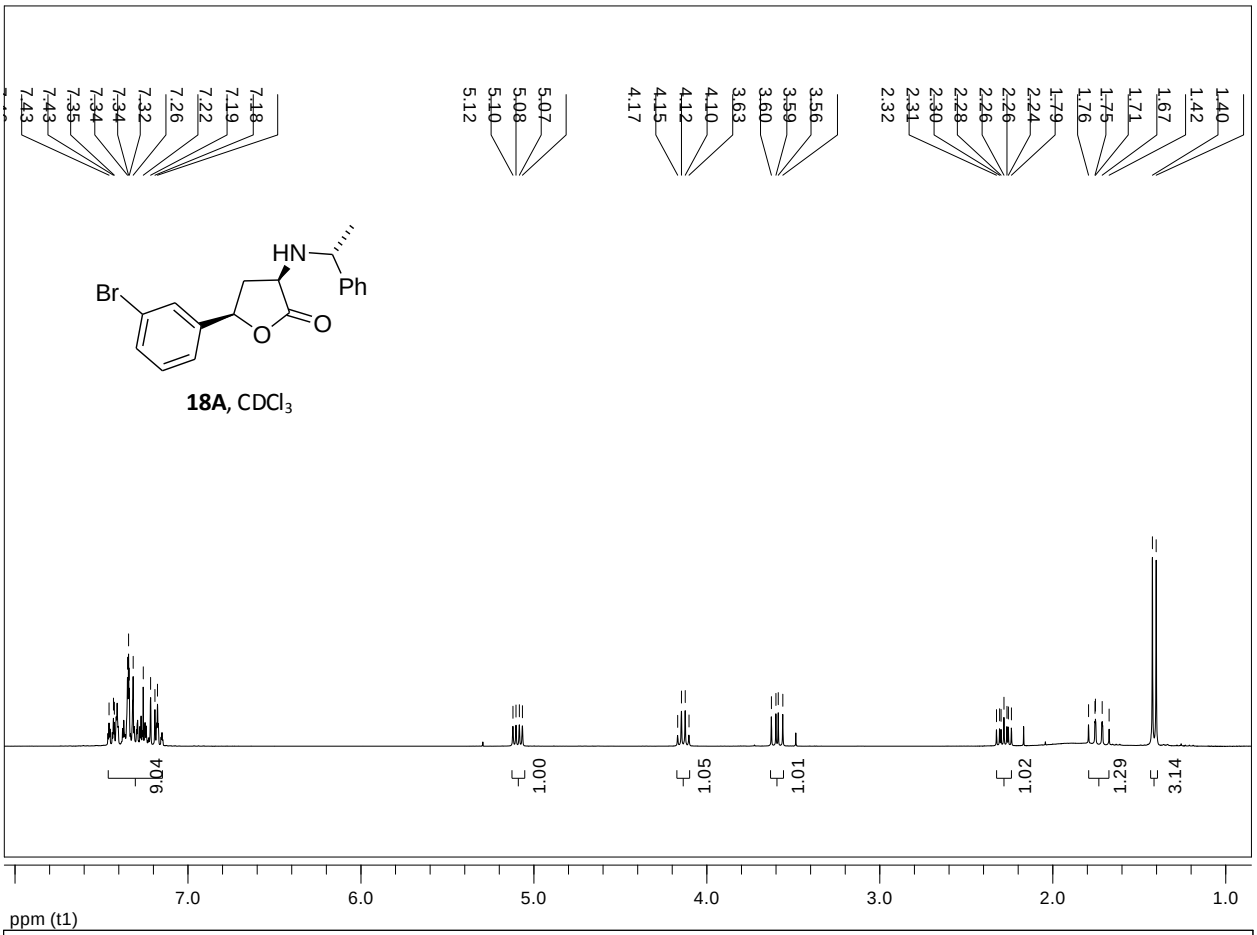
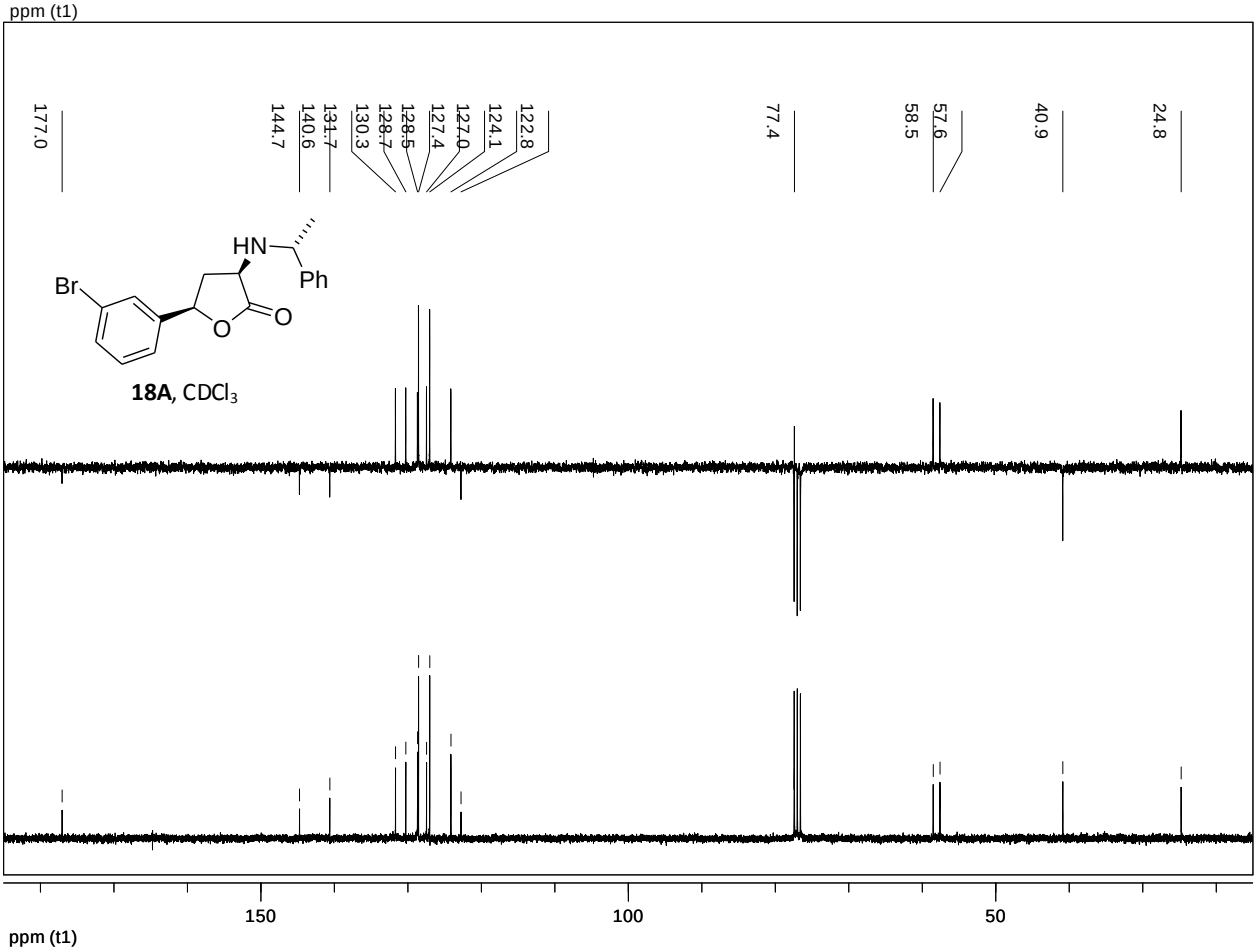
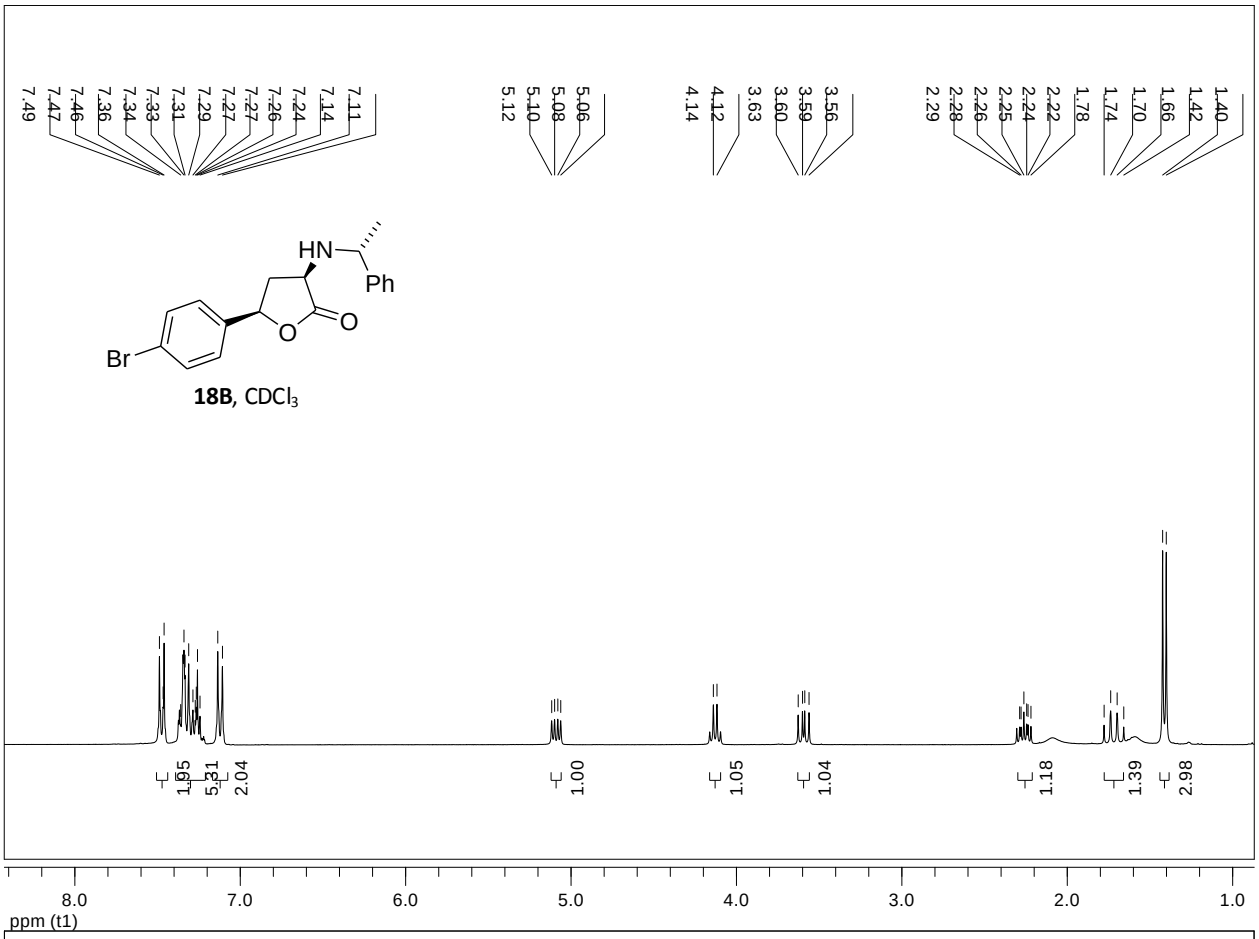
129.8
128.6
127.5
127.0
125.7
113.1
74.5
58.1
55.1
38.3
24.5
HN
Ph
Br
S
O
O
17C, CDCl3
150
100
50
ppm (t1)



18A, $CDCl_3$



18A, $CDCl_3$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7.11
5.12
5.10
5.08
5.06
4.14
4.12
3.63
3.60
3.59
3.56
2.29
2.28
2.26
2.25
2.24
2.22
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1.74
1.70
1.66
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Ph
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O
Br
18B, CDCl3
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5.01
4.04
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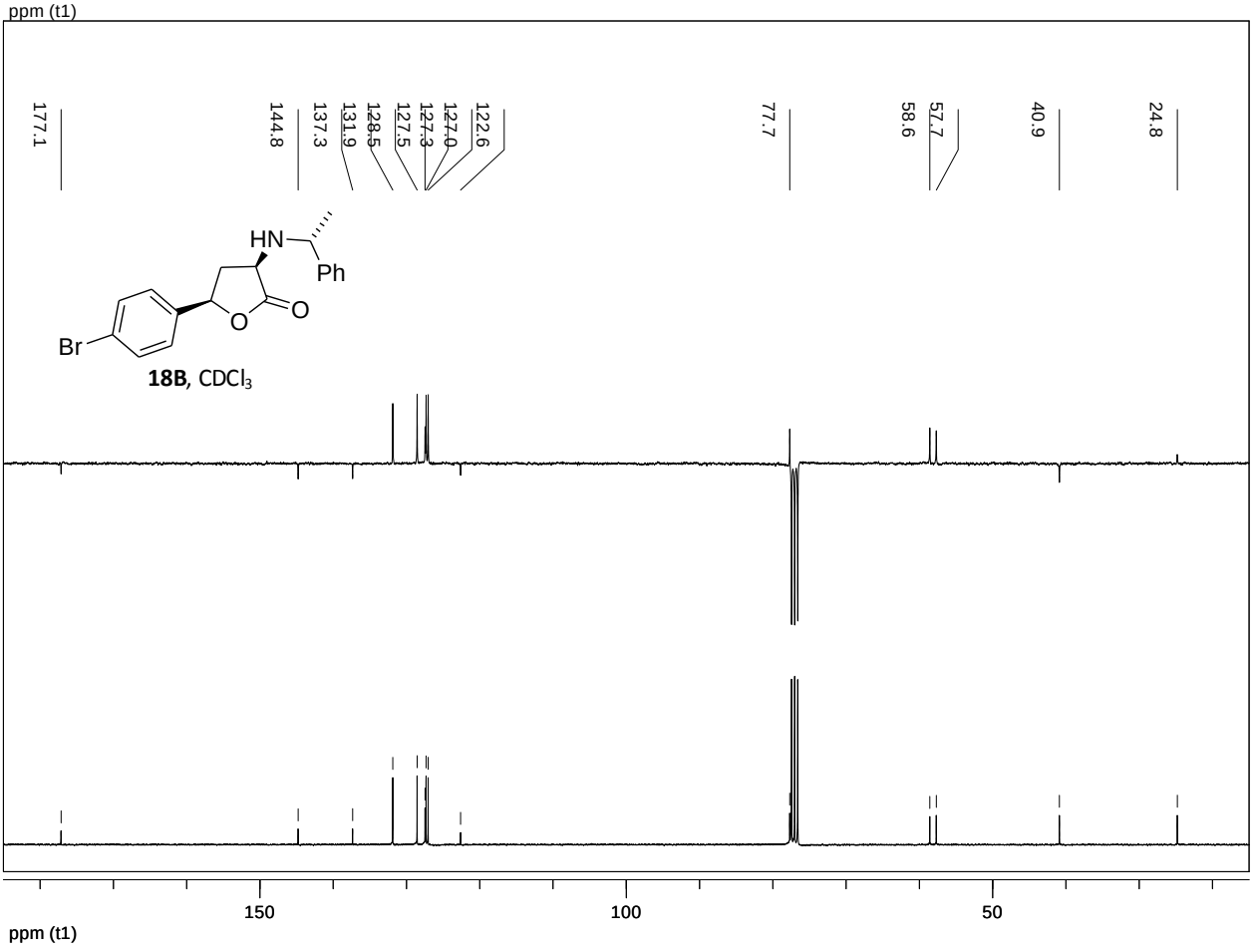
ppm (t1)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127.0
122.6
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40.9
24.8
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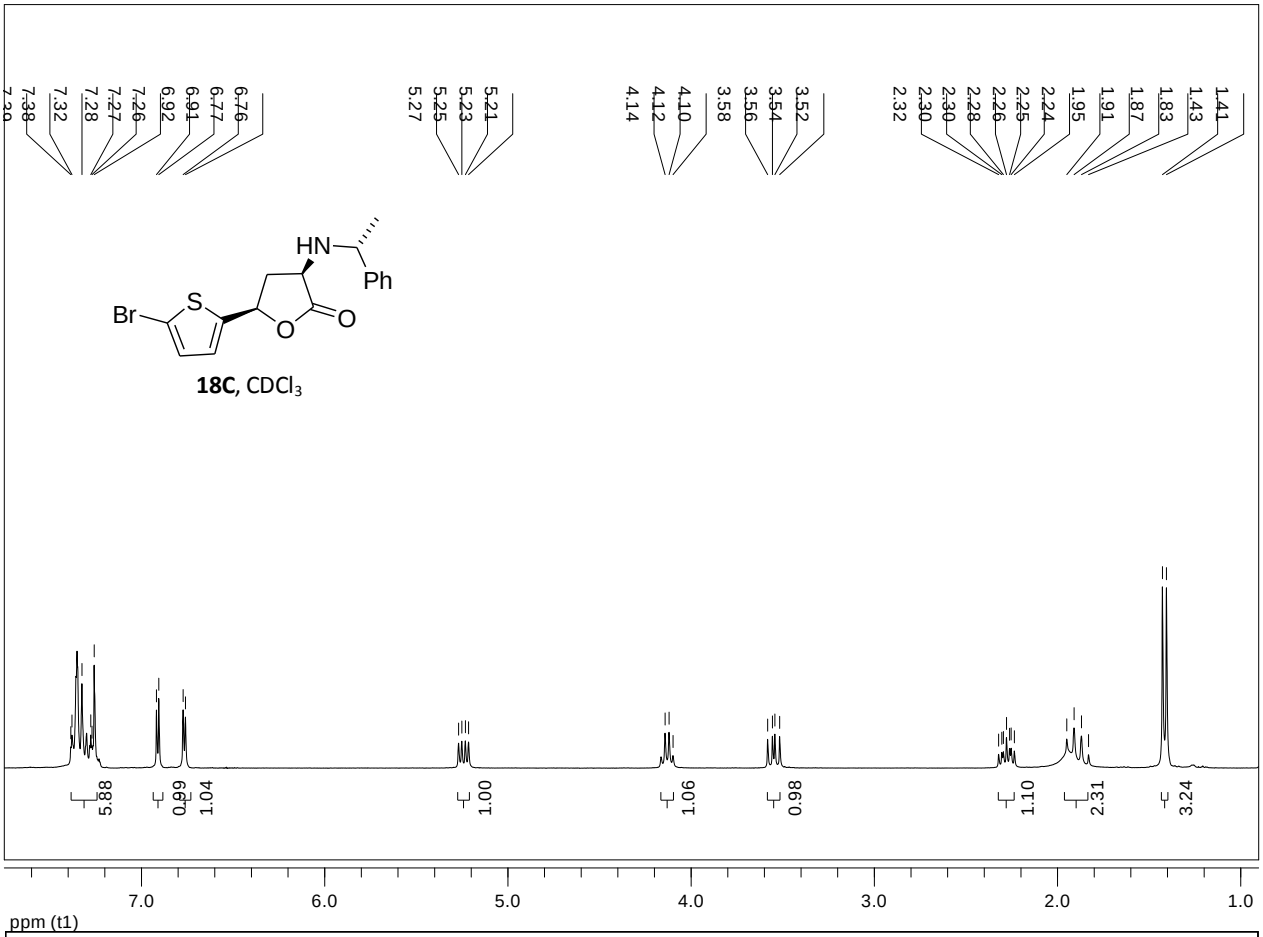
Ph
O
O
Br
18B, CDCl3
150
100
50
ppm (t1)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5.21
4.14
4.12
4.10
3.58
3.56
3.54
3.52
2.32
2.30
2.28
2.26
2.25
2.24
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1.91
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1.41
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Ph
Br
S
O
O
18C, CDCl3
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0.90
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1.00
0.90
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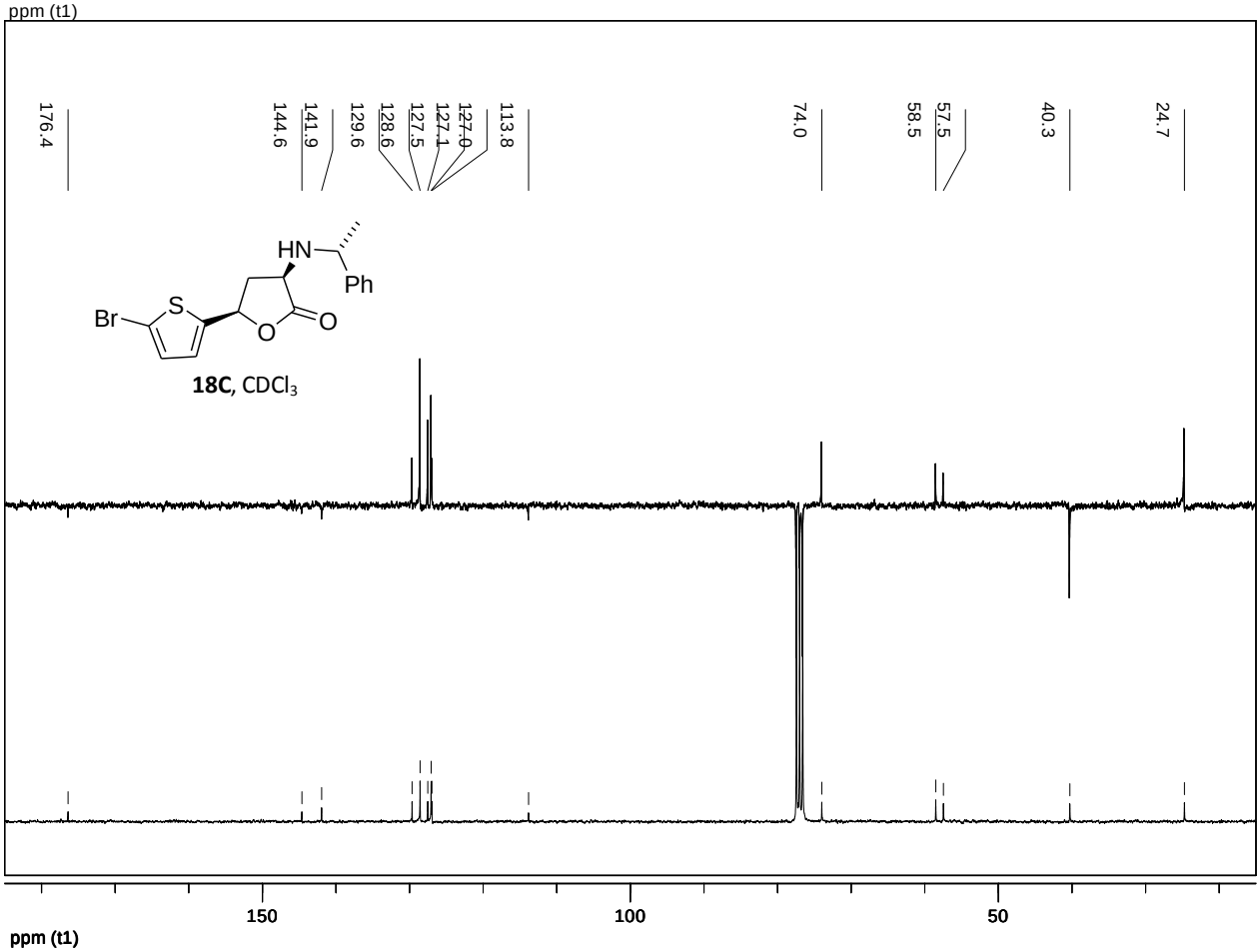
ppm (t1)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128.6
127.5
127.1
127.0
113.8
74.0
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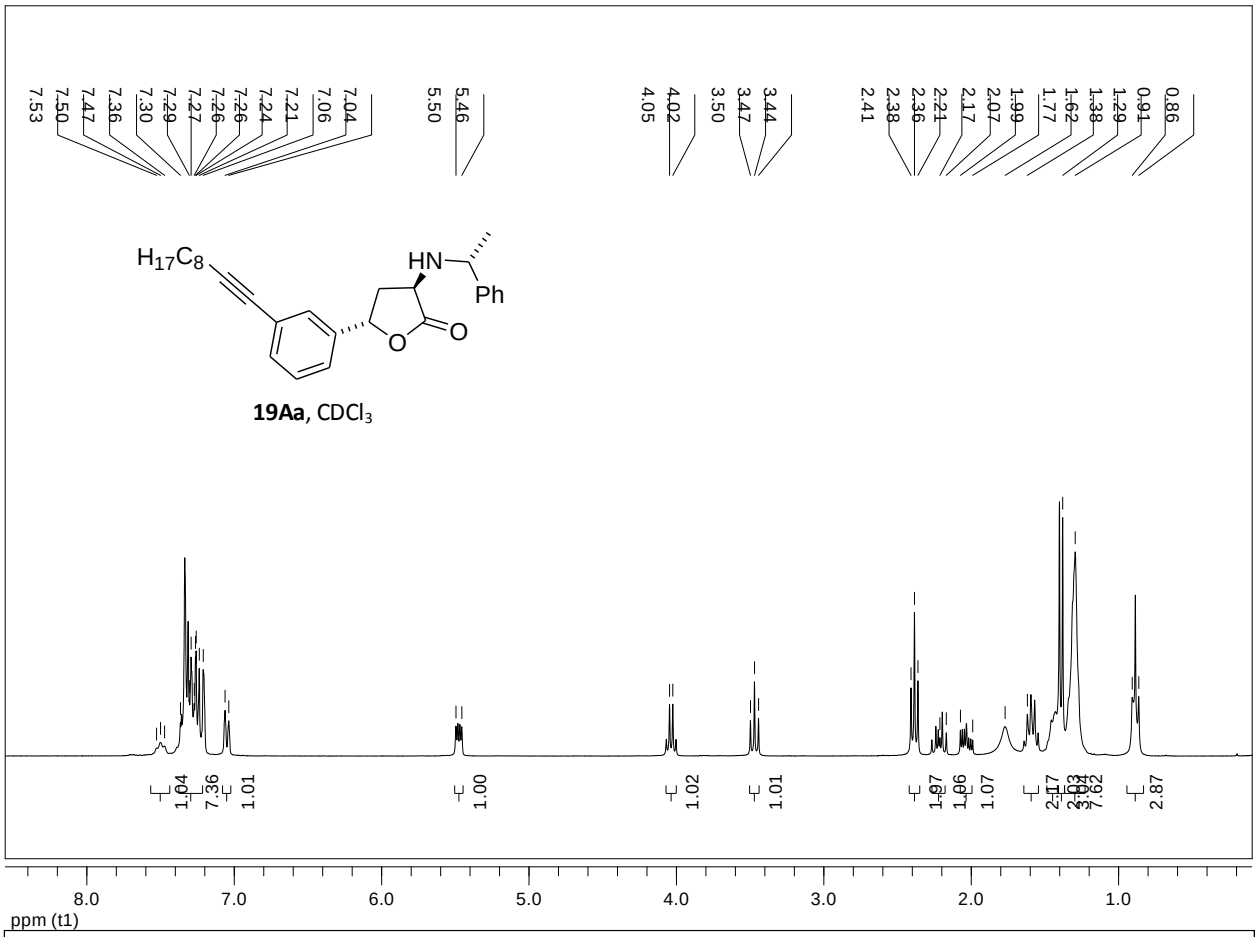
57.5
40.3
24.7
HN
Ph
Br
S
O
O
18C, CDCl3
150
100
50
ppm (t1)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3.44
2.41
2.38
2.36
2.21
2.17
2.07
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1.77
1.62
1.38
1.29
0.91
0.86
H17C8
HN
Ph
O
O
19Aa, CDCl3
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3.96
1.01
1.00
2.01
1.01
7.61
1.06
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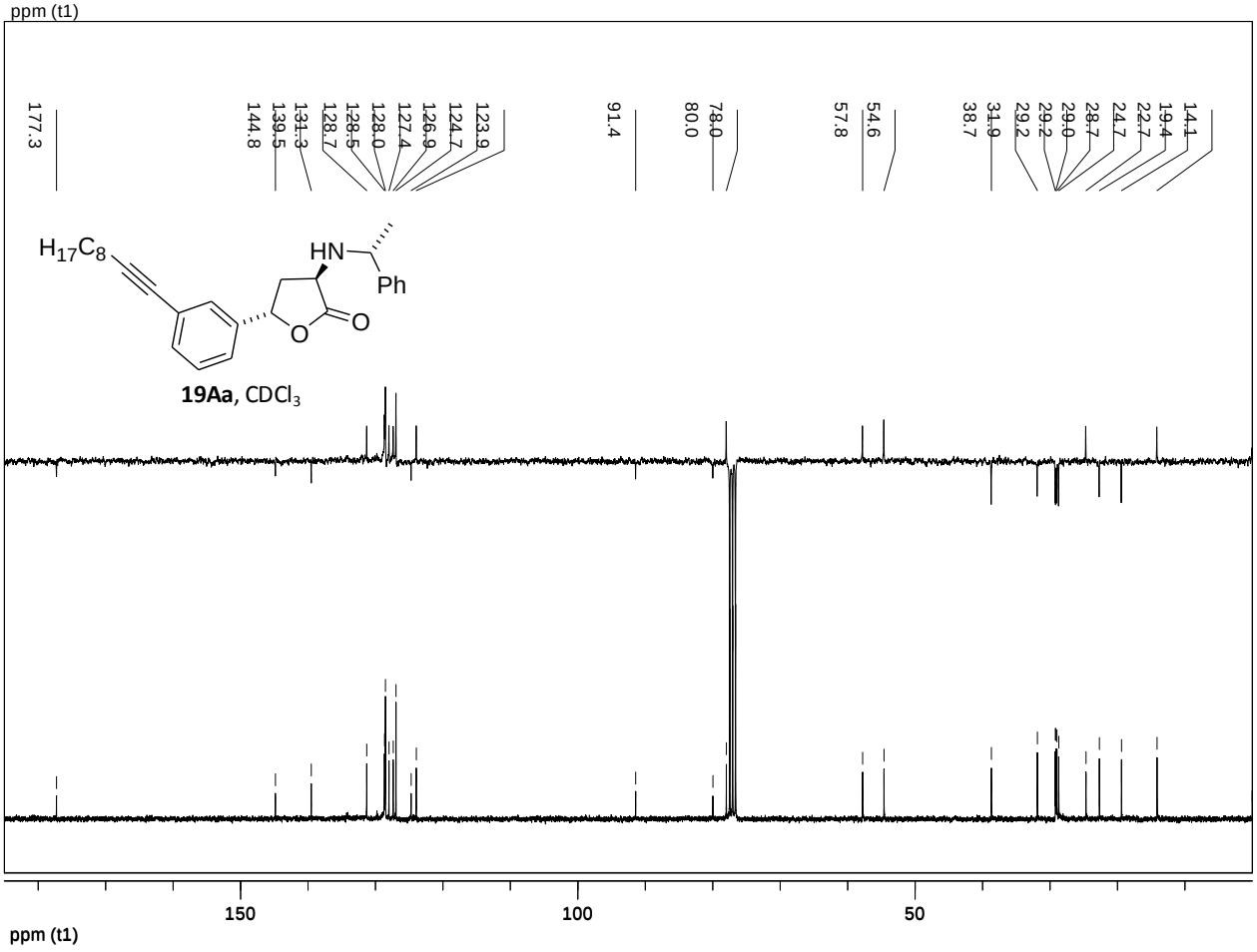
ppm (t1)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126.9
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91.4
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57.8
54.6
38.7
31.9
29.2
29.2
29.0
28.7
24.7
22.7
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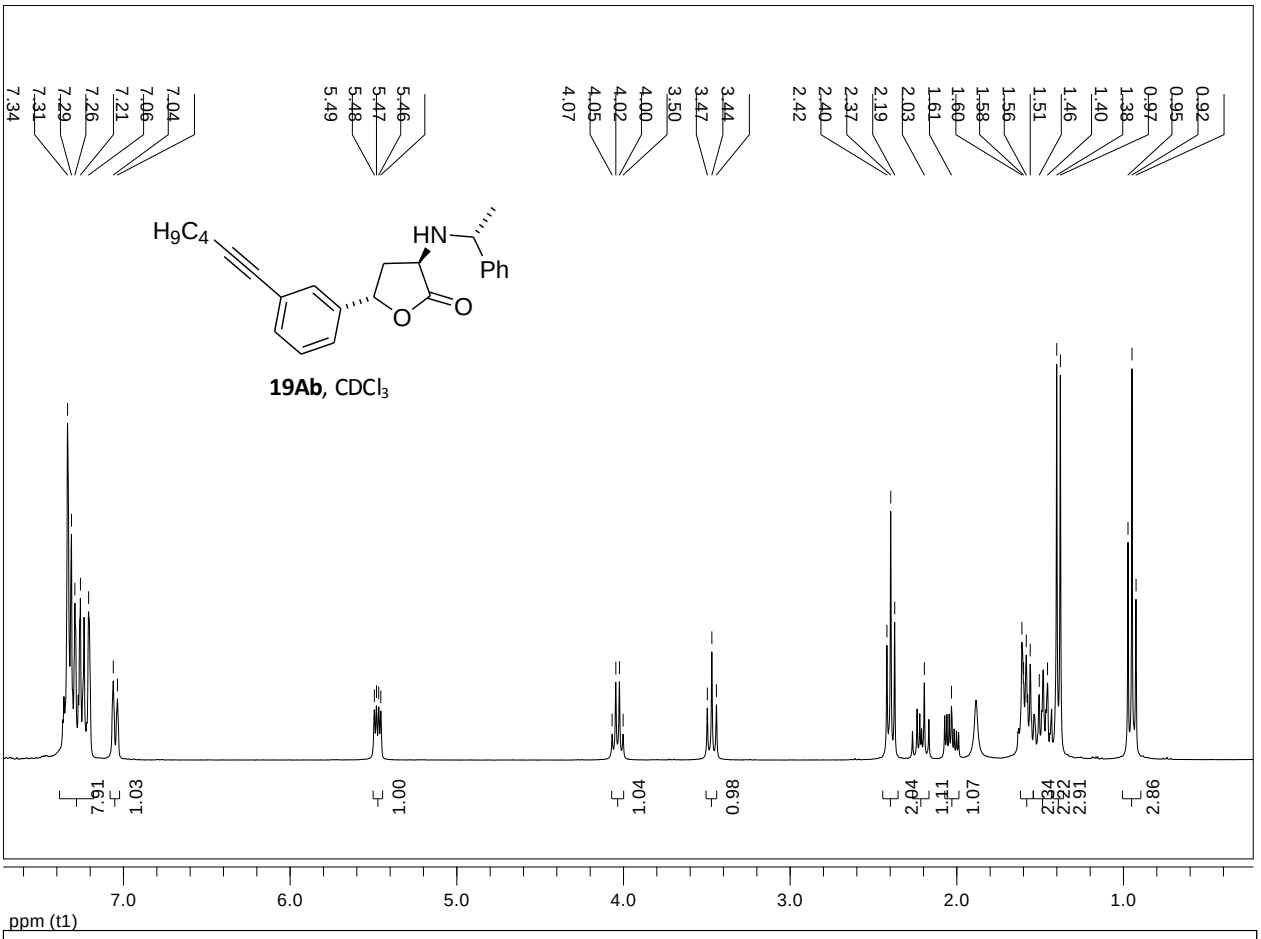
14.1
H17C8
HN
Ph
O
O
19Aa, CDCl3
150
100
50
ppm (t1)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4.05
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4.00
3.50
3.47
3.44
2.42
2.40
2.37
2.19
2.03
1.61
1.60
1.58
1.56
1.51
1.46
1.40
1.38
0.97
0.95
0.92
H9C4
HN
Ph
O
O
19Ab, CDCl3
1.03
7.91
1.00
1.04
8.60
2.04
1.11
1.07
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3.0
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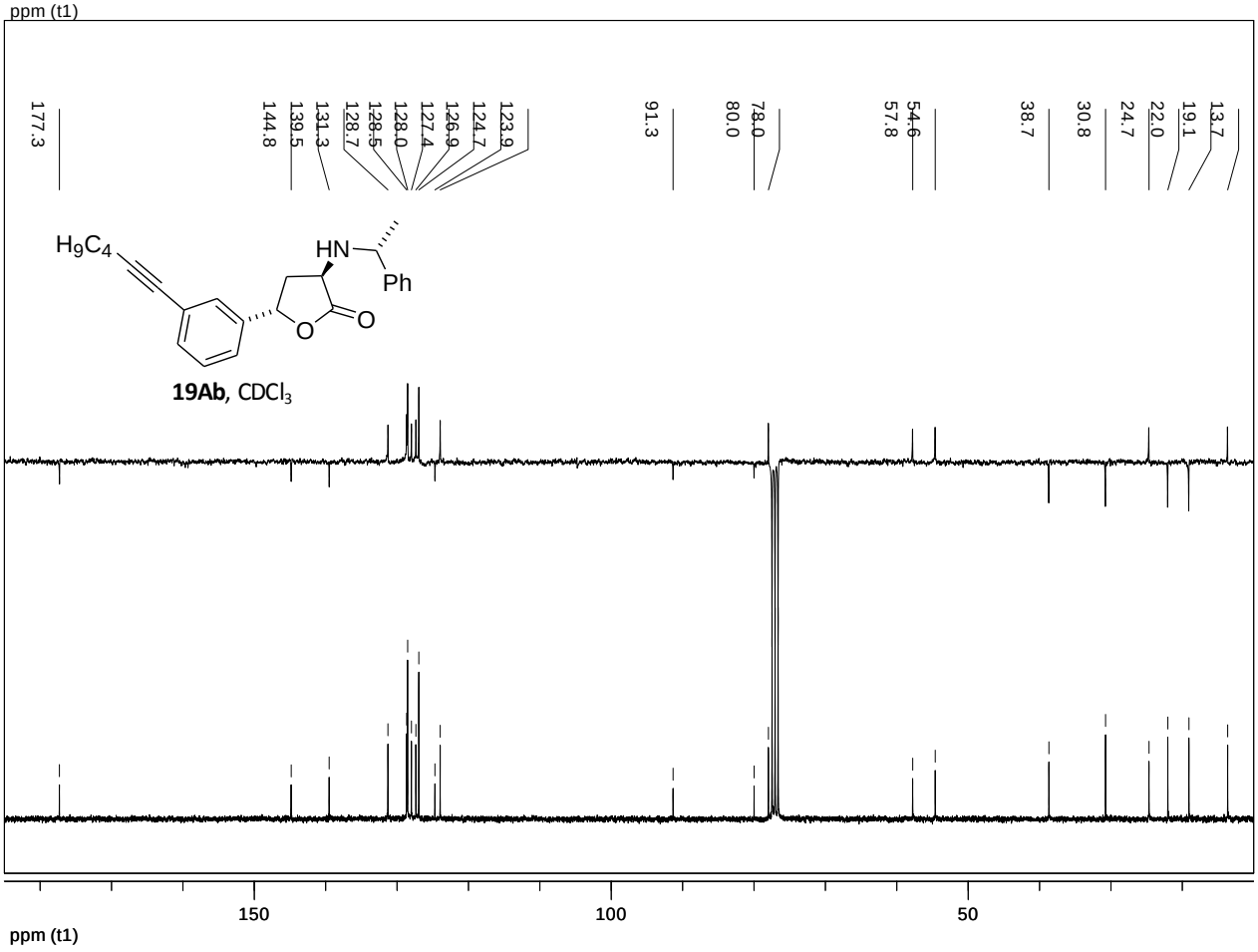
1.0
ppm (t1)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123.9
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80.0
78.0
57.8
54.6
38.7
30.8
24.7
22.0
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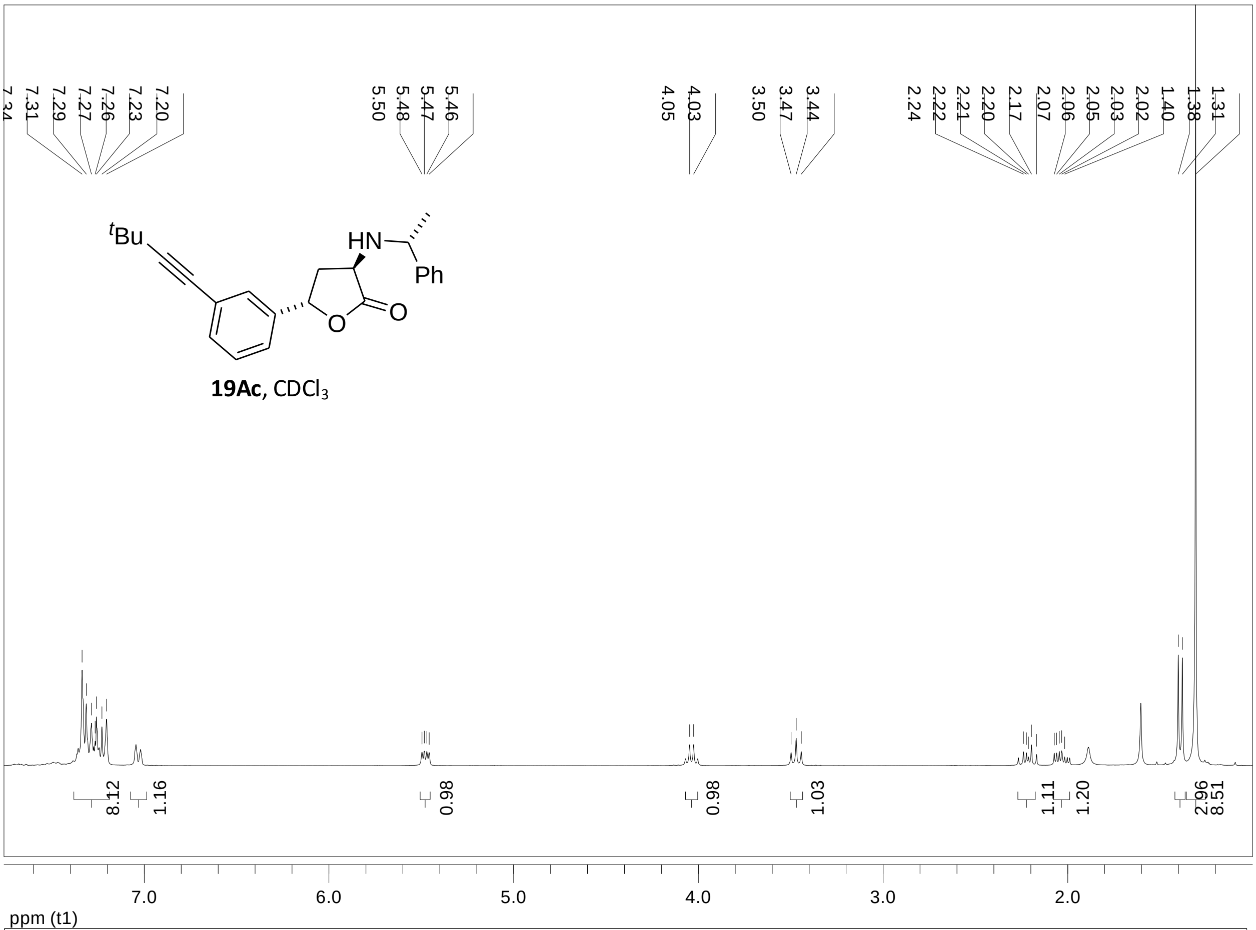
13.7
H9C4
HN
Ph
O
O
19Ab, CDCl3
150
100
50
ppm (t1)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4.05 4.03
3.50 3.47 3.44
2.24 2.22 2.21 2.20 2.17 2.07 2.06 2.05 2.03 2.02 1.40 1.38 1.31
tBu
HN
Ph
O
O
19Ac, CDCl3
8.12 1.16 0.98 0.98 1.03 1.11 1.20 2.96 8.51
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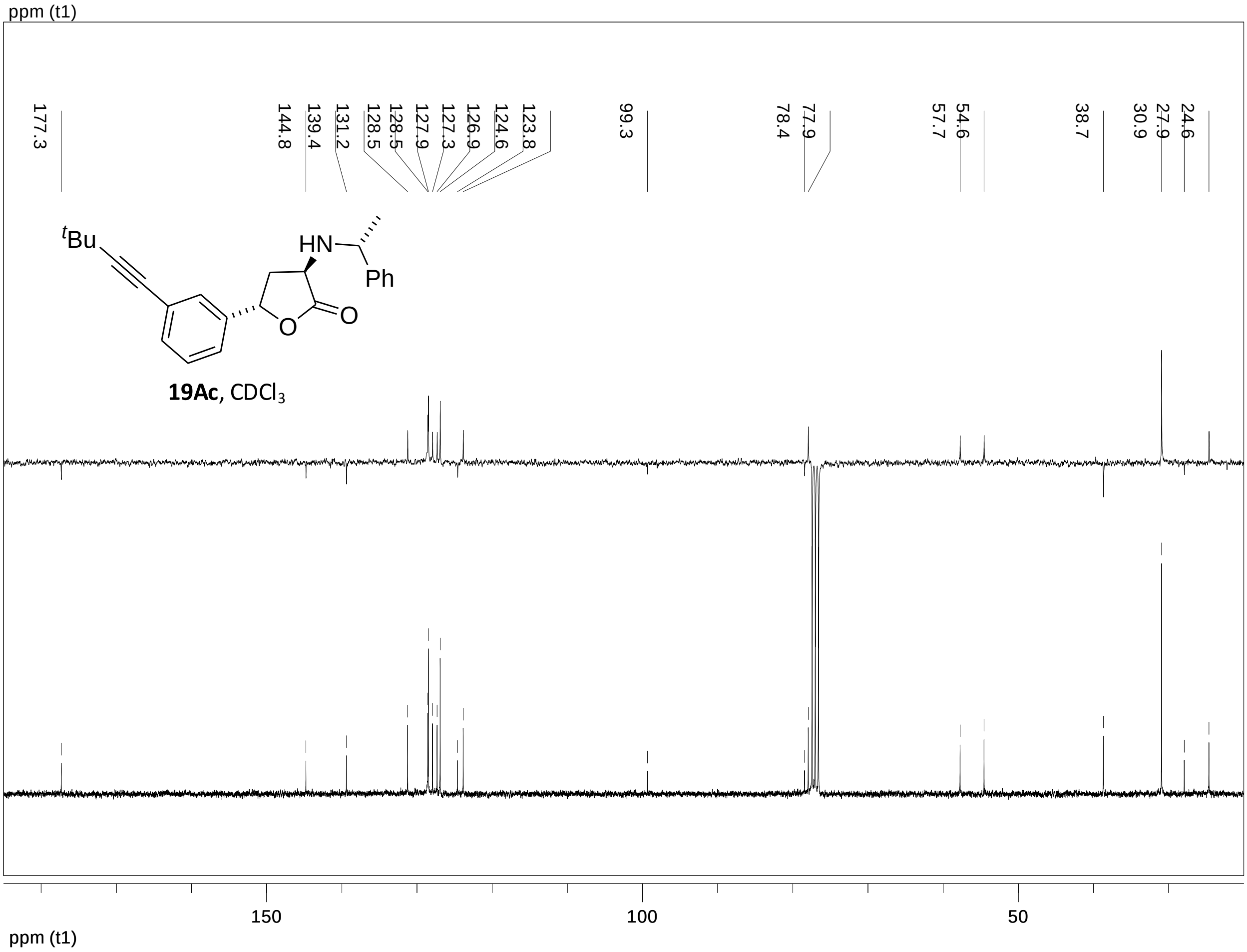
ppm (t1)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99.3
78.4 77.9
57.7 54.6
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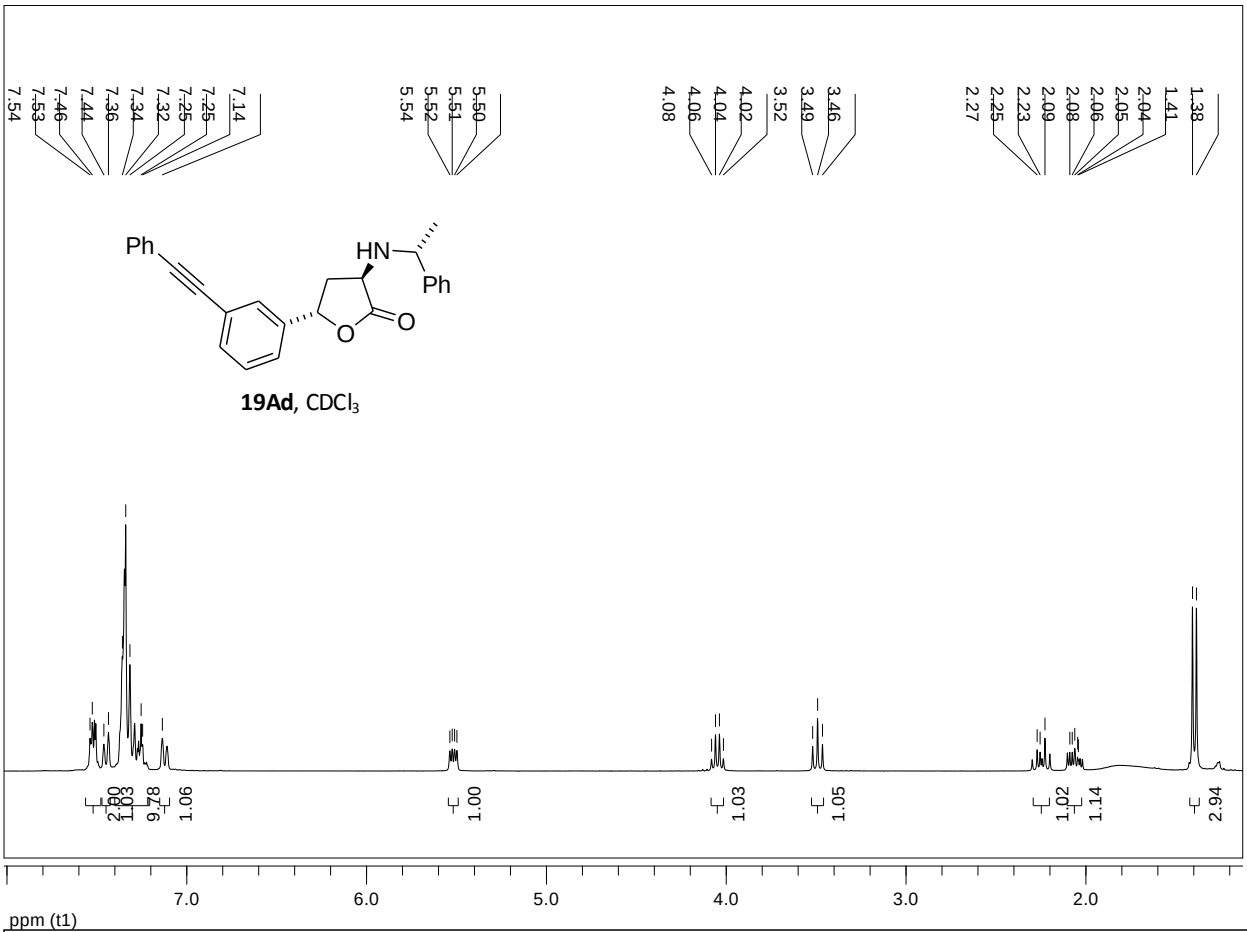
Ph
O
O
19Ac, CDCl3
150 100 50
ppm (t1)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5.50
4.08
4.06
4.04
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2.25
2.23
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2.08
2.06
2.05
2.04
1.41
1.38
Ph
HN
Ph
O
O
19Ad, CDCl3
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3.01
8.76
9.01
1.00
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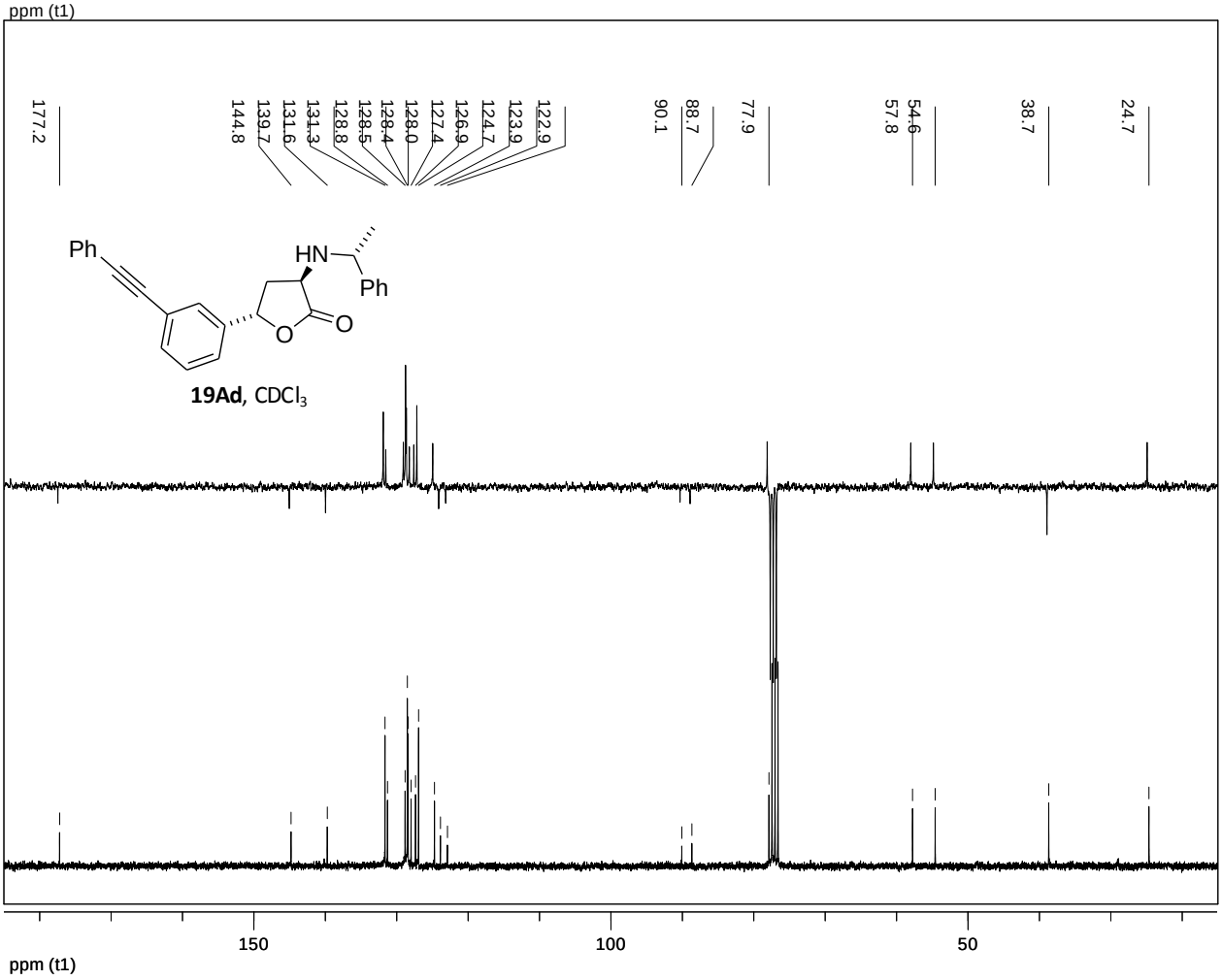
ppm (t1)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123.9
122.9
90.1
88.7
77.9
57.8
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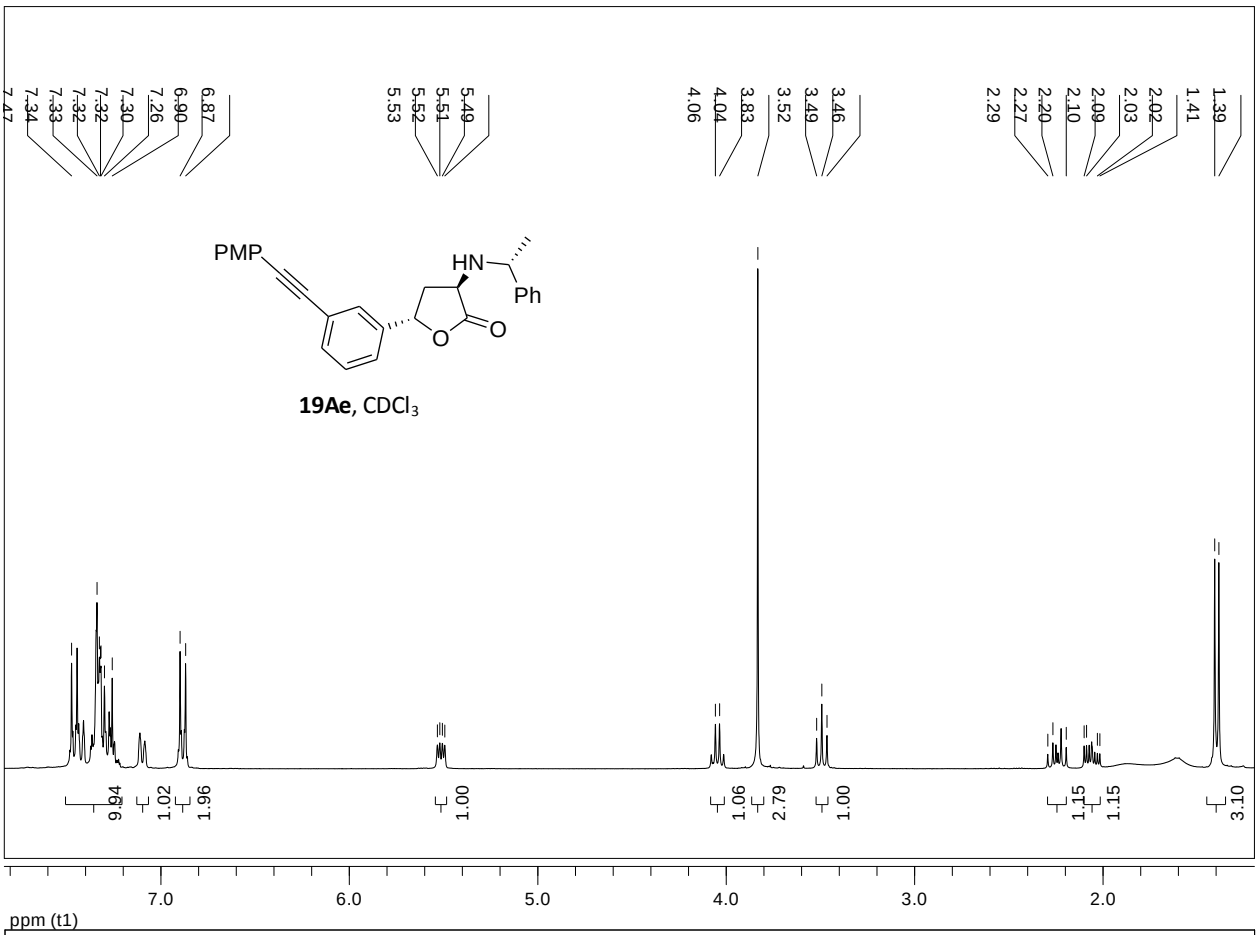
38.7
24.7
Ph
HN
Ph
O
O
19Ad, CDCl3
150
100
50
ppm (t1)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3.52
3.49
3.46
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2.27
2.20
2.10
2.09
2.03
2.02
1.41
1.39
PMP
HN
Ph
O
O
19Ae, CDCl3
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1.02
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1.00
1.06
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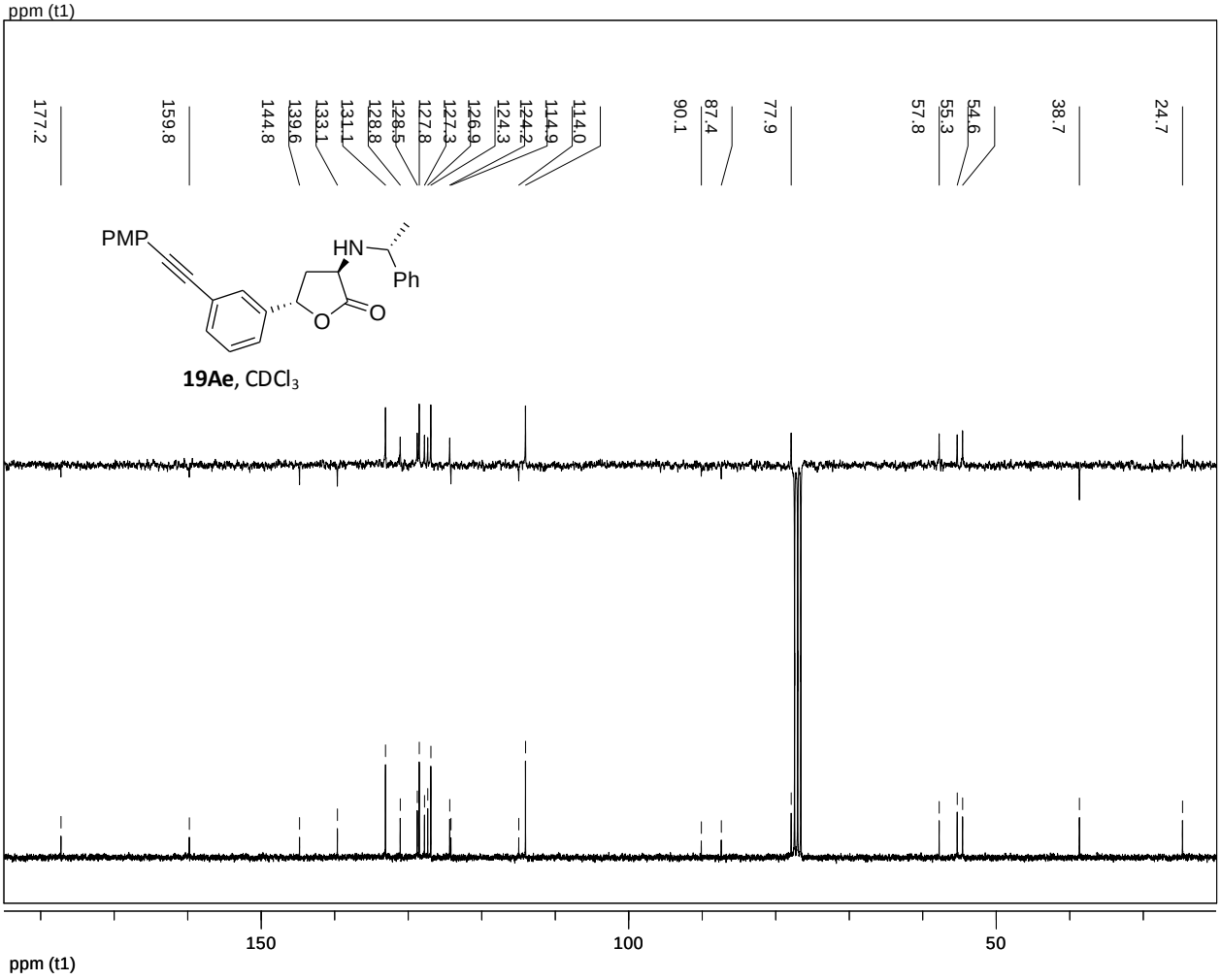
ppm (t1)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124.2
114.9
114.0
90.1
87.4
77.9
57.8
55.3
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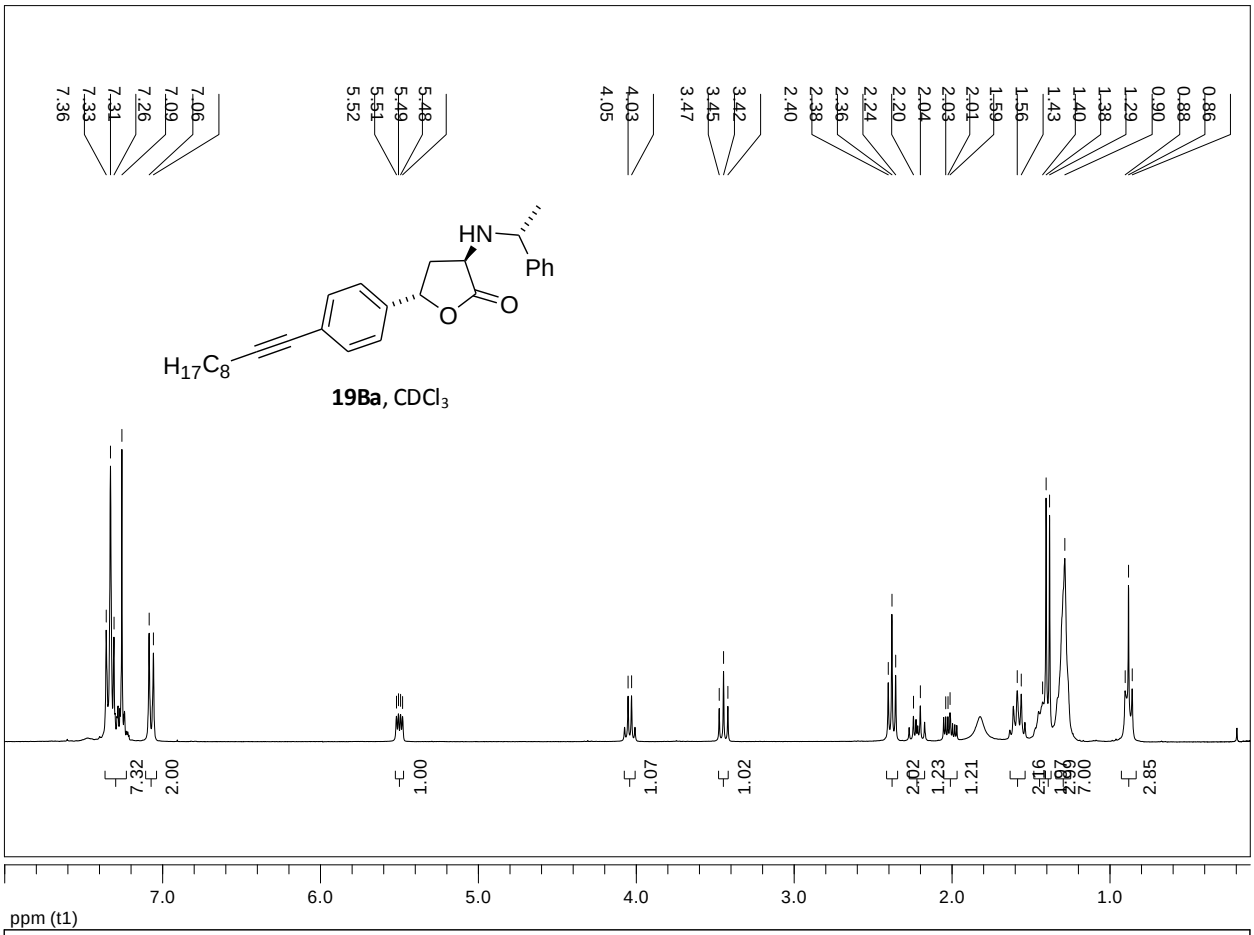
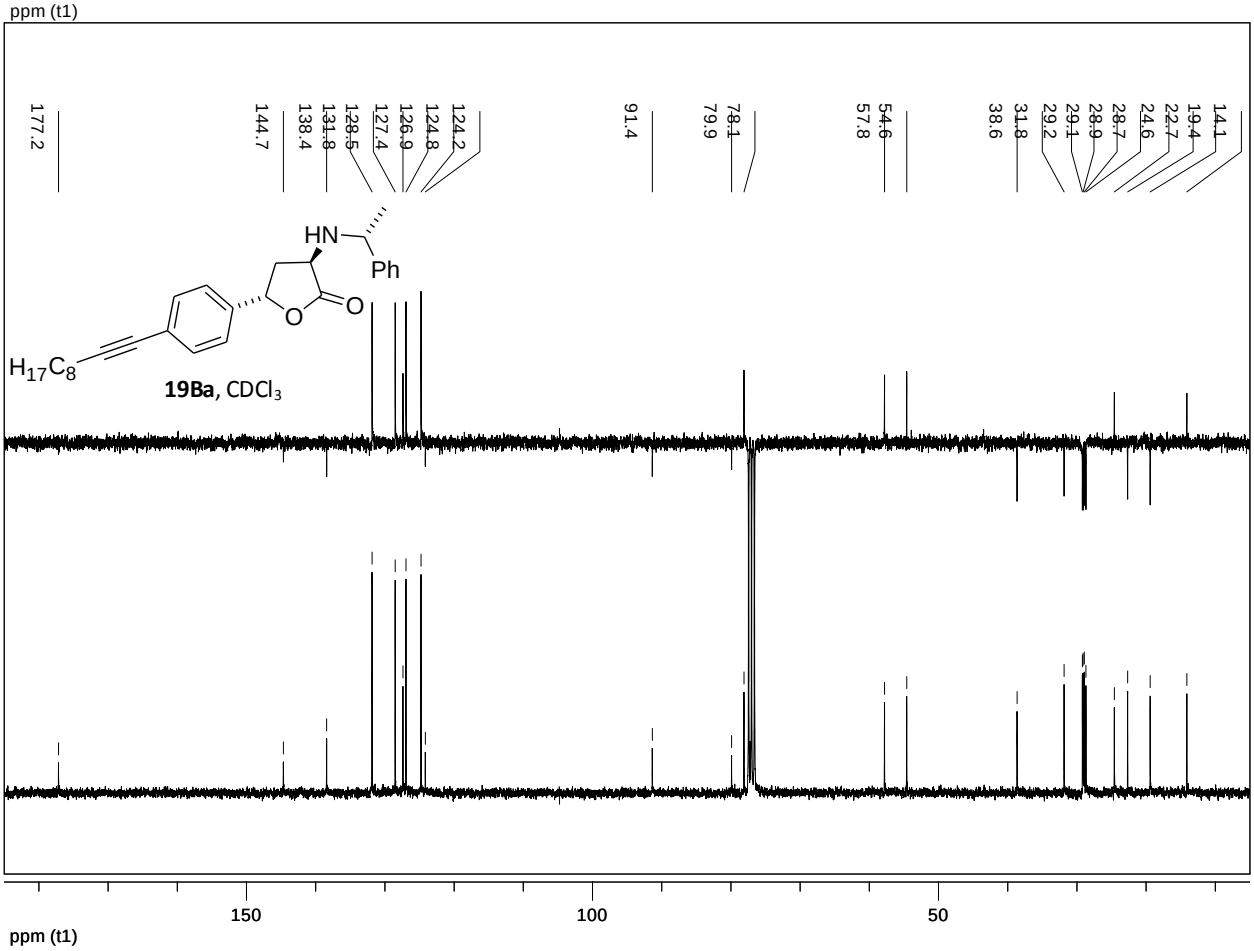
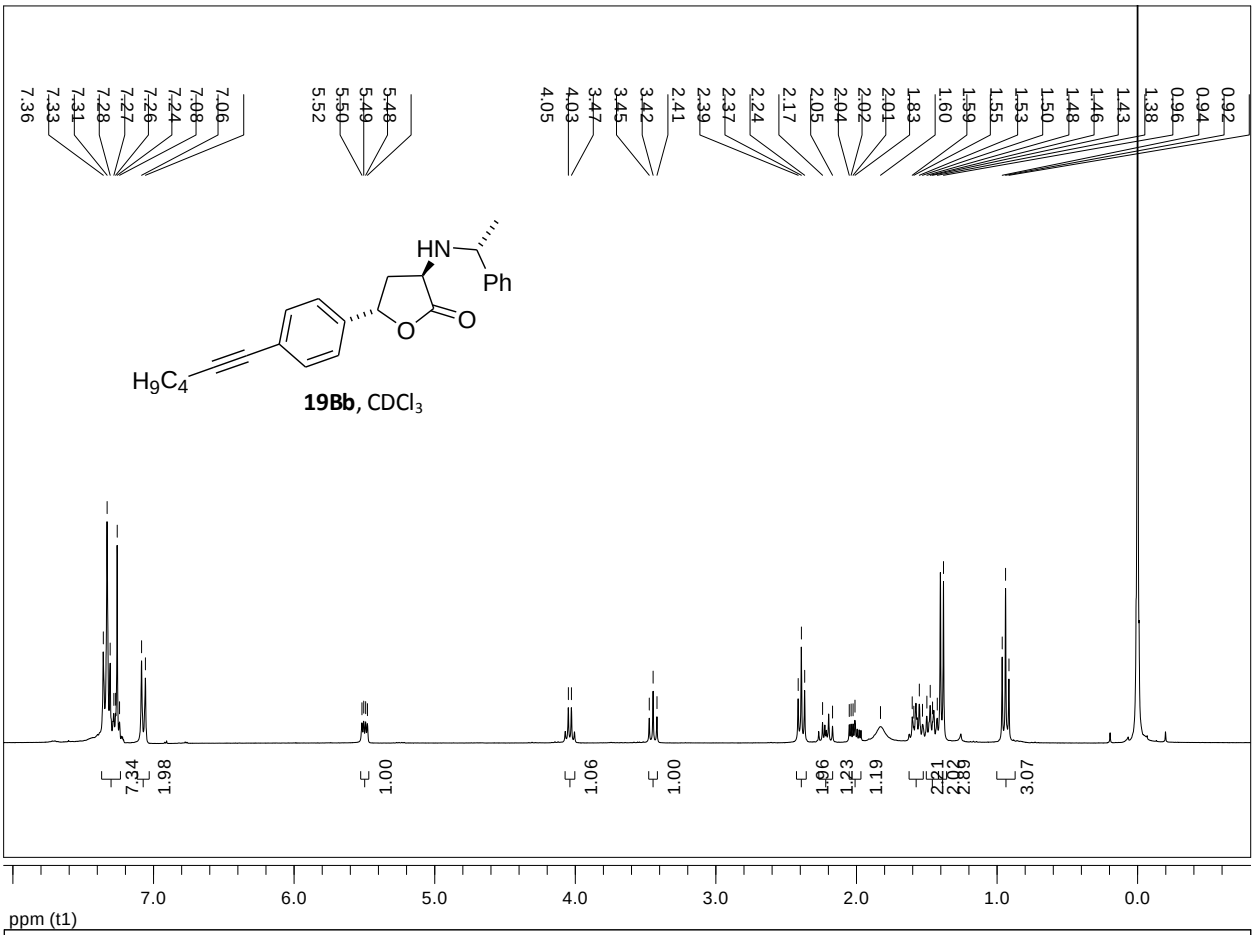
24.7
PMP
HN
Ph
O
O
19Ae, CDCl3
150
100
50
ppm (t1)



19Ba, $CDCl_3$



19Ba, $CDCl_3$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7.08
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5.50
5.49
5.48
4.05
4.03
3.47
3.45
3.42
2.41
2.39
2.37
2.24
2.17
2.05
2.04
2.02
2.01
1.83
1.60
1.59
1.55
1.53
1.50
1.48
1.46
1.43
1.38
0.96
0.94
0.92
HN
Ph
O
O
H_9C_4
19Bb, $CDCl_3$
1.98
1.00
1.06
1.00
1.19
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7.0
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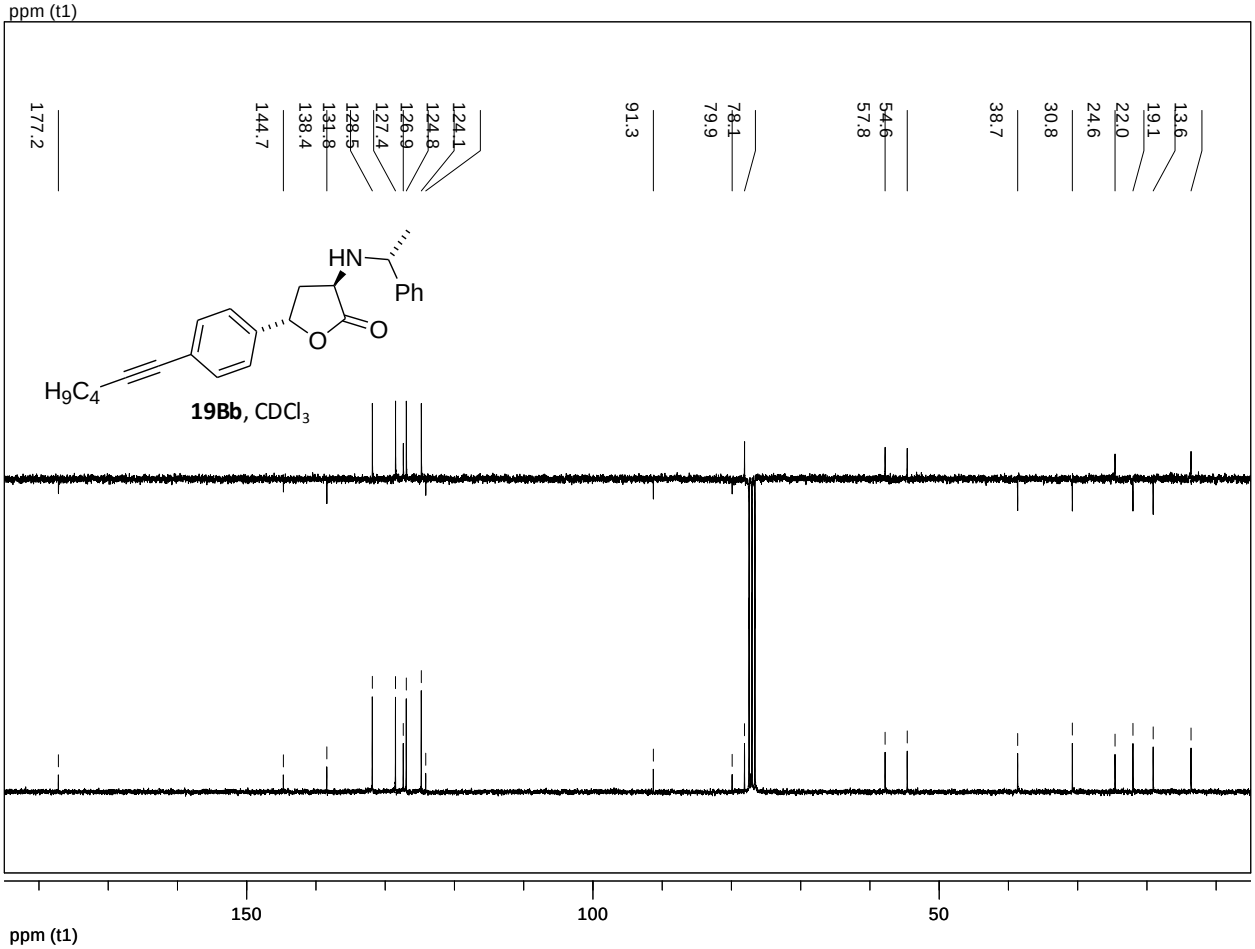
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)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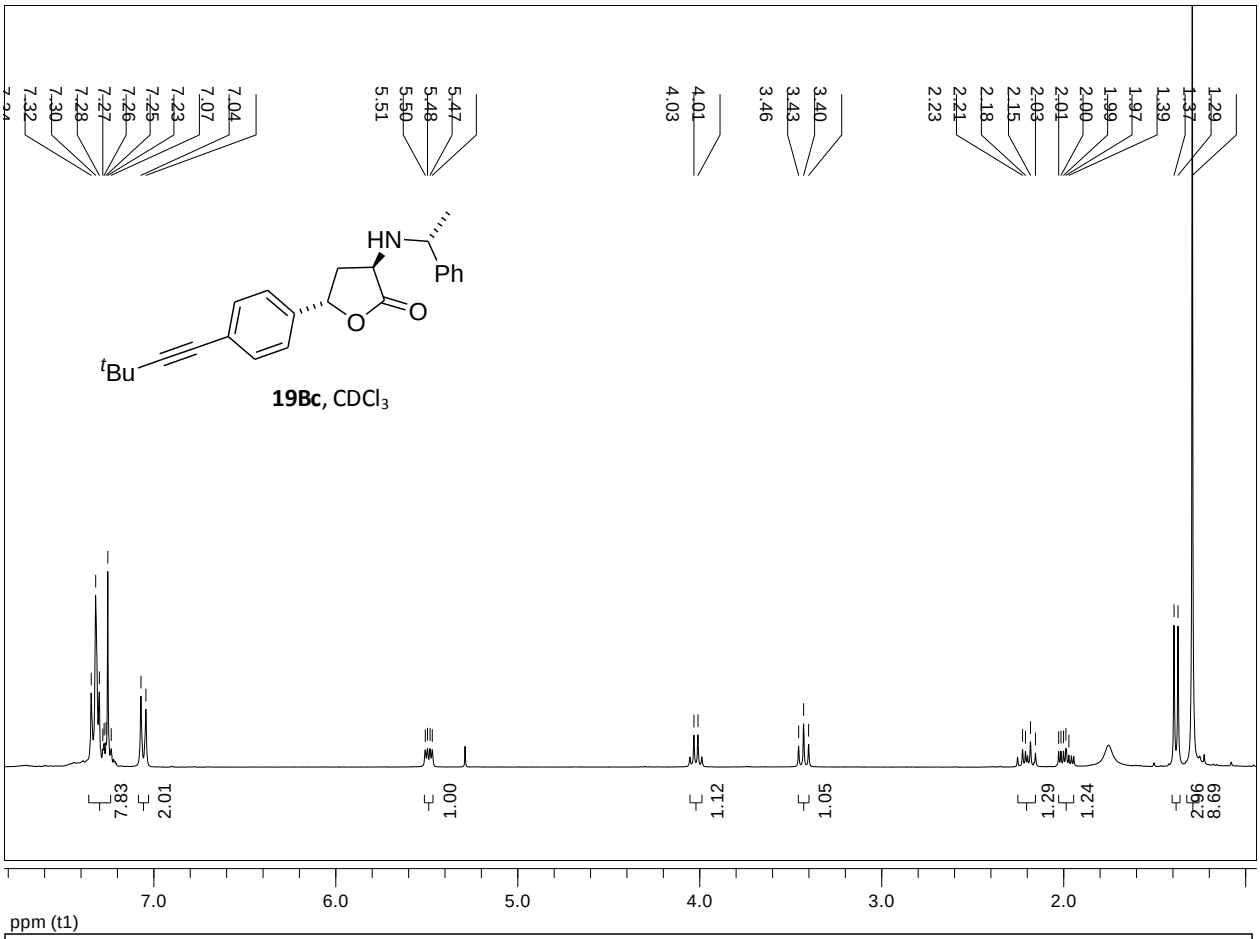
131.8
128.5
127.4
126.9
124.8
124.1
91.3
79.9
78.1
57.8
54.6
38.7
30.8
24.6
22.0
19.1
13.6
HN
Ph
O
O
H_9C_4
19Bb, $CDCl_3$
150
100
50
ppm (t1)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7.26
7.25
7.23
7.07
7.04
5.51
5.50
5.48
5.47
4.03
4.01
3.46
3.43
3.40
2.23
2.21
2.18
2.15
2.03
2.01
2.00
1.99
1.97
1.39
1.37
1.29
HN
Ph
O
O
tBu
19Bc, CDCl3
3.83
2.01
1.00
2.12
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1.24
9.96
9.98
7.0
6.0
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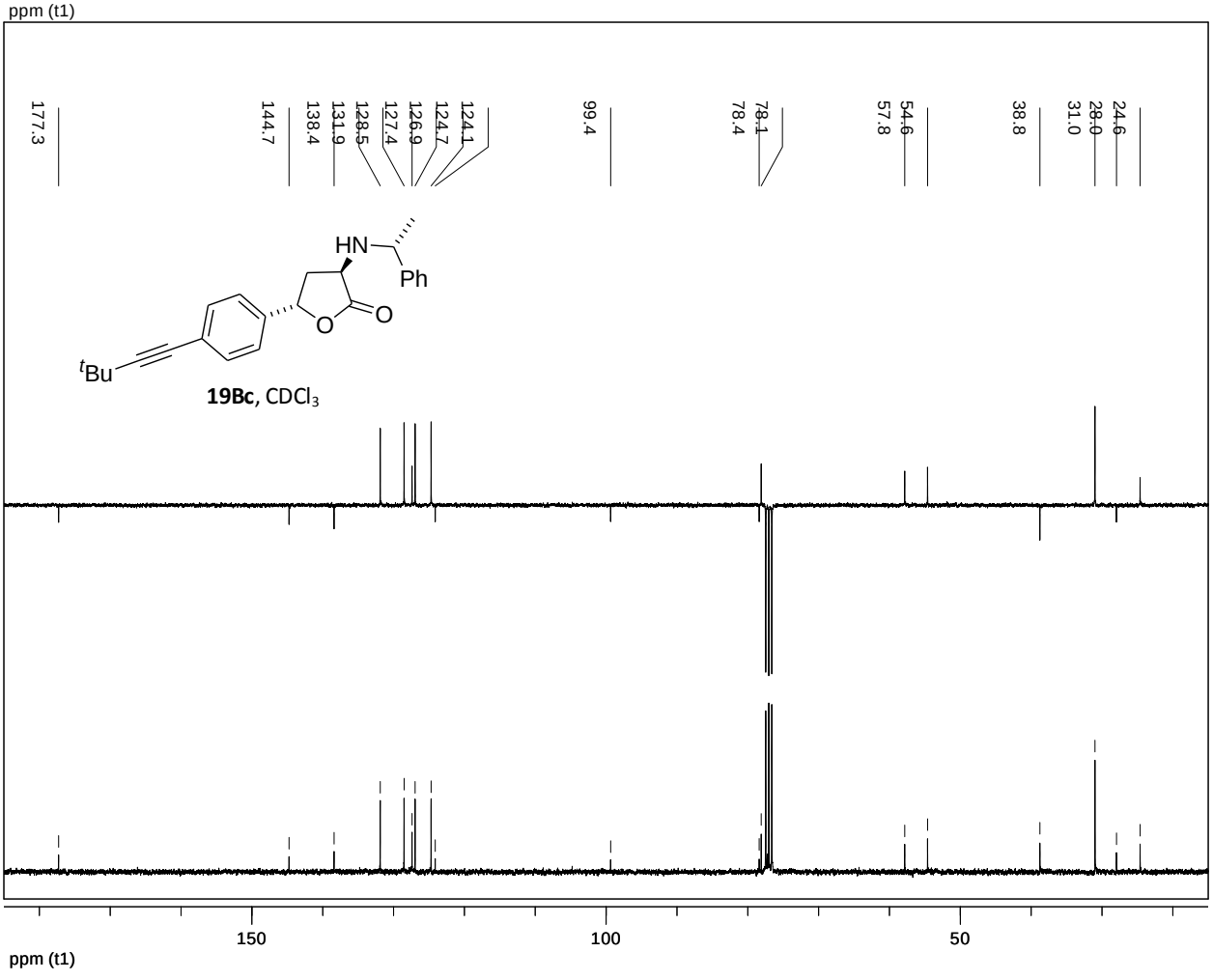
4.0
3.0
2.0
ppm (t1)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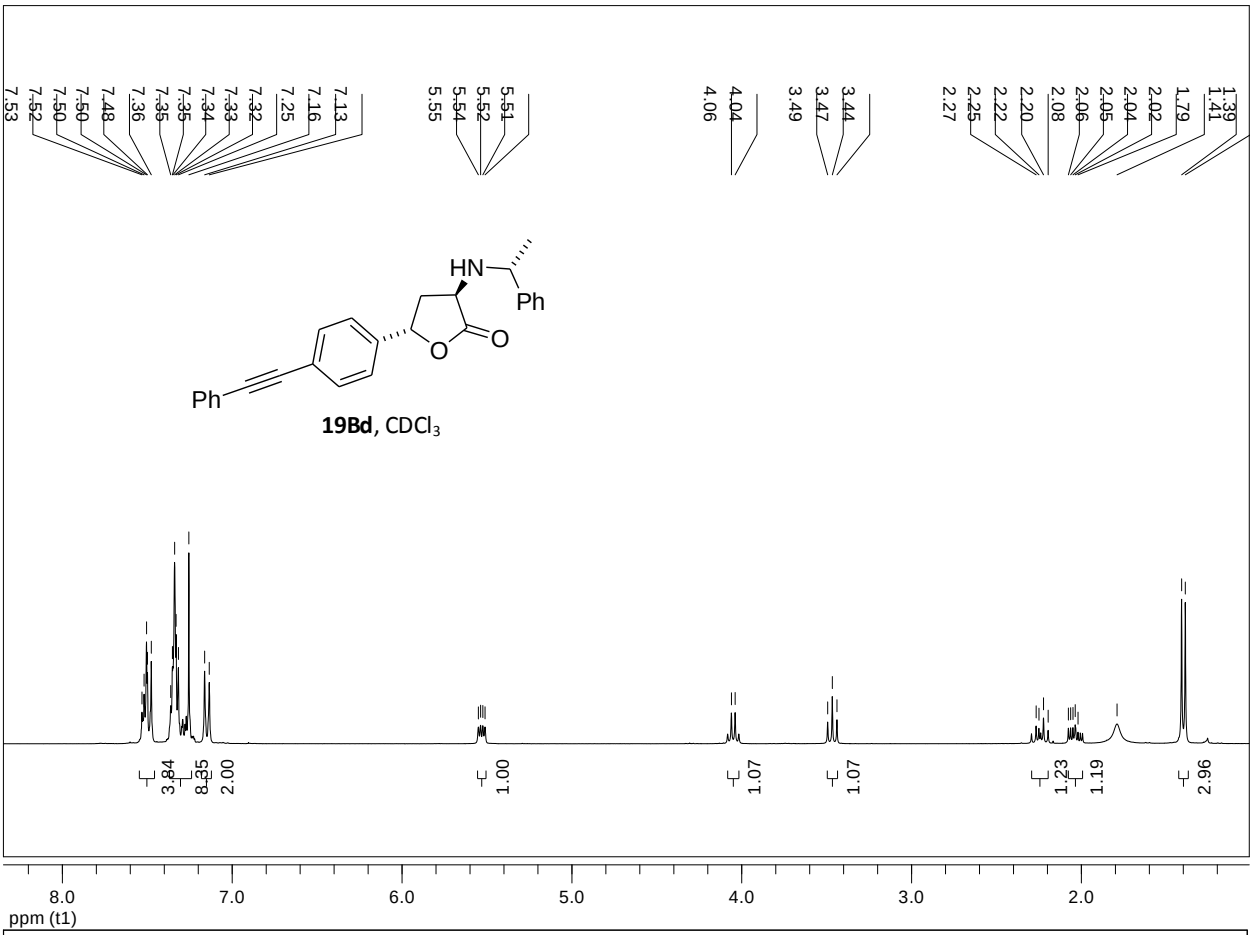
131.9
128.5
127.4
126.9
124.7
124.1
99.4
78.4
78.1
57.8
54.6
38.8
31.0
28.0
24.6
HN
Ph
O
O
tBu
19Bc, CDCl3
150
100
50
ppm (t1)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7.36
7.35
7.35
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7.33
7.32
7.25
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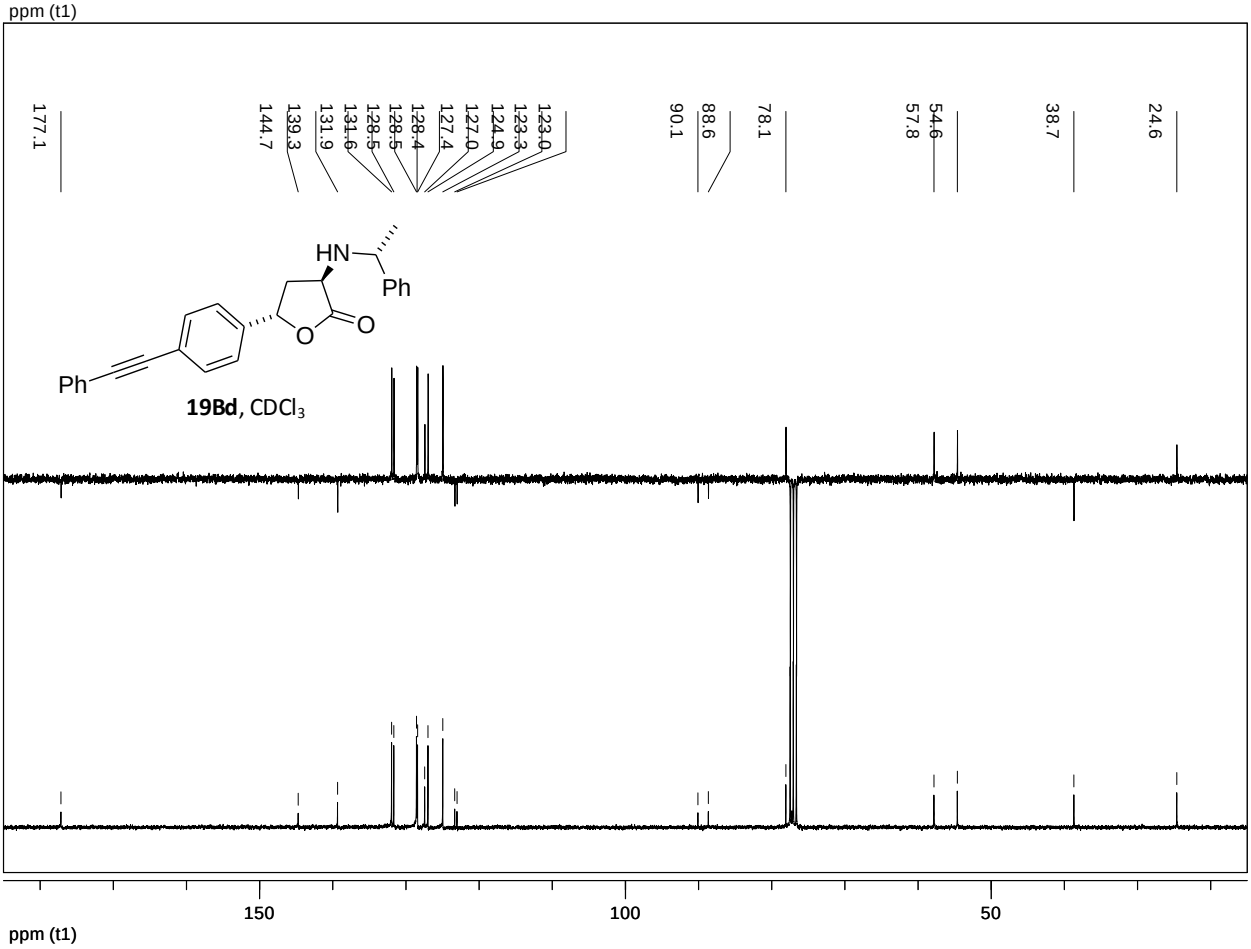
7.13
5.55
5.54
5.52
5.51
4.06
4.04
3.49
3.47
3.44
2.27
2.25
2.22
2.20
2.08
2.06
2.05
2.04
2.02
1.79
1.41
1.39
HN
Ph
O
O
Ph
19Bd, CDCl3
3.84
5.85
2.00
1.00
1.07
1.07
1.22
1.19
9.96
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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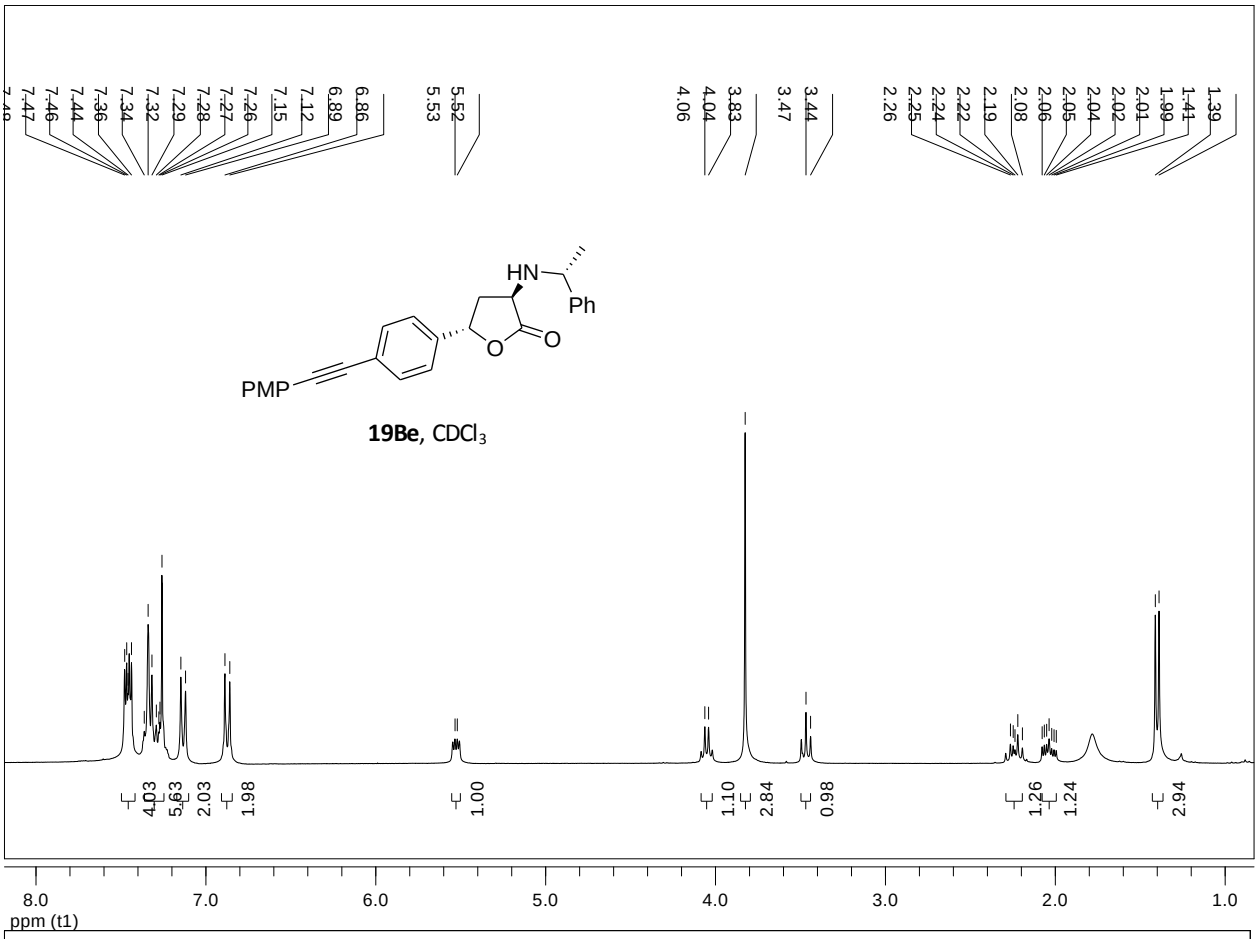
128.5
128.5
128.4
127.4
127.0
124.9
123.3
123.0
90.1
88.6
78.1
57.8
54.6
38.7
24.6
HN
Ph
O
O
Ph
19Bd, CDCl3
150
100
50
ppm (t1)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Ph
O
O
PMP
19Be, CDCl3
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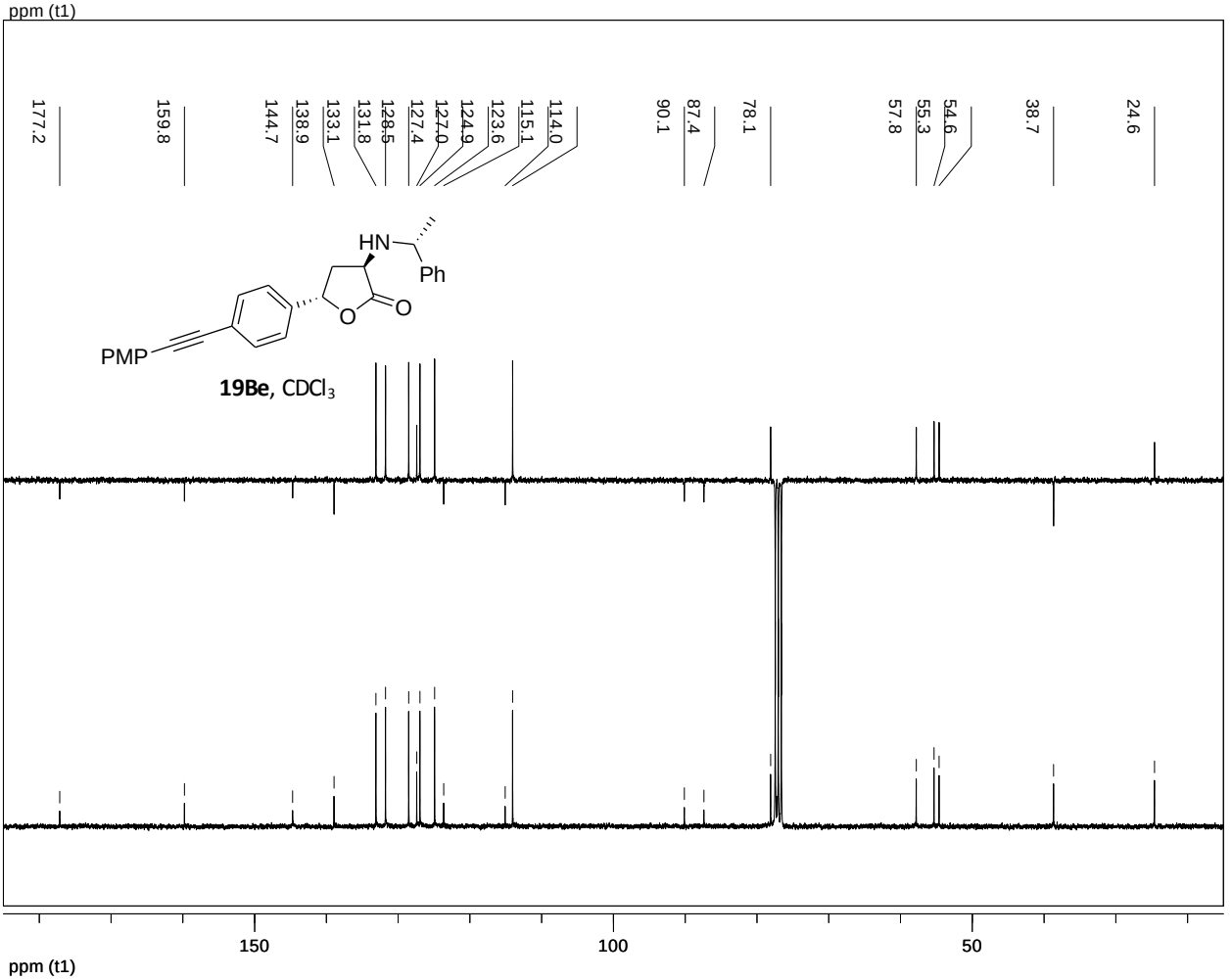
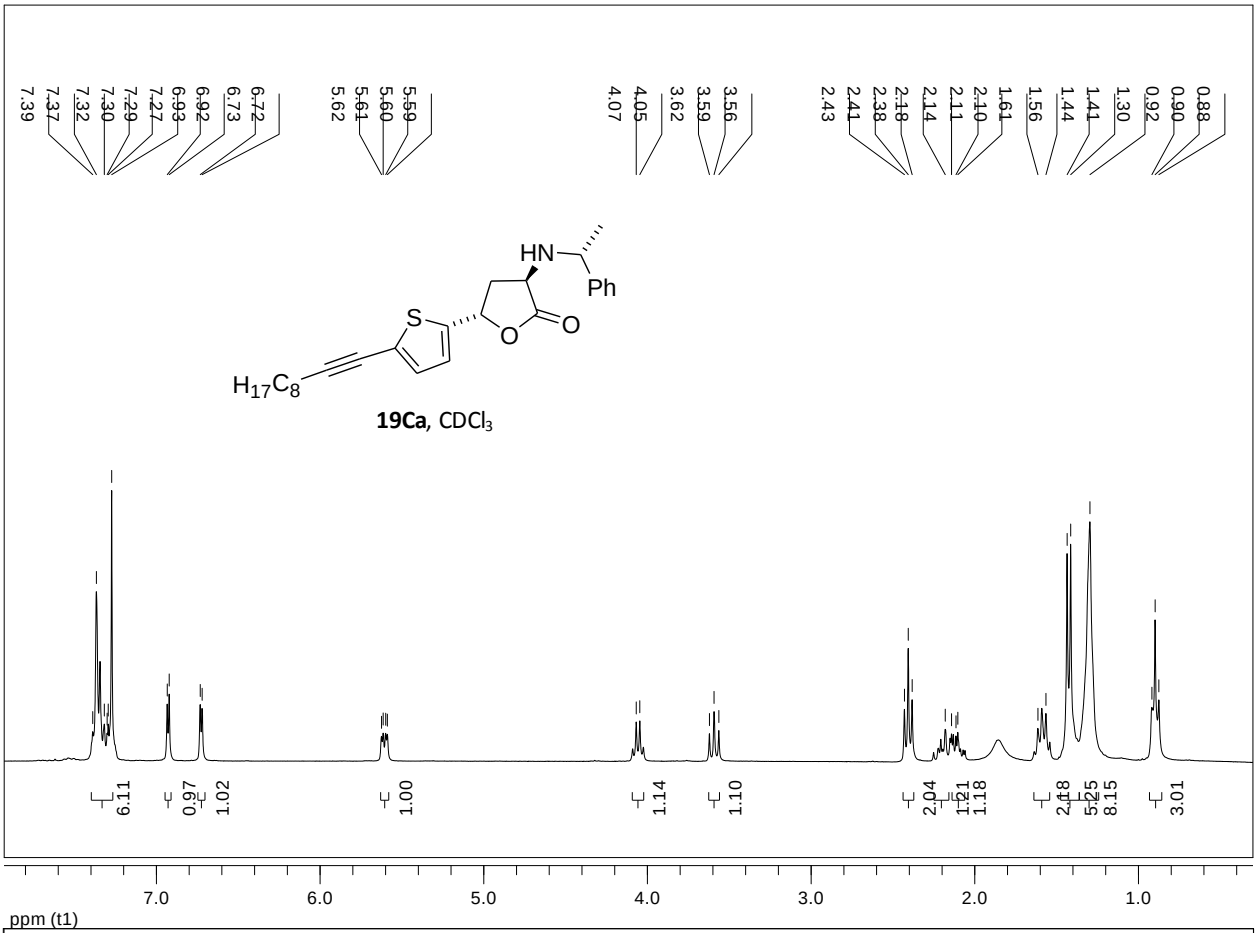
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


HN
Ph
O
O
PMP
19Be, CDCl3
150
100
50
ppm (t1)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7.37
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7.27
6.93
6.92
6.73
6.72
5.62
5.61
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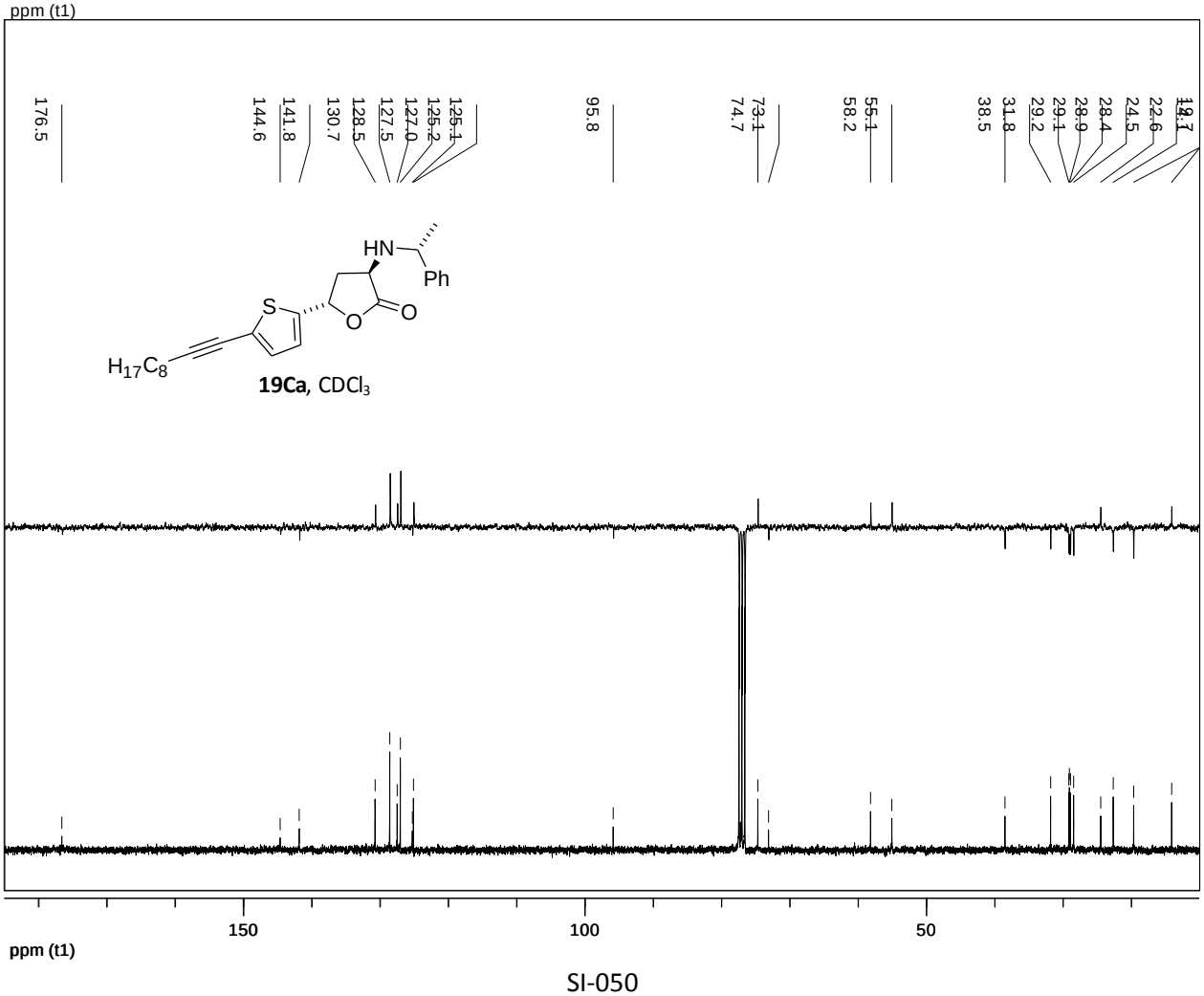
5.59
4.07
4.05
3.62
3.59
3.56
2.43
2.41
2.38
2.18
2.14
2.11
2.10
1.61
1.56
1.44
1.41
1.30
0.92
0.90
0.88
HN
Ph
S
O
O
H17C8
19Ca, CDCl3
9.11
0.97
1.02
1.00
1.14
1.10
2.04
1.21
1.18
2.18
5.25
8.15
3.01
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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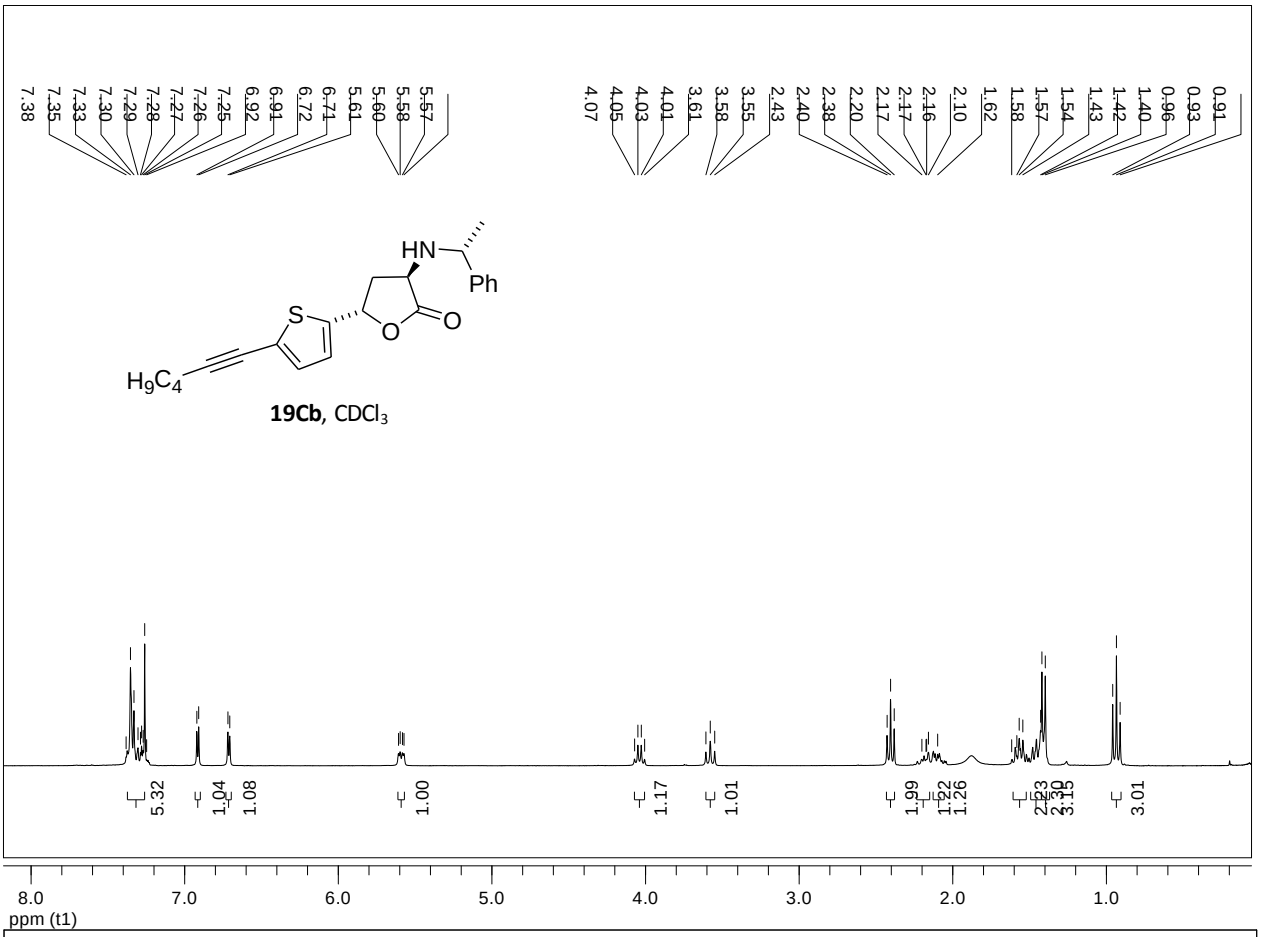
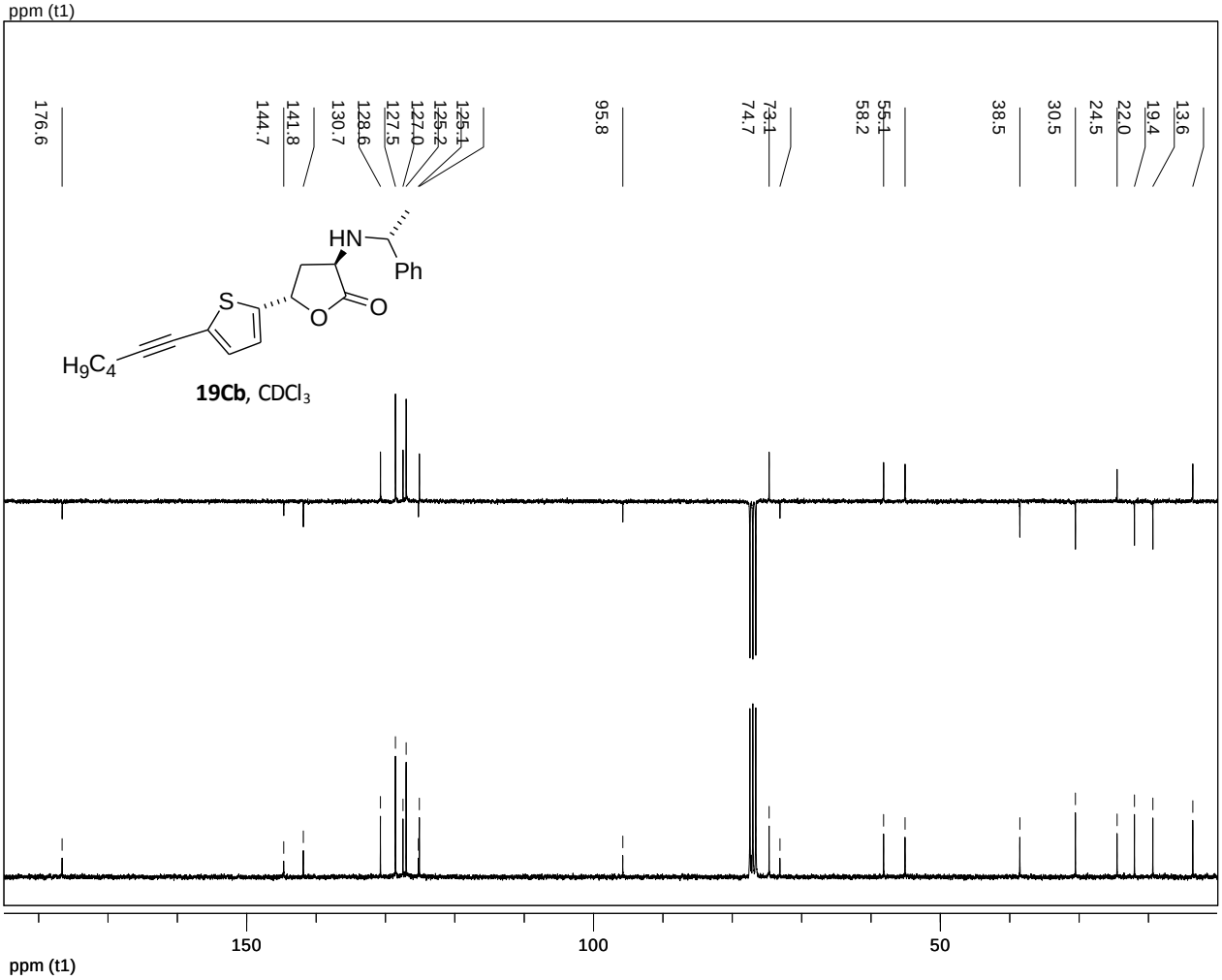
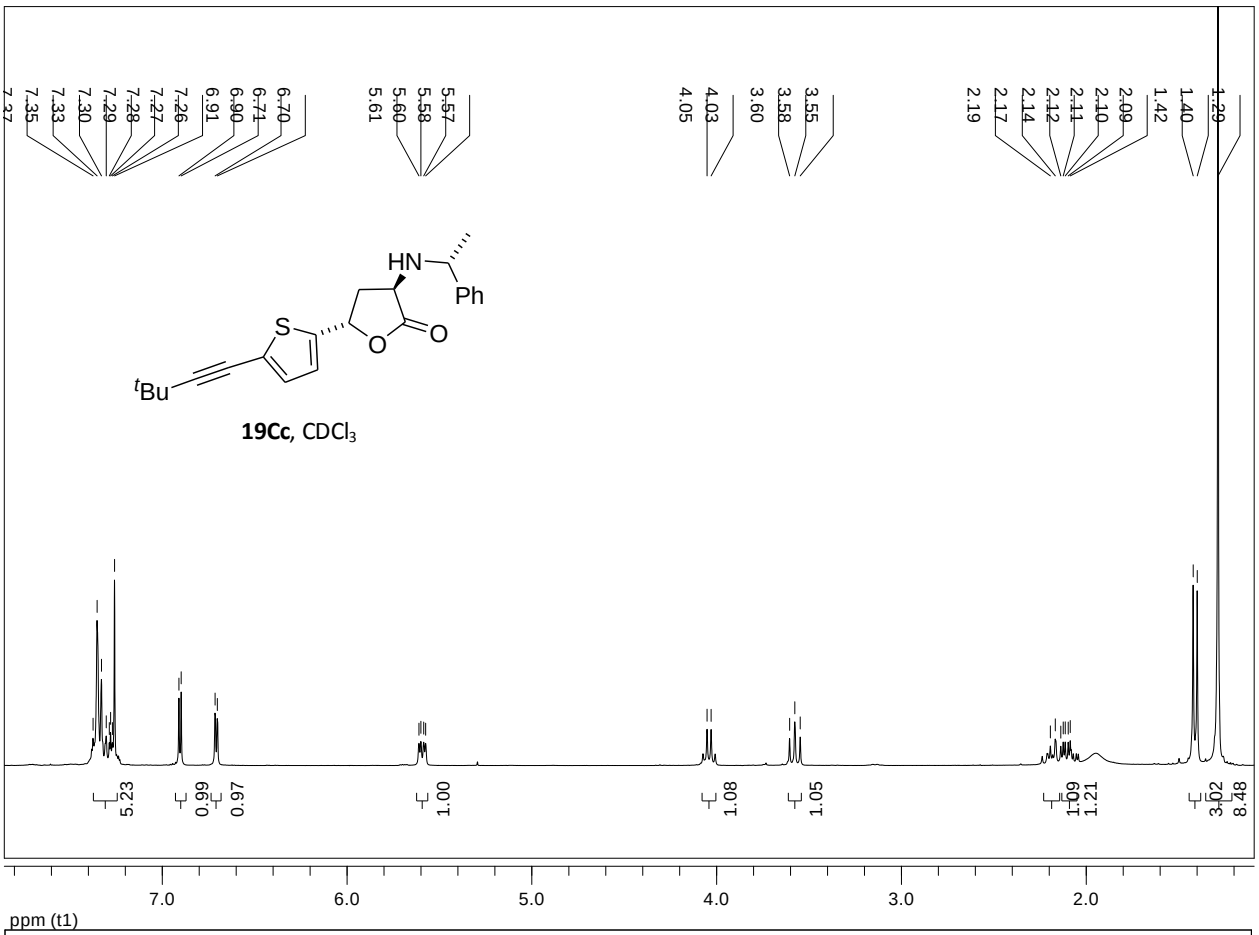
144.6
141.8
130.7
128.5
127.5
127.0
125.2
125.1
95.8
74.7
73.1
58.2
55.1
38.5
31.8
29.2
29.1
28.9
28.4
24.5
22.6
14.1
HN
Ph
S
O
O
H17C8
19Ca, CDCl3
150
100
50
ppm (t1)



19Cb, $CDCl_3$



19Cb, $CDCl_3$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7.27
7.26
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6.90
6.71
6.70
5.61
5.60
5.58
5.57
4.05
4.03
3.60
3.58
3.55
2.19
2.17
2.14
2.12
2.11
2.10
2.09
1.42
1.40
1.29
HN
Ph
S
O
O
tBu
19Cc, CDCl3
5.23
6.60
4.70
1.00
1.08
5.01
1.09
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20.03
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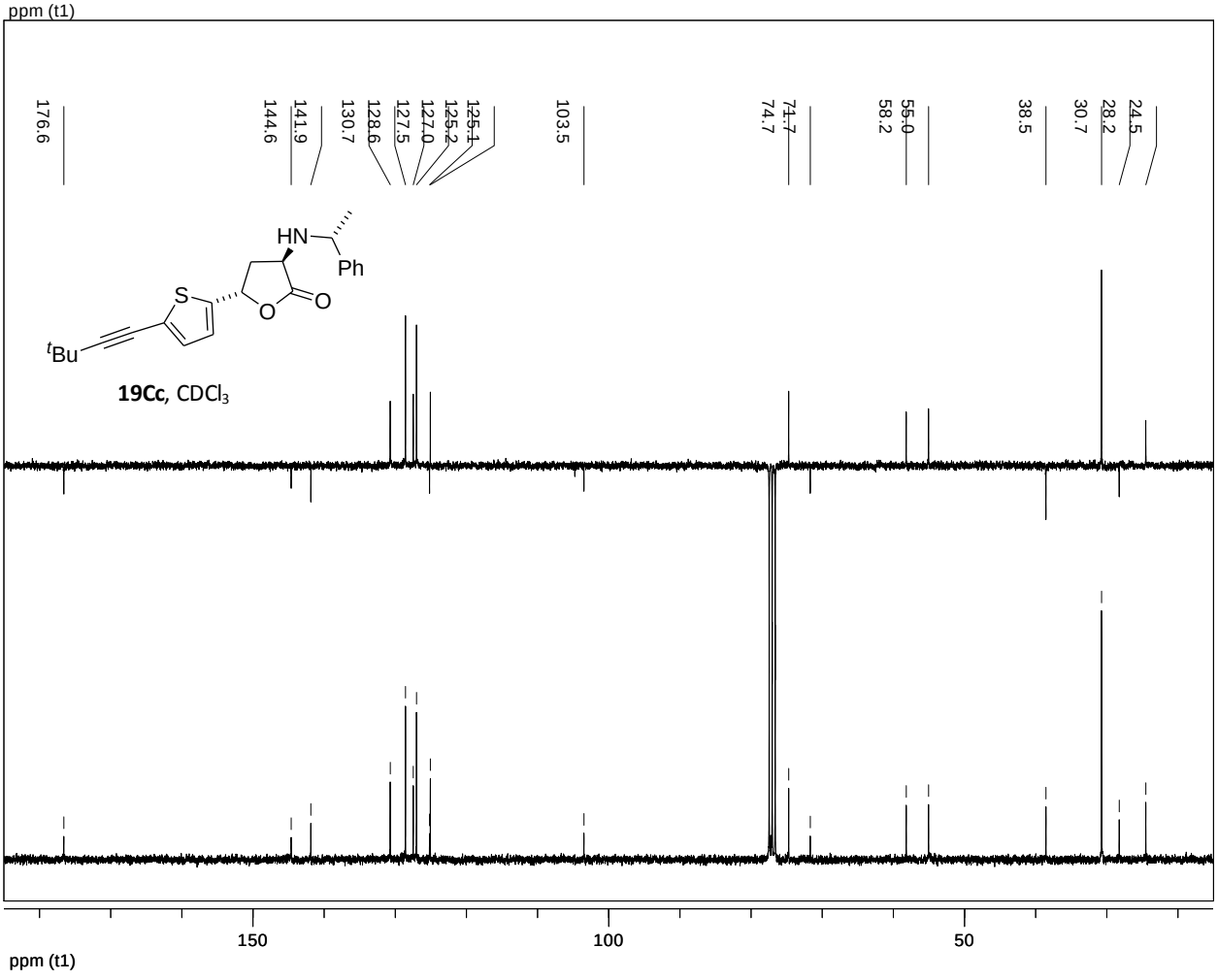
6.0
5.0
4.0
3.0
2.0
ppm (t1)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144.6
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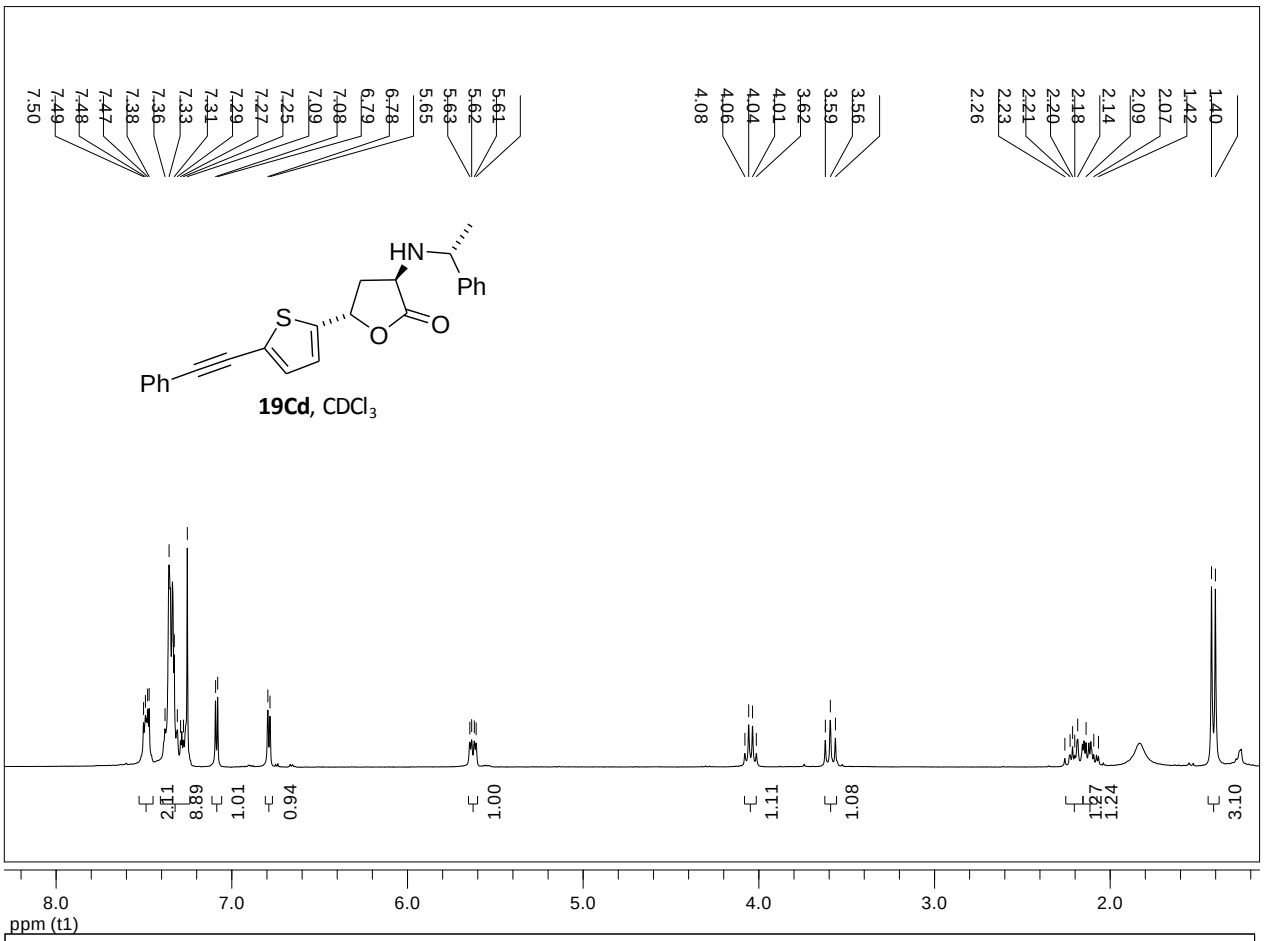
130.7
128.6
127.5
127.0
125.2
125.1
103.5
74.7
71.7
58.2
55.0
38.5
30.7
28.2
24.5
HN
Ph
S
O
O
tBu
19Cc, CDCl3
150
100
50
ppm (t1)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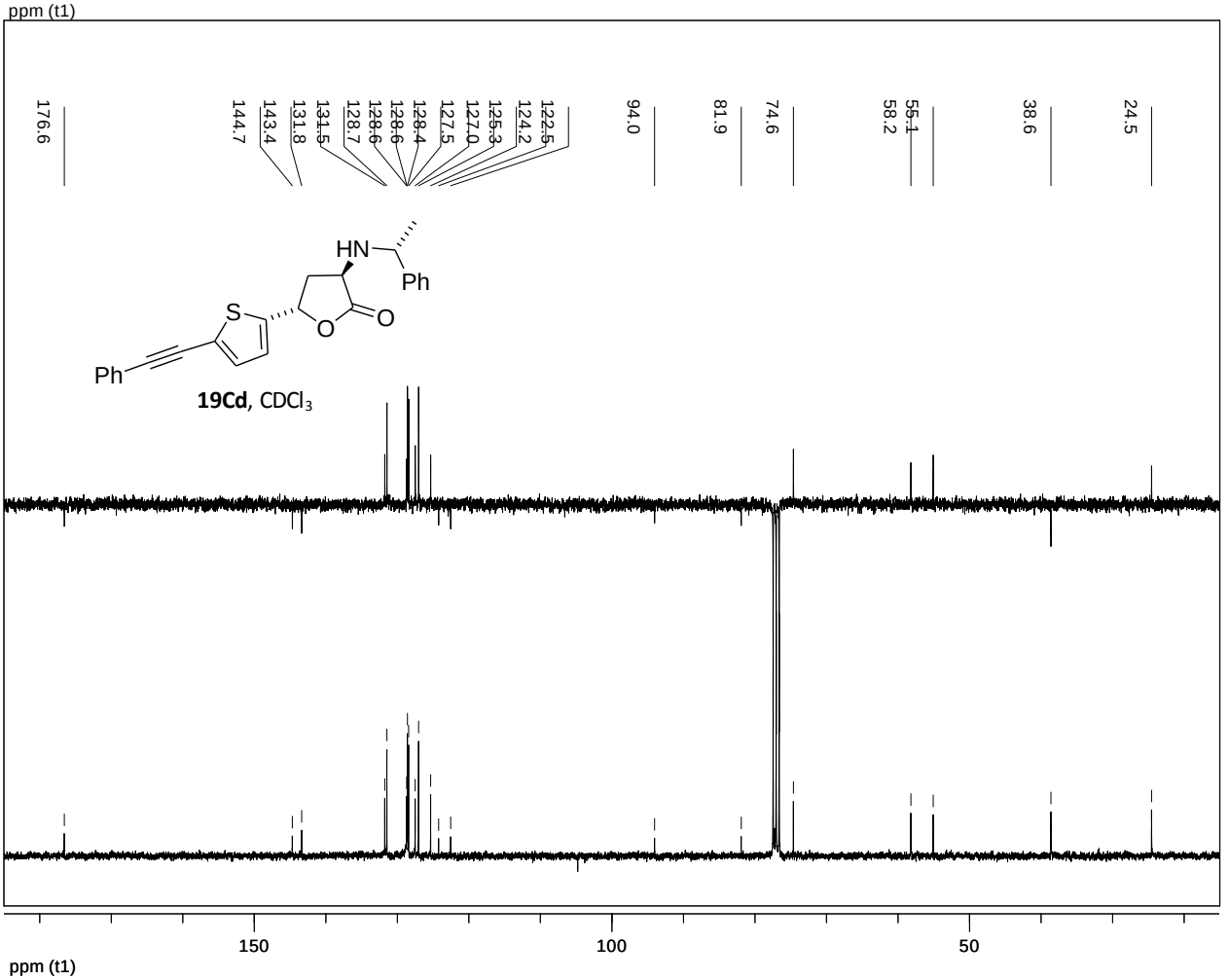
7.27
7.25
7.09
7.08
6.79
6.78
5.65
5.63
5.62
5.61
4.08
4.06
4.04
4.01
3.62
3.59
3.56
2.26
2.23
2.21
2.20
2.18
2.14
2.09
2.07
1.42
1.40
HN
Ph
S
O
O
Ph
19Cd, CDCl3
1.12
1.12
6.88
1.01
0.94
1.00
1.11
1.08
7.21
7.11
3.10
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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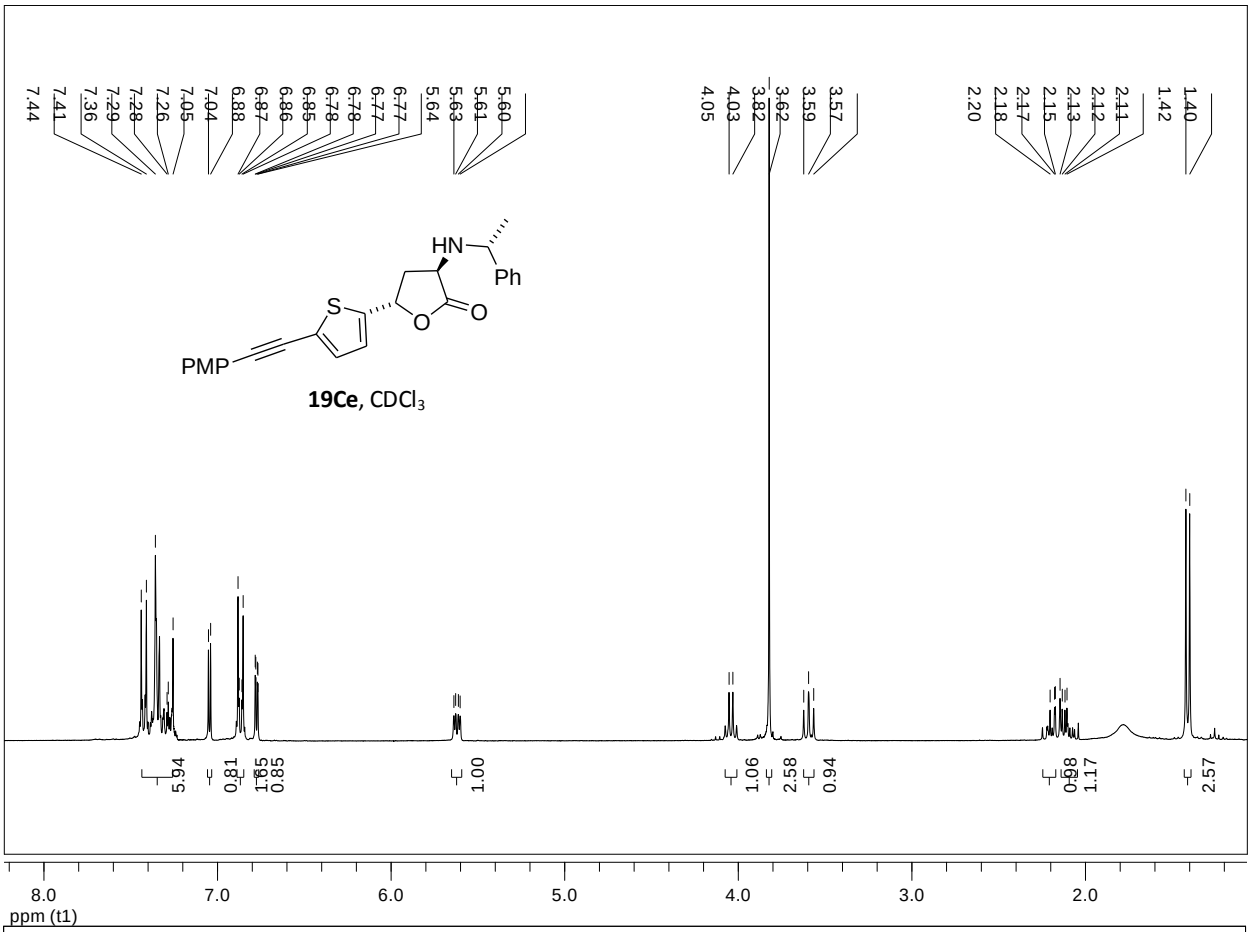
144.7
143.4
131.8
131.5
128.7
128.6
128.6
128.4
127.5
127.0
125.3
124.2
122.5
94.0
81.9
74.6
55.1
58.2
38.6
24.5
HN
Ph
S
O
O
Ph
19Cd, CDCl3
150
100
50
ppm (t1)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7.26
7.05
7.04
6.88
6.87
6.86
6.85
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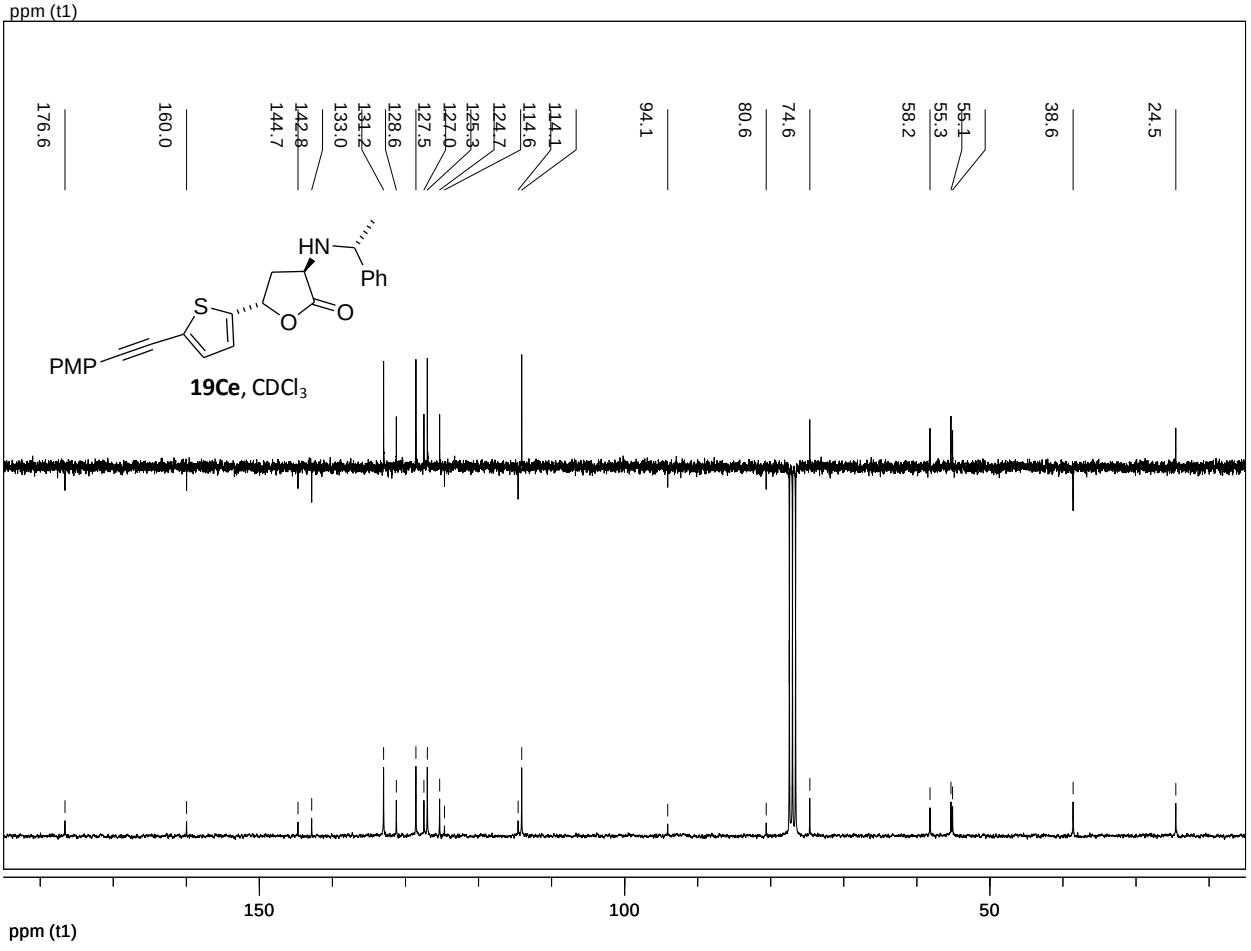
6.78
6.77
6.77
5.64
5.63
5.61
5.60
4.05
4.03
3.82
3.62
3.59
3.57
2.20
2.18
2.17
2.15
2.13
2.12
2.11
1.42
1.40
HN
Ph
S
O
O
PMP
19Ce, CDCl3
4.96
1.80
5.81
5.80
1.00
9.06
8.52
4.04
8.60
11.17
4.57
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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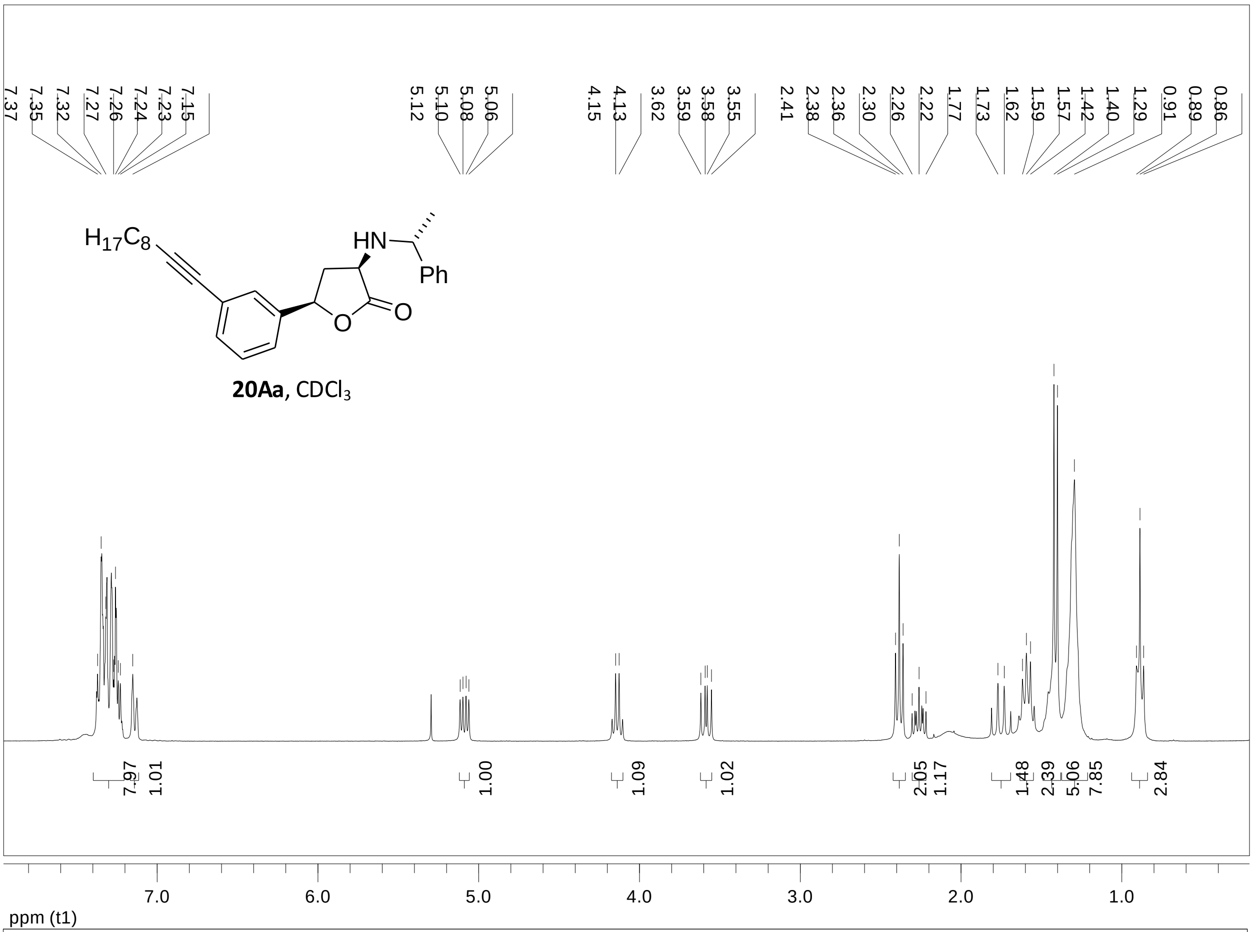
142.8
133.0
131.2
128.6
127.5
127.0
125.3
124.7
114.6
114.1
94.1
80.6
74.6
58.2
55.3
55.1
38.6
24.5
HN
Ph
S
O
O
PMP
19Ce, CDCl3
150
100
50
ppm (t1)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5.12 5.10 5.08 5.06
4.15 4.13 3.62 3.59 3.58 3.55
2.41 2.38 2.36 2.30 2.26 2.22 1.77 1.73 1.62 1.59 1.57 1.42 1.40 1.29 0.91 0.89 0.86
H17C8
HN
Ph
O
O
20Aa, CDCl3
7.97 1.01 1.00 1.09 1.02 2.05 1.17 1.48 2.39 5.06 7.85 2.84
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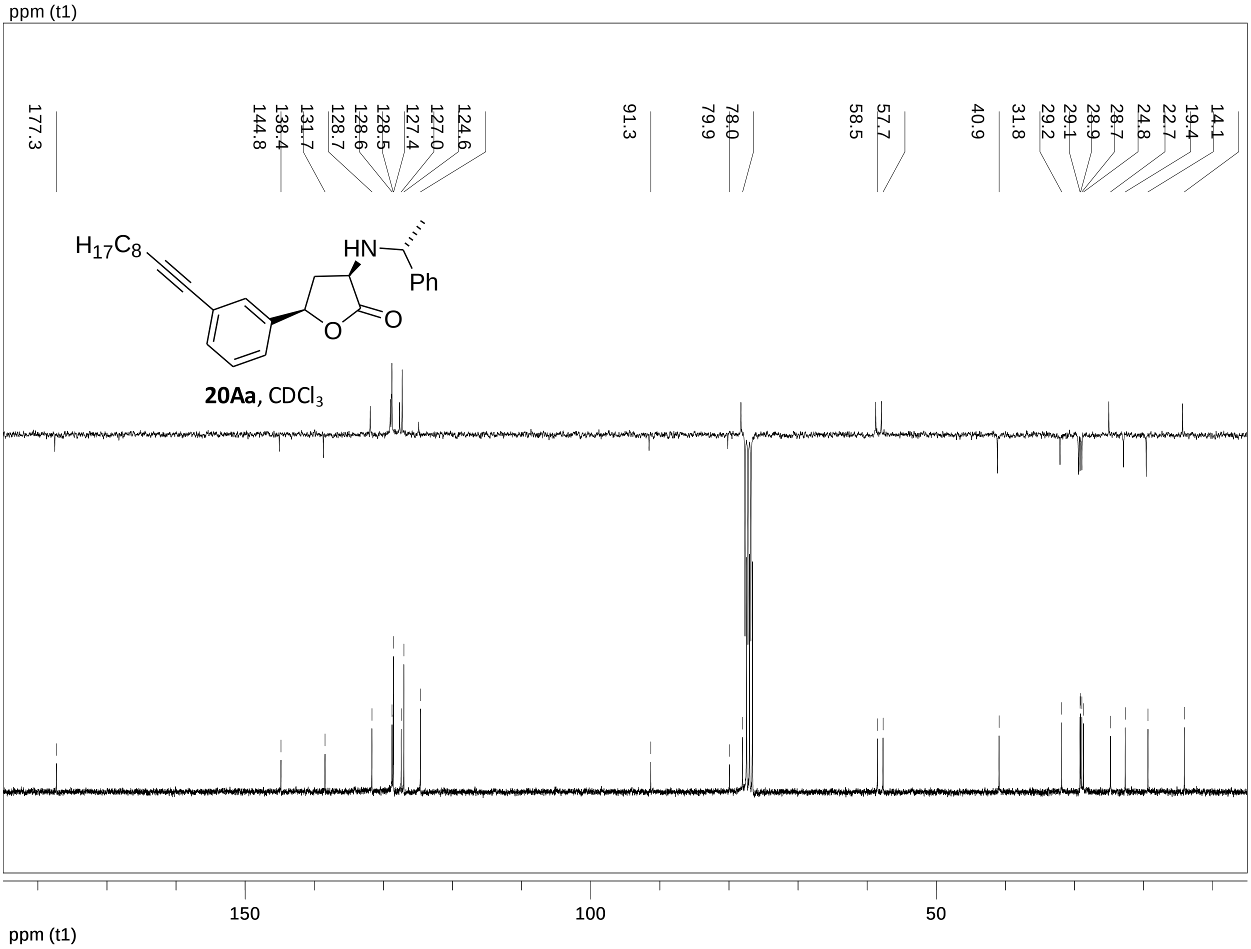
ppm (t1)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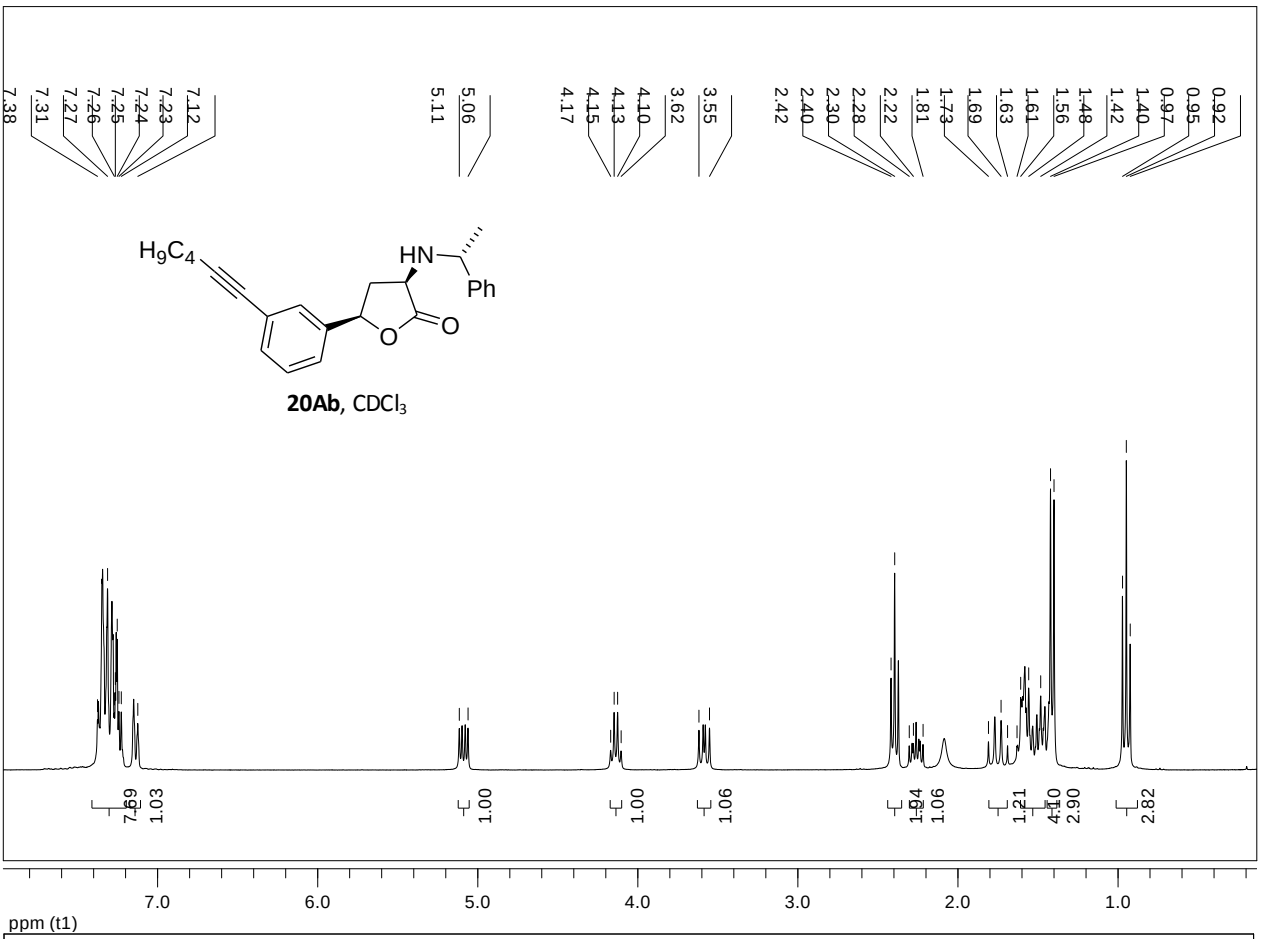
144.8 138.4 131.7 128.7 128.6 128.5 127.4 127.0 124.6
91.3 79.9 78.0
58.5 57.7
40.9 31.8 29.2 29.1 28.9 28.7 24.8 22.7 19.4 14.1
H17C8
HN
Ph
O
O
20Aa, CDCl3
150 100 50
ppm (t1)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7.23
7.12
5.11
5.06
4.17
4.15
4.13
4.10
3.62
3.55
2.42
2.40
2.30
2.28
2.22
1.81
1.73
1.69
1.63
1.61
1.56
1.48
1.42
1.40
0.97
0.95
0.92
H9C4
HN
Ph
O
O
20Ab, CDCl3
7.69
1.03
1.00
1.00
1.06
1.94
1.06
1.21
4.10
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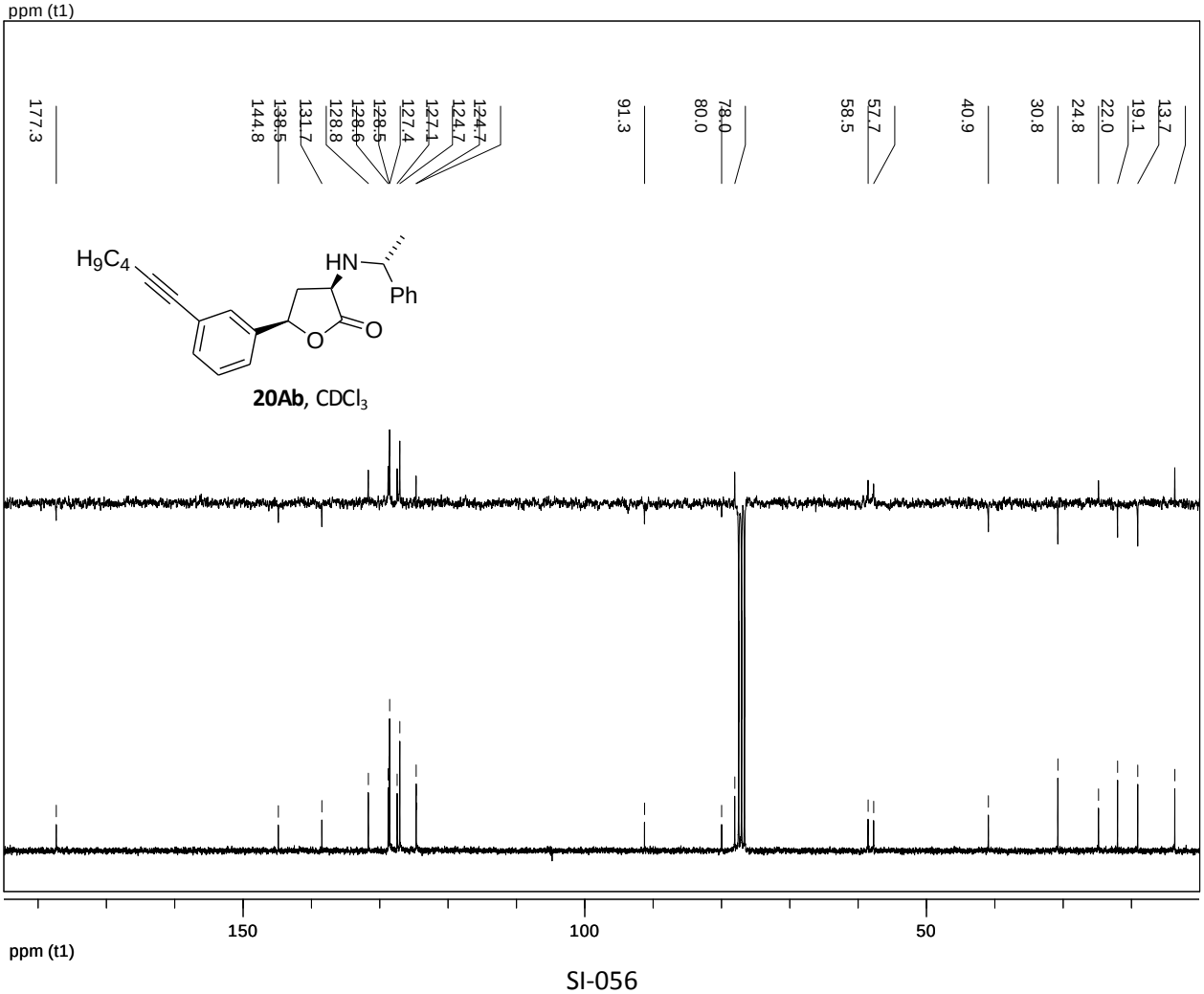
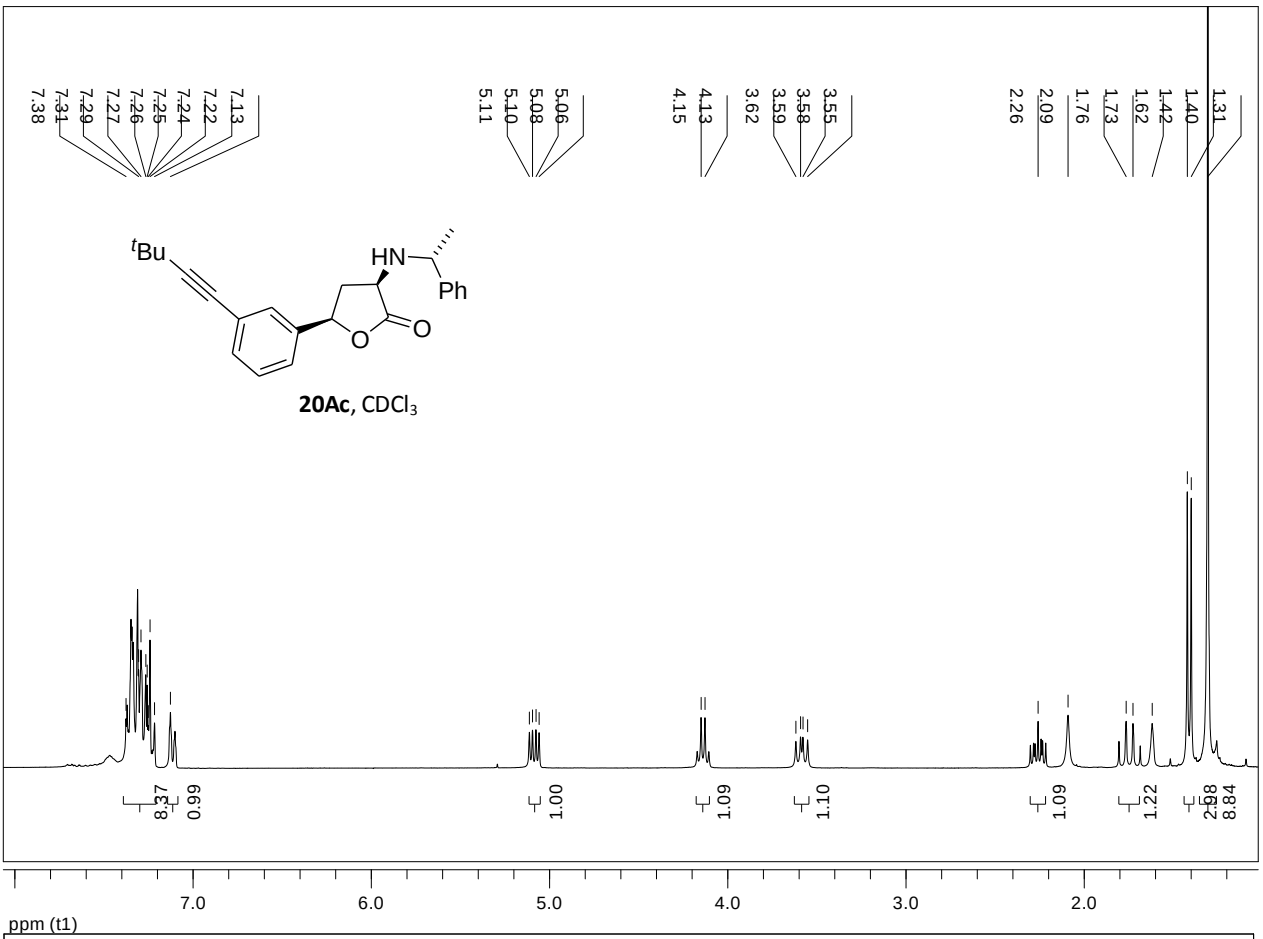
2.82
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


177.3
144.8
138.5
131.7
128.8
128.6
128.5
127.4
127.1
124.7
124.7
91.3
80.0
78.0
58.5
57.7
40.9
30.8
24.8
22.0
19.1
13.7
H9C4
HN
Ph
O
O
20Ab, CDCl3
150
100
50
ppm (t1)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7.13
5.11
5.10
5.08
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3.62
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2.26
2.09
1.76
1.73
1.62
1.42
1.40
1.31
tBu
HN
Ph
O
O
20Ac, CDCl3
8.37
0.99
1.00
1.09
1.10
1.09
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8.52
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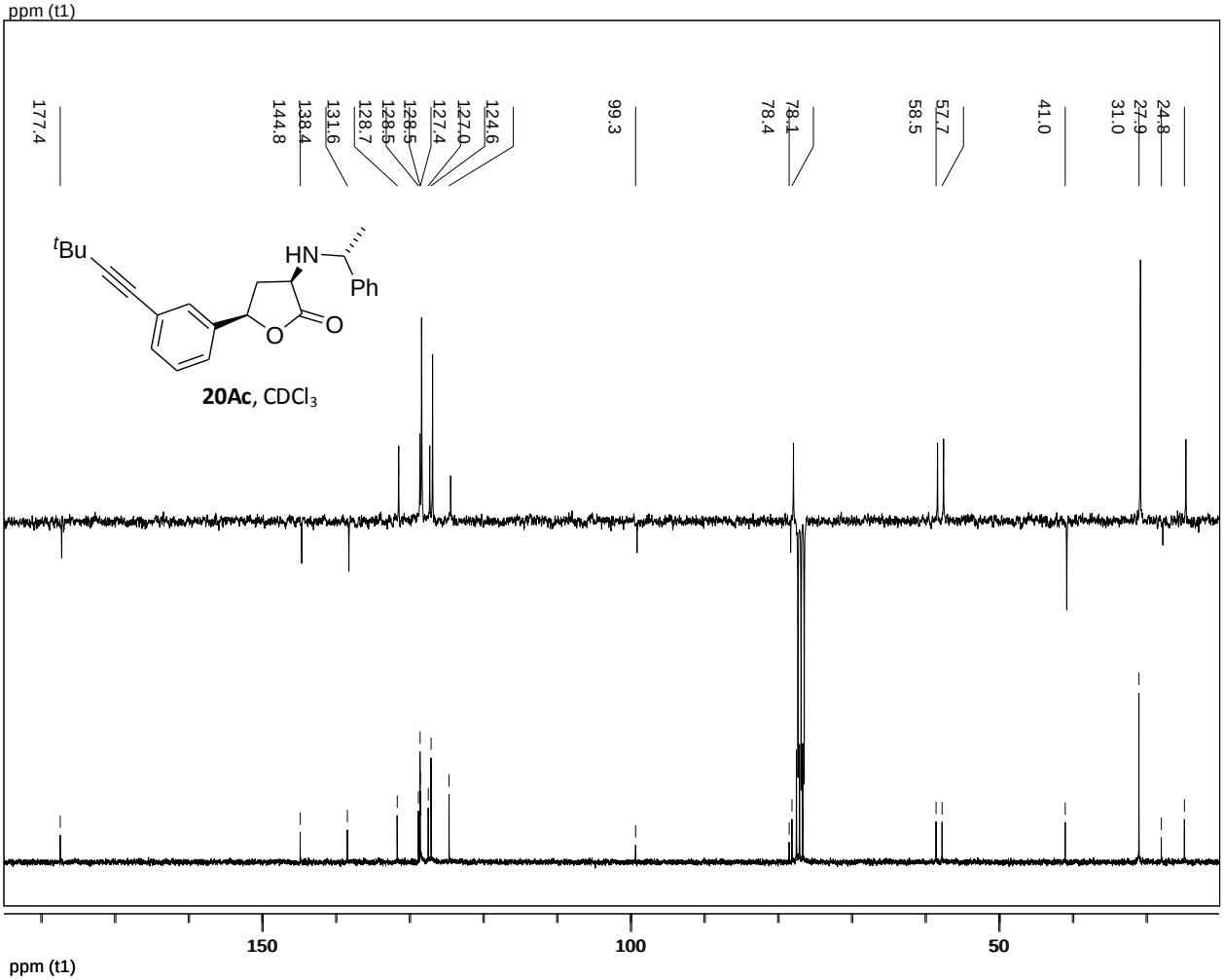
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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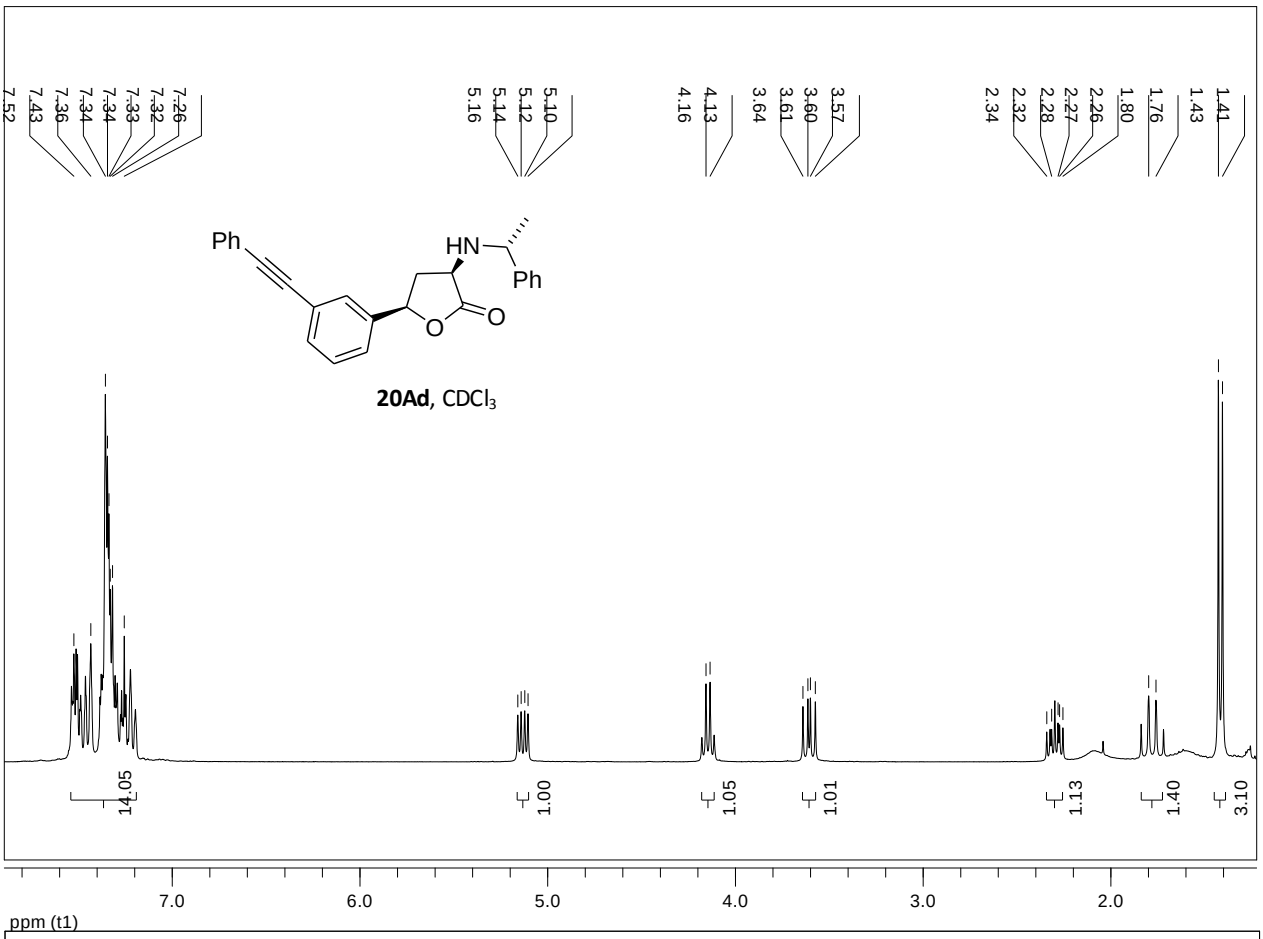
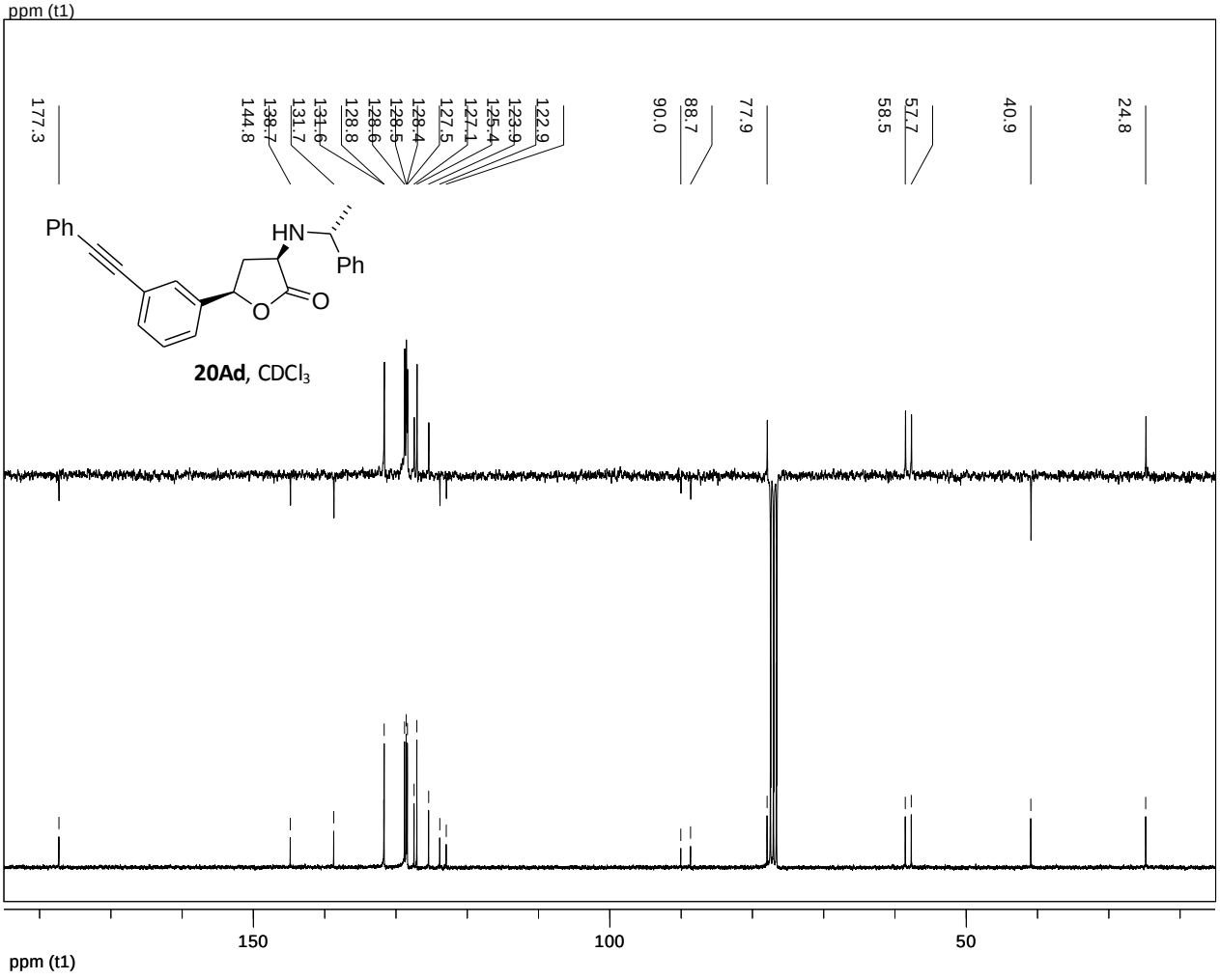
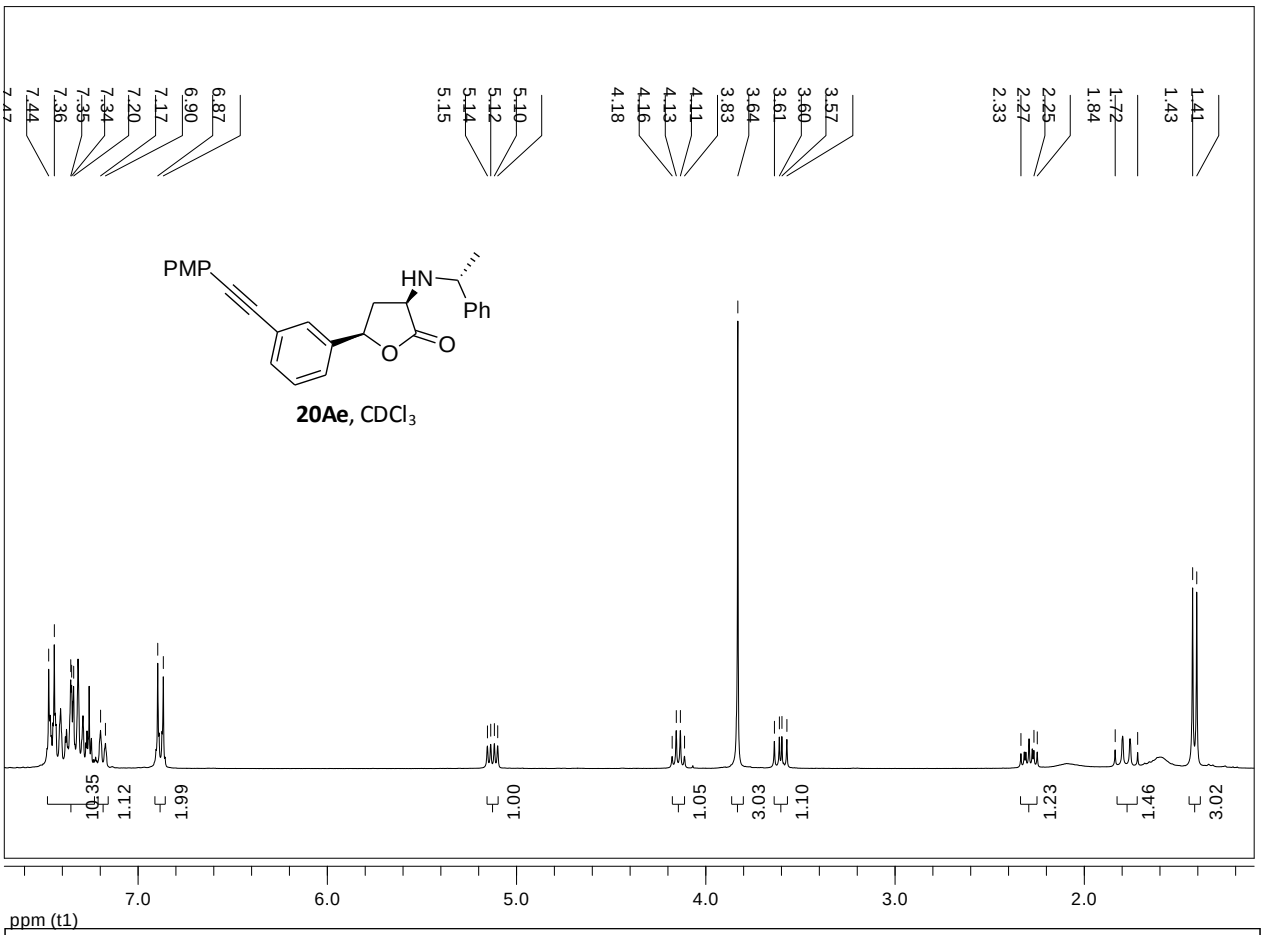
128.5
127.4
127.0
124.6
99.3
78.4
78.1
58.5
57.7
41.0
31.0
27.9
24.8
tBu
HN
Ph
O
O
20Ac, CDCl3
150
100
50
ppm (t1)



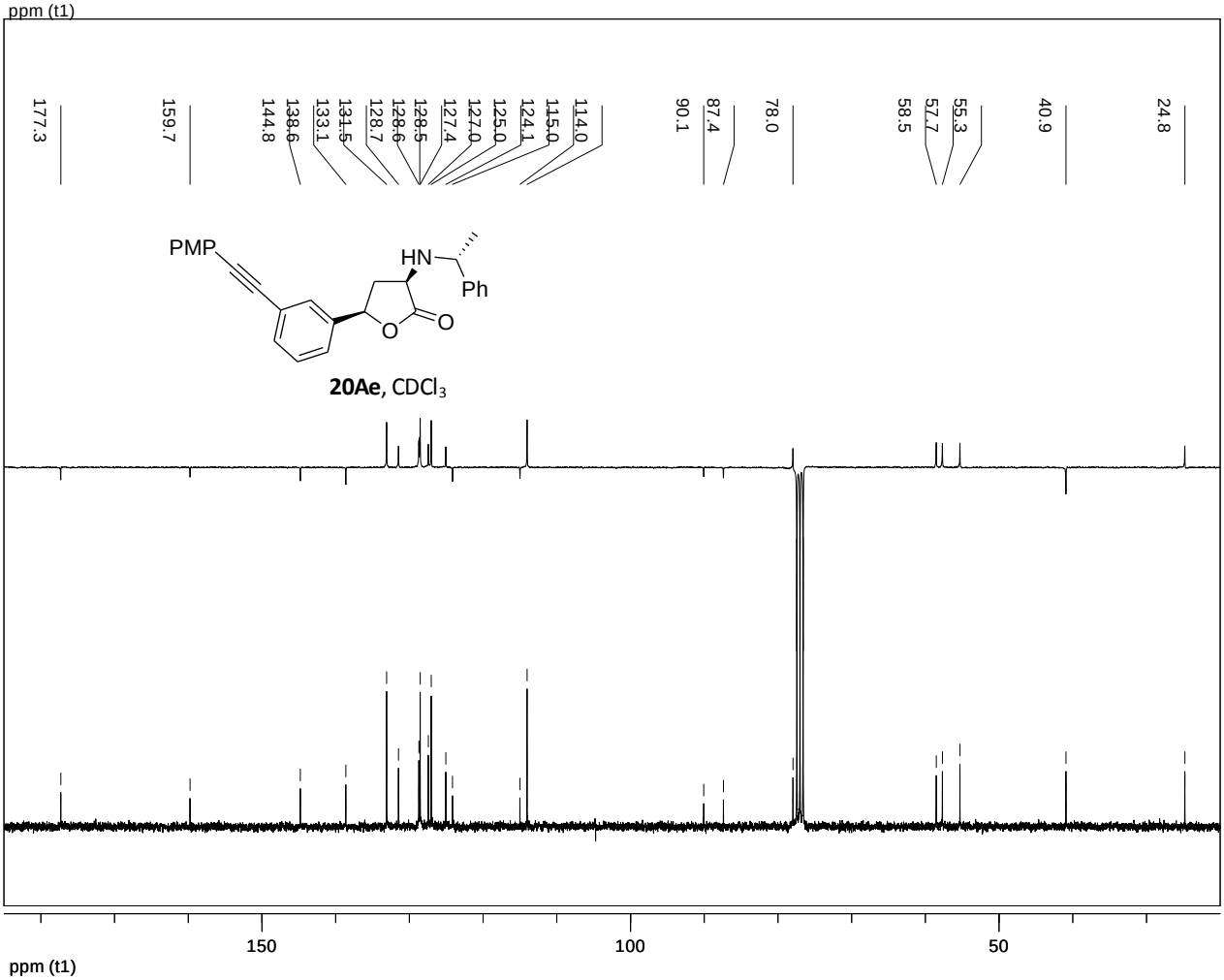
20Ad, $CDCl_3$



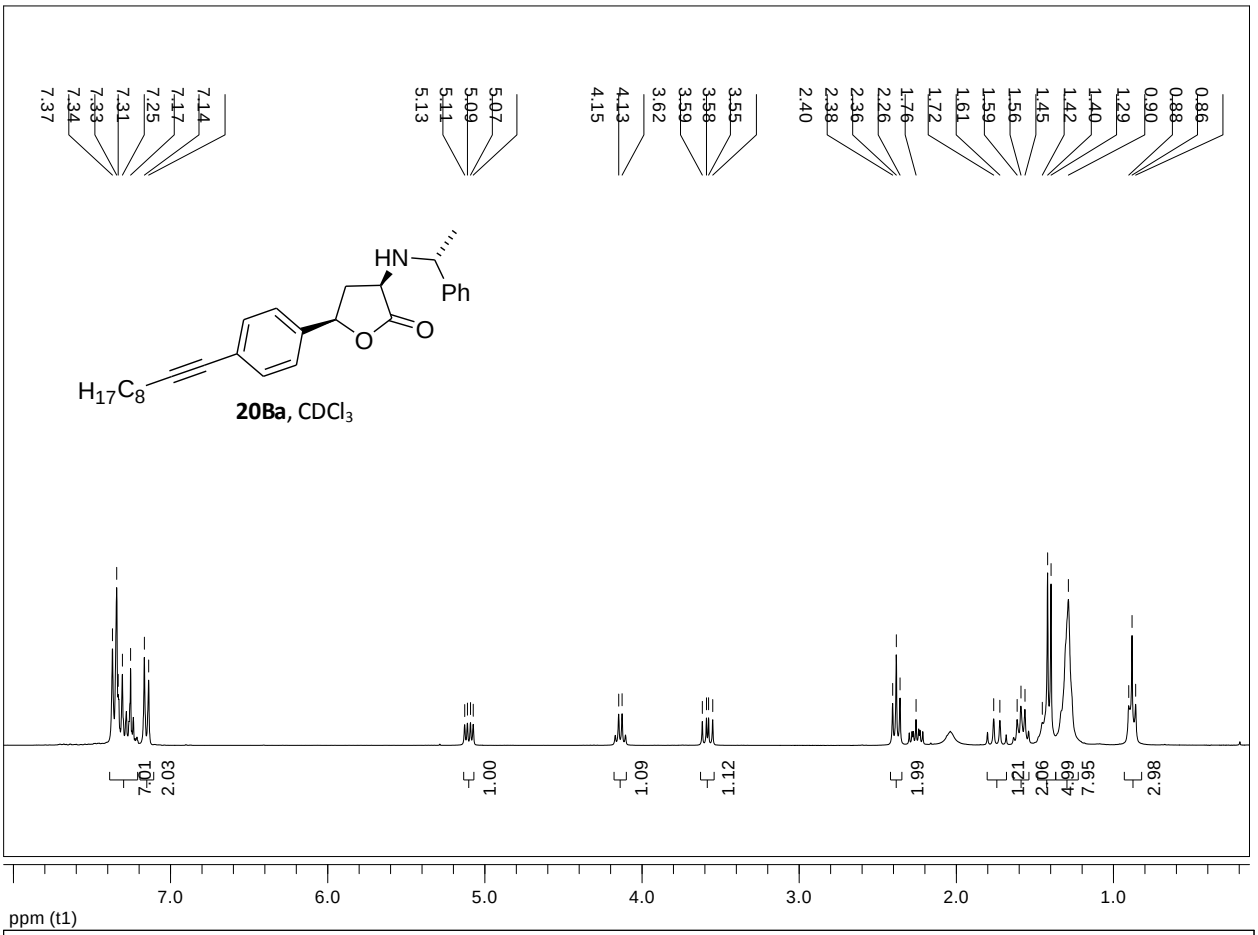
20Ad, $CDCl_3$



20Ae, $CDCl_3$



20Ae, $CDCl_3$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7.14
5.13
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5.09
5.07
4.15
4.13
3.62
3.59
3.58
3.55
2.40
2.38
2.36
2.26
1.76
1.72
1.61
1.59
1.56
1.45
1.42
1.40
1.29
0.90
0.88
0.86
HN
Ph
O
O
$H_{17}C_8$
20Ba, $CDCl_3$
2.08
1.01
1.00
1.09
1.12
1.99
1.21
2.00
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2.98
7.0
6.0
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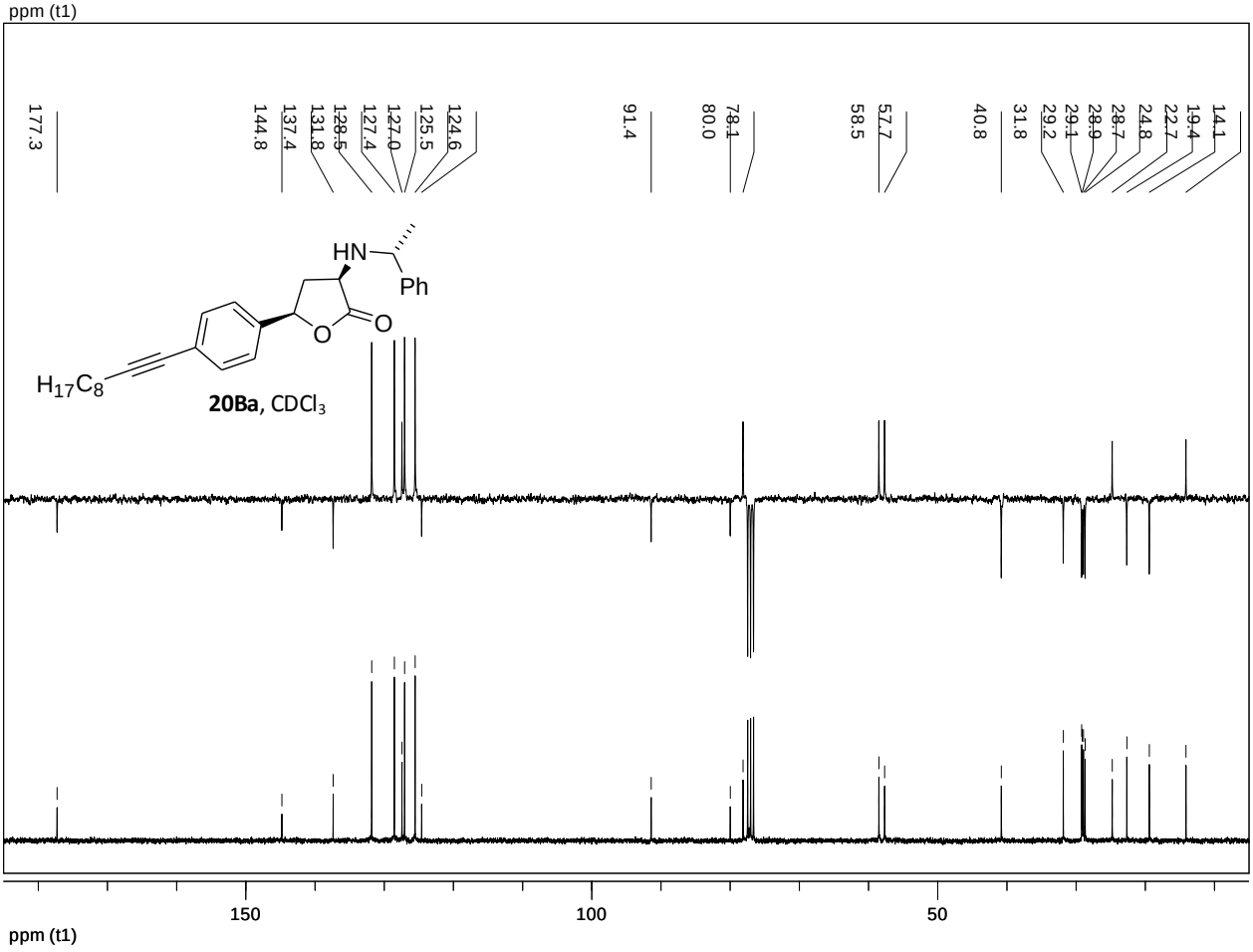
4.0
3.0
2.0
1.0
ppm (t1)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131.8
128.5
127.4
127.0
125.5
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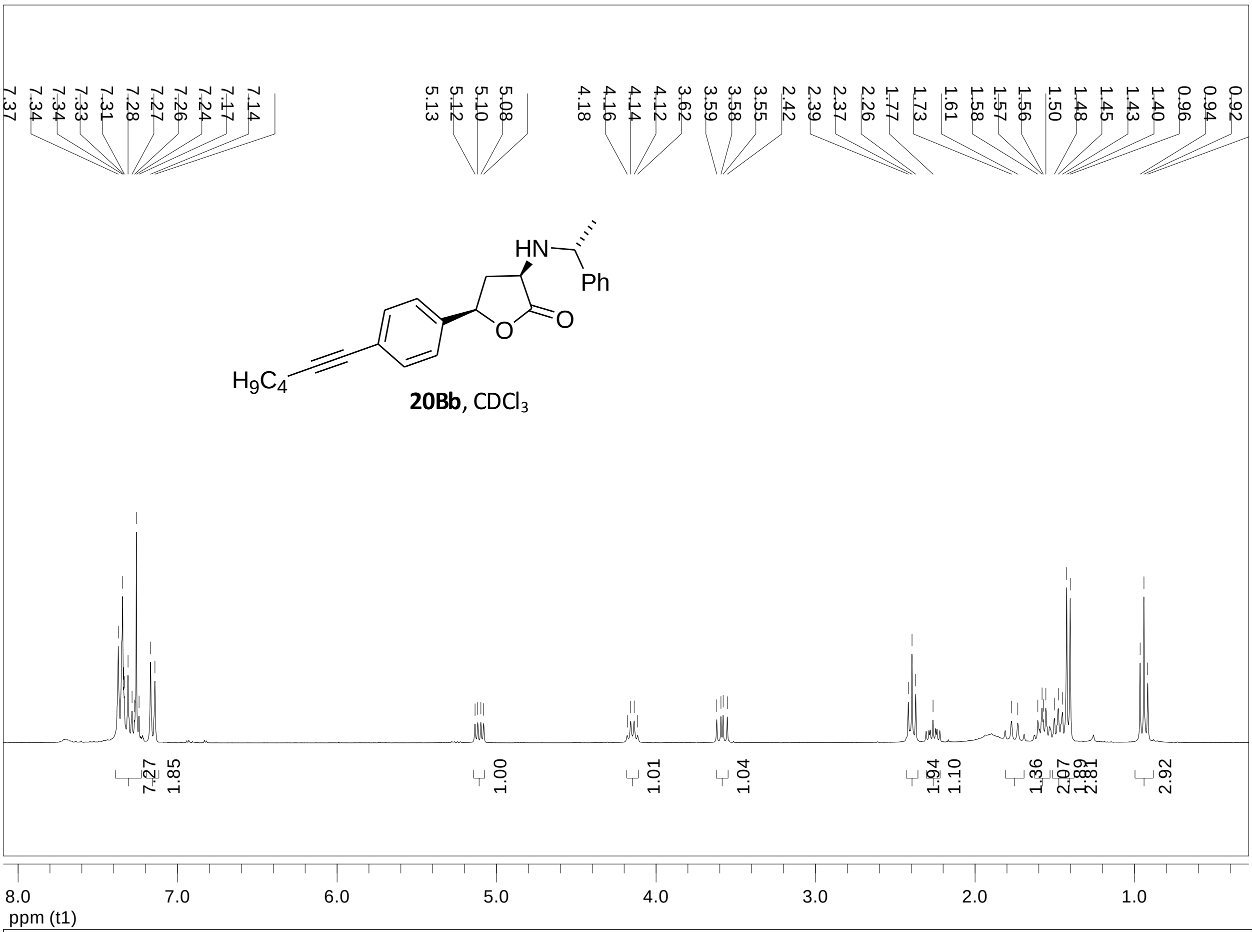
91.4
80.0
78.1
58.5
57.7
40.8
31.8
29.2
29.1
28.9
28.7
24.8
22.7
19.4
14.1
HN
Ph
O
O
$H_{17}C_8$
20Ba, $CDCl_3$
150
100
50
ppm (t1)



7.37 7.34 7.34 7.33 7.31 7.28 7.27 7.26 7.24 7.17 7.14
5.13 5.12 5.10 5.08
4.18 4.16 4.14 4.12 3.62 3.59 3.58 3.55 2.42 2.39 2.37 2.26 1.77 1.73 1.61 1.58 1.57 1.56 1.50 1.48 1.45 1.43 1.40 0.96 0.94 0.92
HN
Ph
O
O
H_9C_4
20Bb, $CDCl_3$
7.27 1.85 1.00 1.01 1.04 1.94 1.10 1.36 2.07 1.89 2.81 2.92
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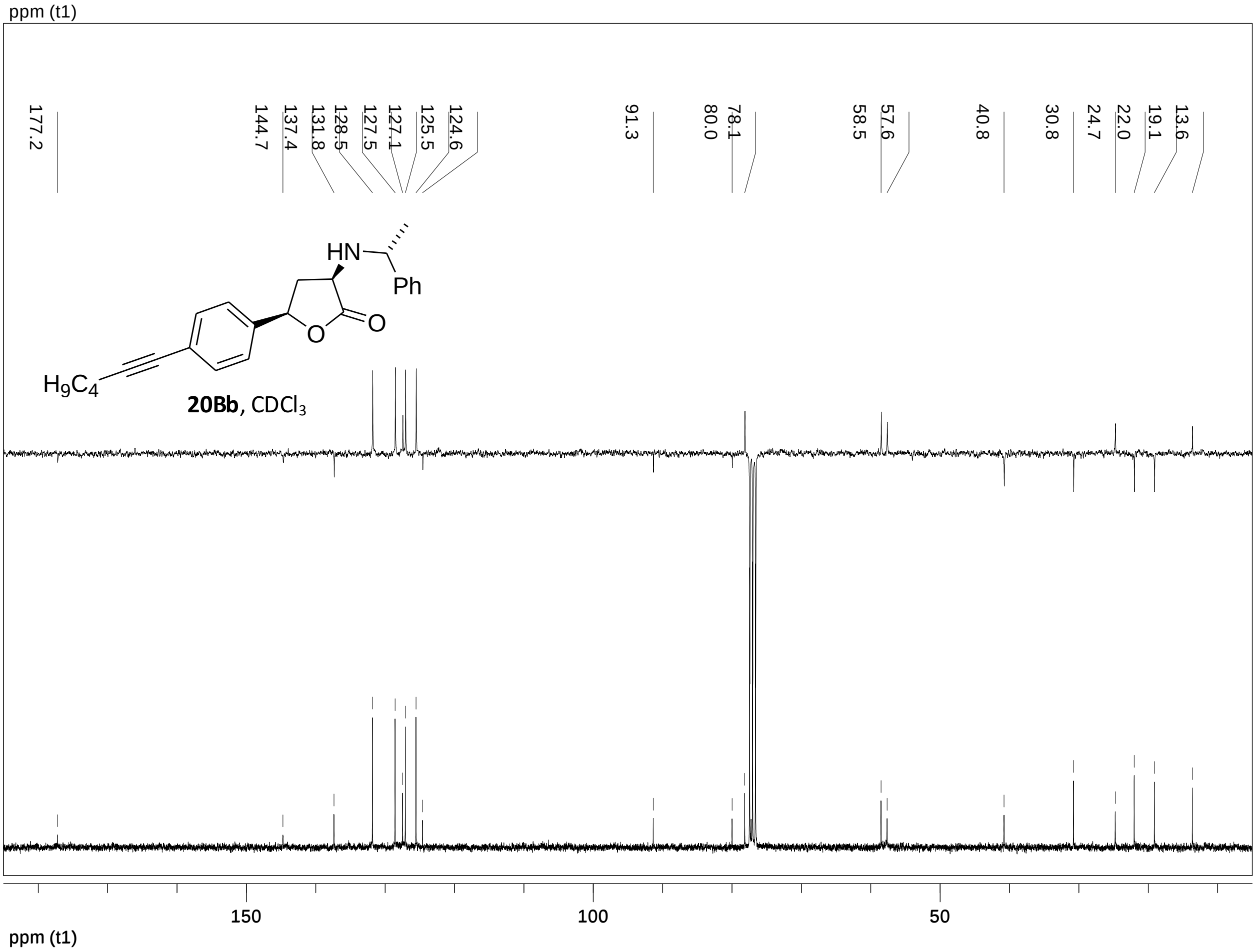
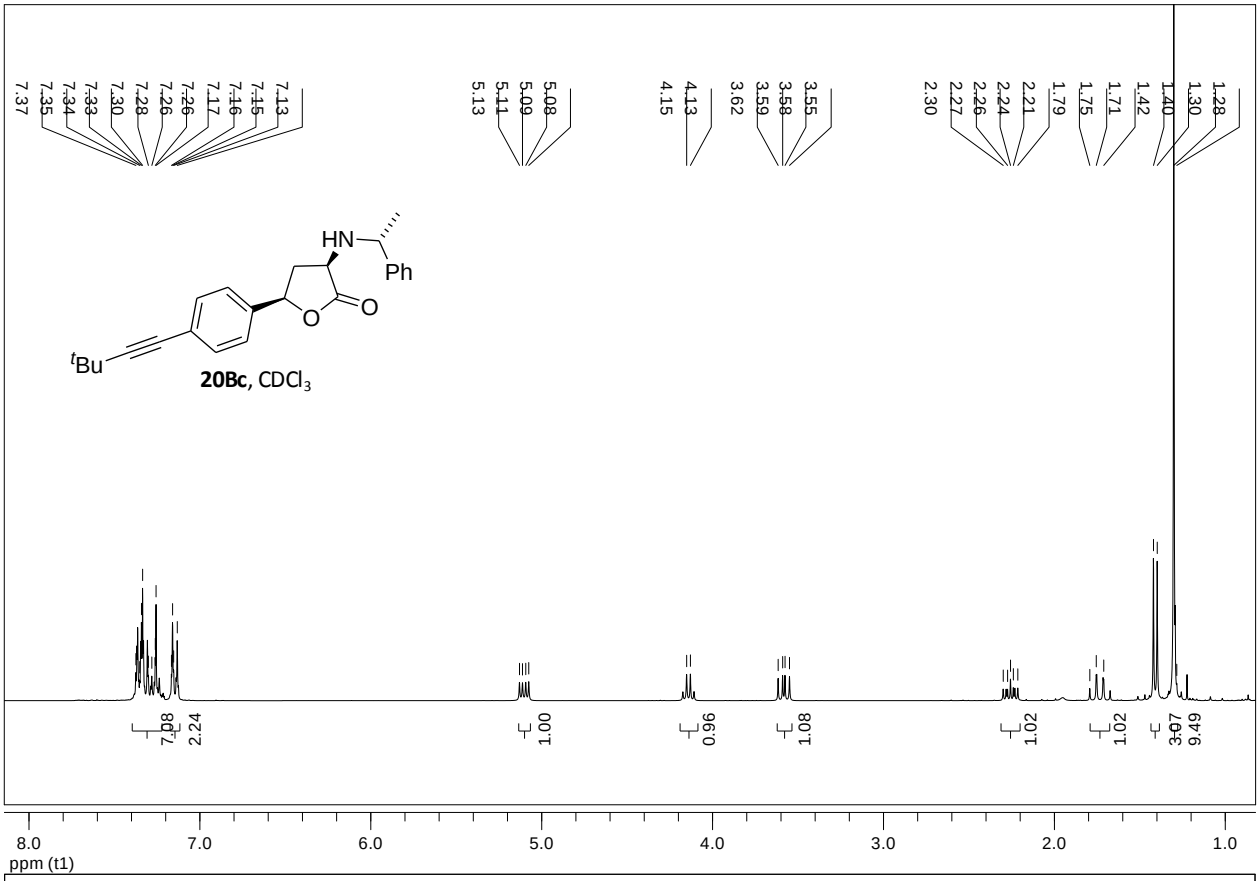
ppm (t1)



177.2
144.7 137.4 131.8 128.5 127.5 127.1 125.5 124.6
91.3 80.0 78.1
58.5 57.6
40.8
30.8 24.7 22.0 19.1 13.6
HN
Ph
O
O
H_9C_4
20Bb, $CDCl_3$
150 100 50
ppm (t1)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5.11
5.09
5.08
4.15
4.13
3.62
3.59
3.58
3.55
2.30
2.27
2.26
2.24
2.21
1.79
1.75
1.71
1.42
1.40
1.30
1.28
HN
Ph
O
O
tBu
20Bc, CDCl3
2.24
1.08
1.00
0.96
1.08
1.02
1.02
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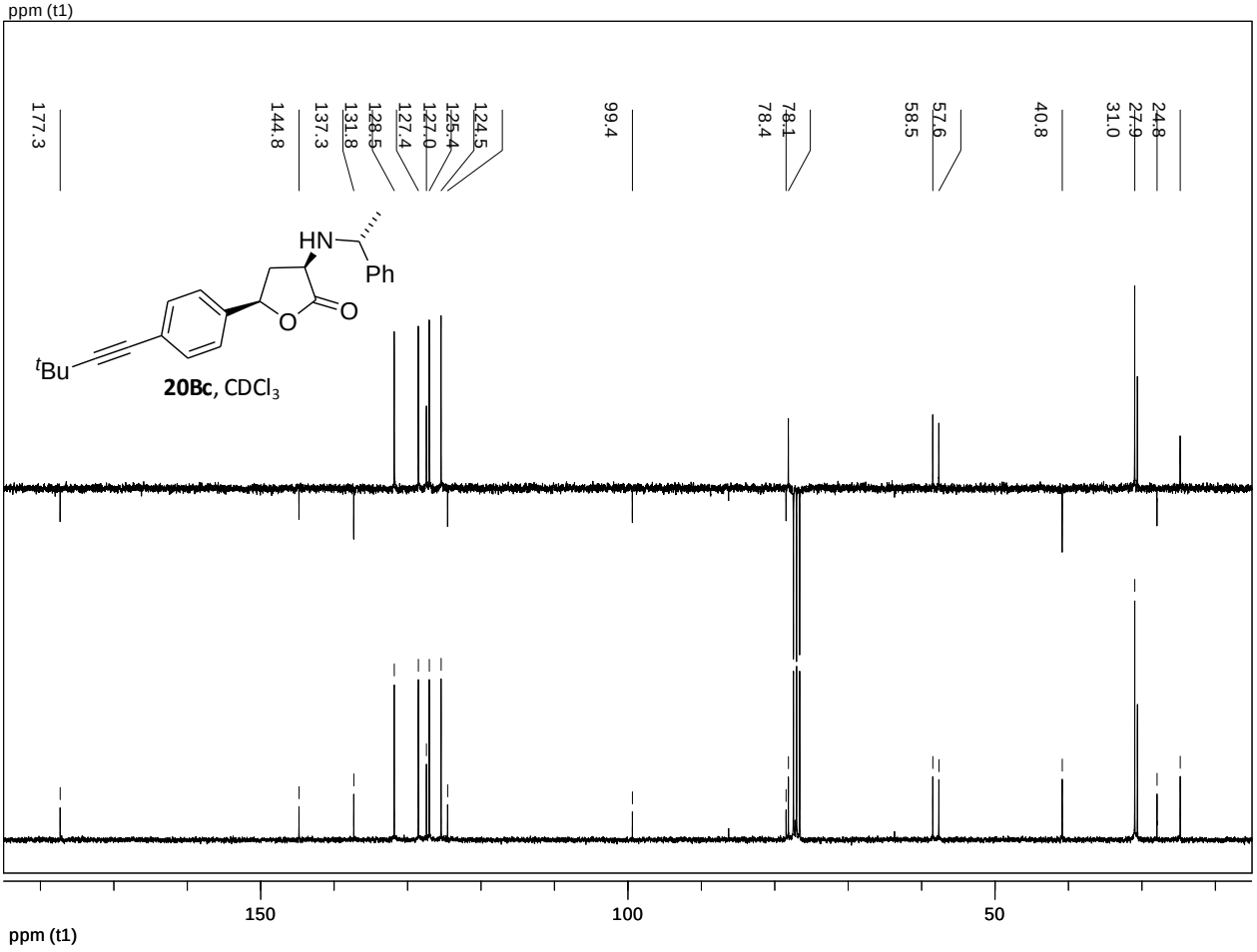
2.0
1.0
ppm (t1)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125.4
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78.4
78.1
58.5
57.6
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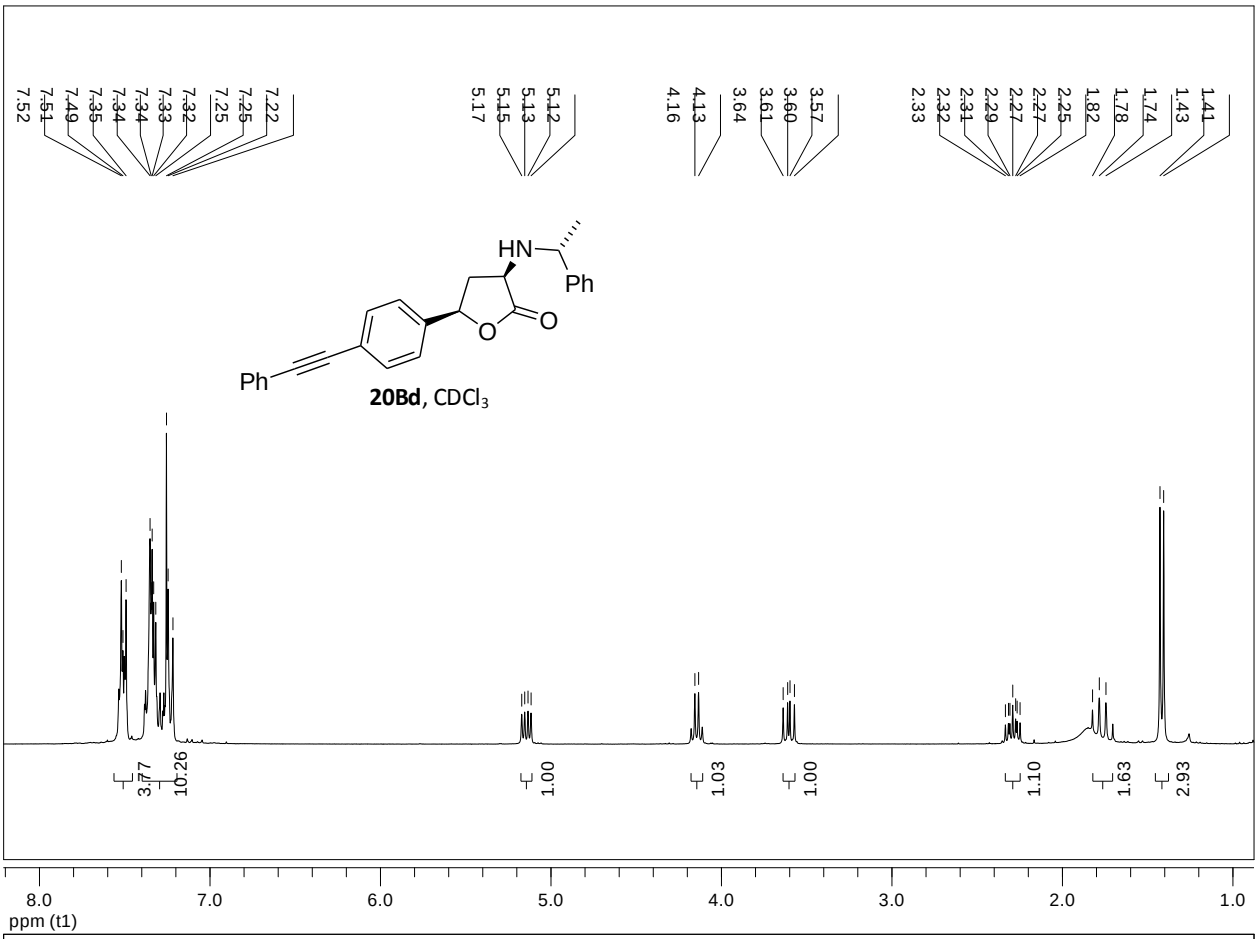
24.8
HN
Ph
O
O
tBu
20Bc, CDCl3
150
100
50
ppm (t1)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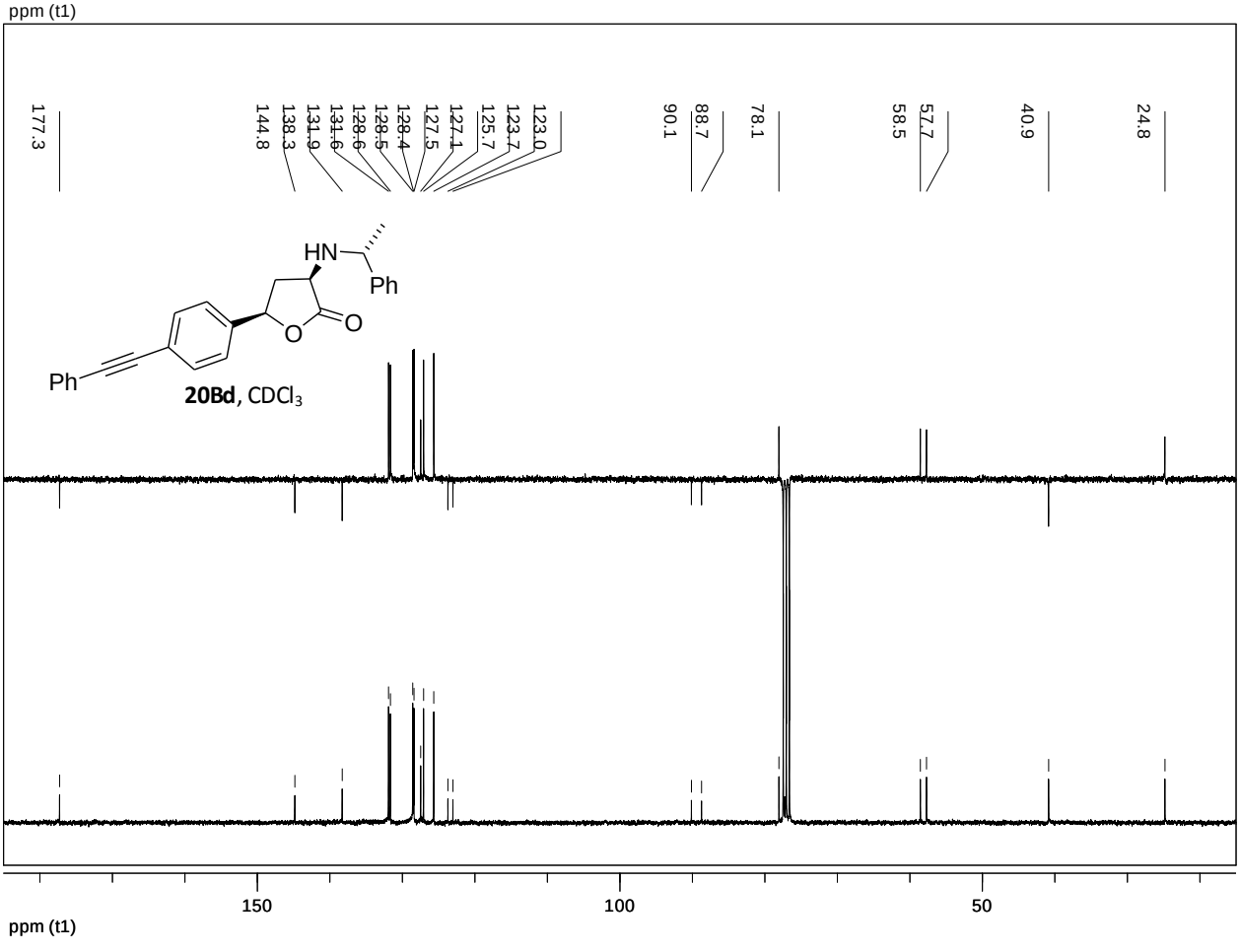
5.17
5.15
5.13
5.12
4.16
4.13
3.64
3.61
3.60
3.57
2.33
2.32
2.31
2.29
2.27
2.27
2.25
1.82
1.78
1.74
1.43
1.41
HN
Ph
O
O
Ph
20Bd, CDCl3
3.47
10.26
1.00
1.03
1.00
1.10
1.63
2.93
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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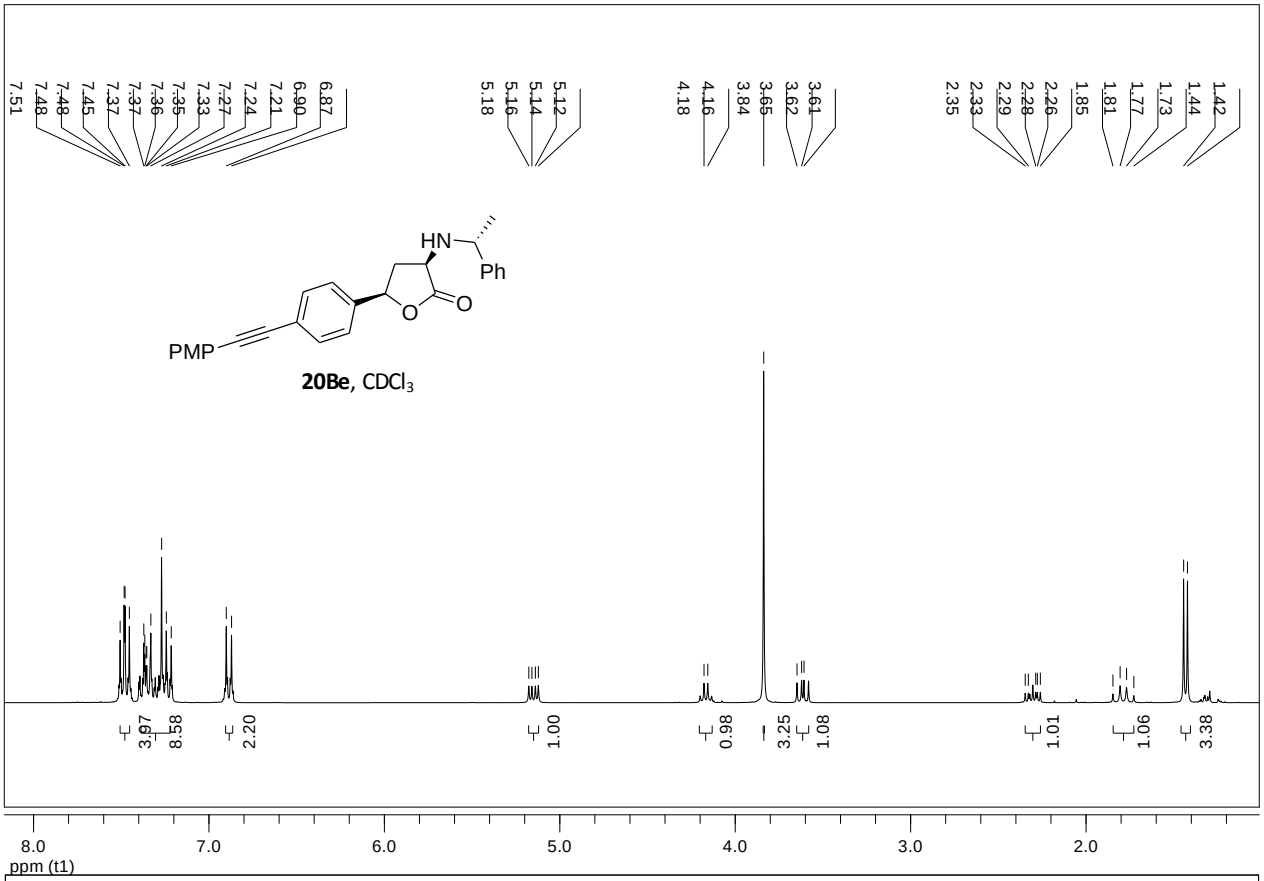
138.3
131.9
131.6
128.6
128.5
128.4
127.5
127.1
125.7
123.7
123.0
90.1
88.7
78.1
58.5
57.7
40.9
24.8
HN
Ph
O
O
Ph
20Bd, CDCl3
150
100
50
ppm (t1)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7.37
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7.35
7.33
7.27
7.24
7.21
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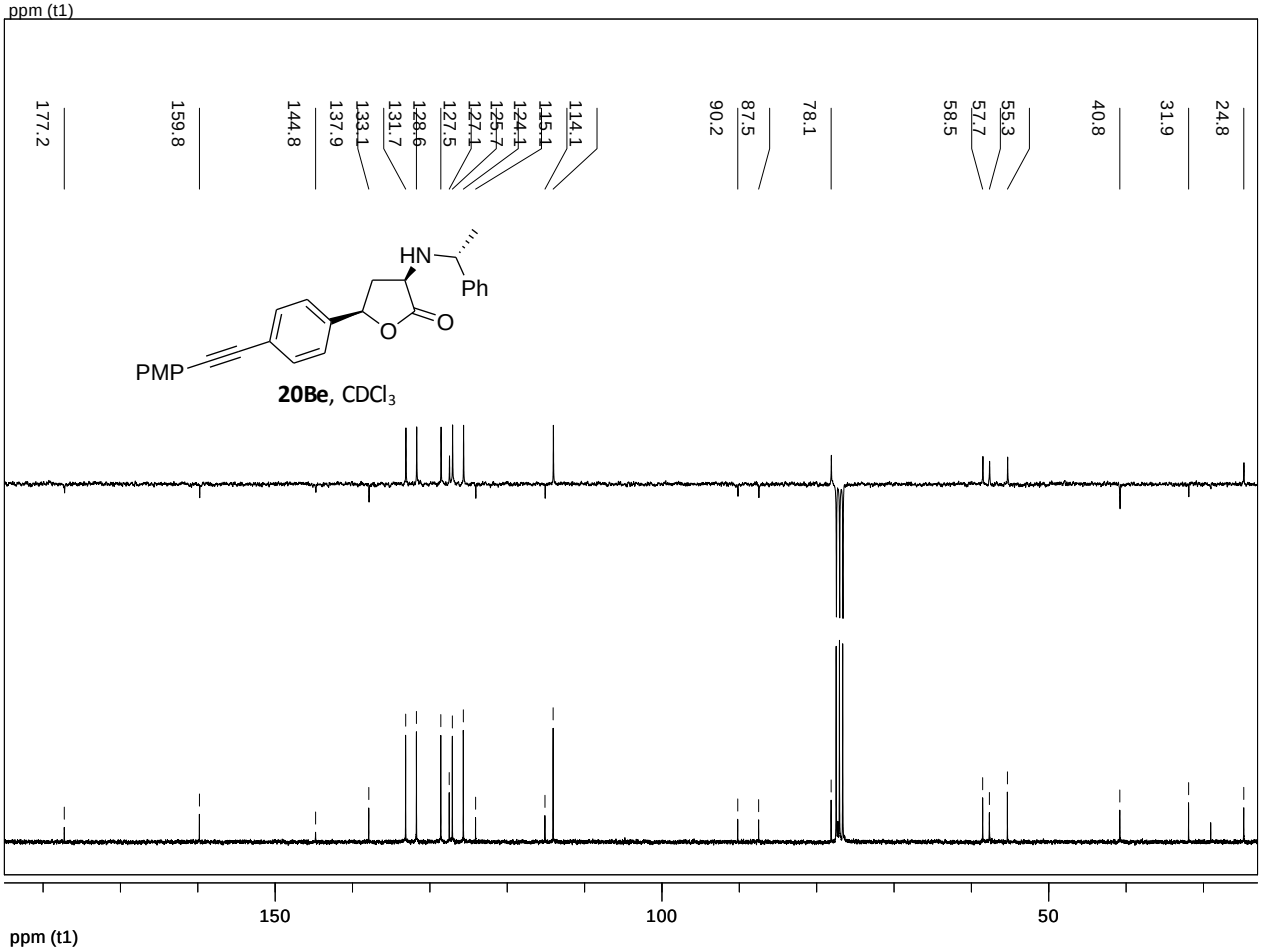
6.87
5.18
5.16
5.14
5.12
4.18
4.16
3.84
3.65
3.62
3.61
2.35
2.33
2.29
2.28
2.26
1.85
1.81
1.77
1.73
1.44
1.42
HN
Ph
O
O
PMP
20Be, CDCl3
3.97
8.58
2.20
1.00
0.98
3.25
1.08
1.01
1.06
3.38
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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159.8
144.8
137.9
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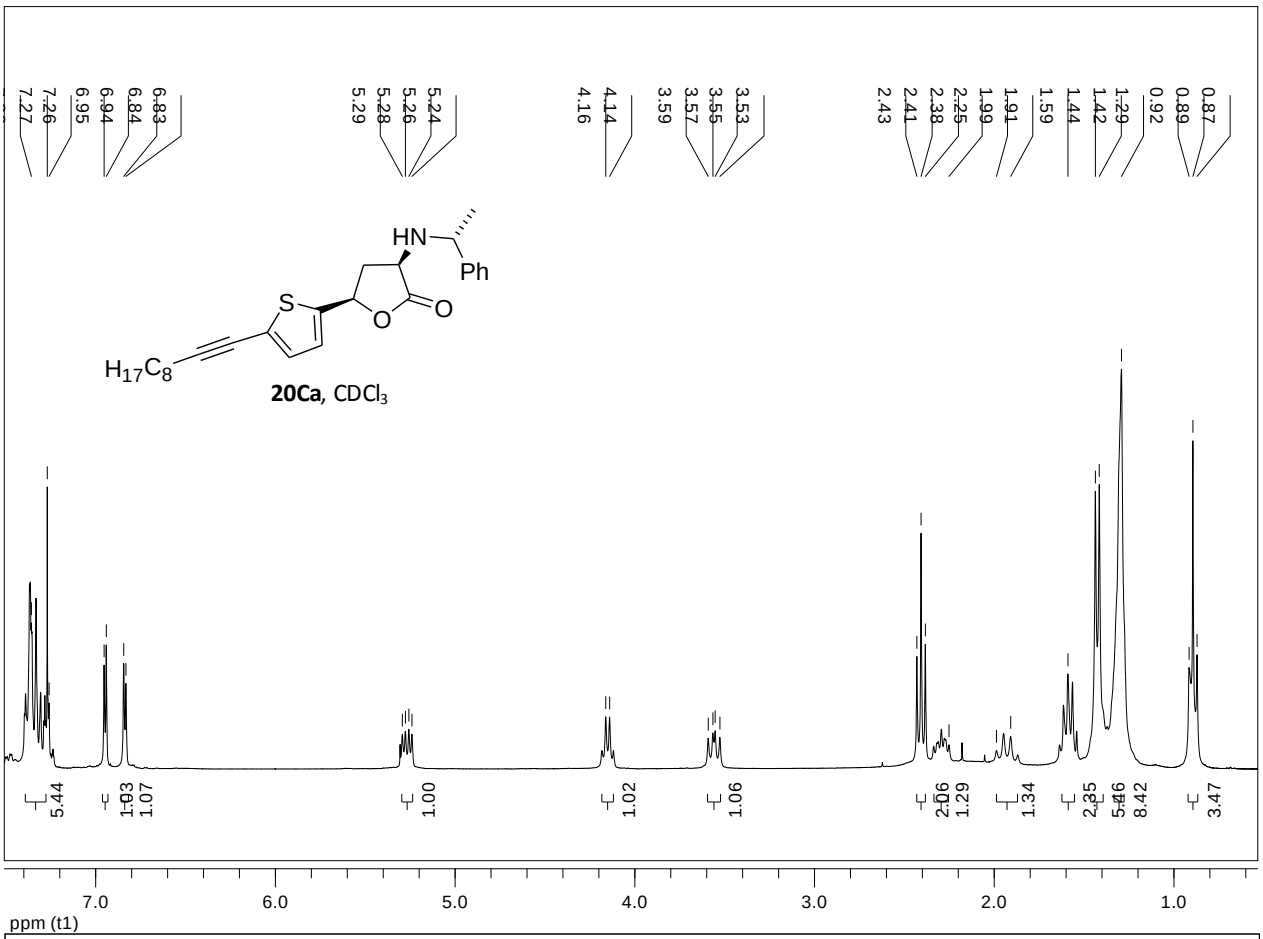
131.7
128.6
127.5
127.1
125.7
124.1
115.1
114.1
90.2
87.5
78.1
58.5
57.7
55.3
40.8
31.9
24.8
HN
Ph
O
O
PMP
20Be, CDCl3
150
100
50
ppm (t1)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5.24
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4.14
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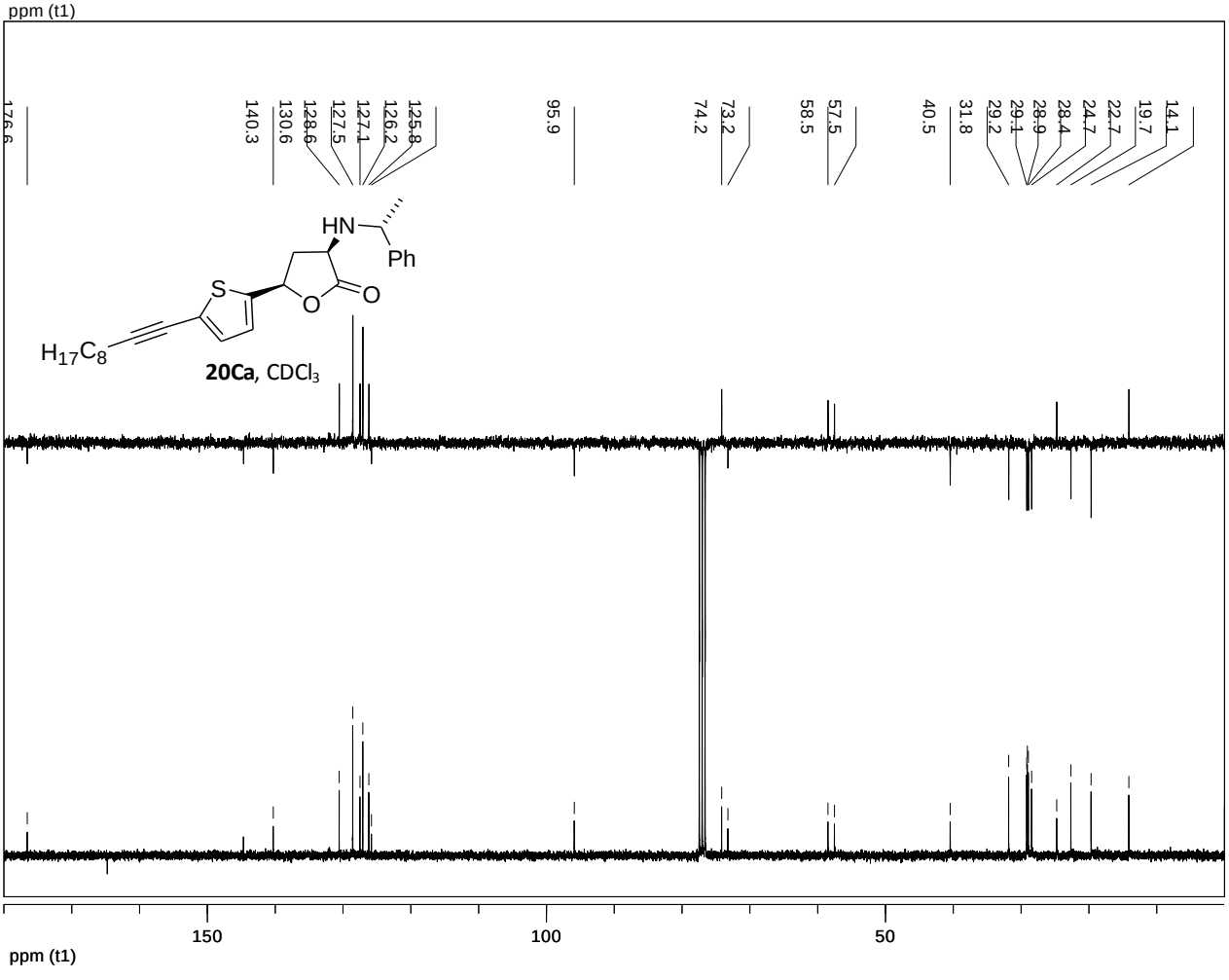
3.57
3.55
3.53
2.43
2.41
2.38
2.25
1.99
1.91
1.59
1.44
1.42
1.29
0.92
0.89
0.87
HN
Ph
S
O
O
$H_{17}C_8$
20Ca, $CDCl_3$
5.44
3.03
3.01
1.00
1.02
1.06
9.02
6.21
1.34
5.82
9.45
2.48
3.47
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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130.6
128.6
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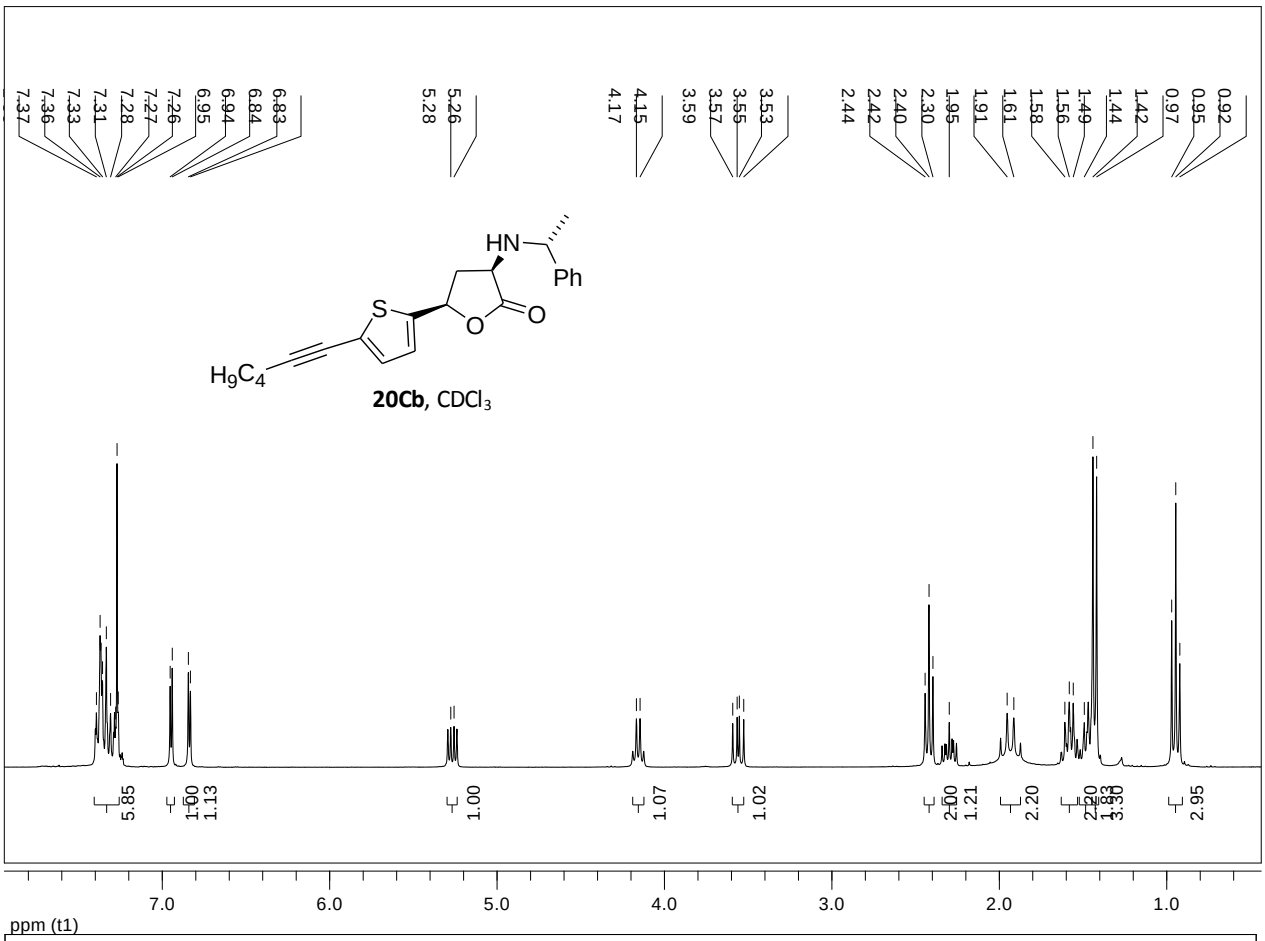
127.1
126.2
125.8
95.9
74.2
73.2
58.5
57.5
40.5
31.8
29.2
29.1
28.9
28.4
24.7
22.7
19.7
14.1
HN
Ph
S
O
O
$H_{17}C_8$
20Ca, $CDCl_3$
150
100
50
ppm (t1)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7.31
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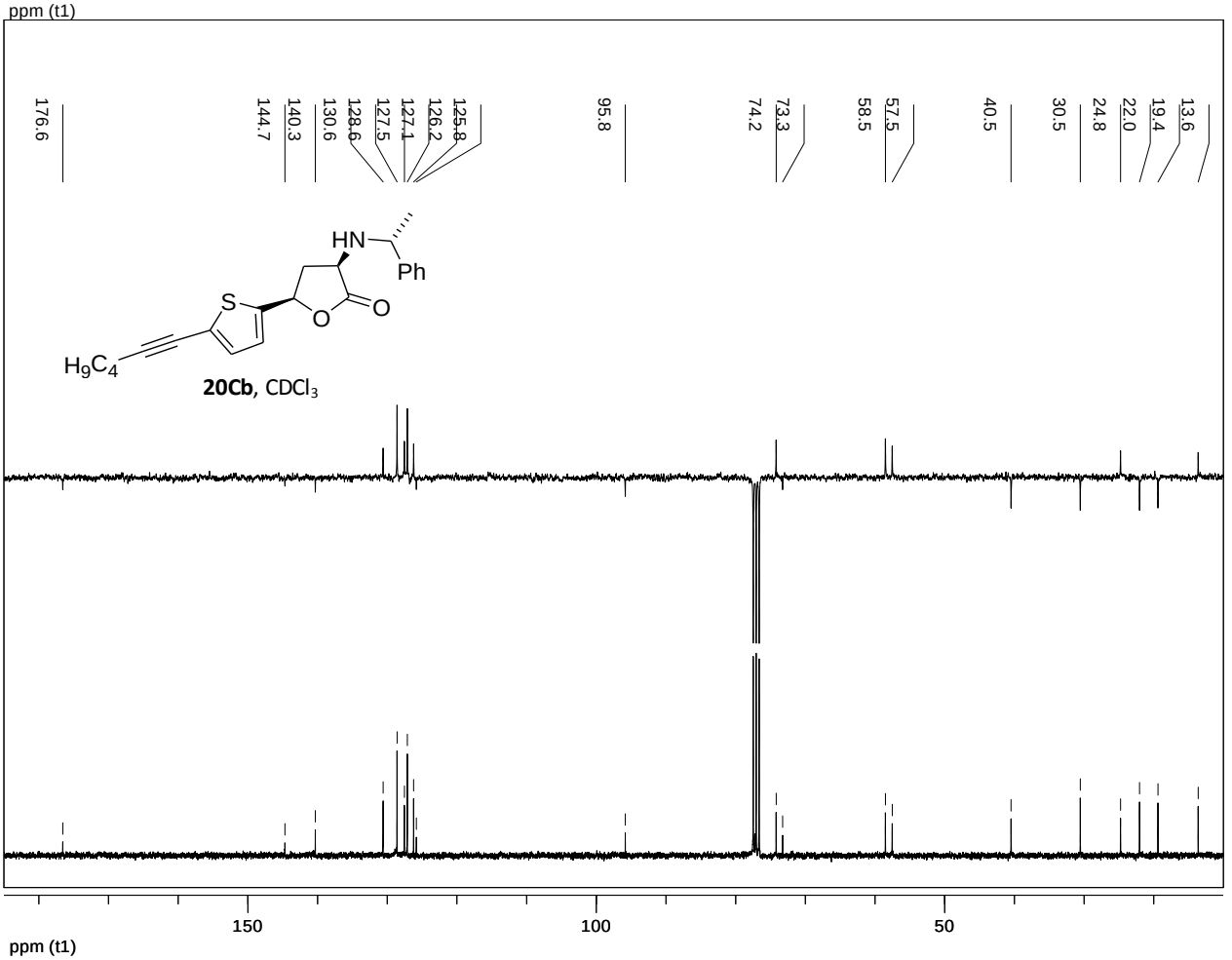
7.27
7.26
6.95
6.94
6.84
6.83
5.28
5.26
4.17
4.15
3.59
3.57
3.55
3.53
2.44
2.42
2.40
2.30
1.95
1.91
1.61
1.58
1.56
1.49
1.44
1.42
0.97
0.95
0.92
HN
Ph
S
O
O
H9C4
20Cb, CDCl3
5.85
1.00
1.13
1.00
1.07
2.01
2.00
1.21
2.20
2.20
1.83
3.00
5.62
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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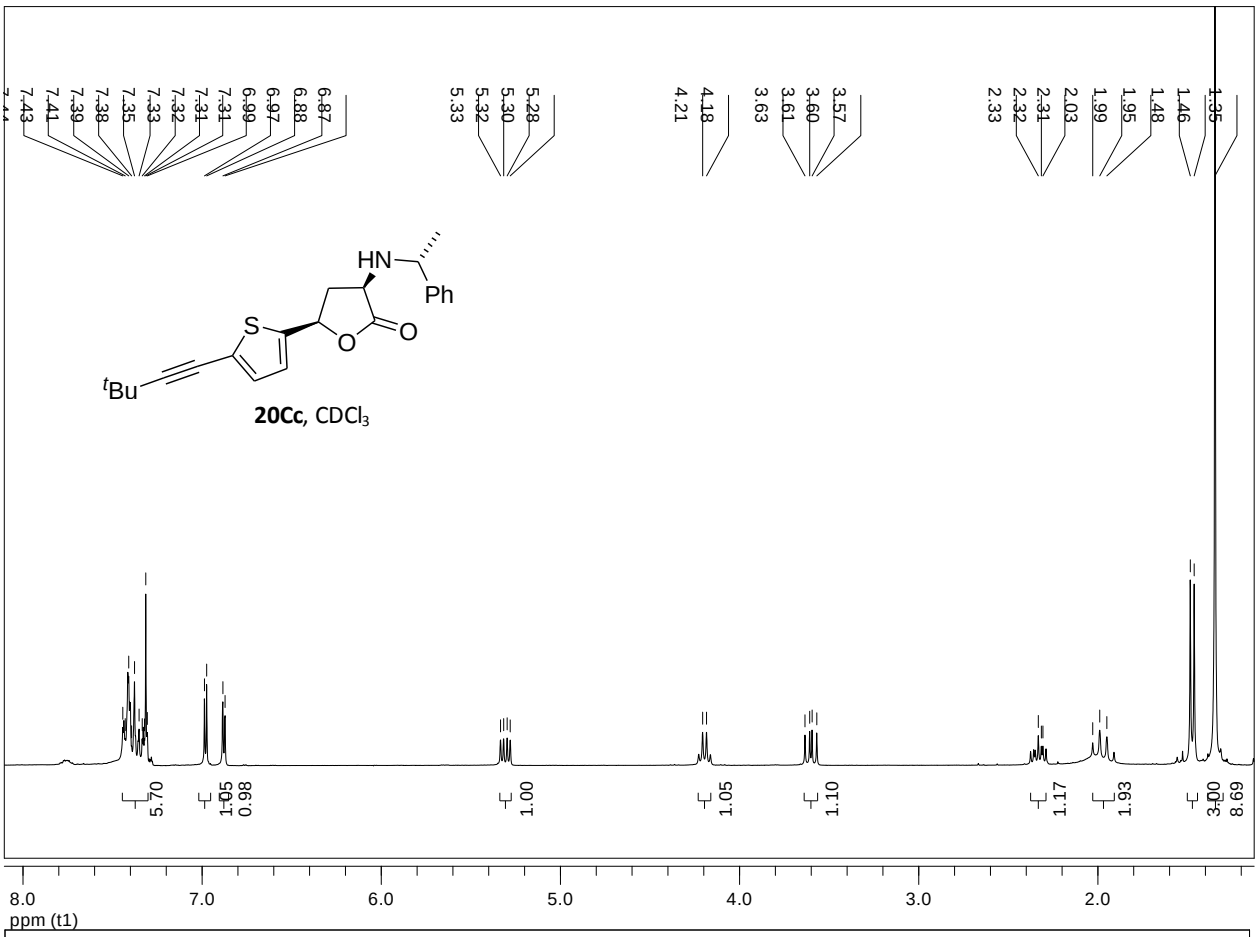
130.6
128.6
127.5
127.1
126.2
125.8
95.8
74.2
73.3
58.5
57.5
40.5
30.5
24.8
22.0
19.4
13.6
HN
Ph
S
O
O
H9C4
20Cb, CDCl3
150
100
50
ppm (t1)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6.97
6.88
6.87
5.33
5.32
5.30
5.28
4.21
4.18
3.63
3.61
3.60
3.57
2.33
2.32
2.31
2.03
1.99
1.95
1.48
1.46
1.35
HN
Ph
S
O
O
tBu
20Cc, CDCl3
5.70
1.05
8.60
1.00
1.05
1.10
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7.0
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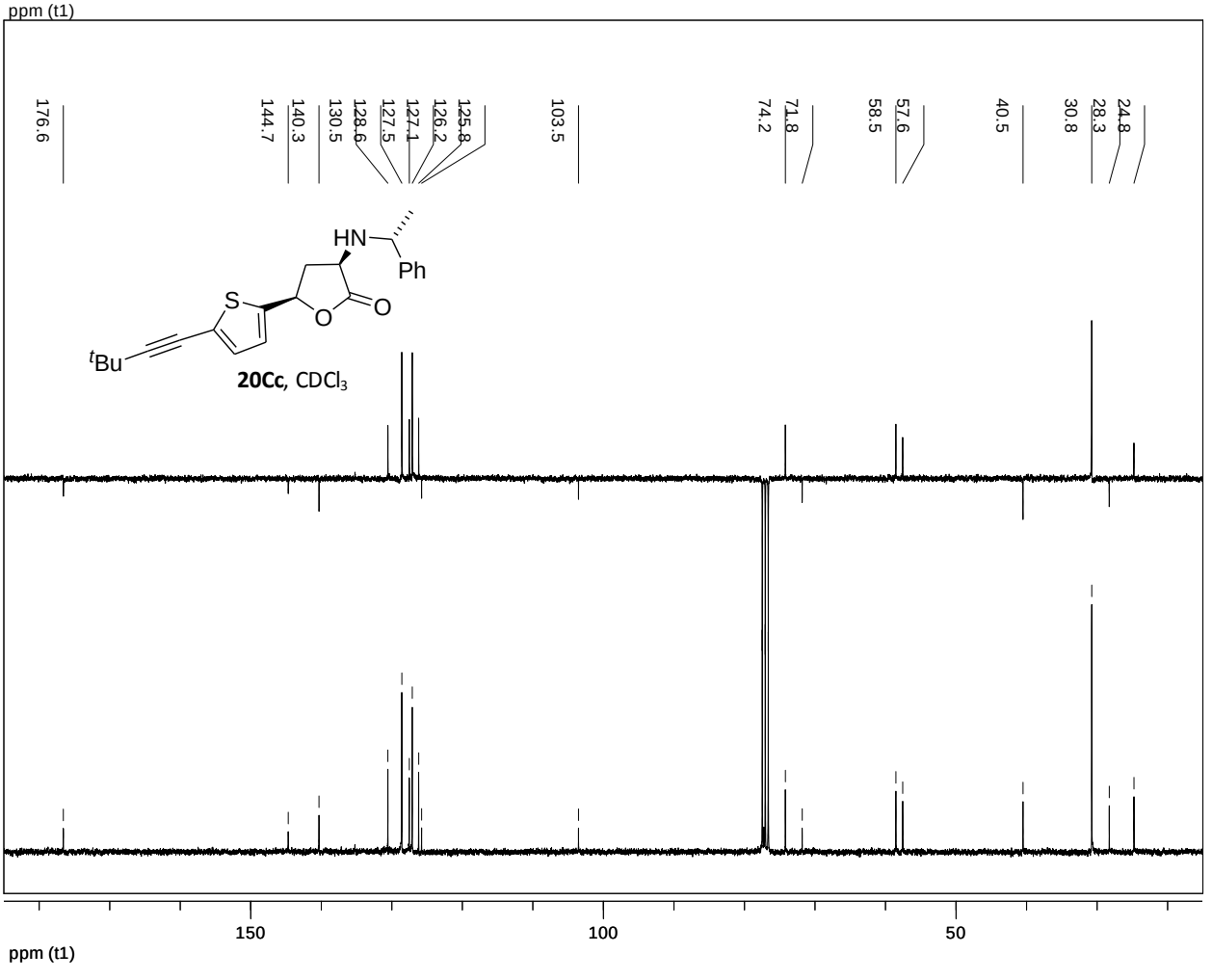
5.0
4.0
3.0
2.0
ppm (t1)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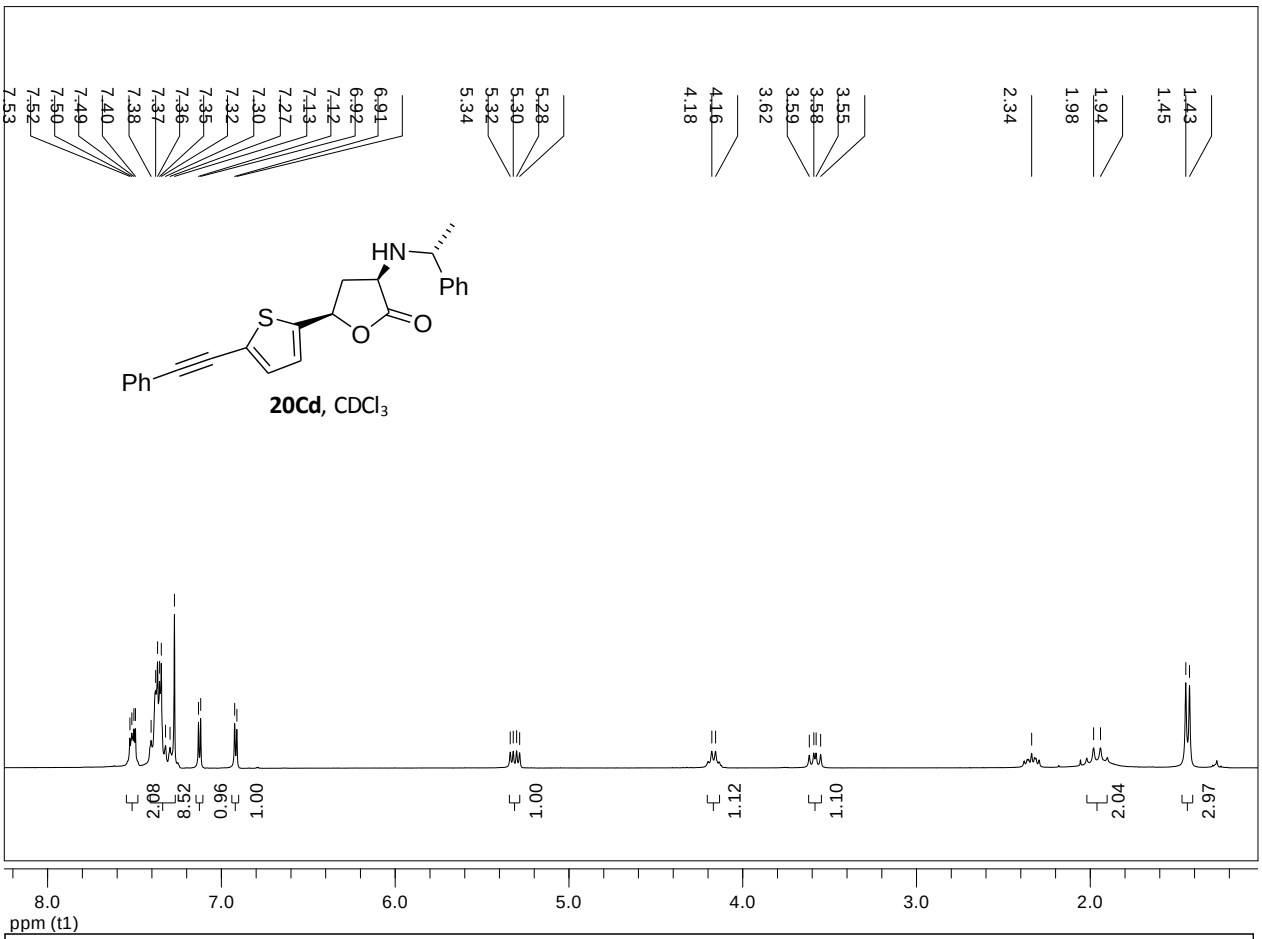
144.7
140.3
130.5
128.6
127.5
127.1
126.2
125.8
103.5
74.2
71.8
58.5
57.6
40.5
30.8
28.3
24.8
HN
Ph
S
O
O
tBu
20Cc, CDCl3
150
100
50
ppm (t1)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7.32
7.30
7.27
7.13
7.12
6.92
6.91
5.34
5.32
5.30
5.28
4.18
4.16
3.62
3.59
3.58
3.55
2.34
1.98
1.94
1.45
1.43
HN
Ph
S
O
O
Ph
20Cd, CDCl3
2.97
2.04
1.12
1.10
1.00
1.00
2.08
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1.00
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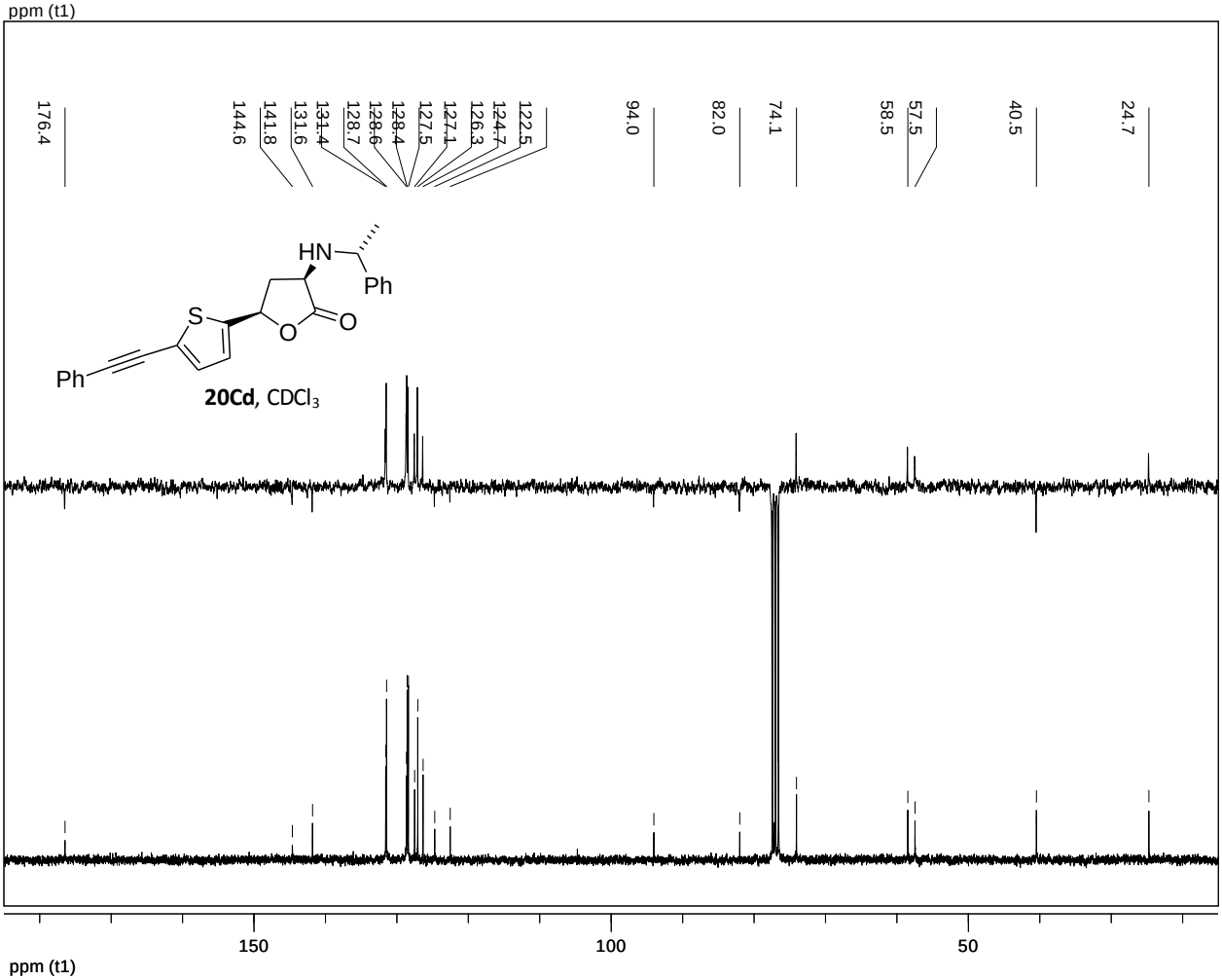
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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128.7
128.6
128.4
127.5
127.1
126.3
124.7
122.5
94.0
82.0
74.1
58.5
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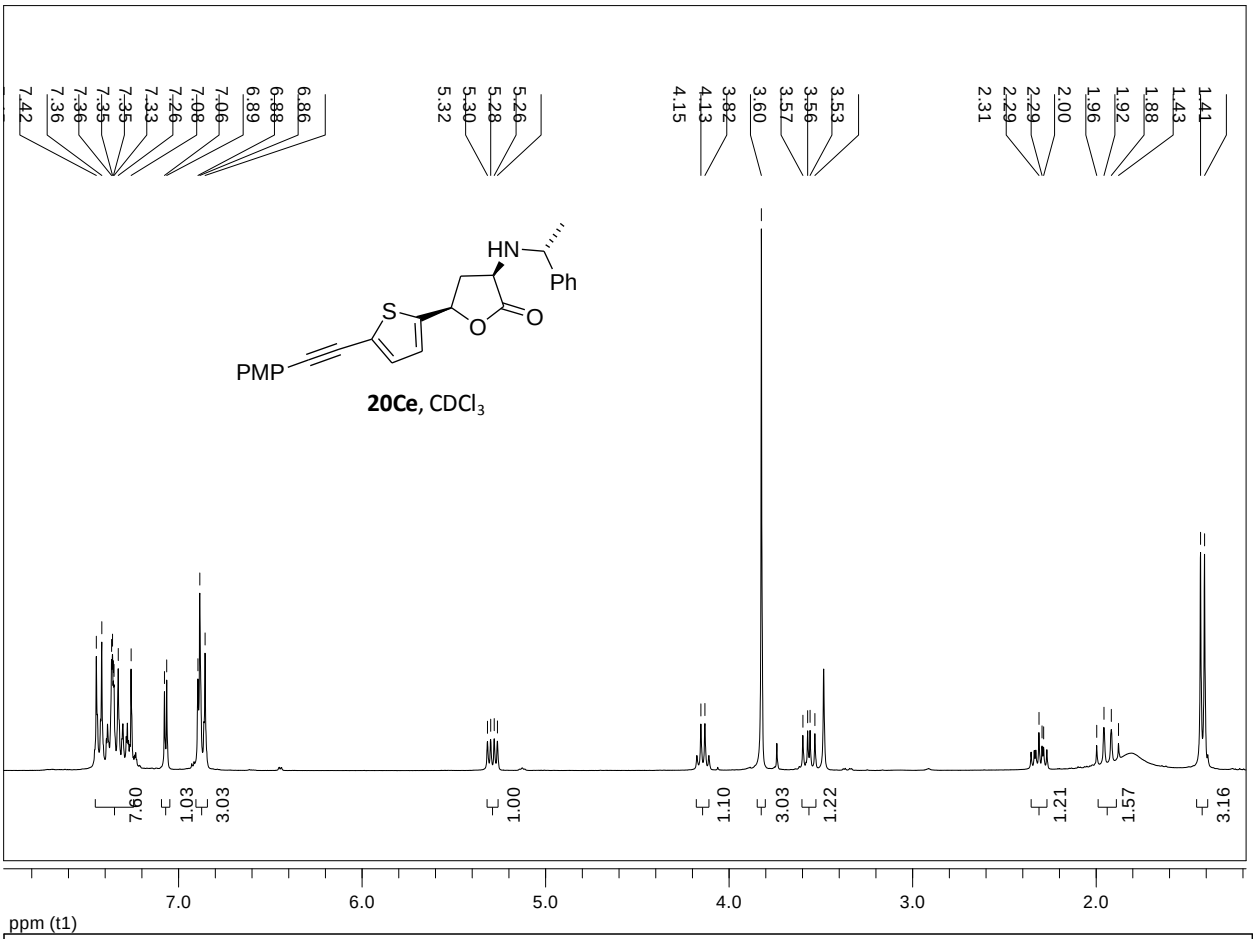
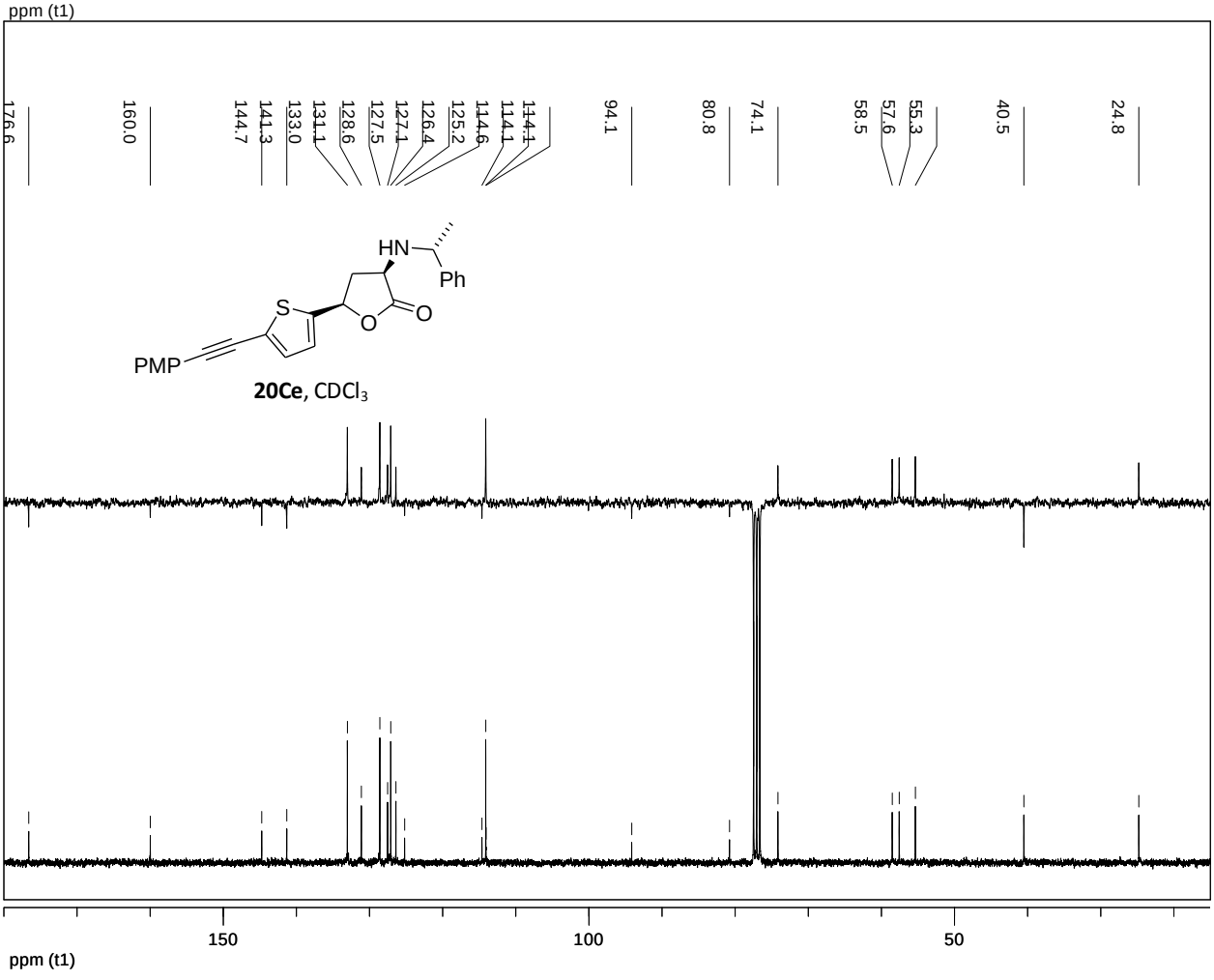
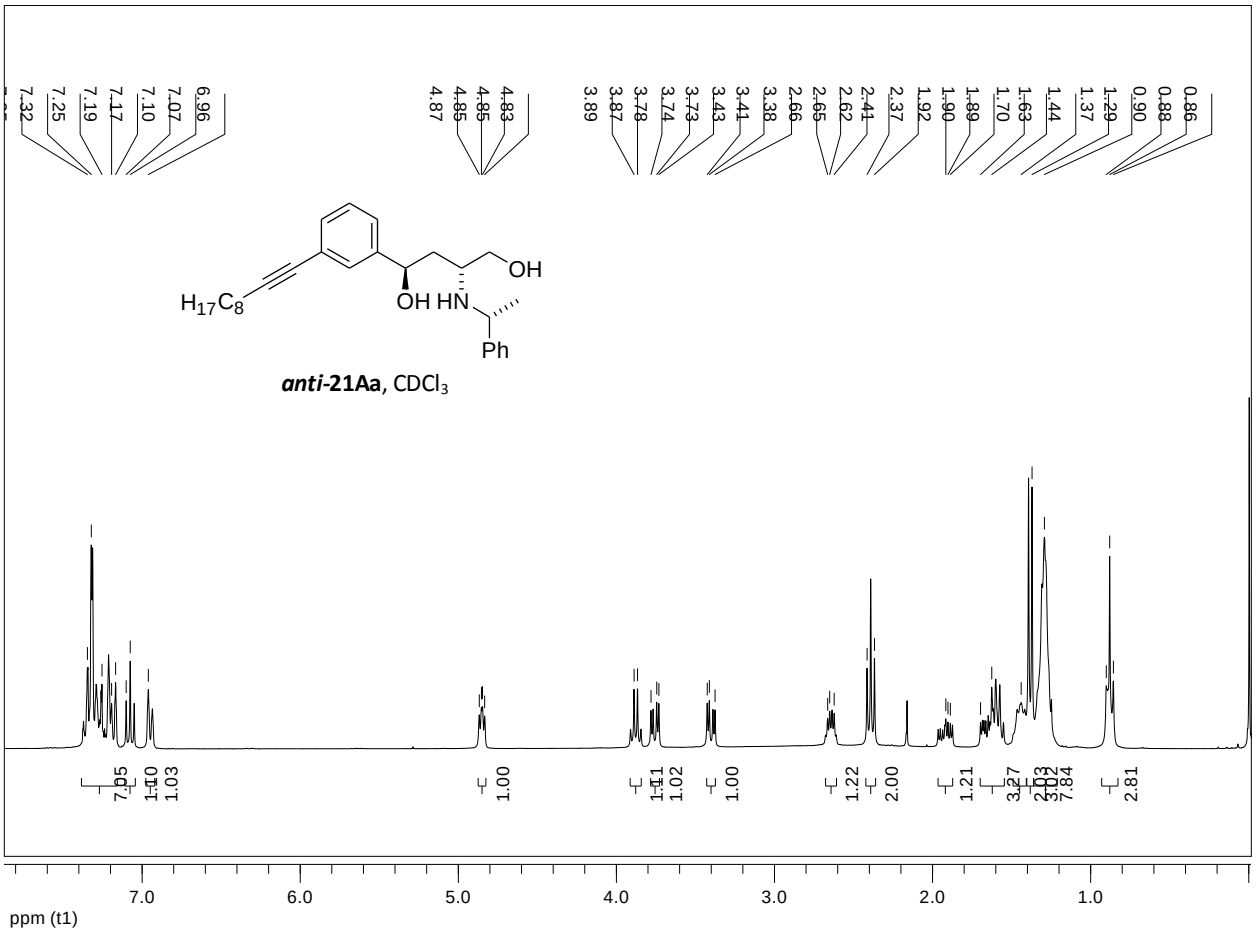
40.5
24.7
HN
Ph
S
O
O
Ph
20Cd, CDCl3
150
100
50
ppm (t1)



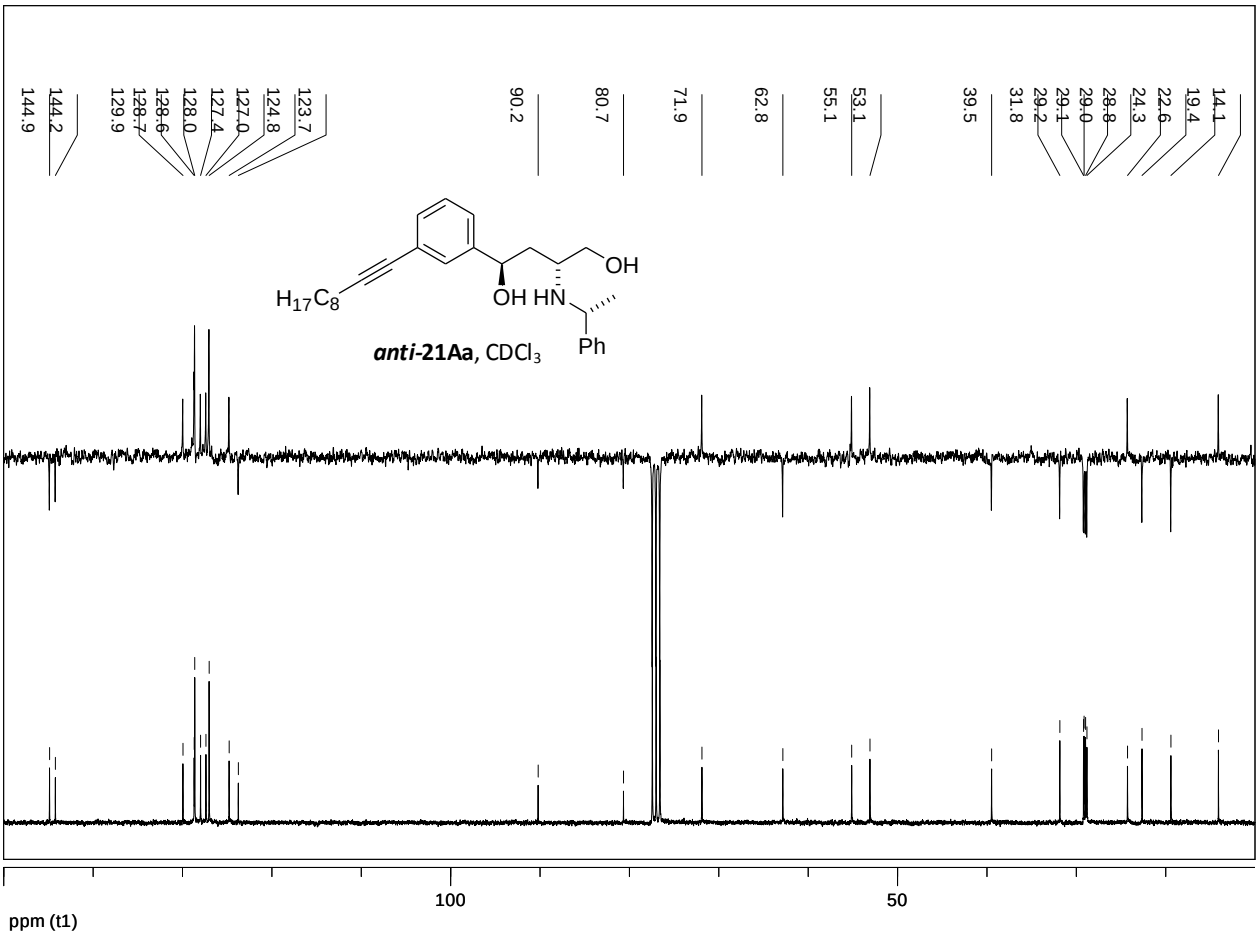
20Ce, $CDCl_3$



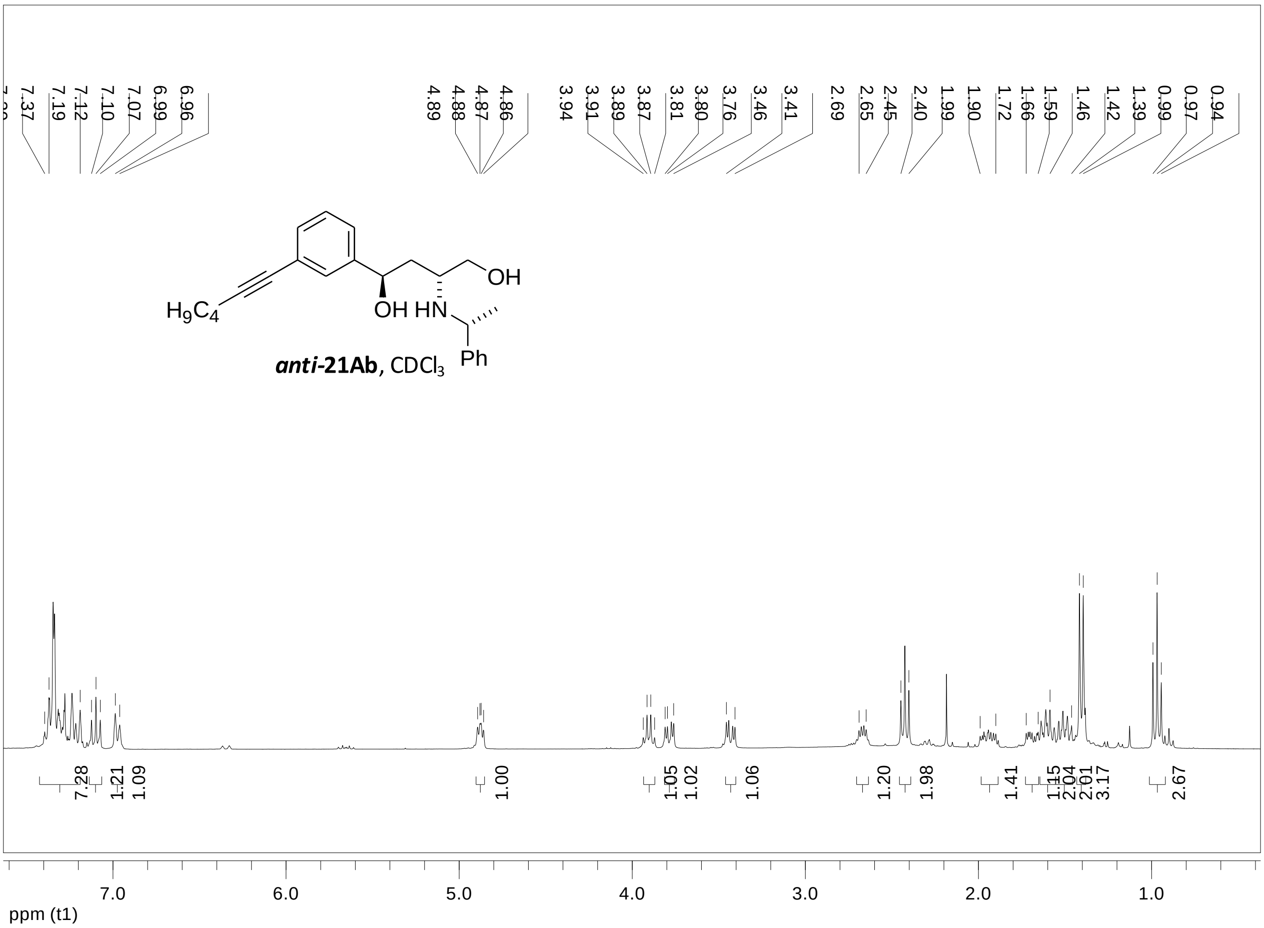
20Ce, $CDCl_3$

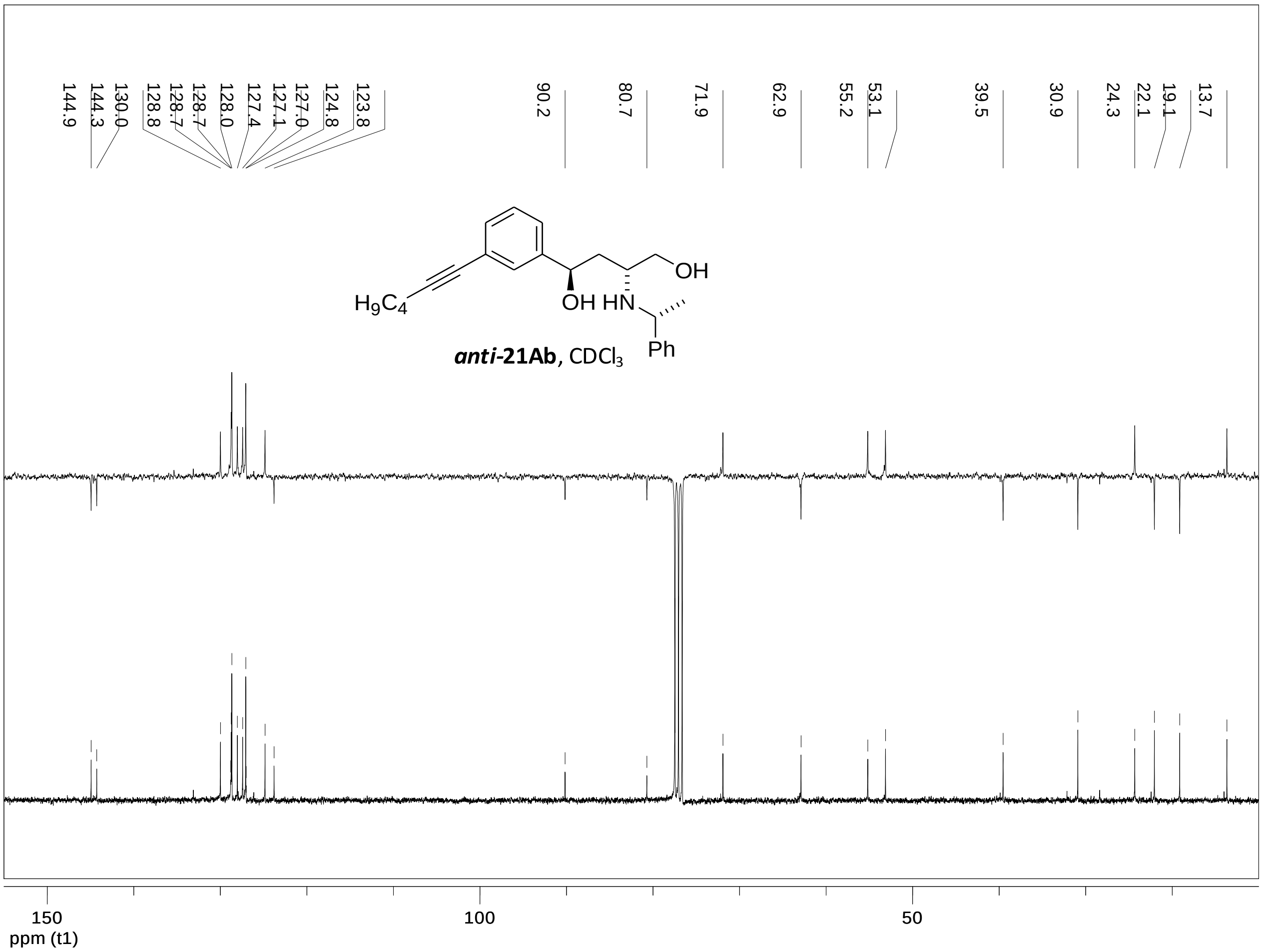


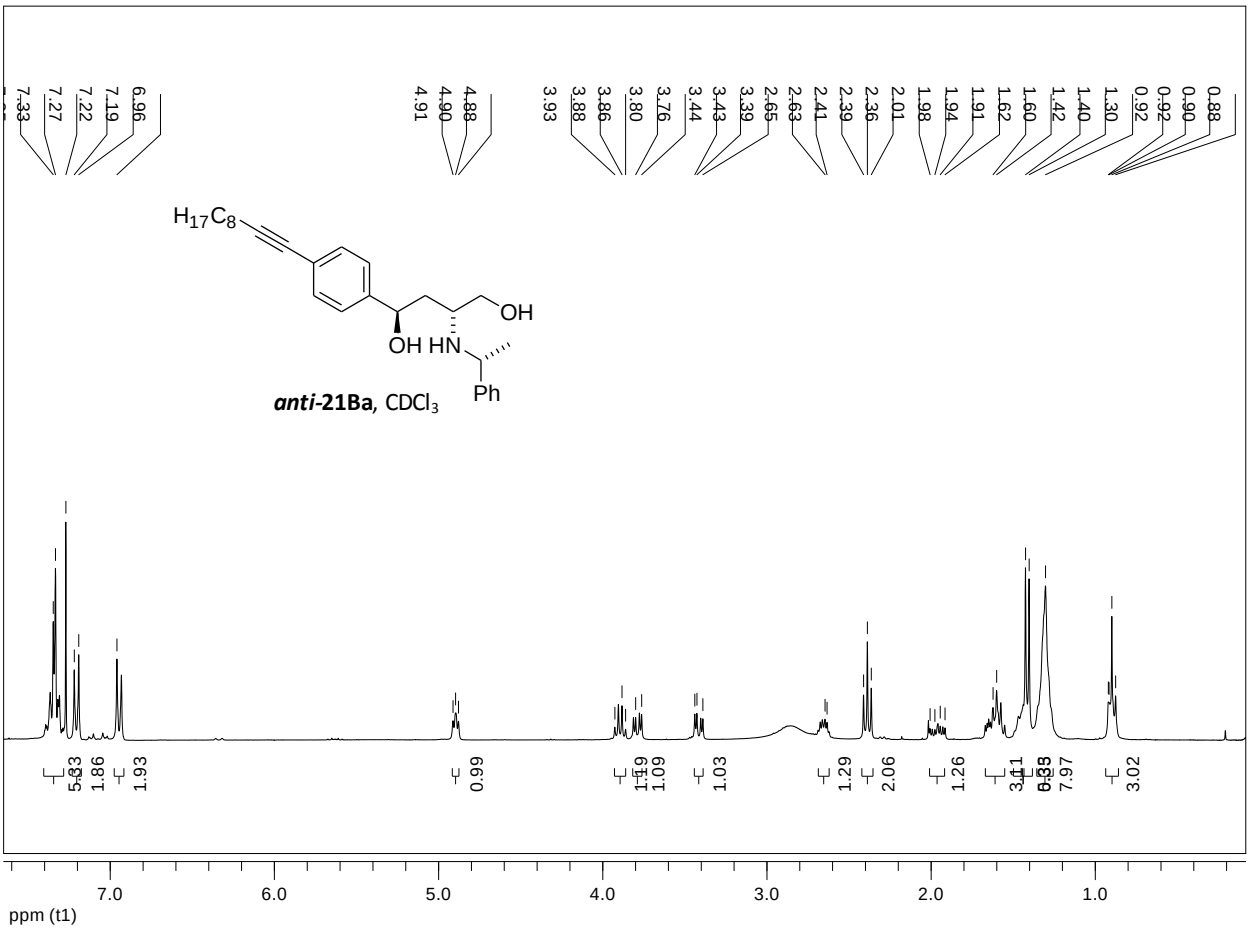
***anti*-21Aa**, $CDCl_3$



***anti*-21Aa**, $CDCl_3$



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3.44
3.43
3.39
2.65
2.63
2.41
2.39
2.36
2.01
1.98
1.94
1.91
1.62
1.60
1.42
1.40
1.30
0.92
0.92
0.90
0.88
H17C8
OH
OH HN
Ph
anti-21Ba, CDCl3
5.33
1.86
1.93
0.99
1.19
1.09
1.03
1.29
2.06
1.26
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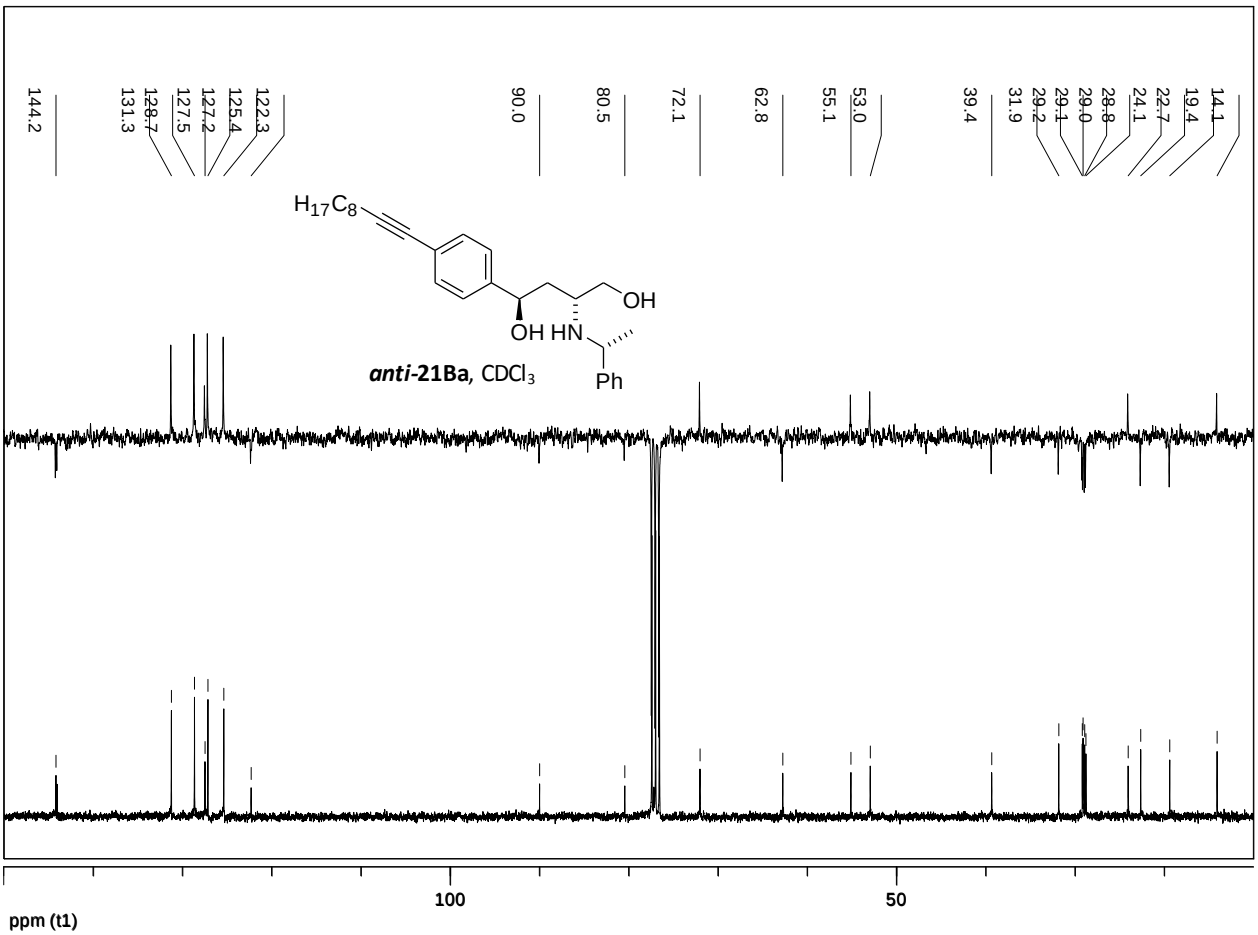
3.02
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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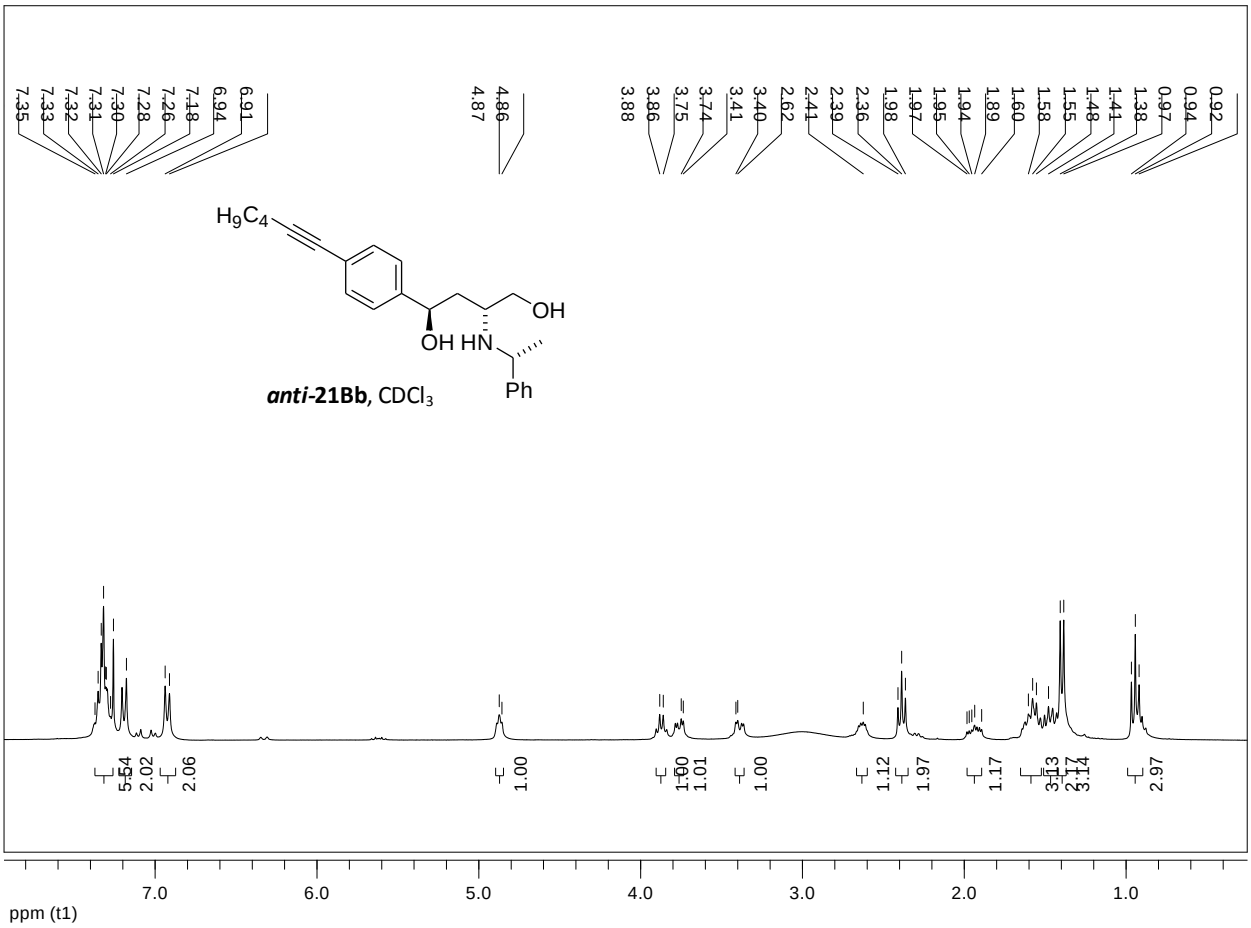
127.5
127.2
125.4
122.3
90.0
80.5
72.1
62.8
55.1
53.0
39.4
31.9
29.2
29.1
29.0
28.8
24.1
22.7
19.4
14.1
H17C8
OH
OH HN
Ph
anti-21Ba, CDCl3
100
50
ppm (t1)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6.94
6.91
4.87
4.86
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3.86
3.75
3.74
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1.98
1.97
1.95
1.94
1.89
1.60
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1.55
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1.41
1.38
0.97
0.94
0.92
H9C4
OH
OH HN
Ph
anti-21Bb, CDCl3
5.54
2.02
2.06
1.00
1.00
1.01
1.00
1.12
1.97
1.17
3.13
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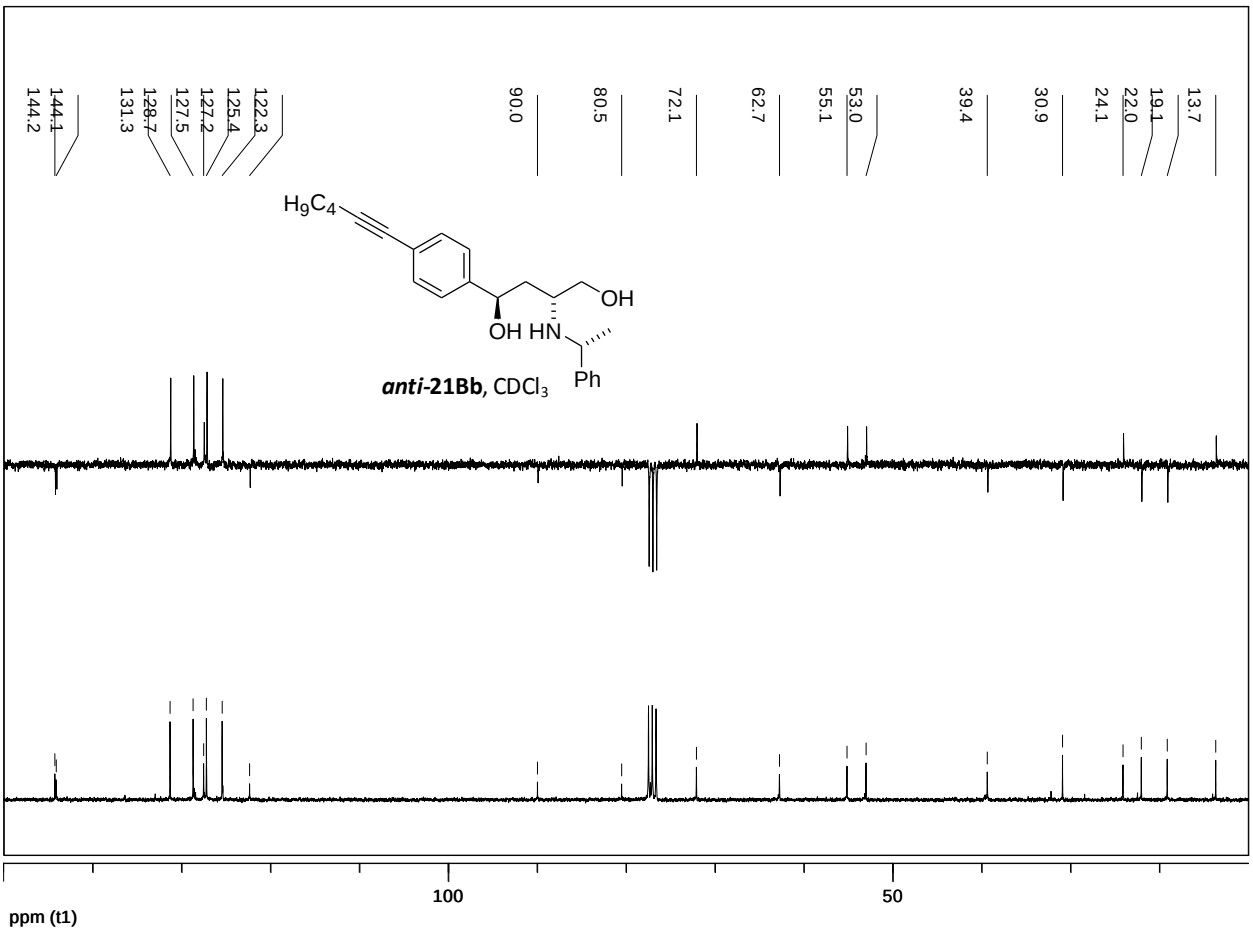
2.97
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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127.2
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72.1
62.7
55.1
53.0
39.4
30.9
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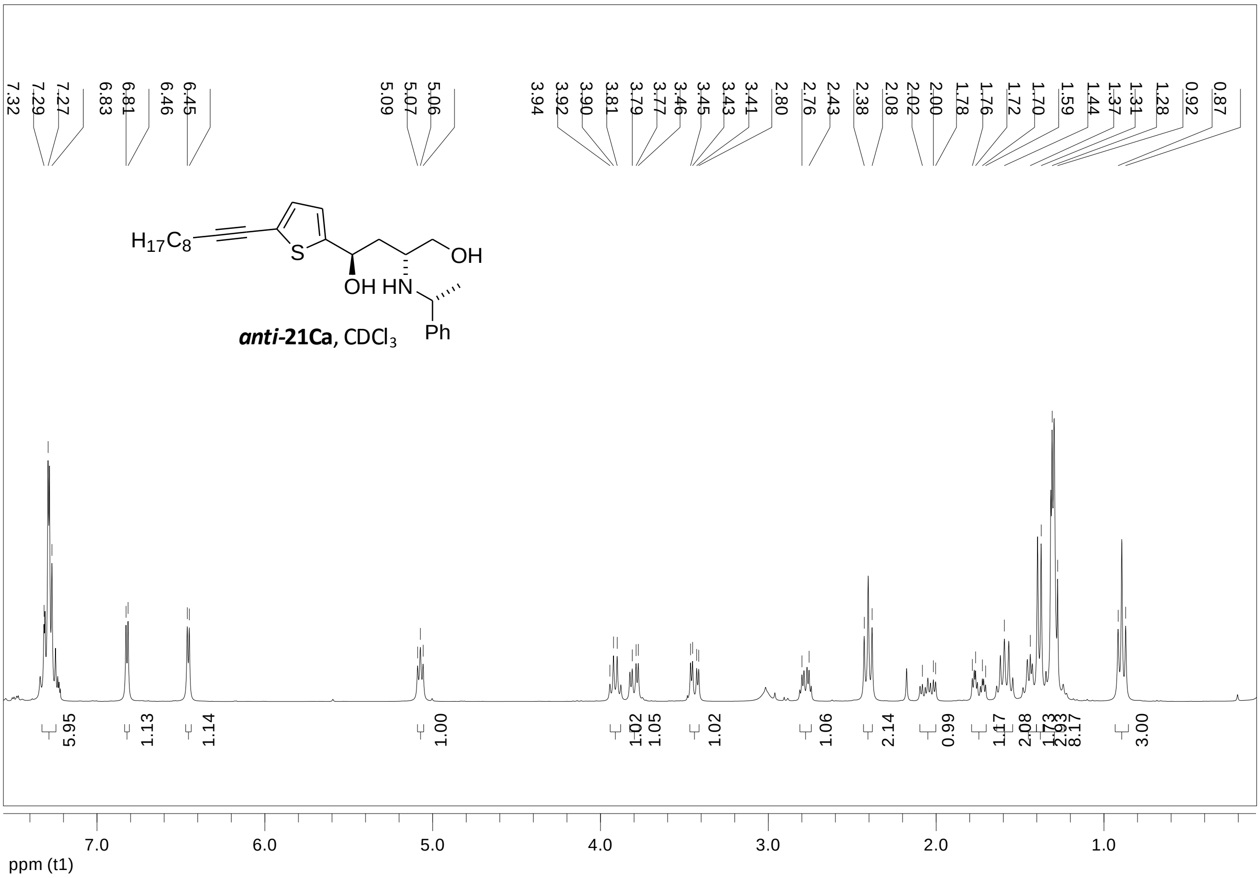
19.1
13.7
H9C4
OH
OH HN
Ph
anti-21Bb, CDCl3
100
50
ppm (t1)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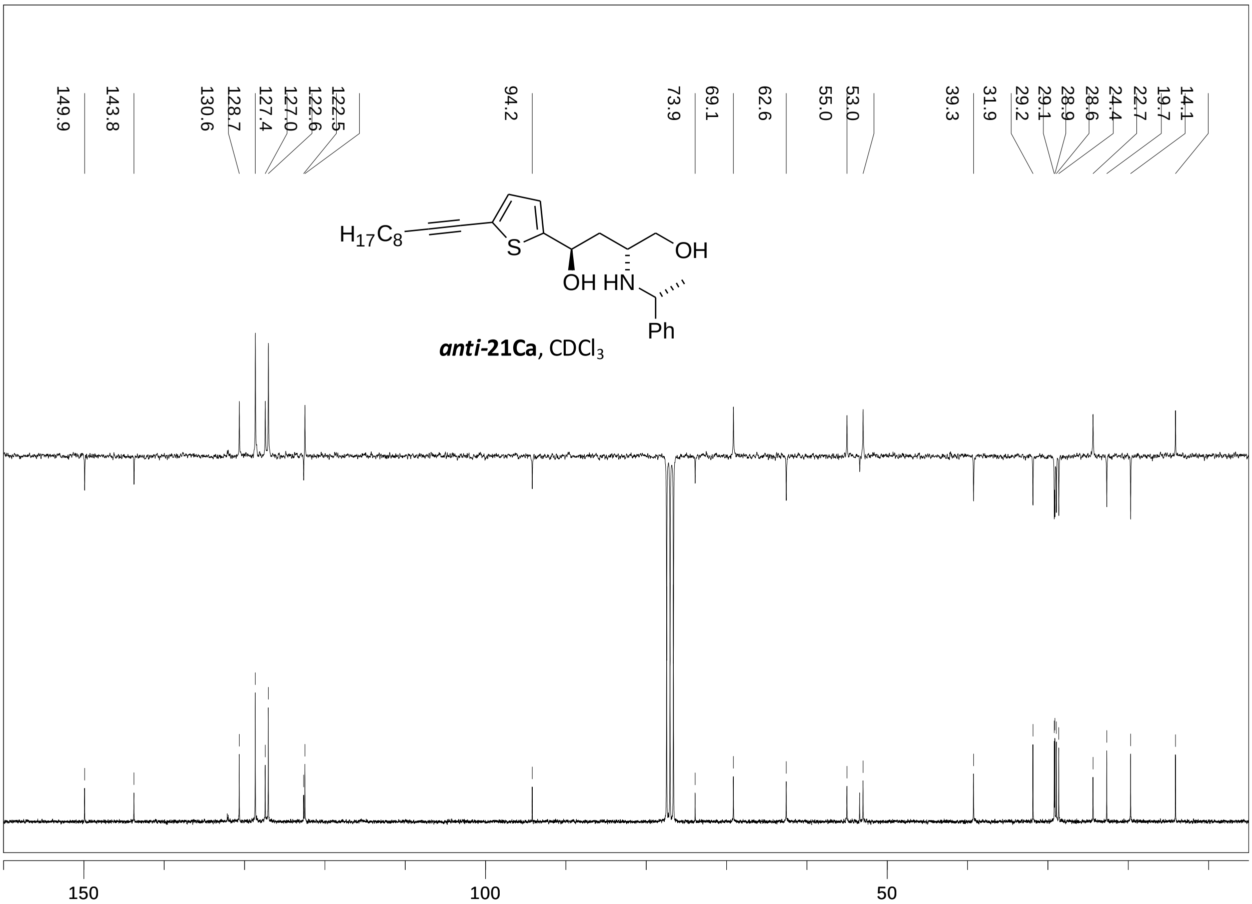
6.45
5.09
5.07
5.06
3.94
3.92
3.90
3.81
3.79
3.77
3.46
3.45
3.43
3.41
2.80
2.76
2.43
2.38
2.08
2.02
2.00
1.78
1.76
1.72
1.70
1.59
1.44
1.37
1.31
1.28
0.92
0.87
$H_{17}C_8$
S
OH
HN
OH
Ph
anti-21Ca, CDCl3
5.95
1.13
1.14
1.00
1.02
1.05
1.02
1.06
2.14
0.99
1.17
2.08
1.73
2.93
8.17
3.00
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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122.5
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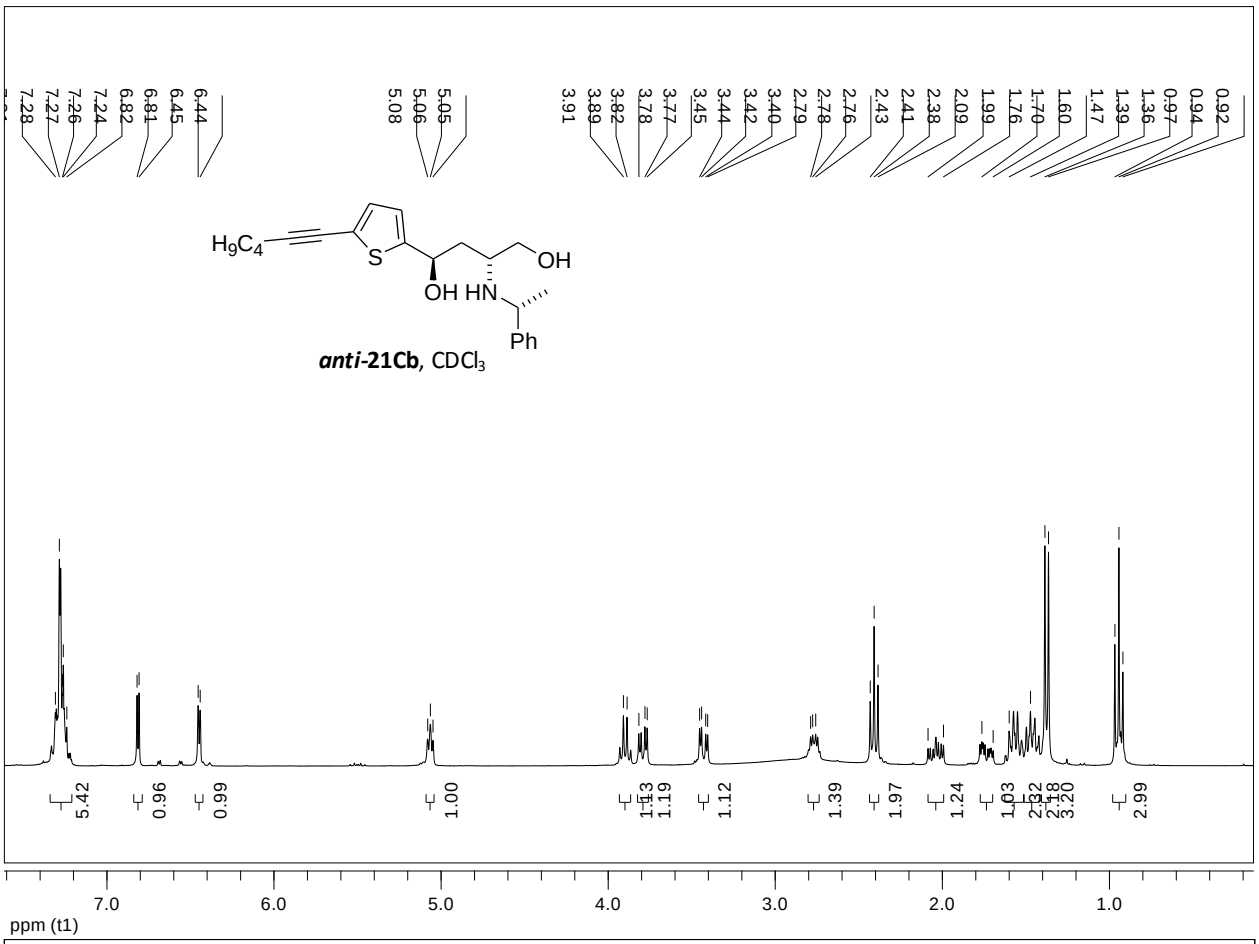
73.9
69.1
62.6
55.0
53.0
39.3
31.9
29.2
29.1
28.9
28.6
24.4
22.7
19.7
14.1
$H_{17}C_8$
S
OH
HN
OH
Ph
anti-21Ca, CDCl3
150
100
50
ppm (t1)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6.44
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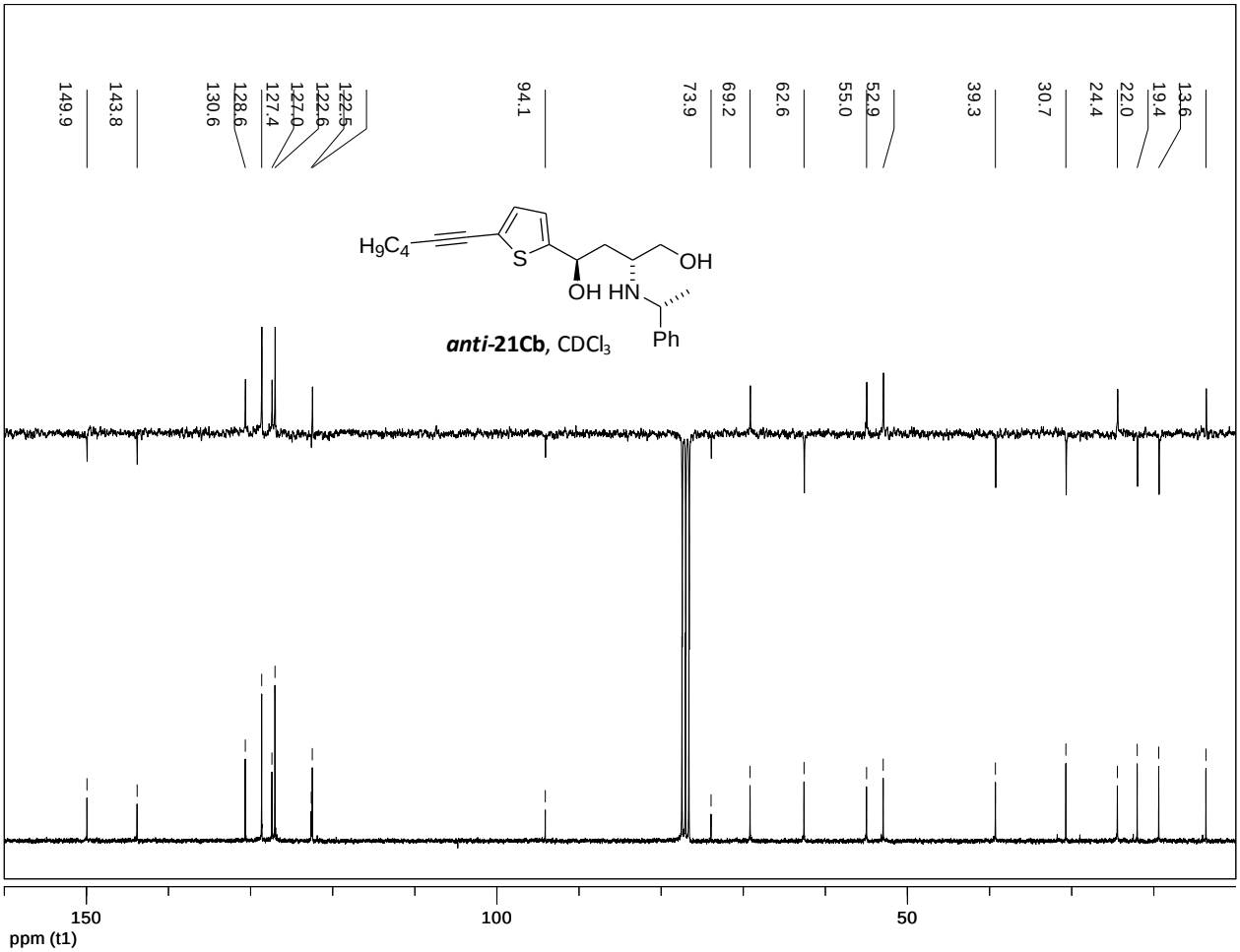
5.06
5.05
3.91
3.89
3.82
3.78
3.77
3.45
3.44
3.42
3.40
2.79
2.78
2.76
2.43
2.41
2.38
2.09
1.99
1.76
1.70
1.60
1.47
1.39
1.36
0.97
0.94
0.92
H9C4
S
OH
OH HN
Ph
anti-21Cb, CDCl3
5.42
0.96
0.99
1.00
1.13
1.19
1.12
1.39
1.97
1.27
1.01
3.20
6.99
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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73.9
69.2
62.6
55.0
52.9
39.3
30.7
24.4
22.0
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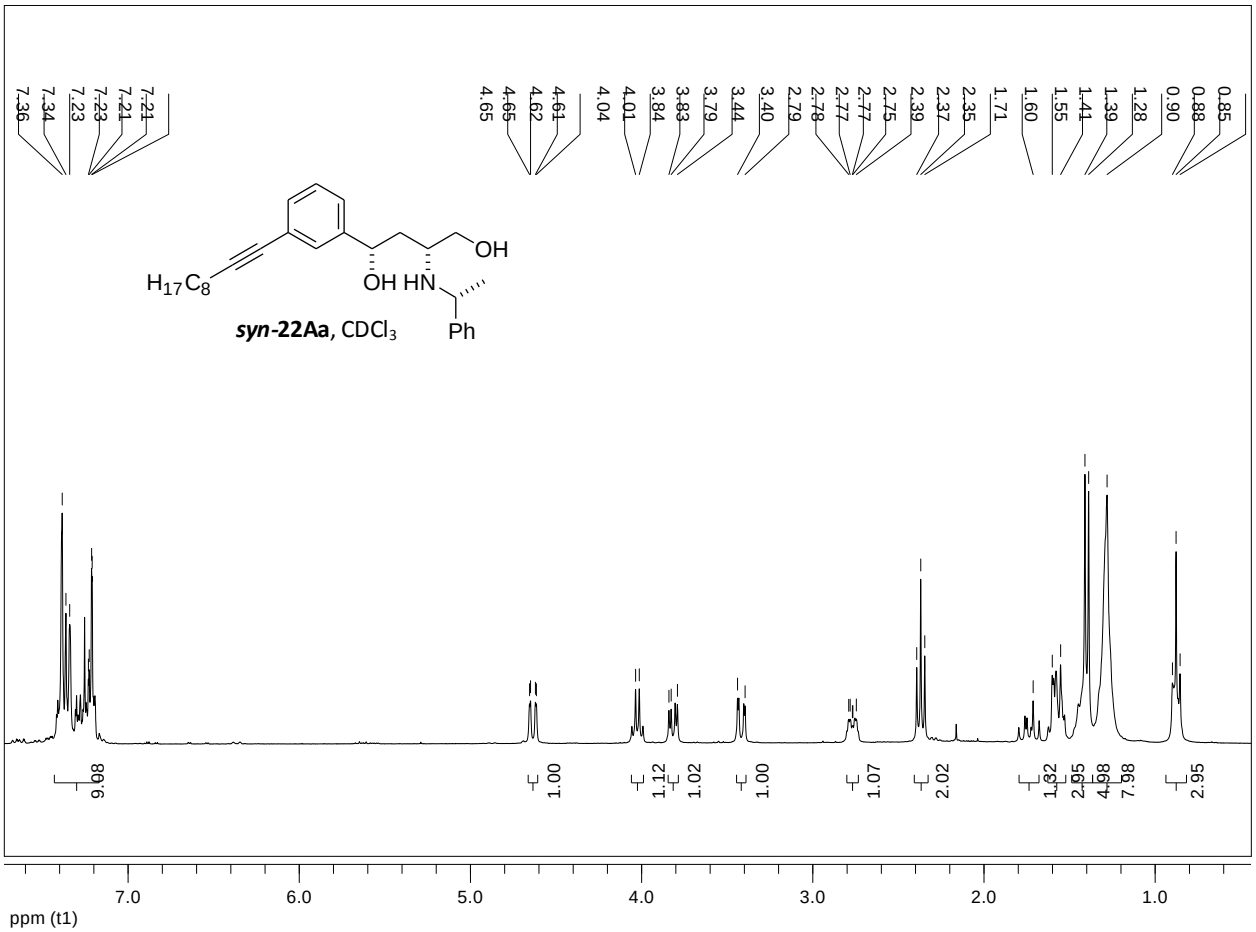
13.6
H9C4
S
OH
OH HN
Ph
anti-21Cb, CDCl3
150
100
50
ppm (t1)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4.65
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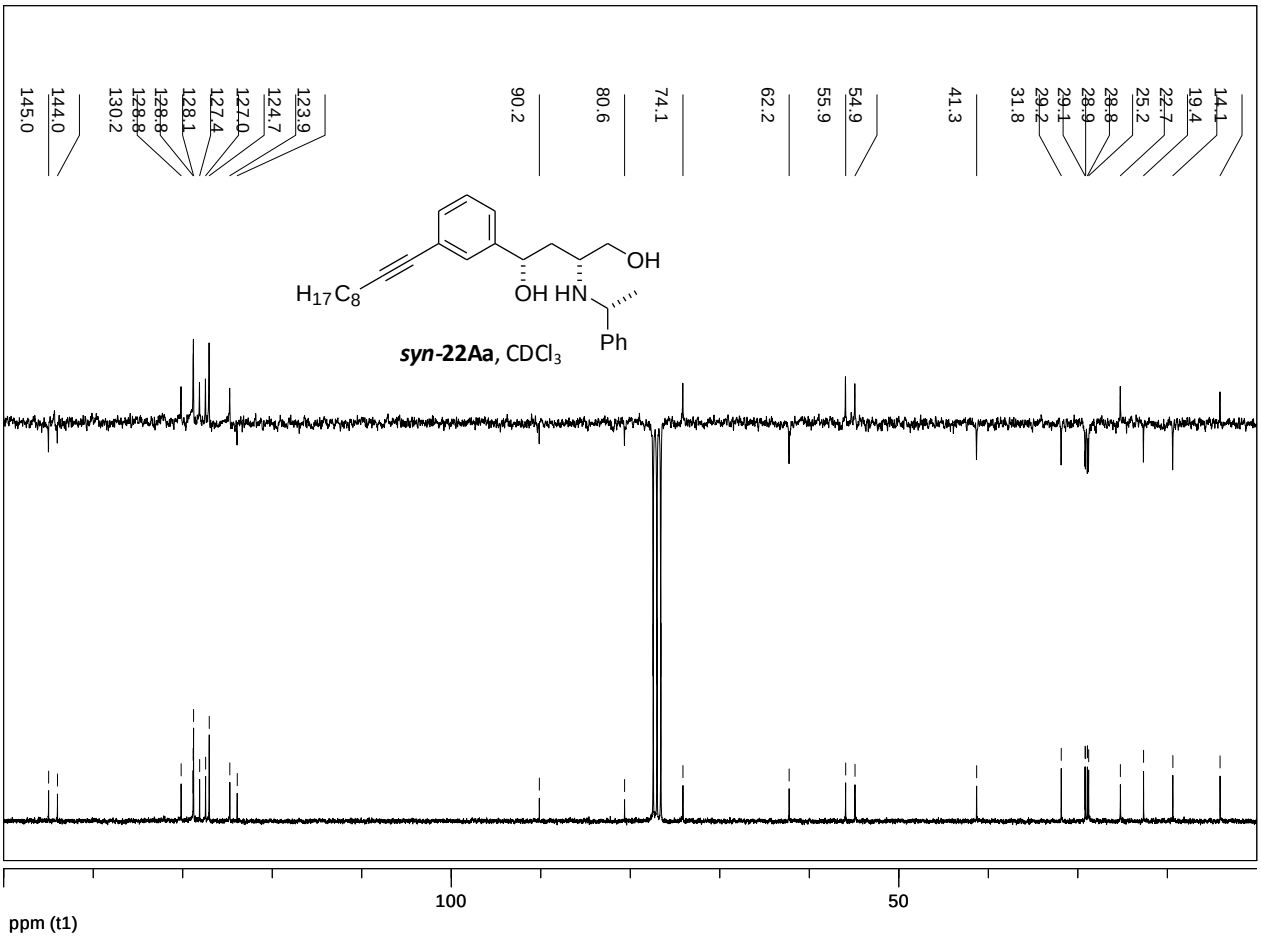
4.61
4.04
4.01
3.84
3.83
3.79
3.44
3.40
2.79
2.78
2.77
2.77
2.75
2.39
2.37
2.35
1.71
1.60
1.55
1.41
1.39
1.28
0.90
0.88
0.85
OH
H17C8
OH HN
Ph
syn-22Aa, CDCl3
9.08
1.00
1.12
2.01
1.00
1.07
2.02
2.07
2.52
8.04
7.98
2.95
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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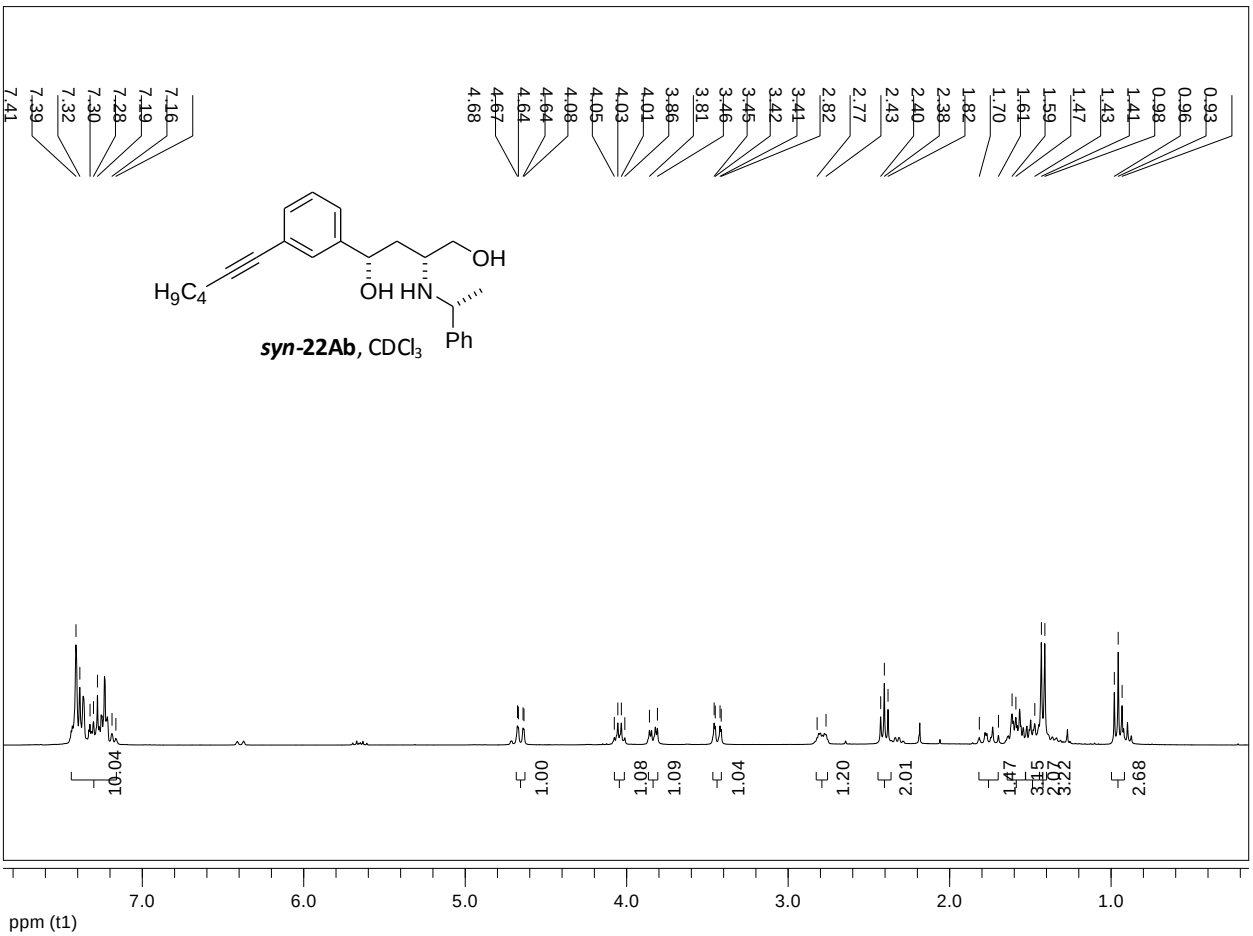
128.8
128.1
127.4
127.0
124.7
123.9
90.2
80.6
74.1
62.2
55.9
54.9
41.3
31.8
29.2
29.1
28.9
28.8
25.2
22.7
19.4
14.1
OH
H17C8
OH HN
Ph
syn-22Aa, CDCl3
100
50
ppm (t1)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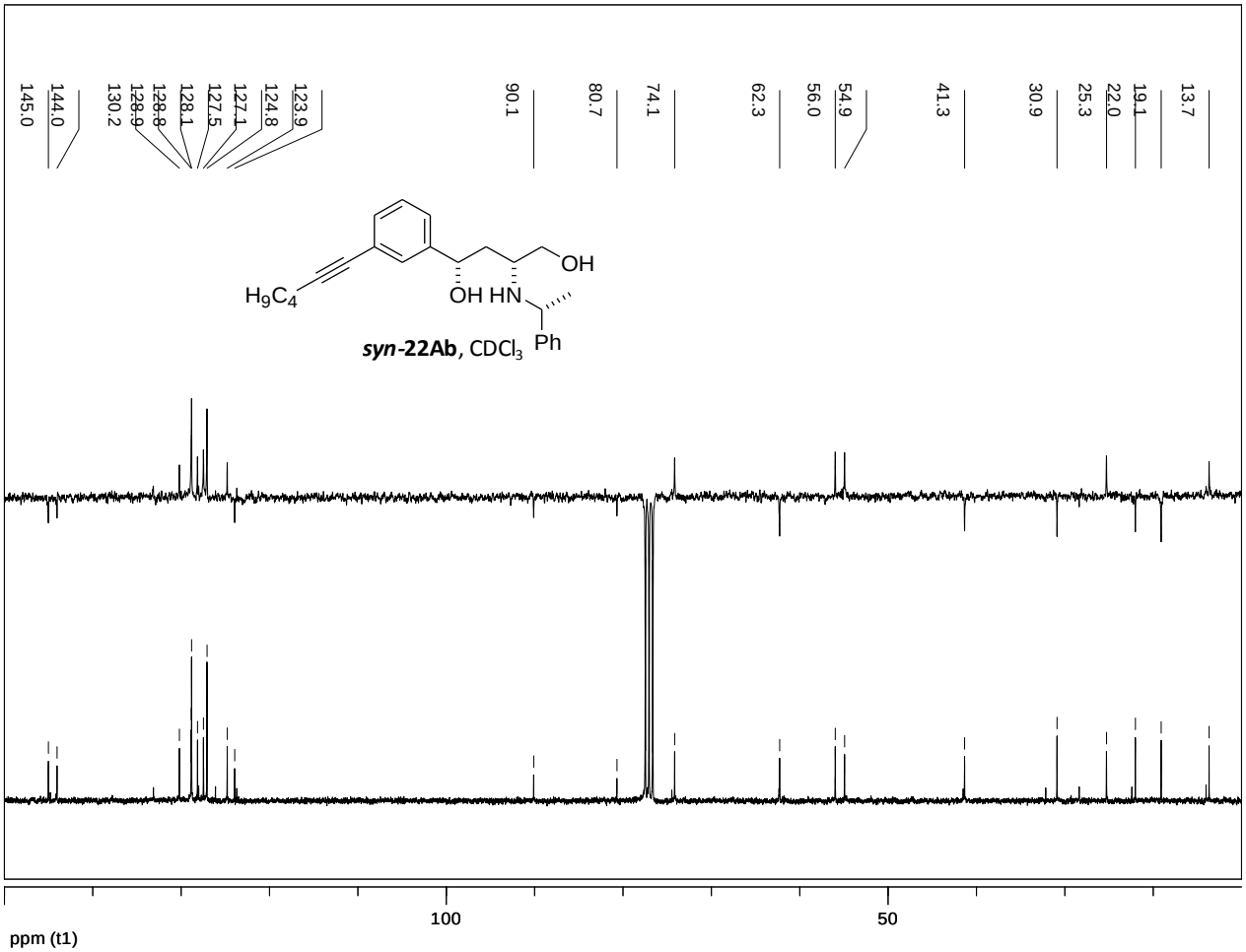
7.19
7.16
4.68
4.67
4.64
4.64
4.08
4.05
4.03
4.01
3.86
3.81
3.46
3.45
3.42
3.41
2.82
2.77
2.43
2.40
2.38
1.82
1.70
1.61
1.59
1.47
1.43
1.41
0.98
0.96
0.93
OH
H9C4
OH HN
Ph
syn-22Ab, CDCl3
16.04
1.00
1.08
1.09
1.04
1.20
2.01
1.47
3.15
2.22
2.68
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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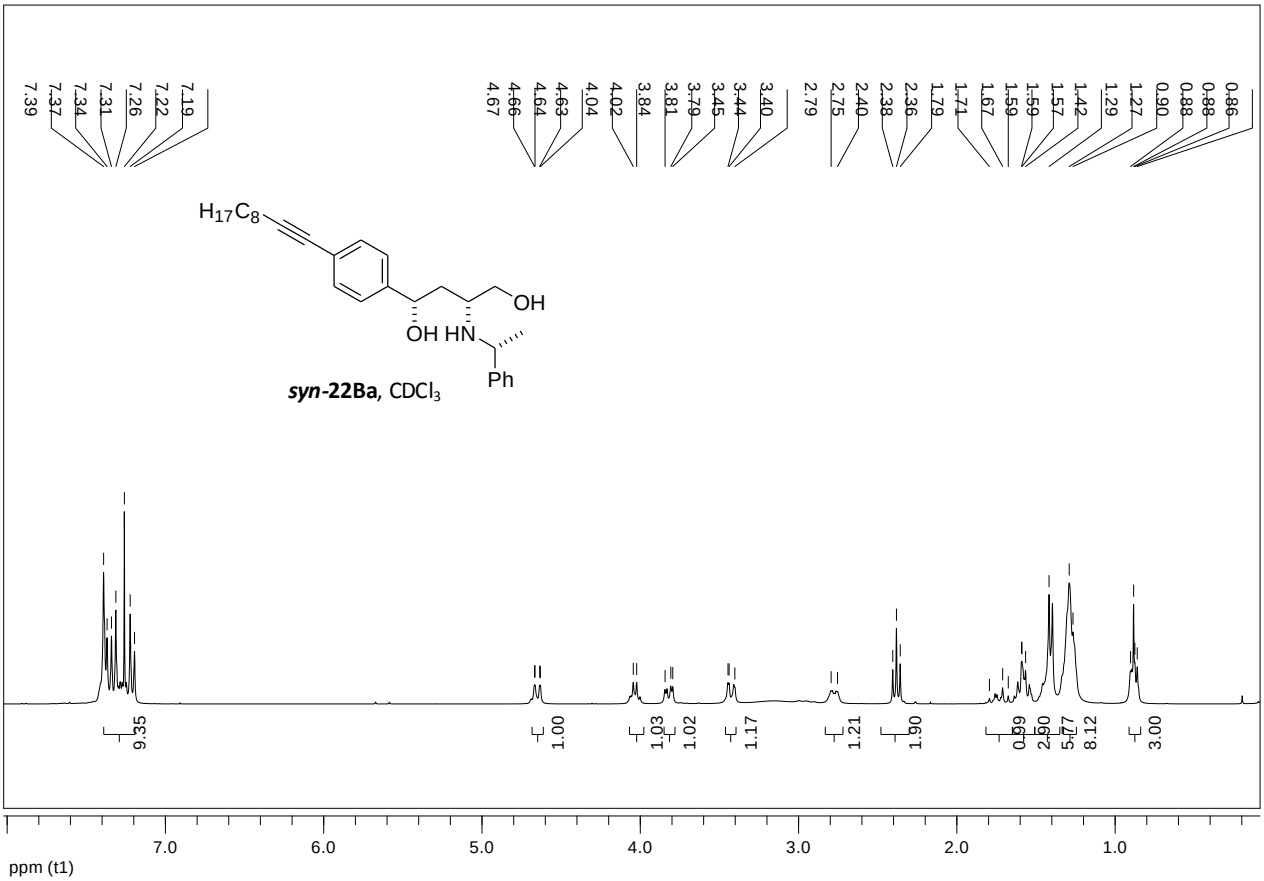
144.0
130.2
128.9
128.8
128.1
127.5
127.1
124.8
123.9
90.1
80.7
74.1
62.3
56.0
54.9
41.3
30.9
25.3
22.0
19.1
13.7
OH
H9C4
OH HN
Ph
syn-22Ab, CDCl3
100
50
ppm (t1)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7.22
7.19
4.67
4.66
4.64
4.63
4.04
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3.81
3.79
3.45
3.44
3.40
2.79
2.75
2.40
2.38
2.36
1.79
1.71
1.67
1.59
1.59
1.57
1.42
1.29
1.27
0.90
0.88
0.88
0.86
H17C8
OH
OH HN
Ph
syn-22Ba, CDCl3
9.35
1.00
1.03
1.02
1.17
1.21
1.90
6.69
6.90
7.75
8.12
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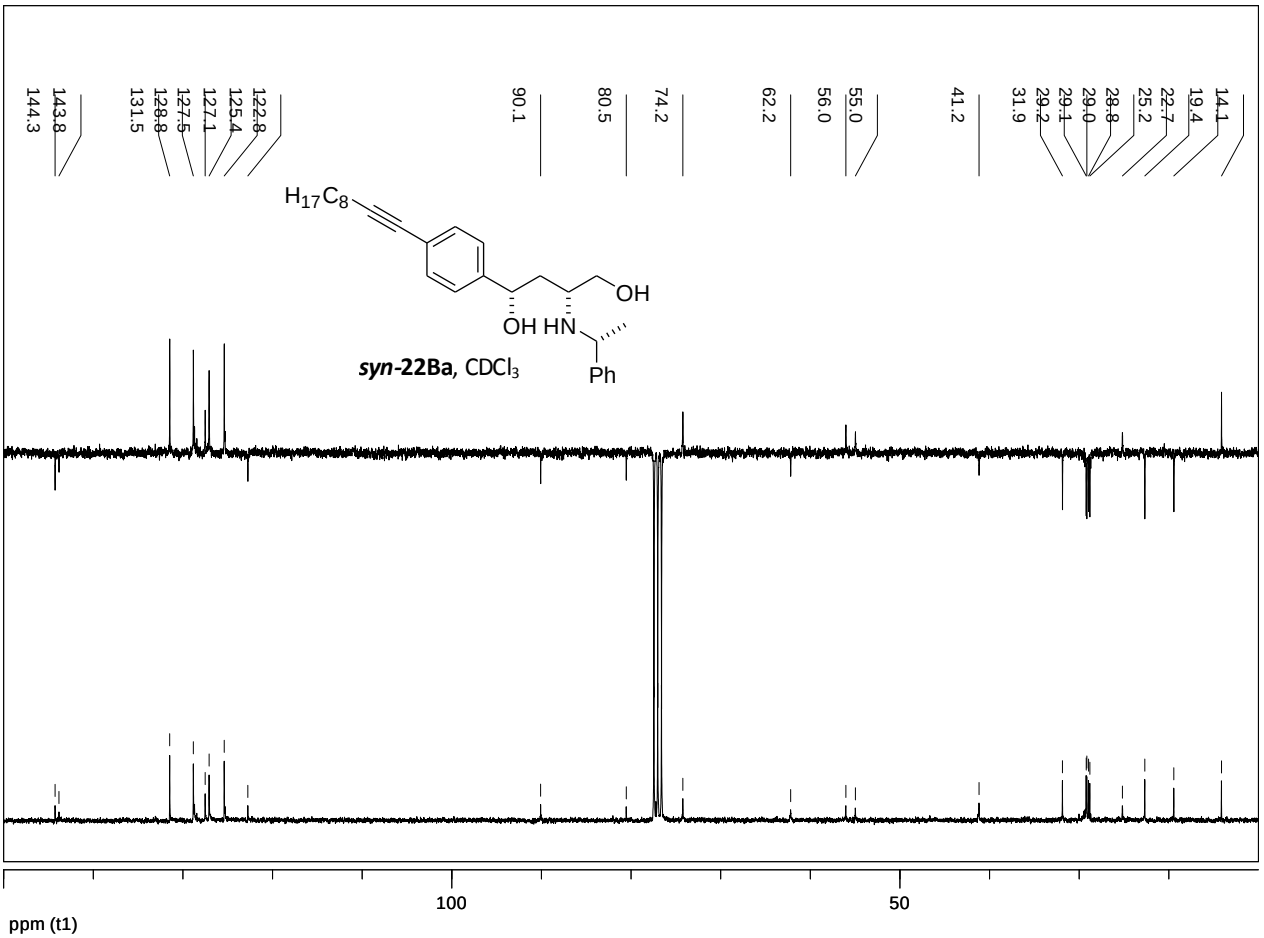
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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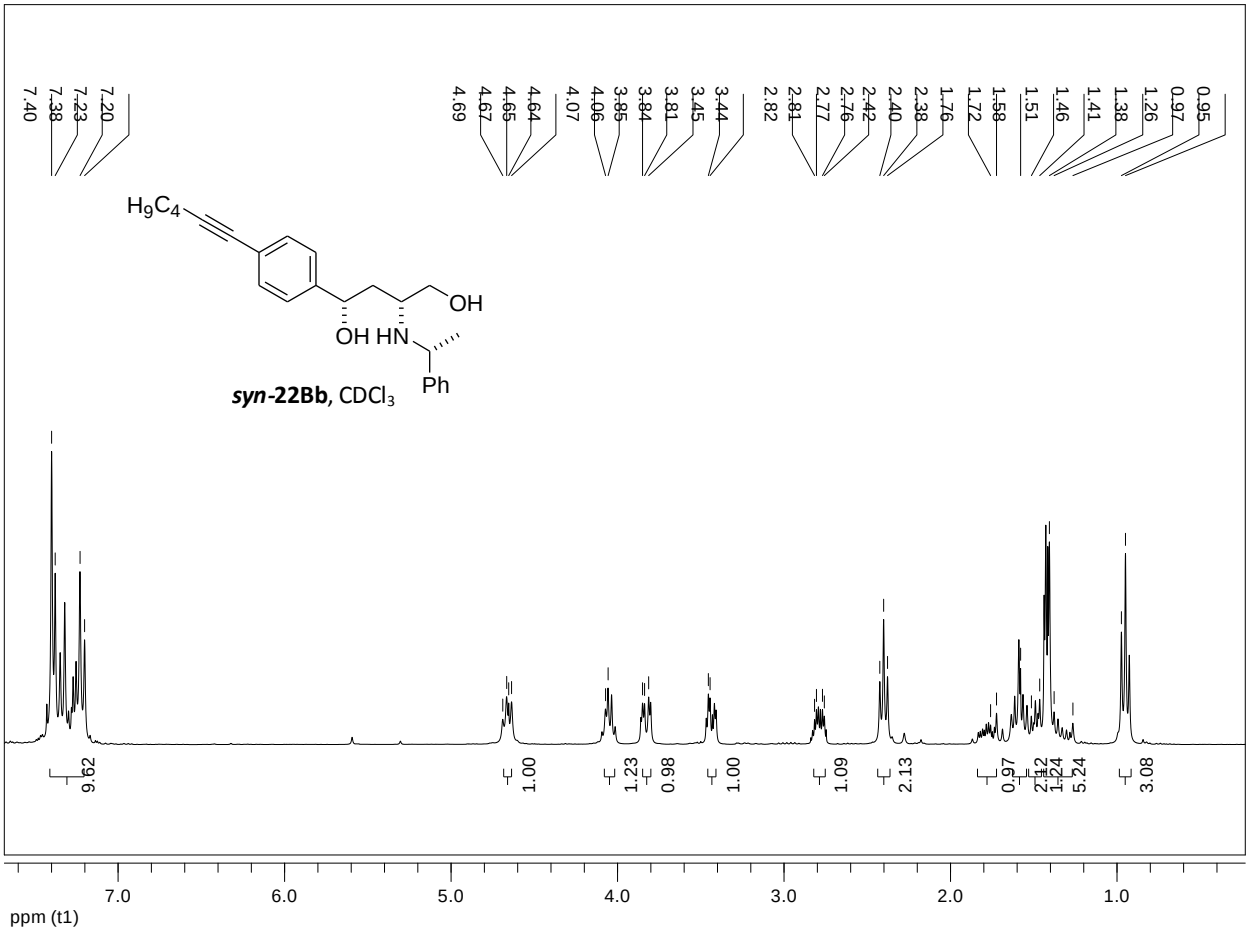
127.1
125.4
122.8
90.1
80.5
74.2
62.2
56.0
55.0
41.2
31.9
29.2
29.1
29.0
28.8
25.2
22.7
19.4
14.1
H17C8
OH
OH HN
Ph
syn-22Ba, CDCl3
100
50
ppm (t1)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4.07
4.06
3.85
3.84
3.81
3.45
3.44
2.82
2.81
2.77
2.76
2.42
2.40
2.38
1.76
1.72
1.58
1.51
1.46
1.41
1.38
1.26
0.97
0.95
H9C4
OH
OH HN
Ph
syn-22Bb, CDCl3
9.62
1.00
1.23
0.98
1.00
1.09
2.13
0.97
2.12
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5.24
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6.0
5.0
4.0
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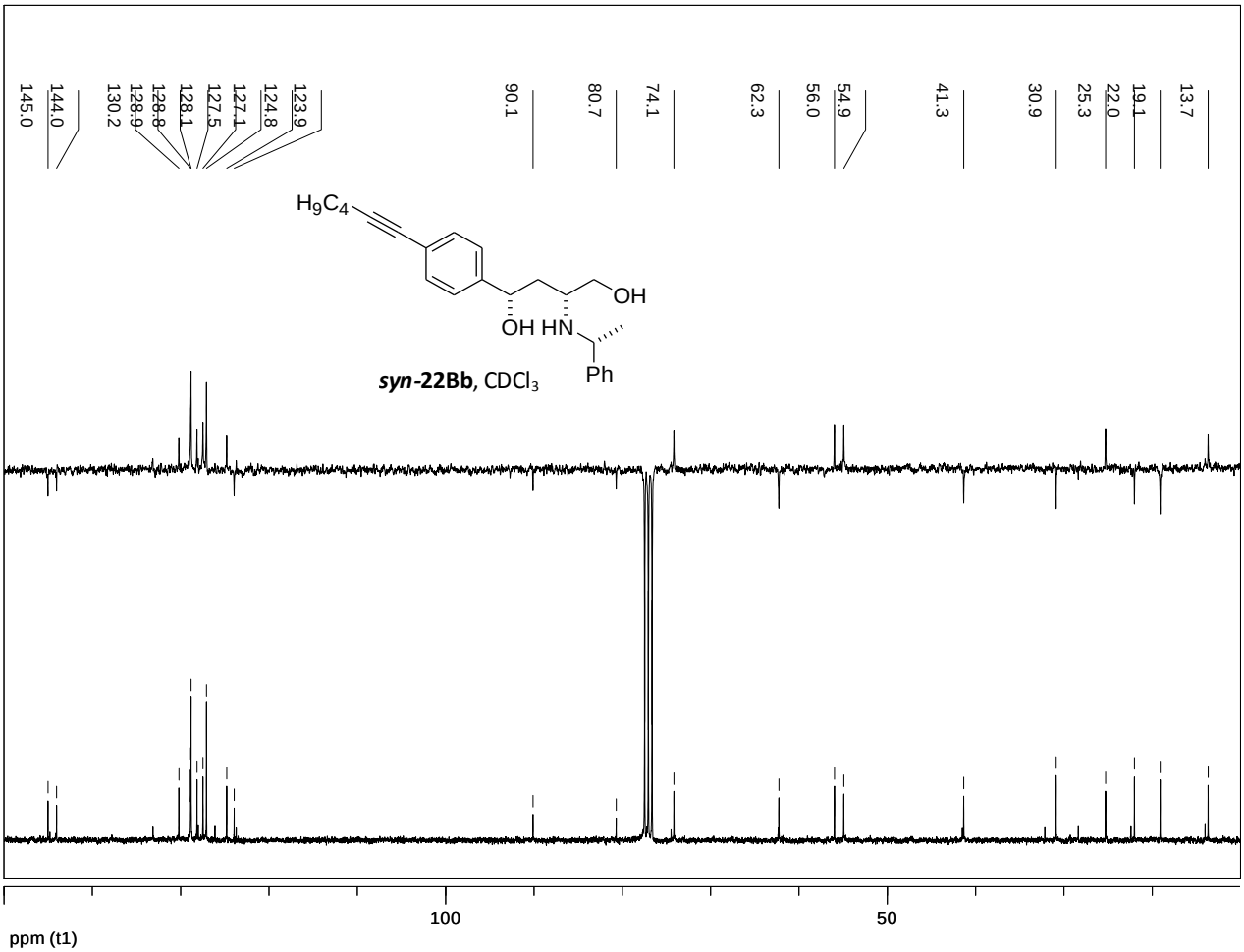
2.0
1.0
ppm (t1)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144.0
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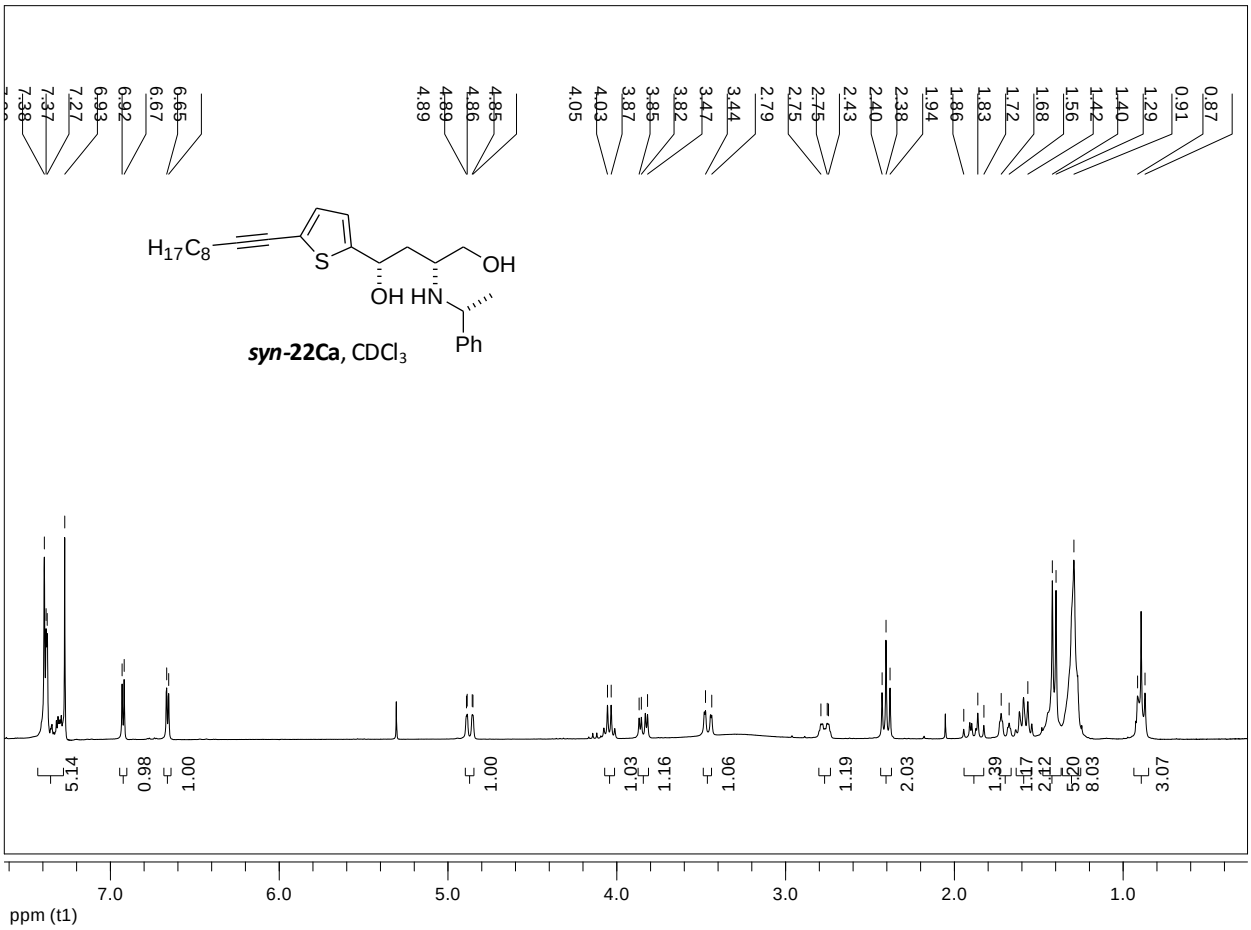
128.9
128.8
128.1
127.5
127.1
124.8
123.9
90.1
80.7
74.1
62.3
56.0
54.9
41.3
30.9
25.3
22.0
19.1
13.7
H9C4
OH
OH HN
Ph
syn-22Bb, CDCl3
100
50
ppm (t1)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6.67
6.65
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4.89
4.86
4.85
4.05
4.03
3.87
3.85
3.82
3.47
3.44
2.79
2.75
2.75
2.43
2.40
2.38
1.94
1.86
1.83
1.72
1.68
1.56
1.42
1.40
1.29
0.91
0.87
H17C8
S
OH
OH HN
Ph
syn-22Ca, CDCl3
1.14
0.98
1.00
1.00
1.03
1.16
1.06
1.19
2.03
1.39
1.77
2.12
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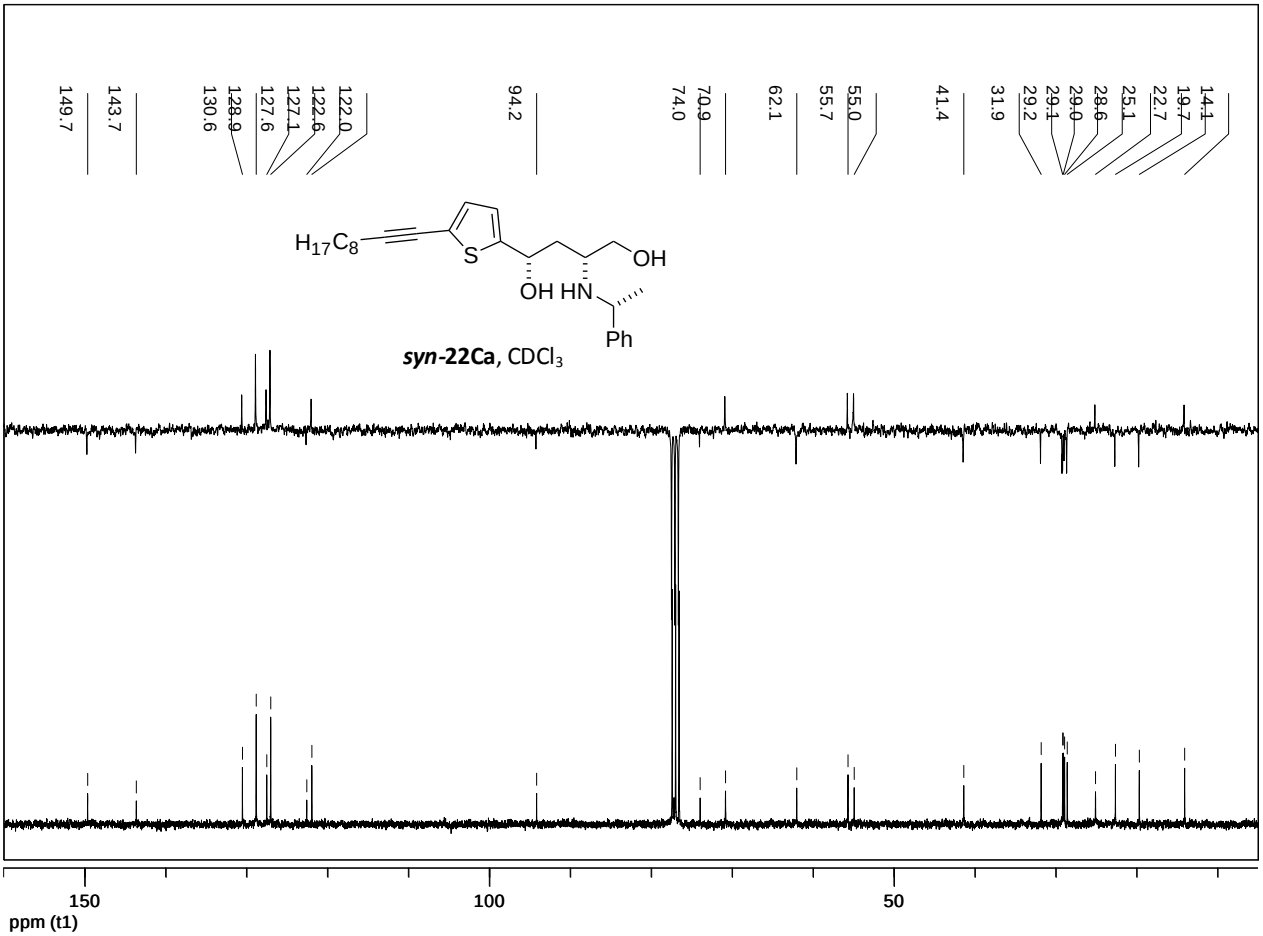
8.03
3.07
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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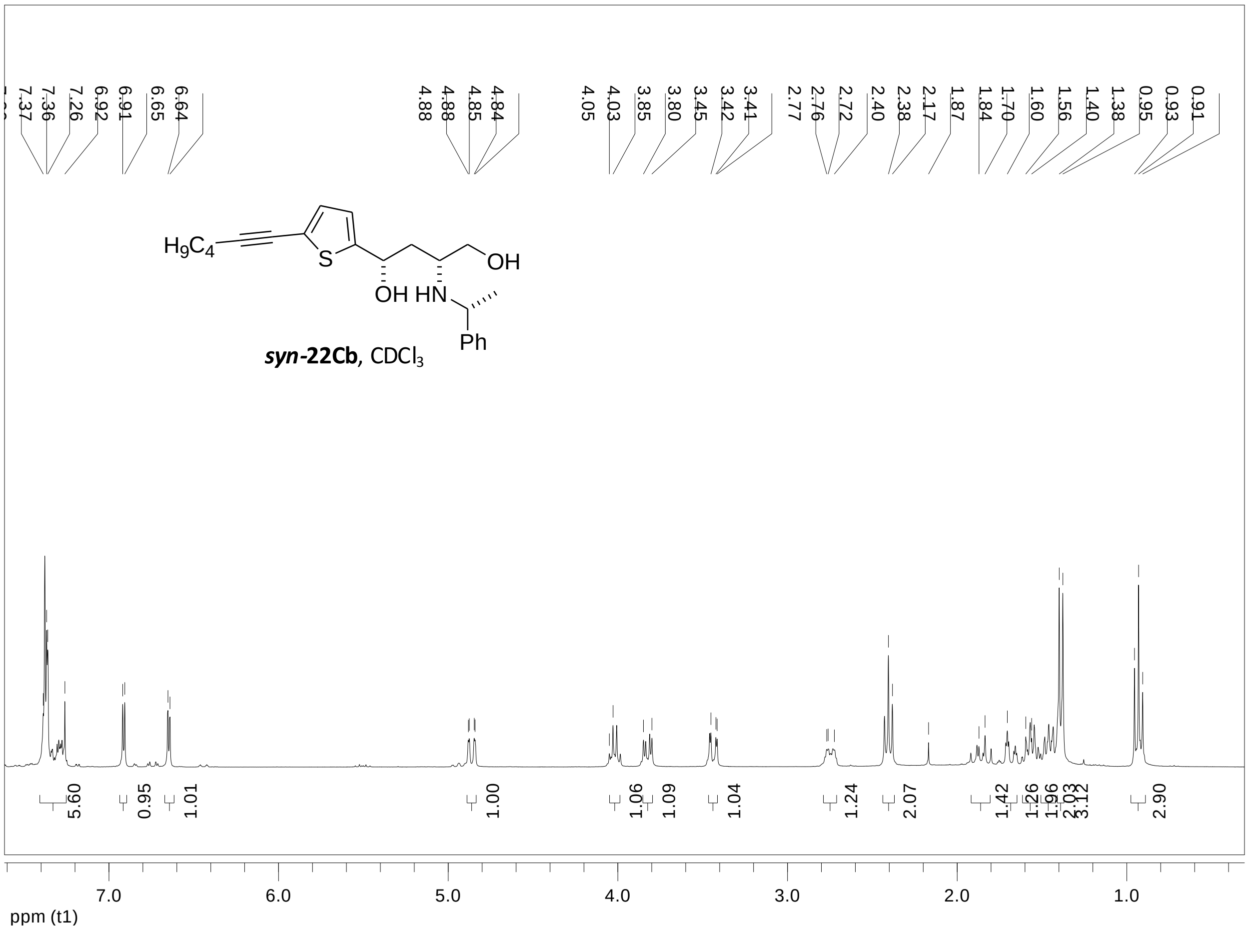
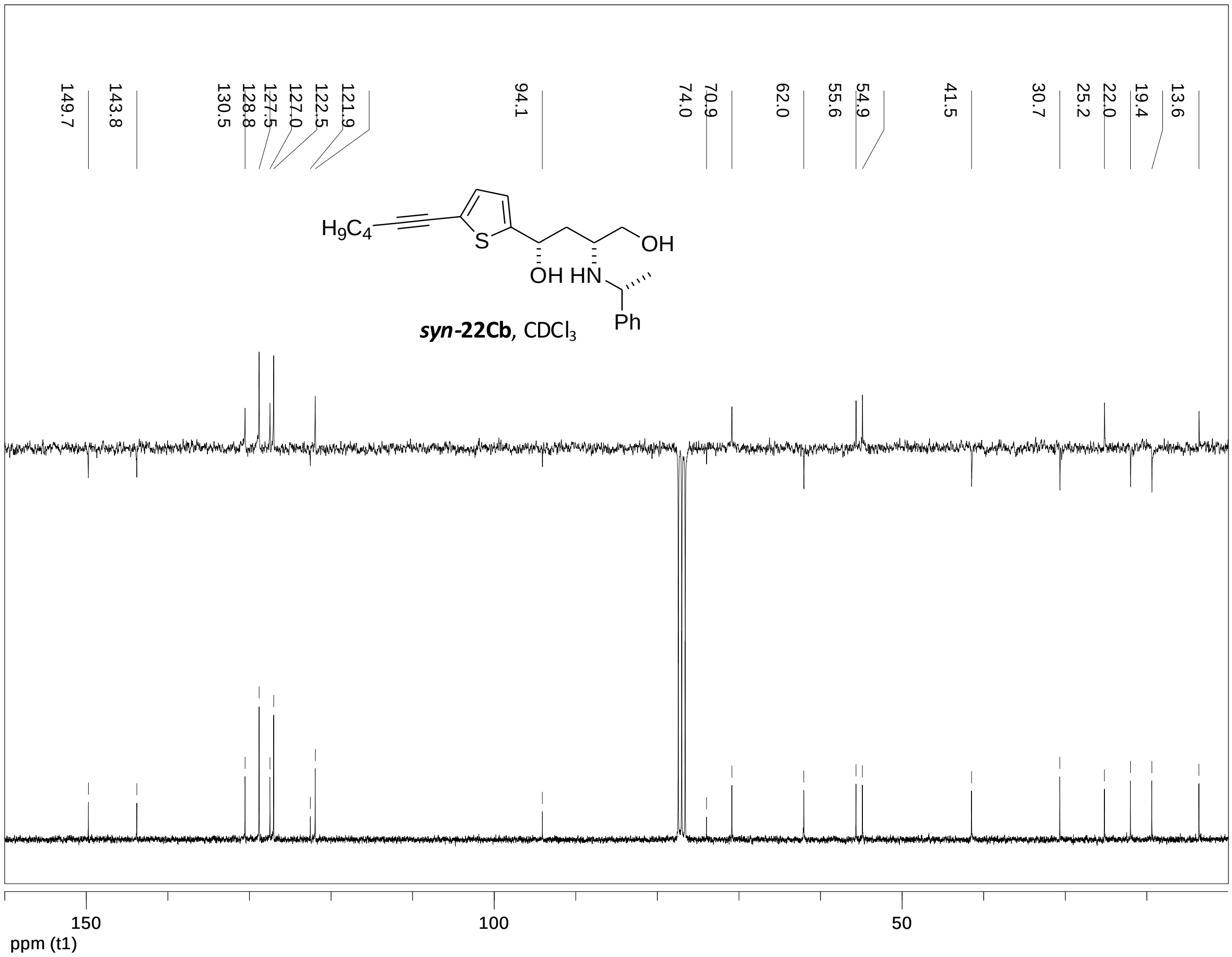
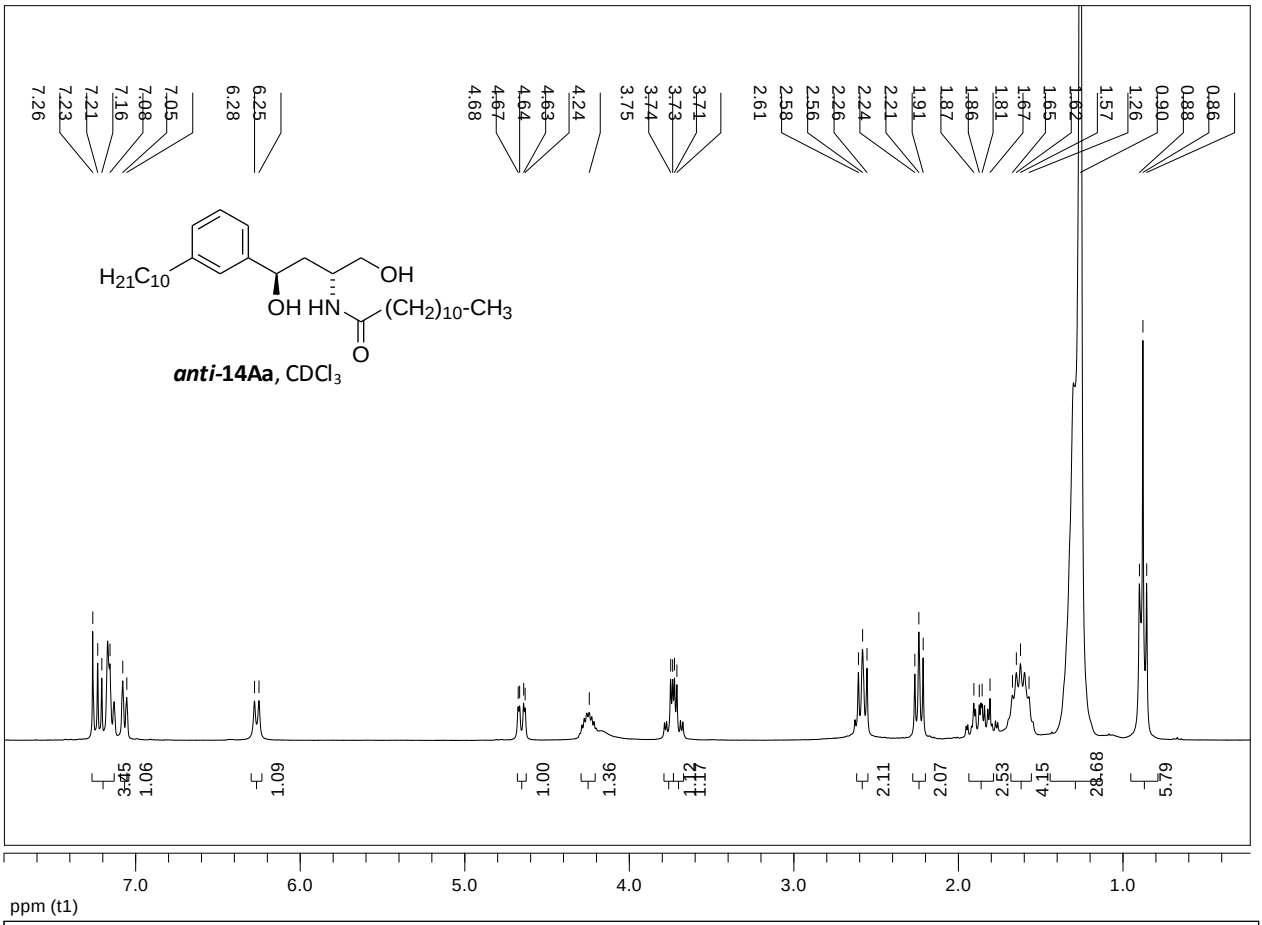
127.6
127.1
122.6
122.0
94.2
74.0
70.9
62.1
55.7
55.0
41.4
31.9
29.2
29.1
29.0
28.6
25.1
22.7
19.7
14.1
H17C8
S
OH
OH HN
Ph
syn-22Ca, CDCl3
150
100
50
ppm (t1)


syn-22Cb, CDCl3
ppm (t1)


syn-22Cb, CDCl3
ppm (t1)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7.05
6.28
6.25
4.68
4.67
4.64
4.63
4.24
3.75
3.74
3.73
3.71
2.61
2.58
2.56
2.26
2.24
2.21
1.91
1.87
1.86
1.81
1.67
1.65
1.62
1.57
1.26
0.90
0.88
0.86
3.45
3.04
0.90
1.00
1.00
1.36
1.12
1.17
2.11
2.07
2.53
4.15
28.68
5.79
7.0
6.0
5.0
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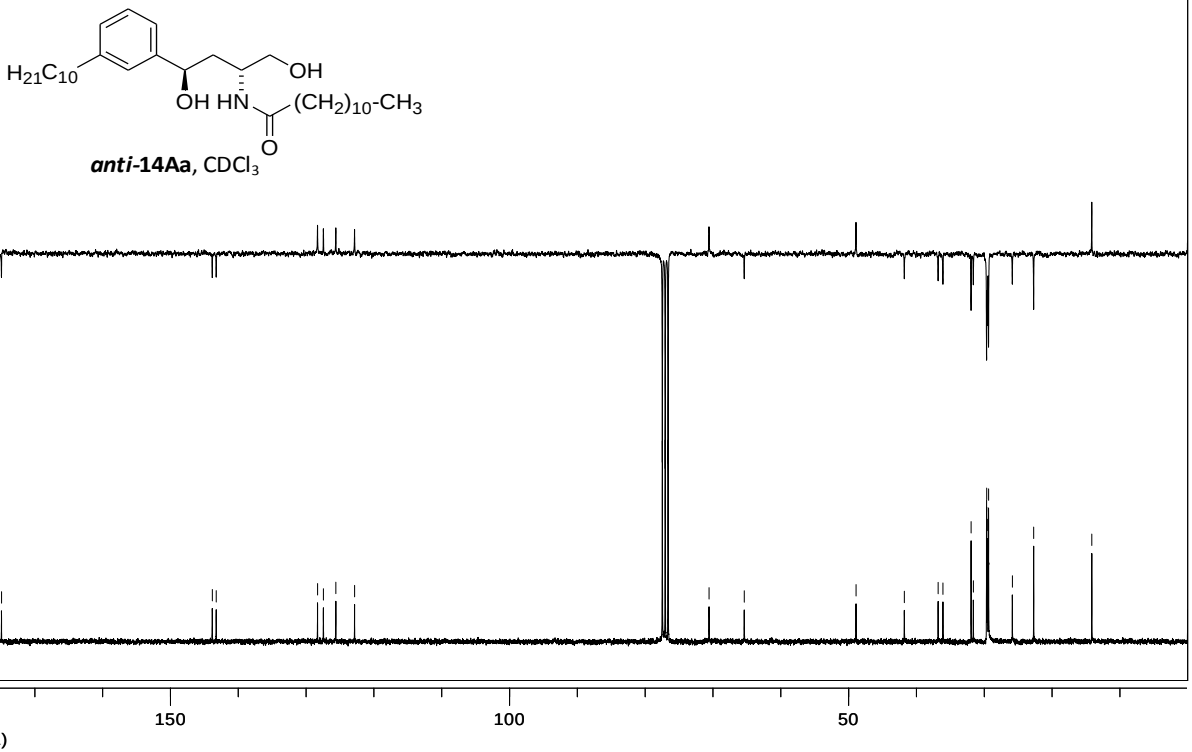
3.0
2.0
1.0
ppm (t1)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128.3
127.4
125.6
122.8
70.6
65.4
48.9
41.8
36.8
36.1
31.9
31.6
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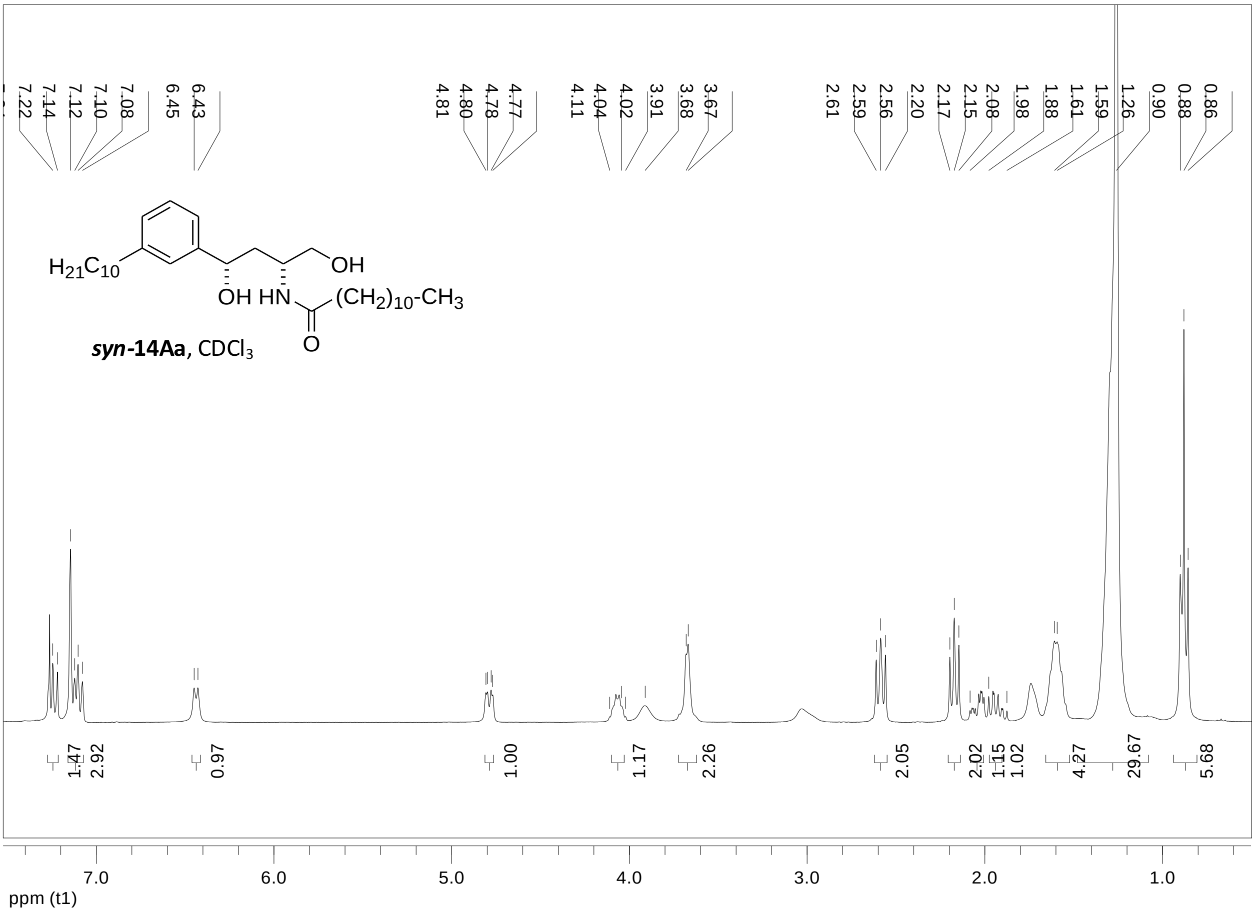
22.7
14.1
150
100
50
ppm (t1)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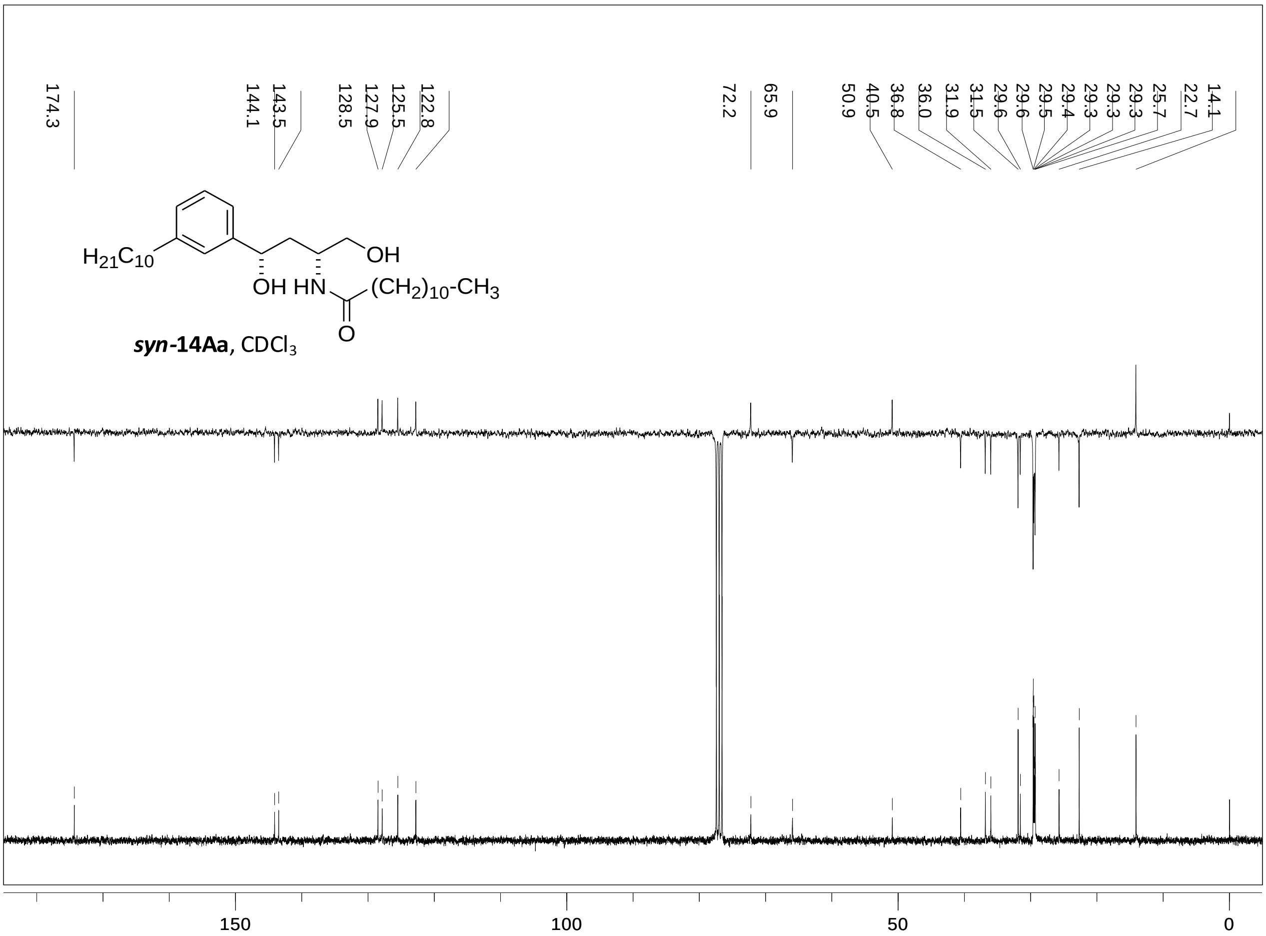
H21C10
OH HN (CH2)10-CH3
OH
O
syn-14Aa, CDCl3
1.47 2.92 0.97 1.00 1.17 2.26 2.05 2.02 1.15 1.02 4.27 29.67 5.68
7.0 6.0 5.0 4.0 3.0 2.0 1.0
ppm (t1)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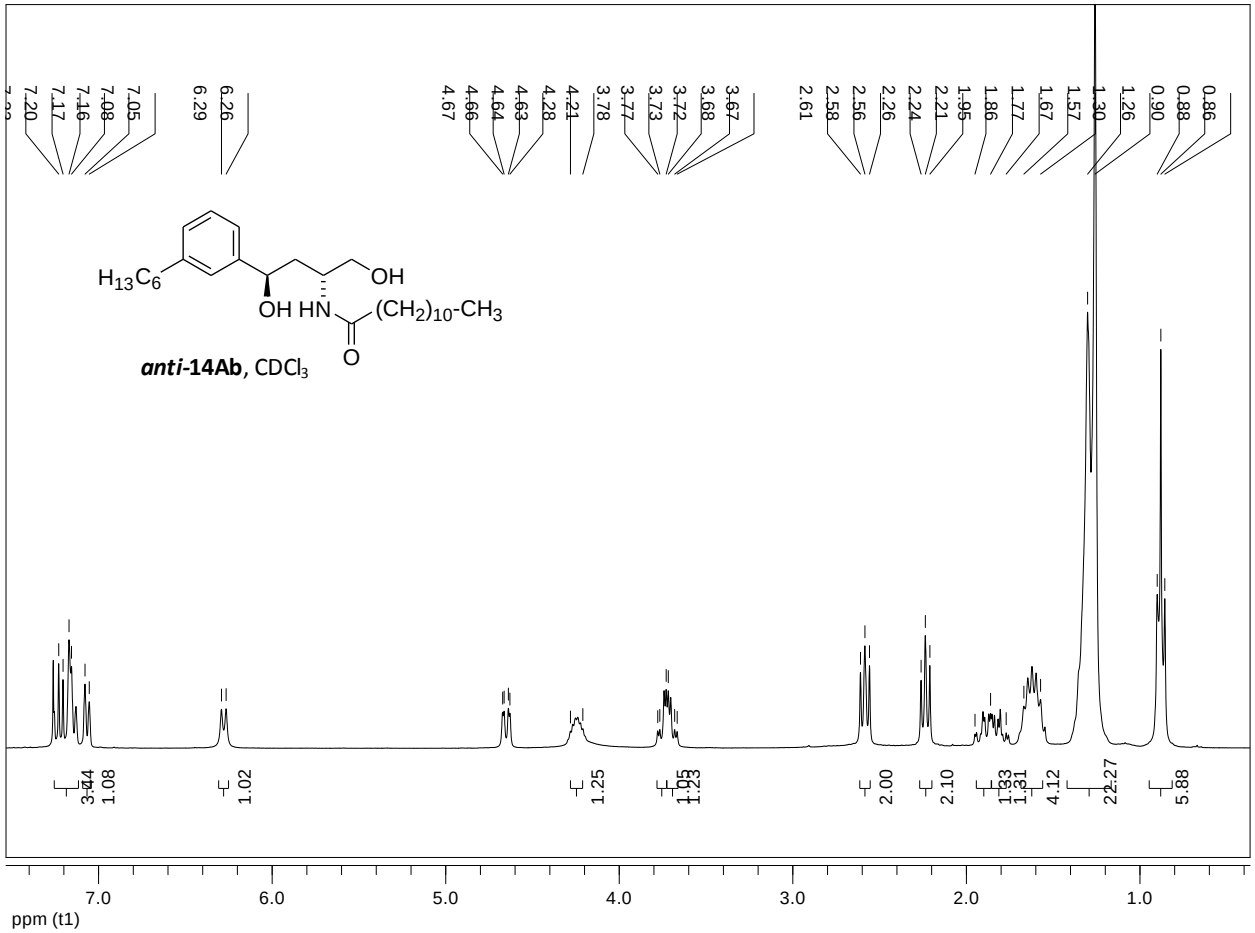
H21C10
OH HN (CH2)10-CH3
OH
O
syn-14Aa, CDCl3
150 100 50 0
ppm (t1)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6.26
4.67
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4.64
4.63
4.28
4.21
3.78
3.77
3.73
3.72
3.68
3.67
2.61
2.58
2.56
2.26
2.24
2.21
1.95
1.86
1.77
1.67
1.57
1.30
1.26
0.90
0.88
0.86
3.44
1.08
1.02
1.25
1.05
2.00
2.10
1.33
1.31
4.12
2.27
5.88
OH
OH HN
(CH2)10-CH3
O
anti-14Ab, CDCl3
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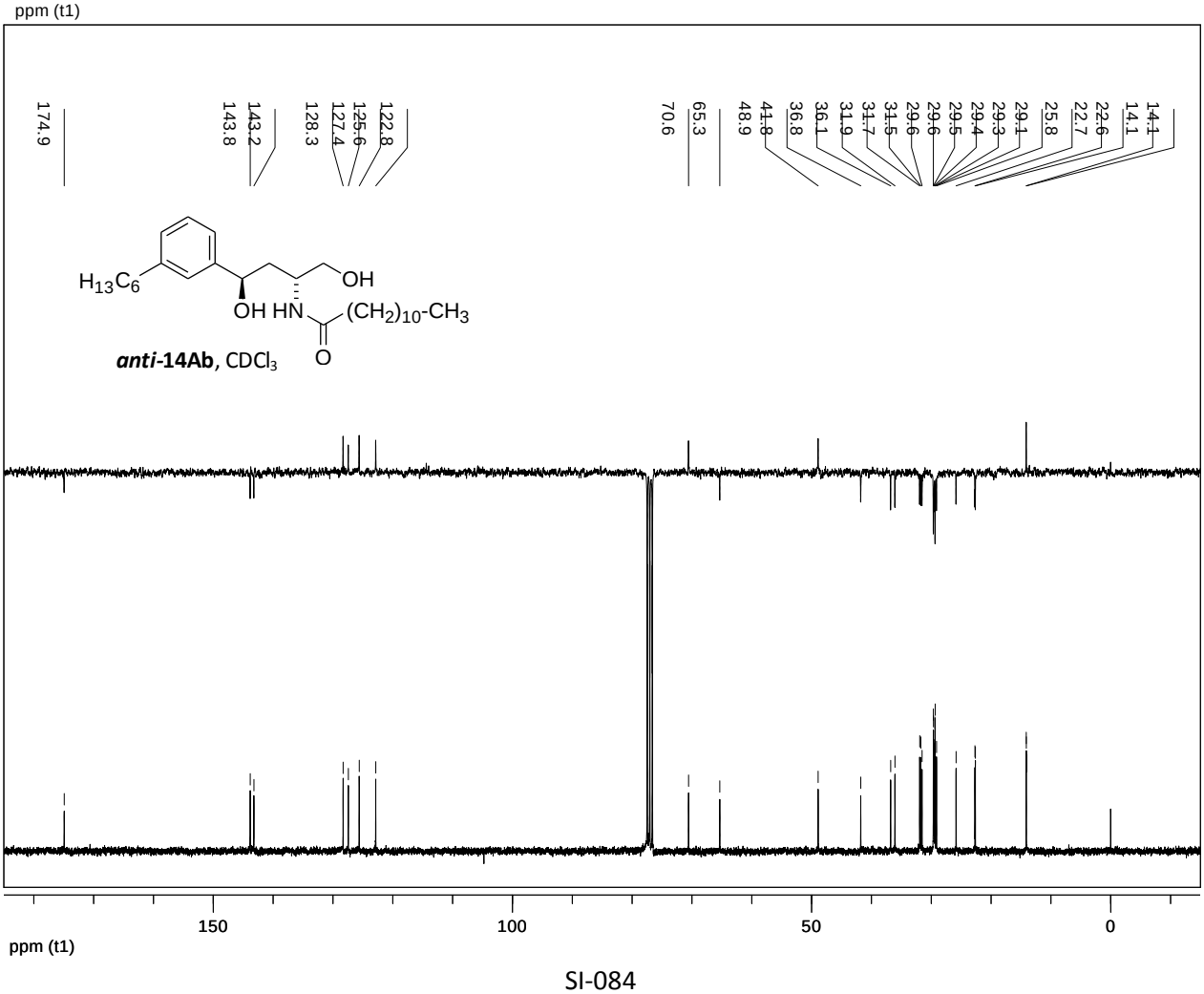
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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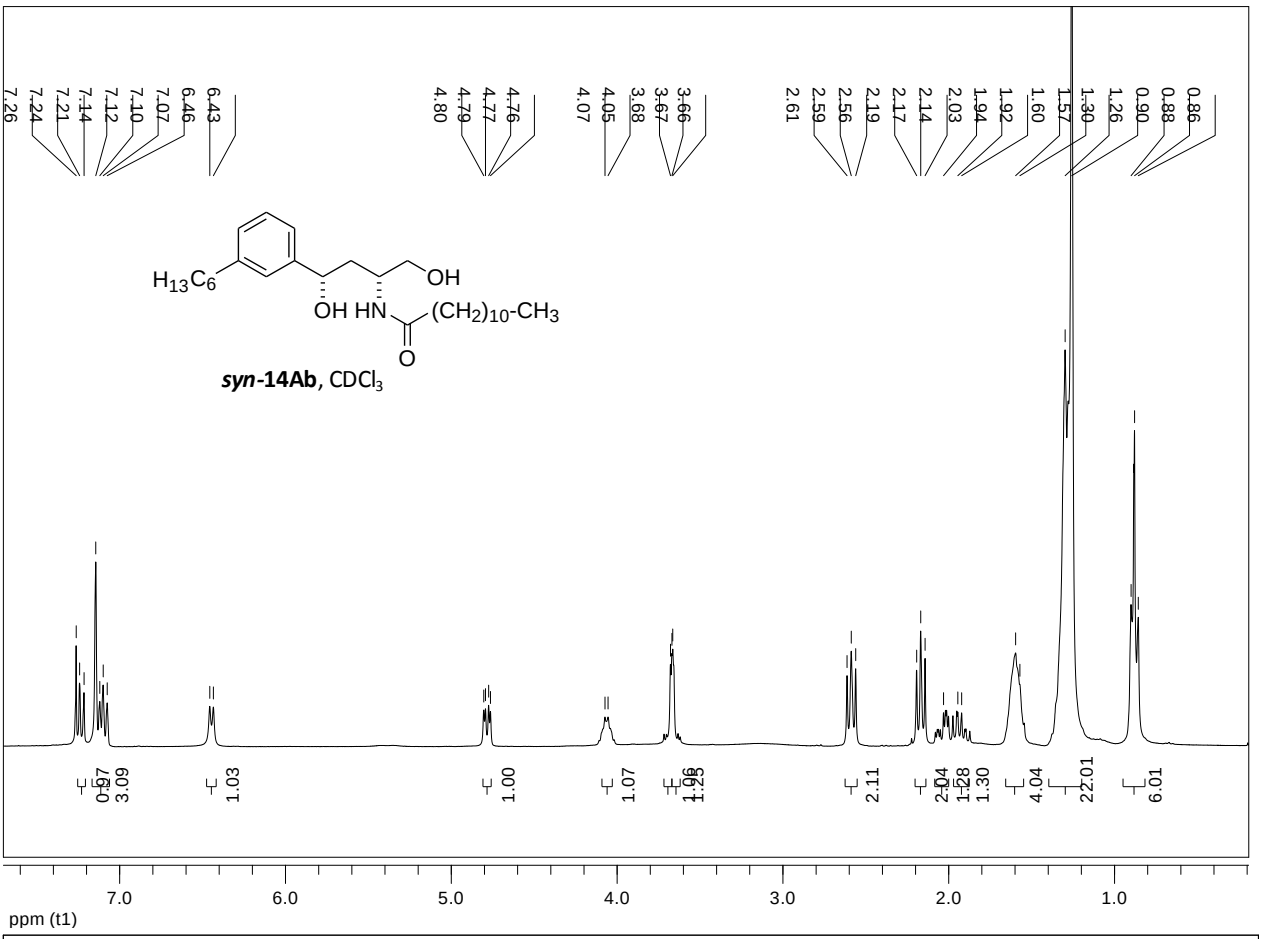
143.8
143.2
128.3
127.4
125.6
122.8
70.6
65.3
48.9
41.8
36.8
36.1
31.9
31.7
31.5
29.6
29.6
29.5
29.4
29.3
29.1
25.8
22.7
22.6
14.1
14.1
OH
OH HN
(CH2)10-CH3
O
anti-14Ab, CDCl3
150
100
50
0
ppm (t1)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4.79
4.77
4.76
4.07
4.05
3.68
3.67
3.66
2.61
2.59
2.56
2.19
2.17
2.14
2.03
1.94
1.92
1.60
1.57
1.30
1.26
0.90
0.88
0.86
H13C6
OH
OH HN
(CH2)10-CH3
O
syn-14Ab, CDCl3
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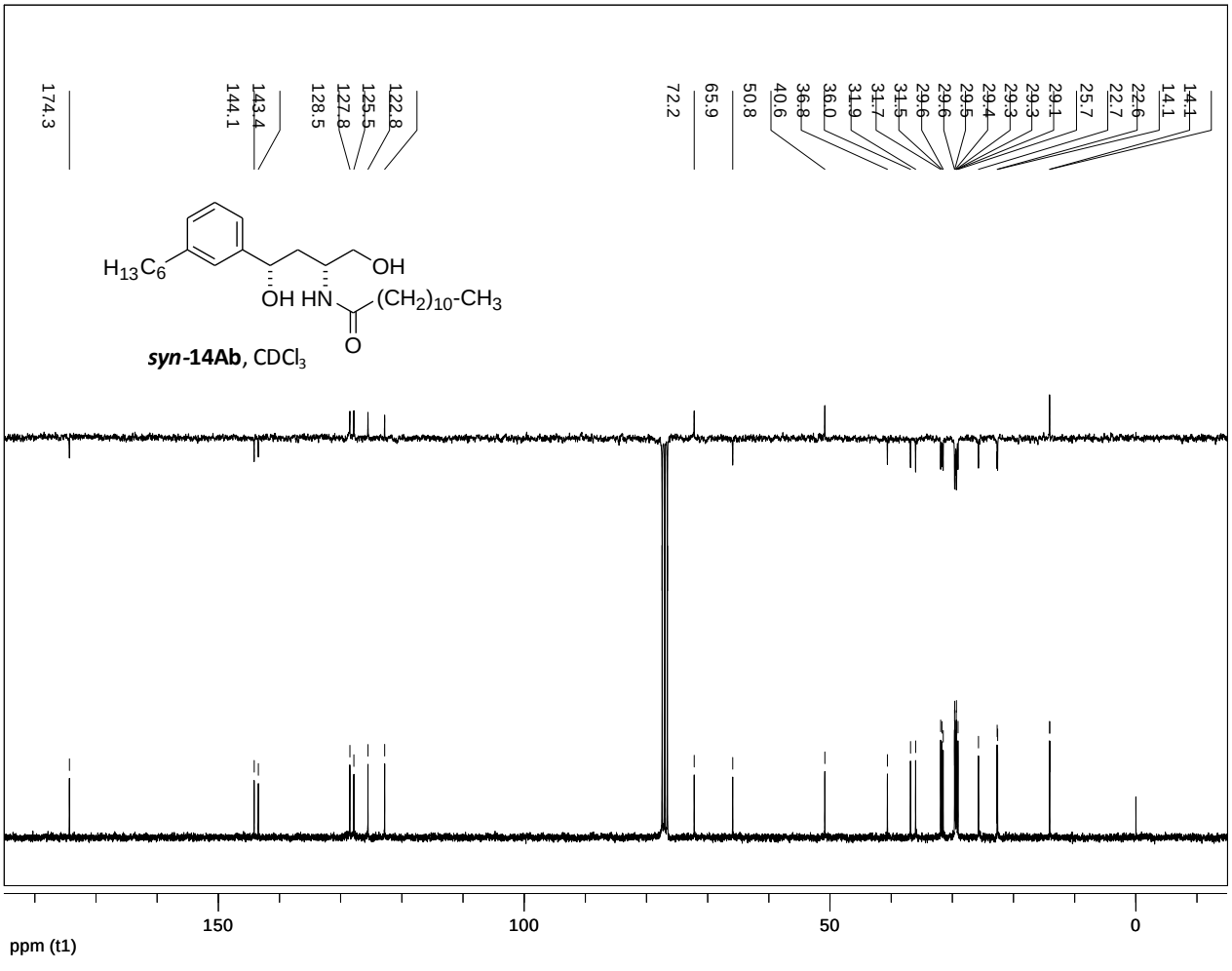
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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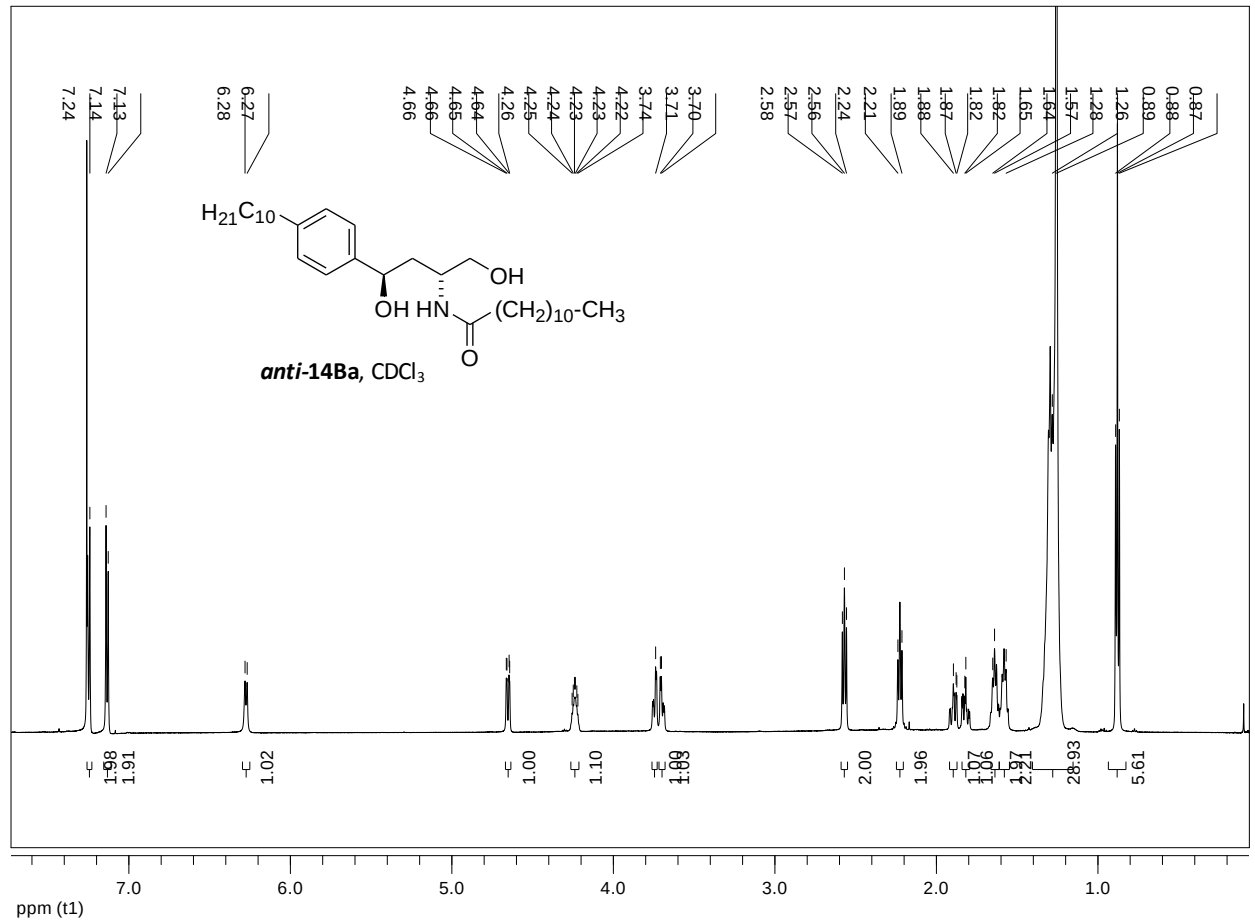
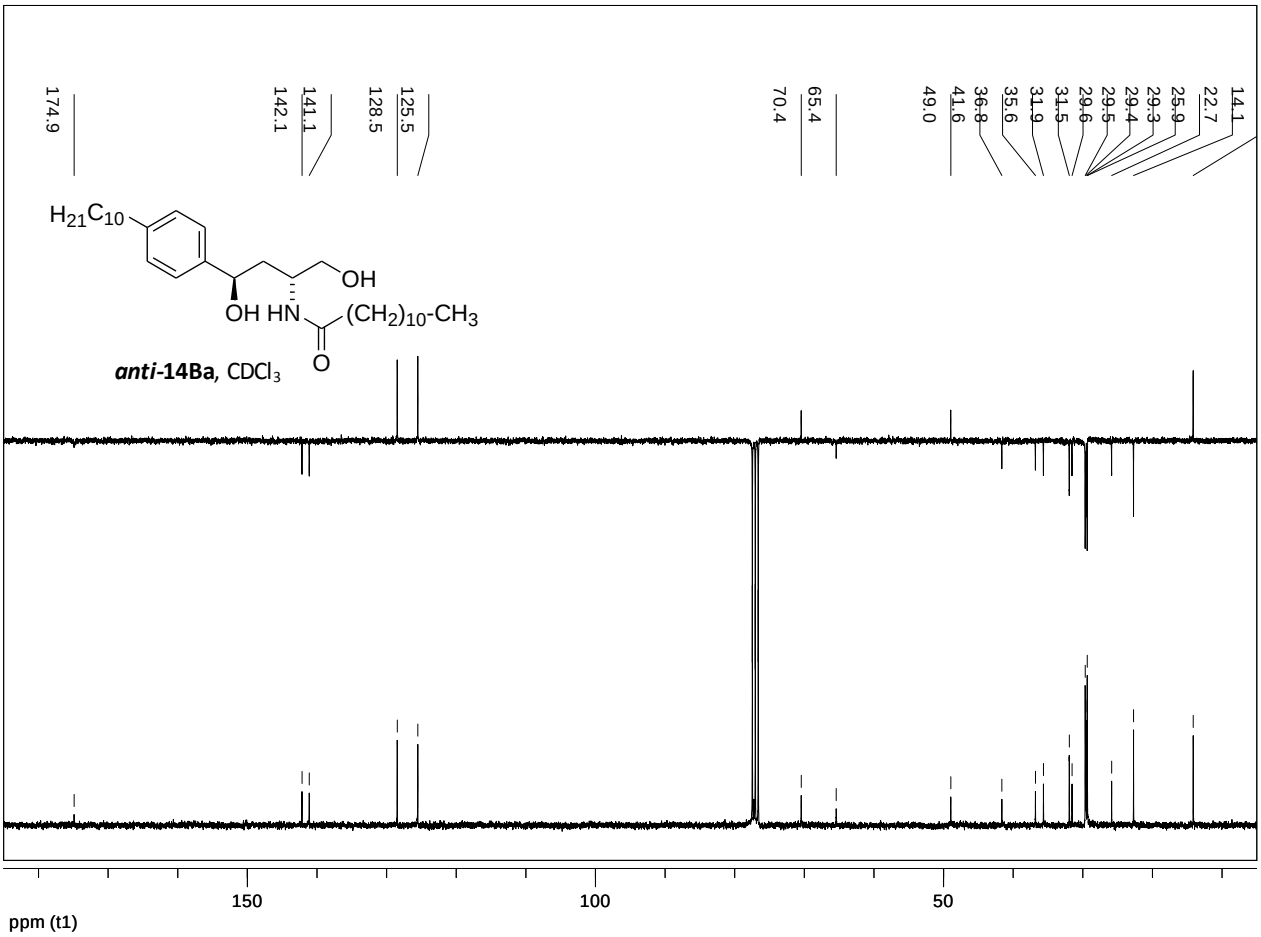
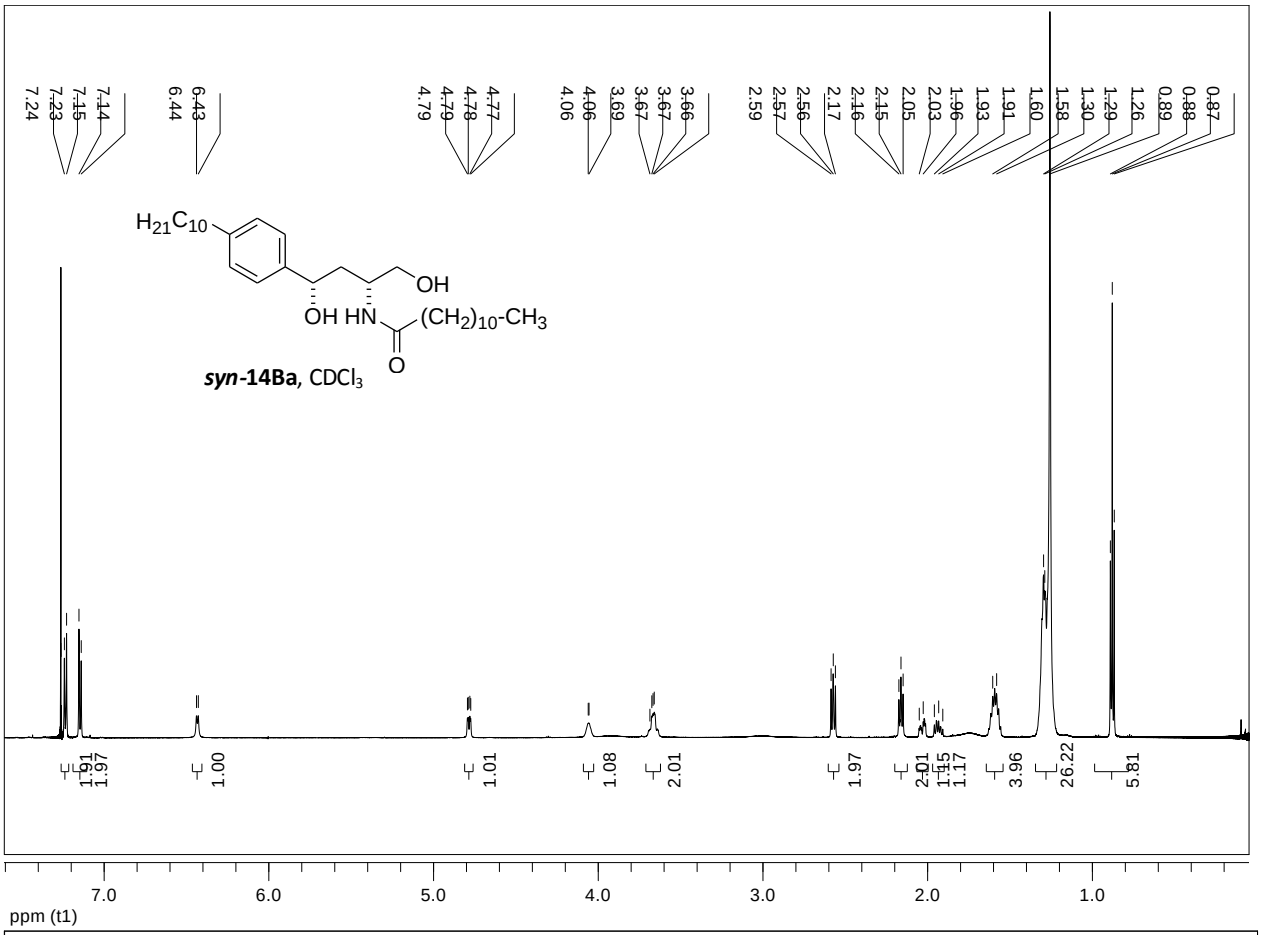
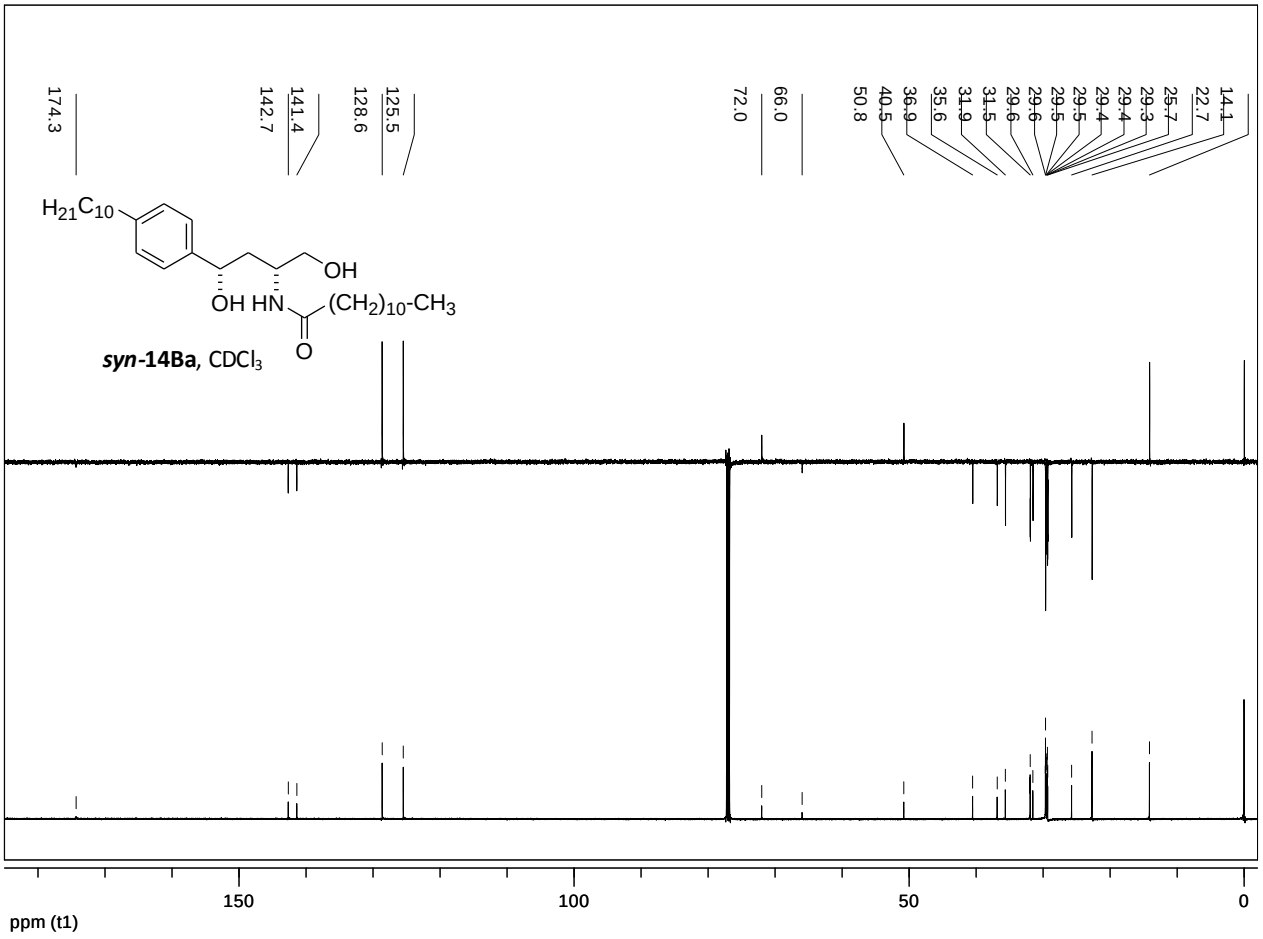
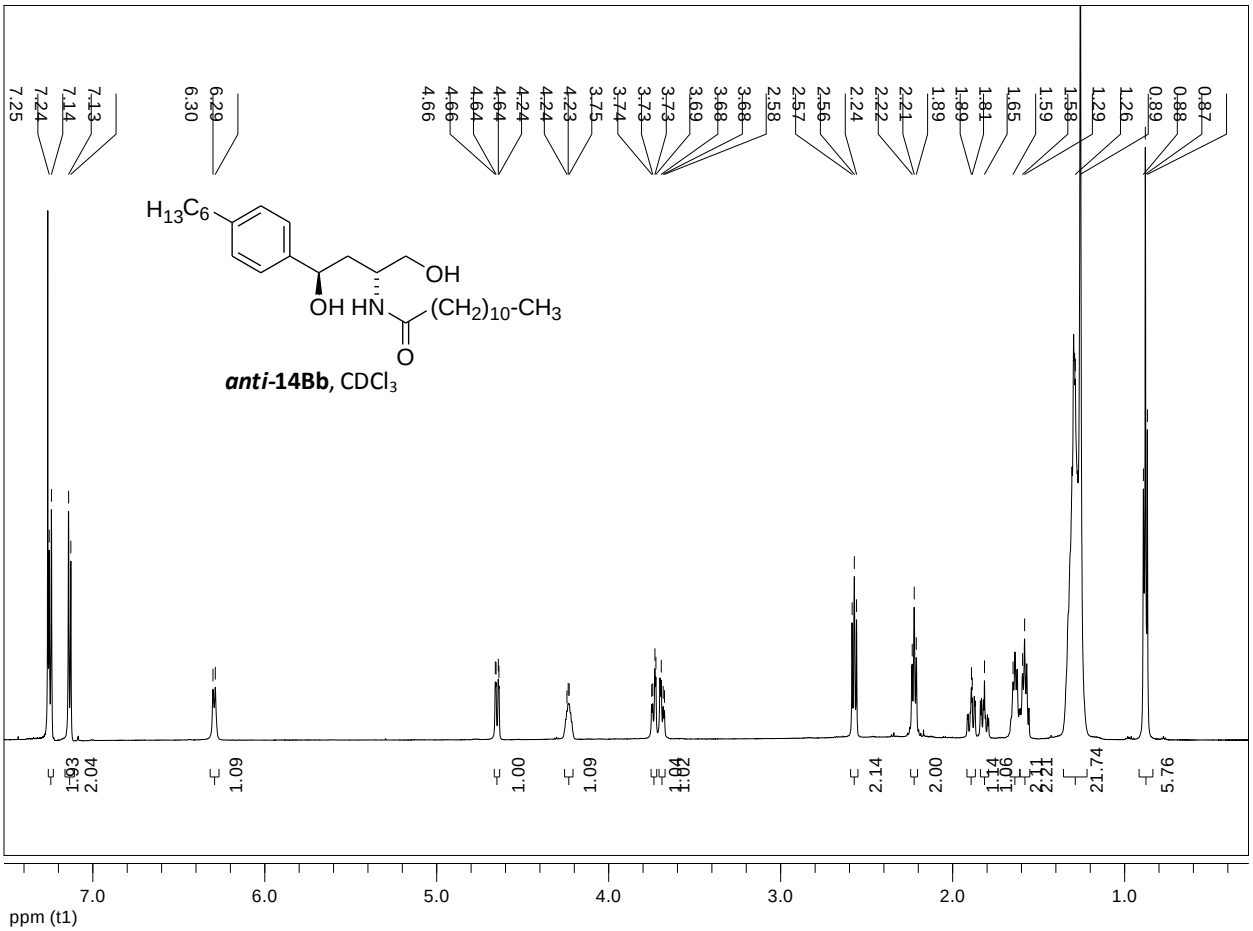
143.4
128.5
127.8
125.5
122.8
72.2
65.9
50.8
40.6
36.8
36.0
31.9
31.7
31.5
29.6
29.6
29.5
29.4
29.3
29.3
29.1
25.7
22.7
22.6
14.1
14.1
H13C6
OH
OH HN
(CH2)10-CH3
O
syn-14Ab, CDCl3
150
100
50
0
ppm (t1)


7.24
7.14
7.13
6.28
6.27
4.66
4.65
4.64
4.26
4.25
4.24
4.23
4.22
3.74
3.71
3.70
2.58
2.57
2.56
2.24
2.21
1.89
1.88
1.87
1.82
1.65
1.64
1.57
1.28
1.26
0.89
0.88
0.87
1.91
0.86
1.02
1.00
1.10
2.00
1.96
19.5
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)
H21C10
OH
OH HN
(CH2)10-CH3
O
anti-14Ba, CDCl3

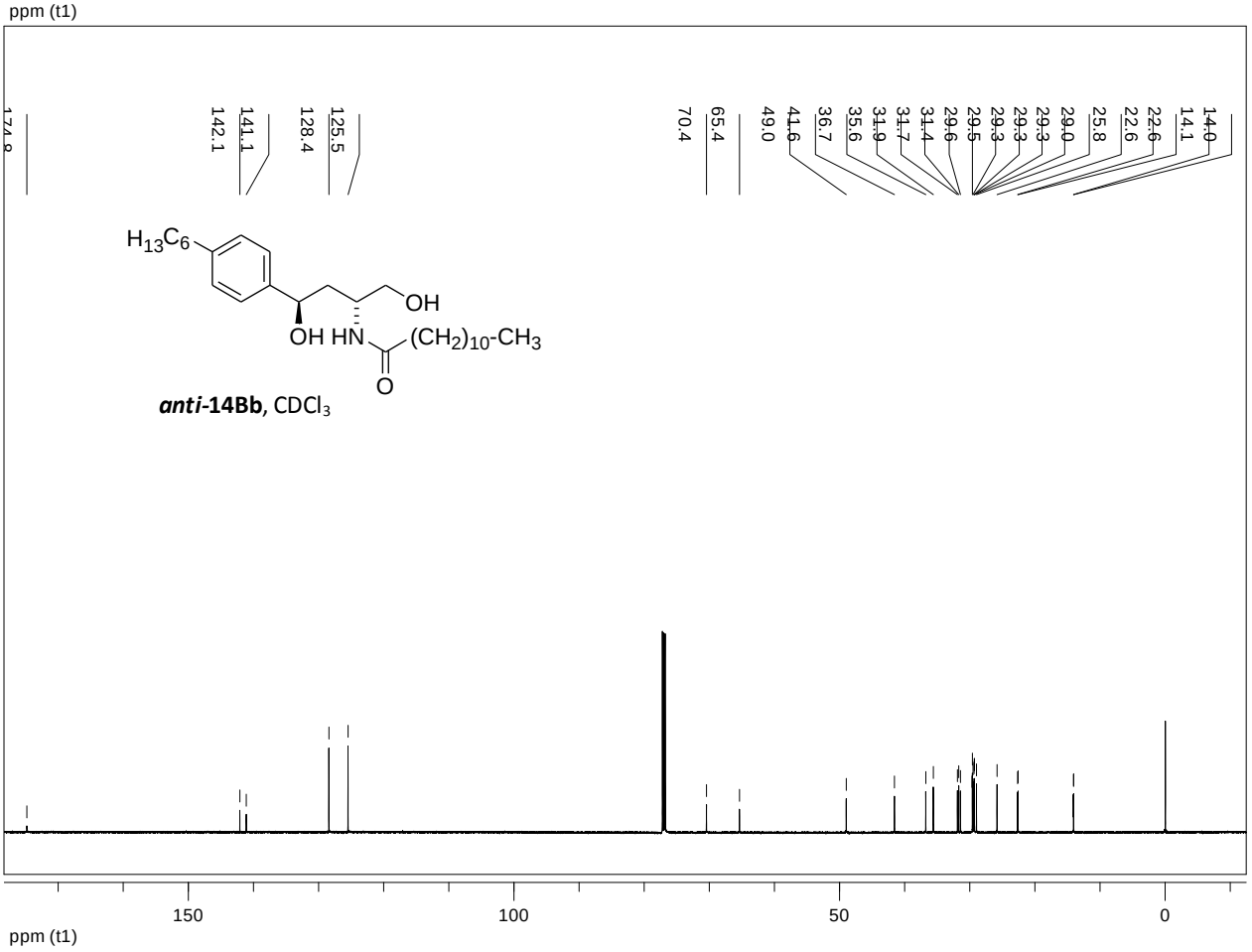

174.9
142.1
141.1
128.5
125.5
70.4
65.4
49.0
41.6
36.8
35.6
31.9
31.5
29.6
29.5
29.4
29.3
25.9
22.7
14.1
150
100
50
ppm (t1)
H21C10
OH
OH HN
(CH2)10-CH3
O
anti-14Ba, CDCl3


7.24
7.23
7.15
7.14
6.44
6.43
4.79
4.78
4.77
4.06
3.69
3.67
3.66
2.59
2.57
2.56
2.17
2.16
2.15
2.05
2.03
1.96
1.93
1.91
1.60
1.58
1.30
1.29
1.26
0.89
0.88
0.87
$H_{21}C_{10}$
OH
OH HN
$(CH_2)_{10}$-CH_3
O
syn-**14Ba**, $CDCl_3$
1.00
1.01
1.08
2.01
1.97
3.96
26.22
5.81
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

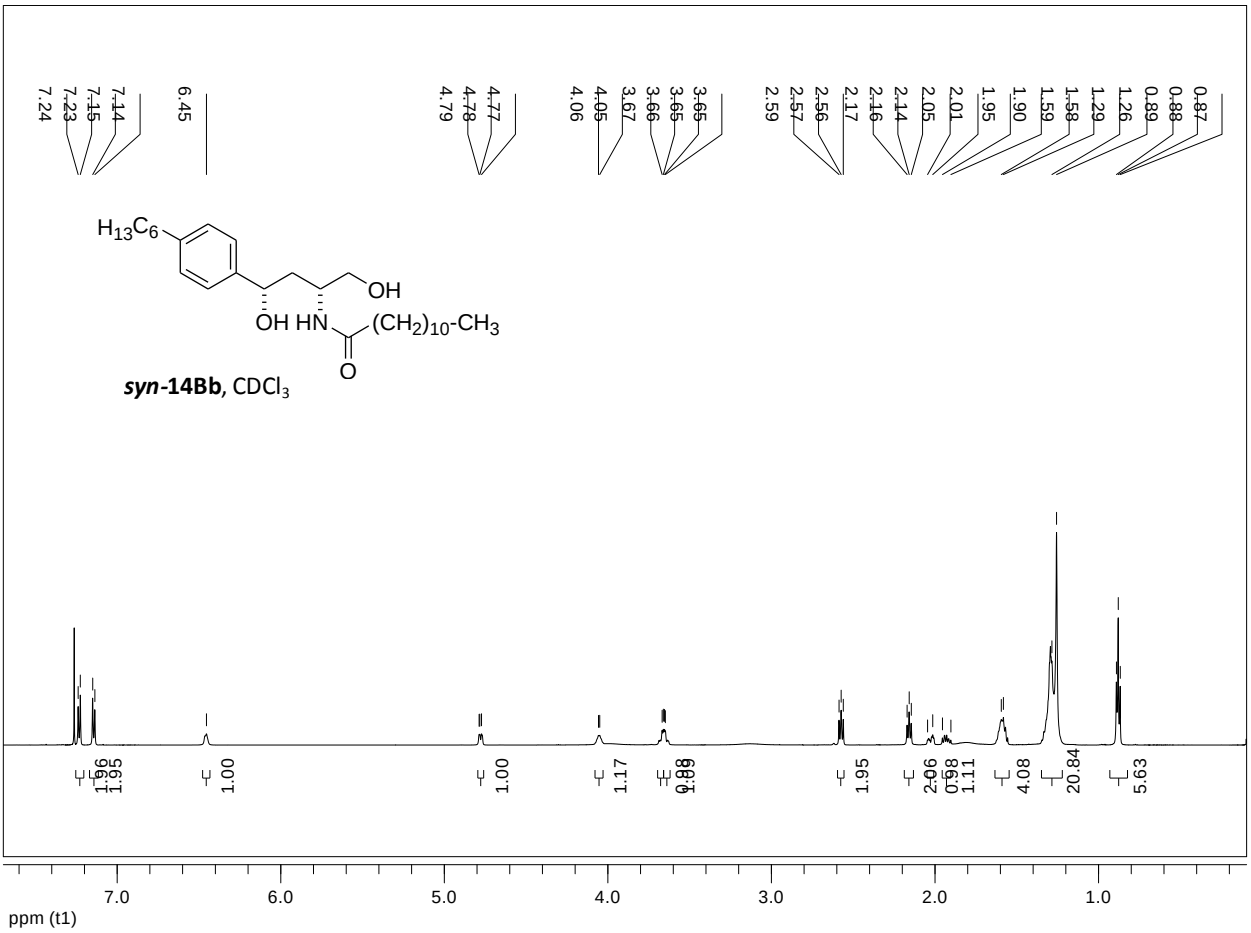

174.3
142.7
141.4
128.6
125.5
72.0
66.0
50.8
40.5
36.9
35.6
31.9
31.5
29.6
29.6
29.5
29.5
29.4
29.4
29.3
25.7
22.7
14.1
$H_{21}C_{10}$
OH
OH HN
$(CH_2)_{10}$-CH_3
O
syn-**14Ba**, $CDCl_3$
150
100
50
0
ppm (t1)

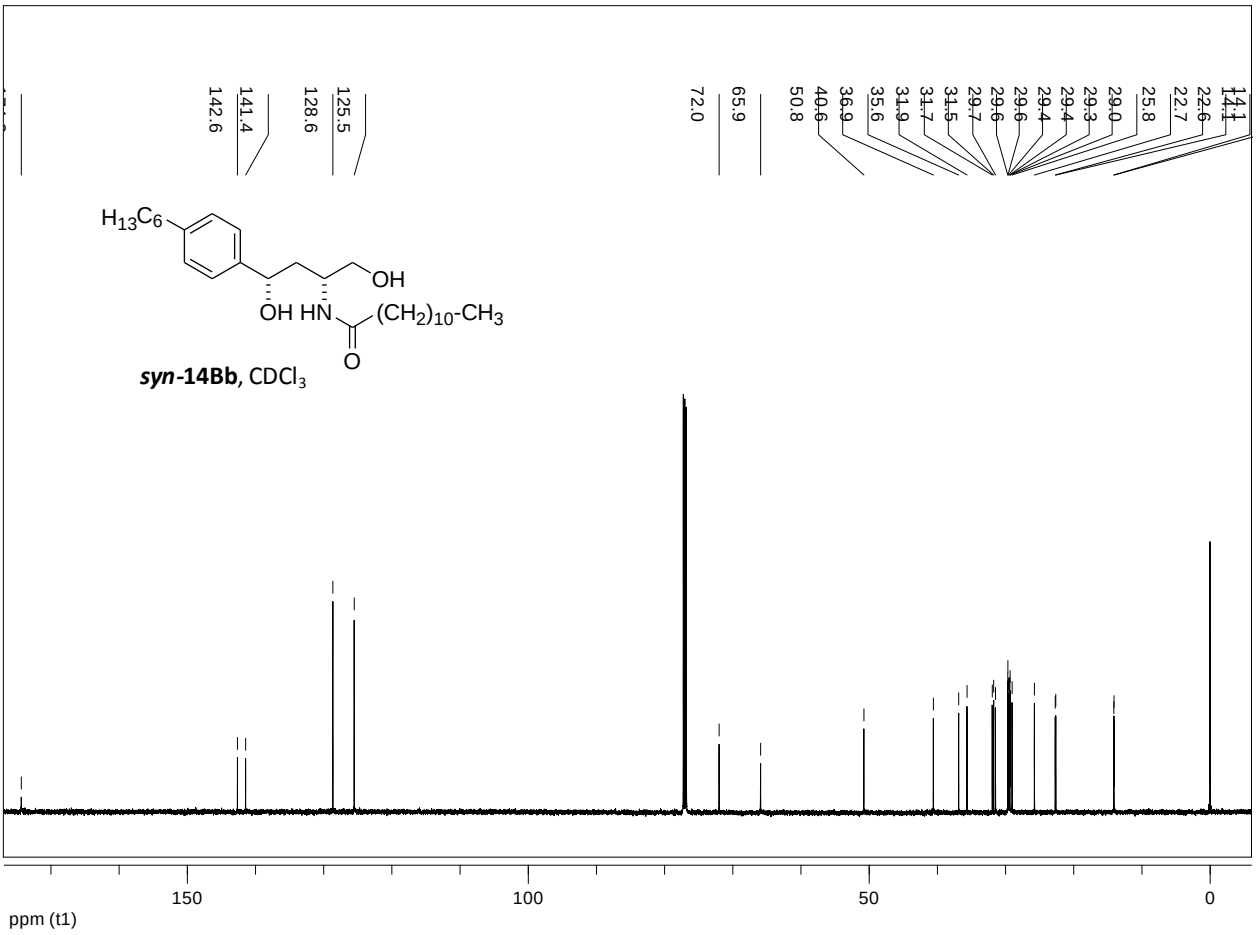


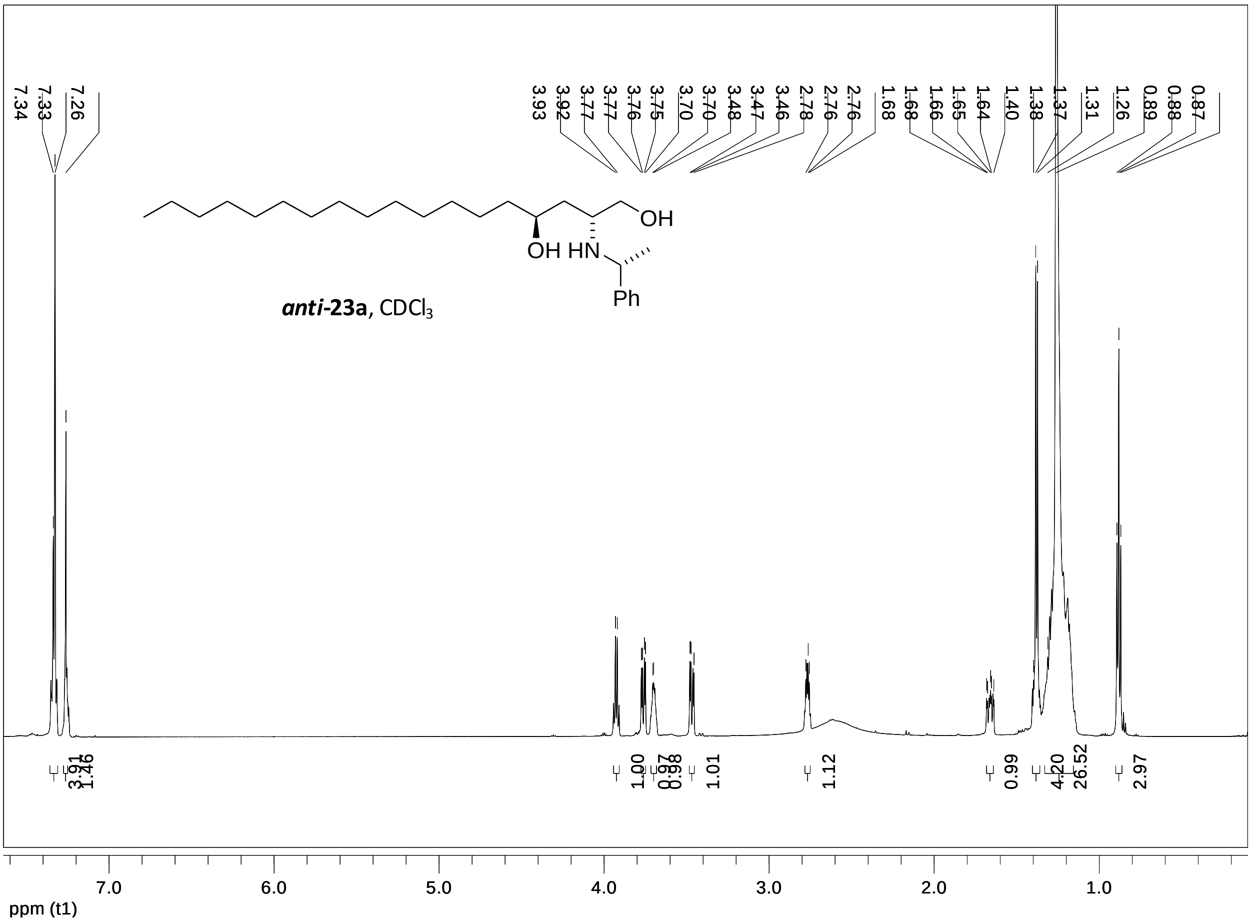
***anti*-14Bb**, $CDCl_3$

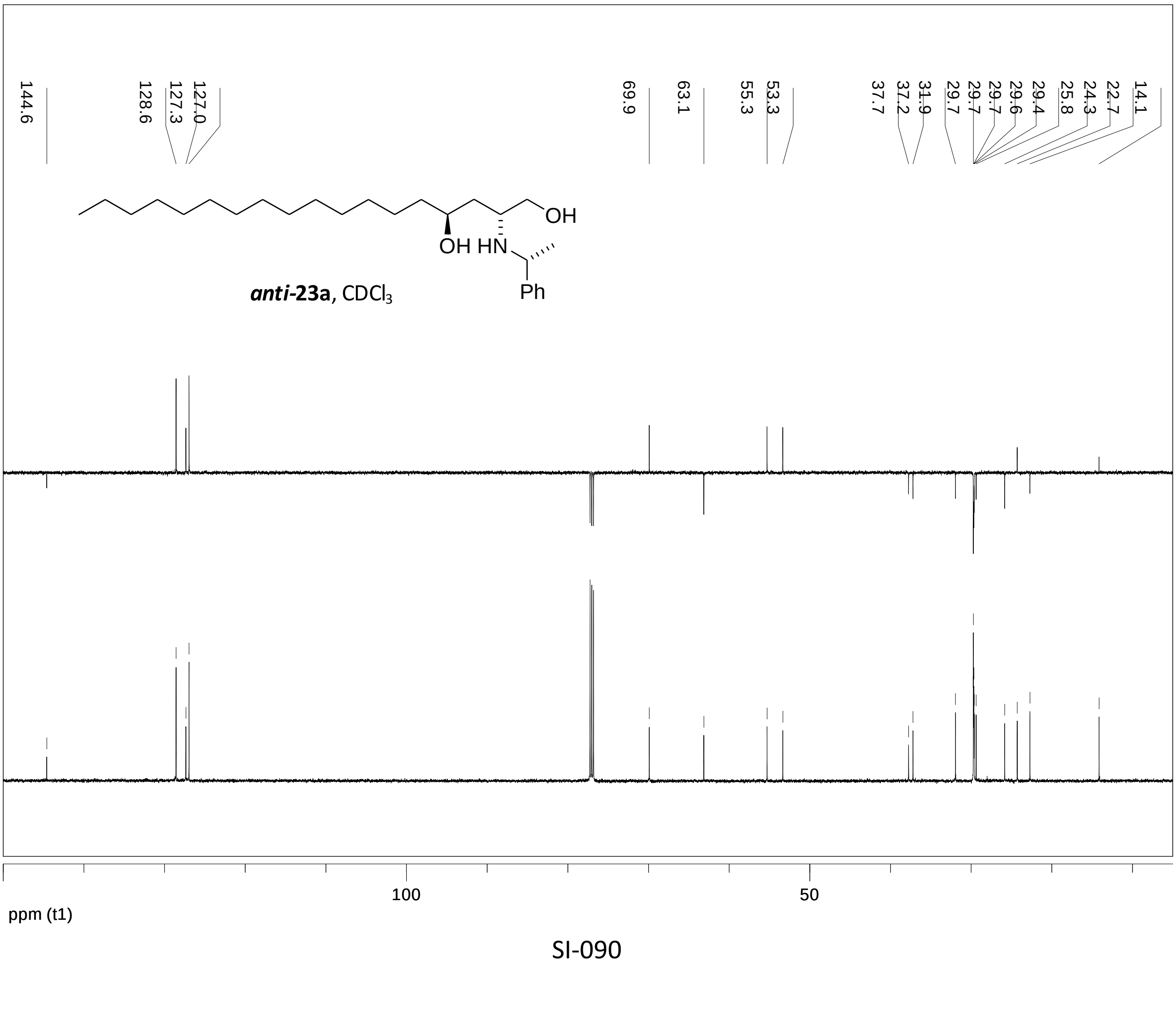


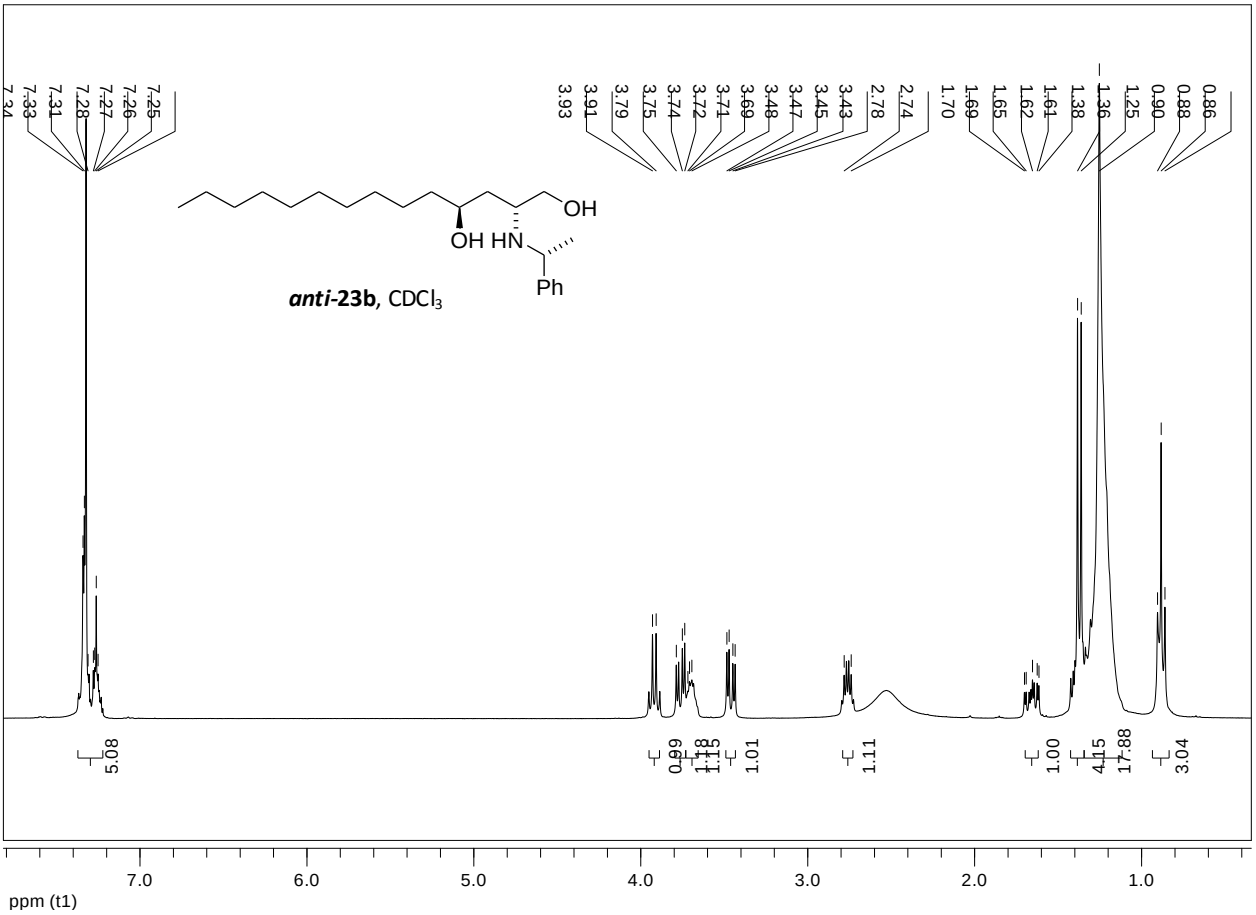
***anti*-14Bb**, $CDCl_3$

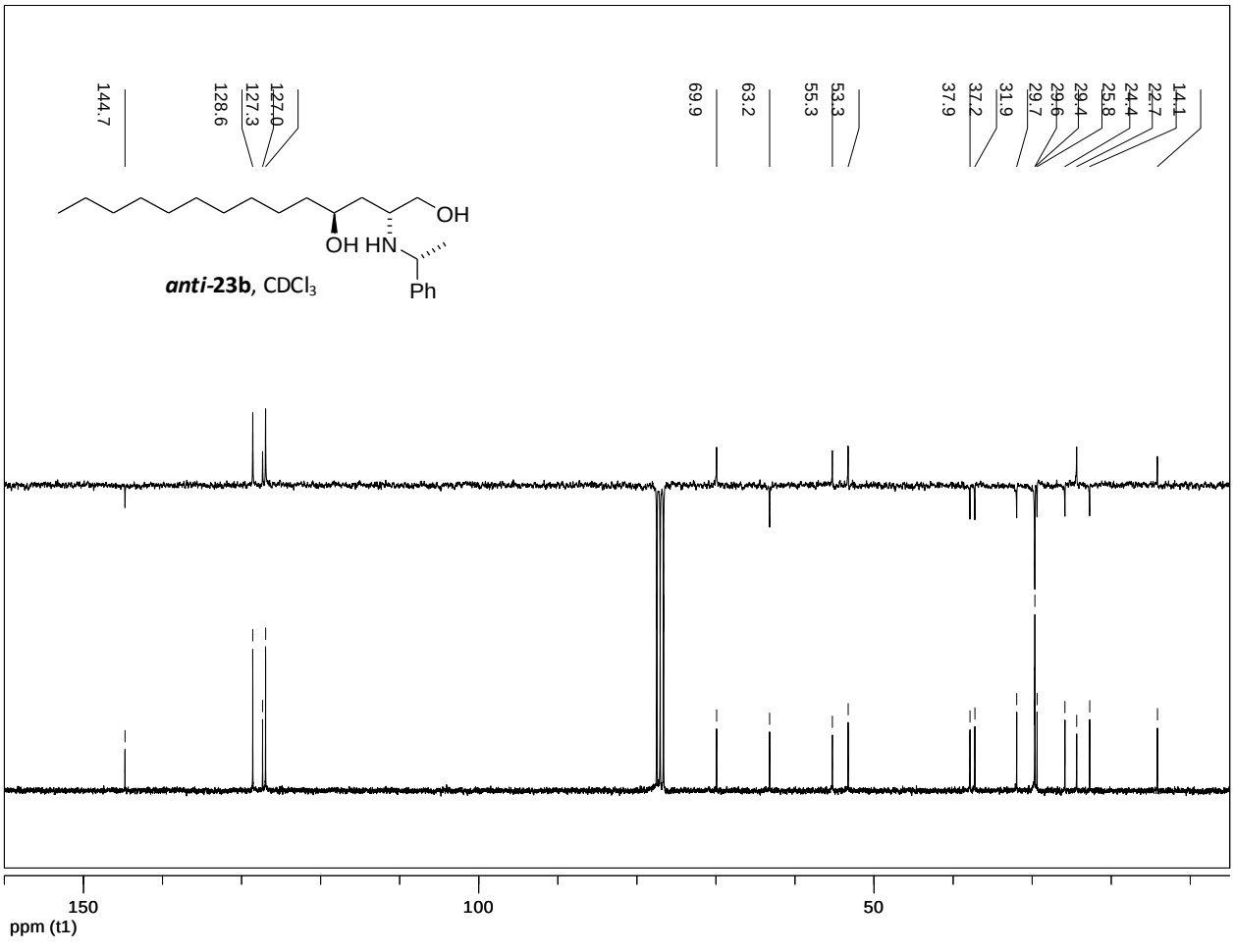

7.24
7.23
7.15
7.14
6.45
4.79
4.78
4.77
4.06
4.05
3.67
3.66
3.65
3.65
2.59
2.57
2.56
2.17
2.16
2.14
2.05
2.01
1.95
1.90
1.59
1.58
1.29
1.26
0.89
0.88
0.87
H13C6
OH
OH HN
(CH2)10-CH3
O
syn-14Bb, CDCl3
1.00
1.00
1.17
1.95
4.08
20.84
5.63
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

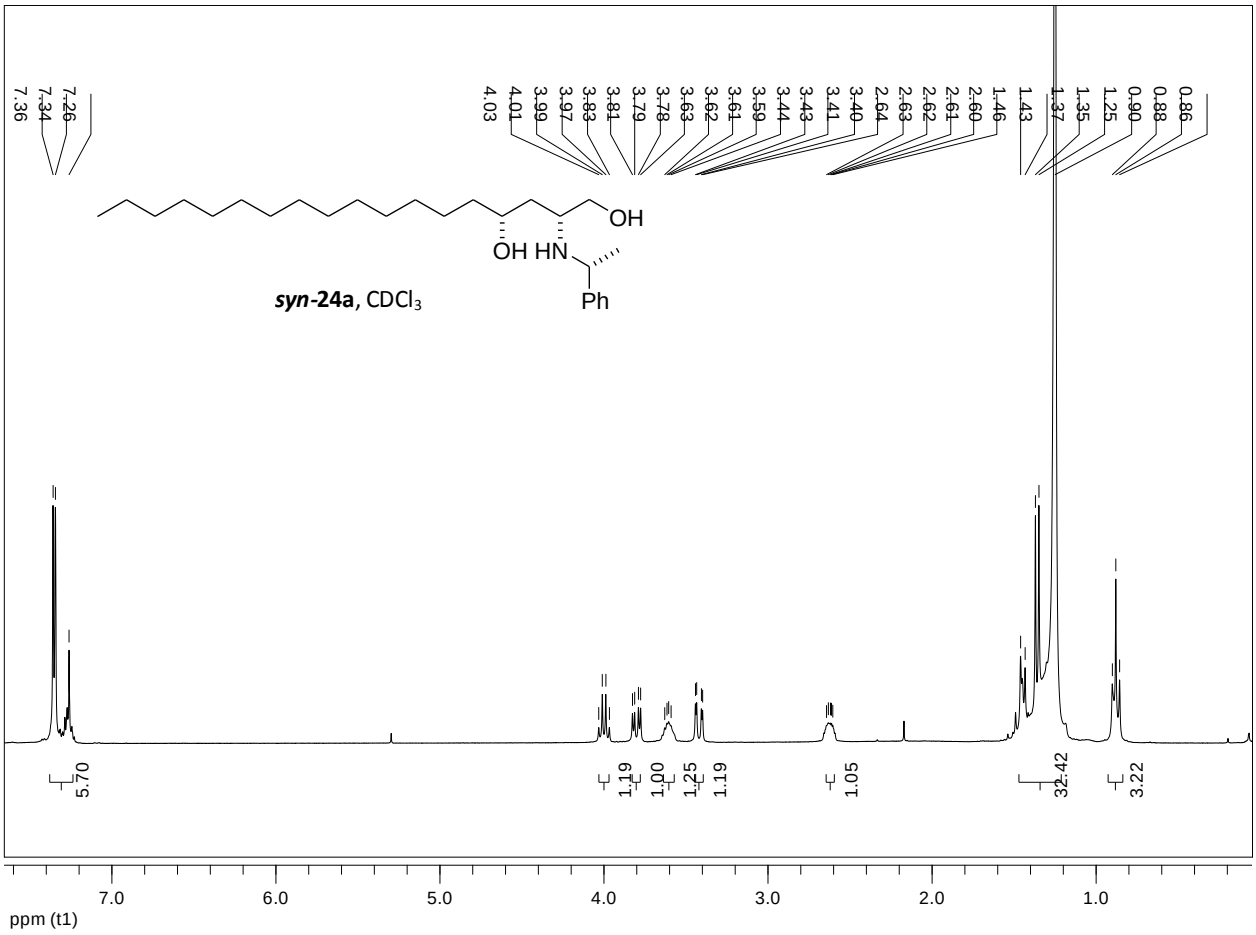

142.6
141.4
128.6
125.5
72.0
65.9
50.8
40.6
36.9
35.6
31.9
31.7
31.5
29.7
29.6
29.6
29.4
29.4
29.3
29.0
25.8
22.7
22.6
14.1
14.1
H13C6
OH
OH HN
(CH2)10-CH3
O
syn-14Bb, CDCl3
150
100
50
0
ppm (t1)

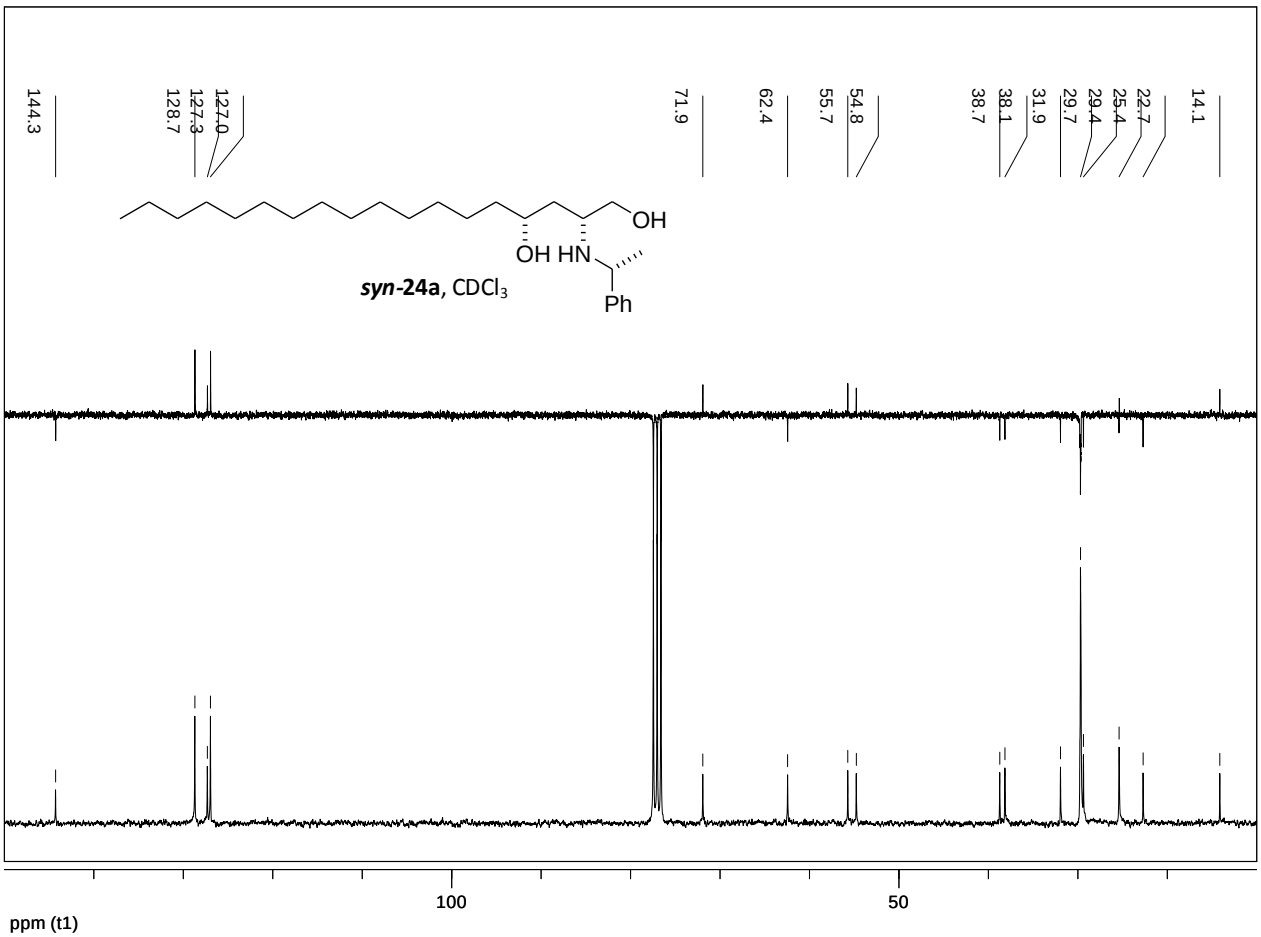

7.34
7.33
7.26
3.93
3.92
3.77
3.77
3.76
3.75
3.70
3.70
3.48
3.47
3.46
2.78
2.76
2.76
1.68
1.68
1.66
1.65
1.64
1.40
1.38
1.37
1.31
1.26
0.89
0.88
0.87
OH
OH HN
Ph
anti-23a, CDCl3
3.71
1.16
1.00
0.97
0.98
1.01
1.12
0.99
4.20
26.52
2.97
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

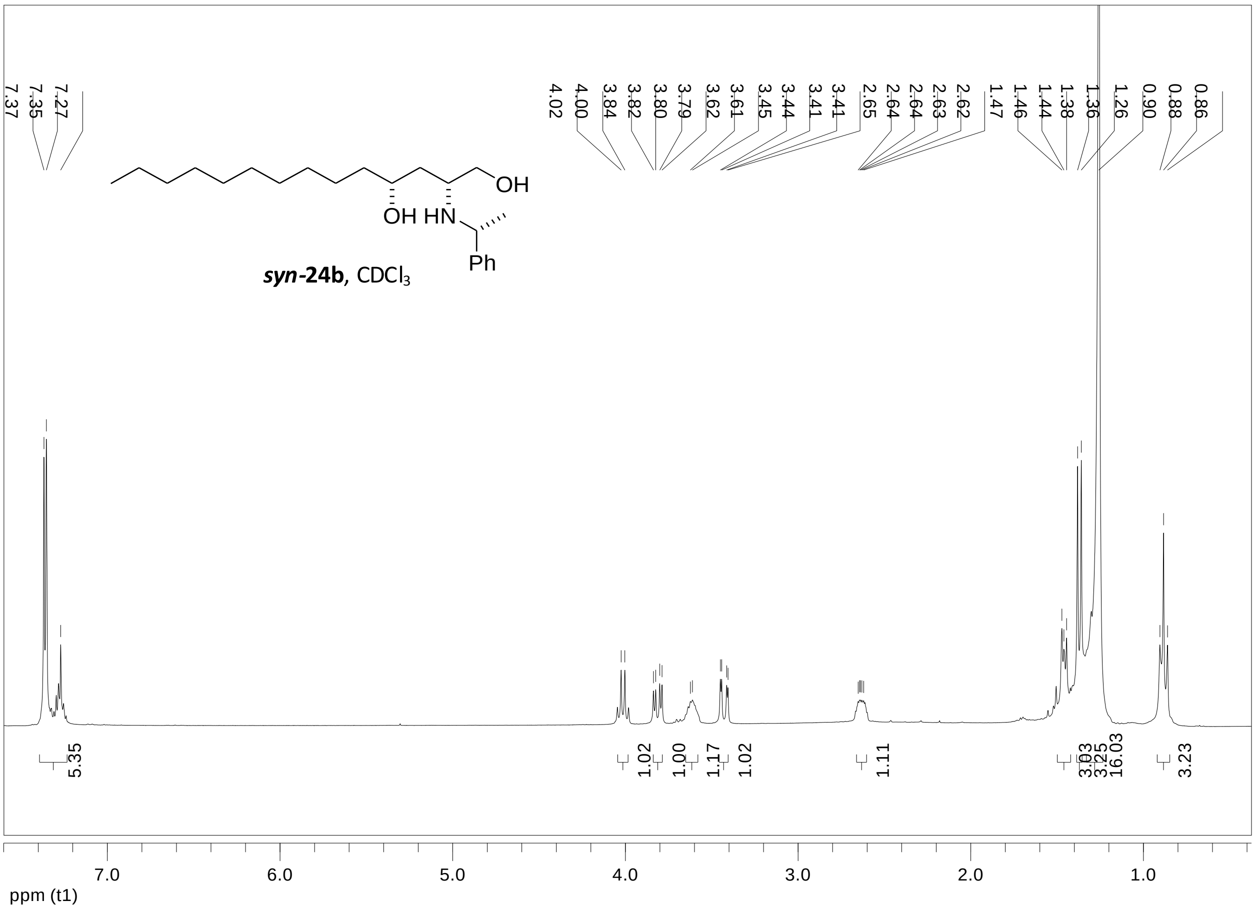

144.6
128.6
127.3
127.0
69.9
63.1
55.3
53.3
37.7
37.2
31.9
29.7
29.7
29.7
29.6
29.4
25.8
24.3
22.7
14.1
OH
OH HN
Ph
anti-23a, CDCl3
100
50
ppm (t1)

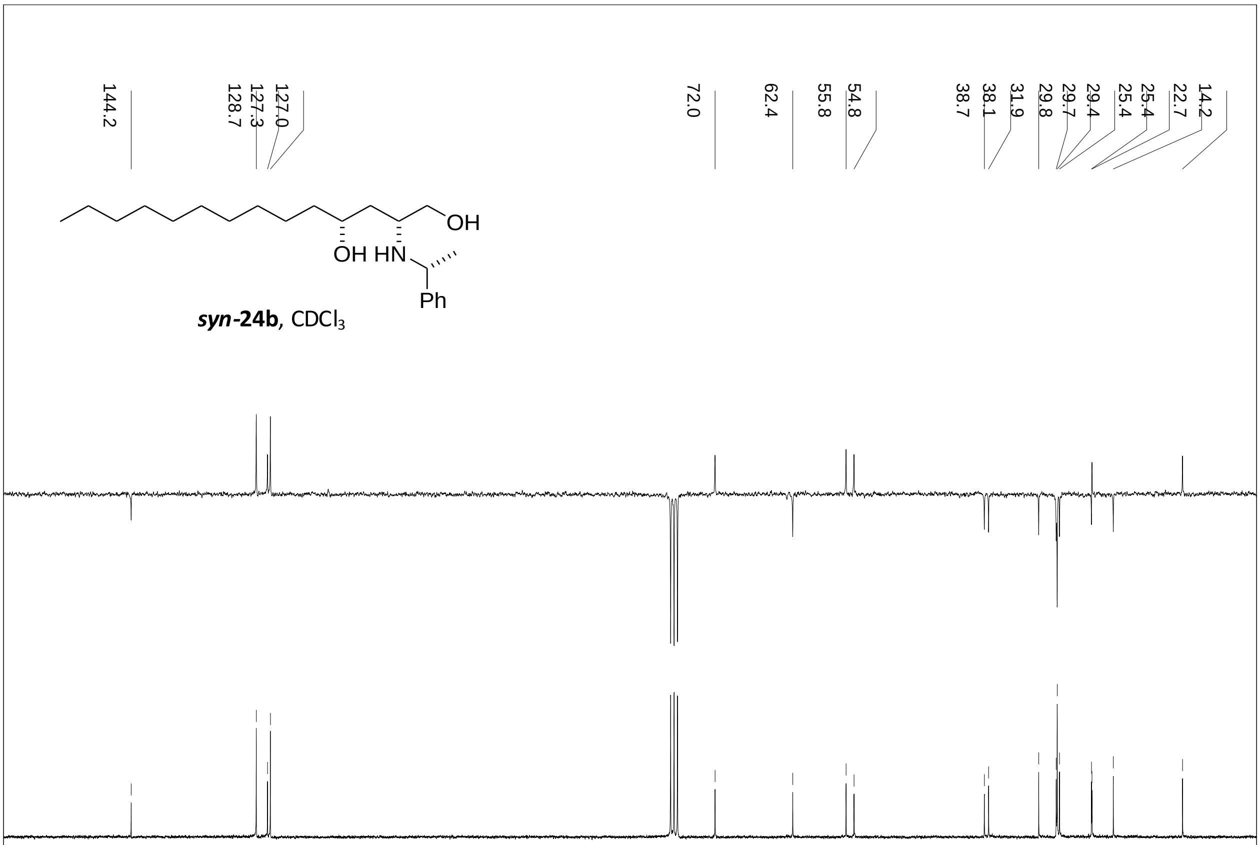

7.34
7.33
7.31
7.28
7.27
7.26
7.25
3.93
3.91
3.79
3.75
3.74
3.72
3.71
3.69
3.48
3.47
3.45
3.43
2.78
2.74
1.70
1.69
1.65
1.62
1.61
1.38
1.36
1.25
0.90
0.88
0.86
OH
OH HN
Ph
anti-23b, CDCl3
5.08
0.99
1.18
1.15
1.01
1.11
1.00
4.15
17.88
3.04
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

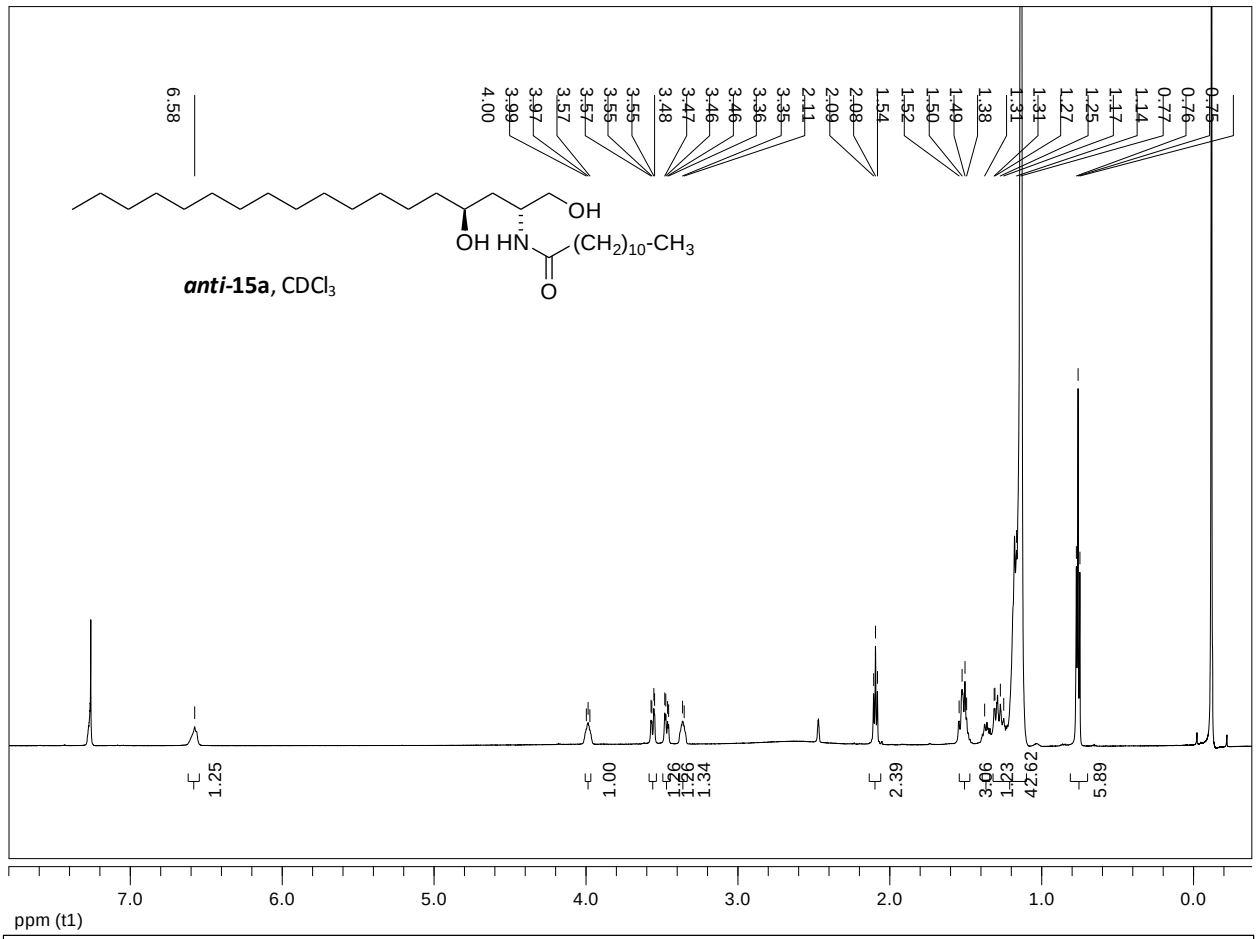

144.7
128.6
127.3
127.0
69.9
63.2
55.3
53.3
37.9
37.2
31.9
29.7
29.6
29.4
25.8
24.4
22.7
14.1
OH
OH HN
Ph
anti-23b, CDCl3
150
100
50
ppm (t1)

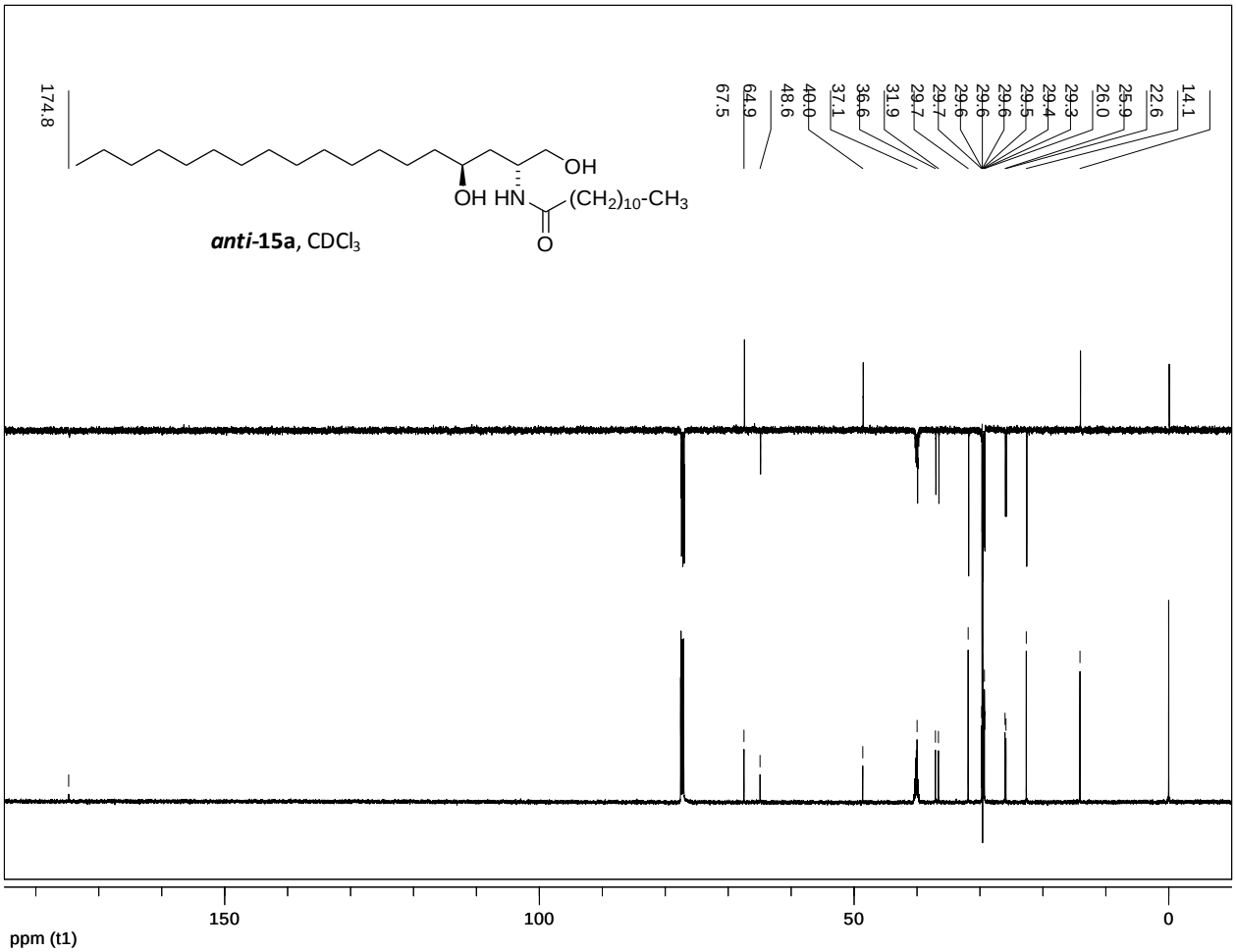

7.36
7.34
7.26
4.03
4.01
3.99
3.97
3.83
3.81
3.79
3.78
3.63
3.62
3.61
3.59
3.44
3.43
3.41
3.40
2.64
2.63
2.62
2.61
2.60
1.46
1.43
1.37
1.35
1.25
0.90
0.88
0.86
OH
OH HN
Ph
syn-24a, CDCl3
5.70
1.19
1.00
1.25
1.19
1.05
32.42
3.22
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

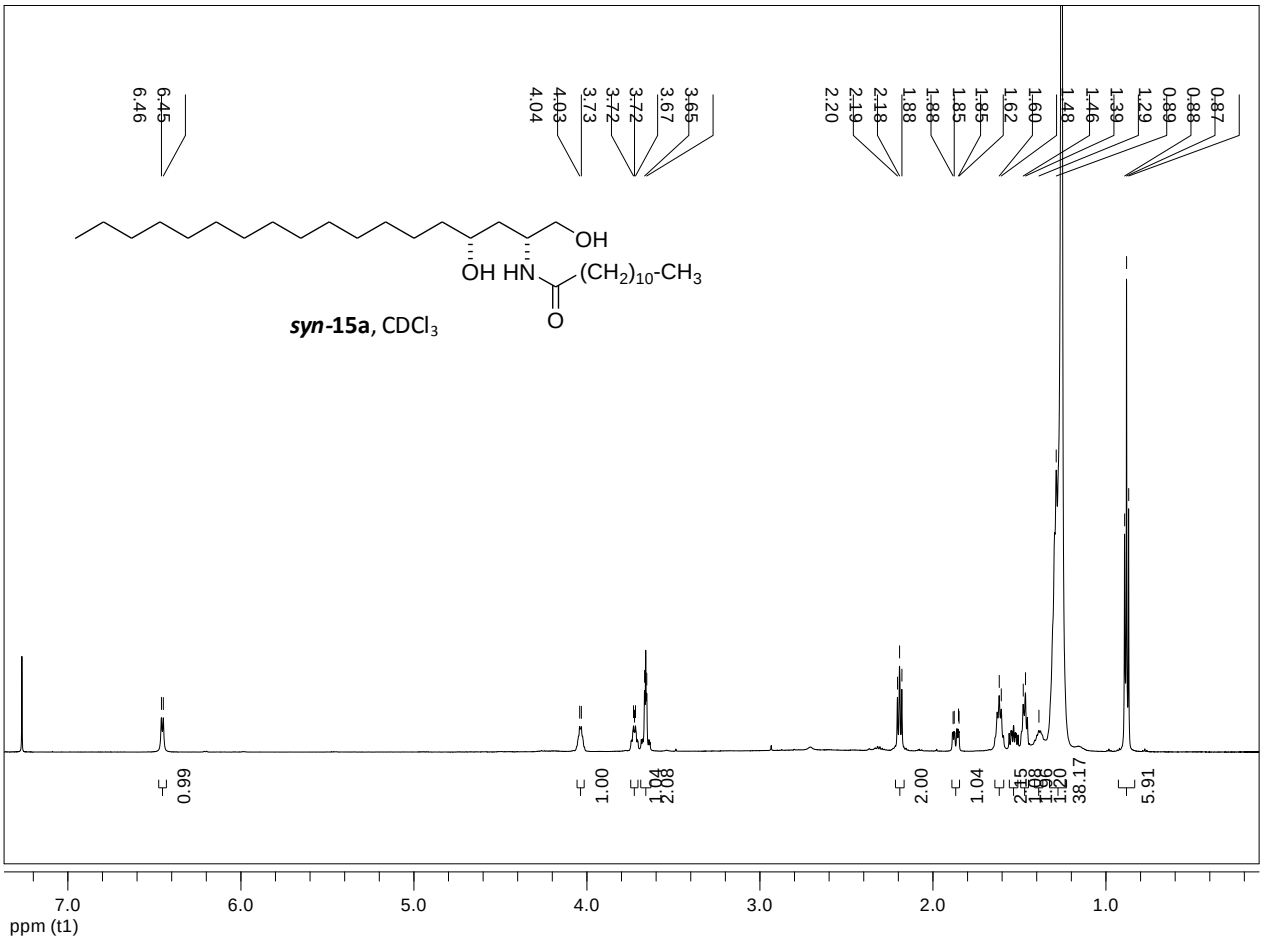

144.3
128.7
127.3
127.0
71.9
62.4
55.7
54.8
38.7
38.1
31.9
29.7
29.4
25.4
22.7
14.1
OH
OH HN
Ph
syn-24a, CDCl3
100
50
ppm (t1)

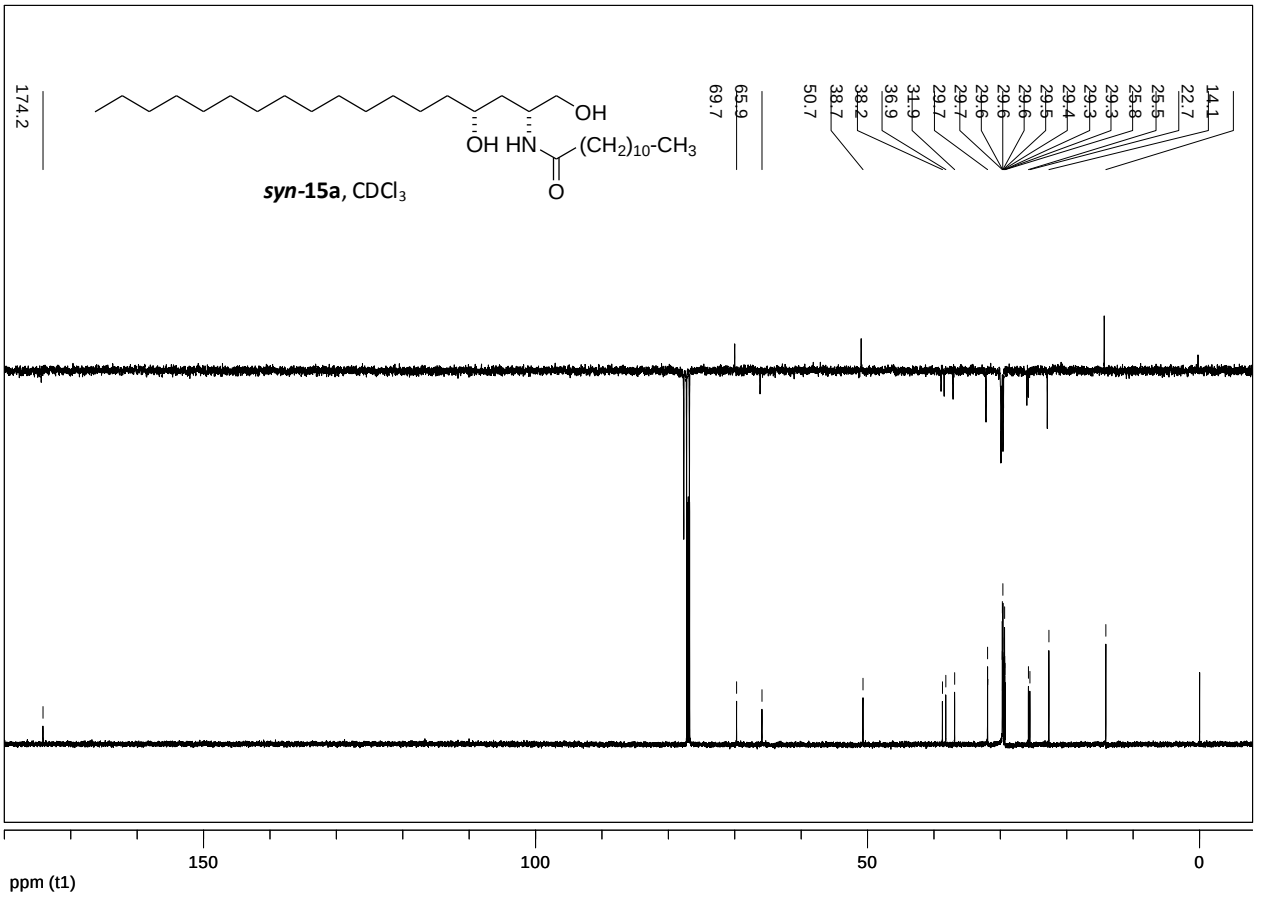

7.37 7.35 7.27 4.02 4.00 3.84 3.82 3.80 3.79 3.62 3.61 3.45 3.44 3.41 3.41 2.65 2.64 2.64 2.63 2.62 1.47 1.46 1.44 1.38 1.36 1.26 0.90 0.88 0.86
OH HN OH Ph
syn-24b, CDCl3
5.35 1.02 1.00 1.17 1.02 1.11 3.03 3.25 16.03 3.23
7.0 6.0 5.0 4.0 3.0 2.0 1.0
ppm (t1)

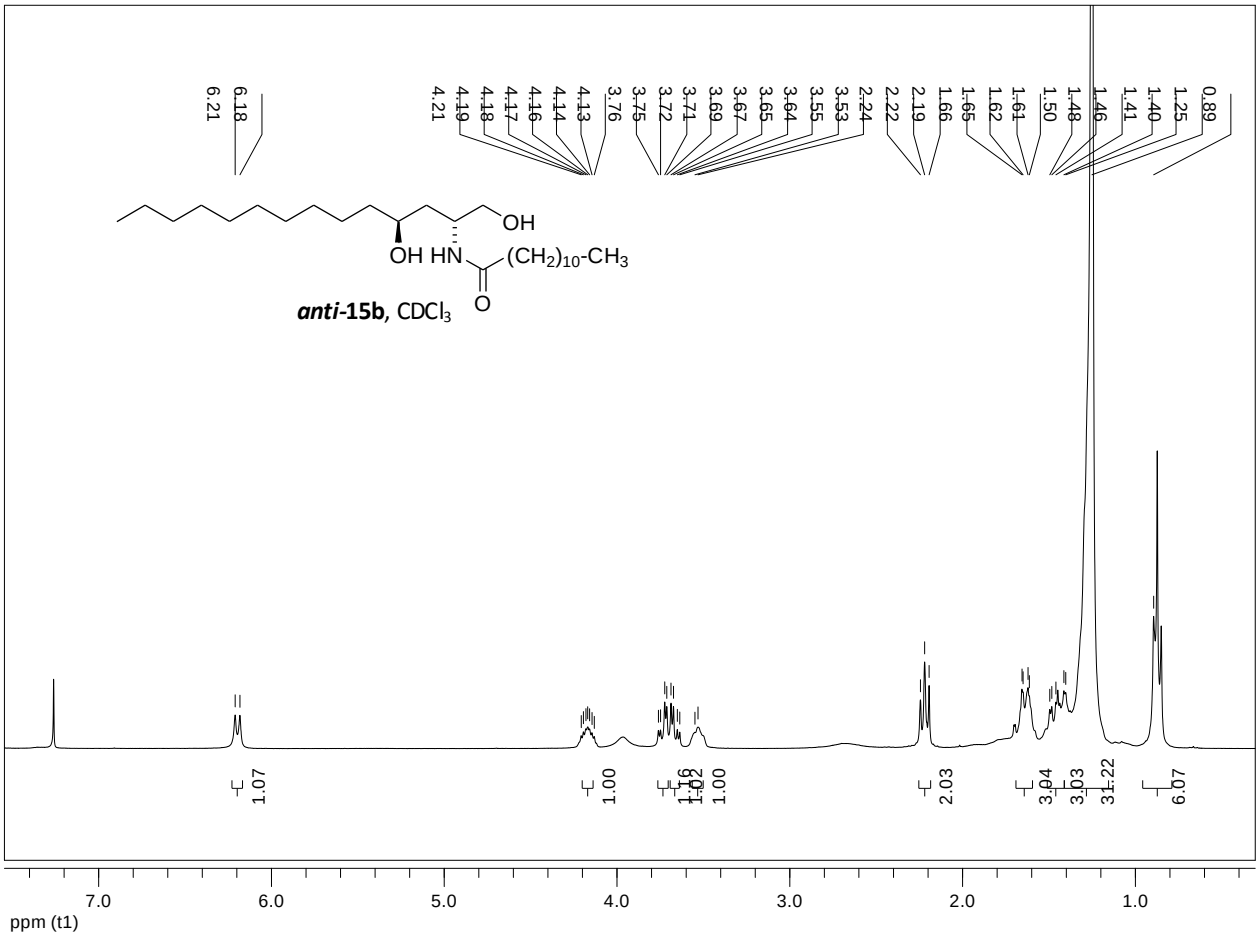

144.2 128.7 127.3 127.0 72.0 62.4 55.8 54.8 38.7 38.1 31.9 29.8 29.7 29.4 25.4 25.4 22.7 14.2
OH HN OH Ph
syn-24b, CDCl3
150 100 50
ppm (t1)

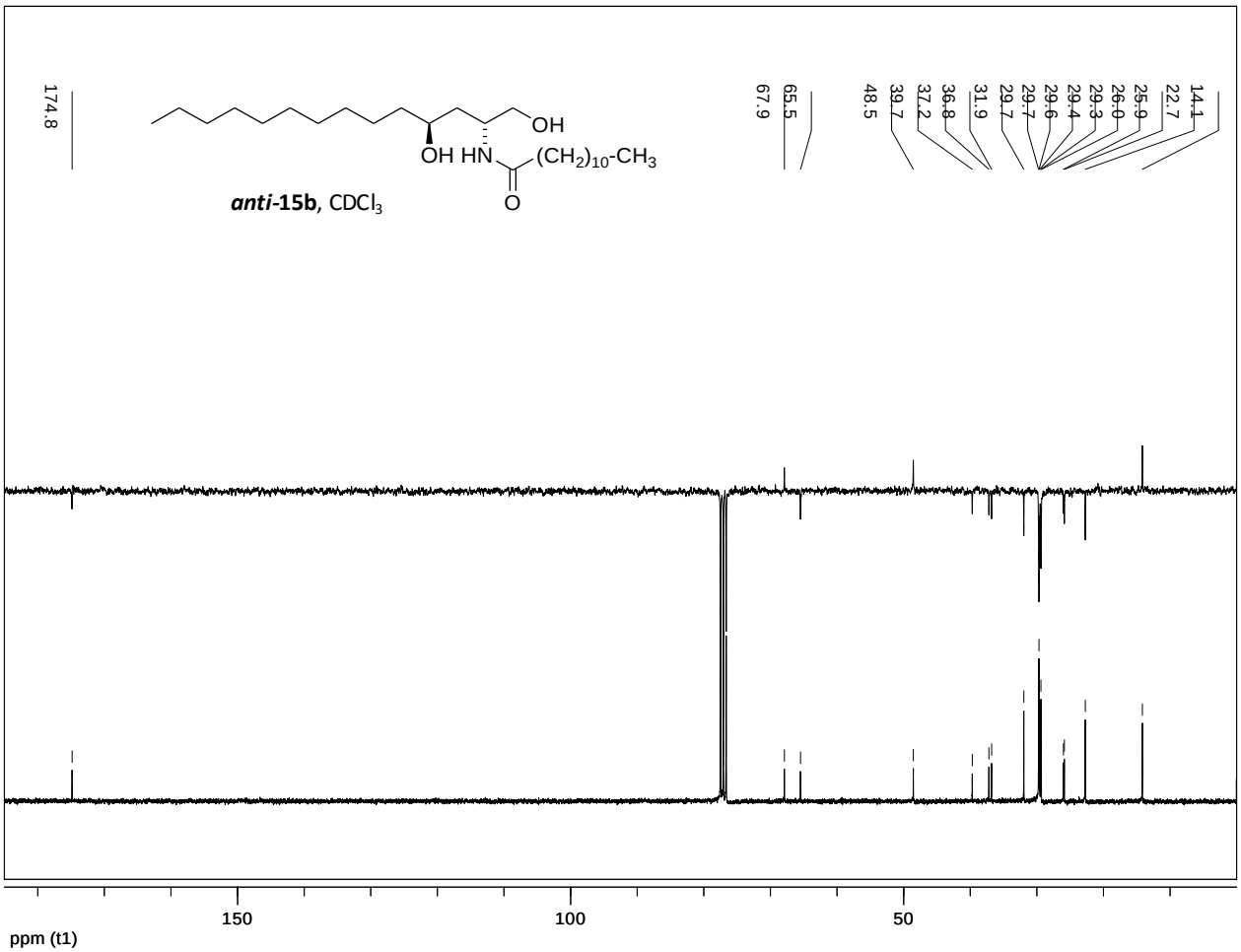

6.58
4.00
3.99
3.97
3.57
3.57
3.55
3.55
3.48
3.47
3.46
3.46
3.36
3.35
2.11
2.09
2.08
1.54
1.52
1.50
1.49
1.38
1.31
1.31
1.27
1.25
1.17
1.14
0.77
0.76
0.75
OH
OH HN
(CH2)10-CH3
O
anti-15a, CDCl3
1.25
1.00
1.55
0.96
1.11
1.34
2.39
3.96
13.71
29.27
3.18
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

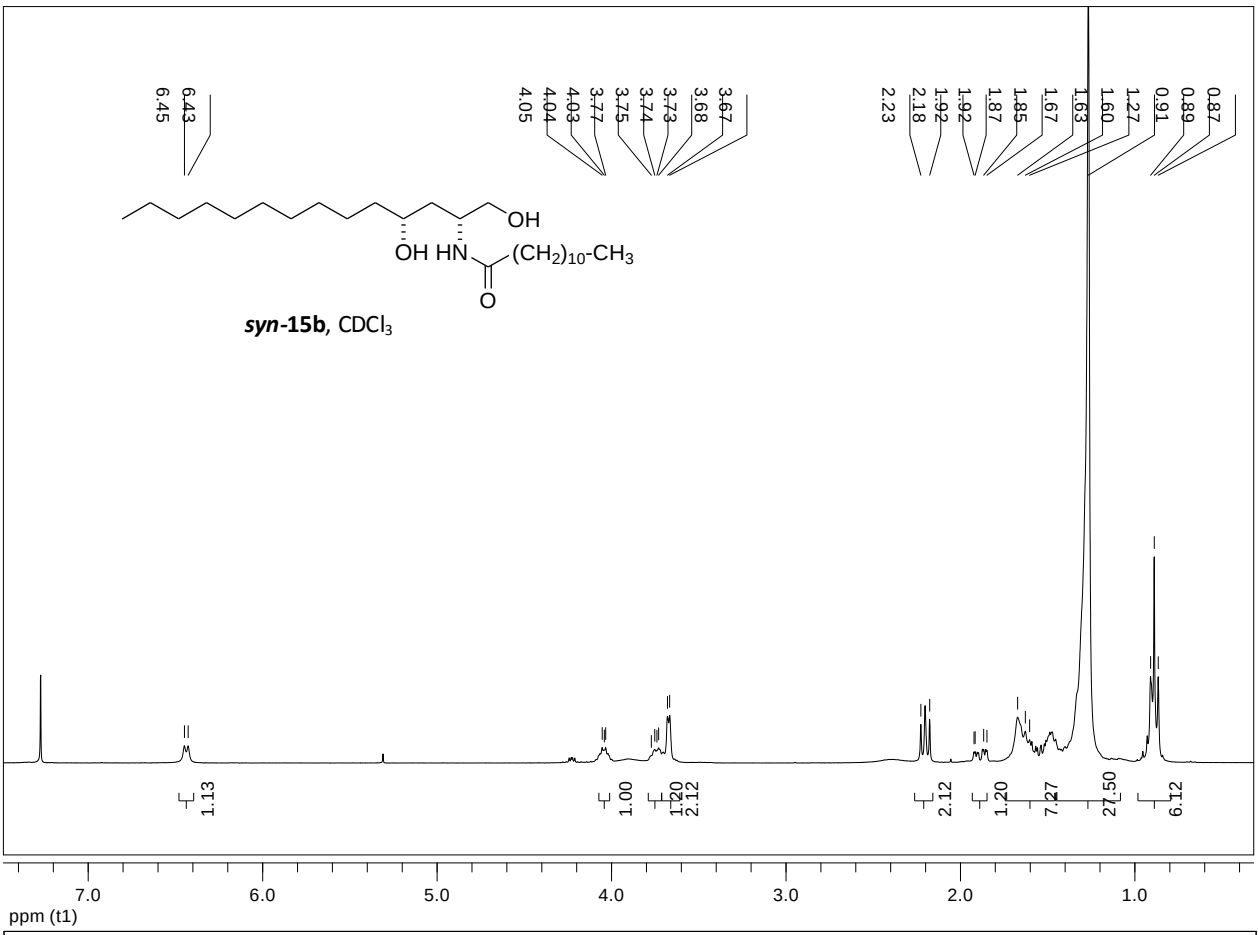

174.8
67.5
64.9
48.6
40.0
37.1
36.6
31.9
29.7
29.7
29.6
29.6
29.6
29.5
29.4
29.3
26.0
25.9
22.6
14.1
OH
OH HN
(CH2)10-CH3
O
anti-15a, CDCl3
150
100
50
0
ppm (t1)


6.46
6.45
4.04
4.03
3.73
3.72
3.72
3.67
3.65
2.20
2.19
2.18
1.88
1.88
1.85
1.85
1.62
1.60
1.48
1.46
1.39
1.29
0.89
0.88
0.87
OH
OH HN
(CH2)10-CH3
O
syn-15a, CDCl3
0.99
1.00
1.04
2.08
2.00
1.04
2.15
1.98
1.98
1.20
38.17
5.91
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

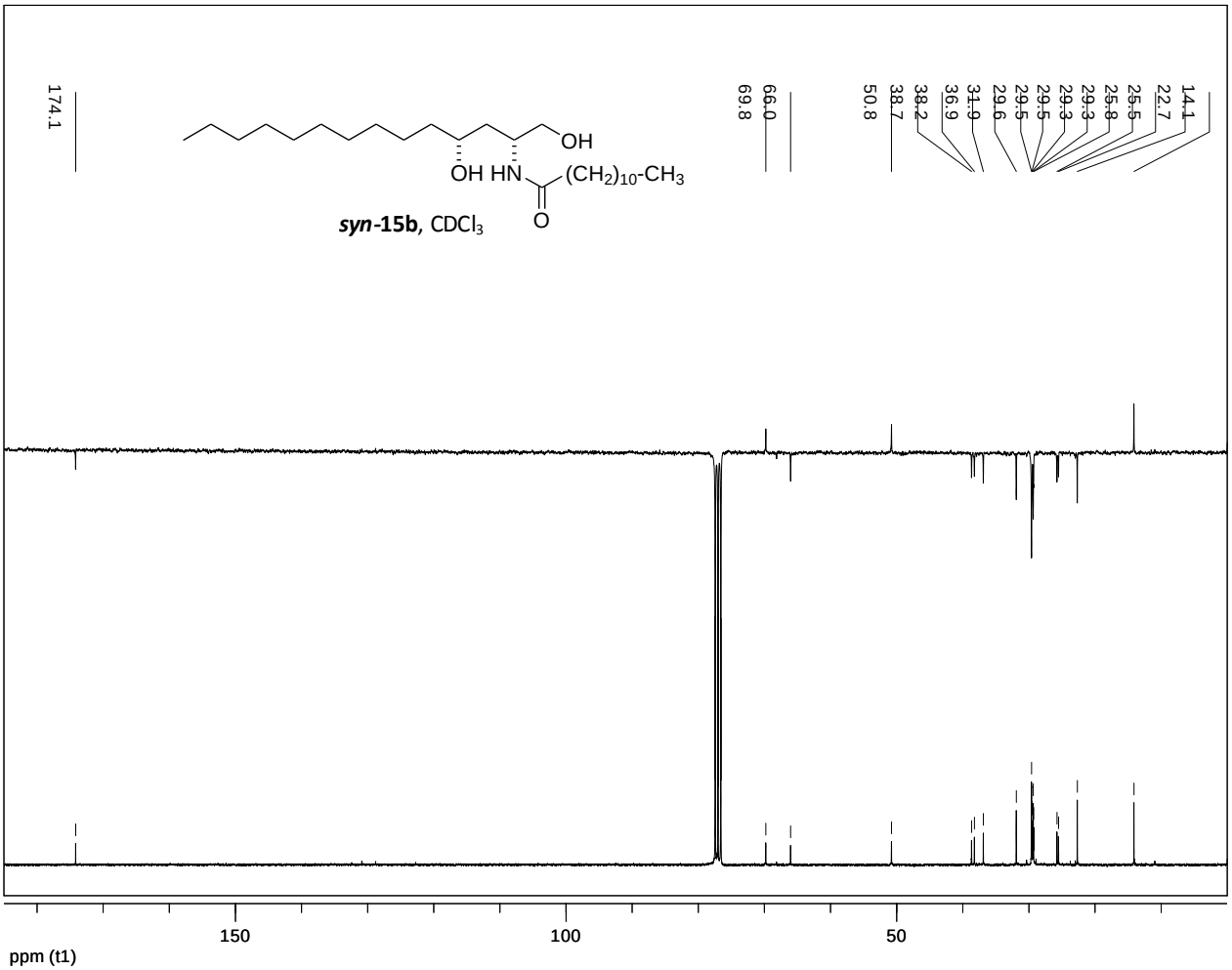

174.2
69.7
65.9
50.7
38.7
38.2
36.9
31.9
29.7
29.7
29.6
29.6
29.6
29.5
29.4
29.3
29.3
25.8
25.5
22.7
14.1
OH
OH HN
(CH2)10-CH3
O
syn-15a, CDCl3
150
100
50
0
ppm (t1)


6.21
6.18
4.21
4.19
4.18
4.17
4.16
4.14
4.13
3.76
3.75
3.72
3.71
3.69
3.67
3.65
3.64
3.55
3.53
2.24
2.22
2.19
1.66
1.65
1.62
1.61
1.50
1.48
1.46
1.41
1.40
1.25
0.89
OH
OH HN
(CH2)10-CH3
O
anti-15b, CDCl3
1.07
1.00
1.00
2.03
3.04
3.03
3.22
6.07
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


174.8
67.9
65.5
48.5
39.7
37.2
36.8
31.9
29.7
29.7
29.6
29.4
29.3
26.0
25.9
22.7
14.1
OH
OH HN
(CH2)10-CH3
O
anti-15b, CDCl3
150
100
50
ppm (t1)



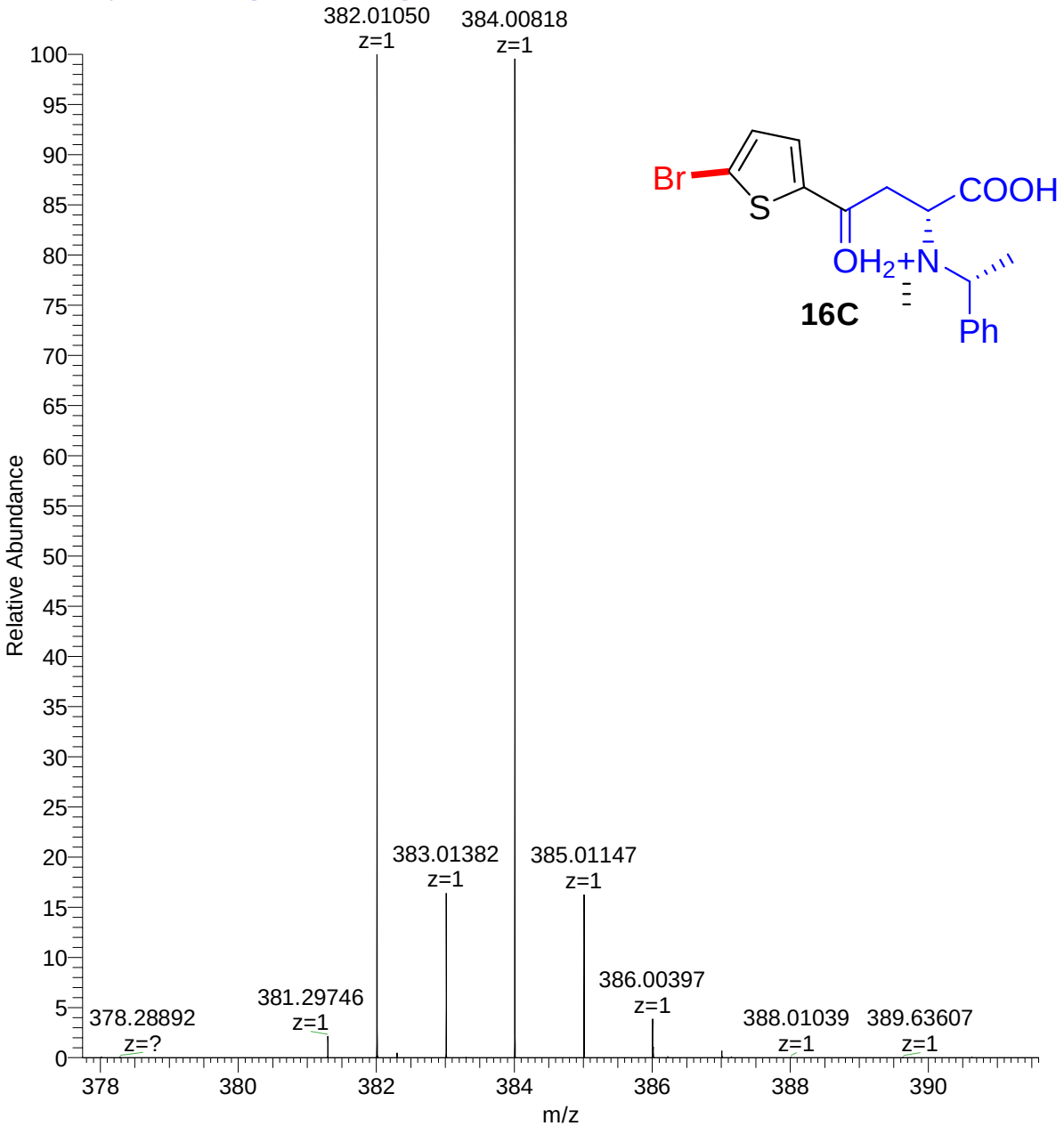
***syn*-15b**, $CDCl_3$



***syn*-15b**, $CDCl_3$

AD-519 (16C) HESI/HRMS positive

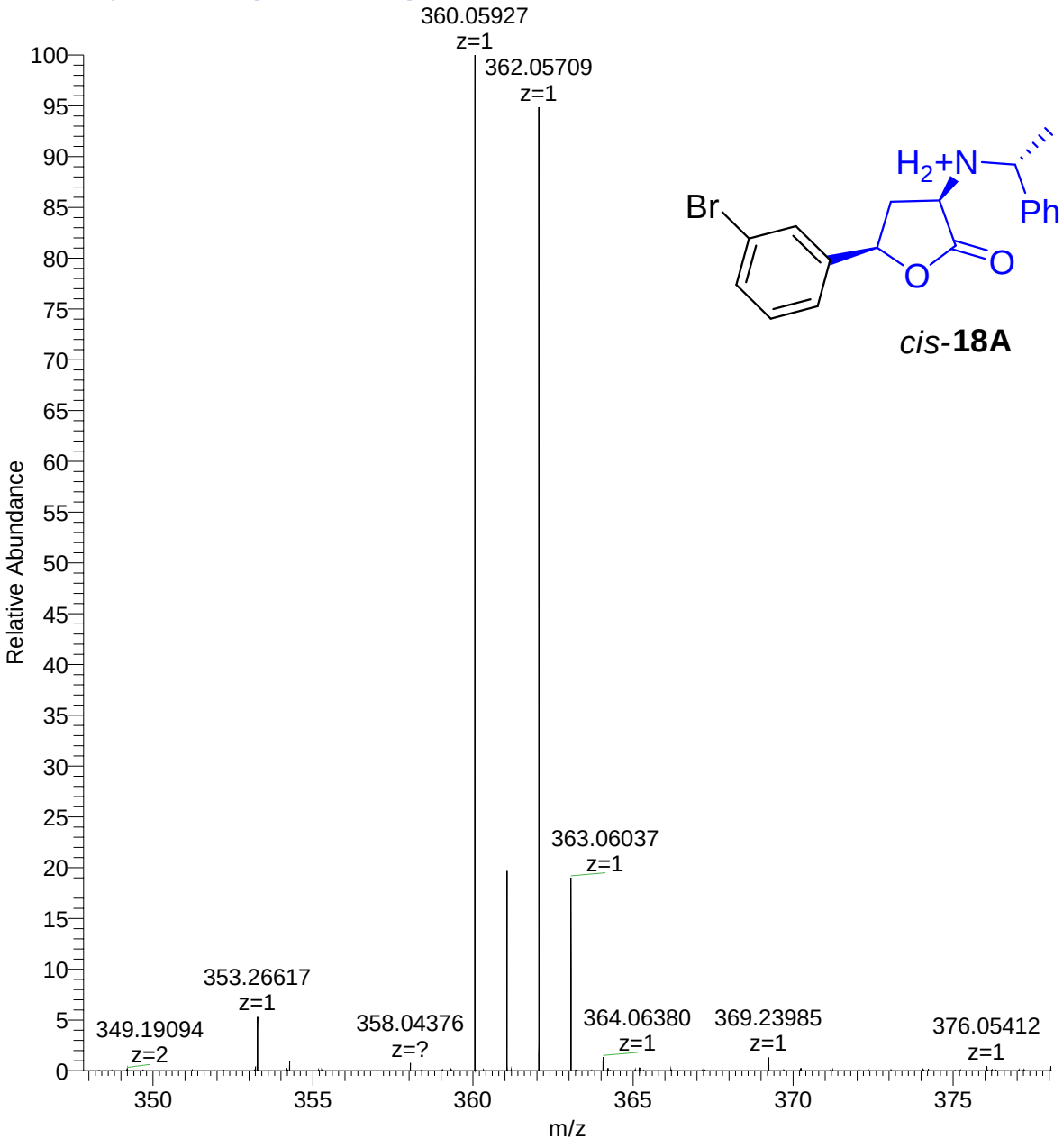
AD_519(16C)_160128-01 #1-8 RT: 0.00-0.26 AV: 8 NL: 1.73E8
T: FTMS + p ESI Full ms [50.00-2000.00]



$[M+H]^+$ = 382.01050 calcd. 382.01070

AD 1182 (cis 18A) HESI/HRMS positive

AD_1182(cis18A)_160128-02 #1-9 RT: 0.01-0.29 AV: 9 NL: 1.05E8
T: FTMS + p ESI Full ms [50.00-2000.00]

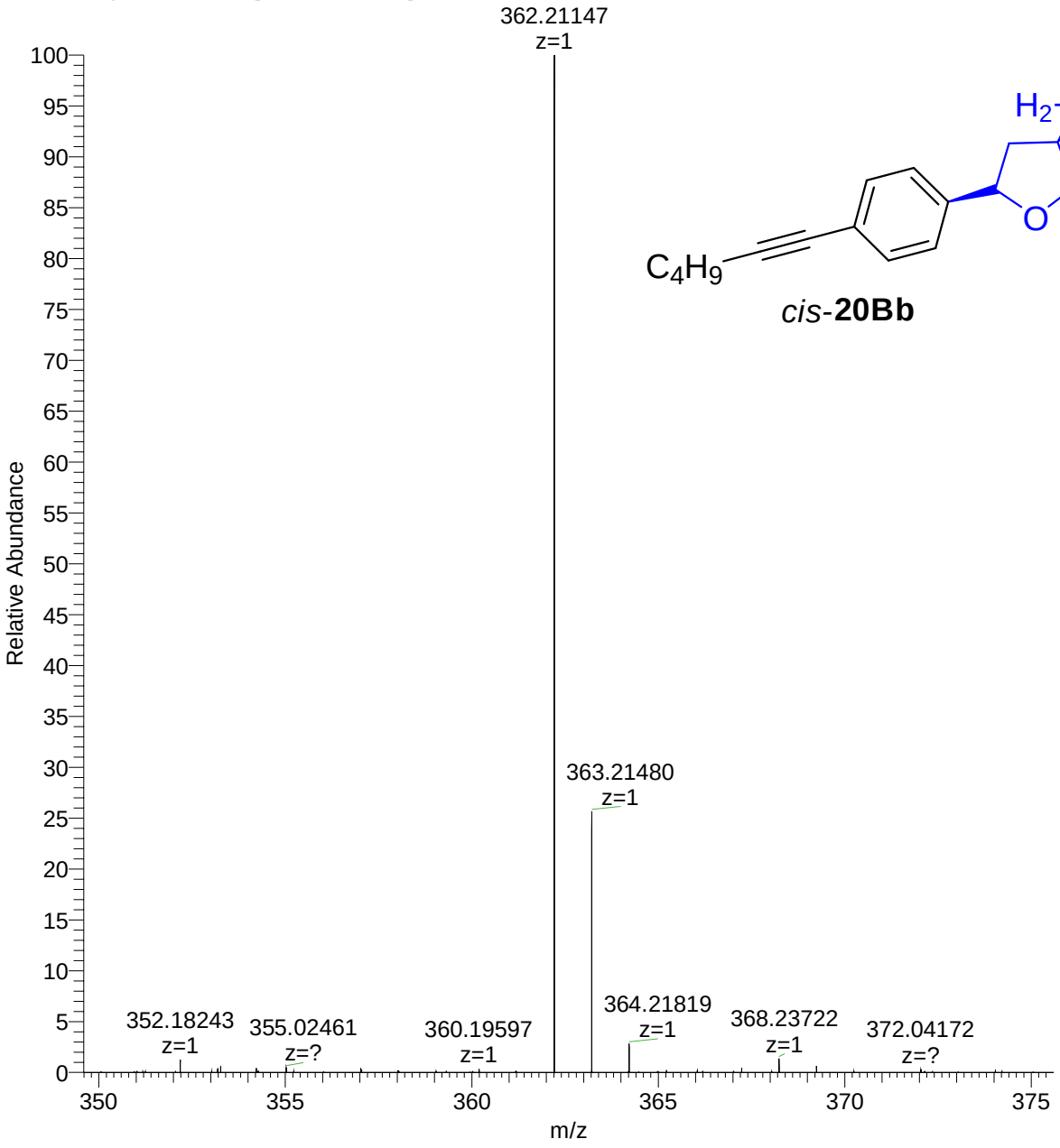


cis-**18A**

$[M+H]^+$ = 360.05927 calcd. 360.05937

AD-1258-(20Bb) HESI/HRMS positive

AD_1258_(20Bb)_160201-03 #1-5 RT: 0.01-0.15 AV: 5 NL: 1.41E7
T: FTMS + p ESI Full ms [50.00-2000.00]

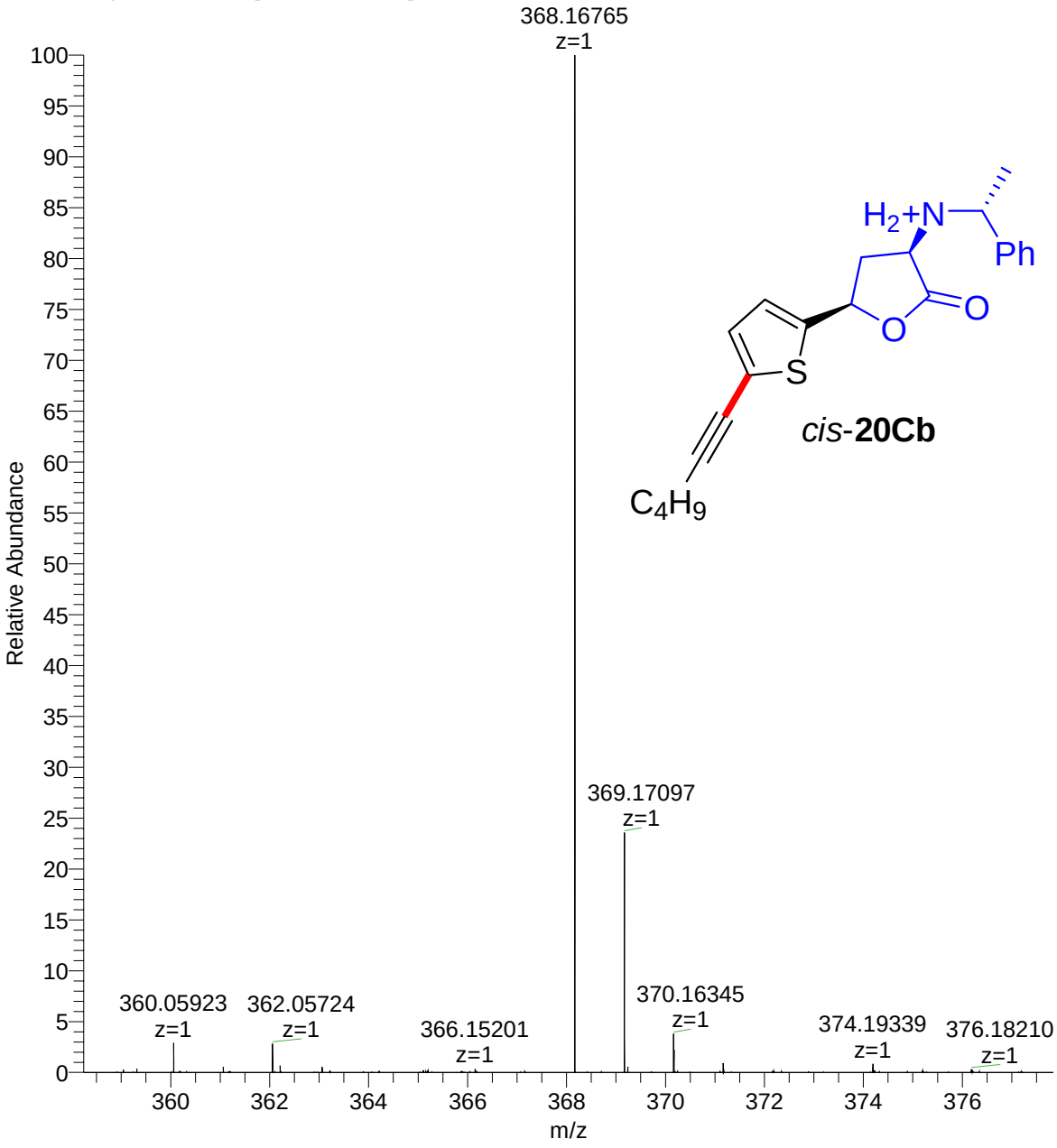


cis-**20Bb**

$[M+H]^+$ = 362.21147 calcd. 362.21146

AD 1232 (cis 20Cb) HESI/HRMS positive

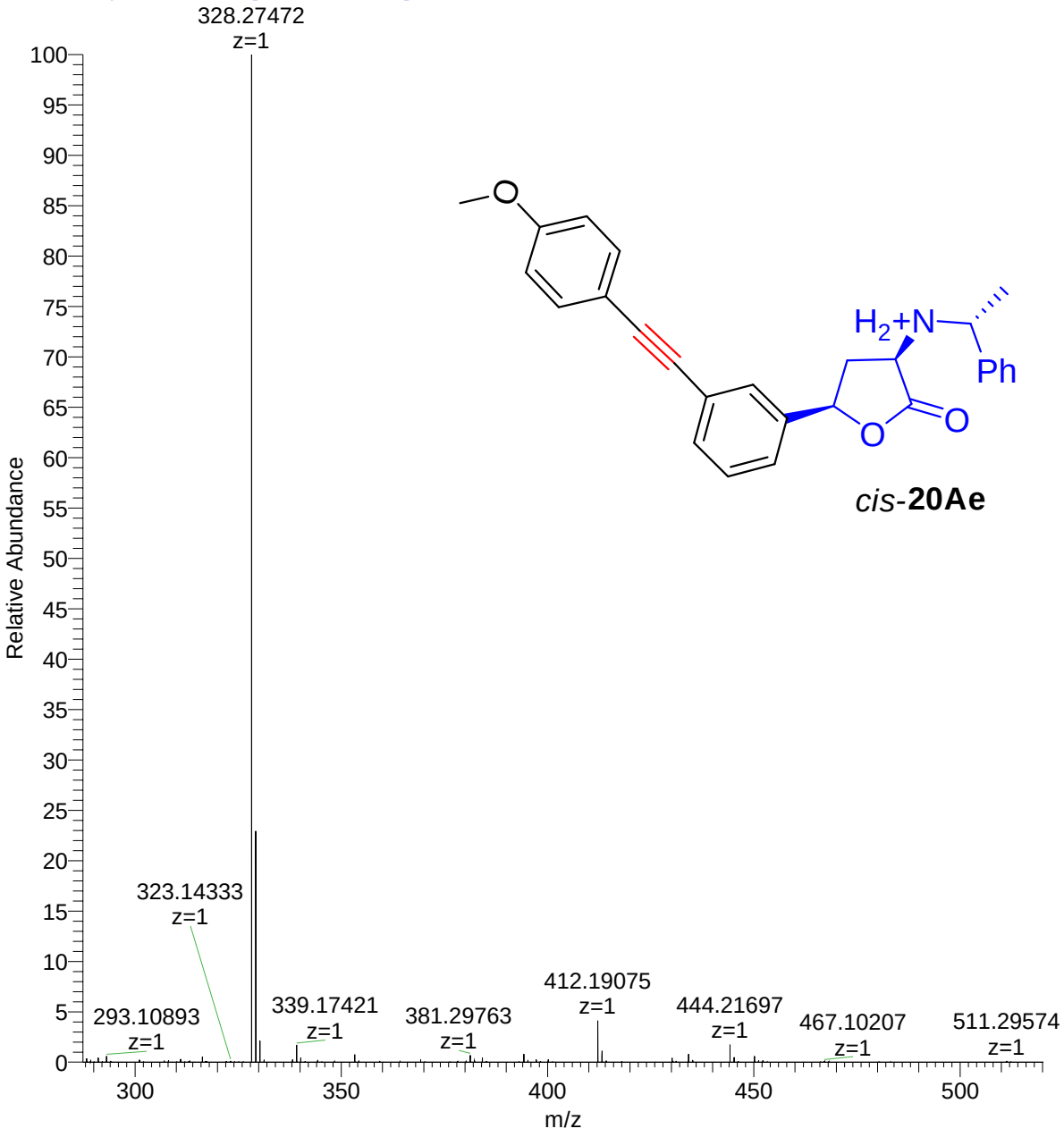
AD_1232(cis20Cb)_160128-04 #14-19 RT: 0.47-0.65 AV: 6 NL: 1.78E7
T: FTMS + p ESI Full ms [50.00-2000.00]



$[M+H]^+$ = 368.16765 calcd. 366.16788

AD-1412-(20Ae) HESI/HRMS positive

AD_1412_(20Ae)_160201-04 #1-4 RT: 0.00-0.16 AV: 4 NL: 1.33E6
T: FTMS + p ESI Full ms [50.00-2000.00]

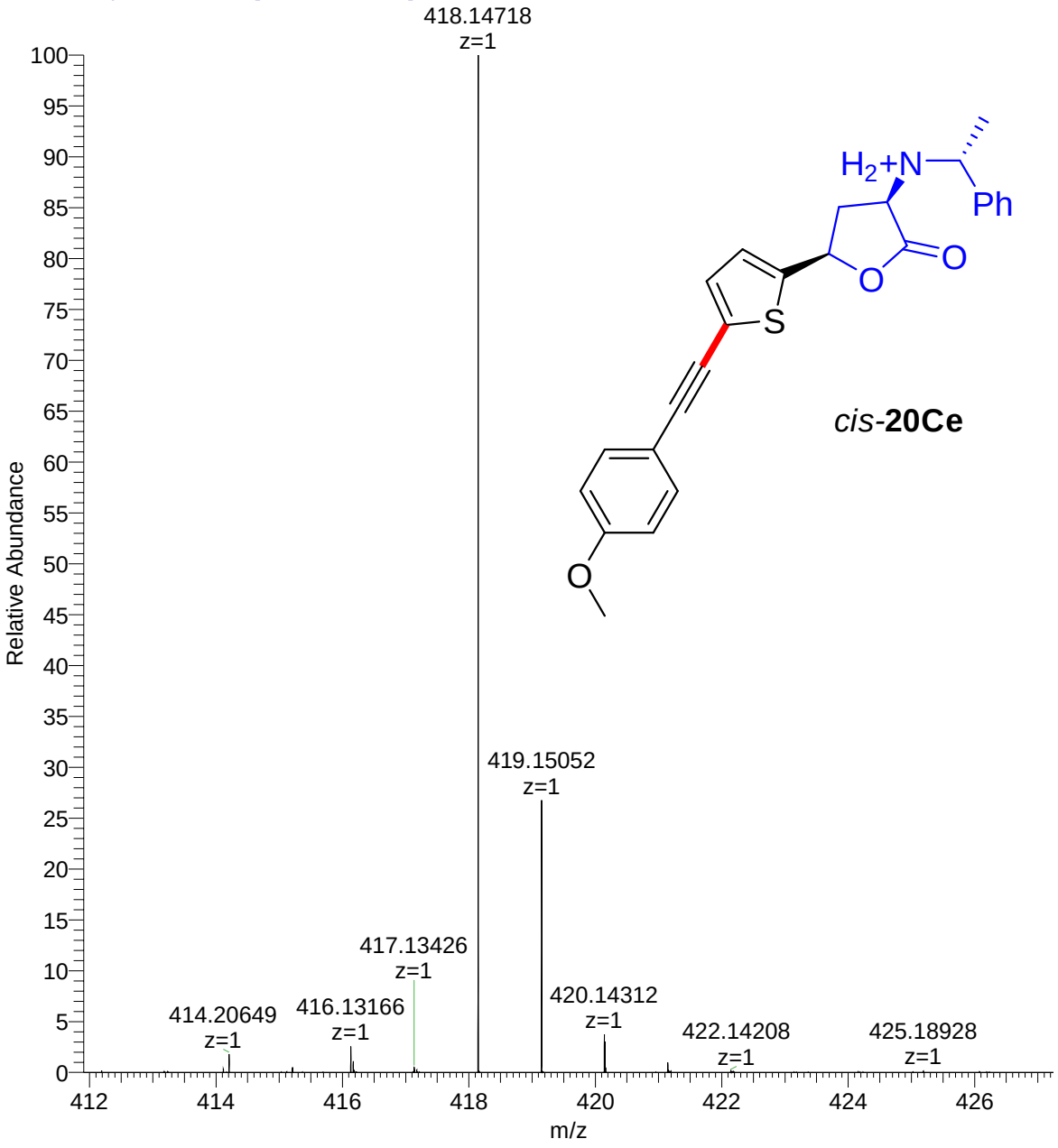


cis-**20Ae**

$[M+H]^+$ = 412.19075 calcd. 412.19072

AD 1322 (cis 20Ce) HESI/HRMS positive

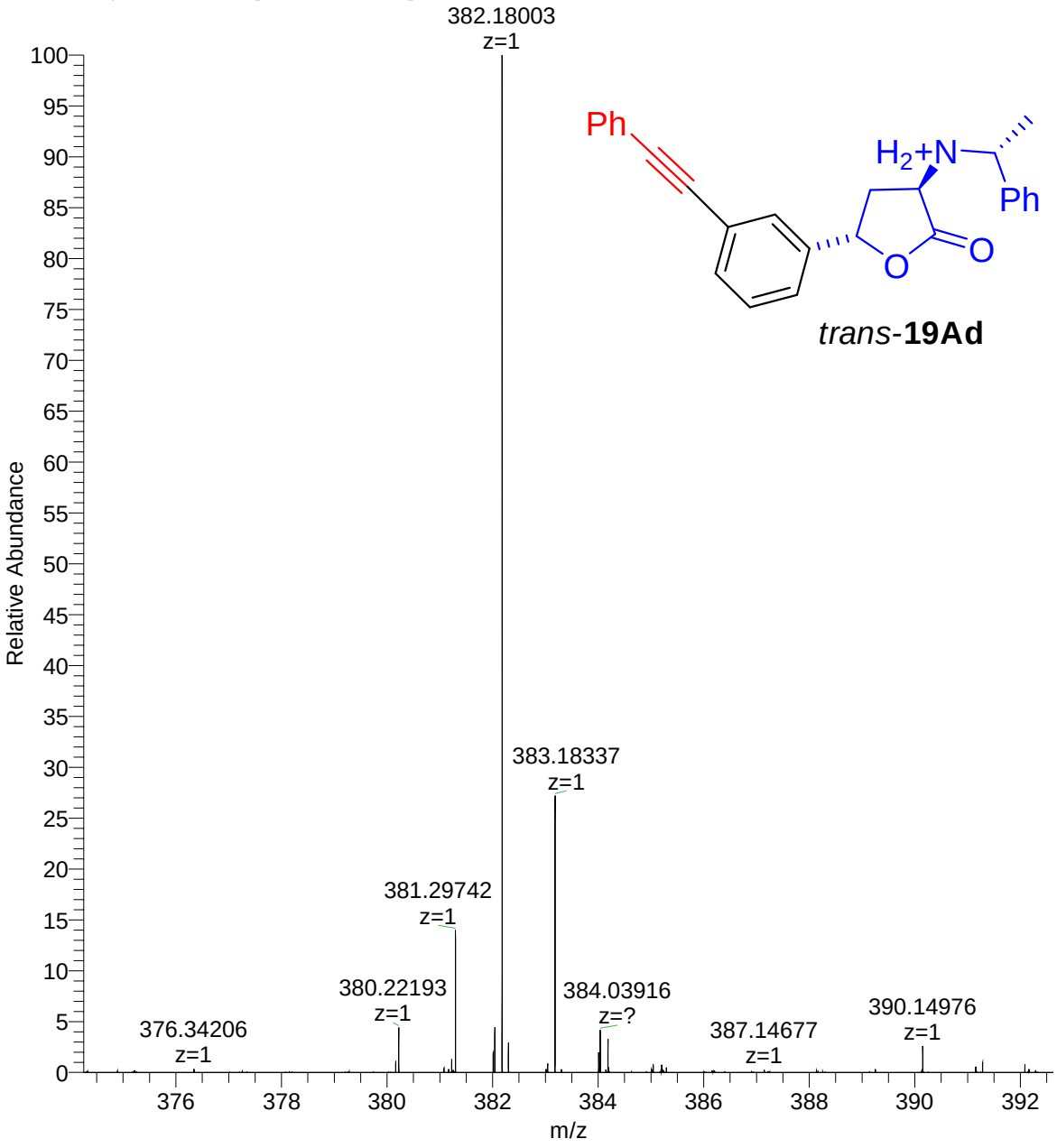
AD_1322cis20Ce)_160128-06 #3-14 RT: 0.08-0.47 AV: 12 NL: 4.20E7
T: FTMS + p ESI Full ms [50.00-2000.00]



$[M+H]^+$ = 418.14718 calcd. 418.14714

AD 1254 (trans19Ad) HESI/HRMS positive

AD_1254(trans19Ad)_160128-07 #19-22 RT: 0.65-0.76 AV: 4 NL: 2.61E6
T: FTMS + p ESI Full ms [50.00-2000.00]

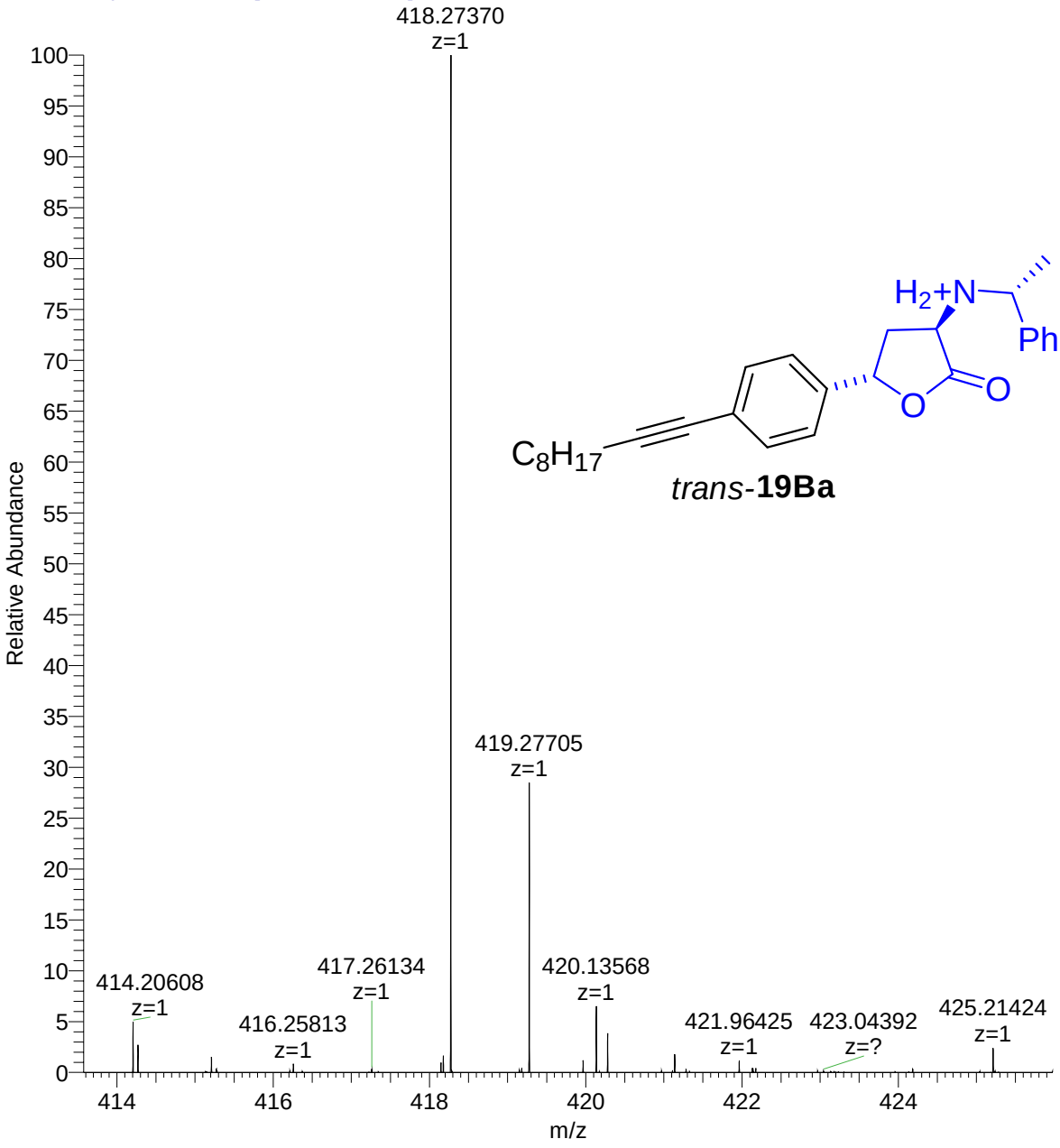


trans-**19Ad**

$[M+H]^+$ = 382.18003 calcd. 382.18016

AD 1261 (trans19Ba) HESI/HRMS positive

AD_1261(trans19Ba)_160128-08 #19-23 RT: 0.75-0.89 AV: 5 NL: 1.98E6
T: FTMS + p ESI Full ms [50.00-2000.00]

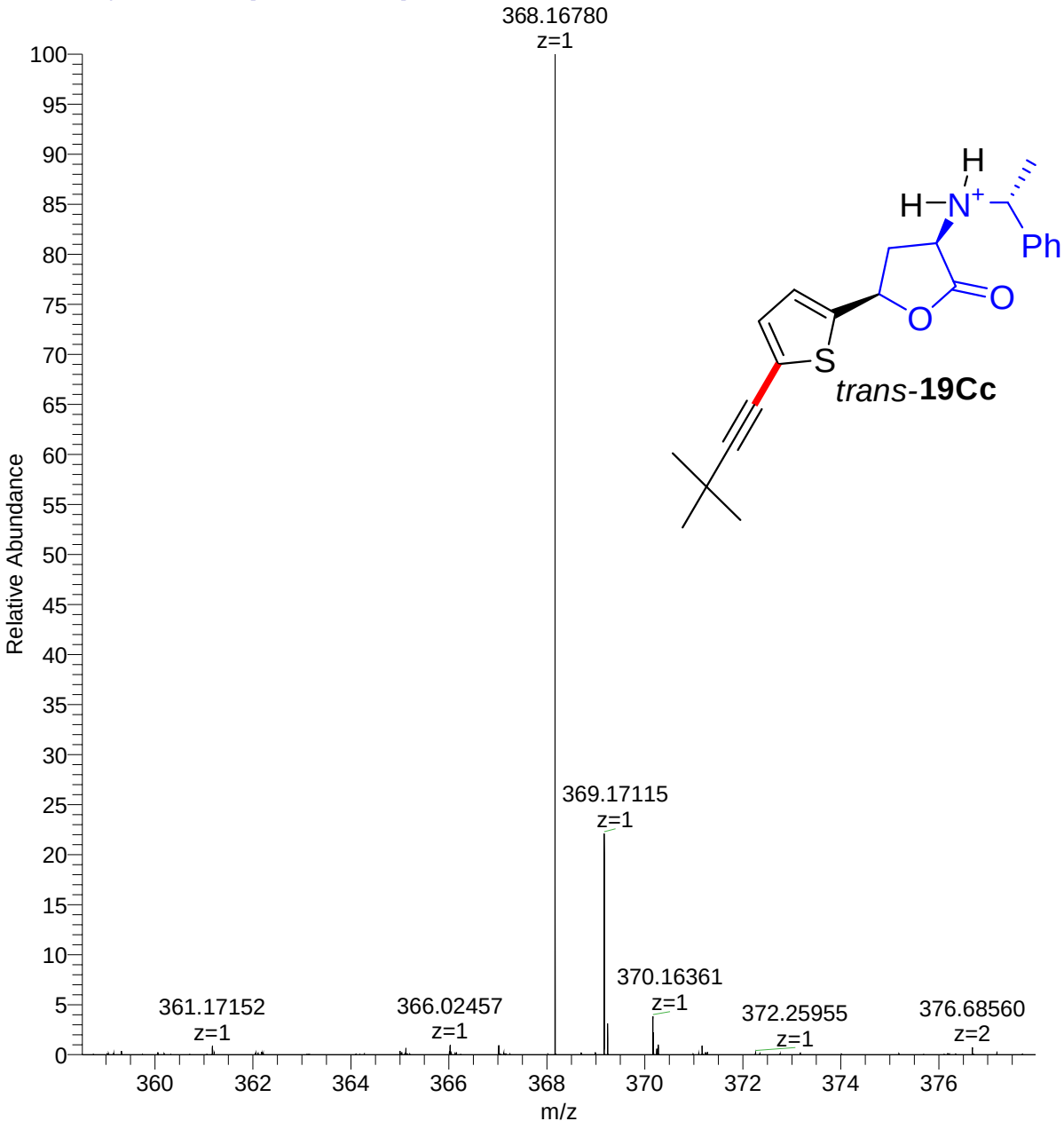


trans-**19Ba**

$[M+H]^+$ = 418.27370 calcd. 418.27406

AD 1245 (trans19Cc) HESI/HRMS positive

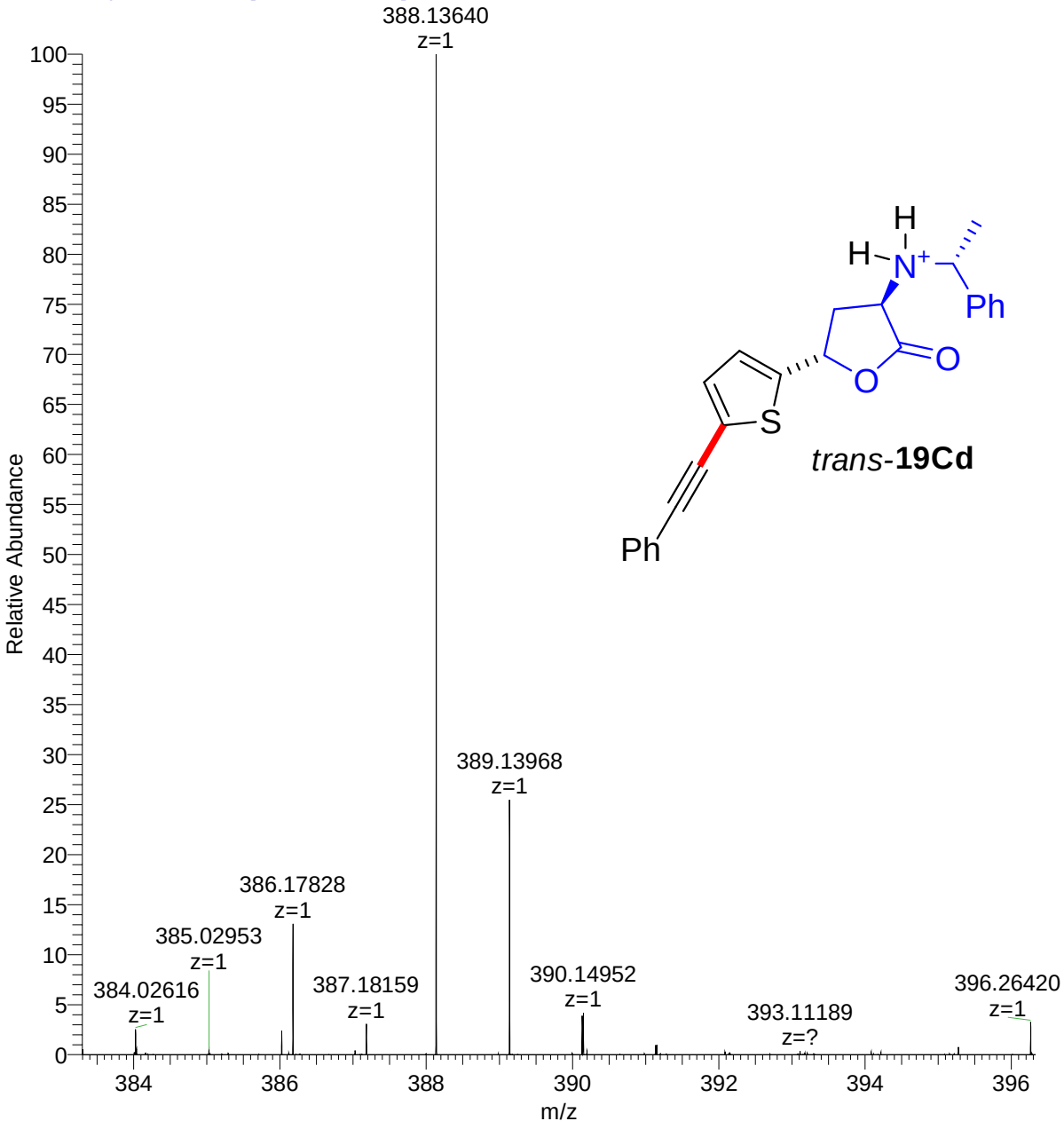
AD_1245(trans19Cc)_160128-10 #4-10 RT: 0.11-0.36 AV: 7 NL: 2.00E6
T: FTMS + p ESI Full ms [50.00-2000.00]



$[M+H]^+$ = 368.16780 calcd. 368.16788

AD 1249 (transCd) HESI/HRMS positive

AD_1249(transCd)_160128-11 #2-19 RT: 0.04-0.71 AV: 18 NL: 3.88E6
T: FTMS + p ESI Full ms [50.00-2000.00]

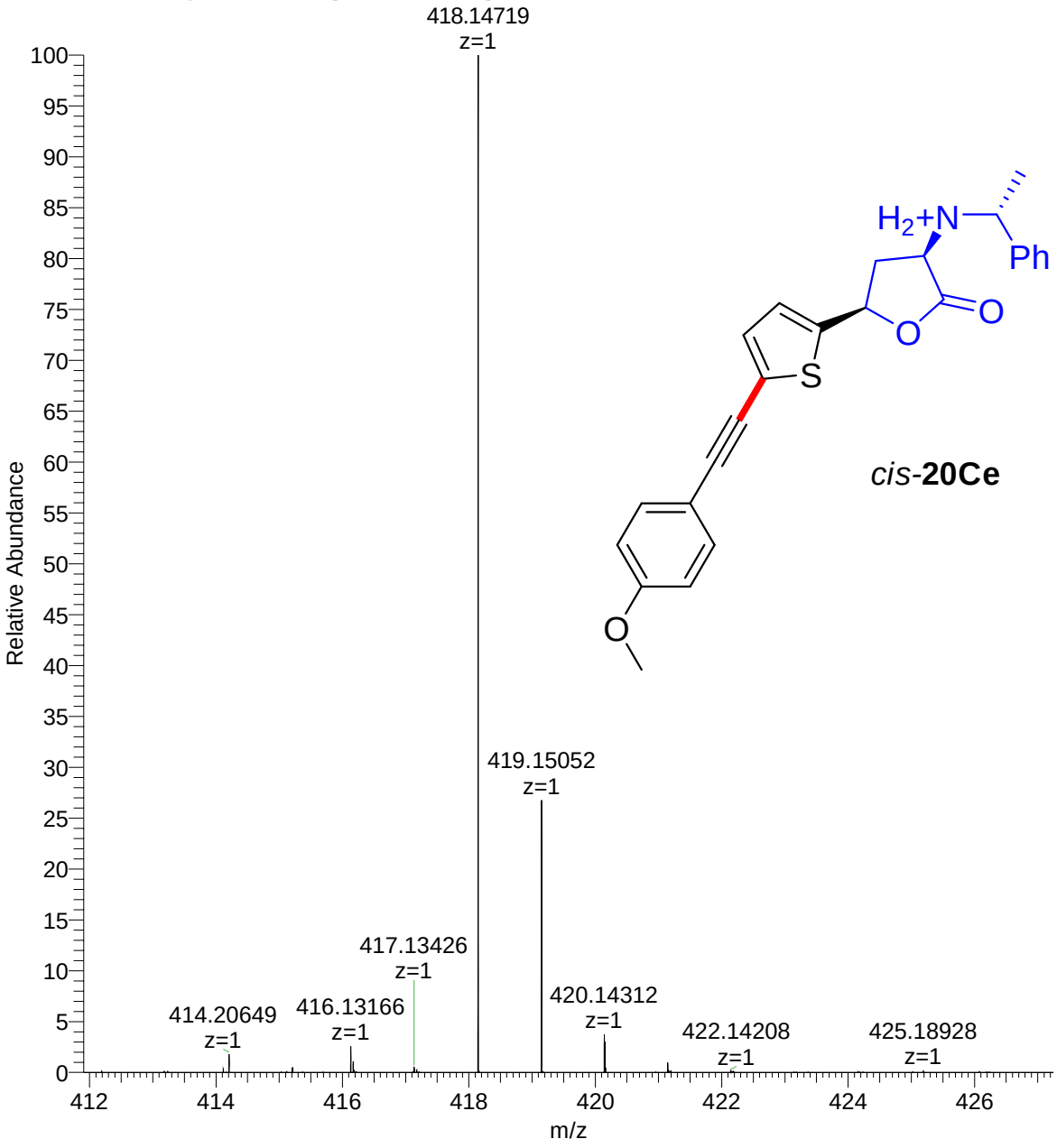


trans-**19Cd**

$[M+H]^+$ = 388.13640 calcd. 388.13658

AD 1393 (trans19Ce) HESI/HRMS positive

AD_1393trans19Ce)_160128-06 #3-14 RT: 0.08-0.47 AV: 12 NL: 4.20E7 T: FTMS + p ESI Full ms [50.00-2000.00]

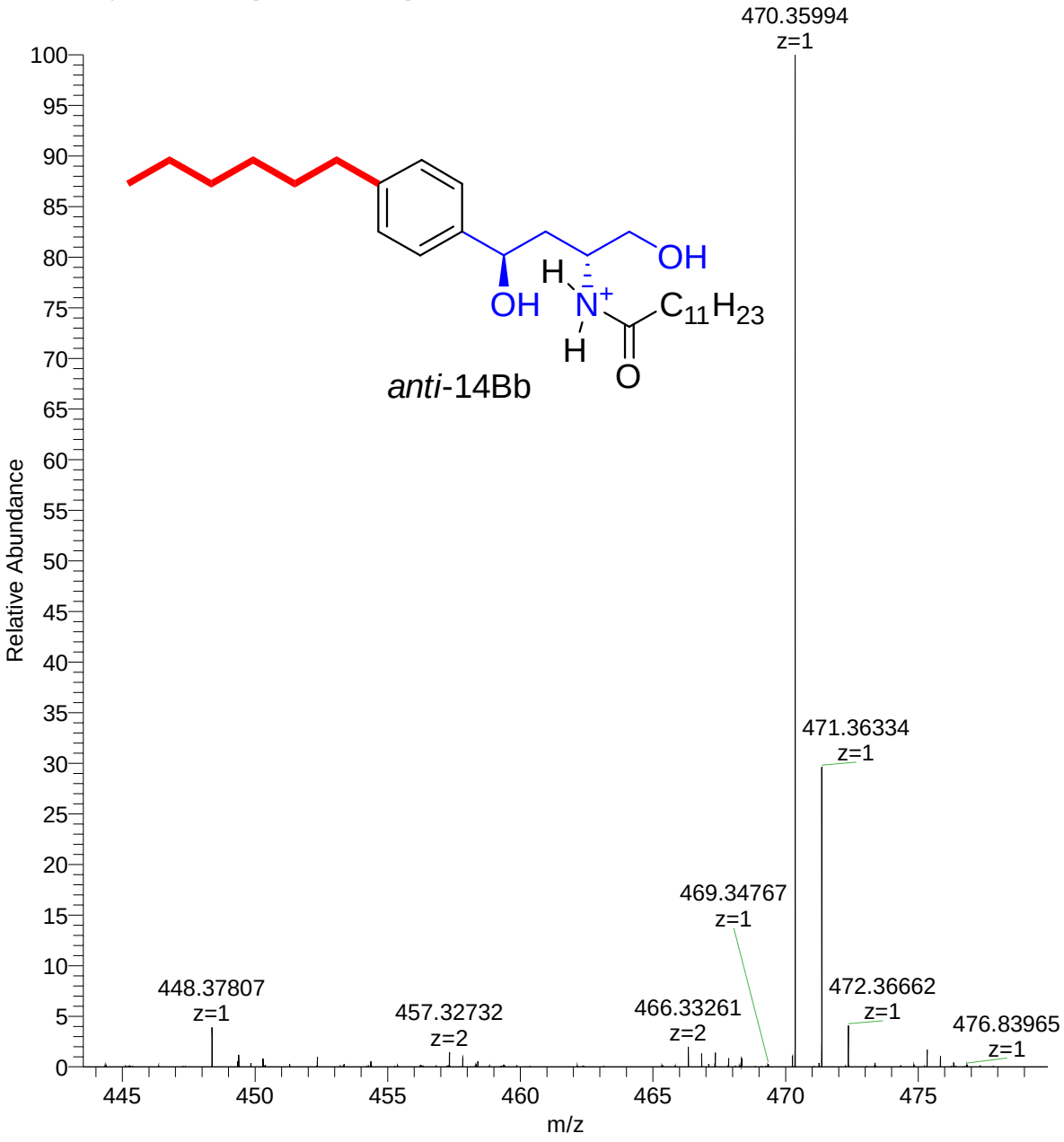


cis-**20Ce**

$[M+H]^+$ = 418.14719 calcd. 418.14714

AD 1285 (anti14Bb) HESI/HRMS positive

AD_1285(anti14Bb)_160128-12 #3-21 RT: 0.08-0.86 AV: 19 NL: 9.68E5
T: FTMS + p ESI Full ms [50.00-2000.00]

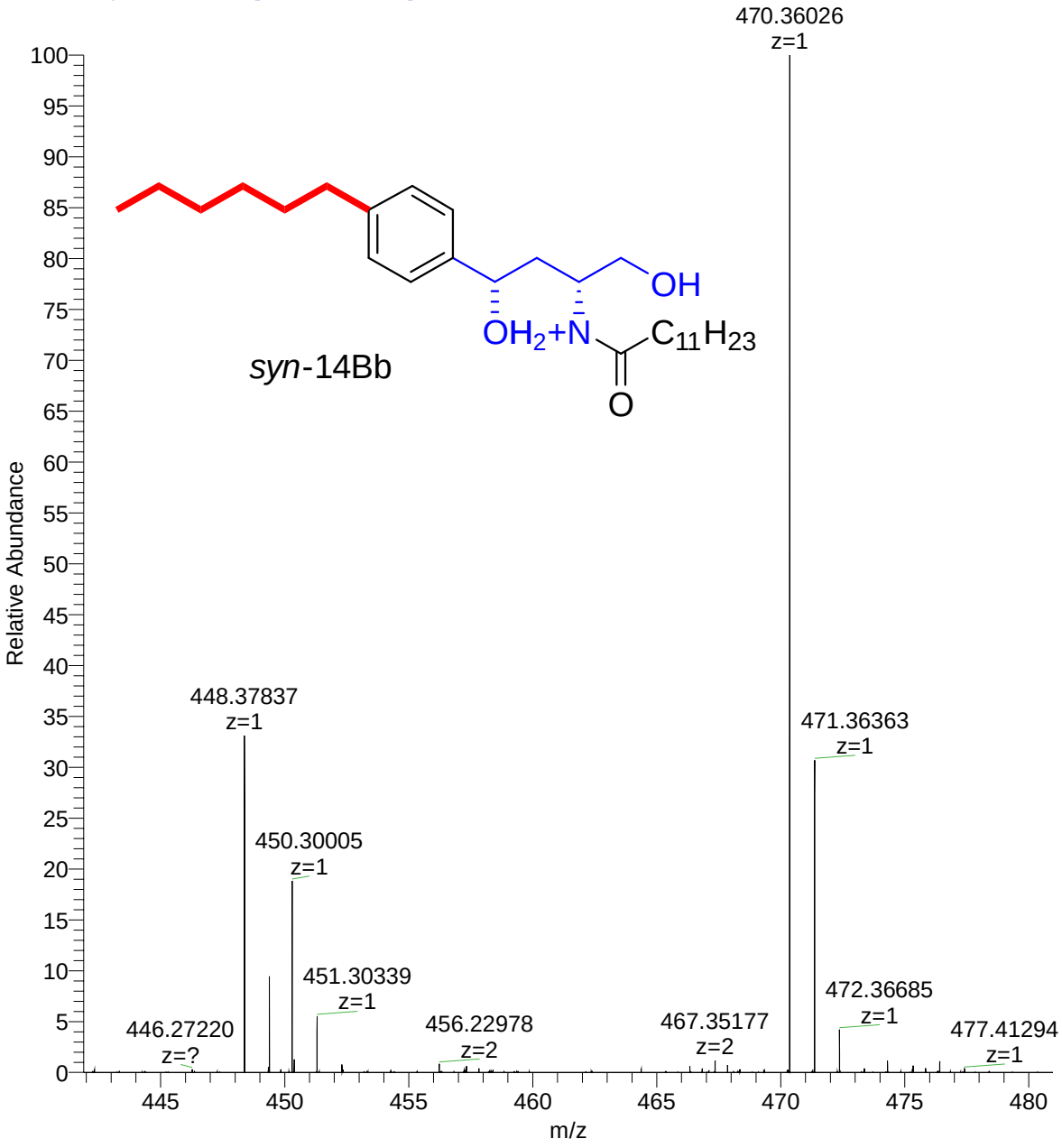


$[M+H]^+$ = 448.37807 calcd. 448.37852

$[M+Na]^+$ = 470.35994

AD 1286 (syn14Bb) HESI/HRMS positive

AD_1286(syn14Bb)_160128-09 #3-16 RT: 0.08-0.59 AV: 14 NL: 3.74E6
T: FTMS + p ESI Full ms [50.00-2000.00]

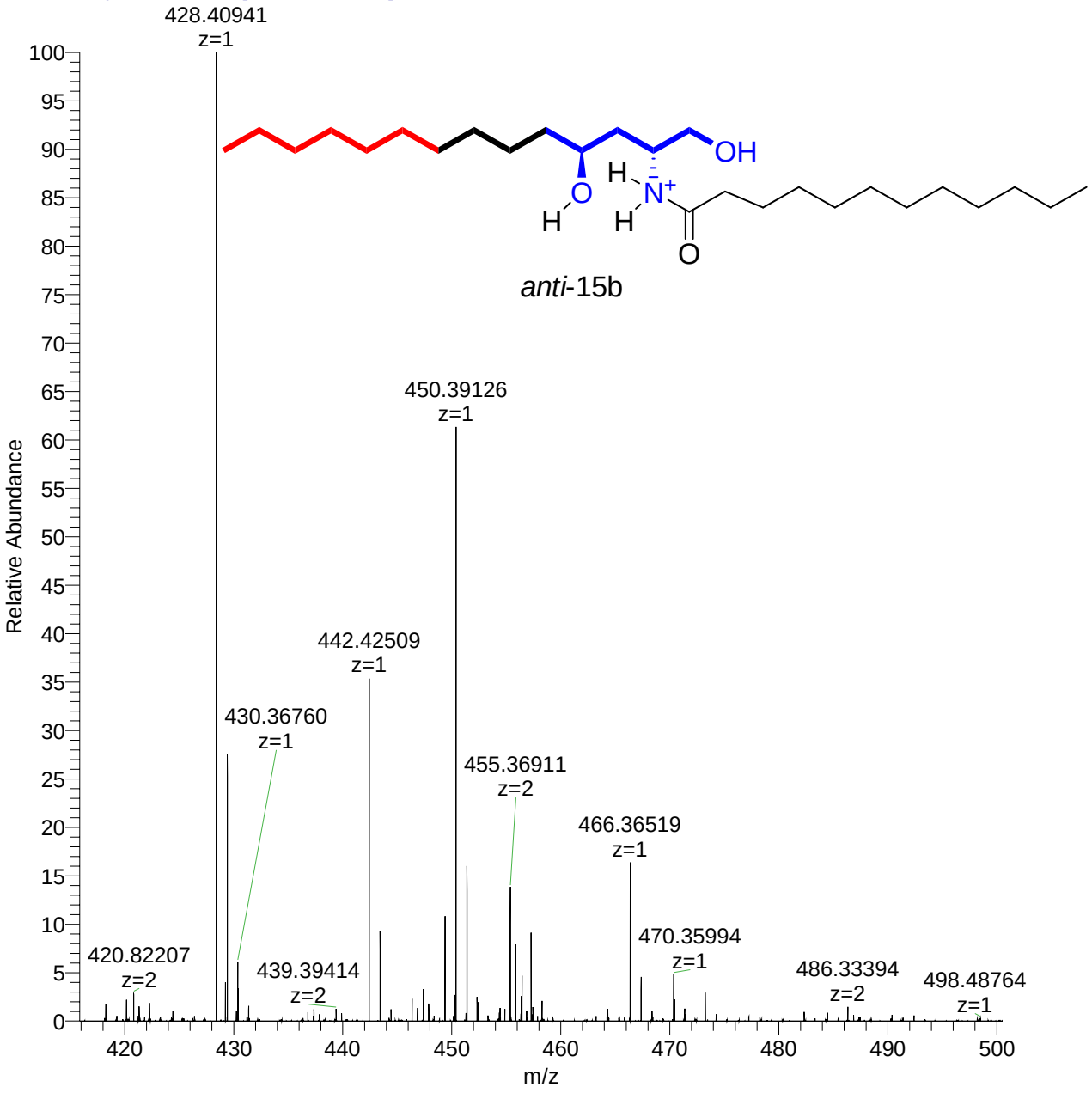


$[M+H]^+$ = 448.37837 calcd. 448.37852

$[M+Na]^+$ = 470.36026

AD 1286 (anti15b) HESI/HRMS positive

AD_1406(anti15b)_160128-13 #2-26 RT: 0.04-0.96 AV: 25 NL: 3.03E6
T: FTMS + p ESI Full ms [50.00-2000.00]



$[M+H]^+$ = 428.40941 calcd. 428.40982

$[M+Na]^+$ = 450.39126