Per(poly)fluoroalkanesulfinamides Assisted Diastereoselective Three-Component Inverse-Electron-Demand Aza Diels－Alder Reaction

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Supplementary Information

Contents

General

Unless otherwise mentioned, solvents and reagents were purchased from commercial sources and used as received. THF was freshly distilled over Na/benzophenone, CH_2Cl_2 was distilled over CaH_2. Melting points were measured on a Melt-Temp apparatus and uncorrected. ^{1}H NMR spectra were recorded on Bruker AM-300 or Mercury 300 (300 MHz) spectrometers with TMS as the internal standard. ^{19}F NMR spectra were recorded on Bruker AM-300 or Mercury 300 (282 MHz) spectrometers with $CFCl_3$ as the external standard. ^{13}C NMR spectra were recorded on DPX-400 (100.7 MHz) spectrometer. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Mass spectra were taken on a HP5989A spectrometer. HRMS data were obtained on a high-resolution mass spectrometer in the ESI or EI mode. α,β-Unsaturated ketones (aldehydes) were prepared according to the literature.[1]

General Procedure for the Preparation of Perfluoroalkanesulfinamides 2a–2d.

To a flask containing $HN(SiMe_3)_2$ (16 mL, 0.075 mol) was added dropwise per(poly)fluoroalkanesulfinyl chloride (0.075 mol) at 0 °C. After addition, stirring was continued for 2 h at room temperature. The TMS substituted sulfinamide intermediate was obtained by distillation under reduced pressure, which was further stirred with saturated aqueous ammonium chloride solution and purified by short column chromatography to give the target product **2**.[2]

2-Chloro-1,1,2,2-tetrafluoroethanesulfinamide (2a): ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.96 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$): δ -67.29 (m, 2F), -121.10 (dd, J_{AB} = 231.2 Hz, Δν = 3.45, 2F).

Trifluoromethanesulfinamide (2b): ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.97 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$): δ -80.92 (s, 3F).

Difluoro(phenyl)methanesulfinamide (2c): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62-7.50 (m, 5H), 4.00 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$): δ -105.04 (dd, J_{AB} = 226.4 Hz, Δν = 4.40, 2F).

Perfluorobutanesulfinamide (2d): ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.86 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$): δ -81.22 (m, 3F), -121.93 (m, 2F), -122.46 (ddt, J = 430.3, 243.4, 8.46 Hz, 2F), -126.48—-126.55 (m, 2F).

(S_s)-2-Chloro-1,1,2,2-tetrafluoroethanesulfinamide (2a): A solution of **5**[3] (0.5 mmol) in CH_2Cl_2 (7 mL) was added slowly to LiHMDS (1 mmol) in CH_2Cl_2 (3 mL) in 3h at -78 °C under the protection of N_2. After addition, saturated ammonium chloride aqueous solution (5 mL) was added immediately. The resulting mixture was extracted with CH_2Cl_2 (5 mL×3), washed with brine (10 mL), dried over Na_2SO_4 and purified by silica gel chromatography (EtOAc/ Petroleum ether: 1/5) to afford a white solid (72% yield): mp 42—43 °C; $[\alpha]_D^{20}$ = -15.4542 (c = 0.9850, $CHCl_3$, >99%ee).

General Procedure for the Preparation of Tetrahydropyridines 4a–4v.

To a solution of α, β-unsaturated ketone **1** (0.5 mmol), sulfinamide **2** (0.6 mmol) and vinyl ether **3** (1.0 mmol) in CH_2Cl_2 (1 mL), $Ti(OPr^i)_4$ (1.5 mmol) was added and the resulting mixture was stirred in a sealed vial at room temperature and monitored by TLC. After reaction, the mixture was poured into an equal volume of brine with rapid stirring and filtered through celite. The filter cake was washed with CH_2Cl_2 (3 mL × 3). The combined filtrate was washed with brine (6 mL), dried over Na_2SO_4. After the removal of solvents under vacuum, the residue was purified by column chromatography on silica gel to afford **4**.

4a-major endo: white solid, 147 mg, 65%; mp 55—57 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33—7.19 (5H, m, ArH), 6.25 (1H, d, J = 3.3 Hz, =C*H*), 5.52 (1H, s, NC*H*O), 3.68 (1H, dt, J = 8.7, 2.4 Hz, C*H*Ph), 3.58 (1H, dq, J = 9.3, 6.9 Hz, OC*H*HCH$_3$), 3.37 (1H, dq, J = 9.3, 6.9 Hz, OC*H*HCH$_3$), 2.63 (1H, ddd, J = 14.7, 9.0, 3.3 Hz, CH_aH$_e$), 2.41 (1H, d, J = 14.7 Hz, CH$_a$$H_e$), 1.05 (3H, t, J = 6.9, OCH$_2$$CH_3$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.38 (s, 3F), -67.88 (s, 2F), -116.51 (dd, J_{AB} = 226.4 Hz, Δν = 12.20, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 128.7, 128.5, 127.0, 121.6 (m), 120.7 (q, J = 272.5 Hz), 76.5, 63.6, 35.7, 34.8, 14.8; FT-IR (KBr): ν_{max}

2983, 2900, 1668, 1494, 1456, 1392, 1341, 1308, 1251, 1188, 1177, 1143, 1116, 1056, 952, 929, 786, 703 cm^{-1}; EIHRMS: *m/z* 453.0401 (M^+, $C_{16}H_{15}ClF_7NO_2$ S requires 453.0400).

4b-major endo: colorless oil, 122 mg, 63%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39－7.20 (5H, m, ArH), 6.27 (1H, d, *J* = 3.6 Hz, =C*H*), 5.46 (1H, t, *J* = 2.7 Hz, NC*H*O), 3.71－3.69 (1H, m, C*H*Ph), 3.58 (1H, dq, *J* = 9.3, 6.9 Hz, OC*H*HCH$_3$), 3.37 (1H, dq, *J* = 9.3, 6.9 Hz,OC*H*HCH$_3$), 2.41 (2H, m, CH_aH_e), 1.05 (3H, t, *J* = 6.9, OCH$_2$CH_3); ^{19}F NMR (282 MHz, $CDCl_3$): δ -63.95 (s, 3F), -73.97 (s, 3F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.2, 128.5, 128.4, 128.3, 121.6 (m), 120.7 (q, *J* = 272.2 Hz), 76.5, 63.4, 35.4, 34.6, 14.5; FT-IR (neat): ν_{max} 2981, 1668, 1494, 1455, 1394, 1339, 1305, 1250, 1189, 1126, 1061, 9542, 932, 701 cm^{-1}; EIMS (*m/z*, %): 387 (M^+, 1.34), 342 (2.52), 318 (34.25), 270 (2.92), 224 (48.42), 183 (100.00), 77 (8.44); EIHRMS: *m/z* 387.0731 (M^+, $C_{15}H_{15}F_6NO_2S$ requires 387.0728).

4c-major endo: white solid**,** 93.5 mg, 42%; mp 96－98 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63－7.46 (5H, m, ArH), 7.36－7.17 (5H, m, ArH), 6.21 (1H, d, *J* = 3.9 Hz, =C*H*), 5.57 (1H, t, *J* = 2.6 Hz, NC*H*O), 3.78－3.66 (1H, m, C*H*Ph), 3.60 (1H, dq, *J* = 9.3, 6.9 Hz, OC*H*HCH$_3$), 3.37 (1H, dq, *J* = 9.3, 6.9 Hz,OC*H*HCH$_3$), 2.62 (1H, ddd, *J* = 14.7, 9.3, 3.0 Hz, CH_aH$_e$), 2.41 (1H, d, *J* = 14.7 Hz, CH$_a$$H_e$), 1.04 (3H, t, *J* = 6.9, OCH$_2$CH_3); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.43 (s, 3F), -105.43 (dd, J_{AB} = 210.1 Hz, Δν =15.22, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 131.9, 129.7, 129.0, 128.5, 128.2, 126.5, 126.0, 121.0 (q, *J* = 272.2 Hz), 119.9 (m), 76.0, 63.0, 35.6, 34.8, 14.7; FT-IR (KBr): ν_{max} 3066, 3032, 2978, 1663, 1604, 1494, 1454, 1394, 1338, 1303, 1278, 1189, 1142, 1068, 956, 932, 888, 758, 699 cm^{-1}; EIMS (*m/z*, %): 445 (M^+, 0.58), 400 (0.90), 270 (7.09), 225 (11.55), 183 (22.75), 127 (100.00), 77 (9.98); EIHRMS *m/z* 445.1131 (M^+, $C_{21}H_{20}F_5NO_2S$ requires 445.1135).

4d-major endo: colorless oil, 146.3 mg, 59%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39－7.13 (5H, m, ArH), 6.26 (1H, d, *J* = 3.6 Hz, =C*H*), 5.53 (1H, s, NC*H*O), 3.74－3.64 (1H, m, C*H*Ph), 3.58 (1H, dq, *J* = 9.3, 6.9 Hz, OC*H*HCH$_3$), 3.37 (1H, dq, *J* = 9.3, 6.9 Hz,OC*H*HCH$_3$), 2.56－2.34 (2H, m, CH_aH_e), 1.06 (3H, t, *J* = 6.9, OCH$_2$CH_3); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.73 (s, 3F), -80.8－82.0 (m, 3F), -118.2 (dd, J_{AB} = 238.8 Hz, Δν = 12.34, 2F), -122.6 (s, 2F), -126.7 (t, *J*= 304.8 Hz, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 128.4, 128.3, 126.8, 121.5 (m), 120.7 (q, *J* = 272.7 Hz), 76.2, 63.4, 35.5, 34.6, 14.5; FT-IR (neat): ν_{max} 2982, 1668, 1605, 1495, 1394, 1350, 1339, 1304, 1240, 1195, 1139, 1143, 1061, 955, 932, 746, 700, 691 cm^{-1}; EIMS (*m/z*, %): 318 (M^+ − C_4F_9, 32.86), 270 (6.36), 225 (23.42), 183 (100.00), 77 (21.12); EIHRMS: *m/z* 537.0636 (M^+, $C_{18}H_{15}F_{12}NO_2S$ requires 537.0632).

4e-major endo: colorless oil; 151.9 mg, 63%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35－7.17 (5H, m, ArH), 6.27 (1H, d, *J* = 3.6 Hz, =C*H*), 5.47 (1H, t, *J* = 2.4 Hz, NC*H*O), 3.75－3.65 (1H, m, C*H*Ph), 3.31 (1H, dd, *J* = 9.3, 6.3 Hz, OC*H*HCH(CH$_3$)$_2$), 3.12 (1H, dd, *J* = 9.3, 6.0 Hz, OCH*H*CH(CH$_3$)$_2$), 2.52 (1H, ddd, *J* = 14.4, 9.0, 3.0 Hz, CH_aH$_e$), 2.45 (1H, d, *J* = 14.4 Hz, CH$_a$$H_e$), 1.74－1.58 (1H, m, OCH$_2$C*H*(CH$_3$)$_2$), 0.77 (3H, d, *J* = 6.3 Hz, OCH$_2$CH(CH_3)$_2$), 0.74 (3H, d, *J* = 6.9 Hz, OCH$_2$CH(CH_3)$_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.05 (s, 3F), -67.63 (dd, J_{AB} = 183.3 Hz, Δν = 0.20, 2F), -116.32 (dd, J_{AB} = 226.4 Hz, Δν = 12.22, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.4, 128.3, 128.2, 126.7, 121.2 (m), 120.7 (q, *J* = 272.5 Hz), 76.9, 76.8, 75.1, 35.2, 34.5, 28.1, 19.2, 19.1; FT-IR (neat): ν_{max} 2961, 2875, 1666, 1604, 1494, 1473, 1454, 1394, 1340, 1303, 1250, 1180, 1140, 1057, 1013, 948, 929, 788, 701 cm^{-1}; HREIMS: *m/z* 481.0720 (M^+, $C_{18}H_{19}ClF_7NO_2S$ requires 481.0713).

4f-major endo: colorless oil; 161.3 mg, 67%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36－7.15 (5H, m, ArH), 6.26 (1H, d, *J* = 3.3 Hz, =C*H*), 5.49 (1H, s, NC*H*O), 3.71－3.67 (1H, m, C*H*Ph), 3.53 (1H, dt, *J* = 9.6, 6.3 Hz, OC*H*HC$_3$H$_7$), 3.31 (1H, dt, *J* = 9.6, 6.3 Hz, OC*H*HC$_3$H$_7$), 2.51 (1H, ddd, *J* = 14.4, 9.0, 3.0 Hz, CH_aH$_e$), 2.42 (1H, d, *J* = 14.4 Hz, CH$_a$$H_e$), 1.45－1.31 (2H, OCH$_2CH_2CH_2CH_3$), 1.30－1.10 (2H, OCH$_2CH_2CH_2CH_3$), 0.83 (3H, t, *J* = 6.9, OC$_3$H$_6$CH_3); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.07 (s, 3F), -67.66 (s, 2F), -116.28 (dd, J_{AB} = 226.4 Hz, Δν =12.26, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 128.5, 126.9, 121.3 (m), 120.9 (q, *J* = 272.5 Hz), 76.9, 76.8, 68.1, 35.6, 34.7, 31.4, 19.4, 13.9; FT-IR (neat): ν_{max} 2961, 2936, 2875, 1667, 1494, 1392, 1339, 1303, 1249, 1219, 1180, 1141, 1077, 1057, 1013, 948, 893, 789, 701 cm^{-1}; EIHRMS: *m/z* 481.0708 (M^+, $C_{18}H_{19}ClF_7NO_2S$ requires 481.0713).

4g-major endo: colorless oil; 158.8 mg, 63%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.32－7.19 (5H, m, ArH), 6.27 (1H, d, J = 2.7 Hz, =C*H*), 5.61 (1H, s, NC*H*O), 3.73－3.64 (1H, m, C*H*Ph), 3.60－3.46 (1H, m, OC*H*(CH_2)$_5$), 2.51 (1H, ddd, J = 14.4, 9.0, 3.0 Hz, C$H_a$$H_e$), 2.36 (1H, d, J = 14.4 Hz, C$H_a$$H_e$), 1.82－1.05 (10H, m, OCH(CH_2)$_5$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.97 (s, 3F), -68.42 (m, 2F), -117.15 (dd, J_{AB} = 226.4 Hz, Δν =12.40, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 128.5, 128.2, 126.6, 121.7 (m), 120.6 (q, J = 272.2 Hz), 73.7, 35.4, 34.9, 32.6, 30.7, 25.6, 23.5, 23.1; FT-IR (neat): ν_{max} 2937, 2860, 1668, 1605, 1494, 1454, 1337, 1303, 1251, 1180, 1139, 1056, 942, 896, 858, 789, 700cm^{-1}; EIMS: (*m/z*, %): 408 (M^+ − $C_6H_{11}O$, 4.09), 372 (M^+ − C_2F_4Cl, 38.00), 324 (2.94), 290 (64.72), 246 (100.00), 225 (37.83), 183 (40.32), 83 (63.87), 55 (44.69); EIHRMS: *m/z* 507.0875 (M^+, $C_{20}H_{21}ClF_7NO_2S$ requires 507.0870).

4h-major endo: colorless oil, as a 10/1 mixture with the minor *endo* diastereomer; 107.4 mg, 46%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.37－7.20 (5H, m, ArH), 6.22 (1H, d, J = 3.0 Hz, =C*H*), 5.64 (1H,s, NC*H*O), 5.34 (2H, d, J = 5.6 Hz, =CH_2), 4.25 (1H, s, C*H*Ph), 3.64 (1H, dq, J = 9.3, 6.9 Hz, OC*H*HCH_3), 3.45 (1H, dq, J = 9.3, 6.9 Hz,OC*H*HCH_3), 1.14 (3H, t, J = 6.9 Hz, OCH_2CH_3); ^{19}F NMR (282 MHz, $CDCl_3$): δ -65.06 (s, 3F), -68.54 (s, 2F), -115.07 (dd, J_{AB} = 222.2 Hz, Δν = 9.86, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.7, 141.3, 128.6, 128.3, 127.1, 122.7, 120.6 (q, J = 272.5 Hz), 117.8, 80.3, 63.2, 44.0, 14.8; FT-IR (neat): ν_{max} 3313, 2981, 2932, 1669, 1603, 1496, 1446, 1403, 1326, 1311, 1261, 1185, 1139, 1089, 1045, 934, 901, 790, 703 cm^{-1}; EIMS (*m/z*, %): 330 (M^+ − C_2F_4Cl, 47.34), 282 (5.31), 236 (100.00), 216 (54.15), 115 (17.45), 91 (10.78), 77 (6.92); EIHRMS: *m/z* 465.0392 (M^+, $C_{17}H_{15}ClF_7NO_2S$ requires 465.0400).

4j-major endo: white solid, mp 61－63 °C; 172.4 mg, 65%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.29－7.16 (2H, m, ArH), 6.90－6.81 (2H, m, ArH), 6.21 (1H, d, J = 3.0 Hz, =C*H*), 5.45 (1H, s, NC*H*O), 4.14－4.04 (1H, m, C*H*Ph), 3.85 (3H, s, OCH_3), 3.29 (1H, dd, J = 9.3, 6.3 Hz, OC*H*HCH(CH_3)$_2$), 3.10 (1H, dd, J = 9.3, 6.0 Hz, OCH*H*CH(CH_3)$_2$), 2.45 (1H, ddd, J = 14.4, 9.0, 2.7 Hz, C$H_a$$H_e$), 2.45 (1H, d, J = 14.4 Hz, C$H_a$$H_e$), 1.72－1.56 (1H, m, O$CH_2$C*H*($CH_3$)$_2$), 0.77 (3H, d, J = 6.3 Hz, OCH_2CH(CH_3)$_2$), 0.72 (3H, d, J = 6.3 Hz, OCH_2CH(CH_3)$_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.05 (s, 3F), -68.36 (m, 2F), -116.99 (dd, J_{AB} = 226.4 Hz, Δν = 12.38, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.0, 131.1, 129.8, 127.8, 121.4, 120.8 (q, J = 272.4 Hz), 120.1, 109.9, 77.2, 75.0, 55.2, 33.0, 28.6, 28.1, 19.2, 19.1; FT-IR (KBr): ν_{max} 2960, 1662, 1602, 1493, 1472, 1338, 1301, 1249, 1195, 1181, 1141, 1121, 1056, 949, 863, 787, 751 cm^{-1}; EIHRMS: *m/z* 511.0818 (M^+, $C_{19}H_{21}ClF_7NO_3S$ requires 511.0819).

4k-major endo: colorless oil; 149.8 mg, 59%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.19 (2H, J = 8.7 Hz, ArH), 6.80 (2H, J = 8.7 Hz, ArH), 6.21 (1H, d, J = 3.6 Hz, =C*H*), 5.44 (1H, s, NC*H*O), 3.77 (3H, s, OCH_3), 3.67－3.55 (1H, m, C*H*Ph), 3.29 (1H, dd, J = 9.0, 6.9 Hz, OC*H*HCH(CH_3)$_2$), 3.11 (1H, dd, J = 9.3, 6.3 Hz, OCH*H*CH(CH_3)$_2$), 2.47 (1H, ddd, J = 14.7, 9.0, 3.3 Hz, C$H_a$$H_e$), 2.38 (1H, d, J = 14.7 Hz, C$H_a$$H_e$), 1.74－1.60 (1H, m, O$CH_2$C*H*($CH_3$)$_2$), 0.78 (3H, d, J = 6.6 Hz, OCH_2CH(CH_3)$_2$), 0.74 (3H, d, J = 6.6 Hz, OCH_2CH(CH_3)$_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.77 (s, 3F), -68.38 (s, 2F), -117.09 (dd, J_{AB} = 226.4 Hz, Δν = 12.15, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 135.7, 129.3, 121.8 (m), 120.7 (q, J = 272.2 Hz), 113.7, 76.8, 75.1, 55.2, 34.7, 28.1, 18.8; FT-IR (neat): ν_{max} 2961, 2934, 2876, 1668, 1612, 1514, 1466, 1394, 1340, 1304, 1255, 1180, 1140, 1058, 948, 896, 829, 789 cm^{-1}; EIHRMS: *m/z* 511.0821 (M^+, $C_{19}H_{21}ClF_7NO_3S$ requires 511.0819).

4l-major endo: white solid, mp 44－46 °C; 159.0 mg, 64%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.18 (2H, J = 7.8 Hz, ArH), 7.10 (2H, J = 7.8 Hz, ArH), 6.24 (1H, d, J = 3.0 Hz, =C*H*), 5.47 (1H, s, NC*H*O), 3.70－3.60 (1H, m, C*H*Ph), 3.31 (1H, dd, J = 9.0, 6.3 Hz, OC*H*HCH(CH_3)$_2$), 3.14 (1H, dd, J = 9.0, 6.0 Hz, OCH*H*CH(CH_3)$_2$), 2.51 (1H, ddd, J = 14.7, 9.0, 3.3 Hz, C$H_a$$H_e$), 2.38 (1H, d, J = 14.7 Hz, C$H_a$$H_e$), 2.32 (3H, s, C$H_3$), 1.76－1.62 (1H, m, O$CH_2$C*H*($CH_3$)$_2$), 0.80 (3H, d, J = 6.6 Hz, OCH_2CH(CH_3)$_2$), 0.77 (3H, d, J = 6.6 Hz, OCH_2CH(CH_3)$_2$); ^{19}F NMR

(282 MHz, $CDCl_3$): δ -64.83 (s, 3F), -68.40 (s, 2F), -117.14 (dd, J_{AB} = 226.4 Hz, Δν = 12.17, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 136.3, 129.0, 128.1, 125.0 (m), 121.9, 120.8 (q, *J* = 272.4 Hz), 76.8, 75.1, 35.0, 34.7, 28.1, 20.9, 19.2, 19.1; FT-IR (KBr): ν_{max} 2963, 1664, 1513, 1338, 1305, 1249, 1119, 1057, 947, 817, 789 cm^{-1}; EIHRMS: *m/z* 495.0873 (M^+, $C_{19}H_{21}ClF_7NO_2S$ requires 495.0870).

4m-major endo: colorless oil; 172.9 mg, 67%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27 (2H, *J* = 8.7 Hz, ArH), 7.22 (2H, *J* = 8.7 Hz, ArH), 6.20 (1H, d, *J* = 3.3 Hz, =C*H*), 5.47 (1H, s, NC*H*O), 3.73－3.62 (1H, m, C*H*Ph), 3.30 (1H, dd, *J* = 9.0, 6.3 Hz, OC*H*HCH(CH_3)$_2$), 3.12 (1H, dd, *J* = 9.0, 6.0 Hz, OCH*H*CH(CH_3)$_2$), 2.50 (1H, ddd, *J* = 14.4, 9.0, 3.0 Hz, CH_aH_e), 2.41 (1H, d, *J* = 14.4 Hz, CH_aH_e), 1.74－1.58 (1H, m, $OCH_2CH(CH_3)_2$), 0.77 (3H, d, *J* = 6.6 Hz, $OCH_2CH(CH_3)_2$), 0.74 (3H, d, *J* = 6.6 Hz, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.86 (s, 3F), -68.46 (s, 2F), -117.05 (dd, J_{AB} = 226.4 Hz, Δν = 12.02, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 132.7, 129.8, 128.6, 120.8 (q, *J* = 272.4 Hz), 120.3 (m), 76.9, 75.4, 34.9, 34.5, 28.3, 19.4, 19.3; FT-IR (neat): ν_{max} 2963, 2877, 1667, 1493, 1395, 1342, 1303, 1249, 1179, 1058, 948, 896, 790 cm^{-1}; EIHRMS: *m/z* 515.0331 (M^+, $C_{18}H_{18}Cl_2F_7NO_2S$ requires 515.0324).

4n-major endo: colorless oil; 165.7 mg, 59%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42 (2H, *J* = 8.7 Hz, ArH), 7.17 (2H, *J* = 8.7 Hz, ArH), 6.20 (1H, d, *J* = 3.3 Hz, =C*H*), 5.48 (1H, s, NC*H*O), 3.73－3.60 (1H, m, C*H*Ph), 3.31 (1H, dd, *J* = 9.0, 6.3 Hz, OC*H*HCH(CH_3)$_2$), 3.13 (1H, dd, *J* = 9.0, 6.3 Hz, OCH*H*CH(CH_3)$_2$), 2.50 (1H, ddd, *J* = 14.4, 9.3, 2.7 Hz, CH_aH_e), 2.41 (1H, d, *J* = 14.4 Hz, CH_aH_e), 1.74－1.59 (1H, m, $OCH_2CH(CH_3)_2$), 0.78 (3H, d, *J* = 6.9 Hz, $OCH_2CH(CH_3)_2$), 0.74 (3H, d, *J* = 6.9 Hz, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.78 (s, 3F), -68.39 (s, 2F), -116.97 (dd, J_{AB} = 226.4 Hz, Δν = 12.27, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4, 131.4, 130.0, 122.0, 120.6 (q, *J* = 272.8 Hz), 120.0 (m), 76.7, 75.1, 34.7, 34.3, 28.1, 19.2, 19.1; FT-IR (neat): ν_{max} 2962, 2929, 2876, 1668, 1490, 1394, 1341, 1303, 1249, 1180, 1124, 1058, 1012, 948, 895, 789 cm^{-1}; EIMS (*m/z*, %): 424 (M^+ − C_2F_4Cl, 31.72), 376 (6.24), 302 (60.22), 261 (29.46), 57 (100.00); EIHRMS: *m/z* 558.9812 (M^+, $C_{18}H_{18}BrClF_7NO_2S$ requires 558.9818).

4o-major endo: colorless oil; 108.52 mg, 46%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 (1H, d, *J* = 2.1 Hz, ArH), 6.28 (1H, dd, *J* = 3.0, 2.1 Hz, ArH), 6.24 (1H, d, *J* = 3.3 Hz, ArH), 6.07 (1H, d, *J* = 3.3 Hz, =C*H*), 5.50 (1H, s, NC*H*O), 3.82－3.73 (1H, m, C*H*Ph), 3.22 (1H, dd, *J* = 9.0, 6.3 Hz, OC*H*HCH$_3$), 3.13 (1H, dd, *J* = 9.0, 6.0 Hz,OC*H*HCH$_3$), 2.67 (2H, d, *J* = 14.7, CH_aH_e), 2.27 (1H, ddd, *J* = 14.7, 9.0, 2.7 Hz, CH_aH_e), 1.68－1.53 (1H, m, $OCH_2CH(CH_3)_2$), 0.73 (3H, d, *J* = 3.6 Hz, $OCH_2CH(CH_3)_2$), 0.71 (3H, d, *J* = 3.6 Hz, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.74 (s, 3F), -68.27 (dd, J_{AB} = 183.3 Hz, Δν = 0.20, 2F), -116.65 (dd, J_{AB} = 226.4 Hz, Δν = 12.59, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.9, 140.9, 120.6 (q, *J* = 272.3 Hz), 116.9 (q, *J* = 5.3 Hz), 110.3, 105.6, 76.4, 74.7, 69.8, 30.7, 29.2, 28.0, 19.0, 18.9; FT-IR (neat): ν_{max} 2962, 2877, 1670, 1615, 1506, 1474, 1395, 1338, 1314, 1289, 1260, 1181, 1122, 1060, 1013, 948, 894, 790 cm^{-1}; EIMS (*m/z*, %): 336 (M^+ − C_2F_4Cl, 12.31), 236 (100.00), 214 (25.35), 184 (29.00), 57 (41.27); EIHRMS: *m/z* 471.0501 (M^+, $C_{16}H_{17}ClF_7NO_3S$ requires 471.0506).

4p-major endo: white solid, mp 64－66 °C; 159.1 mg, 60%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (1H, d, *J* = 8.1 Hz, ArH), 7.91 (1H, d, *J* = 7.5 Hz, ArH), 7.77 (1H, dd, *J* = 6.9, 2.7 Hz, ArH), 7.61－7.47 (2H, m, ArH), 7.45－7.36 (2H, m, ArH), 6.39 (1H, d, *J* = 3.3 Hz, =C*H*), 5.48 (1H, s, NC*H*O), 3.50－3.41 (1H, m, C*H*Ph), 3.31 (1H, dd, *J* = 8.7, 6.9 Hz, OC*H*HCH$_3$), 3.07 (1H, dd, *J* = 9.0, 6.0 Hz,OC*H*HCH$_3$), 2.56 (2H, d, *J* = 13.8, CH_aH_e), 2.70 (1H, ddd, *J* = 13.8, 9.9, 3.0 Hz, CH_aH_e), 1.69－1.56 (1H, m, $OCH_2CH(CH_3)_2$), 0.76 (3H, d, *J* = 6.9 Hz, $OCH_2CH(CH_3)_2$), 0.70 (3H, d, *J* = 6.9 Hz, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.67 (s, 3F), -68.26 (s, 2F), -116.87 (dd, J_{AB} = 226.7 Hz, Δν = 12.45, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 134.0, 130.4, 129.4, 127.5, 126.7, 126.3, 125.4, 125.2, 122.1, 121.1, 120.7 (q, *J* = 272.2 Hz), 77.0, 76.7, 75.1, 34.0, 30.1, 28.1, 19.2, 19.1; FT-IR (KBr): ν_{max} 3064, 2961, 2933, 2876, 1943, 1668, 1600, 1511, 1473, 1396, 1340, 1305, 1247, 1178, 1140, 1059, 1013, 948, 896, 860, 798, 782, 651 cm^{-1}; EIMS (*m/z*, %): 531 (M^+, 5.44), 348 (3.48), 275

(52.94), 274 (100.00), 148 (8.28), 127 (11.59), 57 (23.57); EIHRMS: *m/z* 531.0868 (M^+, $C_{22}H_{21}ClF_7NO_2S$ requires 531.0870).

4q-major endo: colorless oil; 99.5 mg, 38%; ^{1}H NMR (300 MHz, $CDCl_3$): δ7.32－7.24 (2H, m, ArH), 7.23－7.14 (3H, m, ArH), 6.02 (1H, d, *J* = 3.3 Hz, =C*H*), 5.44 (1H, s, NC*H*O), 3.26 (1H, dd, *J* = 9.0, 6.9 Hz, OC*H*HPr^i), 3.17 (1H, dd, *J* = 9.3, 6.0 Hz, OCH*H*Pr^i), 2.62 (2H, t = 6.9 Hz, $CH_2CH_2CH_2$Ph), 2.32 (1H, s (b), C*H*Ph), 2.16 (1H, d, *J* = 14.4 Hz, CH_aH_e), (1H, ddd, *J* = 14.4, 7.8, 1.2 Hz, CH_aH_e), 1.84－1.58 (5H, m, $CH_2CH_2CH_2$Ph, $OCH_2CH(CH_3)_2$), 0.83 (3H, d, *J* = 6.9, $OCH_2CH(CH_3)_2$), 0.80 (3H, d, *J* = 6.9, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.42 (s, 3F), -68.14 (s, 2F), -116.56 (dd, J_{AB} = 226.4 Hz, Δν = 12.57, 2F); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.0, 128.4, 126.0, 122.1, 120.8 (q, *J* = 272.5 Hz), 77.2, 74.7, 35.8, 35.1, 30.3, 29.0, 28.1, 19.3, 19.2; FT-IR (neat): ν_{max} 2961, 2933, 2872, 1666, 1606, 1497, 1455, 1394, 1343, 1297, 1257, 1237, 1179, 1123, 1059, 946, 909, 788, 736, 700 cm^{-1}; EIMS (*m/z*, %): 388 (M^+ − C_2F_4Cl, 11.96), 340 (1.73), 266 (18.39), 91 (100.00), 57 (47.29); EIHRMS: *m/z* 450.0532 (M^+ − OBu^i, $C_{17}H_{16}ClF_7NOS$ requires 450.0529).

4r-major endo: colorless oil; 73.9 mg, 32%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.04 (1H, d, *J* = 3.9 Hz, =C*H*), 5.45 (1H, s, NC*H*O), 3.28 (1H, dd, *J* = 9.0, 6.9 Hz, OC*H*HPr^i), 3.18 (1H, dd, *J* = 9.3, 6.0 Hz, OCH*H*Pr^i), 2.29 (1H, s (b), C*H*Ph), 2.16 (1H, d, *J* = 14.1 Hz, CH_aH_e), 2.02 (1H, dd, *J* = 14.1, 8.4 Hz, CH_aH_e), 1.84－1.68 (1H, m, $OCH_2CH(CH_3)_2$), 1.67－1.54 (2H, m, $CH_2(CH_2)_2CH_3$), 1.44－1.27 (4H, m, $CH_2(CH_2)_2CH_3$), 0.91 (3H, t, *J* = 6.9, $(CH_2)_3CH_3$), 0.85 (6H, d, *J* = 6.9, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.59 (s, 3F), -68.29 (s, 2F), -116.78 (dd, J_{AB} = 226.4 Hz, Δν = 12.53, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 122.5 (m), 120.8 (q, *J* = 272.2 Hz), 77.2, 74.6, 35.2, 30.4, 30.3 29.3, 28.1, 22.5, 19.2, 19.1, 13.9; FT-IR (neat): ν_{max} 2963, 2934, 2876, 1666, 1470, 1395, 1344, 1297, 1179, 1142, 1056, 1012, 948, 898, 789 cm^{-1}; EIMS (*m/z*, %): 388 (M^+ − OBu^i, 5.25), 326 (M^+ − C_2F_4Cl, 19.09), 204 (21.28), 57 (100.00); EIHRMS: *m/z* 461.1028 (M^+, $C_{16}H_{23}ClF_7NO_2S$ requires 461.1026).

4s-major endo: colorless oil; 117.2 mg, 47%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35－7.19 (5H, m, ArH), 6.24 (1H, s, =C*H*), 5.50 (1H, s, NC*H*O), 3.74－3.68 (1H, m, C*H*Ph), 3.43 (1H, dd, *J* = 9.0, 6.3 Hz, OC*H*HPr^i), 3.14 (1H, dd, *J* = 9.0, 6.3 Hz, OCH*H*Pr^i), 2.49 (1H, ddd, *J* = 14.4, 9.3, 2.7 Hz, CH_aH_e), 2.27 (1H, d, *J* = 14.4 Hz, CH_aH_e), 1.69 (1H, m, $OCH_2CH(CH_3)_2$), 0.78 (3H, d, *J* = 6.9, $OCH_2CH(CH_3)_2$), 0.74 (3H, d, *J* = 6.9, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -50.13 (dd, J_{AB} = 230.7 Hz, Δν = 15.81, 2F), -68.29 (s, 2F), -116.61 (dd, J_{AB} = 230.7 Hz, Δν =12.65, 2F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 128.3, 128.2, 126.6.5, 119.6 (m), 76.9, 76.8, 75.3, 35.3, 34.5, 28.2, 19.3, 19.2; FT-IR (neat): ν_{max} 2962, 2876, 2212, 1656, 1604, 1496, 1473, 1455, 1392, 1342, 1288, 1258, 1235, 1216, 1178, 1152, 1121, 1056, 1022, 949, 898, 788, 700 cm^{-1}; EIMS: (*m/z*, %): 424 (M^+ − OBu^i, 4.32), 362 (M^+ − C_2F_4Cl, 37.81), 314 (7.82), 240 (48.70), 91 (32.52), 77 (24.71), 57 (100.00); EIHRMS: *m/z* 497.0415 (M^+, $C_{18}H_{19}Cl_2F_6NO_2S$ requires 497.0418).

4t-major endo: pale yellow solid, mp 51－53 °C; 180.5 mg, 68%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38－7.19 (5H, m, ArH), 6.69 (1H, *J* = 3.0 Hz, =C*H*), 5.41 (1H, *J* = 2.4 Hz, NC*H*O), 5.26－5.10 (1H, m, $CO_2CH_2CH(CH_3)_2$), 3.68 (1H, d, *J* = 9.3 Hz, C*H*Ph), 3.43 (1H, dd, *J* = 9.6, 6.9 Hz, OC*H*HPr^i), 3.22 (1H, dd, *J* = 9.3, 6.0 Hz, OCH*H*Pr^i), 2.66 (1H, ddd, *J* = 15.0, 10.2, 3.6 Hz, CH_aH_e), 2.37 (1H, d, *J* = 15.0 Hz, CH_aH_e), 1.83－1.69 (1H, m, $OCH_2CH(CH_3)_2$), 1.32 (6H, d, *J* = 6.3 Hz, $OCH_2CH(CH_3)_2$), 0.83 (3H, d, *J* = 6.9 Hz, $OCH_2CH(CH_3)_2$), 0.81 (3H, d, *J* = 6.9 Hz, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -67.32 (dd, J_{AB} = 181.3 Hz, Δν = 0.38, 2F), -116.43 (dd, J_{AB} = 226.7 Hz, Δν =11.95, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 144.3, 130.8, 128.4, 126.8, 126.7, 74.9, 70.0, 36.7, 35.8, 28.2, 21.7, 21.6, 19.3, 19.2; FT-IR (KBr): ν_{max} 2960, 2874, 1716, 1640, 1493, 1468, 1455, 1390, 1377, 1286, 1245, 1220, 1173, 1088, 1057, 1024, 974, 896, 789, 768, 701 cm^{-1}; EIHRMS: *m/z* 456.0663 (M^+ − Pr^i, $C_{18}H_{19}ClF_4NO_4S$ requires 531.0870).

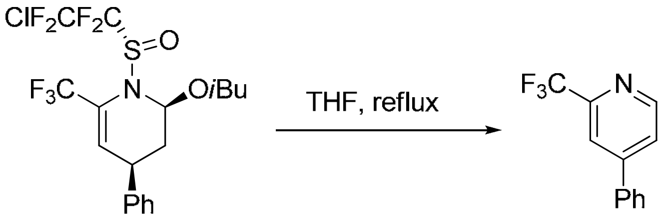
4v-major endo: white solid, mp 109－111 °C; 131.2 mg, 56.6%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 (1H, s, =C*H*), 7.37－7.21 (5H, m, ArH), 4.93 (1H, s, NC*H*O), 3.85 (1H, d, *J* = 7.2 Hz, C*H*Ph), 3.22 (1H, dd, *J* = 8.3, 6.5 Hz, OC*H*HPr^i), 2.86 (1H, dd, *J* = 8.3, 6.5 Hz, OCH*H*Pr^i), 2.53 (1H, ddd, *J* = 13.8, 2.7, 2.4 Hz, CH_aH_e), 2.26 (1H, ddd, *J* = 13.8, 7.2, 2.7 Hz, CH_aH_e), 0.93 (1H, m, $OCH_2CH(CH_3)_2$), 0.69 (3H, d, *J* = 6.9, $OCH_2CH(CH_3)_2$), 0.60

(3H, d, J = 6.9, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -67.37 (s, 2F), -116.58 (dd, J_{AB} = 230.7 Hz, Δν = 8.43, 2F); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.1, 133.2, 128.4, 127.8, 127.0, 118.1, 95.5, 83.8, 75.7, 37.2, 34.2, 28.2, 18.9, 18.8; FT-IR (KBr): ν_{max} 2960, 2874, 2212, 1631, 1449, 1386, 1365, 1268, 1142, 1105, 1058, 1012, 976, 894, 799, 747, 698 cm^{-1}; Anal. Calcd. for $C_{18}H_{19}ClF_4N_2O_2S$: C, 49.26; H, 4.36; N, 6.38. Found: C, 49.39; H, 4.63; N, 6.19.

4v-minor endo: colorless oil, 42.8 mg, 19.5%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.39－7.15 (6H, m, ArH, =C*H*), 5.15 (1H, t, J = 3.3 Hz, NC*H*O), 3.82 (1H, dd, J = 6.6, 3.6 Hz, C*H*Ph), 3.20 (1H, dd, J = 8.4, 6.5 Hz, OC*H*HPr^i), 2.92 (1H, dd, J = 8.4, 6.5 Hz, OCH*H*Pr^i), 2.54 (1H, dt, J = 13.8, 3.9 Hz, CH_aH_e), 2.27 (1H, ddd, J = 13.8, 7.2, 2.7 Hz, CH_aH_e), 1.48 (1H, m, $OCH_2CH(CH_3)_2$), 0.66 (3H, d, J = 6.3, $OCH_2CH(CH_3)_2$), 0.58 (3H, d, J = 6.3, $OCH_2CH(CH_3)_2$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -68.07 (m, 2F), -115.25 (dd, J_{AB} = 222.4 Hz, Δν =11.73, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 135.7, 128.5, 127.6, 127.1, 118.1, 94.9, 83.1, 76.1, 37.6, 34.8, 28.1, 18.8; EIMS (*m/z*, %): 438 (M^+, 1.15), 365 (5.58), 303 (49.82), 229 (43.02), 203 (46.96), 181 (50.13), 140 (64.96), 57 (100.00); EIHRMS: *m/z* 438.0801 (M^+, $C_{18}H_{19}ClF_4N_2O_2S$ requires 438.0792).

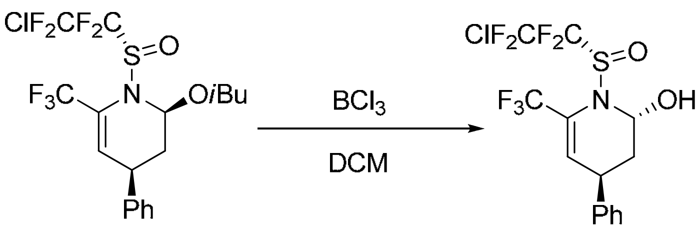
(S_s, 2*S*, 4*R*)-6-major endo: $[\alpha]_D^{28}$ = +131.8° ($CHCl_3$, *c* 1.0); Enantiomeric excess: > 99.9%, HPLC (OD column) 0.7 mL/min (n-hexane/isopropanol = 98/2): t_R 8.0 (minor), t_R 8.8 (major).

Transformations of Cycloadduct.



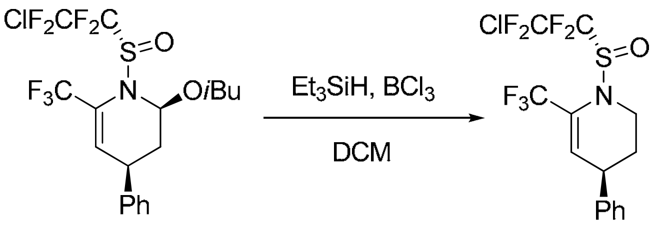
(S_s, 2*S*, 4*R*)-**6** **7**

Compound (S_s, 2*S*, 4*R*)-**6** (70 mg, 0.15 mmol) was dissolved in THF (2 mL) and the mixture was refluxed overnight. After removal of the solvent, the residue was purified by column chromatography to give product **7** as a colorless oil (17.4 mg, 52% yield); ^1H NMR (300 MHz, $CDCl_3$): δ 8.77 (1H, d, J = 5.1 Hz), 7.90 (1H, s), 7.71－7.63 (3H, m), 7.57－7.45 (3H, m); ^{19}F NMR (282 MHz, $CDCl_3$): δ -67.97 (s, 3F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.1, 136.5, 129.5, 129.0, 126.7, 123.8, 121.7, 120.6 (q, J_{AB} = 271.4 Hz), 118.1 (m); FT-IR (neat): ν_{max} 2956, 2926, 2854, 1693, 1606, 1460, 1378, 1336, 1261, 1183, 1149, 1089, 1023, 803, 762, 697 cm^{-1}; LRMS (ESI): *m/z* 224.0 (M^++1); EIHRMS: *m/z* 223.0607 (M^+, $C_{12}H_8F_3N$ requires 223.0609).



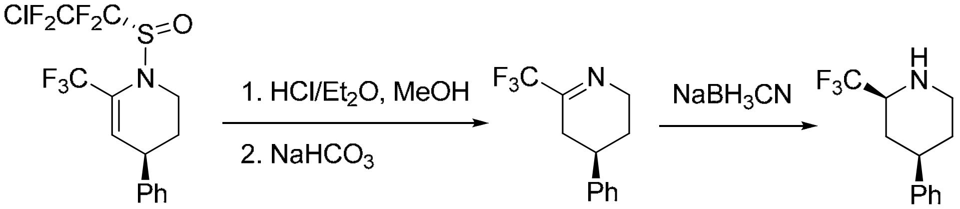
(S_s, 2*S*, 4*R*)-**6** **8**

To a solution of compound (S_s, 2*S*, 4*R*)-**6** (0.1 mmol) in CH_2Cl_2 (1 mL), was added BCl_3 (dissolved in CH_2Cl_2, 0.1 mmol) at 0 °C. The mixture was stirred at that temperature for 1 h and then quenched with 5 mL saturated aqueous NH_4Cl solution. The resulted mixture was extracted with CH_2Cl_2 (5 mL × 3). The combined organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography to afford **8** as a white solid (24.7 mg, 58% yield); mp 114—115 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40—7.18 (5H, m, ArH), 6.22 (1H, s, =C*H*), 5.93(1H, s, NC*H*(OH)), 3.86 (1H, m, C*H*Ph), 2.67 (1H, s, NCH(O*H*)), 2.43 (1H, dddd, *J* = 13.8, 6.6, 2.7, 1.2 Hz, C$H_a$$H_e$), 1.84 (1H, t, *J* = 13.8 Hz, $CH_a$$H_e$); ^{19}F NMR (282 MHz, $CDCl_3$): δ -65.22 (s, 3F), -68.38 (s, 2F), -114.53 (dd, J_{AB} = 222.5 Hz, Δν =14.75, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 129.1, 127.6, 127.5, 122.6 (m), 120.6 (q, J_{AB} = 271.6 Hz), 77.3, 73.7, 36.8, 34.4; FT-IR (KBr): ν_{max} 3421, 1662, 1495, 1455, 1395, 1303, 1207, 1183, 1153, 1126, 1105, 1053, 811, 701 cm^{-1}; EIMS (*m/z*, %): 290 (M^+ − C_2F_4Cl, 40.89), 242 (5.94), 224 (32.52), 183 (100.00), 77 (24.89); EIHRMS: *m/z* 425.0089 (M^+, $C_{14}H_{11}ClF_7NO_2S$ requires 425.0087); $[\alpha]_D^{27}$ = +53.6° ($CHCl_3$, *c* 1.0).



(S_s, 2*S*, 4*R*)-**6** **9**

To a solution of compound (S_s, 2*S*, 4*R*)-**6** (0.3 mmol) and Et_3SiH (0.9 mmol) in CH_2Cl_2 (3 mL), was added BCl_3 (dissolved in CH_2Cl_2, 0.9 mmol) at 0 °C. The mixture was stirred at room temperature for 2 h and then quenched with saturated aqueous NH_4Cl solution. The resulted mixture was extracted with CH_2Cl_2 (6 mL × 3). The combined organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography to afford **9** as a colorless oil (78.2 mg, 65% yield); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40—7.17 (5H, m, ArH), 6.06 (1H, d, *J* = 2.4 Hz, =C*H*), 4.04 (1H, d, *J* = 13.2 Hz), 3.71—3.60 (1H, m, C*H*Ph), 3.50 (1H, t, *J* = 11.7 Hz), 2.34—2.23 (1H, m), 1.98—1.56 (1H, m); ^{19}F NMR (282 MHz, $CDCl_3$): δ -64.97 (s, 3F), -68.58 (s, 2F), -114.84 (dd, J_{AB} = 222.5 Hz, Δν =10.73, 2F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.7, 128.9, 127.4, 127.3, 120.4 (q, J_{AB} = 271.8 Hz), 119.7 (dd, J_{AB} = 5.3 Hz, Δν = 0.05), 39.9, 38.7, 31.0; FT-IR (neat): ν_{max} 2937, 2871, 1656, 1494, 1454, 1390, 1347, 1294, 1263, 1183 (b), 1135 (b), 1059, 1015, 967, 793, 701, 642 cm^{-1}; EIMS (*m/z*, %): 274 (M^+ − C_2F_4Cl, 100.00), 226 (19.36), 224 (34.83), 183 (32.45), 91 (26.73), 77 (10.95); EIHRMS: *m/z* 409.0132 (M^+, $C_{14}H_{11}ClF_7NOS$ requires 409.0138); $[\alpha]_D^{25}$ = +117.0° ($CHCl_3$, *c* 1.0).



9 **10** **11**

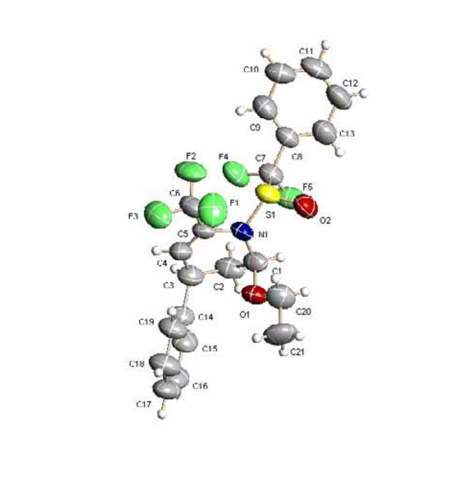
To a solution of compound **9** (0.3 mmol) in MeOH (5 mL) was added HCl/Et_2O (1M, 5 mL), and the mixture was stirred at 50 °C for 1h. The reaction mixture was then evaporated. The residue was dissolved in CH_2Cl_2, and washed with saturated aqueous $NaHCO_3$ solution. The organic phase was dried and concentrated to give imine **10** without further purification.

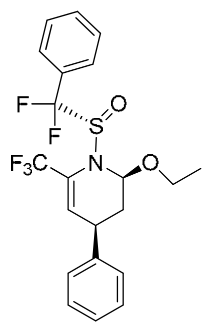
The above imine was dissolved in MeOH (3 mL), $NaBH_3CN$ (0.75 mmol) and a few drops of glacial AcOH was added at 0 °C. The resulting mixture was stirred at room temperature for 2h. Then the reaction mixture was concentrated and CH_2Cl_2 (5 mL) was added. The organic phase was washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography to afford **11** as a colorless oil[4] (48.9 mg, 71% total yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36－7.28 (2H, m, ArH), 7.27－7.19 (3H, m, ArH), 3.36－3.22 (2H, m, H-2 and H-6), 2.82 (1H, td, J = 12.4, 2.5 Hz, H-6), 2.65 (1H, tt, J = 12.4, 3.2 Hz, H-4), 2.05 (1H, d, J = 12.4 Hz, H-3), 1.86 (1H, d, J = 12.4 Hz, H-5), 1.76 (1H, s, NH), 1.67 (1H, qd, J = 12.4, 4.0 Hz, H-3), 1.64 (1H, q, J = 12.4 Hz, H-5); ^{19}F NMR (282 MHz, $CDCl_3$): δ -77.73 (s, 3F); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.0, 128.6, 126.7, 126.6, 125.6 (q, J_{AB} = 273.6 Hz), 58.4 (q, J_{AB} = 28.6 Hz),, 46.1, 41.6, 33.1, 32.3; FT-IR (neat): ν_{max} 3335, 2929, 2848, 1603, 1494, 1453, 1395, 1373, 1270, 1230, 1176, 1147, 1129, 1100, 814, 759, 263.78 in^{-1}; EIMS (m/z, %): 230 (M^+ + H, 8.76), 229 (M^+, 58.07), 160 (100.00), 104 (20.37), 91 (20.09), 77 (14.85), 56 (71.78); EIHRMS: m/z 229.1079 (M^+, $C_{12}H_{14}F_3N$ requires 229.1078); $[\alpha]_D^{23}$ = -6.5° (MeOH, c 1.4); Enantiomeric excess: 98 %, HPLC (Lux 5μ Cellulose-2 column) 0.3 mL/min (n-hexane/isopropanol = 99/1): t_R 18.3 (minor), t_R 19.4 (major).

Determination of the Stereochemistry of the Products

a) Stereochemistry *endo*

It is well-known that the Diels-Alder reaction of N-sulfinyl-1-aza-1,3-dienes takes place with very high *endo*-selectivity[5]. We have confirmed this stereochemistry by X-ray diffraction analysis of **4c** (see below). The data of X-ray structure of **4c** are found at the end of the Supporting Information.

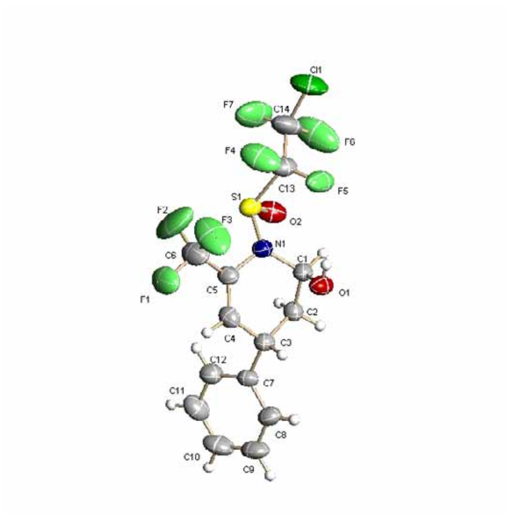


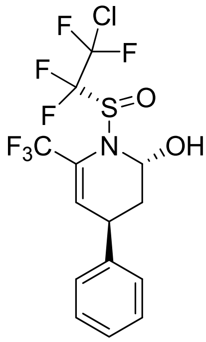


4c

b) Relative Stereochemistry of Product **8**

The Lewis acid-promoted nucleophilic replacement of the alkoxy group is known to proceed with inversion of configuration[5c, 5d]. We have confirmed this stereochemistry by X-ray diffraction analysis of (±)-**7** (see below). Data of X-ray structure of (±)-**7** are found at the end of the Supporting Information.

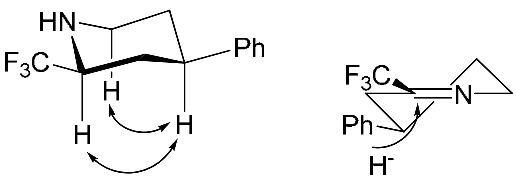




8

c) Relative Stereochemistry of Product **11**

The relative stereochemistry of **11** has been established by NMR. ^{1}H NMR experiments allowed proton assignment, while the 2D-NOESY experiments were decisive for the determination of relative stereochemistry. Some critical NOE contacts are shown in the Figure below. On the other hand, the relative stereochemistry is in agreement with the anticipated[6] axial addition of hydride to the specific half-chaired imine intermediate **10**.



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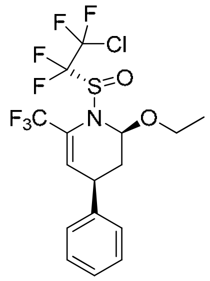
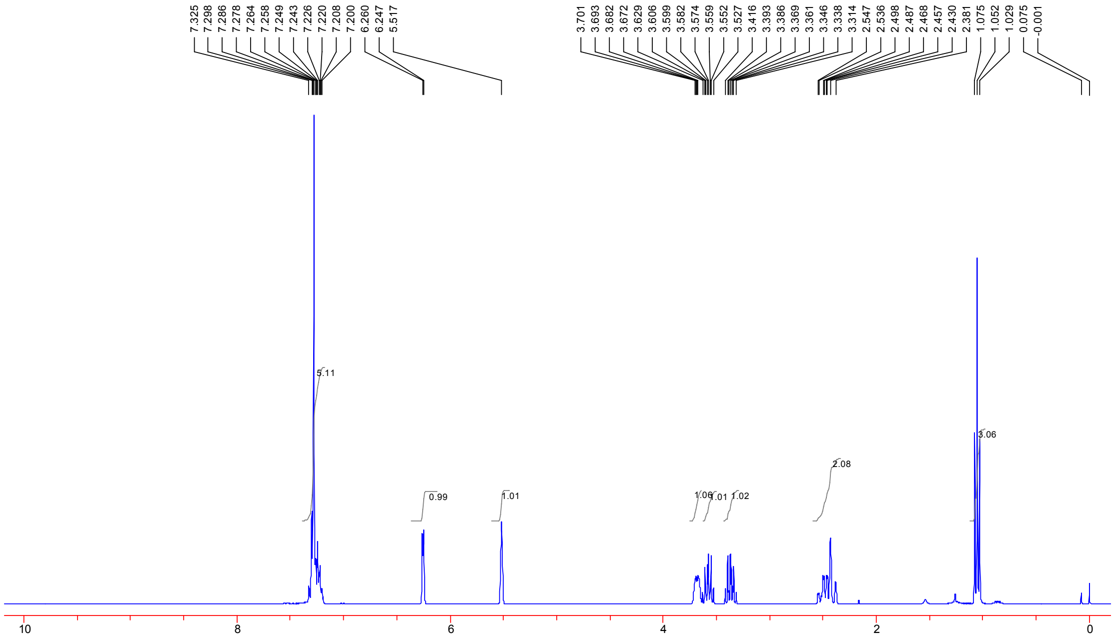
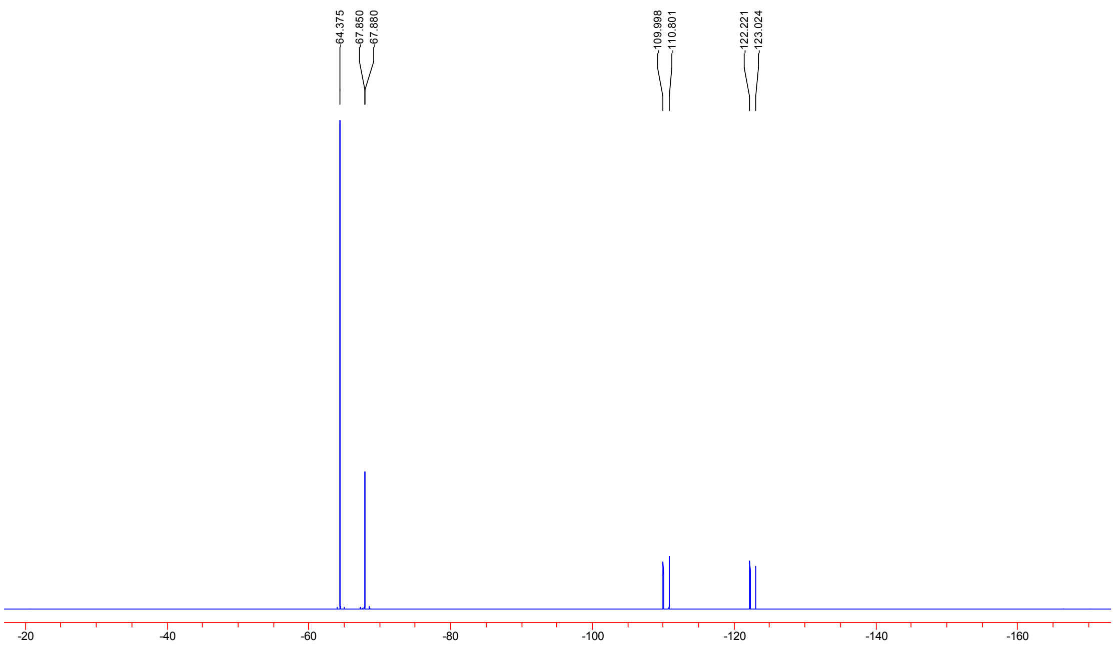
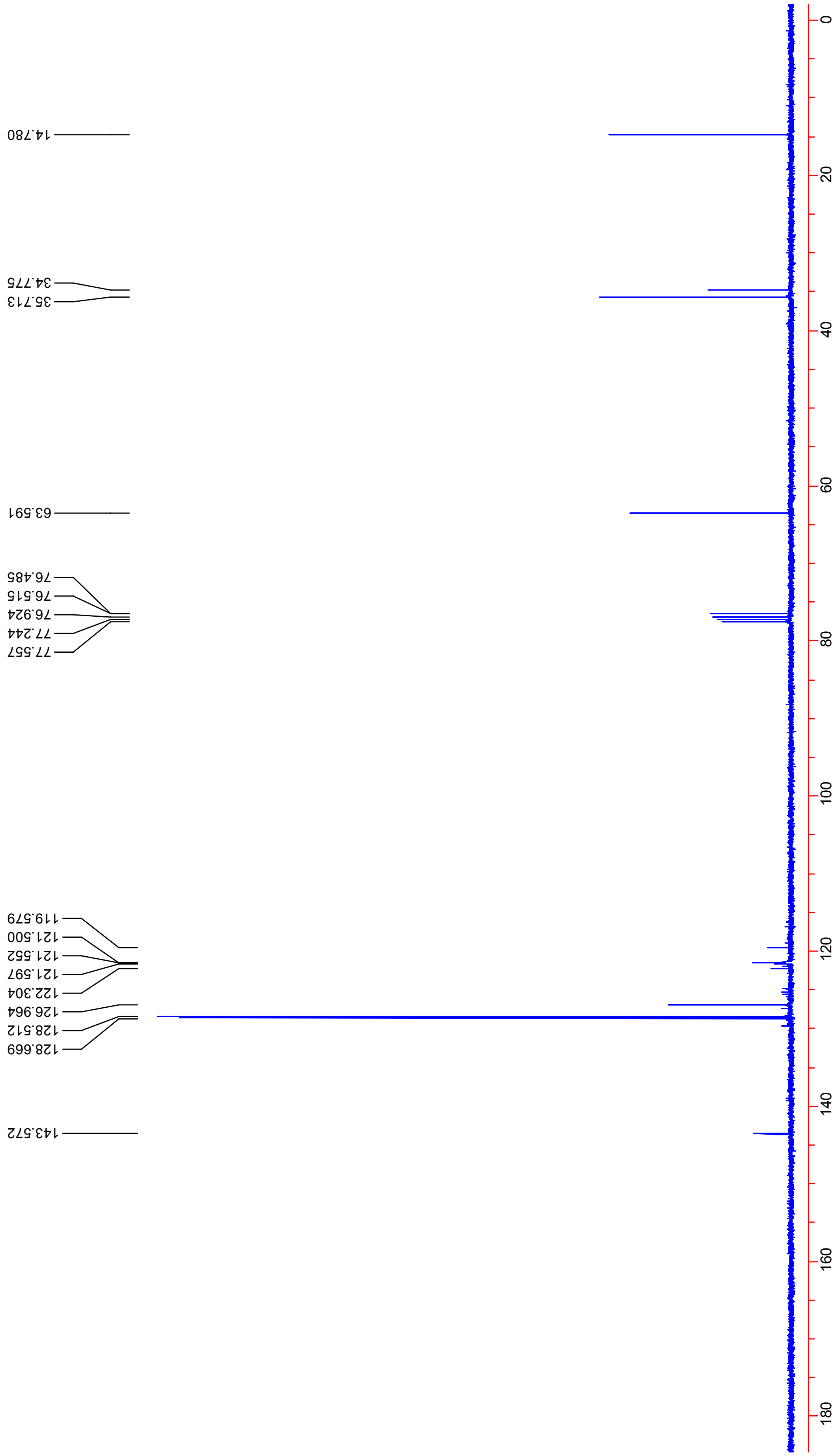
NMR Spectra



4a–major endo



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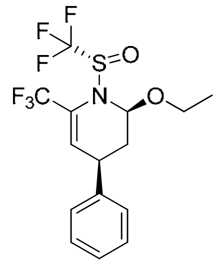
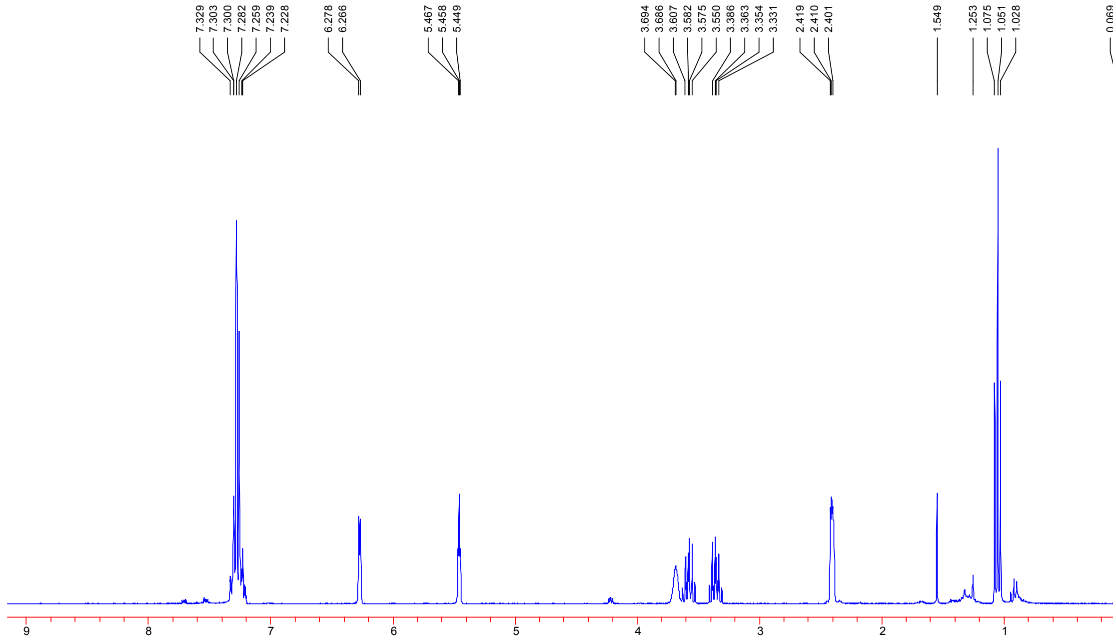
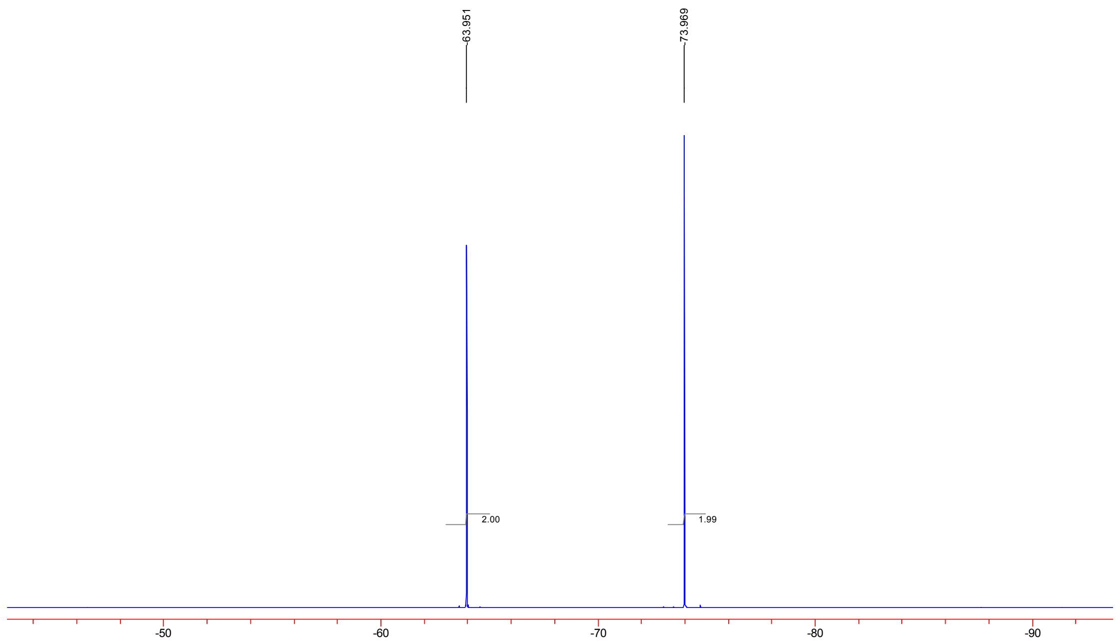
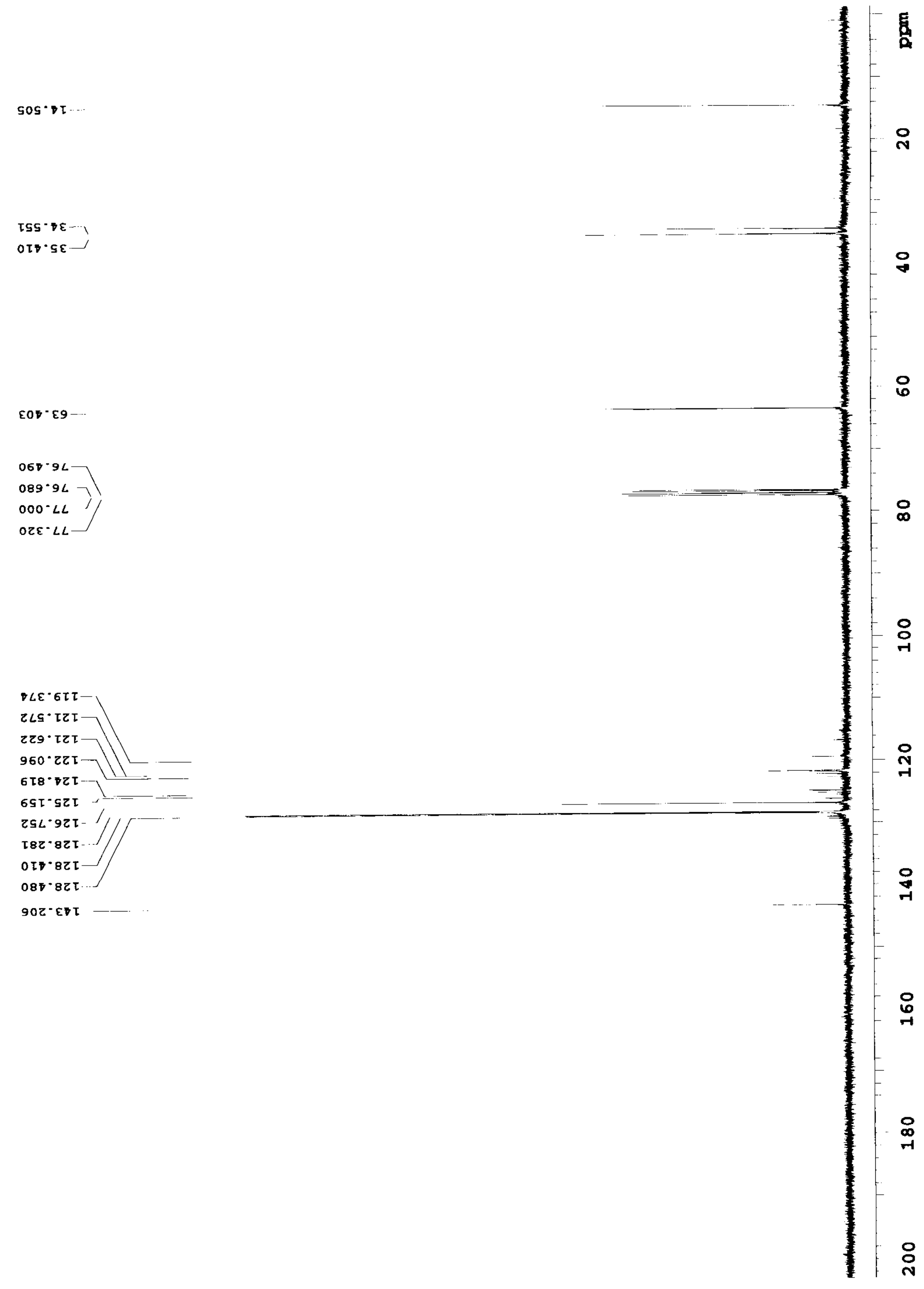


4b–major endo



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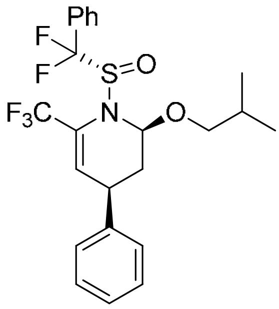
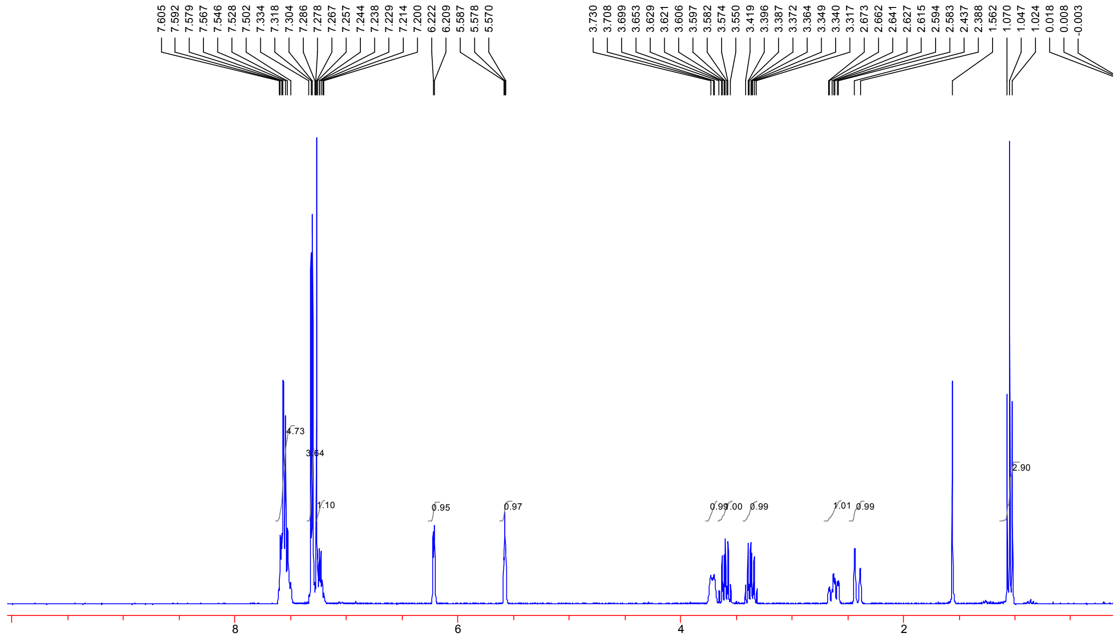
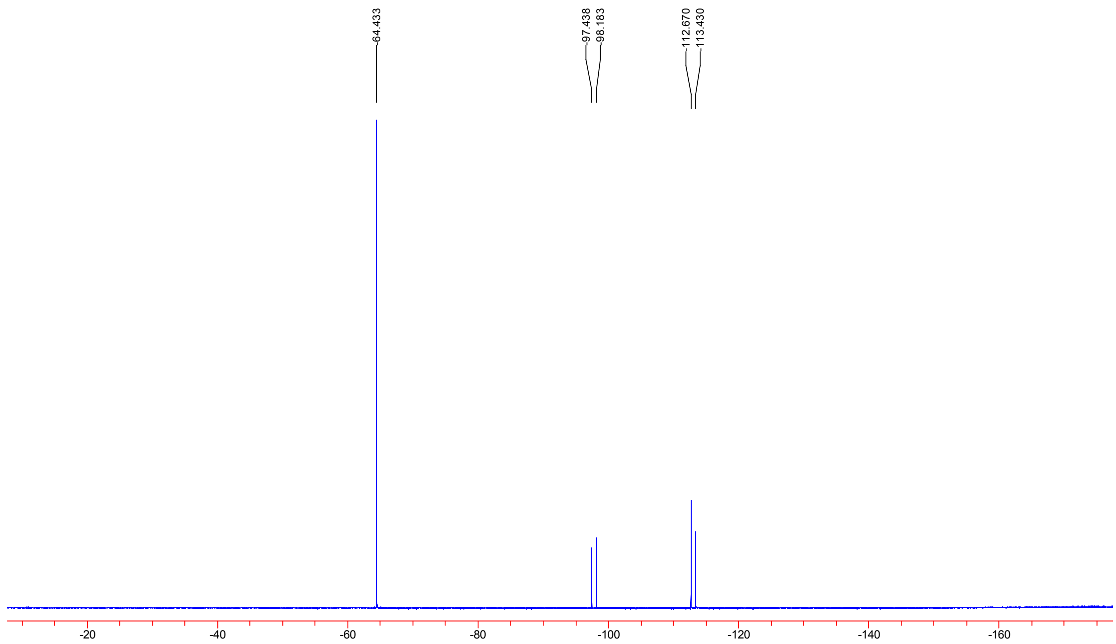
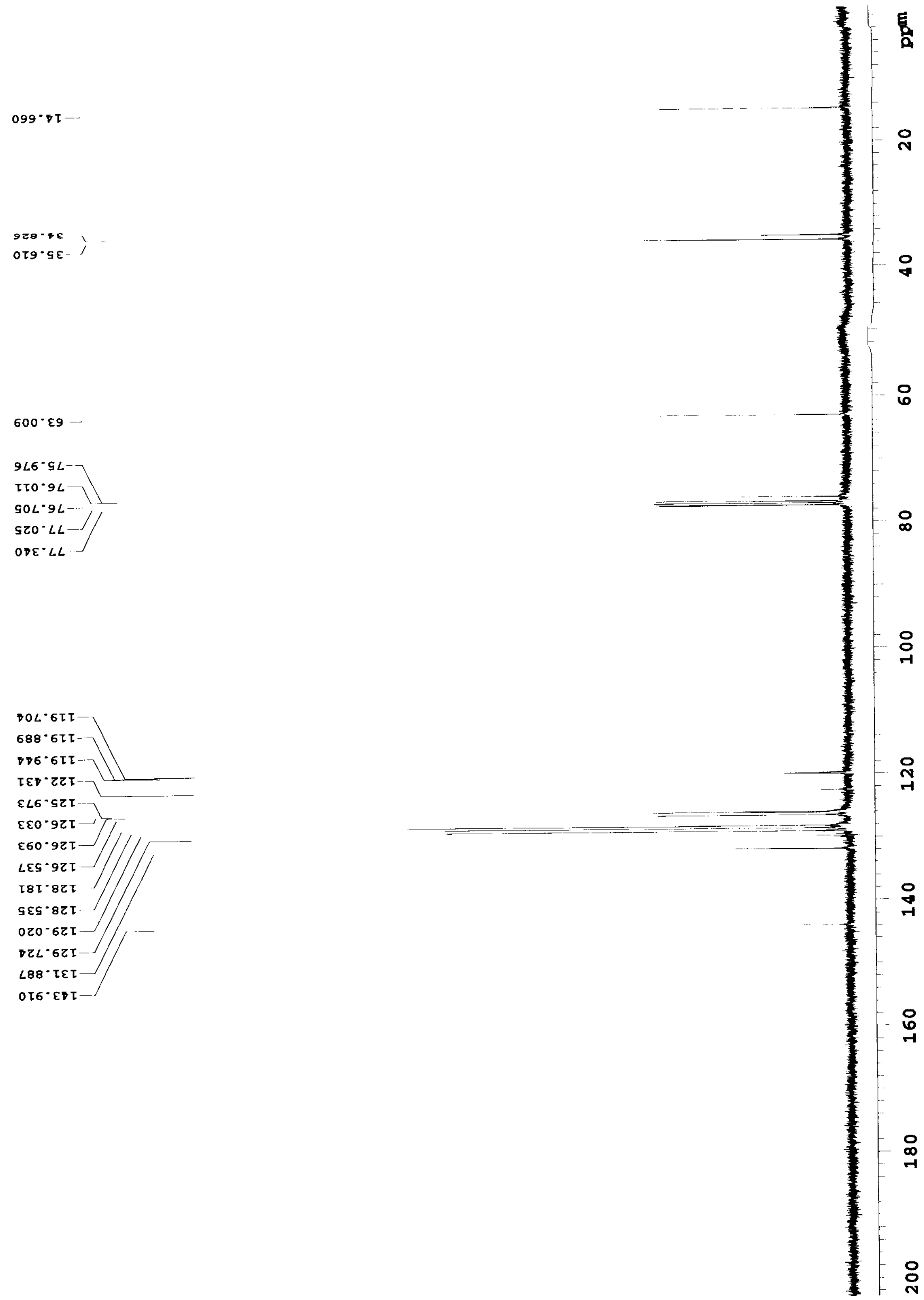


4c–major endo



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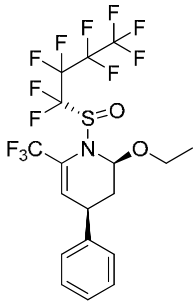

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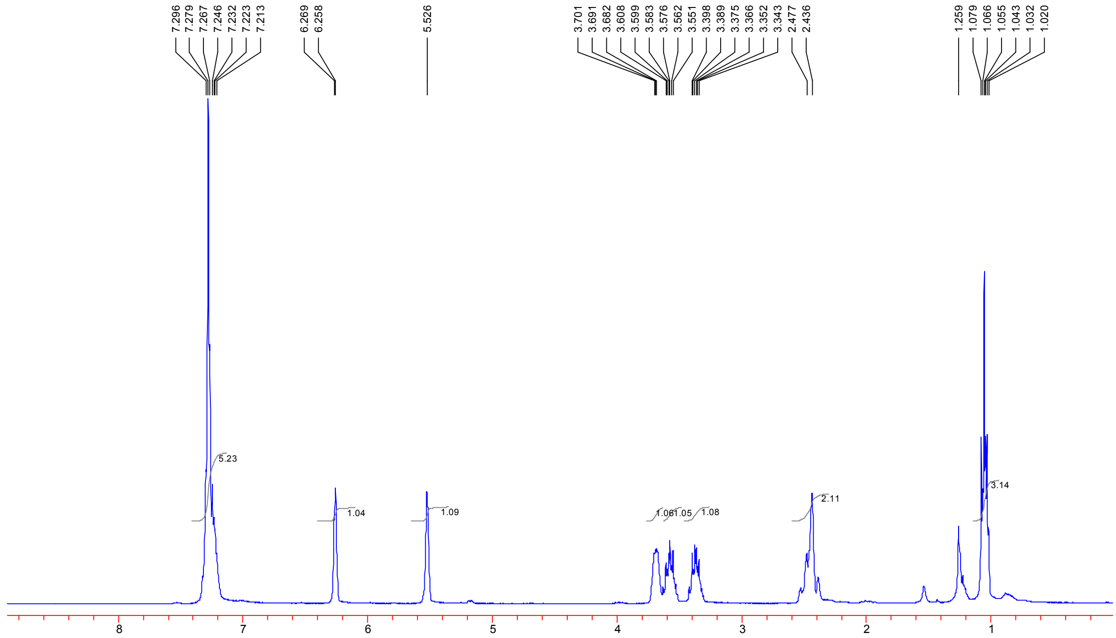

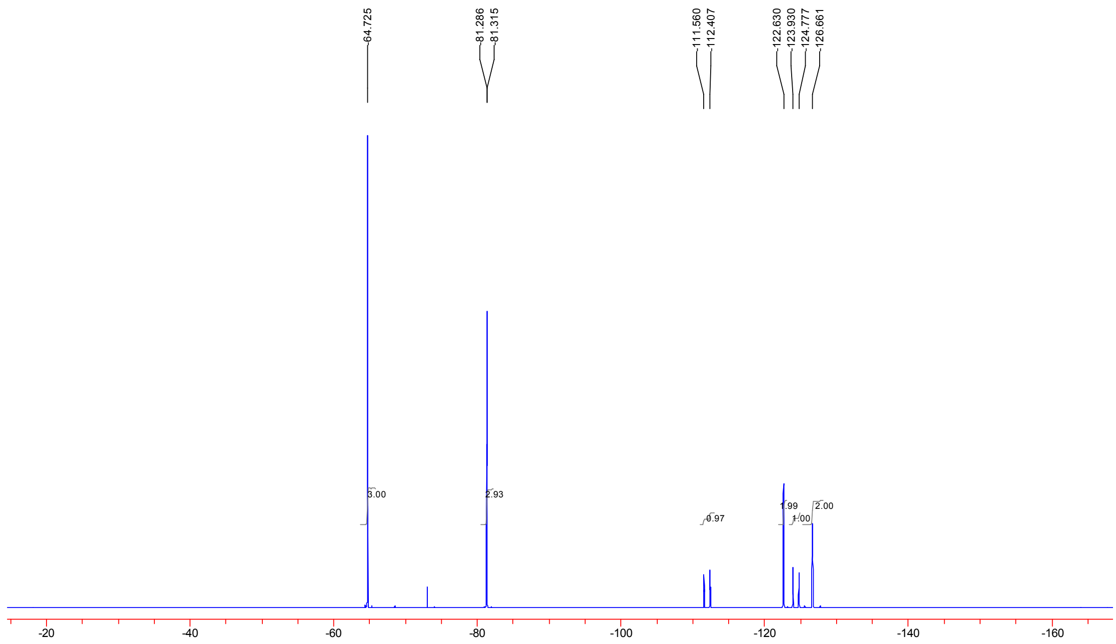

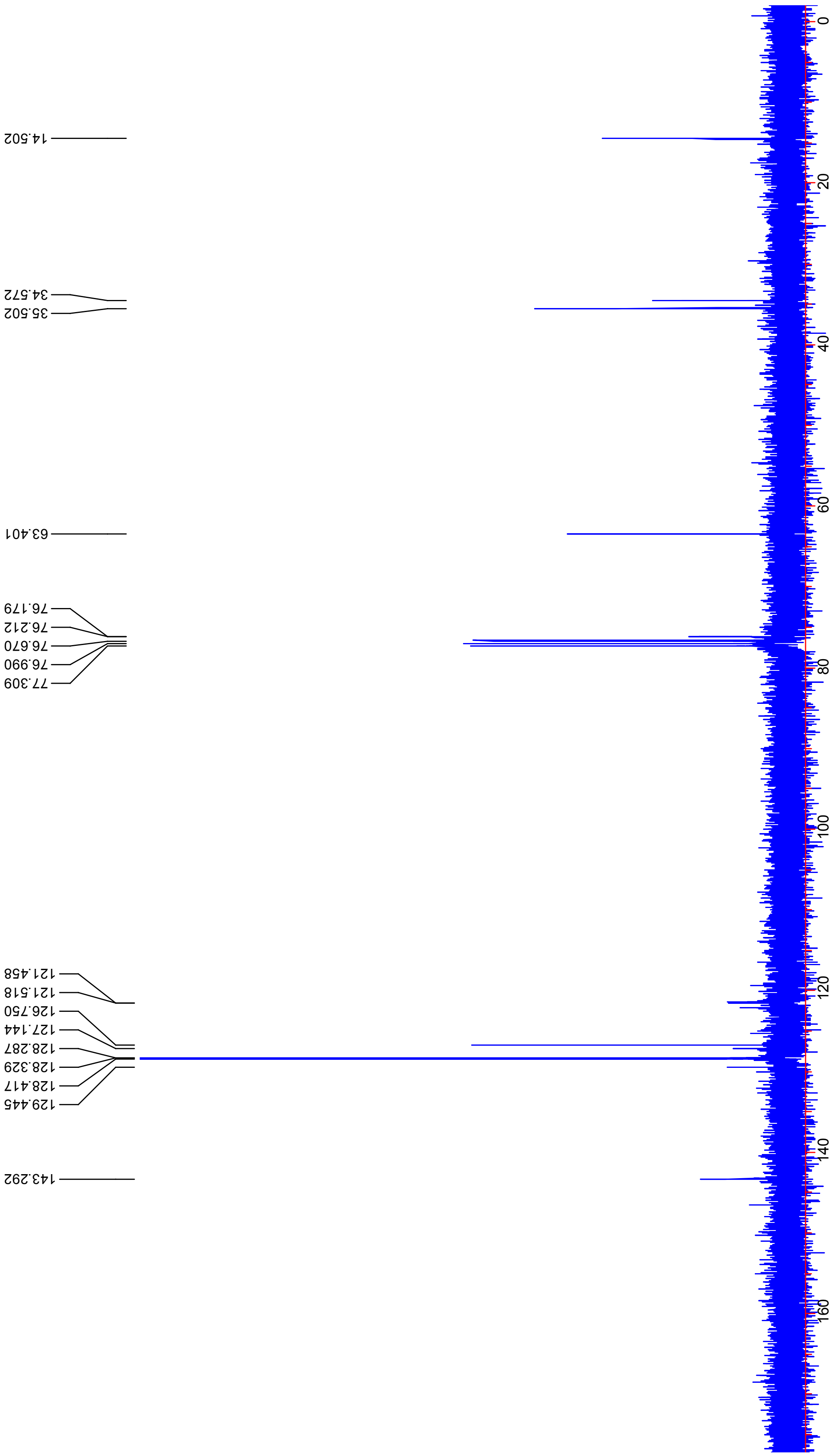
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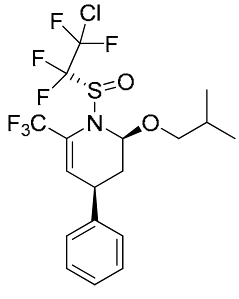
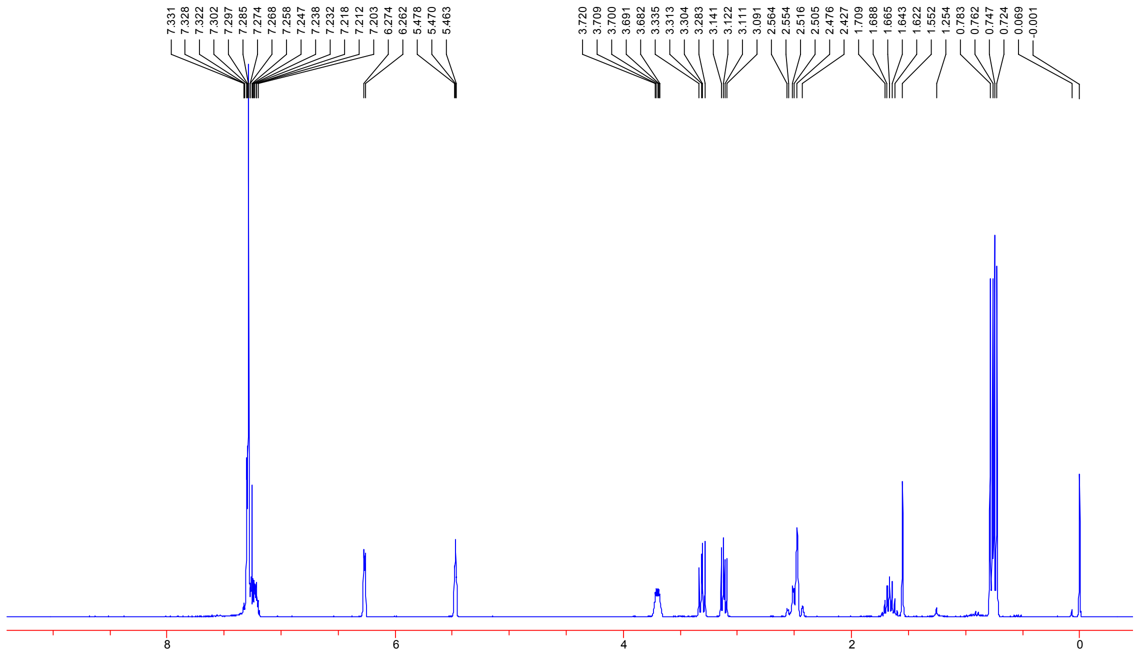
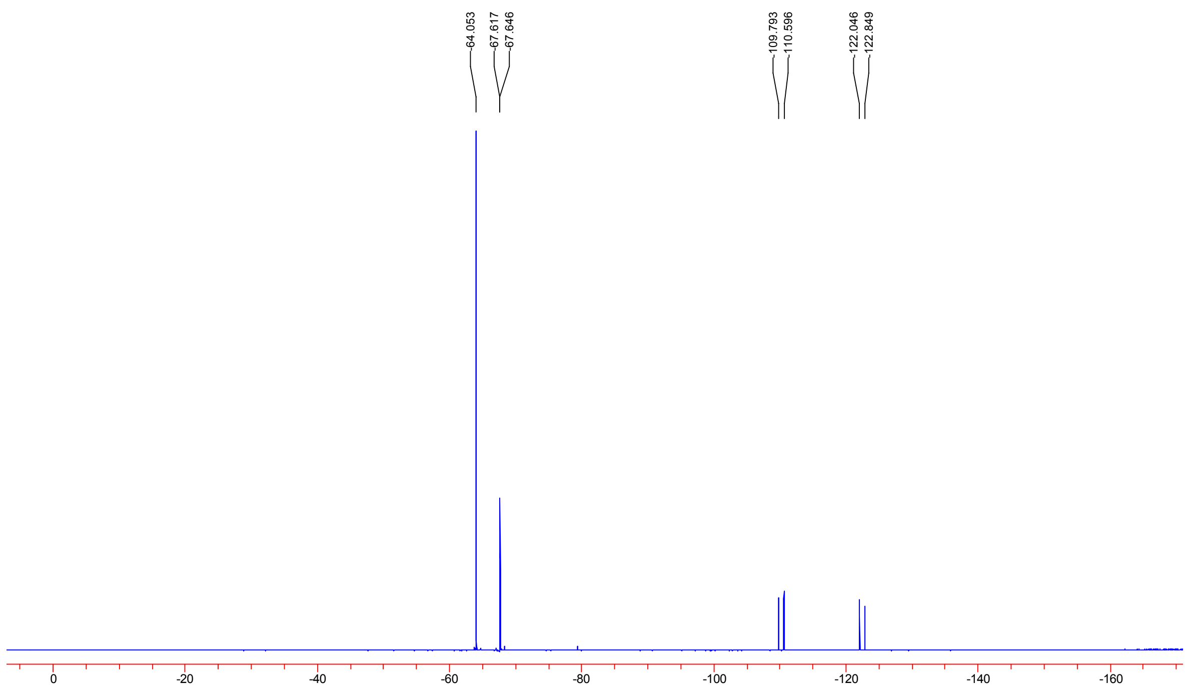
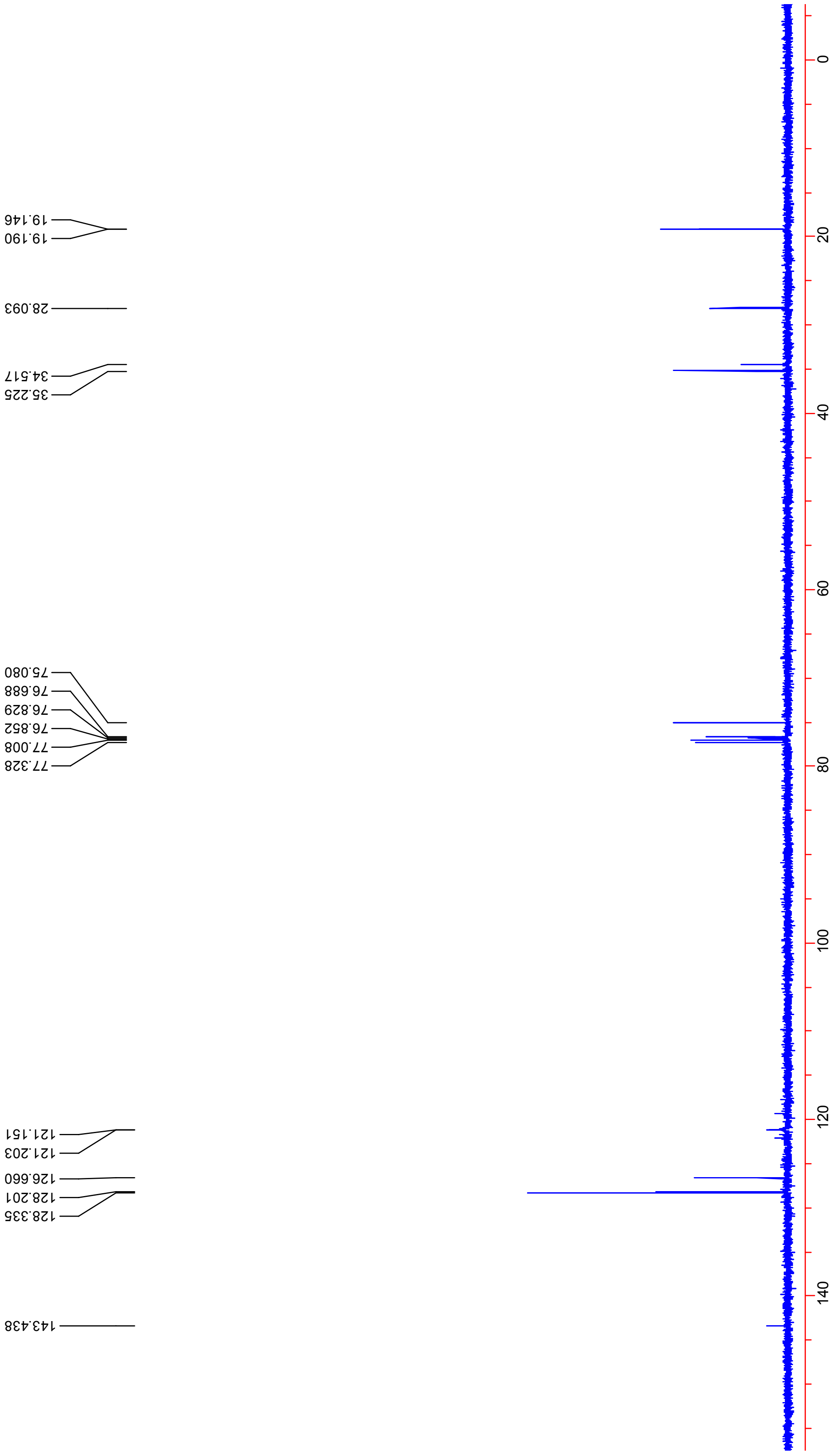


4e–major endo



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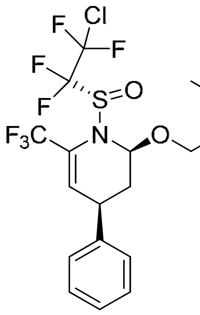
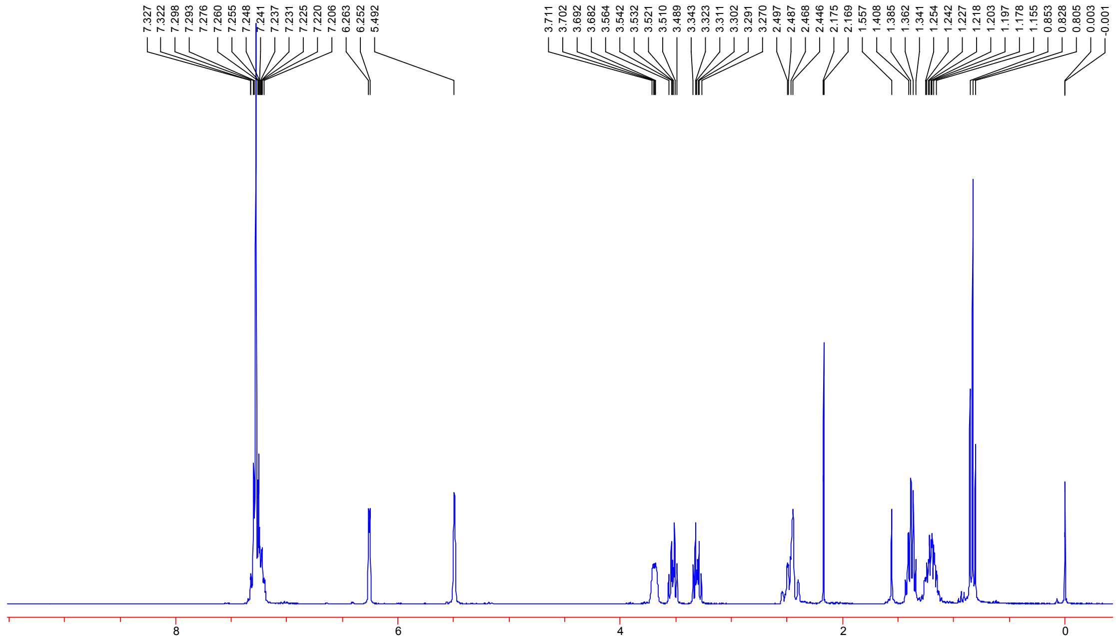
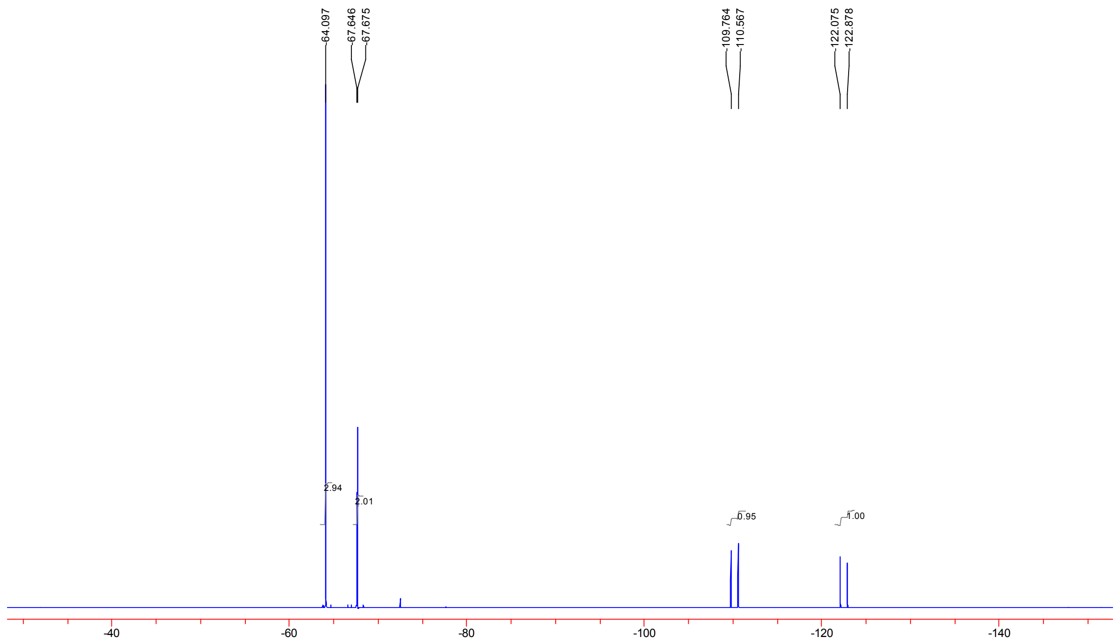
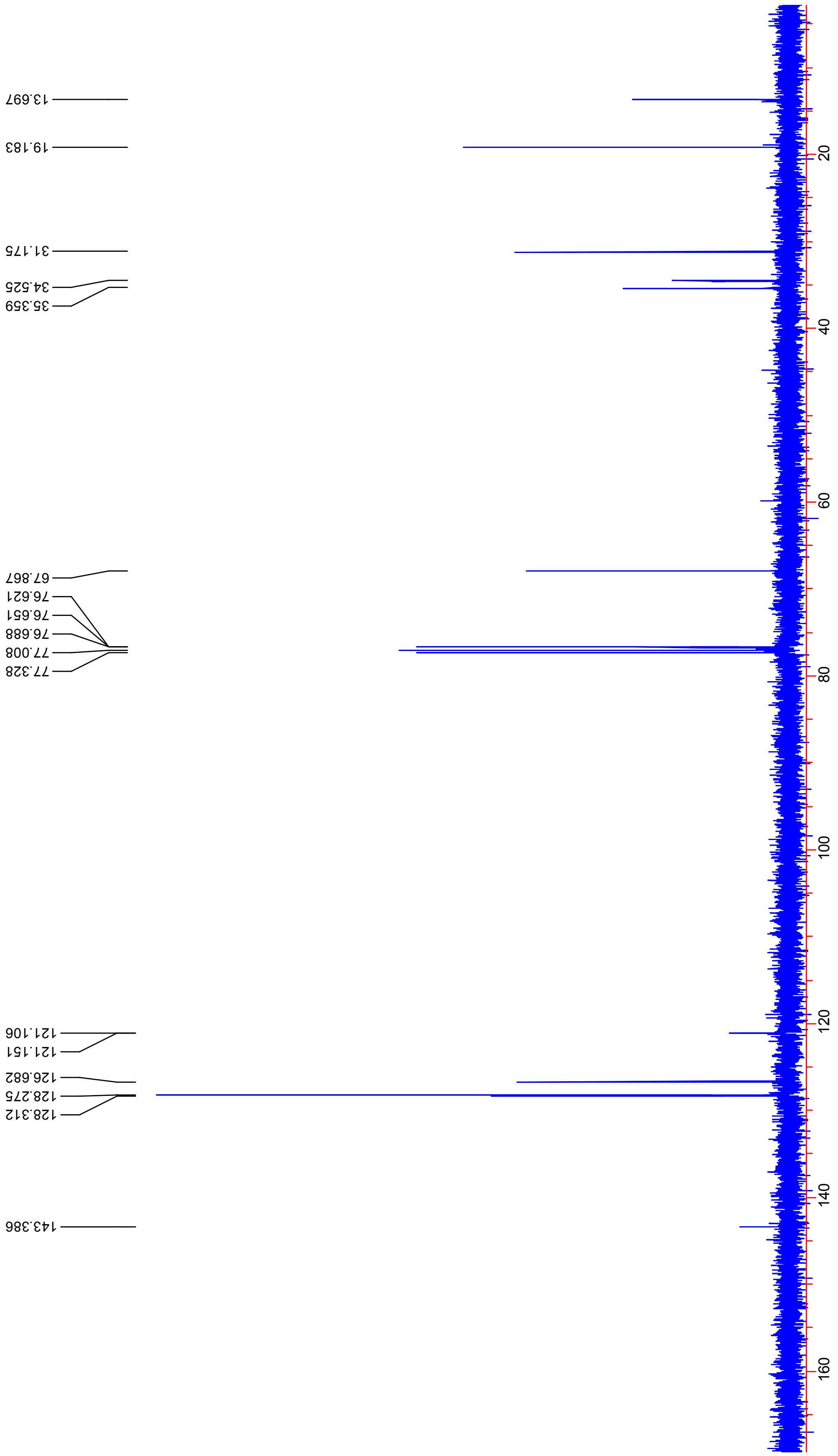


4f– major endo



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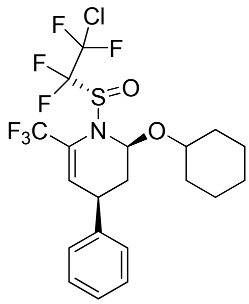
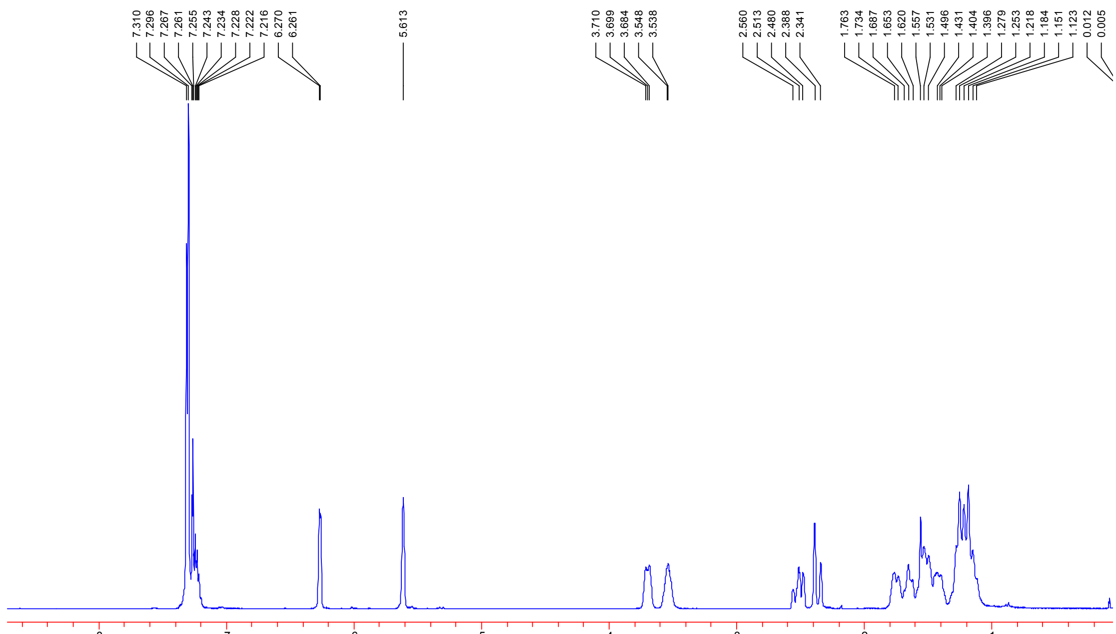
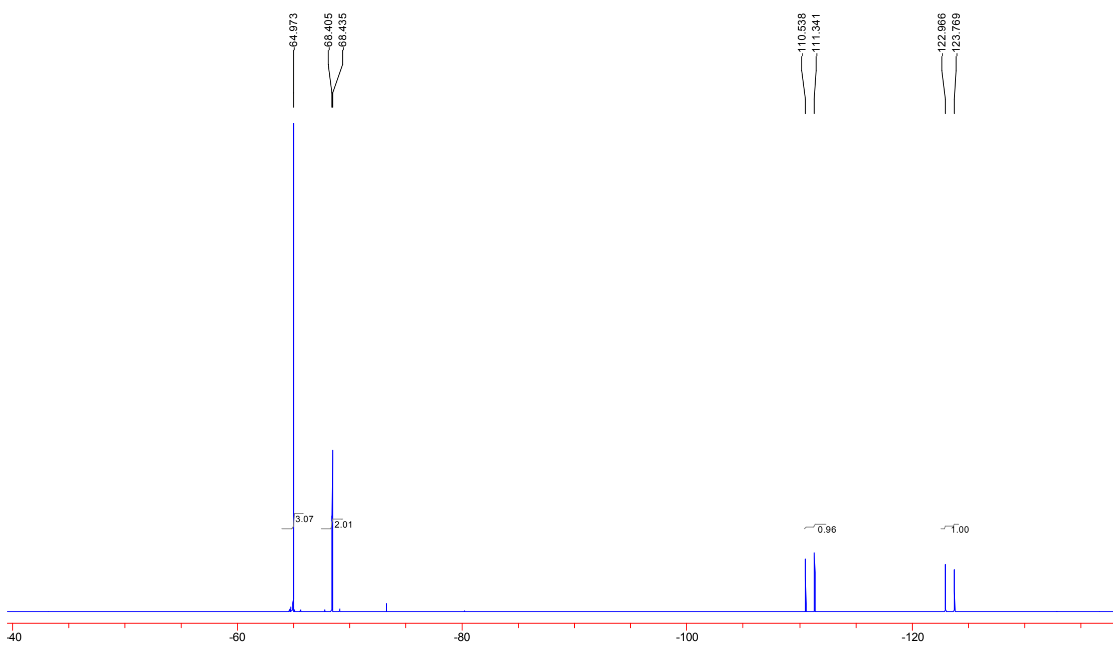
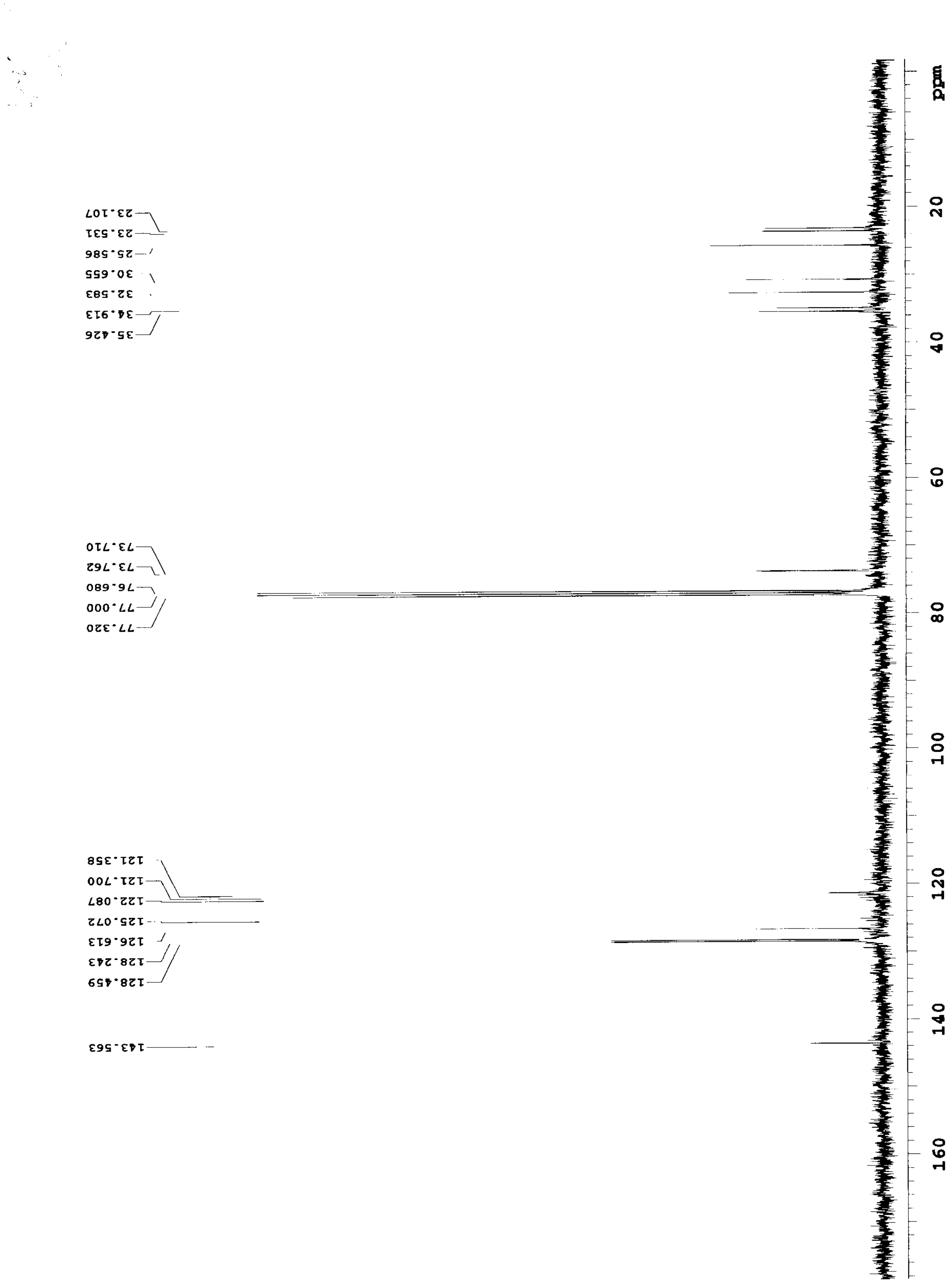


4g– major endo



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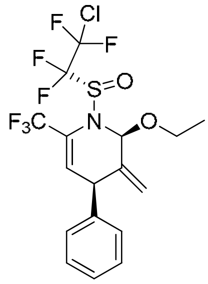
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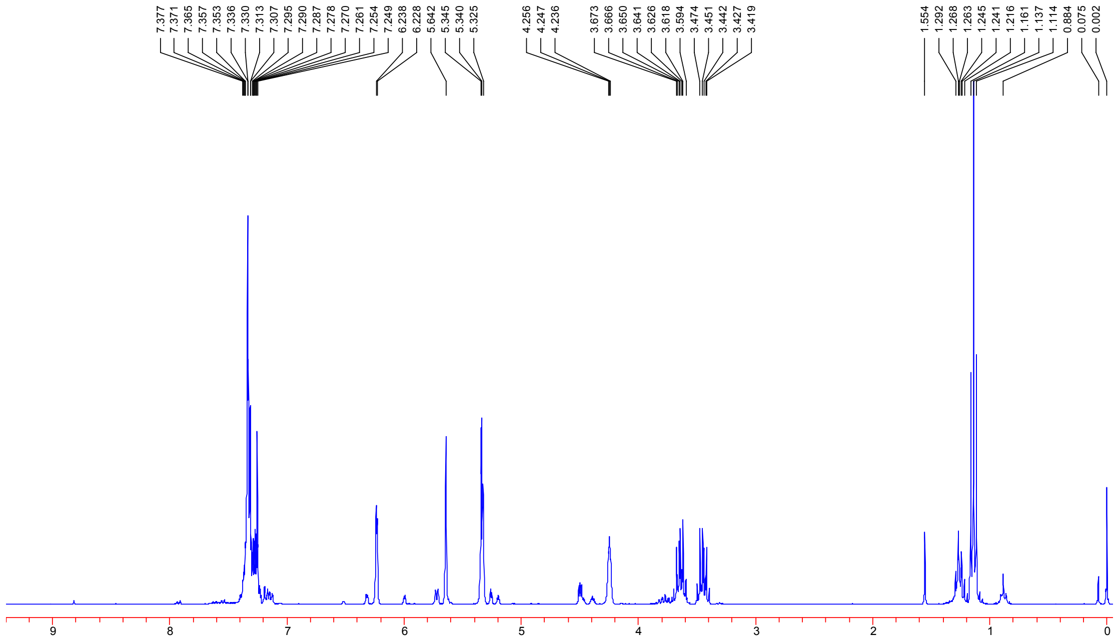
N
O

4h– endo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9
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5
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3
2
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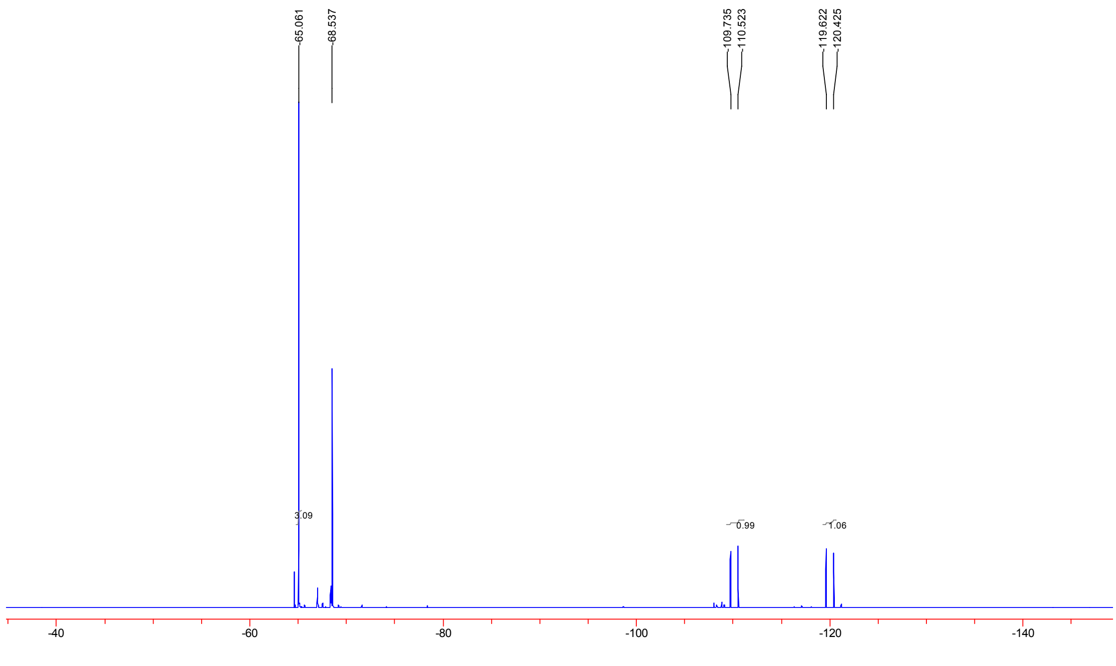
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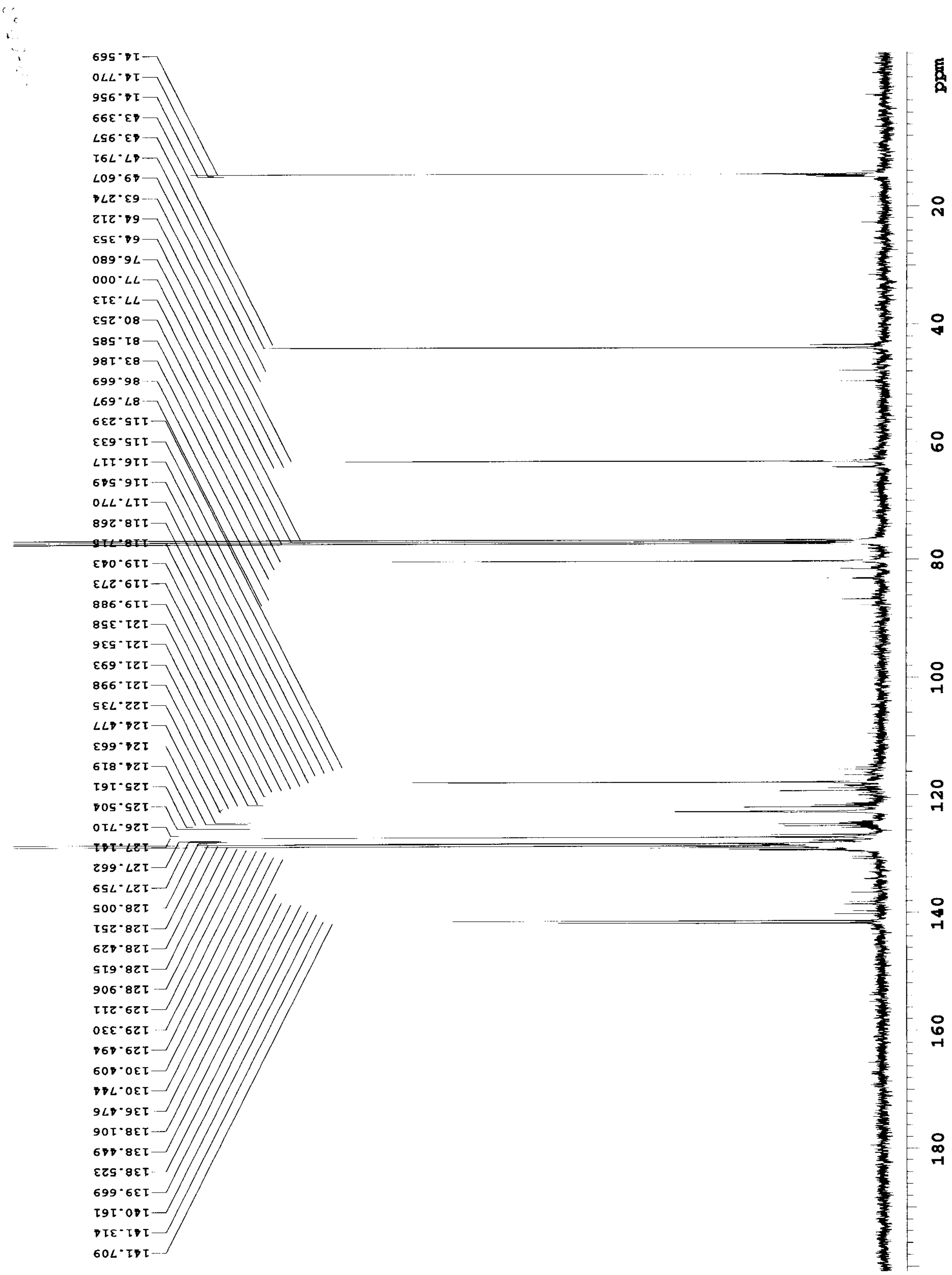
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77.313
80.253
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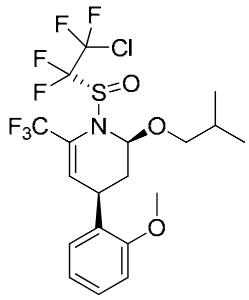
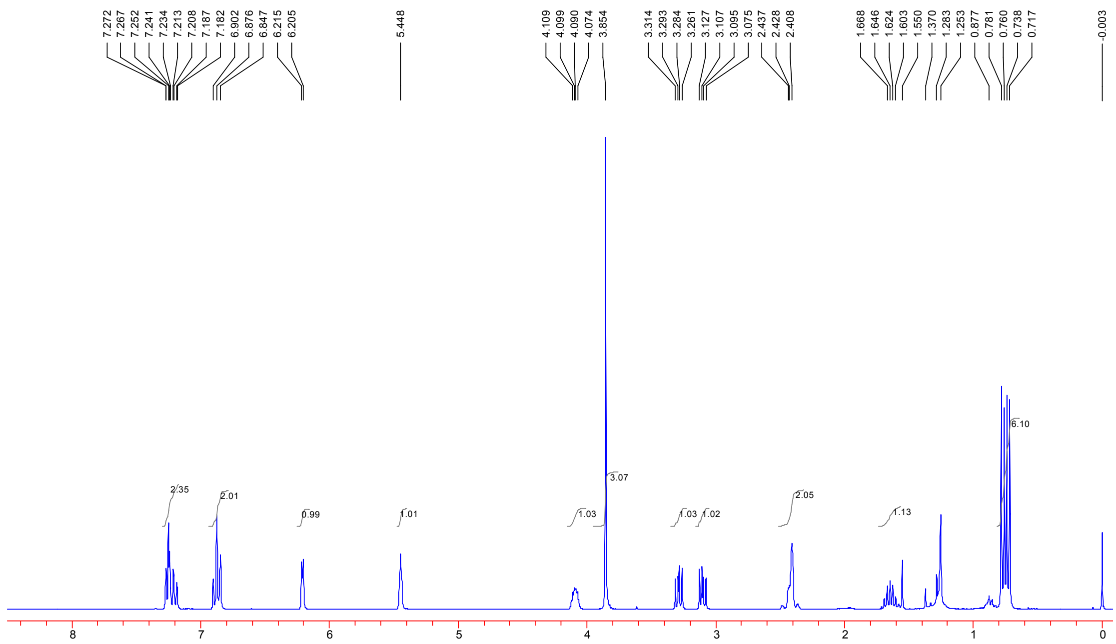
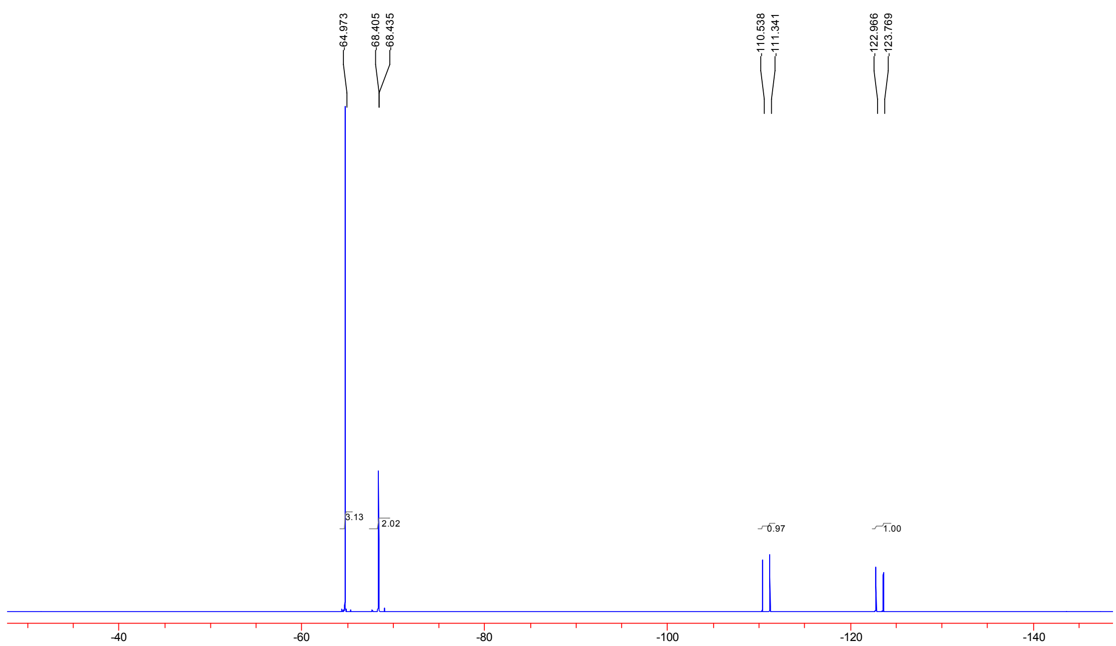
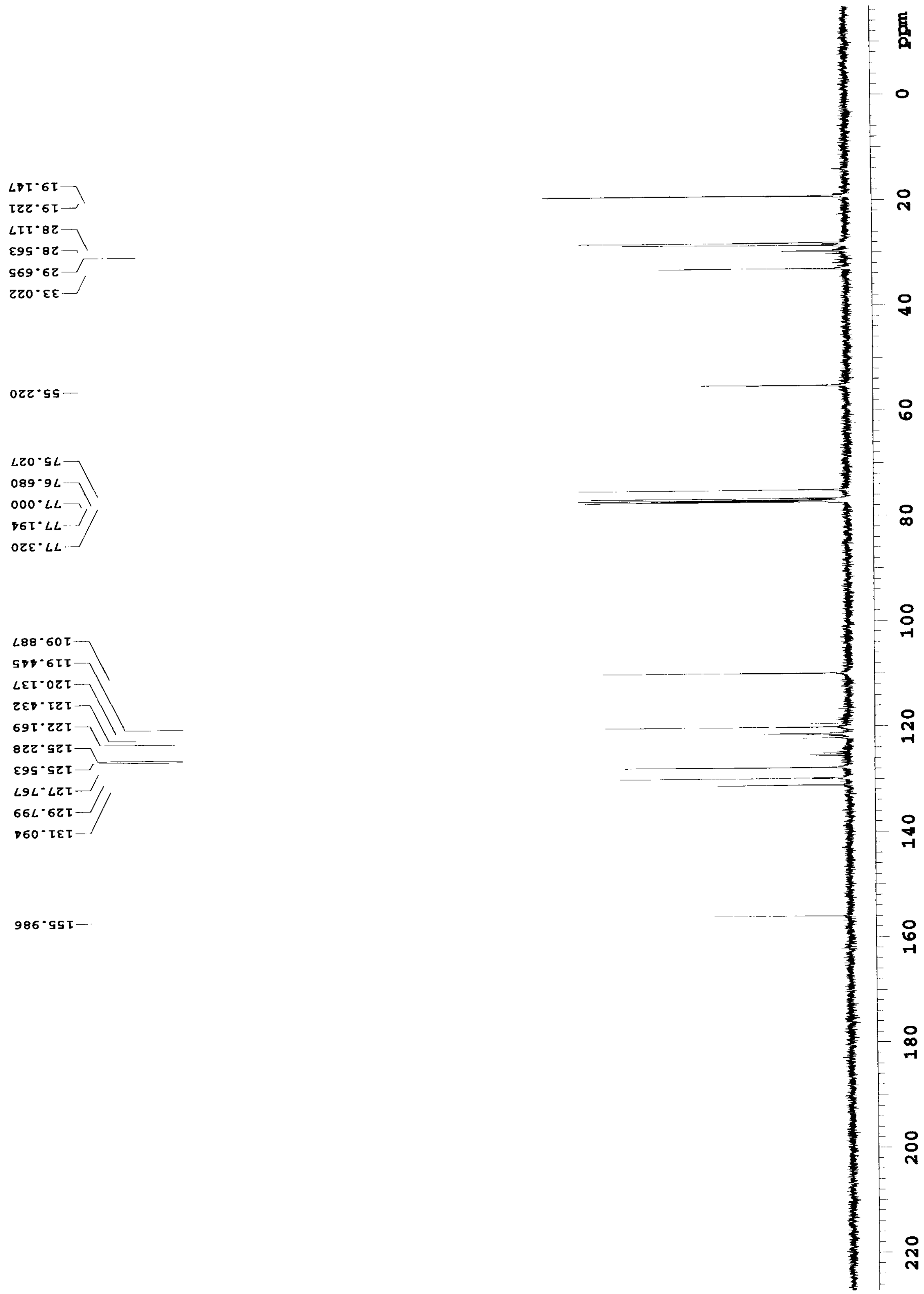


4j–major endo



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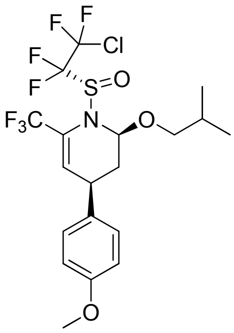
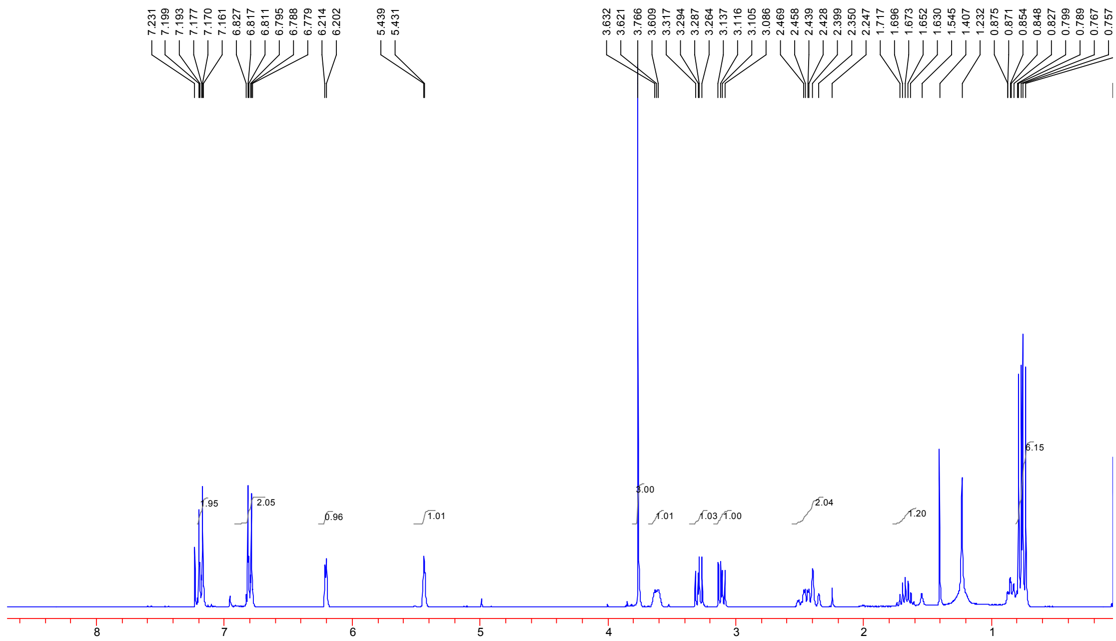
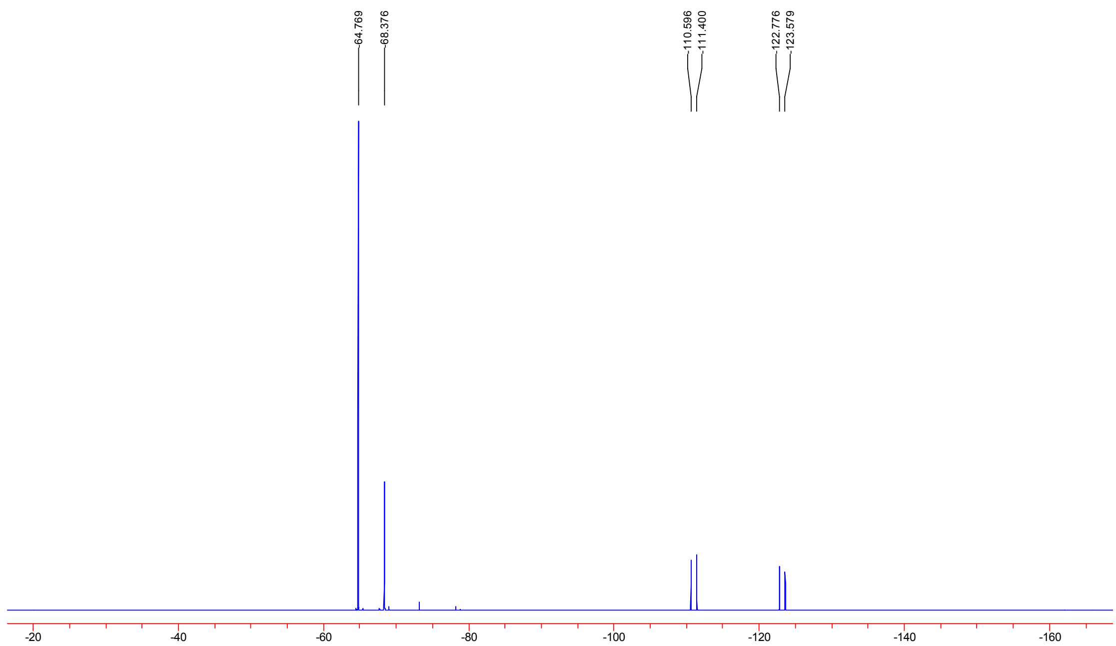
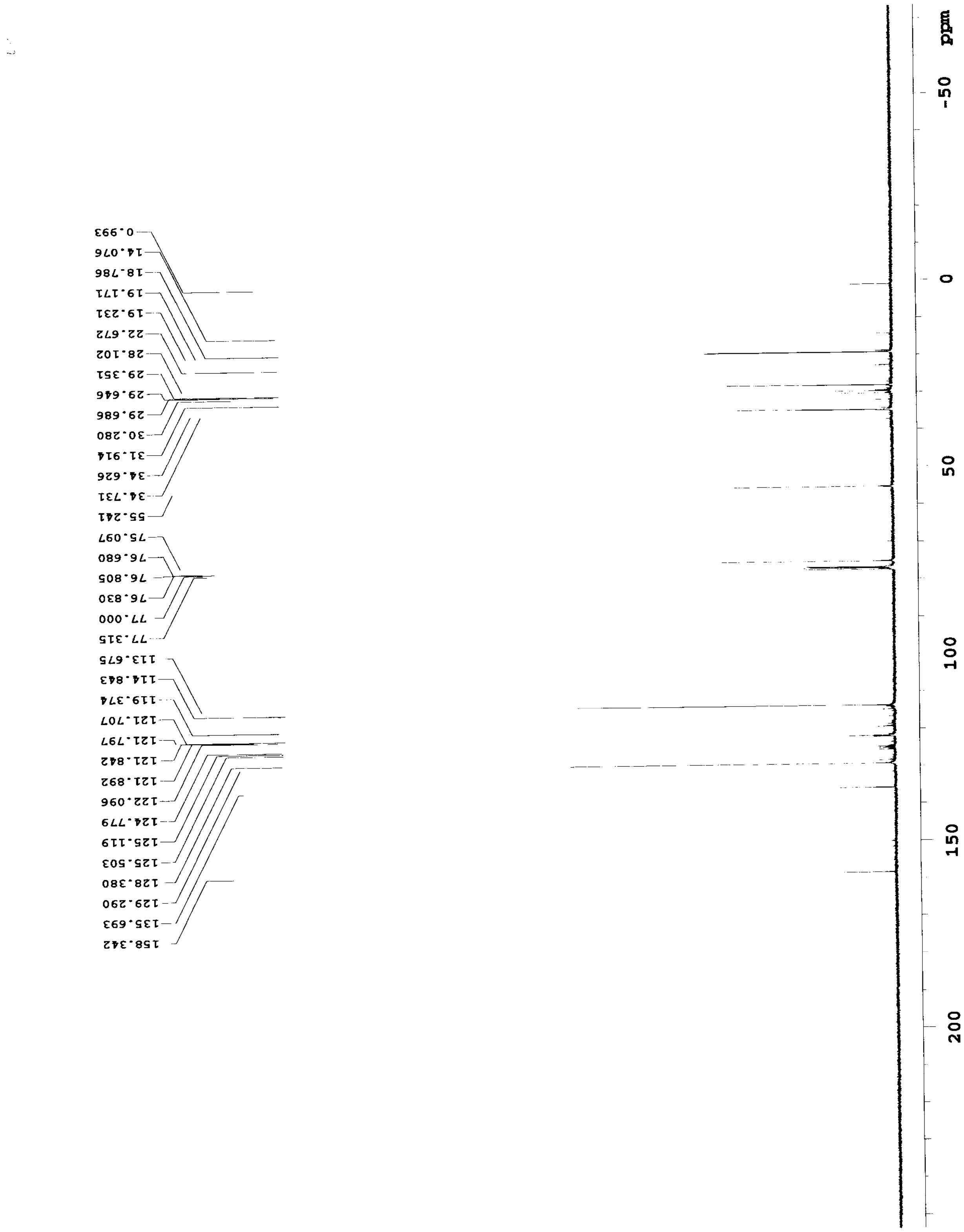


4k–major endo



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77.000
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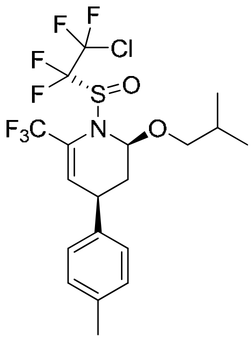
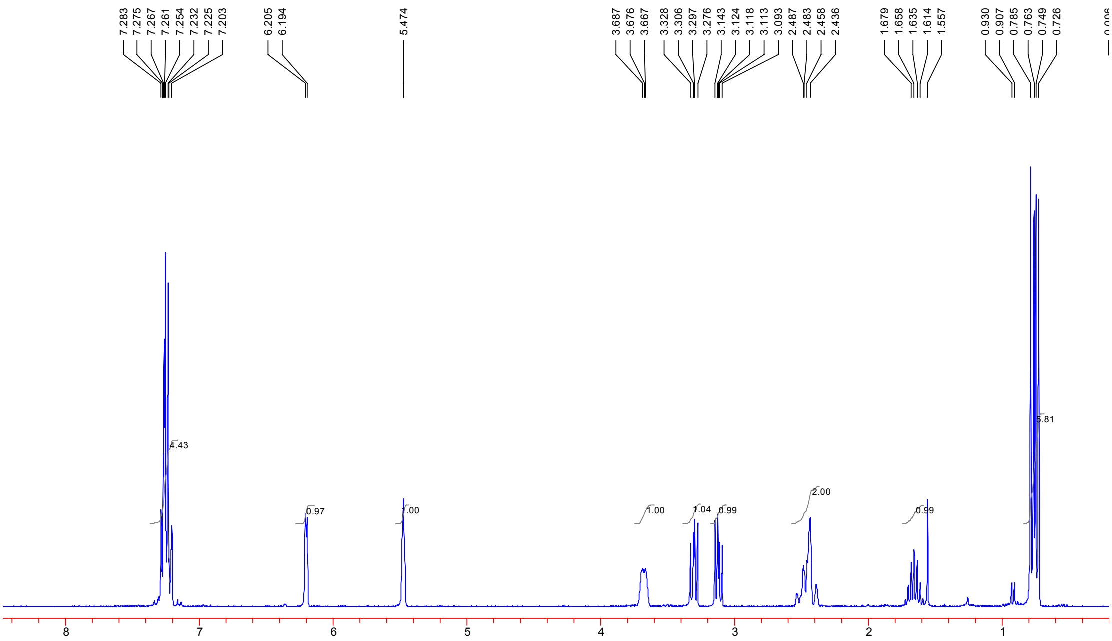
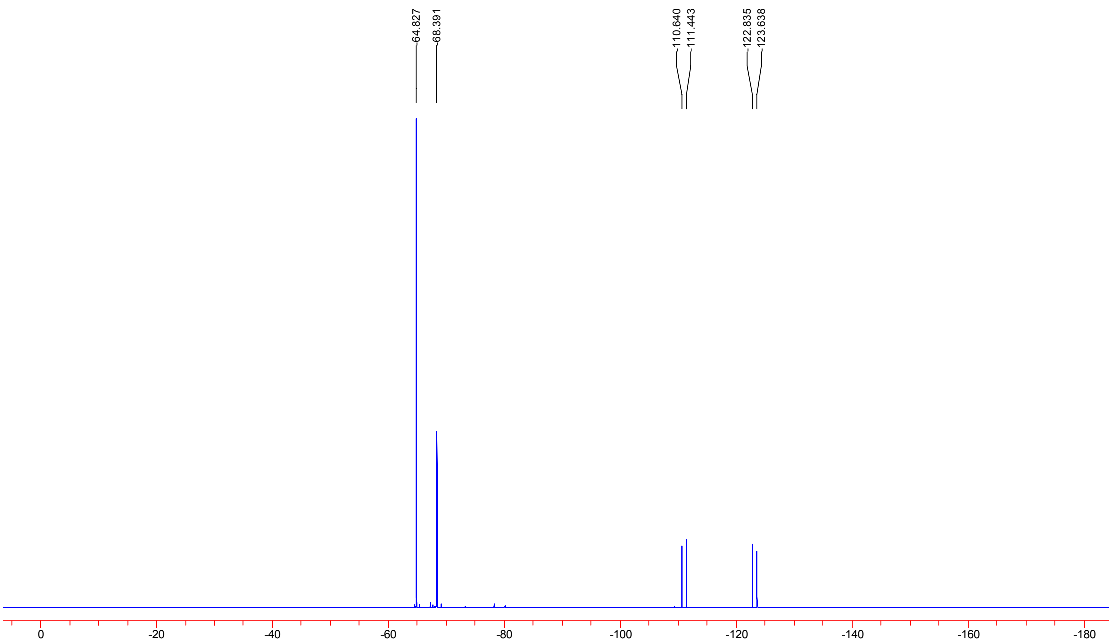
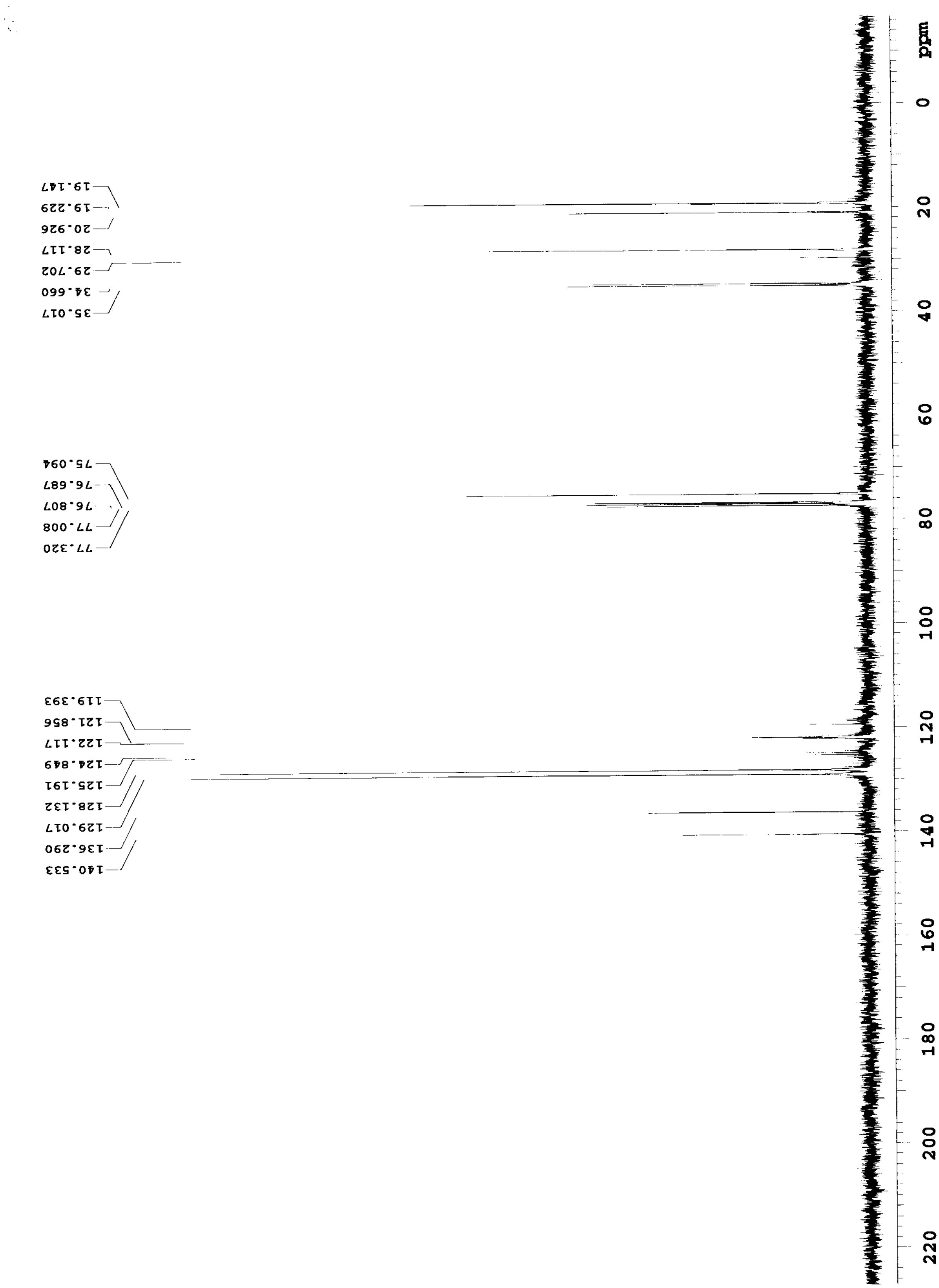


4l–major endo



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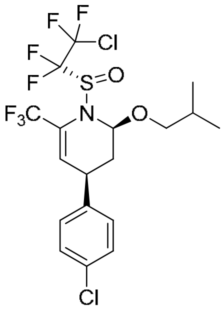
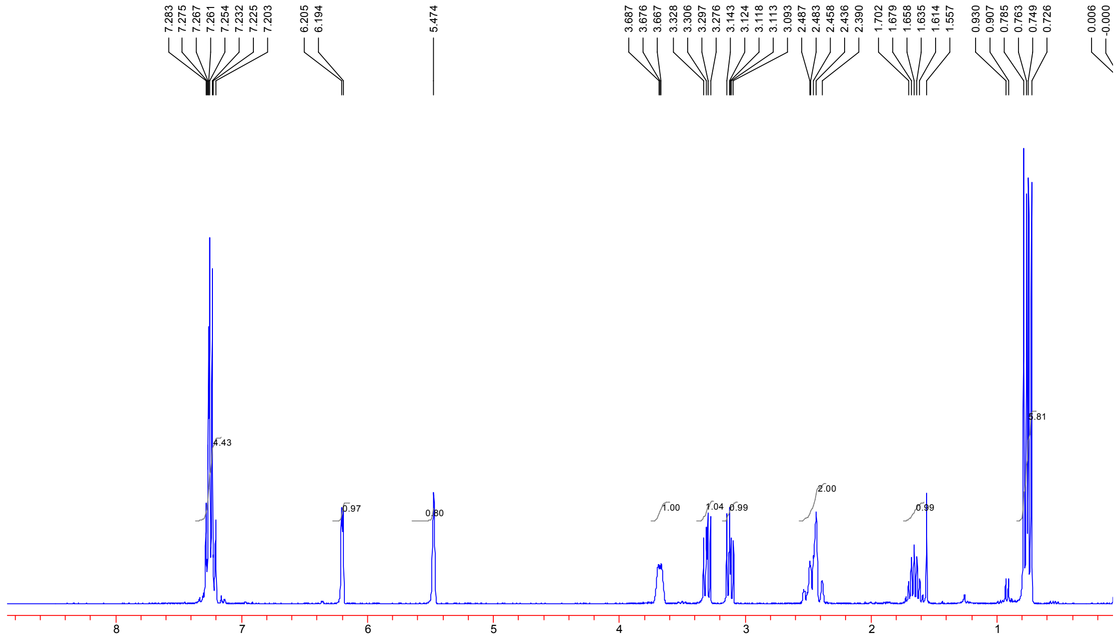
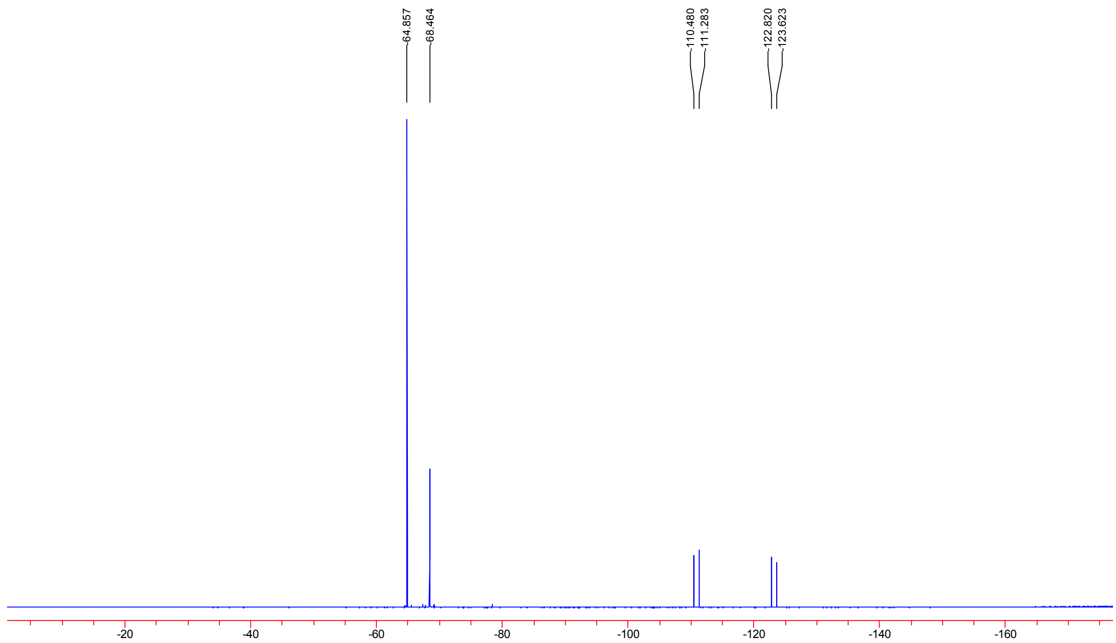
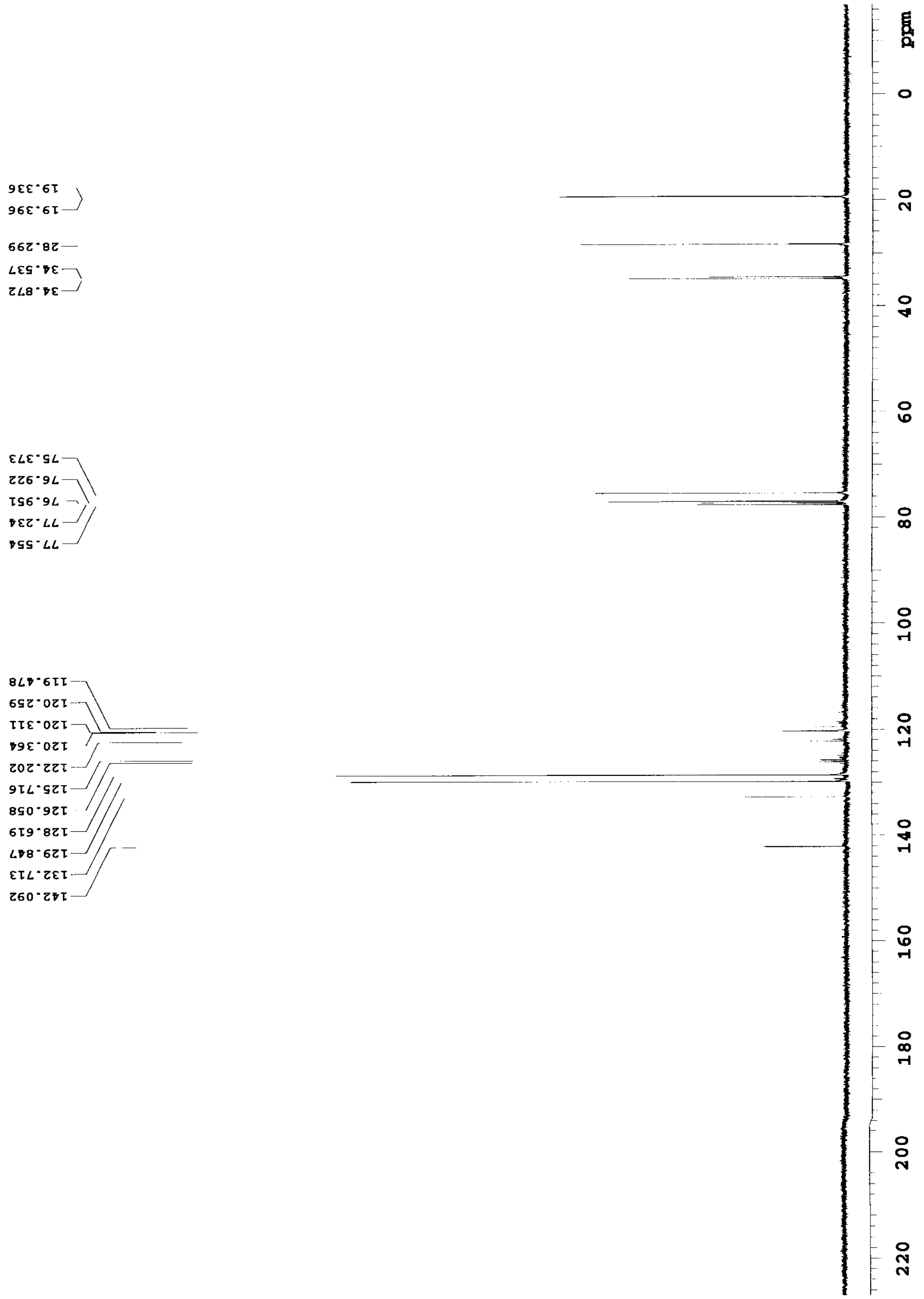


4m–major endo



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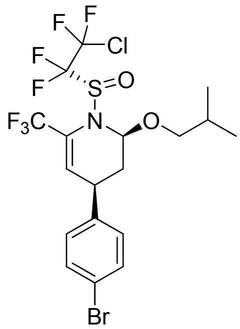
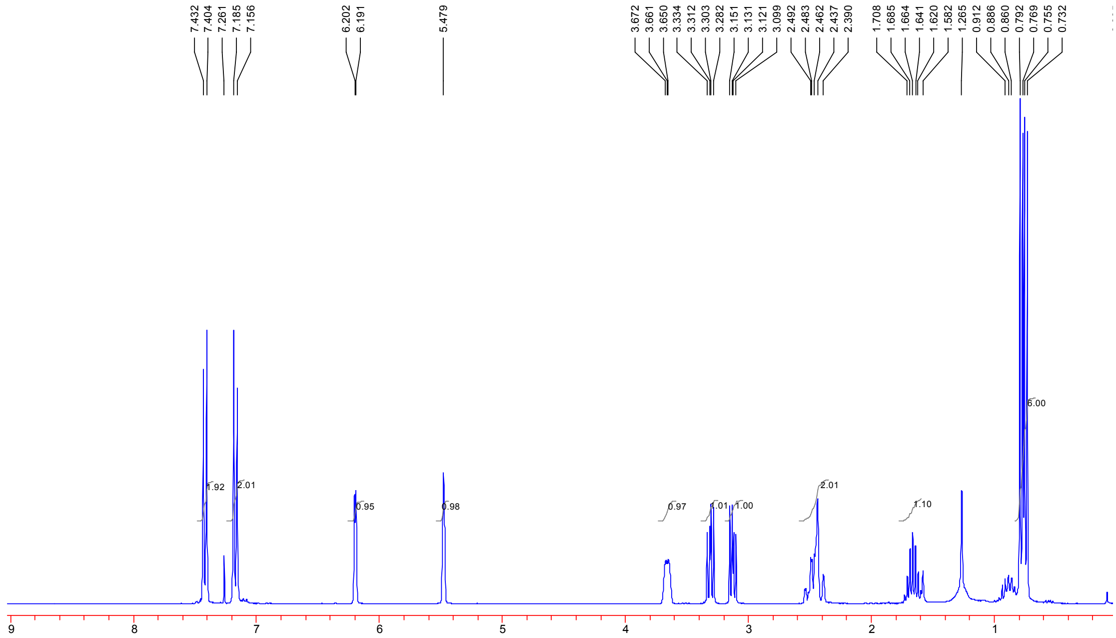
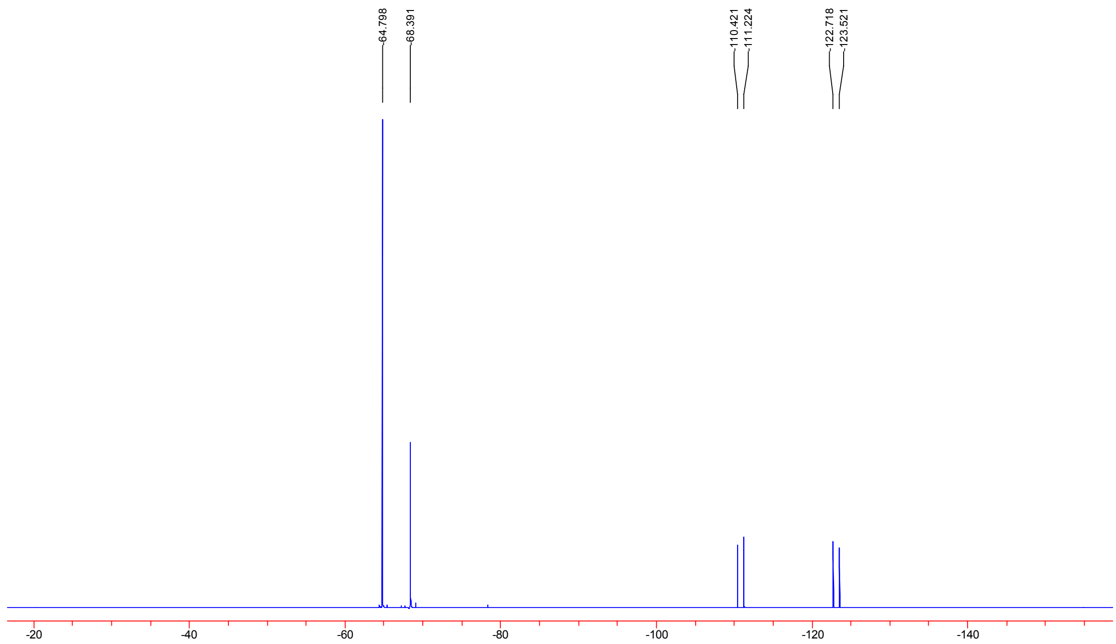
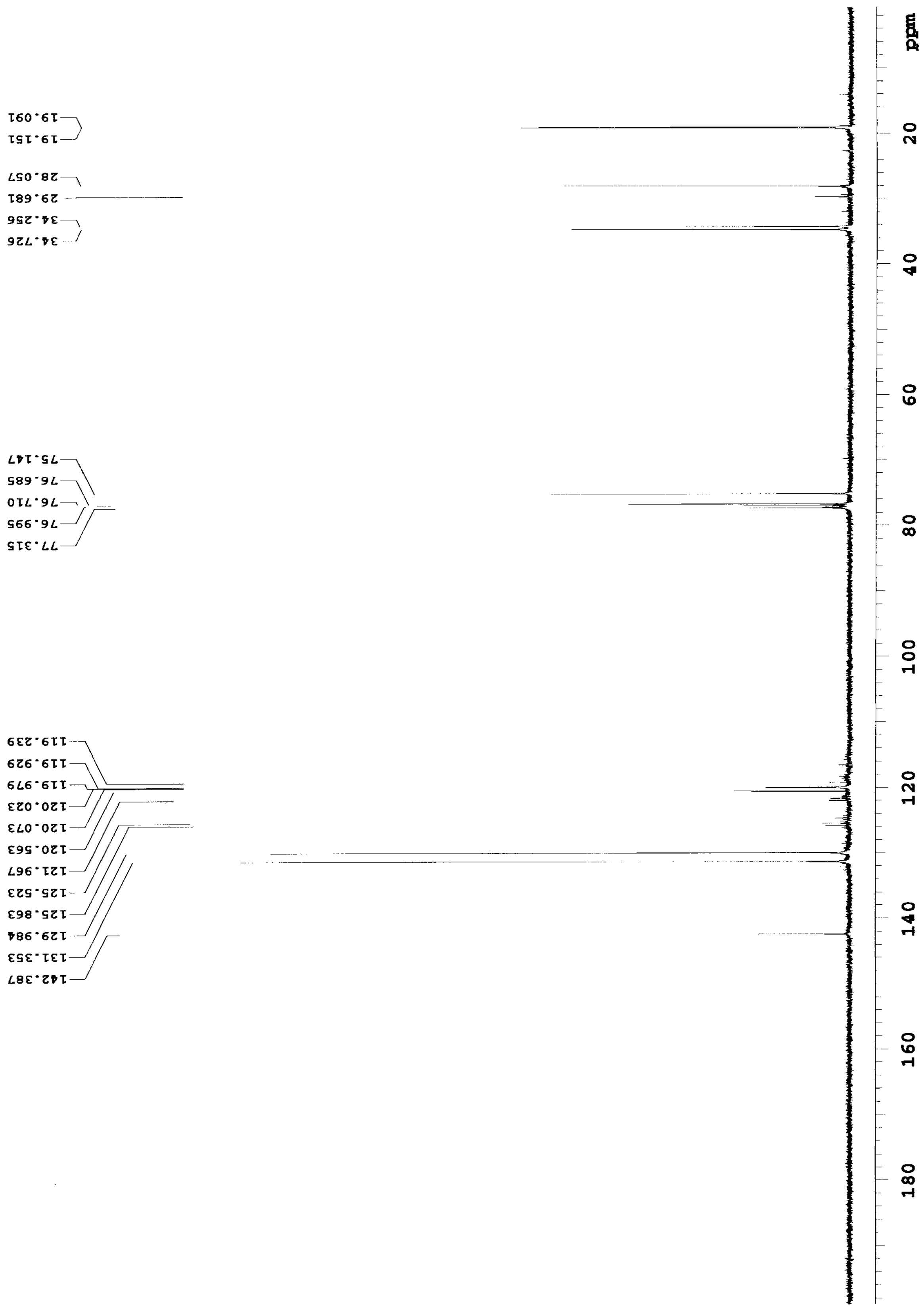


4n–major endo



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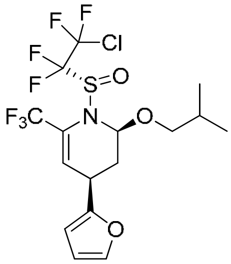
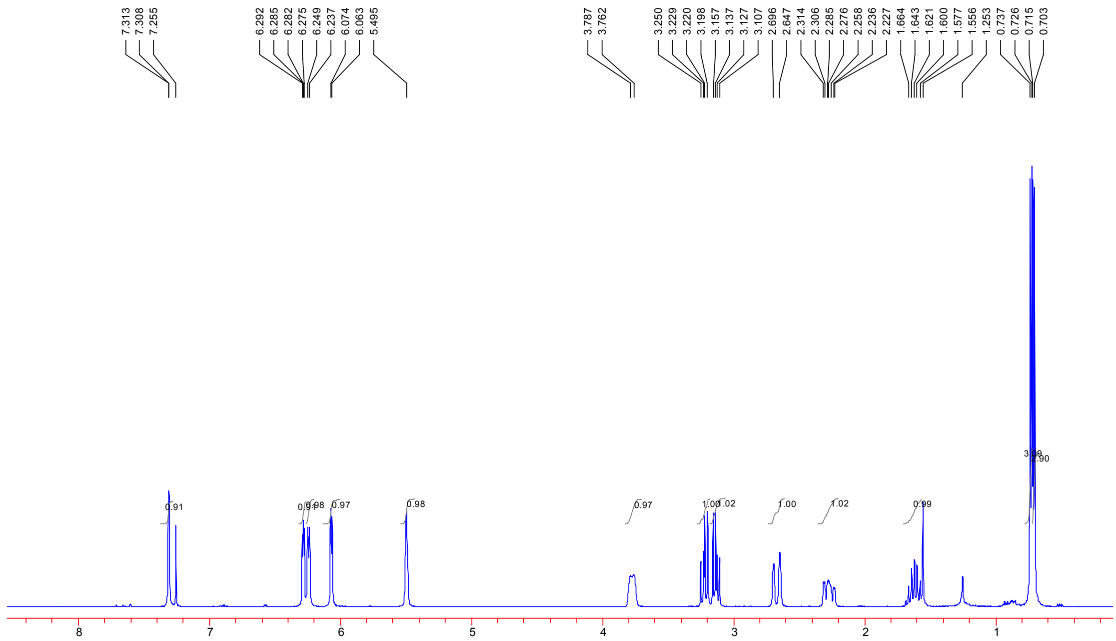
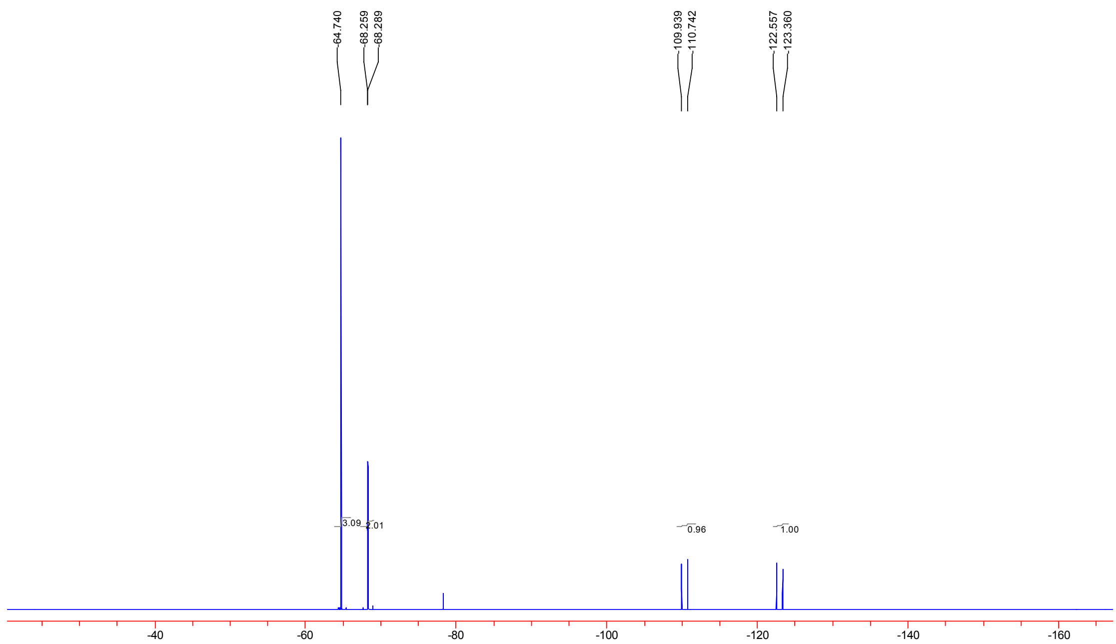
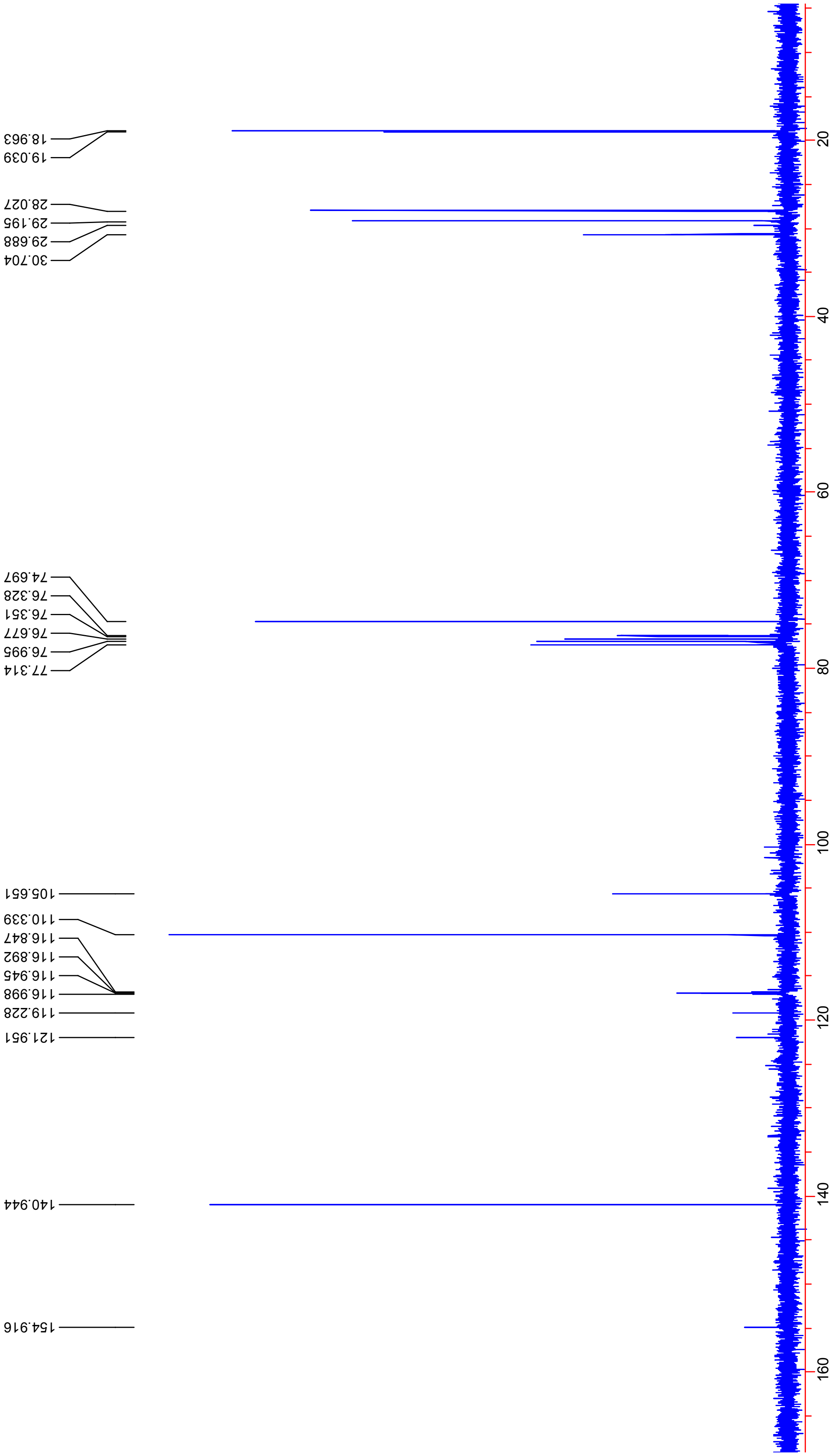


4o–major endo



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76.677
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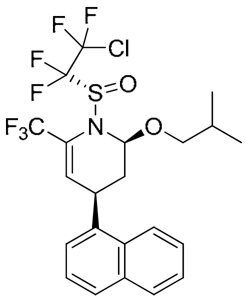
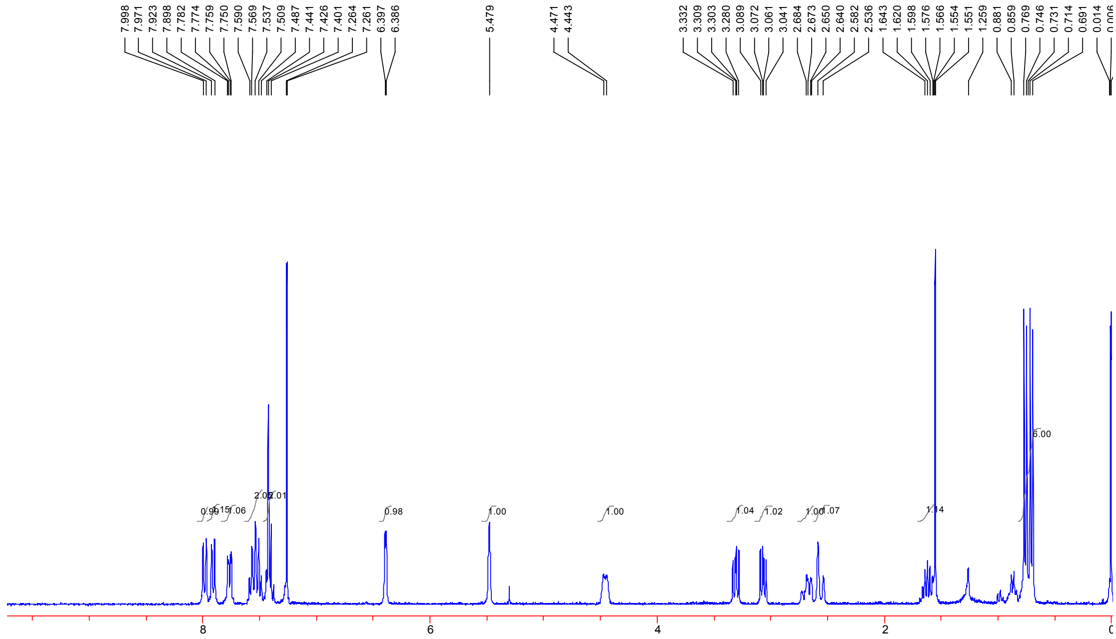
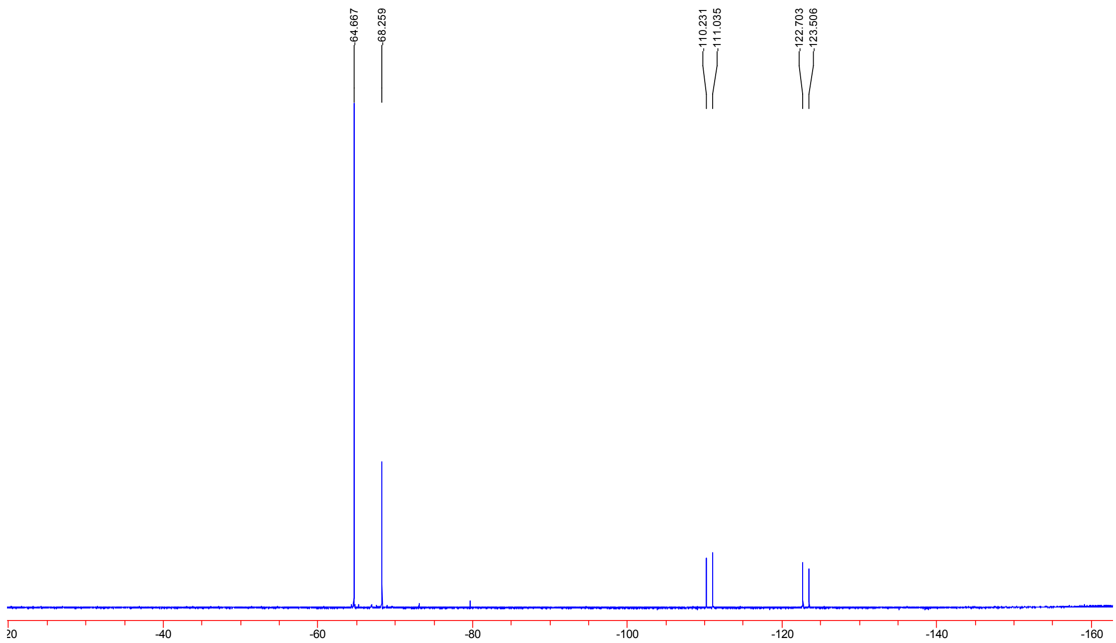
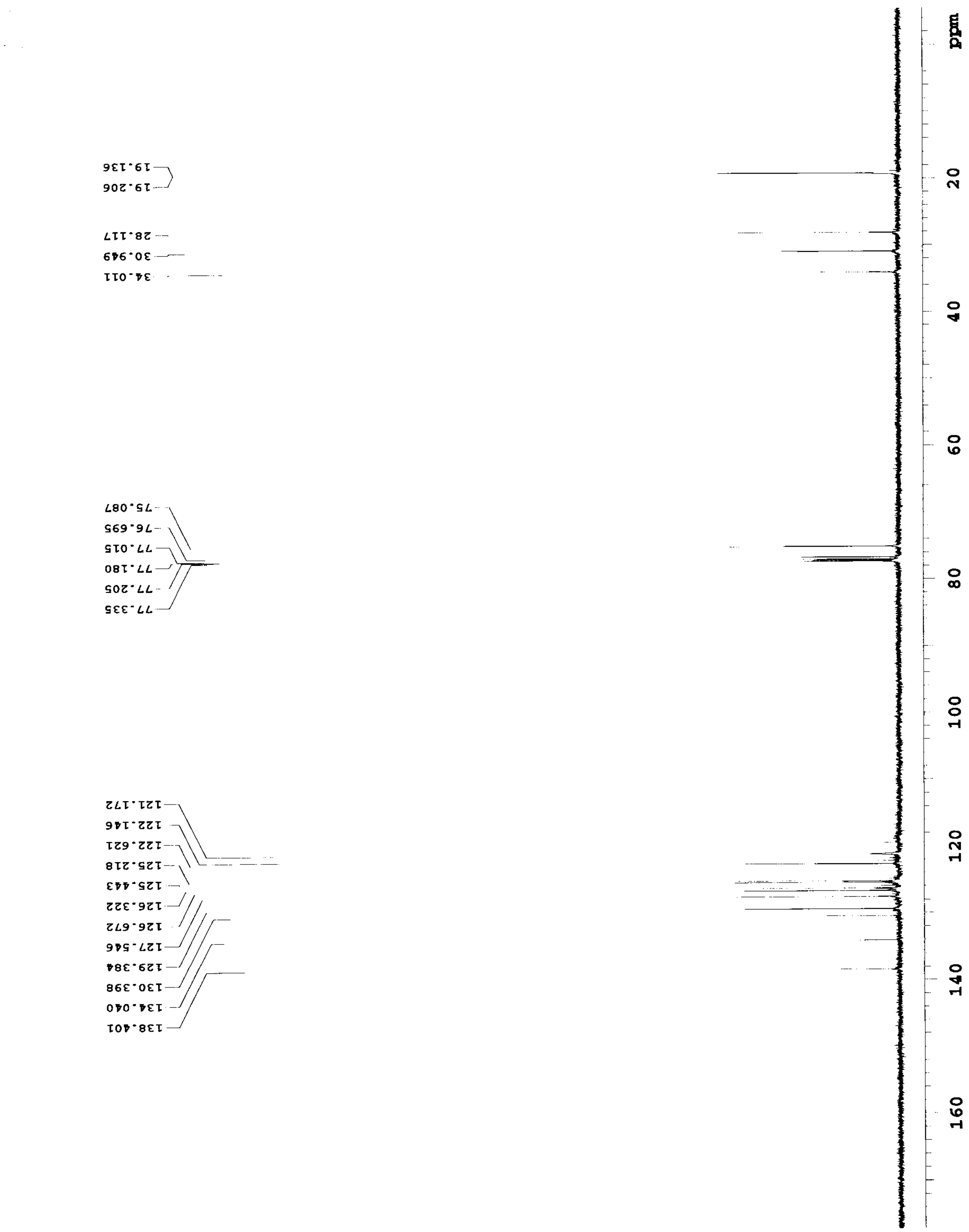


4p–major endo



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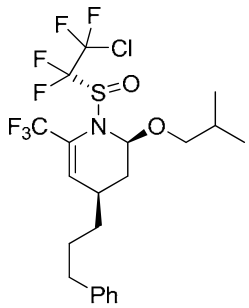
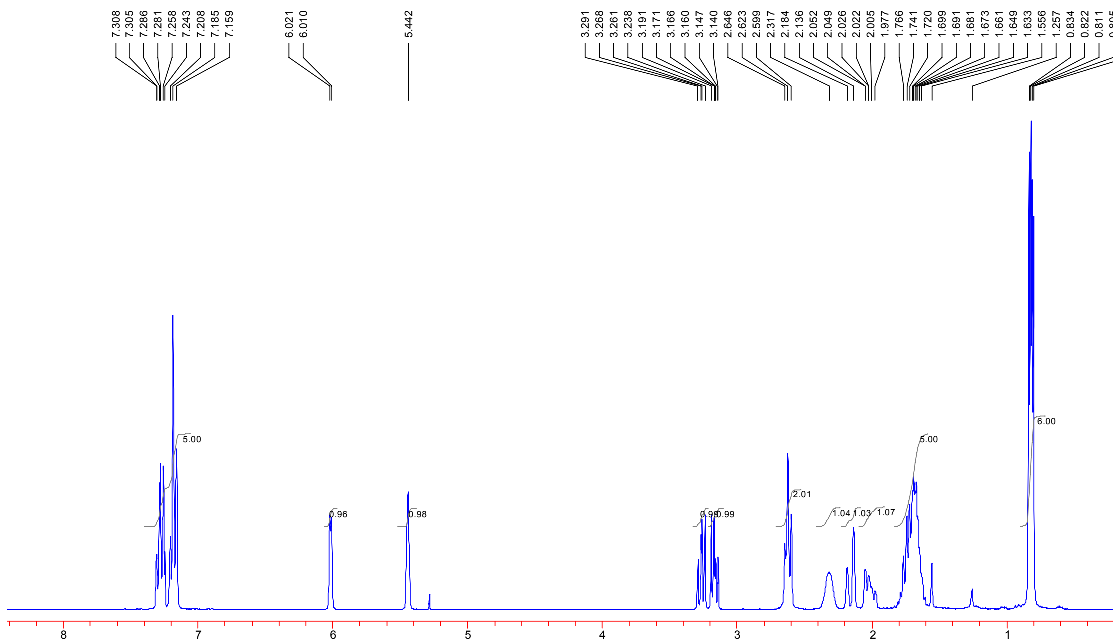
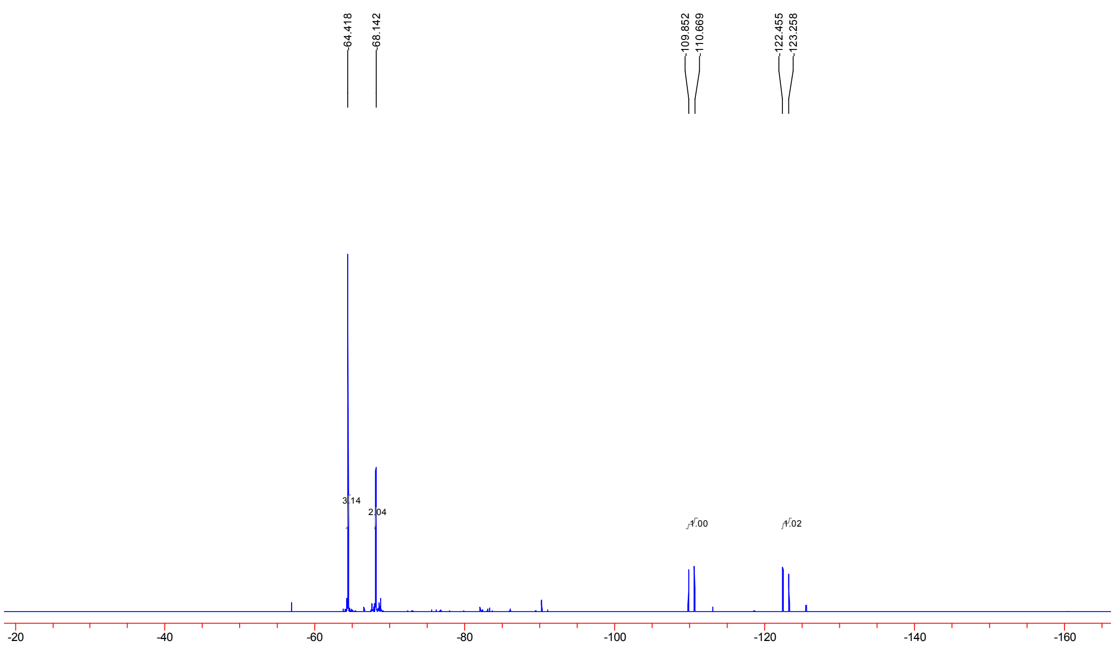
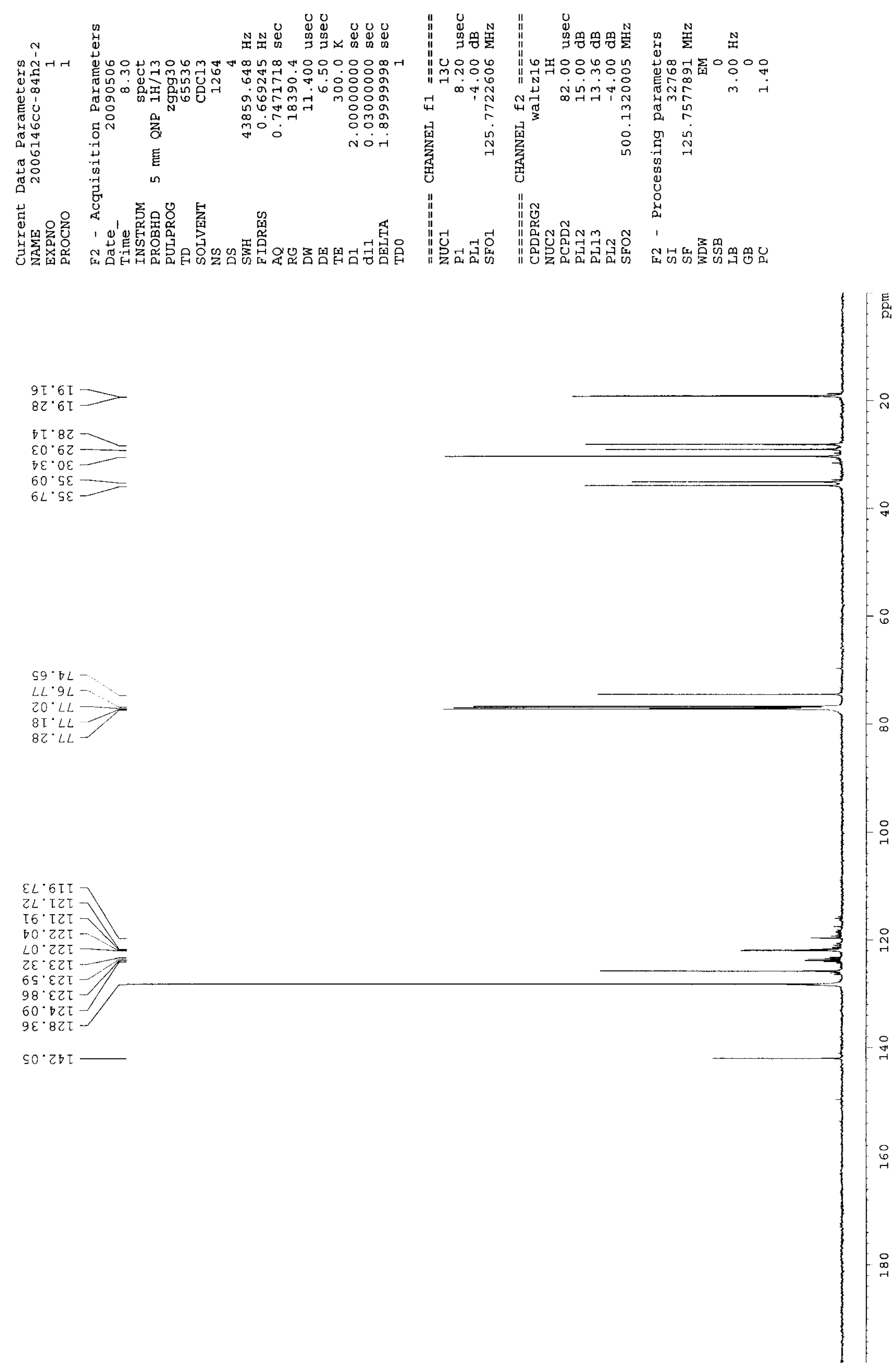


4q–major endo



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AQ 0.7471718 sec
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DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
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P1 8.20 usec
PL1 -4.00 dB
SFO1 125.7722606 MHz
======== CHANNEL f2 ========
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WDW EM
SSB 0
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GB 0
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29.03
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35.09
35.79
74.65
76.77
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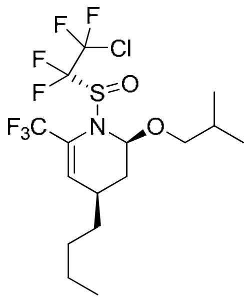
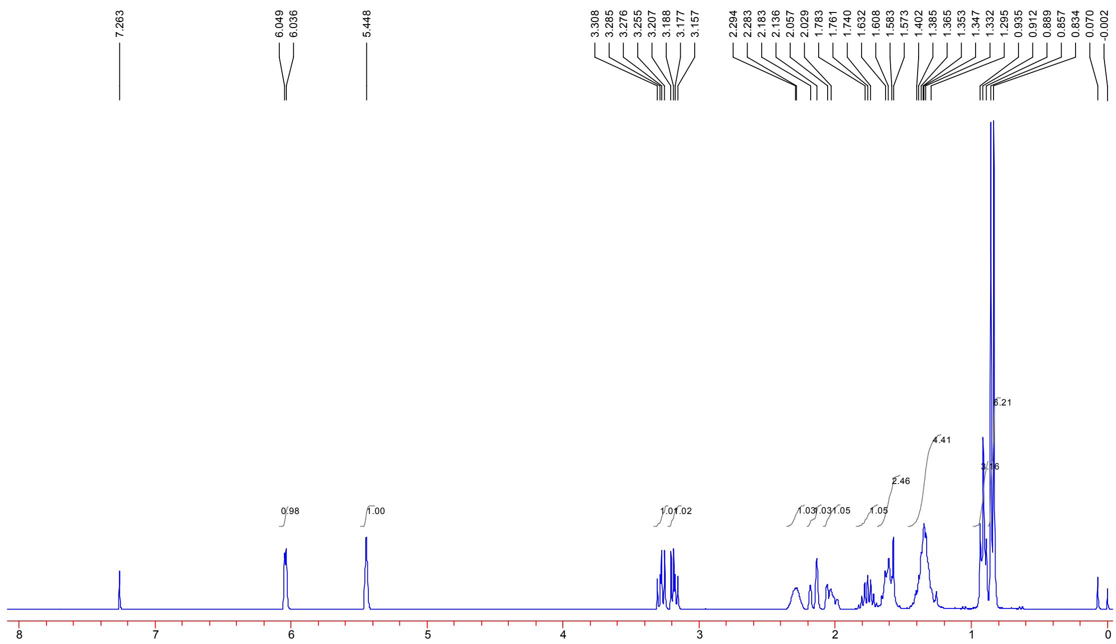
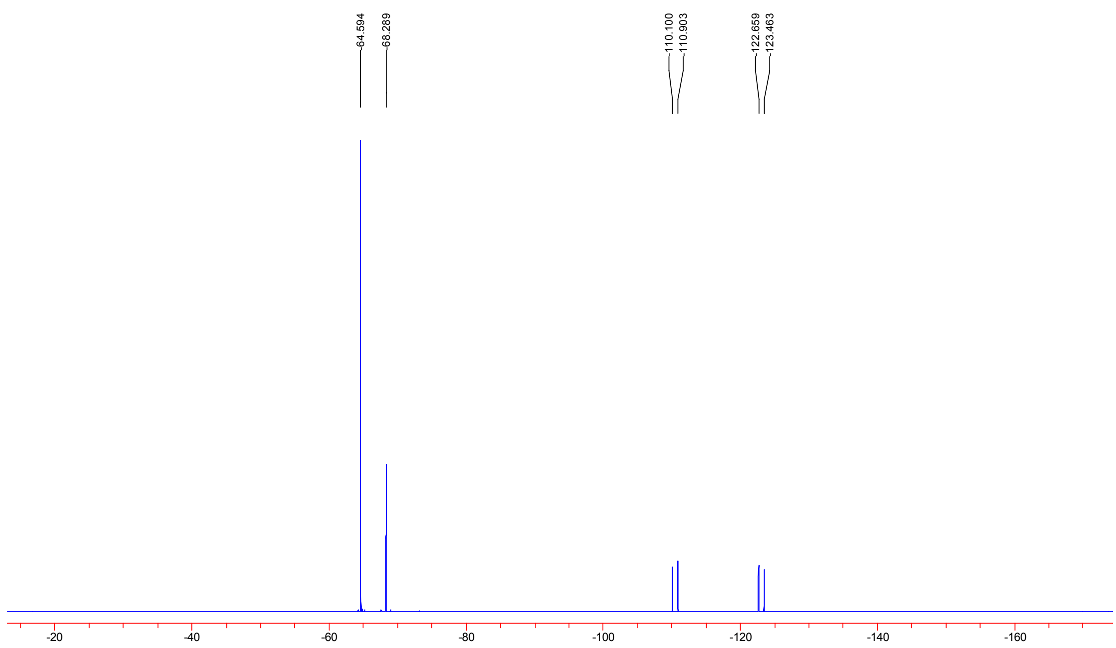
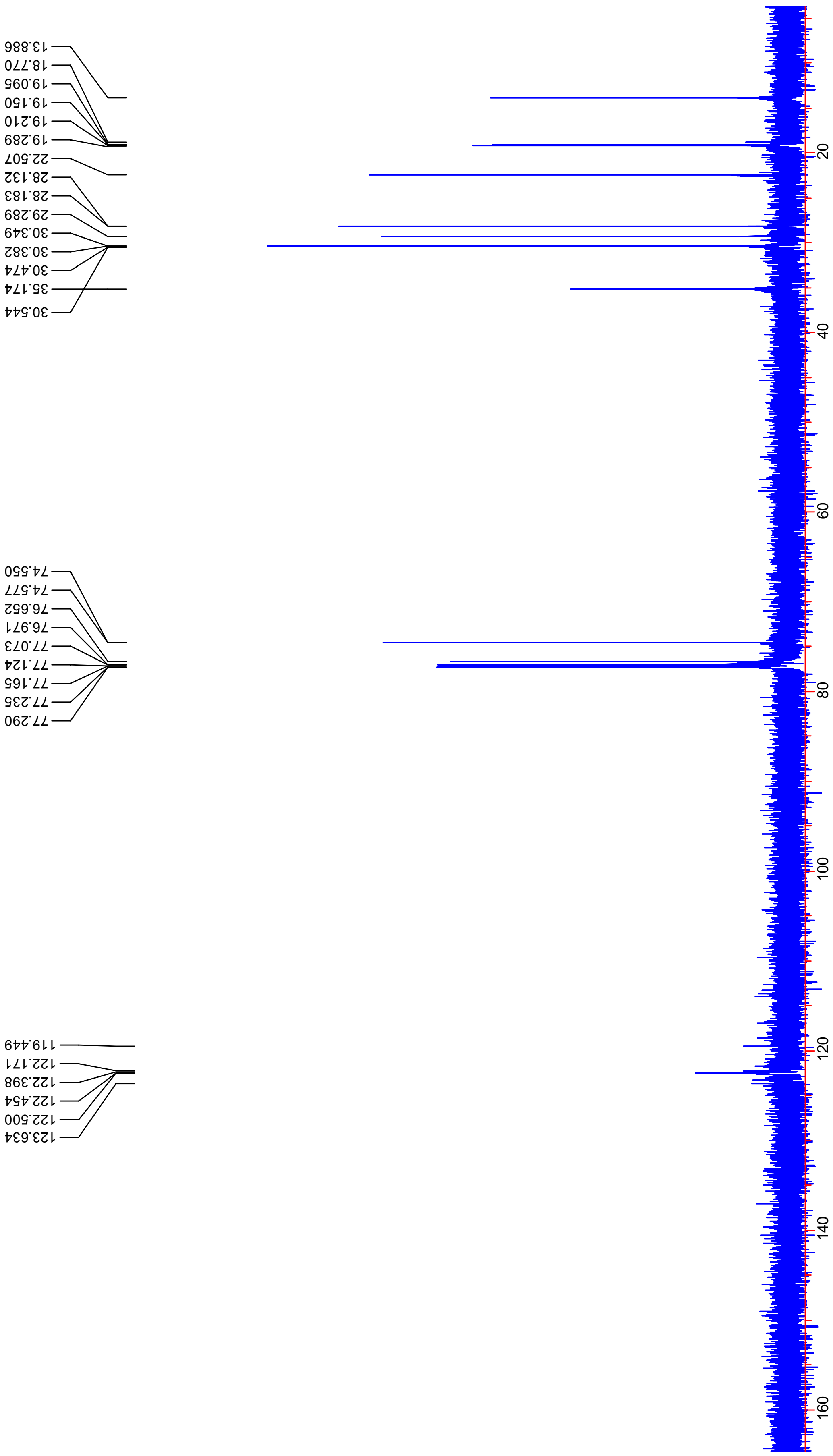


4r–major endo



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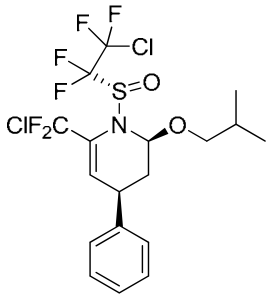
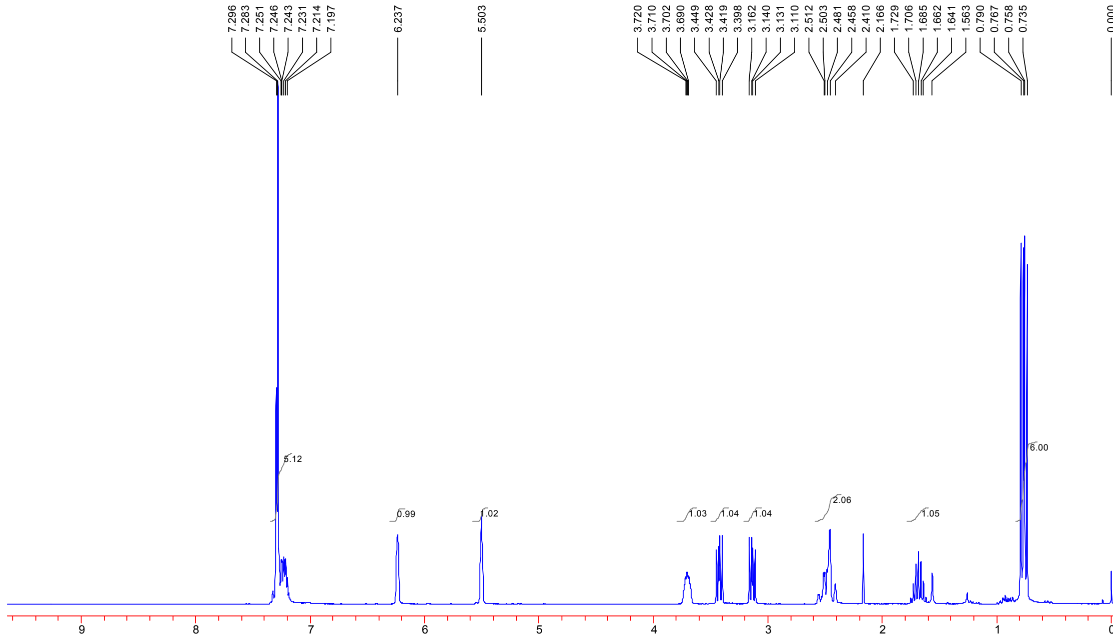
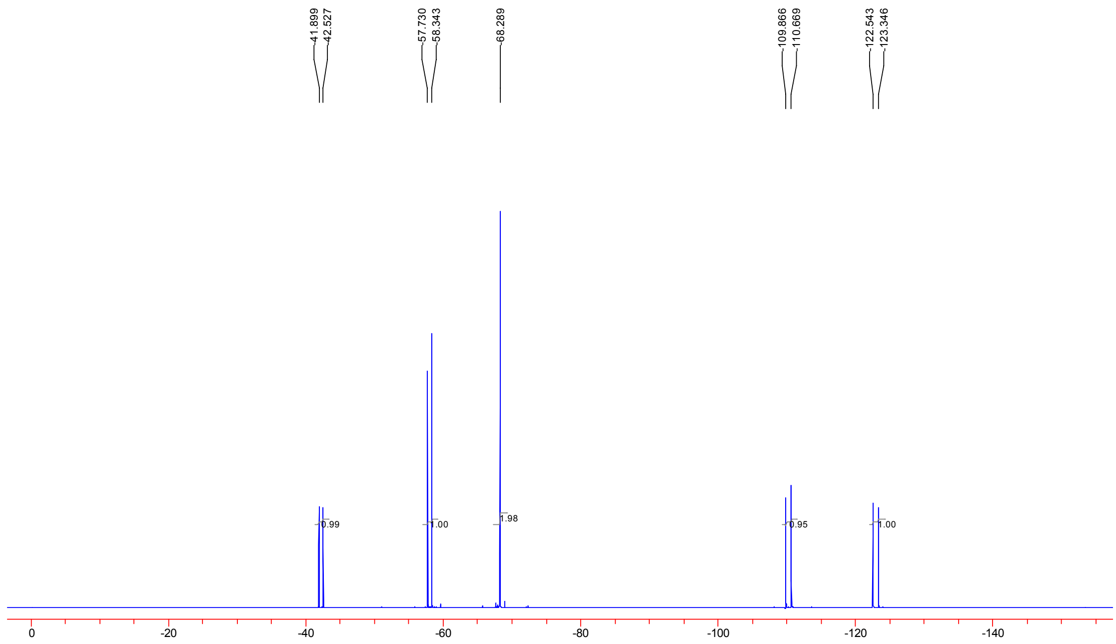
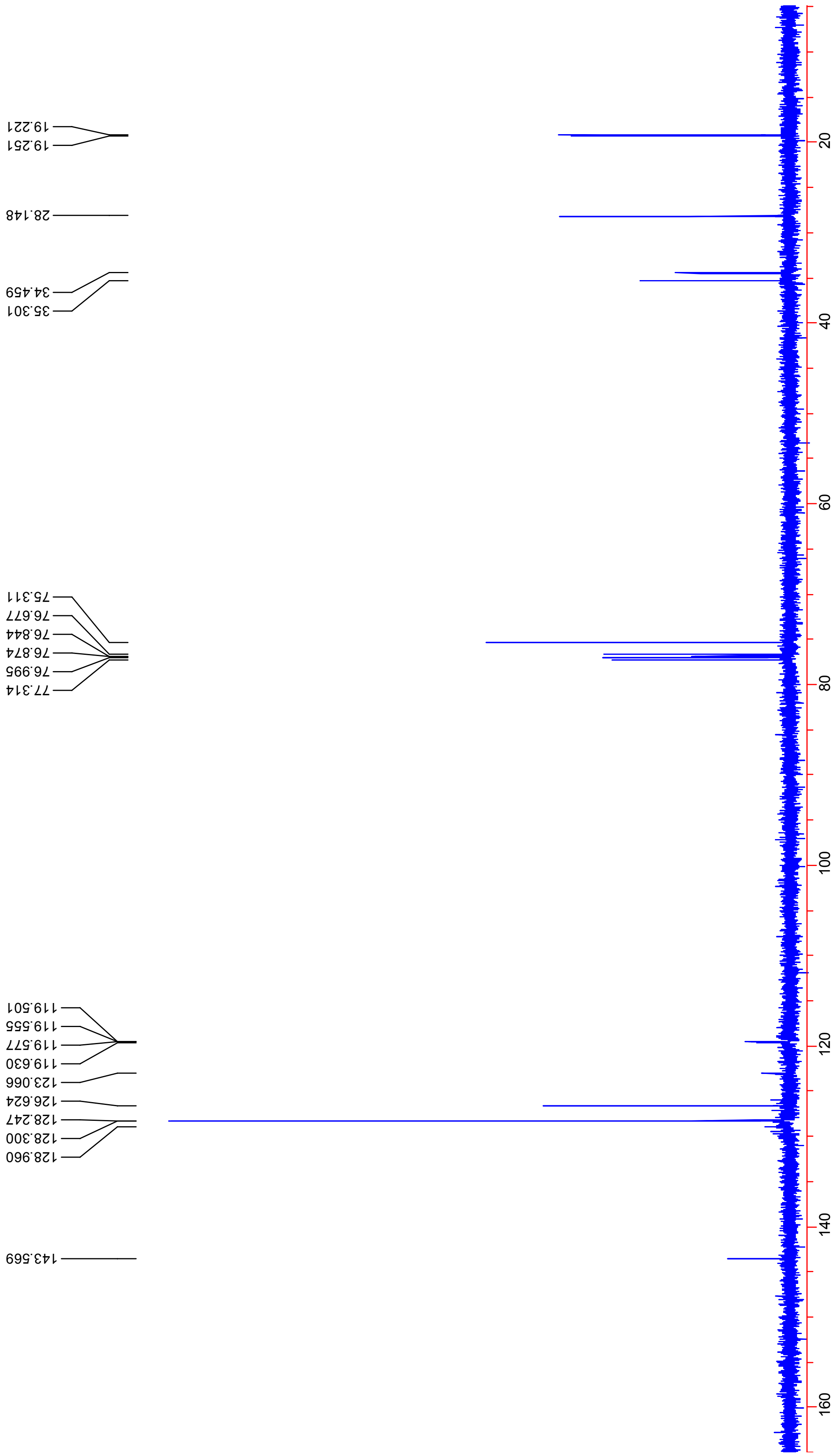


4s–major endo



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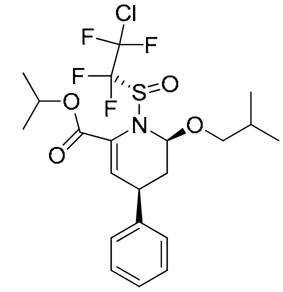
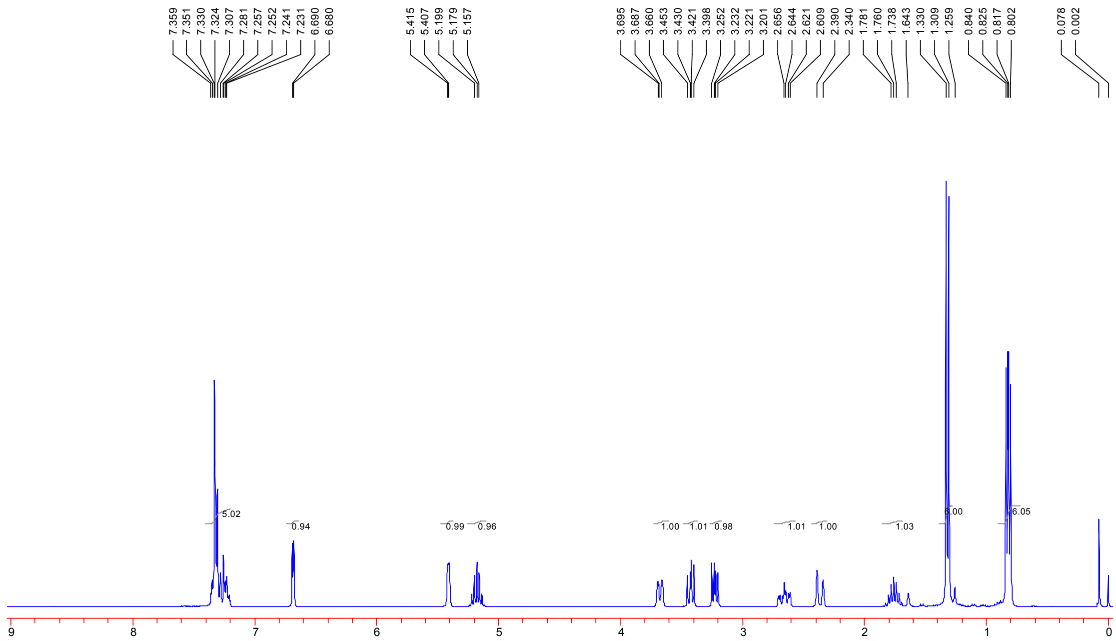
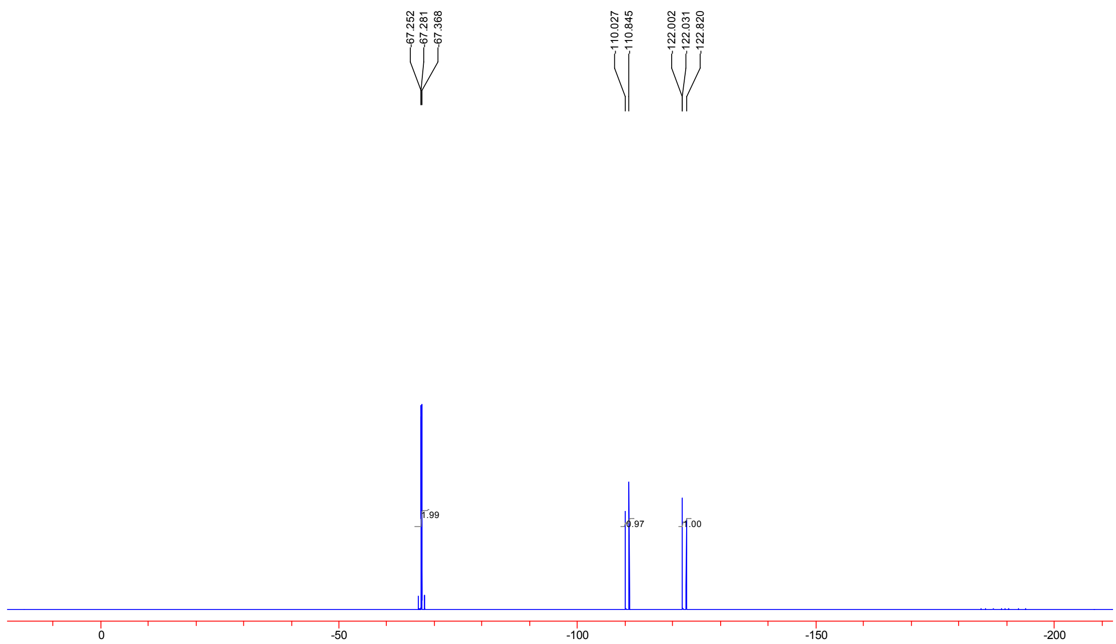
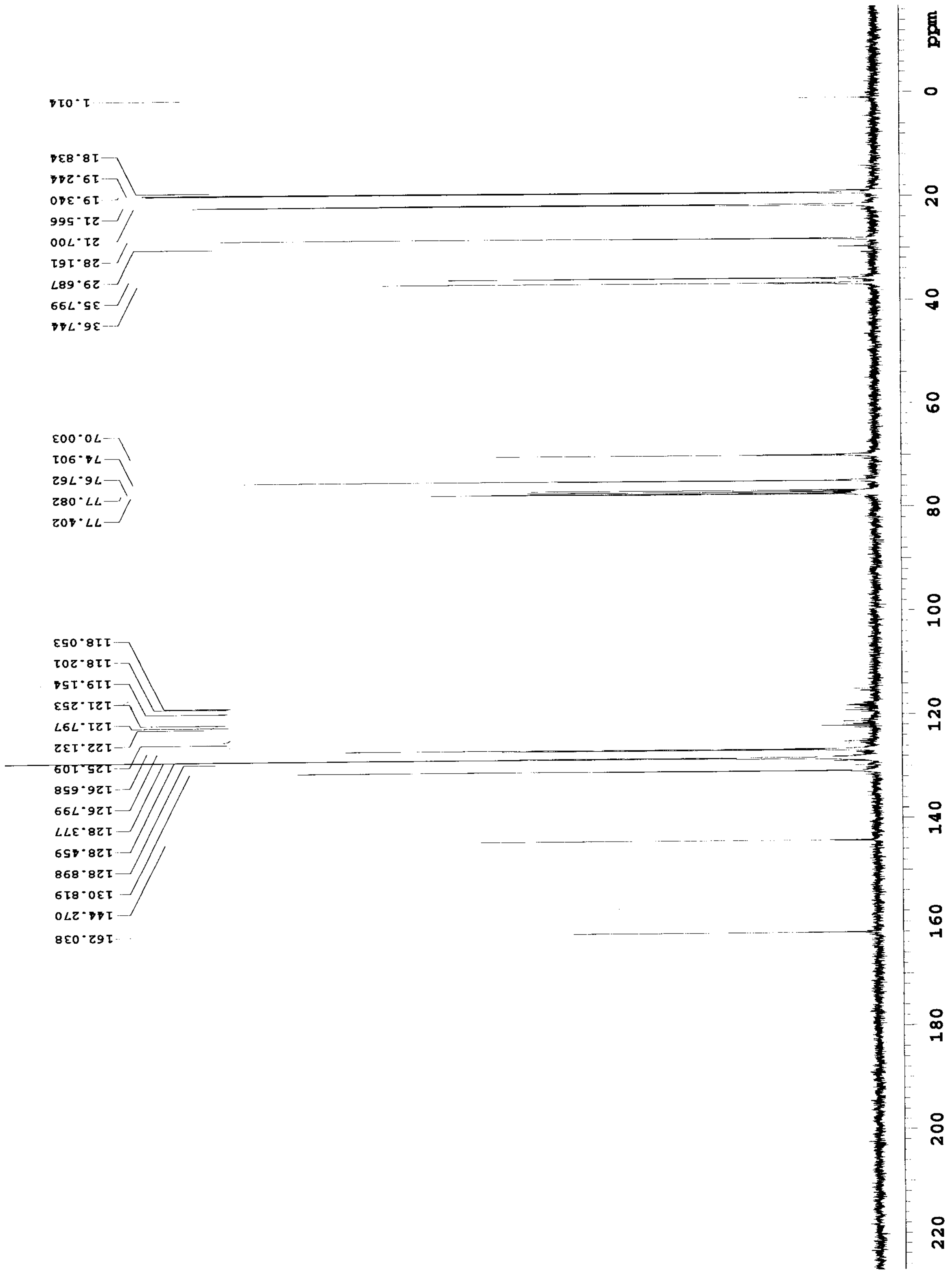


4t–major endo



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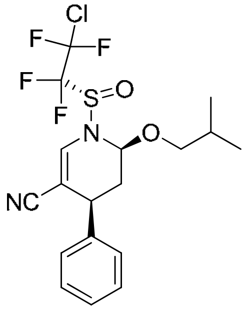
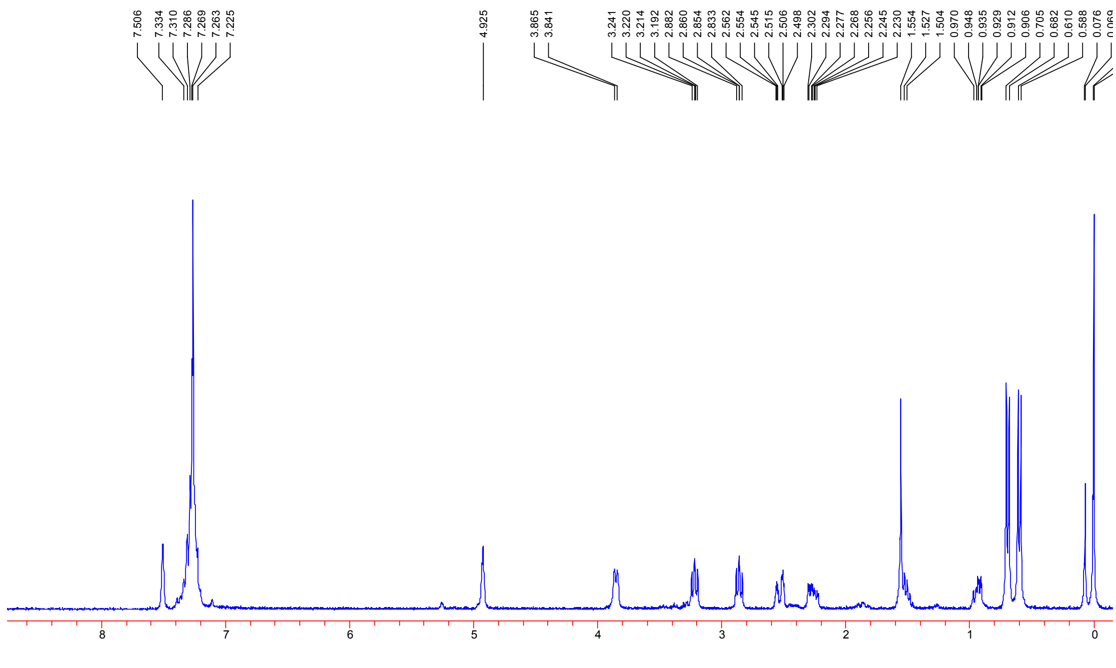
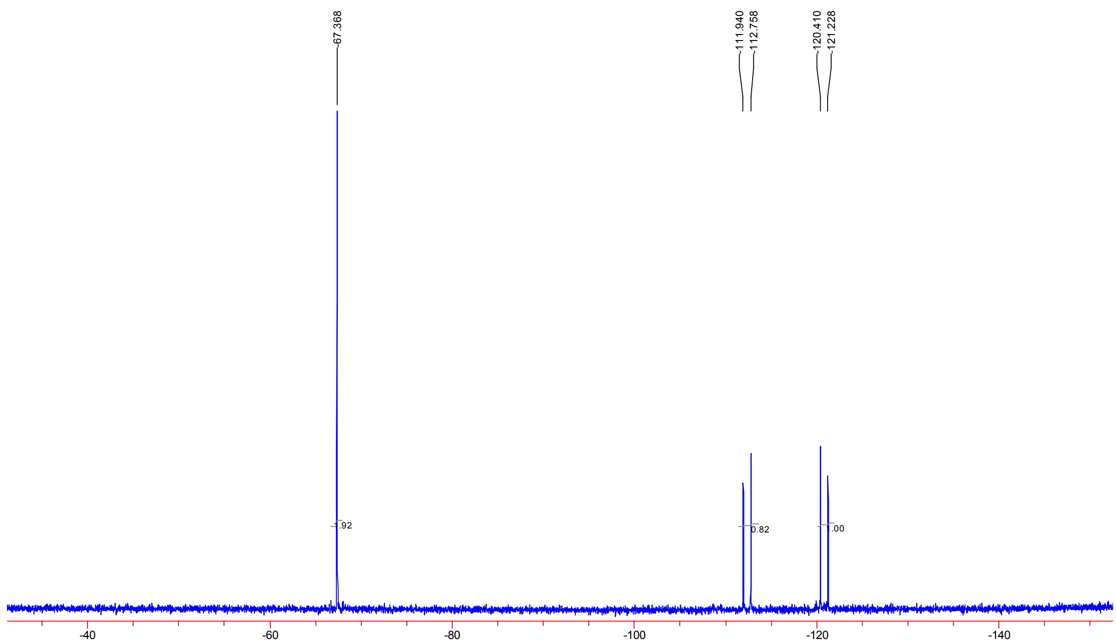
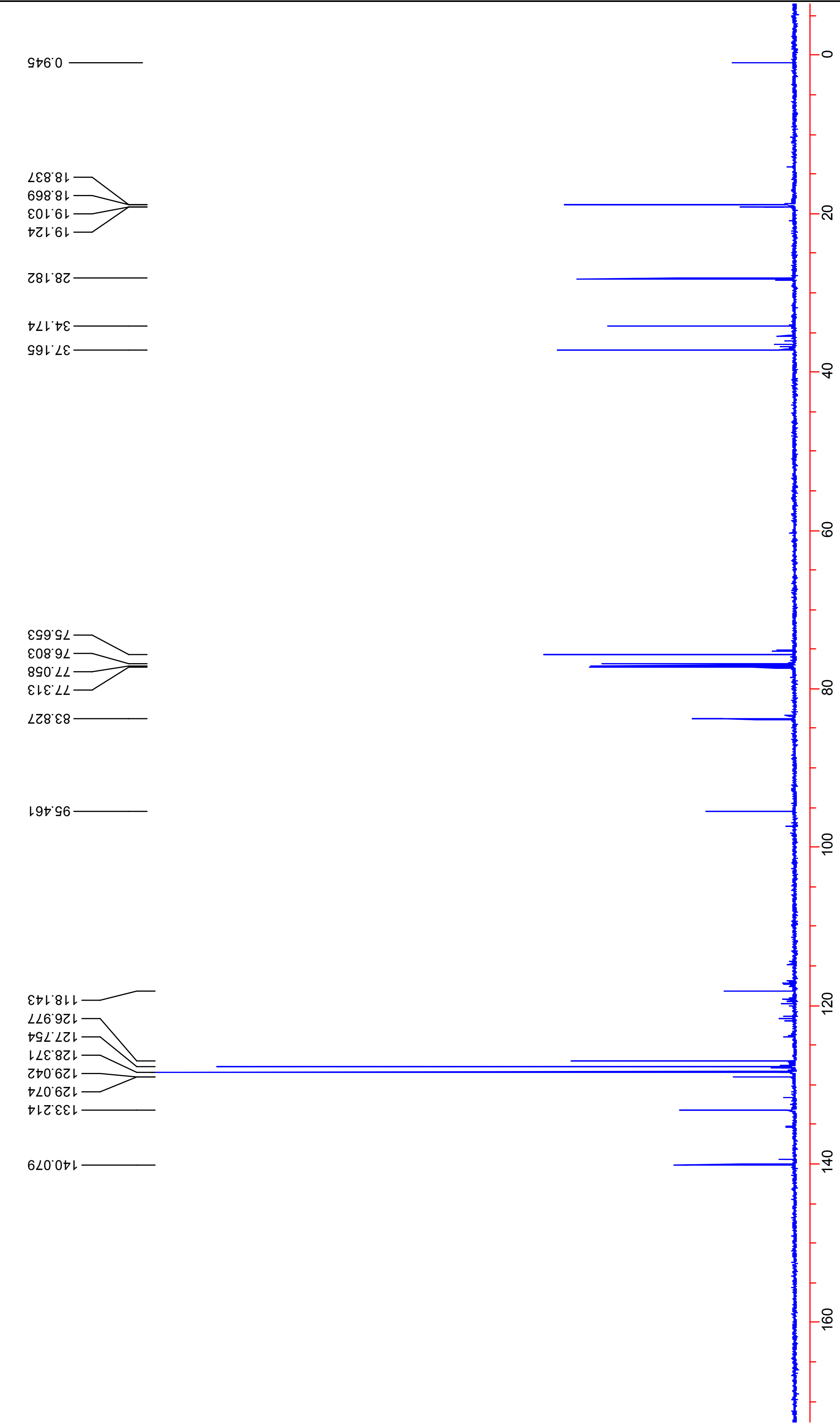


4v–major endo



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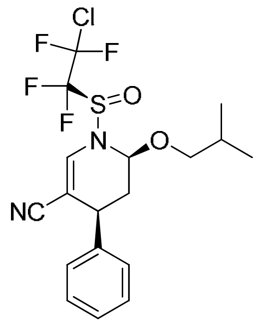
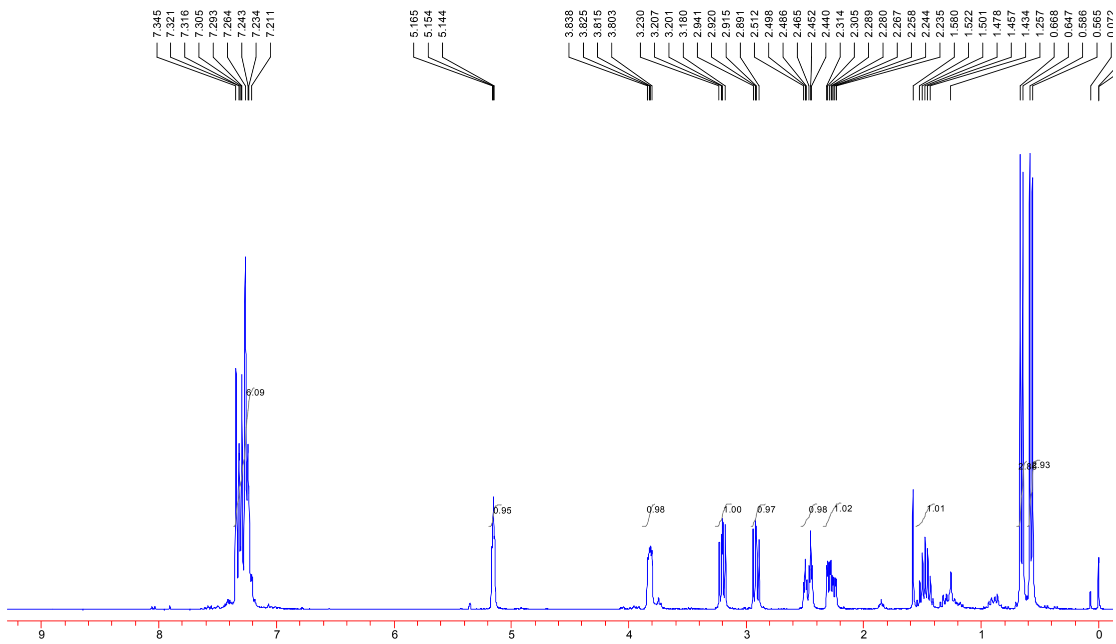
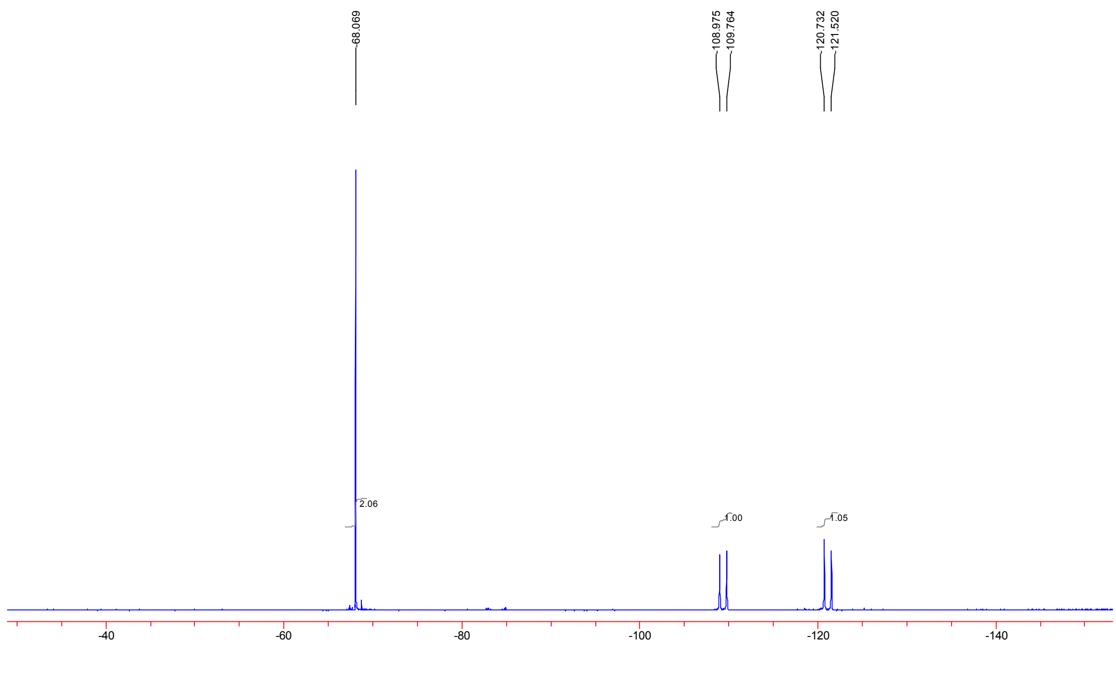
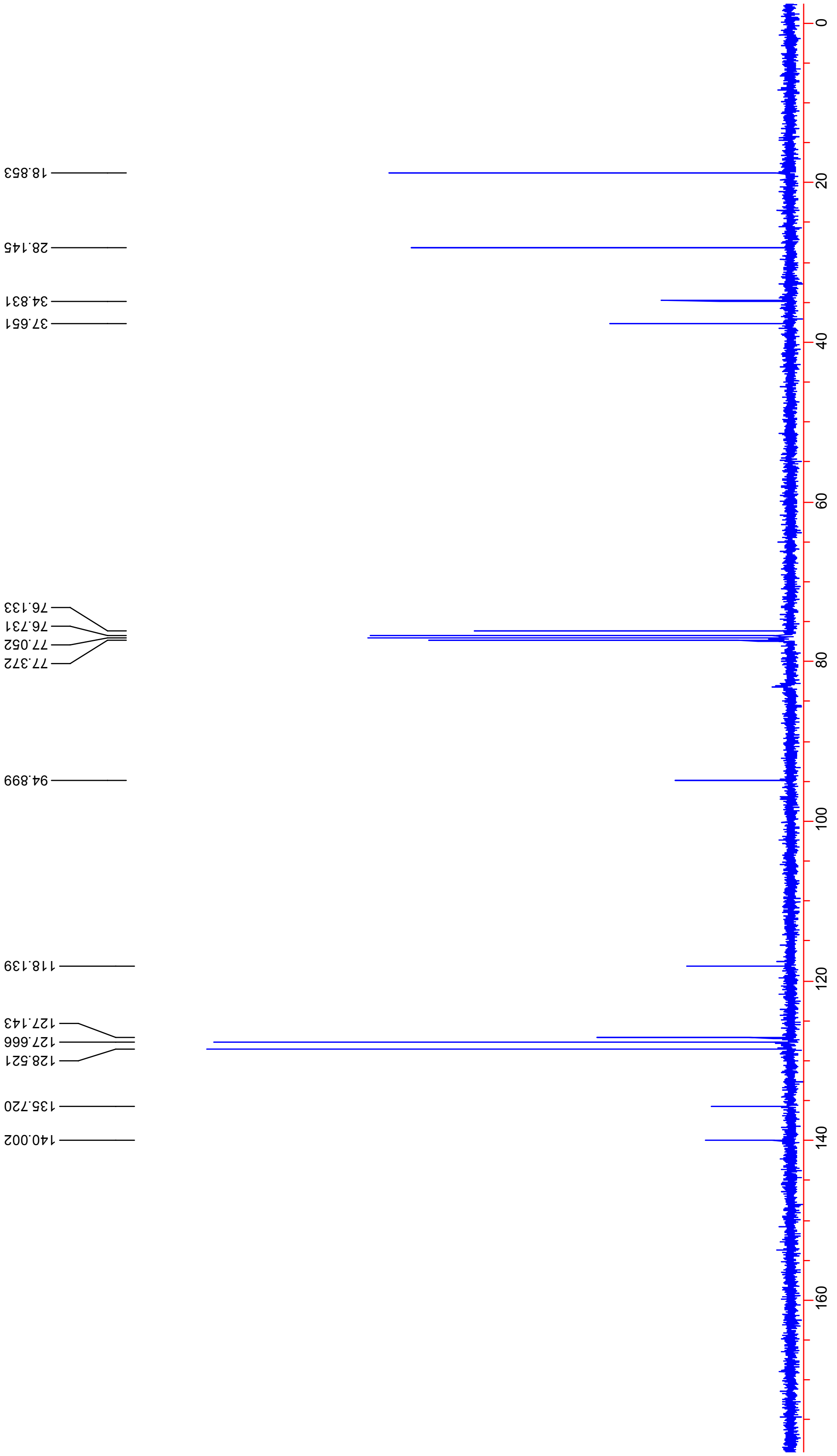


4v–minor endo






18.853
28.145
34.831
37.651
76.133
76.731
77.052
77.372
94.899
118.139
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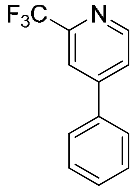
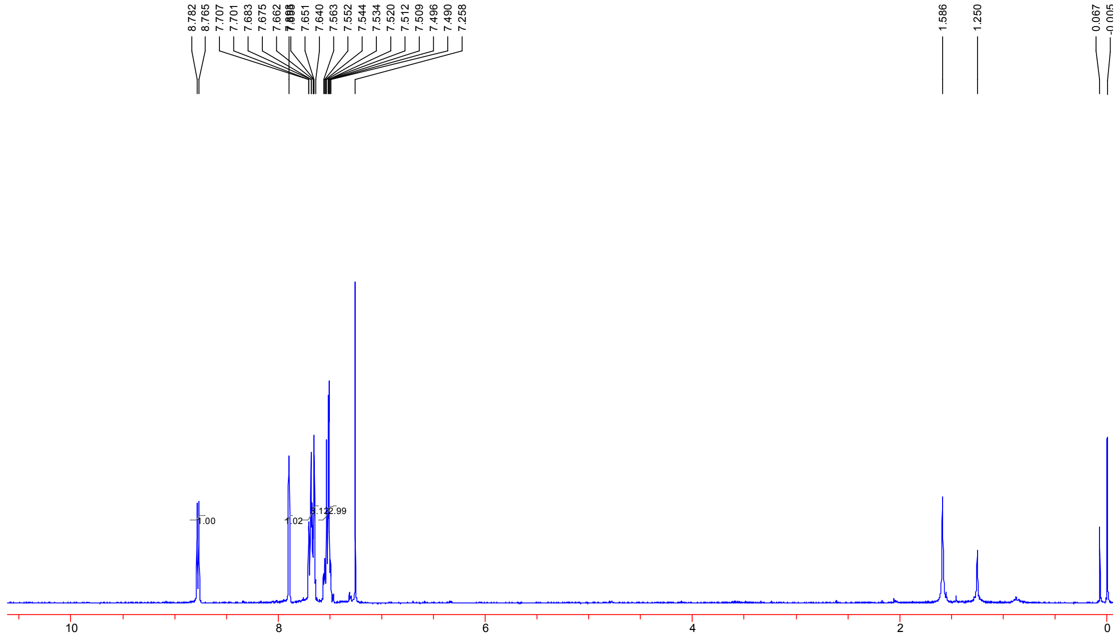
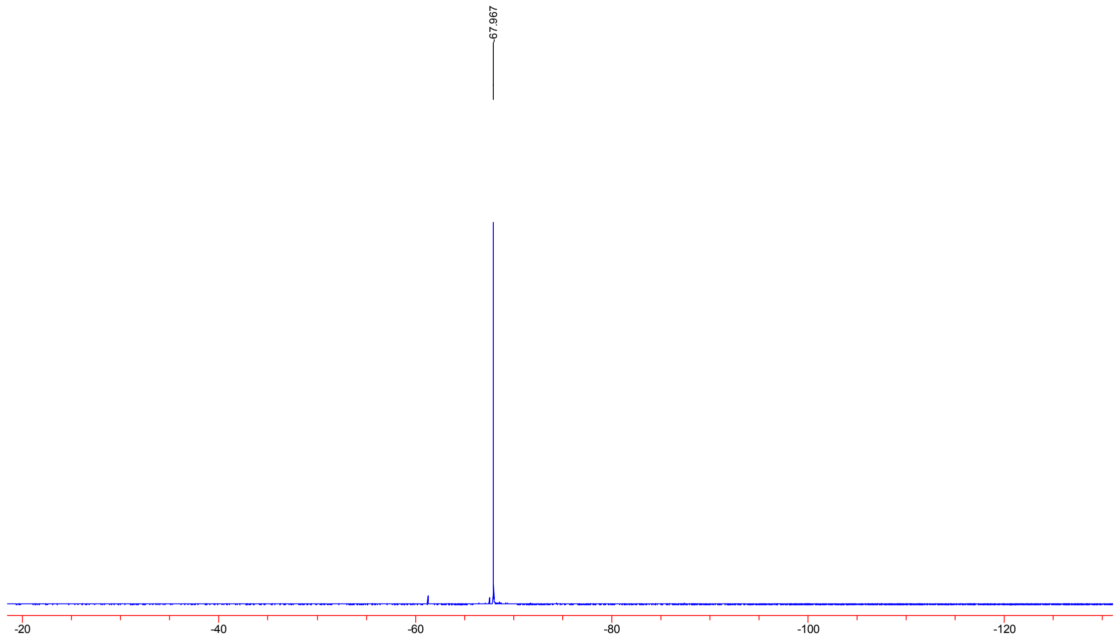
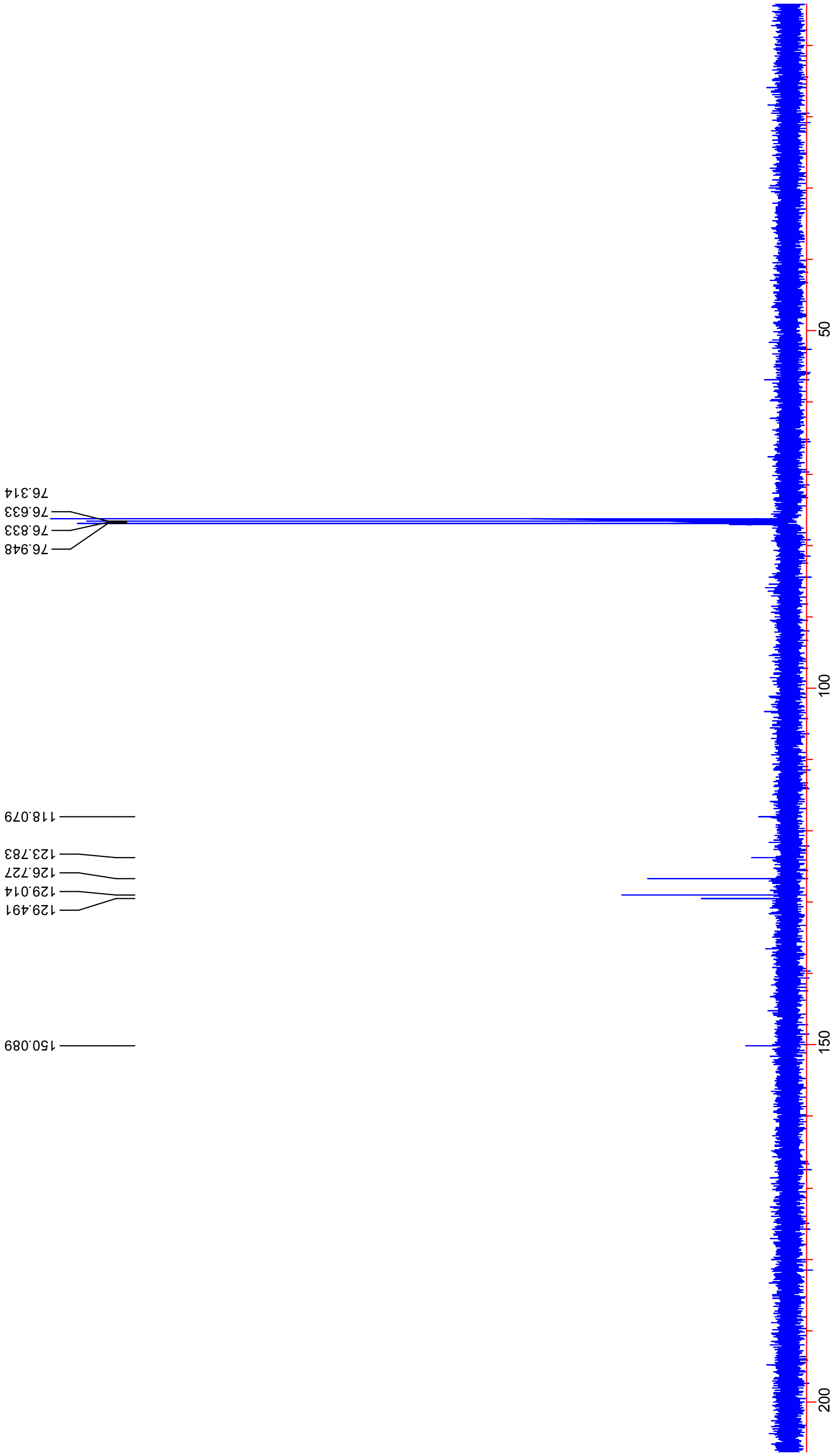
127.666
128.521
135.720
140.002
0
20
40
60
80
100
120
140
160

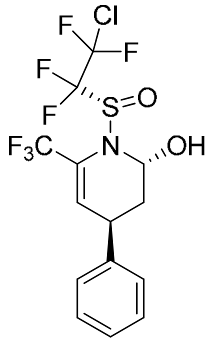

F3C
N

7

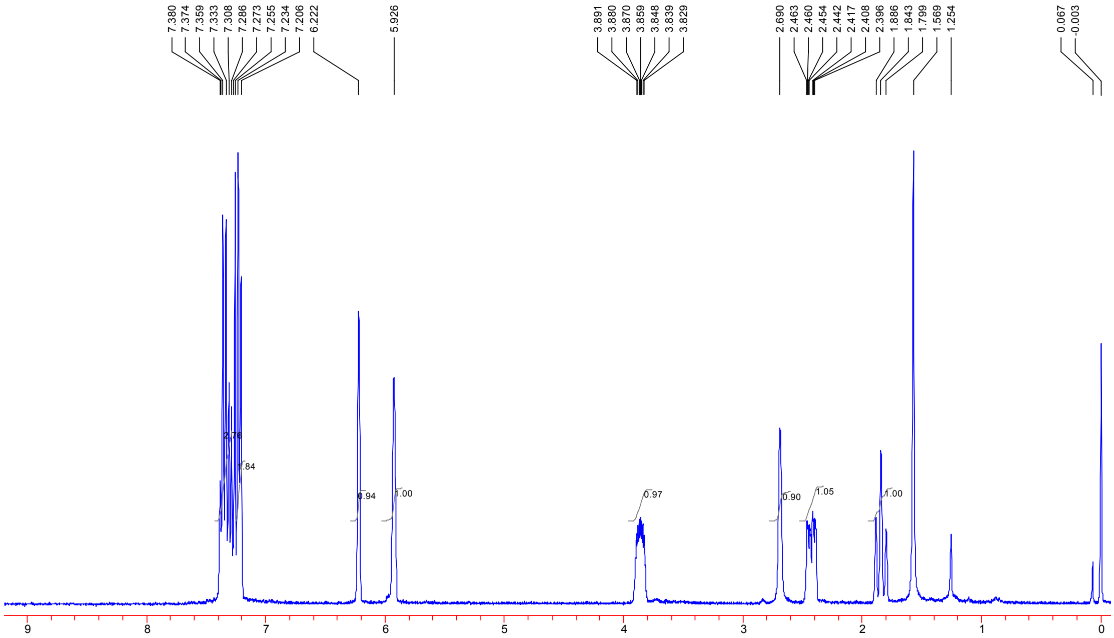

8.782
8.765
7.707
7.701
7.683
7.675
7.662
7.651
7.640
7.563
7.552
7.544
7.534
7.520
7.512
7.509
7.496
7.490
7.258
1.586
1.250
0.067
1.00
1.02
10
8
6
4
2
0

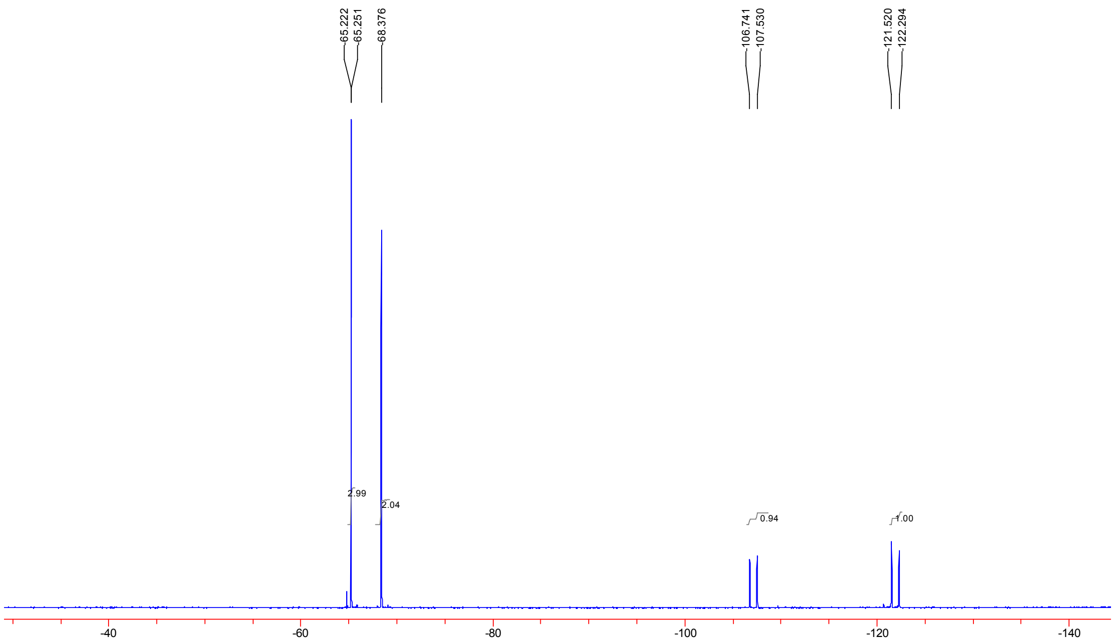

-67.967
-20
-40
-60
-80
-100
-120

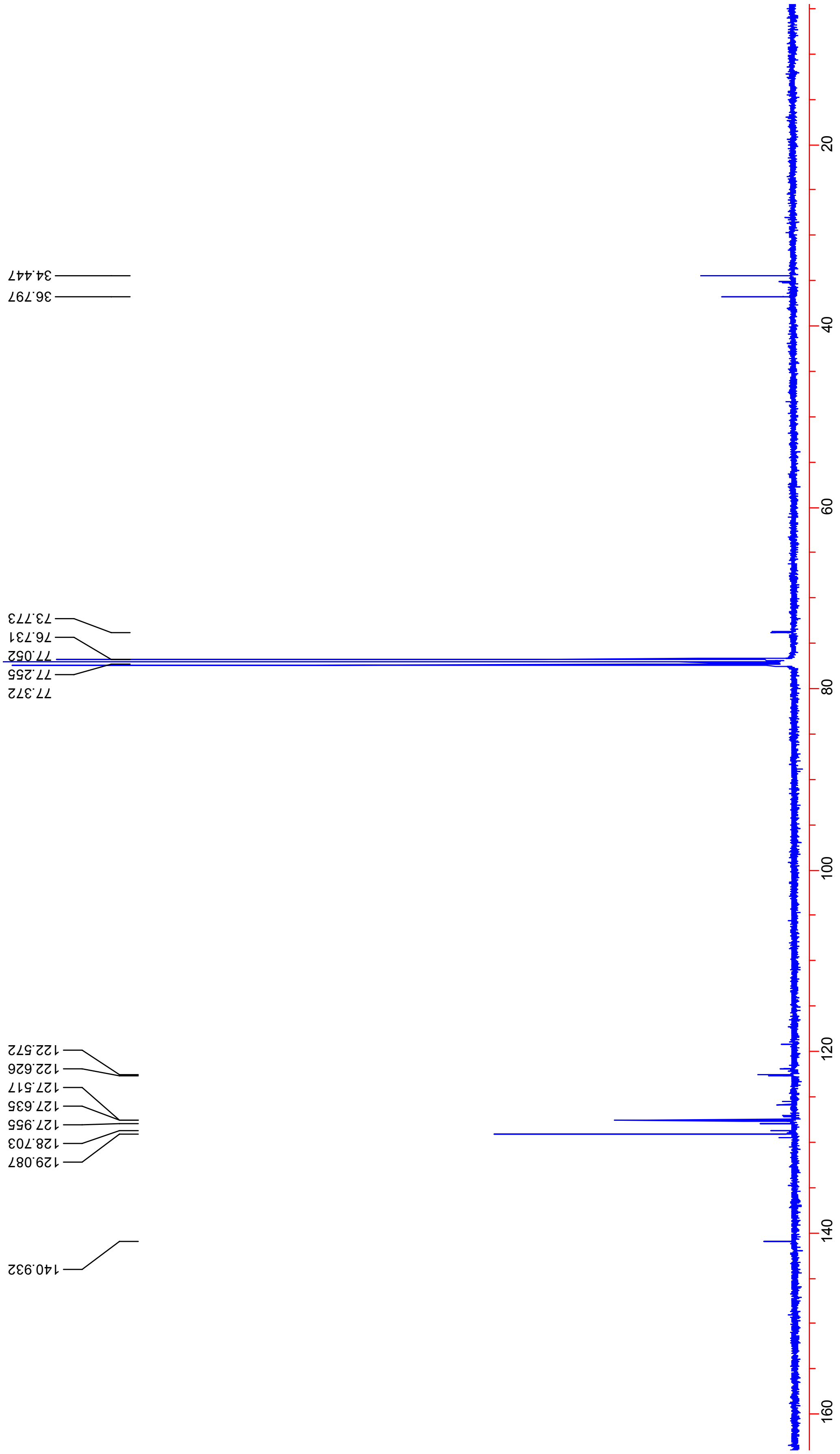

76.314
76.633
76.833
76.948
118.079
123.783
126.727
129.014
129.491
150.089
50
100
150
200



8



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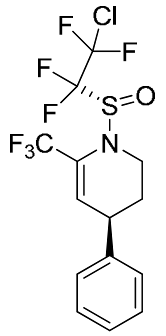
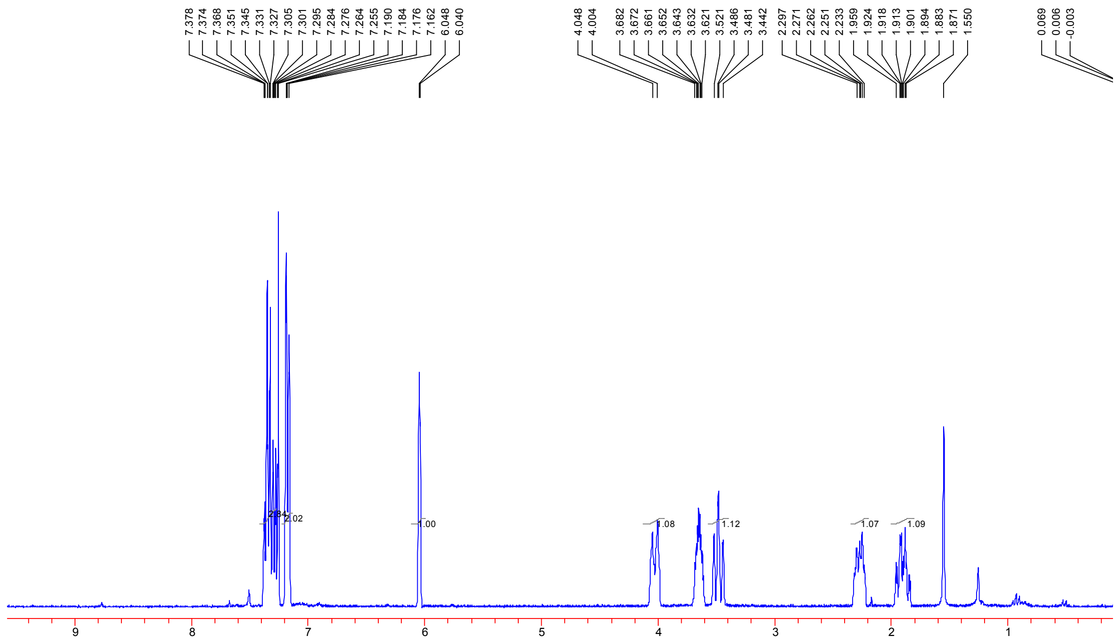
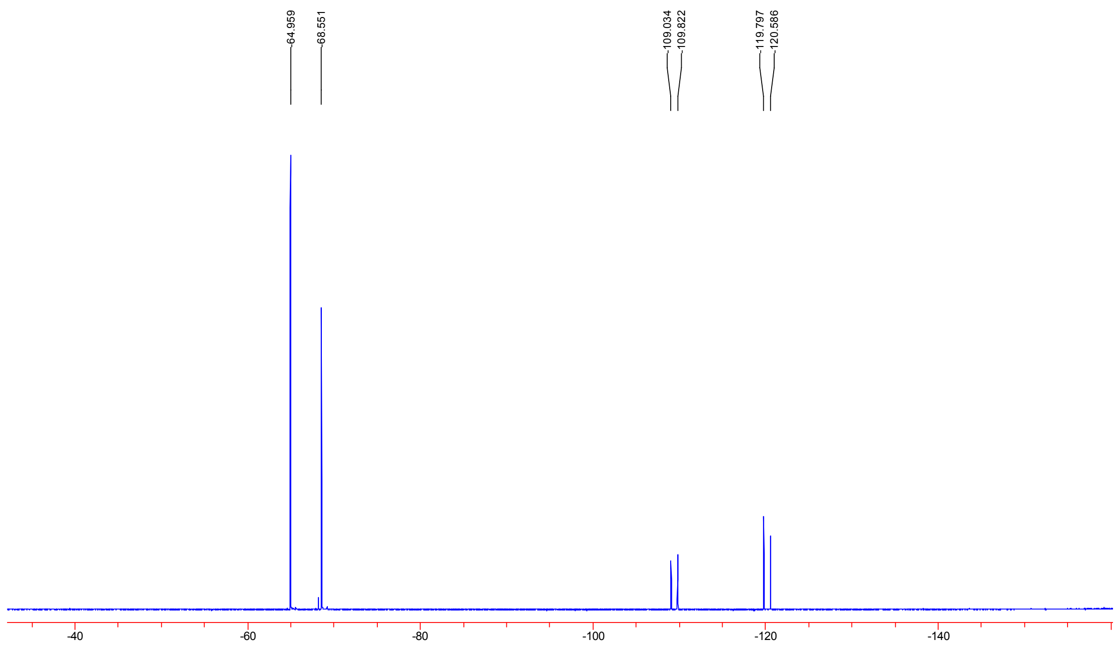
36.797
73.773
76.731
77.052
77.255
77.372
122.572
122.626
127.517
127.635
127.955
128.703
129.087
140.932
20
40
60
80
100
120
140
160


F
Cl
F
F
F
S=O
N
F3C

9


7.378
7.374
7.368
7.351
7.345
7.331
7.327
7.305
7.301
7.295
7.284
7.276
7.264
7.255
7.190
7.184
7.176
7.162
6.048
6.040
4.048
4.004
3.682
3.672
3.661
3.652
3.643
3.632
3.621
3.521
3.486
3.481
3.442
2.297
2.271
2.262
2.251
2.233
1.959
1.924
1.918
1.913
1.901
1.894
1.883
1.871
1.550
0.069
0.006
-0.003
2.84
2.02
1.00
1.08
1.12
1.07
1.09
9
8
7
6
5
4
3
2
1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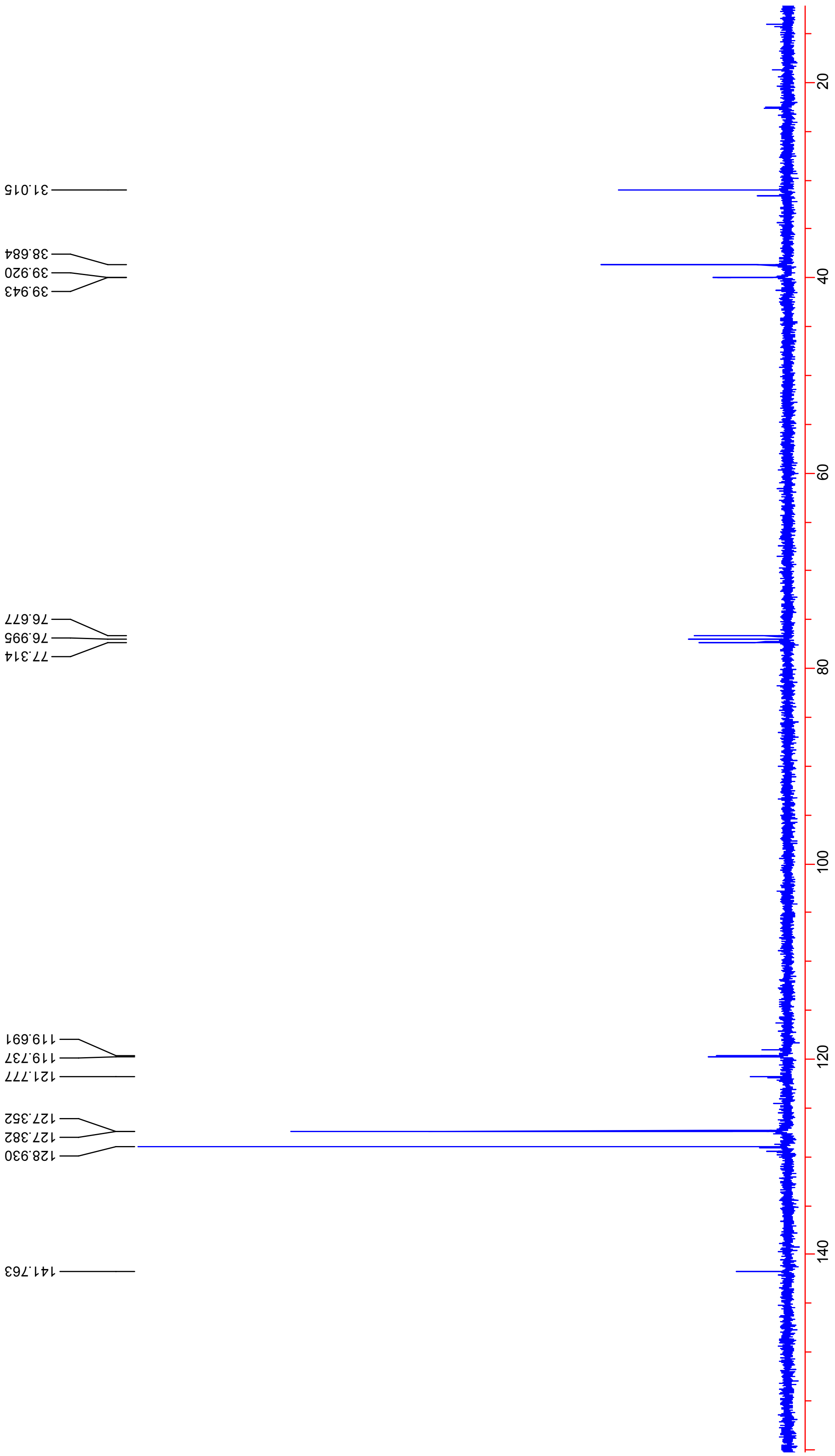
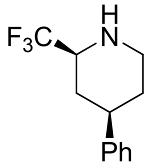
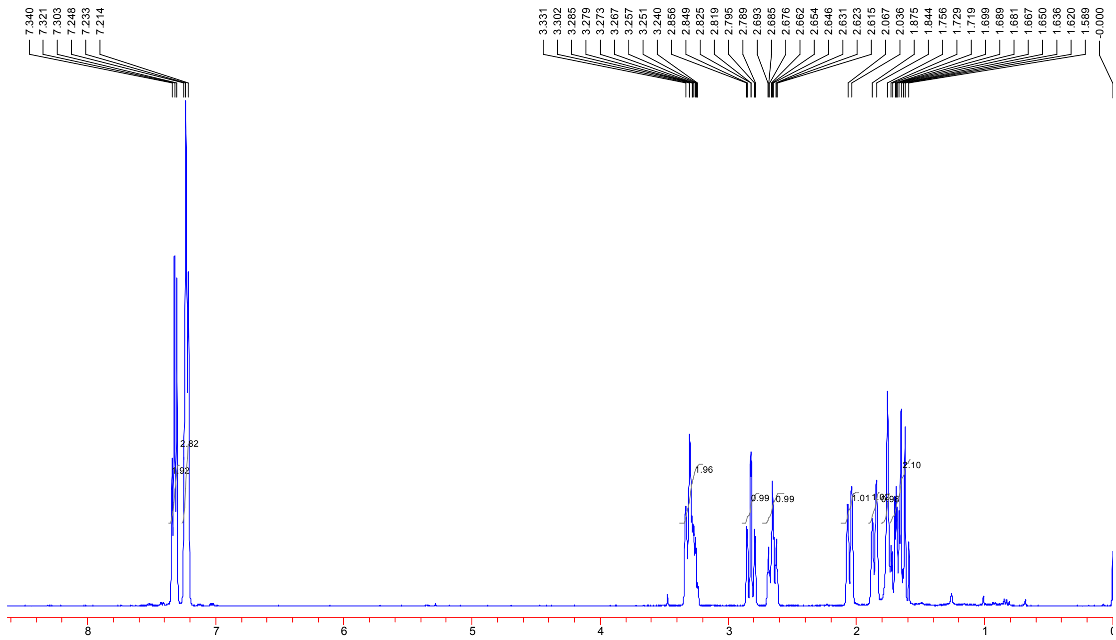
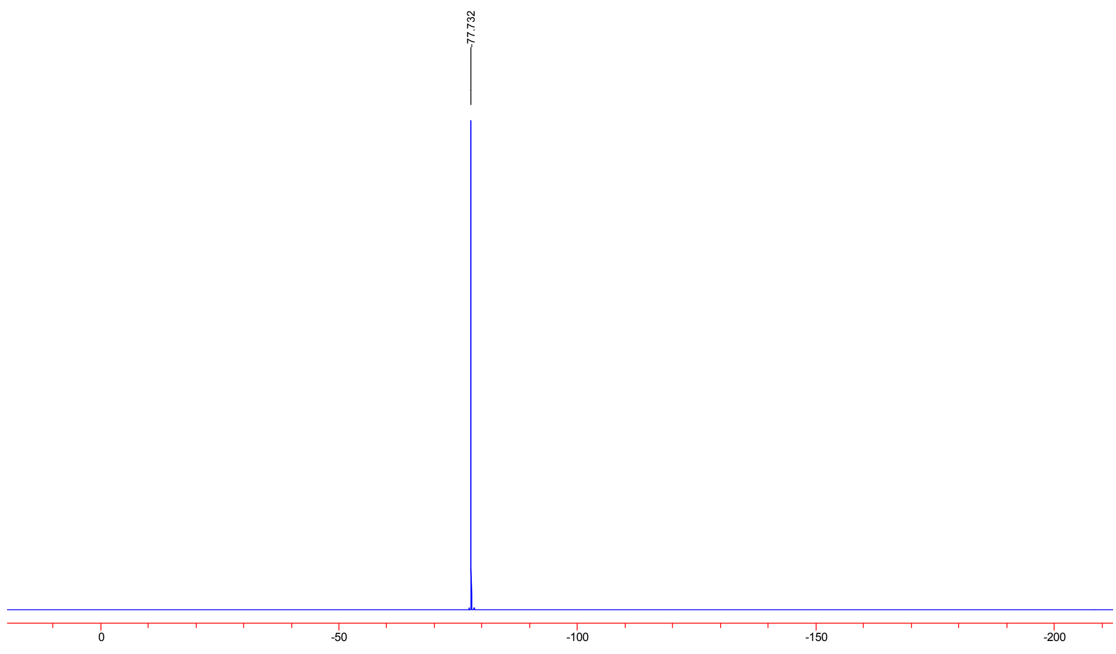
-68.551
-109.034
-109.822
-119.797
-120.586
-40
-60
-80
-100
-120
-140

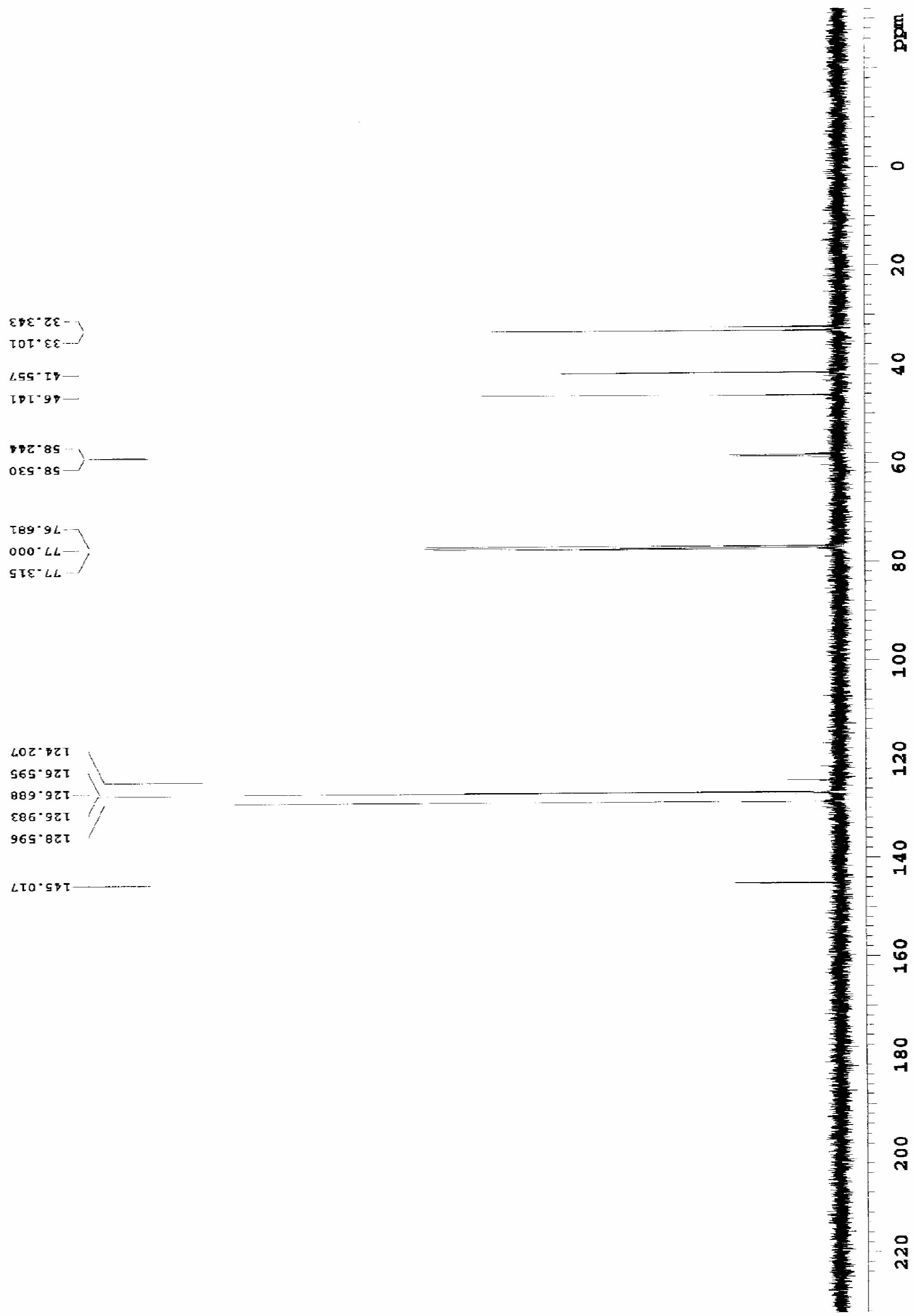

31.015
38.684
39.920
39.943
76.677
76.995
77.314
119.691
119.737
121.777
127.352
127.382
128.930
141.763
20
40
60
80
100
120
140



11






32.343
33.101
41.557
46.141
58.244
58.530
76.681
77.000
77.315
124.207
126.595
126.688
126.983
128.596
145.017
ppm
0
20
40
60
80
100
120
140
160
180
200
220