Supporting Information

Asymmetric Synthesis of spiro[benzofuran-pyrrolidine]-indolinedione *via* Bifunctional Urea Catalyzed [3+2]-annulation Reaction

Sankar Bharani,[a] Biddika Anandarao,[a] L. Raju Chowhan,[b] Pallepogu Raghavaiah,[c] and Madavi S. Prasad*[a]

[a]*Asymmetric Synthesis and Catalysis Laboratory, Department of Chemistry, Central University of Tamil Nadu, Thiruvarur, 610 005, India*

shivaprasad@cutn.ac.in* and *shivacutn@gmail.com

[b]*School of Physical Sciences, Jawaharlal Nehru University, New Delhi, 110067, India*

[c]*Department of Chemistry, Central University of Karnataka, Kadaganchi, Kalaburagi- 585 367, India*

Table of Contents

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) and DMSO-D6 (δ = 39.0).

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/100mL. 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.

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-j' was prepared by following the reported literature procedure.[1]

General Procedure B: *Preparation of alkylidene 2-cumaranone enophiles:*

2a-2v were synthesized using a literature report.[2] All the NMRs were consistent with the literature.

General Procedure C: *[3+2]-cycloaddition:*

To an oven-dried vial containing catalyst **3b** (2.5 mol%), the arylidene cumaranone enophile **2** (1.0 equiv.) was added followed by the addition of Ketimine **1** (1.1 equiv.) in DCM (0.5 mL). The crude reaction mixture was directly loaded into the column and purified by flash column chromatography using hexane/ EtOAc (7:3) to avoid racemisation.

General Procedure D: Racemic reaction of *[3+2]-cycloaddition:*

To an oven-dried vial containing catalyst DABCO (20 mol%), the arylidene cumaranone enophile **2** (1.0 equiv.) was added followed by the addition of Ketimine **1** (1.1 equiv.) in toluene (0.5 mL). After the completion of the reaction, monitored through TLC, the crude reaction mixture was directly loaded into the column and purified by flash column chromatography using hexane/ EtOAc (7:3). In the case of reactions where precipitation is observed, they are subjected to a centrifuge process followed by hexane wash resulting in the desired product.

General Procedure E: *synthetic application: m-CPBA oxidation: [3]*

To an oven-dried vial containing **4d** (1 equiv.), *m*-CPBA (2.1 equiv.) was added in DCM (0.1 M). The resulting mixture was stirred at RT for 72 hours; The reaction mixture was diluted with 5 mL of DCM, washed with 10% Na_2SO_4 solution (2×5mL), saturated $NaHCO_3$ solution (2×5 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.

General Procedure F: *synthetic application: [4]*

To an oven-dried vial containing **4i'** (1 equiv.), 4-acetamidobenzenesulfonyl azide (1.0 equiv.)c CuI (5 mol%) and NEt_3 (6 mol%) was added in EtOH (0.1 M) under N_2. The resulting mixture was stirred at 70^{o}C for 3 hours; The reaction mixture was diluted with 5 mL of DCM, washed with saturated $NaHCO_3$ solution (2×5 mL), dried over Na_2SO_4 and concentrated in vacuo. Then the crude product was directly purified by column chromatography using DCM with 1% NEt_3 as a mobile phase.

References:

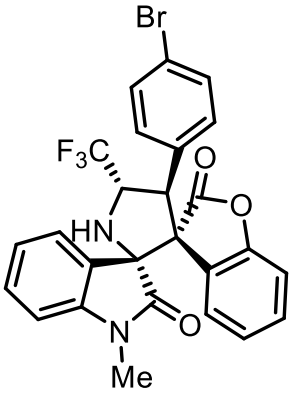
1) X. Wang, D. Huang, K. H. Wang, J. Liu, W. Zong, J. Wang, J. Su, and Y. Hu, *Appl Organometal Chem*. 2019, **33**, 4995.

2) H. J. Ma, K. Gao, X. L. Wag, J. Y. Zeng, Y. Yang, and Y. Jiang, *Org. Biomol. Chem.*, 2023,**21**, 6312-6316

3) W. C. Yuan, L. Yang, J. Q. Zhao, H. Y. Du, Z. H. Wang, Y. You, Y. P. Zhang, J. Li, W. Zhang, and M. Q. Zhou, *Org. Lett.* 2022, **24**, 25, 4603–4608.

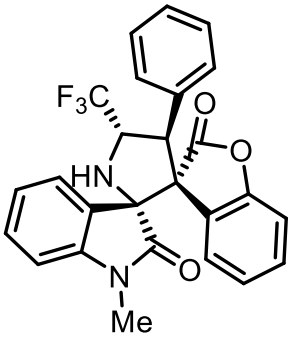
4) P. Shanmugam, M. Damodiran, K. Selvakumar, and P. T. Perumal, *J. Heterocyclic Chem*., 2009, **46**, 919-924.

(2'R,3R,4'S,5'S)-4'-(4-bromophenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4a):



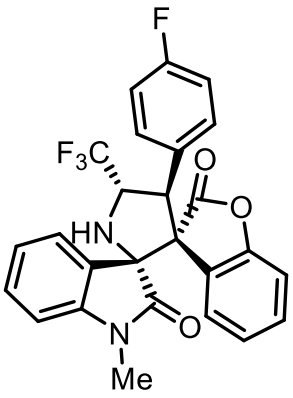
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4a** in 89% yield as a white solid with M. P. 239 - 241 °C; The enantiomeric ratio (*er*) was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 9.303 min (minor), t_R = 24.131 min (major), **$[\alpha]_D^{25}$ = -82.273 (CH_2Cl_2, *c* = 0.9 g/100mL, CH_2Cl_2 for 90:10 *er*)**; **IR (neat) ν_{max}** 3329, 1797, 1720, 1122, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.78 (1H, dd, *J* = 7.6, 1.5 Hz), 7.33 (1H, td, J = 7.6, 1.2 Hz), 7.28 (1H, td, *J* = 7.8, 1.5 Hz), 7.24 – 7.20 (2H, m), 7.17 (1H, td, *J* = 7.7, 1.2 Hz), 6.93 (2H, d, *J* = 8.5 Hz), 6.76 (1H, dd, *J* = 8.0, 0.8 Hz), 6.74 (1H, dd, *J* = 7.6, 0.8 Hz), 6.70 (1H, d, *J* = 7.7 Hz), 6.65 (1H, td, J = 7.6, 0.9 Hz), 5.57 (1H, d, *J* = 10.7 Hz), 4.86 – 4.47 (1H, m), 3.21 (3H, s), 2.85 (1H, d, *J* = 5.6 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.0 (C, C-*C*=O), 171.9 (C, N-*C*=O), 152.9 (C), 144.2 (C), 131.5 (2CH), 131.2 (C), 130.6 (CH), 130.6 (CH), 130.1 (2CH), 126.4 (CH), 125.4 (CF3, q, *J* = 279 Hz), 125.3 (CH), 123.8 (C), 123.6 (CH), 123.4 (C), 122.4 (C), 121.9 (CH), 111.7 (CH), 108.3 (CH), 71.5 (C), 65.9 (C), 60.9 (CH, q, *J* = 31 Hz), 50.1 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.60; **HRMS (ESI)** m/z: 565.0345 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_3BrNa$; Found 565.03316.

(2'R,3R,4'S,5'S)-1''-methyl-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4b):



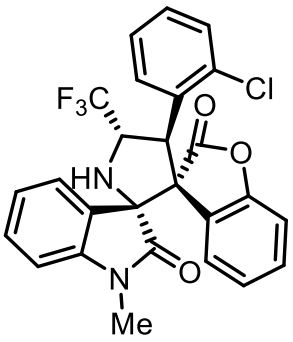
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4b** in 83% yield as a white solid with M. P. 250 - 252 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 7.935 min (minor), t_R = 16.749 min (major), **$[\alpha]_D^{25}$ = -4.000 (CH_2Cl_2, *c* = 0.1 g/100mL, CH_2Cl_2 for 79:21 *er*)**; **IR (neat) ν_{max}** 3340, 1793, 1720, 1462, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 (1H, d, *J* = 7.0 Hz), 7.31 (1H, t, *J* = 7.6 Hz), 7.24 (1H, td, *J* = 7.7, 1.0 Hz), 7.16 (1H, td, *J* = 7.6, 0.8 Hz), 7.12 – 7.05 (5H, m), 6.76 (1H, d, *J* = 7.3 Hz), 6.70 (2H, t, *J* = 7.2 Hz), 6.64 (1H, t, *J* = 7.6 Hz), 5.60 (1H, d, *J* = 10.7 Hz), 4.94 – 4.85 (1H, m), 3.22 (3H, s), 2.86 (1H, d, *J* = 5 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.1 (C, C-*C*=O), 172.1 (C, N-*C*=O), 152.8 (C), 144.2 (C), 132.0 (C), 130.5 (CH), 130.3 (CH), 128.4 (2CH), 128.3 (2CH), 128.1 (CH), 126.5 (CH), 125.5 (CF3, q, *J* = 279 Hz), 125.4 (CH), 123.9 (C), 123.8 (C), 123.5 (CH), 121.9 (CH), 111.4 (CH), 108.3 (CH), 71.5 (C), 66.3 (C), 60.8 (CH, q, *J* = 32 Hz), 50.7 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.53; **HRMS (ESI)** m/z: 487.1240 $[M + Na]^+$, calcd for $C_{26}H_{19}O_3N_2F_3Na$; Found 487.1235.

(2'R,3R,4'S,5'S)-4'-(4-fluorophenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4c):



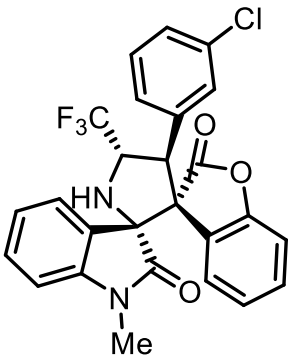
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4c** in 86% yield as a white solid with M. P. 247 - 249 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 17.268 min (minor), t_R = 38.553 min (major), **$[\alpha]_D^{25}$ = -81.633 (CH_2Cl_2, *c* = 0.5 g/100mL, CH_2Cl_2 for 91:9 *er*)**; **IR (neat) ν_{max}** 3344, 1793, 1724, 1172, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 (1H, d, *J* = 7.3 Hz), 7.33 (1H, t, *J* = 7.4 Hz), 7.27 (1H, t, *J* = 7.2 Hz), 7.17 (1H, t, *J* = 7.6 Hz), 7.03 (2H, q, *J* = 3.2 Hz), 6.80 – 6.74 (4H, m), 6.70 (1H, d, *J* = 7.8 Hz), 6.65 (1H, t, *J* = 7.6 Hz), 5.59 (1H, d, *J* = 10.7 Hz), 4.86 – 4.78 (1H, m), 3.21 (3H, s), 2.86 (1H, d, *J* = 5 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.1 (C, C-*C*=O), 171.9 (C, N-*C*=O), 162.4 (C, C-F, d, *J* = 246 Hz), 152.9 (C), 144.2 (C), 130.6 (CH), 130.5 (CH), 130.1 (CH), 130.0 (CH), 127.8 (C, d, *J* = 3Hz), 126.4 (CH), 125.4 (CF3, q, *J* = 279 Hz), 125.4 (CH), 123.9 (C), 123.6 (CH), 123.5 (CH), 121.9 (CH), 115.4 (CH), 115.2 (CH), 111.6 (CH), 108.3 (CH), 71.4 (C), 66.1 (C), 61.2 (CH, q, *J* = 31 Hz), 50.3 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.55, -113.6; **HRMS (ESI)** m/z: 505.1146 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_4Na$; Found 505.1138.

(2'R,3R,4'R,5'S)-4'-(2-chlorophenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione(4d):



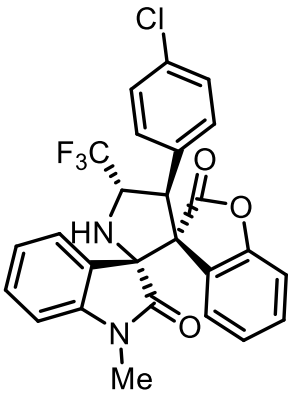
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4d** in 88% yield as a white solid with M. P. 254 - 256 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 12.372 min (minor), t_R = 42.681 min (major), **$[\alpha]_D^{25}$ = -37.333 (CH_2Cl_2, *c* = 0.6 g/100mL, CH_2Cl_2 for 98:2 *er*)**; **IR (neat) ν_{max}** 3332, 1797, 1724, 1126, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.33 (1H, d, *J* = 7.4 Hz), 7.43 (1H, t, *J* = 7.5 Hz), 7.31 (2H, t, *J* = 7.5 Hz), 7.21 (1H, t, *J* = 7.8 Hz), 7.13 (2H, q, J = 7.8 Hz), 6.95 – 6.90 (4H, m), 6.69 (1H, t, *J* = 7.7 Hz), 6.39 (1H, d, *J* = 10.8 Hz), 5.15 (1H, d, *J* = 8.6 Hz), 4.94 – 4.88 (1H, m), 3.11 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.4 (C, C-*C*=O), 171.6 (C, N-*C*=O), 152.4 (C), 144.5 (C), 134.7 (C), 131.1 (CH), 130.9 (CH), 130.7 (C), 130.6 (CH), 130.1 (CH), 130.0 (CH), 128.5 (CH), 126.7 (CH), 126.6 (CF3, q, *J* = 279 Hz), 126.4 (CH), 124.3 (CH), 123.4 (C), 123.3 (C), 121.6 (CH), 111.3 (CH), 108.8 (CH), 72.1 (C), 65.6 (C), 62.0 (CH, q, *J* = 30 Hz), 45.9 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.62; **HRMS (ESI)** m/z: 521.0850 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_3ClNa$; Found 521.0846.

(2'R,3R,4'S,5'S)-4'-(3-chlorophenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4e):



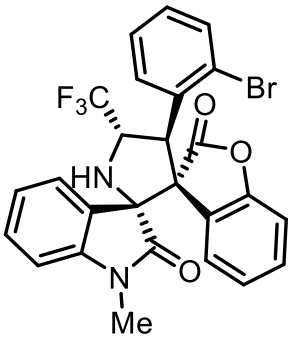
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4e** in 67% yield as a white solid with M. P. 249 - 251 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 15.886 min (minor), t_R = 38.616 min (major), **$[\alpha]_D^{25}$ = -98.200 (CH_2Cl_2, *c* = 0.5 g/100mL, CH_2Cl_2 for 80:20 *er*)**; **IR (neat) ν_{max}** 3332, 1797, 1705, 1080, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.20 (1H, d, *J* = 7.5 Hz), 7.39 (1H, td, *J* = 7.5, 0.8 Hz), 7.32 (1H, td, *J* = 7.7, 1.0 Hz), 7.22 – 7.15 (3H, m), 7.13 (1H, br s), 7.07 (1H, d, *J* = 7.2 Hz), 6.89 (2H, t, *J* = 7.8 Hz), 6.76 (1H, d, *J* = 7.3 Hz), 6.65 (1H, d, *J* = 7.5 Hz), 5.41 (1H, d, *J* = 10.0 Hz), 5.16 (2H, s), 3.10 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.3 (C, C-*C*=O), 172.5 (C, N-*C*=O), 152.1 (C), 144.2 (C), 135.7 (C), 133.3 (C), 131.0 (CH), 130.9 (CH), 130.6 (CH), 128.6 (CH), 128.5 (CH), 127.9 (CH), 127.7 (CH), 126.2 (CH), 124.4 (CH), 123.8 (CF3, q, *J* = 279 Hz), 123.3 (C), 123.2 (C), 121.7 (CH), 111.1 (CH), 108.8 (CH), 72.3 (C), 66.6 (C), 60.1 (CH, q, *J* = 30 Hz), 50.6 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.54; **HRMS (ESI)** m/z: 521.0850 [M + Na]$^+$, calcd for $C_{26}H_{18}O_3N_2F_3ClNa$; Found 521.0832.

(2'R,3R,4'S,5'S)-4'-(4-chlorophenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4f):



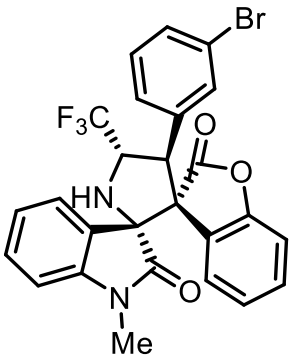
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4f** in 96% yield as a white solid with M. P. 252 - 254 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 95:5, flow rate 1.0 mL/min, λ = 254 nm), t_R = 33.715 min (major), t_R = 36.913 min (major), **$[\alpha]_D^{25}$ = -41.633 (CH_2Cl_2, *c* = 0.5 g/100mL, CH_2Cl_2 for 75:25 *er*)**; **IR (neat) ν_{max}** 3352, 1801, 1720, 1141, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.18 (1H, d, *J* = 7.2 Hz), 7.38 – 7.22 (2H, m), 7.21 – 7.19 (3H, m), 7.12 (2H, d, *J* = 8.4 Hz), 6.90 (2H, m), 6.75 (1H, d, *J* = 7.6 Hz), 6.65 (1H, t, *J* = 7.6 Hz), 5.41 (1H, d, *J* = 10.4 Hz), 5.15 – 5.08 (2H, m), 3.10 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.3 (C, C-*C*=O), 172.5 (C, N-*C*=O), 152.1 (C, d, *J* = 2 Hz), 144.2 (C), 133.1 (C), 132.2 (C), 130.9 (CH), 130.9 (CH), 130.6 (2CH), 128.7 (2CH), 127.9 (CH), 126.6 (CF3, q, *J* = 279 Hz), 126.1 (CH), 124.4 (CH), 123.3 (C), 123.2 (C), 121.7 (CH), 111.1 (CH), 108.8 (CH), 72.3 (C), 66.6 (C), 60.2 (CH, q, *J* = 34 Hz), 50.4 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.51; **HRMS (ESI)** m/z: 521.0850 [M + Na]$^+$, calcd for $C_{26}H_{18}O_3N_2F_3ClNa$; Found 521.0832.

(2'R,3R,4'R,5'S)-4'-(2-bromophenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4g):



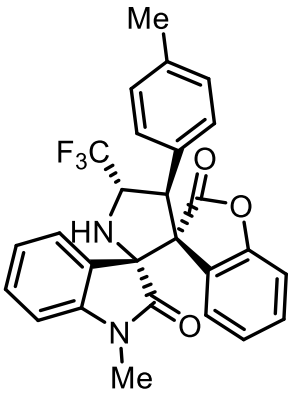
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4g** in 92% yield as a white solid with M. P. 263 - 265 °C; **$[\alpha]_D^{25}$ = -38.888 (CH_2Cl_2, *c* = 0.6 g/100mL)**; **IR (neat) ν_{max}** 3332, 1797, 1720, 1076, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.35 (1H, d, *J* = 7.5 Hz), 7.54 (1H, d, *J* = 7.6 Hz), 7.45 (1H, t, *J* = 7.5 Hz), 7.37 (1H, t, *J* = 7.8 Hz), 7.21 (1H, t, J = 7.7 Hz), 7.07 – 7.04 (2H, m), 6.97 – 6.89 (4H, m), 6.68 (1H, t, *J* = 7.6 Hz), 6.39 (1H, d, *J* = 10.8 Hz), 5.14 (1H, d, *J* = 8.6 Hz), 4.91 – 4.81 (1H, m), 3.11 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.3 (C, C-*C*=O), 171.6 (C, N-*C*=O), 152.5 (C), 144.5 (C), 133.7 (CH), 132.4 (C), 131.2 (CH), 130.9 (CH), 130.7 (CH), 130.4 (CH), 128.6 (CH), 127.2 (CH), 126.5 (CF3, q, *J* = 279 Hz), 126.4 (CH), 125.8 (C), 124.3 (CH), 123.4 (C), 123.2 (C), 121.6(CH), 111.3 (CH), 108.7 (CH), 72.1 (C), 65.7 (C), 62.4 (CH, q, *J* = 30 Hz), 48.5 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.53; **HRMS (ESI)** m/z: 565.0345 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_3BrNa$; Found 565.0339.

(2'R,3R,4'S,5'S)-4'-(3-bromophenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4h):



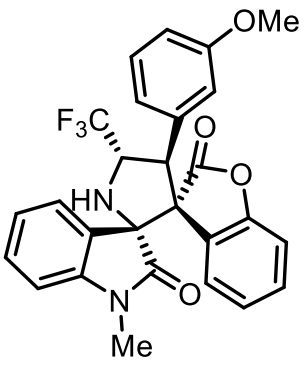
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4h** in 83% yield as a white solid with M. P. 251 - 253 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 16.487 min (minor), t_R = 42.577 min (major), **$[\alpha]_D^{25}$ = -52.383 (CH_2Cl_2, *c* = 1.3 g/100mL, CH_2Cl_2 for 81:19 *er*)**; **IR (neat) ν_{max}** 3317, 1793, 1716, 1122, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.20 (1H, d, *J* = 6.9 Hz), 7.39 (1H, td, *J* = 7.6, 0.9 Hz), 7.35 – 7.30 (2H, m), 7.24 (1H, br s), 7.21 (1H, td, *J* = 7.8, 1.0 Hz), 7.11 (2H, d, *J* = 5.1 Hz), 6.90 (2H, t, *J* = 7.6 Hz), 6.75 (1H, d, *J* = 6.9 Hz), 6.65 (1H, td, *J* = 7.5, 0.7 Hz), 5.39 (1H, d, *J* = 10.2 Hz), 5.14 (2H, s), 3.10 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.3 (C, C-*C*=O), 172.5 (C, N-*C*=O), 152.1 (C), 144.2 (C), 135.8 (C), 131.5 (CH), 131.3 (CH), 131.0 (CH), 130.9 (CH), 130.8 (CH), 128.0 (CH), 127.9 (CH), 126.2 (CH), 124.4 (CH), 123.9 (CF3, q, *J* = 243 Hz), 123.2 (C), 123.2 (C), 121.9 (C), 121.7 (CH), 111.2 (CH), 108.8 (CH), 72.3 (C), 66.6 (C), 60.1 (CH, q, *J* = 30 Hz), 50.6 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.53; **HRMS (ESI)** m/z: 565.0345 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_3BrNa$; Found 565.0335.

(2'R,3R,4'S,5'S)-1''-methyl-4'-(p-tolyl)-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4i):



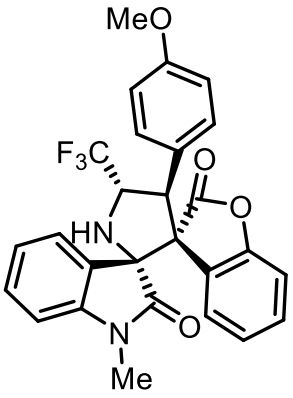
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4i** in 81% yield as a white solid with M. P. 258 - 260 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 17.072 min (minor), t_R = 44.914 min (major), **$[\alpha]_D^{25}$ = -82.712 (CH_2Cl_2, *c* = 0.9 g/100mL, CH_2Cl_2 for 85:15 *er*)**; **IR (neat) ν_{max}** 3325, 1789, 1716, 1083, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.24 (1H, d, *J* = 7.4 Hz), 7.41 (1H, t, J = 7.3 Hz), 7.34 (1H, td, *J* = 7.9, 0.8 Hz), 7.25 (1H, td, *J* = 7.7, 0.8 Hz), 7.02 – 6.94 (5H, m), 6.90 (1H, d, *J* = 7.8 Hz), 6.81 (1H, d, *J* = 9.5 Hz), 6.69 (1H, t, *J* = 7.6 Hz), 5.44 (1H, d, *J* = 10 Hz), 5.13 – 5.06 (2H, m), 3.14 (3H, s), 2.18 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.4 (C, C-*C*=O), 172.7 (C, N-*C*=O), 152.2 (C), 144.2 (C), 137.6 (C), 130.8 (CH), 130.7 (CH), 130.0 (C), 129.3 (2CH), 128.7 (2CH), 127.9 (CH), 126.7 (CF3, q, *J* = 279 Hz), 126.1 (CH), 124.3 (CH), 123.7 (C), 123.5 (C), 121.6 (CH), 111.0 (CH), 108.8 (CH), 72.3 (C), 66.7 (C), 60.4 (CH, q, *J* = 30 Hz), 50.7 (CH), 26.5 (CH_3), 20.9 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.38; **HRMS (ESI)** m/z: 501.1396 $[M + Na]^+$, calcd for $C_{27}H_{21}O_3N_2F_3Na$; Found 501.1389.

(2'R,3R,4'S,5'S)-4'-(3-methoxyphenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4j):



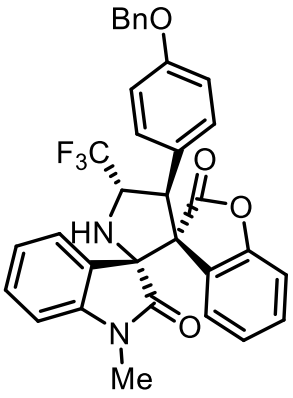
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4j** in 93% yield as a white solid with M. P. 249 - 251 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 19.397 min (minor), t_R = 49.566 min (major), **$[\alpha]_D^{25}$ = -82.211 (CH_2Cl_2, *c* = 1.0 g/100mL, CH_2Cl_2 for 92:8 *er*)**; **IR (neat) ν_{max}** 3325, 1797, 1716, 1141, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.19 (1H, d, *J* = 7.2 Hz), 7.37 (1H, t, *J* = 7.6 Hz), 7.29 (1H, td, *J* = 7.6, 0.8 Hz), 7.19 (1H, td, *J* = 7.7, 0.9 Hz), 7.04 (1H, t, *J* = 7.9 Hz), 6.87 (2H, dd, *J* = 13.3, 7.8 Hz), 6.75 (1H, d, *J* = 7.2 Hz), 6.69 – 6.62 (3H, m), 6.56 (1H, br s), 5.38 (1H, d, *J* = 10.2 Hz), 5.10 – 5.03 (2H, s), 3.56 (3H, s), 3.09 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.4 (C, C-*C*=O), 172.7 (C, N-*C*=O), 159.2 (C), 152.2 (C), 144.3 (C), 134.7 (C), 130.9 (CH), 130.8 (CH), 129.8 (CH), 128.0 (CH), 126.1 (CH), 124.3 (CH), 123.8 (CF3, q, *J* = 279 Hz), 123.7 (C), 123.5 (C), 121.6 (CH), 121.2 (CH), 114.4 (CH), 113.8 (CH), 111.1 (CH), 108.8 (CH), 72.3 (C), 66.7 (C), 60.3 (CH, q, *J* = 30 Hz), 55.4 (CH_3), 50.9 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.44; **HRMS (ESI)** m/z: 517.1346 $[M + Na]^+$, calcd for $C_{27}H_{21}O_4N_2F_3Na$; Found 517.1341.

(2'R,3R,4'S,5'S)-4'-(4-methoxyphenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4k):



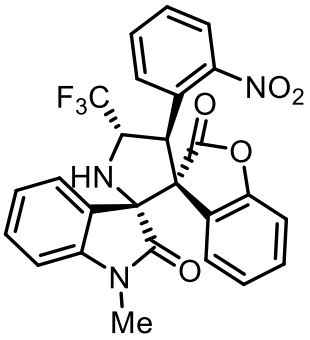
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4k** in 73% yield as a white solid with M. P. 229 - 221 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 21.427 min (minor), t_R = 56.208 min (major), **$[\alpha]_D^{25}$ = -28.407 (CH_2Cl_2, *c* = 0.6 g/100mL, CH_2Cl_2 for 71:29 *er*)**; **IR (neat) ν_{max}** 3753, 2364, 1801, 1720, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.17 (1H, d, *J* = 7.1 Hz), 7.35 (1H, td, *J* = 7.6, 0.8 Hz), 7.28 (1H, td, *J* = 7.9, 1.1 Hz), 7.18 (1H, td, *J* = 7.7, 1.0 Hz), 6.97 (2H, d, *J* = 8.8 Hz), 6.86 (2H, dd, *J* = 12.7, 7.8 Hz), 6.75 (1H, d, *J* = 7.1 Hz), 6.66 – 6.61 (3H, m), 5.35 (1H, d, *J* = 10.3 Hz), 5.04 – 4.95 (2H, m), 3.60 (3H, s), 3.07 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.5 (C, C-*C*=O), 172.7 (C, N-*C*=O), 159.1 (C), 152.2 (C), 144.2 (C), 130.8 (CH), 130.7 (CH), 129.9 (2CH), 127.9 (CH), 126.7 (CF3, q, *J* = 279 Hz), 126.1 (CH), 124.8 (C), 124.3 (CH), 123.7 (C), 123.6 (C), 121.6 (CH), 114.0 (2CH), 111.0 (CH), 108.8 (CH), 72.2 (C), 66.7 (C), 60.5 (CH, q, *J* = 30 Hz), 55.3 (CH_3), 50.5 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.38; **HRMS (ESI)** m/z: 517.1346 $[M + Na]^+$, calcd for $C_{27}H_{21}O_4N_2F_3Na$; Found 517.1340.

(2'R,3R,4'S,5'S)-4'-(4-(benzyloxy)phenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4l):



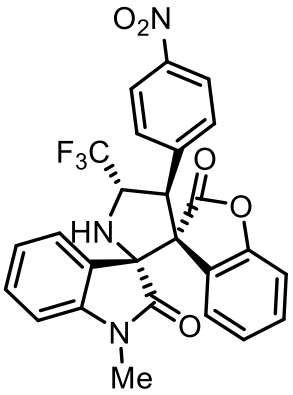
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4l** in 76% yield as a white solid with M. P. 229 - 231 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 12.732 min (minor), t_R = 14.981 min (major), **$[\alpha]_D^{25}$ = +5.790 (CH_2Cl_2, *c* = 0.6 g/100mL, CH_2Cl_2 for 61:39 *er*)**; **IR (neat) ν_{max}** 3371, 1801, 1724, 1612, 1141, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.16 (1H, d, *J* = 7.4 Hz), 7.39 – 7.28 (7H, m), 7.19 (1H, t, *J* = 7.8 Hz), 6.99 (2H, d, J = 8.7 Hz), 6.87 (2H, dd, *J* = 12.4, 7.8 Hz), 6.75 (3H, d, *J* = 8.7 Hz), 6.63 (1H, t, *J* = 7.6 Hz), 5.36 (1H, d, *J* = 9.9 Hz), 5.05 – 4.98 (2H, m), 4.92 (2H, s), 3.08 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.5 (C, C-*C*=O), 172.8 (C, N-*C*=O), 158.3 (C), 152.1 (C), 144.2 (C), 137.2 (C), 130.9 (CH), 130.8 (CH), 129.9 (CH), 128.9 (3CH), 128.4 (CH), 128.3 (3CH), 127.9 (CH), 126.7 (CF3, q, *J* = 279 Hz), 126.0 (CH), 125.0 (C), 124.4 (CH), 123.7 (C), 123.5 (C), 121.7 (CH), 114.8 (CH), 111.0 (CH), 108.8 (CH), 72.3 (C), 69.5 (CH_2), 66.7 (C), 60.5 (CH, q, *J* = 30 Hz), 50.5 (CH), 26.4 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.40; **HRMS (ESI)** m/z: 593.1659 $[M + Na]^+$, calcd for $C_{33}H_{25}O_4N_2F_3Na$; Found 593.1650.

(2'R,3R,4'S,5'S)-1''-methyl-4'-(2-nitrophenyl)-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4m):



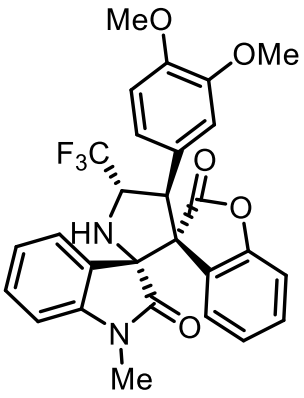
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4m** in 63% yield as a white solid with M. P. 234 - 236 °C; **$[\alpha]_D^{25}$ = 0.000 (CH_2Cl_2, *c* = 0.5 g/100mL)**; **IR (neat) ν_{max}** 2364, 1793, 1720, 1531,1126 and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 – 7.79 (1H, m), 7.67 (1H, dd, *J* = 8.0, 1.3 Hz), 7.37 – 7.27 (3H, m), 7.21 – 7.13 (3H, m), 6.84 – 6.79 (2H, m), 6.69 – 6.65 (2H, m), 6.50 (1H, d, *J* = 10.6 Hz), 4.86 – 4.78 (1H, m), 3.19 (3H, s), 2.95 (1H, d, *J* = 5.2 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 175.2 (C, C-*C*=O), 171.1 (C, N-*C*=O), 153.3 (C), 151.4 (C), 144.4 (C), 131.1 (CH), 130.9 (CH), 130.6 (CH), 129.1 (2CH), 126.9 (CH), 125.9 (C), 125.4 (CH), 125.2 (CF3, q, *J* = 279 Hz), 125.1 (CH), 123.7 (C), 123.5 (CH), 123.0 (C), 121.8 (CH), 111.8 (CH), 108.4 (CH), 71.7 (C), 65.5 (C), 62.2 (CH, q, *J* = 32 Hz), 43.3 (CH), 26.6 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.65; **HRMS (ESI)** m/z: 532.1091 $[M + Na]^+$, calcd for $C_{26}H_{18}O_5N_3F_3Na$; Found 532.1070.

(2'R,3R,4'S,5'S)-1''-methyl-4'-(4-nitrophenyl)-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4n):



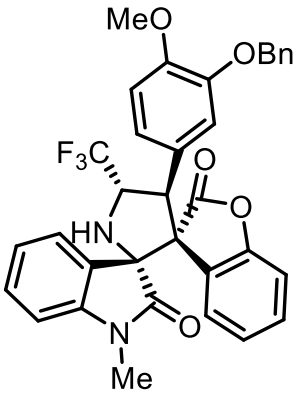
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4n** in 77% yield as a white solid with M. P. 232 - 234 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.550 min (major), t_R = 18.315 min (minor), **$[\alpha]_D^{25}$ = -66.305 (CH_2Cl_2, *c* = 0.7 g/100mL, CH_2Cl_2 for 76:24 *er*)**; **IR (neat) ν_{max}** 3375, 1801, 1724, 1612, 1350, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.19 (1H, d, *J* = 6.9 Hz), 7.98 (2H, d, *J* = 8.8 Hz), 7.42 (2H, d, *J* = 8.8 Hz), 7.37 (1H, td, *J* = 7.6, 1.2 Hz), 7.30 (1H, td, *J* = 7.7, 1.1 Hz), 7.20 (1H, td, *J* = 7.6, 1.1 Hz), 6.91 (1H, d, *J* = 7.8 Hz), 6.86 (1H, dd, *J* = 7.9, 0.6 Hz), 6.72 (1H, d, *J* = 6.8 Hz), 6.64 (1H, td, *J* = 7.5, 0.6 Hz), 5.54 (1H, d, *J* = 10.1 Hz), 5.28 – 5.17 (2H, m), 3.10 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.2 (C, C-*C*=O), 172.3 (C, N-*C*=O), 152.1 (C), 147.6 (C), 144.3 (C), 140.9 (C), 131.2 (CH), 131.1 (CH), 130.3 (2CH), 127.9 (CH), 126.2 (CH), 124.6 (CH), 123.7 (CF3, q, *J* = 279 Hz), 123.7 (2CH), 123.0 (C), 122.9 (C), 121.7 (CH), 111.2 (CH), 108.9 (CH), 72.6 (C), 66.6 (C), 60.3 (CH, q, *J* = 30 Hz), 50.6 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.61; **HRMS (ESI)** m/z: 532.1091 $[M + Na]^+$, calcd for $C_{26}H_{18}O_5N_3F_3Na$; Found 532.1078.

(2'R,3R,4'S,5'S)-4'-(3,4-dimethoxyphenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4o):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4o** in 83% yield as a white solid with M. P. 236 - 238 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 15.287 min (minor), t_R = 17.907 min (major), **$[\alpha]_D^{25}$ = +9.441 (CH_2Cl_2, *c* = 0.6 g/100mL, CH_2Cl_2 for 53:47 *er*)**; **IR (neat) ν_{max}** 1801, 1720, 1519, 1465, 1265, 1141, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.21 (1H, d, *J* = 7.4 Hz), 7.39 (1H, t, *J* = 7.5 Hz), 7.32 (1H, t, *J* = 7.7 Hz), 7.20 (1H, t, *J* = 7.6 Hz), 6.89 (2H, t, *J* = 8.0 Hz), 6.80 (1H, d, *J* = 7.4 Hz), 6.71 (1H, d, *J* = 8.4 Hz), 6.65 (1H, t, *J* = 7.5 Hz), 6.60 (1H, dd, *J* = 8.4, 1.7 Hz), 6.48 (1H, d, *J* = 1.7 Hz), 5.34 (1H, d, *J* = 10.2 Hz), 5.05 – 4.96 (2H, m), 3.61 (3H, s), 3.74 (3H, s), 3.09 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.5 (C, C-*C*=O), 172.7 (C, N-*C*=O), 152.2 (C), 148.7 (C, d, *J* = 3.7 Hz), 148.3 (C, d, *J* = 3.9 Hz), 144.2 (C), 130.8 (2CH, d, *J* = 9.6 Hz), 128.0 (CH), 126.6 (CF3, q, *J* = 279 Hz), 126.2 (CH), 125.0 (C, d, *J* = 3.3 Hz), 124.3 (CH), 123.8 (C), 123.6 (C), 121.6 (2CH), 111.8 (CH, d, *J* = 8 Hz), 111.5 (CH, d, *J* = 5.9 Hz), 111.2 (CH), 108.8 (CH), 72.0 (C), 66.7 (C), 60.6 (CH, q, *J* = 30 Hz), 55.7 (CH_3, d, *J* = 31 Hz), 55.6 (CH_3, d, *J* = 29 Hz), 50.9 (CH), 26.4 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.45; **HRMS (ESI)** m/z: 547.1451 $[M + Na]^+$, calcd for $C_{28}H_{23}O_5N_2F_3Na$; Found 547.1444.

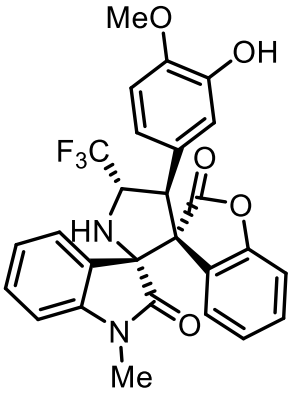
(2'R,3R,4'S,5'S)-4'-(3-(benzyloxy)-4-methoxyphenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4p):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4p** in 79% yield as a white solid with M. P. 243 - 245 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IA column (hexane/EtOAc = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 11.512 min (minor), t_R = 26.732 min (major), **$[\alpha]_D^{25}$ = -44.977 (CH_2Cl_2, *c* = 0.5 g/100mL, CH_2Cl_2 for 76:24 *er*)**; **IR (neat) ν_{max}** 3325, 1801, 1720, 1161, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.15 (1H, d, *J* = 7.4 Hz), 7.36 – 7.25 (7H, m), 7.13 (1H, t, *J* = 7.3 Hz), 6.83 (2H, d, *J* = 7.9 Hz), 6.74 (1H, d, *J* = 7.5 Hz), 6.68 (1H, d, *J* = 8.4 Hz), 6.61 – 6.55 (3H, m), 5.27 (1H, d, *J* = 10.8 Hz), 5.00 (1H, d, *J* = 8.5 Hz), 4.93 – 4.83 (1H, m), 4.75 (1H, d, *J* = 11.6 Hz), 4.52 (1H, d, *J* = 11.6 Hz), 3.56 (3H, s), 3.03 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.5 (C, C-*C*=O), 172.6 (C, N-*C*=O), 152.3 (C, d, *J* = 1 Hz), 149.2 (C, d, *J* = 5 Hz), 147.4 (C, d, *J* = 4 Hz), 144.3 (C), 137.2 (C, d, *J* = 3 Hz), 130.8 (CH, d, *J* = 6 Hz), 128.9 (2CH), 128.4 (CH), 128.2 (2CH, d, *J* = 4 Hz), 128.1 (CH), 126.7 (CF3, q, *J* = 280 Hz), 126.2 (CH), 125.0 (C, d, *J* = 4 Hz), 124.3 (CH), 123.9 (C, d, *J* = 1 Hz), 123.6 (C, d, *J* = 2 Hz), 122.2 (CH), 121.6 (CH), 113.9 (CH, d, *J* = 13 Hz), 111.9 (CH, d, *J* = 8 Hz), 111.2 (CH), 108.8 (CH), 72.0 (C,

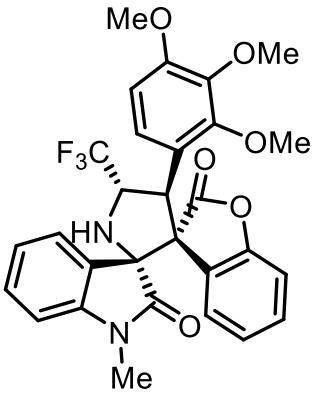
d, *J* = 2 Hz), 70.7 (CH_2), 70.6 (C), 66.7 (C), 60.6 (CH, q, *J* = 30 Hz), 55.7 (CH_3, d, *J* = 3 Hz), 50.9 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-*D*$_6$)** δ -70.45; **HRMS (ESI)** m/z: 623.1764 $[M + Na]^+$, calcd for $C_{34}H_{27}O_5N_2F_3Na$; Found 623.1761.

(2'R,3R,4'S,5'S)-4'-(3-hydroxy-4-methoxyphenyl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4q):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4q** in 74% yield as a white solid with M. P. 217 - 219 °C; **$[\alpha]_D^{25}$ = -14.419 (CH_2Cl_2, *c* = 0.8 g/100mL)**; **IR (neat) ν_{max}** 3325, 1797, 1712, 1130, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-*D*$_6$)** δ 8.83 (1H, s), 8.08 (1H, d, *J* = 7 Hz), 7.29 (1H, td, *J* = 7.4, 0.8 Hz), 7.23 (1H, td, *J* = 7.7, 1.1 Hz), 7.12 (1H, td, *J* = 7.6, 0.9 Hz), 6.81 (2H, t, *J* = 7.1 Hz), 6.67 (1H, d, *J* = 7.1 Hz), 6.59 – 6.55 (2H, m), 6.40 – 6.37 (2H, m), 5.20 (1H, d, *J* = 10.8 Hz), 4.92 (1H, d, *J* = 8.8 Hz), 4.87 – 4.77 (1H, m), 3.55 (3H, s), 3.02 (3H, s); **^{13}C NMR (100 MHz, DMSO-*D*$_6$, DEPT-135)** δ 175.4 (C, C-*C*=O), 172.8 (C, N-*C*=O), 152.2 (C), 147.6 (C), 146.2 (C), 144.2 (C), 130.8 (CH), 130.7 (CH), 127.9 (CH), 126.7 (CF3, q, *J* = 279 Hz), 125.9 (CH), 125.2 (C), 124.3 (CH), 123.9 (C), 123.6 (C), 121.6 (CH), 119.6 (CH), 116.0 (CH), 111.9 (CH), 111.0 (CH), 108.8 (CH), 72.3 (C), 66.7 (C), 60.6 (CH, q, *J* = 30 Hz), 55.7 (CH_3), 50.5 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-*D*$_6$)** δ -70.32; **HRMS (ESI)** m/z: 533.1295 $[M + Na]^+$, calcd for $C_{27}H_{21}O_5N_2F_3Na$; Found 533.1294.

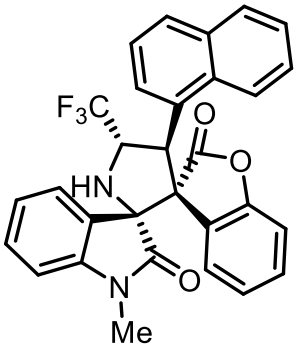
(2'R,3R,4'S,5'S)-1''-methyl-5'-(trifluoromethyl)-4'-(2,3,4-trimethoxyphenyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4r):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4r** in 93% yield as a white solid with M. P. 268 - 270 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 15.412 min (minor), t_R = 17.203 min (major), **$[\alpha]_D^{25}$ = +300.461 (CH_2Cl_2, *c* = 1.1 g/100mL, CH_2Cl_2 for 99:1 *er*)**; **IR (neat) ν_{max}** 3325, 1797, 1720, 1107, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-*D*$_6$)** δ 8.16 (1H, d, *J* = 6.9 Hz), 7.33 (2H, quin, *J* = 6.2 Hz), 7.20 (1H, t, *J* = 7.6 Hz), 6.89 (2H, d, *J* = 7.7 Hz), 6.85 (1H, d, *J* = 7.4 Hz), 6.65 (2H, dd, *J* = 16.8, 7.6 Hz), 6.41 (1H, d, *J* = 8.9 Hz), 5.90 (1H, d, *J* = 10.8 Hz), 4.97 (1H, d *J* = 8.8 Hz), 4.88 – 4.82 (1H, m), 3.70 (3H, s), 3.64 (3H, s), 3.61 (3H, s), 3.10 (3H, s); **^{13}C NMR (100 MHz, DMSO-*D*$_6$, DEPT-135)** δ 175.5 (C, C-*C*=O), 172.0 (C, N-*C*=O), 153.1 (C), 152.6 (CH), 152.4 (C, d, *J* = 2 Hz), 144.5 (C), 141.3 (C, d, *J* = 5 Hz), 130.8 (CH), 130.6 (CH), 128.1 (CH), 126.7 (CF3, q, *J* = 279 Hz), 126.2 (CH), 128.1 (CH), 126.2 (CH), 124.2 (C, d, *J* = 2 Hz), 123.9 (CH), 123.7 (C, d, *J* = 3 Hz), 121.5 (CH), 118.6 (C, d, *J* = 3 Hz), 110.9 (CH), 108.7 (CH), 107.0 (CH, d, *J* = 3 Hz), 72.1 (C), 61.6 (CH, q, *J* = 30 Hz), 61.3 (CH_3), 60.6 (CH_3), 55.6 (CH_3, d, *J* = 3 Hz), 43.9 (CH),

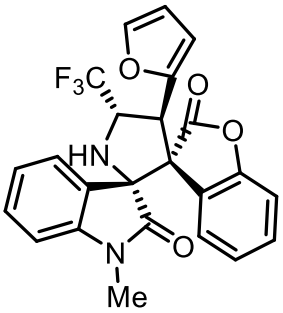
26.5 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.08; **HRMS (ESI)** m/z: 577.1557 $[M + Na]^+$, calcd for $C_{29}H_{25}O_6N_2F_3Na$; Found 577.1559.

(2'R,3R,4'S,5'S)-1''-methyl-4'-(naphthalen-1-yl)-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4s):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4s** in 81% yield as a white solid with M. P. 280 - 282 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 92:8, flow rate 0.4 mL/min, λ = 254 nm), t_R = 14.504 min (minor), t_R = 15.828 min (major), **$[\alpha]_D^{25}$ = +16.000 (CH_2Cl_2, *c* = 0.1 g/100mL, CH_2Cl_2 for 76:24 *er*)**; **IR (neat) ν_{max}** 3329, 1793, 1712, 1145, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.34 (1H, d, *J* = 7.4 Hz), 8.27 (1H, d, *J* = 8.7 Hz), 7.79 (1H, d, *J* = 7.8 Hz), 7.64 (1H, d, *J* = 8.1 Hz), 7.35 (1H, t, *J* = 7.1 Hz), 7.45 (1H, d, *J* = 7.4 Hz), 7.40 (1H, t, *J* = 8.4 Hz), 7.29 – 7.22 (2H, m), 7.16 (1H, t, *J* = 7.7 Hz), 7.07 (1H, t, *J* = 7.8 Hz), 6.88 (1H, d, *J* = 7.7 Hz), 6.81 (1H, d, *J* = 7.3 Hz), 6.72 (2H, t, *J* = 8.4 Hz), 6.63 (1H, t, *J* = 7.4 Hz), 5.13 (1H, d, *J* = 8.6 Hz), 5.08 – 5.02 (1H, m), 3.11 (3H, s);**^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.8 (C, C-*C*=O), 172.5 (C, N-*C*=O), 152.5 (C), 144.4 (C), 133.8 (C), 132.2 (C), 130.9 (2CH, d, *J* = 3 Hz), 129.2 (CH), 128.9 (CH), 128.5 (2CH), 127.2 (CH), 127.1 (CH), 126.7 (CF3, q, *J* = 279 Hz), 126.3 (2CH), 124.9 (CH), 124.4 (CH), 123.7 (C), 123.5 (C), 123.0 (CH), 121.8 (CH), 111.2 (CH), 108.9 (CH), 72.3 (C), 65.9 (C), 62.0 (CH, q, *J* = 30 Hz), 43.9 (CH), 26.6 (CH_3);**^{19}F NMR (376MHz, DMSO-D_6)** δ -70.57; **HRMS (ESI)** m/z: 537.1396 $[M + Na]^+$, calcd for $C_{30}H_{21}O_3N_2F_3Na$; Found 537.1389.

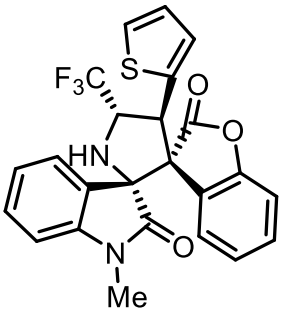
(2'R,3R,4'S,5'S)-4'-(furan-2-yl)-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4t):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4t** in 87% yield as a white solid with M. P. 241 - 244 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 44.518 min (major), t_R = 47.097 min (minor), **$[\alpha]_D^{25}$ = -88.250 (CH_2Cl_2, *c* = 0.8 g/100mL, CH_2Cl_2 for 72:28 *er*)**; **IR (neat) ν_{max}** 1801, 1716, 1614, 1139, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 – 7.65 (1H, m), 7.28 – 7.25 (2H, m), 7.17 (1H, td, *J* = 8.8, 3.8 Hz), 7.05 – 7.04 (1H, m), 6.85 – 6.79 (1H, m), 6.69 (1H, d, *J* = 7.8 Hz), 6.63 (2H, d, *J* = 4.3 Hz), 6.09 – 6.07 (2H, m), 5.61 (1H, d, *J* = 10.4 Hz), 4.93 – 4.84 (1H, m), 3.18 (3H, s), 2.91 – 2.88 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 175.7 (C, C-*C*=O), 171.9 (C, N-*C*=O), 152.8 (C), 147.2 (C), 144.2 (C), 142.6 (CH), 130.6 (CH), 130.3 (CH), 126.4 (CH), 125.3 (CF_3, q, *J* = 279 Hz), 125.1 (CH), 124.0 (C), 123.6 (CH), 123.4 (C), 121.9 (CH), 111.2 (CH), 110.2 (CH), 108.8 (CH), 108.3

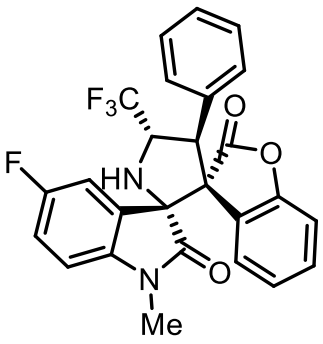
(CH), 71.7 (C), 64.5 (C), 60.9 (CH, q, *J* = 32 Hz), 45.1 (CH), 26.4 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.99; **HRMS (ESI)** m/z: 477.1033 $[M + Na]^+$, calcd for $C_{24}H_{17}O_4N_2F_3Na$; Found 477.1018.

(2'R,3R,4'S,5'S)-1''-methyl-4'-(thiophen-2-yl)-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4u):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4u** in 83% yield as a white solid with M. P. 237 - 241 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 11.905 min (major), t_R = 13.214 min (minor), **$[\alpha]_D^{25}$ = -127.529 (CH_2Cl_2, *c* = 0.9 g/100mL, CH_2Cl_2 for 86:14 *er*)**; **IR (neat) ν_{max}** 2922, 1801, 1716, 1141, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82 – 7.79 (1H, m), 7.35 (2H, dquin, *J* = 6.6, 1.4 Hz), 7.17 (1H, td, *J* = 7.7, 1.2 Hz), 7.01 (1H, dd, *J* = 5.0, 1.0 Hz), 6.88 – 6.87 (1H, m), 6.84 – 6.82 (1H, m), 6.78 – 6.73 (2H, m), 6.70 (1H, d, *J* = 7.8 Hz), 6.65 (1H, td, *J* = 7.6, 0.9 Hz), 5.91 (1H, d, *J* = 10.5 Hz), 4.69 – 4.61 (1H, m), 3.20 (3H, s), 2.87 (1H, d, *J* = 3.9 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.0 (C, C-*C*=O), 171.8 (C, N-*C*=O), 153.2 (C), 144.2 (C), 134.5 (C), 130.8 (CH), 130.6 (CH), 128.1 (CH), 126.8 (CH), 126.4 (CH), 125.9 (CH), 125.4 (CH), 125.3 (CF_3, q, *J* = 280 Hz), 123.9 (CH), 123.8 (C), 123.8 (C), 121.9 (CH), 111.6 (CH), 108.3 (CH), 71.2 (C), 65.7 (C), 63.9 (CH, q, *J* = 31 Hz), 47.0 (CH), 26.5 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.44; **HRMS (ESI)** m/z: 493.0804 $[M + Na]^+$, calcd for $C_{24}H_{17}O_3N_2F_3NaS$; Found 493.0791.

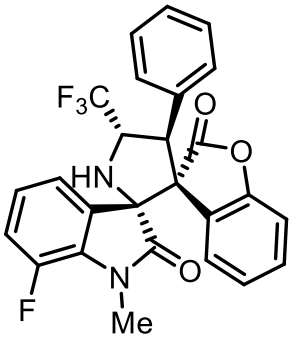
(2'R,3R,4'S,5'S)-5''-fluoro-1''-methyl-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4w):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4w** in 91% yield as a white solid with M. P. 250 - 252 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.763 min (major), t_R = 11.426 min (minor), **$[\alpha]_D^{25}$ = -98.881 (CH_2Cl_2, *c* = 1.3 g/100mL, CH_2Cl_2 for 93:7 *er*)**; **IR (neat) ν_{max}** 3336, 1793, 1720, 1168, and 763 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.10 (1H, d, *J* = 7.4 Hz), 7.32 (1H, t, *J* = 7.4 Hz), 7.25 (1H, t, *J* = 7.6 Hz), 7.05 – 6.98 (6H, m), 6.86 – 6.80 (2H, m), 6.49 (1H, dd, *J* = 9.1, 2.5 Hz), 5.31 (1H, d, *J* = 10.6 Hz), 5.12 (1H, d, *J* = 8.4 Hz), 5.07 – 4.99 (1H, m), 3.03 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.2 (C, C-*C*=O), 172.4 (C, N-*C*=O), 157.5 (C-F, d, *J* = 235 Hz), 152.2 (C), 140.5 (C), 132.9 (C), 131.0 (CH), 128.8 (2CH), 128.7 (2CH), 128.5 (CH), 127.9 (CH), 126.6 (CF3, q, *J* = 279 Hz), 125.1 (C), 124.4 (CH), 123.3 (C), 117.1 (CH, d, *J* = 24 Hz), 114.3 (CH, d, *J* = 26 Hz), 111.2 (CH), 109.6 (CH, d, *J* = 8 Hz), 72.5 (C), 66.7 (C), 60.2 (CH, q, *J* = 30 Hz),

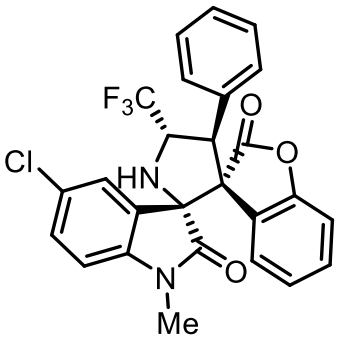
50.9 (CH), 26.7 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.54, -121.54; **HRMS (ESI)** m/z: 505.1146 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_4Na$; Found 505.1142.

(2'R,3R,4'S,5'S)-7''-fluoro-1''-methyl-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4x):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4x** in 96% yield as a white solid with M. P. 216 - 218 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 8.976 min (major), t_R = 9.736 min (minor), **$[\alpha]_D^{25}$ = -147.960 (CH_2Cl_2, *c* = 0.8 g/100mL, CH_2Cl_2 for 95:5 *er*)**; **IR (neat) ν_{max}** 3325, 1793, 1708, 1083, and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 (1H, d, *J* = 6.9 Hz), 7.31 (1H, t, *J* = 7.5 Hz), 7.24 (1H, td, *J* = 7.7, 1.0 Hz), 7.11 – 7.04 (5H, m), 6.92 – 6.87 (1H, m), 6.73 (1H, d, *J* = 7.8 Hz), 6.60 – 6.55 (2H, m), 5.57 (1H, d, *J* = 10.7 Hz), 4.94 – 4.85 (1H, m), 3.43 (3H, d, *J* = 2.9 Hz), 2.85 (1H, d, *J* = 5.8 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 175.9 (C, C-*C*=O), 171.9 (C, N-*C*=O), 152.8 (C), 147.3 (C-F, d, *J* = 242 Hz), 131.8 (C), 130.9 (C, d, *J* = 9 Hz), 130.5 (CH), 128.4 (2CH), 128.3 (2CH), 128.2 (CH), 126.9 (C, d, *J* = 3 Hz), 126.6 (CH), 125.4 (CF3, q, *J* = 279 Hz), 123.5 (CH), 123.4 (C), 122.2 (CH, d, *J* = 6 Hz), 121.3 (CH, d, *J* = 3 Hz), 118.5 (CH, d, *J* = 19 Hz), 111.5 (CH), 71.5 (C, d, *J* = 2 Hz), 66.3 (C), 60.7 (CH, q, *J* = 31 Hz), 50.6 (CH_2), 29.1 (CH_3, d, *J* = 6 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.51, -135.49; **HRMS (ESI)** m/z: 505.1146 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_4Na$; Found 505.1147.

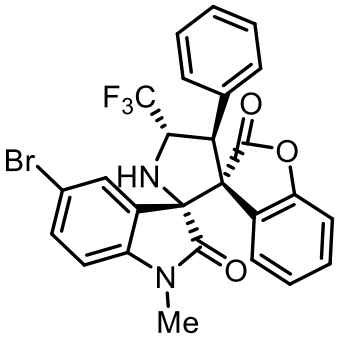
(2'R,3R,4'S,5'S)-5''-chloro-1''-methyl-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4y):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4y** in 93% yield as a white solid with M. P. 251 - 253 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.537 min (major), t_R = 10.854 min (minor), **$[\alpha]_D^{25}$ = -93.400 (CH_2Cl_2, *c* = 0.5 g/100mL, CH_2Cl_2 for 95:5 *er*)**; **IR (neat) ν_{max}** 3356, 1797, 1720, 1138, and 752 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.10 (1H, d, *J* = 7.8 Hz), 7.32 (1H, td, *J* = 7.6, 0.9 Hz), 7.25 (1H, td, *J* = 7.9, 1.1 Hz), 7.21 (1H, dd, *J* = 8.4, 2.2 Hz), 7.07 – 7.01 (5H, m), 6.87 (1H, d, *J* = 8.4 Hz), 6.83 (1H, dd, *J* = 7.8, 0.6 Hz), 6.70 (1H, d, *J* = 2.1 Hz), 5.29 (1H, d, *J* = 10.7 Hz), 5.14 (1H, d, *J* = 8.4 Hz), 5.09 – 4.99 (1H, m), 3.03 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 175.1 (C, C-*C*=O), 172.4 (C, N-*C*=O), 152.2 (C), 143.1 (C), 132.9 (C), 131.0 (CH), 130.6 (CH), 128.8 (2CH), 128.7 (2CH), 128.5 (CH), 127.9 (CH), 126.7 (CF3, q, *J* = 279 Hz), 126.6 (CH), 125.7 (C), 125.3 (C), 124.3 (CH), 123.2 (C), 111.2 (CH), 110.2 (CH), 72.4 (C), 66.7

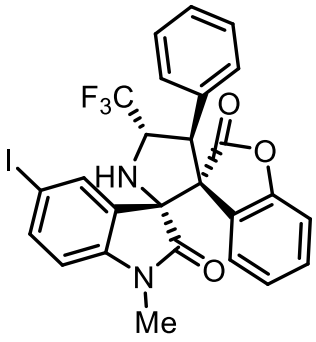
(C), 60.2 (CH, q, *J* = 30 Hz), 50.9 (CH), 26.6 (CH_3); **^{19}F NMR (376MHz, DMSO-D_6)** δ -70.62; **HRMS (ESI)** m/z: 521.0850 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_3ClNa$; Found 521.0834.

(2'R,3R,4'S,5'S)-5''-bromo-1''-methyl-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4z):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4z** in 91% yield as a white solid with M. P. 241 - 243 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.763 min (major), t_R = 11.008 min (minor), **$[\alpha]_D^{25}$ = -68.250 (CH_2Cl_2, *c* = 0.4 g/100mL, CH_2Cl_2 for 95:5 *er*)**; **IR (neat) ν_{max}** 2924, 2854, 1805, 1732, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 (1H, d, *J* = 6.8 Hz), 7.37 (1H, td, *J* = 7.5, 0.5 Hz), 7.30 (2H, td, *J* = 7.8, 1.6 Hz), 7.13 – 7.05 (5H, m), 6.88 (1H, d, *J* = 1.9 Hz), 6.77 (1H, d, *J* = 7.9 Hz), 6.58 (1H, d, *J* = 8.3 Hz), 5.53 (1H, d, *J* = 10.7 Hz), 4.93 – 4.84 (1H, m), 3.20 (3H, s), 2.84 (1H, d, *J* = 4.8 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 175.7 (C, C-*C*=O), 171.9 (C, N-*C*=O), 152.8 (C), 143.1 (C), 133.2 (C), 131.8 (C), 130.7 (CH), 128.9 (CH), 128.4 (2CH), 128.4 (2CH), 128.2 (CH), 126.4 (CH), 126.0 (C), 125.4 (CF3, q, *J* = 280 Hz), 123.7 (CH), 123.3 (C), 114.4 (C), 111.7 (CH), 109.6 (CH), 71.5 (C), 66.2 (C), 60.8 (CH, q, *J* = 31 Hz), 50.5 (CH), 26.6 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.61; **HRMS (ESI)** m/z: 565.0345 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_3BrNa$; Found 565.0326.

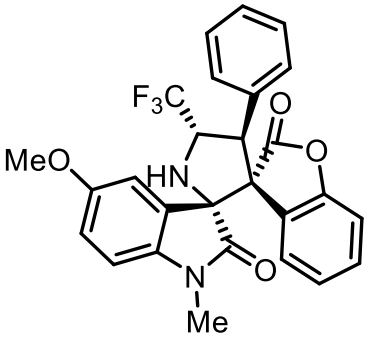
(2'R,3R,4'S,5'S)-5''-iodo-1''-methyl-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4a'):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4a'** in 85% yield as a white solid with M. P. 254 - 256 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.892 min (major), t_R = 11.098 min (minor), **$[\alpha]_D^{25}$ = -13.491 (CH_2Cl_2, *c* = 1.1 g/100mL, CH_2Cl_2 for 96:4 *er*)**; **IR (neat) ν_{max}** 3356, 1801, 1728, 1138, and 756 cm^{-1}; **^{1}H NMR (400 MHz, DMSO-D_6)** δ 8.09 (1H, dd, *J* = 7.6, 1.0 Hz), 7.46 (1H, dd, *J* = 8.2, 1.7 Hz), 7.34 – 7.24 (2H, m), 7.07 – 7.02 (5H, m), 6.97 (1H, d, *J* = 1.7 Hz), 6.81 (1H, dd, *J* = 7.8, 0.9 Hz), 6.69 (1H, d, *J* = 8.2 Hz), 5.26 (1H, d, *J* = 10.7 Hz), 5.11 (1H, d, *J* = 8.4 Hz), 5.08 – 4.98 (1H, m), 3.01 (3H, s); **^{13}C NMR (100 MHz, DMSO-D_6, DEPT-135)** δ 174.9 (C, C-*C*=O), 172.4 (C, N-*C*=O), 152.2 (C), 143.9 (C), 139.1 (C), 134.9 (CH), 133.0 (C), 130.9 (CH), 128.8 (2CH), 128.7 (2CH), 128.5 (CH), 128.0 (CH), 126.6 (CF3, q, *J* = 287 Hz), 125.7 (C), 124.2 (CH), 123.3 (C), 111.2 (2CH, d, *J* = 3 Hz), 84.4 (C), 72.4 (C), 66.7 (C), 60.3 (CH, q, *J* = 30 Hz), 50.8 (CH), 26.5 (CH_3);

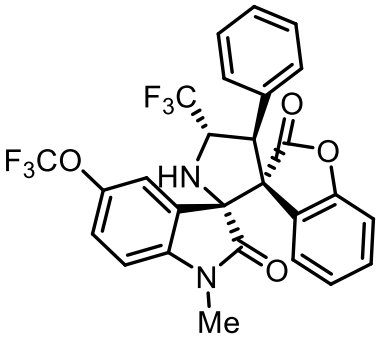
^{19}F NMR (376MHz, DMSO-D_6) δ -70.66; **HRMS (ESI)** m/z: 613.0206 $[M + Na]^+$, calcd for $C_{26}H_{18}O_3N_2F_3INa$; Found 613.0194.

(2'R,3R,4'S,5'S)-5''-methoxy-1''-methyl-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4b'):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4b'** in 96% yield as a white solid with M. P. 236 - 238 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 12.904 min (major), t_R = 15.651 min (minor), **$[\alpha]_D^{25}$ = -83.825 (CH_2Cl_2, *c* = 0.8 g/100mL, CH_2Cl_2 for 98:2 *er*)**; **IR (neat) ν_{max}** 3020, 1801, 1720, 1215, and 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (1H, dd, *J* = 7.6, 1.0 Hz), 7.34 (1H, td, *J* = 7.6, 1.0 Hz), 7.28 – 7.26 (1H, m), 7.12 – 7.06 (5H, m), 6.75 (1H, d, *J* = 7.9 Hz), 6.70 (1H, dd, *J* = 8.5, 2.5 Hz), 6.60 (1H, d, *J* = 8.5 Hz), 6.37 (1H, d, *J* = 2.5 Hz), 5.62 (1H, d, *J* = 10.6 Hz), 4.90 (1H, t, *J* = 7.1 Hz), 3.45 (3H, s), 3.19 (3H, s), 2.85 (1H, s); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 175.9 (C, C-*C*=O), 171.9 (C, N-*C*=O), 155.2 (C), 152.9 (C), 137.5 (C), 132.0 (CH), 130.4 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 126.6 (CH), 125.5 (CF3, q, *J* = 280 Hz), 125.1 (C), 123.8 (C), 123.4 (CH), 115.7 (CH), 112.4 (C), 112.4 (CH), 111.6 (CH), 108.7 (CH), 108.7 (C), 71.7 (C), 66.2 (C), 60.8 (CH, q, *J* = 31 Hz), 55.7 (CH_3), 50.6 (CH), 26.5 (CH_3, d, *J* = 2 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.43; **HRMS (ESI)** m/z: 517.1346 $[M + Na]^+$, calcd for $C_{27}H_{21}O_4N_2F_3Na$; Found 517.1332.

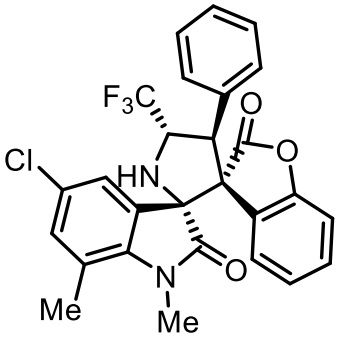
(2'R,3R,4'S,5'S)-1''-methyl-4'-phenyl-5''-(trifluoromethoxy)-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4c'):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4c'** in 94% yield as a white solid with M. P. 248 - 250 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 8.334 min (major), t_R = 8.964 min (minor), **$[\alpha]_D^{25}$ = -157.792 (CH_2Cl_2, *c* = 0.7 g/100mL, CH_2Cl_2 for 98:2 *er*)**; **IR (neat) ν_{max}** 1789, 1728, 1462, 1219, 1134, and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (1H, dd, *J* = 7.6, 1.0 Hz), 7.37 (1H, td, *J* = 7.6, 0.9 Hz), 7.29 (1H, td, *J* = 7.9, 1.4 Hz), 7.16 – 7.05 (6H, m), 6.77 (1H, d, *J* = 7.9 Hz), 6.72 – 6.70 (2H, m), 5.56 (1H, d, *J* = 10.7 Hz), 4.96 – 4.88 (1H, m), 3.24 (3H, s), 2.89 (1H, br s); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.1 (C, C-*C*=O), 171.9 (C, N-*C*=O), 152.8 (C), 143.8 (C), 142.7 (C), 131.7 (C), 130.8 (CH), 128.4 (4CH), 128.3 (CH), 126.3 (CH), 125.6 (C), 125.4 (CF3, q, *J* = 279 Hz), 123.8 (CH), 123.7 (CH), 123.1 (C), 120.2 (OCF_3, d, *J* = 255 Hz), 119.7 (CH), 111.6 (CH), 108.6 (CH), 71.5 (C), 66.2 (C), 60.8 (CH, q,

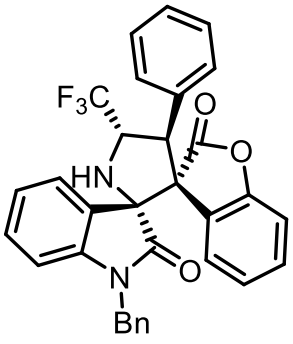
J = 31 Hz), 50.5 (CH), 26.6 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -58.68, -71.50; **HRMS (ESI)** m/z: 571.1063 $[M + Na]^+$, calcd for $C_{27}H_{18}O_4N_2F_6Na$; Found 571.1058.

(2'R,3R,4'S,5'S)-5''-chloro-1'',7''-dimethyl-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4d'):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4d'** in 98% yield as a white solid with M. P. 250 - 252 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 9.783 min (major), t_R = 11.759 min (minor), **$[\alpha]_D^{25}$ = -92.698 (CH_2Cl_2, *c* = 1.0 g/100mL, CH_2Cl_2 for 97:3 *er*)**; **IR (neat) ν_{max}** 3383, 1786, 1739, 1462, 1087 and 702 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.78 (1H, dd, *J* = 7.6, 1.0 Hz), 7.34 (1H, td, *J* = 7.5, 1.0 Hz), 7.27 (1H, td, *J* = 7.9, 1.4 Hz), 7.13 – 7.04 (5H, m), 6.88 (1H, d, *J* = 1.6 Hz), 6.75 (1H, d, *J* = 7.9 Hz), 6.65 (1H, d, *J* = 2.1 Hz), 5.54 (1H, d, *J* = 10.7 Hz), 4.92 – 4.84 (1H,m), 3.48 (3H, s), 2.80 (1H, d, *J* = 4.2 Hz), 2.45 (3H, s); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.8 (C, C-*C*=O), 171.9 (C, N-*C*=O), 152.8 (C), 140.4 (C), 133.6 (CH), 131.8 (C), 130.6 (CH), 128.4 (2CH), 128.3 (2CH), 128.2 (CH), 126.7 (C), 126.6 (CH), 126.4 (C), 125.4 (CF3, q, *J* = 279 Hz), 123.8 (CH), 123.6 (CH), 123.2 (C), 121.2 (C),111.6 (CH), 71.0 (C), 66.4 (C), 60.7 (CH, q, *J* = 31 Hz), 50.6 (CH), 29.9 (CH_3), 18.9 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.52; **HRMS (ESI)** m/z: 535.1007 $[M + Na]^+$, calcd for $C_{27}H_{20}O_3N_2F_3ClNa$; Found 535.0993.

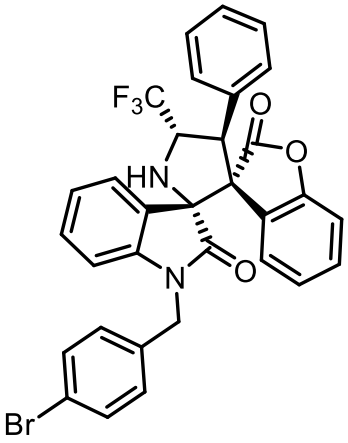
(2'R,3R,4'S,5'S)-1''-benzyl-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4f'):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4f'** in 83% yield as a white solid with M. P. 136 - 138 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 80:20, flow rate 0.5 mL/min, λ = 254 nm), t_R = 8.786 min (major), t_R = 9.376 min (minor), **$[\alpha]_D^{25}$ = -127.093 (CH_2Cl_2, *c* = 0.9 g/100mL, CH_2Cl_2 for 88:12 *er*)**; **IR (neat) ν_{max}** 3341, 1801, 1724, 1130, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82 (1H, d, *J* = 7.4 Hz), 7.41 – 7.06 (6H, m), 7.23 (1H, td, *J* = 7.8, 1.0 Hz), 7.14 – 7.06 (5H, m), 7.03 (1H, td, *J* = 7.7, 1.0 Hz), 6.75 (2H, q, *J* = 9.0 Hz), 6.60 (1H, t, *J* = 7.6 Hz), 6.56 (1H, d, *J* = 6.6 Hz), 5.69 (1H, d, *J* = 10.7 Hz), 5.25 (1H, d, *J* = 15.6 Hz), 4.97 – 4.89 (1H, m), 4.60 (1H, d, *J* = 15.6 Hz), 2.92 (1H, s); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.2 (C, C-*C*=O), 172.2 (C, N-*C*=O), 152.9 (C), 143.7 (C), 135.4 (C), 131.9 (CH), 130.4 (CH), 130.4 (CH), 128.8 (2CH), 128.4 (2CH), 128.3 (2CH), 128.1 (CH), 127.7 (2CH), 127.7 (CH), 126.6 (CH), 125.6 (CF3, q, *J* = 279 Hz), 125.5 (CH), 124.1 (C), 123.7 (C), 123.5 (CH), 121.9 (CH), 111.5 (CH),

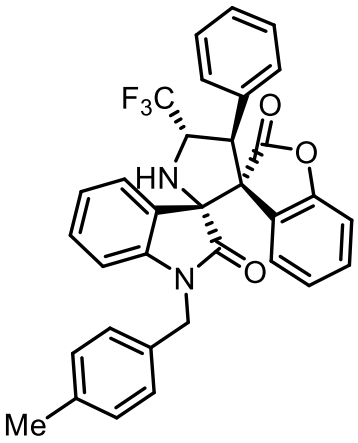
109.5 (CH), 71.4 (C), 66.2 (C), 60.7 (CH, q, *J* = 31 Hz), 51.0 (CH), 44.7 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.51; **HRMS (ESI)** m/z: 563.1553 $[M + Na]^+$, calcd for $C_{32}H_{23}O_3N_2F_3Na$; Found 563.1541.

(2'R,3R,4'S,5'S)-1''-(4-bromobenzyl)-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4g'):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4g'** in 86% yield as a white solid with M. P. 147 - 149 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 16.552 min (major), t_R = 18.943 min (minor), **$[\alpha]_D^{25}$ = -123.699 (CH_2Cl_2, *c* = 0.7 g/100mL, CH_2Cl_2 for 90:10 *er*)**; **IR (neat) ν_{max}** 3371, 1801, 1720, 1161, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 (1H, d, *J* = 7.4 Hz), 7.48 (2H, d, *J* = 8.4 Hz), 7.34 – 7.23 (4H, m), 7.12 – 7.02 (6H, m), 6.77 (1H, d, *J* = 7.6 Hz), 6.73 (1H, d, *J* = 7.9 Hz), 6.62 (1H, t, *J* = 7.7 Hz), 6.51 (1H, d, *J* = 7.8 Hz), 5.66 (1H, d, *J* = 10.7 Hz), 5.22 (1H, d, *J* = 15.7 Hz), 4.97 – 4.88 (1H, m), 4.50 (1H, d, *J* = 15.7 Hz), 2.91 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.2 (C, C-*C*=O), 172.2 (C, N-*C*=O), 152.8 (C), 143.4 (C), 134.5 (C), 131.9 (2CH), 131.9 (C), 130.5 (2CH, d, *J* = 5 Hz), 129.5 (2CH), 128.4 (2CH), 128.3 (2CH), 128.2 (CH), 126.5 (CH), 125.6 (CH), 125.5 (CF3, q, *J* = 279 Hz), 124.0 (C), 123.6 (C), 123.6 (CH), 122.1 (CH), 121.7 (C), 111.6 (CH), 109.2 (CH), 71.4 (C), 66.2 (C), 60.7 (CH, q, *J* = 30 Hz), 51.0 (CH), 44.1 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.57; **HRMS (ESI)** m/z: 641.0658 $[M + Na]^+$, calcd for $C_{32}H_{22}O_3N_2F_3BrNa$; Found 641.0638.

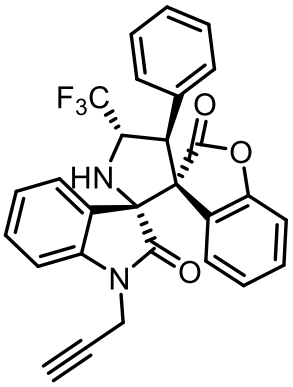
(2'R,3R,4'S,5'S)-1''-(4-methylbenzyl)-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4h'):



Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4h'** in 84% yield as a white solid with M. P. 138 - 140 °C; The enantiomeric ratio *(er)* was determined by chiral stationary phase HPLC using a DAICEL IC column (hexane/EtOAc = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 18.136 min (major), t_R = 23.715 min (minor), **$[\alpha]_D^{25}$ = -111.292 (CH_2Cl_2, *c* = 0.9 g/100mL, CH_2Cl_2 for 86:14 *er*)**; **IR (neat) ν_{max}** 2924, 1801, 1728, 1215, and 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 (1H, dd, *J* = 7.5, 0.6 Hz), 7.50 – 7.46 (3H, m), 7.40 (1H, td, *J* = 7.7, 1.2 Hz), 7.33 (2H, d, *J* = 7.9 Hz), 7.28 – 7.22 (5H, m), 7.18 (1H, td, *J* = 7.7, 1.0 Hz), 6.92 (1H, d, *J* = 7.4 Hz), 6.88 (1H, d, *J* = 7.7 Hz), 6.75 (2H, d, *J* = 8.8 Hz), 5.87 (1H, d, *J* = 10.7 Hz), 5.37 (1H, d, *J* = 15.4 Hz), 5.15 – 5.06 (1H, m), 4.72 (1H, d, *J* = 15.4 Hz), 3.10 (1H, d, *J* = 3.8 Hz), 2.47 (3H, s); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.1 (C, C-*C*=O), 172.1 (C, N-*C*=O), 152.8 (C), 143.7 (C), 137.4 (C), 132.4 (C), 132.0 (C), 130.4 (CH), 130.4 (CH), 129.5 (2CH), 128.5

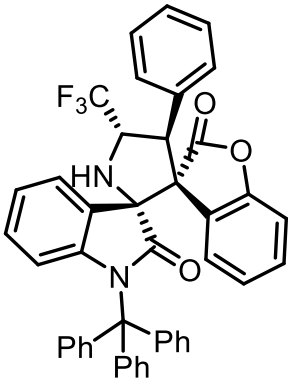
(2CH), 128.1 (CH), 127.8 (2CH), 126.6 (CH), 125.6 (CF3, q, *J* = 279 Hz), 125.4 (C), 123.7 (C), 123.5 (CH), 121.9 (CH), 111.5 (CH), 109.5 (CH), 71.4 (C), 66.2 (C), 60.7 (CH, q, *J* = 31 Hz), 51.0 (CH), 44.4 (CH_2), 21.1 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.51; **HRMS (ESI)** m/z: 577.1709 $[M + Na]^+$, calcd for $C_{33}H_{25}O_3N_2F_3Na$; Found 577.1692.

(2'R,3R,4'S,5'S)-4'-phenyl-1''-(prop-2-yn-1-yl)-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4i'):



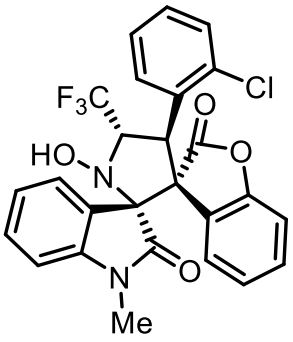
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4i'** in 63% yield as a white solid with M. P. 212 - 214 °C; **$[\alpha]_D^{25}$ = -129.584 (CH_2Cl_2, *c* = 0.8 g/100mL)**; **IR (neat) ν_{max}** 3302, 1797, 1728, 1130, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 (1H, dd, *J* = 7.5, 1.0 Hz), 7.32 (1H, td, *J* = 7.6, 1.0 Hz), 7.24 (1H, dd, *J* = 7.8 Hz), 7.20 (1H, td, *J* = 7.7, 1.2 Hz), 7.13 – 7.03 (5H, m), 6.94 (1H, d, *J* = 7.7 Hz), 6.81 (1H, dd, *J* = 7.6, 0.7 Hz), 6.70 (2H, qd, *J* = 7.8, 0.8 Hz), 5.55 (1H, d, *J* = 10.7 Hz), 4.92 – 4.87 (1H, m), 4.55 (2H, qd, *J* = 18.4, 2.5 Hz), 2.87 (1H, d, *J* = 4.4 Hz), 2.25 (1H, t, *J* = 2.5 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 175.2 (C, C-*C*=O), 171.9 (C, N-*C*=O), 152.9 (C), 142.2 (C), 131.9 (C), 130.4 (2CH), 130.4 (C), 128.4 (2CH), 128.3 (2CH), 128.1 (CH), 126.6 (2CH), 125.3 (CF3, q, *J* = 279 Hz), 125.1 (CH), 123.6 (C), 123.5 (CH), 122.2 (CH), 111.5 (CH), 109.4 (CH), 72.7 (C), 71.4 (C), 66.3 (C), 60.7 (CH, q, *J* = 31 Hz), 50.7 (CH), 29.6 (CH_2); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.58; **HRMS (ESI)** m/z: 511.1240 $[M + Na]^+$, calcd for $C_{28}H_{19}O_3N_2F_3Na$; Found 511.1235.

(2'R,3R,4'S,5'S)-4'-phenyl-5'-(trifluoromethyl)-1''-trityl-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (4j'):



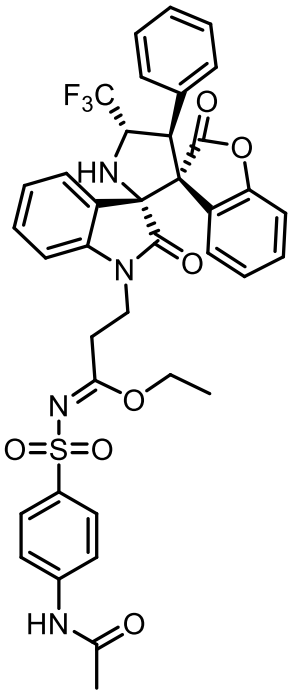
Prepared by following general procedure **C** purified by column chromatography using hexane - Ethyl acetate and isolated product **4j'** in 43% yield as a white solid with M. P. 182 - 184 °C; **$[\alpha]_D^{25}$ = -71.300 (CH_2Cl_2, *c* = 1.0 g/100mL)**; **IR (neat) ν_{max}** 2924, 1805, 1739, 1141, and 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 – 7.73 (1H, m), 7.51 (6H, d, *J* = 7.6 Hz), 7.31 – 7.27 (8H, m), 7.24 – 7.20 (3H, m), 7.13 – 7.07 (5H, m), 6.84 – 6.79 (2H, m), 6.73 (1H, td, *J* = 8.7, 1.2 Hz), 6.51 (1H, t, *J* = 7.6 Hz), 6.26 (1H, d, *J* = 8.2 Hz), 5.36 (1H, d, *J* = 10.7 Hz), 4.92 – 4.86 (1H, m), 2.72 (1H, br s); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 177.8 (C, C-*C*=O), 172.8 (C, N-*C*=O), 153.0 (C), 153.0 (C),144.1 (C), 144.0 (C), 142.2 (C), 132.2 (C), 132.2 (C), 130.2 (CH), 129.5 (6C), 128.5 (CH), 128.5 (2CH), 128.2 (2CH), 128.0 (CH), 127.6 (6CH), 127.0 (CH), 126.8 (3ch), 124.9 (CH), 125.4 (CF3, q, *J* = 279 Hz), 123.6 (C), 123.4 (CH), 121.2 (CH), 116.4 (CH), 111.5 (CH), 75.5 (C), 71.4 (C), 66.5 (C), 60.8 (CH, q, *J* = 31 Hz), 51.1 (CH); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.84; **HRMS (ESI)** m/z: 715.2179 $[M + Na]^+$, calcd for $C_{44}H_{31}O_3N_2F_3Na$; Found 715.2158.

(2'R,3R,4'R,5'S)-4'-(2-chlorophenyl)-1'-hydroxy-1''-methyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indoline]-2,2''-dione (5d):



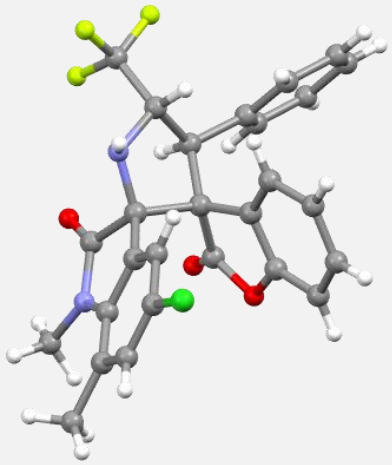
Prepared by following general procedure **E** purified by column chromatography using hexane - Ethyl acetate and isolated product **5d** in 51% yield as a white solid with M. P. 230 - 231 °C; **$[\alpha]_D^{25}$ = -80.500 (CH_2Cl_2, *c* = 0.006 g/100mL)**;**IR (neat) ν_{max}** 3398, 2920, 1724, 1462, and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 (1H, dd, *J* = 8.0, 1.4 Hz), 7.60 (1H, dd, *J* = 7.7, 0.7 Hz), 7.56 (1H, dd, *J* = 7.7, 1.0 Hz), 7.22 – 7.19 (1H, m), 7.18 – 7.11 (2H, m), 7.08 – 7.03 (2H, m), 7.01 – 6.93 (2H, m), 6.59 (1H, d, *J* = 7.6 Hz), 6.53 (1H, d, *J* = 7.8 Hz), 6.09 (1H, d, *J* = 11.9 Hz), 5.64 (1H, s), 5.34 – 5.27 (1H, m), 3.01 (3H, s); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 174.3 (C, C-*C*=O), 173.5 (C, N-*C*=O), 153.3 (C), 144.1 (C), 135.6 (C), 130.7 (2CH), 130.6 (2CH), 130.4 (CH), 130.2 (CH), 129.8 (C), 129.5 (CH), 129.3 (CH), 127.3 (CH), 126.6 (CH), 125.4 (CF3, q, *J* = 278 Hz), 123.9 (CH), 122.9 (CH), 120.4 (C), 120.3 (C), 110.4 (CH), 108.1 (CH), 72.6 (CH, q, *J* = 29 Hz), 41.9 (CH), 26.0 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -70.41; **HRMS (ESI)** m/z: 537.0799 $[M + Na]^+$, calcd for $C_{26}H_{18}O_4N_2F_3ClNa$; Found 537.0789.

ethyl(E)-N-((4-acetamidophenyl)sulfonyl)-3-((2'R,3R,4'S,5'S)-2,2''-dioxo-4'-phenyl-5'-(trifluoromethyl)-2H-dispiro[benzofuran-3,3'-pyrrolidine-2',3''-indolin]-1''-yl)propanimidate (7i'):



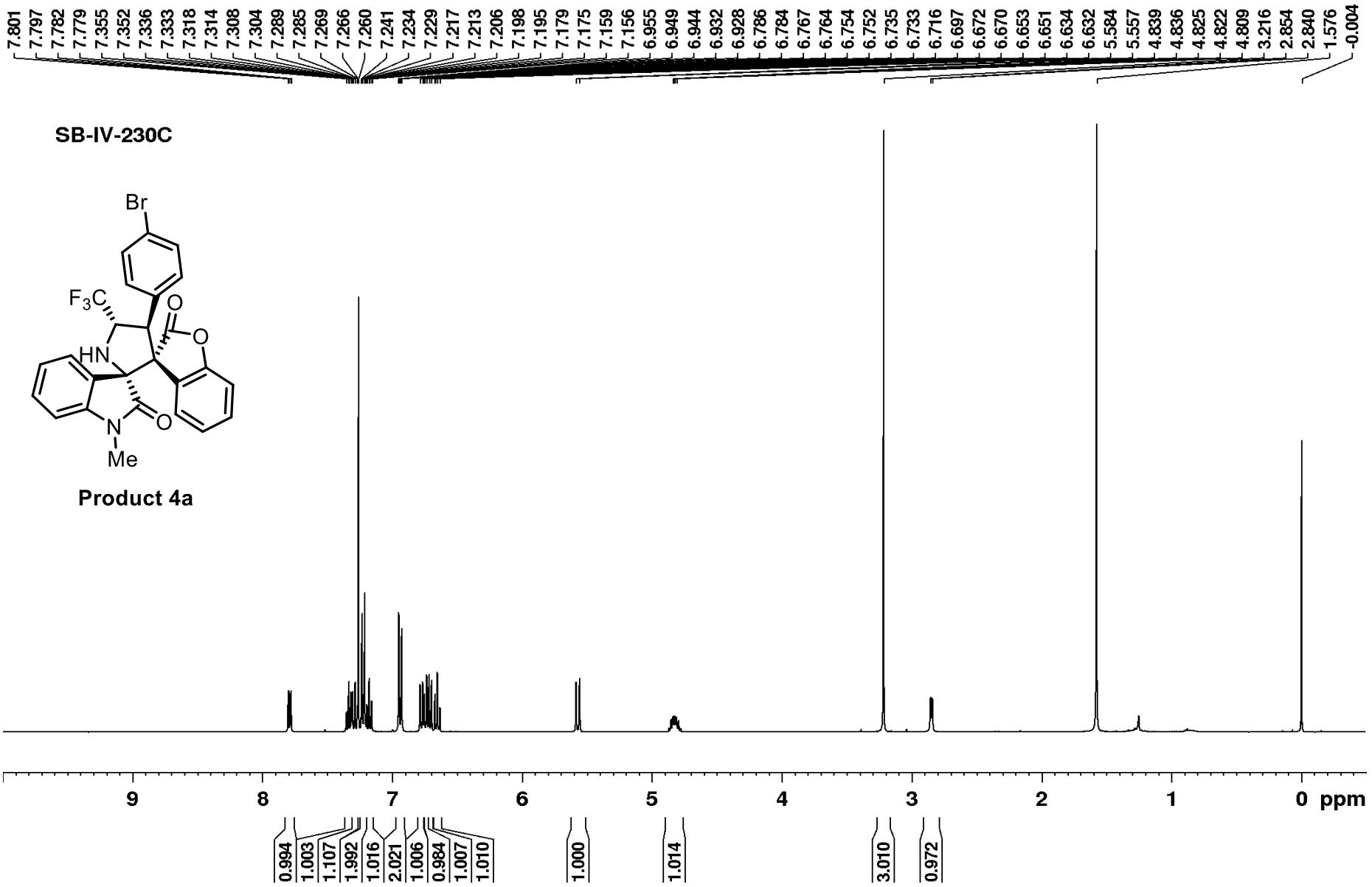
Prepared by following general procedure **F** purified by column chromatography using hexane - Ethyl acetate and isolated product **7i'** in 87% yield as a white solid with M. P. 148 - 150 °C; **$[\alpha]_D^{25}$ = -33.714 ($CHCl_3$, *c* = 0.004 g/100mL)**; **IR (neat) ν_{max}** 2924, 2852, 1801, 1591, and 732 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.85 (1H, dd, *J* = 7.6, 1.0 Hz), 7.81 (2H, dd, *J* = 6.9, 1.8 Hz), 7.61 (2H, d, *J* = 8.2 Hz), 7.46 (1H, s), 7.32 (1H, td, *J* = 1.0 Hz), 7.24 (1H, td, *J* = 7.8, 1.3 Hz), 7.18 (1H, td, *J* = 7.7, 1.1 Hz), 7.11 – 7.04 (5H, m), 6.93 (1H, d, *J* = 7.8 Hz), 6.79 (1H, dd, *J* = 7.7, 0.9 Hz), 6.71 (1H, dd, *J* = 7.9, 0.6 Hz), 6.65 (1H, td, *J* = 7.6, 0.8 Hz), 5.57 (1H, d, *J* = 10.6 Hz), 4.92 – 4.83 (1H, m), 4.22 – 4.06 (4H, m), 3.38 – 3.30 (1H, m), 3.20 – 3.13 (1H, m), 3.10 (1H, d, *J* = 4.8 Hz), 2.21 (3H, s), 1.22 (3H, t, *J* = 7.1 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.1 (C, C-*C*=O), 173.1 (C, N-*C*=O), 172.2 (C, N-*C*=O), 168.6 (C), 152.8 (C), 142.8 (C), 141.6 (C), 136.5 (C), 132.1 (C), 130.6 (CH), 130.3 (2CH), 128.4 (2CH), 128.2 (CH), 128.1 (3CH), 127.9 (CH), 126.8 (CH), 125.7 (CH), 125.6 (CF_3, d, *J* = 281 Hz), 124.2 (C), 123.7 (C), 123.5 (CH), 122.0 (CH), 119.2 (CH), 111.3 (CH), 108.6 (CH), 71.2 (C), 66.2 (C), 65.2 (CH_2), 60.7 (CH, q, *J* = 31 Hz), 50.8 (CH), 36.9 (CH_2), 31.9 (CH_2), 24.8 (CH_3), 13.5 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -71.41; **HRMS (ESI)** m/z: 769.1914 $[M + Na]^+$, calcd for $C_{38}H_{33}O_7N_4F_3NaS$; Found 769.1893.

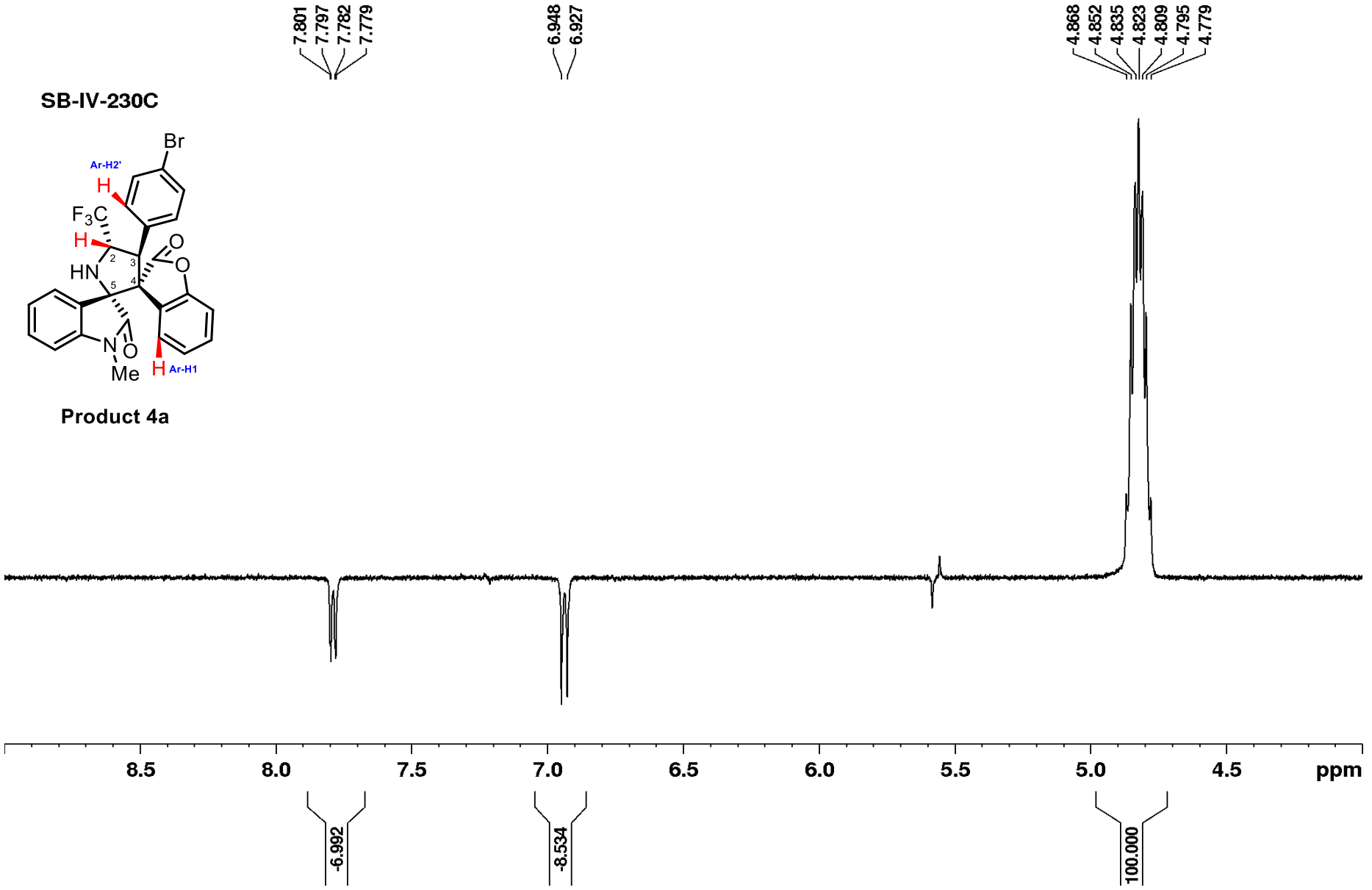
SC-XRD DATA

Crystallographic Data and Structure Refinements Summary of (–)-4d’	
Molecular Structure (ball & stick Diagram) for compound (–)-4d’	
CCDC number	CCDC 2388791
Empirical formula	$C_{27}H_{20}ClF_3N_2O_3$
Formula weight	512.90
Temperature	297.0 K
Wavelength	0.71073 λ
Crystal system	orthorhombic
space group	P 2_1 2_1 2_1
a	6.8332 (9) Å
b	16.149 (2) Å

c	21.497 (3) Å
a	90°
b	90°
g	90°
Volume	2372.1(5) $Å^3$
Z	4
Calculated density	1.436 g/cm^3
Absorption coefficient, m	0.218 mm^{-1}
F (000)	1056.0
Crystal size	0.36 X 0.26 X 0.26 mm^3
θ range for data collection	4.55° to 56.61°
Limiting indices	-9<=h<=9, -21<=k<=21, -28<=l<=28
Reflections collected / unique	81429 / 5878 [R_{int} = 0.0643, R_{sigma} = 0.0275]
Completeness to θ =	28.30 99.8 %
Absorption correction	Multi-scan

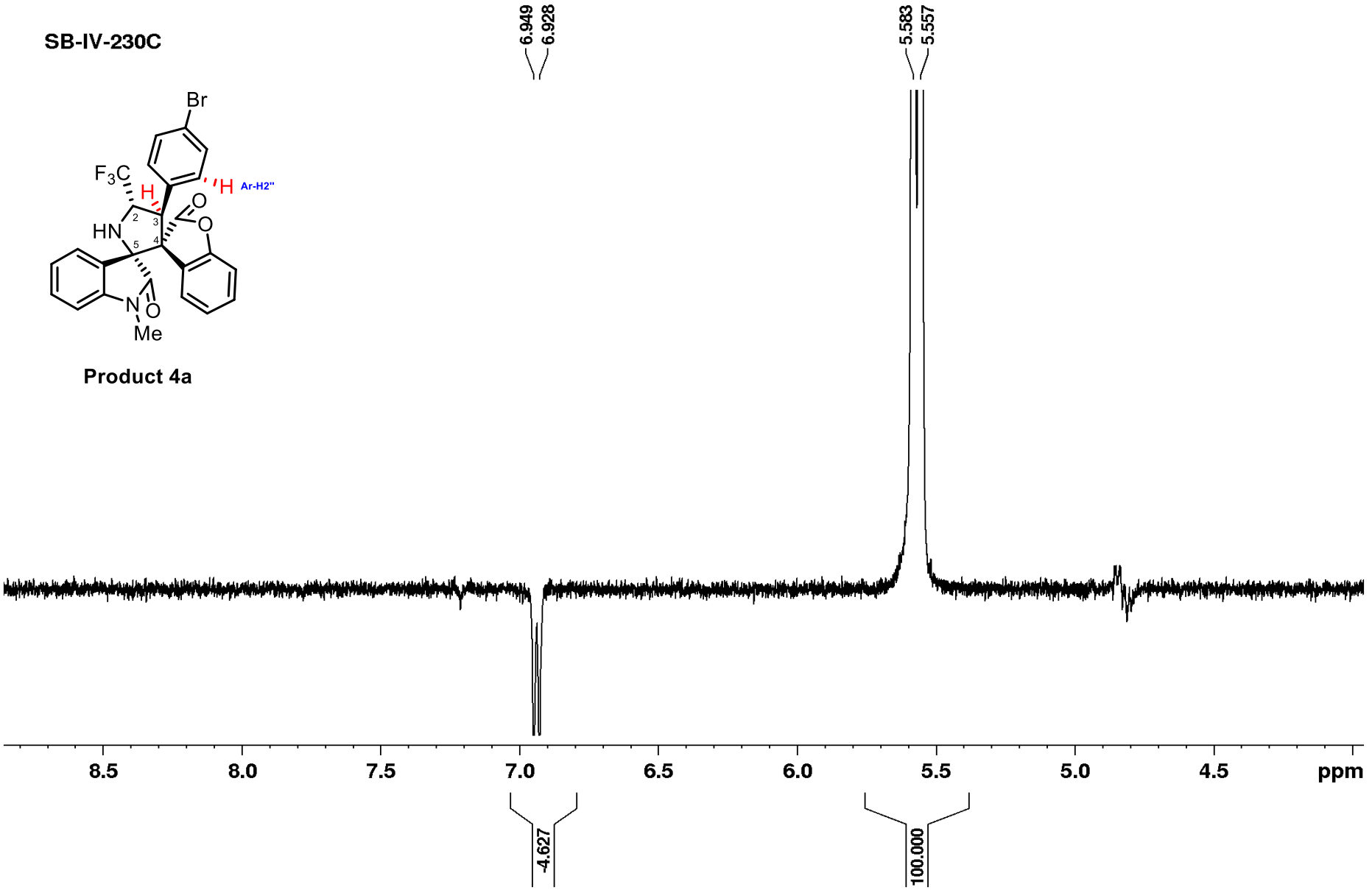
Max. and min. transmission	-
Refinement method	SHELXL 2013/1 (Sheldrick, 2015)'
Data/restraints / parameters	5878 / 0/ 332
Goodness-of-fit on F^2	1.028
Final R indices [I>2sigma(I)]	R1 = 0.0377
R indices (all data)	R1 = 0.0532
Absolute structure parameter	0.01 (3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.18 and -0.24 e.$Å^{-3}$

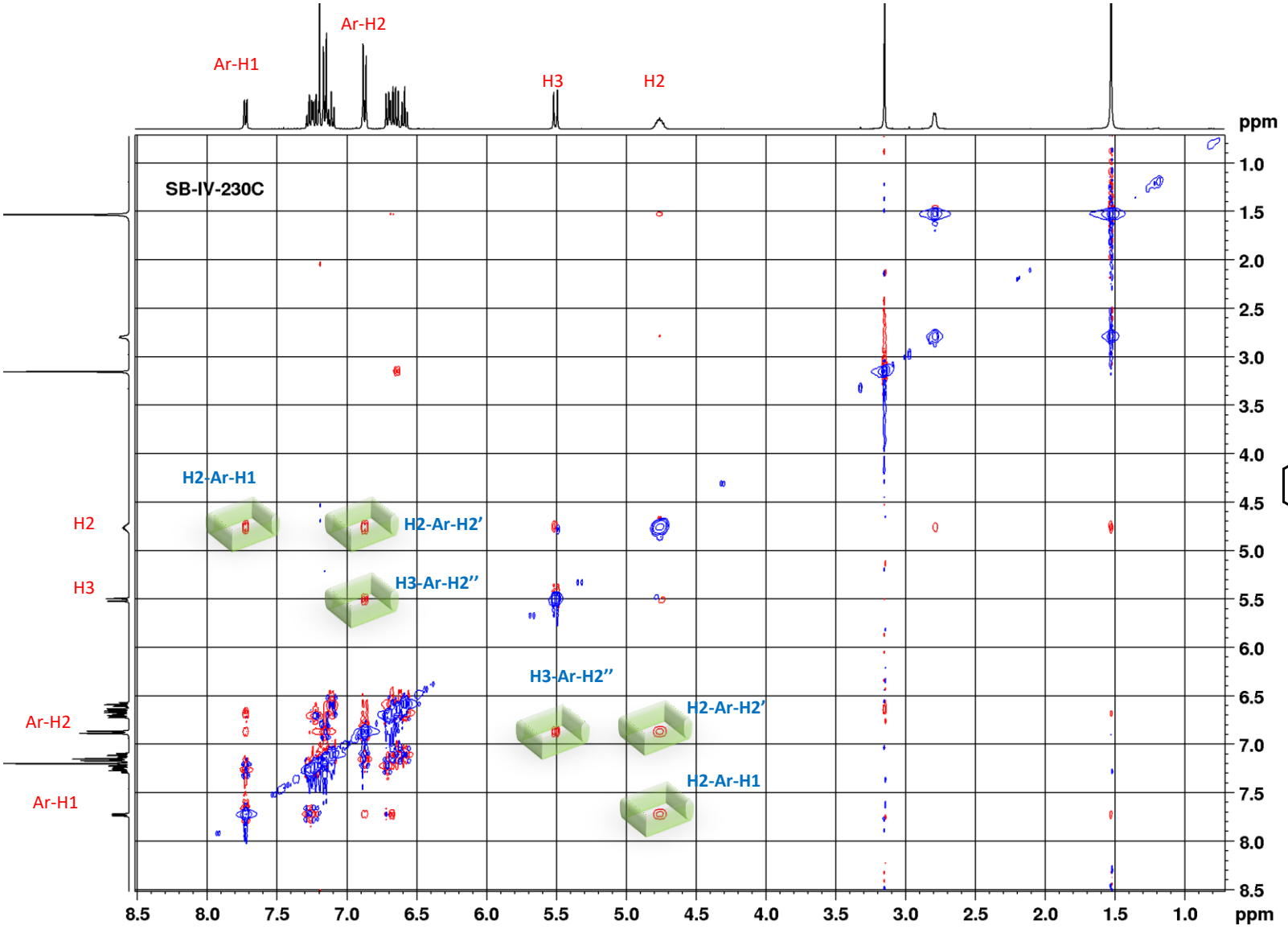

7.801
7.797
7.782
7.779
7.355
7.352
7.336
7.333
7.318
7.314
7.308
7.304
7.289
7.285
7.269
7.266
7.260
7.241
7.234
7.229
7.217
7.213
7.206
7.198
7.195
7.179
7.175
7.159
7.156
6.955
6.949
6.944
6.932
6.928
6.786
6.784
6.767
6.764
6.754
6.752
6.735
6.733
6.716
6.697
6.672
6.670
6.653
6.651
6.634
6.632
5.584
5.557
4.839
4.836
4.825
4.822
4.809
3.216
2.854
2.840
1.576
-0.004
SB-IV-230C
Br
F3C
O
O
HN
O
N
Me
Product 4a
9
8
7
6
5
4
3
2
1
0 ppm
0.994
1.003
1.107
1.992
1.016
2.021
1.006
0.984
1.007
1.010
1.000
1.014
3.010
0.972

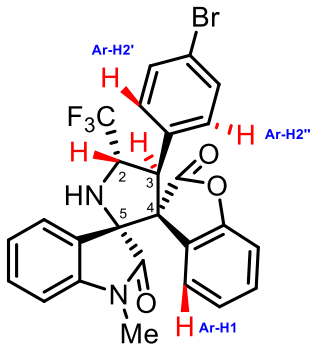

7.801
7.797
7.782
7.779
6.948
6.927
4.868
4.852
4.835
4.823
4.809
4.795
4.779
SB-IV-230C
Br
Ar-H2'
H
F3C
H
HN
2
3
4
5
O
O
N
O
Me
H
Ar-H1
Product 4a
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
ppm
-6.992
-8.534
100.000

SB-IV-230C

Product 4a



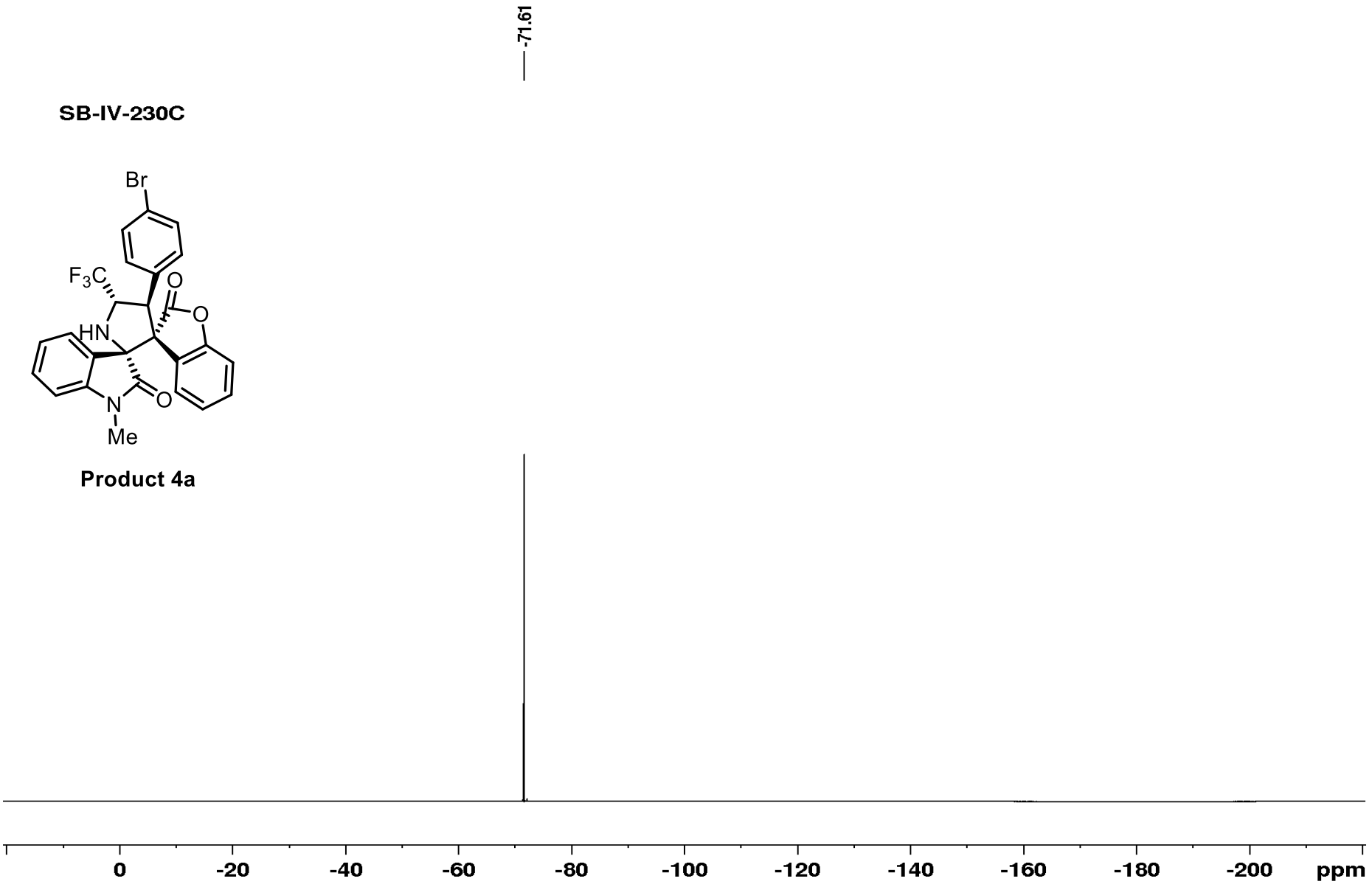

Ar-H1
Ar-H2
H3
H2
ppm
SB-IV-230C
H2-Ar-H1
H2-Ar-H2'
H3-Ar-H2''
H2
H3
Ar-H2
Ar-H1
H3-Ar-H2''
H2-Ar-H2'
H2-Ar-H1
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

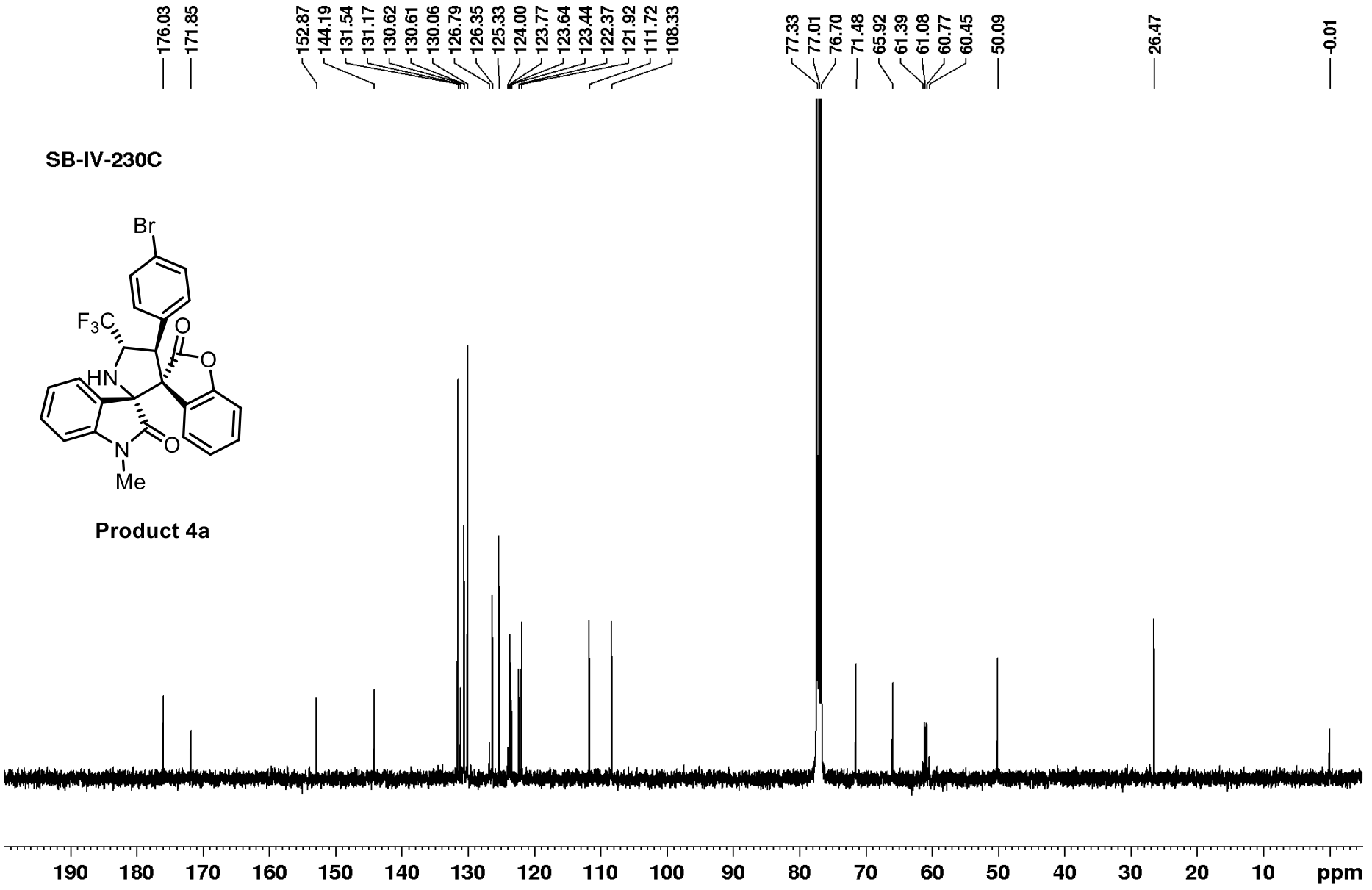

Br
Ar-H2'
H
F3C
H
H
Ar-H2"
O
O
HN
2
3
4
5
N
O
Me
H
Ar-H1

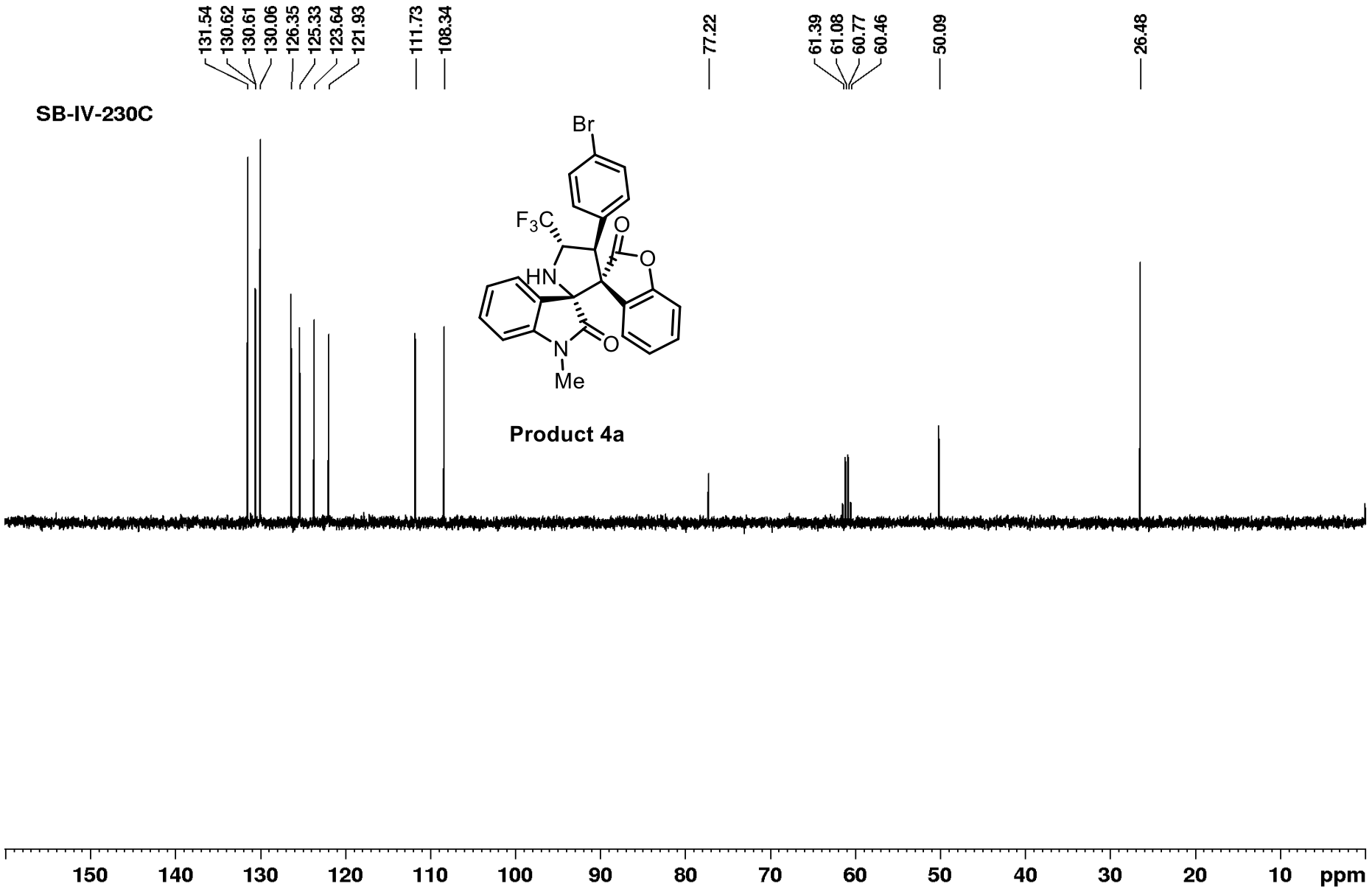
Product 4a

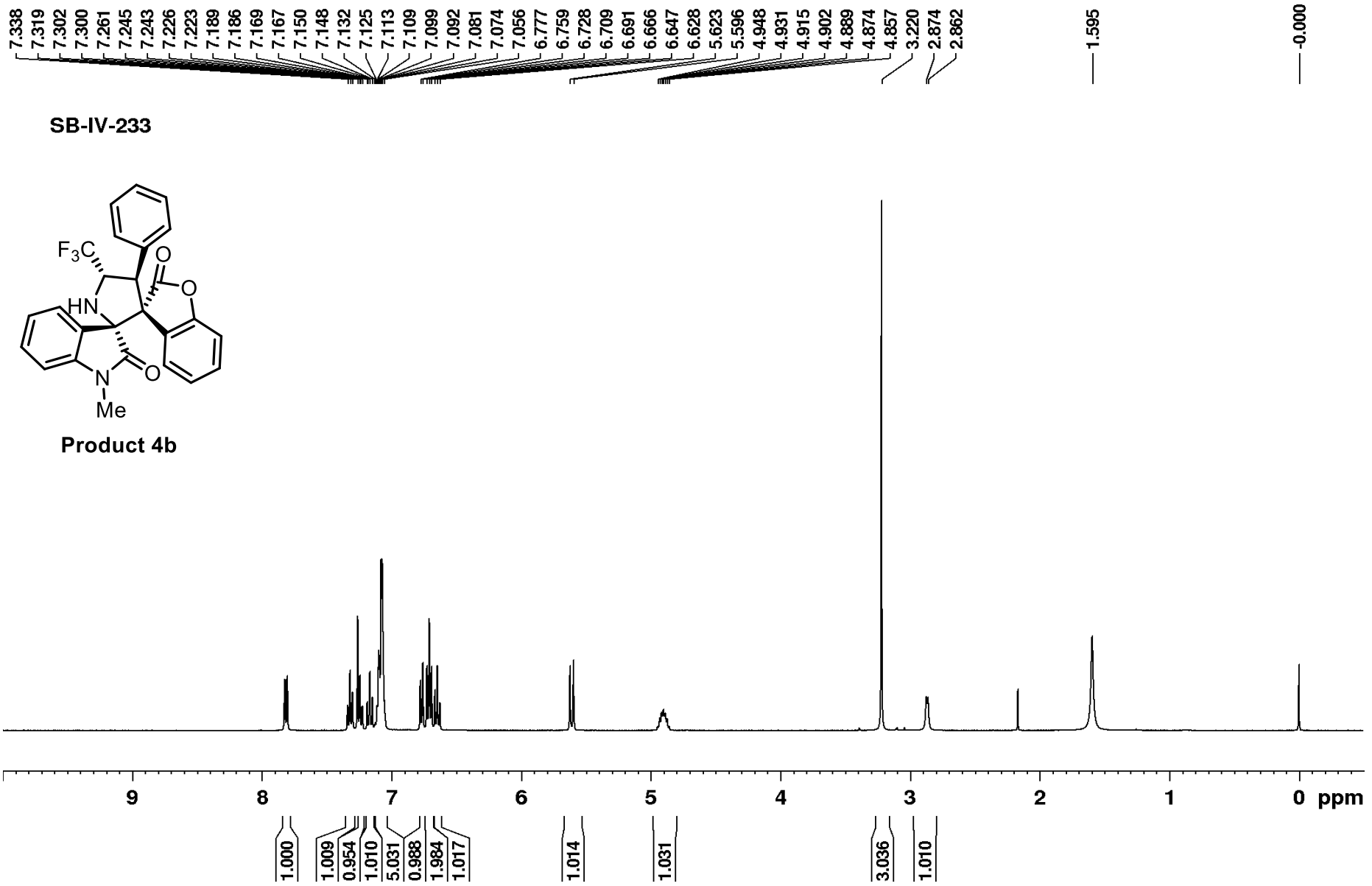
SB-IV-230C

Product 4a



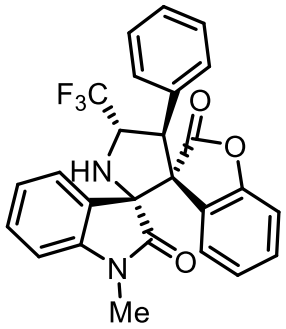

176.03
171.85
152.87
144.19
131.54
131.17
130.62
130.61
130.06
126.79
126.35
125.33
124.00
123.77
123.64
123.44
122.37
121.92
111.72
108.33
77.33
77.01
76.70
71.48
65.92
61.39
61.08
60.77
60.45
50.09
26.47
-0.01
SB-IV-230C
Br
F3C
O
O
HN
O
N
Me
Product 4a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


131.54
130.62
130.61
130.06
126.35
125.33
123.64
121.93
111.73
108.34
77.22
61.39
61.08
60.77
60.46
50.09
26.48
SB-IV-230C
Br
F3C
O
O
HN
N
O
Me
Product 4a
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

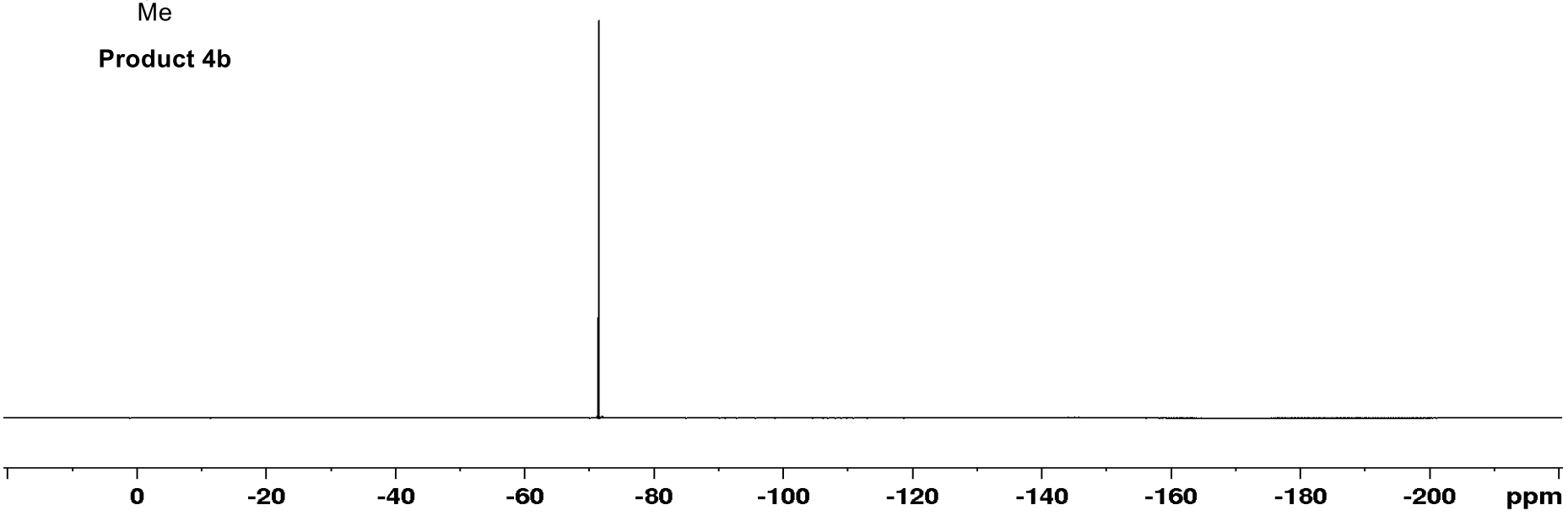

7.338
7.319
7.302
7.300
7.261
7.245
7.243
7.226
7.223
7.189
7.186
7.169
7.167
7.150
7.148
7.132
7.125
7.113
7.109
7.099
7.092
7.081
7.074
7.056
6.777
6.759
6.728
6.709
6.691
6.666
6.647
6.628
5.623
5.596
4.948
4.931
4.915
4.902
4.889
4.874
4.857
3.220
2.874
2.862
1.595
-0.000
SB-IV-233
F3C
O
O
HN
O
N
Me
Product 4b
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.009
0.954
1.010
5.031
0.988
1.984
1.017
1.014
1.031
3.036
1.010

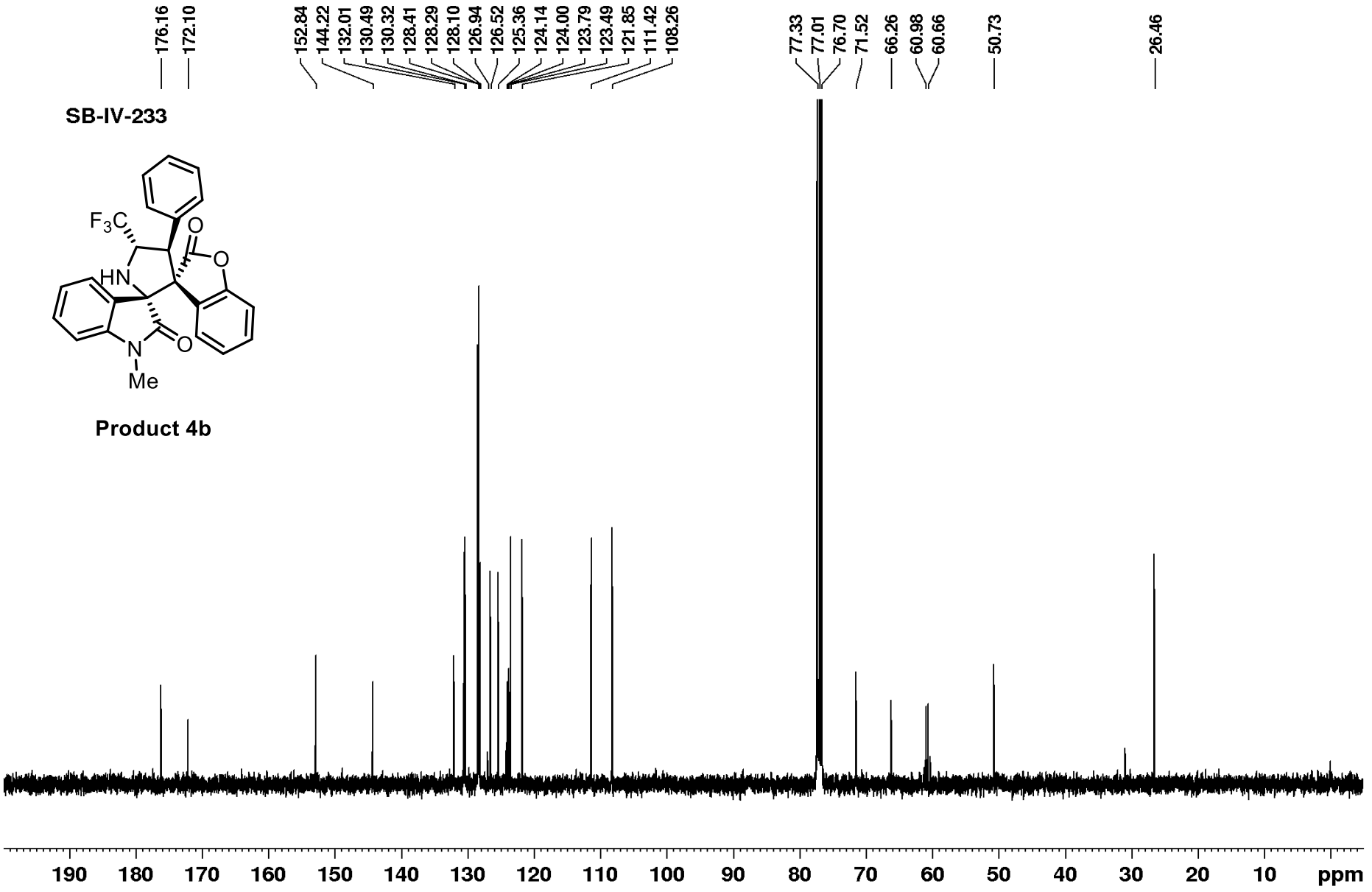
-71.52
-71.54

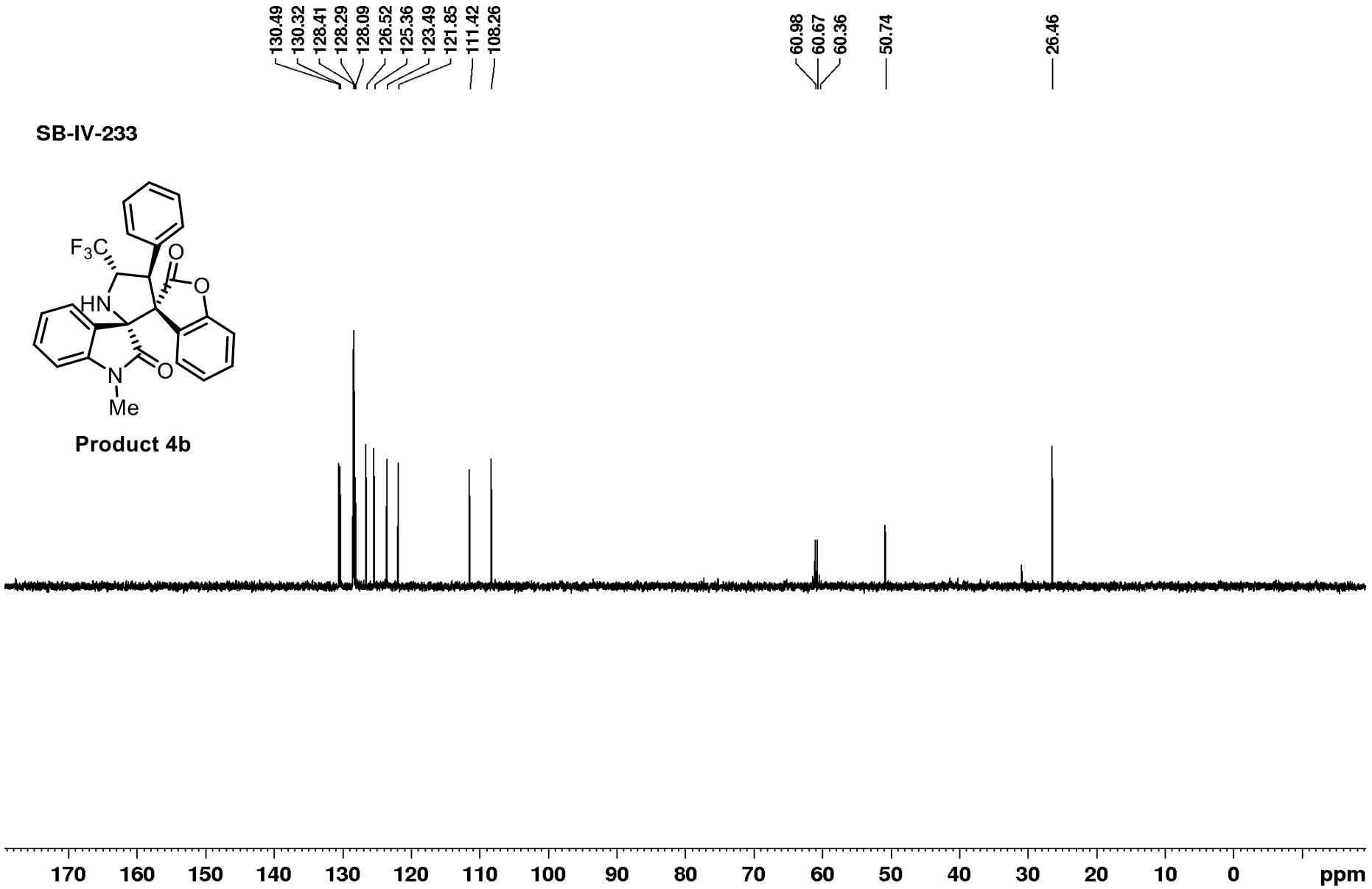
SB-IV-233

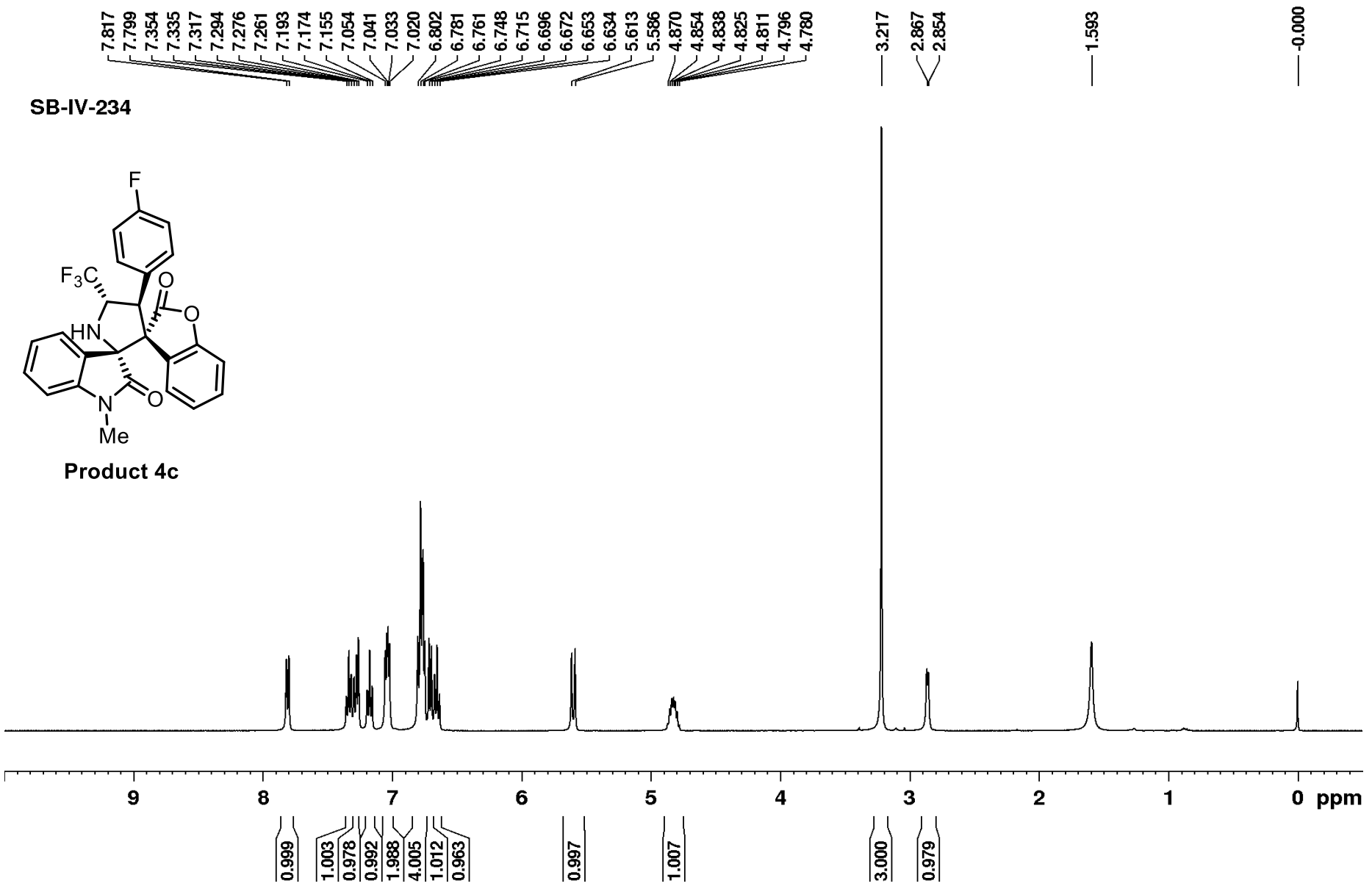


Product 4b



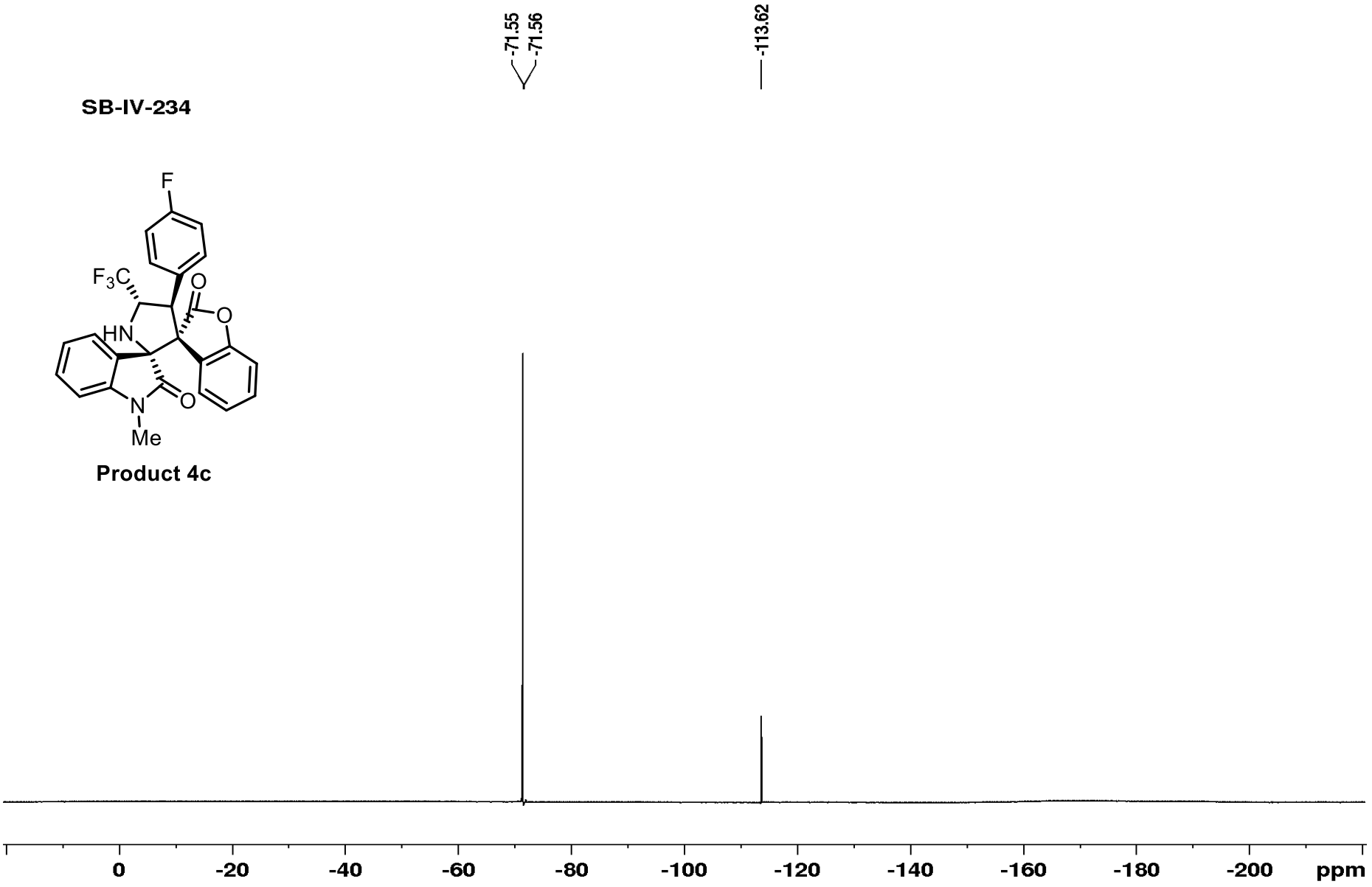

176.16
172.10
152.84
144.22
132.01
130.49
130.32
128.41
128.29
128.10
126.94
126.52
125.36
124.14
124.00
123.79
123.49
121.85
111.42
108.26
77.33
77.01
76.70
71.52
66.26
60.98
60.66
50.73
26.46
SB-IV-233
F3C
HN
O
O
N
O
Me
Product 4b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

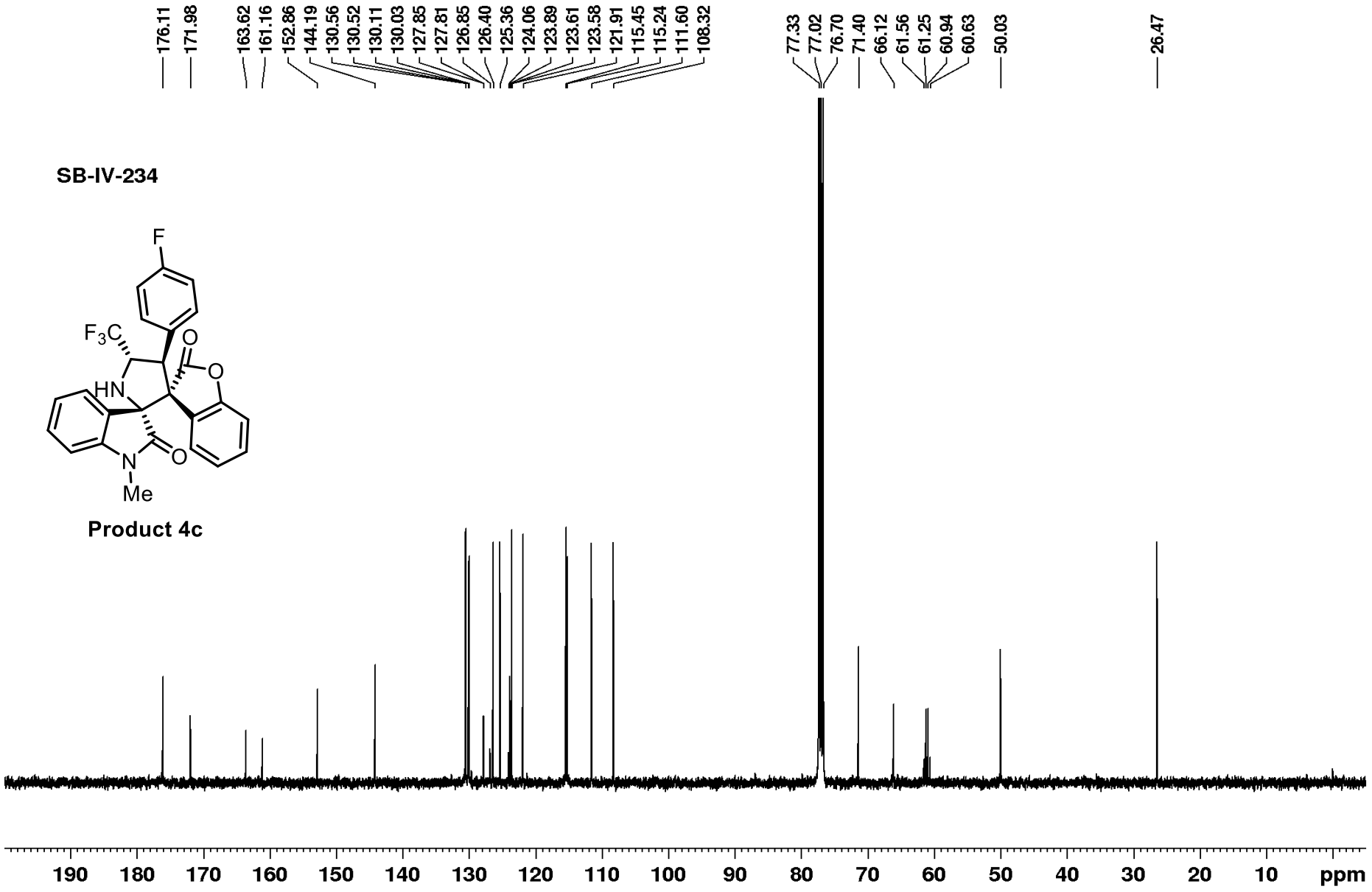

130.49
130.32
128.41
128.29
128.09
126.52
125.36
123.49
121.85
111.42
108.26
60.98
60.67
60.36
50.74
26.46
SB-IV-233
F3C
O
O
HN
O
N
Me
Product 4b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

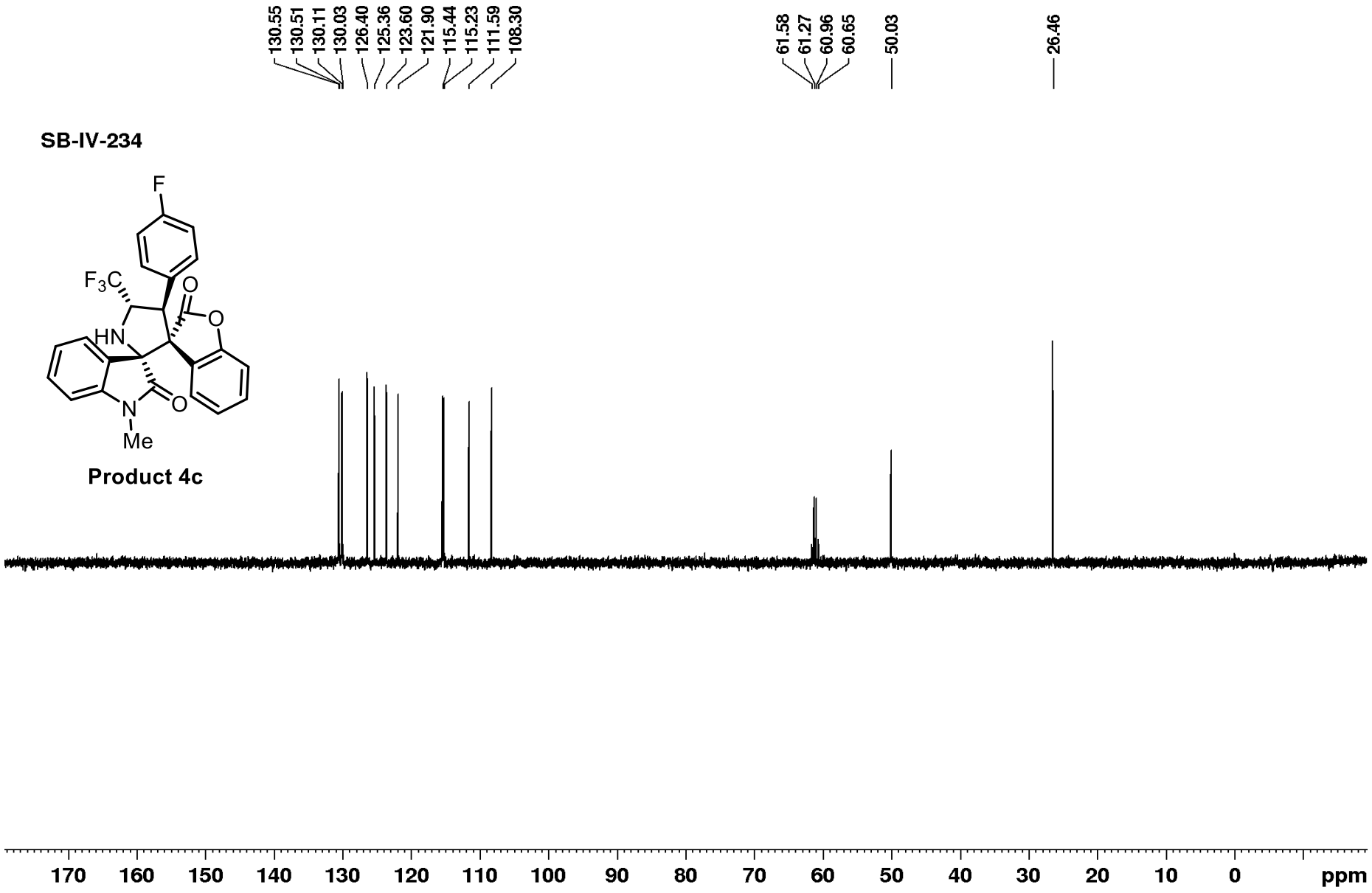

7.817
7.799
7.354
7.335
7.317
7.294
7.276
7.261
7.193
7.174
7.155
7.054
7.041
7.033
7.020
6.802
6.781
6.761
6.748
6.715
6.696
6.672
6.653
6.634
5.613
5.586
4.870
4.854
4.838
4.825
4.811
4.796
4.780
3.217
2.867
2.854
1.593
-0.000
SB-IV-234
F
F3C
O
O
HN
O
N
Me
Product 4c
9
8
7
6
5
4
3
2
1
0 ppm
0.999
1.003
0.978
0.992
1.988
4.005
1.012
0.963
0.997
1.007
3.000
0.979

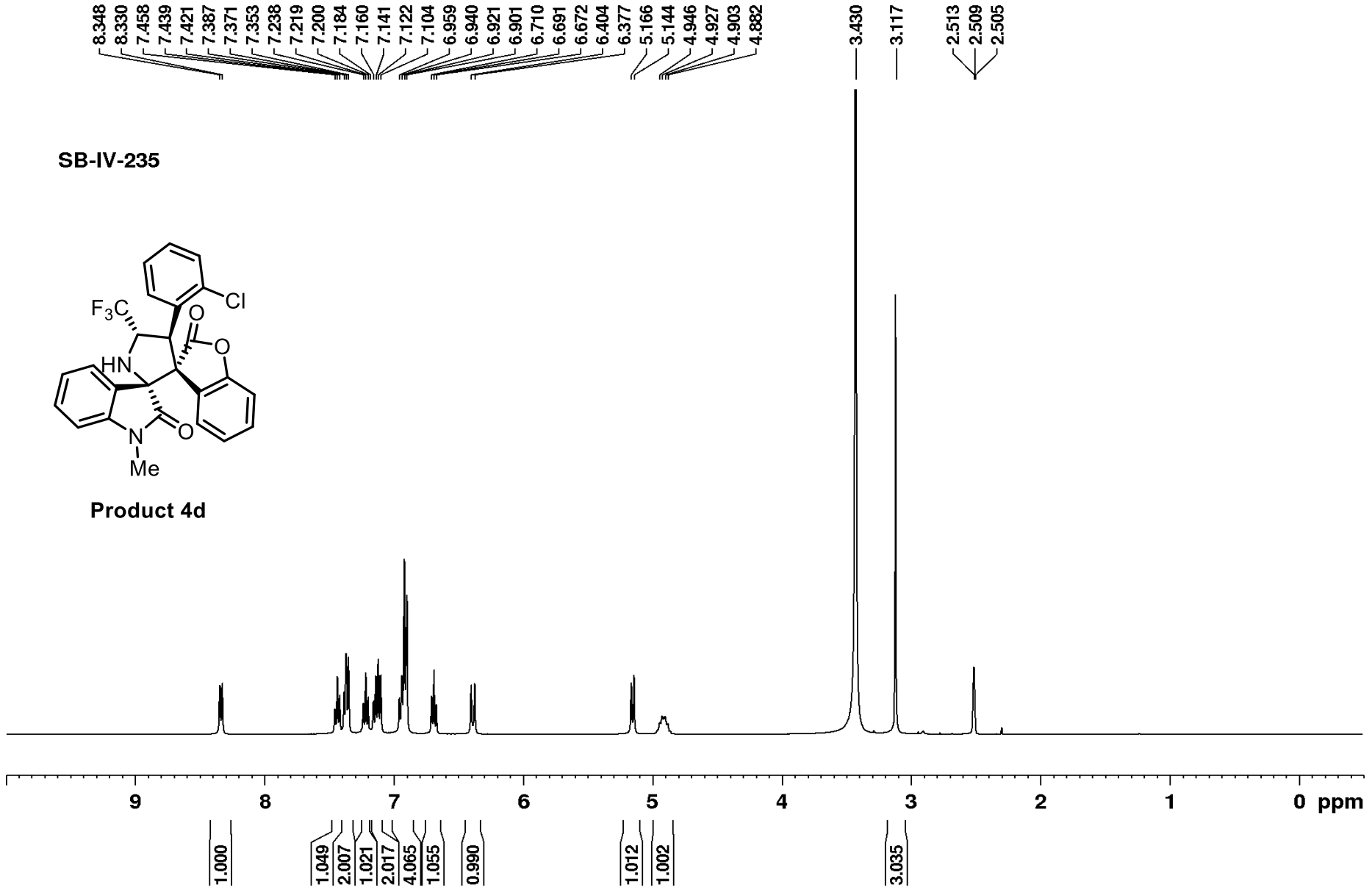
SB-IV-234

Product 4c



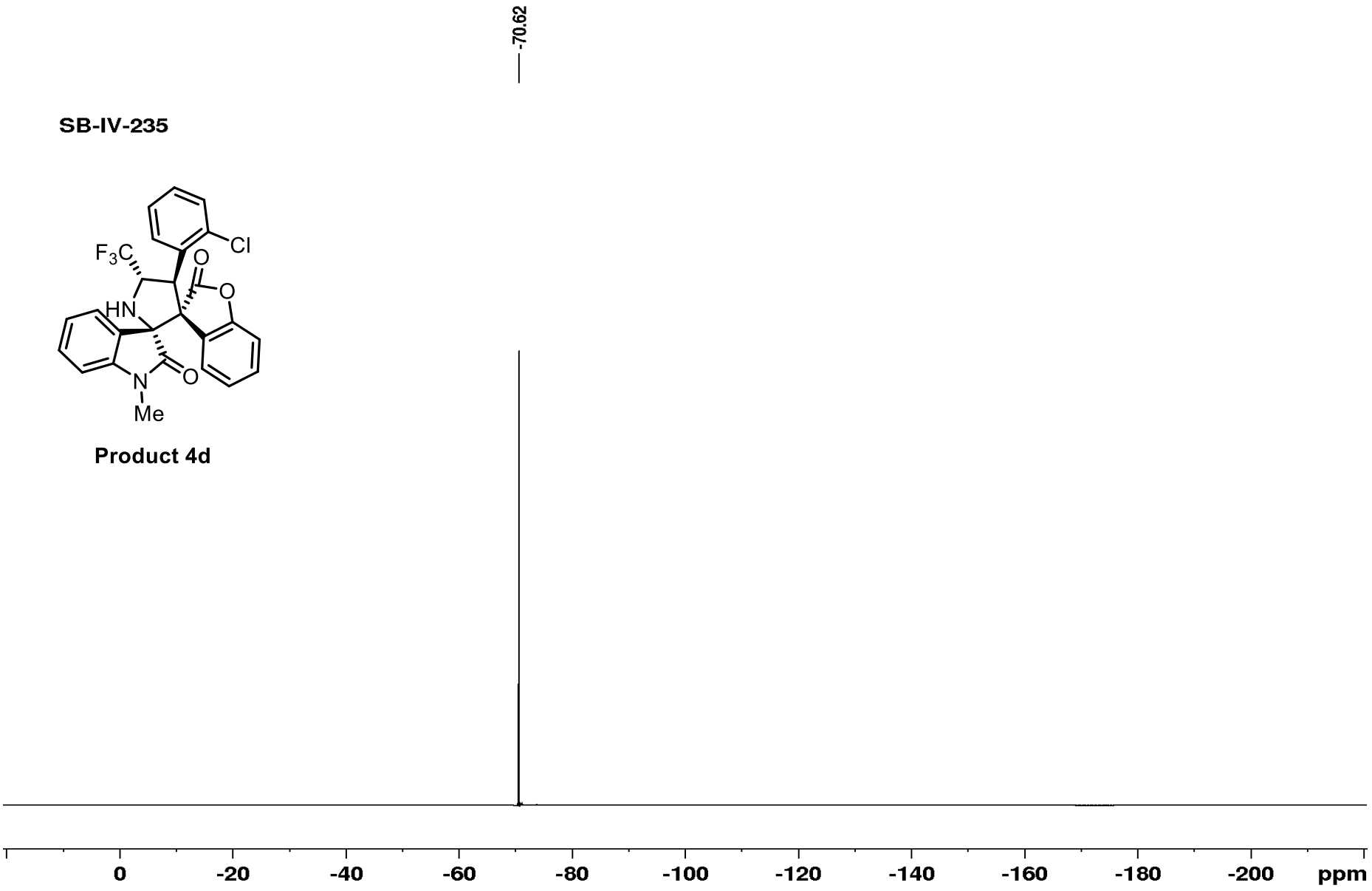

176.11
171.98
163.62
161.16
152.86
144.19
130.56
130.52
130.11
130.03
127.85
127.81
126.85
126.40
125.36
124.06
123.89
123.61
123.58
121.91
115.45
115.24
111.60
108.32
77.33
77.02
76.70
71.40
66.12
61.56
61.25
60.94
60.63
50.03
26.47
SB-IV-234
F
F3C
O
O
HN
O
N
Me
Product 4c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

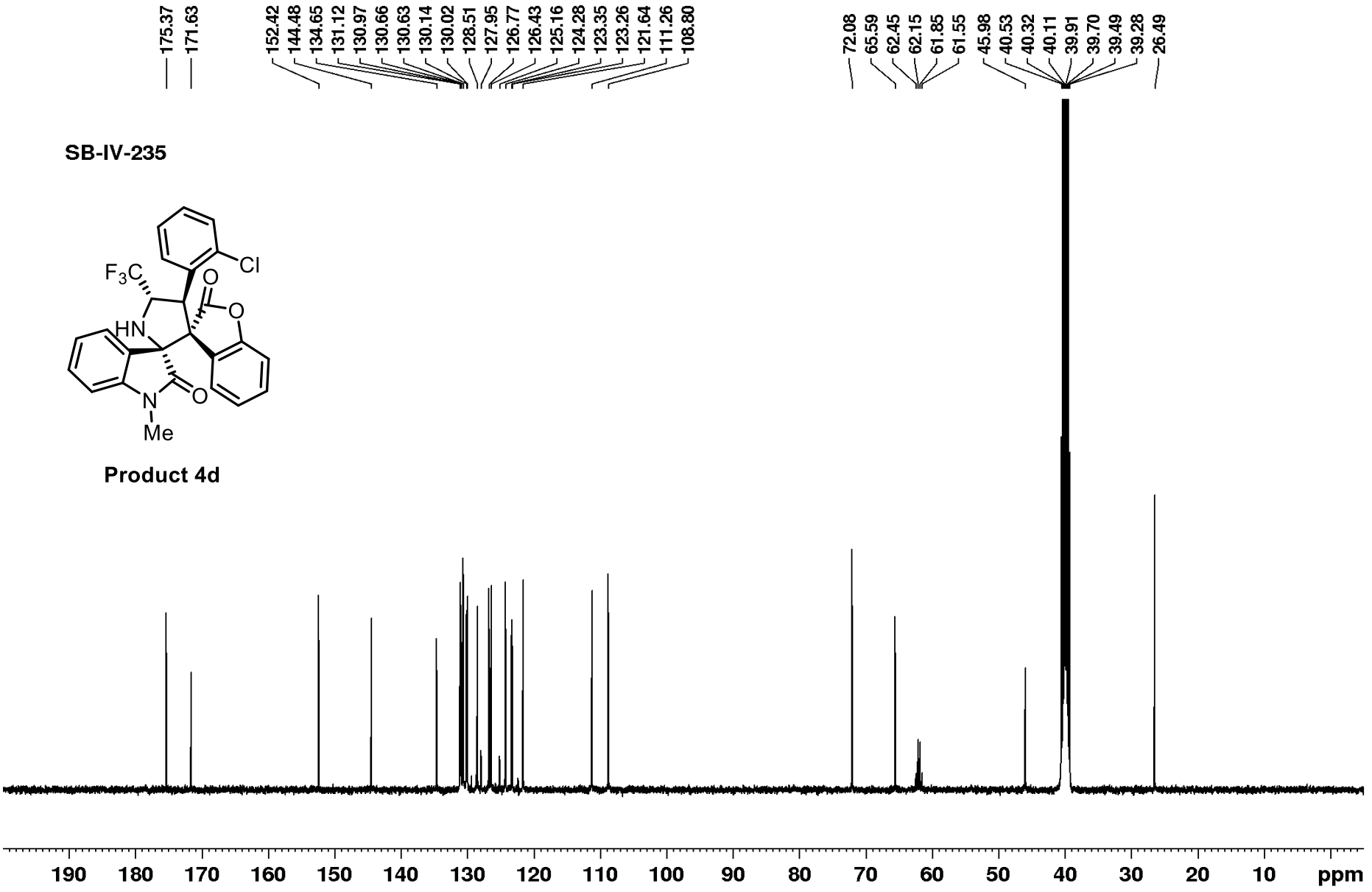

130.55
130.51
130.11
130.03
126.40
125.36
123.60
121.90
115.44
115.23
111.59
108.30
61.58
61.27
60.96
60.65
50.03
26.46
SB-IV-234
F
F3C
O
O
HN
O
N
Me
Product 4c
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

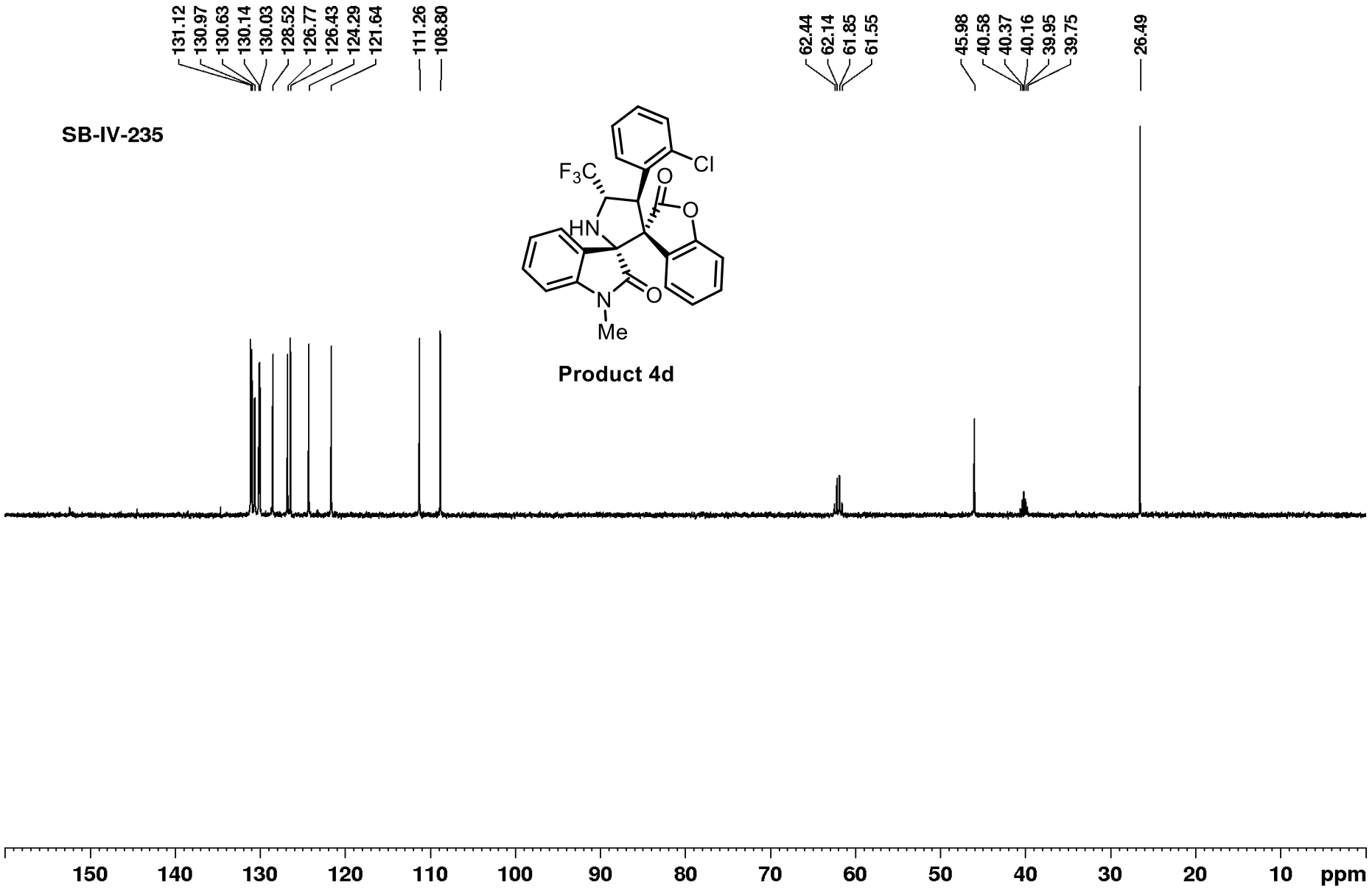

8.348
8.330
7.458
7.439
7.421
7.387
7.371
7.353
7.238
7.219
7.200
7.184
7.160
7.141
7.122
7.104
6.959
6.940
6.921
6.901
6.710
6.691
6.672
6.404
6.377
5.166
5.144
4.946
4.927
4.903
4.882
3.430
3.117
2.513
2.509
2.505
SB-IV-235
F3C
Cl
O
O
HN
O
N
Me
Product 4d
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.049
2.007
1.021
2.017
4.065
1.055
0.990
1.012
1.002
3.035

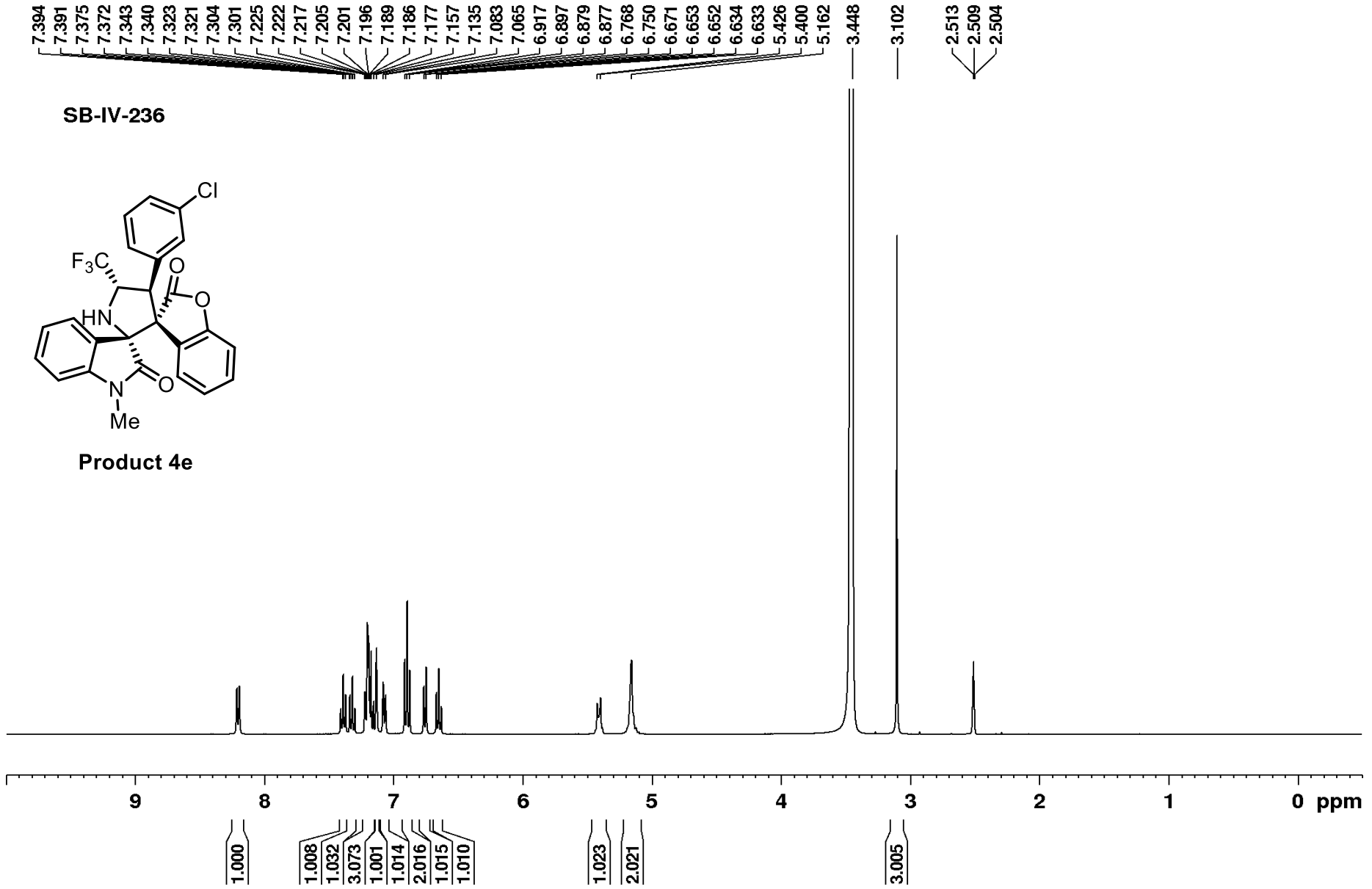
SB-IV-235

Product 4d



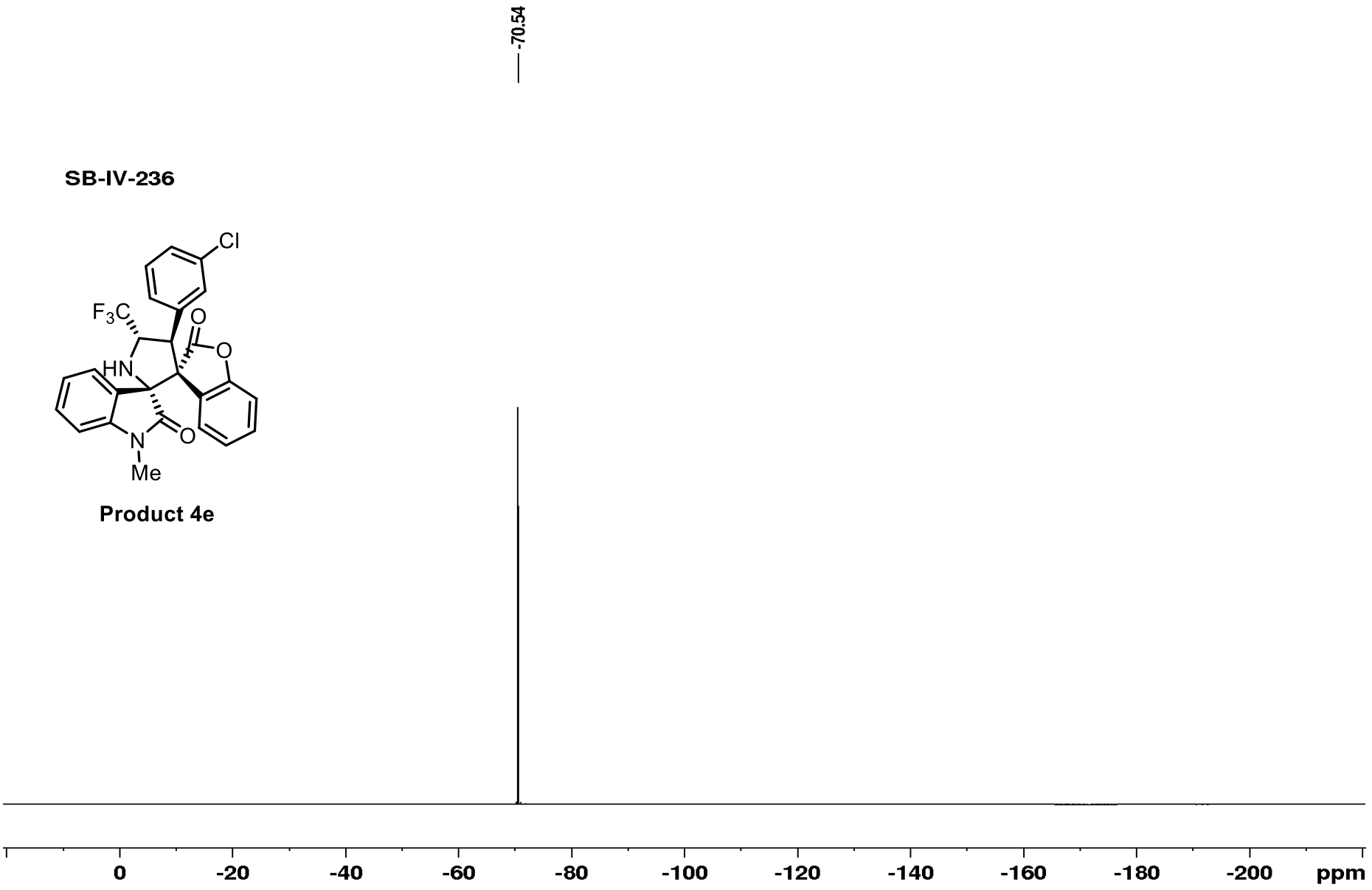

175.37
171.63
152.42
144.48
134.65
131.12
130.97
130.66
130.63
130.14
130.02
128.51
127.95
126.77
126.43
125.16
124.28
123.35
123.26
121.64
111.26
108.80
72.08
65.59
62.45
62.15
61.85
61.55
45.98
40.53
40.32
40.11
39.91
39.70
39.49
39.28
26.49
SB-IV-235
F3C
Cl
O
O
HN
O
N
Me
Product 4d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

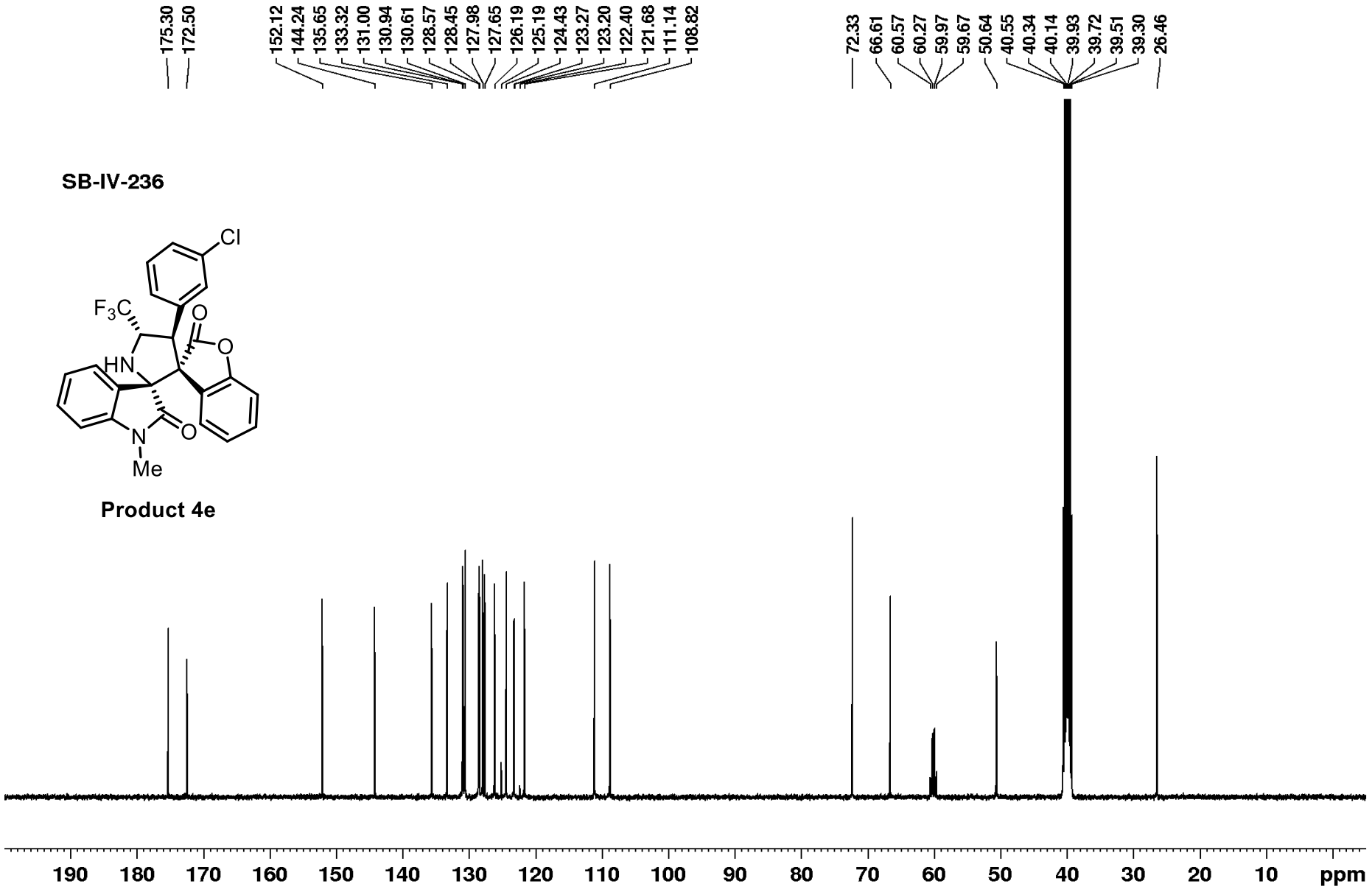

131.12
130.97
130.63
130.14
130.03
128.52
126.77
126.43
124.29
121.64
111.26
108.80
62.44
62.14
61.85
61.55
45.98
40.58
40.37
40.16
39.95
39.75
26.49
SB-IV-235
F3C
Cl
O
O
HN
O
N
Me
Product 4d
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

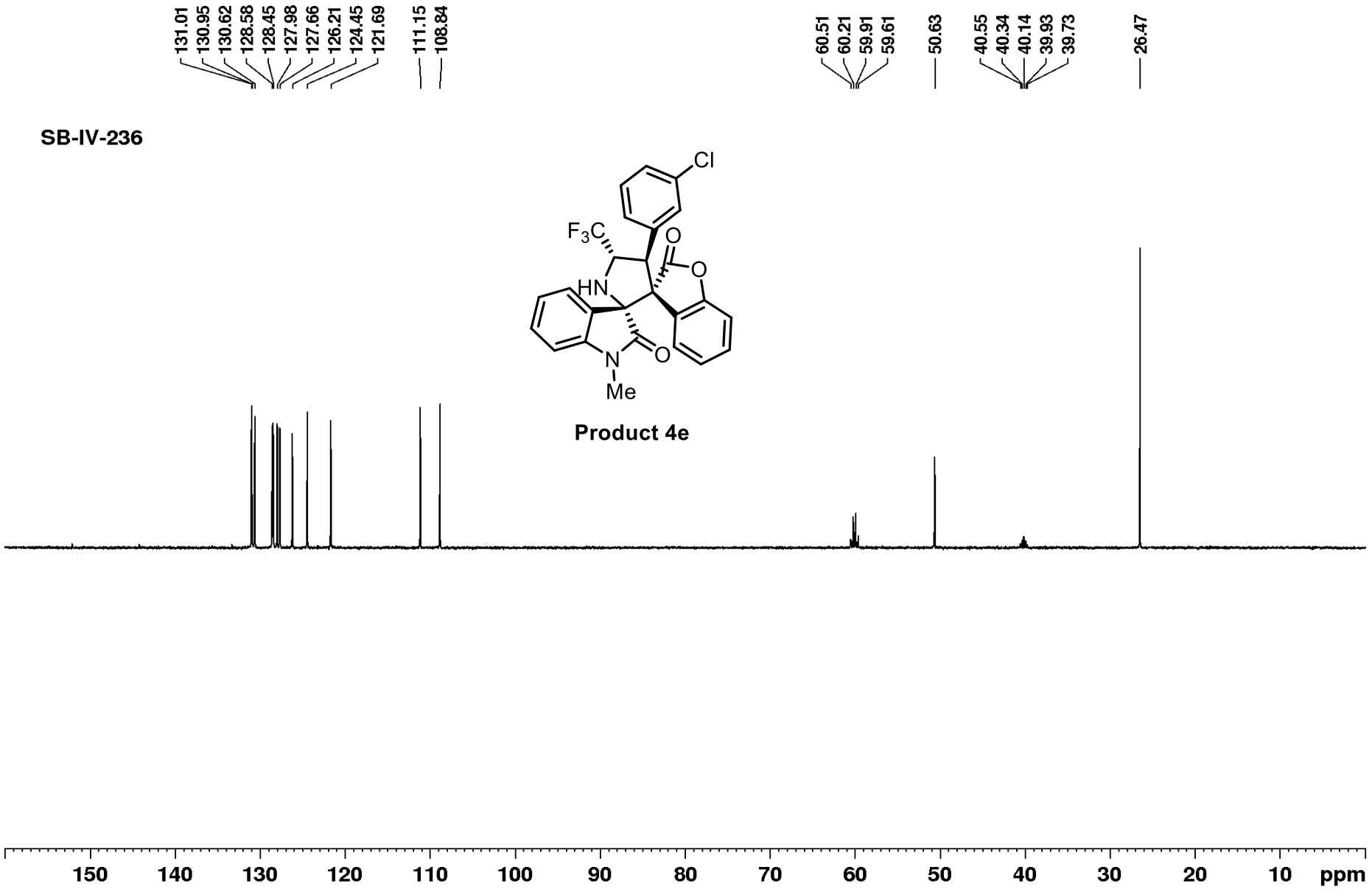

7.394
7.391
7.375
7.372
7.343
7.340
7.323
7.321
7.304
7.301
7.225
7.222
7.217
7.205
7.201
7.196
7.189
7.186
7.177
7.157
7.135
7.083
7.065
6.917
6.897
6.879
6.877
6.768
6.750
6.671
6.653
6.652
6.634
6.633
5.426
5.400
5.162
3.448
3.102
2.513
2.509
2.504
SB-IV-236
Cl
F3C
O
O
HN
O
N
Me
Product 4e
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.008
1.032
3.073
1.001
1.014
2.016
1.015
1.010
1.023
2.021
3.005

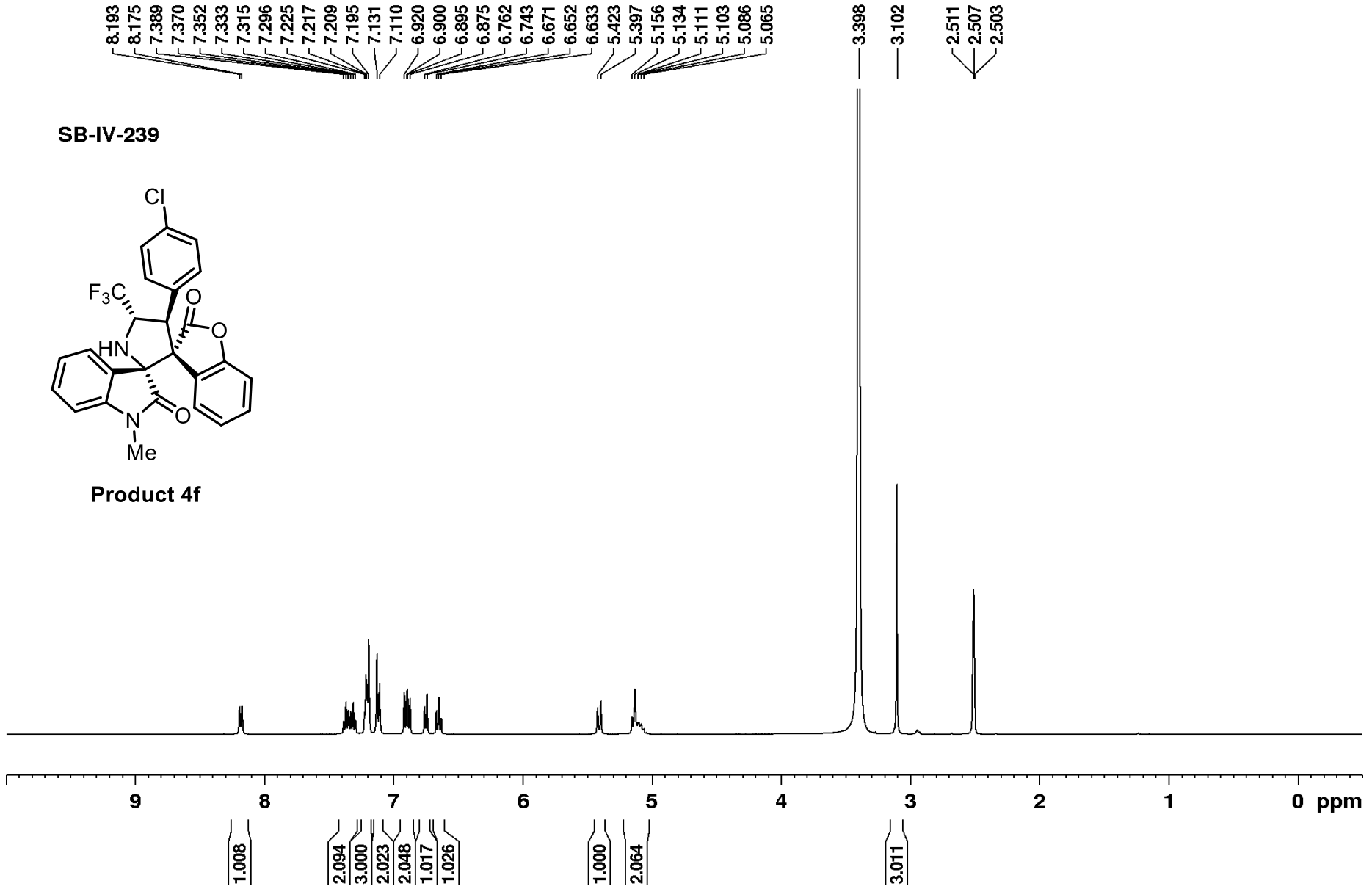
SB-IV-236

Product 4e



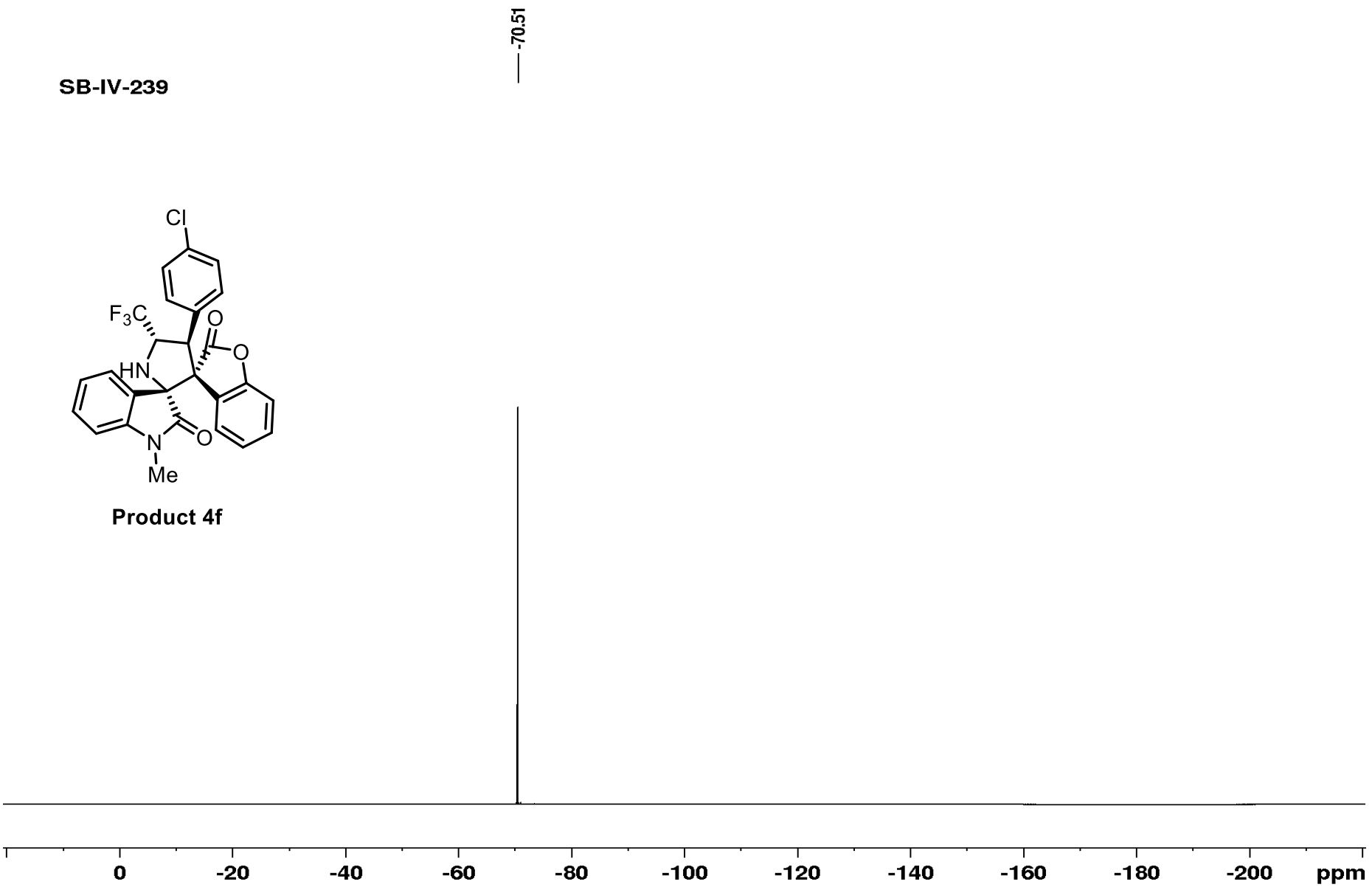

175.30
172.50
152.12
144.24
135.65
133.32
131.00
130.94
130.61
128.57
128.45
127.98
127.65
126.19
125.19
124.43
123.27
123.20
122.40
121.68
111.14
108.82
72.33
66.61
60.57
60.27
59.97
59.67
50.64
40.55
40.34
40.14
39.93
39.72
39.51
39.30
26.46
SB-IV-236
Cl
F3C
O
O
HN
O
N
Me
Product 4e
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

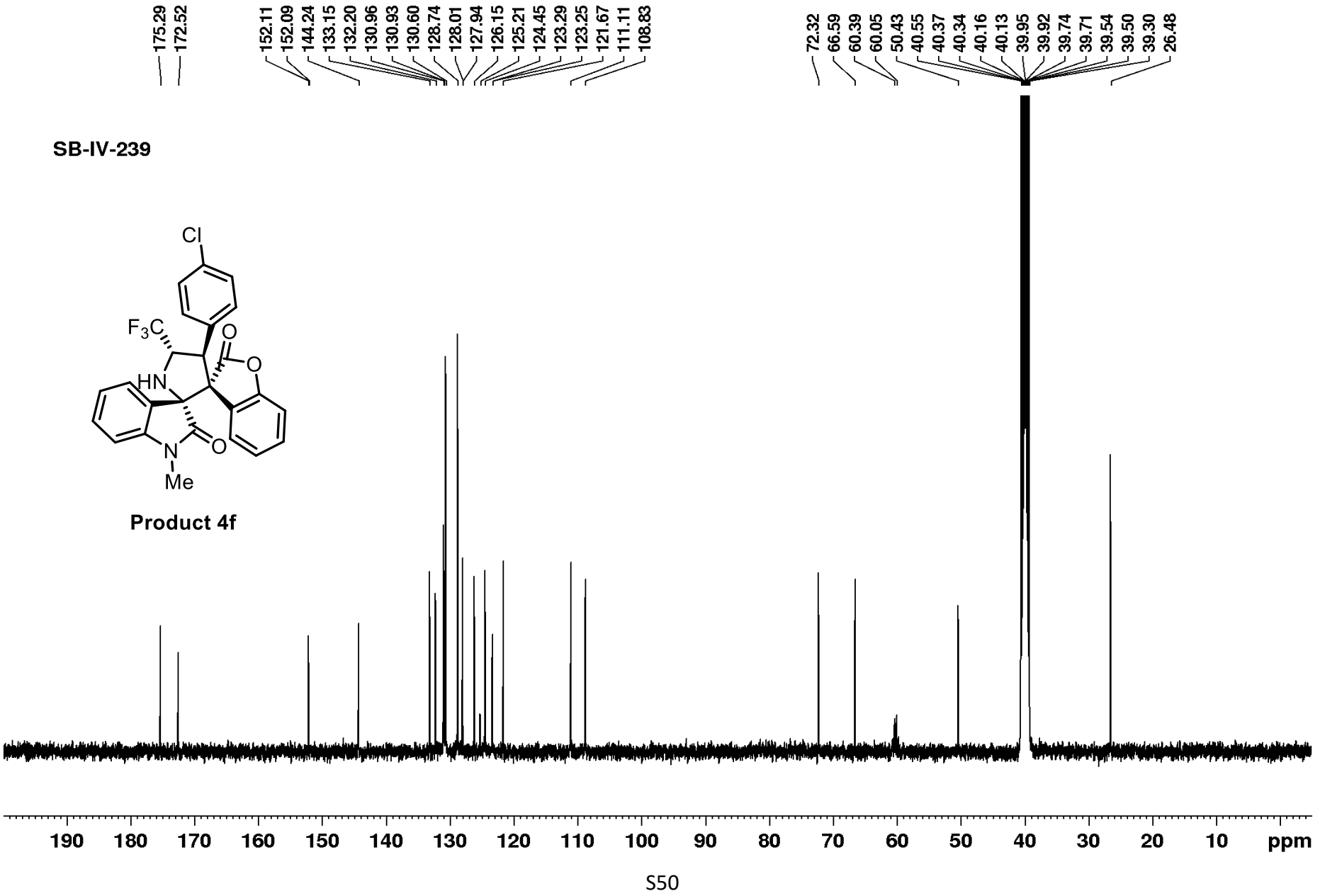

131.01
130.95
130.62
128.58
128.45
127.98
127.66
126.21
124.45
121.69
111.15
108.84
60.51
60.21
59.91
59.61
50.63
40.55
40.34
40.14
39.93
39.73
26.47
SB-IV-236
Cl
F3C
O
O
HN
O
N
Me
Product 4e
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

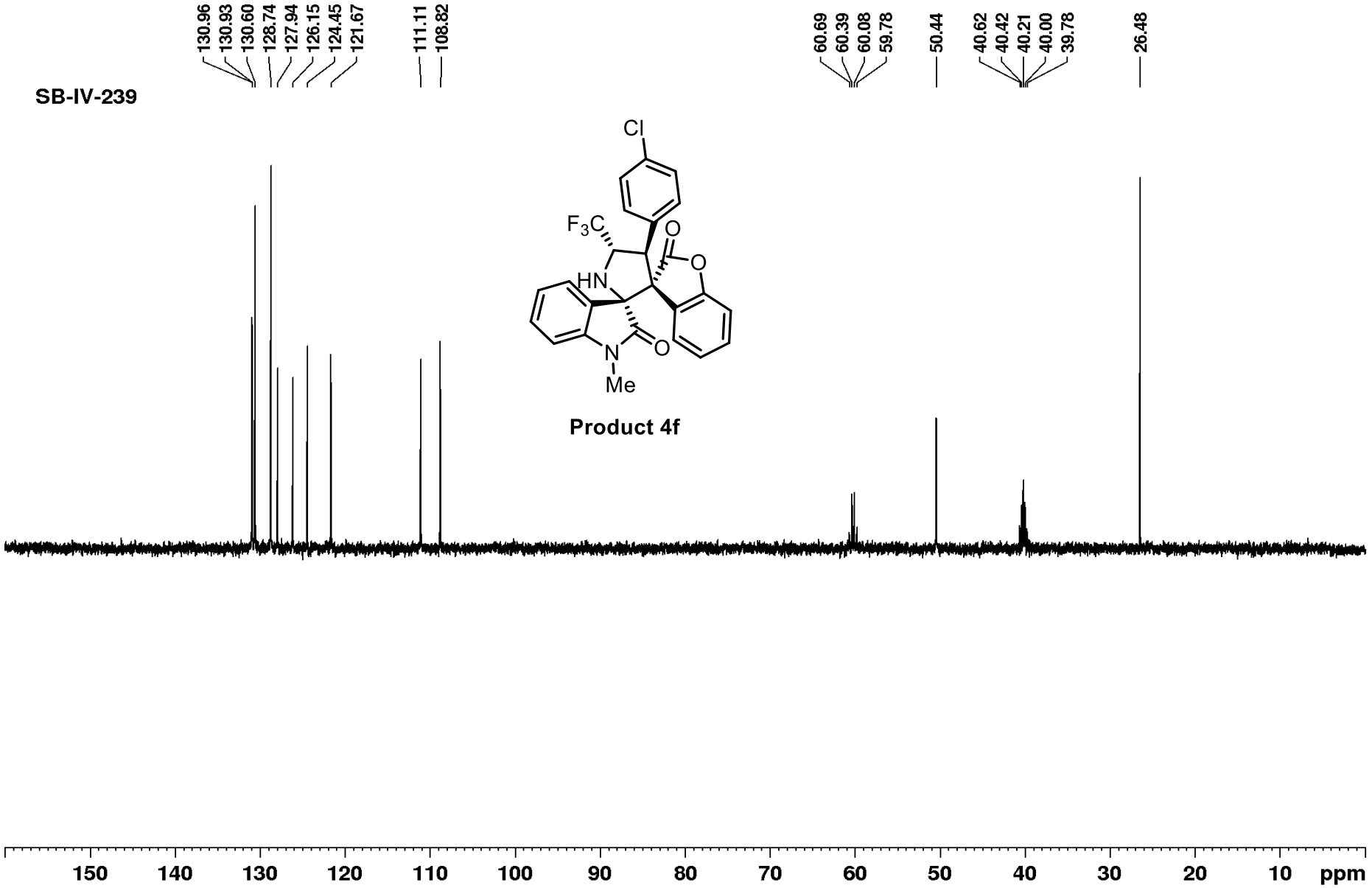

8.193
8.175
7.389
7.370
7.352
7.333
7.315
7.296
7.225
7.217
7.209
7.195
7.131
7.110
6.920
6.900
6.895
6.875
6.762
6.743
6.671
6.652
6.633
5.423
5.397
5.156
5.134
5.111
5.103
5.086
5.065
3.398
3.102
2.511
2.507
2.503
SB-IV-239
Cl
F3C
O
O
HN
O
N
Me
Product 4f
9
8
7
6
5
4
3
2
1
0 ppm
1.008
2.094
3.000
2.023
2.048
1.017
1.026
1.000
2.064
3.011

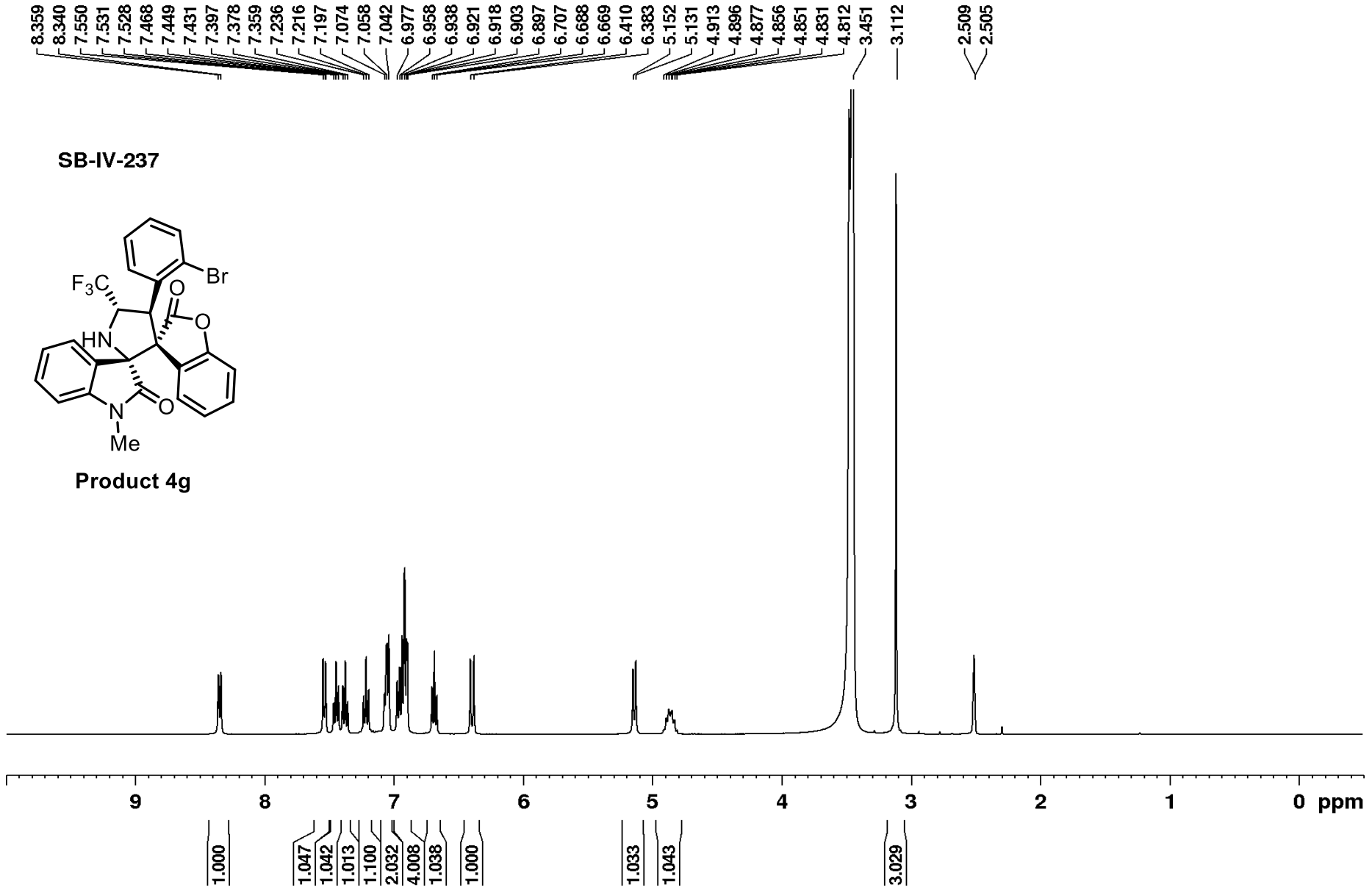
SB-IV-239

Product 4f



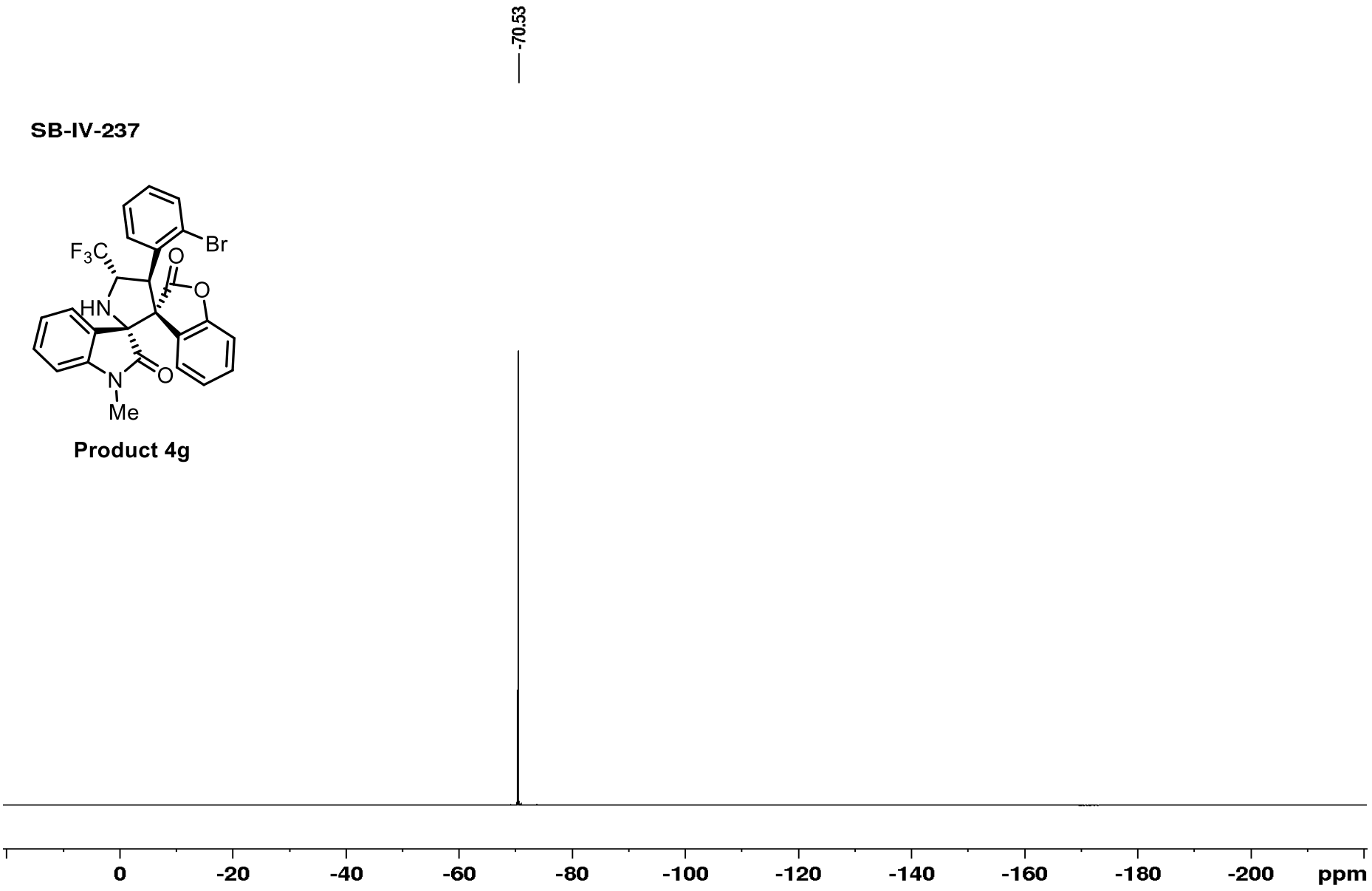

175.29
172.52
152.11
152.09
144.24
133.15
132.20
130.96
130.93
130.60
128.74
128.01
127.94
126.15
125.21
124.45
123.29
123.25
121.67
111.11
108.83
72.32
66.59
60.39
60.05
50.43
40.55
40.37
40.34
40.16
40.13
39.95
39.92
39.74
39.71
39.54
39.50
39.30
26.48
SB-IV-239
Cl
F3C
O
O
HN
N
O
Me
Product 4f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

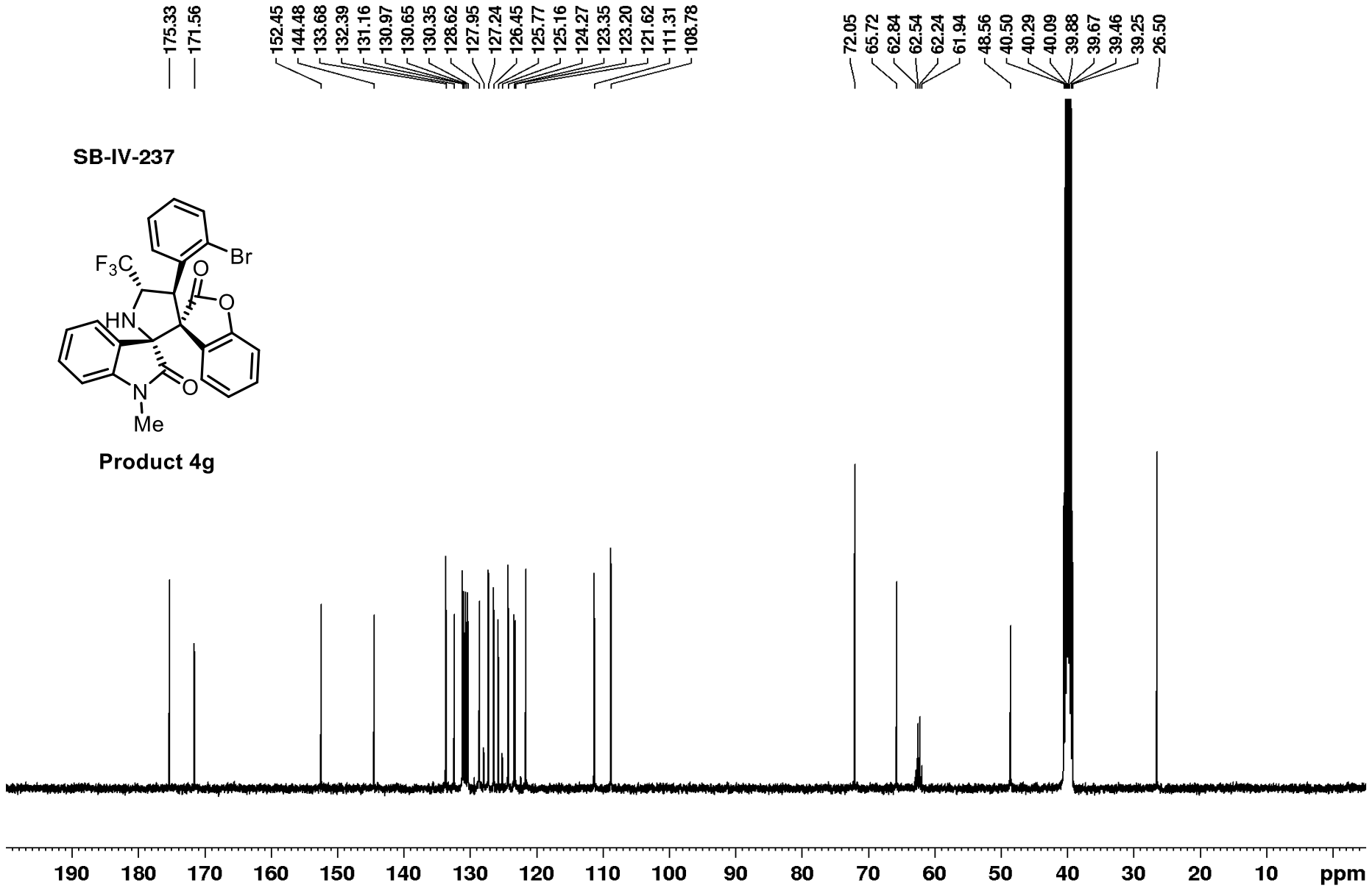

130.96
130.93
130.60
128.74
127.94
126.15
124.45
121.67
111.11
108.82
60.69
60.39
60.08
59.78
50.44
40.62
40.42
40.21
40.00
39.78
26.48
SB-IV-239
Cl
F3C
O
O
HN
O
N
Me
Product 4f
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

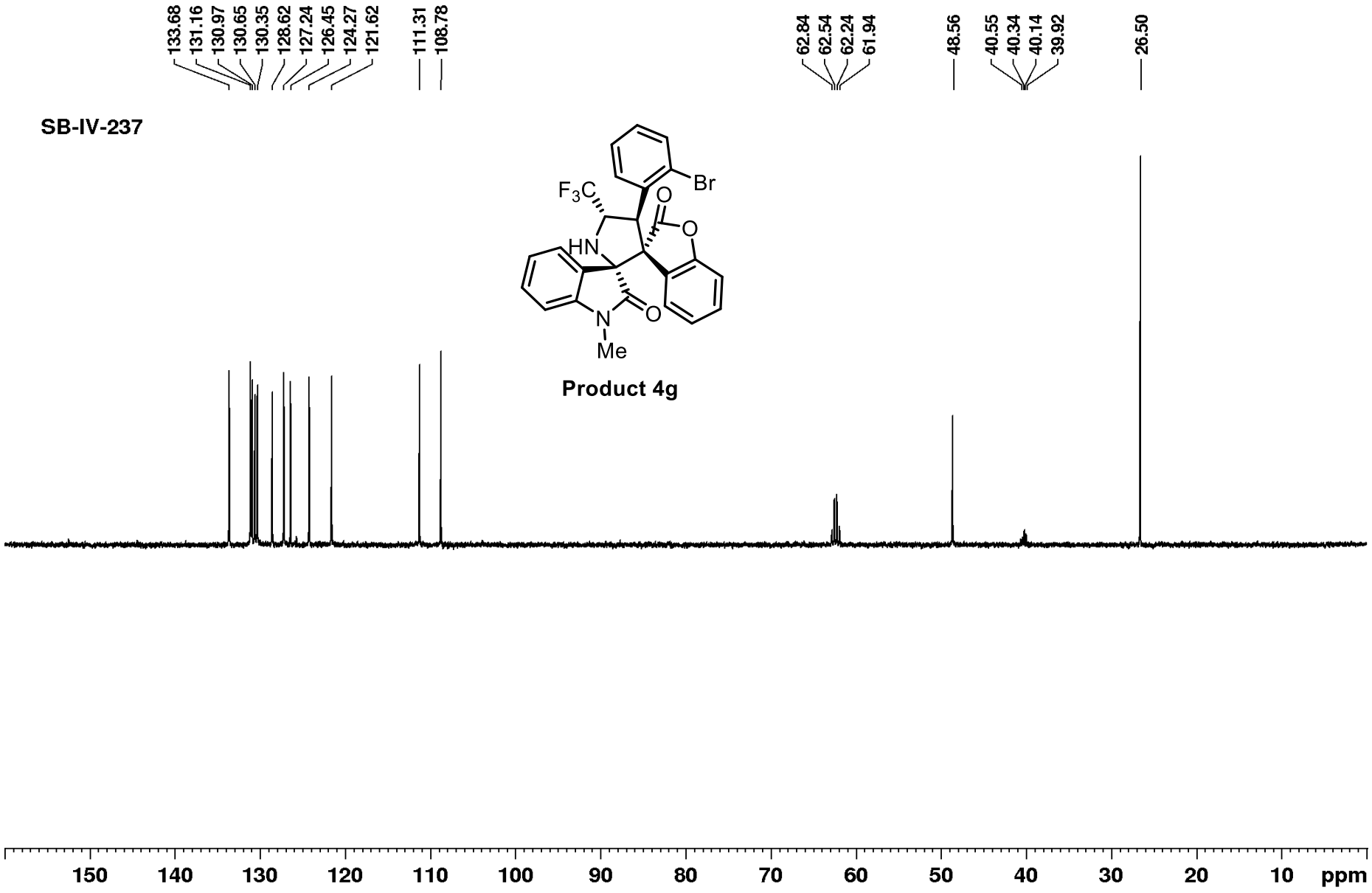

8.359
8.340
7.550
7.531
7.528
7.468
7.449
7.431
7.397
7.378
7.359
7.236
7.216
7.197
7.074
7.058
7.042
6.977
6.958
6.938
6.921
6.918
6.903
6.897
6.707
6.688
6.669
6.410
6.383
5.152
5.131
4.913
4.896
4.877
4.856
4.851
4.831
4.812
3.451
3.112
2.509
2.505
SB-IV-237
F3C
Br
O
O
HN
O
N
Me
Product 4g
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.047
1.042
1.013
1.100
2.032
4.008
1.038
1.000
1.033
1.043
3.029

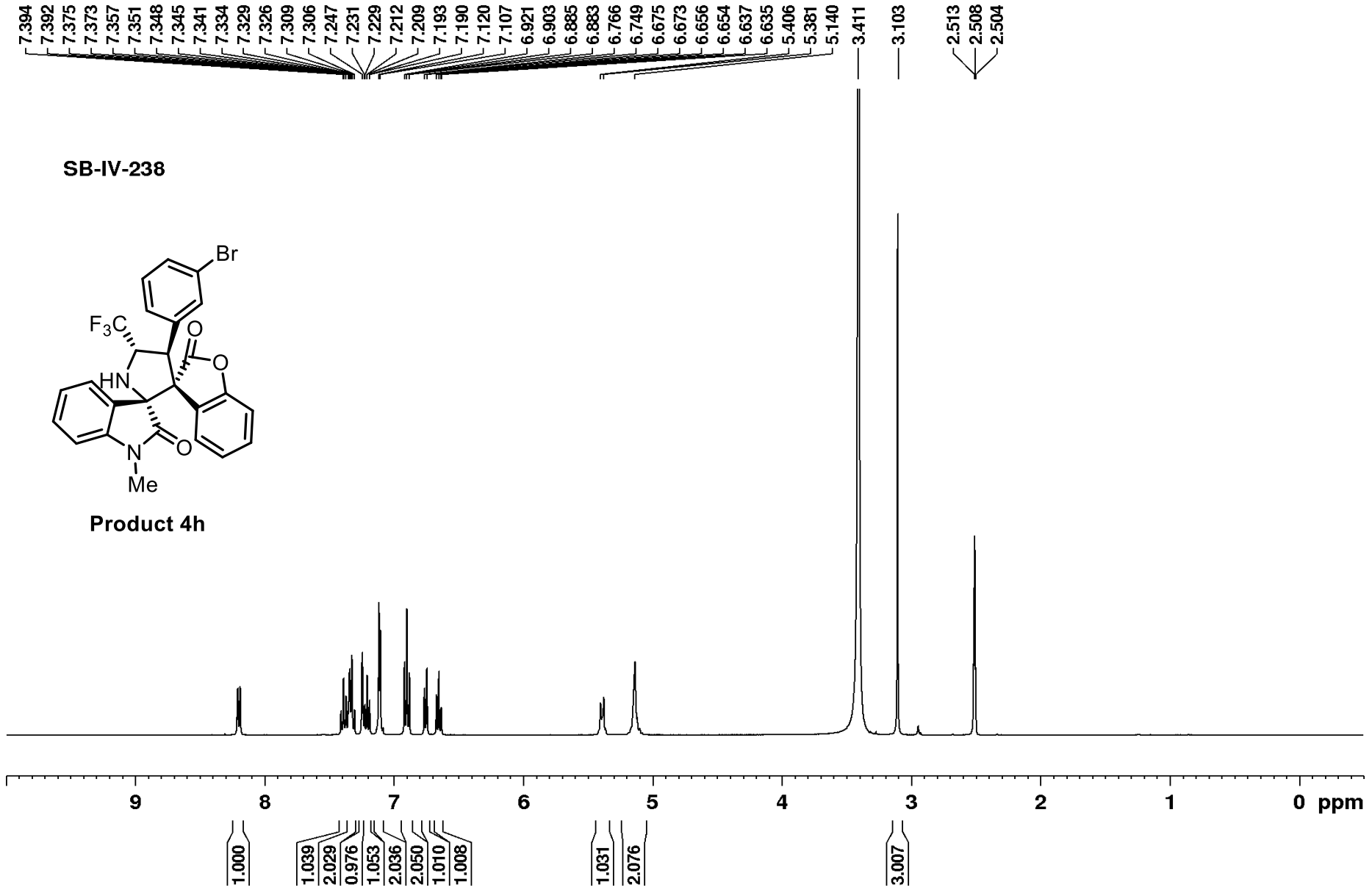
SB-IV-237

Product 4g



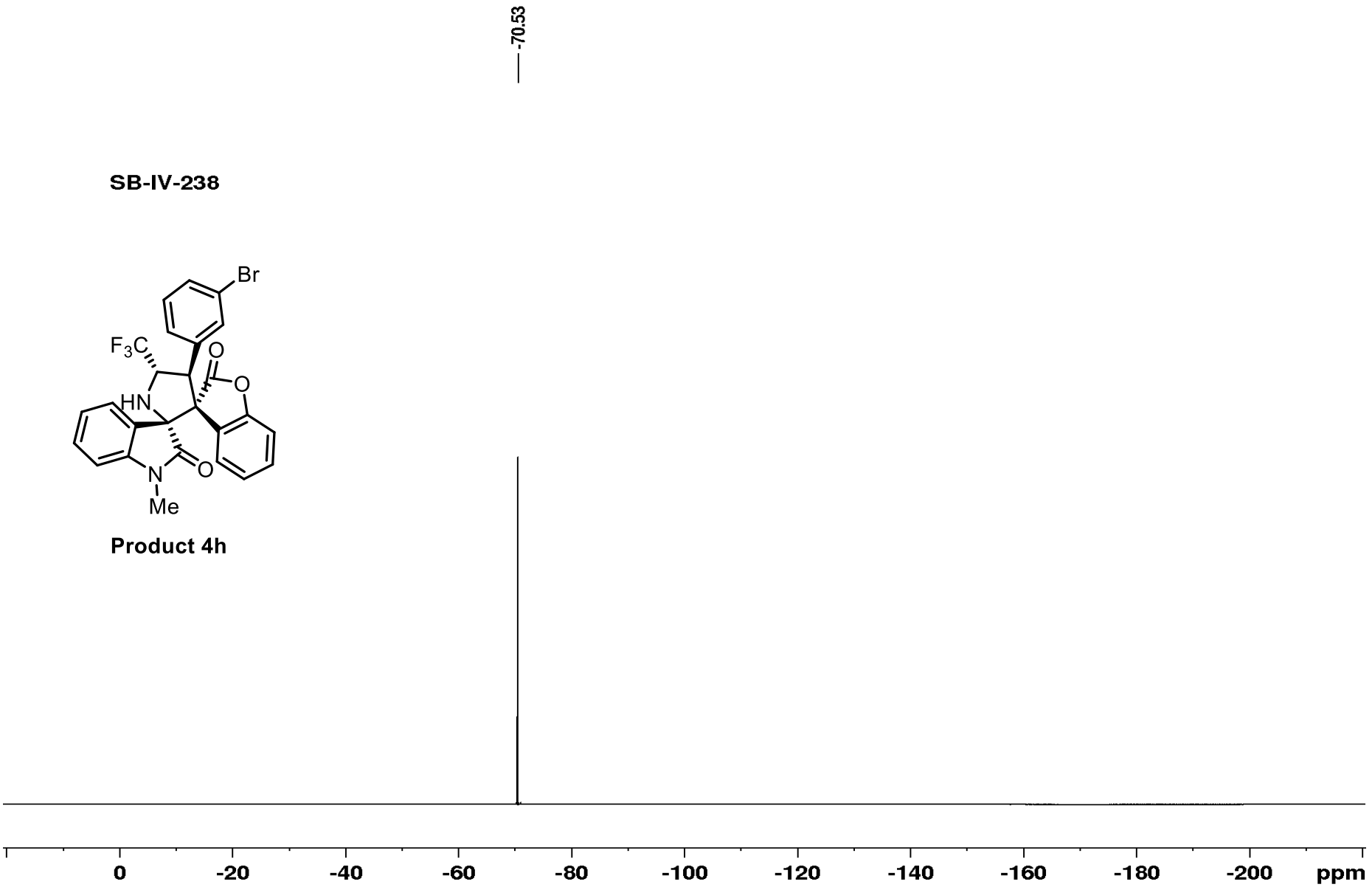

175.33
171.56
152.45
144.48
133.68
132.39
131.16
130.97
130.65
130.35
128.62
127.95
127.24
126.45
125.77
125.16
124.27
123.35
123.20
121.62
111.31
108.78
72.05
65.72
62.84
62.54
62.24
61.94
48.56
40.50
40.29
40.09
39.88
39.67
39.46
39.25
26.50
SB-IV-237
F3C
Br
O
O
HN
O
N
Me
Product 4g
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

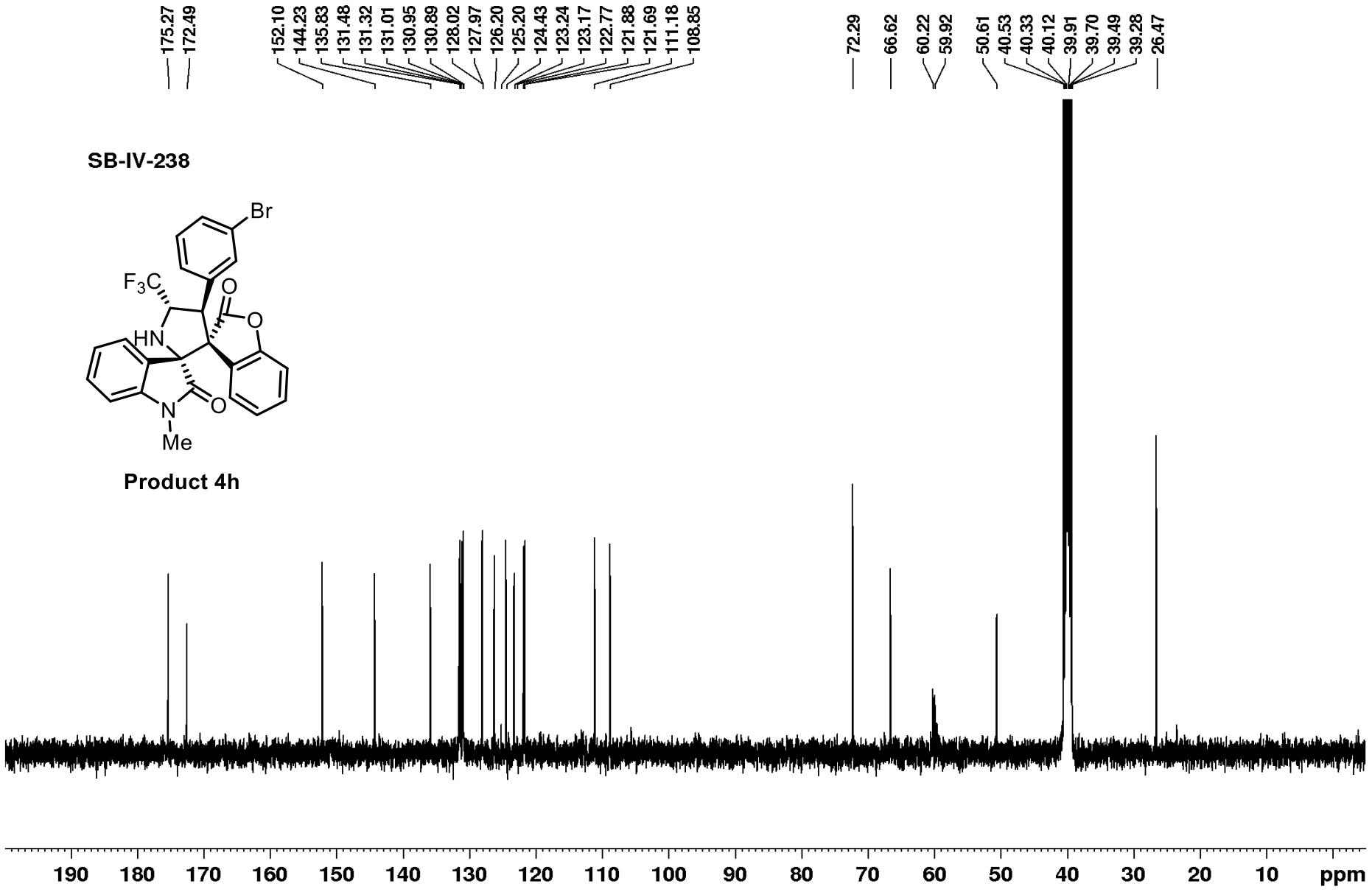

133.68
131.16
130.97
130.65
130.35
128.62
127.24
126.45
124.27
121.62
111.31
108.78
62.84
62.54
62.24
61.94
48.56
40.55
40.34
40.14
39.92
26.50
SB-IV-237
Br
F3C
O
O
HN
O
N
Me
Product 4g
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

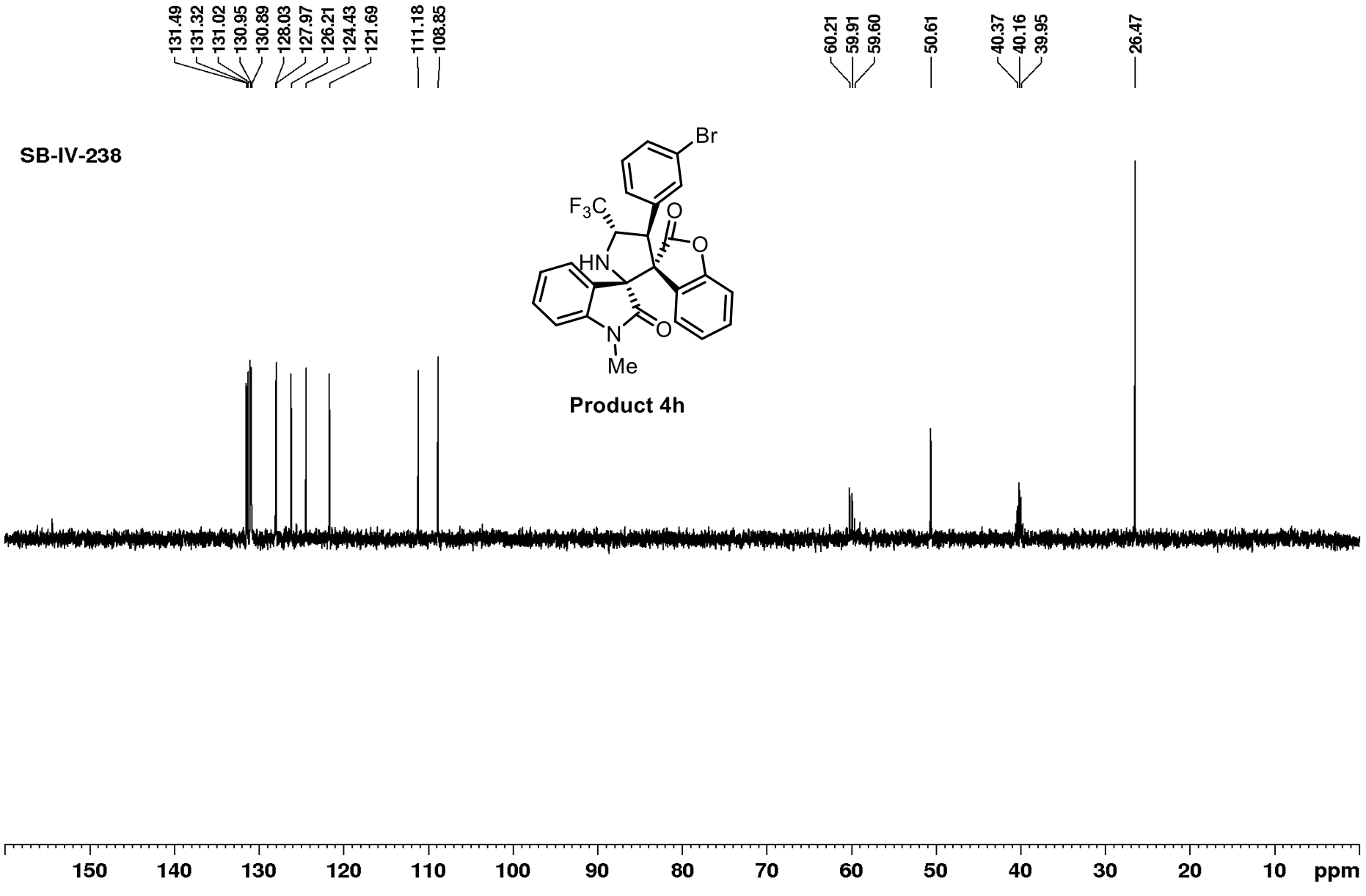

7.394
7.392
7.375
7.373
7.357
7.351
7.348
7.345
7.341
7.334
7.329
7.326
7.309
7.306
7.247
7.231
7.229
7.212
7.209
7.193
7.190
7.120
7.107
6.921
6.903
6.885
6.883
6.766
6.749
6.675
6.673
6.656
6.654
6.637
6.635
5.406
5.381
5.140
3.411
3.103
2.513
2.508
2.504
SB-IV-238
Br
F3C
O
O
HN
O
N
Me
Product 4h
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.039
2.029
0.976
1.053
2.036
2.050
1.010
1.008
1.031
2.076
3.007

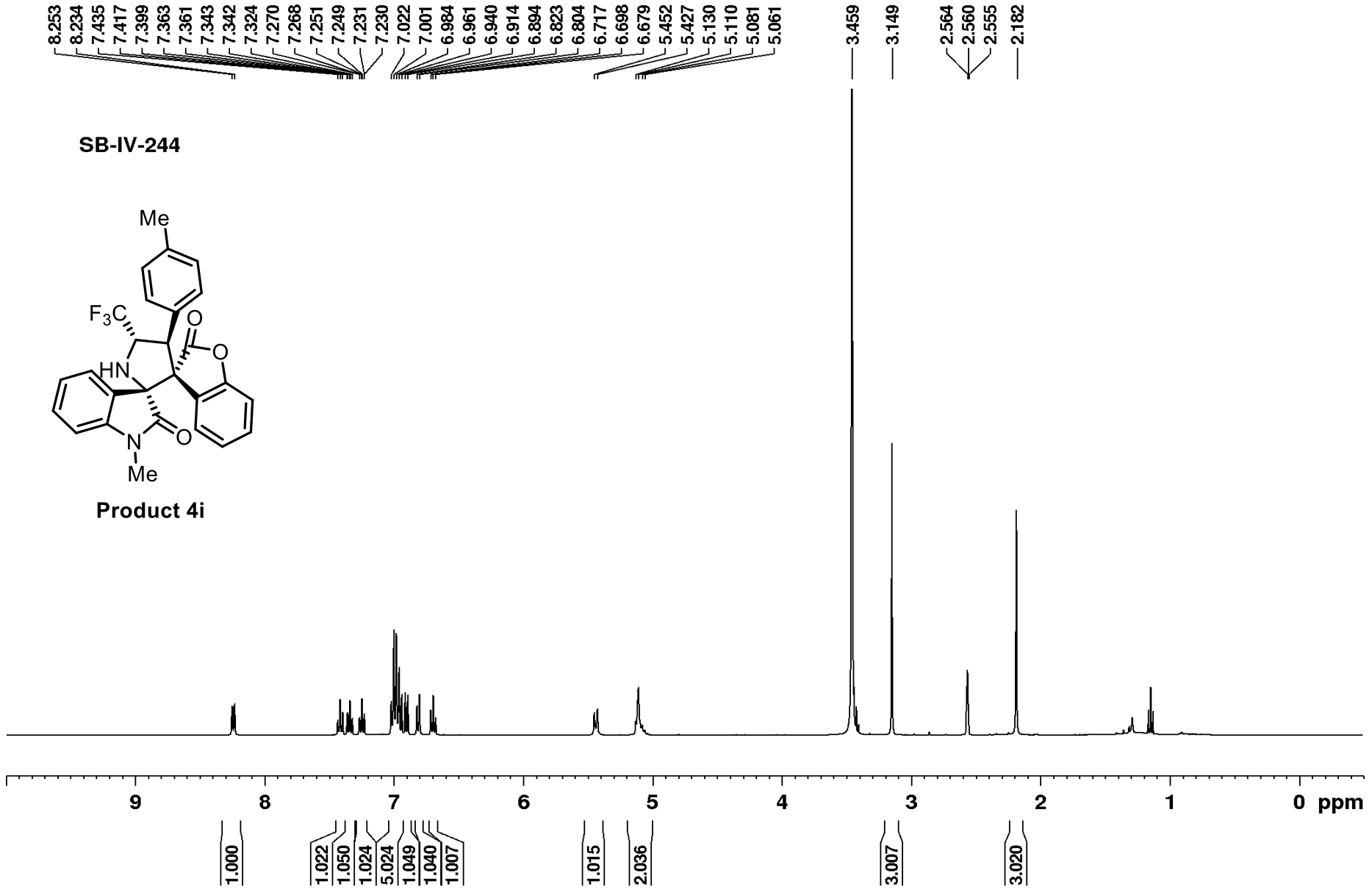
SB-IV-238

Product 4h



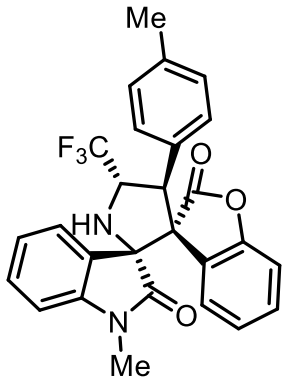

175.27
172.49
152.10
144.23
135.83
131.48
131.32
131.01
130.95
130.89
128.02
127.97
126.20
125.20
124.43
123.24
123.17
122.77
121.88
121.69
111.18
108.85
72.29
66.62
60.22
59.92
50.61
40.53
40.33
40.12
39.91
39.70
39.49
39.28
26.47
SB-IV-238
Br
F3C
O
O
HN
O
N
Me
Product 4h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


131.49
131.32
131.02
130.95
130.89
128.03
127.97
126.21
124.43
121.69
111.18
108.85
60.21
59.91
59.60
50.61
40.37
40.16
39.95
26.47
SB-IV-238
Br
F3C
O
O
HN
N
O
Me
Product 4h
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

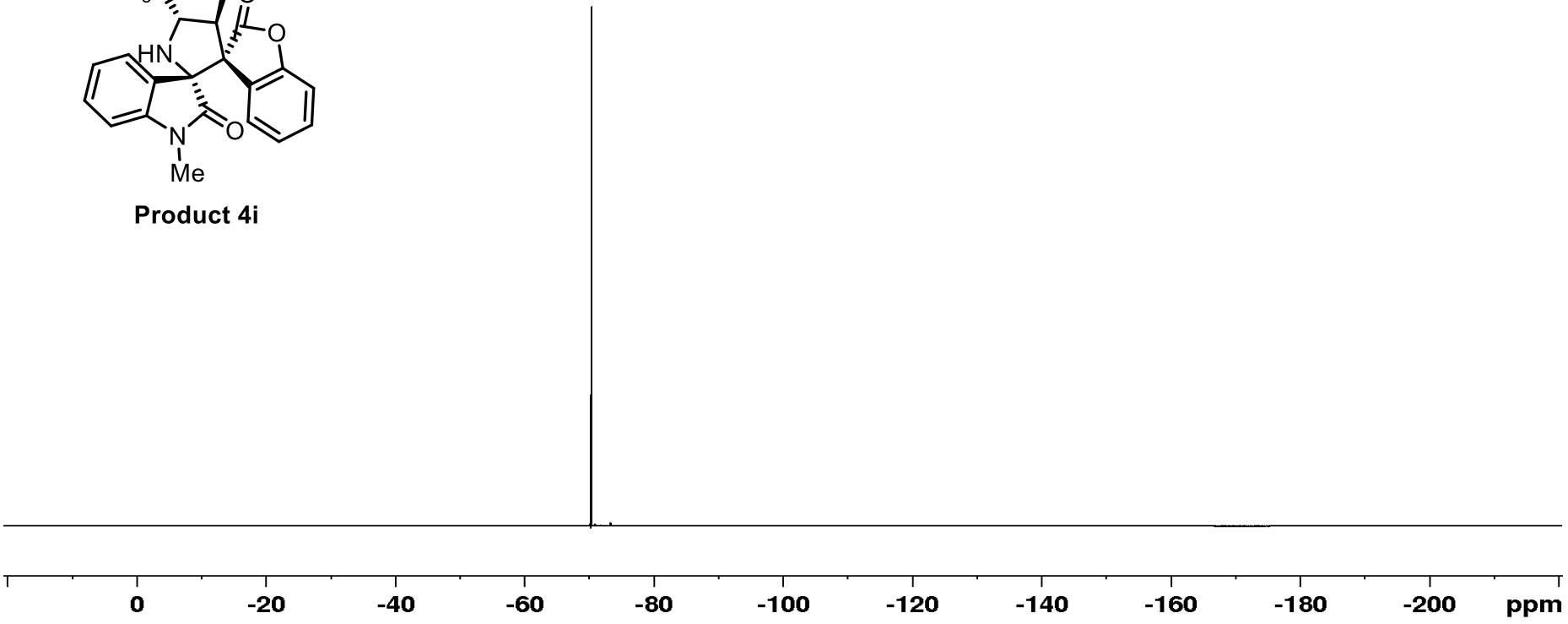

8.253
8.234
7.435
7.417
7.399
7.363
7.361
7.343
7.342
7.324
7.270
7.268
7.251
7.249
7.231
7.230
7.022
7.001
6.984
6.961
6.940
6.914
6.894
6.823
6.804
6.717
6.698
6.679
5.452
5.427
5.130
5.110
5.081
5.061
3.459
3.149
2.564
2.560
2.555
2.182
SB-IV-244
Me
F3C
O
O
HN
O
N
Me
Product 4i
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.022
1.050
1.024
5.024
1.049
1.040
1.007
1.015
2.036
3.007
3.020

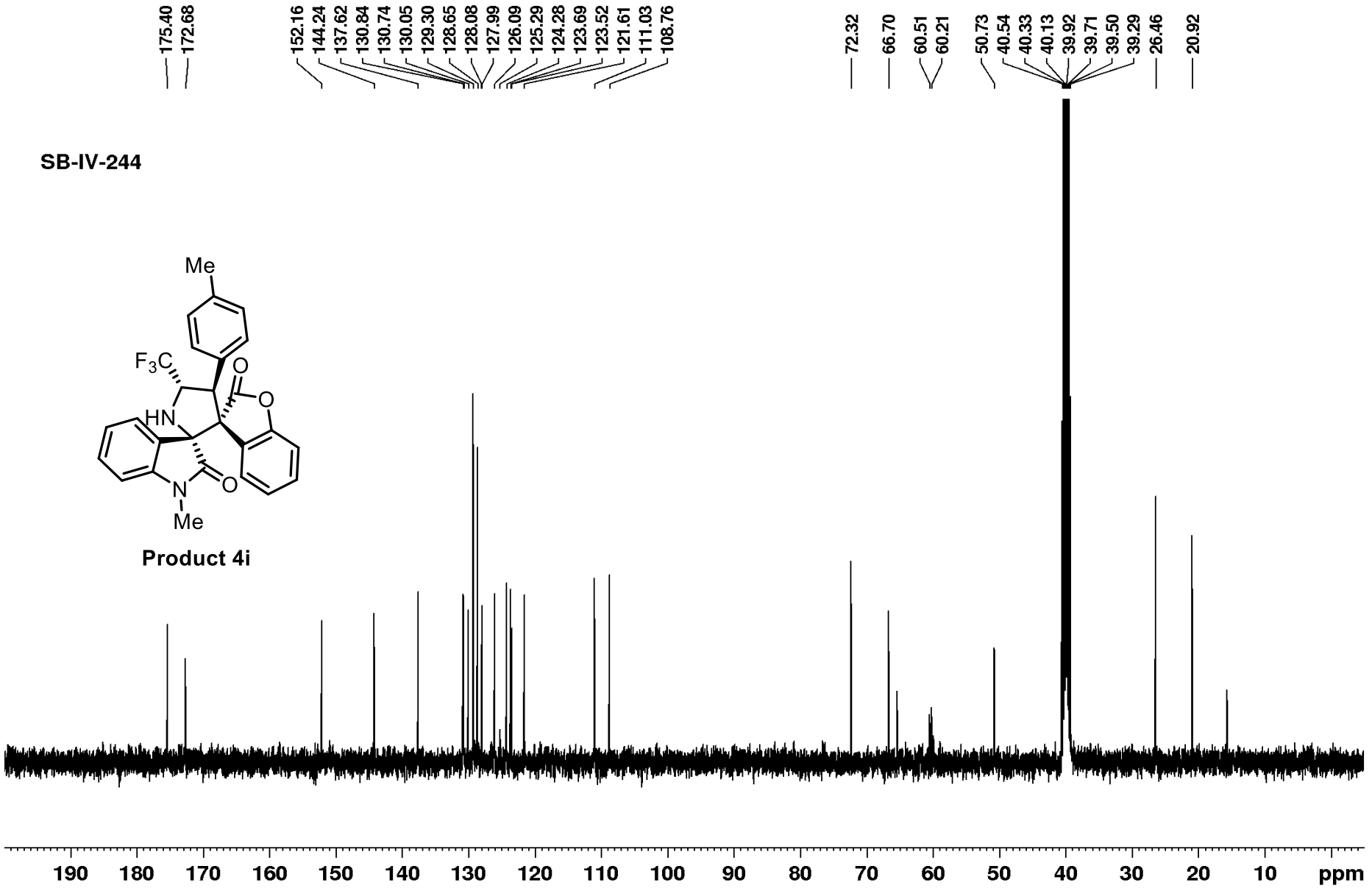
-70.38

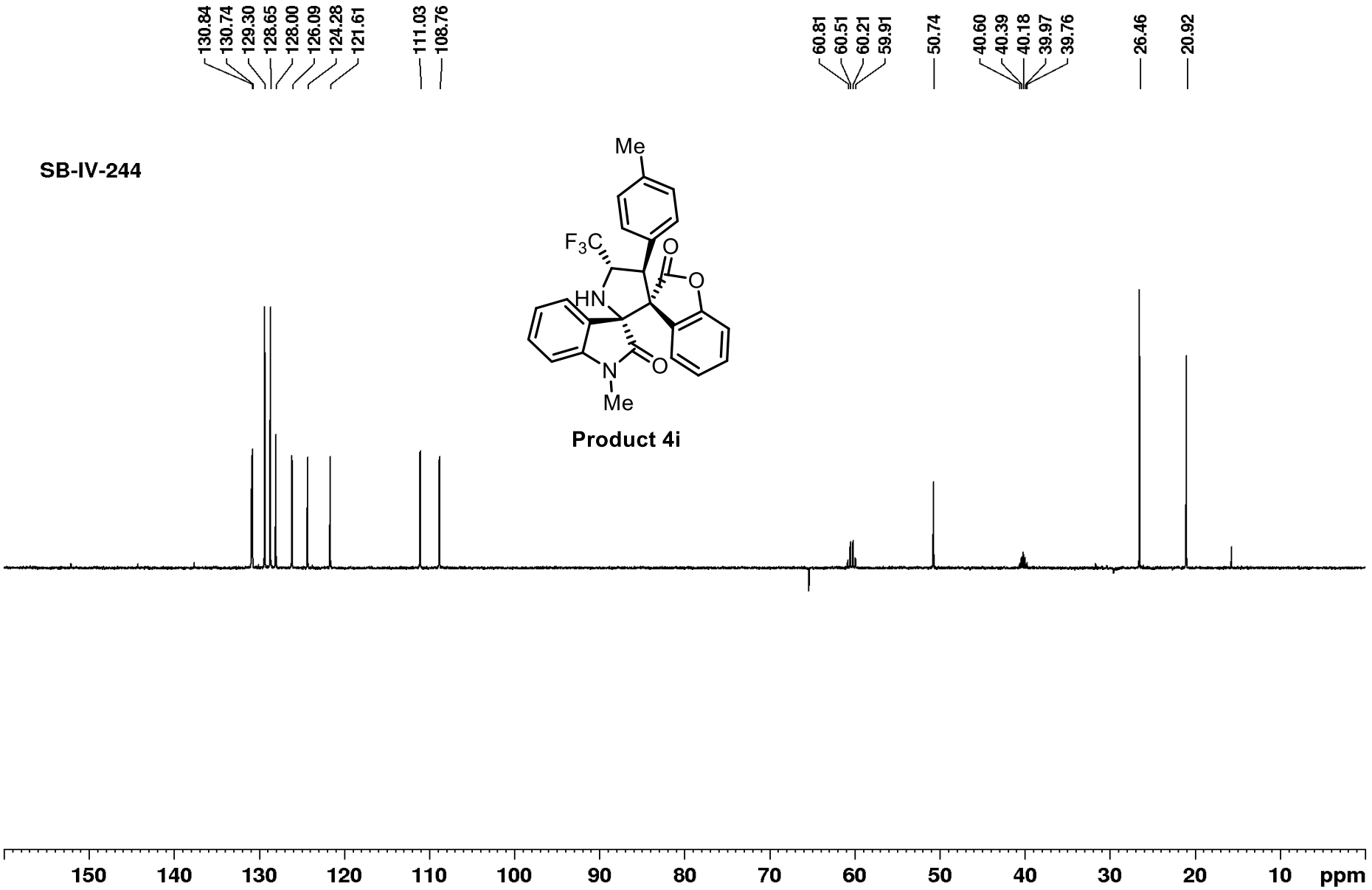
SB-IV-244

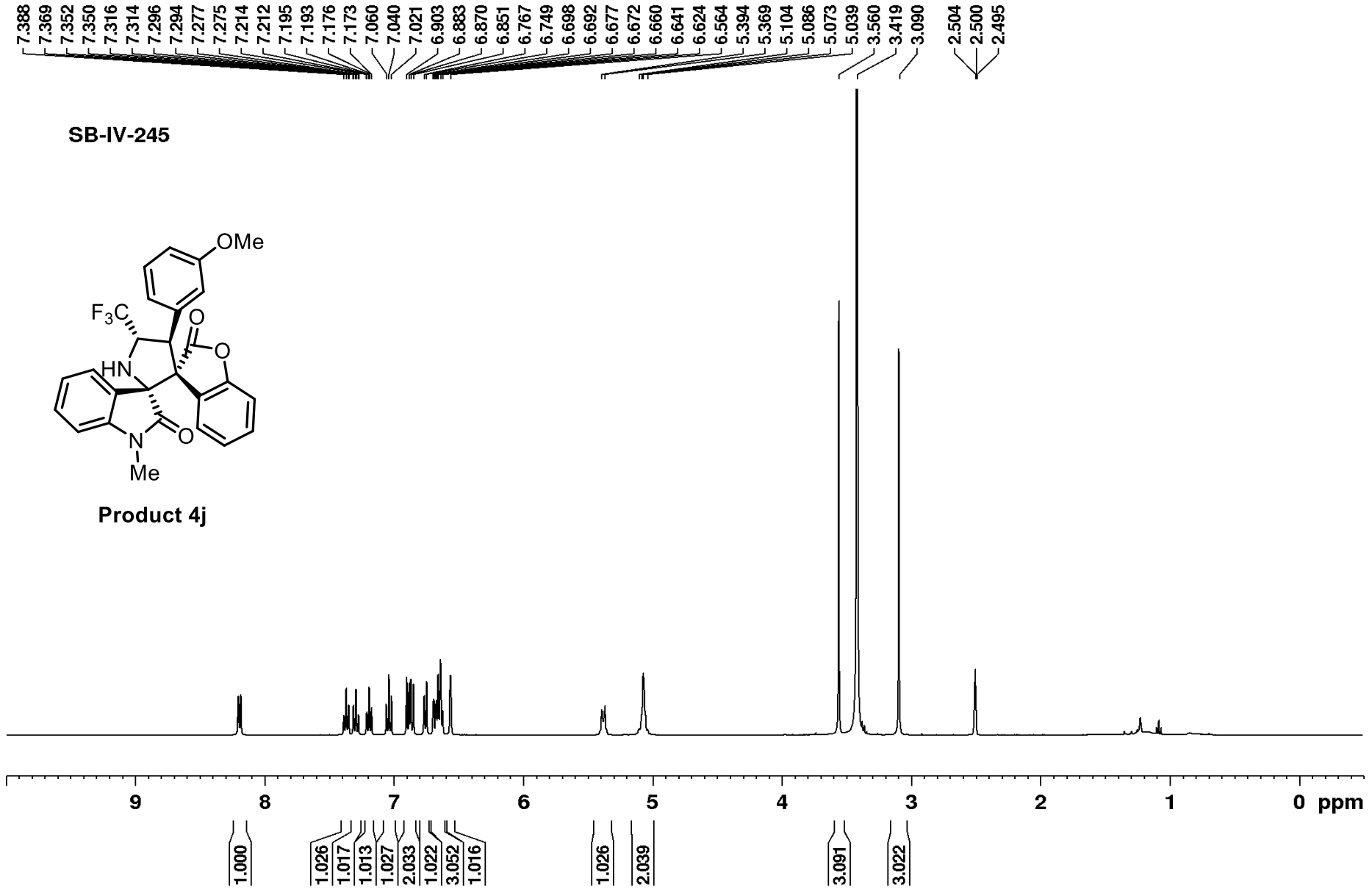


Product 4i



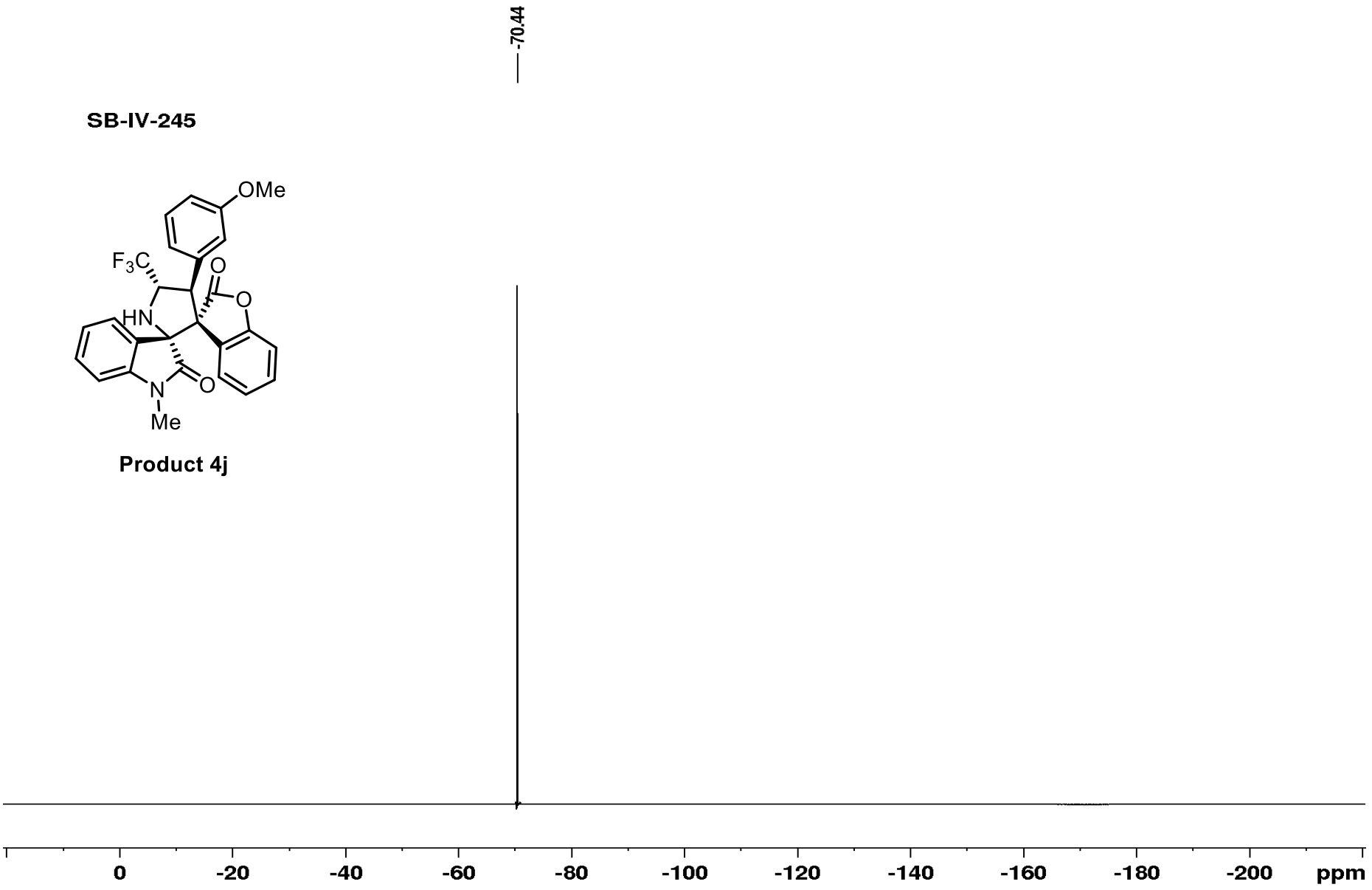

175.40
172.68
152.16
144.24
137.62
130.84
130.74
130.05
129.30
128.65
128.08
127.99
126.09
125.29
124.28
123.69
123.52
121.61
111.03
108.76
72.32
66.70
60.51
60.21
50.73
40.54
40.33
40.13
39.92
39.71
39.50
39.29
26.46
20.92
SB-IV-244
Me
F3C
O
O
HN
N
O
Me
Product 4i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

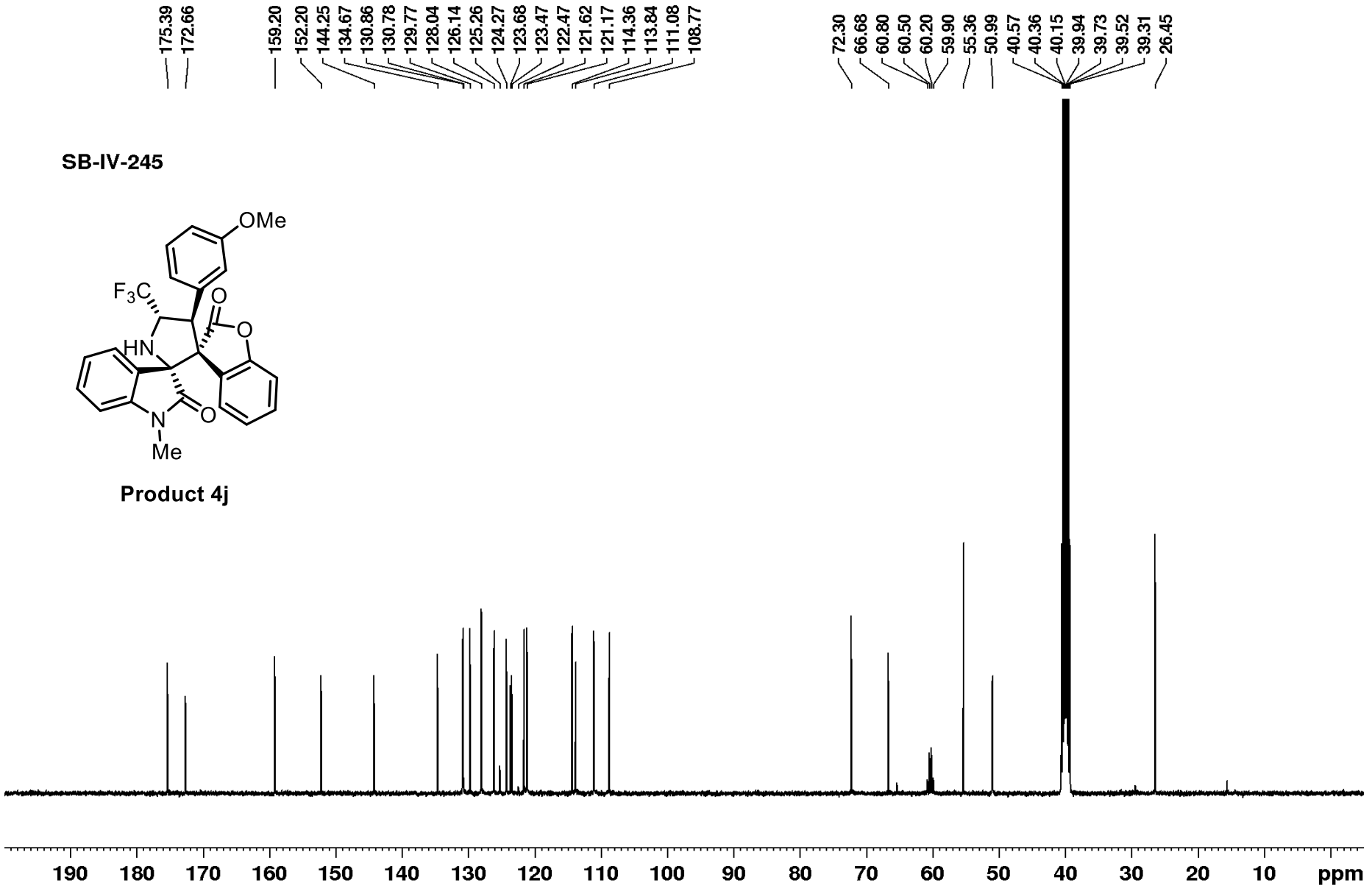

130.84
130.74
129.30
128.65
128.00
126.09
124.28
121.61
111.03
108.76
60.81
60.51
60.21
59.91
50.74
40.60
40.39
40.18
39.97
39.76
26.46
20.92
SB-IV-244
Me
F3C
O
O
HN
O
N
Me
Product 4i
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

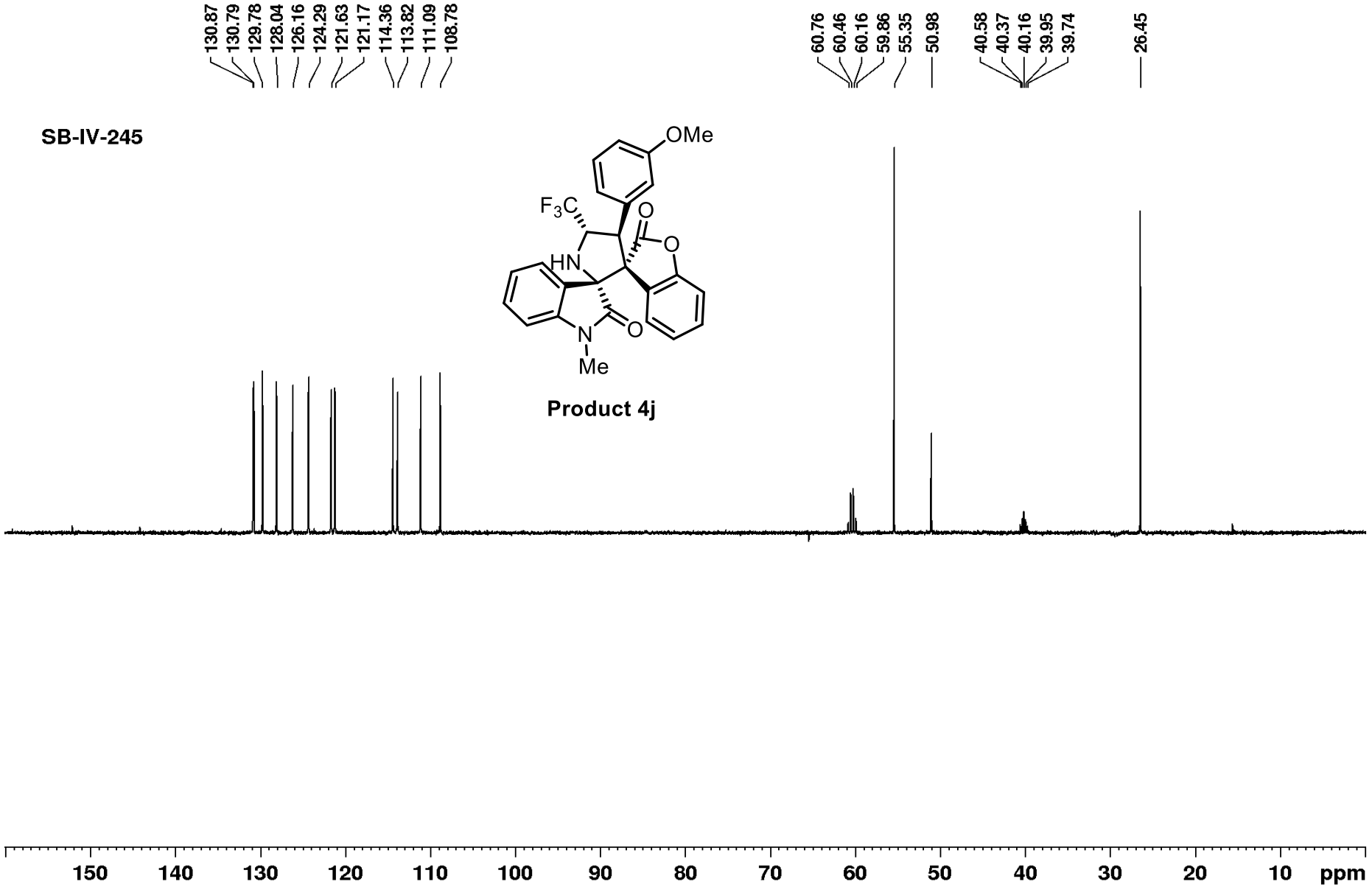

7.388
7.369
7.352
7.350
7.316
7.314
7.296
7.294
7.277
7.275
7.214
7.212
7.195
7.193
7.176
7.173
7.060
7.040
7.021
6.903
6.883
6.870
6.851
6.767
6.749
6.698
6.692
6.677
6.672
6.660
6.641
6.624
6.564
5.394
5.369
5.104
5.086
5.073
5.039
3.560
3.419
3.090
2.504
2.500
2.495
SB-IV-245
OMe
F3C
O
O
HN
O
N
Me
Product 4j
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.026
1.017
1.013
1.027
2.033
1.022
3.052
1.016
1.026
2.039
3.091
3.022

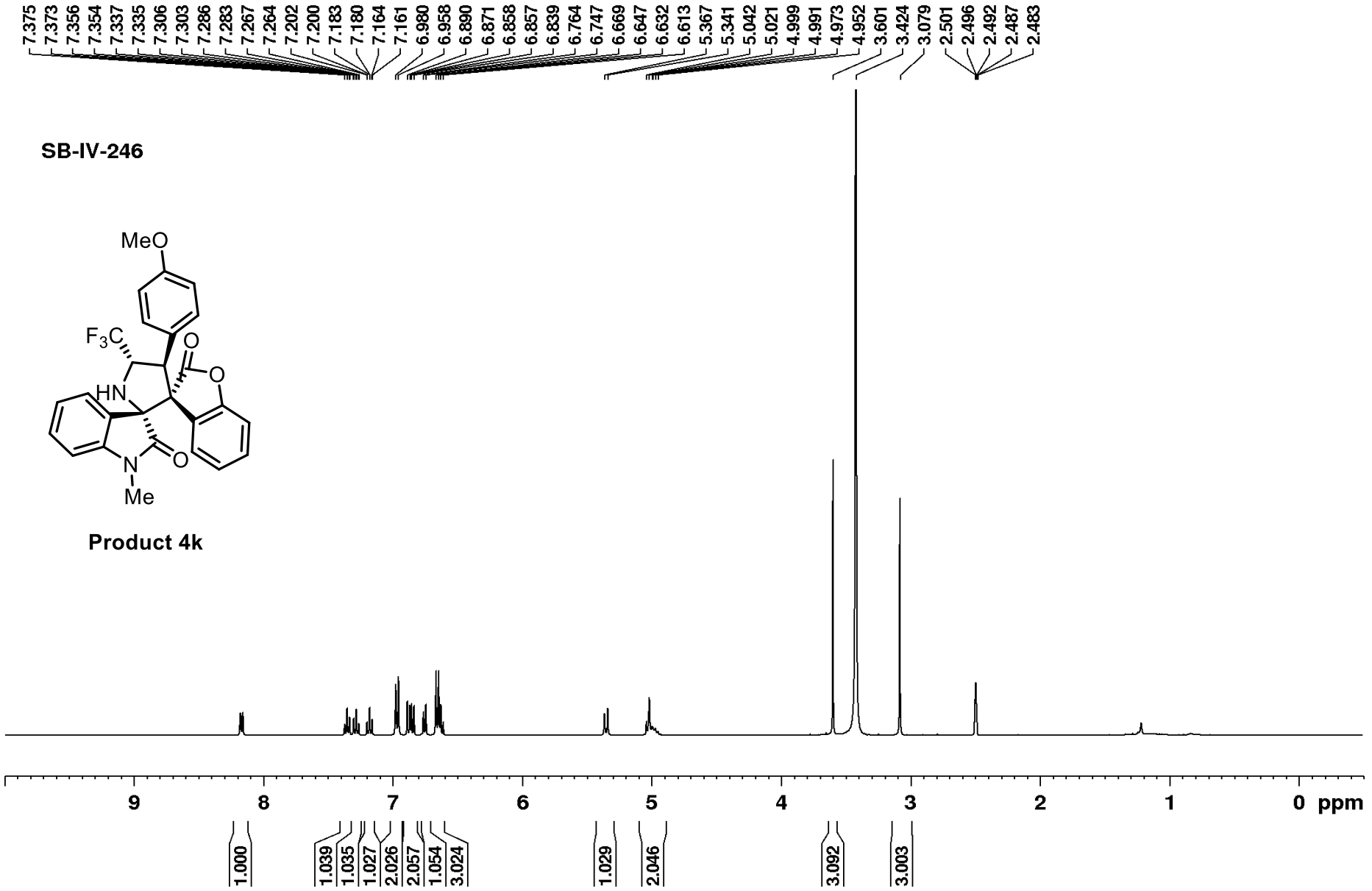
SB-IV-245

Product 4j



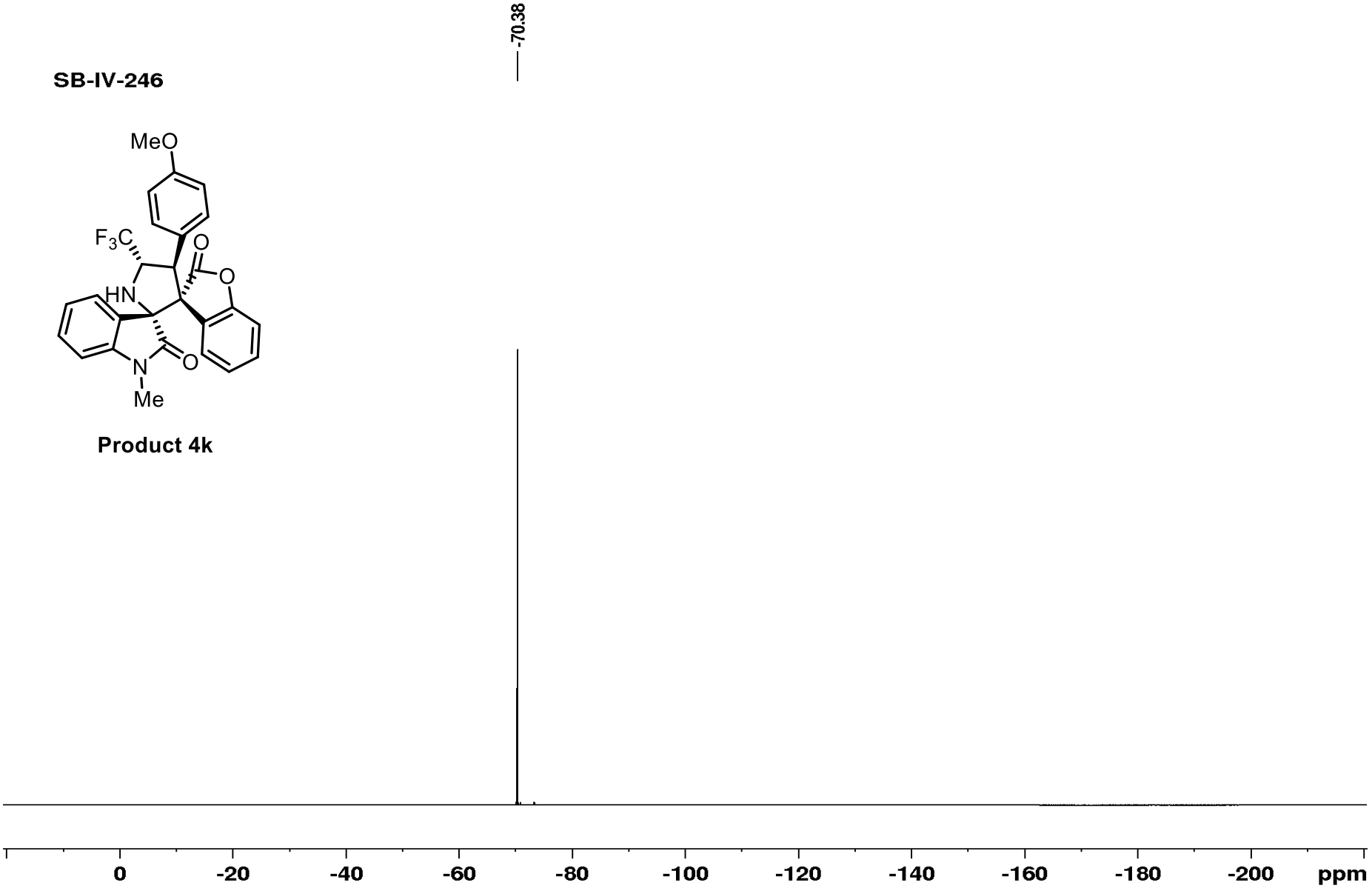

175.39
172.66
159.20
152.20
144.25
134.67
130.86
130.78
129.77
128.04
126.14
125.26
124.27
123.68
123.47
122.47
121.62
121.17
114.36
113.84
111.08
108.77
72.30
66.68
60.80
60.50
60.20
59.90
55.36
50.99
40.57
40.36
40.15
39.94
39.73
39.52
39.31
26.45
SB-IV-245
OMe
F3C
O
O
HN
O
N
Me
Product 4j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

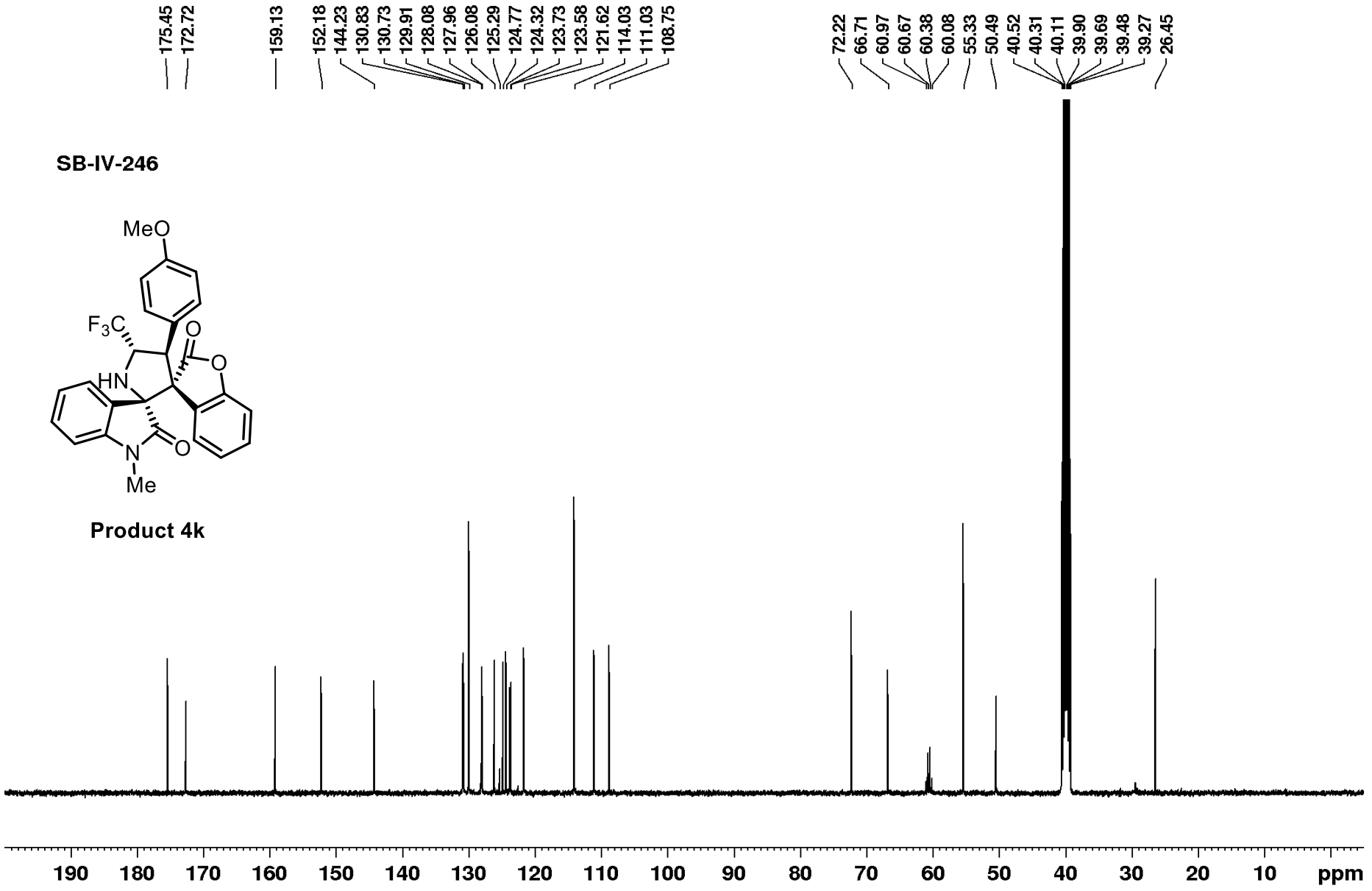

130.87
130.79
129.78
128.04
126.16
124.29
121.63
121.17
114.36
113.82
111.09
108.78
60.76
60.46
60.16
59.86
55.35
50.98
40.58
40.37
40.16
39.95
39.74
26.45
SB-IV-245
OMe
F3C
O
O
HN
O
N
Me
Product 4j
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

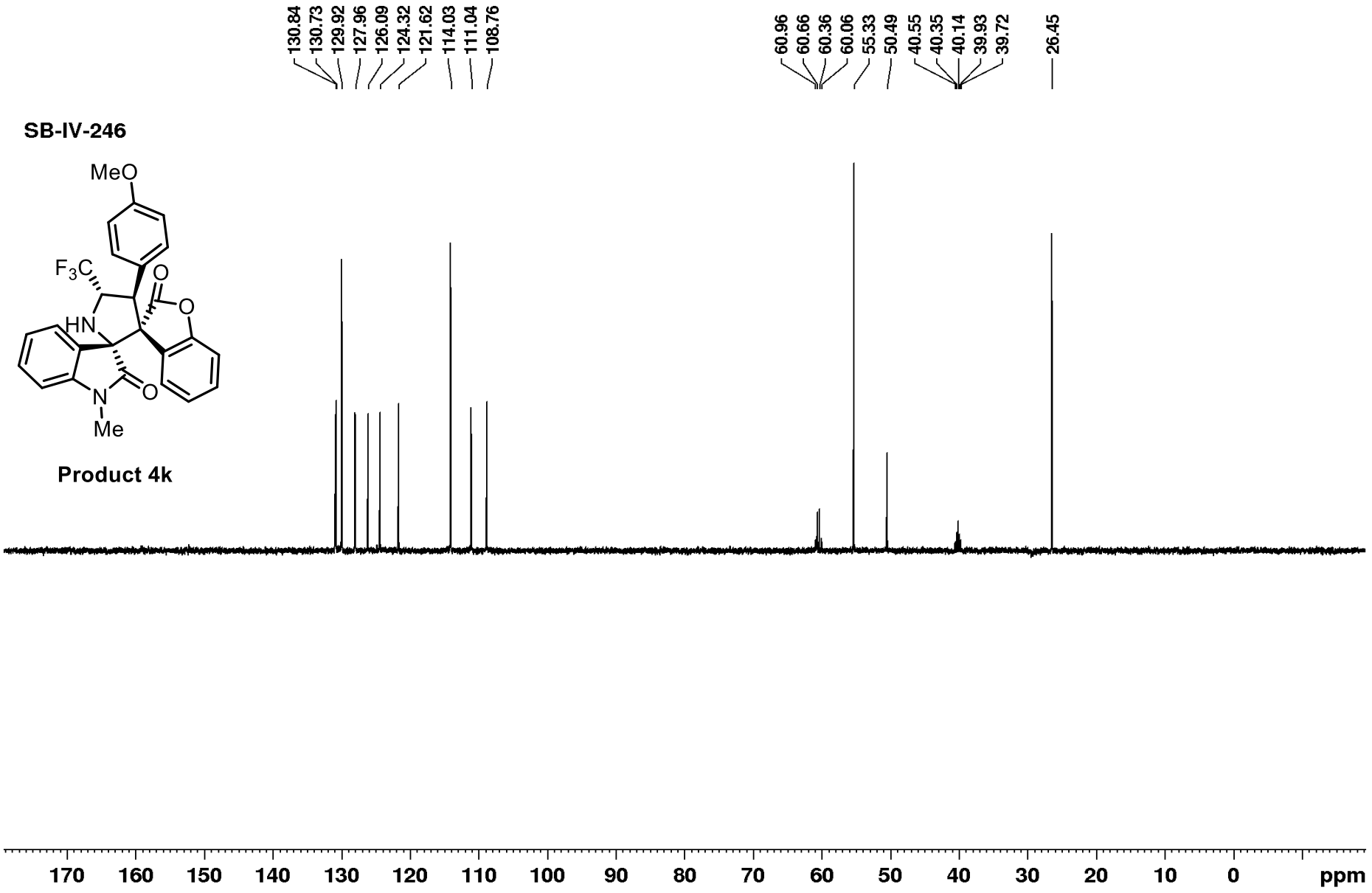

7.375
7.373
7.356
7.354
7.337
7.335
7.306
7.303
7.286
7.283
7.267
7.264
7.202
7.200
7.183
7.180
7.164
7.161
6.980
6.958
6.890
6.871
6.858
6.857
6.839
6.764
6.747
6.669
6.647
6.632
6.613
5.367
5.341
5.042
5.021
4.999
4.991
4.973
4.952
3.601
3.424
3.079
2.501
2.496
2.492
2.487
2.483
SB-IV-246
MeO
F3C
O
O
HN
O
N
Me
Product 4k
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.039
1.035
1.027
2.026
2.057
1.054
3.024
1.029
2.046
3.092
3.003

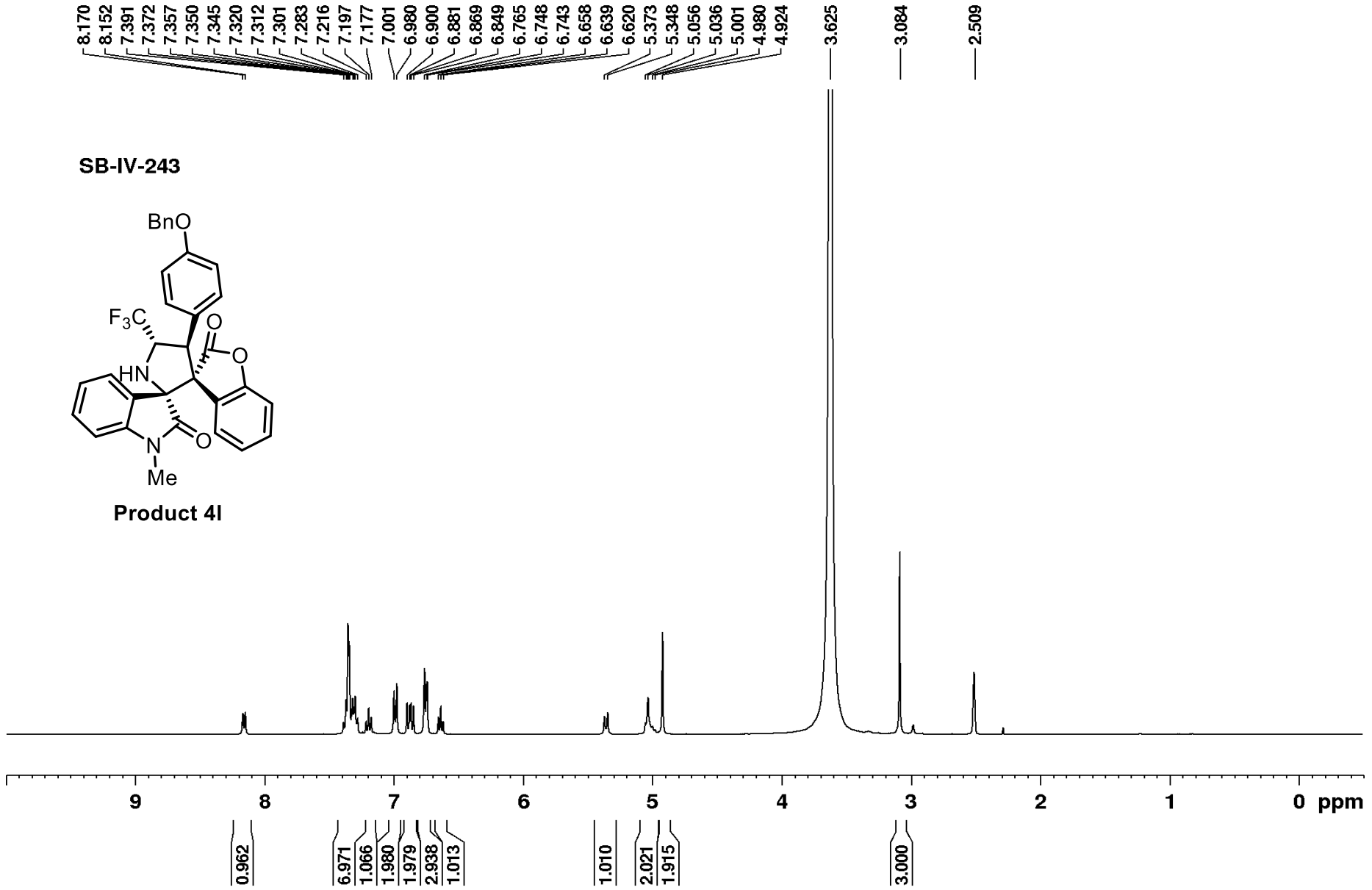
SB-IV-246

Product 4k



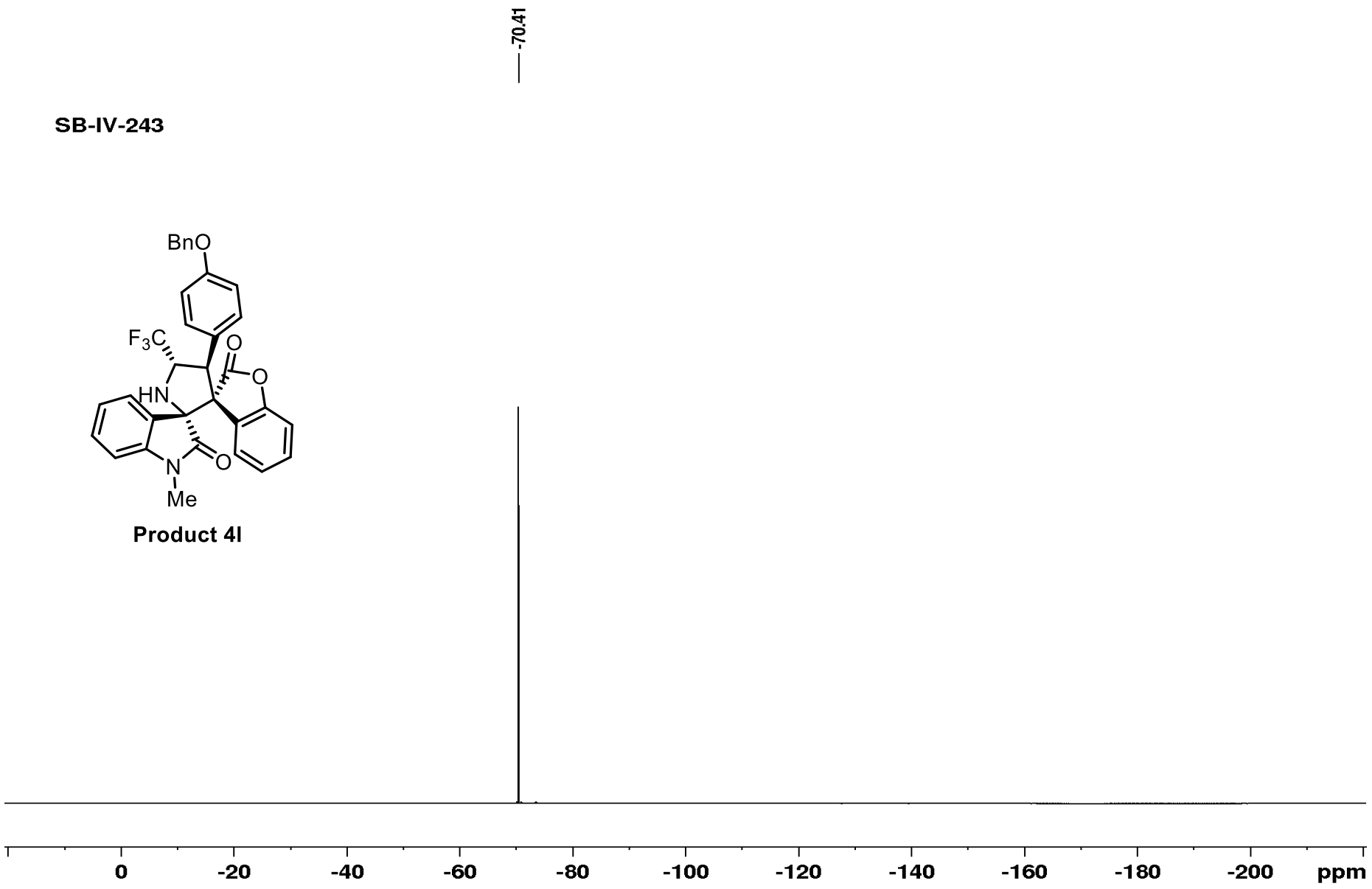

175.45
172.72
159.13
152.18
144.23
130.83
130.73
129.91
128.08
127.96
126.08
125.29
124.77
124.32
123.73
123.58
121.62
114.03
111.03
108.75
72.22
66.71
60.97
60.67
60.38
60.08
55.33
50.49
40.52
40.31
40.11
39.90
39.69
39.48
39.27
26.45
SB-IV-246
MeO
F3C
O
O
HN
O
N
Me
Product 4k
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

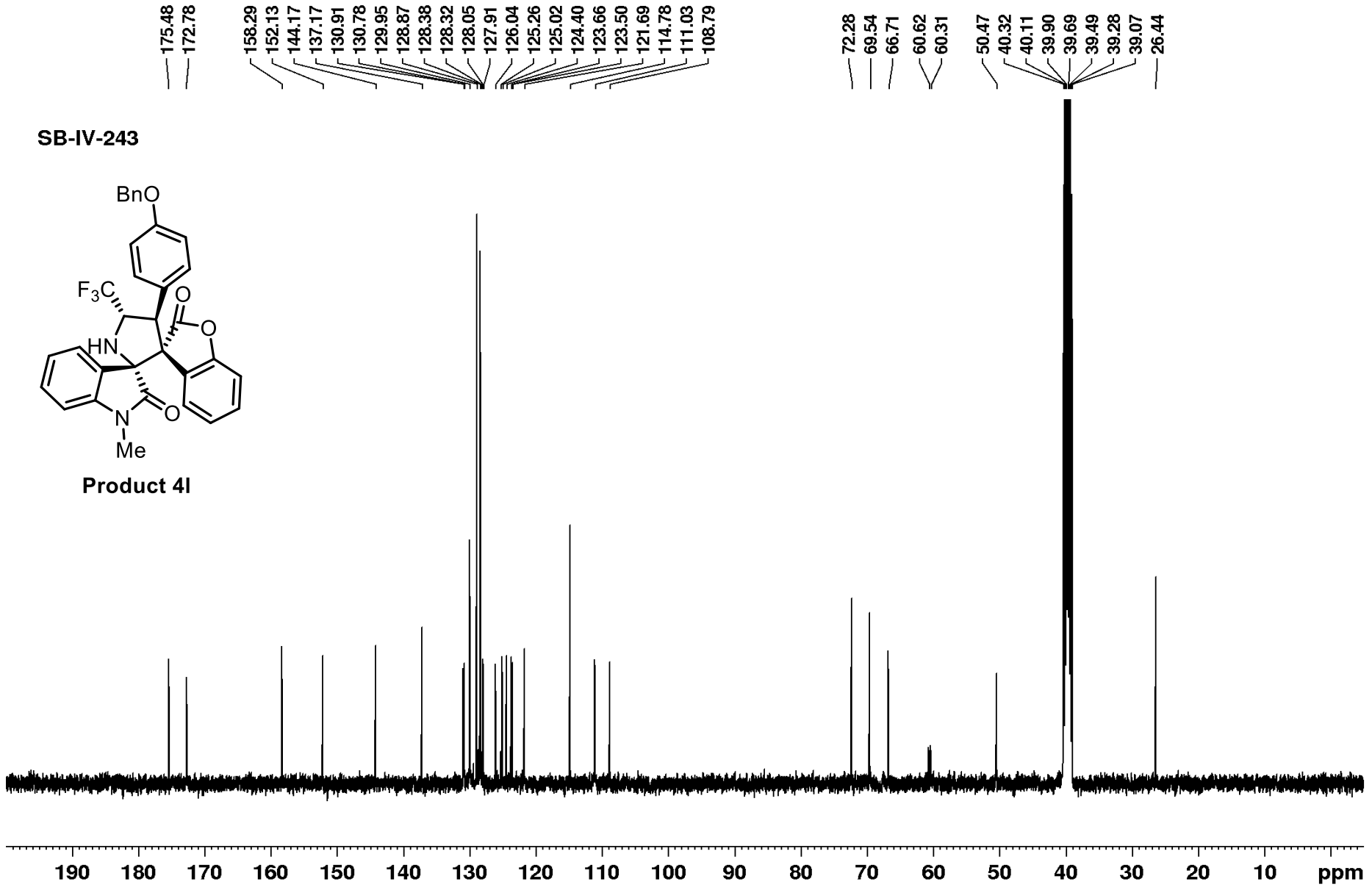

130.84
130.73
129.92
127.96
126.09
124.32
121.62
114.03
111.04
108.76
60.96
60.66
60.36
60.06
55.33
50.49
40.55
40.35
40.14
39.93
39.72
26.45
SB-IV-246
MeO
F3C
O
O
HN
O
N
Me
Product 4k
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

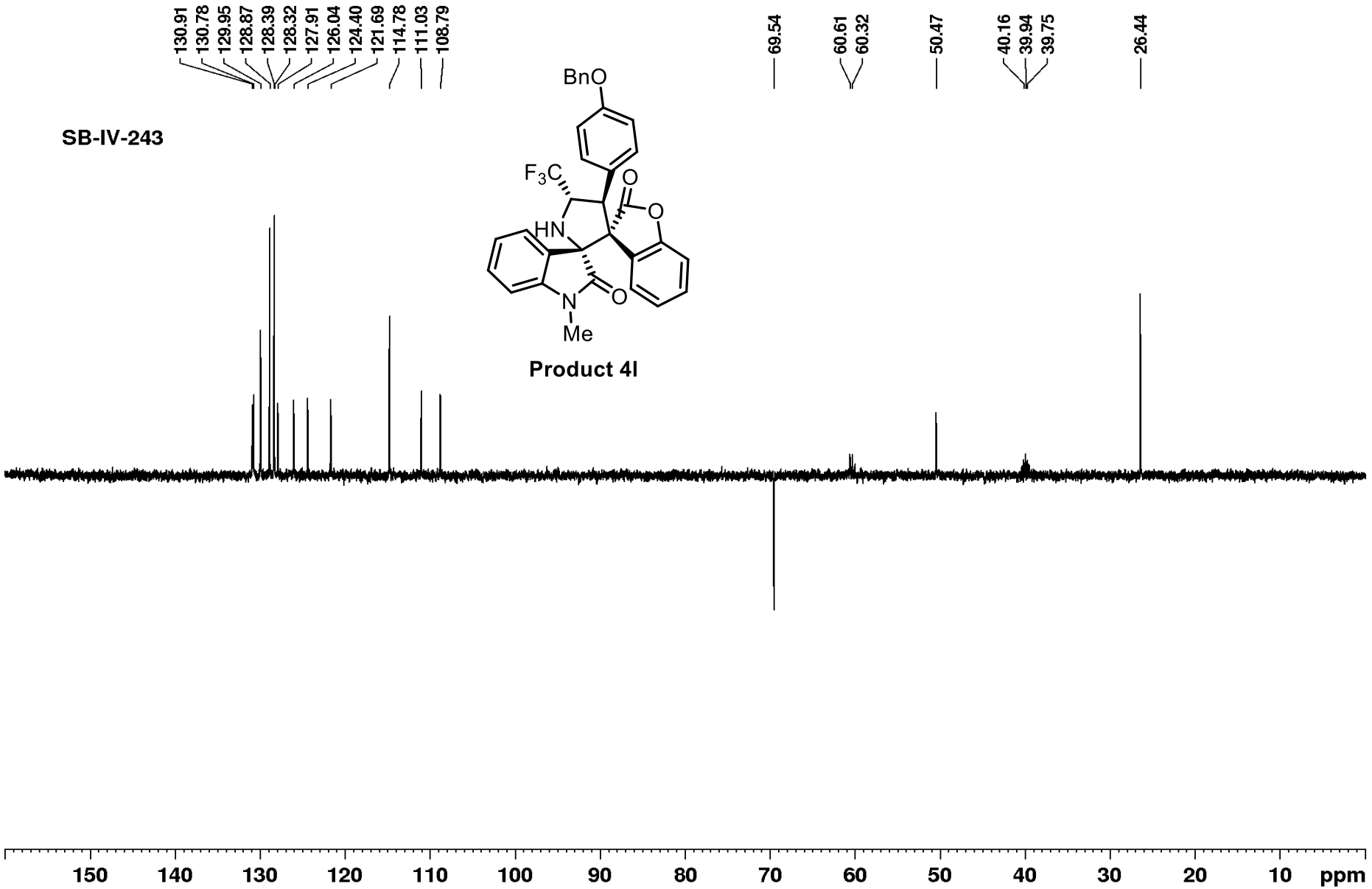

8.170
8.152
7.391
7.372
7.357
7.350
7.345
7.320
7.312
7.301
7.283
7.216
7.197
7.177
7.001
6.980
6.900
6.881
6.869
6.849
6.765
6.748
6.743
6.658
6.639
6.620
5.373
5.348
5.056
5.036
5.001
4.980
4.924
3.625
3.084
2.509
SB-IV-243
BnO
F3C
O
O
HN
O
N
Me
Product 4l
9
8
7
6
5
4
3
2
1
0 ppm
0.962
6.971
1.066
1.980
1.979
2.938
1.013
1.010
2.021
1.915
3.000

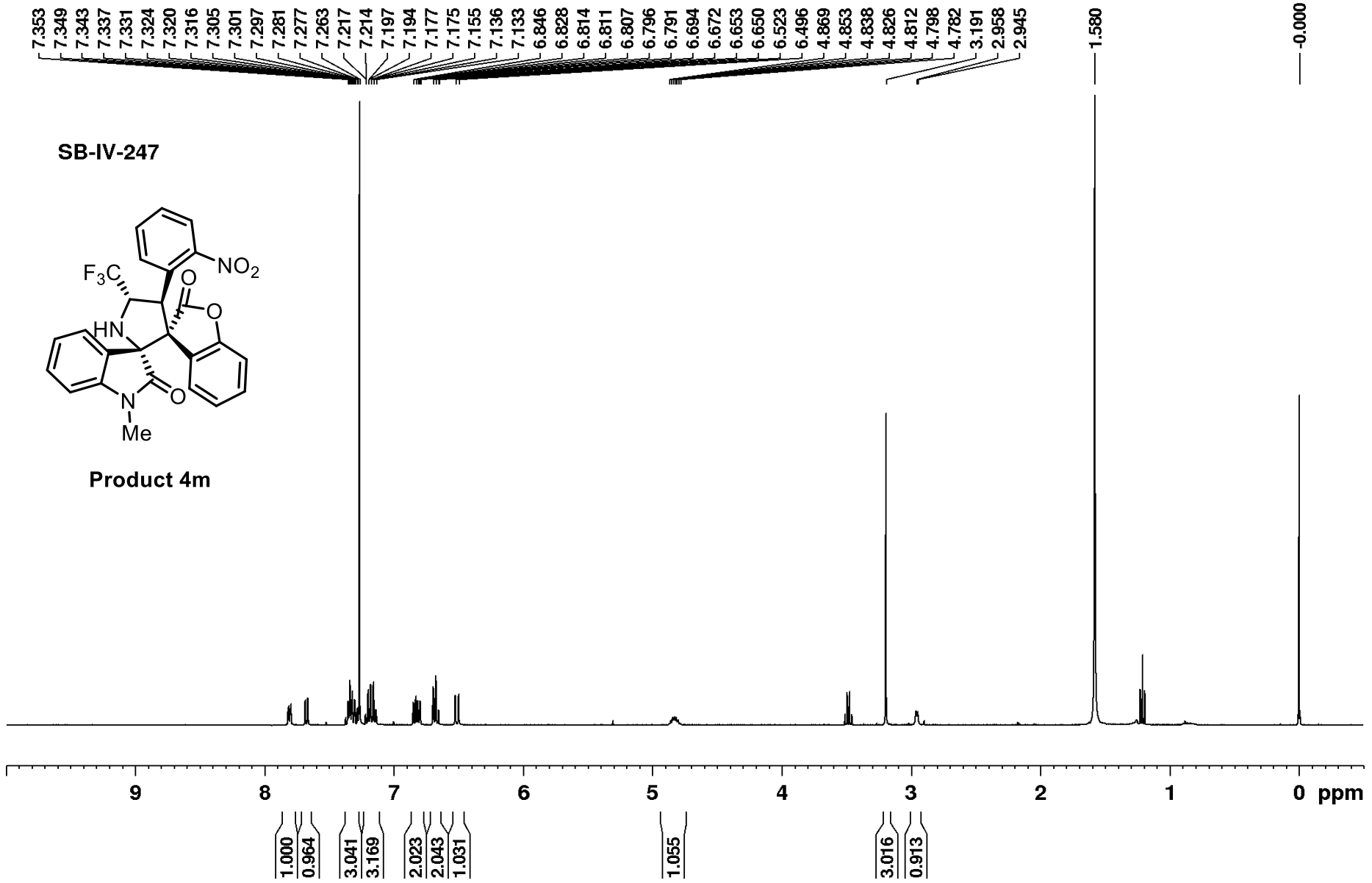
SB-IV-243

Product 4l



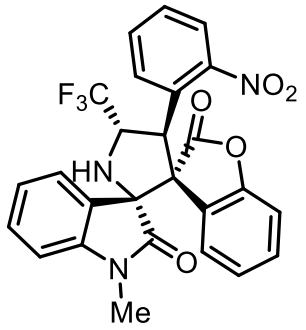

175.48
172.78
158.29
152.13
144.17
137.17
130.91
130.78
129.95
128.87
128.38
128.32
128.05
127.91
126.04
125.26
125.02
124.40
123.66
123.50
121.69
114.78
111.03
108.79
72.28
69.54
66.71
60.62
60.31
50.47
40.32
40.11
39.90
39.69
39.49
39.28
39.07
26.44
SB-IV-243
BnO
F3C
O
O
HN
O
N
Me
Product 4l
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


130.91
130.78
129.95
128.87
128.39
128.32
127.91
126.04
124.40
121.69
114.78
111.03
108.79
69.54
60.61
60.32
50.47
40.16
39.94
39.75
26.44
SB-IV-243
BnO
F3C
O
O
HN
O
N
Me
Product 4l
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

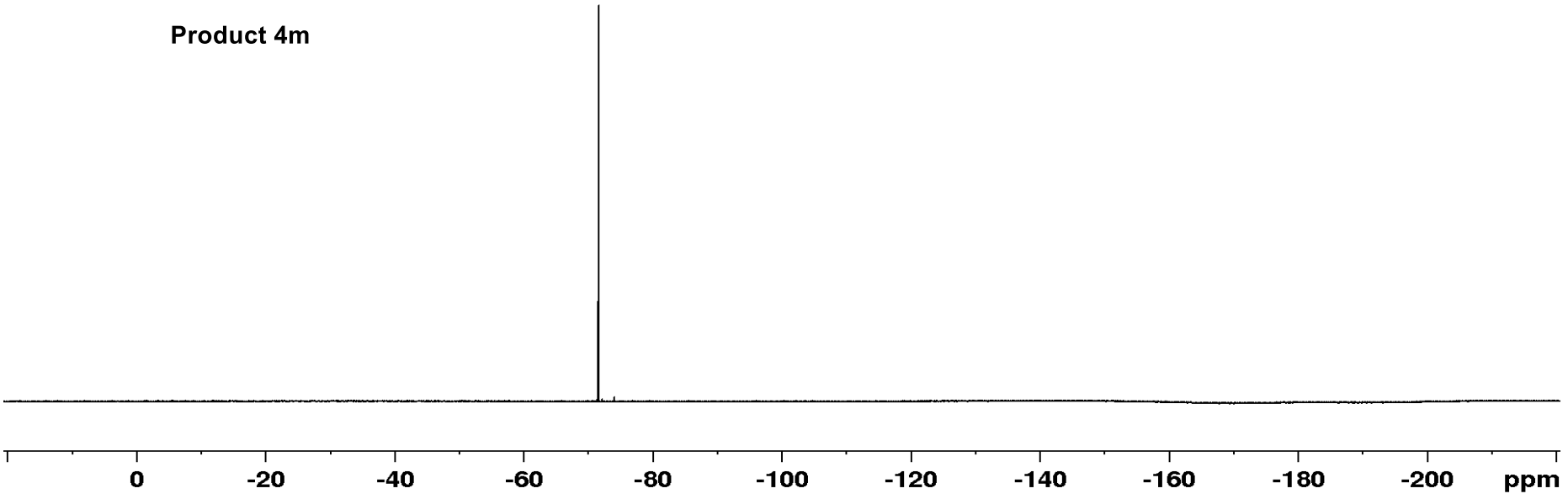

7.353
7.349
7.343
7.337
7.331
7.324
7.320
7.316
7.305
7.301
7.297
7.281
7.277
7.263
7.217
7.214
7.197
7.194
7.177
7.175
7.155
7.136
7.133
6.846
6.828
6.814
6.811
6.807
6.796
6.791
6.694
6.672
6.653
6.650
6.523
6.496
4.869
4.853
4.838
4.826
4.812
4.798
4.782
3.191
2.958
2.945
1.580
-0.000
SB-IV-247
F3C
NO2
HN
O
O
O
N
Me
Product 4m
9
8
7
6
5
4
3
2
1
0 ppm
1.000
0.964
3.041
3.169
2.023
2.043
1.031
1.055
3.016
0.913

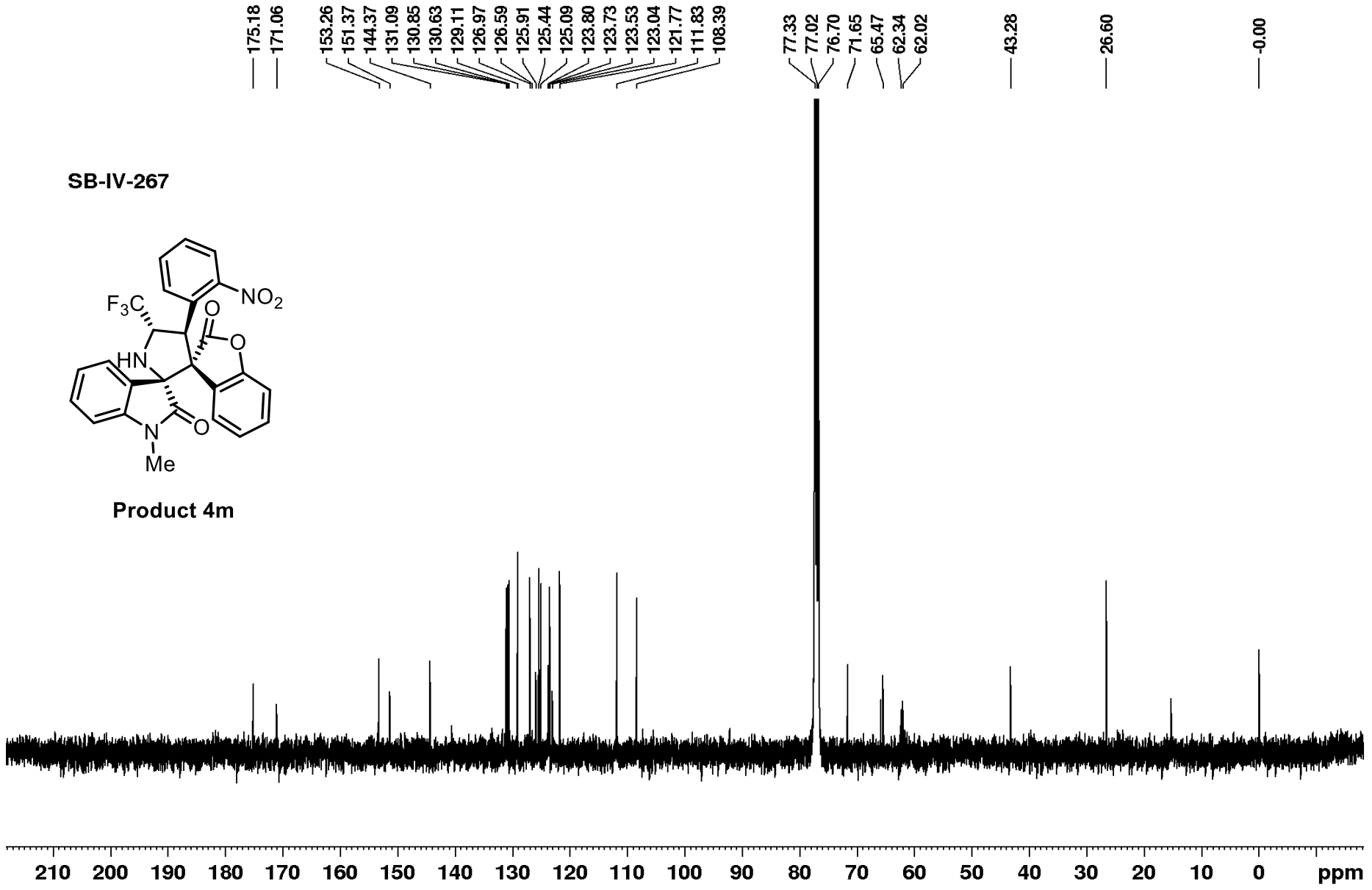
-71.65

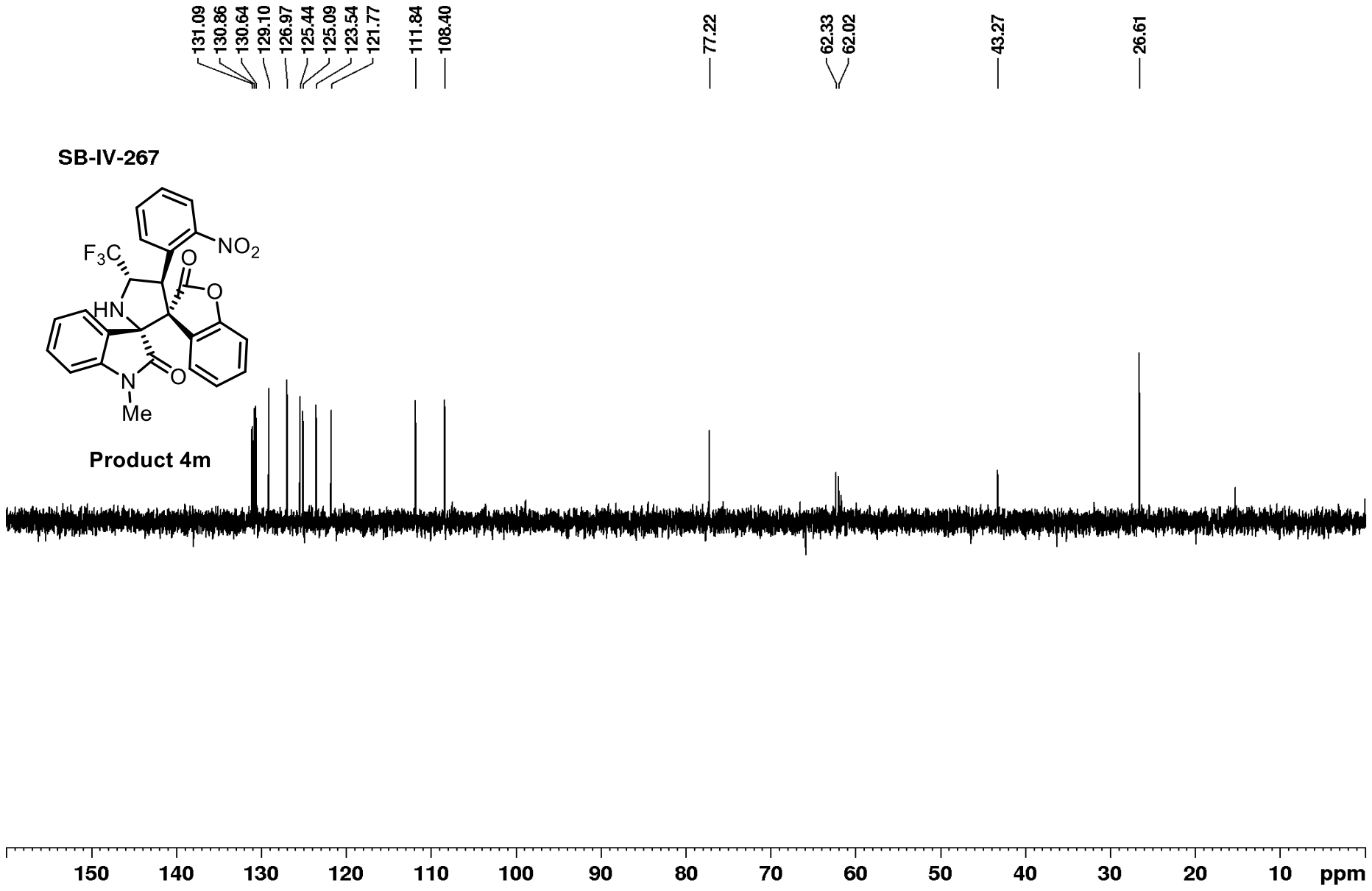
SB-IV-247

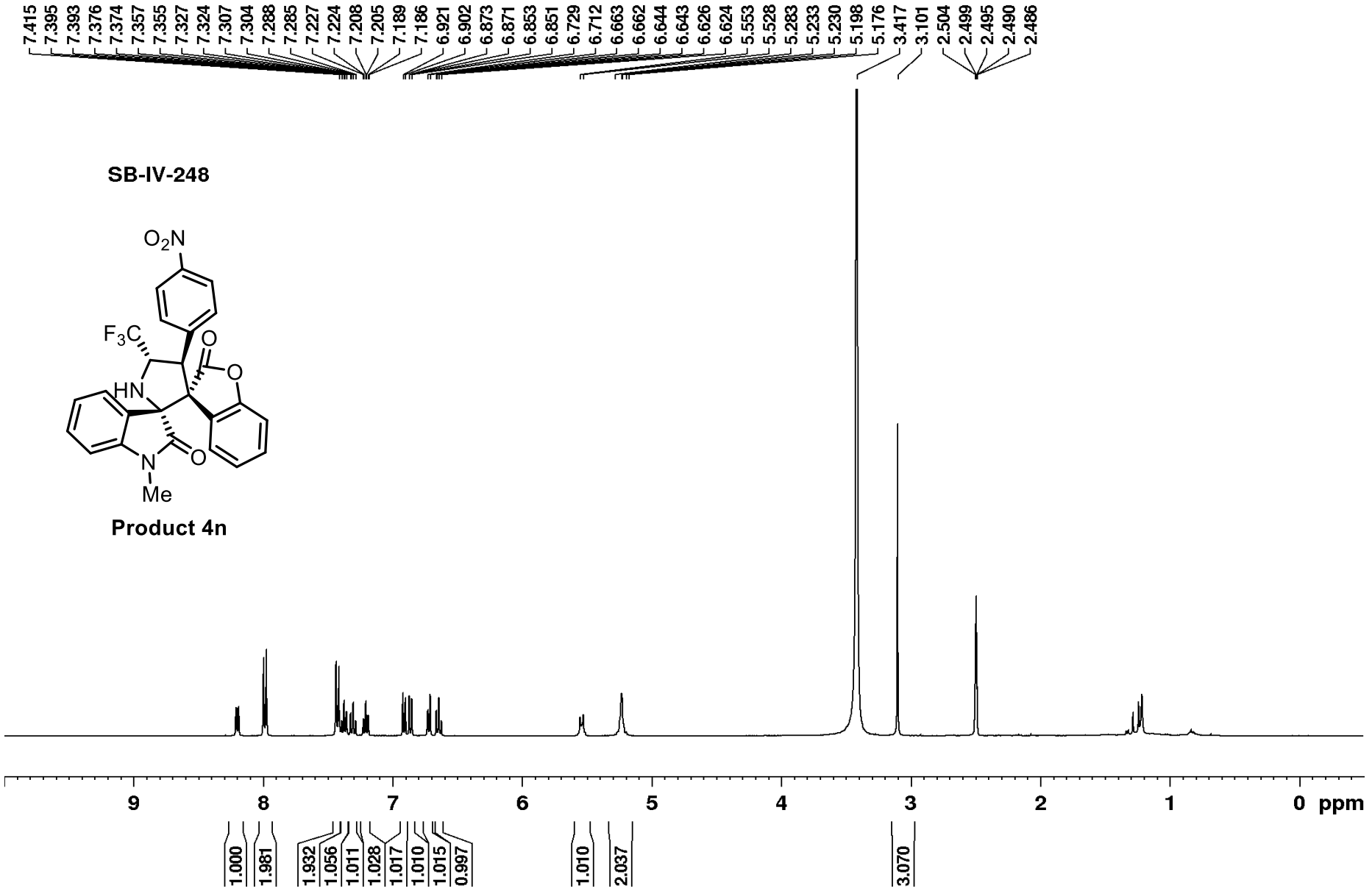


Product 4m



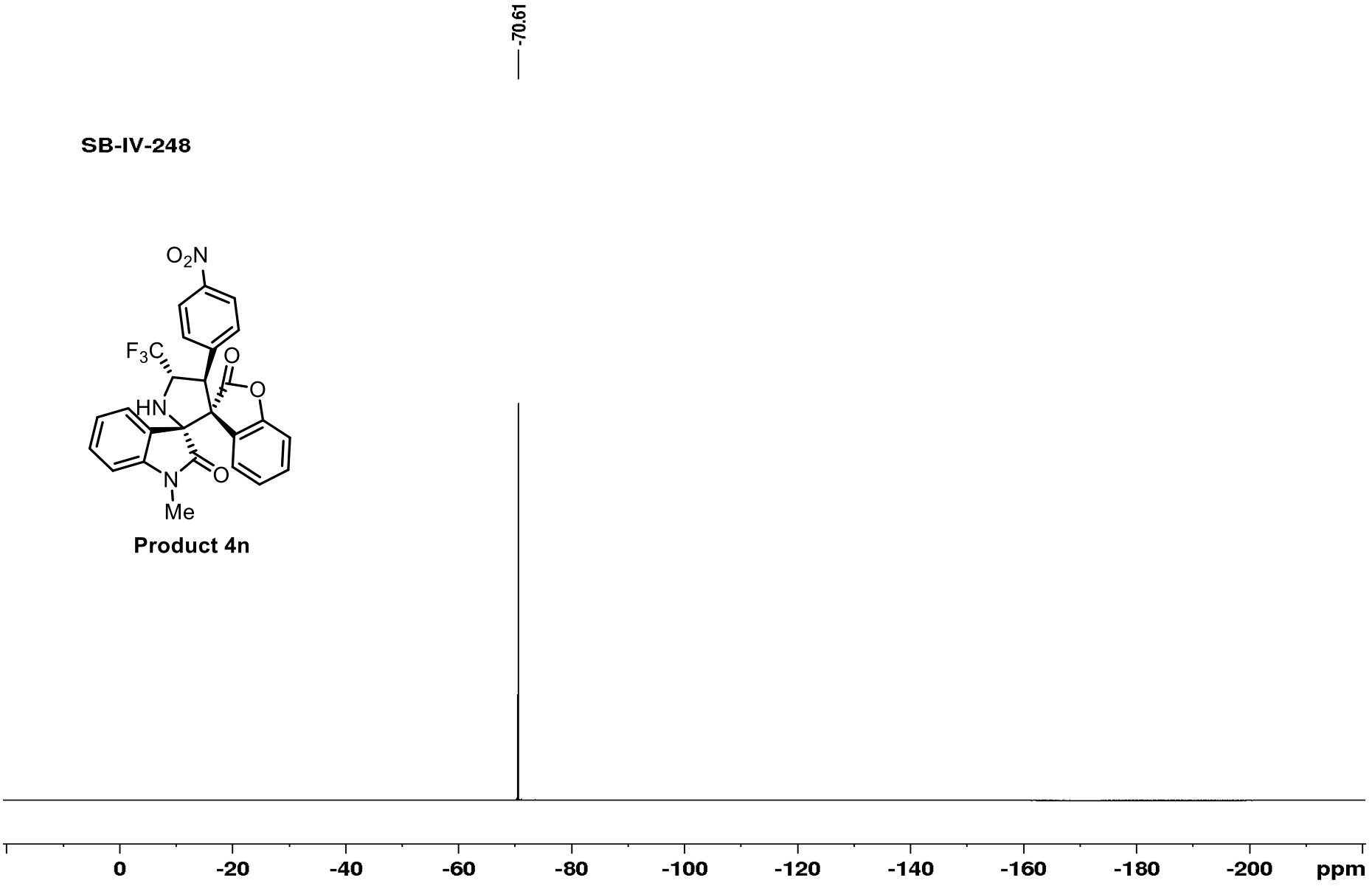

175.18
171.06
153.26
151.37
144.37
131.09
130.85
130.63
129.11
126.97
126.59
125.91
125.44
125.09
123.80
123.73
123.53
123.04
121.77
111.83
108.39
77.33
77.02
76.70
71.65
65.47
62.34
62.02
43.28
26.60
-0.00
SB-IV-267
F3C
NO2
O
O
HN
O
N
Me
Product 4m
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

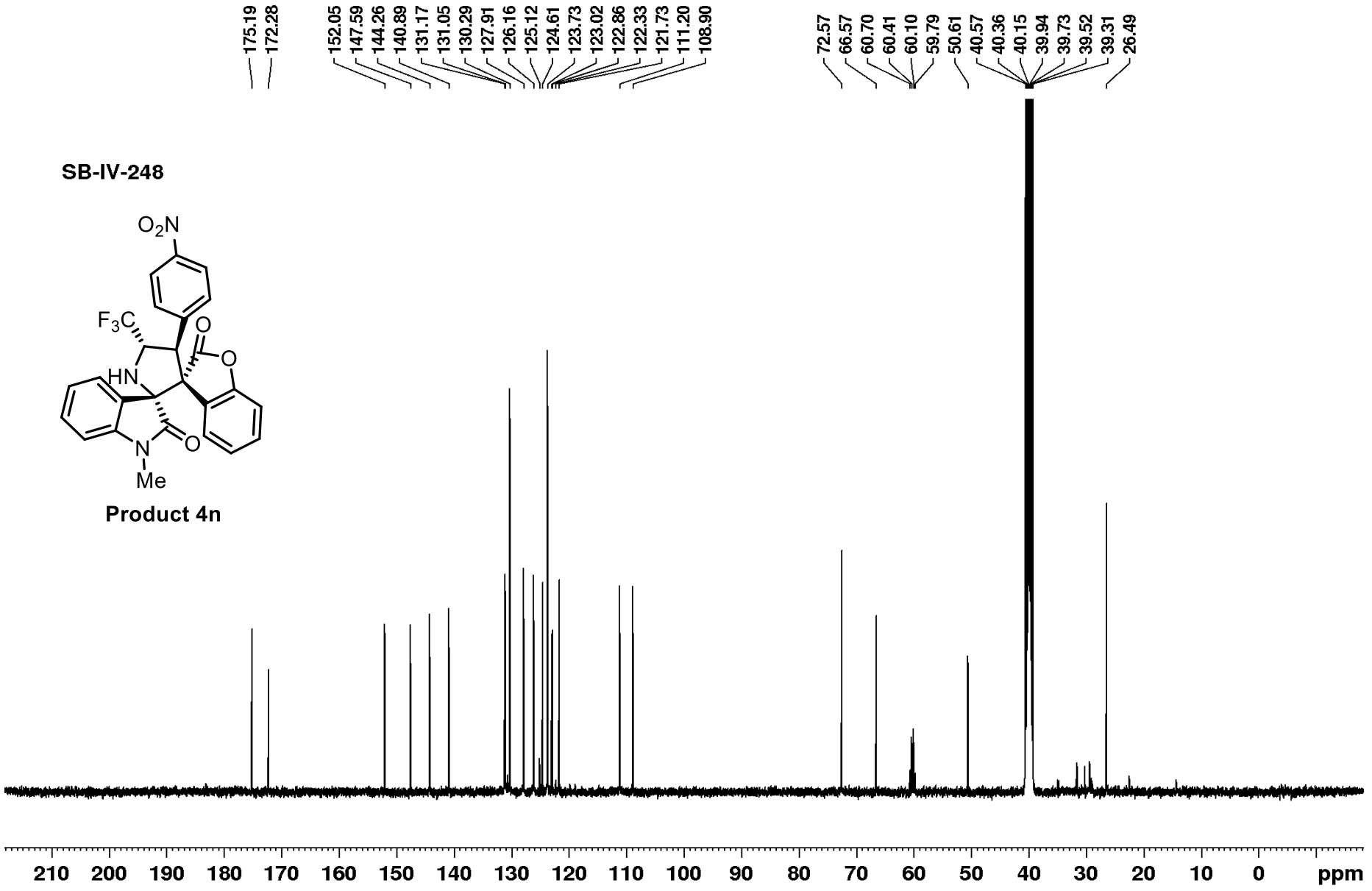

131.09
130.86
130.64
129.10
126.97
125.44
125.09
123.54
121.77
111.84
108.40
77.22
62.33
62.02
43.27
26.61
SB-IV-267
F3C
NO2
O
O
HN
O
N
Me
Product 4m
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

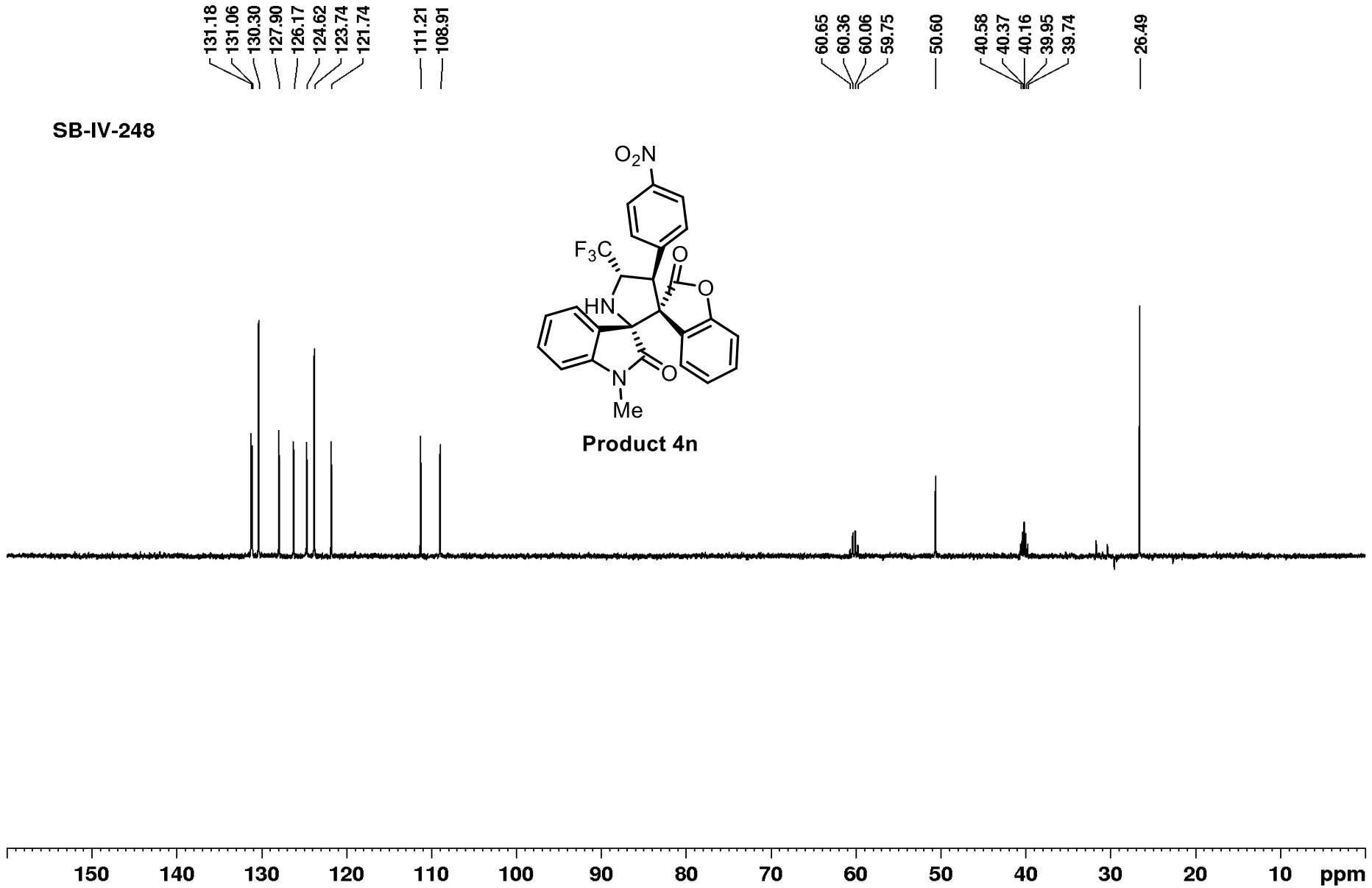

7.415
7.395
7.393
7.376
7.374
7.357
7.355
7.327
7.324
7.307
7.304
7.288
7.285
7.227
7.224
7.208
7.205
7.189
7.186
6.921
6.902
6.873
6.871
6.853
6.851
6.729
6.712
6.663
6.662
6.644
6.643
6.626
6.624
5.553
5.528
5.283
5.233
5.230
5.198
5.176
3.417
3.101
2.504
2.499
2.495
2.490
2.486
SB-IV-248
O2N
F3C
O
O
HN
O
N
Me
Product 4n
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.981
1.932
1.056
1.011
1.028
1.017
1.010
1.015
0.997
1.010
2.037
3.070

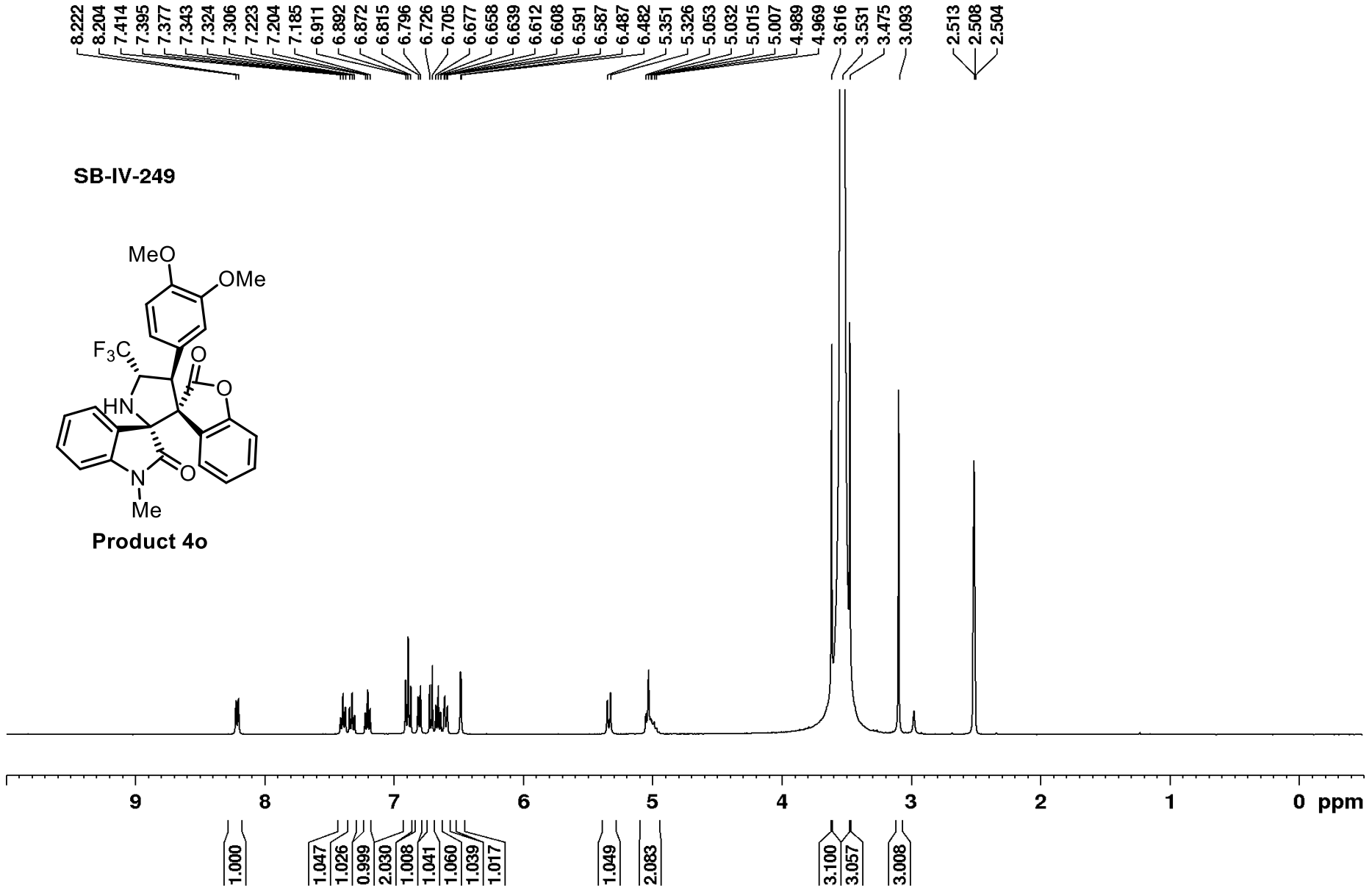
SB-IV-248

Product 4n



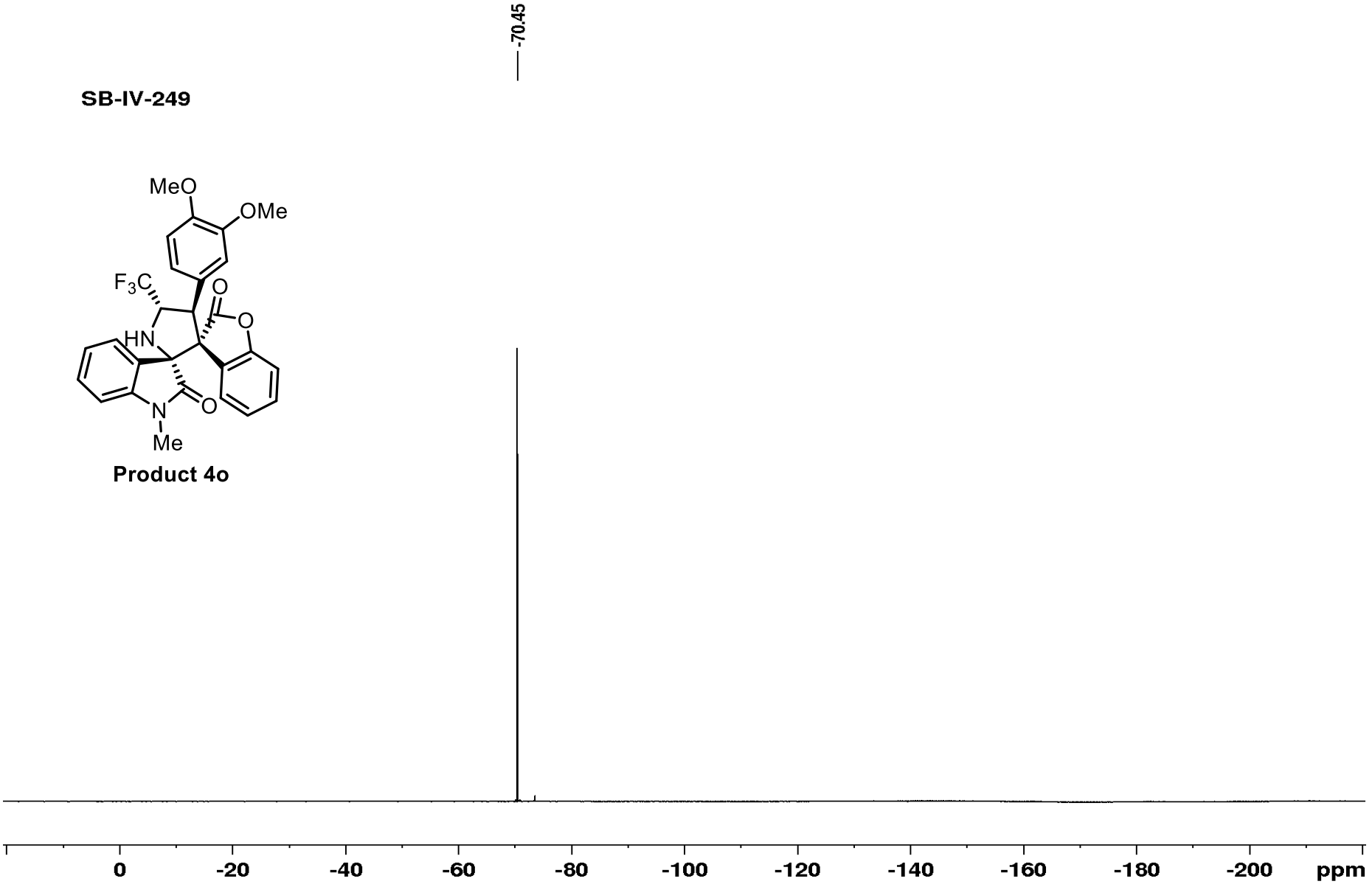

175.19
172.28
152.05
147.59
144.26
140.89
131.17
131.05
130.29
127.91
126.16
125.12
124.61
123.73
123.02
122.86
122.33
121.73
111.20
108.90
72.57
66.57
60.70
60.41
60.10
59.79
50.61
40.57
40.36
40.15
39.94
39.73
39.52
39.31
26.49
SB-IV-248
O2N
F3C
O
O
HN
O
N
Me
Product 4n
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

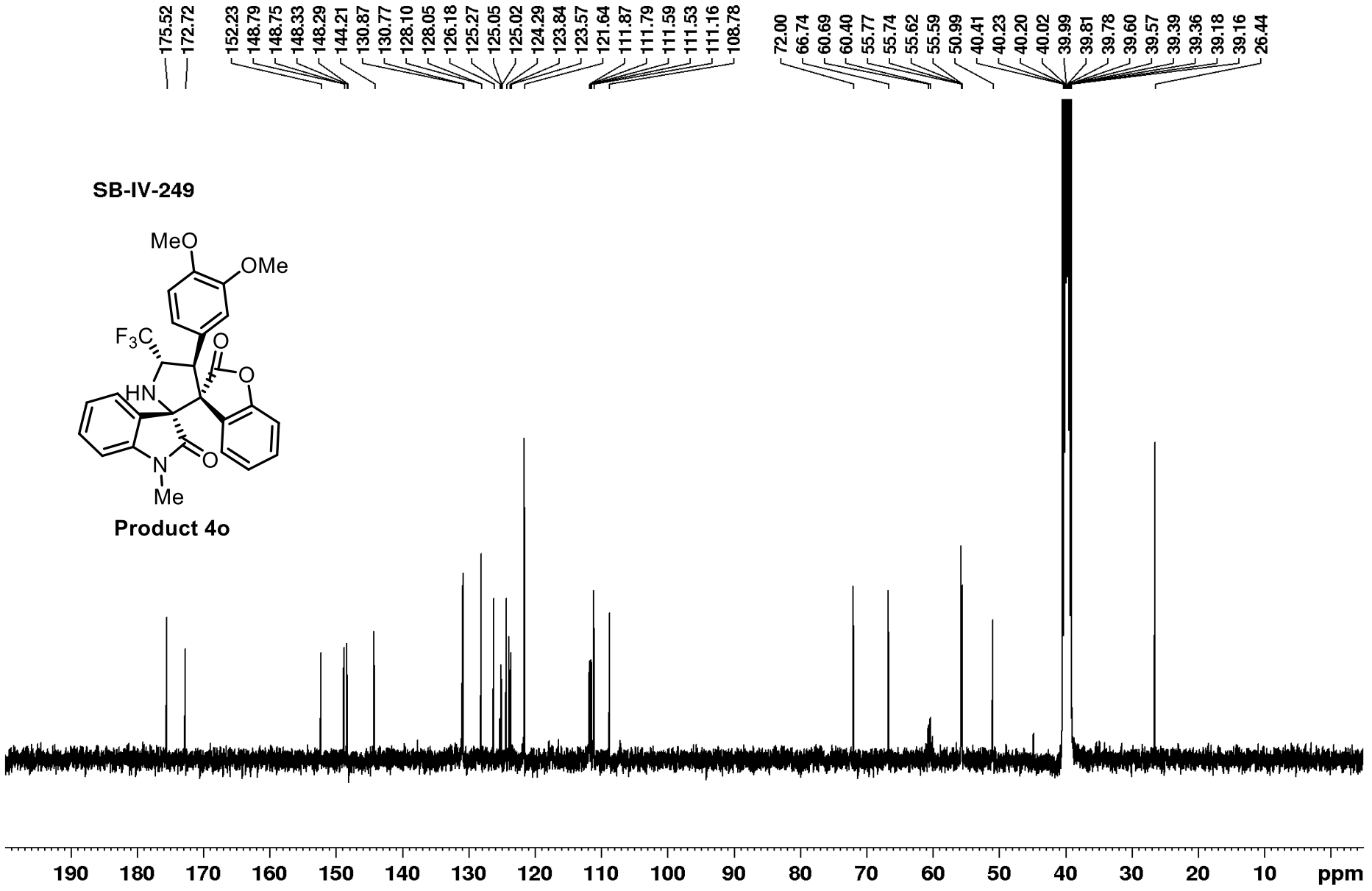

131.18
131.06
130.30
127.90
126.17
124.62
123.74
121.74
111.21
108.91
60.65
60.36
60.06
59.75
50.60
40.58
40.37
40.16
39.95
39.74
26.49
SB-IV-248
O2N
F3C
O
O
HN
O
N
Me
Product 4n
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

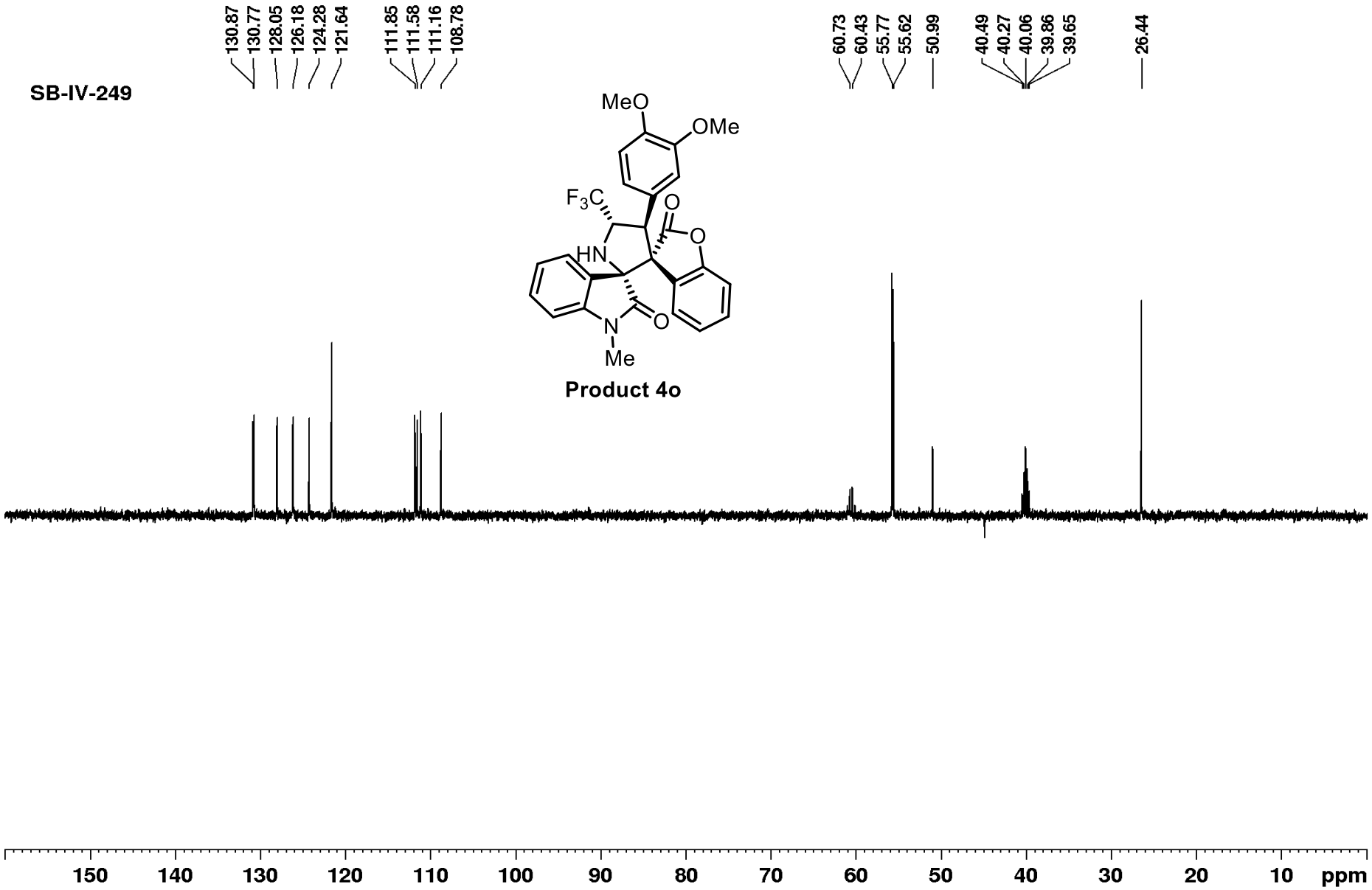

8.222
8.204
7.414
7.395
7.377
7.343
7.324
7.306
7.223
7.204
7.185
6.911
6.892
6.872
6.815
6.796
6.726
6.705
6.677
6.658
6.639
6.612
6.608
6.591
6.587
6.487
6.482
5.351
5.326
5.053
5.032
5.015
5.007
4.989
4.969
3.616
3.531
3.475
3.093
2.513
2.508
2.504
SB-IV-249
MeO
OMe
F3C
O
O
HN
O
N
Me
Product 4o
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.047
1.026
0.999
2.030
1.008
1.041
1.060
1.039
1.017
1.049
2.083
3.100
3.057
3.008

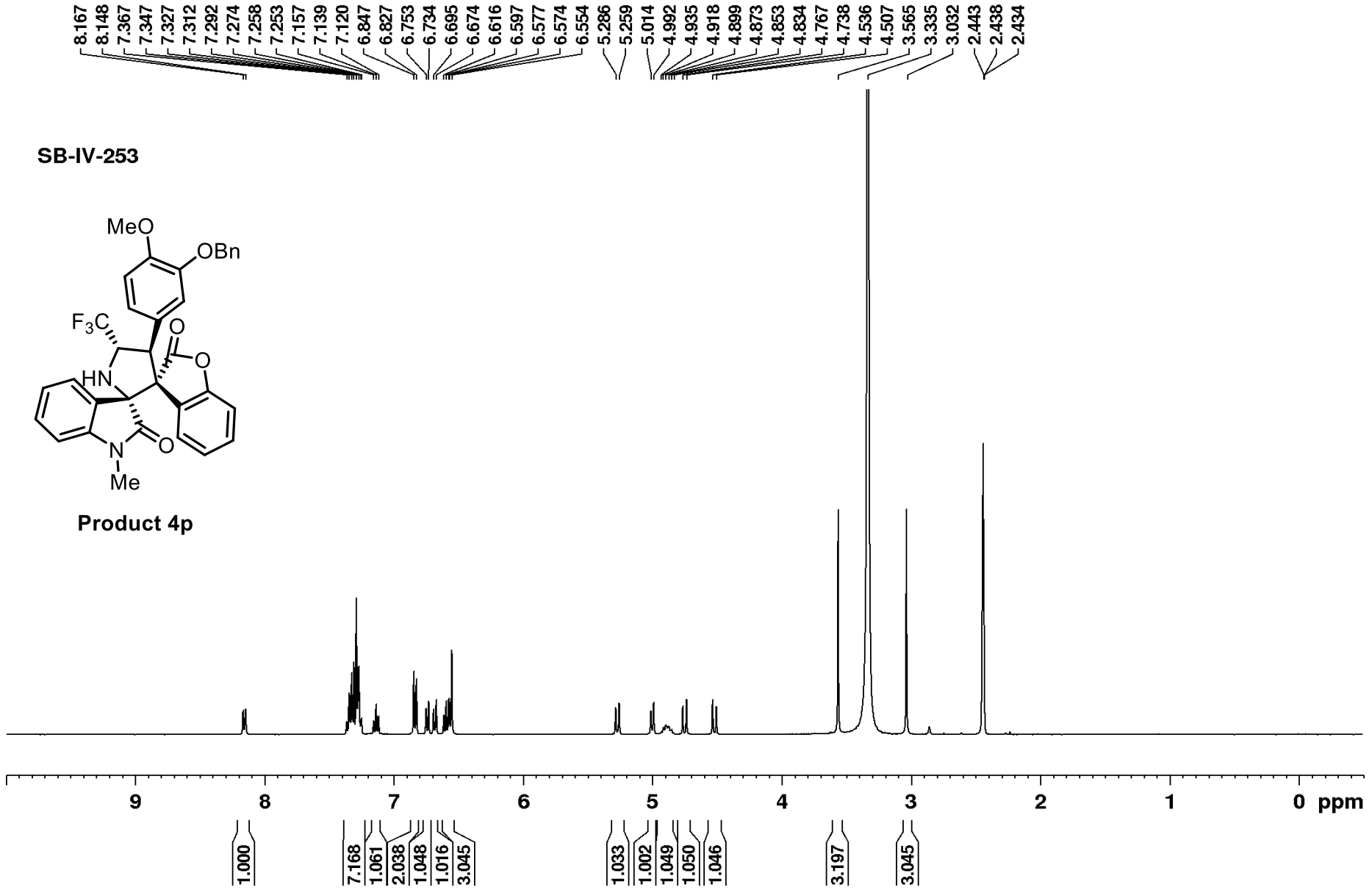
SB-IV-249

Product 4o



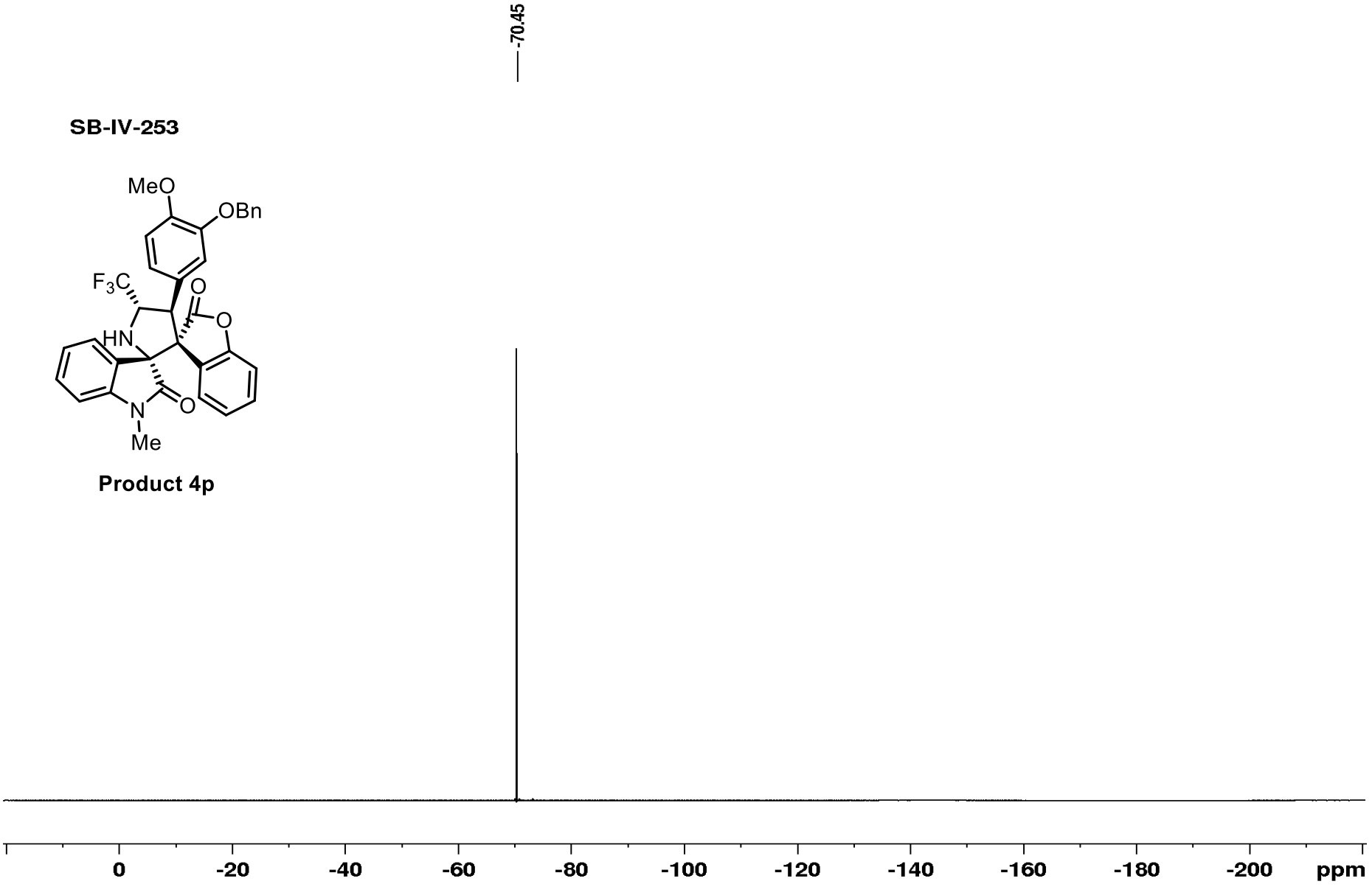

175.52
172.72
152.23
148.79
148.75
148.33
148.29
144.21
130.87
130.77
128.10
128.05
126.18
125.27
125.05
125.02
124.29
123.84
123.57
121.64
111.87
111.79
111.59
111.53
111.16
108.78
72.00
66.74
60.69
60.40
55.77
55.74
55.62
55.59
50.99
40.41
40.23
40.20
40.02
39.99
39.81
39.78
39.60
39.57
39.39
39.36
39.18
39.16
26.44
SB-IV-249
MeO
OMe
F3C
O
O
HN
O
N
Me
Product 4o
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

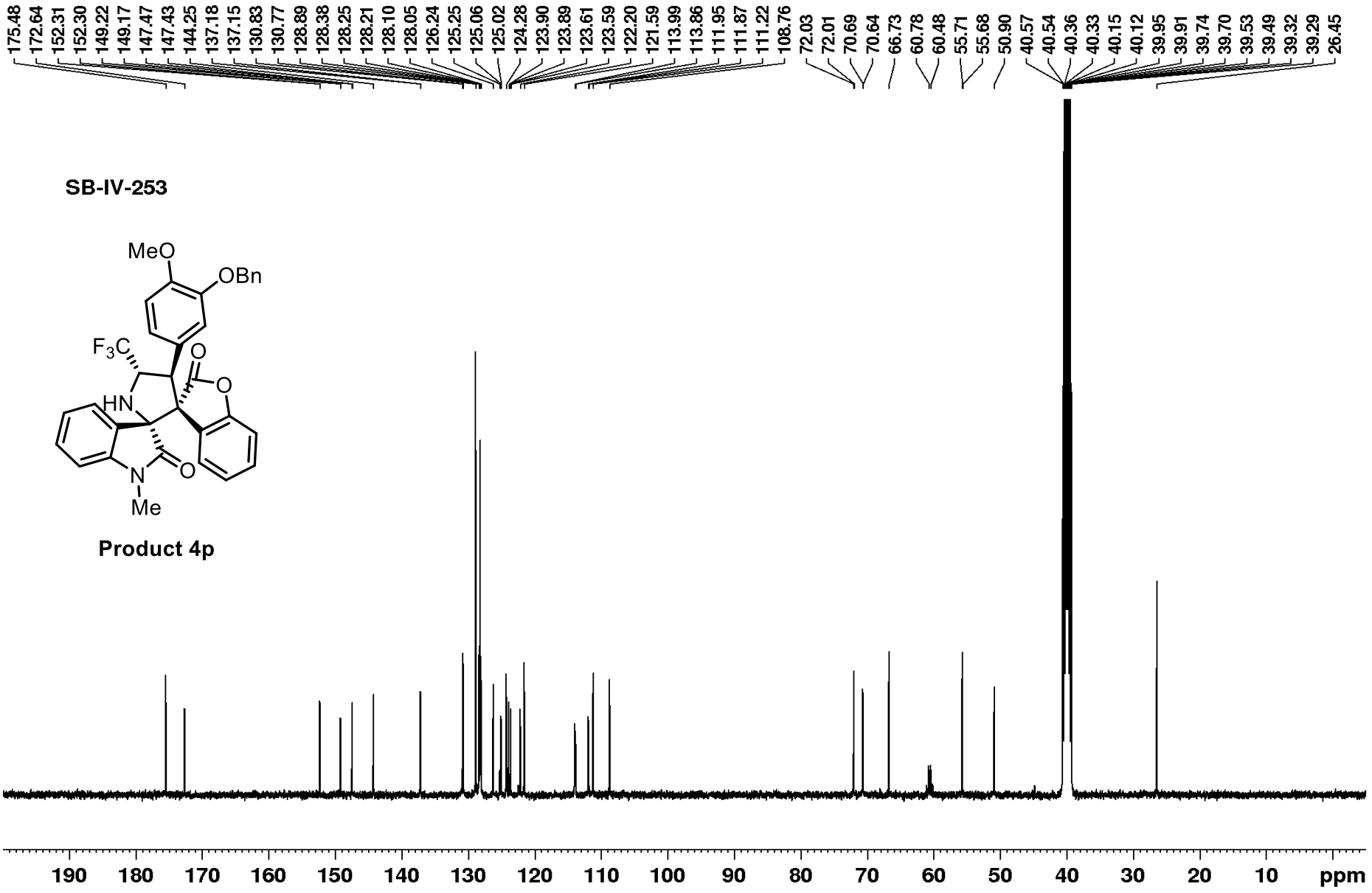

SB-IV-249
130.87
130.77
128.05
126.18
124.28
121.64
111.85
111.58
111.16
108.78
60.73
60.43
55.77
55.62
50.99
40.49
40.27
40.06
39.86
39.65
26.44
MeO
OMe
F3C
HN
O
O
O
N
Me
Product 4o
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

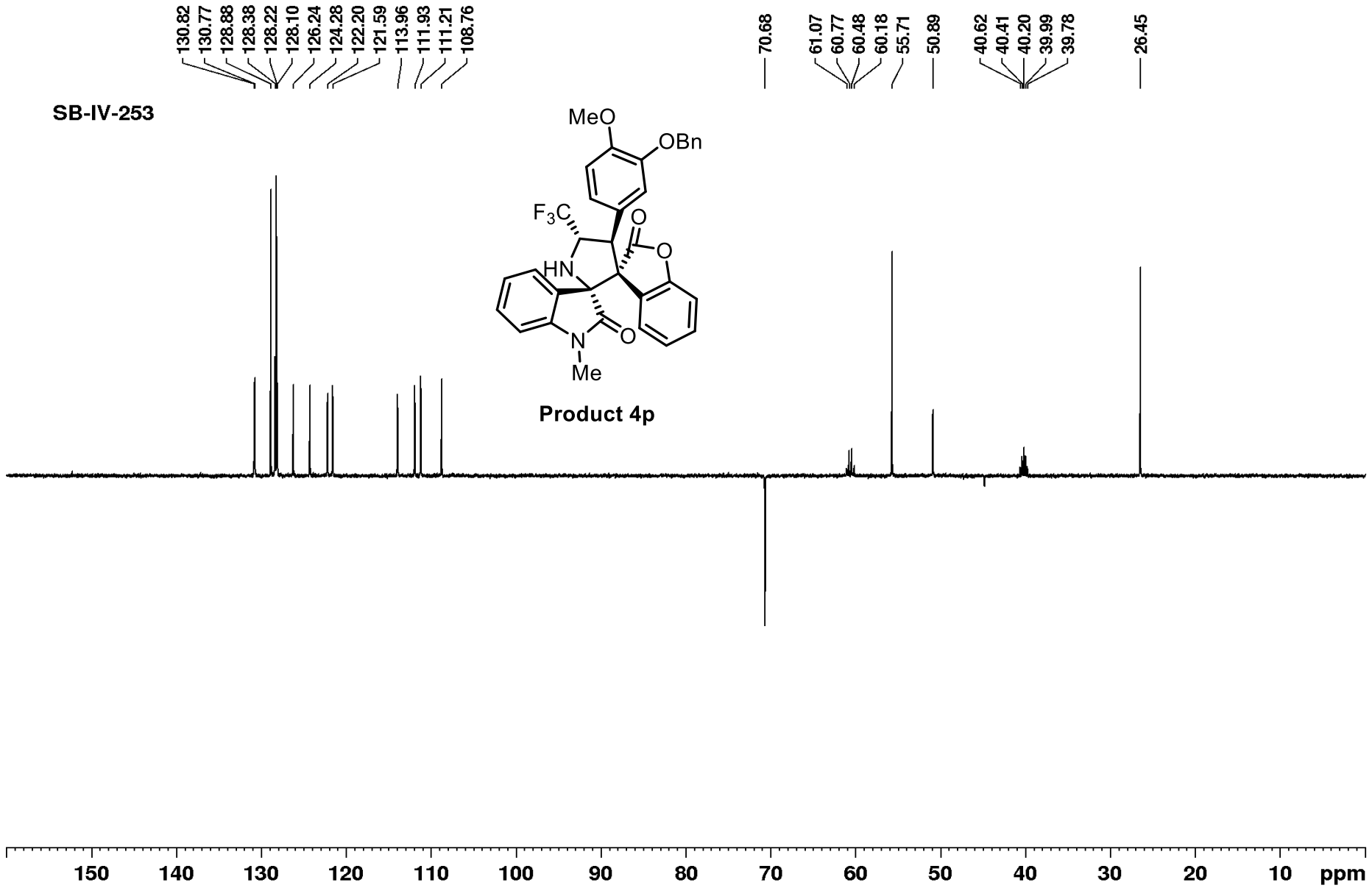

8.167
8.148
7.367
7.347
7.327
7.312
7.292
7.274
7.258
7.253
7.157
7.139
7.120
6.847
6.827
6.753
6.734
6.695
6.674
6.616
6.597
6.577
6.574
6.554
5.286
5.259
5.014
4.992
4.935
4.918
4.899
4.873
4.853
4.834
4.767
4.738
4.536
4.507
3.565
3.335
3.032
2.443
2.438
2.434
SB-IV-253
MeO
OBn
F3C
O
O
HN
O
N
Me
Product 4p
9
8
7
6
5
4
3
2
1
0 ppm
1.000
7.168
1.061
2.038
1.048
1.016
3.045
1.033
1.002
1.049
1.050
1.046
3.197
3.045

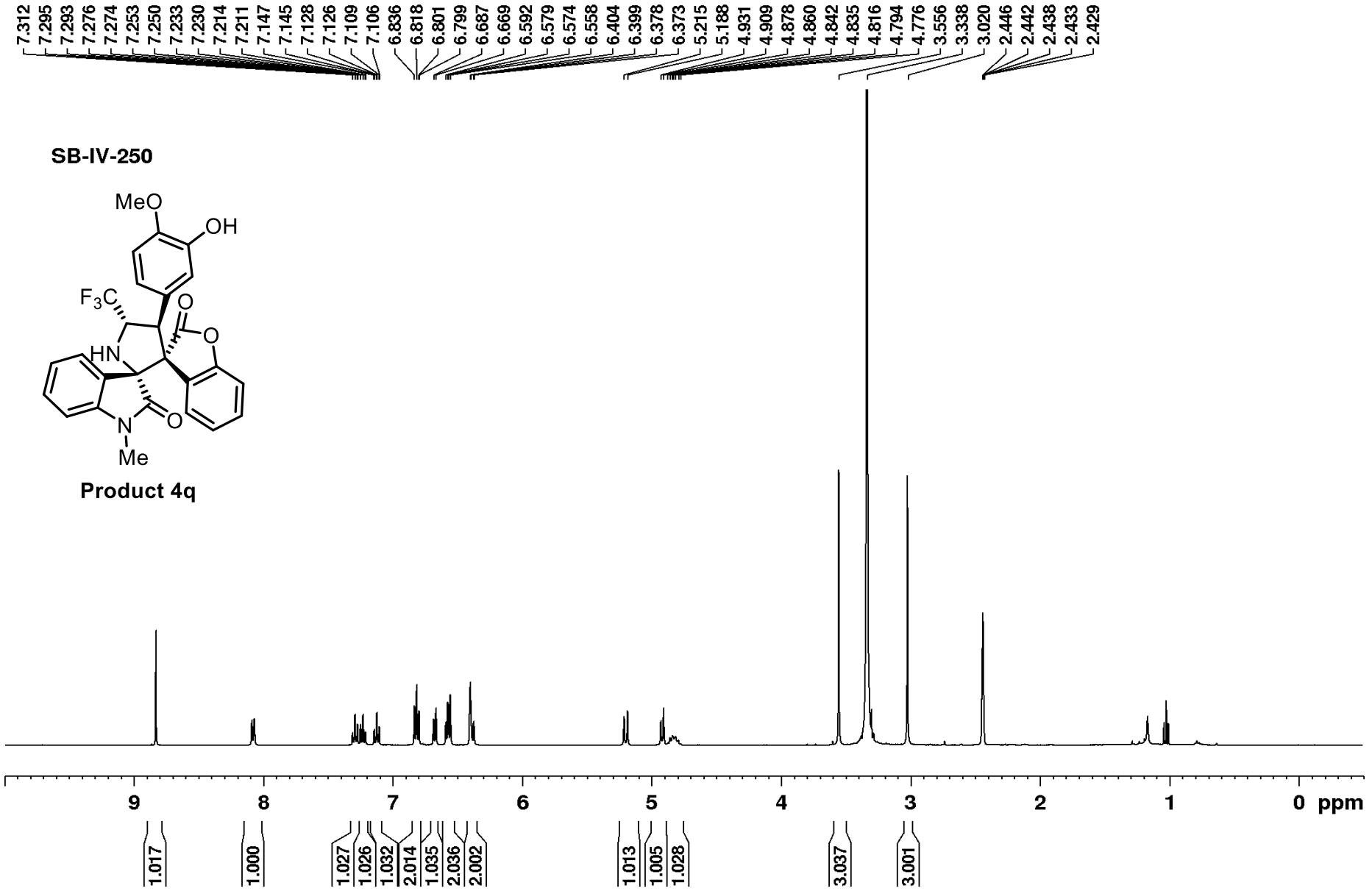
SB-IV-253

Product 4p



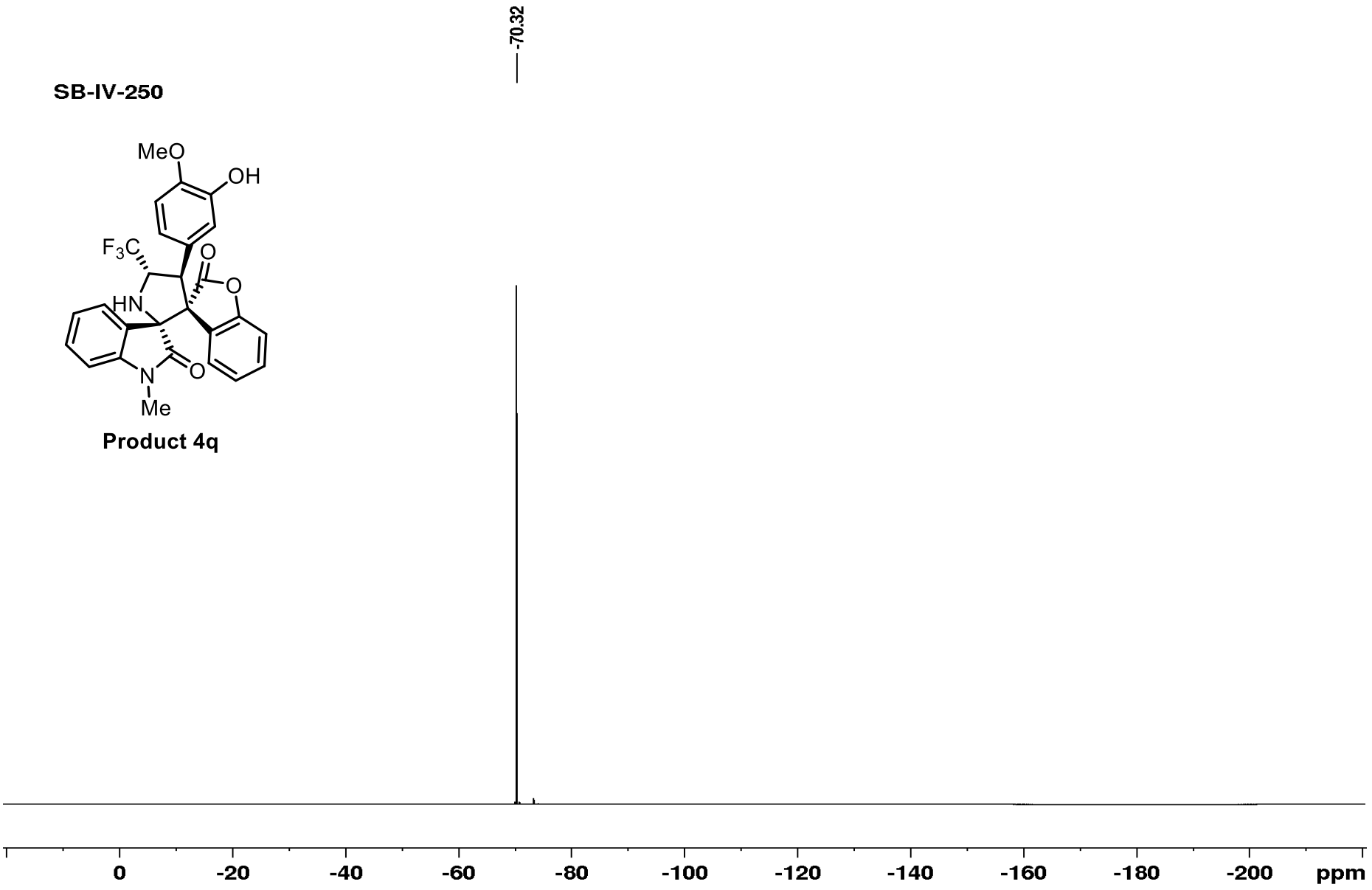

175.48
172.64
152.31
152.30
149.22
149.17
147.47
147.43
144.25
137.18
137.15
130.83
130.77
128.89
128.38
128.25
128.21
128.10
128.05
126.24
125.25
125.06
125.02
124.28
123.90
123.89
123.61
123.59
122.20
121.59
113.99
113.86
111.95
111.87
111.22
108.76
72.03
72.01
70.69
70.64
66.73
60.78
60.48
55.71
55.68
50.90
40.57
40.54
40.36
40.33
40.15
40.12
39.95
39.91
39.74
39.70
39.53
39.49
39.32
39.29
26.45
SB-IV-253
MeO
OBn
F3C
O
O
HN
O
N
Me
Product 4p
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

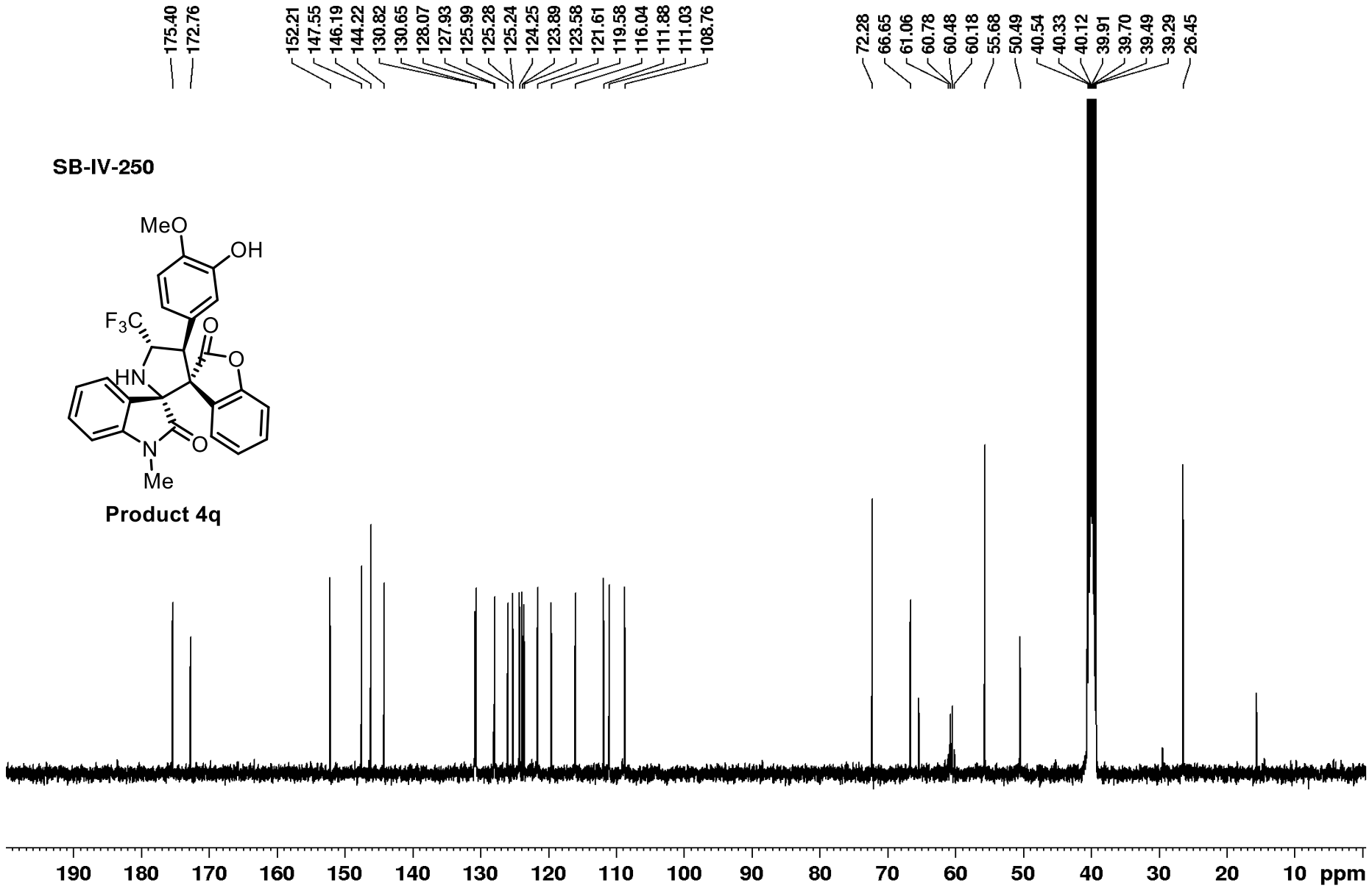

130.82
130.77
128.88
128.38
128.22
128.10
126.24
124.28
122.20
121.59
113.96
111.93
111.21
108.76
70.68
61.07
60.77
60.48
60.18
55.71
50.89
40.62
40.41
40.20
39.99
39.78
26.45
SB-IV-253
MeO
OBn
F3C
O
O
HN
O
N
Me
Product 4p
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

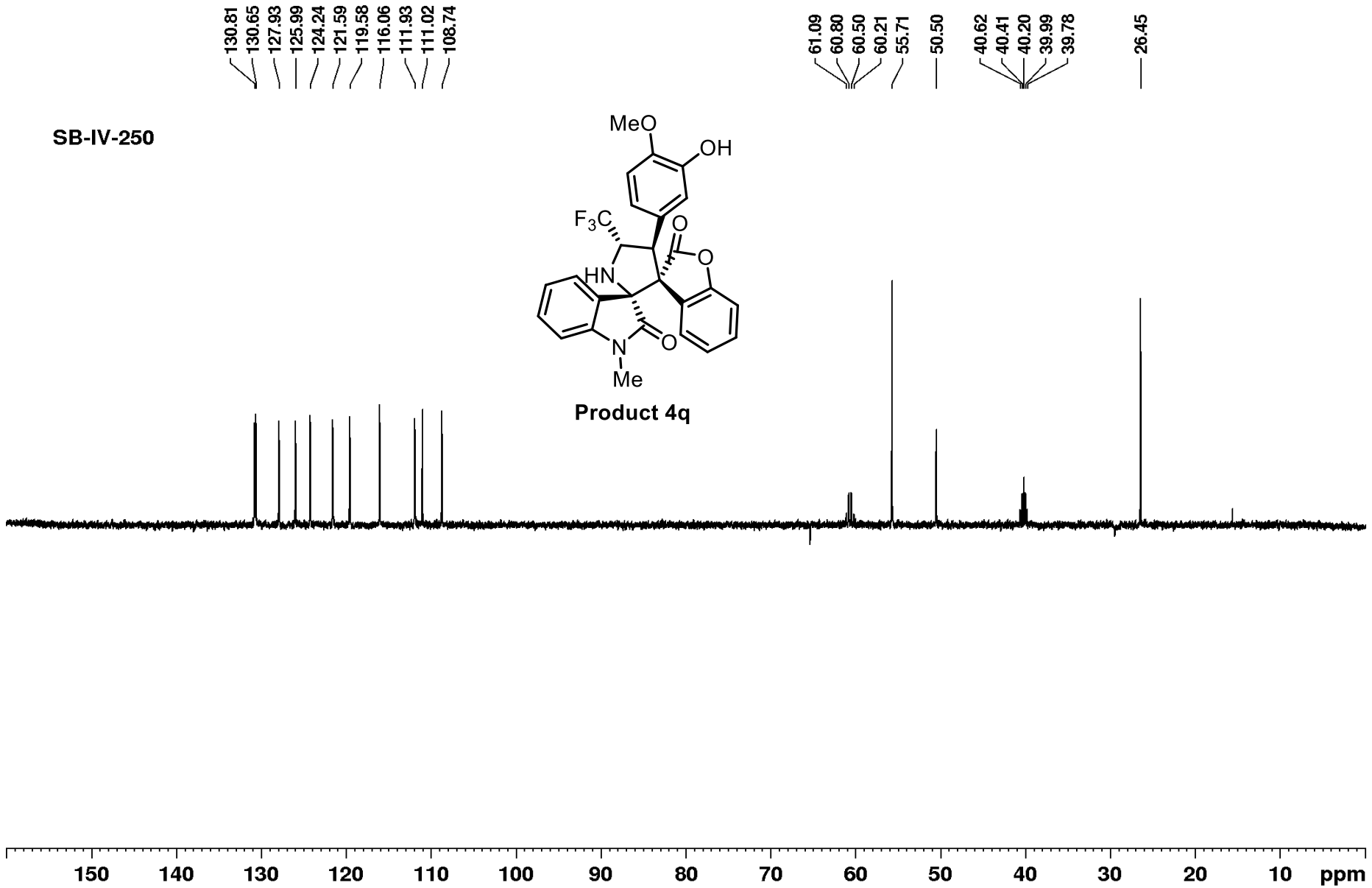

7.312
7.295
7.293
7.276
7.274
7.253
7.250
7.233
7.230
7.214
7.211
7.147
7.145
7.128
7.126
7.109
7.106
6.836
6.818
6.801
6.799
6.687
6.669
6.592
6.579
6.574
6.558
6.404
6.399
6.378
6.373
5.215
5.188
4.931
4.909
4.878
4.860
4.842
4.835
4.816
4.794
4.776
3.556
3.338
3.020
2.446
2.442
2.438
2.433
2.429
SB-IV-250
MeO
OH
F3C
O
O
HN
O
N
Me
Product 4q
9
8
7
6
5
4
3
2
1
0 ppm
1.017
1.000
1.027
1.026
1.032
2.014
1.035
2.036
2.002
1.013
1.005
1.028
3.037
3.001

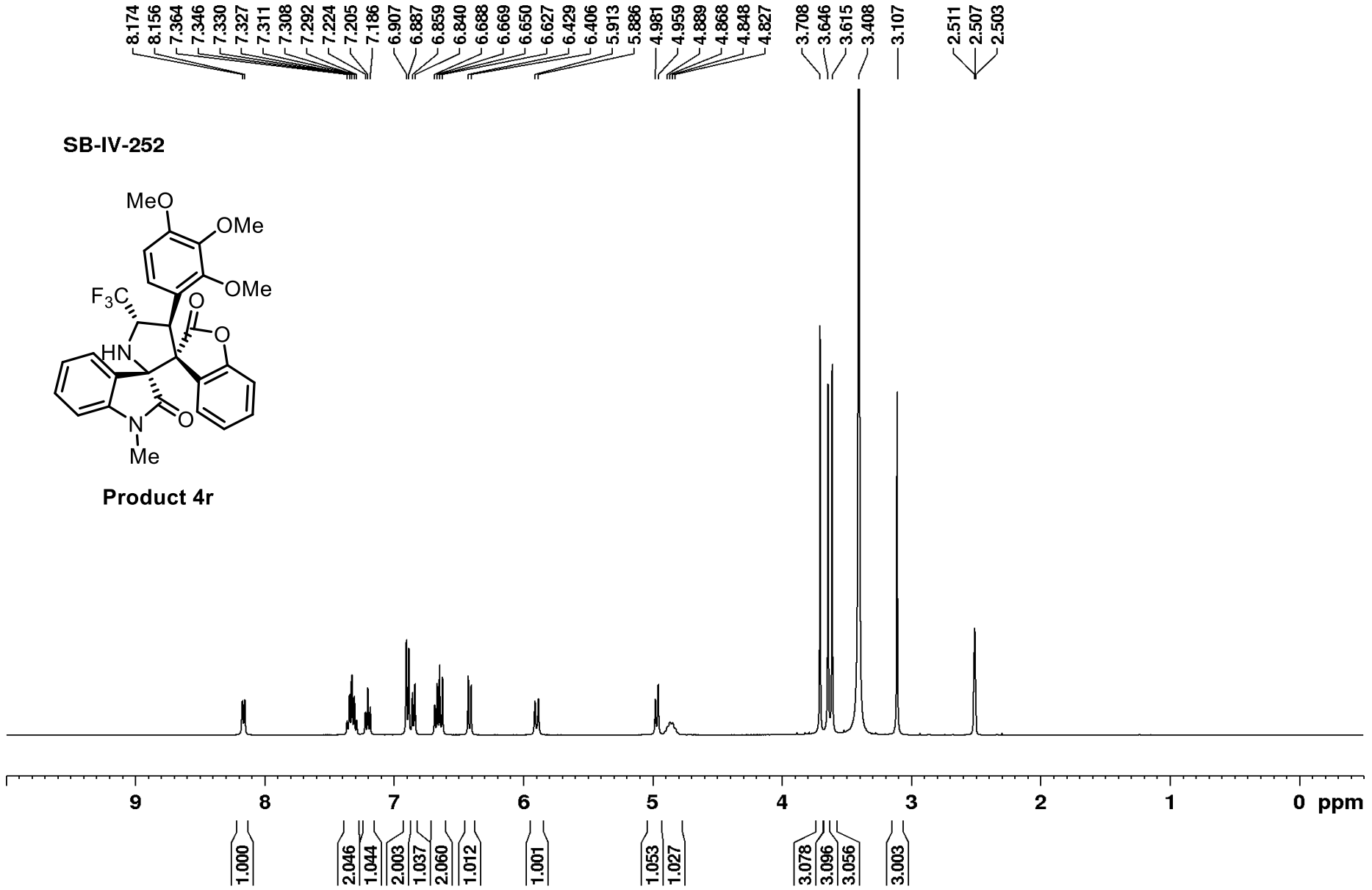
SB-IV-250

Product 4q



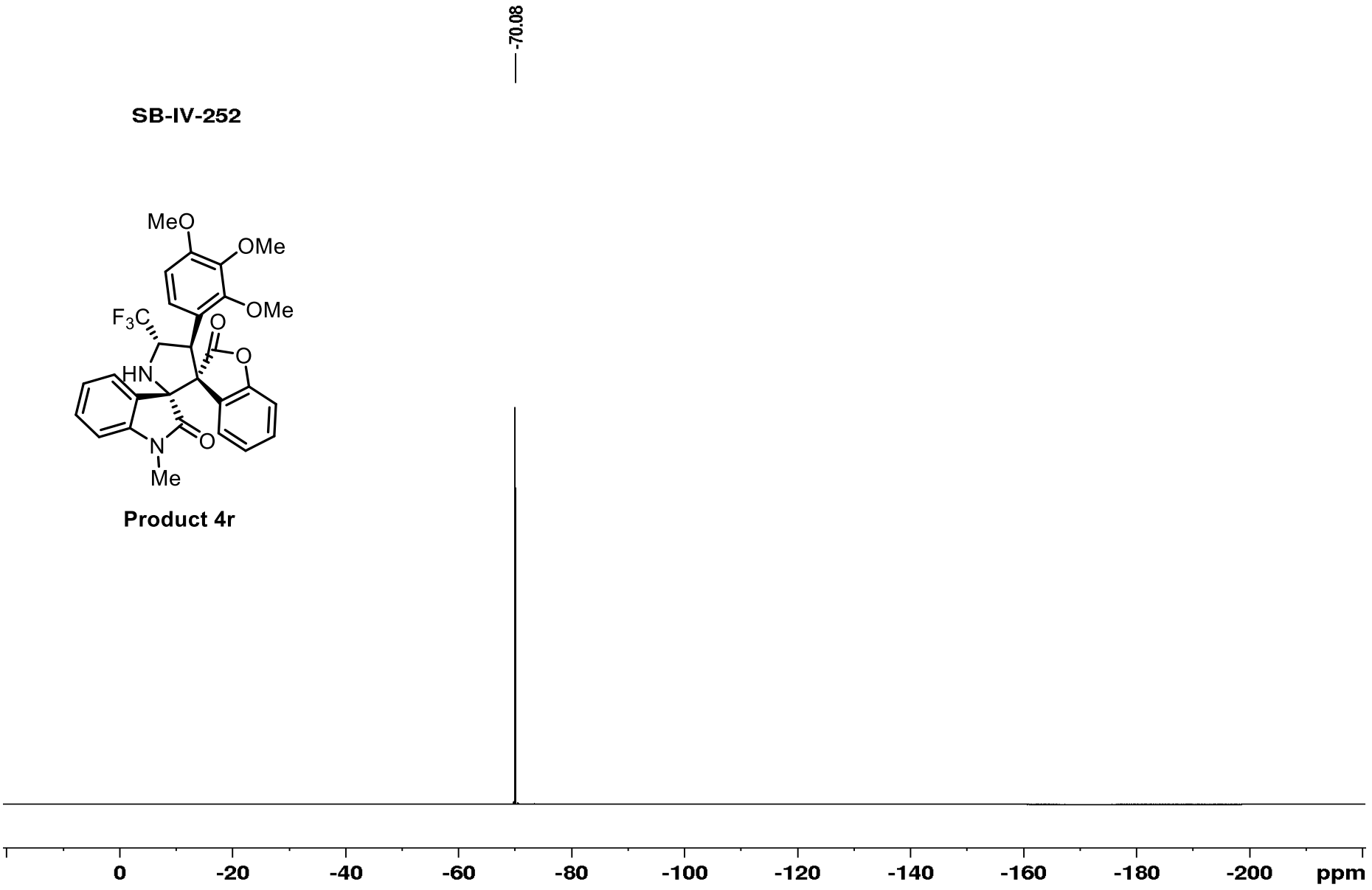

175.40
172.76
152.21
147.55
146.19
144.22
130.82
130.65
128.07
127.93
125.99
125.28
125.24
124.25
123.89
123.58
121.61
119.58
116.04
111.88
111.03
108.76
72.28
66.65
61.06
60.78
60.48
60.18
55.68
50.49
40.54
40.33
40.12
39.91
39.70
39.49
39.29
26.45
SB-IV-250
MeO
OH
F3C
O
O
HN
O
N
Me
Product 4q
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

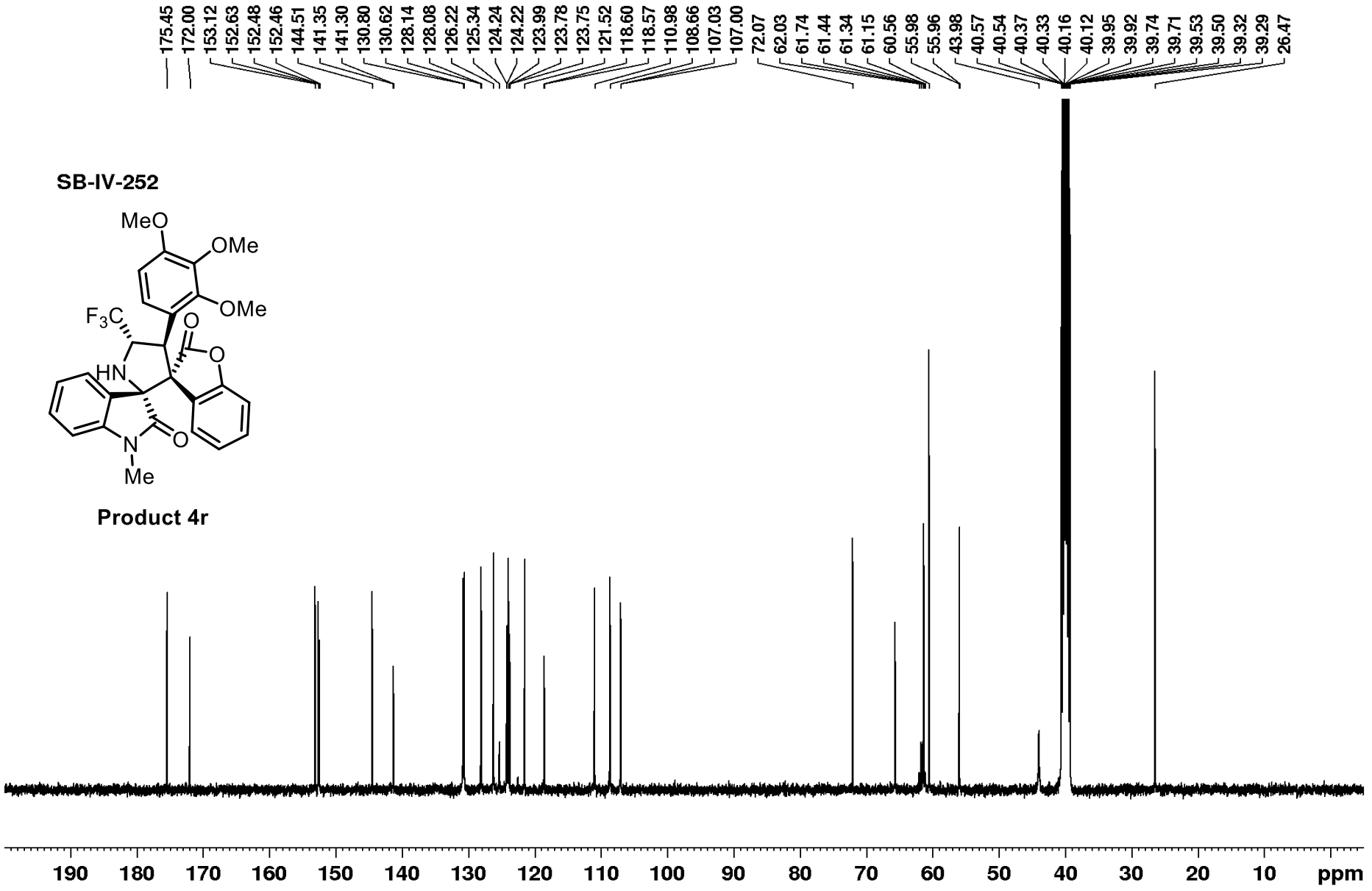

130.81
130.65
127.93
125.99
124.24
121.59
119.58
116.06
111.93
111.02
108.74
61.09
60.80
60.50
60.21
55.71
50.50
40.62
40.41
40.20
39.99
39.78
26.45
SB-IV-250
MeO
OH
F3C
O
O
HN
N
O
Me
Product 4q
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

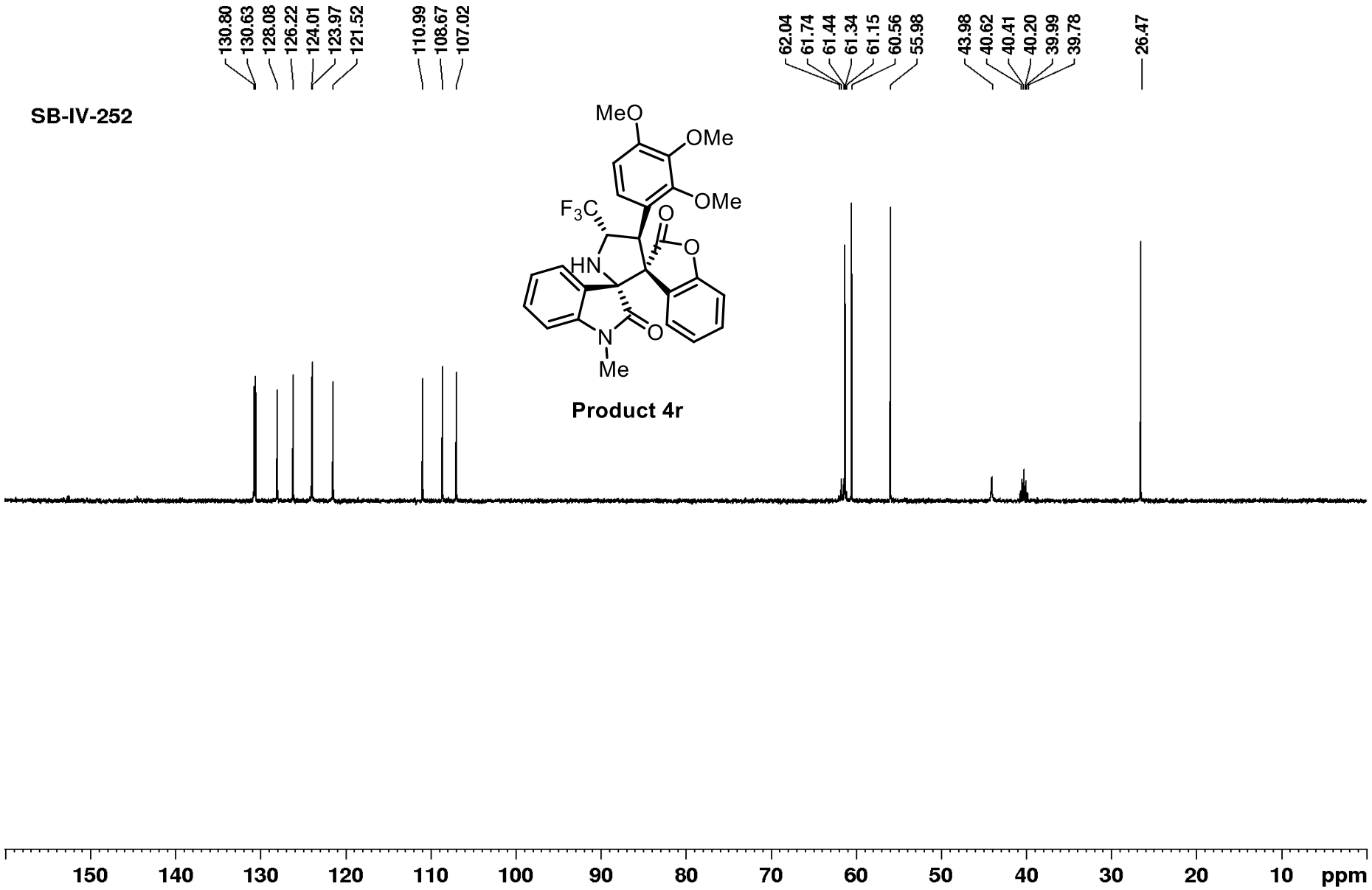

8.174
8.156
7.364
7.346
7.330
7.327
7.311
7.308
7.292
7.224
7.205
7.186
6.907
6.887
6.859
6.840
6.688
6.669
6.650
6.627
6.429
6.406
5.913
5.886
4.981
4.959
4.889
4.868
4.848
4.827
3.708
3.646
3.615
3.408
3.107
2.511
2.507
2.503
SB-IV-252
MeO
OMe
OMe
F3C
O
O
HN
O
N
Me
Product 4r
9
8
7
6
5
4
3
2
1
0 ppm
1.000
2.046
1.044
2.003
1.037
2.060
1.012
1.001
1.053
1.027
3.078
3.096
3.056
3.003

SB-IV-252

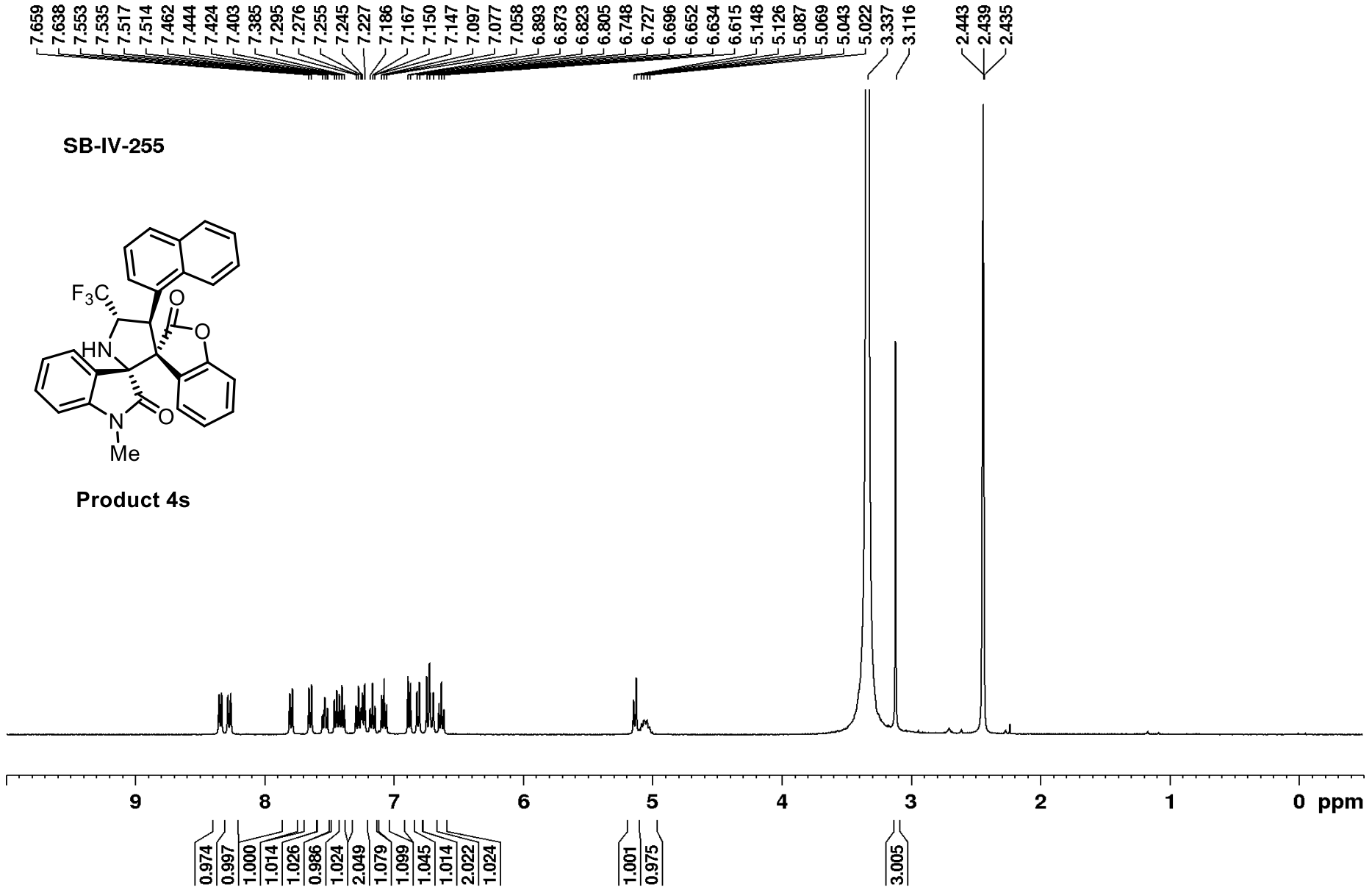
Product 4r




175.45
172.00
153.12
152.63
152.48
152.46
144.51
141.35
141.30
130.80
130.62
128.14
128.08
126.22
125.34
124.24
124.22
123.99
123.78
123.75
121.52
118.60
118.57
110.98
108.66
107.03
107.00
72.07
62.03
61.74
61.44
61.34
61.15
60.56
55.98
55.96
43.98
40.57
40.54
40.37
40.33
40.16
40.12
39.95
39.92
39.74
39.71
39.53
39.50
39.32
39.29
26.47
SB-IV-252
MeO
OMe
OMe
F3C
O
O
HN
O
N
Me
Product 4r
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

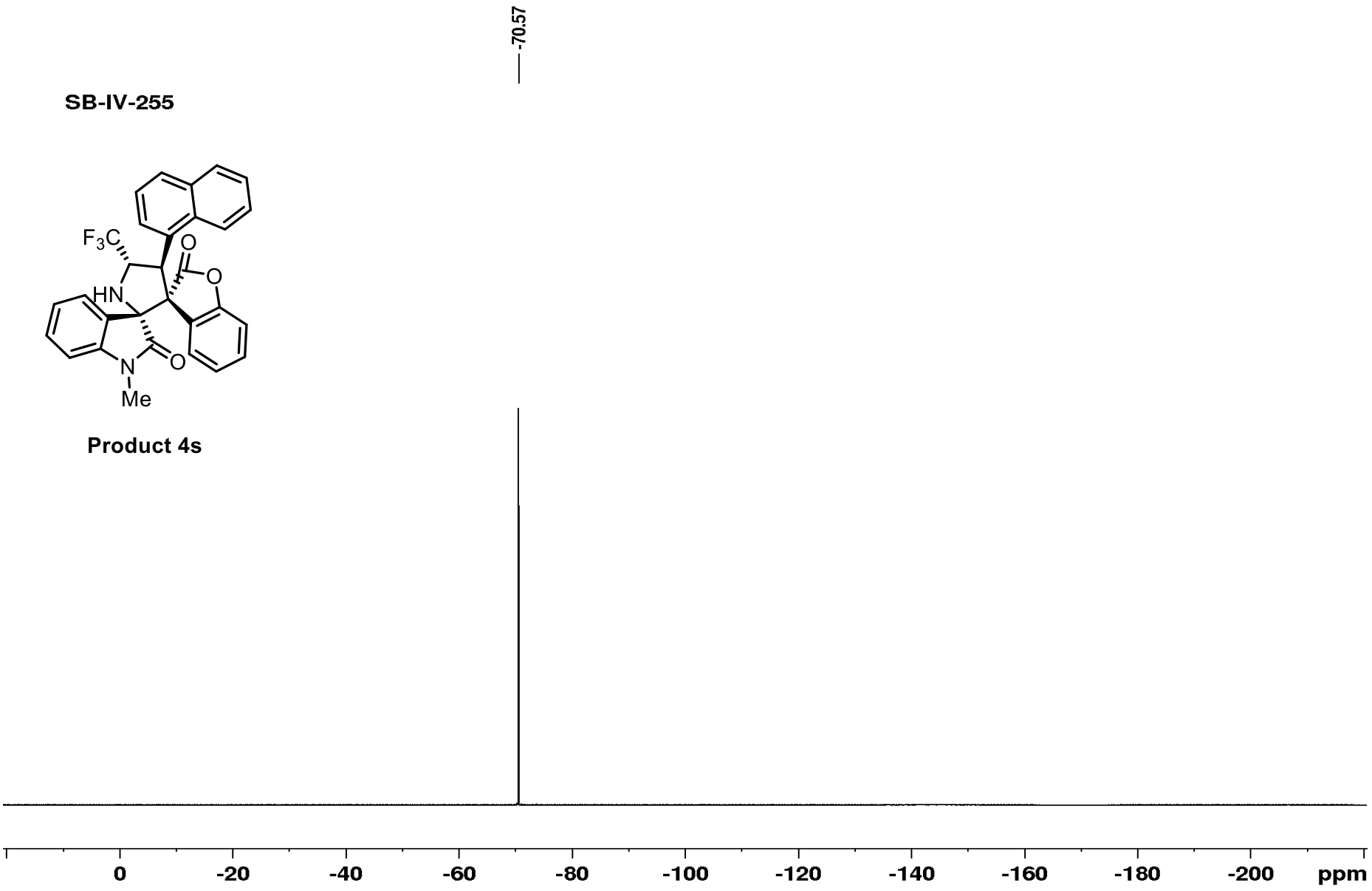

130.80
130.63
128.08
126.22
124.01
123.97
121.52
110.99
108.67
107.02
62.04
61.74
61.44
61.34
61.15
60.56
55.98
43.98
40.62
40.41
40.20
39.99
39.78
26.47
SB-IV-252
MeO
OMe
OMe
F3C
O
O
HN
O
N
Me
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

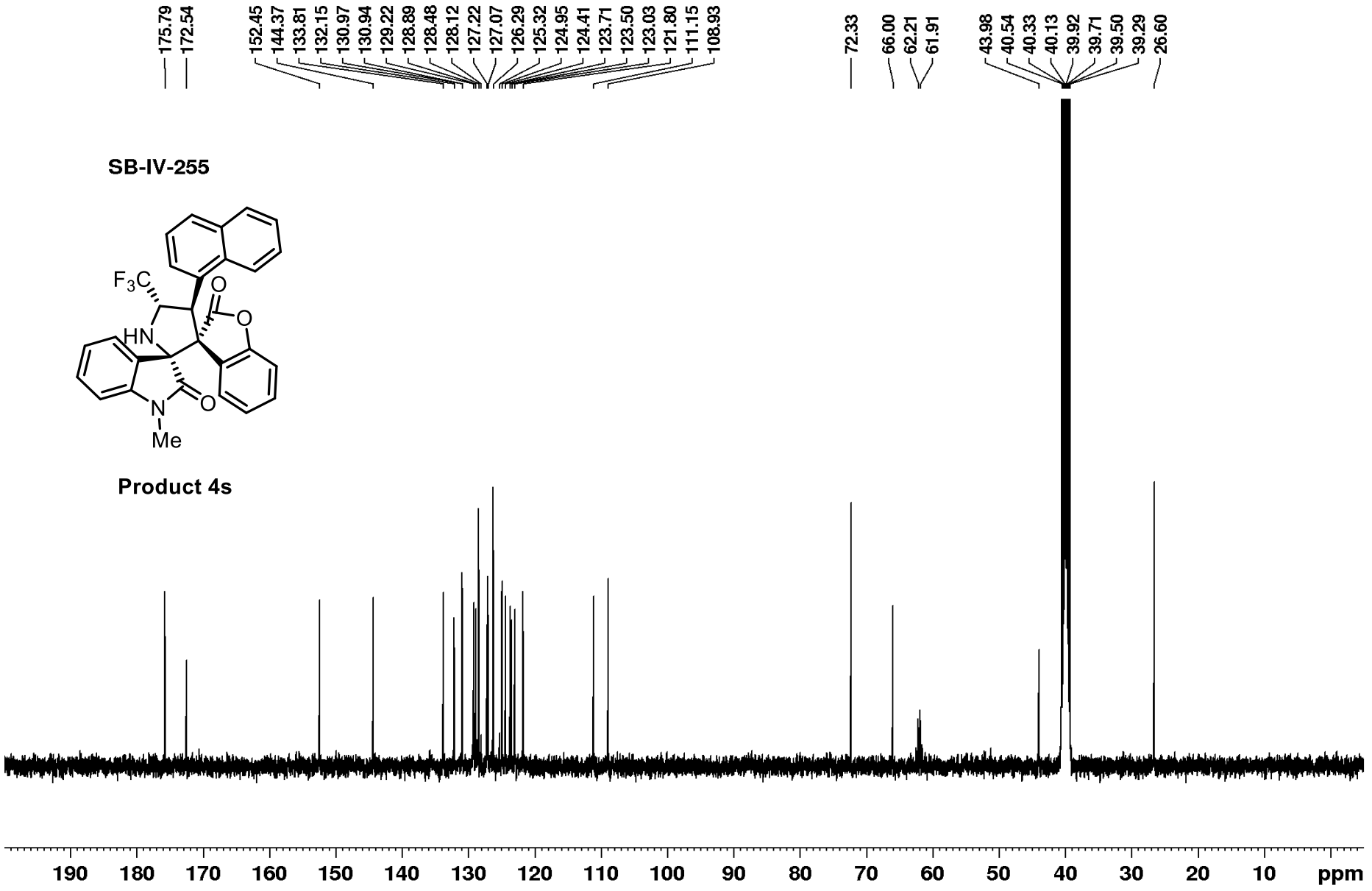
Product 4r

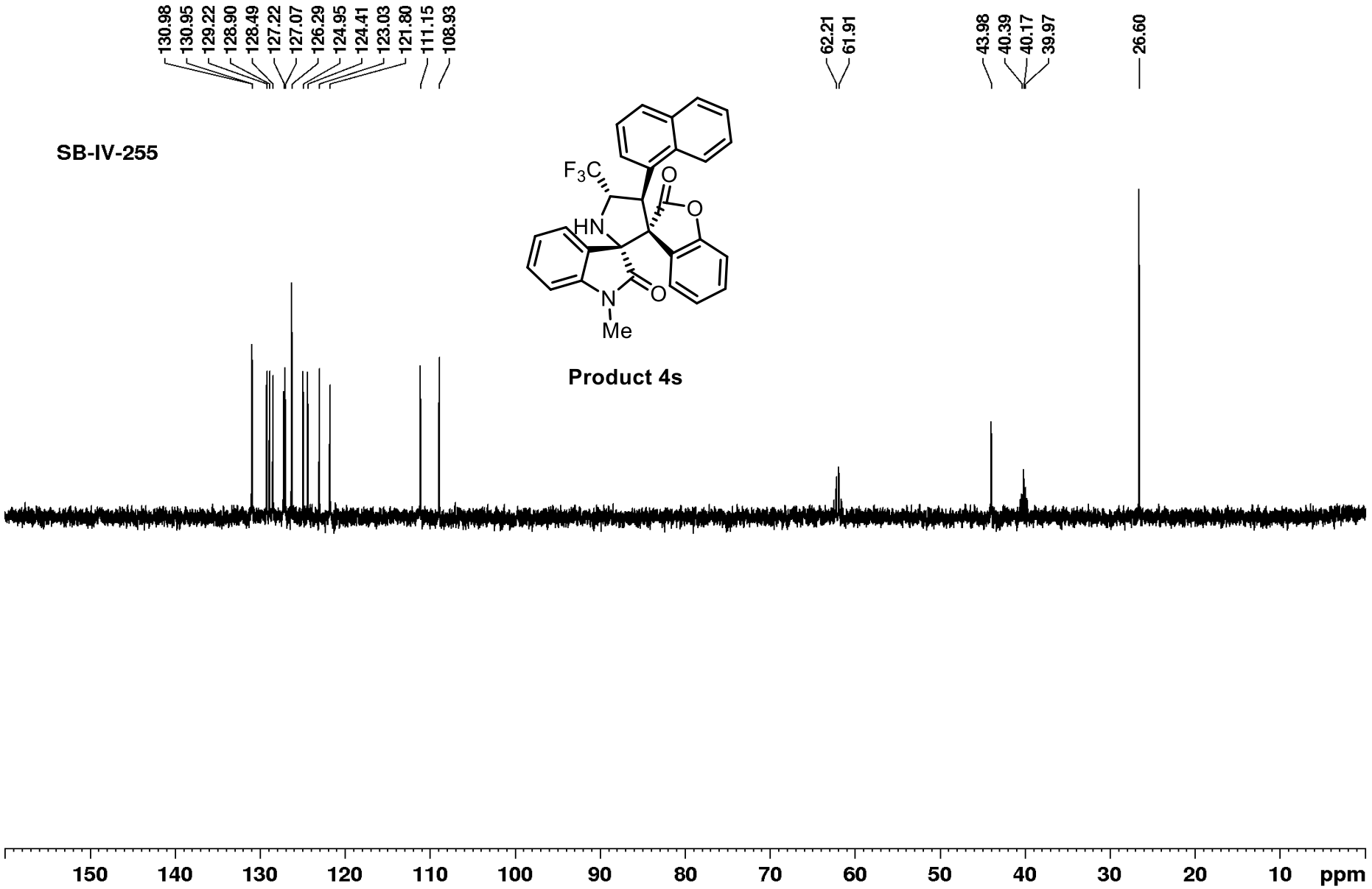

7.659
7.638
7.553
7.535
7.517
7.514
7.462
7.444
7.424
7.403
7.385
7.295
7.276
7.255
7.245
7.227
7.186
7.167
7.150
7.147
7.097
7.077
7.058
6.893
6.873
6.823
6.805
6.748
6.727
6.696
6.652
6.634
6.615
5.148
5.126
5.087
5.069
5.043
5.022
3.337
3.116
2.443
2.439
2.435
SB-IV-255
F3C
O
O
HN
O
N
Me
Product 4s
9
8
7
6
5
4
3
2
1
0 ppm
0.974
0.997
1.000
1.014
1.026
0.986
1.024
2.049
1.079
1.099
1.045
1.014
2.022
1.024
1.001
0.975
3.005

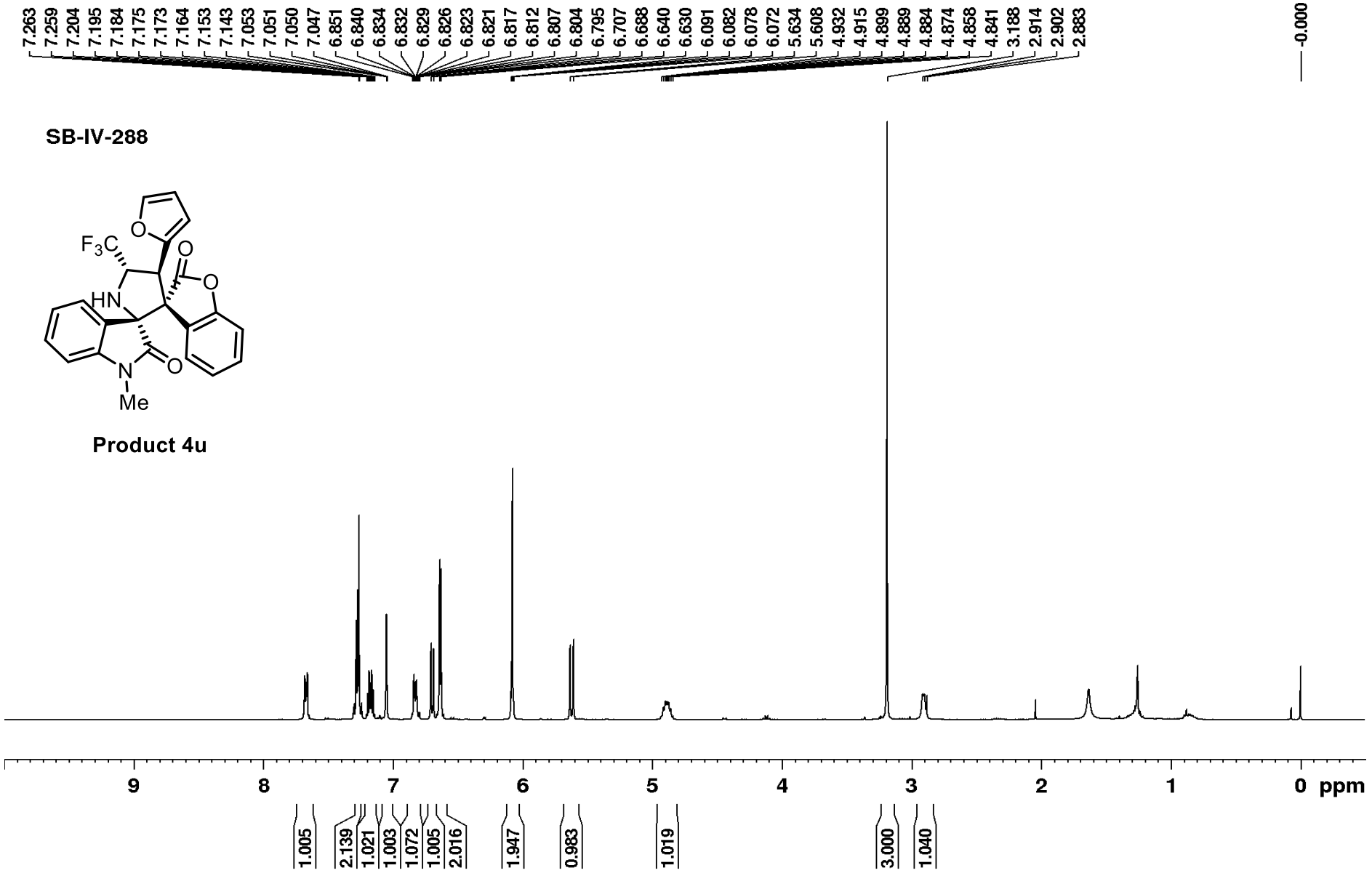
SB-IV-255

Product 4s



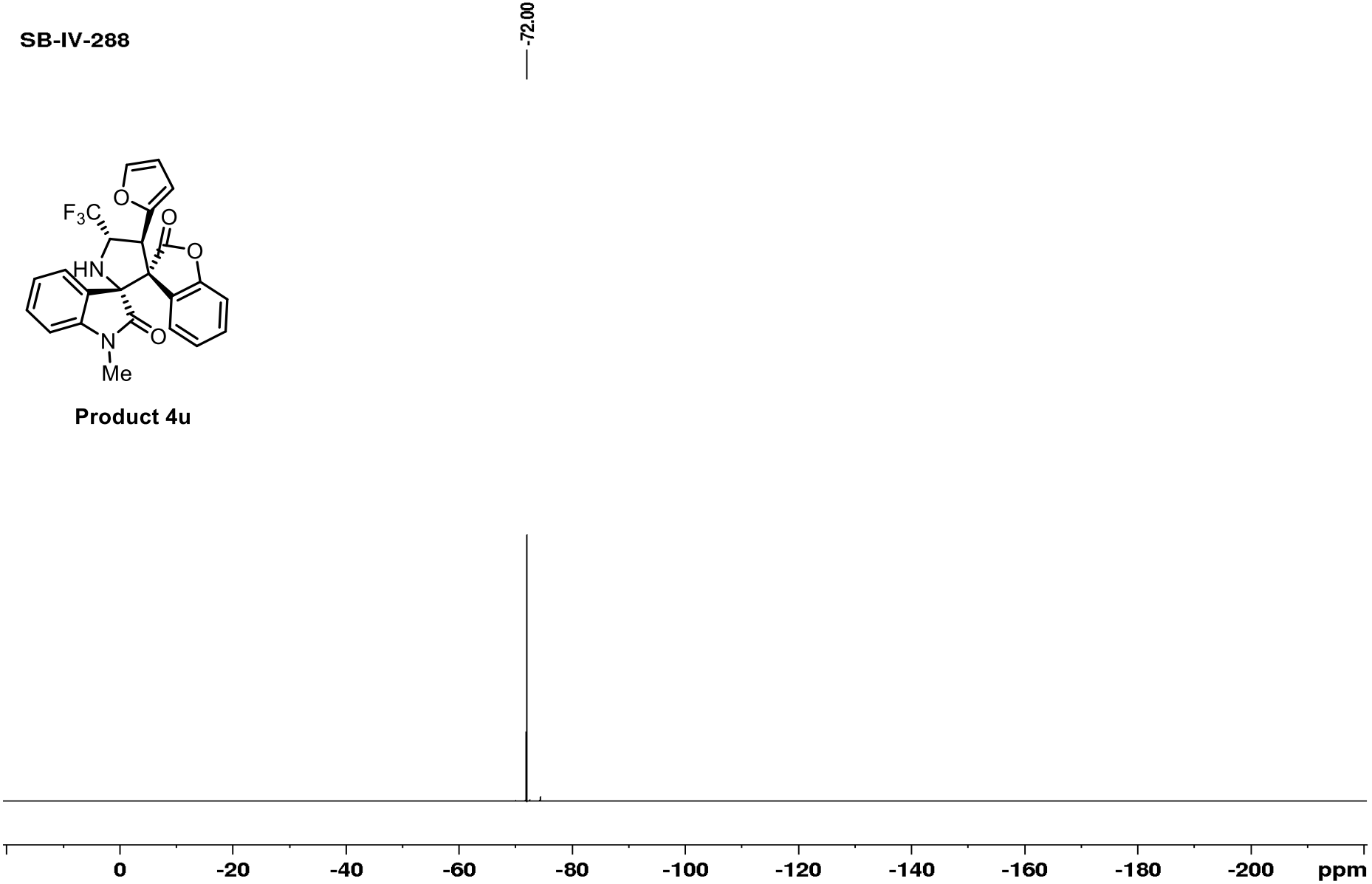

175.79
172.54
152.45
144.37
133.81
132.15
130.97
130.94
129.22
128.89
128.48
128.12
127.22
127.07
126.29
125.32
124.95
124.41
123.71
123.50
123.03
121.80
111.15
108.93
72.33
66.00
62.21
61.91
43.98
40.54
40.33
40.13
39.92
39.71
39.50
39.29
26.60
SB-IV-255
F3C
HN
O
O
O
N
Me
Product 4s
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

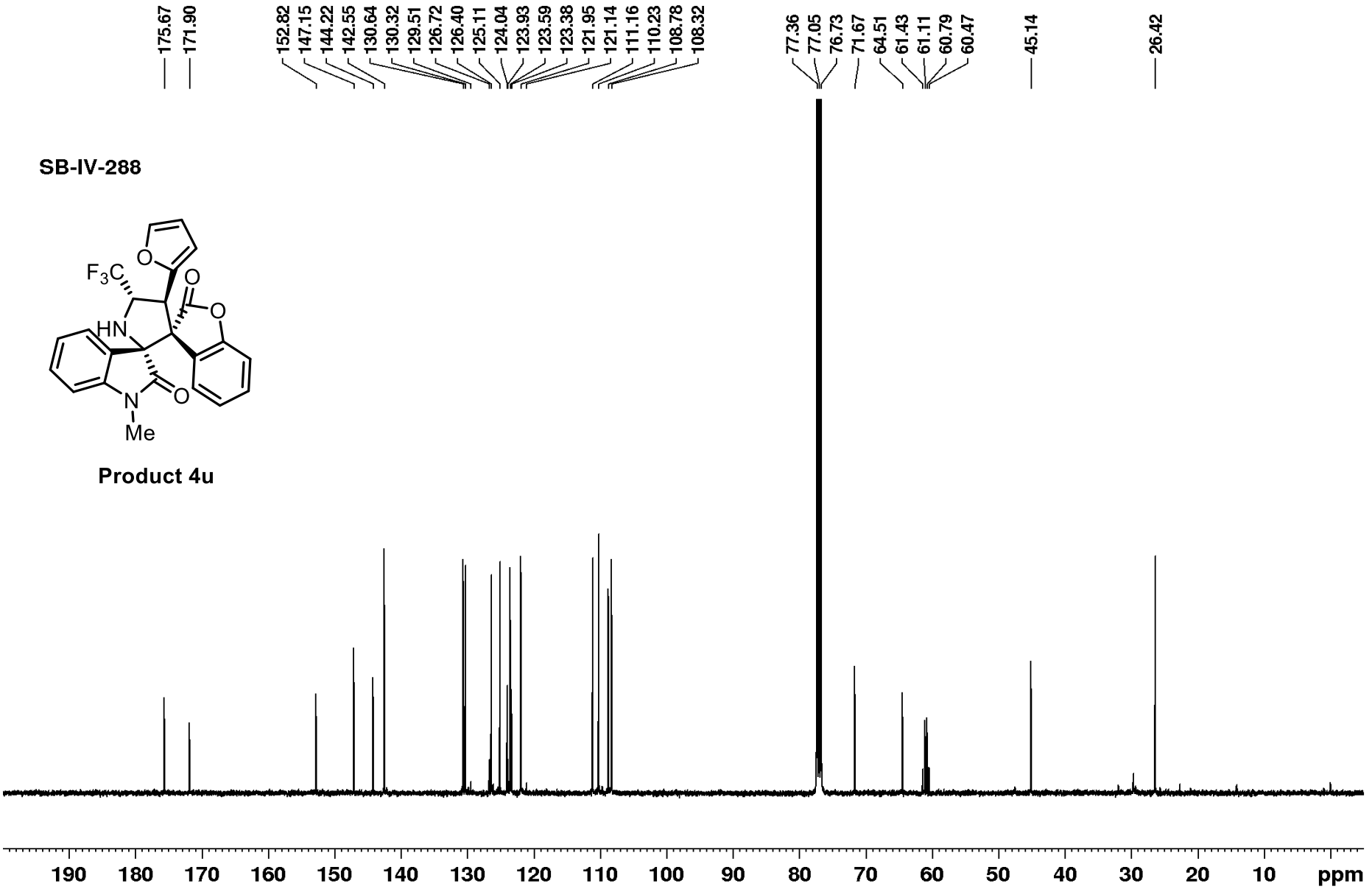

130.98
130.95
129.22
128.90
128.49
127.22
127.07
126.29
124.95
124.41
123.03
121.80
111.15
108.93
62.21
61.91
43.98
40.39
40.17
39.97
26.60
SB-IV-255
F3C
HN
O
O
O
N
Me
Product 4s
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

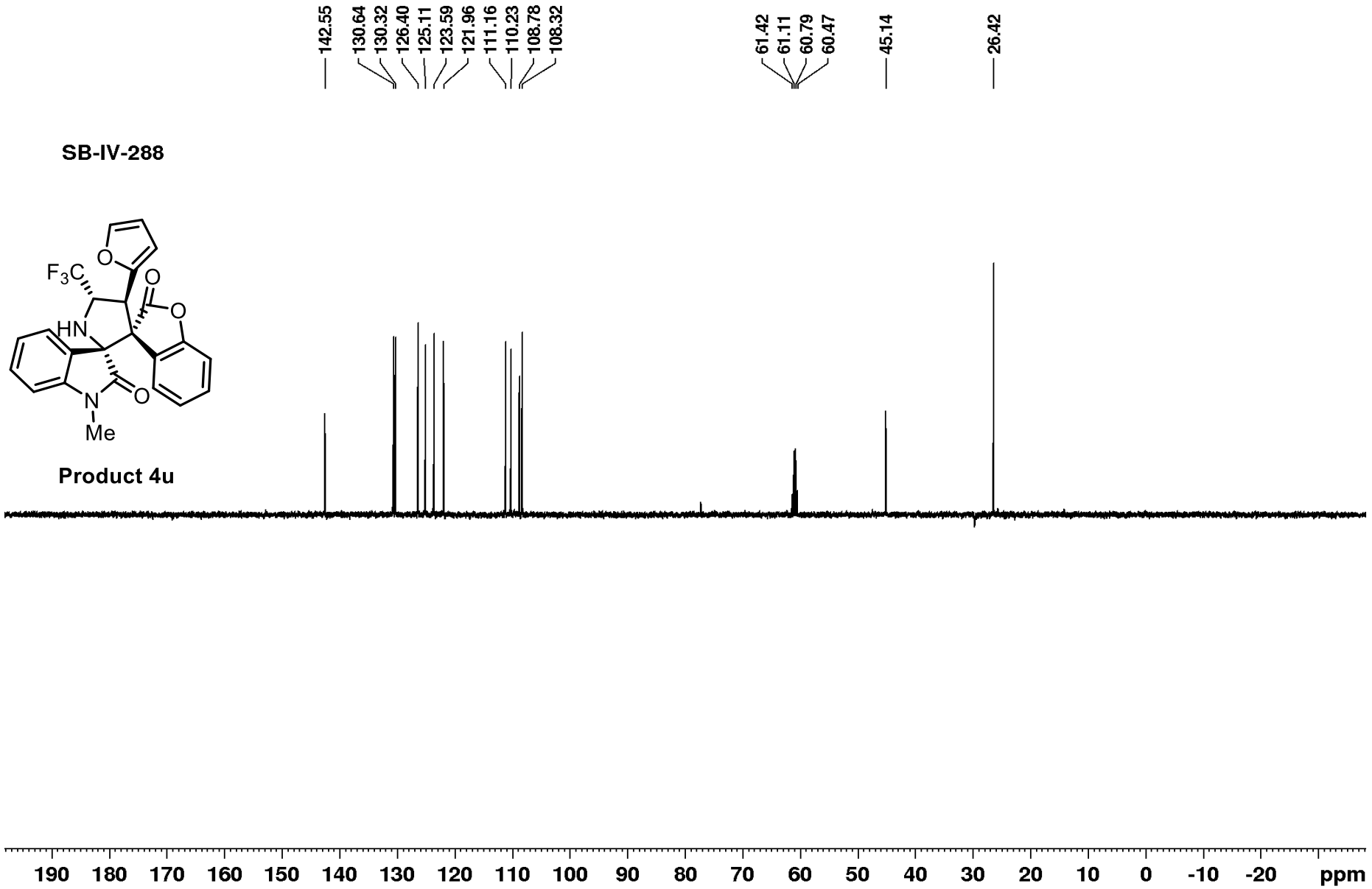

7.263
7.259
7.204
7.195
7.184
7.175
7.173
7.164
7.153
7.143
7.053
7.051
7.050
7.047
6.851
6.840
6.834
6.832
6.829
6.826
6.823
6.821
6.817
6.812
6.807
6.804
6.795
6.707
6.688
6.640
6.630
6.091
6.082
6.078
6.072
5.634
5.608
4.932
4.915
4.899
4.889
4.884
4.874
4.858
4.841
3.188
2.914
2.902
2.883
-0.000
SB-IV-288
F3C
HN
O
O
O
O
N
Me
Product 4u
9
8
7
6
5
4
3
2
1
0 ppm
1.005
2.139
1.021
1.003
1.072
1.005
2.016
1.947
0.983
1.019
3.000
1.040

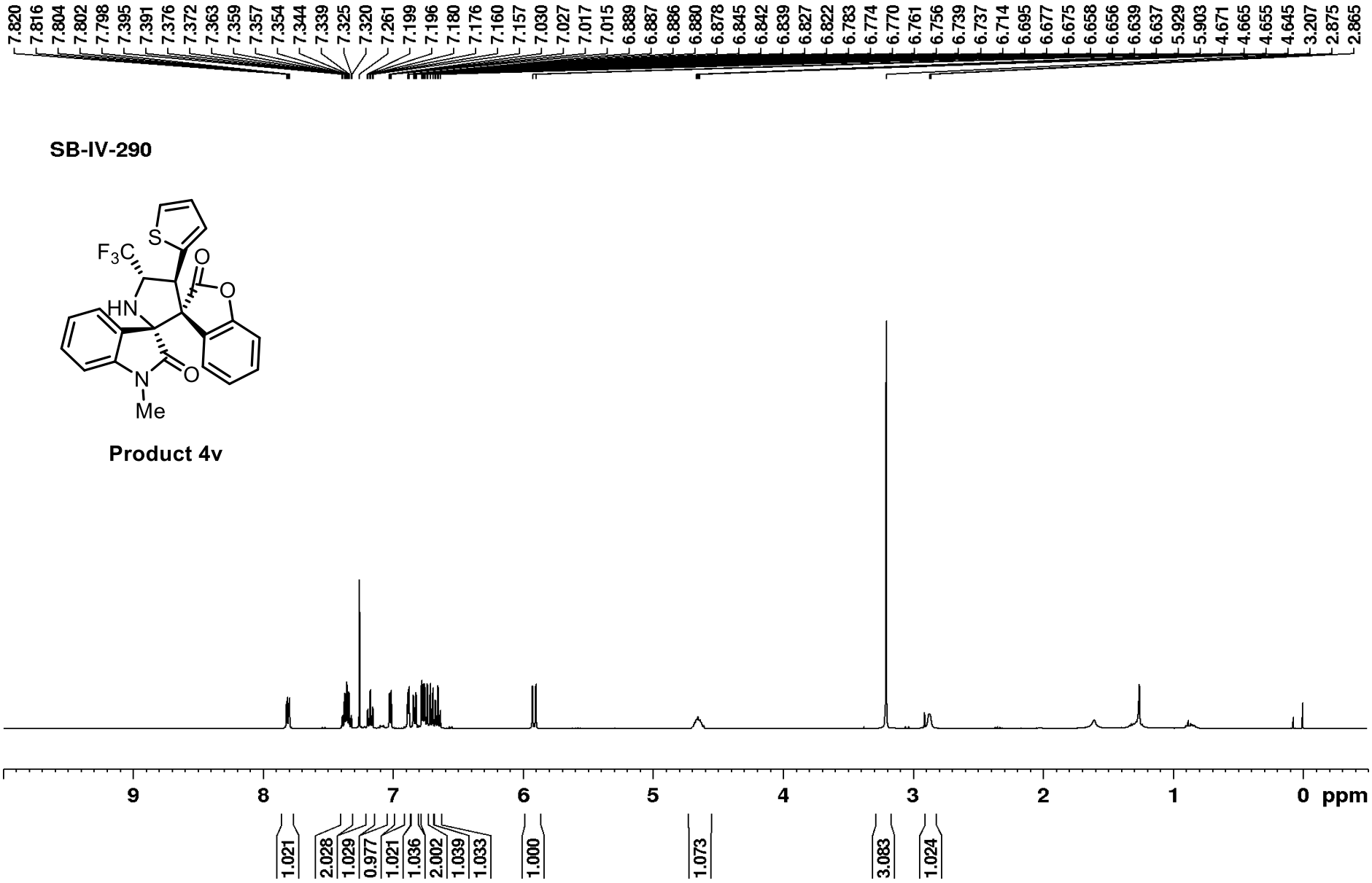
SB-IV-288

Product 4u



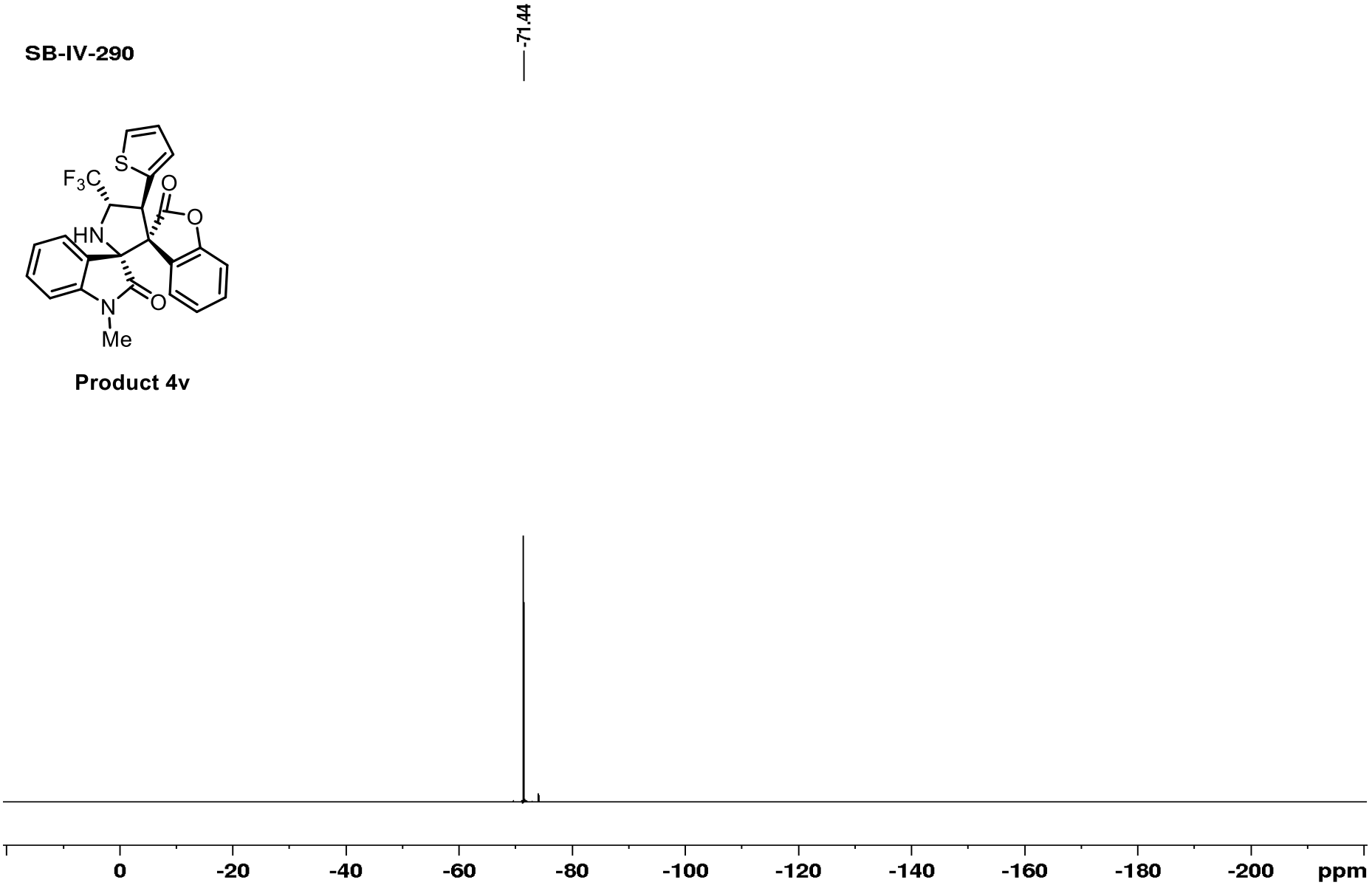

175.67
171.90
152.82
147.15
144.22
142.55
130.64
130.32
129.51
126.72
126.40
125.11
124.04
123.93
123.59
123.38
121.95
121.14
111.16
110.23
108.78
108.32
77.36
77.05
76.73
71.67
64.51
61.43
61.11
60.79
60.47
45.14
26.42
SB-IV-288
F3C
O
O
O
HN
O
N
Me
Product 4u
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

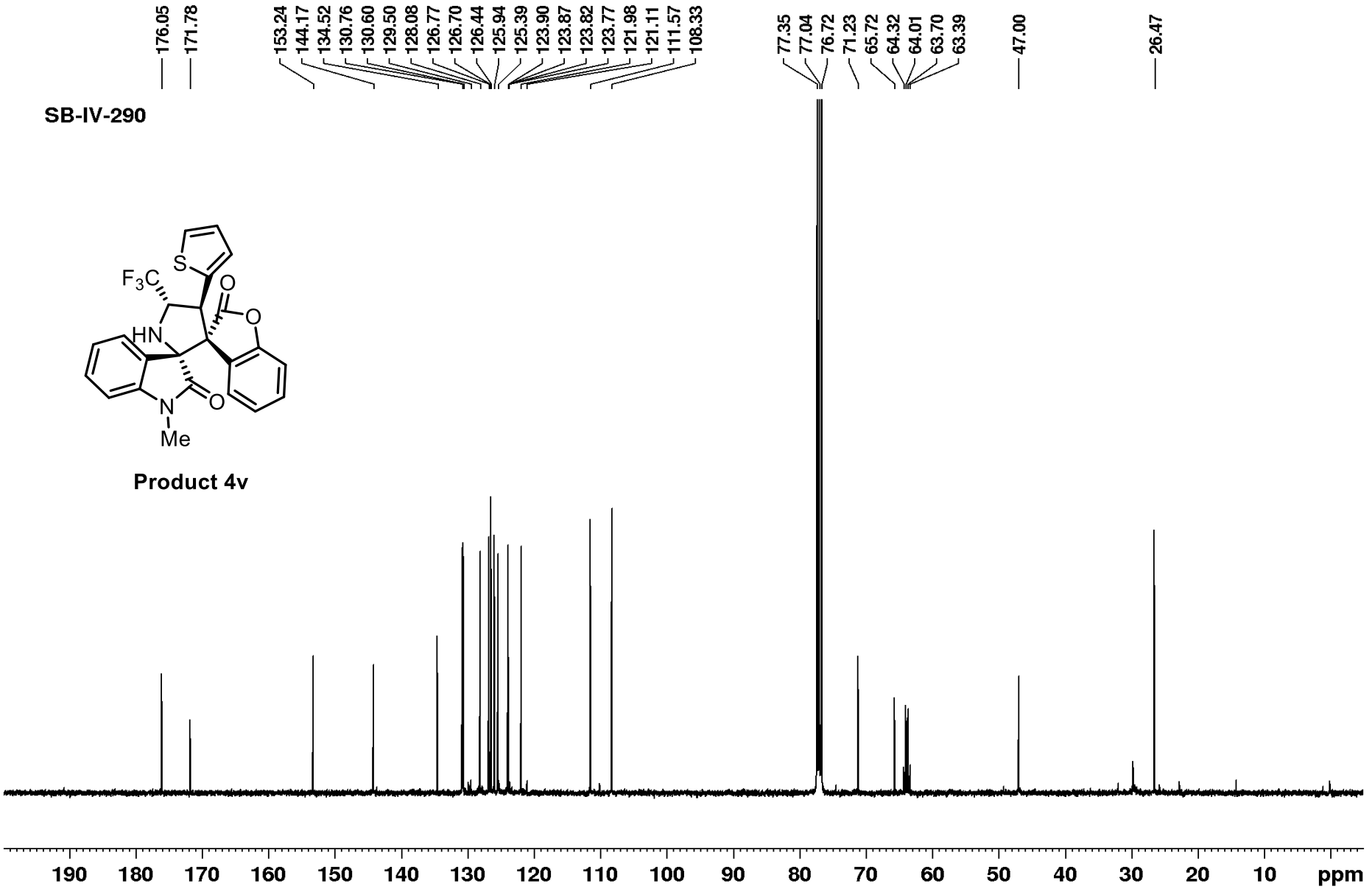

142.55
130.64
130.32
126.40
125.11
123.59
121.96
111.16
110.23
108.78
108.32
61.42
61.11
60.79
60.47
45.14
26.42
SB-IV-288
F3C
O
O
O
HN
O
N
Me
Product 4u
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
ppm


7.820
7.816
7.804
7.802
7.798
7.395
7.391
7.376
7.372
7.363
7.359
7.357
7.354
7.344
7.339
7.325
7.320
7.261
7.199
7.196
7.180
7.176
7.160
7.157
7.030
7.027
7.017
7.015
6.889
6.887
6.886
6.880
6.878
6.845
6.842
6.839
6.827
6.822
6.783
6.774
6.770
6.761
6.756
6.739
6.737
6.714
6.695
6.677
6.675
6.658
6.656
6.639
6.637
5.929
5.903
4.671
4.665
4.655
4.645
3.207
2.875
2.865
SB-IV-290
F3C
S
O
O
HN
O
N
Me
Product 4v
9
8
7
6
5
4
3
2
1
0 ppm
1.021
2.028
1.029
0.977
1.021
1.036
2.002
1.039
1.033
1.000
1.073
3.083
1.024

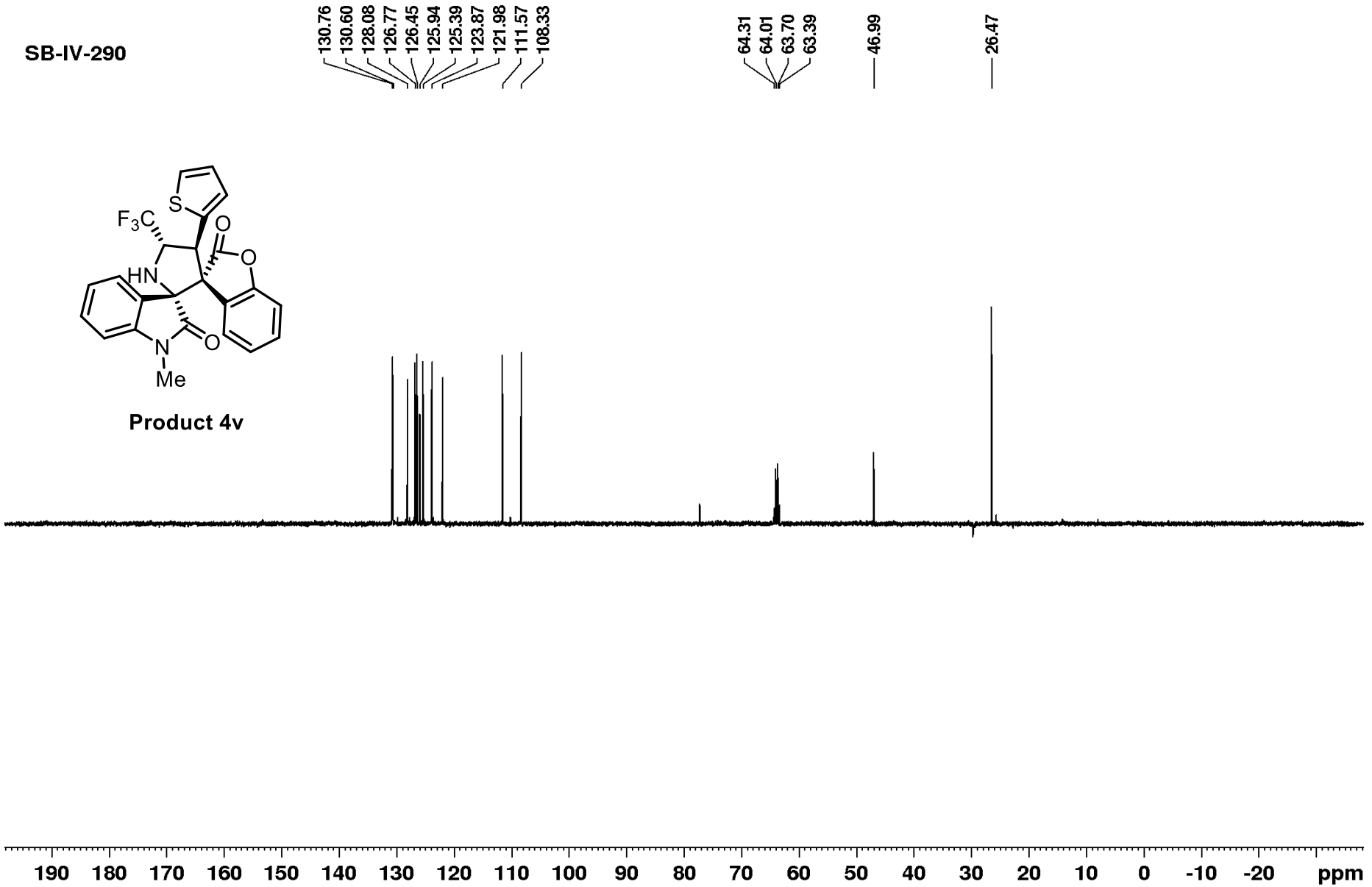
SB-IV-290

Product 4v

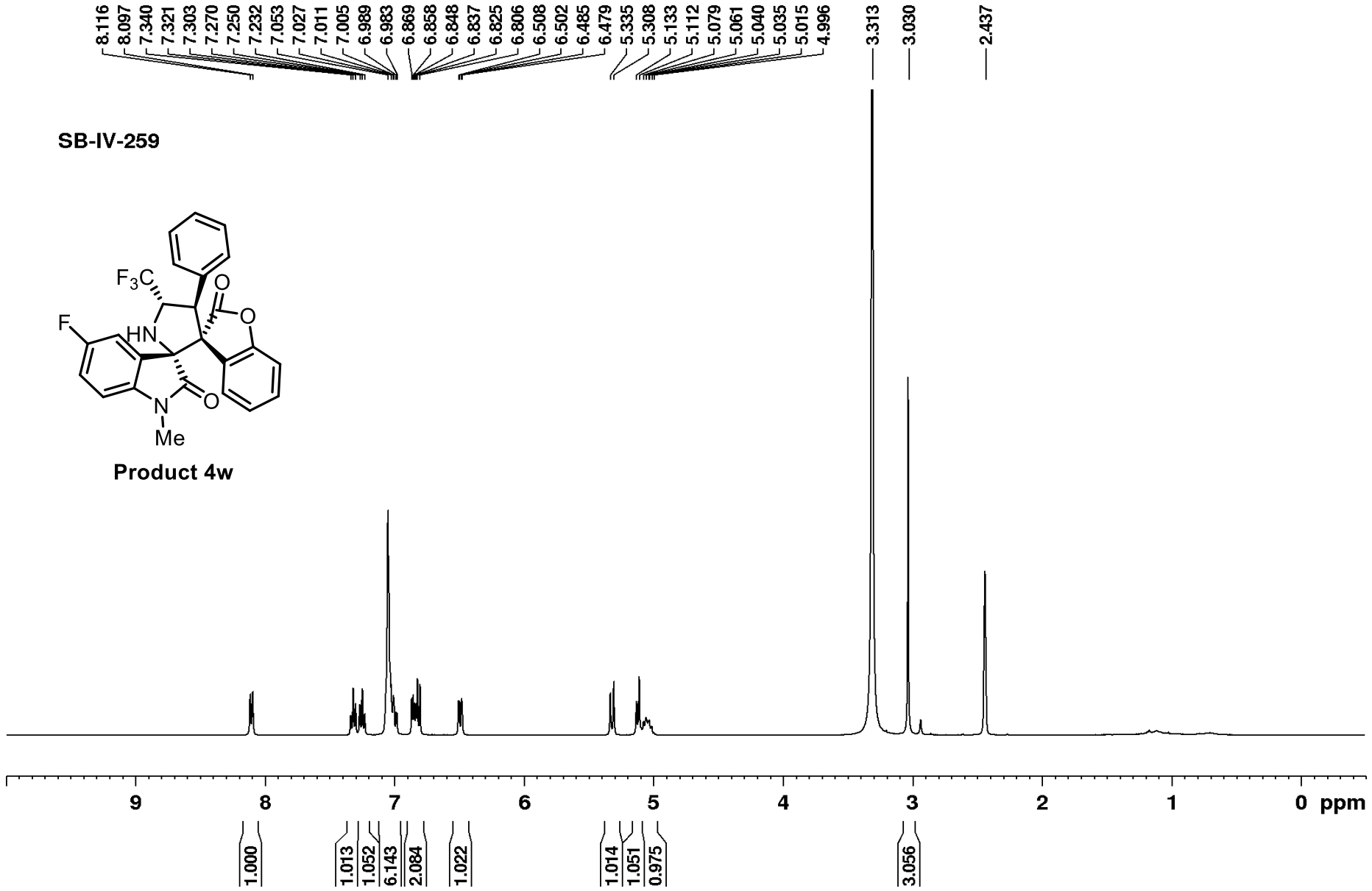



176.05
171.78
153.24
144.17
134.52
130.76
130.60
129.50
128.08
126.77
126.70
126.44
125.94
125.39
123.90
123.87
123.82
123.77
121.98
121.11
111.57
108.33
77.35
77.04
76.72
71.23
65.72
64.32
64.01
63.70
63.39
47.00
26.47
SB-IV-290
S
F3C
O
O
HN
N
O
Me
Product 4v
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

SB-IV-290

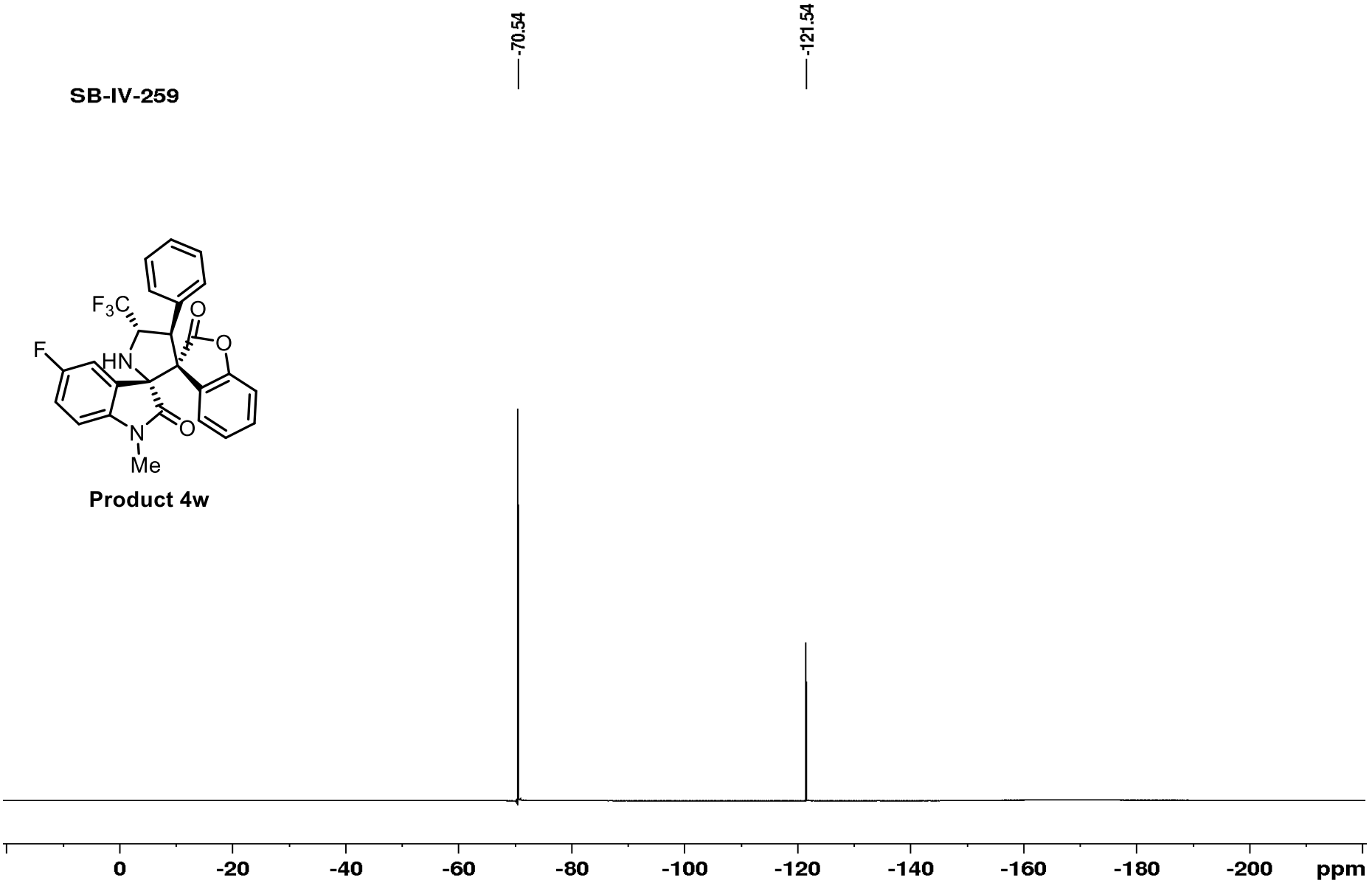


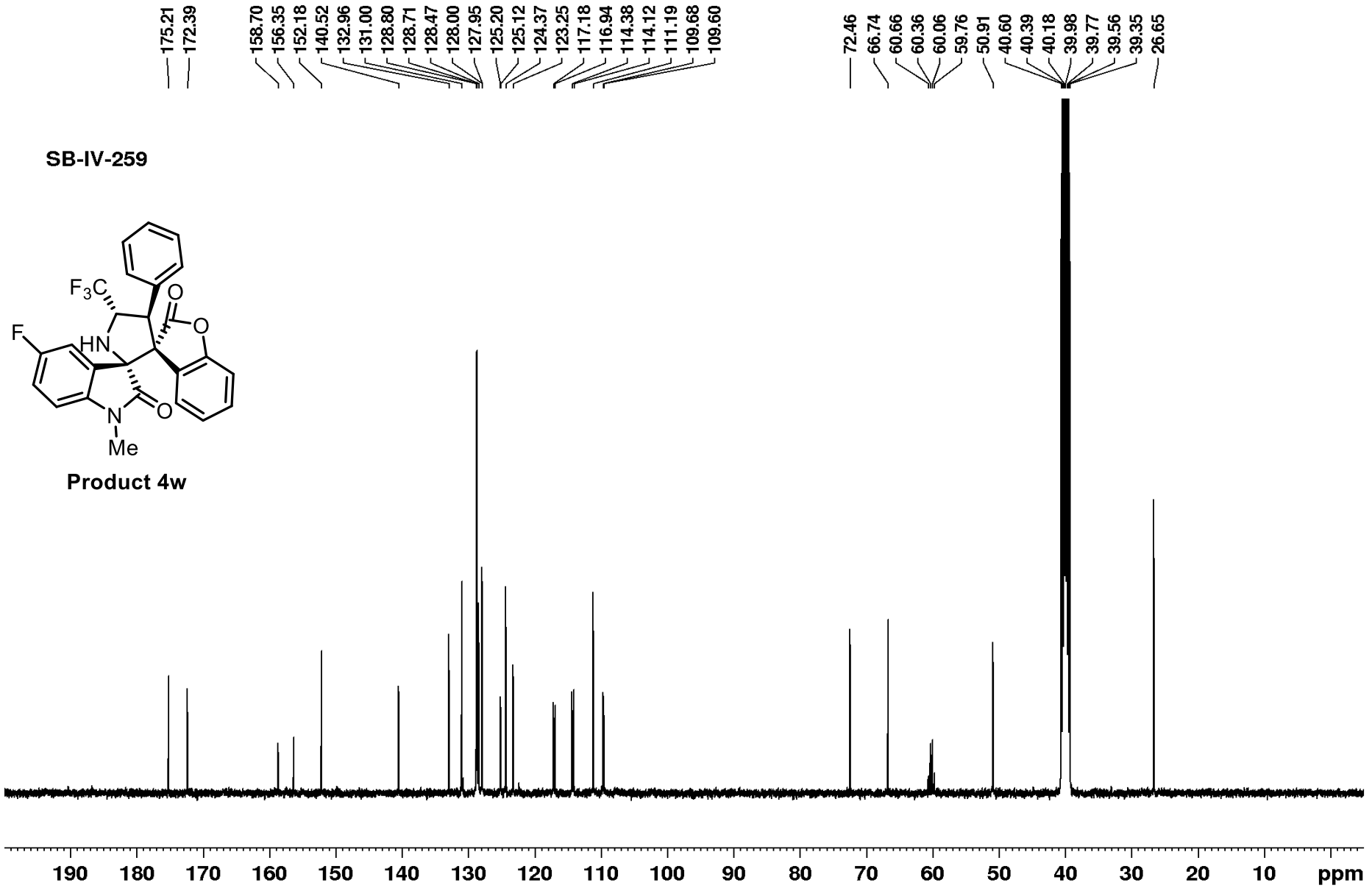
Product 4v

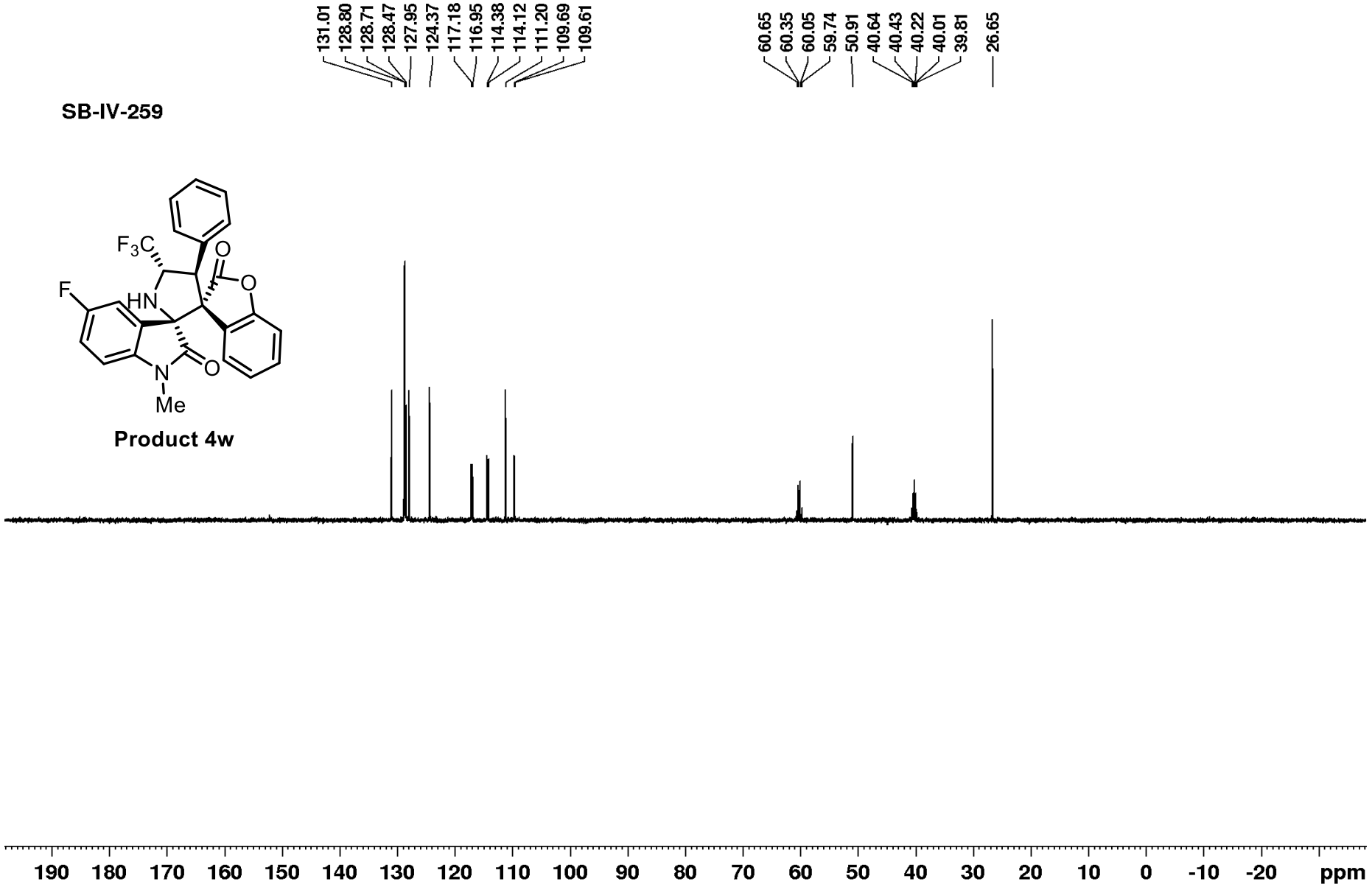

8.116
8.097
7.340
7.321
7.303
7.270
7.250
7.232
7.053
7.027
7.011
7.005
6.989
6.983
6.869
6.858
6.848
6.837
6.825
6.806
6.508
6.502
6.485
6.479
5.335
5.308
5.133
5.112
5.079
5.061
5.040
5.035
5.015
4.996
3.313
3.030
2.437
SB-IV-259
F3C
O
O
F
HN
O
N
Me
Product 4w
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.013
1.052
6.143
2.084
1.022
1.014
1.051
0.975
3.056

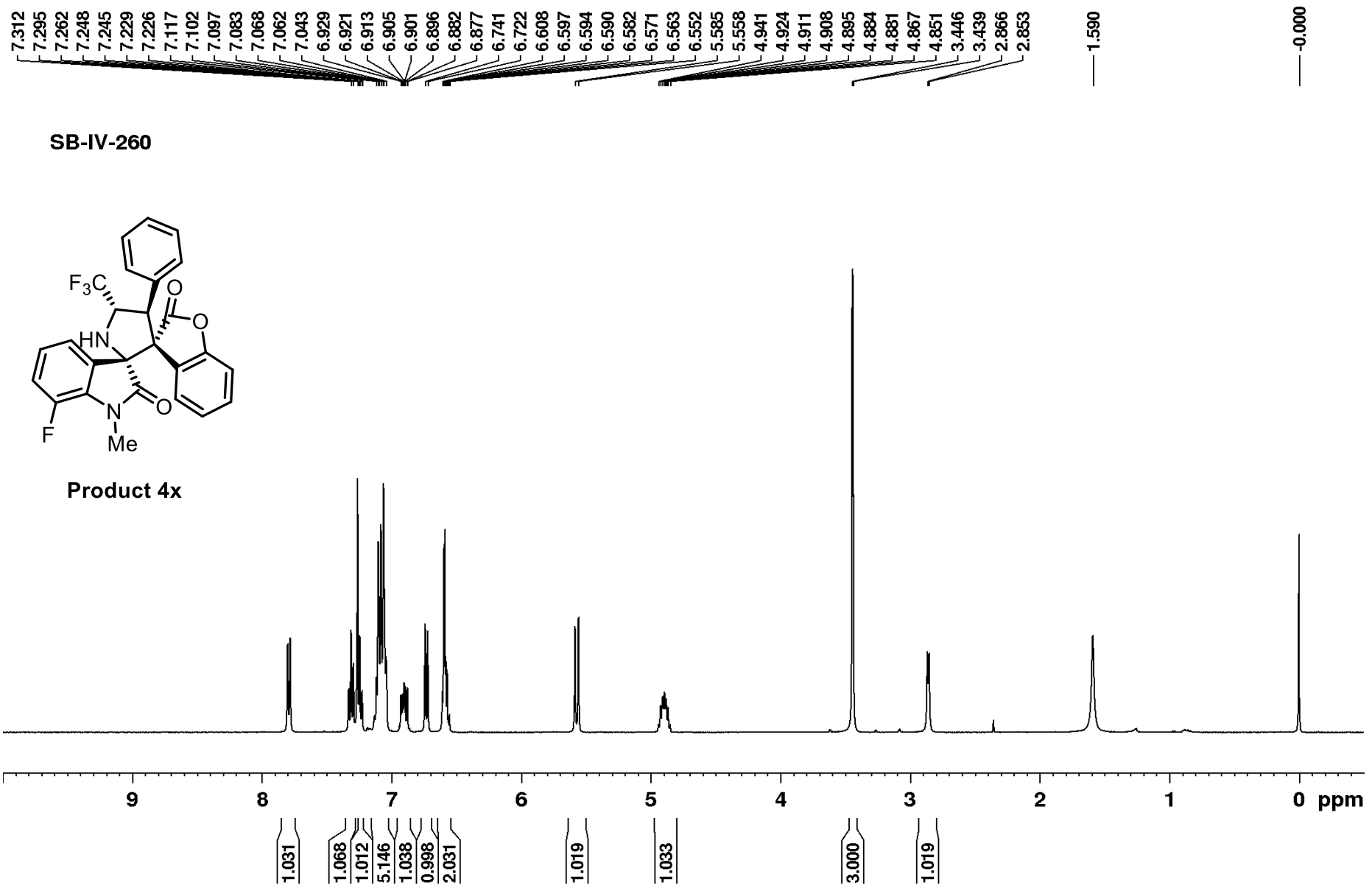
SB-IV-259

Product 4w



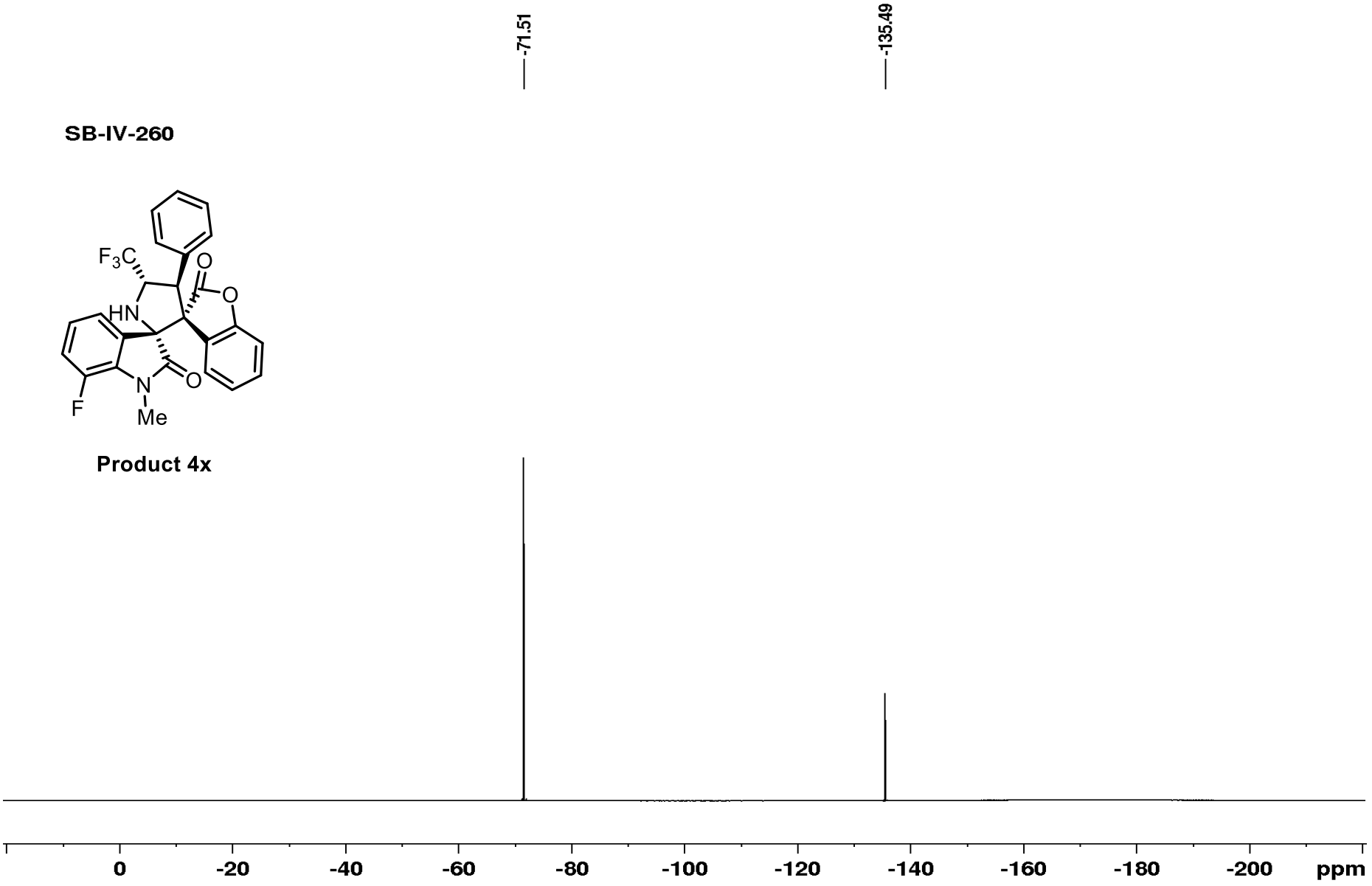

175.21
172.39
158.70
156.35
152.18
140.52
132.96
131.00
128.80
128.71
128.47
128.00
127.95
125.20
125.12
124.37
123.25
117.18
116.94
114.38
114.12
111.19
109.68
109.60
72.46
66.74
60.66
60.36
60.06
59.76
50.91
40.60
40.39
40.18
39.98
39.77
39.56
39.35
26.65
SB-IV-259
F3C
O
O
F
HN
O
N
Me
Product 4w
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

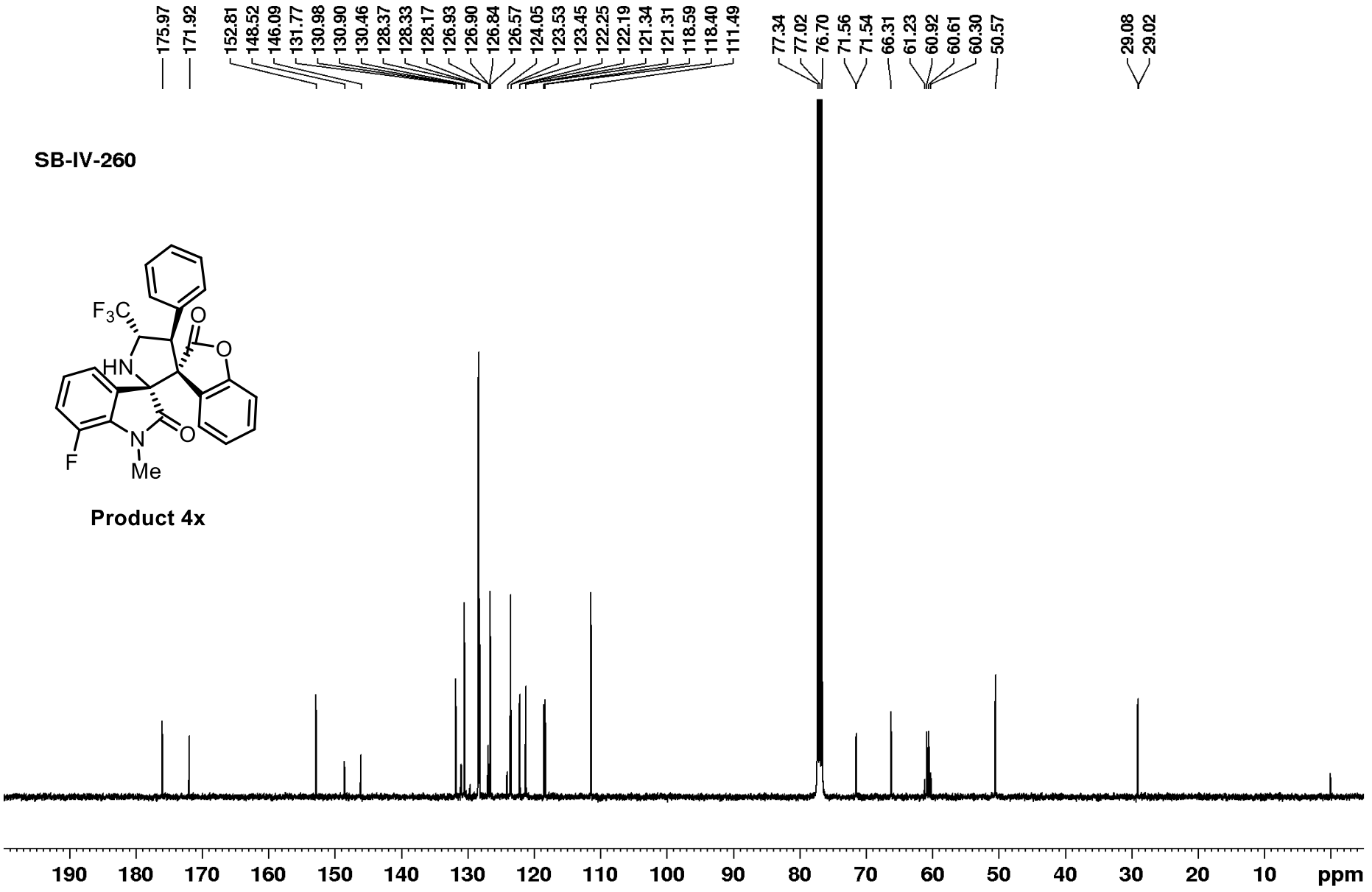

131.01
128.80
128.71
128.47
127.95
124.37
117.18
116.95
114.38
114.12
111.20
109.69
109.61
60.65
60.35
60.05
59.74
50.91
40.64
40.43
40.22
40.01
39.81
26.65
SB-IV-259
F3C
O
O
F
HN
O
N
Me
Product 4w
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 ppm

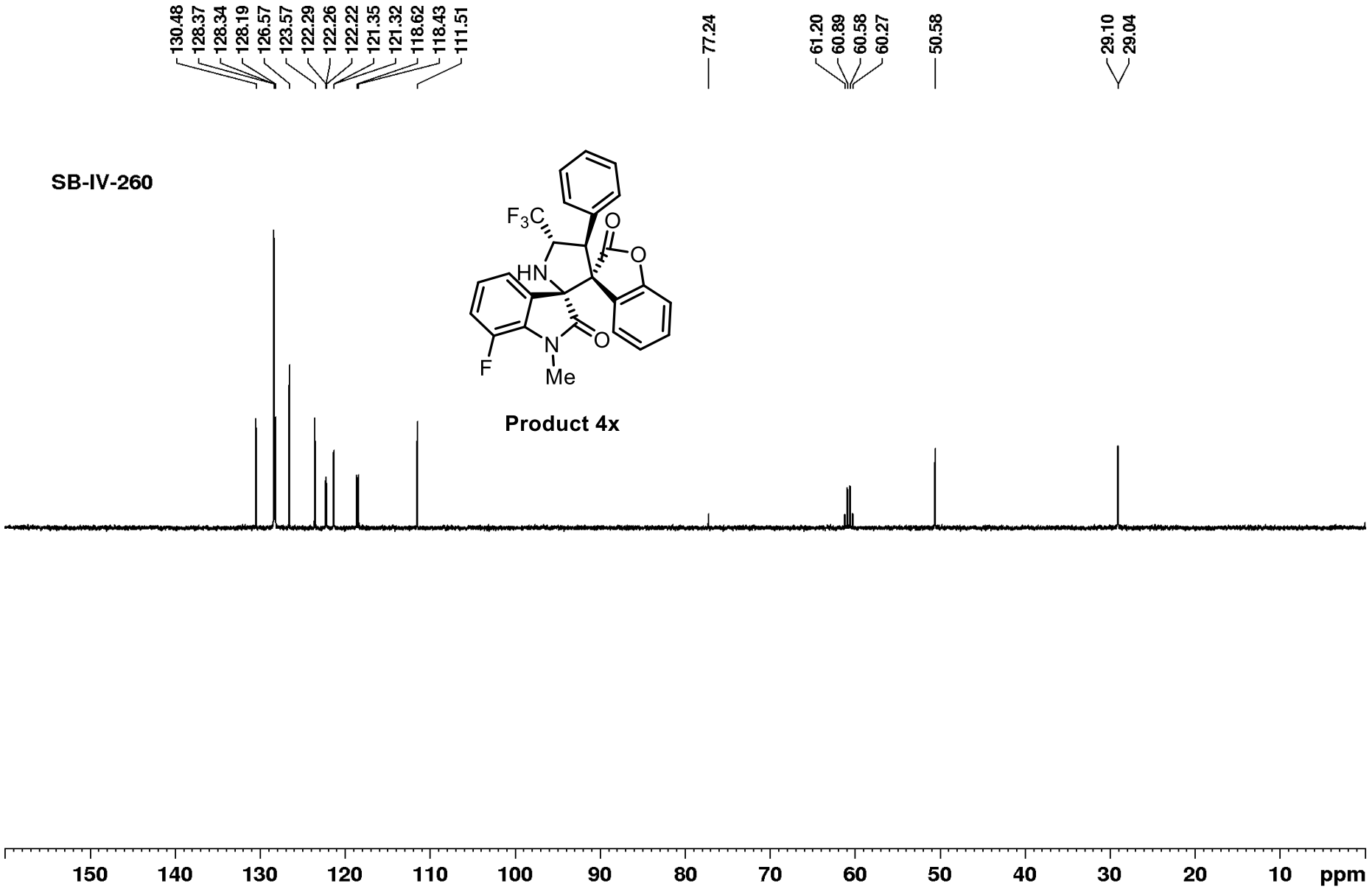

7.312
7.295
7.262
7.248
7.245
7.229
7.226
7.117
7.102
7.097
7.083
7.068
7.062
7.043
6.929
6.921
6.913
6.905
6.901
6.896
6.882
6.877
6.741
6.722
6.608
6.597
6.594
6.590
6.582
6.571
6.563
6.552
5.585
5.558
4.941
4.924
4.911
4.908
4.895
4.884
4.881
4.867
4.851
3.446
3.439
2.866
2.853
1.590
-0.000
SB-IV-260
F3C
O
O
HN
O
N
Me
F
Product 4x
9
8
7
6
5
4
3
2
1
0 ppm
1.031
1.068
1.012
5.146
1.038
0.998
2.031
1.019
1.033
3.000
1.019

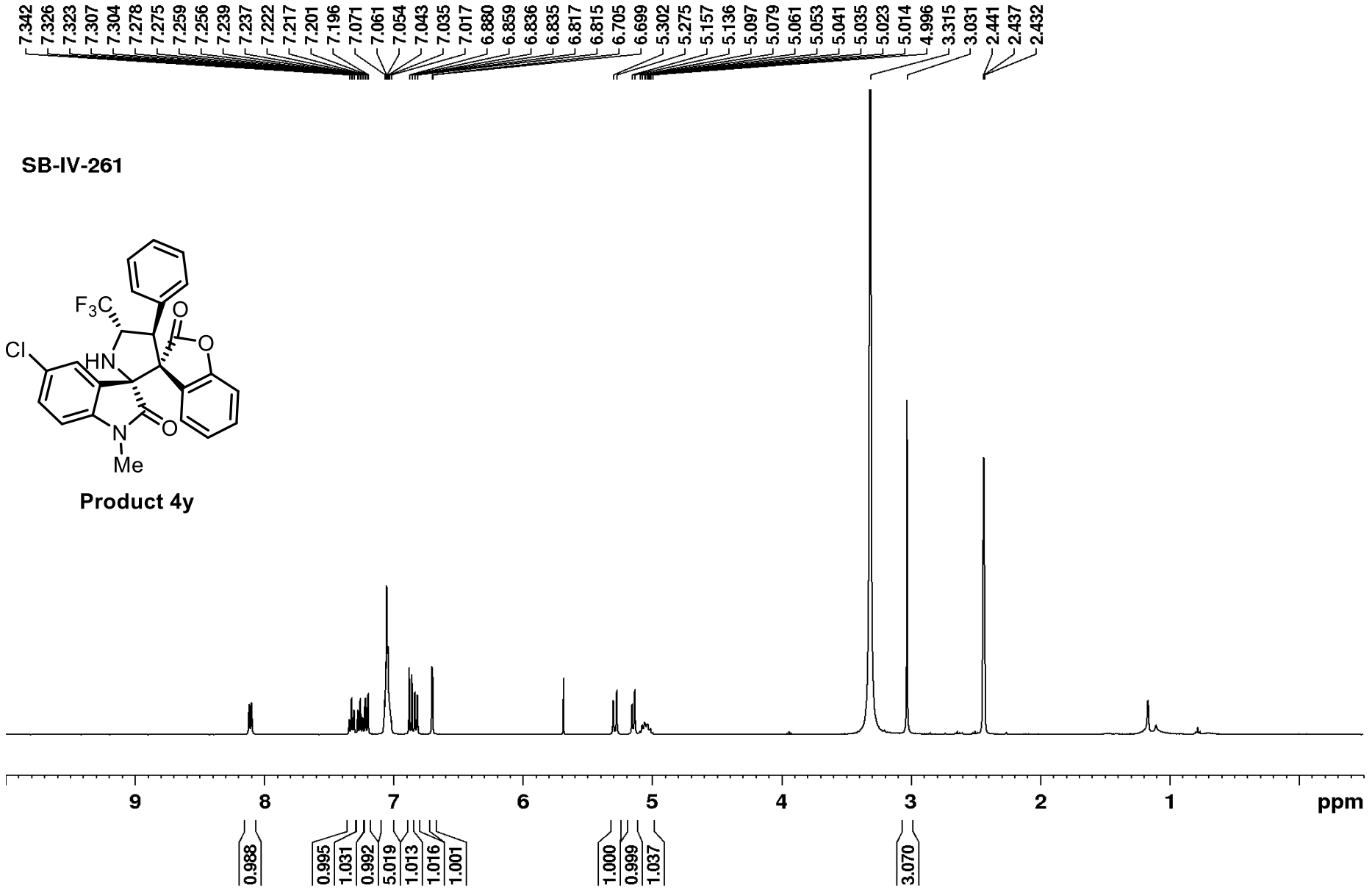
SB-IV-260

Product 4x



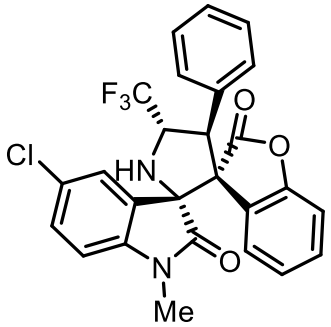

175.97
171.92
152.81
148.52
146.09
131.77
130.98
130.90
130.46
128.37
128.33
128.17
126.93
126.90
126.84
126.57
124.05
123.53
123.45
122.25
122.19
121.34
121.31
118.59
118.40
111.49
77.34
77.02
76.70
71.56
71.54
66.31
61.23
60.92
60.61
60.30
50.57
29.08
29.02
SB-IV-260
F3C
HN
O
O
O
N
Me
F
Product 4x
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


130.48
128.37
128.34
128.19
126.57
123.57
122.29
122.26
122.22
121.35
121.32
118.62
118.43
111.51
77.24
61.20
60.89
60.58
60.27
50.58
29.10
29.04
SB-IV-260
F3C
HN
O
O
O
N
Me
F
Product 4x
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

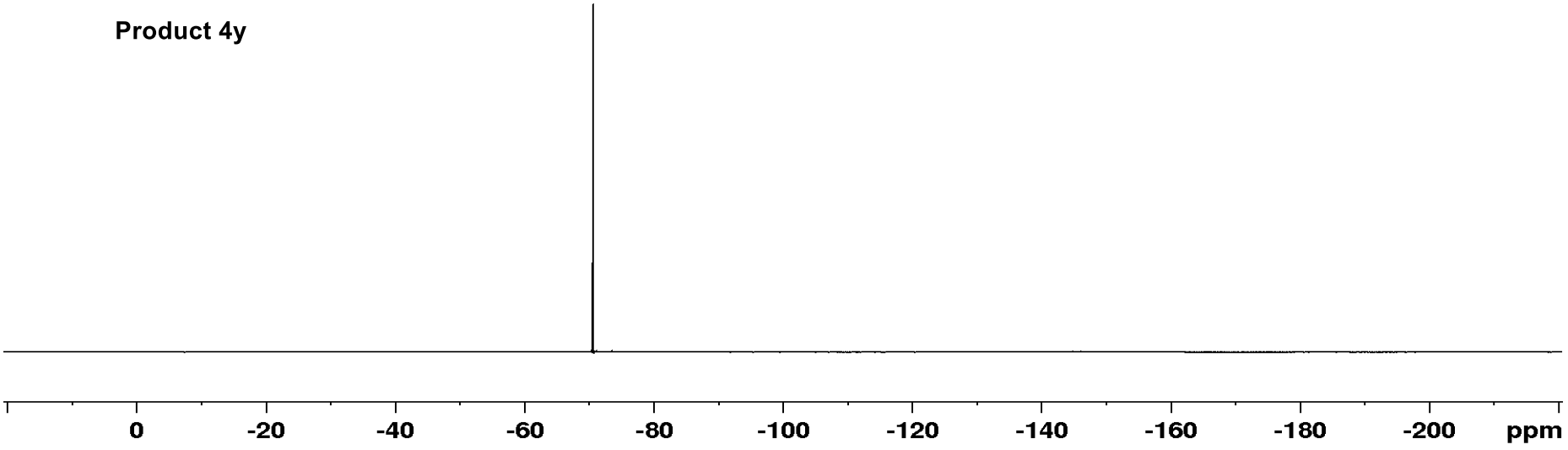

7.342
7.326
7.323
7.307
7.304
7.278
7.275
7.259
7.256
7.239
7.237
7.222
7.217
7.201
7.196
7.071
7.061
7.054
7.043
7.035
7.017
6.880
6.859
6.836
6.835
6.817
6.815
6.705
6.699
5.302
5.275
5.157
5.136
5.097
5.079
5.061
5.053
5.041
5.035
5.023
5.014
4.996
3.315
3.031
2.441
2.437
2.432
SB-IV-261
F3C
O
O
Cl
HN
O
N
Me
Product 4y
9
8
7
6
5
4
3
2
1
ppm
0.988
0.995
1.031
0.992
5.019
1.013
1.016
1.001
1.000
0.999
1.037
3.070

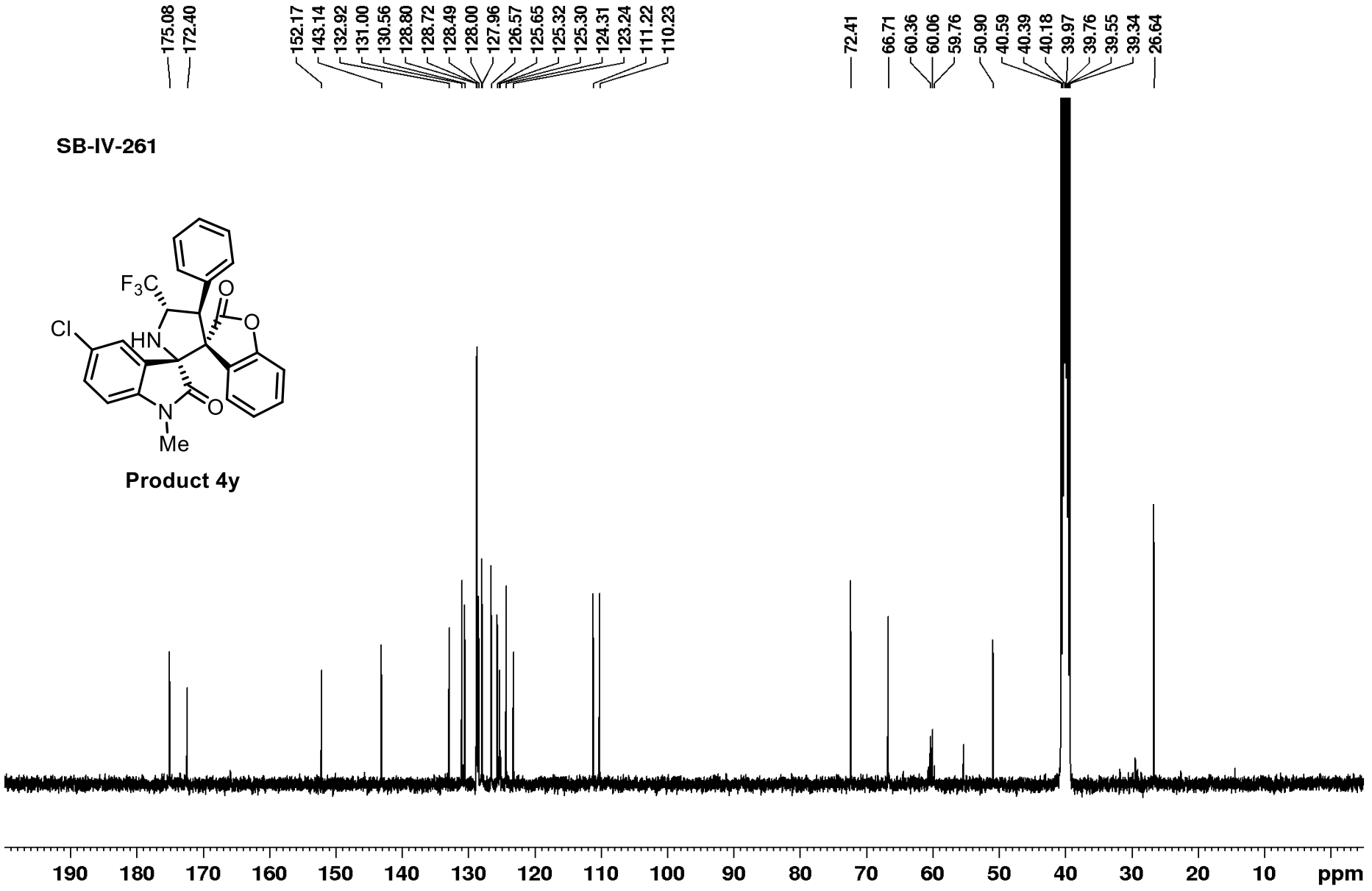
-70.62

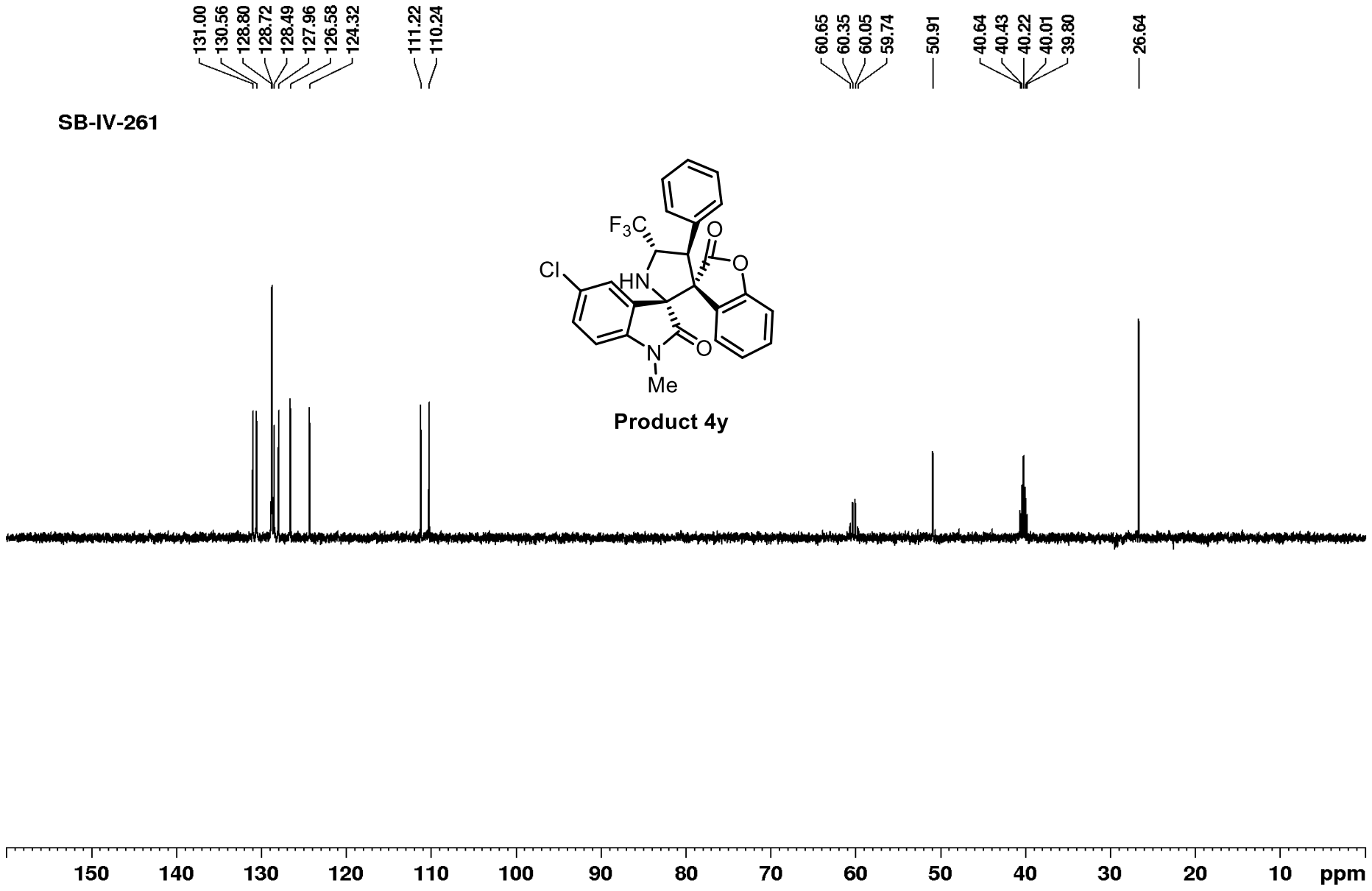
SB-IV-261

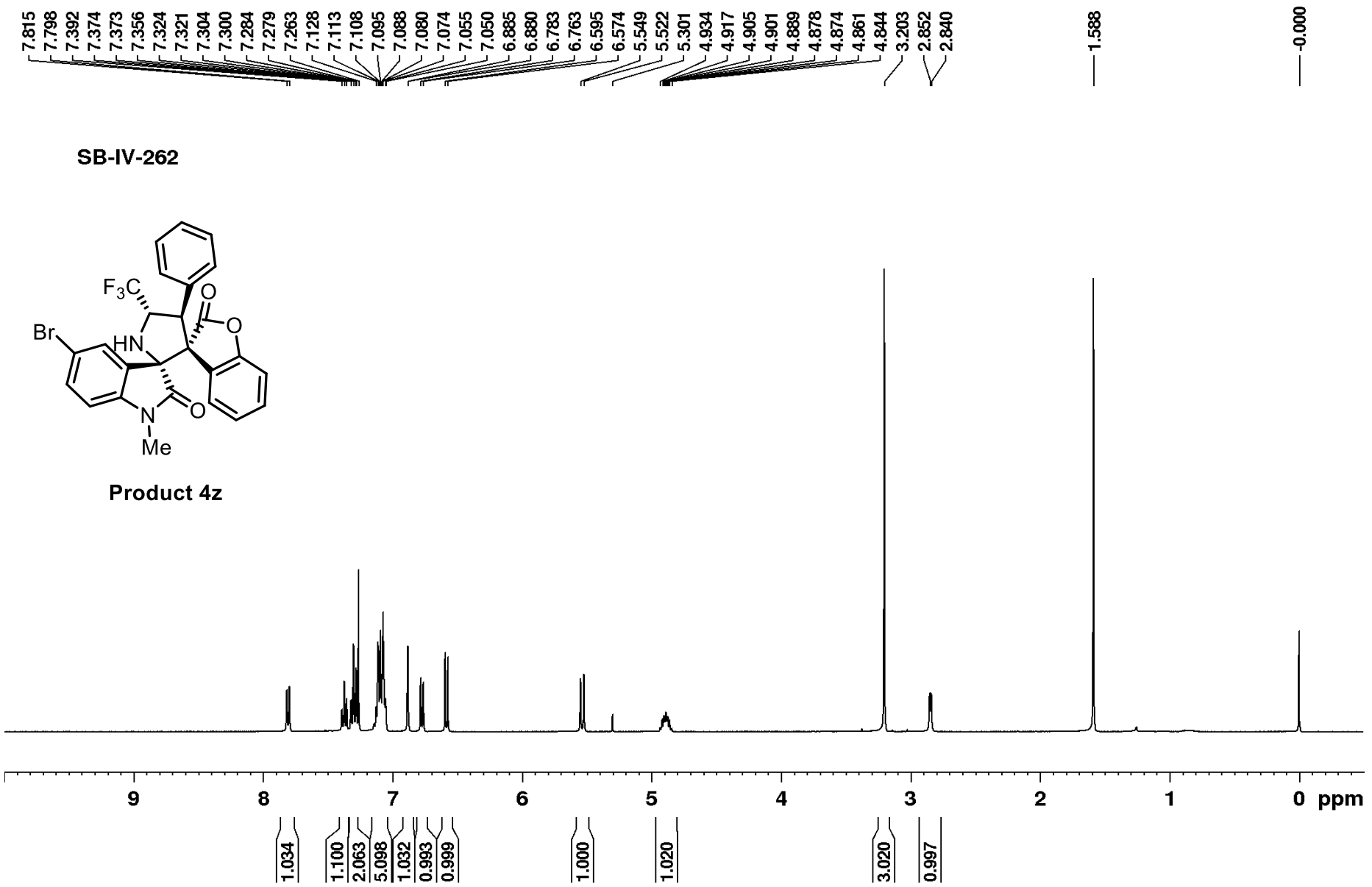


Product 4y



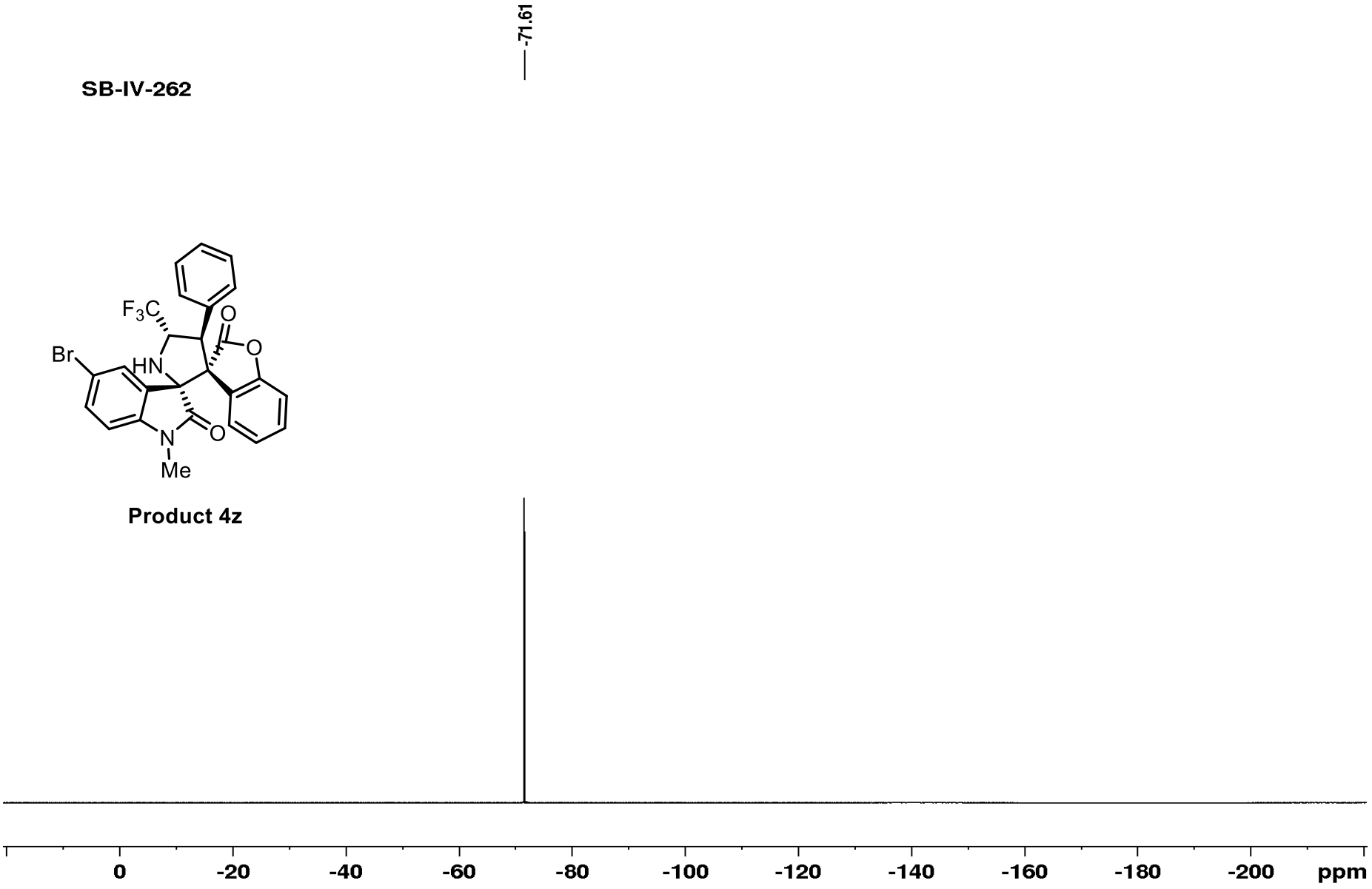

175.08
172.40
152.17
143.14
132.92
131.00
130.56
128.80
128.72
128.49
128.00
127.96
126.57
125.65
125.32
125.30
124.31
123.24
111.22
110.23
72.41
66.71
60.36
60.06
59.76
50.90
40.59
40.39
40.18
39.97
39.76
39.55
39.34
26.64
SB-IV-261
F3C
Cl
HN
O
O
O
N
Me
Product 4y
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

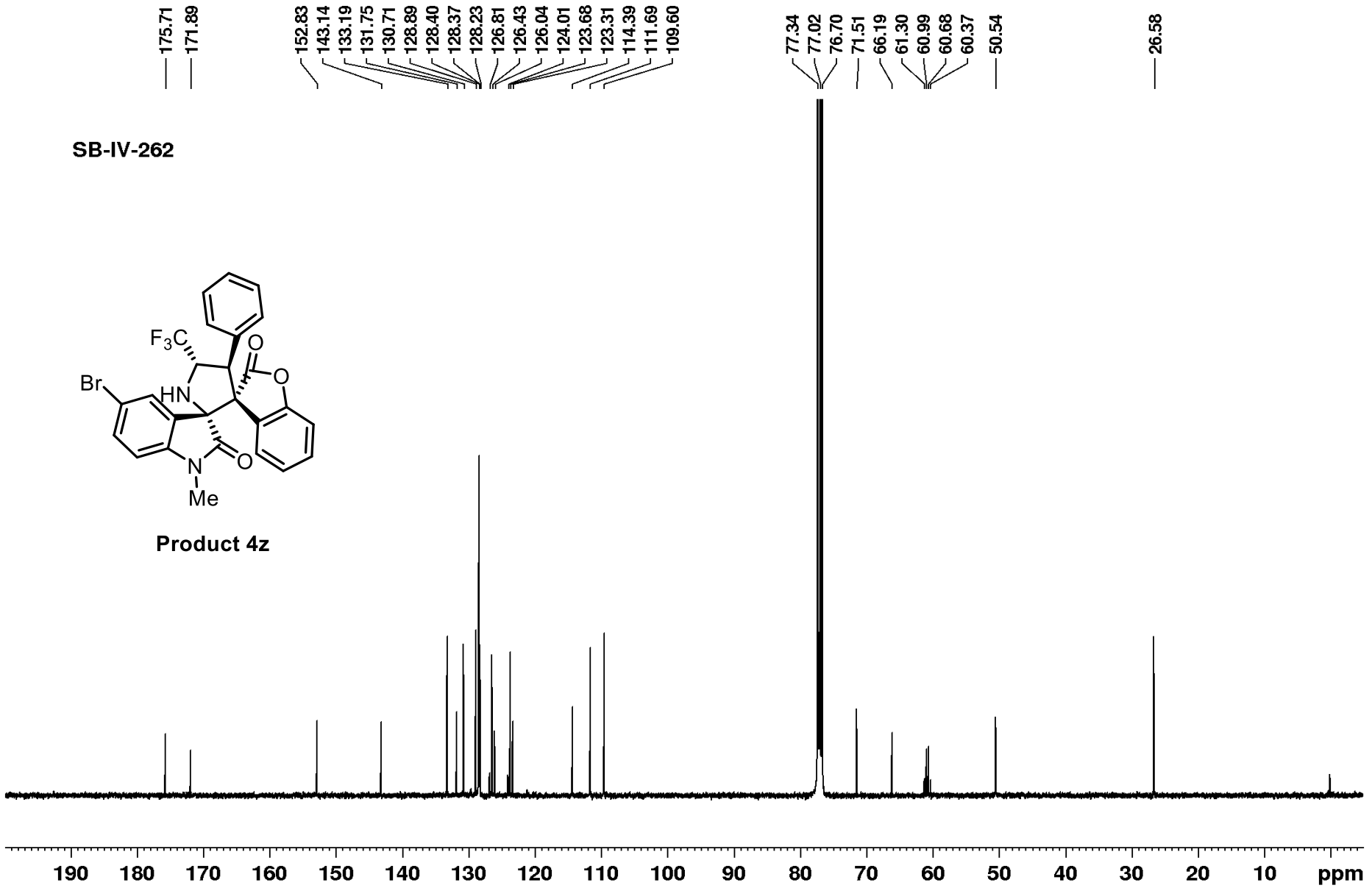

131.00
130.56
128.80
128.72
128.49
127.96
126.58
124.32
111.22
110.24
60.65
60.35
60.05
59.74
50.91
40.64
40.43
40.22
40.01
39.80
26.64
SB-IV-261
F3C
O
O
Cl
HN
O
N
Me
Product 4y
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

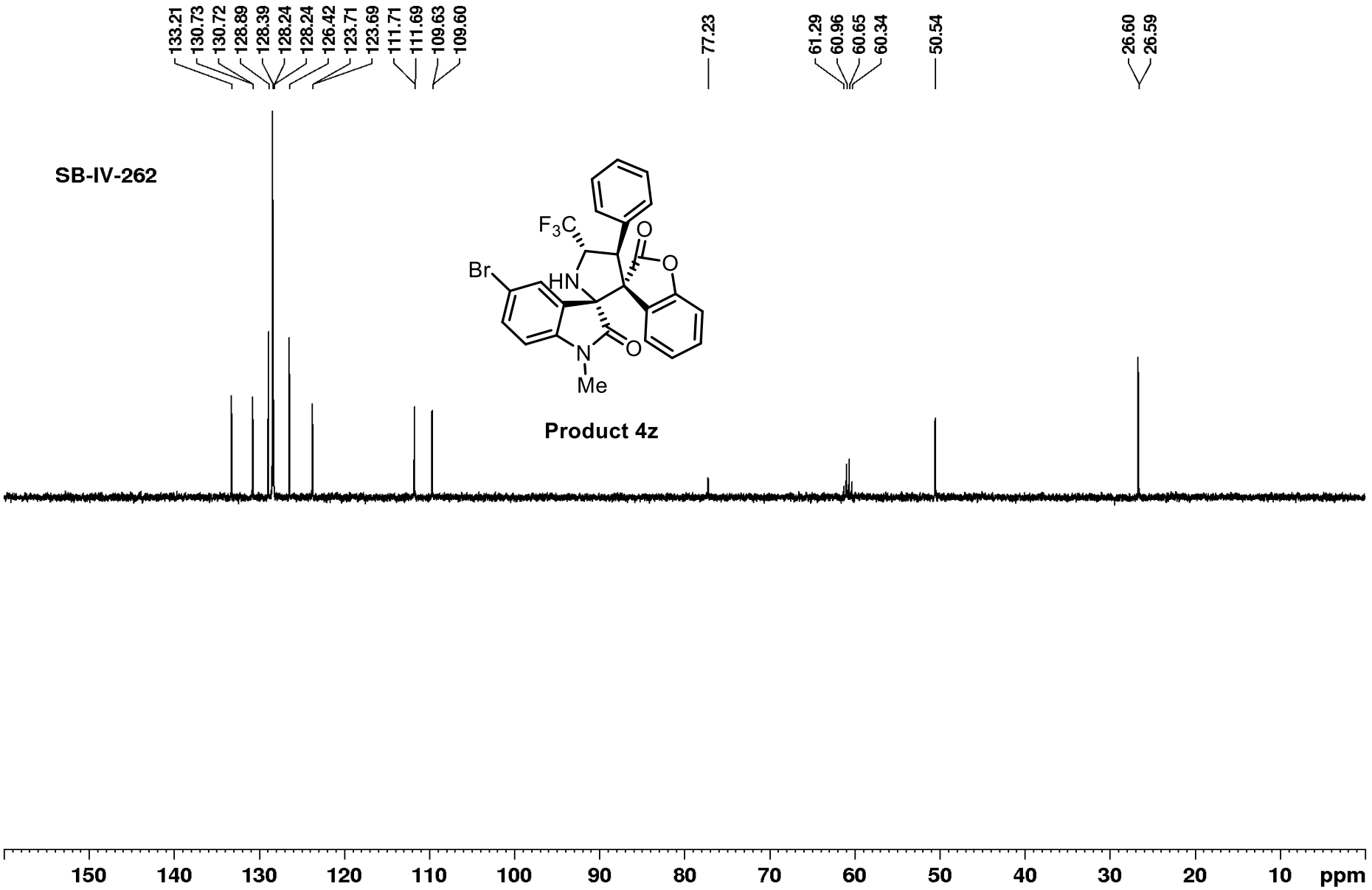

7.815
7.798
7.392
7.374
7.373
7.356
7.324
7.321
7.304
7.300
7.284
7.279
7.263
7.128
7.113
7.108
7.095
7.088
7.080
7.074
7.055
7.050
6.885
6.880
6.783
6.763
6.595
6.574
5.549
5.522
5.301
4.934
4.917
4.905
4.901
4.889
4.878
4.874
4.861
4.844
3.203
2.852
2.840
1.588
-0.000
SB-IV-262
F3C
O
O
Br
HN
O
N
Me
Product 4z
9
8
7
6
5
4
3
2
1
0 ppm
1.034
1.100
2.063
5.098
1.032
0.993
0.999
1.000
1.020
3.020
0.997

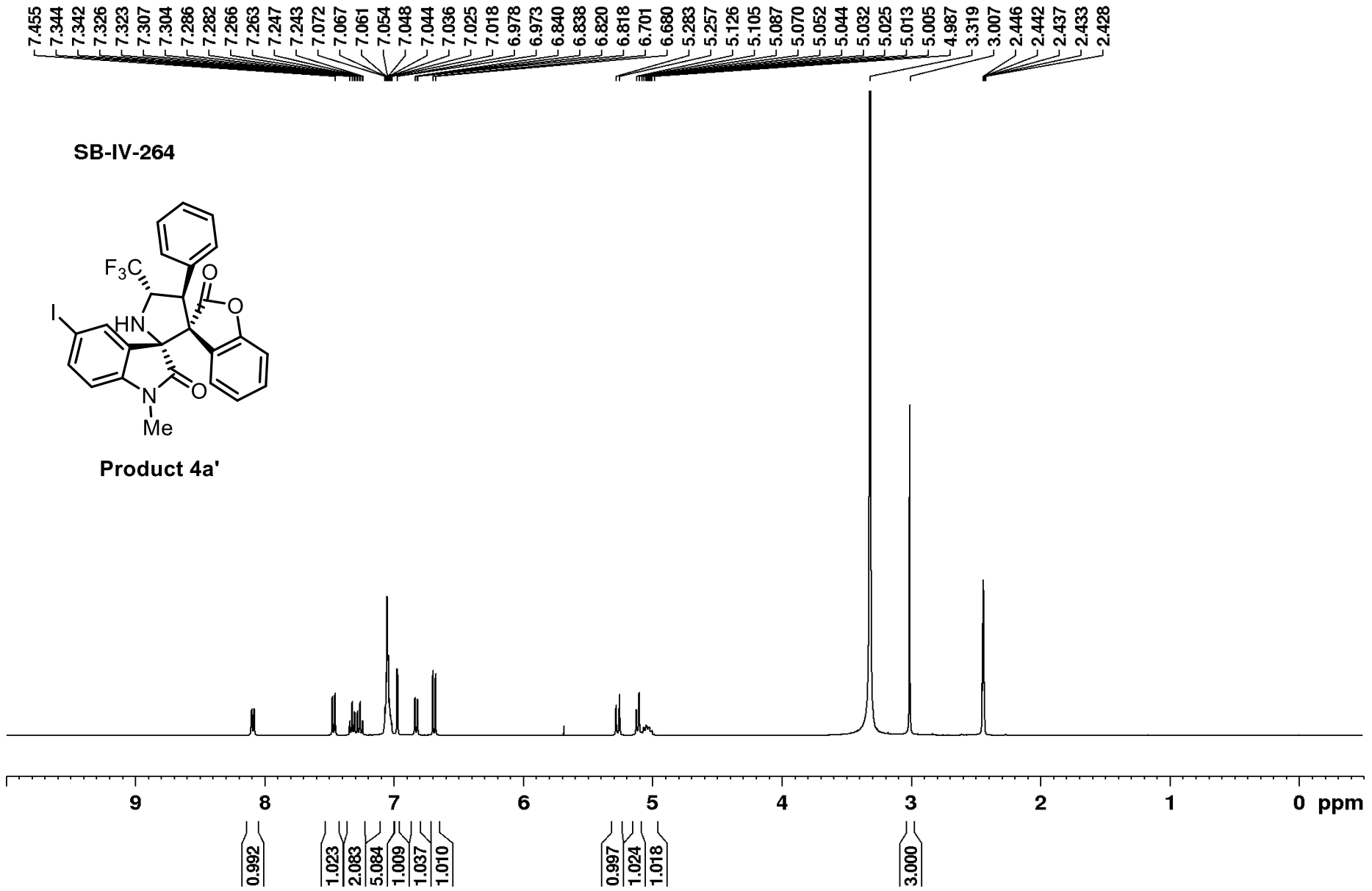
SB-IV-262

Product 4z



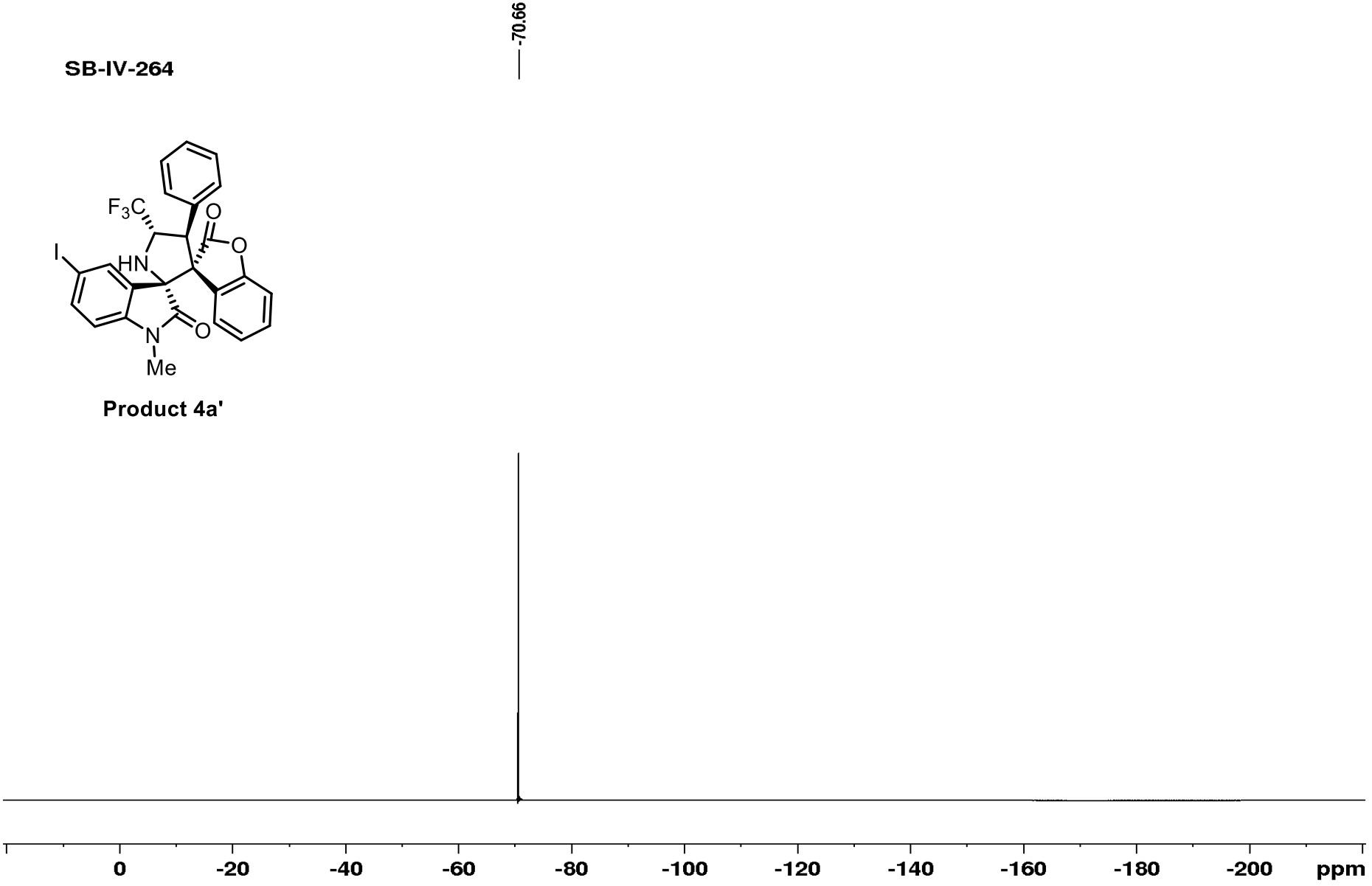

175.71
171.89
152.83
143.14
133.19
131.75
130.71
128.89
128.40
128.37
128.23
126.81
126.43
126.04
124.01
123.68
123.31
114.39
111.69
109.60
77.34
77.02
76.70
71.51
66.19
61.30
60.99
60.68
60.37
50.54
26.58
SB-IV-262
F3C
O
O
Br
HN
O
N
Me
Product 4z
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

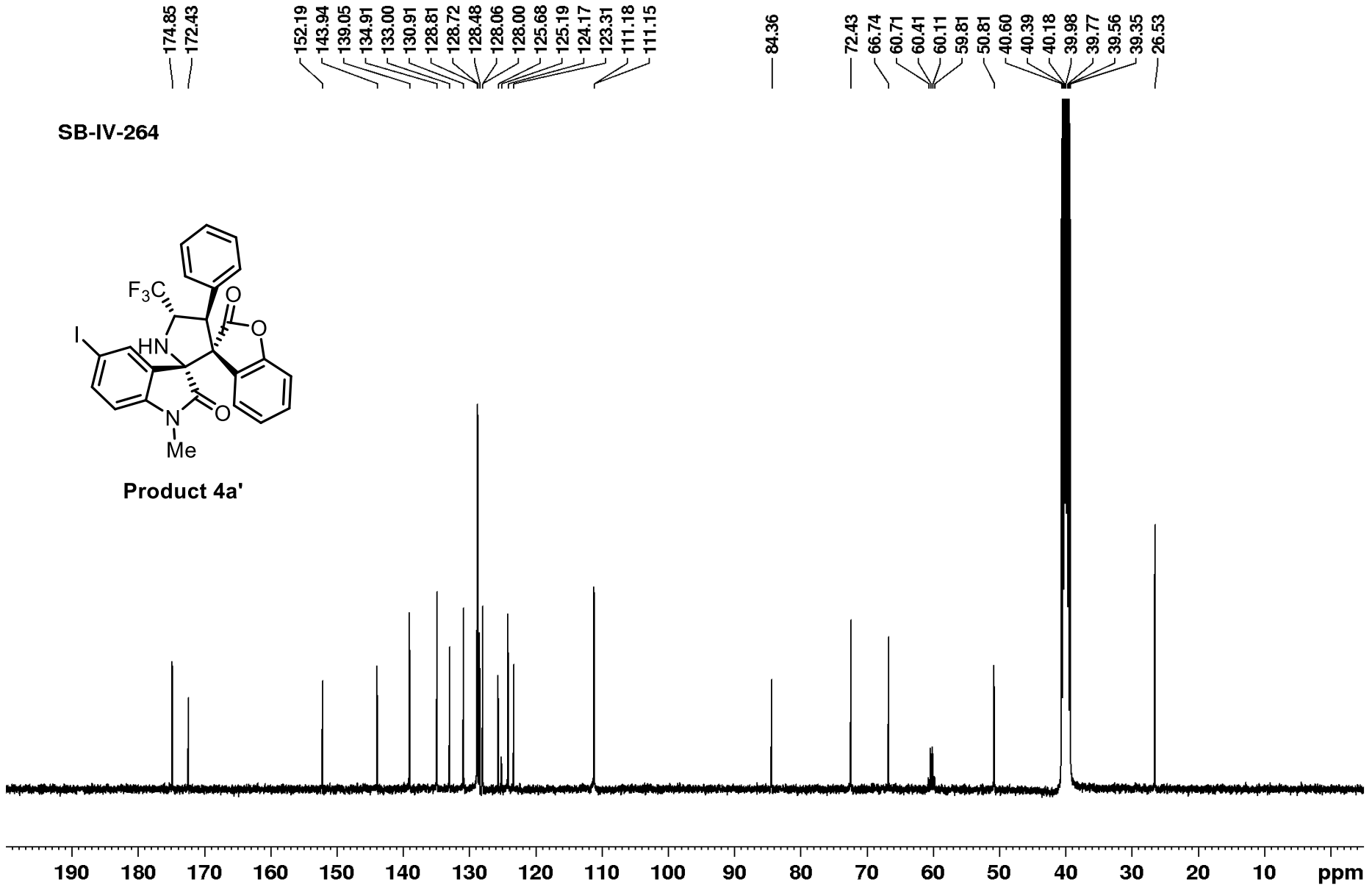

133.21
130.73
130.72
128.89
128.39
128.24
128.24
126.42
123.71
123.69
111.71
111.69
109.63
109.60
77.23
61.29
60.96
60.65
60.34
50.54
26.60
26.59
SB-IV-262
F3C
O
O
Br
HN
O
N
Me
Product 4z
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

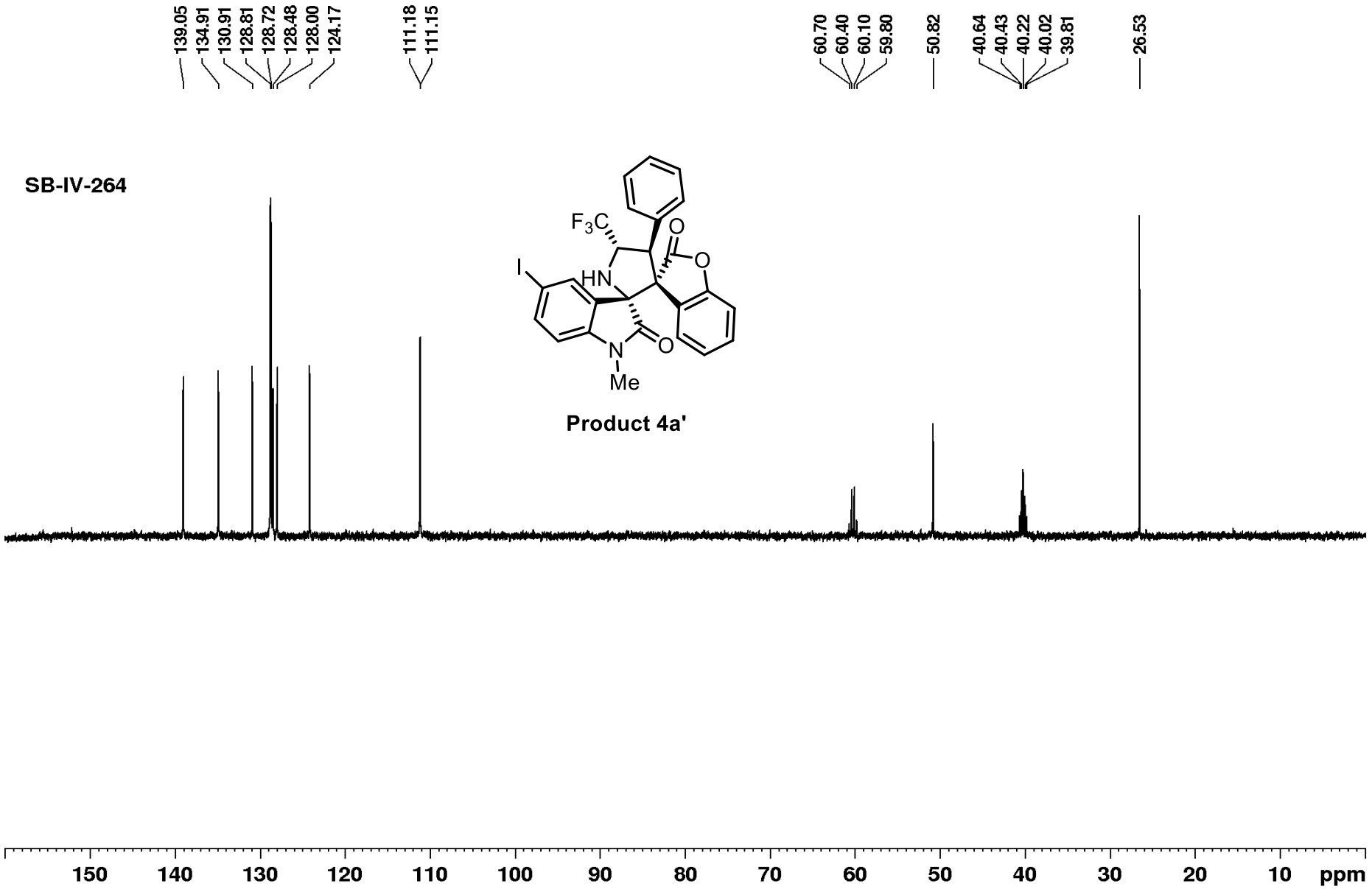

7.455
7.344
7.342
7.326
7.323
7.307
7.304
7.286
7.282
7.266
7.263
7.247
7.243
7.072
7.067
7.061
7.054
7.048
7.044
7.036
7.025
7.018
6.978
6.973
6.840
6.838
6.820
6.818
6.701
6.680
5.283
5.257
5.126
5.105
5.087
5.070
5.052
5.044
5.032
5.025
5.013
5.005
4.987
3.319
3.007
2.446
2.442
2.437
2.433
2.428
SB-IV-264
F3C
O
O
I
HN
O
N
Me
Product 4a'
9
8
7
6
5
4
3
2
1
0 ppm
0.992
1.023
2.083
5.084
1.009
1.037
1.010
0.997
1.024
1.018
3.000

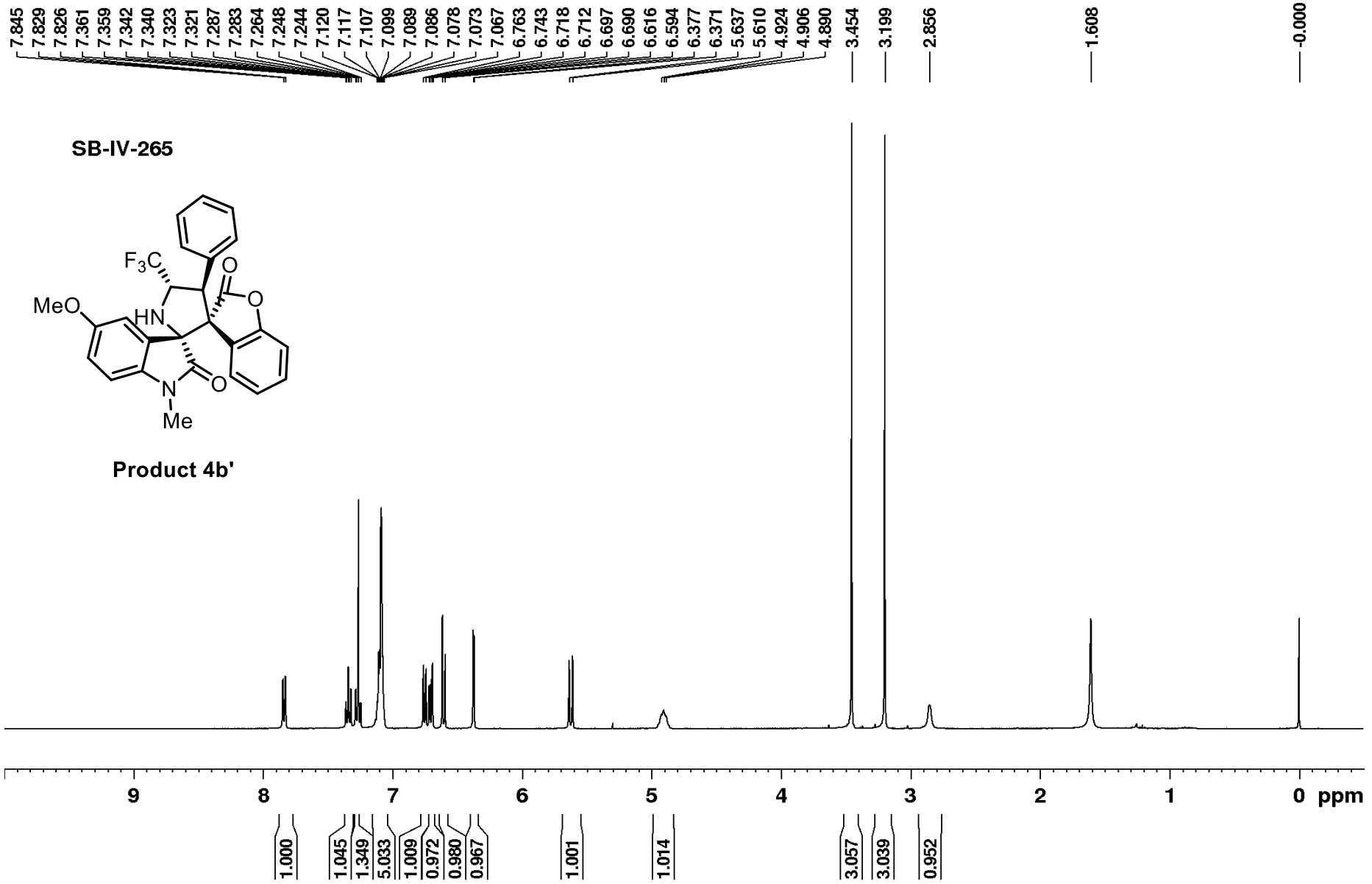
SB-IV-264

Product 4a'



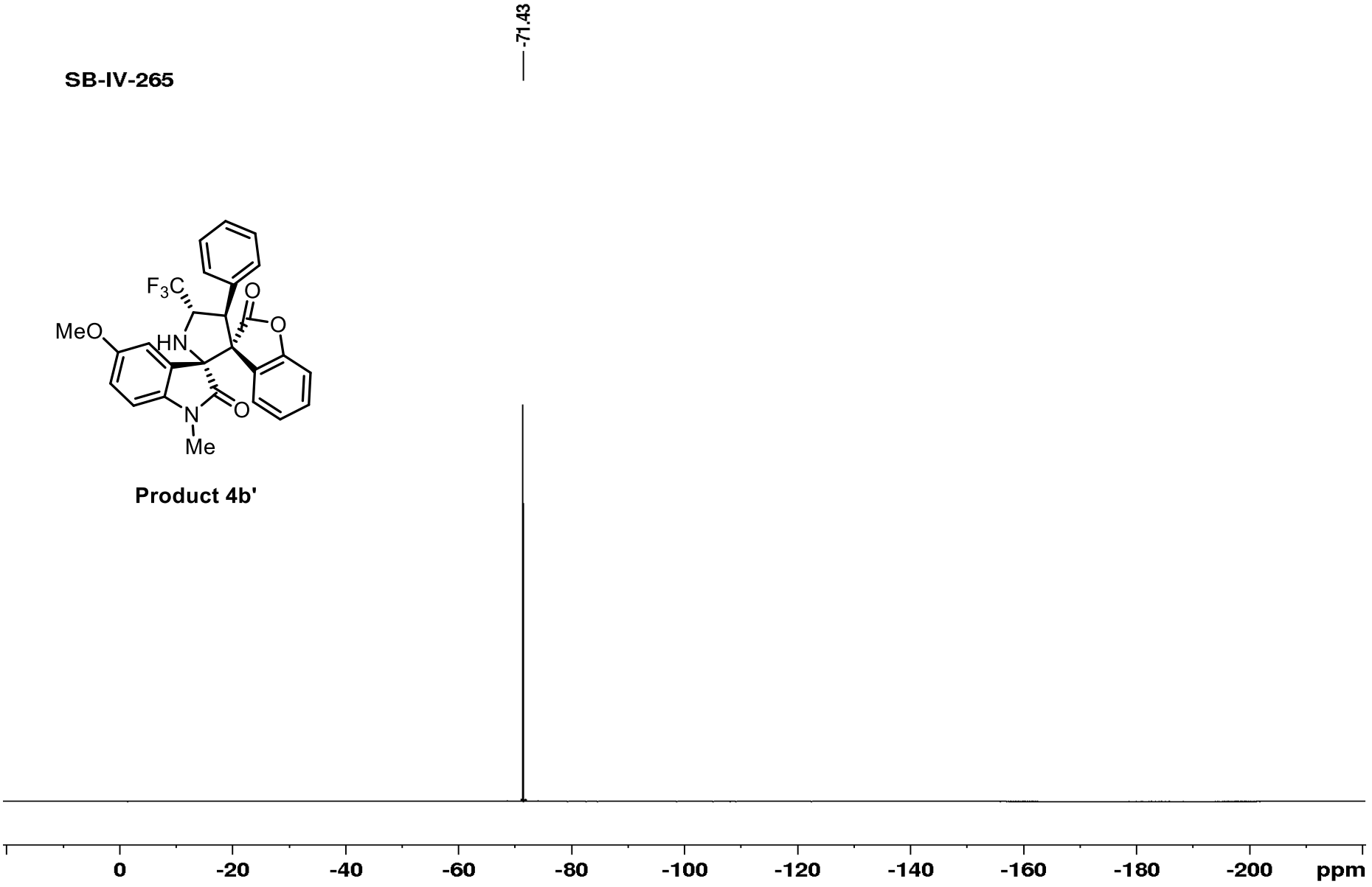

174.85
172.43
152.19
143.94
139.05
134.91
133.00
130.91
128.81
128.72
128.48
128.06
128.00
125.68
125.19
124.17
123.31
111.18
111.15
84.36
72.43
66.74
60.71
60.41
60.11
59.81
50.81
40.60
40.39
40.18
39.98
39.77
39.56
39.35
26.53
SB-IV-264
F3C
O
O
HN
I
N
O
Me
Product 4a'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

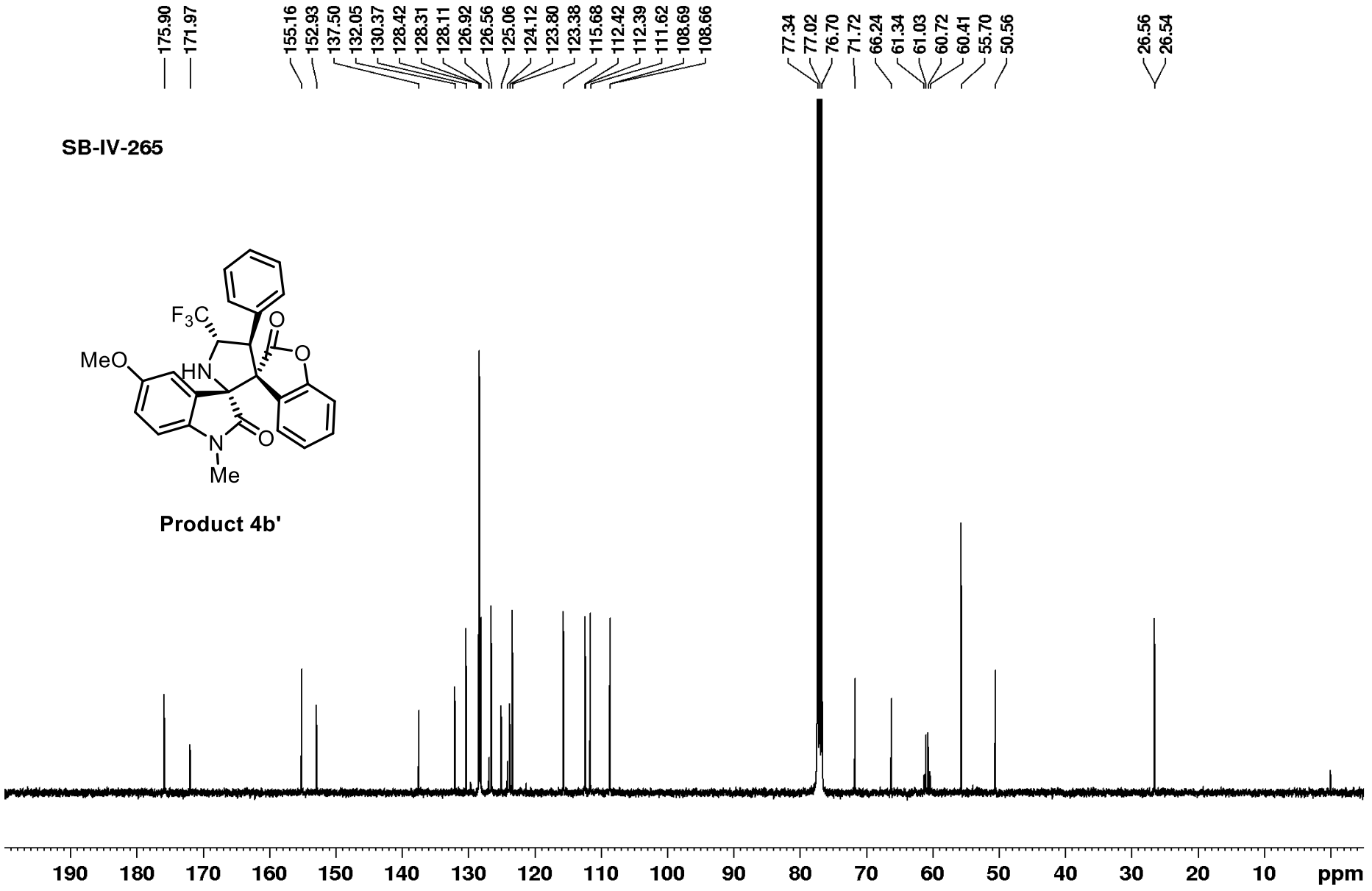

139.05
134.91
130.91
128.81
128.72
128.48
128.00
124.17
111.18
111.15
60.70
60.40
60.10
59.80
50.82
40.64
40.43
40.22
40.02
39.81
26.53
SB-IV-264
F3C
O
O
I
HN
O
N
Me
Product 4a'
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

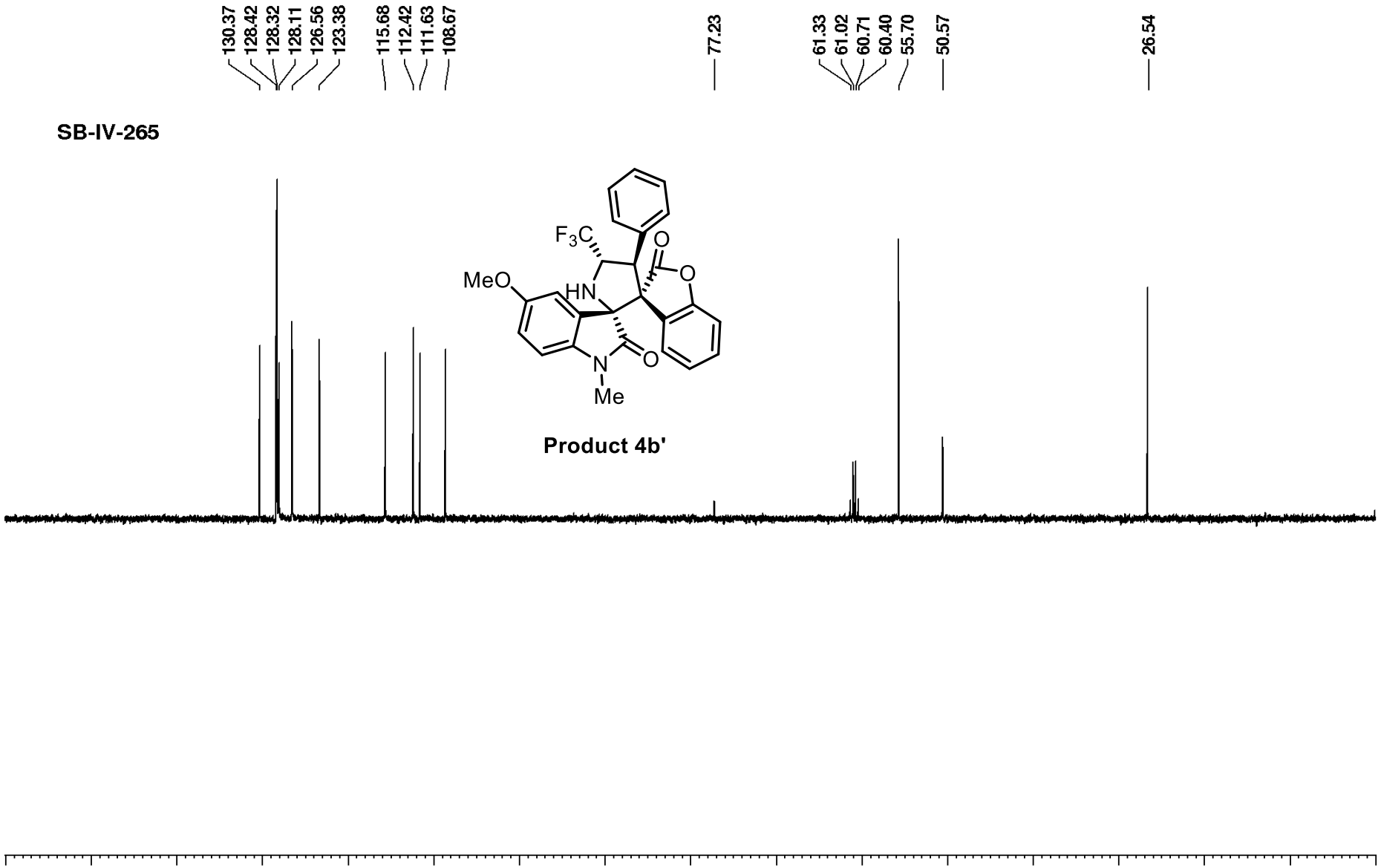

7.845
7.829
7.826
7.361
7.359
7.342
7.340
7.323
7.321
7.287
7.283
7.264
7.248
7.244
7.120
7.117
7.107
7.099
7.089
7.086
7.078
7.073
7.067
6.763
6.743
6.718
6.712
6.697
6.690
6.616
6.594
6.377
6.371
5.637
5.610
4.924
4.906
4.890
3.454
3.199
2.856
1.608
-0.000
SB-IV-265
F3C
O
O
MeO
HN
O
N
Me
Product 4b'
9
8
7
6
5
4
3
2
1
0 ppm
1.000
1.045
1.349
5.033
1.009
0.972
0.980
0.967
1.001
1.014
3.057
3.039
0.952

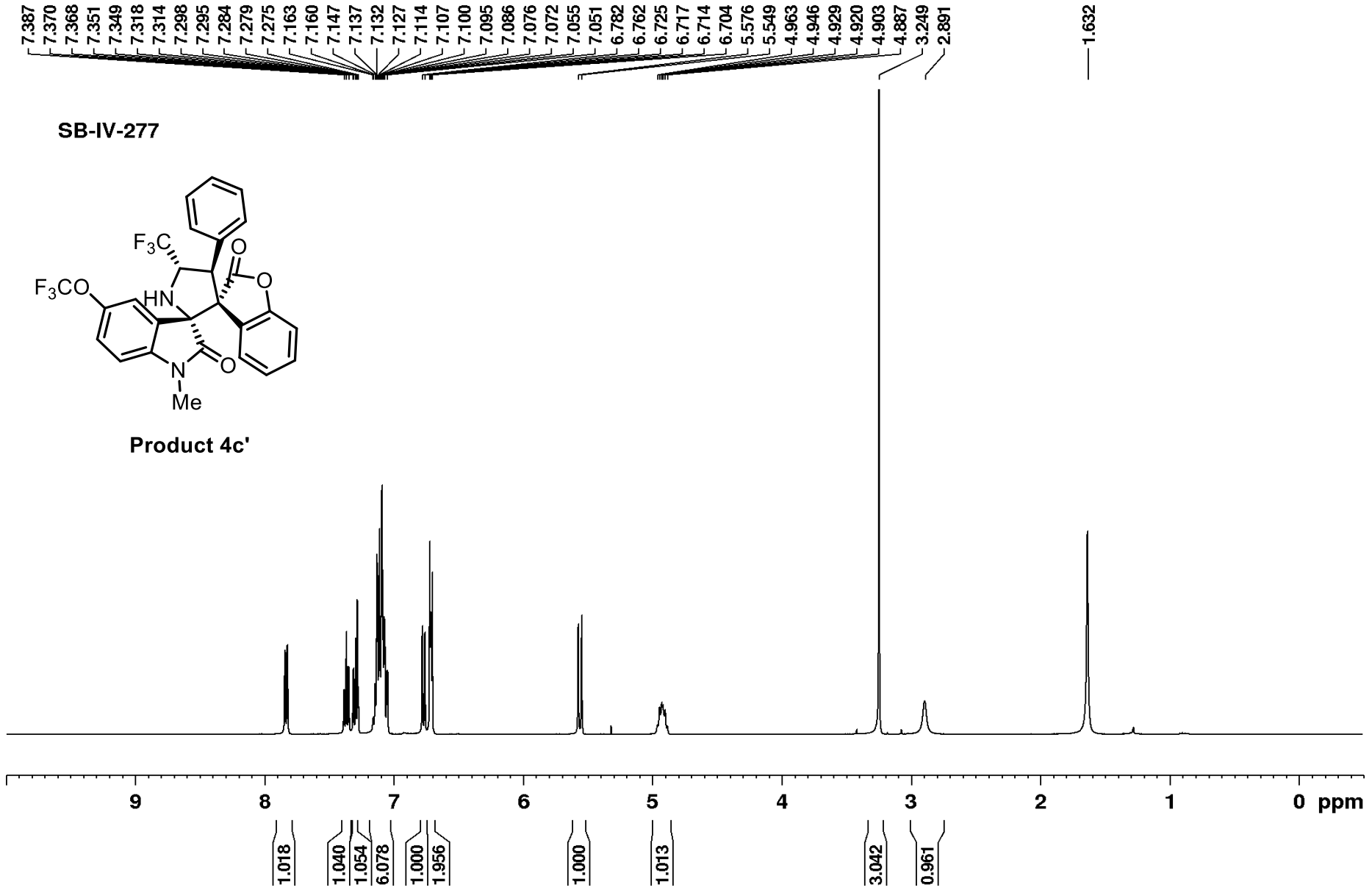
SB-IV-265

Product 4b'




175.90
171.97
155.16
152.93
137.50
132.05
130.37
128.42
128.31
128.11
126.92
126.56
125.06
124.12
123.80
123.38
115.68
112.42
112.39
111.62
108.69
108.66
77.34
77.02
76.70
71.72
66.24
61.34
61.03
60.72
60.41
55.70
50.56
26.56
26.54
SB-IV-265
F3C
O
O
MeO
HN
O
N
Me
Product 4b'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

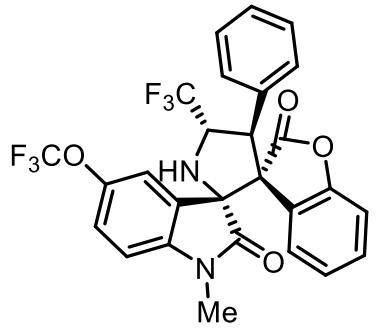

130.37
128.42
128.32
128.11
126.56
123.38
115.68
112.42
111.63
108.67
77.23
61.33
61.02
60.71
60.40
55.70
50.57
26.54
SB-IV-265
F3C
O
O
MeO
HN
O
N
Me
Product 4b'
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


7.387
7.370
7.368
7.351
7.349
7.318
7.314
7.298
7.295
7.284
7.279
7.275
7.163
7.160
7.147
7.137
7.132
7.127
7.114
7.107
7.100
7.095
7.086
7.076
7.072
7.055
7.051
6.782
6.762
6.725
6.717
6.714
6.704
5.576
5.549
4.963
4.946
4.929
4.920
4.903
4.887
3.249
2.891
1.632
SB-IV-277
F3C
O
F3CO
O
HN
O
N
Me
Product 4c'
9
8
7
6
5
4
3
2
1
0 ppm
1.018
1.040
1.054
6.078
1.000
1.956
1.000
1.013
3.042
0.961

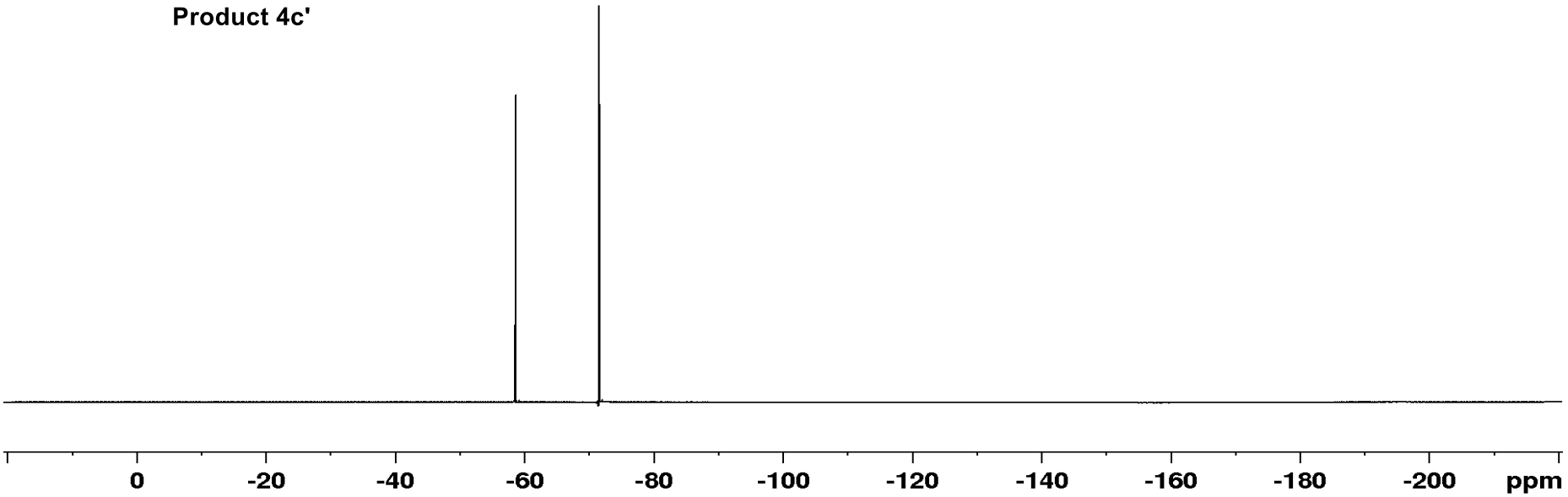
-58.68

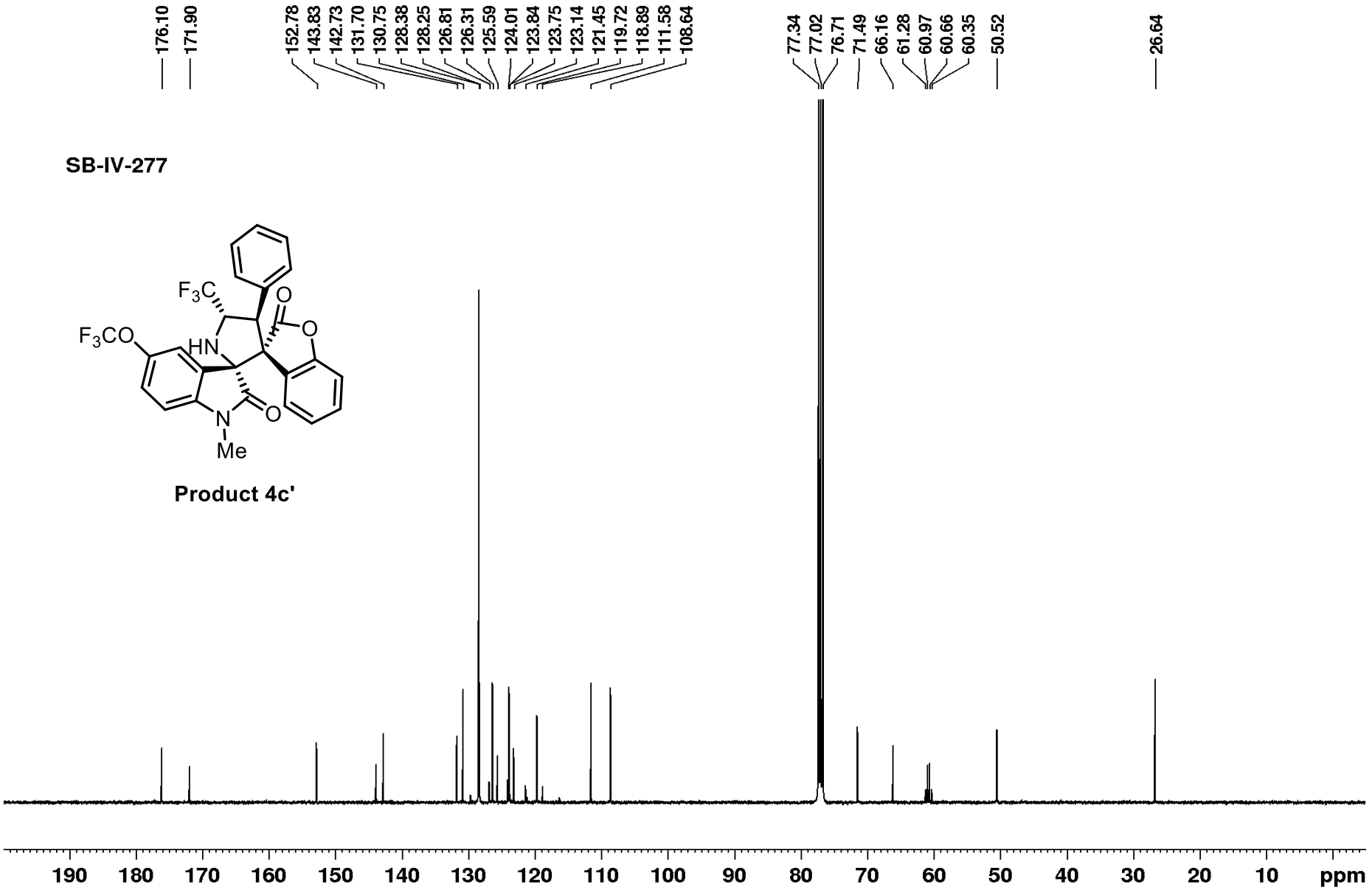
-71.51

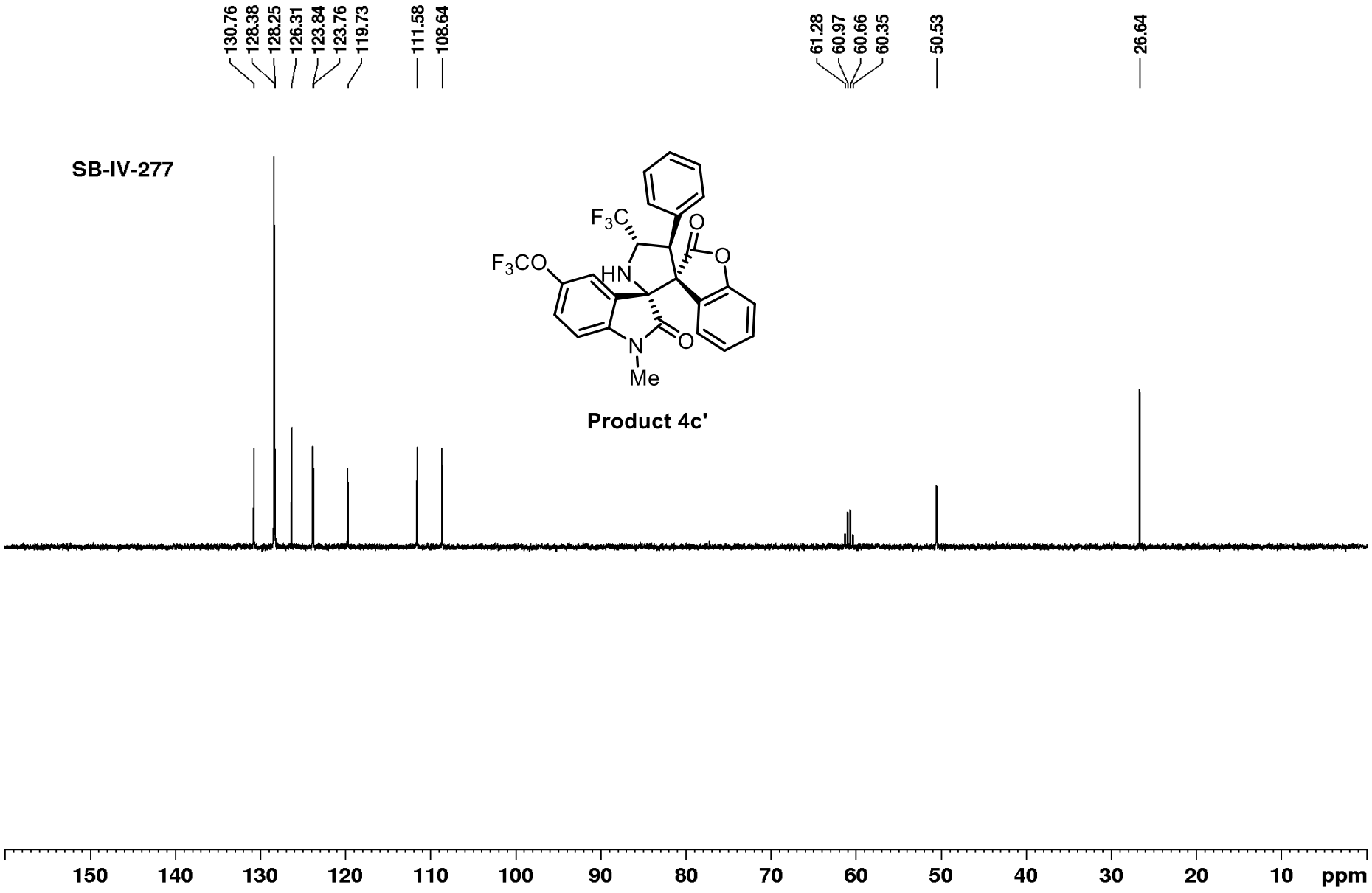
SB-IV-277

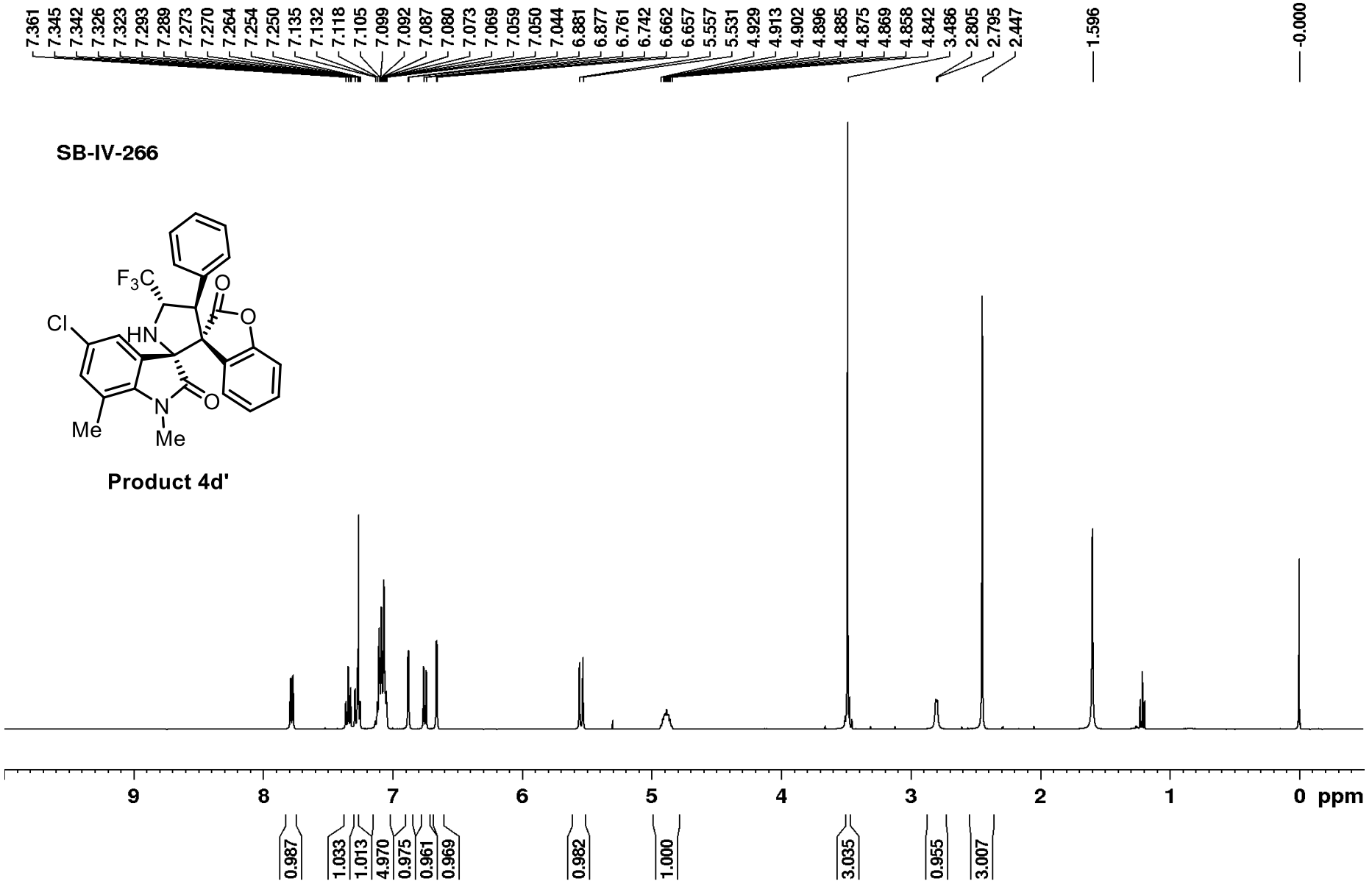


Product 4c'



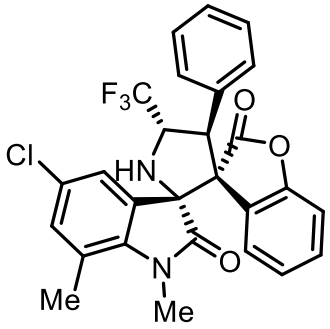

176.10
171.90
152.78
143.83
142.73
131.70
130.75
128.38
128.25
126.81
126.31
125.59
124.01
123.84
123.75
123.14
121.45
119.72
118.89
111.58
108.64
77.34
77.02
76.71
71.49
66.16
61.28
60.97
60.66
60.35
50.52
26.64
SB-IV-277
F3C
O
O
F3CO
HN
O
N
Me
Product 4c'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


130.76
128.38
128.25
126.31
123.84
123.76
119.73
111.58
108.64
61.28
60.97
60.66
60.35
50.53
26.64
SB-IV-277
F3C
O
F3CO
HN
O
N
O
Me
Product 4c'
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

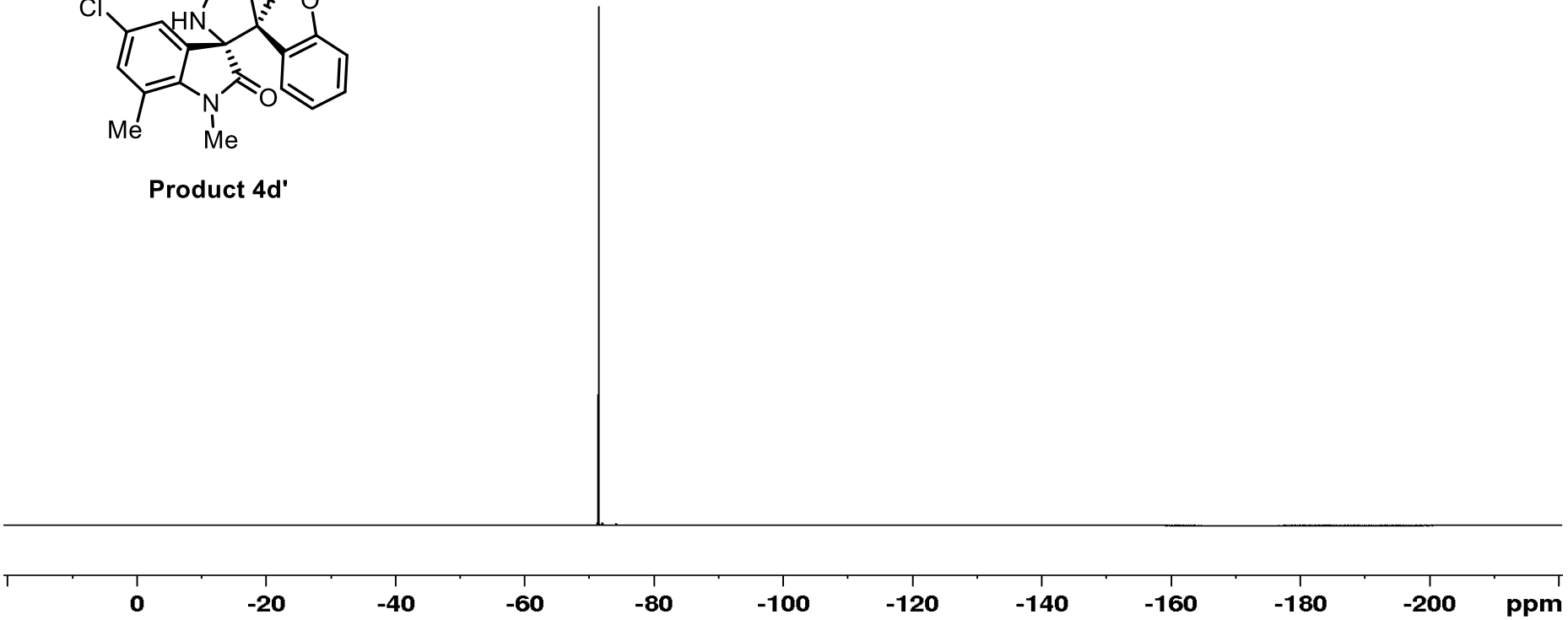

7.361
7.345
7.342
7.326
7.323
7.293
7.289
7.273
7.270
7.264
7.254
7.250
7.135
7.132
7.118
7.105
7.099
7.092
7.087
7.080
7.073
7.069
7.059
7.050
7.044
6.881
6.877
6.761
6.742
6.662
6.657
5.557
5.531
4.929
4.913
4.902
4.896
4.885
4.875
4.869
4.858
4.842
3.486
2.805
2.795
2.447
1.596
-0.000
SB-IV-266
F3C
O
O
Cl
HN
O
N
Me
Me
Product 4d'
9
8
7
6
5
4
3
2
1
0 ppm
0.987
1.033
1.013
4.970
0.975
0.961
0.969
0.982
1.000
3.035
0.955
3.007

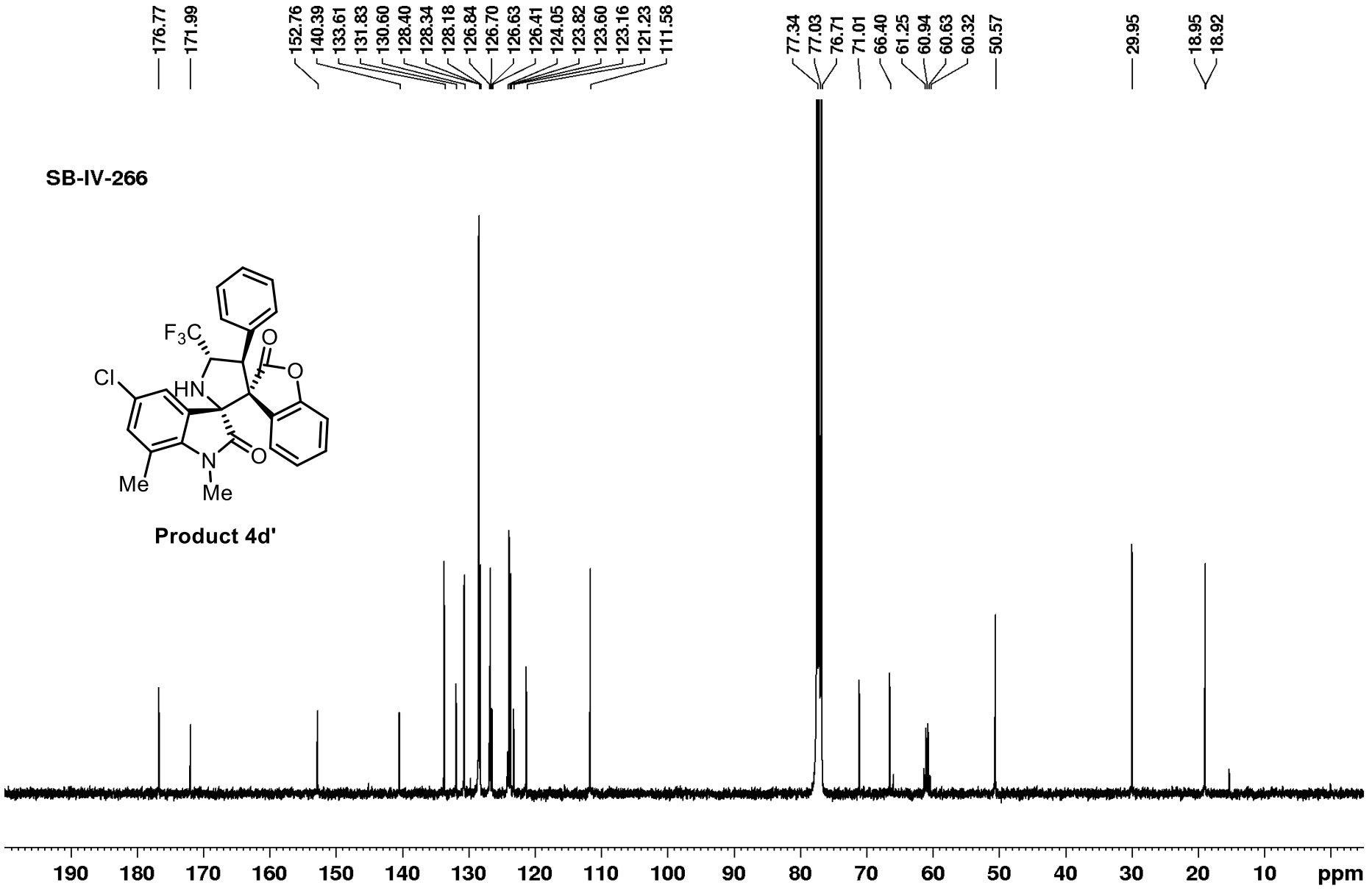
SB-IV-266

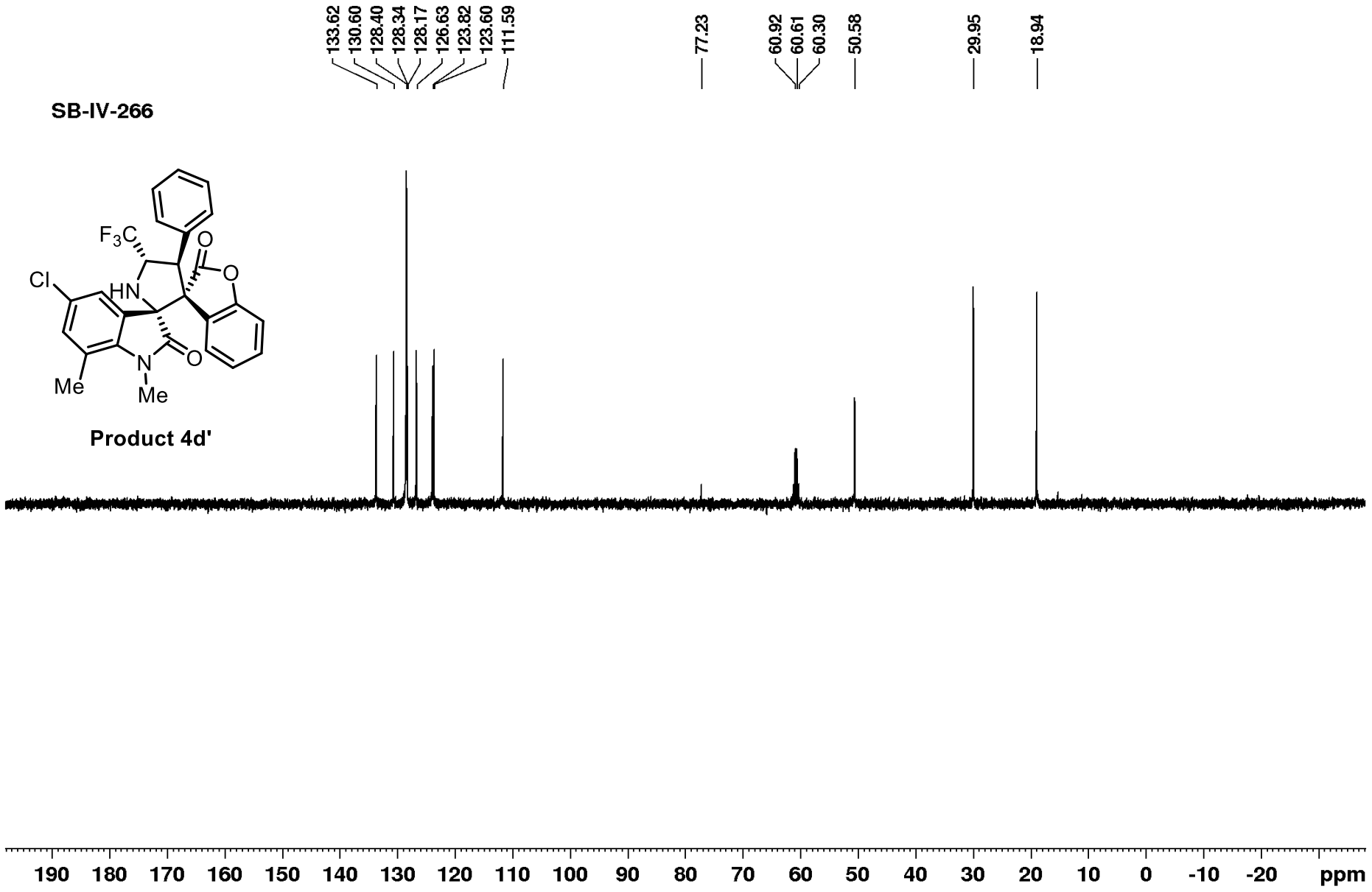
-71.52

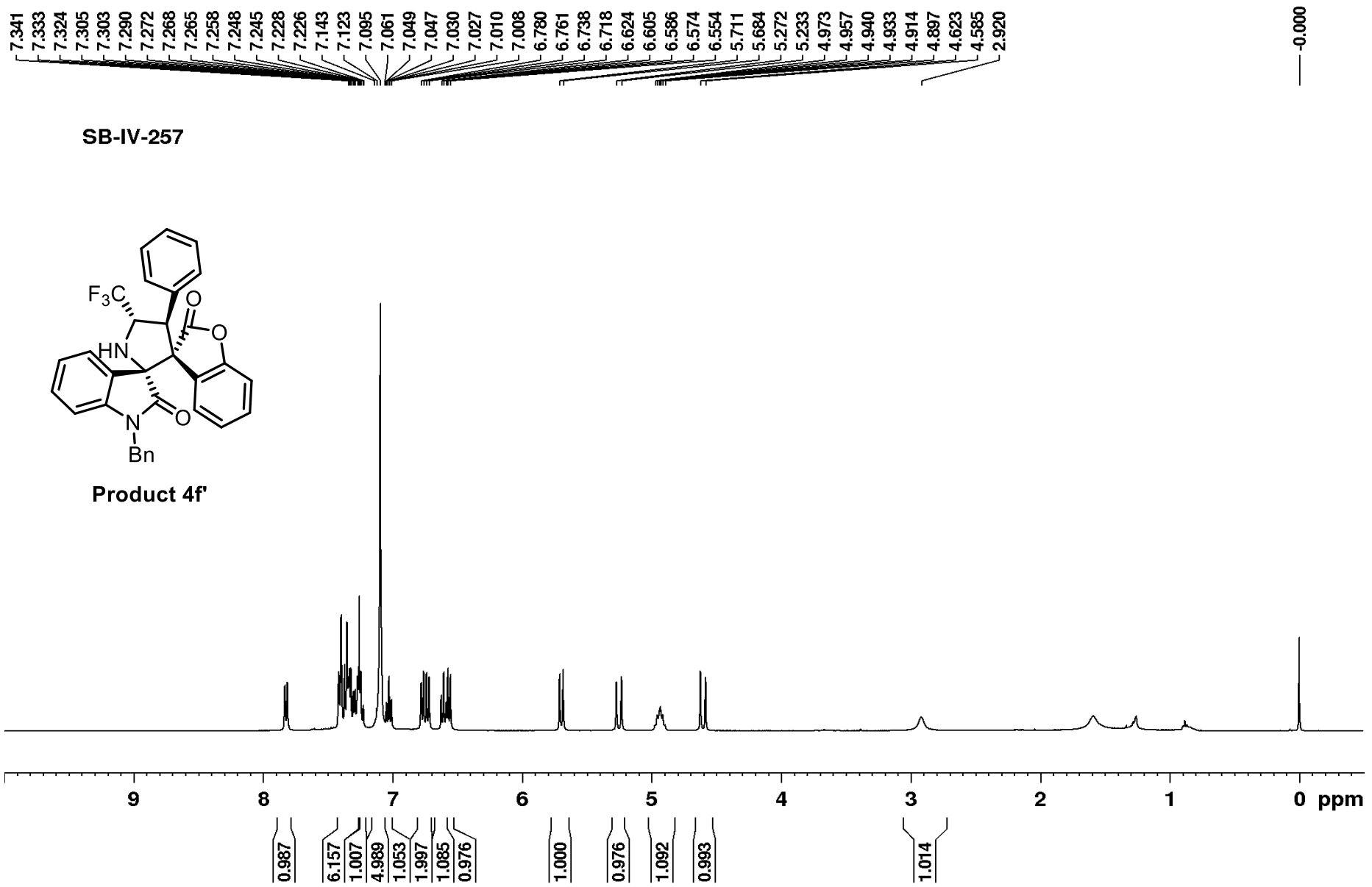


Product 4d'



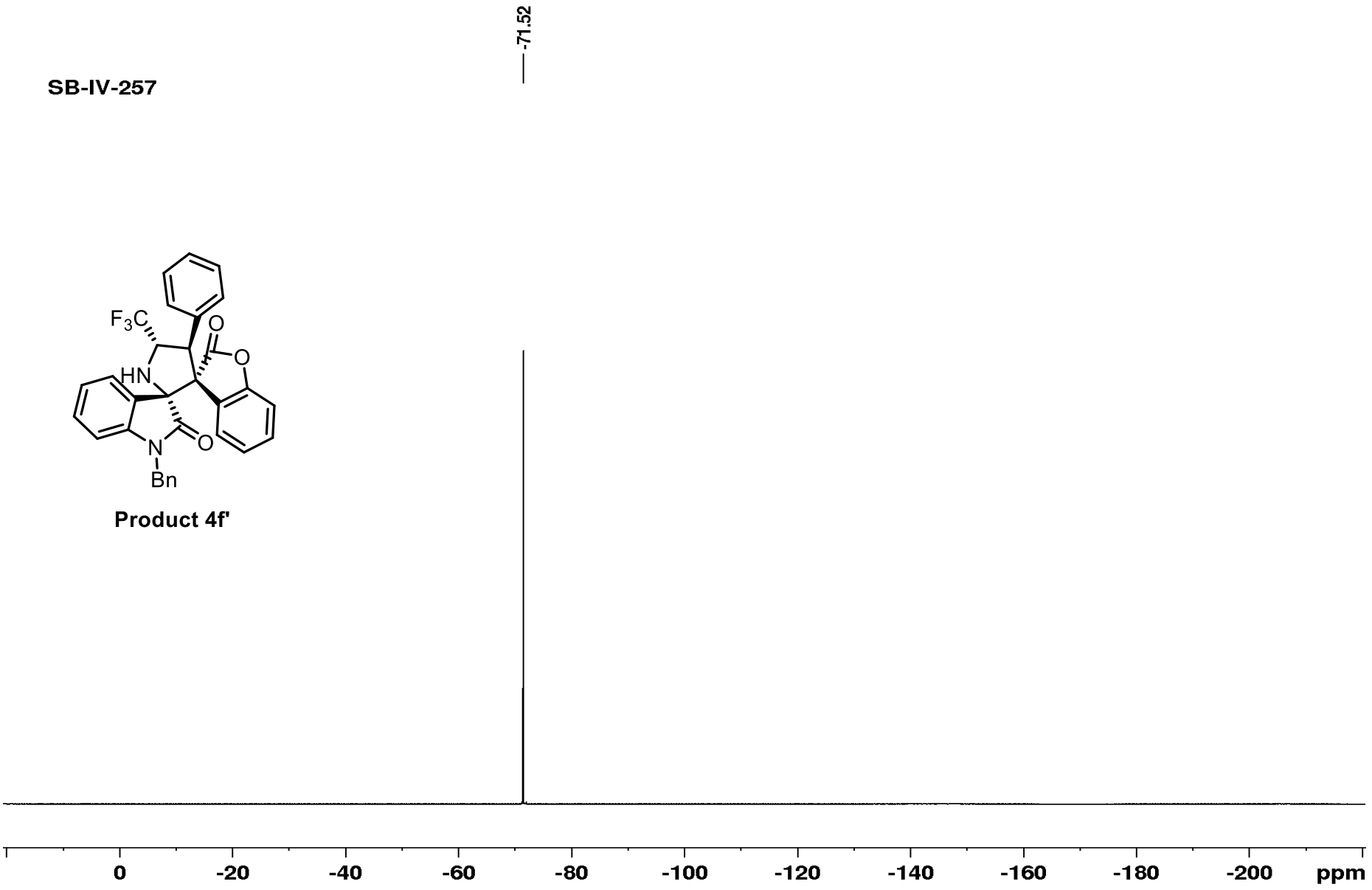

176.77
171.99
152.76
140.39
133.61
131.83
130.60
128.40
128.34
128.18
126.84
126.70
126.63
126.41
124.05
123.82
123.60
123.16
121.23
111.58
77.34
77.03
76.71
71.01
66.40
61.25
60.94
60.63
60.32
50.57
29.95
18.95
18.92
SB-IV-266
F3C
O
O
Cl
HN
O
N
Me
Me
Product 4d'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

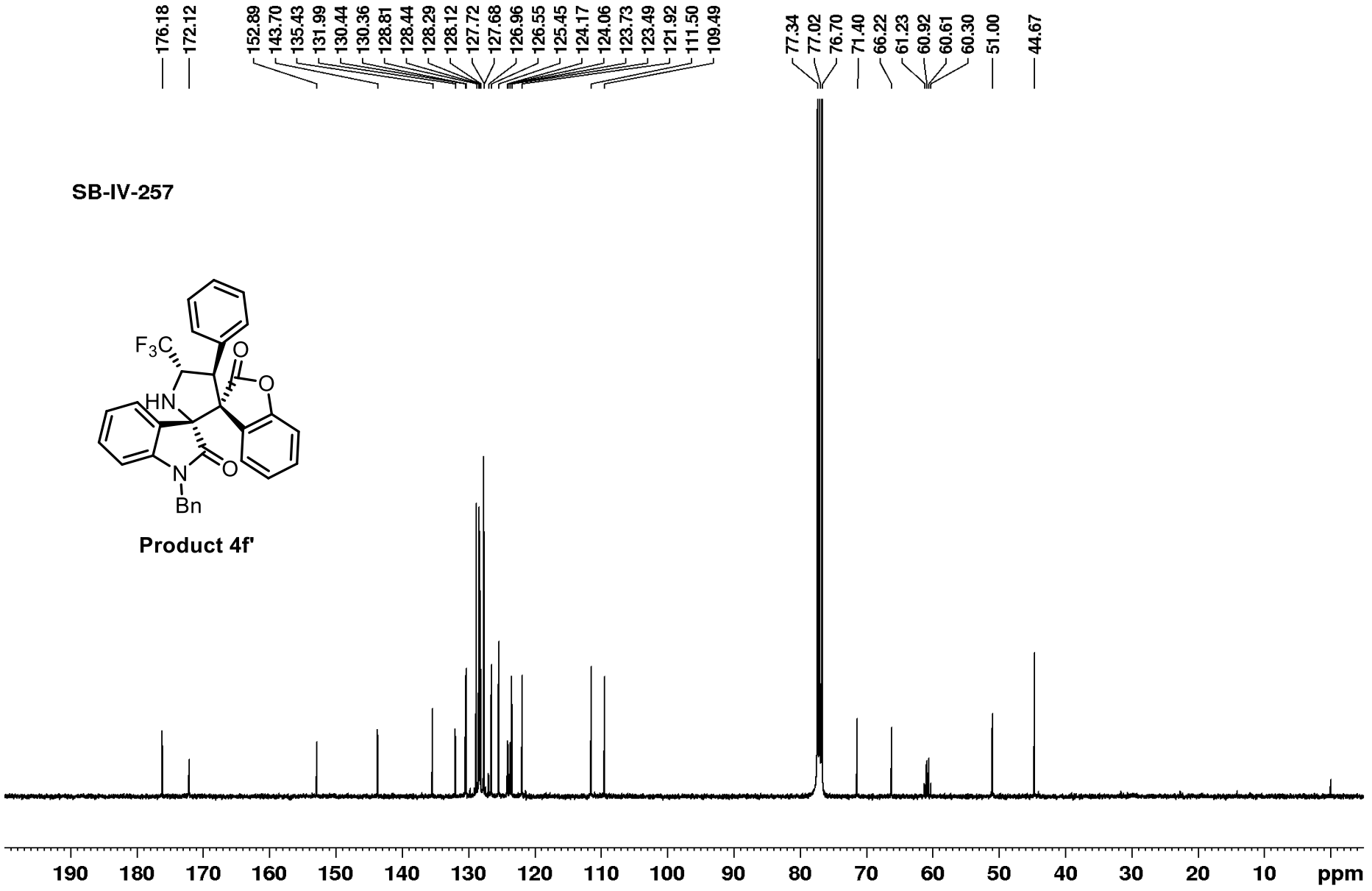

133.62
130.60
128.40
128.34
128.17
126.63
123.82
123.60
111.59
77.23
60.92
60.61
60.30
50.58
29.95
18.94
SB-IV-266
F3C
O
O
Cl
HN
O
N
Me
Me
Product 4d'
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 ppm

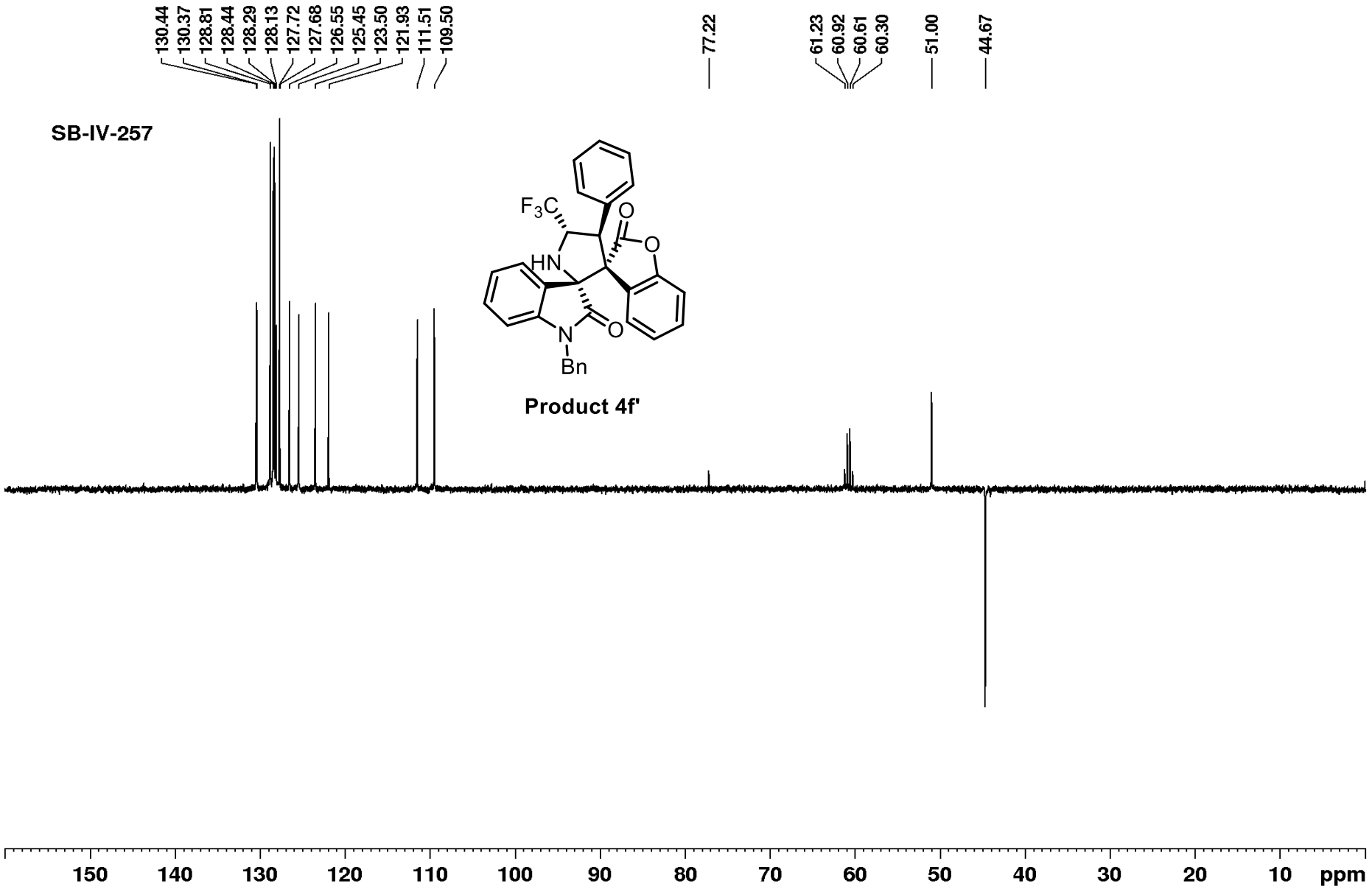

7.341
7.333
7.324
7.305
7.303
7.290
7.272
7.268
7.265
7.258
7.248
7.245
7.228
7.226
7.143
7.123
7.095
7.061
7.049
7.047
7.030
7.027
7.010
7.008
6.780
6.761
6.738
6.718
6.624
6.605
6.586
6.574
6.554
5.711
5.684
5.272
5.233
4.973
4.957
4.940
4.933
4.914
4.897
4.623
4.585
2.920
-0.000
SB-IV-257
F3C
HN
O
O
N
O
Bn
Product 4f'
9
8
7
6
5
4
3
2
1
0 ppm
0.987
6.157
1.007
4.989
1.053
1.997
1.085
0.976
1.000
0.976
1.092
0.993
1.014

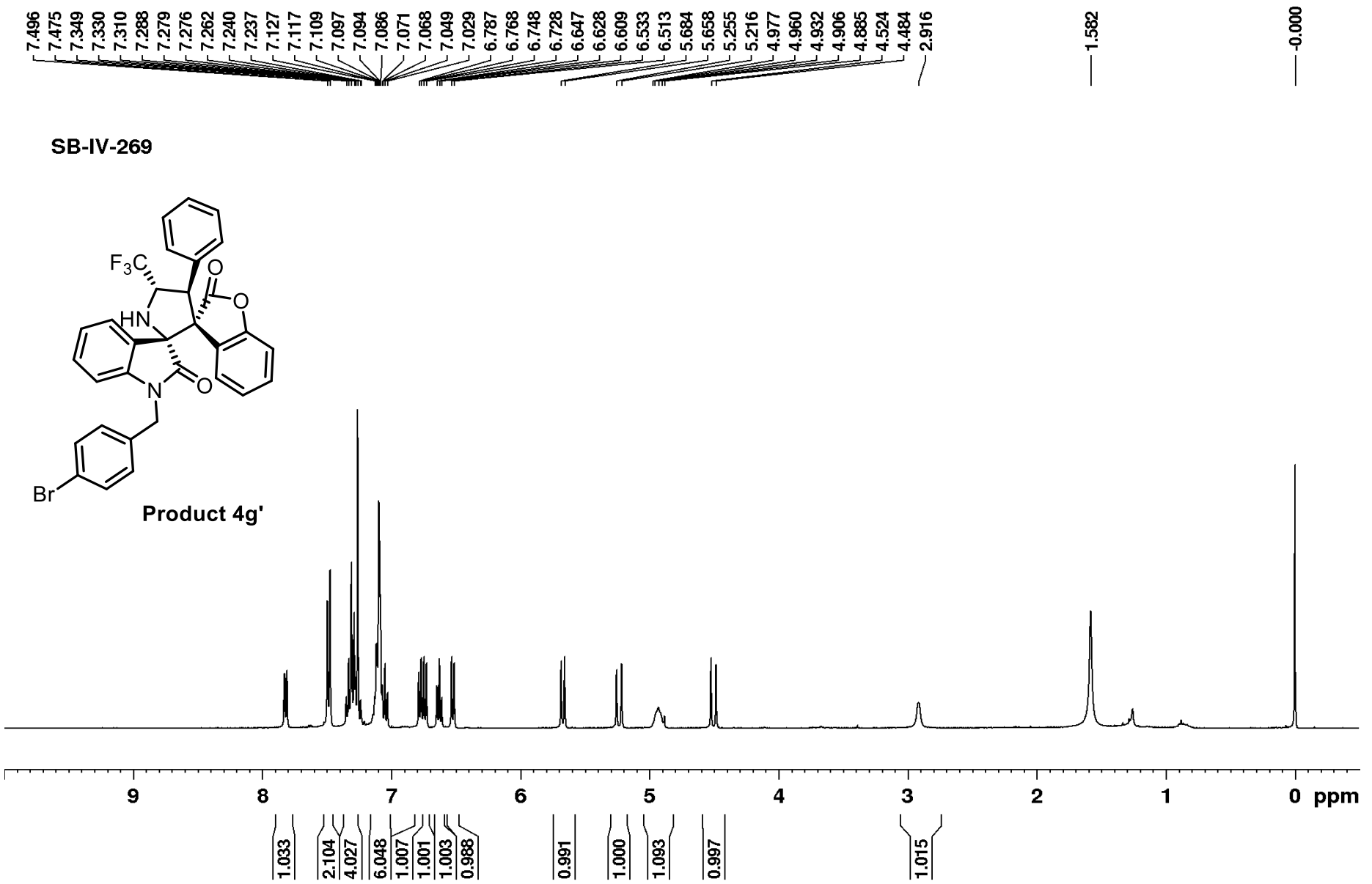
SB-IV-257

Product 4f'



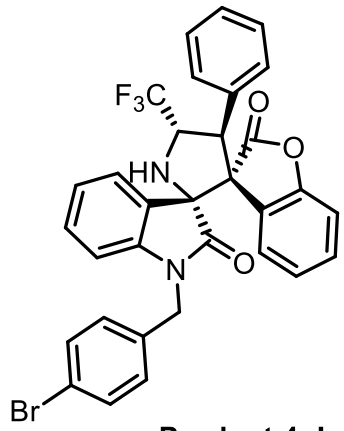

176.18
172.12
152.89
143.70
135.43
131.99
130.44
130.36
128.81
128.44
128.29
128.12
127.72
127.68
126.96
126.55
125.45
124.17
124.06
123.73
123.49
121.92
111.50
109.49
77.34
77.02
76.70
71.40
66.22
61.23
60.92
60.61
60.30
51.00
44.67
SB-IV-257
F3C
HN
O
O
N
O
Bn
Product 4f'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


130.44
130.37
128.81
128.44
128.29
128.13
127.72
127.68
126.55
125.45
123.50
121.93
111.51
109.50
77.22
61.23
60.92
60.61
60.30
51.00
44.67
SB-IV-257
F3C
O
O
HN
O
N
Bn
Product 4f'
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

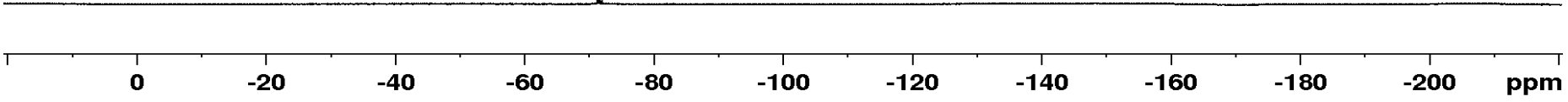

7.496
7.475
7.349
7.330
7.310
7.288
7.279
7.276
7.262
7.240
7.237
7.127
7.117
7.109
7.097
7.094
7.086
7.071
7.068
7.049
7.029
6.787
6.768
6.748
6.728
6.647
6.628
6.609
6.533
6.513
5.684
5.658
5.255
5.216
4.977
4.960
4.932
4.906
4.885
4.524
4.484
2.916
1.582
-0.000
SB-IV-269
F3C
O
O
HN
O
N
Br
Product 4g'
9
8
7
6
5
4
3
2
1
0 ppm
1.033
2.104
4.027
6.048
1.007
1.001
1.003
0.988
0.991
1.000
1.093
0.997
1.015

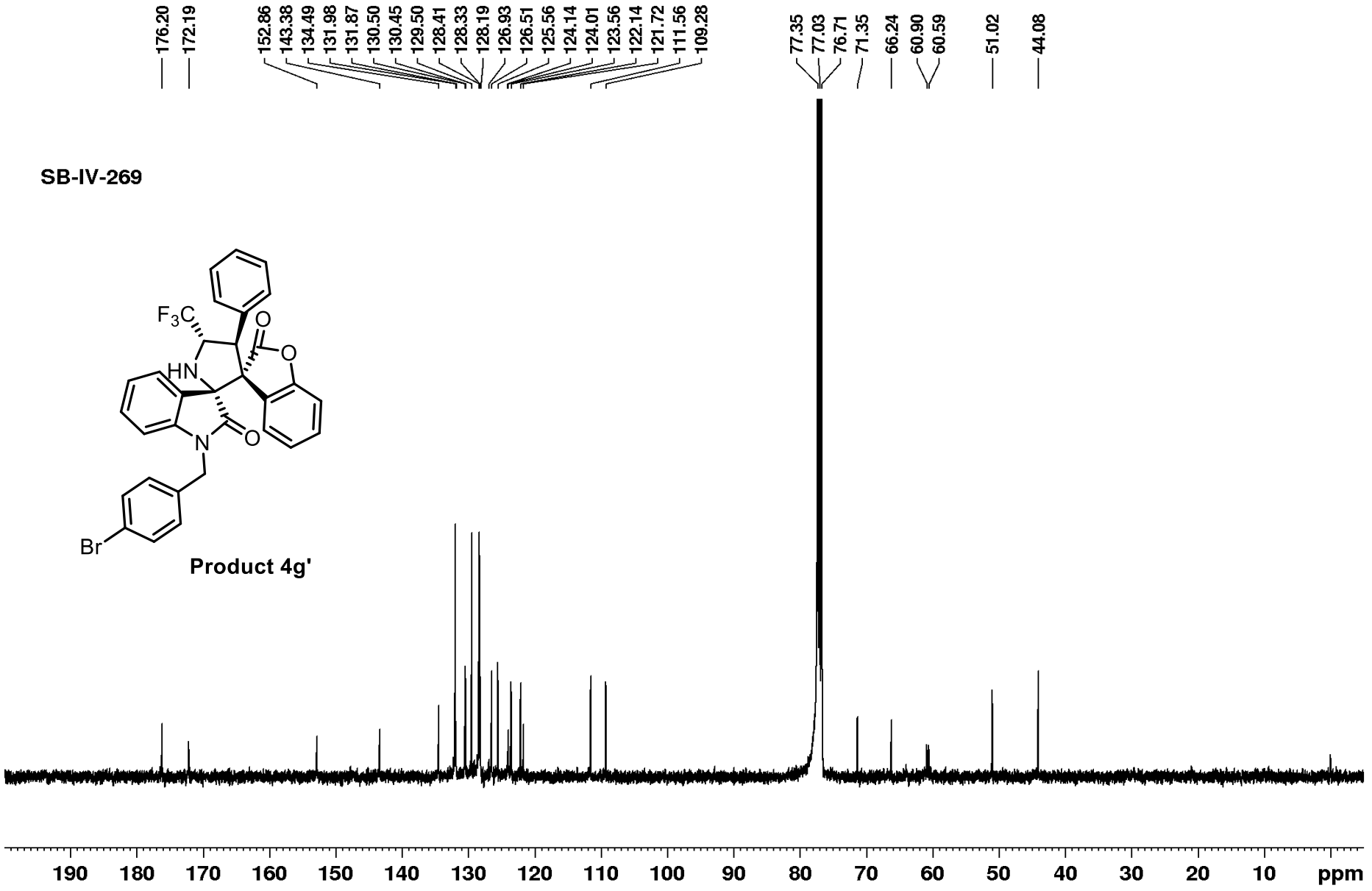
SB-IV-269

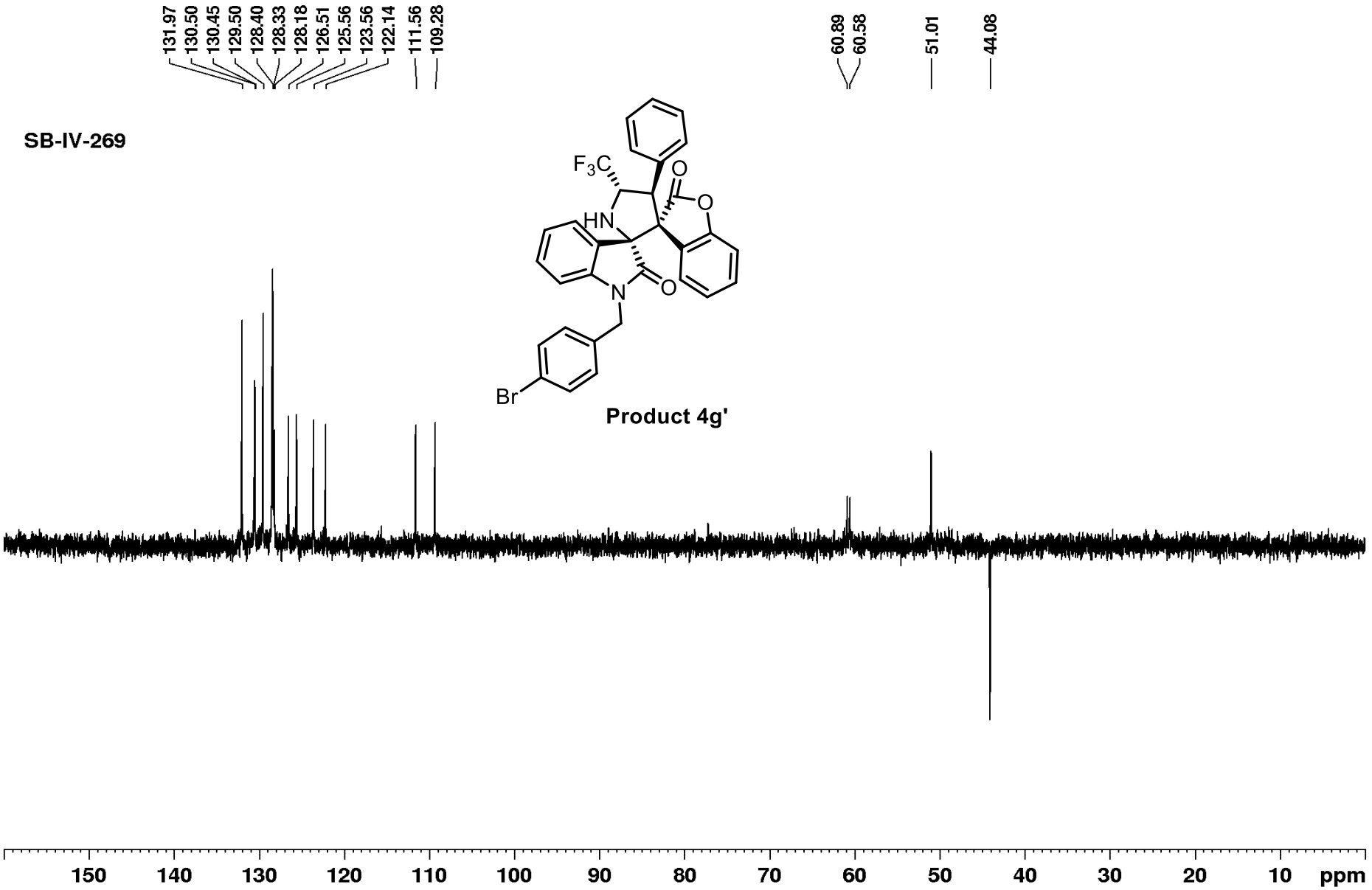
-71.57

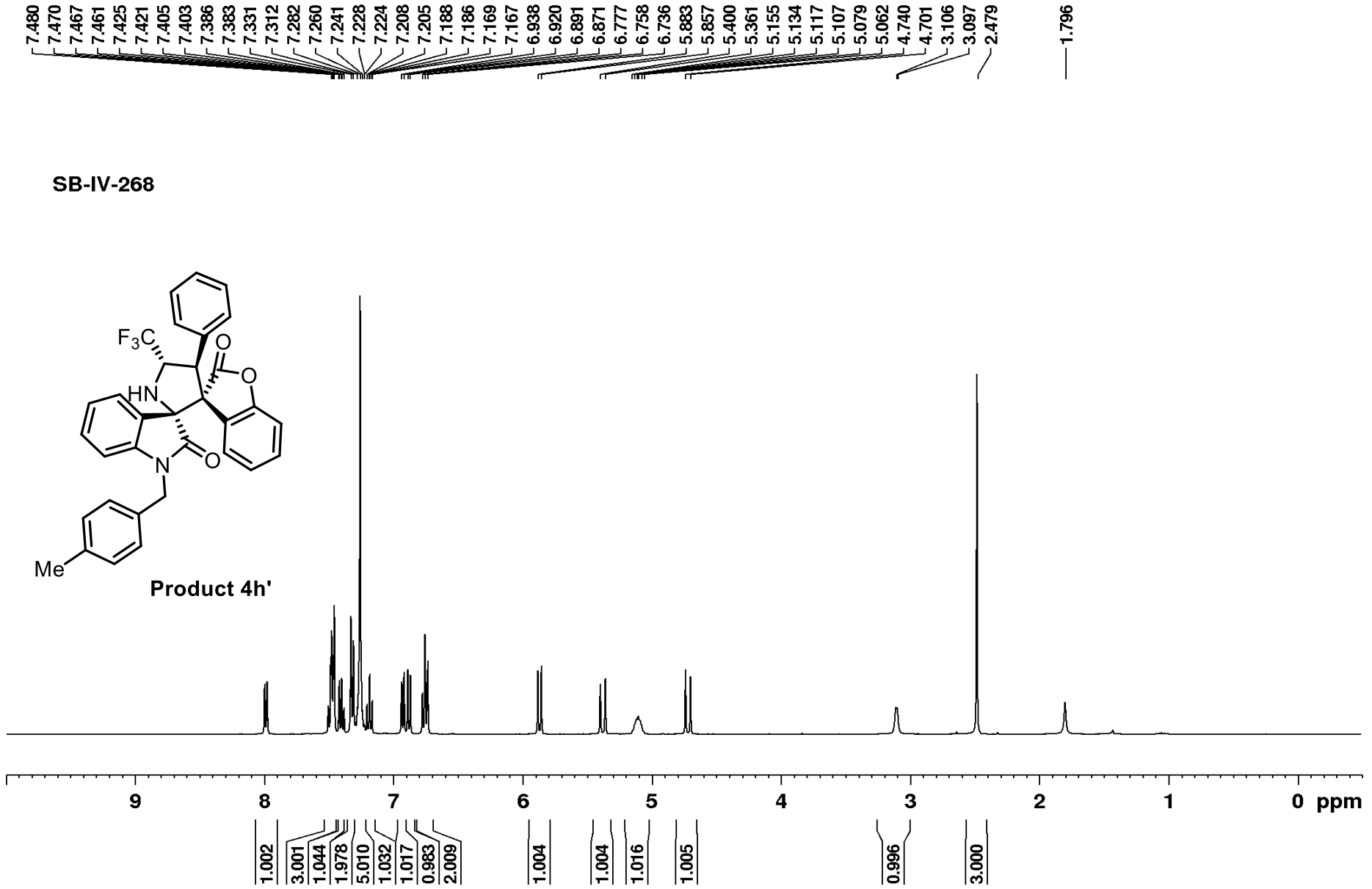


Product 4g'



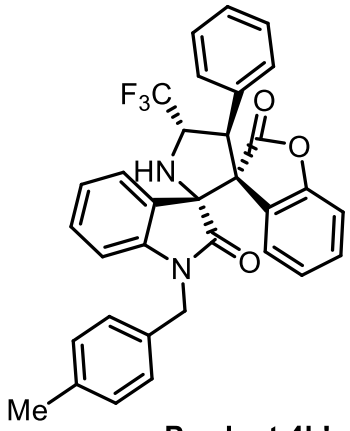

176.20
172.19
152.86
143.38
134.49
131.98
131.87
130.50
130.45
129.50
128.41
128.33
128.19
126.93
126.51
125.56
124.14
124.01
123.56
122.14
121.72
111.56
109.28
77.35
77.03
76.71
71.35
66.24
60.90
60.59
51.02
44.08
SB-IV-269
F3C
HN
O
O
N
O
Br
Product 4g'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


131.97
130.50
130.45
129.50
128.40
128.33
128.18
126.51
125.56
123.56
122.14
111.56
109.28
60.89
60.58
51.01
44.08
SB-IV-269
F3C
HN
O
O
N
O
Br
Product 4g'
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

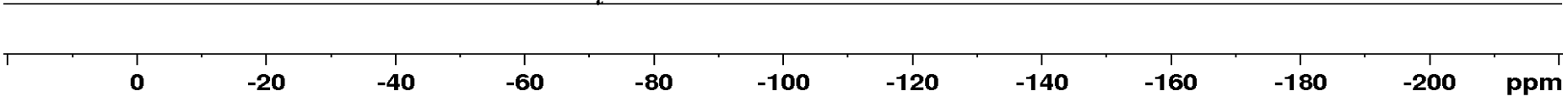

7.480
7.470
7.467
7.461
7.425
7.421
7.405
7.403
7.386
7.383
7.331
7.312
7.282
7.260
7.241
7.228
7.224
7.208
7.205
7.188
7.186
7.169
7.167
6.938
6.920
6.891
6.871
6.777
6.758
6.736
5.883
5.857
5.400
5.361
5.155
5.134
5.117
5.107
5.079
5.062
4.740
4.701
3.106
3.097
2.479
1.796
SB-IV-268
F3C
O
O
HN
O
N
Me
Product 4h'
9
8
7
6
5
4
3
2
1
0 ppm
1.002
3.001
1.044
1.978
5.010
1.032
1.017
0.983
2.009
1.004
1.004
1.016
1.005
0.996
3.000

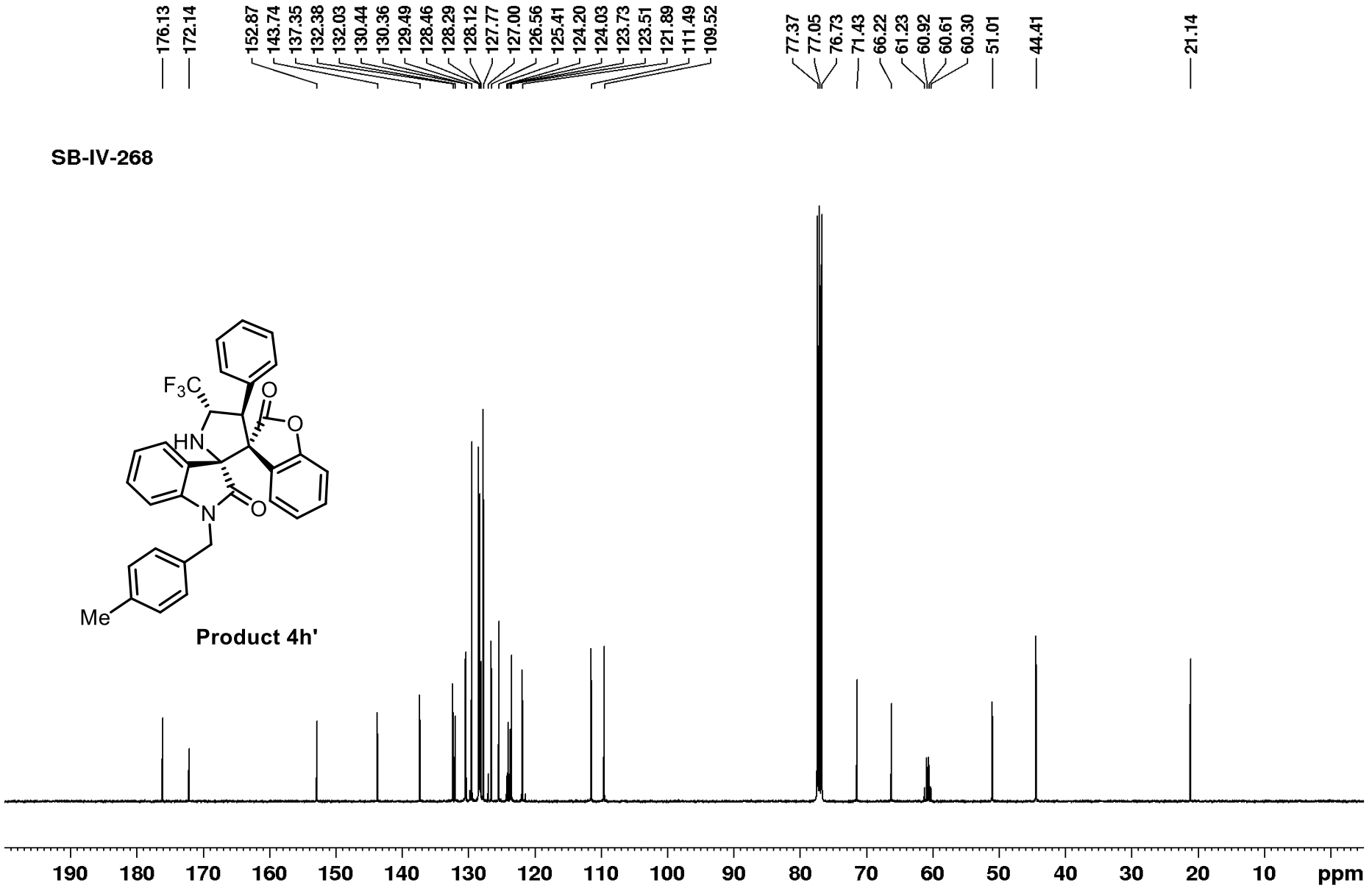
SB-IV-268

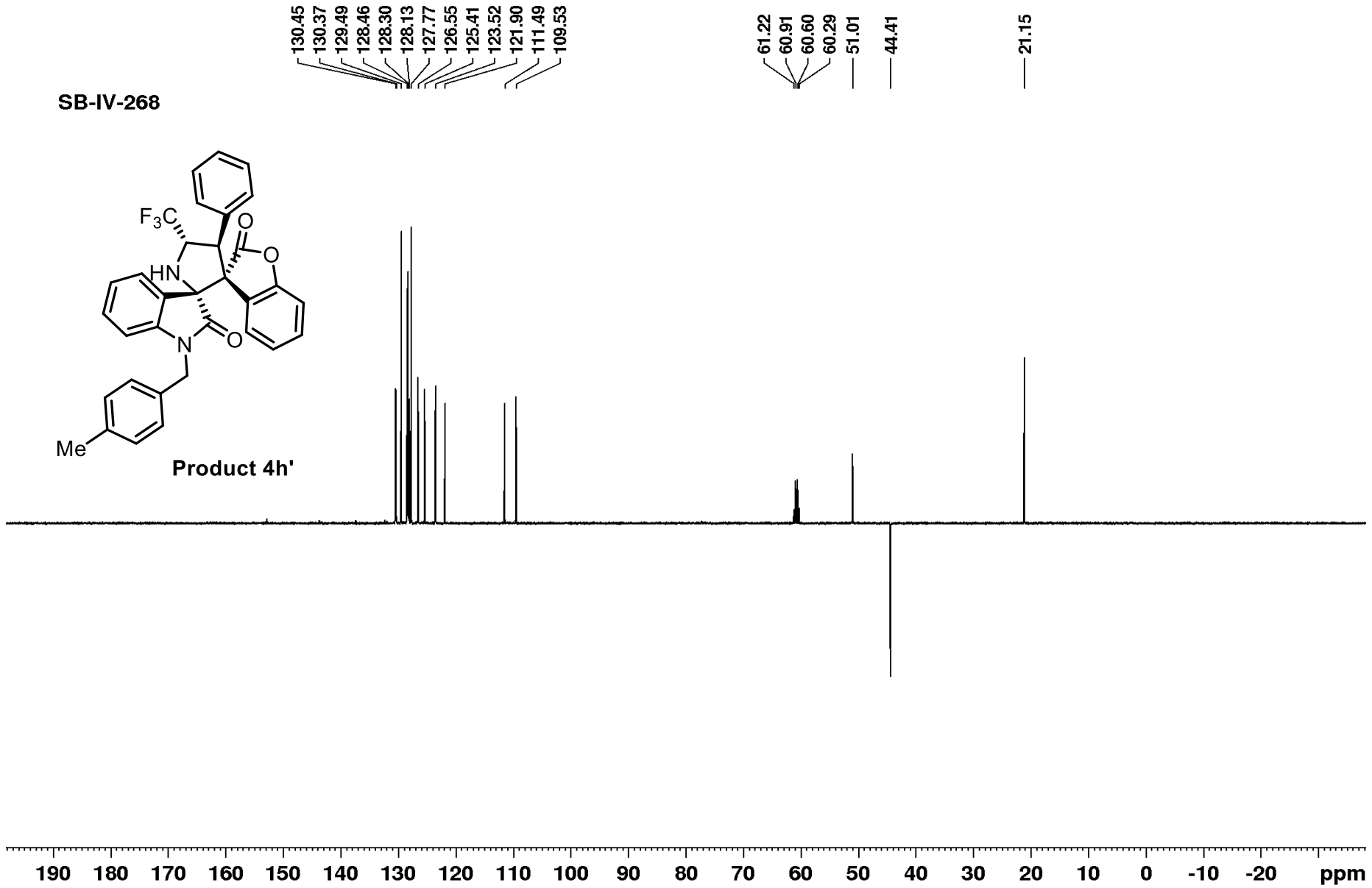
-71.52

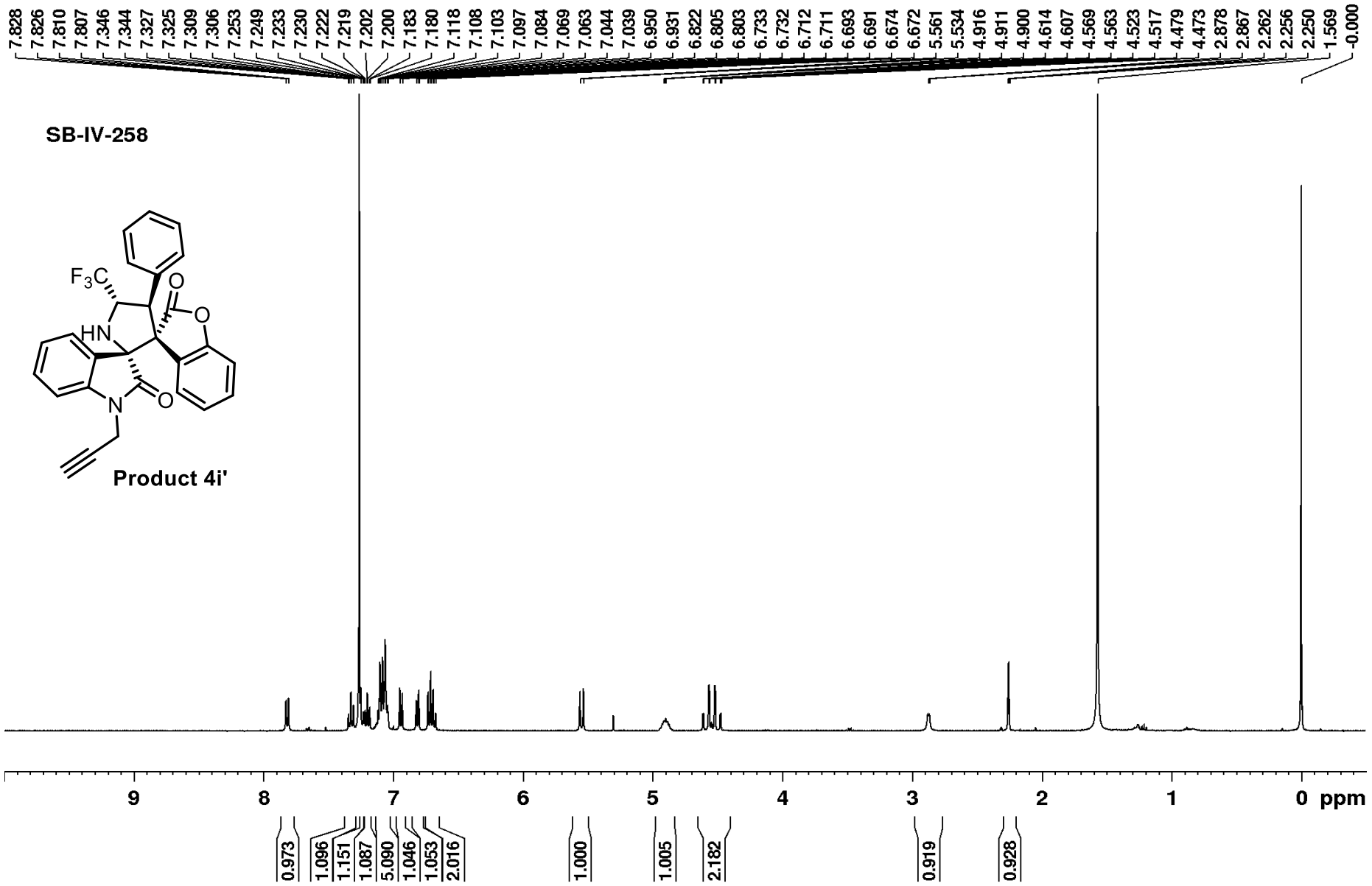


Product 4h'



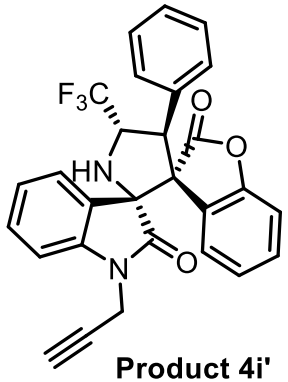

176.13
172.14
152.87
143.74
137.35
132.38
132.03
130.44
130.36
129.49
128.46
128.29
128.12
127.77
127.00
126.56
125.41
124.20
124.03
123.73
123.51
121.89
111.49
109.52
77.37
77.05
76.73
71.43
66.22
61.23
60.92
60.61
60.30
51.01
44.41
21.14
SB-IV-268
F3C
HN
O
O
N
O
Me
Product 4h'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


130.45
130.37
129.49
128.46
128.30
128.13
127.77
126.55
125.41
123.52
121.90
111.49
109.53
61.22
60.91
60.60
60.29
51.01
44.41
21.15
SB-IV-268
F3C
HN
O
O
N
O
Me
Product 4h'
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 ppm

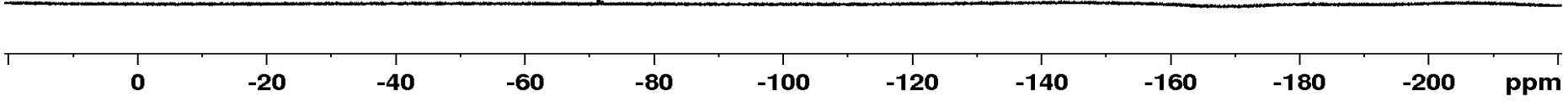

7.828
7.826
7.810
7.807
7.346
7.344
7.327
7.325
7.309
7.306
7.253
7.249
7.233
7.230
7.222
7.219
7.202
7.200
7.183
7.180
7.118
7.108
7.103
7.097
7.084
7.069
7.063
7.044
7.039
6.950
6.931
6.822
6.805
6.803
6.733
6.732
6.712
6.711
6.693
6.691
6.674
6.672
5.561
5.534
4.916
4.911
4.900
4.614
4.607
4.569
4.563
4.523
4.517
4.479
4.473
2.878
2.867
2.262
2.256
2.250
1.569
-0.000
SB-IV-258
F3C
O
O
HN
O
N
Product 4i'
9
8
7
6
5
4
3
2
1
0 ppm
0.973
1.096
1.151
1.087
5.090
1.046
1.053
2.016
1.000
1.005
2.182
0.919
0.928

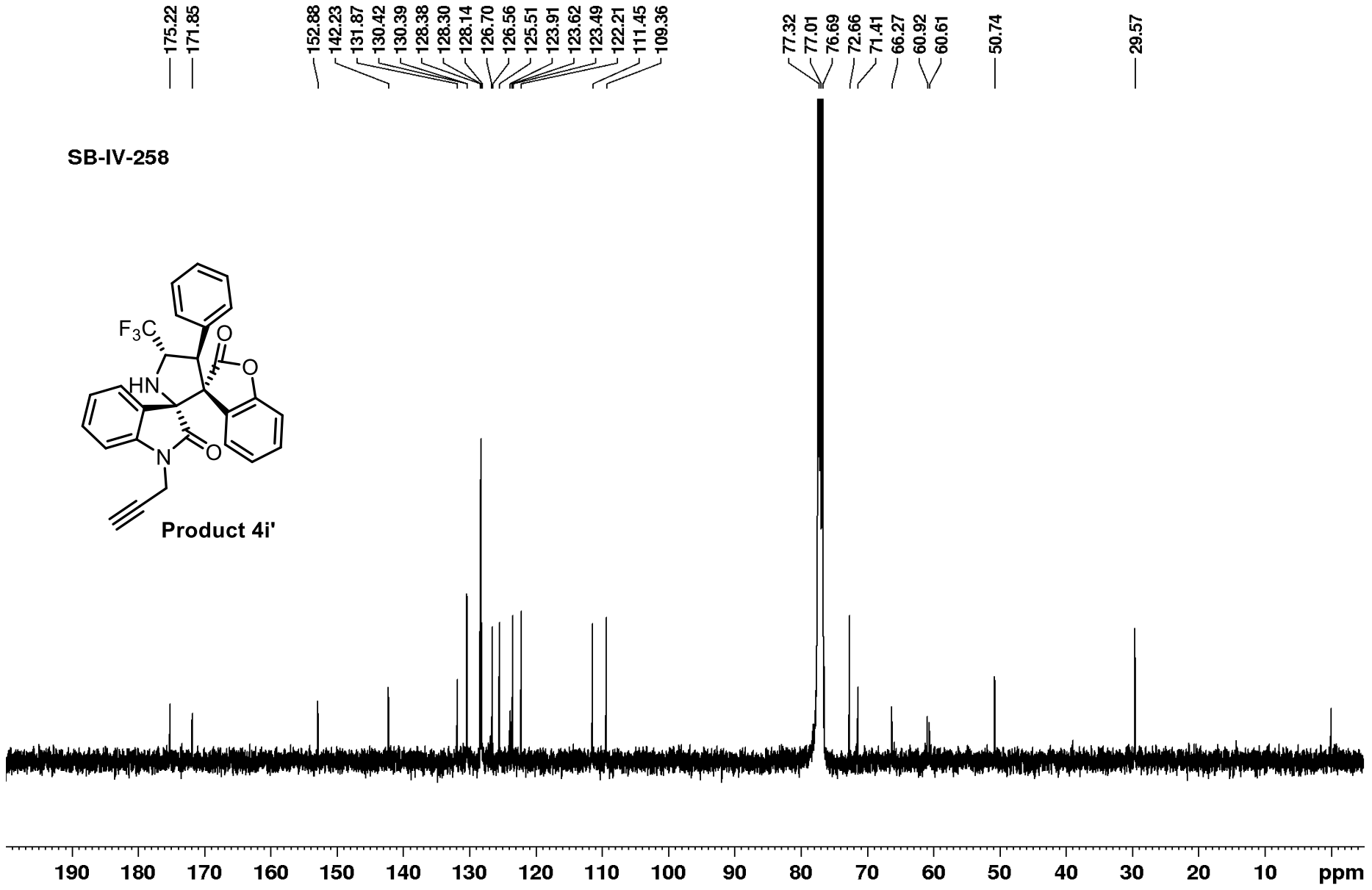
SB-IV-258

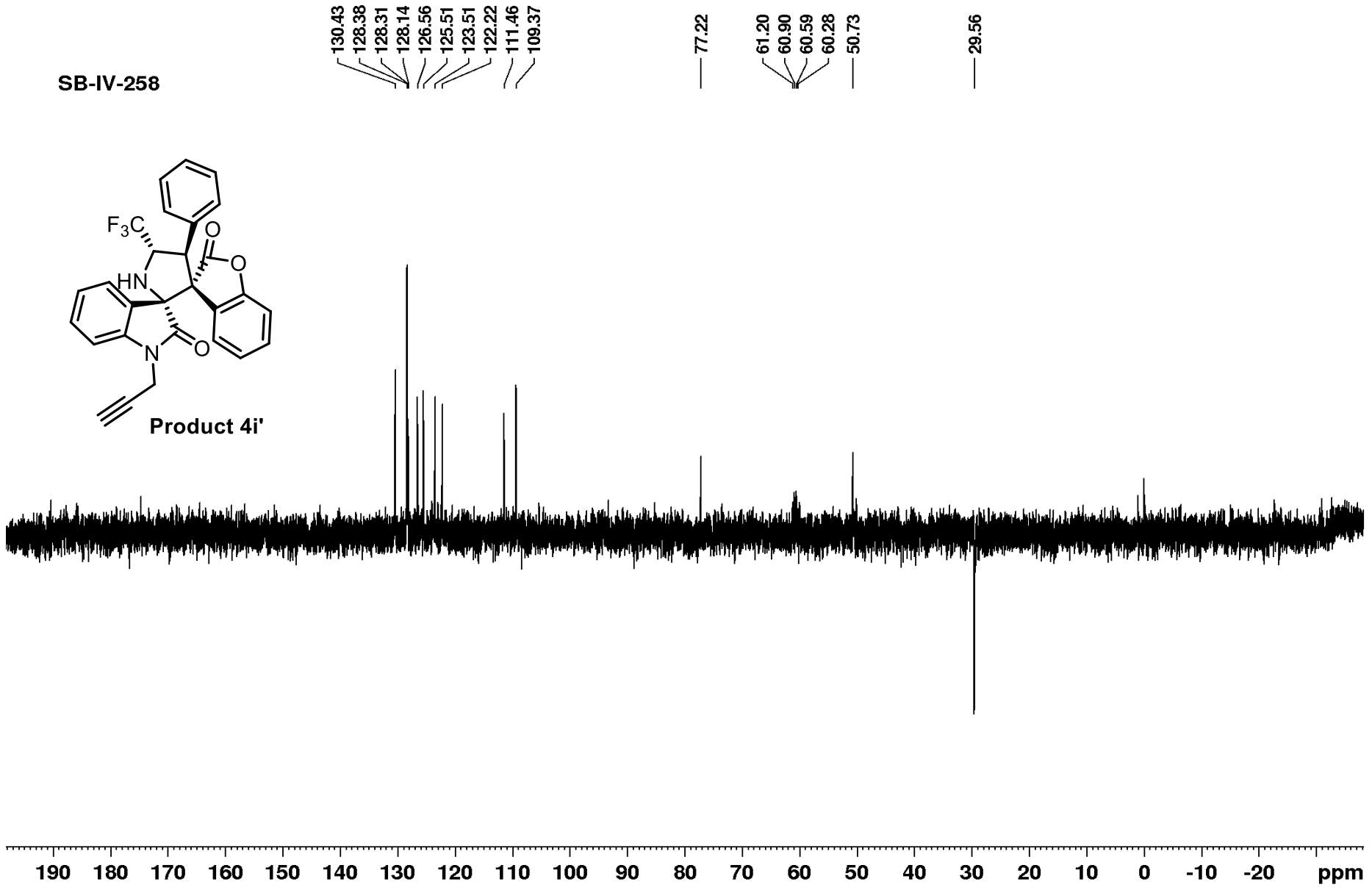
-71.58

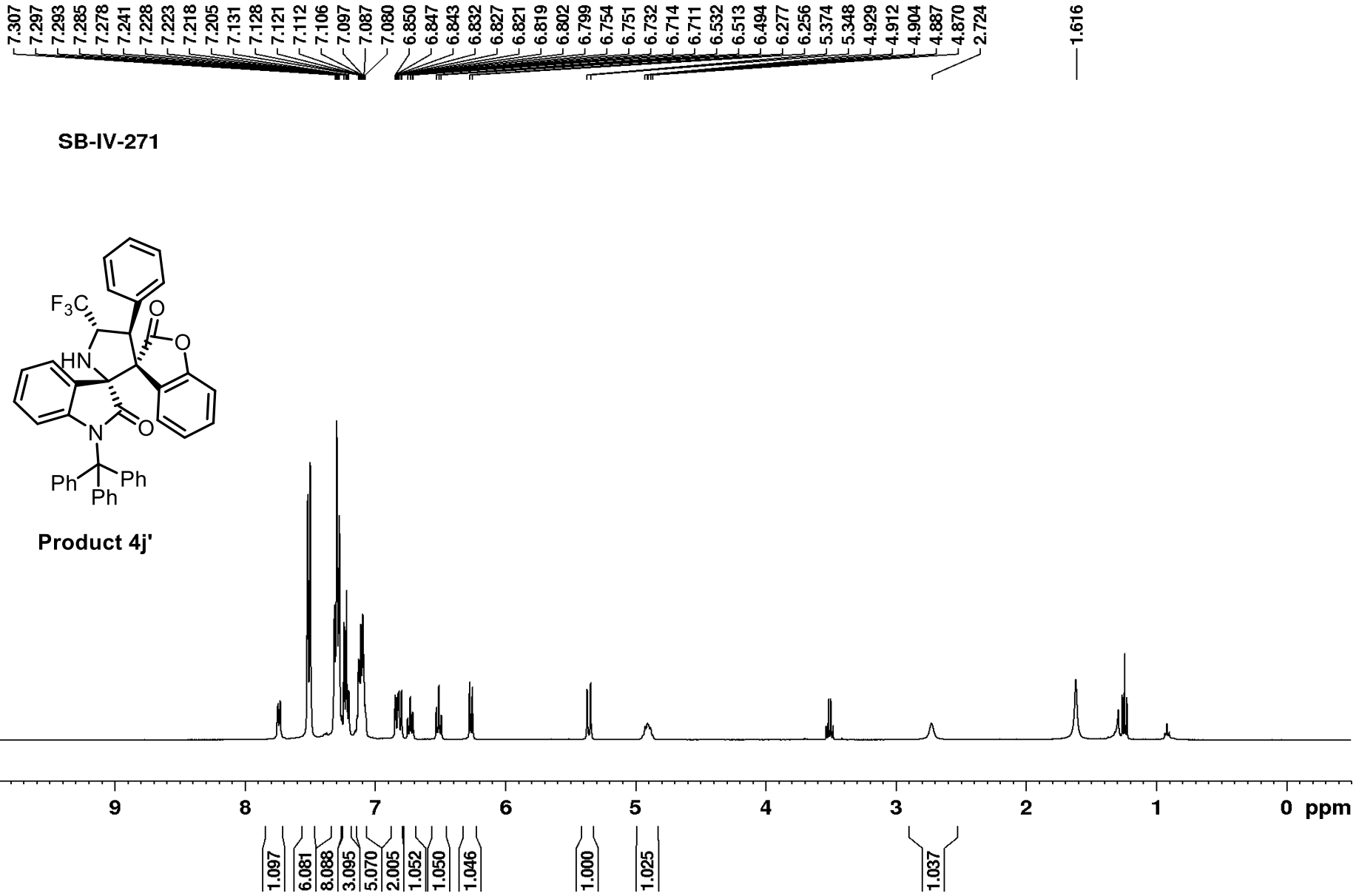


Product 4i'



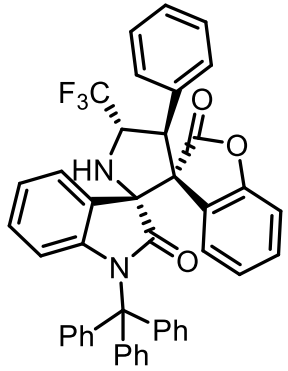

175.22
171.85
152.88
142.23
131.87
130.42
130.39
128.38
128.30
128.14
126.70
126.56
125.51
123.91
123.62
123.49
122.21
111.45
109.36
77.32
77.01
76.69
72.66
71.41
66.27
60.92
60.61
50.74
29.57
SB-IV-258
F3C
HN
O
O
O
N
Product 4i'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


SB-IV-258
130.43
128.38
128.31
128.14
126.56
125.51
123.51
122.22
111.46
109.37
77.22
61.20
60.90
60.59
60.28
50.73
29.56
F3C
HN
O
O
O
N
Product 4i'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
ppm

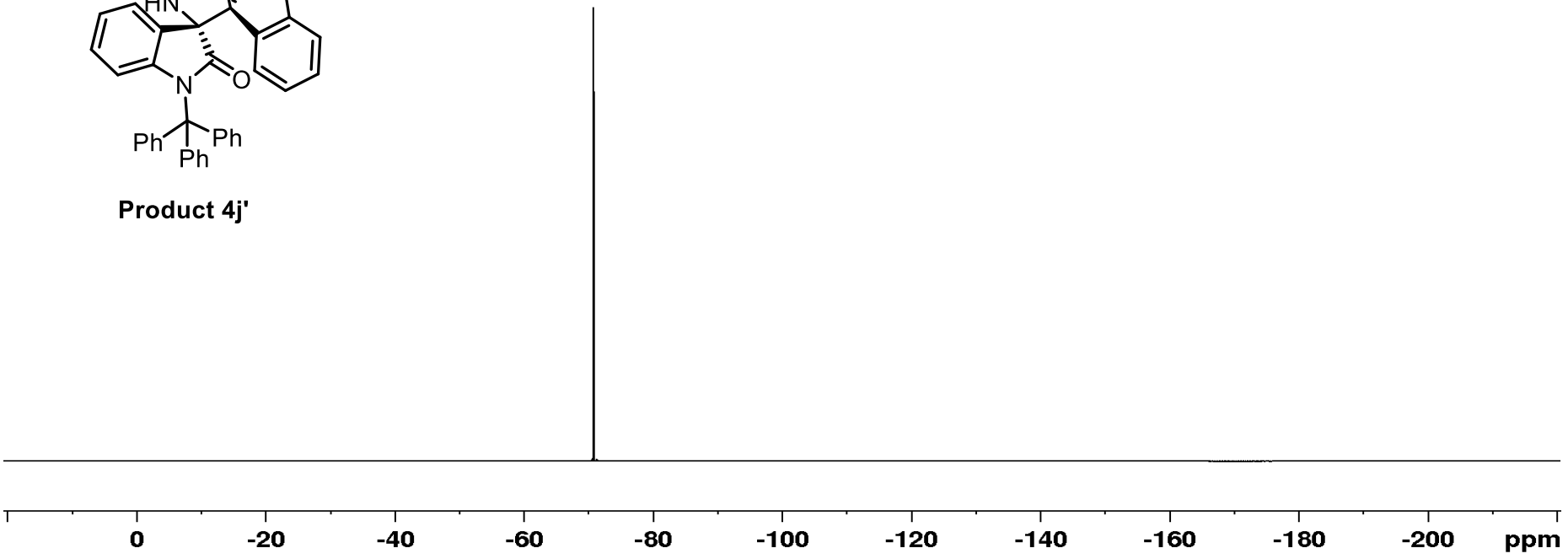

7.307
7.297
7.293
7.285
7.278
7.241
7.228
7.223
7.218
7.205
7.131
7.128
7.121
7.112
7.106
7.097
7.087
7.080
6.850
6.847
6.843
6.832
6.827
6.821
6.819
6.802
6.799
6.754
6.751
6.732
6.714
6.711
6.532
6.513
6.494
6.277
6.256
5.374
5.348
4.929
4.912
4.904
4.887
4.870
2.724
1.616
SB-IV-271
F3C
HN
O
O
N
O
Ph
Ph
Ph
Product 4j'
9
8
7
6
5
4
3
2
1
0 ppm
1.097
6.081
8.088
3.095
5.070
2.005
1.052
1.050
1.046
1.000
1.025
1.037

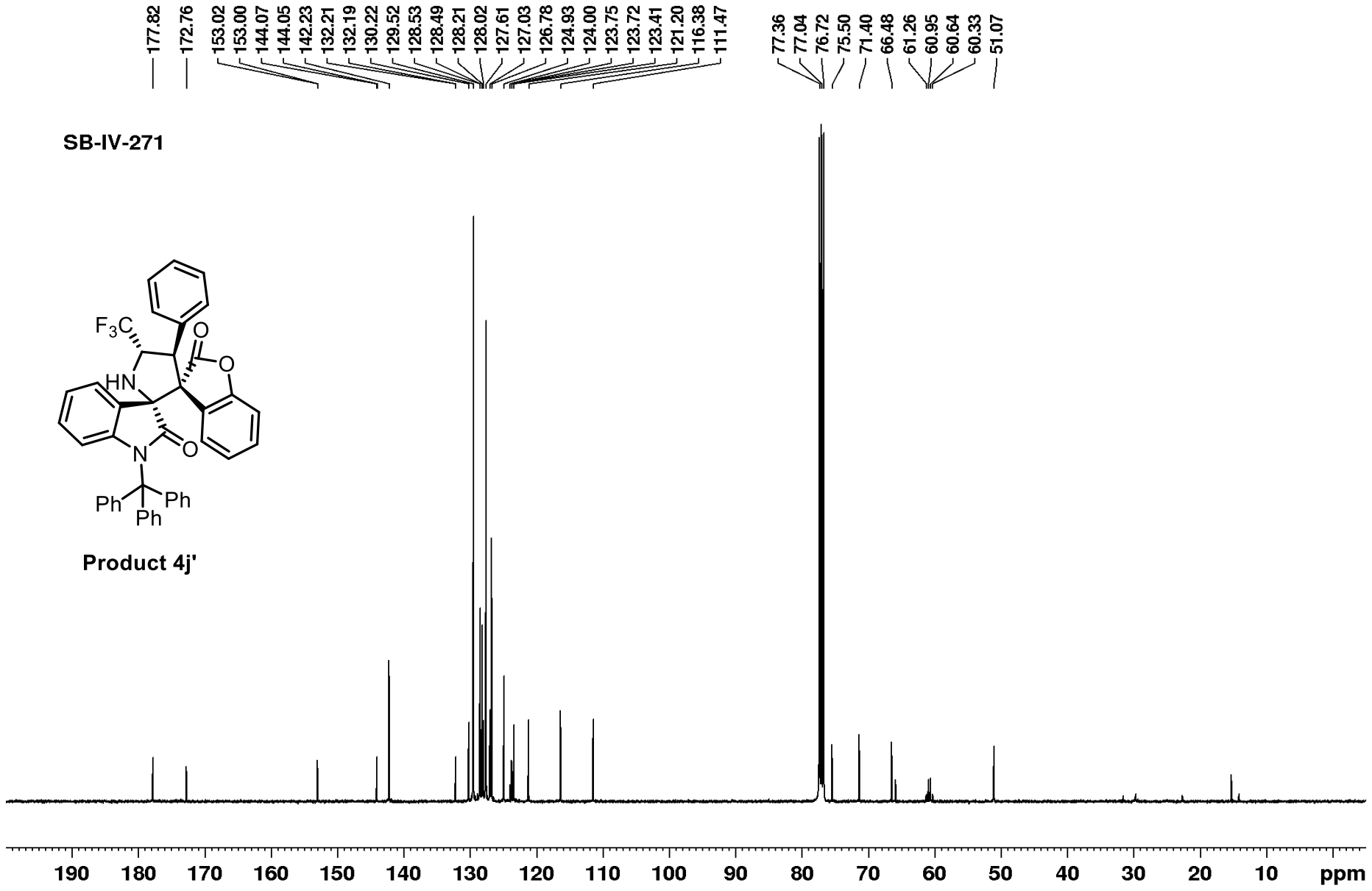
SB-IV-271

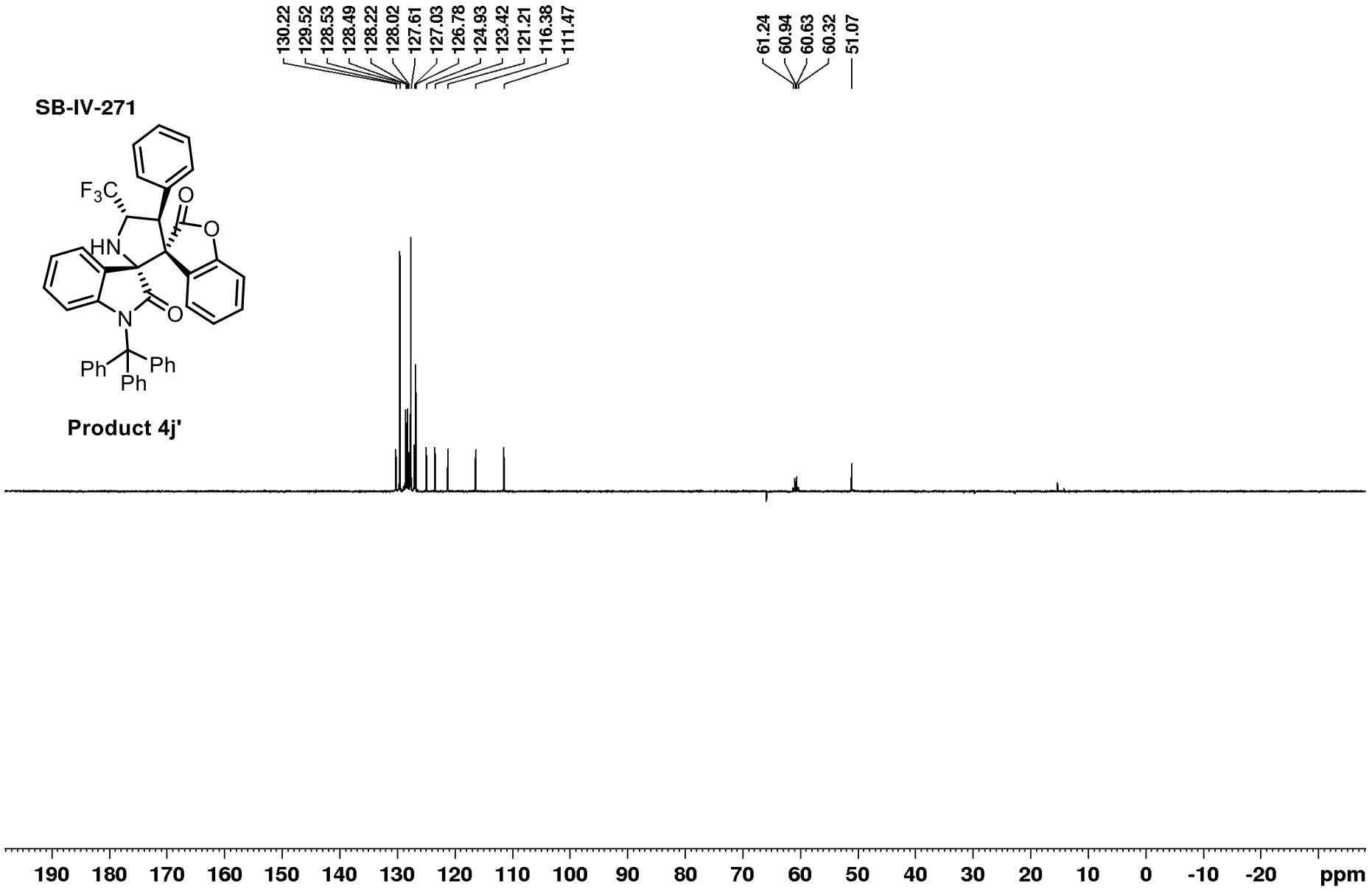
-70.84

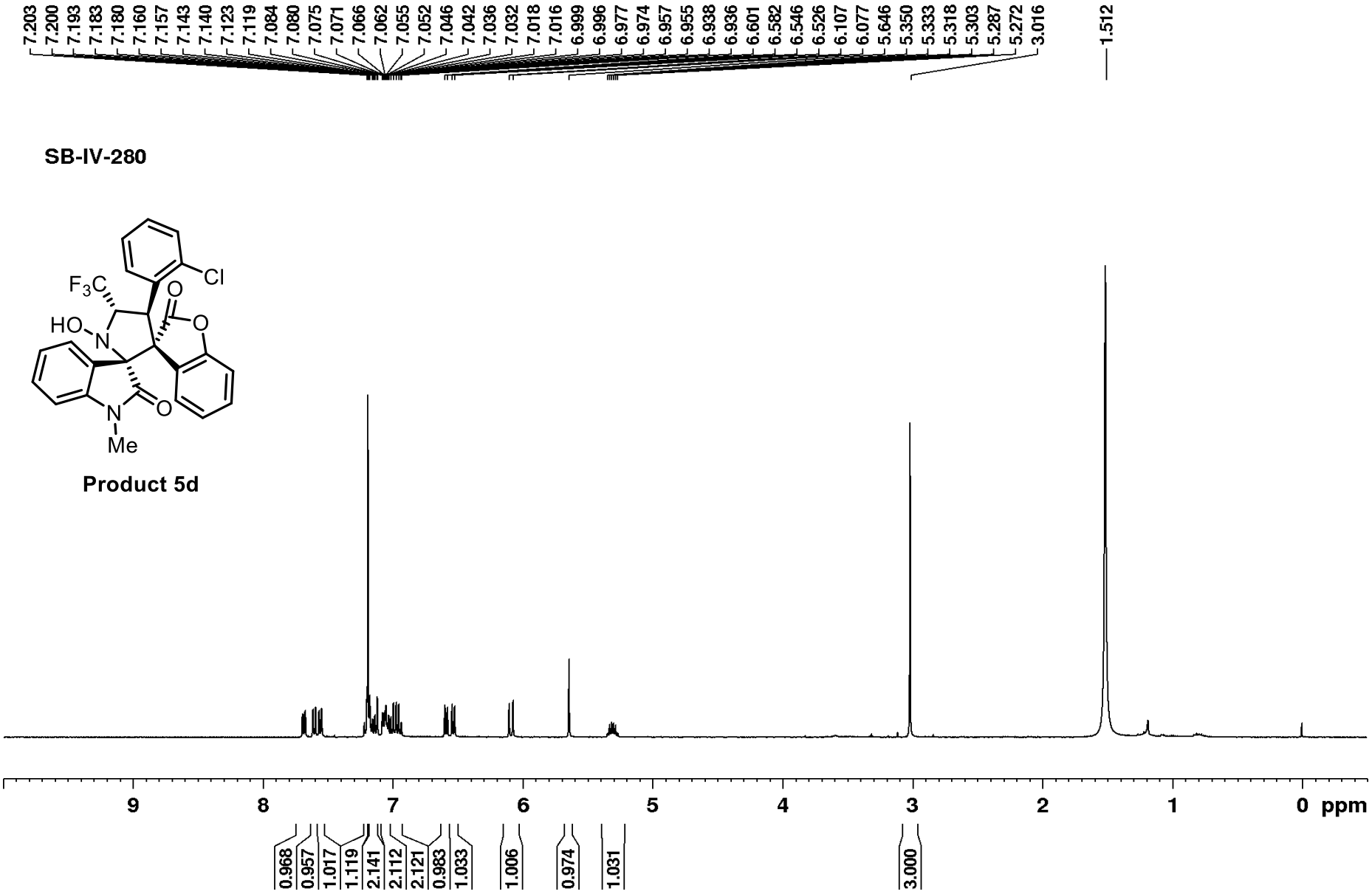


Product 4j'



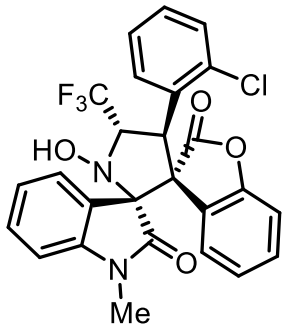

177.82
172.76
153.02
153.00
144.07
144.05
142.23
132.21
132.19
130.22
129.52
128.53
128.49
128.21
128.02
127.61
127.03
126.78
124.93
124.00
123.75
123.72
123.41
121.20
116.38
111.47
77.36
77.04
76.72
75.50
71.40
66.48
61.26
60.95
60.64
60.33
51.07
SB-IV-271
F3C
O
O
HN
O
N
Ph
Ph
Ph
Product 4j'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


130.22
129.52
128.53
128.49
128.22
128.02
127.61
127.03
126.78
124.93
123.42
121.21
116.38
111.47
61.24
60.94
60.63
60.32
51.07
SB-IV-271
F3C
HN
O
O
N
O
Ph
Ph
Ph
Product 4j'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
ppm

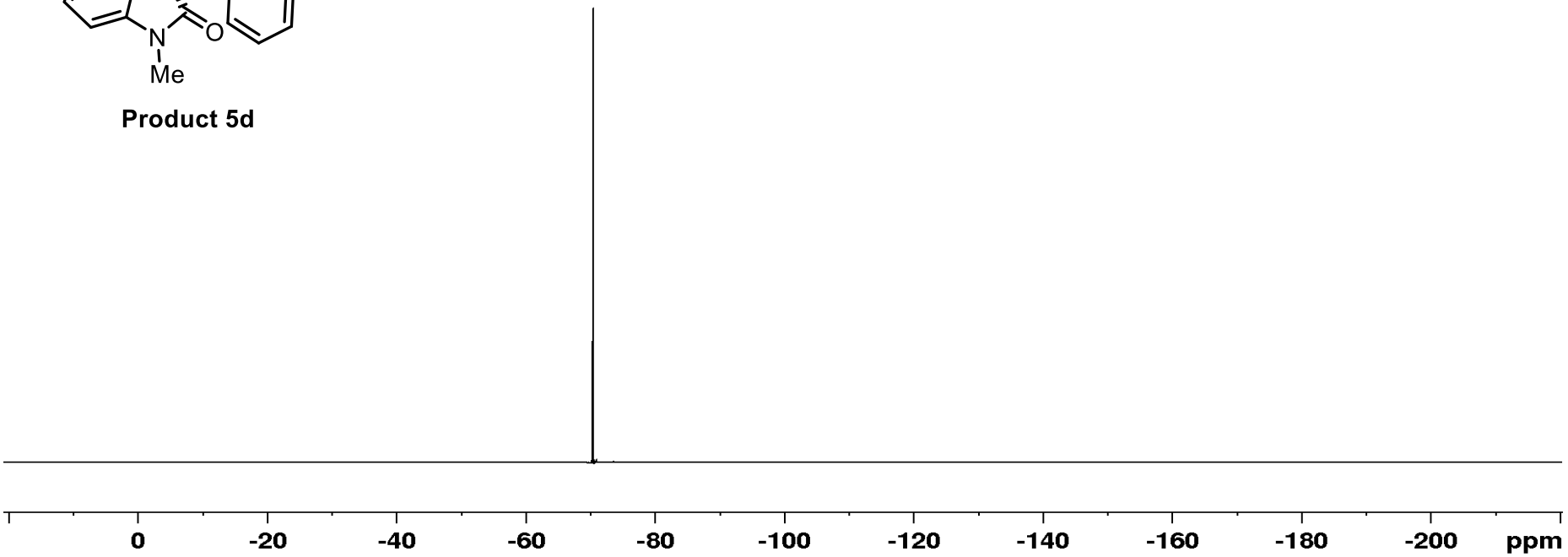

7.203
7.200
7.193
7.183
7.180
7.160
7.157
7.143
7.140
7.123
7.119
7.084
7.080
7.075
7.071
7.066
7.062
7.055
7.052
7.046
7.042
7.036
7.032
7.018
7.016
6.999
6.996
6.977
6.974
6.957
6.955
6.938
6.936
6.601
6.582
6.546
6.526
6.107
6.077
5.646
5.350
5.333
5.318
5.303
5.287
5.272
3.016
1.512
SB-IV-280
F3C
Cl
HO
N
O
O
O
N
Me
Product 5d
9
8
7
6
5
4
3
2
1
0 ppm
0.968
0.957
1.017
1.119
2.141
2.112
2.121
0.983
1.033
1.006
0.974
1.031
3.000

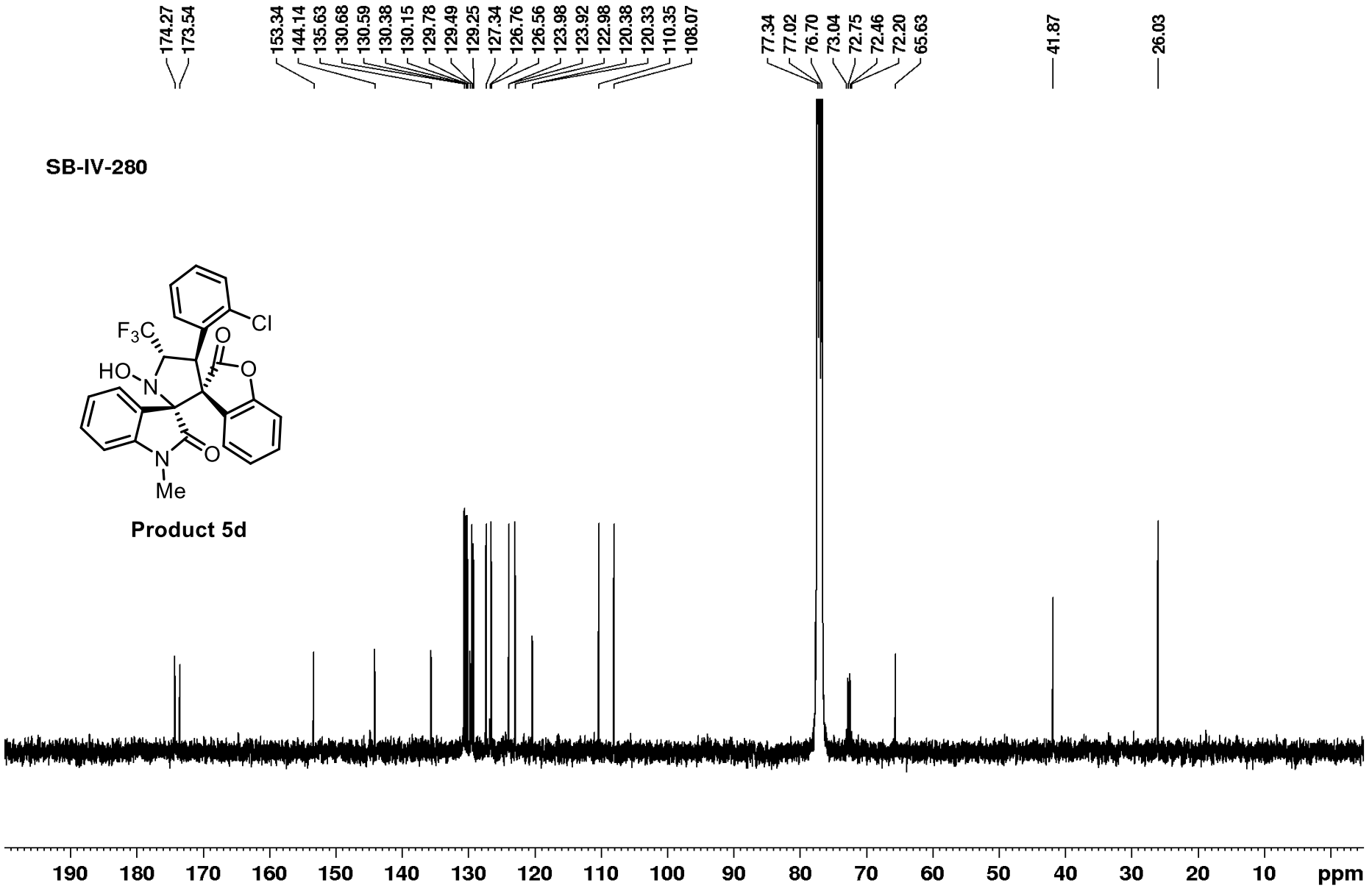
SB-IV-280

-70.41



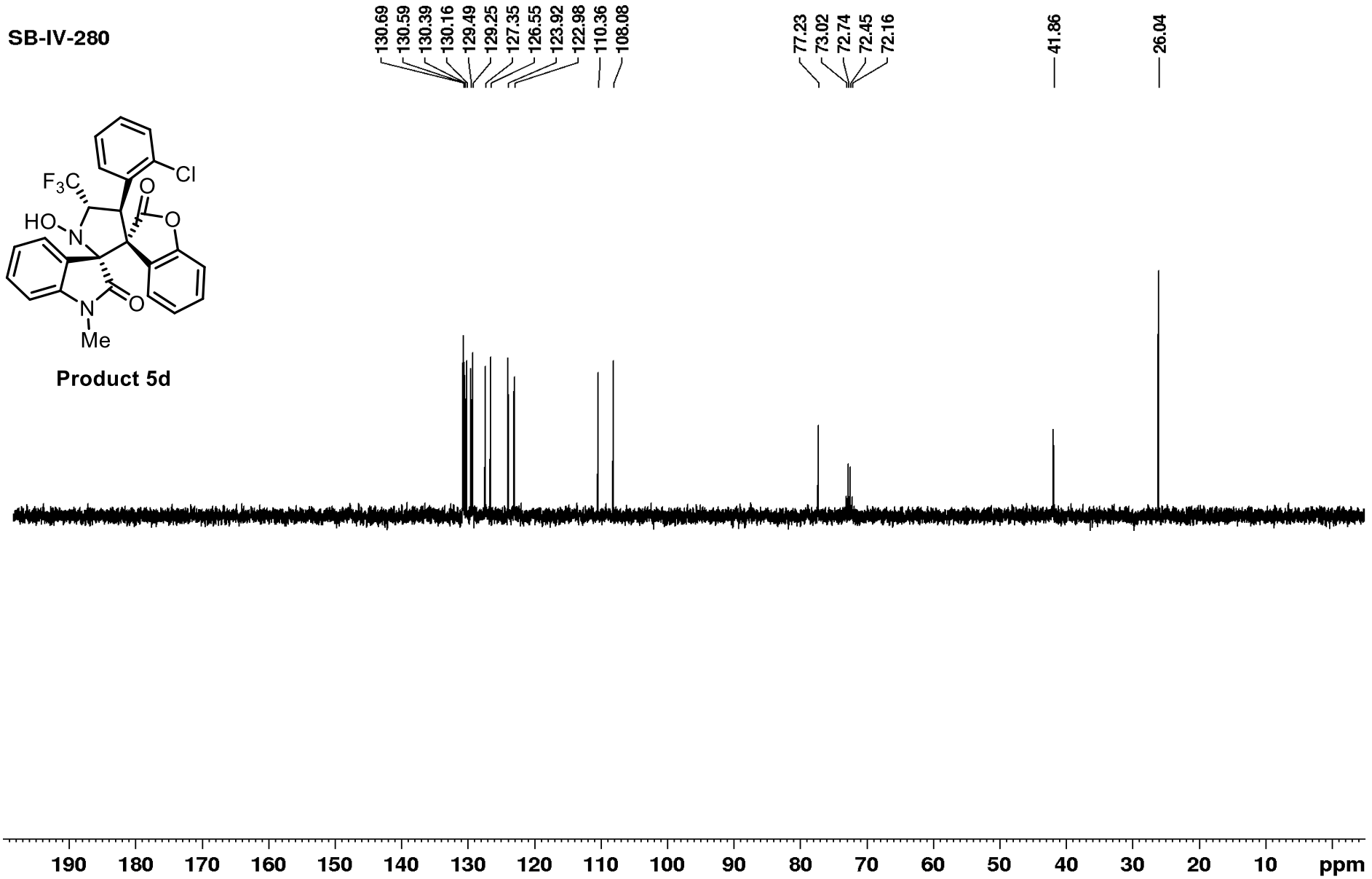
Product 5d

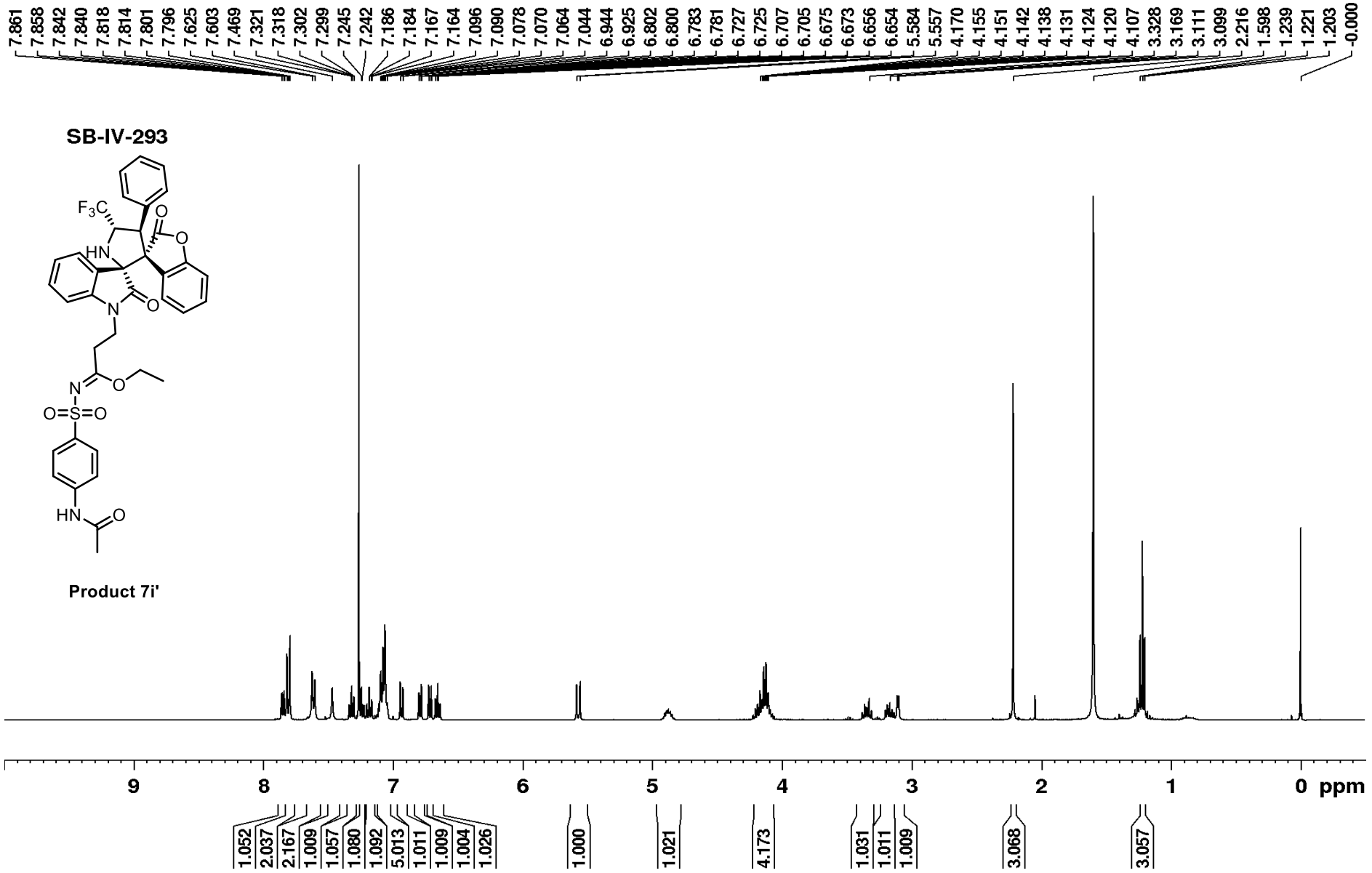



174.27
173.54
153.34
144.14
135.63
130.68
130.59
130.38
130.15
129.78
129.49
129.25
127.34
126.76
126.56
123.98
123.92
122.98
120.38
120.33
110.35
108.07
77.34
77.02
76.70
73.04
72.75
72.46
72.20
65.63
41.87
26.03
SB-IV-280
F3C
Cl
HO
N
O
O
O
N
Me
Product 5d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

SB-IV-280

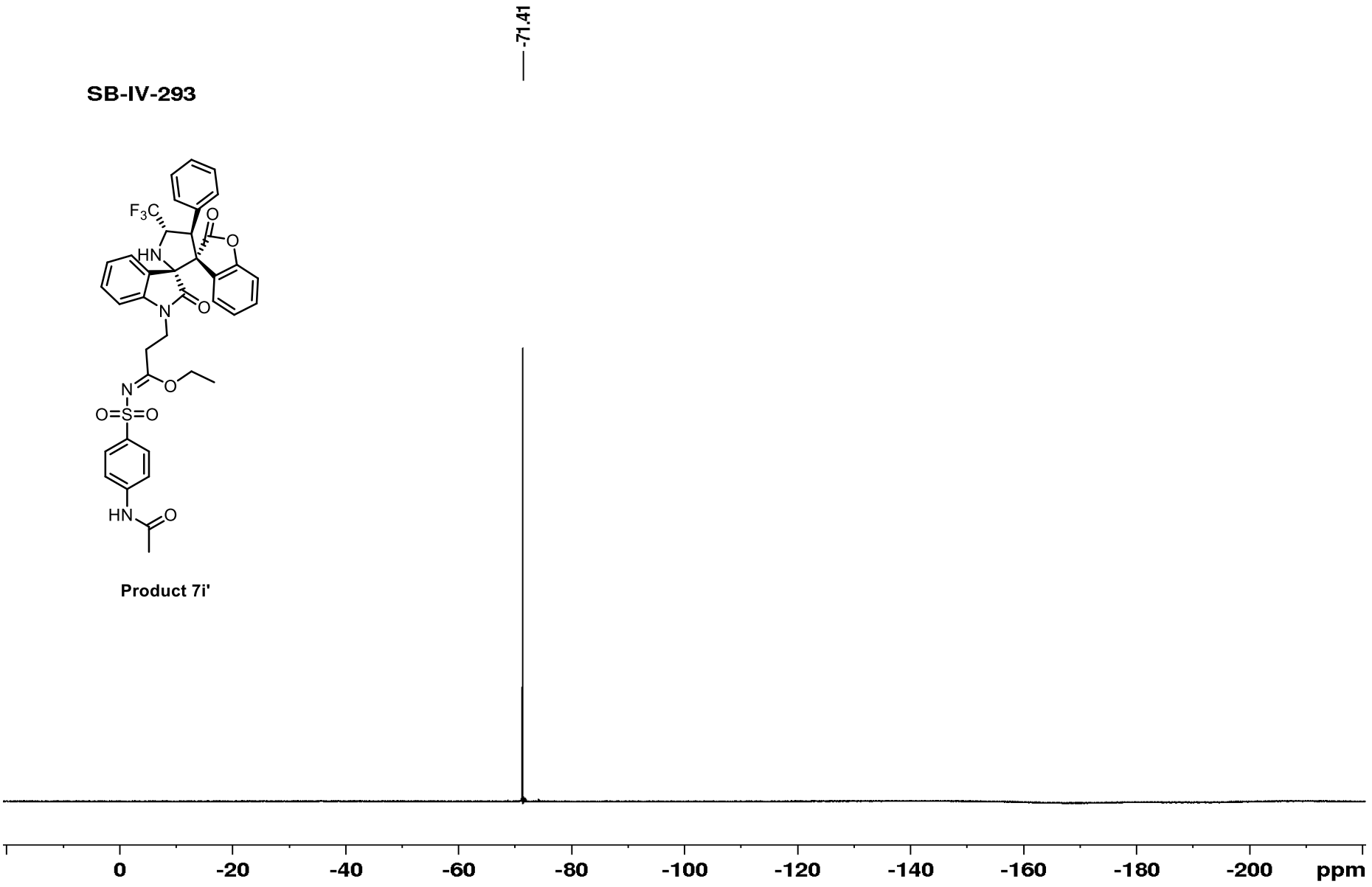
Product 5d

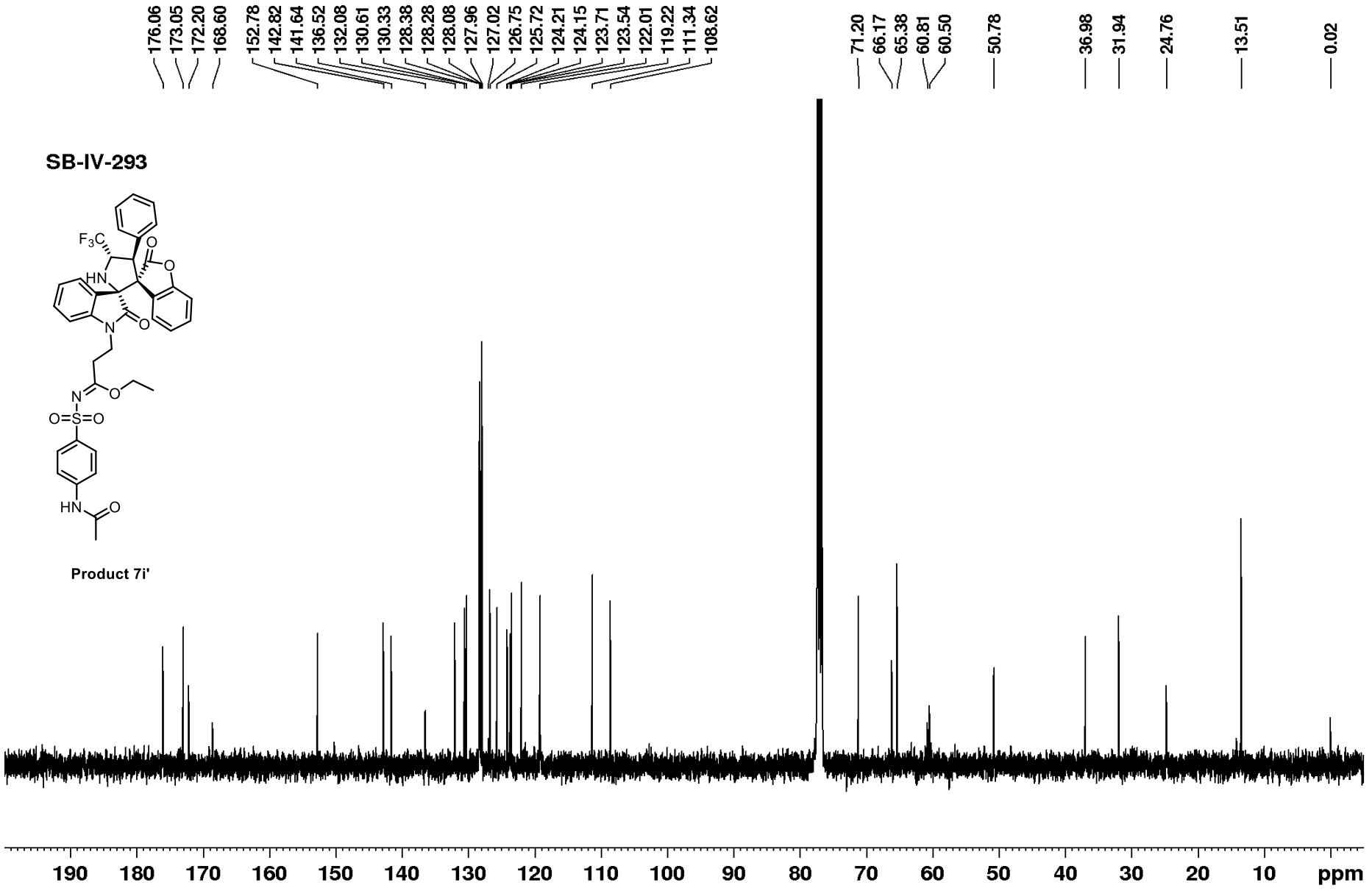


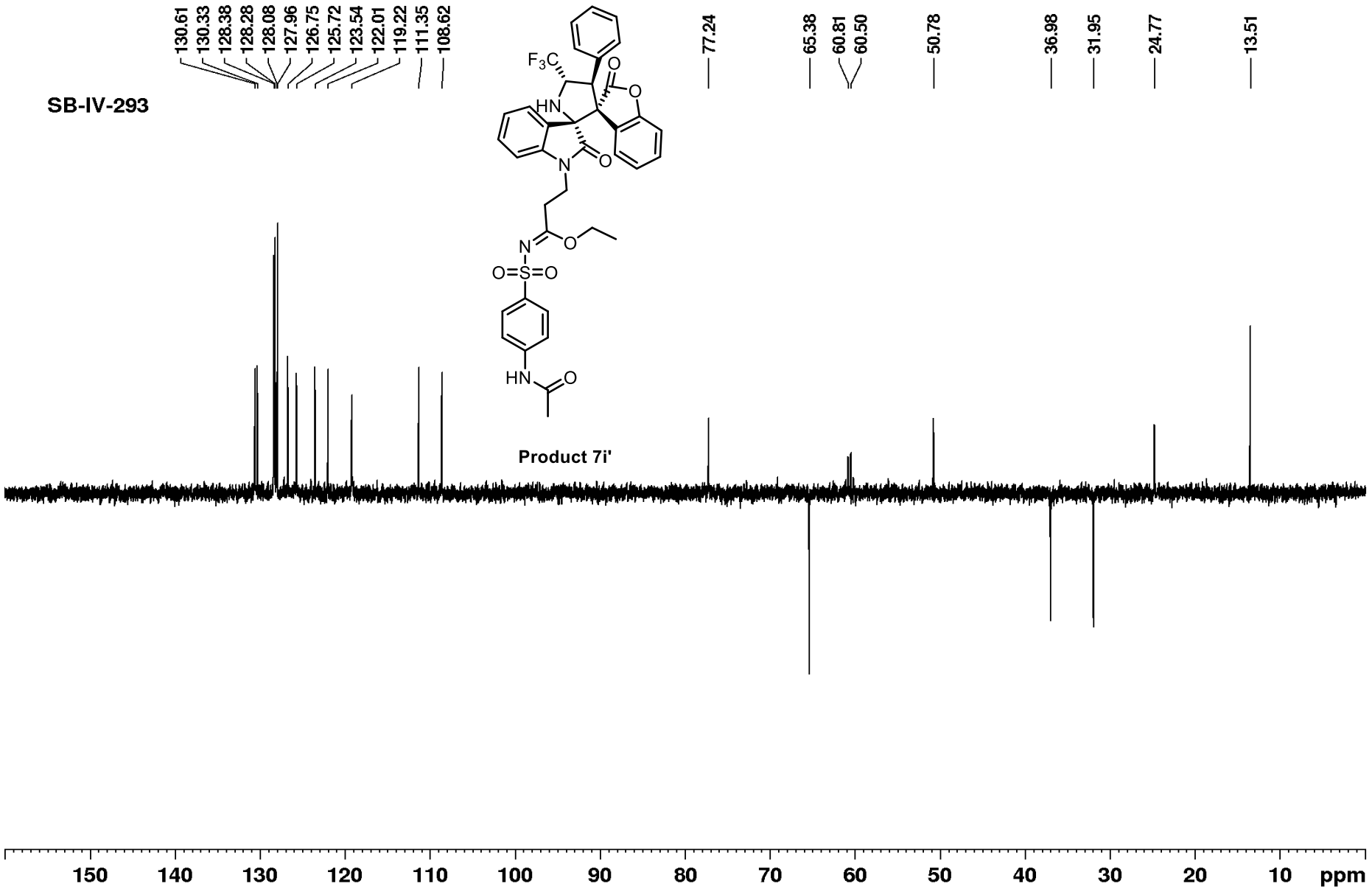

7.861
7.858
7.842
7.840
7.818
7.814
7.801
7.796
7.625
7.603
7.469
7.321
7.318
7.302
7.299
7.245
7.242
7.186
7.184
7.167
7.164
7.096
7.090
7.078
7.070
7.064
7.044
6.944
6.925
6.802
6.800
6.783
6.781
6.727
6.725
6.707
6.705
6.675
6.673
6.656
6.654
5.584
5.557
4.170
4.155
4.151
4.142
4.138
4.131
4.124
4.120
4.107
3.328
3.169
3.111
3.099
2.216
1.598
1.239
1.221
1.203
-0.000
SB-IV-293
Product 7i'
9
8
7
6
5
4
3
2
1
0 ppm
1.052
2.037
2.167
1.009
1.057
1.080
1.092
5.013
1.011
1.009
1.004
1.026
1.000
1.021
4.173
1.031
1.011
1.009
3.068
3.057

SB-IV-293

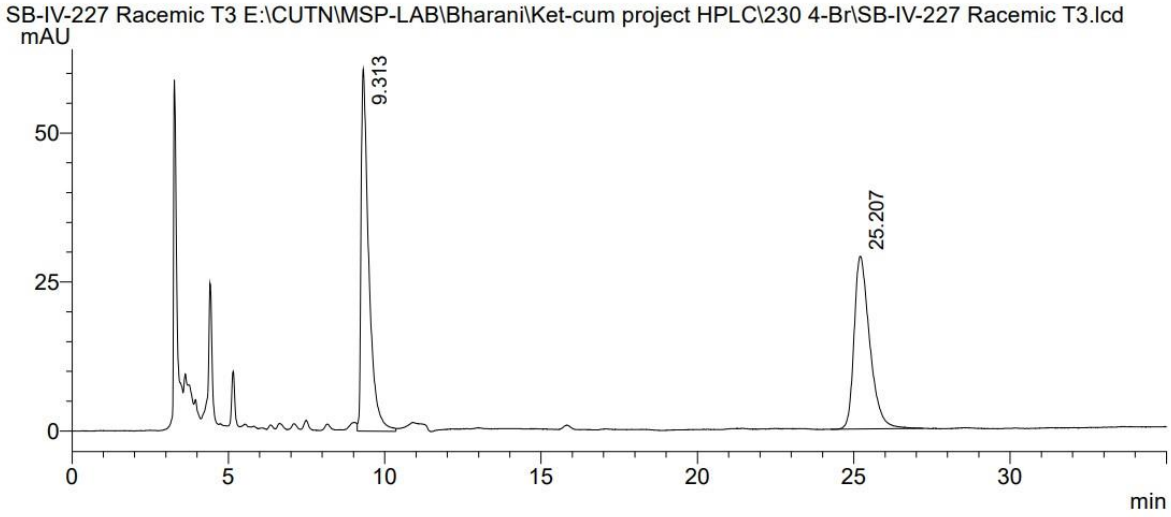
Product 7i'




176.06
173.05
172.20
168.60
152.78
142.82
141.64
136.52
132.08
130.61
130.33
128.38
128.28
128.08
127.96
127.02
126.75
125.72
124.21
124.15
123.71
123.54
122.01
119.22
111.34
108.62
71.20
66.17
65.38
60.81
60.50
50.78
36.98
31.94
24.76
13.51
0.02
SB-IV-293
Product 7i'
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


SB-IV-293
130.61
130.33
128.38
128.28
128.08
127.96
126.75
125.72
123.54
122.01
119.22
111.35
108.62
77.24
65.38
60.81
60.50
50.78
36.98
31.95
24.77
13.51
Product 7i'
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

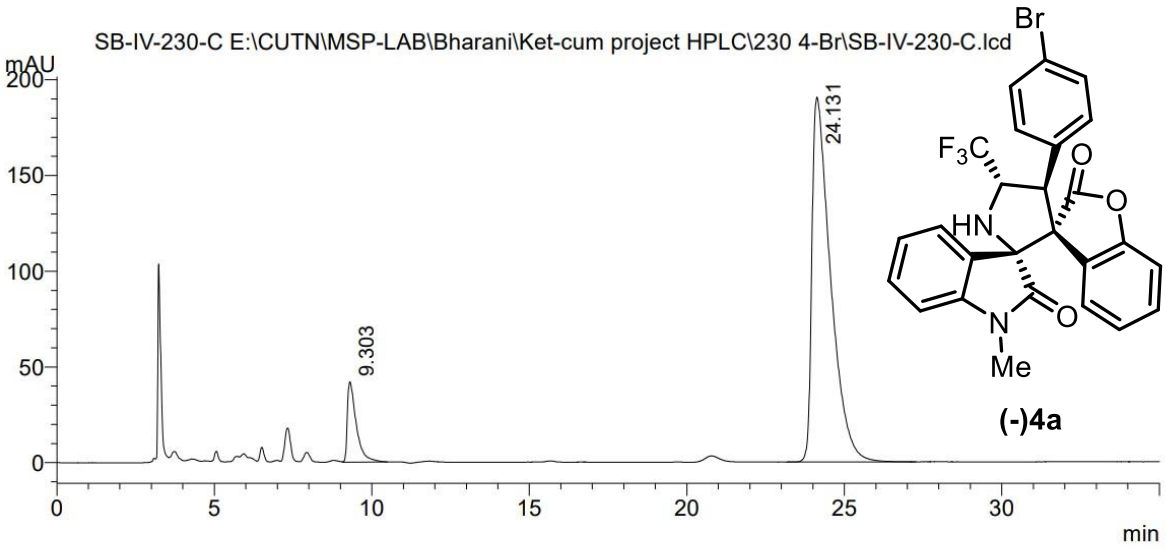
HPLC of racemic **4a**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.313	1040619	60705	50.896
2	25.207	1003985	28972	49.104
Total		2044604	89677	100.000

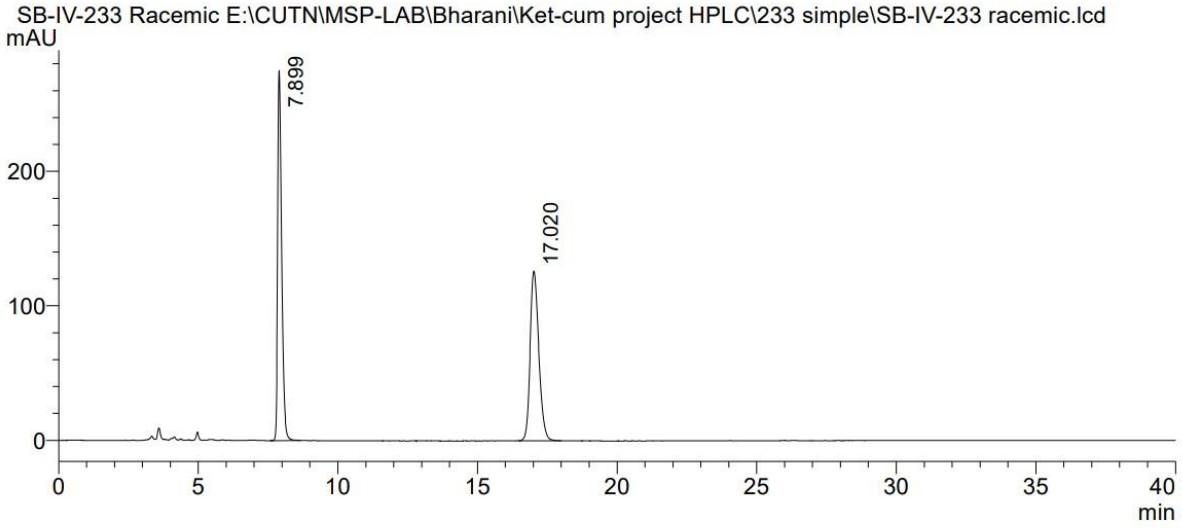
HPLC of chiral **4a: 90:10 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.303	827065	42023	9.521
2	24.131	7860079	190603	90.479
Total		8687144	232626	100.000

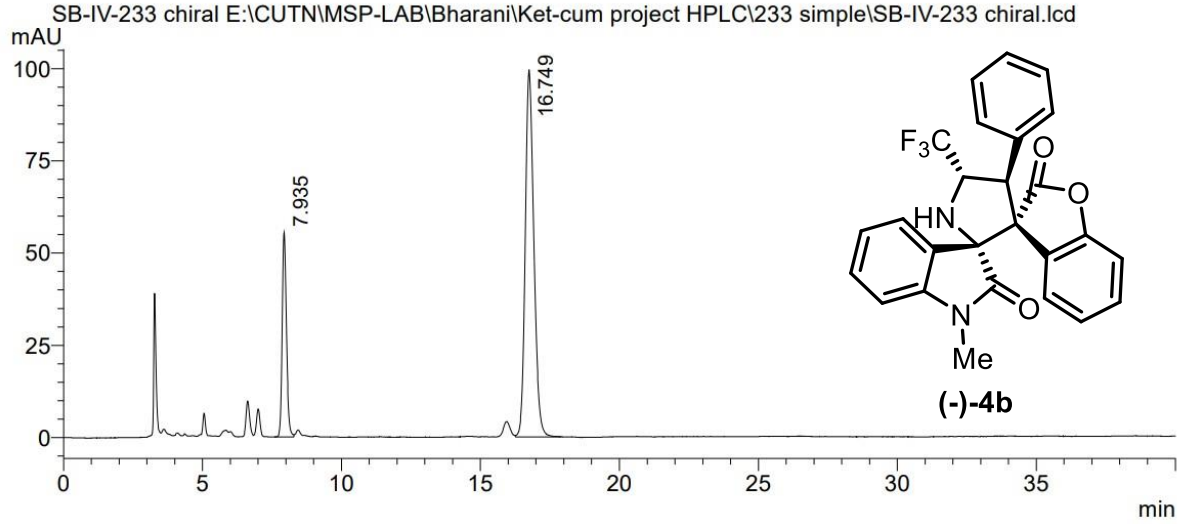
HPLC of racemic **4b**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	7.899	2725957	274751	50.070
2	17.020	2718380	126084	49.930
Total		5444336	400835	100.000

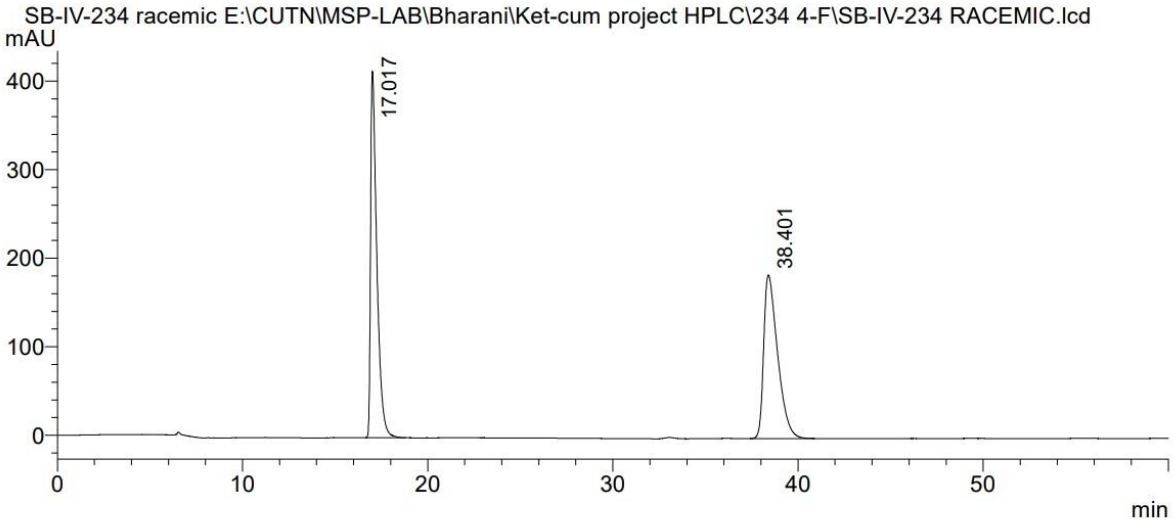
HPLC of chiral **4b: 79:21 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	7.935	581635	55447	21.391
2	16.749	2137435	99503	78.609
Total		2719071	154950	100.000

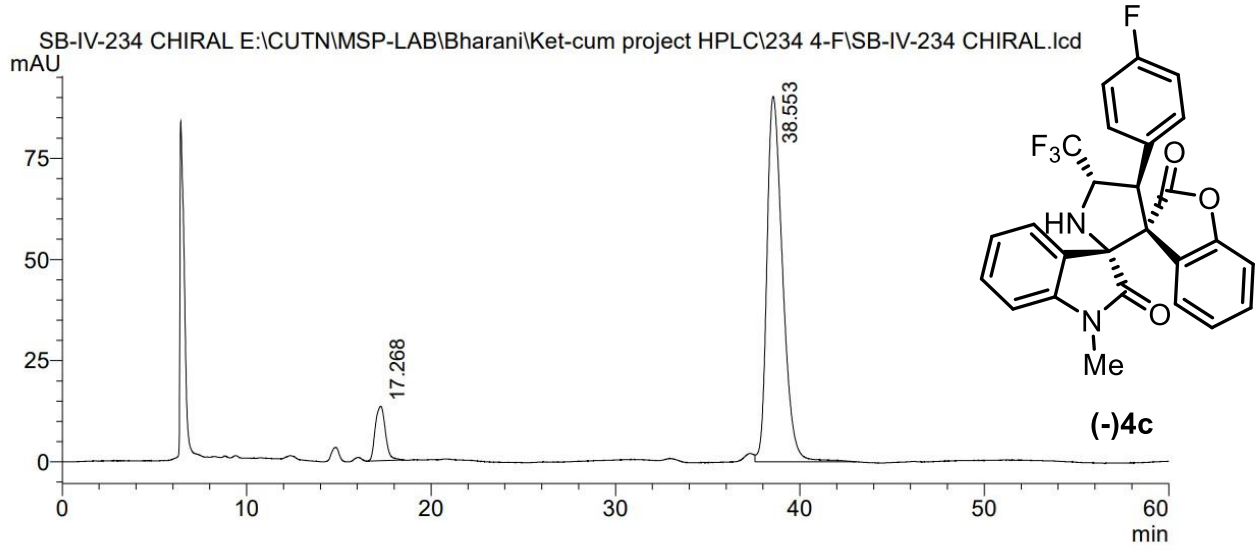
HPLC of racemic **4c**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	17.017	9704574	413915	50.206
2	38.401	9625025	184707	49.794
Total		19329598	598622	100.000

HPLC of chiral **4c: 91:9 *er***

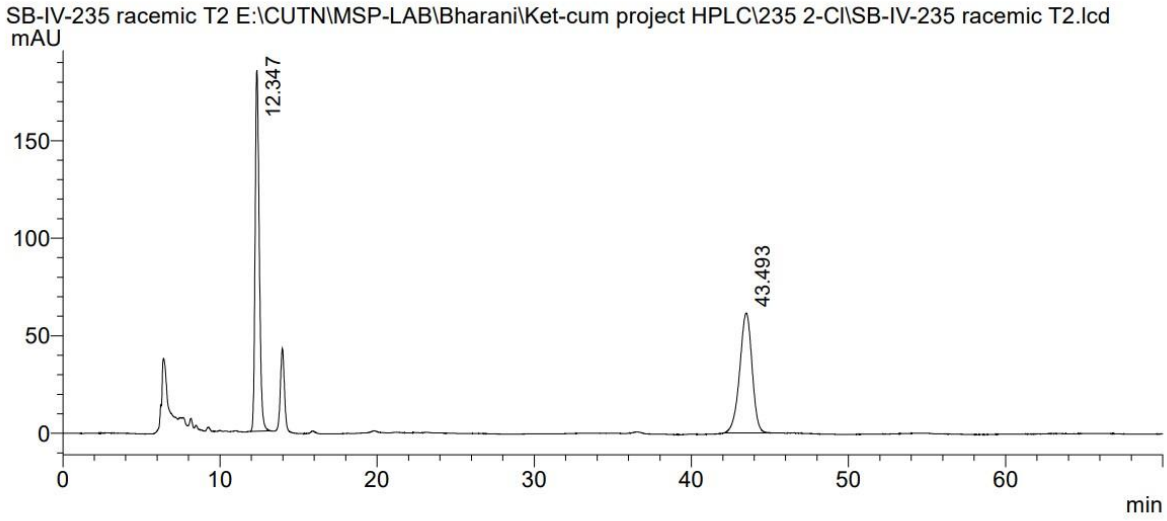


(-)4c

PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	17.268	513440	13441	8.771
2	38.553	5340192	90289	91.229
Total		5853632	103731	100.000

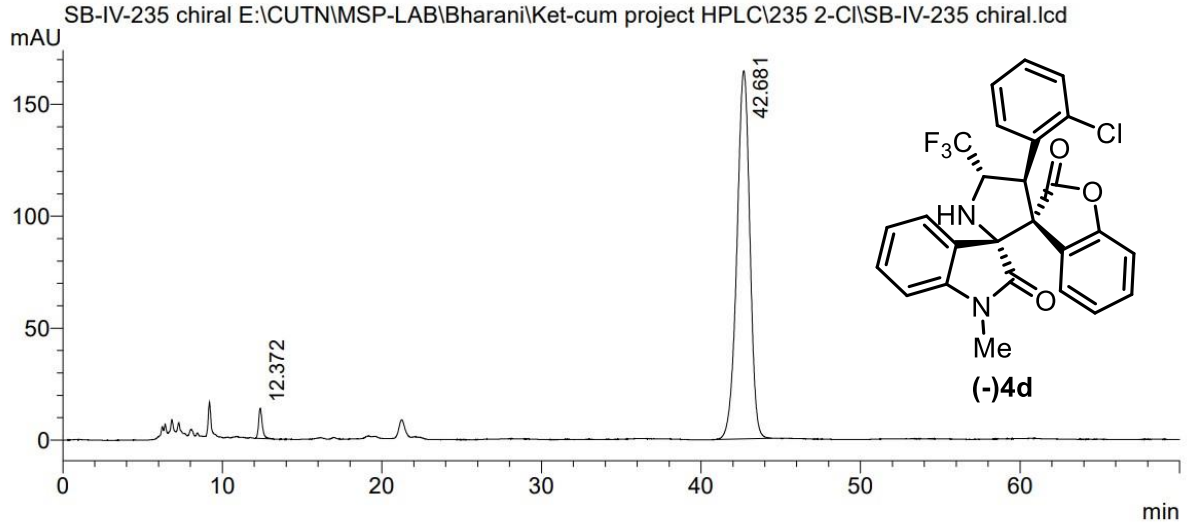
HPLC of racemic **4d**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.347	3403021	184708	50.275
2	43.493	3365733	61497	49.725
Total		6768753	246204	100.000

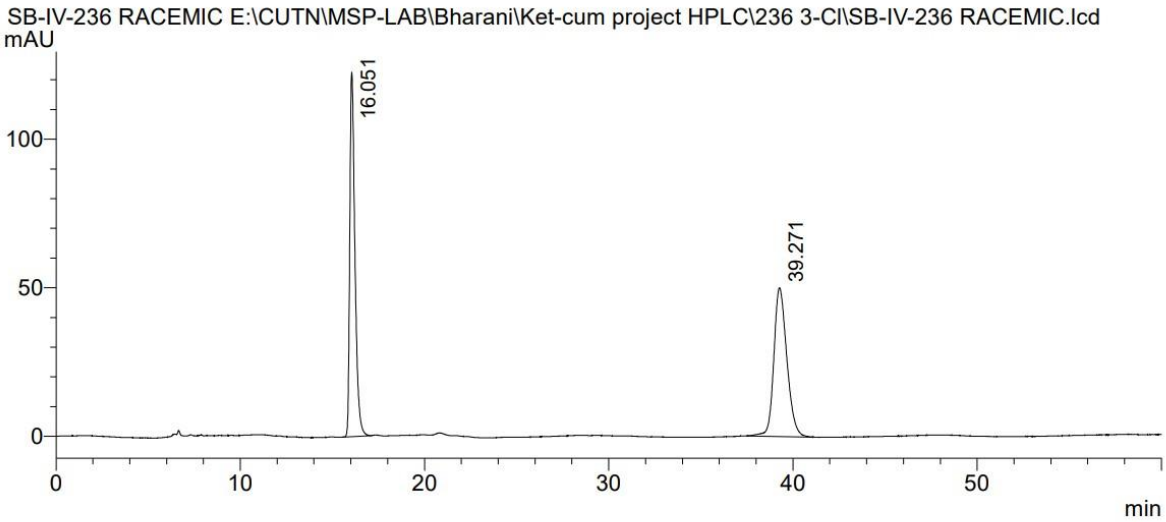
HPLC of chiral **4d: 98:2** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.372	213326	13440	2.252
2	42.681	9259419	164437	97.748
Total		9472745	177876	100.000

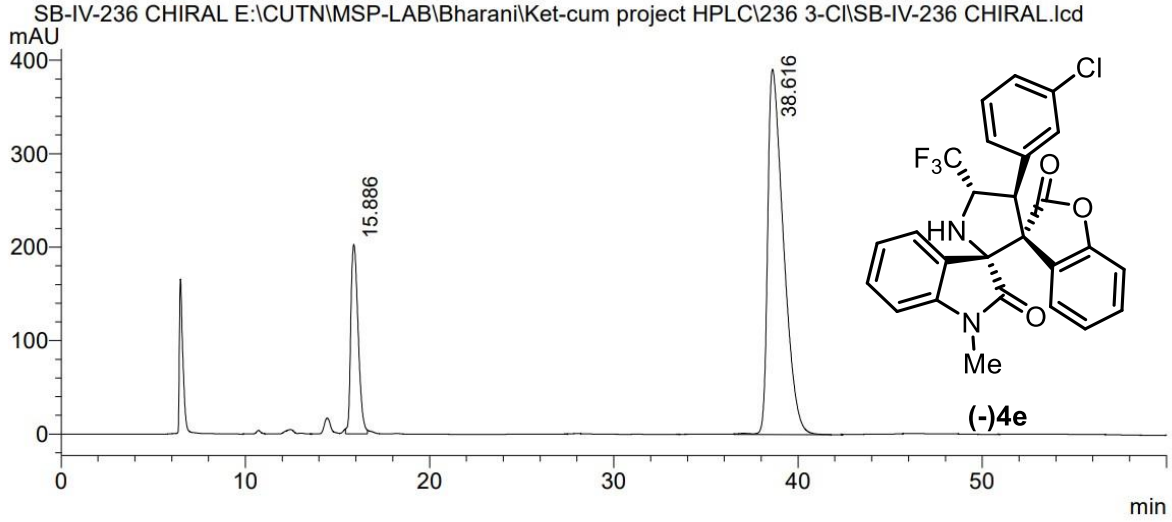
HPLC of racemic **4e**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	16.051	2385183	122673	49.254
2	39.271	2457481	50023	50.746
Total		4842664	172696	100.000

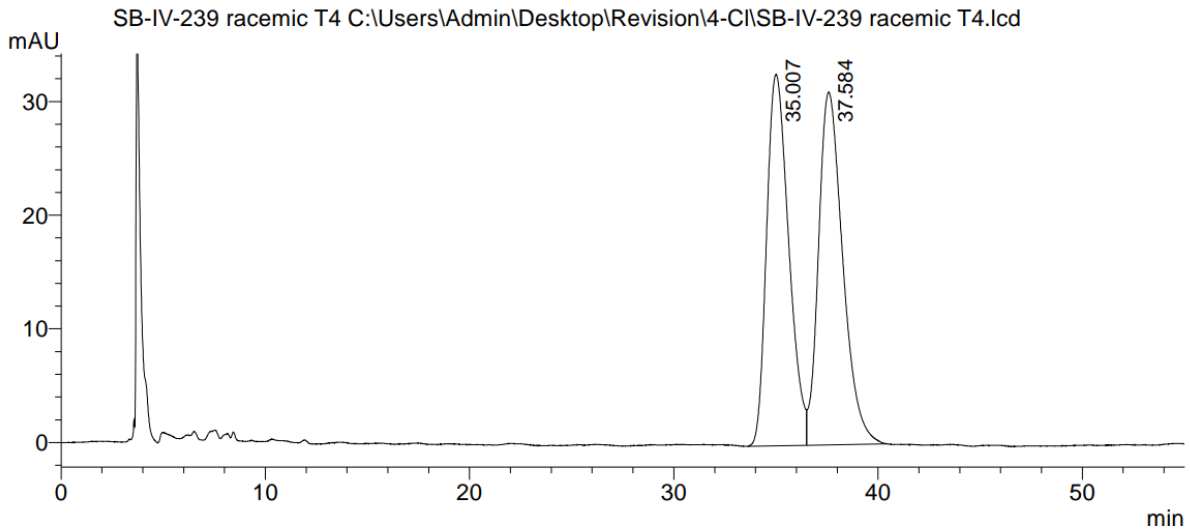
HPLC of chiral **4e: 80:20** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	15.886	5659671	202788	19.574
2	38.616	23254784	390852	80.426
Total		28914456	593640	100.000

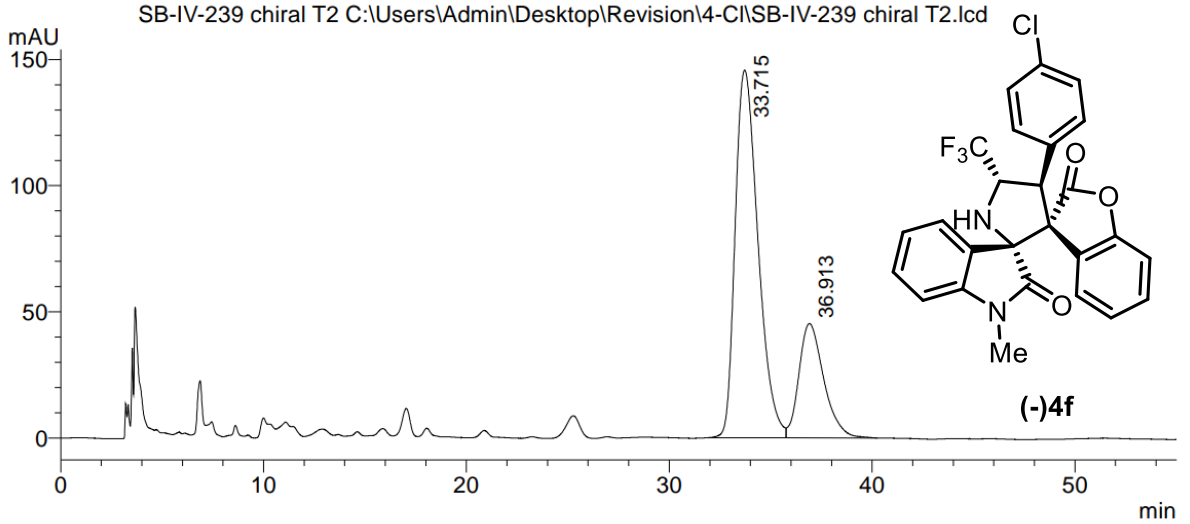
HPLC of racemic **4f**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	35.007	2459039	32678	48.927
2	37.584	2566887	31036	51.073
Total		5025927	63714	100.000

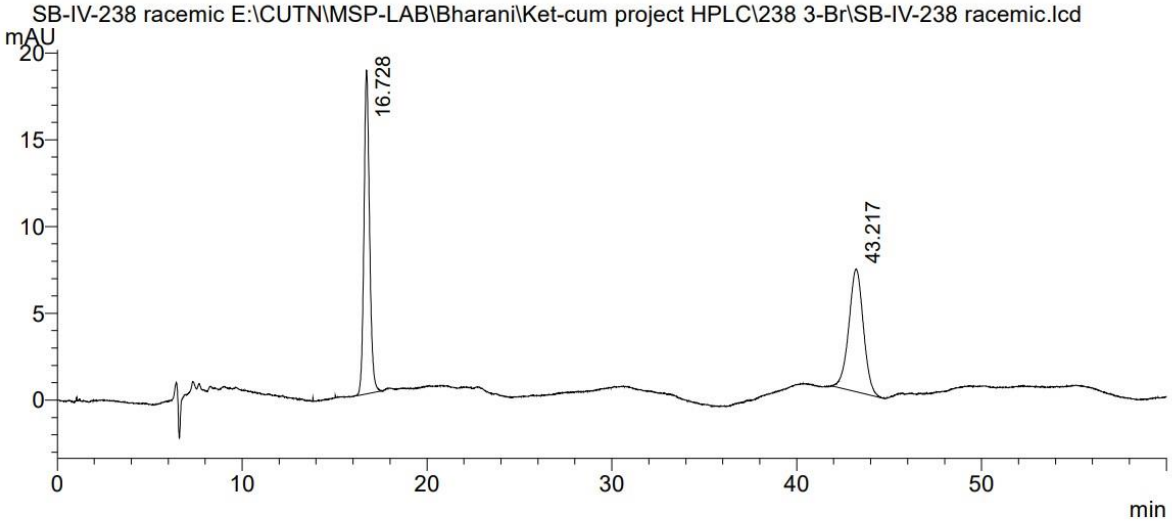
HPLC of chiral **4f: 75:25 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	33.715	11420540	145738	74.727
2	36.913	3862569	45300	25.273
Total		15283109	191038	100.000

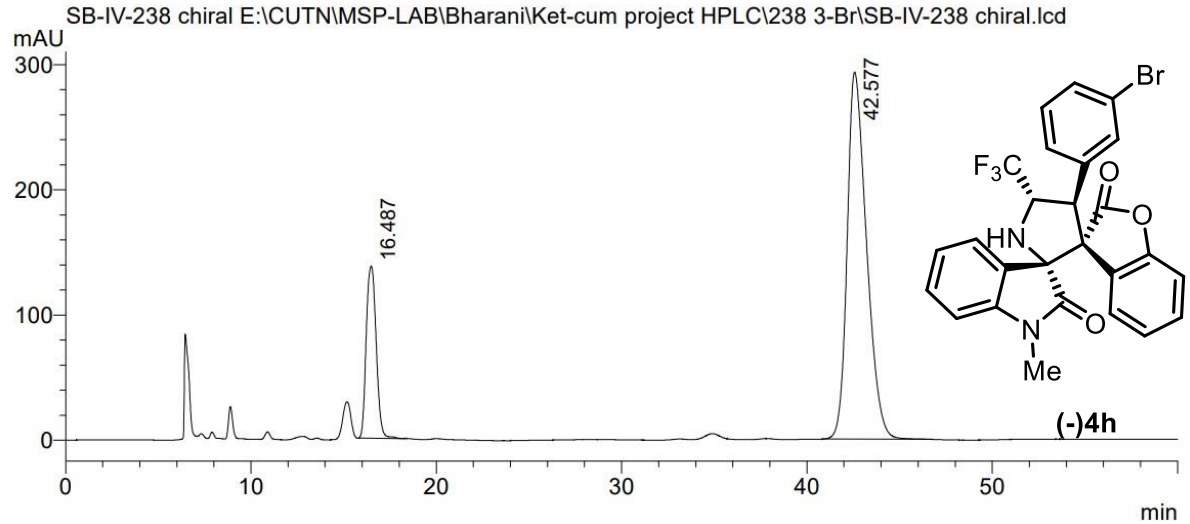
HPLC of racemic **4h**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	16.728	391074	18649	50.227
2	43.217	387542	7079	49.773
Total		778617	25728	100.000

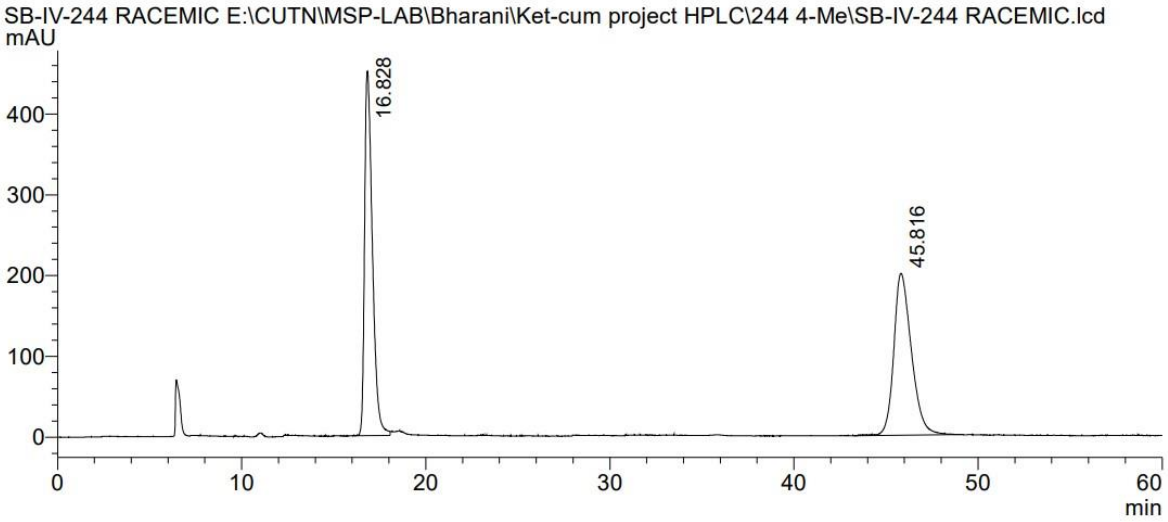
HPLC of chiral **4h: 81:19** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	16.487	5123536	137601	19.397
2	42.577	21290139	293174	80.603
Total		26413675	430775	100.000

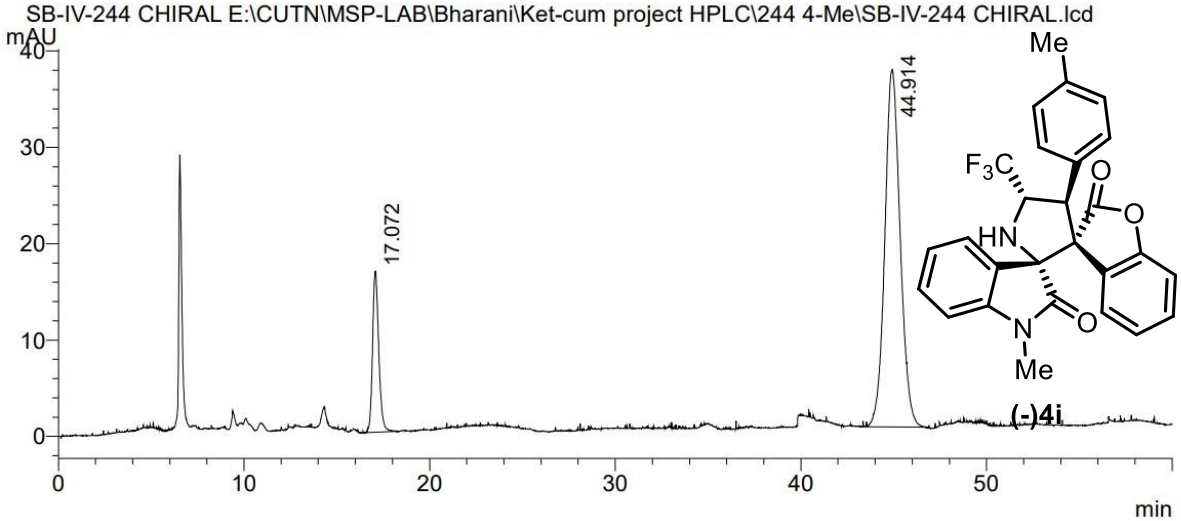
HPLC of racemic **4i**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	16.828	13345206	451227	49.930
2	45.816	13382781	200279	50.070
Total		26727987	651506	100.000

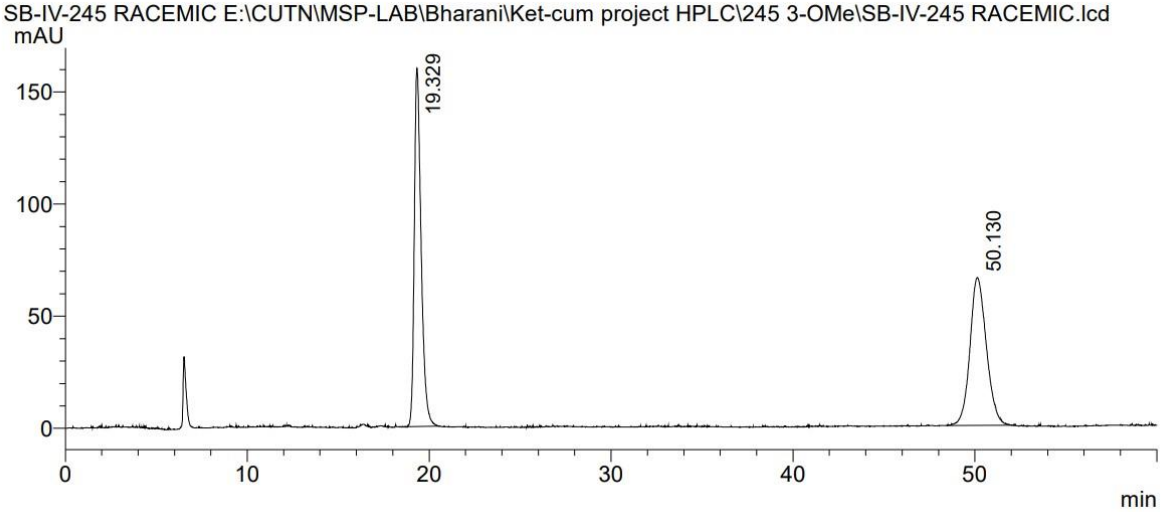
HPLC of chiral **4i: 85:15** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	17.072	386063	16728	15.336
2	44.914	2131256	37082	84.664
Total		2517318	53810	100.000

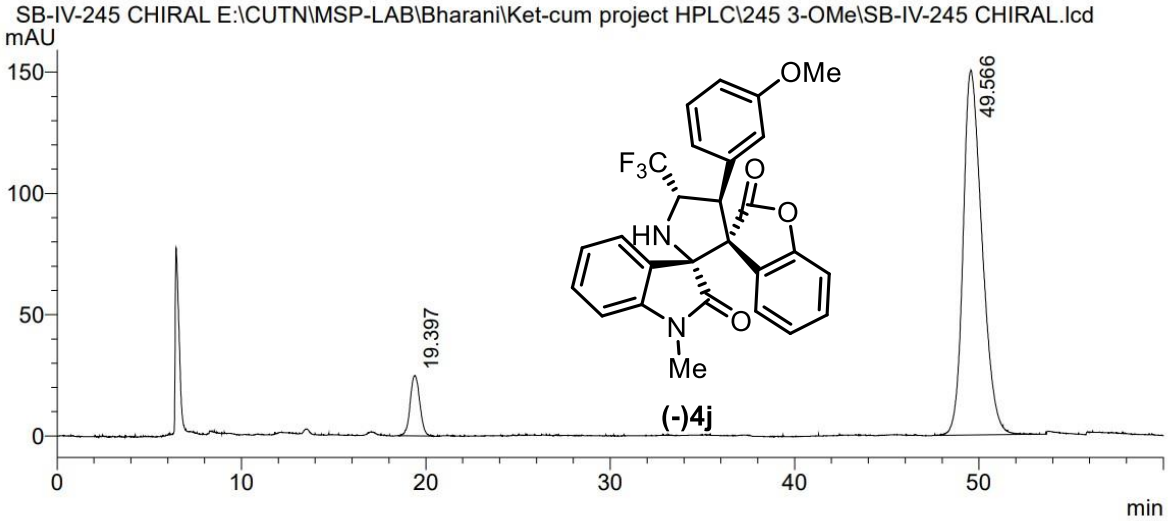
HPLC of racemic **4j**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	19.329	4167604	159829	50.085
2	50.130	4153491	65855	49.915
Total		8321096	225684	100.000

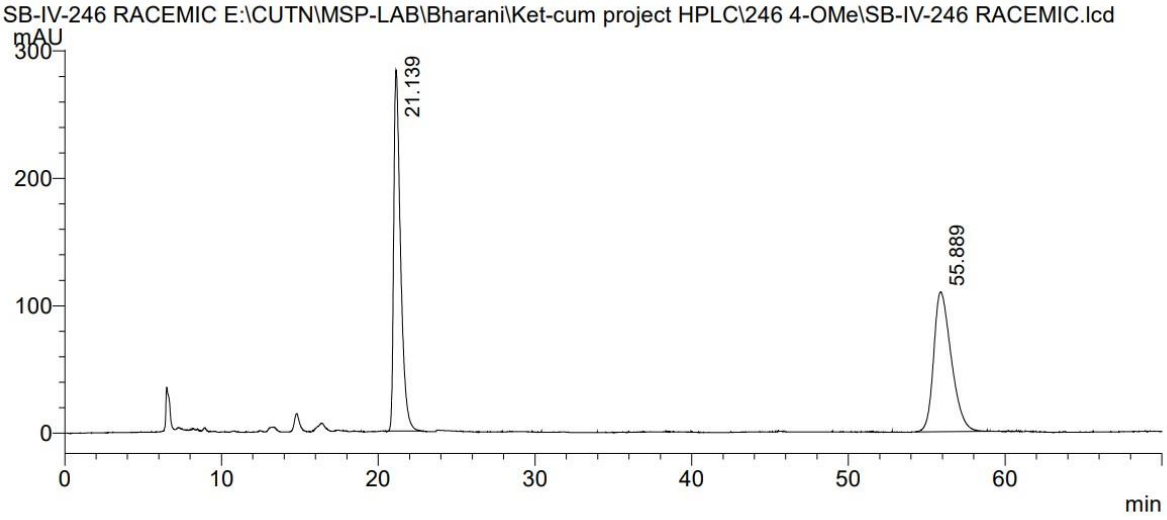
HPLC of chiral **4j: 92:8 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	19.397	899758	24849	7.727
2	49.566	10744354	150370	92.273
Total		11644112	175219	100.000

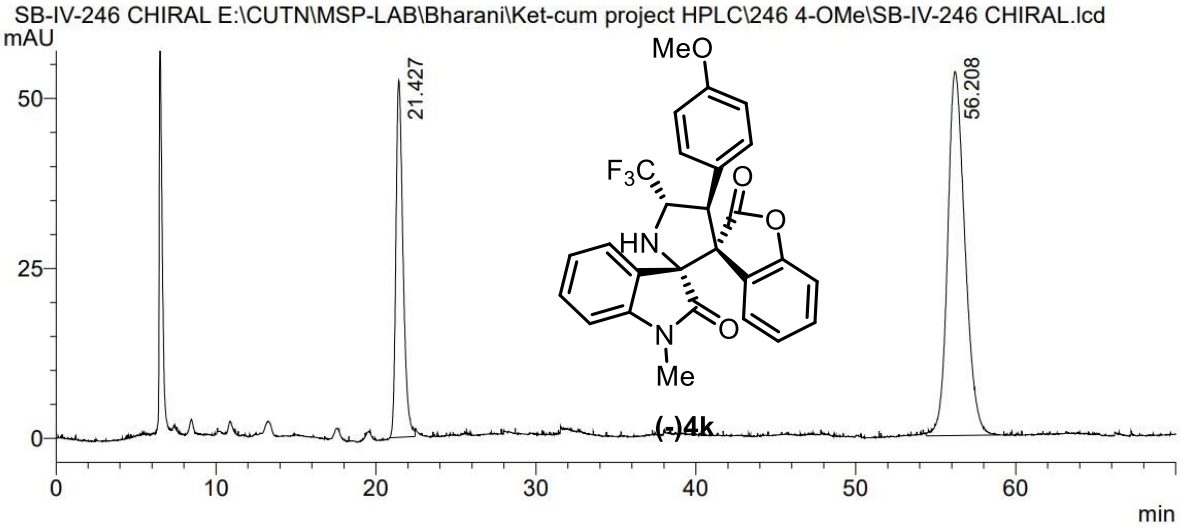
HPLC of racemic **4k**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	21.139	8575165	283449	50.141
2	55.889	8527082	109587	49.859
Total		17102247	393036	100.000

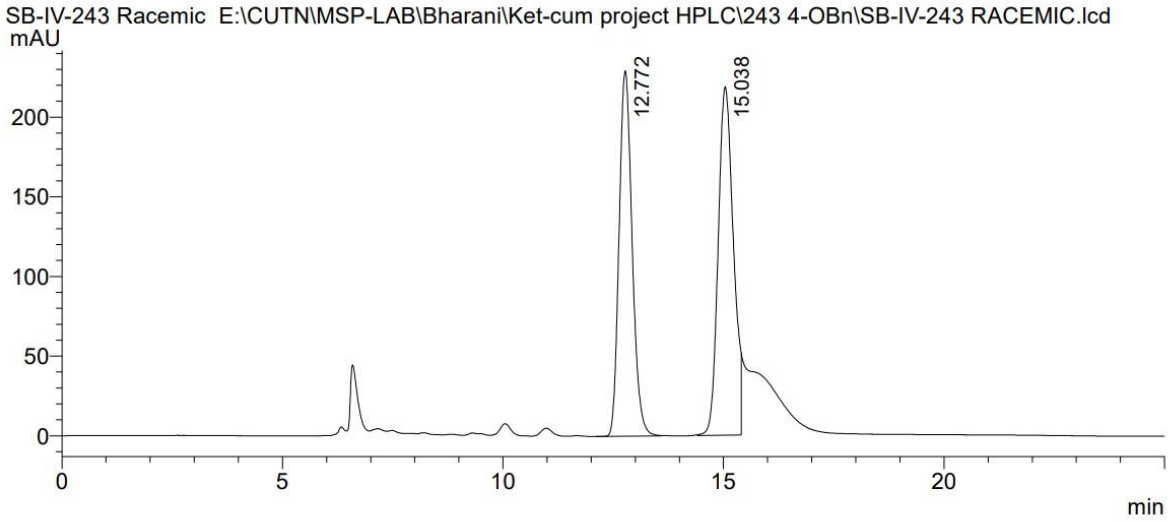
HPLC of chiral **4k: 71:29 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	21.427	1620417	52488	28.704
2	56.208	4024792	53554	71.296
Total		5645208	106042	100.000

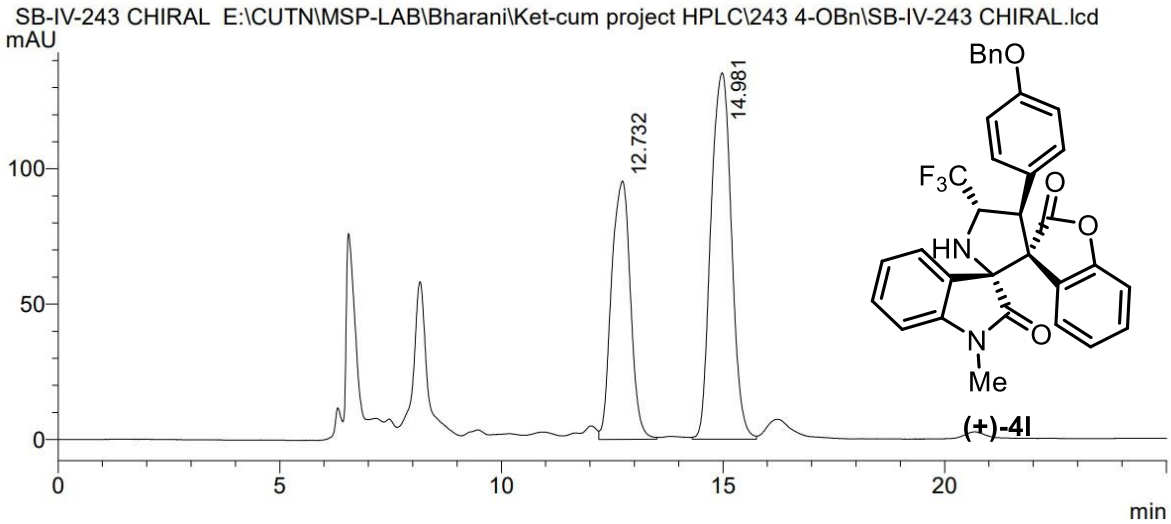
HPLC of racemic **4l**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.772	4706090	229232	47.291
2	15.038	5245276	218743	52.709
Total		9951366	447975	100.000

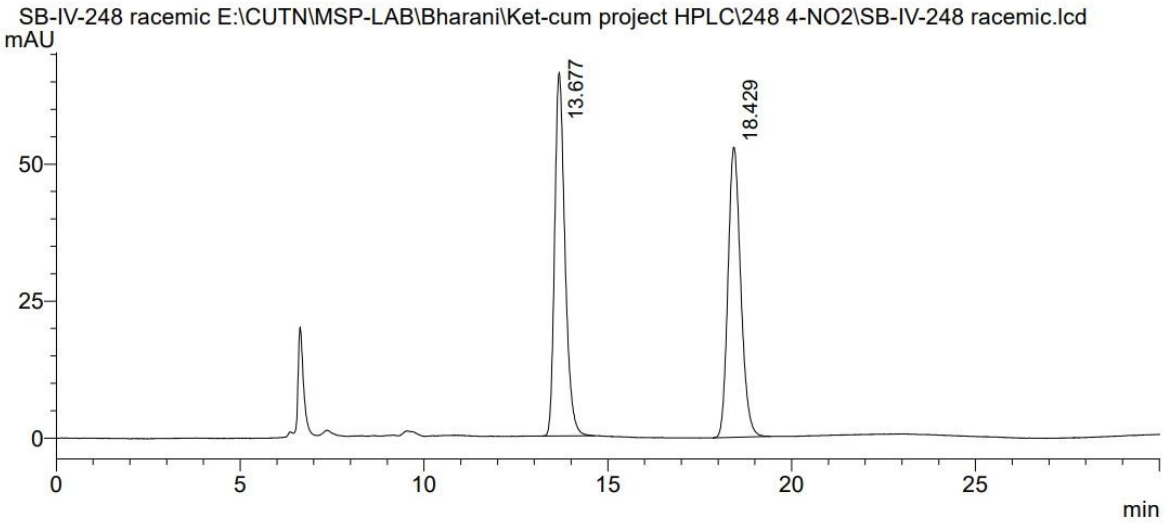
HPLC of chiral **4l: 61:39** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.732	2844209	95424	39.459
2	14.981	4363837	135304	60.541
Total		7208046	230728	100.000

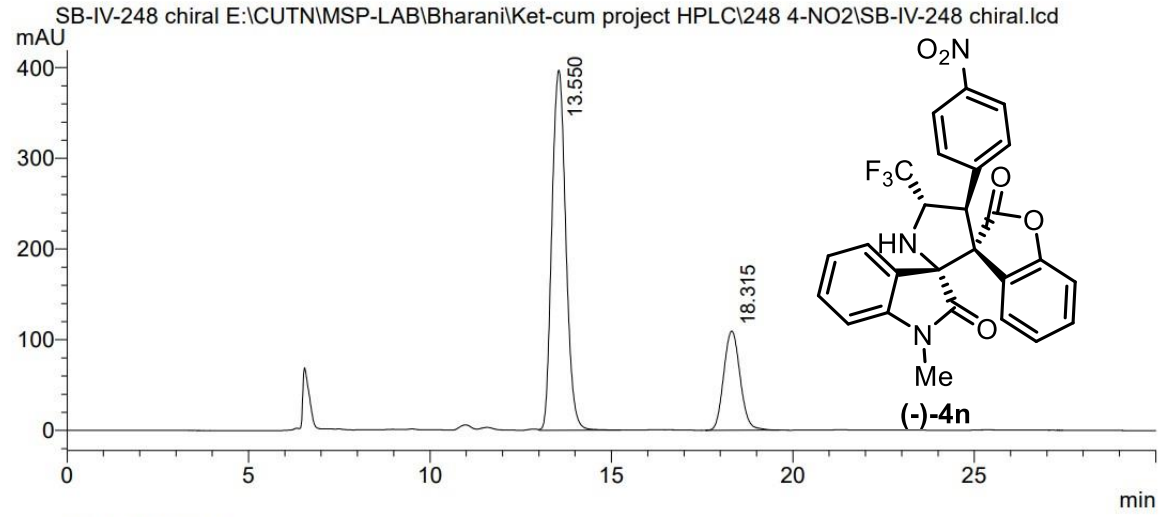
HPLC of racemic **4n**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	13.677	1292196	66279	50.267
2	18.429	1278460	52979	49.733
Total		2570657	119259	100.000

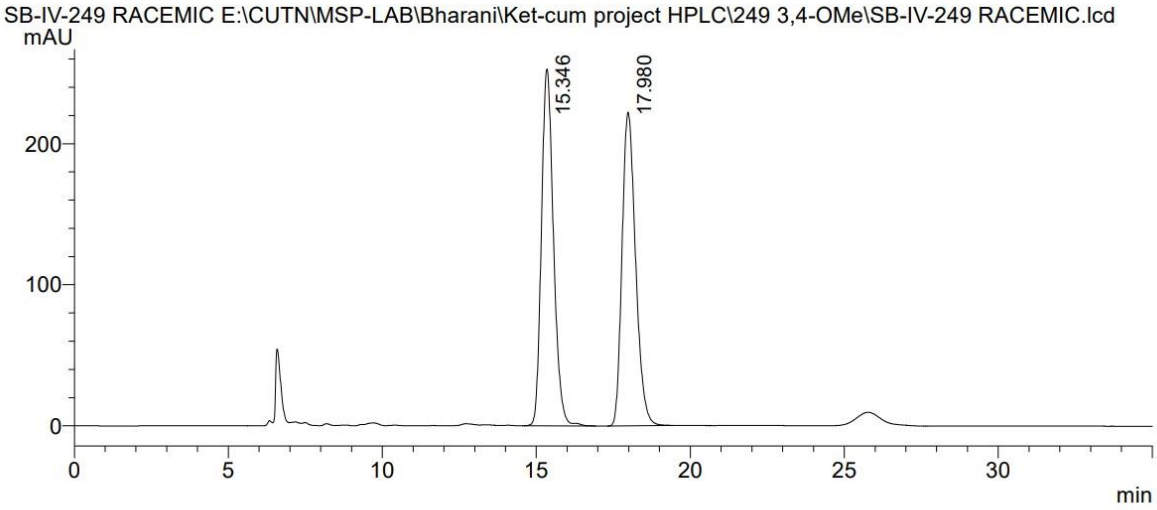
HPLC of chiral **4n: 76:24** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	13.550	10586700	396817	75.455
2	18.315	3443842	109402	24.545
Total		14030542	506219	100.000

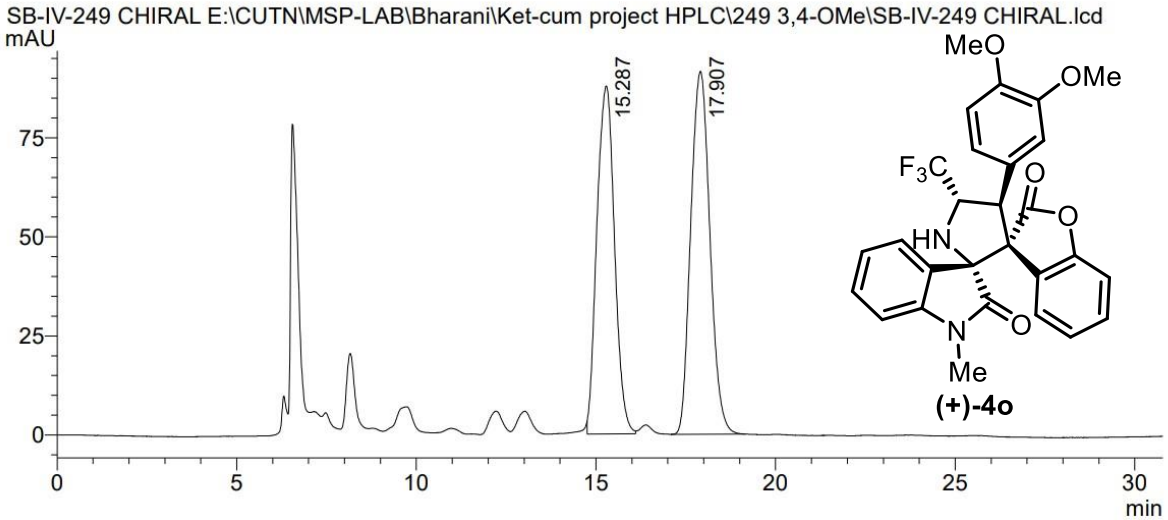
HPLC of racemic **4o**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	15.346	6892213	252888	50.349
2	17.980	6796774	222229	49.651
Total		13688987	475117	100.000

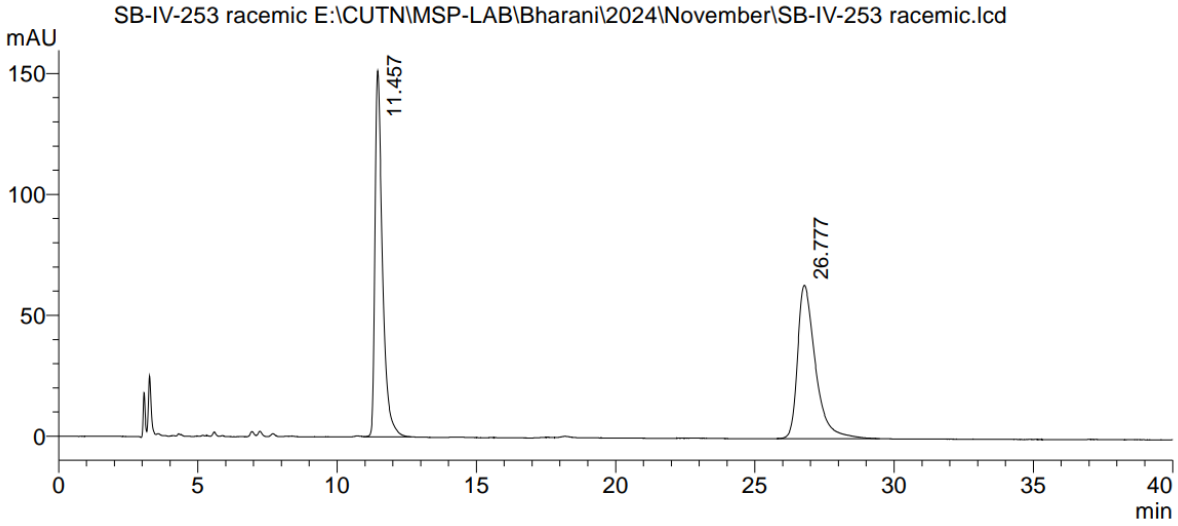
HPLC of chiral **4o: 53:47** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	15.287	2998244	87802	46.933
2	17.907	3390091	91546	53.067
Total		6388335	179348	100.000

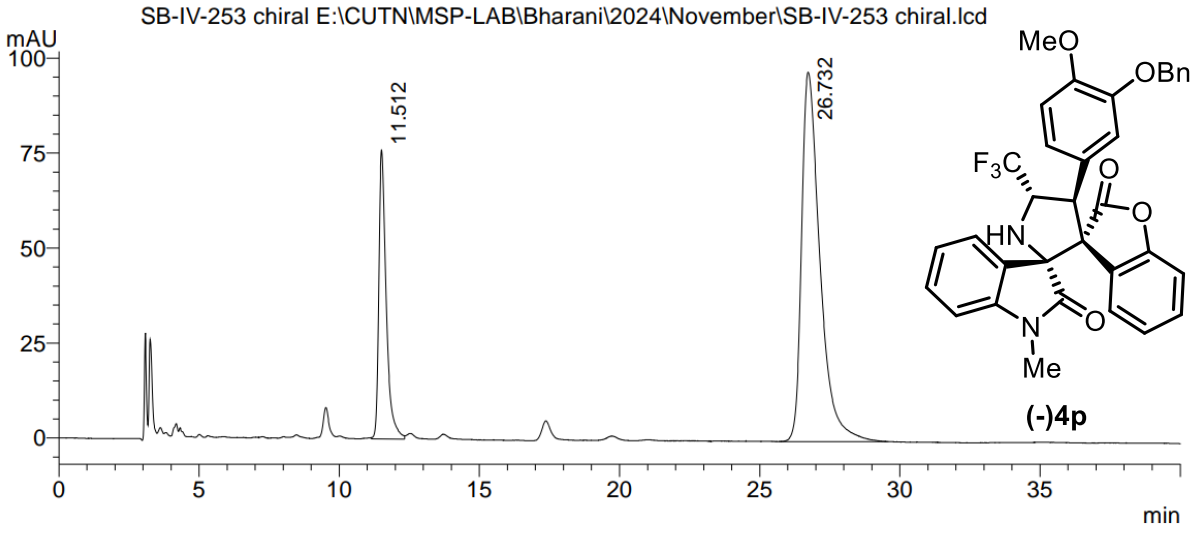
HPLC of racemic **4p**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	11.457	2820693	151375	50.009
2	26.777	2819685	63402	49.991
Total		5640378	214776	100.000

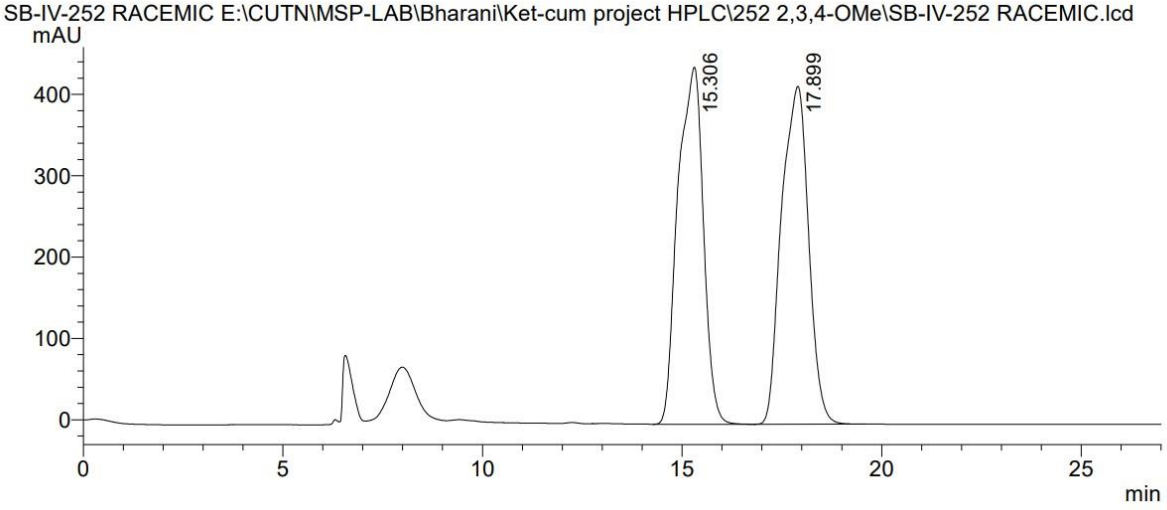
HPLC of chiral **4p: 76:24** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	11.512	1399730	76007	23.997
2	26.732	4433172	97227	76.003
Total		5832902	173234	100.000

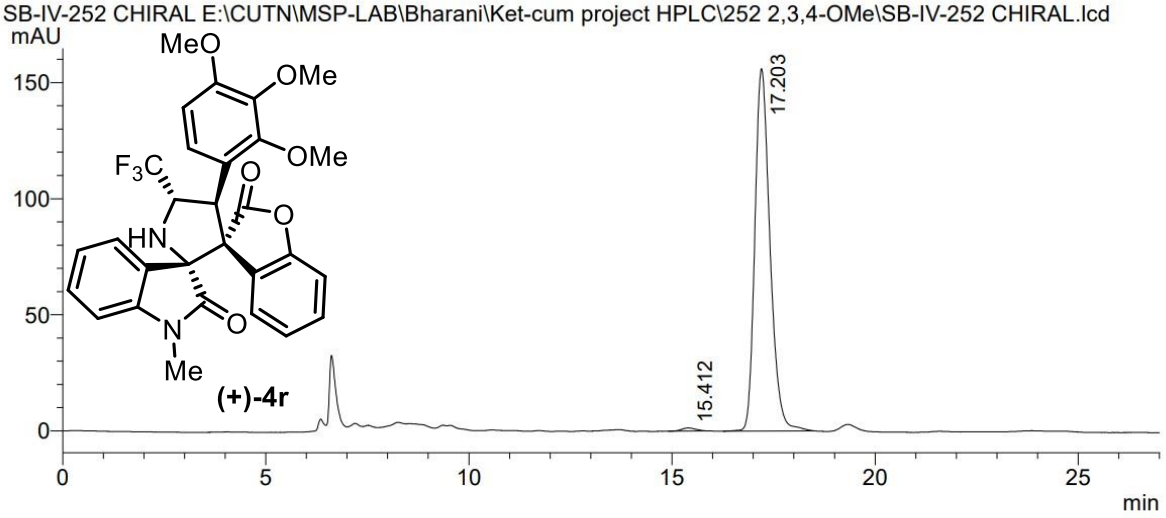
HPLC of racemic **4r**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	15.306	19473109	438847	49.891
2	17.899	19558362	415320	50.109
Total		39031472	854167	100.000

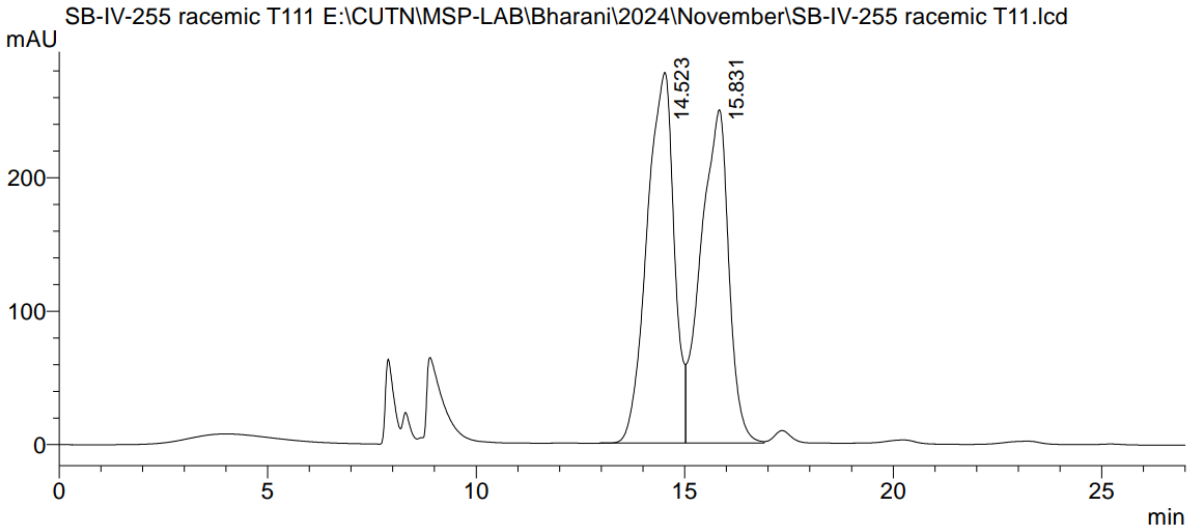
HPLC of chiral **4r: 99:1 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	15.412	34832	1387	0.855
2	17.203	4040995	156016	99.145
Total		4075826	157403	100.000

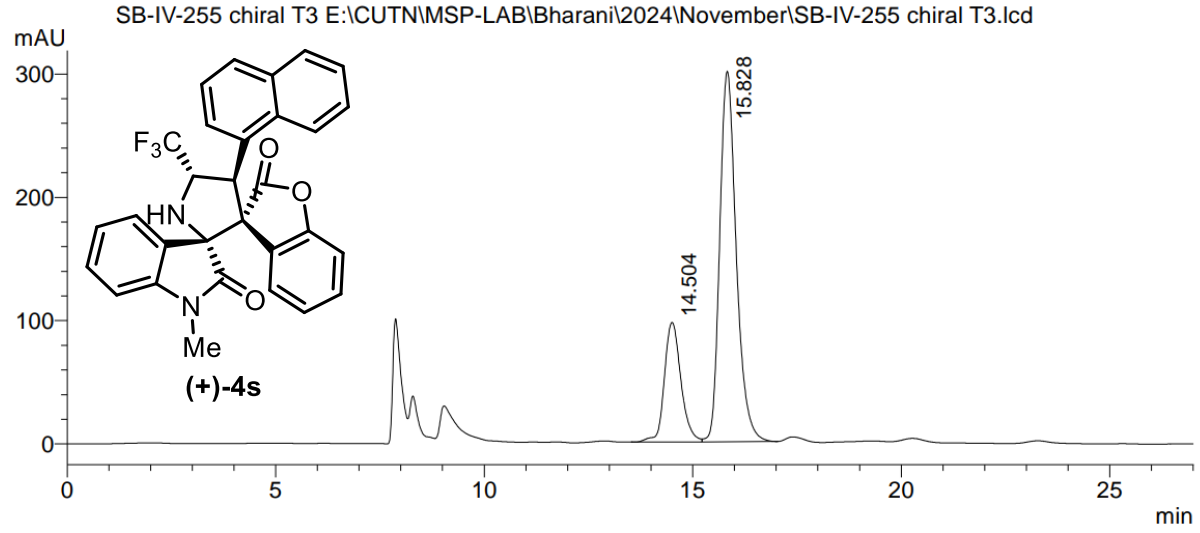
HPLC of racemic **4s**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	14.523	12526614	277578	51.793
2	15.831	11659363	249694	48.207
Total		24185977	527273	100.000

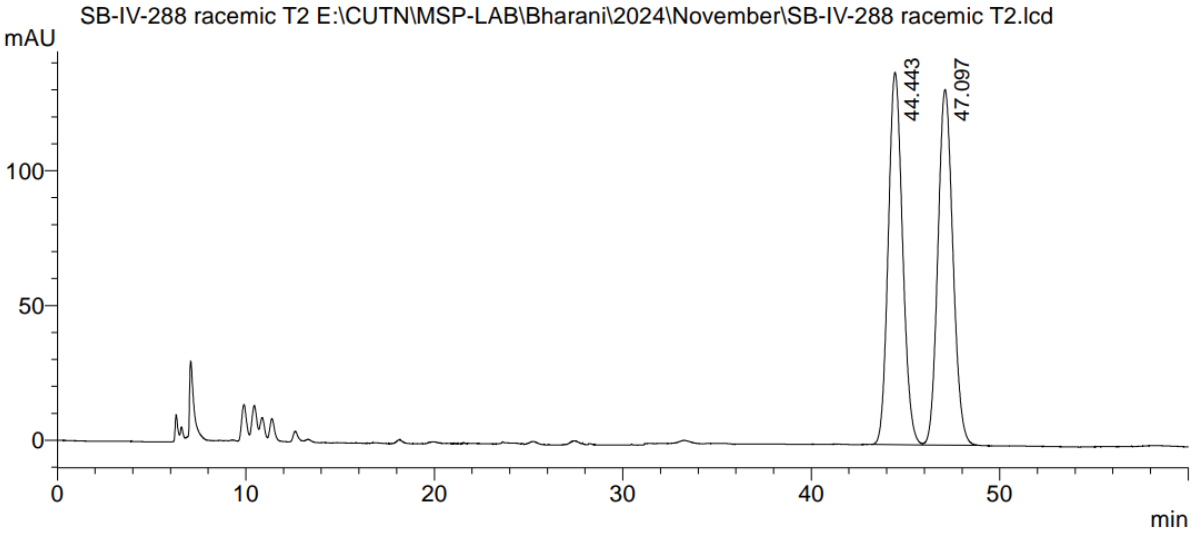
HPLC of chiral **4s: 76:24** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	14.504	2683554	97042	24.470
2	15.828	8282976	300335	75.530
Total		10966531	397376	100.000

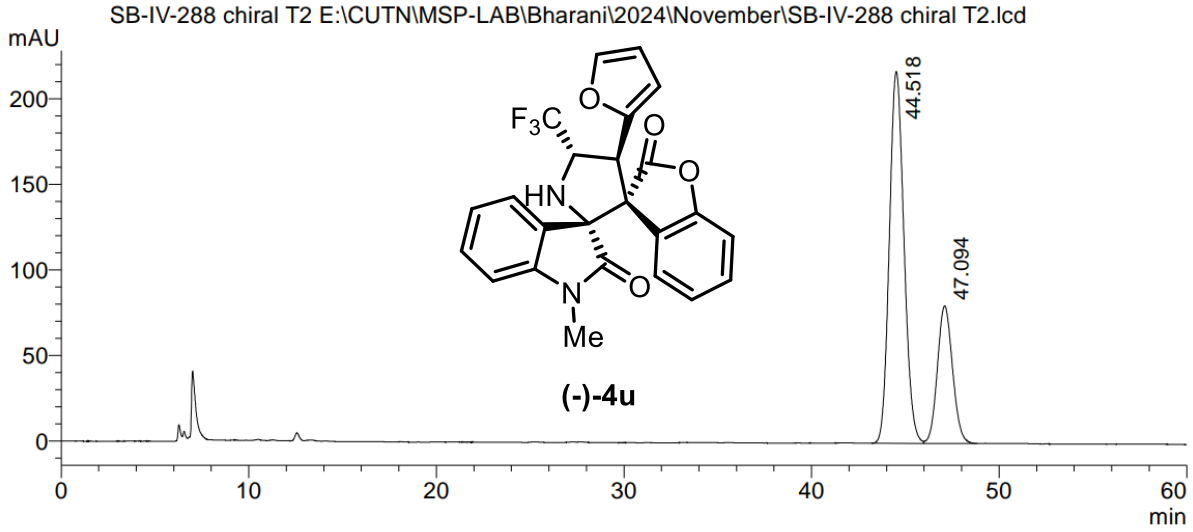
HPLC of racemic **4u**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	44.443	7294348	138098	49.951
2	47.097	7308539	131907	50.049
Total		14602887	270005	100.000

HPLC of chiral **4u: 72:28** ***er***

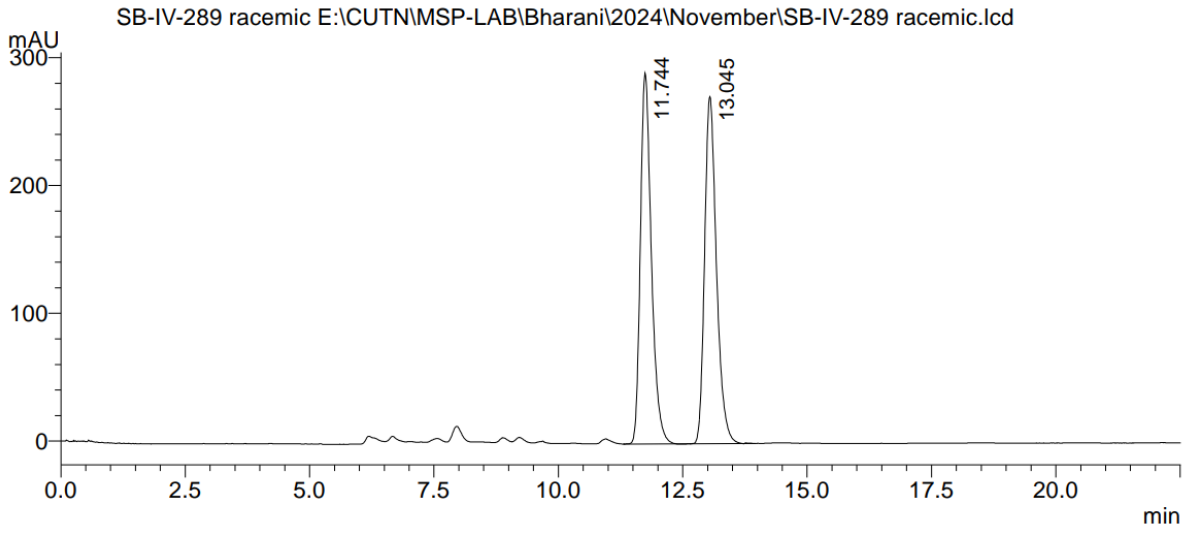


(-)-4u

PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	44.518	11770684	217245	72.293
2	47.094	4511292	80365	27.707
Total		16281976	297611	100.000

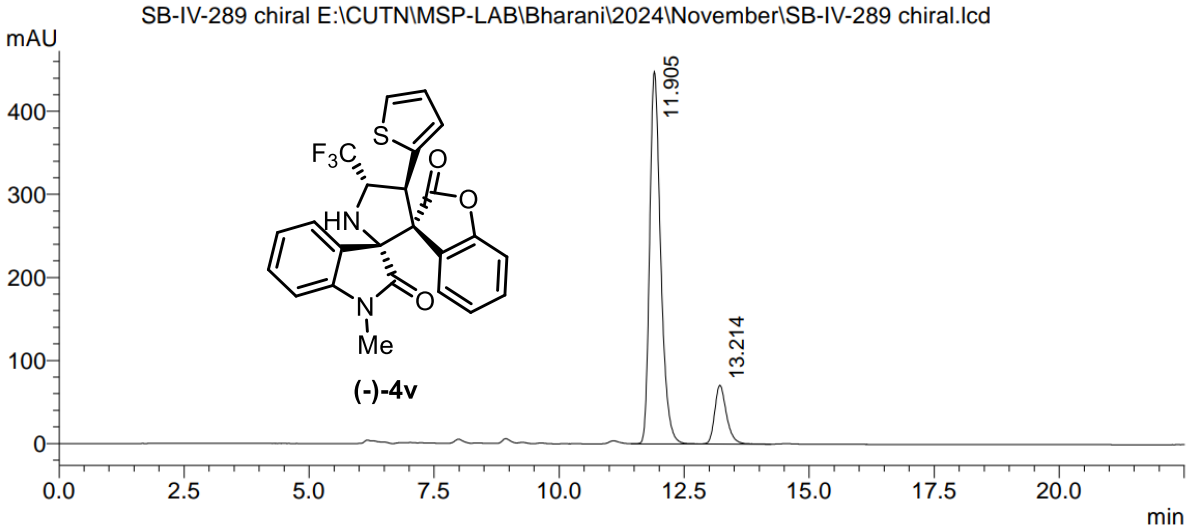
HPLC of racemic **4v**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	11.744	4456177	290225	49.734
2	13.045	4503927	271704	50.266
Total		8960103	561928	100.000

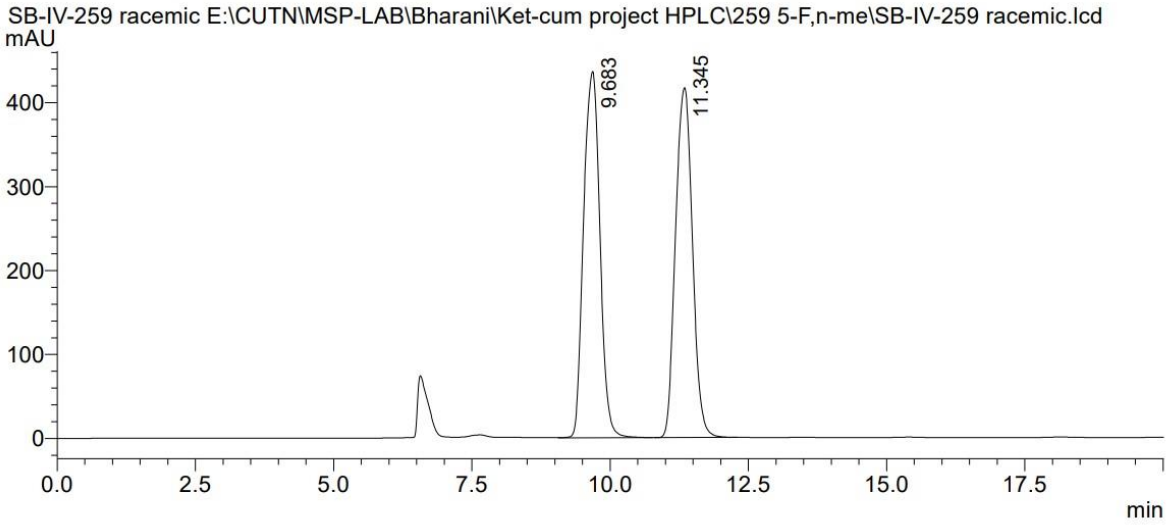
HPLC of chiral **4v: 86:14 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	11.905	6848295	448162	85.480
2	13.214	1163323	70851	14.520
Total		8011618	519013	100.000

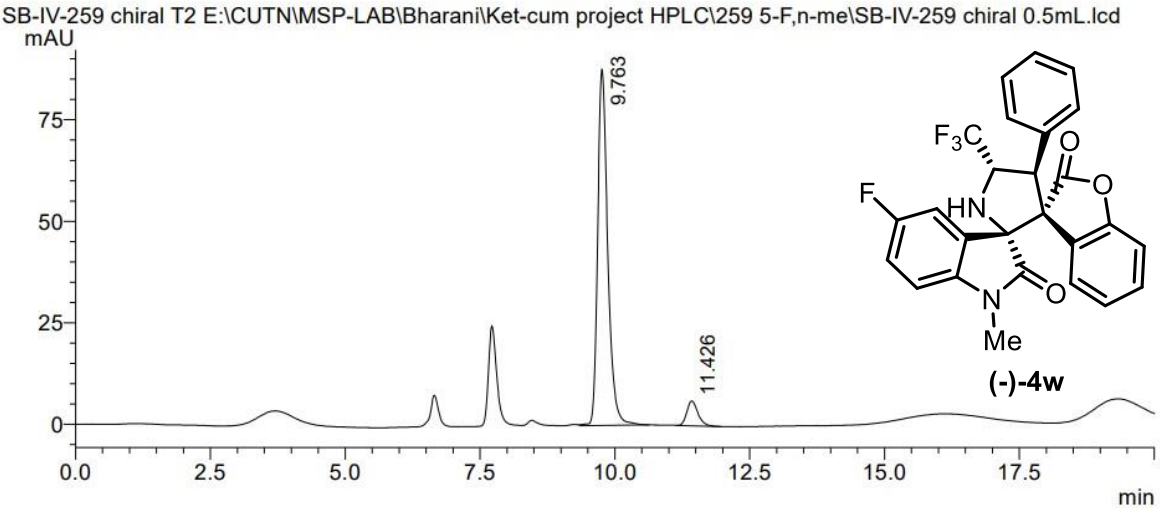
HPLC of racemic **4w**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.683	8976163	436291	50.272
2	11.345	8879191	416714	49.728
Total		17855354	853005	100.000

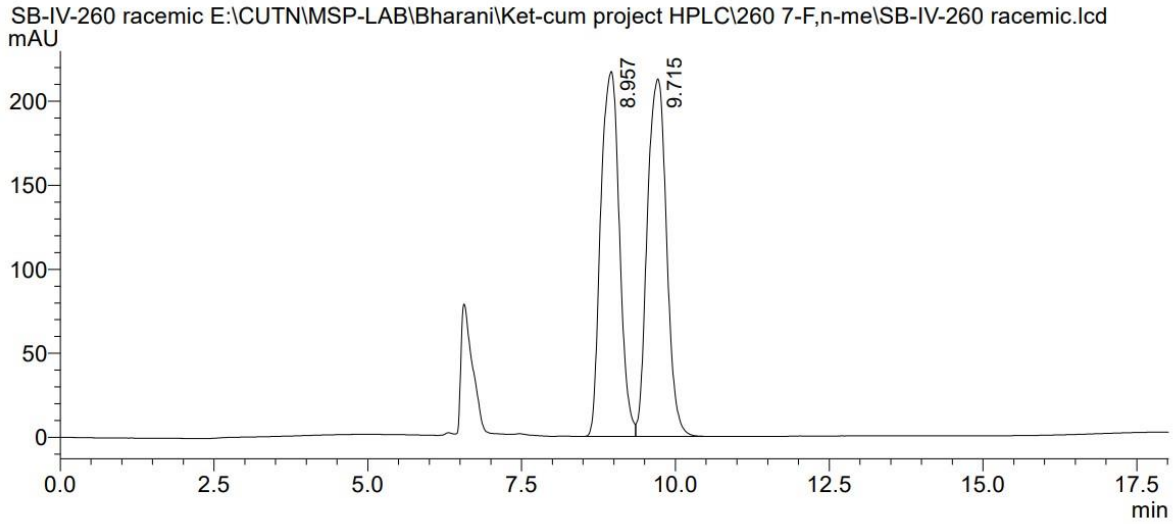
HPLC of chiral **4w: 93:7 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.763	1138579	87600	92.878
2	11.426	87306	6128	7.122
Total		1225885	93728	100.000

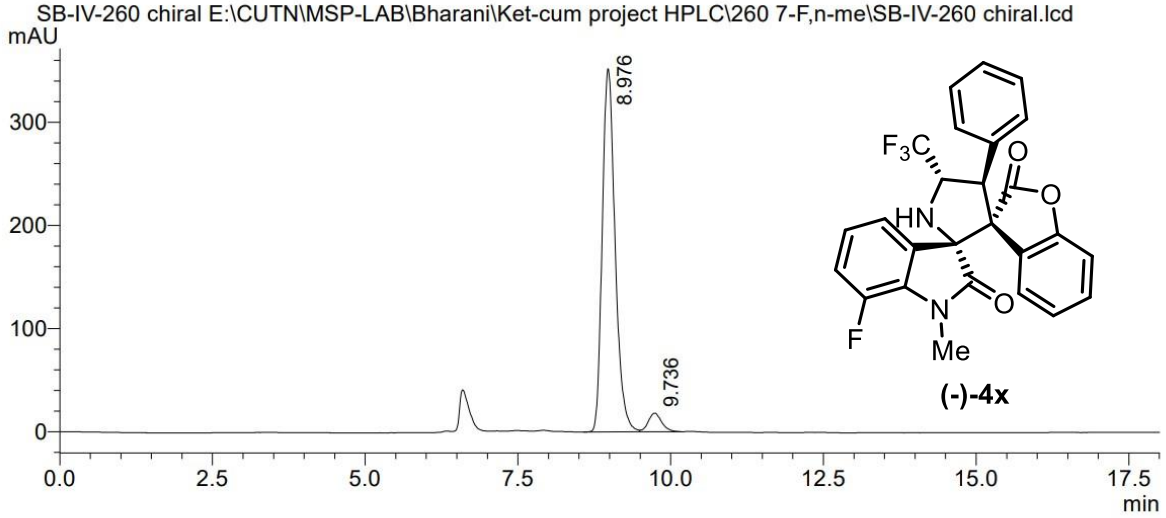
HPLC of racemic **4x**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.957	4588388	217187	49.771
2	9.715	4630534	212867	50.229
Total		9218922	430053	100.000

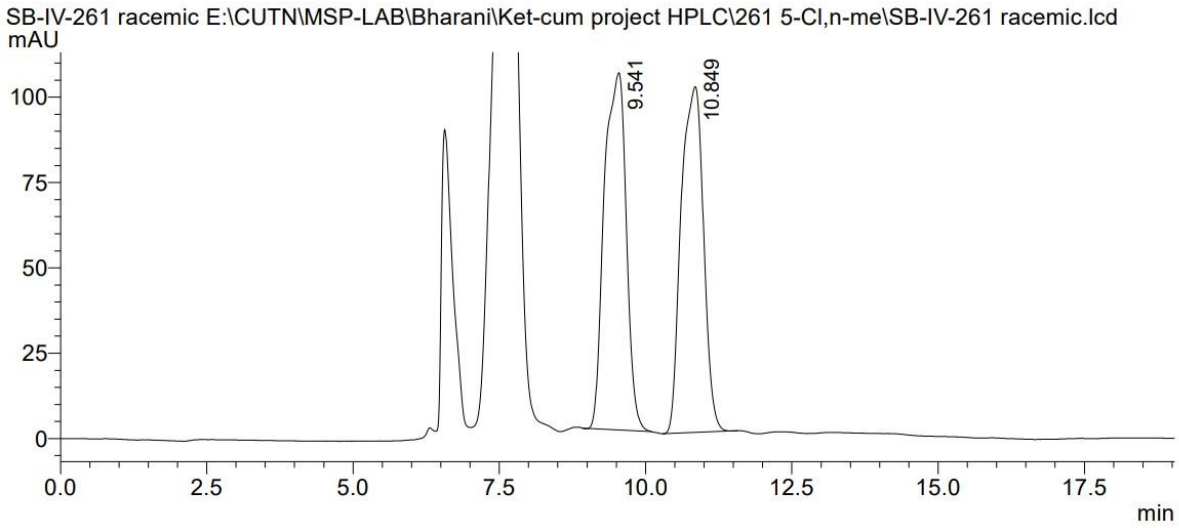
HPLC of chiral **4x: 95:5** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.976	5132224	351914	94.906
2	9.736	275484	18037	5.094
Total		5407709	369951	100.000

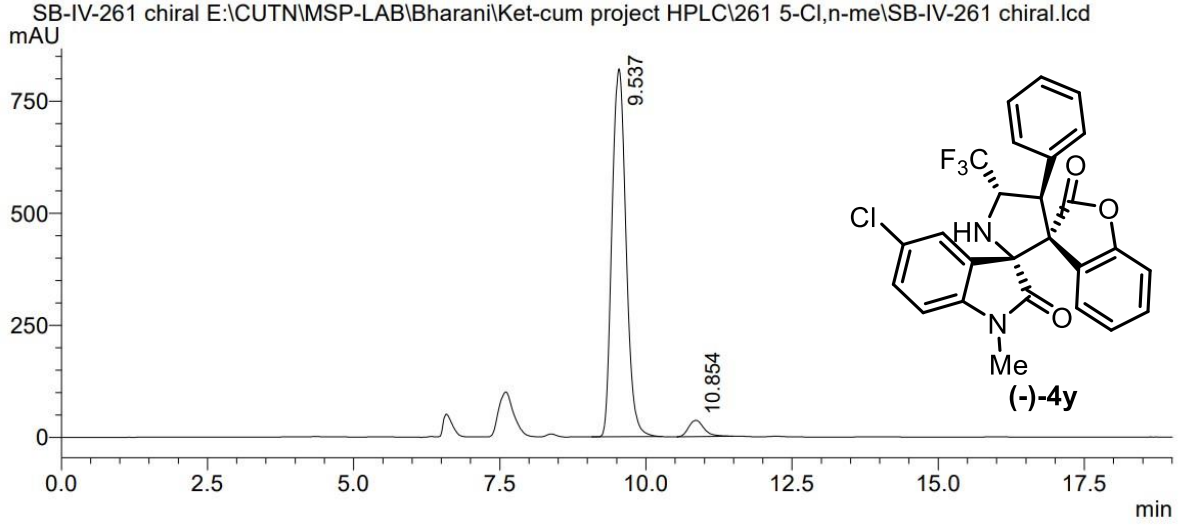
HPLC of racemic **4y**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.541	2729125	104589	50.377
2	10.849	2688278	101320	49.623
Total		5417403	205909	100.000

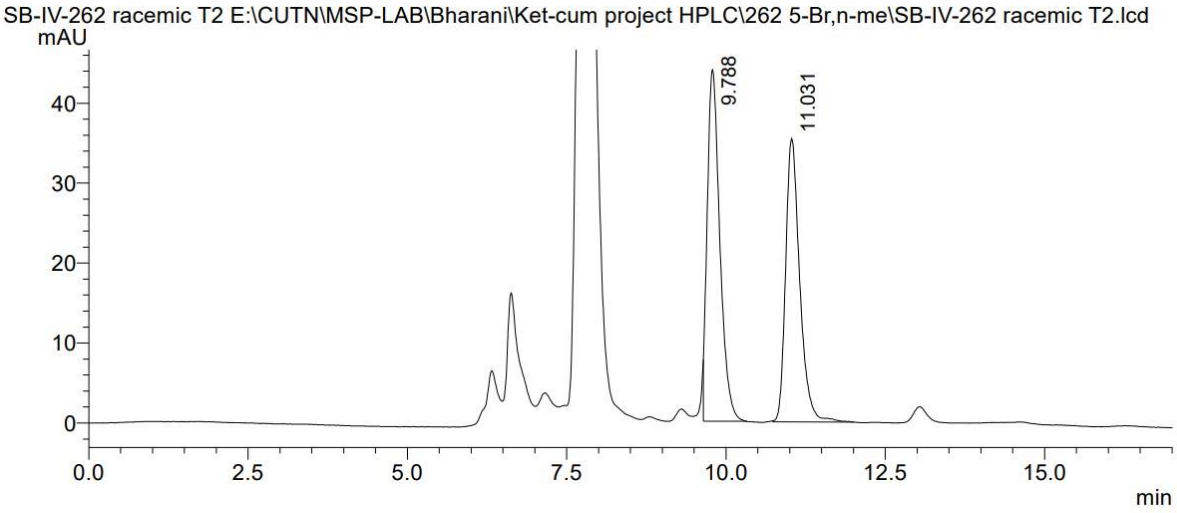
HPLC of chiral **4y: 95:5 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.537	13725263	820198	95.433
2	10.854	656844	36053	4.567
Total		14382107	856252	100.000

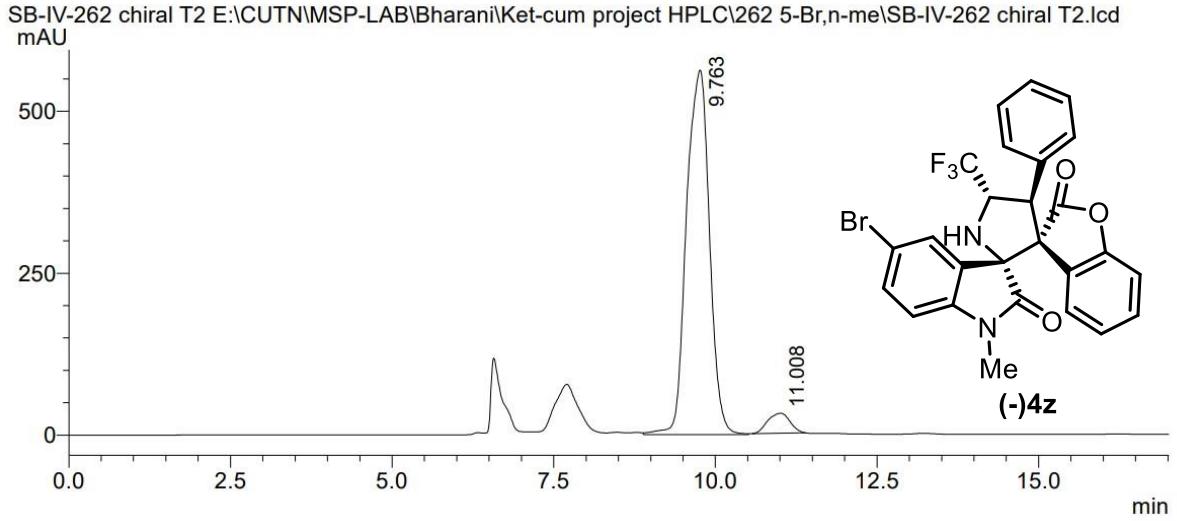
HPLC of racemic **4z**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.788	603704	43977	52.555
2	11.031	545003	35452	47.445
Total		1148706	79429	100.000

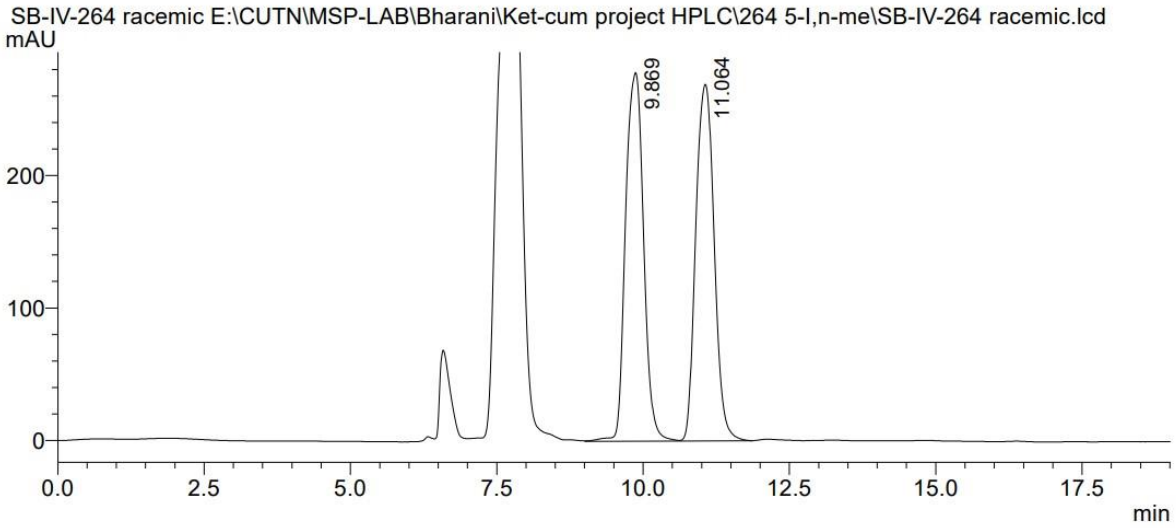
HPLC of chiral **4z: 95:5 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.763	13925525	562503	94.954
2	11.008	740001	30902	5.046
Total		14665526	593404	100.000

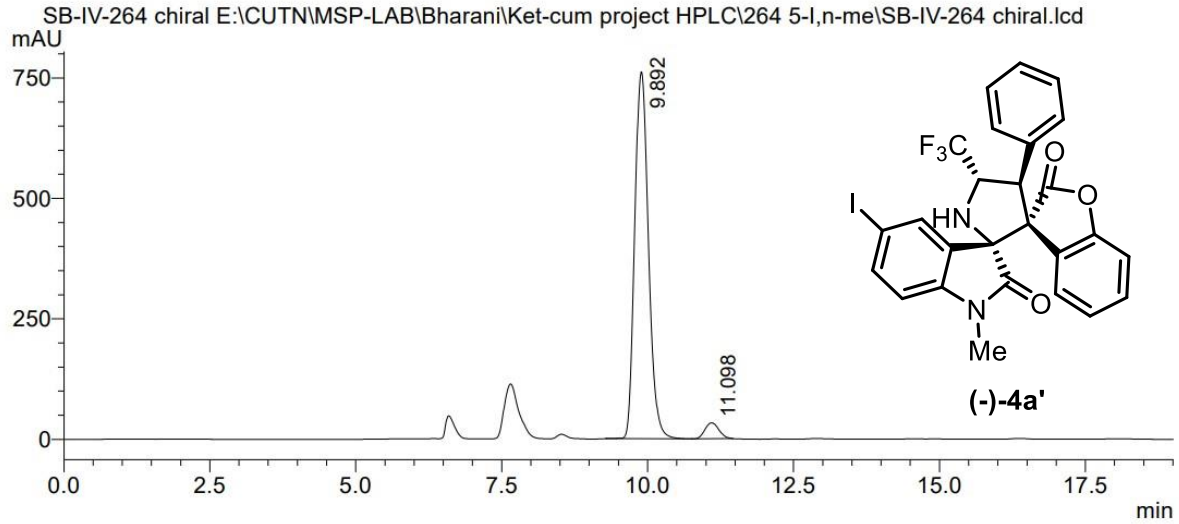
HPLC of racemic **4a'**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.869	5966021	278105	50.309
2	11.064	5892647	269191	49.691
Total		11858667	547296	100.000

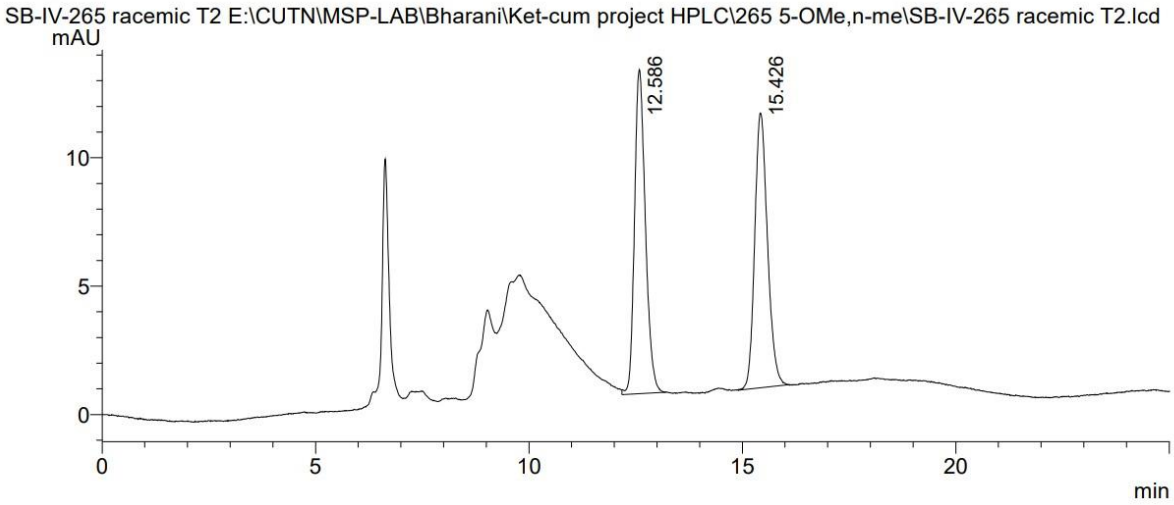
HPLC of chiral **4a': 96:4** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.892	12460381	760941	95.795
2	11.098	547026	32984	4.205
Total		13007407	793925	100.000

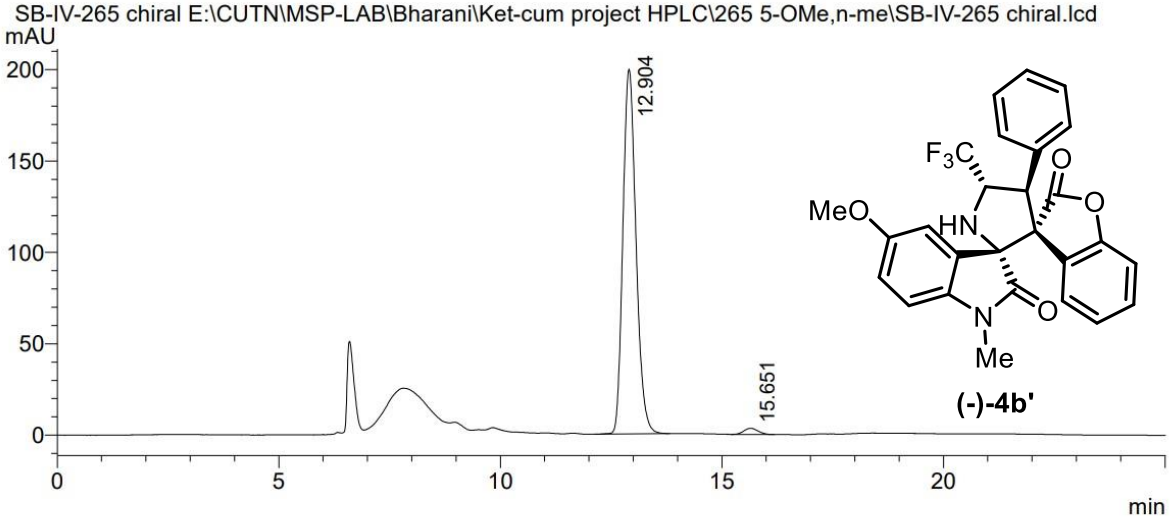
HPLC of racemic **4b'**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.586	223619	12625	50.060
2	15.426	223081	10706	49.940
Total		446700	23331	100.000

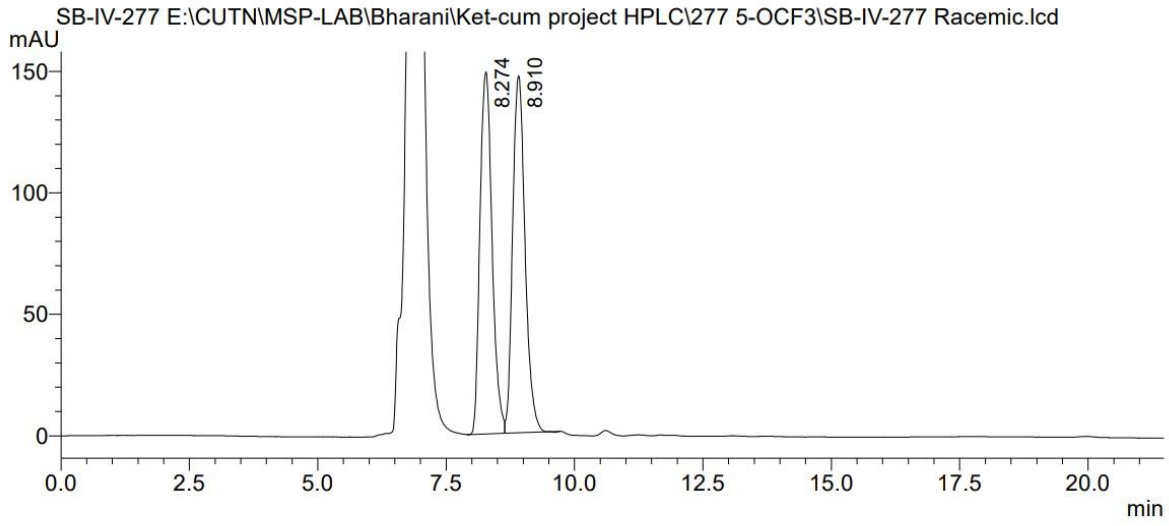
HPLC of chiral **4b': 98:2** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	12.904	4104098	199482	98.204
2	15.651	75057	3354	1.796
Total		4179155	202835	100.000

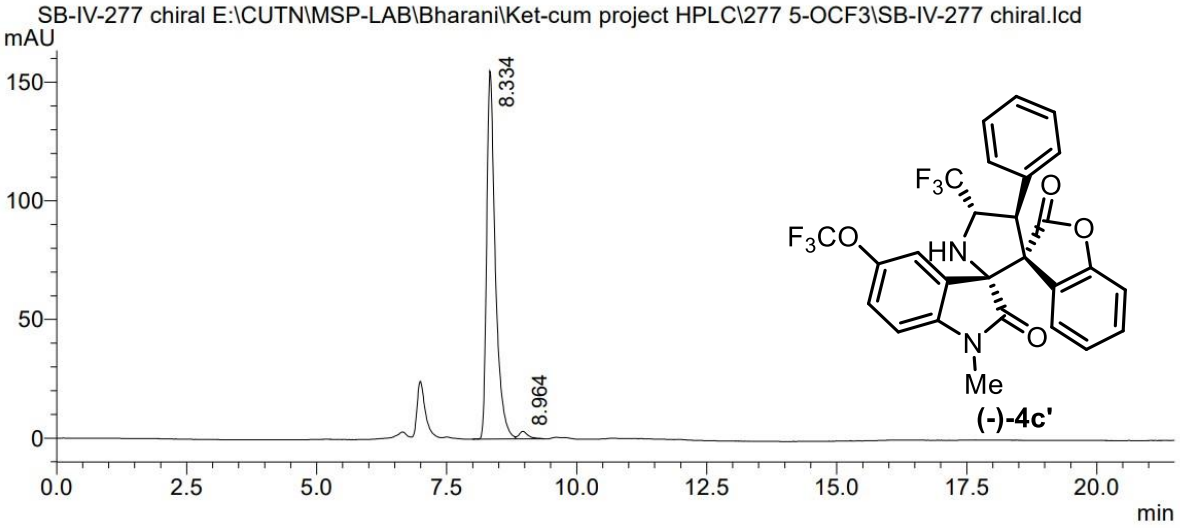
HPLC of racemic **4c'**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.274	2443751	148950	49.796
2	8.910	2463729	146913	50.204
Total		4907480	295863	100.000

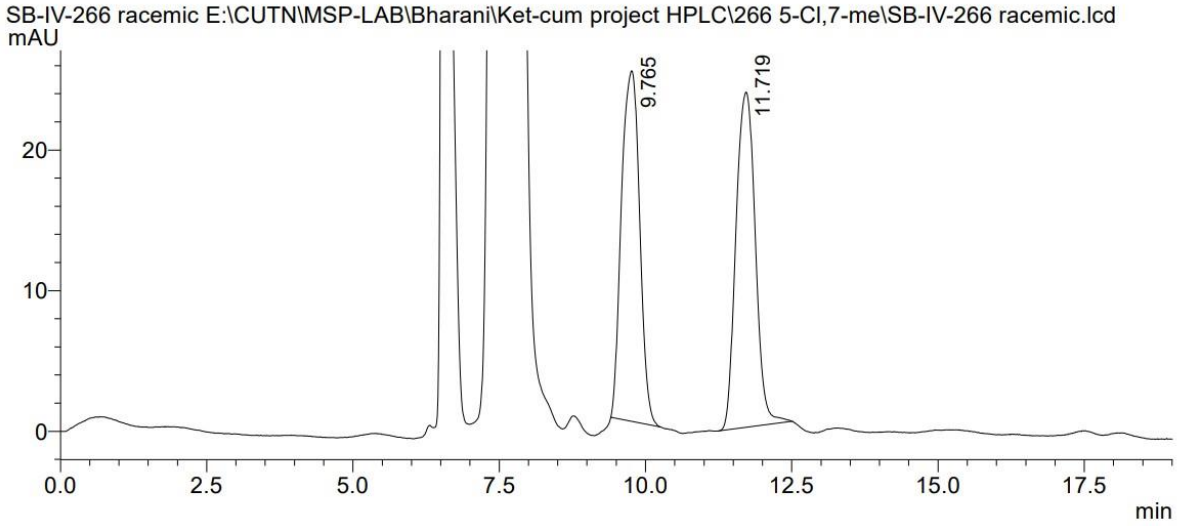
HPLC of chiral **4c': 98:2** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.334	1796705	155097	97.906
2	8.964	38422	3141	2.094
Total		1835126	158238	100.000

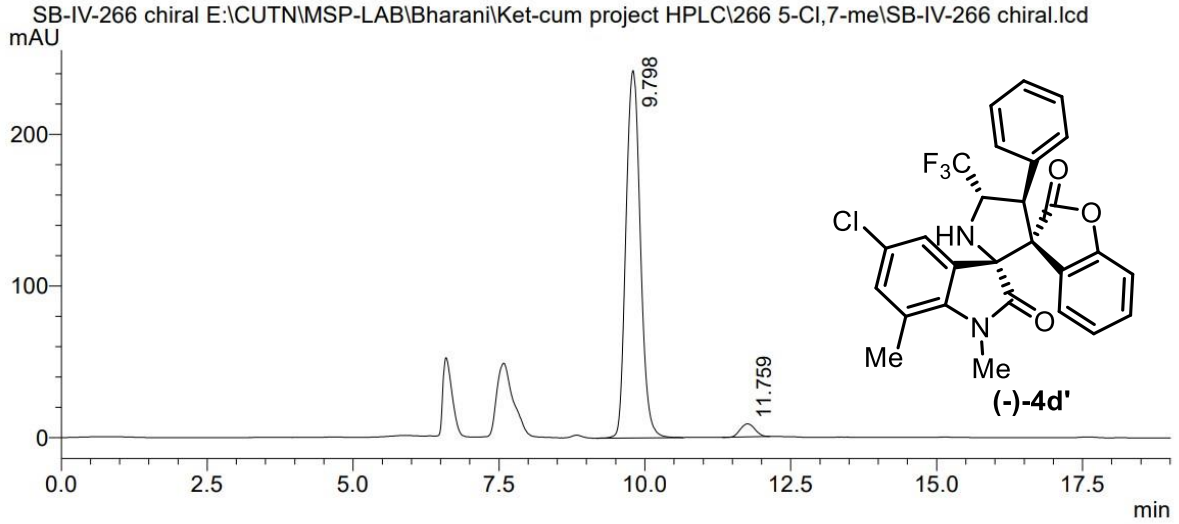
HPLC of racemic **4d'**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.765	538319	24917	49.572
2	11.719	547608	23823	50.428
Total		1085928	48740	100.000

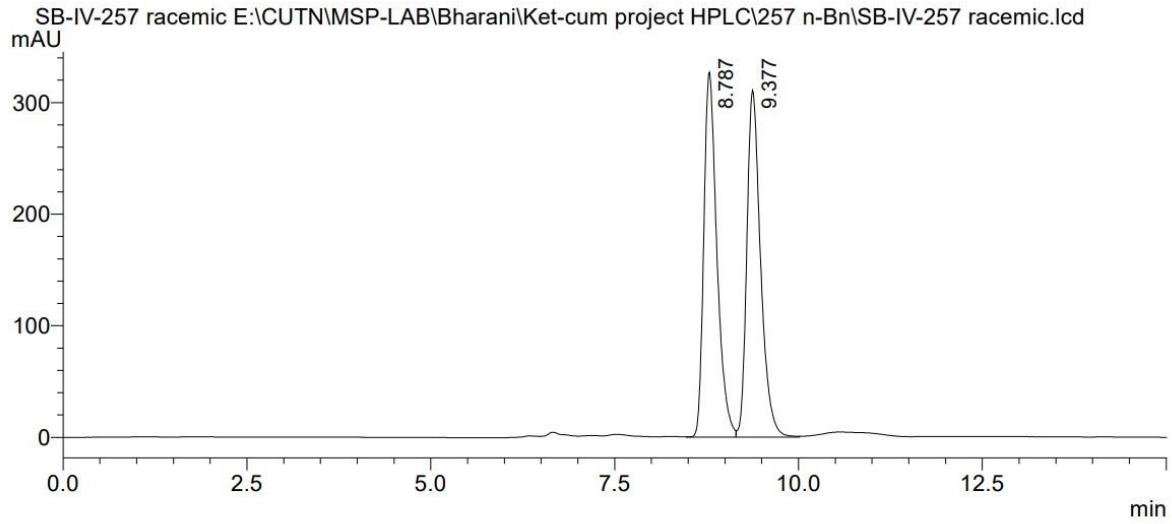
HPLC of chiral **4d': 97:3** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	9.798	4163209	242328	96.522
2	11.759	150018	8583	3.478
Total		4313227	250910	100.000

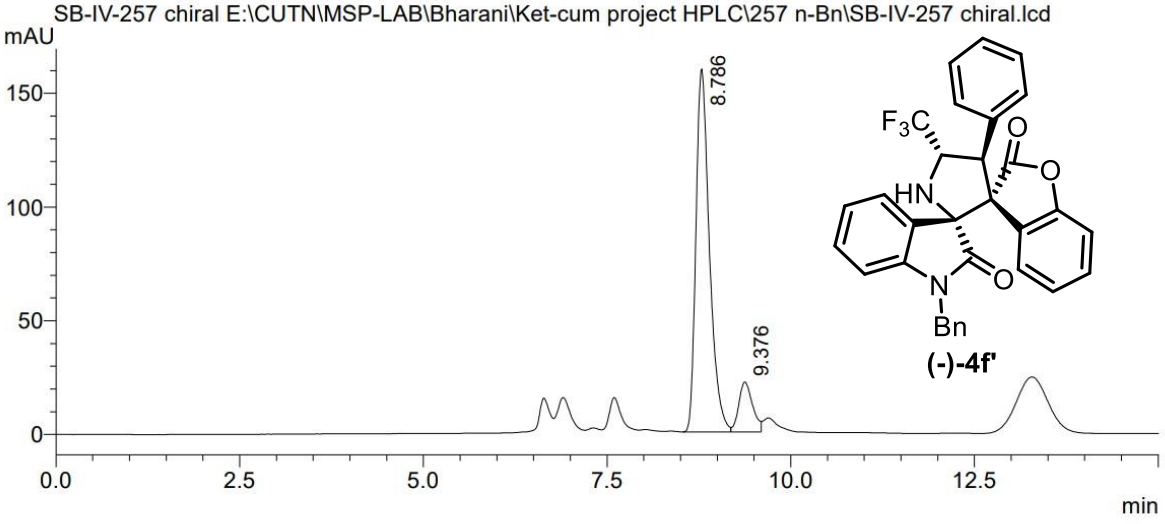
HPLC of racemic **4f'**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.787	4064442	327083	50.043
2	9.377	4057536	310865	49.957
Total		8121978	637949	100.000

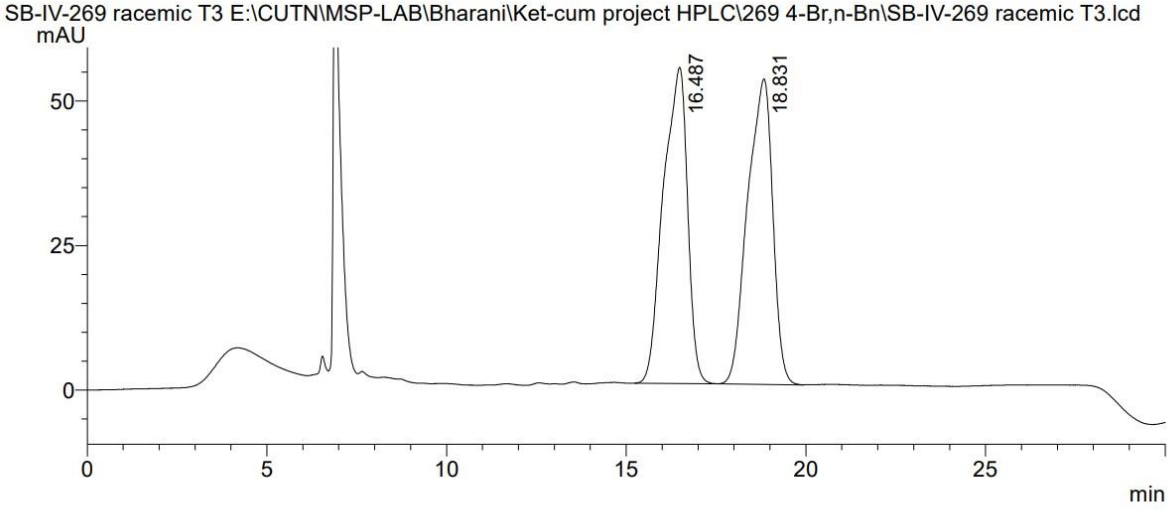
HPLC of chiral **4f': 88:12** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.786	2039026	159481	87.576
2	9.376	289257	21985	12.424
Total		2328283	181466	100.000

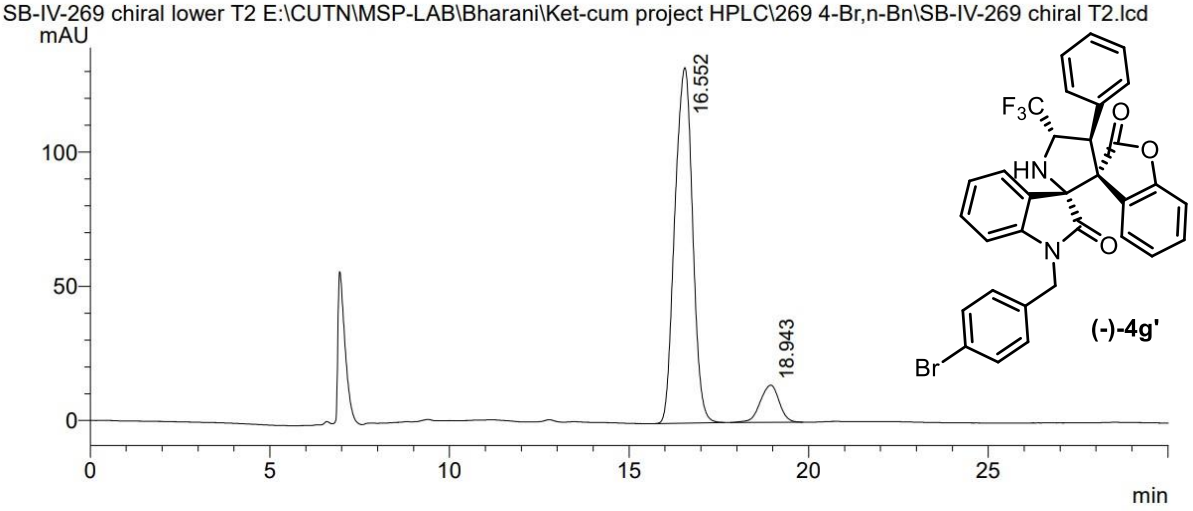
HPLC of racemic **4g'**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	16.487	2553748	54650	49.858
2	18.831	2568305	52825	50.142
Total		5122053	107475	100.000

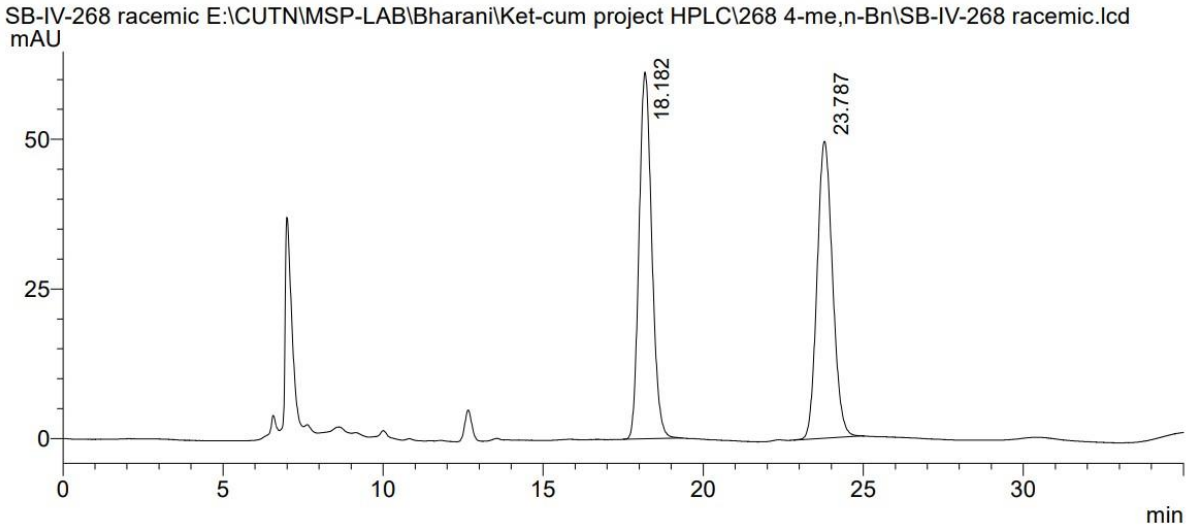
HPLC of chiral **4g': 90:10 *er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	16.552	4557159	132392	89.965
2	18.943	508326	13813	10.035
Total		5065485	146206	100.000

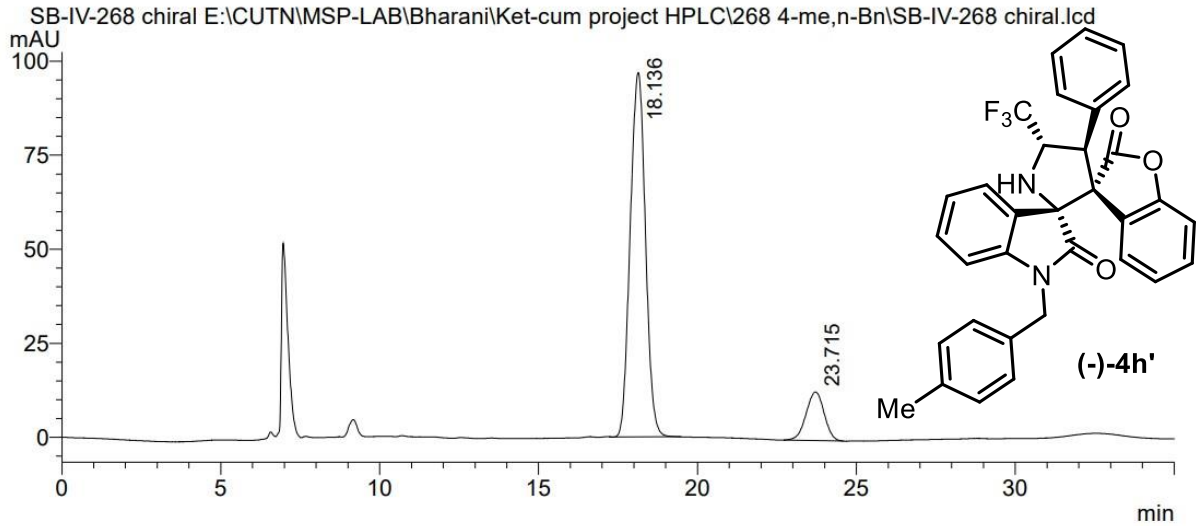
HPLC of racemic **4h'**



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.182	1690540	61241	50.365
2	23.787	1666058	49583	49.635
Total		3356598	110824	100.000

HPLC of chiral **4h': 86:14** ***er***



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.136	3233406	96811	86.314
2	23.715	512681	12956	13.686
Total		3746087	109768	100.000