

**A regio- and stereocontrolled approach to the synthesis of 4-CF₃-substituted
spiro[chromeno[3,4-*c*]pyrrolidine-oxindoles] *via* reversible [3+2] cycloaddition of azomethine
ylides generated from isatins and sarcosine to 3-nitro-2-(trifluoromethyl)-2*H*-chromenes**

Igor B. Kutyashev, Maria V. Ulitko, Alexey Yu. Barkov, Nikolay S. Zimnitskiy,
Vladislav Yu. Korotaev,* Vyacheslav Ya. Sosnovskikh

Institute of Natural Sciences and Mathematics, Ural Federal University,
620000 Ekaterinburg, Russian Federation

Supporting Information

Table of Contents

1.	Experimental procedures	S2–S3
2.	Analytical characterization data of products	S3–S20
3.	X-ray crystallography studies	S20–S21
4.	References	S21
5.	NMR spectra of copounds 5 , 5'j and 6	S22–S88
6.	NMR spectra of copounds 7	S89–S92
7.	NMR spectra of copounds 8	S93–S112
8.	2D ¹ H– ¹ H NOESY spectrum of the mixture of compounds 5f , 5'f and 6f	S113
9.	NMR spectra of the mixtures of isomers 5 and 5'	S114–S131

Experimental procedures

General

IR spectra were recorded on a Shimadzu IRSpirit-T spectrometer equipped with an ATR accessory. NMR spectra were recorded on Bruker DRX-400 (^1H , 400 MHz; ^{19}F , 376 MHz), Bruker Avance-400 (^1H , 400 MHz; ^{19}F , 376 MHz; ^{13}C , 101 MHz) and Bruker Avance III-500 (^1H , 500 MHz; ^{19}F , 471 MHz ^{13}C , 126 MHz) spectrometers in $\text{DMSO-}d_6$ or CDCl_3 . The chemical shifts (δ) are reported in ppm relative to the internal standard TMS (^1H NMR), C_6F_6 (^{19}F NMR) and to residual signals of the solvents (^{13}C NMR). 2D ^1H - ^1H NOESY spectrum was acquired on a Bruker Avance-400 spectrometer with 0.3 s mixing time. The HRMS spectra were obtained using the UHR-QqTOF maXis Impact HD (Bruker Daltonics) mass spectrometer. Elemental analysis was performed on a PerkinElmer PE 2400 automatic analyzer. Melting points were determined on an SMP40 apparatus. The starting 3-nitro-2*H*-chromenes **4a–k** were prepared according to described procedures.¹ For the study of antitumor activity, the human cervical carcinoma cells HeLa, obtained from the Bank of Cell Cultures of the Institute of Cytology of the Russian Academy of Sciences, St.-Petersburg, Russia, was used.

General procedure for synthesis of spiro[chromenopyrrolidine-oxindoles] **5**, **6** and **7**

Method A: A mixture of the corresponding nitrochromene **4** (1.0 mmol), isatin **1** (1.0 mmol) and sarcosine (0.13 g, 1.5 mmol) was stirred in 2-propanol (4 mL) at 55–60 °C for 3.5–9 h (see table 1) and the reaction progress was monitored by TLC. Upon completion, the mixture was filtered off. Water (1.5 mL) was added to the filtrate, and the precipitate was filtered off. Combined precipitates were washed with water and dried on air. In some cases, additional recrystallisation from the mixture 2-propanol– H_2O (80:20) was necessary.

Method B: A mixture of the corresponding nitrochromene **4** (1.0 mmol), isatin **1** (1.0 mmol) and sarcosine (0.13 g, 1.5 mmol) was refluxed in 1,4-dioxane (8 mL) for 48 or 72 h (see Table 1). After that, the mixture was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (elution with chloroform). After removal of the solvents under reduced pressure, the solid formed was recrystallized from hexane–dichloromethane (2:1).

Assessment of *in vitro* cytotoxic activity of compounds **5** and **6**

The cells were seeded into 96-well microplates in a seeding dose of 2×10^5 cells/mL and cultured for 24 h in the DMME medium with glutamine (1%) in the presence of 10% fetal calf serum and gentamicin (50 mg/L) at 37 °C in a humidified atmosphere with 5% v/v CO_2 . Then the tested compounds **5** and **6** were added to the wells in various concentrations (10^{-7} M, 10^{-6} M, 10^{-5} M, 10^{-4} M). Cells with compounds were incubated for 48 h, after which cell viability was assessed using the standard MTT test,² based on

the reduction of the yellow tetrazole salt by living cell mitochondrial dehydrogenases to formazan crystals, soluble in DMSO. Experiments were performed in 3 replicates, with negative (culture medium), positive (10^{-3} M solution of hydrogen peroxide in phosphate buffer solution) controls and solvent control (DMSO). The results of the MTT test were evaluated by comparing the optical density of the formazan solution measured on a flatbed scanner ELx800 (BioTek, USA) at a wavelength of 570 nm in the experimental and control wells and the cytotoxicity index (IC) was calculated. The cytotoxicity index was determined for each concentration of the studied substances. Using probit-regression, the IC_{50} score (the concentration of the substance that is required for 50% inhibition of cell survival) was calculated. The parameters of the arithmetic mean value and the standard error were calculated. The differences in the average values according to the Mann-Whitney test with $p < 0.05$ were considered reliable. For the statistical analysis Microsoft Excel and Statistika 2009 were used.

Analytical characterization data of products

Compound 4h

6-Bromo-8-ethoxy-3-nitro-2-(trifluoromethyl)-2H-chromene (4h). Yield 85%, mp 107–108 °C, yellow powder. IR (ATR): 1645, 1563, 1517, 1462, 1424, 1396, 1375, 1358, 1336 cm^{-1} . ^1H NMR (500 MHz, CDCl_3) δ 1.46 (t, $J = 7.0$ Hz, 3H, Me), 4.12 (q, $J = 7.0$ Hz, 2H, OCH_2), 6.14 (q, $J = 6.2$ Hz, 1H, H-4), 7.11 (d, $J = 1.4$ Hz, 1H, H-7), 7.16 (d, $J = 1.4$ Hz, 1H, H-5), 8.01 (s, 1H, H-4). ^{19}F NMR (471 MHz, $\text{DMSO}-d_6$) δ 84.0 (d, CF_3 , $J = 6.2$ Hz). ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ 14.5, 65.7, 69.8 (q, $^2J = 34.5$ Hz, C-4), 115.3, 118.6, 122.0, 122.5 (q, $^1J = 288.2$ Hz, CF_3), 124.4, 131.5, 134.5, 141.9, 148.2. Anal. Calcd for $\text{C}_{12}\text{H}_9\text{BrF}_3\text{NO}_4$: C, 39.16; H, 2.46; N, 3.81. Found: C, 38.95; H, 2.61; N, 3.63.

Compounds 5, 5', 6 and 7

(3R*,3aS*,4S*,9bR*)-2-Methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5a). Method A. Yield 219 mg (0.523 mmol, 52%), mp 224–225 °C (decomp.), white powder. IR (ATR): 3271, 1715, 1620, 1556, 1491, 1473, 1458, 1376, 1354, 1330 cm^{-1} . ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 1.86 (s, 3H, Me), 2.84 (d, $J = 9.1$ Hz, 1H, H-1a), 4.12 (dd, $J = 9.1, 6.5$ Hz, 1H, H-1b), 4.75 (d, $J = 6.5$ Hz, 1H, H-9b), 5.32 (q, $J = 7.1$ Hz, 1H, H-4), 6.95 (dd, $J = 7.7, 1.0$ Hz, 1H, H-7'), 7.10 (d, $J = 7.9$ Hz, 1H, H-6), 7.15 (t, $J = 7.7$ Hz, 1H, H-8), 7.17 (td, $J = 7.7, 1.0$ Hz, 1H, H-5'), 7.27 (td, $J = 7.8, 1.3$ Hz, 1H, H-7), 7.42 (td, $J = 7.7, 1.0$ Hz, 1H, H-6'), 7.53 (dd, $J = 7.7, 1.3$ Hz, 1H, H-9), 7.59 (dd, $J = 7.7, 1.0$ Hz, 1H, H-4'), 10.79 (s, 1H, NH). ^{19}F NMR (471 MHz, $\text{DMSO}-d_6$) δ 95.8 (d, $J = 7.1$ Hz, CF_3). ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ 34.5, 38.6, 59.7, 73.8 (q, $^2J = 29.7$ Hz, C-4), 79.9, 97.2, 110.4, 116.5, 122.5, 122.7 (q, $^1J = 289.8$ Hz, CF_3), 123.6, 124.0, 127.0, 127.1, 128.1,

128.6, 131.0, 144.0, 149.2, 174.6. Anal. Calcd for C₂₀H₁₆F₃N₃O₄·0.33H₂O: C, 56.47; H, 3.95; N, 9.88. Found: C, 56.60; H, 3.54; N, 9.89.

(3S*,3aS*,4S*,9bR*)-2-Methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'a). This compound was not obtained in a pure form. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.99 (s, 3H, Me), 3.29 (t, *J* = 8.7 Hz, 1H, H-1a), 3.91 (t, *J* = 8.7 Hz, 1H, H-1b), 4.85 (t, *J* = 8.7 Hz, 1H, H-9b), 5.62 (q, *J* = 6.8 Hz, 1H, H-4), 6.91 (dd, *J* = 7.7, 1.0 Hz, 1H, H-7'), 6.99 (dd, *J* = 7.7, 1.0 Hz, 1H, H-4'), 7.04 (td, *J* = 7.7, 1.0 Hz, 1H, H-5'), 7.06 (d, *J* = 8.0 Hz, 1H, H-6), 7.14–7.20 (m, 1H, H-8), 7.24–7.30 (m, 1H, H-7), 7.36 (td, *J* = 7.7, 1.0 Hz, 1H, H-6'), 7.45 (dd, *J* = 7.7, 1.3 Hz, 1H, H-9), 11.00 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 97.5 (d, *J* = 6.8 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 33.9, 41.8, 56.2, 74.7 (q, ²*J* = 32.4 Hz, C-4), 75.2, 99.2, 110.1, 116.6, 122.8 (q, ¹*J* = 290.6 Hz, CF₃), 123.0, 123.6, 123.9, 124.1, 124.3, 128.4, 128.5, 130.9, 142.6, 151.7, 174.1.

(1S*,3aS*,4S*,9bR*)-2-Methyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6a). Method B. Yield 205 mg (0.489 mmol, 49%), mp 252–253 °C (decomp.), white powder. IR (ATR): 3371, 1721, 1692, 1623, 1552, 1489, 1470, 1457, 1393, 1339 cm⁻¹. ¹H NMR (500 MHz, DMSO-*d*₆) δ 2.06 (s, 3H, Me), 3.68 (d, *J* = 12.3 Hz, 1H, H-3a), 4.44 (d, *J* = 12.3 Hz, 1H, H-3b), 4.53 (s, 1H, H-9b), 5.69 (q, *J* = 5.9 Hz, 1H, H-4), 6.23 (d, *J* = 7.8 Hz, 1H, H-9), 6.85 (t, *J* = 7.6 Hz, 1H, H-8), 6.90 (d, *J* = 7.7 Hz, 1H, H-7'), 7.11 (d, *J* = 7.8 Hz, 1H, H-6), 7.18 (t, *J* = 7.7 Hz, 1H, H-5'), 7.23 (t, *J* = 7.6 Hz, 1H, H-7), 7.40 (t, *J* = 7.7 Hz, 1H, H-6'), 7.68 (d, *J* = 7.7 Hz, 1H, H-4'), 10.67 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 90.1 (d, *J* = 5.9 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 33.9, 50.1, 56.6, 75.0 (q, ²*J* = 31.8 Hz, C-4), 76.1, 89.0, 110.2, 117.1, 118.0, 122.3 (q, ¹*J* = 281.9 Hz, CF₃), 123.0, 123.2, 125.0, 125.8, 126.6, 128.9, 130.6, 142.8, 151.1, 176.3. HRMS (ESI) calcd for C₂₀H₁₇F₃N₃O₄ [M+H]⁺ 420.1166, found 420.1164.

(3R*,3aS*,4S*,9bR*)-2,8-Dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5b). Method A. Yield 173 mg (0.400 mmol, 40%), mp 203–204 °C (decomp.), white powder. IR (ATR): 3239, 1715, 1623, 1558, 1503, 1472, 1371, 1331 cm⁻¹. ¹H NMR (500 MHz, DMSO-*d*₆) δ 1.86 (s, 3H, Me), 2.29 (s, 3H, Me), 2.84 (d, *J* = 9.1 Hz, 1H, H-1a), 4.10 (dd, *J* = 9.1, 6.5 Hz, 1H, H-1b), 4.68 (d, *J* = 6.5 Hz, 1H, H-9b), 5.26 (q, *J* = 7.2 Hz, 1H, H-4), 6.94 (d, *J* = 7.8 Hz, 1H, H-7'), 6.98 (d, *J* = 8.2 Hz, 1H, H-6), 7.05 (dd, 1H, *J* = 8.2, 1.5 Hz, H-7), 7.15 (td, *J* = 7.7, 0.8 Hz, 1H, H-5'), 7.32 (d, *J* = 1.5, 1H, H-9), 7.42 (td, *J* = 7.7, 1.1 Hz, 1H, H-6'), 7.58 (d, *J* = 7.5 Hz, 1H, H-4'), 10.78 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 95.9 (d, *J* = 7.2 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 20.3, 34.5, 38.6, 59.7, 73.9 (q, ²*J* = 29.8 Hz, C-4), 79.9, 97.3, 110.4, 116.2, 122.5, 122.7 (q, ¹*J* = 289.7 Hz, CF₃), 123.6, 126.7, 127.1, 128.6, 128.7, 131.0, 133.0, 144.0, 147.1, 174.7. Anal. Calcd for C₂₁H₁₈F₃N₃O₄·0.33H₂O: C, 57.40; H, 4.28; N, 9.56. Found: C, 57.56; H, 4.02; N, 9.56.

(3S*,3aS*,4S*,9bR*)-2,8-Dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'b). This compound was not obtained in a pure

form. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 1.97 (s, 3H, Me), 2.28 (s, 3H, Me), 3.28 (t, $J = 8.7$ Hz, 1H, H-1a), 3.87 (t, $J = 8.7$ Hz, 1H, H-1b), 4.78 (t, $J = 8.7$ Hz, 1H, H-9b), 5.53 (q, $J = 6.8$ Hz, 1H, H-4), 6.90 (dd, $J = 7.7, 1.0$ Hz, 1H, H-7'), 6.93 (d, $J = 8.2$ Hz, 1H, H-6), 6.96 (dd, $J = 7.7, 1.0$ Hz, 1H, H-4'), 7.03 (td, $J = 7.7, 1.0$ Hz, 1H, H-5'), 7.06 (dd, 1H, $J = 8.2, 1.5$ Hz, 1H, H-7), 7.24 (d, $J = 1.5$, 1H, H-9), 7.35 (td, $J = 7.7, 1.0$ Hz, 1H, H-6'), 10.98 (s, 1H, NH). ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ 97.5 (d, $J = 6.8$ Hz, CF_3). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ 20.3, 33.9, 41.8, 56.2, 74.9 (q, $^2J = 32.6$ Hz, C-4), 75.3, 99.4, 110.2, 116.3, 122.9 (q, $^1J = 283.8$ Hz, CF_3), 123.6, 124.1, 124.3, 128.6, 128.9, 130.9, 142.7, 149.6, 174.2 (two signals are masked).

(1S*,3aS*,4S*,9bR*)-2,8-Dimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6b). Method B. Yield 221 mg (0.510 mmol, 51%), mp 245–246 °C (decomp.), white powder. IR (ATR): 3205, 1691, 1621, 1558, 1502, 1468, 1390, 1341 cm^{-1} . ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ 1.92 (s, 3H, Me), 2.07 (s, 3H, Me), 3.68 (d, $J = 12.2$ Hz, 1H, H-3a), 4.43 (d, $J = 12.2$ Hz, 1H, H-3b), 4.45 (s, 1H, H-9b), 5.64 (q, $J = 5.9$ Hz, 1H, H-4), 5.96 (br s, 1H, H-9), 6.91 (d, $J = 7.6$ Hz, 1H, H-7'), 6.99 (d, $J = 8.4$ Hz, 1H, H-6), 7.03 (br d, $J = 8.4$, 1H, H-7), 7.19 (t, $J = 7.6$ Hz, 1H, H-5'), 7.42 (t, $J = 7.6$ Hz, 1H, H-6'), 7.66 (d, $J = 7.6$ Hz, 1H, H-4'), 10.66 (s, 1H, NH). ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ 90.1 (d, $J = 5.9$ Hz, CF_3). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ 20.3, 34.0, 50.3, 56.7, 75.1 (q, $^2J = 30.6$ Hz, C-4), 76.2, 89.0, 110.1, 116.9, 117.7, 122.3 (q, $^1J = 281.8$ Hz, CF_3), 123.1, 125.0, 126.1, 126.7, 129.5, 130.6, 131.9, 142.9, 149.1, 176.4. HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{F}_3\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 434.1322, found 434.1322.

(3R*,3aS*,4S*,9bR*)-8-Methoxy-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5c). Method A. Yield 229 mg (0.510 mmol, 51%), mp 193–194 °C, white powder. IR (ATR): 3184, 1703, 1619, 1559, 1500, 1469, 1383, 1330 cm^{-1} . ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ 1.86 (s, 3H, Me), 2.88 (d, $J = 9.2$ Hz, 1H, H-1a), 3.76 (s, 3H, MeO), 4.10 (dd, $J = 9.2, 6.5$ Hz, 1H, H-1b), 4.71 (d, $J = 6.5$ Hz, 1H, H-9b), 5.24 (q, $J = 7.1$ Hz, 1H, H-4), 6.83 (dd, $J = 8.8, 3.0$ Hz, 1H, H-7), 6.94 (dd, $J = 7.7, 1.0$ Hz, 1H, H-7'), 7.02 (d, 1H, $J = 8.8$ Hz, H-6), 7.11 (d, $J = 3.0$ Hz, 1H, H-9), 7.14 (td, $J = 7.7, 1.0$ Hz, 1H, H-5'), 7.42 (td, $J = 7.7, 1.0$ Hz, 1H, H-6'), 7.59 (dd, $J = 7.7, 1.0$ Hz, 1H, H-4'), 10.79 (s, 1H, NH). ^{19}F NMR (376 MHz, $\text{DMSO-}d_6$) δ 95.9 (d, $J = 7.1$ Hz, CF_3). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ 34.5, 39.0, 55.4, 59.7, 74.0 (q, $^2J = 29.5$ Hz, C-4), 80.0, 97.3, 110.4, 113.0, 114.0, 117.3, 122.5, 122.8 (q, $^1J = 289.7$ Hz, CF_3), 123.6, 127.2, 128.0, 131.1, 142.9, 144.0, 155.6, 174.7. HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{F}_3\text{N}_3\text{O}_5$ $[\text{M}+\text{H}]^+$ 450.1271, found 450.1266.

(3S*,3aS*,4S*,9bR*)-8-Methoxy-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'c). This compound was not obtained in a pure form. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 1.97 (s, 3H, Me), 3.28 (t, $J = 8.7$ Hz, 1H, H-1a), 3.76 (s, 3H, MeO), 3.89 (t, $J = 8.7$ Hz, 1H, H-1b), 4.81 (t, $J = 8.7$ Hz, 1H, H-9b), 5.55 (q, $J = 6.8$ Hz, 1H, H-4), 6.84 (dd, $J = 8.8, 3.0$ Hz, 1H, H-7), 6.90 (dd, $J = 7.7, 1.0$ Hz, 1H, H-7'), 6.97 (dd, $J = 7.7, 1.0$ Hz, 1H, H-4'),

6.98 (d, $J = 8.8$ Hz, 1H, H-6), 7.03 (td, $J = 7.7, 1.0$ Hz, 1H, H-5'), 7.35 (td, $J = 7.7, 1.0$ Hz, 1H, H-6'), 10.99 (s, 1H, NH). ^{19}F NMR (376 MHz, DMSO- d_6) δ 97.4 (d, $J = 6.7$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 33.9, 42.1, 54.8, 56.2, 74.9 (q, $^2J = 31.9$ Hz, C-4), 75.2, 99.3, 110.2, 112.8, 114.3, 117.4, 122.8 (q, $^1J = 284.5$ Hz, CF_3), 123.9, 124.1, 124.2, 126.2, 130.9, 142.7, 143.8, 155.5, 174.2.

(1S*,3aS*,4S*,9bR*)-8-Methoxy-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (6c). Method B. Yield 145 mg (0.323 mmol, 32%), mp 193–194 °C, white powder. IR (ATR): 3183, 1705, 1620, 1557, 1500, 1469, 1337 cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6) δ 2.08 (s, 3H, Me), 3.33 (s, 3H, MeO), 3.69 (d, $J = 12.3$ Hz, 1H, H-3a), 4.43 (d, $J = 12.3$ Hz, 1H, H-3b), 4.46 (s, 1H, H-9b), 5.58 (q, $J = 5.9$ Hz, 1H, H-4), 5.72 (d, $J = 2.9$ Hz, 1H, H-9), 6.80 (dd, 1H, $J = 8.9, 2.9$ Hz, H-7), 6.91 (d, $J = 7.6$ Hz, 1H, H-7'), 7.04 (d, $J = 8.9$ Hz, 1H, H-6), 7.19 (t, $J = 7.6$ Hz, 1H, H-5'), 7.40 (t, $J = 7.6$ Hz, 1H, H-6'), 7.67 (d, $J = 7.6$ Hz, 1H, H-4'), 10.68 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 90.0 (d, $J = 5.9$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 34.0, 50.5, 54.7, 56.7, 75.4 (q, $^2J = 31.8$ Hz, C-4), 76.2, 89.0, 109.6, 110.2, 115.0, 118.1, 118.7, 122.3 (q, $^1J = 281.8$ Hz, CF_3), 123.1, 125.1, 126.6, 130.6, 142.9, 145.0, 154.4, 176.3. HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{19}\text{F}_3\text{N}_3\text{O}_5$ $[\text{M}+\text{H}]^+$ 450.1271, found 450.1272.

(3R*,3aS*,4S*,9bR*)-6-Ethoxy-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5d). Method A. Yield 176 mg (0.380 mmol, 38%), mp 181–182 °C (decomp.), white powder. IR (ATR): 3231, 1703, 1621, 1553, 1488, 1471, 1454, 1398, 1372, 1326 cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6) δ 1.36 (t, $J = 7.0$ Hz, 3H, Me), 1.85 (s, 3H, Me), 2.80 (d, $J = 9.1$ Hz, 1H, H-1a), 4.07–4.17 (m, 3H, H-1b, OCH_2), 4.72 (d, $J = 6.6$ Hz, 1H, H-9b), 5.37 (q, $J = 7.1$ Hz, 1H, H-4), 6.95 (dd, $J = 7.7, 1.0$ Hz, 1H, H-7'), 6.96 (d, $J = 7.2$ Hz, 1H, H-7), 7.03–7.09 (m, 2H, H-8, H-9), 7.17 (td, $J = 7.7, 1.0$ Hz, 1H, H-5'), 7.42 (td, $J = 7.7, 1.0$ Hz, 1H, H-6'), 7.57 (dd, $J = 7.7$ Hz, 1H, H-4'), 10.78 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 96.0 (d, $J = 7.1$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 14.7, 34.5, 38.7, 59.7, 64.0, 73.8 (q, $^2J = 29.8$ Hz, C-4), 79.9, 97.3, 110.4, 111.7, 119.6, 122.6, 123.6, 122.7 (q, $^1J = 289.6$ Hz, CF_3), 123.8, 127.1, 128.3, 131.0, 138.8, 144.0, 147.3, 174.6. Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{F}_3\text{N}_3\text{O}_5$: C, 57.02; H, 4.35; N, 9.07. Found: C, 57.01; H, 4.11; N, 9.02.

(3S*,3aS*,4S*,9bR*)-6-Ethoxy-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'd). This compound was not obtained in a pure form. ^1H NMR (500 MHz, DMSO- d_6) δ 1.30 (t, $J = 7.0$ Hz, 3H, Me), 1.98 (s, 3H, Me), 3.28 (t, $J = 8.8$ Hz, 1H, H-1a), 3.87 (t, $J = 8.8$ Hz, 1H, H-1b), 4.00–4.11 (m, 2H, OCH_2), 4.81 (t, $J = 8.8$ Hz, 1H, H-9b), 5.58 (q, $J = 6.7$ Hz, 1H, H-4), 6.90 (dd, $J = 7.7, 1.0$ Hz, 1H, H-7'), 6.93–7.00 (m, 3H, H-7, H-4', H-5'), 7.01–7.09 (m, 2H, H-8, H-9), 7.35 (td, $J = 7.7, 1.1$ Hz, 1H, H-6'), 10.98 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 97.4 (d, $J = 6.7$ Hz, CF_3).

(1S*,3aS*,4S*,9bR*)-6-Ethoxy-2-methyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6d). Method B. Yield 182 mg (0.393 mmol, 39%),

mp 215–216 °C (decomp.), white powder. IR (ATR): 3362, 1700, 1619, 1558, 1471, 1368, 1328 cm⁻¹. ¹H NMR (500 MHz, DMSO-*d*₆) δ 1.32 (t, *J* = 6.7 Hz, 3H, Me), 2.05 (s, 3H, Me), 3.67 (d, *J* = 12.3 Hz, 1H, H-3a), 3.95–4.10 (m, 2H, OCH₂), 4.43 (d, *J* = 12.3 Hz, 1H, H-3b), 4.50 (s, 1H, H-9b), 5.61 (q, *J* = 5.8 Hz, 1H, H-4), 5.80 (d, *J* = 7.9 Hz, 1H, H-9), 6.74 (t, *J* = 7.9 Hz, 1H, H-8), 6.85–6.93 (m, 2H, H-7, H-7'), 7.17 (t, *J* = 7.6 Hz, 1H, H-5'), 7.39 (t, *J* = 7.6 Hz, 1H, H-6'), 7.66 (d, *J* = 7.6 Hz, 1H, H-4'), 10.66 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 90.2 (d, *J* = 5.8 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 14.5, 33.8, 50.2, 56.6, 64.1, 75.1 (q, ²*J* = 31.7 Hz, C-4), 76.1, 89.1, 110.2, 112.7, 116.8, 119.0, 122.3 (q, ¹*J* = 281.8 Hz, CF₃), 122.9, 123.0, 124.9, 126.8, 130.5, 141.1, 142.8, 147.4, 176.2. HRMS (ESI) calcd for C₂₂H₂₁F₃N₃O₅ [M+H]⁺ 464.1428, found 464.1423.

(3R*,3aS*,4S*,9bR*)-8-Chloro-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5e). Method A. Yield 295 mg (0.650 mmol, 65%), mp 226–227 °C (decomp.), white powder. IR (ATR): 3249, 3236, 1715, 1623, 1559, 1483, 1471, 1370, 1332 cm⁻¹. ¹H NMR (500 MHz, DMSO-*d*₆) δ 1.86 (s, 3H, Me), 2.87 (d, *J* = 9.4 Hz, 1H, H-1a), 4.11 (dd, *J* = 9.4, 6.5 Hz, 1H, H-1b), 4.79 (d, *J* = 6.5 Hz, 1H, H-9b), 5.40 (q, *J* = 7.1 Hz, 1H, H-4), 6.95 (d, *J* = 7.7 Hz, 1H, H-7'), 7.15 (td, *J* = 7.4, 0.9 Hz, 1H, H-5'), 7.16 (d, *J* = 8.6 Hz, 1H, H-6), 7.32 (dd, *J* = 8.6, 2.4 Hz, 1H, H-7), 7.43 (td, *J* = 7.7, 1.1 Hz, 1H, H-6'), 7.55 (d, *J* = 7.6 Hz, 1H, H-4'), 7.72 (d, *J* = 2.4 Hz, 1H, H-9), 10.82 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 95.9 (d, *J* = 7.1 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.4, 38.6, 59.6, 73.8 (q, ²*J* = 29.9 Hz, C-4), 79.9, 96.8, 110.4, 118.3, 122.5, 122.6 (q, ¹*J* = 289.7 Hz, CF₃), 123.4, 127.1, 127.7, 128.0, 128.2, 129.3, 131.1, 144.0, 148.1, 174.5. Anal. Calcd for C₂₀H₁₅ClF₃N₃O₄·0.5H₂O: C, 51.90; H, 3.48; N, 9.08. Found: C, 51.98; H, 3.42; N, 9.11.

(3S*,3aS*,4S*,9bR*)-8-Chloro-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'e). This compound was not obtained in a pure form. ¹H NMR (500 MHz, DMSO-*d*₆) δ 1.98 (s, 3H, Me), 3.27 (t, *J* = 8.7 Hz, 1H, H-1a), 3.91 (t, *J* = 8.7 Hz, 1H, H-1b), 4.84 (t, *J* = 8.7 Hz, 1H, H-9b), 5.71 (q, *J* = 6.9 Hz, 1H, H-4), 6.91 (d, *J* = 7.8 Hz, 1H, H-7'), 6.99 (d, 1H, *J* = 7.7 Hz, H-4'), 7.04 (td, *J* = 7.7, 1.0 Hz, 1H, H-5'), 7.10 (d, *J* = 8.7 Hz, 1H, H-6), 7.32 (dd, *J* = 8.6, 2.4 Hz, 1H, H-7), 7.36 (td, *J* = 7.7, 1.1 Hz, 1H, H-6'), 7.69 (d, *J* = 2.4 Hz, 1H, H-9), 11.00 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 97.6 (d, *J* = 6.9 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.0, 41.2, 56.4, 74.3 (q, ²*J* = 31.9 Hz, C-4), 75.3, 98.5, 110.3, 118.4, 122.8 (q, ¹*J* = 285.0 Hz, CF₃), 124.0, 122.4, 124.3, 125.6, 127.7, 128.2, 128.4, 131.0, 142.8, 150.2, 174.1.

(1S*,3aS*,4S*,9bR*)-8-Chloro-2-methyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6e). Method B. Yield 274 mg (0.604 mmol, 60%), mp 275–276 °C (decomp.), white powder. IR (ATR): 3250, 1712, 1621, 1560, 1472, 1370, 1332 cm⁻¹. ¹H NMR (500 MHz, DMSO-*d*₆) δ 2.08 (s, 3H, Me), 3.67 (d, *J* = 12.3 Hz, 1H, H-3a), 4.45 (d, *J* = 12.3 Hz, 1H, H-3b), 4.60 (s, 1H, H-9b), 5.72 (q, *J* = 5.8 Hz, 1H, H-4), 6.12 (br s, 1H, H-9), 6.93 (d, *J* = 7.7 Hz, 1H, H-7'), 7.15–7.24 (m, 2H, H-5', H-6), 7.31 (dd, *J* = 8.7, 2.0 Hz, 1H, H-7), 7.43 (t, *J* = 7.6, 1H, H-6'), 7.70

(d, $J = 7.4$ Hz, 1H, H-4'), 10.76 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 90.0 (d, $J = 5.8$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 34.0, 49.7, 56.5, 75.1 (q, $^2J = 31.8$ Hz, C-4), 76.1, 88.3, 110.3, 119.2, 120.0, 122.1 (q, $^1J = 282.7$ Hz, CF_3), 123.2, 125.3, 126.1, 126.8, 129.0, 130.9, 142.7, 142.8, 149.9, 176.3. HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{ClF}_3\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 454.0776, found 454.0779.

(3R*,3aS*,4S*,9bR*)-8-Bromo-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5f). Method A. Yield 310 mg (0.622 mmol, 62%), mp 205–206 °C (decomp.), creamy powder. IR (ATR): 3250, 1715, 1694, 1622, 1561, 1470, 1369, 1333 cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6) δ 1.86 (s, 3H, Me), 2.86 (d, $J = 9.4$ Hz, 1H, H-1a), 4.10 (dd, $J = 9.4, 6.5$ Hz, 1H, H-1b), 4.79 (d, $J = 6.5$ Hz, 1H, H-9b), 5.39 (q, $J = 7.1$ Hz, 1H, H-4), 6.95 (d, $J = 7.8$ Hz, 1H, H-7'), 7.10 (d, $J = 8.7$ Hz, 1H, H-6), 7.15 (t, $J = 7.7$ Hz, 1H, H-5'), 7.42 (td, $J = 7.7, 0.8$ Hz, 1H, H-6'), 7.45 (dd, $J = 8.7, 2.3$ Hz, 1H, H-7), 7.55 (d, $J = 7.6$ Hz, 1H, H-4'), 7.84 (d, $J = 2.3$ Hz, 1H, H-9), 10.81 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 95.7 (d, $J = 7.1$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 34.5, 38.6, 59.7, 73.8 (q, $^2J = 29.9$ Hz, C-4), 80.0, 96.9, 110.5, 115.7, 118.9, 122.6 (q, $^1J = 289.6$ Hz, CF_3), 122.7, 123.5, 127.2, 129.8, 131.1, 131.2 (2C), 143.9, 148.7, 174.6. Anal. Calcd for $\text{C}_{20}\text{H}_{15}\text{BrF}_3\text{N}_3\text{O}_4 \cdot 0.33\text{H}_2\text{O}$: C, 47.64; H, 3.13; N, 8.33. Found: C, 47.88; H, 3.11; N, 8.36.

(3S*,3aS*,4S*,9bR*)-8-Bromo-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'f). This compound was not obtained in a pure form. ^1H NMR (500 MHz, DMSO- d_6) δ 1.97 (s, 3H, Me), 3.26 (t, $J = 8.7$ Hz, 1H, H-1a), 3.90 (t, $J = 8.7$ Hz, 1H, H-1b), 4.84 (t, $J = 8.7$ Hz, 1H, H-9b), 5.72 (q, $J = 7.0$ Hz, 1H, H-4), 6.91 (d, $J = 7.7$ Hz, 1H, H-7'), 6.99 (d, $J = 7.7$ Hz, 1H, H-4'), 7.03 (d, $J = 8.7$ Hz, 1H, H-6), 7.04 (t, $J = 7.7$ Hz, 1H, H-5'), 7.36 (td, $J = 7.7, 1.2$ Hz, 1H, H-6'), 7.45 (dd, $J = 8.7, 2.3$ Hz, 1H, H-7), 7.71 (d, $J = 2.3$ Hz, 1H, H-9), 10.99 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 97.6 (d, $J = 7.0$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 34.0, 41.0, 56.5, 74.2 (q, $^2J = 33.2$ Hz, C-4), 75.3, 98.5, 110.2, 115.5, 118.9, 122.4, 122.8 (q, $^1J = 287.9$ Hz, CF_3), 123.8, 123.9, 124.3, 126.0, 131.0, 142.8, 150.6, 174.0 (one signals is masked).

(1S*,3aS*,4S*,9bR*)-8-Bromo-2-methyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6f). Method B. Yield 259 mg (0.520 mmol, 52%), mp 265–266 °C (decomp.), creamy powder. IR (ATR): 3247, 1710, 1692, 1622, 1557, 1483, 1468, 1413, 1339 cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6) δ 2.08 (s, 3H, Me), 3.67 (d, $J = 12.3$ Hz, 1H, H-3a), 4.45 (d, $J = 12.3$ Hz, 1H, H-3b), 4.60 (s, 1H, H-9b), 5.72 (q, $J = 5.8$ Hz, 1H, H-4), 6.27 (d, $J = 2.4$ Hz, 1H, H-9), 6.93 (d, $J = 7.7$ Hz, 1H, H-7'), 7.12 (d, $J = 8.8$ Hz, 1H, H-6), 7.20 (t, $J = 7.4$ Hz, 1H, H-5'), 7.40–7.46 (m, 2H, H-7, H-6'), 7.69 (d, $J = 7.4$ Hz, 1H, H-4'), 10.76 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 90.0 (d, $J = 5.8$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 33.9, 49.7, 56.5, 75.0 (q, $^2J = 31.9$ Hz, C-4), 76.1, 88.3, 110.2, 114.6, 119.4, 120.4, 122.1 (q, $^1J = 281.8$ Hz, CF_3), 123.2, 125.2, 126.0, 128.5, 130.8, 131.7, 142.7, 150.3, 176.2. Anal. Calcd for $\text{C}_{20}\text{H}_{15}\text{BrF}_3\text{N}_3\text{O}_4$: C, 48.21; H, 3.03; N, 8.43. Found: C, 48.06; H, 3.00; N, 8.15.

(3R*,3aS*,4S*,9bR*)-6,8-Dibromo-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5g). Method A. Yield 353 mg (0.612 mmol, 61%), mp 223–224 °C (decomp.), creamy powder. IR (ATR): 3192, 1712, 1621, 1559, 1471, 1453, 1372, 1330 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.86 (s, 3H, Me), 2.87 (d, *J* = 9.6 Hz, 1H, H-1a), 4.11 (dd, *J* = 9.6, 6.4 Hz, 1H, H-1b), 4.87 (d, *J* = 6.4 Hz, 1H, H-9b), 5.60 (q, *J* = 6.9 Hz, 1H, H-4), 6.96 (d, *J* = 7.8 Hz, 1H, H-7'), 7.16 (t, *J* = 7.7 Hz, 1H, H-5'), 7.44 (t, *J* = 7.5 Hz, 1H, H-6'), 7.51 (d, *J* = 7.5 Hz, 1H, H-4'), 7.83 (d, *J* = 2.1 Hz, 1H, H-7), 7.90 (d, *J* = 2.1 Hz, 1H, H-9), 10.85 (s, 1H, NH). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ 95.5 (d, *J* = 6.9 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.4, 59.5, 74.1 (q, ²*J* = 30.3 Hz, C-4), 79.8, 96.7, 110.5, 111.2, 115.9, 122.3 (q, ¹*J* = 289.3 Hz, CF₃), 122.6, 123.2, 126.8, 130.8, 131.1, 131.2, 133.4, 144.0, 145.7, 174.4 (one signal is masked). HRMS (ESI) calcd for C₂₀H₁₅Br₂F₃N₃O₄ [M+H]⁺ 575.9376, found 575.9378.

(3S*,3aS*,4S*,9bR*)-6,8-Dibromo-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'g). This compound was not obtained in a pure form. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.96 (s, 3H, Me), 3.24 (t, *J* = 8.7 Hz, 1H, H-1a), 3.86 (t, *J* = 8.7 Hz, 1H, H-1b), 4.88 (t, *J* = 8.7 Hz, 1H, H-9b), 6.01 (q, *J* = 7.0 Hz, 1H, H-4), 6.92 (d, *J* = 7.8 Hz, 1H, H-7'), 7.03–7.07 (m, 2H, H-4', H-5'), 7.34–7.70 (m, 1H, H-6'), 7.76 (d, *J* = 2.2 Hz, 1H, H-9), 7.83 (d, *J* = 2.2 Hz, 1H, H-7), 11.06 (s, 1H, NH). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ 97.0 (d, *J* = 7.0 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.0, 40.9, 56.6, 74.0 (q, ²*J* = 32.9 Hz, C-4), 75.2, 98.1, 110.3, 111.4, 115.6, 122.5 (q, ¹*J* = 286.5 Hz, CF₃), 122.3, 123.4, 124.4, 127.8, 130.5, 130.9, 133.5, 142.7, 147.5, 173.8.

(1S*,3aS*,4S*,9bR*)-6,8-Dibromo-2-methyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6g). Method B. Yield 312 mg (0.541 mmol, 54%), mp 282–283 °C (decomp.), creamy powder. IR (ATR): 3209, 1696, 1622, 1553, 1455, 1338 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 2.07 (s, 3H, Me), 3.68 (d, *J* = 12.3 Hz, 1H, H-3a), 4.46 (d, *J* = 12.3 Hz, 1H, H-3b), 4.71 (s, 1H, H-9b), 5.79 (q, *J* = 5.8 Hz, 1H, H-4), 6.26 (s, 1H, H-9), 6.93 (d, *J* = 7.6 Hz, 1H, H-7'), 7.21 (t, *J* = 7.5 Hz, 1H, 6'), 7.44 (t, *J* = 7.5 Hz, 1H, 5'), 7.71 (d, *J* = 7.4 Hz, 1H, H-4'), 7.85 (s, 1H, H-7), 10.79 (s, 1H, NH). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ 90.0 (d, *J* = 5.8 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.0, 49.8, 56.3, 75.4 (q, ²*J* = 32.2 Hz, C-4), 76.1, 88.1, 110.2, 111.9, 114.7, 121.8, 121.9 (q, ¹*J* = 281.8 Hz, CF₃), 123.2, 125.4, 125.8, 128.0, 130.9, 134.3, 142.6, 147.2, 176.1. HRMS (ESI) calcd for C₂₀H₁₅Br₂F₃N₃O₄ [M+H]⁺ 575.9376, found 575.9361.

(3R*,3aS*,4S*,9bR*)-8-Bromo-6-ethoxy-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5h). Method A. Yield 239 mg (0.441 mmol, 44%), mp 201–202 °C (decomp.), light-yellow powder. IR (ATR): 3086, 1711, 1622, 1557, 1472, 1424, 1374, 1331 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.35 (t, *J* = 6.9 Hz, 3H, Me), 1.85 (s, 3H, Me), 2.82 (d, *J* = 9.4 Hz, 1H, H-3a), 4.02–4.20 (m, 3H, H-1b, OCH₂), 4.75 (d, *J* = 6.4 Hz, 1H, H-9b), 5.43 (q, *J* = 7.0 Hz, 1H, H-4), 6.94 (d, *J* = 7.7 Hz, 1H, H-7'), 7.14 (d, *J* = 1.9 Hz, 1H, H-7), 7.16 (t, *J* = 7.7 Hz,

1H, H-5'), 7.34 (d, $J = 1.9$ Hz, 1H, H-9), 7.42 (t, $J = 7.7$ Hz, 1H, H-6'), 7.52 (d, $J = 7.6$ Hz, 1H, H-4'), 10.80 (s, 1H, NH). ^{19}F NMR (376 MHz, DMSO- d_6) δ 95.9 (d, $J = 7.0$ Hz, CF₃). ^{13}C NMR (126 MHz, DMSO- d_6) δ 14.5, 34.4, 38.6, 59.5, 64.6, 73.8 (q, $^2J = 30.0$ Hz, C-4), 79.9, 97.0, 110.4, 114.8, 115.4, 122.1, 122.5 (q, $^1J = 289.8$ Hz, CF₃), 122.6, 123.5, 127.1, 130.3, 131.1, 138.3, 144.0, 148.3, 174.5. Anal. Calcd for C₂₂H₁₉BrF₃N₃O₅: C, 48.73; H, 3.53; N, 7.75. Found: C, 48.87; H, 3.67; N, 7.81.

(3S*,3aS*,4S*,9bR*)-8-Bromo-6-ethoxy-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'h). This compound was not obtained in a pure form. ^1H NMR (400 MHz, DMSO- d_6) δ 1.30 (t, $J = 6.9$ Hz, 3H, Me), 1.86 (s, 3H, Me), 3.24 (t, $J = 8.5$ Hz, 1H, H-1a), 3.87 (t, $J = 8.5$ Hz, 1H, H-1b), 4.78 (t, $J = 8.5$ Hz, 1H, H-9b), 5.70 (q, $J = 6.8$ Hz, 1H, H-4), 6.92 (d, $J = 7.7$ Hz, 1H, H-7'), 7.00 (d, $J = 7.6$ Hz, 1H, H-4'), 7.05 (td, $J = 7.7, 0.9$ Hz, 1H, H-5'), 7.15 (d, $J = 1.9$ Hz, 1H, H-7), 7.25 (d, $J = 1.9$ Hz, 1H, H-9), 7.37 (td, $J = 7.7, 1.1$ Hz, 1H, H-6'), 10.99 (s, 1H, NH) (signals of OCH₂ are masked). ^{19}F NMR (376 MHz, DMSO- d_6) δ 97.4 (d, $J = 6.7$ Hz, CF₃). 14.4, 34.0, 41.0, 56.5, 64.8, 74.2 (q, $^2J = 32.3$ Hz, C-4), 75.3, 98.7, 110.2, 115.3, 115.5, 122.0, 122.4, 122.7 (q, $^1J = 284.2$ Hz, CF₃), 123.8, 124.3, 126.6, 131.0, 140.4, 142.7, 148.3, 174.0.

(1S*,3aS*,4S*,9bR*)-8-Bromo-6-ethoxy-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6h). Method B. Yield 337 mg (0.622 mmol, 62%), mp 252–253 °C (decomp.), creamy powder. IR (ATR): 3200, 1695, 1623, 1554, 1471, 1427, 1396, 1372, 1339 cm⁻¹. ^1H NMR (400 MHz, DMSO- d_6) δ 1.31 (t, $J = 6.9$ Hz, 3H, Me), 2.06 (s, 3H, Me), 3.66 (d, $J = 12.3$ Hz, 1H, H-3a), 3.99–4.13 (m, 2H, OCH₂), 4.44 (d, $J = 12.3$ Hz, 1H, H-3b), 4.55 (s, 1H, H-9b), 5.64 (q, $J = 5.8$ Hz, 1H, H-4), 5.85 (d, $J = 1.8$ Hz, 1H, H-9), 6.92 (d, $J = 7.7$ Hz, 1H, H-7'), 7.11 (d, $J = 1.8$ Hz, 1H, H-7), 7.19 (t, $J = 7.6$ Hz, 1H, 5'), 7.42 (t, $J = 7.6$ Hz, 1H, 6'), 7.68 (d, $J = 7.6$ Hz, 1H, H-4'), 10.74 (s, 1H, NH). ^{19}F NMR (376 MHz, DMSO- d_6) δ 90.1 (d, $J = 5.8$ Hz, CF₃). ^{13}C NMR (126 MHz, DMSO- d_6) δ 14.3, 33.9, 49.7, 56.5, 64.7, 75.1 (q, $^2J = 32.1$ Hz, C-4), 76.1, 88.5, 110.2, 114.4, 115.5, 119.3, 120.7, 122.2 (q, $^1J = 281.9$ Hz, CF₃), 123.1, 125.2, 126.2, 130.8, 140.3, 142.8, 148.4, 176.2. Anal. Calcd for C₂₂H₁₉BrF₃N₃O₅: C, 48.73; H, 3.53; N, 7.75. Found: C, 48.46; H, 3.56; N, 7.38.

(3R*,3aS*,4S*,9bR*)-2-Methyl-3a,8-dinitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5i). Method A. Yield 312 mg (0.672 mmol, 67%), mp 218–219 °C (decomp.), white powder. IR (ATR): 3414, 1722, 1623, 1591, 1562, 1527, 1485, 1467, 1380, 1348, 1323 cm⁻¹. ^1H NMR (500 MHz, DMSO- d_6) δ 1.85 (s, 3H, Me), 2.92 (d, $J = 9.5$ Hz, 1H, H-1a), 4.15 (dd, $J = 9.5, 6.2$ Hz, 1H, H-1b), 4.98 (d, $J = 6.2$ Hz, 1H, H-9b), 5.62 (q, $J = 6.9$ Hz, 1H, H-4), 6.96 (d, $J = 7.6$ Hz, 1H, H-7'), 7.16 (t, $J = 7.6$ Hz, 1H, H-5'), 7.40 (d, $J = 9.0$ Hz, 1H, H-6), 7.44 (t, $J = 7.6, 1.1$ Hz, 1H, H-6'), 7.52 (d, $J = 7.6$ Hz, 1H, H-4'), 8.17 (dd, $J = 9.0, 2.3$ Hz, 1H, H-7), 8.62 (d, $J = 2.3$ Hz, 1H, H-9), 10.85 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 95.4 (d, $J = 6.9$ Hz, CF₃). ^{13}C NMR (126 MHz, DMSO- d_6) δ 34.4, 38.7, 59.6, 73.7 (q, $^2J = 30.1$ Hz, C-4), 79.8, 96.4, 110.5, 117.7, 122.5 (q,

$^1J = 289.4$ Hz, CF₃), 122.6, 123.3, 124.0, 124.8, 127.1, 128.5, 131.2, 143.6, 144.0, 154.2, 174.5. HRMS (ESI) calcd for C₂₀H₁₆F₃N₄O₆ [M+H]⁺ 465.1016, found 465.1014.

(3S*,3aS*,4S*,9bR*)-2-Methyl-3a,8-dinitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-

spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'i). This compound was not obtained in a pure form. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.97 (s, 3H, Me), 3.27 (t, $J = 8.6$ Hz, 1H, H-1a), 3.97 (t, $J = 8.6$ Hz, 1H, H-1b), 4.96 (t, $J = 8.6$ Hz, 1H, H-9b), 5.99 (q, $J = 6.8$ Hz, 1H, H-4), 6.94 (d, $J = 7.7$ Hz, 1H, H-7'), 6.97 (d, $J = 7.7$ Hz, 1H, H-4'), 7.06 (t, $J = 7.7$ Hz, 1H, H-5'), 7.30 (d, 1H, $J = 9.0$ Hz, H-6), 7.37 (t, $J = 7.7$ Hz, 1H, H-6'), 8.16 (dd, $J = 9.0, 2.7$ Hz, 1H, H-7), 8.46 (d, $J = 2.7$ Hz, 1H, H-9), 11.01 (s, 1H, NH). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ 97.5 (d, $J = 6.8$ Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.0, 40.4, 56.8, 73.7 (q, $^2J = 32.7$ Hz, C-4), 75.3, 97.3, 110.3, 117.9, 122.3, 122.6 (q, $^1J = 285.7$ Hz, CF₃), 123.5, 124.2, 124.4, 124.6, 125.7, 130.9, 142.8, 143.2, 155.7, 173.9.

(1S*,3aS*,4S*,9bR*)-2-Methyl-3a,8-dinitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-

spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6i). Method B. Yield 319 mg (0.688 mmol, 69%), mp 252–253 °C (decomp.), white powder. IR (ATR): 3211, 1695, 1620, 1588, 1557, 1539, 1486, 1473, 1464, 1394, 1372, 1323 cm⁻¹. ¹H NMR (500 MHz, DMSO-*d*₆) δ 2.10 (s, 3H, Me), 3.71 (d, $J = 12.2$ Hz, 1H, H-3a), 4.50 (d, $J = 12.2$ Hz, 1H, H-3b), 4.77 (s, 1H, H-9b), 5.90 (q, $J = 5.8$ Hz, 1H, H-4), 6.93 (d, $J = 7.7$ Hz, 1H, H-7'), 7.10 (d, $J = 2.7$ Hz, 1H, H-9), 7.24 (t, $J = 7.7$ Hz, 1H, H-5'), 7.42 (d, $J = 9.0$ Hz, 1H, H-6), 7.46 (td, $J = 7.7, 1.0$ Hz, 1H, H-6'), 7.76 (d, $J = 7.7$ Hz, 1H, H-4'), 8.13 (dd, $J = 9.0, 2.7$ Hz, 1H, H-7), 10.74 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 90.1 (d, $J = 5.8$ Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.1, 49.6, 56.5, 75.3 (q, $^2J = 32.2$ Hz, C-4), 76.2, 87.7, 110.5, 118.7, 119.0, 122.0 (q, $^1J = 282.0$ Hz, CF₃), 122.2, 123.4, 124.8, 125.5, 125.7, 131.0, 142.4, 142.6, 155.7, 176.3. HRMS (ESI) calcd for C₂₀H₁₆F₃N₄O₆ [M+H]⁺ 465.1016, found 465.1021.

(3R*,3aS*,4S*,9bR*)-2-Methyl-3a-nitro-4-phenyl-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-

c]pyrrole-3,3'-indolin]-2'-one (5j). Method A. Yield 128 mg (0.299 mmol, 30%), mp 185–186 °C (decomp.), light-yellow powder. IR (ATR): 3238, 1714, 1612, 1543, 1489, 1469, 1454, 1364, 1324 cm⁻¹. ¹H NMR (500 MHz, DMSO-*d*₆) δ 1.90 (s, 3H, Me), 2.96 (d, $J = 8.9$ Hz, 1H, H-1a), 4.14 (dd, $J = 8.9, 6.8$ Hz, 1H, H-1b), 4.98 (d, $J = 6.8$ Hz, 1H, H-9b), 5.55 (s, 1H, H-4), 6.77 (d, $J = 7.8$ Hz, 1H, H-6), 6.94 (d, $J = 7.6$ Hz, 1H, H-7'), 7.00 (d, $J = 7.8$ Hz, 2H, H_o Ph), 7.06–7.20 (m, 4H, Ar, Ph), 7.24 (t, $J = 7.6$ Hz, 1H, H-5'), 7.43 (t, $J = 7.6$ Hz, 1H, H-6'), 7.58 (d, $J = 7.2$ Hz, 1H, Ar), 7.70 (d, $J = 7.6$ Hz, 1H, H-4'), 10.66 (s, 1H, NH). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.7, 38.5, 60.1, 79.0, 80.1, 100.0, 110.2, 117.4, 122.2, 122.9, 124.5, 127.5, 127.9, 128.0, 128.2 (2C), 128.5 (2C), 128.6, 129.4, 130.7, 143.7, 144.0, 150.2, 175.3. HRMS (ESI) calcd for C₂₅H₂₂N₃O₄ [M+H]⁺ 428.1605, found 428.1611.

(3S*,3aS*,4S*,9bR*)-2-Methyl-3a-nitro-4-phenyl-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-

c]pyrrole-3,3'-indolin]-2'-one (5'j). Yield 85 mg (0.199 mmol, 20%), mp 229–230 °C (decomp.), white powder. IR (ATR): 3271, 1715, 1620, 1556, 1491, 1473, 1458, 1376, 1354, 1330 cm⁻¹. ¹H NMR (500

MHz, DMSO-*d*₆) δ 1.99 (s, 3H, Me), 3.98 (t, $J = 9.2$ Hz, 1H, H-1b), 4.96 (dd, $J = 9.5, 5.7$ Hz, 1H, H-9b), 5.86 (s, 1H, H-4), 6.62 (d, $J = 7.9$ Hz, 1H, H-6), 6.89 (d, $J = 7.7$ Hz, 1H, H-7'), 6.94–7.36 (m, 9H, Ar, Ph), 7.41 (d, $J = 7.6$ Hz, 1H, H-4'), 10.68 (s, 1H, NH) (H-1a proton is masked by H₂O). ¹H NMR (500 MHz, CDCl₃) δ 2.23 (s, 3H, Me), 3.70 (dd, $J = 8.9, 5.7$ Hz, 1H, H-1a), 4.25 (t, $J = 8.9$ Hz, 1H, H-1b), 4.97 (dd, $J = 8.9, 5.7$ Hz, 1H, H-9b), 5.60 (s, 1H, H-4), 6.65 (d, $J = 7.9$ Hz, 1H, H-6), 6.84 (d, $J = 7.7$ Hz, 1H, H-7'), 7.01–7.38 (m, 11H, Ar, Ph), 7.86 (s, 1H, NH). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.4, 59.1, 75.4, 76.9, 101.0, 109.9, 117.4, 121.6, 122.4, 123.7, 124.9, 126.9, 127.7 (2C), 127.8, 128.1, 128.2 (2C), 128.5, 130.7, 136.7, 143.2, 150.3, 174.3 (one signal is masked). HRMS (ESI) calcd for C₂₅H₂₂N₃O₄ [M+H]⁺ 428.1605, found 428.1600.

(1S*,3aS*,4S*,9bR*)-2-Methyl-3a-nitro-4-phenyl-1,3a,4,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6j). Method B. Yield 200 mg (0.468 mmol, 47%), mp 264–265 °C, creamy powder. IR (ATR): 3260, 1714, 1618, 1590, 1547, 1490, 1473, 1456, 1359, 1327 cm⁻¹. ¹H NMR (500 MHz, DMSO-*d*₆) δ 2.06 (s, 3H, Me), 3.80 (d, $J = 7.1$ Hz, 1H, H-3a), 3.96 (d, $J = 7.1$ Hz, 1H, H-3b), 4.39 (s, 1H, H-9b), 5.94 (s, 1H, H-4), 6.28 (d, $J = 8.2$ Hz, 1H, H-9), 6.79 (t, $J = 7.7$ Hz, 1H, H-8), 6.92 (d, $J = 7.8$ Hz, 1H, H-7'), 7.00 (d, $J = 7.8$ Hz, 1H, H-6), 7.13–7.20 (m, 2H, H-5', H-7), 7.32–7.37 (m, 2H, Ph), 7.40 (t, $J = 7.7$ Hz, 1H, H-6'), 6.43–7.50 (m, 3H, Ph), 7.61 (d, $J = 7.3$ Hz, 1H, H-4'), 10.60 (s, 1H, NH); ¹³C NMR (126 MHz, DMSO-*d*₆): δ 34.0, 50.2, 56.9, 76.3, 78.6, 94.8, 110.0, 117.3, 119.0, 122.1, 122.8, 124.7, 125.7, 126.5 (2C), 127.5, 128.4, 128.6 (2C), 129.3, 130.3, 134.2, 142.9, 153.6, 176.3. HRMS (ESI) calcd for C₂₅H₂₂N₃O₄ [M+H]⁺ 428.1605, found 428.1613.

(3R*,3aS*,4S*,9bR*)-1',2-Dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5k). Method A. Yield 122 mg (0.282 mmol, 28%), mp 167–168 °C (decomp.), creamy powder. IR (ATR): 1703, 1611, 1555, 1492, 1470, 1371, 1339 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.80 (s, 3H, Me), 2.87 (d, $J = 9.2$ Hz, 1H, H-1a), 3.11 (s, 3H, Me), 4.14 (dd, $J = 9.2, 6.4$ Hz, 1H, H-1b), 4.78 (d, $J = 6.4$ Hz, 1H, H-9b), 5.31 (q, $J = 7.1$ Hz, 1H, H-4), 7.11 (d, $J = 8.0$ Hz, 1H, H-6), 7.14–7.57 (m, 6H, Ar), 7.63 (d, $J = 7.5$ Hz, 1H, H-4'). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ 95.8 (d, CF₃, $J = 7.1$ Hz). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 25.7, 34.4, 38.6, 59.9, 73.7 (q, ² $J = 29.8$ Hz, C-4), 79.7, 97.5, 109.4, 116.5, 122.7 (q, ¹ $J = 289.8$ Hz, CF₃), 122.9, 123.2, 124.1, 126.8, 126.9, 128.1, 128.6, 131.2, 145.2, 149.1, 173.0. Anal. Calcd for C₂₁H₁₈F₃N₃O₄: C, 58.20; H, 4.19; N, 9.70. Found: C, 58.11; H, 4.08; N, 9.44.

(3S*,3aS*,4S*,9bR*)-1',2-Dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'k). This compound was not obtained in a pure form. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.93 (s, 3H, Me), 3.15 (s, 3H, Me), 3.29 (t, $J = 8.7$ Hz, 1H, H-1a), 3.93 (t, $J = 8.7$ Hz, 1H, H-1b), 4.86 (t, $J = 8.7$ Hz, 1H, H-9b), 5.57 (q, $J = 7.0$ Hz, 1H, H-4), 6.96 (d, $J = 7.7$ Hz, 1H, H-7'), 7.00 (d, $J = 7.7$ Hz, 1H, H-4'), 7.03 (t, $J = 7.7, 1.0$ Hz, 1H, H-5'), 7.07 (d, $J = 8.0$ Hz,

1H, H-6), 7.14–7.21 (m, 1H, H-8), 7.23–7.31 (m, 1H, H-7), 7.36 (t, $J = 7.7$ Hz, 1H, H-6'), 7.47 (d, $J = 7.7$, 1H, H-9). ^{19}F NMR (471 MHz, DMSO- d_6) δ 97.0 (d, $J = 7.0$ Hz, CF₃).

(1S*,3aS*,4S*,9bR*)-1',2-Dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6k). Method B. Yield 238 mg (0.550 mmol, 55%), mp 220–221 °C (decomp.), creamy powder. IR (ATR): 1703, 1612, 1555, 1492, 1471, 1371, 1340 cm⁻¹. ^1H NMR (500 MHz, DMSO- d_6) δ 2.01 (s, 3H, Me), 2.93 (s, 3H, Me), 3.70 (d, $J = 12.2$ Hz, 1H, H-3a), 4.46 (d, $J = 12.2$ Hz, 1H, H-3b), 4.58 (s, 1H, H-9b), 5.69 (q, $J = 5.7$ Hz, 1H, H-4), 6.13 (d, $J = 7.8$ Hz, 1H, H-9), 6.80 (t, $J = 7.6$ Hz, 1H, H-8), 7.10 (d, $J = 7.8$ Hz, 1H, H-7'), 7.14 (d, $J = 7.8$ Hz, 1H, H-6), 7.22 (t, $J = 7.5$ Hz, 1H, H-5'), 7.27 (t, $J = 7.6$ Hz, 1H, H-7), 7.52 (t, $J = 7.7$ Hz, 1H, H-6'), 7.74 (d, $J = 7.4$ Hz, 1H, H-4'). ^{19}F NMR (471 MHz, DMSO- d_6) δ 90.0 (d, $J = 5.7$ Hz, CF₃). ^{13}C NMR (126 MHz, DMSO- d_6) δ 25.5, 34.9, 50.1, 56.7, 75.1 (q, $^2J = 32.0$ Hz, C-4), 75.9, 89.1, 109.3, 117.3, 117.9, 122.3 (q, $^1J = 282.4$ Hz, CF₃), 123.2, 123.8, 124.7, 125.6, 125.9, 129.0, 130.8, 144.2, 151.1, 174.3. HRMS (ESI) calcd for C₂₀H₁₉F₃N₃O₄ [M+H]⁺ 434.1322, found 434.1317.

(3R*,3aS*,4S*,9bR*)-8-Chloro-1',2-dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5I). Method A. Yield 202 mg (0.432 mmol, 43%), mp 197–198 °C (decomp.), white powder. IR (ATR): 1702, 1611, 1564, 1470, 1371, 1351 cm⁻¹. ^1H NMR (500 MHz, DMSO- d_6) δ 1.80 (s, 3H, Me), 2.89 (d, $J = 9.4$ Hz, 1H, H-1a), 3.10 (s, 3H, Me), 4.13 (dd, $J = 9.4, 6.7$ Hz, 1H, H-1b), 4.81 (d, $J = 6.7$ Hz, 1H, H-9b), 5.38 (q, $J = 7.0$ Hz, 1H, H-4), 7.16 (d, $J = 8.7$ Hz, 1H, H-6), 7.19 (t, $J = 7.6$ Hz, 1H, H-7'), 7.24 (t, $J = 7.6$ Hz, 1H, H-5'), 7.33 (dd, $J = 8.7, 2.2$ Hz, 1H, H-7), 7.54 (t, $J = 7.6$ Hz, 1H, H-6'), 7.60 (d, $J = 7.6$ Hz, 1H, H-4') 7.72 (d, $J = 2.2$ Hz, 1H, H-9). ^{19}F NMR (471 MHz, DMSO- d_6) δ 95.7 (d, CF₃, $J = 7.0$ Hz). ^{13}C NMR (126 MHz, DMSO- d_6) δ 25.8, 34.4, 38.7, 59.8, 73.7 (q, $^2J = 29.6$ Hz, C-4), 79.7, 97.1, 109.5, 118.4, 122.6 (q, $^1J = 289.7$ Hz, CF₃), 122.7, 123.3, 126.8, 127.8, 128.2, 128.3, 129.3, 131.3, 145.3, 148.1, 172.9. HRMS (ESI) calcd for C₂₁H₁₈ClF₃N₃O₄ [M+H]⁺ 468.0932, found 468.0933.

(3S*,3aS*,4S*,9bR*)-8-Chloro-1',2-dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'1). This compound was not obtained in a pure form. ^1H NMR (500 MHz, DMSO- d_6) δ 1.92 (s, 3H, Me), 3.14 (s, 3H, Me), 3.29 (t, $J = 8.6$ Hz, 1H, H-1a), 3.93 (t, $J = 8.6$ Hz, 1H, H-1b), 4.85 (t, $J = 8.6$ Hz, 1H, H-9b), 5.67 (q, $J = 6.7$ Hz, 1H, H-4), 7.03 (d, $J = 7.6$ Hz, 1H, H-7'), 7.10 (d, $J = 8.7$ Hz, 1H, H-6), 7.12–20 (m, 2H, H-4', H-5'), 7.33 (dd, $J = 8.7, 2.2$ Hz, 1H, H-7), 7.47 (t, $J = 7.6$ Hz, 1H, H-6'), 7.60 (d, $J = 2.2$ Hz, 1H, H-9). ^{19}F NMR (471 MHz, DMSO- d_6) δ 97.3 (d, $J = 6.7$ Hz, CF₃).

(1S*,3aS*,4S*,9bR*)-8-Chloro-1',2-dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6I). Method B. Yield 169 mg (0.361 mmol, 36%), mp 269–270 °C (decomp.), white powder. IR (ATR): 1704, 1610, 1545, 1467, 1373, 1336 cm⁻¹. ^1H NMR (400 MHz, DMSO- d_6) δ 2.03 (s, 3H, Me), 2.95 (s, 3H, Me), 3.69 (d, $J = 12.2$ Hz, 1H, H-3a), 4.47 (d, $J =$

12.2 Hz, 1H, H-3b), 4.65 (s, 1H, H-9b), 5.72 (q, $J = 5.7$ Hz, 1H, H-4), 6.03 (s, 1H, H-9), 7.14–7.33 (m, 4H, H-6, H-7, H-5', H-7'), 7.55 (t, $J = 7.5$ Hz, 1H, H-6'), 7.76 (d, $J = 7.5$ Hz, 1H, H-4'). ^{19}F NMR (376 MHz, DMSO- d_6) δ 90.0 (d, $J = 5.7$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 25.5, 33.8, 49.8, 75.1 (q, $^2J = 31.1$ Hz, C-4), 75.8, 88.3, 99.4, 109.2, 119.1, 119.7, 122.0 (q, $^1J = 281.7$ Hz, CF_3), 123.8, 124.8, 125.2, 125.3, 126.7, 128.9, 130.9, 144.1, 149.8, 173.2. HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{18}\text{ClF}_3\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 468.0932, found 468.0932.

(3R*,3aS*,4S*,9bR*)-2,5'-Dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5m). Method A. Yield 182 mg (0.420 mmol, 42%), mp 164–165 °C (decomp.), white powder. IR (ATR): 3242, 1707, 1624, 1560, 1492, 1474, 1458, 1363, 1340 cm^{-1} . ^1H NMR (400 MHz, DMSO- d_6) δ 1.85 (s, 3H, Me), 2.33 (s, 3H, Me), 2.82 (d, $J = 9.1$ Hz, 1H, H-1a), 4.12 (dd, $J = 9.1, 6.6$ Hz, 1H, H-1b), 4.74 (d, $J = 6.6$ Hz, 1H, H-9b), 5.36 (q, $J = 7.1$ Hz, 1H, H-4), 6.84 (d, $J = 7.8$ Hz, 1H, H-7'), 7.12 (d, $J = 8.0$ Hz, 1H, H-6), 7.16 (t, $J = 7.7$ Hz, 1H, H-8), 7.23 (d, $J = 7.8$ Hz, 1H, H-6'), 7.27 (t, $J = 7.8$ Hz, 1H, H-7), 7.40 (s, 1H, H-4'), 7.53 (dd, $J = 7.7$ Hz, 1H, H-9). 10.68 (s, 1H, NH). ^{19}F NMR (376 MHz, DMSO- d_6) δ 95.9 (d, $J = 7.1$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 20.9, 34.5, 38.6, 59.8, 73.8 (q, $^2J = 29.7$ Hz, C-4), 80.0, 97.2, 110.4, 116.5, 122.7 (q, $^1J = 290.3$ Hz, CF_3), 123.6, 124.0, 127.1, 127.7, 128.0, 128.5, 131.2, 131.3, 141.5, 149.2, 174.5. HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{F}_3\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 434.1322, Found: 434.1320.

(3S*,3aS*,4S*,9bR*)-2,5'-Dimethyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'm). This compound was not obtained in a pure form. ^1H NMR (400 MHz, DMSO- d_6) δ 1.98 (s, 3H, Me), 2.25 (s, 3H, Me), 3.29 (t, $J = 8.7$ Hz, 1H, H-1a), 3.89 (t, $J = 8.7$ Hz, 1H, H-1b), 4.84 (t, $J = 8.7$ Hz, 1H, H-9b), 5.62 (q, $J = 6.8$ Hz, 1H, H-4), 6.80 (d, $J = 7.8$ Hz, 1H, H-7'), 6.81 (s, 1H, H-4'), 7.07 (d, $J = 8.0$ Hz, 1H, H-6), 7.13–7.32 (m, 3H, H-7, H-8, H-6'), 7.46 (d, $J = 7.7$ Hz, 1H, H-9), 10.91 (s, 1H, NH). ^{19}F NMR (376 MHz, DMSO- d_6) δ 97.4 (d, $J = 6.8$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 20.6, 33.9, 41.8, 56.2, 74.7 (q, $^2J = 32.9$ Hz, C-4), 75.2, 99.3, 109.9, 116.5, 123.1 (q, $^1J = 285.3$ Hz, CF_3), 123.0, 124.4, 124.5, 128.3, 128.4, 128.6, 131.1, 131.4, 140.2, 151.7, 174.1.

(1S*,3aS*,4S*,9bR*)-2,5'-Dimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6m). Method B. Yield 214 mg (0.494 mmol, 49%), mp 285–286 °C (decomp.), white powder. IR (ATR): 3194, 1687, 1627, 1552, 1492, 1469, 1458, 1414, 1395, 1336 cm^{-1} . ^1H NMR (400 MHz, DMSO- d_6) δ 2.06 (s, 3H, Me), 2.33 (s, 3H, Me), 3.67 (d, $J = 12.3$ Hz, 1H, H-3a), 4.43 (d, $J = 12.3$ Hz, 1H, H-3b), 4.49 (s, 1H, H-9b), 5.67 (q, $J = 5.9$ Hz, 1H, H-4), 6.25 (d, $J = 7.7$ Hz, 1H, H-9), 6.79 (d, $J = 7.9$ Hz, 1H, H-7'), 6.85 (t, $J = 7.6$ Hz, 1H, H-8), 7.10 (d, $J = 7.8$ Hz, 1H, H-6), 7.20 (d, $J = 7.9$ Hz, 1H, H-6'), 7.22 (t, $J = 7.6$ Hz, 1H, H-7), 7.52 (s, 1H, H-4'), 10.56 (s, 1H, NH). ^{19}F NMR (376 MHz, DMSO- d_6) δ 90.0 (d, $J = 5.9$ Hz, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 20.6, 33.9, 50.2, 56.7, 75.1 (q, $^2J = 31.7$ Hz, C-4), 76.1, 89.1, 109.9, 117.1, 118.1, 122.3 (q, $^1J = 281.9$ Hz,

CF₃), 123.2, 125.5, 125.9, 126.7, 128.9, 130.8, 132.1, 140.3, 151.1, 176.2. HRMS (ESI) calcd for C₂₁H₁₉F₃N₃O₄ [M+H]⁺ 434.1322, found 434.1322.

(3R*,3aS*,4S*,9bR*)-5',8-Dichloro-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5n). Method A Yield 234 mg (0.480 mmol, 48%), mp 195–196 °C (decomp.), white powder. IR (ATR): 3169, 3113, 1710, 1620, 1562, 1475, 1448, 1375, 1357 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.87 (s, 3H, Me), 2.90 (d, *J* = 9.4 Hz, 1H, H-1a), 4.11 (dd, *J* = 9.4, 6.5 Hz, 1H, H-1b), 4.77 (d, *J* = 6.5 Hz, 1H, H-9b), 5.62 (q, *J* = 7.0 Hz, 1H, H-4), 6.96 (d, *J* = 8.9 Hz, 1H, H-7'), 7.18 (d, *J* = 8.7 Hz, 1H, H-6), 7.32 (dd, *J* = 8.7, 2.4 Hz, 1H, H-7), 7.46–7.51 (m, 2H, H-4', H-6'), 7.71 (d, *J* = 2.4 Hz, 1H, H-9), 10.96 (s, 1H, NH). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ 95.7 (d, *J* = 7.0 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.4, 38.6, 59.6, 73.5 (q, ²*J* = 29.8 Hz, C-4), 79.8, 97.1, 111.8, 118.3, 122.6 (q, ¹*J* = 289.6 Hz, CF₃), 125.4, 126.5, 127.2, 127.8, 128.1, 128.2, 129.1, 131.0, 142.9, 148.1, 174.3. HRMS (ESI) calcd for C₂₀H₁₅Cl₂F₃N₃O₄ [M+H]⁺ 488.0386, found 488.0380.

(3S*,3aS*,4S*,9bR*)-5',8-Dichloro-2-methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,9b-tetrahydro-2H-spiro[chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5'n). This compound was not obtained in a pure form. ¹H NMR (400 MHz, DMSO-*d*₆) δ 2.00 (s, 3H, Me), 3.25 (t, *J* = 8.7 Hz, 1H, H-1a), 3.89 (t, *J* = 8.7 Hz, 1H, H-1b), 4.85 (t, *J* = 8.7 Hz, 1H, H-9b), 5.81 (q, *J* = 6.8 Hz, 1H, H-4), 6.95 (d, *J* = 8.9 Hz, 1H, H-7'), 7.02 (d, *J* = 2.1 Hz, 1H, H-4'), 7.10 (d, *J* = 8.8 Hz, 1H, H-6), 7.37 (dd, *J* = 8.8, 2.4 Hz), 7.42 (dd, *J* = 8.9, 2.1 Hz, 1H, H-6'), 7.60 (d, *J* = 2.4 Hz, 1H, H-9), 10.90 (s, 1H, NH). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ 97.3 (d, *J* = 6.8 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.0, 40.9, 56.6, 73.8 (q, ²*J* = 32.6 Hz, C-4), 75.2, 98.3, 111.7, 118.5, 122.7 (q, ¹*J* = 285.9 Hz, CF₃), 124.2, 125.4, 125.8, 126.4, 127.6, 128.3, 130.9, 141.7, 149.9, 173.6 (one signal is masked).

(1S*,3aS*,4S*,9bR*)-5',8-Dichloro-2-methyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6n). Method B. Yield 201 mg (0.412 mmol, 41%), mp 269–270 °C (decomp.), white powder. IR (ATR): 3190, 1695, 1624, 1557, 1483, 1446, 1337 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 2.08 (s, 3H, Me), 3.64 (d, *J* = 12.3 Hz, 1H, H-3a), 4.45 (d, *J* = 12.3 Hz, 1H, H-3b), 4.77 (s, 1H, H-9b), 5.66 (q, *J* = 5.8 Hz, 1H, H-4), 6.17 (d, *J* = 2.2 Hz, 1H, H-9), 6.94 (d, *J* = 8.3 Hz, 1H, H-7'), 7.20 (d, *J* = 8.8 Hz, 1H, H-6), 7.32 (dd, *J* = 8.8, 2.2 Hz, 1H, H-7), 7.49 (dd, *J* = 8.3, 2.2 Hz, 1H, H-6'), 7.90 (d, *J* = 2.2 Hz, 1H, H-4'), 10.89 (s, 1H, NH). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ 90.0 (d, *J* = 5.8 Hz, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 34.0, 49.2, 56.5, 75.0 (q, ²*J* = 32.0 Hz, C-4), 76.2, 88.0, 111.7, 119.2, 119.9, 122.1 (q, ¹*J* = 281.9 Hz, CF₃), 125.4, 125.9, 126.7, 127.3, 128.3, 129.0, 130.7, 141.6, 149.9, 176.0. HRMS (ESI) calcd for C₂₀H₁₅Cl₂F₃N₃O₄ [M+H]⁺ 488.0386, found 488.0389.

(1S*,3aS*,4S*,9bR*)-1'-Benzyl-2-methyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6o). Method B. Yield 183 mg (0.359 mmol, 36%), mp 178–179 °C (decomp.), white powder. IR (ATR): 1698, 1610, 1558, 1486, 1464, 1367, 1345 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 2.05 (s, 3H, Me), 3.73 (d, *J* = 12.2 Hz, 1H, H-3a), 4.51 (d, *J* = 12.2 Hz,

1H, H-3b), 4.62 (d, $J = 15.8$ Hz, 1H, CHHP), 4.67 (s, 1H, H-9b), 4.82 (d, $J = 15.8$ Hz, 1H, CHHP), 5.80 (q, $J = 5.8$ Hz, 1H, H-4), 6.14 (d, $J = 7.8$, 1H, H-9), 6.77 (t, $J = 7.5$ Hz, 1H, H-8), 6.89 (d, $J = 6.8$ Hz, 2H, Ph), 6.96 (d, $J = 7.8$ Hz, 1H, H-7'), 7.12–7.22 (m, 4H, H-6, Ph), 7.24 (t, $J = 7.4$ Hz, 1H, H-5'), 7.28 (t, $J = 7.6$ Hz, 1H, H-7), 7.41 (dt, $J = 7.8, 1.0$ Hz, 1H, H-6'), 7.79 (d, $J = 7.3$ Hz, 1H, H-4'). ^{19}F NMR (376 MHz, DMSO- d_6) δ 90.0 (d, $J = 5.8$ Hz, CF₃). ^{13}C NMR (126 MHz, DMSO- d_6) δ 33.9, 42.4, 50.1, 56.7, 75.0 (q, $^2J = 31.7$ Hz, C-4), 75.9, 88.6, 109.9, 117.2, 117.4, 122.3 (q, $^1J = 282.2$ Hz, CF₃), 123.3, 123.8, 125.0, 125.8, 126.0, 126.8 (2C), 127.3, 128.4 (2C), 129.1, 130.6, 135.3, 143.3, 151.0, 174.5. HRMS (ESI) calcd for C₂₇H₂₃F₃N₃O₄ [M+H]⁺ 510.1635, found 510.1628.

(3R*,3aS*,4*S,11cR*)-2-Methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,11c-tetrahydro-2H-spiro[benzo[5,6]chromeno[3,4-c]pyrrole-3,3'-indolin]-2'-one (5p). Method A. Yield 220 mg (0.469 mmol, 47%), mp 166–167 °C (decomp.), creamy powder. IR (ATP): 3149, 1706, 1622, 1556, 1470, 1367, 1327 cm⁻¹. ^1H NMR (500 MHz, DMSO- d_6) δ 1.84 (s, 3H, Me), 2.78 (d, $J = 9.0$ Hz, 1H, H-1a), 4.31 (dd, $J = 9.0, 6.7$ Hz, 1H, H-1b), 5.25 (d, $J = 6.7$ Hz, 1H, H-11c), 5.49 (q, $J = 7.1$ Hz, 1H, H-4), 6.98 (d, $J = 7.6$ Hz, 1H, Ar), 7.20 (td, $J = 7.6, 0.7$ Hz, 1H, Ar), 7.37 (d, $J = 8.9$ Hz, 1H, Ar), 7.45 (td, $J = 7.6, 1.0$ Hz, 1H, Ar), 7.54 (t, $J = 7.4$ Hz, 1H, Ar), 7.67 (t, $J = 7.4$ Hz, 1H, Ar), 7.70 (d, $J = 8.2$ Hz, 1H, Ar), 7.92 (d, $J = 8.8$ Hz, 1H, Ar), 8.00 (d, $J = 8.1$ Hz, 1H, Ar), 8.09 (d, $J = 8.4$ Hz, 1H, Ar), 8.32 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 96.3 (d, $J = 7.1$ Hz, CF₃). ^{13}C NMR (126 MHz, DMSO- d_6) δ 34.4, 36.2, 58.1, 73.8 (q, $^2J = 29.8$ Hz, C-4), 80.0, 97.7, 110.5, 117.4, 119.3, 122.5, 122.6, 122.7 (q, $^1J = 289.8$ Hz, CF₃), 123.5, 124.9, 127.0, 127.6, 128.9, 129.1, 130.1, 130.4, 131.1, 144.0, 146.9, 174.6. HRMS (ESI) calcd for C₂₄H₁₉F₃N₃O₃ [M+H]⁺ 470.1322, found 470.1330.

(1S*,3aS*,4S*,9bR*)-2-Methyl-3a-nitro-4-(trifluoromethyl)-1,3a,4,11c-tetrahydro-2H-spiro[benzo[5,6]chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (6p). Method B. Yield 179 mg (0.382 mmol, 38%), mp 268–269 °C (decomp.), white powder. IR (ATP): 3289, 1720, 1626, 1602, 1565, 1517, 1470, 1395, 1353, 1321 cm⁻¹. ^1H NMR (500 MHz, DMSO- d_6) δ 2.05 (s, 3H, Me), 3.95 (d, $J = 10.2$ Hz, 1H, H-1a), 4.22 (d, $J = 10.2$ Hz, 1H, H-1b), 5.20 (s, 1H, H-11c), 6.33 (q, $J = 6.2$ Hz, 1H, H-4), 6.63 (d, $J = 7.8$ Hz, 1H, Ar), 6.66 (d, $J = 8.7$ Hz, 1H, Ar), 6.84 (t, $J = 7.6$ Hz, 1H, Ar), 7.20–7.29 (m, 2H, Ar), 7.37 (d, $J = 7.6$ Hz, 1H, Ar), 7.81 (d, $J = 8.5$ Hz, 2H, Ar), 7.95 (d, $J = 7.2$ Hz, 1H, Ar), 10.12 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 91.7 (d, $J = 6.2$ Hz, CF₃). ^{13}C NMR (126 MHz, DMSO- d_6) δ 35.1, 48.5, 56.9, 71.8 (q, $^2J = 30.6$ Hz, C-4), 73.5, 83.7, 110.2, 111.2, 117.4, 122.1, 122.3, 122.8 (q, $^1J = 282.8$ Hz, CF₃), 124.1, 125.9 (2C), 128.4, 128.5, 129.4, 129.5, 130.0, 131.1, 142.7, 149.1, 175.5. HRMS (ESI) calcd for C₂₄H₁₉F₃N₃O₃ [M+H]⁺ 470.1322, found 470.1325.

(3S*,5'S*)-1,1''-Dibenzyl-3'-methyldispiro[indoline-3,4'-oxazolidine-5',3''-indoline]-2,2''-dione (7a). Method A. Yield 108 mg (0.431 mmol, 43%), mp 192–193 °C (lit.³ 191–192 °C), white powder. IR (ATP): 1717, 1610, 1488, 1461, 1351, 1306, 1168, 756, 698 cm⁻¹. ^1H NMR (500 MHz, DMSO- d_6) δ 2.27 (s, 3H, Me), 3.71 (d, $J = 9.8$ Hz, 1H, CHH), 3.80 (d, $J = 9.8$ Hz, 1H, CHH), 4.86 (d, $J = 15.8$ Hz, 1H,

CHHPh), 4.89 ($J = 15.7$ Hz, 1H, CHHPh), 4.93 (d, $J = 15.8$ Hz, 1H, CHHPh), 4.98 ($J = 15.7$ Hz, 1H, CHHPh), 6.93 (d, $J = 7.9$ Hz, 1H, Ar), 6.96 (d, $J = 7.9$ Hz, 1H, Ar), 7.13 (t, $J = 7.5$ Hz, 1H, Ar), 7.15 (d, $J = 7.5$ Hz, 1H, Ar), 7.24–7.38 (m, 12H, Ar), 7.70 (d, $J = 7.6$ Hz, 1H, Ar), 7.82 (d, $J = 7.6$ Hz, 1H, Ar). ^{13}C NMR (101 MHz, DMSO- d_6) δ 34.0, 42.6, 42.8, 59.9, 81.2, 95.4, 109.3, 109.6, 123.0, 123.2, 124.4, 125.6, 126.5, 127.1 (2C), 127.2 (3C), 127.4, 127.5, 128.6 (2C), 128.7 (2C), 130.3, 131.2, 136.1, 136.2, 142.9, 143.6, 174.0, 175.2. HRMS (ESI) calcd for $\text{C}_{32}\text{H}_{28}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 502.2125, found 502.2125.

(3S*,5'S*)-5,5'',7,7''-Tetrabromo-3'-methylspiro[indoline-3,4'-oxazolidine-5',3''-indoline]-2,2''-dione (7b). Method A. Yield 224 mg (0.703 mmol, 70%), mp 288–289 °C (decomp.), creamy powder. IR (ATP): 3186, 1732, 1710, 1615, 1584, 1452, 1273, 1222, 1169, 1109, 798, 731 cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6) δ 2.24 (s, 3H, Me), 3.58 (d, $J = 10.0$ Hz, 1H, CHH), 3.67 (d, $J = 10.0$ Hz, 1H, CHH), 7.64 (d, $J = 1.4$ Hz, 1H, Ar), 7.78 (br s, 2H, Ar), 7.84 (t, $J = 1.4$ Hz, 1H, Ar), 11.03 (s, 1H, NH), 11.14 (s, 1H, NH). ^{13}C NMR (126 MHz, DMSO- d_6) δ 33.6, 59.6, 82.0, 95.5, 103.2, 103.9, 114.2, 114.6, 127.4, 128.1, 128.5, 131.2, 134.9, 135.9, 141.4, 141.9, 175.1, 175.8. HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{12}\text{Br}_4\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 637.7566, found 637.7558.

(1S*,3S*,3aS*,4S*,9bR*)-2,3-Dimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (8a). Method A. Yield 387 mg (0.894 mmol, 89%), mp 234–235 °C (decomp.), white powder. IR (ATP): 3396, 1713, 1620, 1552, 1492, 1488, 1473, 1462, 1402, 1383, 1344, 1331 cm^{-1} . ^1H NMR (400 MHz, DMSO- d_6) δ 1.24 (d, $J = 5.9$ Hz, 3H, Me), 2.04 (s, 3H, Me), 4.03 (q, $J = 5.9$ Hz, 1H, H-3), 4.89 (s, 1H, H-9b), 6.01 (q, $J = 7.1$ Hz, 1H, H-4), 6.24 (d, $J = 7.7$ Hz, 1H, H-9), 6.86 (t, $J = 7.6$ Hz, 1H, H-8), 6.93 (d, $J = 7.7$ Hz, 1H, H-7'), 7.06 (d, $J = 8.1$ Hz, 1H, H-6), 7.18–7.28 (m, H-7, H-5'), 7.43 (t, $J = 7.7$ Hz, 1H, H-6'), 7.58 (d, $J = 7.4$ Hz, 1H, H-4'), 10.67 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 97.1 (br s, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 14.9, 32.7, 49.4, 61.4, 75.2, 75.8 (q, $^2J = 32.8$ Hz, C-4), 95.0, 110.4, 117.8, 118.9, 123.1 (q, $^1J = 281.9$ Hz, CF_3), 123.3, 123.5, 124.4, 126.2, 127.8, 129.2, 130.6, 142.8, 151.8, 176.6. HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{F}_3\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 434.1322, found 434.1320.

(1S*,3S*,3aS*,4S*,9bR*)-2,3,8-Trimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (8b). Method A. Yield 380 mg (0.850 mmol, 85%), mp 223–224 °C (decomp.), white powder. IR (ATP): 3206, 1692, 1622, 1564, 1502, 1488, 1471, 1404, 1343 cm^{-1} . ^1H NMR (400 MHz, DMSO- d_6) δ 1.22 (d, $J = 5.8$ Hz, 3H, Me), 1.93 (s, 3H, Me), 2.04 (s, 3H, Me), 4.02 (q, $J = 5.8$ Hz, 1H, H-3), 4.83 (s, 1H, H-9b), 5.88–6.07 (m, 2H, H-4, H-9), 6.88–6.97 (m, 2H, H-7, H-7'), 7.01 (d, $J = 8.2$ Hz, 1H, H-6), 7.24 (t, $J = 7.5$ Hz, 1H, H-5'), 7.44 (t, $J = 7.6$ Hz, 1H, H-6'), 7.56 (d, $J = 7.4$ Hz, 1H, H-4'), 10.67 (s, 1H, NH). ^{19}F NMR (471 MHz, DMSO- d_6) δ 97.1 (br s, CF_3). ^{13}C NMR (126 MHz, DMSO- d_6) δ 14.9, 20.2, 32.7, 49.6, 61.4, 75.3, 75.8 (q, $^2J = 32.7$ Hz, C-4), 95.0, 110.2, 116.7, 117.4, 123.2 (q, $^1J = 282.1$ Hz, CF_3), 123.3, 124.3, 126.4, 127.9, 129.7, 130.6, 132.2, 142.8, 149.7, 176.6. HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{21}\text{F}_3\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 448.1479, found 448.1475.

(1S*,3S*,3aS*,4S*,9bR*)-Methoxy-2,3-dimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (8c). Method A. Yield 408 mg (0.881 mmol, 88%), mp 236–237 °C (decomp.), white powder. IR (ATP): 3175, 1698, 1623, 1565, 1500, 1471, 1423, 1339 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.22 (d, *J* = 5.9 Hz, 3H, Me), 2.06 (s, 3H, Me), 3.35 (s, 3H, MeO), 4.01 (q, *J* = 5.9 Hz, 1H, H-3), 4.86 (s, 1H, H-9b), 5.72 (br s, 1H, H-9), 5.90 (q, *J* = 7.0 Hz, 1H, H-4), 6.78 (br d, 1H, *J* = 8.7 Hz, H-7), 6.94 (d, *J* = 7.7 Hz, 1H, H-7'), 7.00 (d, *J* = 8.7 Hz, 1H, H-6), 7.25 (t, *J* = 7.5 Hz, 1H, H-5'), 7.43 (t, *J* = 7.6 Hz, 1H, H-6'), 7.57 (d, *J* = 7.4 Hz, 1H, H-4'), 10.70 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 97.0 (br s, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 15.0, 32.8, 49.8, 54.7, 61.4, 75.3, 76.2 (q, ²*J* = 32.9 Hz, C-4), 95.1, 109.9, 110.3, 115.3, 117.9, 118.3, 123.1 (q, ¹*J* = 282.0 Hz, CF₃), 123.3, 124.4, 127.8, 130.6, 142.9, 145.7, 154.6, 176.6. HRMS (ESI) calcd for C₂₂H₂₁F₃N₃O₅ [M+H]⁺ 464.1428, found 464.1436.

(1S*,3S*,3aS*,4S*,9bR*)-6-Ethoxy-2,3-dimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (8d). Method A. Yield 459 mg (0.962 mmol, 96%), mp 225–226 °C (decomp.), white powder. IR (ATP): 3290, 1709, 1620, 1561, 1487, 1470, 1409, 1341, 1331 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.22 (d, *J* = 5.7 Hz, 3H, Me), 1.30 (t, *J* = 6.7 Hz, 3H, Me), 2.01 (s, 3H, Me), 3.92–4.11 (m, 3H, OCH₂, H-3), 4.85 (s, 1H, H-9b), 5.81 (d, *J* = 7.9 Hz, 1H, H-9), 5.96 (q, *J* = 5.9 Hz, 1H, H-4), 6.75 (t, *J* = 7.9 Hz, 1H, H-8), 6.82–6.95 (m, 2H, H-7, H-7'), 7.21 (t, *J* = 7.5 Hz, 1H, H-5'), 7.41 (t, *J* = 7.6 Hz, 1H, H-6'), 7.56 (d, *J* = 7.4 Hz, 1H, H-4'), 10.61 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 97.4 (br s, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 14.5, 14.8, 32.6, 49.4, 61.4, 64.1, 75.2, 75.6 (q, ²*J* = 32.7 Hz, C-4), 95.1, 110.3, 112.9, 117.1, 119.1, 123.2 (q, ¹*J* = 282.6 Hz, CF₃), 123.2, 123.4, 124.3, 128.0, 130.5, 141.6, 142.8, 147.4, 176.5. HRMS (ESI) calcd for C₂₃H₂₃F₃N₃O₅ [M+H]⁺ 478.1584, found 478.1593.

(1S*,3S*,3aS*,4S*,9bR*)-8-Chloro-2,3-dimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (8e). Method A. Yield 435 mg (0.929 mmol, 93%), mp 242–243 °C (decomp.), white powder. IR (ATP): 3214, 1692, 1622, 1562, 1484, 1469, 1448, 1405, 1343, 1333 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.24 (d, *J* = 6.1 Hz, 3H, Me), 2.04 (s, 3H, Me), 4.04 (q, *J* = 6.1 Hz, 1H, H-3), 4.89 (s, 1H, H-9b), 6.02 (q, *J* = 7.1 Hz, 1H, H-4), 6.17 (d, *J* = 2.1 Hz, 1H, H-9), 6.95 (d, *J* = 7.7 Hz, 1H, H-7'), 7.13 (d, *J* = 8.8 Hz, 1H, H-6), 7.24 (t, *J* = 7.5 Hz, 1H, H-5'), 7.28 (dd, *J* = 8.8, 2.1 Hz, 1H, H-7), 7.45 (t, *J* = 7.6, 1H, H-6'), 7.59 (d, *J* = 7.4 Hz, 1H, H-4'), 10.75 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 97.2 (br s, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 14.9, 32.6, 49.1, 61.5, 75.2, 75.7 (q, ²*J* = 32.8 Hz, C-4), 94.3, 110.3, 119.0, 120.2, 123.0 (q, ¹*J* = 282.4 Hz, CF₃), 123.4, 124.6, 125.9, 127.1, 127.3, 129.2, 130.8, 142.7, 150.5, 176.5. HRMS (ESI) calcd for C₂₁H₁₈F₃ClN₃O₄ [M+H]⁺ 468.0932, found 468.0940.

(1S*,3S*,3aS*,4S*,9bR*)-6,8-Dibromo-2,3-dimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (8f). Method A. Yield 539 mg

(0.912 mmol, 91%), mp 251–252 °C (decomp.), white powder. IR (ATP): 3370, 1710, 1694, 1620, 1565, 1472, 1453, 1407, 1338 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.24 (d, *J* = 5.8 Hz, 3H, Me), 2.02 (s, 3H, Me), 4.11 (q, *J* = 5.8 Hz, 1H, H-3), 4.95 (s, 1H, H-9b), 6.14 (q, *J* = 6.7 Hz, 1H, H-4), 6.38 (s, 1H, H-9), 6.94 (d, *J* = 7.6 Hz, 1H, H-7'), 7.24 (t, *J* = 7.5 Hz, 1H, 6'), 7.44 (t, *J* = 7.5 Hz, 1H, 5'), 7.60 (d, *J* = 7.4 Hz, 1H, H-4'), 7.81 (s, 1H, H-7), 10.70 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 97.2 (br s, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 14.6, 32.5, 48.9, 61.6, 75.2, 75.6 (q, ²*J* = 32.8 Hz, C-4), 94.2, 110.2, 111.9, 115.1, 122.8 (q, ¹*J* = 283.7 Hz, CF₃), 122.9, 123.3, 124.9, 127.2, 128.4, 130.8, 134.4, 142.6, 147.8, 176.2. HRMS (ESI) calcd for C₂₁H₁₇F₃Br₂N₃O₄ [M+H]⁺ 591.9512, found 591.9526.

(1S*,3S*,3aS*,4S*,9bR*)-2,3-Dimethyl-3a,8-dinitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-*c*]pyrrole-1,3'-indolin]-2'-one (8g). Method A. Yield 378 mg (0.791 mmol, 79%), mp 228–229 °C (decomp.), white powder. IR (ATP): 3186, 1693, 1622, 1562, 1533, 1485, 1475, 1464, 1403, 1342 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.28 (d, *J* = 6.0 Hz, 3H, Me), 2.06 (s, 3H, Me), 4.10 (q, *J* = 6.0 Hz, 1H, H-3), 5.02 (s, 1H, H-9b), 6.21 (q, *J* = 6.9 Hz, 1H, H-4), 6.95 (d, *J* = 7.6 Hz, 1H, H-7'), 7.16 (br s, 1H, H-9), 7.29 (t, *J* = 7.6 Hz, 1H, H-5'), 7.36 (d, *J* = 9.0 Hz, 1H, H-6), 7.48 (t, *J* = 7.6, 1H, H-6'), 7.64 (d, *J* = 7.6 Hz, 1H, H-4'), 7.98 (dd, *J* = 9.0, 1.9 Hz, 1H, H-7), 10.70 (s, 1H, NH). ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ 97.1 (br s, CF₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 14.7, 32.6, 48.9, 61.6, 75.3, 75.6 (q, ²*J* = 33.0 Hz, C-4), 93.5, 110.5, 118.4, 119.6, 122.6, 122.8 (q, ¹*J* = 282.7 Hz, CF₃), 123.5, 124.8, 125.0, 127.0, 130.9, 142.5, 142.6, 156.3, 176.5. HRMS (ESI) calcd for C₂₁H₁₈F₃N₄O₆ [M+H]⁺ 479.1173, found 479.1182.

(1S*,3S*,3aS*,4R*,9bR*)-2,3-Dimethyl-3a-nitro-4-phenyl-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-*c*]pyrrole-1,3'-indolin]-2'-one (8h). Method A. Yield 419 mg (0.949 mmol, 95%), mp 234–235 °C (decomp.), creamy powder. IR (ATP): 3145, 1706, 1617, 1589, 1542, 1489, 1472, 1456, 1334 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 0.97 (d, *J* = 6.3 Hz, 3H, Me), 2.05 (s, 3H, Me), 4.27 (q, *J* = 6.3 Hz, 1H, H-3), 4.86 (s, 1H, H-9b), 6.14 (s, 1H, H-4), 6.35 (d, *J* = 7.7 Hz, 1H, H-9), 6.78 (t, *J* = 7.7 Hz, 1H, H-8), 6.91 (d, *J* = 7.6 Hz, 1H, H-7'), 7.06 (d, *J* = 8.0 Hz, 1H, H-6), 7.10 (t, *J* = 7.9 Hz, H-7), 7.21 (t, *J* = 7.6 Hz, 1H, H-6'), 7.36–7.44 (m, 6H, Ph, H-5'), 7.58 (d, *J* = 7.6 Hz, 1H, H-4'), 10.54 (s, 1H, NH). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 14.7, 32.5, 49.7, 61.4, 75.2, 78.1, 97.1, 110.1, 117.3, 120.4, 122.4, 122.9, 124.5, 126.1, 127.8 (2C), 128.0 (2C), 128.5, 128.7, 128.8, 130.2, 135.3, 142.8, 153.4, 176.5. HRMS (ESI) calcd for C₂₆H₂₄N₃O₄ [M+H]⁺ 442.1761, found 442.1768.

(1S*,3S*,3aS*,4R*,9bR*)-1',2,3-Trimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-*c*]pyrrole-1,3'-indolin]-2'-one (8i). Method A. Yield 389 mg (0.870 mmol, 87%), mp 196–197 °C (decomp.), white powder. IR (ATP): 1695, 1616, 1559, 1490, 1474, 1456, 1408, 1374, 1340 cm⁻¹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.24 (d, *J* = 6.3 Hz, 3H, Me), 1.98 (s, 3H, Me), 2.91 (s, 3H, Me), 4.06 (q, *J* = 6.3 Hz, 1H, H-3), 4.91 (s, 1H, H-9b), 6.00 (q, *J* = 6.9 Hz, 1H, H-4), 6.15 (d, *J* = 7.5 Hz, 1H, H-9), 6.81 (t, *J* = 7.6 Hz, 1H, H-8), 7.05 (d, *J* = 8.1 Hz, 1H, H-6), 7.12–7.24 (m, H-7, H-5'), 7.32 (d, *J*

= 7.7 Hz, 1H, H-7'), 7.54 (t, $J = 7.7$ Hz, 1H, H-6'), 7.63 (d, $J = 7.3$ Hz, 1H, H-4'). ^{19}F NMR (376 MHz, DMSO- d_6) δ 97.3 (br s, CF₃). ^{13}C NMR (126 MHz, DMSO- d_6) δ 14.9, 25.6, 32.6, 49.4, 61.5, 75.1, 75.6 (q, $^2J = 32.5$ Hz, C-4), 95.0, 109.4, 117.1, 117.9, 123.2 (q, $^1J = 282.7$ Hz, CF₃), 123.4, 124.0, 124.1, 125.9, 127.1, 129.3, 130.7, 144.2, 151.7, 174.5. HRMS (ESI) calcd for C₂₂H₂₁N₃O₄ [M+H]⁺ 448.1479, found 448.1483.

(1S*,3S*,3aS*,4R*,9bR*)-2,3,5'-Trimethyl-3a-nitro-4-(trifluoromethyl)-2,3,3a,9b-tetrahydro-4H-spiro[chromeno[3,4-c]pyrrole-1,3'-indolin]-2'-one (8j). Method A. Yield 312 mg (0.698 mmol, 70%), mp 270–271 °C (decomp.), white powder. IR (ATP): 3173, 3078, 1689, 1625, 1584, 1567, 1560, 1489, 1469, 1456, 1406, 1386, 1340 cm⁻¹. ^1H NMR (400 MHz, DMSO- d_6) δ 1.22 (d, $J = 6.3$ Hz, 3H, Me), 2.03 (s, 3H, Me), 2.38 (s, 3H, Me), 3.99 (q, $J = 6.3$ Hz, 1H, H-3), 4.87 (s, 1H, H-9b), 6.01 (q, $J = 7.2$ Hz, 1H, H-4), 6.25 (d, $J = 7.8$ Hz, 1H, H-9), 6.82 (d, $J = 7.9$ Hz, 1H, H-7'), 6.86 (td, $J = 7.8, 1.0$ Hz, H-8), 7.06 (d, $J = 7.8$ Hz, 1H, H-6), 7.17–7.26 (m, H-7, H-6'), 7.39 (s, 1H, H-4'), 10.60 (s, 1H, NH). ^{19}F NMR (376 MHz, DMSO- d_6) δ 97.0 (br s, CF₃). ^{13}C NMR (126 MHz, DMSO- d_6) δ 15.0, 20.7, 32.8, 49.5, 61.4, 75.3, 75.9 (q, $^2J = 33.1$ Hz, C-4), 95.2, 110.1, 117.0, 117.8, 123.1 (q, $^1J = 281.7$ Hz, CF₃), 123.6, 124.8, 126.2, 127.8, 129.2, 130.9, 132.4, 140.3, 151.8, 176.6. Anal. Calcd for C₂₂H₂₀F₃N₃O₄: C, 59.06; H, 4.51; N, 9.39. Found: C, 58.66; H, 4.43; N, 9.28.

X-ray crystallography

Crystals of **5a**, **6l** and **8e** were grown by the slow evaporation of an acetonitrile solution. Diffraction data were collected on a an Xcalibur Eos (compound **5a**) or on an Xcalibur 3 (compounds **6l** and **7e**) automatic diffractometer using the standard procedure (Mo-K α radiation ($\lambda = 0.71073$ Å) or Cu-K α radiation ($\lambda = 1.54184$ Å), graphite monochromator, ω -scanning, 295(2) K). An empirical adjustment for absorption was introduced. The structures were solved by direct methods and refined by the full-matrix least-squares method using the SHELX-97 program package.⁴ All non-hydrogen atoms were refined with anisotropic atomic displacement and hydrogen atoms were included at the calculated positions using a riding model. The geometrical parameters were analysed using the programs OLEX2.⁵

Crystal data for 5a (C₂₀H₁₆F₃N₃O₄, 419.36). Trigonal crystals, space group $R\bar{3}$, $a = 29.7240(10)$, $b = 29.7240(10)$ and $c = 11.0656(4)$ Å, $V = 8466.9(5)$ Å³, $D_c = 1.480$, absorption coefficient $\mu(\text{Mo-K}\alpha) = 0.124$ mm⁻¹, $Z = 18$. The intensities of 4853 independent reflections ($R_{\text{int}} = 0.0292$) were measured. The final discrepancy factors $R_1 = 0.0469$, $wR_2 = 0.1390$, GooF = 1.004 for 3616 reflections with $I > 2\sigma(I)$; $R_1 = 0.0655$, $wR_2 = 0.1523$ (all data). Largest different peaks and holes: 0.23 and -0.25 e Å⁻³. Completeness to $\theta = 29.12^\circ$ (97.73%). Deposition number CCDC 1939937.

Crystal data for 6l (C₂₁H₁₇ClF₃N₃O₄, 467.83). Monoclinic crystals, space group $P2_1/n$, $a = 10.726(9)$, $b = 12.407(4)$ and $c = 15.495(6)$ Å, $\beta = 107.72(5)^\circ$, $V = 1964.2(19)$ Å³, $D_c = 1.582$, absorption coefficient $\mu(\text{Cu-K}\alpha) = 2.315 \text{ mm}^{-1}$, $Z = 4$. The intensities of 3461 independent reflections ($R_{\text{int}} = 0.0466$) were measured. The final discrepancy factors $R_1 = 0.0441$, $wR_2 = 0.1265$, GooF = 1.013 for 2798 reflections with $I > 2\sigma(I)$; $R_1 = 0.0503$, $wR_2 = 0.1311$ (all data). Largest different peaks and holes: 0.23 and -0.30 e \AA^{-3} . Completeness to $\theta = 66.92^\circ$ (98.9%). Deposition number CCDC 1939936.

Crystal data for 8e (C₂₁H₁₇ClF₃N₃O₄, 467.83). Monoclinic crystals, space group $P2_1/n$, $a = 14.1874(8)$, $b = 8.4578(6)$ and $c = 17.2415(9)$ Å, $\beta = 95.519(5)^\circ$, $V = 2059.3(2)$ Å³, $D_c = 1.509$, absorption coefficient $\mu(\text{Mo-K}\alpha) = 0.247 \text{ mm}^{-1}$, $Z = 4$. The intensities of 5568 independent reflections ($R_{\text{int}} = 0.0338$) were measured. The final discrepancy factors $R_1 = 0.0576$, $wR_2 = 0.1624$, GooF = 1.062 for 3478 reflections with $I > 2\sigma(I)$; $R_1 = 0.0989$, $wR_2 = 0.2107$ (all data). Largest different peaks and holes: 0.27 and -0.32 e \AA^{-3} . Completeness to $\theta = 26.00^\circ$ (99.9%). Deposition number CCDC 1939935.

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- 3 P.-J. Xia, J. Li, Y.-L. Qian, Q.-L. Zhao, H.-Y. Xiang, J.-A. Xiao, X.-Q. Chen, H. Yang, *J. Org. Chem.*, 2018, **83**, 2948.
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- 5 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339.

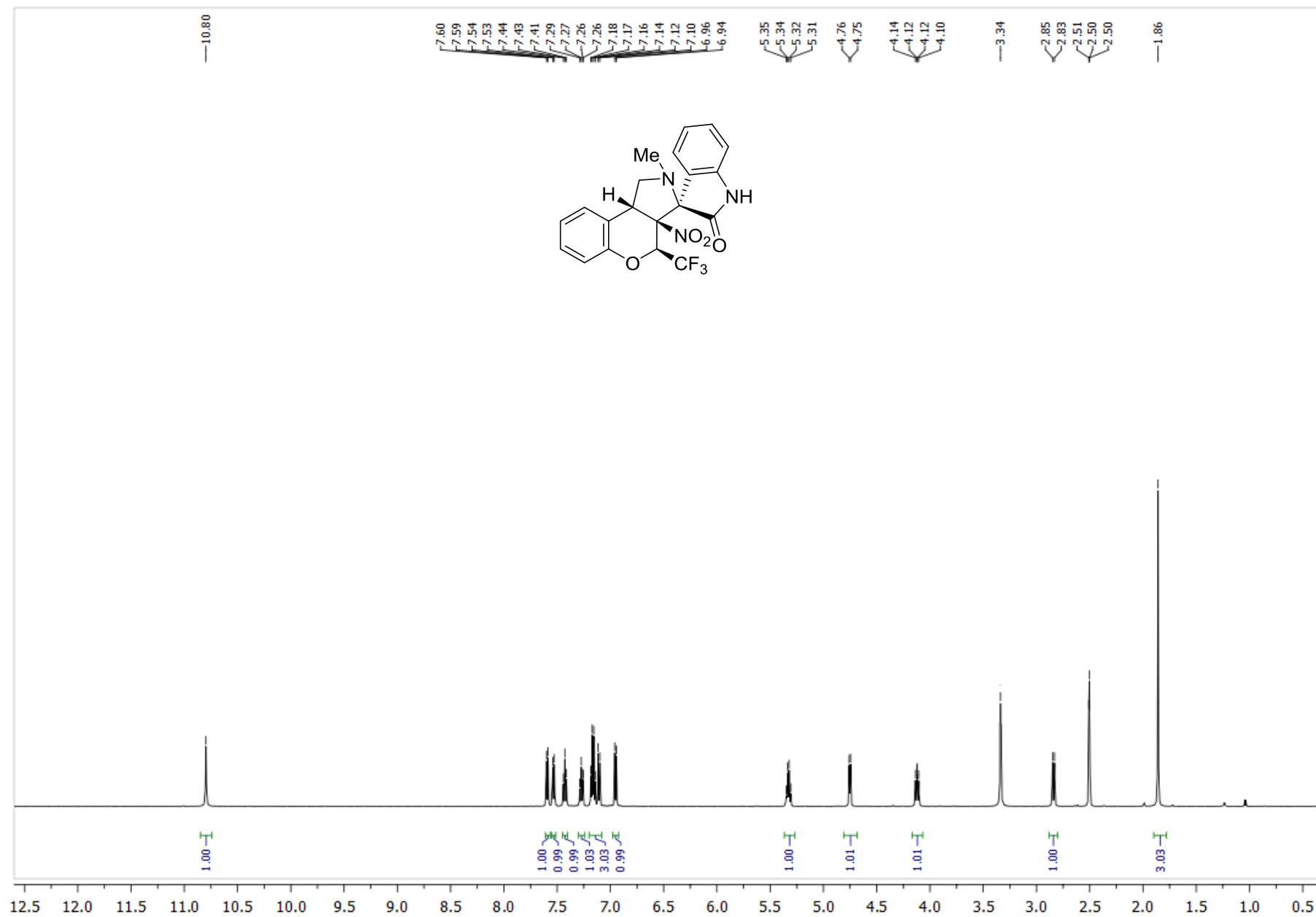


Figure S1. Copy of ¹H NMR spectrum of **5a** in DMSO-*d*₆

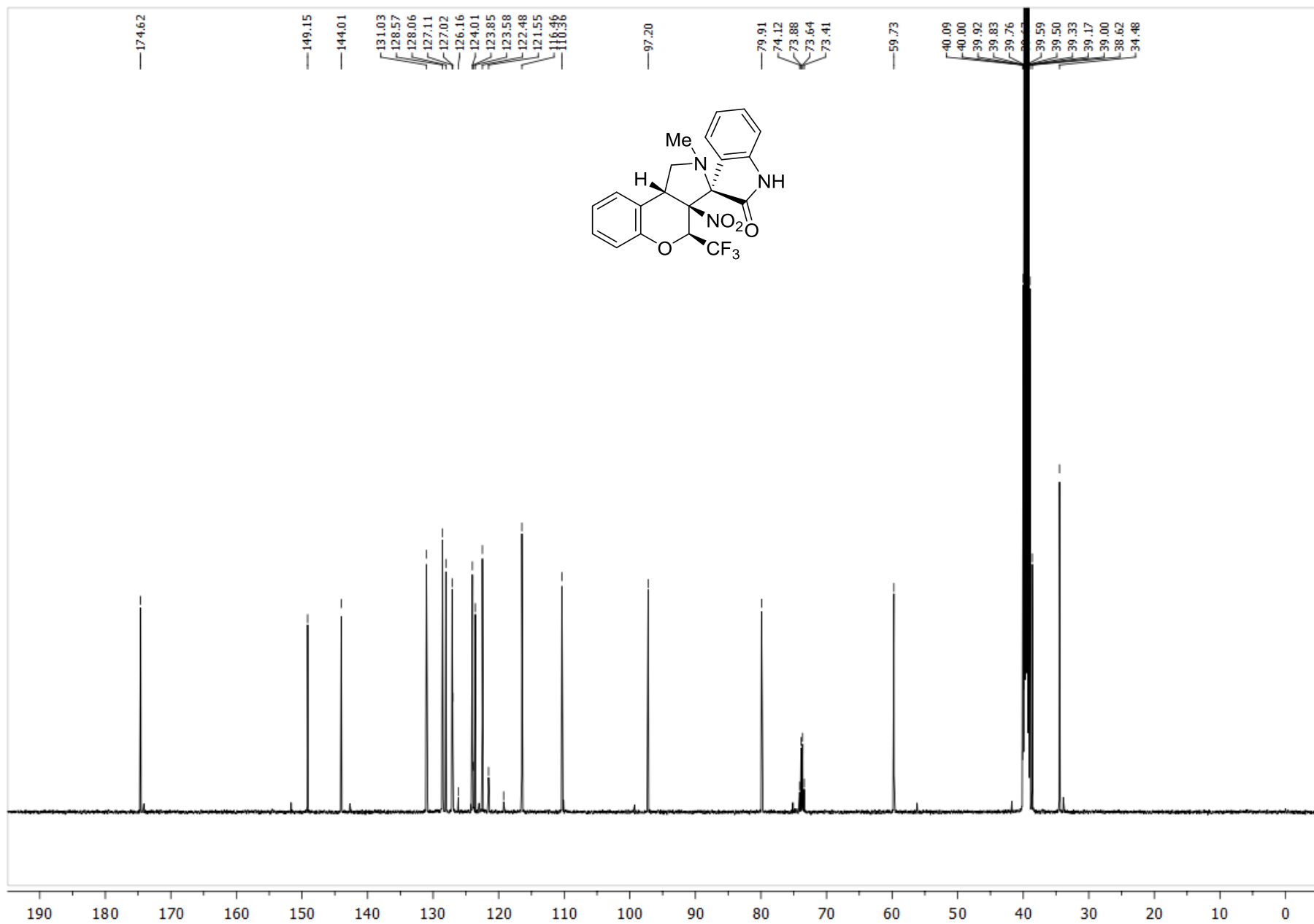


Figure S2. Copy of ^{13}C NMR spectrum of **5a** in $\text{DMSO-}d_6$

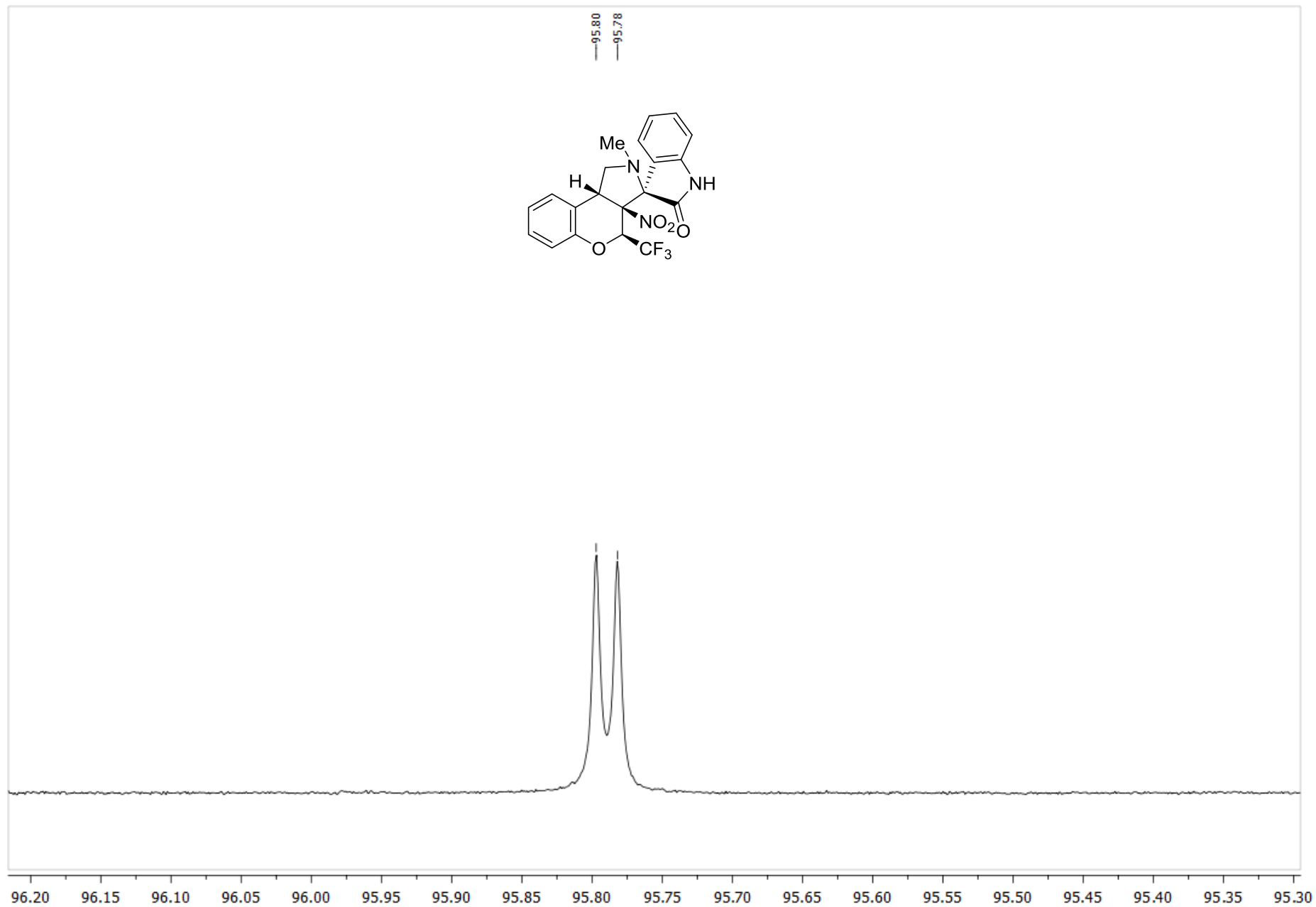


Figure S3. Copy of ^{19}F NMR spectrum of **5a** in $\text{DMSO-}d_6$

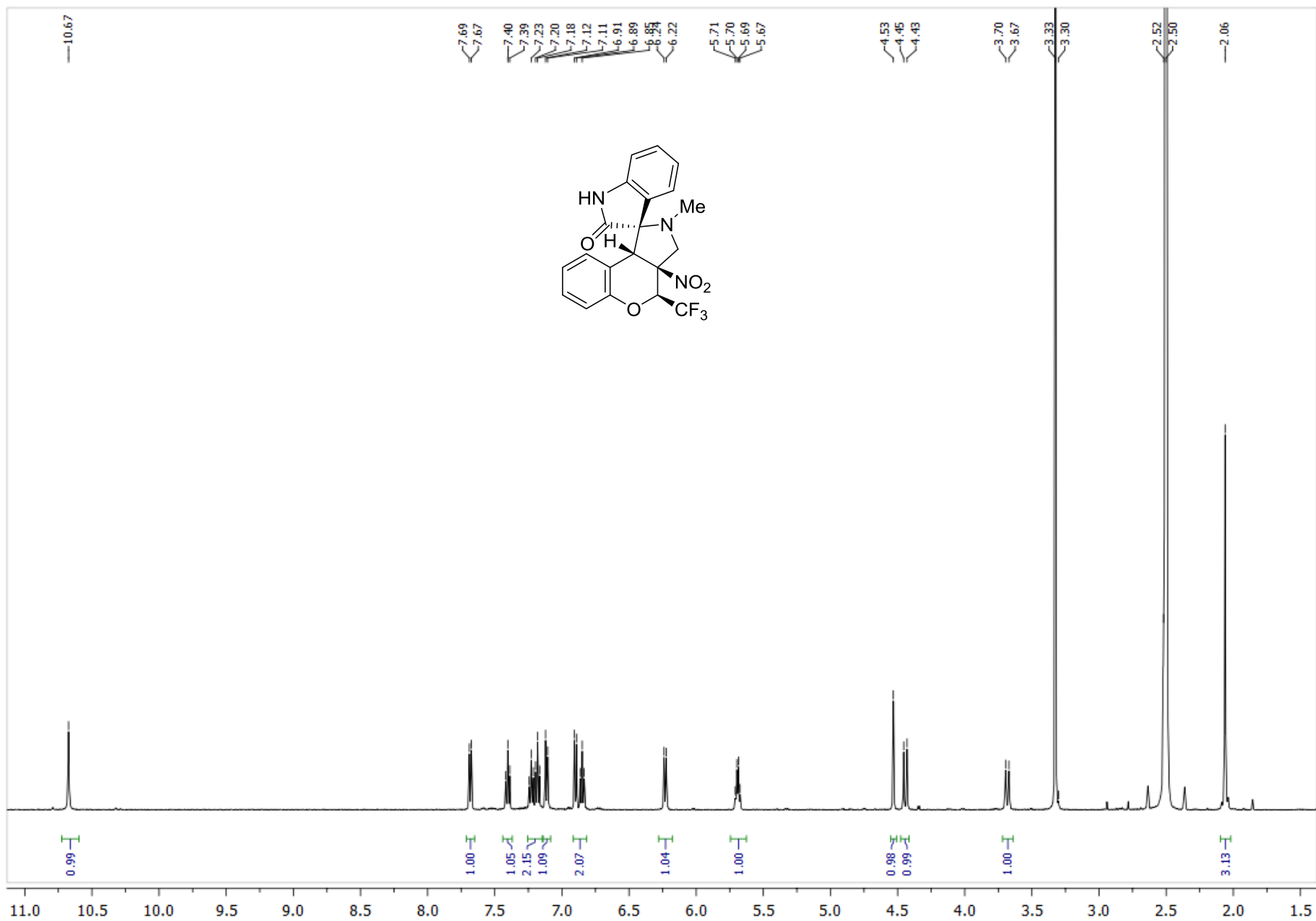


Figure S4. Copy of ¹H NMR spectrum of **6a** in DMSO-*d*₆

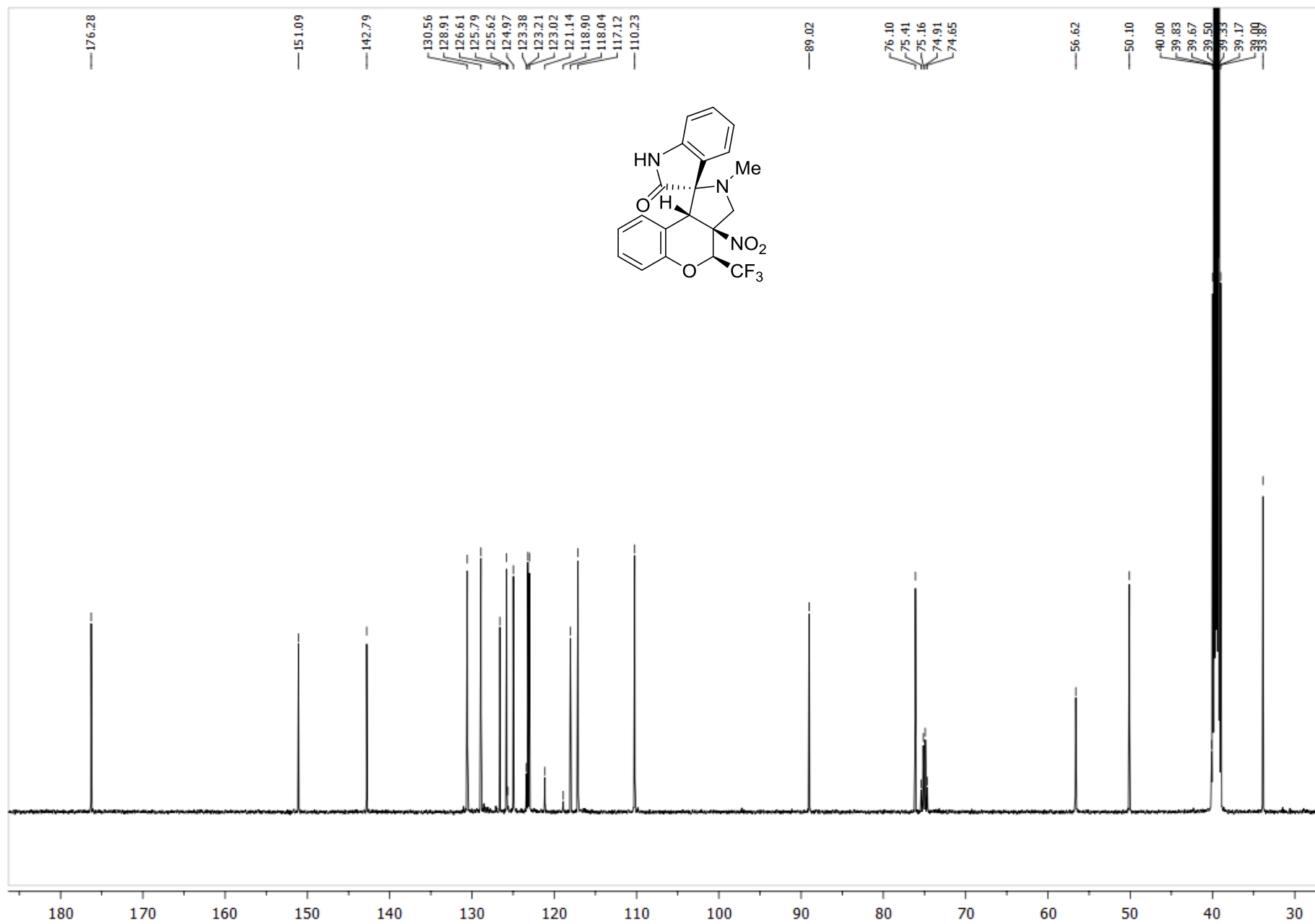


Figure S5. Copy of ¹³C NMR spectrum of **6a** in DMSO-*d*₆

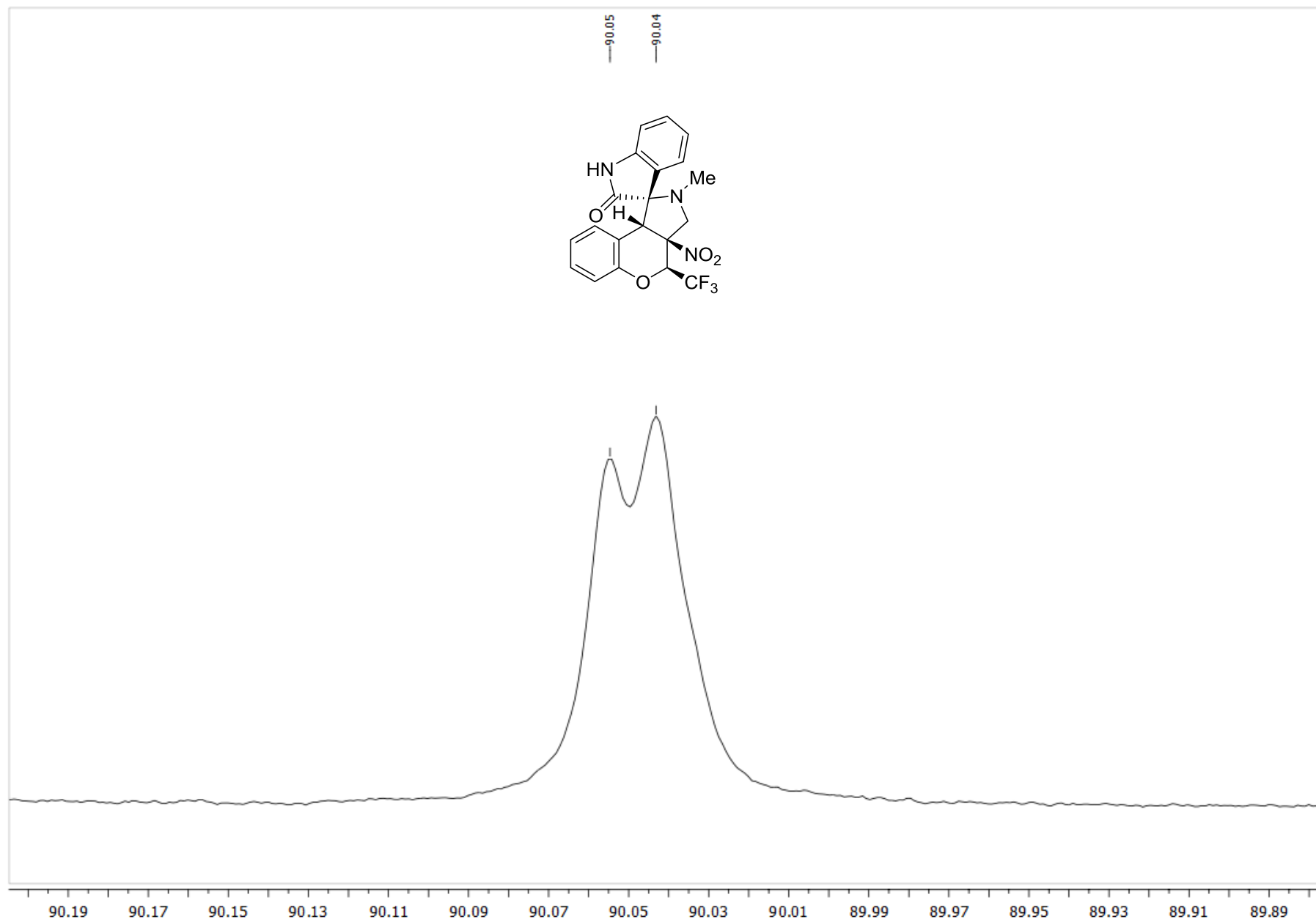


Figure S6. Copy of ^{19}F NMR spectrum of **6a** in $\text{DMSO-}d_6$

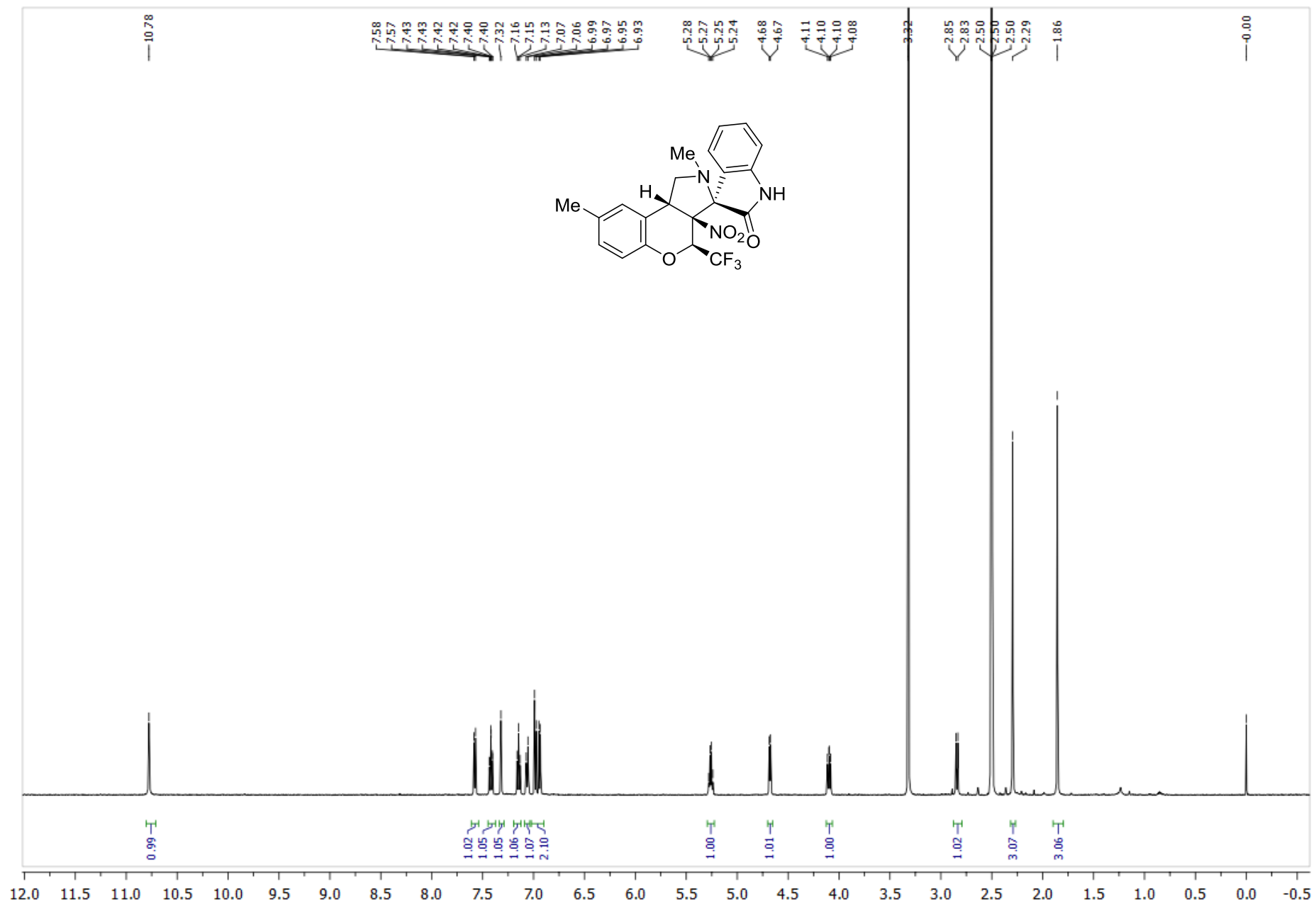


Figure S7. Copy of ¹H NMR spectrum of **5b** in DMSO-*d*₆

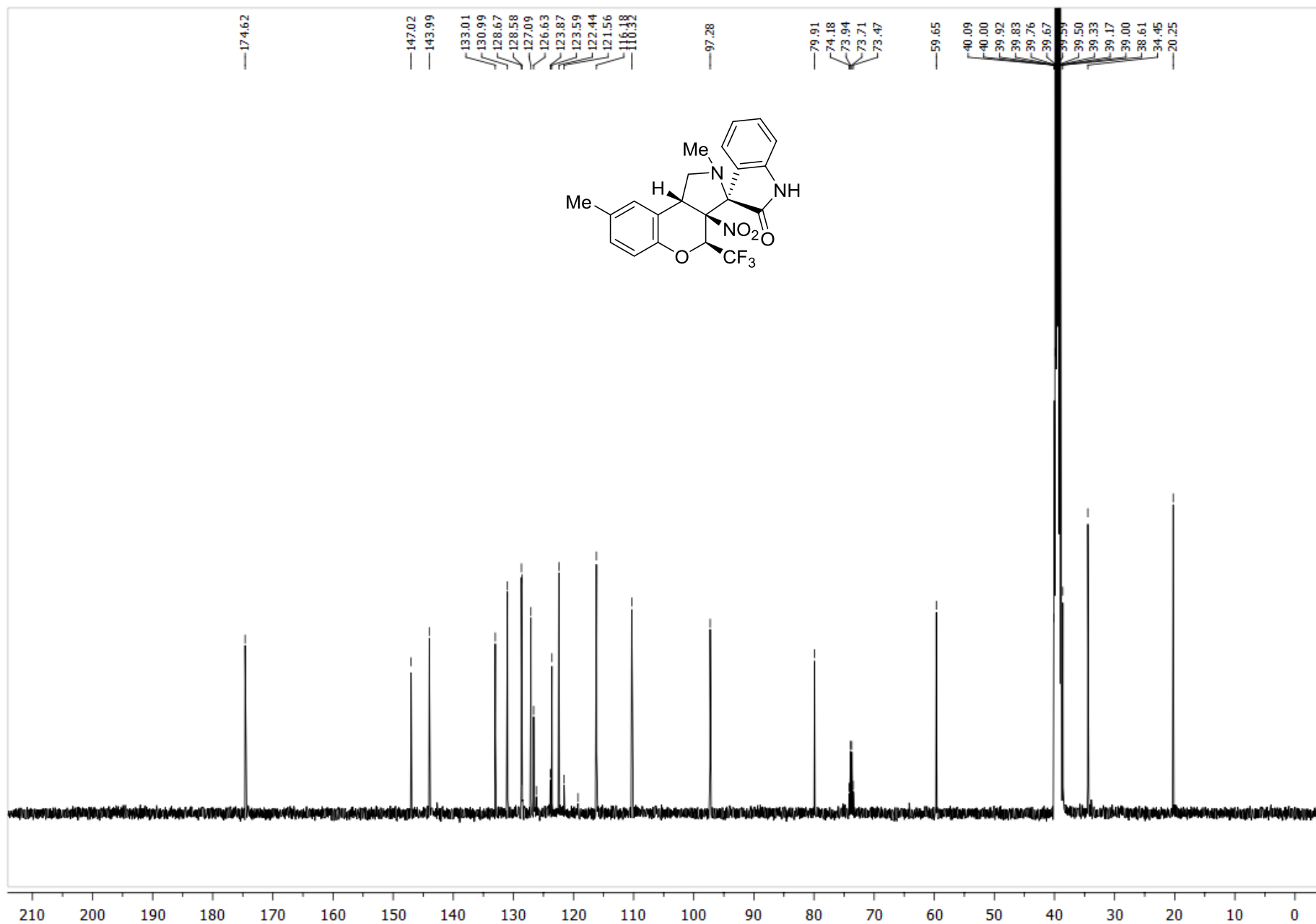


Figure S8. Copy of ¹³C NMR spectrum of **5b** in DMSO-*d*₆

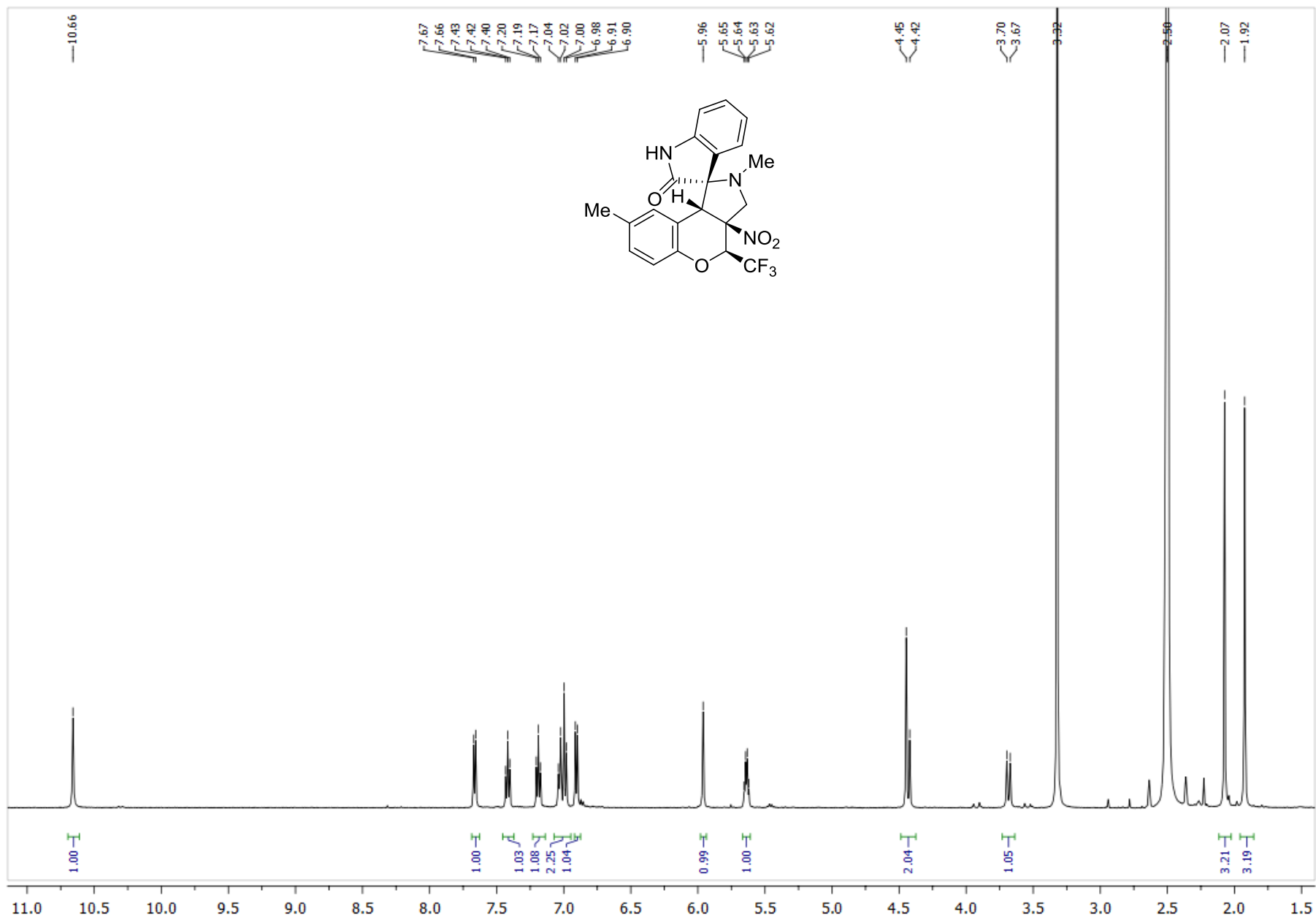


Figure S9. Copy of ¹H NMR spectrum of **6b** in DMSO-*d*₆

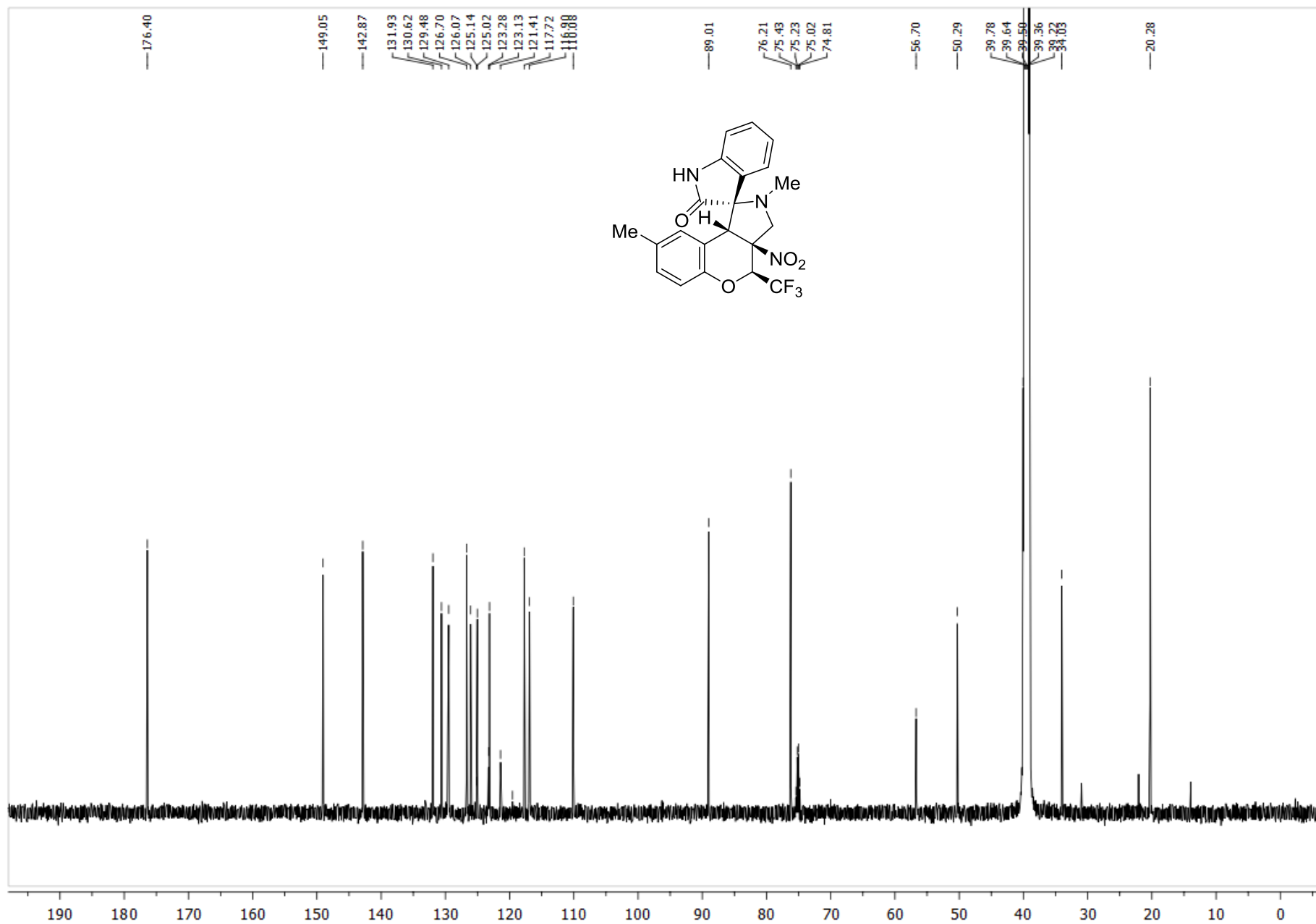


Figure S10. Copy of ¹³C NMR spectrum of **6b** in DMSO-*d*₆

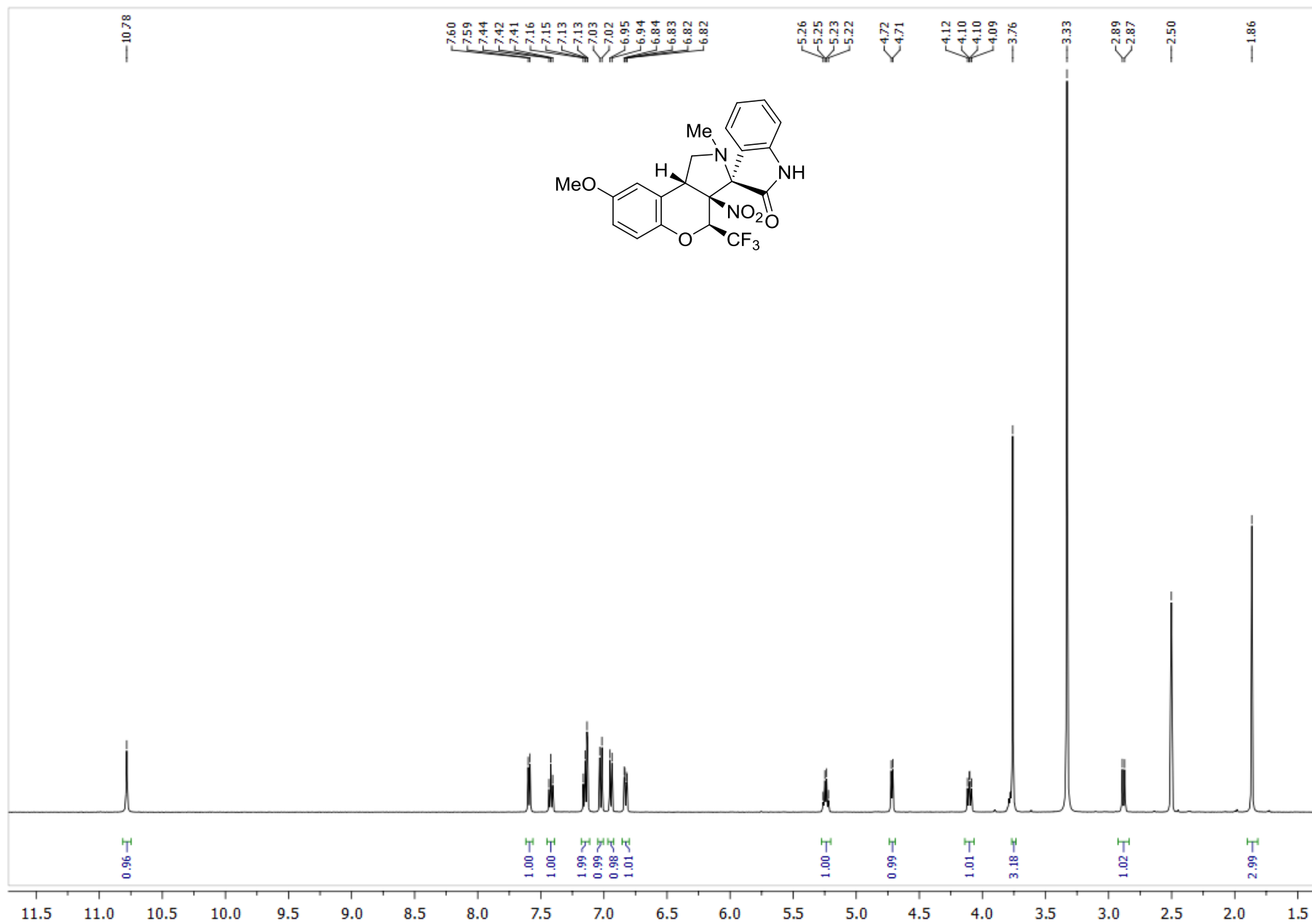


Figure S11. Copy of ¹H NMR spectrum of **5c** in DMSO-*d*₆

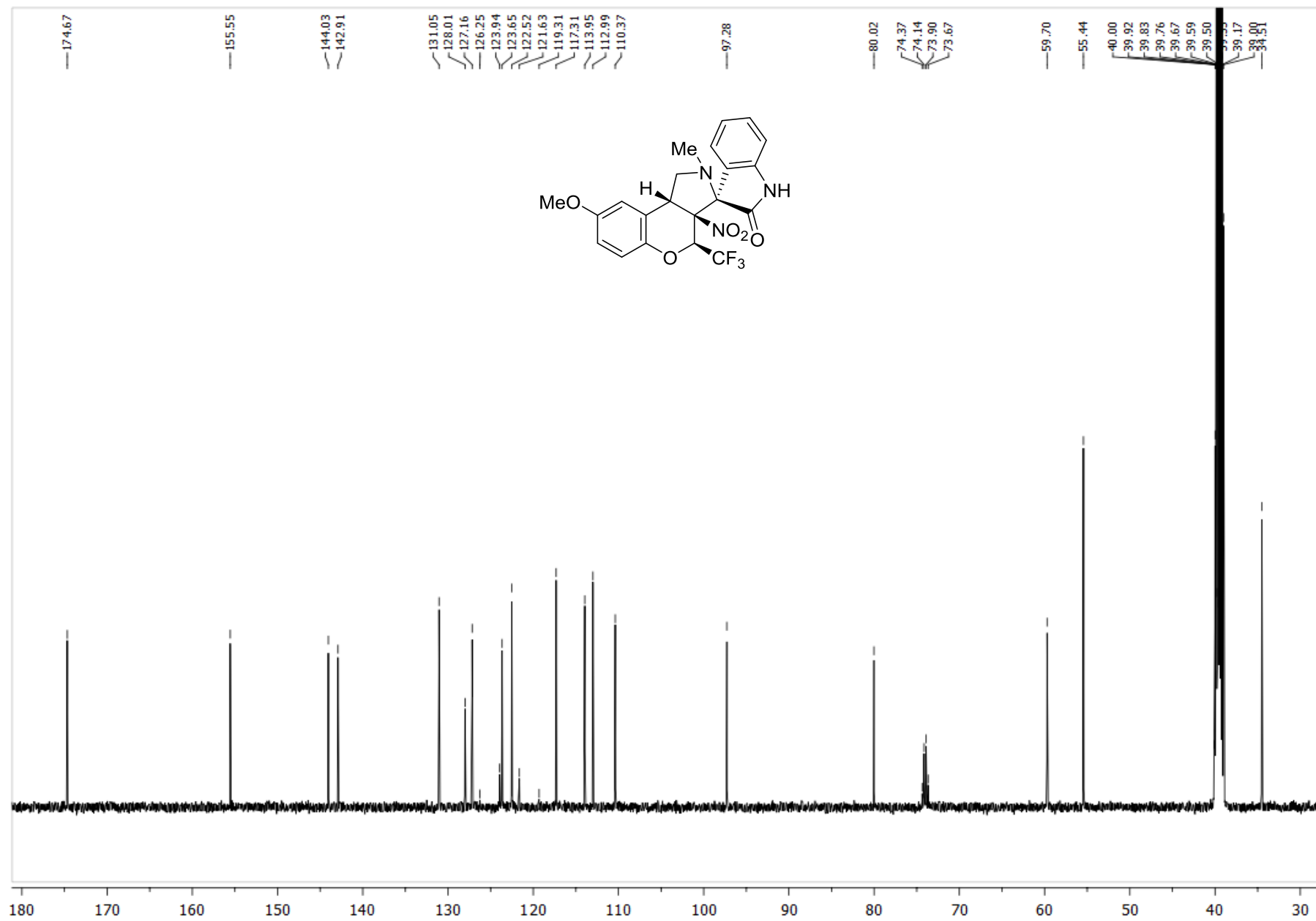


Figure S12. Copy of ¹³C NMR spectrum of **5c** in DMSO-*d*₆

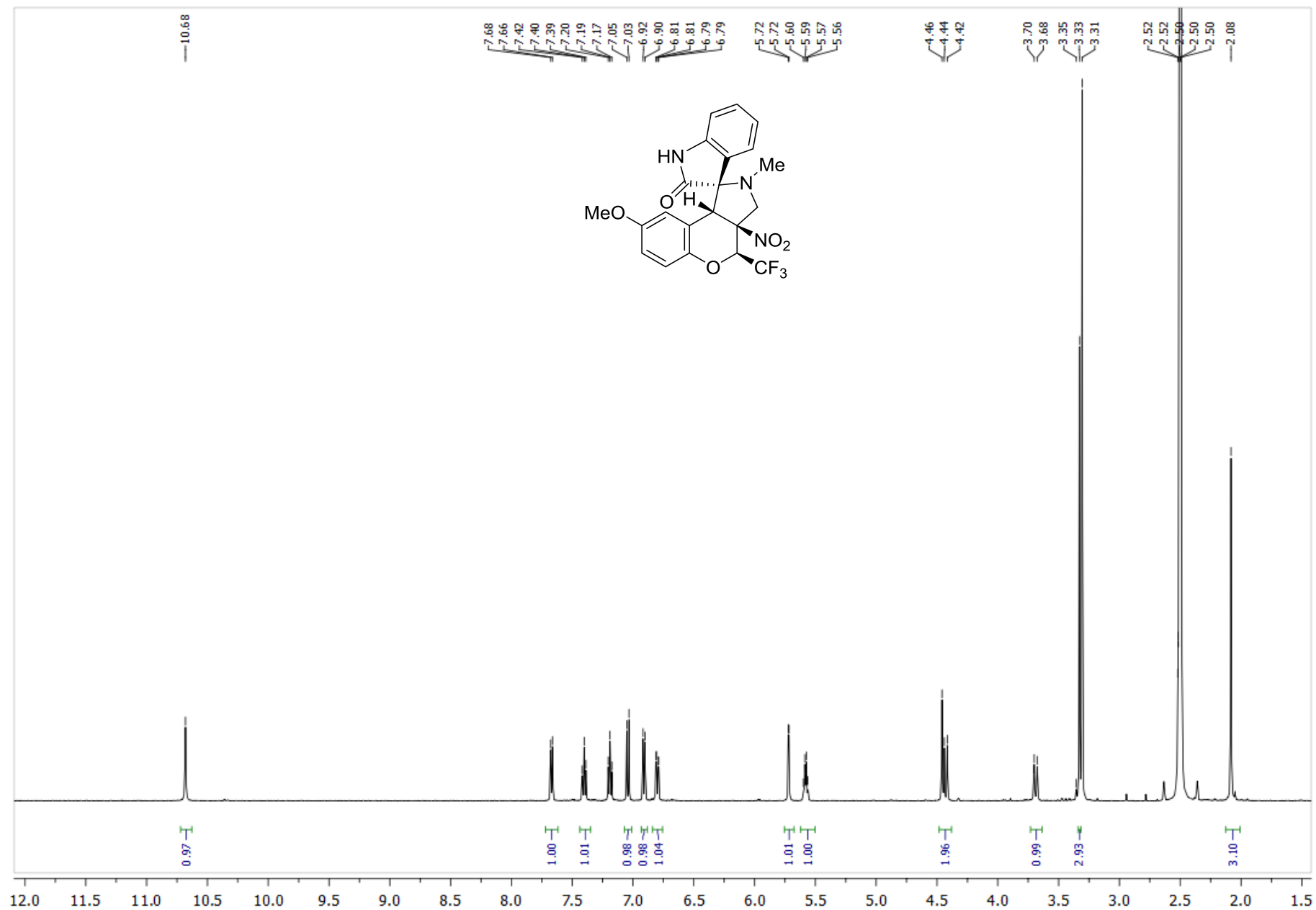


Figure S13. Copy of ¹H NMR spectrum of **6c** in DMSO-*d*₆

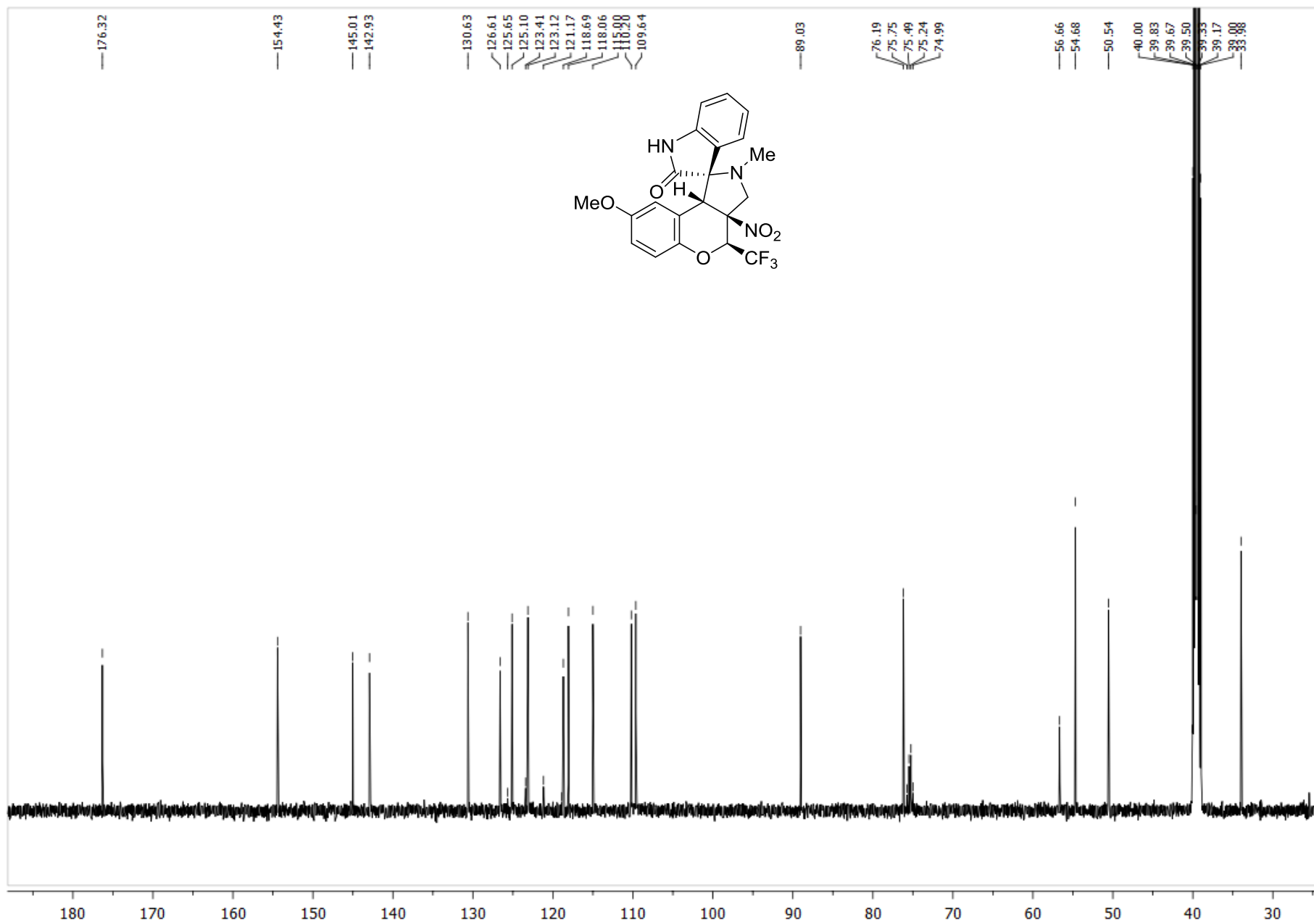


Figure S14. Copy of ¹³C NMR spectrum of **6c** in DMSO-*d*₆

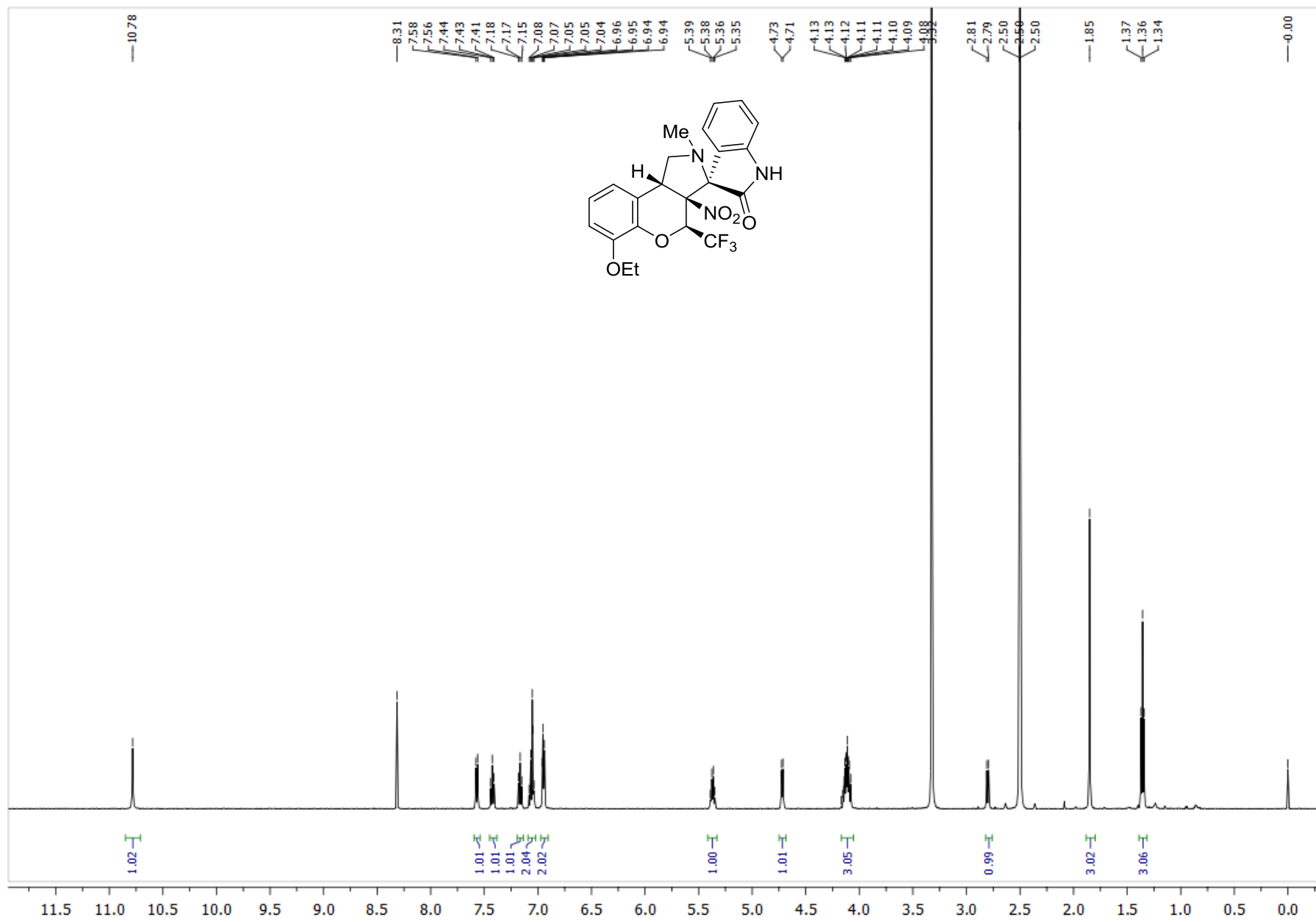


Figure S15. Copy of ¹H NMR spectrum of **5d** in DMSO-*d*₆

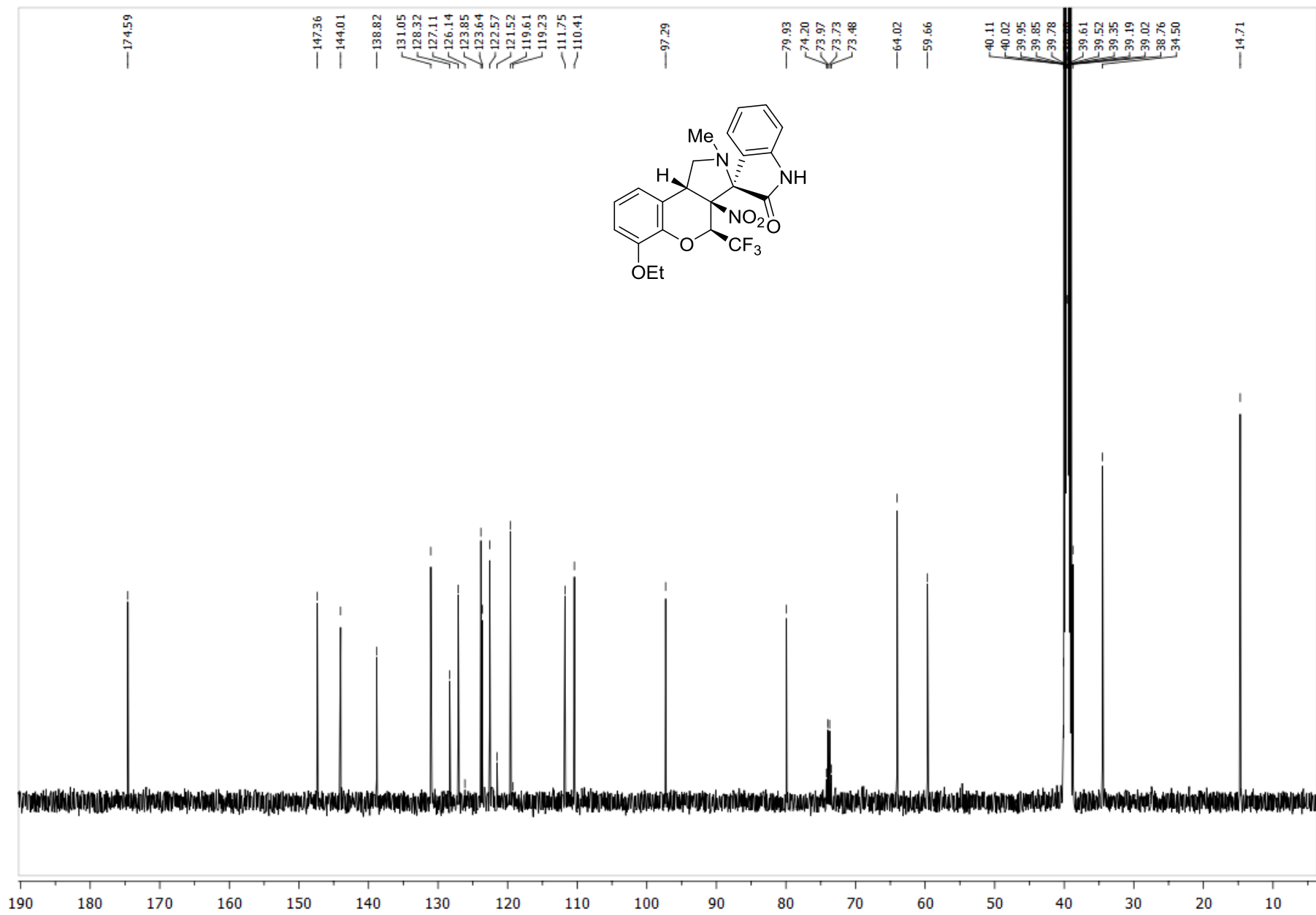


Figure S16. Copy of ¹³C NMR spectrum of **5d** in DMSO-*d*₆

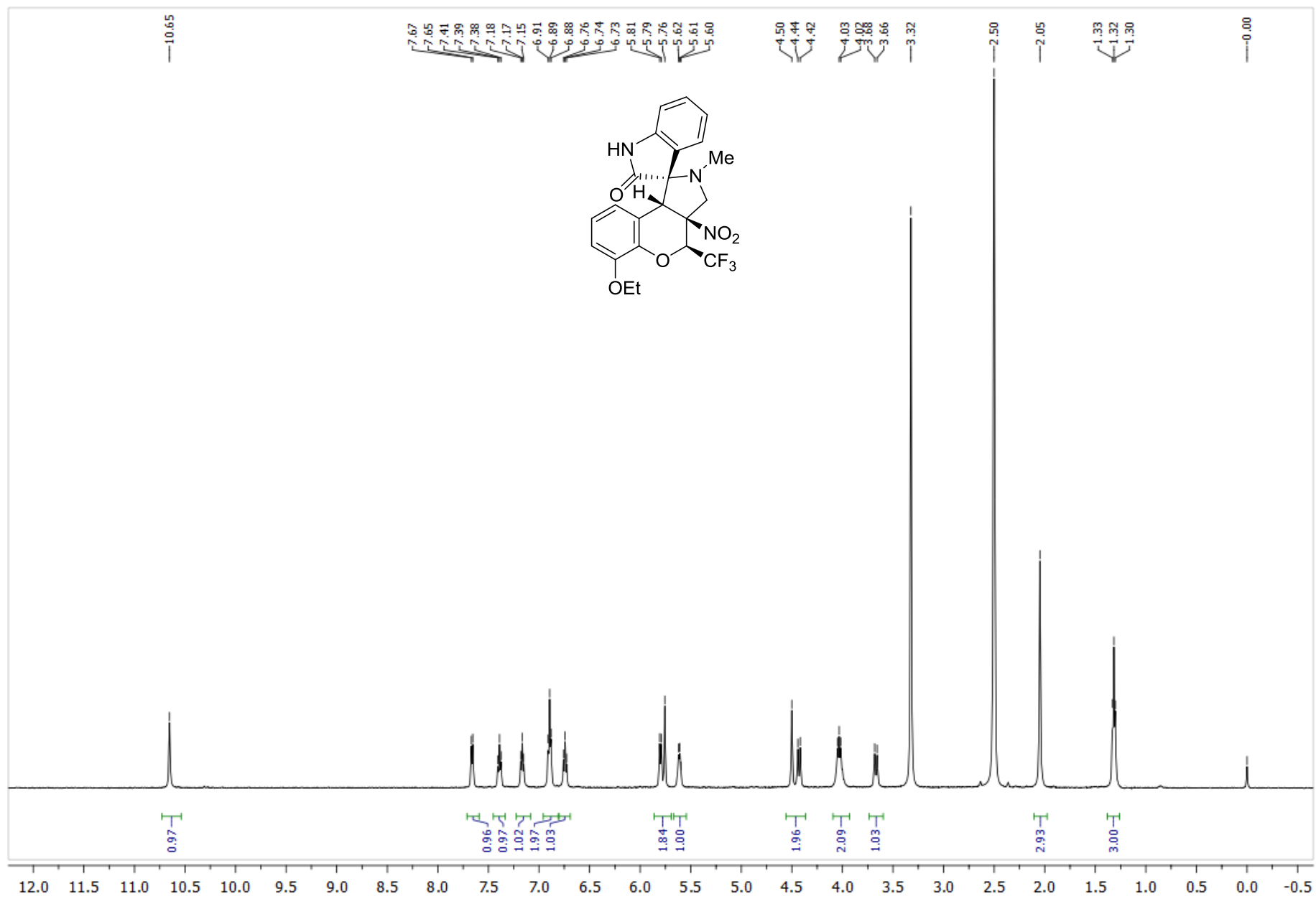


Figure S17. Copy of ¹H NMR spectrum of **6d** in DMSO-*d*₆

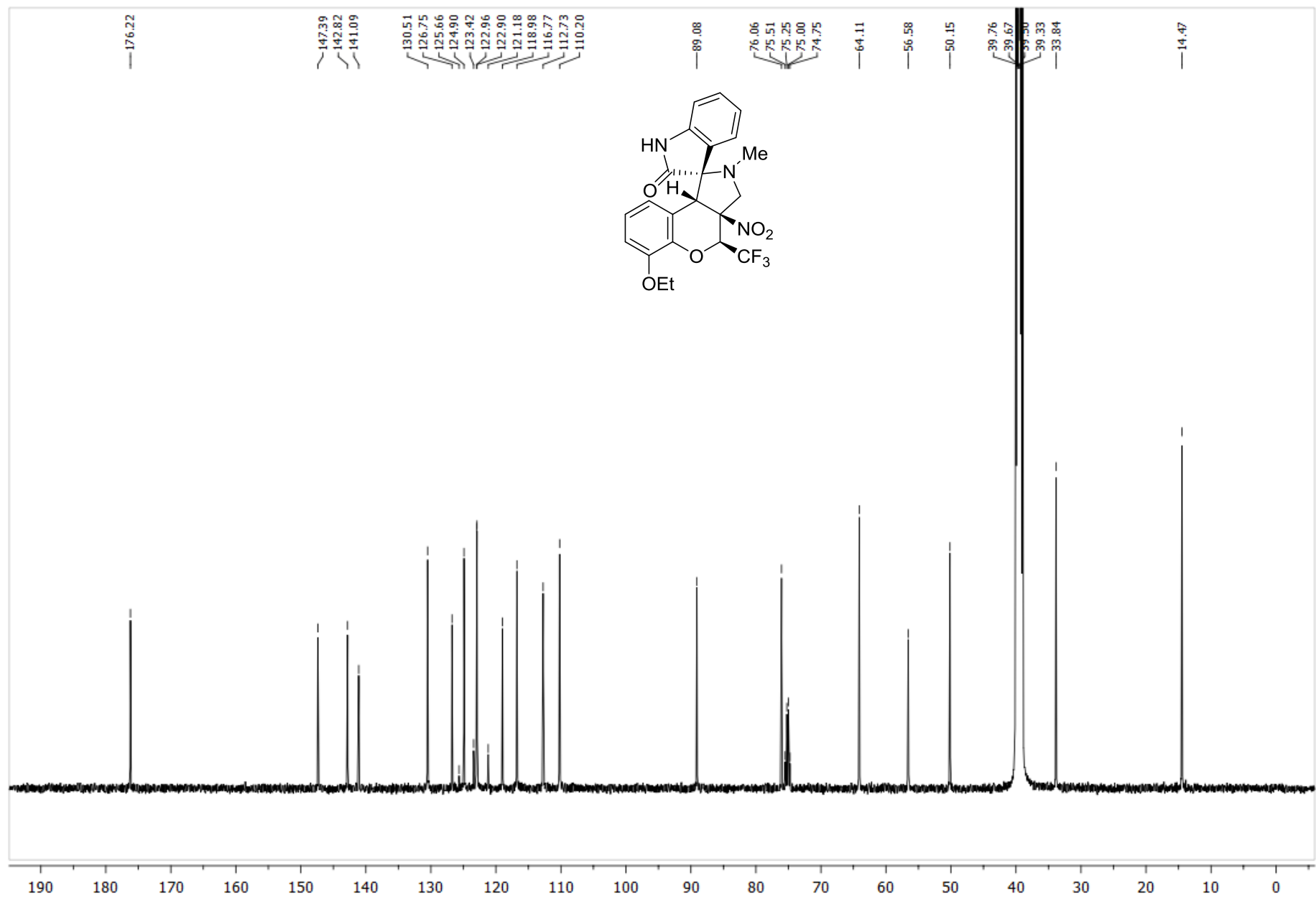


Figure S18. Copy of ¹³C NMR spectrum of **6d** in DMSO-*d*₆

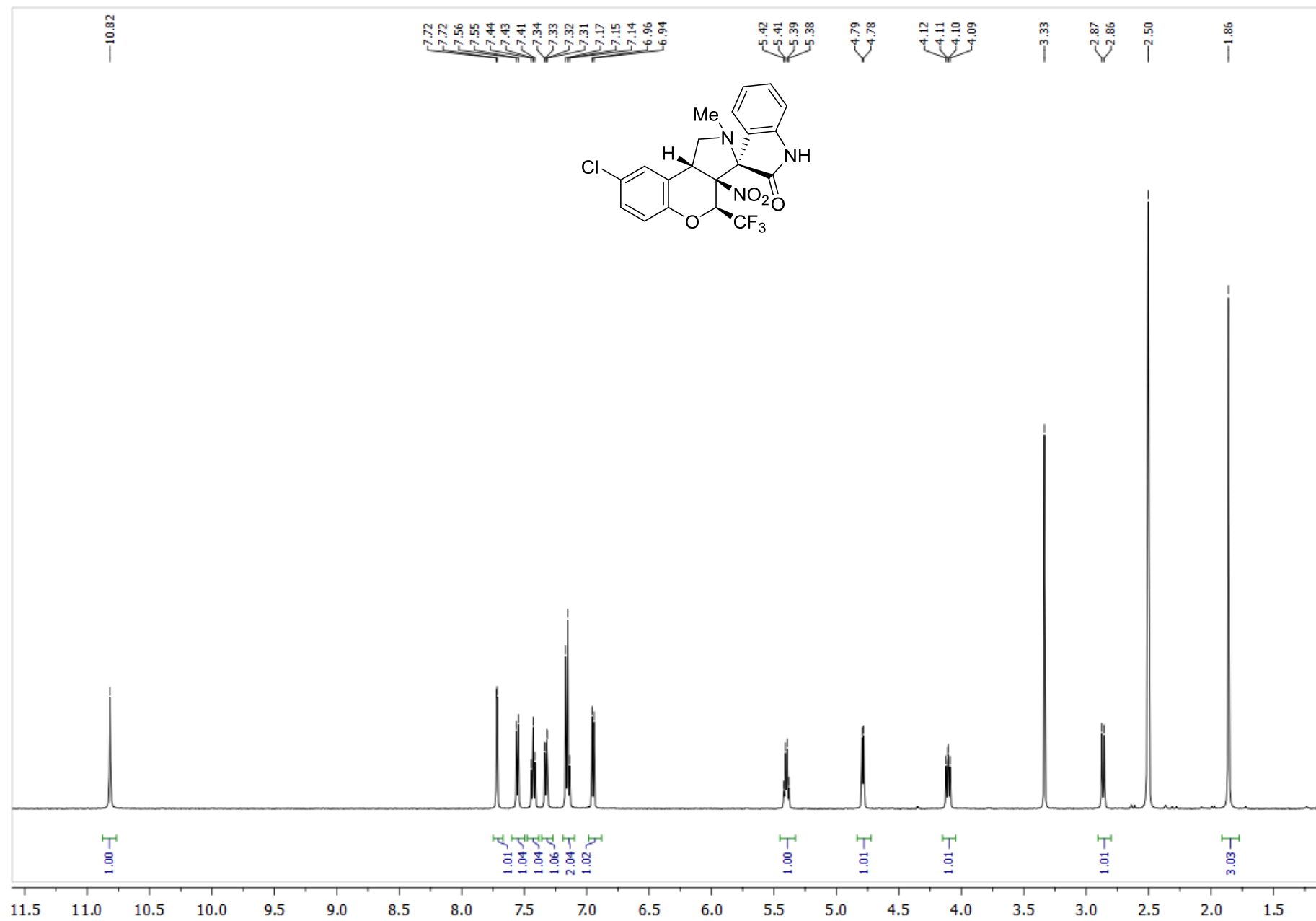


Figure S19. Copy of ^1H NMR spectrum of **5e** in $\text{DMSO-}d_6$

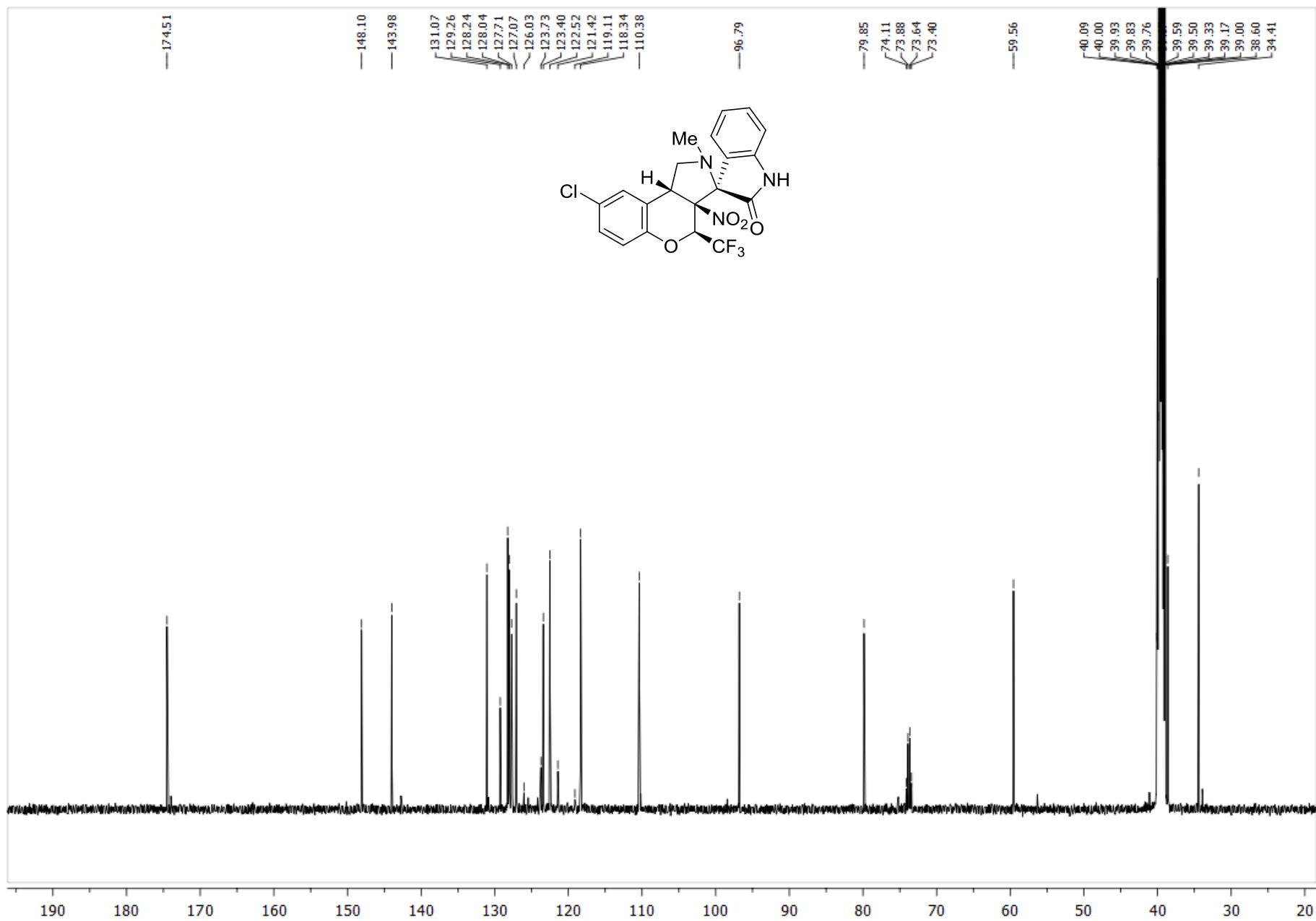


Figure S20. Copy of ^{13}C NMR spectrum of **5e** in $\text{DMSO-}d_6$

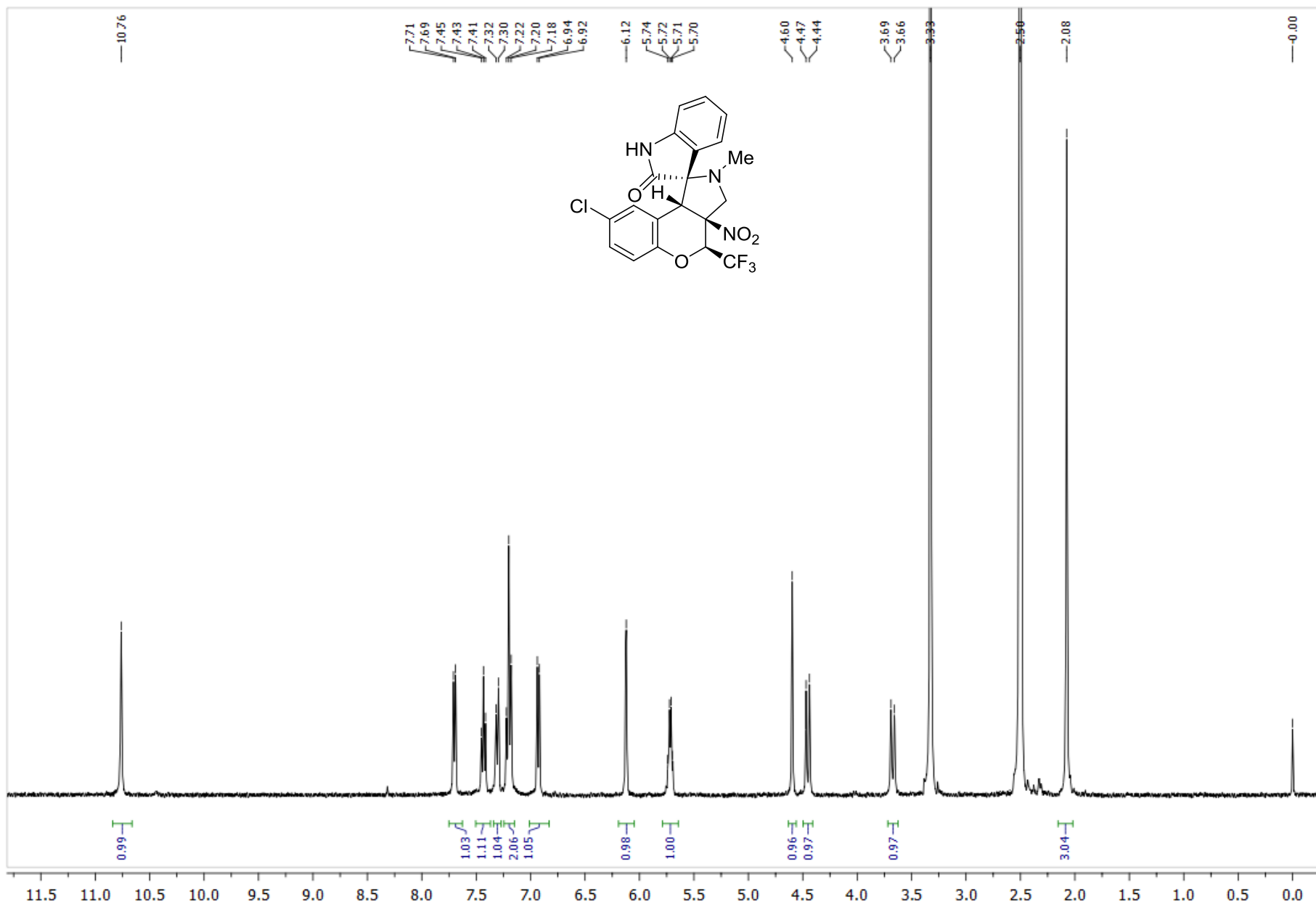


Figure S21. Copy of ^1H NMR spectrum of **6e** in $\text{DMSO-}d_6$

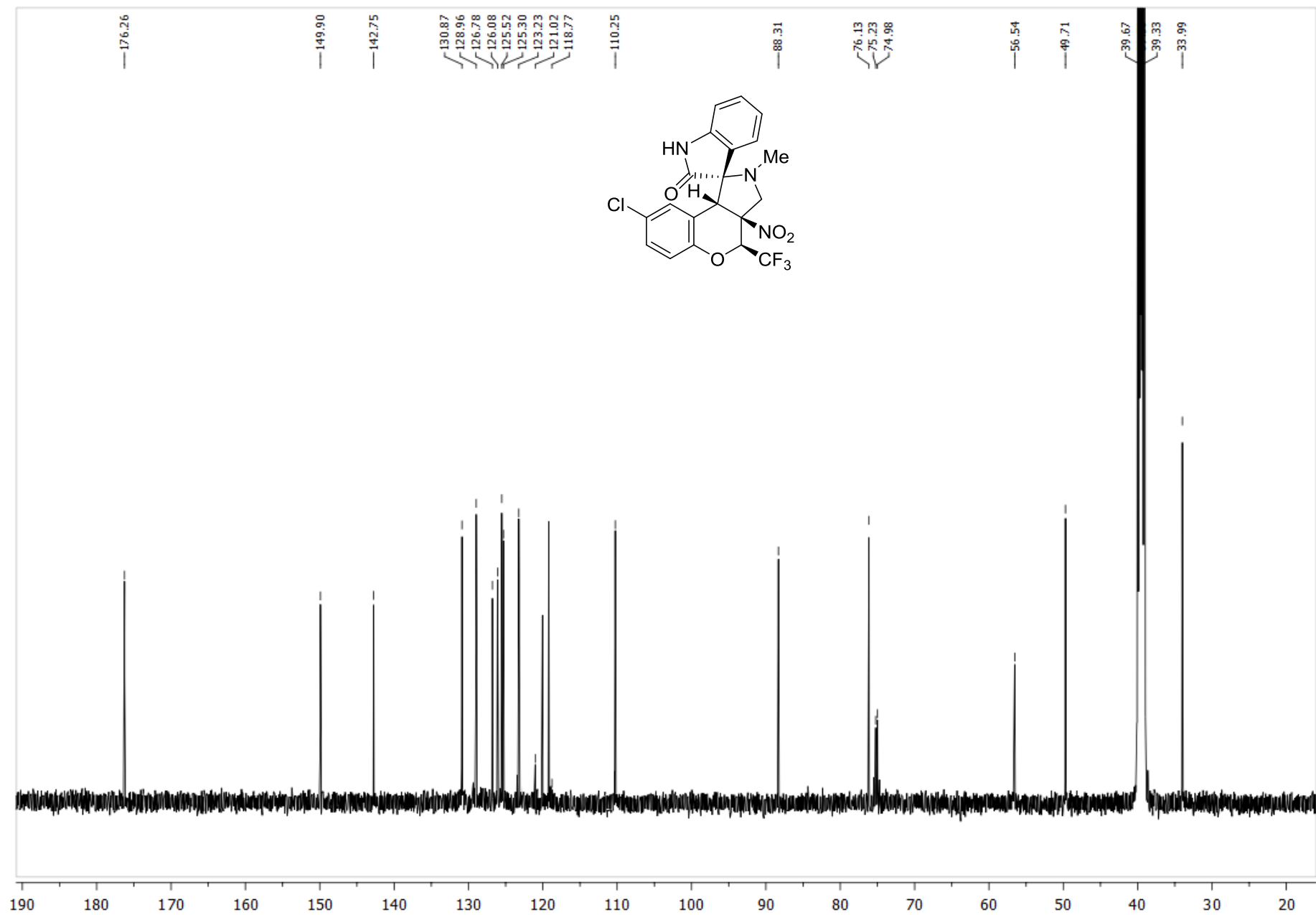


Figure S22. Copy of ^{13}C NMR spectrum of **6e** in $\text{DMSO-}d_6$

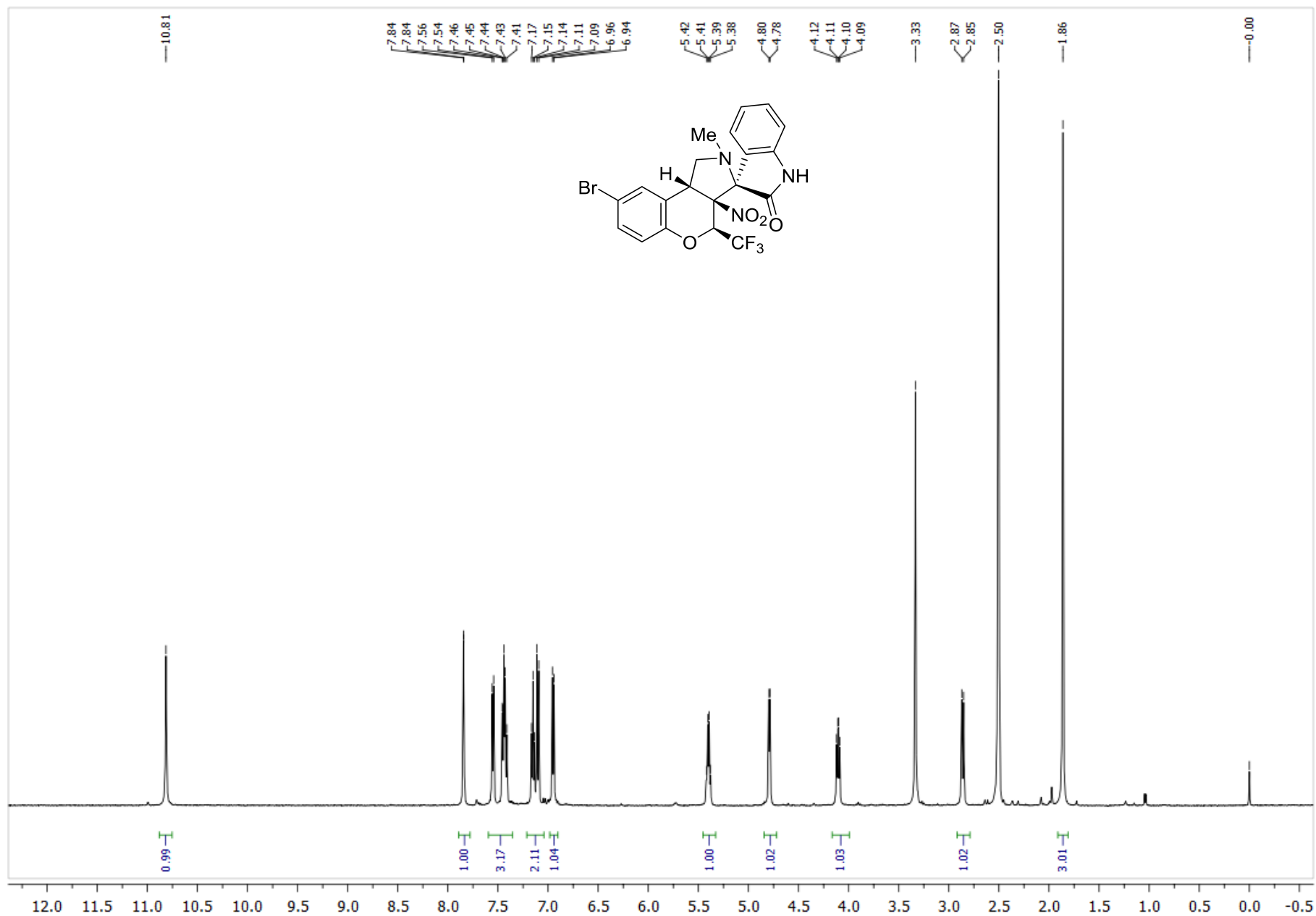


Figure S23. Copy of ^1H NMR spectrum of **5f** in $\text{DMSO}-d_6$

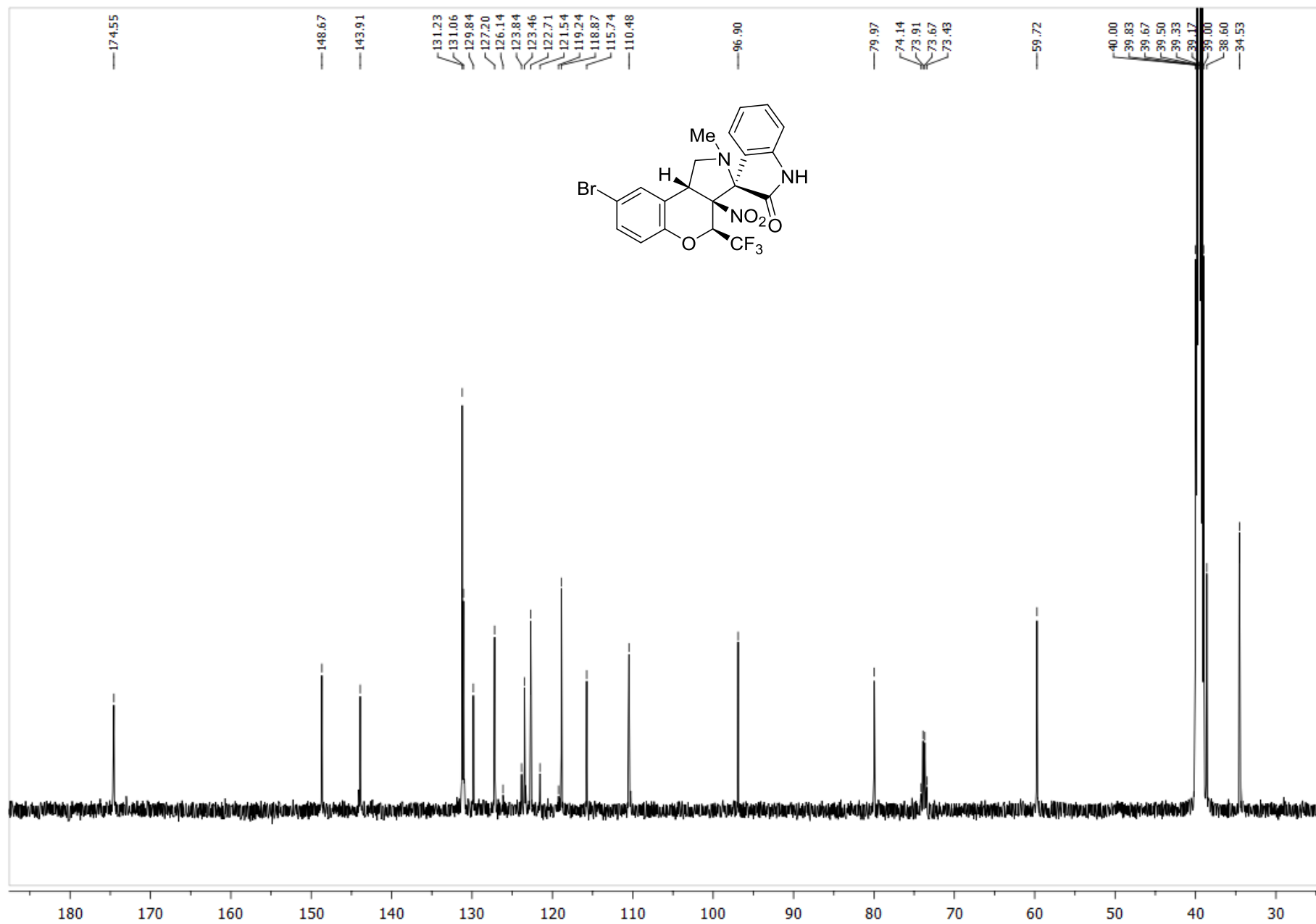


Figure S24. Copy of ^{13}C NMR spectrum of **5f** in $\text{DMSO-}d_6$

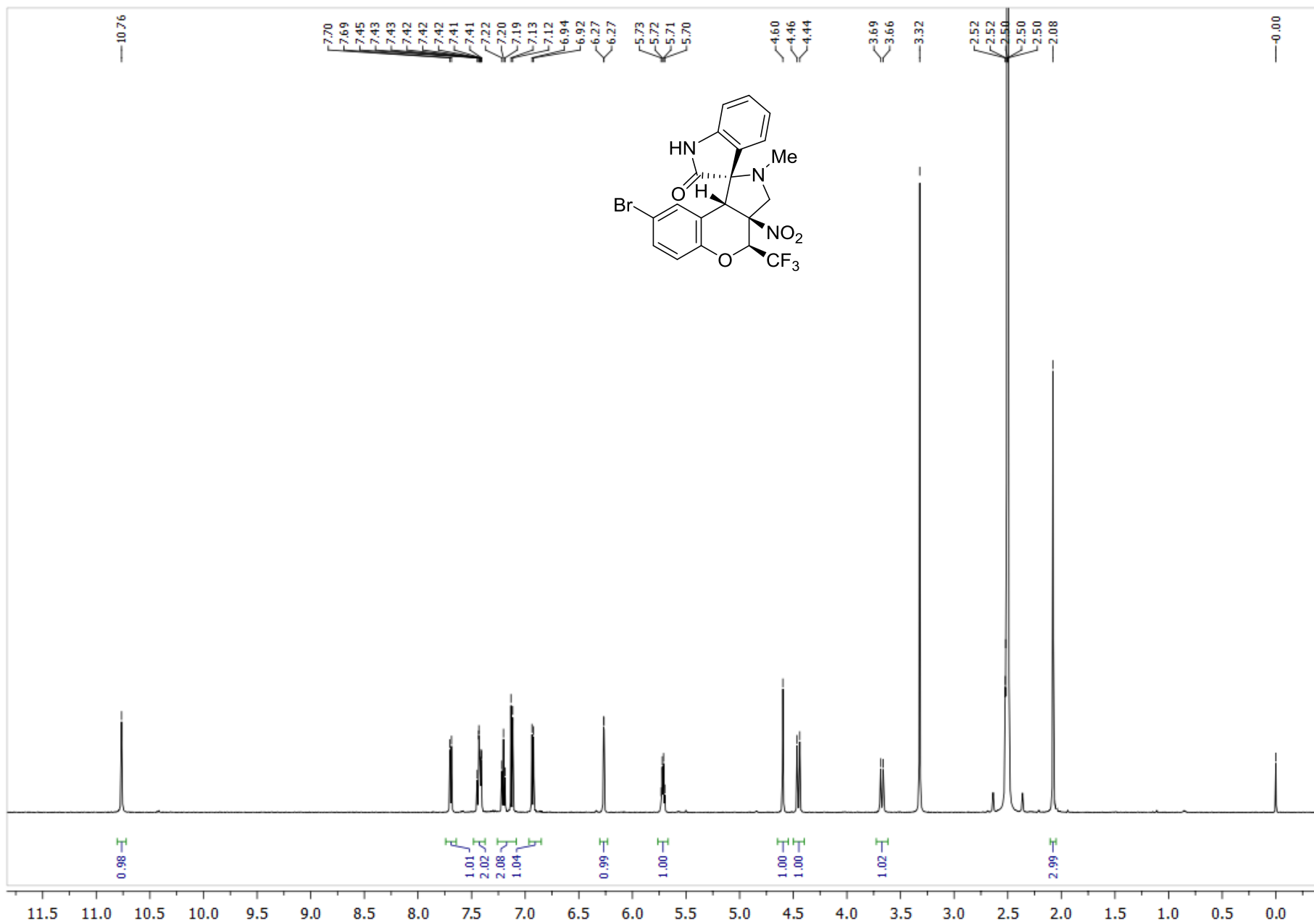


Figure S25. Copy of $^1\text{H NMR}$ spectrum of **6f** in $\text{DMSO-}d_6$

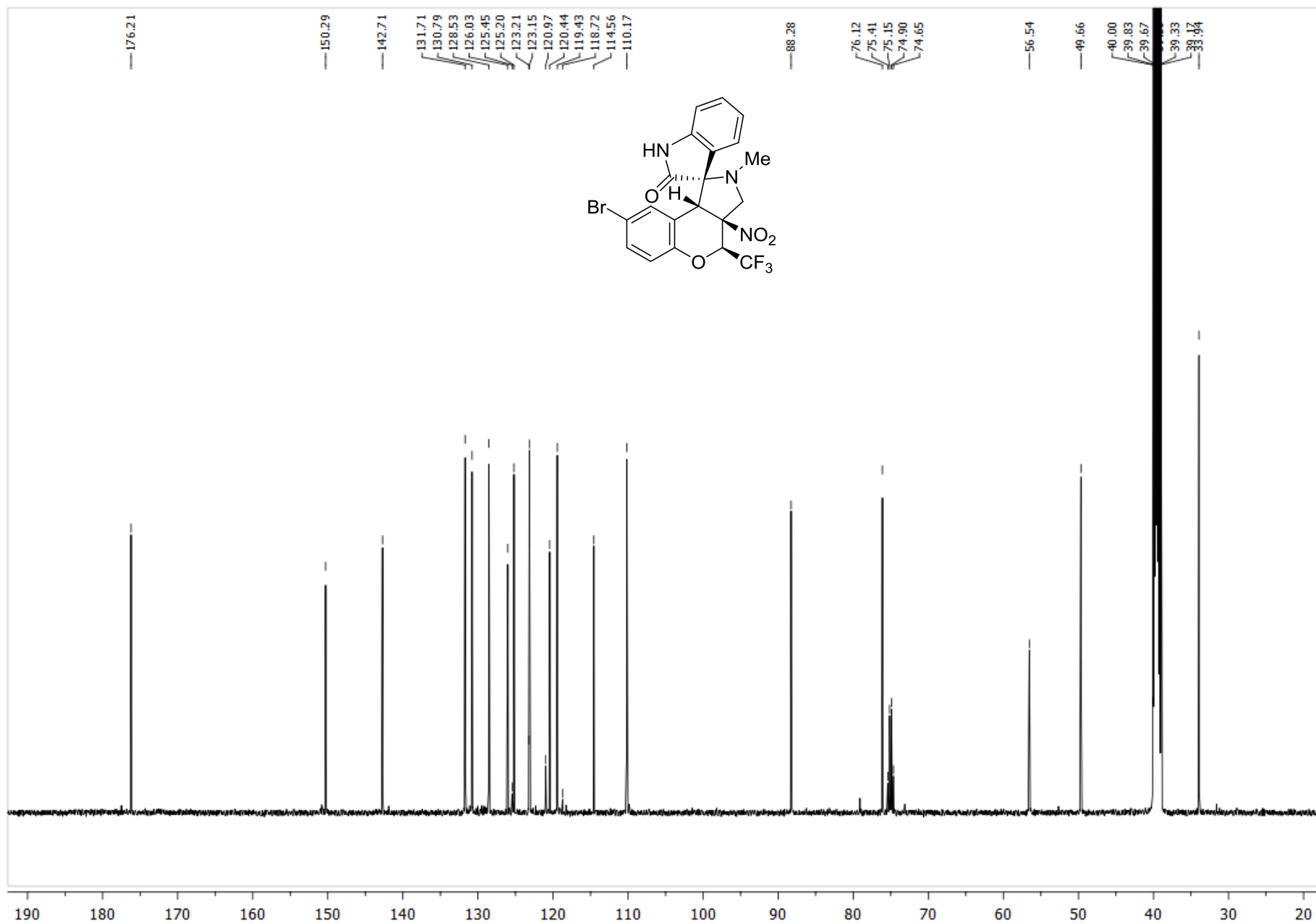


Figure S26. Copy of ^{13}C NMR spectrum of **6f** in $\text{DMSO-}d_6$

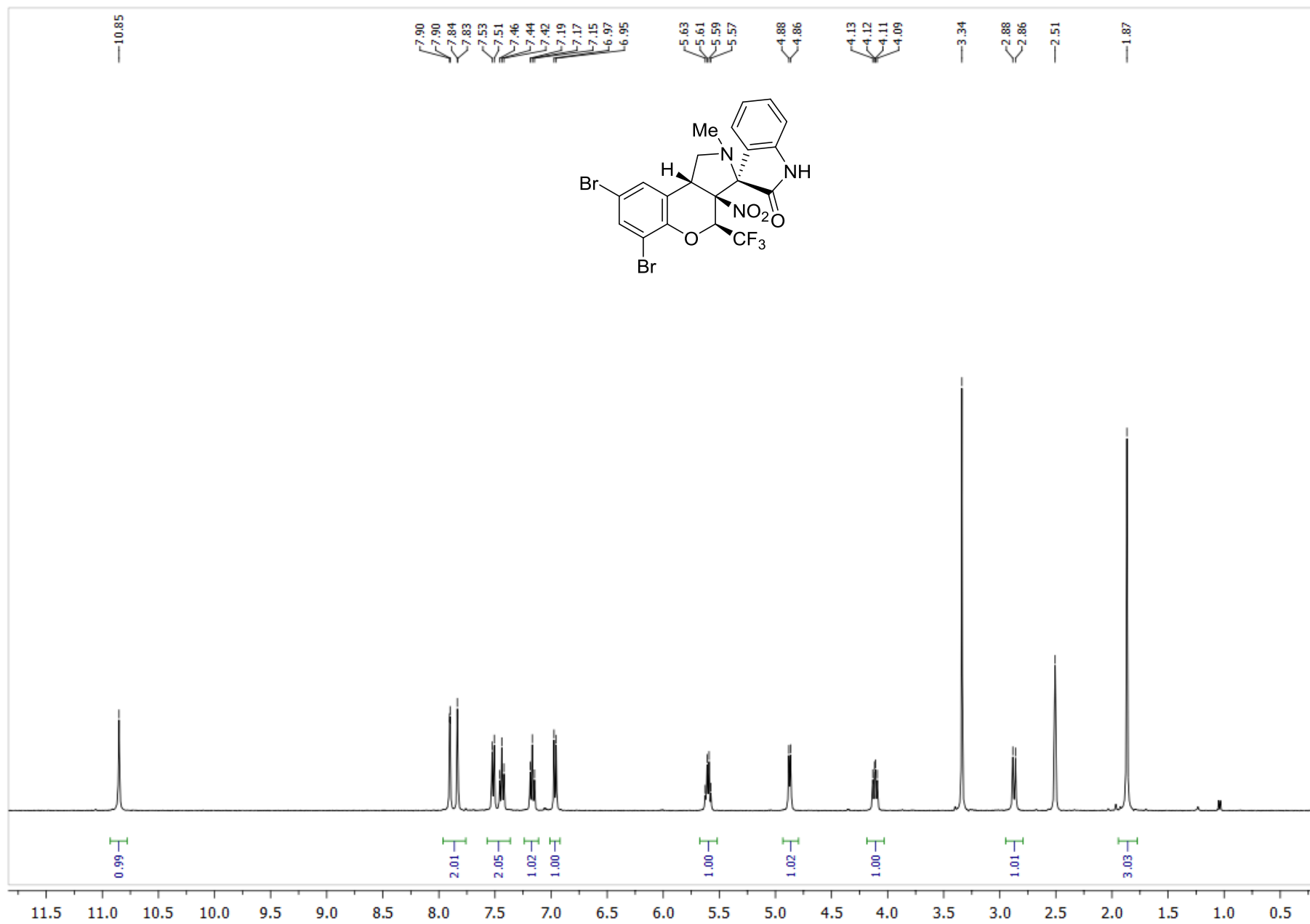


Figure S27. Copy of ¹H NMR spectrum of **5g** in DMSO-*d*₆

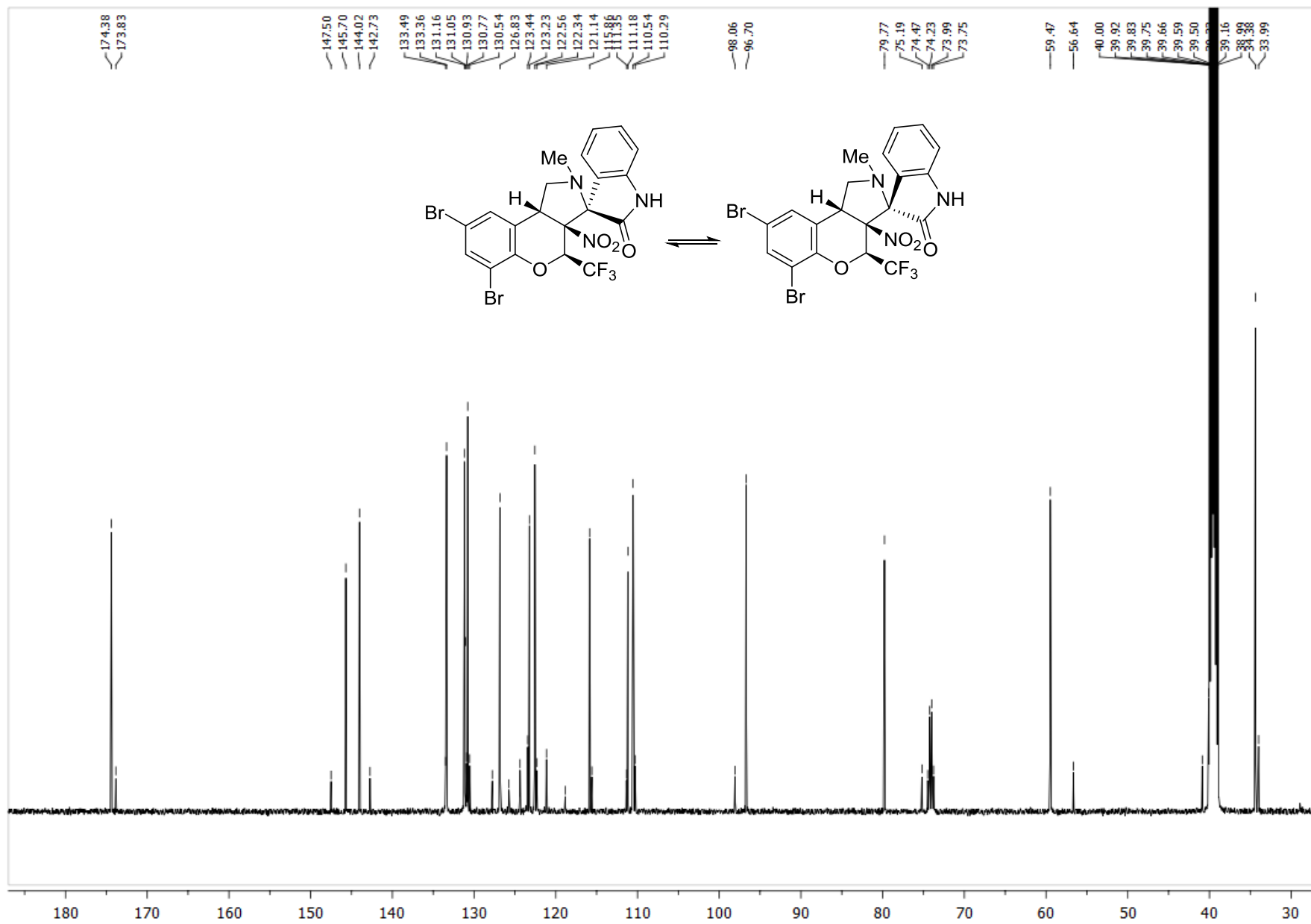


Figure S28. Copy of ^{13}C NMR spectrum of **5g** + **5'g** in $\text{DMSO-}d_6$

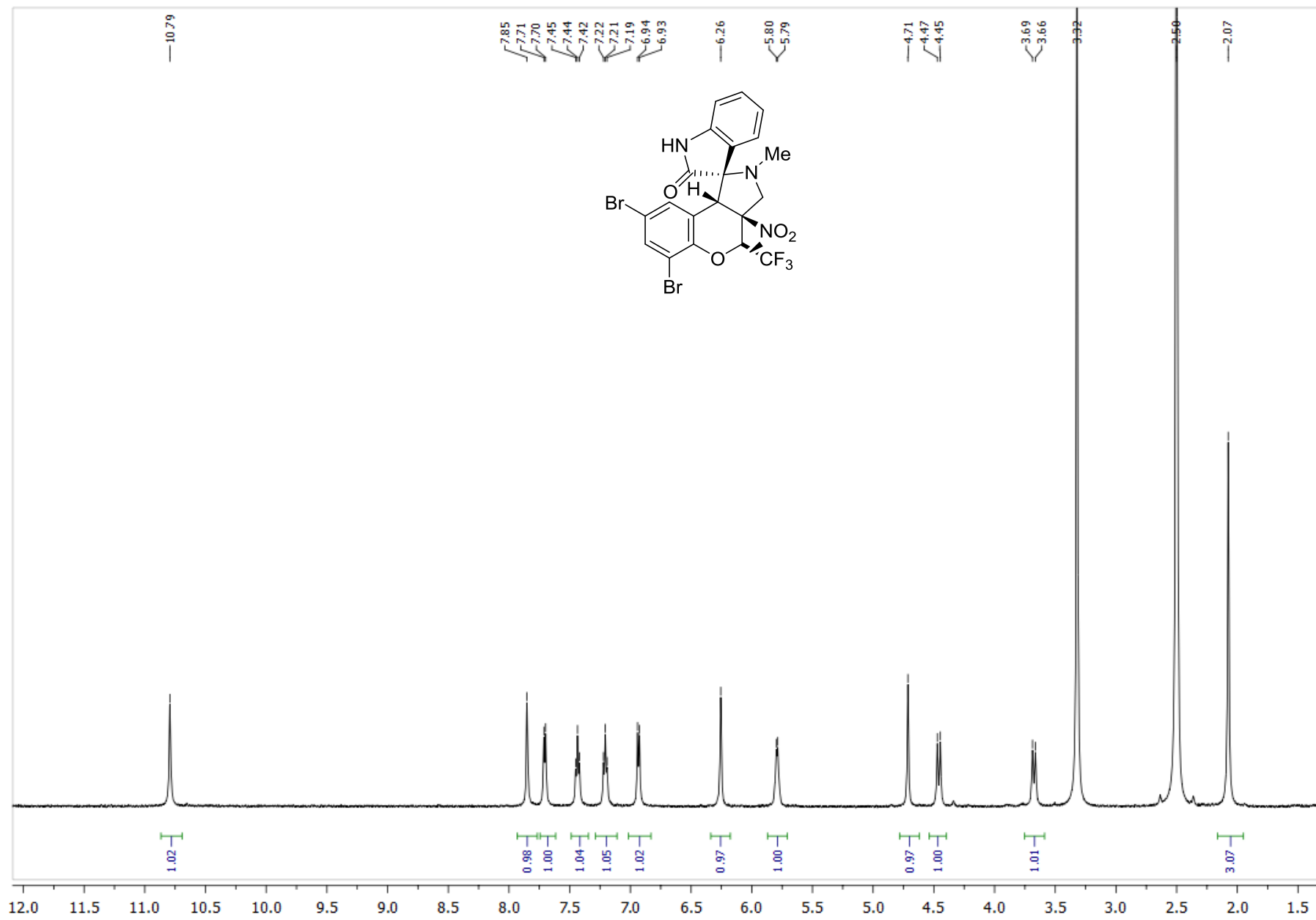


Figure S29. Copy of ¹H NMR spectrum of **6g** in DMSO-*d*₆

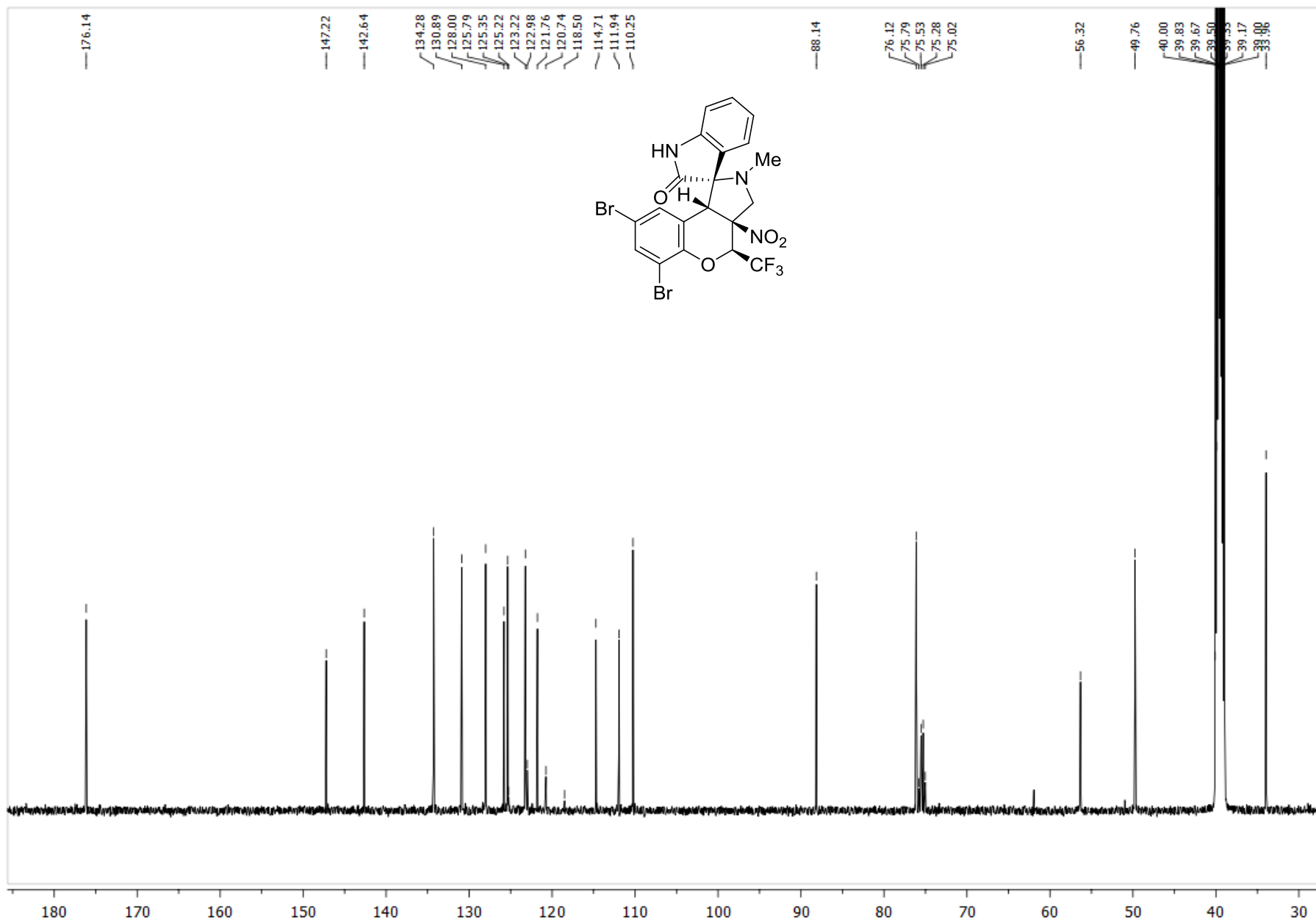


Figure S30. Copy of ^{13}C NMR spectrum of **6g** in $\text{DMSO-}d_6$

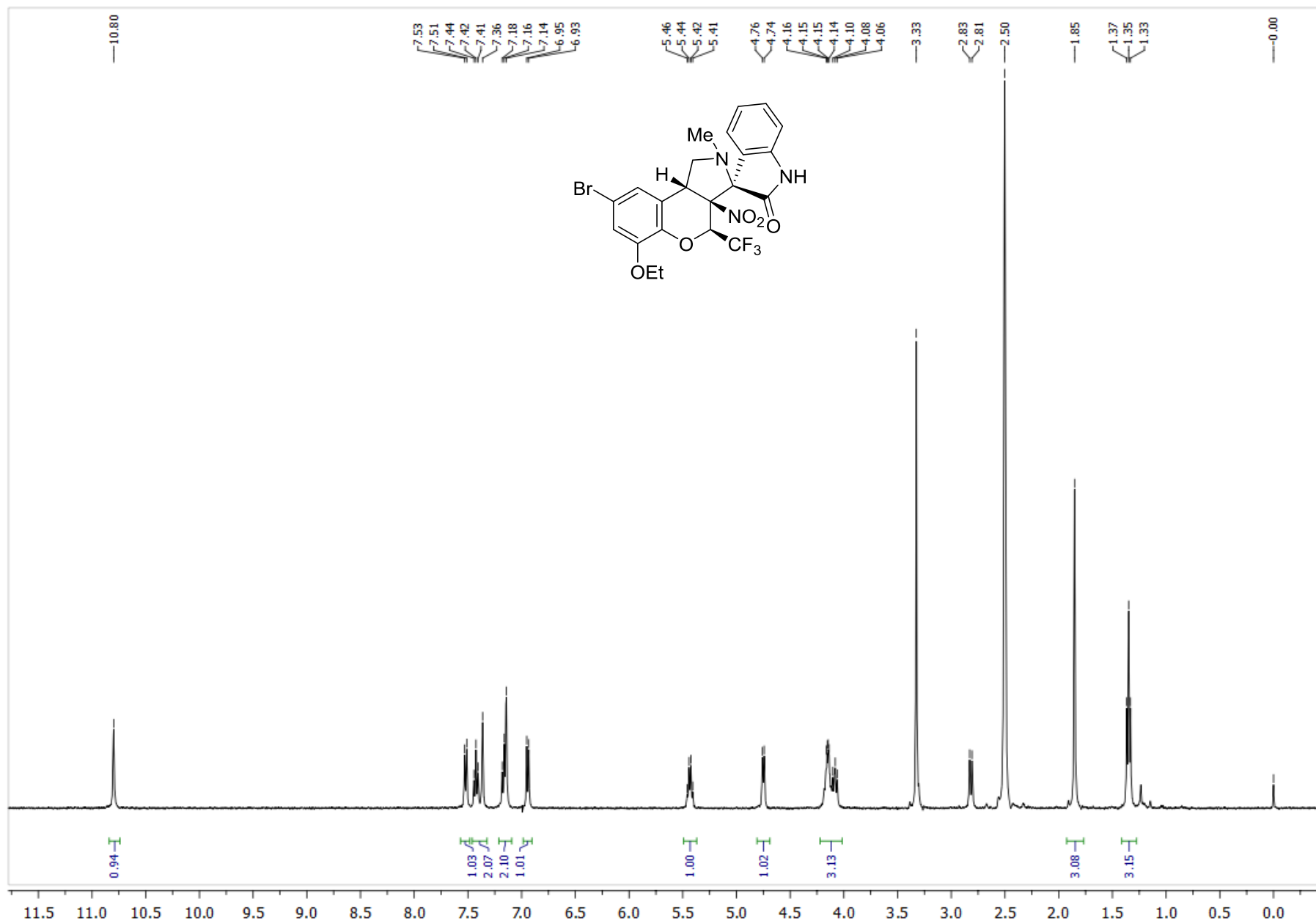


Figure S31. Copy of ¹H NMR spectrum of **5h** in DMSO-*d*₆

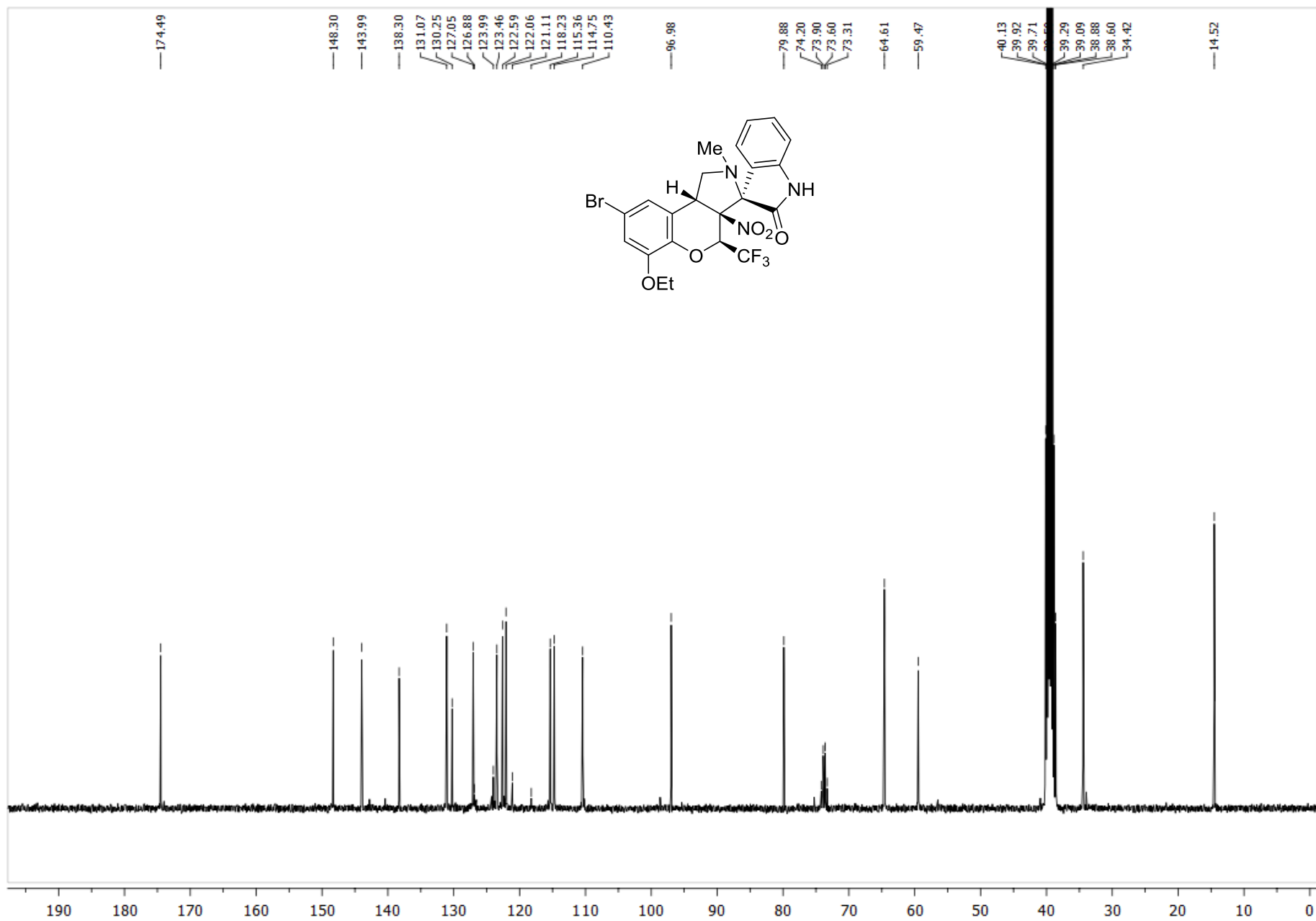


Figure S32. Copy of ¹³C NMR spectrum of **5h** in DMSO-*d*₆

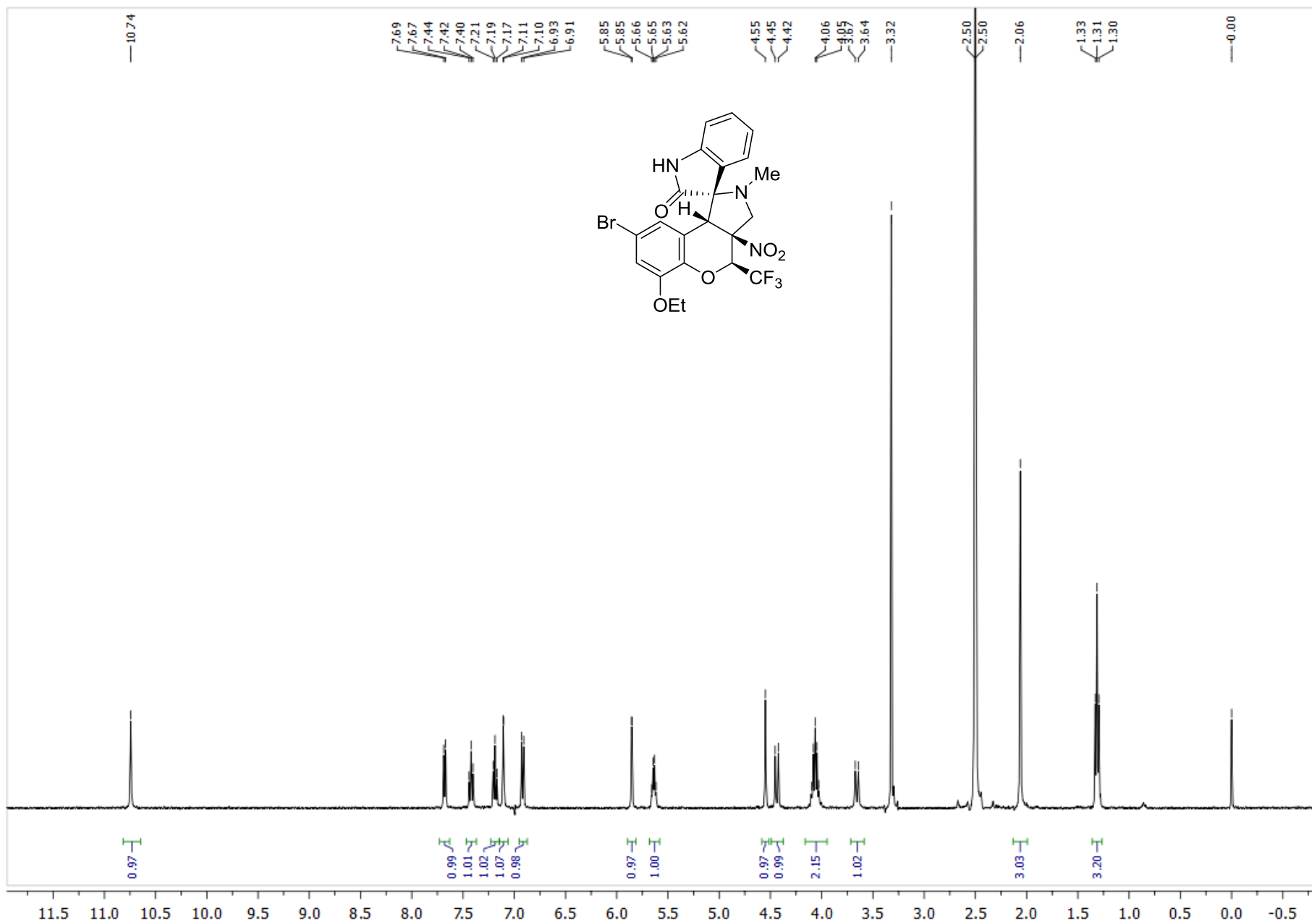


Figure S33. Copy of ¹H NMR spectrum of **6h** in DMSO-*d*₆

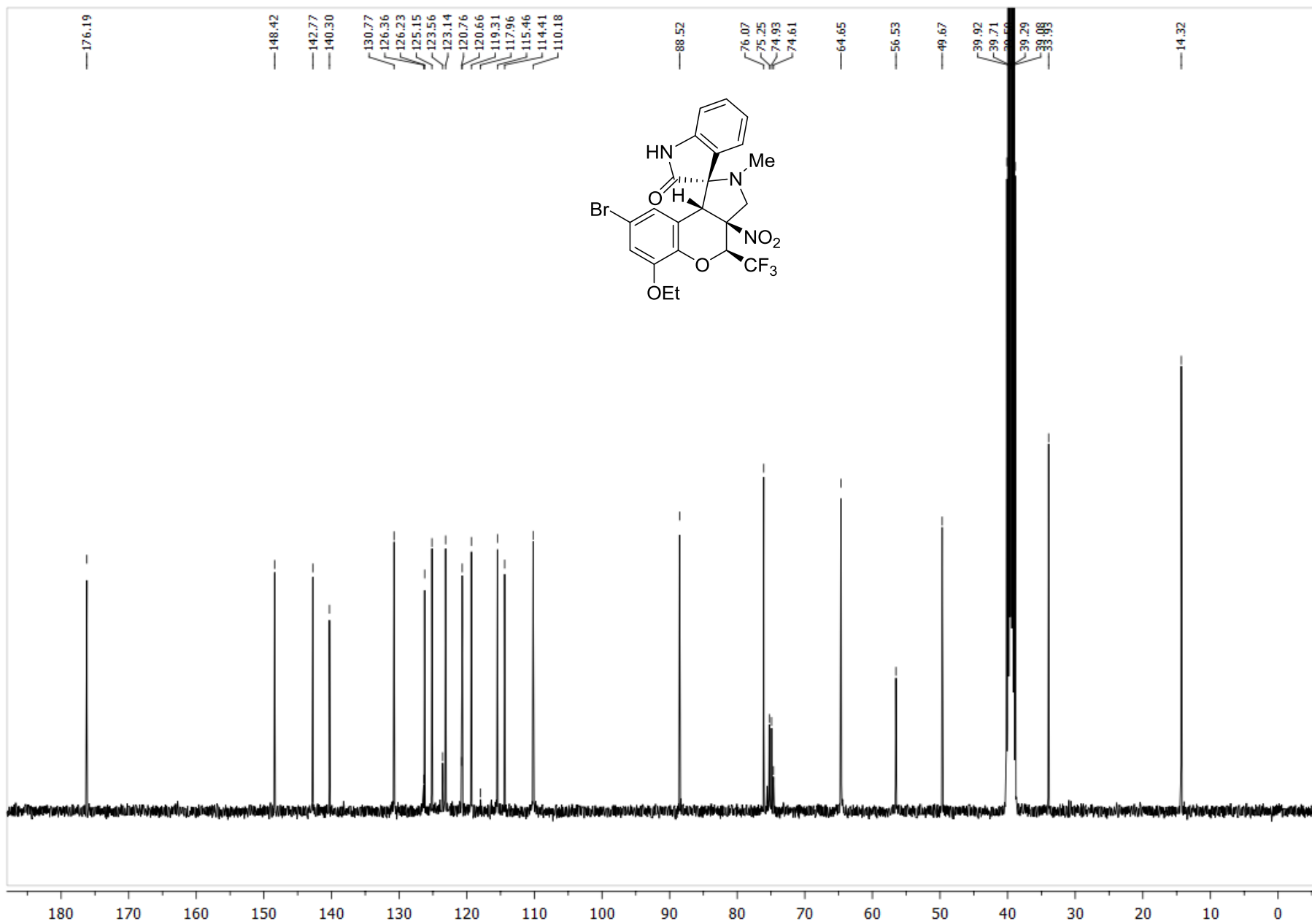


Figure S34. Copy of ¹³C NMR spectrum of **6h** in DMSO-*d*₆

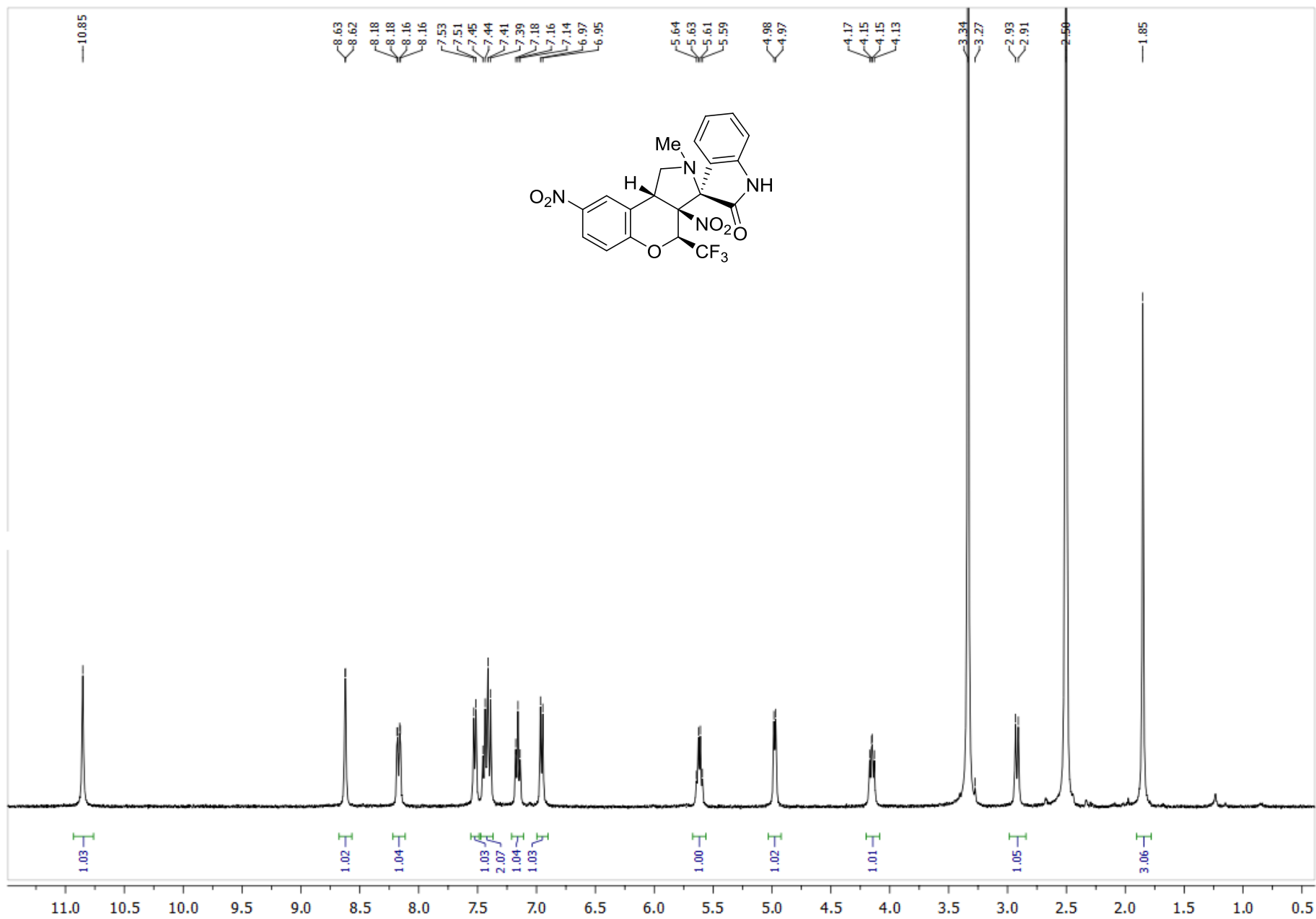


Figure S35. Copy of ¹H NMR spectrum of **5i** in DMSO-*d*₆

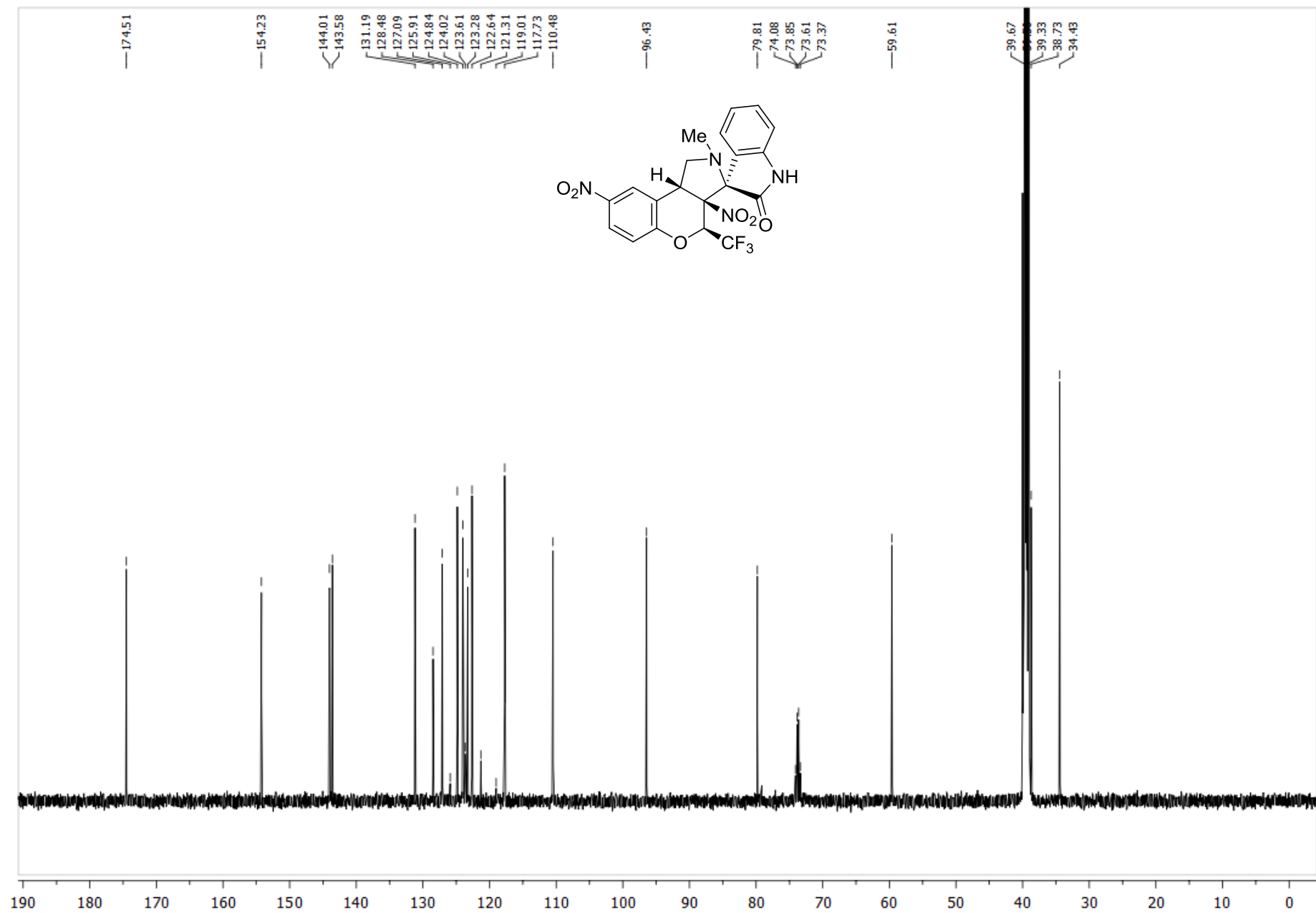


Figure S36. Copy of ^{13}C NMR spectrum of **5i** in $\text{DMSO-}d_6$

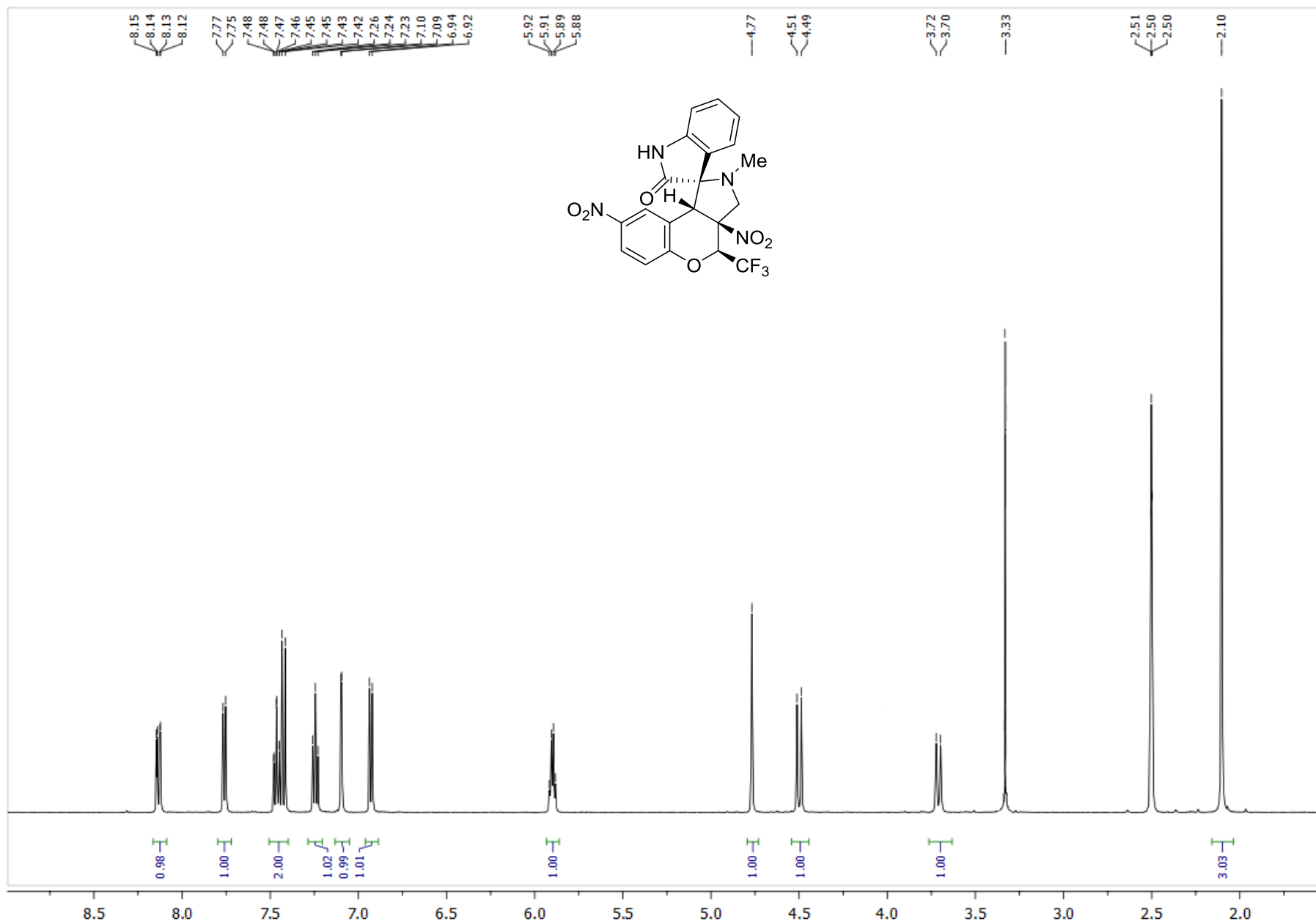


Figure S37. Copy of ¹H NMR spectrum of **6i** in DMSO-*d*₆

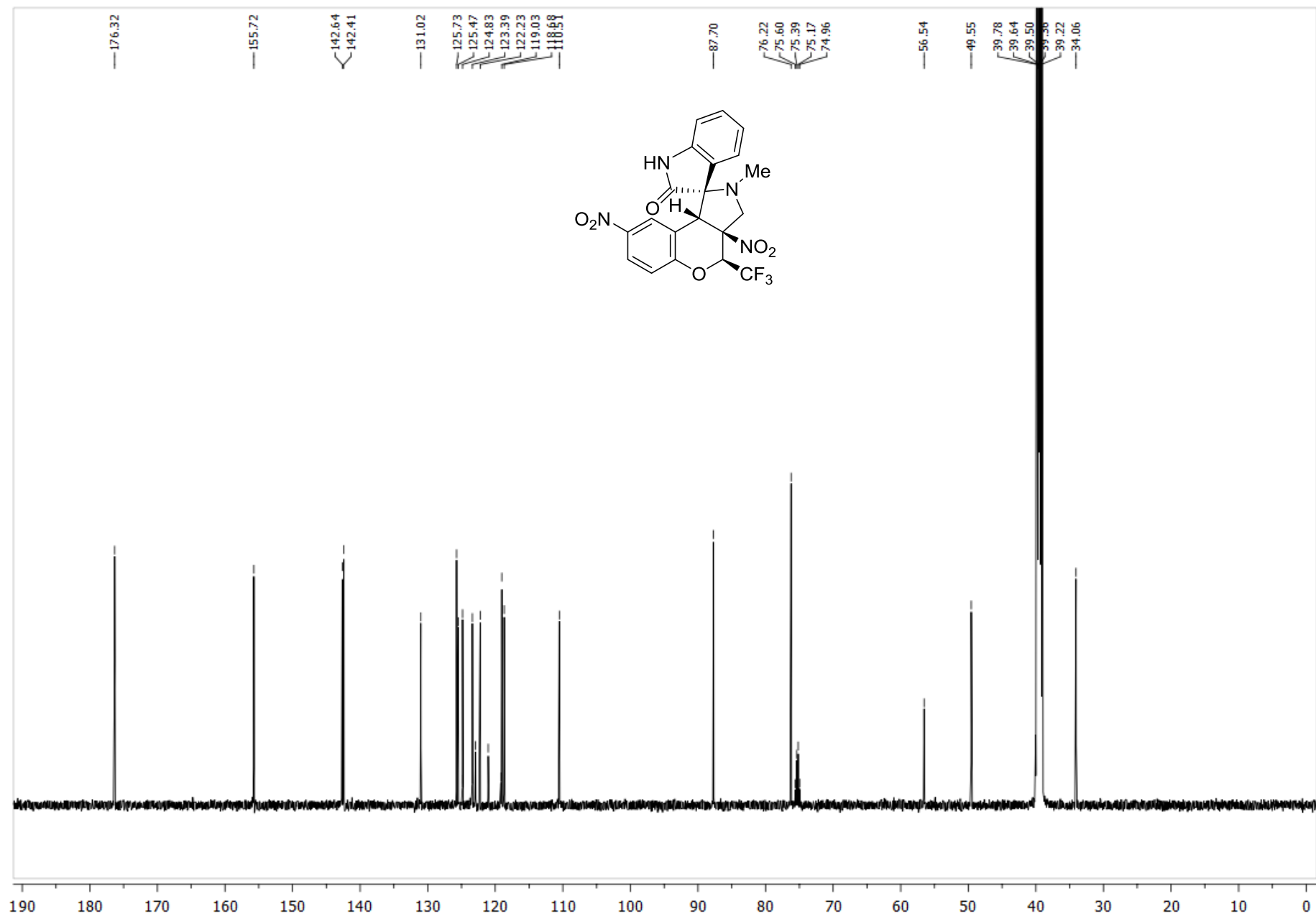


Figure S38. Copy of ¹³C NMR spectrum of **6i** in DMSO-*d*₆

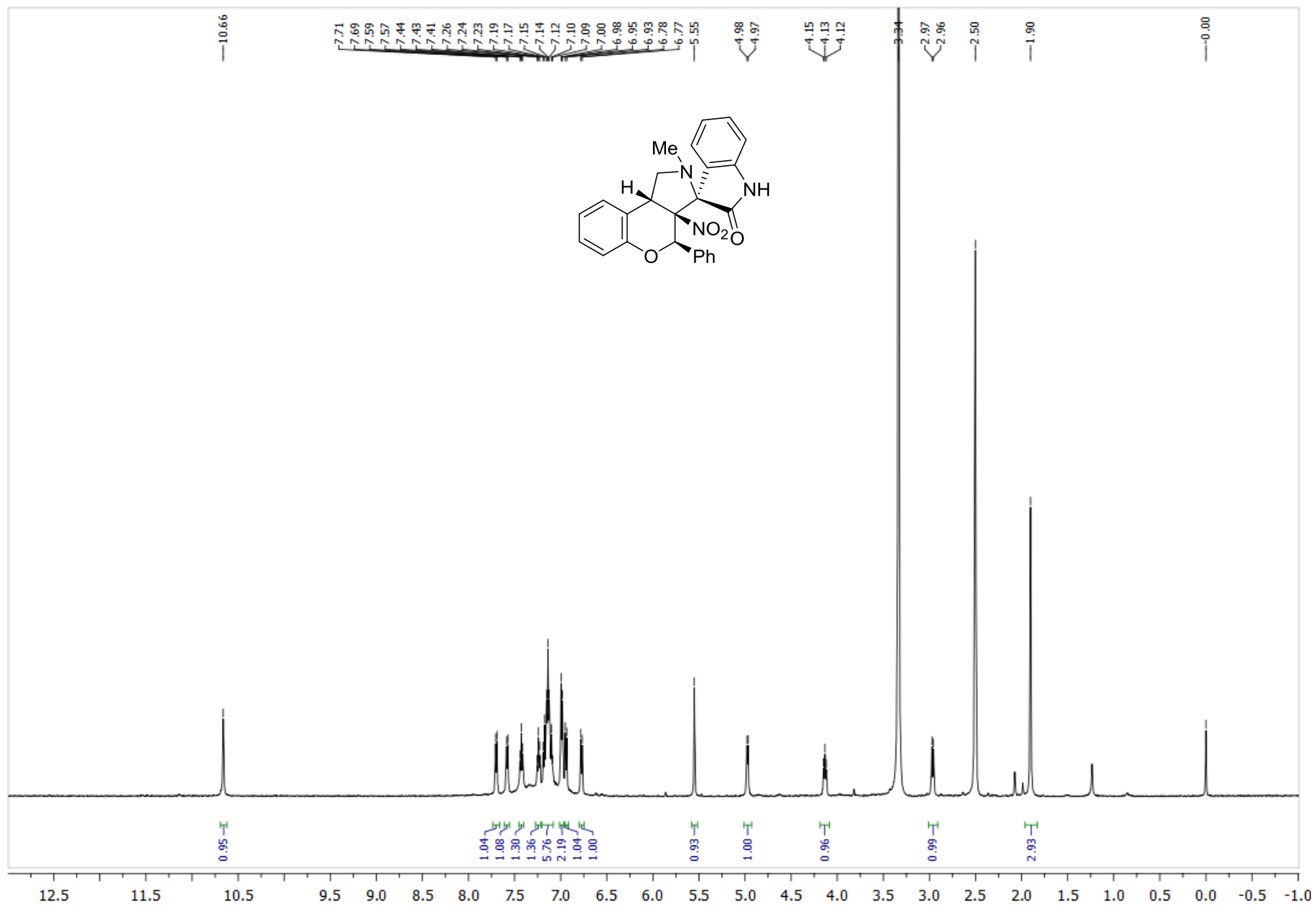


Figure S39. Copy of ¹H NMR spectrum of **5j** in DMSO-*d*₆

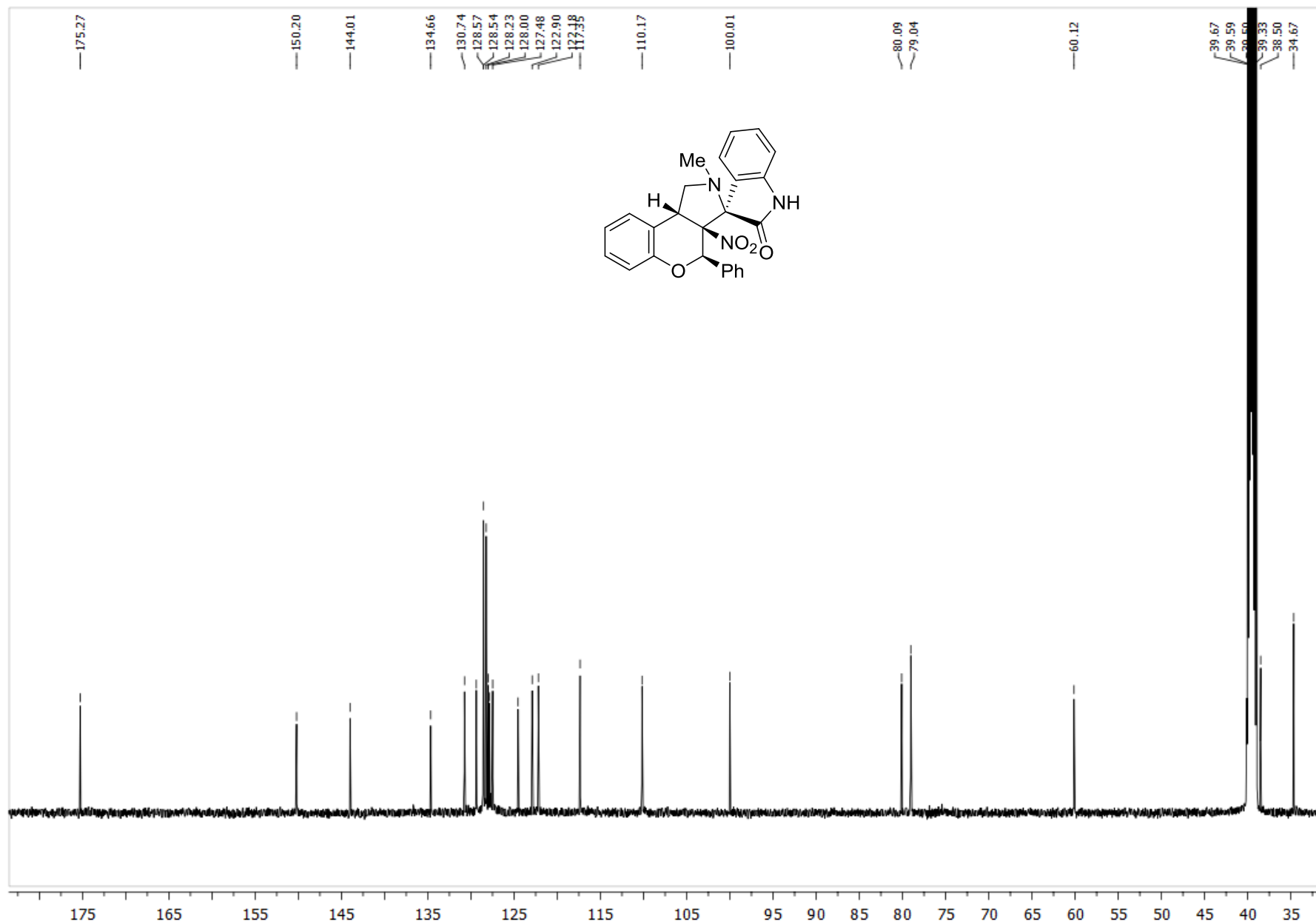


Figure S40. Copy of ^{13}C NMR spectrum of **5j** in $\text{DMSO-}d_6$

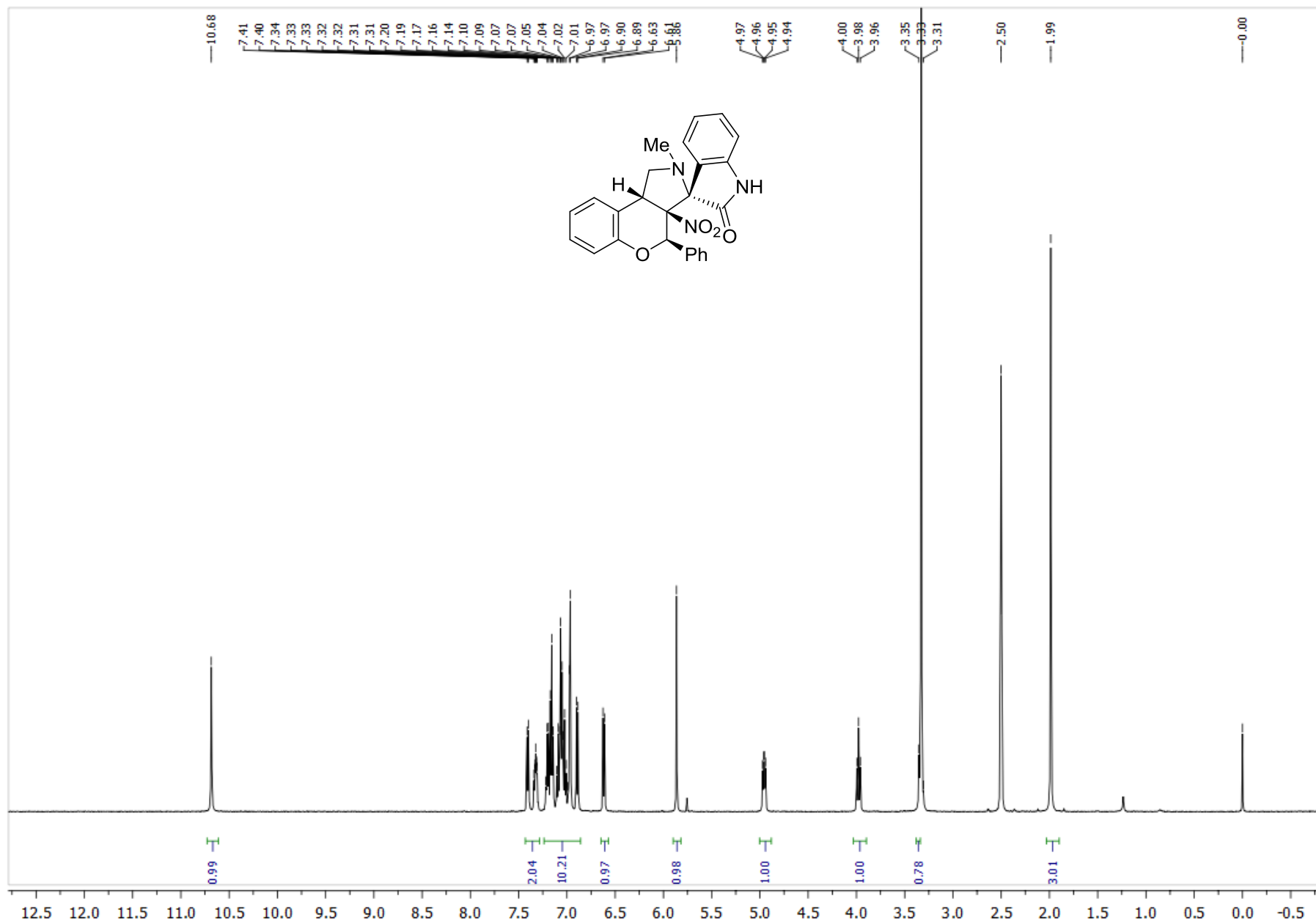


Figure S41. Copy of ¹H NMR spectrum of 5'j in DMSO-*d*₆

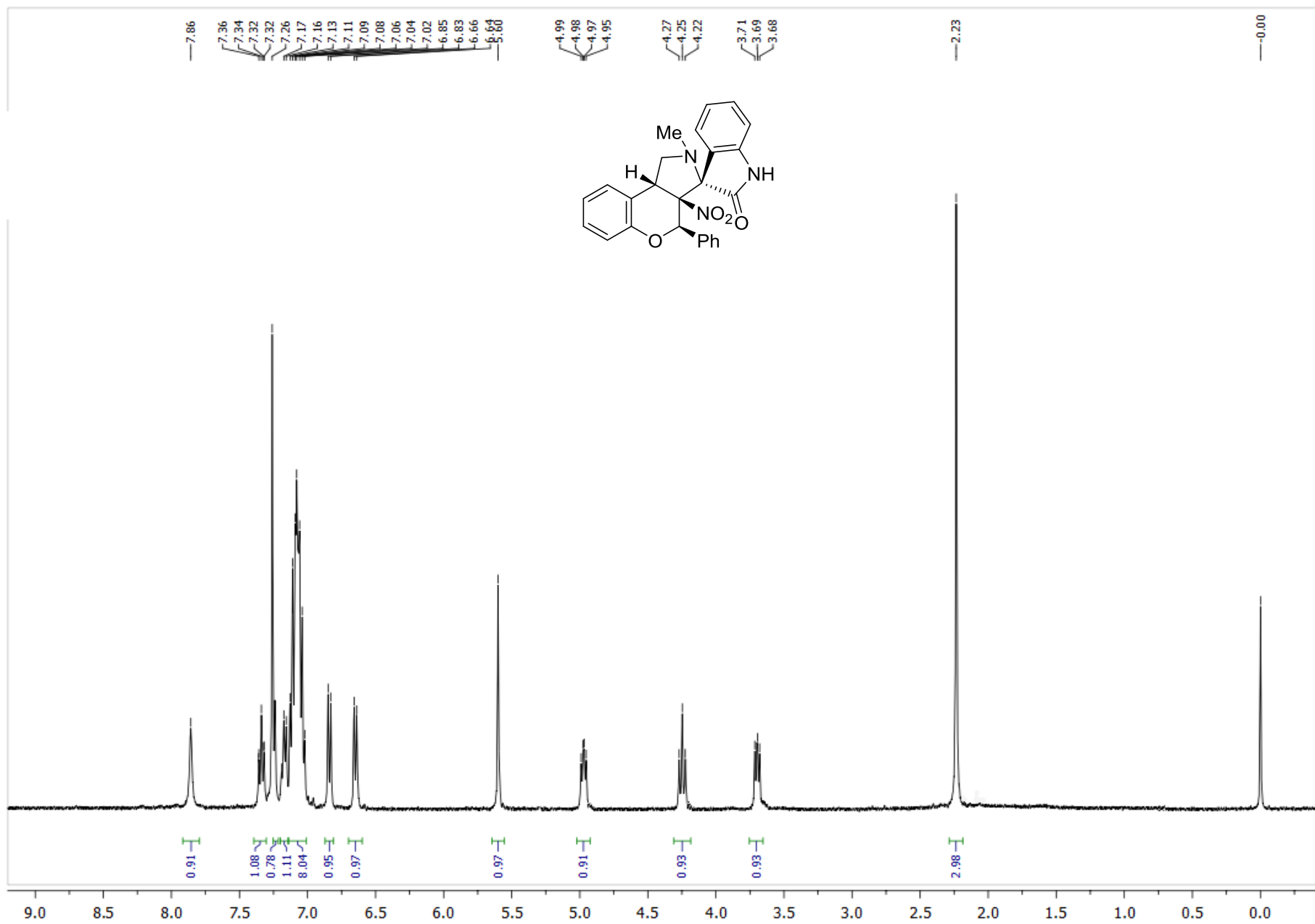


Figure S42. Copy of ¹H NMR spectrum of **5j** in CDCl₃

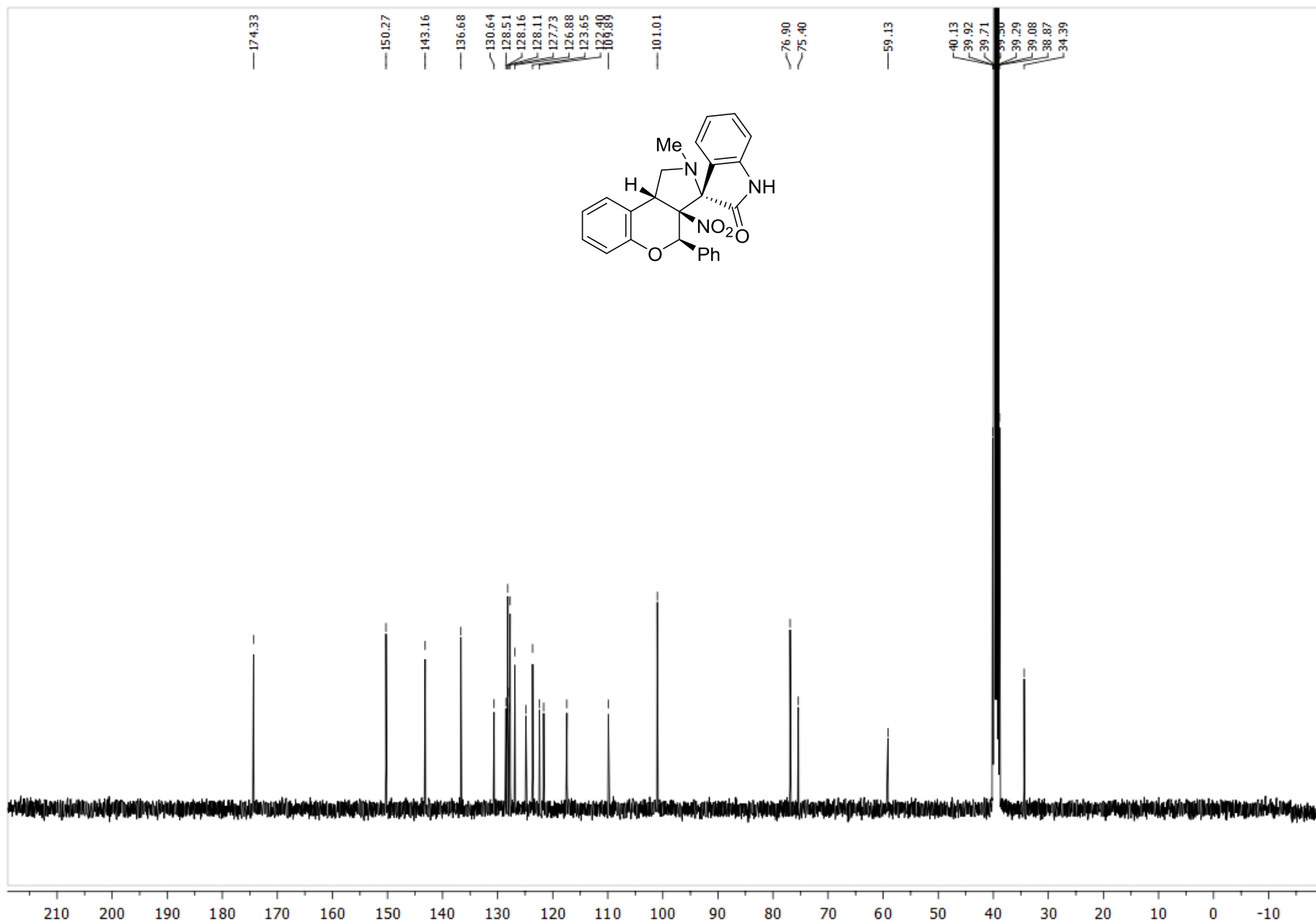


Figure S43. Copy of ¹³C NMR spectrum of **5j** in DMSO-*d*₆

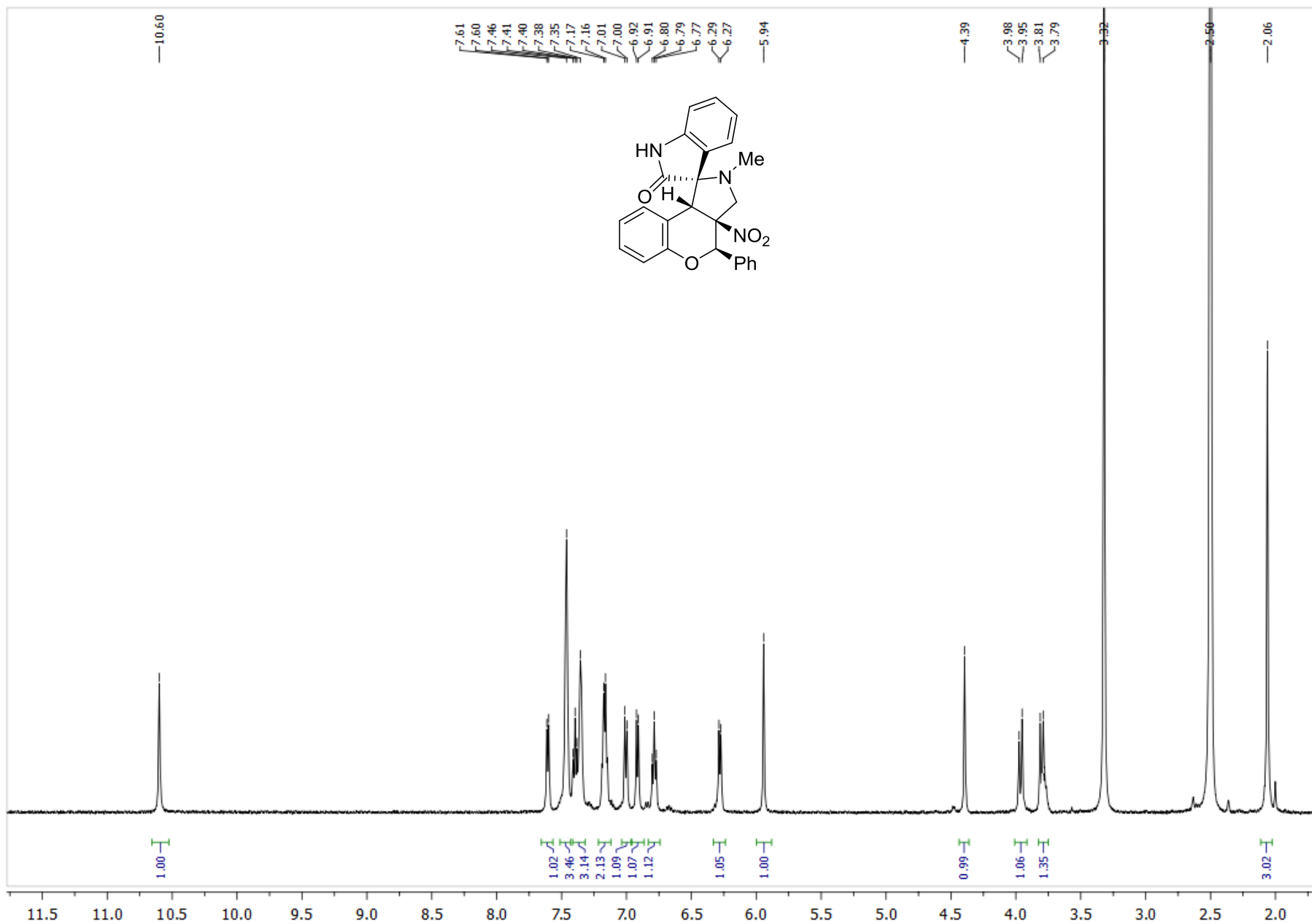


Figure S44. Copy of ¹H NMR spectrum of **6j** in DMSO-*d*₆

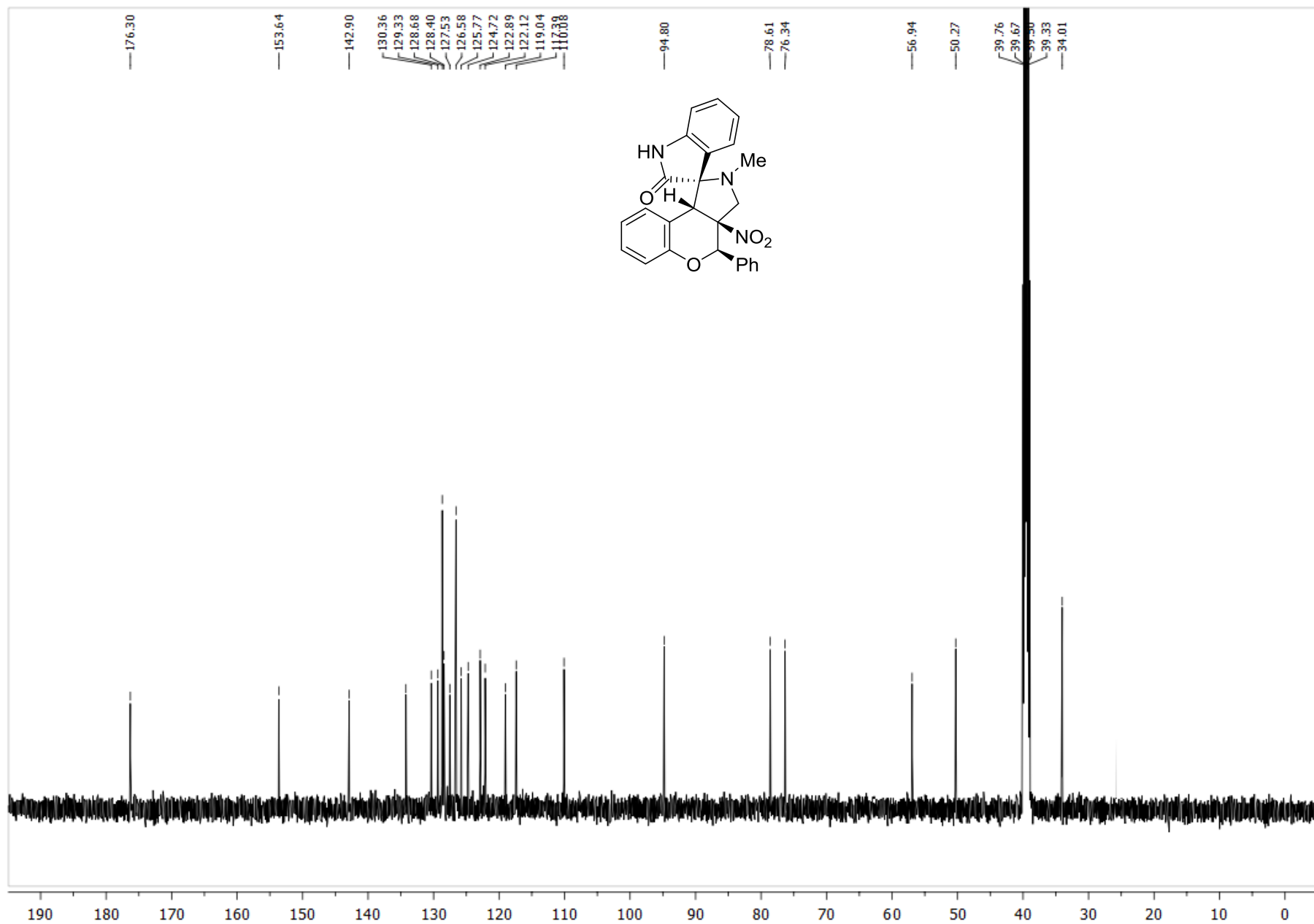


Figure S45. Copy of ^{13}C NMR spectrum of **6j** in $\text{DMSO-}d_6$

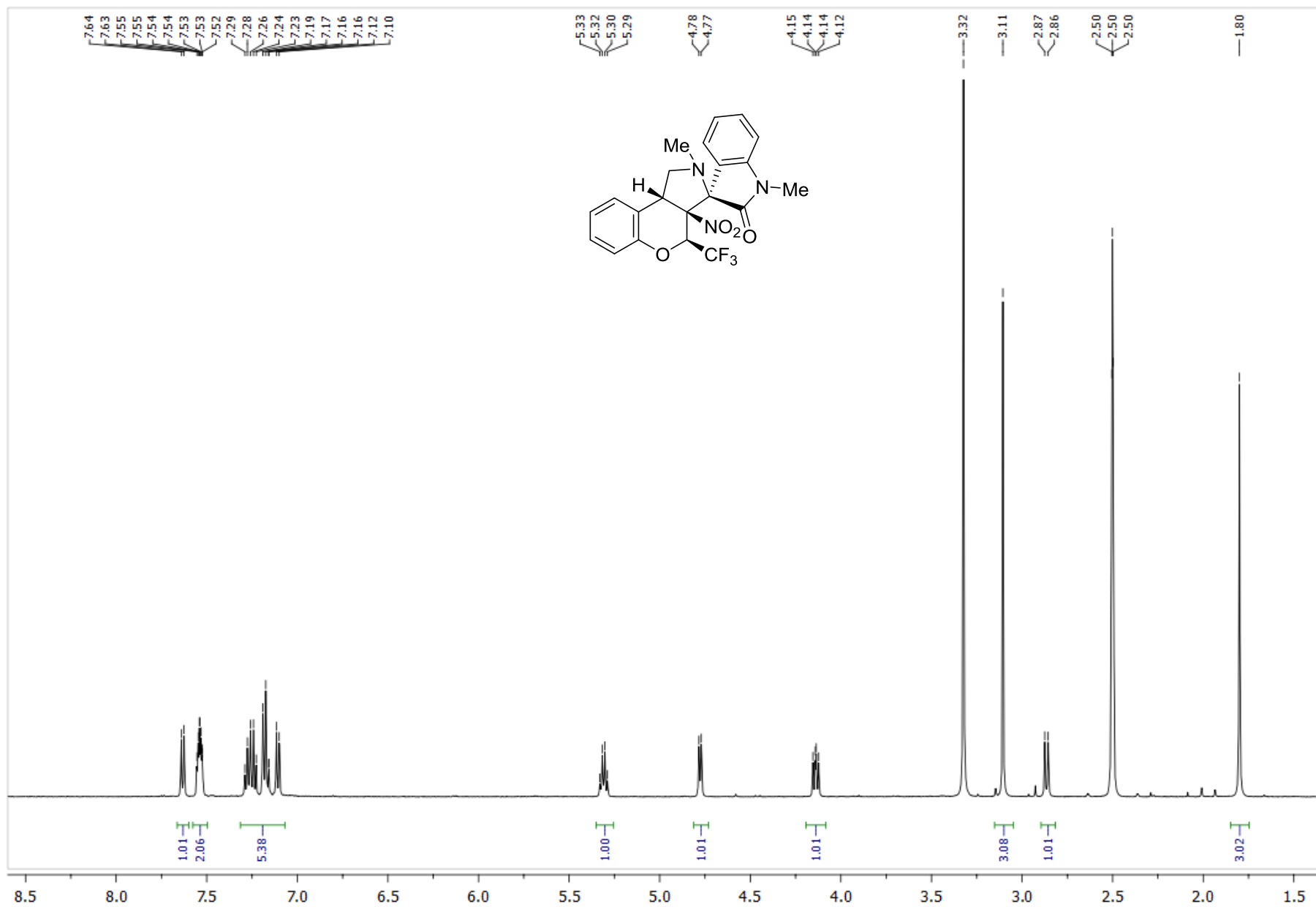


Figure S46. Copy of ^1H NMR spectrum of **5k** in $\text{DMSO-}d_6$

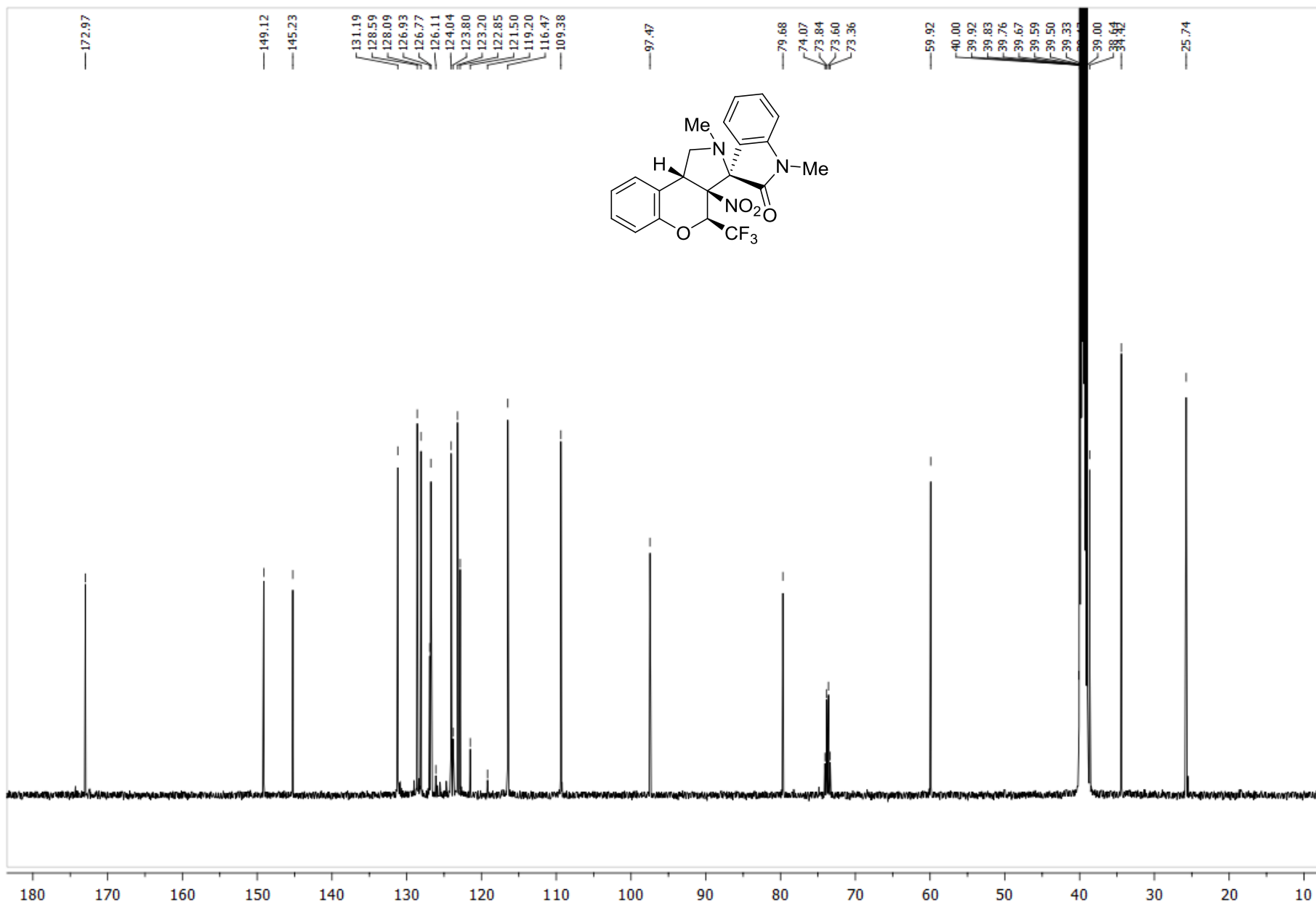


Figure S47. Copy of ^{13}C NMR spectrum of **5k** in $\text{DMSO-}d_6$

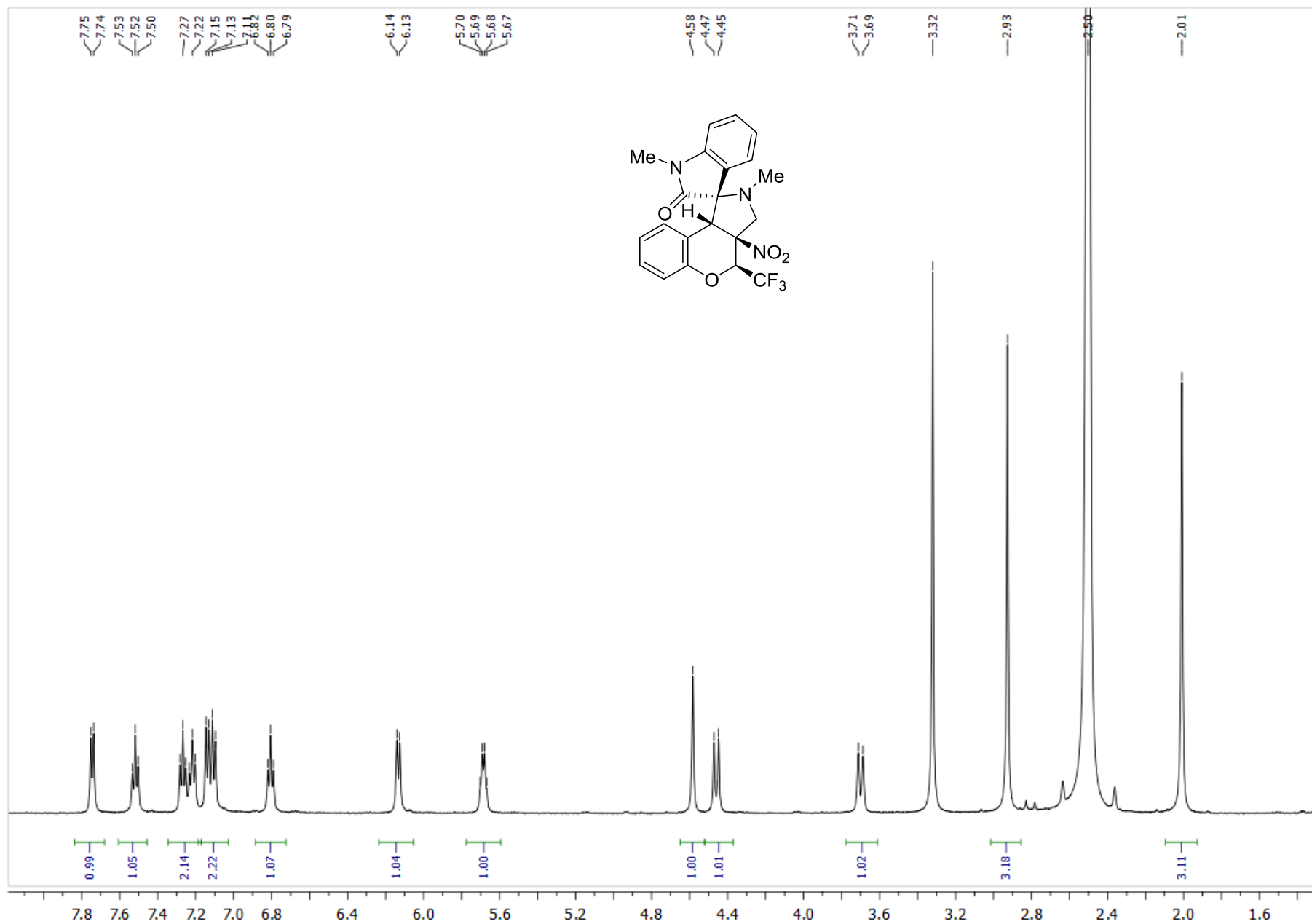


Figure S48. Copy of ^1H NMR spectrum of **6k** in $\text{DMSO-}d_6$

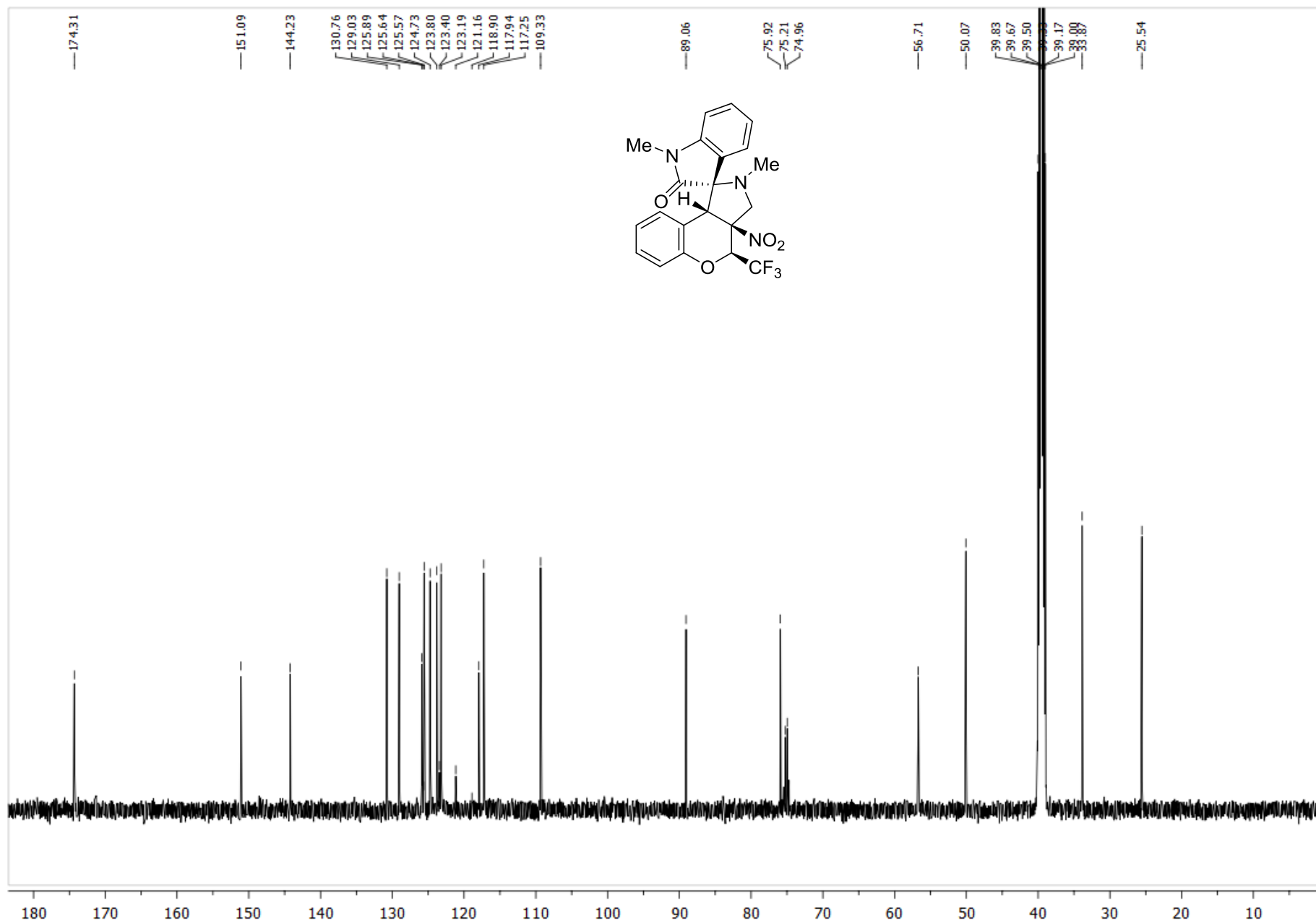


Figure S49. Copy of ¹³C NMR spectrum of **6k** in DMSO-*d*₆

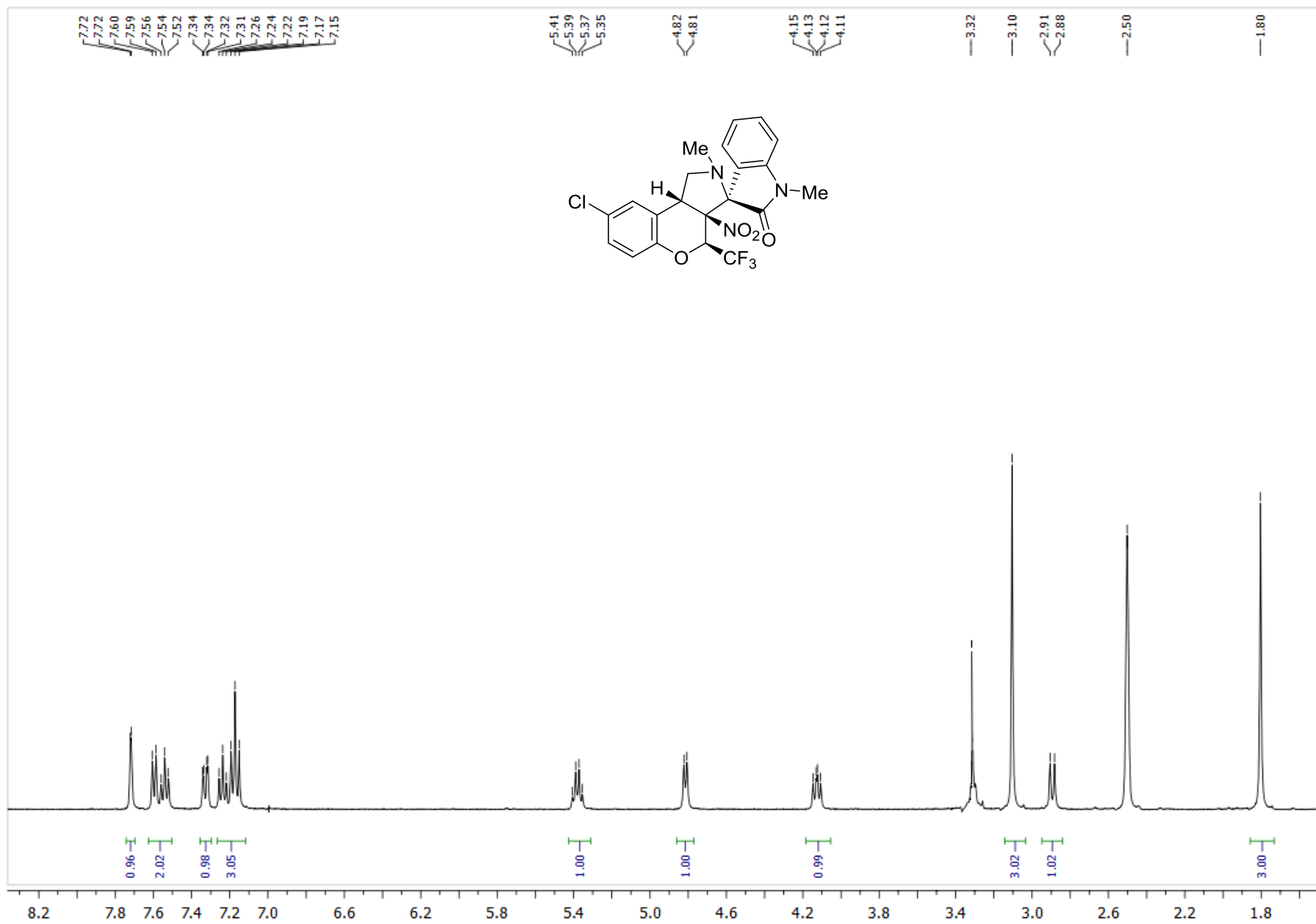


Figure S50. Copy of ¹H NMR spectrum of **51** in DMSO-*d*₆

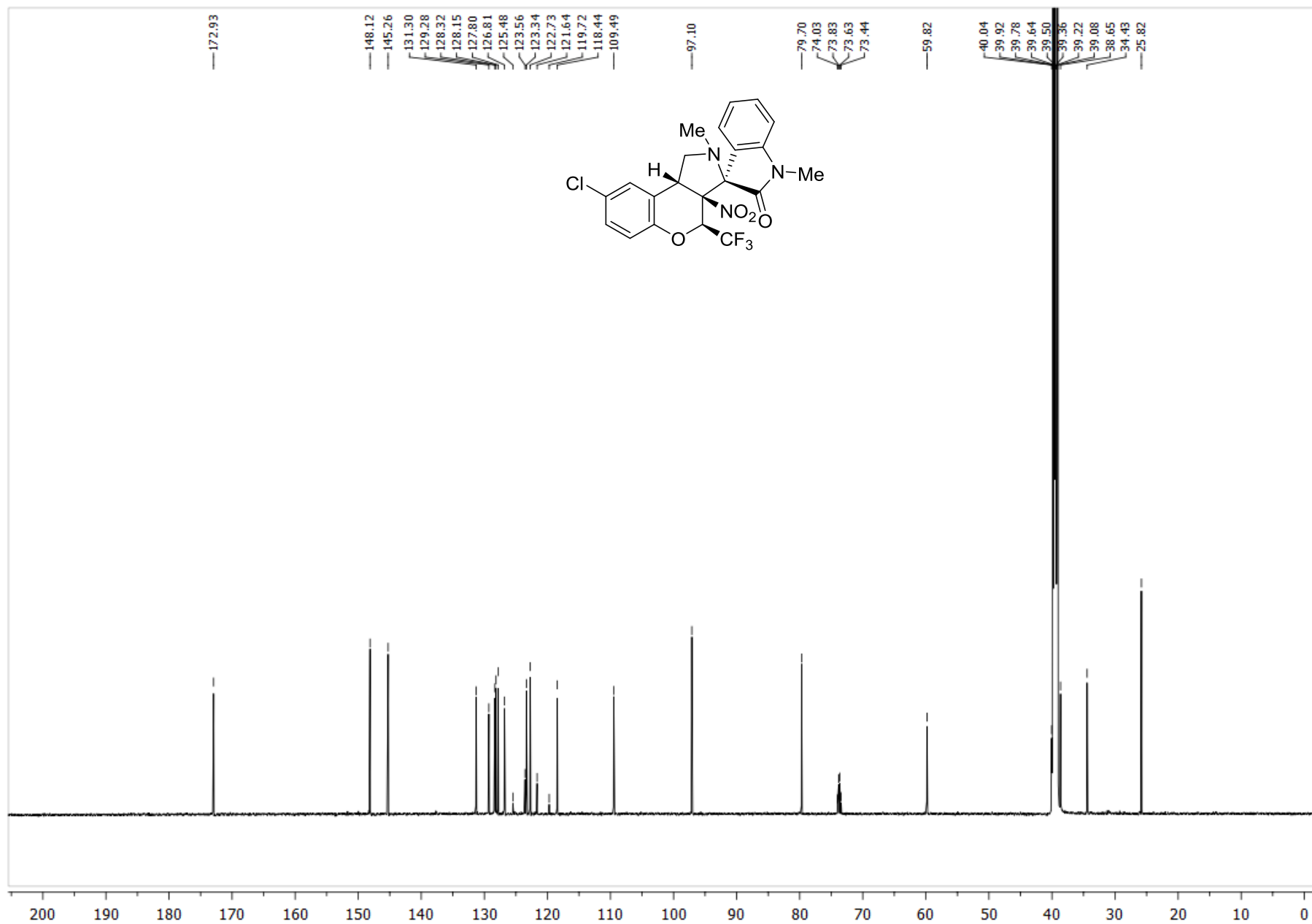


Figure S51. Copy of ¹³C NMR spectrum of **51** in DMSO-*d*₆

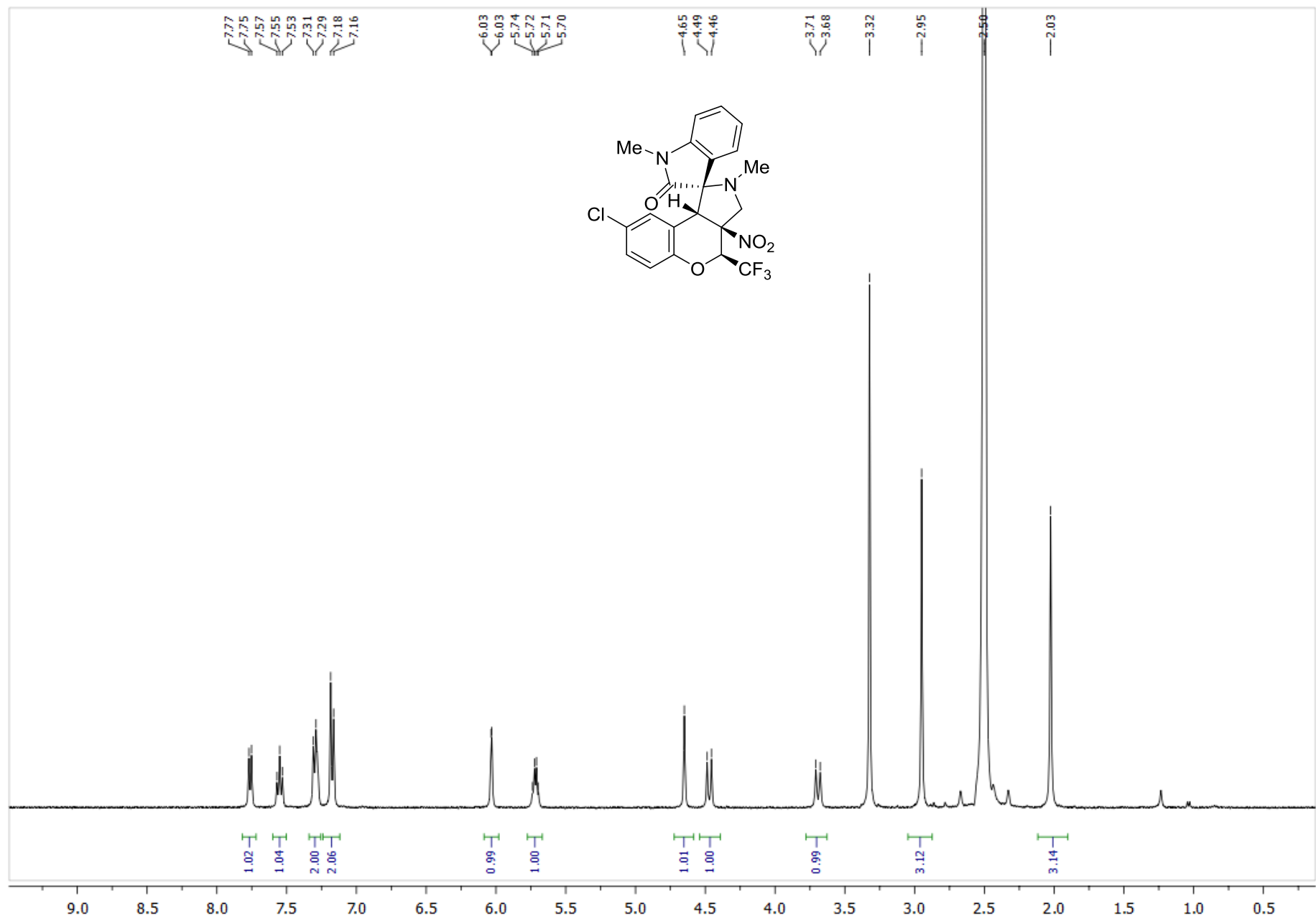


Figure S52. Copy of ¹H NMR spectrum of **6l** in DMSO-*d*₆

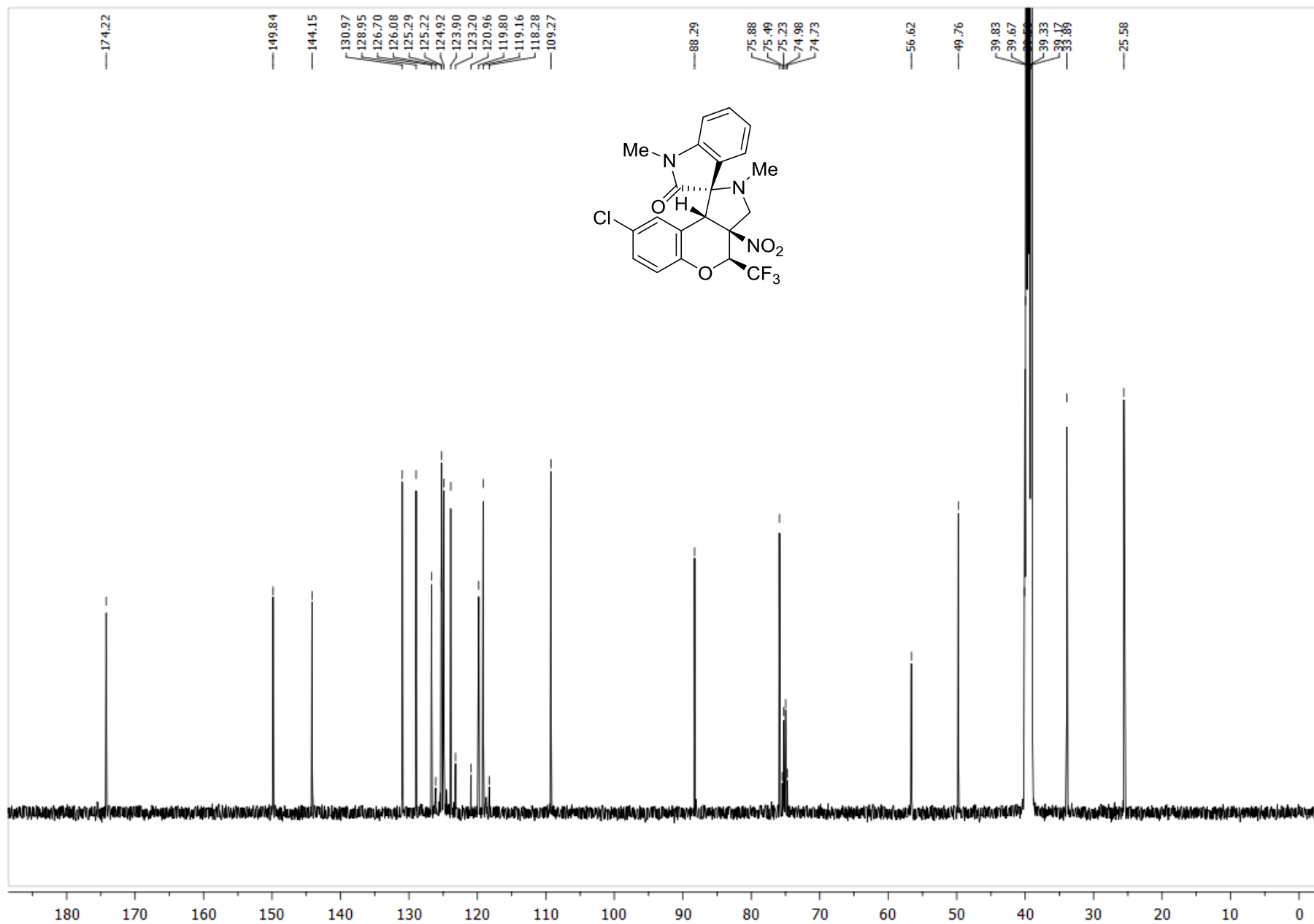


Figure S53. Copy of ¹³C NMR spectrum of **61** in DMSO-*d*₆

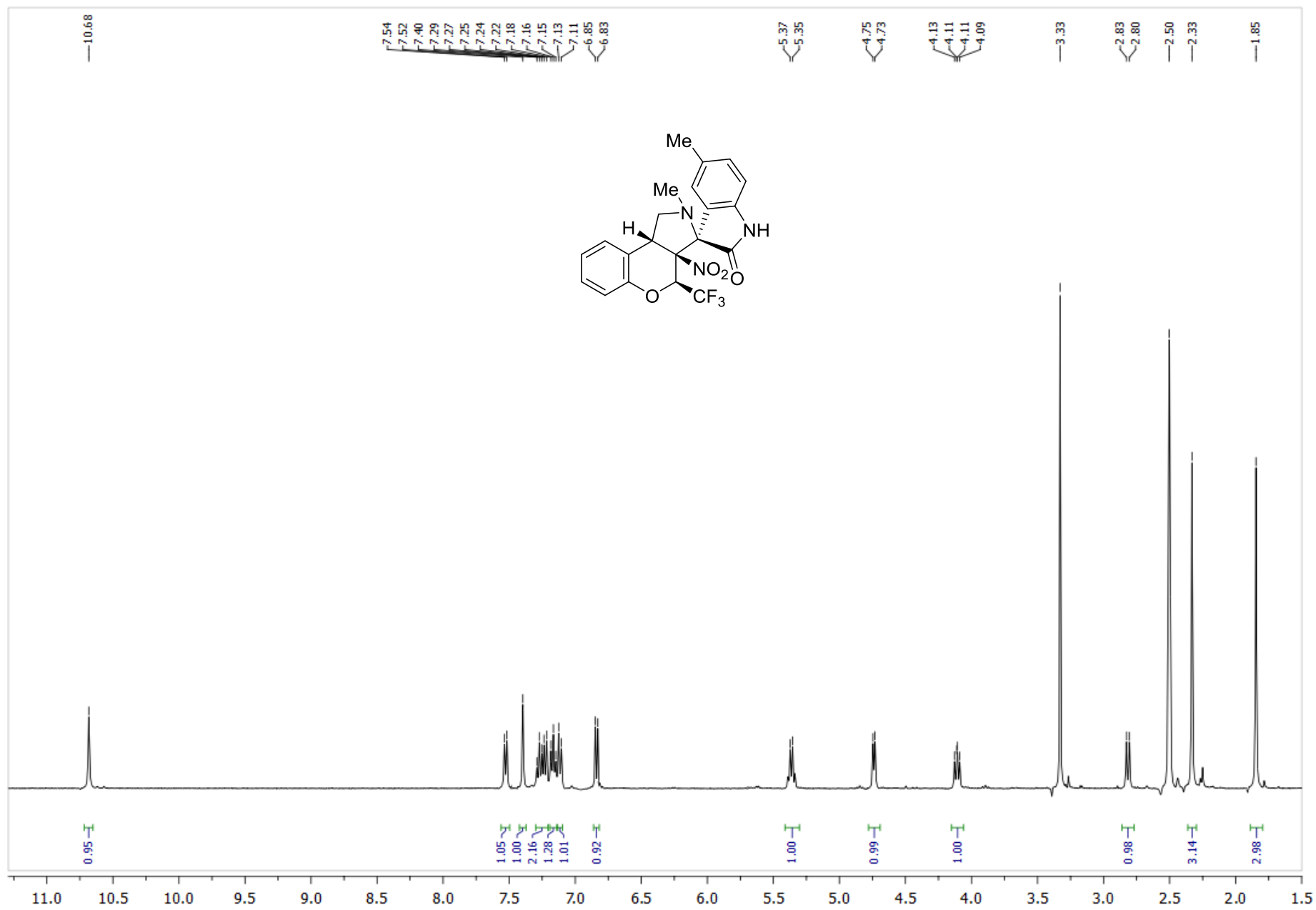


Figure S54. Copy of ¹H NMR spectrum of **5m** in DMSO-*d*₆

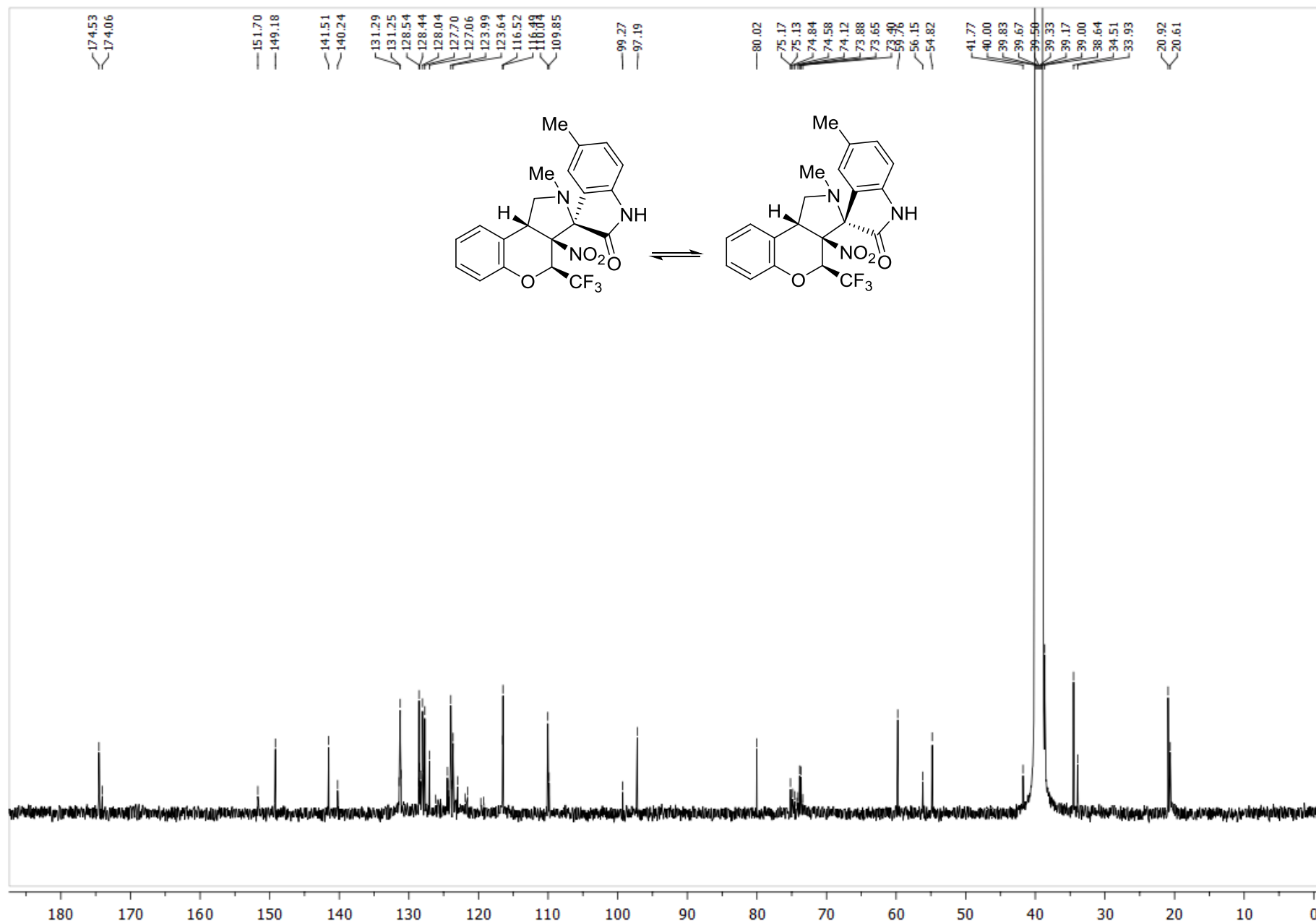


Figure S55. Copy of ^{13}C NMR spectrum of **5m** in $\text{DMSO-}d_6$

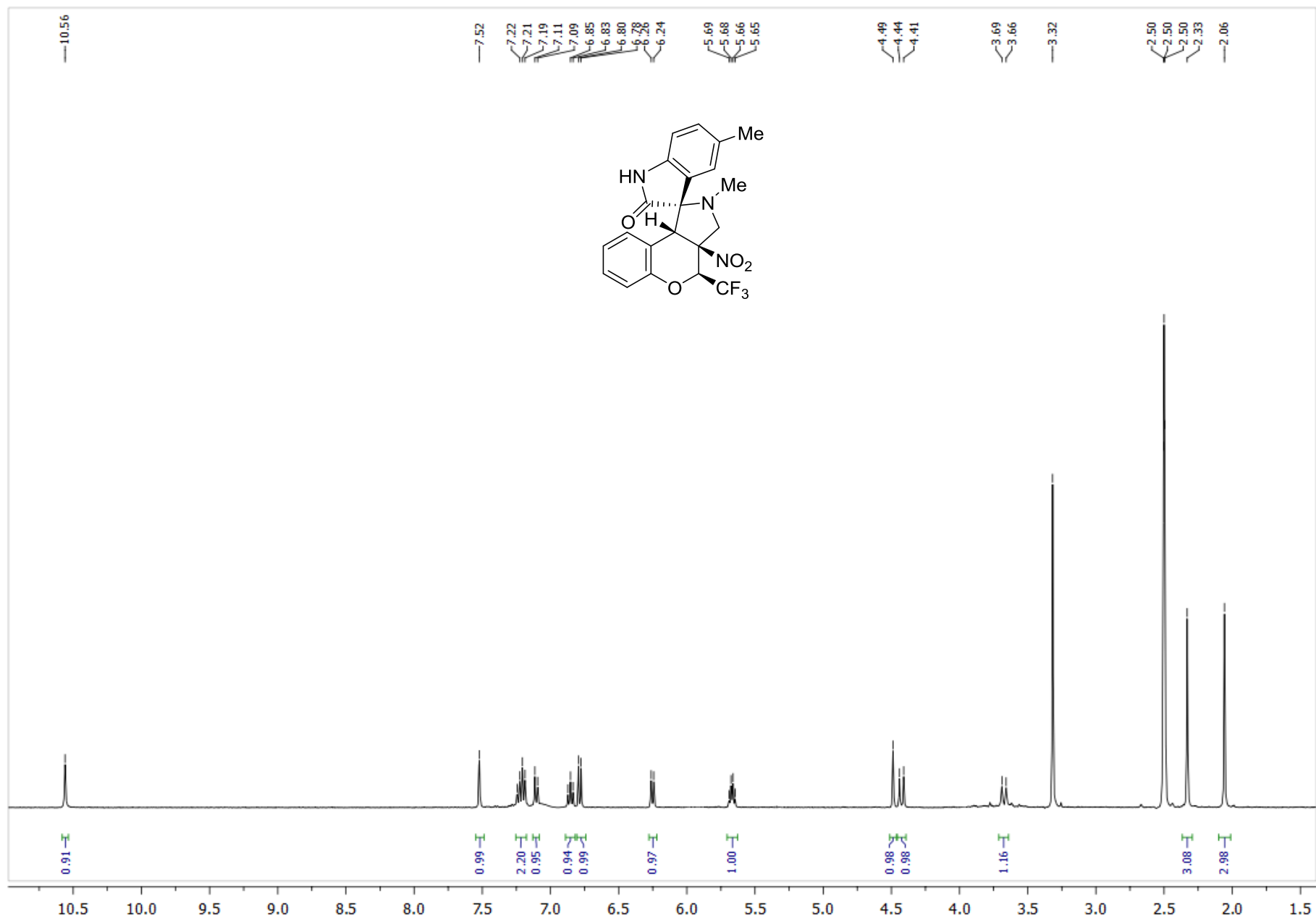


Figure S56. Copy of ¹H NMR spectrum of **6m** in DMSO-*d*₆

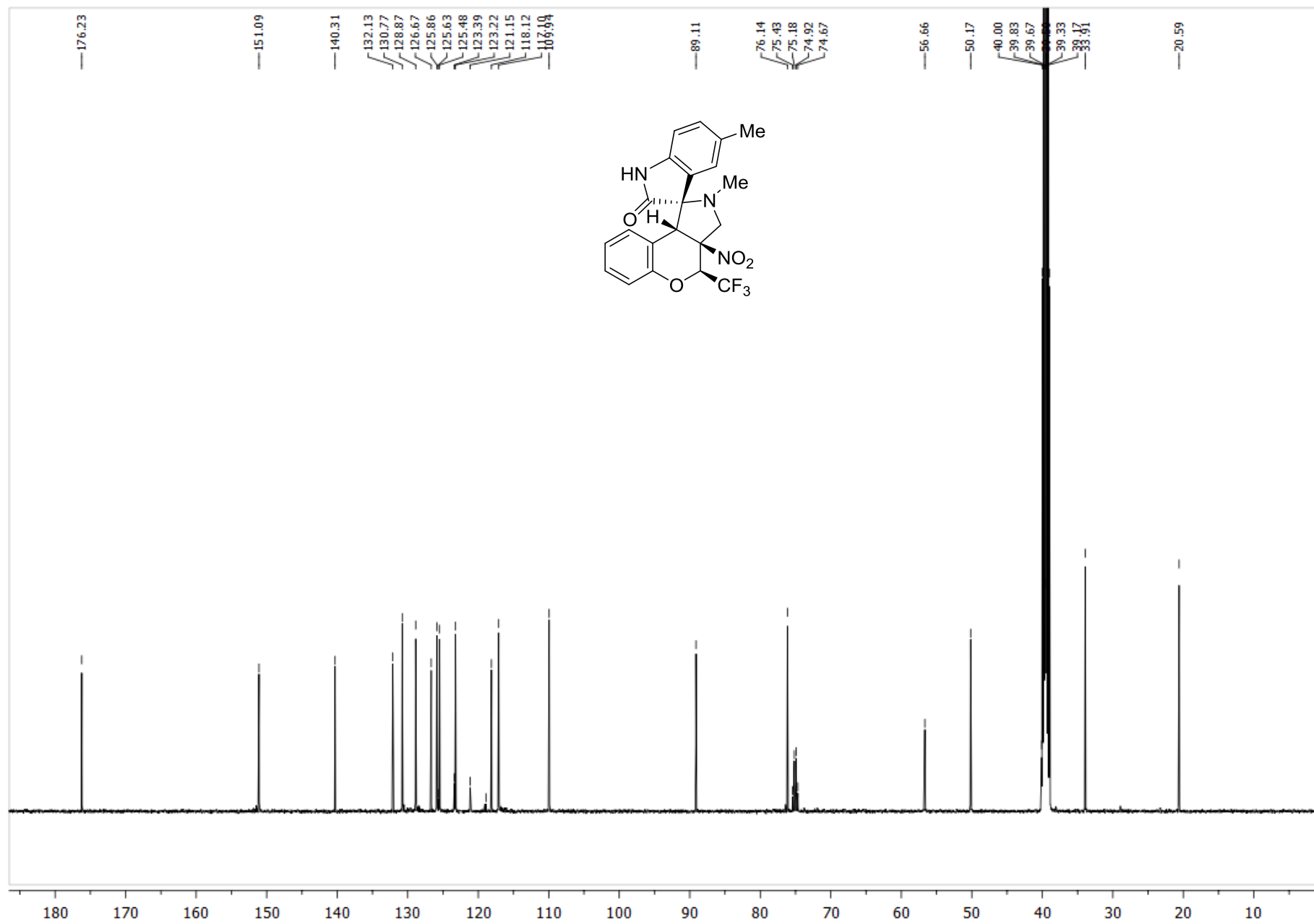


Figure S57. Copy of ^{13}C NMR spectrum of **6m** in $\text{DMSO-}d_6$

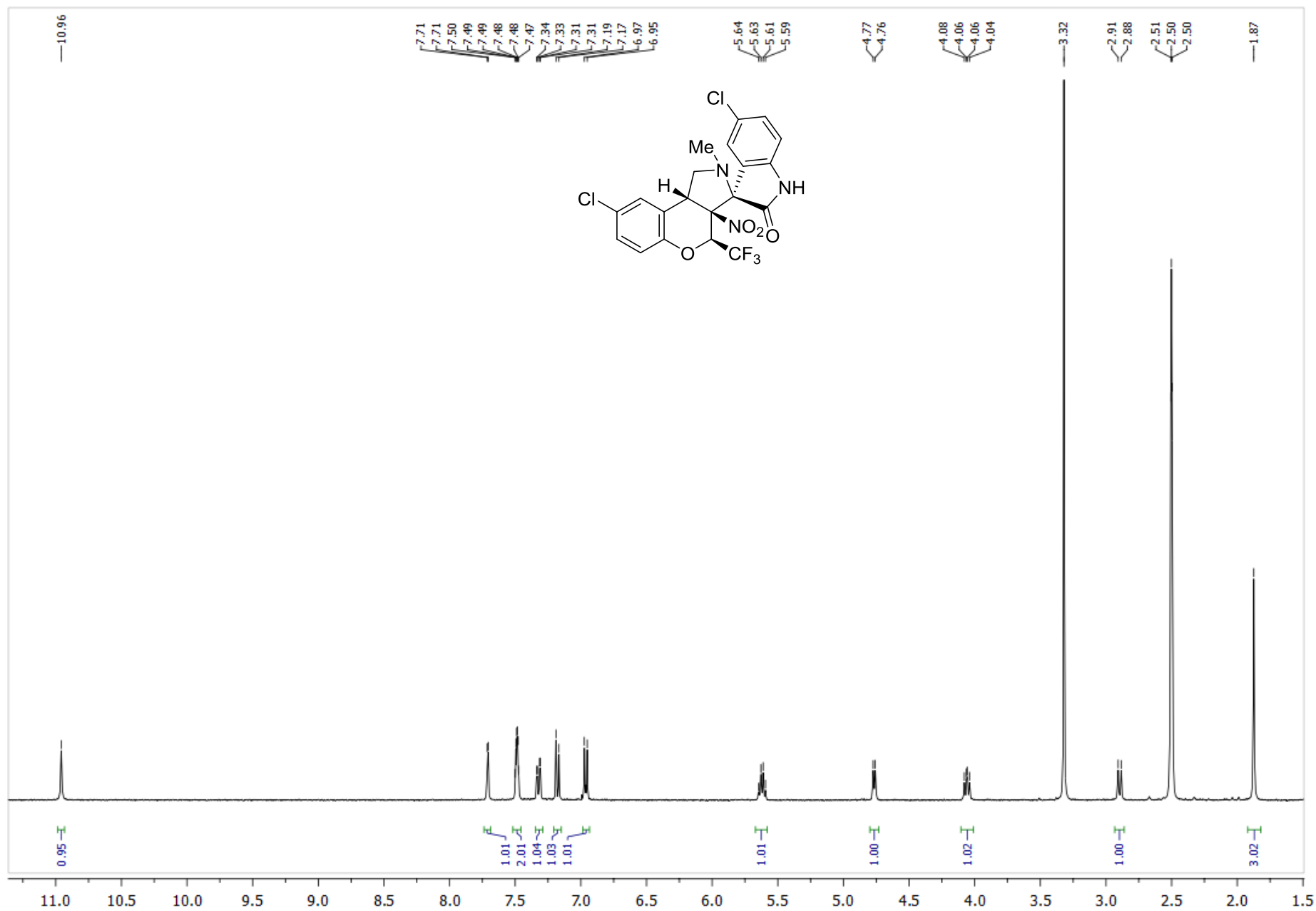


Figure S58. Copy of ^1H NMR spectrum of **5n** in $\text{DMSO-}d_6$

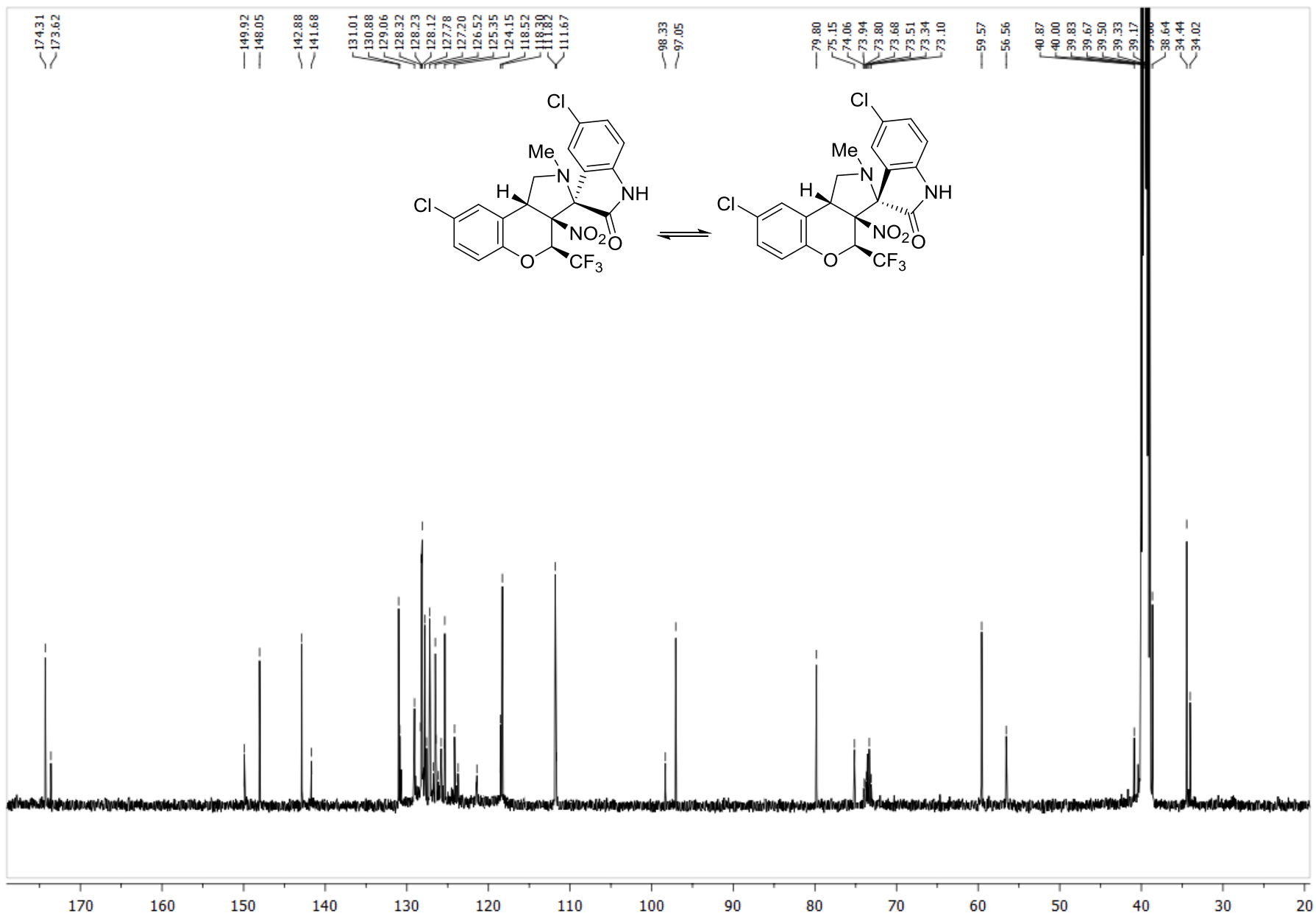


Figure S59. Copy of ^{13}C NMR spectrum of **5n** in $\text{DMSO-}d_6$

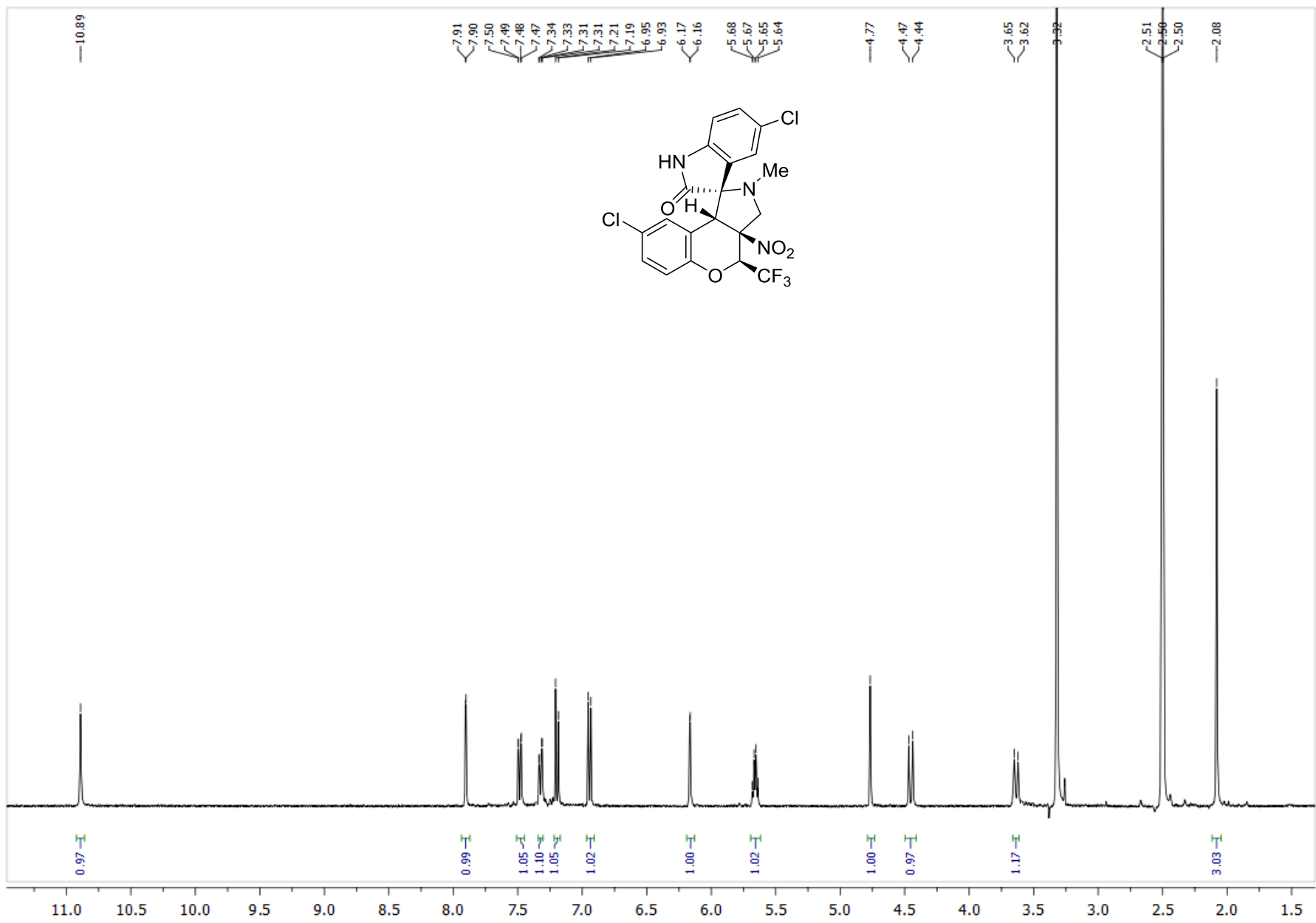


Figure S60. Copy of ^1H NMR spectrum of **6n** in $\text{DMSO-}d_6$

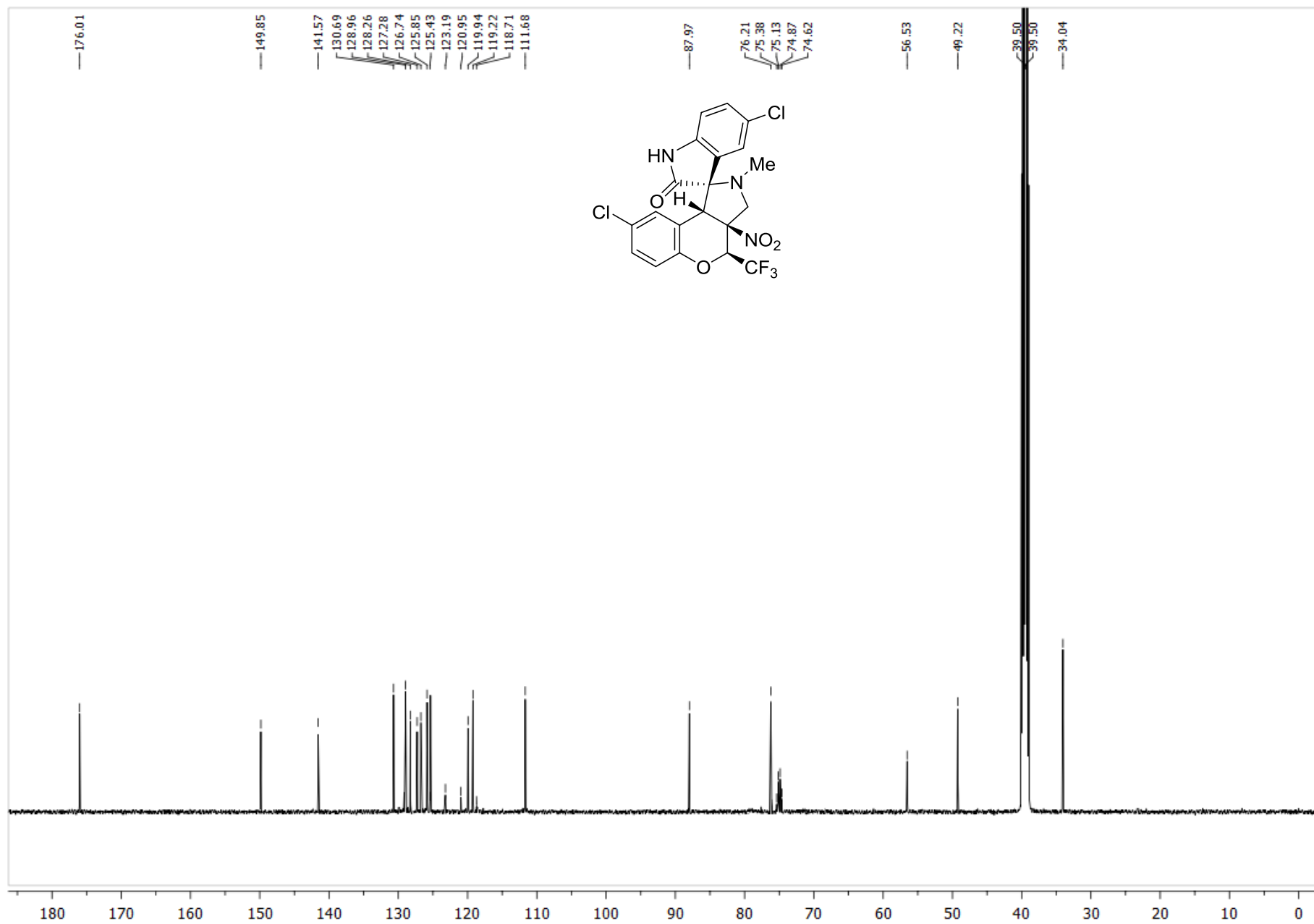


Figure S61. Copy of ¹³C NMR spectrum of **6n** in DMSO-*d*₆

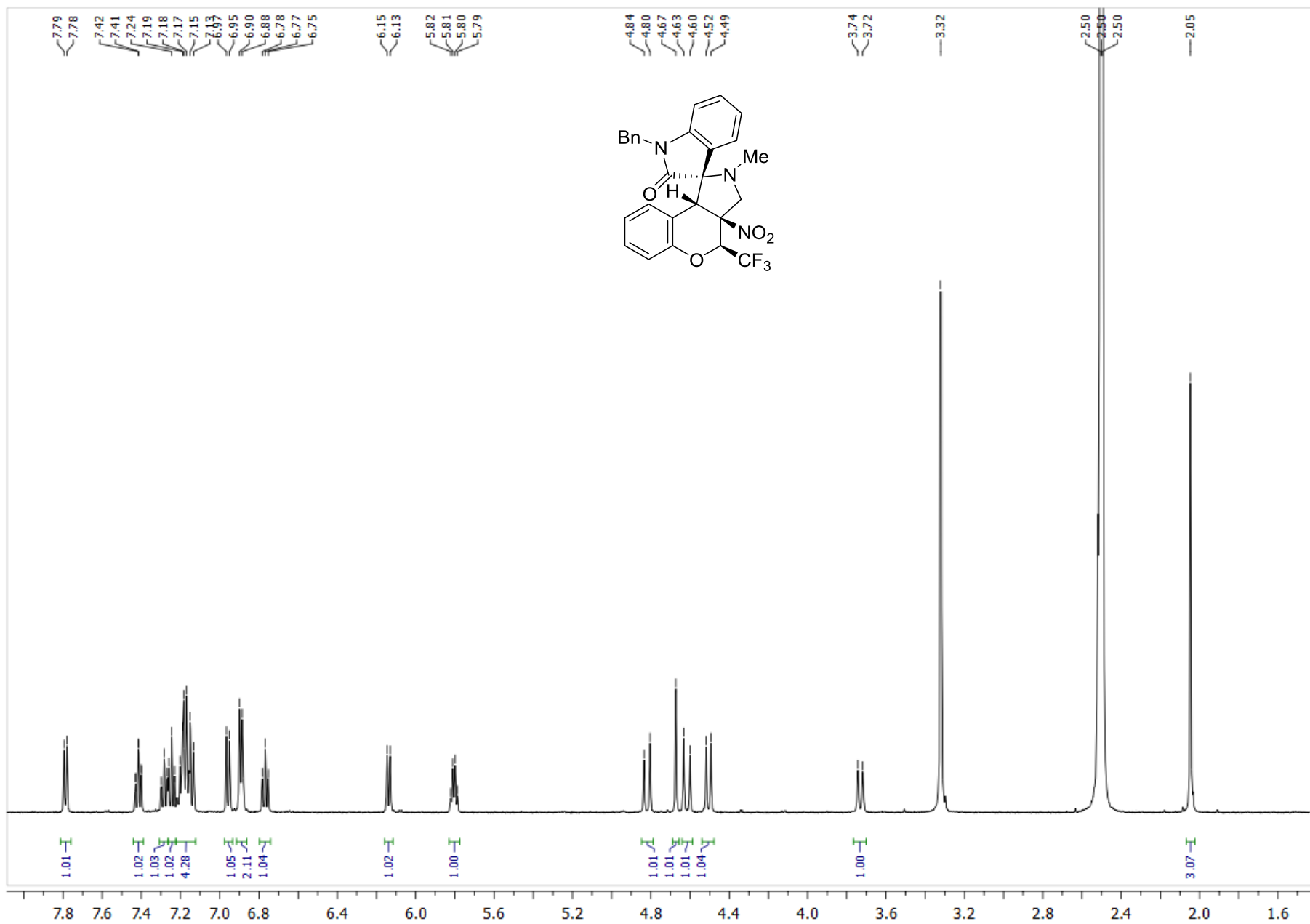


Figure S62. Copy of ¹H NMR spectrum of **60** in DMSO-*d*₆

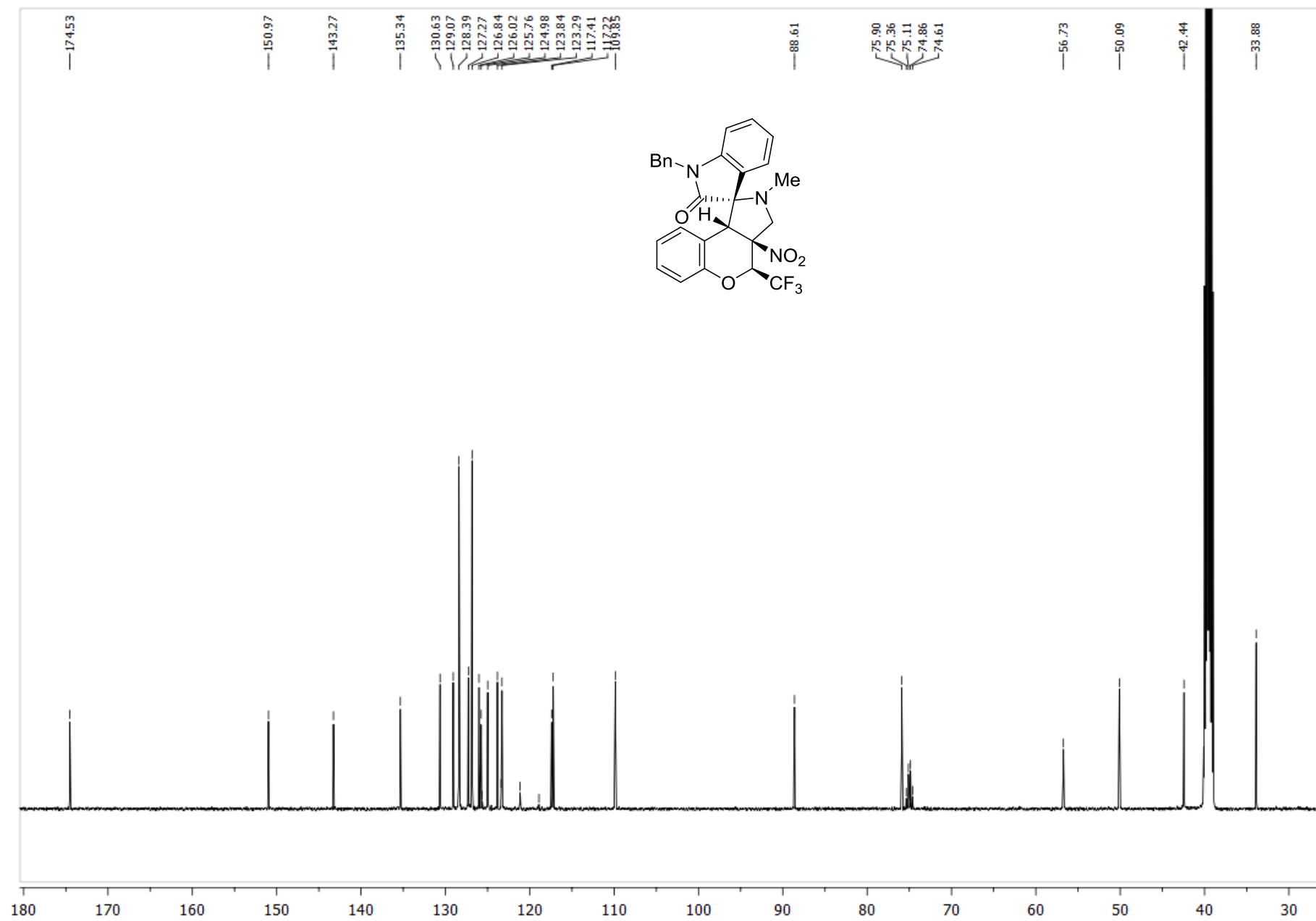


Figure S63. Copy of ^{13}C NMR spectrum of **6o** in $\text{DMSO-}d_6$

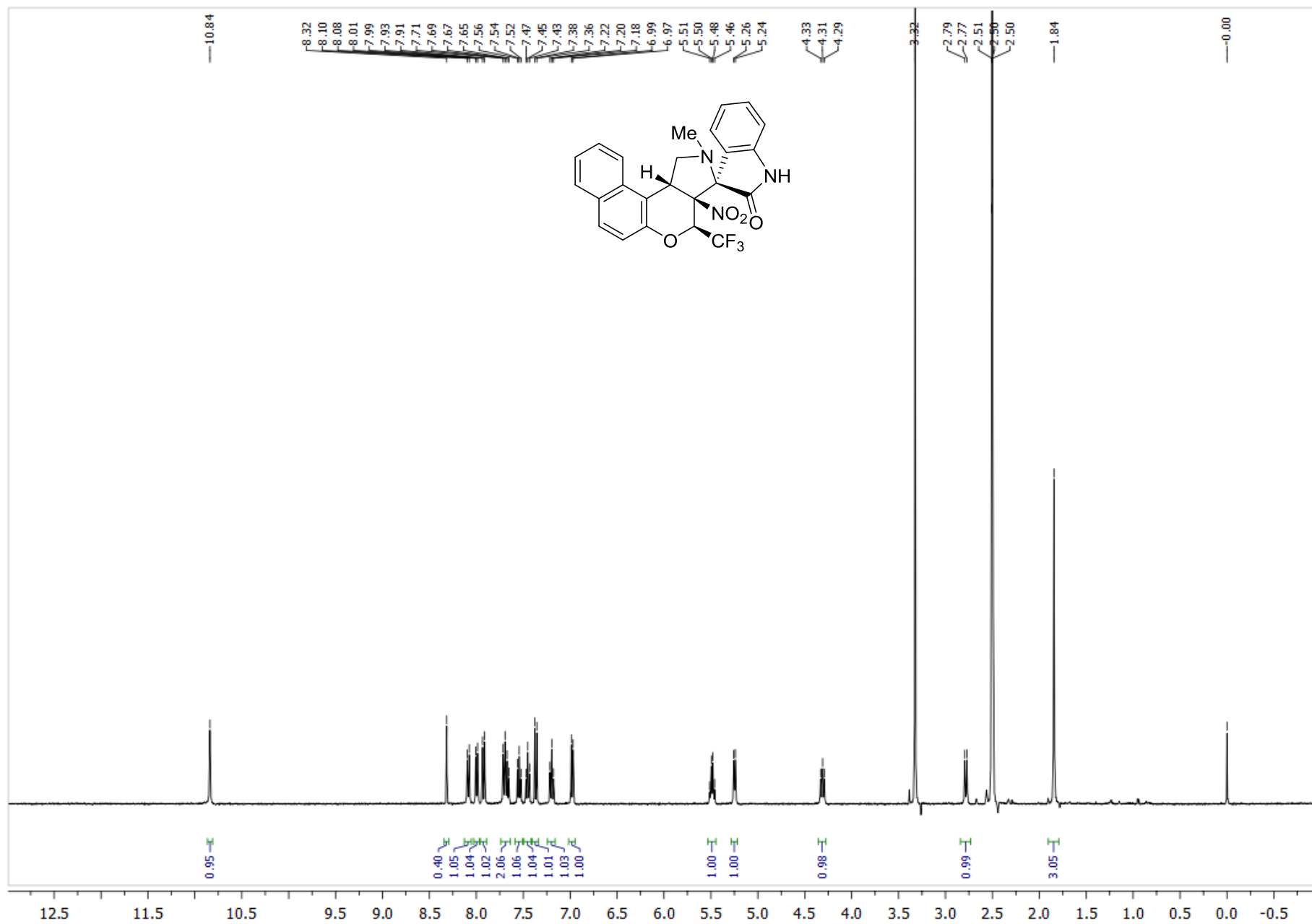


Figure S64. Copy of ¹H NMR spectrum of **5p** in DMSO-*d*₆

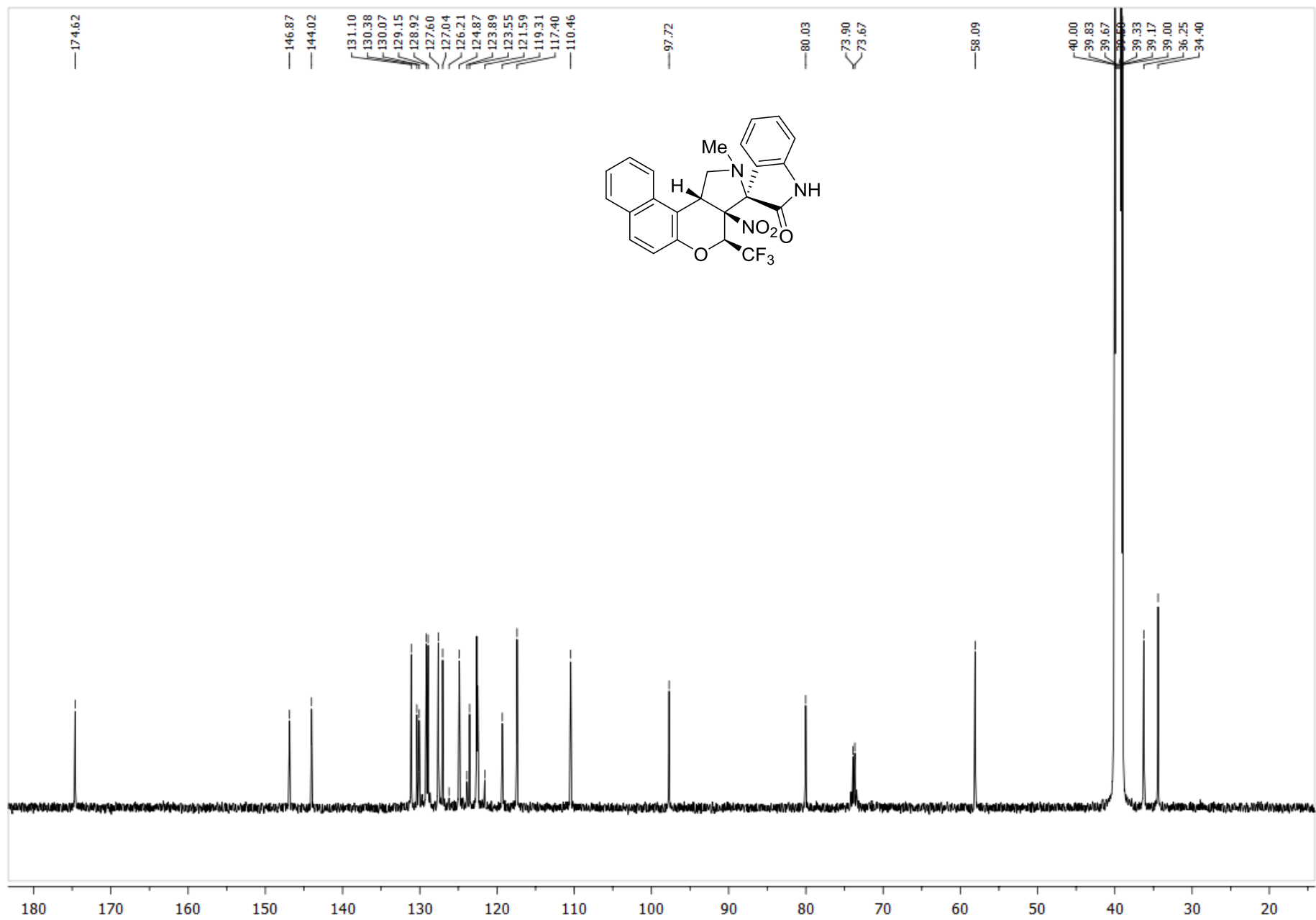


Figure S65. Copy of ^{13}C NMR spectrum of **5p** in $\text{DMSO-}d_6$

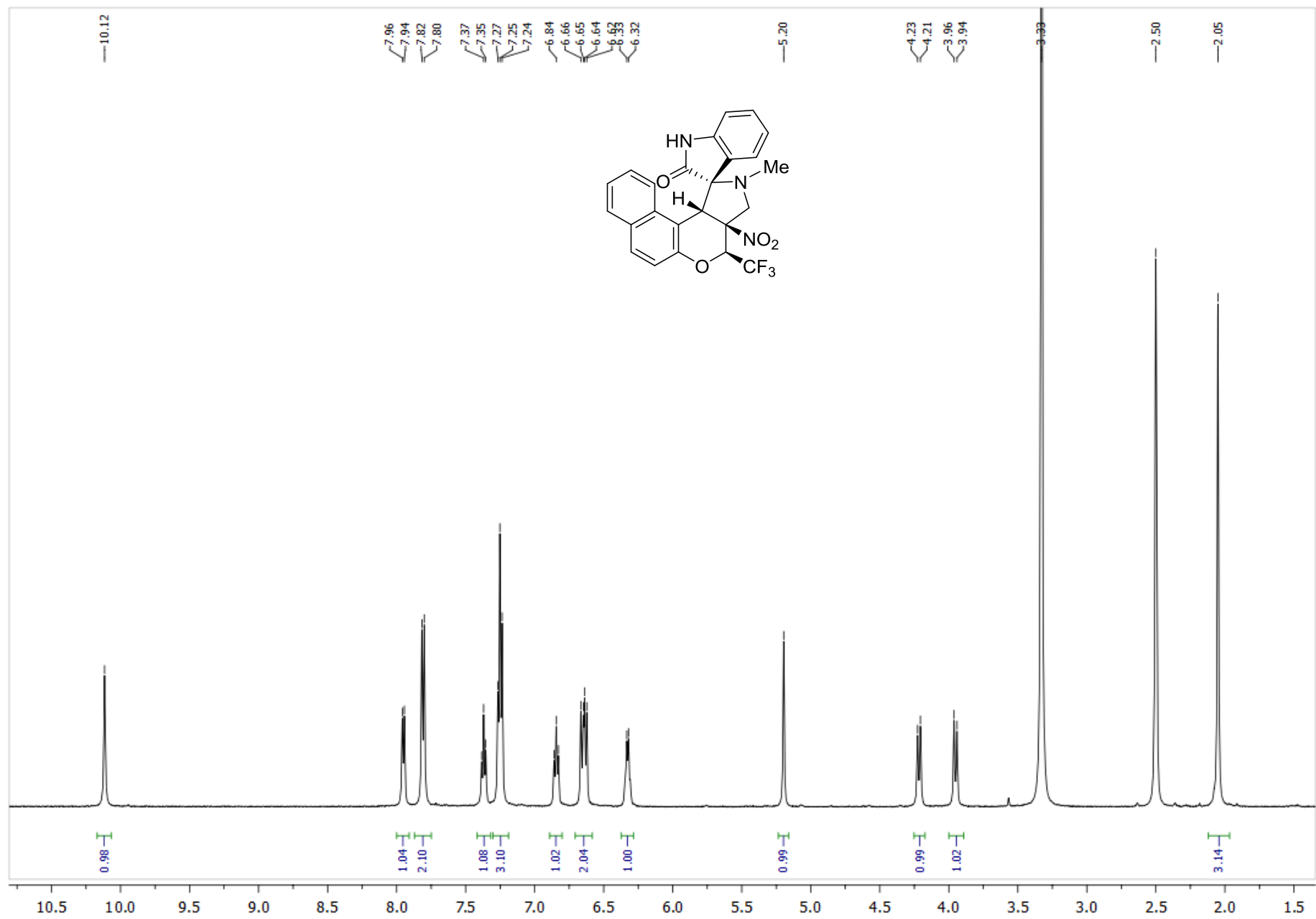


Figure S66. Copy of ¹H NMR spectrum of **6p** in DMSO-*d*₆

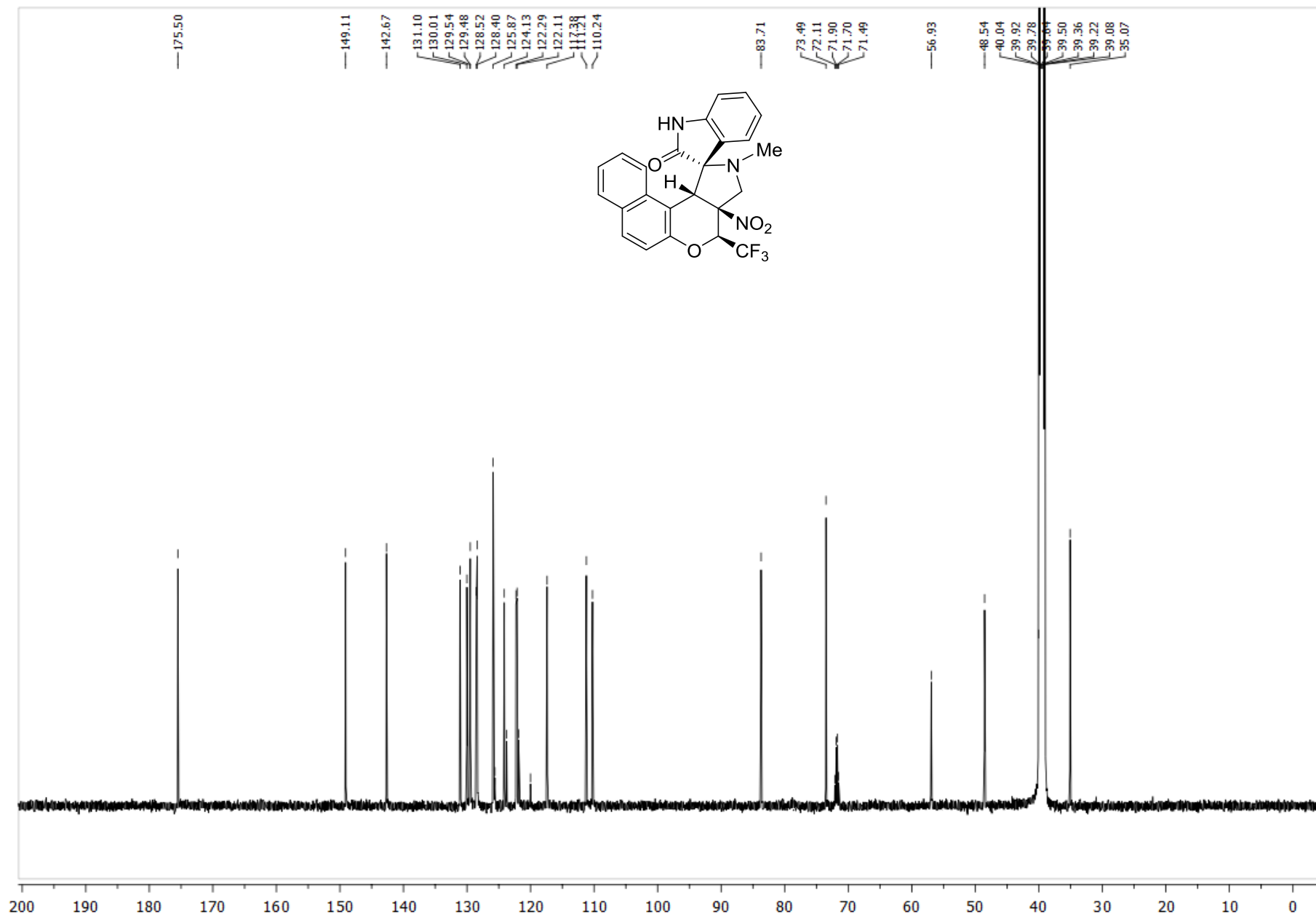


Figure S67. Copy of ¹³C NMR spectrum of **6p** in DMSO-*d*₆

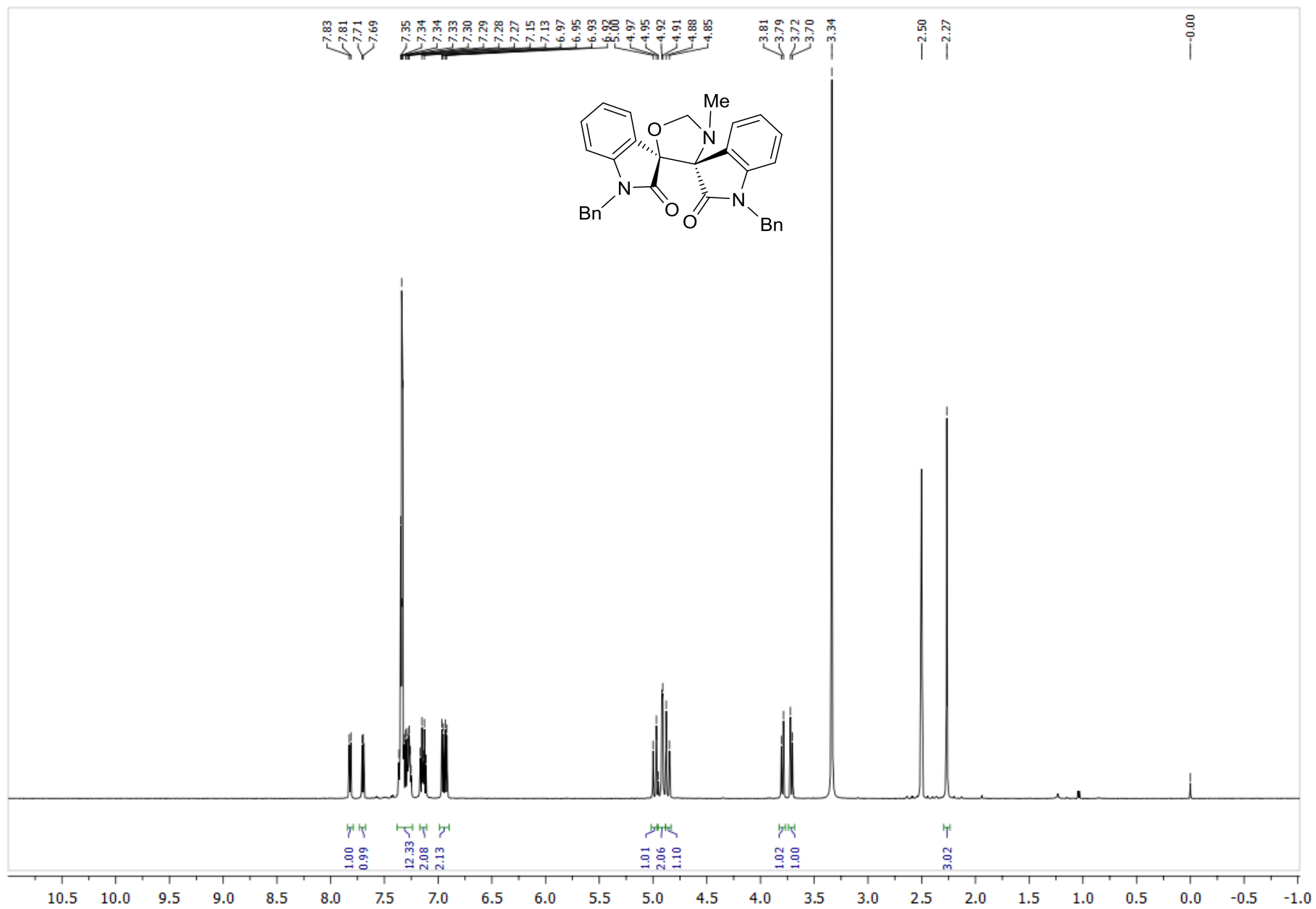


Figure S68. Copy of ^1H NMR spectrum of **7a** in DMSO- d_6

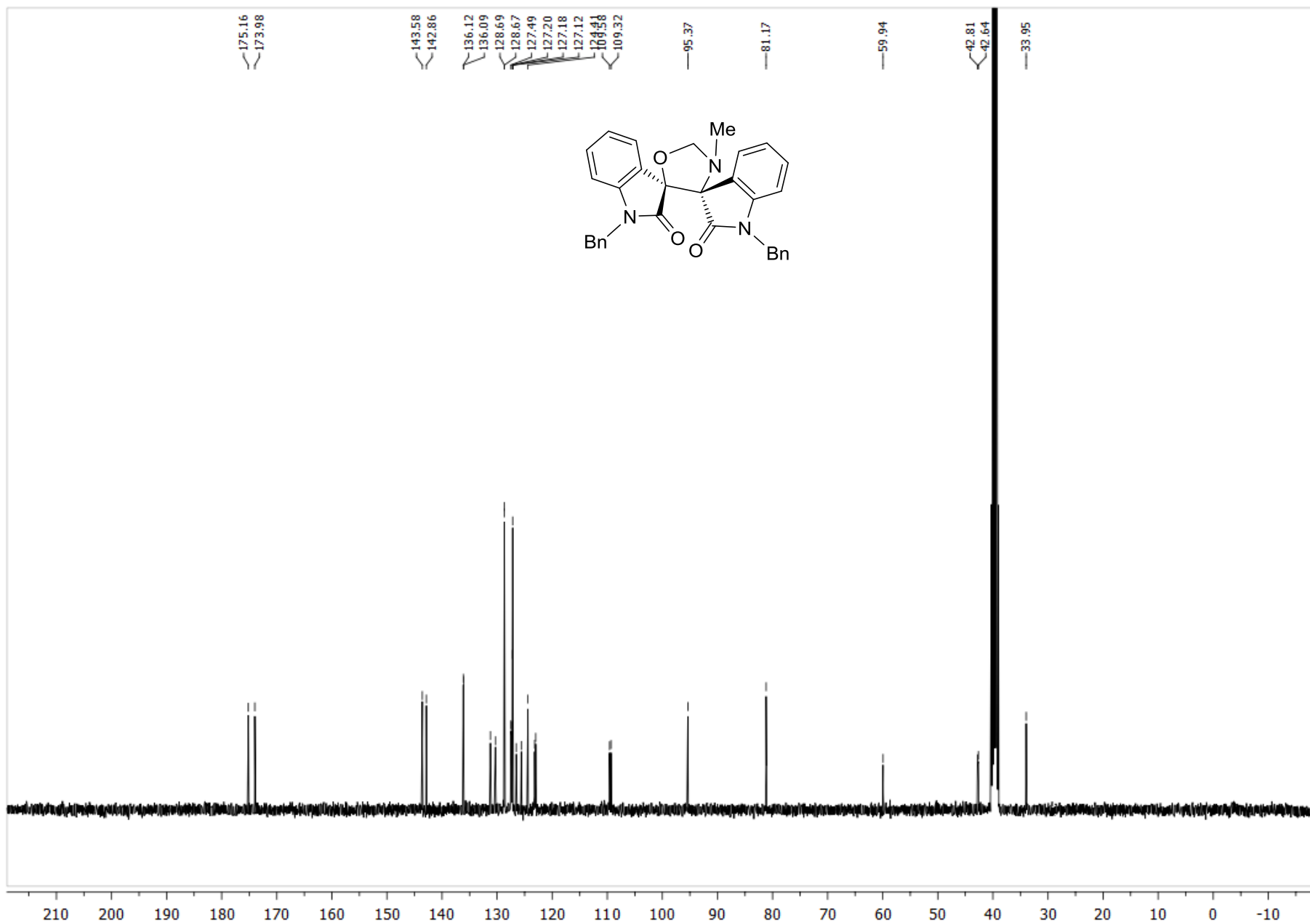


Figure S69. Copy of ^{13}C NMR spectrum of **7a** in $\text{DMSO-}d_6$

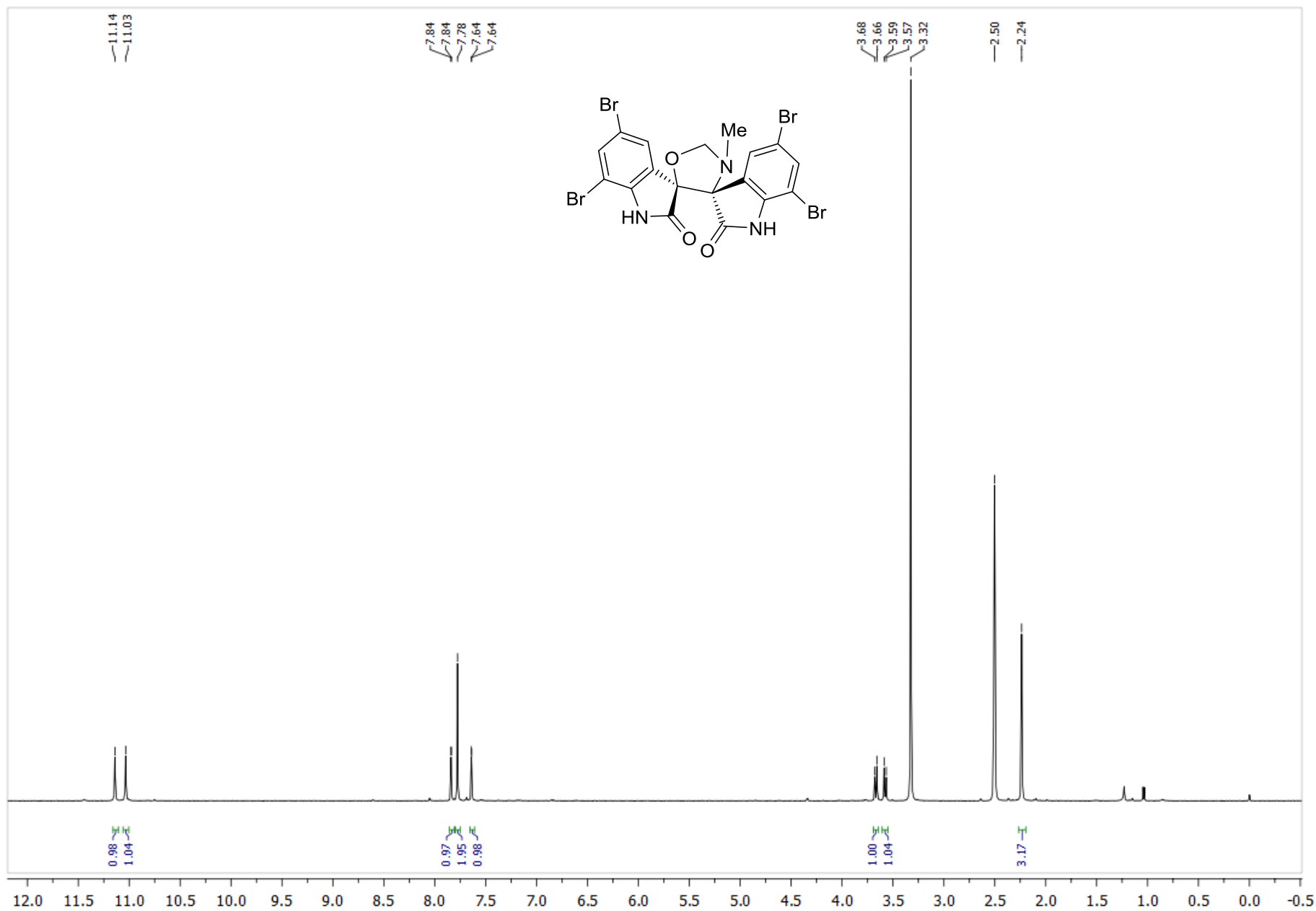


Figure S70. Copy of ¹H NMR spectrum of **7b** in DMSO-*d*₆

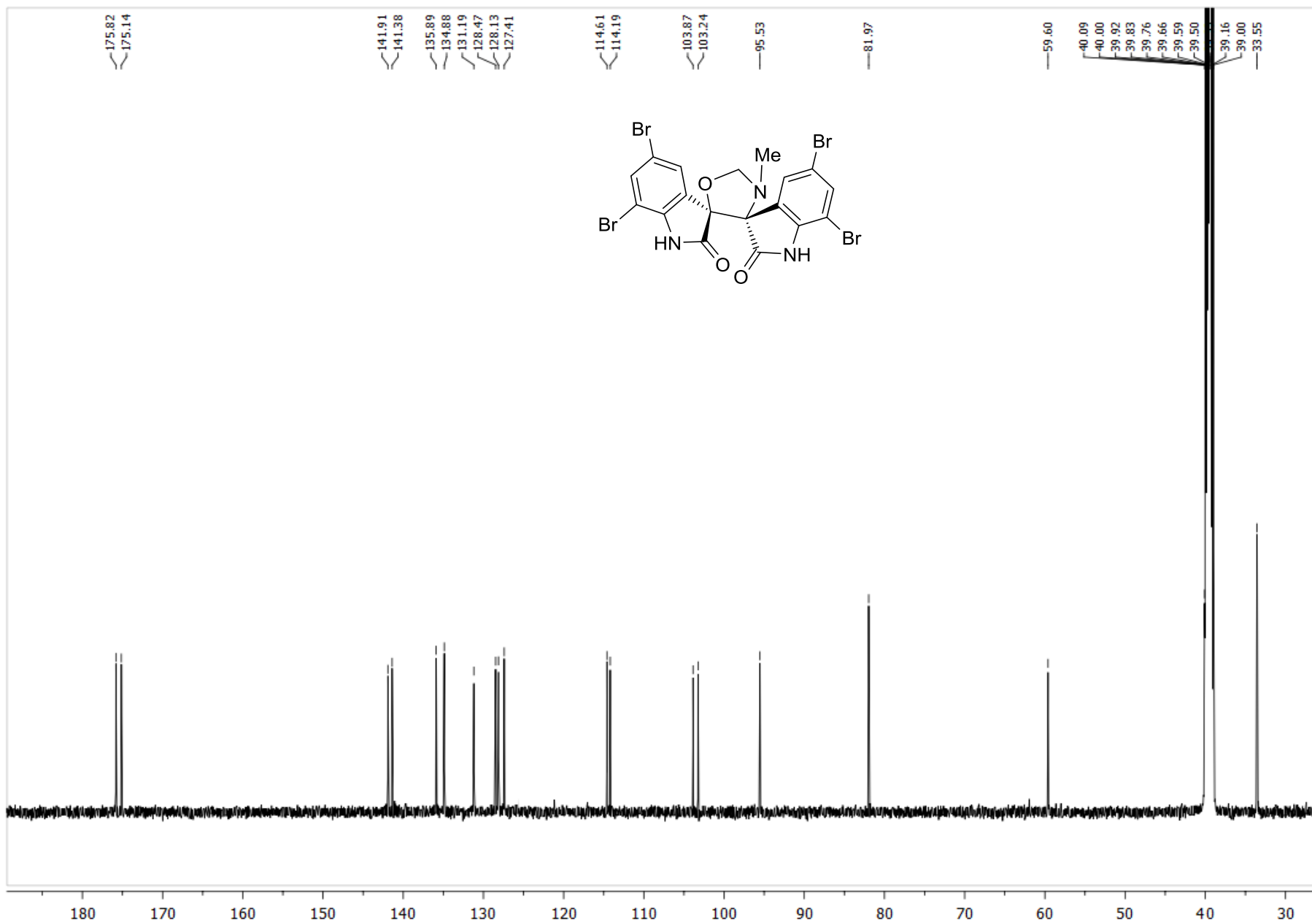


Figure S71. Copy of ^{13}C NMR spectrum of **7b** in $\text{DMSO-}d_6$

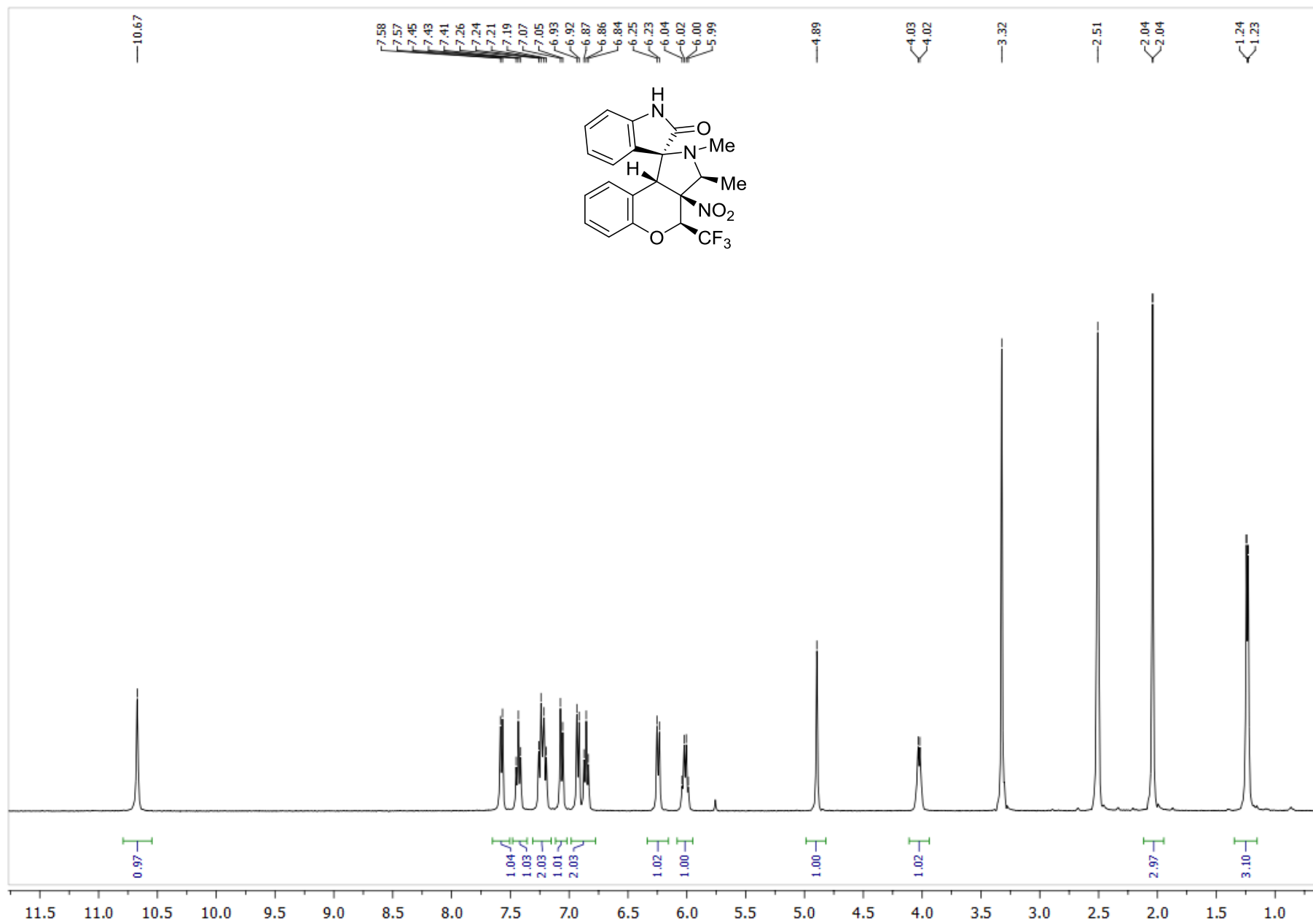


Figure S72. Copy of ^1H NMR spectrum of **8a** in $\text{DMSO}-d_6$

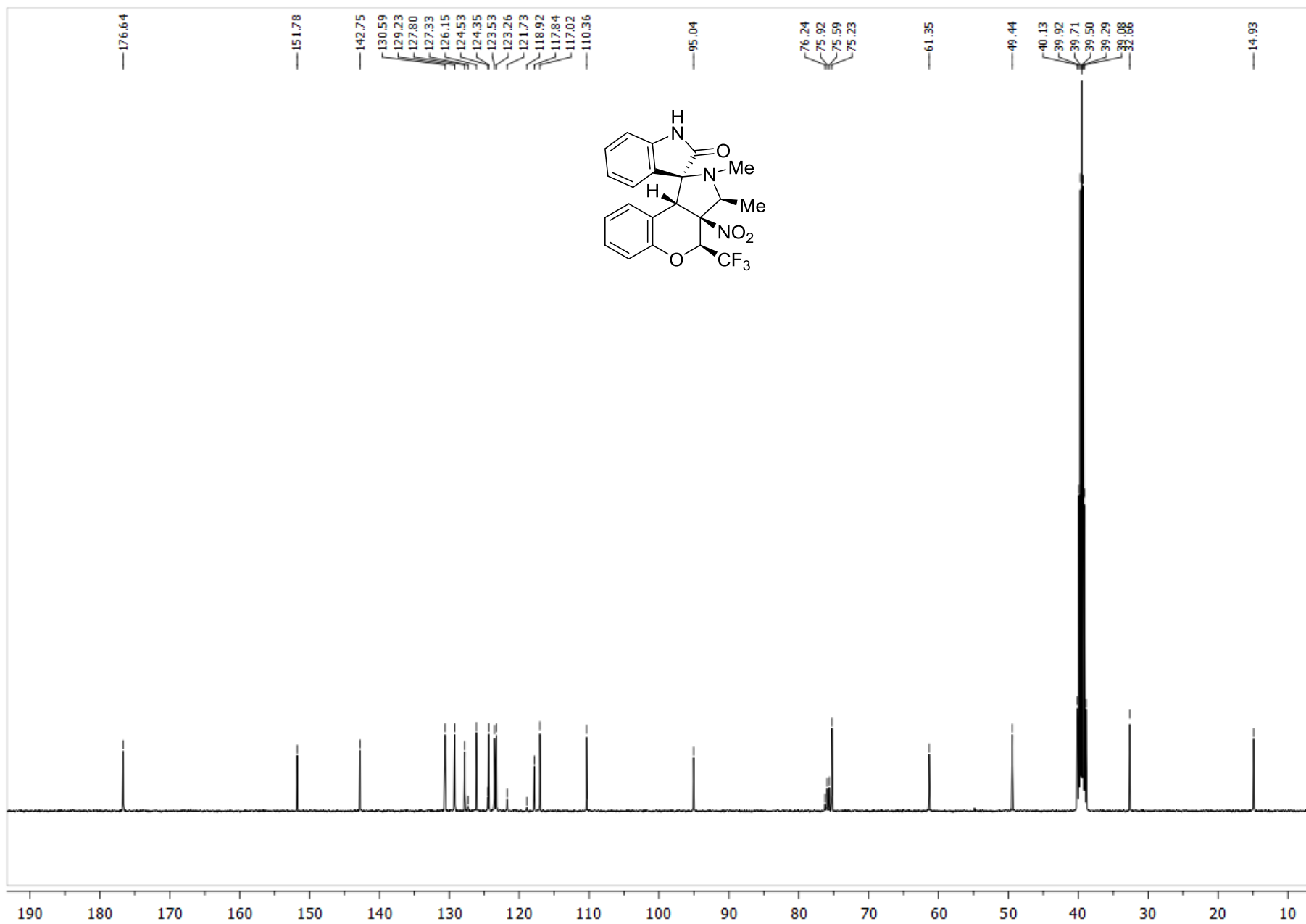


Figure S73. Copy of ¹³C NMR spectrum of **8a** in DMSO-*d*₆

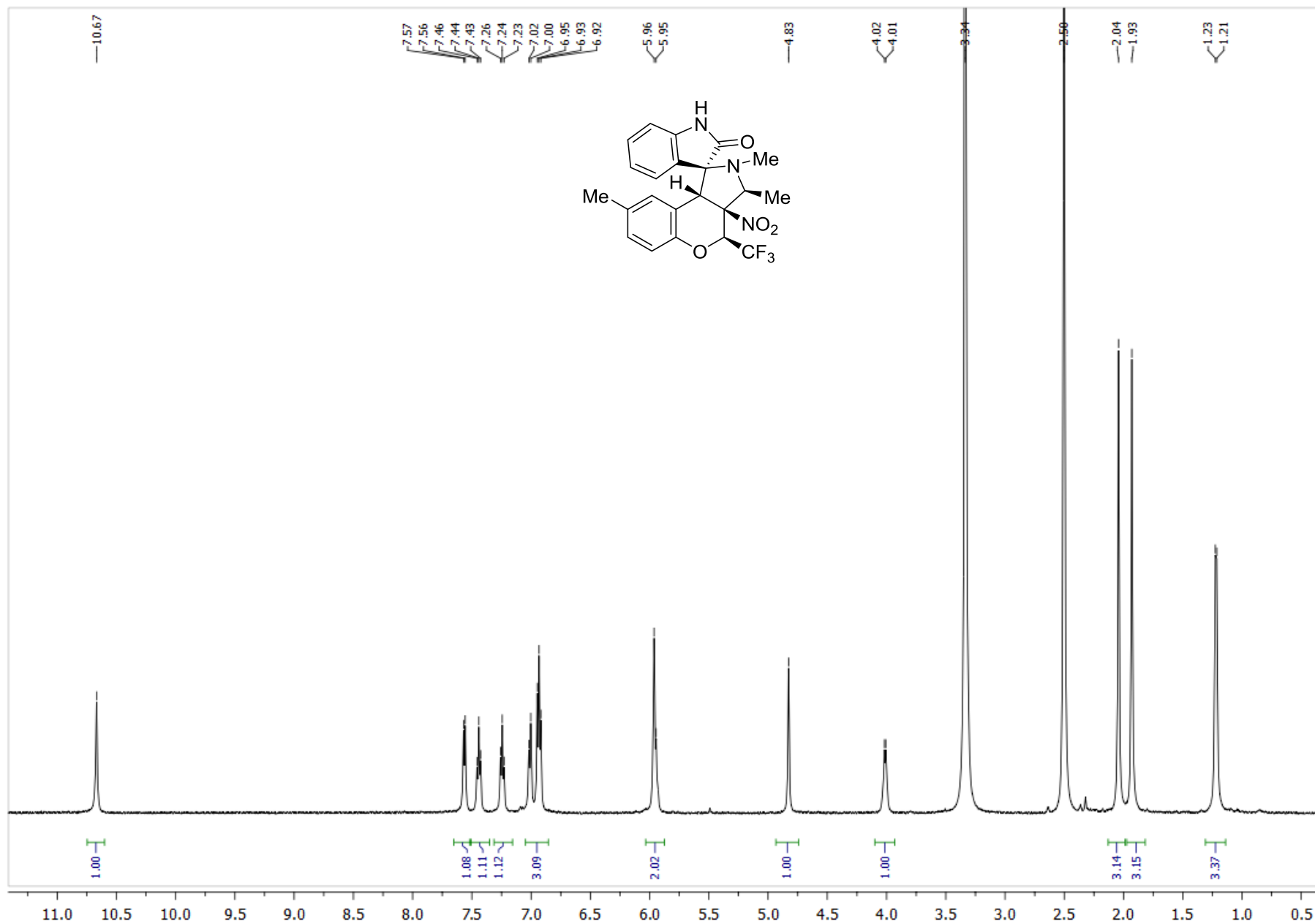


Figure S74. Copy of ¹H NMR spectrum of **8b** in DMSO-*d*₆

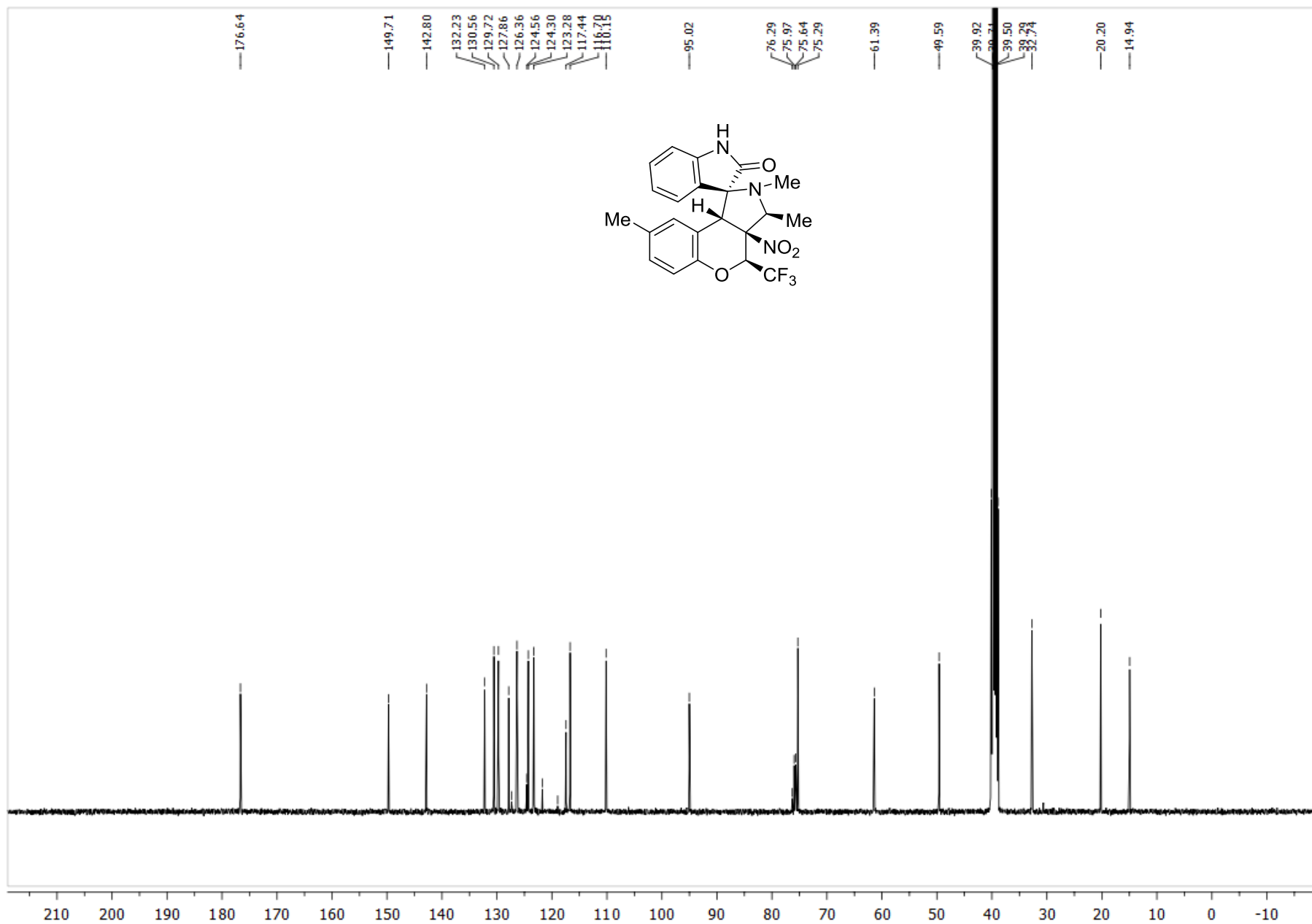


Figure S75. Copy of ¹³C NMR spectrum of **8b** in DMSO-*d*₆

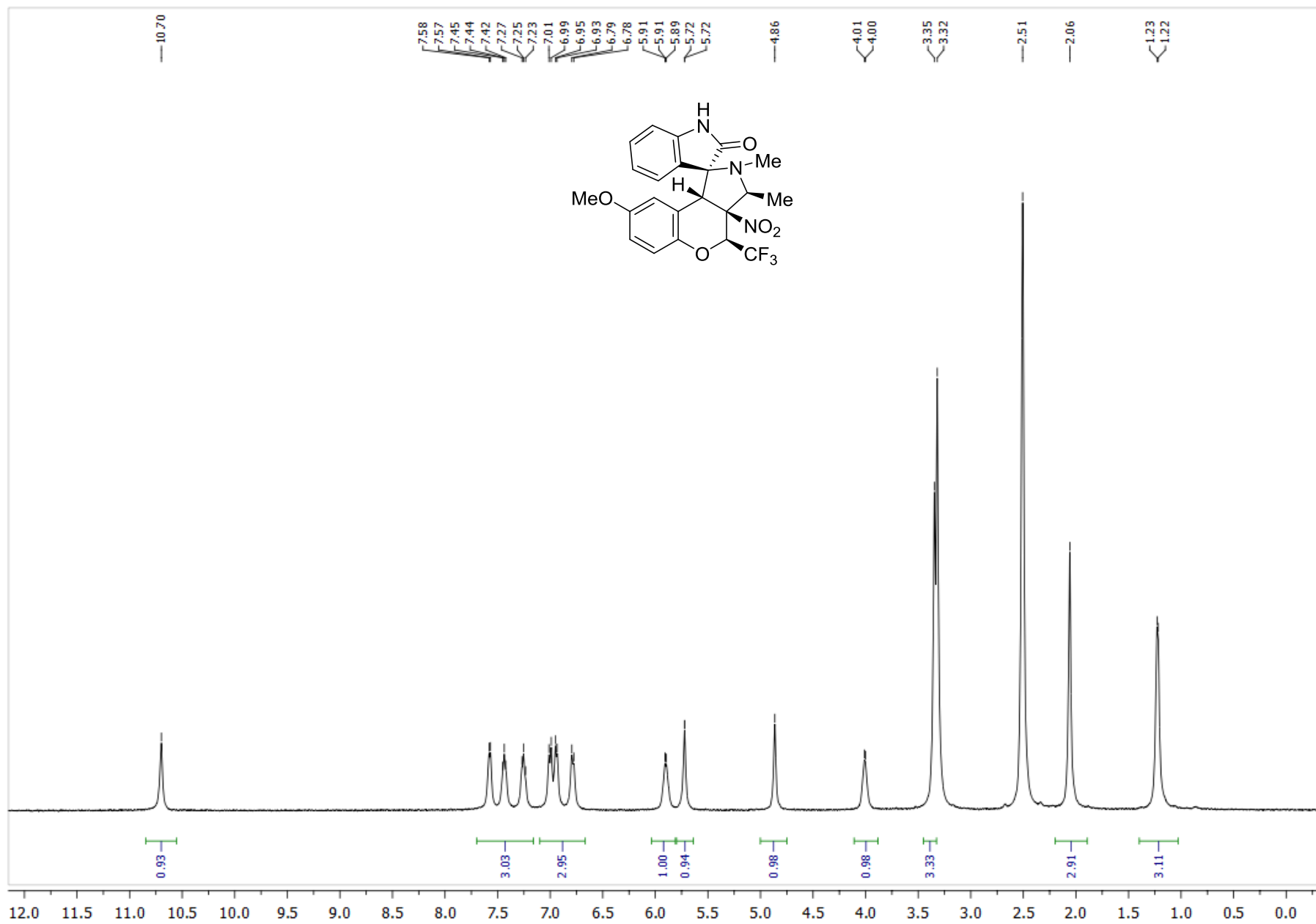


Figure S76. Copy of ^1H NMR spectrum of **8c** in $\text{DMSO-}d_6$

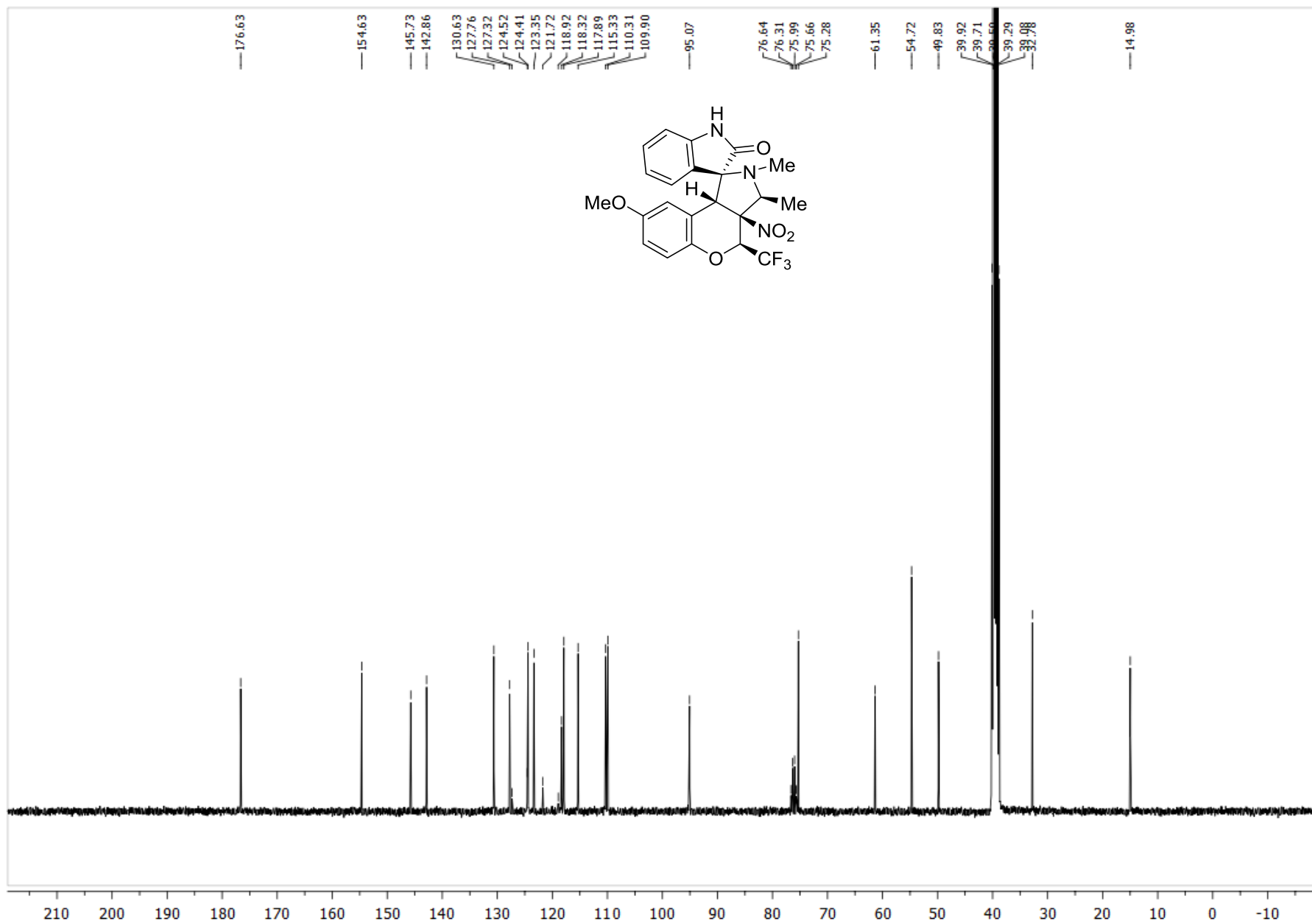


Figure S77. Copy of ¹³C NMR spectrum of **8c** in DMSO-*d*₆

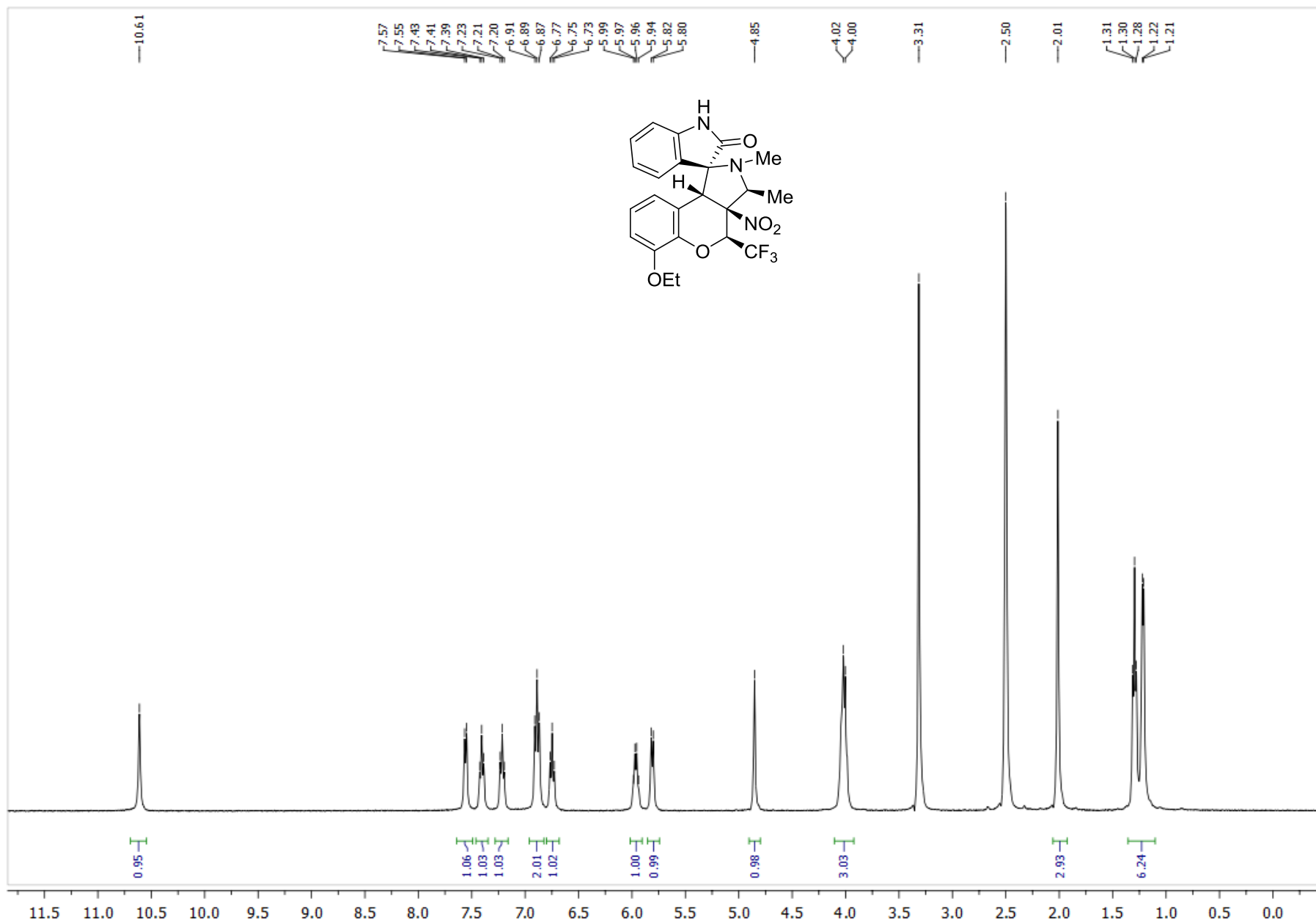


Figure S78. Copy of ^1H NMR spectrum of **8d** in DMSO- d_6

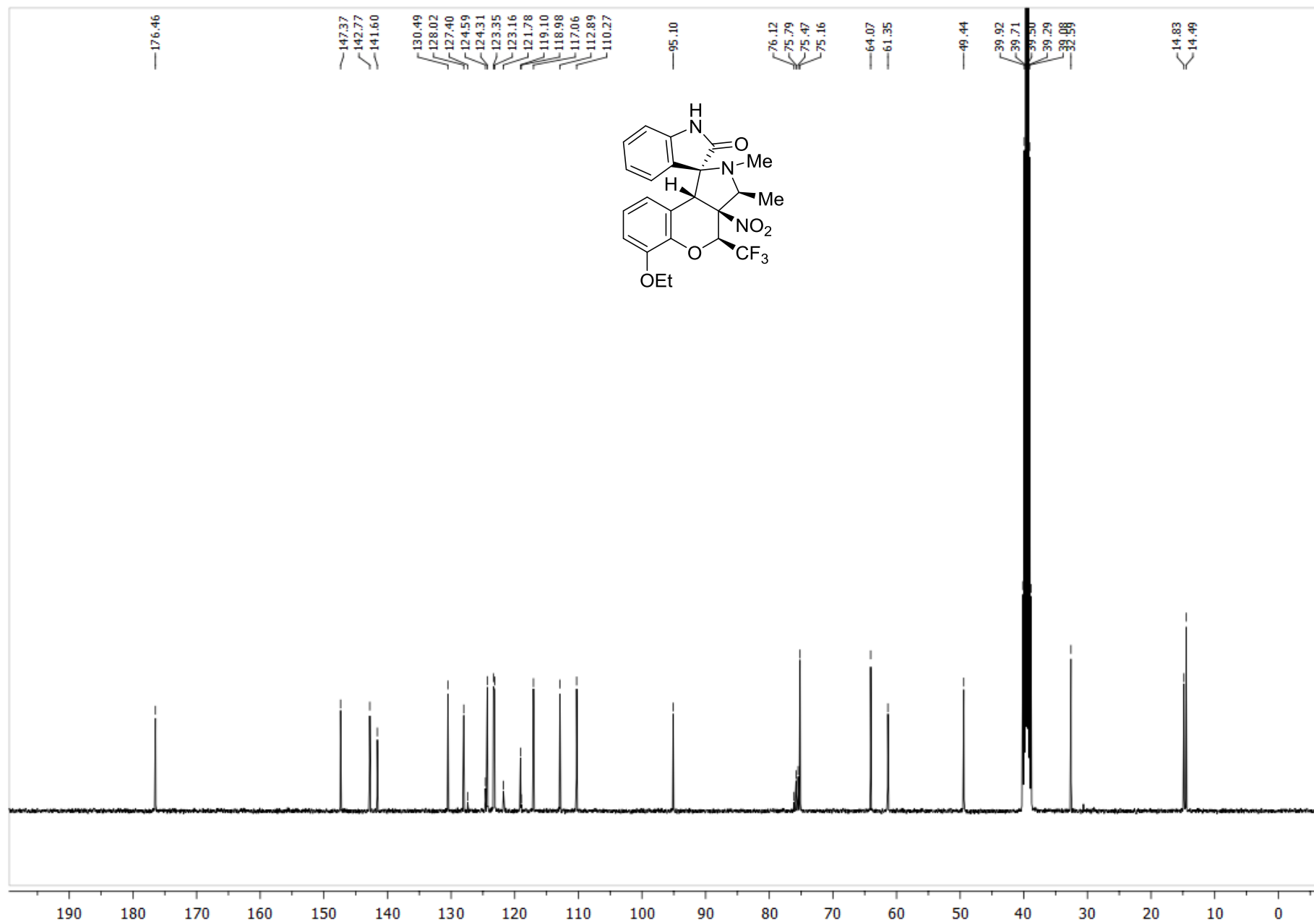


Figure S79. Copy of ¹³C NMR spectrum of **8d** in DMSO-*d*₆

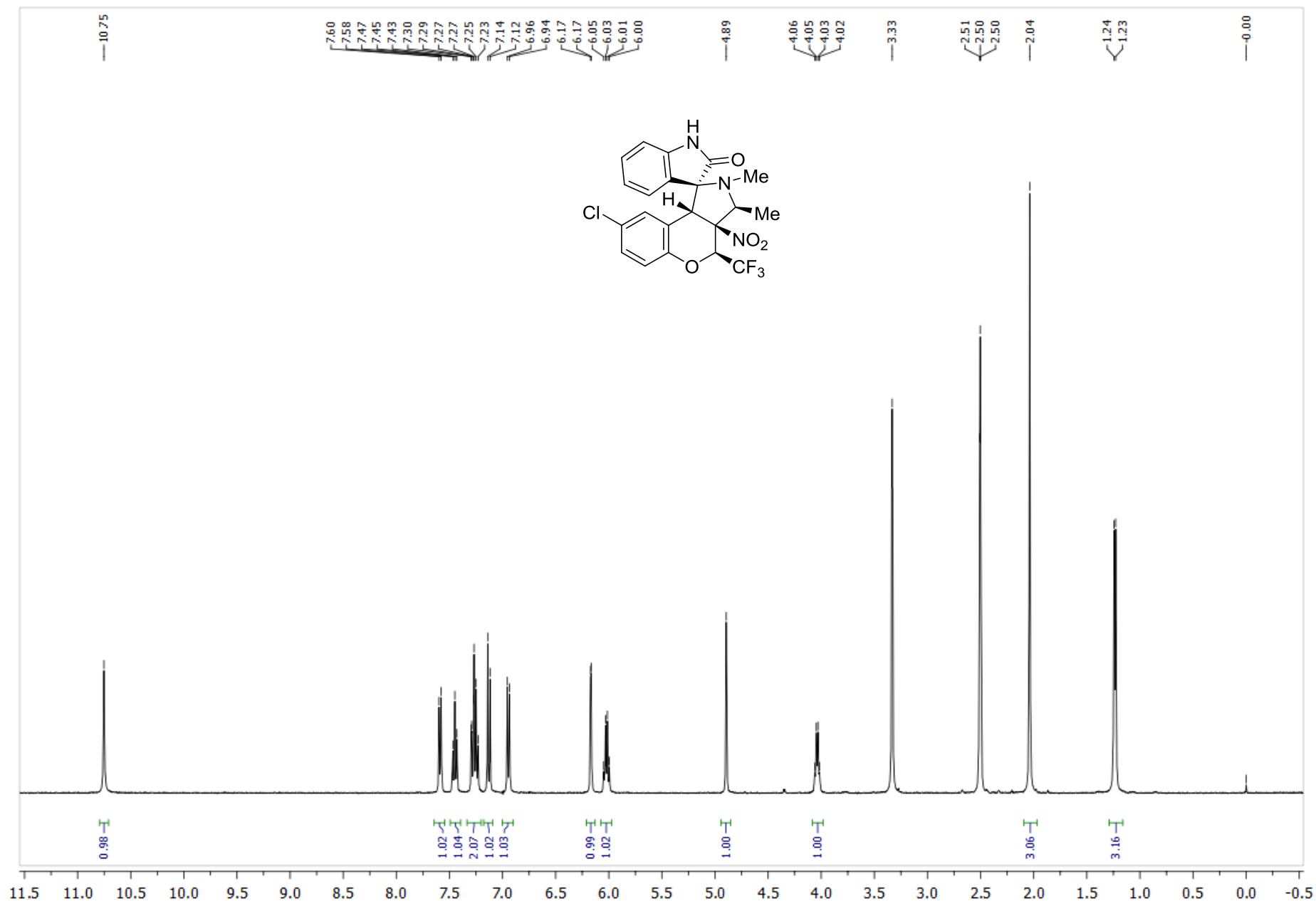


Figure S80. Copy of ^1H NMR spectrum of **8e** in $\text{DMSO}-d_6$

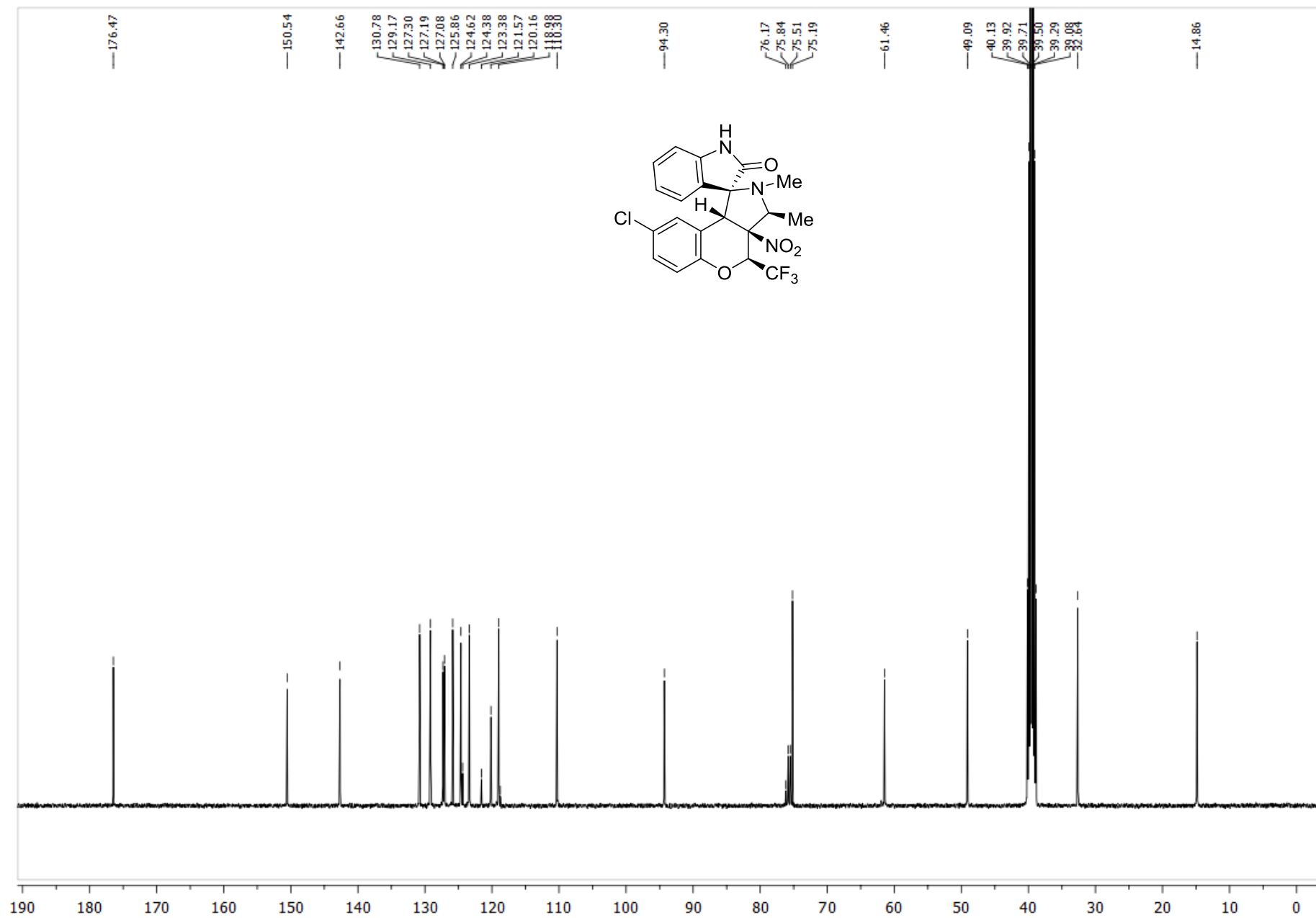


Figure S81. Copy of ^{13}C NMR spectrum of **8e** in $\text{DMSO-}d_6$

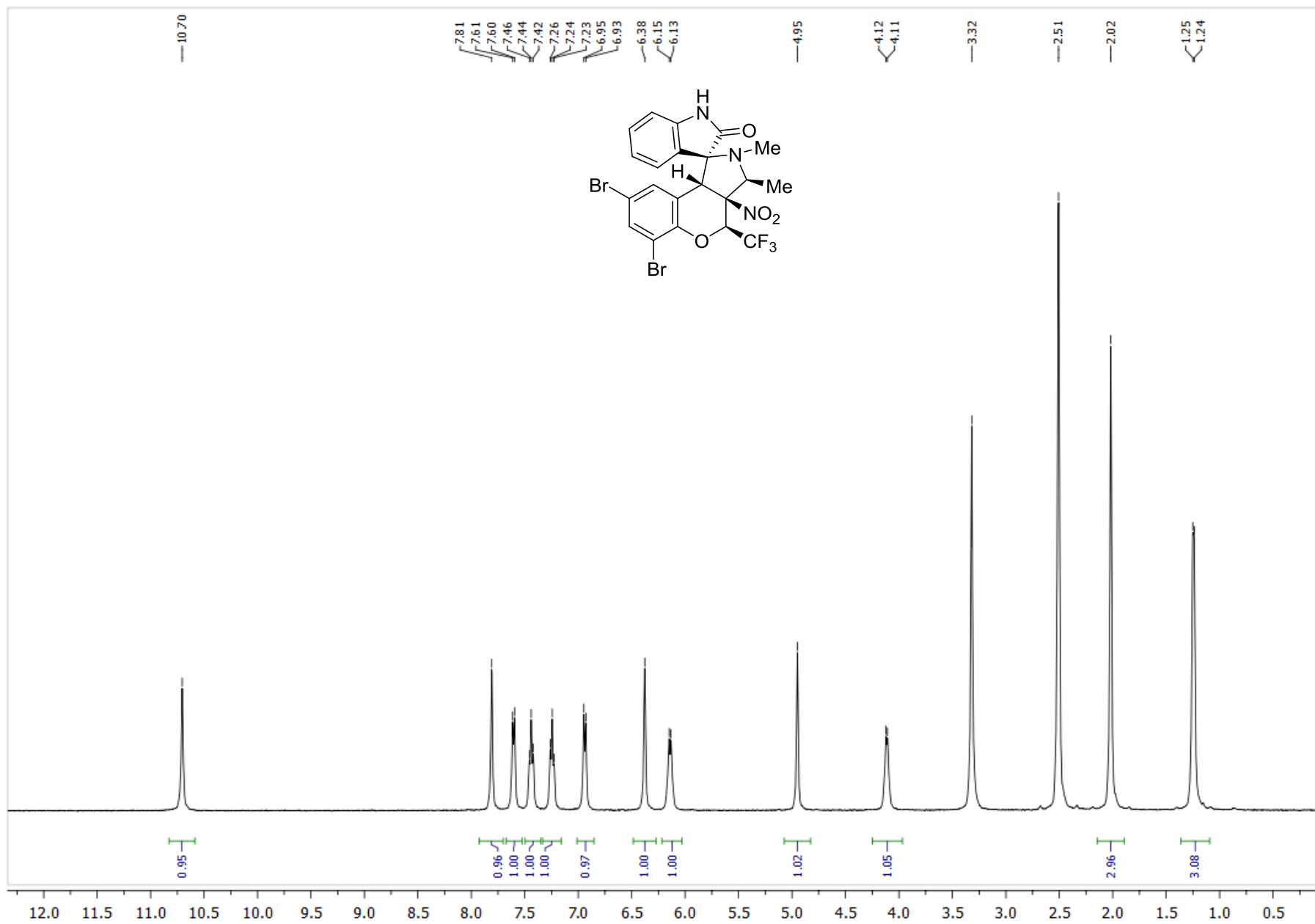


Figure S82. Copy of ¹H NMR spectrum of **8f** in DMSO-*d*₆

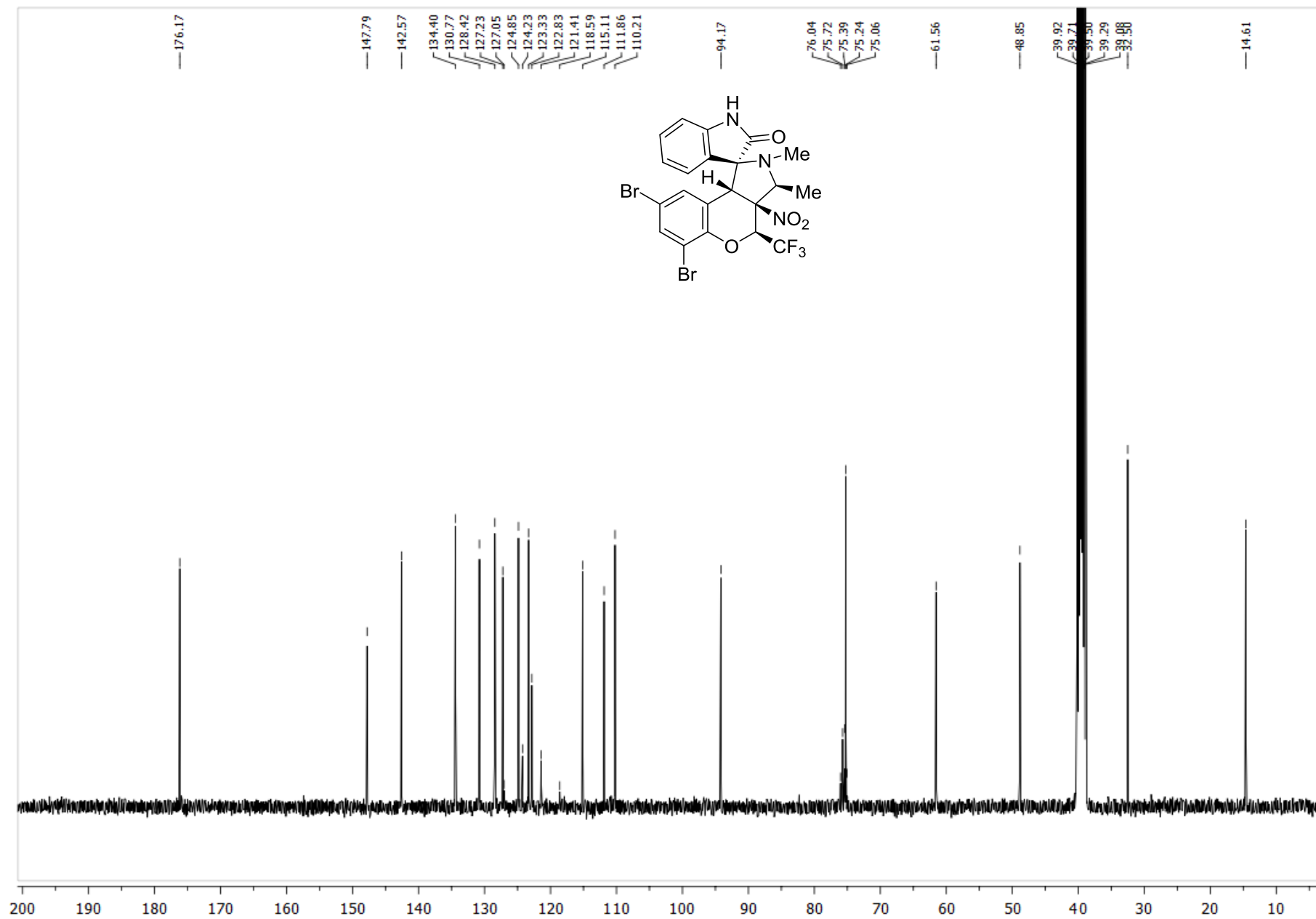


Figure S83. Copy of ¹³C NMR spectrum of **8f** in DMSO-*d*₆

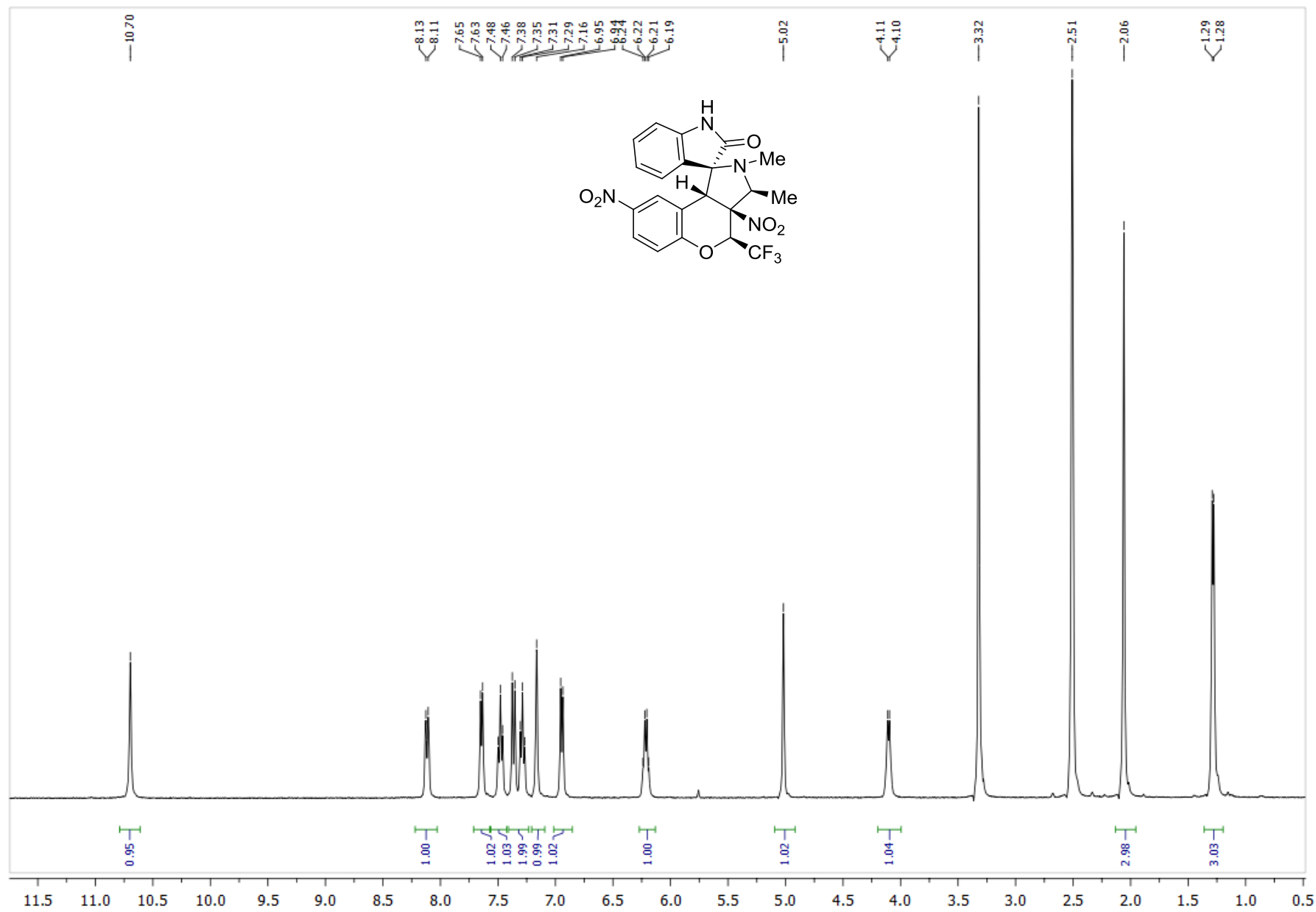


Figure S84. Copy of ^1H NMR spectrum of **8g** in $\text{DMSO-}d_6$

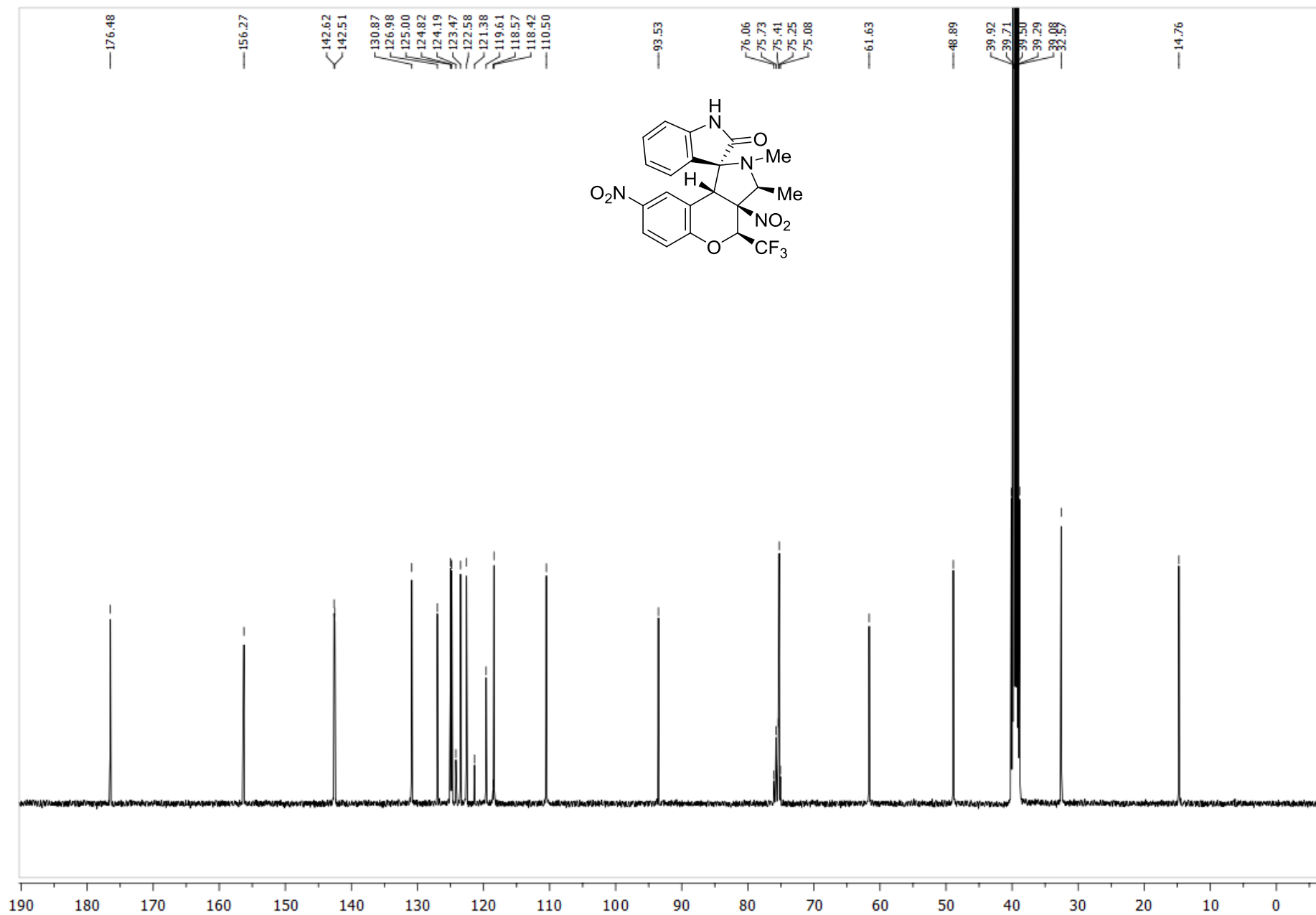


Figure S85. Copy of ¹³C NMR spectrum of **8g** in DMSO-*d*₆

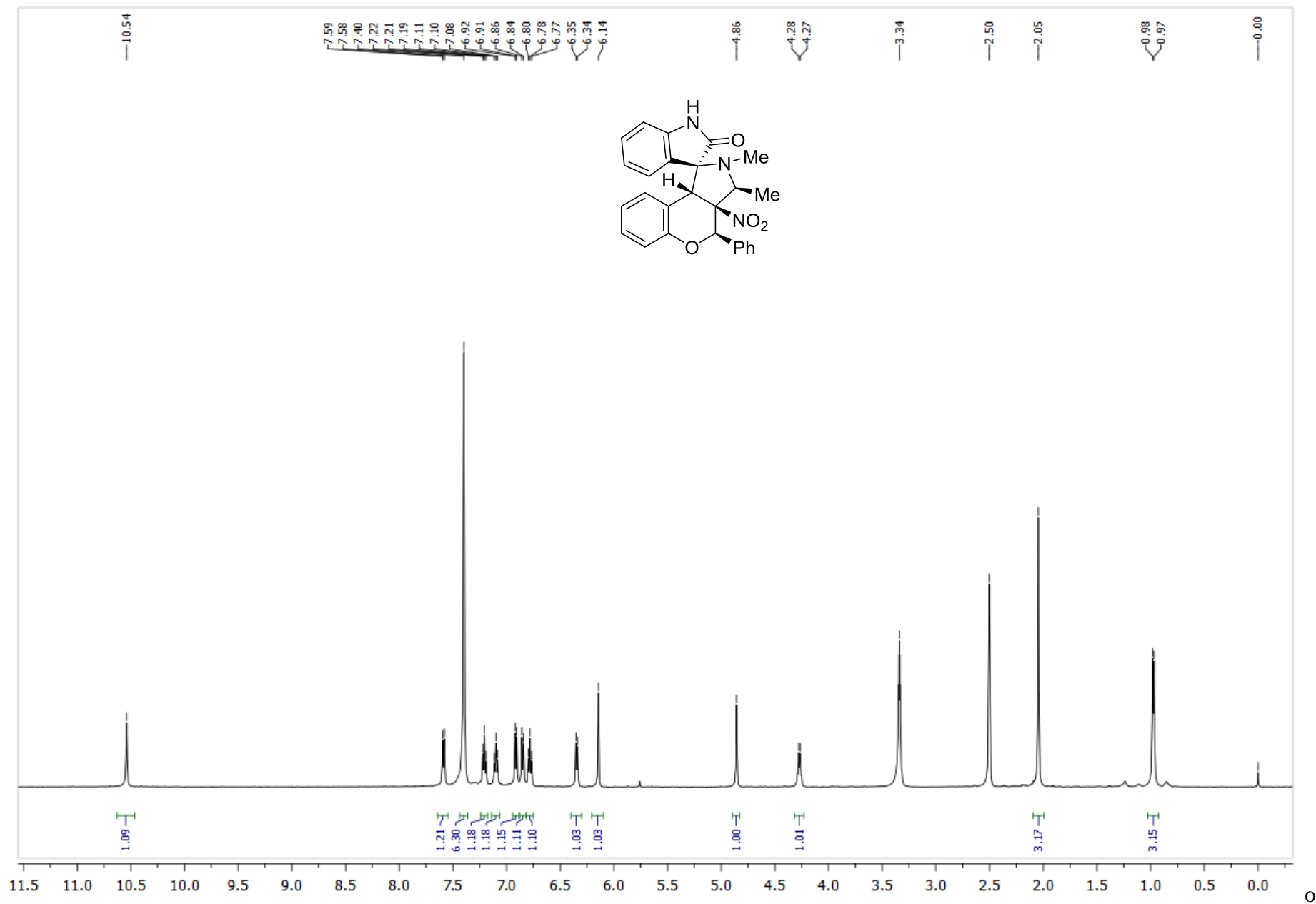


Figure S86. Copy of ^1H NMR spectrum of **8h** in $\text{DMSO-}d_6$

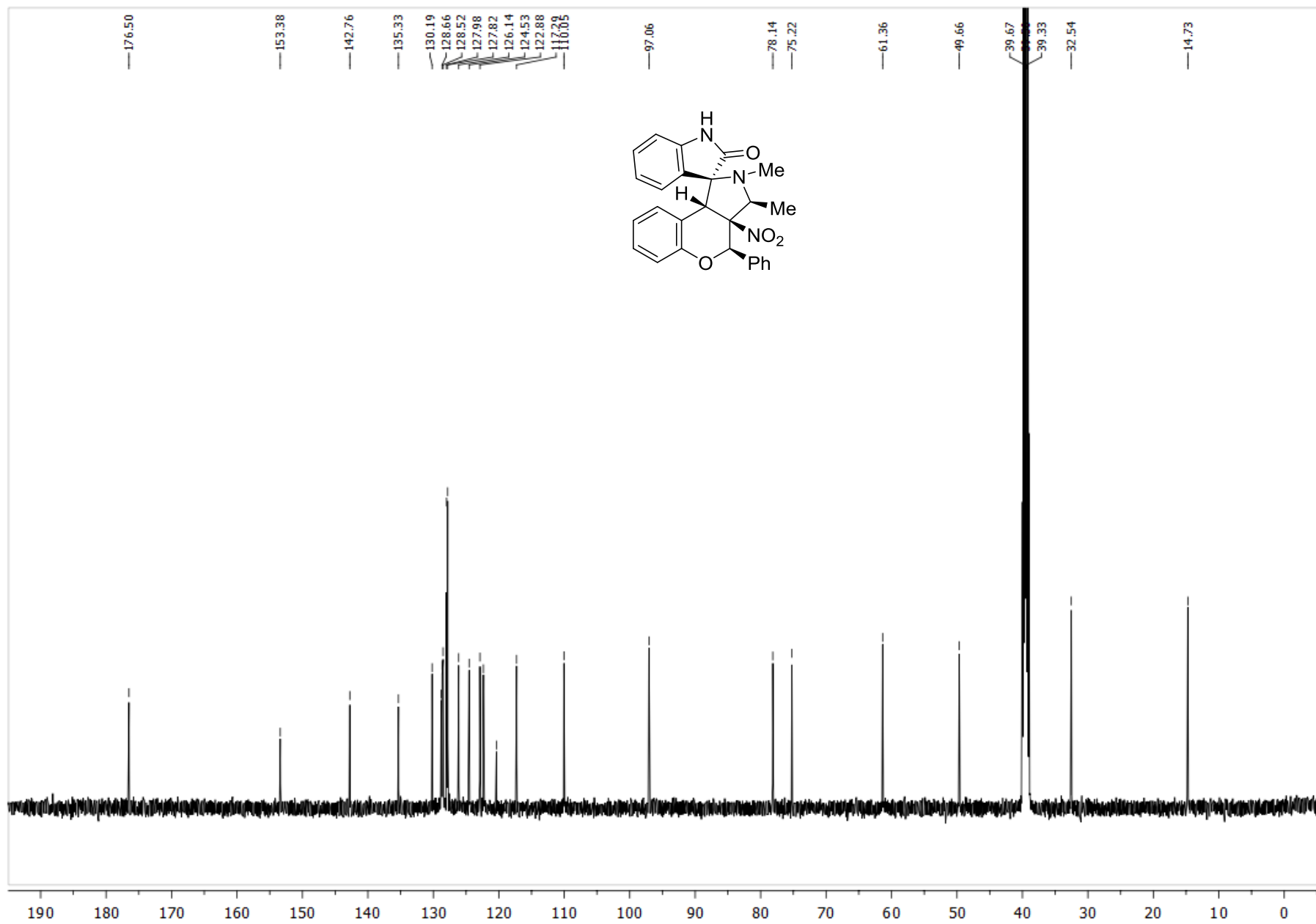


Figure S87. Copy of ¹³C NMR spectrum of **8h** in DMSO-*d*₆

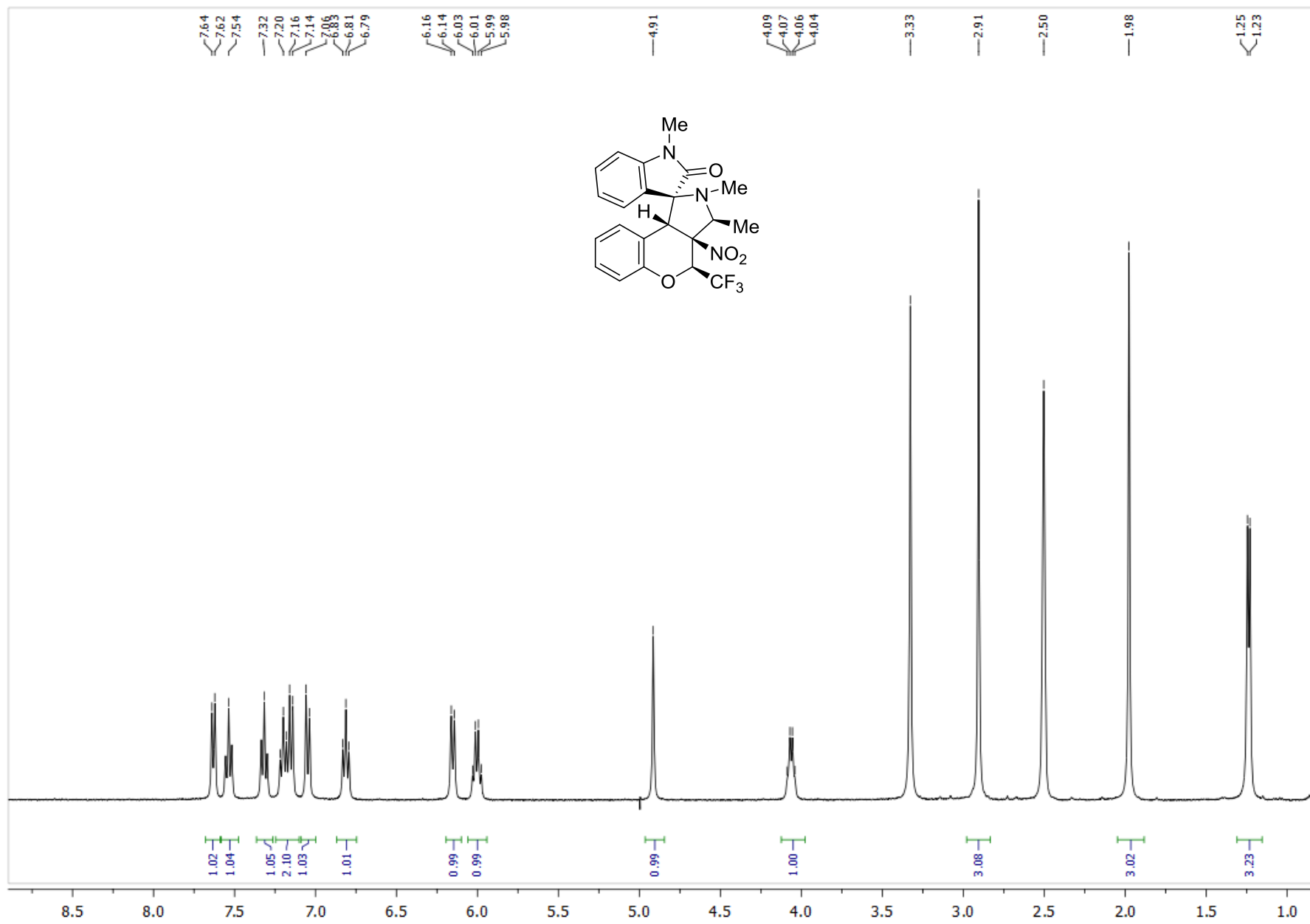


Figure S88. Copy of ¹H NMR spectrum of **8i** in DMSO-*d*₆

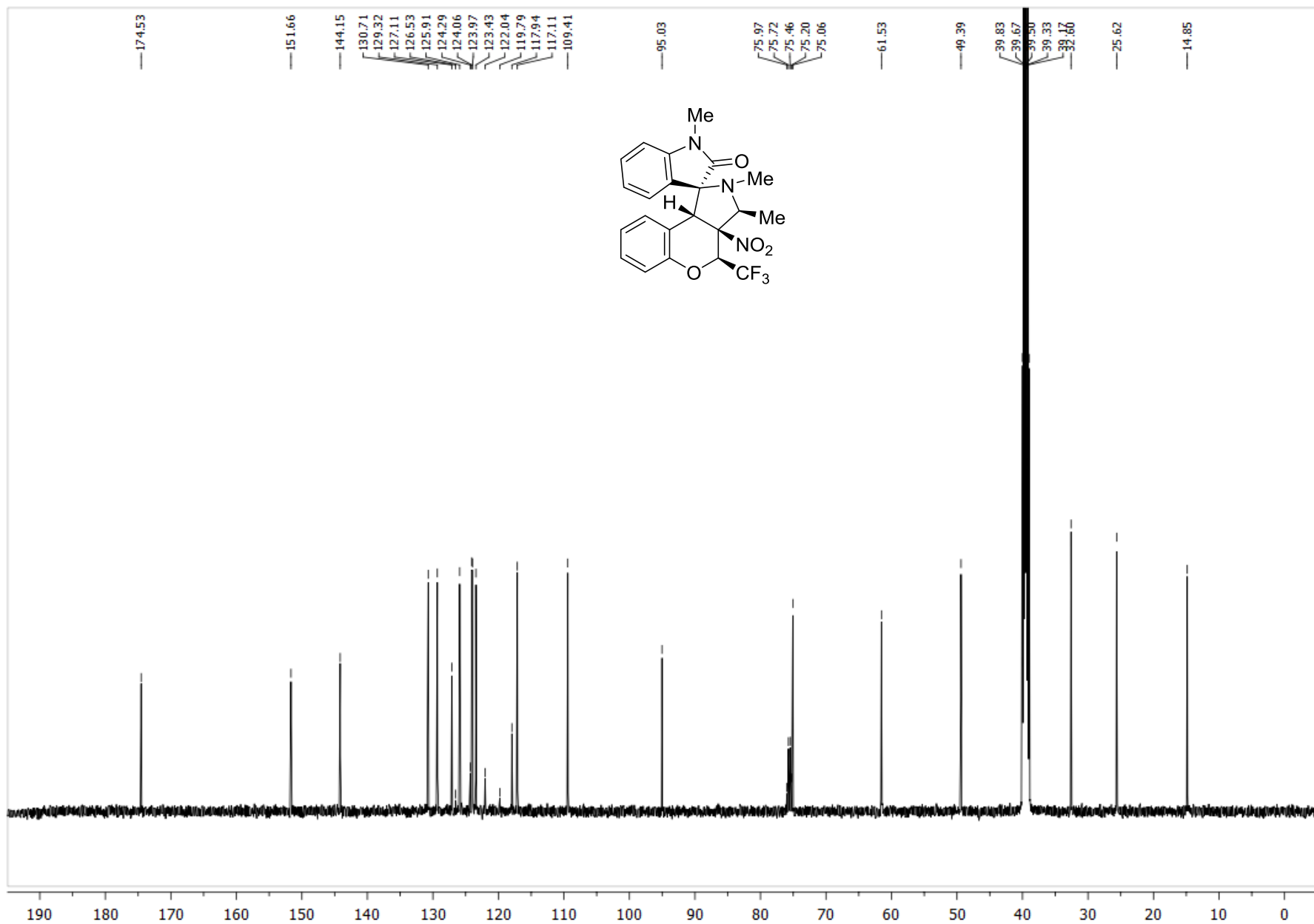


Figure S89. Copy of ¹³C NMR spectrum of **8i** in DMSO-*d*₆

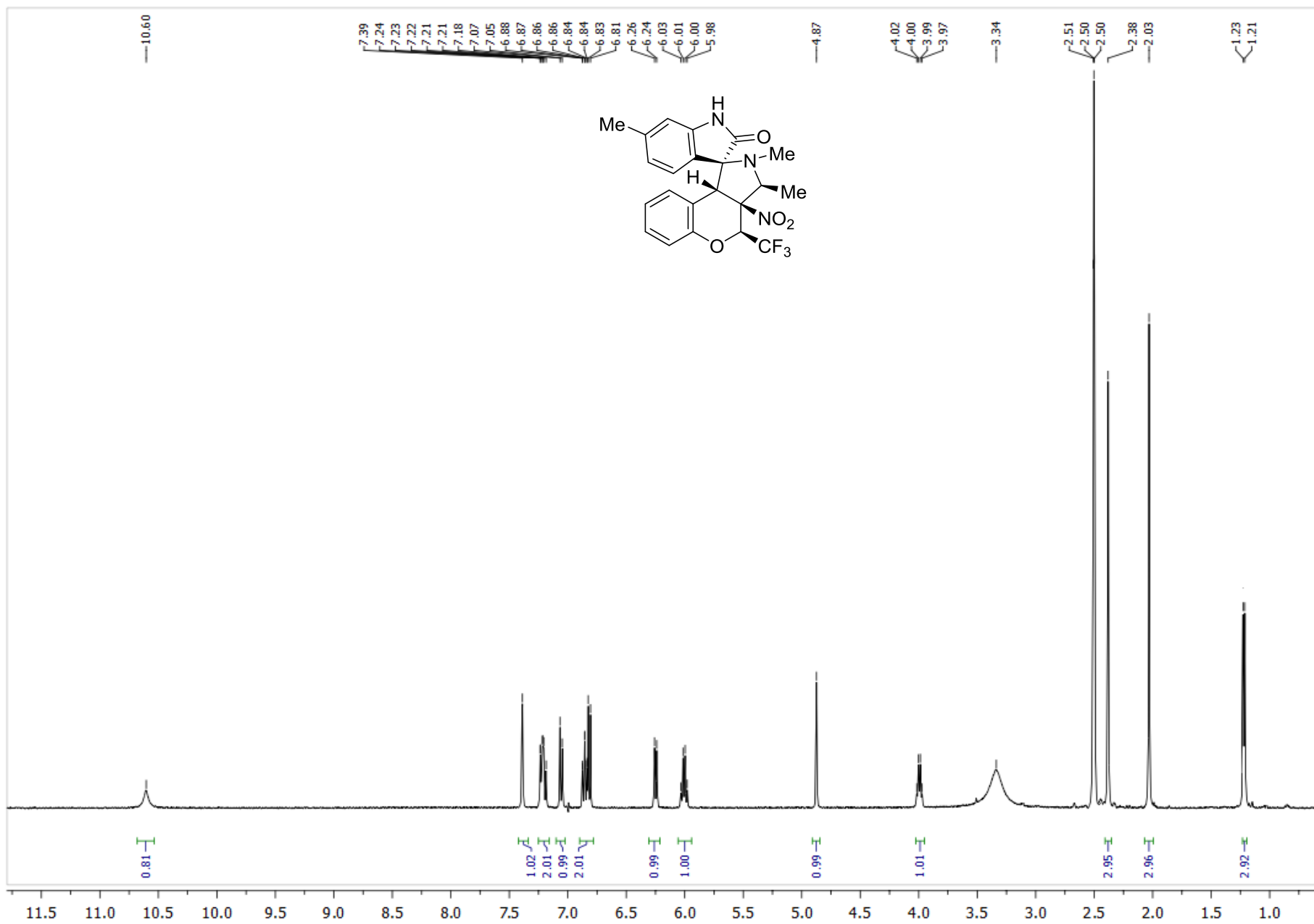


Figure S90. Copy of ^1H NMR spectrum of **8j** in $\text{DMSO-}d_6$

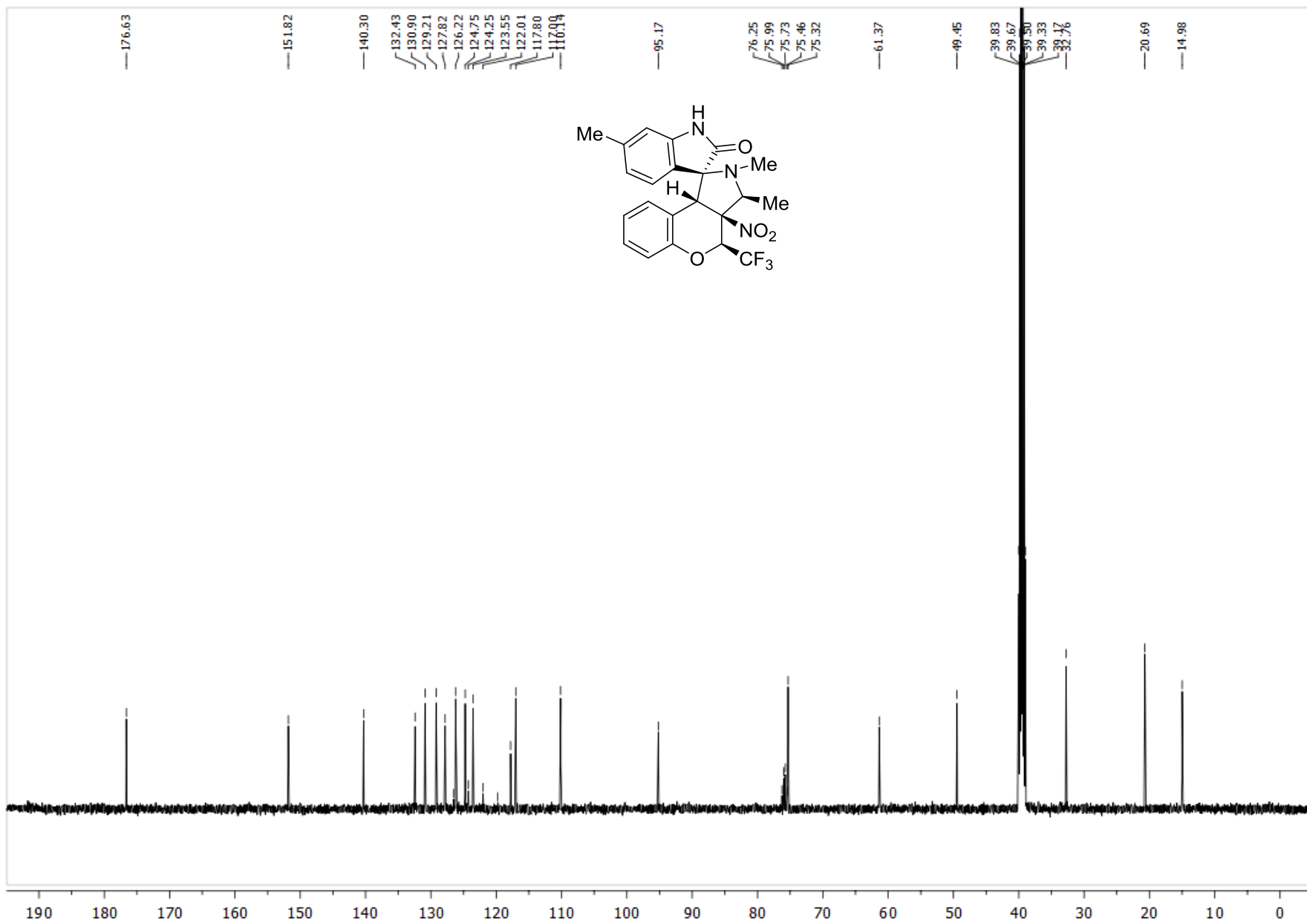


Figure S91. Copy of ¹³C NMR spectrum of **8j** in DMSO-*d*₆

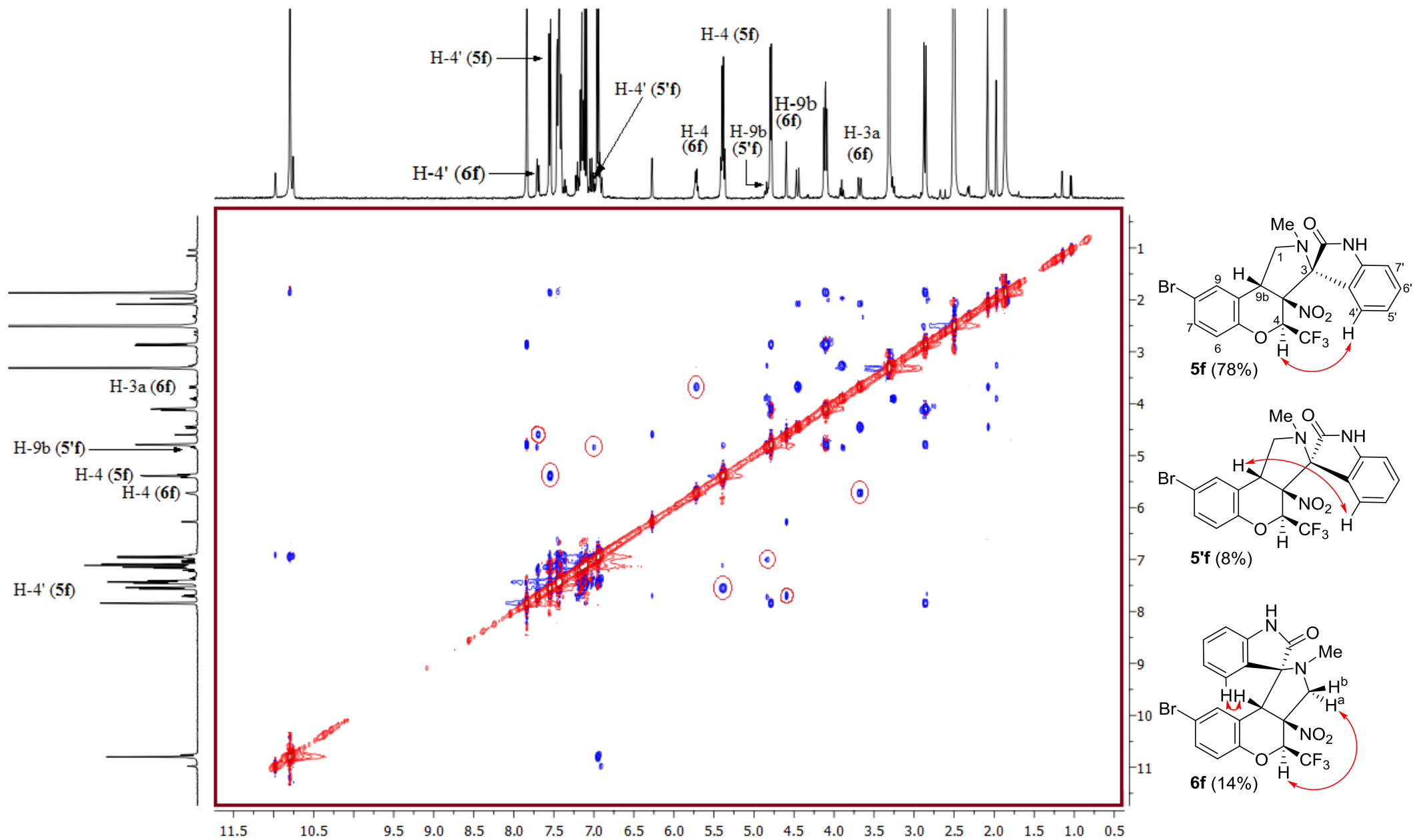


Figure S92. Copy of 2D ^1H - ^1H NOESY spectrum of the mixture of isomers **5f**, **5'f** and **6f** in $\text{DMSO-}d_6$

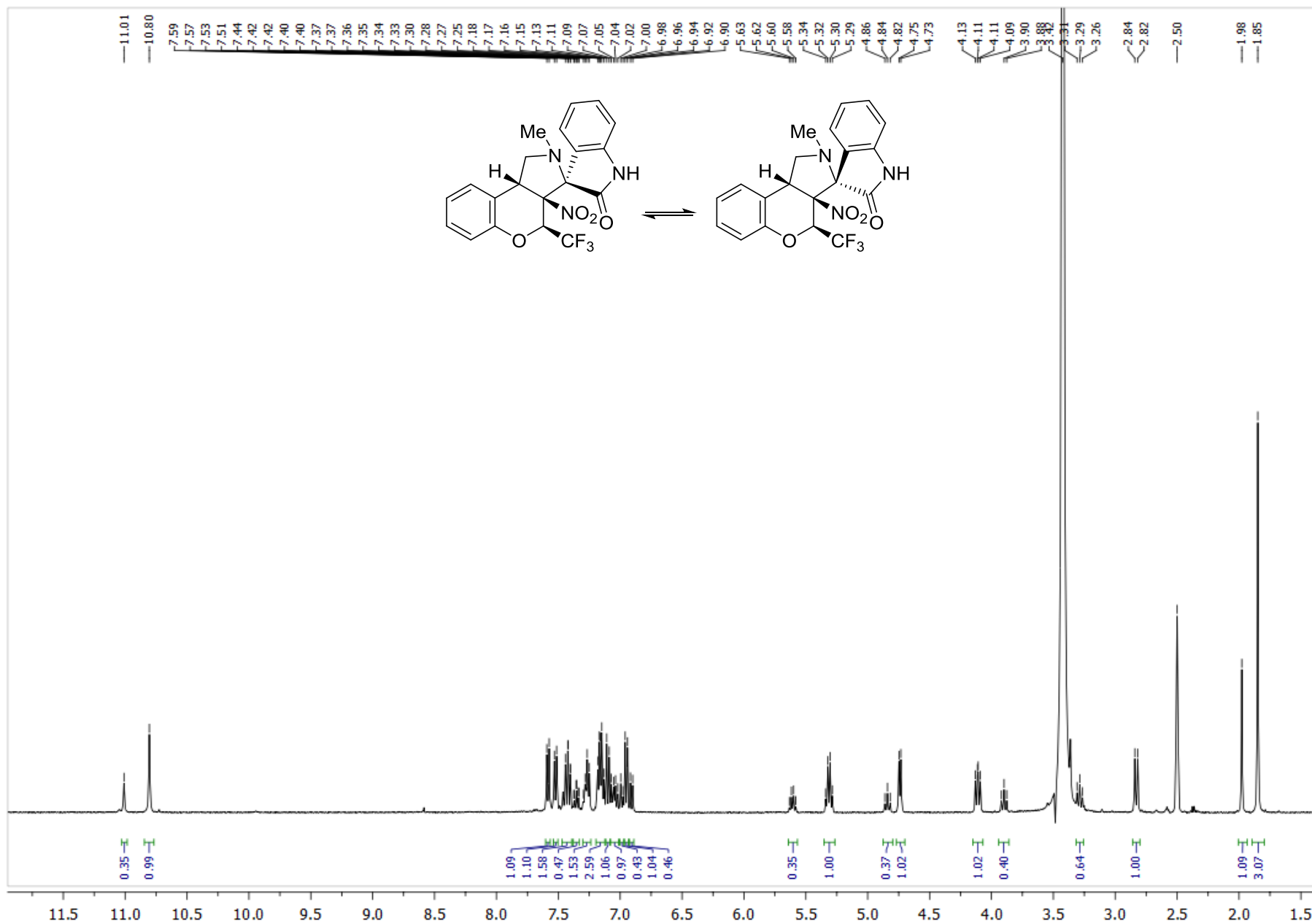


Figure S93. Copy of ^1H NMR spectrum of the mixture of isomers **5a** and **5'a** after keeping in $\text{DMSO-}d_6$ for 37 days

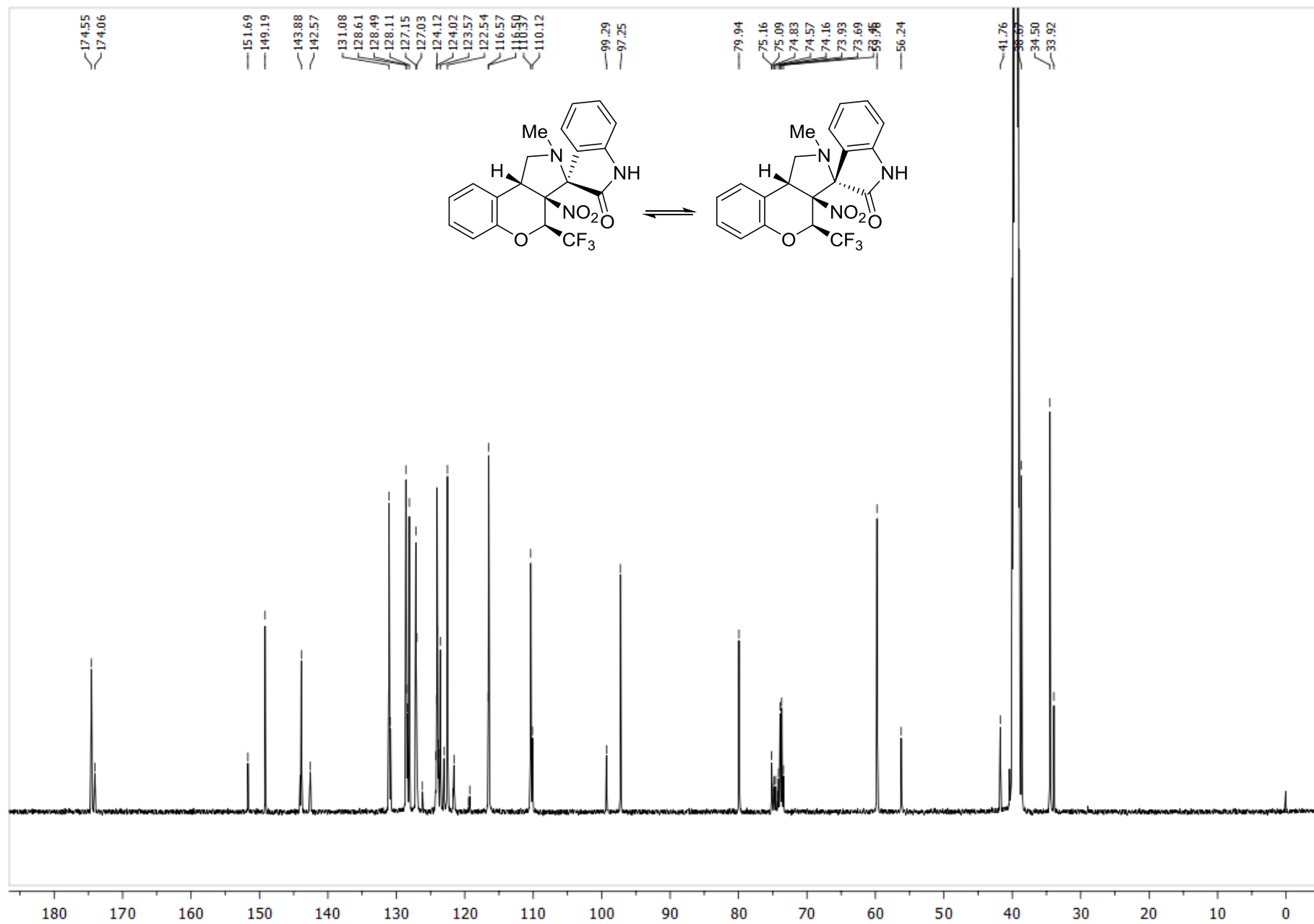


Figure S94. Copy of ¹³C NMR spectrum of the mixture of isomers **5a** and **5'a** after keeping in DMSO-*d*₆ for 37 days

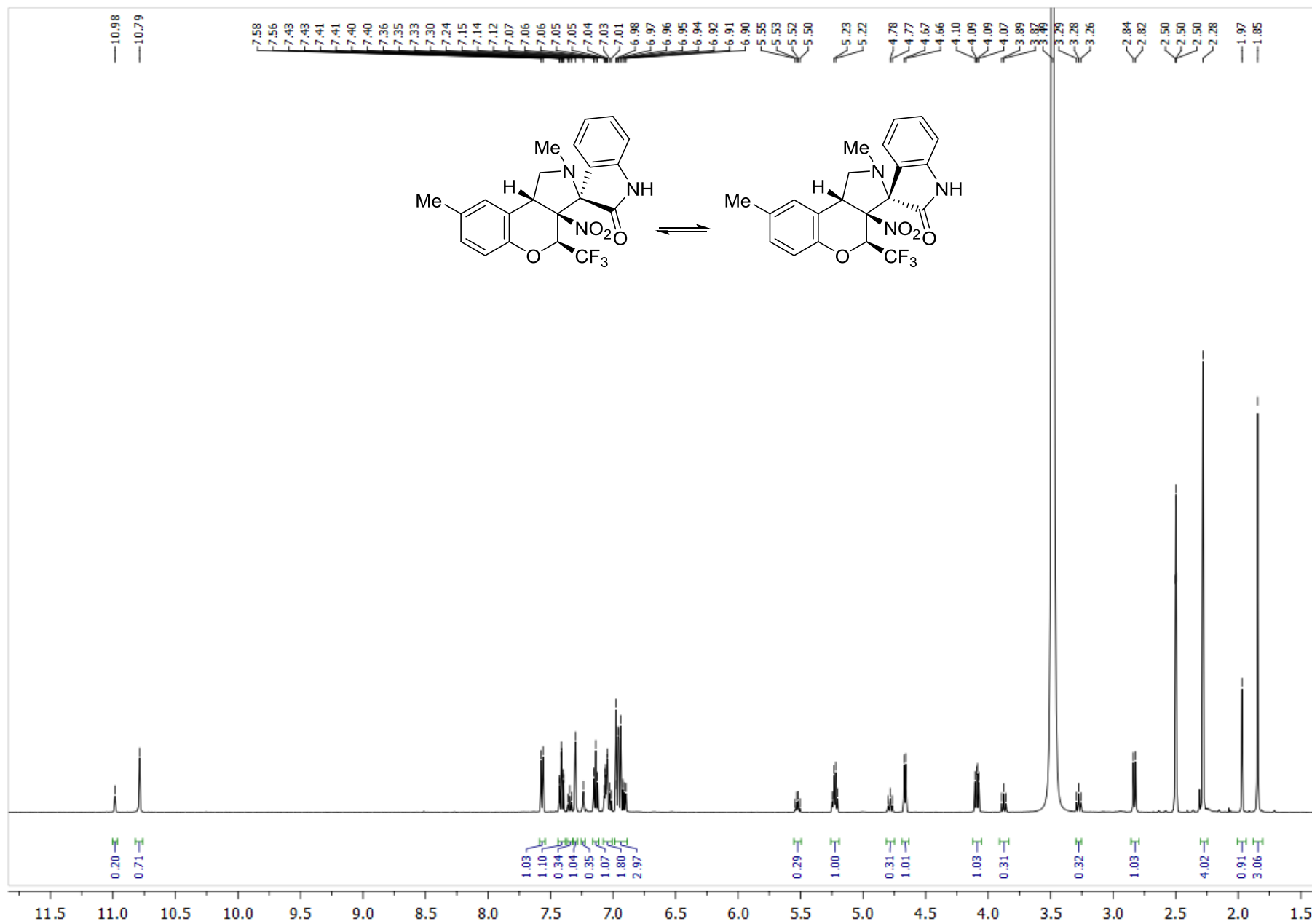


Figure S95. Copy of ¹H NMR spectrum of the mixture of isomers **5b** and **5'b** after keeping in DMSO-*d*₆ for 7 days

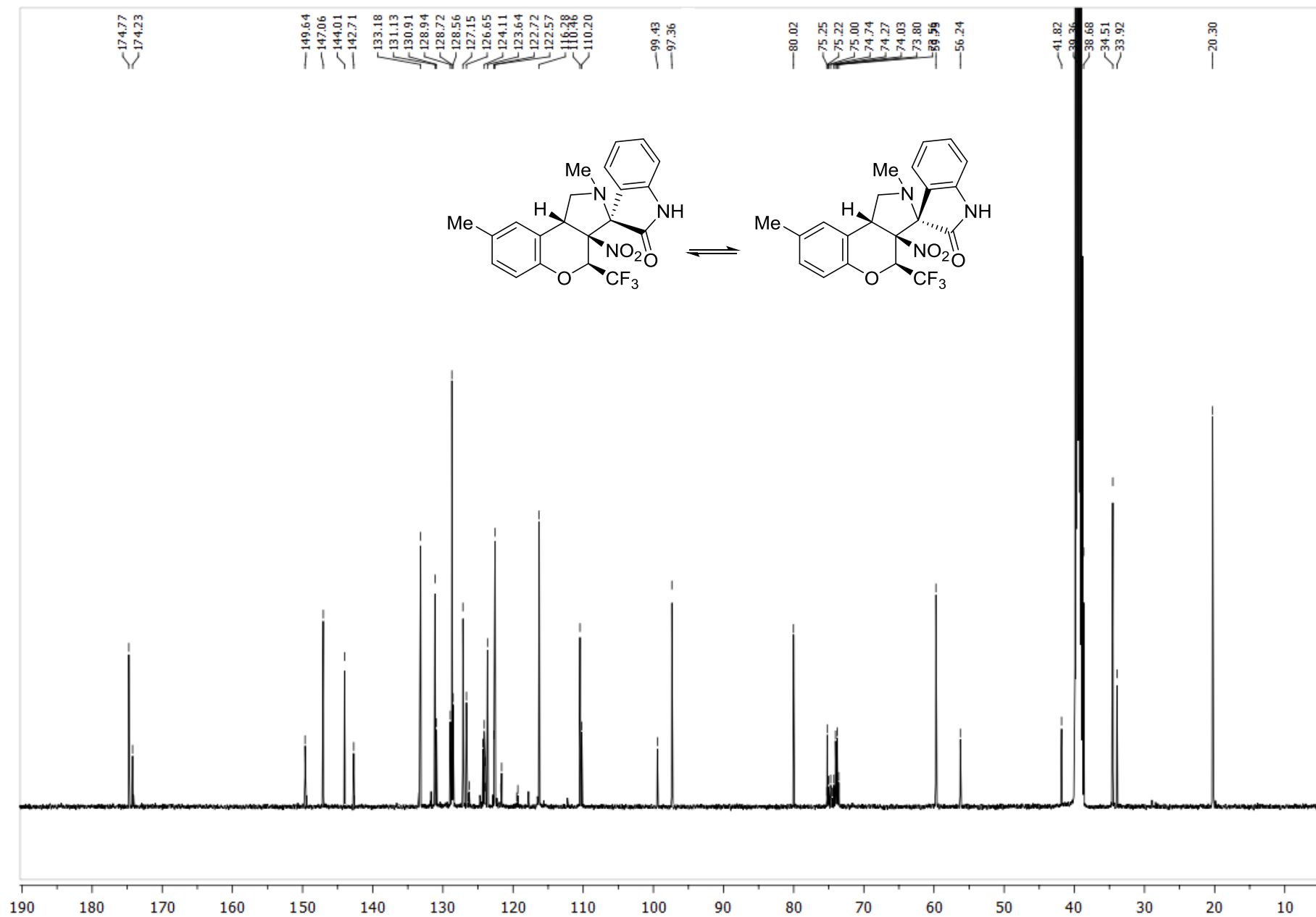


Figure S96. Copy of ¹³C NMR spectrum of the mixture of isomers **5b** and **5'b** after keeping in DMSO-*d*₆ for 14 days

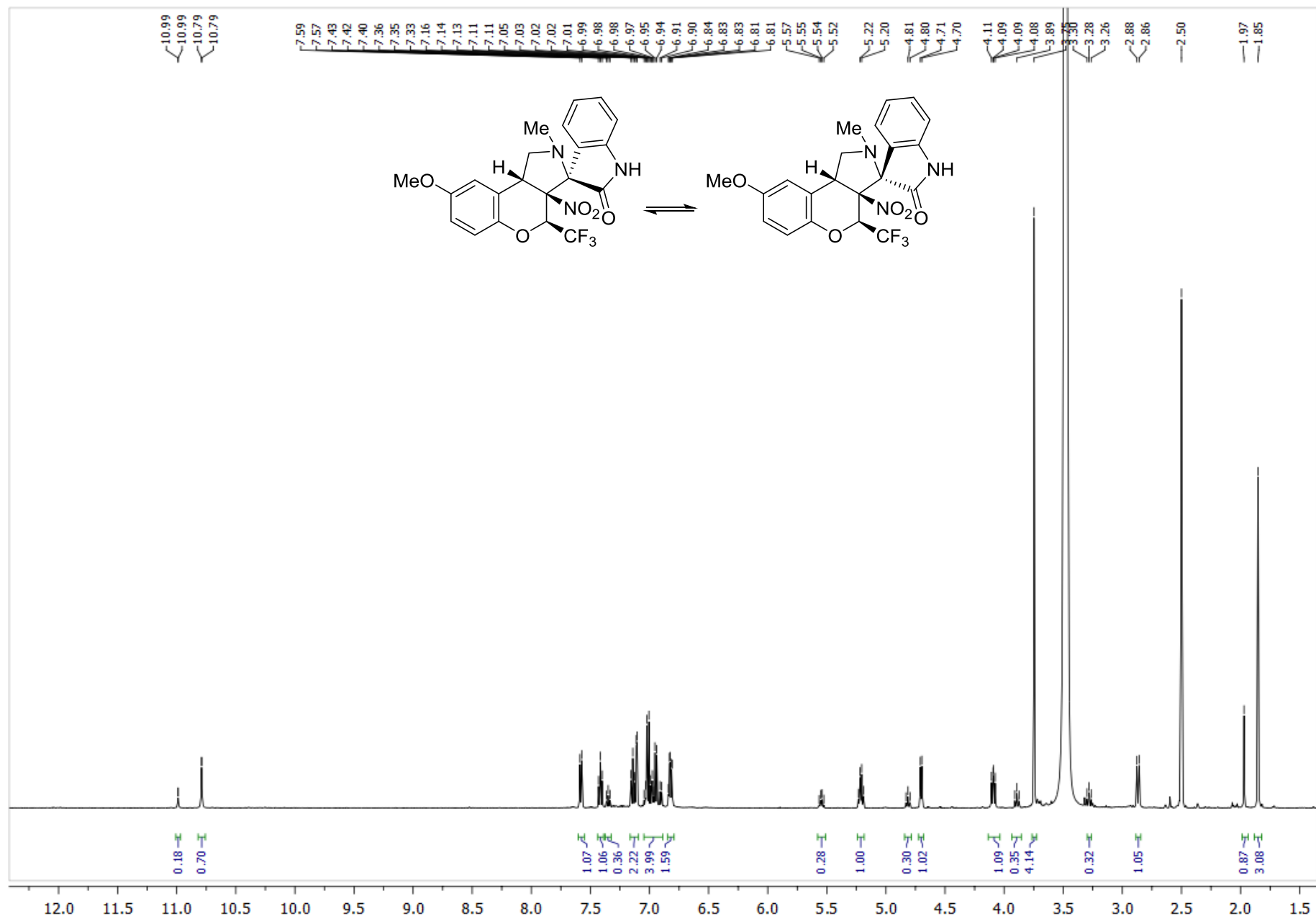


Figure S97. Copy of ^1H NMR spectrum of the mixture of isomers **5c** and **5'c** after keeping in $\text{DMSO-}d_6$ for 7 days

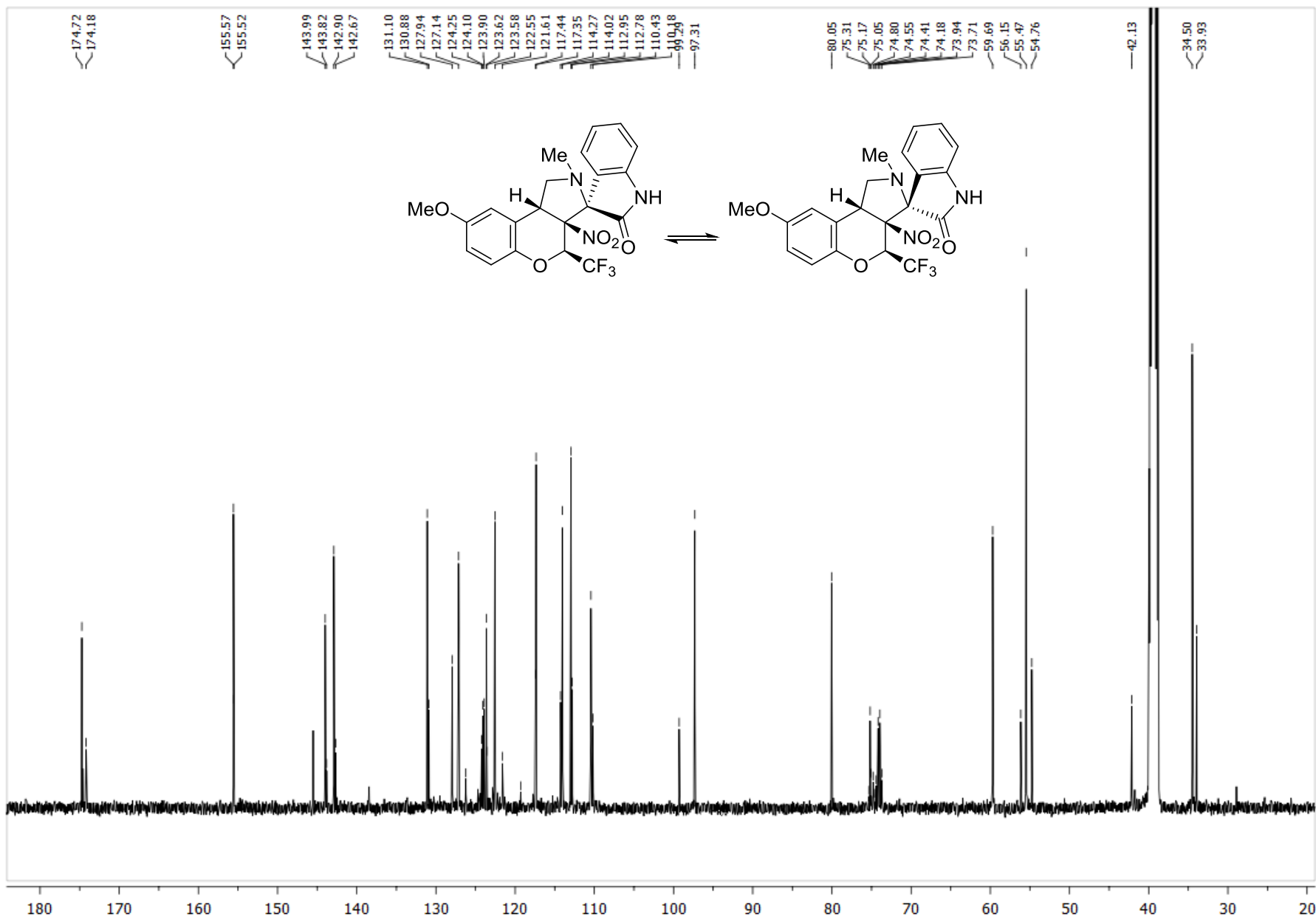


Figure S98. Copy of ¹³C NMR spectrum of the mixture of isomers **5c** and **5'c** after keeping in DMSO-*d*₆ for 14 days

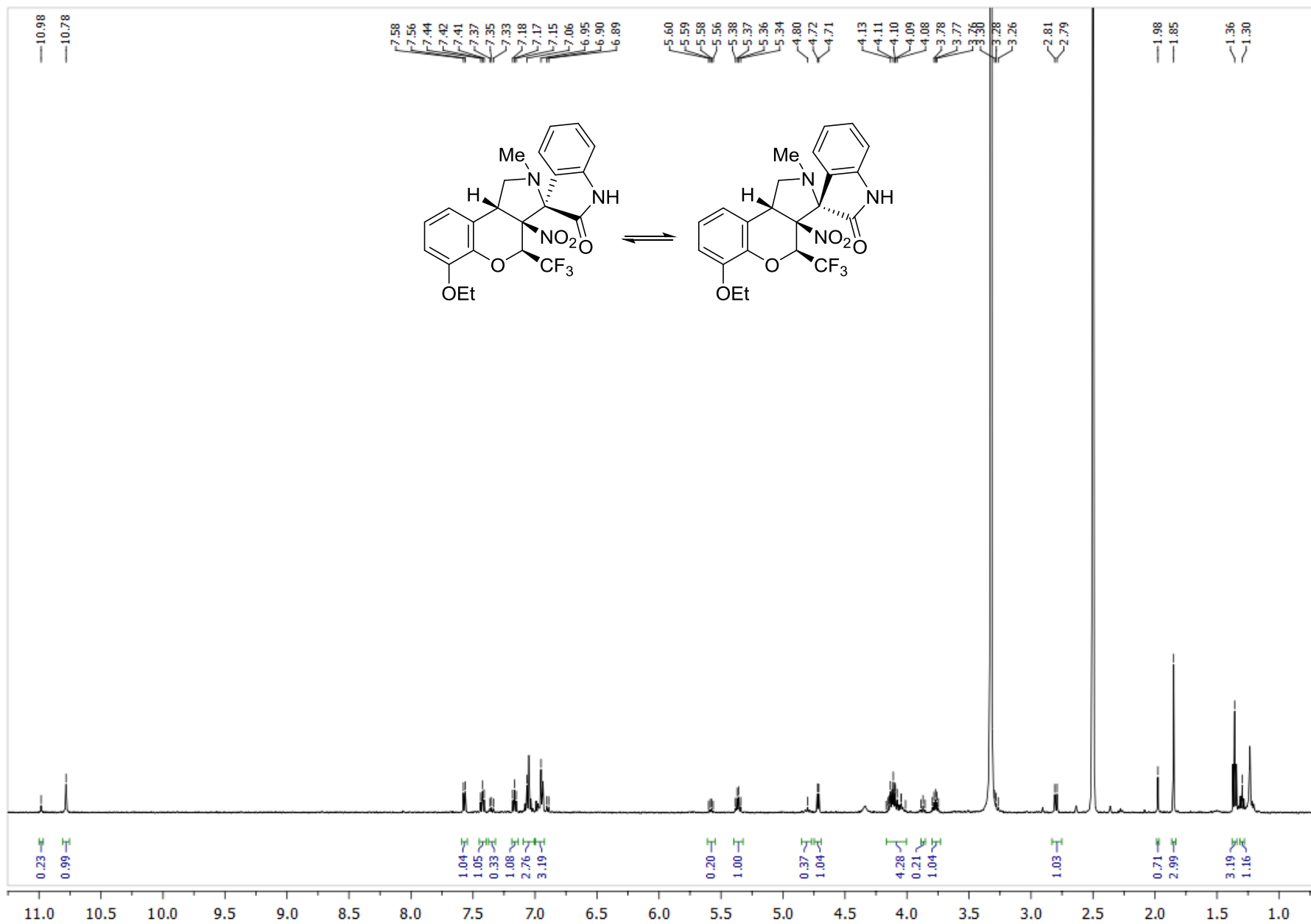


Figure S99. Copy of ^1H NMR spectrum of the mixture of isomers **5d** and **5'd** after keeping in $\text{DMSO-}d_6$ for 7 days

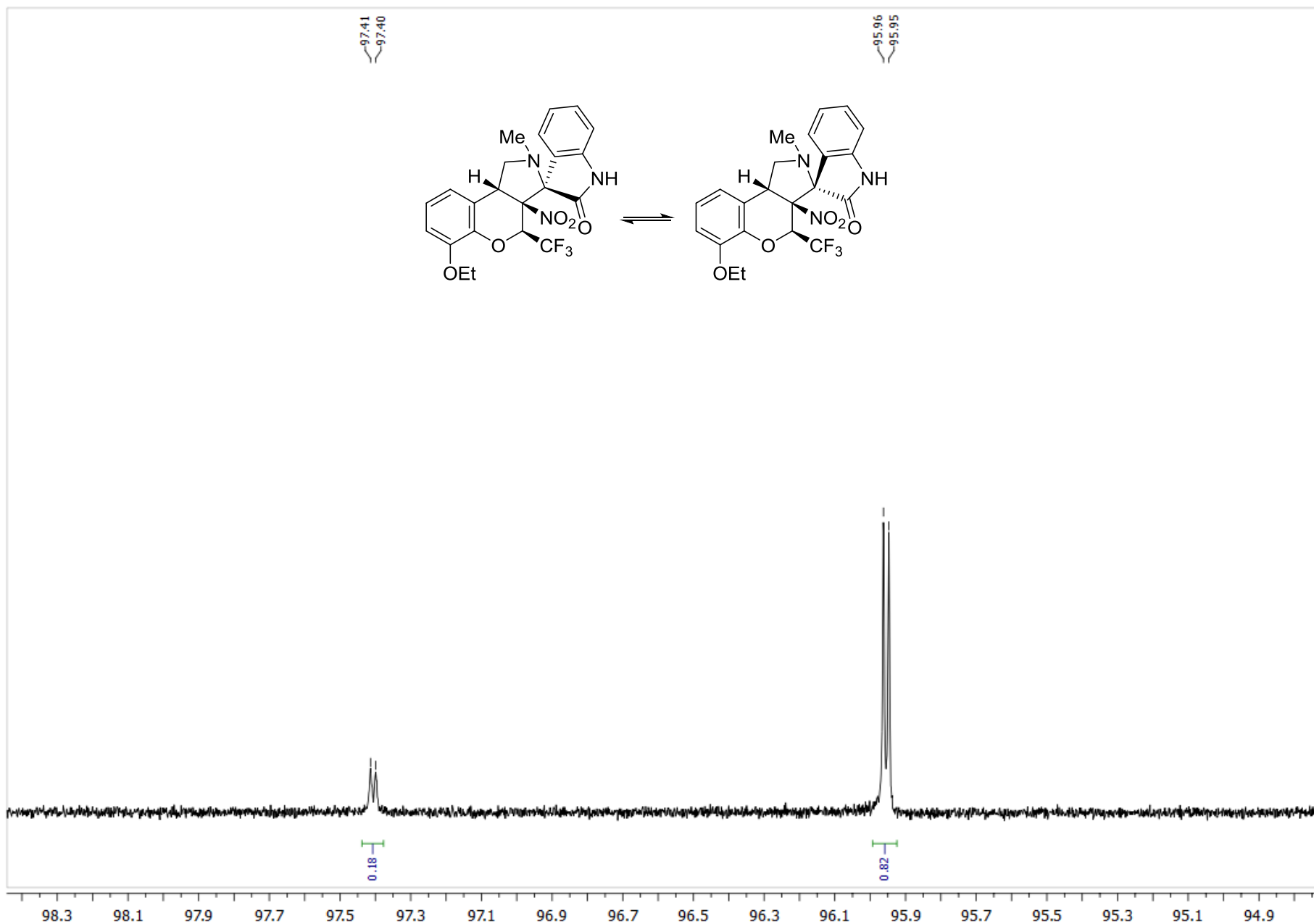


Figure S100. Copy of ^{19}F NMR spectrum of the mixture of isomers **5d** and **5'd** after keeping in $\text{DMSO-}d_6$ for 7 days

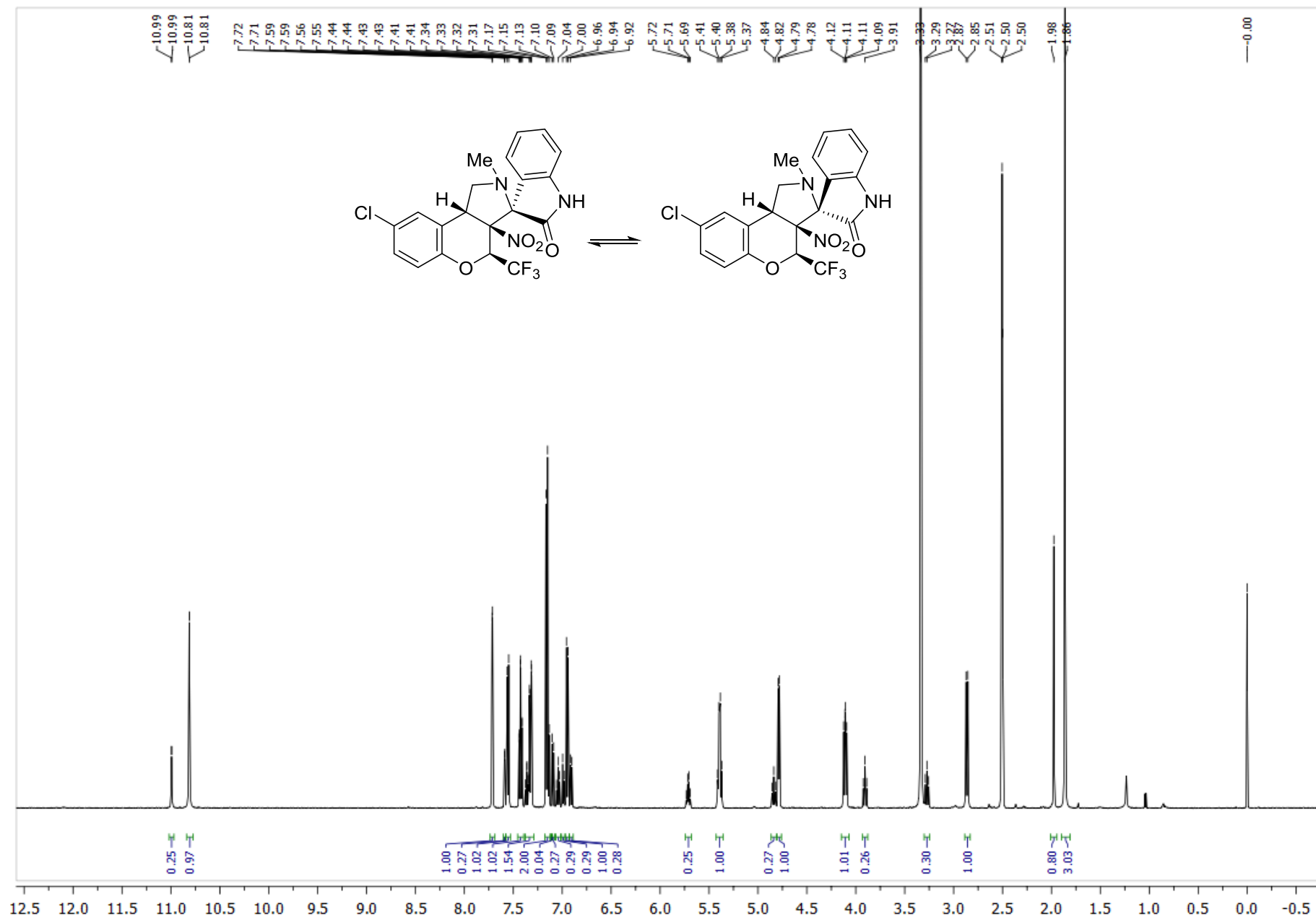


Figure S101. Copy of ^1H NMR spectrum of the mixture of isomers **5e** and **5'e** after keeping in $\text{DMSO-}d_6$ for 7 days

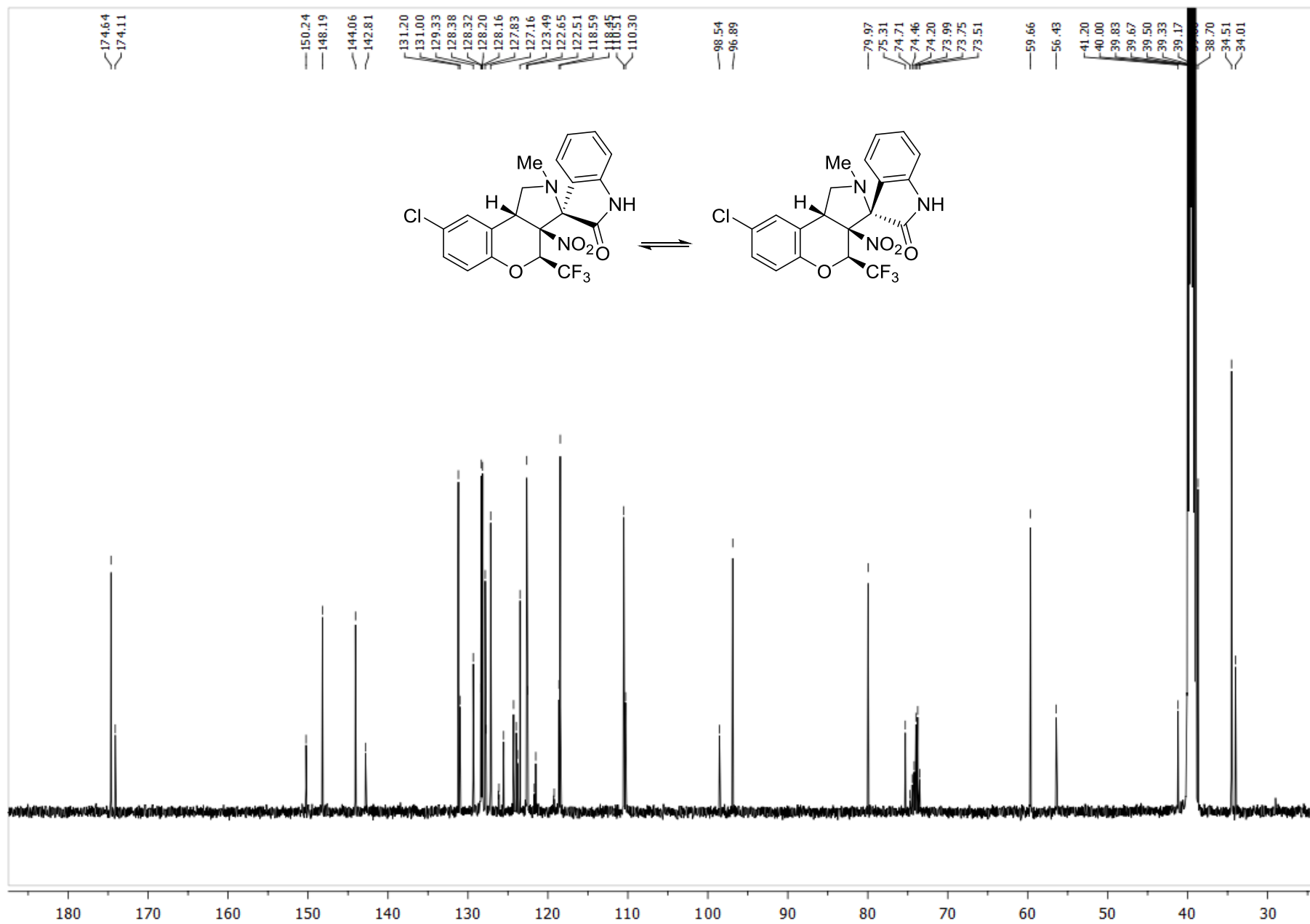


Figure S102. Copy of ¹³C NMR spectrum of the mixture of isomers **5e** and **5'e** after keeping in DMSO-*d*₆ for 14 days

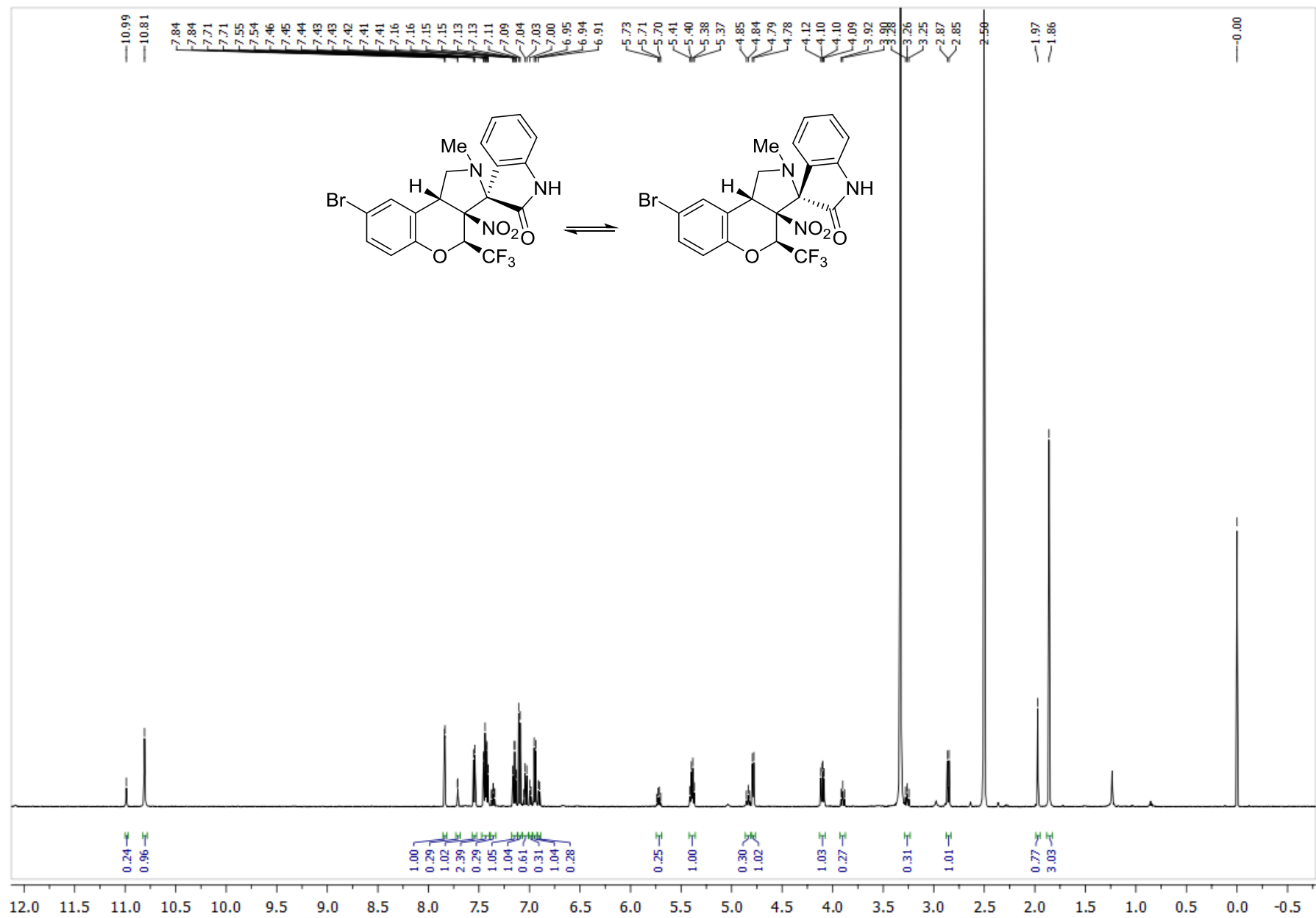


Figure S103. Copy of ¹H NMR spectrum of the mixture of isomers **5f** and **5'f** after keeping in DMSO-*d*₆ for 7 days

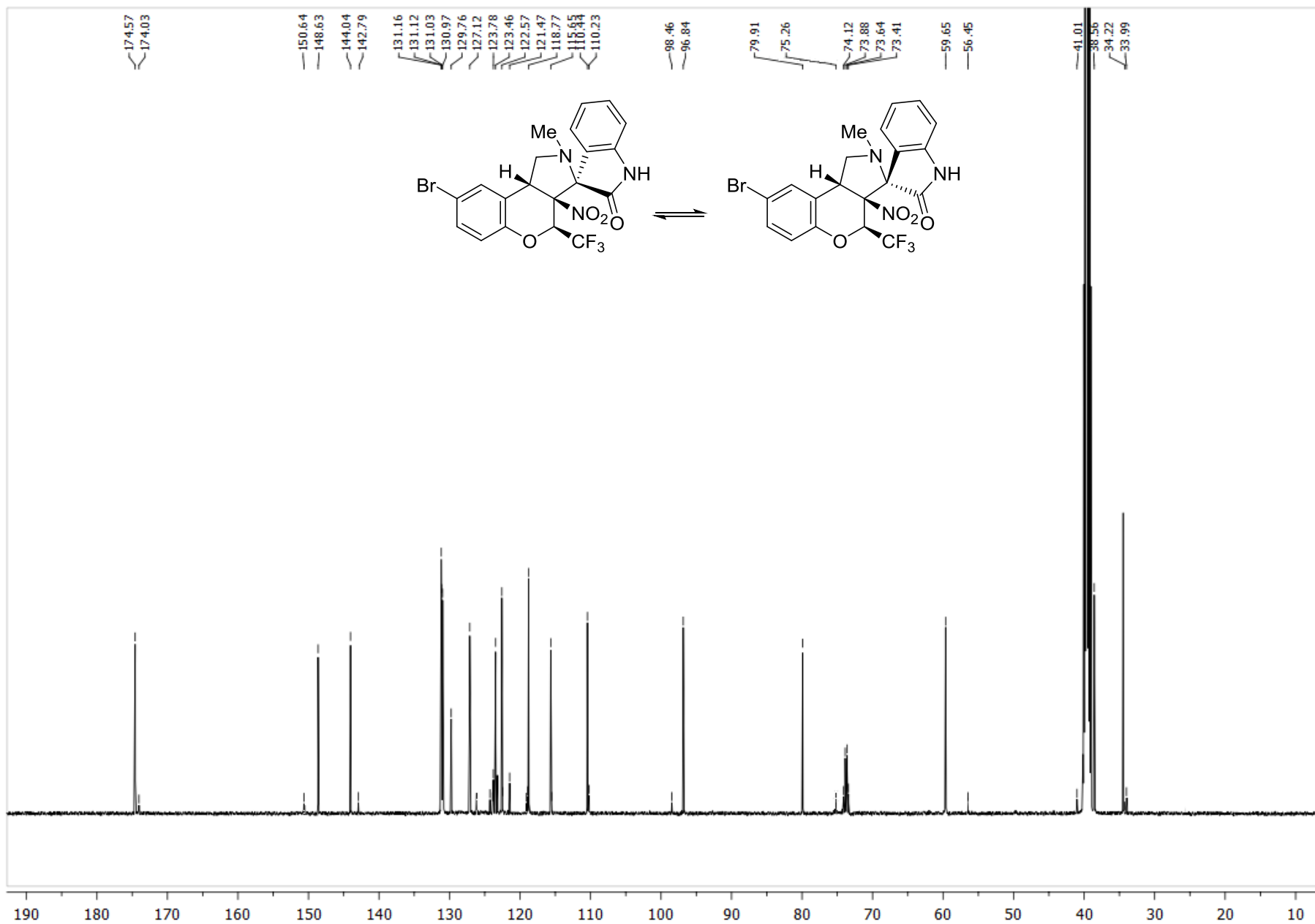


Figure S104. Copy of ¹³C NMR spectrum of the mixture of isomers **5f** and **5'f** after keeping in DMSO-*d*₆ for 7 days

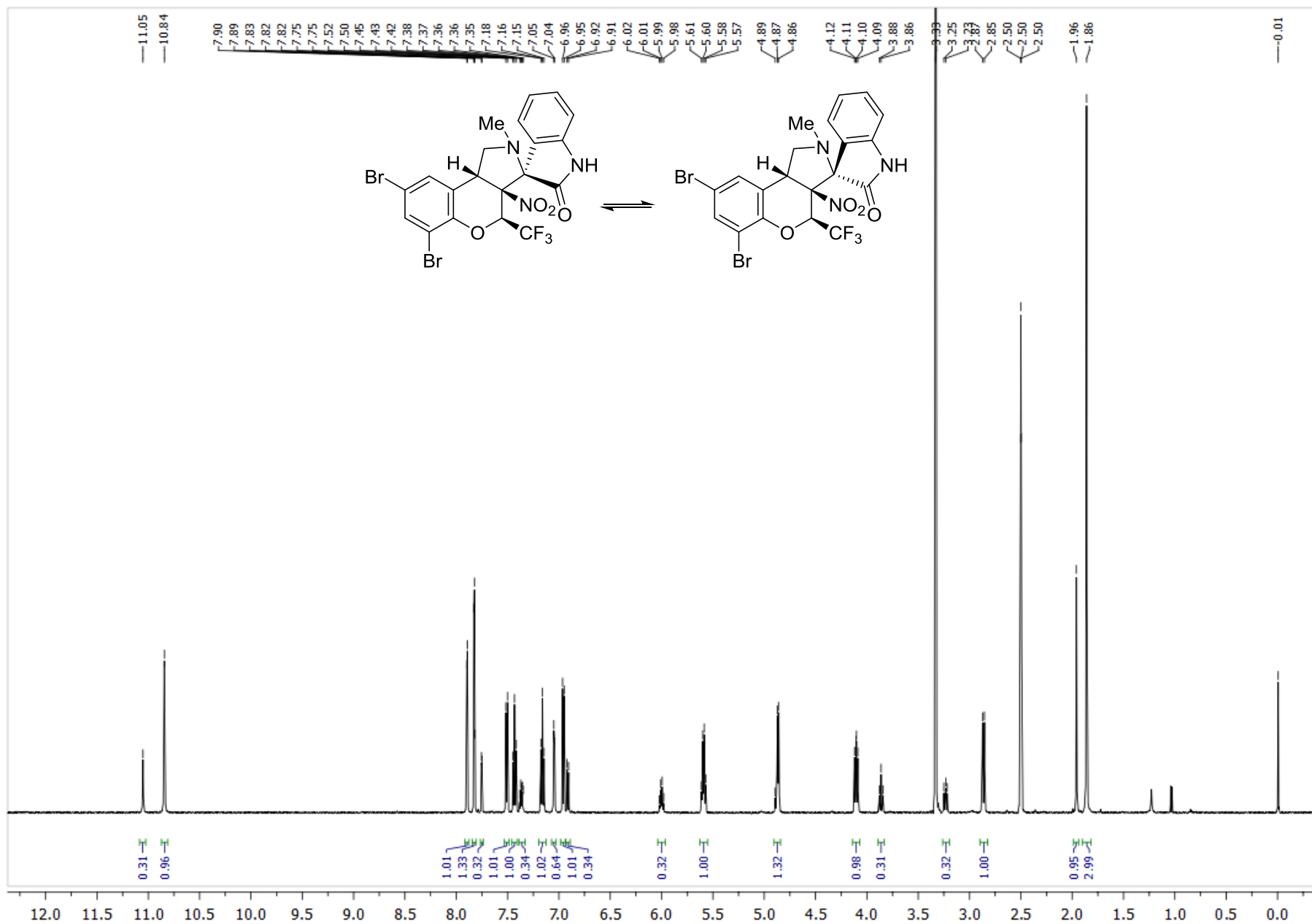


Figure S105. Copy of ^1H NMR spectrum of the mixture of isomers **5g** and **5'g** after keeping in $\text{DMSO-}d_6$ for 7 days

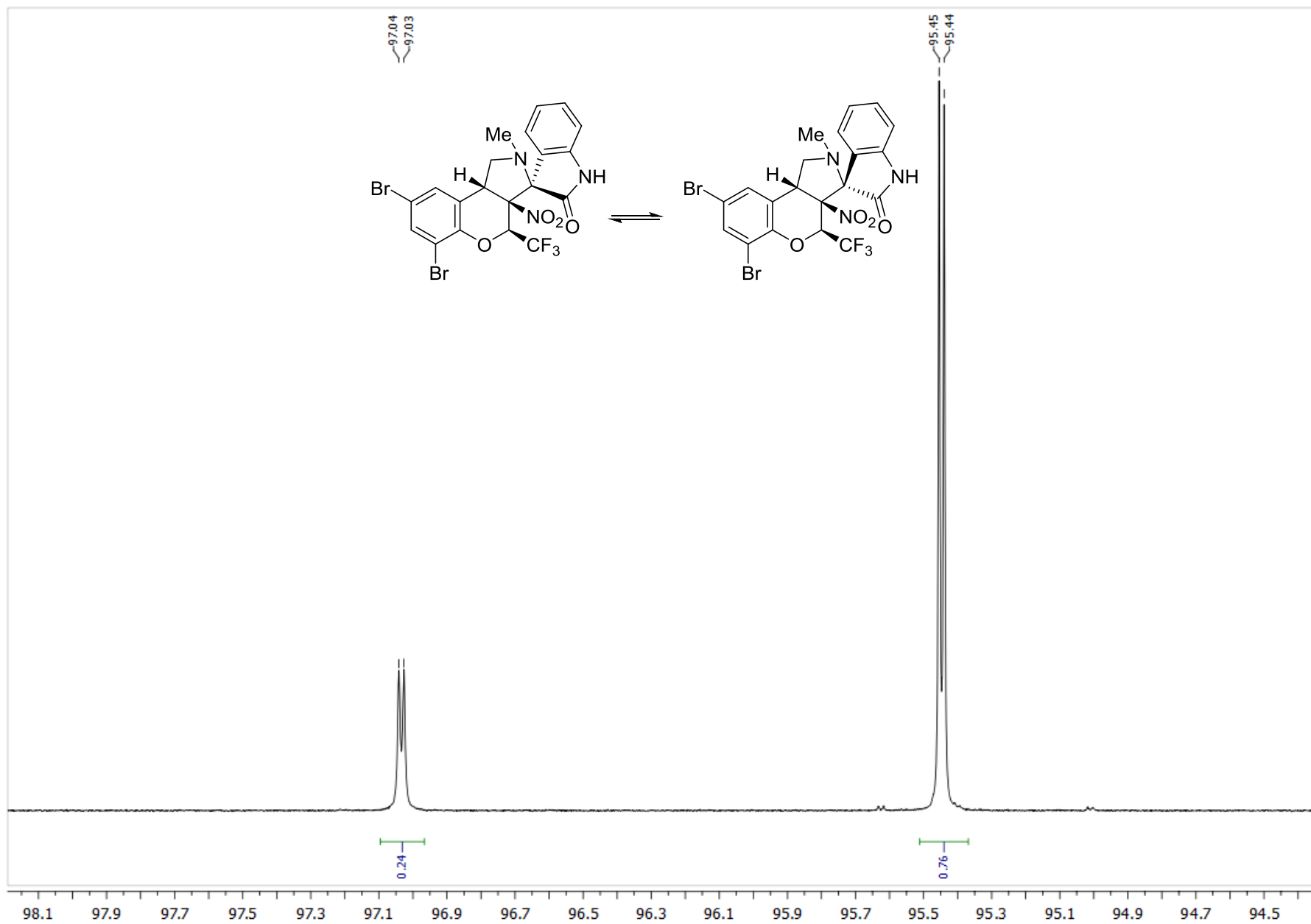


Figure S106. Copy of ^{19}F NMR spectrum of the mixture of isomers **5g** and **5'g** after keeping in $\text{DMSO-}d_6$ for 7 days

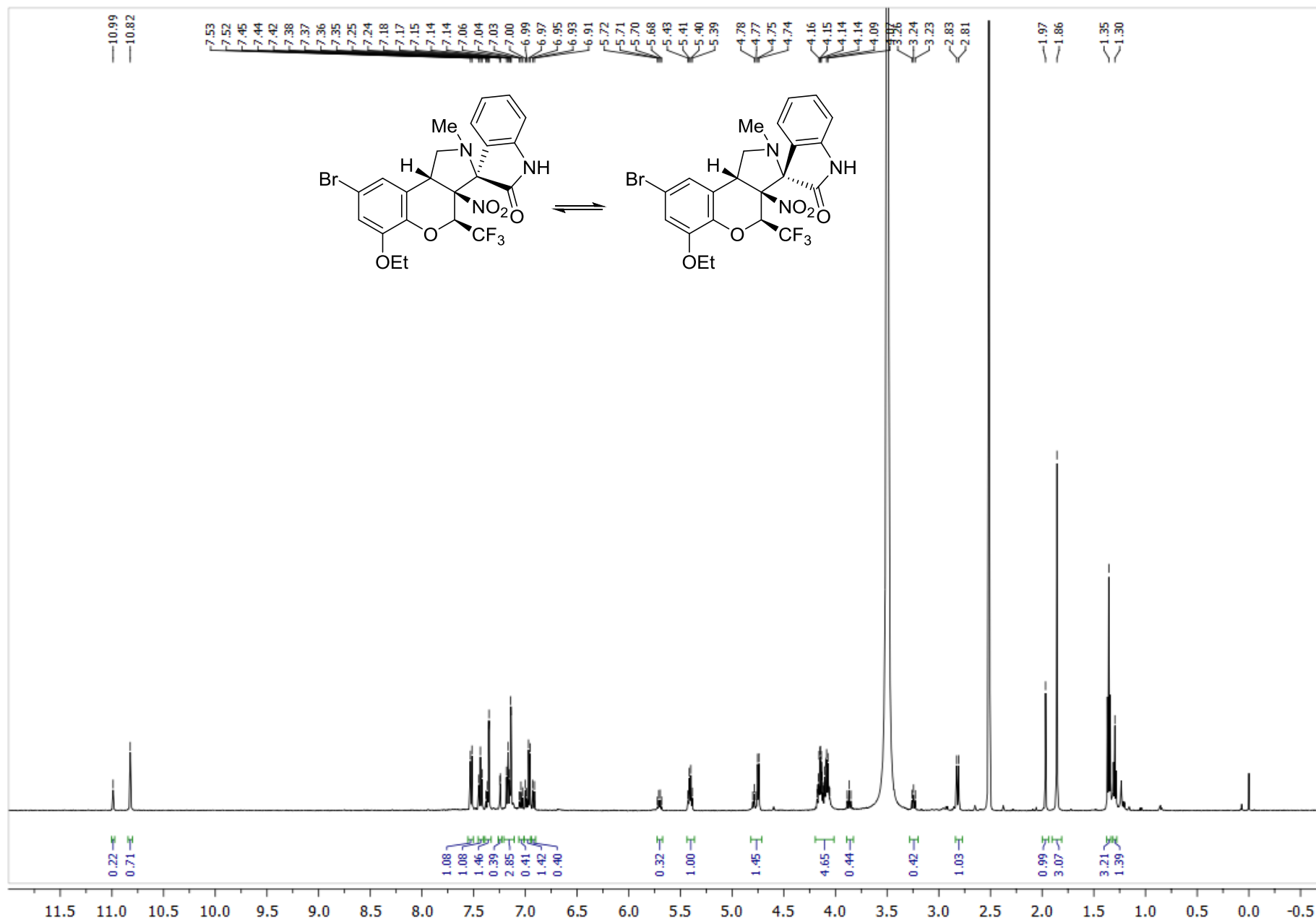


Figure S107. Copy of ¹H NMR spectrum of the mixture of isomers **5h** and **5'h** after keeping in DMSO-*d*₆ for 7 days

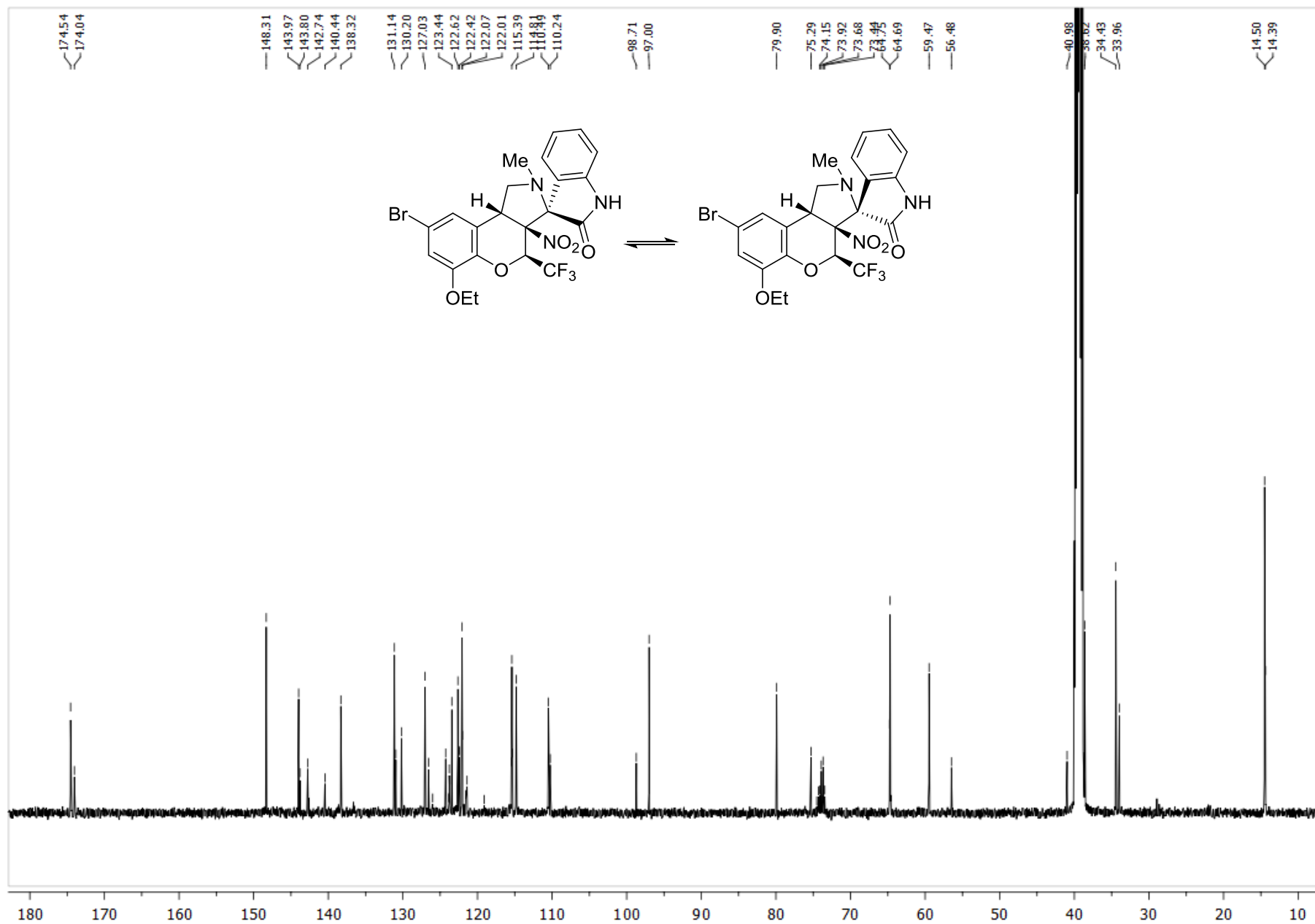


Figure S108. Copy of ¹³C NMR spectrum of the mixture of isomers **5h** and **5'h** after keeping in DMSO-*d*₆ for 7 days

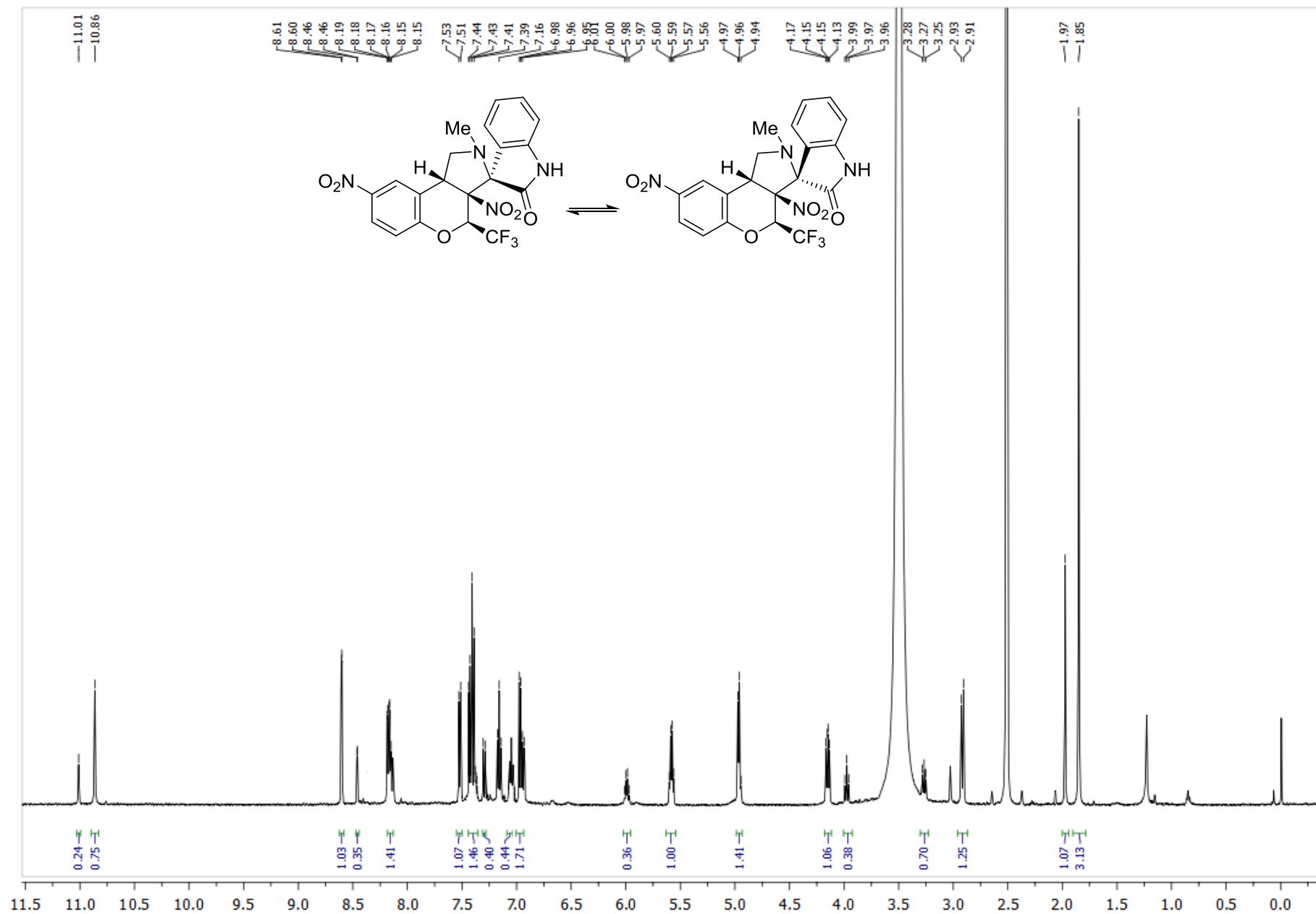


Figure S109. Copy of ^1H NMR spectrum of the mixture of isomers **5i** and **5'i** after keeping in $\text{DMSO-}d_6$ for 7 days

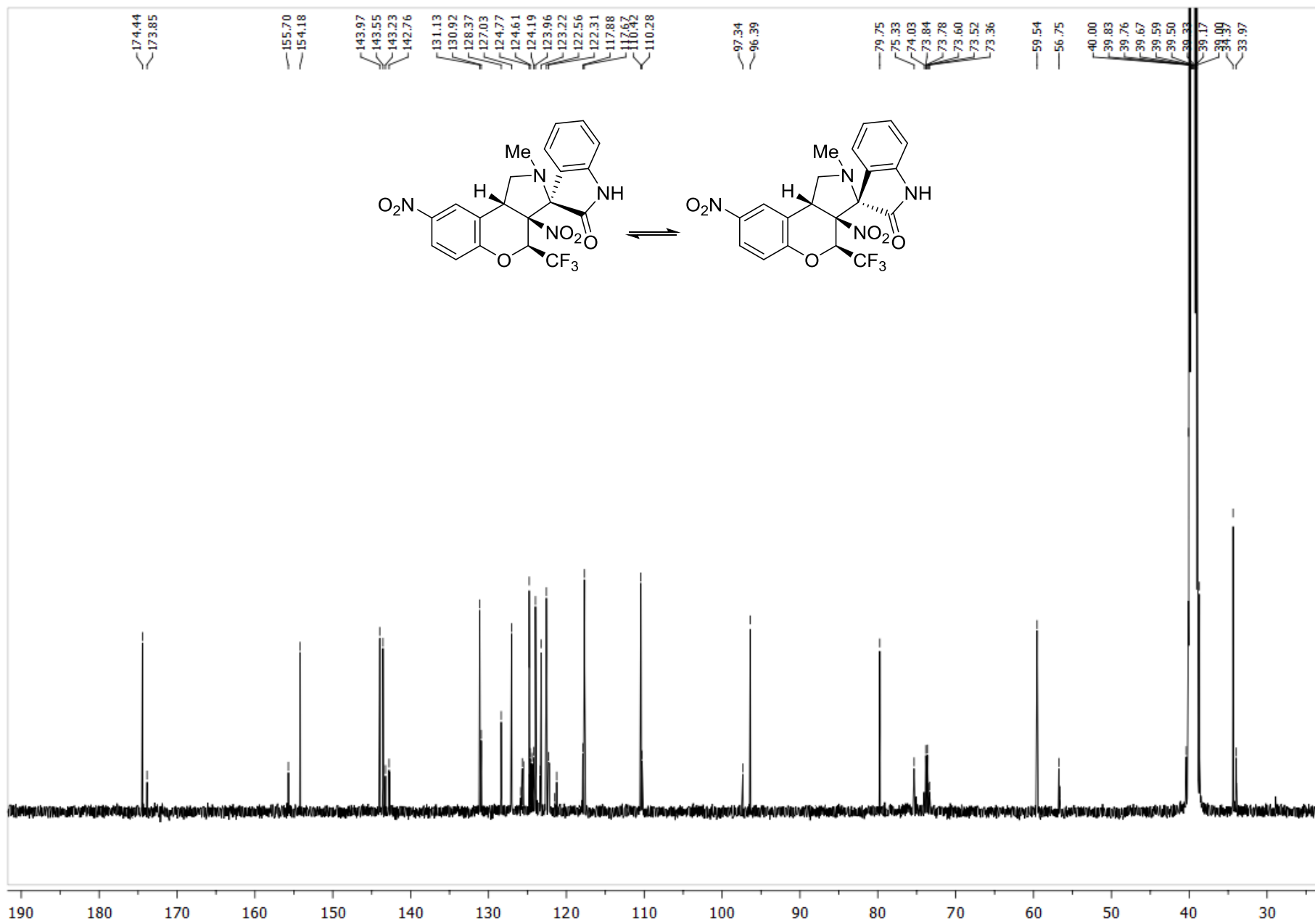


Figure S110. Copy of ¹³C NMR spectrum of the mixture of isomers **5i** and **5'i** after keeping in DMSO-*d*₆ for 7 days