

Supporting Information

DABCO-promoted highly diastereo- and regioselective construction of C-3 functionalized spirooxindoles *via* [3+2] cycloaddition of 2-aryl/heteroarylidene-1*H*-indene-1,3(2*H*)-diones with *N*-2,2,2-trifluoroethylisatin ketimines at ambient conditions

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EXPERIMENTAL SECTION

1.1 General Experimental Procedures

Nuclear Magnetic Resonance Spectroscopy: ^1H NMR spectra were acquired on Bruker AVIII400 (400 MHz) spectrometer and were referenced to TMS and residual non-deuterated solvent peak in CDCl_3 ($\delta = 7.26$). 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 CDCl_3 ($\delta = 77.0$) and DMSO-D_6 ($\delta = 39.0$).

Mass Spectrometry: High-resolution mass spectra (HRMS) were recorded by the Thermo Fisher spectrometer using electrospray ionization (ESI⁺). The parent ion $[\text{M}+\text{H}]^+$ $[\text{M}+\text{Na}]^+$ 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 $\text{cm}^2 \text{g}^{-1}$. Concentrations are reported in g/mL. Temperatures are reported in $^\circ\text{C}$ (typically 25°C).

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

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

Materials:

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

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

1a-g were prepared by following the reported literature procedure.¹

General Procedure B: *Preparation of indane-1,3-dione enophiles:*

2a-2z were synthesized using a literature report.² All the NMR's were consistent with the literature.

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

To an oven dried vial containing catalyst **3c** (0.05 equiv.), the indane-1,3-dione enophile (1.0 equiv.) was added followed by the addition of Ketimine (1.1 equiv.) in toluene (0.2M). The resulting mixture was stirred at RT for 5-12 hours; the crude product was directly purified by centrifugal process.

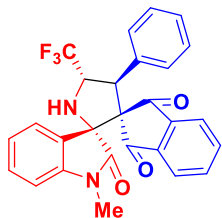
General Procedure D: *Catalytic asymmetric reaction:*

To an oven dried vial containing Quinine (5mol%), enophile (**2**) was added followed by the addition of Ketimine (**1**) in DCM (0.1M). The resulting mixture was stirred at RT for 5 hours; the crude product was directly purified by column chromatography.

References:

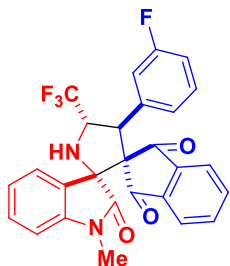
- 1) Wang, X, Huang, D, Wang, K-H, et al. Tin powder promoted synthesis of trifluoroethylamine-containing 3,3'-disubstituted oxindoles. *Appl Organometal Chem.* 2019; 33:e4995.
- 2) Zhi-Feng Hao, Shi-Jie Zhu, Yong-Jia Hao, Wen-Hui Zhang, Ying Zhou, You-Ping Tian and Chuan-Wen Lei. *New J. Chem.*, 2021,45, 18776-18780.

(2'R,4'S,5'S)-1''-methyl-4'-phenyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4a):



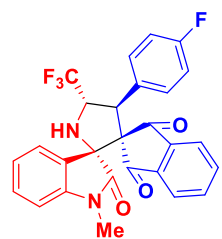
Prepared by following general procedure **D** purified by centrifuge using hexane and isolated product **4a** in 91% yield as a white solid with M. P. 246 - 250 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak I-A column (hexane/EtOAc = 75:25, flow rate 0.5 mL/min, λ = 254 nm), t_R = 17.842 min (minor), t_R = 41.064 min (major), $[\alpha]_D^{25}$ = **-53.000 (CHCl₃, c = 0.12 g/100ml for 87%ee)**; IR (neat) ν_{\max} 1741, 1691, 1618, 1462, 1350 and 752 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.69 - 7.51 (4H, d, m), 7.21 - 7.17 (3H, m), 7.14 - 7.02 (4H, m), 6.81 (1H, t, J = 7.7 Hz), 6.59 (1H, d, J = 7.8 Hz), 5.45 (1H, d, J = 10.6 Hz), 5.30 - 5.20 (1H, m), 3.17 (1H, s), 3.16 (3H, s); **¹³C NMR (100 MHz, CDCl₃+DMSO-d₆ (2drops), DEPT-135)** δ 197.6 (C, C=O), 195.3 (C, C=O), 175.2 (C, N-C=O), 143.6 (C), 141.7 (C), 141.5 (C), 136.1 (CH), 135.9 (CH), 132.8 (C), 130.3 (CH), 125.9 (CF₃, q, J = 278 Hz), 128.6 (2CH), 128.2 (2CH), 127.7 (CH), 125.3 (CH), 122.9 (C), 122.6 (2CH), 121.8 (CH), 108.1 (CH), 71.1 (C), 70.8 (C), 60.7 (CH, q, J = 31 Hz), 47.6 (CH), 24.8 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -172.74; HRMS (ESI) m/z : 499.1240 [M + Na]⁺, calcd for C₂₇H₁₉F₃N₂O₃Na; Found 499.1247.

4'-(3-fluorophenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4b):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4b** in 72% yield as a white solid with M. P. 245 °C.; IR (neat) ν_{\max} 1703, 1612, 1253, 1116 and 756 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.73-7.56 (4H, d, m), 7.71 - 7.05 (3H, m), 7.01 - 6.94 (2H, m), 6.83-6.73 (2H, m), 6.60 (1H, d, J = 7.8 Hz), 5.45 (1H, d, J = 10.6 Hz), 5.25 - 5.15 (1H, m), 3.17 (1H, s), 3.16 (3H, s); **¹³C NMR (100 MHz, CDCl₃+DMSO-d₆ (2drops), DEPT-135)** δ 197.4 (C, C=O), 195.1 (C, C=O), 175.0 (C, N-C=O), 161.9 (C, C-F, d, J = 244 Hz), 143.6 (C), 141.7 (C), 141.4 (C), 136.2 (CH), 136.1 (CH), 135.7 (C), 135.6 (C), 130.4 (C), 130.0 (CH, d, J = 8 Hz), 125.9 (CF₃, q, J = 279 Hz), 125.3 (2CH), 124.7 (CH, d, J = 3 Hz), 122.8 (2CH), 121.9 (CH), 115.5 (CH, d, J = 23 Hz), 114.8 (CH, d, J = 20 Hz), 108.1 (CH), 71.4 (C), 70.7 (C), 60.9 (CH, q, J = 30 Hz), 48.1 (CH), 26.0 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.84, -112.16; HRMS (ESI) m/z : 517.1145 [M + Na]⁺, calcd for C₂₇H₁₈F₄N₂O₃Na; Found 517.1174.

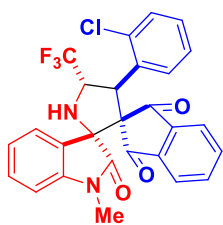
4'-(4-fluorophenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4c):



Prepared by following general procedure **D** purified by centrifuge using hexane and isolated product **4c** in 82% yield as a pale white solid with M. P. 231 °C.; The

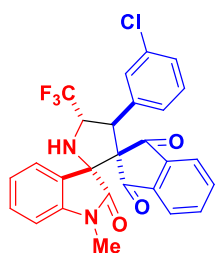
enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak I-A column (hexane/EtOAc = 75:25, flow rate 1 mL/min, λ = 254 nm), t_R = 8.660 min (minor), t_R = 23.451 min (major), $[\alpha]_D^{25}$ = **-2.300 (CHCl₃, c = 0.11 g/100ml for 32%ee)**; IR (neat) ν_{\max} 2360, 1735, 1695, 1263, 1157 and 754 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.72-7.56 (4H, d, m), 7.65 - 7.56 (3H, m), 7.22 - 7.10 (4H, m), 6.80 (3H, q, J = 8.5 Hz), 6.60 (1H, d, J = 7.8 Hz), 5.44 (1H, d, J = 10.6 Hz), 5.25 - 5.15 (1H, m), 3.15 (4H, s); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 198.8 (C, C=O), 195.4 (C, C=O), 175.3 (C, N-C=O), 162.2 (C, C-F, d, J = 246 Hz), 144.3 (C), 142.3 (C), 141.7 (C), 136.1 (2CH), 130.7 (CH), 130.5 (CH), 130.4 (CH), 128.4 (CH, d, J = 4 Hz), 124.7 (CH), 124.2 (CF₃, q, J = 278 Hz), 123.4 (C), 123.1 (CH), 122.9 (CH), 122.3 (CH), 115.6 (CH), 115.4 (CH), 108.4 (CH), 70.8 (C), 70.7 (C), 61.4 (CH, q, J = 30 Hz), 48.8 (CH), 26.4 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.81, -113.89; HRMS (ESI) m/z: 517.1145 [M + Na]⁺, calcd for C₂₇H₁₈F₄N₂O₃Na; Found 517.1151.

4'-(2-chlorophenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4d):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4d** in 73% yield as a white solid with M. P. 248 - 252 °C.; IR (neat) ν_{\max} 2360, 1695, 1612, 1473, 1257 and 754 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.66 - 7.56 (4H, d, m), 7.38 (1H, d, J = 7.9 Hz), 7.22 (1H, d, J = 7.6 Hz), 7.15 (2H, t, J = 7.9 Hz), 7.05 (1H, t, J = 7.6 Hz), 6.97 (1H, t, J = 7.7 Hz), 6.82 (1H, t, J = 7.6 Hz), 6.63 (1H, d, J = 7.8 Hz), 6.37 (1H, d, J = 10.6 Hz), 5.07 - 5.06 (1H, m), 3.21 (4H, s); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 199.2 (C, C=O), 194.4 (C, C=O), 175.4 (C, N-C=O), 144.7 (C), 142.4 (C), 141.5 (C), 136.1 (CH), 135.8 (CH), 135.6 (C), 130.7 (CH), 130.6 (C), 130.3 (CH), 129.1 (CH), 129.0 (CH), 126.6 (CH), 125.6 (CF₃, q, J = 279 Hz), 125.1 (CH), 123.4 (C), 123.3 (CH), 122.8 (CH), 122.2 (CH), 108.3 (CH), 70.6 (C), 70.3 (C), 62.5 (CH, q, J = 30 Hz), 45.1 (CH), 26.4 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.80; HRMS (ESI) m/z: 533.0850 [M + Na]⁺, calcd for C₂₇H₁₈ClF₃N₂O₃Na; Found 533.0860.

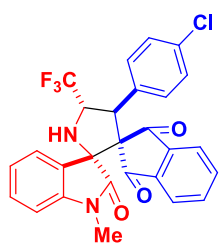
4'-(3-chlorophenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4e):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4e** in 67% yield as a white solid with M. P. 245 - 248 °C.; IR (neat) ν_{\max} 2360, 1707, 1612, 1350, 1255, 1122 and 754 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.73 - 7.56 (4H, d, m), 7.23 (1H, br, s), 7.17-7.03 (5H, m), 6.81 (1H, t, J = 8 Hz), 6.60 (1H, d, J = 7.8 Hz), 5.42 (1H, t, J = 10.6 Hz), 5.25 - 5.15 (1H, m), 3.16 (1H, s), 3.15 (3H, s); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 198.5 (C, C=O), 195.1 (C, C=O), 175.2 (C, N-C=O), 144.3 (C), 142.3 (C), 141.6 (C), 136.1 (2CH), 134.8 (C), 134.3 (C), 130.7 (CH), 129.8 (CH), 128.9 (CH), 128.3 (CH), 127.1 (CH), 125.6 (CF₃, q, J = 279 Hz), 124.7 (CH), 123.2 (C), 123.2

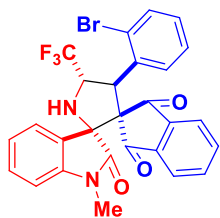
(CH), 122.9 (CH), 122.3 (CH), 108.4 (CH), 70.8 (C), 70.7 (C), 61.2 (CH, q, $J = 31$ Hz), 48.9 (CH), 26.4 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -72.82; HRMS (ESI) m/z : 511.1030 [M + H]⁺, calcd for C₂₇H₁₉ClF₃N₂O₃; Found 511.1044.

4'-(4-chlorophenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4f):



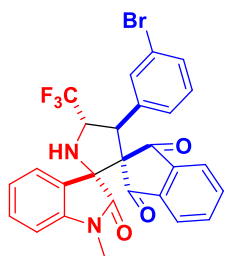
Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4f** in 96% yield as a lace white solid with M. P. 221 - 225 °C.; IR (neat) ν_{\max} 2360, 1703, 1614, 1261, 1132 and 759 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.72 - 7.57 (4H, d, m), 7.18 - 7.07 (6H, m), 6.81 (1H, t, $J = 7.6$ Hz), 6.59 (1H, d, $J = 7.8$ Hz), 5.47 (1H, d, $J = 10.6$ Hz), 5.26 - 5.15 (1H, m), 3.16 (1H, s), 3.15 (3H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 198.6 (C, C=O), 195.2 (C, C=O), 175.2 (C, N-C=O), 144.2 (C), 142.3 (C), 141.6 (C), 136.1 (2CH), 133.9 (C), 131.2 (C), 130.7 (CH), 130.2 (2CH), 128.7 (2CH), 125.7 (CF₃, q, $J = 278$ Hz), 124.6 (CH), 123.2 (C), 123.2 (CH), 122.9 (CH), 122.3 (CH), 108.4 (CH), 70.8 (C), 70.7 (C), 61.2 (CH, q, $J = 31$ Hz), 48.7 (CH), 26.4 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -72.84; HRMS (ESI) m/z : 533.0850 [M + Na]⁺, calcd for C₂₇H₁₈ClF₃N₂O₃Na; Found 533.0858.

4'-(2-bromophenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4g):



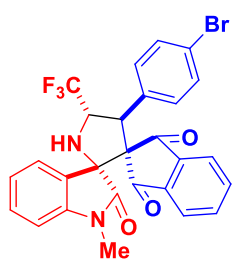
Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4g** in 72% yield as a white solid with M. P. 240- 244 °C.; IR (neat) ν_{\max} 2360, 1737, 1693, 1255, 1116 and 763 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.77 - 7.58 (4H, d, m), 7.38 (2H, d, $J = 8.0$ Hz), 7.23 (1H, d, $J = 7.6$ Hz), 7.15 (1H, t, $J = 7.2$ Hz), 7.08 (1H, t, $J = 7.3$ Hz), 6.90 (1H, t, $J = 7.9$ Hz), 6.83 (1H, t, $J = 7.6$ Hz), 6.63 (1H, d, $J = 7.8$ Hz), 6.41 (1H, d, $J = 10.6$ Hz), 5.08 - 4.98 (1H, m), 3.21 (3H, s), 3.20 (1H, d, $J = 6.9$ Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 199.2 (C, C=O), 194.3 (C, C=O), 175.3 (C, N-C=O), 144.7 (C), 142.5 (C), 141.5 (C), 136.1 (CH), 135.8 (CH), 133.8 (CH), 132.4 (C), 130.7 (CH), 129.3 (CH), 129.2 (CH), 127.2 (CH), 126.4 (C), 125.6 (CF₃, q, $J = 279$ Hz), 125.1 (CH), 123.4 (C), 123.3 (CH), 122.8 (CH), 122.2 (CH), 108.3 (CH), 70.7 (C), 70.3 (C), 62.9 (CH, q, $J = 30$ Hz), 47.8 (CH), 26.4 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -172.69; HRMS (ESI) m/z : 577.0345 [M + Na]⁺, calcd for C₂₇H₁₈BrF₃N₂O₃Na; Found 577.0357.

4'-(3-bromophenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4h):



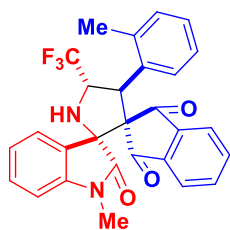
Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4h** in 63% yield as a white solid with M. P. 250 - 254 °C.; IR (neat) ν_{\max} 3317, 1703, 1612, 1352, 1265, 1163 and 754 cm^{-1} ; **¹H NMR (400 MHz, CDCl₃)** δ 7.74 - 7.57 (4H, d, m), 7.38 (1H, br, s), 7.20-7.11 (4H, m), 6.98 (1H, t, J = 7.9 Hz), 6.82 (1H, t, J = 7.64 Hz), 6.60 (1H, d, J = 7.8 Hz), 5.41 (1H, d, J = 10.6 Hz), 5.24 - 5.14 (1H, m), 3.16 (1H, s), 3.15 (3H, s); **¹³C NMR (100 MHz, CDCl₃+DMSO-d₆ (2drops), DEPT-135)** δ 198.0 (C, C=O), 194.8 (C, C=O), 174.9 (C, N-C=O), 143.9 (C), 141.9 (C), 141.4 (C), 135.9 (CH), 135.9 (CH), 134.9 (C), 131.6 (CH), 130.9 (CH), 130.5 (CH), 129.8 (CH), 127.3 (CH), 125.4 (CF₃, q, J = 279 Hz), 124.5 (CH), 122.9 (CH), 122.9 (C), 122.7 (CH), 122.2 (C), 122.1 (CH), 108.1 (CH), 70.7 (C), 70.5 (C), 60.8 (CH, q, J = 31 Hz), 48.5 (CH), 26.1 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.81; HRMS (ESI) m/z : 577.0345 [M + Na]⁺, calcd for C₂₇H₁₈BrF₃N₂O₃Na; Found 5577.0360.

4'-(4-bromophenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4i):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4i** in 85% yield as a lace white solid with M. P. 226 - 230 °C.; IR (neat) ν_{\max} 2360, 1726, 1614, 1257, 1120 and 758 cm^{-1} ; **¹H NMR (400 MHz, CDCl₃)** δ 7.73 - 7.57 (4H, d, m), 7.24 (2H, d, J = 8.5 Hz), 7.16-7.10 (4H, m), 6.81 (1H, t, J = 7.6 Hz), 6.59 (1H, d, J = 7.8 Hz), 5.41 (1H, d, J = 10.6 Hz), 5.26 - 5.15 (1H, m), 3.18 (1H, s), 3.15 (3H, s); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 198.6 (C, C=O), 195.2 (C, C=O), 175.2 (C, N-C=O), 144.2 (C), 142.3 (C), 141.6 (C), 136.1 (2CH), 131.7 (CH), 131.7 (C), 130.7 (2CH), 130.5 (2CH), 125.6 (CF₃, q, J = 278 Hz), 124.6 (CH), 123.2 (C), 123.2 (CH), 122.9 (CH), 122.3 (CH), 122.1 (C), 108.4 (CH), 70.8 (C), 70.6 (C), 61.2 (CH, q, J = 31 Hz), 48.7 (CH), 26.4 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.84; HRMS (ESI) m/z : 577.0345 [M + Na]⁺, calcd for C₂₇H₁₈BrF₃N₂O₃Na; Found 577.0353.

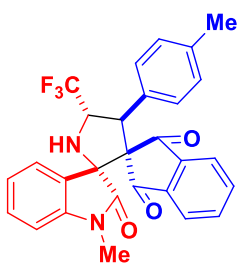
1''-methyl-4'-(o-tolyl)-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4j):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4j** in 64% yield as a pale yellow solid with M. P. 240 - 244 °C.; IR (neat) ν_{\max} 2360, 1726, 1693, 1469, 1253, 1114 and 756 cm^{-1} ; **¹H NMR (400 MHz, CDCl₃)** δ 7.80 (1H, d, J = 7.24 Hz), 7.63 - 7.52 (3H, m), 7.32 - 7.28 (1H, m), 7.22 (1H, d, J = 7.56 Hz), 7.14 (1H, t, J = 6.9 Hz), 6.99 - 6.92 (3H, m), 6.83 (1H, t, J = 7.6 Hz), 6.61 (1H, d, J = 7.7 Hz), 6.07 (1H, d, J = 10.7 Hz), 5.11 - 5.03 (1H, m), 3.22 - 3.18 (4H, m), 2.42 (3H, s); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 199.6 (C, C=O), 195.7 (C, C=O), 175.5 (C, N-C=O), 144.4 (C), 142.2 (C), 141.9 (C), 138.2 (C), 135.9 (2CH), 131.1 (2CH), 130.5 (C),

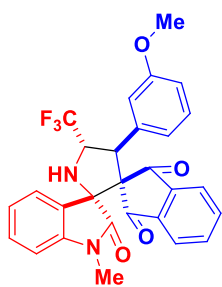
127.6 (CH), 127.4 (CH), 125.8 (CF₃, q, *J* = 278 Hz), 125.8 (CH), 124.9 (CH), 123.5 (C), 123.1 (CH), 122.9 (CH), 122.2 (CH), 108.3 (CH), 70.8 (C), 70.5 (C), 62.7 (CH, q, *J* = 31 Hz), 44.5 (CH), 26.4 (CH₃), 19.7 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -72.89; HRMS (ESI) *m/z*: 513.1396 [M + Na]⁺, calcd for C₂₈H₂₁F₃N₂O₃Na; Found 513.1404.

1''-methyl-4'-(p-tolyl)-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4k):



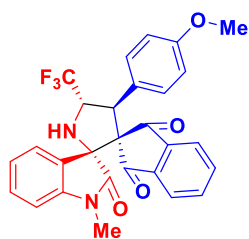
Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4k** in 68% yield as a lace white solid with M. P. 216 - 220 °C.; IR (neat) ν_{\max} 2360, 1703, 1261, 1114 and 754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.71 - 7.51 (4H, d, m), 7.17 (1H, d, *J* = 7.5 Hz), 7.13-7.08 (3H, m), 6.89 (2H, d, *J* = 8.0 Hz), 6.81 (1H, t, *J* = 7.6 Hz), 6.59 (1H, d, *J* = 7.8 Hz), 5.42 (1H, d, *J* = 10.6 Hz), 5.27 - 5.17 (1H, m), 3.17 - 3.15 (4H, s), 2.13 (3H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 198.9 (C, C=O), 195.6 (C, C=O), 175.4 (C, N-C=O), 144.3 (C), 142.4 (C), 141.8 (C), 137.6 (C), 135.8 (CH), 135.8 (CH), 130.5 (CH), 129.4 (C), 129.3 (2C), 128.6 (2C), 125.8 (CF₃, q, *J* = 279 Hz), 124.7 (CH), 123.6 (C), 123.0 (CH), 122.8 (CH), 122.2 (CH), 108.3 (CH), 70.9 (C), 70.7 (C), 61.2 (CH, q, *J* = 30 Hz), 49.3 (CH), 26.4 (CH₃), 20.9 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -72.73; HRMS (ESI) *m/z*: 513.1396 [M + Na]⁺, calcd for C₂₈H₂₁F₃N₂O₃Na; Found 513.1406.

4'-(3-methoxyphenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4l):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4l** in 78% yield as a white solid with M. P. 260 - 263 °C.; IR (neat) ν_{\max} 2360, 2341, 1610, 1346, 1257, 1114 and 690 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.72 - 7.54 (4H, d, m), 7.18 (1H, d, *J* = 7.5 Hz), 7.12 (1H, d, *J* = 7.7 Hz), 7.0 (1H, t, *J* = 7.9 Hz), 6.83 - 6.79 (2H, m), 6.73 (1H, br, m), 6.61 - 6.57 (2H, m), 5.43 (1H, d, *J* = 10.6 Hz), 5.25 - 5.19 (1H, m), 3.66 (3H, m), 3.19 (1H, s), 3.16 (3H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 198.8 (C, C=O), 195.6 (C, C=O), 175.4 (C, N-C=O), 159.3 (C), 144.3 (C), 142.4 (C), 141.7 (C), 135.9 (CH), 134.1 (C), 130.6 (CH), 129.5 (2CH), 125.8 (CF₃, q, *J* = 279 Hz), 124.8 (CH), 123.5 (C), 123.1 (CH), 122.9 (CH), 122.3 (CH), 120.9 (CH), 114.2 (CH), 113.9 (CH), 108.3 (CH), 70.9 (C), 70.6 (C), 61.2 (CH, q, *J* = 31 Hz), 55.1 (CH), 49.7 (CH), 26.4 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -72.76; HRMS (ESI) *m/z*: 529.1345 [M + Na]⁺, calcd for C₂₈H₂₁F₃N₂O₄Na; Found 529.1375.

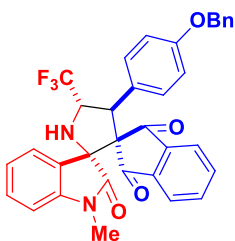
4'-(4-methoxyphenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4m):



Prepared by following general procedure **D** purified by centrifuge using hexane and isolated product **4m** in 77% yield as a pearl white solid with M. P. 208 - 210 °C.; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak I-A column (hexane/EtOAc = 75:25, flow rate 1 mL/min, $\lambda = 254$ nm), $t_R = 10.729$ min (minor), $t_R = 30.295$ min (major), $[\alpha]_D^{25} = -8.969$ (CHCl₃, $c = 0.11$ g/100ml for 38%ee); IR (neat) ν_{\max} 2360, 1701, 1514,

1269, 1114 and 759 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.71 - 7.52 (4H, d, m), 7.18 - 7.10 (4H, m), 6.81 (1H, t, $J = 7.6$ Hz), 6.63 - 6.58 (3H, m), 5.41 (1H, d, $J = 10.7$ Hz), 5.24 - 5.13 (1H, m), 3.64 (3H, m), 3.15 (3H, s), 3.14 (1H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 199.0 (C, C=O), 195.7 (C, C=O), 175.4 (C, N-C=O), 159.0 (C), 144.3 (C), 142.4 (C), 141.7 (C), 135.9 (CH), 130.5 (CH), 129.8 (CH), 125.8 (CF₃, q, $J = 278$ Hz), 124.7 (CH), 124.4 (C), 123.6 (C), 123.0 (CH), 122.8 (CH), 122.2 (CH), 113.8 (3CH), 108.3 (CH), 70.9 (C), 70.6 (C), 61.3 (CH, q, $J = 30$ Hz), 55.0 (CH), 49.0 (CH), 26.4 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -72.73; HRMS (ESI) m/z : 529.1345 [M + Na]⁺, calcd for C₂₈H₂₁F₃N₂O₄Na; Found 529.1344.

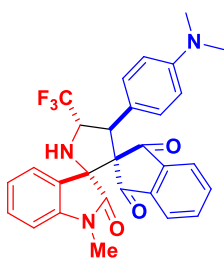
4'-(4-(benzyloxy)phenyl)-1''-methyl-5''-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (**4n**):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4n** in 83% yield as a white solid with M. P. 230 °C.; IR (neat) ν_{\max} 2360, 1703, 1612, 1249, 1116 and 761 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.71 - 7.54 (4H, d, m), 7.34 - 7.27 (5H, m), 7.18 - 7.09 (4H, m), 6.81 (1H, t, $J = 7.6$ Hz), 6.70 (2H, d, $J = 8.7$ Hz), 6.59 (1H, d, $J = 7.8$ Hz), 5.41 (1H, d, $J = 10.6$ Hz), 5.24 - 5.14 (1H, m), 4.89 - 4.83 (2H, m), 3.17 (1H, s), 3.15 (3H, s); ¹³C NMR (100

MHz, CDCl₃, DEPT-135) δ 199.0 (C, C=O), 195.7 (C, C=O), 175.4 (C, N-C=O), 158.3 (C), 144.3 (C), 142.4 (C), 141.7 (C), 136.6 (C), 135.8 (C), 130.5 (CH), 129.9 (2CH), 128.5 (3CH), 127.9 (CH), 127.5 (2CH), 125.8 (CF₃, q, $J = 279$ Hz), 124.7 (CH), 124.7 (C), 123.6 (C), 123.1 (CH), 122.8 (CH), 122.3 (CH), 114.7 (2CH), 108.3 (CH), 70.9 (C), 70.6 (C), 69.8 (CH₂), 61.3 (CH, q, $J = 30$ Hz), 49.7 (CH), 26.4 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -72.71; HRMS (ESI) m/z : 605.1658 [M + Na]⁺, calcd for C₃₄H₂₅F₃N₂O₄Na; Found 605.1670.

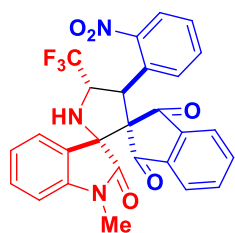
4'-(4-(dimethylamino)phenyl)-1''-methyl-5''-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (**4o**):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4o** in 54% yield as a pale yellow solid with M. P. 230 - 235 °C.; IR (neat) ν_{\max} 2927, 1701, 1614, 1263, 1118, 765 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.71 - 7.52 (4H, d, m), 7.18 (1H, d, $J = 7.7$ Hz), 7.12 - 7.05 (3H, m), 6.80 (1H, t, $J = 7.6$ Hz), 6.58 (1H, d, $J = 7.8$ Hz), 6.43 (2H, d, $J = 8.7$ Hz), 5.37 (1H, d, $J = 10.7$ Hz), 5.20 - 5.18 (1H, m), 3.15 (4H, s), 2.78 (6H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-

135) δ 199.3 (C, C=O), 195.9 (C, C=O), 175.6 (C, N-C=O), 149.8 (C), 144.3 (C), 142.6 (C), 141.9 (C), 135.7 (2CH), 130.4 (CH), 129.5 (2CH), 125.9 (CF₃, q, J = 279 Hz), 124.7 (CH), 123.8 (C), 123.0 (CH), 122.8 (CH), 122.2 (CH), 119.6 (C), 112.2 (2CH), 108.2 (CH), 71.0 (C), 70.6 (C), 61.3 (CH, q, J = 30 Hz), 49.2 (CH), 40.2 (2CH₃), 26.4 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.67; HRMS (ESI) m/z : 542.1662 [M + Na]⁺, calcd for C₂₉H₂₄F₃N₃O₃Na; Found 542.1670.

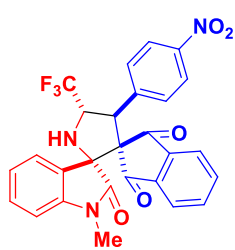
1''-methyl-4'-(2-nitrophenyl)-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4p):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4p** in 94% yield as a light brown solid with M. P. 225-230 °C.; IR (neat) ν_{\max} 1734, 1697, 1527, 1350, 1132, 1116 and 754 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.73 - .7.71 (1H, d, m), 7.64 – 7.56 (3H, m), 7.51 (1H, d, J = 7.8 Hz), 7.34 (1H, t, J = 7.6 Hz), 7.24 – 7.10 (3H, m), 6.80 (1H, t, J = 7.6 Hz), 6.58 (1H, d, J = 7.8 Hz), 6.37 (1H, d, J = 10.6 Hz), 5.21 – 5.17 (1H, m), 3.18 (1H, s), 3.14 (3H, s); **¹³C**

NMR (100 MHz, CDCl₃, DEPT-135) δ 198.8 (C, C=O), 193.9 (C, C=O), 174.6 (C, N-C=O), 151.4 (C), 144.6 (C), 142.1 (C), 141.4 (C), 136.3 (CH), 135.9 (CH), 131.8 (CH), 130.8 (CH), 129.6 (CH), 128.9 (CH), 126.6 (C), 125.4 (CF₃, q, J = 279 Hz), 124.9 (CH), 124.7 (CH), 123.5 (CH), 122.9 (C), 122.8 (CH), 122.1 (CH), 108.4 (CH), 71.0 (C), 70.7 (C), 62.1 (CH, q, J = 31 Hz), 41.8 (CH), 26.5 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.82; HRMS (ESI) m/z : 544.1090 [M + Na]⁺, calcd for C₂₇H₁₈F₃N₃O₅Na; Found 544.1090.

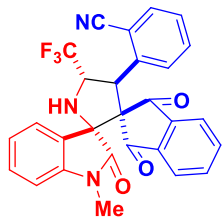
1''-methyl-4'-(4-nitrophenyl)-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4q):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4q** in 65% yield as a white solid with M. P. 244 - 248 °C.; IR (neat) ν_{\max} 2360, 1703, 1612, 1346, 1118 and 758 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.99 (1H, d, J = 8.8 Hz), 7.72 (1H, d, J = 7.9 Hz), 7.67 - 7.58 (3H, m), 7.44 (2H, d, J = 8.8 Hz), 7.16 – 7.11 (2H, m), 6.82 (1H, t, J = 7.7 Hz), 6.60 (1H, d, J = 7.8 Hz), 5.56 (1H, d, J = 10.6 Hz), 5.36 - 5.26 (1H, m), 3.19 (1H, d, J = 9.3 Hz),

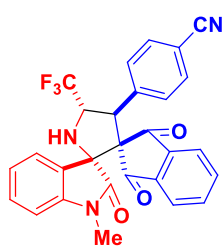
3.15 (3H, s); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 198.2 (C, C=O), 194.7 (C, C=O), 174.9 (C, N-C=O), 147.5 (C), 144.2 (C), 142.1 (C), 141.5 (C), 140.4 (C), 136.4 (CH), 136.4 (C), 130.9 (CH), 129.9 (2CH), 125.5 (CF₃, q, J = 279 Hz), 124.5 (CH), 123.7 (2CH), 123.3 (CH), 123.0 (CH), 122.8 (C), 122.4 (CH), 108.5 (CH), 71.1 (C), 70.7 (C), 61.2 (CH, q, J = 31 Hz), 48.5 (CH), 26.4 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.96; HRMS (ESI) m/z : 544.1090 [M + Na]⁺, calcd for C₂₇H₁₈F₃N₃O₅Na; Found 544.1083.

2-(1''-methyl-1,2'',3-trioxo-5'-(trifluoromethyl)-1,3-dihydrodispiro[indene-2,3'-pyrrolidine-2',3''-indolin]-4'-yl)benzonitrile (4r):



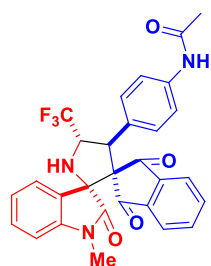
Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4p** in 82% yield as a pale yellow solid with M. P. 265 - 270 °C.; IR (neat) ν_{\max} 1737, 1699, 1494, 1253, 1136 and 761 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.78 (1H, d, $J = 6.9$ Hz), 7.67 – 7.48 (5H, m), 7.37 (1H, t, $J = 7.4$ Hz), 7.21 – 7.11 (3H, m), 6.80 (1H, t, $J = 7.5$ Hz), 6.59 (1H, d, $J = 7.7$ Hz), 6.15 (1H, br s), 5.16 (1H, br s), 3.2 – 3.19 (4H, m); $^{13}\text{C NMR}$ (100 MHz, $\text{DMSO}-d_6$, DEPT-135) δ 198.9 (C, C=O), 193.5 (C, C=O), 174.6 (C, N-C=O), 144.6 (C), 142.3 (2C), 141.6 (2C), 136.6 (C), 136.3 (CH), 136.0 (CH), 134.0 (CH), 132.5 (CH), 130.8 (CH), 128.6 (CH), 125.5 (CF_3 , q, $J = 279$ Hz), 124.7 (CH), 123.5 (CH), 122.9 (CH), 122.8 (CN), 122.1 (CH), 108.4 (2CH), 70.8 (C), 70.6 (C), 62.9 (CH, q, $J = 32$ Hz), 46.6 (CH), 26.6 (CH_3); $^{19}\text{F NMR}$ (376MHz, CDCl_3) δ -72.83; HRMS (ESI) m/z : 524.1192 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{28}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_3\text{Na}$; Found 524.1183.

4-(1''-methyl-1,2'',3-trioxo-5'-(trifluoromethyl)-1,3-dihydrodispiro[indene-2,3'-pyrrolidine-2',3''-indolin]-4'-yl)benzonitrile (4s):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4s** in 73% yield as a white solid with M. P. 235 – 240 °C.; IR (neat) ν_{\max} 2233, 1699, 1352, 1261, 1118 and 731 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.71 – 7.58 (4H, d, m), 7.43 – 7.35 (4H, m), 7.15 - 7.10 (2H, m), 7.87 (2H, t, $J = 7.6$ Hz), 6.59 (1H, d, $J = 7.8$ Hz), 5.50 (1H, d, $J = 10.6$ Hz), 5.29 - 5.26 (1H, m), 3.19 (1H, d, $J = 8.9$ Hz), 3.14 (3H, s); $^{13}\text{C NMR}$ (100 MHz, CDCl_3 , DEPT-135) δ 198.2 (C, C=O), 194.8 (C, C=O), 174.9 (C, N-C=O), 144.2 (C), 142.1 (C), 141.5 (C), 138.4 (C), 136.4 (CH), 136.3 (2CH), 130.9 (CH), 129.7 (2CH), 125.5 (CF_3 , q, $J = 279$ Hz), 124.6 (CH), 123.3 (CH), 123.0 (CH), 122.9 (C), 122.4 (CH), 118.2 (C), 112.0 (C), 108.5 (CH), 70.9 (C), 70.7 (C), 61.3 (CH, q, $J = 31$ Hz), 48.9 (CH), 26.4 (CH_3); $^{19}\text{F NMR}$ (376MHz, CDCl_3) δ -72.95; HRMS (ESI) m/z : 524.1192 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{28}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_3\text{Na}$; Found 524.1216.

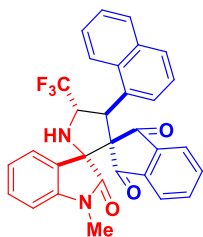
N-(4-(1''-methyl-1,2'',3-trioxo-5'-(trifluoromethyl)-1,3-dihydrodispiro[indene-2,3'-pyrrolidine-2',3''-indolin]-4'-yl)phenyl)acetamide (4t):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4t** in 74% yield as a white solid with M. P. 213 – 215 °C.; IR (neat) ν_{\max} 2360, 1705, 1610, 1261, 1120 and 754 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.71 – 7.57 (4H, d, m), 7.24 – 7.09 (6H, m), 7.00 (1H, br, s), 6.80 (1H, t, $J = 7.4$ Hz), 6.58 (1H, d, $J = 7.3$ Hz), 5.41 (1H, d, $J = 10.2$ Hz), 5.22 - 5.20 (1H, m), 3.14 (4H, s), 2.07 (3H, s); $^{13}\text{C NMR}$ (100 MHz, $\text{CDCl}_3 + \text{DMSO}-d_6$ (2drops), DEPT-135) δ 198.1 (C, C=O), 195.4 (C, C=O), 175.3 (C, N-C=O), 168.8 (C, N-C=O), 143.7 (C), 142.0 (C), 142.0 (C), 141.6 (C), 138.7 (C), 136.0 (CH), 135.9 (CH), 130.4 (CH), 129.0 (2CH), 127.2 (C), 125.9 (CF_3 , q, $J = 279$ Hz), 125.0

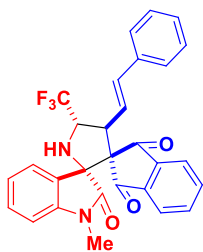
(CH), 123.1 (C), 122.8 (CH), 122.8 (CH), 122.0 (CH), 119.2 (2CH), 108.1 (CH), 71.1 (C), 70.7 (C), 61.1 (CH, q, $J = 30$ Hz), 48.5 (CH), 26.2 (CH₃), 24.1 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.75; HRMS (ESI) m/z : 556.1454 [M + Na]⁺, calcd for C₂₉H₂₂F₃N₃O₄Na; Found 556.1454.

1''-methyl-4'-(naphthalen-1-yl)-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4u):



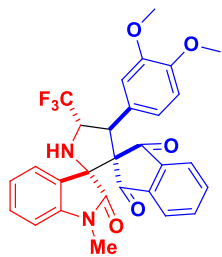
Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4u** in 79% yield as a pale yellow solid with M. P. 258 - 262 °C.; IR (neat) ν_{\max} 2360, 1703, 1612, 1263, 1120 and 758 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 8.36 (1H, d, $J = 8.7$ Hz), 7.65 (1H, d, $J = 7.7$ Hz), 7.61 (1H, d, $J = 8.1$ Hz), 7.56 – 7.51 (3H, m), 7.47 (1H, t, $J = 6.4$ Hz), 7.40 – 7.33 (2H, m), 7.29 – 7.22 (3H, m), 7.15 (1H, t, $J = 7.7$ Hz), 6.83 (1H, t, $J = 7.6$ Hz), 6.71 (1H, d, $J = 10.5$ Hz), 6.65 (1H, d, $J = 7.8$ Hz), 5.39 - 5.29 (1H, m), 3.30 (1H, d, $J = 9.1$ Hz), 3.25 (3H, s); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 199.2 (C, C=O), 195.6 (C, C=O), 175.8 (C, N-C=O), 144.6 (C), 142.2 (C), 141.5 (C), 135.6 (CH), 135.6 (CH), 133.8 (C), 132.0 (C), 130.6 (CH), 128.5 (CH), 128.5 (CH), 128.4 (CH), 126.8 (CH), 125.8 (CH), 125.8 (CF₃, q, $J = 278$ Hz), 125.7 (CH), 125.1 (CH), 124.5 (CH), 123.8 (CH), 123.7 (C), 122.8 (CH), 122.6 (CH), 122.3 (CH), 108.4 (CH), 71.0 (C), 70.3 (C), 62.3 (CH, q, $J = 30$ Hz), 43.6 (CH), 26.5 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.74; HRMS (ESI) m/z : 549.1396 [M + Na]⁺, calcd for C₃₁H₂₁F₃N₂O₃Na; Found 549.1413.

(E)-1''-methyl-4'-styryl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4v):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4v** in 56% yield as a yellowish white solid with M. P. 230 - 234 °C.; IR (neat) ν_{\max} 2360, 1703, 1612, 1263, 1120 and 758 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.87 (1H, d, $J = 7.52$ Hz), 7.73 – 7.62 (3H, m), 7.20 – 7.09 (7H, m), 6.80 (1H, t, $J = 7.6$ Hz), 6.62 – 6.57 (2H, m), 5.91 (1H, dd, $J = 9.6, 9.6$ Hz), 4.91 (1H, t, $J = 9.6$ Hz), 4.78 -4.70 (1H, m), 3.13 (3H, s), 3.06 (1H, d, $J = 8.8$ Hz); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 199.2 (C, C=O), 195.0 (C, C=O), 175.2 (C, N-C=O), 144.2 (C), 142.6 (C), 141.7 (C), 136.3 (CH), 136.2 (CH), 136.1 (CH), 135.9 (C), 130.6 (CH), 128.4 (2CH), 127.9 (CH), 126.5 (2CH), 125.7 (CF₃, q, $J = 278$ Hz), 124.4 (CH), 123.4 (CH), 123.3 (C), 122.9 (CH), 122.2 (CH), 121.3 (CH), 108.3 (CH), 70.9 (C), 70.1 (C), 63.2 (CH, q, $J = 30$ Hz), 48.2 (CH), 26.3 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.61; HRMS (ESI) m/z : 525.1396 [M + Na]⁺, calcd for C₂₉H₂₁F₃N₂O₃Na; Found 525.1412.

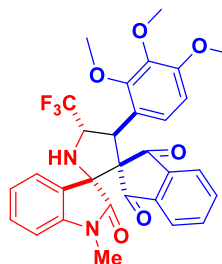
4'-(3,4-dimethoxyphenyl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4w):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4w** in 74% yield as a white solid with M. P. 222 - 224 °C.; IR (neat) ν_{\max} 2360, 1703, 1261, 1026 and 761 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.73 - 7.69 (1H, m), 7.64 - 7.55 (3H, m), 7.17 (1H, d, $J = 7.6$ Hz), 7.12 (1H, t, $J = 7.7$ Hz), 6.83 - 6.87 (2H, m), 6.68 (1H, s), 6.60 (2H, d, $J = 8.2$ Hz), 5.41 (1H, d, $J = 10.6$ Hz), 5.23 - 5.13 (1H, m), 3.74 (3H, s), 3.71 (3H, s), 3.16 (3H, s), 3.15 (1H, d, $J = 8.9$ Hz); ^{13}C

NMR (100 MHz, CDCl_3 , DEPT-135) δ 199.1 (C, C=O), 195.8 (C, C=O), 175.5 (C, N-C=O), 148.4 (2C), 144.3 (C), 142.5 (C), 141.8 (C), 136.0 (2CH), 135.9 (CH), 130.6 (CH), 125.8 (CF_3 , q, $J = 279$ Hz), 124.8 (CH), 124.6 (C), 123.0 (CH), 122.3 (CH), 120.8 (CH), 111.9 (CH), 110.8 (CH), 108.3 (CH), 70.9 (C), 70.5 (C), 61.3 (CH, q, $J = 31$ Hz), 55.8 (CH_3), 55.6 (CH_3), 49.6 (CH), 26.4 (CH_3); $^{19}\text{F NMR}$ (376MHz, CDCl_3) δ -72.74; HRMS (ESI) m/z : 559.1451 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{29}\text{H}_{23}\text{F}_3\text{N}_2\text{O}_5\text{Na}$; Found 559.1451.

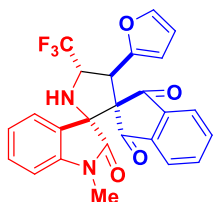
1''-methyl-5'-(trifluoromethyl)-4'-(2,3,4-trimethoxyphenyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4x):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4x** in 60% yield as a white solid with M. P. 228 - 232 °C.; IR (neat) ν_{\max} 1741, 1693, 1494, 1153, 1006 and 858 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.67 - 7.64 (2H, m), 7.58 - 7.55 (2H, m), 7.22 (1H, d, $J = 7.2$ Hz), 7.15 (1H, t, $J = 7.7$ Hz), 6.92 (1H, d, $J = 8.9$ Hz), 6.81 (1H, t, $J = 7.6$ Hz), 6.64 (1H, d, $J = 7.8$ Hz), 6.44 (1H, d, $J = 8.8$ Hz), 5.90 (1H, d, $J = 10.6$ Hz), 5.10 - 4.97 (1H, m), 3.81 (3H, s),

3.70 (3H, s), 3.50 (3H, s), 3.23 (3H, s), 3.17 (1H, d, $J = 9.7$ Hz); $^{13}\text{C NMR}$ (100 MHz, CDCl_3 , DEPT-135) δ 199.5 (C, C=O), 194.7 (C, C=O), 175.7 (C, N-C=O), 153.0 (C), 152.3 (C), 144.8 (C), 142.9 (C), 141.7 (C), 141.3 (C), 135.7 (CH), 135.3 (CH), 130.4 (CH), 125.9 (CF_3 , q, $J = 278$ Hz), 125.1 (CH), 124.0 (C), 122.9 (2C), 122.5 (CH), 122.1 (CH), 118.4 (C), 108.2 (CH), 106.5 (CH), 70.9 (C), 69.7 (C), 61.4 (CH, q, $J = 30$ Hz), 60.8 (CH_3), 60.4 (CH_3), 55.7 (CH_3), 43.5 (CH), 26.4 (CH_3); $^{19}\text{F NMR}$ (376MHz, CDCl_3) δ -72.20; HRMS (ESI) m/z : 589.1556 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{30}\text{H}_{25}\text{F}_3\text{N}_2\text{O}_6\text{Na}$; Found 589.1571.

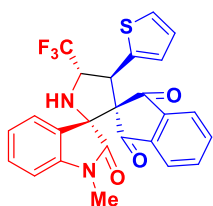
4'-(furan-2-yl)-1''-methyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4y):



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4y** in 60% yield as a white solid with M. P. 221 - 224 °C.; IR (neat) ν_{\max} 1753, 1708, 1259, 1126 and 750 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.08 (1H, d, $J = 6.7$ Hz), 7.72 (1H, d, $J = 7.9$ Hz), 7.68 - 7.62 (2H, m), 7.18 - 7.12 (2H, m), 7.01 (1H, s), 6.82 (1H, t, $J = 7.6$ Hz), 6.61 (1H, d, $J = 7.8$ Hz), 6.15 (1H, d, $J = 3.2$

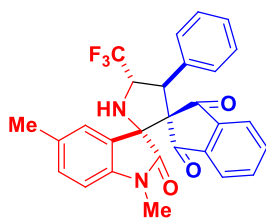
H_z), 6.06 – 6.05 (1H, m), 5.53 (1H, d, *J* = 10.3 Hz), 5.11 - 5.05 (1H, m), 3.20 – 3.16 (4H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 198.1 (C, C=O), 194.8 (C, C=O), 175.2 (C, N-C=O), 147.2 (C), 144.4 (C), 142.4 (CH), 142.2 (C), 141.4 (CH), 135.9 (2CH), 130.7 (CH), 125.5 (CF₃, q, *J* = 278 Hz), 124.8 (CH), 123.2 (CH), 123.1 (C), 122.9 (CH), 122.3 (CH), 110.2 (CH), 109.3 (CH), 108.4 (CH), 70.1 (C), 69.1 (C), 61.5 (CH, q, *J* = 31 Hz), 43.8 (CH), 26.4 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -73.01; HRMS (ESI) *m/z*: 489.1032 [M + Na]⁺, calcd for C₂₅H₁₇F₃N₂O₄Na; Found 489.1039.

1''-methyl-4'-(thiophen-2-yl)-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4z):



Prepared by following general procedure D purified by centrifuge using hexane and isolated product **4z** in 64% yield as a white solid with M. P. 242 - 245 °C.; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak I-A column (hexane/EtOAc = 75:25, flow rate 0.5 mL/min, λ = 254 nm), *t_R* = 19.104 min (minor), *t_R* = 51.333 min (major), [*α*]_D²⁵ = -16.321 (CHCl₃, *c* = 0.11 g/100ml for 90%*ee*); IR (neat) *ν*_{max} 1703, 1618, 1492, 1236, 1120 and 732 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.78 (1H, d, *J* = 7.0 Hz), 7.69 – 7.58 (3H, m), 7.17 – 7.11 (2H, m), 6.98 (1H, d, *J* = 5.1 Hz), 6.91 (1H, d, *J* = 3.4 Hz), 6.82 (1H, t, *J* = 7.5 Hz), 6.73 – 6.71 (1H, m), 6.60 (1H, d, *J* = 7.8 Hz), 5.74 (1H, d, *J* = 10.4 Hz), 5.14 - 5.03 (1H, m), 3.17 (1H, d, *J* = 10.6 Hz), 3.15 (3H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 198.9 (C, C=O), 195.0 (C, C=O), 175.2 (C, N-C=O), 144.3(C), 142.5 (CH), 141.9 (C), 135.9 (2CH), 134.9 (CH), 134.7 (CH), 127.7 (CH), 126.6 (CH), 125.5 (CF₃, q, *J* = 279 Hz), 125.3 (CH), 124.7 (CH), 123.3 (CH), 123.2 (C), 122.9 (CH), 122.3 (C), 108.4 (CH), 70.6 (C), 70.5 (C), 63.4 (CH, q, *J* = 31 Hz), 45.3 (CH), 26.4 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -72.74; HRMS (ESI) *m/z*: 505.0804 [M + Na]⁺, calcd for C₂₅H₁₇F₃N₂O₃SNa; Found 505.0809.

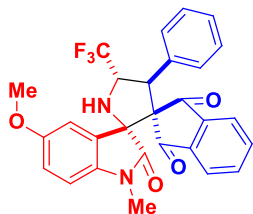
1'',5''-dimethyl-4'-phenyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4a'):



Prepared by following general procedure C purified by centrifuge using hexane and isolated product **4a'** in 89% yield as a white solid with M. P. 260 - 265 °C.; IR (neat) *ν*_{max} 1722, 1604, 1352, 1253 and 746 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.70 - 7.53 (4H, m), 7.21 (2H, d, *J* = 7.4 Hz), 7.11 – 7.02 (3H, m), 6.99 (1H, s), 6.90 (1H, d, *J* = 7.9 Hz), 6.56 (1H, d, *J* = 7.9 Hz), 5.46 (1H, d, *J* = 10.6 Hz), 5.30 - 5.20 (1H, m), 3.15 (1H, d, *J* = 12.1 Hz), 3.13 (3H, s), 2.16 (3H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 198.8 (C, C=O), 195.5 (C, C=O), 175.4 (C, N-C=O), 142.4 (C), 141.8 (C), 141.8 (C), 135.8 (CH), 132.6 (C), 131.8 (C), 130.8 (CH), 128.8 (2CH), 128.5 (2CH), 127.9 (CH), 125.8 (CF₃, q, *J* = 278 Hz), 125.6 (CH), 123.5 (C), 123.1 (CH), 122.7 (2CH), 108.0 (CH), 71.0 (C), 70.7 (C),

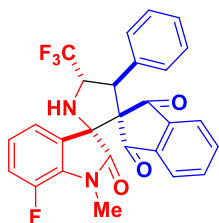
61.1 (CH, q, $J = 31$ Hz), 49.6 (CH), 26.4 (CH₃), 21.0 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.73; HRMS (ESI) m/z : 513.1396 [M + Na]⁺, calcd for C₂₈H₂₁F₃N₂O₃Na; Found 513.1410.

5''-methoxy-1''-methyl-4'-phenyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4b'):



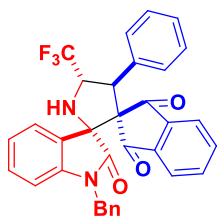
Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4b'** in 94% yield as a pale yellow solid with M. P. 240 - 245 °C.; IR (neat) ν_{\max} 1703, 1496, 1253, 1112 and 696 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.71 - 7.54 (4H, m), 7.21 (2H, d, $J = 7.2$ Hz), 7.10 - 7.01 (3H, m), 6.83 (1H, d, $J = 2.4$ Hz), 6.64 (1H, dd, $J = 2.4, 2.4$ Hz), 6.51 (1H, d, $J = 8.8$ Hz), 5.51 (1H, d, $J = 10.6$ Hz), 5.28 - 5.25 (1H, m), 3.67 (3H, s), 3.18 (1H, d, $J = 8.4$ Hz), 3.10 (3H, s); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 198.9 (C, C=O), 195.4 (C, C=O), 175.2 (C, N-C=O), 155.5 (C), 142.4 (C), 141.7 (C), 137.6 (C), 135.9 (CH), 132.5 (C), 128.7 (2CH), 128.5 (2CH), 128.0 (CH), 125.8 (CF₃, q, $J = 278$ Hz), 124.7 (C), 123.1 (CH), 122.8 (CH), 115.1 (CH), 112.3 (CH), 108.8 (CH), 71.0 (C), 70.1 (C), 61.1 (CH, q, $J = 31$ Hz), 55.8 (O-CH₃), 49.7 (CH), 26.5 (CH₃); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.71; HRMS (ESI) m/z : 529.1345 [M + Na]⁺, calcd for C₂₈H₂₁F₃N₂O₄Na; Found 529.1336.

7''-fluoro-1''-methyl-4'-phenyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4c'):



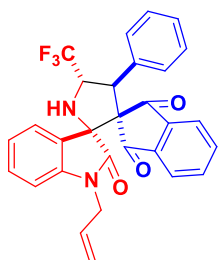
Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4c'** in 88% yield as a white solid with M. P. 250 - 255 °C.; IR (neat) ν_{\max} 1703, 1629, 1244, 1159 and 725 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.69 - 7.56 (4H, m), 7.19 (2H, d, $J = 7.6$ Hz), 7.10 - 6.99 (4H, m), 6.88 - 6.73 (2H, m), 5.43 (1H, d, $J = 10.6$ Hz), 5.29 - 5.19 (1H, m), 3.39 (3H, d, $J = 2.8$ Hz), 3.16 (1H, d, $J = 9.2$ Hz); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 198.6 (C, C=O), 195.3 (C, C=O), 175.2 (C, N-C=O), 147.2 (C, CF, d, $J = 242$ Hz), 142.3 (C), 141.6 (C), 136.0 (2CH, d, $J = 8$ Hz), 132.2 (C), 131.1 (C, d, $J = 9$ Hz), 128.7 (2CH), 128.5 (2CH), 128.1 (CH), 126.5 (C, d, $J = 3$ Hz), 125.7 (CF₃, q, $J = 279$ Hz), 123.0 (2CH, d, $J = 36$ Hz), 122.8 (CH), 122.7 (CH), 120.8 (CH, d, $J = 3$ Hz), 118.7 (CH, d, $J = 19$ Hz), 71.0 (C), 70.5 (C, d, $J = 3$ Hz), 61.1 (CH, q, $J = 31$ Hz), 49.7 (CH), 28.9 (CH₃, d, $J = 6$ Hz); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.76, -135.26; HRMS (ESI) m/z : 517.1145 [M + Na]⁺, calcd for C₂₇H₁₈F₄N₂O₃Na; Found 517.1159.

1''-benzyl-4'-phenyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4d'):



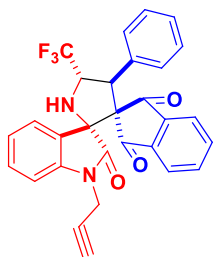
Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4d'** in 64% yield as a white solid with M. P. 275 - 280 °C.; IR (neat) ν_{\max} 1703, 1610, 1456, 1255, 1130 and 758 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.68 - 7.52 (4H, m), 7.35 (4H, d, J = 4.4 Hz), 7.30 - 7.26 (3H, m), 7.18 (1H, d, J = 7.6 Hz), 7.13 - 7.04 (3H, m), 6.97 (1H, t, J = 9.4 Hz), 6.77 (1H, t, J = 7.6 Hz), 6.44 (1H, d, J = 8 Hz), 5.50 (1H, d, J = 10.6 Hz), 5.35 - 5.25 (2H, m), 4.41 (1H, d, J = 15.5 Hz), 3.19 (1H, d, J = 9.3 Hz); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 198.6 (C, C=O), 195.4 (C, C=O), 175.4 (C, N-C=O), 143.6 (C), 142.4 (C), 141.8 (C), 135.9 (CH), 135.9 (CH), 135.6 (CH), 132.5 (C), 130.5 (CH), 128.9 (2CH), 128.5 (2CH), 128.5 (2CH), 128.0 (CH), 127.7 (2CH), 127.6 (CH), 125.8 (CF₃, q, J = 279 Hz), 124.8 (CH), 123.6 (C), 122.9 (CH), 122.9 (CH), 122.3 (CH), 109.4 (CH), 71.0 (C), 70.9 (C), 61.1 (CH, q, J = 31 Hz), 49.5 (CH), 44.4 (CH₂); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.88; HRMS (ESI) m/z : 575.1553 [M + Na]⁺, calcd for C₃₃H₂₃F₃N₂O₃Na; Found 575.1555.

1''-allyl-4'-phenyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4e')



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4e'** in 70% yield as a white solid with M. P. 240 - 245 °C.; IR (neat) ν_{\max} 1703, 1612, 1359, 1263 and 754 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.69 - 7.53 (4H, m), 7.23 - 7.17 (3H, m), 7.11 - 7.02 (4H, m), 6.80 (1H, t, J = 7.6 Hz), 6.59 (1H, d, J = 7.6 Hz), 5.87 - 5.77 (1H, m), 5.44 (1H, d, J = 10.6 Hz), 5.32 - 5.16 (3H, m), 4.16 - 4.56 (1H, m), 4.01 (1H, dd, J = 6, 5.9 Hz), 3.17 (1H, d, J = 8.8 Hz); **¹³C NMR (100 MHz, CDCl₃, DEPT-135)** δ 198.7 (C, C=O), 195.3 (C, C=O), 175.1 (C, N-C=O), 143.5 (C), 142.4 (C), 141.7 (C), 135.9 (CH), 135.8 (CH), 132.5 (C), 131.3 (CH), 130.4 (CH), 128.8 (CH), 128.5 (2CH), 128.0 (CH), 125.8 (CF₃, q, J = 278 Hz), 124.8 (CH), 123.5 (C), 122.9 (CH), 122.8 (CH), 122.2 (CH), 117.8 (CH₂), 109.2 (CH), 71.1 (C), 70.7 (C), 61.1 (CH, q, J = 31 Hz), 49.5 (CH), 42.7 (CH₂); **¹⁹F NMR (376MHz, CDCl₃)** δ -72.81; HRMS (ESI) m/z : 525.1396 [M + Na]⁺, calcd for C₂₉H₂₁F₃N₂O₃Na; Found 525.1410.

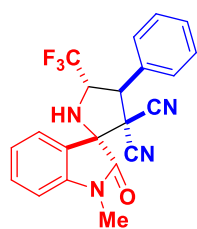
4'-phenyl-1''-(prop-2-yn-1-yl)-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (4f')



Prepared by following general procedure **C** purified by centrifuge using hexane and isolated product **4f'** in 78% yield as a white solid with M. P. 253 - 257 °C.; IR (neat) ν_{\max} 1716, 1612, 1357, 1261 and 752 cm⁻¹; **¹H NMR (400 MHz, CDCl₃)** δ 7.68 - 7.52 (4H, m), 7.22 - 7.20 (3H, m), 7.16 - 7.02 (4H, m), 6.84 (2H, q, J = 7.6 Hz), 5.39 (1H, d, J = 10.6 Hz), 5.32 - 5.22 (1H, m), 4.55 (1H, dd, J = 2.4, 2.4 Hz), 4.40 (1H, dd, J = 2.4, 2.4 Hz), 3.19 (1H, d, J = 9.1 Hz), 2.2 (1H, t, J = 2.4 Hz); **¹³C NMR**

(100 MHz, CDCl₃, DEPT-135) δ 198.6 (C, C=O), 195.1 (C, C=O), 174.3 (C, N-C=O), 142.4 (C), 142.2 (C), 141.7 (C), 135.9 (CH), 135.8 (CH), 132.4 (C), 130.5 (CH), 128.8 (2CH), 128.5 (2CH), 128.0 (CH), 125.7 (CF₃, q, *J* = 278Hz), 124.9 (CH), 123.4 (C), 123.0 (CH), 122.8 (CH), 122.6 (CH), 109.4 (CH), 76.4 (CH), 72.5 (C), 71.0 (C), 70.7 (C), 61.1 (CH, q, *J* = 31 Hz), 49.5 (CH), 29.4 (CH₂); ¹⁹F NMR (376MHz, CDCl₃) δ -72.87; HRMS (ESI) *m/z*: 523.1240 [M + Na]⁺, calcd for C₂₉H₁₉F₃N₂O₃Na; Found 5223.1245.

(3R,4'S,5'S)-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (4aa''):



Prepared by following general procedure **C** purified by column chromatography using hexane/EtOAc and isolated product **4aa''** in 58% yield as a white solid with M. P. 187 - 194 °C.; IR (neat) ν_{\max} 2250, 1701, 1454, 1176, 1138 and 694 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.79 (1H, d, *J* = 7.4 Hz), 7.60 – 7.58 (2H, m), 7.50 -7.47 (4H, m), 7.22 (1H, t, *J* = 7.7 Hz), 6.93 (1H, d, *J* = 7.8 Hz), 5.44 (1H, d, *J* = 10.8 Hz), 4.84 – 4.74 (1H, m), 3.27 (3H, s), 2.94 (1H, d, *J* = 7.6 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 173.3 (C, N-C=O), 144.4 (C), 132.5 (CH), 130.1 (CH), 129.4 (CH), 129.5 (C), 128.9 (CH), 124.9 (CH), 124.5 (CF₃, q, *J* = 278 Hz), 123.9 (CH), 121.9 (C), 111.2 (2CN), 109.4 (CH), 70.8 (C), 59.9 (CH, q, *J* = 32 Hz), 51.6 (C), 51.4 (CH), 26.7 (CH₃); ¹⁹F NMR (376MHz, CDCl₃) δ -73.469; HRMS (ESI) *m/z*: 419.1090 [M + Na]⁺, calcd for C₂₁H₁₅F₃N₄ONa; Found 419.1098.

Crystal Structure of 4a

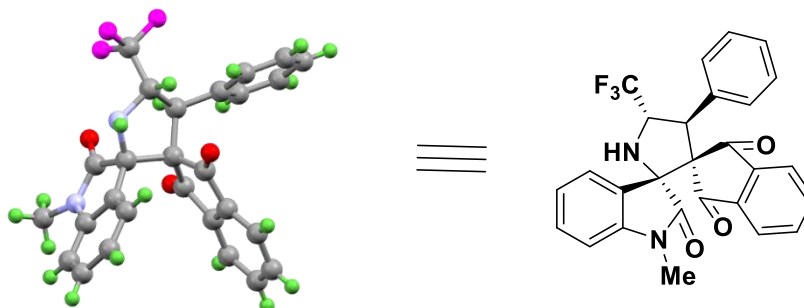
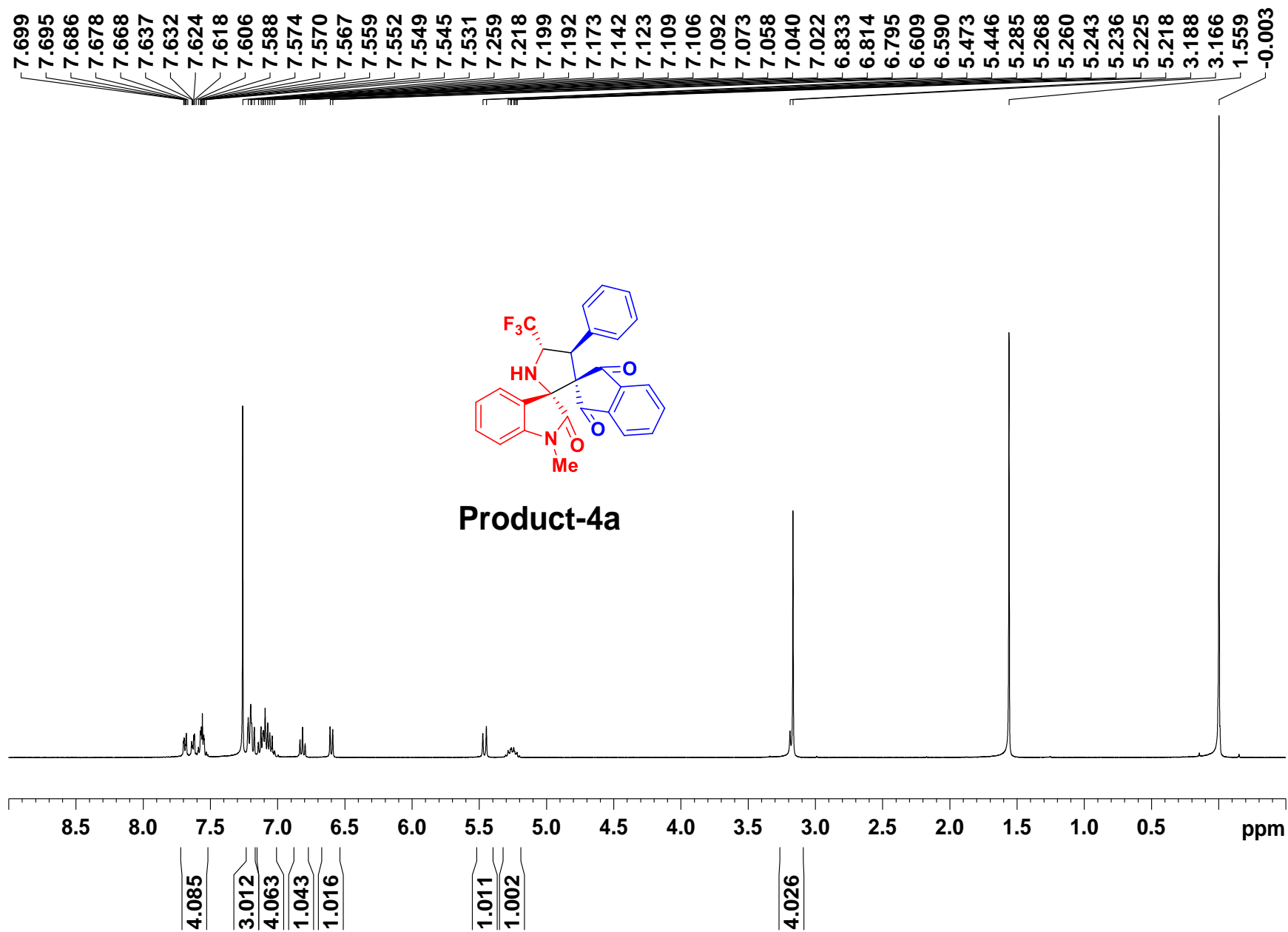


Table 1. Crystal data and structure refinement for me.

Identification code	ME
Empirical formula	C ₂₇ H ₁₉ F ₃ N ₂ O ₃
Formula weight	476.44
Temperature	296(2) K
Wavelength	0.71073 Å

Crystal system	Orthorhombic
Space group	Pbca
Unit cell dimensions	a = 12.0771(4) Å α = 90°. b = 19.0403(7) Å β = 90°. c = 20.1521(8) Å γ = 90°.
Volume	4634.0(3) Å ³
Z	8
Density (calculated)	1.366 Mg/m ³
Absorption coefficient	0.106 mm ⁻¹
F(000)	1968
Crystal size	0.200 x 0.150 x 0.100 mm ³
Theta range for data collection	2.139 to 25.672°.
Index ranges	-14 ≤ h ≤ 14, -22 ≤ k ≤ 23, -24 ≤ l ≤ 24
Reflections collected	69301
Independent reflections	4398 [R(int) = 0.0962]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7452 and 0.6676
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	4398 / 0 / 322
Goodness-of-fit on F ²	1.106
Final R indices [I > 2σ(I)]	R1 = 0.0447, wR2 = 0.0984
R indices (all data)	R1 = 0.1227, wR2 = 0.1421
Extinction coefficient	0.0010(2)
Largest diff. peak and hole	0.253 and -0.188 e.Å ⁻³



197.62
195.33

175.18

143.61
141.74
141.46
136.05
135.91
132.79
130.31
130.16
128.59
128.24
127.74
127.38
125.26
124.60
122.98
122.64
121.89
121.82
108.06

78.54

78.21

77.89

71.13

70.80

61.16

60.87

60.56

60.27

48.76

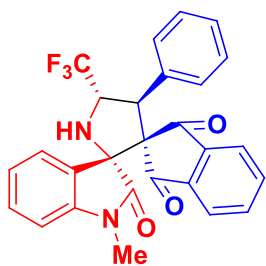
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39.88

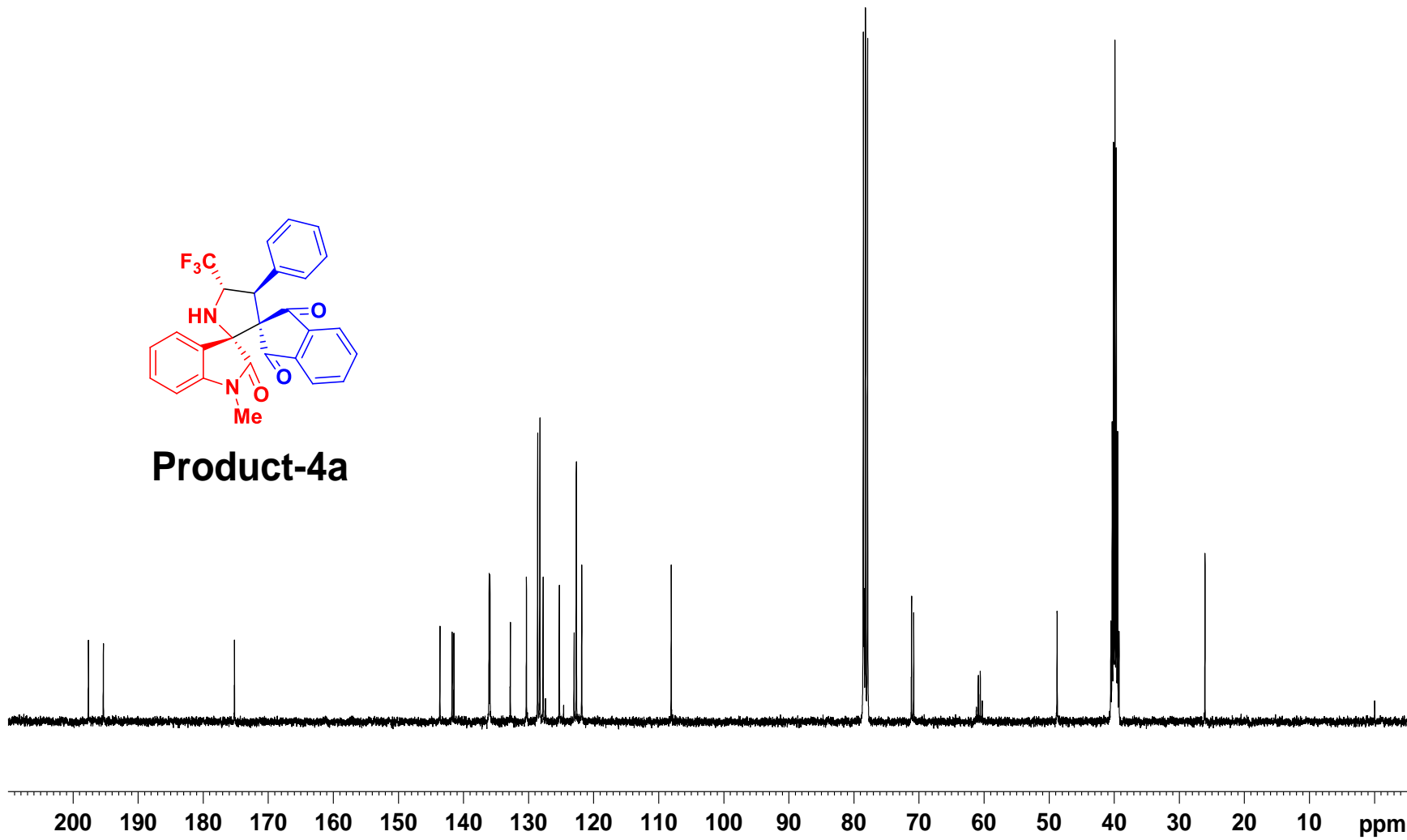
39.67

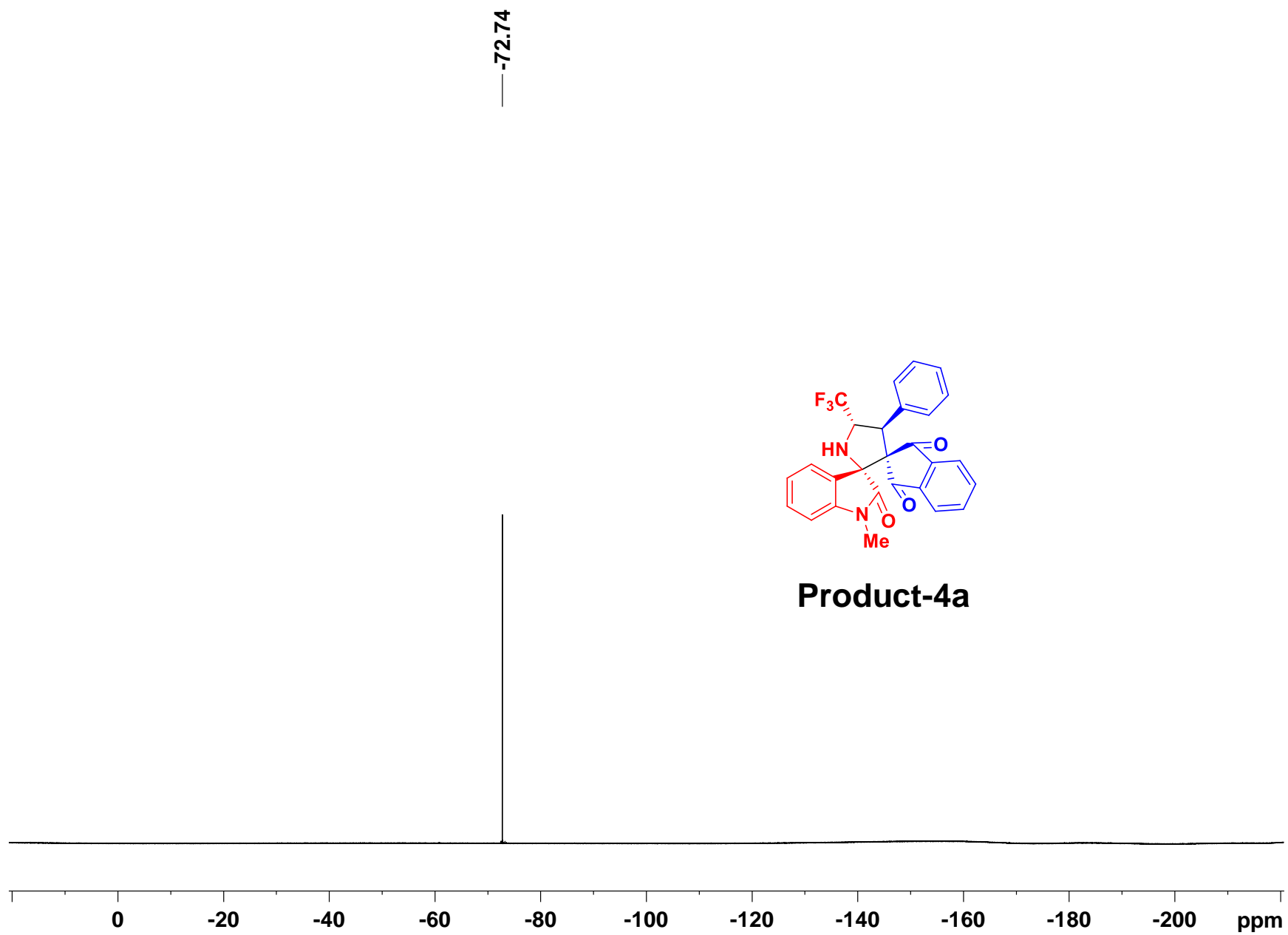
26.04

-0.01

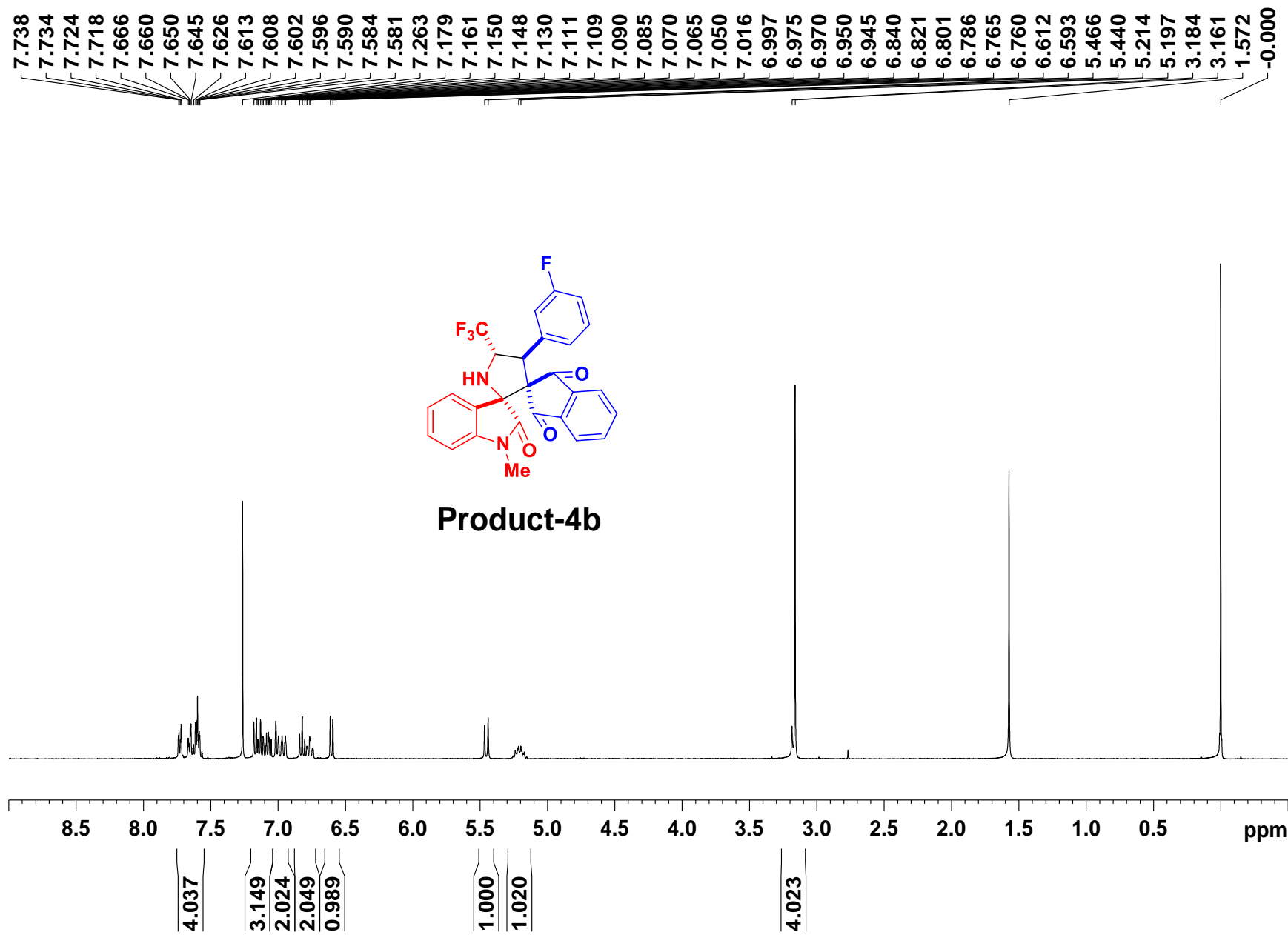


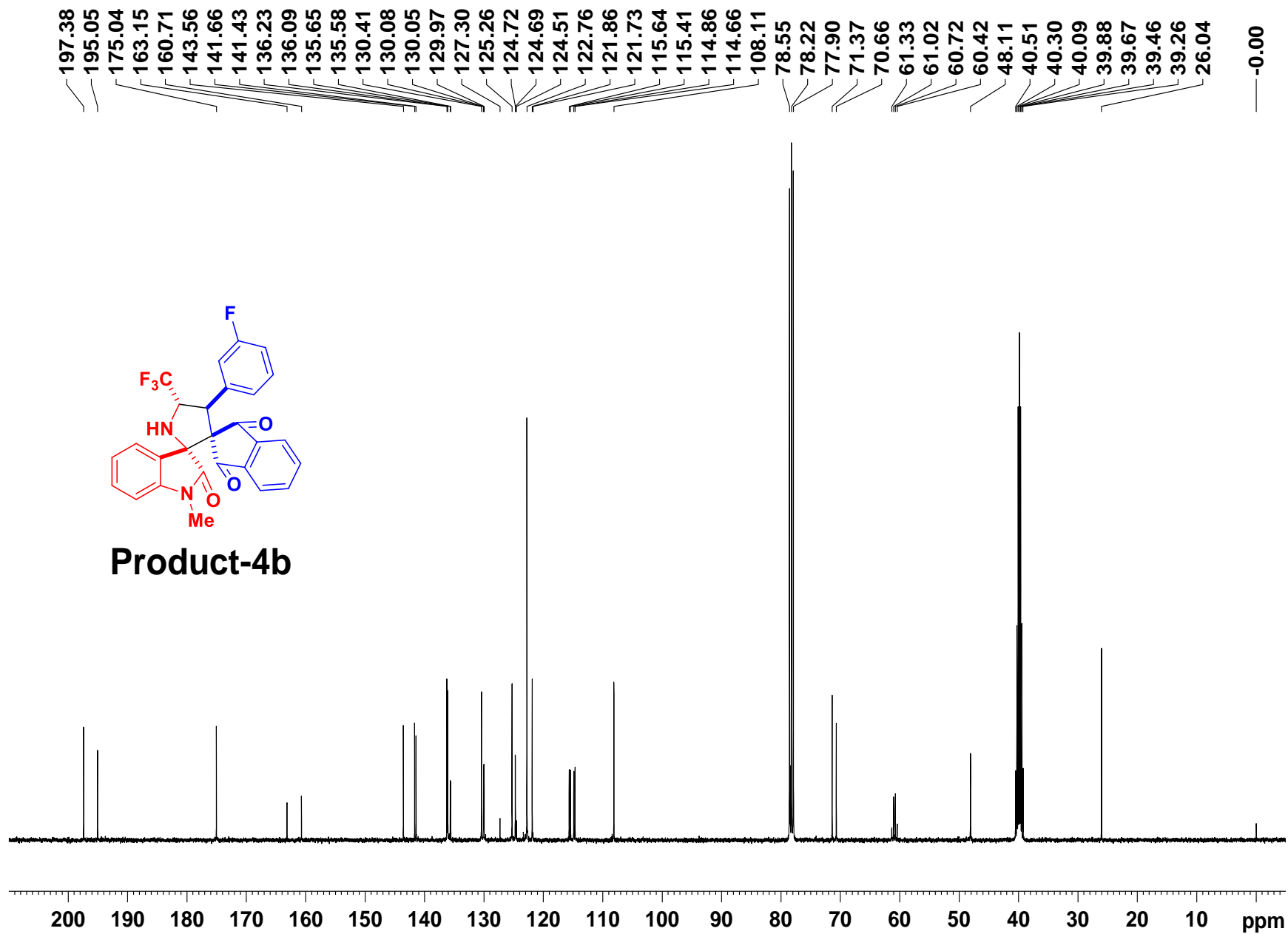
Product-4a



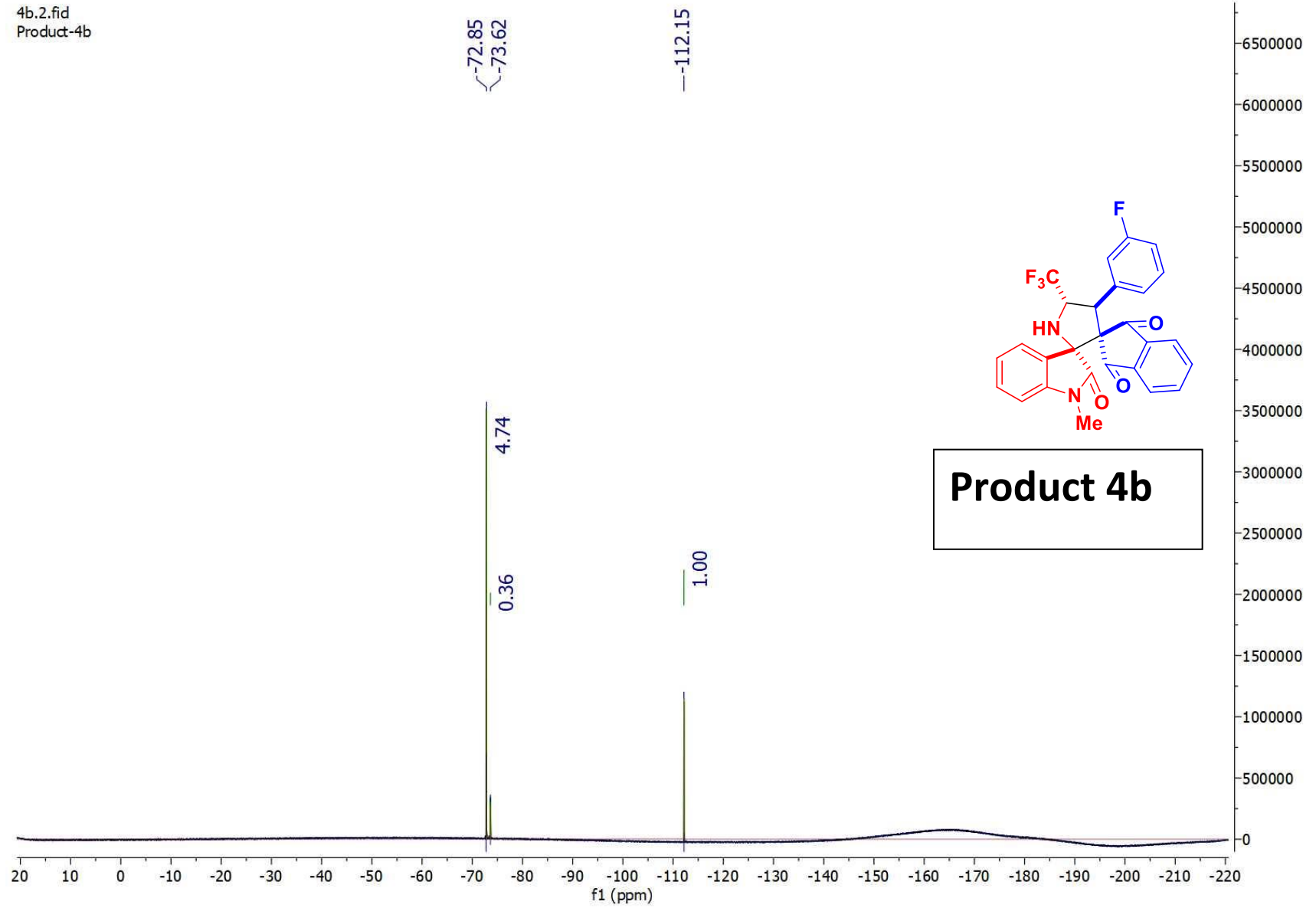


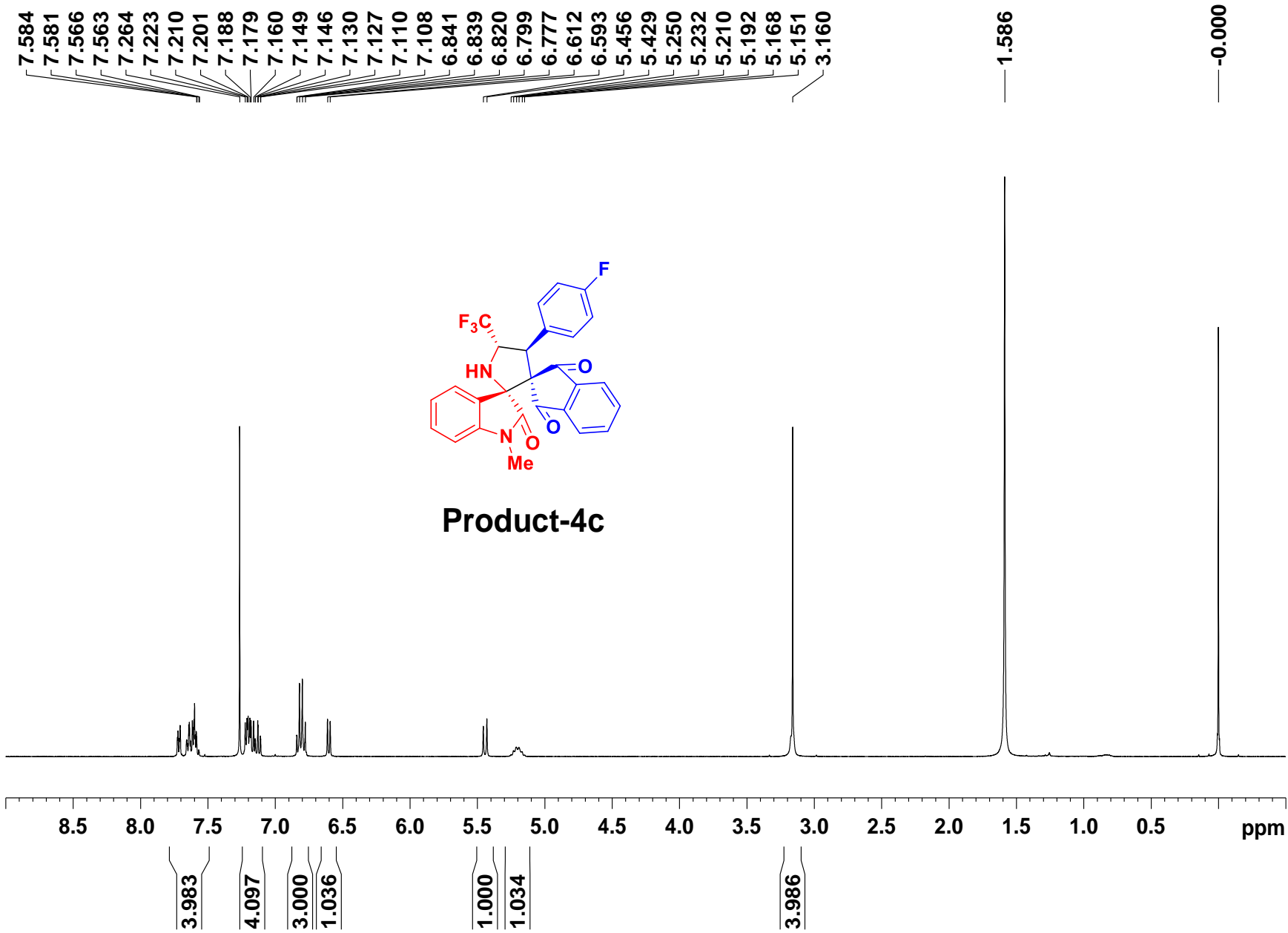
S21





4b.2.fid
Product-4b





198.80
195.36

175.30
163.46
161.00
144.27
142.33
141.68
136.06
130.66
130.49
130.41
129.87
128.38
128.34
127.09
124.69
124.31
123.38
123.13
122.87
122.31
121.53
115.59
115.38
108.36

77.35

77.04

76.72

70.82

70.65

61.82

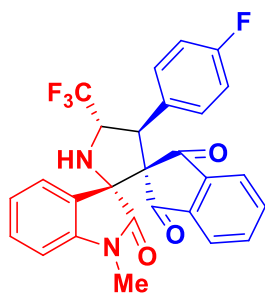
61.51

61.21

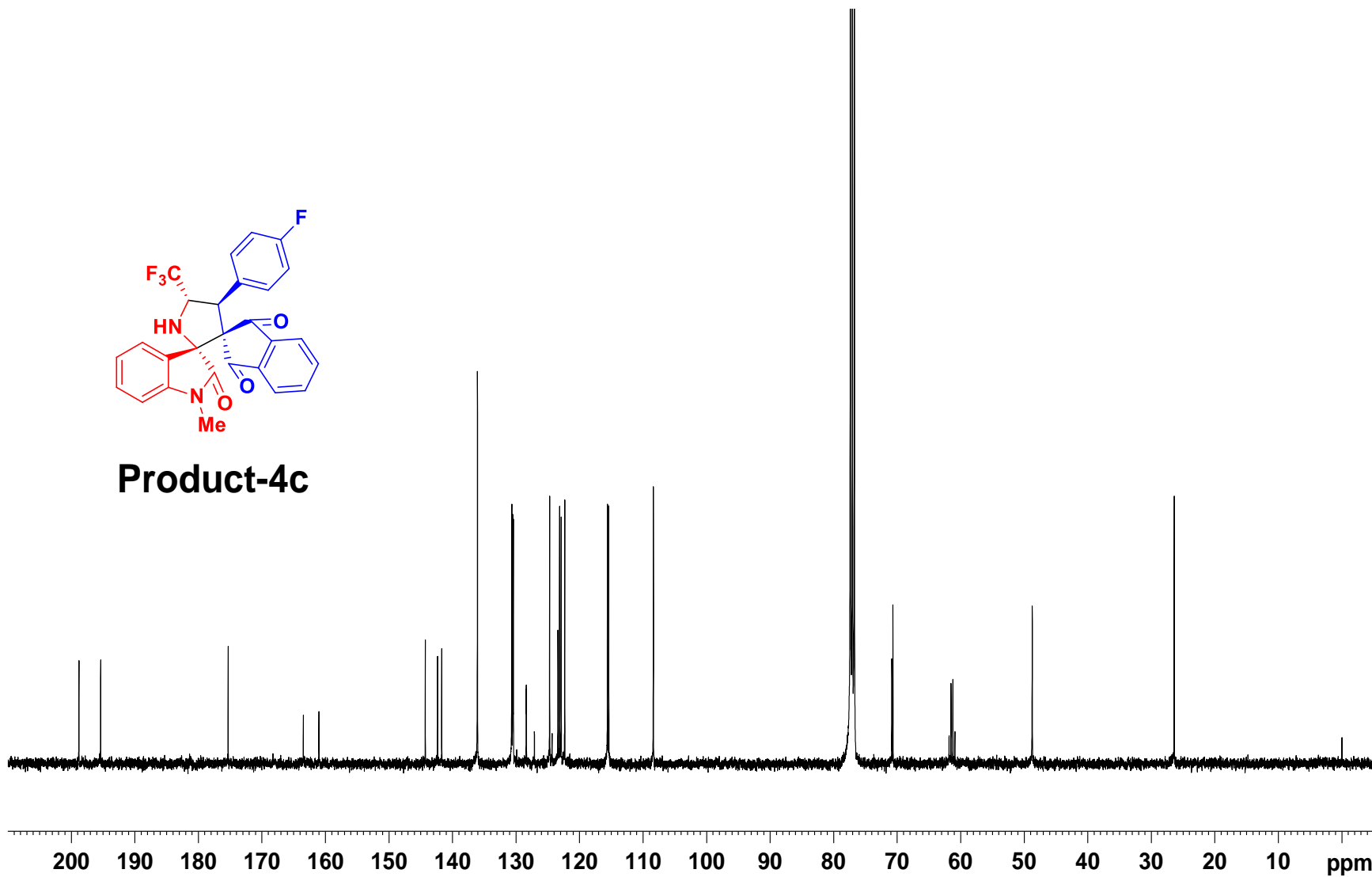
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48.77

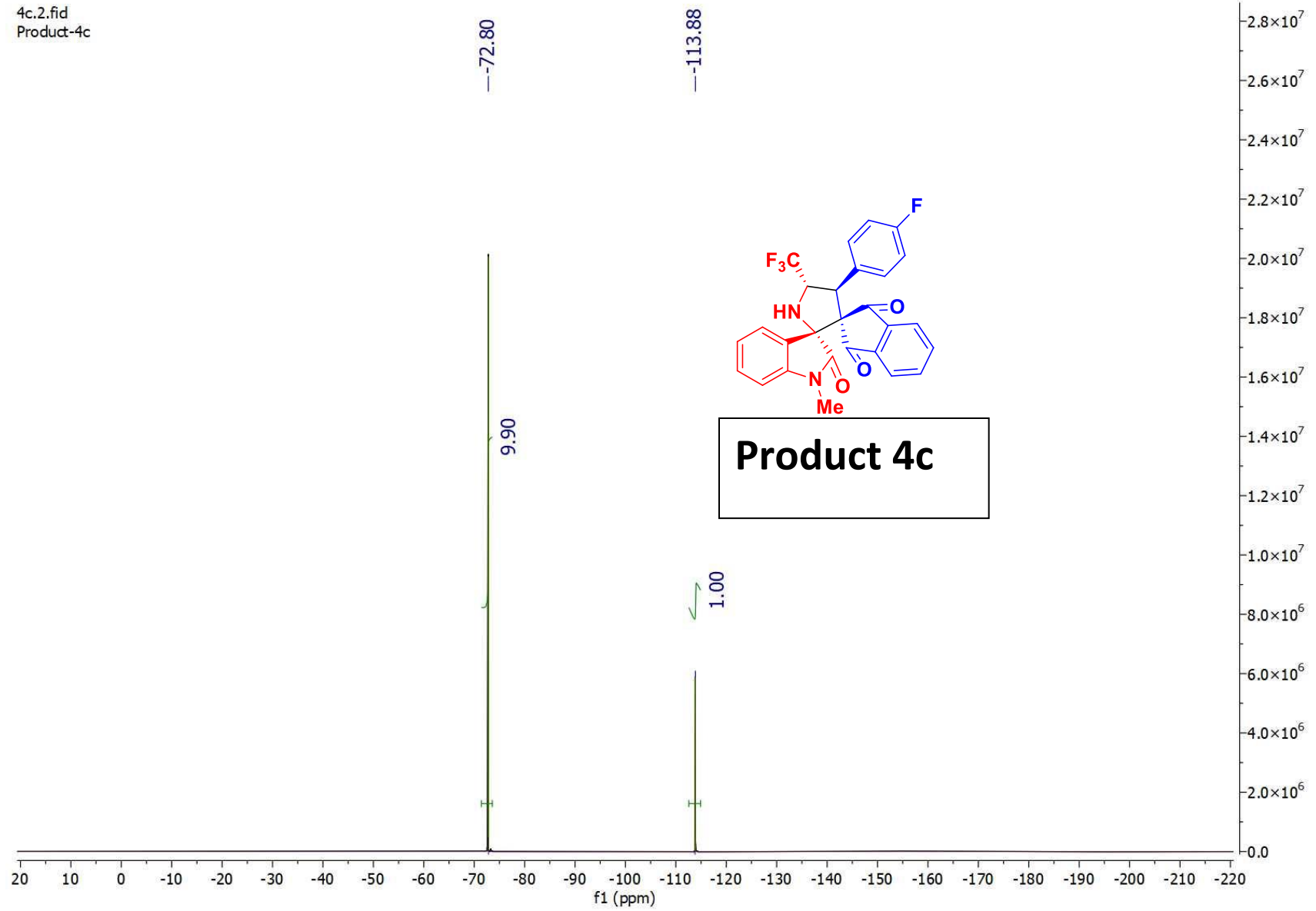
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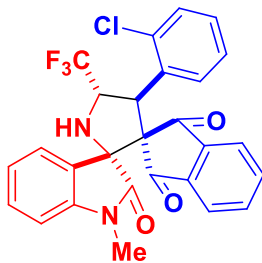
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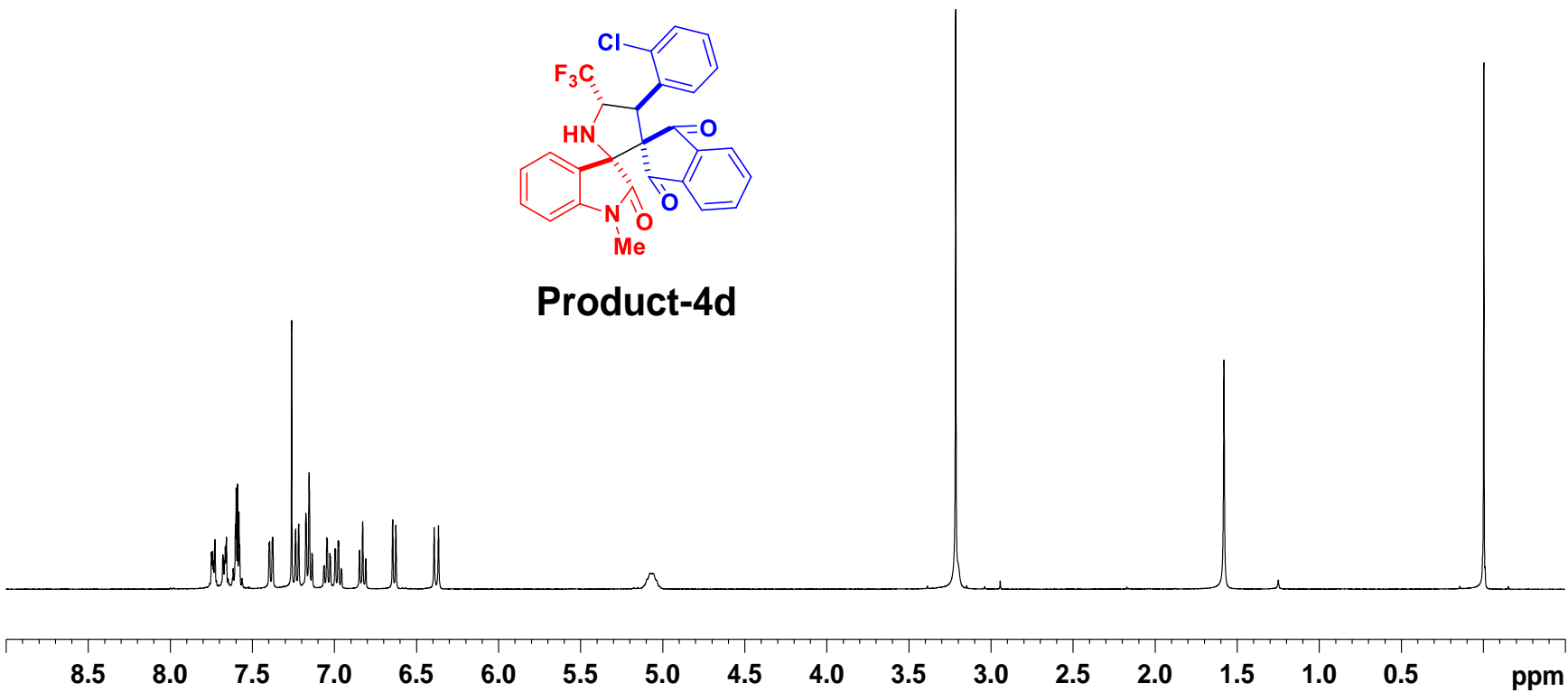
4c.2.fid
Product-4c



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7.736
7.727
7.679
7.676
7.669
7.664
7.658
7.616
7.603
7.598
7.590
7.581
7.577
7.563
7.397
7.394
7.378
7.374
7.260
7.236
7.217
7.173
7.154
7.136
7.134
7.064
7.061
7.046
7.043
7.027
7.023
6.997
6.993
6.977
6.974
6.959
6.955
6.846
6.827
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5.077
5.061
3.214
1.579
-0.004



Product-4d

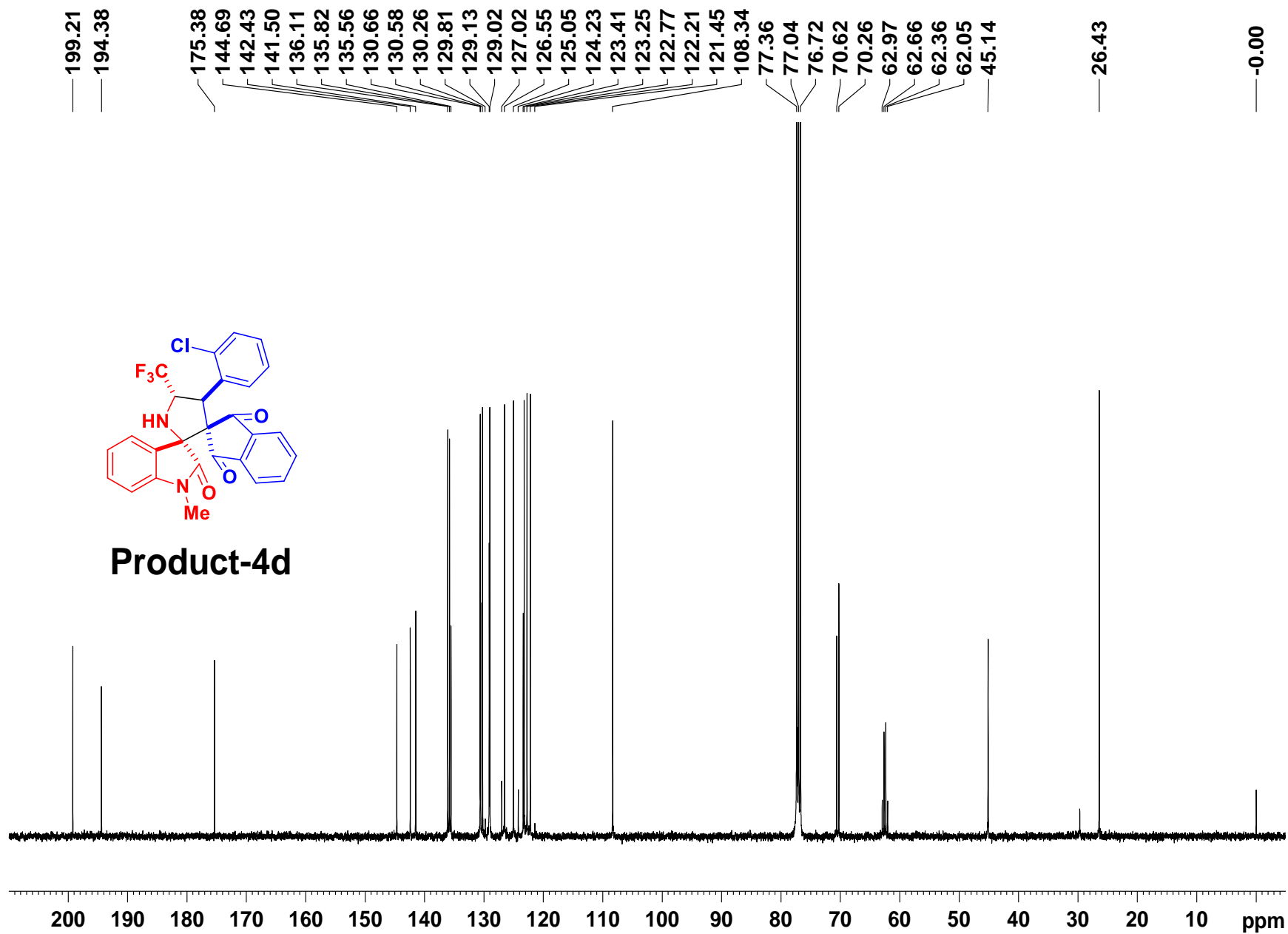


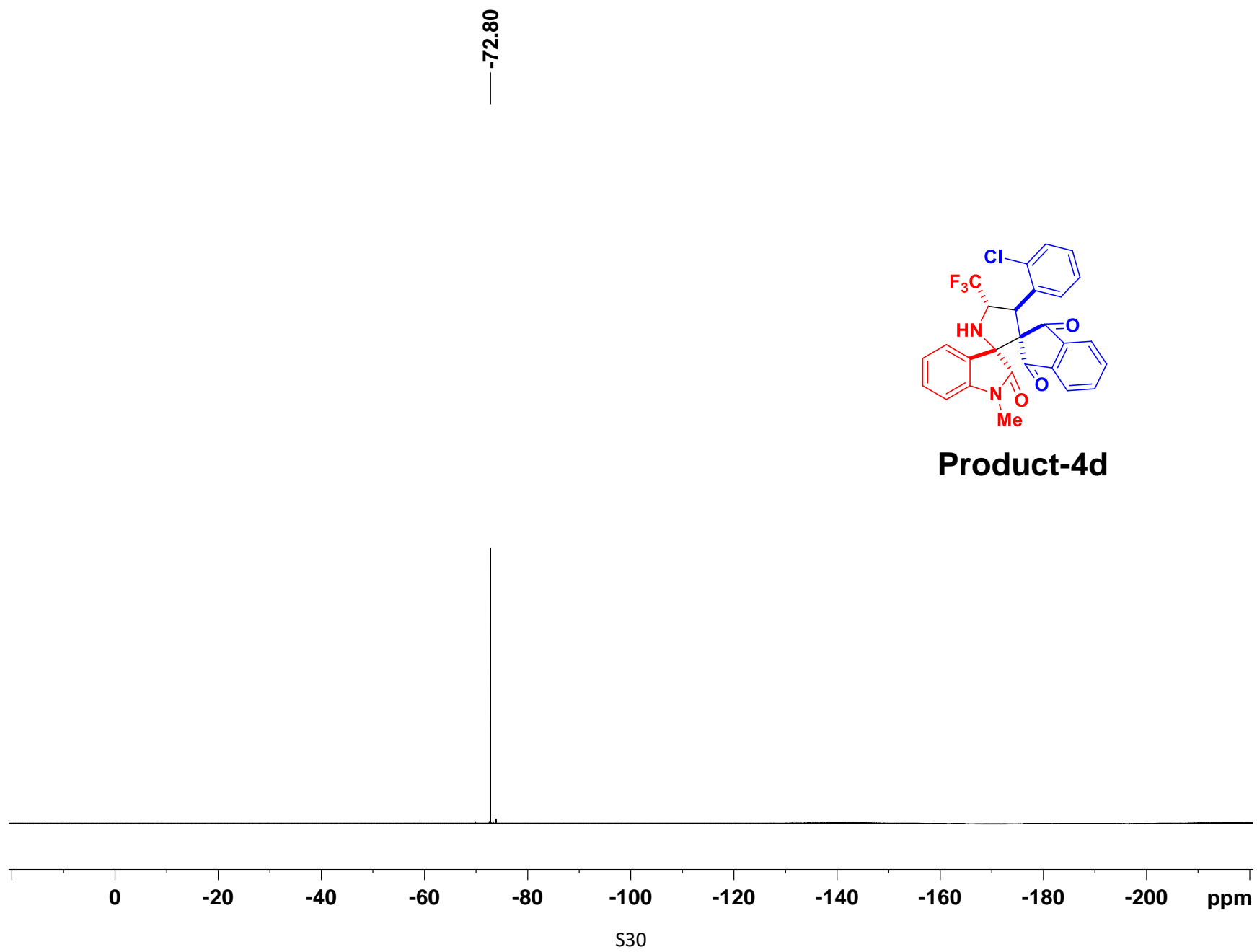
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1.069
1.079
2.073
0.948
1.061
1.063
1.010
0.994

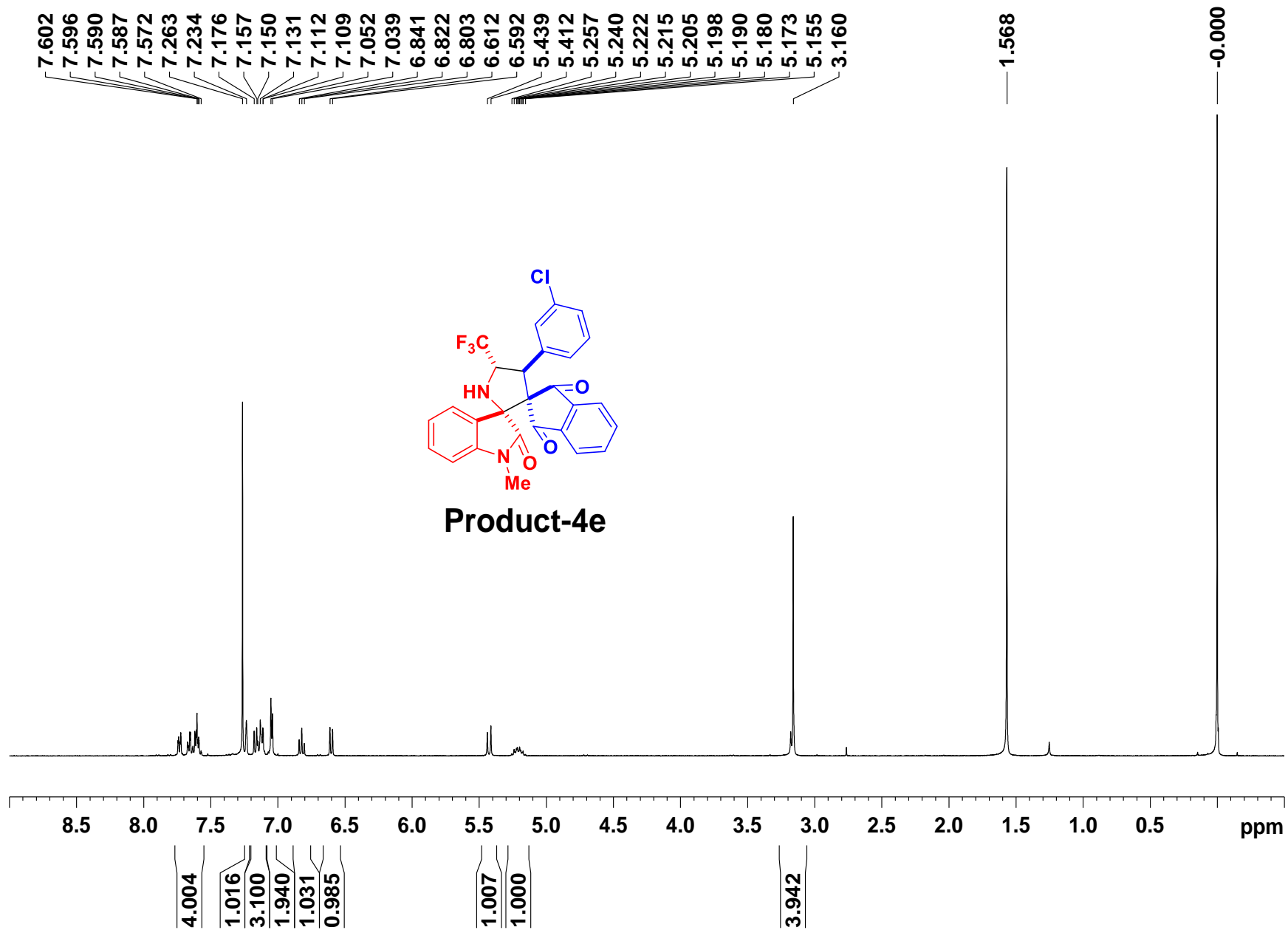
1.046

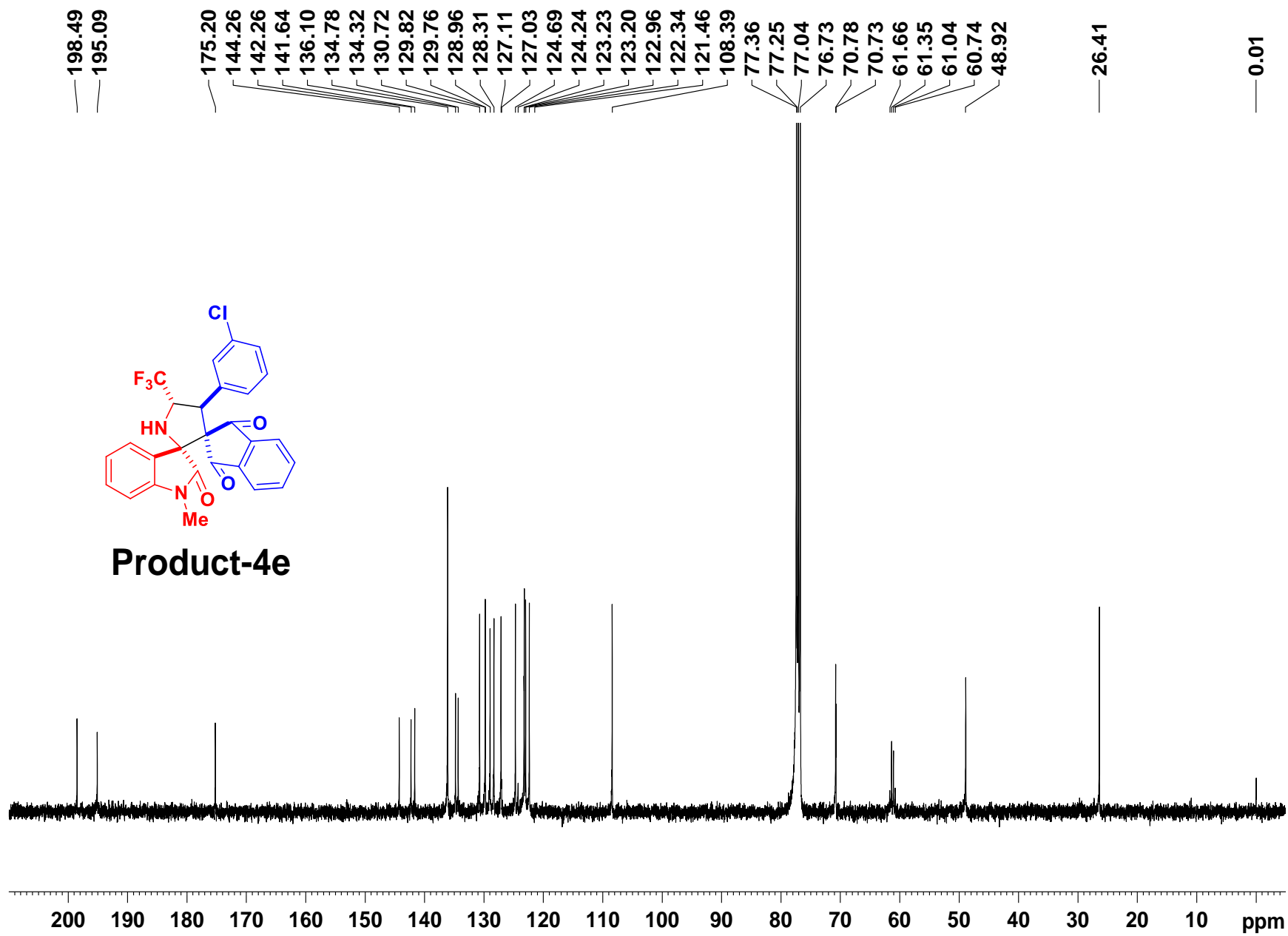
S28

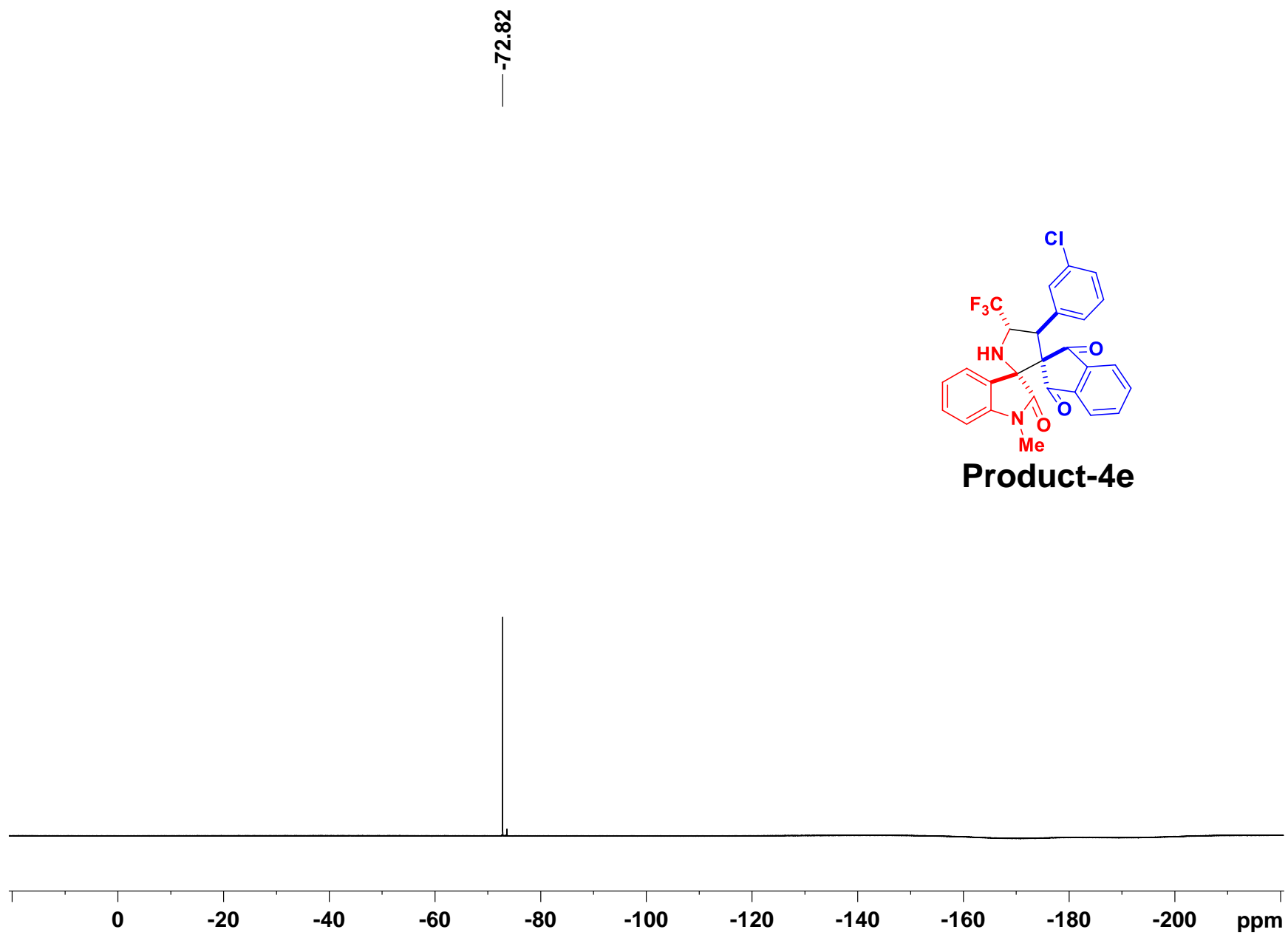
4.078



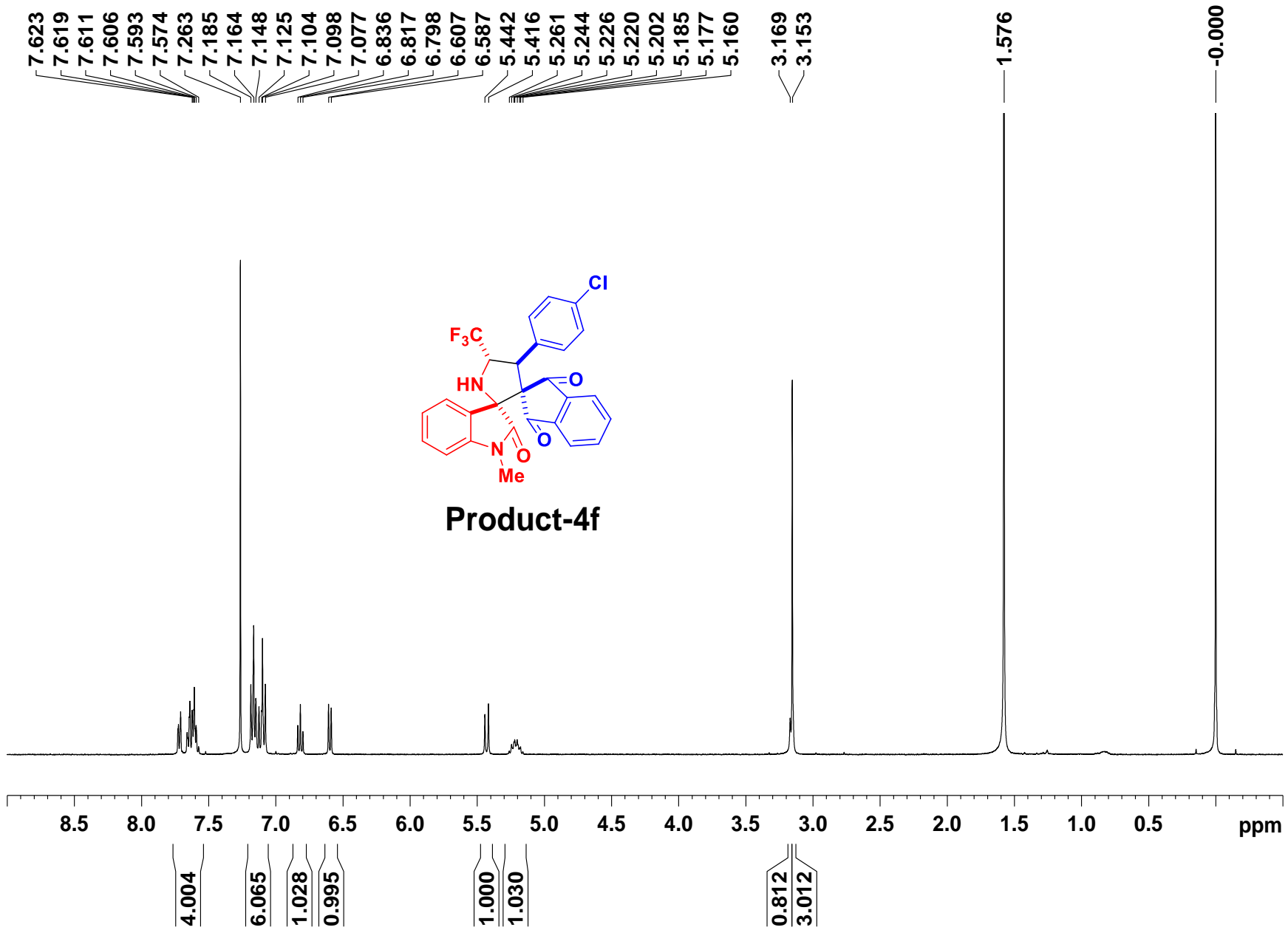


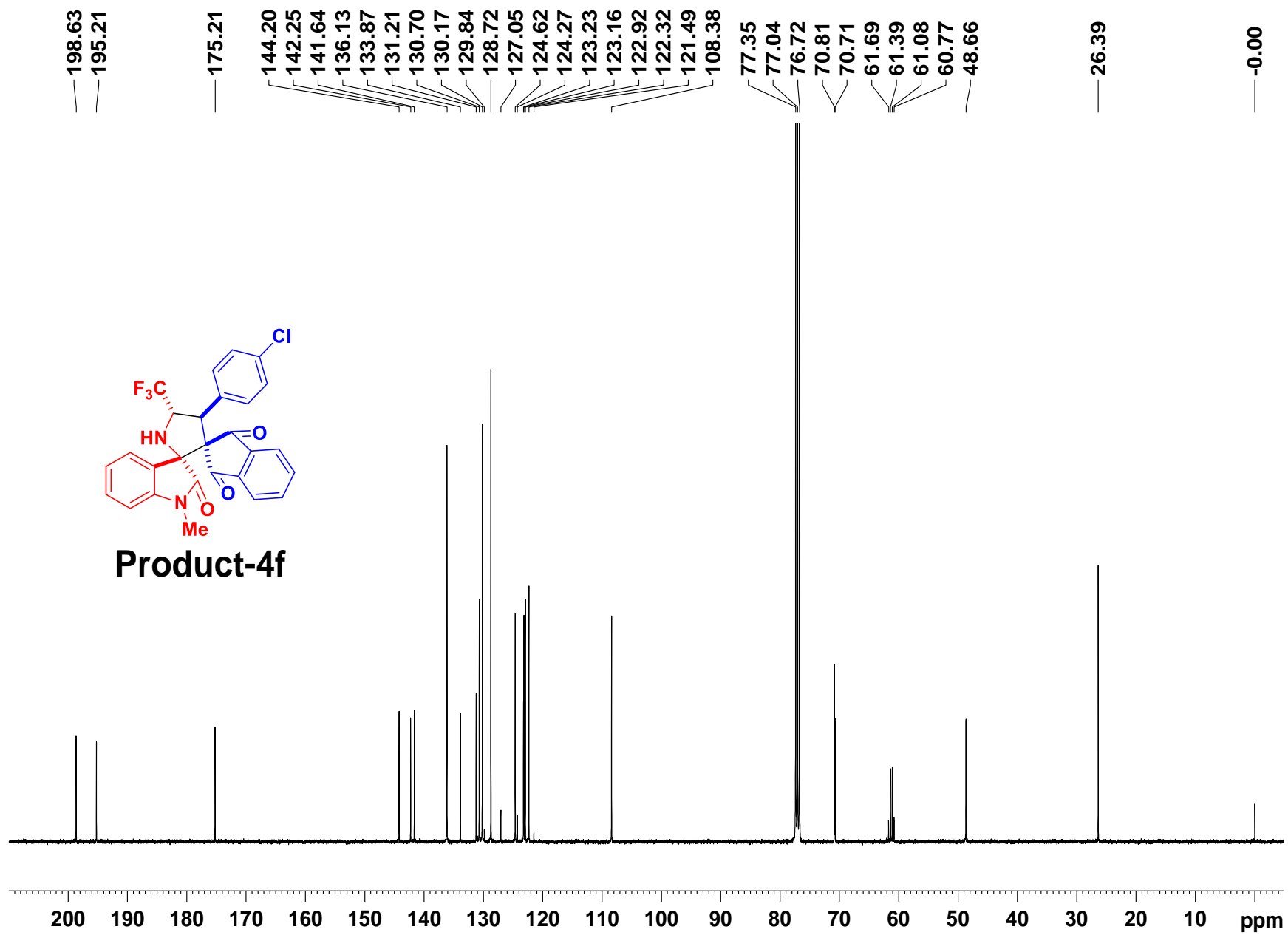




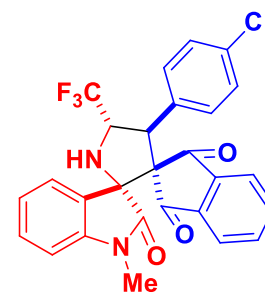


S33

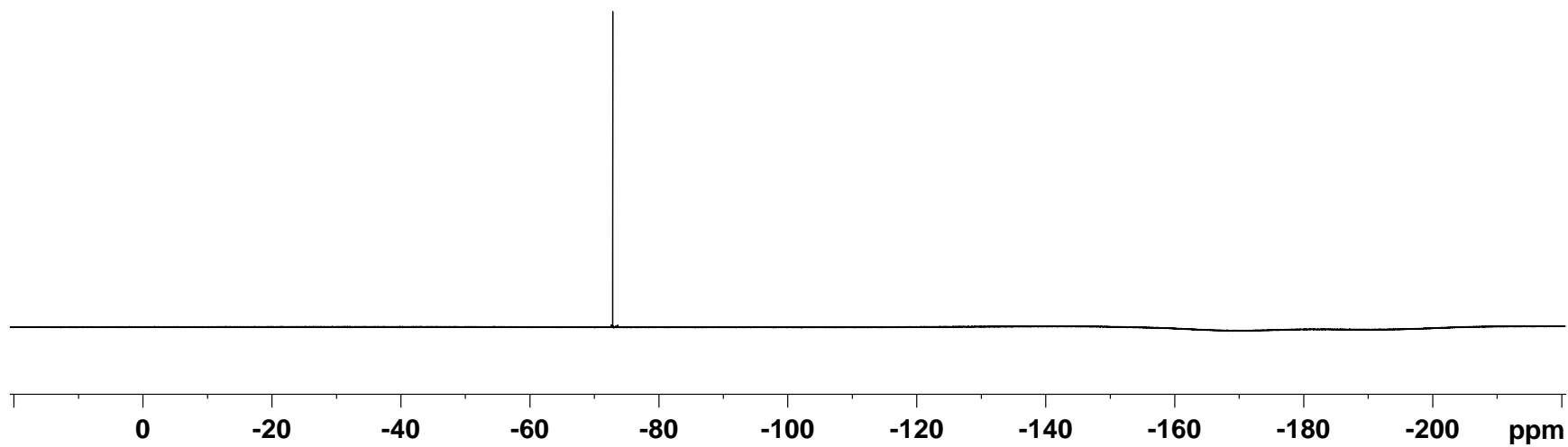


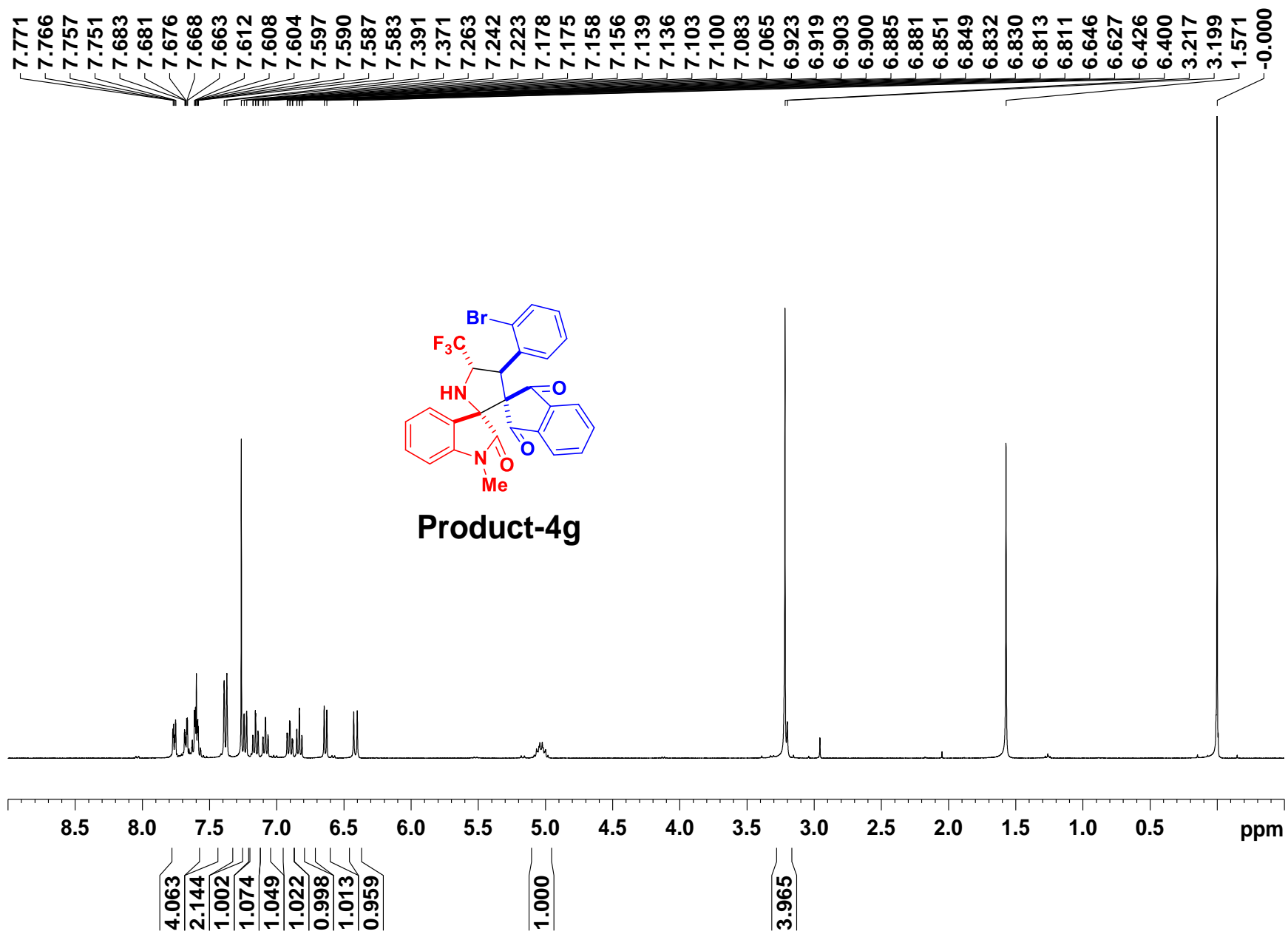


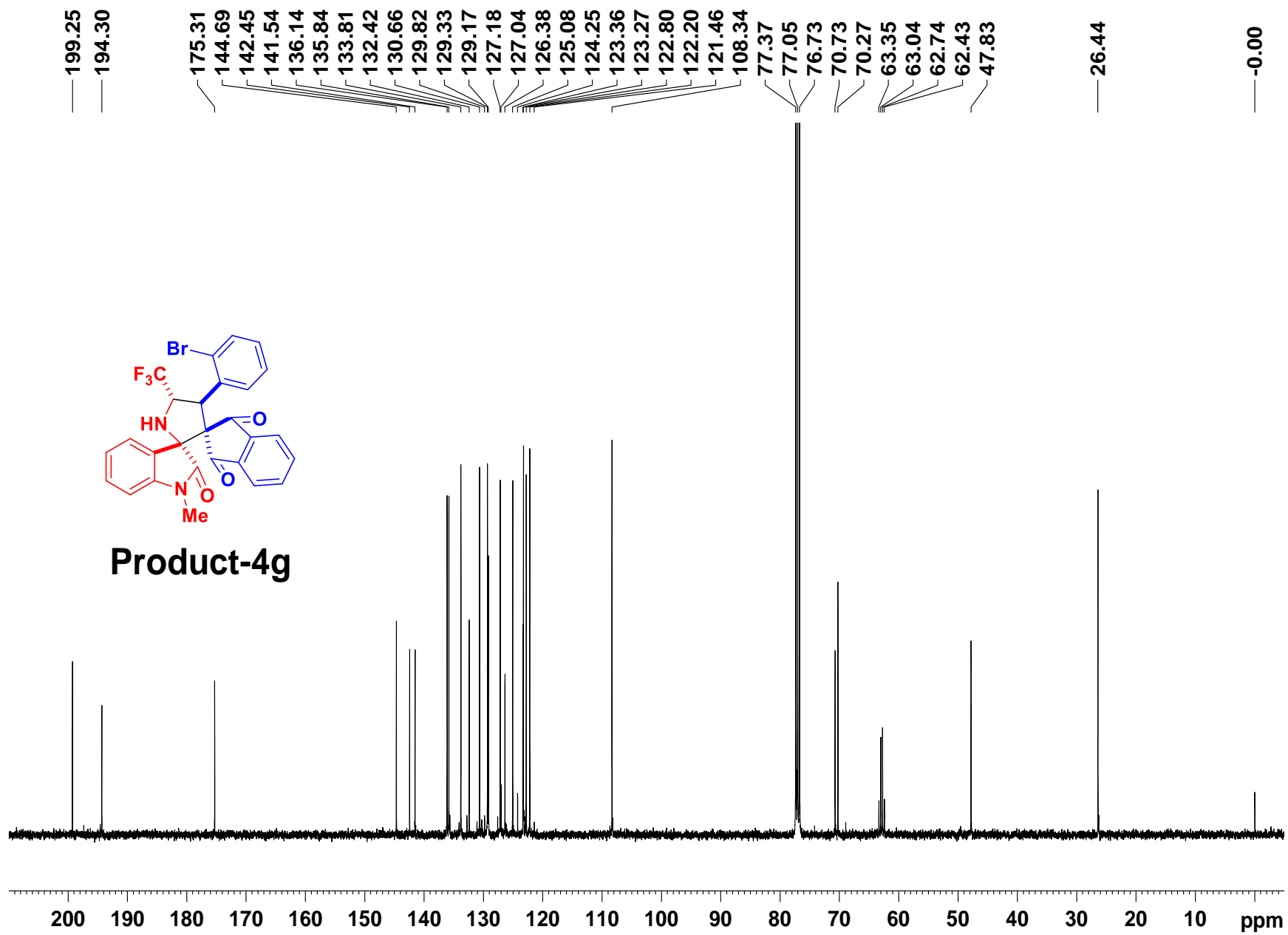
—72.84



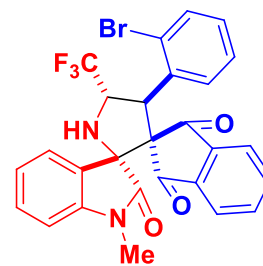
Product-4f



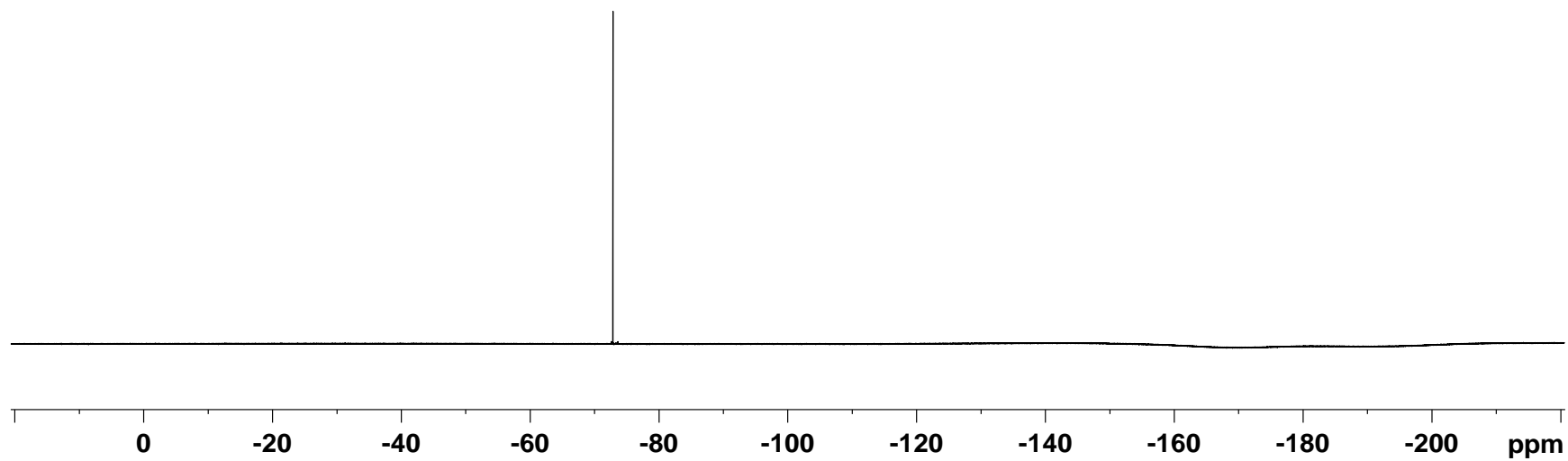


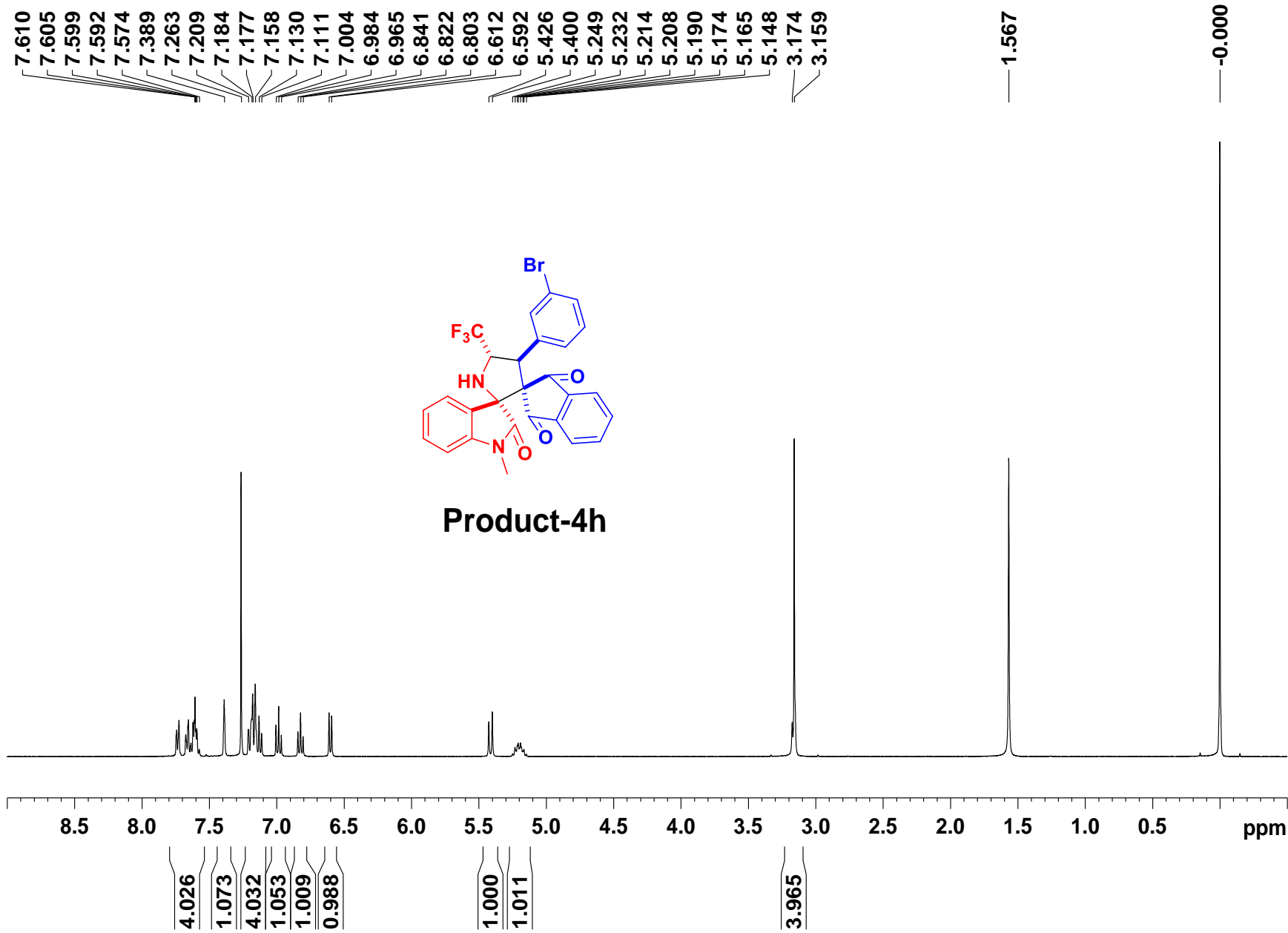


— -72.84



Product-4g

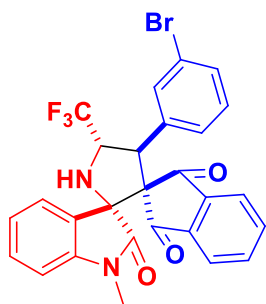




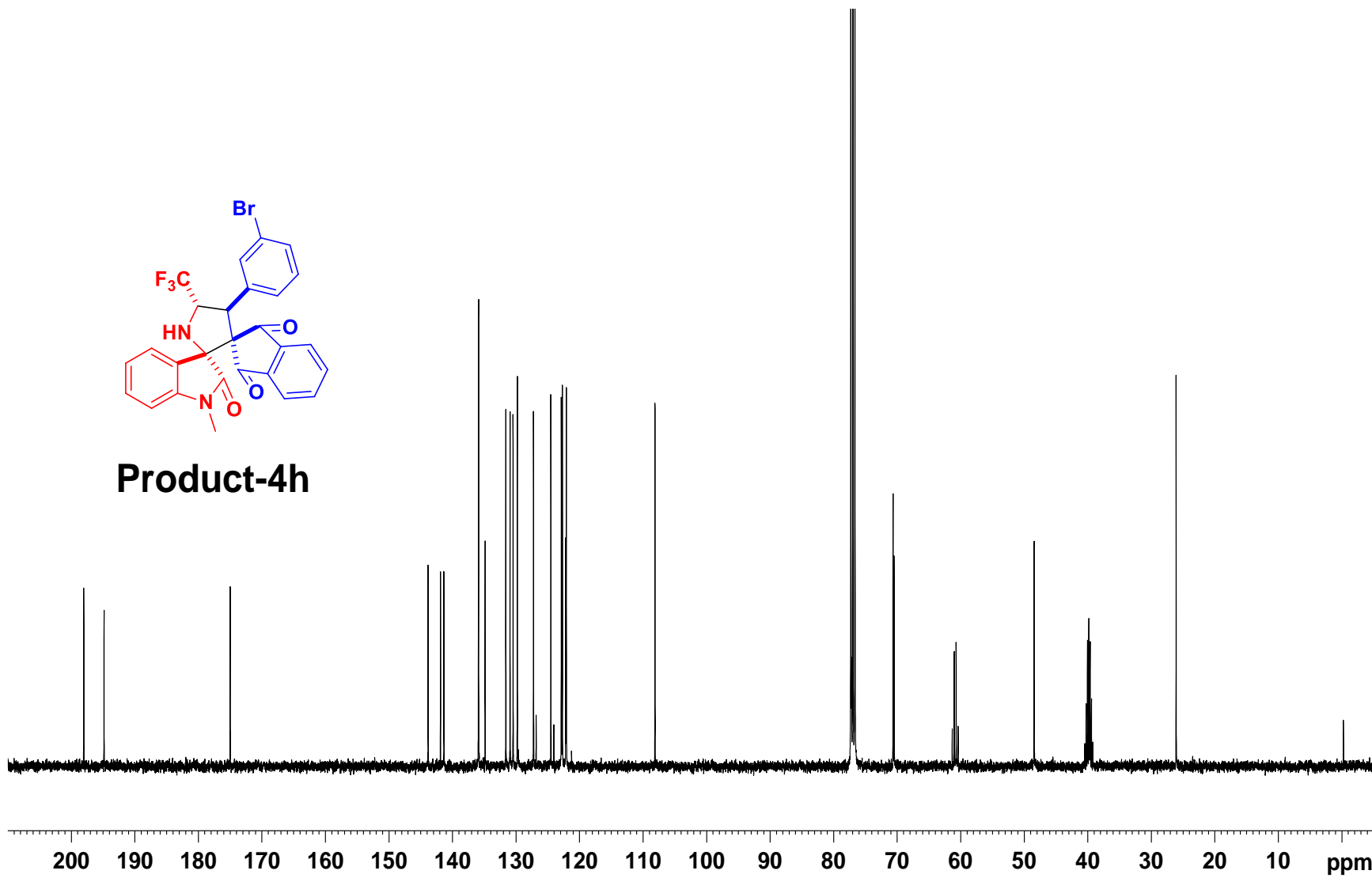
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194.84

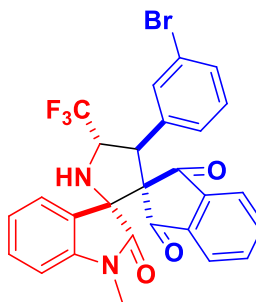
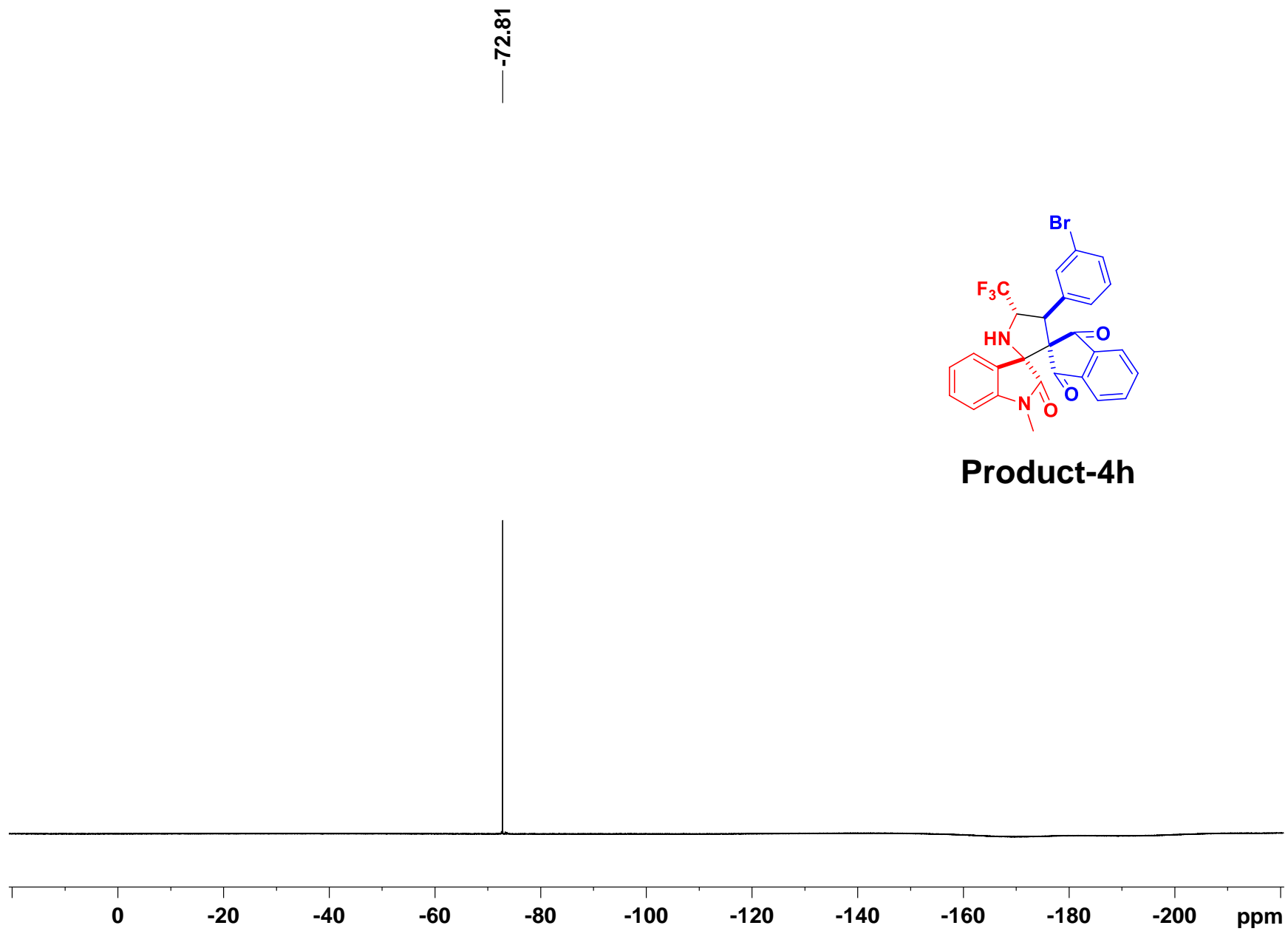
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135.91
134.88
131.63
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127.27
126.86
124.53
124.07
122.90
122.87
122.72
122.20
122.10
121.28
108.14
77.31
76.99
76.68
70.68
70.50
61.35
61.05
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40.07
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39.65
39.44
39.23
26.12

-0.22

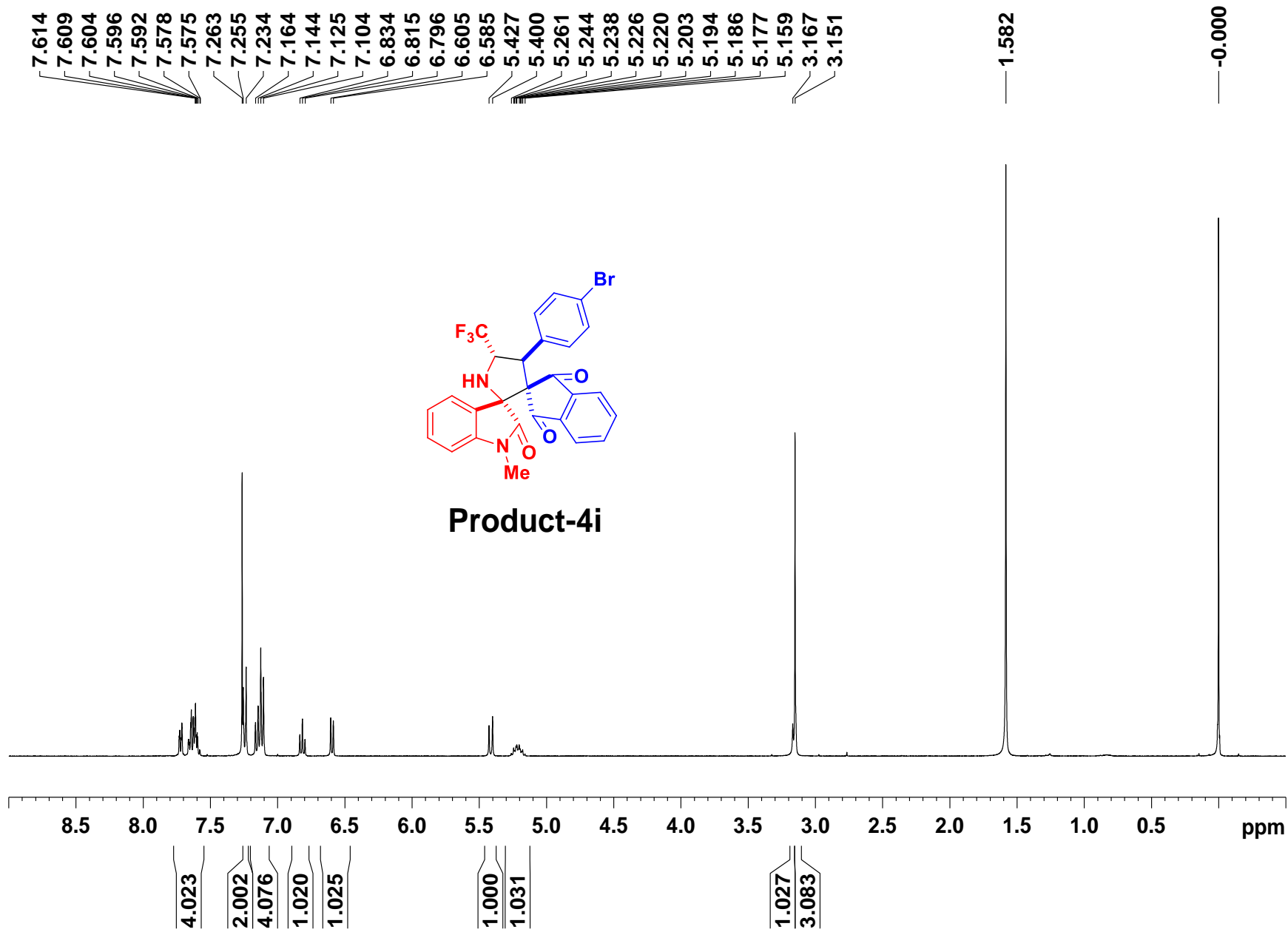


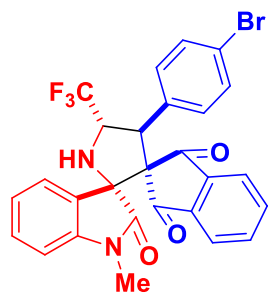
Product-4h



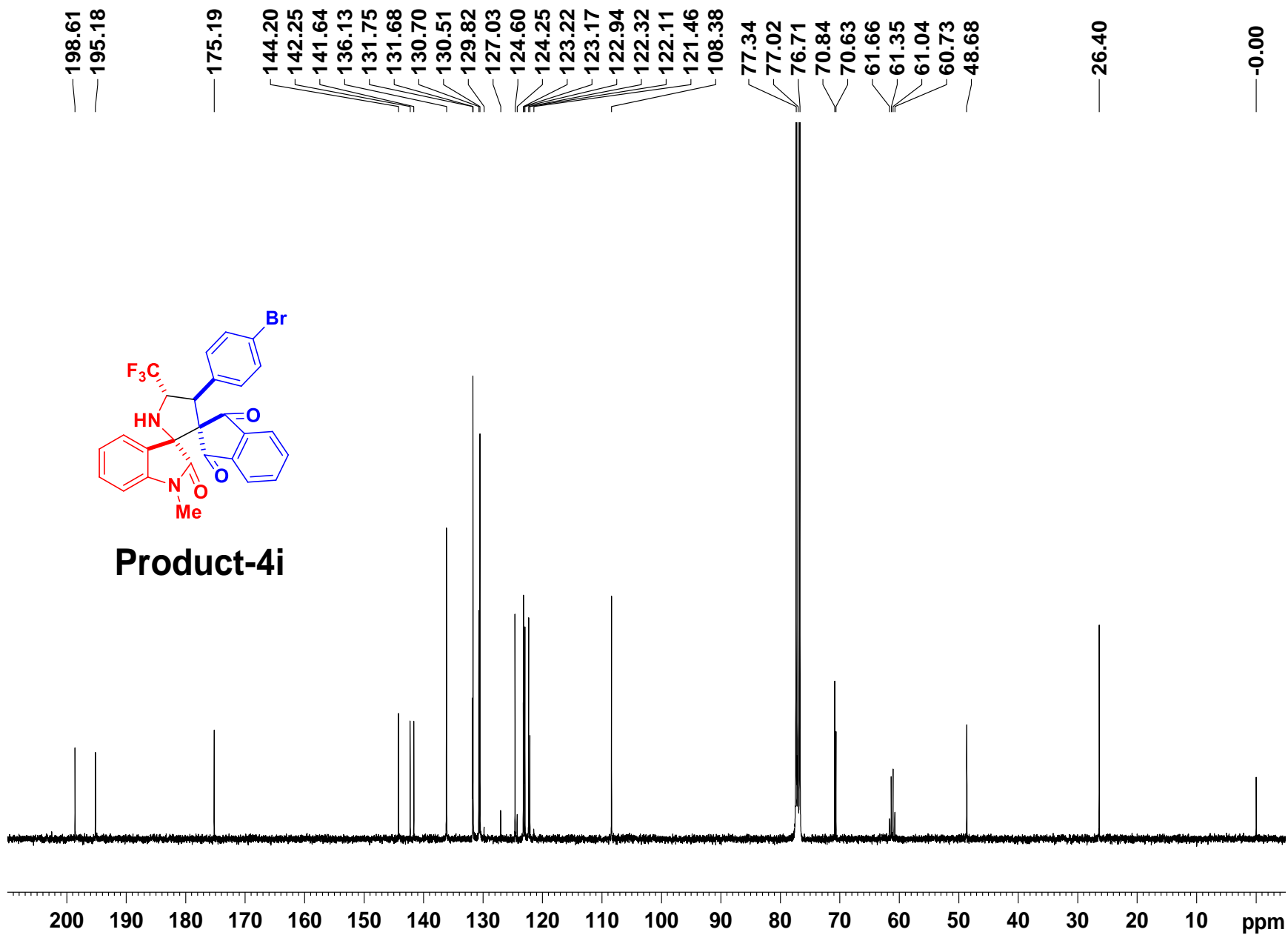


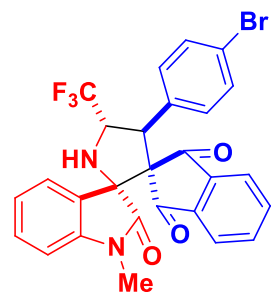
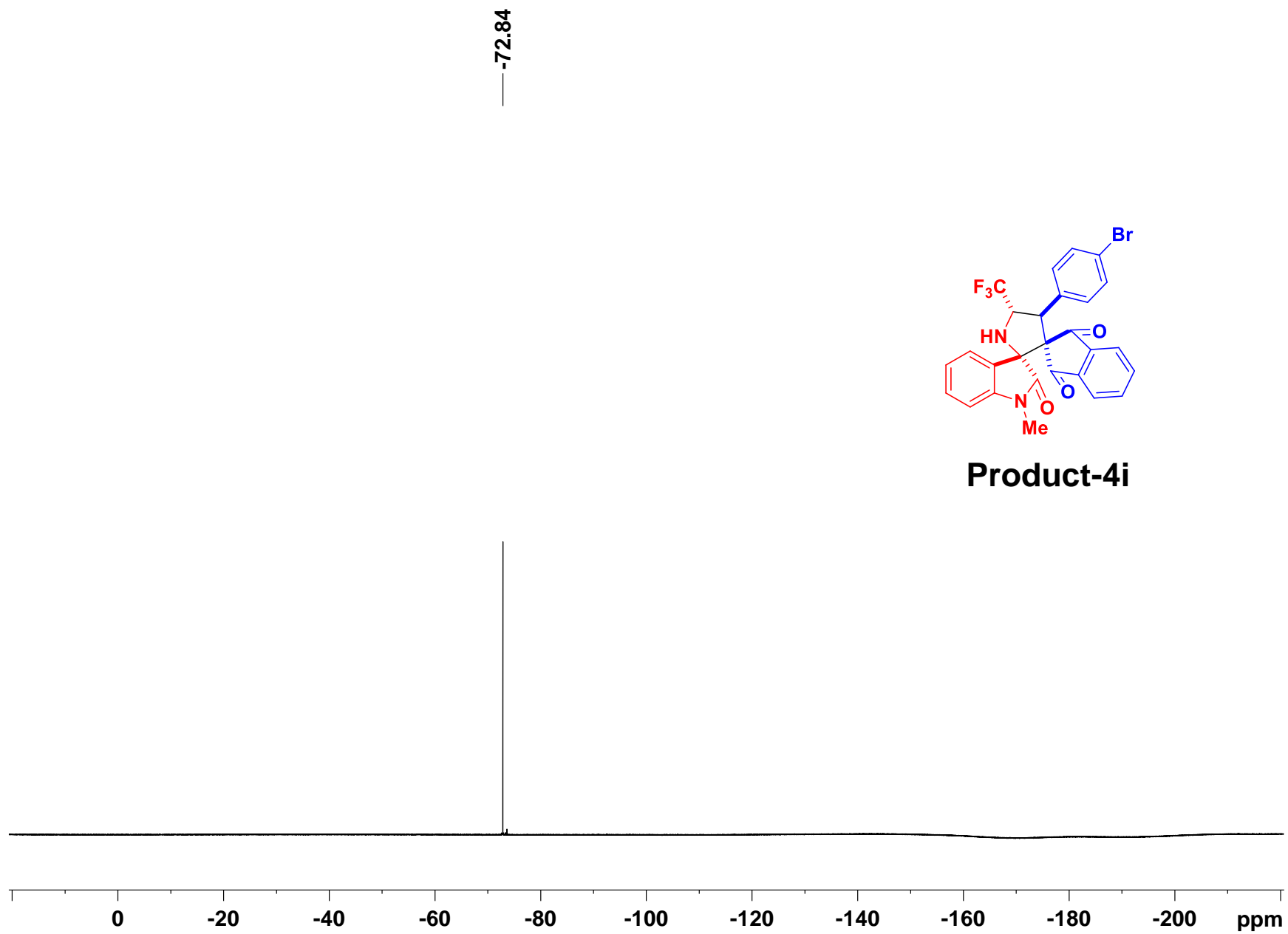
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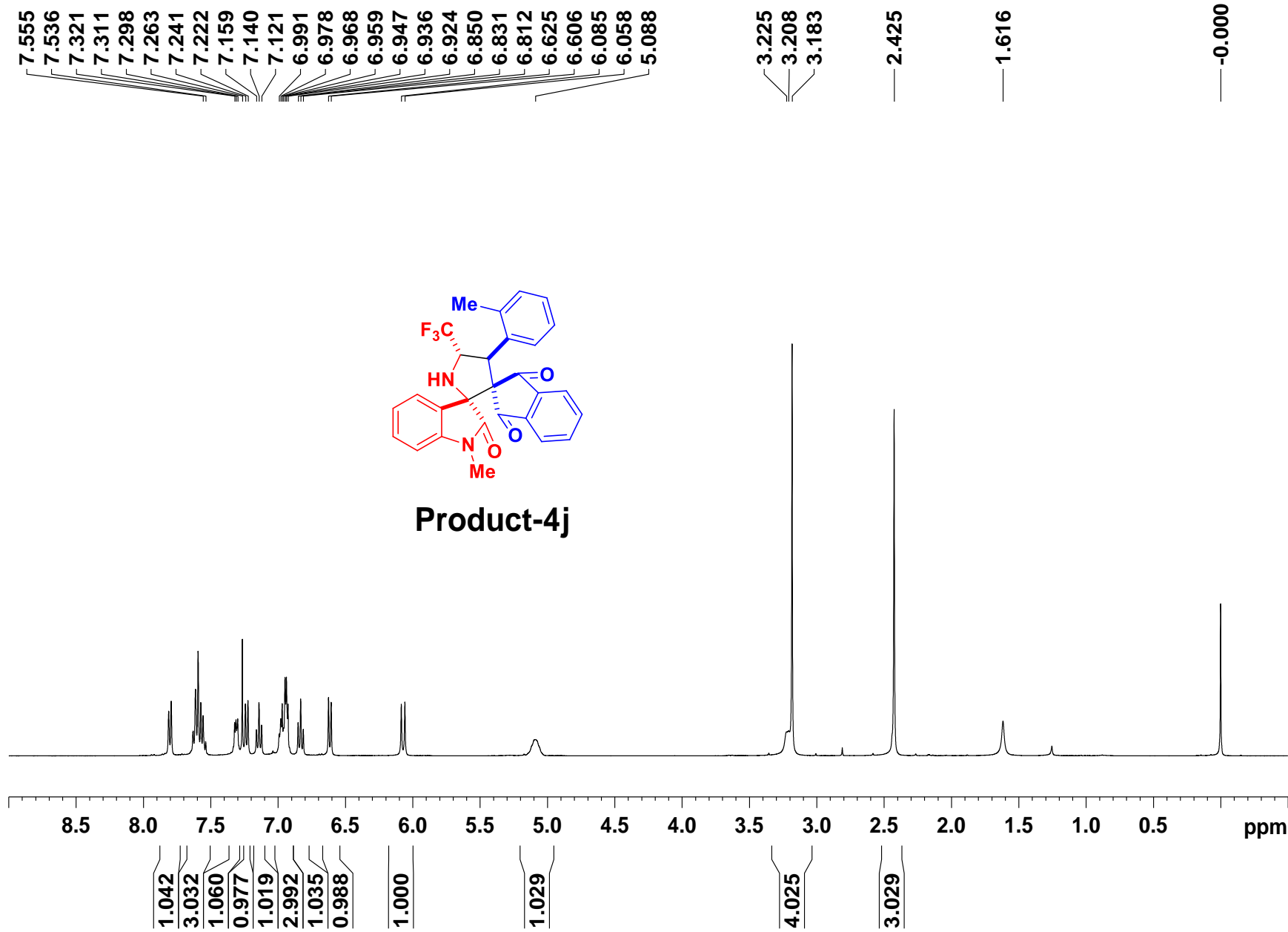


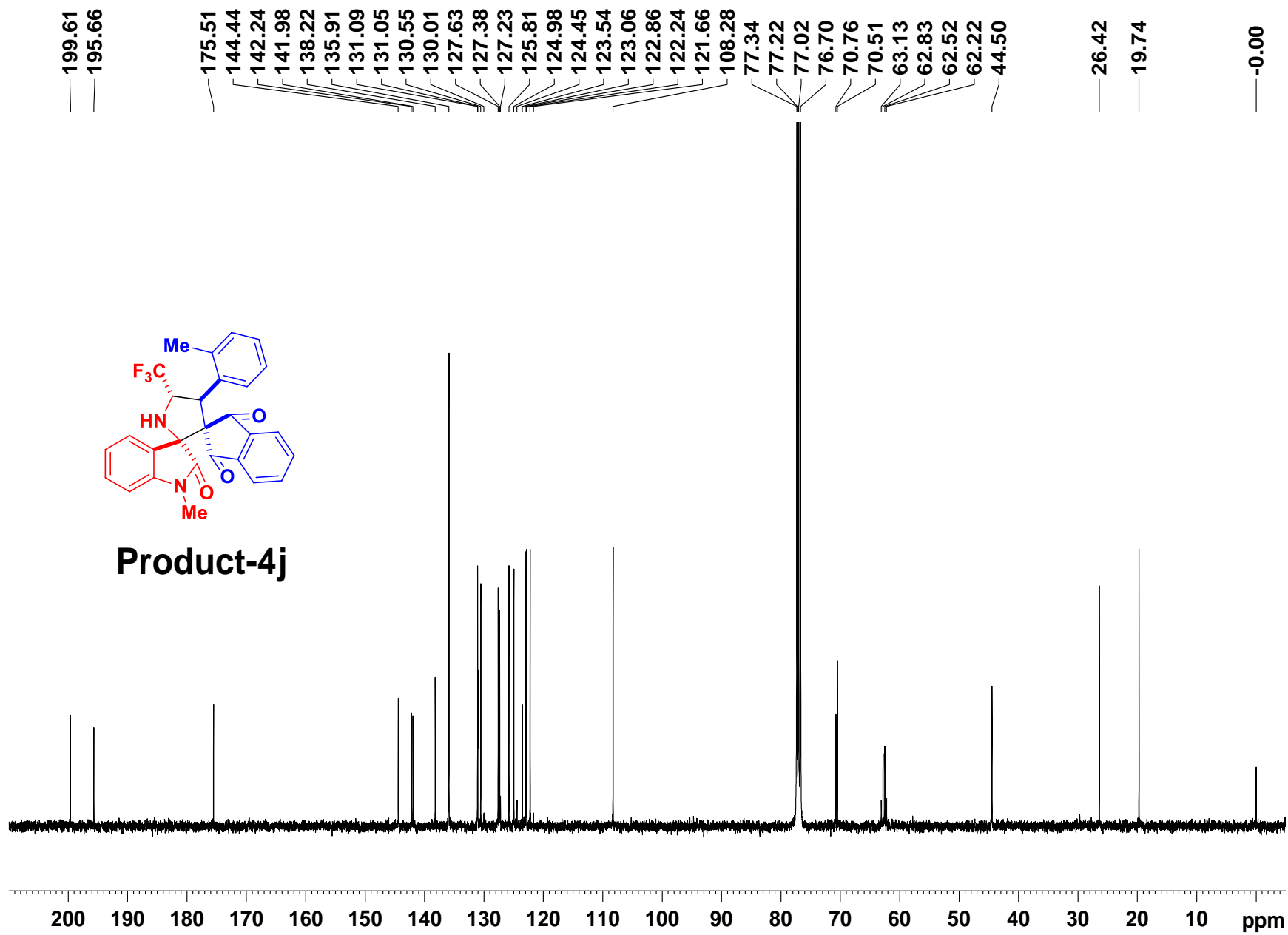
Product-4i

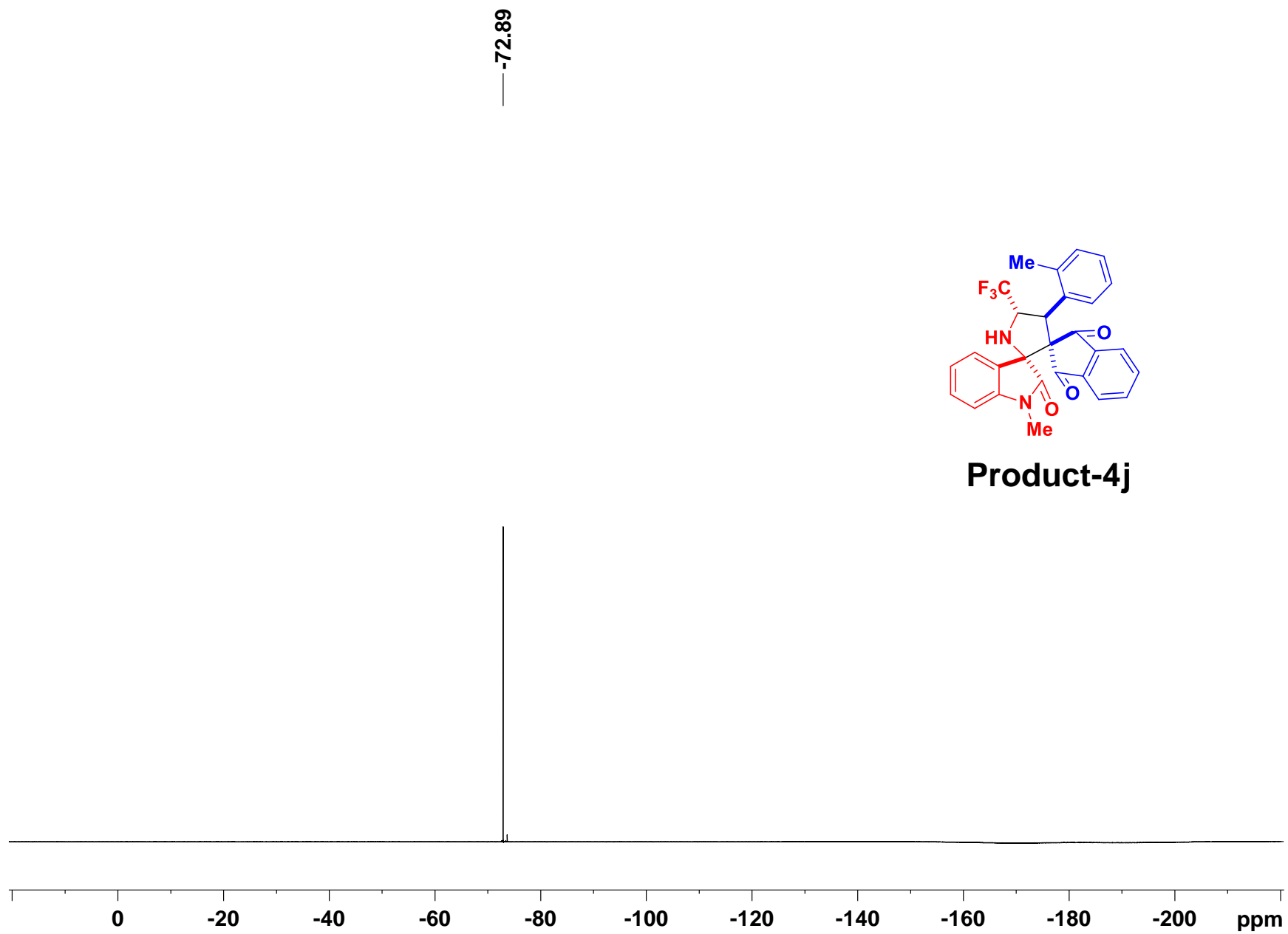


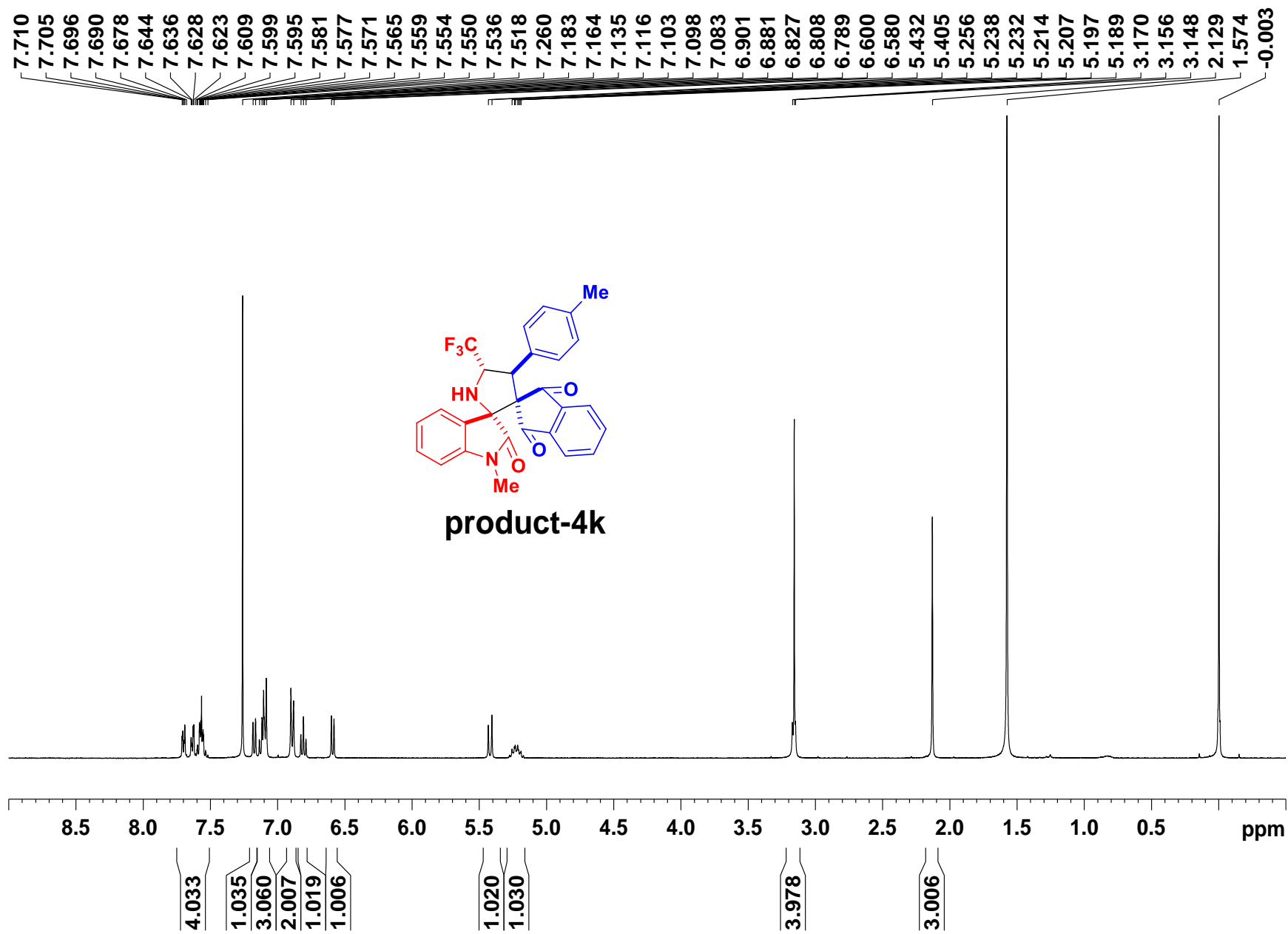


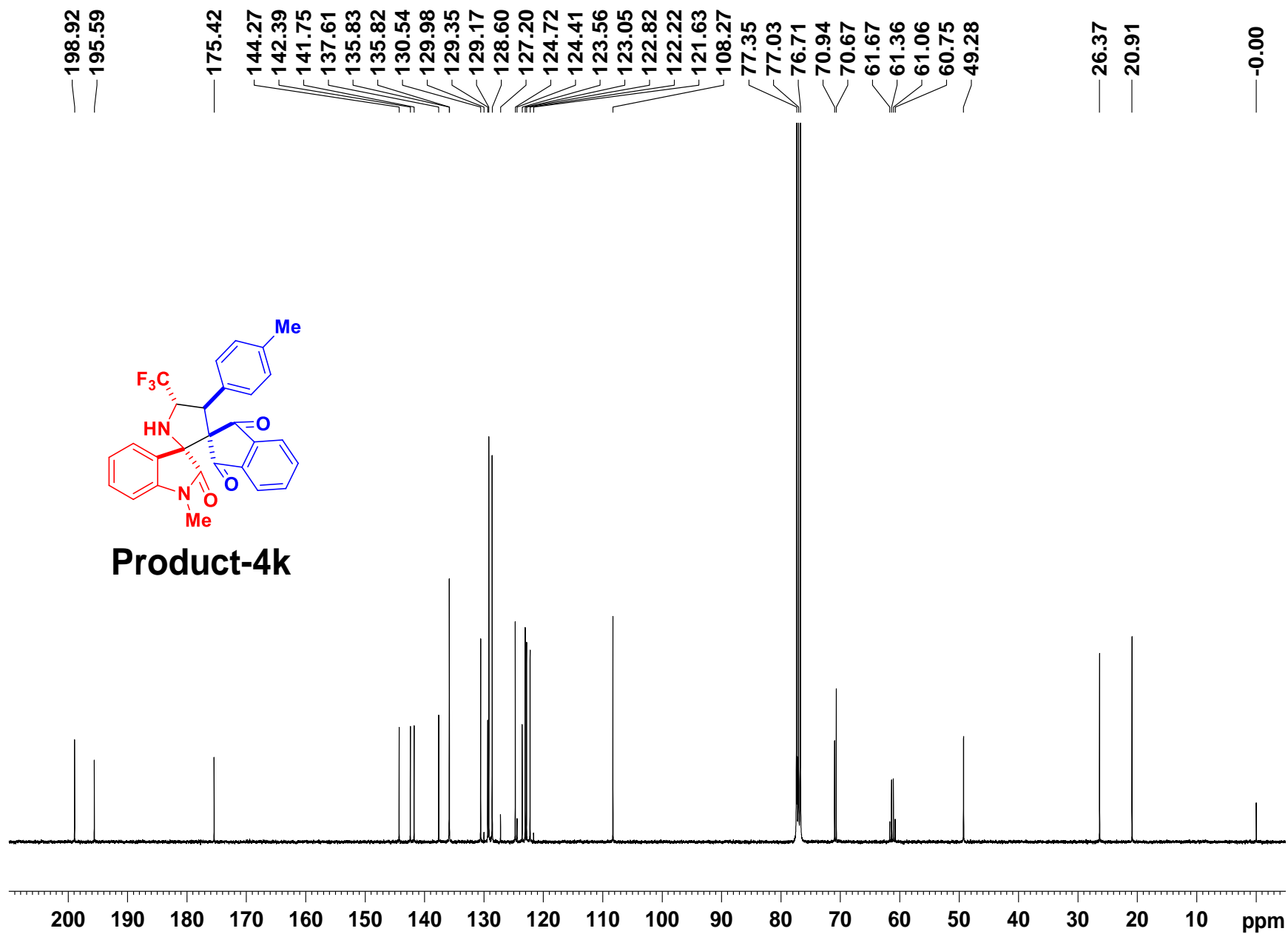
Product-4i



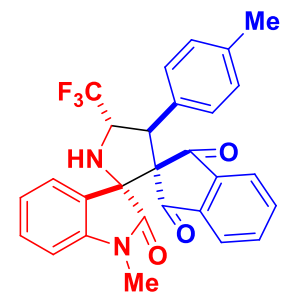




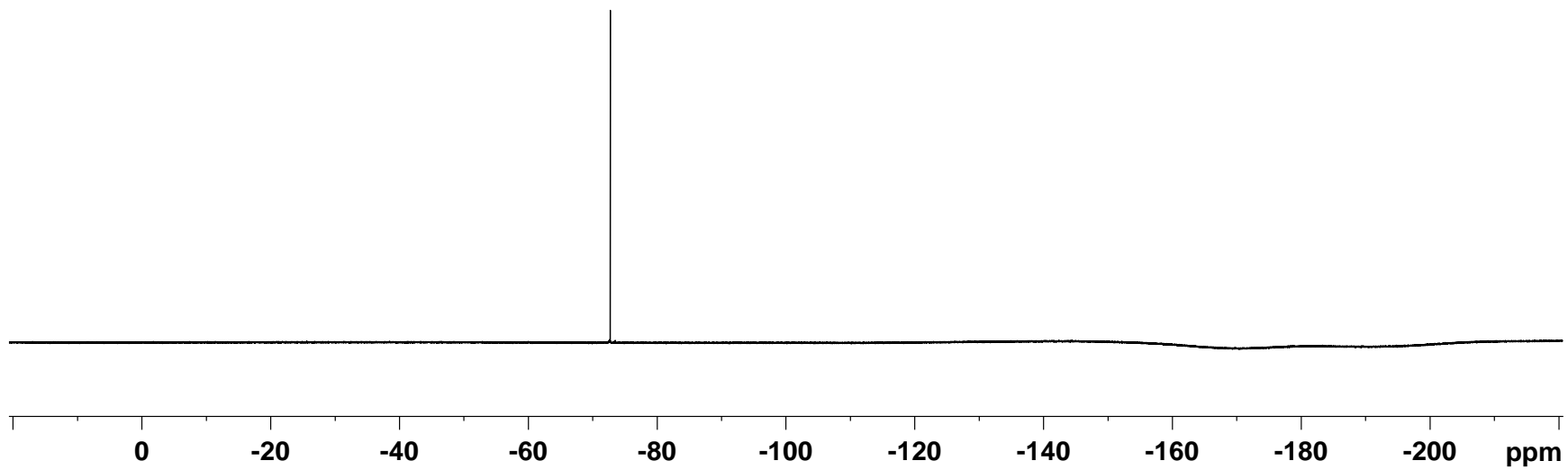




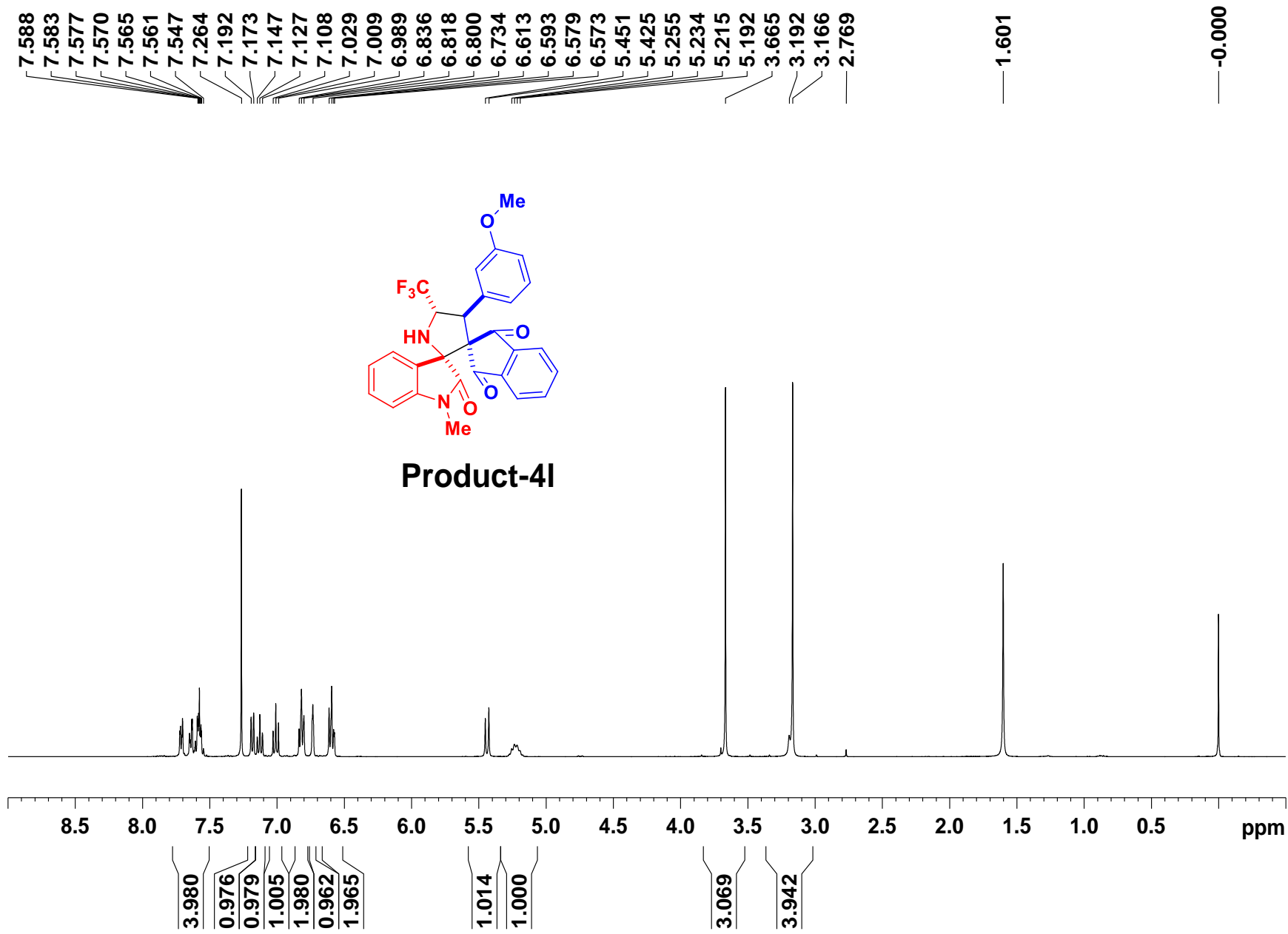
—72.73



Product-4k



S51

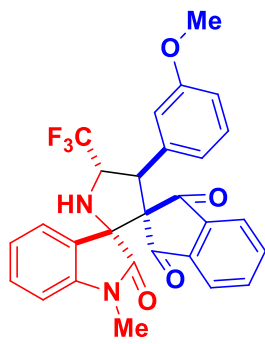


198.77
195.56

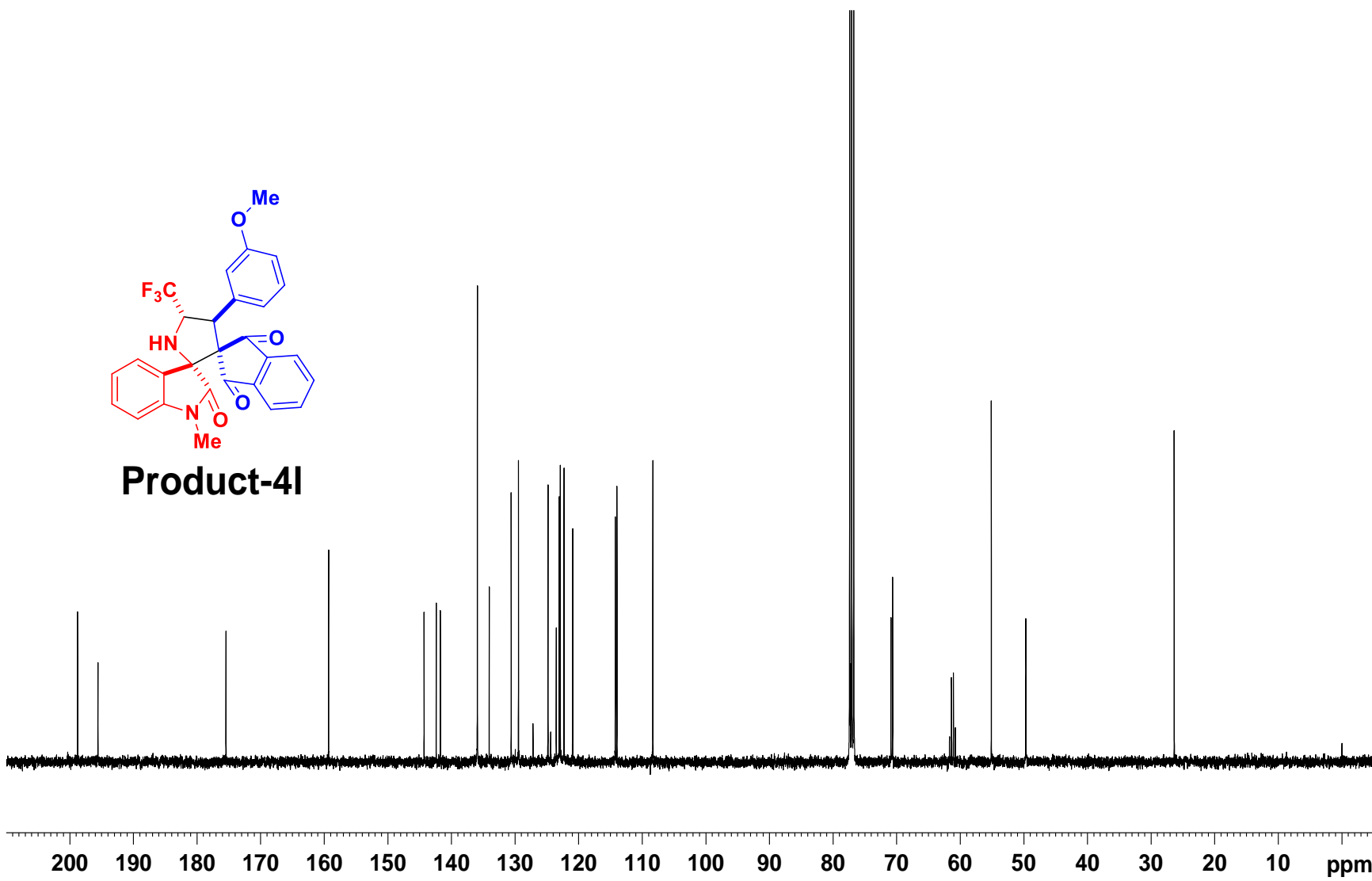
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159.30
144.30
142.38
141.73
135.91
134.05
130.60
129.95
129.45
127.17
124.80
124.38
123.50
123.05
122.88
122.29
121.60
120.92
114.22
113.96
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61.68
61.37
61.06
60.76
55.13
49.72

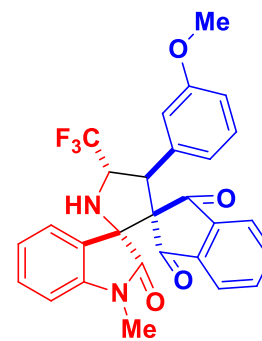
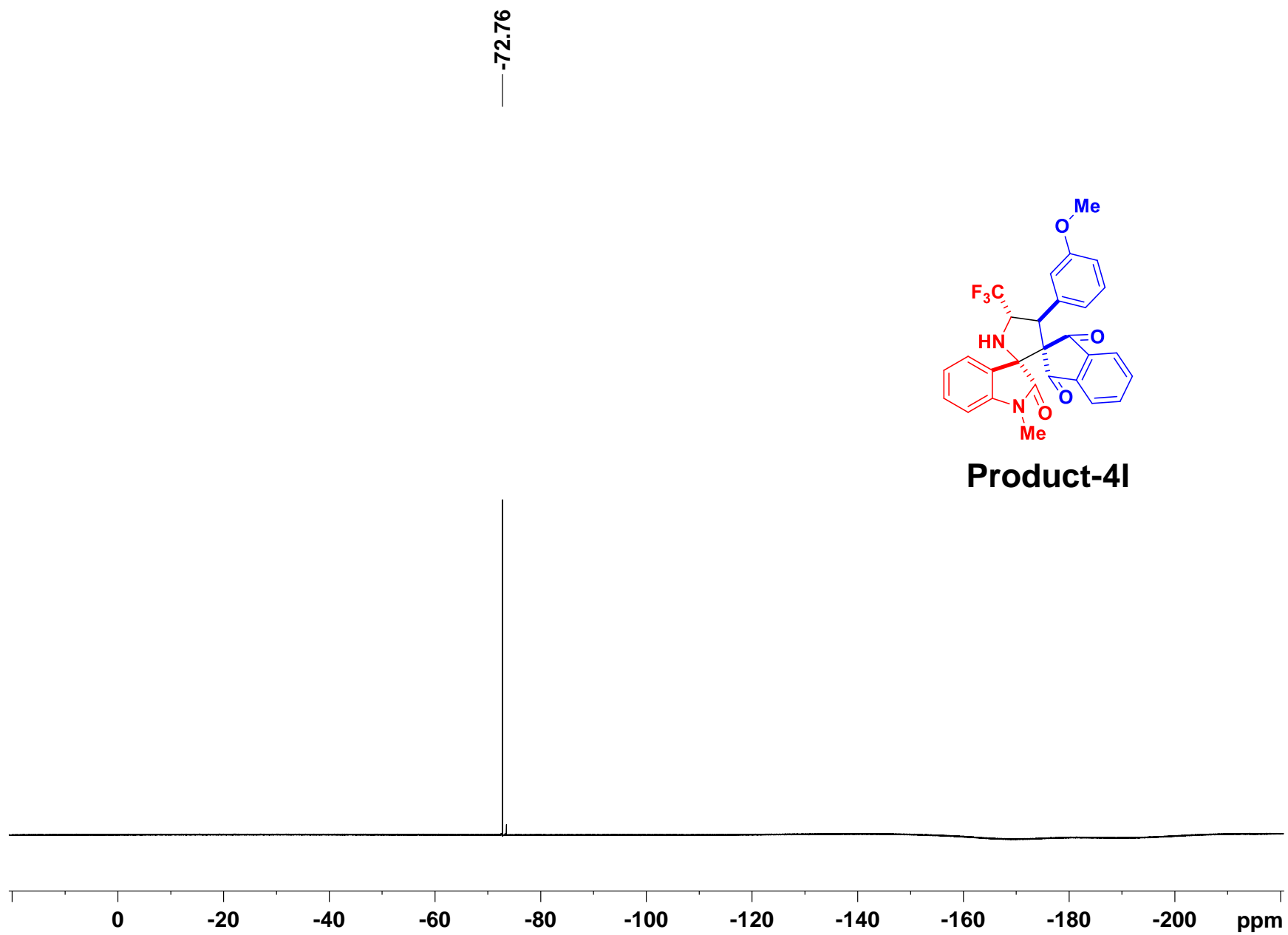
26.38

0.01

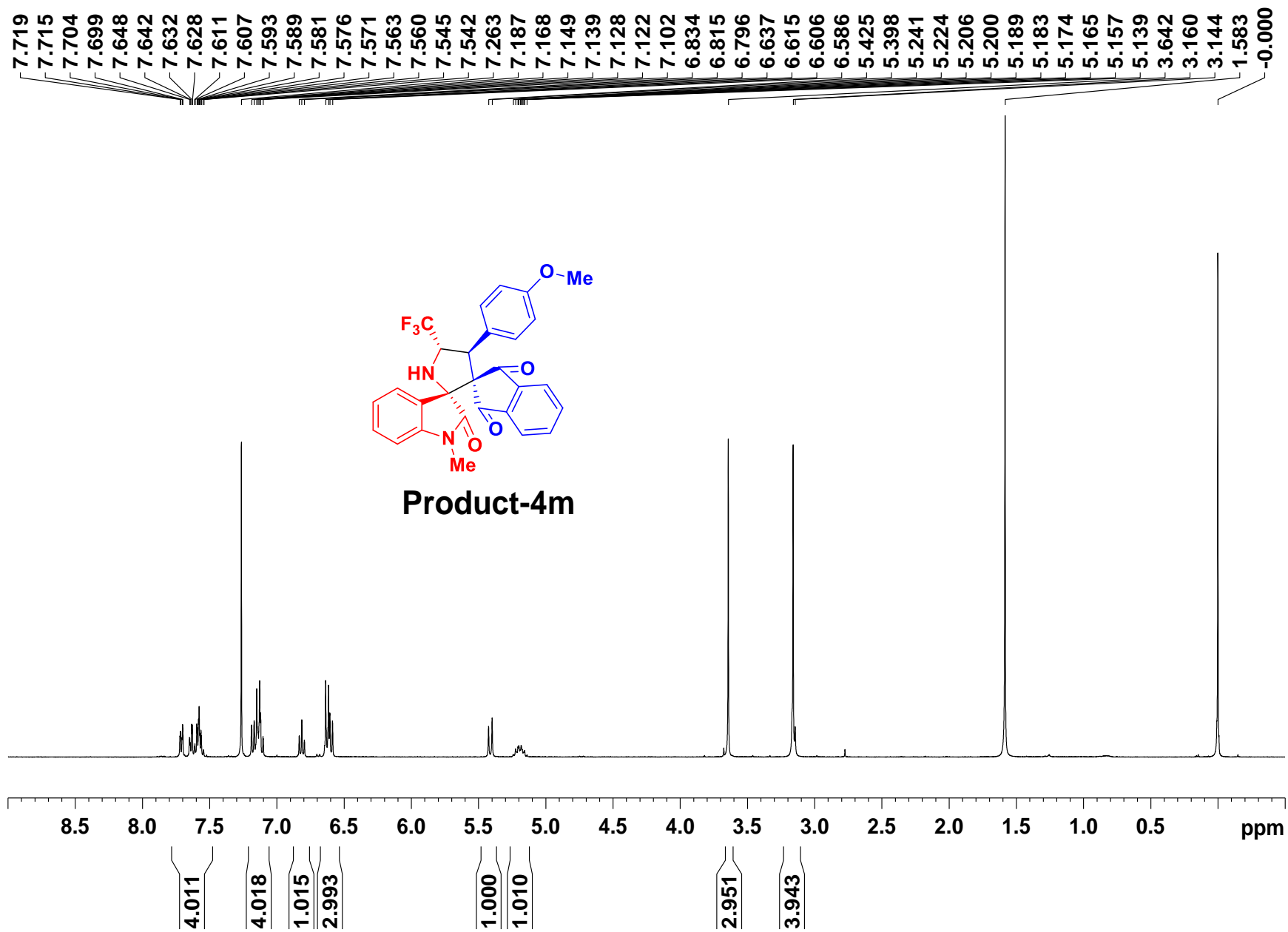


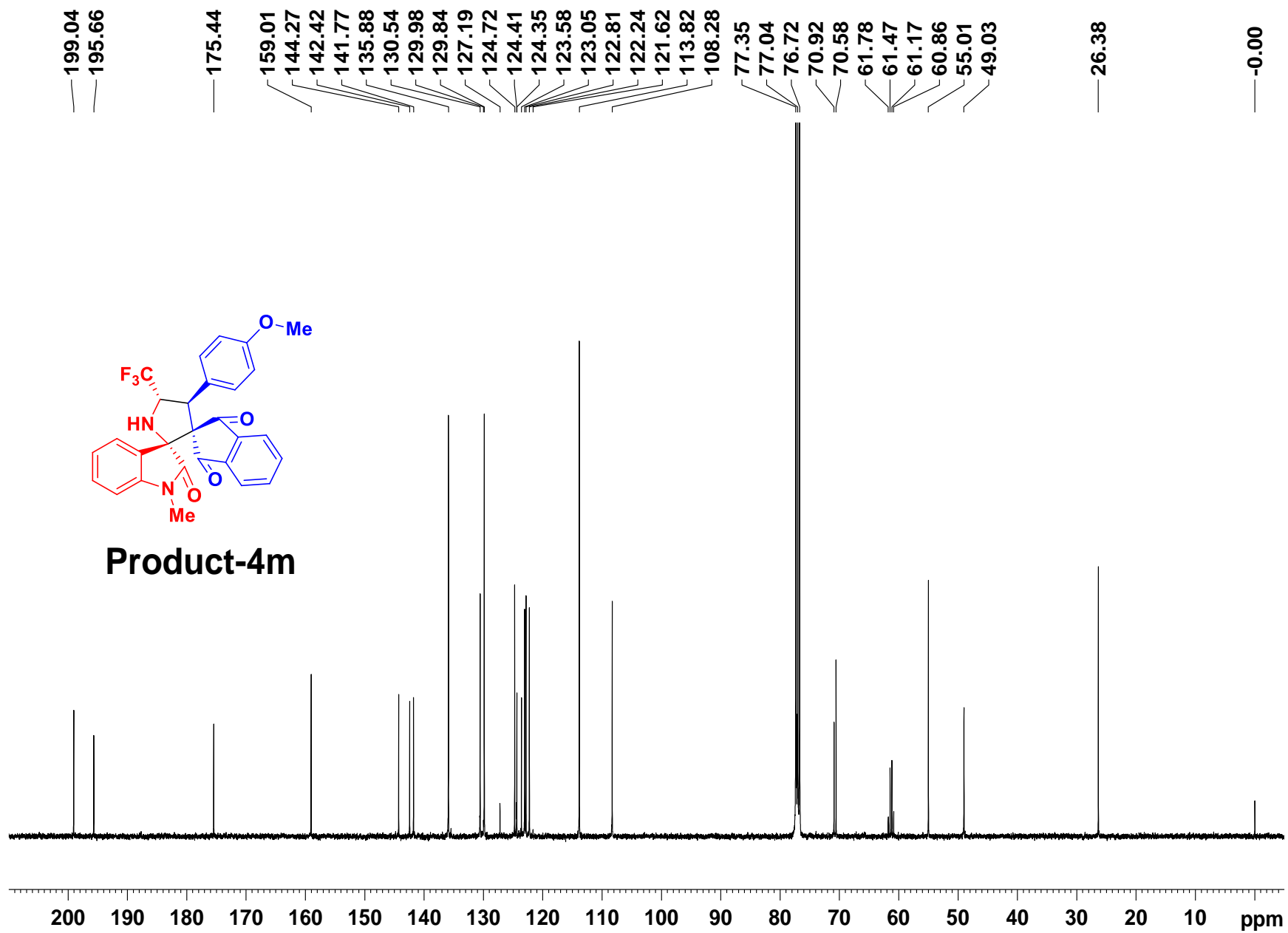
Product-4I



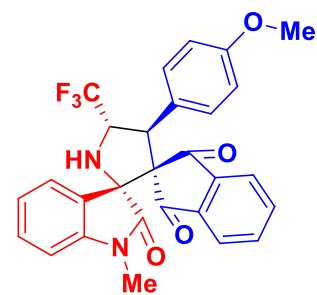


Product-4I

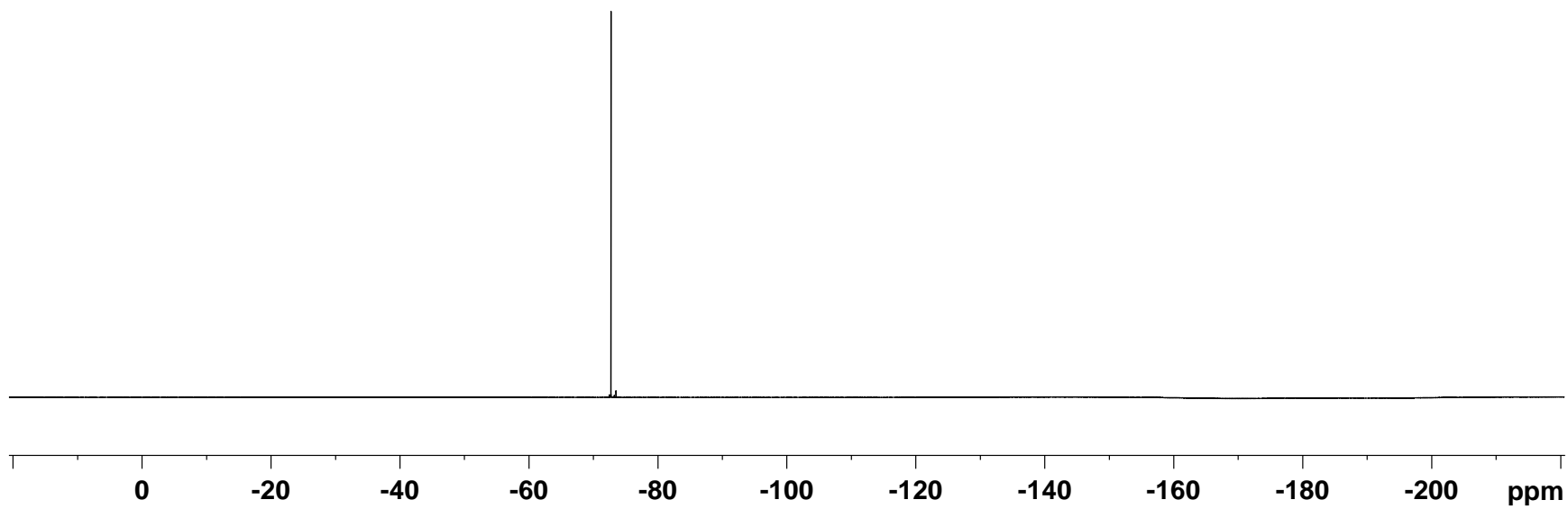


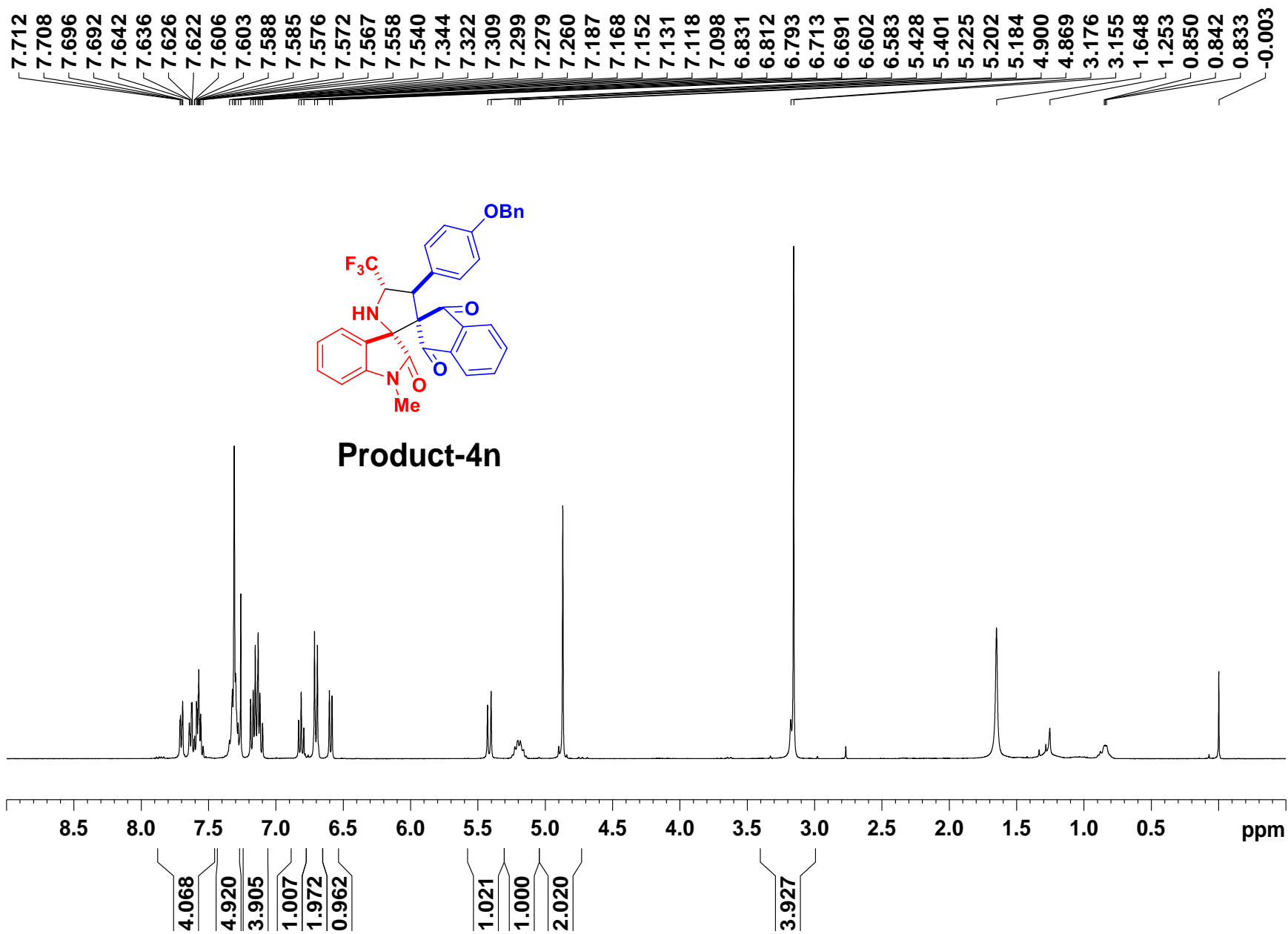


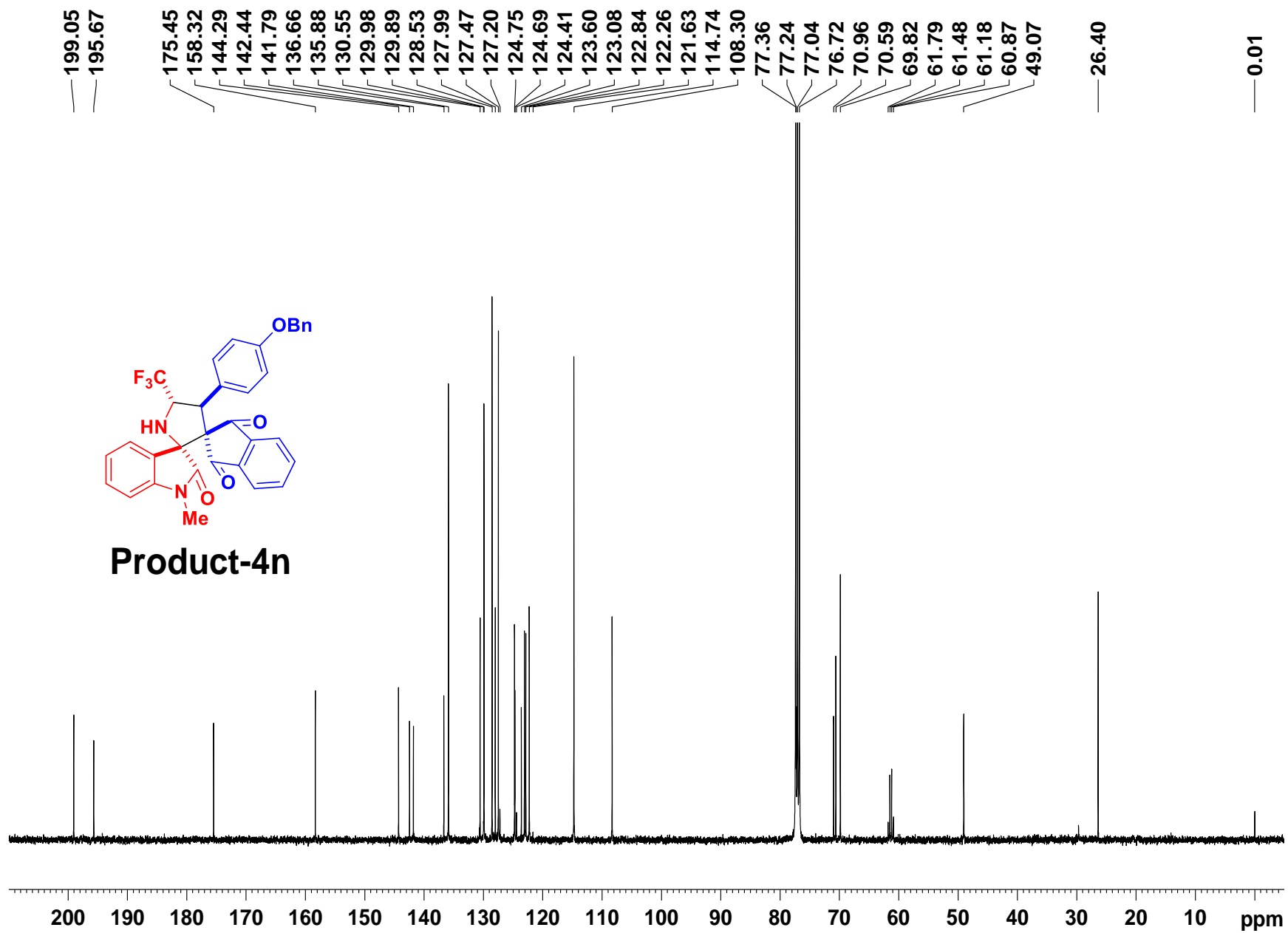
—72.73



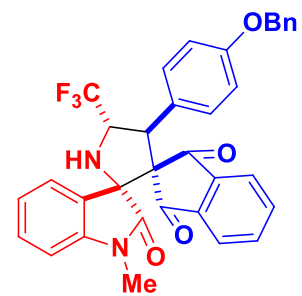
Product-4m



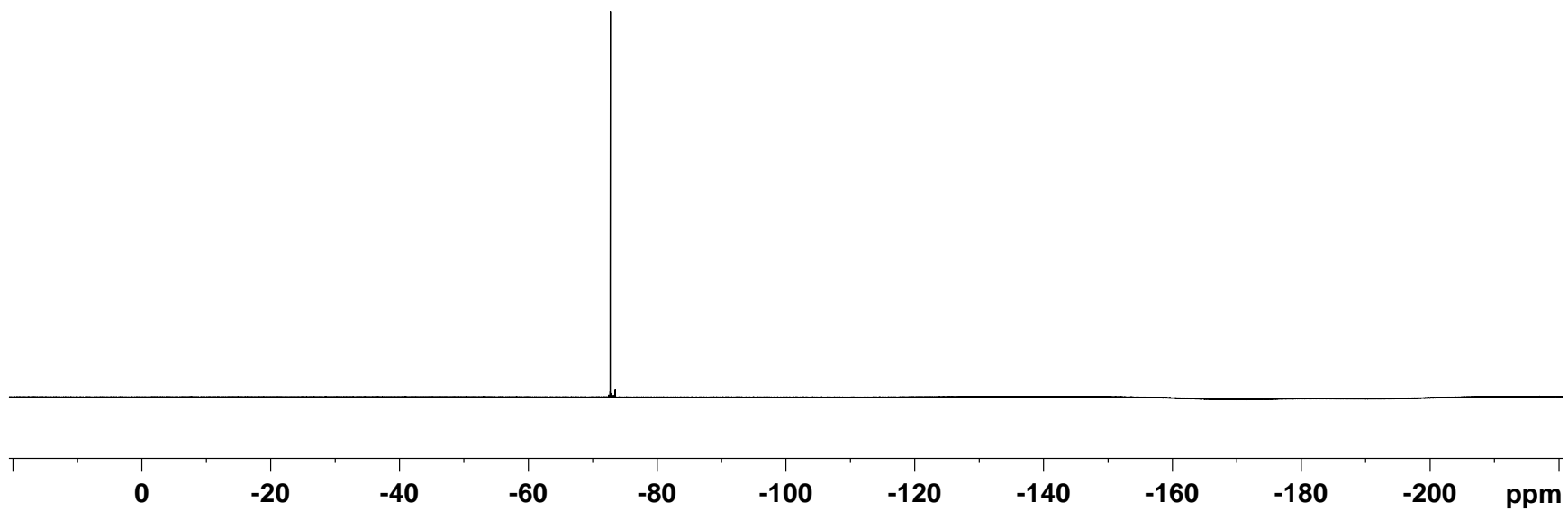




—72.71



Product-4n



S60

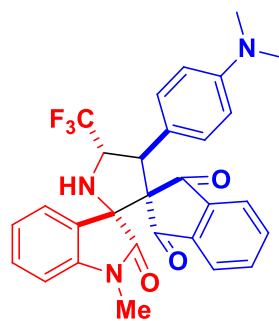
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7.079
7.057
6.824
6.806
6.787
6.595
6.575
6.445
6.423
5.385
5.359
5.201
5.185

— 3.154

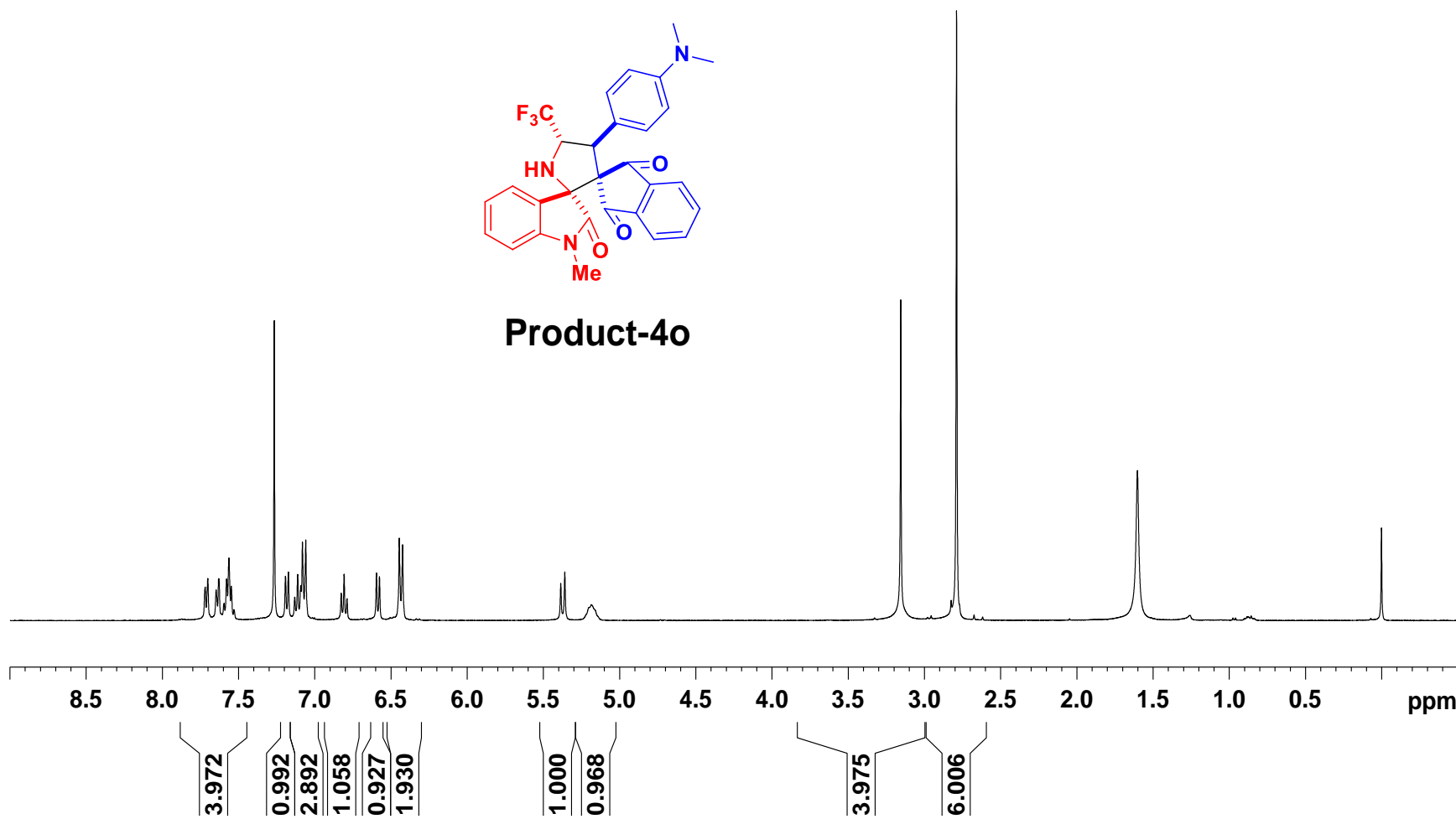
— 2.788

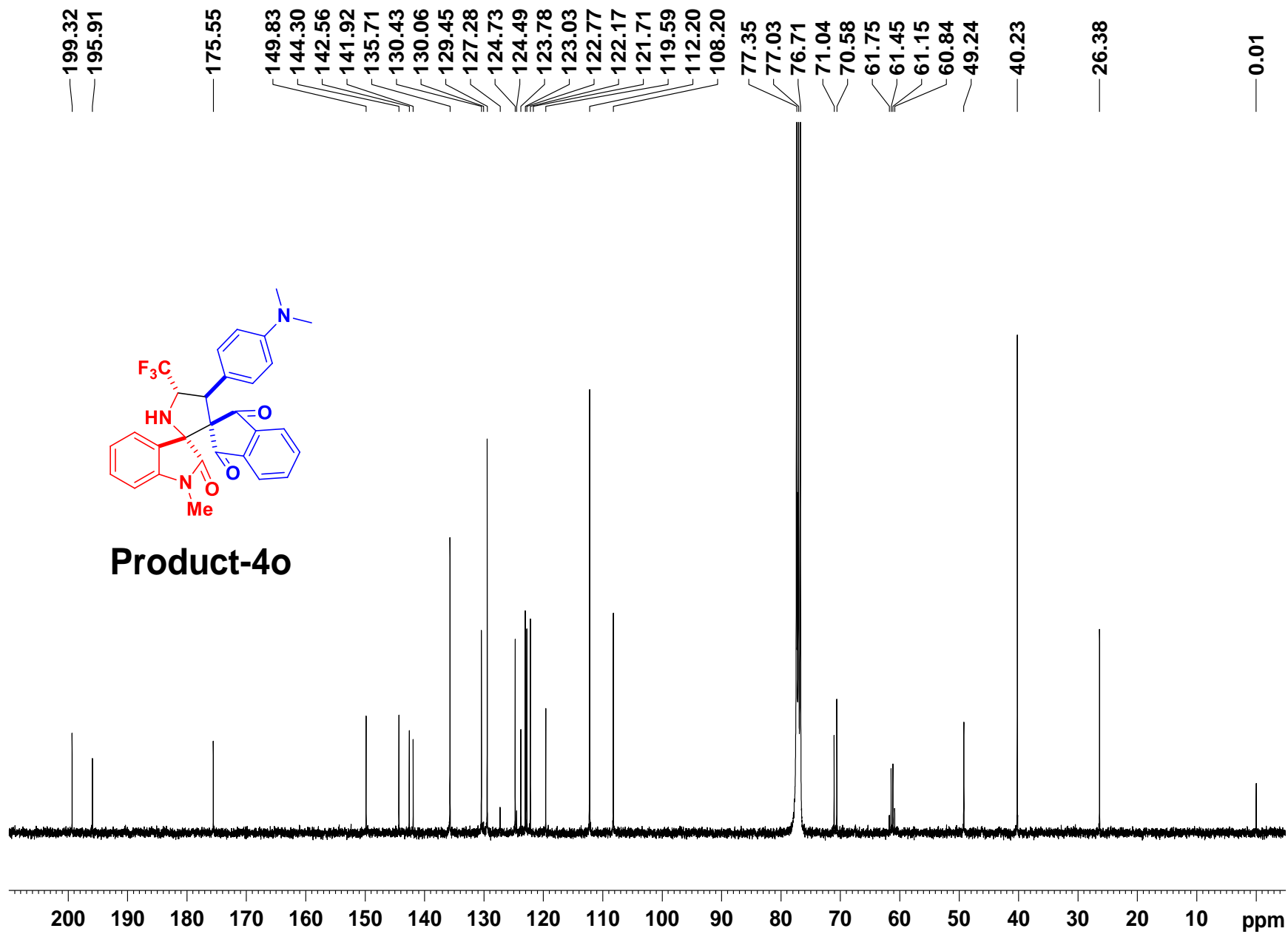
— 1.601

— -0.000

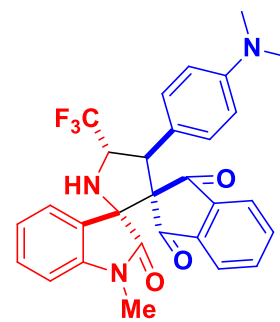


Product-4o

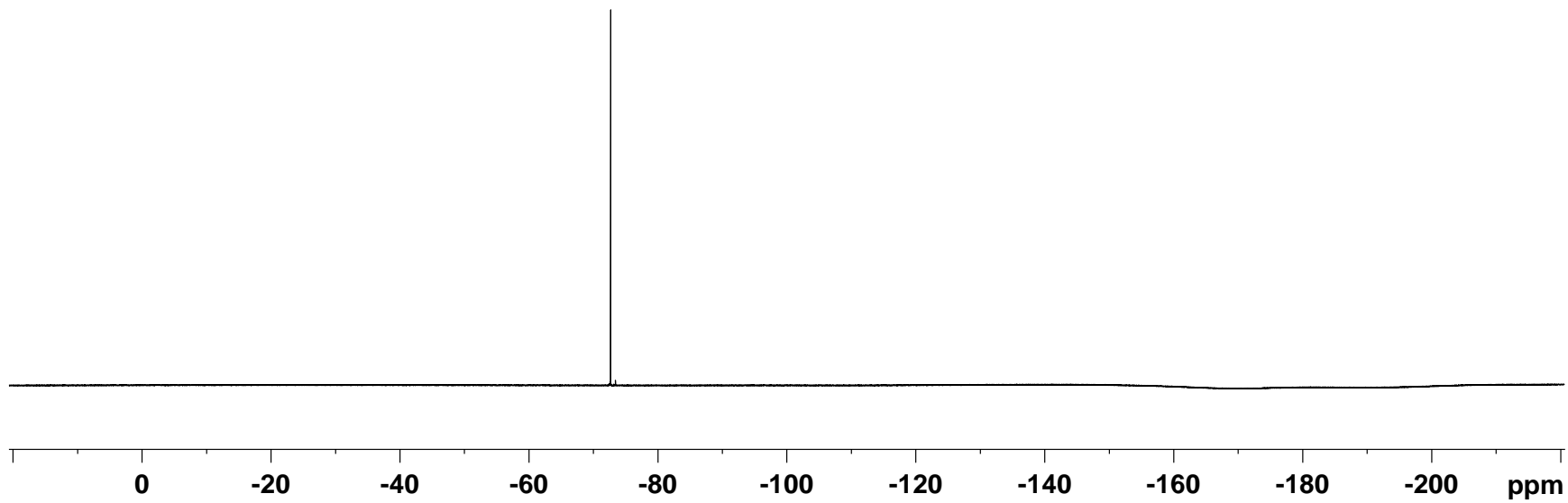


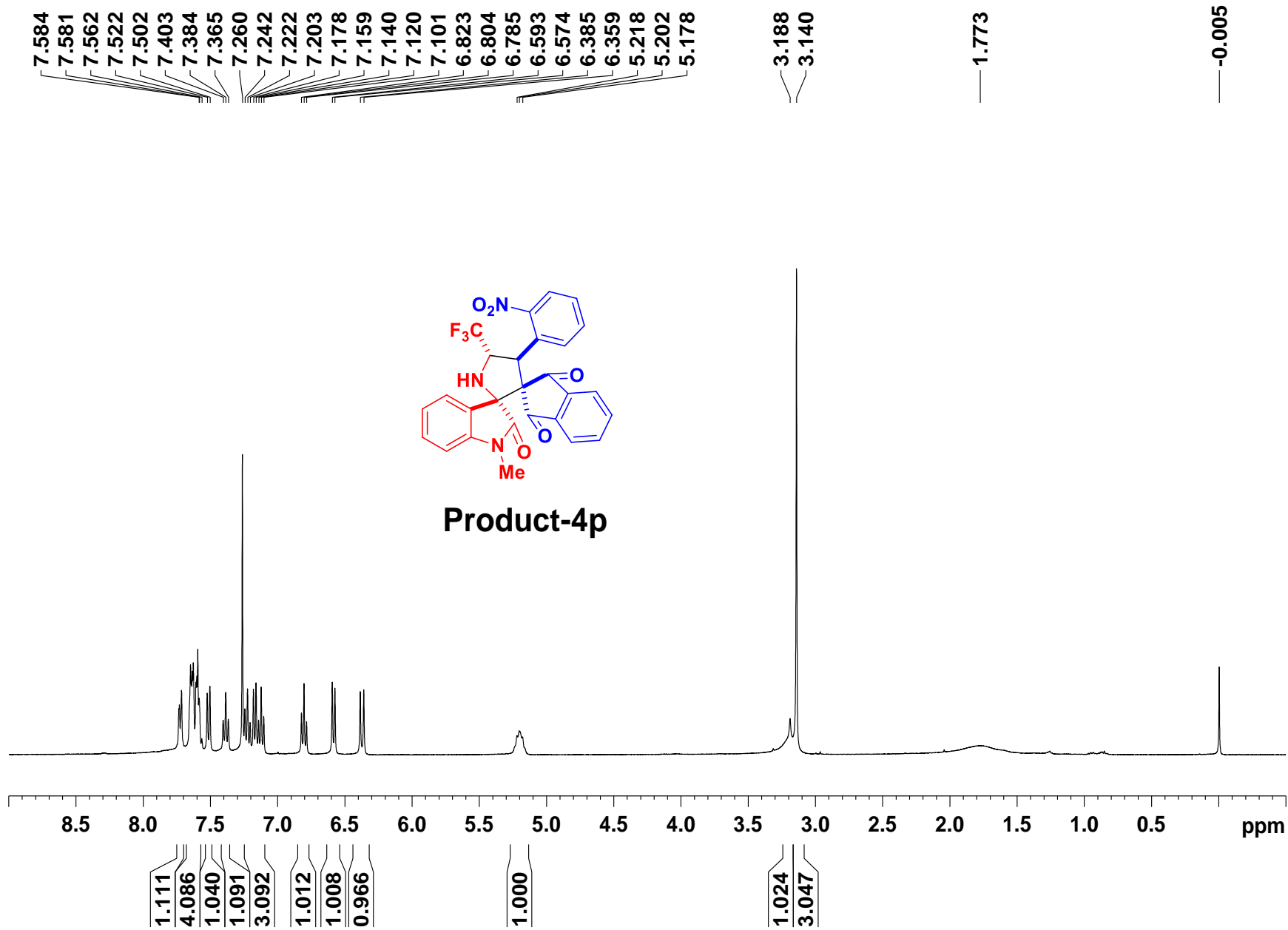


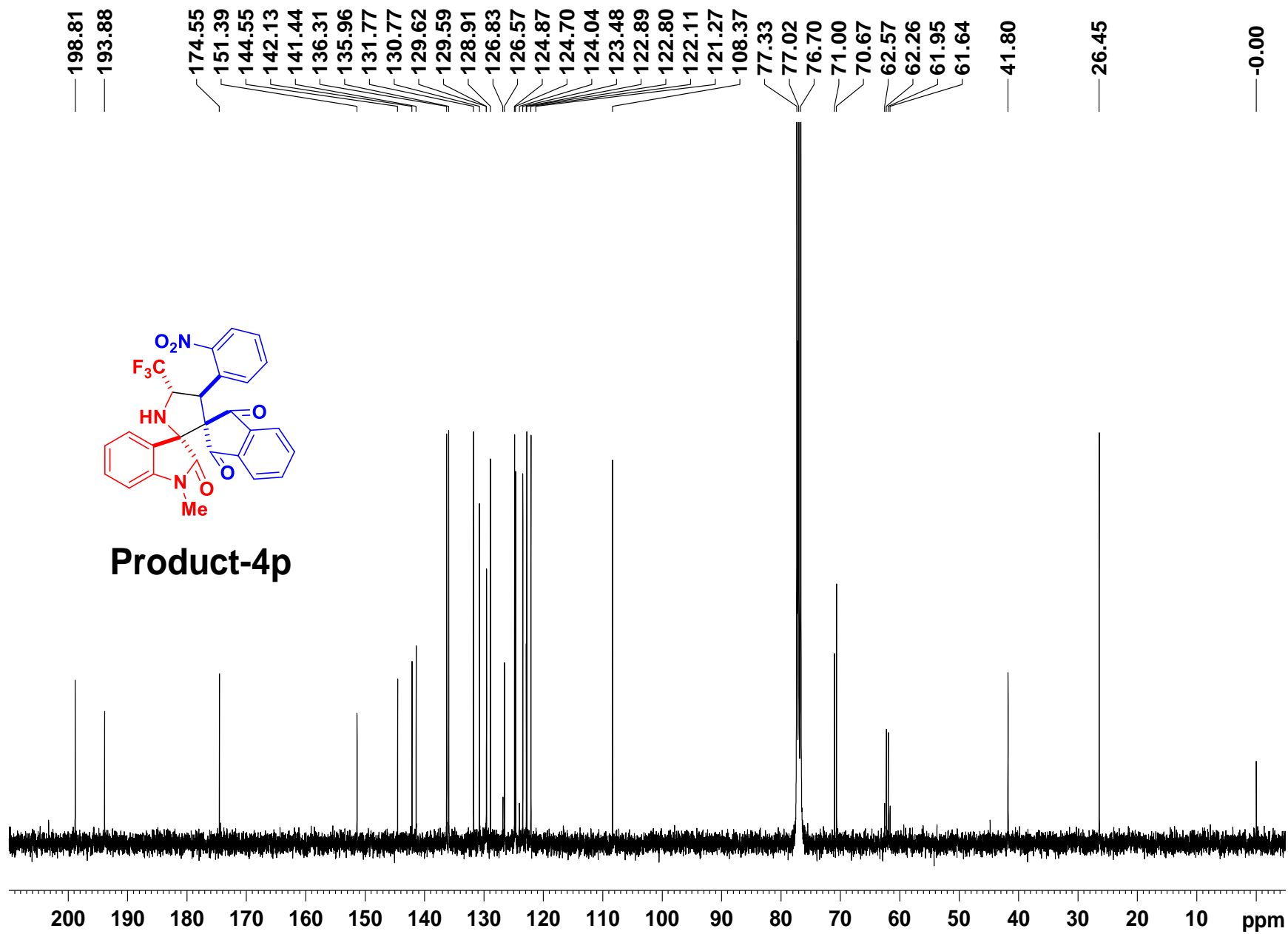
—72.67

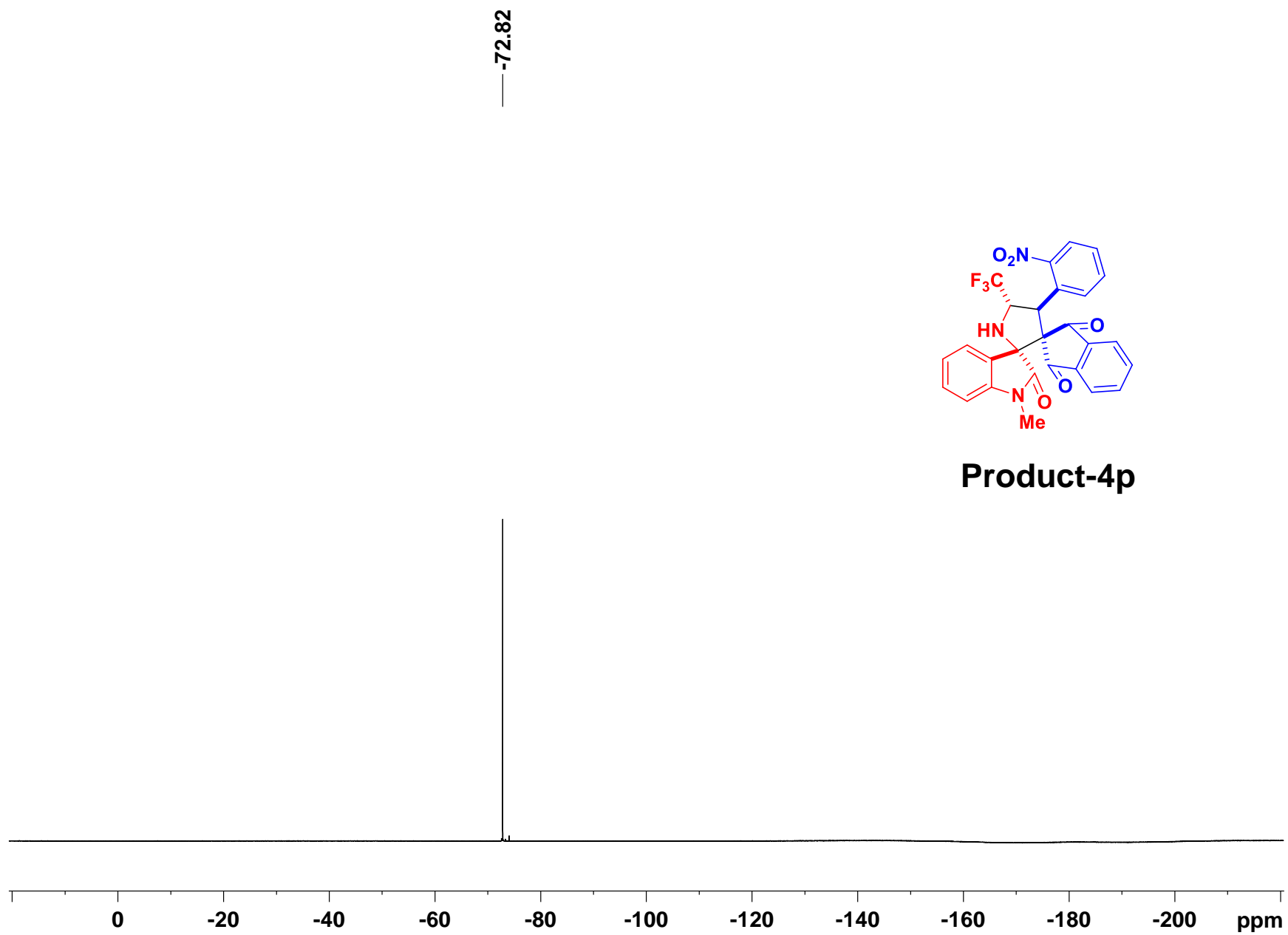


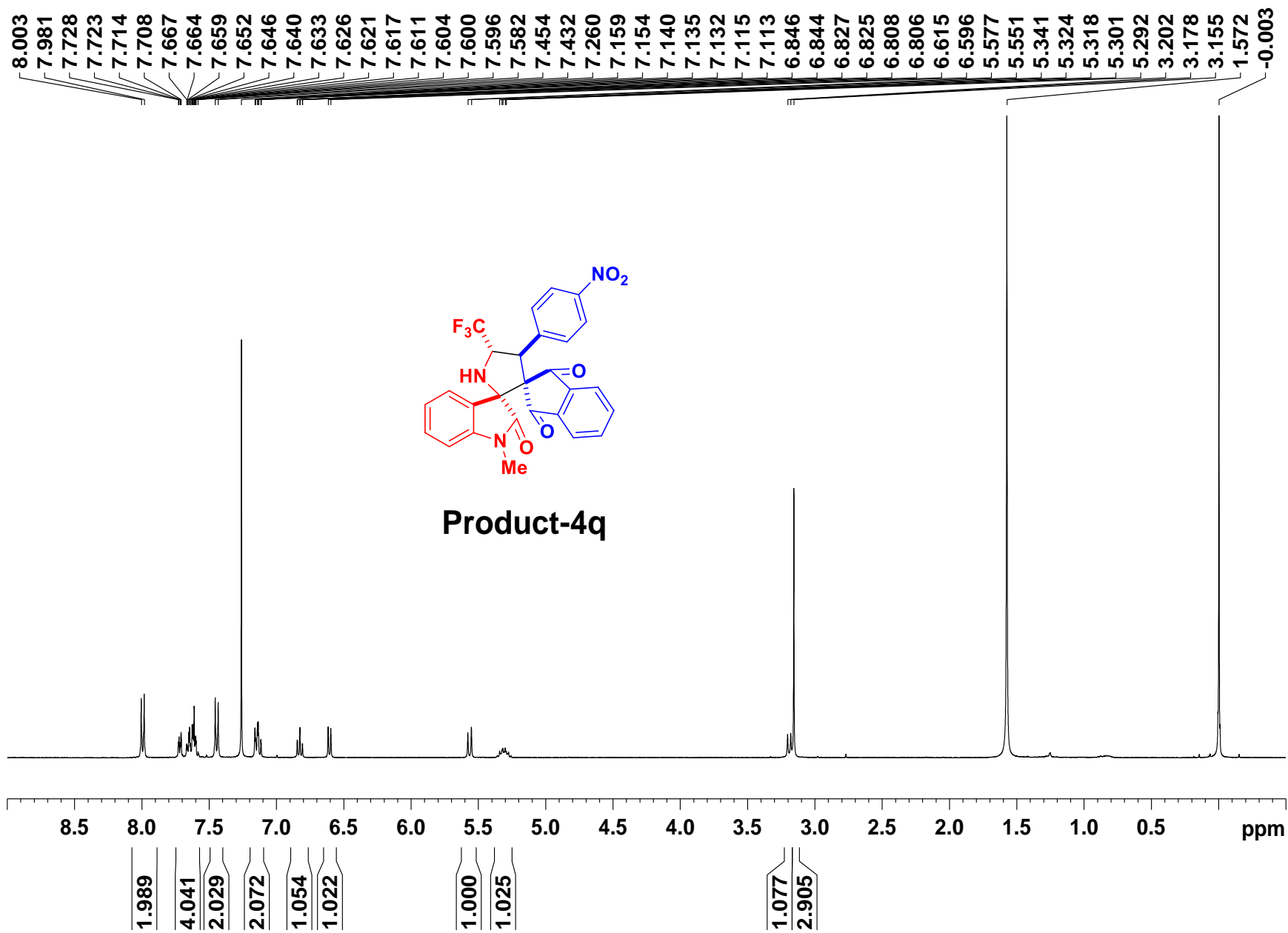
Product-4o

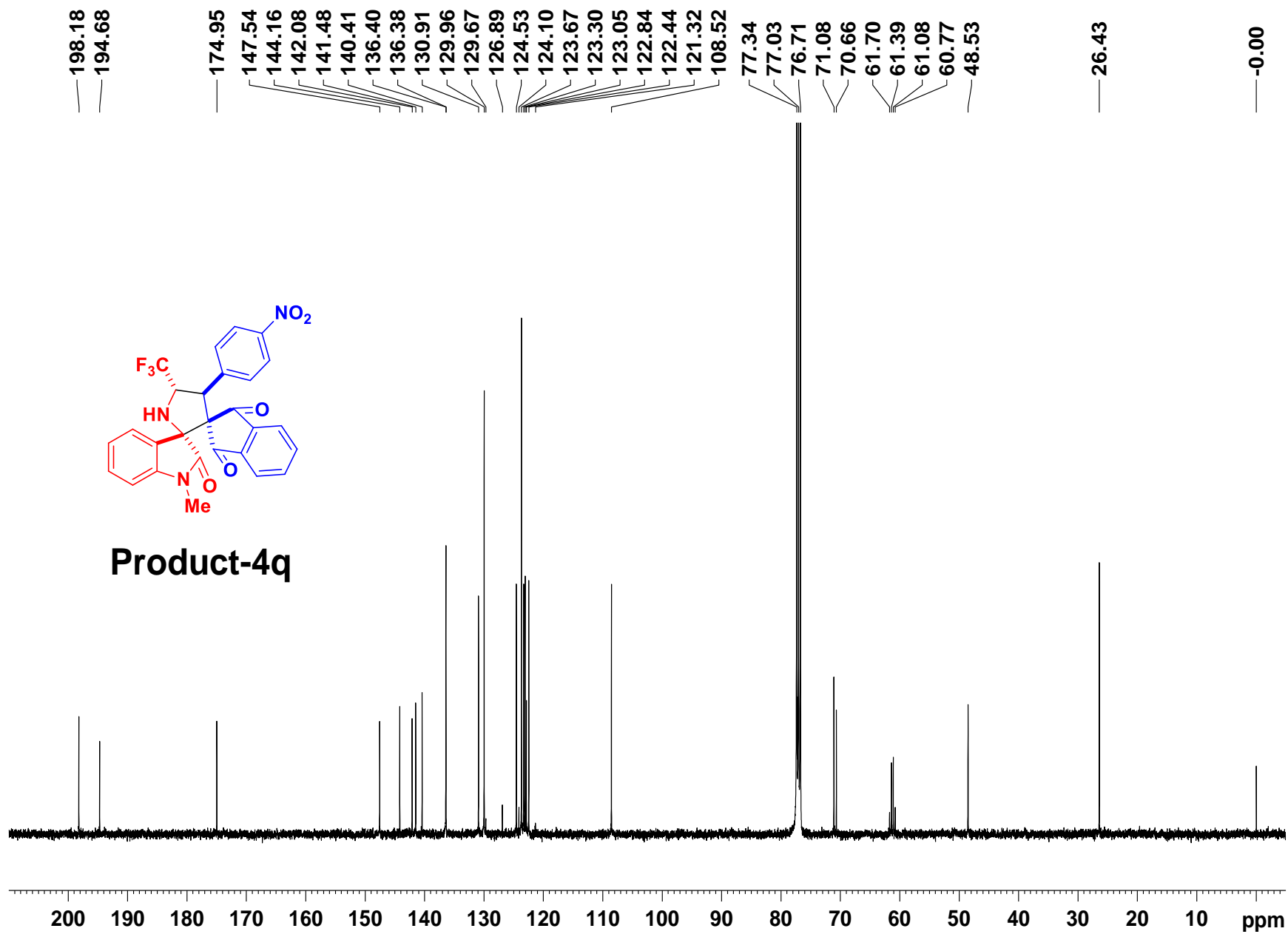


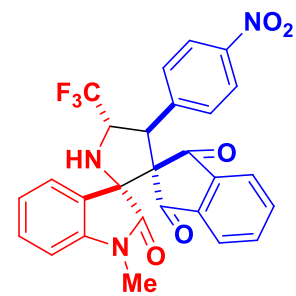
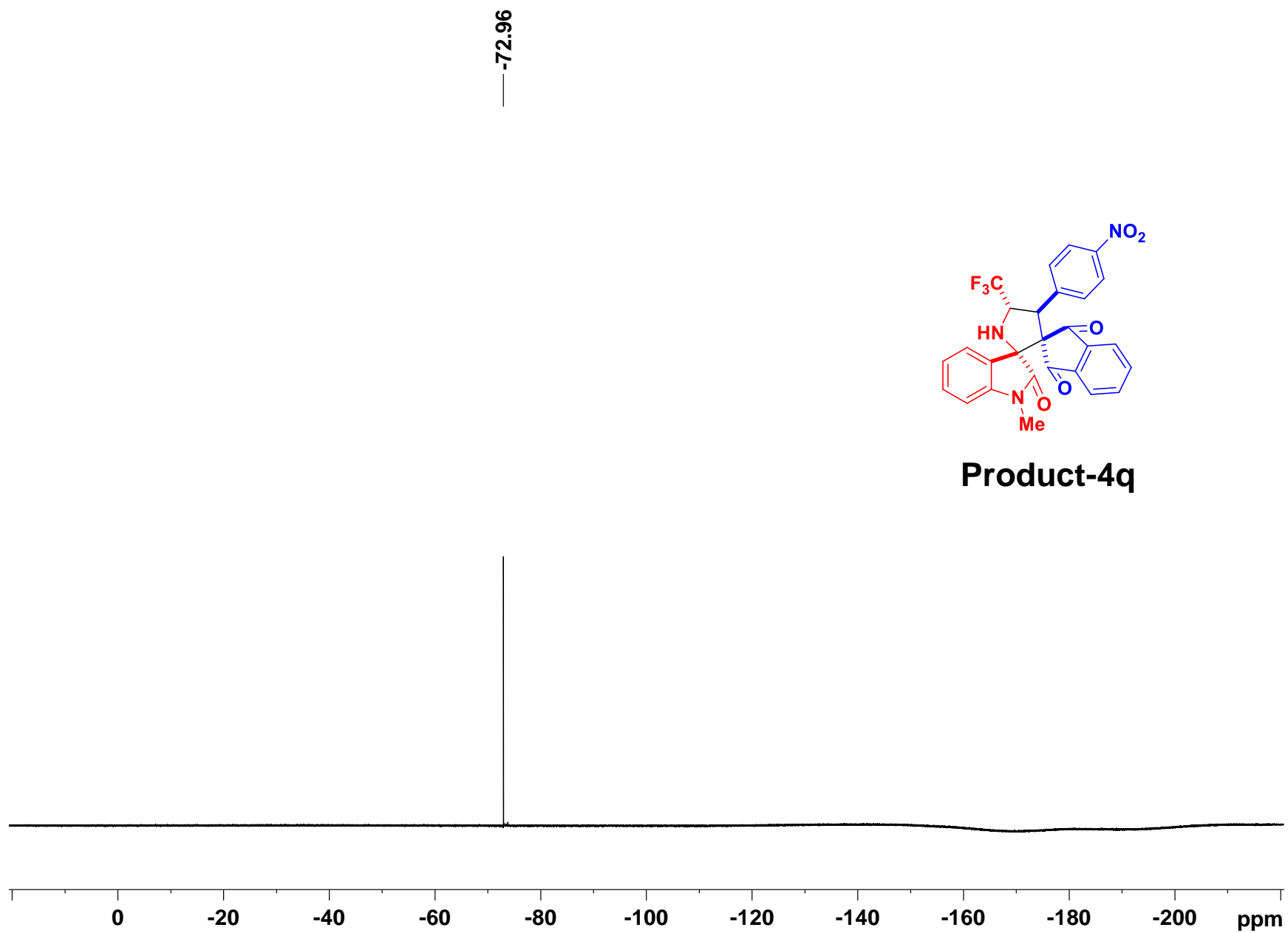




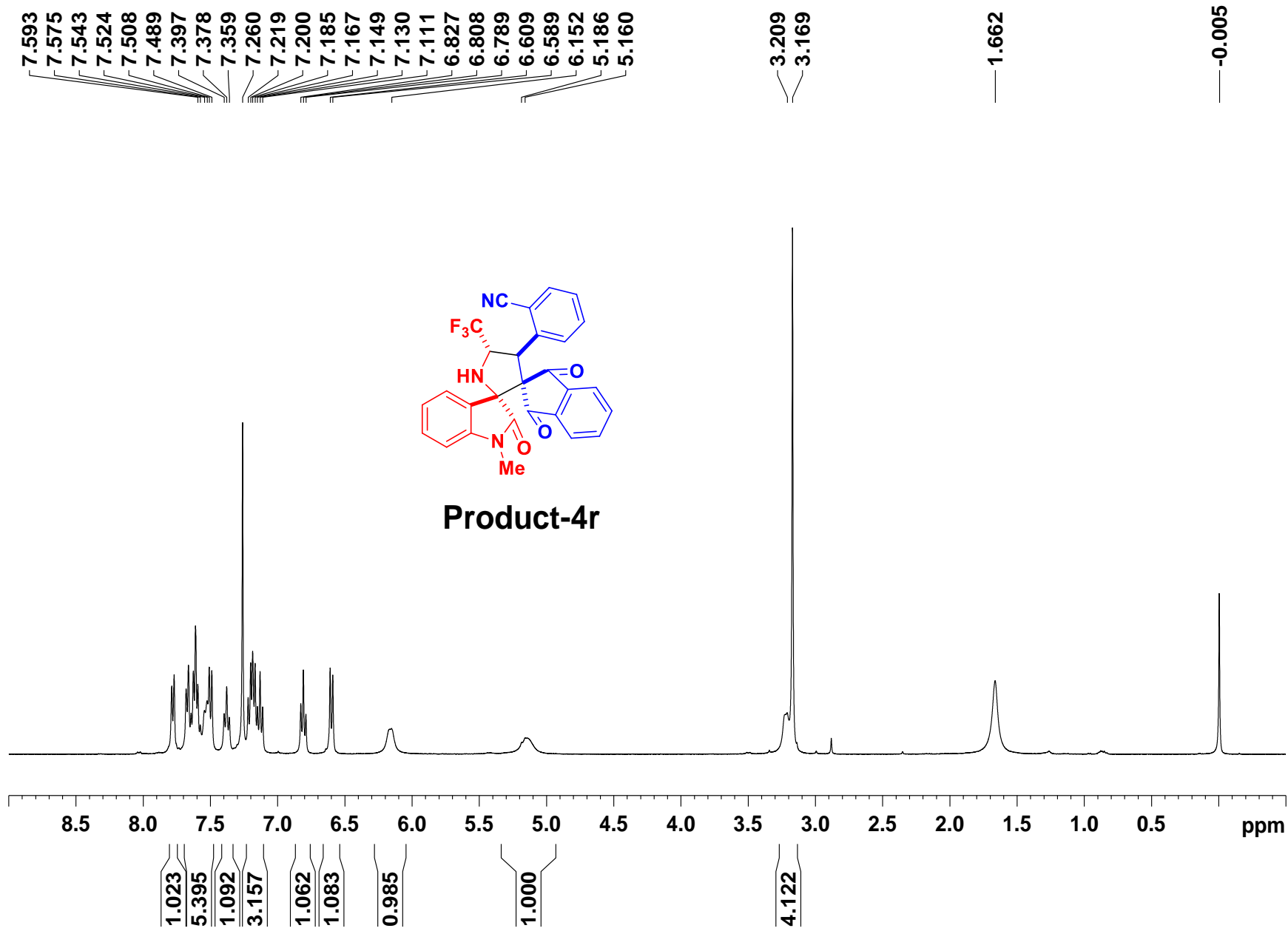


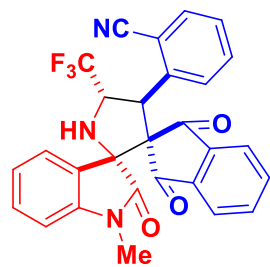




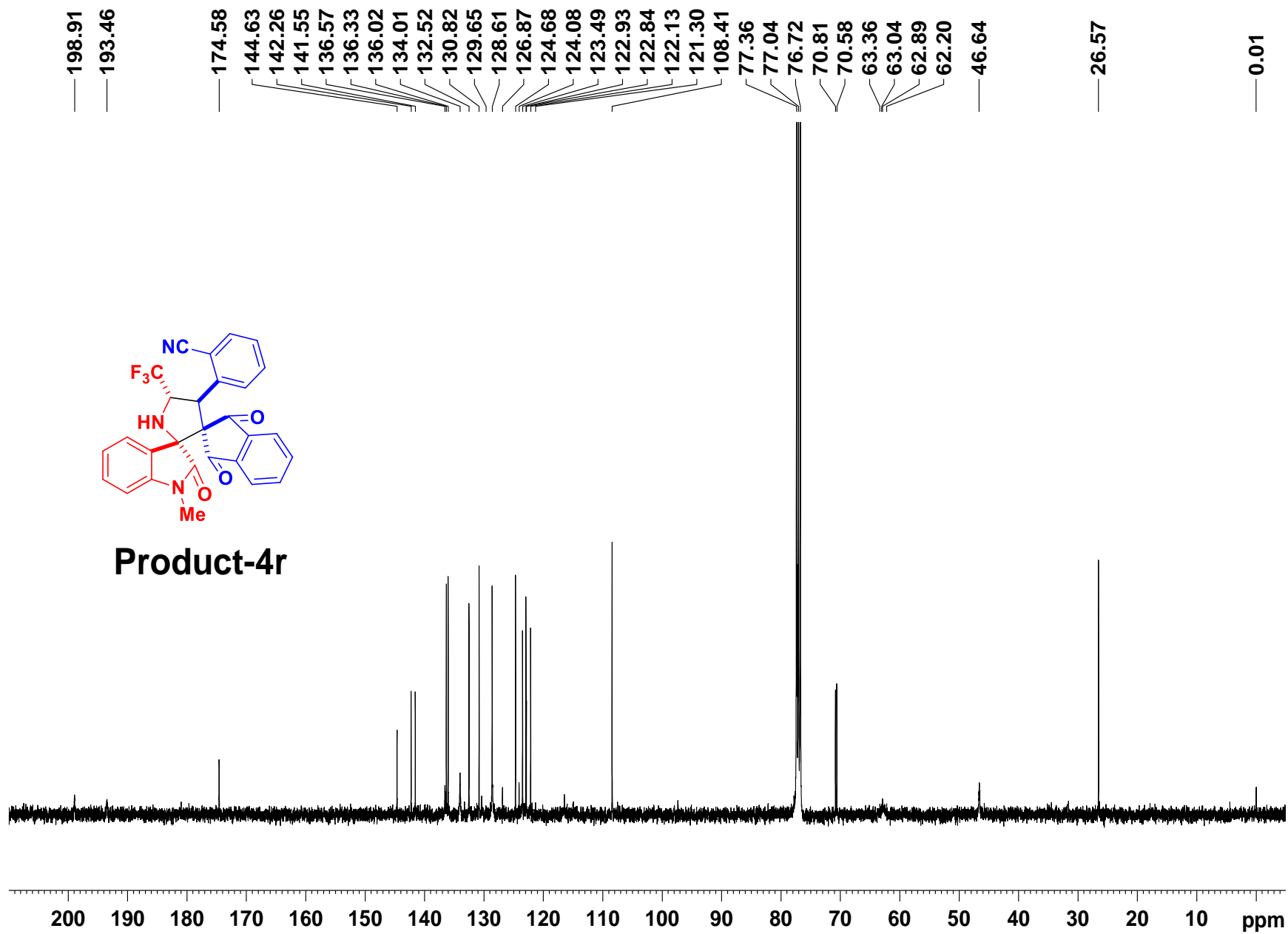


Product-4q

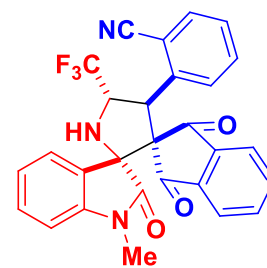




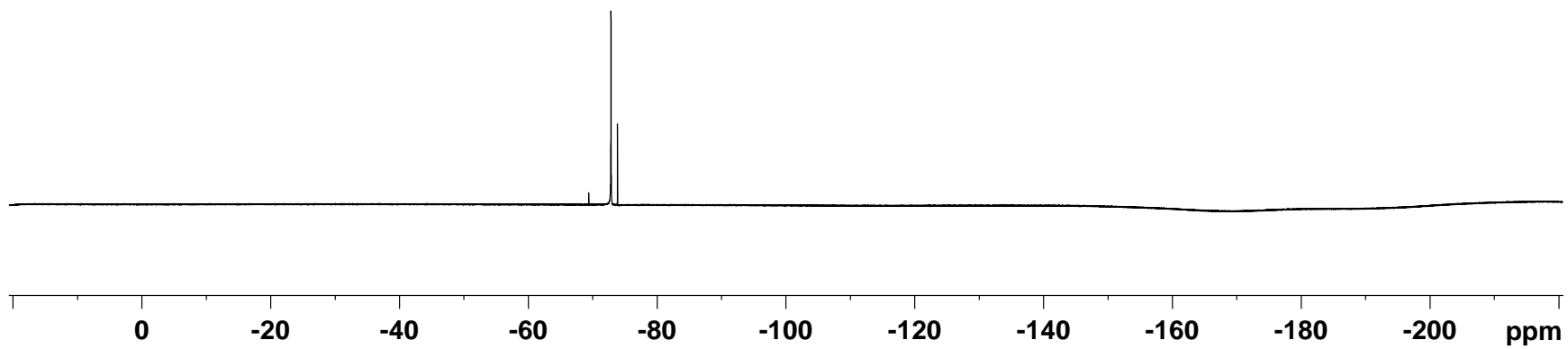
Product-4r

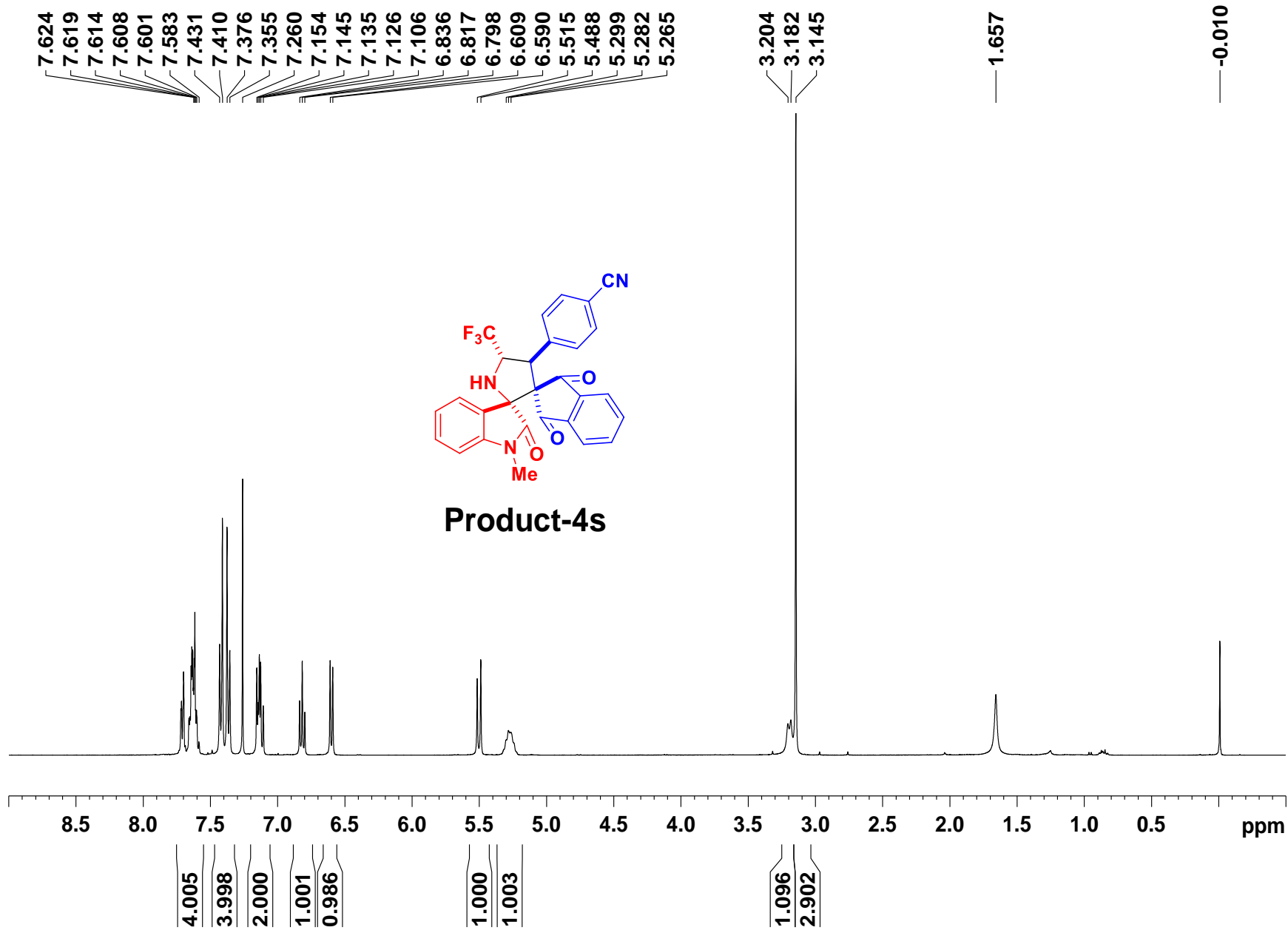


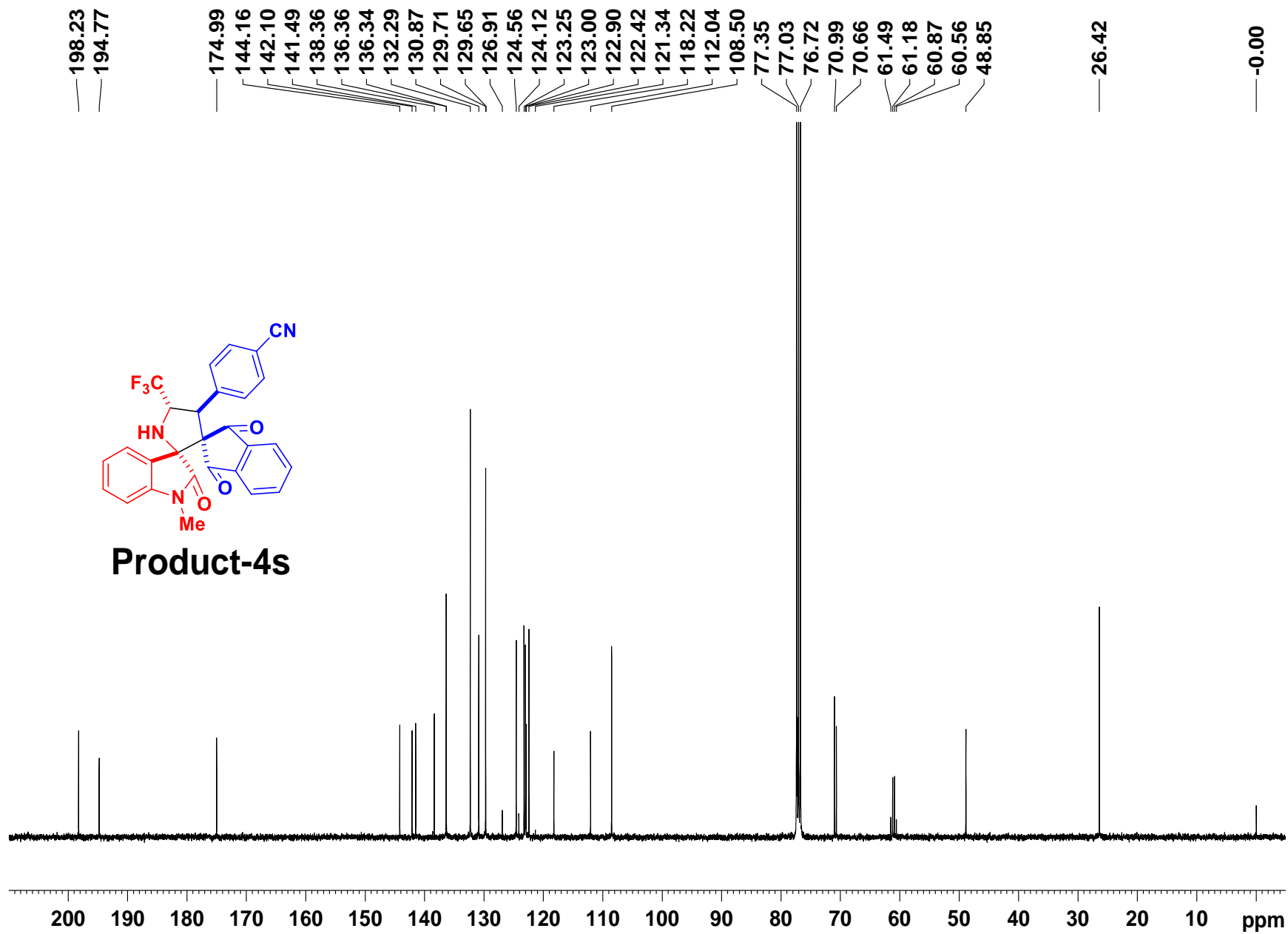
-72.83
-73.83

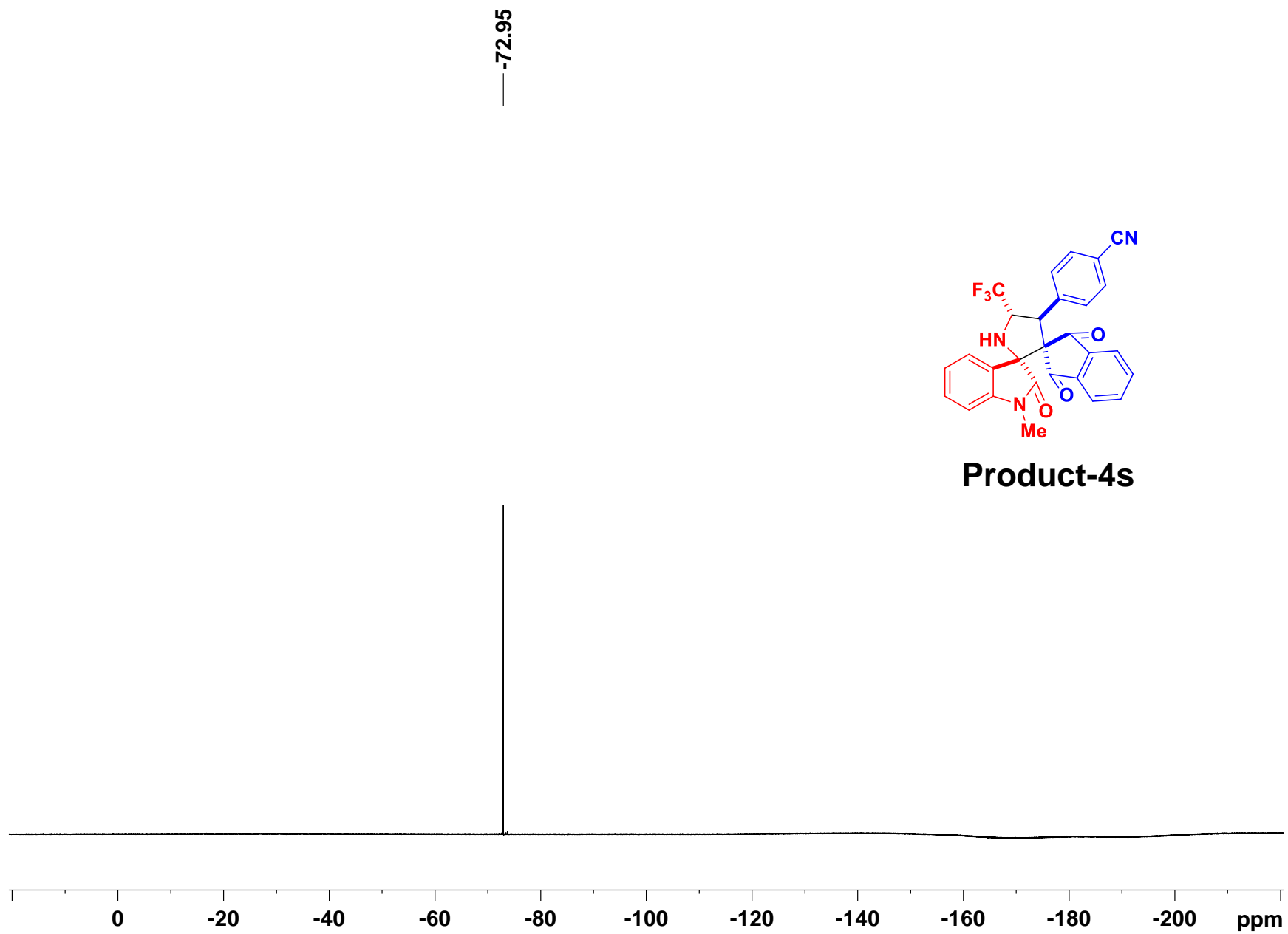


Product-4r









S75

7.645
7.628
7.608
7.592
7.578
7.300
7.264
7.244
7.195
7.177
7.159
7.138
7.119
7.101
7.005
6.831
6.813
6.793
6.601
6.583
5.432
5.406
5.229
5.211

3.152

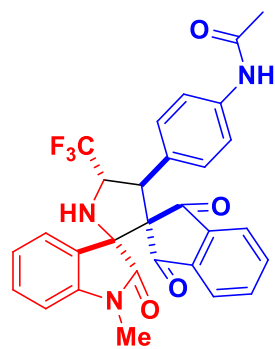
2.078

1.586

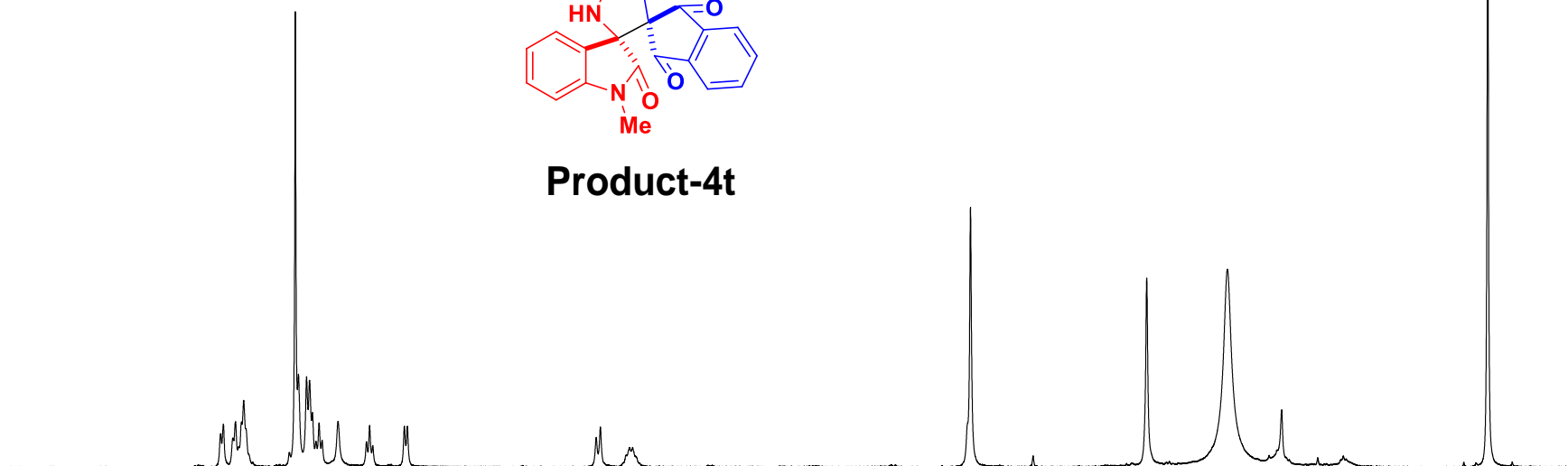
1.256

0.880

-0.000



Product-4t



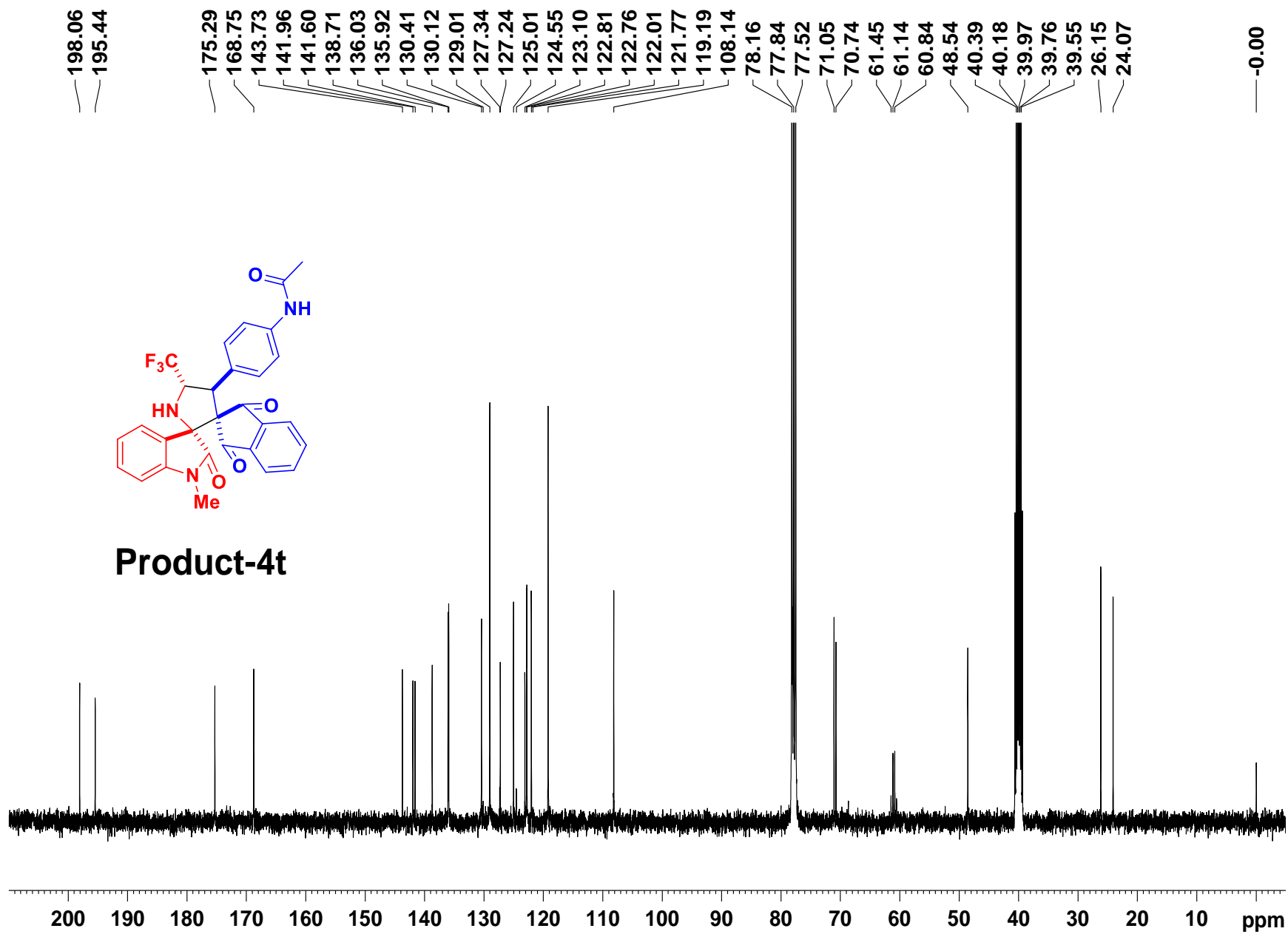
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

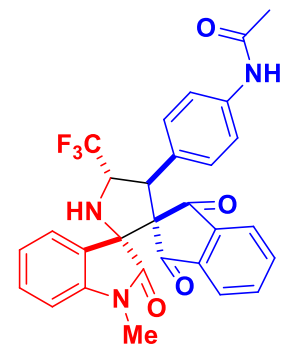
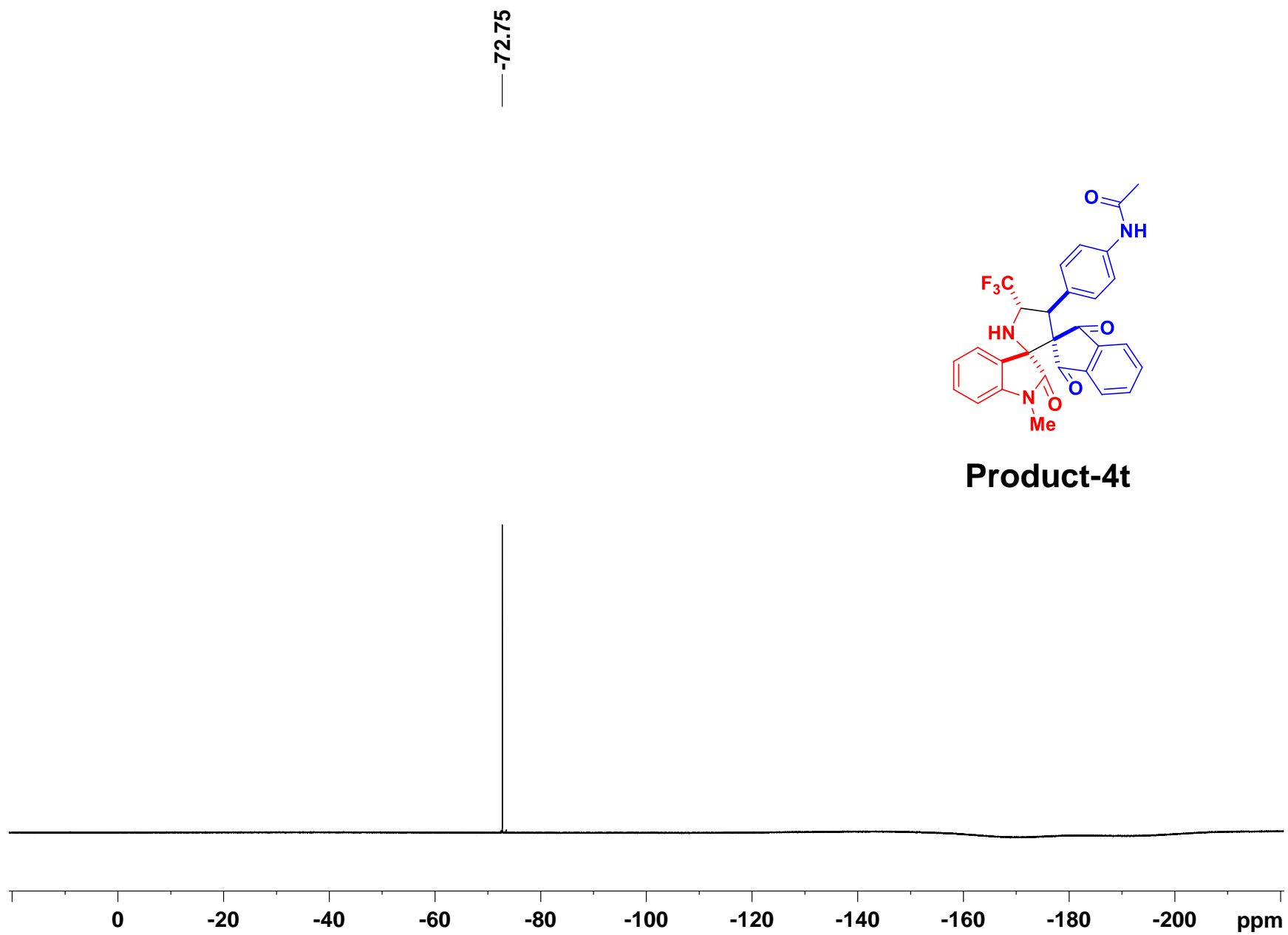
4.061
6.078
1.070
1.058
1.063

1.000
1.040

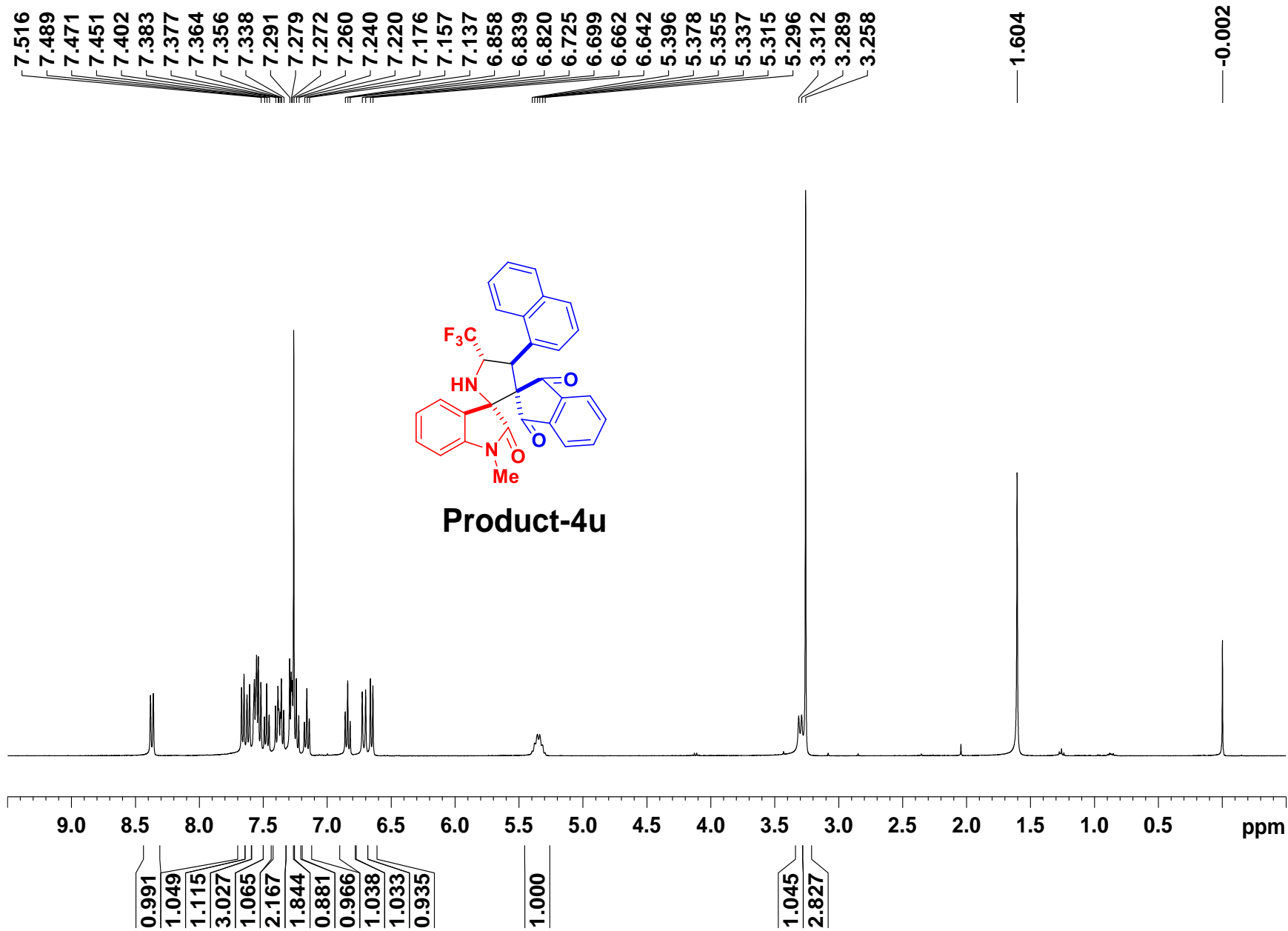
3.944

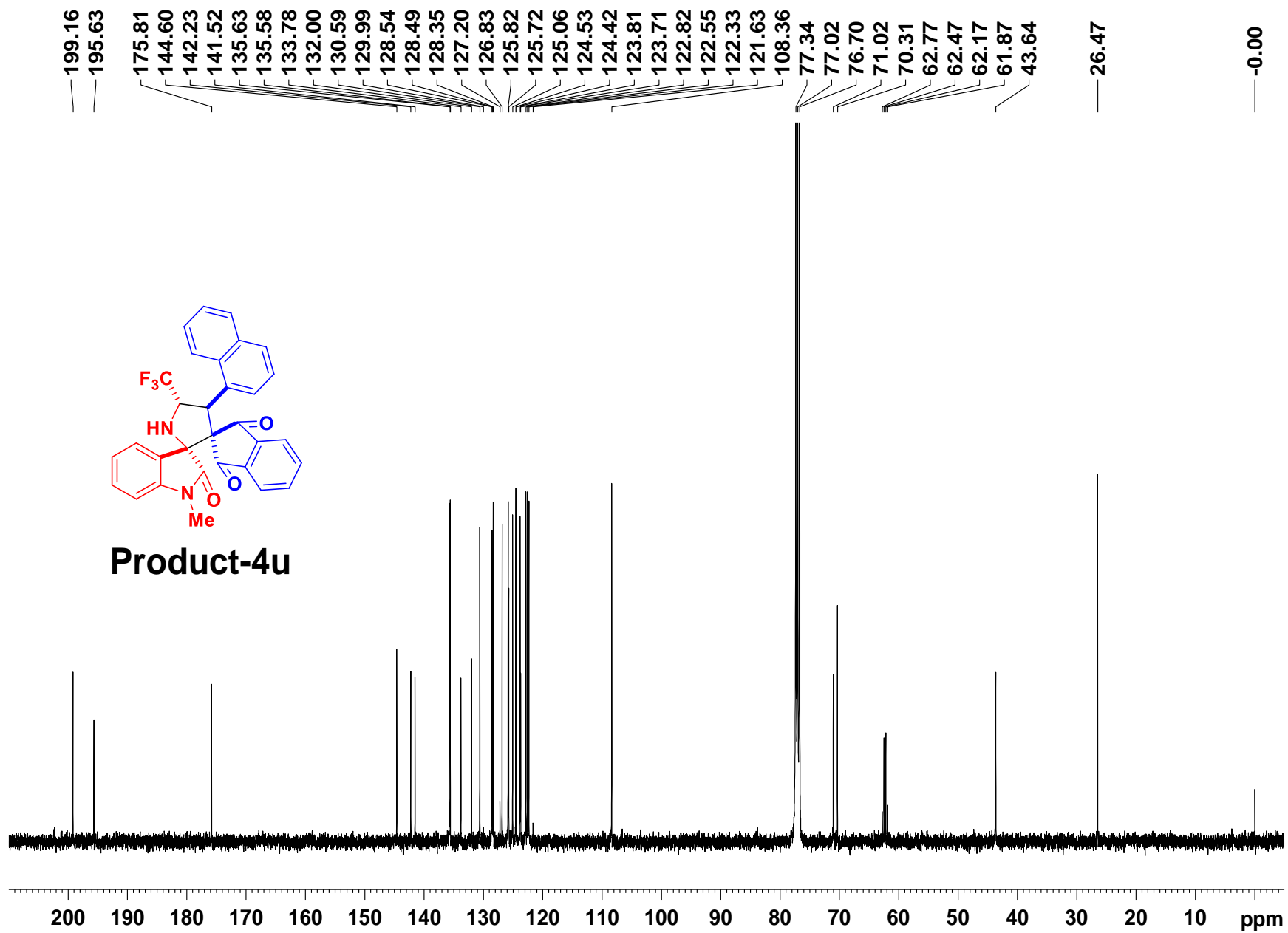
3.119



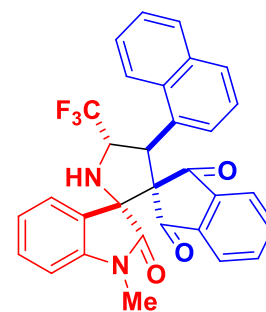


Product-4t

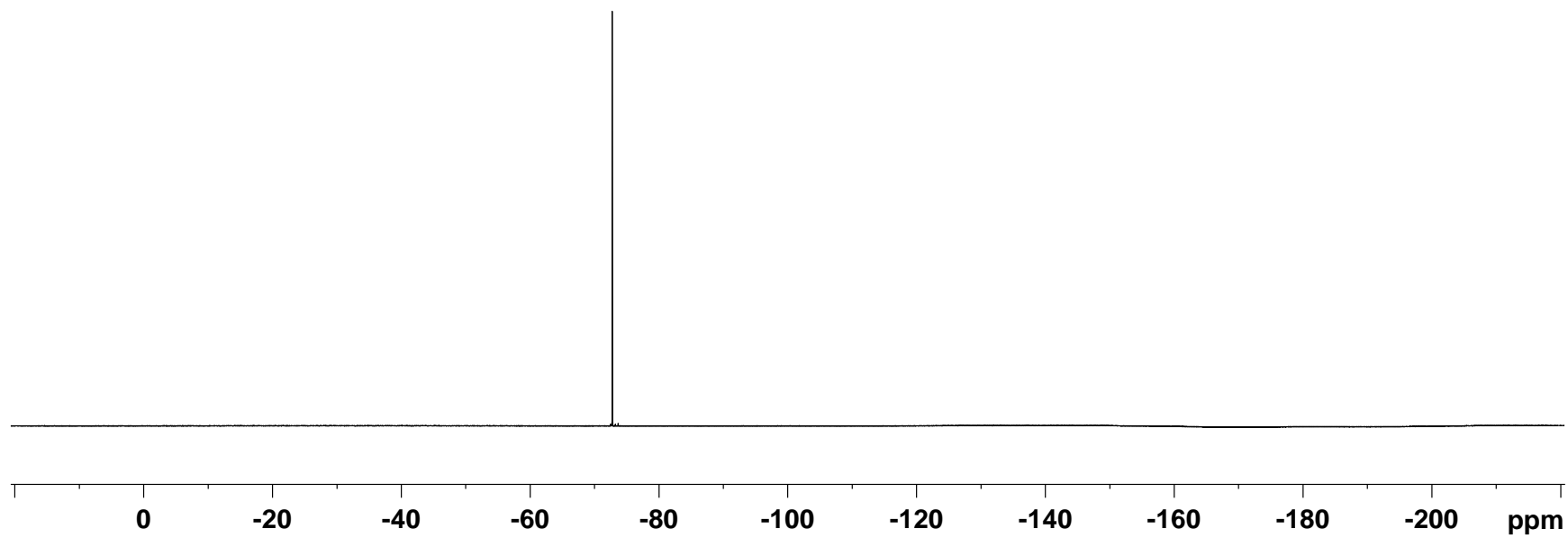




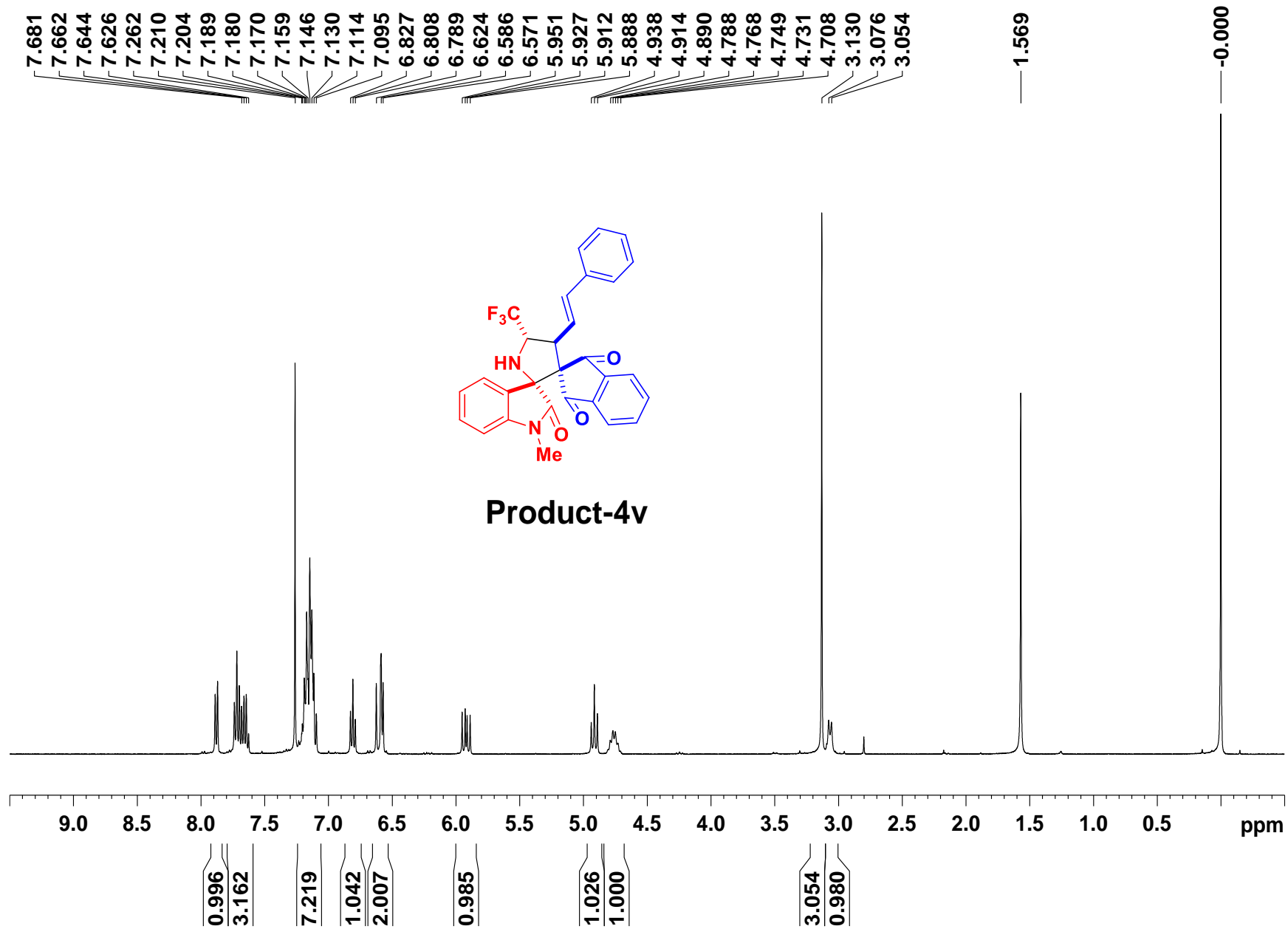
—72.74

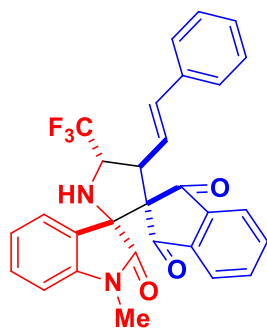


Product-4u

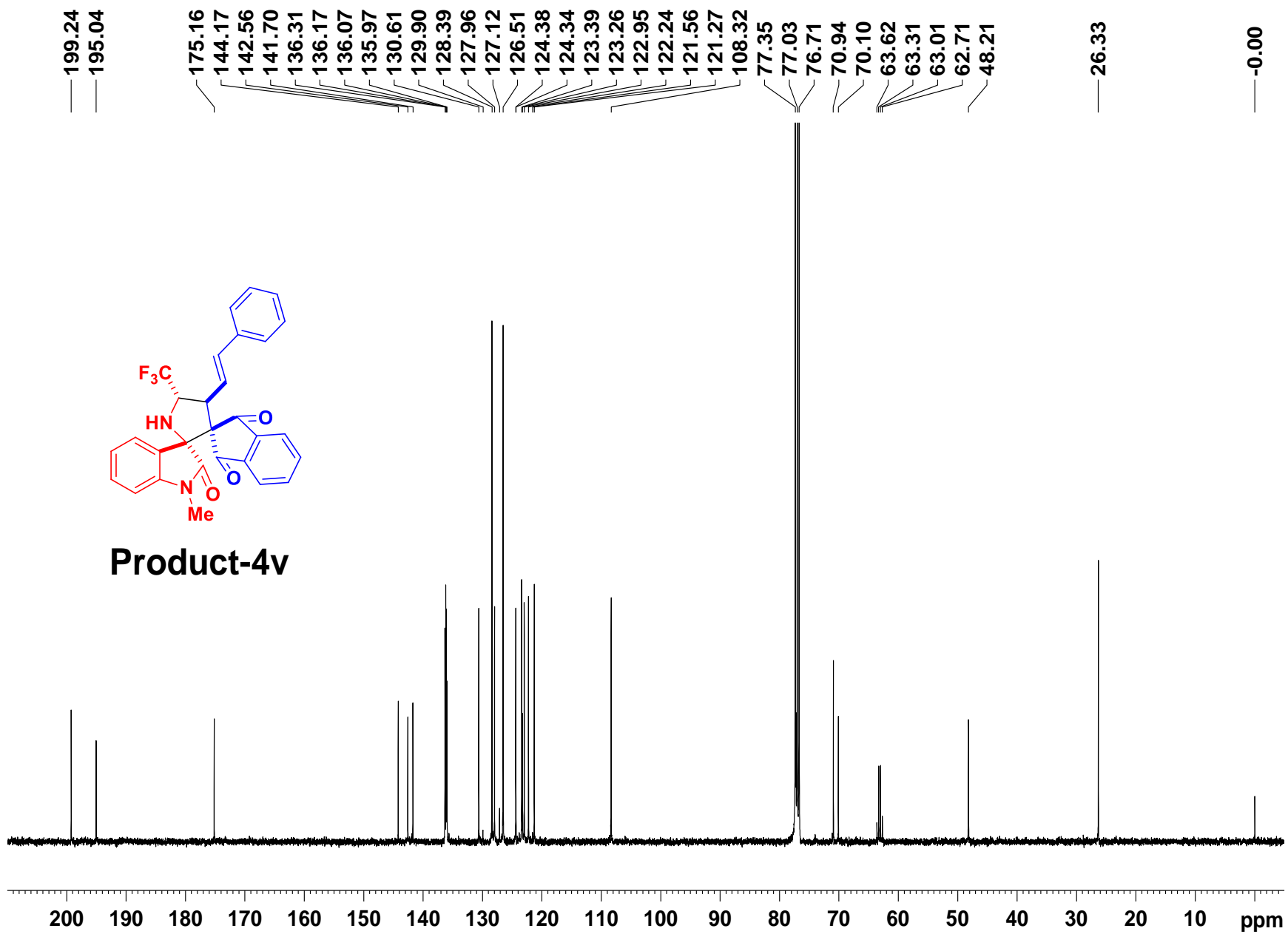


S81

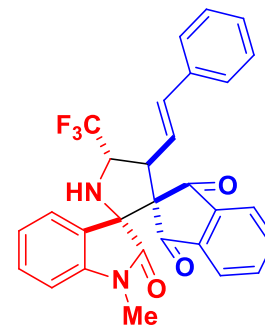




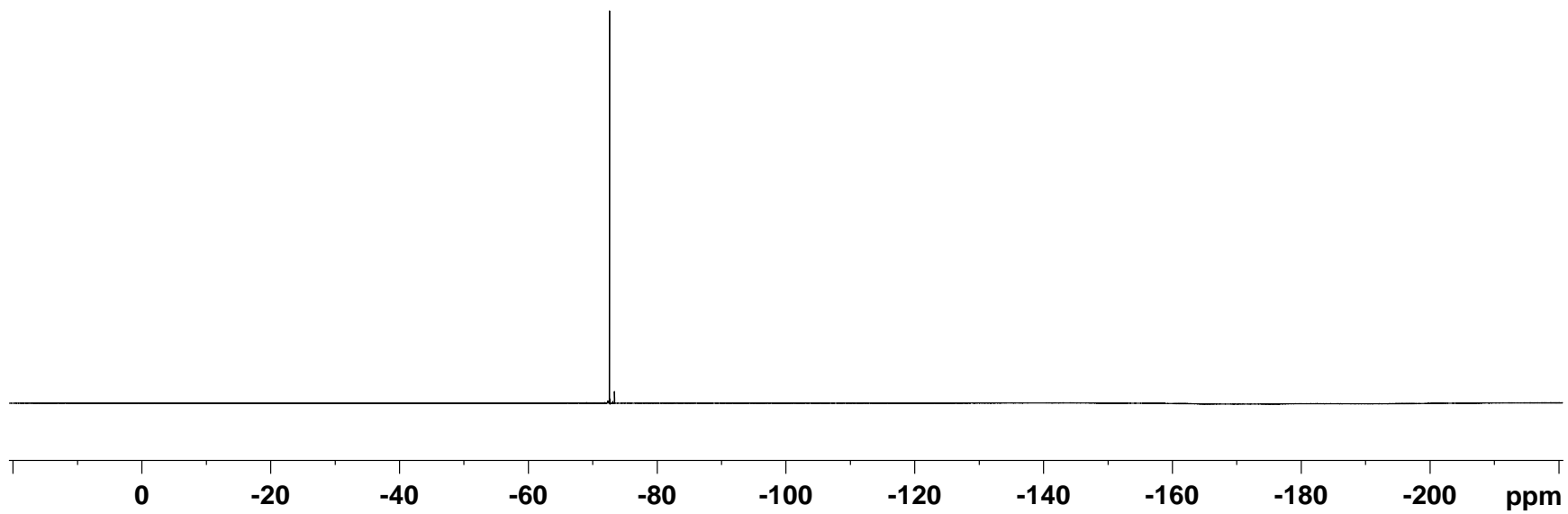
Product-4v



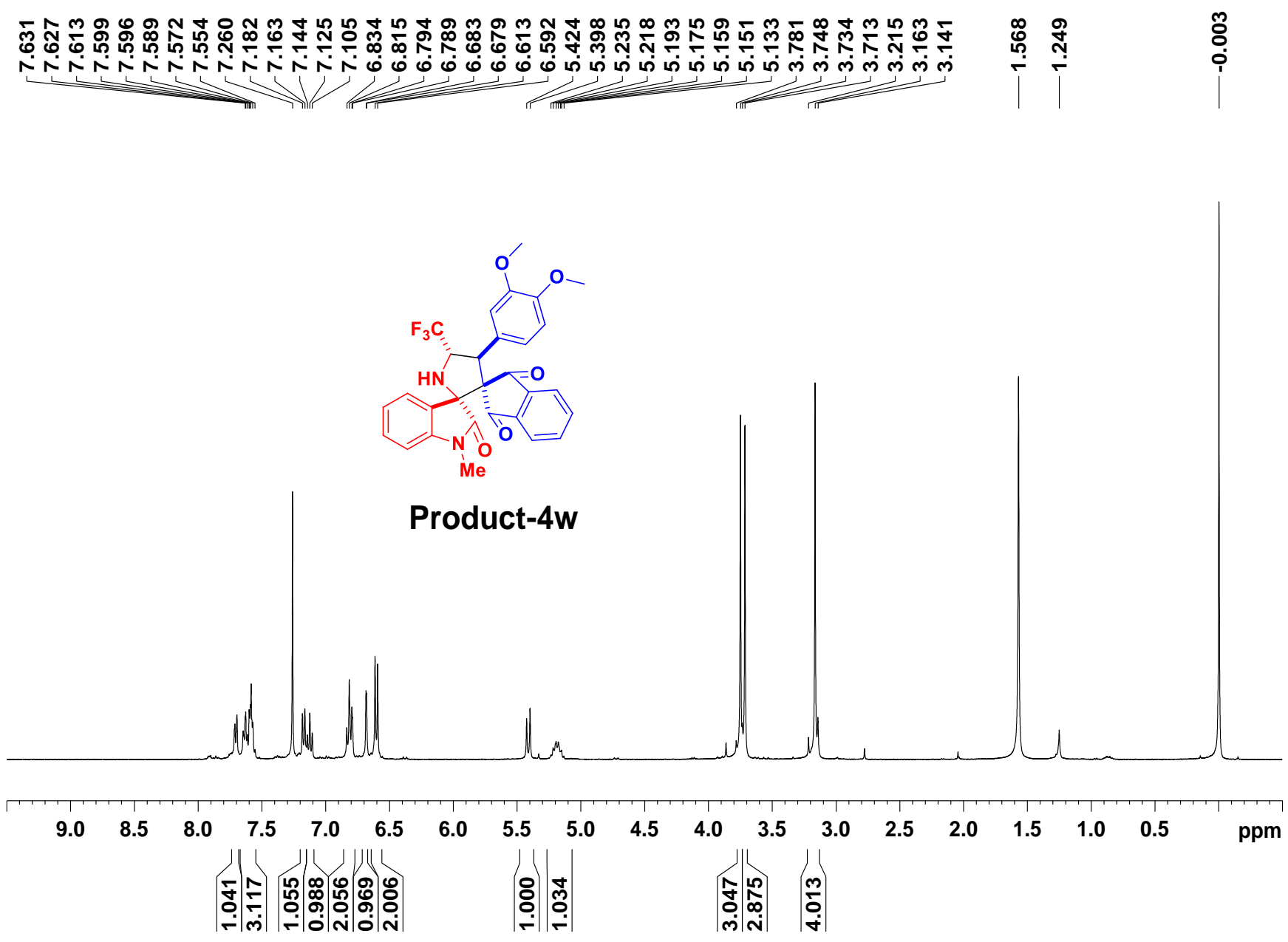
—72.61



Product-4v



S84

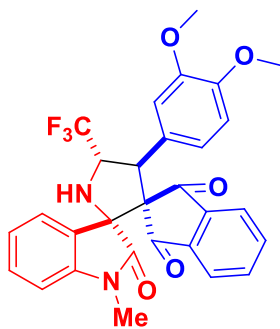


199.14
195.84

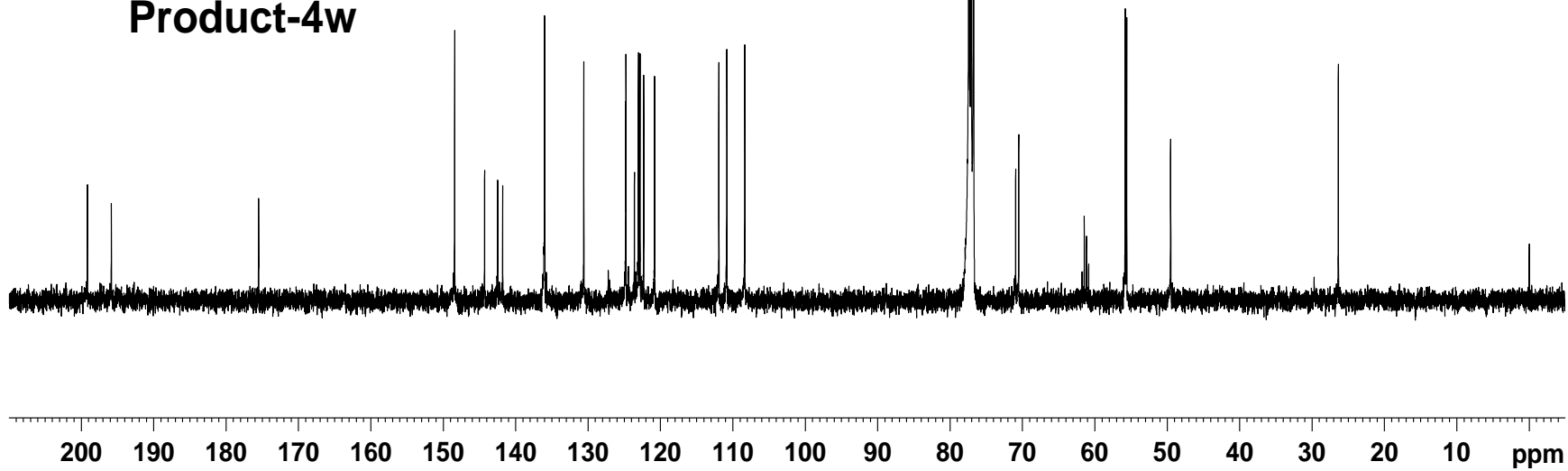
175.49
148.41
144.28
142.47
141.78
136.00
135.97
130.57
129.97
127.18
124.80
124.75
124.40
123.59
123.02
122.81
122.30
121.62
120.79
111.92
110.81
108.33
77.36
77.04
76.73
70.92
70.50
61.75
61.45
61.14
60.84
55.78
55.61
49.56

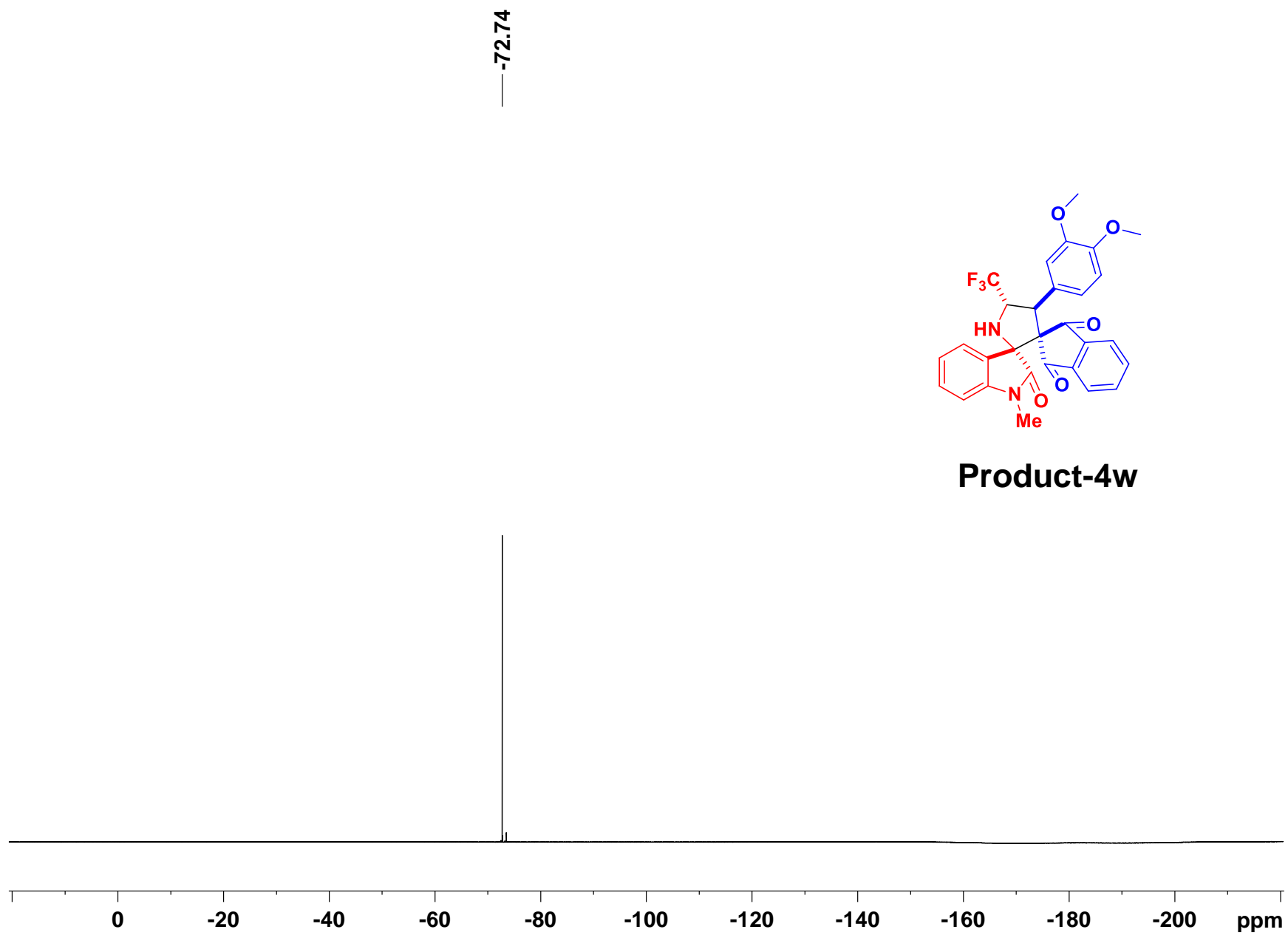
26.38

0.01

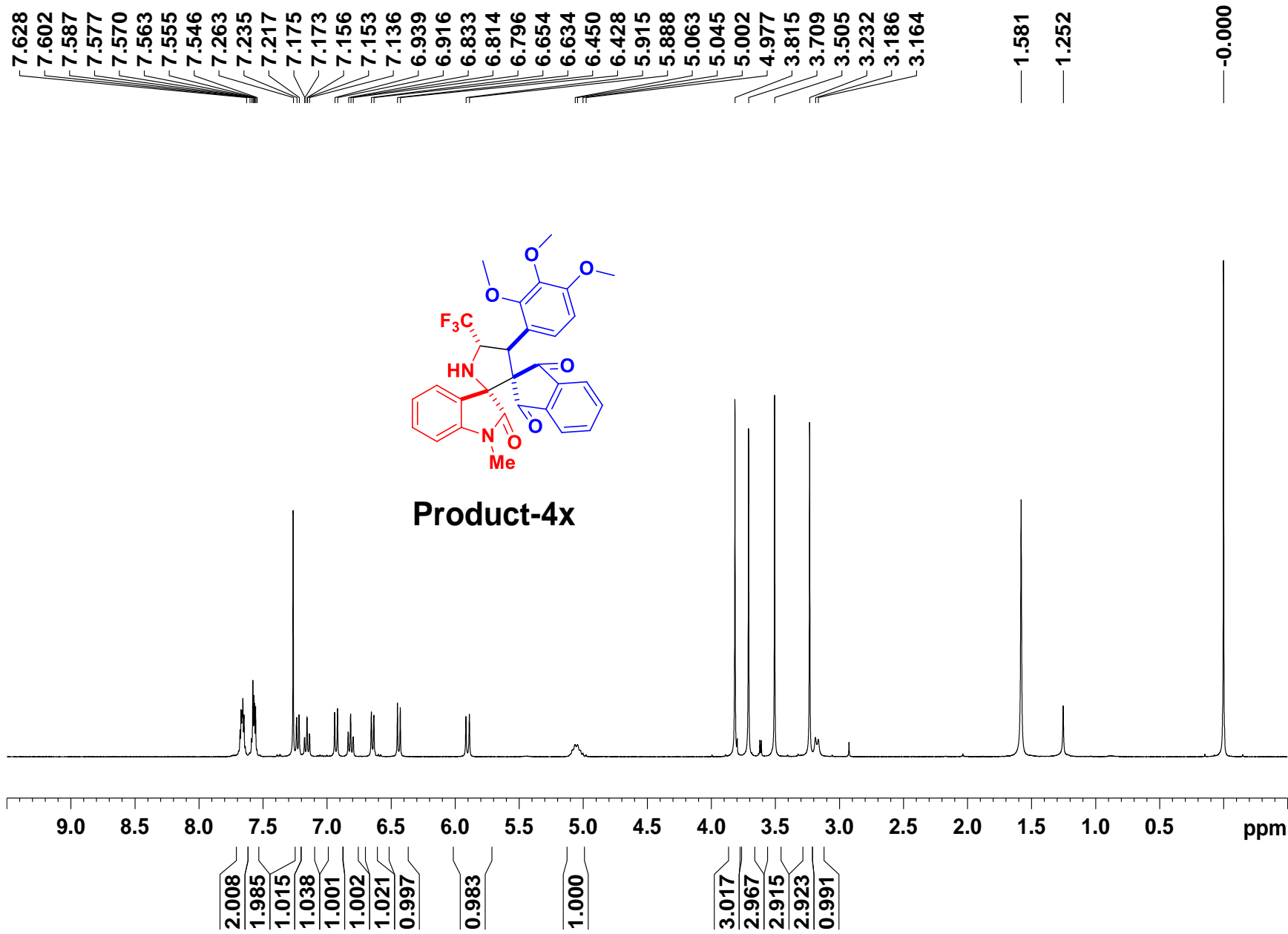


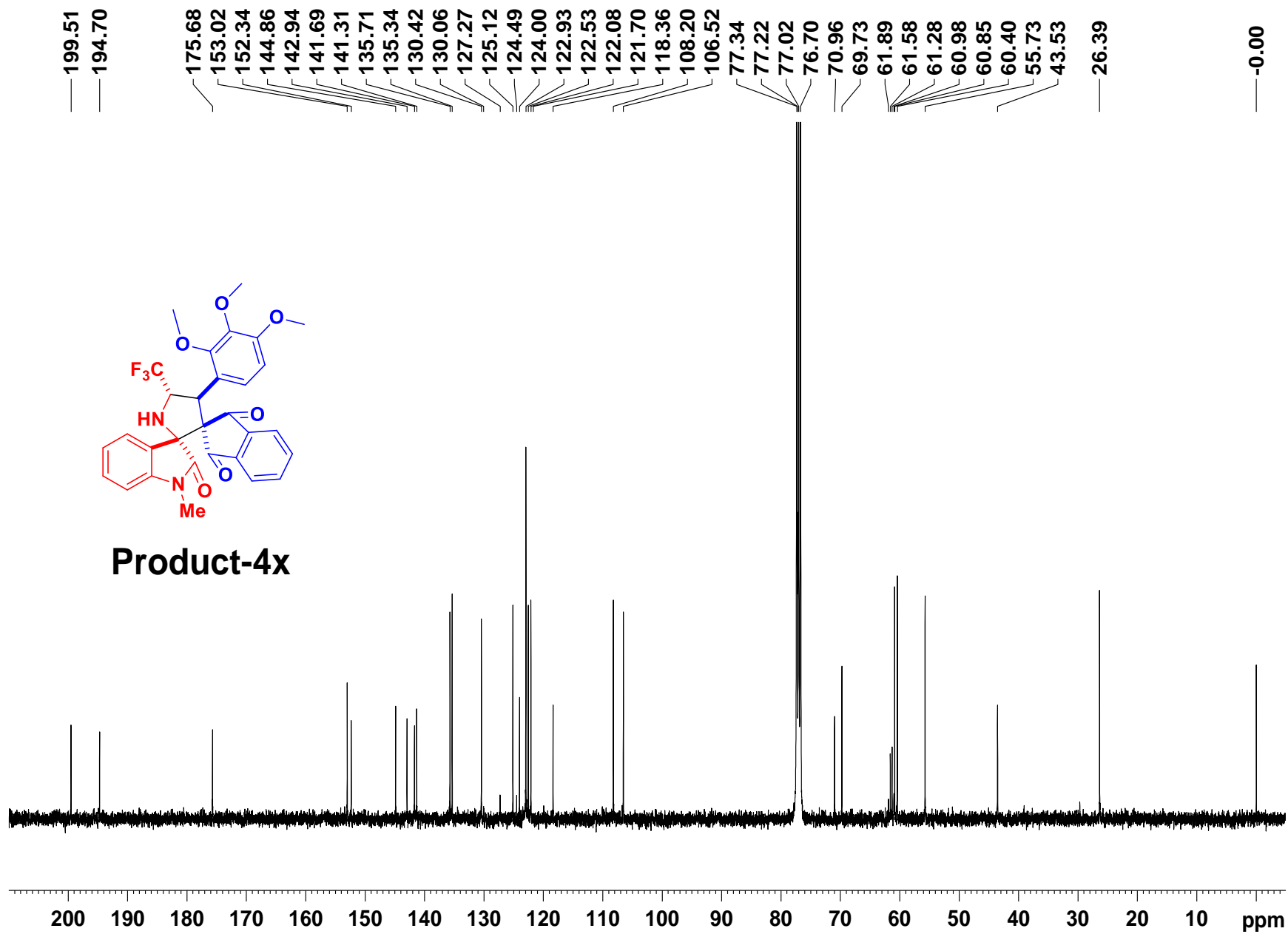
Product-4w



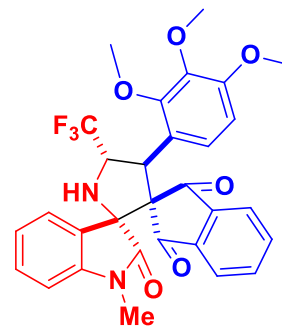


S87

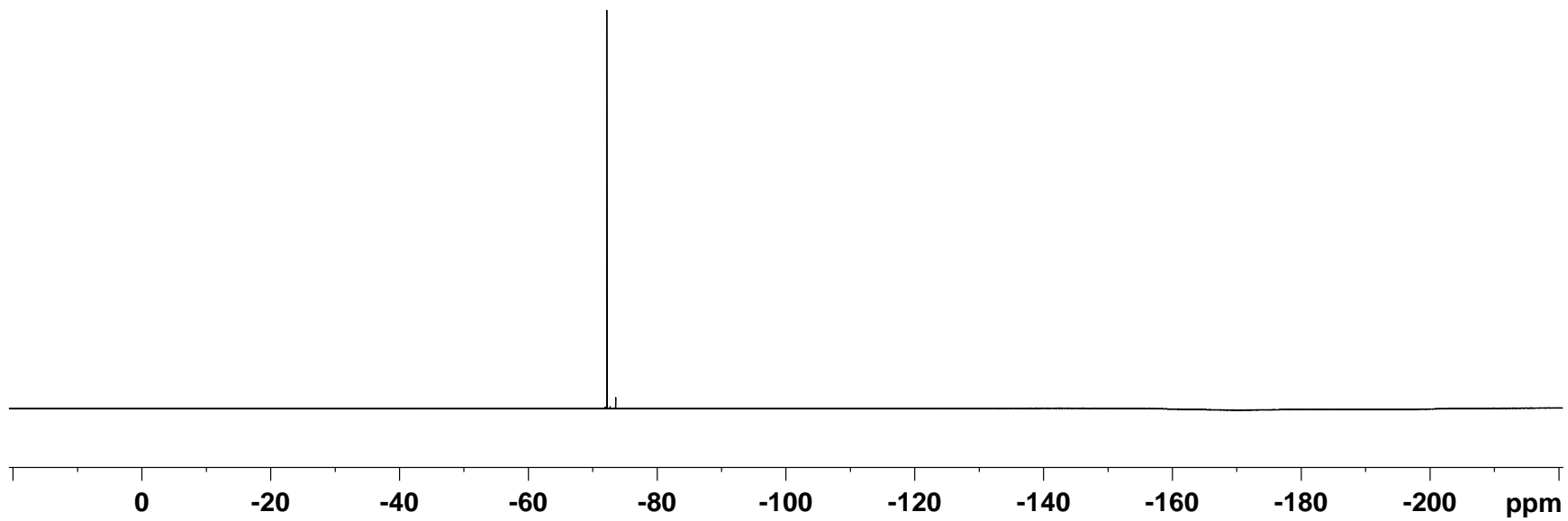




— -72.20



Product-4x

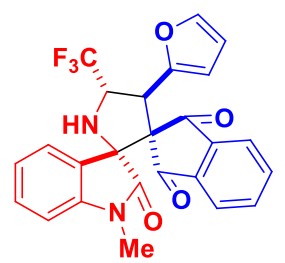


S90

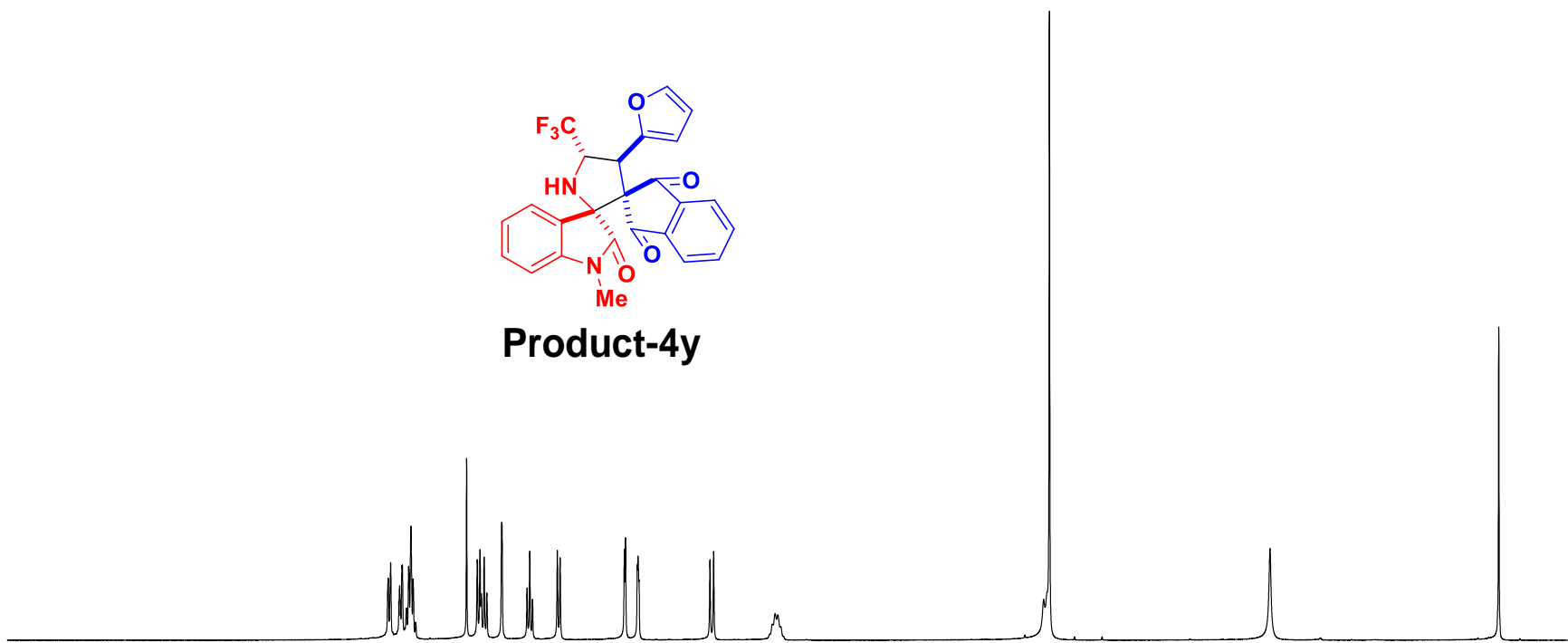
7.815
7.798
7.737
7.721
7.717
7.688
7.673
7.671
7.656
7.642
7.624
7.265
7.190
7.171
7.161
7.142
7.122
7.018
6.839
6.820
6.801
6.626
6.607
6.154
6.146
6.064
6.059
6.052
5.552
5.526
5.114
5.093
5.074
5.056
3.204
3.163

— 1.610

— -0.000



Product-4y



10 9 8 7 6 5 4 3 2 1 ppm

1.123
1.023
2.018
2.097
1.028
1.083
1.028
1.012
0.954
1.000
1.030
4.126

198.11
194.85

175.17

147.15

144.40

142.44

142.22

141.39

135.88

130.67

129.67

126.88

124.82

124.10

123.24

123.12

122.97

122.31

121.32

110.24

109.27

108.35

77.34

77.02

76.70

70.14

69.09

61.62

61.30

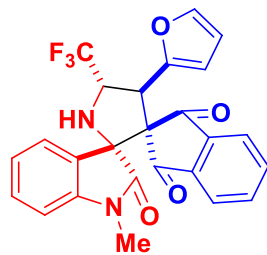
60.99

60.68

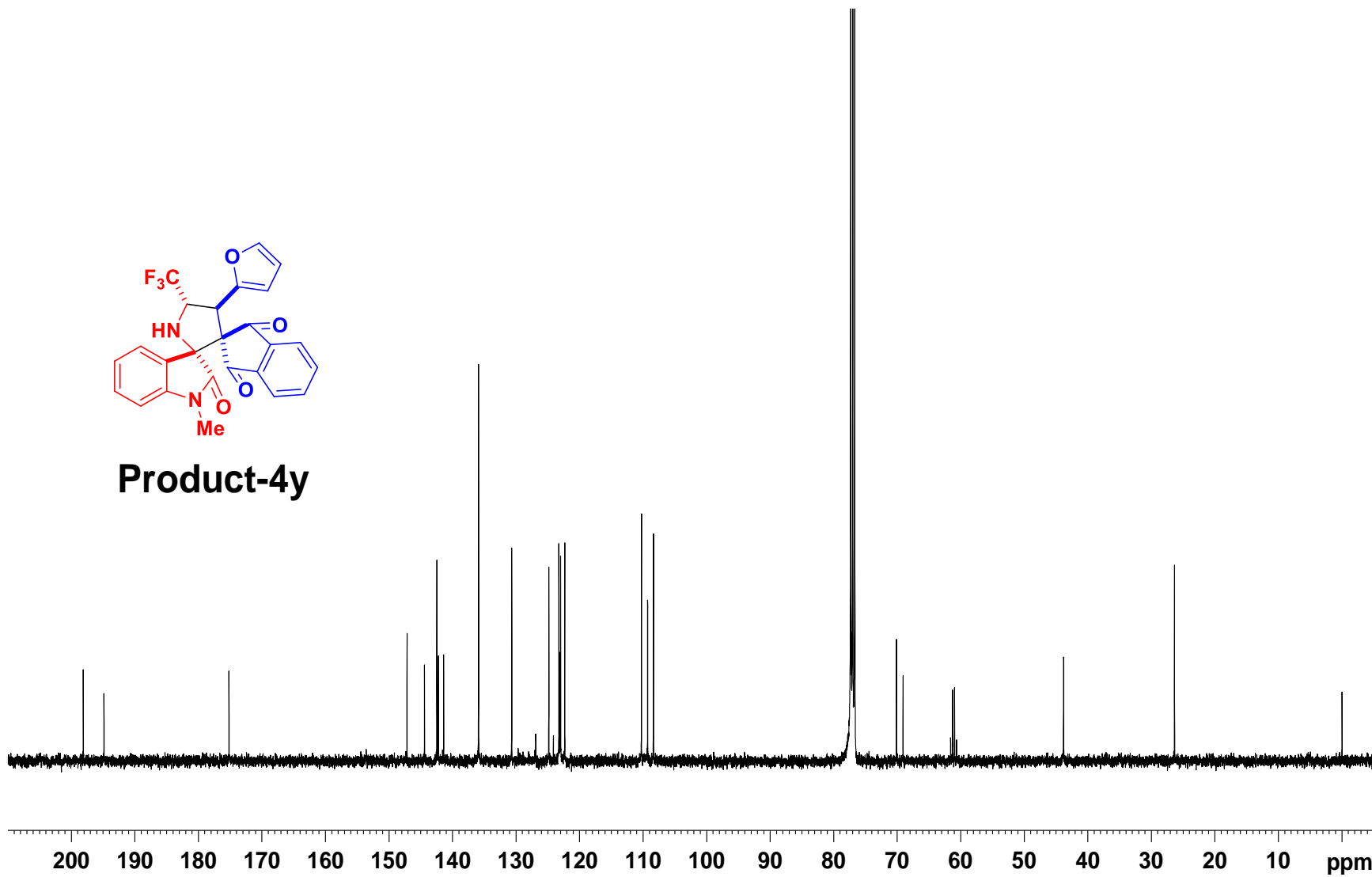
43.83

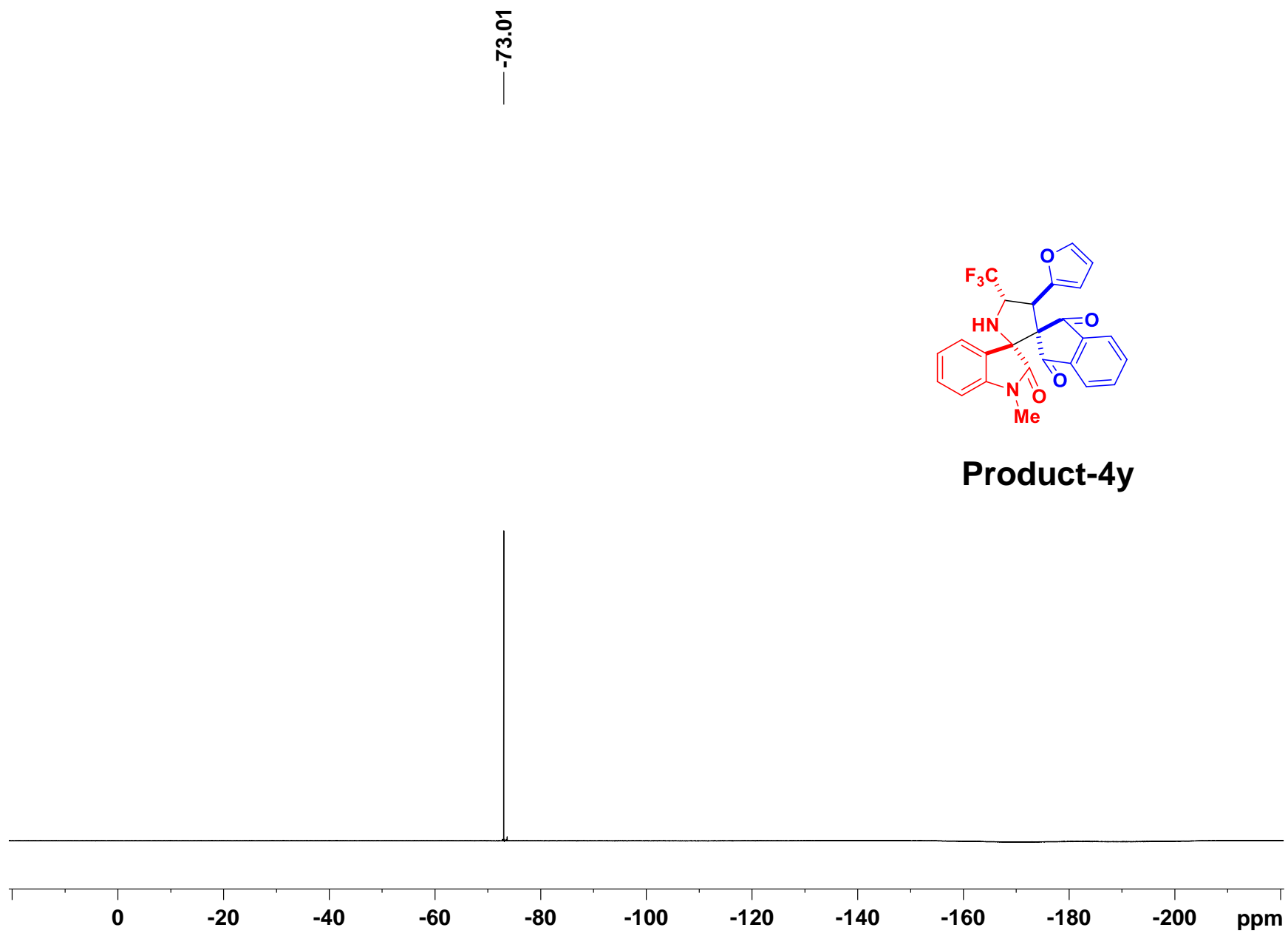
26.37

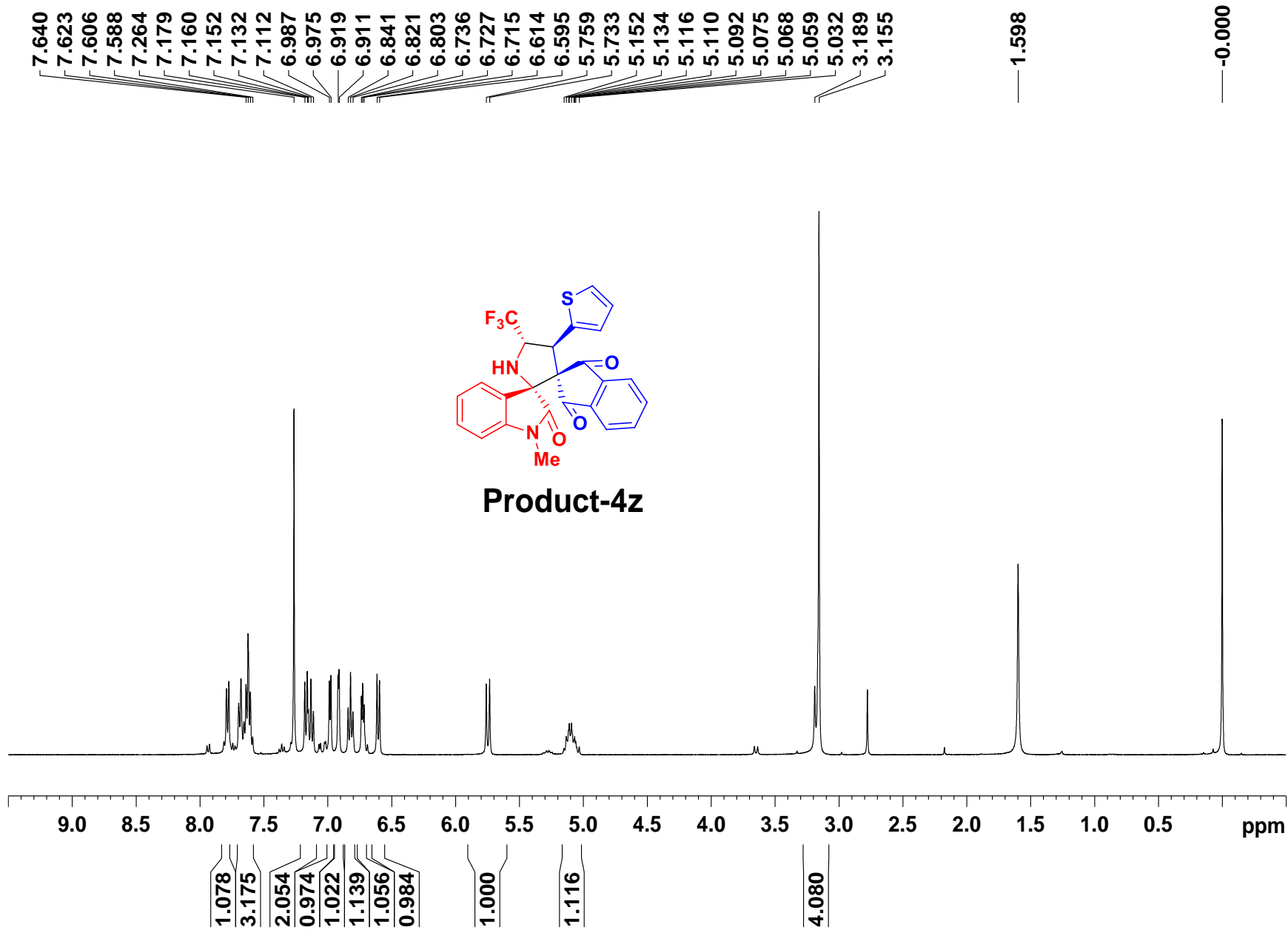
-0.00

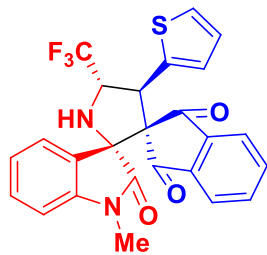


Product-4y

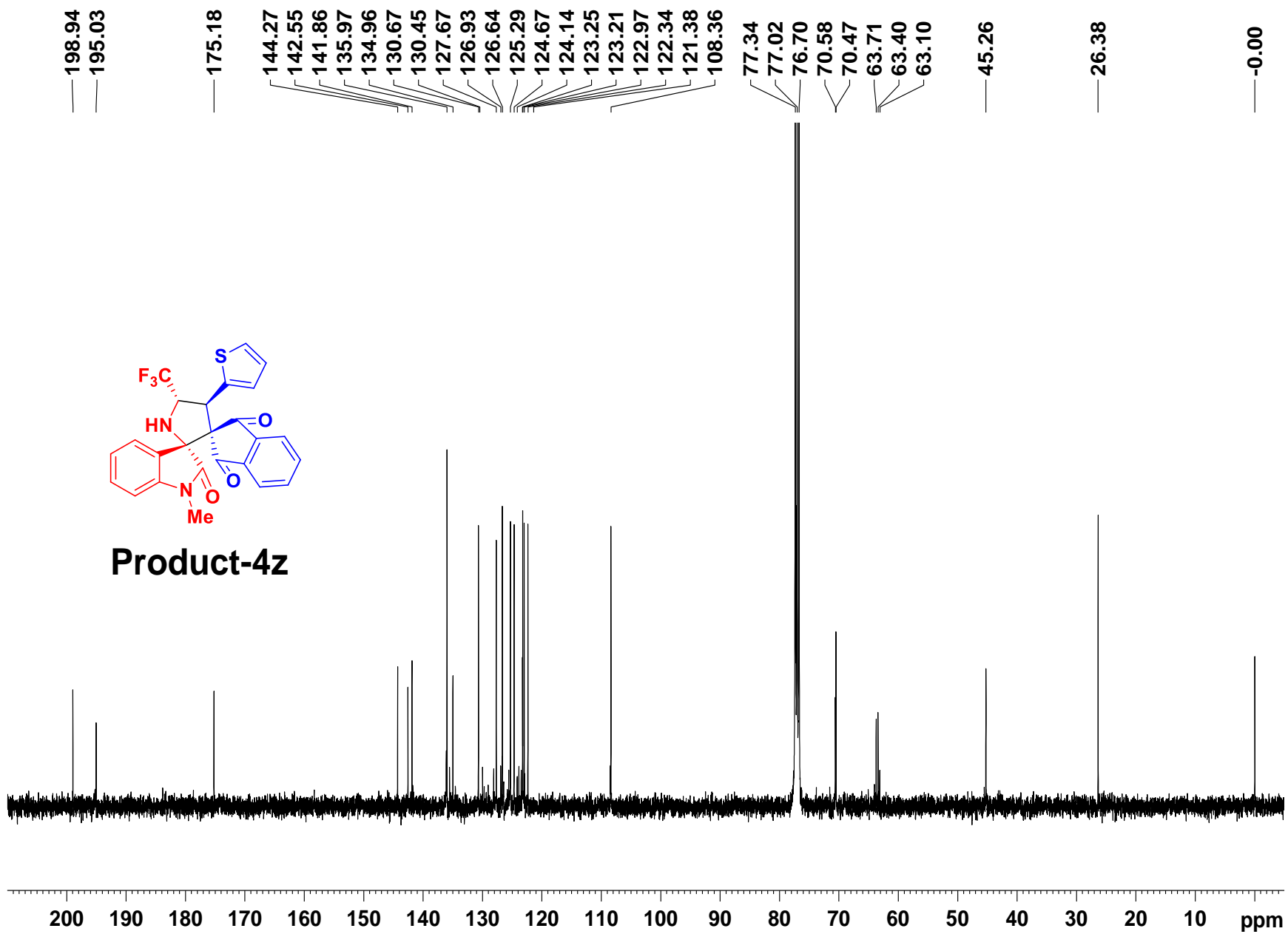




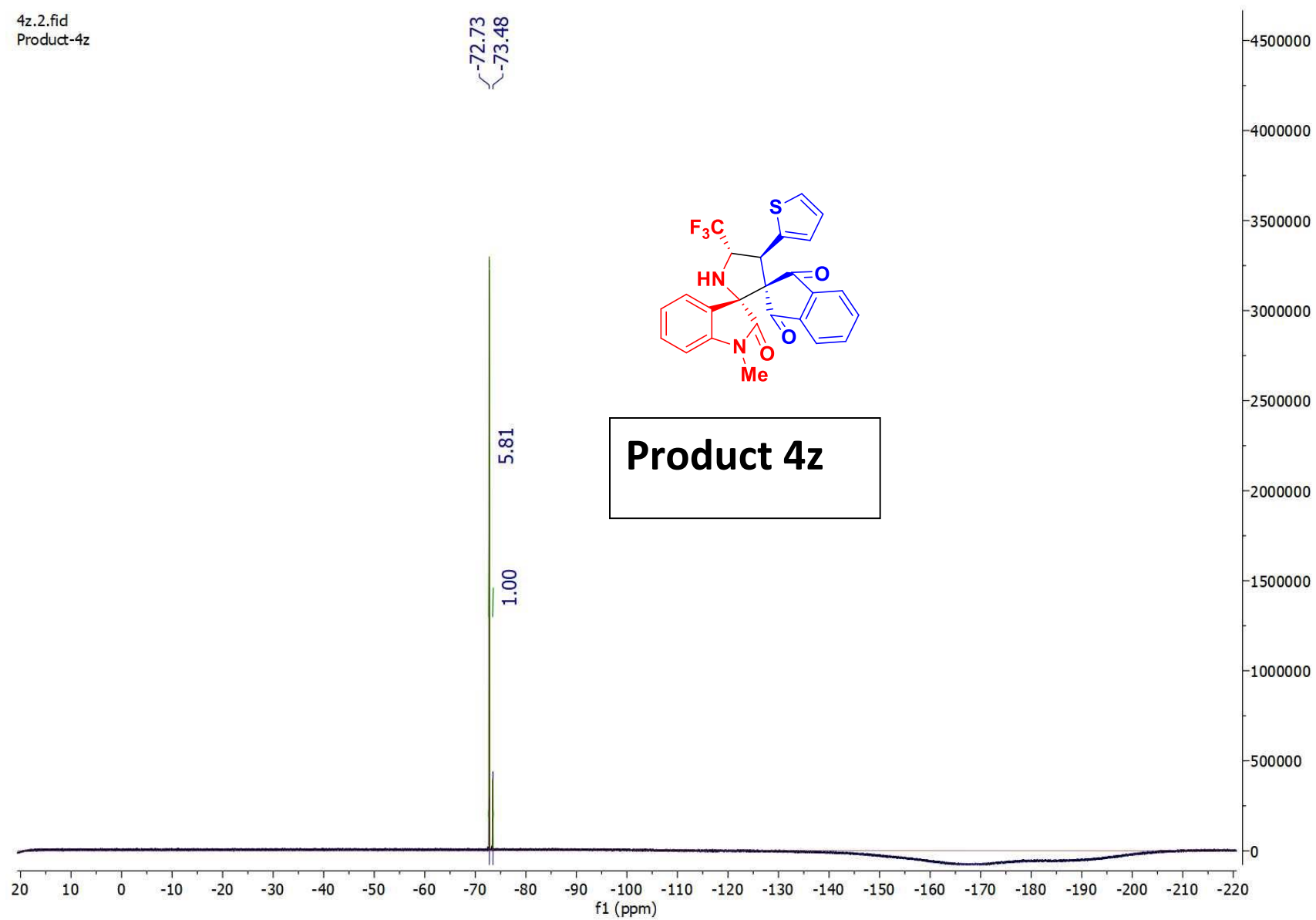


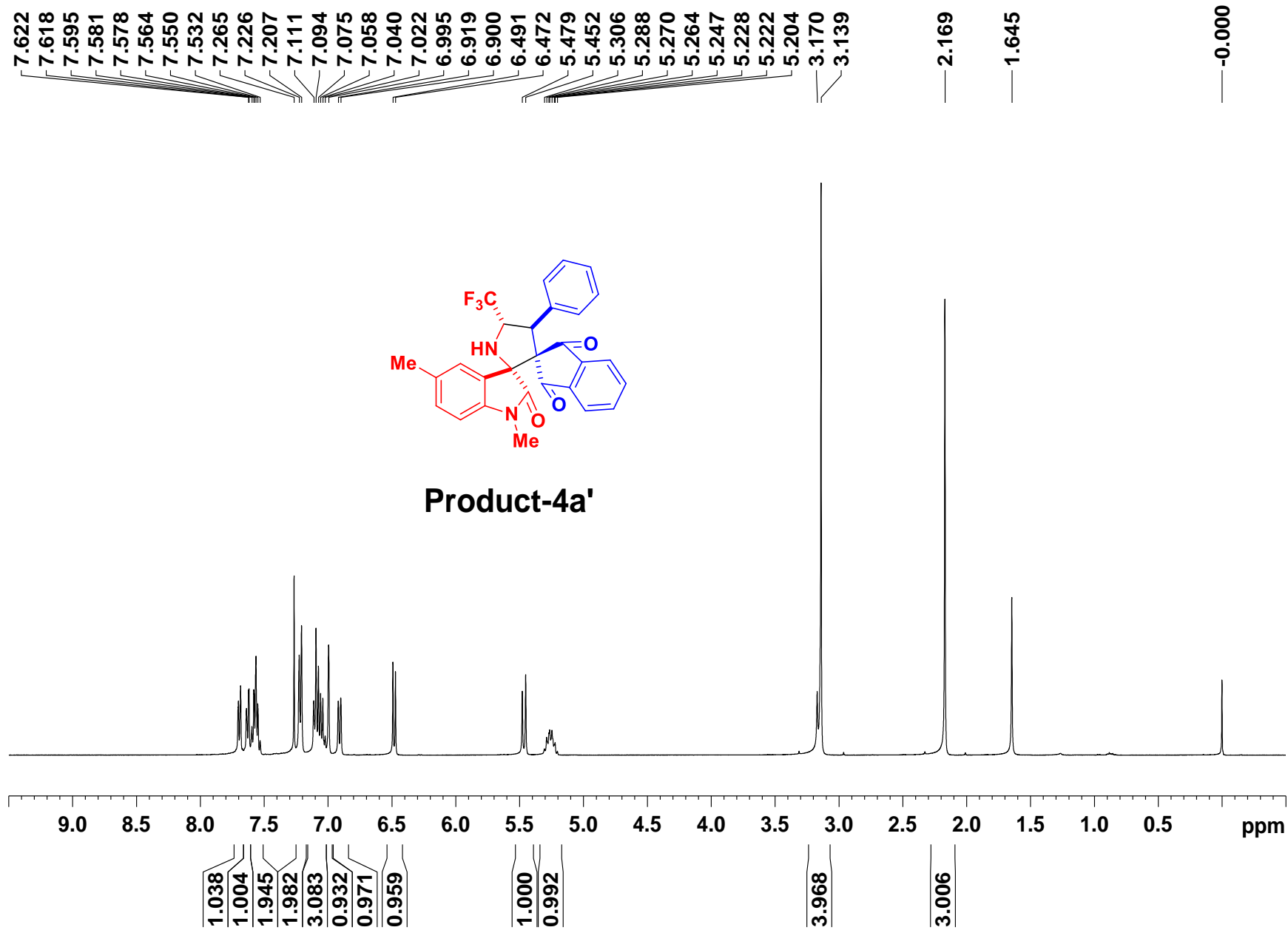


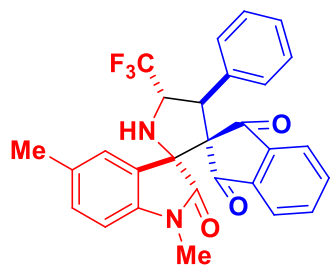
Product-4z



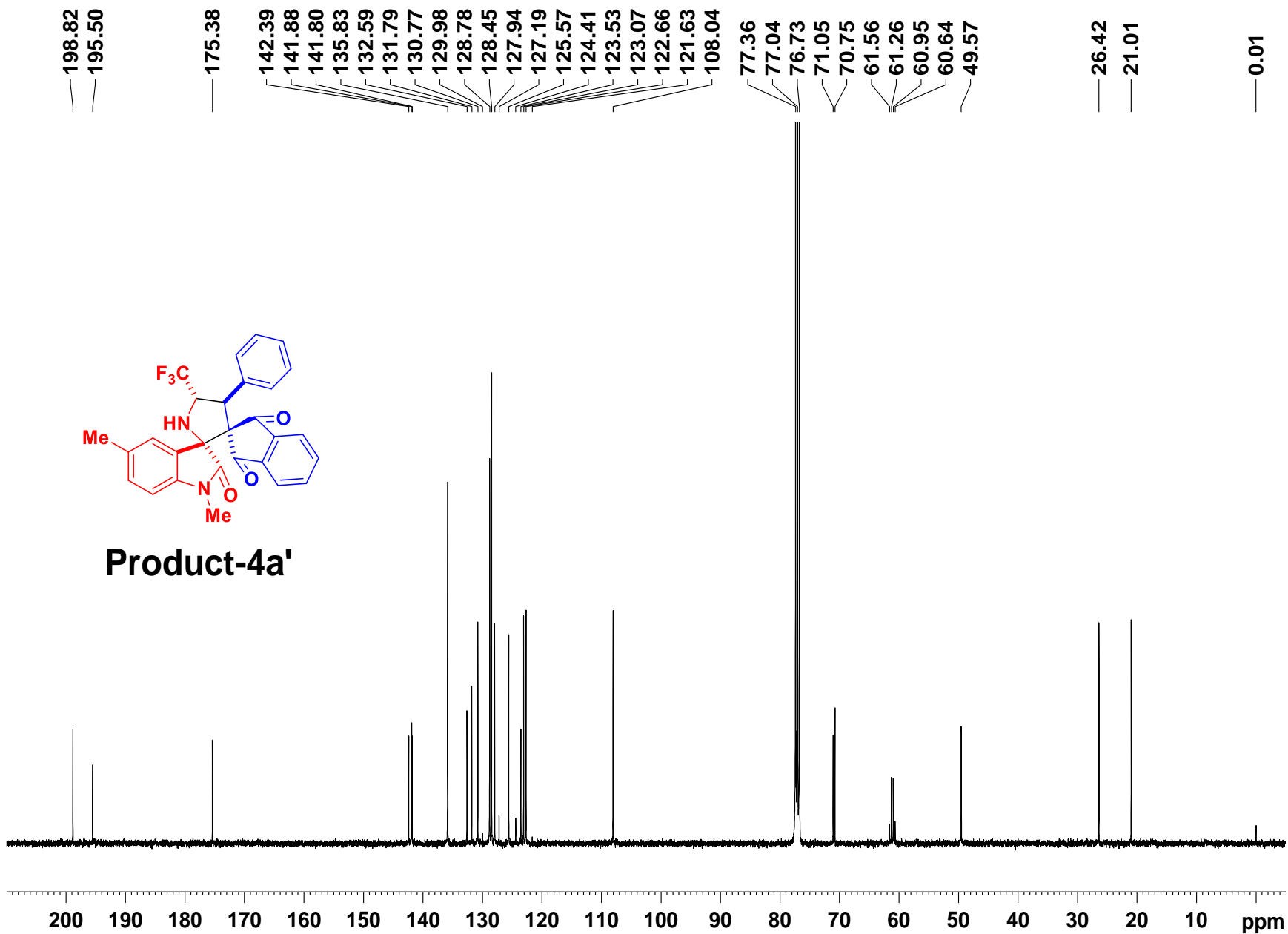
4z.2.fid
Product-4z



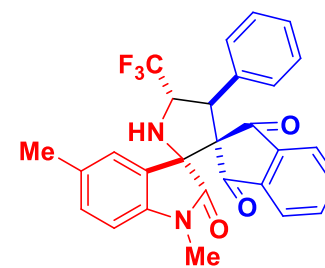




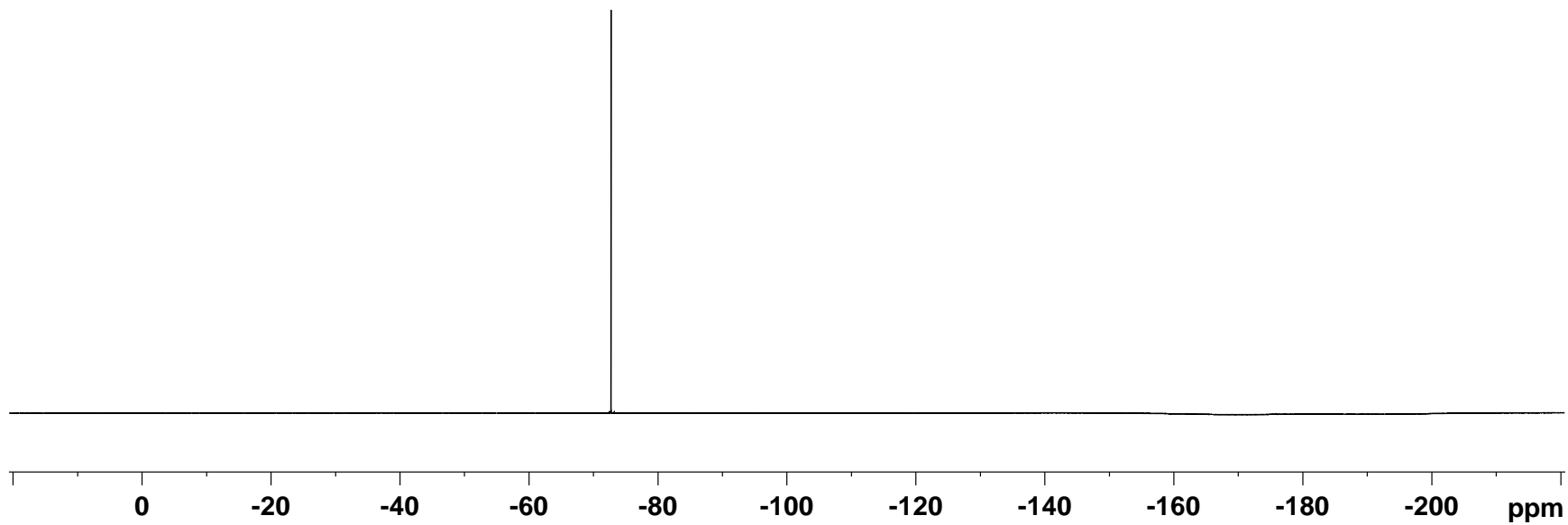
Product-4a'

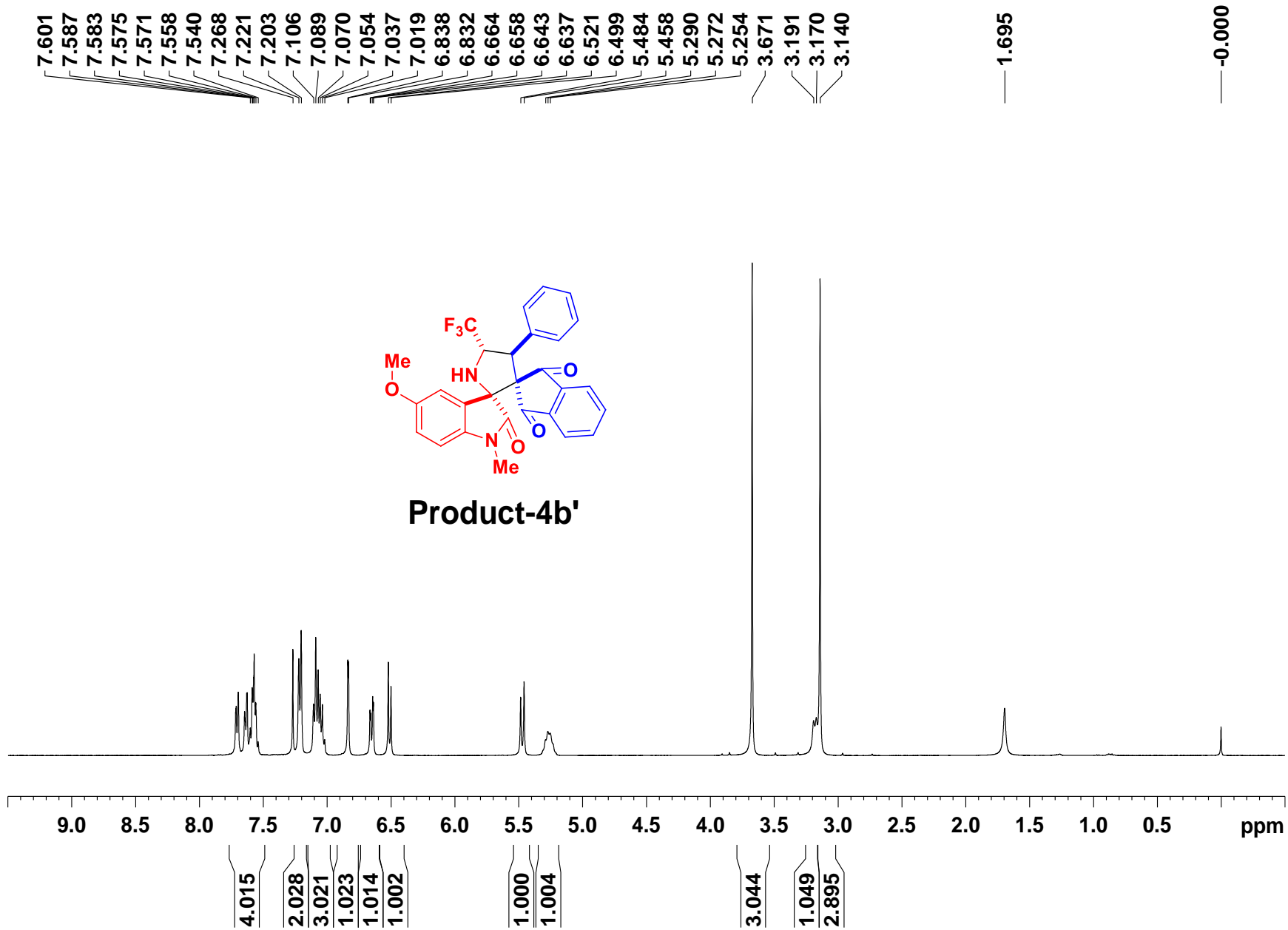


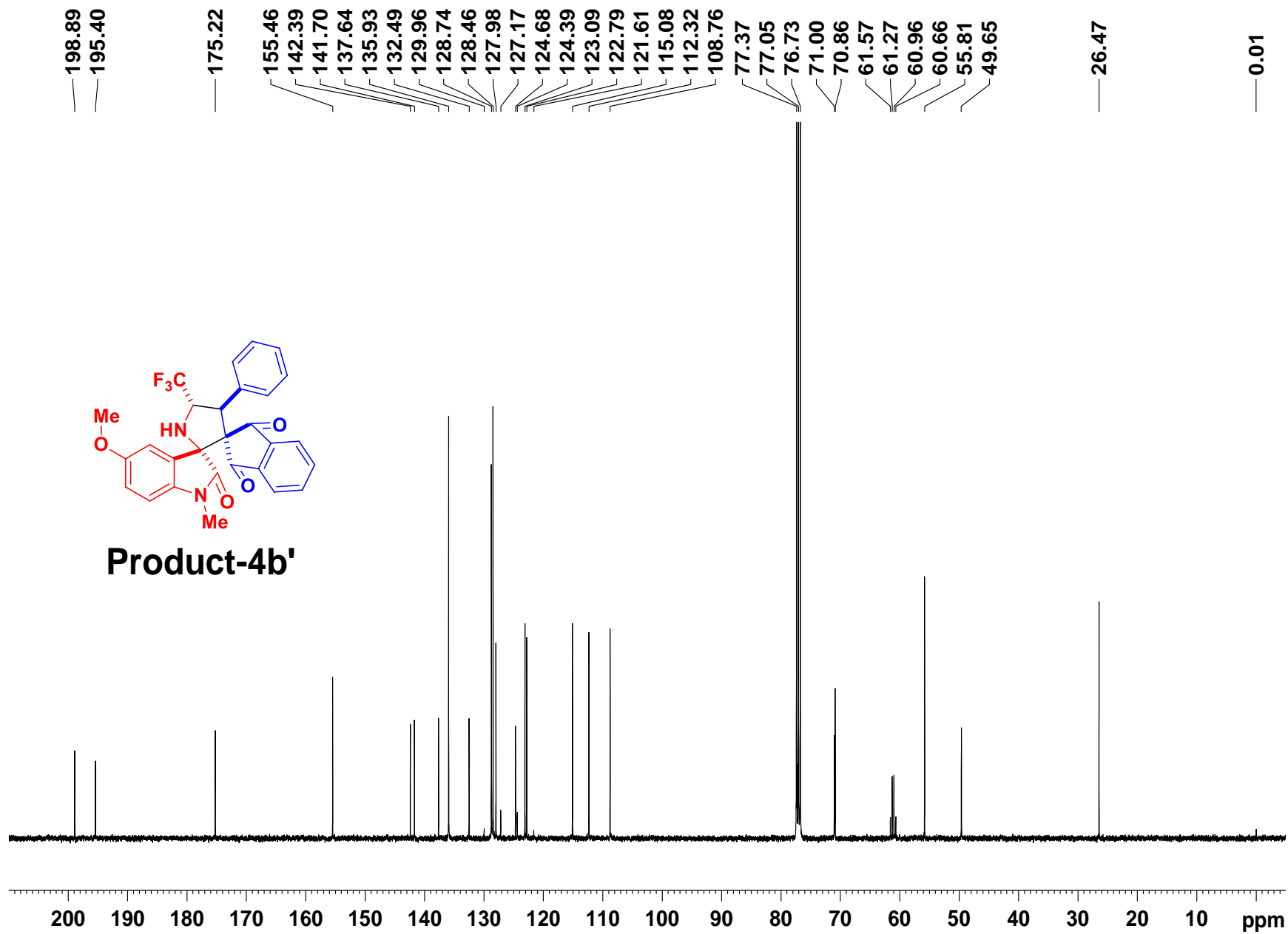
—72.73



Product-4a'

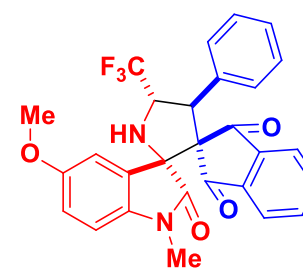




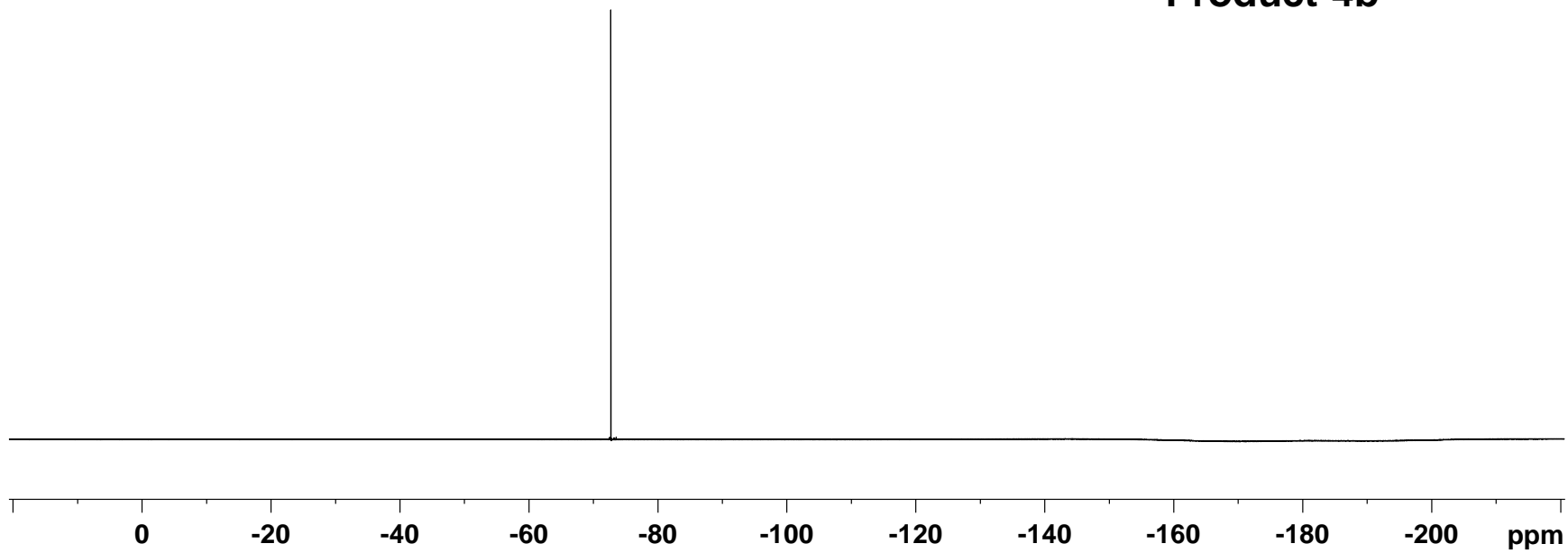


S101

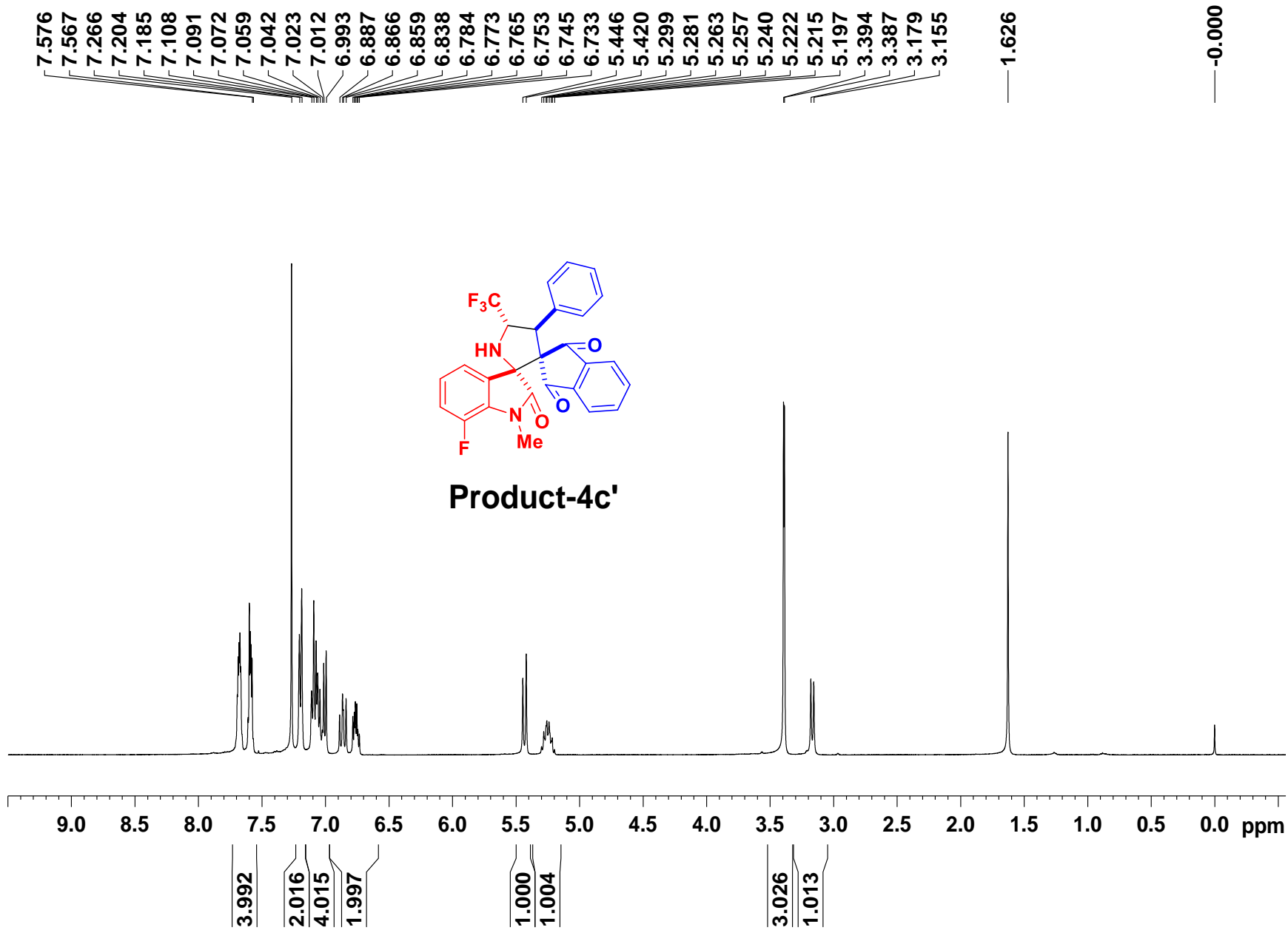
—72.71

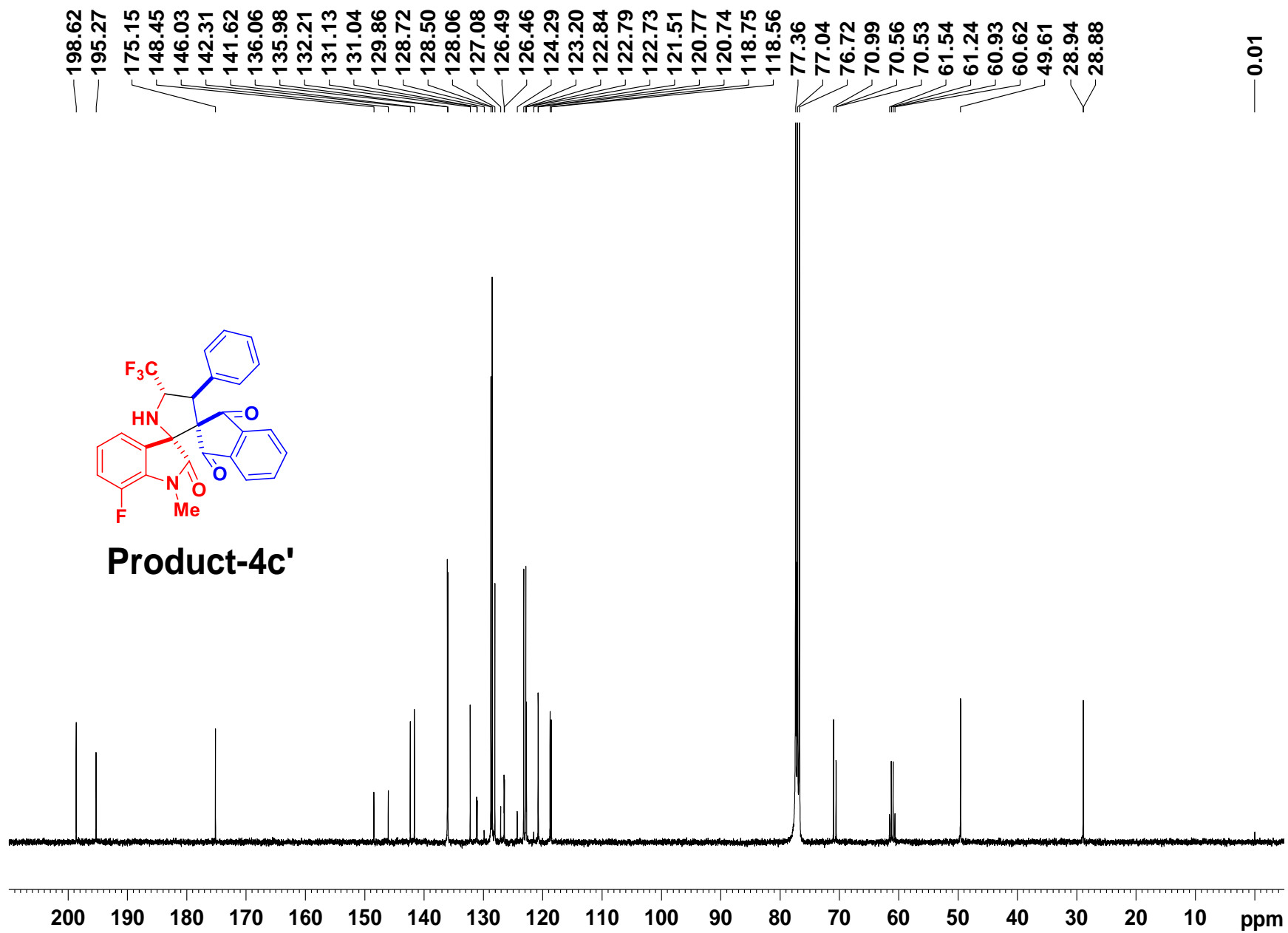


Product-4b'

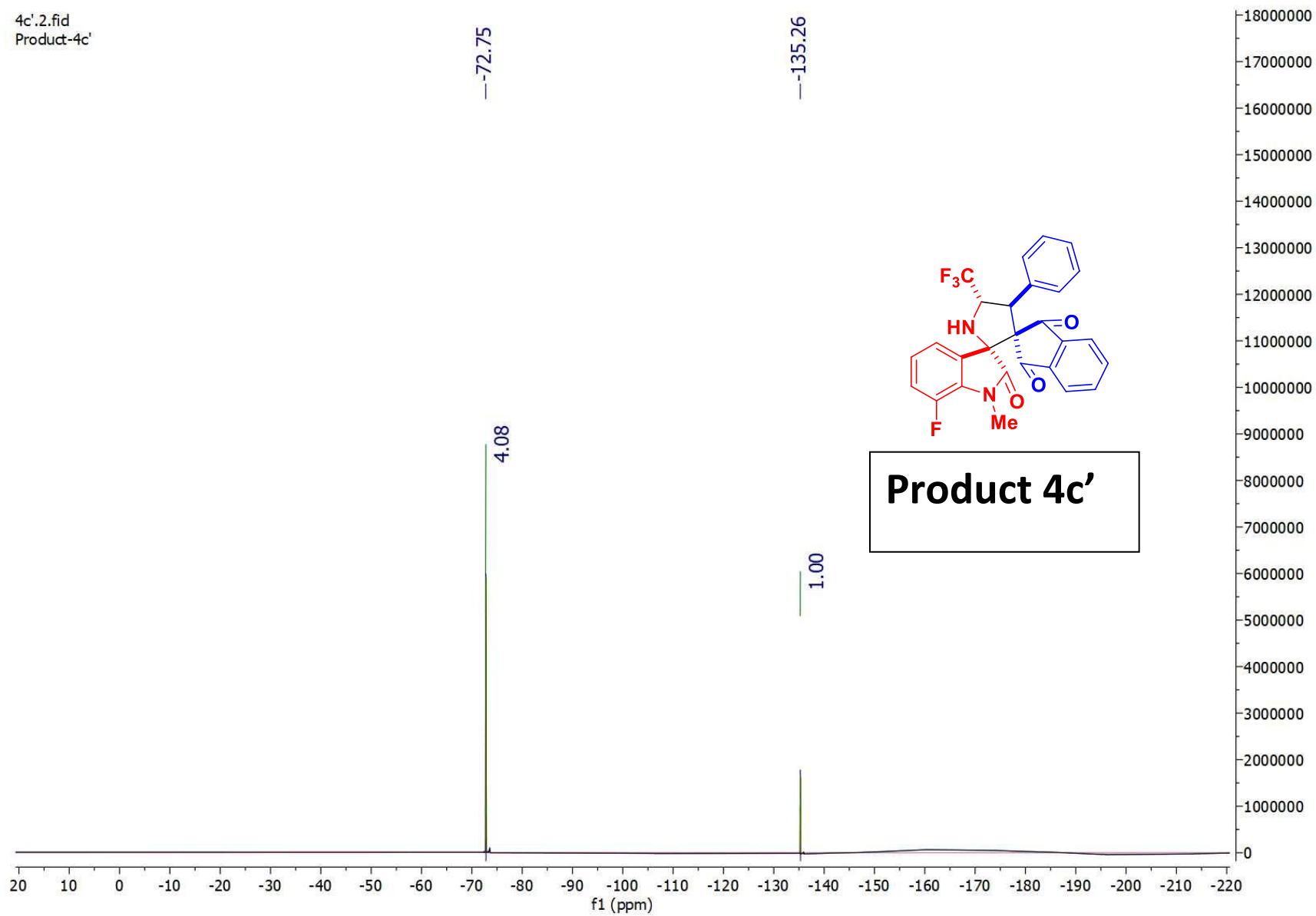


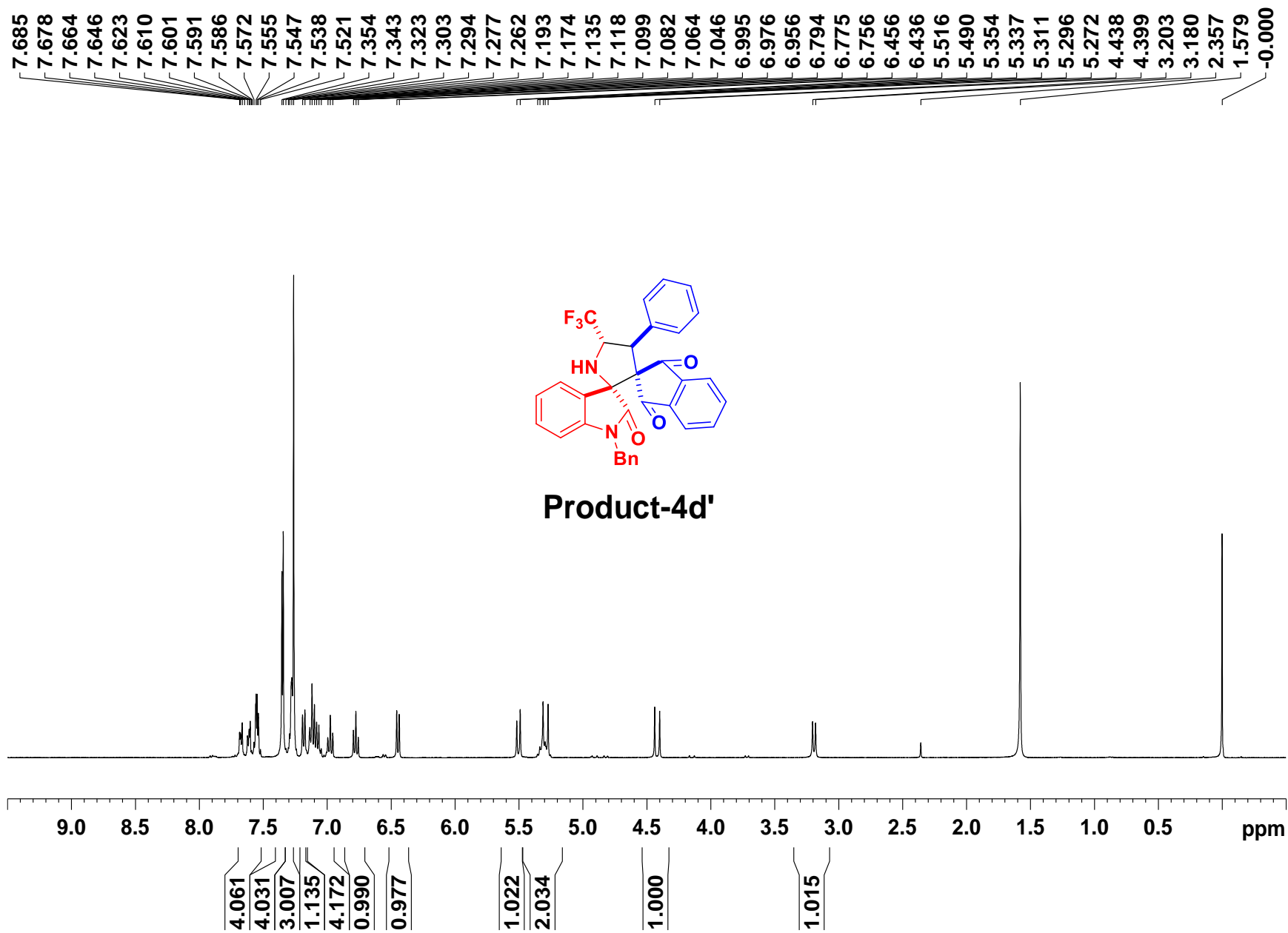
S102

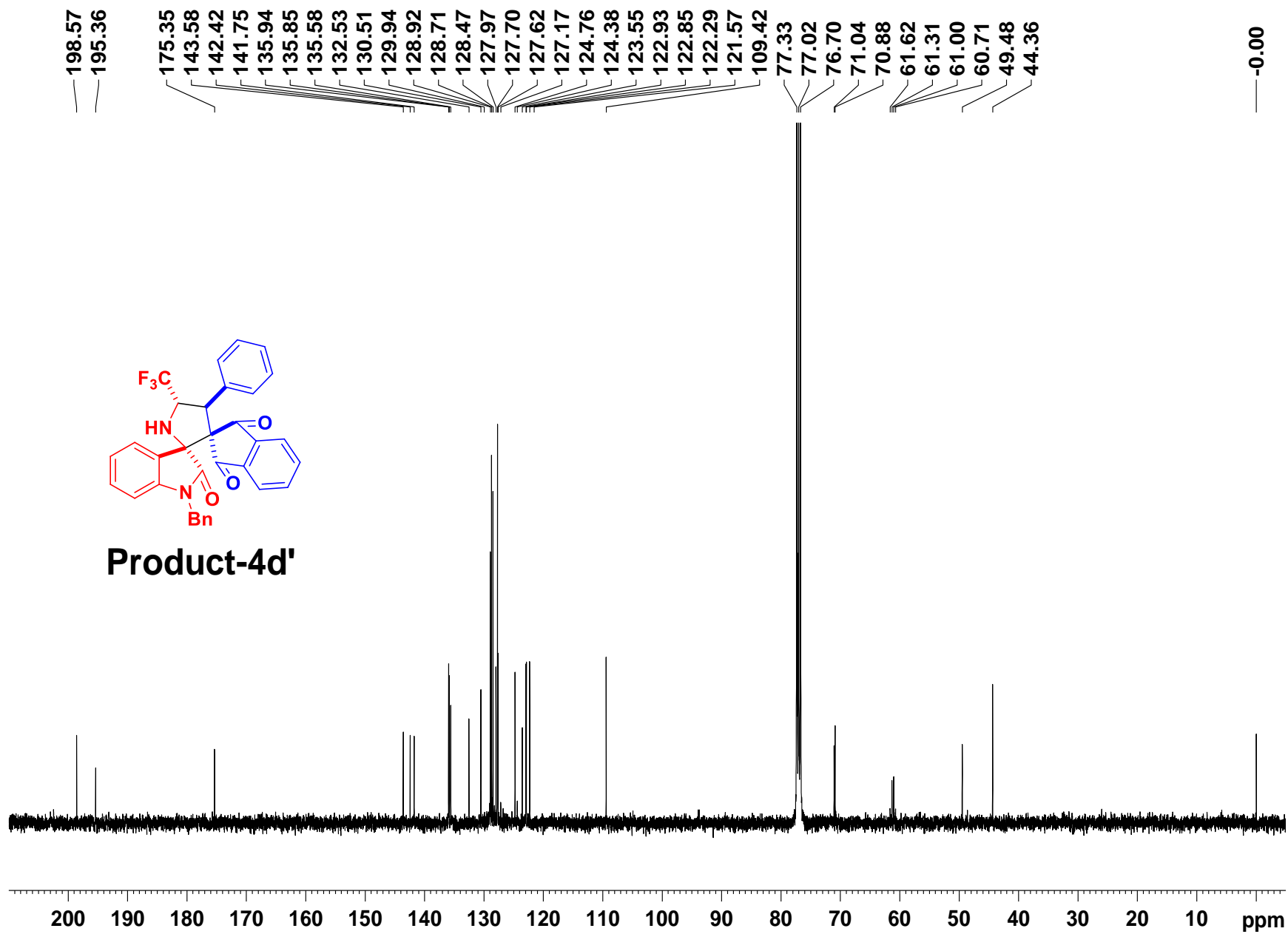


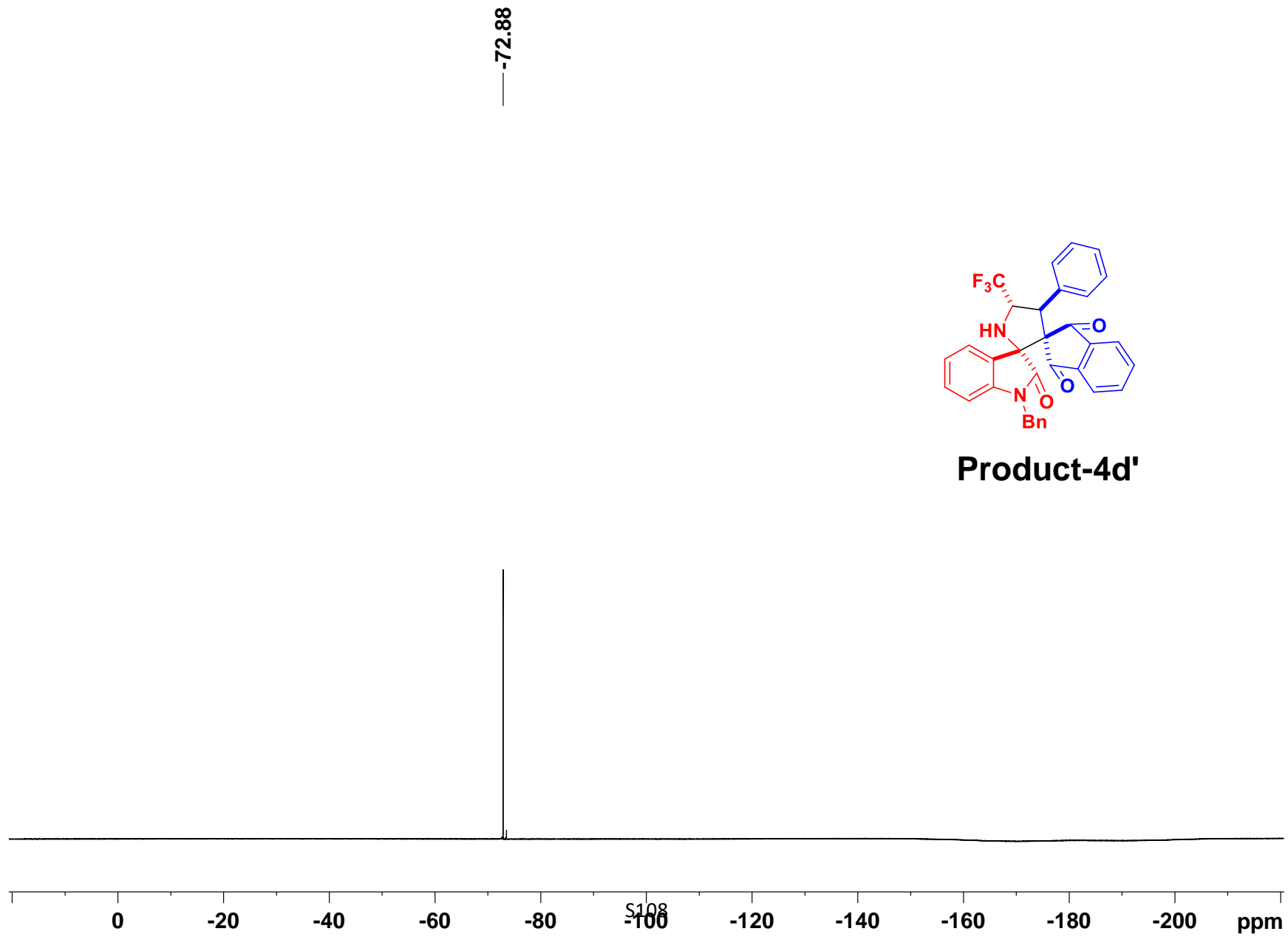


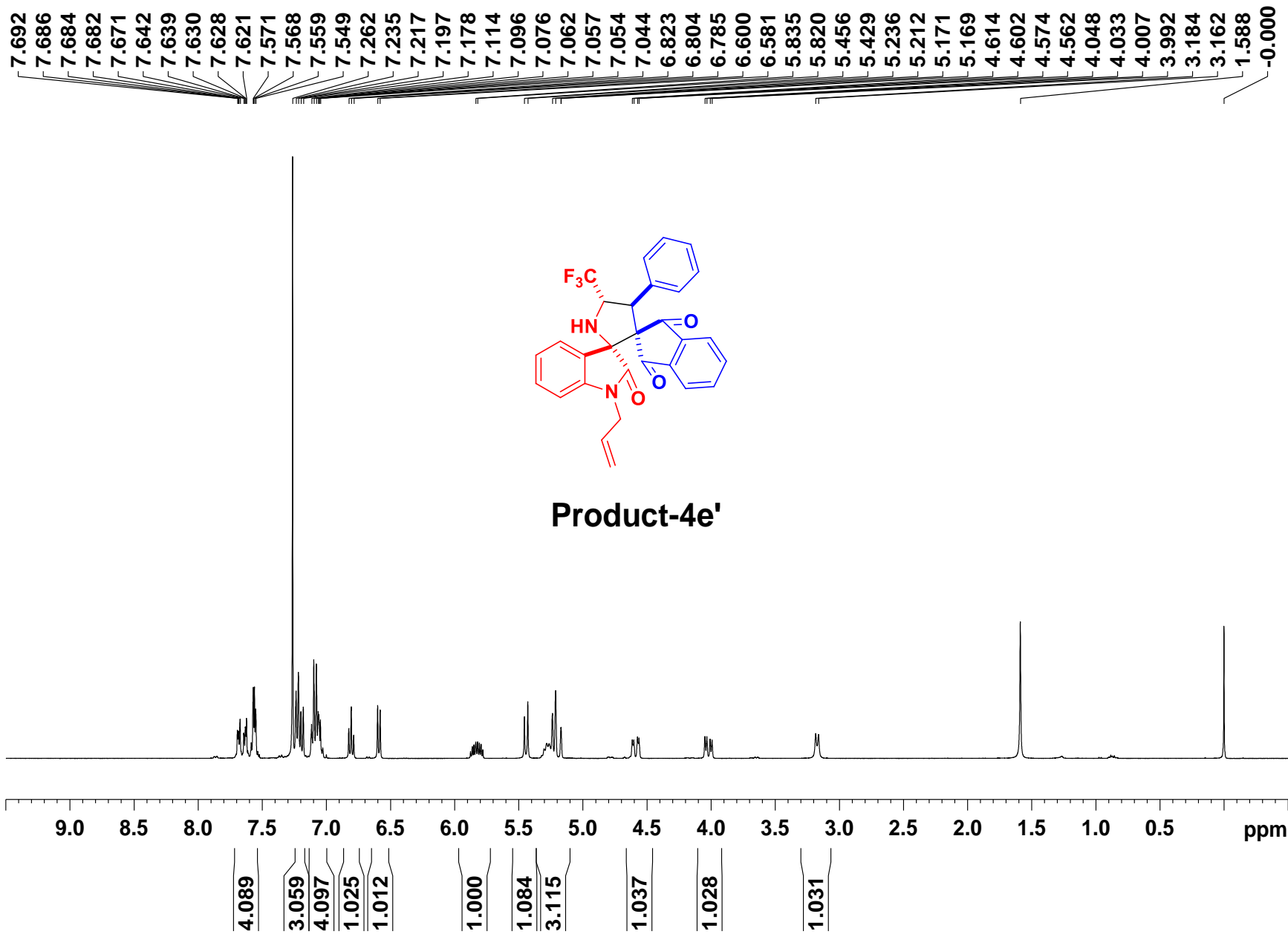
4c'.2.fid
Product-4c'

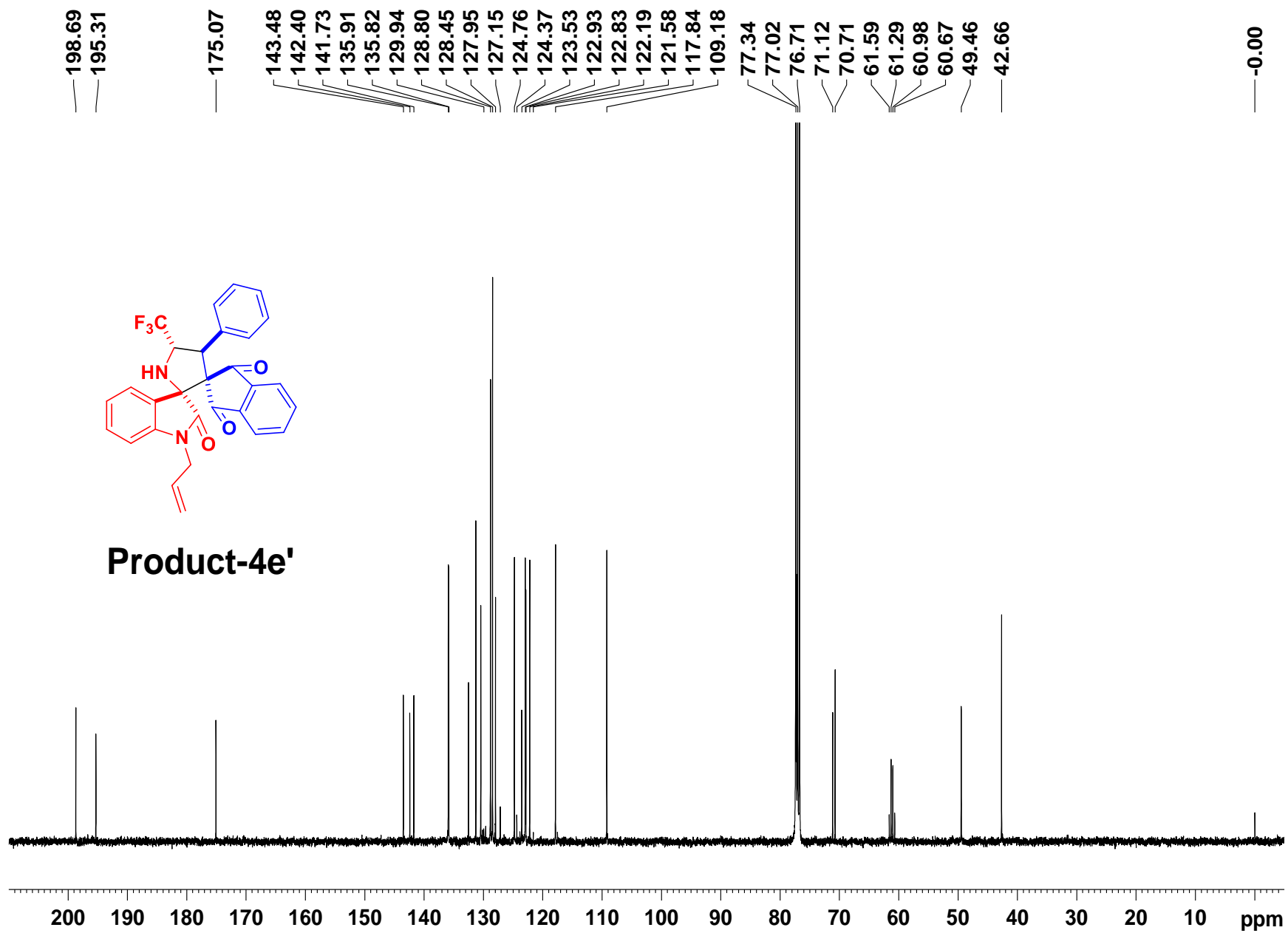


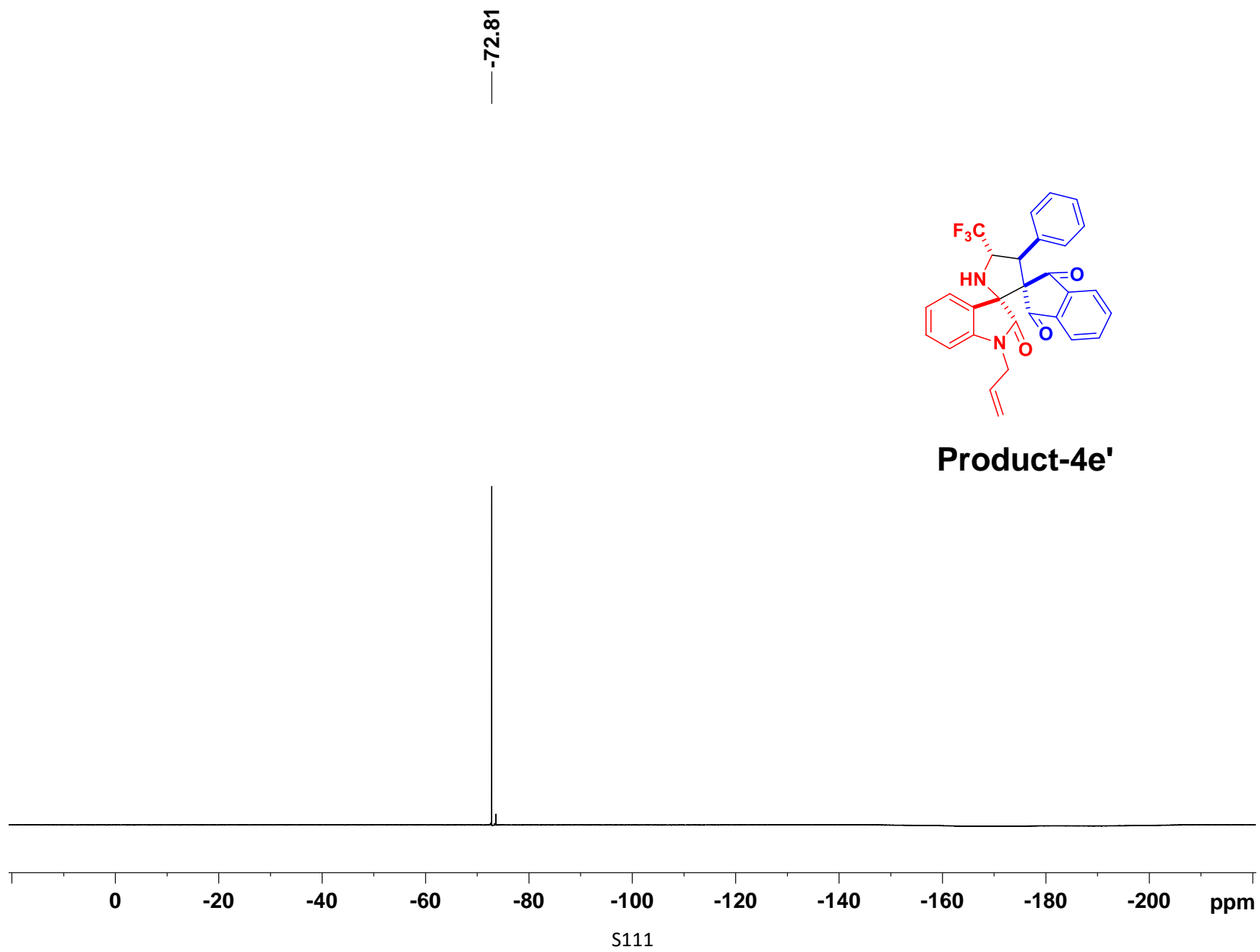




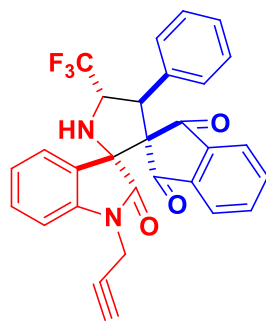




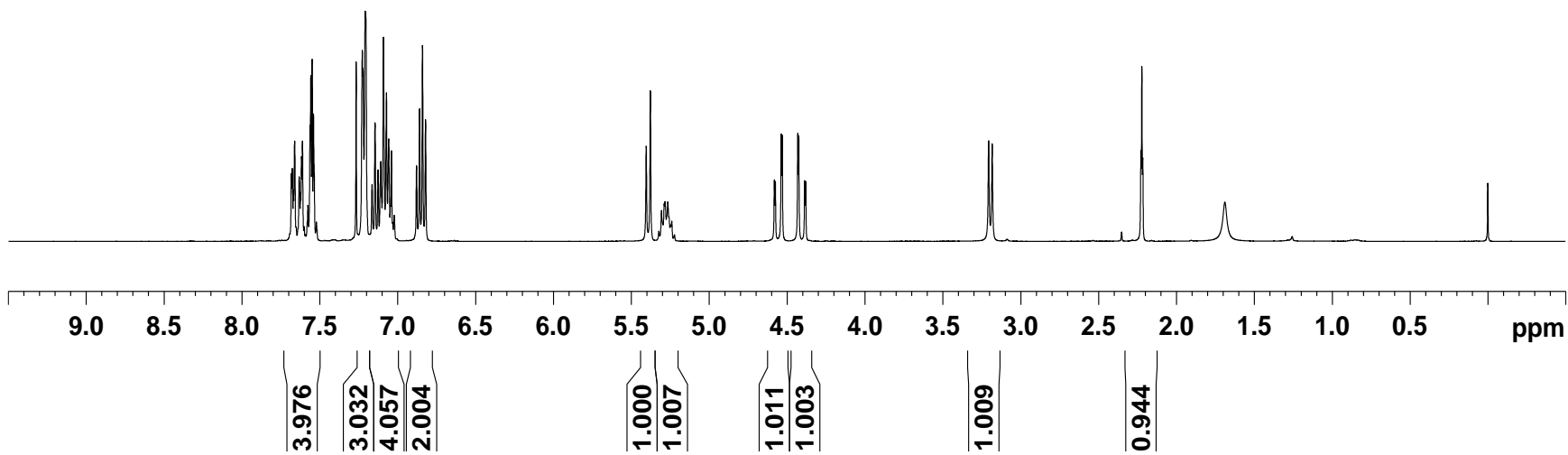


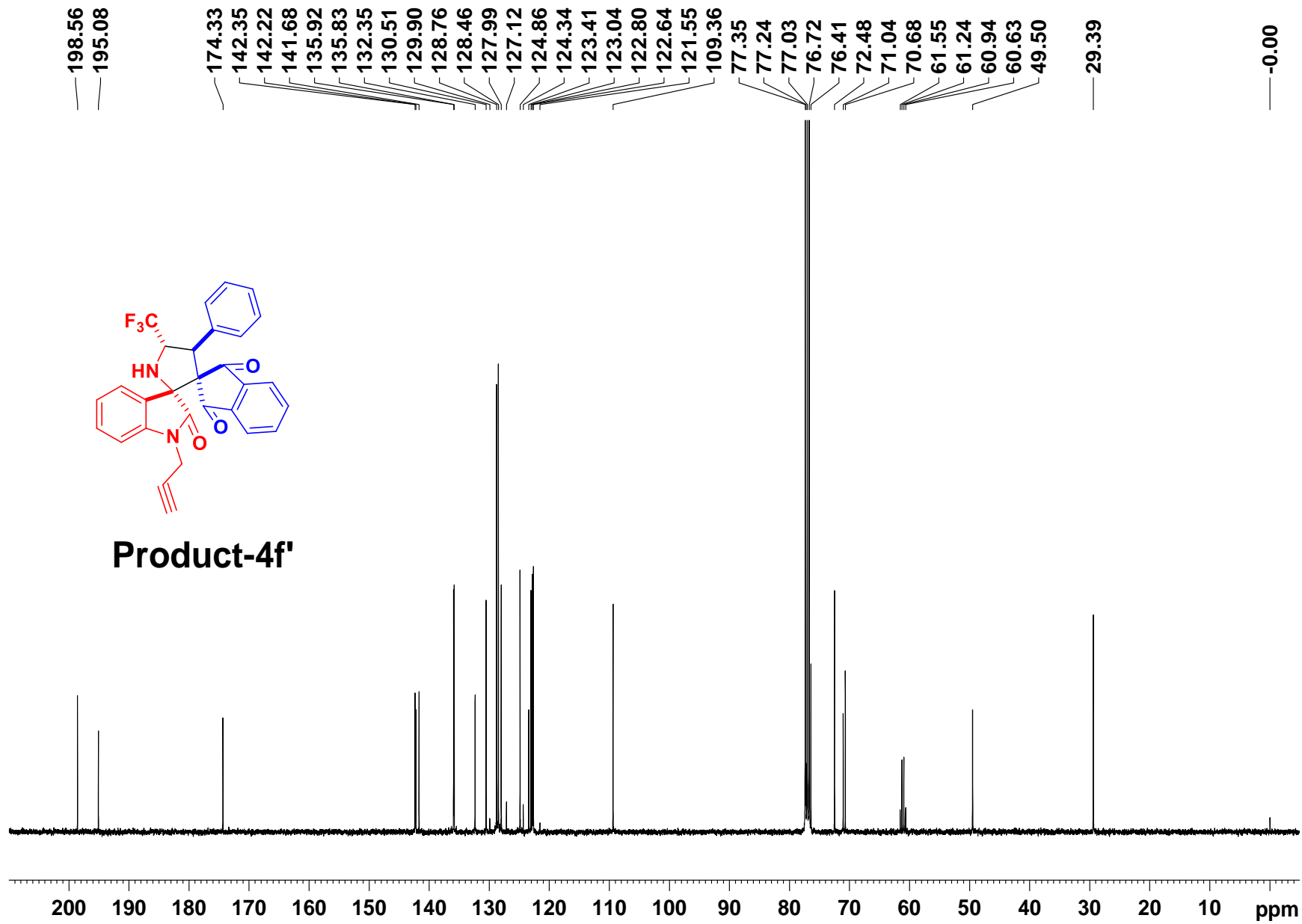


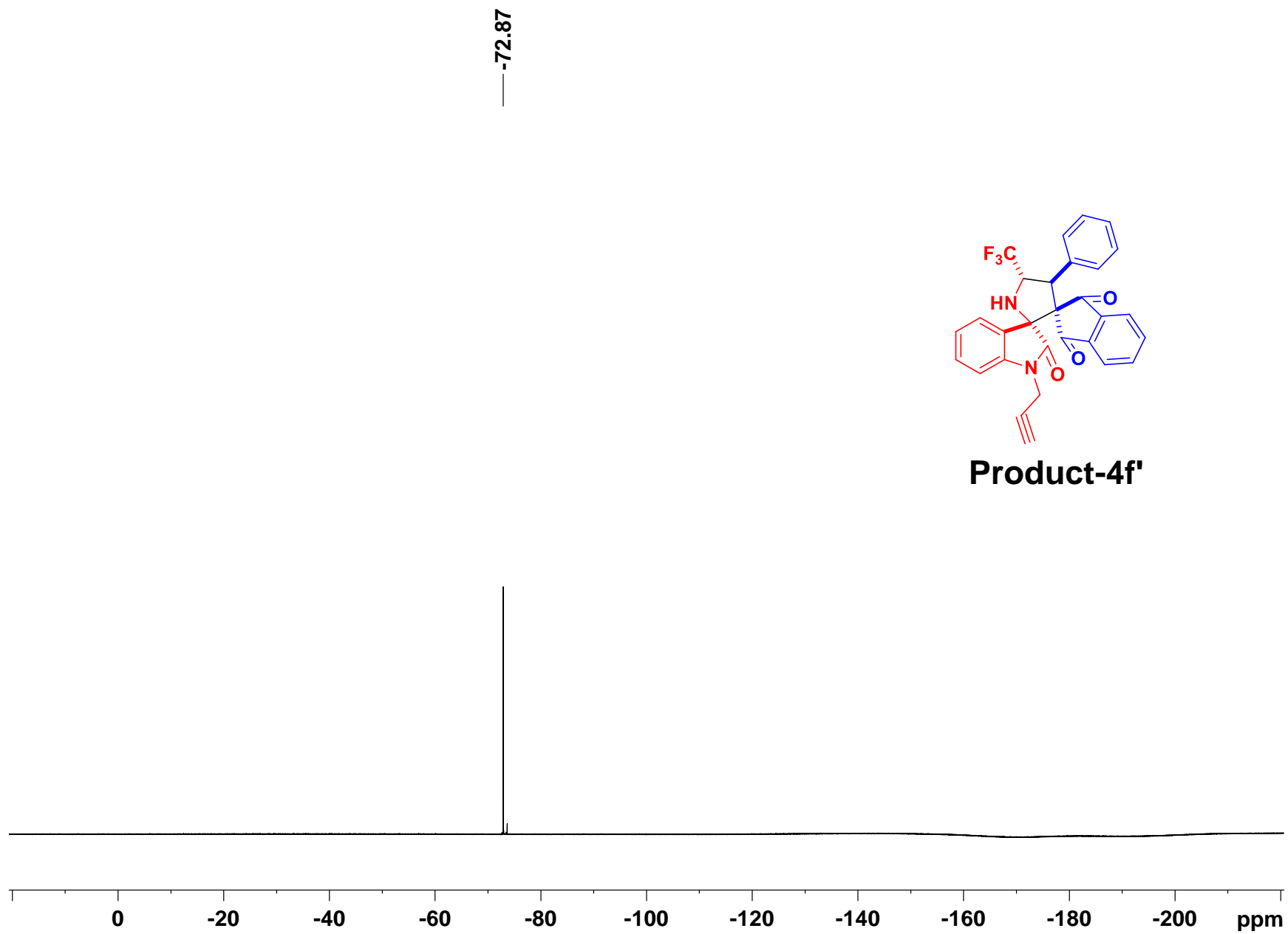
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7.669
7.661
7.632
7.623
7.617
7.611
7.576
7.562
7.557
7.549
7.540
7.266
7.227
7.222
7.208
7.204
7.164
7.145
7.126
7.108
7.091
7.072
7.057
7.046
7.040
6.878
6.859
6.840
6.821
5.404
5.377
5.288
5.283
5.265
4.581
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4.537
4.531
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4.424
4.386
4.380
3.205
3.182
2.227
2.221
2.215
1.688
-0.000



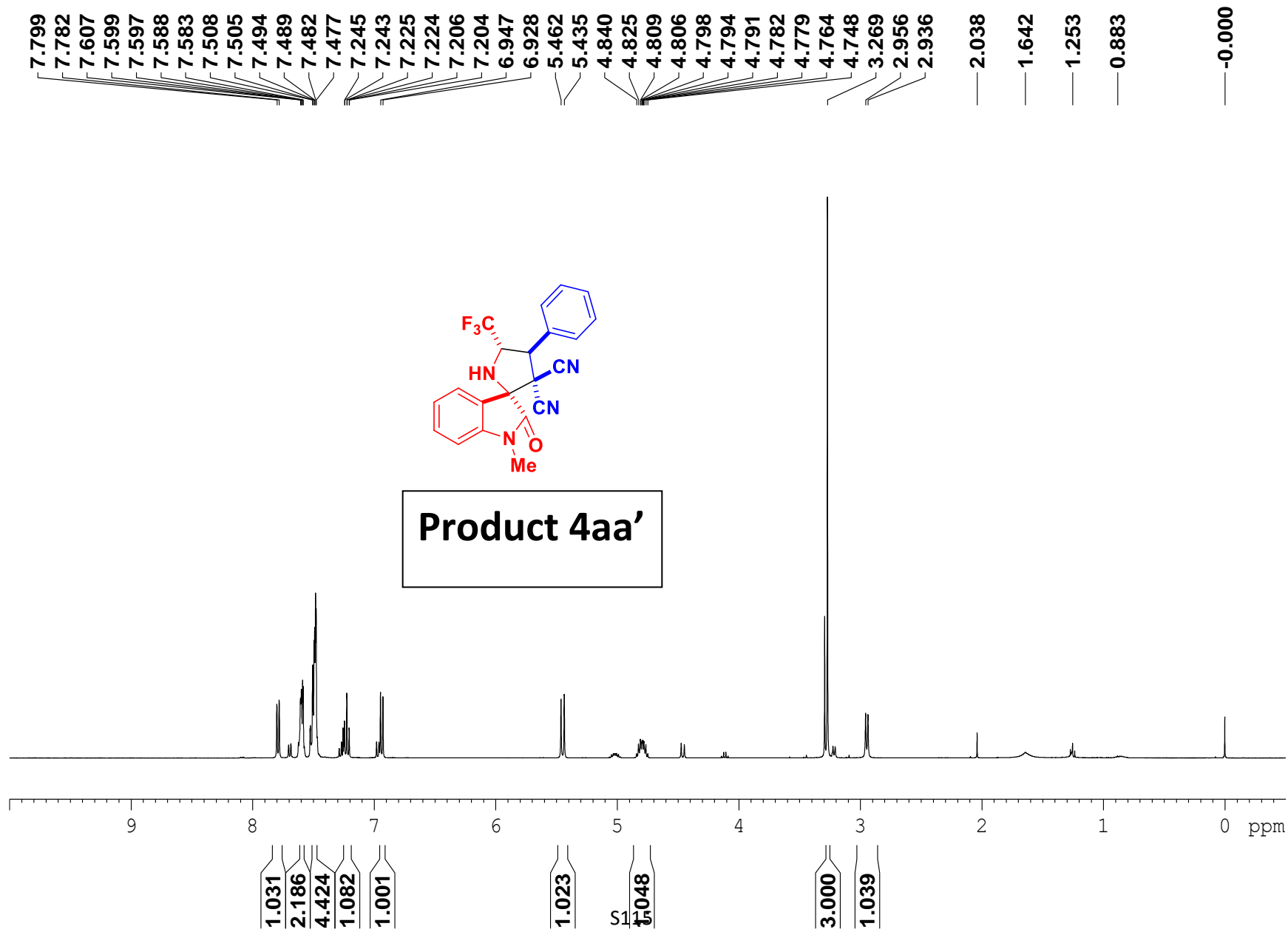
Product-4f'

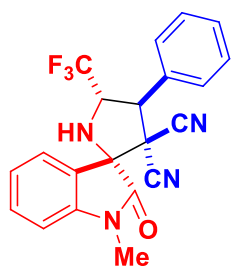




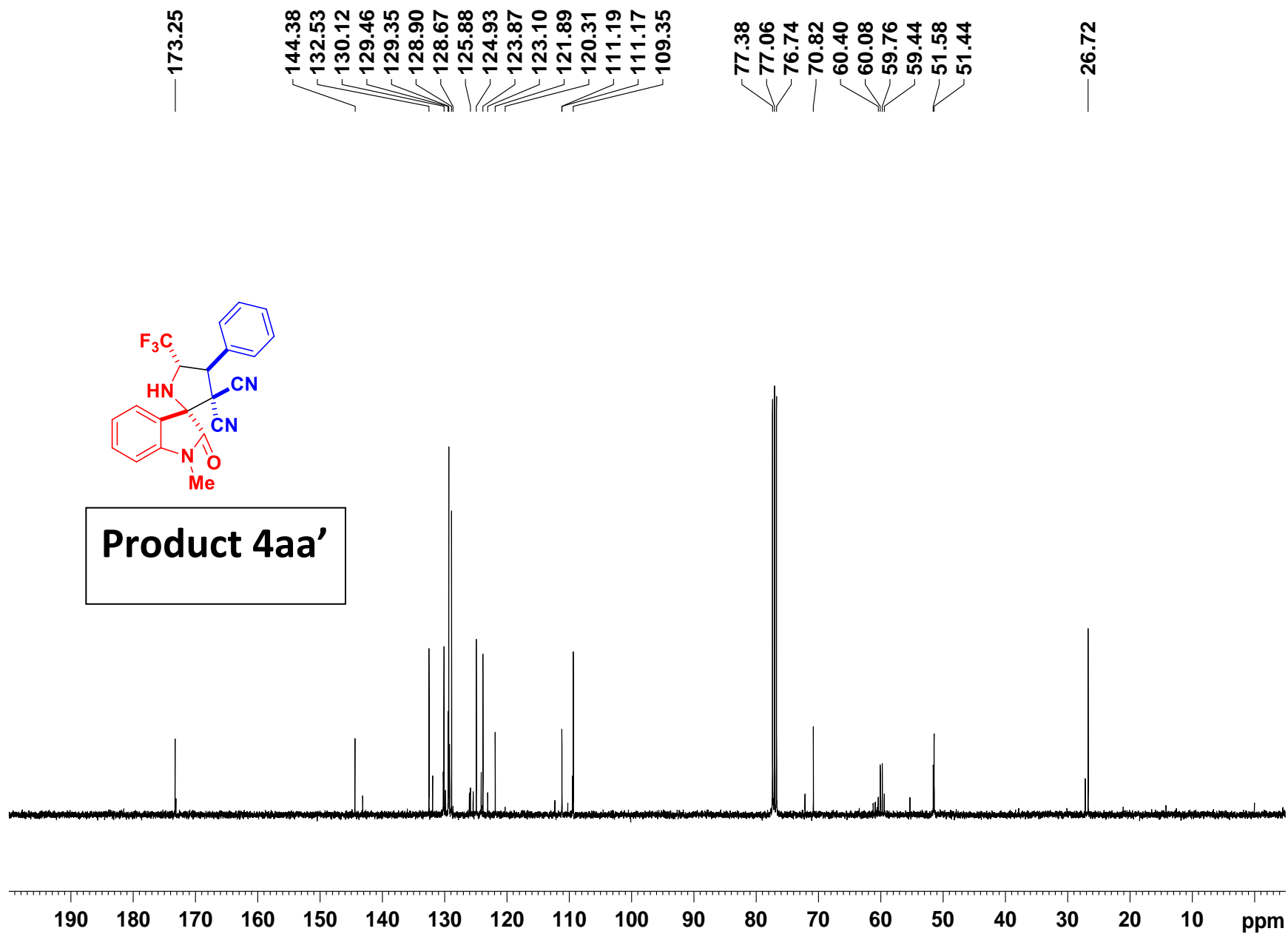


S114



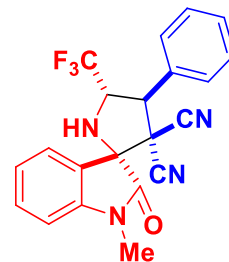


Product 4aa'

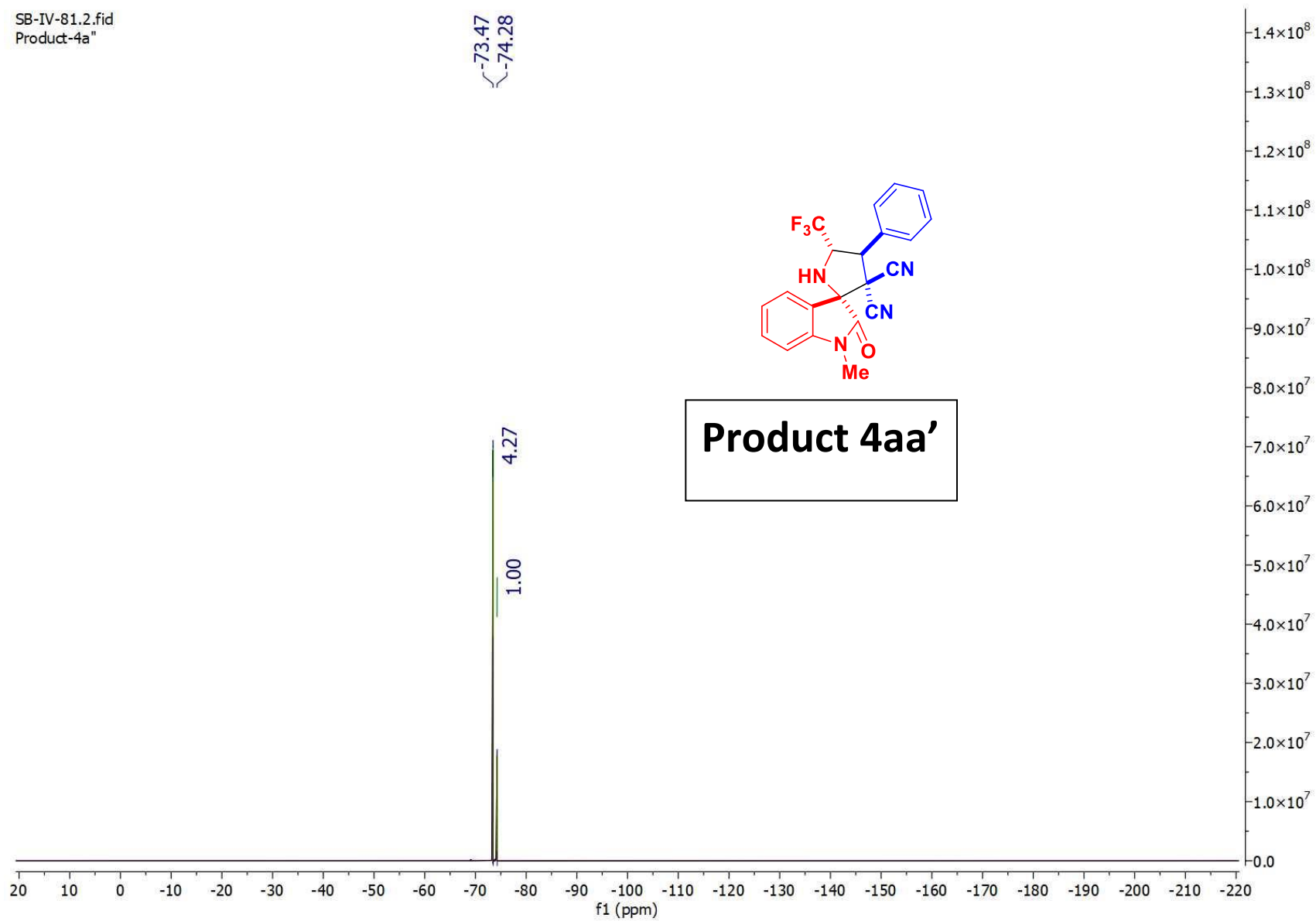


SB-IV-81.2.fid
Product-4a''

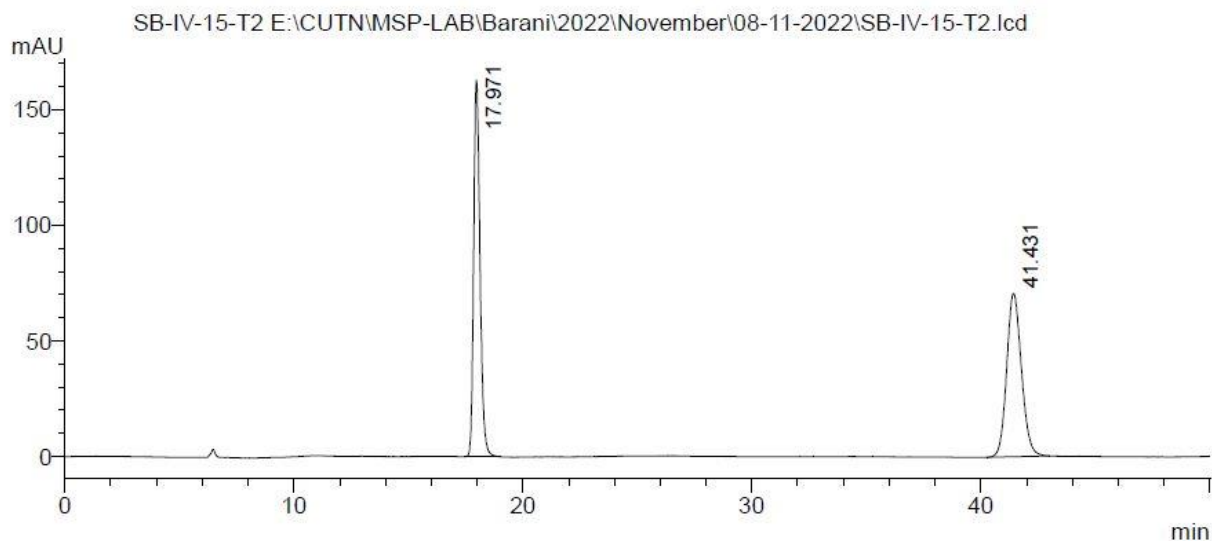
-73.47
-74.28



Product 4aa'



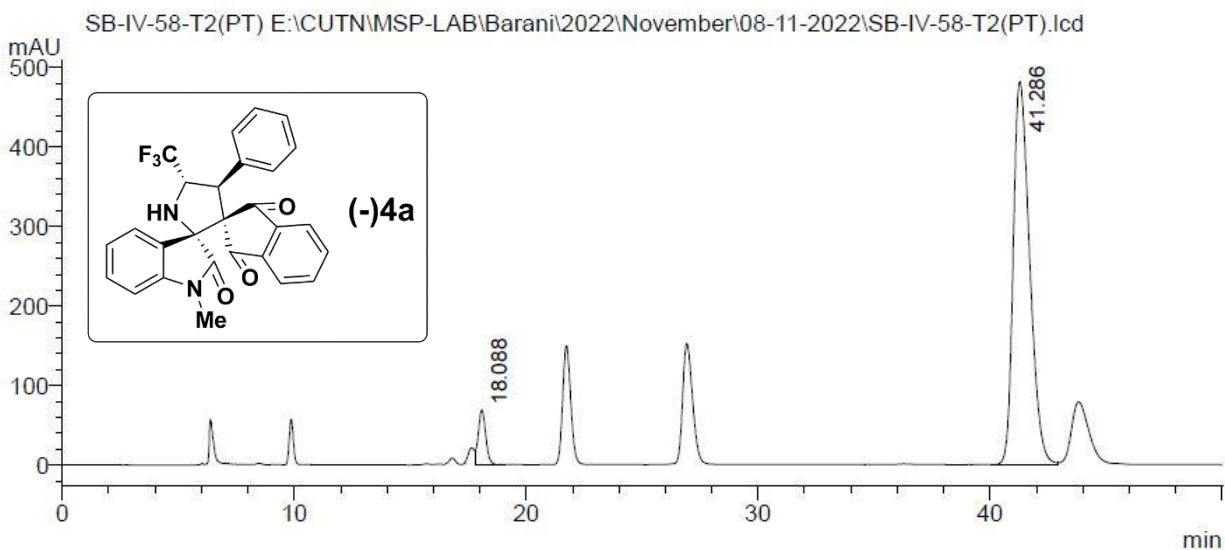
HPLC data of racemic 4a



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	17.971	3139022	162774	49.797
2	41.431	3164587	70692	50.203
Total		6303609	233466	100.000

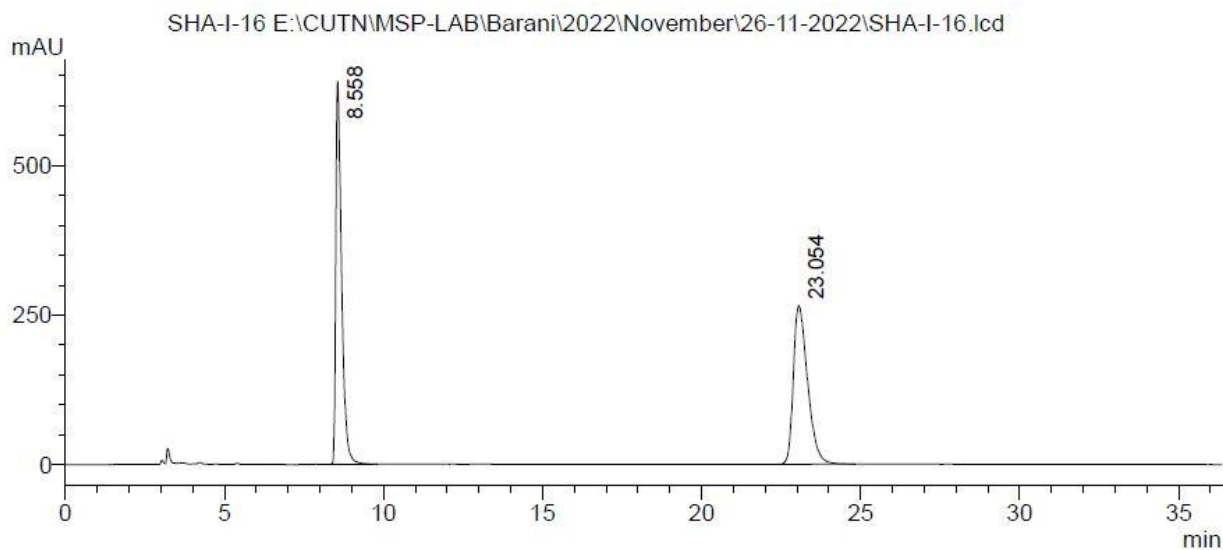
HPLC data of chiral 4a : 87% ee



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.088	1566722	69194	6.199
2	41.286	23708096	481993	93.801
Total		25274818	551187	100.000

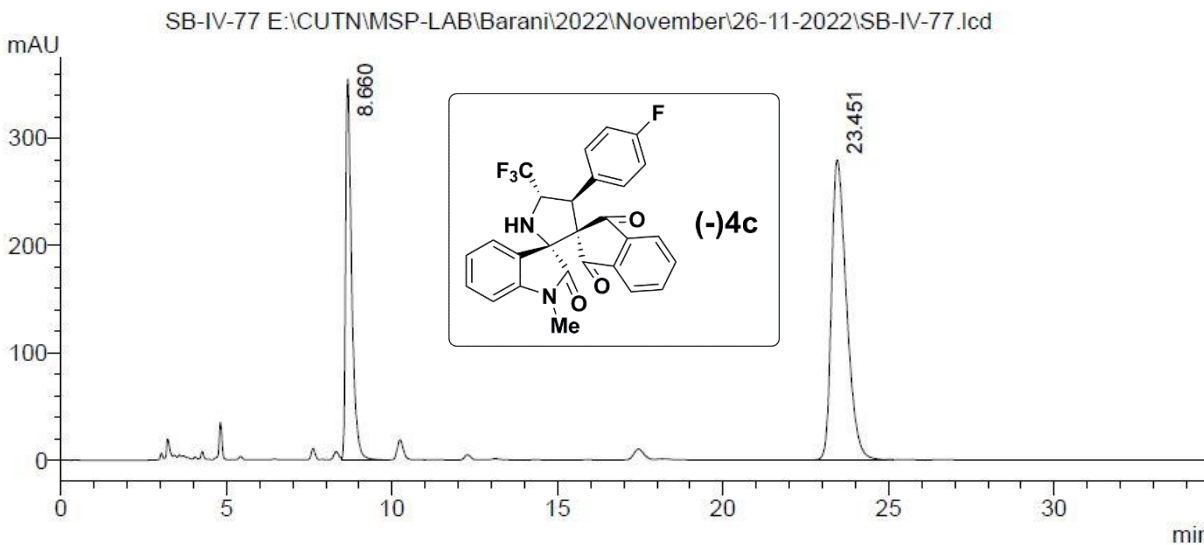
HPLC data of racemic 4c



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.558	8197741	640339	49.772
2	23.054	8272916	265373	50.228
Total		16470657	905711	100.000

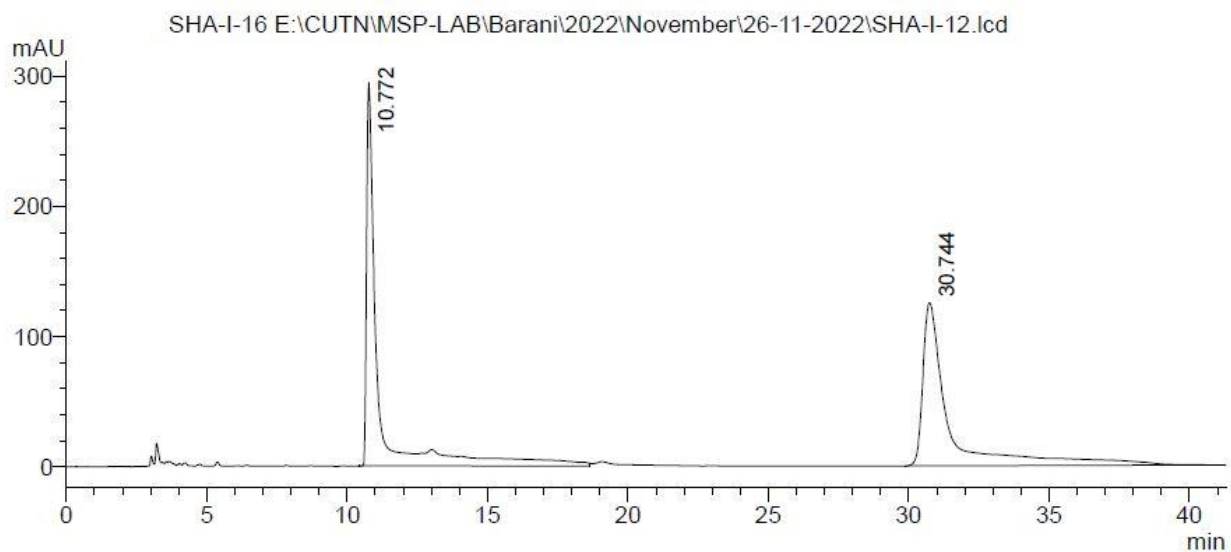
HPLC data of chiral 4c : 32% ee



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	8.660	4528142	354976	33.828
2	23.451	8857571	279422	66.172
Total		13385714	634398	100.000

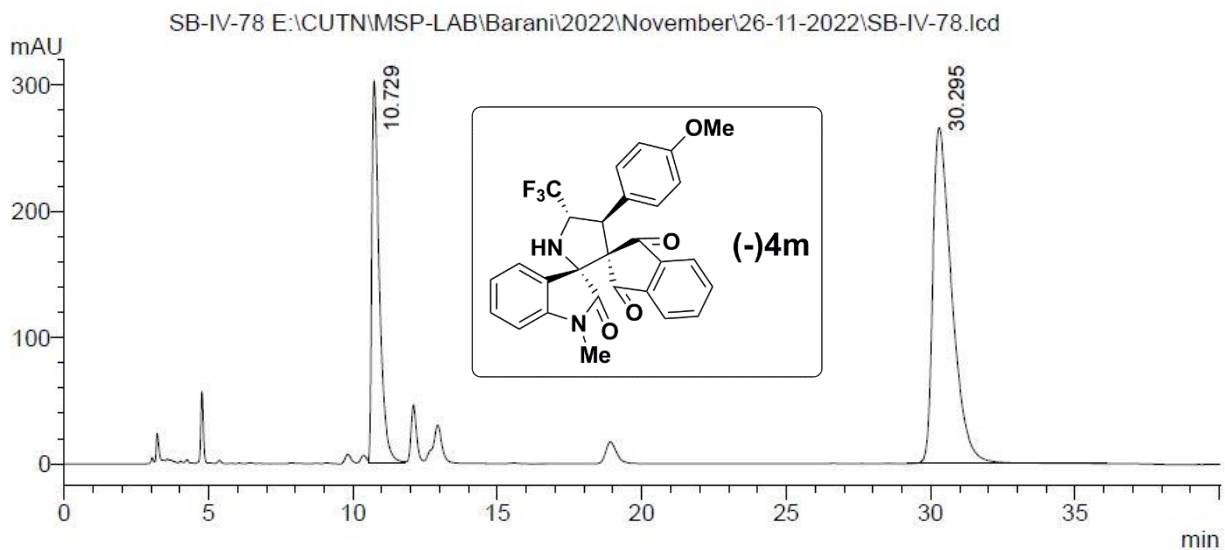
HPLC data of racemic 4m



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.772	8234468	294133	50.562
2	30.744	8051369	125143	49.438
Total		16285837	419277	100.000

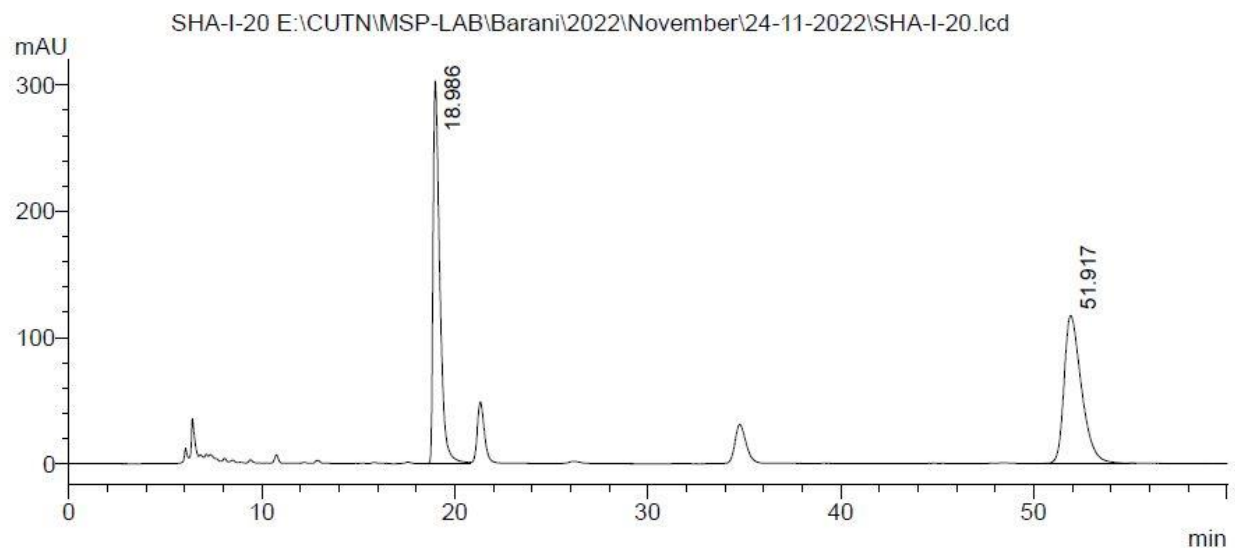
HPLC data of chiral 4m : 38% ee



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	10.729	5480166	303134	30.953
2	30.295	12224808	266192	69.047
Total		17704973	569326	100.000

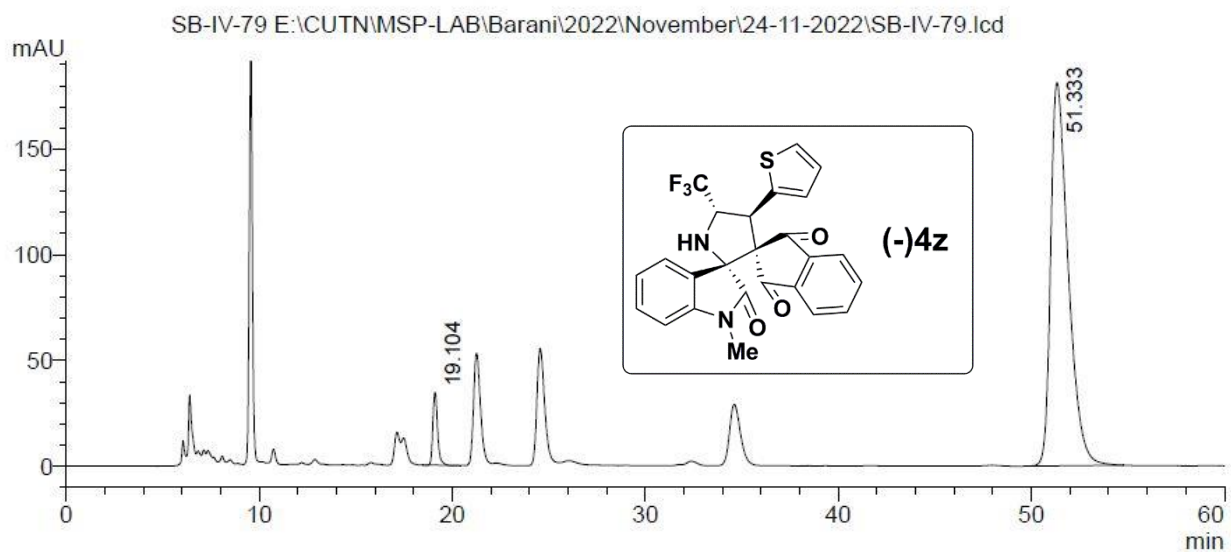
HPLC data of racemic 4z



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	18.986	7317794	303097	49.837
2	51.917	7365640	117171	50.163
Total		14683434	420268	100.000

HPLC data of chiral 4z : 90% ee



PDA Ch1 254nm

Peak #	Ret. Time (min)	Area	Height	Area%
1	19.104	585200	34533	4.845
2	51.333	11494299	181323	95.155
Total		12079500	215857	100.000