Supporting Information

N-2,2,2-trifluoroethylisatinketimine as a 1,2-dipolarophile for [3+2]- addition to access optically pure spirothiazolidine oxindoles

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EXPERIMENTAL SECTION

1.1 General Experimental Procedures

Nuclear Magnetic Resonance Spectroscopy: ^{1}H NMR spectra were acquired on Bruker AVIII400 (400 MHz) spectrometer and were referenced to TMS and residual non-deuterated solvent peak in CDCl3 (δ = 7.26). Chemical shifts (δH and δC) are reported in parts per million (ppm), with signal splitting recorded as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet and unresolved peaks (m). Coupling constants (*J*) are mentioned in Hz and are presented as observed. ^{13}C NMR spectra were obtained on Bruker AVIII400 (100 MHz) spectrometers and were referenced to solvent peaks in CDCl3 (δ = 77.0).

Mass Spectrometry: High-resolution mass spectra (HRMS) were recorded by the Thermo Fisher spectrometer using electrospray ionization (ESI^{+}). The parent ion $[M+H]^{+}$, $[M+Na]^{+}$ is calculated to 4 decimal places from the molecular formula, and all values are within a tolerance of 5 ppm.

Specific rotations: Optical rotations were recorded on an Anton Parr MCP100 polarimeter with a path length of 1 dm (using the sodium D line, 589 nm). Specific rotations ($[\alpha]^{D}$) are reported in units of 10^{-1} deg cm^2 g^{-1}. Concentrations are reported in g/mL. Temperatures are reported in °C (typically 25 °C).

Infrared Spectroscopy: Absorption spectra were obtained on a Shimadzu FT-IR spectrometer. Wavelengths of maximum absorbance (vmax) are quoted in wavenumbers (cm ^{1}). Only selected characteristic IR absorption data are provided for each compound.

Single Crystal XRD: Data was collected from the Sophisticated Analytical Instrumental Facility, Indian Institute of Technology Madras- Chennai.

Materials*:*

Unless otherwise stated, all reactions were carried out in oven-dried glassware, using anhydrous reaction solvents. All other commercially available reagents and solvents were either used as received and/or dried and purified before use using standard procedures.

General Procedure A: *Preparation of isatin-derived ketimines:*

1a-g was prepared by following the reported literature procedure.[1]

General Procedure B: *Preparation of racemic molecules **4a – 4w**:*

To an oven-dried vial containing catalyst DABCO **3** (0.05 equiv.), the 1,4-dithaine-2,5-diol **2** (0.7 equiv.) was added followed by the addition of Ketimine **1** (1.0 equiv.) in EtOH (1M) and toluene (0.12 M). The resulting mixture was stirred at RT for 6 hours; the crude product was directly purified by preparative TLC.

General Procedure C: *Preparation of chiral molecules **4a – 4w:***

To an oven dried vial containing catalyst **3e** (0.025 equiv.), the 1,4-dithaine-2,5-diol **2** (0.7 equiv.) was added followed by the addition of Ketimine **1** (1.0 equiv.) in $CHCl_3$ (0.1 M). The resulting mixture was stirred at RT for 19-24 hours; the crude reaction mixture was directly loaded into the column and purified by flash column chromatography using hexane/ EtOAc (10:1) to avoid racemization.

General Procedure D: *Preparation of compound **5a**:*

Compound **5a** was prepared by following the reported literature procedure.[2]

General Procedure E: *Preparation of compound **6a**:*

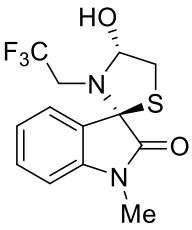
To an oven-dried vial containing **4a** (1 equiv.), MCPBA (5 equiv.) was added in DCM (0.06 M). The resulting mixture was stirred at RT for 24 hours; The reaction mixture was diluted with 15 mL of EtOAc, washed with 10% Na_2SO_4 solution (2×10mL), saturated $NaHCO_3$ solution (2×10 mL), dried over Na_2SO_4 and concentrated in vacuo. Then the crude product was directly purified by column chromatography using hexane/ EtOAc (3:1) as a mobile phase.

References:

1) Wang, X, Huang, D, Wang, K-H, et al. Tin powder promoted synthesis of trifluoroethylamine-containing 3,3′-disubstituted oxindoles. *Appl Organometal Chem*. 2019, **33**, 4995.

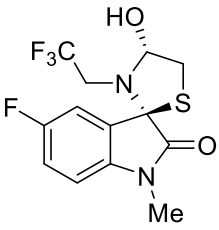
2) P. Cheng, W. Guo, P. Chen, Y. Liu, X. Du and C. Li, Chem. Commun. 2016, **52**, 3418.

(3R,4'R)-4'-hydroxy-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4a):



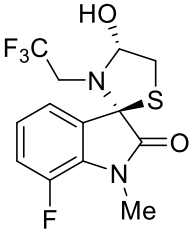
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4a** in 92% yield as a white solid with M. P. 205 - 208 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.645 min (minor), t_R = 12.583 min (major), **$[\alpha]_D^{25}$ = -59.834 ($CHCl_3$, *c* = 0.72 g/100mL, $CHCl_3$ for 95% *ee*)**; IR (neat) ν_{max} 1716,1612, 1269, 1130, 1103, and 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (1H, d, *J* = 7.5 Hz), 7.37 (1H, t, *J* = 7.8 Hz), 7.18 (1H, t, *J* = 7.6 Hz), 6.85 (1H, d, *J* = 7.8 Hz), 5.59 (1H, d, *J* = 11.9 Hz), 5.46 (1H, dd, *J* = 4.6, 11.9 Hz), 3.79 – 3.69 (2H, m), 3.36 (1H, d, *J* = 10.5 Hz), 3.23 (3H, s), 2.46 – 2.36 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.9 (C, N-*C*=O), 143.1 (C), 130.8 (CH), 126.4 (CH), 126.3 (C), 124.4 (CH), 124.4 (CF_3, q, *J* = 277 Hz), 108.9 (CH), 88.1 (CH), 77.1 (C), 44.5 (CH_2, q, *J* = 33 Hz), 40.3 (CH_2), 26.9 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.91; HRMS (ESI) m/z: 341.05420 $[M + Na]^+$, calcd for $C_{13}H_{13}O_2N_2F_3NaS$; Found 341.05293.

(3R,4'R)-5-fluoro-4'-hydroxy-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4b):



Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4b** in 84% yield as a colourless semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 12.711 min (minor), t_R = 15.332 min (major), **$[\alpha]_D^{25}$ = -71.049 ($CHCl_3$, *c* = 0.68 g/100mL, $CHCl_3$ for 99% *ee*)**; IR (neat) ν_{max} 3317, 2924, 1697, 1273, 1149 and 786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (1H, dd, *J* = 2.4, 7.5 Hz), 7.10 – 7.05 (1H, m), 6.79 (1H, dd, *J* = 3.9, 8.6 Hz), 5.51 (1H, d, *J* = 12.0 Hz), 5.44 (1H, dd, *J* = 4.3, 12 Hz), 3.81 – 3.70 (2H, m), 3.36 (1H, d, *J* = 10.4 Hz), 3.23 (3H, s), 2.45 – 2.34 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.7 (C, N-*C*=O), 160.2 (C-F, d, *J* = 242 Hz), 138.9 (C, d, *J* = 2 Hz), 128.4 (C, d, *J* = 7 Hz), 124.3 (CF_3, q, *J* = 276 Hz), 117.4 (CH, d, *J* = 24 Hz), 114.3 (CH, d, *J* = 25 Hz), 109.7 (CH, d, *J* = 8 Hz), 88.3 (CH), 77.1 (C), 44.7 (CH_2, q, *J* = 34 Hz), 40.4 (CH_2), 27.1 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.96, -117.53; HRMS (ESI) m/z: 359.0447 $[M + Na]^+$, calcd for $C_{13}H_{12}O_2N_2F_4NaS$; Found 359.0444.

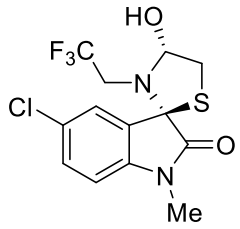
(3R,4'R)-7-fluoro-4'-hydroxy-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4c):



Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4c** in 96% yield as a white solid with M. P. 124 - 127 °C.; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.260 min (minor), t_R = 11.502 min (major), **$[\alpha]_D^{25}$ = -**

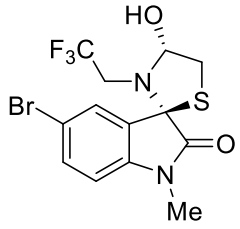
81.941 ($CHCl_3$, *c* = 0.88 g/100mL, $CHCl_3$ for 91% *ee*); IR (neat) ν_{max} 1693, 1477, 1149, 1107, 1014 and 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.25 (1H, m), 7.13 – 7.05 (2H, m), 5.44 (2H, s), 3.80 – 3.70 (2H, m), 3.43 (3H, d, *J* = 2.7 Hz), 3.35 (1H, d, *J* = 10.5 Hz), 2.48 – 2.37 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.7 (C, N-*C*=O), 147.7 (C-F, d, *J* = 244 Hz), 129.7 (C, d, *J* = 9 Hz), 129.4 (C, d, *J* = 2 Hz), 124.9 (CH, d, *J* = 6 Hz), 124.3 (CF_3, q, *J* = 277 Hz), 122.2 (CH, d, *J* = 3 Hz), 118.6 (CH, d, *J* = 19 Hz), 88.2 (CH, d, *J* = 2 Hz), 76.8 (C), 44.6 (CH_2, q, *J* = 33 Hz), 40.4 (CH_2), 29.6 (CH_3, d, *J* = 6 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.89, -135.87; HRMS (ESI) m/z: 359.04478 $[M + Na]^+$, calcd for $C_{13}H_{12}O_2N_2F_4NaS$; Found 359.04514.

(3R,4'R)-5-chloro-4'-hydroxy-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4d):



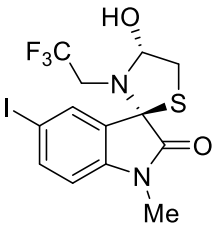
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4d** in 75% yield as a colourless semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.789 min (minor), t_R = 10.995 min (major), **$[\alpha]_D^{25}$ = -42.218 ($CHCl_3$, *c* = 0.56 g/100mL, $CHCl_3$ for 87% *ee*)**; IR (neat) ν_{max} 1689, 1149, 1095, 1018, 817 and 547 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (1H, s), 7.34 (1H, d, *J* = 8.3 Hz), 6.79 (1H, d, *J* = 8 Hz), 5.47 – 5.40 (2H, m), 3.80 – 3.70 (2H, m), 3.36 (1H, d, *J* = 10.4 Hz), 3.23 (3H, s), 2.45 – 2.36 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.5 (C, N-*C*=O), 141.6 (C), 130.8 (CH), 129.9 (C), 128.3 (C), 126.8 (CH), 124.3 (CF_3, q, *J* = 276 Hz), 109.9 (CH), 88.3 (CH), 76.9 (C), 44.7 (CH_2, q, *J* = 34 Hz), 40.5 (CH_2), 27.1 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.96; HRMS (ESI) m/z: 375.01523 $[M + Na]^+$, calcd for $C_{13}H_{12}ClO_2N_2F_3NaS$; Found 375.01559.

(3R,4'R)-5-bromo-4'-hydroxy-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4e):



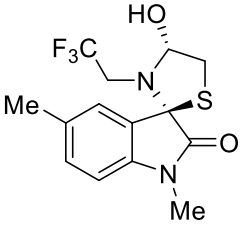
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4e** in 71% yield as a white solid with M. P. 183 - 188 °C.; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 12.777 min (minor), t_R = 15.335 min (major), **$[\alpha]_D^{25}$ = -52.029 ($CHCl_3$, *c* = 0.69 g/100mL, $CHCl_3$ for 87% *ee*)**; IR (neat) ν_{max} 1685, 1608, 1149, 1022, 975 and 813 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (1H, d, *J* = 0.9 Hz), 7.48 (1H, dd, *J* = 2, 8.3 Hz), 6.73 (1H, d, *J* = 8.3 Hz), 5.46 – 5.38 (2H, m), 3.79 – 3.69 (2H, m), 3.35 (1H, d. *J* = 10.4 Hz), 3.21 (3H, s), 2.44 – 2.33 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.3 (C, N-*C*=O), 142.1 (C), 133.7 (CH), 129.6 (CH), 128.6 (C), 124.3 (CF_3, q, *J* = 277 Hz), 117.1 (C), 110.4 (CH), 88.3 (CH), 76.8 (C), 44.7 (CH_2, q, *J* = 34 Hz), 40.5 (CH_2), 27.1 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.89; HRMS (ESI) m/z: 418.96472 $[M + Na]^+$, calcd for $C_{13}H_{12}BrO_2N_2F_3NaS$; Found 418.96350.

(3R,4'R)-4'-hydroxy-5-iodo-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4f):



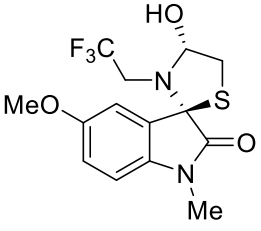
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4f** in 53% yield as a yellowish white solid with M. P. 115 - 119 °C.; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 19.087 min (minor), t_R = 24.236 min (major), **$[\alpha]_D^{25}$ = -17.000 ($CHCl_3$, *c* = 0.10 g/mL, $CHCl_3$ for 88% *ee*)**; IR (neat) ν_{max} 1689, 1604, 1481, 1149, 1103 and 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (1H, s), 7.68 (1H, dd, *J* = 1.6, 8.2 Hz), 6.62 (1H, d, *J* = 8.2 Hz), 5.45 – 5.37 (2H, m), 3.78 – 3.68 (2H, m), 3.34 (1H, d. *J* = 10.4 Hz), 3.20 (3H, s), 2.44 – 2.33 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.1 (C, N-*C*=O), 142.8 (C), 139.6 (CH), 135.3 (CH), 128.6 (C), 124.3 (CF_3, q, *J* = 277 Hz), 110.9 (CH), 88.3 (CH), 86.9 (C), 76.6 (C), 44.7 (CH_2, q, *J* = 34 Hz), 40.5 (CH_2), 27.0 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.97; HRMS (ESI) m/z: 466.95085 $[M + Na]^+$, calcd for $C_{13}H_{12}IO_2N_2F_3NaS$; Found 466.95175.

(3R,4'R)-4'-hydroxy-1,5-dimethyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4g):



Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4g** in 88% yield as a white solid with M. P. 148 - 152 °C.; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.755 min (minor), t_R = 12.956 min (major), **$[\alpha]_D^{25}$ = -56.837 ($CHCl_3$, *c* = 0.87 g/100mL, $CHCl_3$ for 93% *ee*)**; IR (neat) ν_{max} 1681, 1273, 1141, 1103, 1026 and 817 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (1H, s), 7.16 (1H, d, *J* = 7.9 Hz), 6.73 (1H, t, *J* = 7.9 Hz), 5.65 (1H, d, *J* = 11.9 Hz), 5.45 (1H, dd, *J* = 4.6, 11.9 Hz), 3.78 – 3.67 (2H, m), 3.35 (1H, d, *J* = 10.5 Hz), 3.21 (3H, s), 2.46 – 2.38 (1H, m), 2.35 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.8 (C, N-*C*=O), 140.8 (C), 134.3 (C), 131.1 (CH), 127.0 (CH), 126.2 (C), 124.4 (CF_3, q, *J* = 277 Hz), 108.7 (CH), 88.1 (CH), 76.8 (C), 44.5 (CH_2, q, *J* = 33 Hz), 40.3 (CH_2), 26.9 (CH_3), 21.1 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.89; HRMS (ESI) m/z: 355.06985 $[M + Na]^+$, calcd for $C_{14}H_{15}O_2N_2F_3NaS$; Found 355.07025.

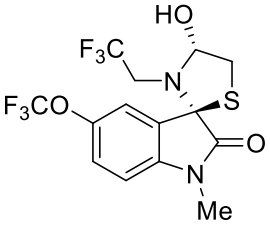
(3R,4'R)-4'-hydroxy-5-methoxy-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4h):



Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4h** in 89% yield as a colourless semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 24.160 min (minor), t_R = 33.342 min (major),

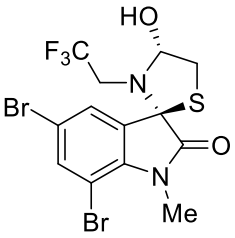
$[\alpha]_D^{25}$ = -57.008 ($CHCl_3$, *c* = 1.40 g/100mL, $CHCl_3$ for 91% *ee*); IR (neat) ν_{max} 3332, 1681, 1496, 1273, 979 and 563 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.08 (1H, d, *J* = 1.6 Hz), 6.89 (1H, d, *J* = 8.8 Hz), 6.75 (1H, d, *J* = 8.8 Hz), 5.68 (1H, d, *J* = 12 Hz), 5.44 (1H, d, *J* = 12 Hz), 3.80 (3H, s), 3.77 – 3.69 (2H, m), 3.35 (1H, d, *J* = 10.4 Hz), 3.20 (3H, s), 2.46 – 2.36 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.6 (C, N-*C*=O), 157.3 (C), 136.4 (C), 127.5 (C), 124.5 (CF_3, q, *J* = 277 Hz), 116.6 (CH), 112.2 (CH), 109.6 (CH), 88.1 (CH), 77.0 (C), 55.9 (CH), 44.5 (CH_2, q, *J* = 33 Hz), 40.3 (CH_2), 26.9 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.82; HRMS (ESI) m/z: 371.06477 $[M + Na]^+$, calcd for $C_{14}H_{15}O_3N_2F_3NaS$; Found 371.06409.

(3R,4'R)-4'-hydroxy-1-methyl-3'-(2,2,2-trifluoroethyl)-5-(trifluoromethoxy)spiro[indoline-3,2'-thiazolidin]-2-one (4i):



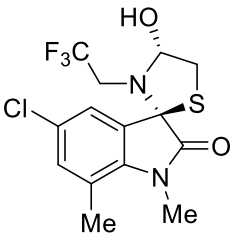
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4i** in 80% yield as a colourless semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.171 min (minor), t_R = 11.492 min (major), **$[\alpha]_D^{25}$ = -53.220 ($CHCl_3$, *c* = 0.29 g100/mL, $CHCl_3$ for 85% *ee*)**; IR (neat) ν_{max} 2924, 1705, 1496, 1257, 1157 and 825 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (1H, s), 7.25 – 7.22 (1H, m), 6.85 (1H, d, *J* = 8.5 Hz), 5.46 – 5.38 (2H, m), 3.81 – 3.71 (2H, m), 3.36 (1H, d. *J* = 10.4 Hz), 3.24 (3H, s), 2.43 – 2.32 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.8 (C, N-*C*=O), 145.9 (C), 141.6 (C), 128.3 (C), 124.2 (CF_3, q, *J* = 277 Hz), 124.1 (CH), 120.4 (OCF_3, q, *J* = 255 Hz), 120.4 (CH), 109.6 (CH), 88.4 (CH), 76.9 (C), 44.7 (CH_2, q, *J* = 34 Hz), 40.5 (CH_2), 21.1 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -58.53, -71.21; HRMS (ESI) m/z: 425.03650 $[M + Na]^+$, calcd for $C_{14}H_{12}O_3N_2F_6NaS$; Found 425.03677.

(3R,4'R)-5,7-dibromo-4'-hydroxy-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4k):



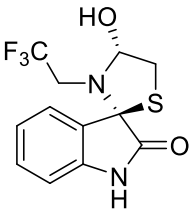
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4k** in 52% yield as a colourless semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.683 min (minor), t_R = 12.082 min (major), **$[\alpha]_D^{25}$ = -76.571 ($CHCl_3$, *c* = 0.35 g/100mL, $CHCl_3$ for 86% *ee*)**; IR (neat) ν_{max} 2924, 1705, 1458, 1149, 1111 and 864 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (1H, d, *J* = 1.9 Hz), 7.54 – 7.53 (1H, m), 5.43 (1H, dd, *J* = 4.4,12.1 Hz), 5.29 (1H, d, *J* = 12.1 Hz), 3.80 – 3.70 (2H, m), 3.58 (3H, s), 3.35 (1H, d, *J* = 10.4 Hz), 2.44 – 2.33 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.9 (C, N-*C*=O), 139.5 (C), 138.2 (CH), 131.6 (C), 128.9 (CH), 124.2 (CF_3, q, *J* = 277 Hz), 117.3 (C), 103.5 (C), 88.4 (CH), 76.2 (C), 44.8 (CH_2, q, *J* = 33 Hz), 40.6 (CH_2), 30.7 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.87; HRMS (ESI) m/z: 496.87523 $[M + Na]^+$, calcd for $C_{13}H_{11}O_2N_2Br_2F_3NaS$; Found 496.87429.

(3R,4'R)-5-chloro-4'-hydroxy-1,7-dimethyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4l):



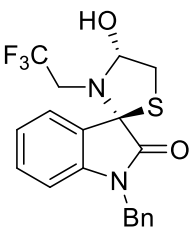
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4l** in 67% yield as a white solid with M. P. 154 - 157 °C.; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.115 min (minor), t_R = 12.256 min (major), **$[\alpha]_D^{25}$ = -73.802 ($CHCl_3$, *c* = 0.43 g/100mL, $CHCl_3$ for 74% *ee*)**; IR (neat) ν_{max} 1701, 1462, 1273, 1107, 1087, and 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (1H, s), 7.08 (1H, s), 5.52 (1H, d, *J* = 11.9 Hz), 5.43 (1H, dd, *J* = 4.4, 11.9 Hz), 3.77 – 3.67 (2H, m), 3.47 (3H, s), 3.34 (1H, d, *J* = 10.4 Hz), 2.53 (3H, s), 2.45 – 2.34 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 178.2 (C, N-*C*=O), 139.3 (C), 134.0 (CH), 129.5 (CH), 129.1 (CH), 124.6 (CH), 124.3 (CF_3, q, *J* = 277 Hz), 122.2 (C), 88.2 (CH), 76.4 (C), 44.6 (CH_2, q, *J* = 34 Hz), 40.5 (CH_2), 30.4 (CH_3), 18.6 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.85; HRMS (ESI) m/z: 389.03088 $[M + Na]^+$, calcd for $C_{14}H_{14}O_2N_2ClF_3NaS$; Found 389.03033.

(3R,4'R)-4'-hydroxy-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4m):



Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4m** in 56% yield as a yellow semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 18.082 min (minor), t_R = 23.175 min (major), **$[\alpha]_D^{25}$ = -85.299 ($CHCl_3$, *c* = 0.77 g/100mL, $CHCl_3$ for 89% *ee*)**; IR (neat) ν_{max} 3224, 2924, 1705, 1149, 1111 and 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (1H, s), 7.47 (1H, d, *J* = 7.5 Hz), 7.31 (1H, t, *J* = 7.7 Hz), 7.15 (1H, d, *J* = 7.6 Hz), 6.89 (1H, d, *J* = 7.8 Hz), 5.48 (1H, dd, *J* = 4.4, 11.9 Hz), 5.40 (1H, d, *J* = 12 Hz), 3.82 – 3.72 (2H, m), 3.36 (1H, d, *J* = 10.5 Hz), 2.59 – 2.48 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 179.7 (C, N-*C*=O), 140.1 (C), 130.8 (CH), 126.9 (C), 126.8 (C), 124.4 (CH), 124.4 (CF_3, q, *J* = 277 Hz), 110.6 (CH), 88.1 (CH), 66.5 (C), 44.5 (CH_2, q, *J* = 34 Hz), 40.3 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.87; HRMS (ESI) m/z: 327.03855 $[M + Na]^+$, calcd for $C_{12}H_{11}O_2N_2F_3NaS$; Found 327.03732.

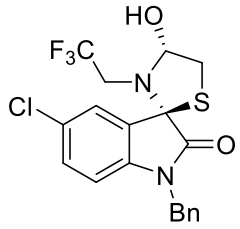
(3R,4'R)-1-benzyl-4'-hydroxy-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4n):



Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4n** in 82% yield as a white solid with M. P. 131 - 135 °C.; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.999 min (minor), t_R = 13.890 min (major), **$[\alpha]_D^{25}$ = -25.280 ($CHCl_3$, *c* = 0.73 g/100mL, $CHCl_3$ for 89% *ee*)**; IR (neat) ν_{max} 1685, 1612, 1276, 1138, 1107, and 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (1H, d, *J* = 7.4 Hz), 7.36 – 7.23 (6H, m), 7.13 (1H, t, *J* = 8 Hz), 6.74 (1H, d, *J* = 7.8 Hz), *5*.62 (1H, d, *J* = 12 Hz), 5.49 (1H, dd, *J* = 4.4, 11.9

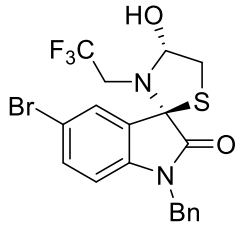
Hz), 4.94 (1H, d, *J* = 15.5 Hz), 4.83 (1H, d, *J* = 15.5 Hz), 3.84 – 3.73 (2H, m), 3.39 (1H, d, *J* = 10.5 Hz), 2.50 – 2.39 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 178.2 (C, N-*C*=O), 142.3 (C), 134.9 (C), 130.8 (CH), 129.1 (2CH), 128.2 (CH), 127.3 (2CH), 126.5 (CH), 126.2 (C), 124.4 (CH), 124.4 (CF_3, q, *J* = 277 Hz), 109.9 (C), 88.1 (CH), 77.2 (C), 44.5 (CH_2), 44.5 (CH_2, q, *J* = 33 Hz), 40.3 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.84; HRMS (ESI) m/z: 417.08550 $[M + Na]^+$, calcd for $C_{19}H_{17}O_2N_2F_3NaS$; Found 417.08658.

(3R,4'R)-1-benzyl-5-chloro-4'-hydroxy-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4o):



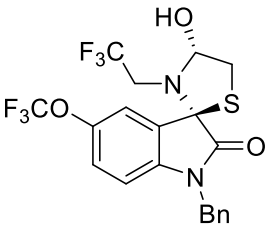
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4o** in 72% yield as a yellow semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.368 min (minor), t_R = 12.620 min (major), **$[\alpha]_D^{25}$ = -45.308 ($CHCl_3$, *c* = 1.45 g/100mL, $CHCl_3$ for 89% *ee*)**; IR (neat) ν_{max} 3340, 2924, 1697, 1481, 1149, and 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.46 (1H, m), 7.37 – 7.26 (4H, m), 7.24 (1H, br s), 7.21 (1H, dd, *J* = 2.2, 8.4 Hz), 6.66 (1H, d, *J* = 8.4 Hz), 5.57 – 5.44 (2H, m), 4.93 (1H, d, *J* = 15.5 Hz), 4.82 (1H, d, *J* = 15.5 Hz), 3.85 – 3.74 (2H, m), 3.39 (1H, d, *J* = 10.5 Hz), 2.47 – 2.37 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.8 (C, N-*C*=O), 140.7 (C), 134.4 (C), 130.8 (CH), 130.2 (C), 129.2 (2CH), 128.4 (C), 128.3 (CH), 127.2 (2CH), 126.8 (CH), 124.3 (CF_3, q, *J* = 277 Hz), 111.0 (CH), 88.3 (CH), 76.9 (C), 44.7 (CH_2), 44.6 (CH_2, q, *J* = 33 Hz), 40.5 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.89; HRMS (ESI) m/z: 451.04653 $[M + Na]^+$, calcd for $C_{19}H_{16}O_2N_2ClF_3NaS$; Found 451.04450.

(3R,4'R)-1-benzyl-5-bromo-4'-hydroxy-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4p):



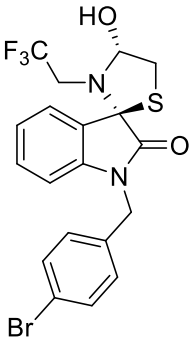
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4p** in 63%yield as a yellow semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.635 min (minor), t_R = 12.967 min (major), **$[\alpha]_D^{25}$ = -38.957 ($CHCl_3$, *c* = 0.93 g/100mL, $CHCl_3$ for 85% *ee*)**; IR (neat) ν_{max} 2924, 1705, 1473, 1273, 1149, and 810 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (1H, s), 7.37 – 7.28 (5H, m), 7.24 (1H, br s), 6.61 (1H, d, *J* = 8.4 Hz), 5.50 – 5.43 (2H, m), 4.87 (2H, q, *J* = 15.5, 43.1 Hz), 3.84 – 3.76 (2H, m), 3.39 (1H, d, *J* = 10.4 Hz), 2.48 – 2.37 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.6 (C, N-*C*=O), 141.2 (C), 134.4 (C), 133.6 (CH), 129.6 (CH), 129.2 (2CH), 128.5 (C), 128.4 (C), 127.2 (2CH), 124.3 (CF_3, q, *J* = 277 Hz), 117.2 (C), 111.5 (CH), 88.3 (CH), 76.9 (C), 44.6 (CH_2, q, *J* = 34 Hz), 44.6 (CH_2), 40.5 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.89; HRMS (ESI) m/z: 494.99602 $[M + Na]^+$, calcd for $C_{19}H_{16}O_2N_2BrF_3NaS$; Found 494.99367.

(3R,4'R)-1-benzyl-4'-hydroxy-3'-(2,2,2-trifluoroethyl)-5-(trifluoromethoxy)spiro[indoline-3,2'-thiazolidin]-2-one (4q):



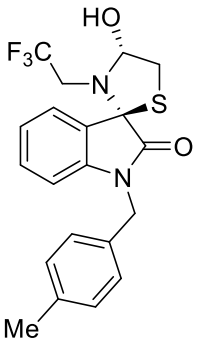
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4q** in 75% yield as a pale yellow solid with M. P. 134 - 137 °C.; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 8.787 min (minor), t_R = 10.142 min (major), **$[\alpha]_D^{25}$ = -30.400 ($CHCl_3$, *c* = 0.12 g/100mL, $CHCl_3$ for 89% *ee*)**; IR (neat) ν_{max} 1693, 1489, 1249, 1145, 1080, and 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (4H, m), 7.27 (2H, d, *J* = 8.4 Hz), 7.11 (1H, d, *J* = 8.4 Hz), 6.73 (1H, d, *J* = 8.5 Hz), 5.51 – 5.42 (2H, m), 4.96 (1H, d, *J* = 15.5 Hz), 4.82 (1H, d, *J* = 15.5 Hz), 3.87 – 3.77 (2H, m), 3.40 (1H, d, *J* = 10.4 Hz), 2.46 – 2.35 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 178.1 (C, N-*C*=O), 145.9 (C), 140.7 (C), 134.4 (C), 129.2 (2CH), 128.4 (CH), 128.4 (C), 127.3 (2CH), 124.2 (CF_3, q, *J* = 276 Hz), 123.9 (CH), 120.4 (CF_3, q, *J* = 256 Hz), 120.3 (CH), 110.6 (CH), 88.4 (CH), 76.9 (C), 44.7 (CH_2), 44.6 (CH_2), 40.5 (CH_2, q, *J* = 34 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -58.49, -71.13; HRMS (ESI) m/z: 501.06780 [M + Na]$^+$, calcd for $C_{20}H_{16}O_3N_2F_6NaS$; Found 501.06880.

(3R,4'R)-1-(4-bromobenzyl)-4'-hydroxy-3'-(2,2,2-trifluoroethyl)-5-(trifluoromethoxy)spiro[indoline-3,2'-thiazolidin]-2-one (4r):



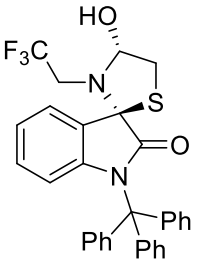
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4r** in 56% yield as a yellow semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex I-A column (hexane/EtOAc = 85:15, flow rate 1 mL/min, λ = 254 nm), t_R = 7.835 min (minor), t_R = 11.093 min (major), **$[\alpha]_D^{25}$ = -46.402 ($CHCl_3$, *c* = 1.20 g/100mL, $CHCl_3$ for 93% *ee*)**; IR (neat) ν_{max} 2924, 1697, 1465, 1342, 1149, and 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.46 (3H, m), 7.28 – 7.24 (1H, m), 7.19 – 7.13 (3H, m), 6.71 (1H, d, *J* = 7.8 Hz), 5.56 – 5.47 (2H, m), 4.92 (1H, d, *J* = 15.6 Hz), 4.74 (1H, d, *J* = 15.6 Hz), 3.83 – 3.73 (2H, m), 3.39 (1H, d, *J* = 10.6 Hz), 2.48 – 2.37 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 178.2 (C, N-*C*=O), 141.9 (C), 133.9 (C), 132.3 (2CH), 130.8 (CH), 129.0 (2CH), 126.6 (CH), 126.2 (C), 124.6 (CH), 123.9 (CF_3, q, *J* = 277 Hz), 122.2 (C), 109.7 (CH), 88.1 (CH), 77.1 (C), 44.5 (CH_2, q, *J* = 34 Hz), 43.9 (CH_2), 40.3 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.78; HRMS (ESI) m/z: 494.9960 [M + Na]$^+$, calcd for $C_{19}H_{16}O_2N_2BrF_3NaS$; Found 494.99513.

(3R,4'R)-4'-hydroxy-1-(4-methylbenzyl)-3'-(2,2,2-trifluoroethyl)-5-(trifluoromethoxy)spiro[indoline-3,2'-thiazolidin]-2-one (4s):



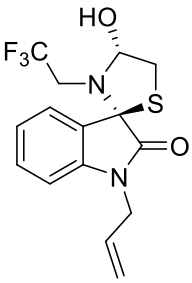
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4s** in 72% yield as a pale yellow solid with M. P. 118 - 123 °C.; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 11.040 min (minor), t_R = 13.563 min (major), **$[\alpha]_D^{25}$ = -43.348 ($CHCl_3$, *c* = 1.06 g/100mL, $CHCl_3$ for 86% *ee*)**; IR (neat) ν_{max} 1681, 1612, 1276, 1138, 1107, and 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (1H, d, *J* = 7.4 Hz), 7.26 – 7.22 (1H, m), 7.18 – 7.10 (5H, m), 6.71 (1H, d, *J* = 7.8 Hz), 5.64 (1H, d, *J* = 12 Hz), 5.48 (1H, dd, *J* = 4.9, 11.9 Hz), 4.84 (2H, q, *J* = 18.2 Hz), 3.83 – 3.72 (2H, m), 3.39 (1H, d, *J* = 10.5 Hz), 2.48 – 2.37 (1H, m), 2.31 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 178.1 (C, N-*C*=O), 142.3 (C), 137.9 (C), 131.8 (C), 130.7 (CH), 129.7 (2CH), 127.3 (2CH), 126.4 (CH), 126.2 (C), 124.4 (CF_3, q, *J* = 277 Hz),124.4 (CH), 109.9 (CH), 88.1 (CH), 77.0 (C), 44.4 (CH_2, q, *J* = 34 Hz), 44.3 (CH_2), 40.3 (CH_2), 21.1 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.84; HRMS (ESI) m/z: 431.10115 $[M + Na]^+$, calcd for $C_{20}H_{19}O_2N_2F_3NaS$; Found 431.09830.

(3R,4'R)-4'-hydroxy-3'-(2,2,2-trifluoroethyl)-1-tritylspiro[indoline-3,2'-thiazolidin]-2-one (4t):



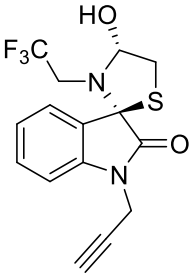
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4t** in 39% yield as a yellow semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.080 min (minor), t_R = 13.494 min (major), **$[\alpha]_D^{25}$ = -4.047 ($CHCl_3$, *c* = 0.96 g/100mL, $CHCl_3$ for 59% *ee*)**; IR (neat) ν_{max} 3348, 2924, 1705, 1458, 1149, 1111, and 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.41 (8H, m), 7.29 – 7.27 (3H, m), 7.25 – 7.19 (5H, m), 7.03 (1H, t, *J* = 7.5 Hz), 6.96 (1H, t, *J* = 7.9 Hz), 6.22 (1H, d, *J* = 8.0 Hz), 5.38 (1H, dd, *J* = 4.3, 11.7 Hz), 5.28 (1H, d, *J* = 11.7 Hz), 3.72 (1H, dd, *J* = 4.6, 10.5 Hz), 3.39 – 3.28 (2H, m), 1.80 – 1.69 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 179.9 (C, N-*C*=O), 143.1 (C), 141.6 (C), 129.4 (CH), 129.3 (CH), 128.8 (6CH), 127.9 (6CH), 127.5 (3C), 127.2 (3CH), 125.8 (CH), 124.2 (CF_3, q, *J* = 277 Hz), 123.9 (CH), 116.1 (CH), 87.6 (CH), 76.9 (C), 43.9 (CH_2, q, *J* = 33 Hz), 44.5 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.92; HRMS (ESI) m/z: 569.1481 $[M + Na]^+$, calcd for $C_{31}H_{25}O_2N_2F_3NaS$; Found 569.14981.

(3R,4'R)-1-allyl-4'-hydroxy-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4u):



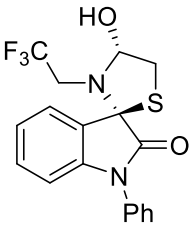
Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4u** in 87% yield as a yellow semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 0.5 mL/min, λ = 254 nm), t_R = 11.102 min (minor), t_R = 12.056 min (major), **$[\alpha]_D^{25}$ = -80.574 ($CHCl_3$, *c* = 0.71 g/100mL, $CHCl_3$ for 63% *ee*)**; IR (neat) ν_{max} 3332, 2924, 1697, 1612, 1149, and 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (1H, d, *J* = 7.5 Hz), 7.33 (1H, d, *J* = 7.8 Hz), 7.16 (1H, t, *J* = 7.5 Hz), 6.84 (1H, d, *J* = 7.8 Hz), 5.87 – 5.78 (1H, m), 5.56 (1H, d, *J* = 12.0 Hz), 5.47 (1H, dd, *J* = 4.5, 12.0 Hz), 5.28 – 5.21 (2H, m), 4.34 – 4.30 (2H, m), 3.80 – 3.70 (2H, m), 3.37 (1H, d, *J* = 10.5 Hz), 2.48 – 2.37 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.7 (C, N-*C*=O), 142.3 (C), 130.7 (CH), 130.4 (CH), 126.5 (CH), 126.2 (C), 124.4 (CH), 124.4 (CF_3, q, *J* = 276 Hz), 118.4 (CH_2),109.8 (CH), 88.1 (CH), 77.1 (C), 44.5 (CH_2, q, *J* = 34 Hz), 42.9 (CH_2), 40.3 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.84; HRMS (ESI) m/z: 367.0698 $[M + Na]^+$, calcd for $C_{15}H_{15}O_2N_2F_3NaS$; Found 367.0697.

(3R,4'R)-4'-hydroxy-1-(prop-2-yn-1-yl)-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4v):



Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4v** in 83% yield as a yellow semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 16.024 min (minor), t_R = 19.021 min (major), **$[\alpha]_D^{25}$ = -38.680 ($CHCl_3$, *c* = 0.69 g/100mL, $CHCl_3$ for 89% *ee*)**; IR (neat) ν_{max} 3294, 2924, 1705, 1612, 1342, 1149, and 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (1H, d, *J* = 7.6 Hz), 7.39 (1H, d, *J* = 7.6 Hz), 7.21 (1H, t, *J* = 8.4 Hz), 7.05 (1H, d, *J* = 7.6 Hz), 5.46 (2H, dd, *J* = 12, 12 Hz), 4.55 (1H, d, *J* = 15.2 Hz), 4.43 (1H, d, *J* = 15.2 Hz), 3.78 – 3.71 (2H, m), 3.35 (1H, d, *J* = 10.8 Hz), 2.25 – 2.41 (1H, m), 2.29 (1H, t, *J* = 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.3 (C, N-*C*=O), 141.3 (C), 130.8 (C), 126.6 (CH), 126.2 (C), 124.8 (CH), 124.3 (CF_3, q, *J* = 277 Hz), 109.9 (CH), 88.1 (CH), 76.9 (C), 75.9 (CH), 73.3 (CH), 44.4 (CH_2, q, *J* = 34 Hz), 40.3 (CH_2), 30.0 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.89; HRMS (ESI) m/z: 365.05420 $[M + Na]^+$, calcd for $C_{15}H_{13}O_2N_2F_3NaS$; Found 365.05363.

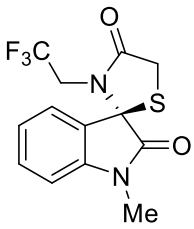
(3R,4'R)-4'-hydroxy-1-phenyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidin]-2-one (4w):



Prepared by following general procedure **C** purified by column chromatography using hexane and isolated product **4w** in 67% yield as a colourless semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 18.229 min (major), t_R = 22.141 min (minor), **$[\alpha]_D^{25}$ = -69.230 ($CHCl_3$,**

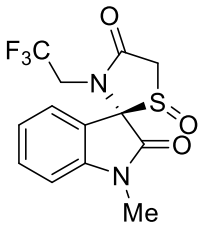
***c* = 1.14 g/100mL, $CHCl_3$ for 93% *ee*)**; IR (neat) ν_{max} 3363, 1705, 1273, 1141, 1080 and 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.53 (3H, m), 7.48 – 7.43 (1H, m), 7.41 – 7.38 (2H, m), 7.30 (1H, t, *J* = 7.7 Hz), 7.21 (1H, t, *J* = 7.5 Hz), 6.81 (1H, d, *J* = 7.9 Hz), 5.51 (1H, dd, *J* = 4.5, 12.1 Hz), 5.42 (1H, d, *J* = 12.1 Hz), 3.89 – 3.78 (2H, m), 3.39 (1H, d, *J* = 10.6 Hz), 2.67 – 2.57 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 177.6 (C, N-*C*=O), 143.3 (C), 133.4 (C), 130.8(CH), 129.9 (2CH), 128.9 (CH), 126.9 (CH), 126.2 (2CH), 126.0 (C), 124.8 (CH), 124.4 (CF_3, q, *J* = 277 Hz), 110.3 (CH), 88.2 (CH), 77.3 (C), 44.6 (CH_2, q, *J* = 33 Hz), 40.3 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.75; HRMS (ESI) m/z: 403.0698 $[M + Na]^+$, calcd for $C_{18}H_{15}O_2N_2F_3NaS$; Found 403.0703.

(R)-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidine]-2,4'-dione (5a):



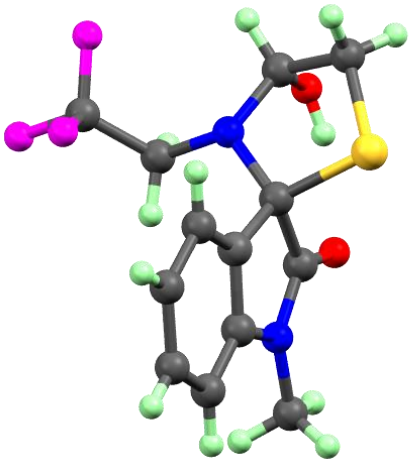
Prepared by following general procedure **D** purified by column chromatography using hexane and isolated product **5a** in 75% yield as a colourless semi solid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Phenomenex cellulose-5 column (hexane/EtOAc = 85:15, flow rate 1 mL/min, λ = 254 nm), t_R = 18.349 min (major), t_R = 19.416 min (minor), **$[\alpha]_D^{25}$ = +3.474 ($CHCl_3$, *c* = 0.17 g/100mL, $CHCl_3$ for 92% *ee*)**; IR (neat) ν_{max} 2924, 1728, 1612, 1465, 1373, 1157, and 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (1H, t, *J* = 7.8 Hz), 7.38 (1H, d, *J* = 7.4 Hz), 7.19 (1H, q, *J* = 7.6 Hz), 6.91 (1H, d, *J* = 7.9 Hz), 4.31 (1H, d, *J* = 15.3 Hz), 3.96 – 3.86 (1H, m), 3.72 (1H, d, *J* = 15.3 Hz), 3.59 – 3.49 (1H, m), 3.21 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 174.2 (C=O), 173.2 (C, N-*C*=O), 144.1 (C), 132.1 (CH), 126.5 (CH), 123.8 (CH), 122.9 (CF_3, q, *J* = 278 Hz), 122.2 (C), 109.4 (CH), 68.2 (C), 43.7 (CH_2, q, *J* = 36 Hz), 32.3 (CH_2), 26.6 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -69.02; HRMS (ESI) m/z: 33.03855 $[M + Na]^+$, calcd for $C_{13}H_{11}O_2N_2F_3NaS$; Found 339.03867.

(1'S,3R)-1-methyl-3'-(2,2,2-trifluoroethyl)spiro[indoline-3,2'-thiazolidine]-2,4'-dione 1'-oxide (6a):



Prepared by following general procedure **E** purified by column chromatography using hexane and isolated product **6a** in 25% yield as a pale-yellow semi solid. **$[\alpha]_D^{25}$ = -84.667 ($CHCl_3$, *c* = 0.15 g/100mL, $CHCl_3$)**; IR (neat) ν_{max} 1720, 1612, 1473, 1373, 1265 and 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (1H, t, *J* = 7.8 Hz), 7.36 (1H, d, *J* = 8.3 Hz), 7.20 – 7.23 (1H, m), 7.03 (1H, d, *J* = 7.9 Hz), 4.66 – 4.39 (1H, m), 4.41 (1H, d, *J* = 16.3 Hz), 3.69 (1H, d, *J* = 16.3 Hz), 3.36 – 3.29 (1H, m), 3.26 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 170.6 (C, N-*C*=O), 168.9 (C, N-*C*=O), 144.2 (C), 132.9 (CH), 127.4 (CH), 124.5 (CH), 123.0 (CF_3, q, *J* = 278 Hz), 115.8 (C), 109.9 (CH), 83.8 (C), 53.2 (CH_2), 43.3 (CH_2, q, *J* = 35 Hz), 26.9 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.09; HRMS (ESI) m/z: 355.03347 $[M + Na]^+$, calcd for $C_{13}H_{11}O_3N_2F_3NaS$; Found 355.03360.

Crystal Structure of 4a



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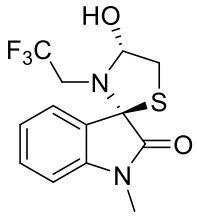
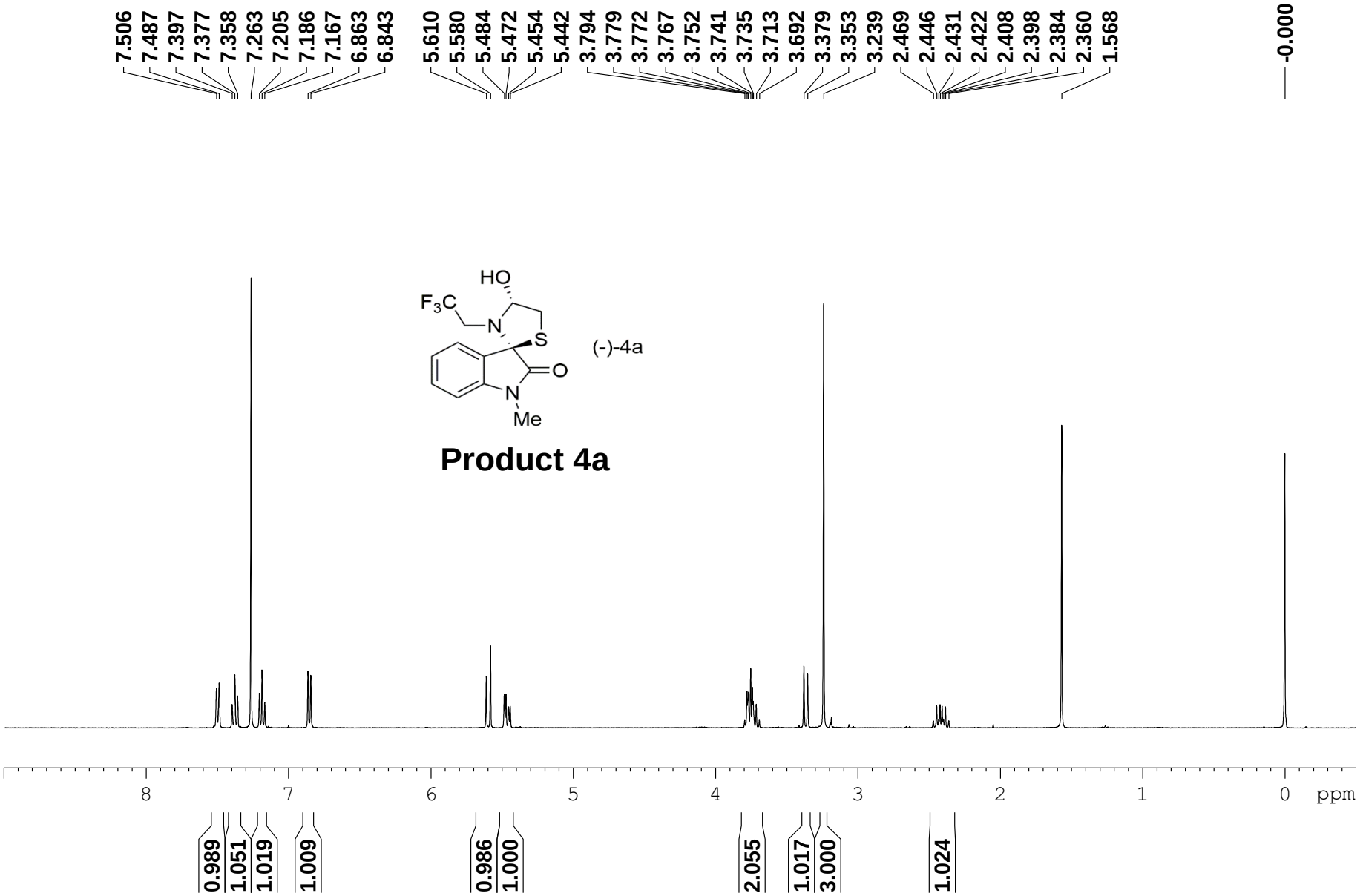


Table 1. Crystal data and structure refinement for sbii4.

Identification code	SB-II-4	
Empirical formula	C13 H13 F3 N2 O2 S	
Formula weight	318.31	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 10.2811(5) Å	α= 90°.
	b = 14.3963(6) Å	β= 116.7220(10)°.
	c = 10.3695(4) Å	γ = 90°.
Volume	1370.87(10) $Å^3$	
Z	4	
Density (calculated)	1.542 Mg/m^3	
Absorption coefficient	0.277 mm^{-1}	
F(000)	656	
Crystal size	0.450 x 0.089 x 0.042 mm^3	
Theta range for data collection	2.830 to 29.596°.	
Index ranges	-14<=h<=14, -19<=k<=20, -14<=l<=14	
Reflections collected	54179	
Independent reflections	3856 [R(int) = 0.0704]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.934 and 0.823	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3856 / 0 / 195
Goodness-of-fit on F^2	1.039
Final R indices [I>2sigma(I)]	R1 = 0.0460, wR2 = 0.1130
R indices (all data)	R1 = 0.0605, wR2 = 0.1250
Extinction coefficient	n/a
Largest diff. peak and hole	0.427 and -0.290 e.$Å^{-3}$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5.472
5.454
5.442
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3.779
3.772
3.767
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3.692
3.379
3.353
3.239
2.469
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2.431
2.422
2.408
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F3C
N
S
O
N
Me
(-)-4a
Product 4a
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6
5
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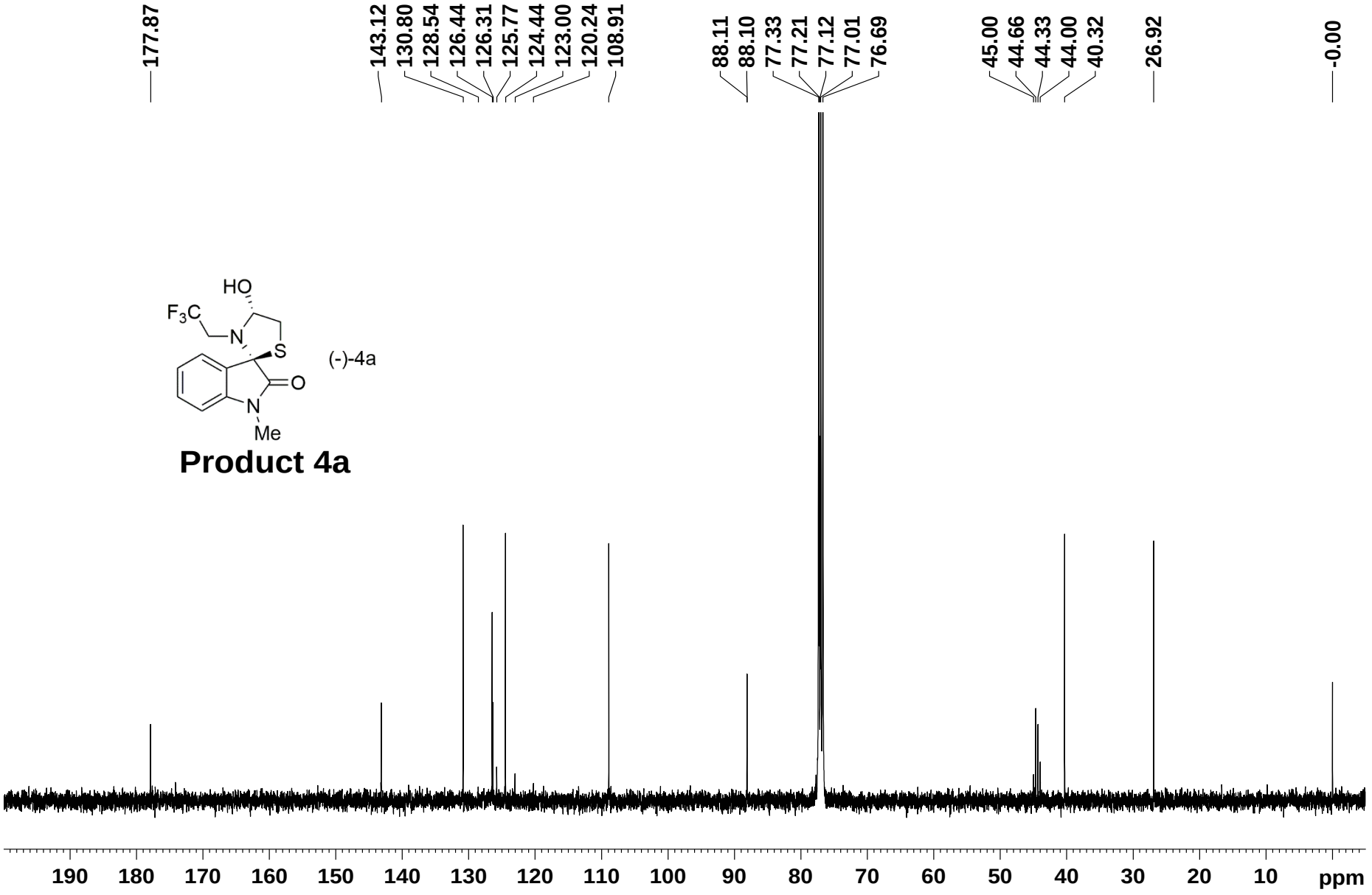
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76.69
45.00
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44.00
40.32
26.92
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F3C
N
S
O
N
Me
(-)-4a
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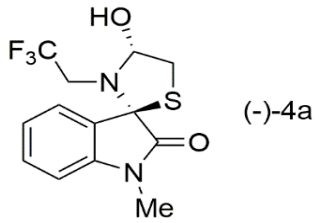
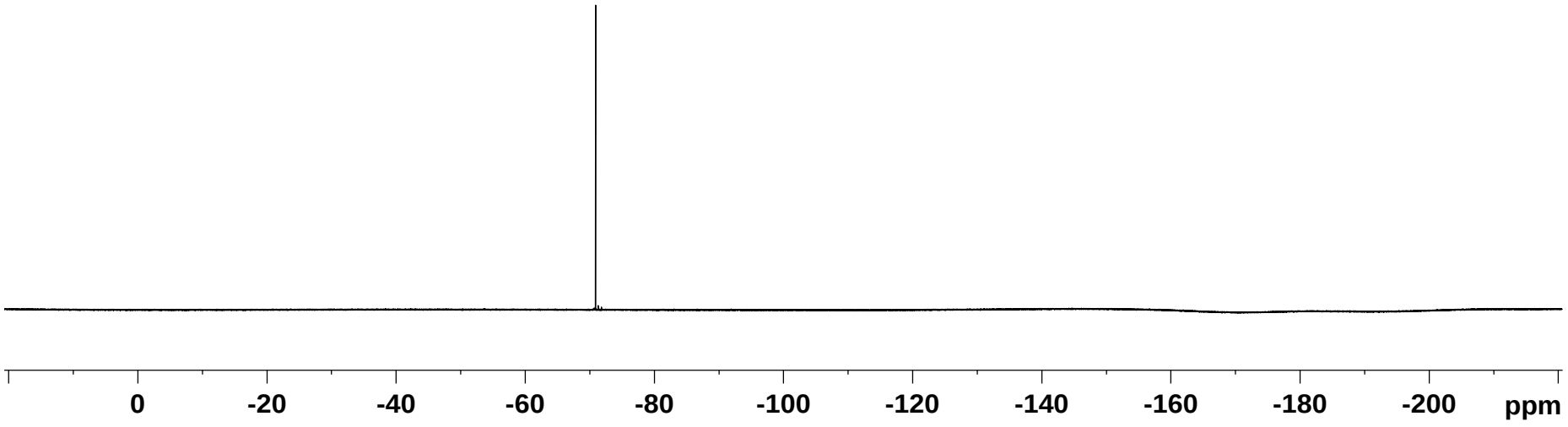
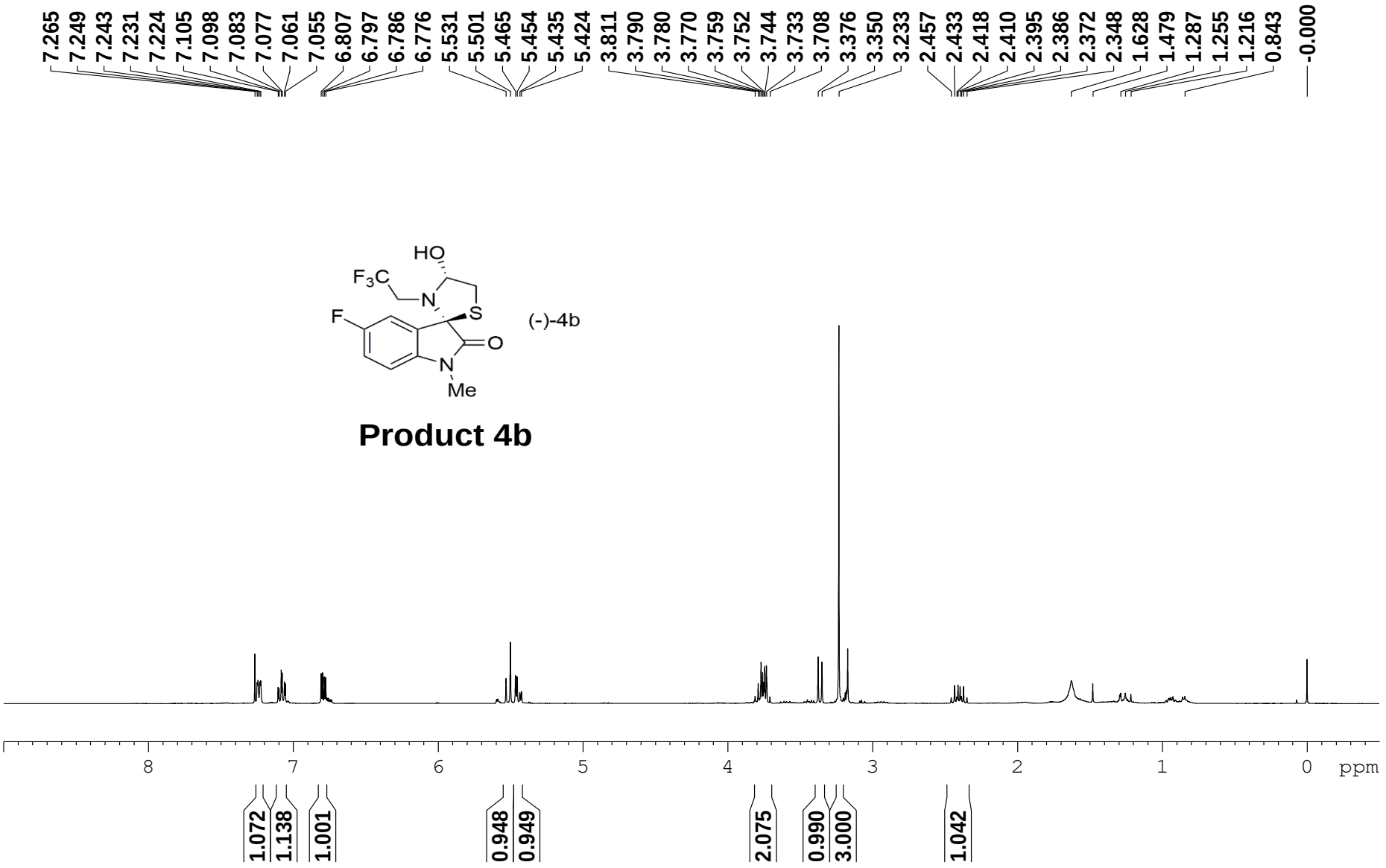


(-)-4a

Product 4a

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S
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Me
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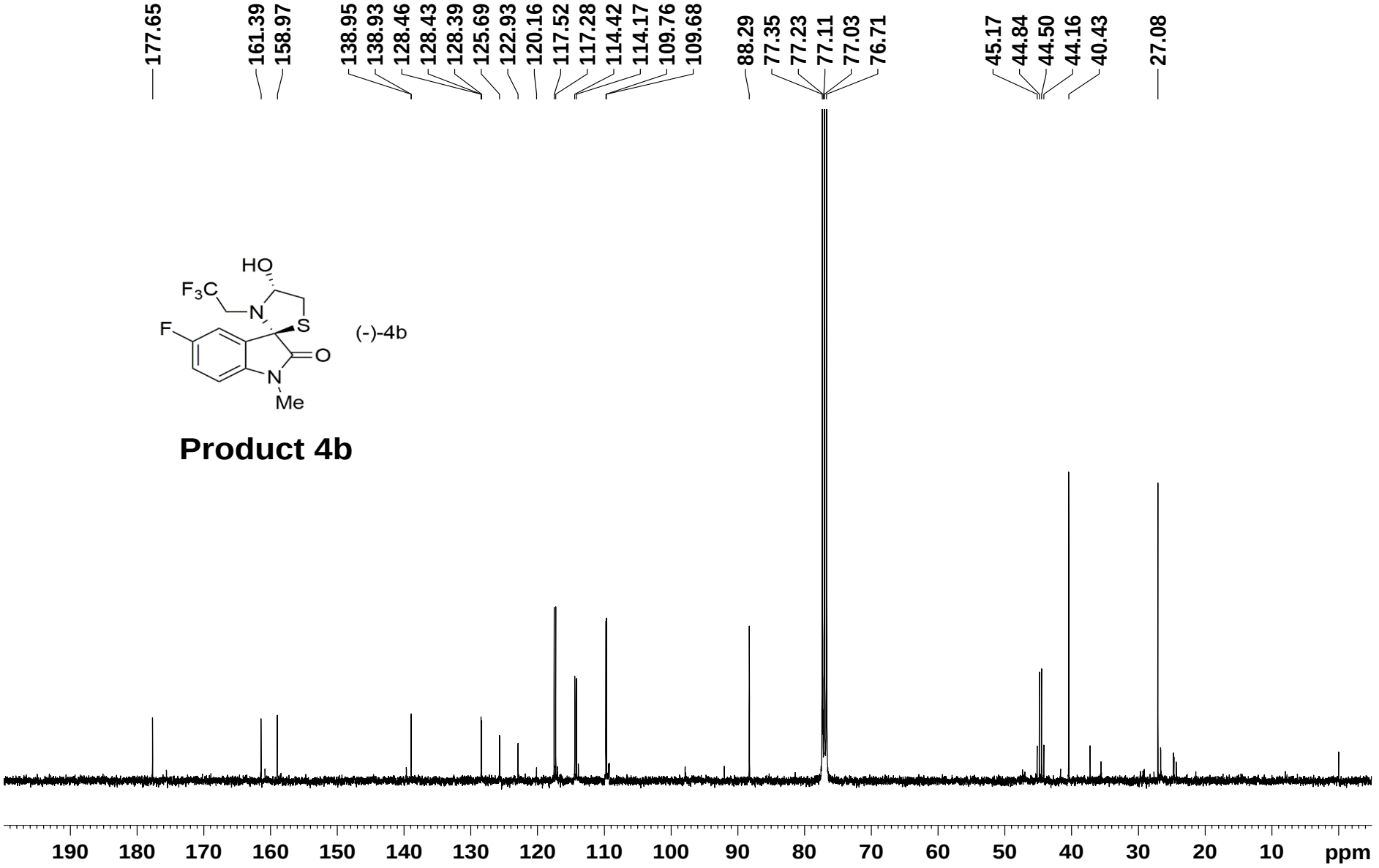
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114.17
109.76
109.68
88.29
77.35
77.23
77.11
77.03
76.71
45.17
44.84
44.50
44.16
40.43
27.08
HO
F3C
N
S
F
O
N
Me
(-)-4b
Product 4b
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150
140
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120
110
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90
80
70
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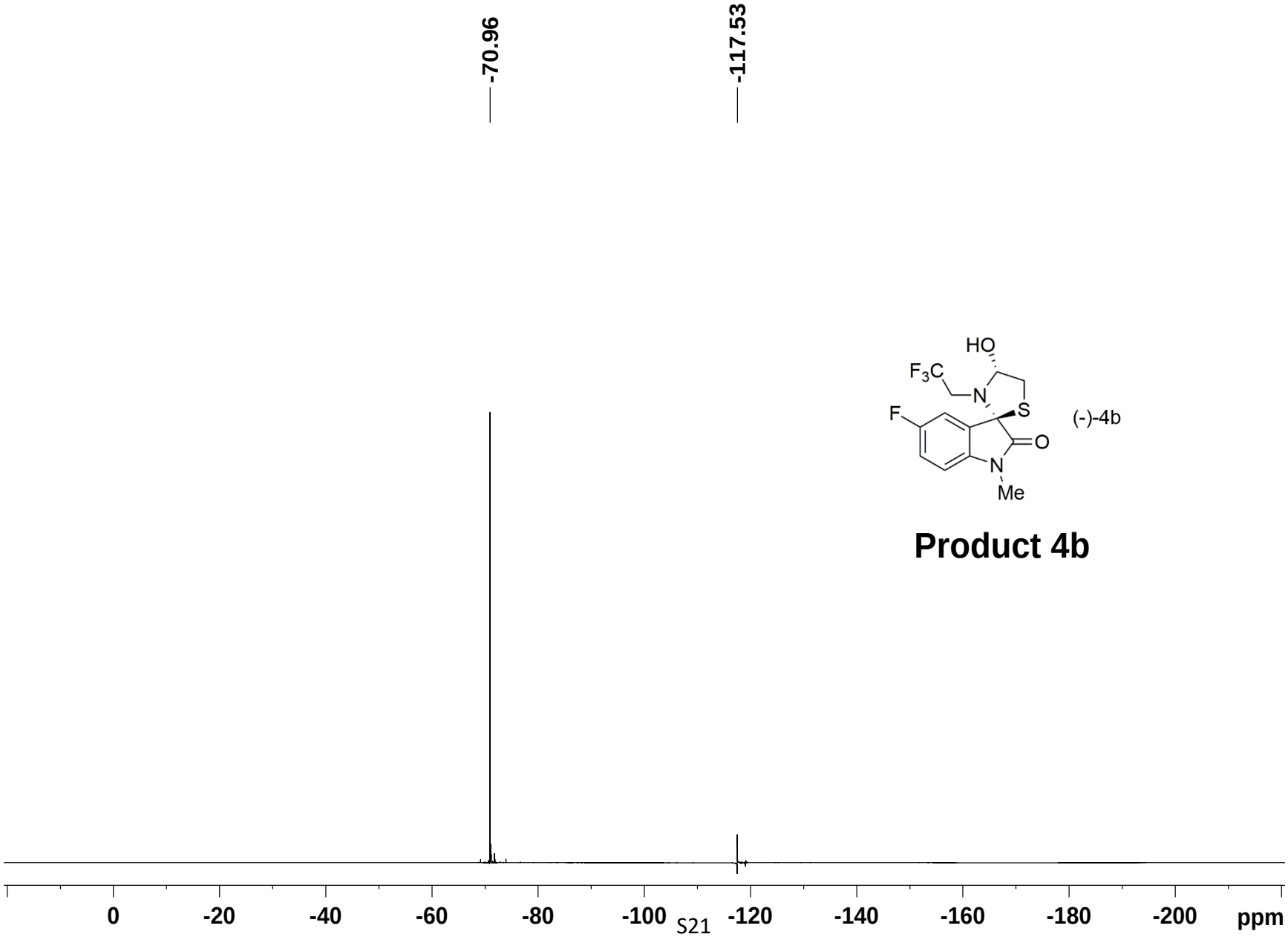
10
ppm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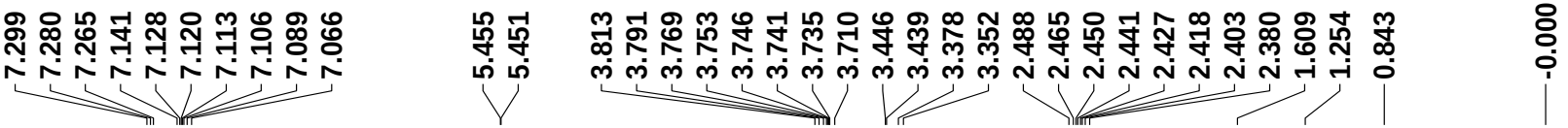
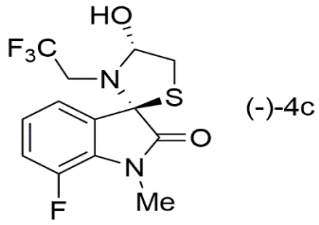
ppm

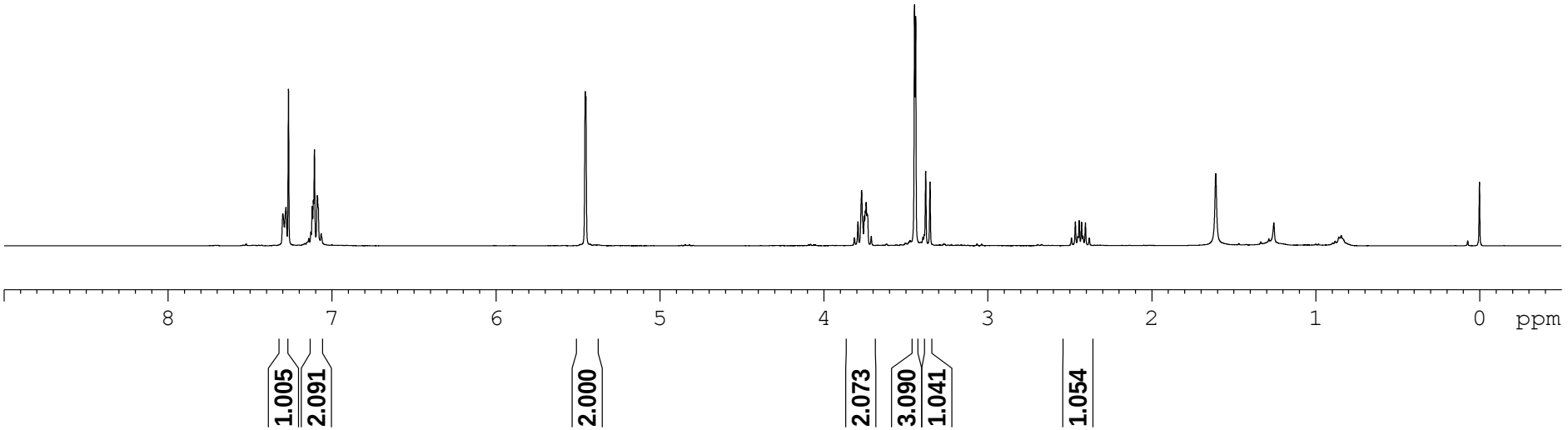
Product 4b

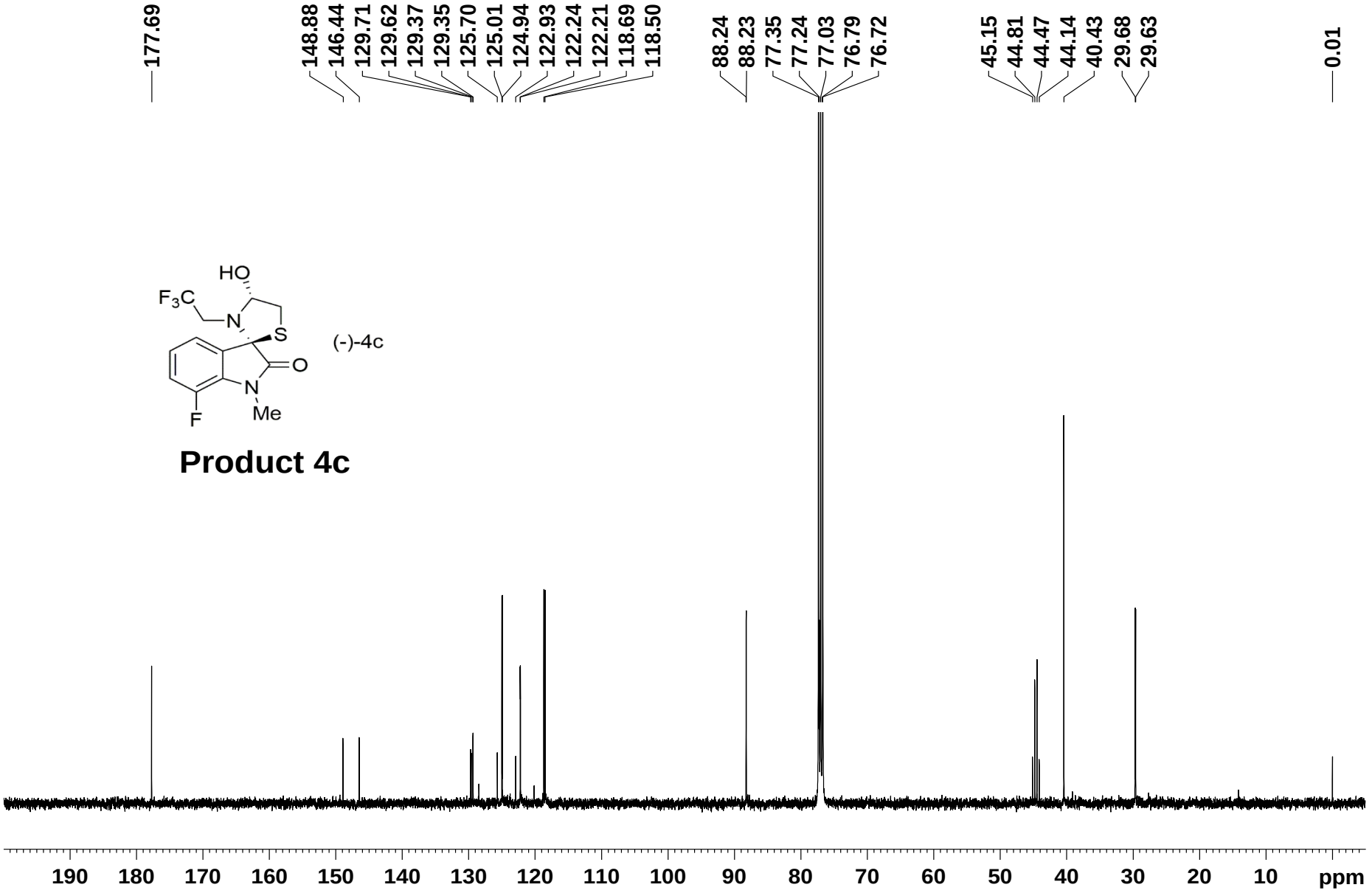




(-)-4c

Product 4c

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88.23
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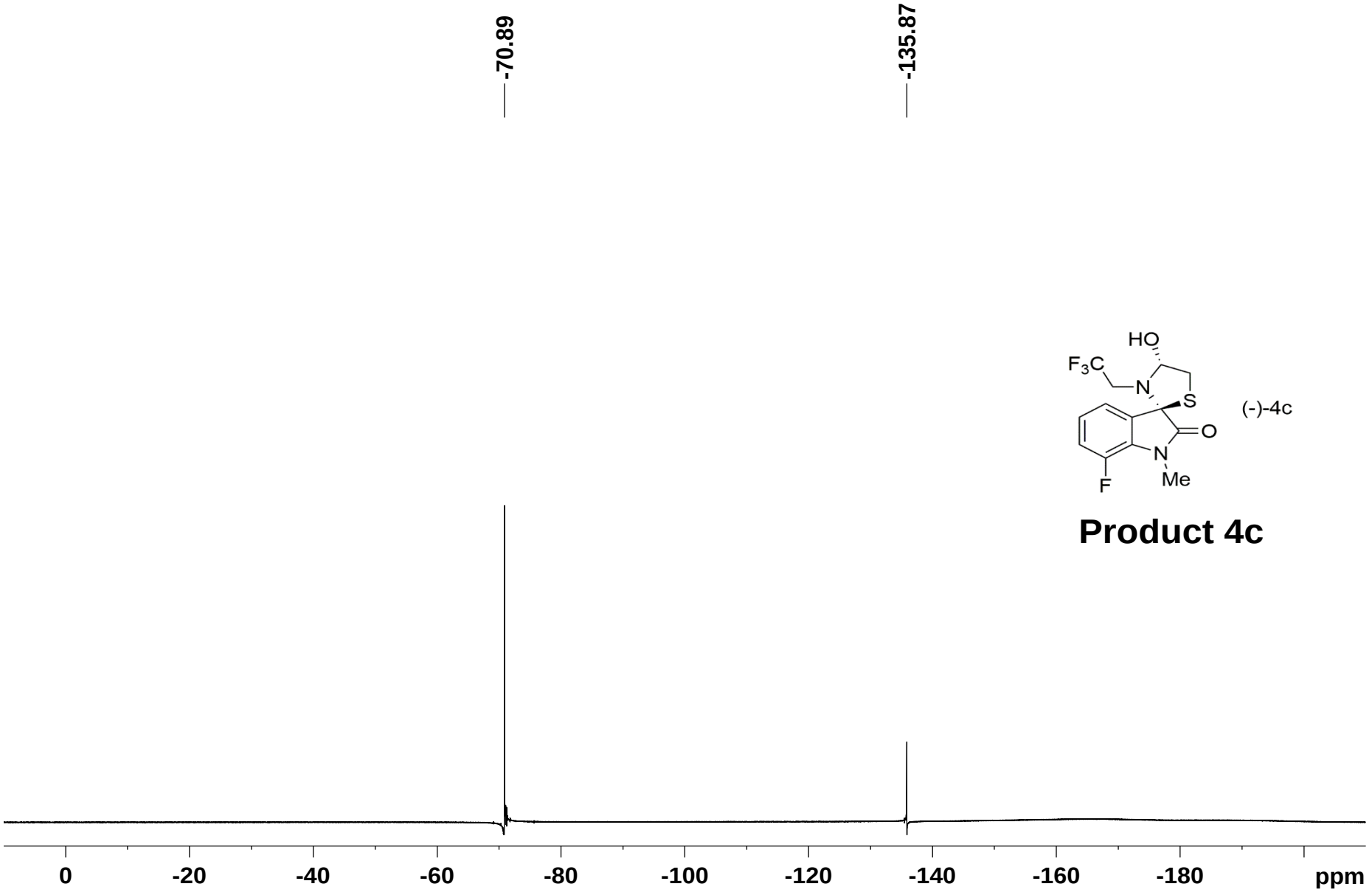
77.03
76.79
76.72
45.15
44.81
44.47
44.14
40.43
29.68
29.63
0.01
HO
F3C
N
S
O
N
Me
F
(-)-4c
Product 4c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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-135.87
HO
F3C
N
S
O
N
Me
F
(-)-4c
Product 4c
0
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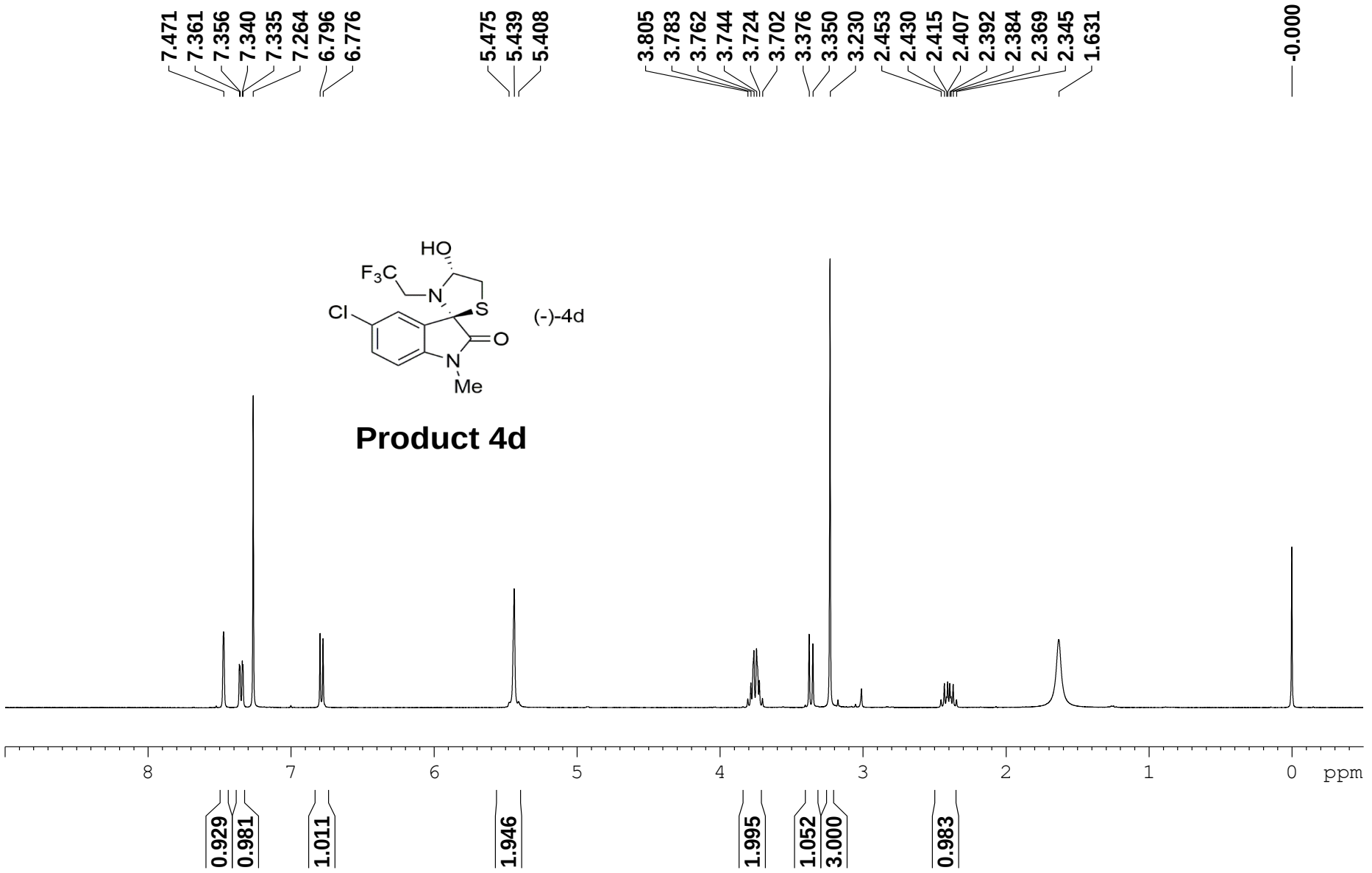
-40
-60
-80
-100
-120
-140
-160
-180
ppm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7.264
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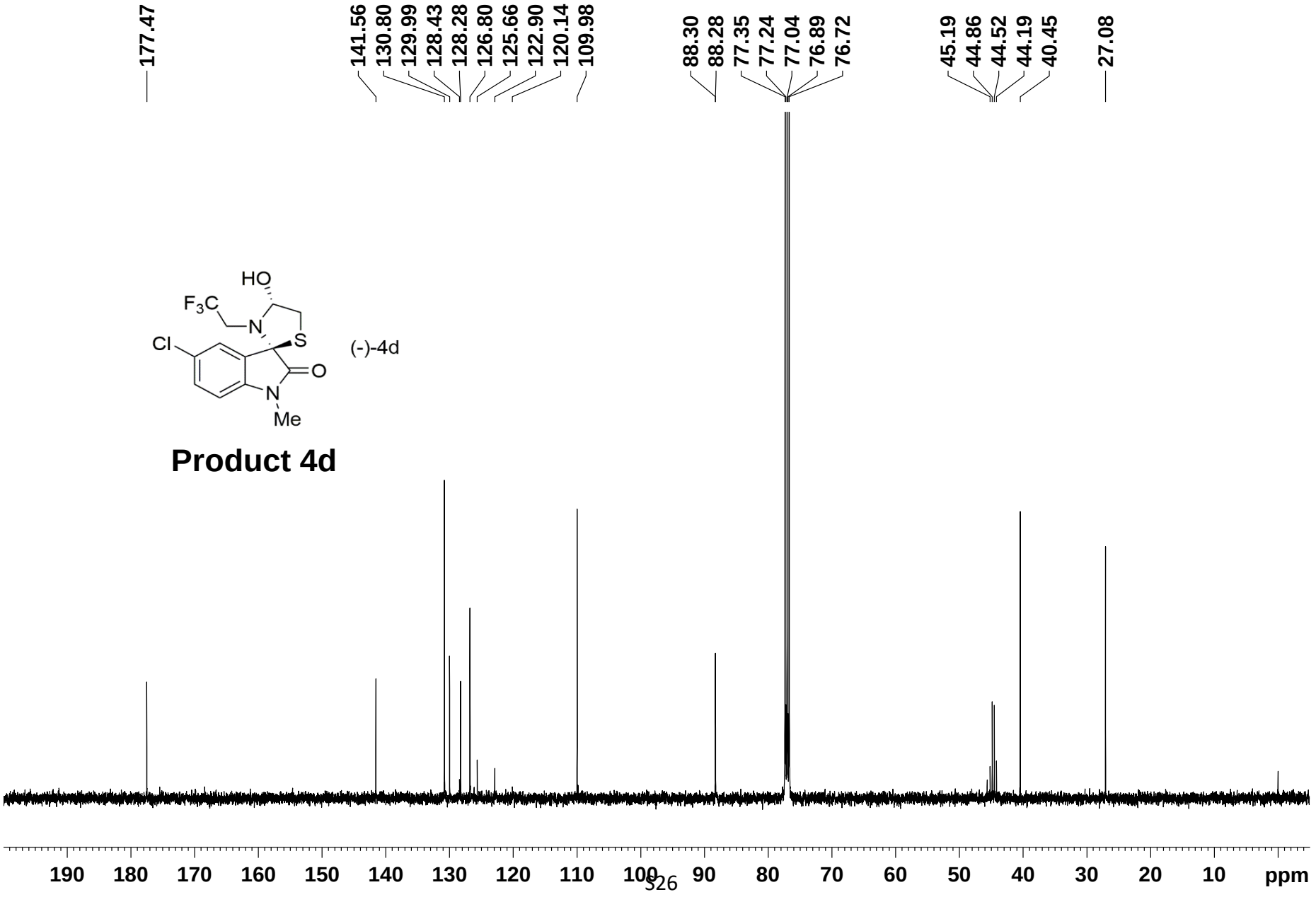
6.776
5.475
5.439
5.408
3.805
3.783
3.762
3.744
3.724
3.702
3.376
3.350
3.230
2.453
2.430
2.415
2.407
2.392
2.384
2.369
2.345
1.631
-0.000
HO
F3C
N
S
Cl
O
N
Me
(-)-4d
Product 4d
8
7
6
5
4
3
2
1
0
ppm
0.929
0.981
1.011
1.946
1.995
1.052
3.000
0.983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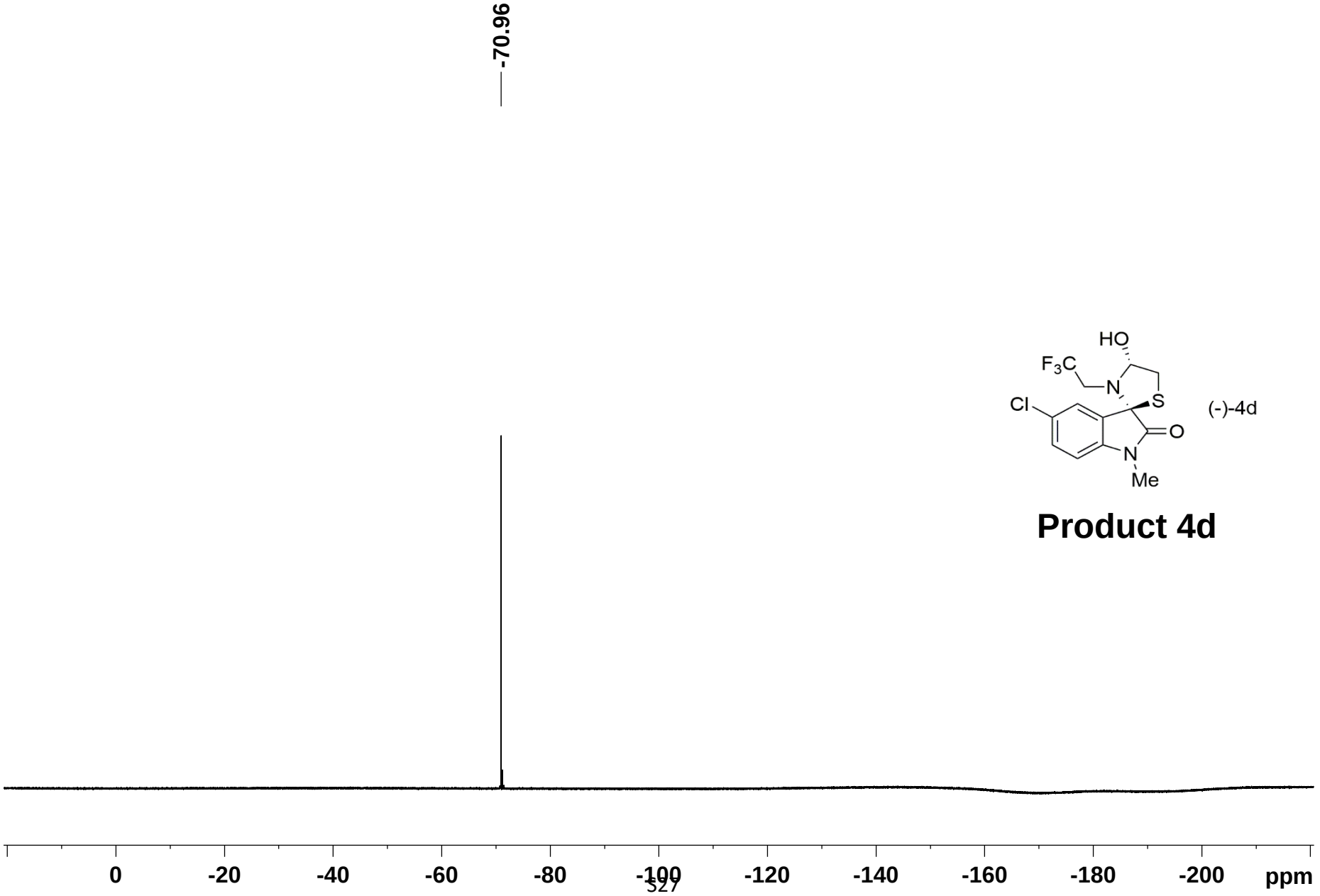
141.56
130.80
129.99
128.43
128.28
126.80
125.66
122.90
120.14
109.98
88.30
88.28
77.35
77.24
77.04
76.89
76.72
45.19
44.86
44.52
44.19
40.45
27.08
HO
F3C
N
S
Cl
O
N
Me
(-)-4d
Product 4d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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F3C
N
S
Cl
O
N
Me
(-)-4d
Product 4d
0
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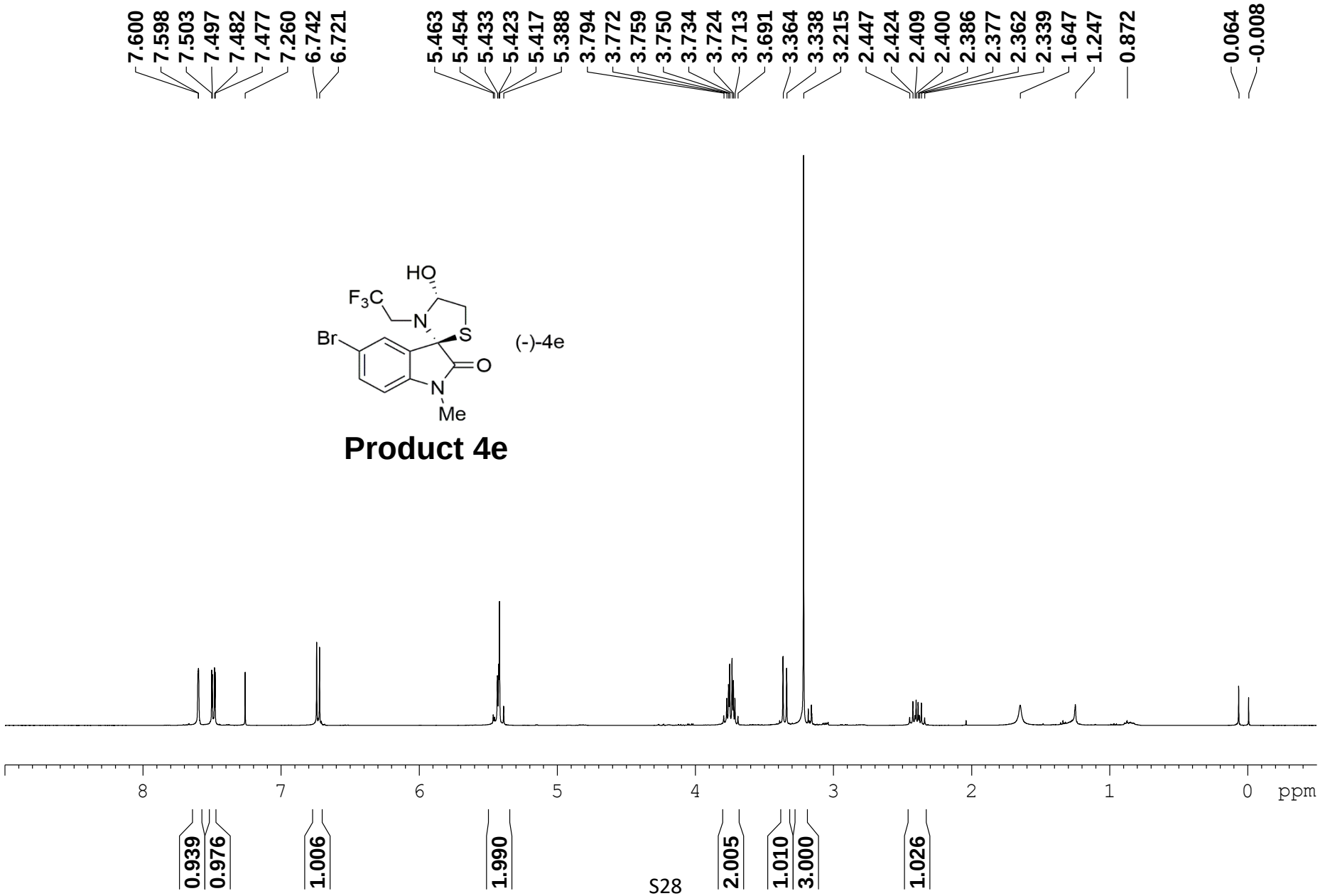
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm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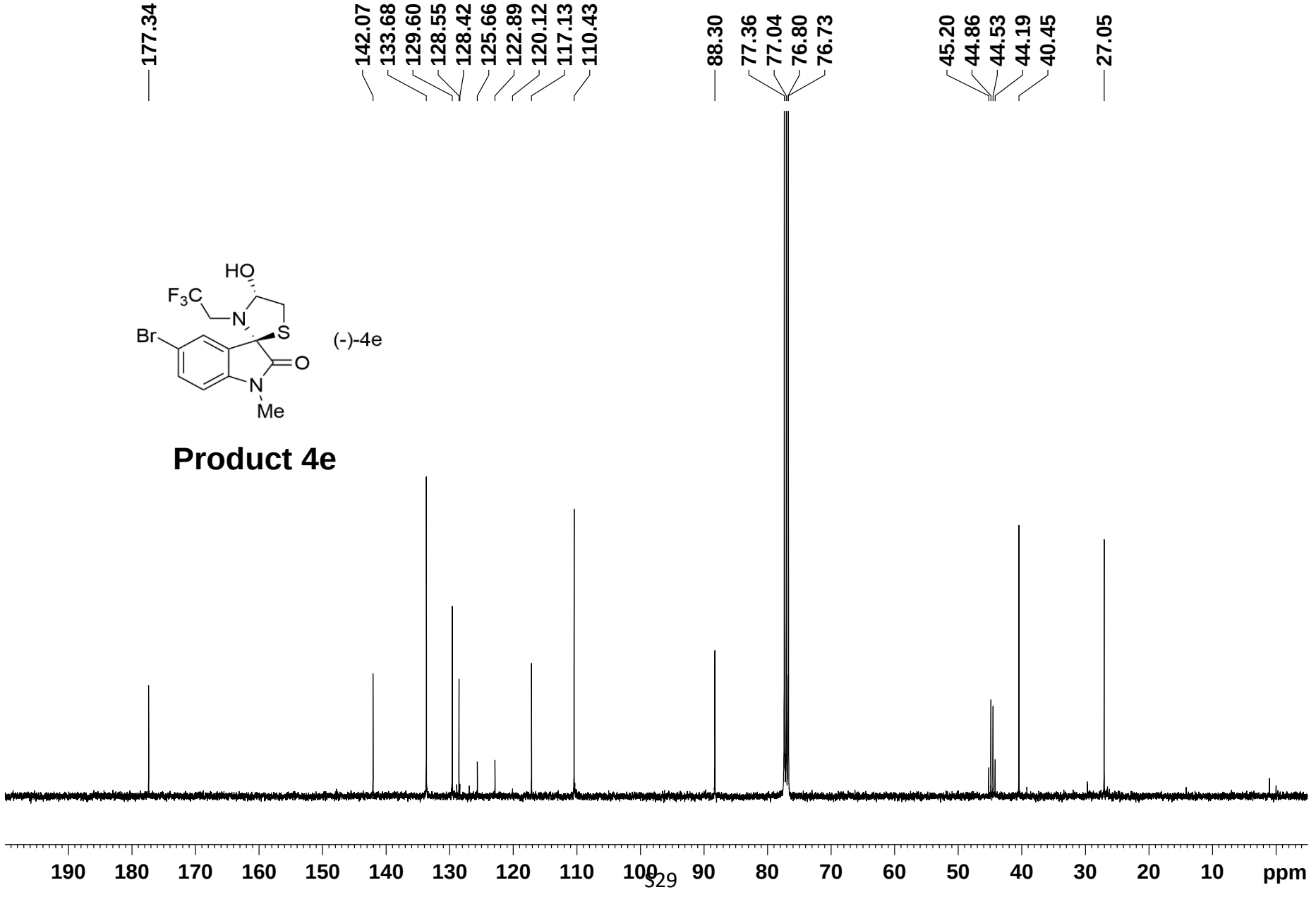
7.598
7.503
7.497
7.482
7.477
7.260
6.742
6.721
5.463
5.454
5.433
5.423
5.417
5.388
3.794
3.772
3.759
3.750
3.734
3.724
3.713
3.691
3.364
3.338
3.215
2.447
2.424
2.409
2.400
2.386
2.377
2.362
2.339
1.647
1.247
0.872
0.064
-0.008
HO
F3C
N
S
Br
O
N
Me
(-)-4e
Product 4e
8
7
6
5
4
3
2
1
0
ppm
0.939
0.976
1.006
1.990
2.005
1.010
3.000
1.026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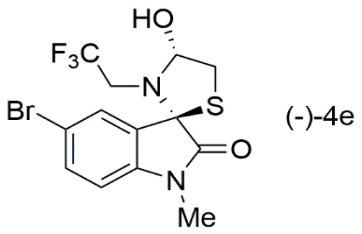
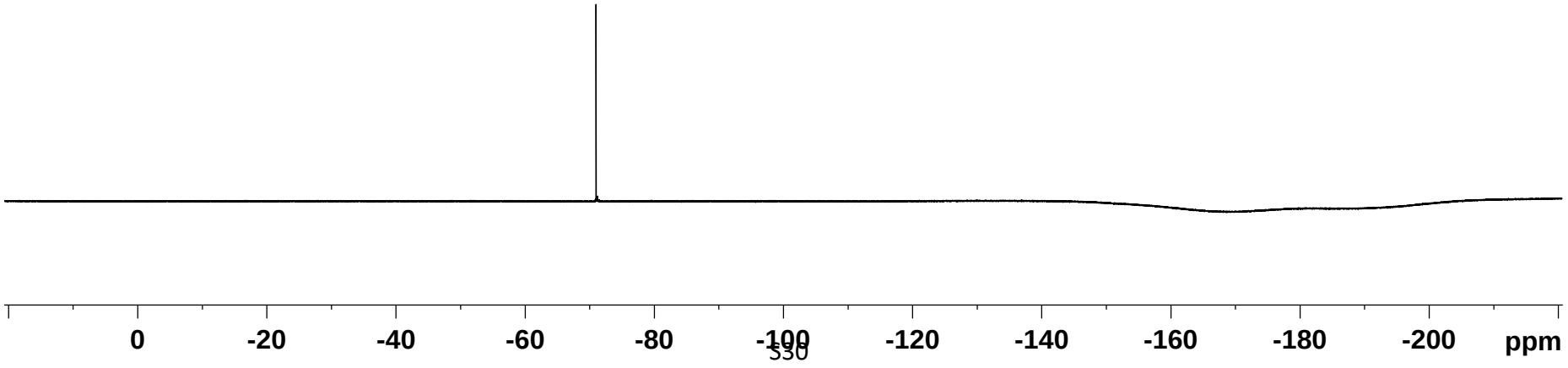
142.07
133.68
129.60
128.55
128.42
125.66
122.89
120.12
117.13
110.43
88.30
77.36
77.04
76.80
76.73
45.20
44.86
44.53
44.19
40.45
27.05
HO
F3C
N
S
Br
O
N
Me
(-)-4e
Product 4e
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

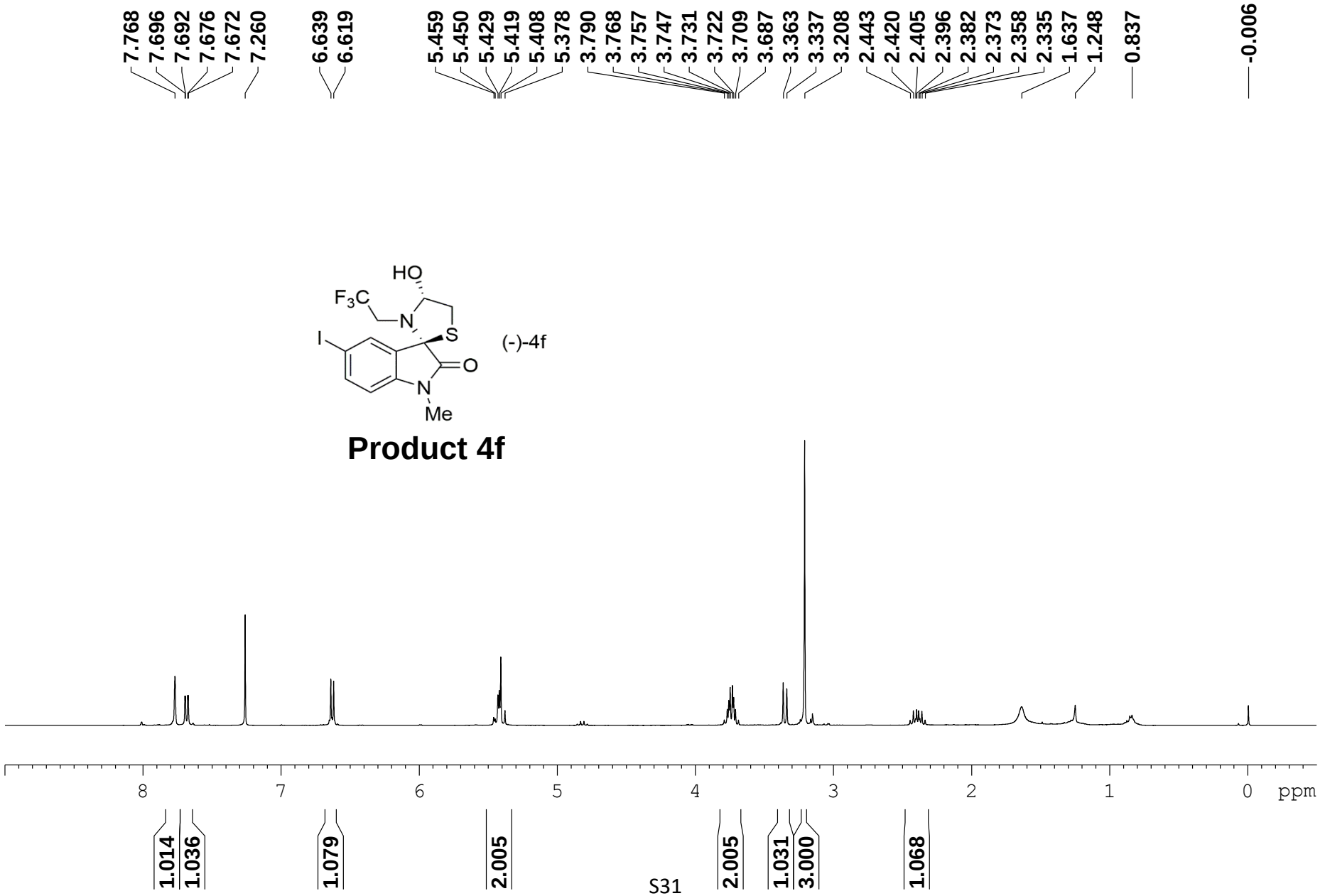
-70.97



(-)-4e

Product 4e

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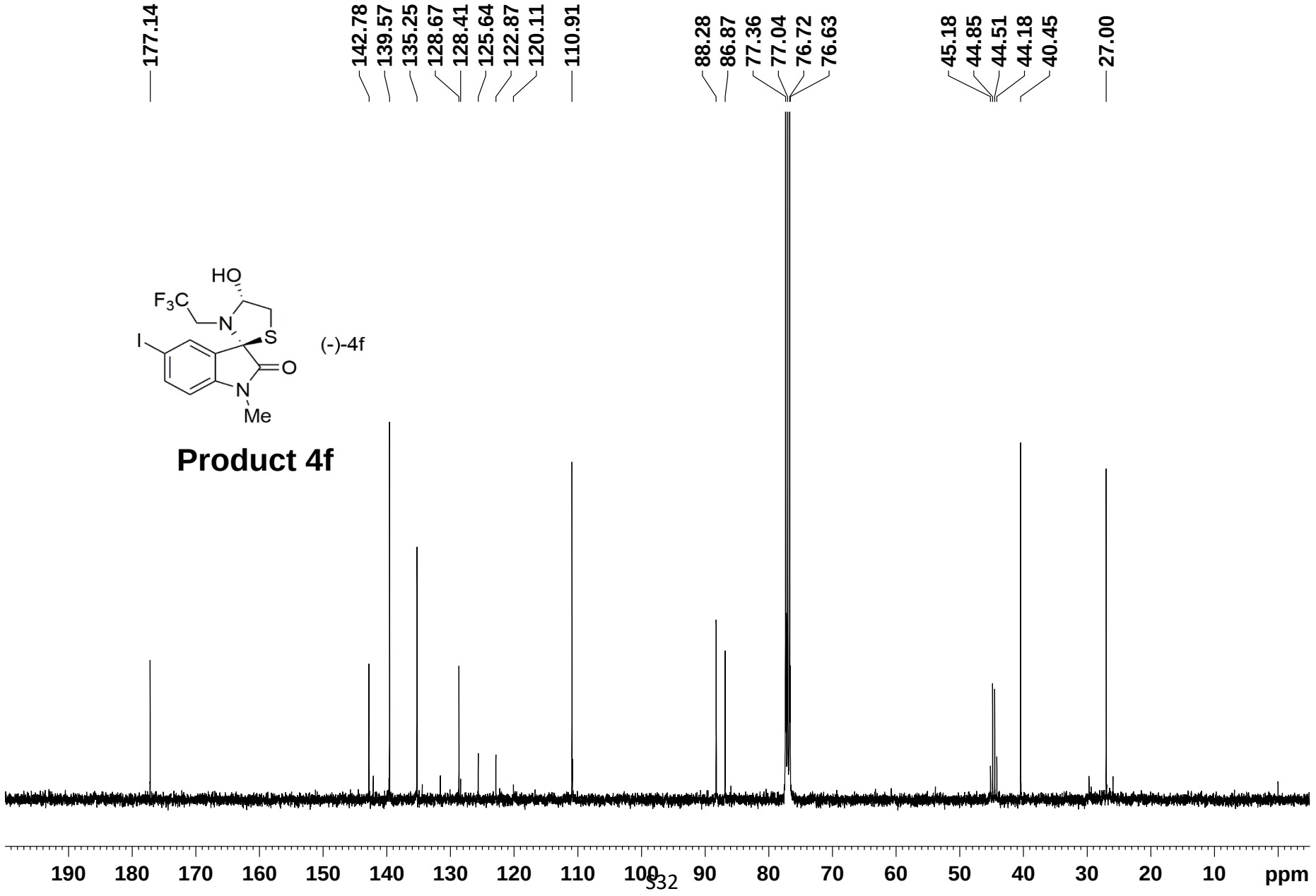
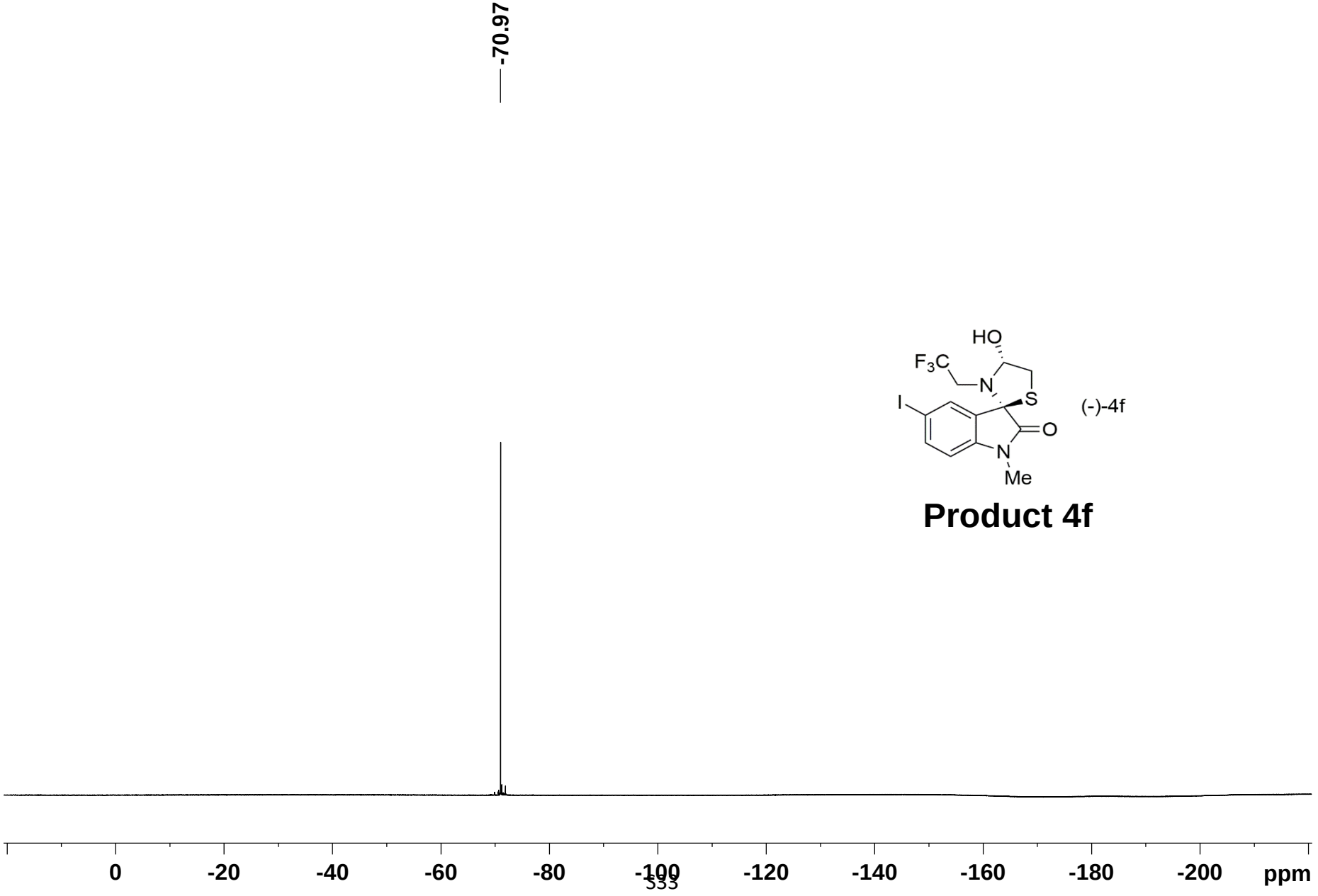
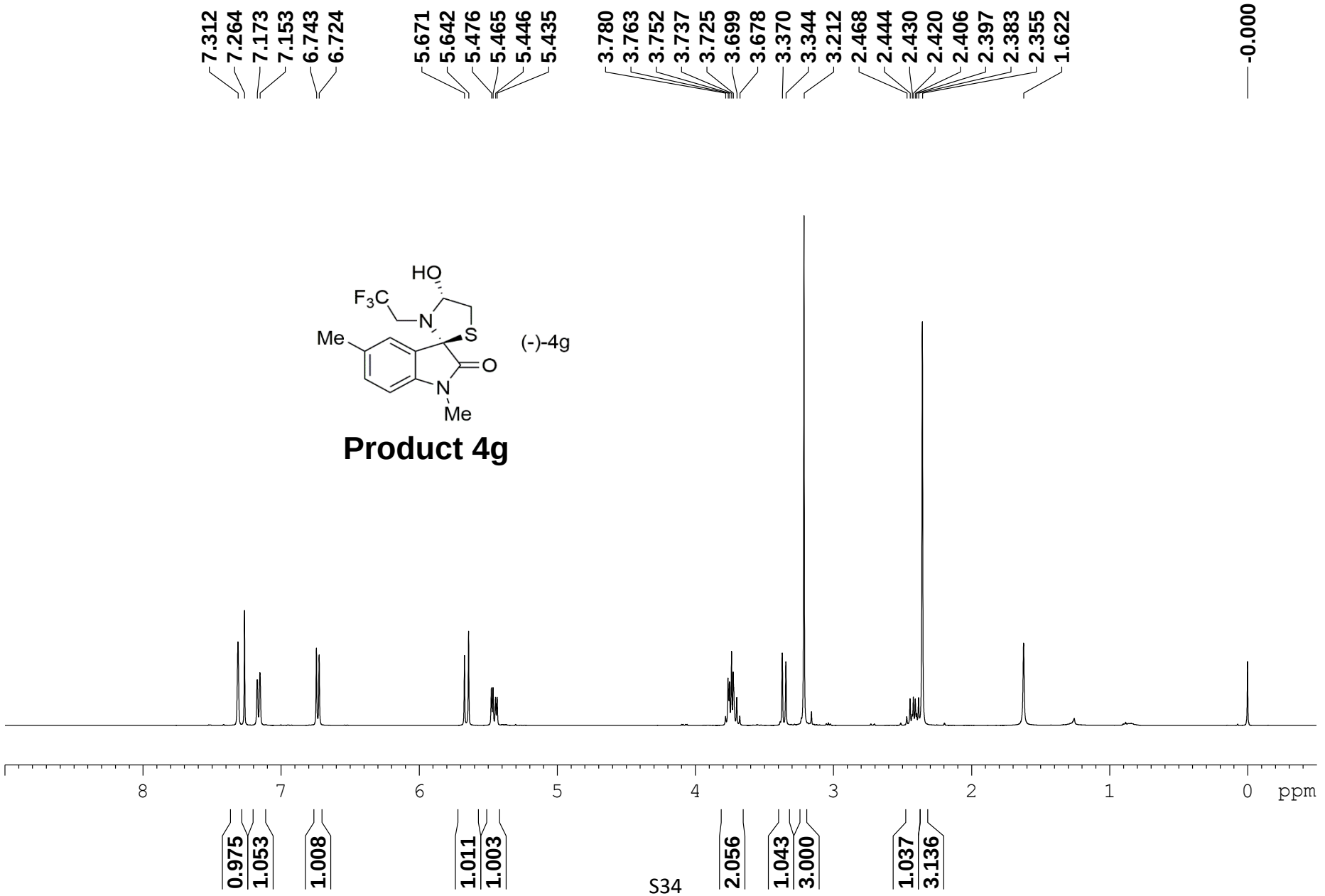
7.696
7.692
7.676
7.672
7.260
6.639
6.619
5.459
5.450
5.429
5.419
5.408
5.378
3.790
3.768
3.757
3.747
3.731
3.722
3.709
3.687
3.363
3.337
3.208
2.443
2.420
2.405
2.396
2.382
2.373
2.358
2.335
1.637
1.248
0.837
-0.006
HO
F3C
N
S
I
O
N
Me
(-)-4f
Product 4f
8
7
6
5
4
3
2
1
0
ppm
1.014
1.036
1.079
2.005
2.005
1.031
3.000
1.068


177.14
142.78
139.57
135.25
128.67
128.41
125.64
122.87
120.11
110.91
88.28
86.87
77.36
77.04
76.72
76.63
45.18
44.85
44.51
44.18
40.45
27.00
HO
F3C
N
S
I
O
N
Me
(-)-4f
Product 4f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


-70.97
HO
F3C
N
S
I
O
N
Me
(-)-4f
Product 4f
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm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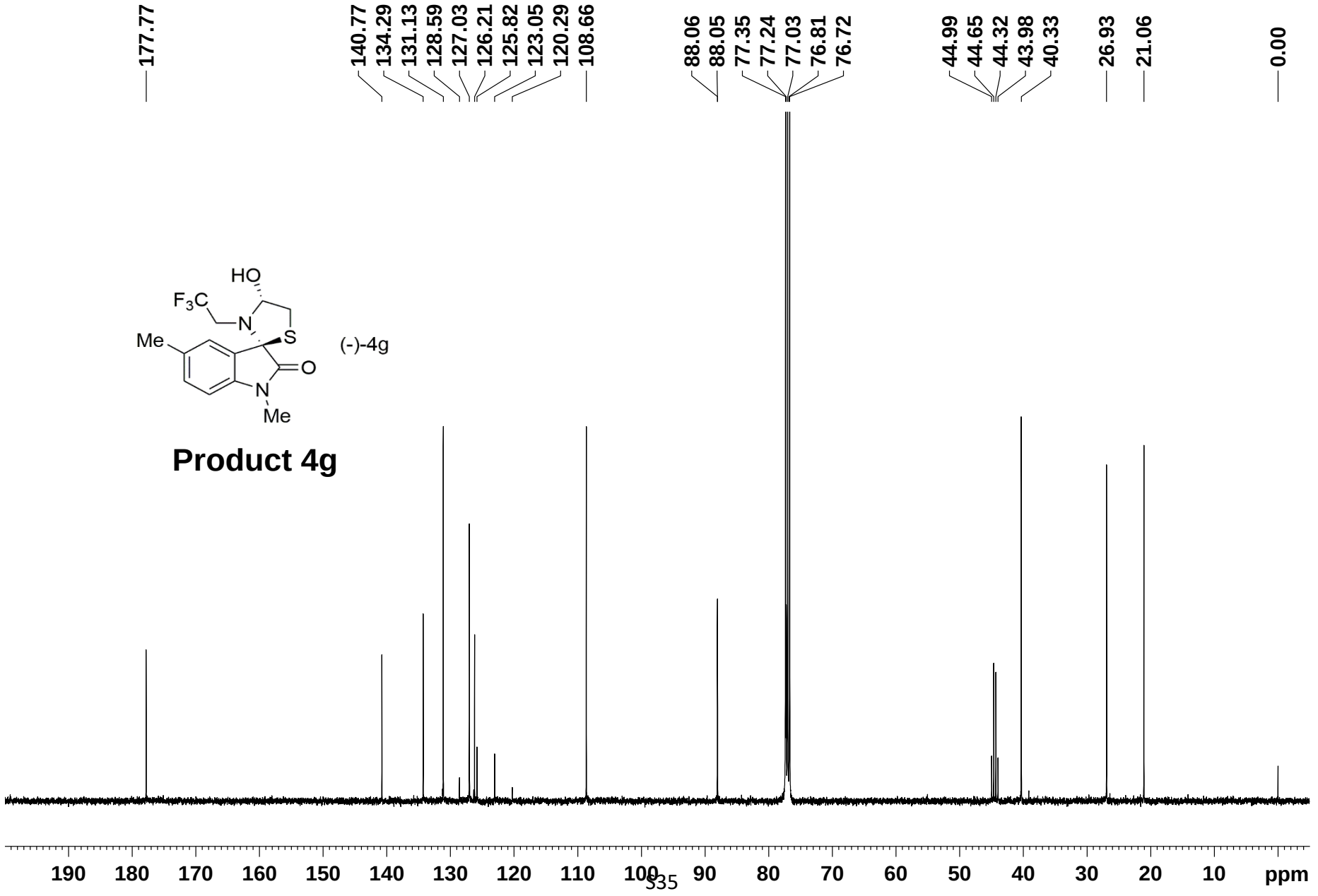
7.264
7.173
7.153
6.743
6.724
5.671
5.642
5.476
5.465
5.446
5.435
3.780
3.763
3.752
3.737
3.725
3.699
3.678
3.370
3.344
3.212
2.468
2.444
2.430
2.420
2.406
2.397
2.383
2.355
1.622
-0.000
HO
F3C
N
S
Me
O
N
Me
(-)-4g
Product 4g
8
7
6
5
4
3
2
1
0
ppm
0.975
1.053
1.008
1.011
1.003
2.056
1.043
3.000
1.037
3.136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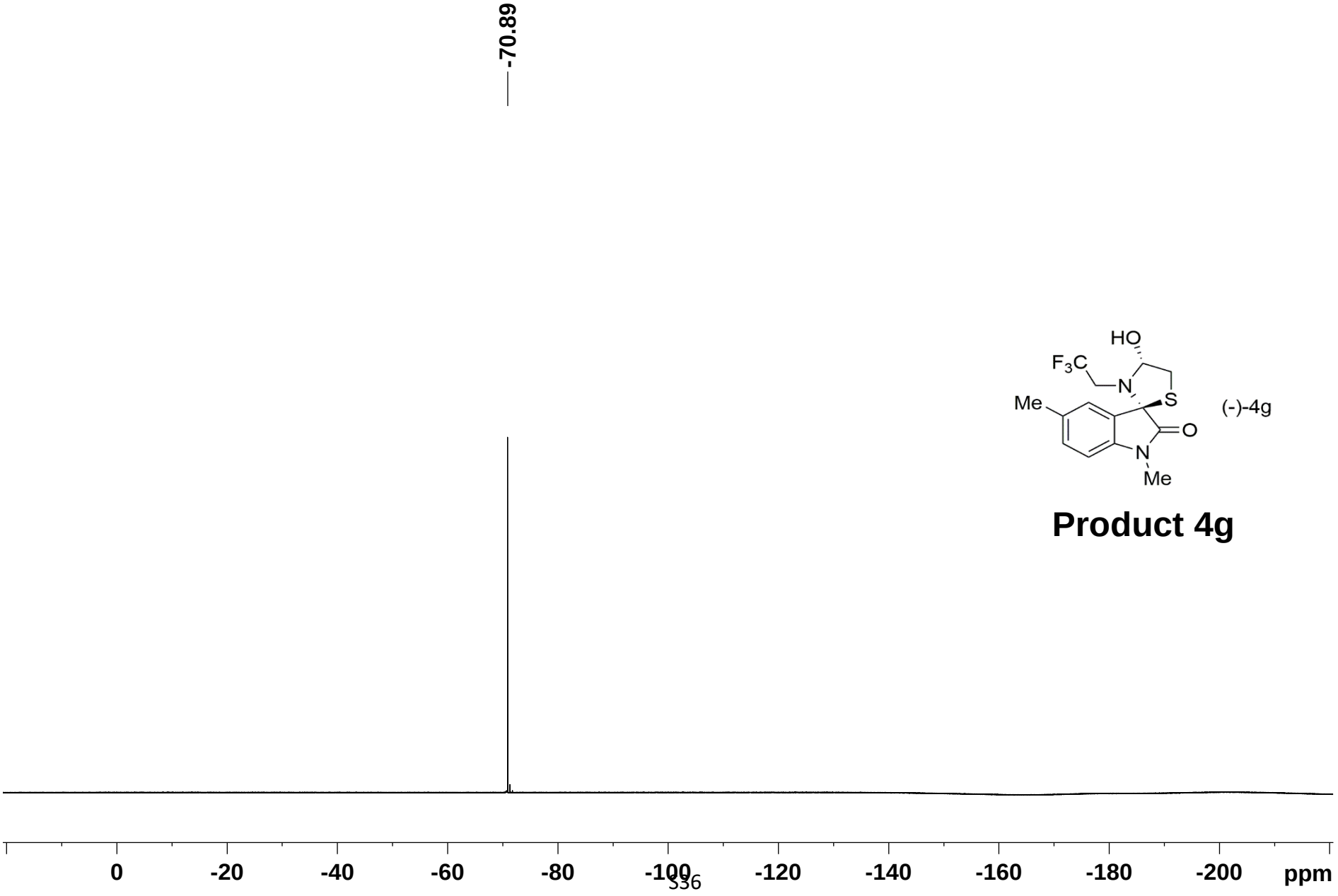
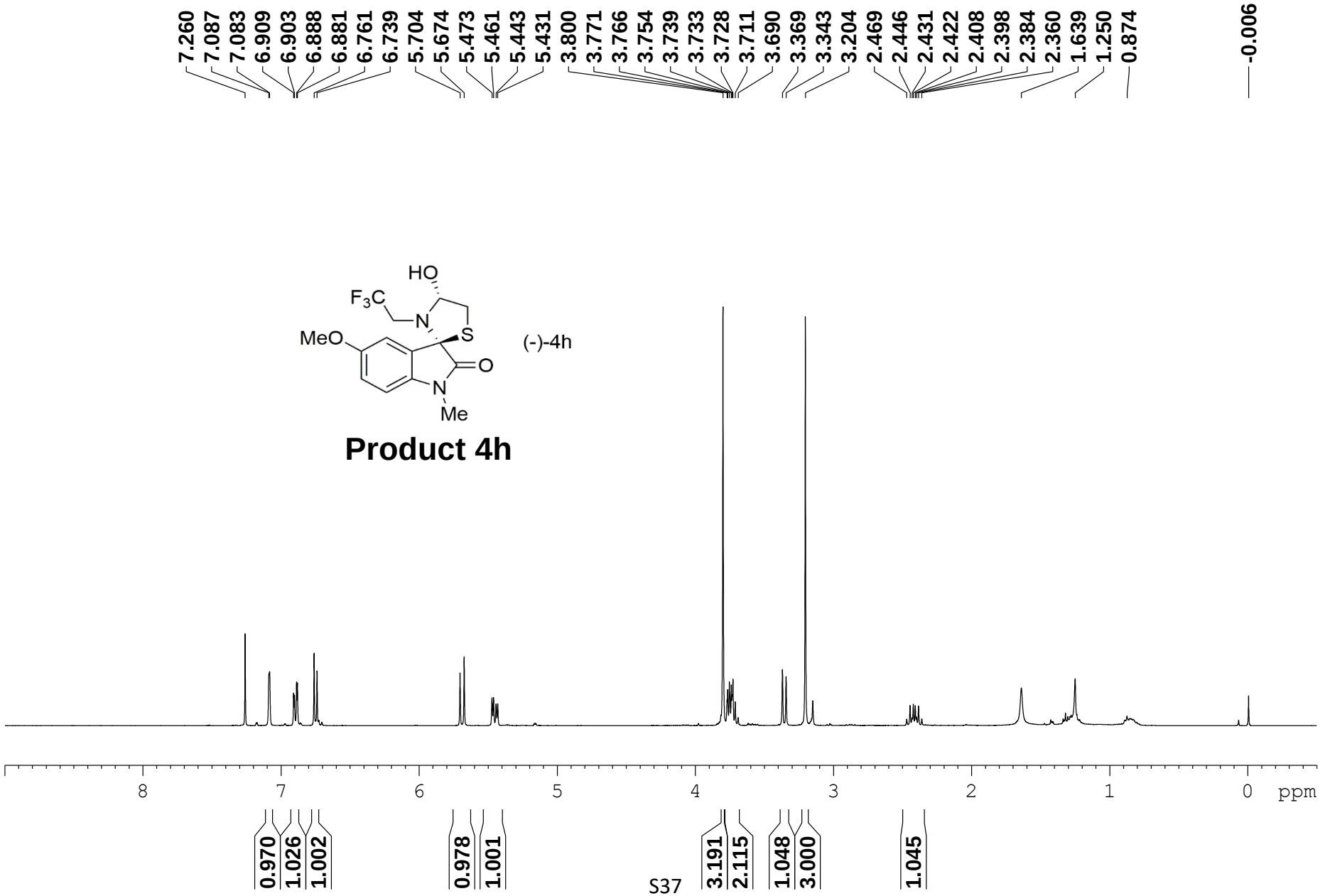
140.77
134.29
131.13
128.59
127.03
126.21
125.82
123.05
120.29
108.66
88.06
88.05
77.35
77.24
77.03
76.81
76.72
44.99
44.65
44.32
43.98
40.33
26.93
21.06
0.00
HO
F3C
N
S
Me
O
N
Me
(-)-4g
Product 4g
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


-70.89
HO
F3C
N
S
Me
O
N
Me
(-)-4g
Product 4g
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm


7.260
7.087
7.083
6.909
6.903
6.888
6.881
6.761
6.739
5.704
5.674
5.473
5.461
5.443
5.431
3.800
3.771
3.766
3.754
3.739
3.733
3.728
3.711
3.690
3.369
3.343
3.204
2.469
2.446
2.431
2.422
2.408
2.398
2.384
2.360
1.639
1.250
0.874
-0.006
HO
F3C
N
S
MeO
O
N
Me
(-)-4h
Product 4h
8
7
6
5
4
3
2
1
0
ppm
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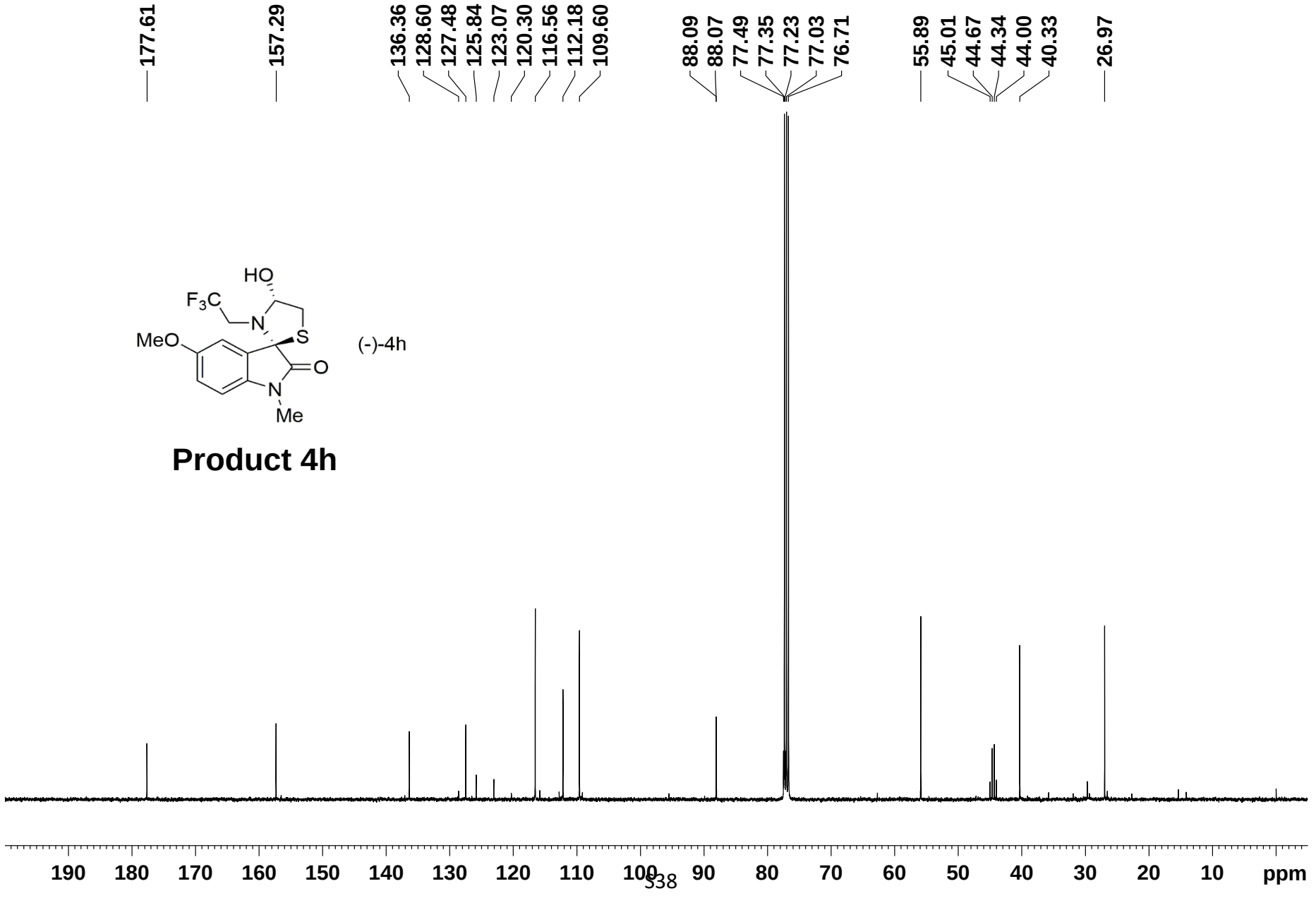
1.026
1.002
0.978
1.001
3.191
2.115
1.048
3.000
1.045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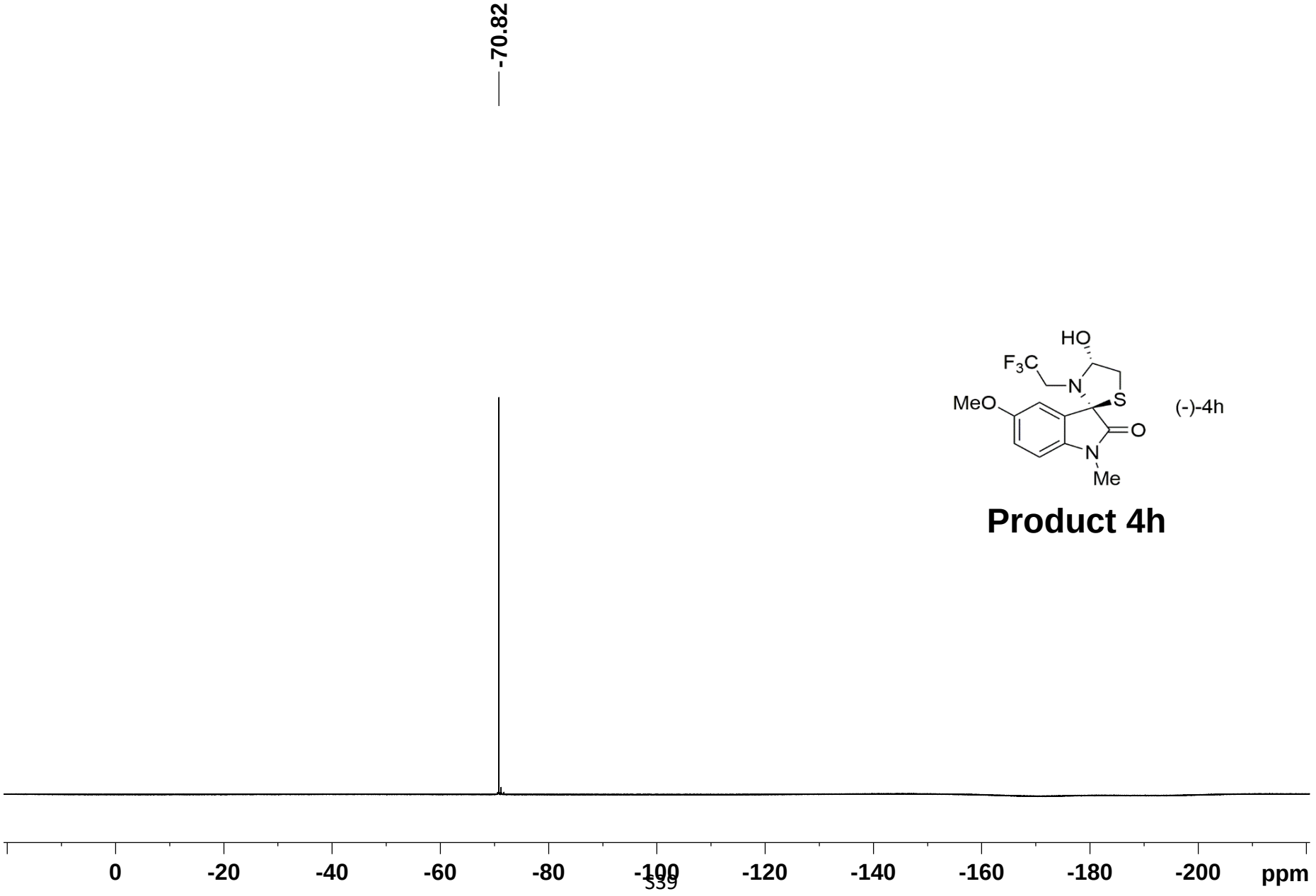
136.36
128.60
127.48
125.84
123.07
120.30
116.56
112.18
109.60
88.09
88.07
77.49
77.35
77.23
77.03
76.71
55.89
45.01
44.67
44.34
44.00
40.33
26.97
HO
F3C
N
S
MeO
O
N
Me
(-)-4h
Product 4h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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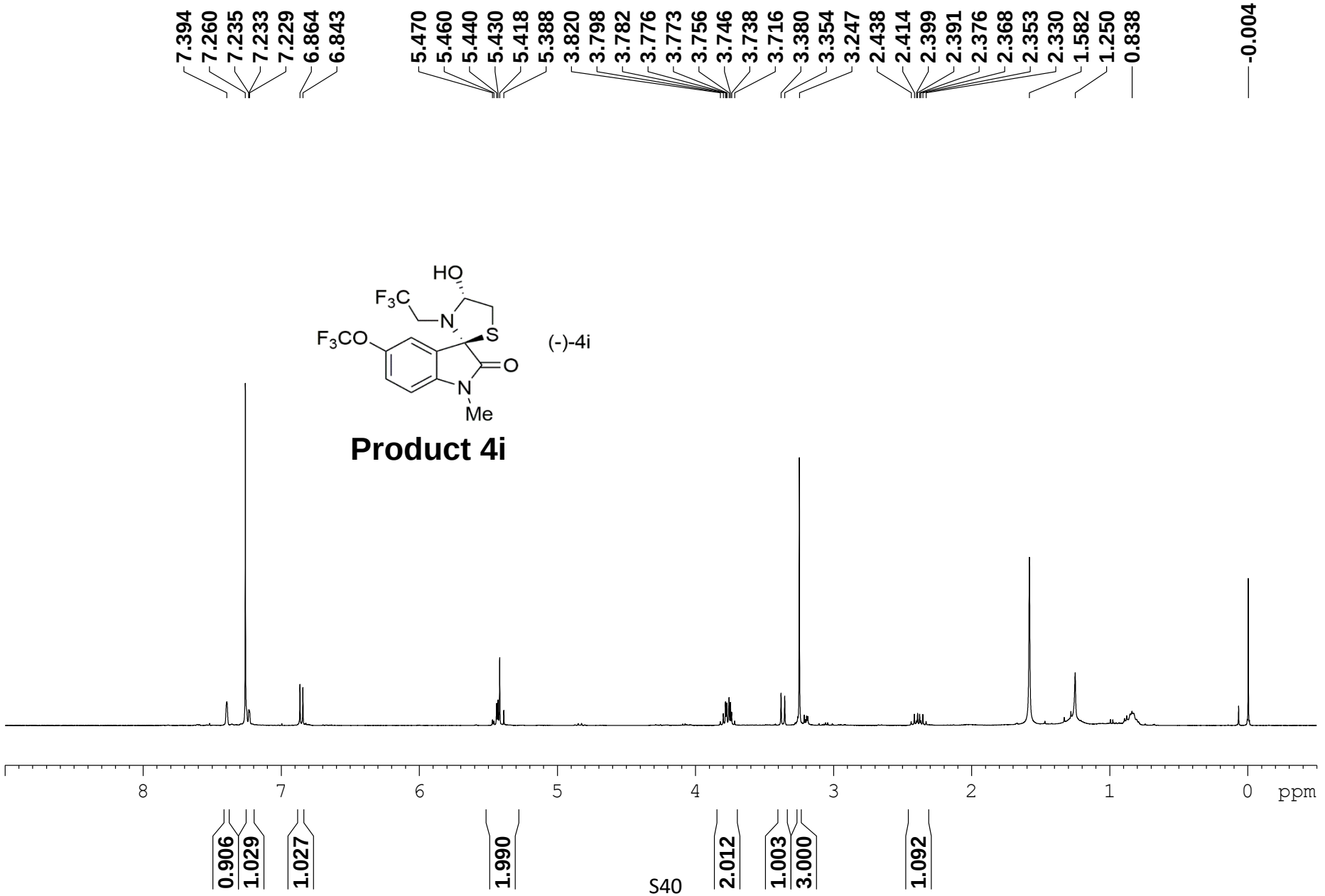
HO
F3C
N
S
MeO
O
N
Me
(-)-4h
Product 4h
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm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7.260
7.235
7.233
7.229
6.864
6.843
5.470
5.460
5.440
5.430
5.418
5.388
3.820
3.798
3.782
3.776
3.773
3.756
3.746
3.738
3.716
3.380
3.354
3.247
2.438
2.414
2.399
2.391
2.376
2.368
2.353
2.330
1.582
1.250
0.838
-0.004
HO
F3C
N
S
F3CO
O
N
Me
(-)-4i
Product 4i
8
7
6
5
4
3
2
1
0
ppm
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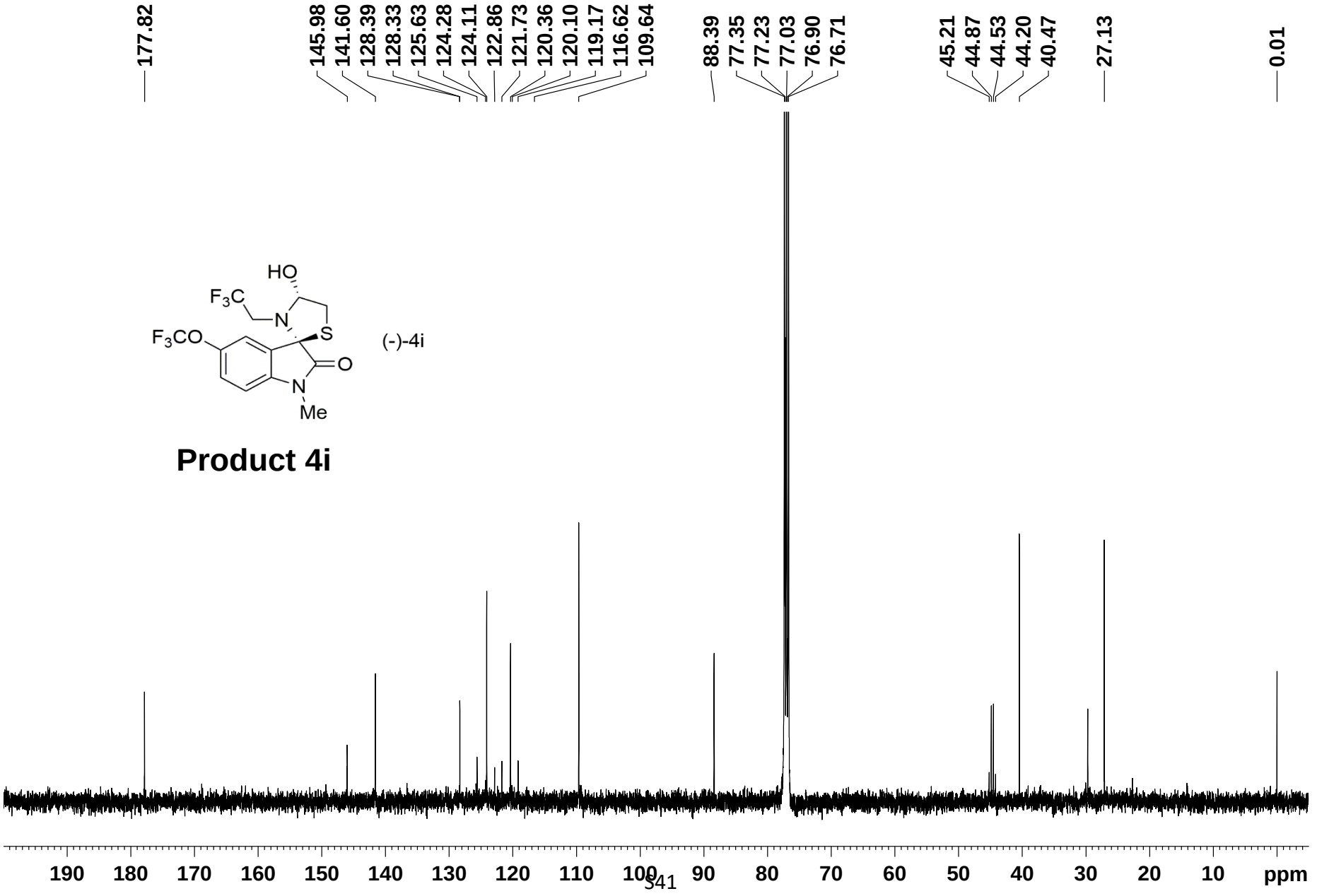
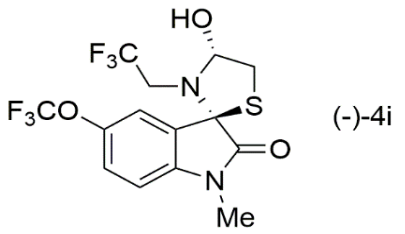
1.027
1.990
2.012
1.003
3.000
1.092


177.82
145.98
141.60
128.39
128.33
125.63
124.28
124.11
122.86
121.73
120.36
120.10
119.17
116.62
109.64
88.39
77.35
77.23
77.03
76.90
76.71
45.21
44.87
44.53
44.20
40.47
27.13
0.01
HO
F3C
N
S
F3CO
O
N
Me
(-)-4i
Product 4i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

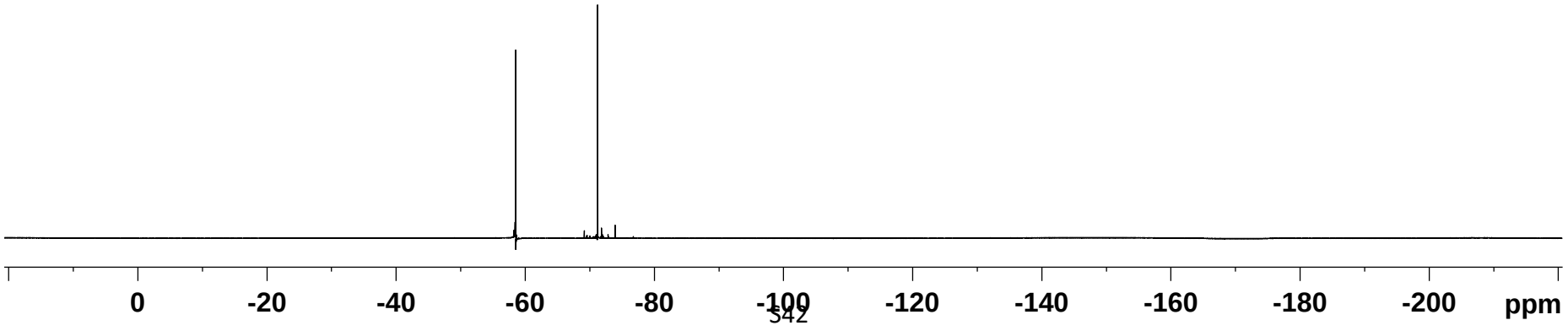
-58.53

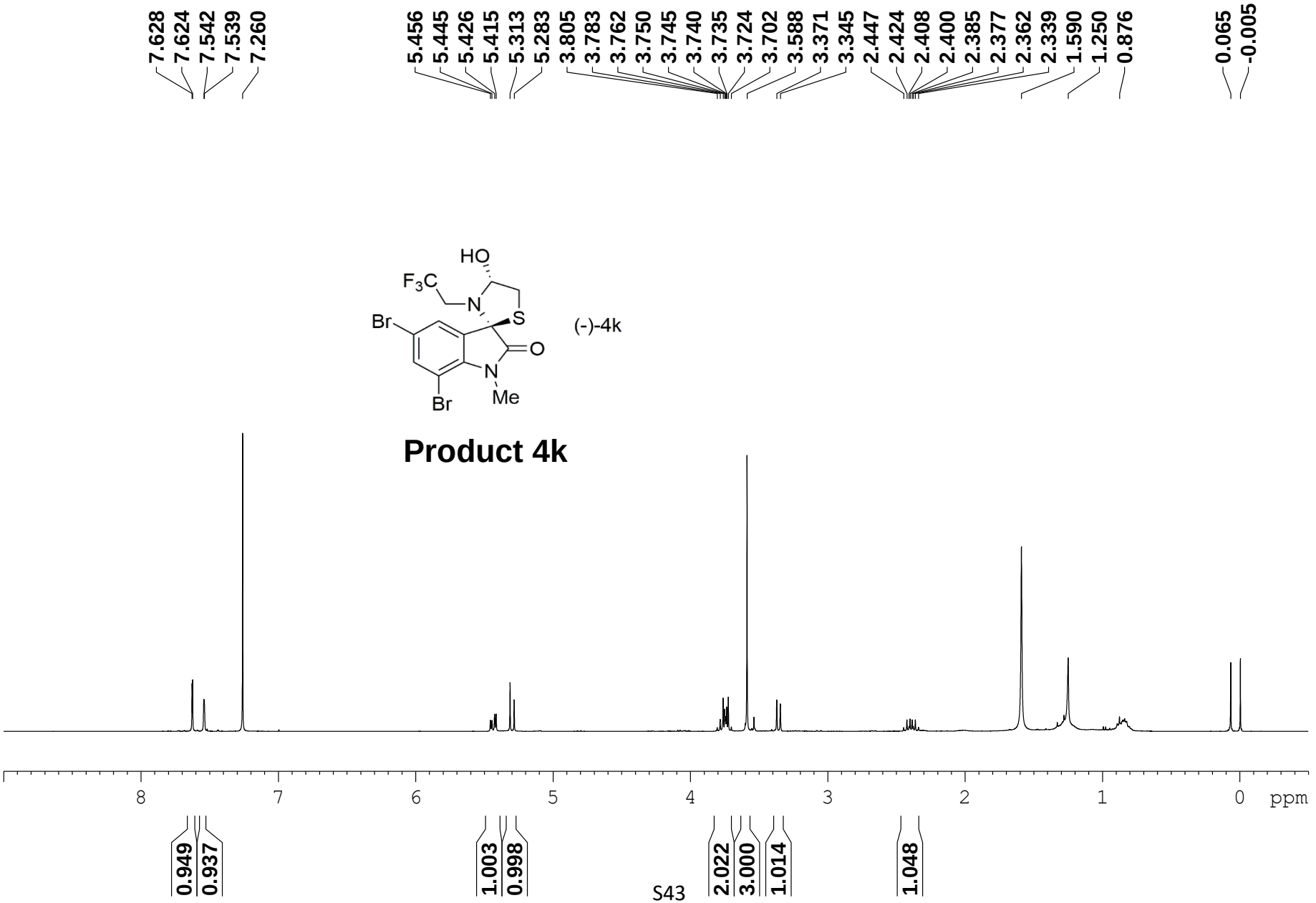
-71.21



(-)-4i

Product 4i

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7.624
7.542
7.539
7.260
5.456
5.445
5.426
5.415
5.313
5.283
3.805
3.783
3.762
3.750
3.745
3.740
3.735
3.724
3.702
3.588
3.371
3.345
2.447
2.424
2.408
2.400
2.385
2.377
2.362
2.339
1.590
1.250
0.876
0.065
-0.005
HO
F3C
N
S
Br
O
N
Me
Br
(-)-4k
Product 4k
8
7
6
5
4
3
2
1
0
ppm
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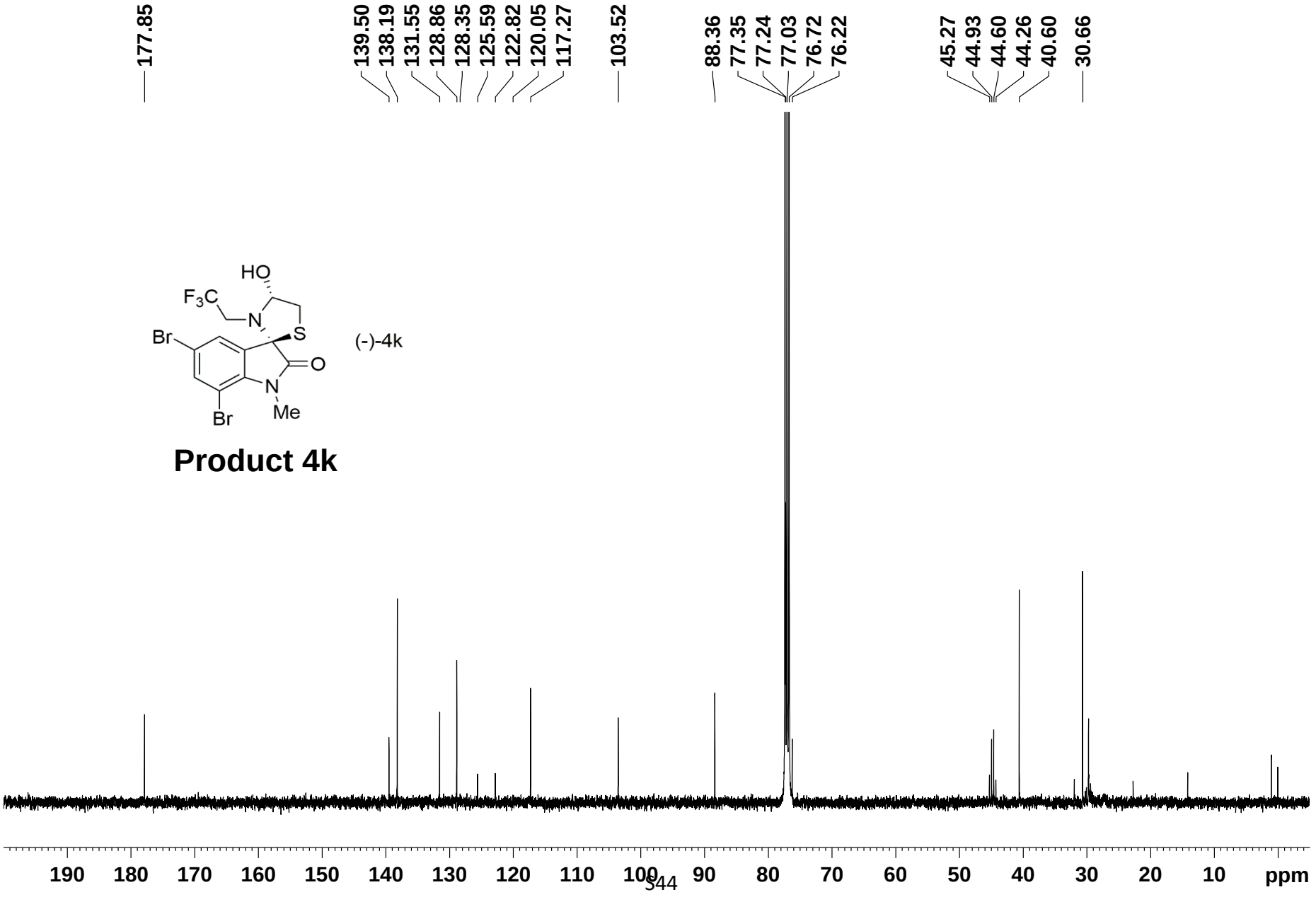
0.937
1.003
0.998
2.022
3.000
1.014
1.048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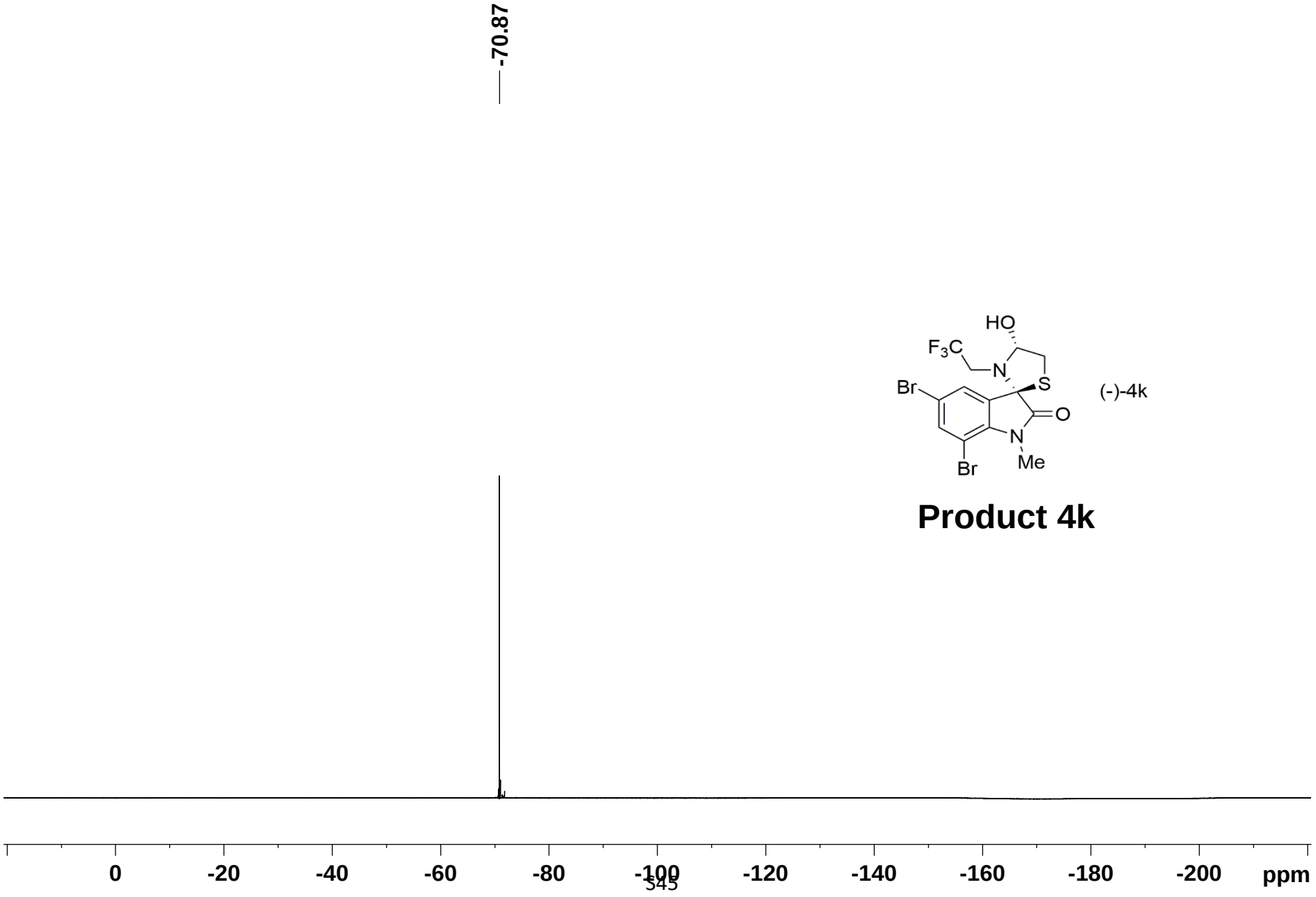
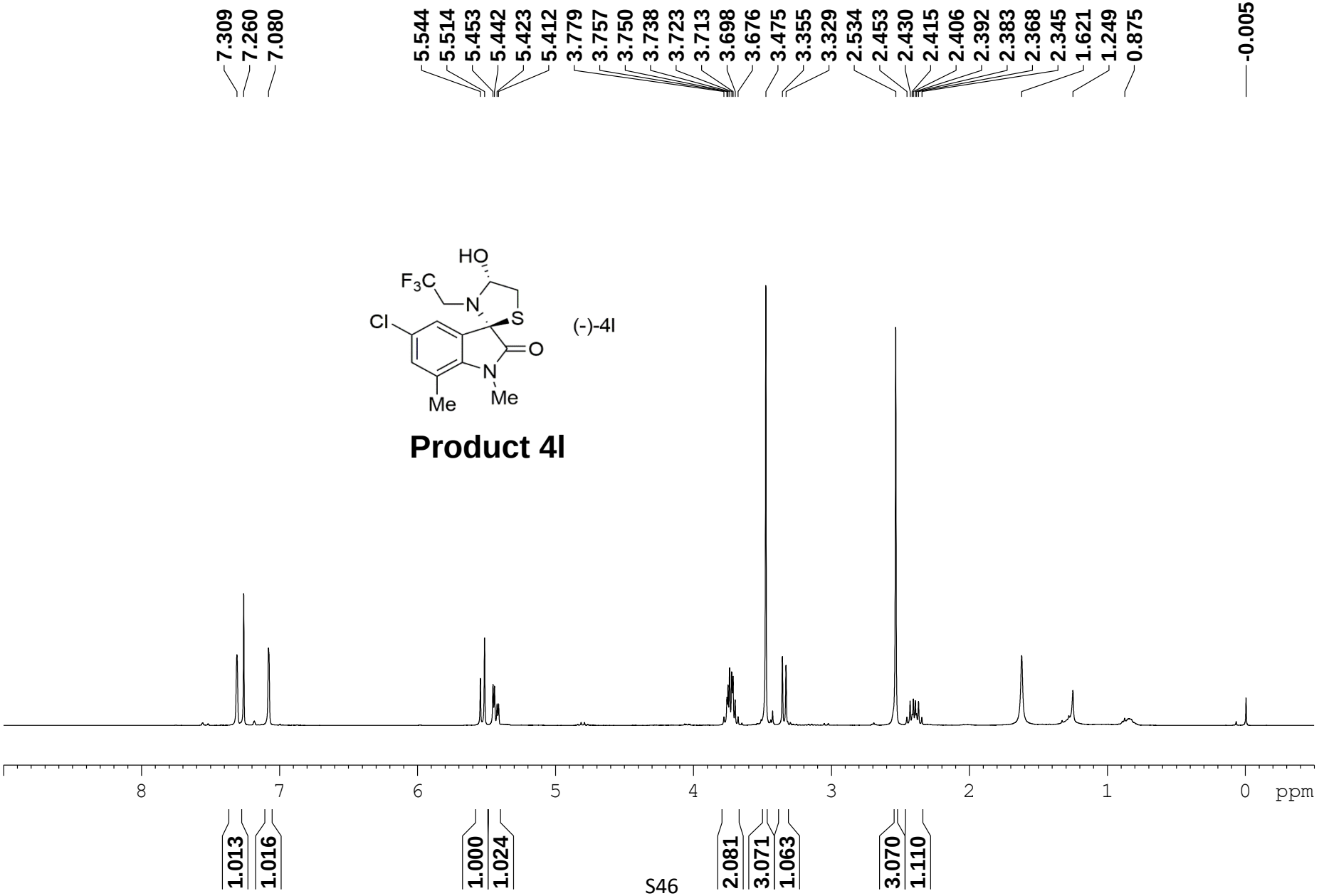
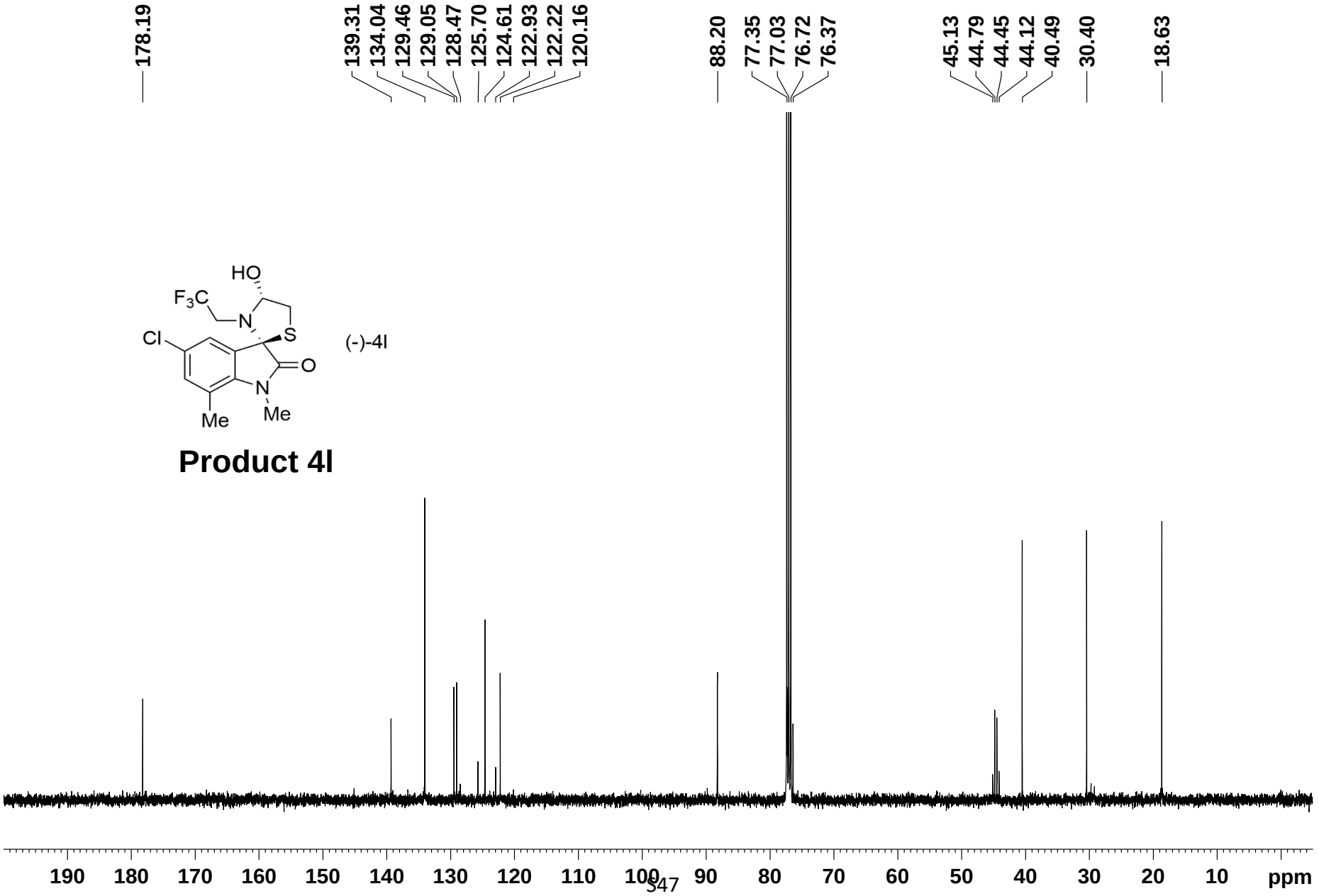
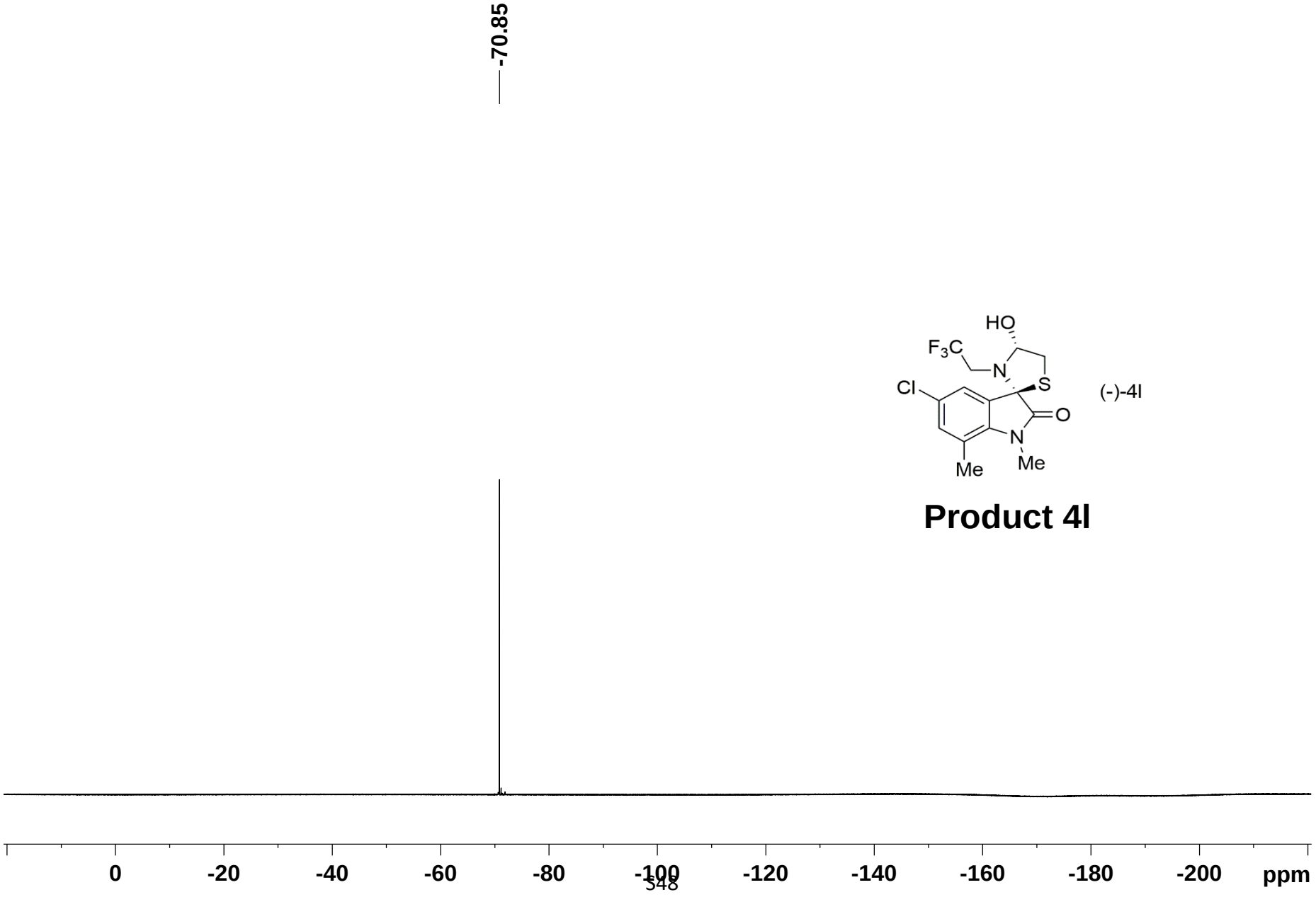
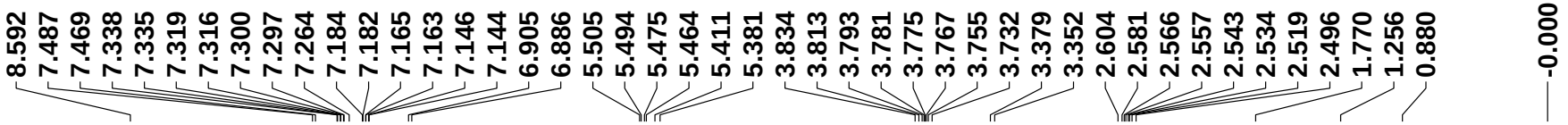
139.50
138.19
131.55
128.86
128.35
125.59
122.82
120.05
117.27
103.52
88.36
77.35
77.24
77.03
76.72
76.22
45.27
44.93
44.60
44.26
40.60
30.66
HO
F3C
N
S
Br
O
N
Me
Br
(-)-4k
Product 4k
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

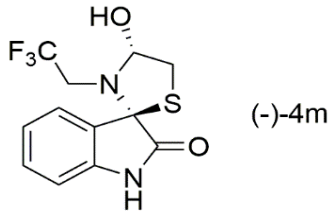

-70.87
HO
F3C
N
S
Br
O
N
Me
Br
(-)-4k
Product 4k
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm


7.309
7.260
7.080
5.544
5.514
5.453
5.442
5.423
5.412
3.779
3.757
3.750
3.738
3.723
3.713
3.698
3.676
3.475
3.355
3.329
2.534
2.453
2.430
2.415
2.406
2.392
2.383
2.368
2.345
1.621
1.249
0.875
-0.005
HO
F3C
N
S
Cl
O
N
Me
Me
(-)-4l
Product 4l
8
7
6
5
4
3
2
1
0
ppm
1.013
1.016
1.000
1.024
2.081
3.071
1.063
3.070
1.110


178.19
139.31
134.04
129.46
129.05
128.47
125.70
124.61
122.93
122.22
120.16
88.20
77.35
77.03
76.72
76.37
45.13
44.79
44.45
44.12
40.49
30.40
18.63
HO
F3C
N
S
Cl
O
N
Me
Me
(-)-4l
Product 4l
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

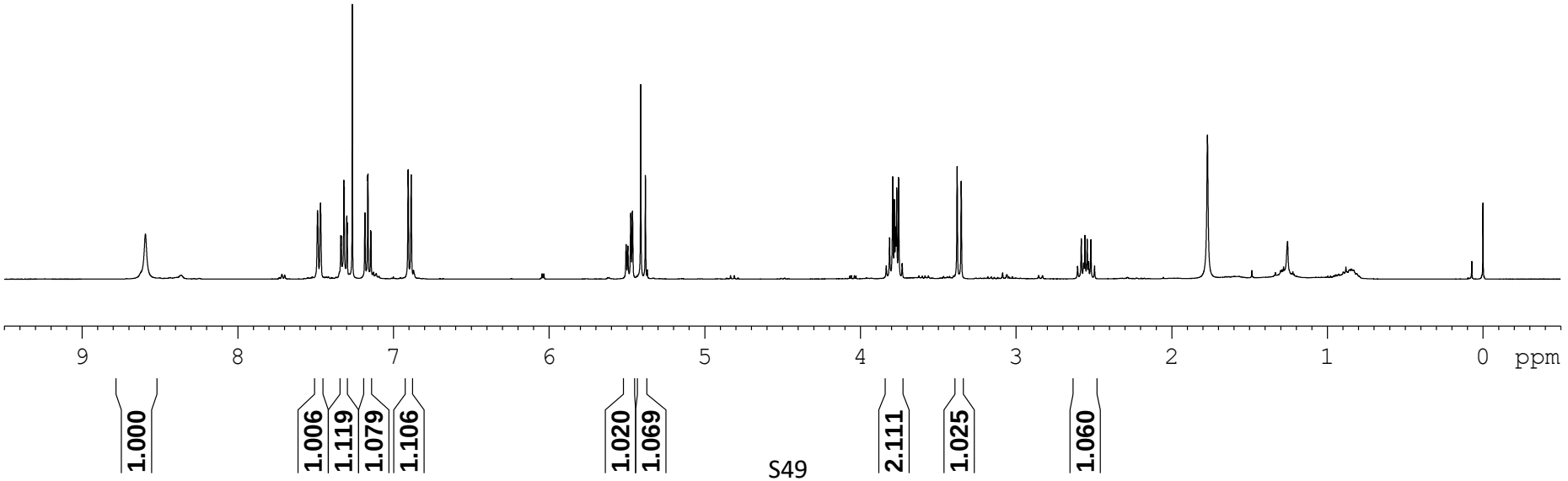

-70.85
HO
F3C
N
S
Cl
O
N
Me
Me
(-)-4l
Product 4l
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

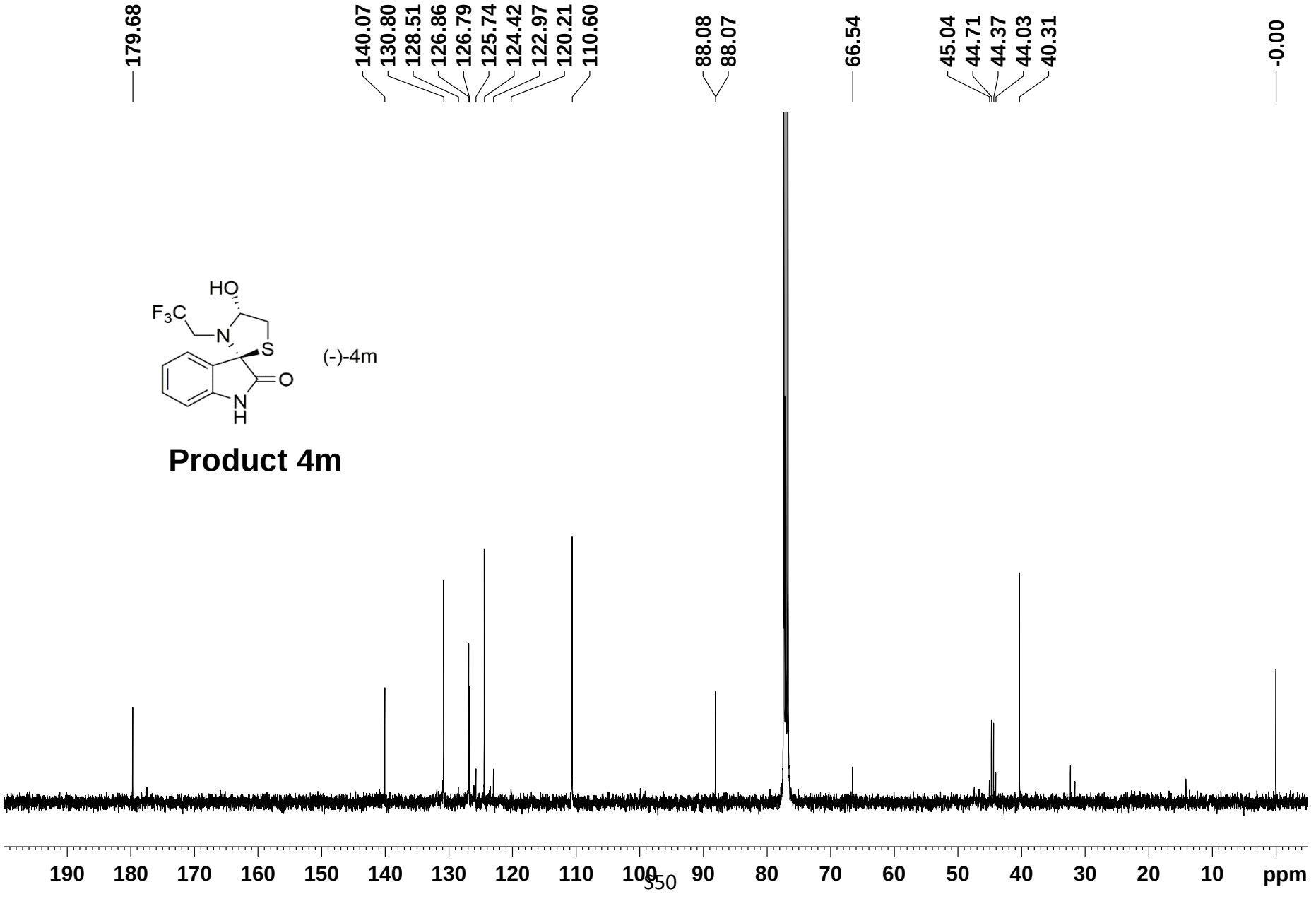


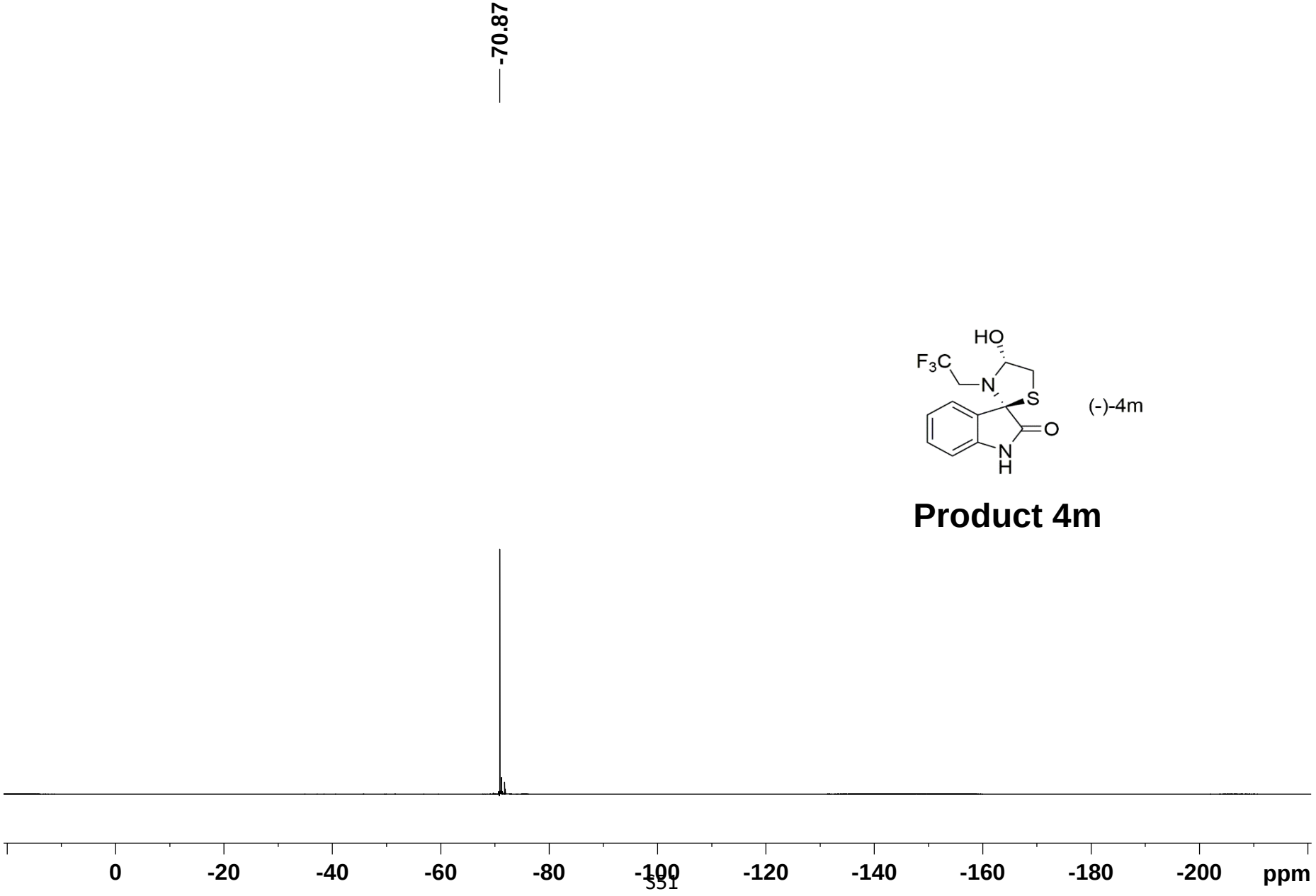


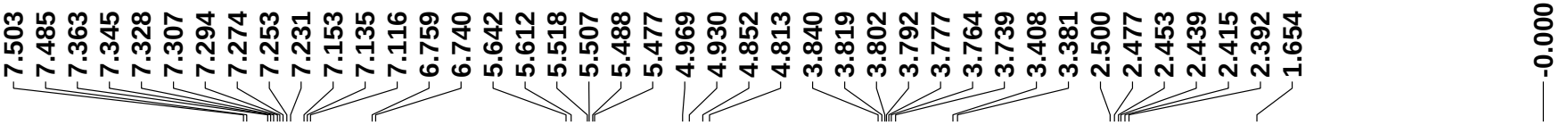
(-)-4m

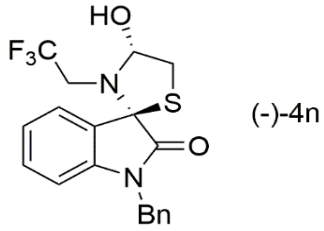
Product 4m




179.68
140.07
130.80
128.51
126.86
126.79
125.74
124.42
122.97
120.21
110.60
88.08
88.07
66.54
45.04
44.71
44.37
44.03
40.31
-0.00
HO
F3C
N
S
O
N
H
(-)-4m
Product 4m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

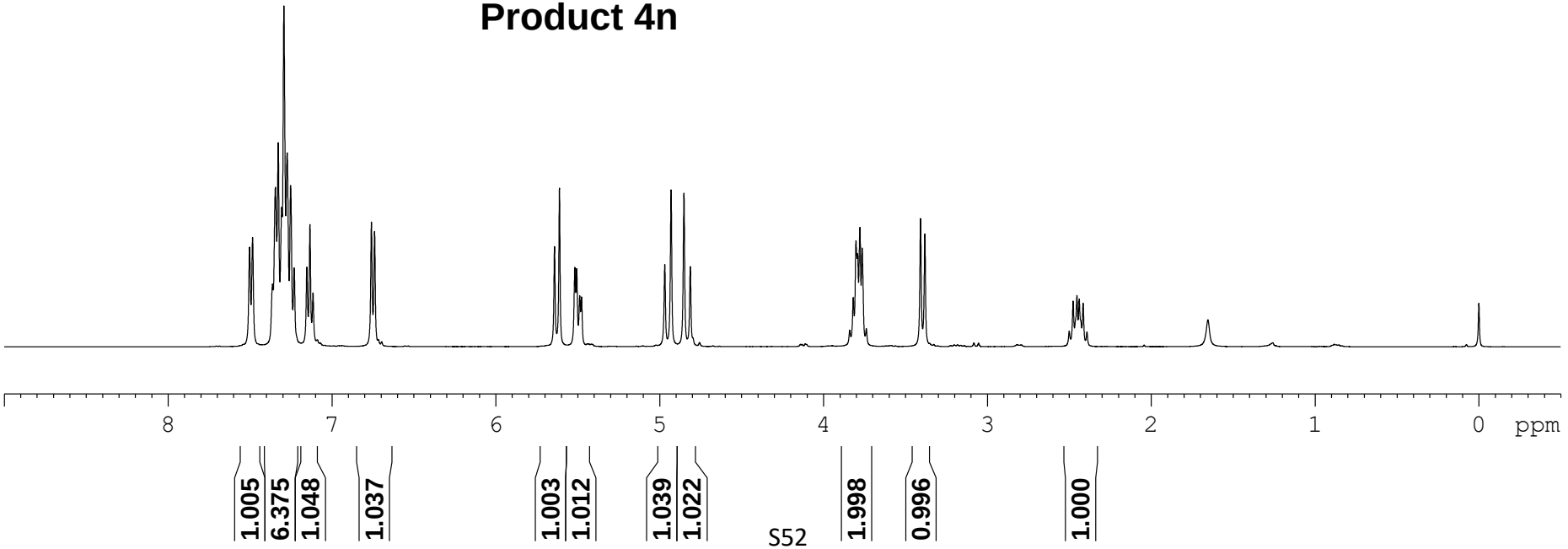

-70.87
HO
F3C
N
S
O
N
H
(-)-4m
Product 4m
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

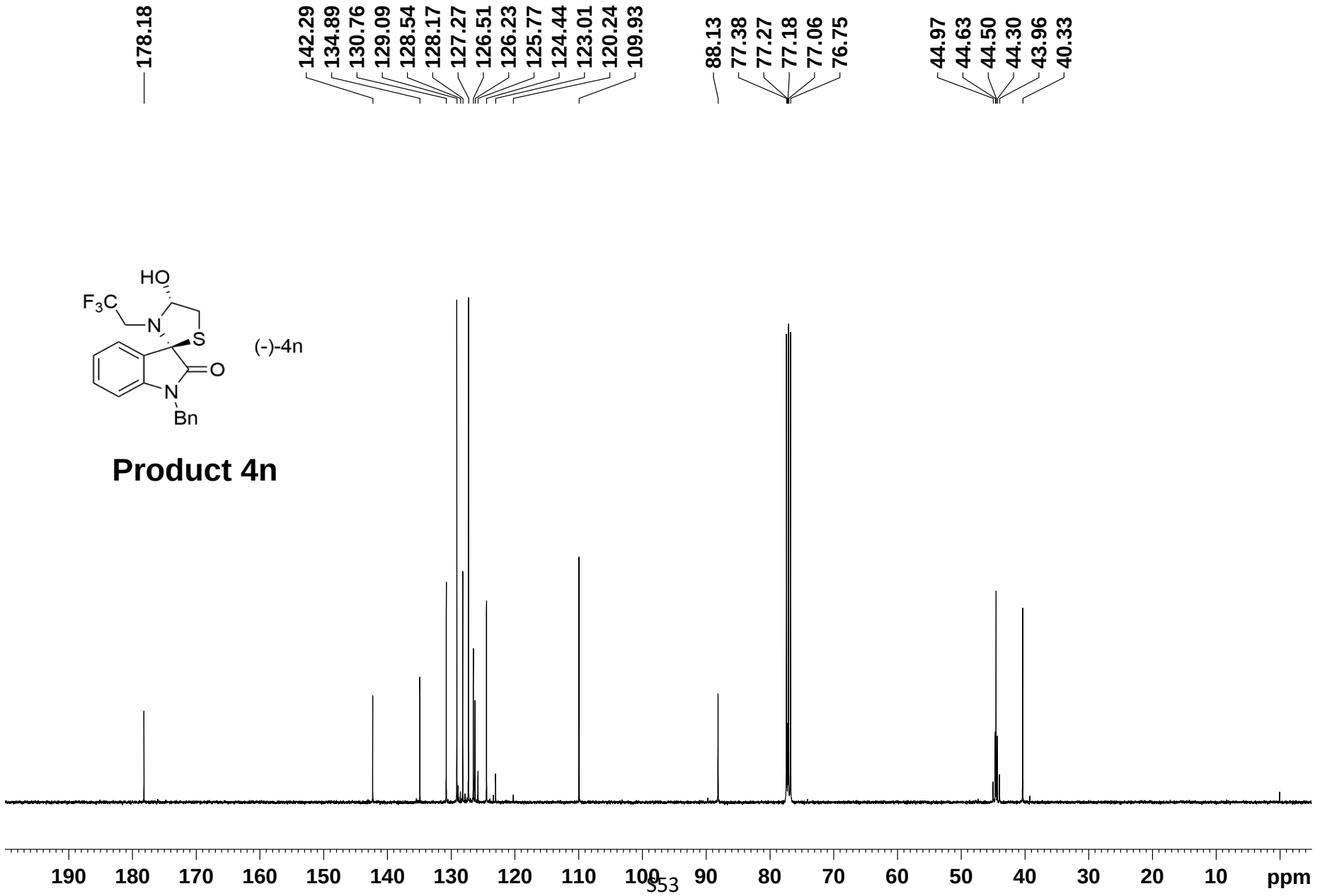


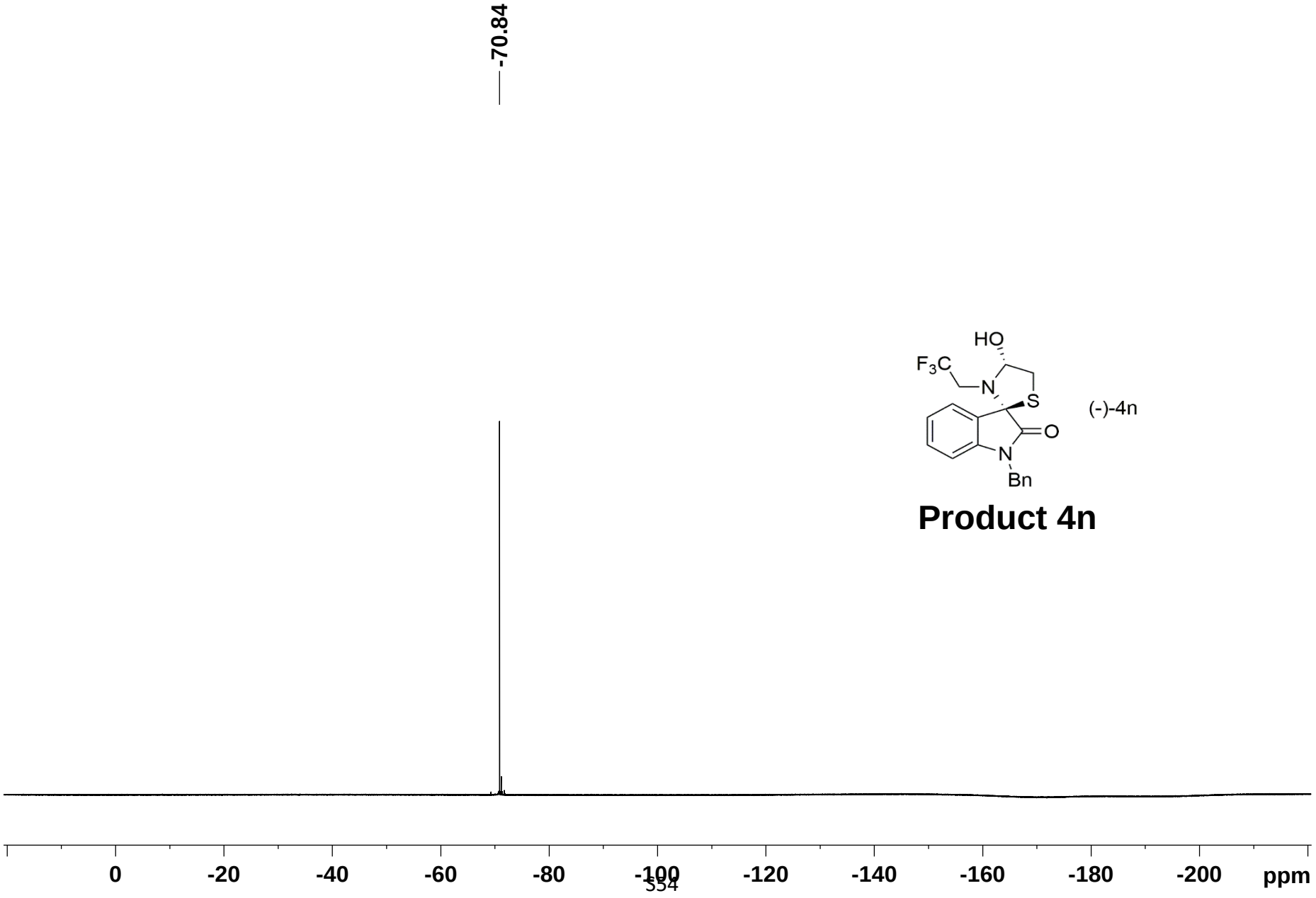


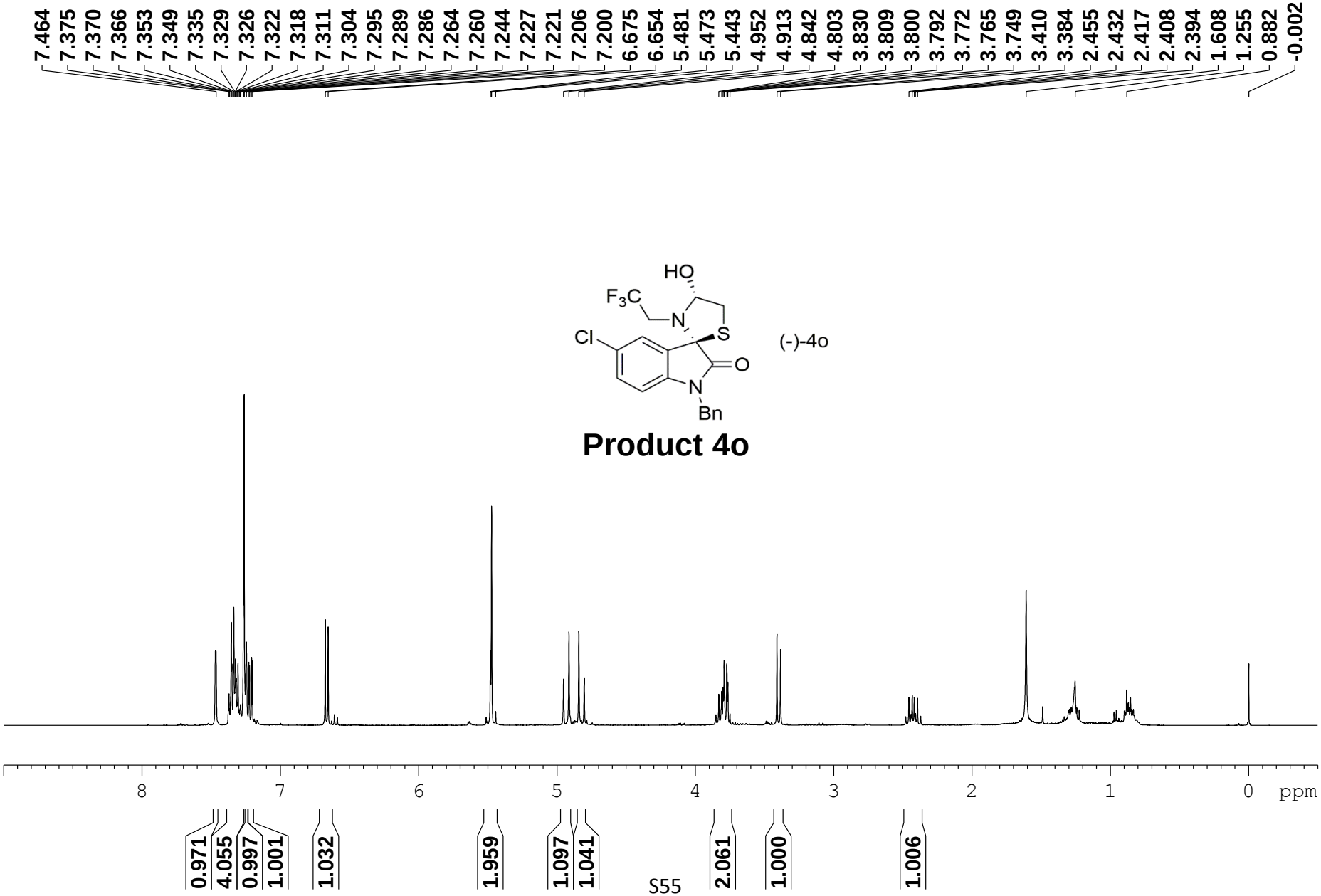
(-)-4n

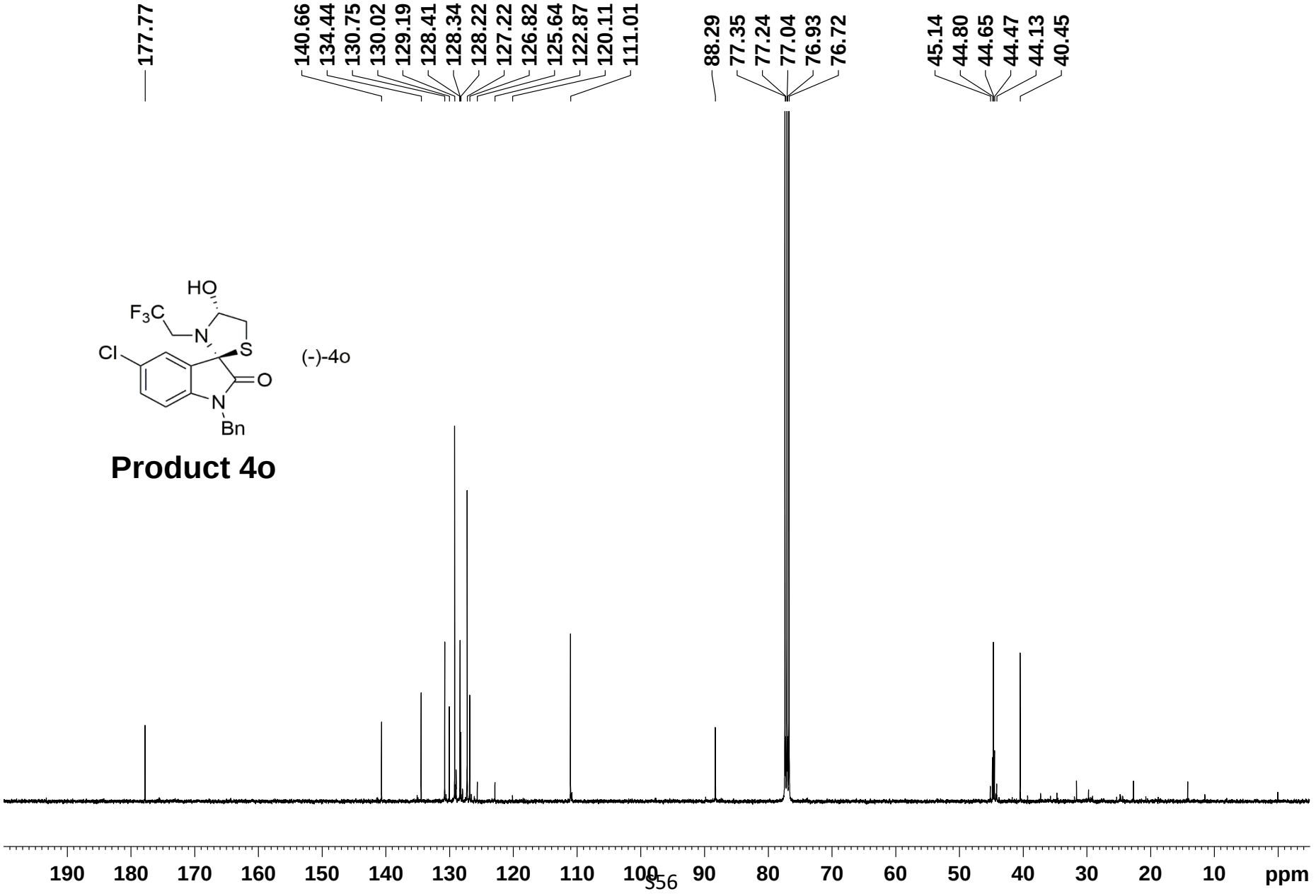
Product 4n

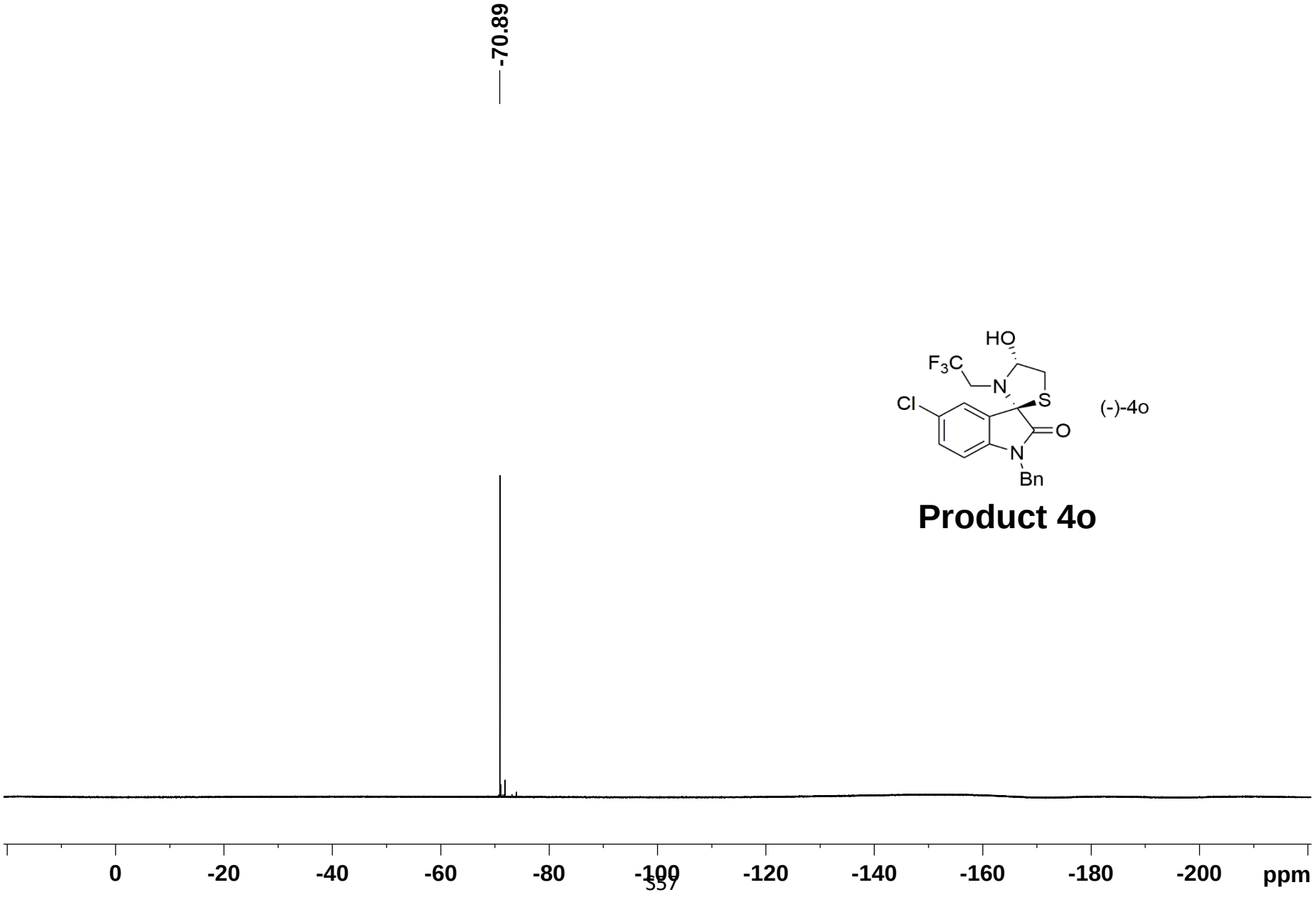


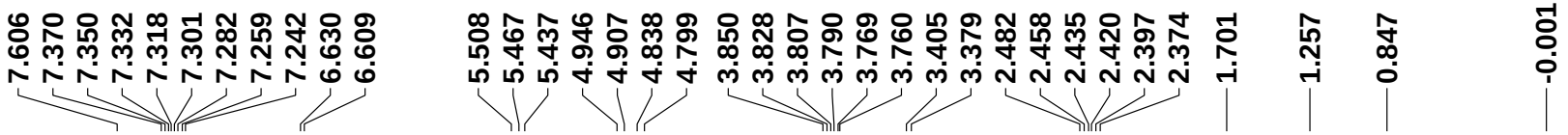

178.18
142.29
134.89
130.76
129.09
128.54
128.17
127.27
126.51
126.23
125.77
124.44
123.01
120.24
109.93
88.13
77.38
77.27
77.18
77.06
76.75
44.97
44.63
44.50
44.30
43.96
40.33
HO
F3C
N
S
O
N
Bn
(-)-4n
Product 4n
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

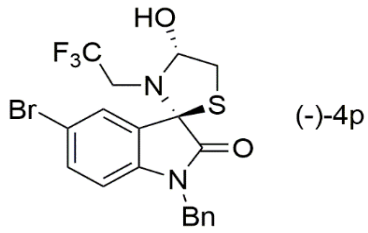

-70.84
HO
F3C
N
S
O
N
Bn
(-)-4n
Product 4n
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm


7.464
7.375
7.370
7.366
7.353
7.349
7.335
7.329
7.326
7.322
7.318
7.311
7.304
7.295
7.289
7.286
7.264
7.260
7.244
7.227
7.221
7.206
7.200
6.675
6.654
5.481
5.473
5.443
4.952
4.913
4.842
4.803
3.830
3.809
3.800
3.792
3.772
3.765
3.749
3.410
3.384
2.455
2.432
2.417
2.408
2.394
1.608
1.255
0.882
-0.002
HO
F3C
N
S
Cl
O
N
Bn
(-)-4o
Product 4o
8
7
6
5
4
3
2
1
0
ppm
0.971
4.055
0.997
1.001
1.032
1.959
1.097
1.041
2.061
1.000
1.006


177.77
140.66
134.44
130.75
130.02
129.19
128.41
128.34
128.22
127.22
126.82
125.64
122.87
120.11
111.01
88.29
77.35
77.24
77.04
76.93
76.72
45.14
44.80
44.65
44.47
44.13
40.45
HO
F3C
N
S
Cl
O
N
Bn
(-)-4o
Product 4o
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

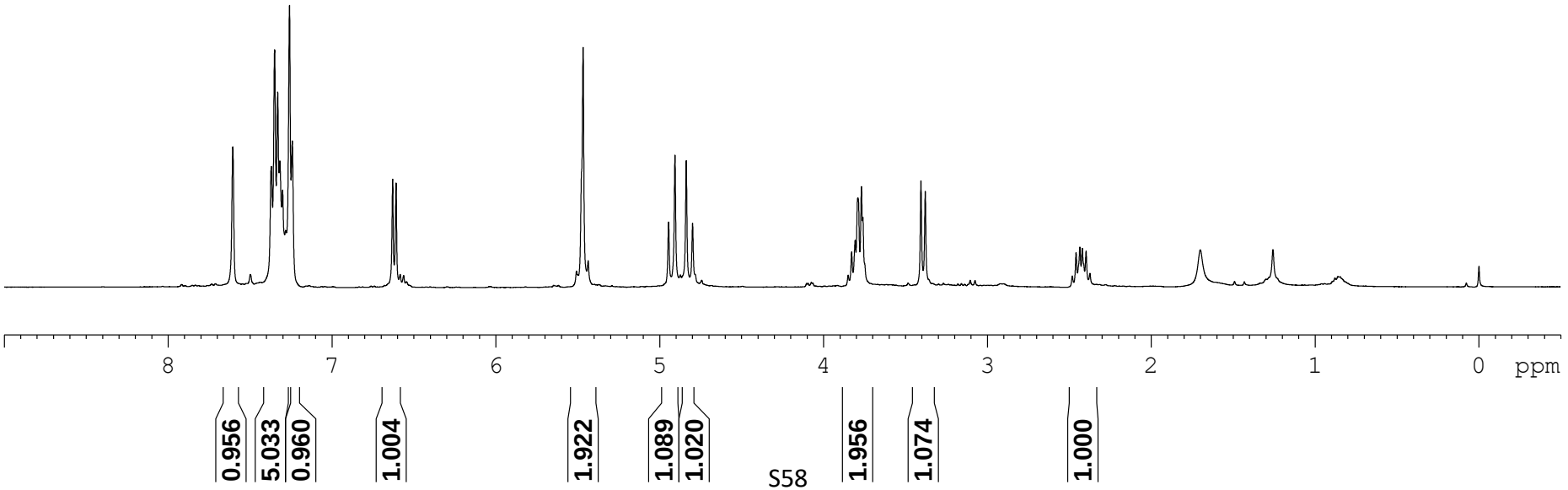

-70.89
HO
F3C
N
S
Cl
O
N
Bn
(-)-4o
Product 4o
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

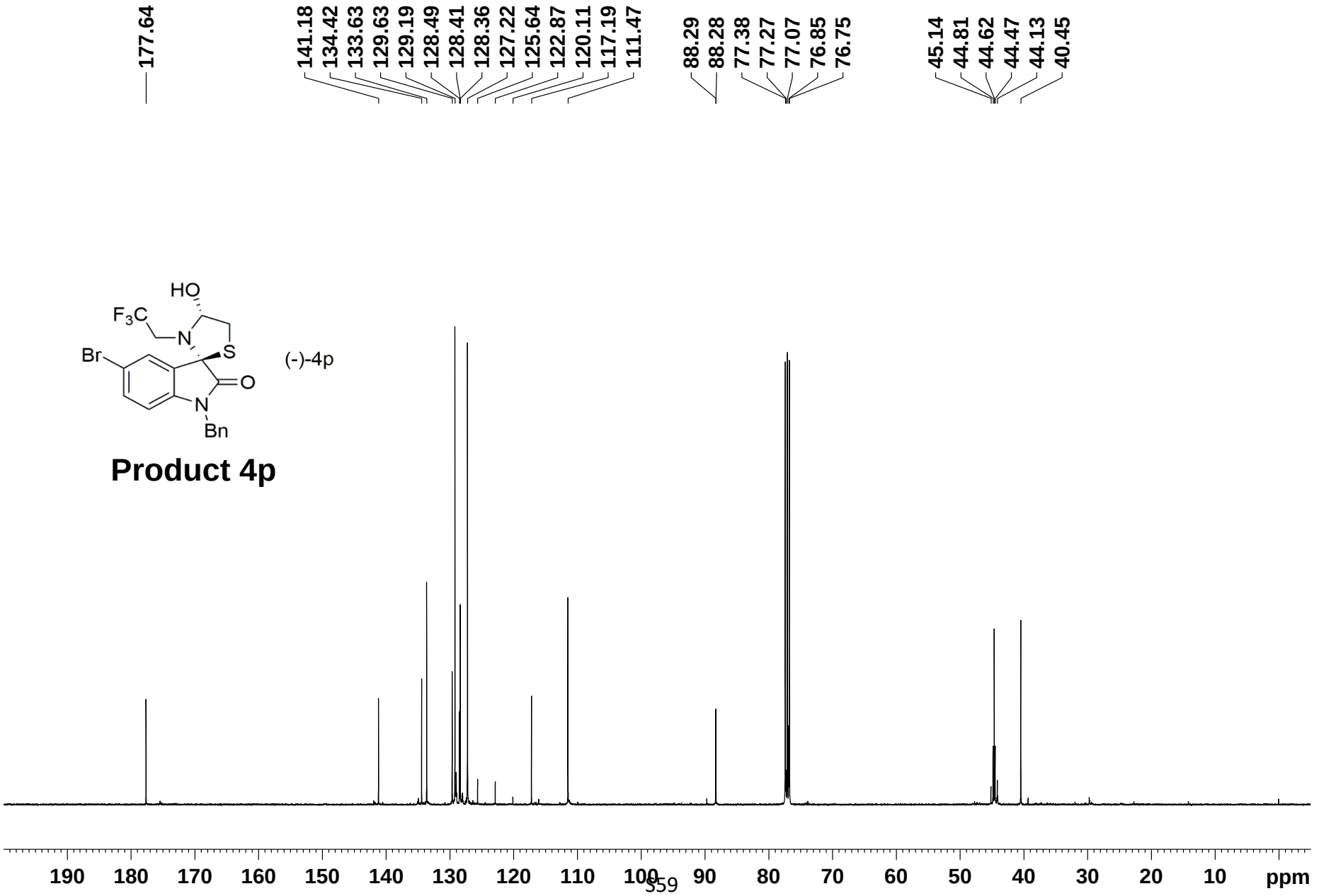


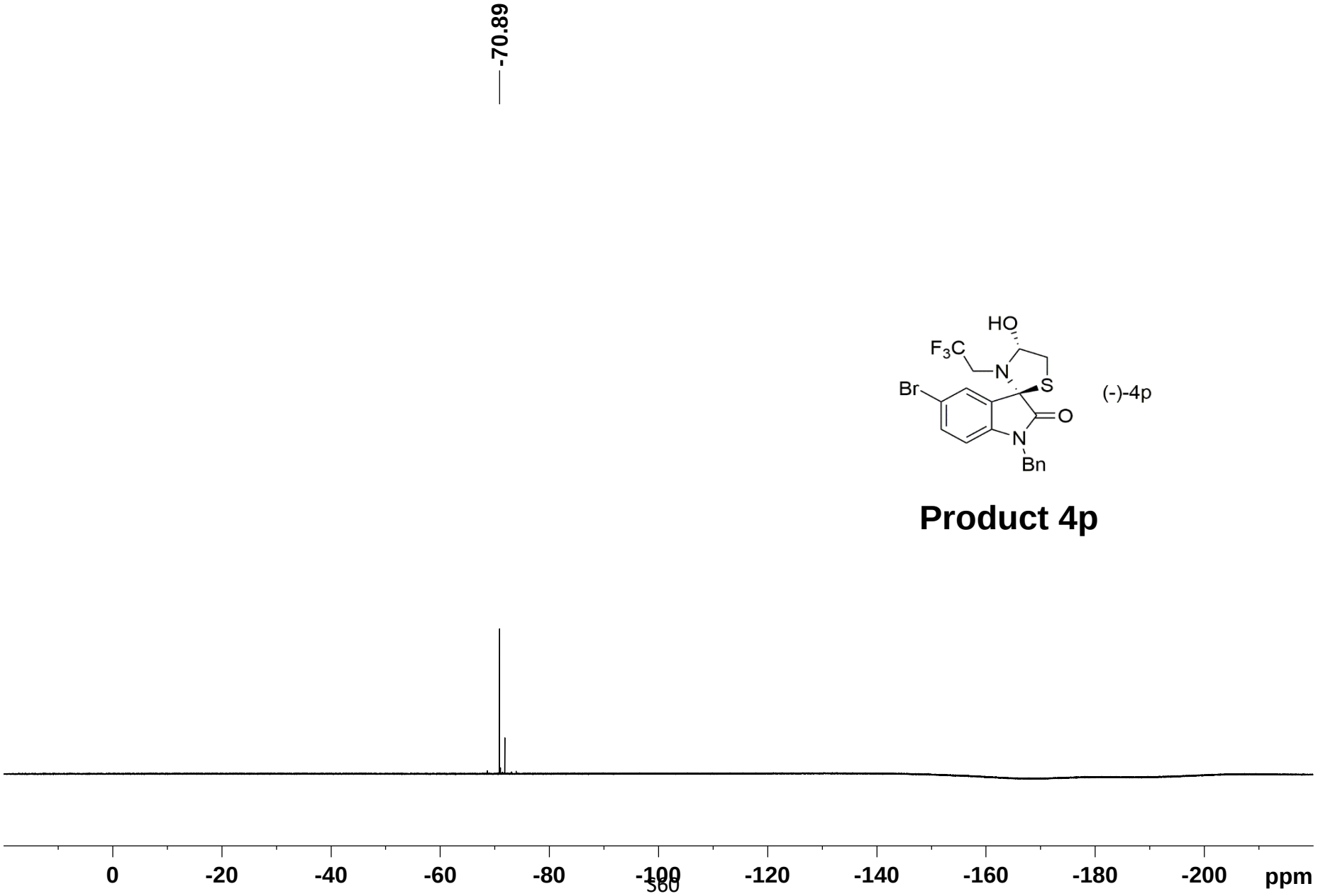


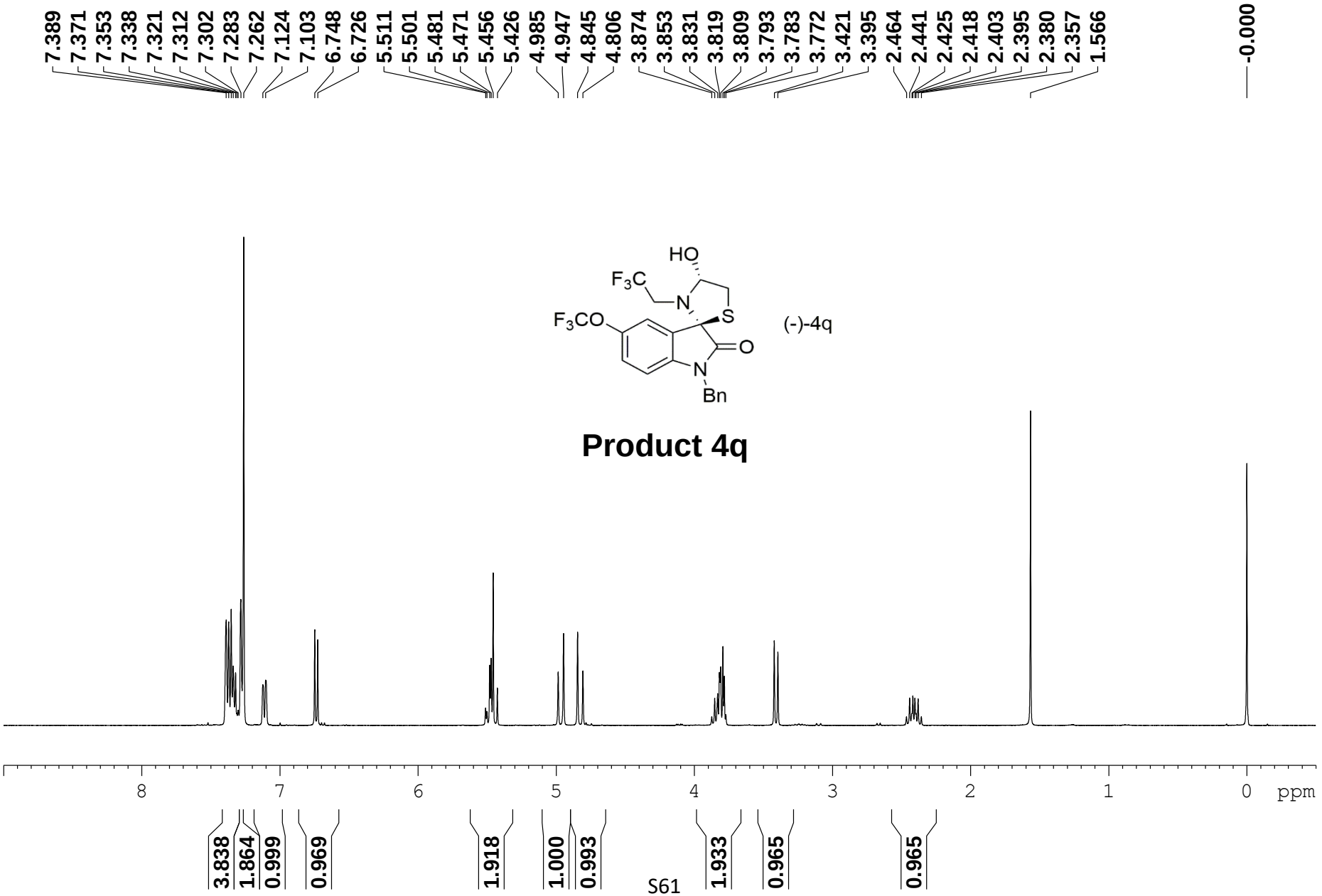
(-)-4p

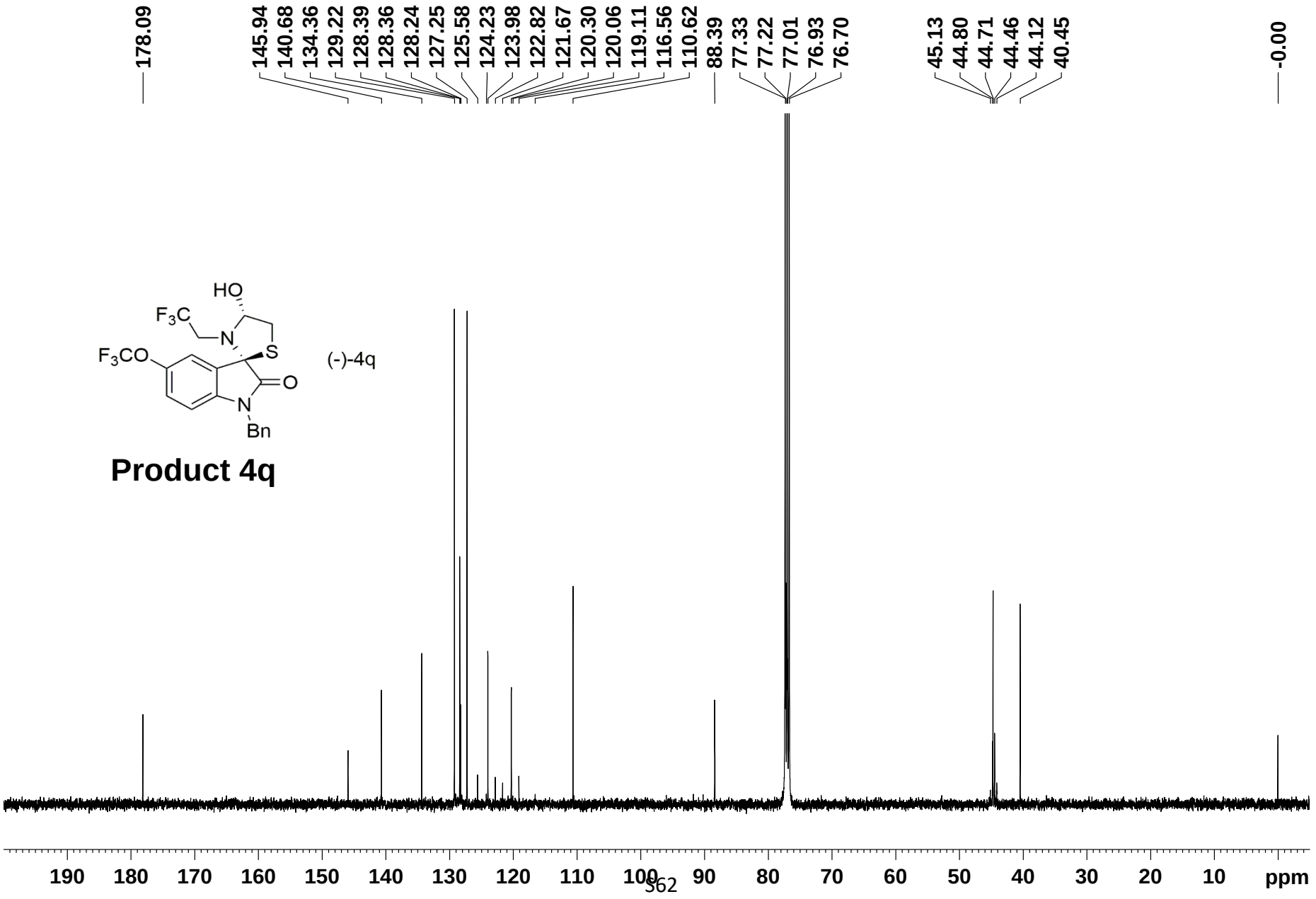
Product 4p

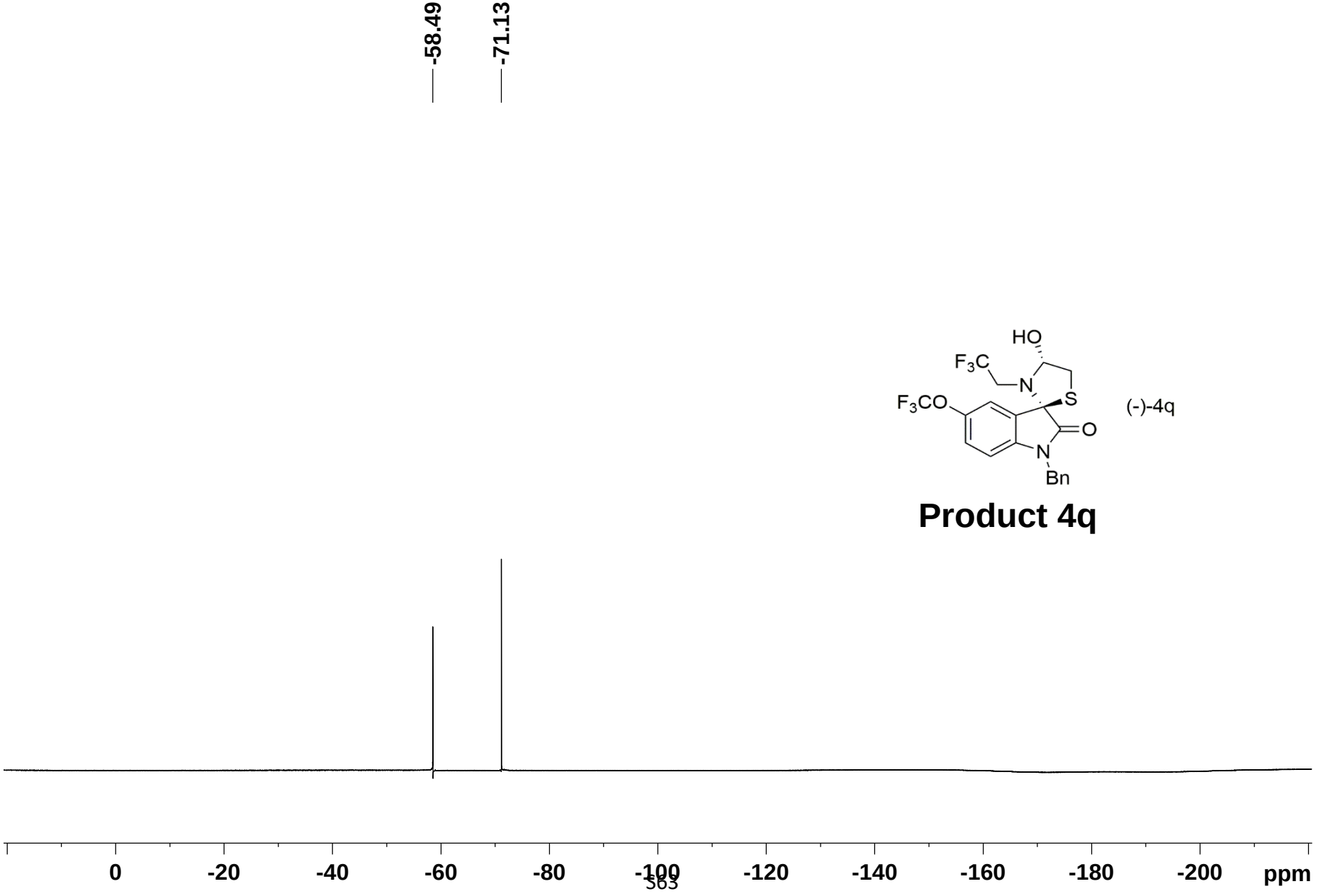


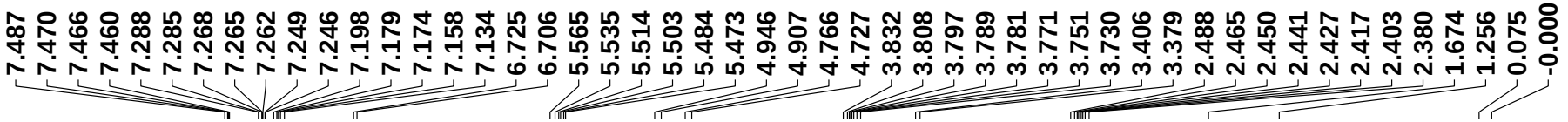

177.64
141.18
134.42
133.63
129.63
129.19
128.49
128.41
128.36
127.22
125.64
122.87
120.11
117.19
111.47
88.29
88.28
77.38
77.27
77.07
76.85
76.75
45.14
44.81
44.62
44.47
44.13
40.45
HO
F3C
N
S
Br
O
N
Bn
(-)-4p
Product 4p
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

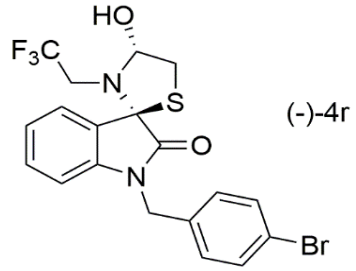

-70.89
HO
F3C
N
S
Br
O
N
Bn
(-)-4p
Product 4p
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm


7.389
7.371
7.353
7.338
7.321
7.312
7.302
7.283
7.262
7.124
7.103
6.748
6.726
5.511
5.501
5.481
5.471
5.456
5.426
4.985
4.947
4.845
4.806
3.874
3.853
3.831
3.819
3.809
3.793
3.783
3.772
3.421
3.395
2.464
2.441
2.425
2.418
2.403
2.395
2.380
2.357
1.566
-0.000
HO
F3C
N
S
F3CO
O
N
Bn
(-)-4q
Product 4q
8
7
6
5
4
3
2
1
0
ppm
3.838
1.864
0.999
0.969
1.918
1.000
0.993
1.933
0.965
0.965


178.09
145.94
140.68
134.36
129.22
128.39
128.36
128.24
127.25
125.58
124.23
123.98
122.82
121.67
120.30
120.06
119.11
116.56
110.62
88.39
77.33
77.22
77.01
76.93
76.70
45.13
44.80
44.71
44.46
44.12
40.45
-0.00
HO
F3C
N
S
F3CO
O
N
Bn
(-)-4q
Product 4q
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

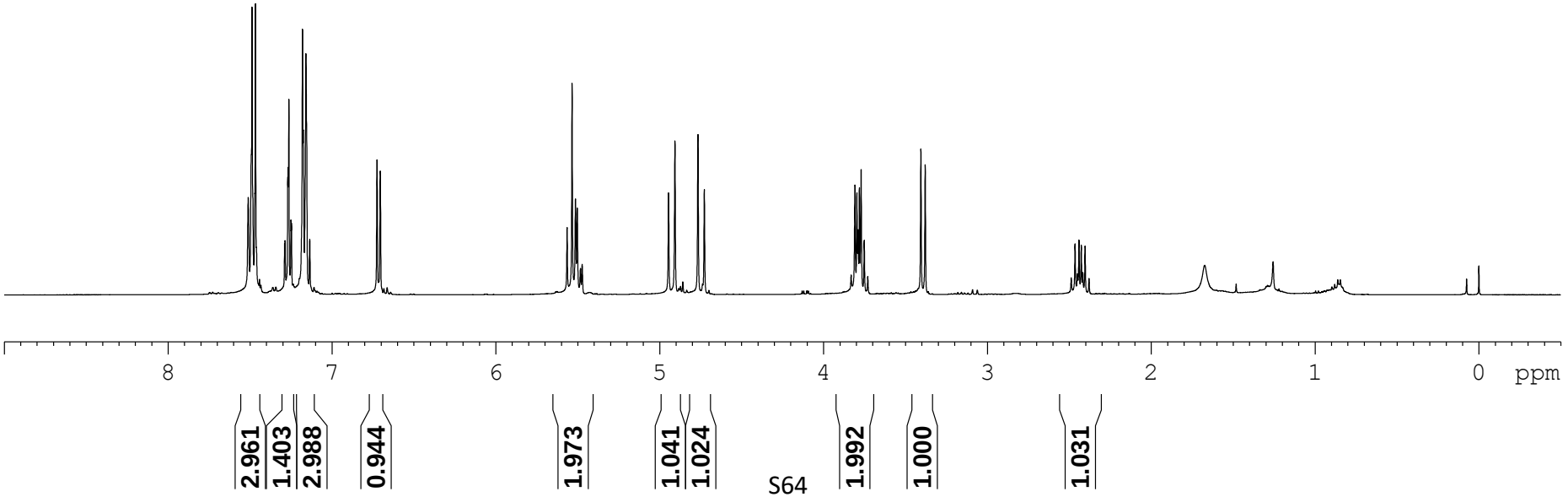

-58.49
-71.13
HO
F3C
N
S
F3CO
O
N
Bn
(-)-4q
Product 4q
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

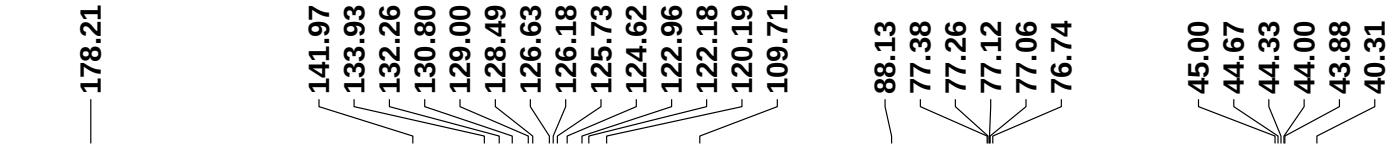


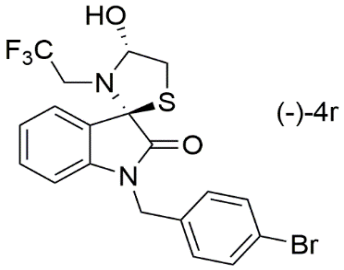


(-)-4r

Product 4r

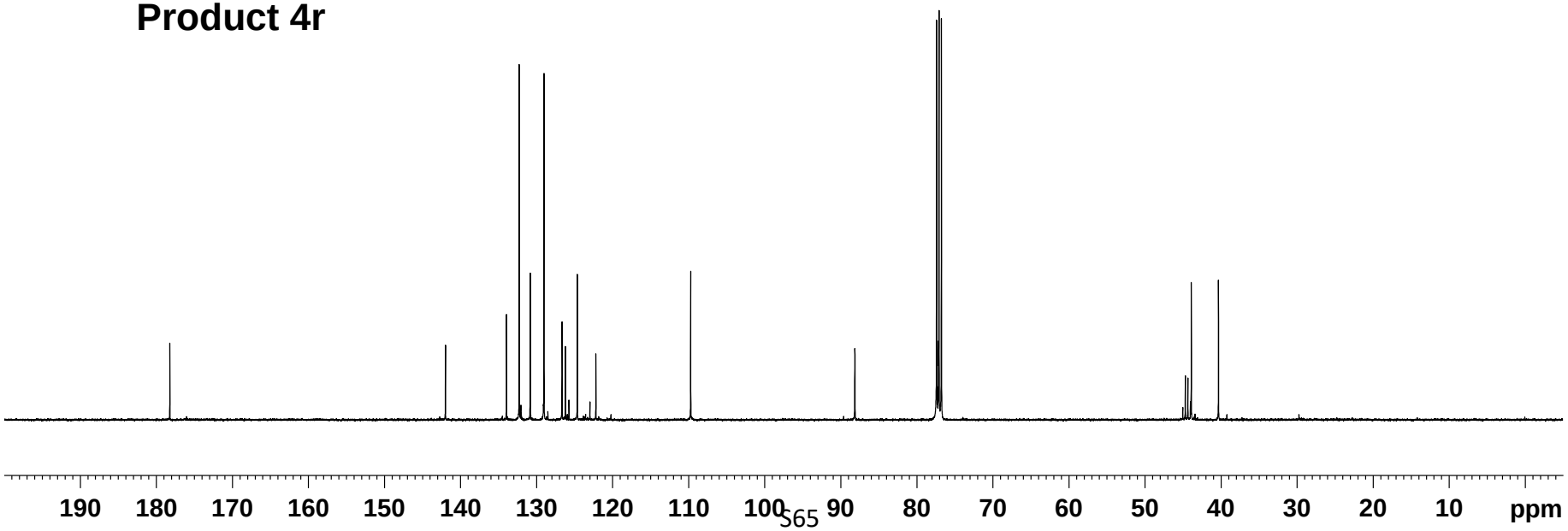


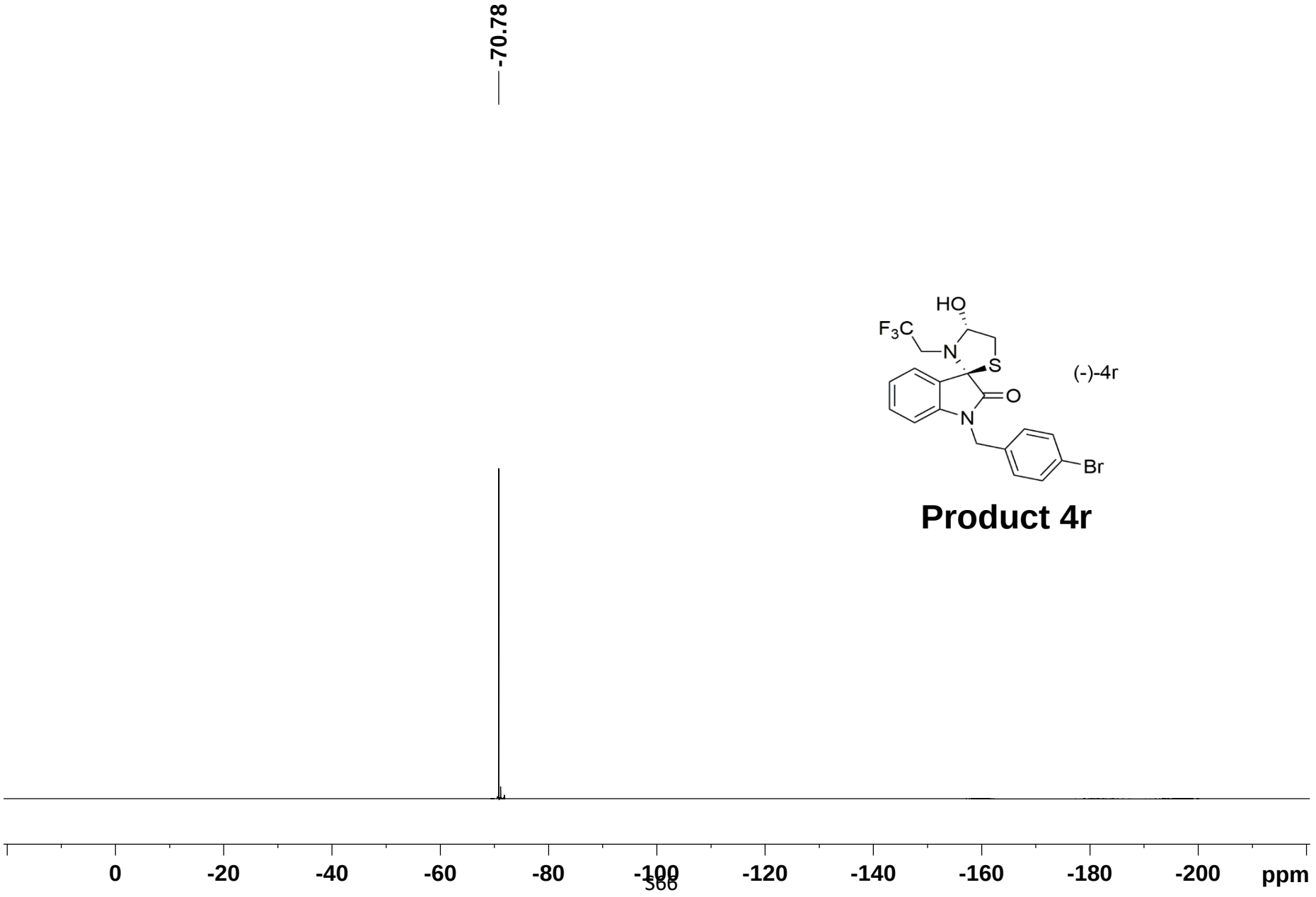


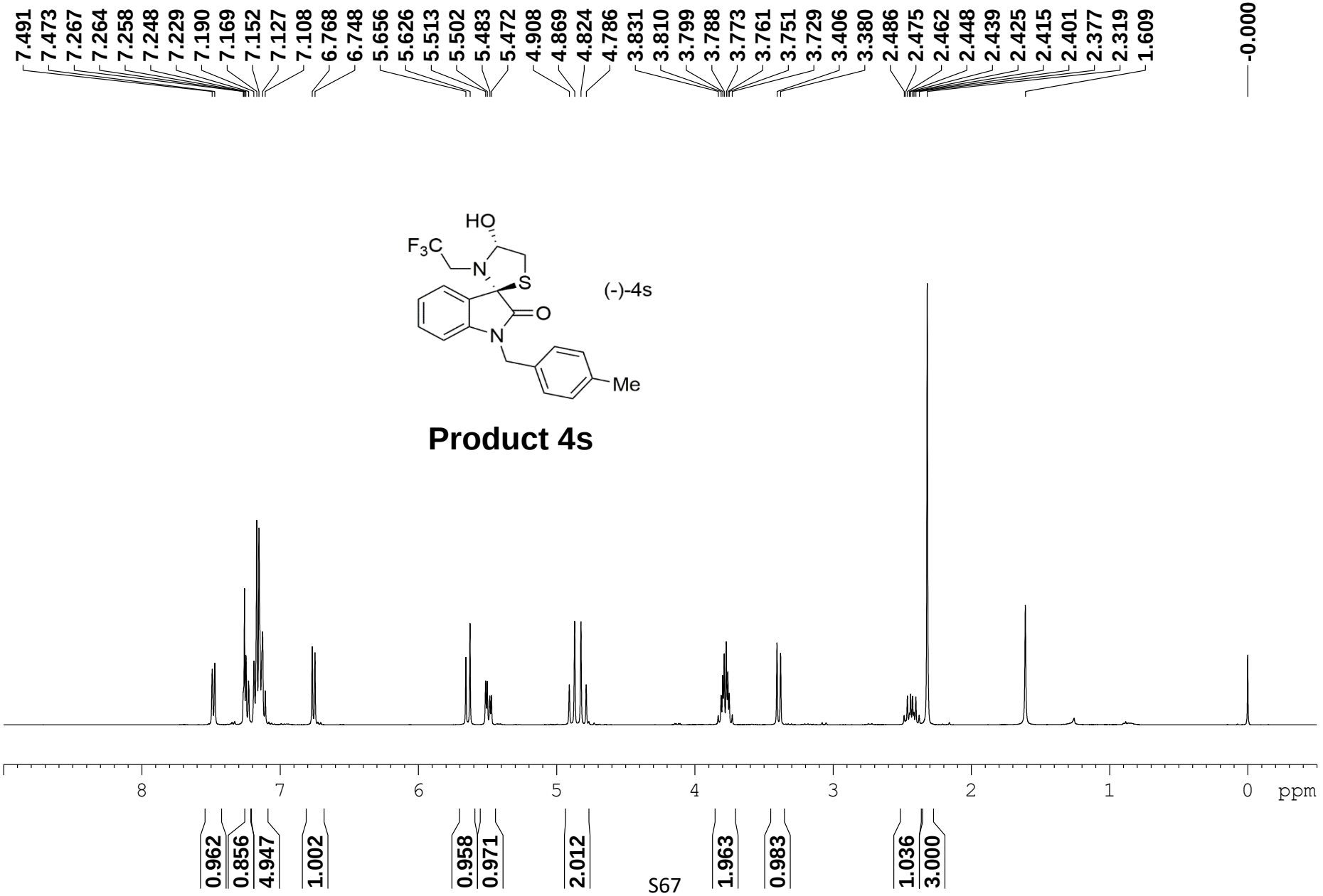


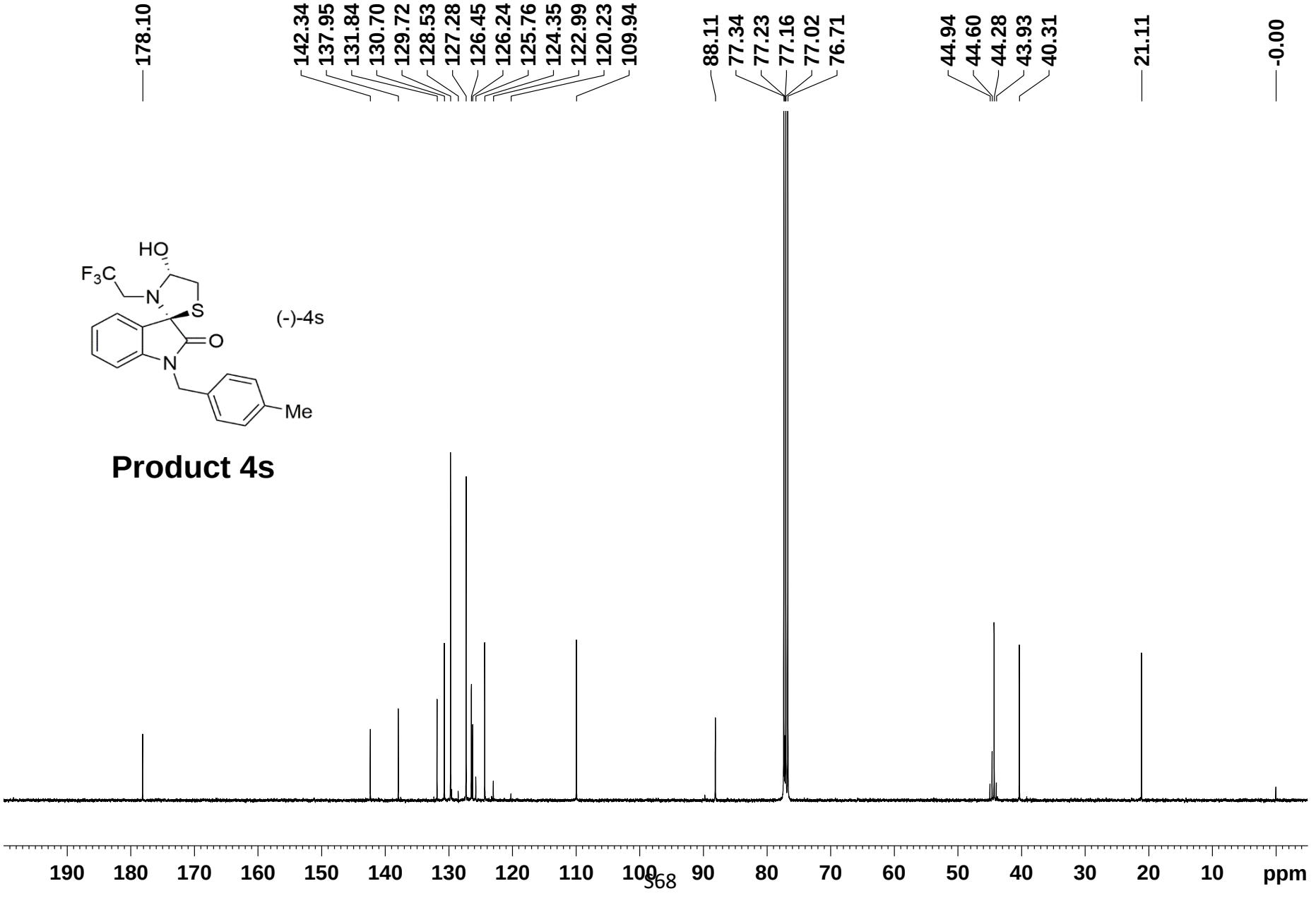
(-)-4r

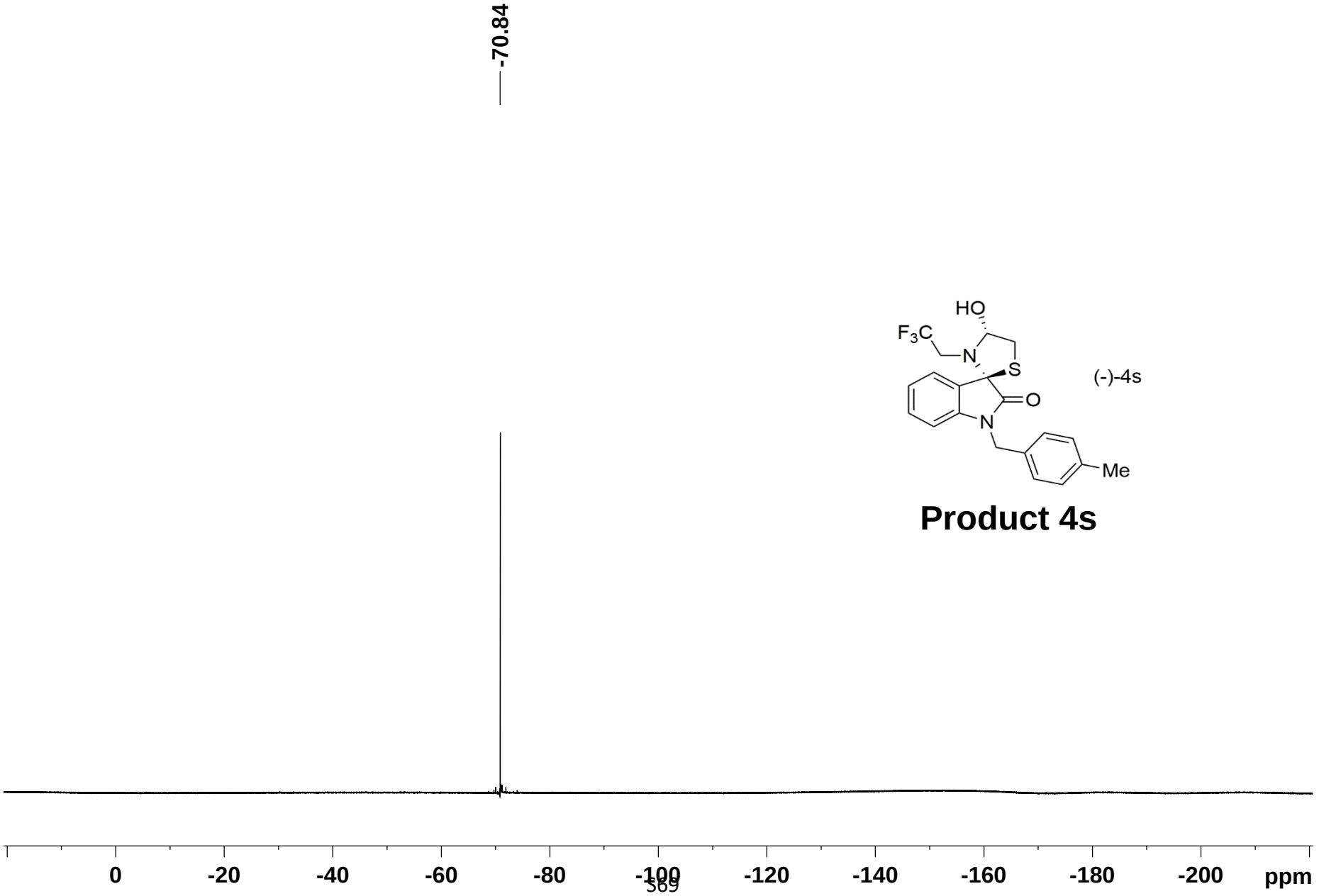
Product 4r



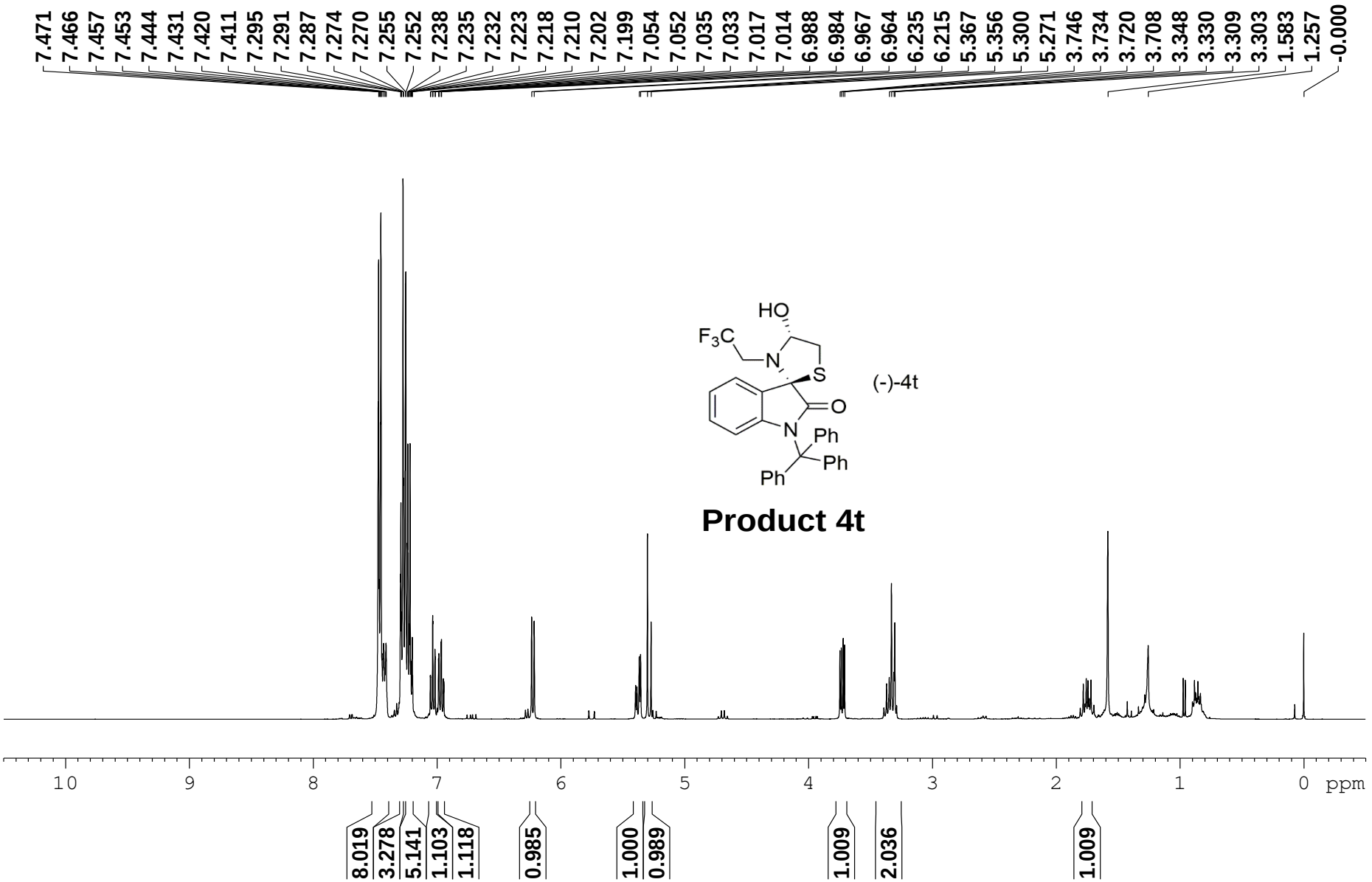

-70.78
HO
F3C
N
S
O
N
Br
(-)-4r
Product 4r
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

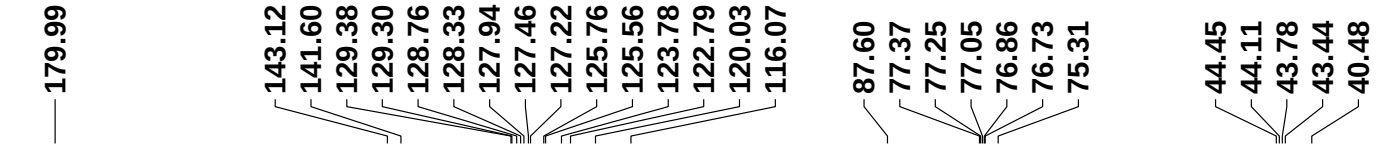

7.491
7.473
7.267
7.264
7.258
7.248
7.229
7.190
7.169
7.152
7.127
7.108
6.768
6.748
5.656
5.626
5.513
5.502
5.483
5.472
4.908
4.869
4.824
4.786
3.831
3.810
3.799
3.788
3.773
3.761
3.751
3.729
3.406
3.380
2.486
2.475
2.462
2.448
2.439
2.425
2.415
2.401
2.377
2.319
1.609
-0.000
HO
F3C
N
S
O
N
Me
(-)-4s
Product 4s
8
7
6
5
4
3
2
1
0
ppm
0.962
0.856
4.947
1.002
0.958
0.971
2.012
1.963
0.983
1.036
3.000

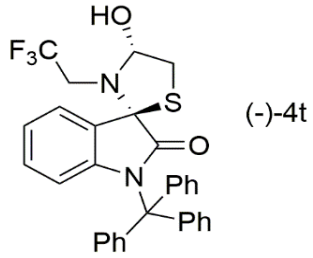

178.10
142.34
137.95
131.84
130.70
129.72
128.53
127.28
126.45
126.24
125.76
124.35
122.99
120.23
109.94
88.11
77.34
77.23
77.16
77.02
76.71
44.94
44.60
44.28
43.93
40.31
21.11
-0.00
HO
F3C
N
S
O
N
Me
(-)-4s
Product 4s
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



Product 4s

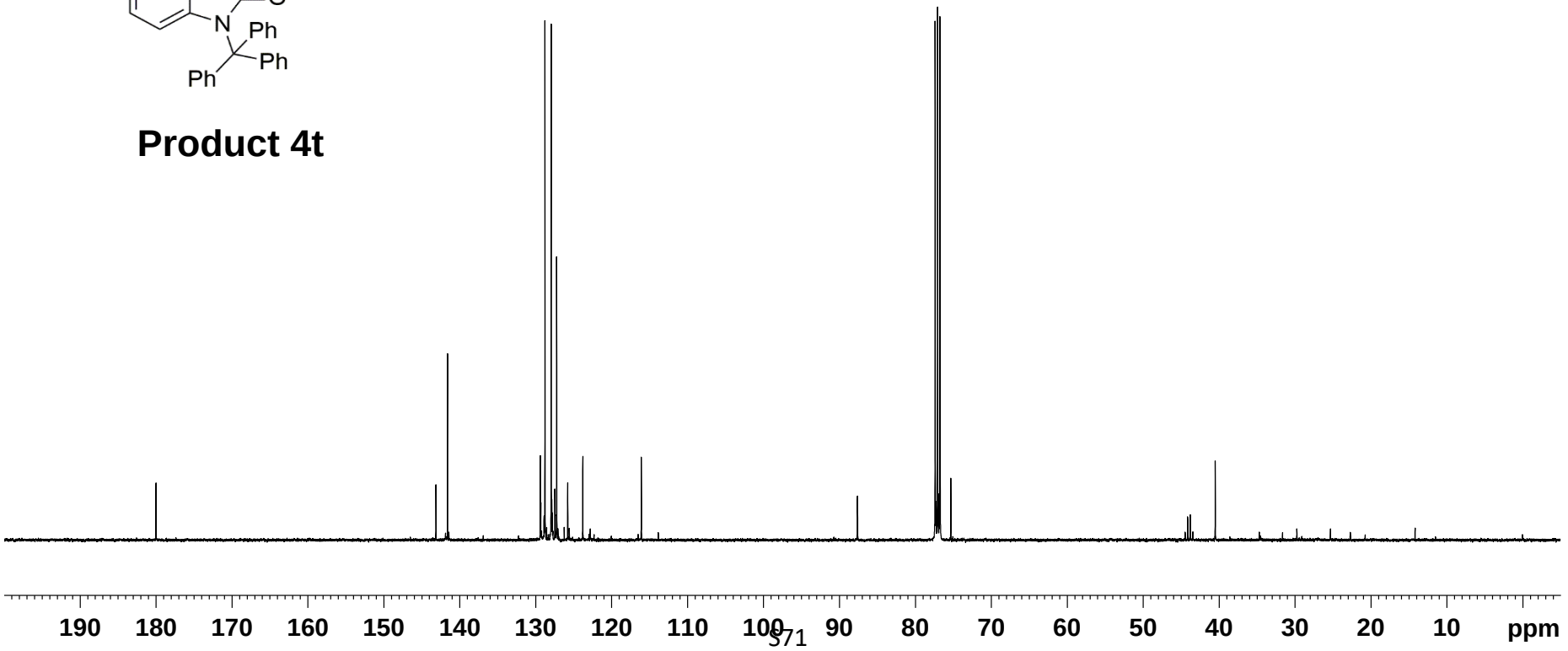

7.471
7.466
7.457
7.453
7.444
7.431
7.420
7.411
7.295
7.291
7.287
7.274
7.270
7.255
7.252
7.238
7.235
7.232
7.223
7.218
7.210
7.202
7.199
7.054
7.052
7.035
7.033
7.017
7.014
6.988
6.984
6.967
6.964
6.235
6.215
5.367
5.356
5.300
5.271
3.746
3.734
3.720
3.708
3.348
3.330
3.309
3.303
1.583
1.257
-0.000
HO
F3C
N
S
O
N
Ph
Ph
Ph
(-)-4t
Product 4t
10
9
8
7
6
5
4
3
2
1
0
ppm
8.019
3.278
5.141
1.103
1.118
0.985
1.000
0.989
1.009
2.036
1.009





(-)-4t

Product 4t



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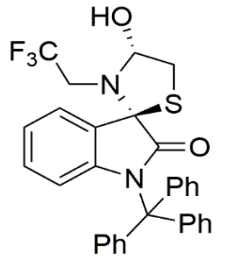

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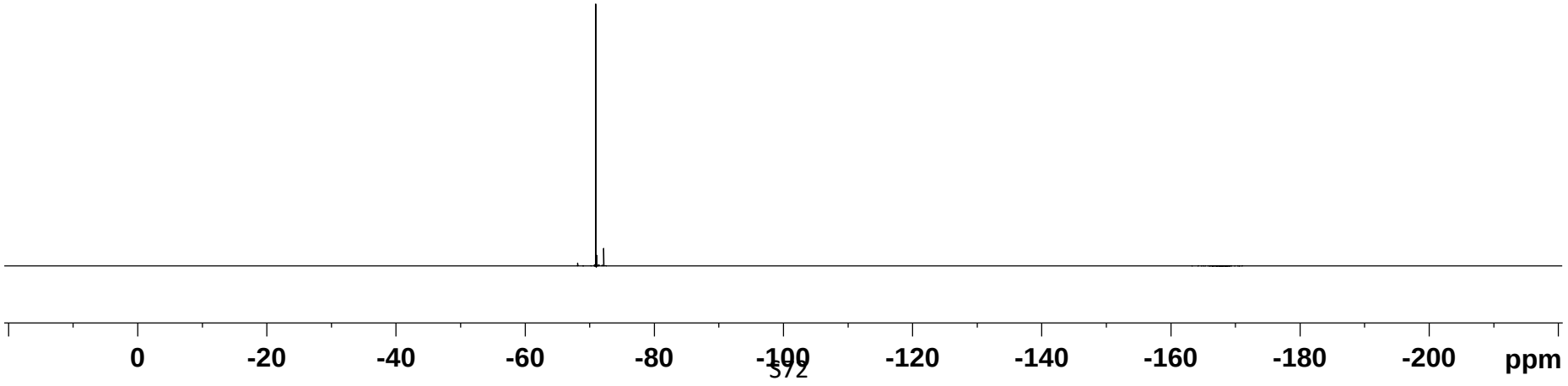
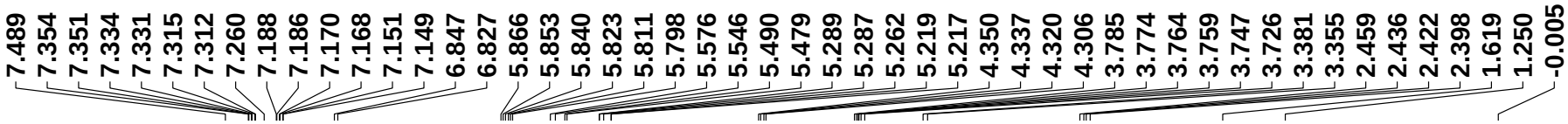
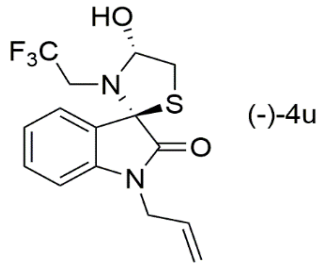
Product 4t







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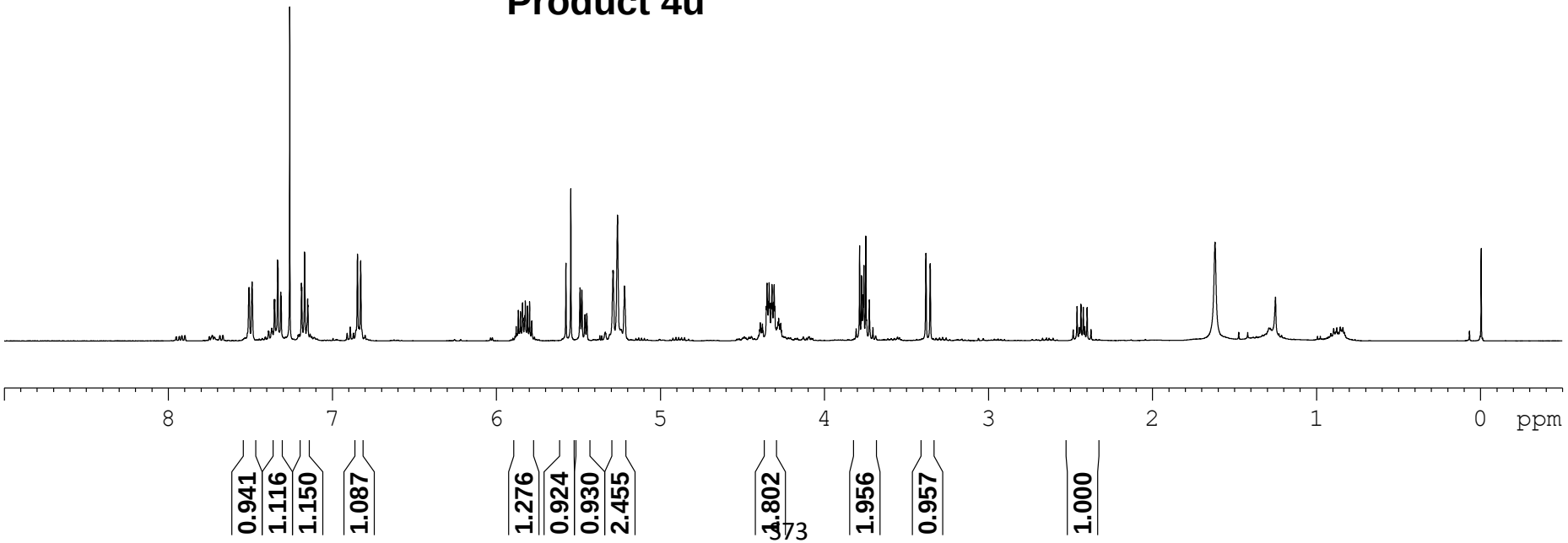
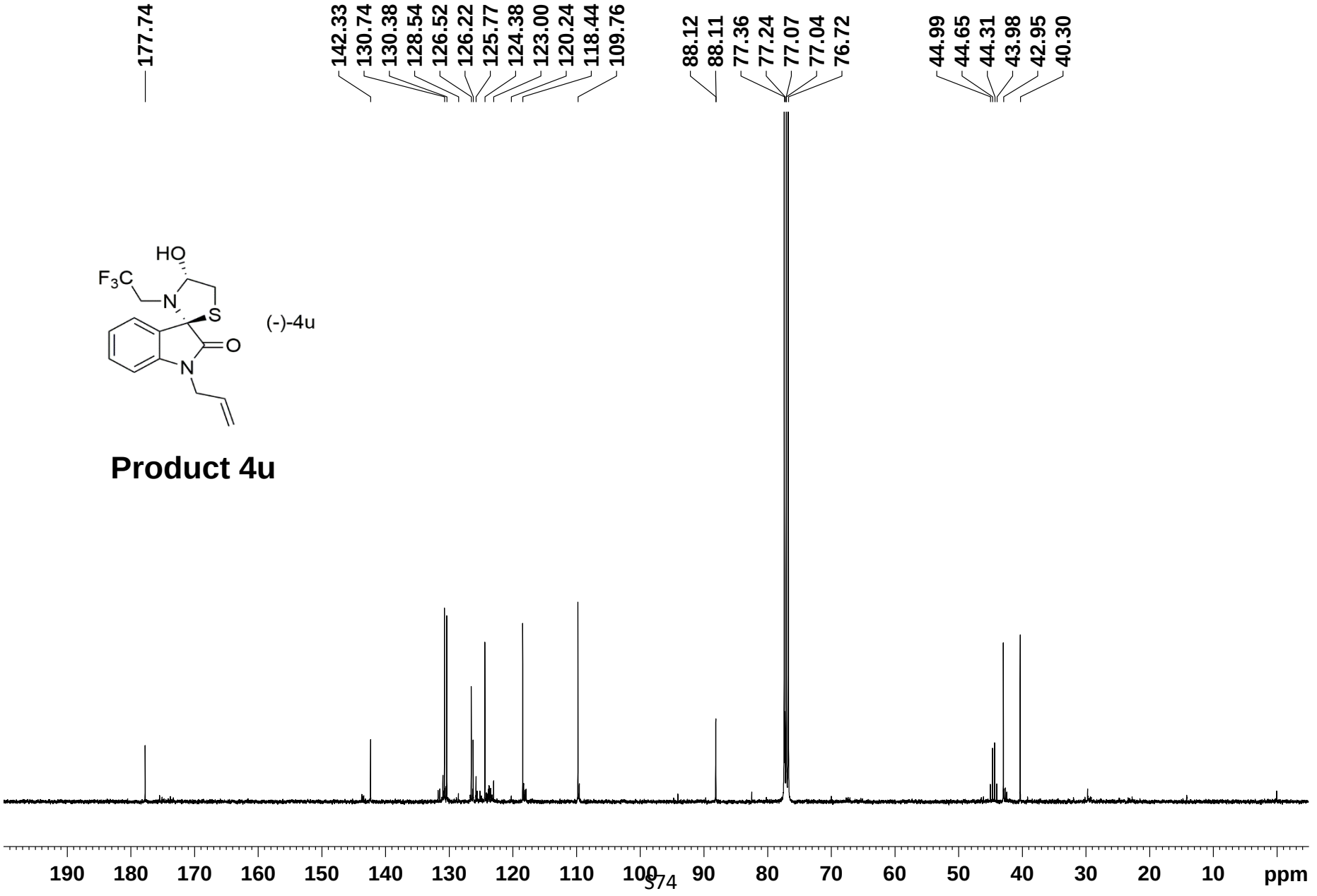
Product 4u

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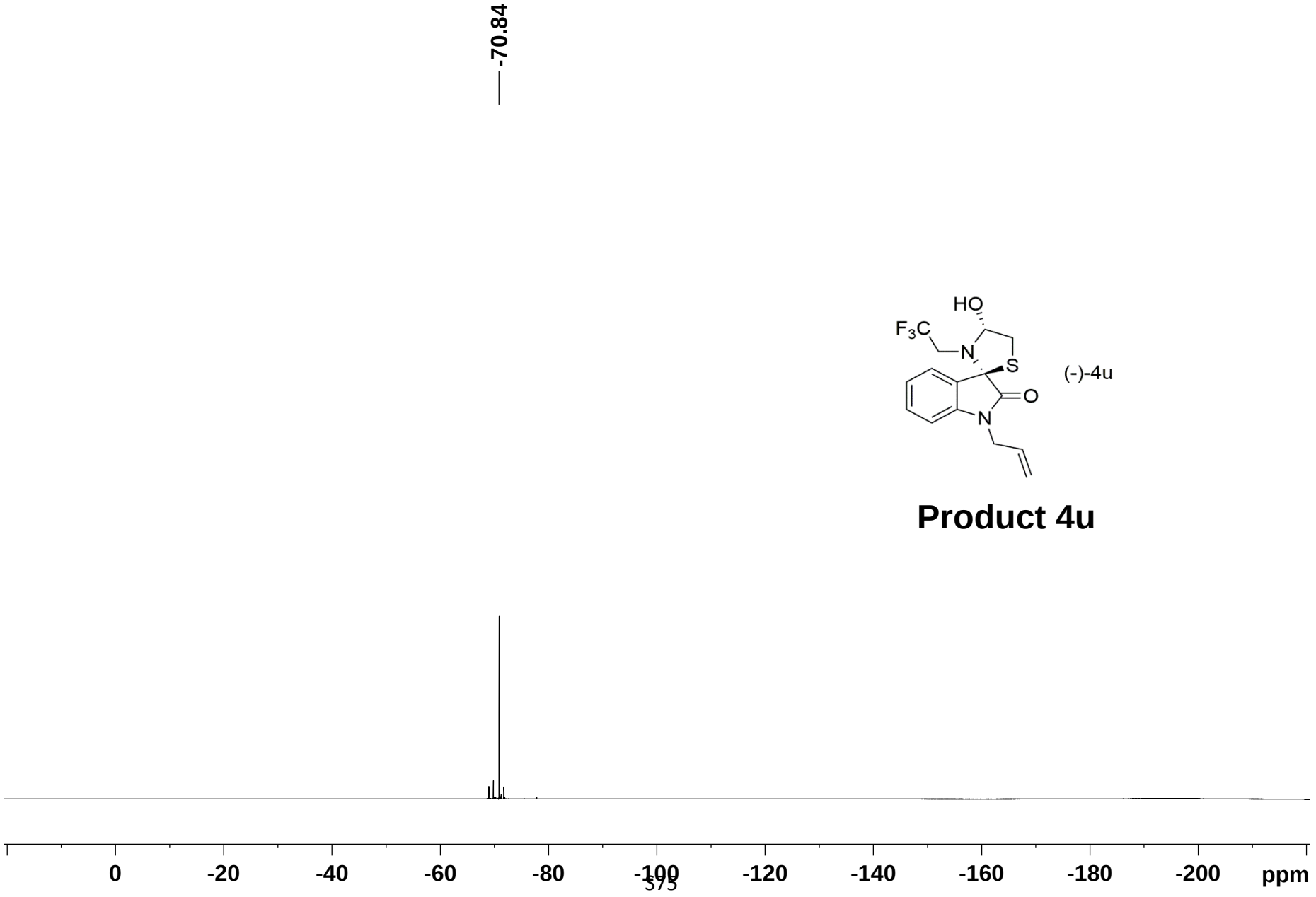
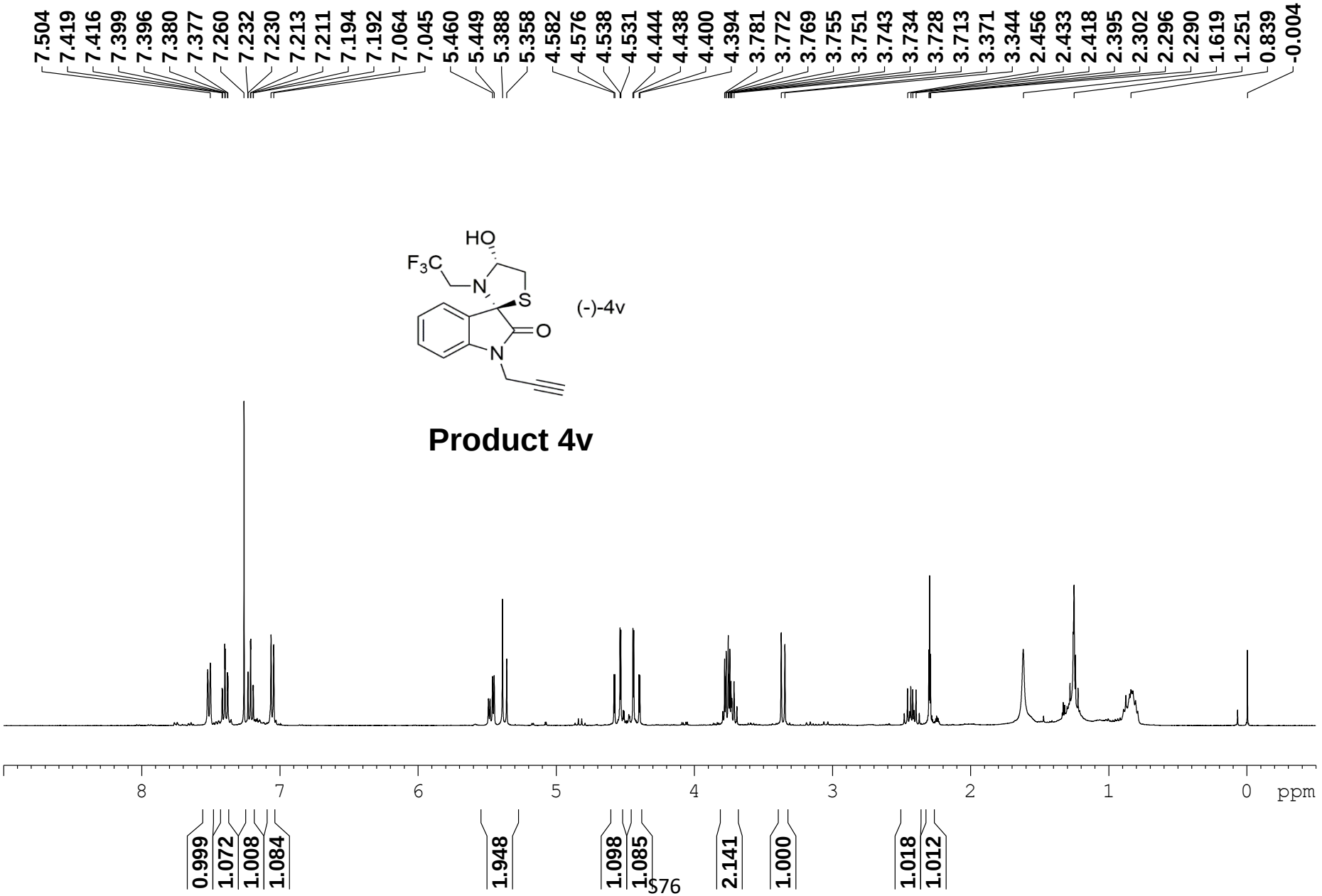
130.74
130.38
128.54
126.52
126.22
125.77
124.38
123.00
120.24
118.44
109.76
88.12
88.11
77.36
77.24
77.07
77.04
76.72
44.99
44.65
44.31
43.98
42.95
40.30
HO
F3C
N
S
O
N
(-)-4u
Product 4u
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



Product 4u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7.380
7.377
7.260
7.232
7.230
7.213
7.211
7.194
7.192
7.064
7.045
5.460
5.449
5.388
5.358
4.582
4.576
4.538
4.531
4.444
4.438
4.400
4.394
3.781
3.772
3.769
3.755
3.751
3.743
3.734
3.728
3.713
3.371
3.344
2.456
2.433
2.418
2.395
2.302
2.296
2.290
1.619
1.251
0.839
-0.004
HO
F3C
N
S
O
N
(-)-4v
Product 4v
8
7
6
5
4
3
2
1
0
ppm
0.999
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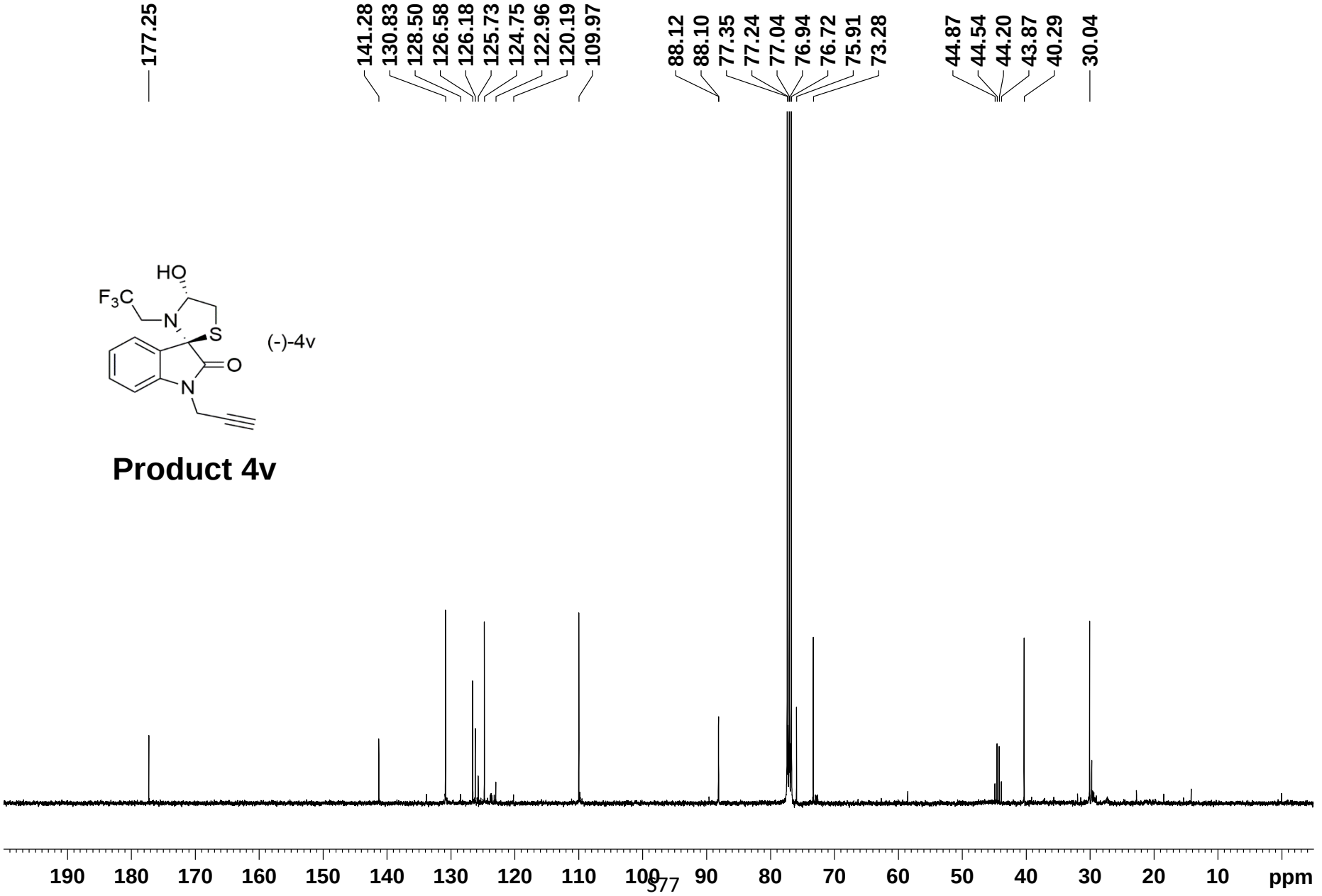
1.008
1.084
1.948
1.098
1.085
2.141
1.000
1.018
1.012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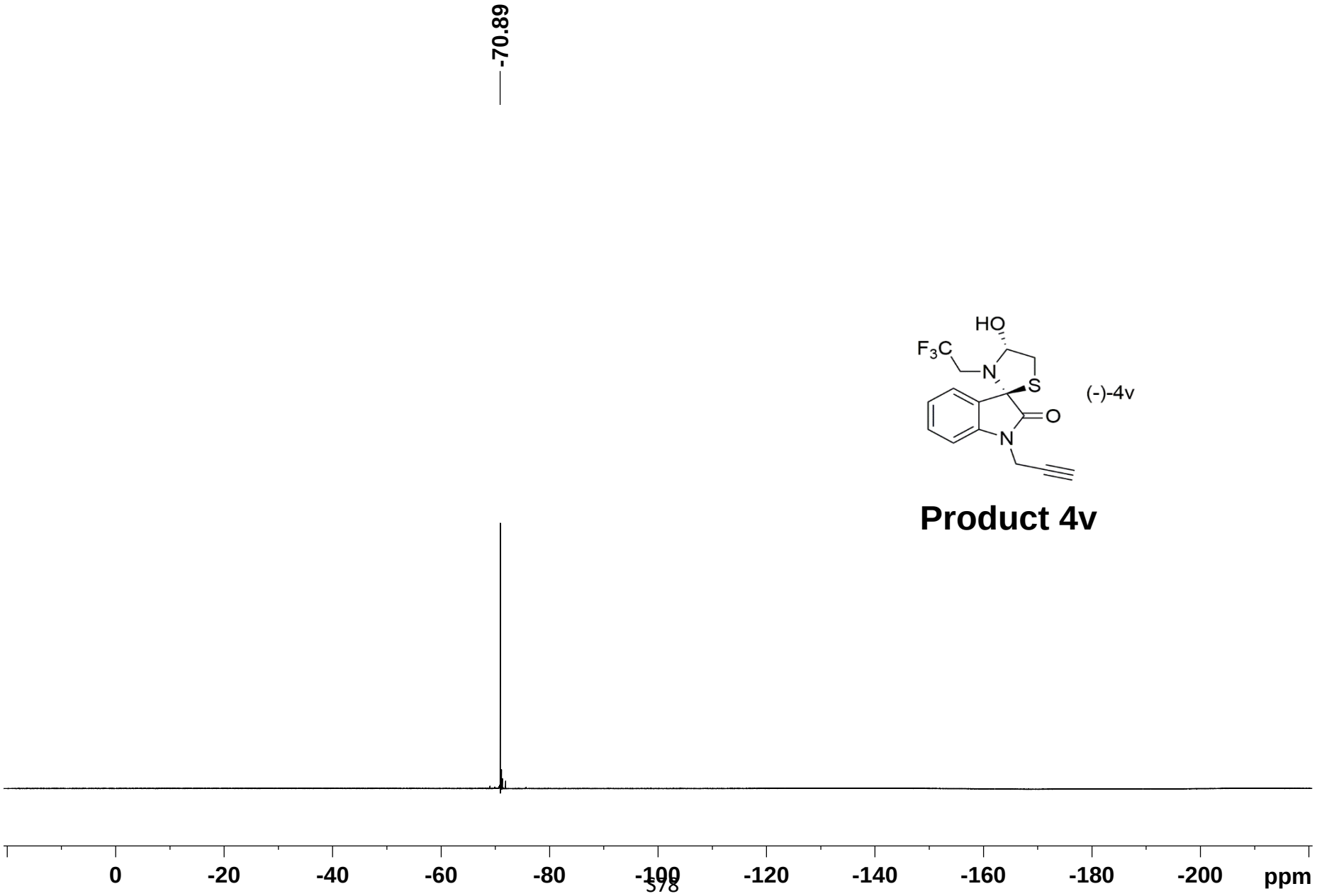
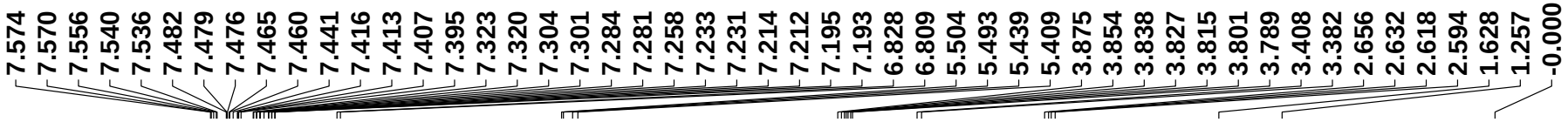
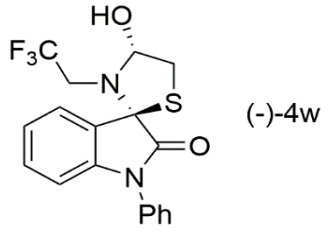
128.50
126.58
126.18
125.73
124.75
122.96
120.19
109.97
88.12
88.10
77.35
77.24
77.04
76.94
76.72
75.91
73.28
44.87
44.54
44.20
43.87
40.29
30.04
HO
F3C
N
S
O
N
(-)-4v
Product 4v
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

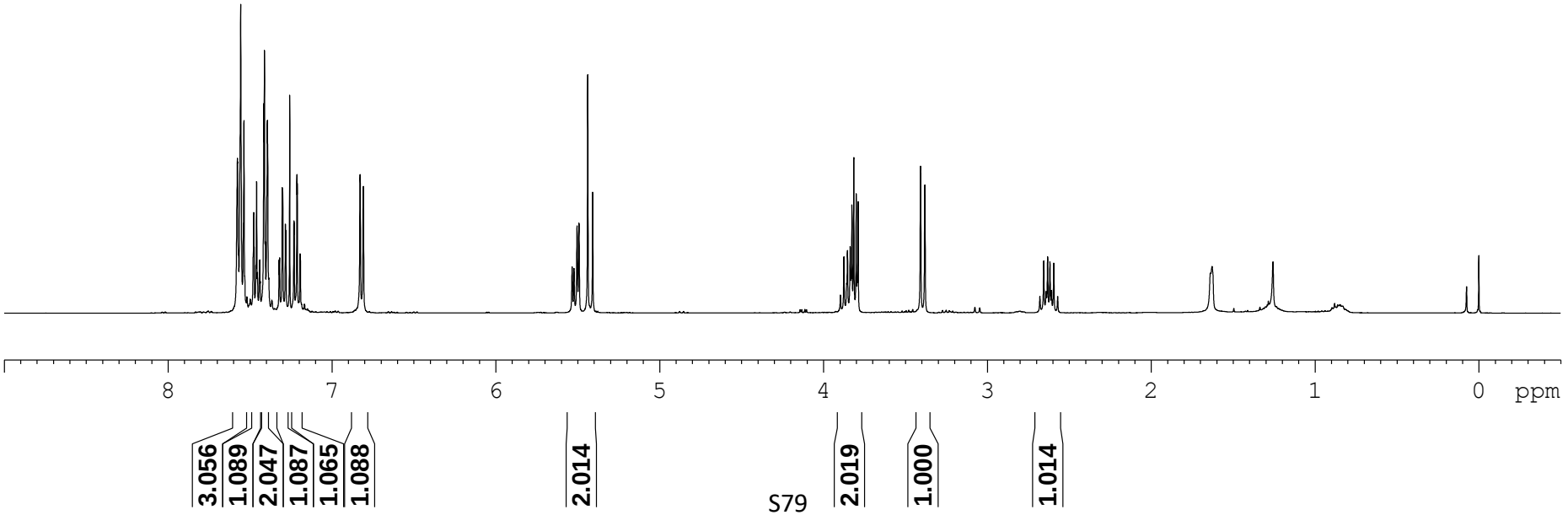

-70.89
HO
F3C
N
S
O
N
(-)-4v
Product 4v
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

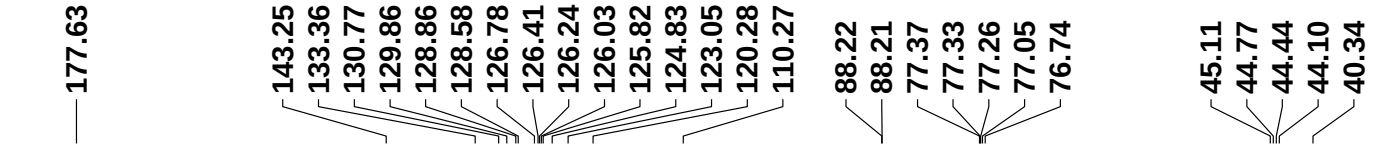


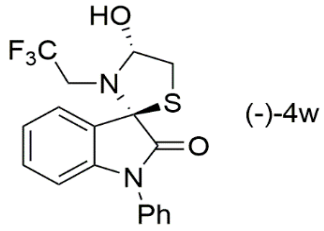


(-)-4w

Product 4w

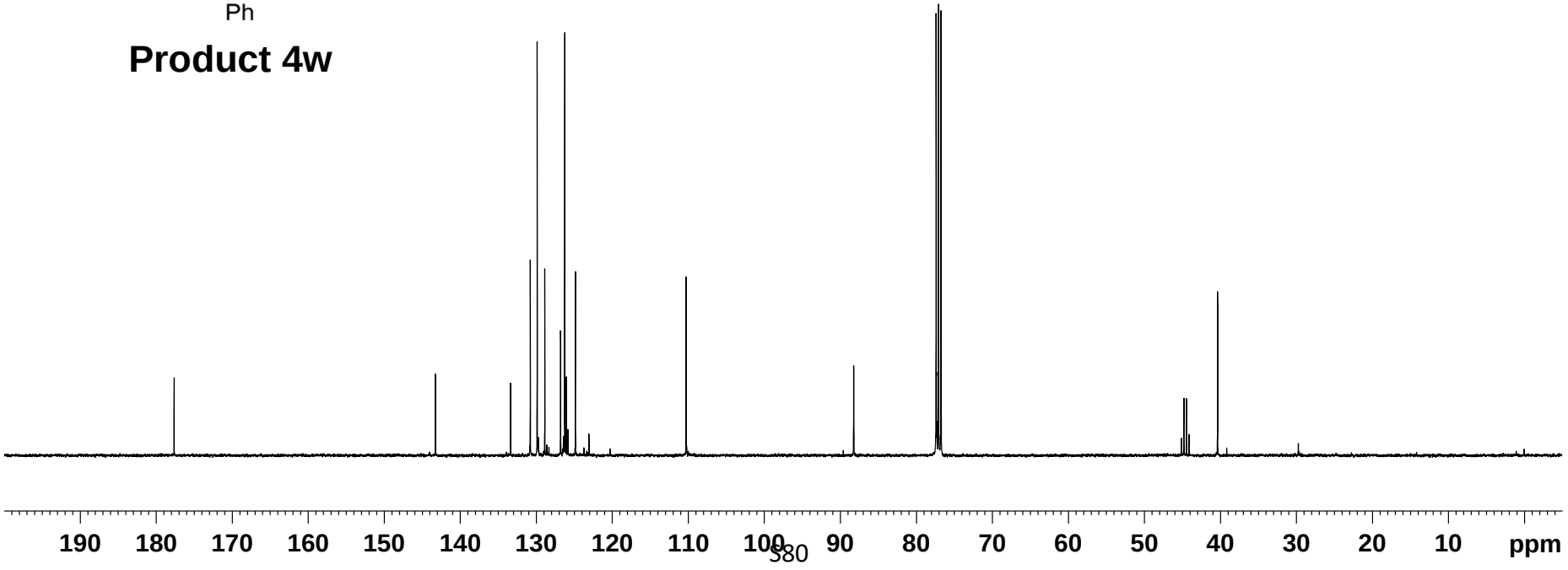


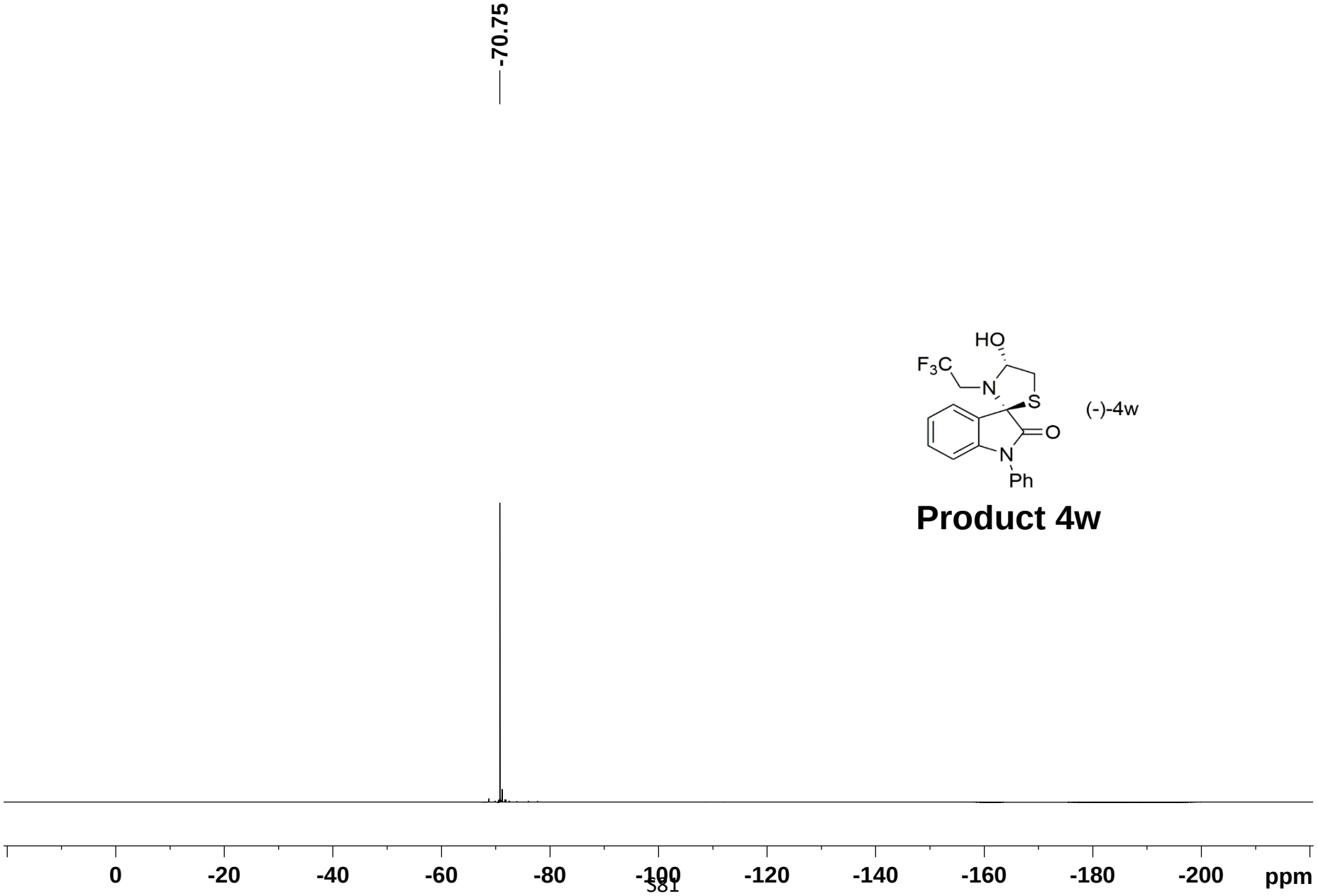


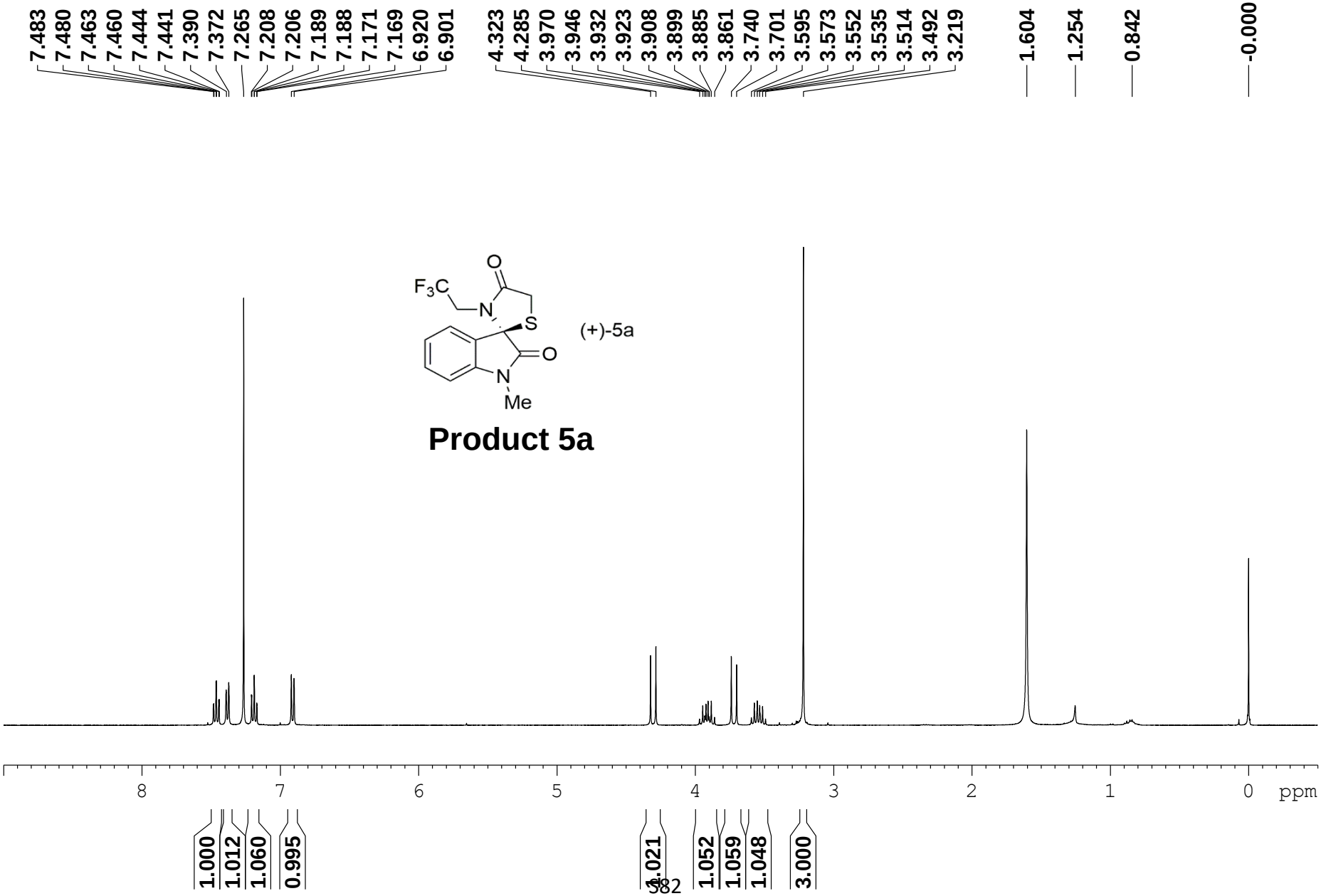


(-)-4w

Product 4w




-70.75
HO
F3C
N
S
O
N
Ph
(-)-4w
Product 4w
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm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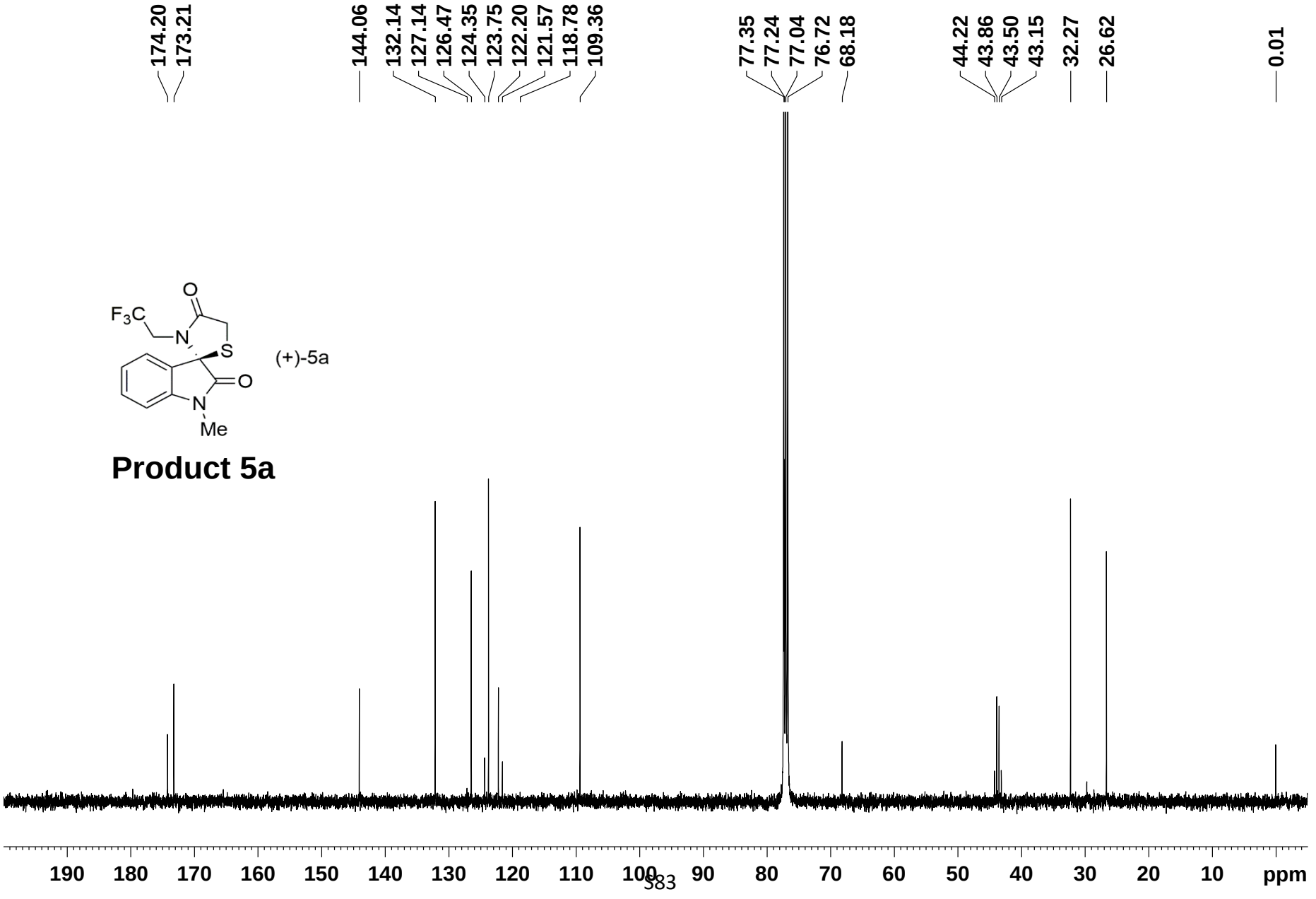
7.441
7.390
7.372
7.265
7.208
7.206
7.189
7.188
7.171
7.169
6.920
6.901
4.323
4.285
3.970
3.946
3.932
3.923
3.908
3.899
3.885
3.861
3.740
3.701
3.595
3.573
3.552
3.535
3.514
3.492
3.219
1.604
1.254
0.842
-0.000
F3C
N
O
S
O
N
Me
(+)-5a
Product 5a
8
7
6
5
4
3
2
1
0
ppm
1.000
1.012
1.060
0.995
1.021
1.052
1.059
1.048
3.000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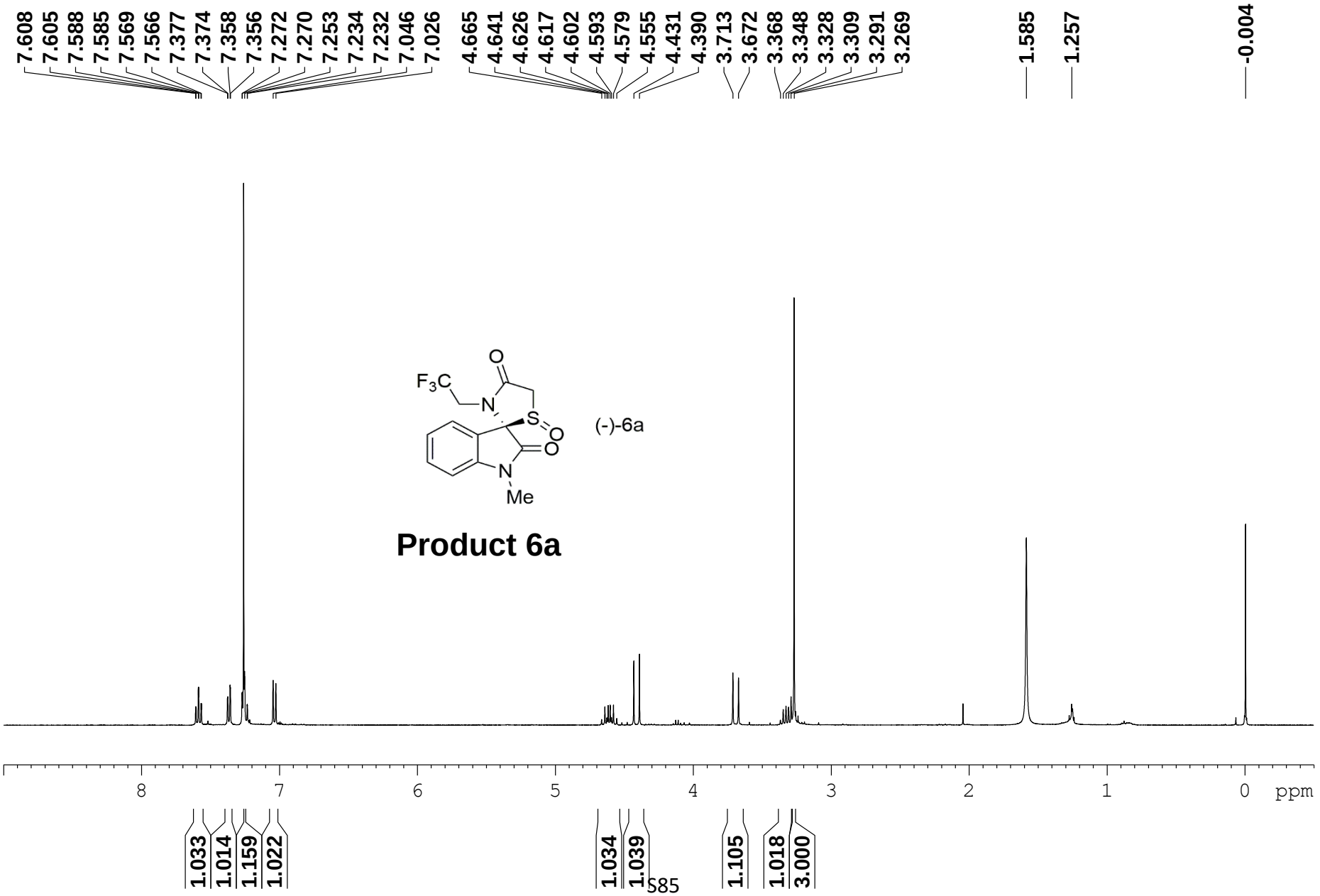
144.06
132.14
127.14
126.47
124.35
123.75
122.20
121.57
118.78
109.36
77.35
77.24
77.04
76.72
68.18
44.22
43.86
43.50
43.15
32.27
26.62
0.01
F3C
N
O
S
O
N
Me
(+)-5a
Product 5a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Product 5a


7.608
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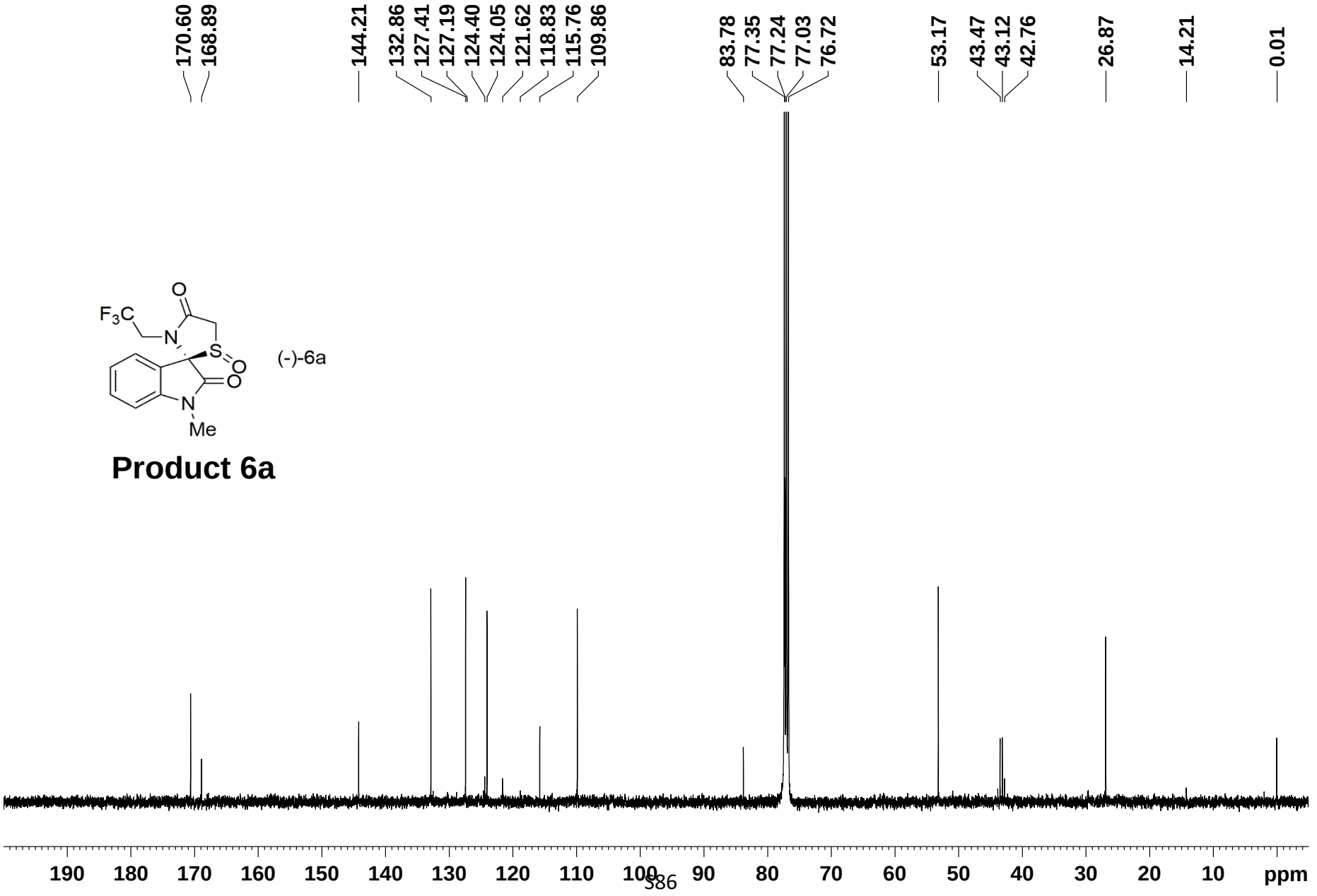
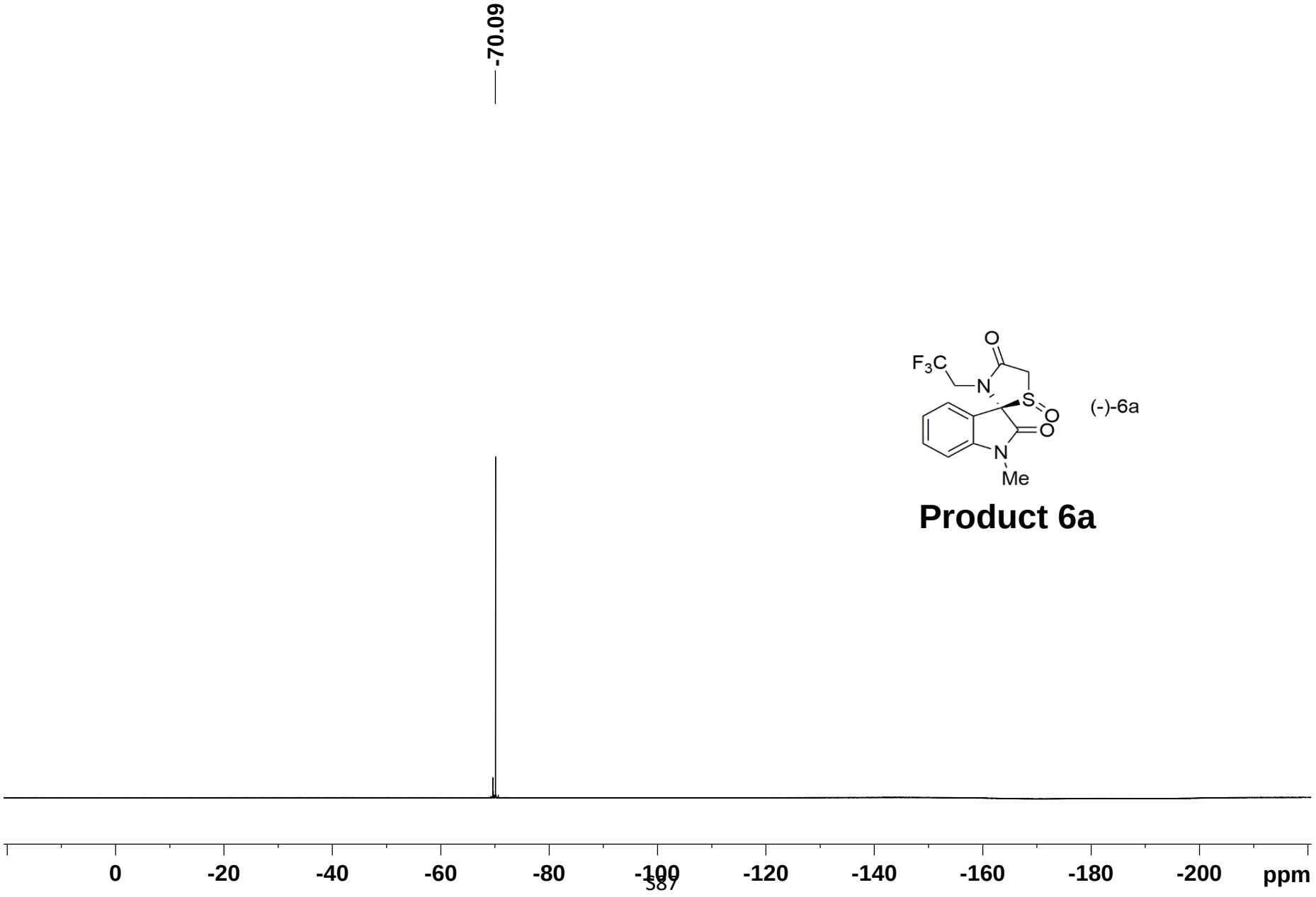
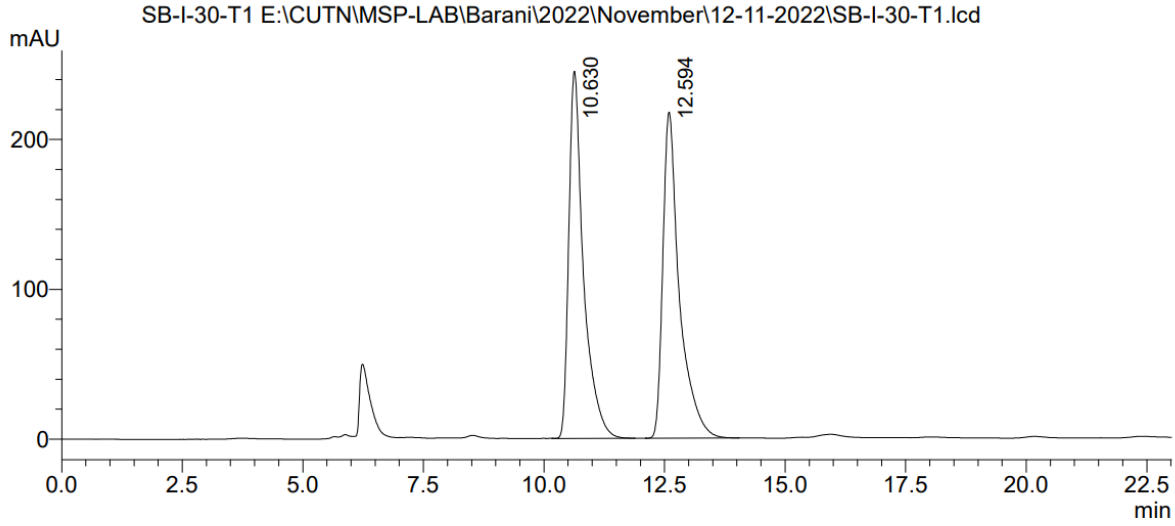
7.585
7.569
7.566
7.377
7.374
7.358
7.356
7.272
7.270
7.253
7.234
7.232
7.046
7.026
4.665
4.641
4.626
4.617
4.602
4.593
4.579
4.555
4.431
4.390
3.713
3.672
3.368
3.348
3.328
3.309
3.291
3.269
1.585
1.257
-0.004
F3C
N
O
S
O
O
N
Me
(-)-6a
Product 6a
8
7
6
5
4
3
2
1
0
ppm
1.033
1.014
1.159
1.022
1.034
1.039
1.105
1.018
3.000


170.60
168.89
144.21
132.86
127.41
127.19
124.40
124.05
121.62
118.83
115.76
109.86
83.78
77.35
77.24
77.03
76.72
53.17
43.47
43.12
42.76
26.87
14.21
0.01
F3C
N
O
S
O
O
N
Me
(-)-6a
Product 6a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



Product 6a

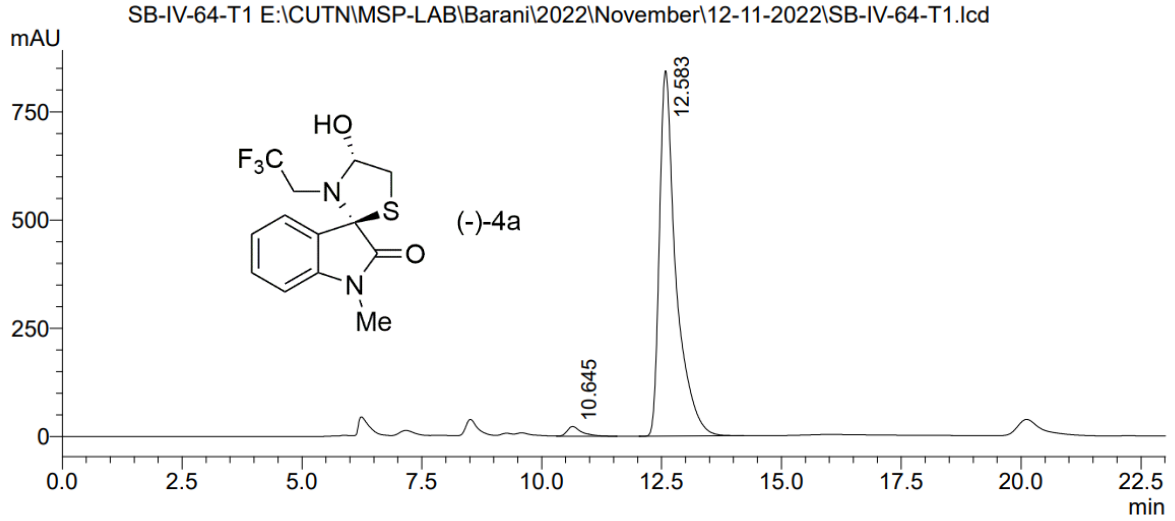
HPLC of racemic **4a**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.630	5186567	244962	49.970
2	12.594	5192725	217629	50.030
Total		10379292	462592	100.000

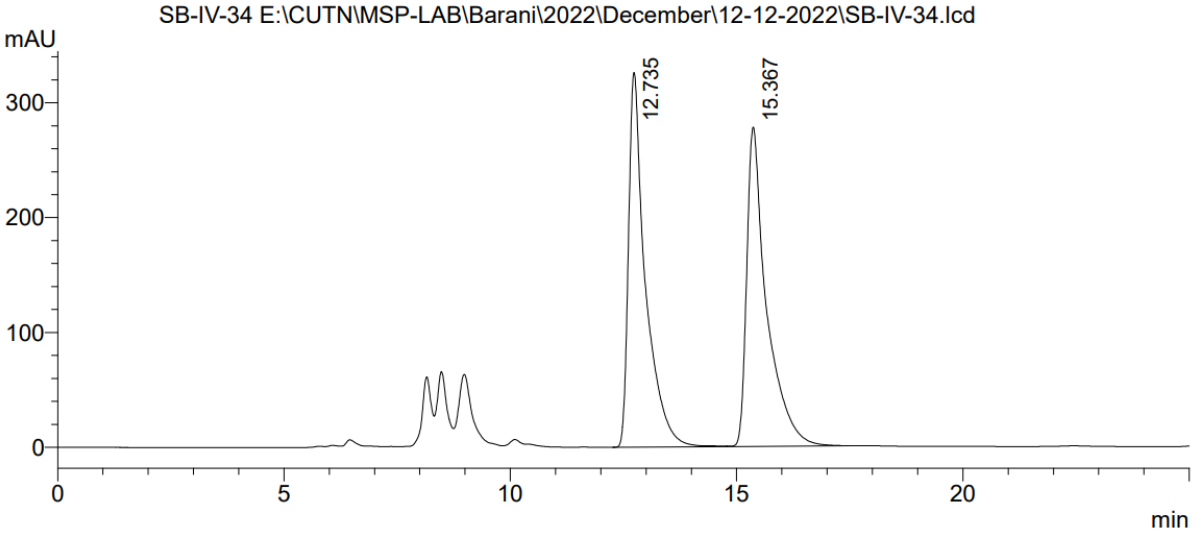
HPLC of chiral **4a: 95% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.645	473594	22574	2.289
2	12.583	20214138	843719	97.711
Total		20687732	866294	100.000

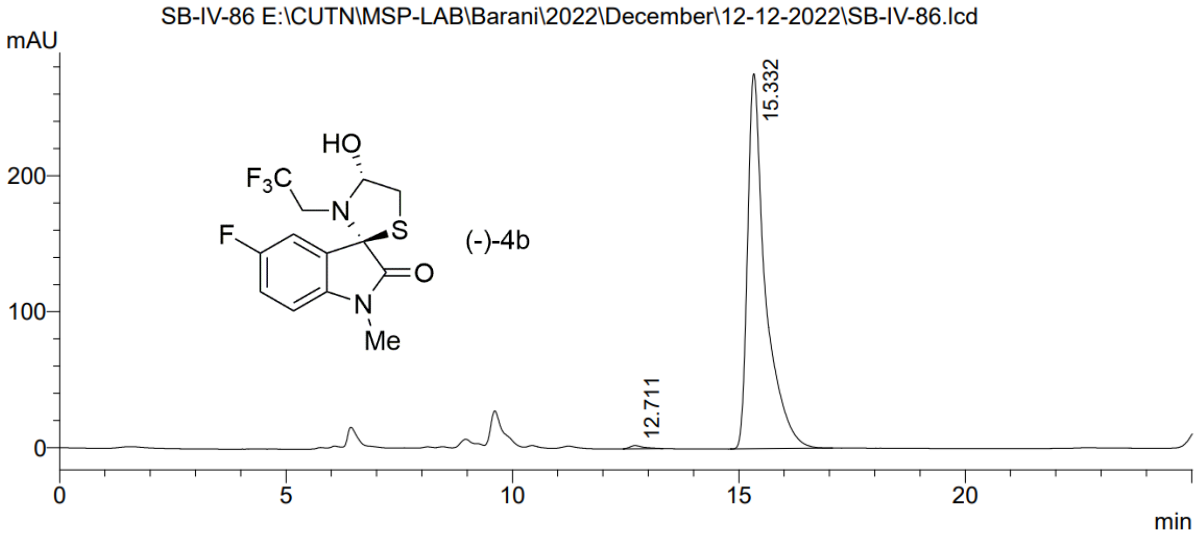
HPLC of racemic **4b**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.735	8469528	326293	49.946
2	15.367	8487920	278111	50.054
Total		16957448	604404	100.000

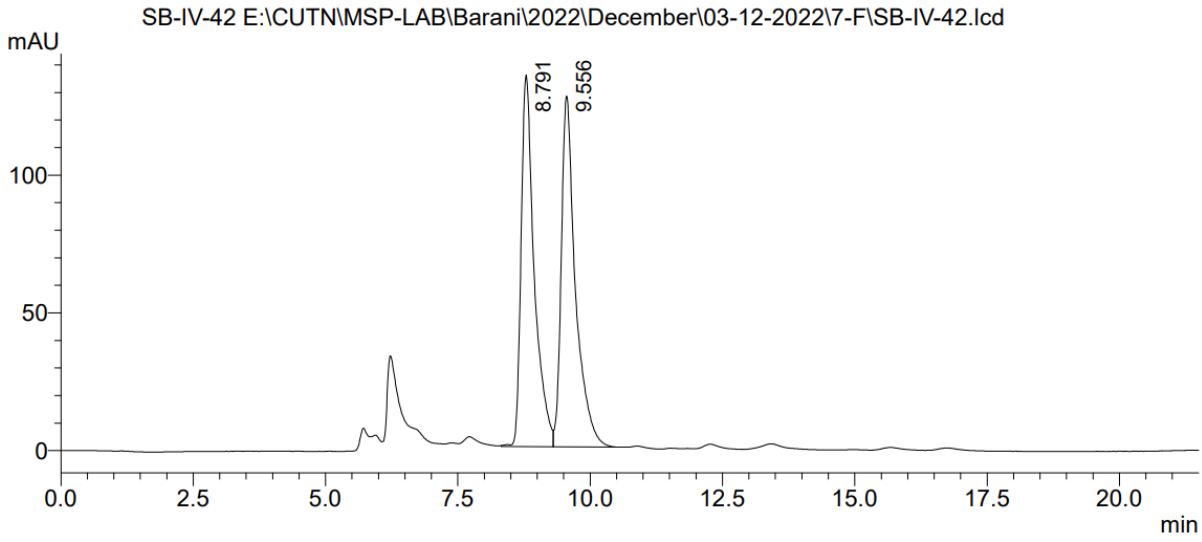
HPLC of chiral **4b: 99% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.711	48687	2373	0.641
2	15.332	7545453	275682	99.359
Total		7594139	278055	100.000

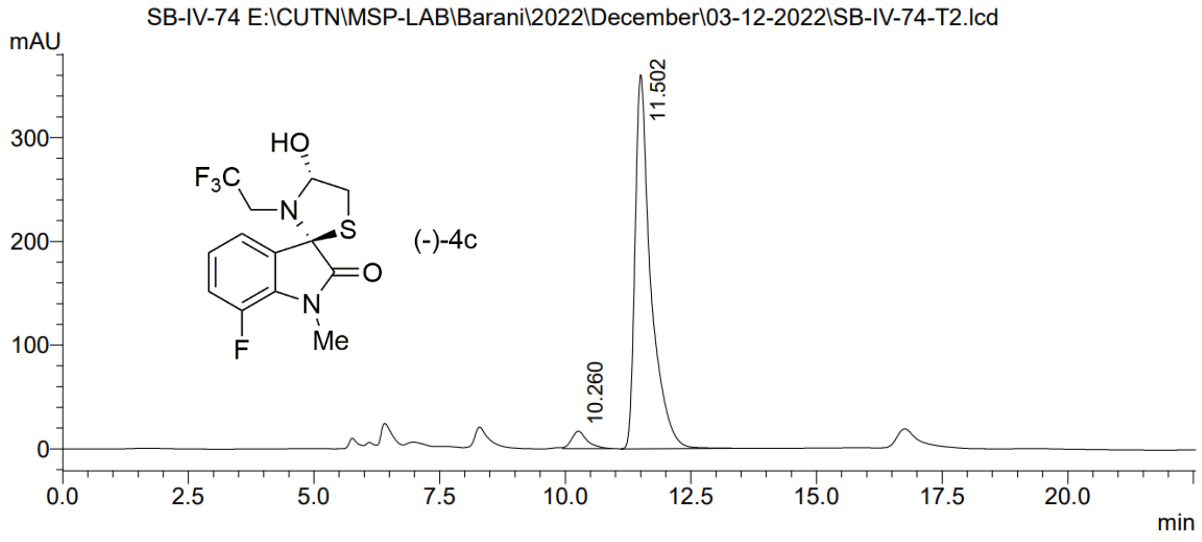
HPLC of racemic **4c**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.791	2328379	134847	49.518
2	9.556	2373697	127316	50.482
Total		4702076	262163	100.000

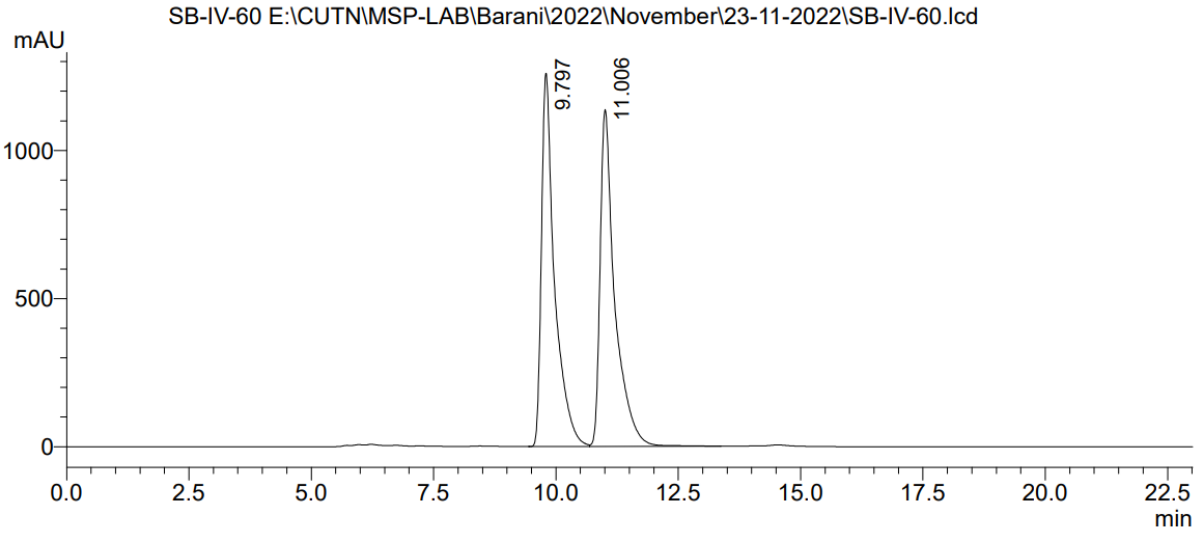
HPLC of chiral **4c: 91% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.260	365441	16931	4.441
2	11.502	7863195	360393	95.559
Total		8228637	377324	100.000

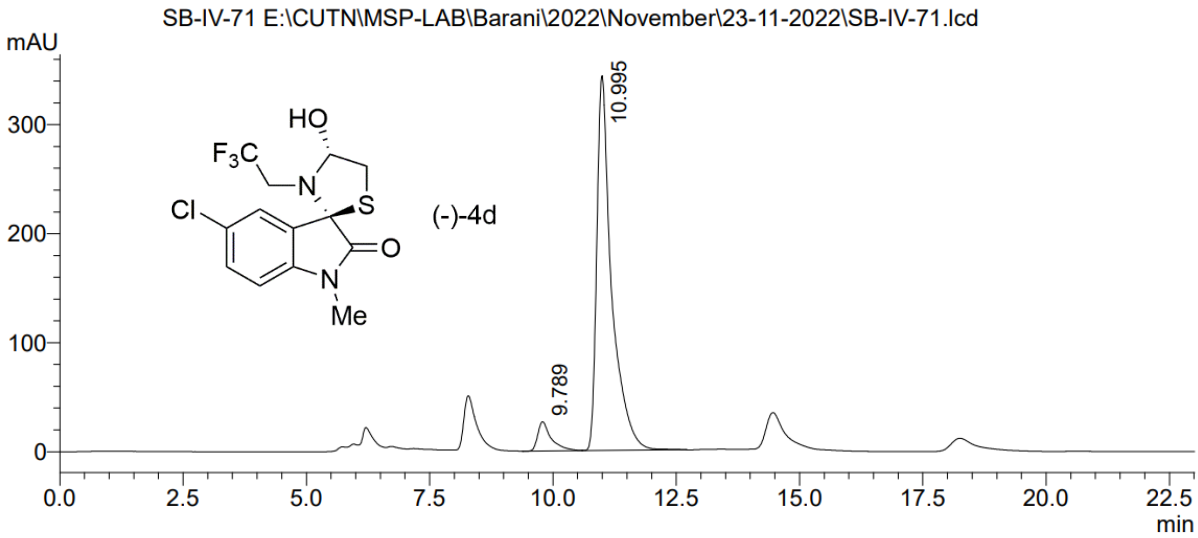
HPLC of racemic **4d**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.797	23523515	1259616	49.766
2	11.006	23744977	1136993	50.234
Total		47268492	2396609	100.000

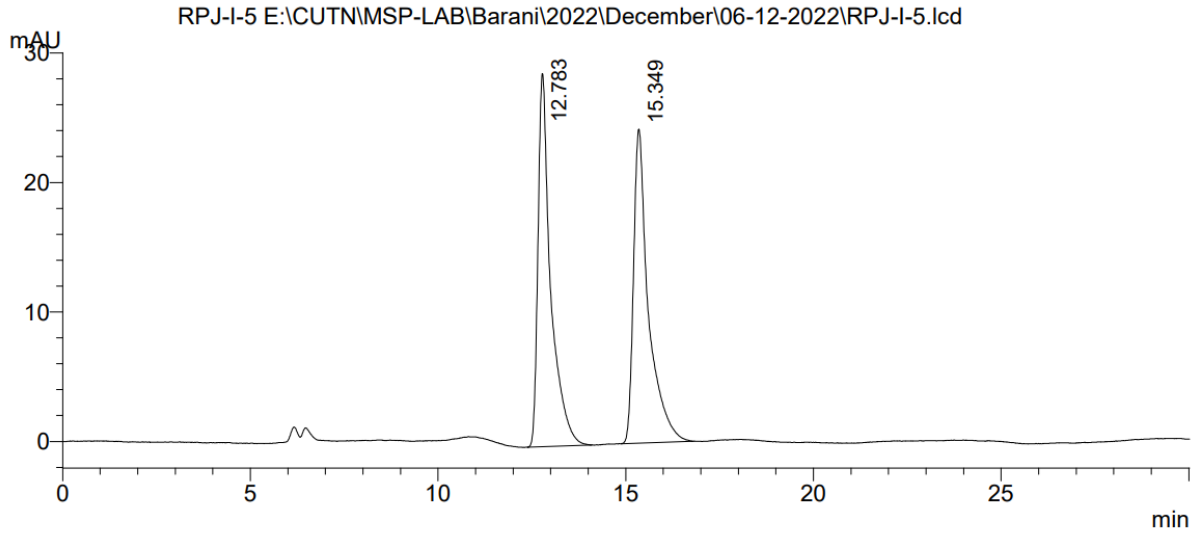
HPLC of chiral **4d: 87% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.789	510647	26889	6.622
2	10.995	7201049	343794	93.378
Total		7711697	370683	100.000

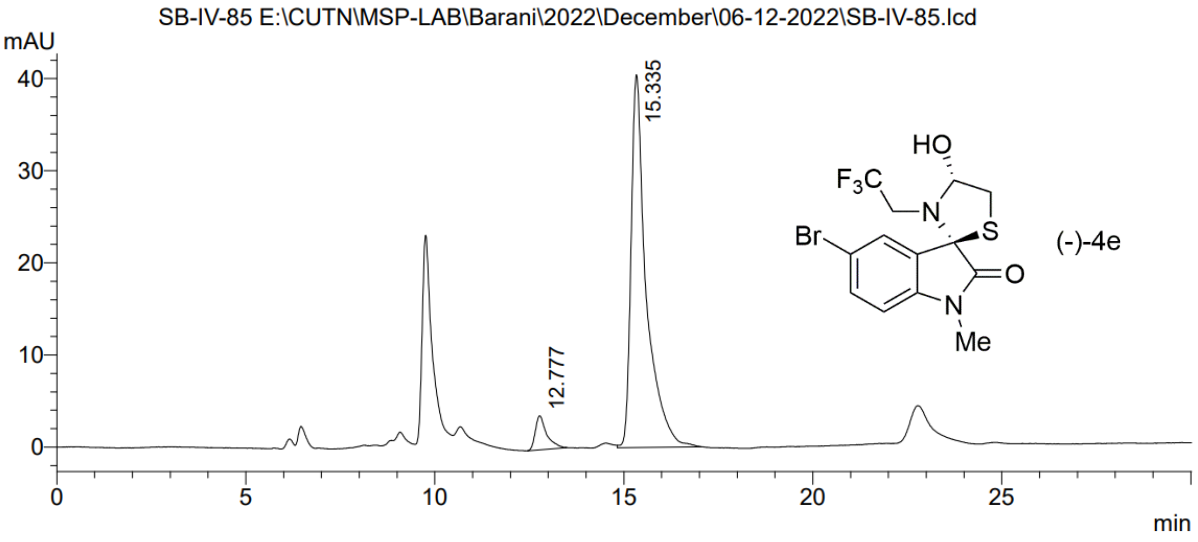
HPLC of racemic **4e**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.783	674801	28818	50.244
2	15.349	668236	24245	49.756
Total		1343037	53063	100.000

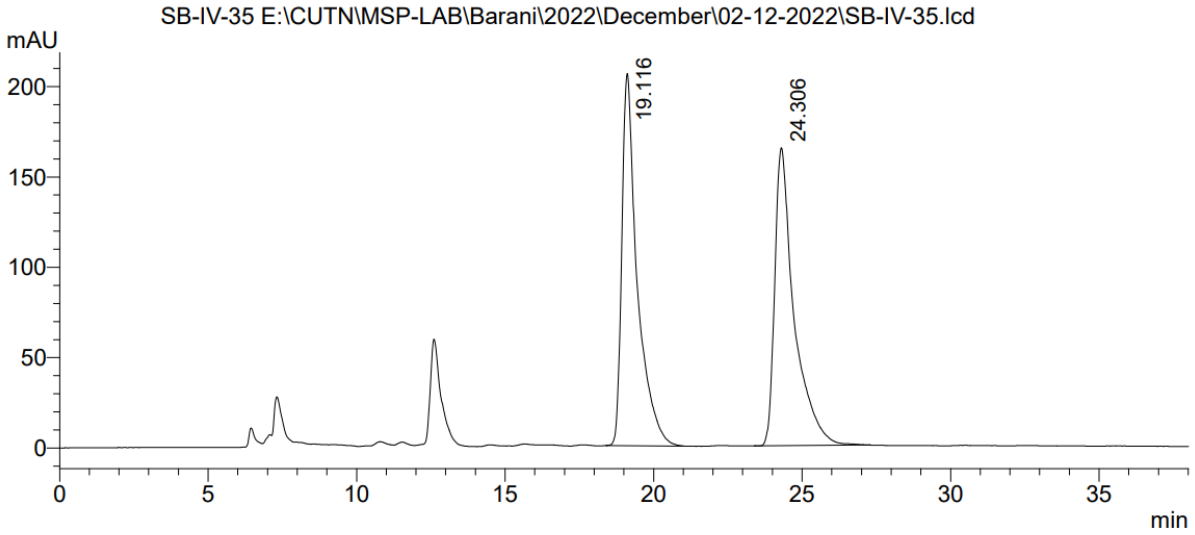
HPLC of chiral **4e: 87% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.777	76294	3689	6.325
2	15.335	1129957	40457	93.675
Total		1206250	44146	100.000

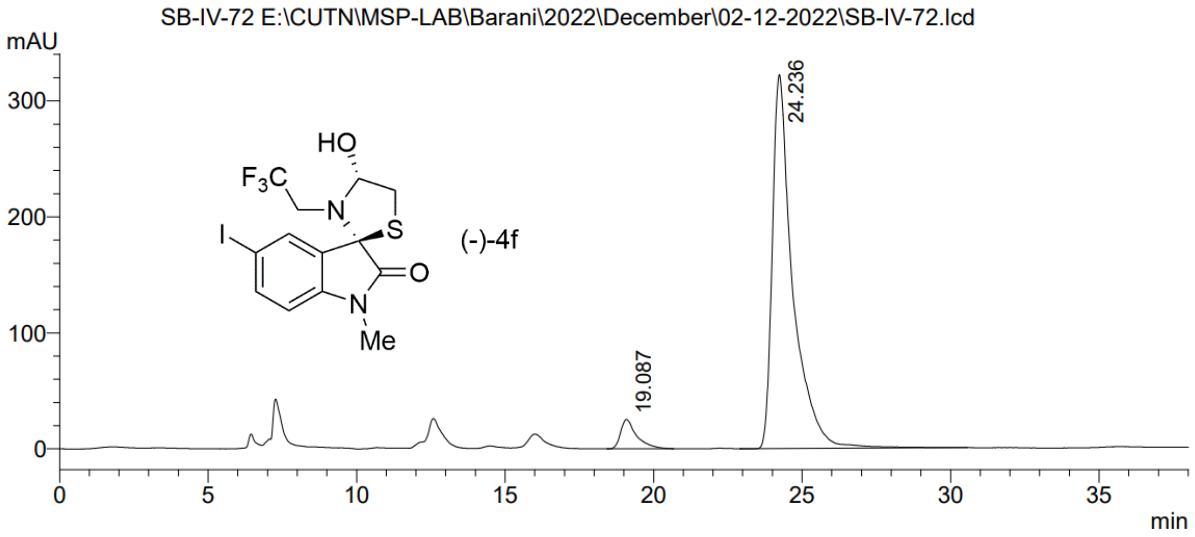
HPLC of racemic **4f**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	19.116	7445503	205957	49.853
2	24.306	7489386	164949	50.147
Total		14934889	370905	100.000

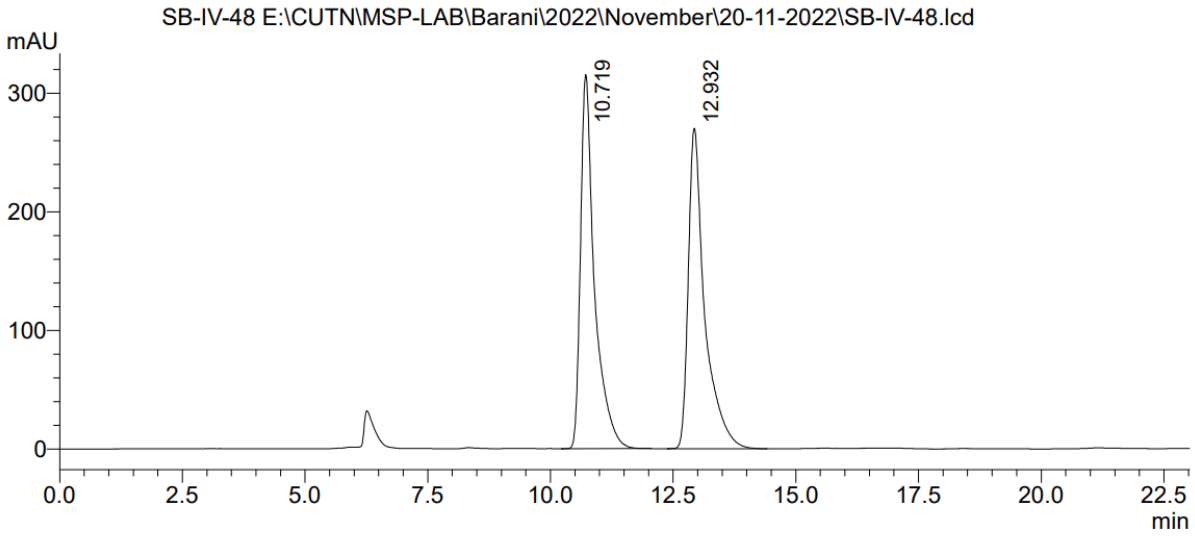
HPLC of chiral **4f: 88% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	19.087	946289	25346	5.768
2	24.236	15460481	322281	94.232
Total		16406770	347627	100.000

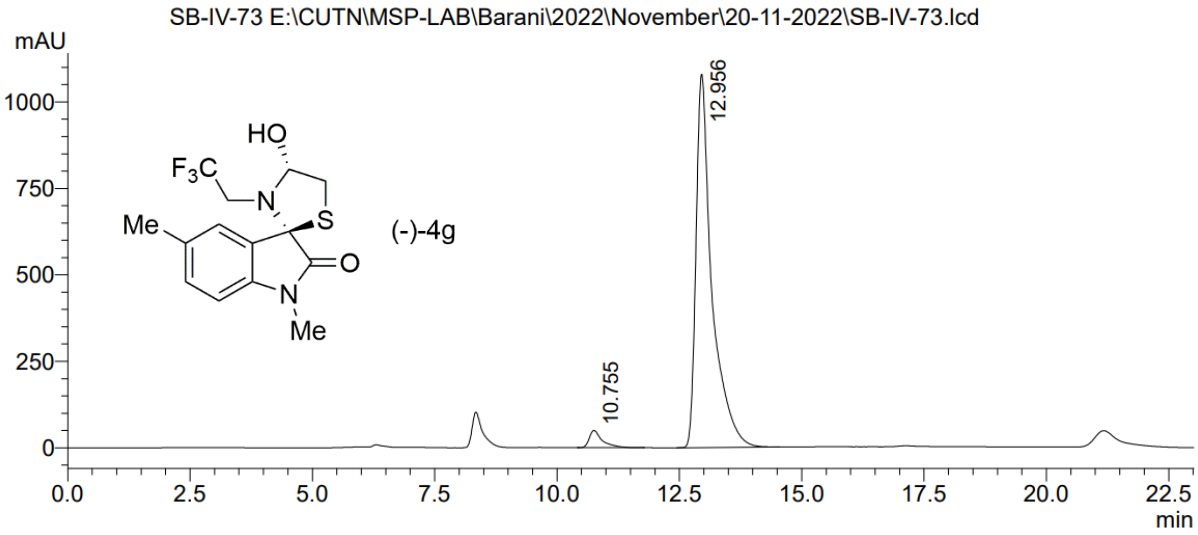
HPLC of racemic **4g**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.719	6257613	315522	49.939
2	12.932	6272984	270461	50.061
Total		12530597	585983	100.000

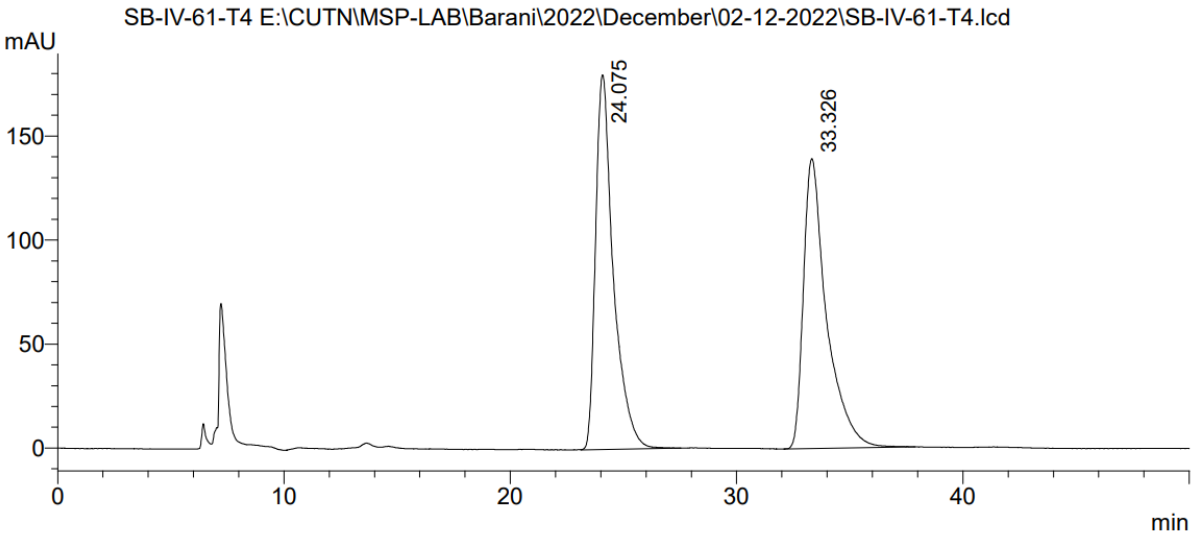
HPLC of chiral **4g: 93%** ***ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.755	931881	50119	3.681
2	12.956	24385574	1079122	96.319
Total		25317455	1129241	100.000

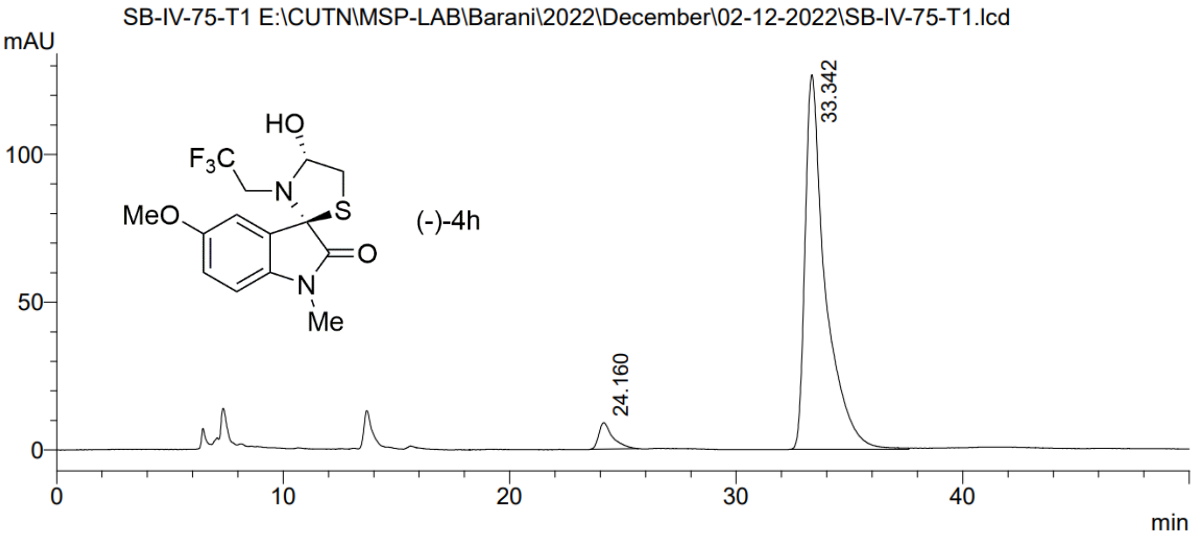
HPLC of racemic **4h**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	24.075	9857041	180094	49.889
2	33.326	9900914	139374	50.111
Total		19757955	319468	100.000

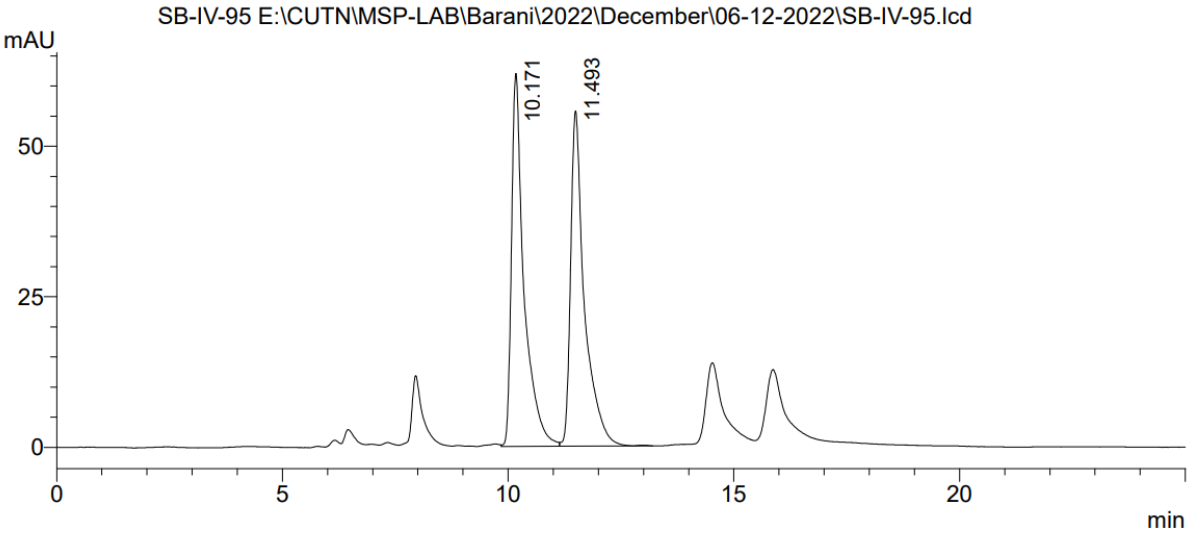
HPLC of chiral **4h: 91% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	24.160	379485	8951	4.571
2	33.342	7921705	126764	95.429
Total		8301190	135716	100.000

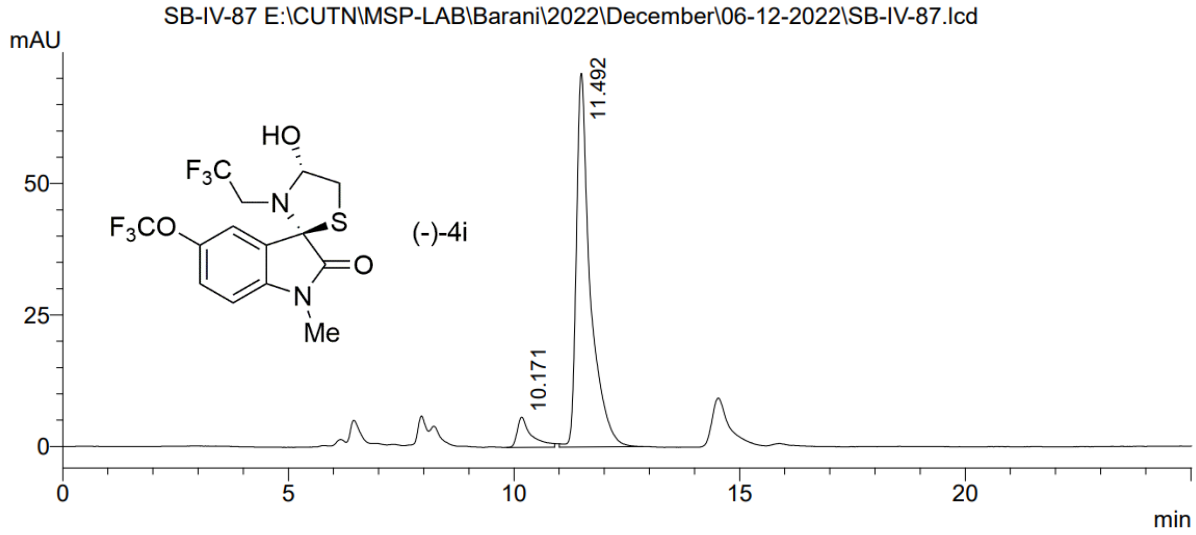
HPLC of racemic **4i**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.171	1193412	61912	50.212
2	11.493	1183354	55650	49.788
Total		2376766	117562	100.000

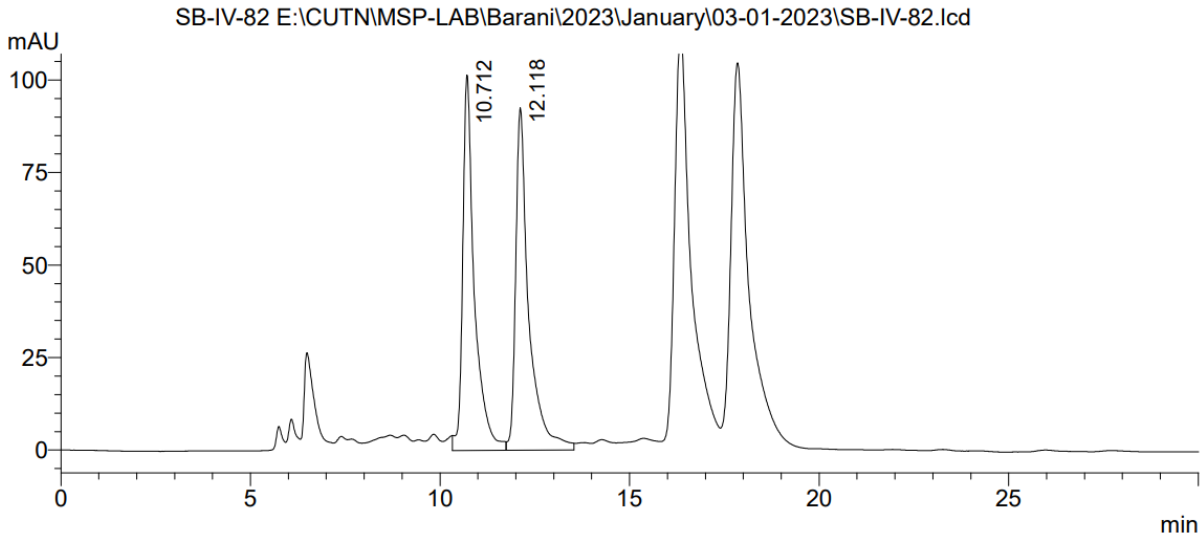
HPLC of chiral **4i**: **85% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.171	124829	5718	7.593
2	11.492	1519233	71048	92.407
Total		1644062	76765	100.000

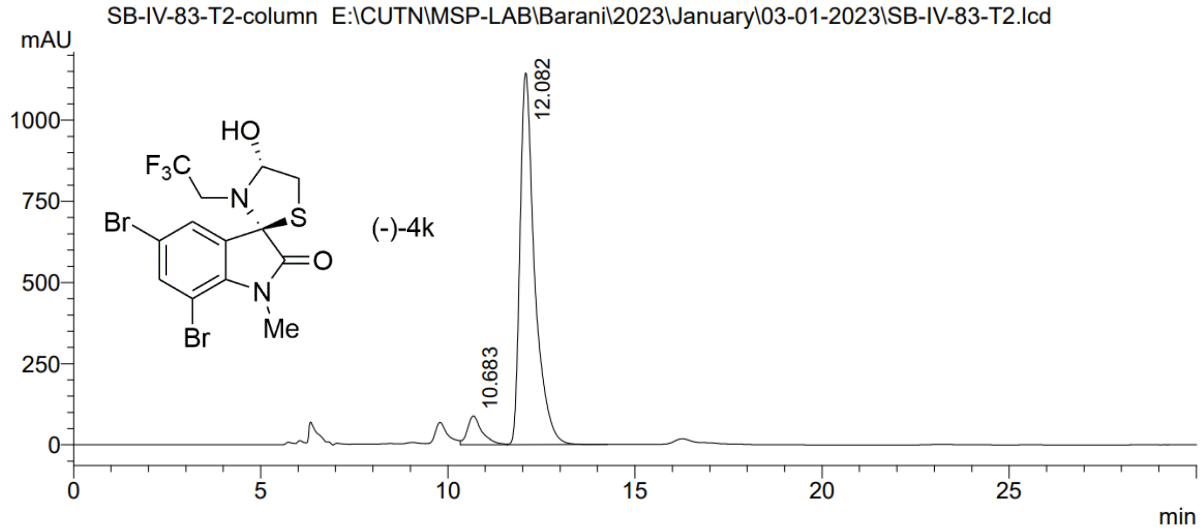
HPLC of racemic **4k**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.712	2172979	101427	49.480
2	12.118	2218658	92513	50.520
Total		4391638	193940	100.000

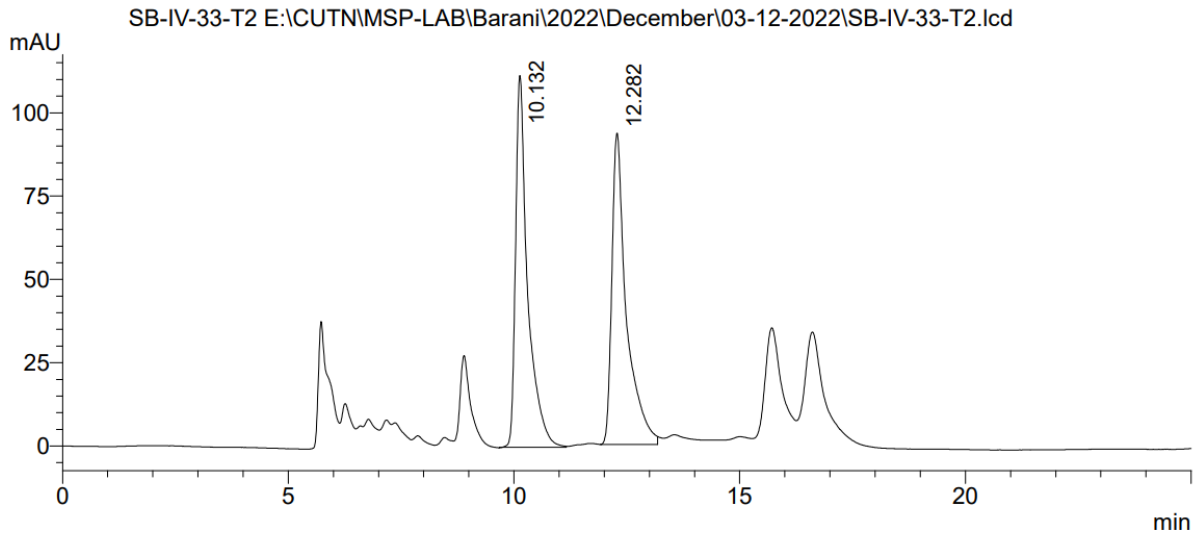
HPLC of chiral **4k: 86% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.683	2398244	88691	7.169
2	12.082	31052535	1144788	92.831
Total		33450779	1233479	100.000

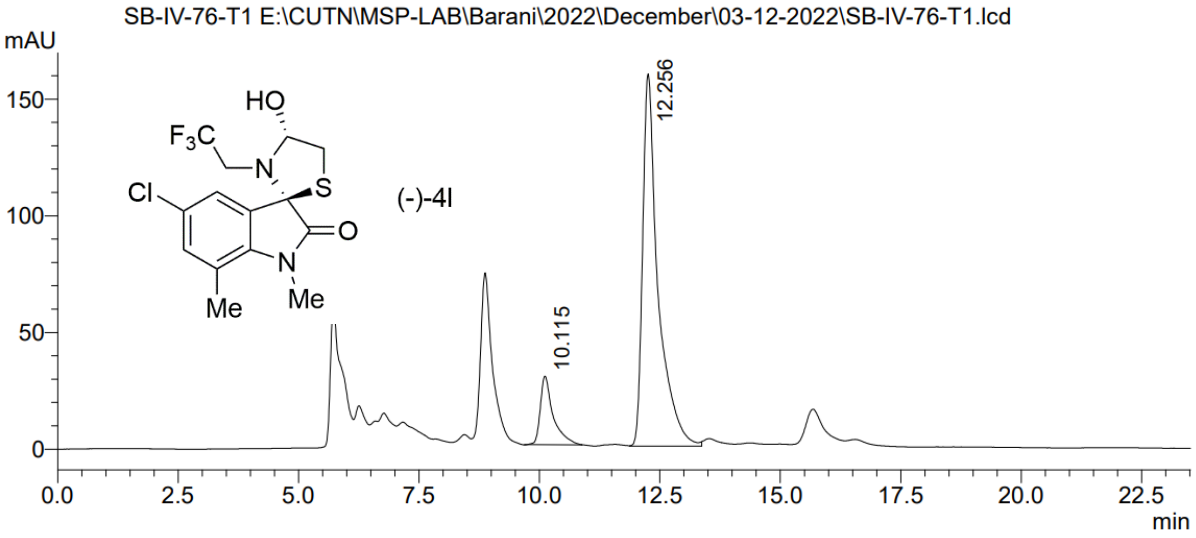
HPLC of racemic **4l**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.132	2071378	111540	49.751
2	12.282	2092076	93459	50.249
Total		4163454	204998	100.000

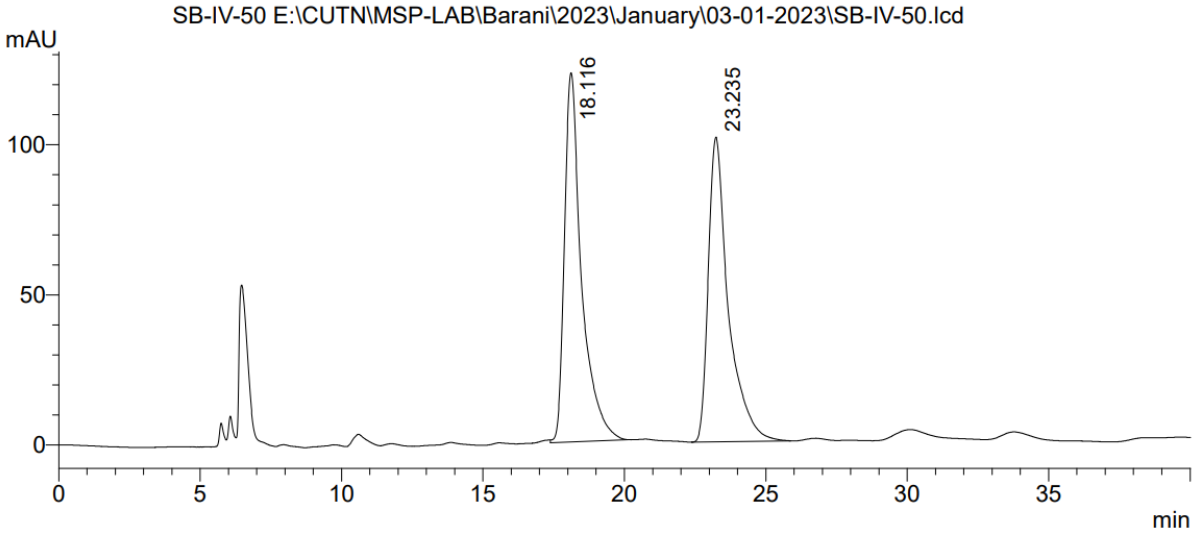
HPLC of chiral **4l: 74% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.115	542019	29349	13.260
2	12.256	3545662	159458	86.740
Total		4087682	188808	100.000

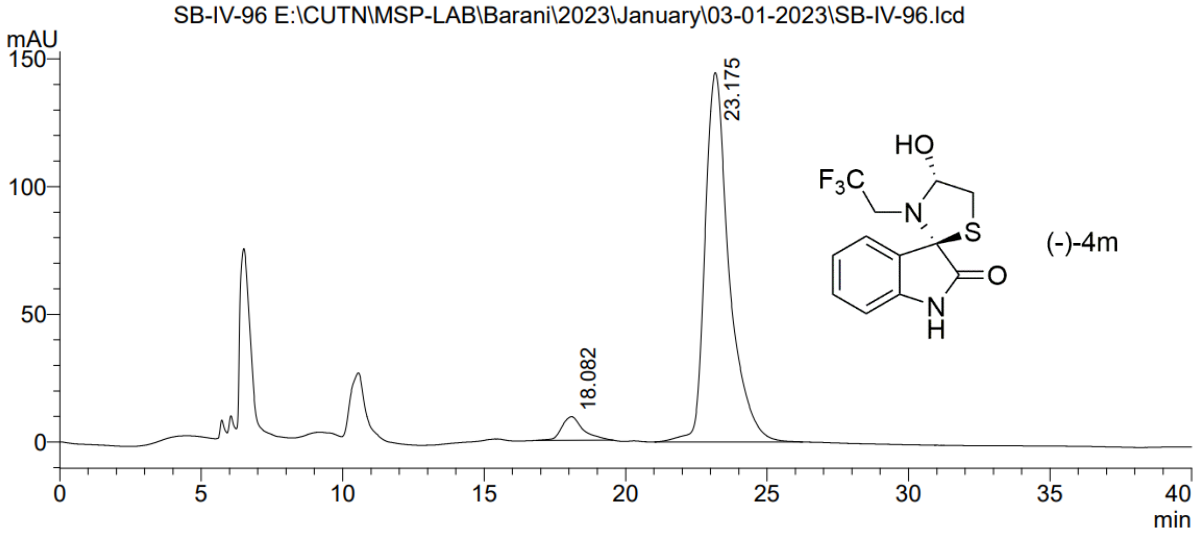
HPLC of racemic **4m**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.116	5162128	122972	50.814
2	23.235	4996753	101548	49.186
Total		10158881	224520	100.000

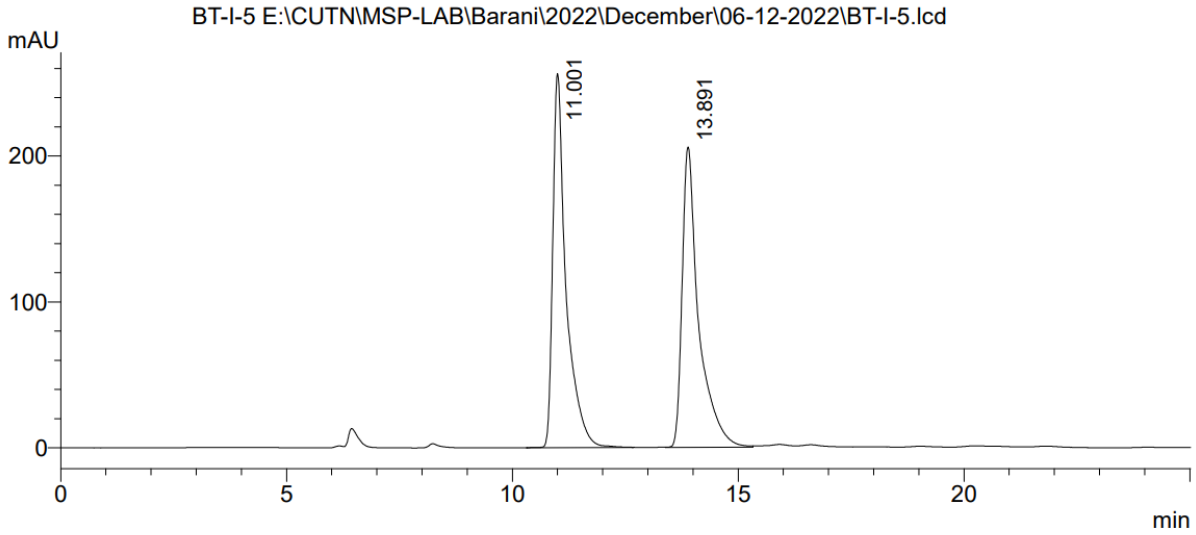
HPLC of chiral **4m: 89% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.082	482762	9247	5.322
2	23.175	8587630	144606	94.678
Total		9070392	153853	100.000

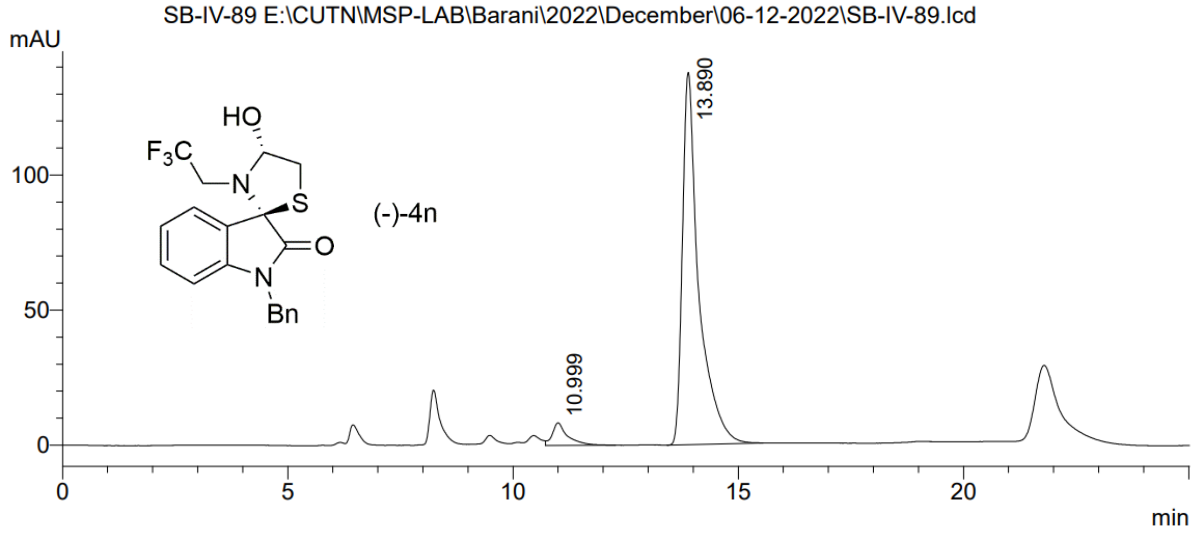
HPLC of racemic **4n**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	11.001	5244471	256313	50.087
2	13.891	5226192	205831	49.913
Total		10470663	462145	100.000

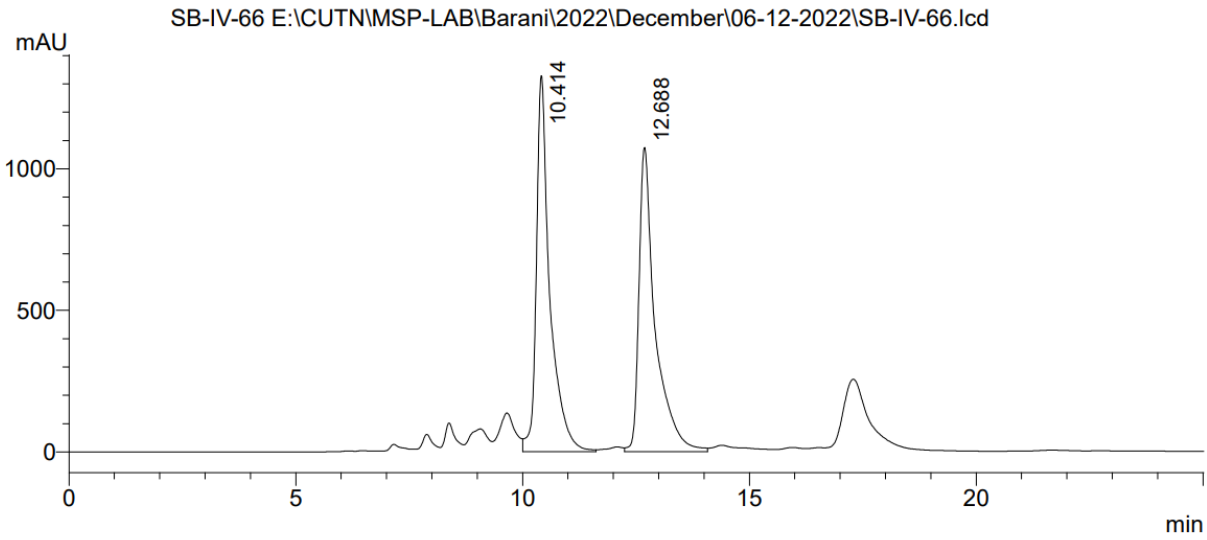
HPLC of chiral **4n: 89% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.999	197459	8340	5.375
2	13.890	3476198	137811	94.625
Total		3673657	146151	100.000

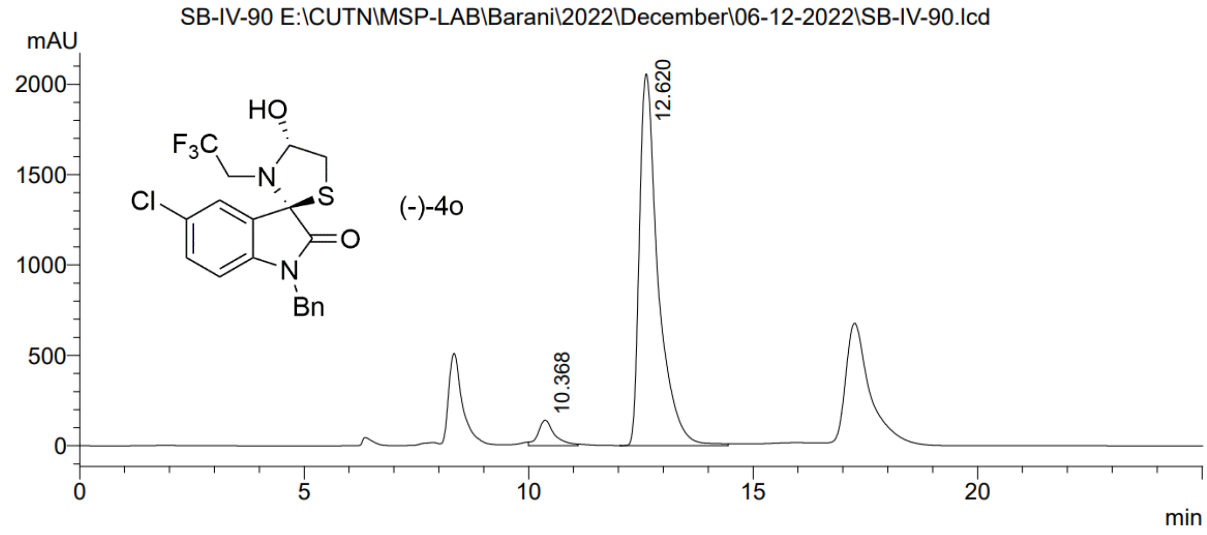
HPLC of racemic **4o**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.414	27344400	1328265	50.576
2	12.688	26721936	1074288	49.424
Total		54066336	2402553	100.000

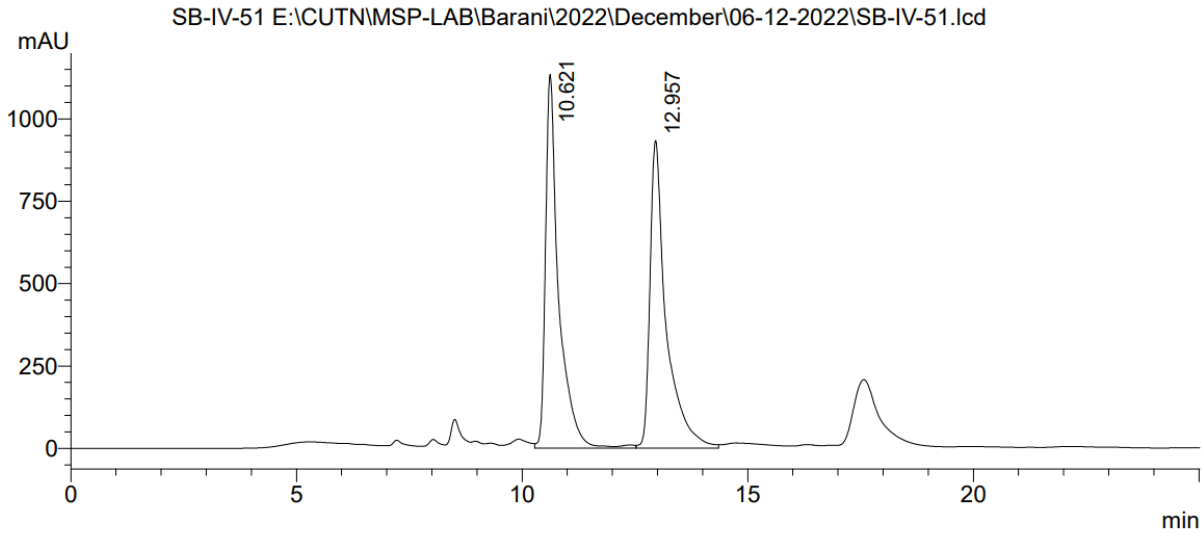
HPLC of chiral **4o: 89% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.368	3590735	140601	5.681
2	12.620	59616576	2056216	94.319
Total		63207311	2196817	100.000

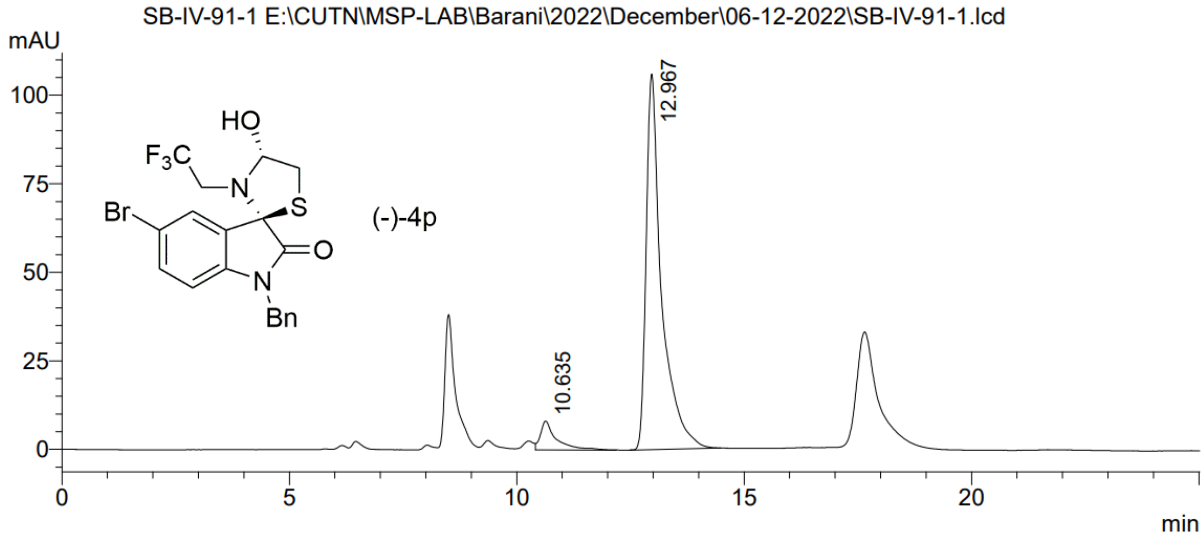
HPLC of racemic **4p**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.621	23024597	1134329	49.729
2	12.957	23275715	934141	50.271
Total		46300313	2068470	100.000

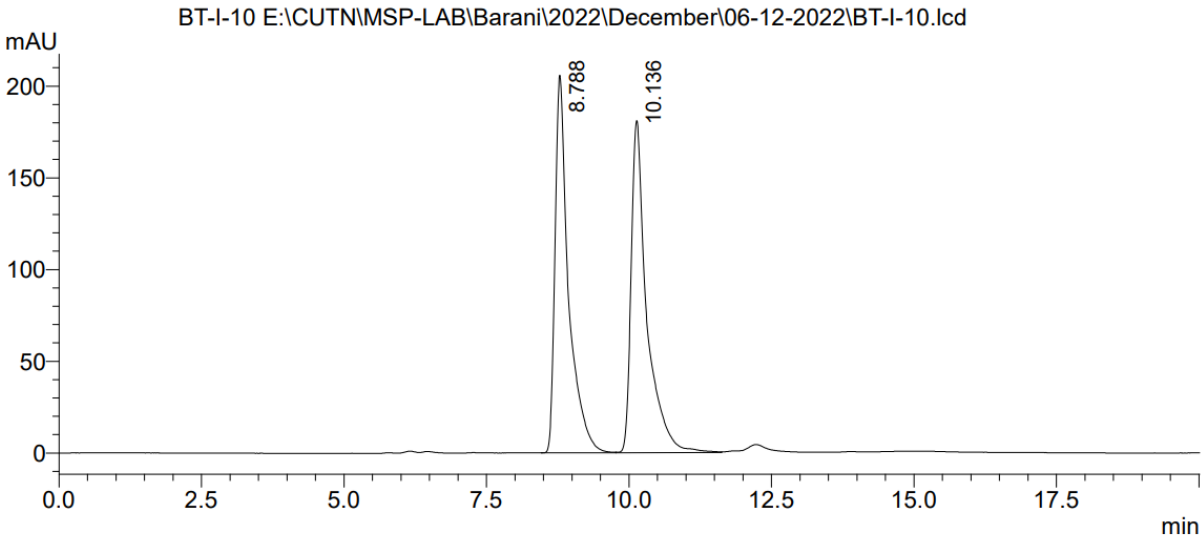
HPLC of chiral **4p: 85% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.635	200205	8174	7.403
2	12.967	2504301	106016	92.597
Total		2704507	114190	100.000

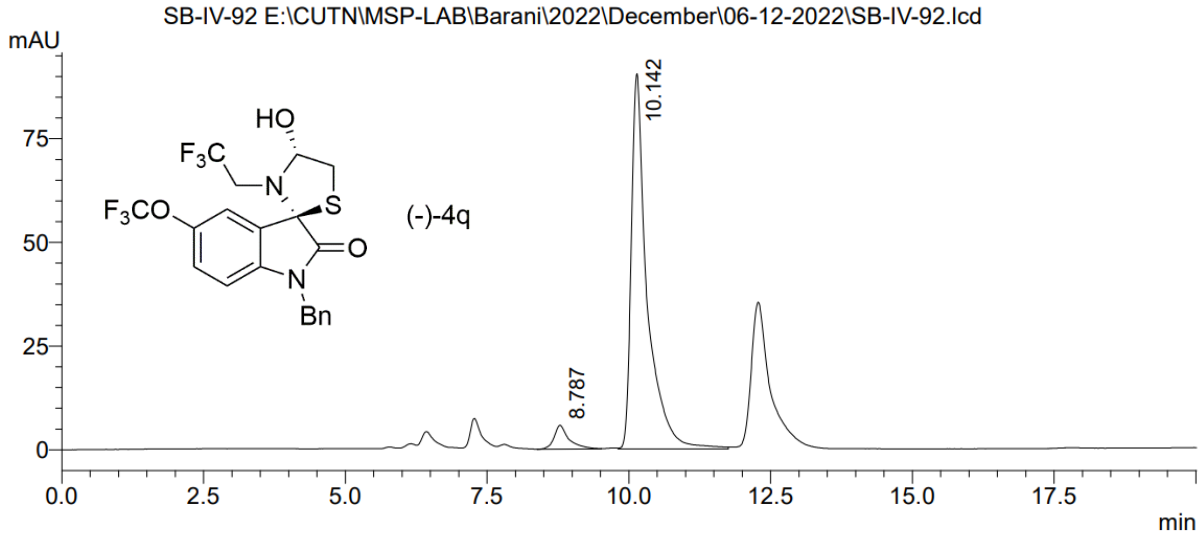
HPLC of racemic **4q**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.788	3390873	205829	49.519
2	10.136	3456807	181073	50.481
Total		6847680	386902	100.000

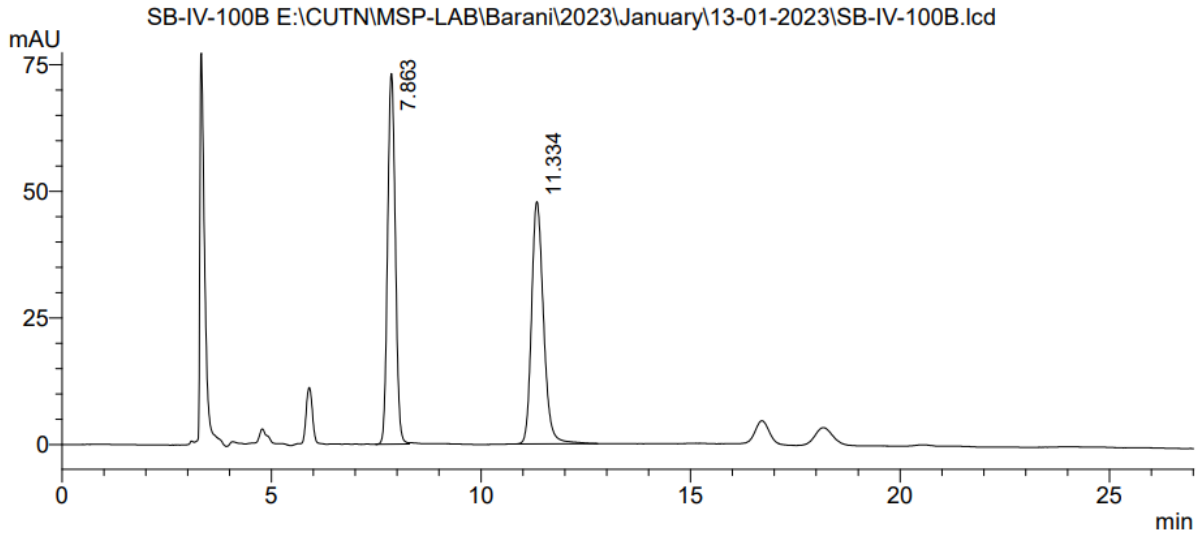
HPLC of chiral **4q: 89% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.787	105723	5757	5.660
2	10.142	1762009	90475	94.340
Total		1867732	96233	100.000

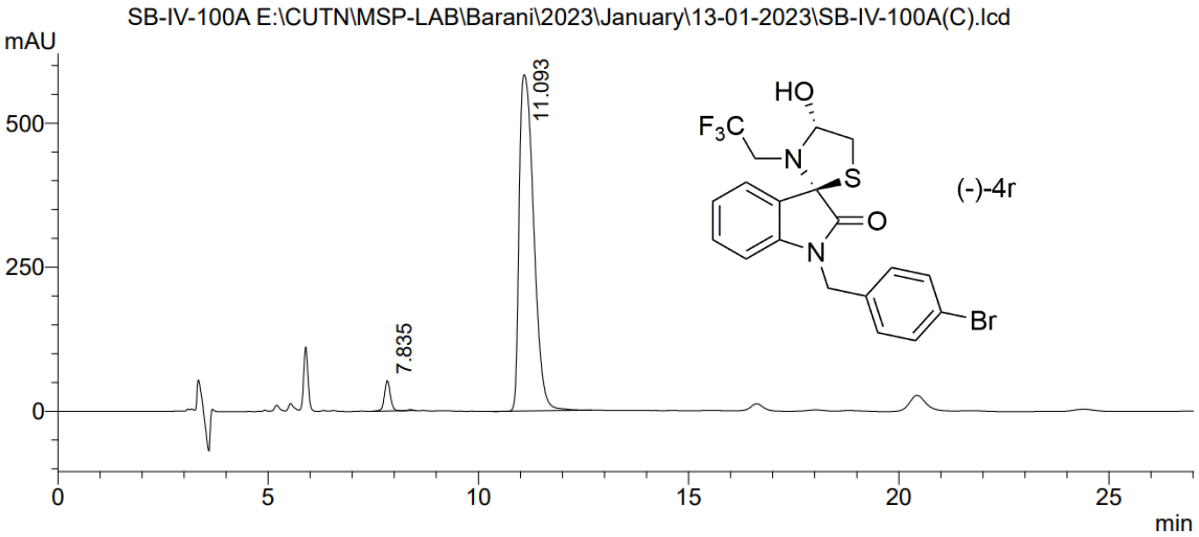
HPLC of racemic **4r**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	7.863	936950	73182	49.625
2	11.334	951109	47826	50.375
Total		1888060	121007	100.000

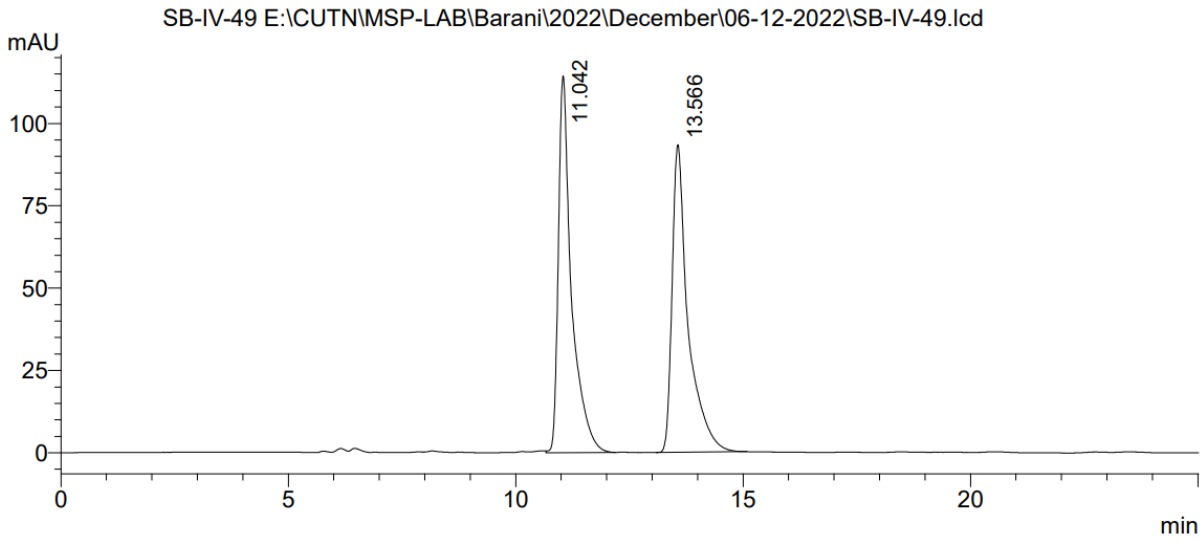
HPLC of chiral **4r: 93% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	7.835	526221	52673	3.626
2	11.093	13985860	583786	96.374
Total		14512081	636459	100.000

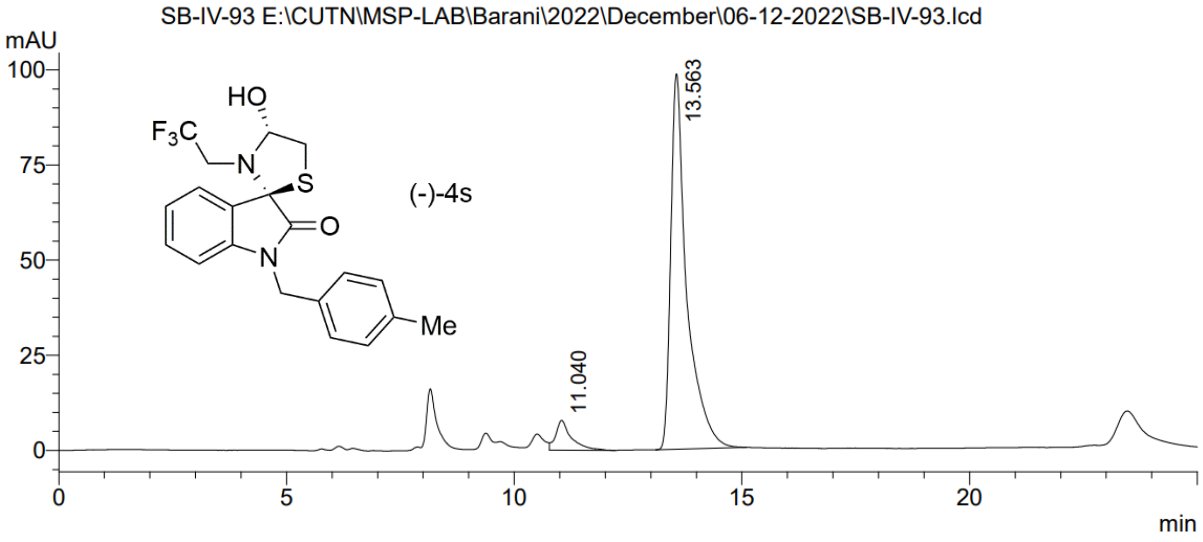
HPLC of racemic **4s**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	11.042	2291813	114389	50.182
2	13.566	2275177	93381	49.818
Total		4566990	207769	100.000

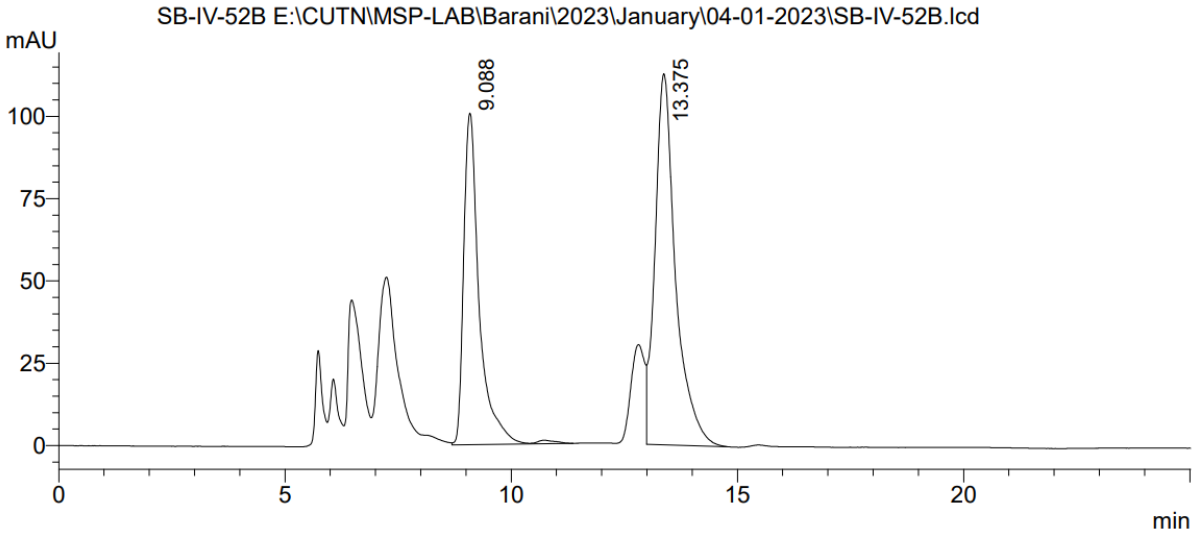
HPLC of chiral **4s: 86% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	11.040	186393	7822	7.170
2	13.563	2413346	98593	92.830
Total		2599739	106415	100.000

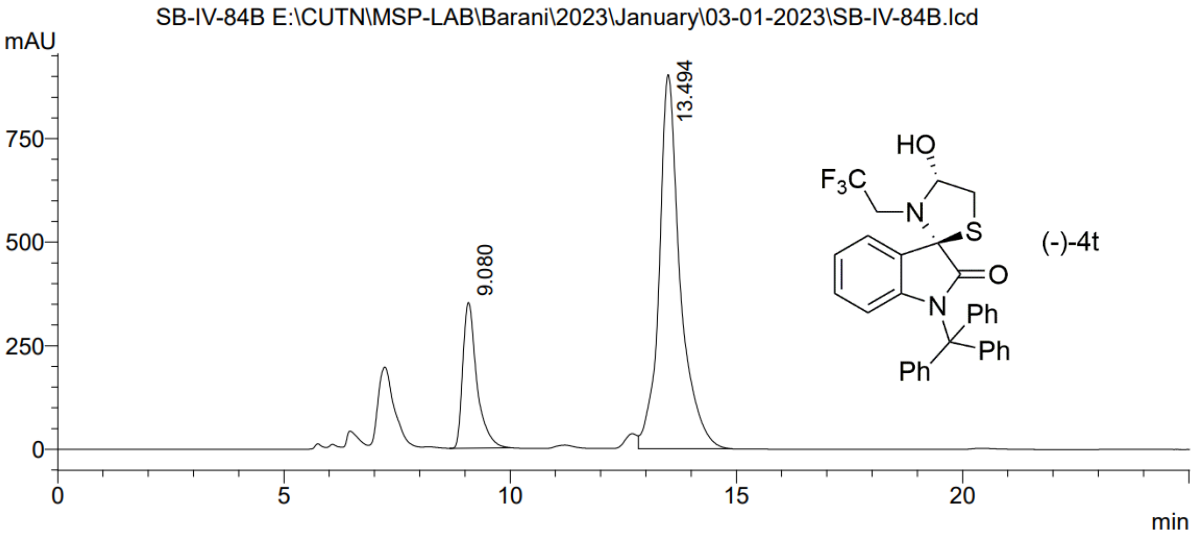
HPLC of racemic **4t**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.088	2411847	100682	40.437
2	13.375	3552588	112742	59.563
Total		5964435	213424	100.000

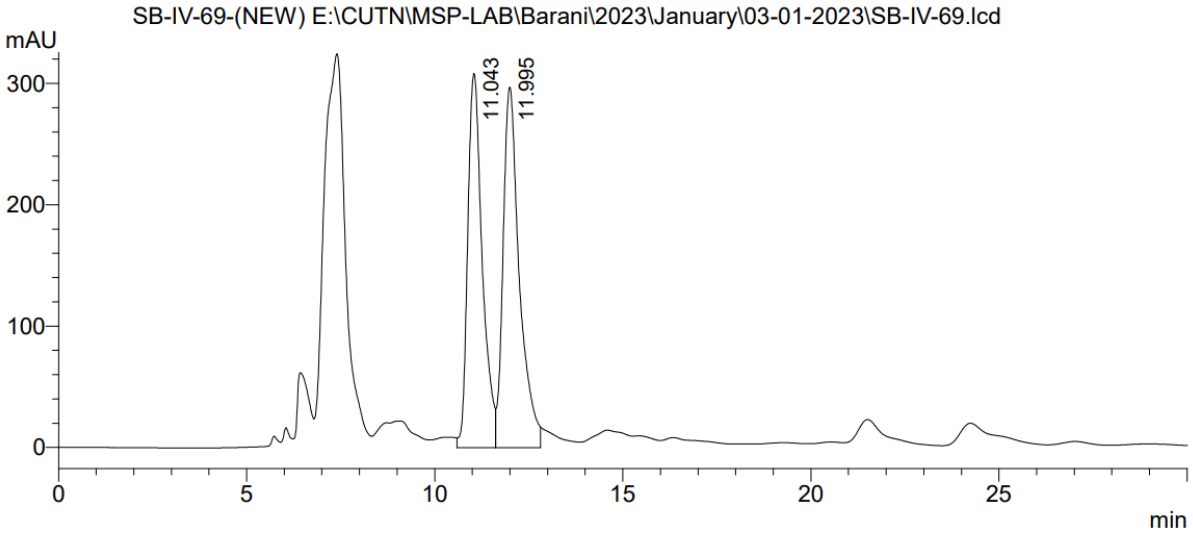
HPLC of chiral **4t: 59% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.080	7583206	351534	20.648
2	13.494	29142793	902921	79.352
Total		36725998	1254455	100.000

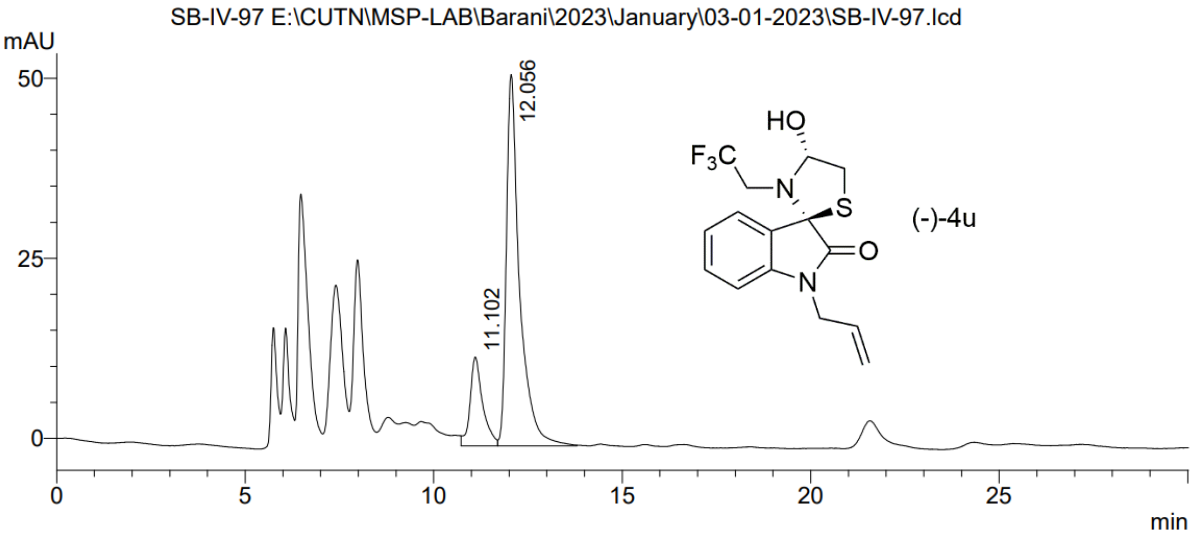
HPLC of racemic **4u**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	11.043	8297897	308492	48.104
2	11.995	8952011	297210	51.896
Total		17249908	605702	100.000

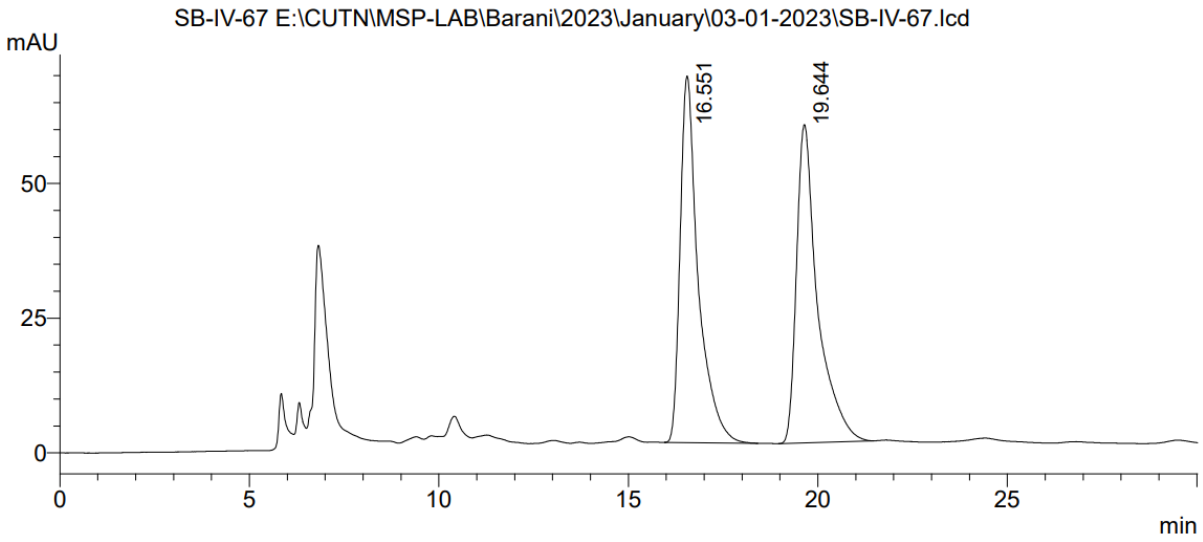
HPLC of chiral **4u: 63% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	11.102	287275	12326	18.579
2	12.056	1258958	51524	81.421
Total		1546234	63850	100.000

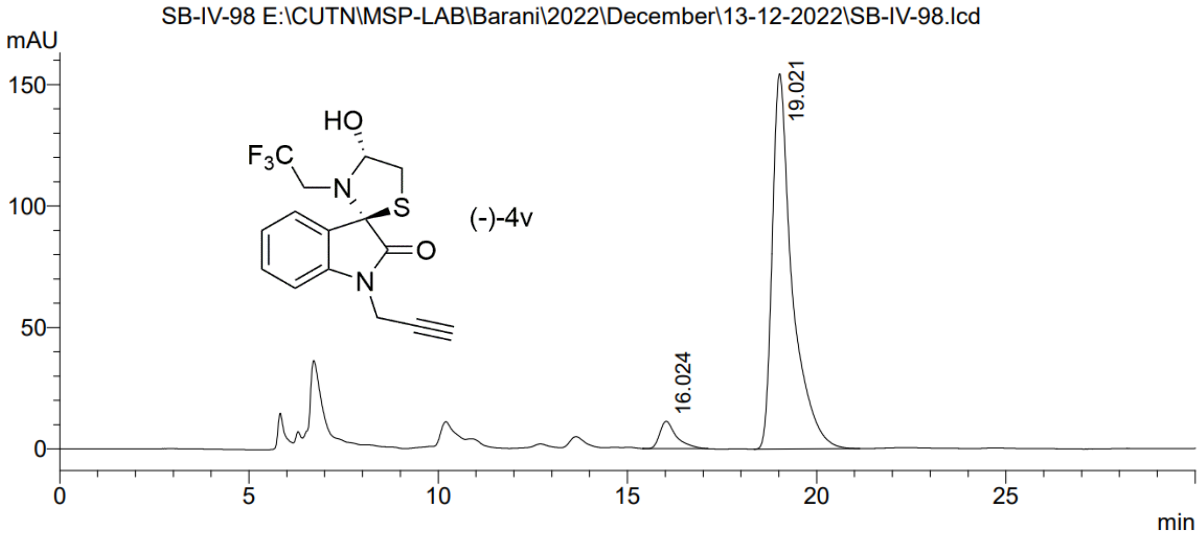
HPLC of racemic **4v**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	16.551	2263524	68068	49.687
2	19.644	2292007	59115	50.313
Total		4555531	127183	100.000

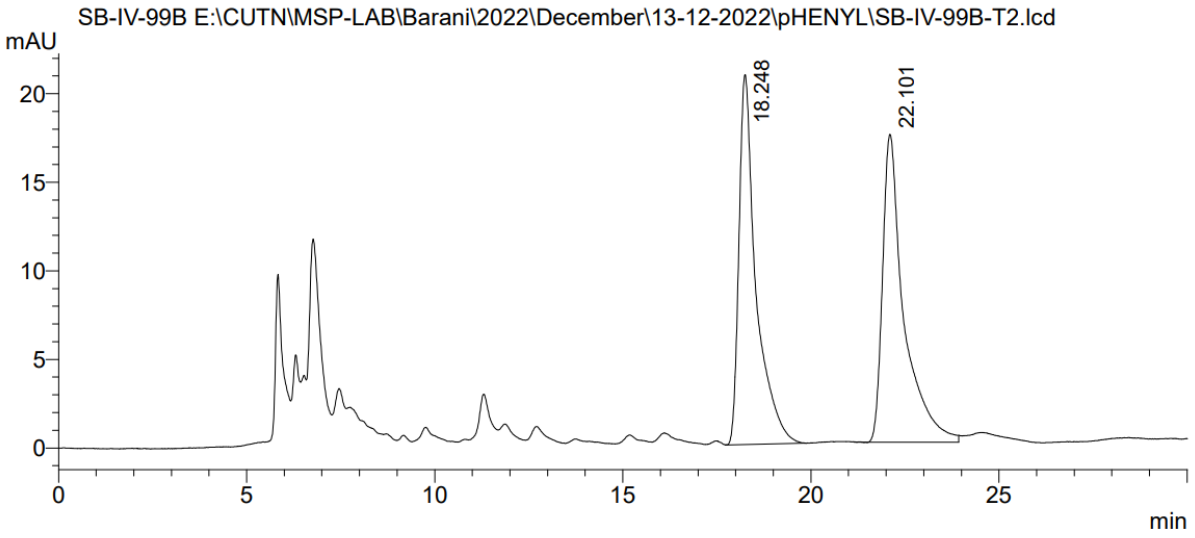
HPLC of chiral **4v: 89% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	16.024	342075	11268	5.696
2	19.021	5663710	154489	94.304
Total		6005785	165757	100.000

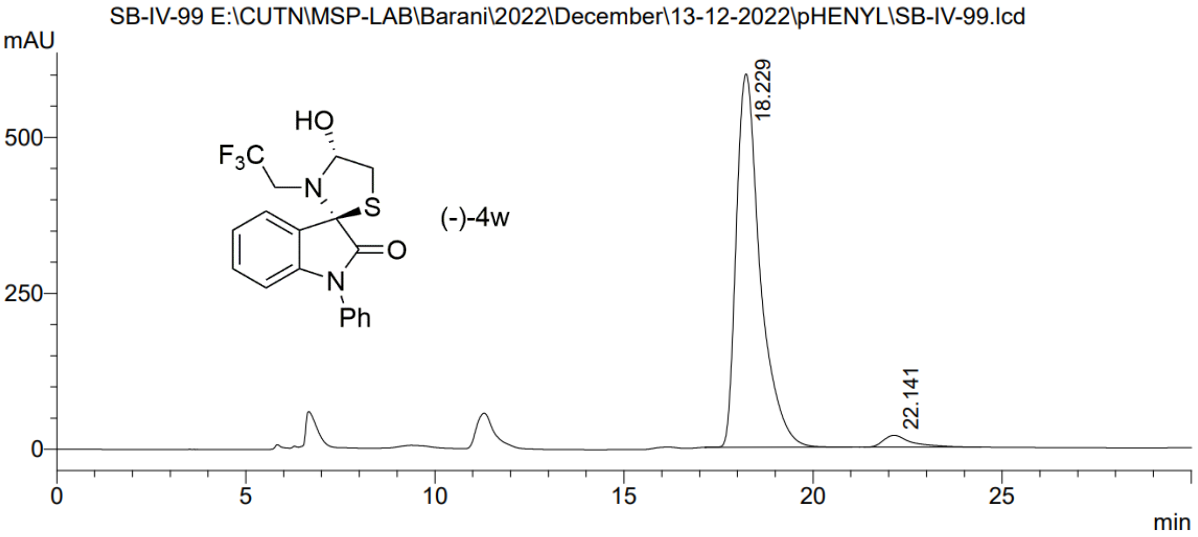
HPLC of racemic **4w**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.248	658551	20883	49.087
2	22.101	683041	17391	50.913
Total		1341593	38274	100.000

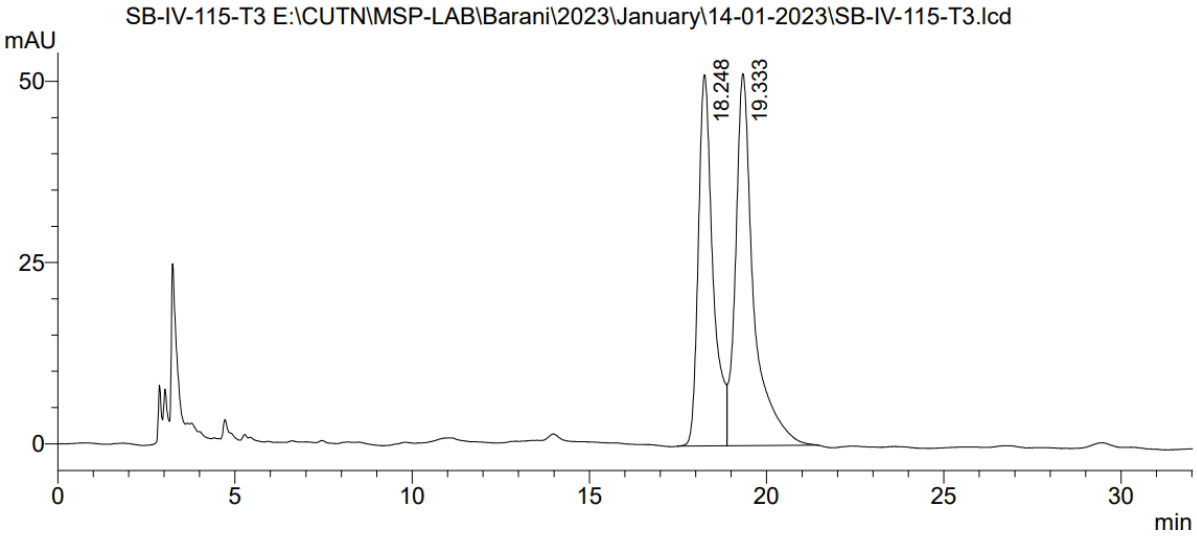
HPLC of chiral **4w: 93% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.229	26313960	598604	96.362
2	22.141	993412	18971	3.638
Total		27307372	617574	100.000

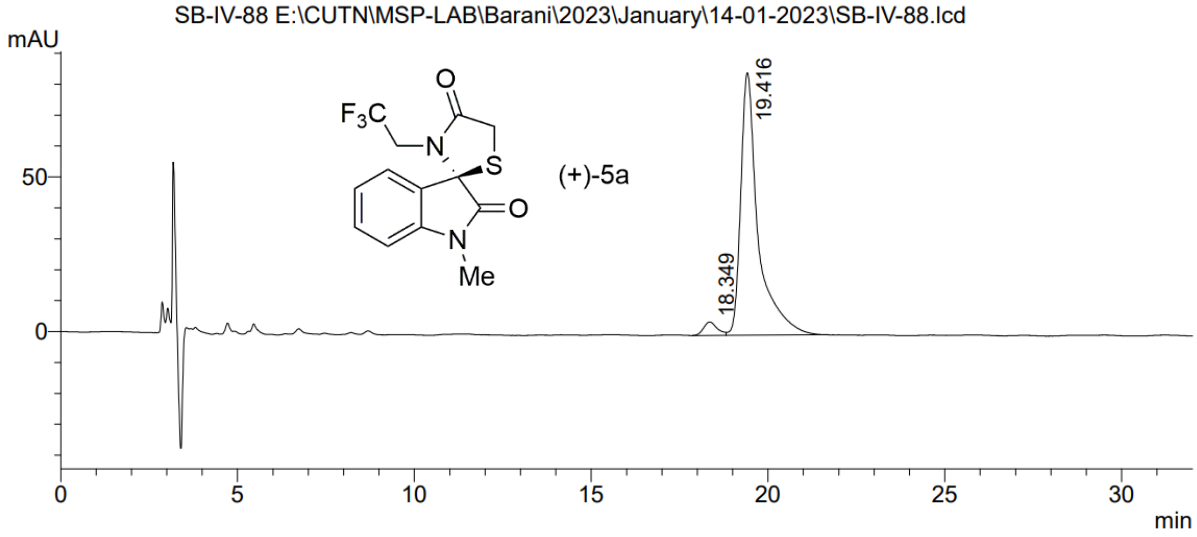
HPLC of racemic **5a**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.248	1477333	51205	44.821
2	19.333	1818766	51298	55.179
Total		3296099	102503	100.000

HPLC of chiral **5a: 92% *ee***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.349	117209	4326	3.882
2	19.416	2901768	84894	96.118
Total		3018977	89220	100.000