A Convenient Synthesis of Novel Isoxazolidine and Isoxazole Isoquinolinones Fused Hybrids

Konstantinos A. Ouzounthanasis [1], Stergios R. Rizos [2] and Alexandros E. Koumbis [1,*]

[1]Laboratory of Organic Chemistry, Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki 54124, Greece
[2]Department of Chemistry and Chemical Biology, Harvard University, 12 Oxford St., Cambridge, 02138, Massachusetts, USA

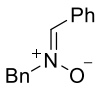
*akoumbis@chem.auth.gr

SUPPORTING INFORMATION

Table of Contents

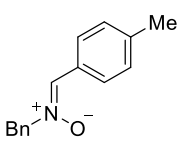
1. Data for compounds **4**

(*Z*)-*N*-Benzyl-1-phenylmethanimine oxide (**4a**)



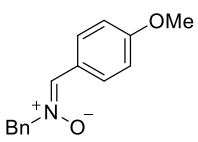
Yield: 97%; white solid; R_f = 0.31 (*n*-hexane/EtOAc 1:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**1**].

(*Z*)-*N*-Benzyl-1-(p-tolyl)methanimine oxide (**4b**)



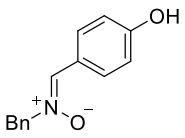
Yield: 97%; white solid; R_f = 0.25 (*n*-hexane/EtOAc 1:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**1**].

(*Z*)-*N*-Benzyl-1-(4-methoxyphenyl)methanimine oxide (**4c**)



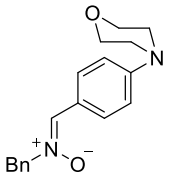
Yield: 99%; white solid; R_f = 0.17 (*n*-hexane/EtOAc 1:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**1**].

(*Z*)-*N*-Benzyl-1-(4-hydroxyphenyl)methanimine oxide (**4d**)



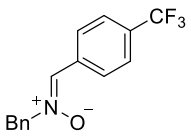
Yield: 91%; white solid; R_f = 0.17 (*n*-hexane/EtOAc 1:3 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**2**].

(*Z*)-*N*-Benzyl-1-(4-morpholinophenyl)methanimine oxide (**4e**)



Yield: 99%; m.p. 190–191 °C; white solid; R_f = 0.08 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 9.1 Hz, 2H), 7.48 – 7.45 (m, 2H), 7.42 – 7.35 (m, 3H), 7.27 (s, 1H), 6.86 (d, *J* = 9.1 Hz, 2H), 5.01 (s, 2H), 3.83 (t, *J* = 4.8 Hz, 4H), 3.24 (t, *J* = 4.8 Hz, 4H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.2, 134.2, 133.5, 130.3, 129.1, 128.8, 128.7, 121.5, 113.9, 70.4, 66.6, 47.8 ppm; FT-IR (neat): v = 3067, 2955, 2857, 1601, 1506, 1456, 1229, 1154, 1111, 923, 825, 702 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{18}H_{20}N_2NaO_2^+$ 319.1417; found 319.1410.

(*Z*)-*N*-Benzyl-1-(4-(trifluoromethyl)phenyl)methanimine oxide (**4f**)



Yield: 99%; white solid; R_f = 0.20 (*n*-hexane/EtOAc 3:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**1**].

1 He, C.-T.; Han, X.-L.; Zhang, Y.-X.; Du, Z.-T.; Si, C.-M.; Wei, B.-G. Sc(OTf)$_3$-Catalyzed [3 + 2]-Cycloaddition of Nitrones with Ynones. *Org. Biomol. Chem*. **2021**, *19*, 457–466.

2 Bortolini, o.; Mulani, I.; De Niro, A.; Maiuolo, L.; Nardi, M.; Russo, B.; Avnet, S. Efficient Synthesis of Isoxazolidine-Substituted Bisphosphonates By 1,3-Dipolar Cycloaddition Reactions. *Tetrahedron* **2011**, *67*, 5635–5641.

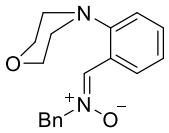
(*Z*)-*N*-Benzyl-1-(2-(trifluoromethyl)phenyl)methanimine oxide (**4g**)

Yield: 98%; white solid; m.p. 54–55 °C; R_f = 0.25 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.40 (d, *J* = 8.1 Hz, 1H), 7.74 (s, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.50 – 7.47 (m, 3H), 7.46 – 7.41 (m, 3H), 5.14 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 133.6, 132.5, 132.1, 129.8, 129.4, 129.3, 129.2, 129.1, 128.8, 127.5, 125.8 (q, *J* = 5.8 Hz), 122.8, 72.2 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ = –58.72 ppm; FT-IR (neat): ν = 3078, 3034, 1580, 1424, 1316, 1292, 1153, 1107, 1036, 773, 714 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{15}H_{12}F_3NNaO^+$ 302.0763; found 302.0768.

(*Z*)-N-Benzyl-1-(2-bromophenyl)methanimine oxide (**4h**)

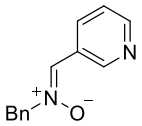
Yield: 98%; white solid; R_f = 0.31 (*n*-hexane/EtOAc 2:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**3**].

(Z)-*N*-Benzyl-1-(2-morpholinophenyl)methanimine oxide (**4i**)



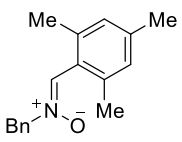
Yield: 99%; white solid; m.p. 144.5–145.5 °C; R_f = 0.20 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.16 (d, *J* = 7.9 Hz, 1H), 7.70 (s, 1H), 7.49 – 7.42 (m, 5H), 7.35 (t, *J* = 7.0 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 5.09 (s, 2H), 3.58 (t, *J* = 3.6 Hz, 4H), 2.78 (t, *J* = 4.5 Hz, 4H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.3, 133.3, 131.2, 130.9, 129.7, 129.2, 128.8, 124.4, 123.9, 118.7, 71.5, 67.0, 53.4 ppm; FT-IR (neat): ν = 3092, 2947, 2857, 1585, 1455, 1329, 1223, 1125, 1111, 931, 760, 701 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{18}H_{20}N_2NaO_2^+$ 319.1417; found 319.1427.

(*Z*)-*N*-Benzyl-1-(pyridin-3-yl)methanimine oxide (**4j**)



Yield: 98%; white solid; m.p. 95–96 °C; R_f =0.12 (*n*-hexane/EtOAc 1:4 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**4**].

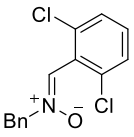
(*Z*)-*N*-Benzyl-1-mesitylmethanimine oxide (**4k**)



Yield: 85%; white solid; m.p. 144–145 °C; R_f = 0.24 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.62 (s, 1H), 7.54 – 7.50 (m, 2H), 7.45 – 7.34 (m, 3H), 6.83 (s, 2H), 5.12 (s, 2H), 2.25 (s, 3H), 2.16 (s, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.5, 137.5, 136.4, 133.2, 129.3, 129.0, 128.3, 125.2, 69.9, 21.1, 19.7 ppm; FT-IR (neat): ν = 3041, 2971, 2914, 1567, 1456, 1192, 1163, 951, 696 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{19}NNaO^+$ 276.1359; found 276.1360.

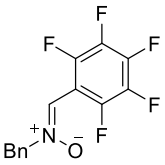
3 Poulsen, P. H.; Vergura, S.; Monleón, A.; Jørgensen, D. K. B.; Jørgensen, K. A. Controlling Asymmetric Remote and Cascade 1,3-Dipolar Cycloaddition Reactions by Organocatalysis. *J. Am. Chem. Soc.* **2016**, *138*, 6412−6415.
4 Delso. I.; Terejo, T.; ^{1}H–^{15}N HMBC as a Valuable Tool for the Identification and Characterization of Nitrones. *Tetrahedron Lett.* **2007**, *48*, 4101–4104.

(*Z*)-*N*-Benzyl-1-(2,6-dichlorophenyl)methanimine oxide (**4l**)



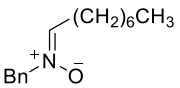
Yield: 99%; white solid; m.p. 164–165 °C; R_f = 0.34 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 – 7.51 (m, 3H), 7.46 – 7.38 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.26 – 7.22 (m, 1H), 5.14 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 135.4, 132.5, 130.9, 130.6, 129.5, 129.1, 129.0, 128.1, 127.9, 70.3 ppm; FT-IR (neat): v = 3064, 3028, 2995, 1556, 1430, 1165, 952, 808, 776, 699 cm^{-1}; HRMS (ESI), *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{11}Cl_2NNaO^+$ 302.0110; found 302.0101.

(*Z*)-*N*-Benzyl-1-(perfluorophenyl)methanimine oxide (**4m**)



Yield: 97%; white solid; R_f = 0.28 (*n*-hexane/EtOAc 3:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**5**].

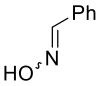
(*Z*)-*N*-Benzyloctan-1-imine oxide (**4n**)



Yield: 93%; white solid; R_f =0.11 (*n*-hexane/EtOAc 1:2 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**6**].

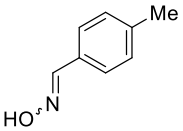
2. Data for compounds **5**

Benzaldehyde oxime (**5a**)



Yield: 99%; white solid; R_f = 0.4 (*n*-hexane/EtOAc 3:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**7**].

4-Methylbenzaldehyde oxime (**5b**)



Yield: 98%; R_f = 0.37 (*n*-hexane/EtOAc 5:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**8**].

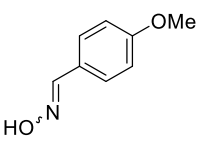
5 Chakraborty, B.; Chettri, E. Synthesis of Some Novel Class of Regioselective Spiro Isoxazolidine Derivatives via 1,3-Dipolar Cycloaddition Reaction of *N*-Benzyl-*C*-fluorosubstituted Phenyl Nitrones in Ionic Liquid. *J. Heterocyclic Chem*. **2018**, *55*, 1157−1165.

6 Katahara, S.; Kobayashi, S.; Fujita, K.; Matsumoto, T.; Sato, T.; Chida, N. An Iridium-Catalyzed Reductive Approach to Nitrones from *N*-Hydroxyamides. *J. Am. Chem. Soc*. **2016**, *138*, 5246−5249.

7 Schierle, S.; Neumann, S.; Heitel, P.; Willems, S.; Kaiser, A.; Pollinger, J.; Merk, D.Design and Structural Optimization of Dual FXR/PPAR*δ* Activators. *J. Med. Chem*. **2020**, *63*, 8369−8379.

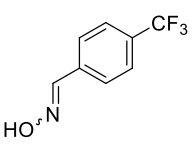
8 Di Nunno, L.; Vitale, P.; Scilimati, A.; Simonea, L.; Capitelli, F. Stereoselective Dimerization of 3-Arylisoxazoles to Cage-Shaped Bis-b-lactams *syn* 2,6-Diaryl-3,7-diazatricyclo[4.2.0.02,5]-octan-4,8-diones Induced by Hindered Lithium Amides. *Tetrahedron* **2007**, *63*, 12388−12395.

4-Methoxybenzaldehyde oxime (**5c**)



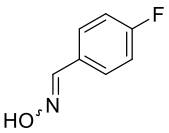
Yield: 96%; white solid; R_f = 0.32 (*n*-hexane/EtOAc 2:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**8**].

4-(Trifluoromethyl)benzaldehyde oxime (**5d**)



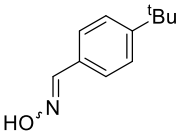
Yield: 98%; white solid; R_f = 0.42 (*n*-hexane/EtOAc 3:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**8**].

4-Fluorobenzaldehyde oxime (**5e**)



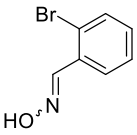
Yield: 99%; white solid; R_f = 0.41 (*n*-hexane/EtOAc 4:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**8**].

4-(*t*-Butyl)benzaldehyde oxime (**5f**)



Yield: 93%; white solid; R_f = 0.38 (*n*-hexane/EtOAc 4:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**9**].

2-Bromobenzaldehyde oxime (**5g**)



Yield: 97%; white solid; R_f = 0.38 (*n*-hexane/EtOAc 4:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**10**].

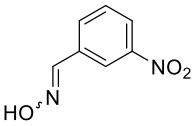
2-(Trifluoromethyl)benzaldehyde oxime (**5h**)

Yield: 96%; white solid; R_f = 0.40 (*n*-hexane/EtOAc 3:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**7**].

9 Tambara, K.; Dan Pantos, G. Conversion of Aldoximes into Nitriles and Amides Under Mild Conditions. *Org. Biomol. Chem.*, **2013**, *11*, 2466−2472.

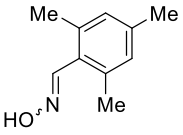
10 Steiger, S. A.; Li, C.; Backos, D. S.; Reigan, P.; Natale, N.R. Dimeric Isoxazolyl-1,4-Dihydropyridines Have Enhanced Binding at the Multi-Drug Resistance Transporter. *Bioorg. Med. Chem.* **2017**, *25*, 3223−3234.

3-Nitrobenzaldehyde oxime (**5i**)



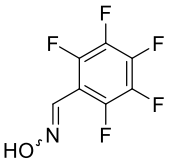
Yield: 99%; white solid; R_f = 0.23 (*n*-hexane/EtOAc 1:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**11**].

2,4,6-Trimethylbenzaldehyde oxime (**5j**)



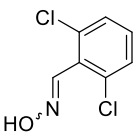
Yield: 97%; white solid; R_f = 0.43 (*n*-hexane/EtOAc 5:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**12**].

2,3,4,5,6-Pentafluorobenzaldehyde oxime (**5k**)



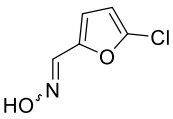
Yield: 90%; white solid; R_f = 0.52 (*n*-hexane/EtOAc 3:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**13**].

2,6-Dichlorobenzaldehyde oxime (**5l**)



Yield: 99%; white solid; R_f = 0.54 (*n*-hexane/EtOAc 4:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**7**].

5-Chlorofuran-2-carbaldehyde oxime (**5m**)



Yield: 88%; white solid; R_f = 0.43 (*n*-hexane/EtOAc 4:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**14**].

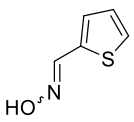
11 Yu, J.; Lu, M. Metal-Free: A Novel and Efficient Aerobic Oxidation of Primary Amines to Oximes Using *N*,*N*′,*N*″-Trihydroxyisocyanuric Acid and Acetaldoxime as Catalysts in Water. *SYNLETT* **2014**, *25*, 1873−1878.

12 McIntosh, M. L.; Naffziger, M. R.; Ashburn, B. O.; Zakharov, L. N.; Carter, R. G. Highly Regioselective Nitrile Oxide Dipolar Cycloadditions with *ortho*-Nitrophenyl Alkynes. *Org. Biomol. Chem.* **2012**, *10*, 9204−9213.

13 Jawalekar, A. M.; Reubsaet, E.; Rutjes F. P. J. T.; van Delft, F. L. Synthesis of Isoxazoles by Hypervalent Iodine-Induced Cycloaddition of Nitrile Oxides to Alkynes. *Chem. Commun.* **2011**, *47*, 3198−3200.

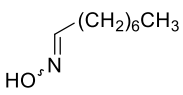
14 Kanemasa, S.; Matsuda, H.; Kamimurac, A.; Kakinami, T. Synthesis of Hydroximoyl Chlorides from Aldoximes and Benzyltrimethylammonium Tetrachloroiodate (BTMA ICl_4). *Tetrahedron* **2000**, *56*, 1057−1064.

Thiophene-2-carbaldehyde oxime (**5n**)



Yield: 83%; white solid; R_f = 0.43 (*n*-hexane/EtOAc 4:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**11**].

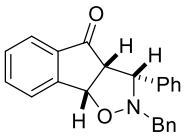
Octanal oxime (**5o**)



Yield: 94%; white solid; R_f = 0.39 (*n*-hexane/EtOAc 2:1 *v/v*). All spectroscopic data were in accordance with those reported in the literature [**15**].

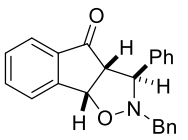
3. Data for compounds **6**, **8** and **7**

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-phenyl-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6a**)



Yield: 50%; white solid; m.p. 159–160 °C; R_f = 0.38 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.79 (tt, *J* = 7.9, 1.9 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.28 – 7.15 (m, 6H), 7.09 (t, *J* = 6.1 Hz, 4H), 5.75 (d, *J* = 6.3 Hz, 1H), 4.20 (d, *J* = 9.3 Hz, 1H), 3.85 – 3.78 (m, 2H), 3.71 (d, *J* = 15.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 201.7, 153.2, 138.7, 137.9, 136.2, 135.8, 130.0, 128.6, 128.6, 128.31, 128.26, 128.1, 127.1, 126.8, 122.1, 78.4, 73.5, 60.1, 58.5 ppm; FT-IR (neat): v = 3058, 3024, 2855, 1715, 1600, 1495, 1455, 1264, 775, 756, 733, 698 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{19}NNaO_2^+$ 364.1308; found 364.1300.

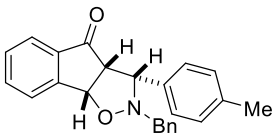
(3*S*,3a*R*,8b*S*)-2-Benzyl-3-phenyl-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7a**)



Yield: 40%; white solid; m.p. 190–191 °C; R_f = 0.50 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.78 (t, *J* = 7.4 Hz, 1H), 7.72 (t, *J* = 7.9 Hz, 2H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.53 (d, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.25 – 7.16 (m, 3H), 7.13 (d, *J* = 6.8 Hz, 2H), 5.81 (d, *J* = 6.4 Hz, 1H), 4.07 (d, *J* = 5.7 Hz, 1H), 3.81 (t, *J* = 6.1 Hz, 1H), 3.66 (dd, *J* = 14.9, 5.2 Hz, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 203.3, 150.8, 138.6, 137.8, 136.5, 135.9, 130.5, 128.8, 128.4, 128.3, 128.2, 128.1, 127.6, 127.0, 123.6, 78.7, 72.2, 63.5, 58.7 ppm; FT-IR (neat): v = 3022, 2915, 2856, 1714, 1604, 1495, 1456, 1348, 1231, 754, 731, 694 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{19}NNaO_2^+$ 364.1308; found 364.1302.

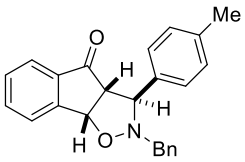
15 Suzuki, K.; Watanabe, T.; Murahashi, S.-I. Oxidation of Primary Amines to Oximes with Molecular Oxygen using 1,1-Diphenyl-2-picrylhydrazyl and WO_3/Al_2O_3 as Catalysts. *J. Org. Chem.* **2013**, *78*, 2301−2310.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(p-tolyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6b**)



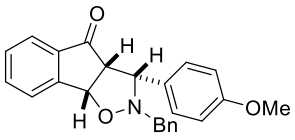
Yield: 40%; white solid; m.p. 145.5–146.5 °C; R_f = 0.70 (*n*-hexane/EtOAc 4:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.79 (tt, *J* = 8.1, 5.8, 2.5 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.23 – 7.15 (m, 3H), 7.10 – 7.06 (m, 4H), 6.96 (d, *J* = 8.0 Hz, 2H), 5.73 (d, *J* = 6.3 Hz, 1H), 4.14 (d, *J* = 9.4 Hz, 1H), 3.80 – 3.76 (m, 2H), 3.67 (d, *J* = 15.3 Hz, 1H), 2.26 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 201.9, 153.4, 138.8, 138.0, 137.3, 135.9, 133.1, 130.1, 129.3, 128.6, 128.4, 128.3, 127.2, 126.9, 122.2, 78.4, 73.4, 60.1, 58.4, 21.2 ppm; FT-IR (neat): v = 3024, 2921, 2852, 1712, 1599, 1346, 1213, 1079, 1042, 814, 773, 734, 695 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{21}NNaO_2^+$ 378.1465; found 378.1472.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(p-tolyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7b**)



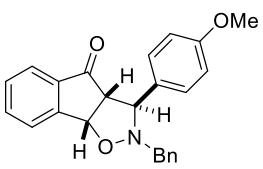
Yield: 37%; white solid; m.p. 159–160 °C; R_f = 0.58 (*n*-hexane/EtOAc 4:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.78 (t, *J* = 7.4 Hz, 1H), 7.72 (t, *J* = 6.3 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 2H), 7.26 – 7.17 (m, 5H), 7.12 (d, *J* = 7.2 Hz, 2H), 5.79 (d, *J* = 6.4 Hz, 1H), 4.01 (d, *J* = 5.8 Hz, 1H), 3.78 (t, *J* = 6.1 Hz, 1H), 3.66 (d, *J* = 14.9 Hz, 1H), 3.61 (d, *J* = 14.7 Hz, 1H), 2.34 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 203.3, 150.8, 137.9, 137.5, 136.5, 135.8, 135.4, 130.5, 129.4, 128.4, 128.3, 128.1, 127.6, 127.0, 123.6, 78.6, 72.1, 63.4, 58.5, 20.9 ppm; FT-IR (neat): v = 3032, 2950, 2843, 1714, 1605, 1350, 1278, 1056, 763, 701 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{21}NNaO_2^+$ 378.1465; found 378.1470.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(4-methoxyphenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6c**)



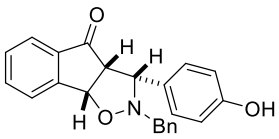
Yield: 47%; white solid; m.p. 130–131 °C; R_f = 0.43 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.82 – 7.77 (m, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 4.5 Hz, 2H), 7.24 – 7.15 (m, 3H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 5.73 (d, *J* = 6.2 Hz, 1H), 4.13 (d, *J* = 9.5 Hz, 1H), 3.81 – 3.74 (m, 2H), 3.72 (s, 3H), 3.66 (d, *J* = 15.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 202.0, 159.2, 153.4, 138.8, 138.0, 135.8, 130.1, 129.8, 128.4, 128.3, 127.8, 127.2, 126.9, 122.2, 114.1, 78.3, 73.2, 60.0, 58.4, 55.4 ppm; FT-IR (neat): v = 3024, 3007, 2844, 1711, 1613 ,1598, 1514, 1254 ,1032, 836, 774, 735 cm^{-1}; HRMS (ESI), *m*/*z*: [M + K]$^+$ calcd for $C_{24}H_{21}KNO_3^+$ 433.1045; found 433.1056.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(4-methoxyphenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7c**)



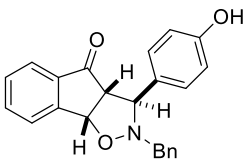
Yield: 24%; white solid; m.p. 127–128 °C; R_f = 0.60 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.78 (t, *J* = 7.4 Hz, 1H), 7.72 (t, *J* = 6.6 Hz, 2H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.25 – 7.16 (m, 3H), 7.13 (d, *J* = 7.3 Hz, 2H), 6.99 (d, *J* = 8.7 Hz, 2H), 5.79 (d, *J* = 6.4 Hz, 1H), 3.99 (br s, 1H), 3.79 (s, 3H), 3.77 (t, *J* = 6.1 Hz, 1H), 3.63 (dd, *J* = 14.7, 5.3 Hz, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 203.3, 159.4, 150.9, 137.9, 136.5, 135.8, 130.5, 130.22, 129.7, 128.3, 128.1, 127.6, 127.0, 123.6, 114.4, 78.6, 71.8, 63.4, 58.4, 55.4 ppm; FT-IR (neat): v = 3032, 2909, 2835, 1718, 1613, 1514, 1248, 1178, 1035, 829, 770, 731 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{21}NNaO_3^+$ 394.1414; found 394.1422.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(4-hydroxyphenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6d**)



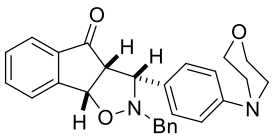
Yield: 45%; white solid; m.p. 202–204 °C; R_f = 0.28 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 9.36 (br s, 1H), 7.81 – 7.76 (m, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.23 – 7.14 (m, 3H), 7.08 (d, *J* = 6.9 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.64 (d, *J* = 8.6 Hz, 2H), 5.71 (d, *J* = 6.3 Hz, 1H), 4.07 (d, *J* = 9.3 Hz, 1H), 3.78 (d, *J* = 15.4 Hz, 1H), 3.72 (dd, *J* = 9.3, 6.3 Hz, 1H), 3.64 (d, *J* = 15.4 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 202.1, 157.4, 153.5, 138.9, 138.1, 135.8, 130.1, 129.8, 128.4, 128.3, 127.1, 126.9, 126.0, 122.1, 115.5, 78.3, 73.5, 60.0, 58.3 ppm; FT-IR (neat): v = 3284, 3024, 2847, 1694, 1600, 1518, 1454, 1274, 1263, 834, 768, 741, 694 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{19}NNaO_3^+$ 380.1257; found 380.1260.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(4-hydroxyphenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7d**)



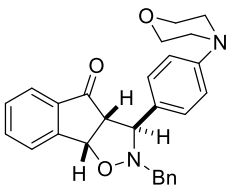
Yield: 26%; white solid; m.p. 189–190 °C; R_f = 0.40 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 9.33 (br s, 1H), 7.77 (t, *J* = 7.4 Hz, 1H), 7.71 (t, *J* = 7.1 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.25 – 7.11 (m, 5H), 6.82 (d, *J* = 8.4 Hz, 2H), 5.77 (d, *J* = 6.4 Hz, 1H), 3.92 (br s, 1H), 3.75 (t, *J* = 6.1 Hz, 1H), 3.66 (d, *J* = 14.8 Hz, 1H), 3.58 (d, *J* = 14.7 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 203.4, 157.5, 150.9, 138.0, 136.5, 135.8, 130.4, 129.7, 128.4, 128.3, 128.1, 127.5, 126.9, 123.6, 115.7, 78.5, 72.0, 63.3, 58.3 ppm; FT-IR (neat): v = 3482, 3024, 2919, 2849, 1699, 1602, 1518, 1348, 1277, 1233, 843, 833, 733, 694 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{19}NNaO_3^+$ 380.1257; found 380.1251.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(4-morpholinophenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6e**)



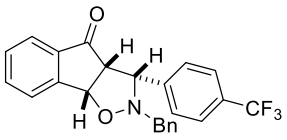
Yield: 43%; white solid; m.p. 151–152 °C; R_f = 0.34 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.79 (ddd, *J* = 8.0, 5.6, 2.7 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.23 – 7.15 (m, 3H), 7.08 (d, *J* = 6.9 Hz, 2H), 6.93 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 5.71 (d, *J* = 6.3 Hz, 1H), 4.08 (d, *J* = 9.3 Hz, 1H), 3.77 (d, *J* = 15.4 Hz, 1H), 3.74 – 3.69 (m, 5H), 3.64 (d, *J* = 15.4 Hz, 1H), 3.11 – 3.04 (m, 4H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 202.0, 153.5, 150.8, 138.8, 138.1, 135.8, 130.0, 129.4, 128.4, 128.2, 127.1, 126.9, 126.0, 122.1, 115.0, 78.3, 73.5, 66.6, 60.0, 58.3, 48.5 ppm; FT-IR (neat): v = 3035, 2950, 2838, 1715, 1612, 1516, 1264, 1234, 1218, 1120, 927, 770, 735 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{27}H_{26}N_2NaO_3^+$ 449.1836; found 449.1832.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(4-morpholinophenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7e**)



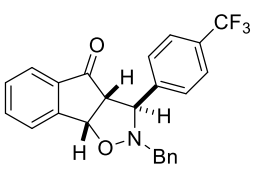
Yield: 26%; white solid; m.p. 219–220 °C; R_f = 0.53 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.78 (t, *J* = 7.4 Hz, 1H), 7.72 (t, *J* = 6.3 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 8.6 Hz, 2H), 7.26 – 7.16 (m, 3H), 7.13 (d, *J* = 7.2 Hz, 2H), 6.99 (d, *J* = 8.7 Hz, 2H), 5.78 (d, *J* = 6.4 Hz, 1H), 3.93 (br s, 1H), 3.78 – 3.74 (m, 4H), 3.67 (d, *J* = 14.9 Hz, 1H), 3.59 (d, *J* = 14.8 Hz, 1H), 3.15 (d, *J* = 5.1 Hz, 4H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 203.3, 151.0, 150.9, 138.0, 136.5, 135.8, 130.4, 129.2, 128.4, 128.3, 128.1, 127.5, 126.9, 123.6, 115.2, 78.5, 72.0, 66.4, 63.3, 58.4, 48.6 ppm; FT-IR (neat): v = 3011, 2966, 2837, 1721, 1610, 1521, 1350, 1234, 1122, 926, 821, 742, 688 cm^{-1}; HRMS (ESI), *m*/*z*: [M + H]$^+$ calcd for $C_{27}H_{27}N_2O_3^+$ 427.2016; found 427.2011.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(4-(trifluoromethyl)phenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6f**)



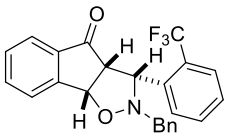
Yield: 54%; white solid; m.p. 145–146 °C; R_f = 0.47 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.80 (ddd, *J* = 7.7, 6.2, 2.1 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.58 – 7.53 (m, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.24 – 7.16 (m, 3H), 7.13 – 7.10 (m, 2H), 5.80 (d, *J* = 6.3 Hz, 1H), 4.36 (d, *J* = 9.3 Hz, 1H), 3.92 (dd, *J* = 9.3, 6.4 Hz, 1H), 3.84 (d, *J* = 15.2 Hz, 1H), 3.75 (d, *J* = 15.2 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 201.5, 153.0, 141.3, 138.5, 137.6, 135.9, 130.1, 129.4, 128.8 (q, *J* = 31.6 Hz), 128.5, 128.3, 127.2, 126.9, 125.4 (q, *J* = 3.9 Hz), 124.7 (q, *J* = 272.1 Hz), 122.3, 78.6, 72.7, 60.2, 58.9 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –62.62 (s, 3F) ppm; FT-IR (neat): v = 3034, 2953, 2922, 1721, 1602, 1329, 1163, 1122, 1068, 833, 752, 699, 590, 452 cm^{-1}; HRMS (ESI), *m*/*z*: [M + H]$^+$ calcd for $C_{24}H_{19}F_3NO_2^+$ 410.1362; found 410.1356.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(4-(trifluoromethyl)phenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7f**)



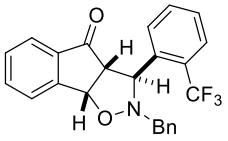
Yield: 24%; white solid; m.p. 170–171 °C; R_f = 0.66 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.83 – 7.72 (m, 7H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.25 – 7.17 (m, 3H), 7.13 (d, *J* = 7.1 Hz, 2H), 5.83 (d, *J* = 6.4 Hz, 1H), 4.24 (d, *J* = 5.4 Hz, 1H), 3.85 (t, *J* = 5.9 Hz, 1H), 3.71 (d, *J* = 14.6 Hz, 1H), 3.67 (d, *J* = 14.8 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 203.0, 150.8, 143.6, 137.5, 136.4, 136.0, 130.6, 129.1, 128.9 (q, *J* = 31.9 Hz), 128.4, 128.2, 127.6, 127.1, 125.7 (q, *J* = 3.9 Hz), 124.4 (q, *J* = 272.2 Hz), 123.7, 78.9, 71.4, 63.6, 59.1 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –62.61 (s, 3F) ppm; FT-IR (neat): v = 3035, 2955, 2850, 1715, 1607, 1331, 1159, 1111, 1068, 855, 762, 703, 463 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{18}F_3NNaO_2^+$ 432.1182; found 432.1189.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(2-(trifluoromethyl)phenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6g**)



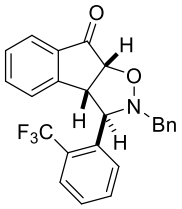
Yield: 31%; white solid; m.p. 155–157 °C; R_f = 0.54 (*n*-hexane/EtOAc 4:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.81 (td, *J* = 7.5, 7.0, 1.3 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.60 – 7.52 (m, 2H), 7.48 – 7.43 (m, 2H), 7.23 – 7.09 (m, 6H), 5.82 (d, *J* = 6.3 Hz, 1H), 4.40 (d, *J* = 9.2 Hz, 1H), 3.84 – 3.80 (m, 2H), 3.76 (d, *J* = 15.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 201.0, 153.0, 138.5, 137.2, 135.7, 134.6 (d, *J* = 1.5 Hz), 132.5, 130.0, 128.9, 128.4, 128.11, 128.09, 128.0 (q, *J* = 29.6 Hz), 127.0, 126.7, 126.0 (q, *J* = 5.7 Hz), 124.6 (q, *J* = 274.0 Hz), 122.0, 78.4, 69.1, 60.0, 58.6 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –58.78 (s, 3F) ppm; FT-IR (neat): v = 3021, 2945, 2883, 1716, 1653, 1455, 1313, 1261, 1165, 1103, 1033, 785, 748, 701, 660 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{18}F_3NNaO_2^+$ 432.1182; found 432.1181.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(2-(trifluoromethyl)phenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7g**)



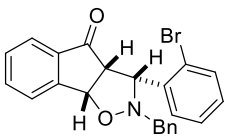
Yield: 24%; white solid; m.p. 152–153 °C; R_f = 0.43 (*n*-hexane/EtOAc 4:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.07 (d, *J* = 7.9 Hz, 1H), 7.83 – 7.73 (m, 5H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.24 – 7.16 (m, 3H), 7.07 (d, *J* = 6.8 Hz, 2H), 5.90 (d, *J* = 6.5 Hz, 1H), 4.48 (d, *J* = 3.8 Hz, 1H), 3.92 (t, *J* = 5.8 Hz, 1H), 3.65 (d, *J* = 14.3 Hz, 1H), 3.61 (d, *J* = 14.4 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 202.1, 151.1, 138.1 (d, *J* = 1.8 Hz), 137.7, 136.4, 136.3, 133.4, 130.9, 130.7, 128.9, 128.6, 128.4, 127.9 (q, *J* = 29.6 Hz), 127.8, 127.4, 126.2 (q, *J* = 5.9 Hz), 124.6 (q, *J* = 274.7 Hz), 124.0, 79.7, 67.7, 64.9, 59.7 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –56.83 (s, 3F) ppm; FT-IR (neat): v = 3021, 2925, 2874, 1716, 1647, 1456, 1312, 1277, 1162, 1121, 1034, 769, 694, 666 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{18}F_3NNaO_2^+$ 432.1182; found 432.1186.

(3*R*,3a*S*,8a*R*)-2-Benzyl-3-(2-(trifluoromethyl)phenyl)-2,3,3a,8a-tetrahydro-8*H*-indeno[1,2-*d*]isoxazol-8-one (**8g**)



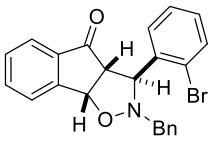
Yield: 16%; white solid; m.p. 165–166 °C; R_f = 0.22 (*n*-hexane/DCM 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.07 (d, *J* = 7.9 Hz, 1H), 7.86 – 7.74 (m, 4H), 7.63 – 7.56 (m, 2H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.25 – 7.17 (m, 3H), 7.09 (d, *J* = 7.1 Hz, 2H), 5.02 (d, *J* = 6.8 Hz, 1H), 4.51 (dd, *J* = 6.8, 4.3 Hz, 1H), 4.40 (d, *J* = 2.8 Hz, 1H), 3.65 (d, *J* = 14.4 Hz, 1H), 3.57 (d, *J* = 14.4 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 201.2, 152.9, 137.9, 137.3, 136.6, 135.1, 133.4, 130.4, 129.4, 128.7, 128.3, 128.2, 127.4 (q, *J* = 29.3 Hz), 127.2, 126.8, 125.9 (q, *J* = 5.8 Hz), 124.5 (q, *J* = 274.4 Hz), 124.2, 81.8, 70.2, 59.3, 57.5 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –56.71 (s, 3F) ppm; FT-IR (neat): v = 2934, 1717, 1647, 1541,1465, 1311, 1161, 1121, 825, 779, 697, 668 cm^{-1}; HRMS (ESI), *m*/*z*: [M + K]$^+$ calcd for $C_{24}H_{18}F_3KNO_2^+$ 448.0921; found 448.0930.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(2-bromophenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6h**)



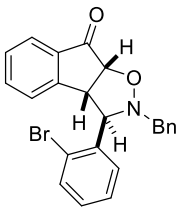
Yield: 28%; white solid; m.p. 139–140 °C; R_f = 0.54 (*n*-hexane/THF 20:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.79 (t, *J* = 7.4 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.25 – 7.17 (m, 5H), 7.12 (d, *J* = 7.0 Hz, 2H), 6.91 – 6.88 (m, 1H), 5.81 (d, *J* = 6.4 Hz, 1H), 4.43 (d, *J* = 9.3 Hz, 1H), 3.96 – 3.90 (m, 2H), 3.78 (d, *J* = 15.2 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 200.8, 152.9, 138.3, 137.1, 135.6, 135.4, 132.8, 129.9, 129.6, 128.7, 128.3, 128.1, 127.8, 127.0, 126.7, 124.2, 121.9, 78.1, 71.9, 58.5, 57.5 ppm; FT-IR (neat): v = 3026, 2945, 2868, 1712, 1602, 1260, 1221, 1015, 766, 748, 697, 620 cm^{-1}; HRMS (ESI), *m*/*z*: [M + H]$^+$ calcd for $C_{23}H_{19}BrNO_2^+$ 420.0594; found 420.0596.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(2-bromophenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7h**)



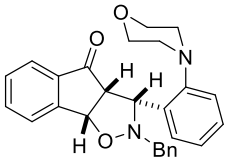
Yield: 20%; white solid; m.p. 148–150 °C; R_f = 0.52 (*n*-hexane/THF 20:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.82 – 7.72 (m, 4H), 7.68 – 7.62 (m, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.29 (td, *J* = 7.7, 1.7 Hz, 1H), 7.23 – 7.15 (m, 3H), 7.06 (d, *J* = 6.9 Hz, 2H), 5.86 (d, *J* = 6.5 Hz, 1H), 4.70 (d, *J* = 4.6 Hz, 1H), 3.91 (dd, *J* = 6.5, 4.7 Hz, 1H), 3.71 (d, *J* = 14.2 Hz, 1H), 3.64 (d, *J* = 14.4 Hz, 1H). ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 202.7, 151.3, 137.7, 137.4, 136.3, 136.0, 133.1, 130.6, 130.3, 130.0, 128.4, 128.3, 128.1, 127.6, 127.1, 123.8, 123.7, 79.3, 70.5, 63.6, 59.4 ppm; FT-IR (neat): v = 3028, 2919, 2870, 1715, 1600, 1472, 1347, 1276, 1233, 1022, 844, 752, 743, 698, 618 cm^{-1}; HRMS (ESI), *m*/*z*: [M + H]$^+$ calcd for $C_{23}H_{19}BrNO_2^+$ 420.0594; found 420.0596.

(3*R*,3a*S*,8a*R*)-2-Benzyl-3-(2-bromophenyl)-2,3,3a,8a-tetrahydro-8*H*-indeno[1,2-*d*]isoxazol-8-one (**8h**)



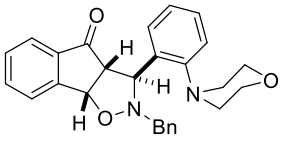
Yield: 23%; white solid; m.p. 123–124 °C; R_f = 0.30 (DCM); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.84 – 7.78 (m, 2H), 7.77 – 7.71 (m, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.31 (td, *J* = 7.7, 1.7 Hz, 1H), 7.25 – 7.17 (m, 3H), 7.08 (d, *J* = 7.0 Hz, 2H), 4.92 (d, *J* = 6.8 Hz, 1H), 4.66 (d, *J* = 3.6 Hz, 1H), 4.46 (dd, *J* = 6.9, 3.7 Hz, 1H), 3.71 (d, *J* = 14.2 Hz, 1H), 3.62 (d, *J* = 14.2 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 201.6, 153.6, 138.5, 137.2, 136.6, 135.2, 133.0, 130.0, 130.0, 129.3, 128.5, 128.4, 128.2, 127.2, 127.1, 124.2, 123.4, 81.9, 73.0, 59.8, 56.7 ppm; FT-IR (neat): v = 3027, 2934, 2896, 1721, 1603, 1472, 1251, 1020, 764, 752, 697, 634 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{18}BrNNaO_2^+$ 442.0413; found 442.0420.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(2-morpholinophenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6i**)



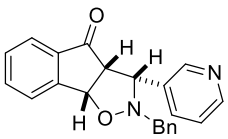
Yield: 42%; white solid; m.p. 186–187 °C; R_f = 0.31 (*n*-hexane/EtOAc 3:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.80 (td, *J* = 7.3, 1.3 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.29 – 7.17 (m, 5H), 7.10 (d, *J* = 6.6 Hz, 2H), 6.92 (td, *J* = 7.5, 1.3 Hz, 1H), 6.78 (dd, *J* = 7.8, 1.6 Hz, 1H), 5.78 (d, *J* = 6.3 Hz, 1H), 4.69 (d, *J* = 9.6 Hz, 1H), 3.88 (dd, *J* = 9.6, 6.3 Hz, 1H), 3.82 (d, *J* = 15.1 Hz, 1H), 3.80 – 3.72 (m, 4H), 3.67 (d, *J* = 15.1 Hz, 1H), 3.08 – 3.03 (m, 2H), 2.81 – 2.76 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 201.8, 153.4, 152.3, 138.7, 137.5, 135.7, 132.5, 129.9, 128.6, 128.5, 128.2, 127.8, 127.1, 126.8, 124.7, 122.1, 121.8, 78.4, 67.2, 67.1, 58.9, 58.3, 53.5 ppm; FT-IR (neat): v = 3030, 2944, 2842, 1715, 1599, 1490, 1454, 1222, 1117, 1080, 928, 742, 704 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{27}H_{26}N_2NaO_3^+$ 449.1836; found 449.1842.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(2-morpholinophenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7i**)



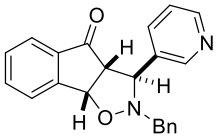
Yield: 34%; white solid; m.p. 183–184 °C; R_f = 0.51 (*n*-hexane/EtOAc 3:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ 7.80 (t, *J* = 7.4 Hz, 1H), 7.77 – 7.71 (m, 3H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.27 – 7.14 (m, 5H), 7.01 (d, *J* = 6.9 Hz, 2H), 5.86 (d, *J* = 6.4 Hz, 1H), 4.94 (d, *J* = 4.6 Hz, 1H), 3.84 (dd, *J* = 6.5, 4.6 Hz, 1H), 3.74 – 3.59 (m, 6H), 3.06 – 3.02 (m, 2H), 2.68 – 2.63 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 203.8, 151.9, 151.5, 137.8, 136.6, 135.9, 134.7, 130.5, 129.1, 128.9, 128.4, 128.1, 127.6, 127.0, 124.9, 123.5, 121.4, 79.2, 66.8, 65.4, 63.6, 59.0, 53.4 ppm; FT-IR (neat): v = 3031, 2892, 2823, 1715, 1598, 1491, 1452, 1294, 1114, 1068, 933, 749, 735 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{27}H_{26}N_2NaO_3^+$ 449.1836; found 449.1833.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(pyridin-3-yl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6j**)



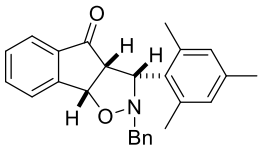
Yield: 55%; white solid; m.p. 149–150 °C; R_f = 0.23 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.44 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.34 (d, *J* = 2.2 Hz, 1H), 7.81 (td, *J* = 7.3, 6.5, 1.9 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.38 (dt, *J* = 8.0, 1.9 Hz, 1H), 7.29 – 7.16 (m, 4H), 7.11 (d, *J* = 7.0 Hz, 2H), 5.81 (d, *J* = 6.3 Hz, 1H), 4.32 (d, *J* = 9.2 Hz, 1H), 3.92 (dd, *J* = 9.3, 6.7 Hz, 1H), 3.84 (d, *J* = 15.1 Hz, 1H), 3.78 (d, *J* = 15.1 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 202.0, 153.1, 149.9, 149.4, 138.5, 137.6, 136.2, 136.1, 132.2, 130.3, 128.48, 128.45, 127.3, 127.0, 123.8, 122.3, 78.6, 70.9, 60.1, 58.8 ppm; FT-IR (neat): v = 3029, 2942, 2844, 1715, 1604, 1424, 1338, 1230, 1023, 967, 874, 766, 750, 719, 700 cm^{-1}; HRMS (ESI), *m*/*z*: [M + K]$^+$ calcd for $C_{22}H_{18}KN_2O_2^+$ 381.1000; found 381.1010.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(pyridin-3-yl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7j**)



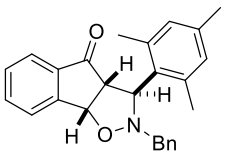
Yield: 27%; white solid; m.p. 172–173 °C; R_f = 0.34 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.69 (d, *J* = 2.2 Hz, 1H), 8.57 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.91 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.80 (td, *J* = 7.4, 1.2 Hz, 1H), 7.77 – 7.73 (m, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.45 (dd, *J* = 7.8, 4.7 Hz, 1H), 7.24 – 7.16 (m, 3H), 7.10 (d, *J* = 7.1 Hz, 2H), 5.86 (d, *J* = 6.4 Hz, 1H), 4.22 (d, *J* = 5.2 Hz, 1H), 3.88 (dd, *J* = 6.5, 5.2 Hz, 1H), 3.70 (d, *J* = 14.5 Hz, 1H), 3.64 (d, *J* = 14.7 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 203.1, 150.9, 149.7, 149.5, 137.5, 136.5, 136.0, 136.0, 134.1, 130.6, 128.4, 128.2, 127.6, 127.1, 123.9, 123.6, 78.8, 69.7, 63.2, 58.7 ppm; FT-IR (neat): v = 3022, 2918, 2856, 1715, 1604, 1426, 1348, 1277, 1029, 944, 840, 762, 733, 715, 696 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{22}H_{18}N_2NaO_2^+$ 365.1260; found 365.1267.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-mesityl-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6k**)



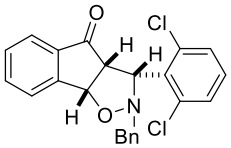
Yield: 32%; white solid; m.p. 177–178 °C; R_f = 0.68 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.78 – 7.70 (m, 3H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.22 – 7.18 (m, 3H), 6.90 (s, 2H), 5.79 (d, *J* = 6.2 Hz, 1H), 4.23 (d, *J* = 8.1 Hz, 1H), 4.01 (dd, *J* = 8.1, 6.2 Hz, 1H), 3.70 (d, *J* = 14.8 Hz, 1H), 3.64 (d, *J* = 14.8 Hz, 1H), 2.54 (br s, 6H), 2.24 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 204.0, 149.9 138.2, 137.7, 137.0, 136.3, 135.7, 130.7, 130.3, 129.9, 128.3, 128.2, 127.7, 127.0, 124.0, 78.8, 69.0, 61.2, 59.7, 21.1, 20.6 ppm; FT-IR (neat): v = 3023, 2926, 2871, 1714, 1605, 1494, 1350, 1278, 1232, 1059, 941, 863, 762, 720 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{26}H_{25}NNaO_2^+$ 406.1778; found 406.1780.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-mesityl-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7k**)



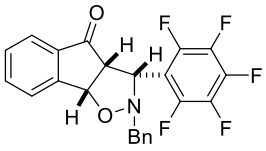
Yield: 20%; white solid; m.p. 191–192 °C; R_f = 0.48 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.81 (td, *J* = 7.4, 1.4 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.23 – 7.16 (m, 3H), 7.09 (d, *J* = 6.9 Hz, 2H), 6.89 (s, 1H), 6.66 (s, 1H), 5.72 (d, *J* = 6.4 Hz, 1H), 4.33 (d, *J* = 9.1 Hz, 1H), 3.83 (d, *J* = 15.5 Hz, 1H), 3.77 (dd, *J* = 9.1, 6.4 Hz, 1H), 3.60 (d, *J* = 15.6 Hz, 1H), 2.38 (s, 3H), 2.20 (s, 3H), 1.80 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 201.3, 153.2, 138.8, 137.5, 137.4, 137.2, 136.2, 135.5, 130.9, 129.8, 129.1, 128.04, 128.00, 127.9, 126.8, 126.7, 121.9, 77.5, 72.0, 58.4, 56.9, 21.9, 20.9, 20.5 ppm; FT-IR (neat): v = 3025, 2916, 2859, 1717, 1653, 1559, 1496, 1464, 1259, 1077, 866, 760, 728 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{26}H_{25}NNaO_2^+$ 406.1778; found 406.1777.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(2,6-dichlorophenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6l**)



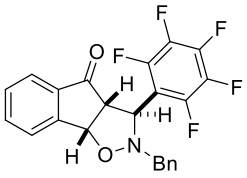
Yield: 40%; white solid; m.p. 193–194 °C; R_f = 0.54 (*n*-hexane/EtOAc 4:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.80 – 7.73 (m, 3H), 7.65 (td, *J* = 7.5, 1.2 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.38 (dd, *J* = 8.5, 7.6 Hz, 1H), 7.23 – 7.14 (m, 5H), 5.87 (d, *J* = 6.1 Hz, 1H), 4.66 (d, *J* = 7.5 Hz, 1H), 4.31 (dd, *J* = 7.6, 6.1 Hz, 1H), 3.80 (d, *J* = 14.4 Hz, 1H), 3.70 (d, *J* = 14.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 203.5, 149.7, 137.7, 136.4, 136.2, 131.4, 131.3, 131.2, 128.6, 128.4, 128.1, 127.5, 124.5, 79.4, 68.8, 60.9, 60.7 ppm; FT-IR (neat): v = 3031, 2898, 2874, 1713, 1610, 1566, 1428, 1288, 1185, 945, 843, 785, 760, 740, 607 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{17}Cl_2NNaO_2^+$ 432.0529; found 432.0536.

(3*R*,3a*R*,8b*S*)-2-Benzyl-3-(perfluorophenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6m**)



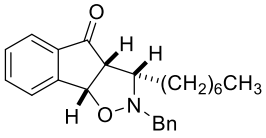
Yield: 18%; white solid; m.p. 163–164 °C; R_f = 0.51 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.82 (t, *J* = 7.4 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.20 – 7.13 (m, 3H), 7.10 – 7.05 (m, 2H), 5.81 (d, *J* = 6.4 Hz, 1H), 4.44 (d, *J* = 8.9 Hz, 1H), 3.95 (d, *J* = 14.4 Hz, 1H), 3.89 – 3.85 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 202.1, 152.6, 138.3, 136.8, 136.3, 130.3, 128.8, 128.3, 127.5, 127.3, 122.5, 78.3, 64.8, 59.8, 57.8 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –130.34 (d, *J* = 21.7 Hz, 1F), –141.56 (d, *J* = 22.5 Hz, 1F), –153.39 (t, *J* = 20.9 Hz, 1F), –161.33 (t, *J* = 18.4 Hz, 1F), –162.11 (t, *J* = 17.7 Hz, 1F) ppm; FT-IR (neat): v = 3025, 2918, 2847, 1706, 1652, 1604, 1522, 1500, 1364, 1270, 1030, 1012, 980, 773, 761, 711, 673 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{14}F_5NNaO_2^+$ 454.0837; found 454.0841.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-(perfluorophenyl)-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7m**)



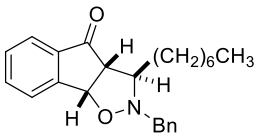
Yield: 37%; white solid; m.p. 131–133 °C; R_f = 0.58 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.81 (t, *J* = 7.3 Hz, 1H), 7.78 – 7.74 (m, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.22 – 7.12 (m, 5H), 5.83 (d, *J* = 6.1 Hz, 1H), 4.36 (d, *J* = 5.5 Hz, 1H), 4.08 (t, *J* = 5.9 Hz, 1H), 3.90 (d, *J* = 13.9 Hz, 1H), 3.79 (d, *J* = 13.8 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 202.9, 150.0, 136.6, 136.3, 136.1, 130.8, 128.5, 128.0, 127.7, 127.3, 123.8, 78.9, 62.2, 61.2, 59.6 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –139.58 (d, *J* = 16.1 Hz, 2F), –153.31 (t, *J* = 20.8 Hz, 1F), –161.79 (td, *J* = 22.2, 8.0 Hz, 2F) ppm; FT-IR (neat): v = 3087, 3033, 2882, 1718, 1652, 1605, 1524, 1503, 1372, 1274, 1230, 1057, 1007, 969, 954, 756, 696, 670 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{14}F_5NNaO_2^+$ 454.0837; found 454.0832.

(3*S*,3a*R*,8b*S*)-2-Benzyl-3-heptyl-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**6n**)



Yield: 21%; white solid; m.p. 59–60 °C; R_f = 0.63 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.74 (t, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.26 – 7.16 (m, 5H), 5.67 (d, *J* = 6.6 Hz, 1H), 4.07 (d, *J* = 14.4 Hz, 1H), 3.82 – 3.74 (m, 2H), 3.03 (q, *J* = 7.3 Hz, 1H), 1.62 – 1.52 (m, 1H), 1.40 – 1.14 (m, 10H), 0.85 (t, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 203.3, 152.5, 138.1, 138.0, 135.9, 130.1, 128.9, 128.4, 127.2, 127.1, 122.4, 78.2, 68.8, 59.1, 57.3, 31.7, 29.4, 29.1, 28.2, 26.6, 22.6, 14.4 ppm; FT-IR (neat): v = 3030, 2925, 2855, 1702, 1603, 1466, 1270, 955, 769, 753, 701 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{29}NNaO_2^+$ 386.2091; found 386.2090.

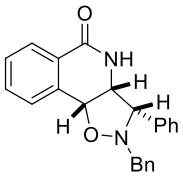
(3*R*,3a*R*,8b*S*)-2-Benzyl-3-heptyl-2,3,3a,8b-tetrahydro-4*H*-indeno[2,1-*d*]isoxazol-4-one (**7n**)



Yield: 55%; white solid; m.p. 64–65 °C; R_f = 0.57 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 7.74 (t, *J* = 7.3 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.28 – 7.18 (m, 3H), 7.15 (d, *J* = 7.2 Hz, 2H), 5.60 (d, *J* = 6.4 Hz, 1H), 3.82 (d, *J* = 14.1 Hz, 1H), 3.65 (d, *J* = 14.0 Hz, 1H), 3.53 (dd, *J* = 6.5, 4.8 Hz, 1H), 3.09 (q, *J* = 5.9 Hz, 1H), 1.73 – 1.64 (m, 1H), 1.62 – 1.54 (m, 1H), 1.54 – 1.40 (m, 2H), 1.33 – 1.24 (m, 7H), 0.88 (t, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 204.1, 151.6, 138.0, 136.4, 135.7, 130.3, 128.7, 128.1, 127.5, 127.0, 123.5, 79.0, 68.4, 61.3, 60.0, 32.0, 31.4, 29.1, 28.8, 25.7, 22.2, 14.0 ppm; FT-IR (neat): v = 3034, 2925, 2857, 1708, 1604, 1466, 1352, 1284, 1232, 771, 760, 703 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{29}NNaO_2^+$ 386.2091; found 386.2085.

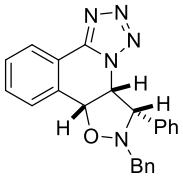
4. Data for compounds **9** and **10**

(3S,3a*R*,9b*R*)-2-Benzyl-3-phenyl-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9a**)



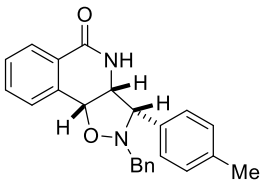
Reaction time: 48 h; yield: 78%; white solid; m.p. 169–170 °C; R_f = 0.14 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.83 (d, *J* = 7.6 Hz, 1H), 7.59 (td, *J* = 7.5, 1.4 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.28 – 7.18 (m, 8H), 7.15 – 7.12 (m, 3H), 5.59 (d, *J* = 7.6 Hz, 1H), 4.76 (td, *J* = 7.7, 3.7 Hz, 1H), 4.28 (d, *J* = 7.7 Hz, 1H), 3.94 (d, *J* = 14.9 Hz, 1H), 3.89 (d, *J* = 15.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.6, 138.1, 137.9, 136.3, 132.5, 129.2, 128.7, 128.5, 128.5, 128.34, 128.25, 128.1, 127.8, 127.2, 126.9, 74.6, 71.9, 60.2, 59.6 ppm; FT-IR (neat): v = 3206, 3074, 2855, 1652, 1582, 1412, 1342, 997, 745, 697 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{20}N_2NaO_2^+$ 379.1417; found 379.1422.

(4a*R*,5*S*,7a*R*)-6-Benzyl-5-phenyl-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**10a**)



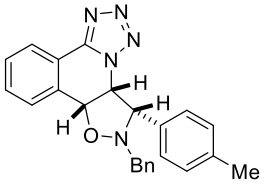
Reaction time: 48 h; yield: 14%; white solid; m.p. 148–150 °C; R_f = 0.36 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 7.2 Hz, 1H), 7.63 – 7.54 (m, 3H), 7.29 – 7.24 (m, 3H), 7.20 – 7.10 (m, 5H), 6.94 (d, *J* = 6.9 Hz, 2H), 5.91 – 5.85 (m, 2H), 4.44 (d, *J* = 7.8 Hz, 1H), 4.07 (d, *J* = 14.9 Hz, 1H), 3.84 (d, *J* = 14.9 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.9, 136.3, 132.3, 129.5, 129.1, 128.7, 128.20, 128.19, 128.1, 128.0, 127.3, 124.9, 119.7, 74.5, 74.3, 63.3, 59.1 ppm; FT-IR (neat): v = 3022, 2859, 1556, 1490, 1447, 983, 788, 738, 702, 694 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{19}N_5NaO^+$ 404.1482; found 404.1476.

(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(*p*-tolyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9b**)



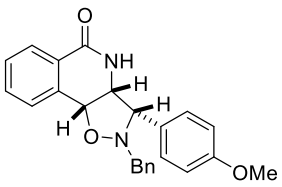
Reaction time: 48 h; yield: 59%; white solid; m.p. 157.5–158.5 °C; R_f = 0.41 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.83 (d, *J* = 7.3 Hz, 1H), 7.59 (td, *J* = 7.5, 1.4 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.27 – 7.15 (m, 6H), 7.07 (d, *J* = 7.9 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 5.59 (d, *J* = 7.8 Hz, 1H), 4.70 (td, *J* = 7.8, 3.8 Hz, 1H), 4.20 (d, *J* = 7.8 Hz, 1H), 3.87 (s, 2H), 2.25 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.3, 138.0, 137.6, 137.0, 132.9, 132.2, 128.99, 128.95, 128.5, 128.4, 128.2, 128.1, 127.7, 127.0, 126.7, 74.4, 71.8, 60.0, 60.0, 20.9 ppm; FT-IR (neat): v = 3206, 3088, 2895, 1652, 1583, 1409 ,1354, 755, 734 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{22}N_2NaO_2^+$ 393.1573; found 393.1573.

(4a*R*,5*S*,7a*R*)-6-Benzyl-5-(*p*-tolyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**10b**)



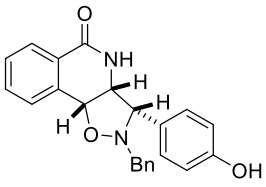
Reaction time: 48 h; yield: 19%; white solid; m.p. 151–152 °C; R_f = 0.57 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 7.2 Hz, 1H), 7.62 – 7.54 (m, 3H), 7.29 – 7.23 (m, 3H), 7.15 – 7.11 (m, 2H), 6.93 (d, *J* = 7.8 Hz, 2H), 6.82 (d, *J* = 7.7 Hz, 2H), 5.89 – 5.83 (m, 2H), 4.40 (d, *J* = 6.2 Hz, 1H), 4.05 (d, *J* = 14.9 Hz, 1H), 3.81 (d, *J* = 15.0 Hz, 1H), 2.22 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.9, 138.9, 136.4, 132.3, 129.46, 129.45, 129.2, 129.0, 128.23, 128.21, 128.1, 128.03, 127.99, 127.2, 124.9, 119.8, 74.5, 74.2, 63.3, 59.0, 21.1 ppm; FT-IR (neat): v = 3067, 3028, 2877, 1557, 1513, 1494 ,1450, 1330, 1111, 1051, 818, 731, 723, 695 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{21}N_5NaO^+$ 418.1638; found 418.1640.

3*S*,3a*R*,9b*R*)-2-Benzyl-3-(4-methoxyphenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9c**)



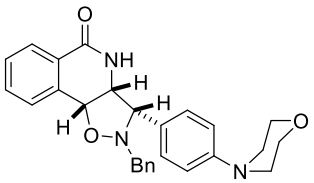
Reaction time: 48 h; yield: 62%; white solid; m.p. 170–171°C; R_f = 0.14 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.86 (d, *J* = 6.9 Hz, 1H), 7.59 (td, *J* = 7.5, 1.4 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.27 – 7.16 (m, 6H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.58 (d, *J* = 7.7 Hz, 1H), 4.68 (td, *J* = 7.7, 3.7 Hz, 1H), 4.19 (d, *J* = 7.7 Hz, 1H), 3.87 (s, 2H), 3.71 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.6, 159.3, 138.3, 138.2, 132.6, 130.5, 128.7, 128.5, 128.4, 128.3, 127.9, 127.7, 127.2, 126.9, 114.1, 74.3, 71.9, 60.0, 59.4, 55.5 ppm; FT-IR (neat): v = 3197, 3087, 1652, 1582, 1513, 1251, 1176, 1031, 829, 757 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{22}N_2NaO_3^+$ 409.1523; found 409.1526.

(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(4-hydroxyphenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9d**)



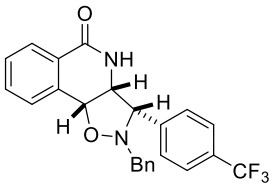
Reaction time: 48 h; yield: 54%; white solid; m.p. 163–164 °C; R_f = 0.12 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 9.38 (s, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.26 – 7.15 (m, 6H), 6.93 (d, *J* = 8.4 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 5.56 (d, *J* = 7.7 Hz, 1H), 4.64 (td, *J* = 7.7, 3.6 Hz, 1H), 4.13 (d, *J* = 7.6 Hz, 1H), 3.86 (d, *J* = 15.2 Hz, 1H), 3.86 (d, *J* = 15.2 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.6, 157.4, 138.4, 138.2, 132.6, 130.5, 128.7, 128.5, 128.4, 127.8, 127.2, 126.9, 126.1, 115.5, 74.5, 71.9, 60.0, 59.4 ppm; FT-IR (neat): v = 3332, 3140, 1645, 1577, 1516, 1454, 1231, 738 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{20}N_2NaO_3^+$ 395.1366; found 395.1370.

(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(4-morpholinophenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9e**)



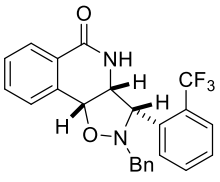
Reaction time: 72 h; yield: 81%; white solid; m.p. 167–168 °C; R_f = 0.25 (*n*-hexane/THF 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.87 (d, *J* = 7.0 Hz, 1H), 7.59 (td, *J* = 7.5, 1.4 Hz, 1H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.26 – 7.15 (m, 6H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 5.56 (d, *J* = 7.7 Hz, 1H), 4.65 (td, *J* = 7.7, 3.7 Hz, 1H), 4.13 (d, *J* = 7.6 Hz, 1H), 3.85 (d, *J* = 15.3 Hz, 1H), 3.84 (d, *J* = 15.1 Hz, 1H), 3.70 (t, *J* = 4.8 Hz, 4H), 3.12 – 3.01 (m, 4H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.6, 151.0, 138.4, 138.2, 132.5, 130.1, 128.67, 128.4, 128.3, 127.8, 127.2, 126.9, 126.1, 115.1, 74.6, 71.9, 66.6, 59.9, 59.4, 48.6 ppm; FT-IR (neat): ν = 3216, 2963, 2853, 1654, 1583, 1518, 1350, 1239, 1122, 926, 762, 734 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{27}H_{27}N_3NaO_3^+$ 464.1945; found 464.1955.

(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(4-(trifluoromethyl)phenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9f**)



Reaction time: 72 h; yield: 70%; white solid; m.p. 165–166 °C; R_f = 0.39 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.81 (d, *J* = 7.7 Hz, 1H), 7.62 – 7.57 (m, 3H), 7.54 (d, *J* = 3.8 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.27 – 7.19 (m, 5H), 5.63 (d, *J* = 7.8 Hz, 1H), 4.84 (td, *J* = 7.9, 3.8 Hz, 1H), 4.41 (d, *J* = 7.9 Hz, 1H), 3.98 (d, *J* = 14.8 Hz, 1H), 3.92 (d, *J* = 14.8 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.6, 141.5, 137.9, 137.9, 132.6, 130.0, 128.7, 128.6, 128.5 (q, *J* = 31.2 Hz), 128.4, 128.1, 127.7, 127.3, 126.9, 125.3 (q, *J* = 3.8 Hz), 124.7 (q, *J* = 272.0 Hz), 73.9, 71.8, 60.3, 59.6 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –62.73 (s, 3F) ppm; FT-IR (neat): ν = 3203, 3086, 2899, 1647, 1584, 1410, 1326, 1165, 1132, 1369,, 758, 735 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{19}F_3N_2NaO_2^+$ 447.1290; found 447.1286.

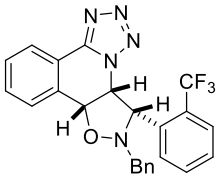
(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(2-(trifluoromethyl)phenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9g**)



Reaction time: 48 h; yield: 65%; white solid; m.p. 175–176 °C; R_f = 0.26 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.87 (d, *J* = 7.0 Hz, 1H), 7.74 (d, *J* = 7.1 Hz, 1H), 7.62 (td, *J* = 7.5, 1.4 Hz, 1H), 7.55 (d, *J* = 3.8 Hz, 1H), 7.52 – 7.44 (m, 3H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.25 – 7.16 (m, 4H), 7.12 (d, *J* = 6.7 Hz, 2H), 5.66 (d, *J* = 7.8 Hz, 1H), 4.75 (td, *J* = 7.8, 4.0 Hz, 1H), 4.38 (d, *J* = 8.5 Hz, 1H), 3.88 (d, *J* = 14.9 Hz, 1H), 3.82 (d, *J* = 14.9 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.5, 137.8, 137.3, 134.5, 132.4, 132.2, 130.7, 129.0 (q, *J* = 34.2 Hz), 128.6, 128.4, 128.3, 128.1, 128.0, 127.6, 127.1, 126.7, 125.9 (q, *J* = 5.7 Hz), 124.5 (q, *J* = 274.0 Hz), 72.0, 71.3, 60.0, 59.9 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –58.99 (s, 3F) ppm; FT-IR (neat): ν = 3196, 3064, 2922, 1682, 1311, 1164,

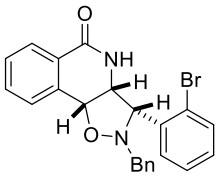
1114, 1103, 1033, 778, 737, 696 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{24}H_{19}F_3N_2NaO_2^+$ 447.1290; found 447.1306.

(4a*R*,5*S*,7a*R*)-6-Benzyl-5-(2-(trifluoromethyl)phenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**10g**)



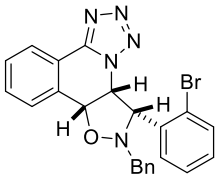
Reaction time: 48 h; yield: 12%; white solid; m.p. 161–162 °C; R_f = 0.51 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.63 – 7.55 (m, 3H), 7.29 (t, *J* = 7.7 Hz, 1H), 7.24 – 7.20 (m, 3H), 7.12 (t, *J* = 7.7 Hz, 1H), 7.10 – 7.06 (m, 2H), 6.87 (d, *J* = 7.8 Hz, 1H), 5.95 (t, *J* = 8.5 Hz, 1H), 5.90 (d, *J* = 8.8 Hz, 1H), 4.81 (d, *J* = 7.8 Hz, 1H), 3.97 (d, *J* = 15.0 Hz, 1H), 3.86 (d, *J* = 15.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.9, 136.2, 135.1, 132.4, 132.1, 131.1 (q, *J* = 1.6 Hz), 129.6, 128.9, 128.2, 128.04, 128.02, 127.9, 127.3, 126.2 (q, *J* = 5.5 Hz), 124.9, 124.1 (q, *J* = 273.7 Hz), 119.5, 74.7, 70.8, 63.6, 59.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ = –58.25 (s, 3F) ppm; FT-IR (neat): ν = 3072, 3040, 2945, 1455, 1309, 1277, 1176, 1114, 1033, 772, 741, 697 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{24}H_{18}F_3N_5NaO^+$ 472.1356; found 472.1349.

(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(2-bromophenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9h**)



Reaction time: 48 h; yield: 65%; white solid; m.p. 159–161 °C; R_f = 0.40 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.81 (d, *J* = 7.5 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 3.8 Hz, 1H), 7.27 – 7.16 (m, 6H), 7.05 (dd, *J* = 6.0, 3.7 Hz, 1H), 5.65 (d, *J* = 7.3 Hz, 1H), 4.83 (td, *J* = 7.5, 3.9 Hz, 1H), 4.55 (d, *J* = 7.6 Hz, 1H), 3.96 (d, *J* = 14.8 Hz, 1H), 3.91 (d, *J* = 14.8 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.7, 137.8, 137.7, 135.5, 132.9, 132.7, 130.7, 130.0, 128.9, 128.7, 128.4, 128.3, 127.88, 127.85, 127.4, 126.9, 124.6, 73.9, 72.2, 60.4, 58.5 ppm; FT-IR (neat): ν = 3190, 3063, 2949, 1675, 1583, 1416, 763, 736 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{23}H_{19}BrN_2NaO_2^+$ 457.0522; found 457.0531,

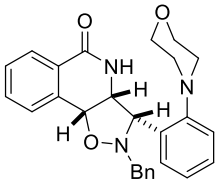
(4a*R*,5*S*,7a*R*)-6-Benzyl-5-(2-bromophenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**10h**)



Reaction time: 48 h; yield: 17%; white solid; m.p. 158–159 °C; R_f = 0.74 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 7.5 Hz, 1H), 7.63 – 7.53 (m, 4H), 7.27 – 7.23 (m, 3H), 7.14 – 7.10 (m, 2H), 7.05 (td, *J* = 7.7, 1.8 Hz, 1H), 6.91 (td, *J* = 7.6, 1.2 Hz, 1H), 6.70 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.02 (t, *J* = 8.4 Hz, 1H), 5.89 (d, *J* = 8.7 Hz, 1H), 4.92 (d, *J* = 8.2 Hz, 1H), 4.06 (d, *J* = 15.0 Hz, 1H), 3.87 (d, *J* = 15.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.8, 135.9, 135.0, 132.9, 132.3, 132.1, 130.2, 129.6, 128.2, 128.1, 127.6, 127.3, 125.5, 124.9, 119.7, 74.5, 73.2, 62.0, 59.0 ppm; FT-IR

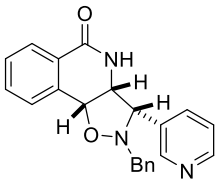
(neat): v = 3067, 2980, 2879, 1481, 1449, 1435, 1376, 1018, 977, 740, 697, 605 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{23}H_{18}BrN_5NaO^+$ 482.0587; found 482.0577.

(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(2-morpholinophenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9i**)



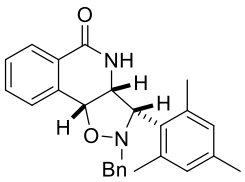
Reaction time: 72 h; yield: 51%; off-white solid; m.p. 162.5–163.5 °C; R_f = 0.20 (*n*-hexane/THF 1:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.88 (d, *J* = 6.9 Hz, 1H), 7.61 (td, *J* = 7.5, 1.4 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.27 – 7.13 (m, 7H), 7.10 (d, *J* = 3.4 Hz, 1H), 7.04 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.98 (td, *J* = 7.9, 7.4, 1.6 Hz, 1H), 5.63 (d, *J* = 7.3 Hz, 1H), 4.83 (td, *J* = 7.3, 3.5 Hz, 1H), 4.75 (d, *J* = 7.3 Hz, 1H), 3.84 (s, 2H), 3.74 (dtd, *J* = 17.1, 10.9, 2.9 Hz, 4H), 2.89 (ddd, *J* = 11.7, 6.1, 3.1 Hz, 2H), 2.77 (ddd, *J* = 8.5, 6.0, 3.2 Hz, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.8, 152.6, 137.92, 137.85, 132.6, 131.7, 130.2, 128.88, 128.87, 128.8, 128.4, 128.3, 128.2, 127.3, 126.9, 124.5, 121.4, 72.2, 69.2, 67.3, 60.0, 58.9, 53.8 ppm; FT-IR (neat): v = 3194, 3062, 2949, 2846, 1675, 1425, 1113, 1031, 741 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + H]^+$ calcd for $C_{27}H_{28}N_3O_3^+$ 442.2125; found 442.2134.

(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(pyridin-3-yl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9j**)



Reaction time: 48 h; yield: 53%; off-white solid; m.p. 164–165 °C; R_f = 0.17 (DCM:acetone 1:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.40 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.29 (d, *J* = 2.1 Hz, 1H), 7.80 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.64 (d, *J* = 3.9 Hz, 1H), 7.60 (td, *J* = 7.5, 1.4 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.34 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.27 – 7.18 (m, 6H), 5.64 (d, *J* = 8.0 Hz, 1H), 4.82 (td, *J* = 8.0, 3.9 Hz, 1H), 4.35 (d, *J* = 8.0 Hz, 1H), 3.99 (d, *J* = 14.7 Hz, 1H), 3.92 (d, *J* = 14.7 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.6, 150.6, 149.1, 138.0, 137.9, 136.7, 132.7, 132.4, 128.7, 128.6, 128.4, 128.0, 127.6, 127.4, 126.9, 123.5, 72.2, 71.7, 60.3, 59.3 ppm; FT-IR (neat): v = 3193, 3051, 2958, 1667, 1496, 1417, 1037, 735, 715 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{22}H_{19}N_3NaO_2^+$ 380.1369; found 380.1360.

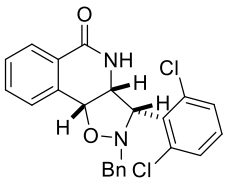
(3*S*,3a*R*,9b*R*)-2-Benzyl-3-mesityl-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9k**)



Reaction time: 48 h; yield: 90%; white solid; m.p. 175–176 °C; R_f = 0.34 (*n*-hexane/EtOAc 2:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.25 (br s, 1H), 8.04 (d, *J* = 7.7 Hz, 1H), 7.60 (td, *J* = 7.4, 1.5 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.27 – 7.17 (m, 5H), 6.88 (s, 2H), 5.43 (d, *J* = 7.5 Hz, 1H), 4.76 (td, *J* = 7.2, 2.5 Hz, 1H), 4.29 (d, *J* = 6.9 Hz, 1H), 3.72 (d, *J* = 14.7 Hz, 1H), 3.66 (d, *J* = 14.8 Hz, 1H), 2.50 (s, 6H), 2.22 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.5, 138.3, 138.1, 137.0, 134.6, 132.4, 130.3, 129.9, 129.3, 129.1, 128.4, 128.2, 127.6, 127.3, 127.0, 76.9, 71.8, 60.7,

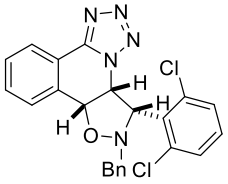
60.1, 21.2, 20.6 ppm; FT-IR (neat): v = 3179, 3044, 2915, 1679, 1586, 1422, 844, 766, 701 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + K]^+$ calcd for $C_{26}H_{26}KN_2O_2^+$ 437.1626; found 437.1635.

(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(2,6-dichlorophenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9l**)



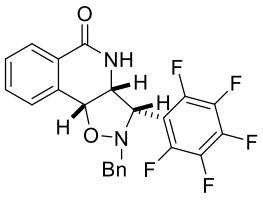
Reaction time: 72 h; yield: 72%; white solid; m.p. 179–180 °C; R_f = 0.43 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.48 (br s 1H), 8.05 (d, *J* = 7.4 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.35 (t, *J* = 8.1 Hz, 1H), 7.24 – 7.13 (m, 5H), 5.53 (d, *J* = 7.2 Hz, 1H), 5.06 (td, *J* = 6.5, 2.4 Hz, 1H), 4.71 (d, *J* = 6.2 Hz, 1H), 3.85 (d, *J* = 14.3 Hz, 1H), 3.72 (d, *J* = 14.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.3, 137.4, 136.2, 134.1, 132.4, 130.9, 130.7, 130.0, 129.8, 129.5, 128.3, 128.0, 127.6, 127.4, 127.1, 77.0, 72.0, 60.9, 60.2 ppm; FT-IR (neat): v = 3176, 3035, 2910, 1661, 1582, 1434, 1416, 783, 762, 736 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{23}H_{18}Cl_2N_2NaO_2^+$ 447.0638; found 447.0644.

(4a*R*,5*S*,7a*R*)-6-Benzyl-5-(2,6-dichlorophenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**10l**)



Reaction time: 72 h; yield: 13%; white solid; m.p. 188–189 °C; R_f = 0.68 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.34 (dd, *J* = 7.2, 1.7 Hz, 1H), 7.69 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.31 – 7.16 (m, 6H), 6.02 (dd, *J* = 6.7, 5.3 Hz, 1H), 5.92 (d, *J* = 6.7 Hz, 1H), 5.08 (d, *J* = 5.3 Hz, 1H), 3.94 (d, *J* = 14.4 Hz, 1H), 3.85 (d, *J* = 14.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.9, 136.5, 132.2, 131.4, 130.9, 130.7, 129.5, 129.1, 128.3, 128.0, 127.3, 126.0, 120.5, 75.53, 75.46, 64.3, 60.1 ppm; FT-IR (neat): v = 3090, 2951, 2919, 1488, 1455, 1435, 1318, 1049, 786, 773, 749, 624 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{23}H_{17}Cl_2N_5NaO^+$ 472.0702; found 472.0711.

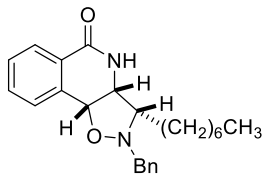
(3*S*,3a*R*,9b*R*)-2-Benzyl-3-(perfluorophenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9m**)



Reaction time: 48 h; yield: 65%; white solid; m.p. 192–193 °C; R_f = 0.18 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.94 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 2.7 Hz, 1H), 7.62 (td, *J* = 7.5, 1.4 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.22 – 7.15 (m, 5H), 5.66 (d, *J* = 7.6 Hz, 1H), 4.85 (td, *J* = 7.5, 3.1 Hz, 1H), 4.59 (d, *J* = 7.4 Hz, 1H), 4.08 (d, *J* = 13.8 Hz, 1H), 4.02 (d, *J* = 13.8 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.6, 137.0, 136.3, 132.6, 129.1, 129.0, 128.7, 128.3, 128.1, 127.6, 127.0, 71.8, 68.0, 60.9, 59.3 ppm; ^{19}F NMR (470 MHz, CDCl3): δ = –133.97 (br s, 1F), –140.75 (br s, 1F), –156.44 (t, *J* = 22.2 Hz, 1F), –164.03 (d, *J* = 276.0 Hz, 2F) ppm; FT-IR (neat): v =

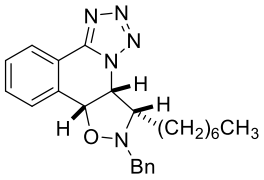
3182, 3052, 2928, 1657, 1522, 1499, 1415, 1348, 970, 738, 693 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{23}H_{15}F_5N_2NaO_2^+$ 469.0946; found 464.0960.

3*S*,3a*R*,9b*R*)-2-Benzyl-3-heptyl-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**9n**)



Reaction time: 48 h; yield: 69%; white solid; m.p. 138–139 °C; R_f = 0.37 (*n*-hexane/EtOAc 1:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.98 – 7.92 (m, 2H), 7.56 (td, *J* = 7.5, 1.4 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.33 – 7.21 (m, 5H), 5.41 (d, *J* = 7.1 Hz, 1H), 4.63 (td, *J* = 6.8, 2.4 Hz, 1H), 4.04 (d, *J* = 13.8 Hz, 1H), 3.98 (d, *J* = 13.8 Hz, 1H), 3.23 (q, *J* = 6.8 Hz, 1H), 1.53 – 1.45 (m, 1H), 1.29 – 1.10 (m, 10H), 0.84 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 163.0, 138.5, 135.8, 132.6, 129.3, 129.2, 129.0, 128.5, 128.1, 127.4, 127.3, 71.1, 70.2, 61.2, 57.9, 31.7, 29.4, 29.1, 28.4, 26.7, 22.6, 14.4 ppm; FT-IR (neat): v = 3209, 2915, 2849, 1664, 1583, 1418, 1339, 761, 727, 694 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{24}H_{30}N_2NaO_2^+$ 401.2199; found 401.2200.

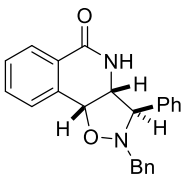
(4a*R*,5*S*,7a*R*)-6-Benzyl-5-heptyl-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**10n**)



Reaction time: 48 h; yield: 11%; white solid; m.p. 119–120 °C; R_f = 0.80 (*n*-hexane/EtOAc 1:1 *v*/*v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.24 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.60 – 7.52 (m, 3H), 7.38 – 7.29 (m, 5H), 5.82 – 5.76 (m, 1H), 4.15 (d, *J* = 13.5 Hz, 1H), 4.09 (d, *J* = 13.6 Hz, 1H), 3.68 (q, *J* = 6.9 Hz, 1H), 1.28 – 1.17 (m, 4H), 1.15 – 1.06 (m, 4H), 1.04 – 0.95 (m, 4H), 0.83 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.3, 136.1, 133.1, 132.4, 129.8, 128.8, 128.7, 128.4, 127.7, 125.4, 119.1, 73.8, 69.1, 61.4, 60.4, 31.6, 29.0, 29.0, 27.3, 26.2, 22.5, 14.0 ppm; FT-IR (neat): v = 3064, 2947, 2926, 2855, 1493, 1455, 1111, 788, 745, 710 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{24}H_{29}N_5NaO^+$ 404.2445; found 404.2435.

5. Data for compounds **12** and **13**

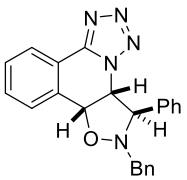
(3*R*,3a*R*,9b*R*)-2-Benzyl-3-phenyl-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12a**)



Yield: 82%; white solid; m.p. 160–161 °C; R_f = 0.11 (*n*-hexane/EtOAc 1:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.36 (br s, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.61 – 7.50 (m, 6H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.28 – 7.18 (m, 4H), 5.23 (d, *J* = 6.2 Hz, 1H), 4.42 (t, *J* = 4.9 Hz, 1H), 4.17 (d, *J* = 4.0 Hz, 1H), 3.97 (d, *J* = 14.4 Hz, 1H), 3.90 (d, *J* = 14.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.6, 138.9, 137.8, 133.8, 132.3, 130.0, 130.0, 128.7, 128.6, 128.14, 128.08, 128.06, 128.0, 127.3,

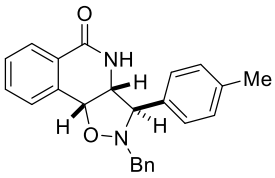
127.1, 78.3, 72.4, 65.0, 60.8 ppm; FT-IR (neat): v = 3179, 3047, 2934, 1668, 1606, 1586, 1419, 1350, 748, 700 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{23}H_{20}N_2NaO_2^+$ 379.1417; found 379.1420.

(4a*R*,5*R*,7a*R*)-6-Benzyl-5-phenyl-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13a**)



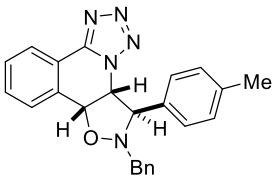
Yield: 14%; white solid; m.p. 170–171 °C; R_f = 0.40 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.32 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.76 (d, *J* = 7.2 Hz, 2H), 7.67 – 7.57 (m, 3H), 7.51 – 7.47 (m, 2H), 7.44 – 7.40 (m, 1H), 7.30 – 7.22 (m, 5H), 5.60 (d, *J* = 6.3 Hz, 1H), 5.24 (dd, *J* = 6.4, 4.4 Hz, 1H), 4.39 (d, *J* = 4.4 Hz, 1H), 3.99 (d, *J* = 14.5 Hz, 1H), 3.77 (d, *J* = 14.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.8, 136.2, 136.1, 132.2, 131.2, 130.9, 129.2, 129.0, 129.0, 128.9, 128.3, 128.2, 127.6, 126.0, 120.5, 78.52, 75.5, 68.3, 59.7 ppm; FT-IR (neat): v = 3081, 3022, 2859, 1555, 1490, 1447, 1157, 983, 788, 738, 702 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{23}H_{19}N_5NaO^+$ 404.1482; found 404.1474.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(p-tolyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12b**)



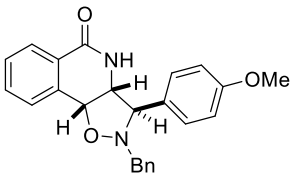
Yield: 72%; white solid; m.p. 156–157 °C; R_f = 0.43 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.33 (br s, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.61 – 7.49 (m, 3H), 7.47 (d, *J* = 7.8 Hz, 2H), 7.28 – 7.17 (m, 7H), 5.22 (d, *J* = 6.2 Hz, 1H), 4.38 (t, *J* = 5.2 Hz, 1H), 4.11 (d, *J* = 4.1 Hz, 1H), 3.95 (d, *J* = 14.5 Hz, 1H), 3.86 (d, *J* = 14.4 Hz, 1H), 2.32 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.6, 137.9, 137.3, 135.8, 133.9, 132.3, 130.00, 129.45, 129.3, 128.7, 128.2, 128.0, 127.3, 127.1, 78.2, 72.4, 64.9, 60.7, 20.9 ppm; FT-IR (neat): v = 3186, 3023, 2924, 1667, 1496, 1418, 1026, 762, 741, 695 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{24}H_{22}N_2NaO_2^+$ 393.1573; found 393.1580.

(4a*R*,5*R*,7a*R*)-6-Benzyl-5-(p-tolyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13a**)



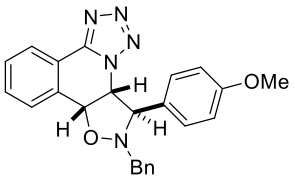
Yield: 14%; white solid; m.p. 162–163 °C; R_f = 0.66 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.31 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.66 – 7.57 (m, 5H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.28 – 7.22 (m, 5H), 5.59 (d, *J* = 6.5 Hz, 1H), 5.22 (dd, *J* = 6.5, 4.6 Hz, 1H), 4.33 (d, *J* = 4.6 Hz, 1H), 3.99 (d, *J* = 14.5 Hz, 1H), 3.73 (d, *J* = 14.5 Hz, 1H), 2.42 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.8, 138.9, 136.6, 133.4, 132.2, 131.2, 130.8, 129.9, 129.2, 128.8, 128.19, 128.15, 127.4, 126.0, 120.5, 78.5, 75.4, 68.4, 59.6, 21.2 ppm; FT-IR (neat): v = 3065, 3031, 2896, 1494, 1452, 1430, 1367, 1318, 1056, 964, 817, 757, 696 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{24}H_{21}N_5NaO^+$ 418.1638; found 418.1644.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(4-methoxyphenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12c**)



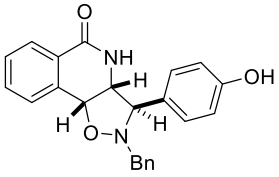
Yield: 83%; white solid; m.p. 151–152 °C; R_f = 0.40 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.31 (br s, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.59 (td, *J* = 7.4, 1.5 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.28 – 7.18 (m, 5H), 6.96 (d, *J* = 8.7 Hz, 2H), 5.22 (d, *J* = 6.3 Hz, 1H), 4.37 (ddd, *J* = 6.2, 4.2, 1.7 Hz, 1H), 4.06 (d, *J* = 4.2 Hz, 1H), 3.94 (d, *J* = 14.5 Hz, 1H), 3.84 (d, *J* = 14.5 Hz, 1H), 3.77 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.6, 159.3, 138.0, 133.9, 132.4, 130.6, 130.0, 130.0, 129.3, 128.7, 128.2, 128.1, 127.3, 127.1, 114.2, 78.1, 72.3, 64.8, 60.5, 55.4 ppm; FT-IR (neat): v = 3175, 3035, 2924, 1672, 1511, 1415, 1249, 1173, 1029, 759 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{22}N_2NaO_3^+$ 409.1523; found 409.1529.

(4a*R*,5*R*,7a*R*)-6-Benzyl-5-(4-methoxyphenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13c**)



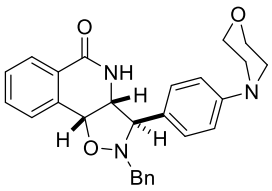
Yield: 14%; white solid; m.p. 139–140 °C; R_f = 0.57 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.31 (dd, *J* = 7.3, 1.7 Hz, 1H), 7.68 – 7.57 (m, 5H), 7.30 – 7.22 (m, 5H), 7.01 (d, *J* = 8.7 Hz, 2H), 5.60 (d, *J* = 6.6 Hz, 1H), 5.22 (dd, *J* = 6.6, 4.6 Hz, 1H), 4.29 (d, *J* = 4.6 Hz, 1H), 3.99 (d, *J* = 14.6 Hz, 1H), 3.86 (s, 3H), 3.73 (d, *J* = 14.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.1, 148.8, 136.5, 132.2, 131.2, 130.8, 130.0, 129.2, 128.8, 128.20, 128.17, 127.4, 126.0, 120.5, 114.6, 78.3, 75.3, 68.3, 59.5, 55.4 ppm; FT-IR (neat): v = 3064, 3032, 2891, 2835, 1612, 1516, 1454, 1247, 1182, 1033, 962, 833, 754, 712, 695 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{21}N_5NaO_2^+$ 434.1587; found 434.1577.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(4-hydroxyphenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12d**)



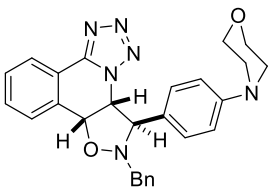
Yield: 75%; white solid; m.p. 161–162.5 °C; R_f = 0.20 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 9.28 (br s, 1H), 8.28 (br s, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 7.59 (td, *J* = 7.4, 1.5 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.28 – 7.17 (m, 5H), 6.81 (d, *J* = 8.4 Hz, 2H), 5.22 (d, *J* = 6.4 Hz, 1H), 4.36 (t, *J* = 4.8 Hz, 2H), 4.00 (d, *J* = 4.3 Hz, 1H), 3.93 (d, *J* = 14.5 Hz, 1H), 3.81 (d, *J* = 14.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.6, 157.4, 138.1, 134.1, 132.4, 130.0, 129.4, 129.3, 128.71, 128.70, 128.2, 128.0, 127.3, 127.1, 115.6, 78.3, 72.3, 64.7, 60.4 ppm; FT-IR (neat): v = 3328, 3196, 3047, 1679, 1520, 1419, 1261, 1179, 765, 728, 699 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{20}N_2NaO_3^+$ 395.1366; found 395.1371.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(4-morpholinophenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12e**)



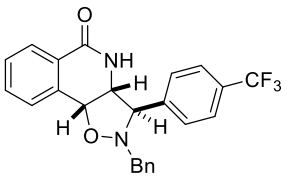
Yield: 84%; white solid; m.p. 158.5–159.5 °C; R_f = 0.17 (*n*-hexane/THF 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.28 (br s, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.59 (td, *J* = 7.4, 1.5 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.28 – 7.18 (m, 5H), 6.96 (d, *J* = 8.5 Hz, 2H), 5.22 (d, *J* = 6.3 Hz, 1H), 4.37 (t, *J* = 4.6 Hz, 1H), 4.02 (d, *J* = 4.3 Hz, 1H), 3.94 (d, *J* = 14.5 Hz, 1H), 3.82 (d, *J* = 14.5 Hz, 1H), 3.75 (t, *J* = 4.8 Hz, 4H), 3.13 (t, *J* = 4.8 Hz, 4H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.6, 151.0, 138.1, 134.0, 132.3, 130.0, 129.4, 128.9, 128.8, 128.7, 128.1, 128.0, 127.3, 127.0, 115.2, 78.2, 72.3, 66.4, 64.7, 60.4, 48.7 ppm; FT-IR (neat): v = 3184, 3043, 2954, 1667, 1516, 1417, 1241, 1123, 930, 734 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{27}H_{27}N_3NaO_3^+$ 464.1945; found 464.1949.

(4a*R*,5*R*,7a*R*)-6-Benzyl-5-(4-morpholinophenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13e**)



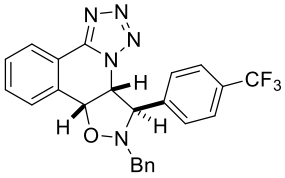
Yield: 14%; white solid; m.p. 164–166 °C; R_f = 0.43 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.31 (dd, *J* = 7.3, 1.7 Hz, 1H), 7.66 – 7.57 (m, 5H), 7.31 – 7.22 (m, 5H), 7.03 (d, *J* = 8.2 Hz, 2H), 5.59 (d, *J* = 6.6 Hz, 1H), 5.22 (dd, *J* = 6.6, 4.6 Hz, 1H), 4.26 (d, *J* = 4.7 Hz, 1H), 3.99 (d, *J* = 14.6 Hz, 1H), 3.90 (t, *J* = 4.8 Hz, 4H), 3.71 (d, *J* = 14.5 Hz, 1H), 3.24 (t, *J* = 4.8 Hz, 4H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.8, 136.7, 132.2, 131.2, 130.8, 129.3, 129.2, 128.8, 128.2, 127.4, 126.0, 120.5, 116.0, 78.4, 75.3, 68.2, 66.8, 59.5, 49.0 ppm; FT-IR (neat): v = 3034, 2949, 2894, 1608, 1516, 1454, 1235, 1118, 1053, 923, 761, 712, 696 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{27}H_{26}N_6NaO_2^+$ 489.2009; found 489.2011.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(4-(trifluoromethyl)phenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12f**)



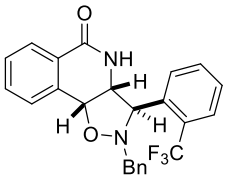
Yield: 85%; white solid; m.p. 158–159 °C; R_f = 0.31 (*n*-hexane/EtOAc 21:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.39 (br s, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.61 (td, *J* = 7.4, 1.5 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.27 – 7.17 (m, 5H), 5.24 (d, *J* = 6.1 Hz, 1H), 4.45 (ddd, *J* = 5.9, 3.9, 1.7 Hz, 1H), 4.31 (d, *J* = 3.8 Hz, 1H), 3.98 (s, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.8, 144.0, 137.7, 134.0, 132.7, 130.3, 129.8, 129.12, 129.07, 128.9 (q, *J* = 27.5 Hz), 128.4, 128.2, 127.6, 127.4, 125.7 (q, *J* = 3.8 Hz), 124.7 (q, *J* = 272.1 Hz), 77.8, 72.8, 65.3, 61.4 ppm; ^{19}F NMR (470 MHz, DMSO-d_6): δ = –62.69 (s, 3F) ppm; FT-IR (neat): v = 3182, 3046, 1668, 1585, 1421, 1328, 1165, 1113, 1070, 837, 759, 699 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{19}F_3N_2NaO_2^+$ 447.1291; found 447.1299.

(4a*R*,5*R*,7a*R*)-6-Benzyl-5-(4-(trifluoromethyl)phenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13f**)



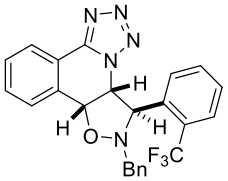
Yield: 14%; white solid; m.p. 164–165 °C; R_f = 0.66 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.33 (dd, *J* = 7.1, 1.7 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.69 – 7.60 (m, 3H), 7.30 – 7.22 (m, 5H), 5.60 (d, *J* = 6.4 Hz, 1H), 5.22 (dd, *J* = 6.4, 4.4 Hz, 1H), 4.47 (d, *J* = 4.3 Hz, 1H), 3.94 (d, *J* = 14.3 Hz, 1H), 3.85 (d, *J* = 14.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.9, 140.7, 135.8, 132.4, 131.22, 131.15 (q, *J* = 32.4 Hz), 131.05, 128.9, 128.8, 128.6, 128.3, 127.7, 126.2 (q, *J* = 3.7 Hz), 126.1, 123.9 (q, *J* = 272.3 Hz), 120.4, 77.9, 75.5, 68.4, 60.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ = –62.72 (s, 3F) ppm; FT-IR (neat): v = 3036, 2881, 1616, 1455, 1322, 1161, 1122, 1112, 1067, 839, 788, 761, 695 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{24}H_{18}F_3N_5NaO^+$ 472.1356; found 472.1357.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(2-(trifluoromethyl)phenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12g**)



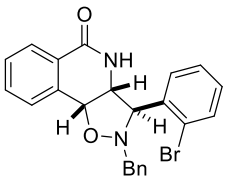
Yield: 82%; white solid; m.p. 158–159 °C; R_f = 0.46 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.08 (d, *J* = 7.3 Hz, 2H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.80 – 7.73 (m, 2H), 7.62 (td, *J* = 7.5, 1.5 Hz, 1H), 7.57 – 7.50 (m, 3H), 7.27 – 7.17 (m, 5H), 5.39 (d, *J* = 6.8 Hz, 1H), 4.49 (td, *J* = 6.8, 6.2, 2.4 Hz, 1H), 4.45 (d, *J* = 4.4 Hz, 2H), 3.86 (s, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.7, 137.6, 137.0, 135.1, 133.0, 132.6, 130.1, 129.4 (q, *J* = 31.5 Hz), 129.32, 129.31, 128.63, 128.61, 128.2, 127.4, 127.3, 127.2, 125.9 (q, *J* = 5.6 Hz), 124.5 (q, *J* = 274.4 Hz), 73.2, 72.1, 65.1, 61.1 ppm; ^{19}F NMR (470 MHz, DMSO-d_6): δ = –57.04 (s, 3F) ppm; FT-IR (neat): v = 3193, 3068, 2944, 1675, 1606, 1411, 1311, 1122, 1034, 771, 754, 699 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + K]^+$ calcd for $C_{24}H_{19}F_3KN_2O_2^+$ 463.1030; found 463.1040.

(4a*R*,5*R*,7a*R*)-6-Benzyl-5-(2-(trifluoromethyl)phenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13g**)



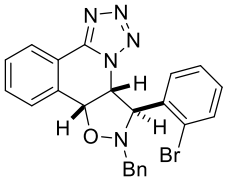
Yield: 14%; white solid; m.p. 178–180 °C; R_f = 0.57 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 7.5 Hz, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.66 – 7.59 (m, 3H), 7.55 (t, *J* = 7.7 Hz, 1H), 7.29 – 7.20 (m, 5H), 5.69 (d, *J* = 6.7 Hz, 1H), 5.42 (dd, *J* = 6.7, 4.8 Hz, 1H), 4.99 (d, *J* = 4.7 Hz, 1H), 3.76 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.0, 136.5, 135.0, 132.6, 132.3, 130.8, 130.6, 130.1, 129.9, 129.6 (q, *J* = 30.1 Hz), 129.1, 128.7, 128.2, 127.5, 126.6 (q, *J* = 5.8 Hz), 126.1, 125.0, 120.0, 75.4, 72.7, 68.3, 60.3 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ = –57.10 (s, 3F) ppm; FT-IR (neat): v = 3040, 2916, 1450, 1312, 1283, 1155, 1126, 1035, 970, 786, 727, 695 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{24}H_{18}F_3N_5NaO^+$ 472.1356; found 472.1364.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(2-bromophenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12h**)



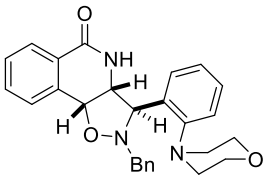
Yield: 87%; white solid; m.p. 150–151 °C; R_f = 0.48 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.55 (br s, 1H), 8.01 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.86 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.64 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.60 (td, *J* = 7.4, 1.5 Hz, 1H), 7.55 (td, *J* = 7.5, 1.5 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.28 (td, *J* = 7.7, 1.7 Hz, 1H), 7.26 – 7.17 (m, 5H), 5.15 (d, *J* = 5.7 Hz, 1H), 4.68 (d, *J* = 3.5 Hz, 1H), 4.47 (ddd, *J* = 5.6, 3.5, 1.7 Hz, 1H), 4.03 (s, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.9, 137.7, 137.6, 134.3, 132.9, 132.5, 130.1, 129.9, 129.8, 129.5, 128.7, 128.2, 128.1, 127.8, 127.4, 127.2, 123.7, 76.0, 72.6, 64.3, 61.7 ppm; FT-IR (neat): v = 3176, 3057, 2905, 1668, 1604, 1584, 1406, 1024, 752 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{19}BrN_2NaO_2^+$ 457.0522; found 457.0535.

4a*R*,5*R*,7a*R*)-6-Benzyl-5-(2-bromophenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13h**)



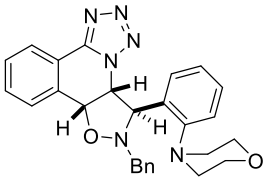
Yield: 12%; white solid; m.p. 174–176 °C; R_f = 0.60 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 7.4 Hz, 1H), 7.90 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.68 – 7.57 (m, 4H), 7.45 (td, *J* = 7.6, 1.3 Hz, 1H), 7.29 – 7.19 (m, 6H), 5.58 (d, *J* = 6.0 Hz, 1H), 5.38 (dd, *J* = 6.0, 3.7 Hz, 1H), 5.16 (d, *J* = 3.7 Hz, 1H), 3.81 (d, *J* = 13.9 Hz, 1H), 3.78 (d, *J* = 14.1 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.1, 136.3, 135.7, 133.7, 132.2, 130.9, 130.4, 130.3, 129.5, 128.8, 128.2, 128.0, 127.5, 126.2, 124.1, 120.4, 75.9, 75.7, 67.50, 60.9 ppm; FT-IR (neat): v = 3064, 2918, 1490, 1474, 1452, 1308, 1050, 961, 778, 756, 746, 696 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{18}BrN_5NaO^+$ 482.0587; found 482.0576.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(2-morpholinophenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12i**)



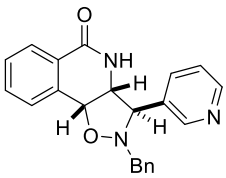
Yield: 84%; white solid; m.p. 140–141 °C; R_f = 0.41 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.09 (br s, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.71 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.62 (td, *J* = 7.5, 1.5 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.36 – 7.29 (m, 2H), 7.27 – 7.17 (m, 6H), 5.27 (d, *J* = 6.5 Hz, 1H), 4.72 (d, *J* = 5.3 Hz, 1H), 4.46 (ddd, *J* = 6.5, 5.3, 2.3 Hz, 1H), 3.94 (d, *J* = 14.3 Hz, 1H), 3.88 (d, *J* = 14.3 Hz, 1H), 3.70 (t, *J* = 4.5 Hz, 4H), 2.86 (dt, *J* = 11.6, 4.5 Hz, 2H), 2.77 (dt, *J* = 11.6, 4.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.9, 152.3, 138.1, 135.4, 134.5, 132.5, 129.5, 129.2, 128.9, 128.7, 128.4, 128.1, 127.7, 127.3, 127.0, 125.4, 122.2, 72.3, 72.1, 66.8, 64.1, 61.2, 53.6 ppm; FT-IR (neat): v = 3177, 3032, 2899, 1667, 1584, 1404, 1342, 1113, 931, 771, 755 cm^{-1}; HRMS (ESI), *m*/*z*: [M + H]$^+$ calcd for $C_{27}H_{28}N_3O_3^+$ 442.2125; found 442.2133.

(4a*R*,5*R*,7a*R*)-6-Benzyl-5-(2-morpholinophenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13i**)



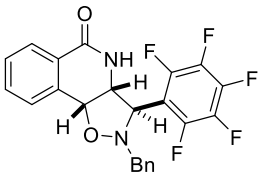
Yield: 8%; white solid; m.p. 168–170 °C; R_f = 0.56 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 7.4 Hz, 1H), 7.85 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.67 – 7.58 (m, 3H), 7.43 (td, *J* = 7.5, 1.6 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.26 – 7.17 (m, 5H), 5.61 (d, *J* = 5.7 Hz, 1H), 5.38 – 5.34 (m, 2H), 3.89 – 3.77 (m, 5H), 3.69 (d, *J* = 13.8 Hz, 1H), 3.09 – 3.04 (m, 2H), 2.77 (br s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.1, 149.1, 136.6, 133.2, 132.2, 130.9, 130.8, 129.8, 129.4, 128.7, 128.2, 127.4, 126.1, 125.9, 122.6, 120.5, 76.0, 71.7, 67.9, 67.3, 60.7, 53.8 ppm; FT-IR (neat): v = 3063, 2892, 2854, 1491, 1451, 1316, 1223, 1114, 1058, 971, 932, 796, 729, 695 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + H]^+$ calcd for $C_{27}H_{27}N_6O_2^+$ 467.2190; found 467.2199.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(pyridin-3-yl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12j**)



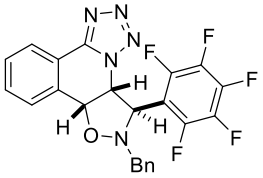
Yield: 64%; off-white solid; m.p. 166–168 °C; R_f = 0.24 (DCM:acetone 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.70 (d, *J* = 2.2 Hz, 1H), 8.51 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.37 (br s, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 7.93 (dt, *J* = 7.8, 2.0 Hz, 1H), 7.61 (td, *J* = 7.4, 1.5 Hz, 1H), 7.58 – 7.52 (m, 2H), 7.40 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.26 – 7.16 (m, 5H), 5.27 (d, *J* = 6.2 Hz, 1H), 4.47 (ddd, *J* = 6.0, 4.0, 1.7 Hz, 1H), 4.20 (d, *J* = 4.0 Hz, 1H), 3.95 (s, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.6, 149.6, 149.3, 137.5, 135.8, 134.5, 133.7, 132.5, 130.1, 129.6, 128.9, 128.2, 128.0, 127.4, 127.3, 123.7, 76.3, 72.5, 64.9, 60.9 ppm; FT-IR (neat): v = 3188, 3061, 2869, 1670, 1418, 1364, 1343, 1028, 763, 733 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{22}H_{19}N_3NaO_2^+$ 380.1369; found 380.1377.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-(perfluorophenyl)-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12m**)



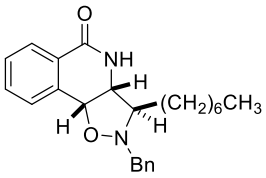
Yield: 81%; white solid; m.p. 182–183 °C; R_f = 0.20 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.36 (br s, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.64 (td, *J* = 7.2, 1.5 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.25 – 7.15 (m, 5H), 5.37 (d, *J* = 6.8 Hz, 1H), 4.77 (ddd, *J* = 7.0, 5.2, 1.9 Hz, 1H), 4.19 (d, *J* = 5.1 Hz, 1H), 4.06 (d, *J* = 13.7 Hz, 1H), 3.90 (d, *J* = 13.6 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.2, 136.5, 132.9, 132.5, 130.3, 129.7, 128.8, 128.0, 127.8, 127.4, 127.3, 72.3, 70.9, 61.9, 60.8 ppm; ^{19}F NMR (470 MHz, DMSO-d_6): δ = –139.38 (d, *J* = 14.6 Hz, 2F), –153.11 (t, *J* = 20.9 Hz, 1F), –161.59 (td, *J* = 22.1, 8.0 Hz, 2F) ppm; FT-IR (neat): v = 3207, 3062, 2956, 1683, 1521, 1504, 1415, 1339, 1131, 1006, 958, 759, 698 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{23}H_{15}F_5N_2NaO_2^+$ 469.0946; found 469.0947

(4a*R*,5*R*,7a*R*)-6-Benzyl-5-(perfluorophenyl)-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13m**)



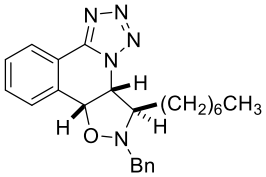
Yield: 12%; white solid; m.p. 175.5–176.5 °C; R_f = 0.33 (*n*–hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.34 (dd, *J* = 7.3, 1.8 Hz, 1H), 7.74 – 7.63 (m, 3H), 7.24 – 7.18 (m, 4H), 5.75 (d, *J* = 6.3 Hz, 1H), 5.55 (dd, *J* = 6.3, 4.6 Hz, 1H), 4.58 (d, *J* = 4.6 Hz, 1H), 4.24 (d, *J* = 13.3 Hz, 1H), 3.78 (d, *J* = 13.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.9, 134.7, 132.5, 131.4, 131.3, 128.7, 128.4, 128.1, 127.9, 126.2, 120.5, 75.5, 69.3, 65.8, 61.0 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ = –139.63 (d, *J* = 15.6 Hz, 2F), –151.74 (t, *J* = 20.8 Hz, 1F), –160.75 (td, *J* = 22.1, 21.3, 8.0 Hz, 2F) ppm; FT-IR (neat): v = 3031, 2913, 1522, 1506, 1455, 1343, 1064, 1012, 959, 948, 755, 710, 699 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{23}H_{14}F_5N_5NaO^+$ 494.1011; found 494.1020.

(3*R*,3a*R*,9b*R*)-2-Benzyl-3-heptyl-2,3,3a,9b-tetrahydroisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**12n**)



Yield: 90%; white solid; m.p. 119.5–120.5 °C; R_f = 0.54 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6, 60 °C): δ = 8.12 (br s, 1H), 8.01 (d, *J* = 7.6 Hz, 1H), 7.58 (td, *J* = 7.4, 1.5 Hz, 1H), 7.53 (td, *J* = 7.5, 1.4 Hz, 1H), 7.48 (d, *J* = 7.3 Hz, 1H), 7.31 – 7.21 (m, 5H), 4.99 (d, *J* = 5.4 Hz, 1H), 4.19 (d, *J* = 4.7 Hz, 1H), 4.01 (d, *J* = 13.7 Hz, 1H), 3.93 (d, *J* = 13.7 Hz, 1H), 3.22 (dd, *J* = 6.6, 2.6 Hz, 1H), 1.54 (q, *J* = 7.3 Hz, 2H), 1.42 – 1.21 (m, 10H), 0.87 (t, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 60 °C): δ = 161.8, 138.2, 134.0, 132.2, 130.0, 129.4, 129.0, 128.3, 128.2, 127.3, 127.1, 73.6, 72.6, 62.3, 61.9, 32.5, 31.4, 29.2, 28.7, 25.4, 22.2, 14.0 ppm; FT-IR (neat): v = 3185, 3034, 2924, 2852, 1667, 1585, 1421, 762, 692 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{30}N_2NaO_2^+$ 401.2199; found 401.2190.

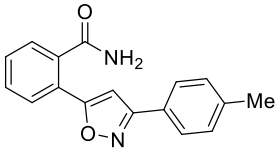
(4a*R*,5*R*,7a*R*)-6-Benzyl-5-heptyl-4a,5,6,7a-tetrahydroisoxazolo[4,5-*c*]tetrazolo[5,1-*a*]isoquinoline (**13n**)



Yield: 9%; white solid; m.p. 126–127 °C; R_f = 0.86 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 7.8 Hz, 1H), 7.65 – 7.56 (m, 3H), 7.33 – 7.24 (m, 5H), 5.34 (d, *J* = 5.4 Hz, 1H), 4.98 (dd, *J* = 5.5, 2.8 Hz, 1H), 3.85 (s, 2H), 3.74 (td, *J* = 6.5, 2.8 Hz, 1H), 1.86 – 1.80 (m, 2H), 1.66 – 1.59 (m, 2H), 1.44 – 1.25 (m, 8H), 0.90 (t, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.1, 136.2, 132.1, 131.0, 130.9, 129.4, 129.1, 128.4, 127.6, 126.0, 120.7, 75.5, 73.4, 65.8, 61.7, 32.8, 31.7, 29.5, 29.1, 25.9, 22.6, 14.1 ppm; FT-IR (neat): v = 3061, 2945, 2923, 2854, 1491, 1455, 1111, 789, 744, 710 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{24}H_{30}N_2NaO_2^+$ 426.2264; found 426.2266.

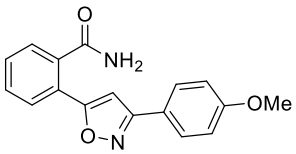
6. Data for compounds **18**

2-(3-(*p*-Tolyl)isoxazol-5-yl)benzamide (**18b**)



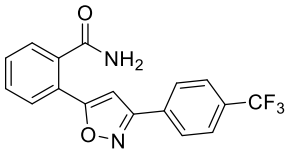
Yield: 89%; white solid; m.p. 176–177 °C; R_f = 0.36 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.00 (br s, 1H), 7.82 – 7.77 (m, 3H), 7.63 – 7.53 (m, 4H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.22 (s, 1H), 2.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.7, 169.6, 162.5, 140.5, 137.4, 130.7, 130.2, 130.0, 128.8, 128.3, 126.9, 126.2, 124.7, 101.0, 21.5 ppm; FT-IR (neat): v = 3333, 3158, 2920, 1663, 1605, 1427, 1388, 918, 797, 758 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{17}H_{14}N_2NaO_2^+$ 301.0947; found 301.0950.

2-(3-(4-Methoxyphenyl)isoxazol-5-yl)benzamide (**18c**)



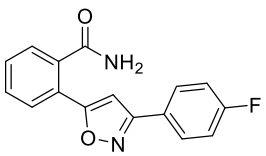
Yield: 87%; white solid; m.p. 175–176 °C; R_f = 0.47 (DCM/acetone 4:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.98 (br s, 1H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.82 – 7.78 (m, 1H), 7.62 – 7.52 (m, 4H), 7.19 (s, 1H), 7.10 (d, *J* = 8.8 Hz, 2H), 3.83 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.7, 169.4, 162.2, 161.2, 137.4, 130.7, 130.0, 128.8, 128.5, 128.3, 124.8, 121.4, 115.1, 100.9, 55.8 ppm; FT-IR (neat): v = 3336, 3164, 1662, 1614, 1433, 1390, 1247, 1026, 832, 799 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{17}H_{14}N_2NaO_3^+$ 317.0897; found 317.0891.

2-(3-(4-(Trifluoromethyl)phenyl)isoxazol-5-yl)benzamide (**18d**)



Yield: 86%; white solid; m.p. 178–179 °C; R_f = 0.17 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.13 (d, *J* = 8.1 Hz, 2H), 8.02 (br s, 1H), 7.92 (d, *J* = 8.1 Hz, 2H), 7.83 – 7.80 (m, 1H), 7.64 – 7.55 (m, 4H), 7.38 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.6, 170.5, 161.7, 137.5, 133.0, 130.99, 130.98 (q, *J* = 32.2 Hz, 1C), 130.2, 129.1, 128.5, 127.9, 126.7 (q, *J* = 4.0 Hz, 1C), 124.6, 124.5 (q, *J* = 272.4 Hz, 1C), 101.5 ppm; ^{19}F NMR (470 MHz, DMSO-d_6) δ = –61.36 (s, 3F) ppm; FT-IR (neat): v = 3377, 3193, 1652, 1441, 1327, 1167, 1122, 1065, 952, 769 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{17}H_{11}F_3N_2NaO_2^+$ 355.0665; found 355.0666.

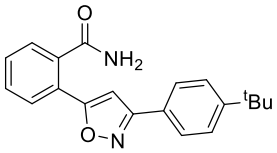
2-(3-(4-Fluorophenyl)isoxazol-5-yl)benzamide (**18e**)



Yield: 88%; white solid; m.p. 175–176 °C; R_f = 0.46 (DCM/acetone 4:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.00 (br s, 1H), 7.98 – 7.93 (m, 2H), 7.82 – 7.78 (m, 1H), 7.63 – 7.53 (m, 4H), 7.42 – 7.36 (m, 2H), 7.26 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.6, 170.0, 163.7 (d, *J* = 247.6 Hz, 1C), 161.7, 137.5, 130.8, 130.1, 129.4 (d, *J* = 8.6 Hz, 1C), 128.9, 128.4, 125.6 (d, *J* = 3.2 Hz, 1C), 124.7,

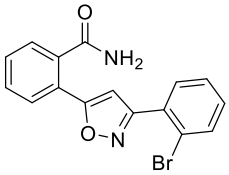
116.7 (d, *J* = 21.9 Hz, 1C), 101.1 ppm; ^{19}F NMR (470 MHz, DMSO-d_6) δ = –110.59 (ddd, *J* = 14.2, 8.9, 5.4 Hz, 1F) ppm; FT-IR (neat): v = 3372, 3181, 1651, 1607, 1438, 1396, 1231, 1159, 950, 784 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{16}H_{11}FN_2NaO_2^+$ 305.0697; found 305.0690.

2-(3-(4-(tert-Butyl)phenyl)isoxazol-5-yl)benzamide (**18f**)



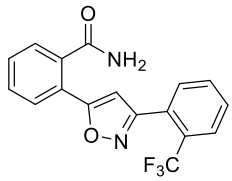
Yield: 91%; white solid; m.p. 165–166 °C; R_f = 0.54 (DCM/acetone 4:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.00 (br s, 1H), 7.84 – 7.80 (m, 3H), 7.62 – 7.53 (m, 6H), 7.22 (s, 1H), 1.32 (s, 9H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.7, 169.6, 162.5, 153.4, 137.4, 130.7, 130.0, 128.8, 128.3, 126.8, 126.4, 126.3, 124.7, 101.1, 35.1, 31.4 ppm; FT-IR (neat): v = 3334, 3162, 2952, 1666, 1626, 1430, 1389, 952, 839, 759 cm^{-1}; HRMS (ESI), *m*/*z*: [M + K]$^+$ calcd for $C_{16}H_{11}FKN_2O_2^+$ 359.1156; found 359.1163.

2-(3-(2-Bromophenyl)isoxazol-5-yl)benzamide (**18g**)



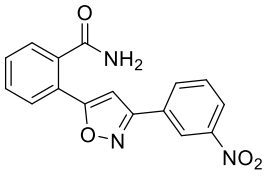
Yiel: 92%; white solid; m.p. 174–175 °C; R_f = 0.18 (*n*-hexane/EtOAc 1:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.02 (br s, 1H), 7.88 – 7.86 (m, 1H), 7.84 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.69 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.62 (br s, 1H), 7.61 – 7.58 (m, 2H), 7.58 – 7.51 (m, 2H), 7.48 (td, *J* = 7.7, 1.8 Hz, 1H), 7.16 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.8, 168.5, 162.7, 137.5, 134.1, 132.3, 131.8, 130.8, 130.3, 130.0, 128.7, 128.5, 128.2, 124.1, 122.0, 104.2 ppm; FT-IR (neat): v = 3373, 3189, 1634, 1605, 1451, 1440, 1395, 952, 760 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{16}H_{11}BrN_2NaO_2^+$ 364.9896; found 364.9890.

2-(3-(2-(Trifluoromethyl)phenyl)isoxazol-5-yl)benzamide (**18h**)



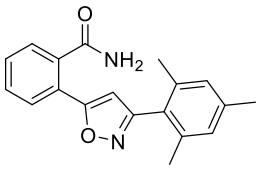
Yield: 89%; white solid; m.p. 153–154 °C; R_f = 0.18 (*n*-hexane/EtOAc 1:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.02 (br s, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.90 – 7.82 (m, 2H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.64 – 7.57 (m, 3H), 7.54 – 7.51 (m, 1H), 7.00 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.8, 168.8, 161.8, 137.5, 133.4, 132.3, 131.0, 130.9, 130.0, 128.6, 128.3, 128.0 (q, *J* = 2.4 Hz, 1C), 127.9 (q, *J* = 30.7 Hz, 1C), 127.2 (q, *J* = 5.4 Hz, 1C), 124.2 (q, *J* = 273.7 Hz, 1C), 123.9, 104.2 (q, *J* = 2.0 Hz, 1C) ppm; ^{19}F NMR (470 MHz, DMSO-d_6) δ = –56.86 (s, 3F) ppm; FT-IR (neat): v = 3362, 3186, 1651, 1392, 1309, 1138, 1114, 954, 772 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{17}H_{11}F_3N_2NaO_2^+$ 355.0665; found 355.0669.

2-(3-(3-Nitrophenyl)isoxazol-5-yl)benzamide (**18i**)



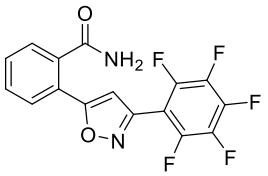
Yield: 83%; white solid; m.p. 247–248 °C; R_f = 0.31 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.66 (br s, 1H), 8.37 (t, *J* = 7.8 Hz, 2H), 8.02 (br s, 1H), 7.89 – 7.80 (m, 2H), 7.64 – 7.56 (m, 4H), 7.48 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.7, 170.5, 161.1, 148.9, 137.5, 133.3, 131.5, 131.0, 130.6, 130.2, 129.1, 128.4, 125.4, 124.5, 121.5, 101.4 ppm; FT-IR (neat): v = 3353, 3171, 2363, 2342, 1660, 1542, 1347, 809, 763, 745 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{16}H_{11}N_3NaO_4^+$ 332.0642; found 332.0652.

2-(3-Mesitylisoxazol-5-yl)benzamide (**18j**)



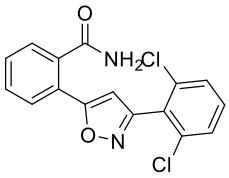
Yield: 90%; white solid; m.p. 177–178 °C; R_f = 0.28 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.86 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.55 (td, *J* = 7.8, 1.4 Hz, 2H), 7.49 (td, *J* = 7.7, 7.2, 1.3 Hz, 1H), 6.94 (s, 2H), 6.58 (s, 1H), 6.16 (br s, 1H), 5.94 (br s, 1H), 2.32 (s, 3H), 2.17 (s, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.2, 167.4, 162.7, 138.9, 137.2, 135.0, 130.3, 130.1, 128.7, 128.4, 127.8, 125.9, 124.9, 104.8, 21.2, 20.3 ppm; FT-IR (neat): v = 3348, 3179, 1658, 1581, 1571, 1487, 1377, 841, 774 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{19}H_{18}N_2NaO_2^+$ 329.1260; found 329.1253.

2-(3-(Perfluorophenyl)isoxazol-5-yl)benzamide (**18k**)



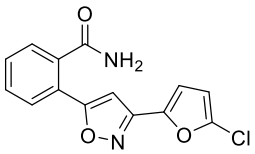
Yield: 84%; white solid; m.p. 218–219 °C; R_f = 0.28 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.05 (br s, 1H), 7.89 – 7.85 (m, 1H), 7.64 (br s, 1H), 7.63 – 7.60 (m, 2H), 7.59 – 7.55 (m, 1H), 7.16 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.6, 170.0, 152.0, 137.5, 131.2, 130.2, 128.9, 128.4, 123.7, 104.1 (t, *J* = 3.3 Hz, 1C) ppm; ^{19}F NMR (470 MHz, DMSO-d_6) δ = –139.21 (dd, *J* = 22.7, 6.7 Hz, 2F), –151.85 (t, *J* = 22.2 Hz, 1F), –161.56 (td, *J* = 21.7, 5.6 Hz, 2F) ppm; FT-IR (neat): v = 3359, 3176, 1653, 1534, 1506, 1400, 1092, 997, 815, 764 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{16}H_7F_5N_2NaO_2^+$ 377.0320; found 377.0329.

2-(3-(2,6-Dichlorophenyl)isoxazol-5-yl)benzamide (**18l**)



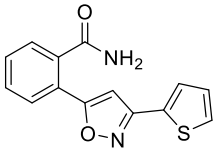
Yield: 93%; white solid; m.p. 197–198 °C; R_f = 0.34 (*n*-hexane/EtOAc 2:3 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.02 (br s, 1H), 7.91 – 7.87 (m, 1H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.63 – 7.57 (m, 4H), 7.54 – 7.51 (m, 1H), 6.97 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.8, 169.2, 159.3, 137.5, 134.9, 132.9, 130.9, 130.0, 129.2, 128.5, 128.3, 128.1, 123.8, 104.5 ppm; FT-IR (neat): v = 3356, 3169, 1648, 1625, 1433, 1406, 1384, 1193, 1124, 780 cm^{-1}; HRMS (ESI), *m*/*z*: [M + K]$^+$ calcd for $C_{16}H_{10}Cl_2KN_2O_2^+$ 370.9751; found 370.9759.

2-(3-(5-Chlorofuran-2-yl)isoxazol-5-yl)benzamide (**18m**)



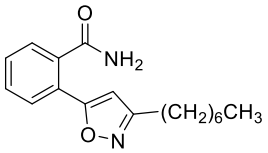
Yield: 80%; white solid; m.p. 172–173 °C; R_f = 0.4 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.00 (br s, 1H), 7.82 – 7.78 (m, 1H), 7.62 – 7.57 (m, 3H), 7.56 – 7.52 (m, 1H), 7.26 (d, *J* = 3.5 Hz, 1H), 7.09 (s, 1H), 6.76 (d, *J* = 3.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.6, 169.7, 154.2, 143.8, 137.7, 137.5, 131.0, 130.1, 128.9, 128.4, 124.1, 114.3, 109.9, 100.3 ppm; FT-IR (neat): v = 3380, 3187, 1645, 1620, 1522, 1429, 1397, 1205, 1014, 766 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{14}H_9ClN_2NaO_3^+$ 311.0194; found 311.0199.

2-(3-(Thiophen-2-yl)isoxazol-5-yl)benzamide (**18n**)



Yield: 79%; white solid; m.p. 171.5–172.5 °C; R_f = 0.34 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.00 (br s, 1H), 7.81 – 7.77 (m, 1H), 7.76 (d, *J* = 4.9 Hz, 1H), 7.71 (d, *J* = 3.4 Hz, 1H), 7.64 – 7.53 (m, 4H), 7.24 (dd, *J* = 5.1, 3.6 Hz, 1H), 7.19 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.6, 169.7, 158.1, 137.5, 130.9, 130.4, 130.1, 129.2, 129.0, 128.7, 128.4, 124.5, 101.1 ppm; FT-IR (neat): v = 3370, 3200, 1625, 1602, 1582, 1428, 1394, 914, 762, 706 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{14}H_{10}N_2NaO_2S^+$ 293.0355; found 293.0354.

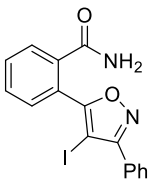
2-(3-Heptylisoxazol-5-yl)benzamide (**18o**)



Yield: 92%; white solid; m.p. 105–106 °C; R_f = 0.46 (*n*-hexane/EtOAc 2:3 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.93 (br s, 1H), 7.77 – 7.73 (m, 1H), 7.58 – 7.51 (m, 3H), 7.49 – 7.45 (m, 1H), 6.64 (s, 1H), 2.64 (t, *J* = 7.6 Hz, 2H), 1.63 (p, *J* = 7.3 Hz, 2H), 1.37 – 1.21 (m, 8H), 0.86 (t, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.9, 168.1, 164.5, 137.4, 130.4, 129.8, 128.5, 128.1, 124.6, 102.7, 31.7, 29.0, 28.9, 28.2, 25.8, 22.6, 14.4 ppm; FT-IR (neat): v = 3363, 3182, 2920, 2850, 1652, 1602, 1463, 1396, 797, 767 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{17}H_{22}N_2NaO_2^+$ 309.1573; found 309.1563.

7. Data for compounds **22**

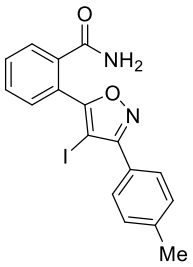
2-(4-Iodo-5-phenylisoxazol-3-yl)benzamide (**22a**)



Yield: 97%; white solid; m.p. 177.5–179 °C; R_f = 0.2 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.02 (br s, 1H), 7.81 – 7.78 (m, 2H), 7.76 – 7.73 (m, 1H), 7.71 – 7.64 (m, 3H), 7.62 – 7.56 (m, 3H), 7.46 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 171.9, 169.3, 163.4, 137.9, 131.3, 131.2, 130.7, 130.6, 129.3, 129.1, 128.9,

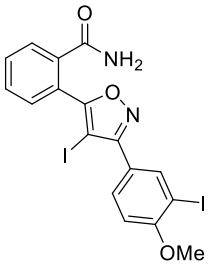
128.8, 126.2, 61.3 ppm; FT-IR (neat): v = 3466, 3144, 1673, 1604, 1379, 982, 766, 699, 515 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_{11}IN_2NaO_2^+$ 412.9757; found 412.9750.

2-(4-Iodo-5-(p-tolyl)isoxazol-3-yl)benzamide (**22b**)



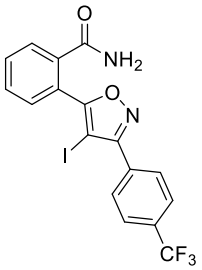
Yield: 99%; white solid; m.p. 184–185 °C; R_f = 0.44 (*n*-hexane/EtOAc 1:2 *v*/*v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 – 7.71 (m, 3H), 7.65 (d, *J* = 6.9 Hz, 1H), 7.58 (dtd, *J* = 17.0, 7.4, 1.6 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 6.13 (br s, 1H), 5.93 (br s, 1H), 2.42 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.3, 169.6, 163.4, 140.3, 136.1, 131.04, 130.9, 130.6, 129.2, 128.6, 128.5, 125.7, 125.4, 59.7, 21.4 ppm; FT-IR (neat): v = 3468, 3153, 1678, 1604, 1379, 1110, 982, 820, 767, 495 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{13}IN_2NaO_2^+$ 426.9914; found 426.9907.

2-(4-Iodo-5-(3-iodo-4-methoxyphenyl)isoxazol-3-yl)benzamide (**22c**)



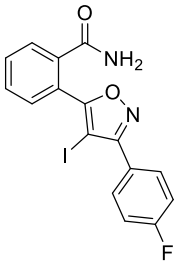
Yield: 88%; white solid; m.p. 195–196 °C; R_f = 0.31 (*n*-hexane/EtOAc 1:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.18 (d, *J* = 2.2 Hz, 1H), 8.02 (br s, 1H), 7.84 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.76 – 7.71 (m, 1H), 7.68 – 7.63 (m, 3H), 7.46 (br s, 1H), 7.21 (d, *J* = 8.6 Hz, 1H), 3.92 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 172.0, 169.3, 161.6, 159.7, 139.1, 137.9, 131.4, 131.2, 130.6, 130.5, 128.8, 126.2, 123.1, 112.2, 86.7, 61.3, 57.2 ppm; FT-IR (neat): v = 34061, 3208, 2930, 1652, 1600, 1397, 1274, 1258, 1046, 987, 728 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{12}I_2N_2NaO_3^+$ 568.8829; found 568.8840.

2-(4-Iodo-5-(4-(trifluoromethyl)phenyl)isoxazol-3-yl)benzamide (**22d**)



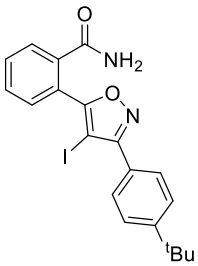
Yield: 99%; white solid; m.p. 174–175 °C; R_f = 0.46 (*n*-hexane/EtOAc 1:2 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.07 – 8.02 (m, 3H), 7.98 (d, *J* = 8.2 Hz, 2H), 7.78 – 7.74 (m, 1H), 7.71 – 7.64 (m, 3H), 7.48 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 172.5, 169.2, 162.5, 137.9, 133.1, 131.4, 131.3, 130.9 (q, *J* = 32.3 Hz, 1C), 130.7, 129.9, 128.8, 126.3 (q, *J* = 3.6 Hz, 1C), 126.0, 124.5 (q, *J* = 272.4 Hz, 1C), 61.3 ppm; ^{19}F NMR (470 MHz, DMSO-d_6) δ = –61.36 (s, 3F) ppm; FT-IR (neat): v = 3469, 3279, 3167, 1675, 1640, 1600, 1319, 1127, 1110, 1067, 766 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + H]^+$ calcd for $C_{17}H_{11}F_3IN_2O_2^+$ 458.9812; found 458.9821.

2-(5-(4-Fluorophenyl)-4-iodoisoxazol-3-yl)benzamide (**22e**)



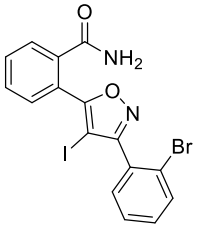
Yield: 97%; white solid; m.p. 151–152 °C; R_f = 0.48 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.03 (br s, 1H), 7.88 – 7.84 (m, 2H), 7.76 – 7.72 (m, 1H), 7.70 – 7.64 (m, 3H), 7.49 – 7.41 (m, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 172.0, 169.2, 163.6 (d, *J* = 247.9 Hz, 1C), 162.6, 137.9, 131.3 (2C), 131.2, 131.2, 130.5, 128.7, 126.1, 125.5 (d, *J* = 3.3 Hz, 1C), 116.4 (d, *J* = 21.9 Hz, 1C), 61.3 ppm; ^{19}F NMR (470 MHz, DMSO-d_6) δ = –110.57 (tt, *J* = 9.2, 5.2 Hz, 1F) ppm; FT-IR (neat): v = 3359, 3151, 1678, 1604, 1482, 1399, 1216, 986, 841, 766 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{16}H_{10}FIN_2NaO_2^+$ 430.9663; found 430.9669.

2-(5-(4-(tert-Butyl)phenyl)-4-iodoisoxazol-3-yl)benzamide (**22f**)



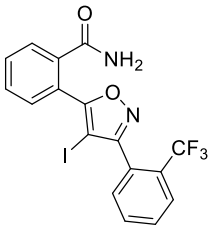
Yield: 97%; white solid; m.p. 215–216 °C; R_f = 0.58 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.02 (br s, 1H), 7.75 – 7.72 (m, 3H), 7.70 – 7.63 (m, 3H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.47 (br s, 1H), 1.34 (s, 9H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 171.7, 169.3, 163.2, 153.27, 137.9, 131.3, 131.1, 130.5, 128.7, 126.2, 126.2, 126.1, 61.2, 35.1, 31.5 ppm; FT-IR (neat): v = 3417, 3198, 2961, 1671, 1611, 1590, 1375, 984, 842, 767 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{20}H_{19}IN_2NaO_2^+$ 469.0383; found 469.0392.

2-(5-(2-Bromophenyl)-4-iodoisoxazol-3-yl)benzamide (**22g**)



Yield: 99%; white solid; m.p. 224–225 °C; R_f = 0.34 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.99 (br s, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.75 – 7.71 (m, 1H), 7.71 – 7.63 (m, 3H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.52 (td, *J* = 7.7, 1.9 Hz, 1H), 7.49 (br s, 1H), 7.45 (dd, *J* = 7.4, 1.9 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.8, 169.3, 165.6, 138.0, 133.4, 132.5, 132.3, 131.2, 131.0, 130.7, 130.5, 128.8, 128.4, 125.7, 123.2, 64.1 ppm; FT-IR (neat): v = 3470, 3313, 3175, 1682, 1662, 1599, 1473, 1379, 982, 760 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{16}H_{10}BrIN_2NaO_2^+$ 490.8863; found 490.8860.

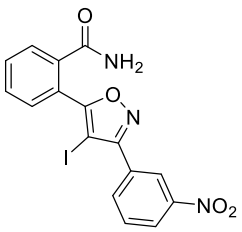
2-(4-Iodo-5-(2-(trifluoromethyl)phenyl)isoxazol-3-yl)benzamide (**22h**)



Yield: 99%; white solid; m.p. 190–191 °C; R_f = 0.37 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.00 – 7.95 (m, 2H), 7.88 (t, *J* = 7.5 Hz, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.75 – 7.72 (m, 1H), 7.70 – 7.65 (m, 3H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.50 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 170.7, 169.3, 164.2, 138.0, 133.1, 132.6, 131.2, 131.2, 131.0, 130.5, 128.9 (d, *J* = 30.6 Hz, 1C), 128.8, 127.8 (q, *J* = 1.7 Hz, 1C), 127.2 (q, *J* = 4.8 Hz, 1C), 125.7, 124.0 (q, *J* = 274.1 Hz, 1C), 64.1 ppm; ^{19}F NMR (470 MHz, DMSO-d_6) δ = –57.17 (s, 3F) ppm; FT-IR (neat): v = 3440, 3115,

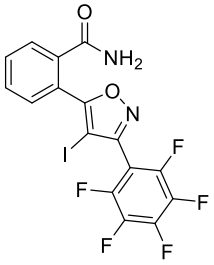
1681, 1656, 1610, 1396, 1316, 1174, 1127, 1032, 766 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{10}F_3IN_2NaO_2^+$ 480.9631; found 480.9627.

2-(4-Iodo-5-(3-nitrophenyl)isoxazol-3-yl)benzamide (**22i**)



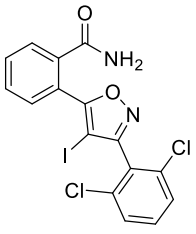
Yield: 99%; white solid; m.p. 222–223 °C; R_f = 0.46 (*n*-hexane/EtOAc 1:2 *v*/*v*); ^1H NMR (500 MHz, DMSO-d_6): δ = 8.65 (t, *J* = 2.0 Hz, 1H), 8.45 (ddd, *J* = 8.3, 2.4, 1.1 Hz, 1H), 8.28 (dt, *J* = 7.7, 1.2 Hz, 1H), 8.05 (br s, 1H), 7.92 (t, *J* = 8.0 Hz, 1H), 7.79 – 7.75 (m, 1H), 7.72 – 7.66 (m, 3H), 7.48 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 172.7, 169.1, 161.6, 148.3, 137.8, 135.2, 131.3, 131.3, 131.3, 130.6, 130.5, 128.8, 125.9, 125.5, 123.3, 61.3 ppm; FT-IR (neat): v = 3458, 3297, 3176, 1660, 1603, 1525, 1386, 1347, 997, 765 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_{10}IN_3NaO_4^+$ 457.9608; found 457.9603.

2-(4-Iodo-5-(perfluorophenyl)isoxazol-3-yl)benzamide (**22k**)



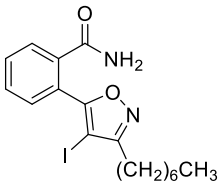
Yield: 99%; white solid; m.p. 178–179 °C; R_f = 0.5 (*n*-hexane/EtOAc 1:2 *v*/*v*); ^1H NMR (500 MHz, DMSO-d_6): δ = 8.07 (br s, 1H), 7.79 – 7.75 (m, 1H), 7.73 – 7.67 (m, 3H), 7.53 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 172.8, 169.1, 155.4, 137.8, 131.5, 131.2, 130.7, 128.8, 125.3, 63.9 ppm; ^{19}F NMR (470 MHz, DMSO-d_6) δ = –138.55 – –138.65 (m, 2F), –149.48 (t, *J* = 22.4 Hz, 1F), –160.55 – –160.71 (m, 2F) ppm; FT-IR (neat): v = 3476, 3200, 1673, 1506, 1494, 1372, 1126, 1021, 990 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_6F_5IN_2NaO_2^+$ 502.9286; found 502.9271.

2-(5-(2,6-Dichlorophenyl)-4-iodoisoxazol-3-yl)benzamide (**22l**)



Yield: 98%; white solid; m.p. 264–265 °C; R_f = 0.48 (*n*-hexane/EtOAc 1:2 *v*/*v*); ^1H NMR (500 MHz, DMSO-d_6): δ = 7.98 (br s, 1H), 7.76 – 7.61 (m, 7H), 7.51 (br s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 171.4, 169.3, 162.9, 138.0, 135.3, 133.4, 131.3, 130.9, 130.5, 129.0, 128.8, 127.9, 125.5, 63.8 ppm; FT-IR (neat): v = 3432, 3111, 1680, 1661, 1605, 1429, 1369, 1193, 1112, 985 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_9Cl_2IN_2NaO_2^+$ 480.8978; found 480.8977.

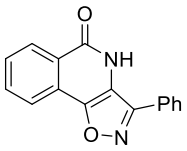
2-(5-Heptyl-4-iodoisoxazol-3-yl)benzamide (**22o**)



Yield: 98%; white solid; m.p. 84–85 °C; R_f = 0.54 (*n*-hexane/EtOAc 1:2 *v/v*); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.79 – 7.73 (m, 1H), 7.62 – 7.54 (m, 3H), 5.85 (br s, 1H), 5.76 (br s, 1H), 2.67 (t, *J* = 7.5 Hz, 2H), 1.76 (p, *J* = 7.6 Hz, 2H), 1.46 – 1.26 (m, 8H), 0.89 (t, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.5, 168.8, 165.3, 135.9, 130.7, 130.6, 128.6, 125.6, 61.4, 31.7, 28.9, 27.2, 26.9, 22.6, 14.1 ppm; FT-IR (neat): v = 3306, 3140, 2926, 2855, 1687, 1667, 1607, 1385, 1047 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{21}IN_2NaO_2^+$ 435.0540; found 435.0550.

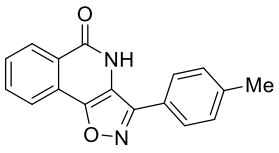
8. Data for compounds **23**

3-Phenylisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23a**)



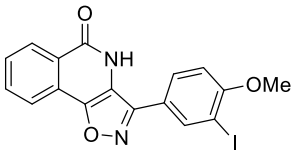
Yield: 78%; white solid; m.p. >250 °C (decomposed); R_f = 0.46 (DCM/acetone 8:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.88 (br s, 1H), 8.35 (dd, *J* = 8.2, 2.4 Hz, 1H), 8.13 – 8.07 (m, 1H), 7.99 – 7.88 (m, 3H), 7.76 (td, *J* = 7.6, 2.3 Hz, 1H), 7.61 – 7.54 (m, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.1, 152.7, 150.1, 138.2, 134.0, 130.9, 130.5, 130.0, 129.4, 129.1, 128.6, 127.0, 125.1, 121.3 ppm; FT-IR (neat): v = 3441, 2924, 1664, 1598, 1346, 769, 689 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_{10}N_2NaO_2^+$ 285.0634; found 285.0639

3-(*p*-Tolyl)isoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23b**)



Yield: 67%; white solid; m.p. >250 °C (decomposed); R_f = 0.64 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, 4% TFA-*d* in $CDCl_3$): δ = 8.55 (d, *J* = 8.1 Hz, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 7.99 (t, *J* = 7.6 Hz, 1H), 7.82 – 7.73 (m, 3H), 7.40 (d, *J* = 7.6 Hz, 2H), 2.47 (s, 3H) ppm; ^{13}C NMR (125 MHz, 4% TFA-*d* in $CDCl_3$): δ = 164.4, 152.5, 151.4, 141.7, 134.9, 130.3, 130.2, 129.4, 127.6, 125.7, 124.0, 122.8, 121.5, 117.4, 21.5 ppm; FT-IR (neat): v = 3094, 2982, 1646, 1596, 1481, 1339, 821, 766, 725 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + K]^+$ calcd for $C_{17}H_{12}KN_2O_2^+$ 315.0530; found 315.0533.

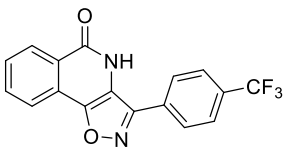
3-(3-Iodo-4-methoxyphenyl)isoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23c**)



Yield: 93%; white solid; m.p. >260 °C (decomposed); R_f = 0.4 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, 4% TFA-*d* in $CDCl_3$): δ = 8.56 (d, *J* = 8.2 Hz, 1H), 8.26 (d, *J* = 2.1 Hz, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 8.01 (t, *J* = 7.6 Hz, 1H), 7.86 – 7.78 (m, 2H), 7.01 (d, *J* = 8.5 Hz, 1H), 3.99 (s, 3H) ppm; ^{13}C NMR (125 MHz, 4% TFA-*d* in $CDCl_3$): δ = 164.5, 160.5, 151.6, 151.0, 138.5, 135.0, 130.4, 129.4, 129.4, 125.6, 121.6, 119.7, 117.2, 111.2, 87.1, 56.6 ppm; FT-IR (neat): v = 3086, 2845, 1652,

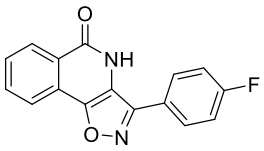
1599, 1480, 1393, 1197, 1154, 1044, 779 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{11}IN_2NaO_3^+$ 440.9707; found 440.9716.

3-(4-(Trifluoromethyl)phenyl)isoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23d**)



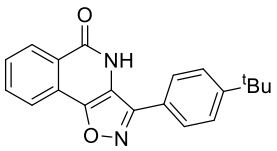
Yield: 81%; white solid; m.p. >255 °C (decomposed); R_f = 0.51 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, 4% TFA-*d* in $CDCl_3$): δ = 8.57 (d, *J* = 8.1 Hz, 1H), 8.24 (d, *J* = 7.9 Hz, 1H), 8.06 – 7.99 (m, 3H), 7.90 – 7.82 (m, 3H) ppm; ^{13}C NMR (125 MHz, 4% TFA-*d* in $CDCl_3$): δ = 164.6, 152.2, 151.4, 135.2, 133.3 (q, *J* = 33.0 Hz, 1C), 130.7, 129.5, 129.1, 128.3, 126.6 (q, *J* = 3.7 Hz, 1C), 125.4, 124.0, 123.6 (q, *J* = 272.5 Hz, 1C), 121.7, 117.3 ppm; ^{19}F NMR (470 MHz, 4% TFA-*d* in $CDCl_3$) δ = –63.18 (s, 3F) ppm; FT-IR (neat): v = 3086, 1652, 1598, 1327, 1198, 1134, 1111, 1070, 841, 770 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_9F_3N_2NaO_2^+$ 353.0508; found 353.0517.

3-(4-Fluorophenyl)isoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23e**)



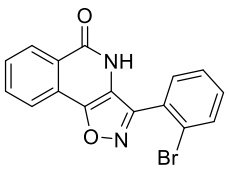
Yield: 89%; white solid; m.p. >270 °C (decomposed); R_f = 0.66 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, 4% TFA-*d* in $CDCl_3$): δ = 8.56 (d, *J* = 8.1 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 8.02 (t, *J* = 7.6 Hz, 1H), 7.90 – 7.81 (m, 3H), 7.31 (t, *J* = 8.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, 4% TFA-*d* in $CDCl_3$): δ = 164.7 (d, *J* = 253.1 Hz, 1C), 164.6, 151.8, 151.8, 135.2, 130.6, 130.0 (d, *J* = 8.7 Hz, 1C), 129.5, 125.5, 124.1, 121.7, 121.5 (d, *J* = 3.4 Hz, 1C), 117.3, 117.0 (d, *J* = 22.0 Hz, 1C) ppm; ^{19}F NMR (470 MHz, 4% TFA-*d* in $CDCl_3$) δ = –107.45 (tt, *J* = 8.9, 5.0 Hz, 1F) ppm; FT-IR (neat): v = 3090, 2981, 1662, 1600, 1485, 1420, 1344, 1235, 828, 760 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_9FN_2NaO_2^+$ 303.0540; found 303.0533.

3-(4-(*tert*-Butyl)phenyl)isoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23f**)



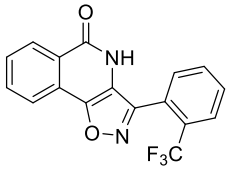
Yield: 78%; white solid; m.p. >265 °C (decomposed); R_f = 0.44 (*n*-hexane/EtOAc 2:1 *v/v*); ^{1}H NMR (500 MHz, 4% TFA-*d* in $CDCl_3$): δ = 8.57 (d, *J* = 8.2 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.00 (t, *J* = 7.6 Hz, 1H), 7.80 (t, *J* = 7.3 Hz, 3H), 7.64 (d, *J* = 7.9 Hz, 2H), 1.40 (s, 9H) ppm; ^{13}C NMR (125 MHz, 4% TFA-*d* in $CDCl_3$): δ = 164.4, 154.8, 152.5, 151.4, 134.9, 130.2, 129.5, 127.5, 126.6, 125.7, 124.0, 122.8, 121.6, 117.6, 35.0, 31.1 ppm; FT-IR (neat): v = 3113, 2965, 1645, 1598, 1340, 1134, 834, 769 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{20}H_{18}N_2NaO_2^+$ 341.1260; found 341.1266.

3-(2-Bromophenyl)isoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23g**)



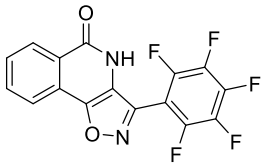
Yield: 58%; white solid; m.p. >240 °C (decomposed); R_f = 0.46 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, 4% TFA-*d* in $CDCl_3$): δ = 8.50 (d, *J* = 8.2 Hz, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 8.02 – 7.94 (m, 1H), 7.78 (q, *J* = 8.0, 7.4 Hz, 2H), 7.65 – 7.57 (m, 1H), 7.50 (dtd, *J* = 21.4, 7.5, 1.6 Hz, 2H) ppm; ^{13}C NMR (125 MHz, 4% TFA-*d* in $CDCl_3$): δ = 163.6, 152.9, 150.9, 134.5, 133.6, 132.3, 132.1, 129.9, 129.5, 128.0, 127.8, 127.4, 125.7, 122.8, 121.5, 118.8 ppm; FT-IR (neat): v = 3077, 2971, 1652, 1596, 1339, 855, 760, 730, 700 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_9BrN_2NaO_2^+$ 362.9740; found 362.9745.

3-(2-(Trifluoromethyl)phenyl)isoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23h**)



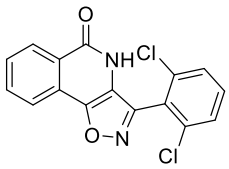
Yield: 61%; white solid; m.p. 238–239 °C; R_f = 0.47 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.91 (br s, 1H), 8.35 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.99 – 7.95 (m, 2H), 7.90 – 7.71 (m, 4H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 161.7, 151.7, 148.9, 134.2, 133.1, 133.1, 131.3, 130.2, 129.3, 129.2 (q, *J* = 30.6 Hz, 1C) 126.9 (q, *J* = 4.9 Hz, 1C), 126.2, 125.1 (q, *J* = 4.1 Hz, 1C), 125.1, 124.1 (q, *J* = 273.7 Hz, 1C), 121.5, 121.4 ppm; ^{19}F NMR (470 MHz, 4% TFA-*d* in $CDCl_3$) δ = –57.79 (s, 3F) ppm; FT-IR (neat): v = 3080, 2981, 1645, 1595, 1341, 1311, 1123, 1068, 1037, 766 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_9F_3N_2NaO_2^+$ 353.0508; found 353.0517.

3-(Perfluorophenyl)isoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23k**)



Yield: 29%; white solid; m.p. >260 °C (decomposed); R_f = 0.47 (*n*-hexane/EtOAc 3:1 *v/v*); ^{1}H NMR (500 MHz, 4% TFA-*d* in $CDCl_3$): δ = 8.58 (d, *J* = 8.1 Hz, 1H), 8.27 (d, *J* = 7.9 Hz, 1H), 8.05 (t, *J* = 7.6 Hz, 1H), 7.86 (t, *J* = 7.7 Hz, 1H) ppm; ^{13}C NMR (125 MHz, 4% TFA-*d* in $CDCl_3$): δ = 164.5, 152.1, 141.5, 135.1, 130.7, 129.6, 125.3, 124.1, 121.6, 118.6 ppm; ^{19}F NMR (470 MHz, 4% TFA-*d* in $CDCl_3$) δ = –137.51 – –137.62 (m, 2F), –147.82 (t, *J* = 20.8 Hz, 1F), –159.30 – –159.44 (m, 2F) ppm; FT-IR (neat): v = 3087, 1649, 1600, 1474, 1342, 1180, 899 cm^{-1}; HRMS (ESI), *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_5F_5N_2NaO_2^+$ 375.0163; found 375.0163.

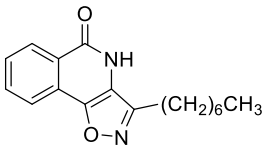
3-(2,6-Dichlorophenyl)isoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23l**)



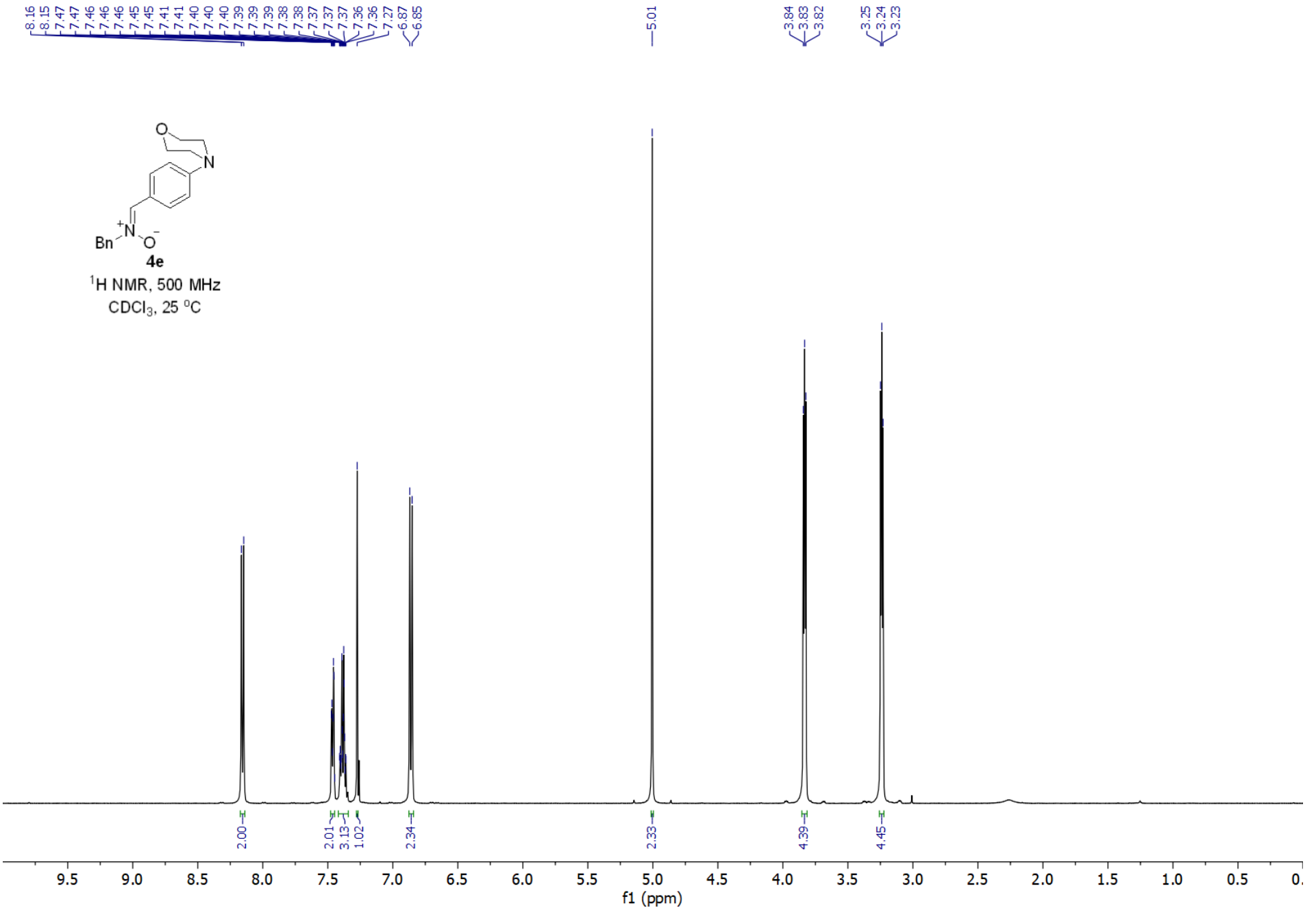
Yield: 46%; white solid; m.p. >270 °C (decomposed); R_f = 0.47 (*n*-hexane/EtOAc 1:1 *v/v*); ^{1}H NMR (500 MHz, 4% TFA-*d* in $CDCl_3$): δ = 8.55 (d, *J* = 8.1 Hz, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 8.01 (t, *J* = 7.7 Hz, 1H), 7.81 (t, *J* = 7.9 Hz, 1H), 7.58 – 7.47 (m, 3H) ppm; ^{13}C NMR (125 MHz, 4% TFA-*d* in $CDCl_3$): δ = 164.3, 151.3, 149.1, 135.9, 134.8, 132.6, 130.2, 129.5, 128.7, 125.7, 124.2, 124.0, 121.6, 118.9

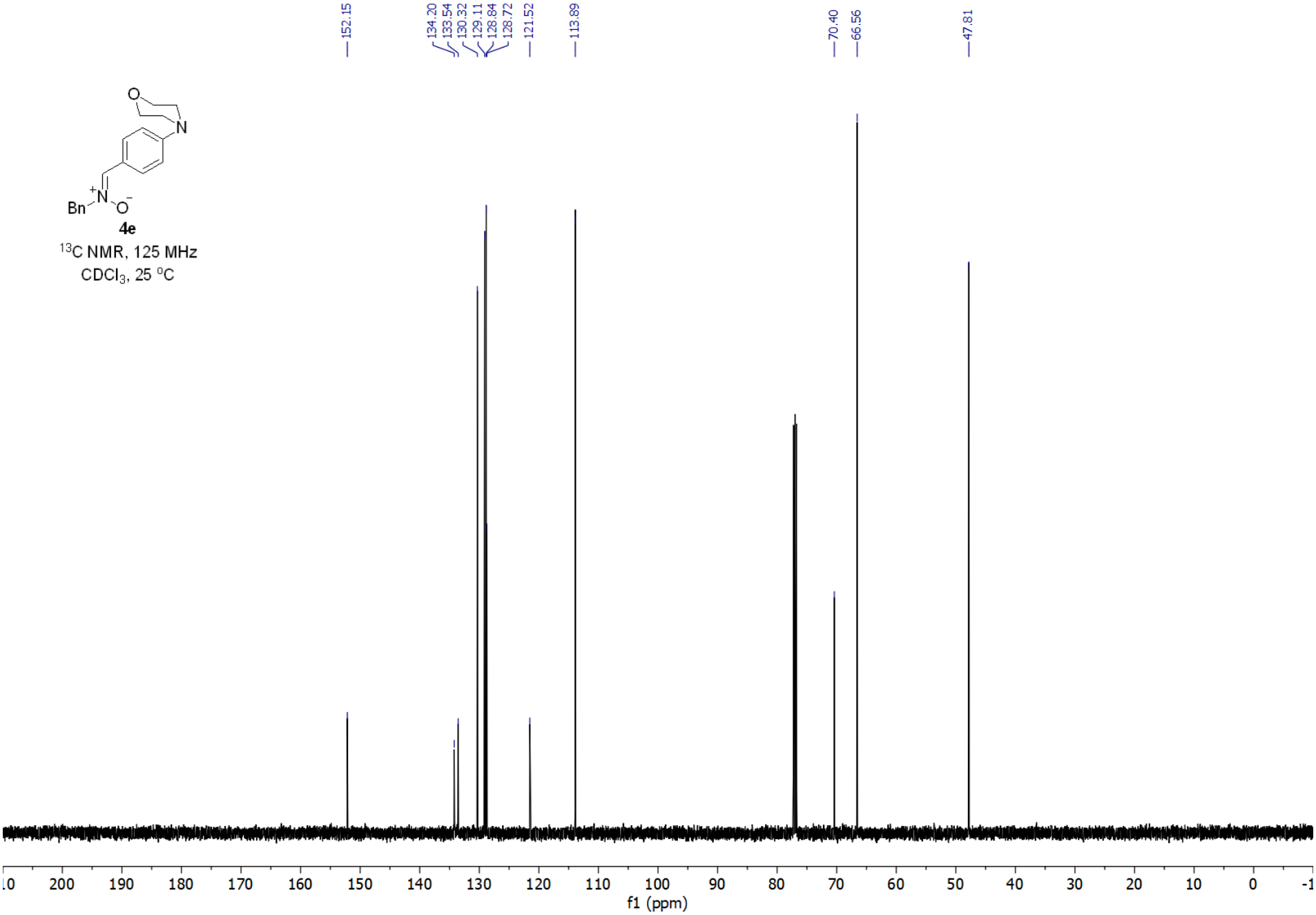
ppm; FT-IR (neat): v = 2914, 1652, 1602, 1434, 1339, 1196, 894, 783, 772 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{16}H_8Cl_2N_2NaO_2^+$ 352.9855; found 352.9863.

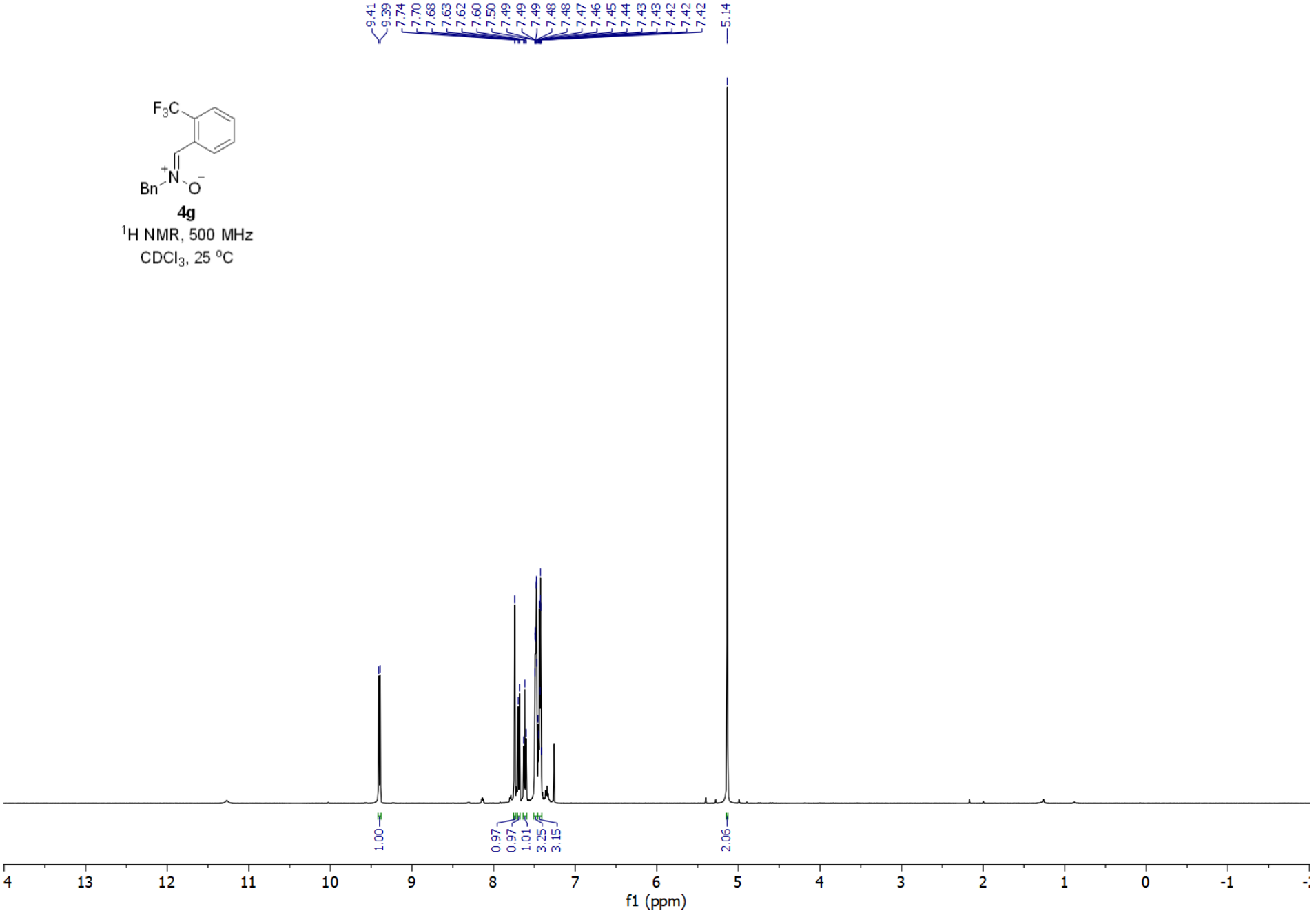
3-Heptylisoxazolo[4,5-*c*]isoquinolin-5(4*H*)-one (**23o**)

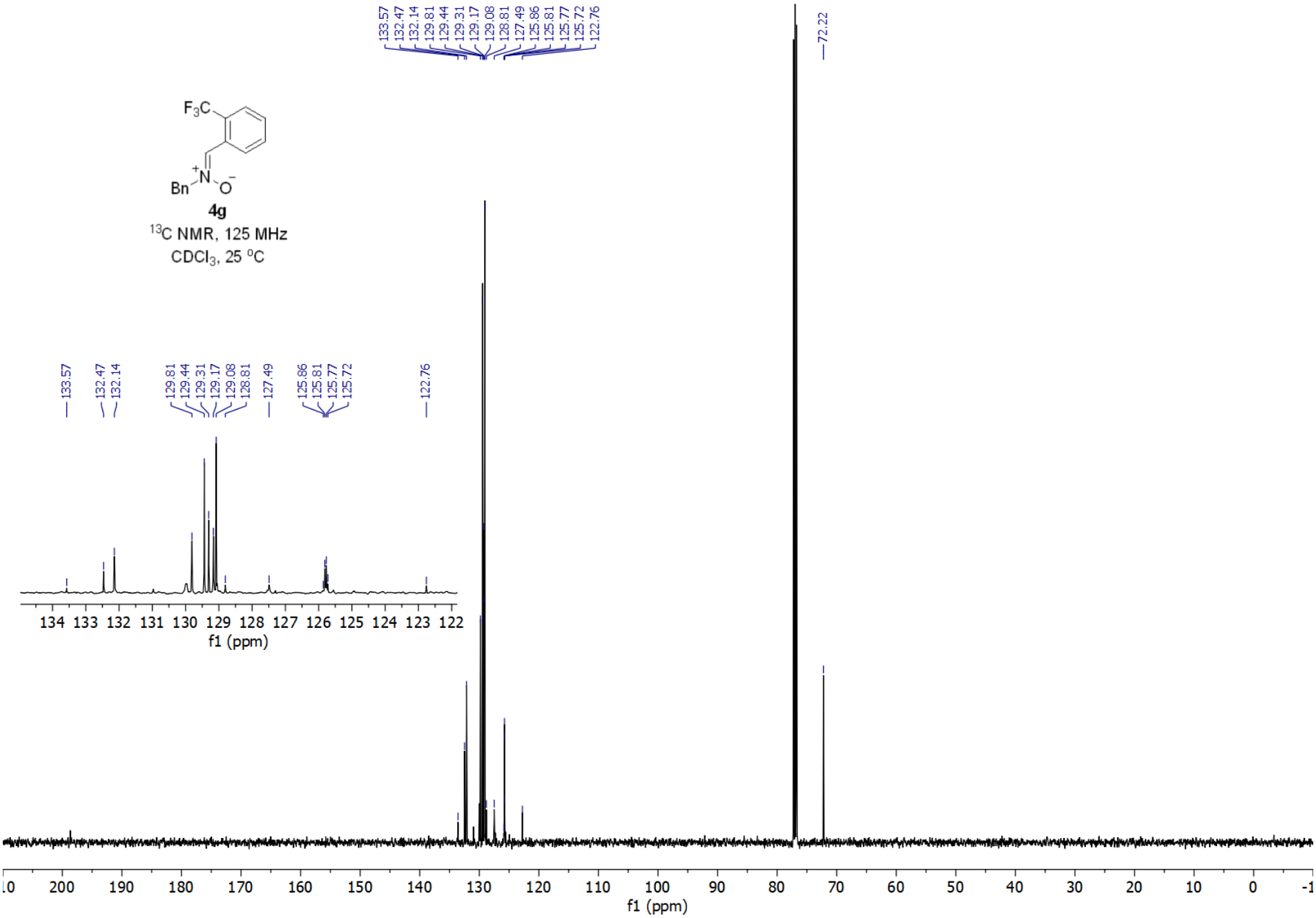


Yield: 80%; white solid; m.p. 177–178 °C; R_f = 0.46 (*n*-hexane/EtOAc 2:1 *v*/*v*); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.94 (br s, 1H), 8.32 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.90 (td, *J* = 7.6, 1.3 Hz, 1H), 7.72 (t, *J* = 7.2 Hz, 1H), 2.84 (t, *J* = 7.6 Hz, 2H), 1.67 (p, *J* = 7.4 Hz, 2H), 1.37 – 1.21 (m, 8H), 0.84 (t, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 161.8, 154.1, 148.4, 133.9, 129.6, 129.3, 126.0, 125.4, 121.2, 120.5, 31.6, 29.0, 28.8, 27.7, 24.1, 22.5, 14.4 ppm; FT-IR (neat): v = 2952, 2924, 2850, 1662, 1602, 1424, 1335, 1241, 859, 764 cm^{-1}; HRMS (ESI), *m*/*z*: [M + Na]$^+$ calcd for $C_{17}H_{20}N_2NaO_2^+$ 307.1417; found 307.1409.


8.16
8.15
7.47
7.47
7.46
7.46
7.46
7.45
7.45
7.41
7.41
7.40
7.40
7.40
7.39
7.39
7.39
7.38
7.38
7.37
7.37
7.37
7.36
7.36
7.27
6.87
6.85
5.01
3.84
3.83
3.82
3.25
3.24
3.23
O
N
Bn
+N
O−
4e
1H NMR, 500 MHz
CDCl3, 25 °C
2.00
2.01
3.13
1.02
2.34
2.33
4.39
4.45
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


152.15
134.20
133.54
130.32
129.11
128.84
128.72
121.52
113.89
70.40
66.56
47.81
O
N
Bn
+N
O−
4e
13C NMR, 125 MHz
CDCl3, 25 °C
f1 (ppm)

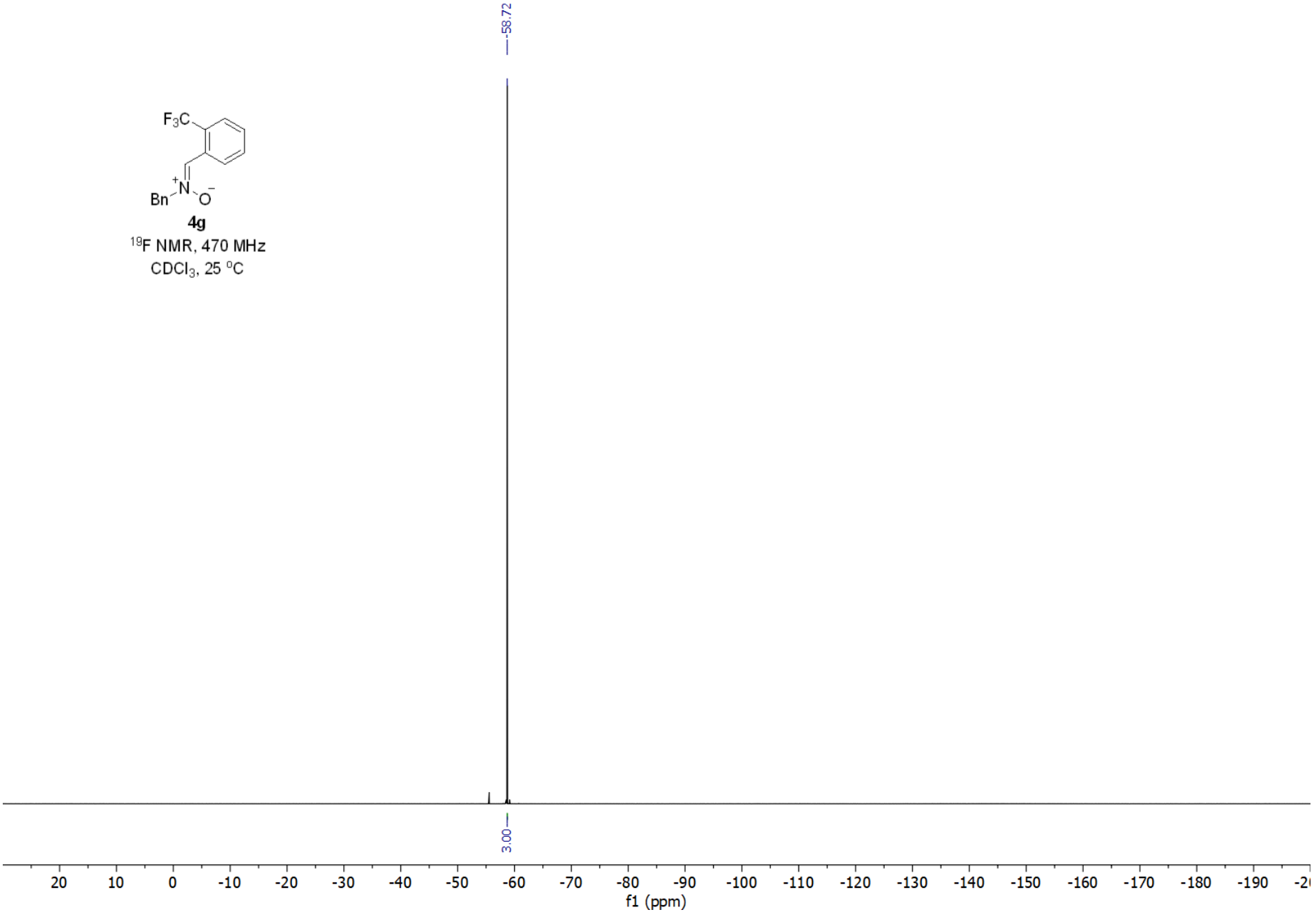

9.41
9.39
7.74
7.70
7.68
7.63
7.62
7.60
7.50
7.49
7.49
7.49
7.48
7.48
7.47
7.46
7.45
7.44
7.43
7.42
7.42
7.42
5.14
F3C
Bn
N
O
4g
1H NMR, 500 MHz
CDCl3, 25 °C
1.00
0.97
0.97
1.01
3.25
3.15
2.06
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

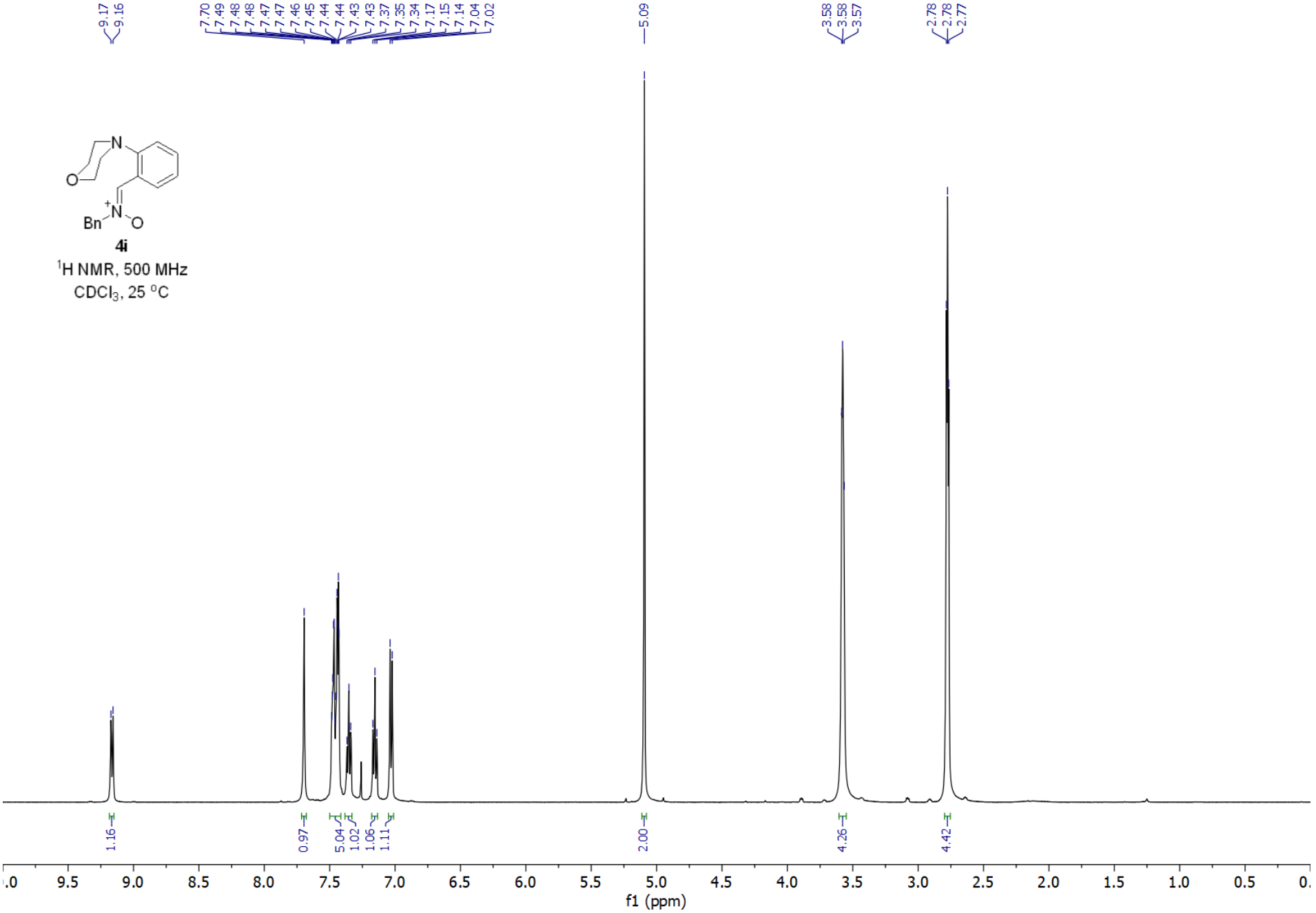

133.57
132.47
132.14
129.81
129.44
129.31
129.17
129.08
128.81
127.49
125.86
125.81
125.77
125.72
122.76
72.22
F3C
Bn
N
O
4g
13C NMR, 125 MHz
CDCl3, 25 °C
f1 (ppm)
f1 (ppm)

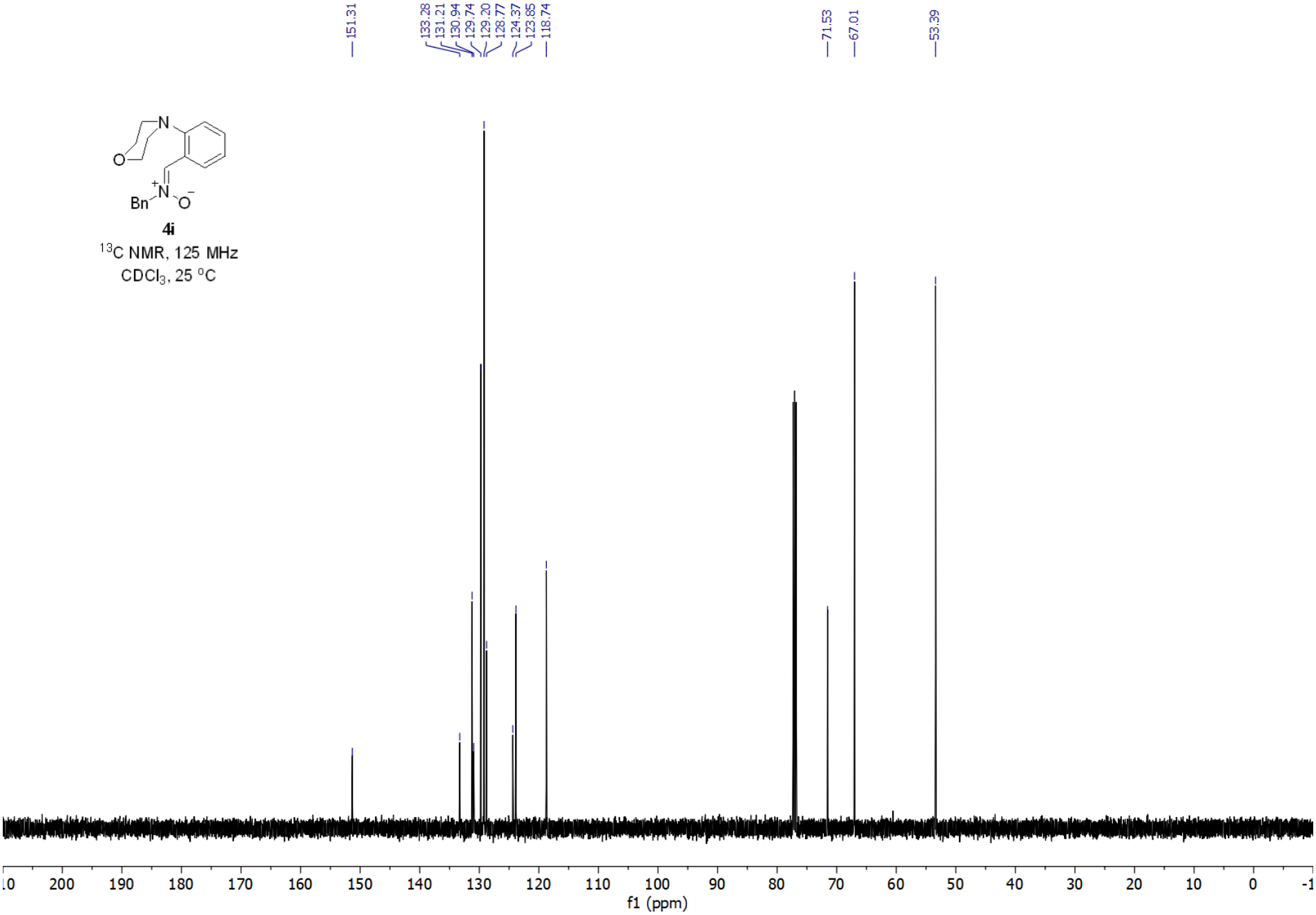
4g

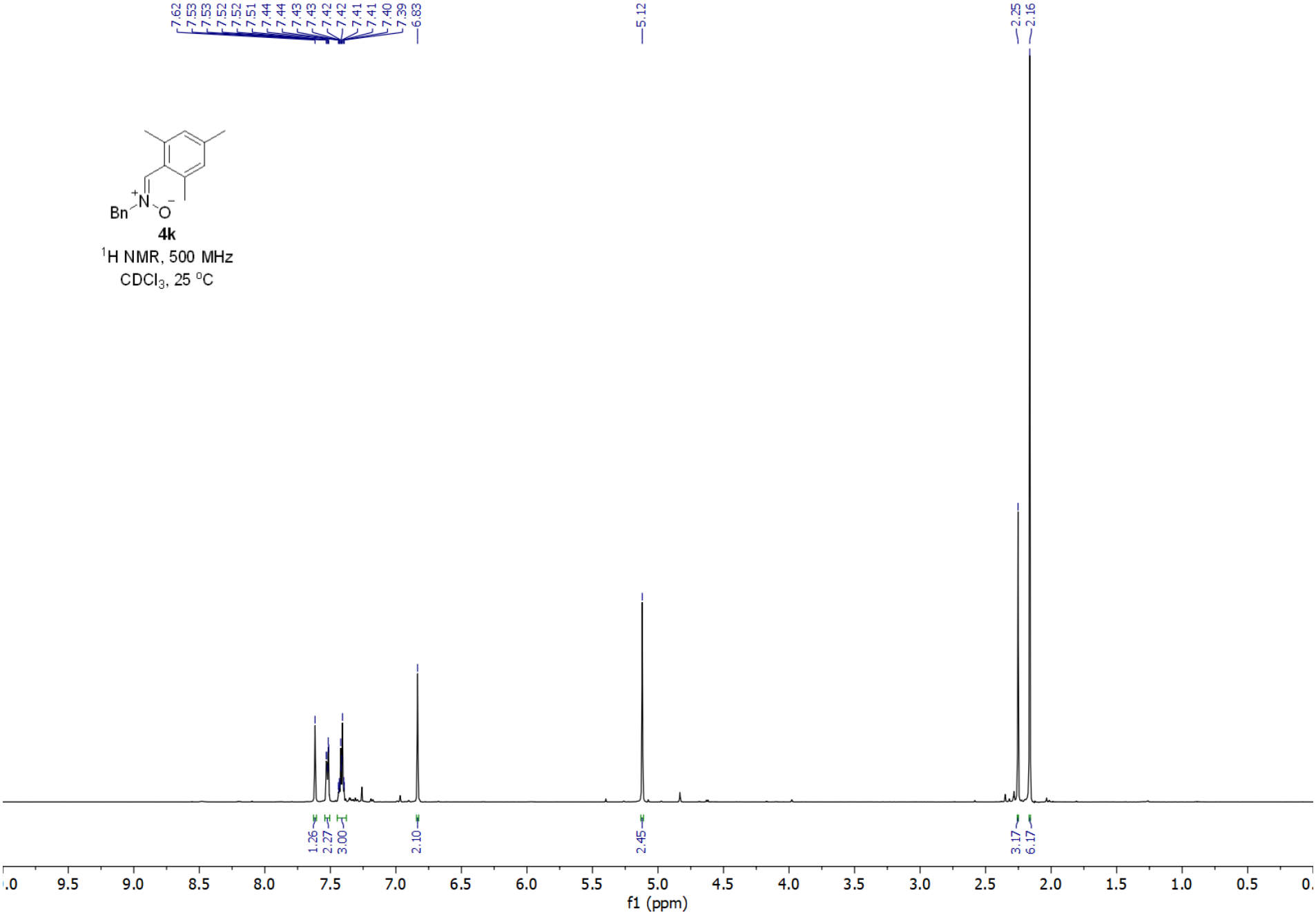
^{19}F NMR, 470 MHz

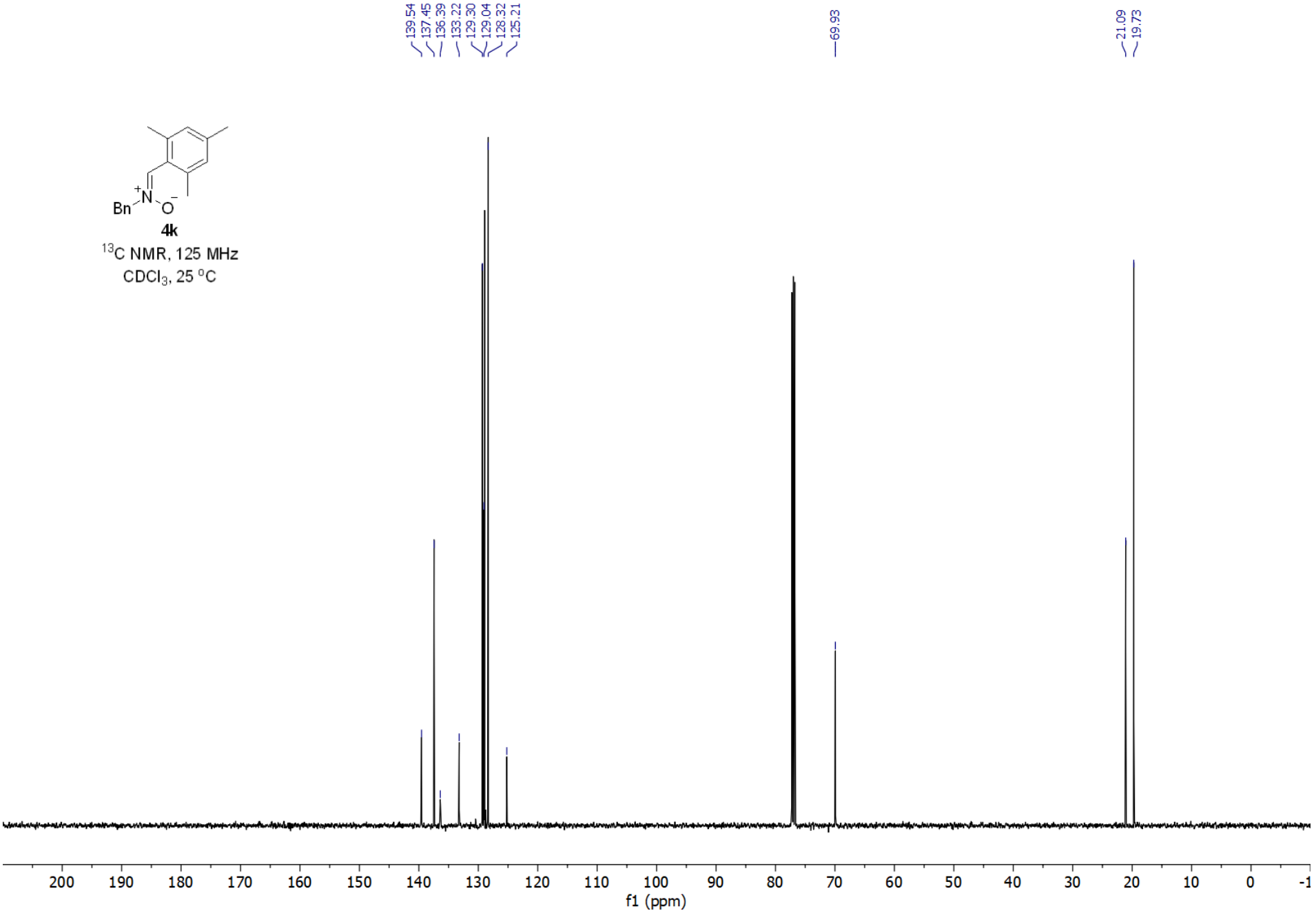
$CDCl_3$, 25 °C

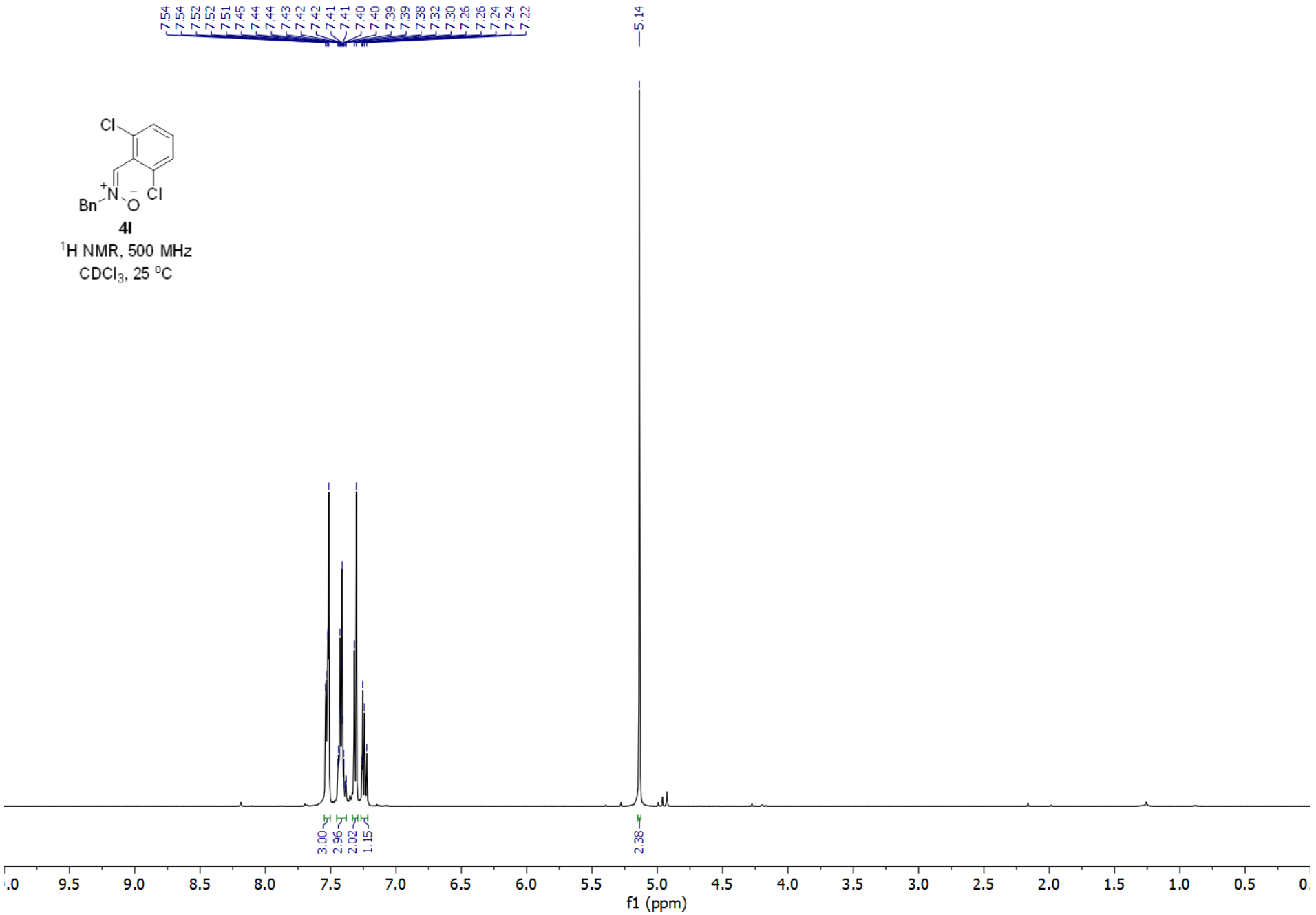



9.17
9.16
7.70
7.49
7.48
7.48
7.47
7.47
7.46
7.45
7.44
7.44
7.43
7.43
7.37
7.35
7.34
7.17
7.15
7.14
7.04
7.02
5.09
3.58
3.58
3.57
2.78
2.78
2.77
Bn
4i
1H NMR, 500 MHz
CDCl3, 25 °C
1.16
0.97
5.04
1.02
1.06
1.11
2.00
4.26
4.42
f1 (ppm)


151.31
133.28
131.21
130.94
129.74
129.20
128.77
124.37
123.85
118.74
71.53
67.01
53.39
Bn
4i
13C NMR, 125 MHz
CDCl3, 25 °C
f1 (ppm)


7.62
7.53
7.53
7.52
7.52
7.51
7.44
7.44
7.43
7.43
7.42
7.42
7.41
7.41
7.40
7.39
6.83
5.12
2.25
2.16
Bn
N
O
4k
1H NMR, 500 MHz
CDCl3, 25 °C
1.26
2.27
3.00
2.10
2.45
3.17
6.17
f1 (ppm)

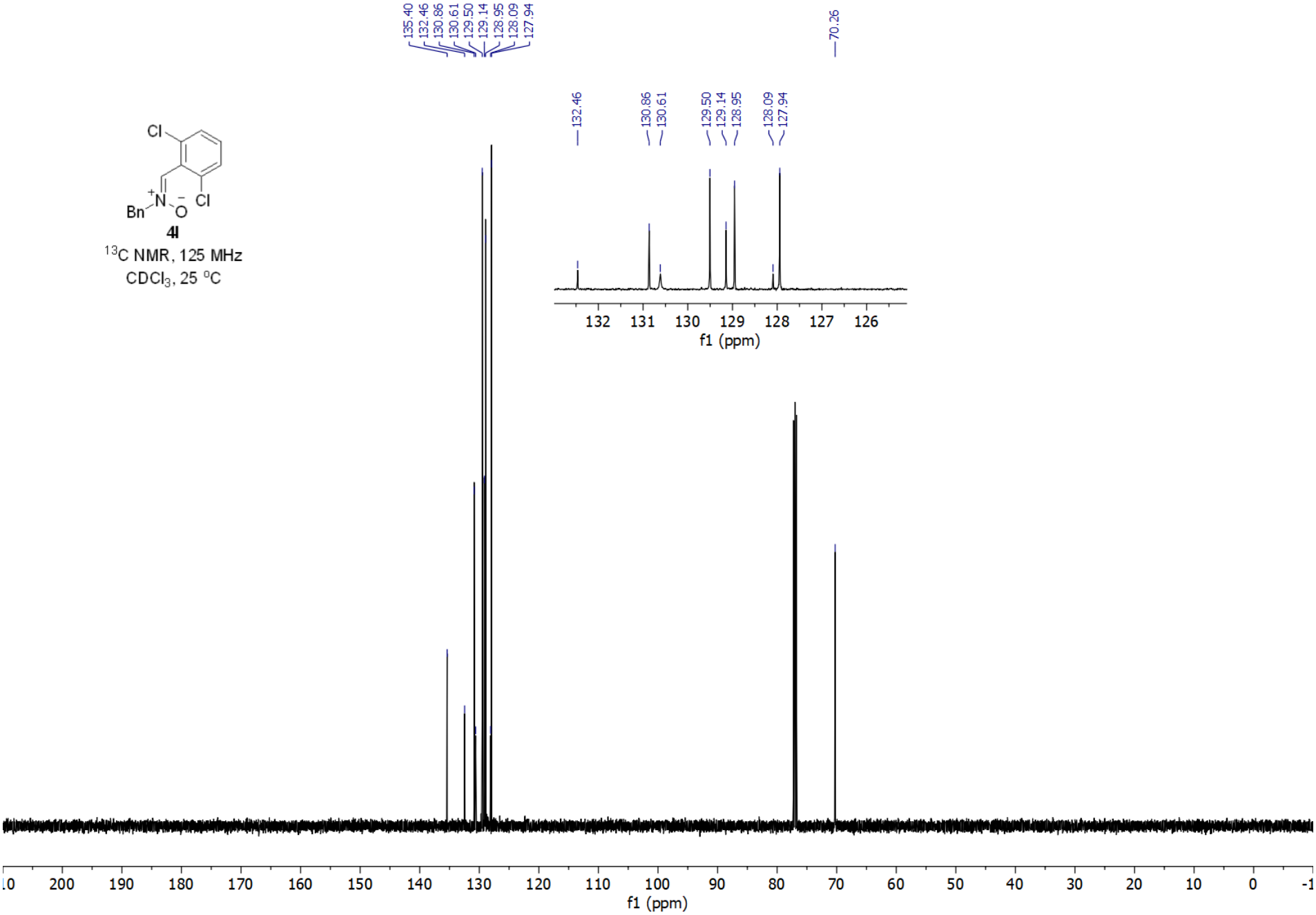

139.54
137.45
136.39
133.22
129.30
129.04
128.32
125.21
69.93
21.09
19.73
Bn
N
O
4k
13C NMR, 125 MHz
CDCl3, 25 °C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

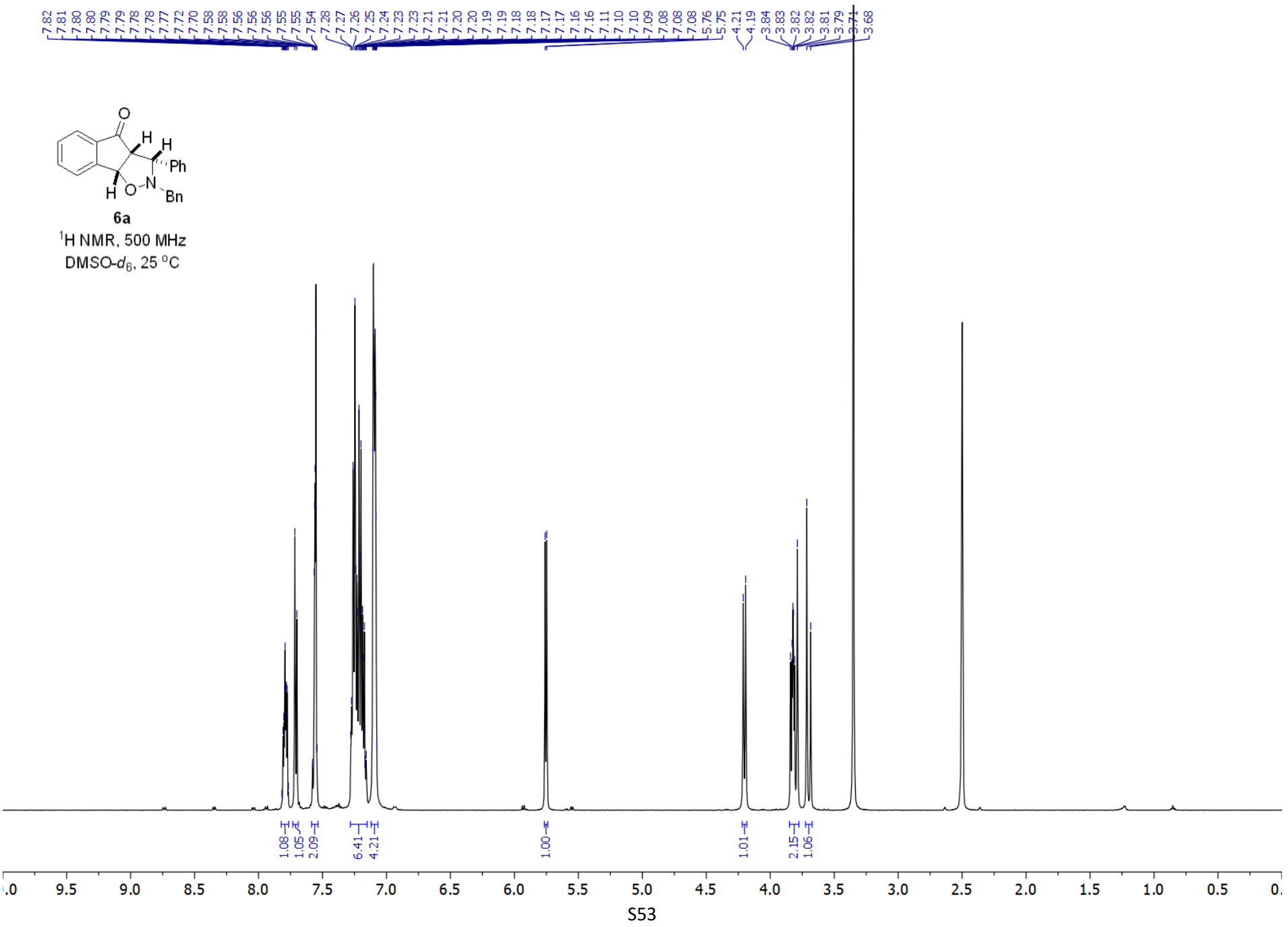


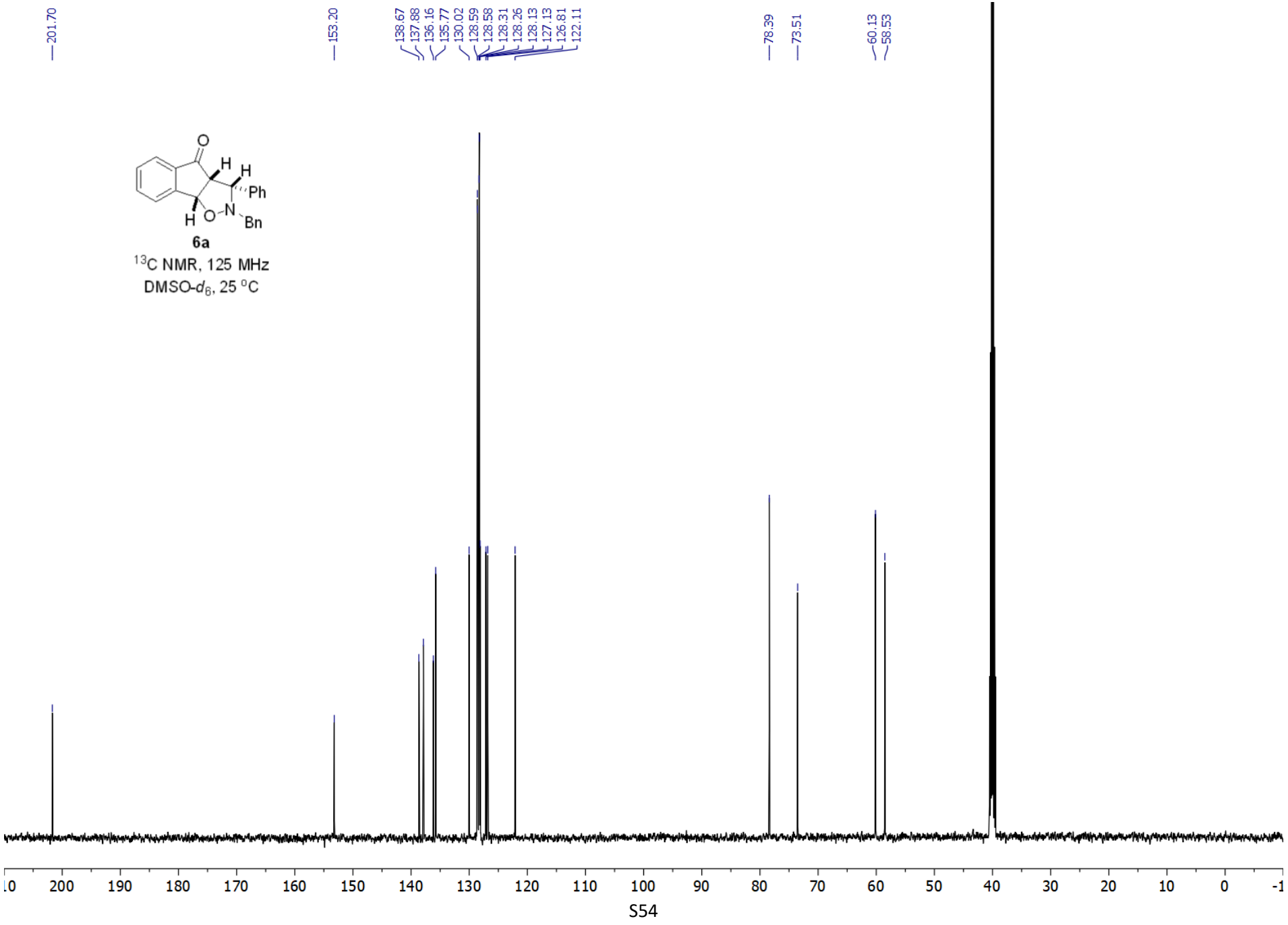
4l

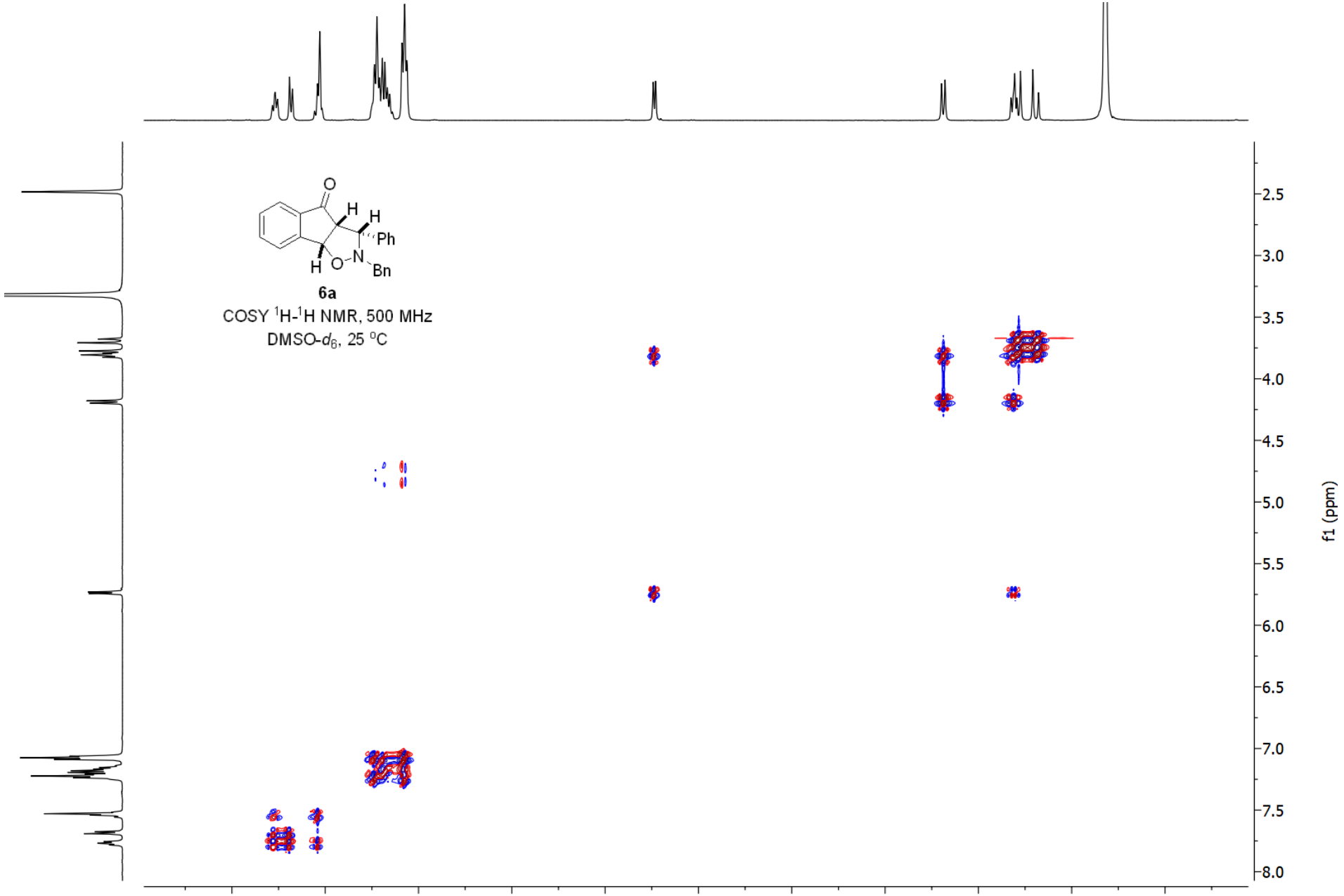
^{1}H NMR, 500 MHz

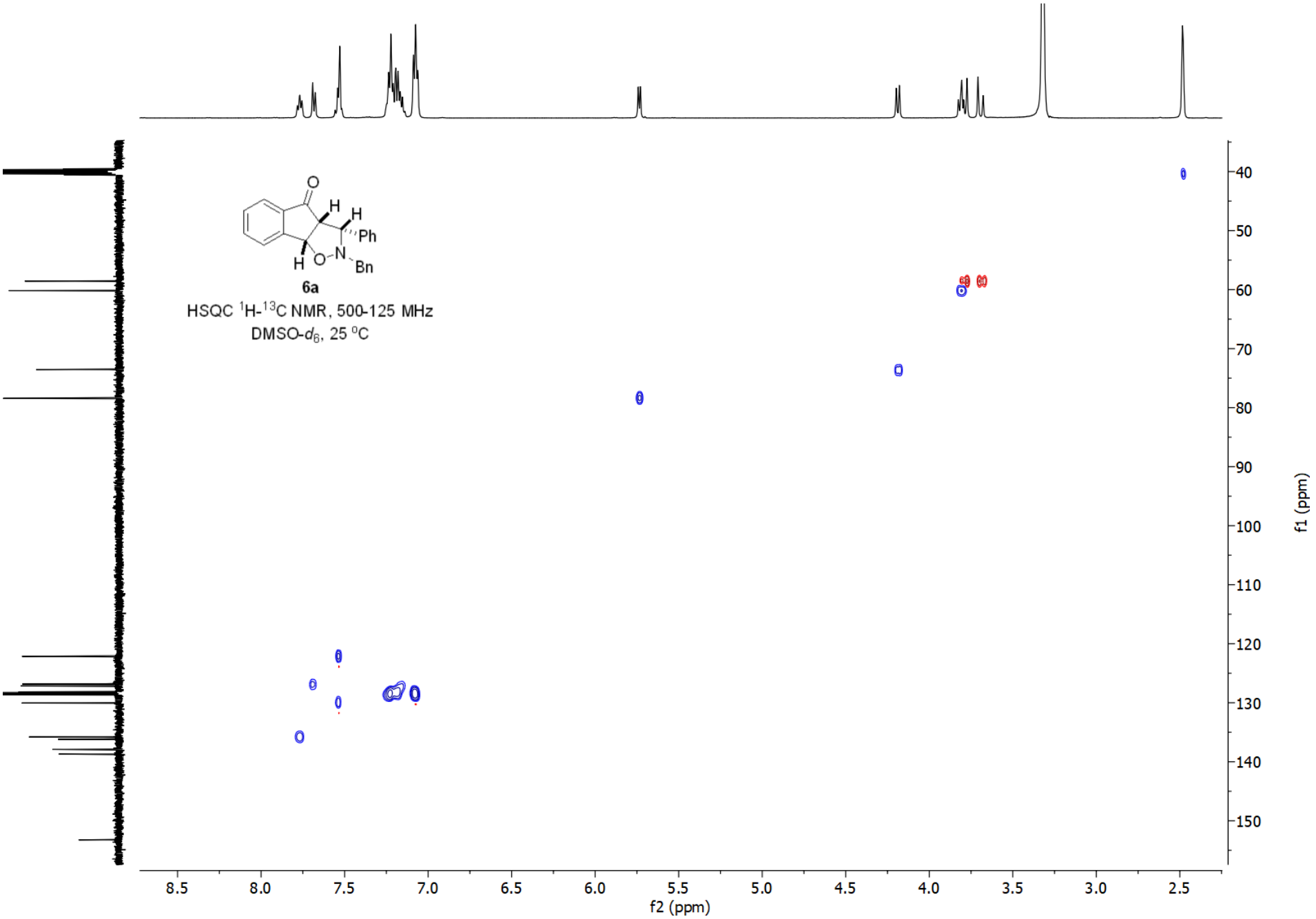
$CDCl_3$, 25 °C

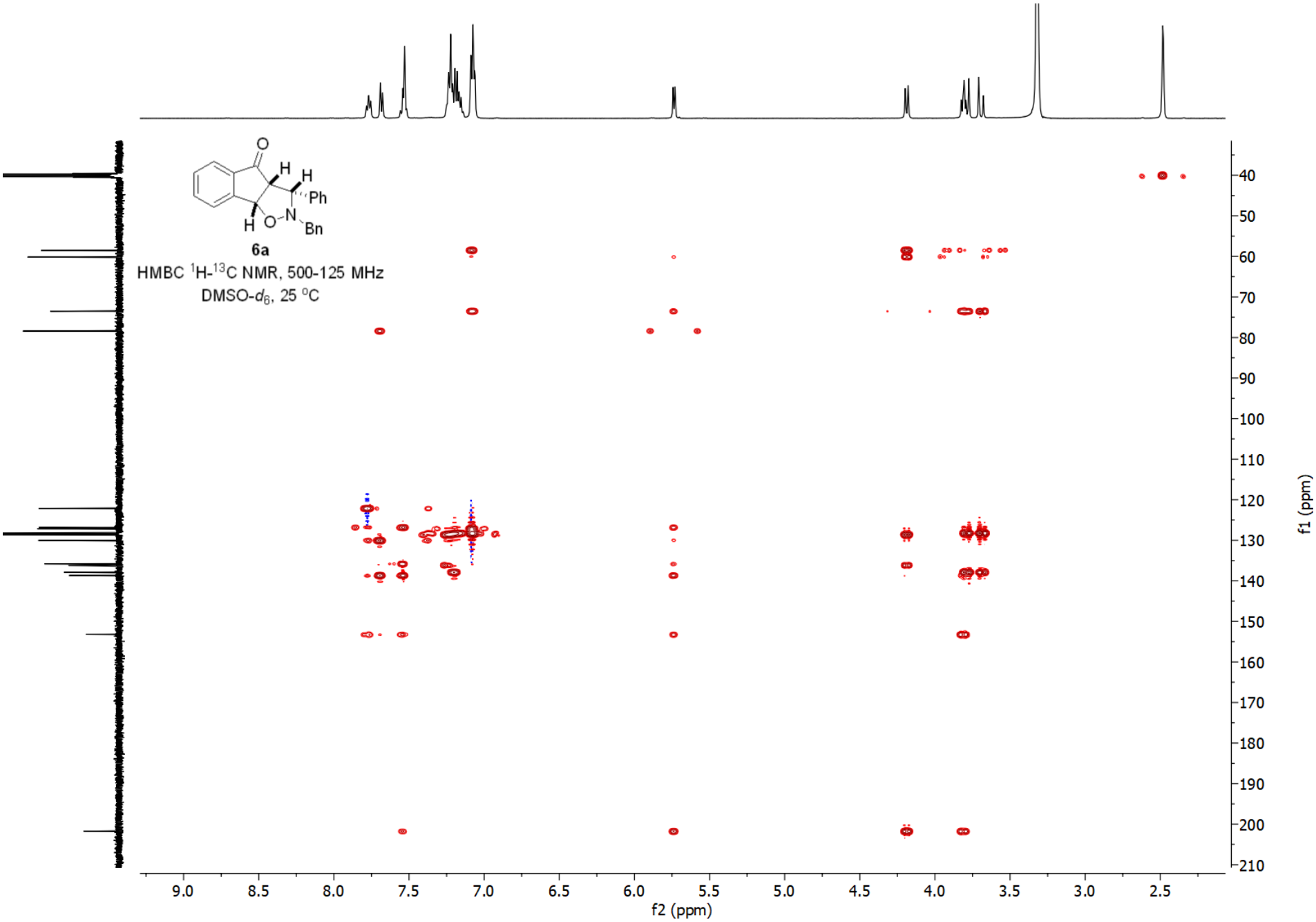

135.40
132.46
130.86
130.61
129.50
129.14
128.95
128.09
127.94
70.26
Cl
Cl
Bn
4l
^{13}C NMR, 125 MHz
$CDCl_3$, 25 ^{o}C
132.46
130.86
130.61
129.50
129.14
128.95
128.09
127.94
132 131 130 129 128 127 126
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

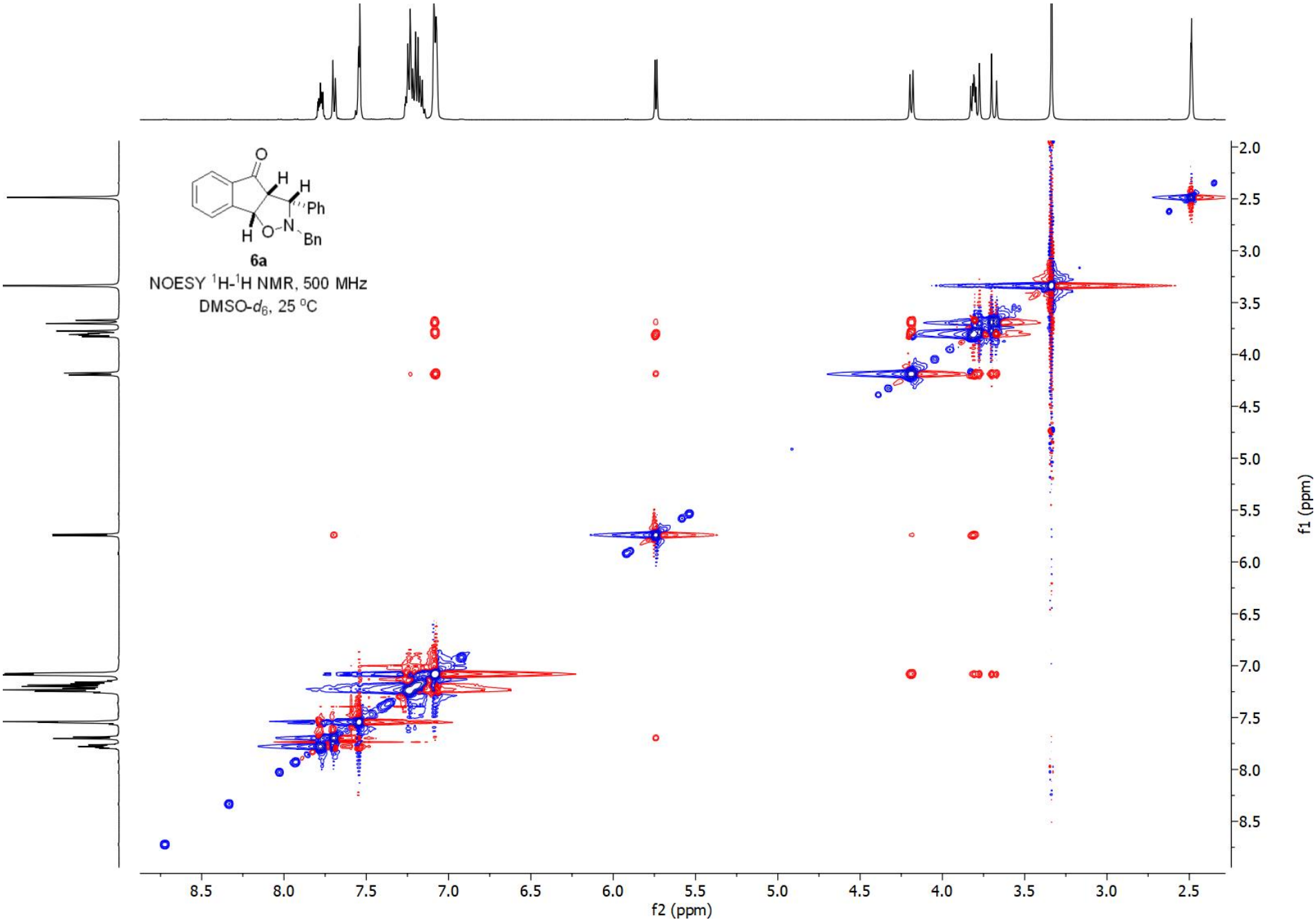

7.82 7.81 7.80 7.80 7.79 7.79 7.78 7.78 7.77 7.72 7.70 7.58 7.58 7.56 7.56 7.56 7.55 7.55 7.54 7.28 7.27 7.26 7.25 7.24 7.23 7.23 7.21 7.21 7.20 7.20 7.19 7.19 7.18 7.17 7.17 7.16 7.16 7.11 7.10 7.10 7.09 7.08 7.08 7.08 5.76 5.75 4.21 4.19 3.84 3.83 3.82 3.82 3.81 3.79 3.71 3.68
O
H
H
Ph
N
O
H
Bn
6a
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.08
1.05
2.09
6.41
4.21
1.00
1.01
2.15
1.06
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

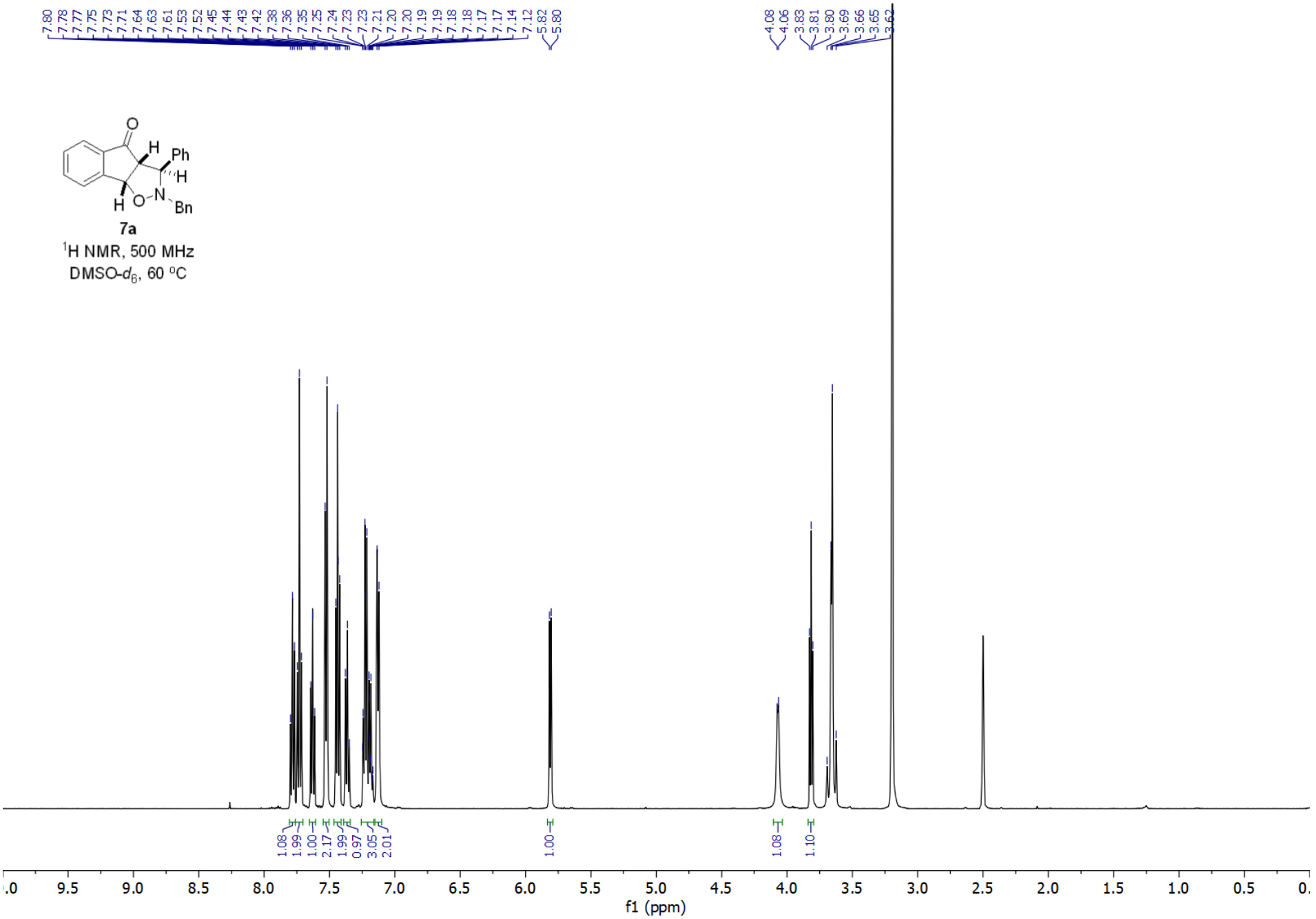

201.70
153.20
138.67
137.88
136.16
135.77
130.02
128.59
128.58
128.31
128.26
128.13
127.13
126.81
122.11
78.39
73.51
60.13
58.53
O
H
H
Ph
H
O
N
Bn
6a
13C NMR, 125 MHz
DMSO-d6, 25 °C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

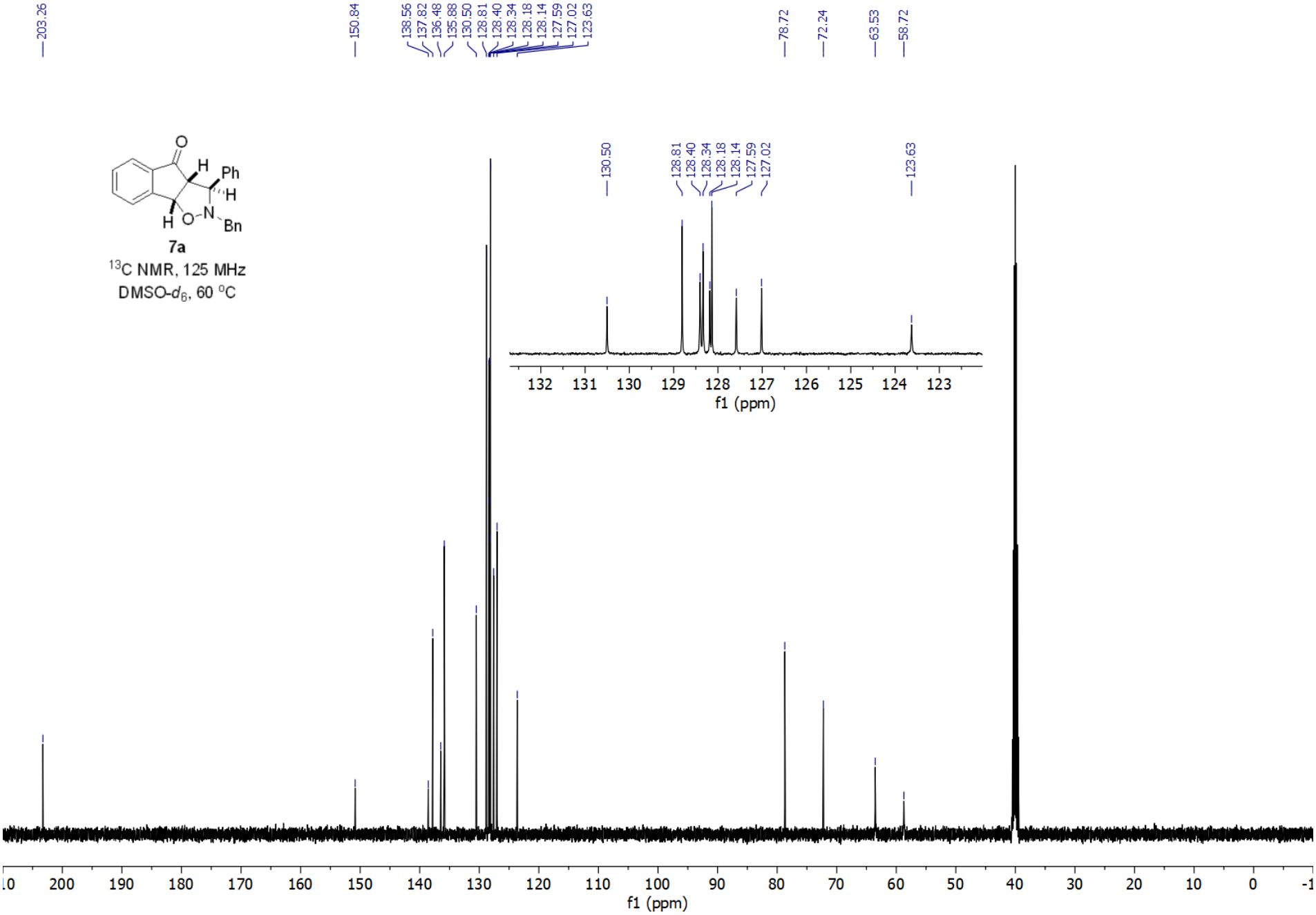

O
H
H
Ph
H
O
N
Bn
6a
COSY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 25 ^{o}C
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f2 (ppm)
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
f1 (ppm)

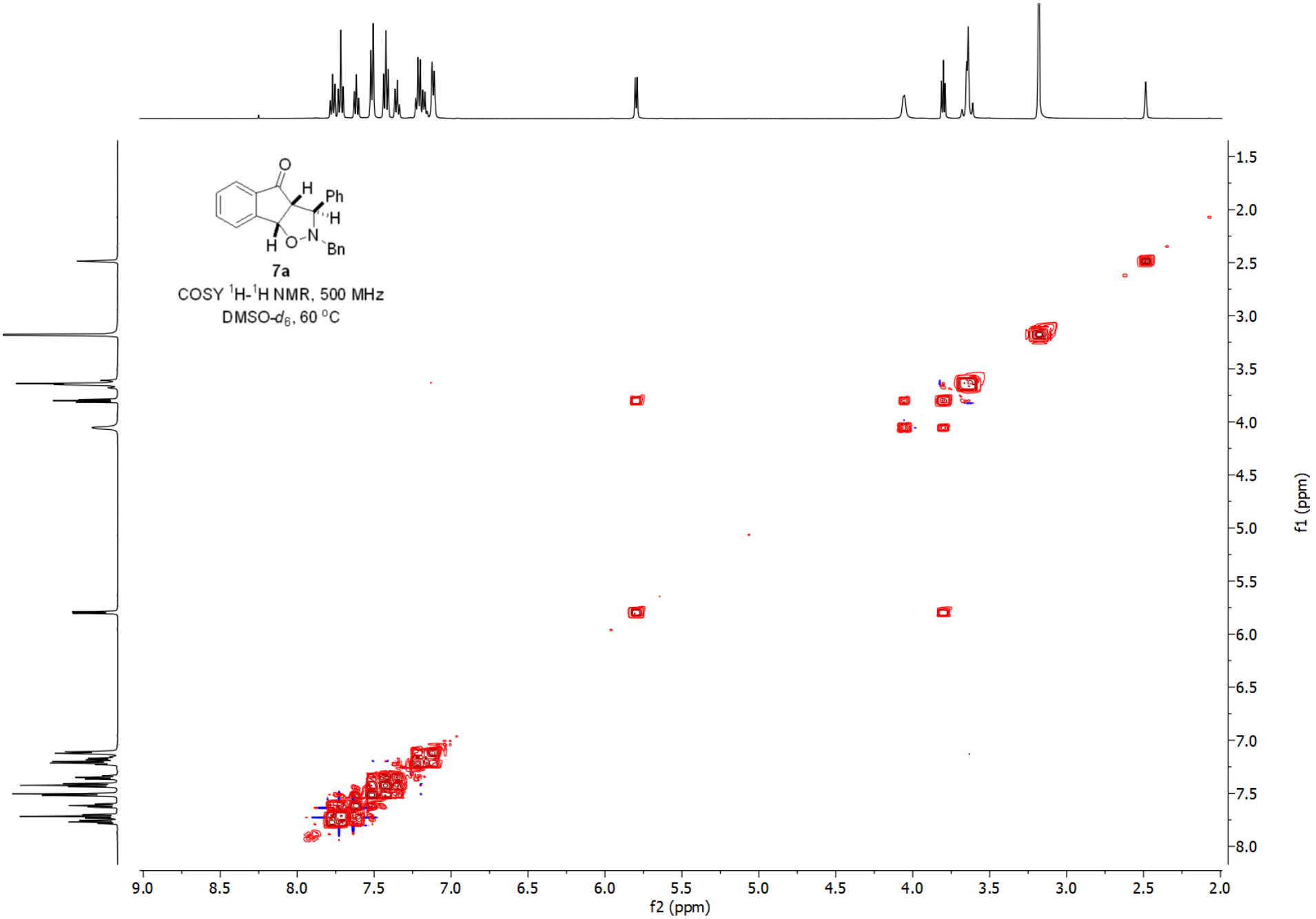

6a
HSQC ^{1}H-^{13}C NMR, 500-125 MHz
DMSO-d_6, 25 ^{0}C
f2 (ppm)
f1 (ppm)

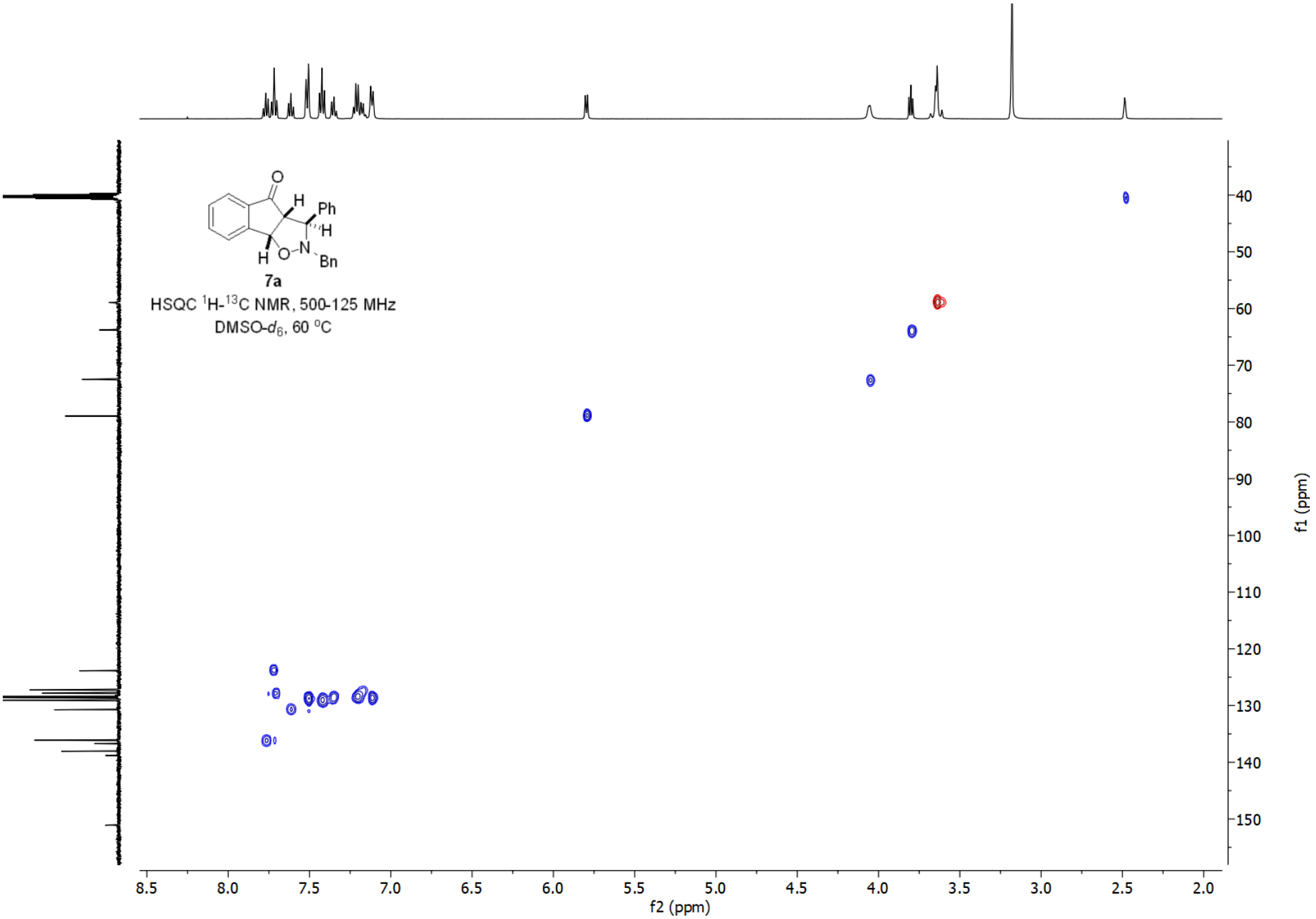

6a
HMBC ^{1}H-^{13}C NMR, 500-125 MHz
DMSO-d_6, 25 ^{o}C
f2 (ppm)
f1 (ppm)

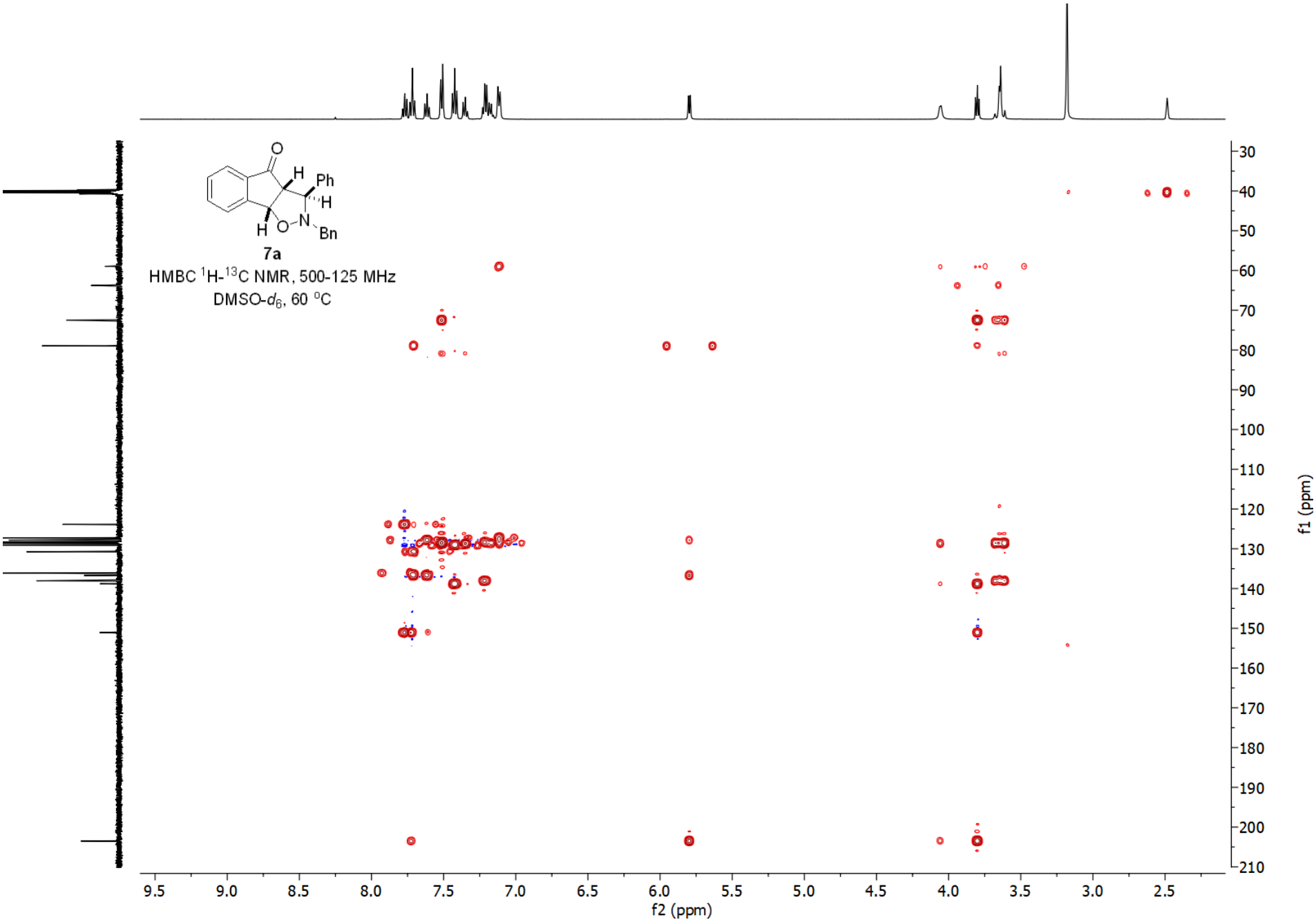

6a
NOESY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 25 ^{o}C
f2 (ppm)
f1 (ppm)

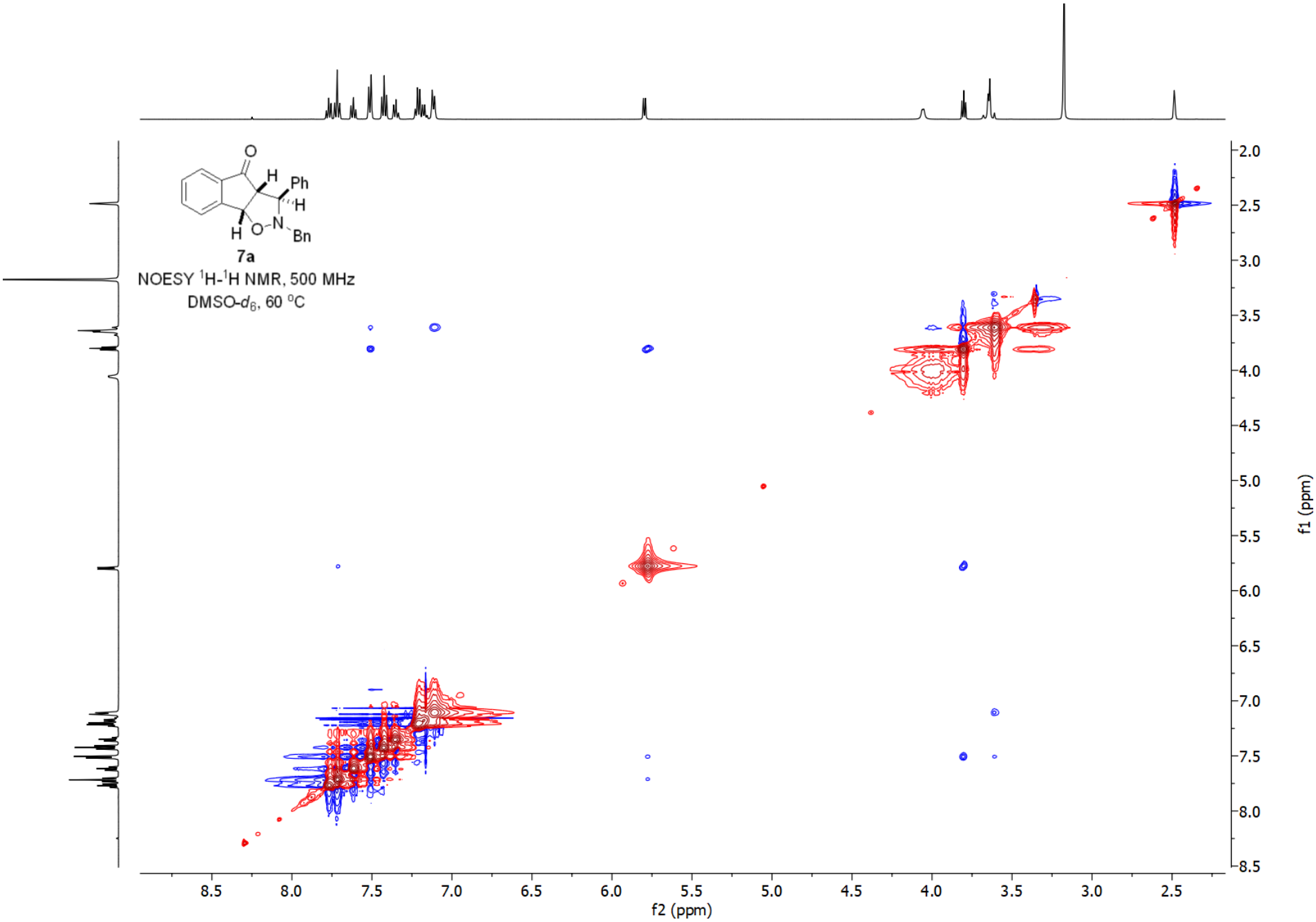

7.80
7.78
7.77
7.75
7.73
7.71
7.64
7.63
7.61
7.53
7.52
7.45
7.44
7.43
7.42
7.38
7.36
7.35
7.25
7.24
7.23
7.23
7.21
7.20
7.20
7.19
7.19
7.18
7.18
7.17
7.17
7.14
7.12
5.82
5.80
4.08
4.06
3.83
3.81
3.80
3.69
3.66
3.65
3.62
O
H
Ph
H
H
O
N
Bn
7a
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.08
1.99
1.00
2.17
1.99
0.97
3.05
2.01
1.00
1.08
1.10
f1 (ppm)

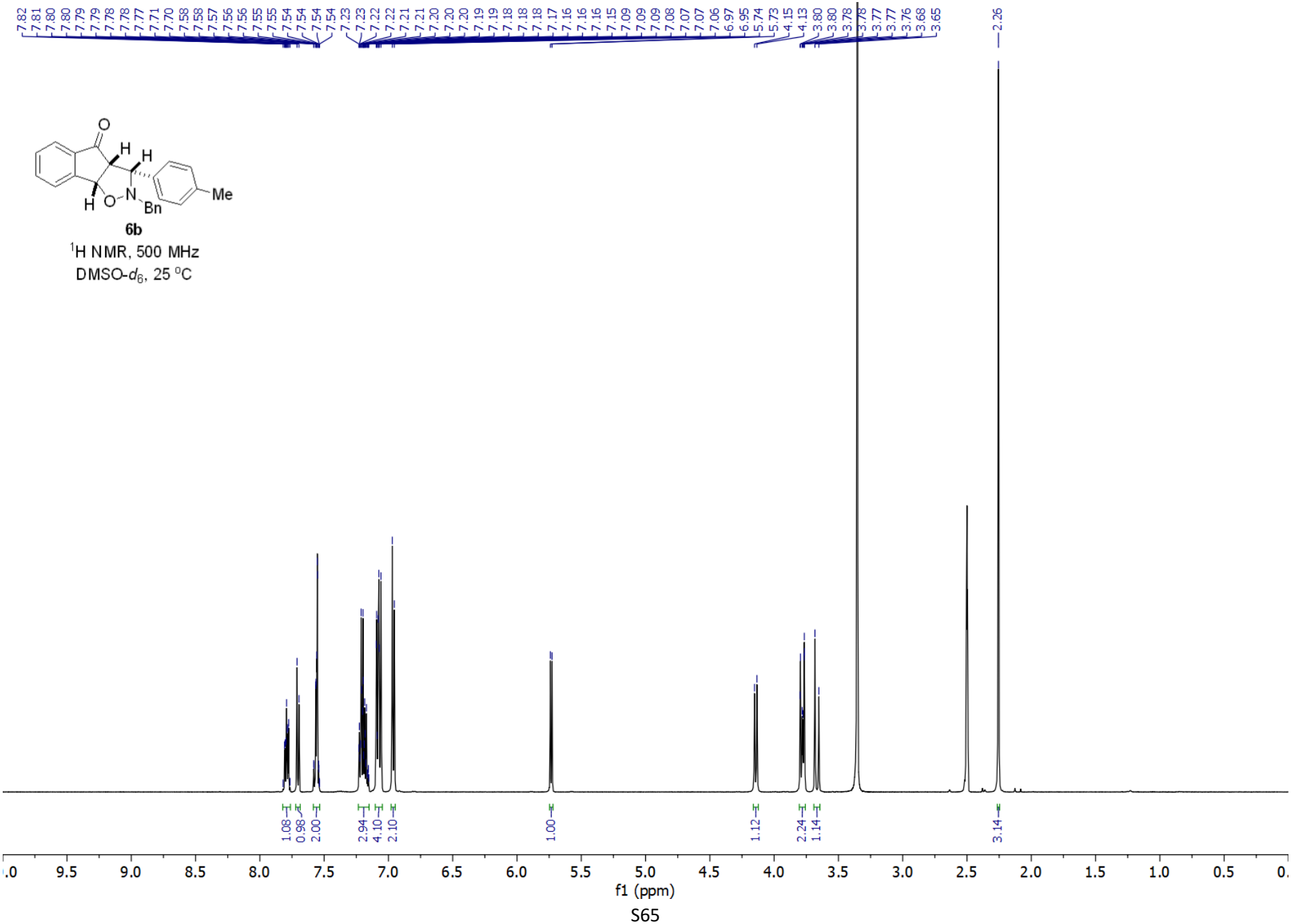

203.26
150.84
138.56
137.82
136.48
135.88
130.50
128.81
128.40
128.34
128.18
128.14
127.59
127.02
123.63
78.72
72.24
63.53
58.72
O
H
Ph
H
H
O
N
Bn
7a
13C NMR, 125 MHz
DMSO-d6, 60 °C
130.50
128.81
128.40
128.34
128.18
128.14
127.59
127.02
123.63
132 131 130 129 128 127 126 125 124 123
f1 (ppm)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

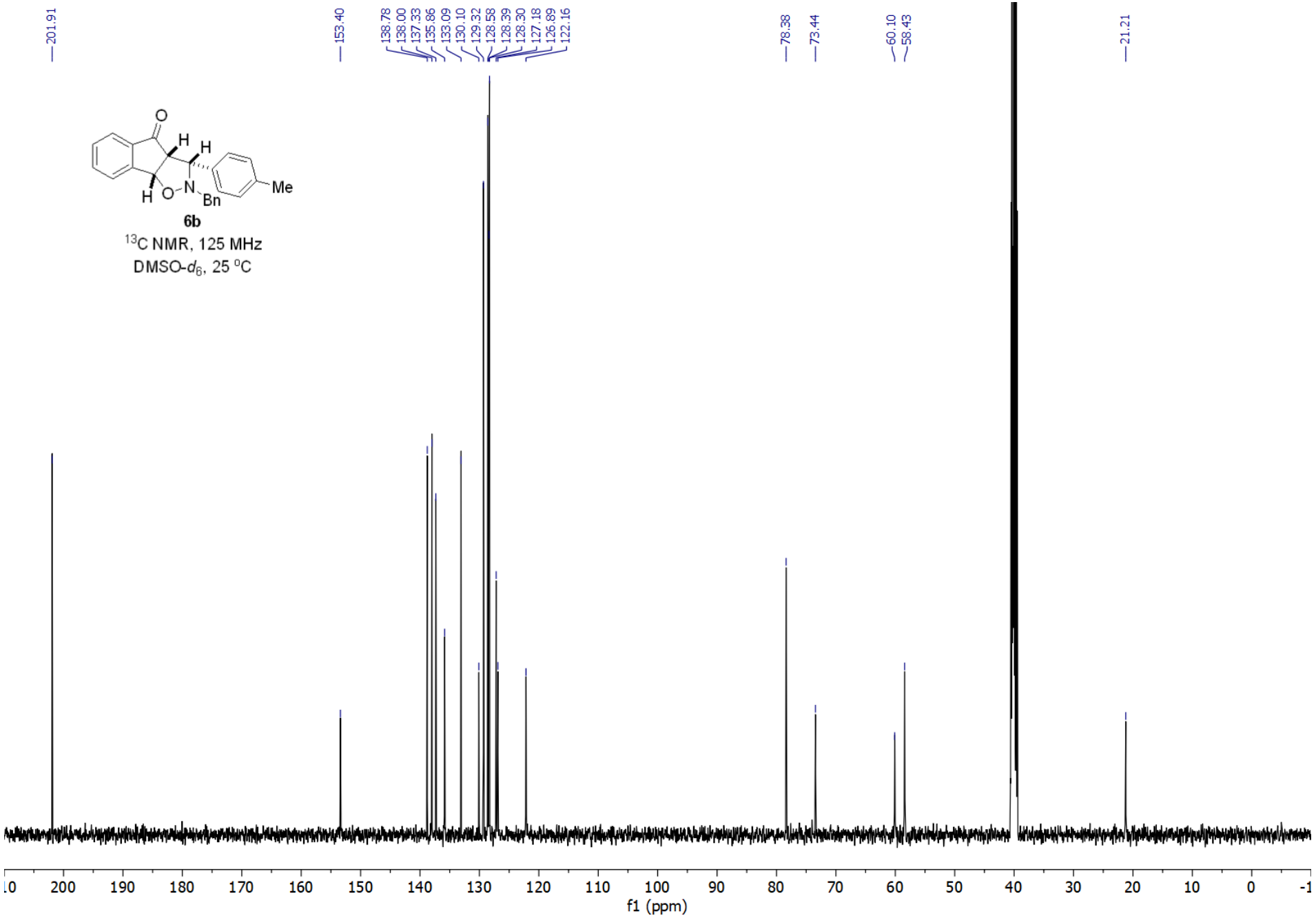

7a
COSY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 60 °C
f2 (ppm)
f1 (ppm)

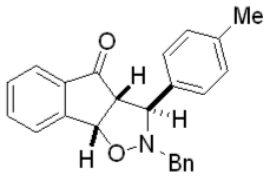

7a
HSQC ^{1}H-^{13}C NMR, 500-125 MHz
DMSO-d_6, 60 ^{0}C
f2 (ppm)
f1 (ppm)


7a
HMBC ^{1}H-^{13}C NMR, 500-125 MHz
DMSO-d_6, 60 ^{o}C
f2 (ppm)
f1 (ppm)


7a
NOESY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 60 ^{o}C
f2 (ppm)
f1 (ppm)


7.82 7.81 7.80 7.80 7.79 7.79 7.78 7.78 7.77 7.71 7.70 7.58 7.58 7.57 7.56 7.56 7.55 7.55 7.54 7.54 7.54 7.54 7.23 7.23 7.22 7.22 7.21 7.21 7.20 7.20 7.20 7.19 7.19 7.18 7.18 7.18 7.17 7.16 7.16 7.16 7.15 7.09 7.09 7.09 7.08 7.07 7.07 7.06 6.97 6.95 5.74 5.73 4.15 4.13 3.80 3.80 3.78 3.78 3.77 3.77 3.76 3.68 3.65 2.26
O
H
H
H
O
N
Bn
Me
6b
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.08 0.98 2.00 2.94 4.10 2.10 1.00 1.12 2.24 1.14 3.14
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

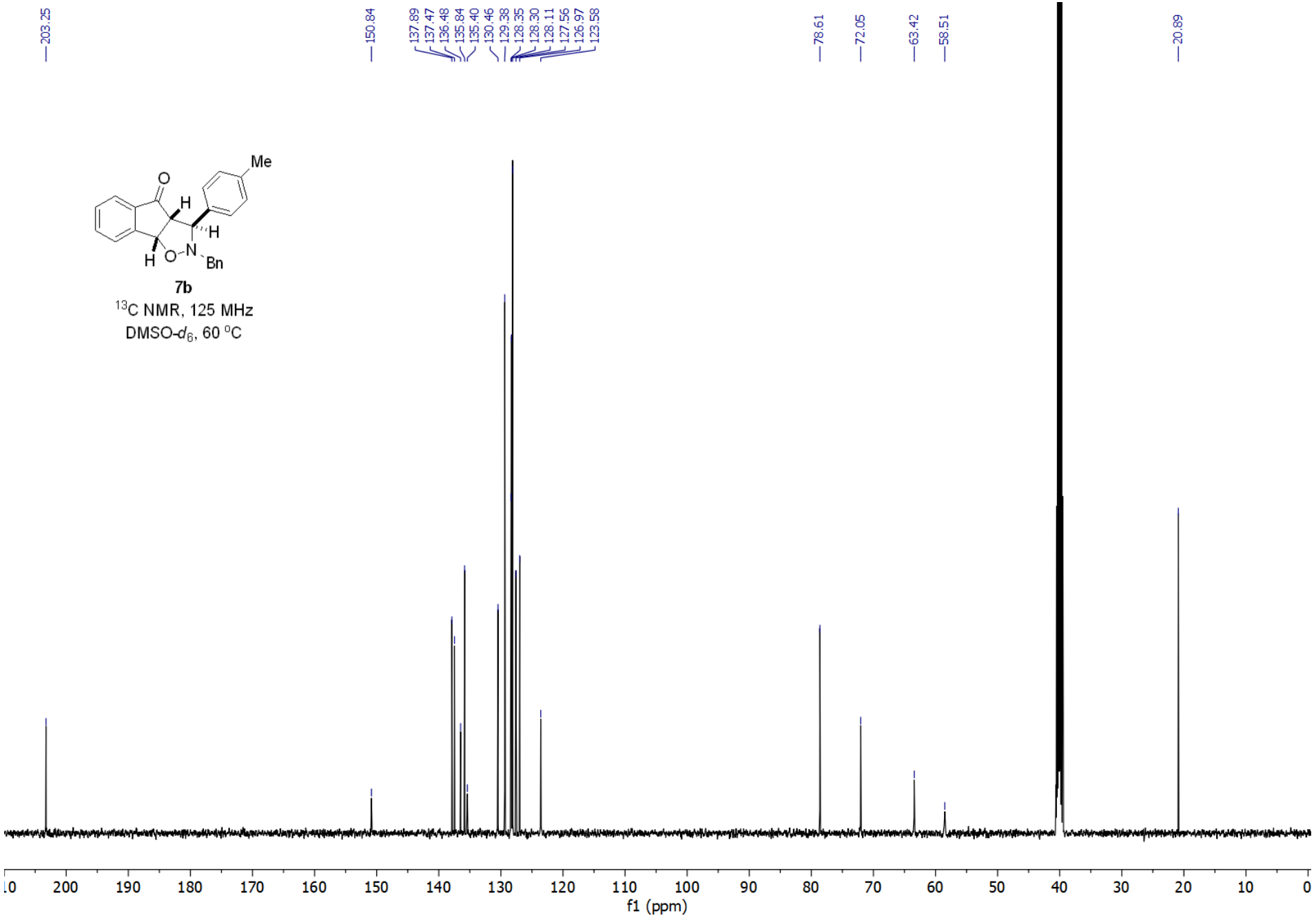

201.91
153.40
138.78
138.00
137.33
135.86
133.09
130.10
129.32
128.58
128.39
128.30
127.18
126.89
122.16
78.38
73.44
60.10
58.43
21.21
O
H
H
H
O
N
Bn
Me
6b
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

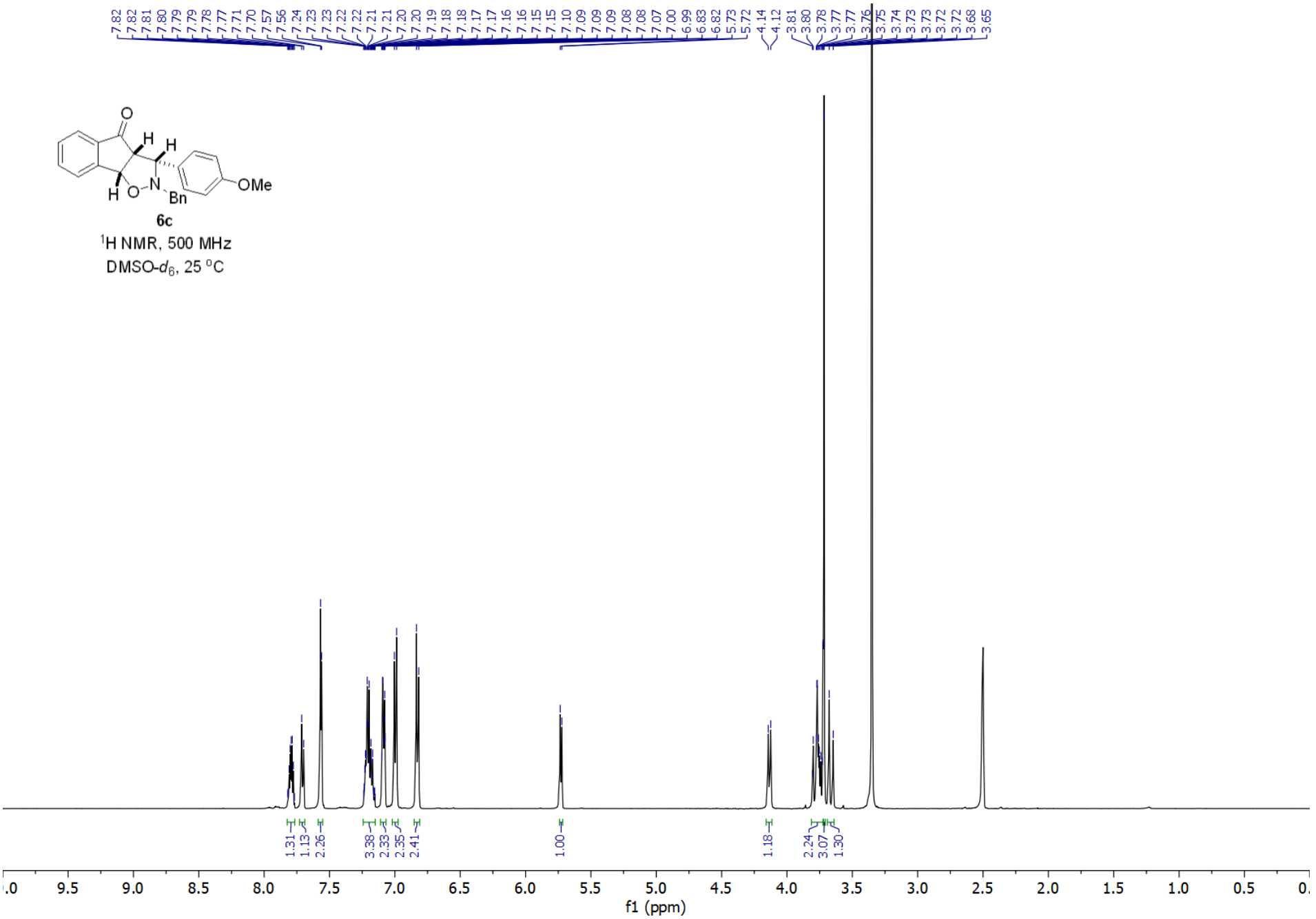


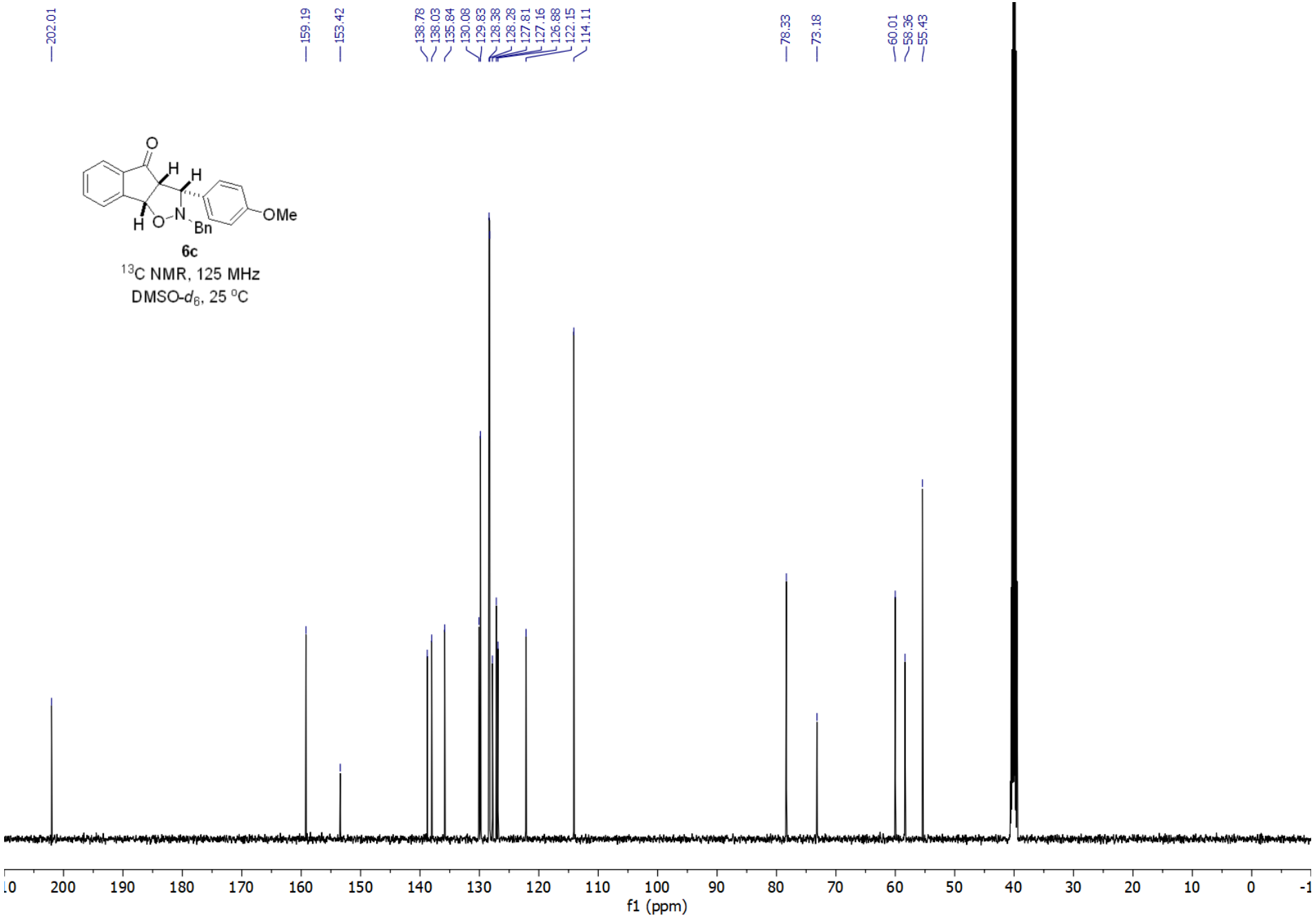
7b

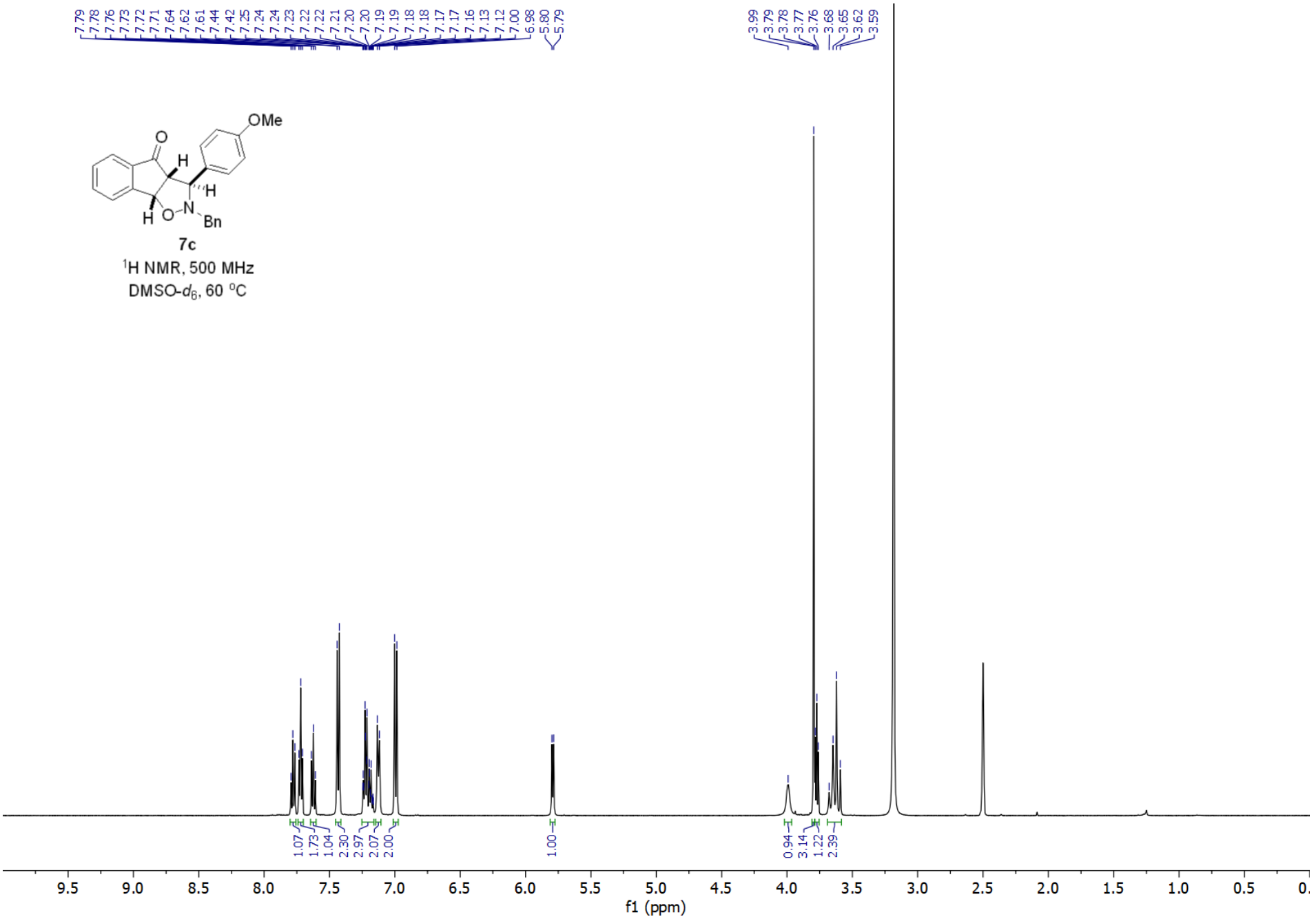
^{1}H NMR, 500 MHz

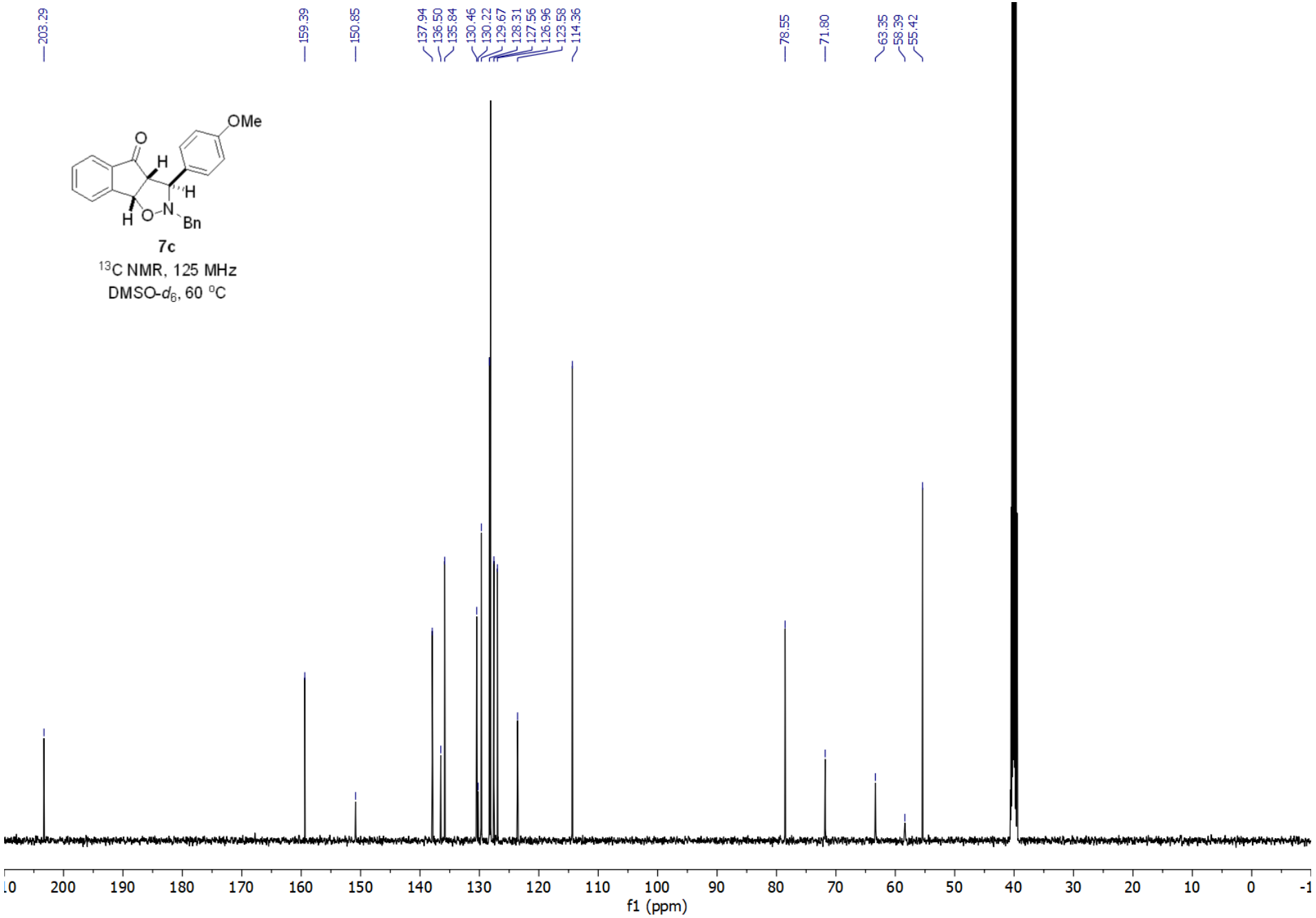
DMSO-d_6, 60 ^{0}C

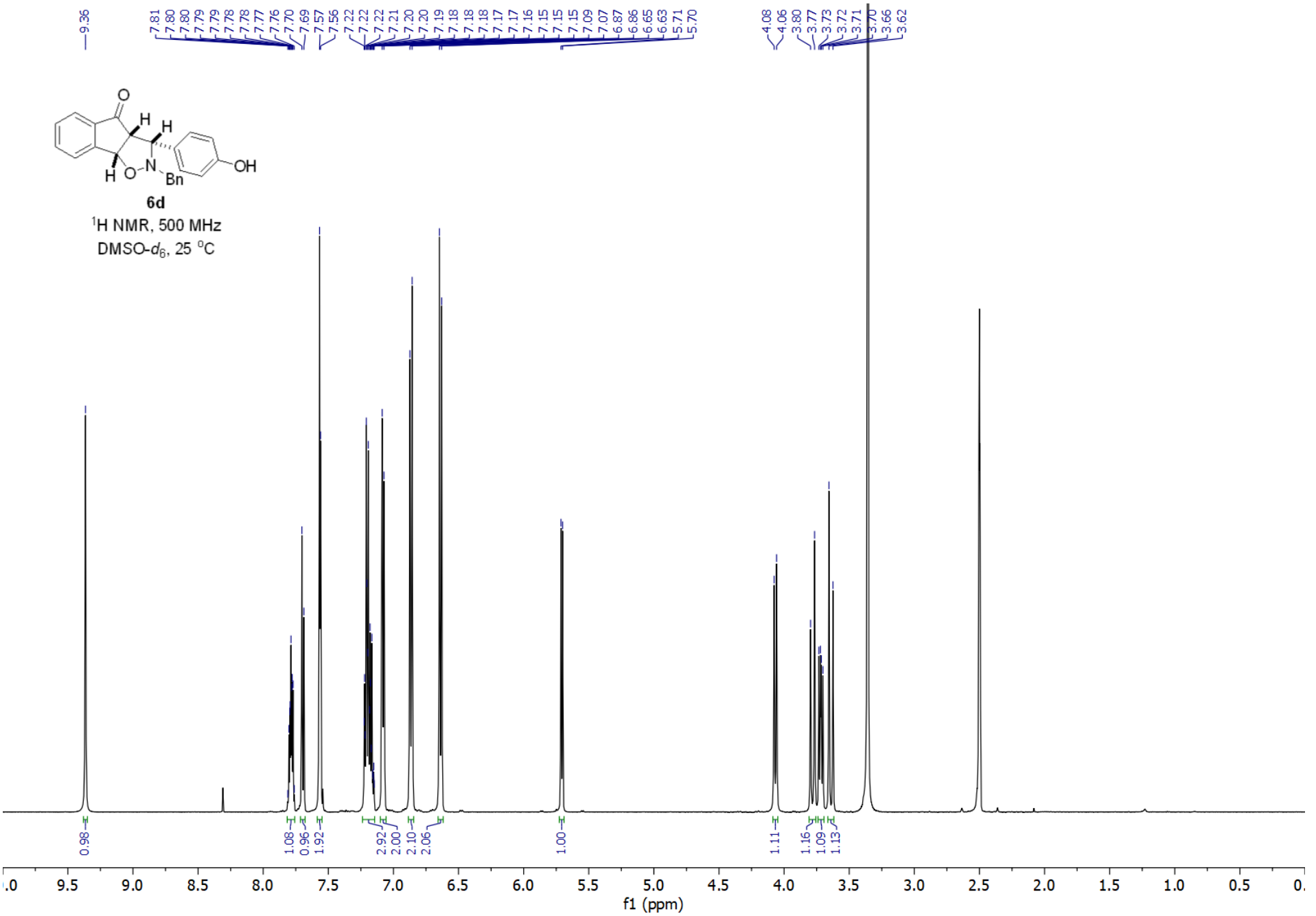

203.25
150.84
137.89
137.47
136.48
135.84
135.40
130.46
129.38
128.35
128.30
128.11
127.56
126.97
123.58
78.61
72.05
63.42
58.51
20.89
Me
O
H
H
H
O
N
Bn
7b
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

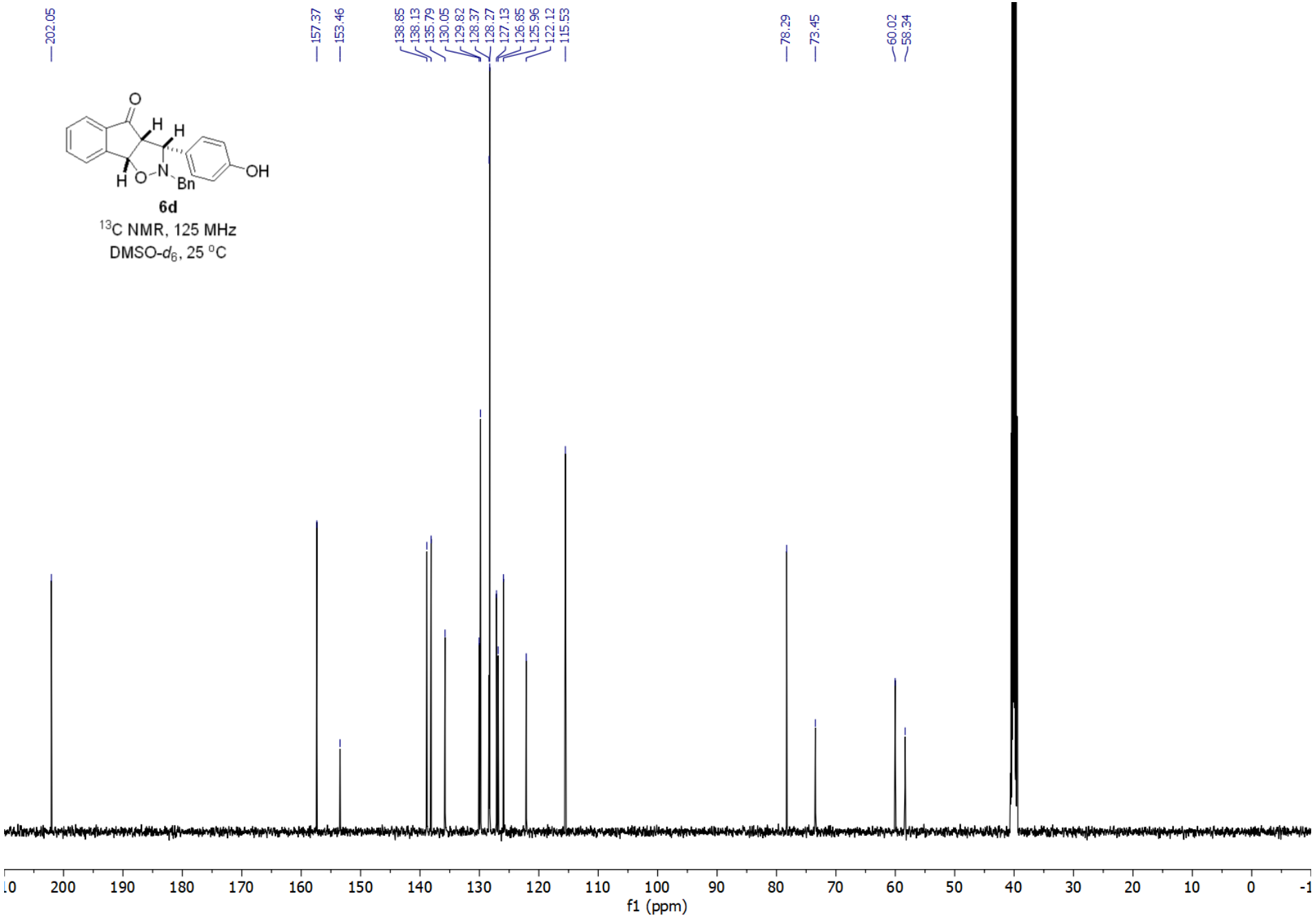

7.82 7.82 7.81 7.80 7.79 7.79 7.78 7.77 7.71 7.70 7.57 7.56 7.24 7.23 7.23 7.22 7.22 7.21 7.21 7.20 7.20 7.19 7.18 7.18 7.17 7.17 7.16 7.16 7.15 7.15 7.10 7.09 7.09 7.09 7.08 7.08 7.07 7.00 6.99 6.83 6.82 5.73 5.72 4.14 4.12 3.81 3.80 3.78 3.77 3.77 3.76 3.75 3.74 3.73 3.73 3.72 3.72 3.68 3.65
O
H
H
H
O
N
Bn
OMe
6c
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.31 1.13 2.26 3.38 2.33 2.35 2.41 1.00 1.18 2.24 3.07 1.30
f1 (ppm)

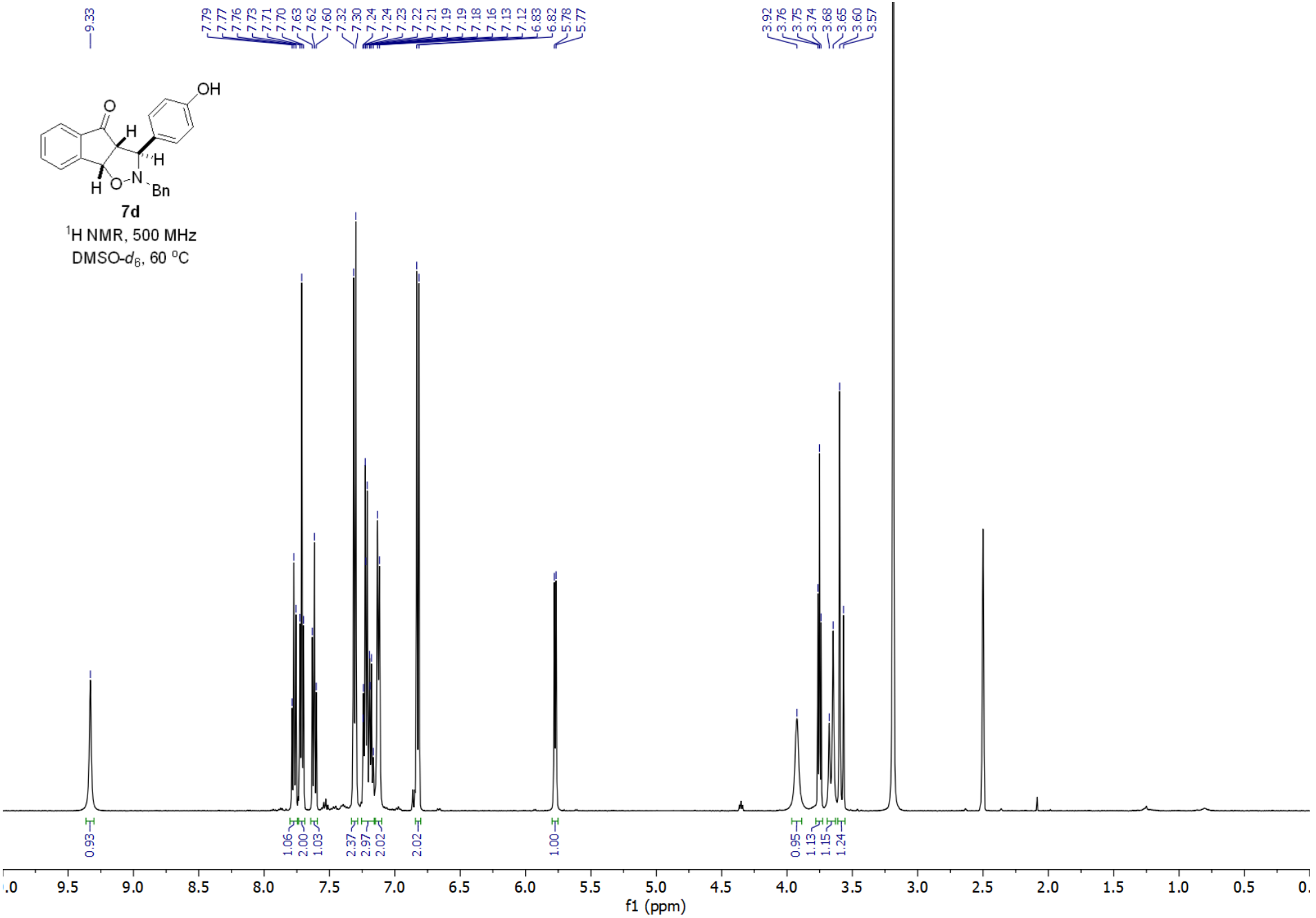

202.01
159.19
153.42
138.78
138.03
135.84
130.08
129.83
128.38
128.28
127.81
127.16
126.88
122.15
114.11
78.33
73.18
60.01
58.36
55.43
O
H
H
H
O
N
Bn
OMe
6c
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

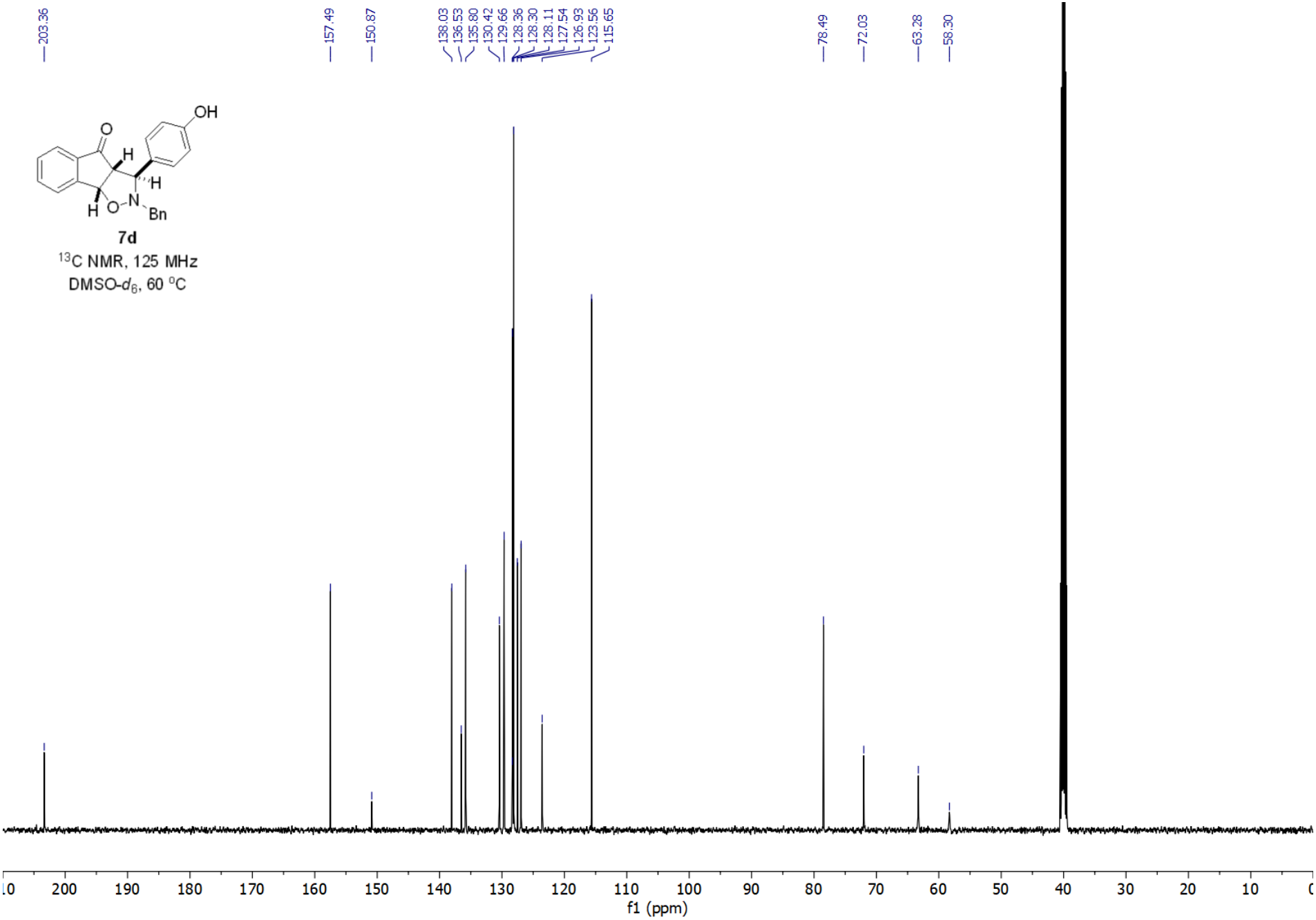

7.79
7.78
7.76
7.73
7.72
7.71
7.64
7.62
7.61
7.44
7.42
7.25
7.24
7.24
7.23
7.22
7.22
7.21
7.20
7.20
7.19
7.19
7.18
7.18
7.17
7.17
7.16
7.13
7.12
7.00
6.98
5.80
5.79
3.99
3.79
3.78
3.77
3.76
3.68
3.65
3.62
3.59
OMe
O
H
H
H
O
N
Bn
7c
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.07
1.73
1.04
2.30
2.97
2.07
2.00
1.00
0.94
3.14
1.22
2.39
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

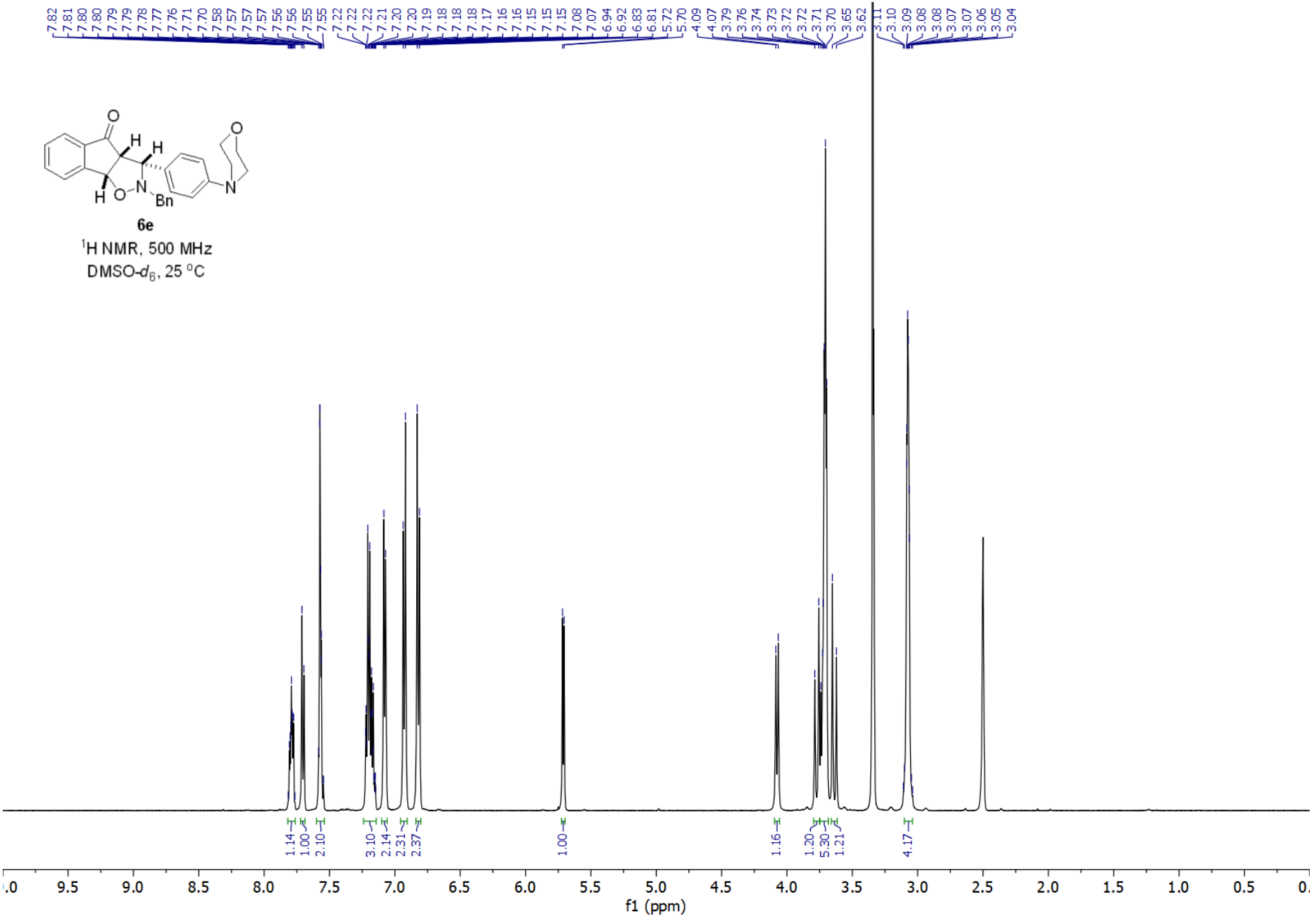

203.29
159.39
150.85
137.94
136.50
135.84
130.46
130.22
129.67
128.31
127.56
126.96
123.58
114.36
78.55
71.80
63.35
58.39
55.42
OMe
O
H
H
H
O
N
Bn
7c
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

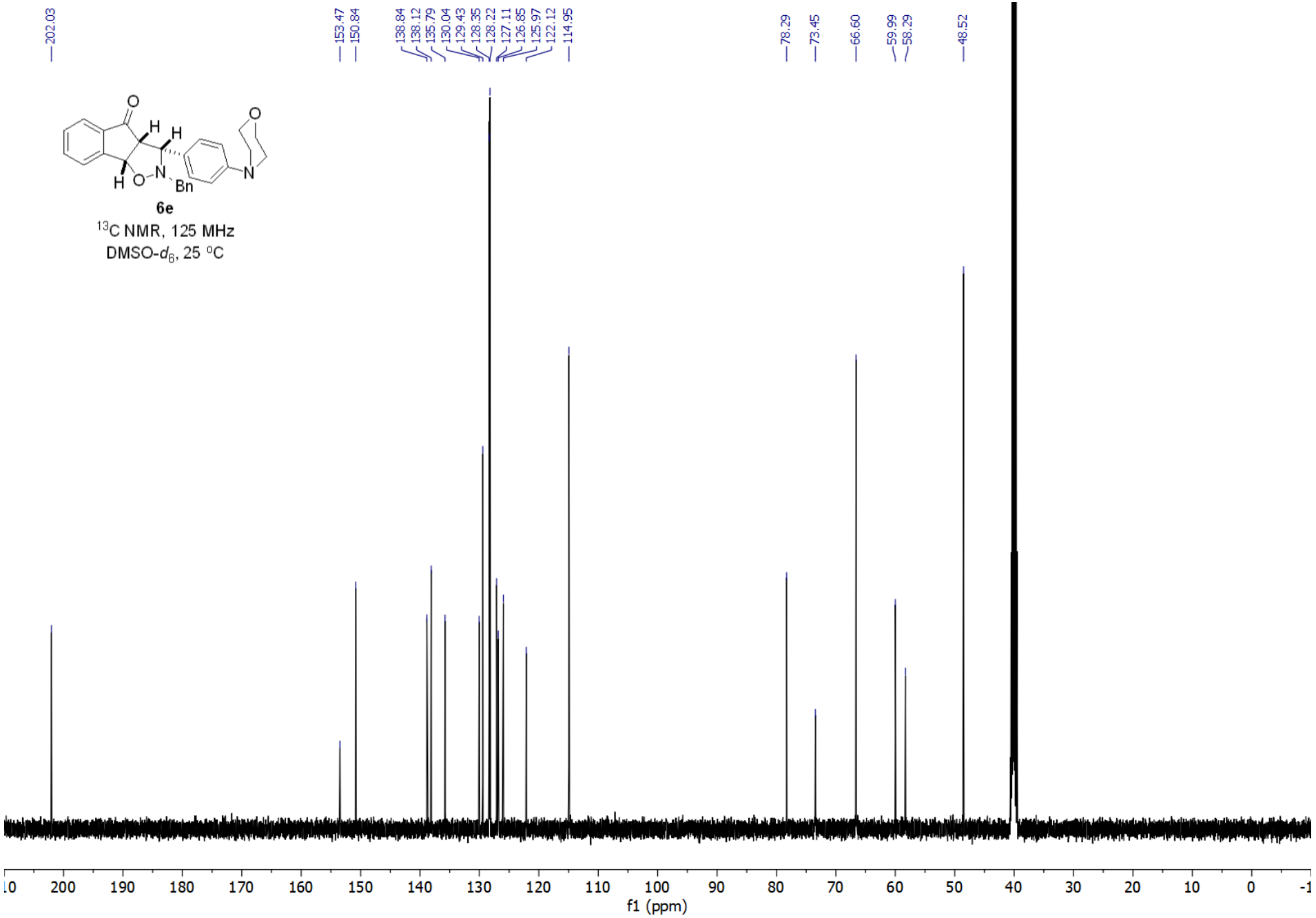

9.36
7.81
7.80
7.80
7.79
7.79
7.78
7.78
7.77
7.76
7.70
7.69
7.57
7.56
7.22
7.22
7.22
7.21
7.20
7.20
7.19
7.18
7.18
7.18
7.17
7.17
7.16
7.15
7.15
7.15
7.09
7.07
6.87
6.86
6.65
6.63
5.71
5.70
4.08
4.06
3.80
3.77
3.73
3.72
3.71
3.70
3.66
3.62
O
H
H
H
O
N
Bn
OH
6d
1H NMR, 500 MHz
DMSO-d6, 25 °C
0.98
1.08
0.96
1.92
2.92
2.00
2.10
2.06
1.00
1.11
1.16
1.09
1.13
f1 (ppm)

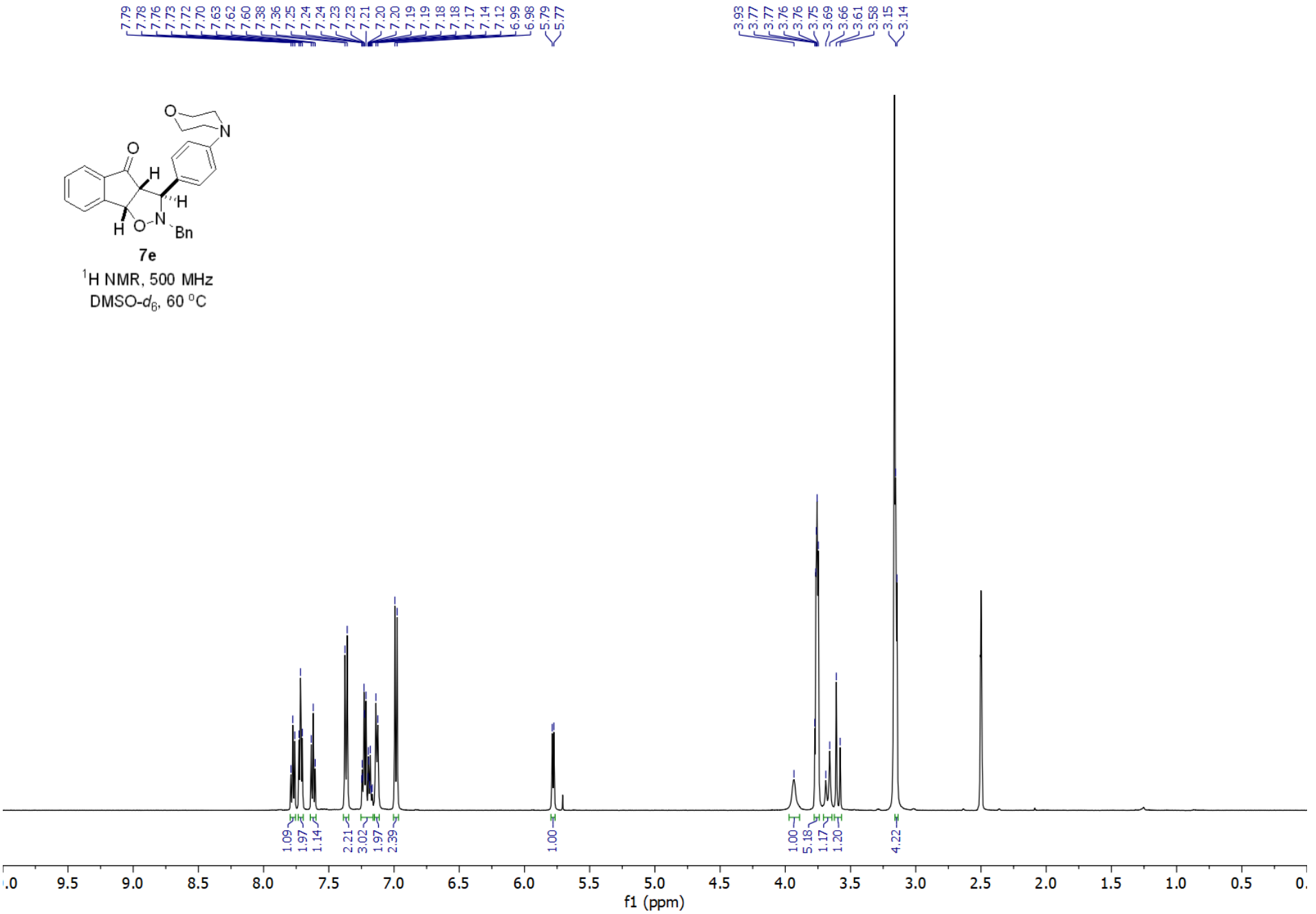

202.05
157.37
153.46
138.85
138.13
135.79
130.05
129.82
128.37
128.27
127.13
126.85
125.96
122.12
115.53
78.29
73.45
60.02
58.34
O
H
H
H
O
N
Bn
OH
6d
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

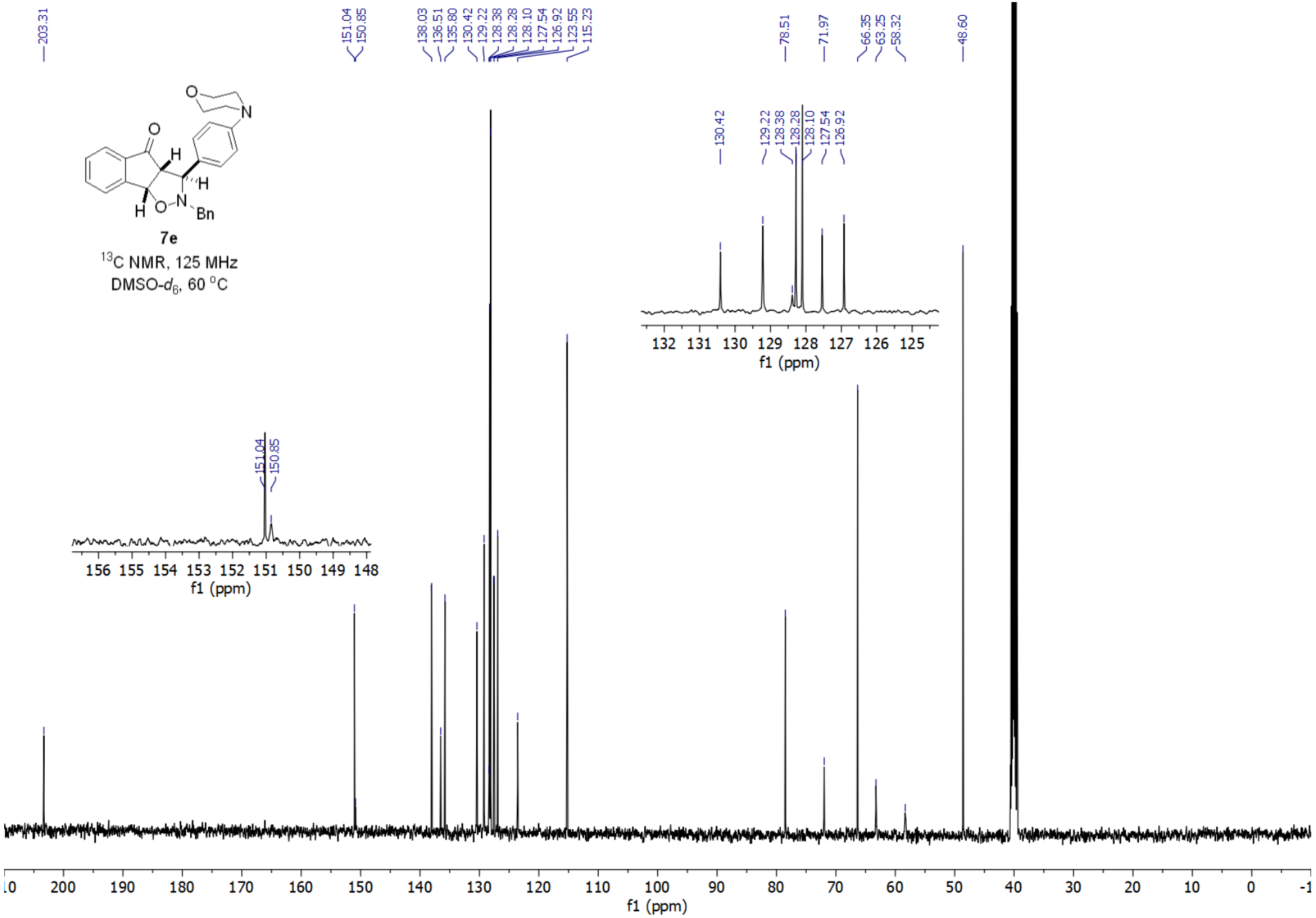

9.33
7.79
7.77
7.76
7.73
7.71
7.70
7.63
7.62
7.60
7.32
7.30
7.24
7.24
7.23
7.22
7.21
7.19
7.19
7.18
7.16
7.13
7.12
6.83
6.82
5.78
5.77
3.92
3.76
3.75
3.74
3.68
3.65
3.60
3.57
OH
O
H
H
O
N
Bn
H
7d
1H NMR, 500 MHz
DMSO-d6, 60 °C
0.93
1.06
2.00
1.03
2.37
2.97
2.02
2.02
1.00
0.95
1.13
1.15
1.24
f1 (ppm)

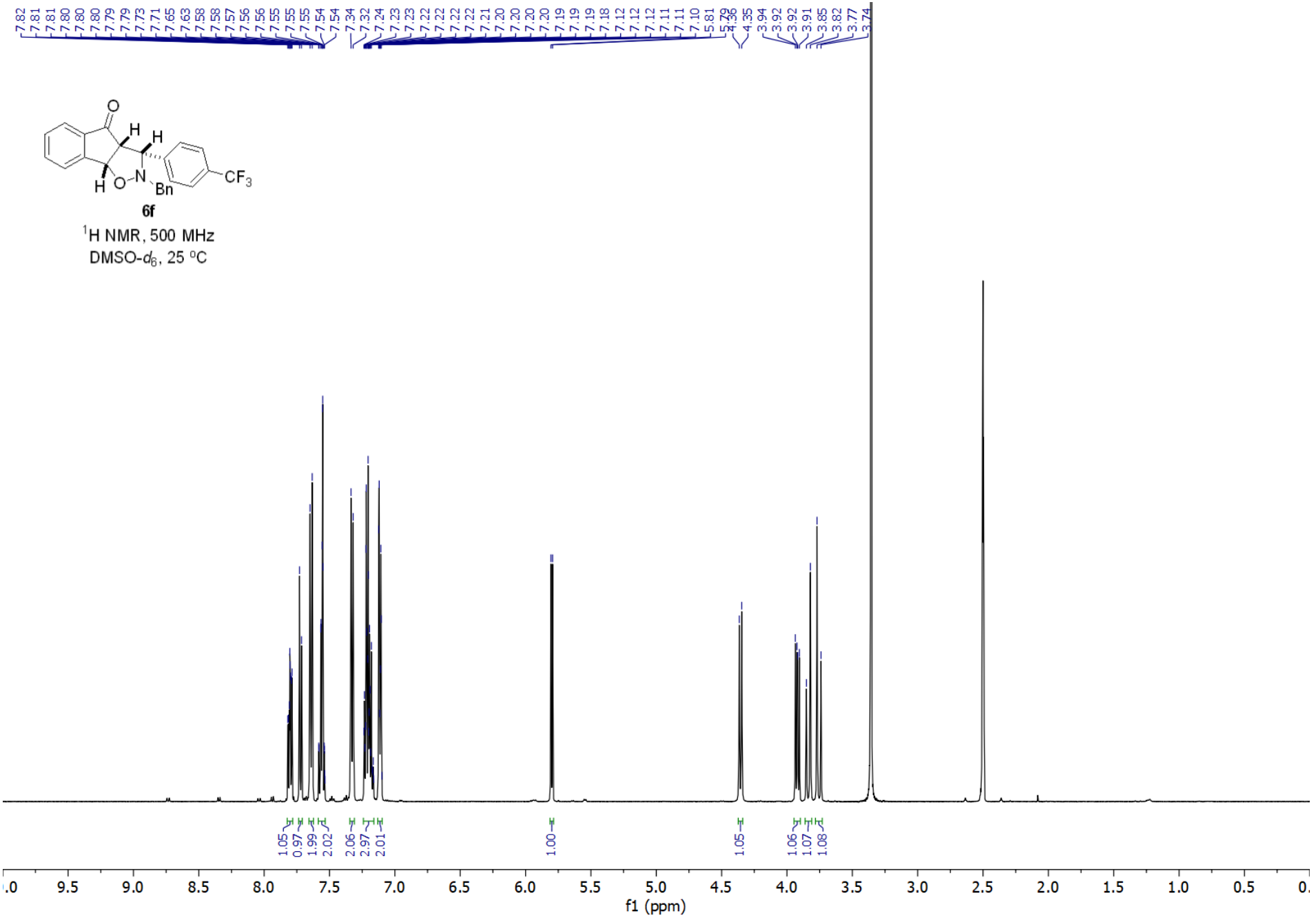

203.36
157.49
150.87
138.03
136.53
135.80
130.42
129.66
128.36
128.30
128.11
127.54
126.93
123.56
115.65
78.49
72.03
63.28
58.30
OH
O
H
H
H
O
N
Bn
7d
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

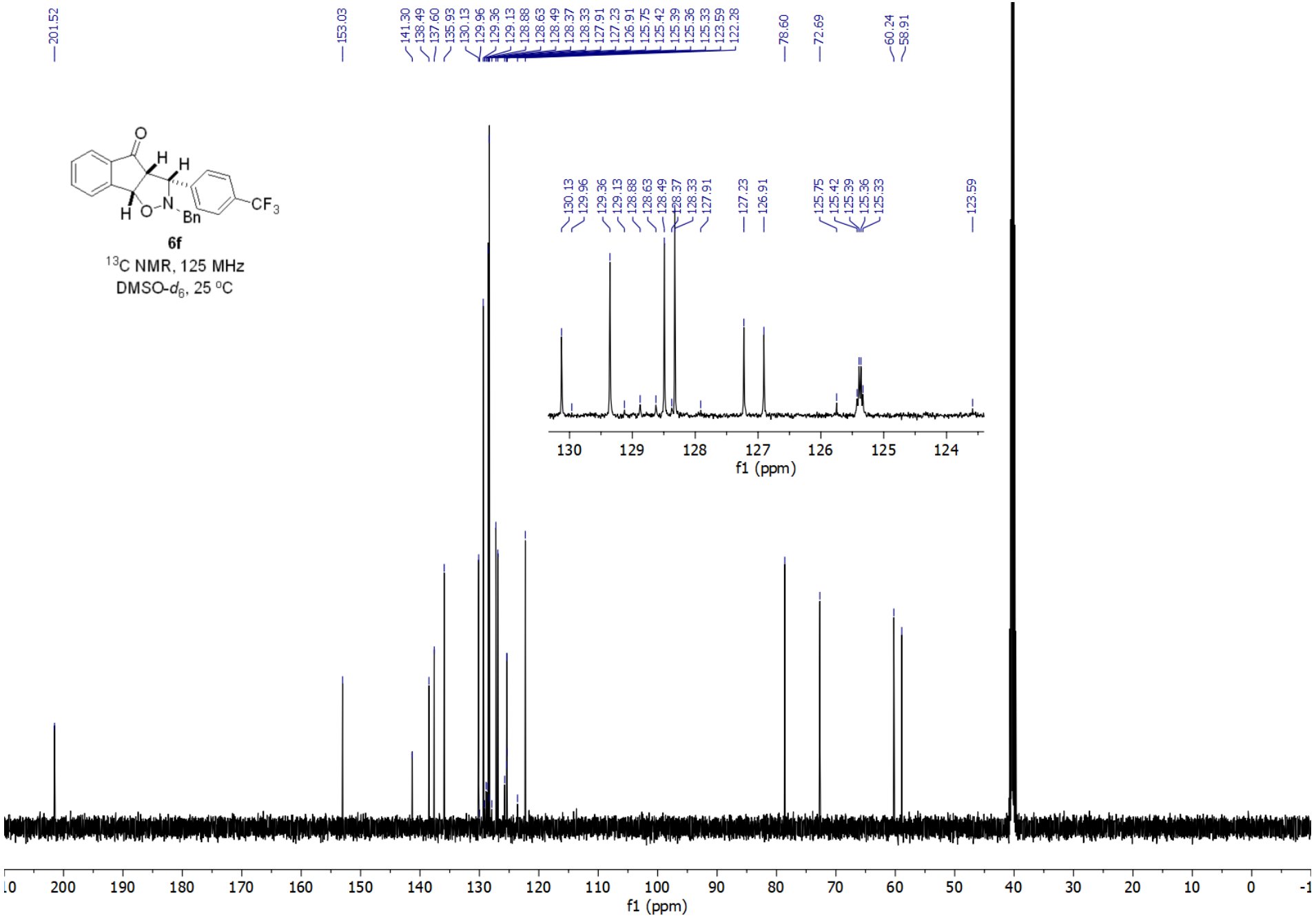

7.82 7.81 7.80 7.80 7.79 7.79 7.78 7.77 7.76 7.71 7.70 7.58 7.57 7.57 7.57 7.56 7.56 7.55 7.55
7.22 7.22 7.21 7.20 7.20 7.19 7.18 7.18 7.17 7.16 7.16 7.15 7.15 7.15 7.08 7.07 6.94 6.92 6.83 6.81 5.72 5.70
4.09 4.07 3.79 3.76 3.74 3.73 3.72 3.72 3.71 3.70 3.65 3.62
3.11 3.10 3.09 3.08 3.08 3.07 3.07 3.06 3.05 3.04
O
H
H
O
N
Bn
O
N
6e
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.14 1.00 2.10 3.10 2.14 2.31 2.37 1.00 1.16 1.20 5.30 1.21 4.17
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


202.03
153.47
150.84
138.84
138.12
135.79
130.04
129.43
128.35
128.22
127.11
126.85
125.97
122.12
114.95
78.29
73.45
66.60
59.99
58.29
48.52
O
H
H
O
N
Bn
O
N
6e
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)


7.79
7.78
7.76
7.73
7.72
7.70
7.63
7.62
7.60
7.38
7.36
7.25
7.24
7.24
7.23
7.23
7.21
7.20
7.20
7.19
7.19
7.18
7.18
7.17
7.14
7.12
6.99
6.98
5.79
5.77
3.93
3.77
3.77
3.76
3.76
3.75
3.69
3.66
3.61
3.58
3.15
3.14
O
N
O
H
H
H
O
N
Bn
7e
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.09
1.97
1.14
2.21
3.02
1.97
2.39
1.00
1.00
5.18
1.17
1.20
4.22
f1 (ppm)


203.31
151.04
150.85
138.03
136.51
135.80
130.42
129.22
128.38
128.28
128.10
127.54
126.92
123.55
115.23
78.51
71.97
66.35
63.25
58.32
48.60
O
N
O
H
H
H
O
N
Bn
7e
13C NMR, 125 MHz
DMSO-d6, 60 °C
130.42
129.22
128.38
128.28
128.10
127.54
126.92
132 131 130 129 128 127 126 125
f1 (ppm)
151.04
150.85
156 155 154 153 152 151 150 149 148
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

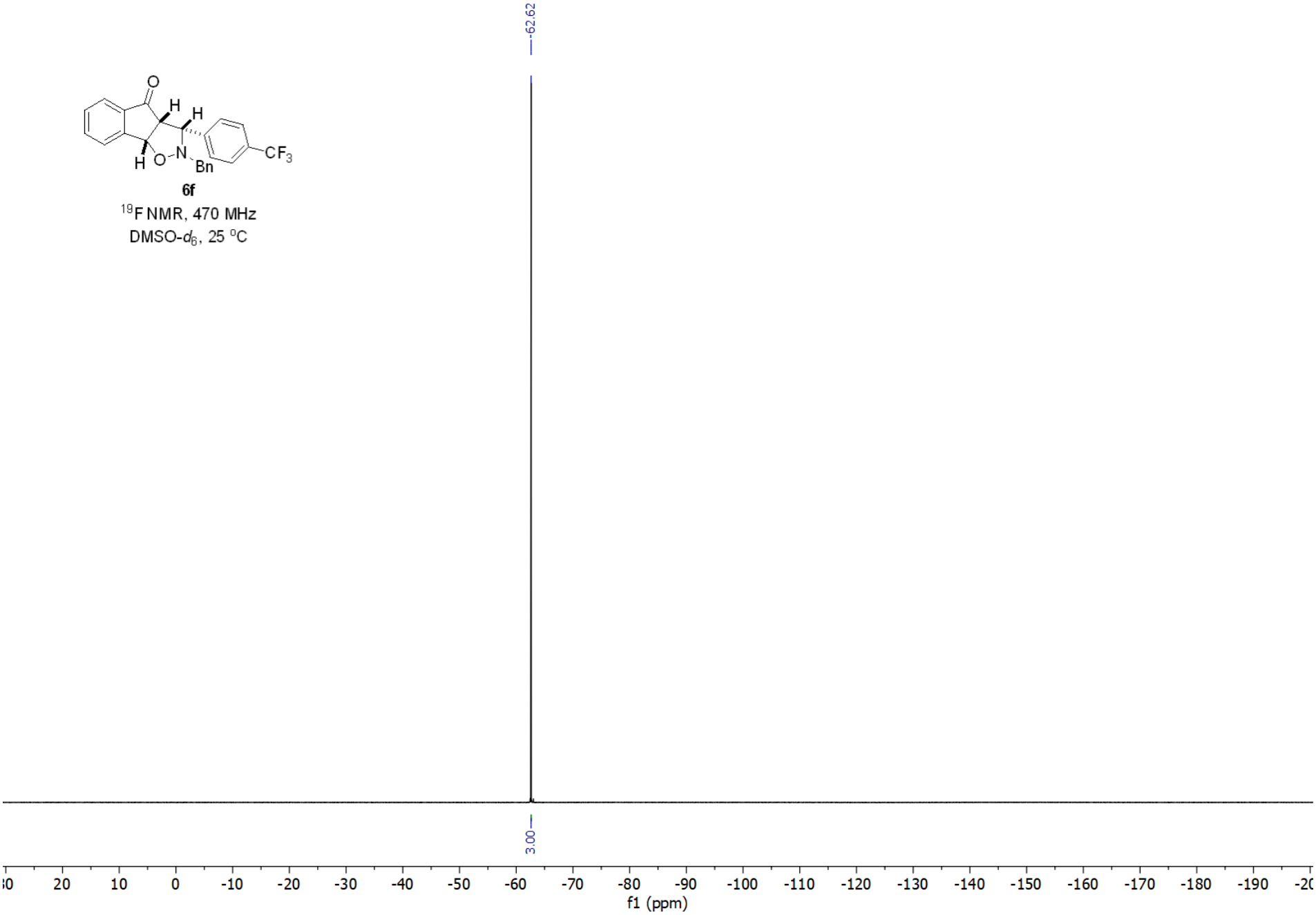

7.82 7.81 7.81 7.80 7.80 7.80 7.79 7.79 7.73 7.71 7.65 7.63 7.58 7.58 7.57 7.56 7.56 7.55 7.55 7.55 7.54 7.54 7.34 7.32 7.24 7.23 7.23 7.22 7.22 7.22 7.22 7.21 7.20 7.20 7.20 7.20 7.19 7.19 7.19 7.18 7.12 7.12 7.11 7.11 7.10 5.81 5.29 4.36 4.35 3.94 3.92 3.92 3.91 3.85 3.82 3.77 3.74
O
H
H
H
O
N
Bn
CF3
6f
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.05 0.97 1.99 2.02 2.06 2.97 2.01 1.00 1.05 1.06 1.07 1.08
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

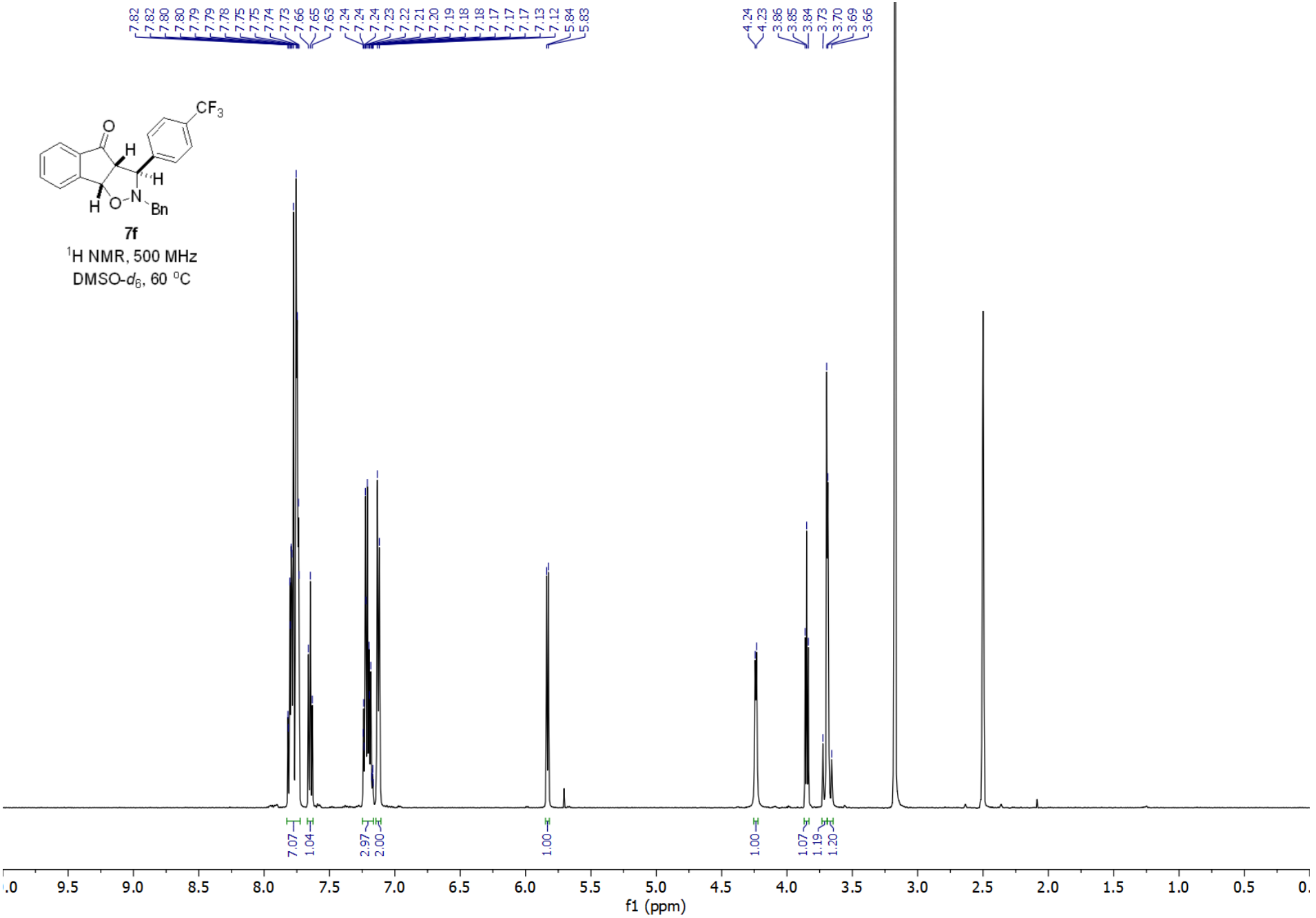

201.52
153.03
141.30
138.49
137.60
135.93
130.13
129.96
129.36
129.13
128.88
128.63
128.49
128.37
128.33
127.91
127.23
126.91
125.75
125.42
125.39
125.36
125.33
123.59
122.28
78.60
72.69
60.24
58.91
O
H
H
H
O
N
Bn
CF3
6f
13C NMR, 125 MHz
DMSO-d6, 25 °C
130.13
129.96
129.36
129.13
128.88
128.63
128.49
128.37
128.33
127.91
127.23
126.91
125.75
125.42
125.39
125.36
125.33
123.59
130
129
128
127
126
125
124
f1 (ppm)
f1 (ppm)

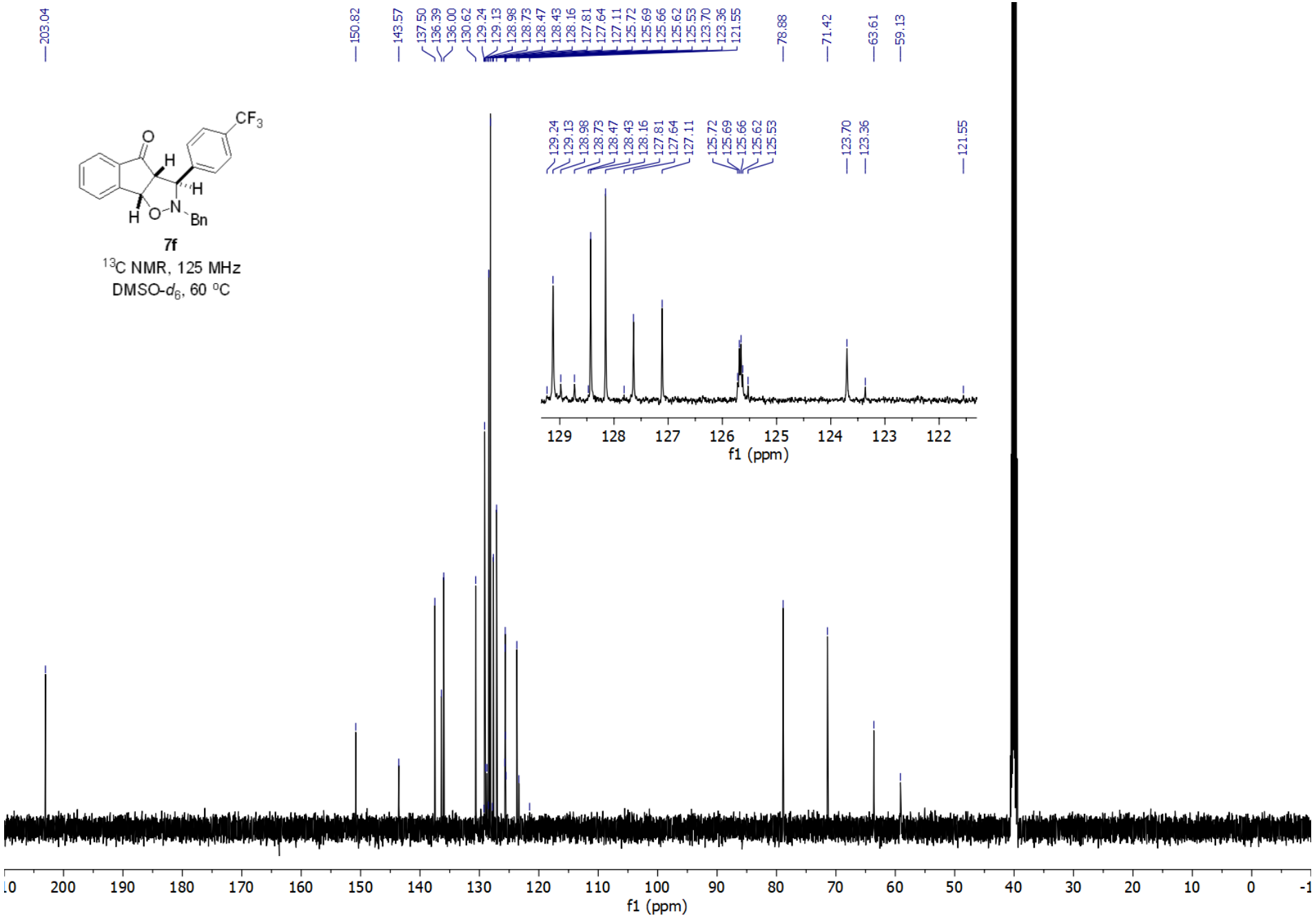
6f

^{19}F NMR, 470 MHz

DMSO-d_6, 25 ^{0}C



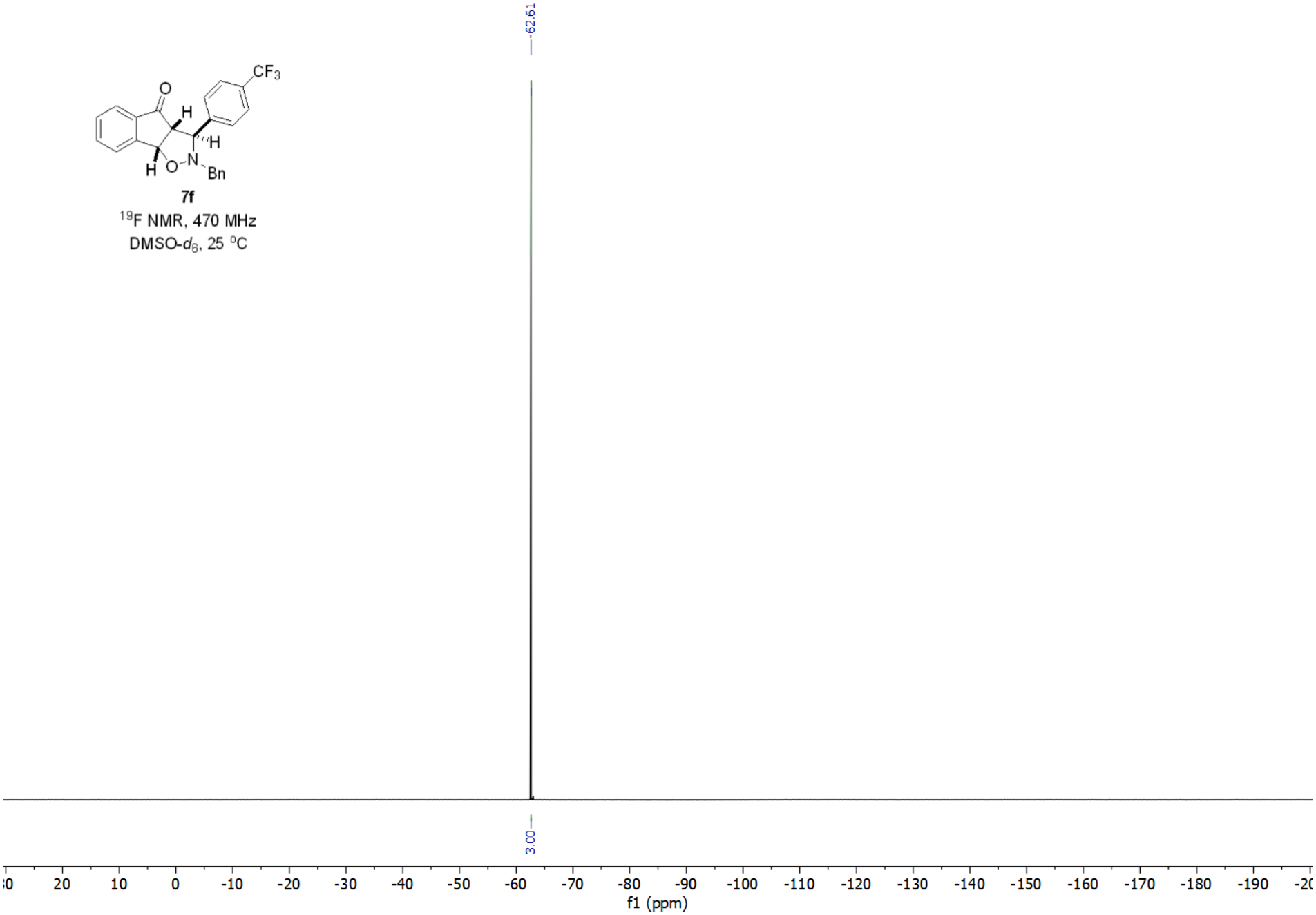

7.82
7.82
7.80
7.80
7.79
7.79
7.78
7.75
7.75
7.74
7.73
7.66
7.65
7.63
7.24
7.24
7.24
7.23
7.22
7.21
7.20
7.19
7.18
7.18
7.17
7.17
7.17
7.13
7.12
5.84
5.83
4.24
4.23
3.86
3.85
3.84
3.73
3.70
3.69
3.66
CF3
O
H
H
H
O
N
Bn
7f
1H NMR, 500 MHz
DMSO-d6, 60 °C
7.07
1.04
2.97
2.00
1.00
1.00
1.07
1.19
1.20
f1 (ppm)

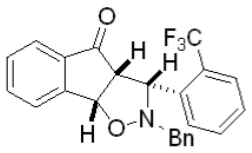

203.04
150.82
143.57
137.50
136.39
136.00
130.62
129.24
129.13
128.98
128.73
128.47
128.43
128.16
127.81
127.64
127.11
125.72
125.69
125.66
125.62
125.53
123.70
123.36
121.55
78.88
71.42
63.61
59.13
CF3
O
H
H
H
O
N
Bn
7f
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)
f1 (ppm)

7f

^{19}F NMR, 470 MHz

DMSO-d_6, 25 ^{0}C

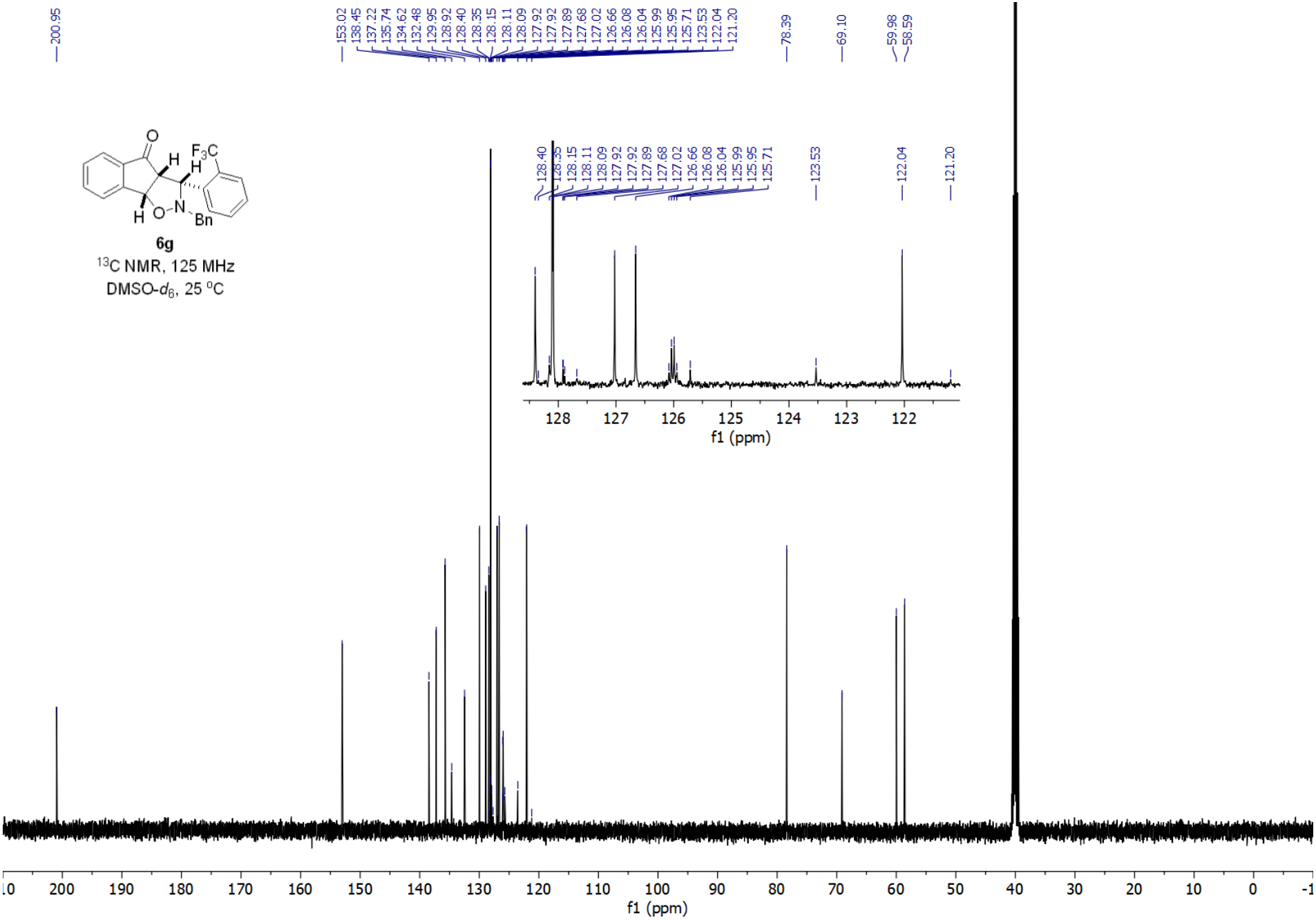




6g

^{1}H NMR, 500 MHz

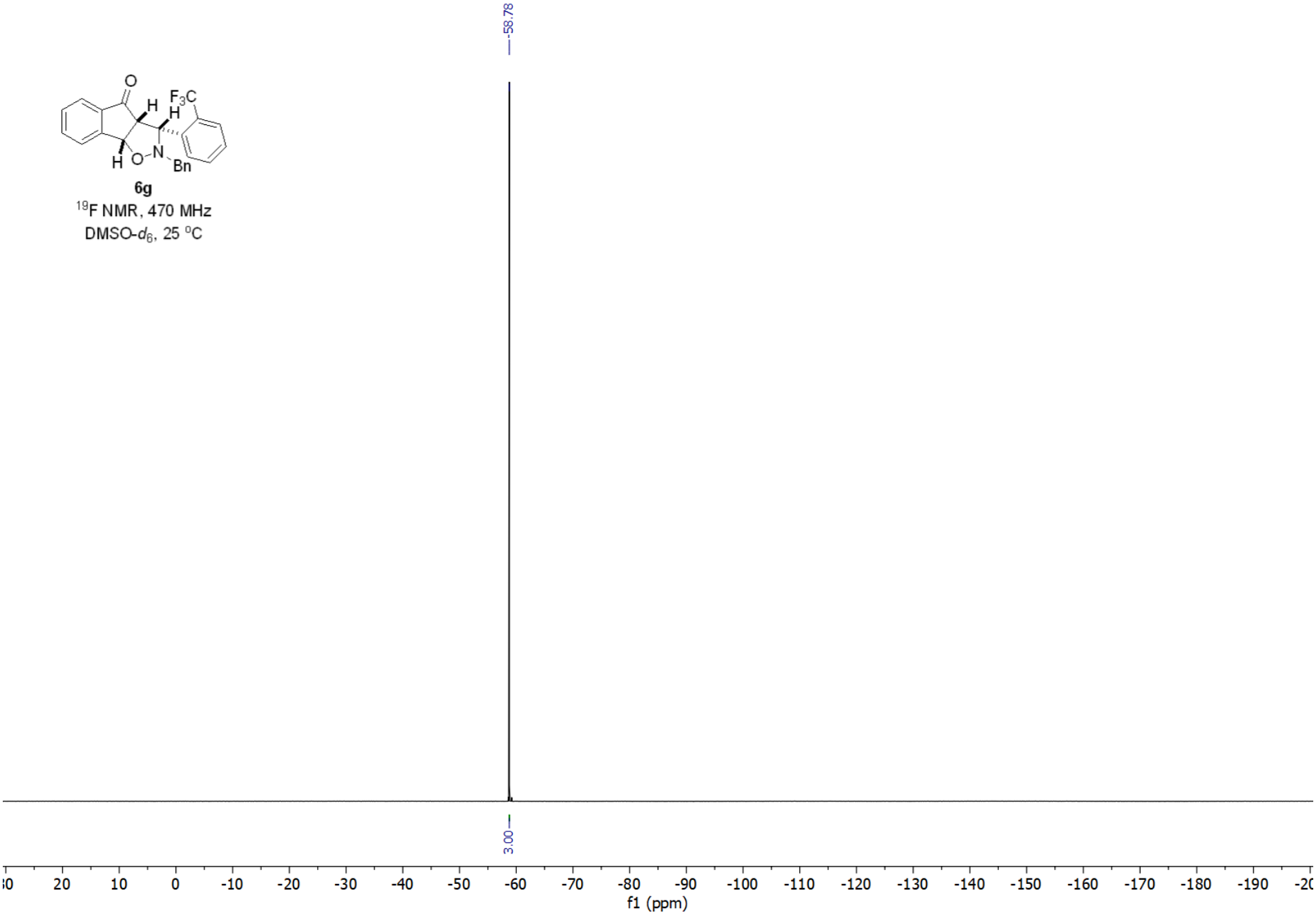
DMSO-d_6, 25 ^{o}C

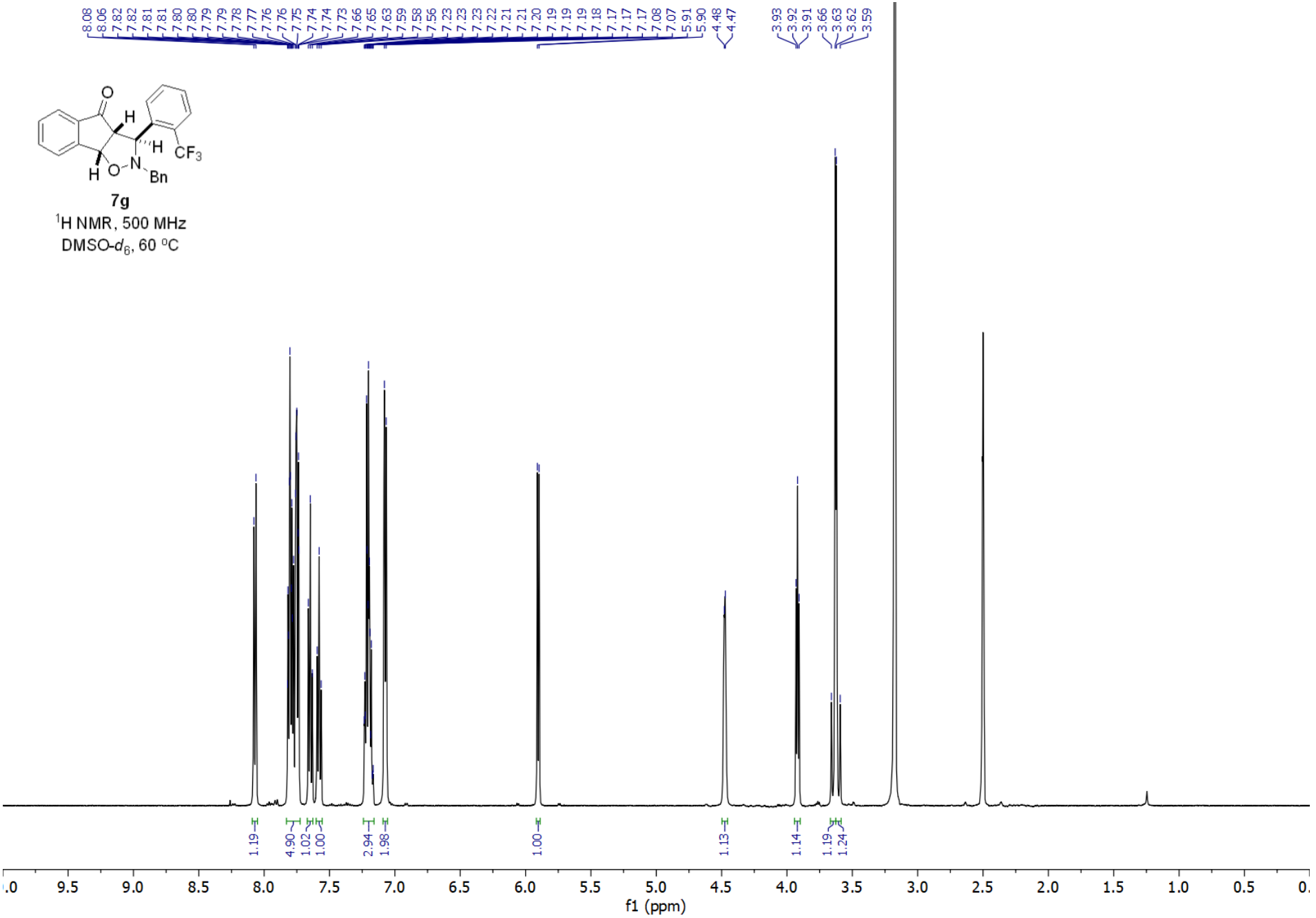

200.95
153.02
138.45
137.22
135.74
134.62
132.48
129.95
128.92
128.40
128.35
128.15
128.11
128.09
127.92
127.92
127.89
127.68
127.02
126.66
126.08
126.04
125.99
125.95
125.71
123.53
122.04
121.20
78.39
69.10
59.98
58.59
O
H
F3C
H
H
O
N
Bn
6g
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)
f1 (ppm)

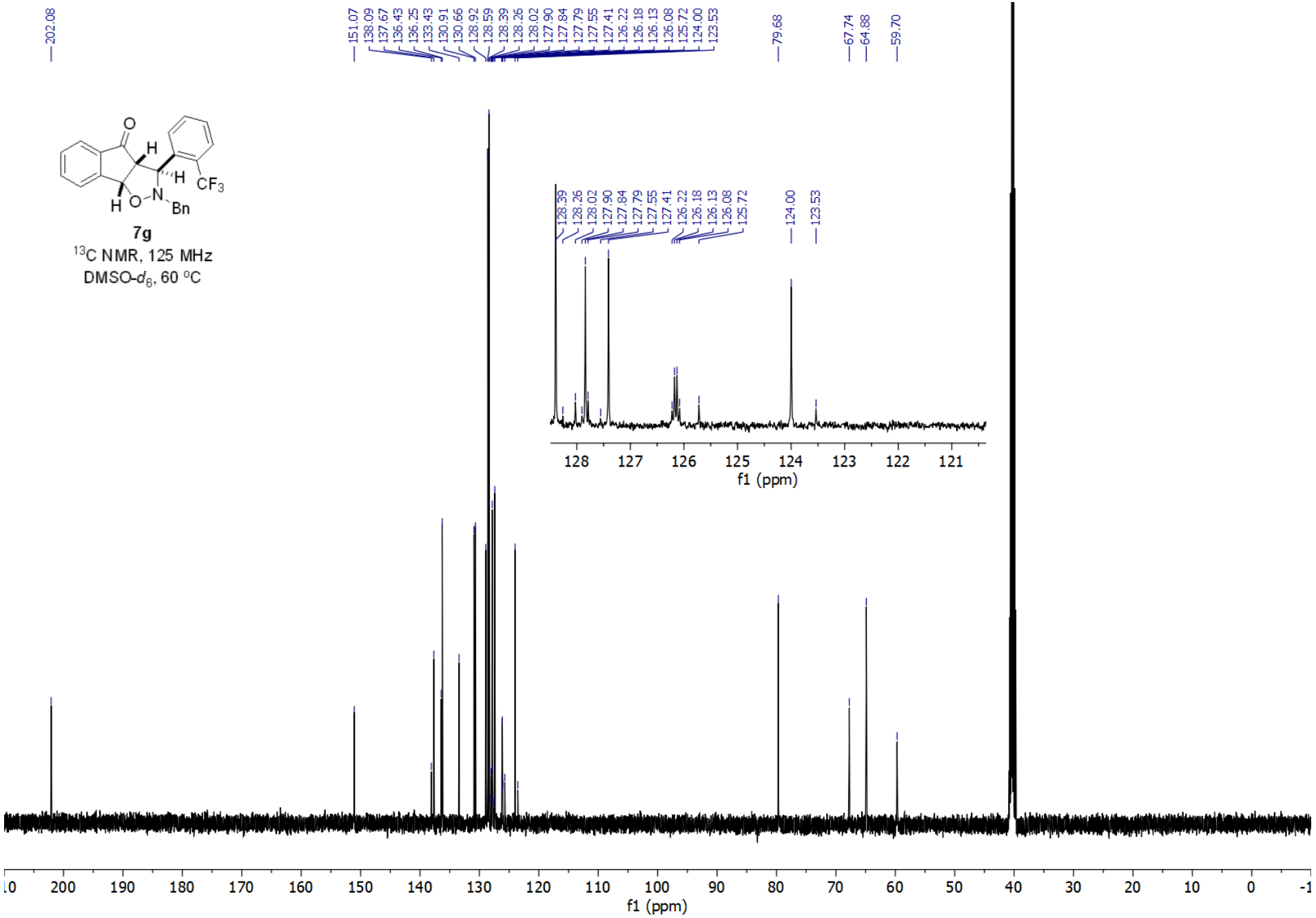
6g

^{19}F NMR, 470 MHz

DMSO-d_6, 25 ^{0}C



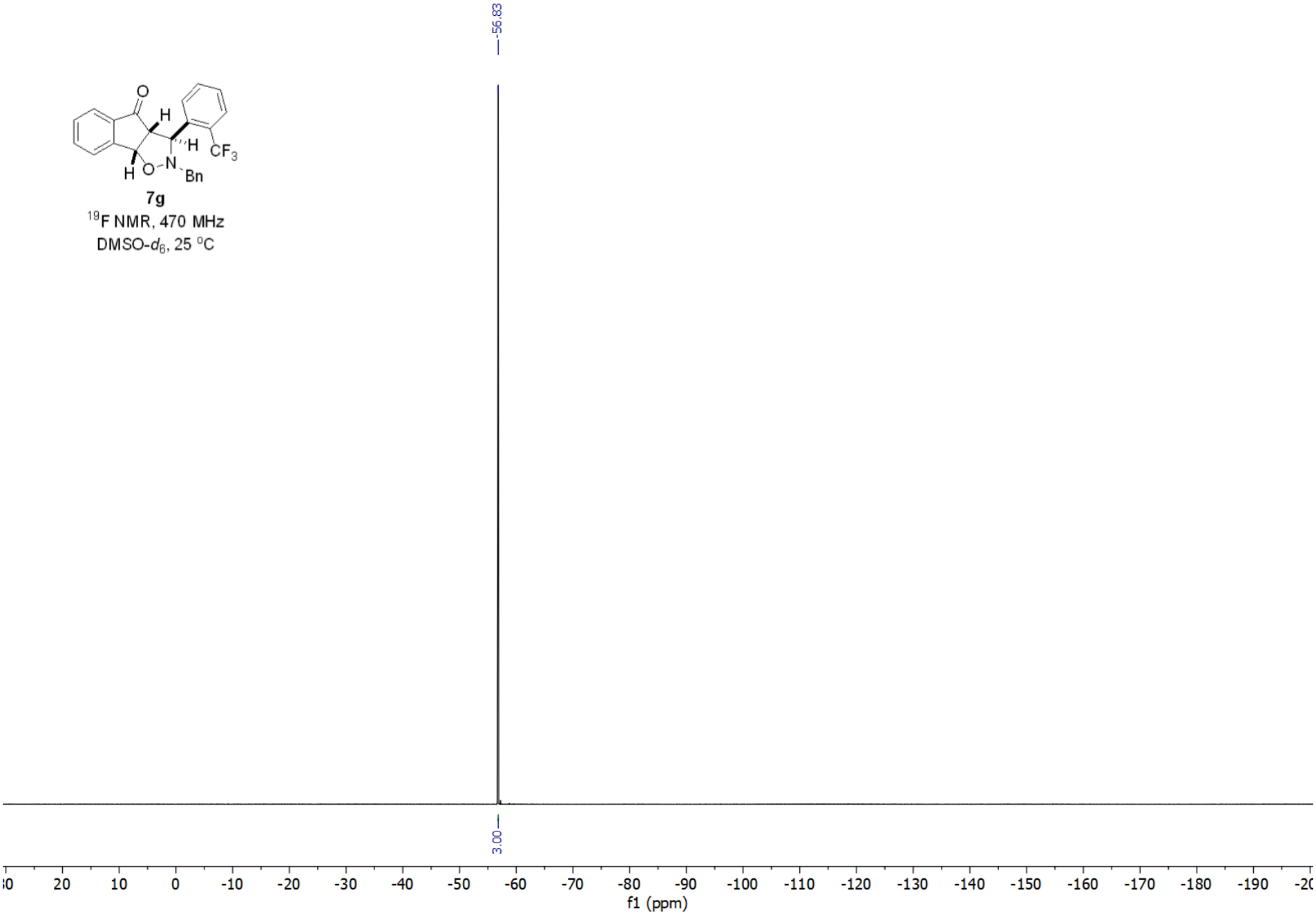

8.08
8.06
7.82
7.82
7.81
7.81
7.80
7.80
7.79
7.79
7.78
7.77
7.76
7.76
7.75
7.74
7.74
7.73
7.66
7.65
7.63
7.59
7.58
7.56
7.23
7.23
7.23
7.22
7.21
7.21
7.20
7.19
7.19
7.19
7.18
7.17
7.17
7.17
7.08
7.07
5.91
5.90
4.48
4.47
3.93
3.92
3.91
3.66
3.63
3.62
3.59
O
H
H
CF3
H
O
N
Bn
7g
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.19
4.90
1.02
1.00
2.94
1.98
1.00
1.13
1.14
1.19
1.24
f1 (ppm)

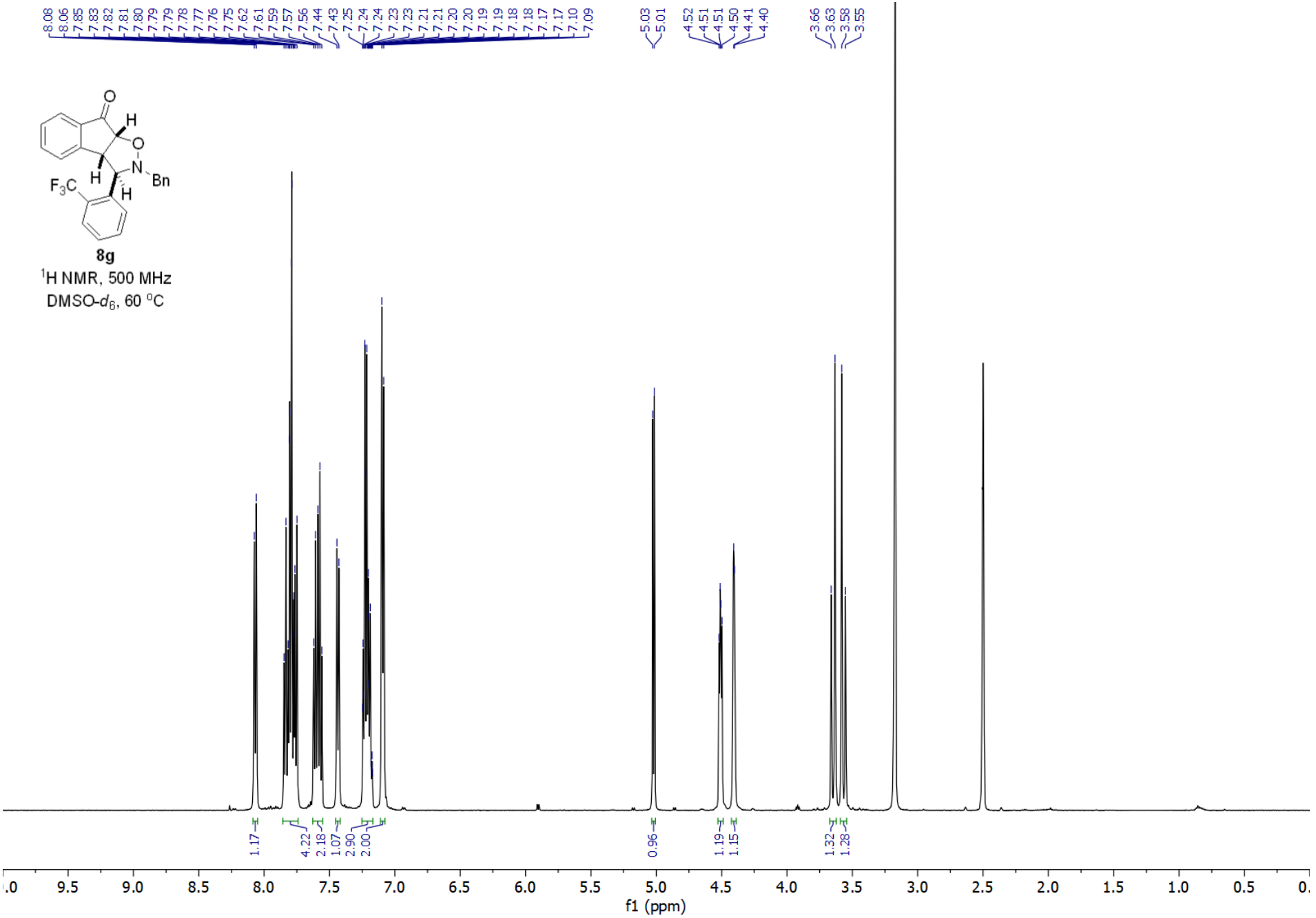

202.08
151.07
138.09
137.67
136.43
136.25
133.43
130.91
130.66
128.92
128.59
128.39
128.26
128.02
127.90
127.84
127.79
127.55
127.41
126.22
126.18
126.13
126.08
125.72
124.00
123.53
79.68
67.74
64.88
59.70
O
H
H
CF3
O
N
H
Bn
7g
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)
f1 (ppm)

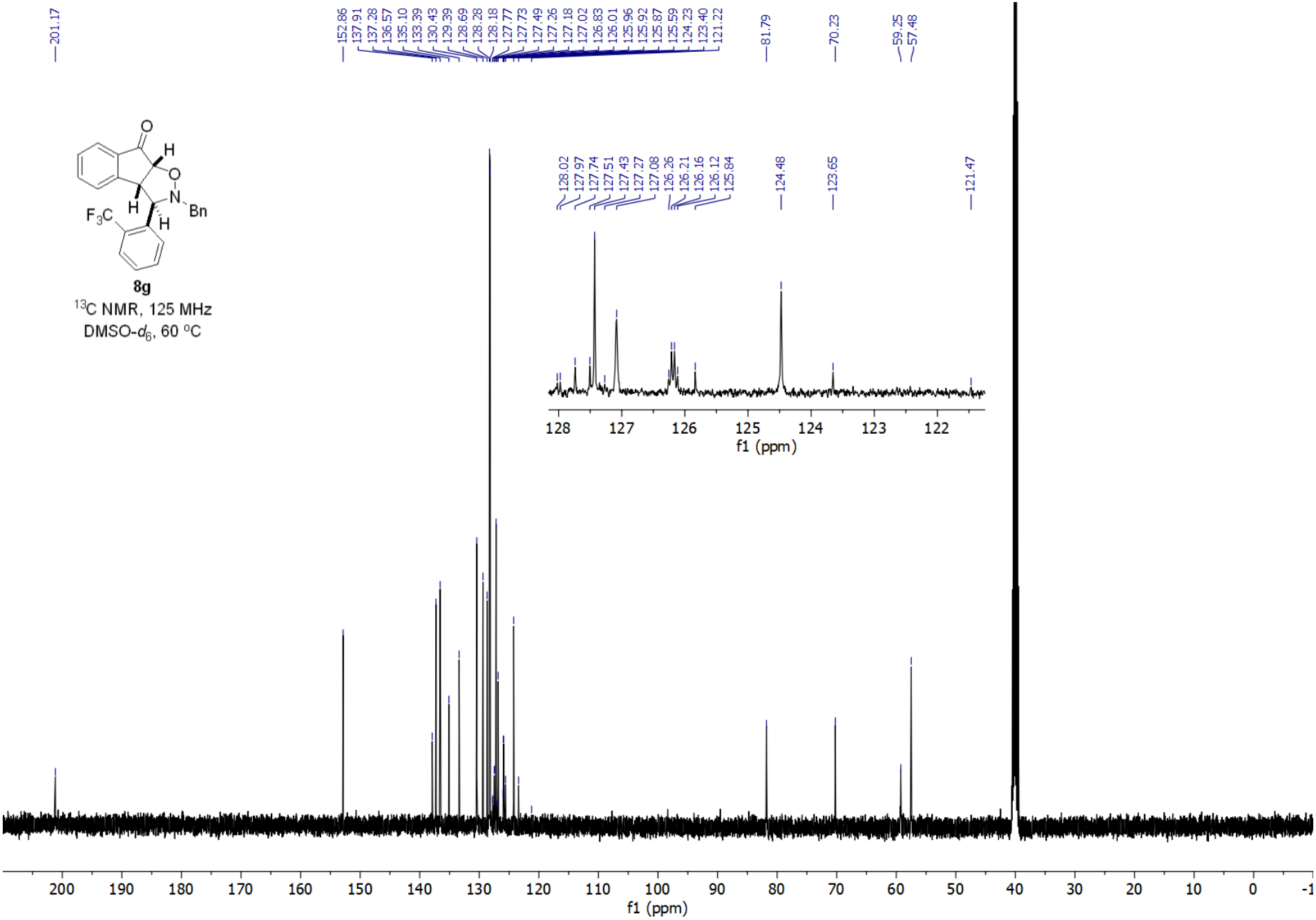
7g

^{19}F NMR, 470 MHz

DMSO-d_6, 25 °C



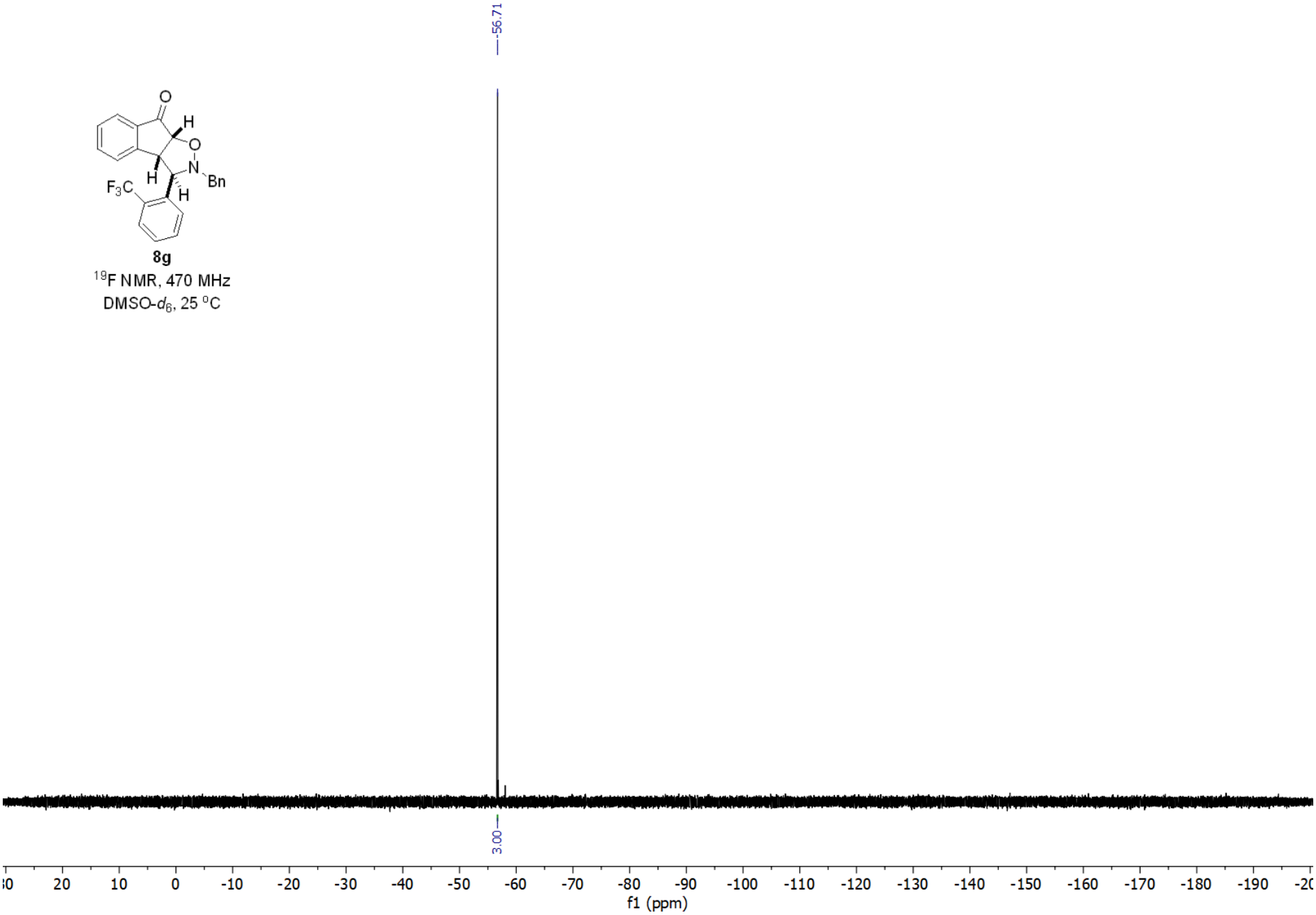

8.08
8.06
7.85
7.83
7.82
7.81
7.80
7.79
7.79
7.78
7.77
7.76
7.75
7.62
7.61
7.59
7.57
7.56
7.44
7.43
7.25
7.24
7.24
7.23
7.23
7.21
7.21
7.20
7.20
7.19
7.19
7.18
7.18
7.17
7.17
7.10
7.09
5.03
5.01
4.52
4.51
4.51
4.50
4.41
4.40
3.66
3.63
3.58
3.55
O
H
O
N
Bn
H
F3C
H
8g
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.17
4.22
2.18
1.07
2.90
2.00
0.96
1.19
1.15
1.32
1.28
f1 (ppm)

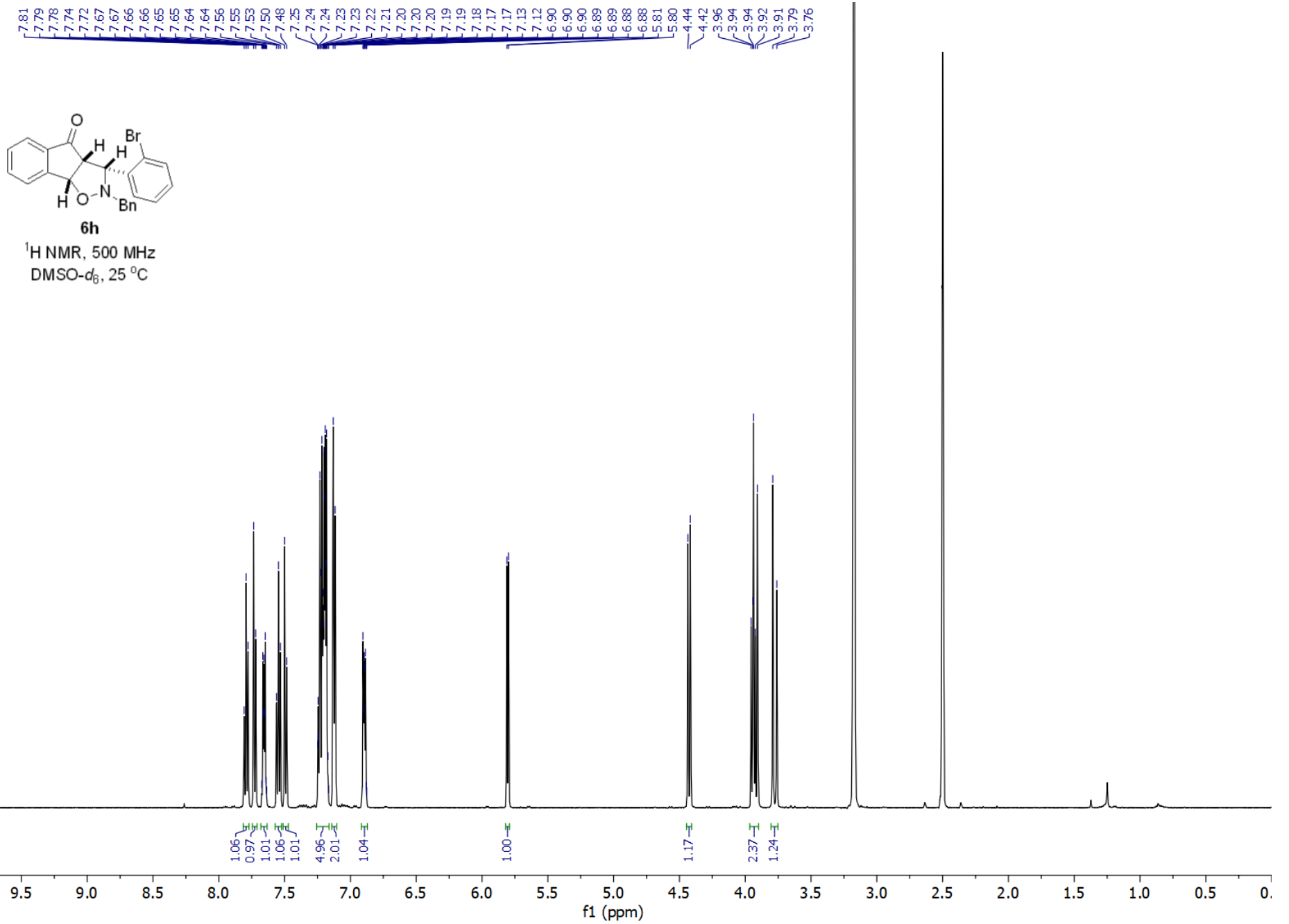

201.17
152.86
137.91
137.28
136.57
135.10
133.39
130.43
129.39
128.69
128.28
128.18
127.77
127.73
127.49
127.26
127.18
127.02
126.83
126.01
125.96
125.92
125.87
125.59
124.23
123.40
121.22
81.79
70.23
59.25
57.48
128.02
127.97
127.74
127.51
127.43
127.27
127.08
126.26
126.21
126.16
126.12
125.84
124.48
123.65
121.47
O
H
O
N
Bn
H
H
F3C
8g
13C NMR, 125 MHz
DMSO-d6, 60 °C
128
127
126
125
124
123
122
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

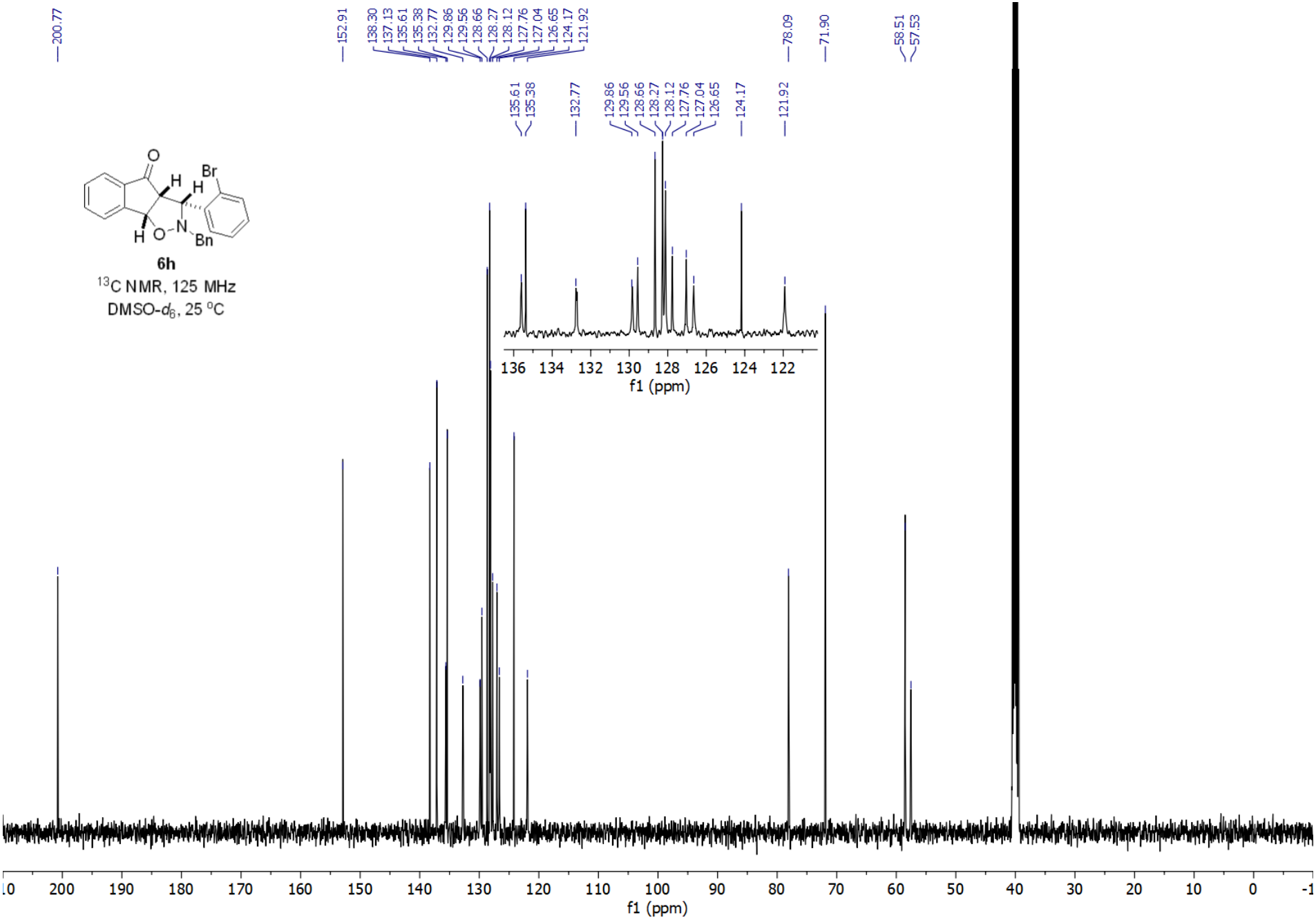
8g

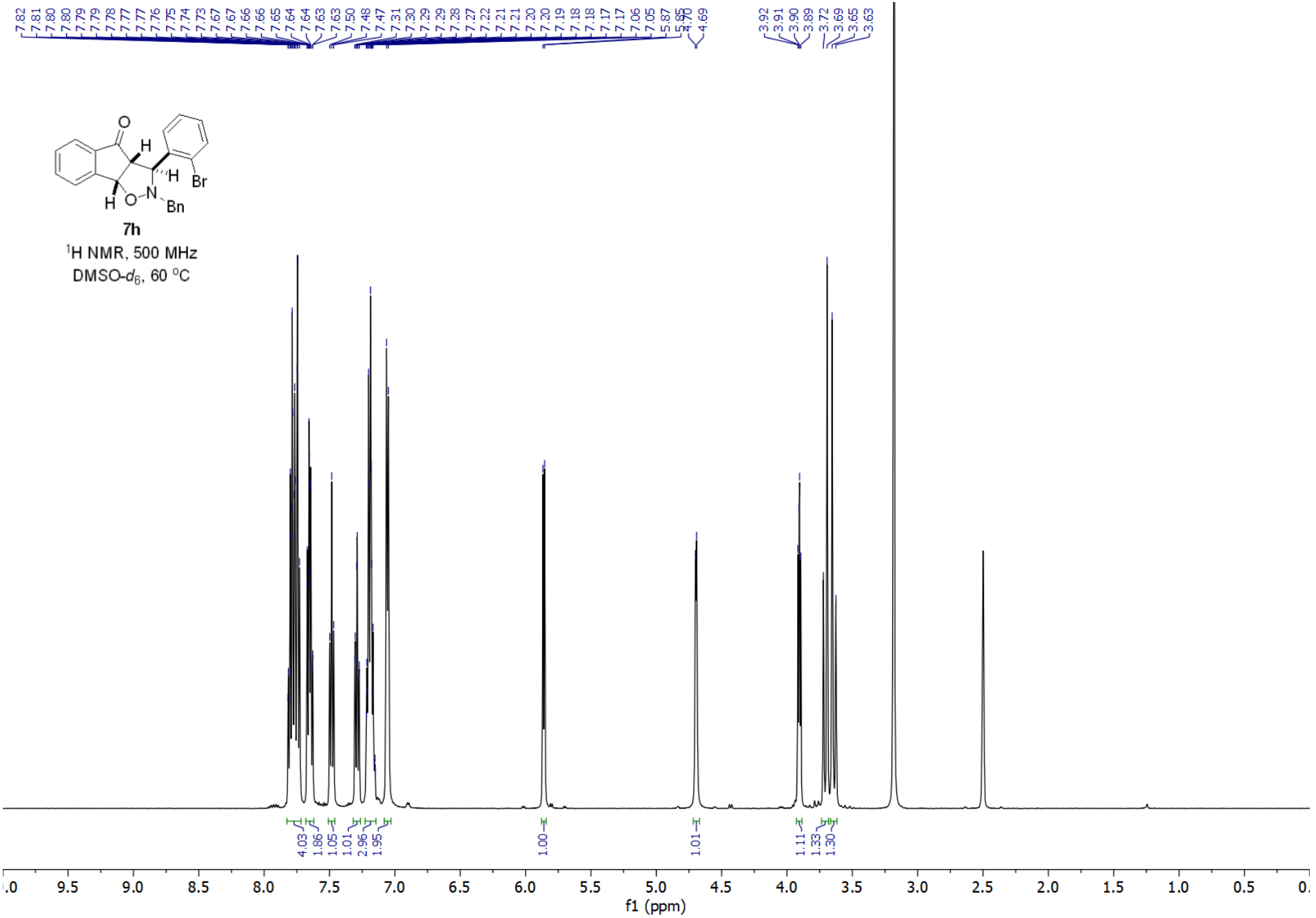
^{19}F NMR, 470 MHz

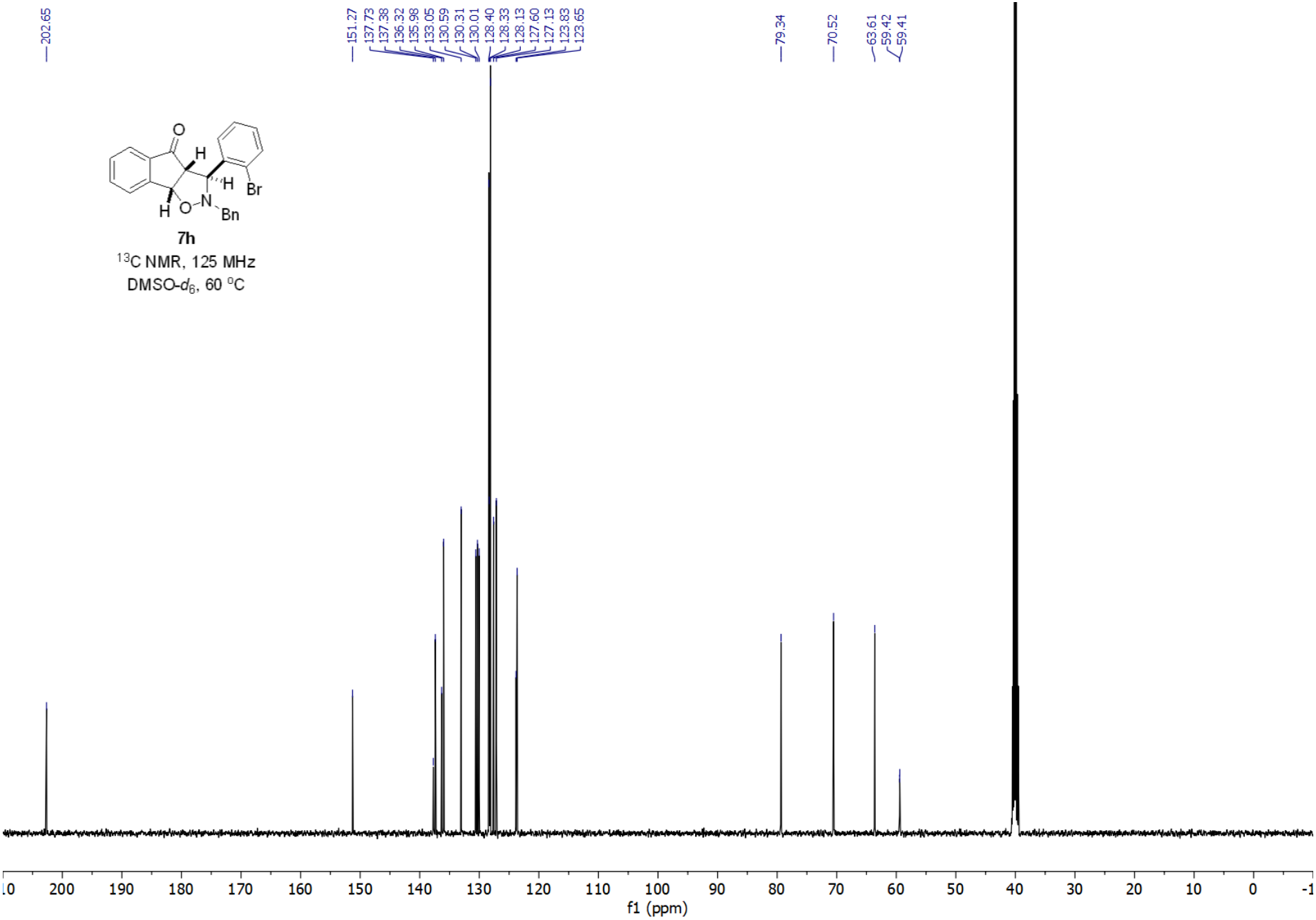
DMSO-d_6, 25 ^{o}C

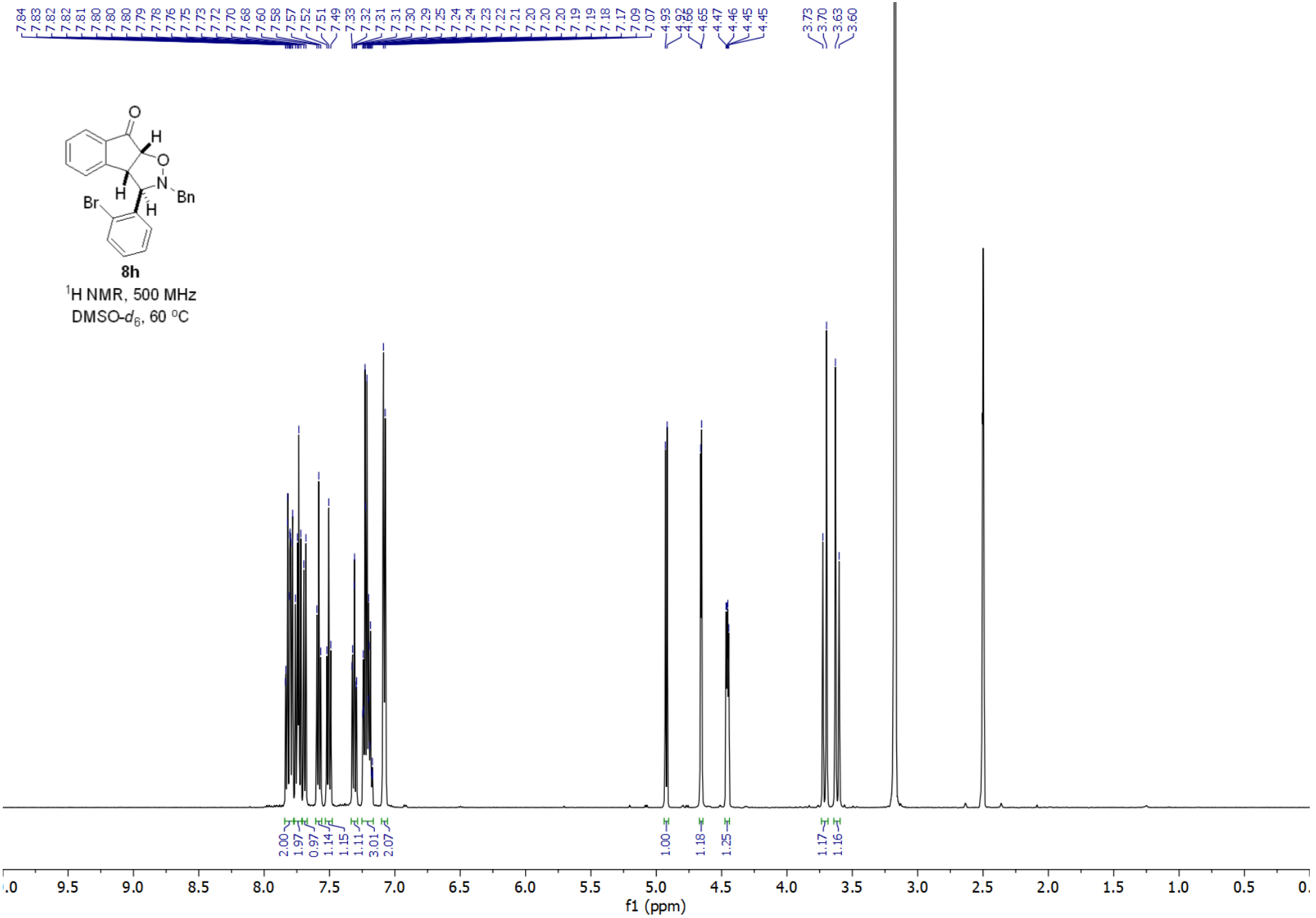


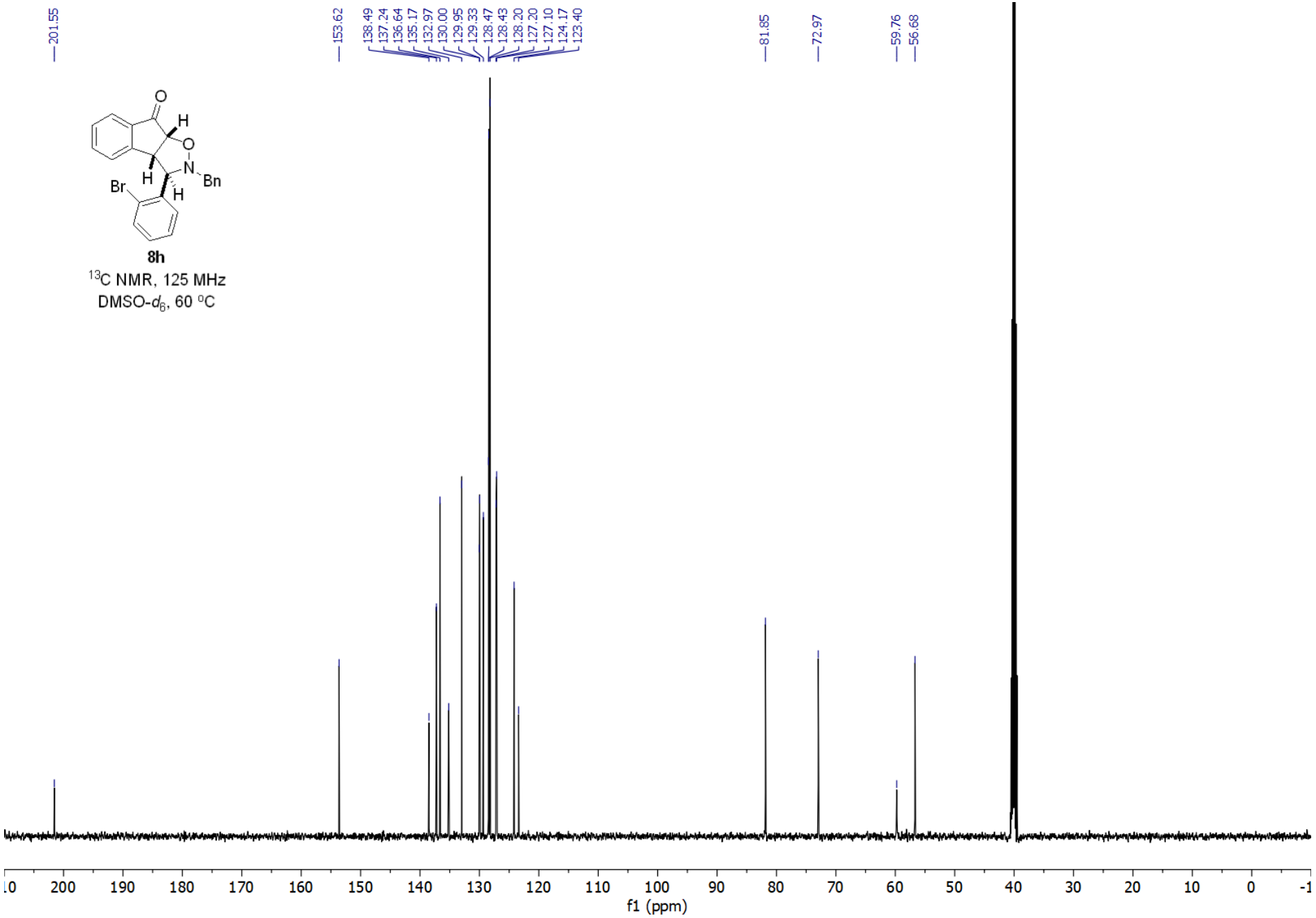

7.81 7.79 7.78 7.74 7.72 7.67 7.67 7.66 7.66 7.65 7.65 7.64 7.64 7.56 7.55 7.53 7.50 7.48 7.25 7.24 7.24 7.23 7.23 7.22 7.21 7.20 7.20 7.20 7.19 7.19 7.18 7.17 7.17 7.13 7.12 6.90 6.90 6.90 6.89 6.89 6.88 6.88 5.81 5.80 4.44 4.42 3.96 3.94 3.94 3.92 3.91 3.79 3.76
O
H
H
Br
H
O
N
Bn
6h
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.06 0.97 1.01 1.06 1.01 4.96 2.01 1.04 1.00 1.17 2.37 1.24
f1 (ppm)

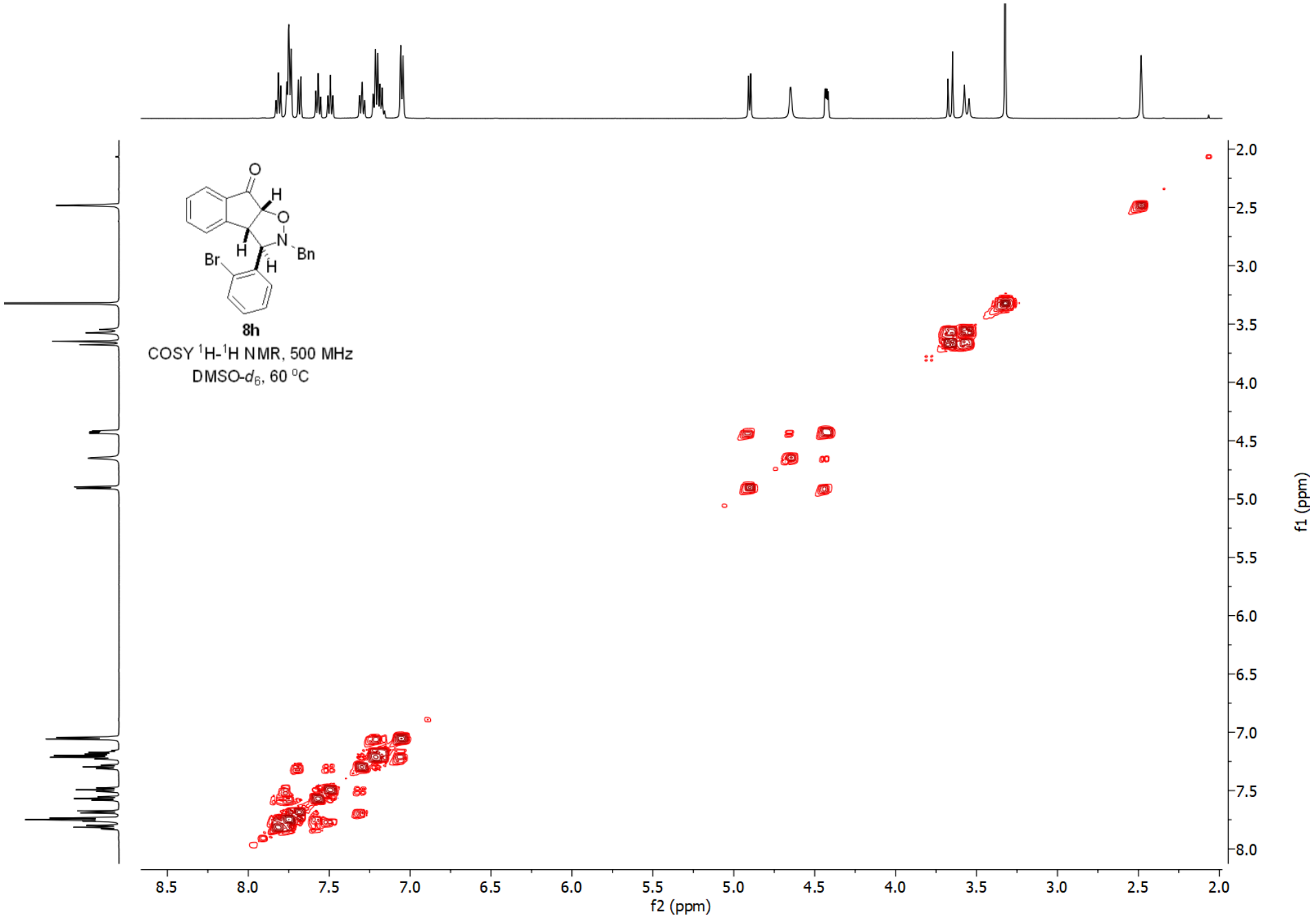

200.77
152.91
138.30
137.13
135.61
135.38
132.77
129.86
129.56
128.66
128.27
128.12
127.76
127.04
126.65
124.17
121.92
78.09
71.90
58.51
57.53
O
H
H
Br
H
O
N
Bn
6h
13C NMR, 125 MHz
DMSO-d6, 25 °C
136 134 132 130 128 126 124 122
f1 (ppm)
f1 (ppm)

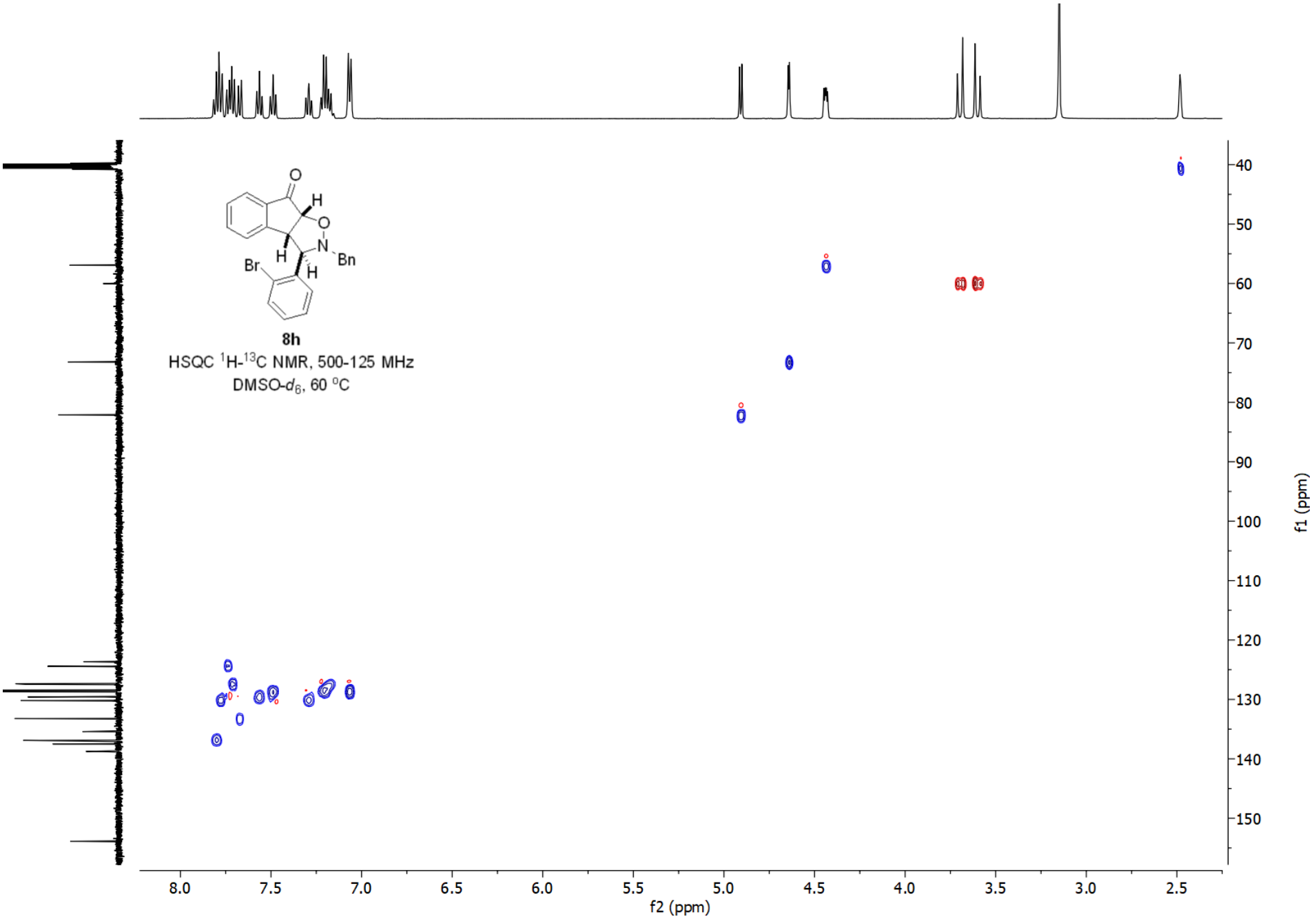

7.82 7.81 7.80 7.80 7.79 7.79 7.78 7.77 7.77 7.76 7.75 7.74 7.73 7.67 7.67 7.66 7.66 7.65 7.64 7.64 7.63 7.63 7.50 7.48 7.47 7.31 7.30 7.29 7.29 7.28 7.27 7.22 7.21 7.21 7.20 7.20 7.19 7.18 7.18 7.17 7.17 7.06 7.05 5.87 4.70 4.69
3.92 3.91 3.90 3.89 3.72 3.69 3.65 3.63
O
H
H
Br
O
N
H
Bn
7h
1H NMR, 500 MHz
DMSO-d6, 60 °C
4.03 1.86 1.05 1.01 2.96 1.95 1.00 1.01 1.11 1.33 1.30
f1 (ppm)

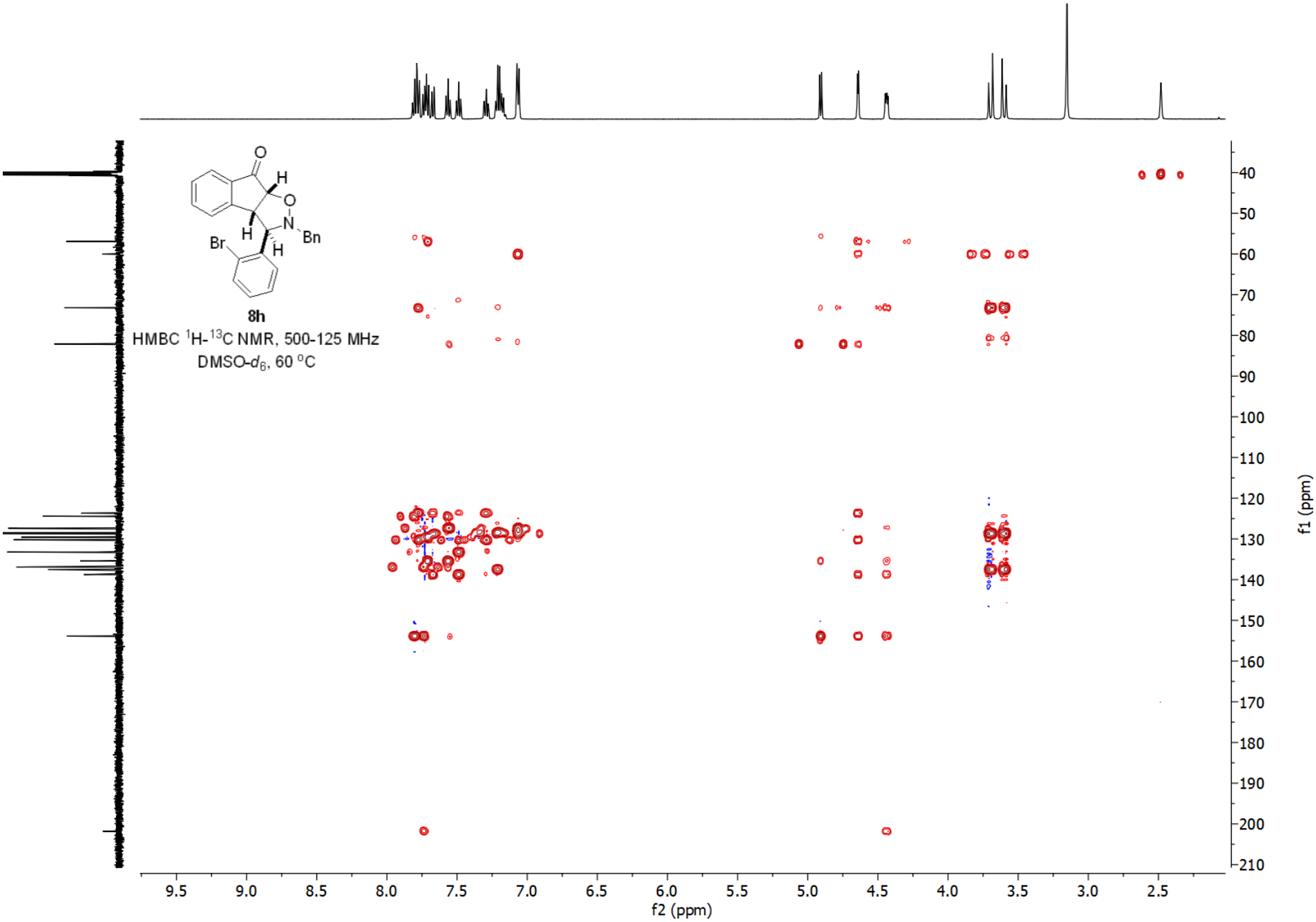

202.65
151.27
137.73
137.38
136.32
135.98
133.05
130.59
130.31
130.01
128.40
128.33
128.13
127.60
127.13
123.83
123.65
79.34
70.52
63.61
59.42
59.41
O
H
H
Br
H
O
N
Bn
7h
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

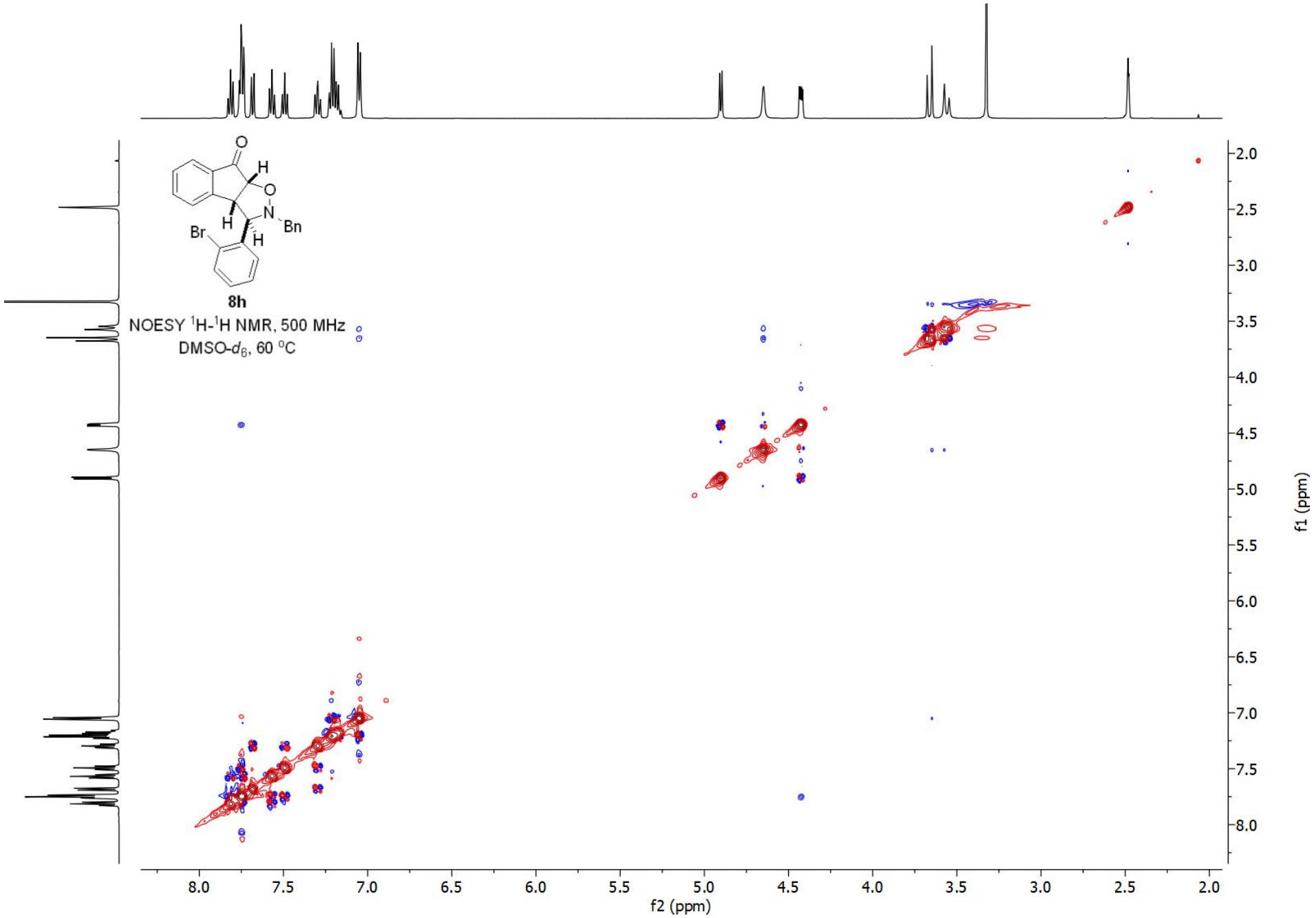

7.84 7.83 7.82 7.82 7.81 7.80 7.80 7.80 7.79 7.78 7.76 7.75 7.73 7.72 7.70 7.68 7.60 7.58 7.57 7.52 7.51 7.49 7.33 7.32 7.31 7.31 7.30 7.29 7.25 7.24 7.24 7.23 7.22 7.21 7.20 7.20 7.20 7.19 7.19 7.18 7.17 7.09 7.07 4.93 4.92 4.66 4.65 4.47 4.46 4.45 4.45 3.73 3.70 3.63 3.60
O
H
O
N
Bn
H
H
Br
8h
1H NMR, 500 MHz
DMSO-d6, 60 °C
2.00 1.97 0.97 1.14 1.15 1.11 3.01 2.07 1.00 1.18 1.25 1.17 1.16
f1 (ppm)

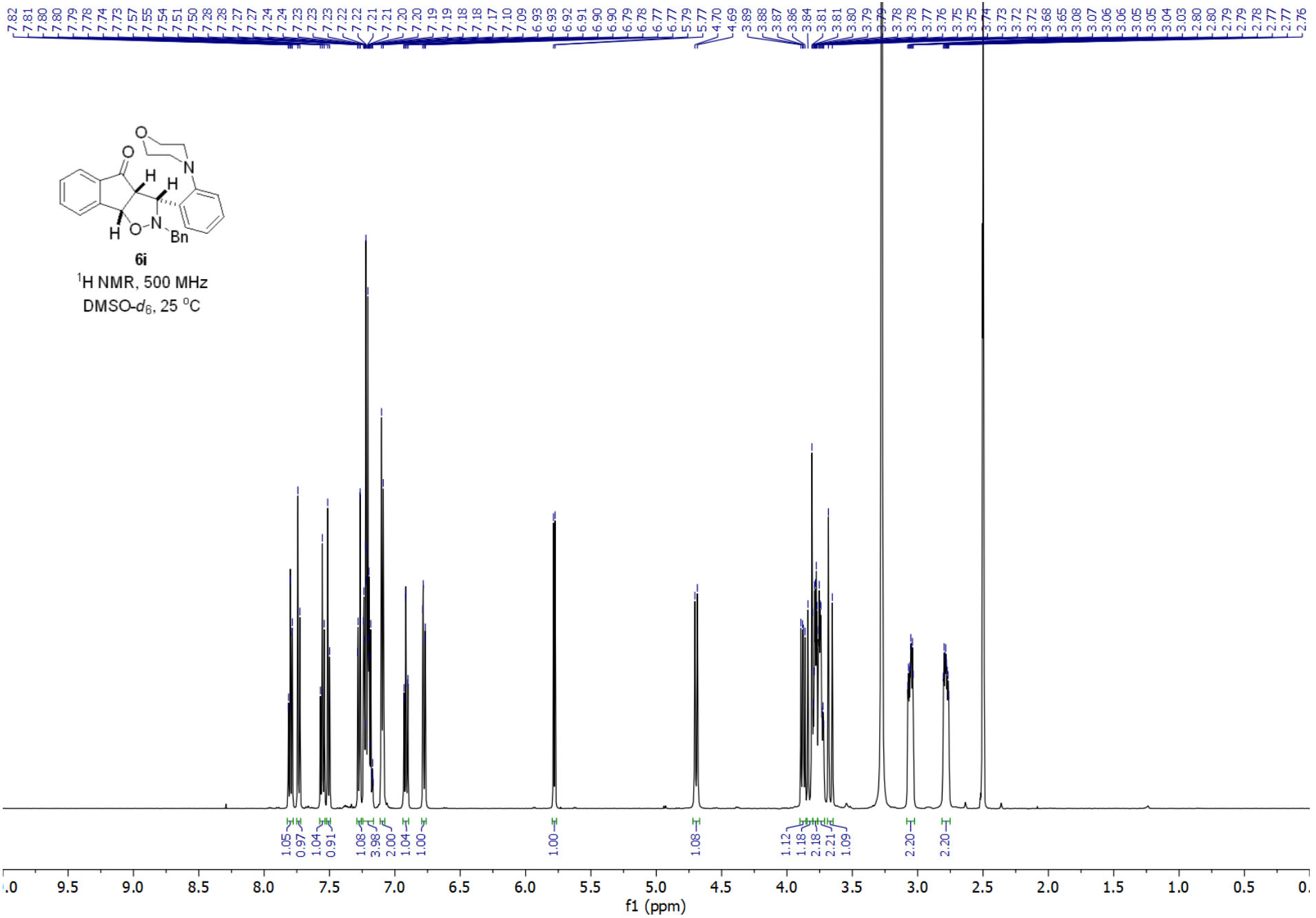

201.55
153.62
138.49
137.24
136.64
135.17
132.97
130.00
129.95
129.33
128.47
128.43
128.20
127.20
127.10
124.17
123.40
81.85
72.97
59.76
56.68
O
H
O
N
Bn
H
Br
H
8h
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

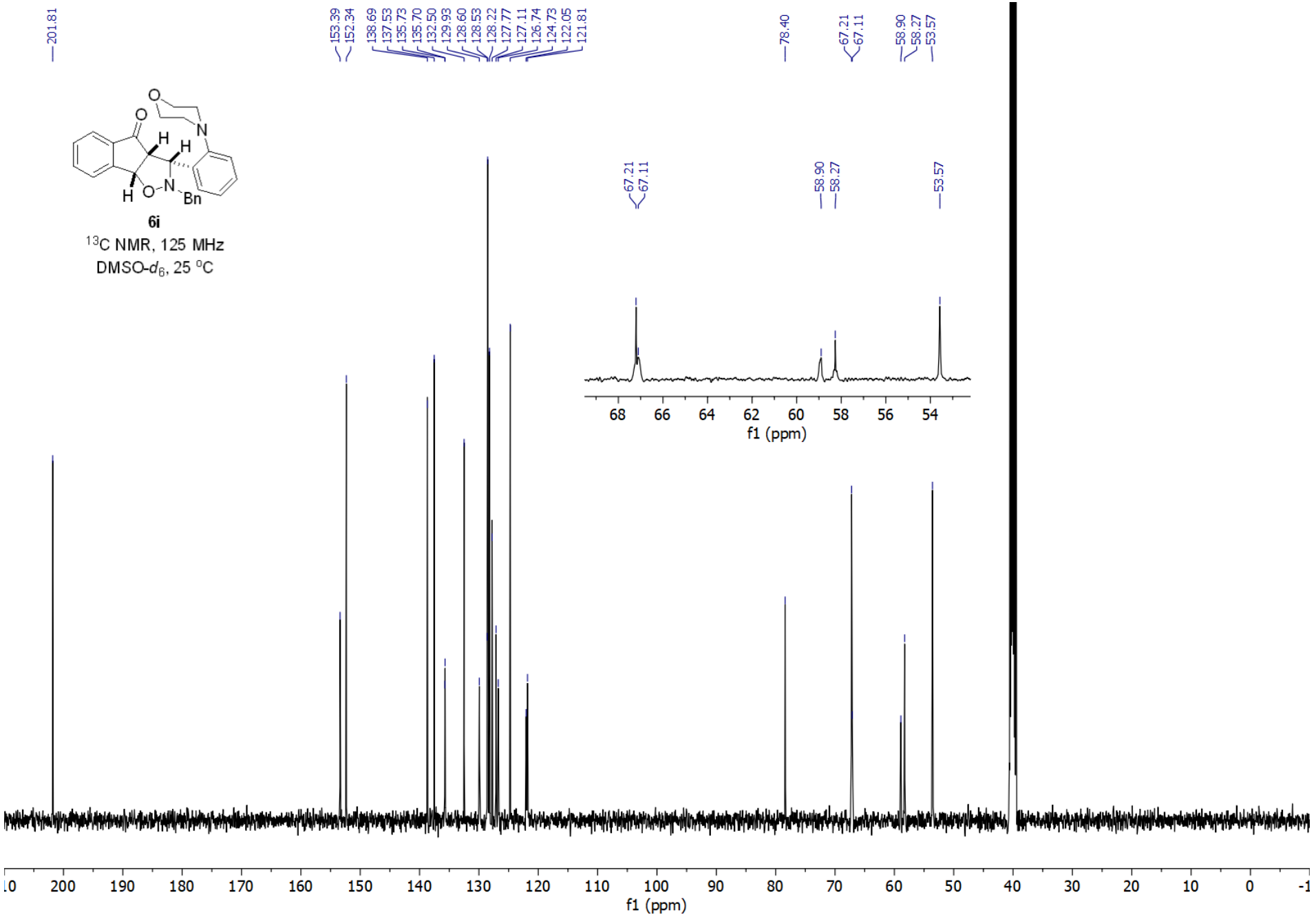

O
H
O
N
Bn
H
H
Br
8h
COSY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 60 °C
f2 (ppm)
f1 (ppm)

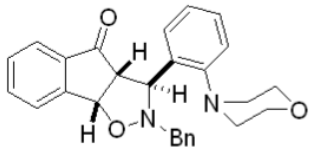

O
H
O
N
Bn
H
Br
H
8h
HSQC ^{1}H-^{13}C NMR, 500-125 MHz
DMSO-d_6, 60 ^{o}C
40
50
60
70
80
90
100
110
120
130
140
150
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
f2 (ppm)


8h
HMBC ^{1}H-^{13}C NMR, 500-125 MHz
DMSO-d_6, 60 ^{o}C
f2 (ppm)
f1 (ppm)


8h
NOESY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 60 ^{o}C
f2 (ppm)
f1 (ppm)


6i
1H NMR, 500 MHz
DMSO-d6, 25 °C
f1 (ppm)


201.81
153.39
152.34
138.69
137.53
135.73
135.70
132.50
129.93
128.60
128.53
128.22
127.77
127.11
126.74
124.73
122.05
121.81
78.40
67.21
67.11
58.90
58.27
53.57
O
O
N
H
H
H
O
N
Bn
6i
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)
f1 (ppm)

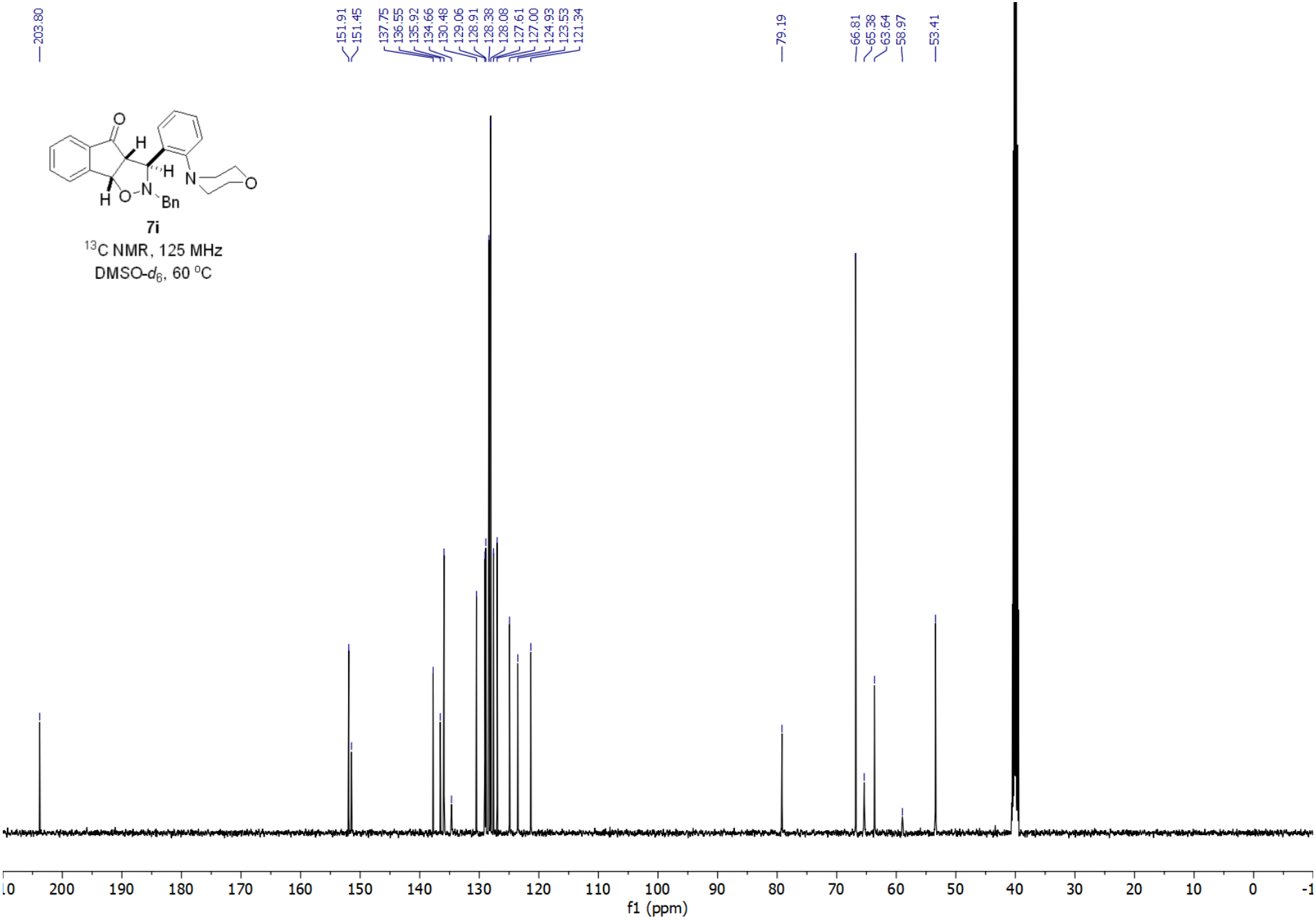


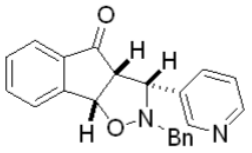
7i

^{1}H NMR, 500 MHz

DMSO-d_6, 60 ^{o}C

f1 (ppm)

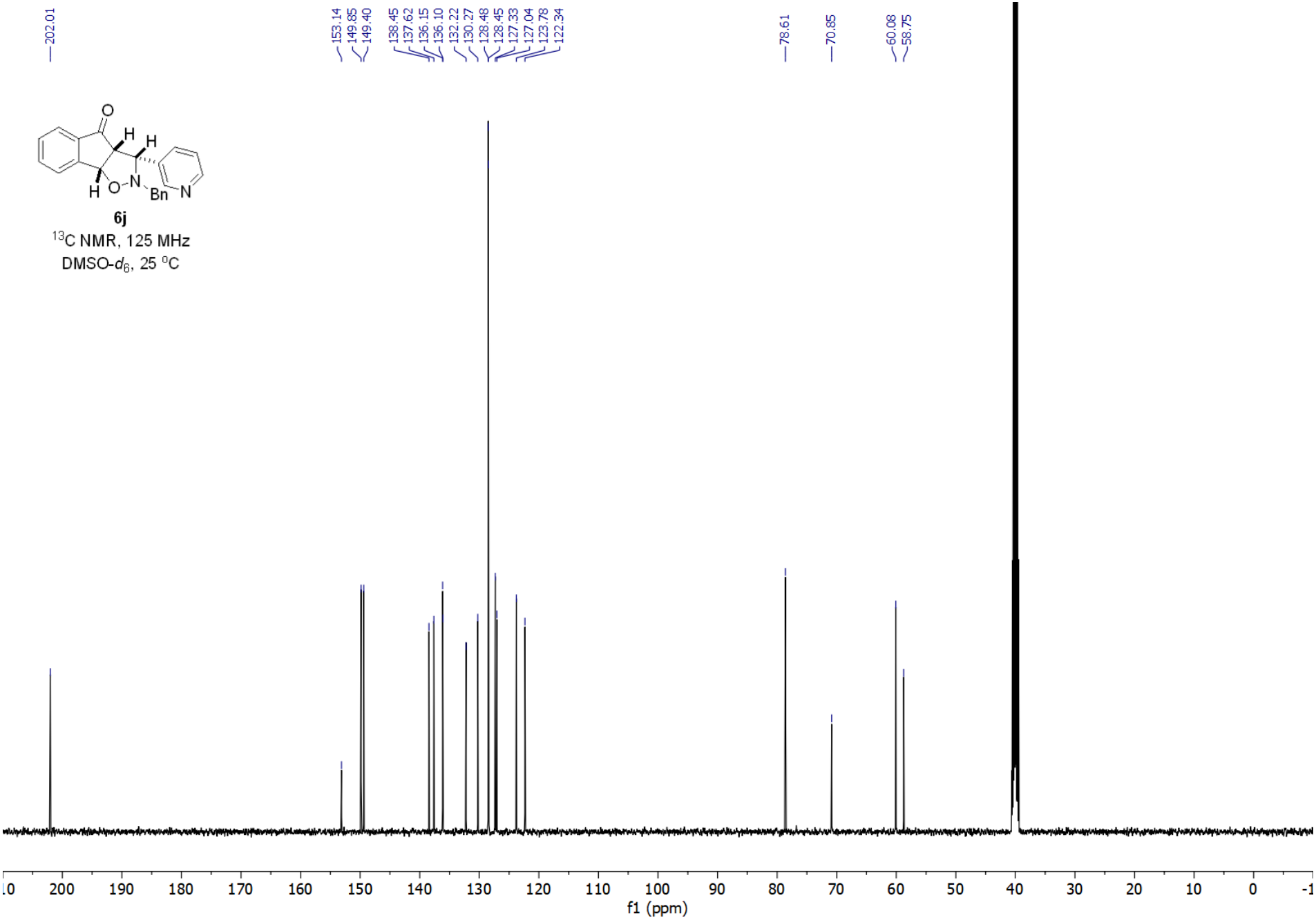

203.80
151.91
151.45
137.75
136.55
135.92
134.66
130.48
129.06
128.91
128.38
128.08
127.61
127.00
124.93
123.53
121.34
79.19
66.81
65.38
63.64
58.97
53.41
O
H
H
N
O
H
O
N
Bn
7i
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

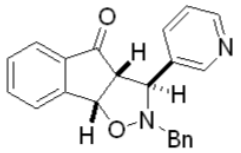


6j

^{1}H NMR, 500 MHz

DMSO-d_6, 25 ^{o}C


202.01
153.14
149.85
149.40
138.45
137.62
136.15
136.10
132.22
130.27
128.48
128.45
127.33
127.04
123.78
122.34
78.61
70.85
60.08
58.75
O
H
H
H
O
N
Bn
N
6j
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

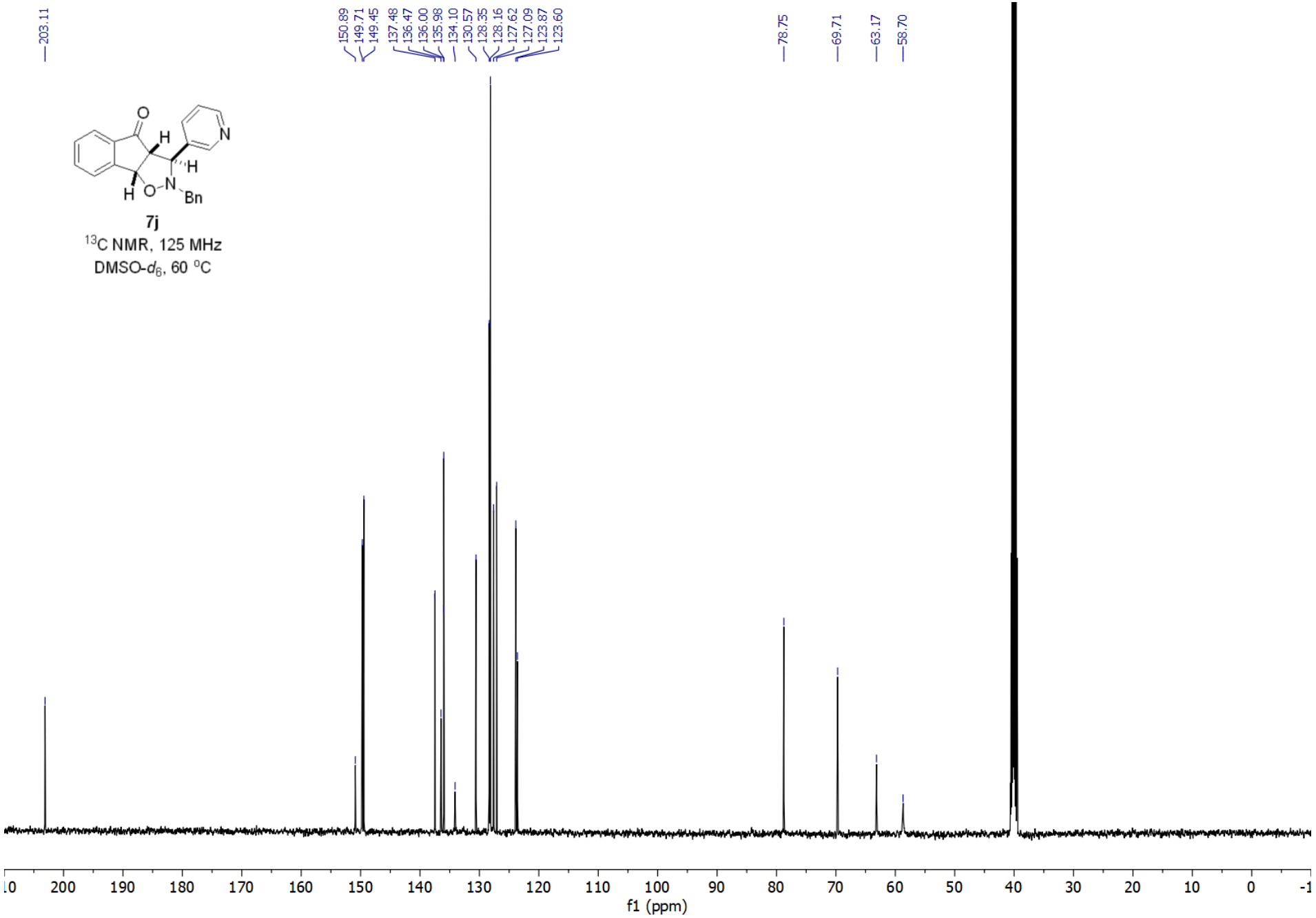


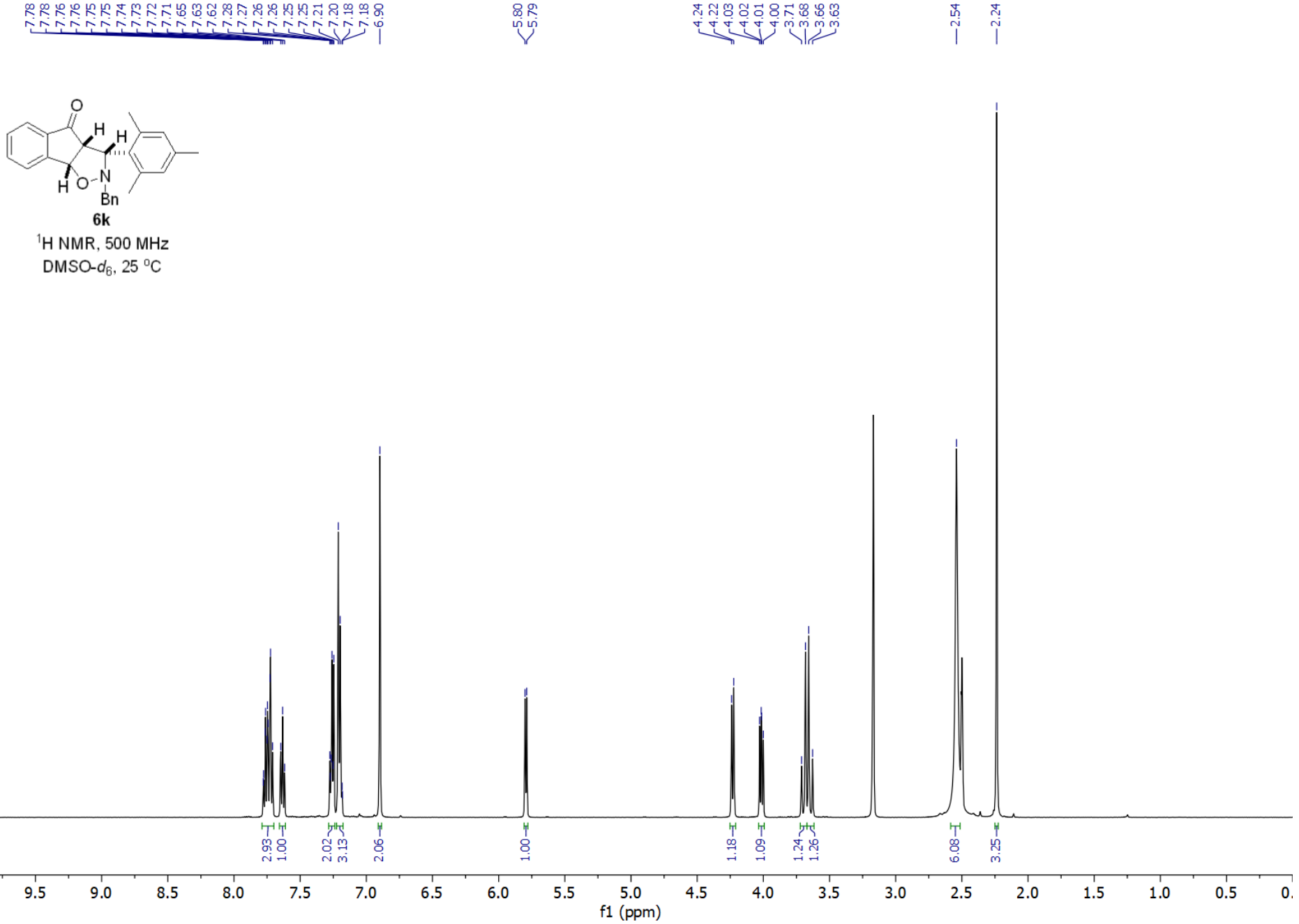
7j

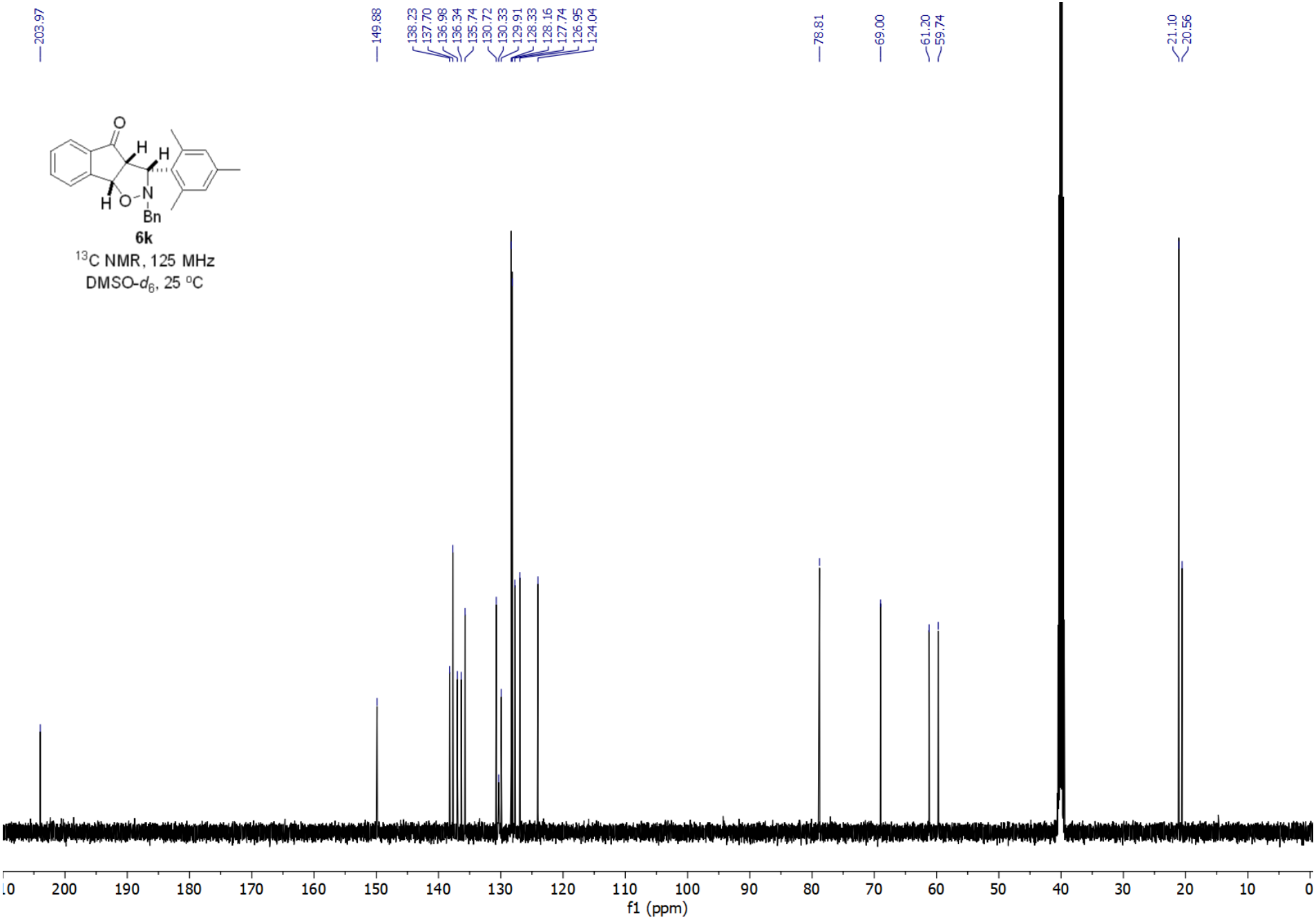
^{1}H NMR, 500 MHz

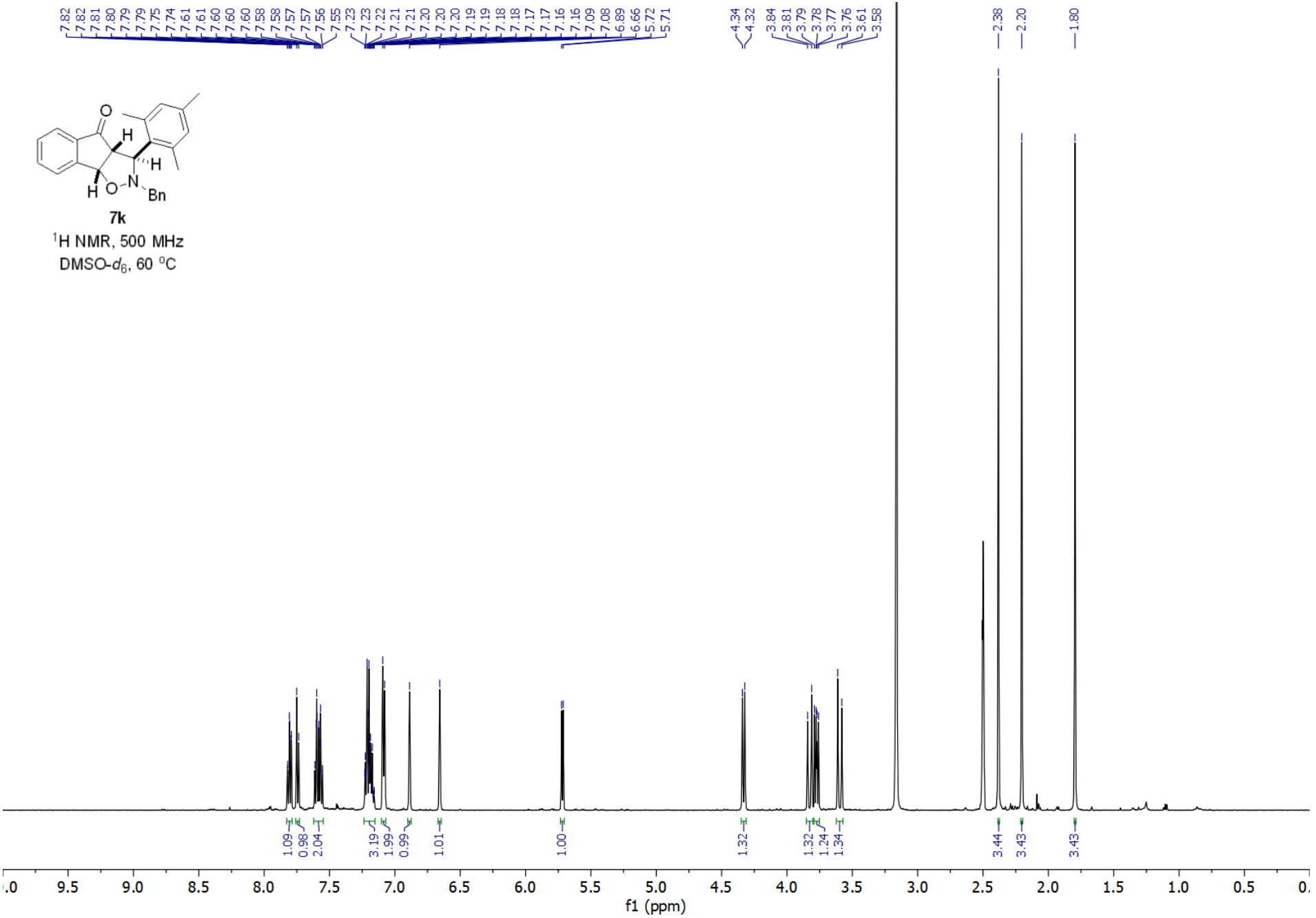
DMSO-d_6, 60 ^{0}C

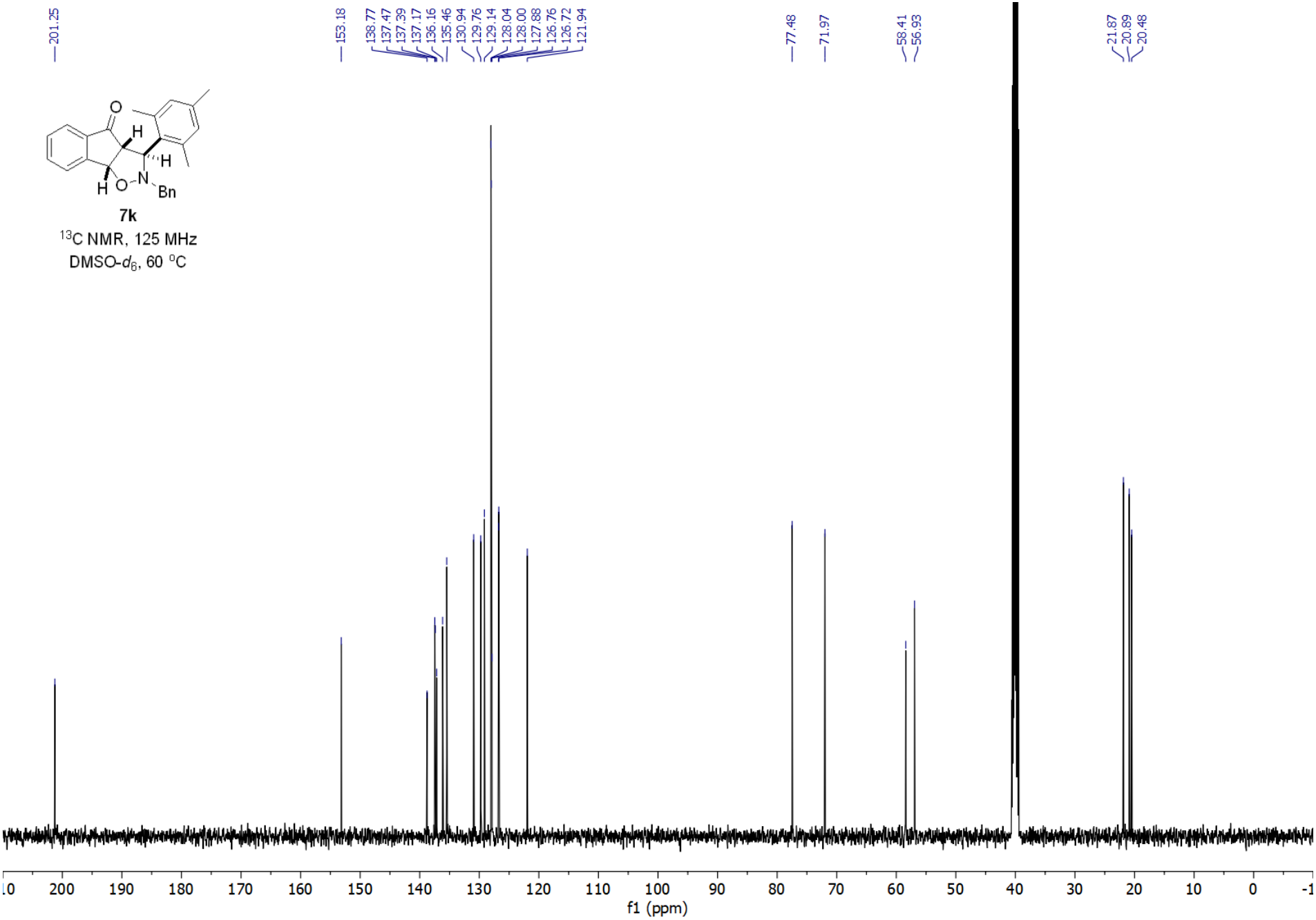
f1 (ppm)

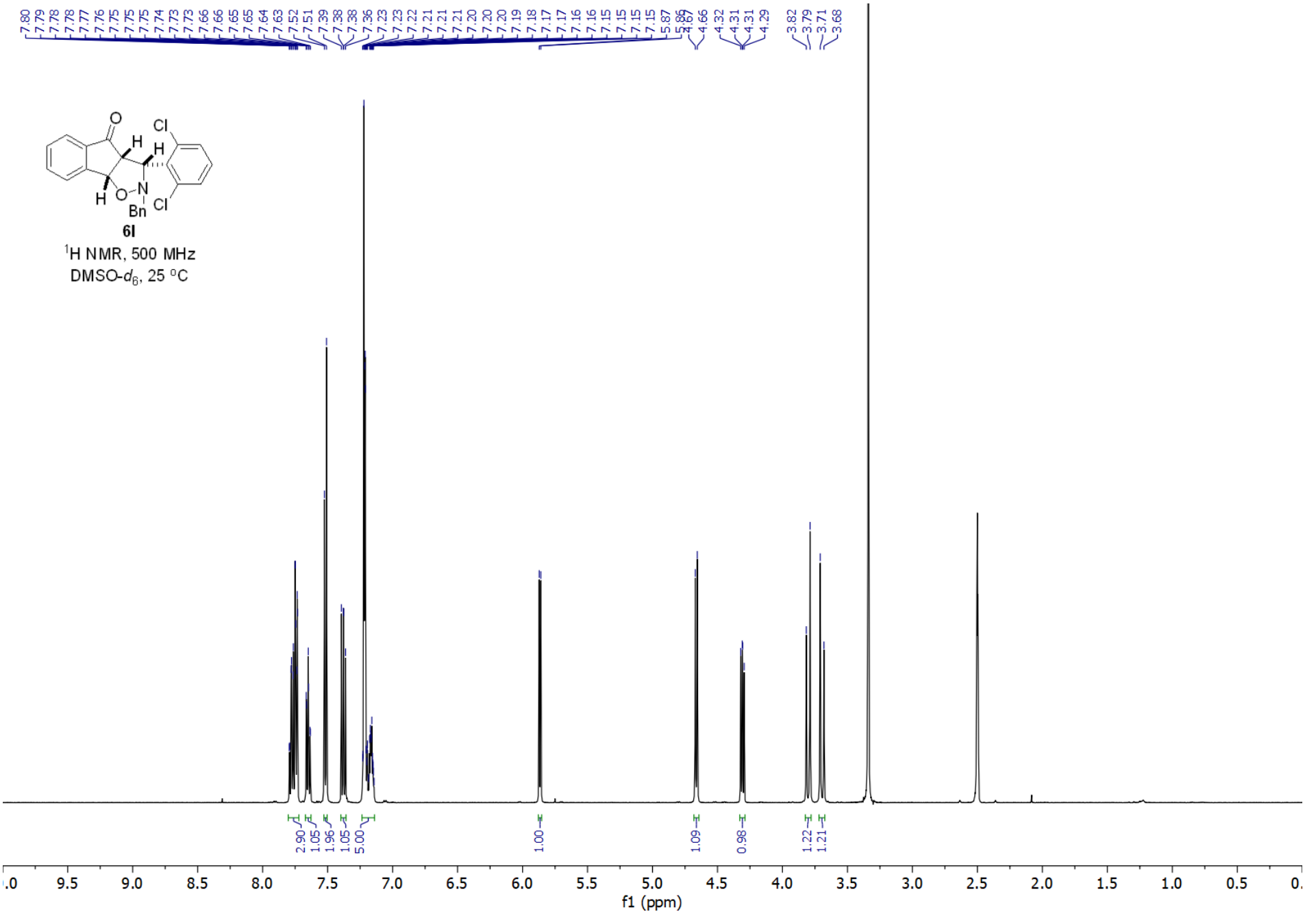

203.11
150.89
149.71
149.45
137.48
136.47
136.00
135.98
134.10
130.57
128.35
128.16
127.62
127.09
123.87
123.60
78.75
69.71
63.17
58.70
O
H
N
H
H
O
N
Bn
7j
13C NMR, 125 MHz
DMSO-d6, 60 °C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

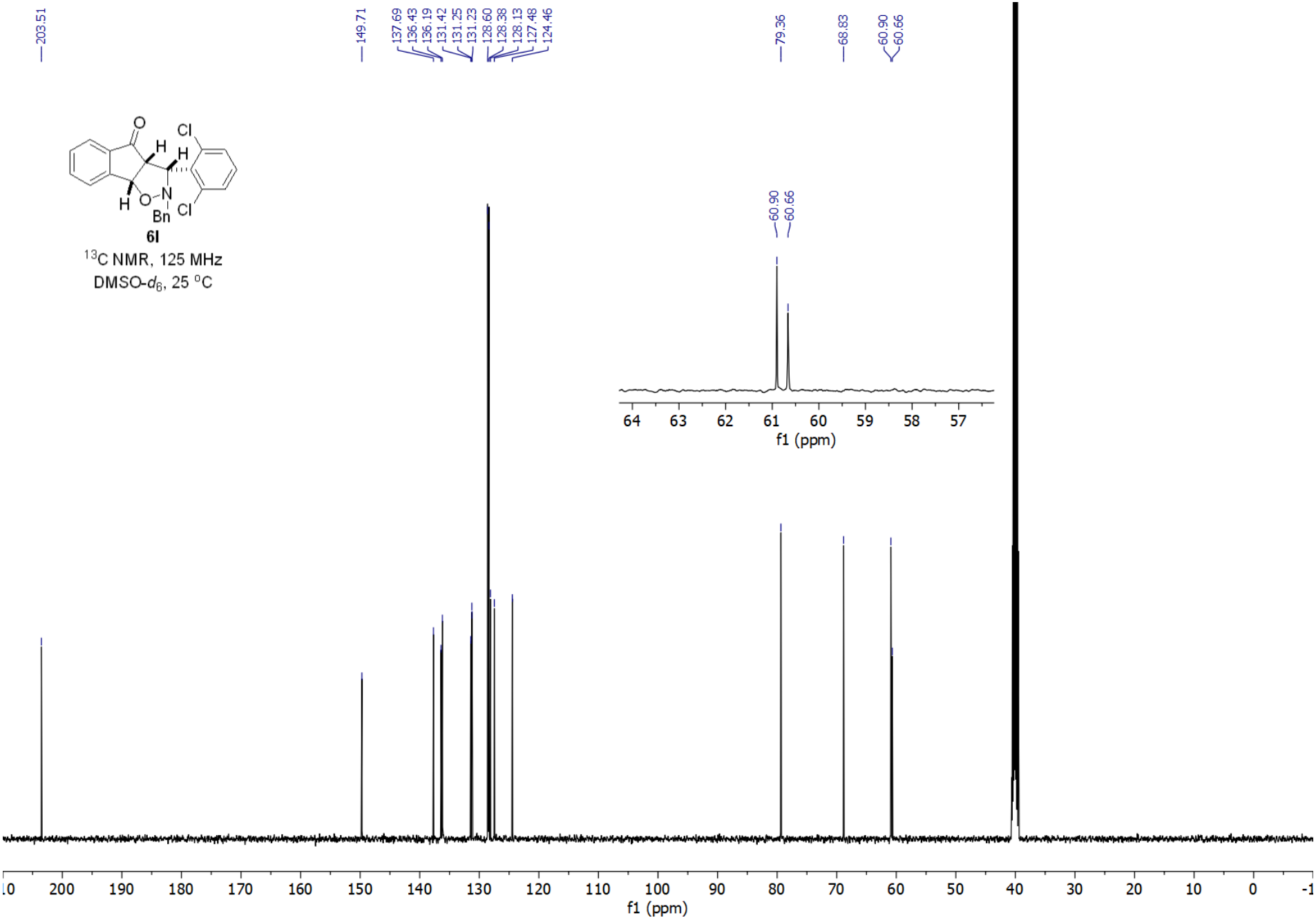

7.78
7.78
7.76
7.76
7.75
7.75
7.74
7.73
7.72
7.71
7.65
7.63
7.62
7.28
7.27
7.26
7.26
7.25
7.25
7.21
7.20
7.18
7.18
6.90
5.80
5.79
4.24
4.22
4.03
4.02
4.01
4.00
3.71
3.68
3.66
3.63
2.54
2.24
O
H
H
H
O
N
Bn
6k
1H NMR, 500 MHz
DMSO-d6, 25 °C
2.93
1.00
2.02
3.13
2.06
1.00
1.18
1.09
1.24
1.26
6.08
3.25
f1 (ppm)

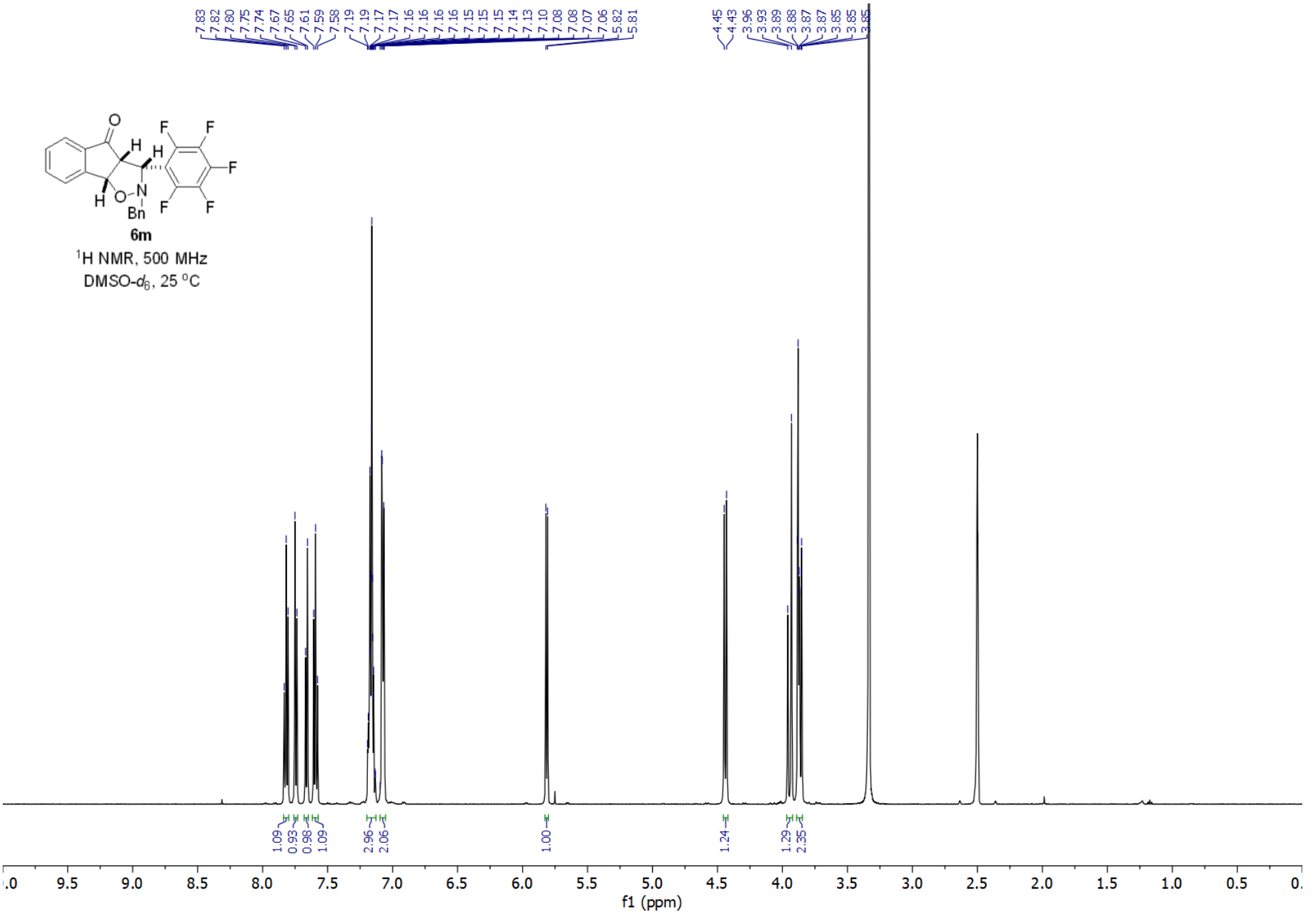

203.97
149.88
138.23
137.70
136.98
136.34
135.74
130.72
130.33
129.91
128.33
128.16
127.74
126.95
124.04
78.81
69.00
61.20
59.74
21.10
20.56
O
H
H
O
N
Bn
6k
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

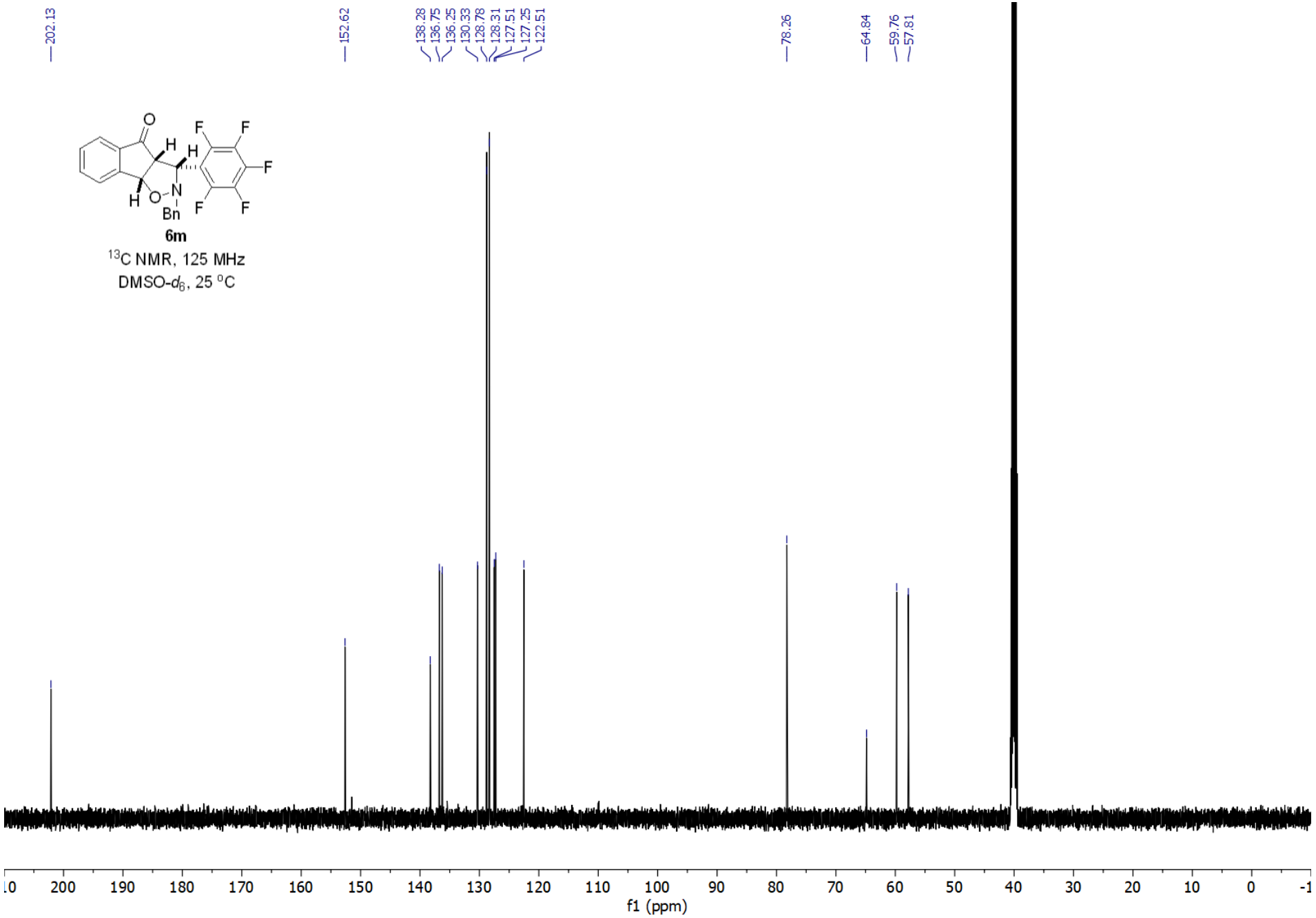

7.82 7.82 7.81 7.80 7.79 7.79 7.75 7.74 7.61 7.61 7.60 7.60 7.60 7.58 7.58 7.57 7.57 7.56 7.55 7.23 7.22 7.21 7.21 7.20 7.20 7.19 7.19 7.18 7.18 7.17 7.17 7.16 7.16 7.09 7.08 6.89 6.66 5.72 5.71
4.34 4.32 3.84 3.81 3.79 3.78 3.77 3.76 3.61 3.58
2.38 2.20 1.80
O H H H O N Bn
7k
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.09 0.98 2.04 3.19 1.99 0.99 1.01 1.00 1.32 1.32 1.24 1.34 3.44 3.43 3.43
f1 (ppm)


201.25
153.18
138.77
137.47
137.39
137.17
136.16
135.46
130.94
129.76
129.14
128.04
128.00
127.88
126.76
126.72
121.94
77.48
71.97
58.41
56.93
21.87
20.89
20.48
O
H
H
H
O
N
Bn
7k
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)


7.80
7.79
7.78
7.78
7.77
7.76
7.75
7.75
7.75
7.74
7.73
7.73
7.66
7.66
7.65
7.65
7.64
7.63
7.52
7.51
7.39
7.38
7.38
7.36
7.23
7.23
7.22
7.21
7.21
7.21
7.20
7.20
7.20
7.19
7.18
7.17
7.17
7.16
7.16
7.15
7.15
7.15
7.15
5.87
4.67
4.66
4.32
4.31
4.31
4.29
3.82
3.79
3.71
3.68
O
H
H
Cl
H
O
N
Bn
Cl
6l
1H NMR, 500 MHz
DMSO-d6, 25 °C
2.90
1.05
1.96
1.05
5.00
1.00
1.09
0.98
1.22
1.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


203.51
149.71
137.69
136.43
136.19
131.42
131.25
131.23
128.60
128.38
128.13
127.48
124.46
79.36
68.83
60.90
60.66
O
H
H
Cl
O
N
Bn
Cl
H
6l
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)
f1 (ppm)

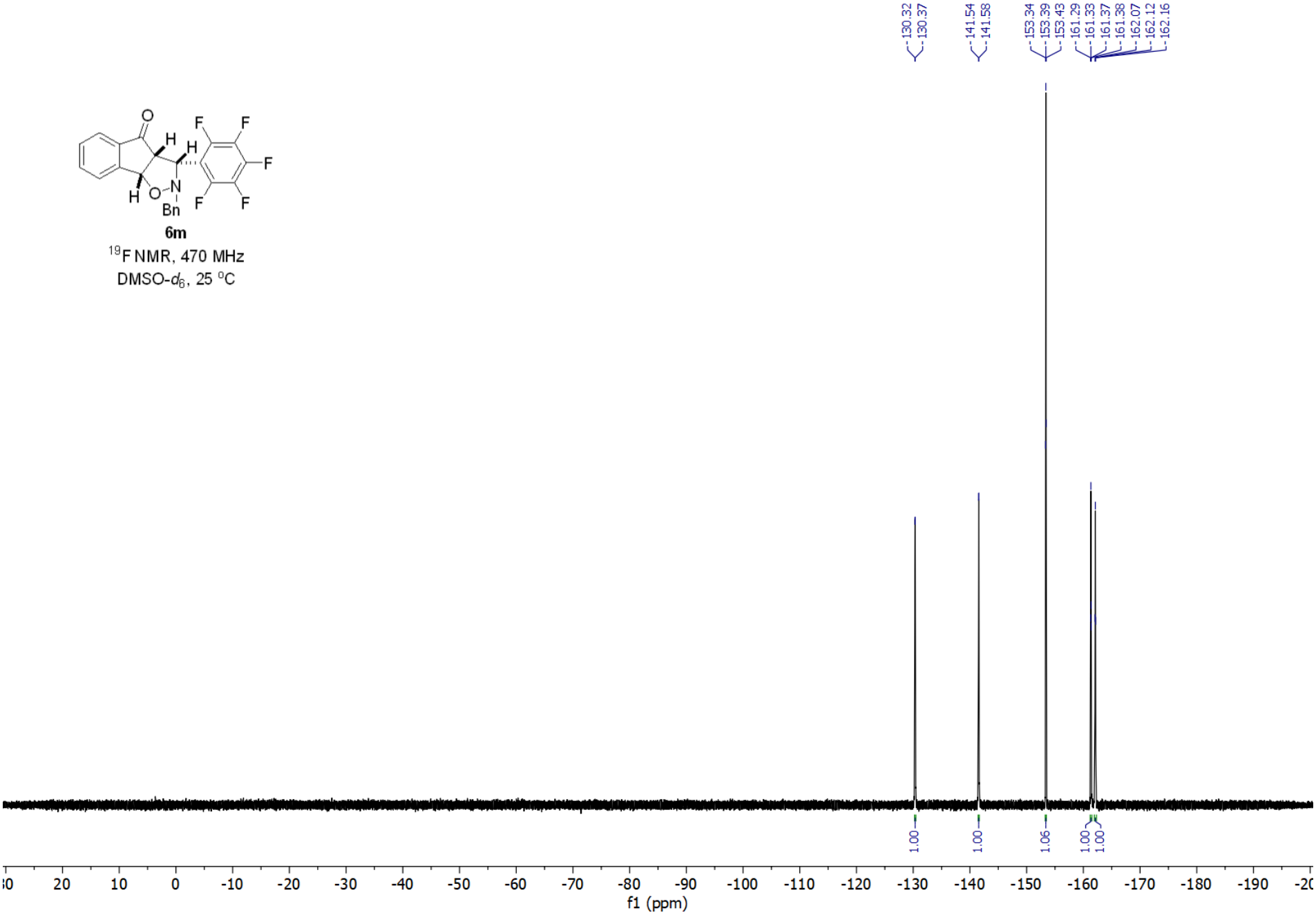

7.83
7.82
7.80
7.75
7.74
7.67
7.65
7.61
7.59
7.58
7.19
7.19
7.17
7.17
7.16
7.16
7.16
7.16
7.15
7.15
7.15
7.14
7.13
7.10
7.08
7.08
7.07
7.06
5.82
5.81
4.45
4.43
3.96
3.93
3.89
3.88
3.87
3.87
3.85
3.85
3.85
O
H
H
F
F
F
F
F
O
N
H
Bn
6m
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.09
0.93
0.98
1.09
2.96
2.06
1.00
1.24
1.29
2.35
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

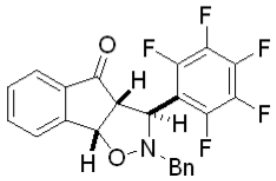

202.13
152.62
138.28
136.75
136.25
130.33
128.78
128.31
127.51
127.25
122.51
78.26
64.84
59.76
57.81
O
H
H
F
F
F
F
F
O
N
Bn
6m
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

6m

^{19}F NMR, 470 MHz

DMSO-d_6, 25 °C

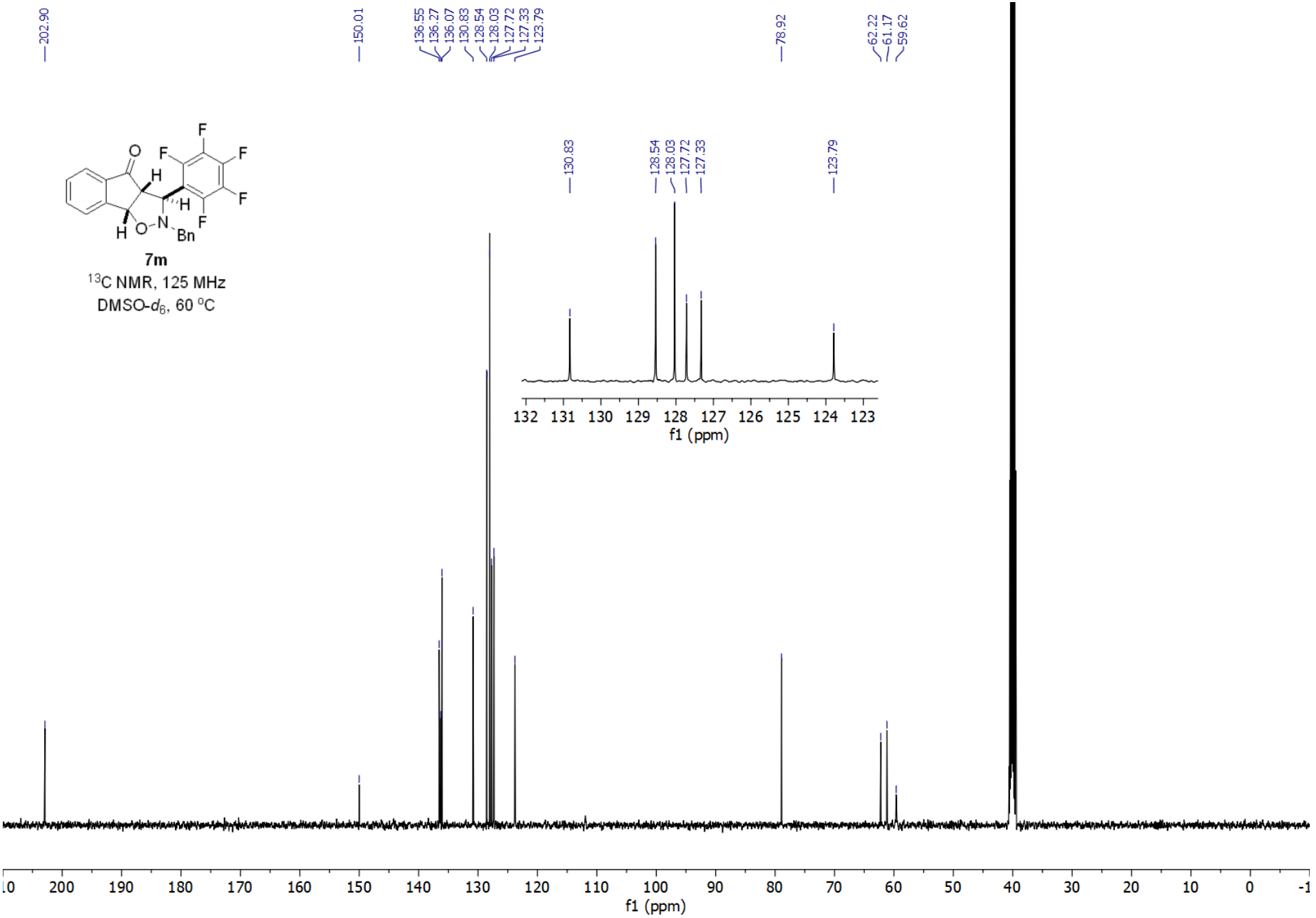




7m

^{1}H NMR, 500 MHz

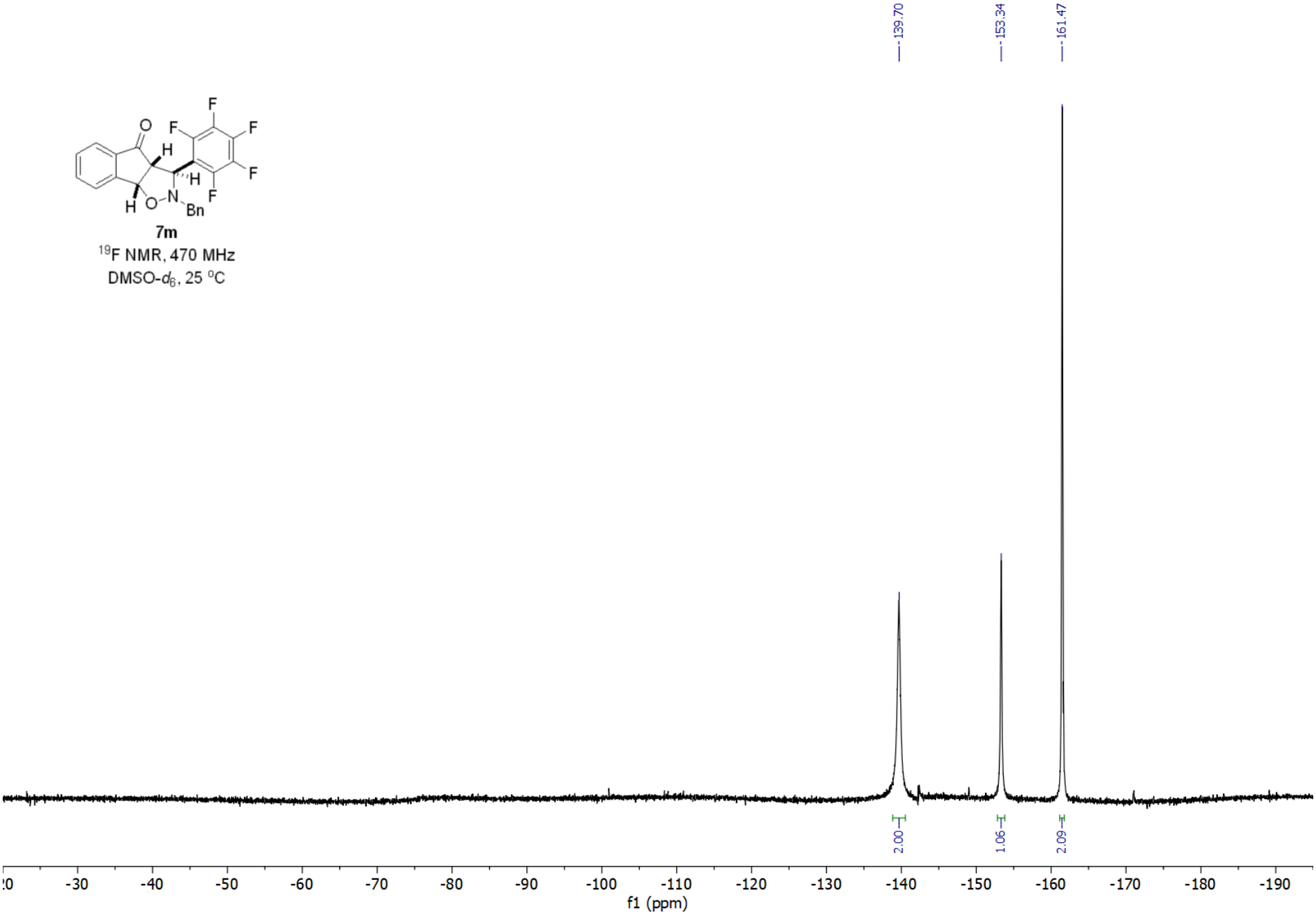
DMSO-d_6, 60 ^{0}C

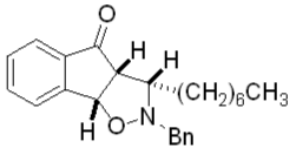

202.90
150.01
136.55
136.27
136.07
130.83
128.54
128.03
127.72
127.33
123.79
78.92
62.22
61.17
59.62
F
F
F
F
F
O
H
H
H
O
N
Bn
7m
13C NMR, 125 MHz
DMSO-d6, 60 °C
130.83
128.54
128.03
127.72
127.33
123.79
132 131 130 129 128 127 126 125 124 123
f1 (ppm)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

7m

^{19}F NMR, 470 MHz

DMSO-d_6, 25 ^{o}C

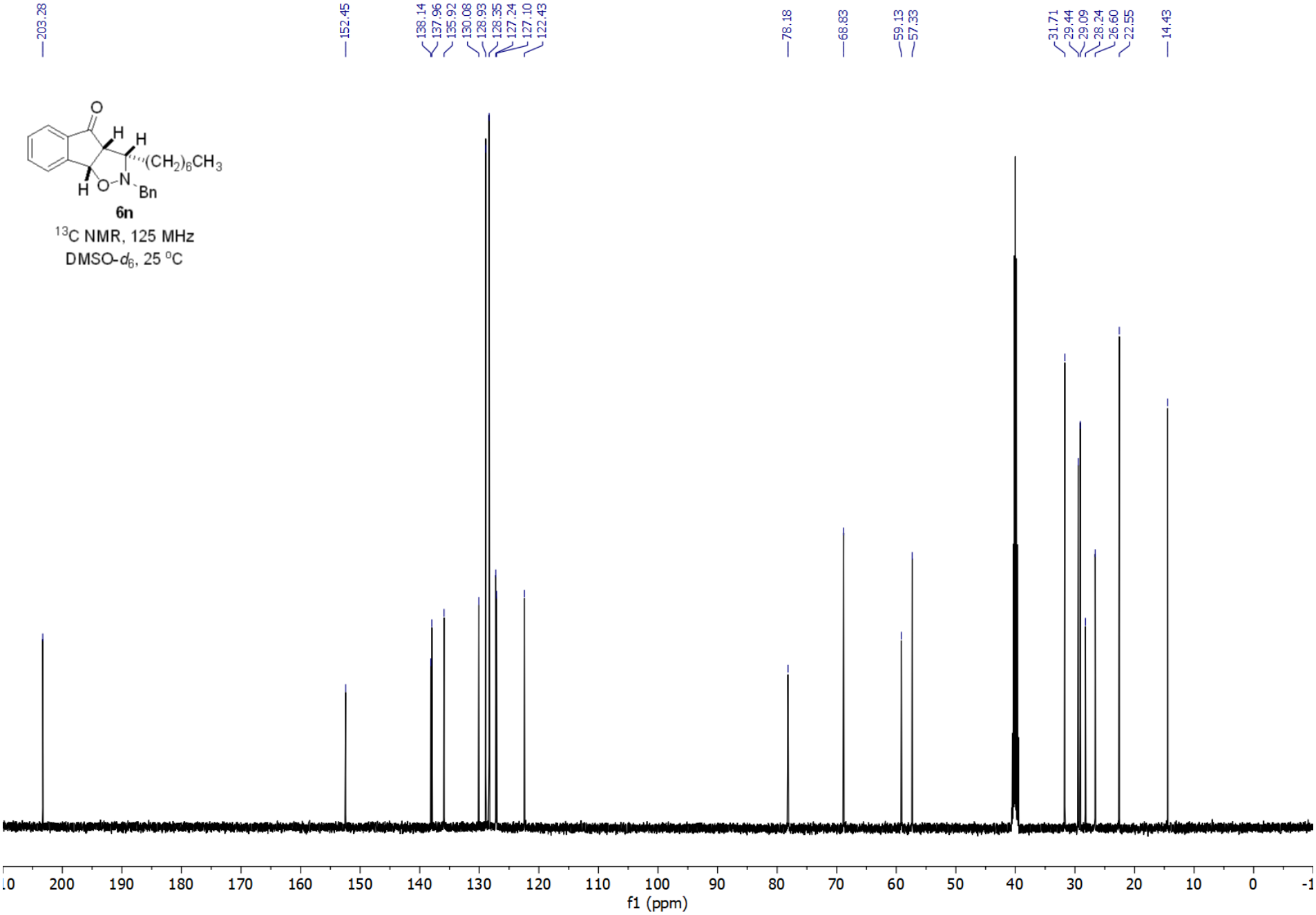


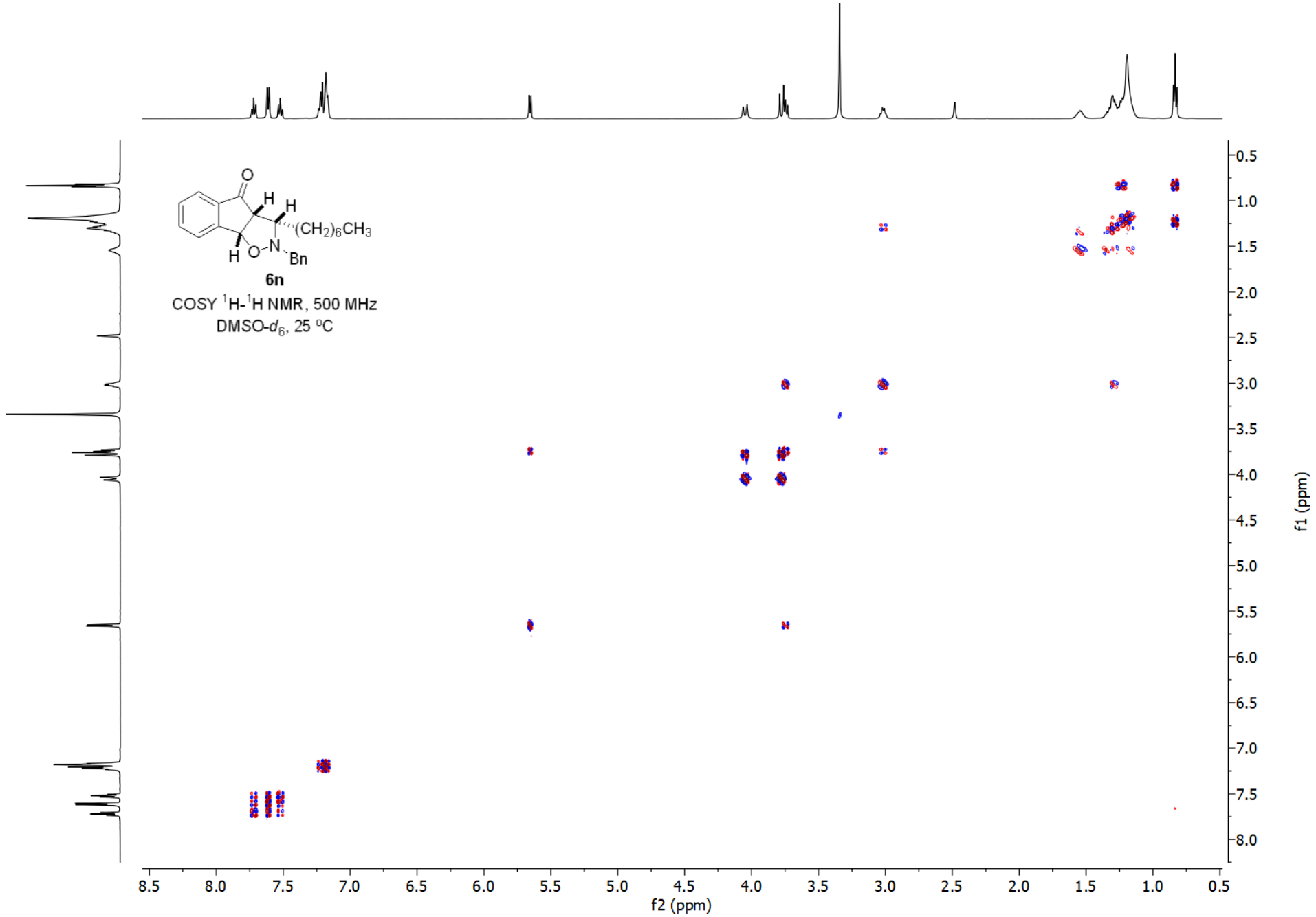


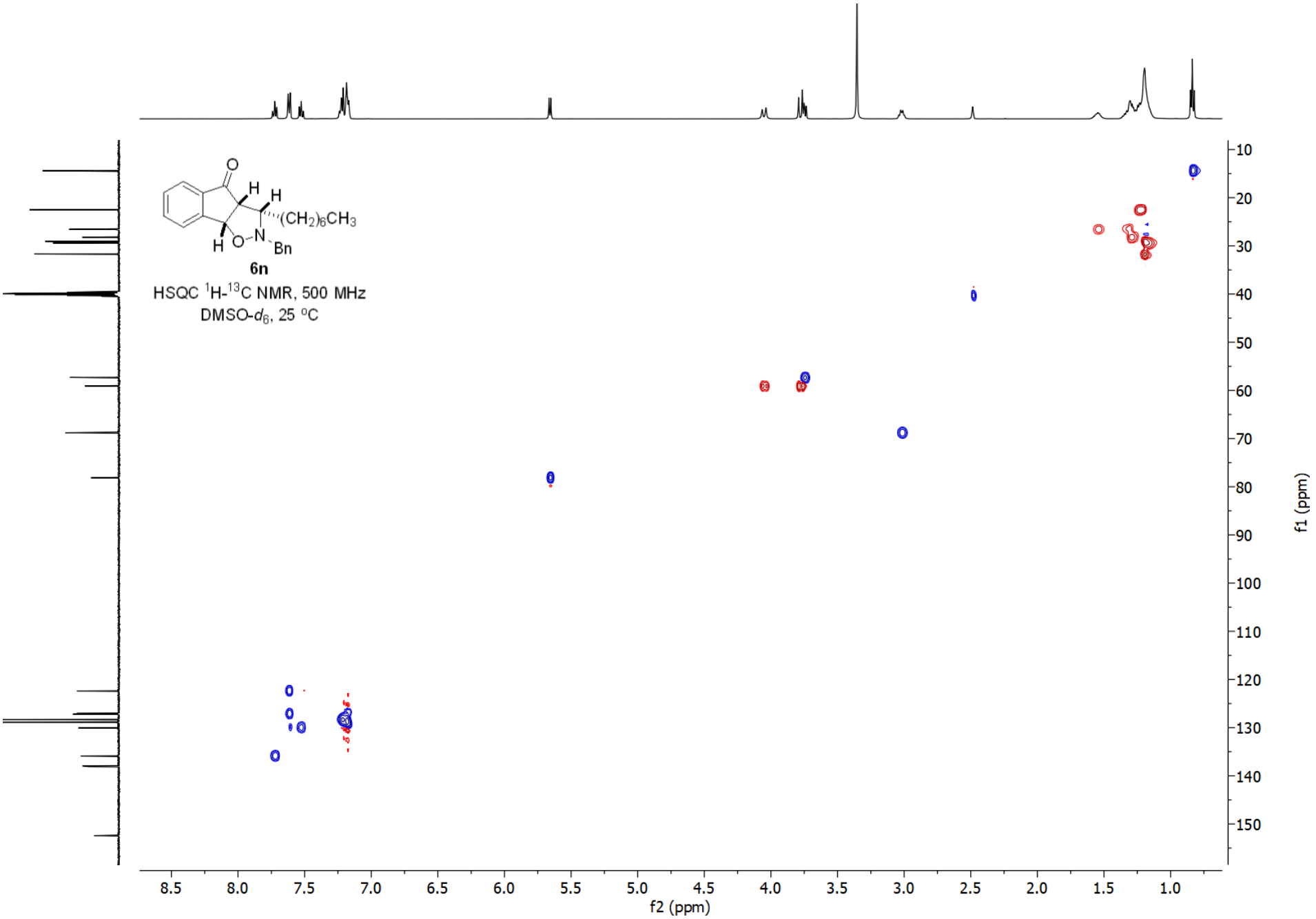
6n

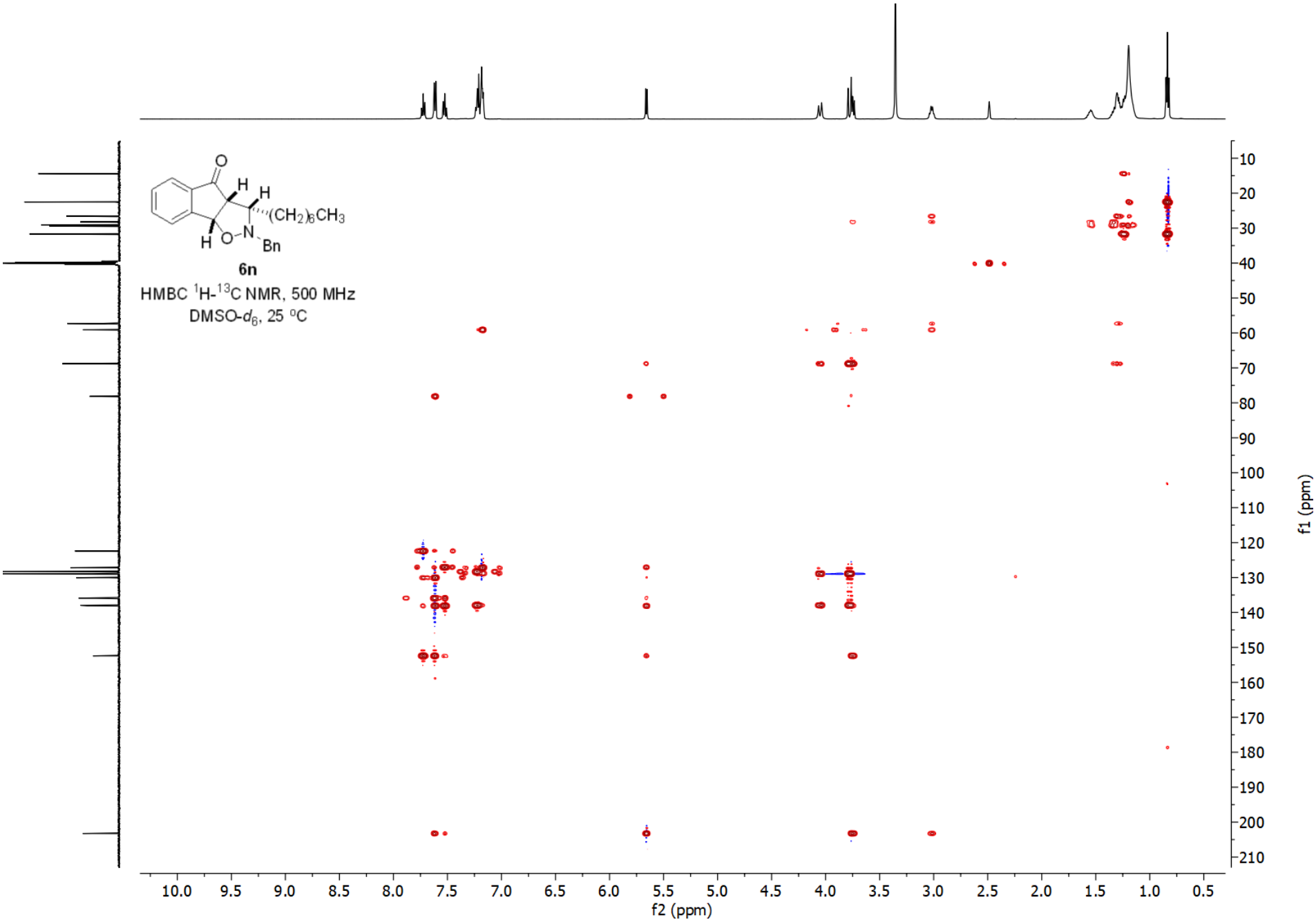
^{1}H NMR, 500 MHz

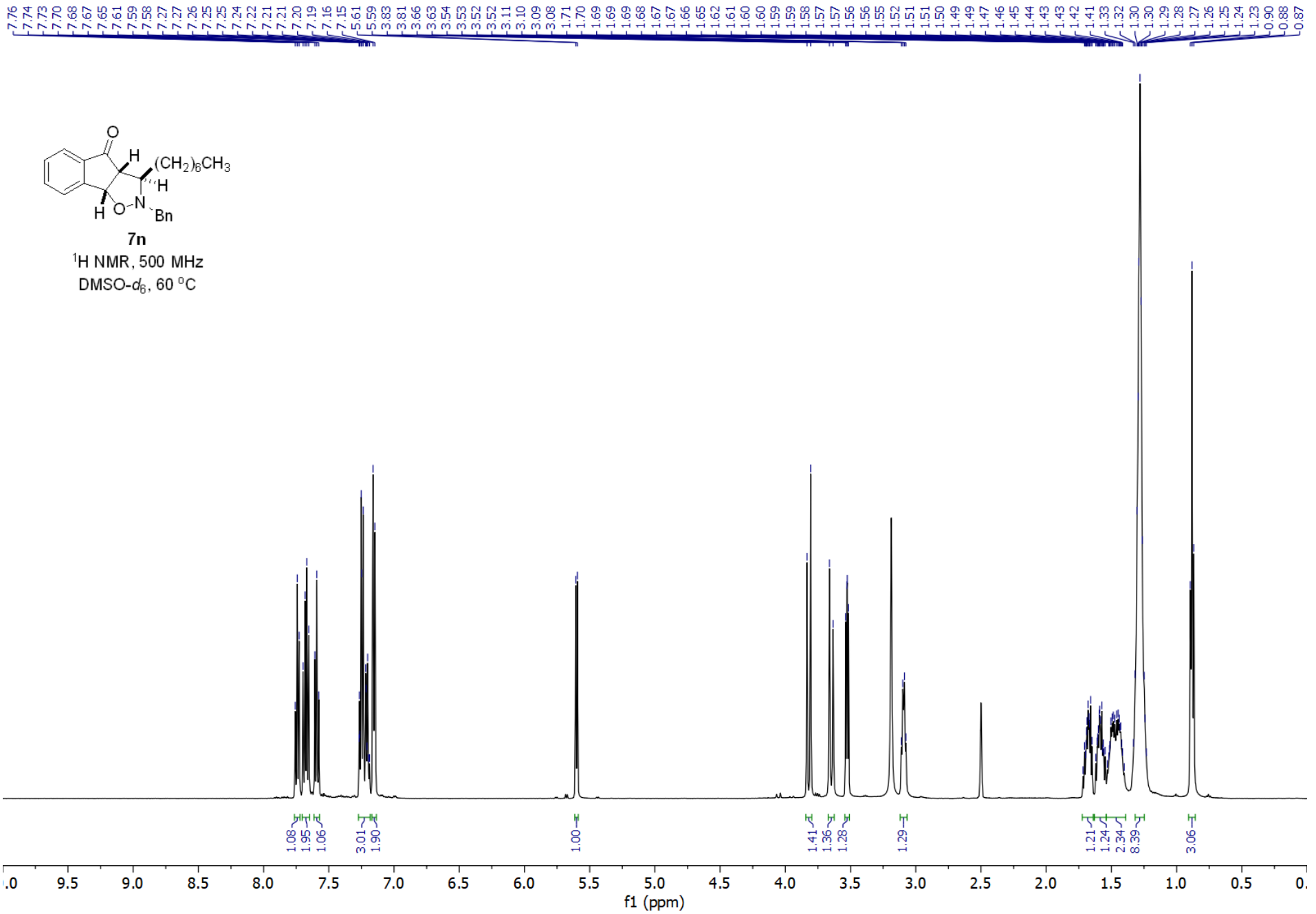
DMSO-d_6, 25 °C

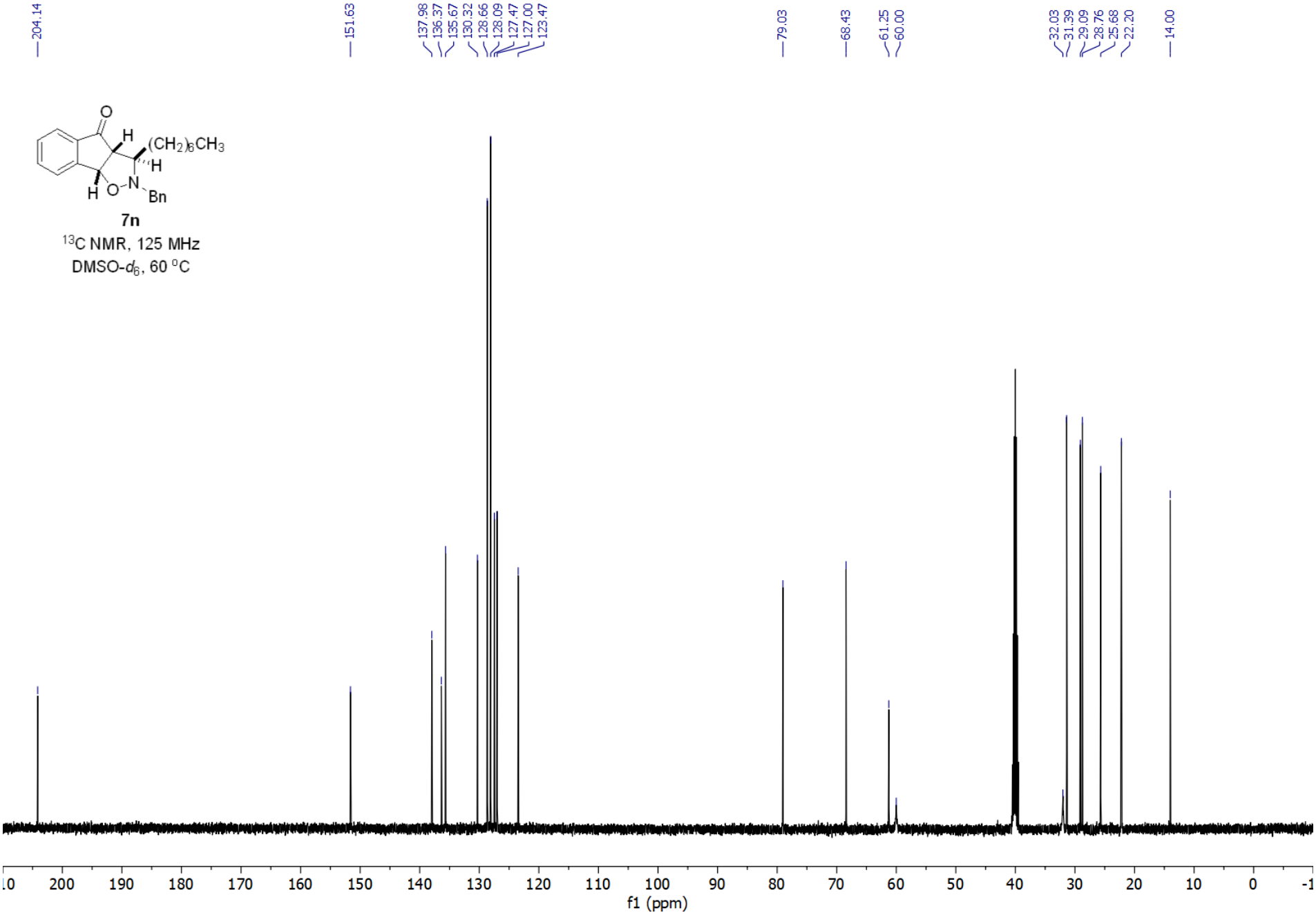

203.28
152.45
138.14
137.96
135.92
130.08
128.93
128.35
127.24
127.10
122.43
78.18
68.83
59.13
57.33
31.71
29.44
29.09
28.24
26.60
22.55
14.43
O
H
H
(CH2)6CH3
H
O
N
Bn
6n
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

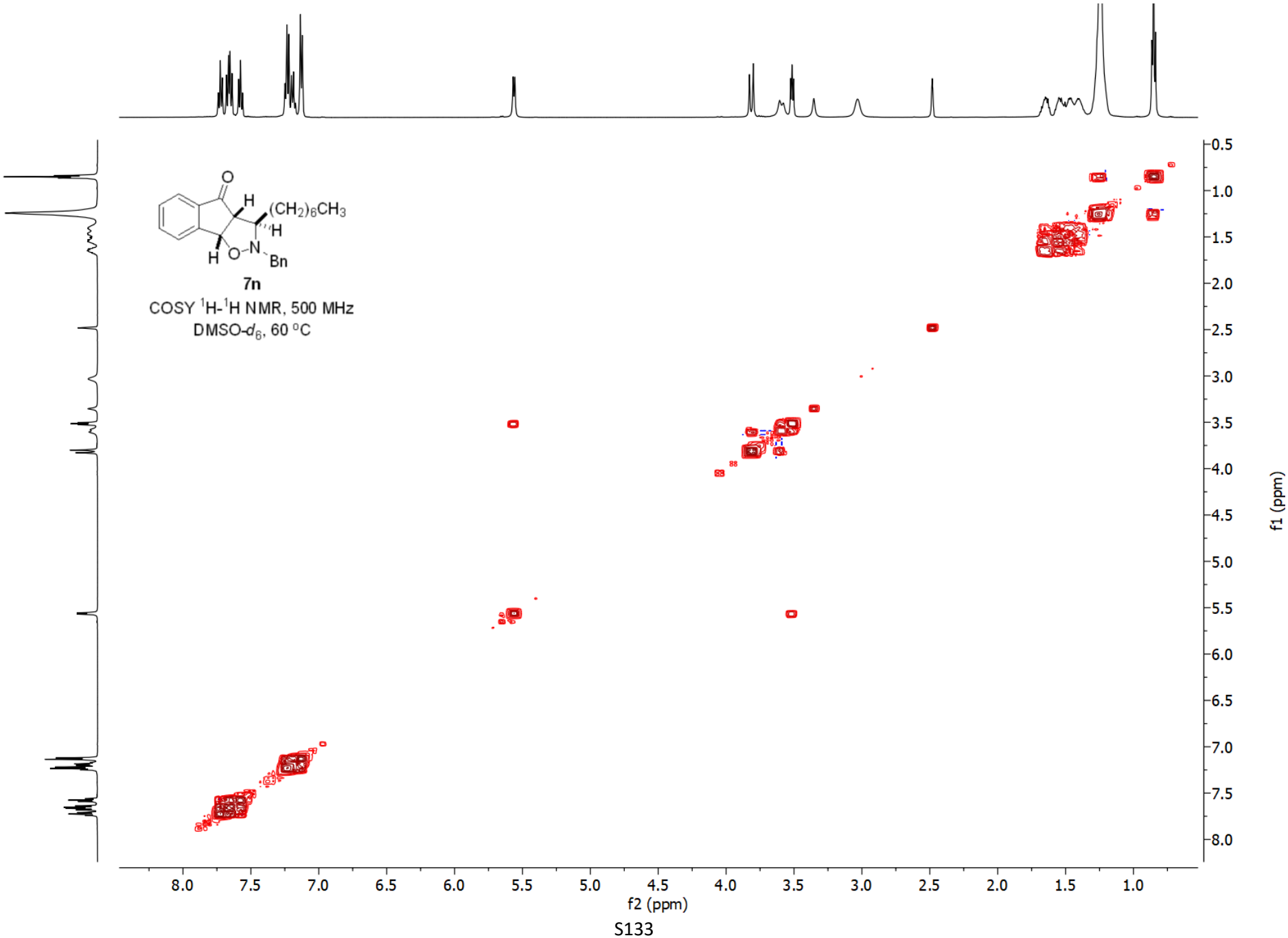

O
H
H
(CH2)6CH3
H
O
N
Bn
6n
COSY 1H-1H NMR, 500 MHz
DMSO-d6, 25 °C
f2 (ppm)
f1 (ppm)

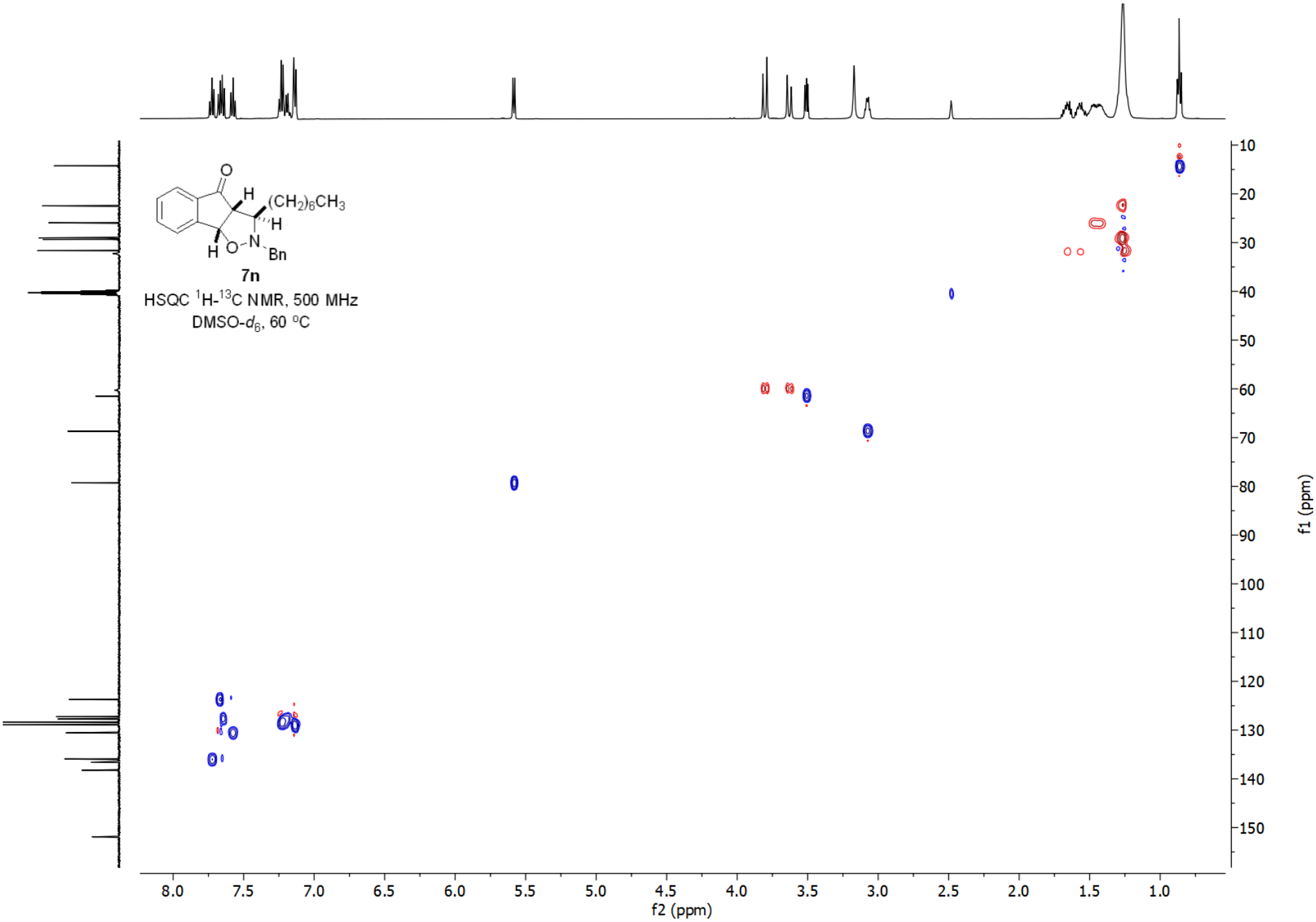

6n
HSQC ^{1}H-^{13}C NMR, 500 MHz
DMSO-d_6, 25 °C
f2 (ppm)
f1 (ppm)

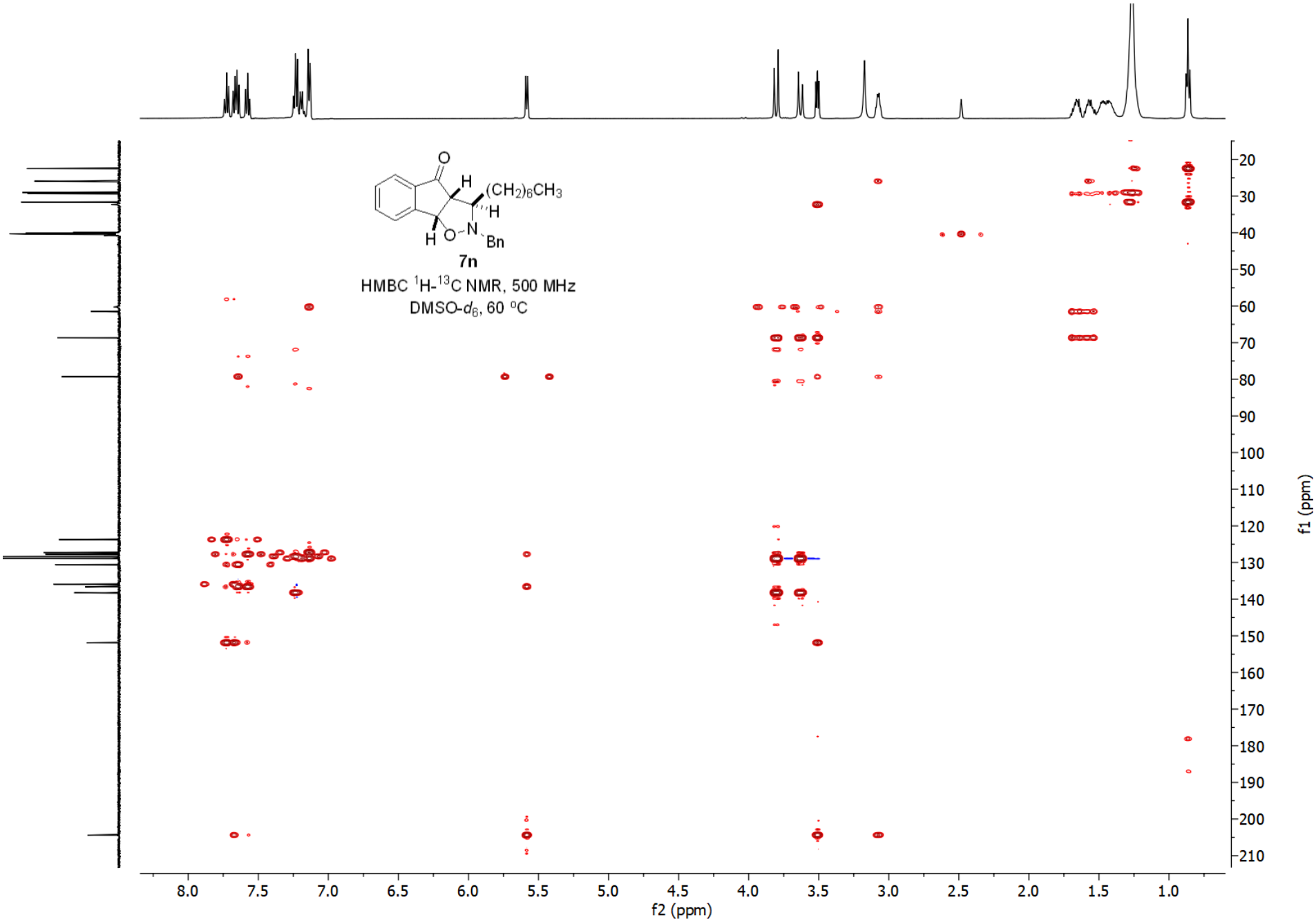

6n
HMBC ^{1}H-^{13}C NMR, 500 MHz
DMSO-d_6, 25 °C
f2 (ppm)
f1 (ppm)

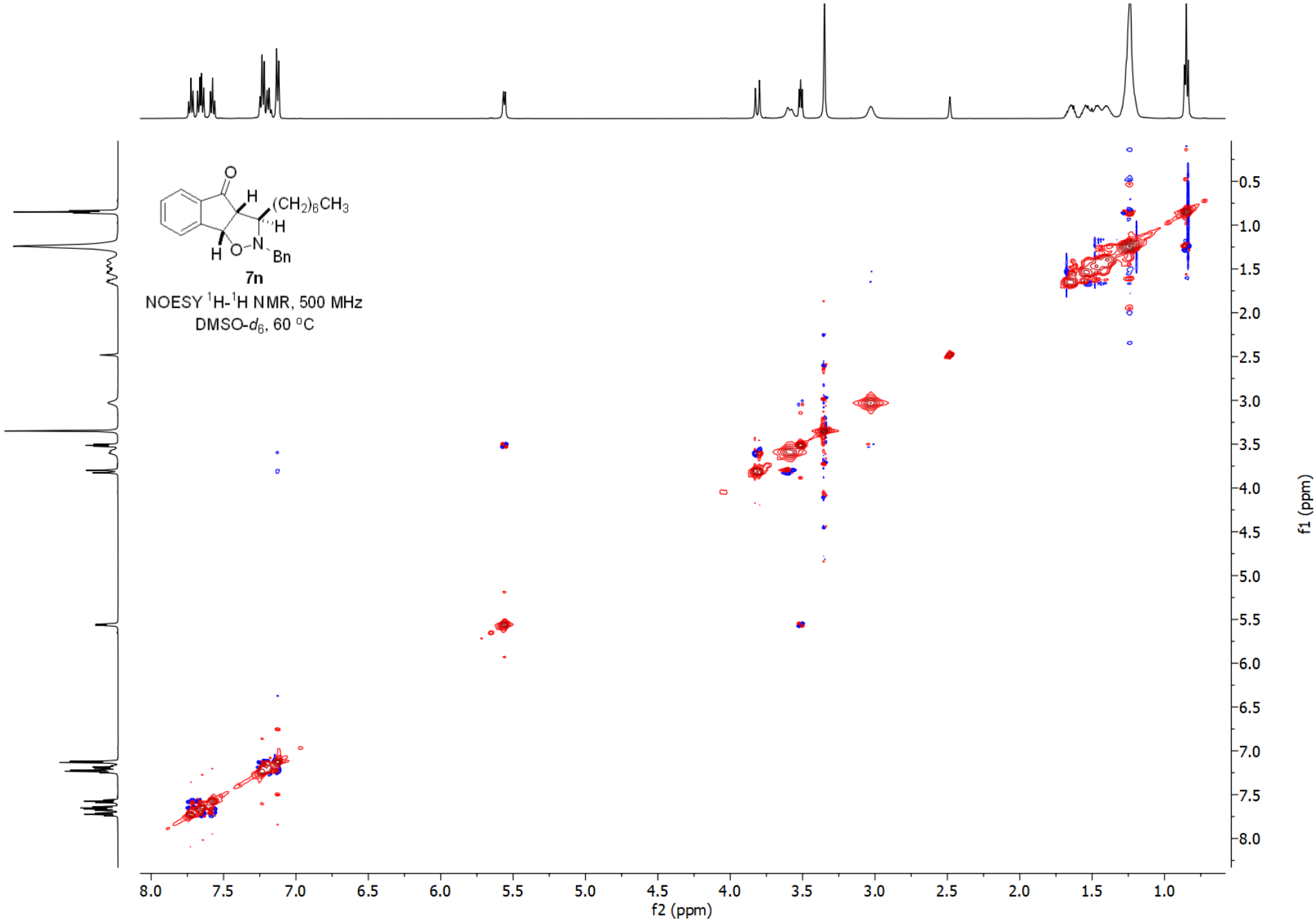

7.76 7.74 7.73 7.70 7.68 7.67 7.65 7.61 7.59 7.58 7.27 7.27 7.26 7.25 7.25 7.24 7.22 7.21 7.21 7.20 7.19 7.16 7.15 5.61 5.59 3.83 3.81 3.66 3.63 3.54 3.53 3.52 3.52 3.11 3.10 3.09 3.08 1.71 1.70 1.69 1.69 1.69 1.68 1.67 1.67 1.66 1.65 1.62 1.61 1.60 1.60 1.59 1.59 1.58 1.57 1.57 1.56 1.56 1.55 1.52 1.51 1.50 1.49 1.49 1.47 1.46 1.45 1.44 1.43 1.42 1.41 1.33 1.32 1.30 1.30 1.29 1.28 1.27 1.26 1.25 1.24 1.23 0.90 0.88 0.87
O
H
(CH2)6CH3
H
H
O
N
Bn
7n
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.08 1.95 1.06 3.01 1.90 1.00 1.41 1.36 1.28 1.29 1.21 1.24 2.34 8.39 3.06
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

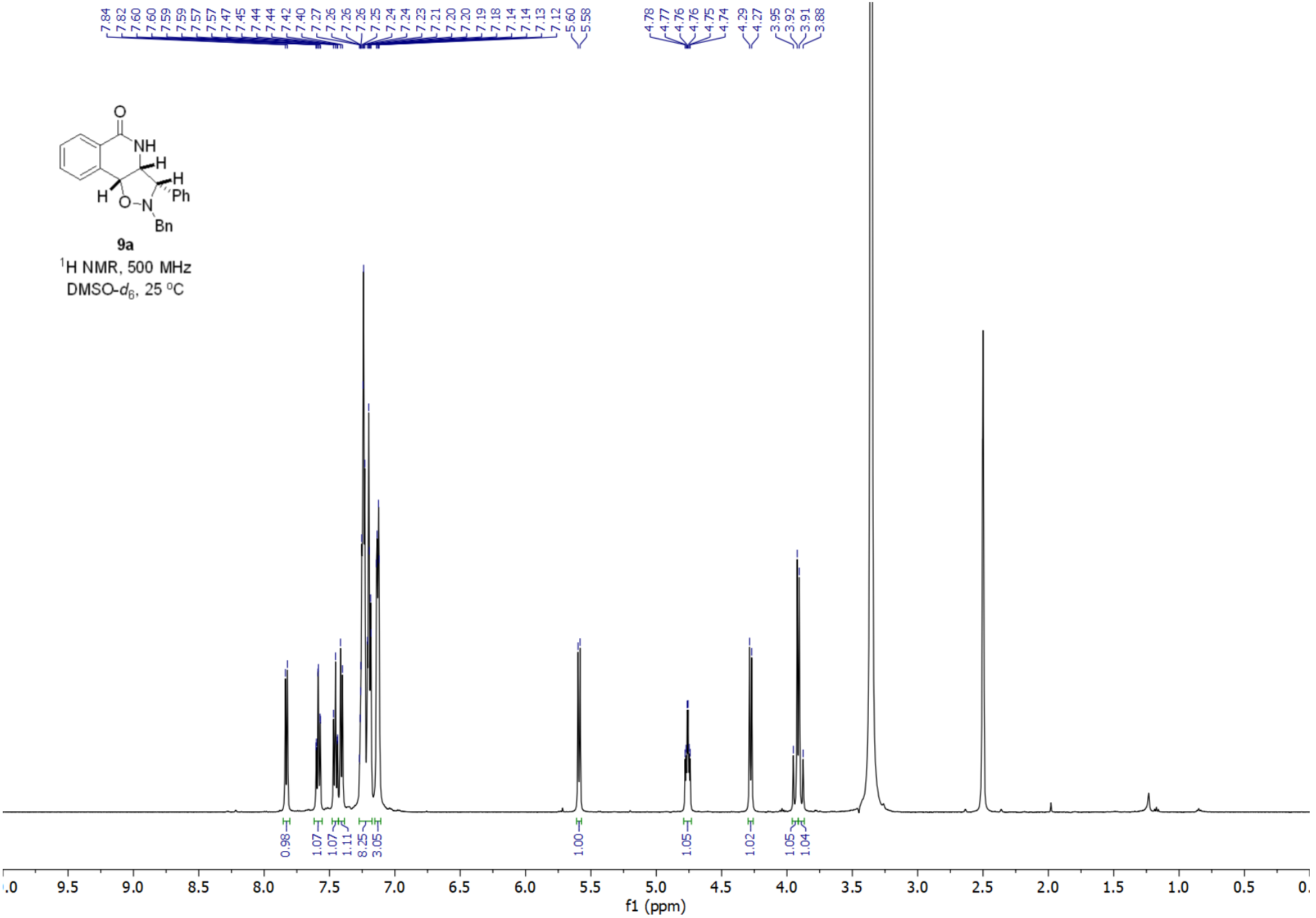

204.14
151.63
137.98
136.37
135.67
130.32
128.66
128.09
127.47
127.00
123.47
79.03
68.43
61.25
60.00
32.03
31.39
29.09
28.76
25.68
22.20
14.00
O
H
(CH2)6CH3
H
H
O
N
Bn
7n
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

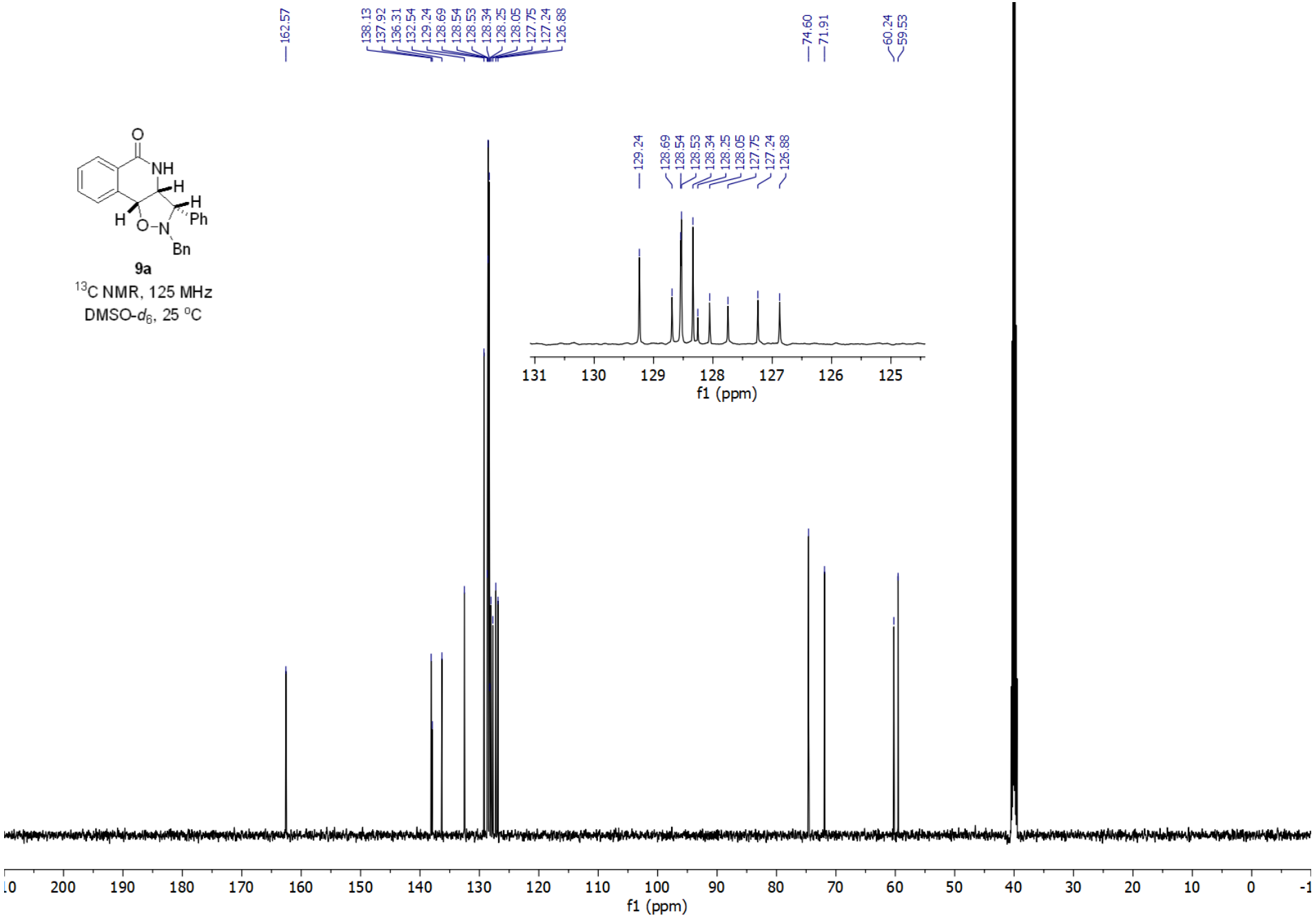

7n
COSY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 60 °C
f2 (ppm)
f1 (ppm)

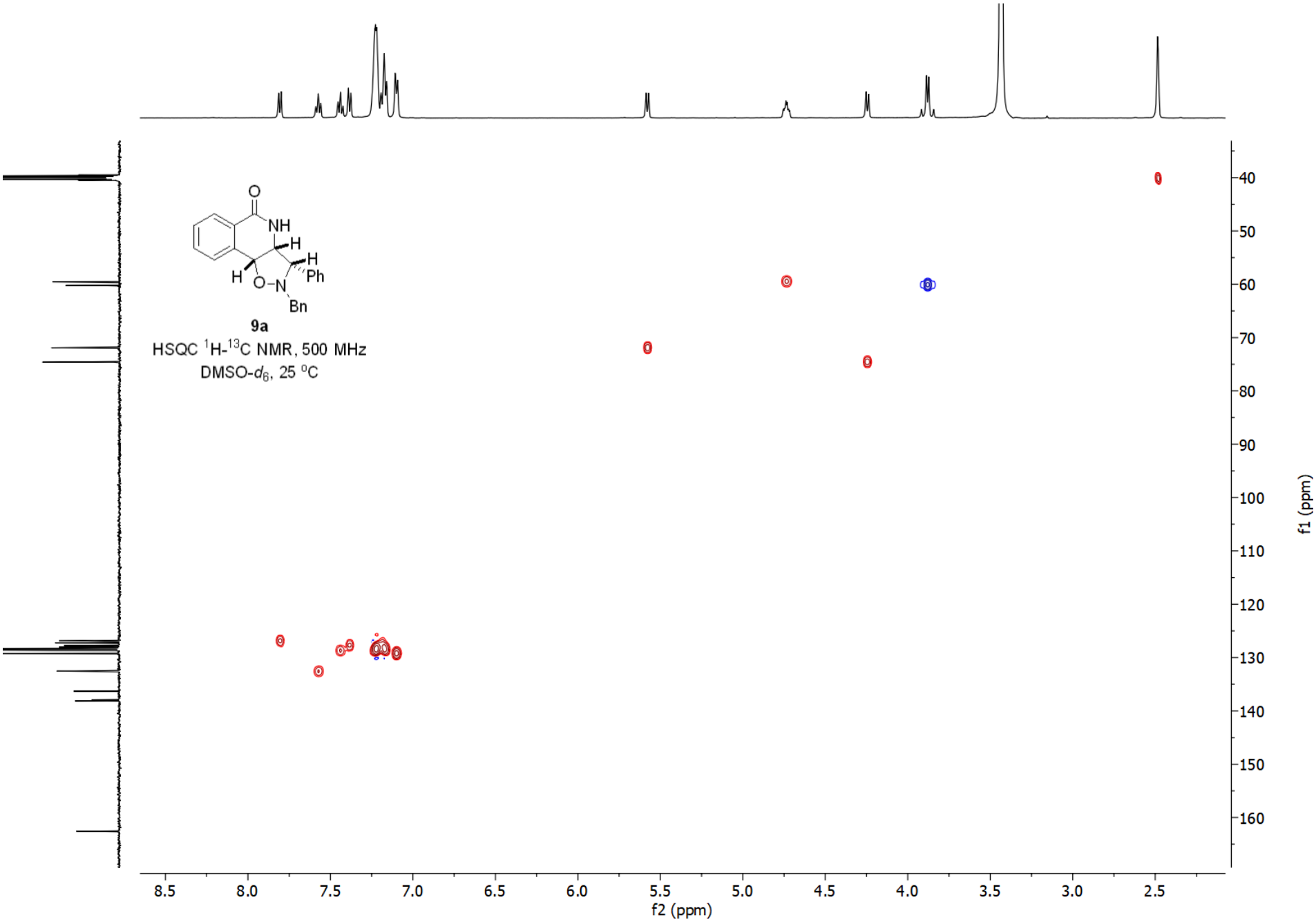

O
H
(CH2)6CH3
H
H
O
N
Bn
7n
HSQC 1H-13C NMR, 500 MHz
DMSO-d6, 60 °C
f2 (ppm)
f1 (ppm)

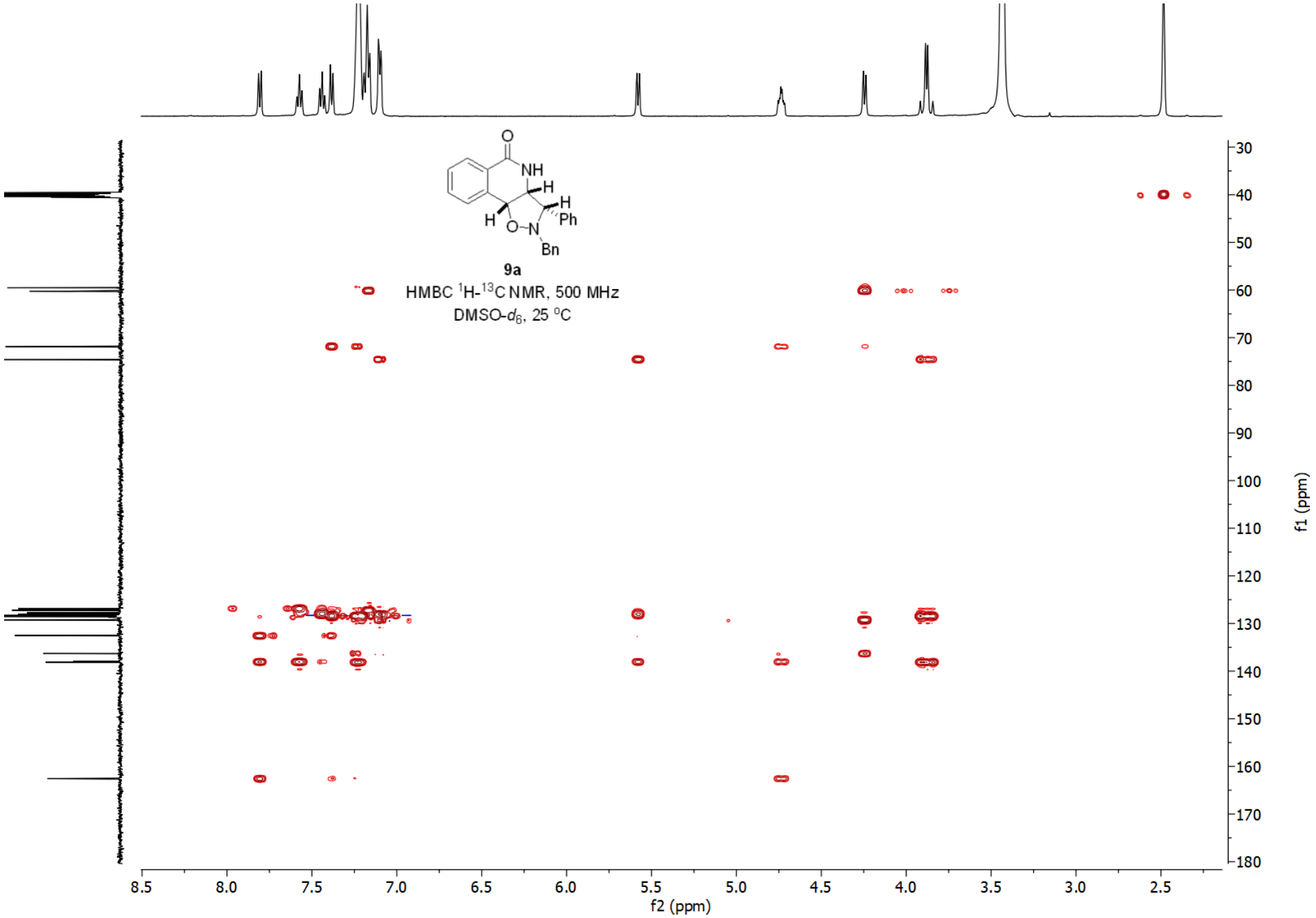

7n
HMBC ^{1}H-^{13}C NMR, 500 MHz
DMSO-d_6, 60 ^{o}C
f2 (ppm)
f1 (ppm)

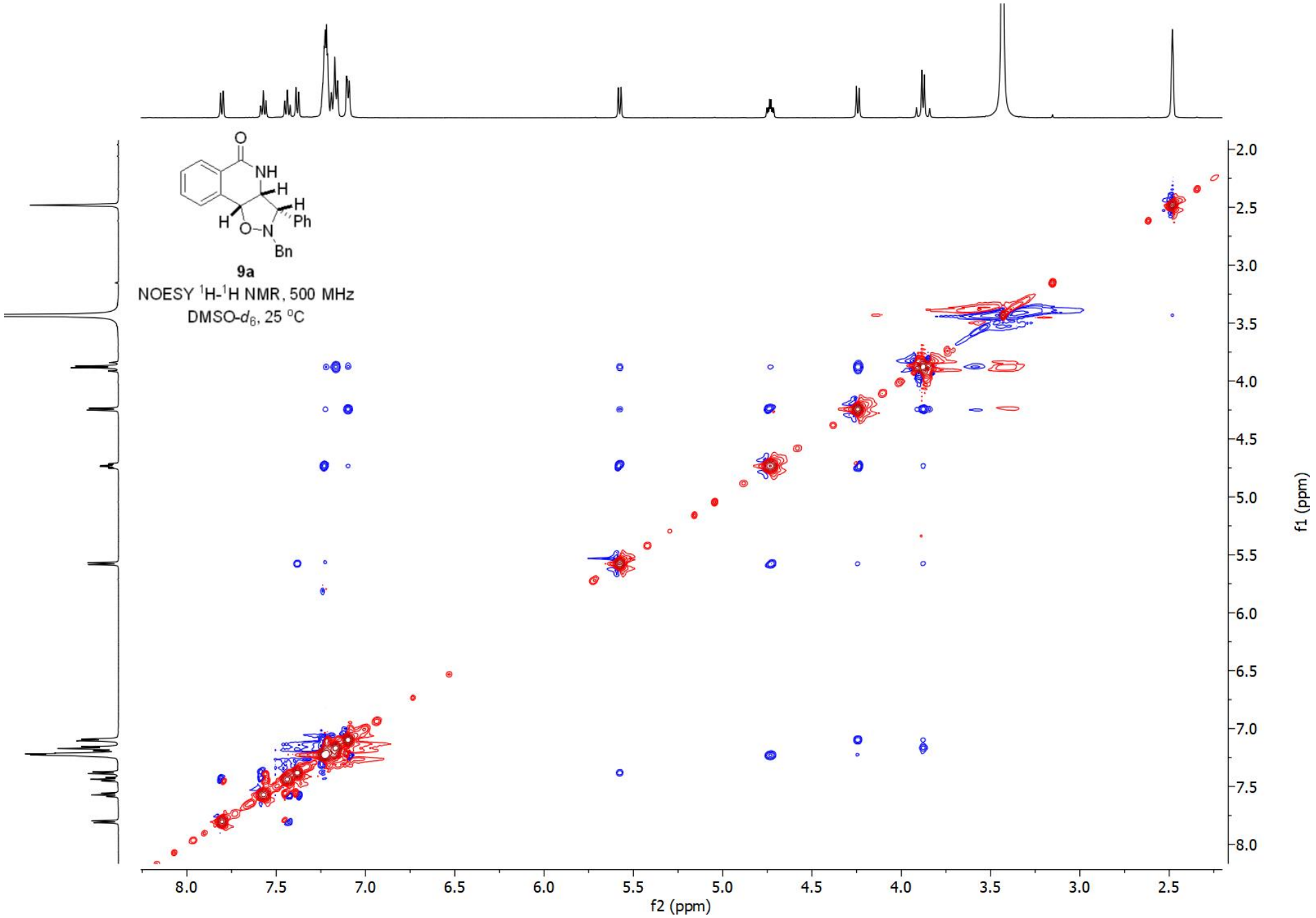

7n
NOESY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 60 °C
f2 (ppm)
f1 (ppm)


7.84
7.82
7.60
7.60
7.59
7.59
7.57
7.57
7.47
7.45
7.44
7.44
7.42
7.40
7.27
7.26
7.26
7.26
7.25
7.24
7.24
7.23
7.21
7.20
7.20
7.19
7.18
7.14
7.14
7.13
7.12
5.60
5.58
4.78
4.77
4.76
4.76
4.75
4.74
4.29
4.27
3.95
3.92
3.91
3.88
O
NH
H
H
H
O
N
Ph
Bn
9a
1H NMR, 500 MHz
DMSO-d6, 25 °C
0.98
1.07
1.07
1.11
8.25
3.05
1.00
1.05
1.02
1.05
1.04
f1 (ppm)


162.57
138.13
137.92
136.31
132.54
129.24
128.69
128.54
128.53
128.34
128.25
128.05
127.75
127.24
126.88
74.60
71.91
60.24
59.53
O
NH
H
H
H
O
N
Ph
Bn
9a
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)
f1 (ppm)


O
NH
H
H
H
O
N
Ph
Bn
9a
HSQC ^{1}H-^{13}C NMR, 500 MHz
DMSO-d_6, 25 ^{o}C
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
f2 (ppm)
40
50
60
70
80
90
100
110
120
130
140
150
160
f1 (ppm)

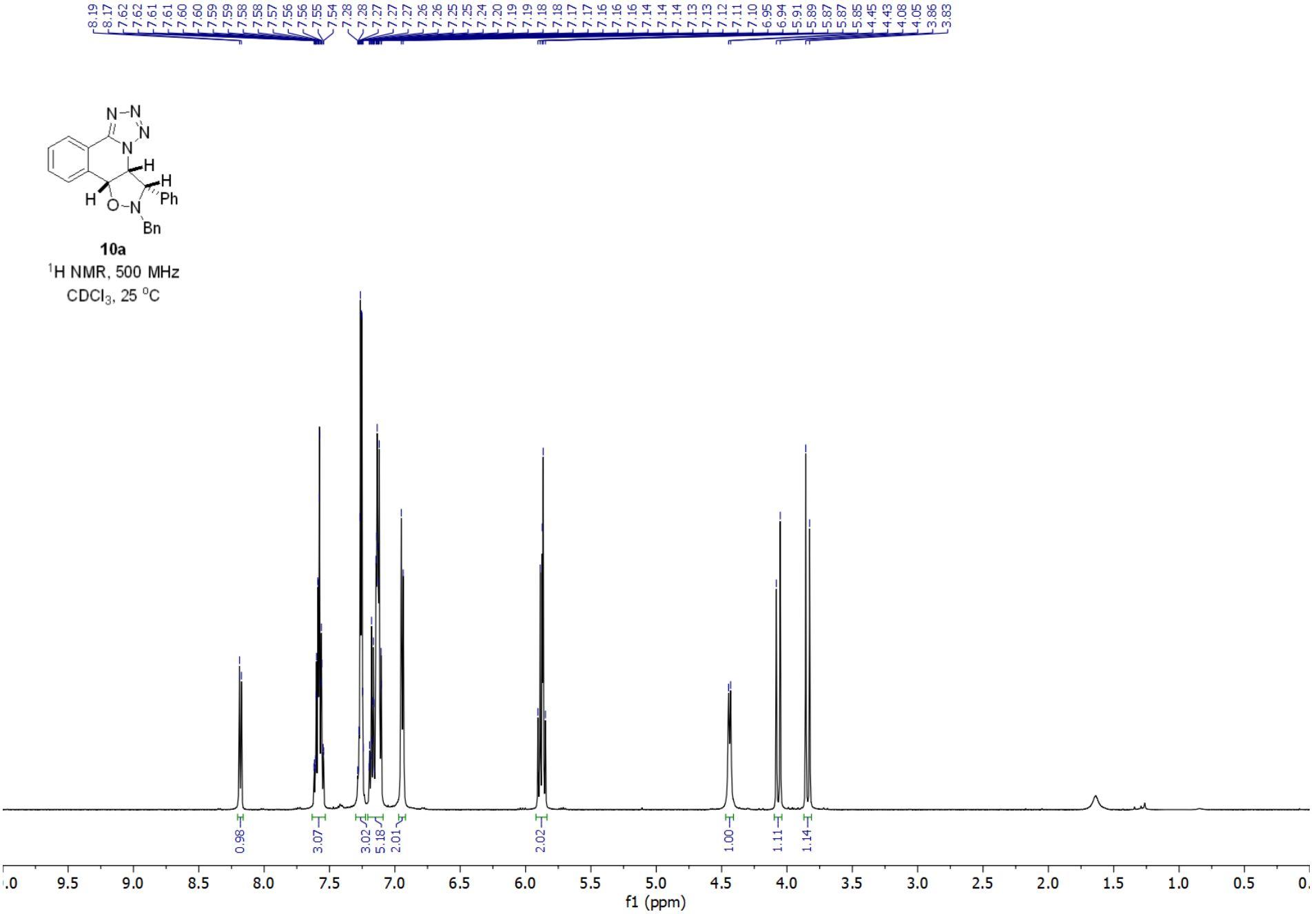

O
NH
H
H
H
Ph
O
N
Bn
9a
HMBC ^{1}H-^{13}C NMR, 500 MHz
DMSO-d_6, 25 ^{o}C
f1 (ppm)
f2 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180

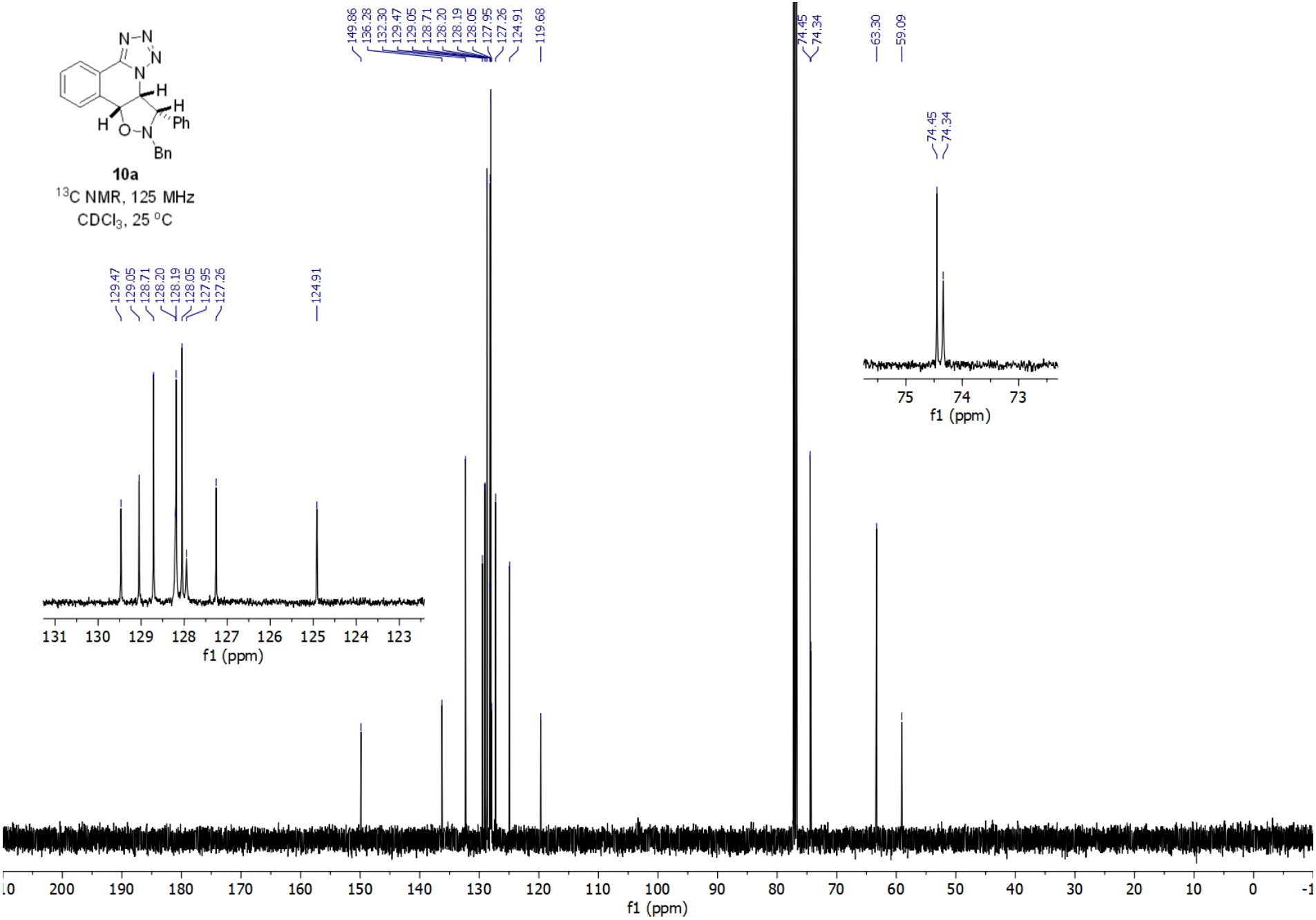

O
NH
H
H
H
Ph
O
N
Bn
9a
NOESY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 25 ^{0}C
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
f2 (ppm)
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
f1 (ppm)

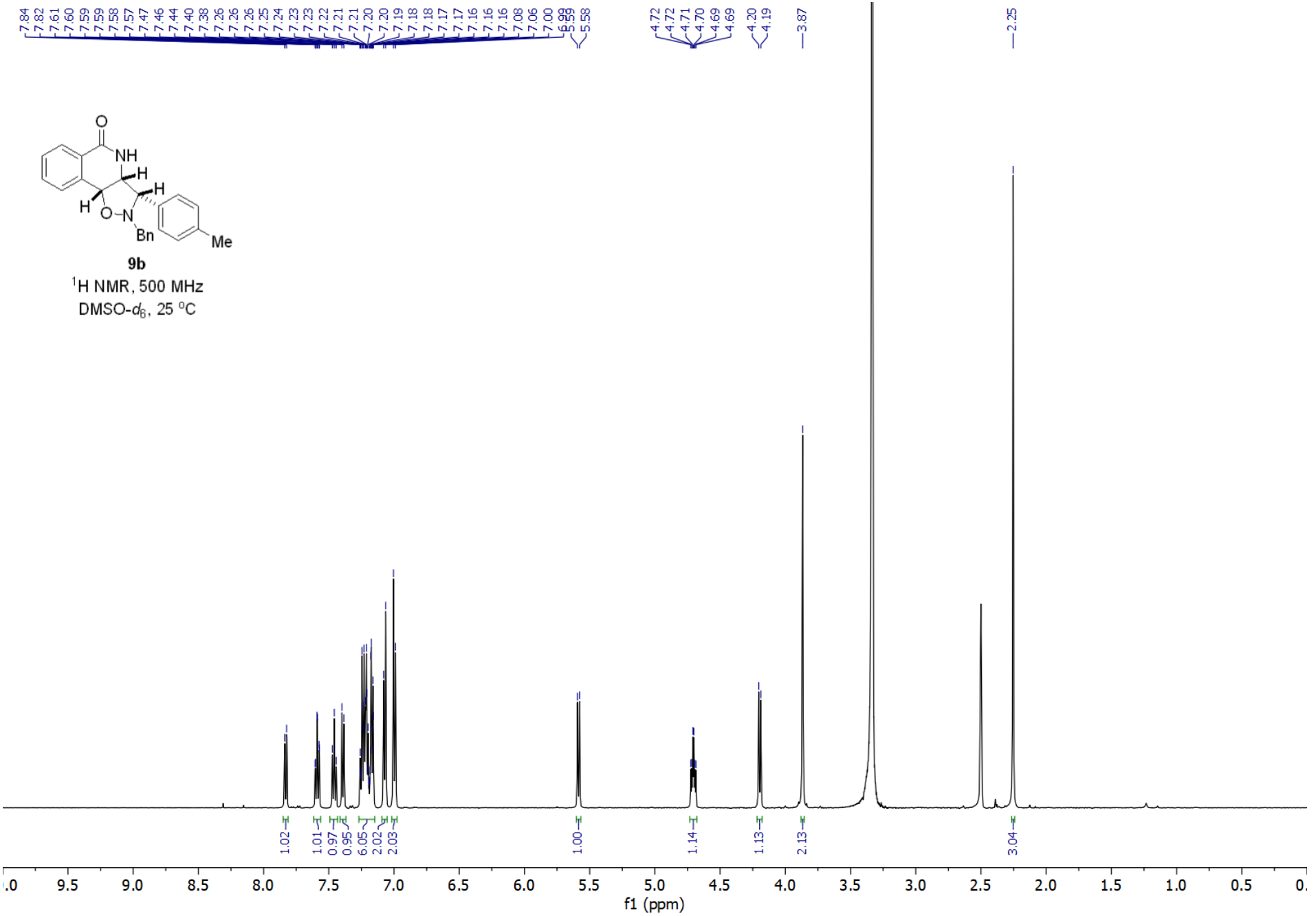
10a

^{1}H NMR, 500 MHz

$CDCl_3$, 25 ^{o}C



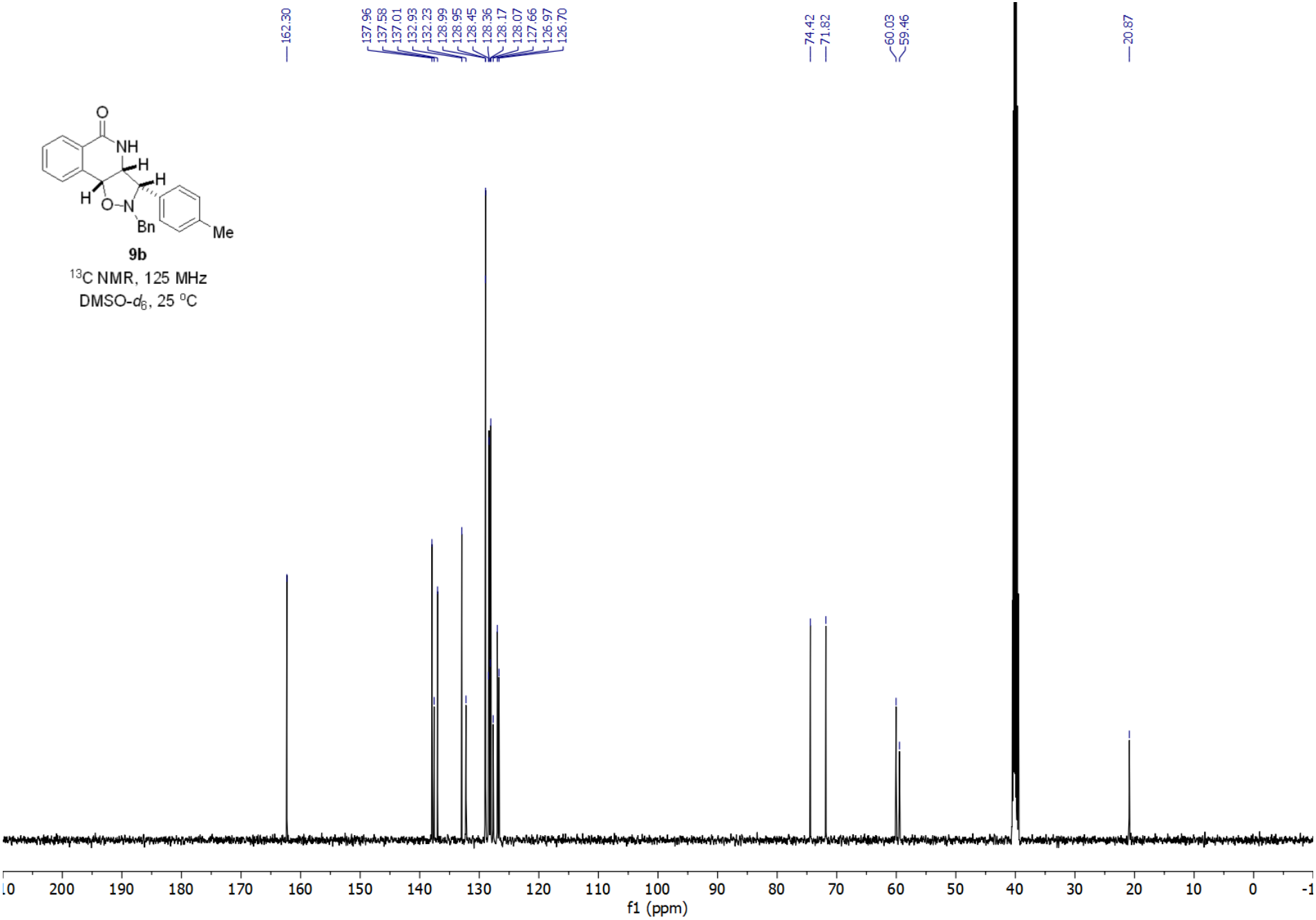

10a
13C NMR, 125 MHz
CDCl3, 25 °C
149.86
136.28
132.30
129.47
129.05
128.71
128.20
128.19
128.05
127.95
127.26
124.91
119.68
74.45
74.34
63.30
59.09
f1 (ppm)

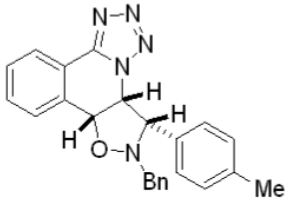

7.84
7.82
7.61
7.60
7.59
7.59
7.58
7.57
7.47
7.46
7.44
7.40
7.38
7.26
7.26
7.26
7.25
7.24
7.23
7.23
7.22
7.21
7.21
7.20
7.20
7.19
7.18
7.18
7.17
7.17
7.16
7.16
7.16
7.08
7.06
7.00
6.99
5.59
5.58
4.72
4.72
4.71
4.70
4.69
4.69
4.20
4.19
3.87
2.25
O
NH
H
H
H
O
N
Bn
Me
9b
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.02
1.01
0.97
0.95
6.05
2.02
2.03
1.00
1.14
1.13
2.13
3.04
f1 (ppm)

9b

^{13}C NMR, 125 MHz

DMSO-d_6, 25 ^{o}C

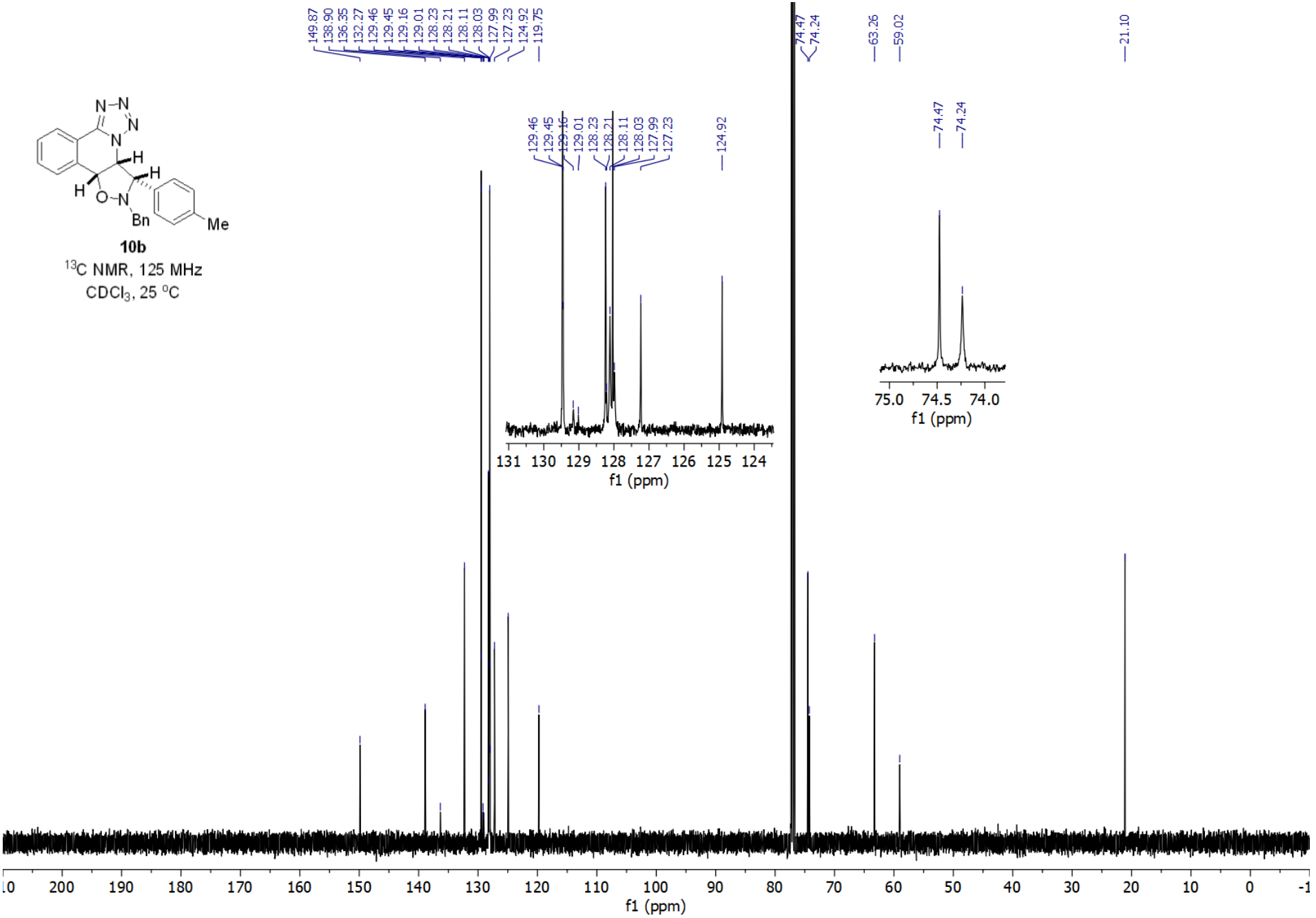


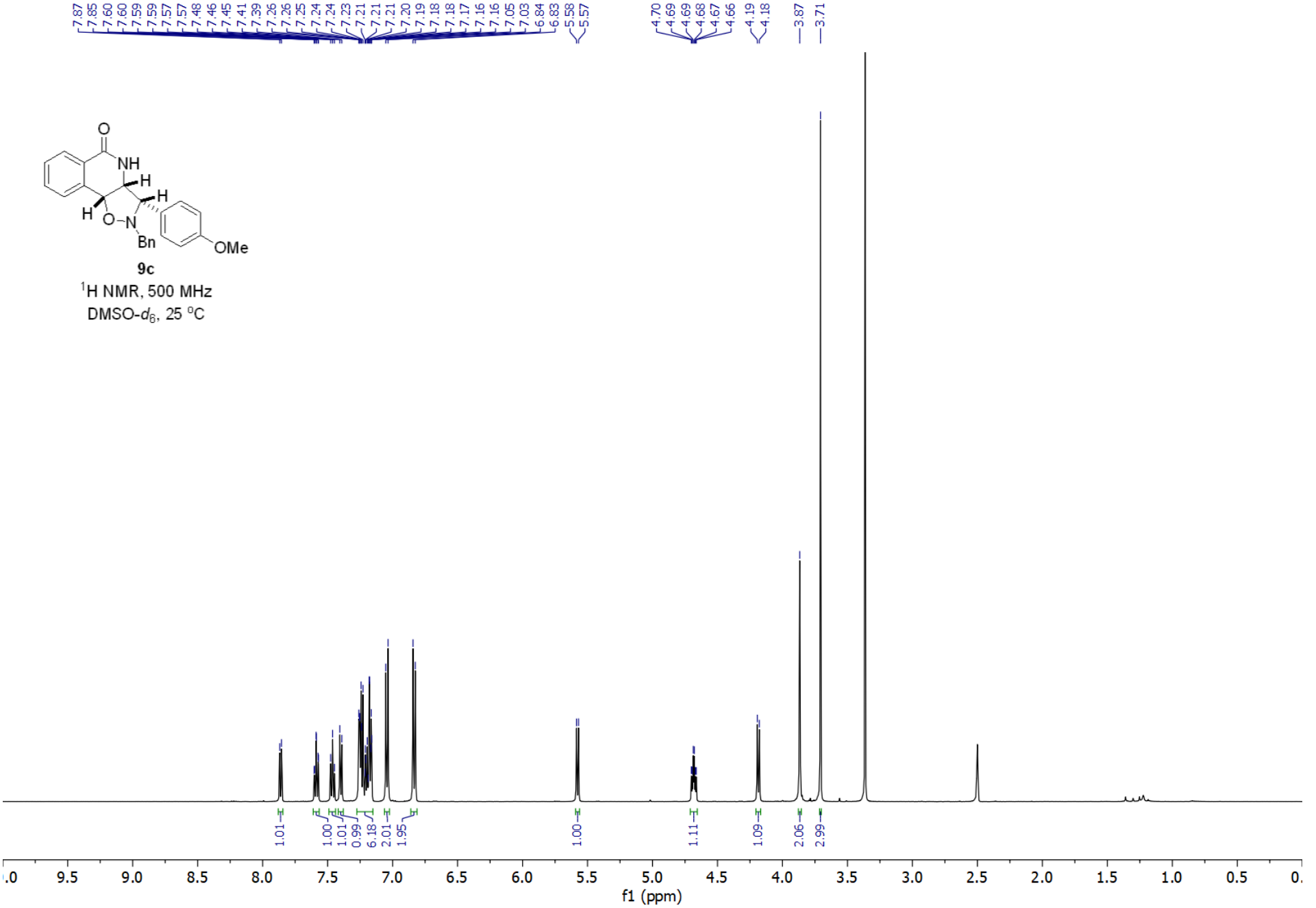


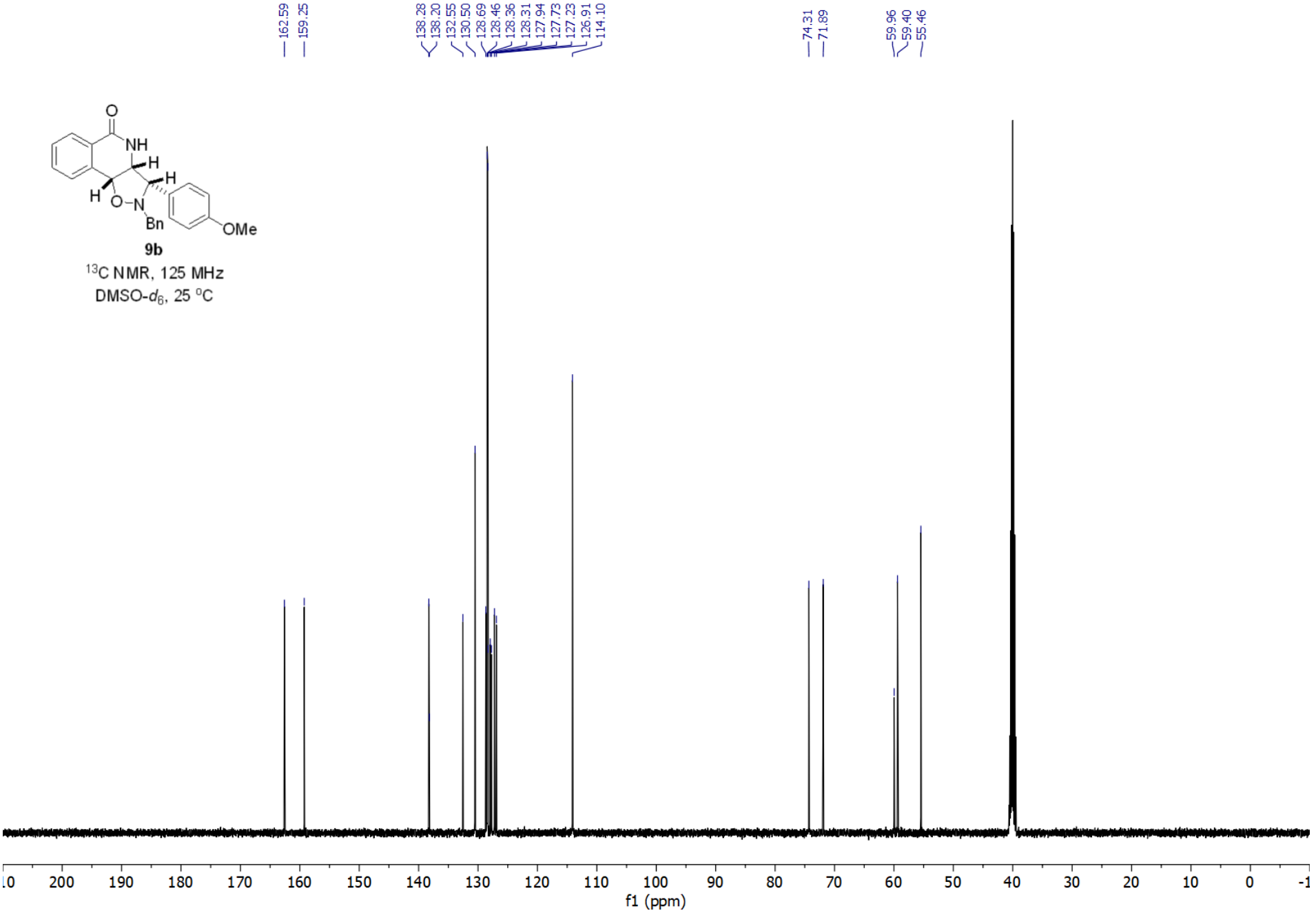
10b

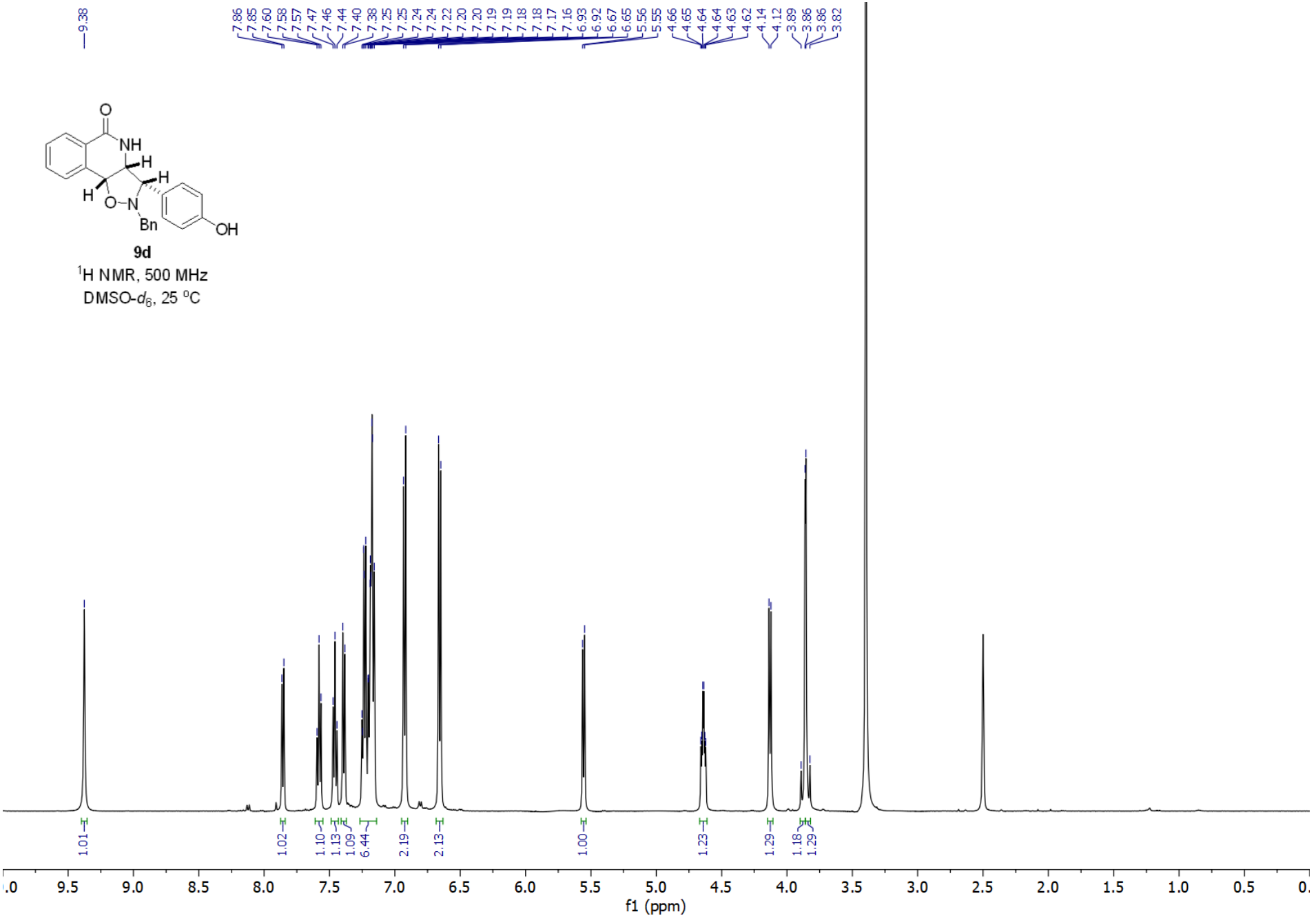
^{1}H NMR, 500 MHz

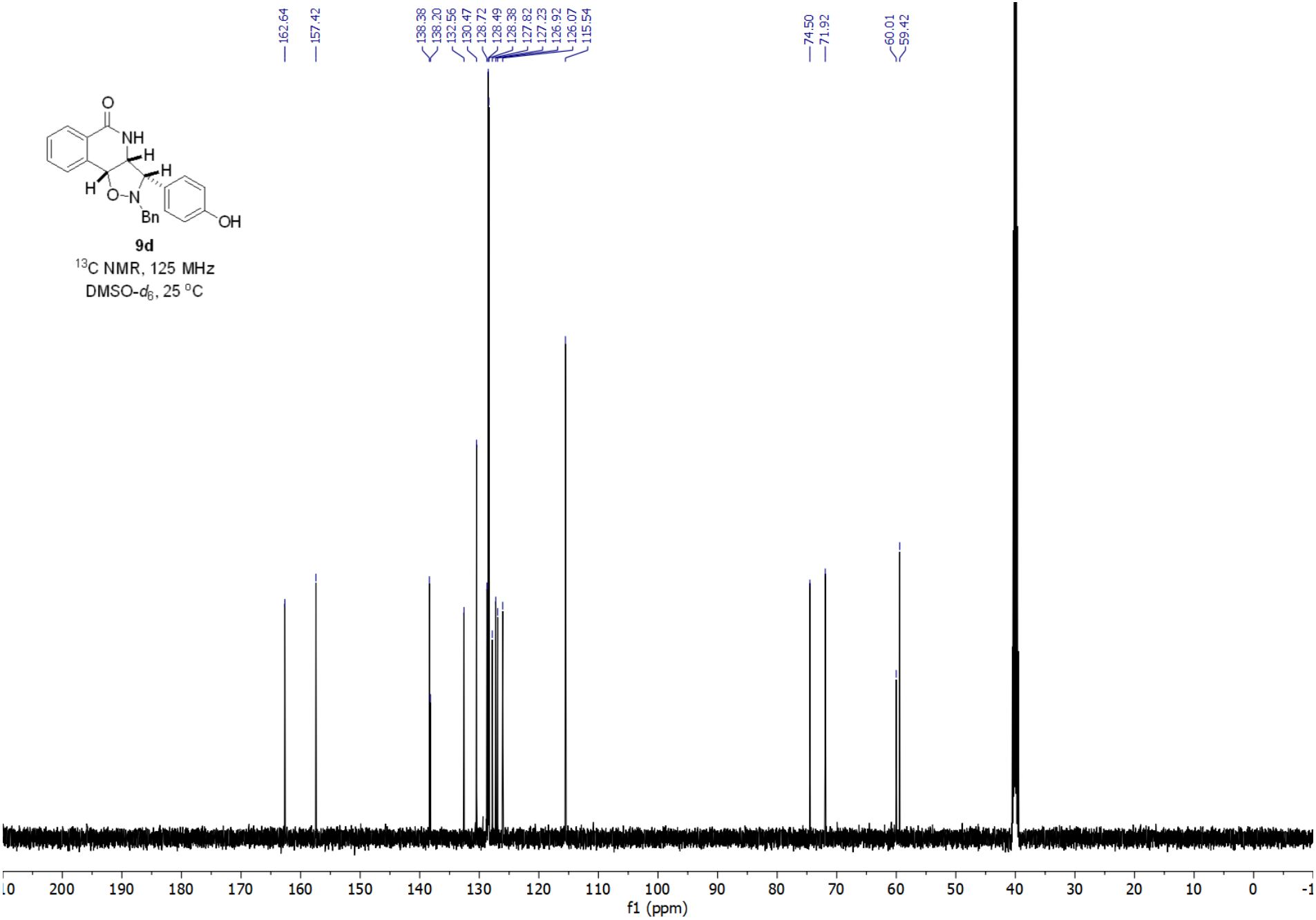
$CDCl_3$, 25 ^oC

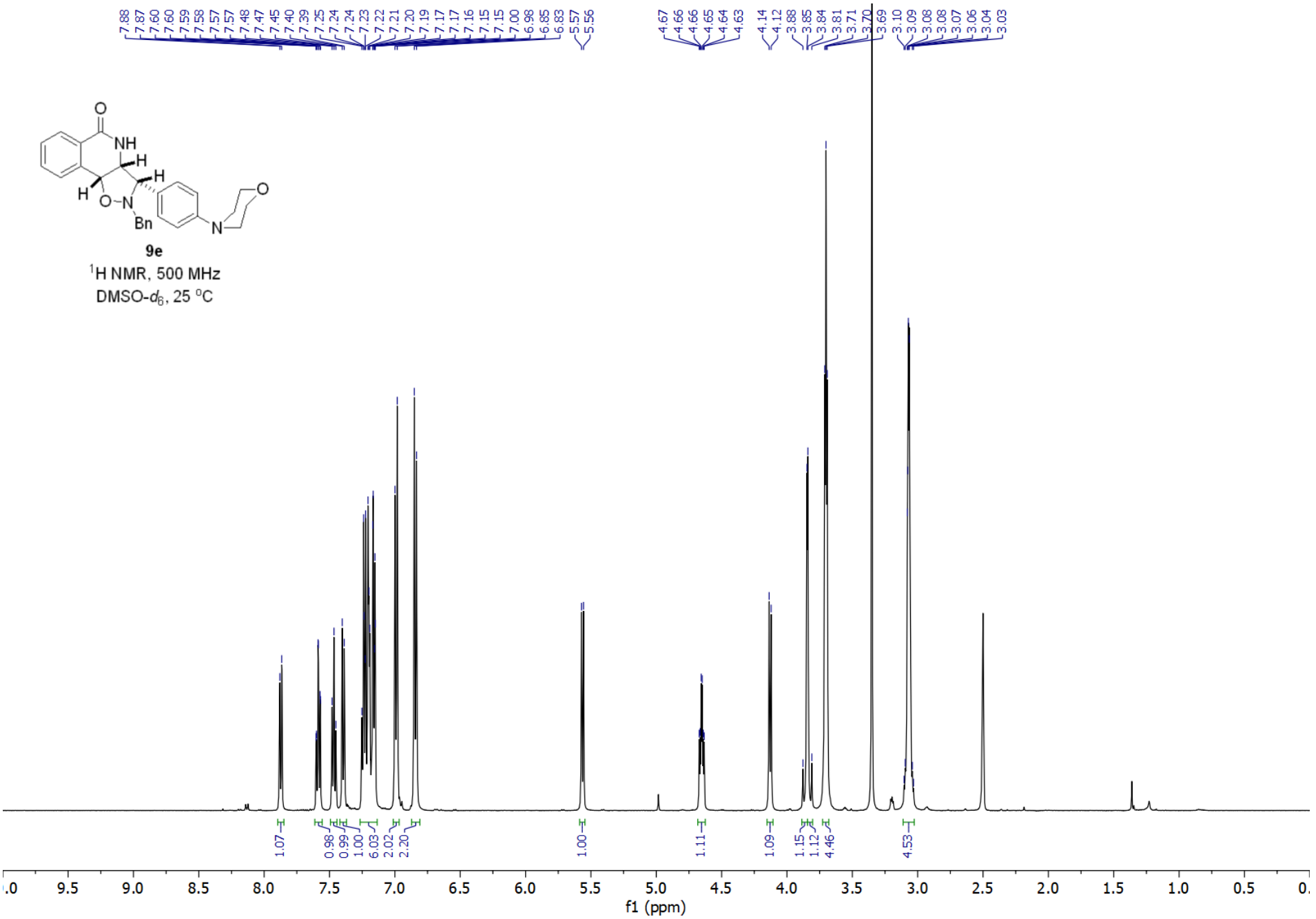

149.87
138.90
136.35
132.27
129.46
129.45
129.16
129.01
128.23
128.21
128.11
128.03
127.99
127.23
124.92
119.75
74.47
74.24
63.26
59.02
21.10
N–N
N
N
H
H
H
O–N
Bn
Me
10b
13C NMR, 125 MHz
CDCl3, 25 °C
131 130 129 128 127 126 125 124
f1 (ppm)
75.0 74.5 74.0
f1 (ppm)
f1 (ppm)

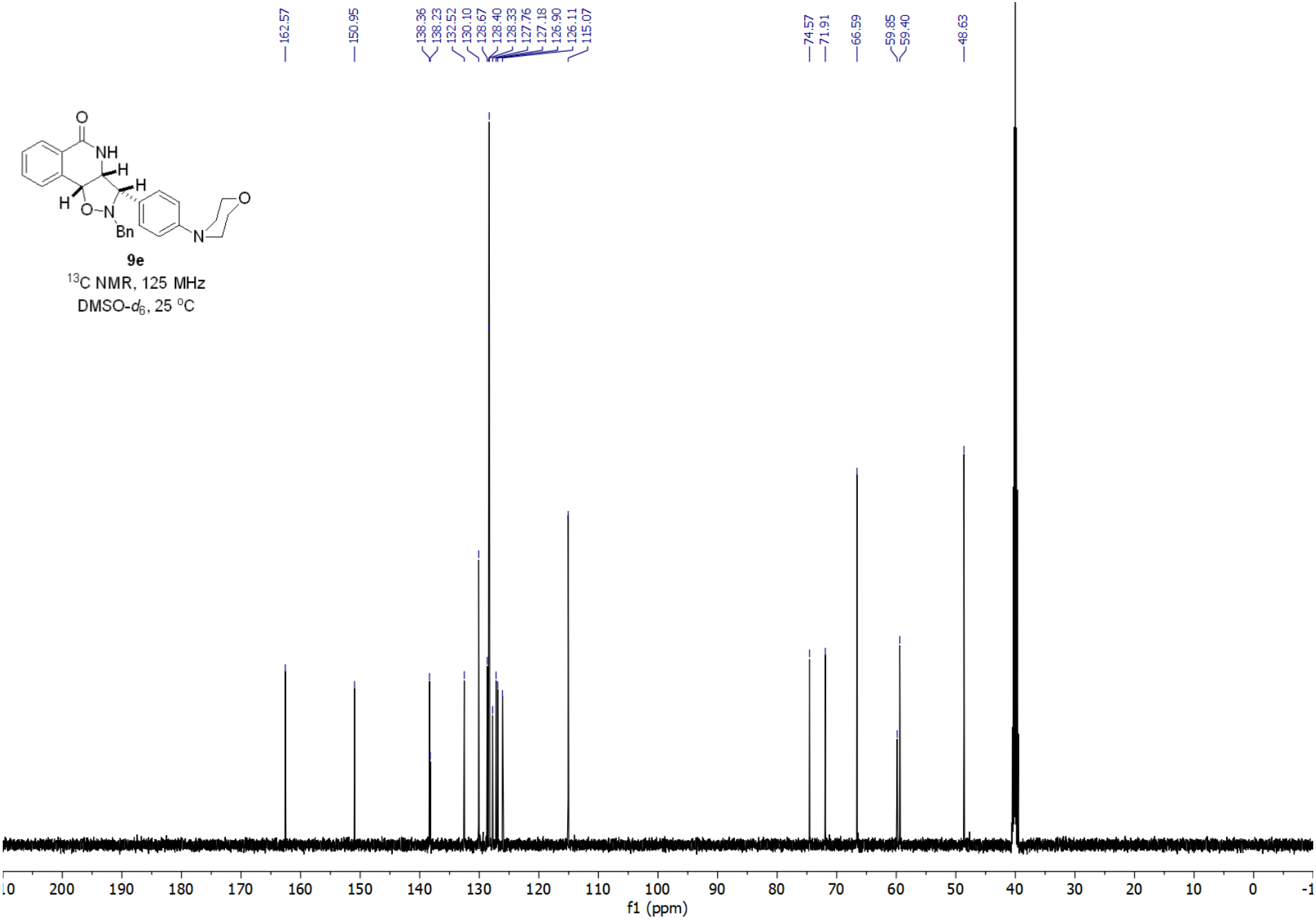

7.87
7.85
7.60
7.60
7.59
7.59
7.57
7.57
7.48
7.46
7.45
7.41
7.39
7.26
7.25
7.24
7.24
7.23
7.21
7.21
7.21
7.20
7.19
7.18
7.18
7.17
7.16
7.16
7.05
7.03
6.84
6.83
5.58
5.57
4.70
4.69
4.69
4.68
4.67
4.66
4.19
4.18
3.87
3.71
O
NH
H
H
H
O
N
Bn
OMe
9c
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.01
1.00
1.01
0.99
6.18
2.01
1.95
1.00
1.11
1.09
2.06
2.99
f1 (ppm)

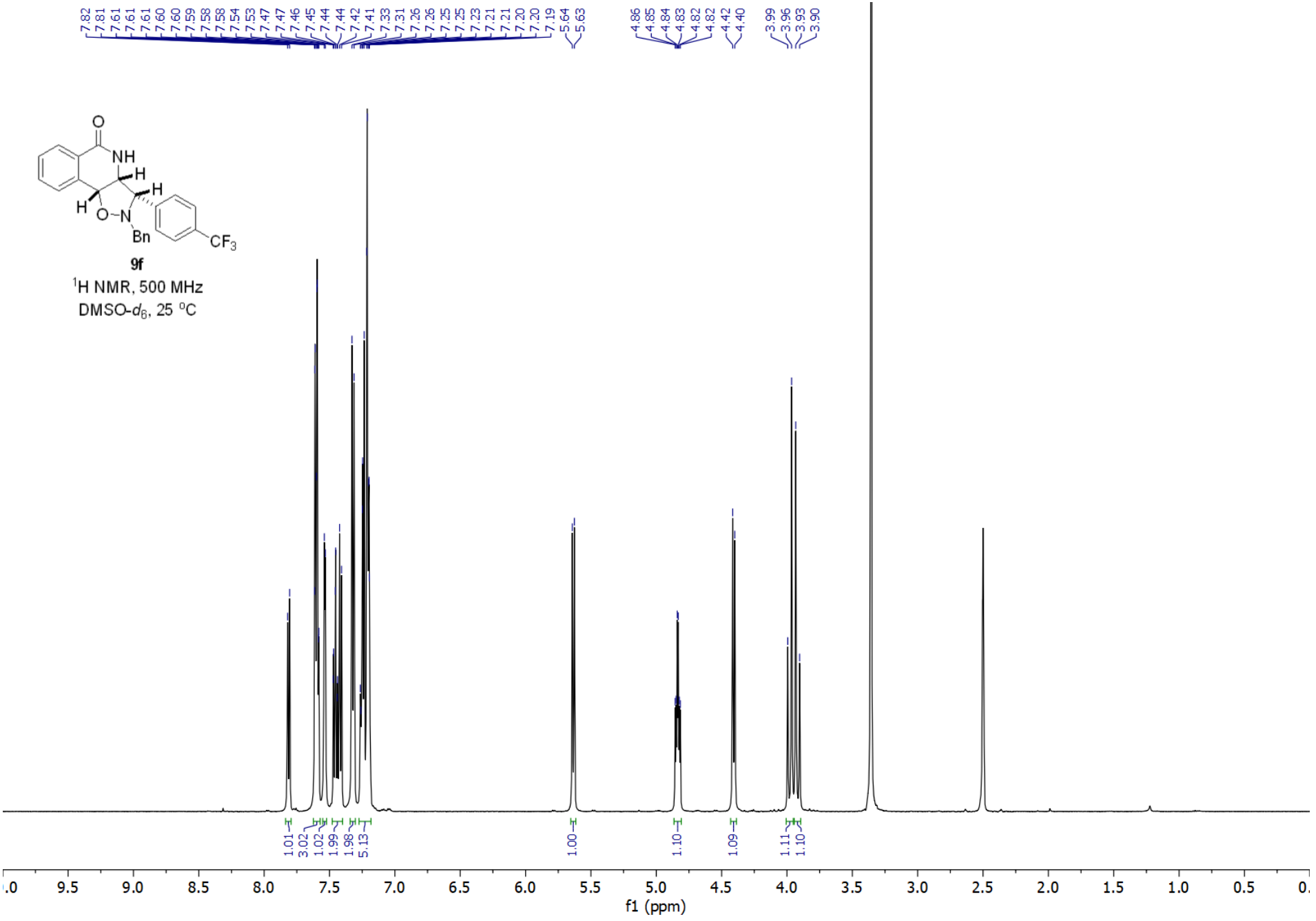

162.59
159.25
138.28
138.20
132.55
130.50
128.69
128.46
128.36
128.31
127.94
127.73
127.23
126.91
114.10
74.31
71.89
59.96
59.40
55.46
O
NH
H
H
H
O
N
Bn
OMe
9b
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

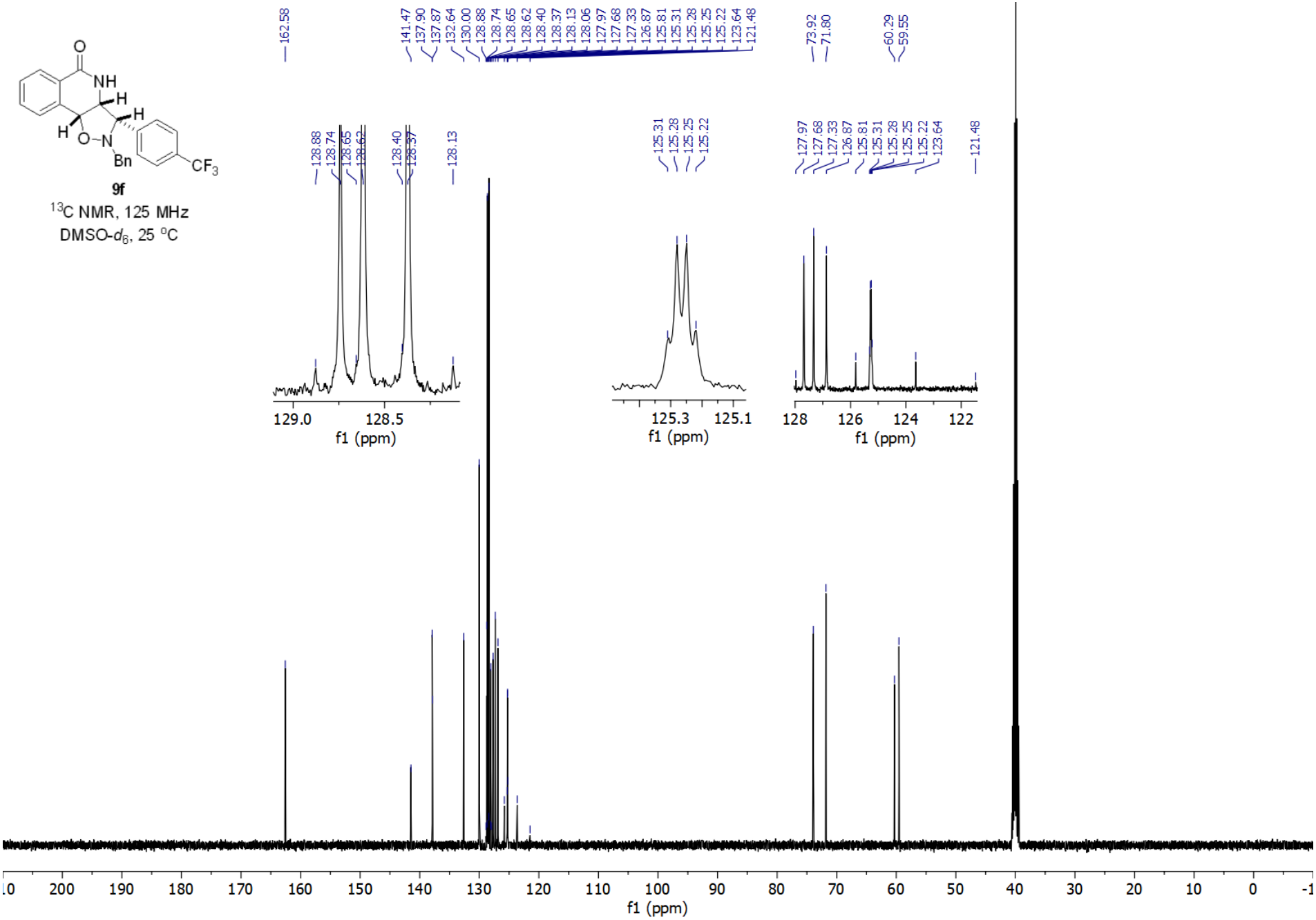

9.38
7.86
7.85
7.60
7.58
7.57
7.47
7.46
7.44
7.40
7.38
7.25
7.25
7.24
7.24
7.22
7.20
7.20
7.19
7.19
7.18
7.18
7.17
7.16
6.93
6.92
6.67
6.65
5.56
5.55
4.66
4.65
4.64
4.64
4.63
4.62
4.14
4.12
3.89
3.86
3.86
3.82
O
NH
H
H
H
O
N
Bn
OH
9d
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.01
1.02
1.10
1.13
1.09
6.44
2.19
2.13
1.00
1.23
1.29
1.18
1.29
f1 (ppm)


162.64
157.42
138.38
138.20
132.56
130.47
128.72
128.49
128.38
127.82
127.23
126.92
126.07
115.54
74.50
71.92
60.01
59.42
O
NH
H
H
H
O
N
Bn
OH
9d
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)


7.88
7.87
7.60
7.60
7.59
7.58
7.57
7.57
7.48
7.47
7.45
7.40
7.39
7.25
7.24
7.24
7.23
7.22
7.21
7.20
7.19
7.17
7.17
7.16
7.15
7.15
7.00
6.98
6.85
6.83
5.57
5.56
4.67
4.66
4.66
4.65
4.64
4.63
4.14
4.12
3.88
3.85
3.84
3.81
3.71
3.70
3.69
3.10
3.09
3.08
3.08
3.07
3.06
3.04
3.03
O
NH
H
H
H
O-N
Bn
N
O
9e
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.07
0.98
0.99
1.00
6.03
2.02
2.20
1.00
1.11
1.09
1.15
1.12
4.46
4.53
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


162.57
150.95
138.36
138.23
132.52
130.10
128.67
128.40
128.33
127.76
127.18
126.90
126.11
115.07
74.57
71.91
66.59
59.85
59.40
48.63
O
NH
H
H
H
O
N
Bn
O
N
9e
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

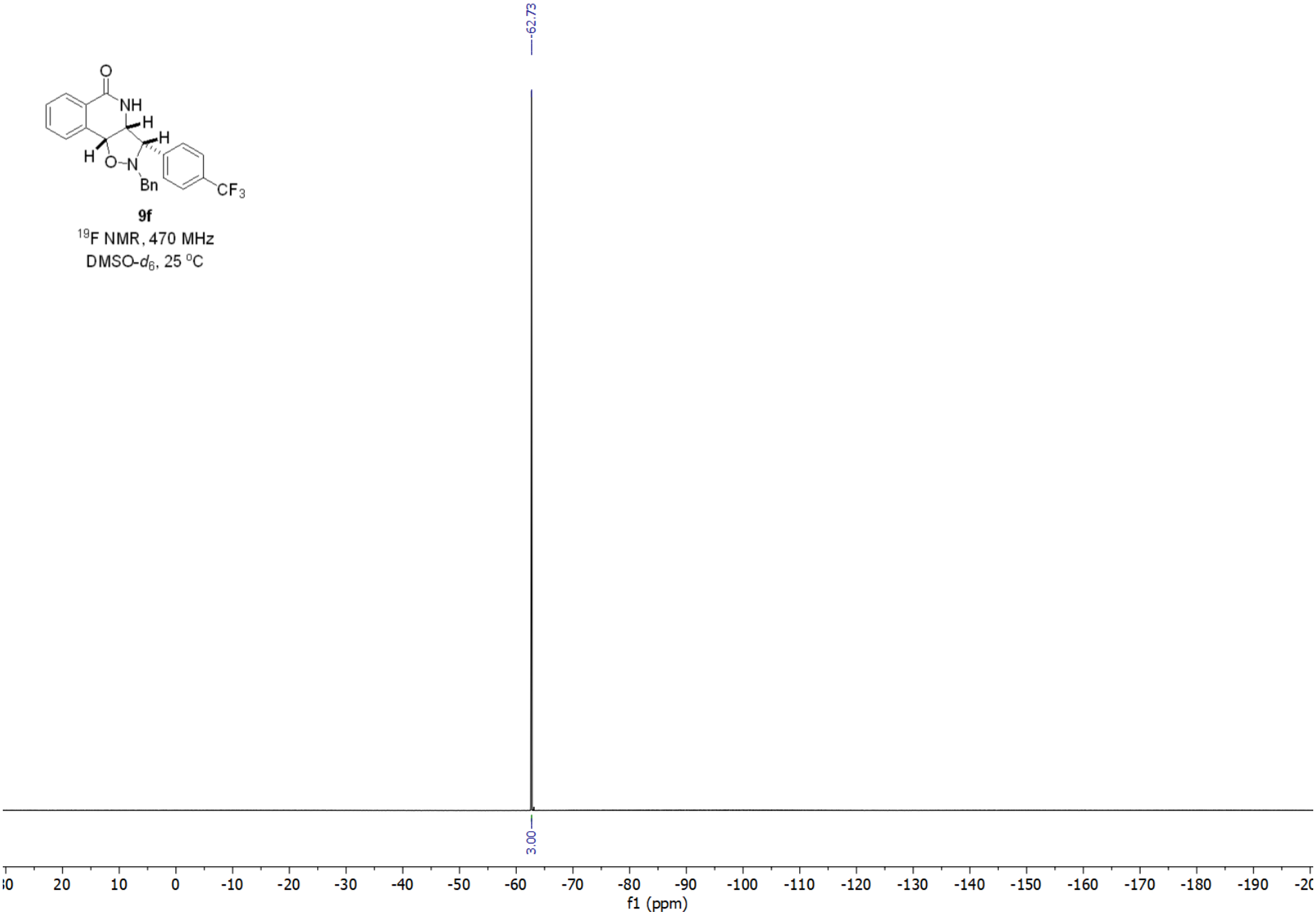

7.82 7.81 7.61 7.61 7.61 7.60 7.60 7.59 7.58 7.58 7.54 7.53 7.47 7.47 7.46 7.45 7.44 7.44 7.42 7.41 7.33 7.31 7.26 7.26 7.25 7.25 7.23 7.21 7.21 7.20 7.20 7.19 5.64 5.63
4.86 4.85 4.84 4.83 4.82 4.82 4.42 4.40
3.99 3.96 3.93 3.90
O
NH
H
H
H
O–N
Bn
CF3
9f
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.01 3.02 1.02 1.99 1.98 5.13 1.00 1.10 1.09 1.11 1.10
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

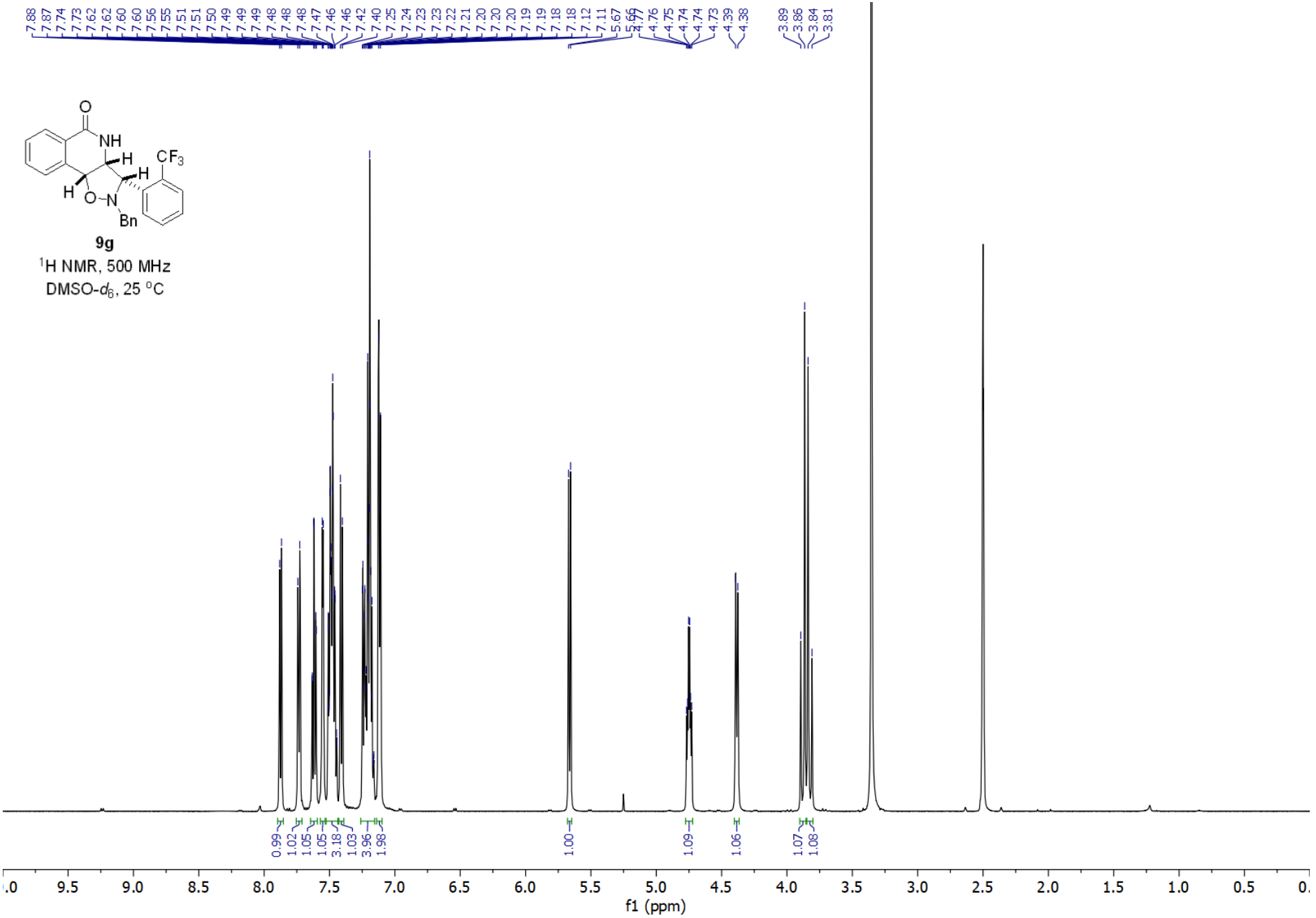

O
NH
H
H
H
O
N
Bn
CF3
9f
13C NMR, 125 MHz
DMSO-d6, 25 °C
162.58
141.47
137.90
137.87
132.64
130.00
128.88
128.74
128.65
128.62
128.40
128.37
128.13
128.06
127.97
127.68
127.33
126.87
125.81
125.31
125.28
125.25
125.22
123.64
121.48
73.92
71.80
60.29
59.55
129.0
128.5
125.3
125.1
128
126
124
122
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1

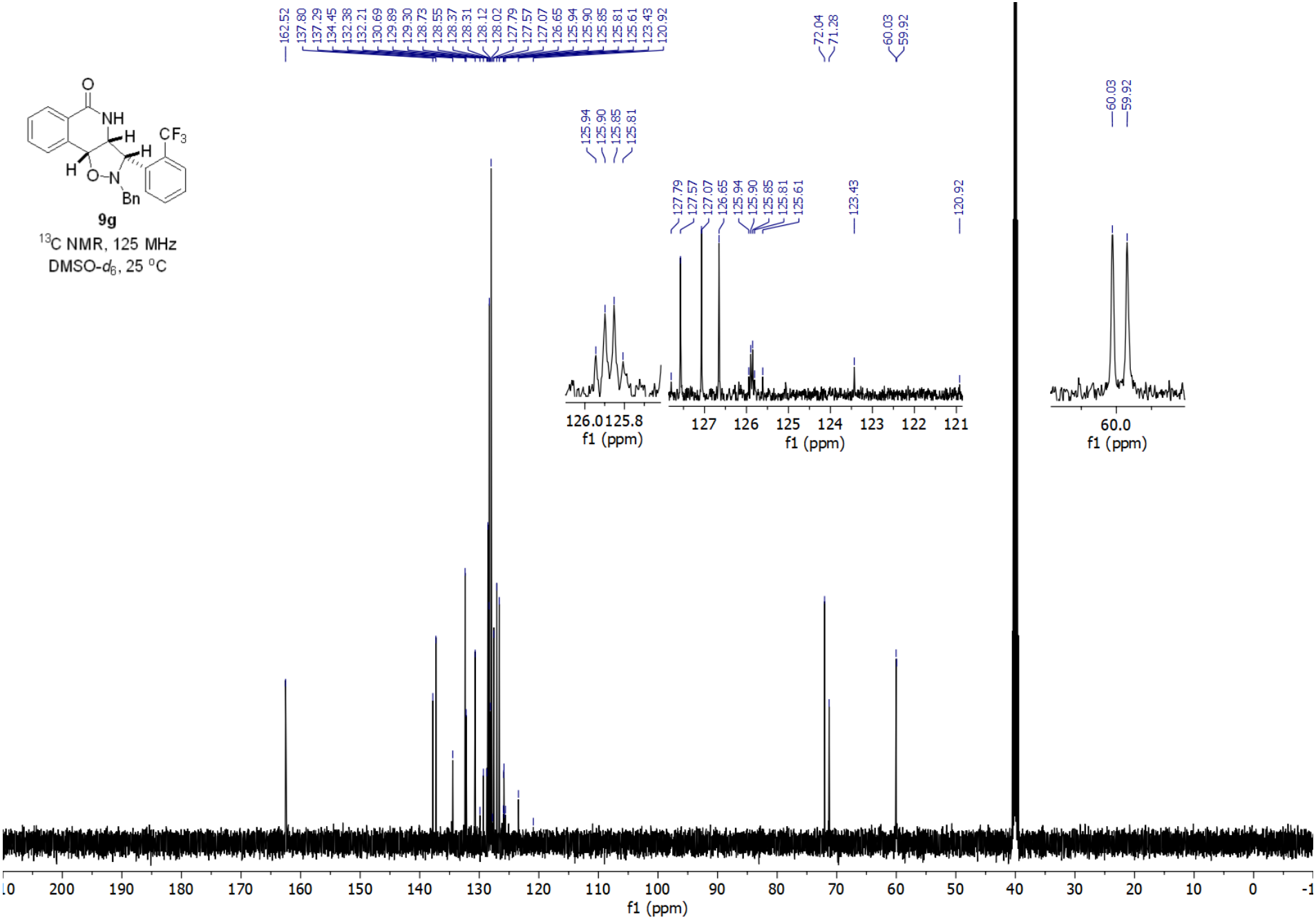
9f

^{19}F NMR, 470 MHz

DMSO-d_6, 25 °C



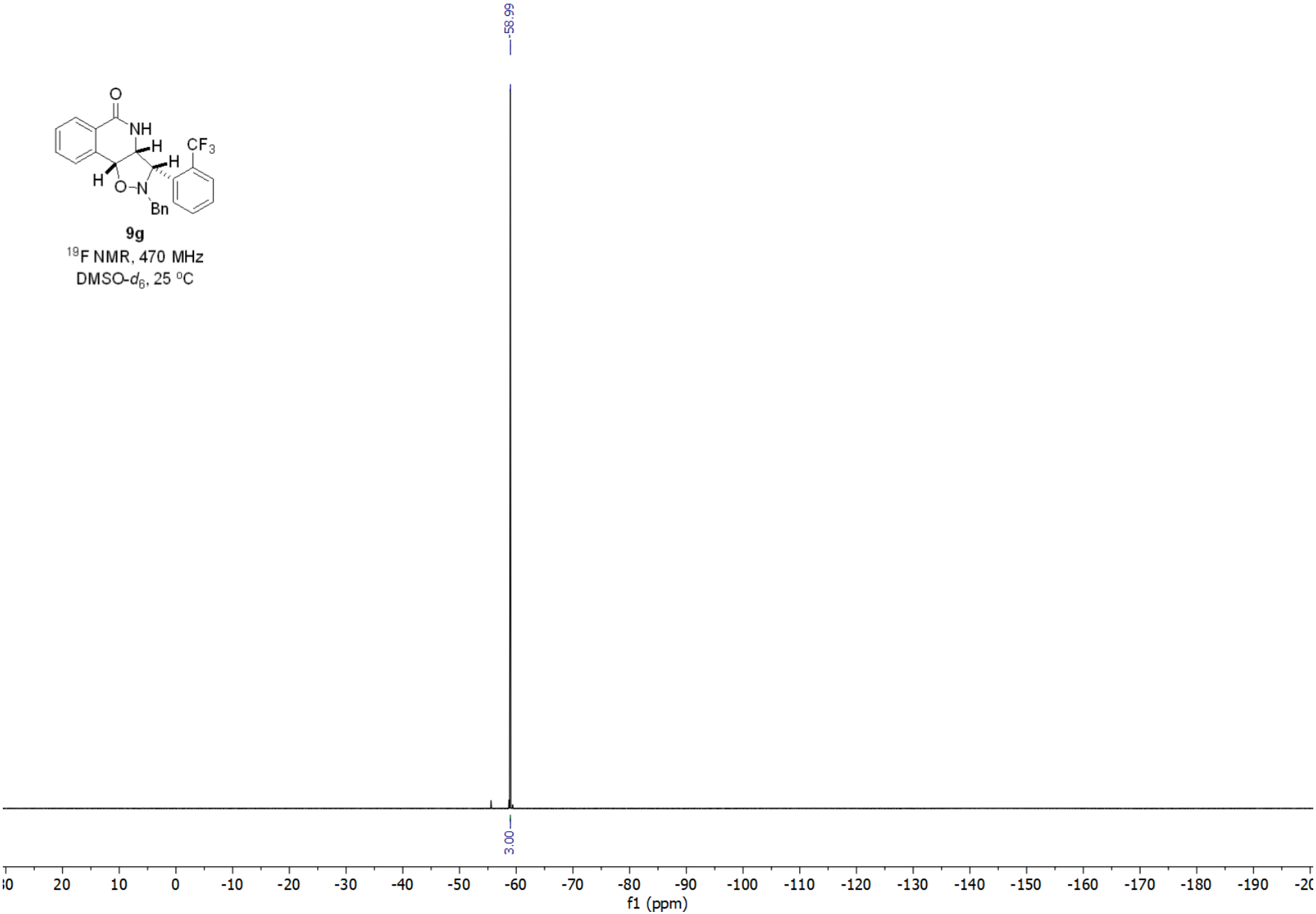

7.88 7.87 7.74 7.73 7.62 7.62 7.60 7.60 7.56 7.55 7.51 7.51 7.50 7.49 7.49 7.49 7.48 7.48 7.48 7.47 7.46 7.46 7.42 7.40 7.25 7.24 7.23 7.23 7.22 7.21 7.20 7.20 7.20 7.19 7.19 7.18 7.18 7.12 7.11 5.67 5.66 4.77 4.76 4.75 4.74 4.74 4.73 4.39 4.38 3.89 3.86 3.84 3.81
O
NH
H
H
H
O
N
Bn
CF3
9g
1H NMR, 500 MHz
DMSO-d6, 25 °C
0.99 1.02 1.05 1.05 3.18 1.03 3.96 1.98 1.00 1.09 1.06 1.07 1.08
f1 (ppm)


9g
^{13}C NMR, 125 MHz
DMSO-d_6, 25 °C
f1 (ppm)

9g

^{19}F NMR, 470 MHz

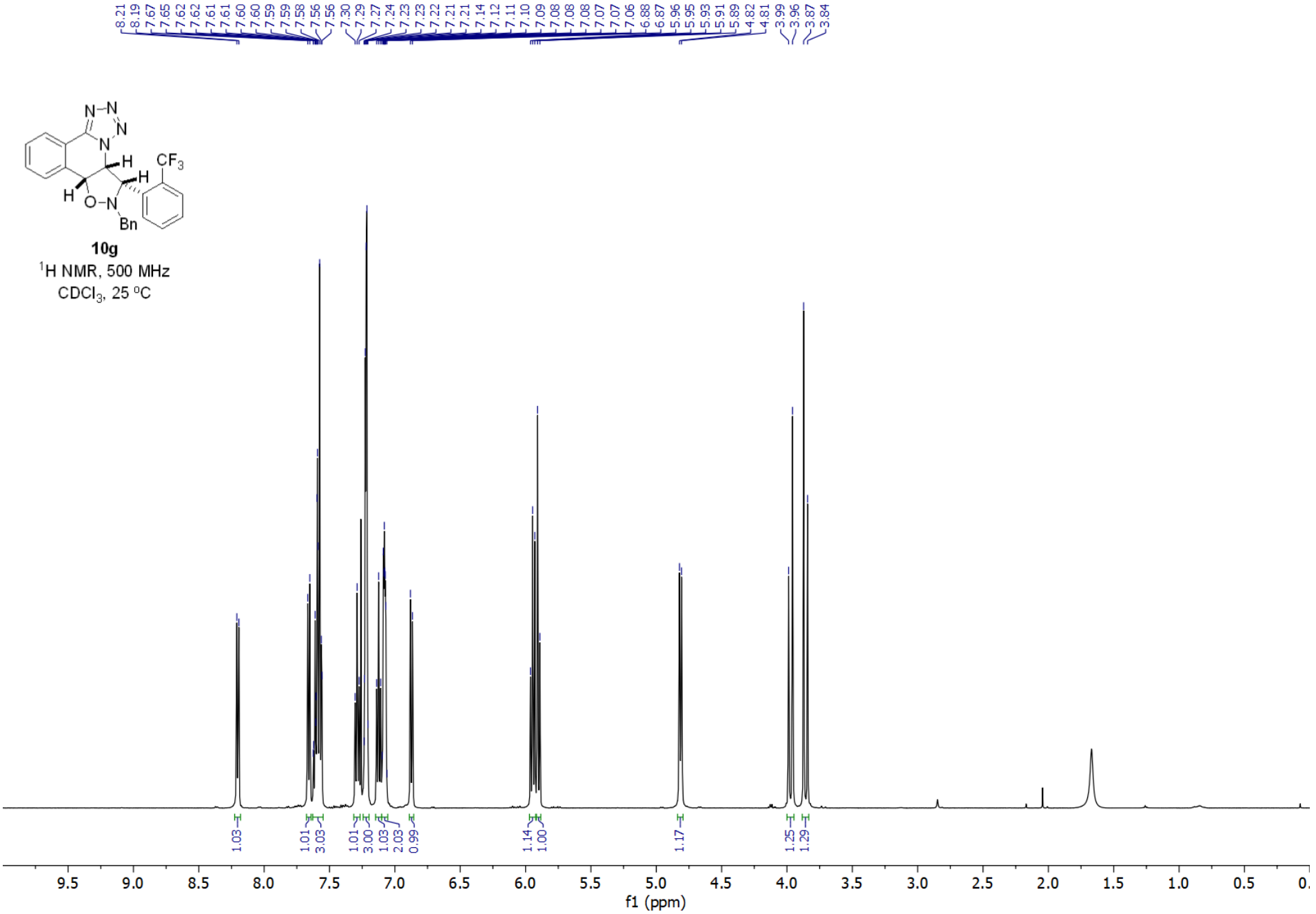
DMSO-d_6, 25 ^{o}C

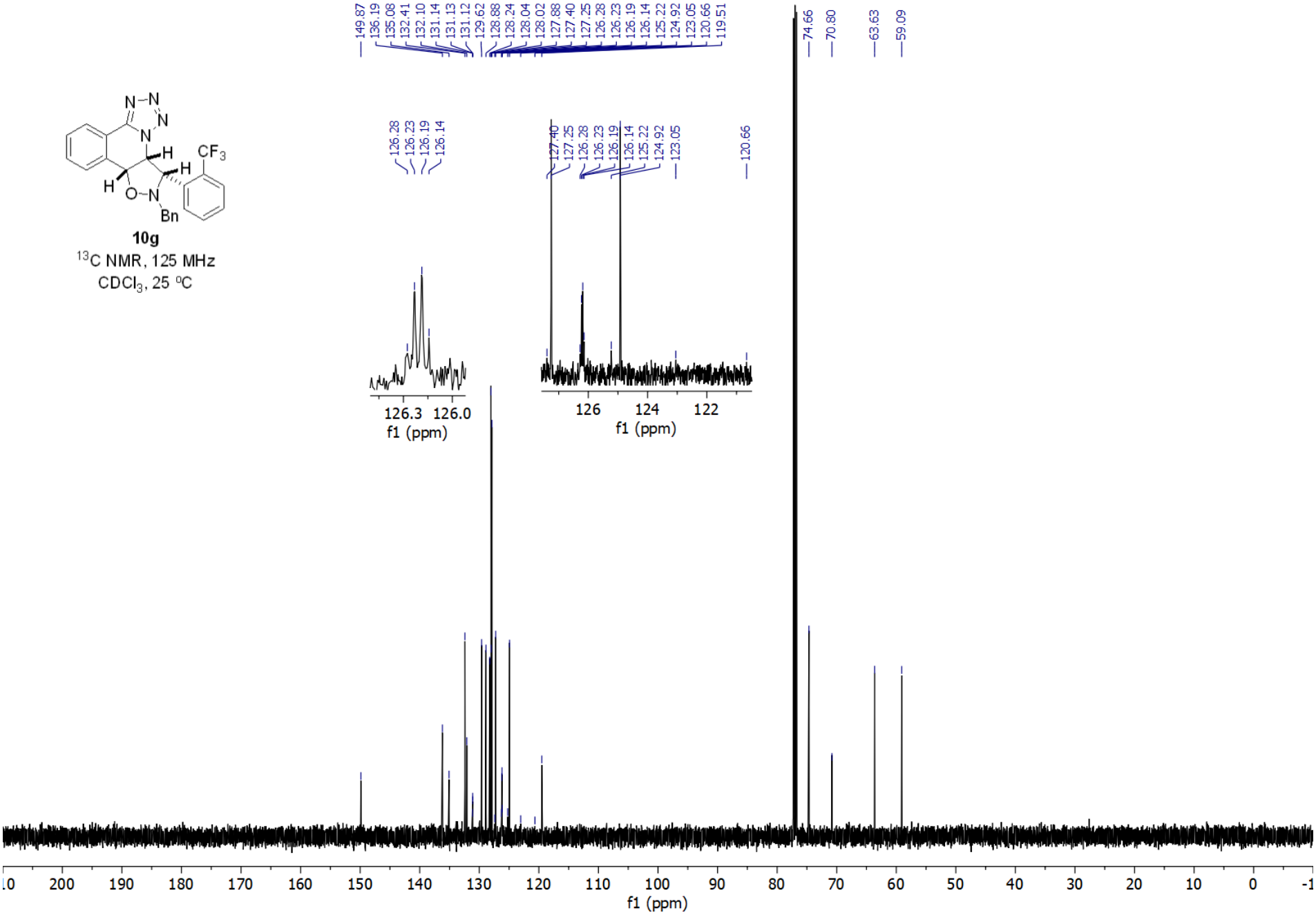


10g

^{1}H NMR, 500 MHz

$CDCl_3$, 25 ^oC

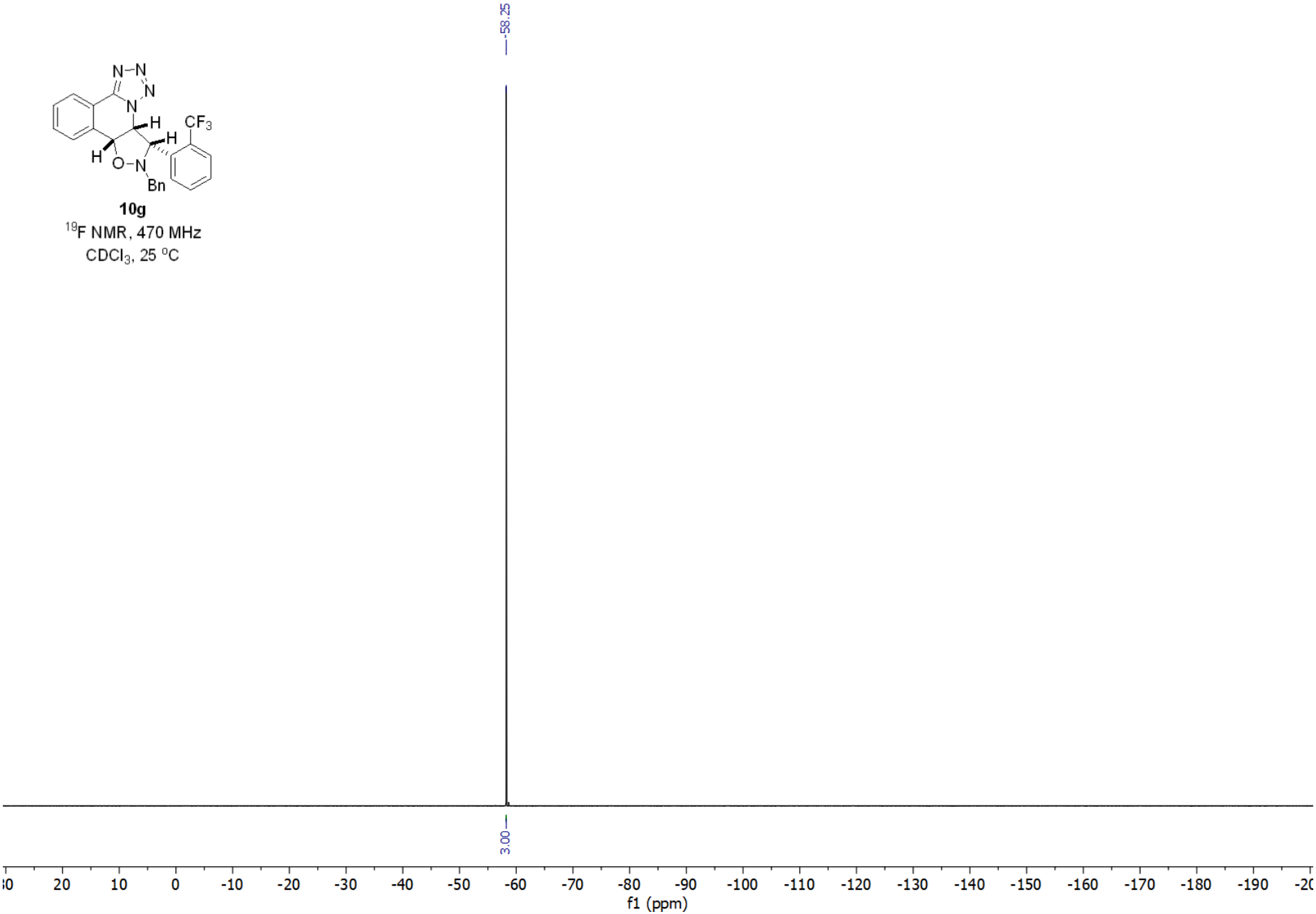


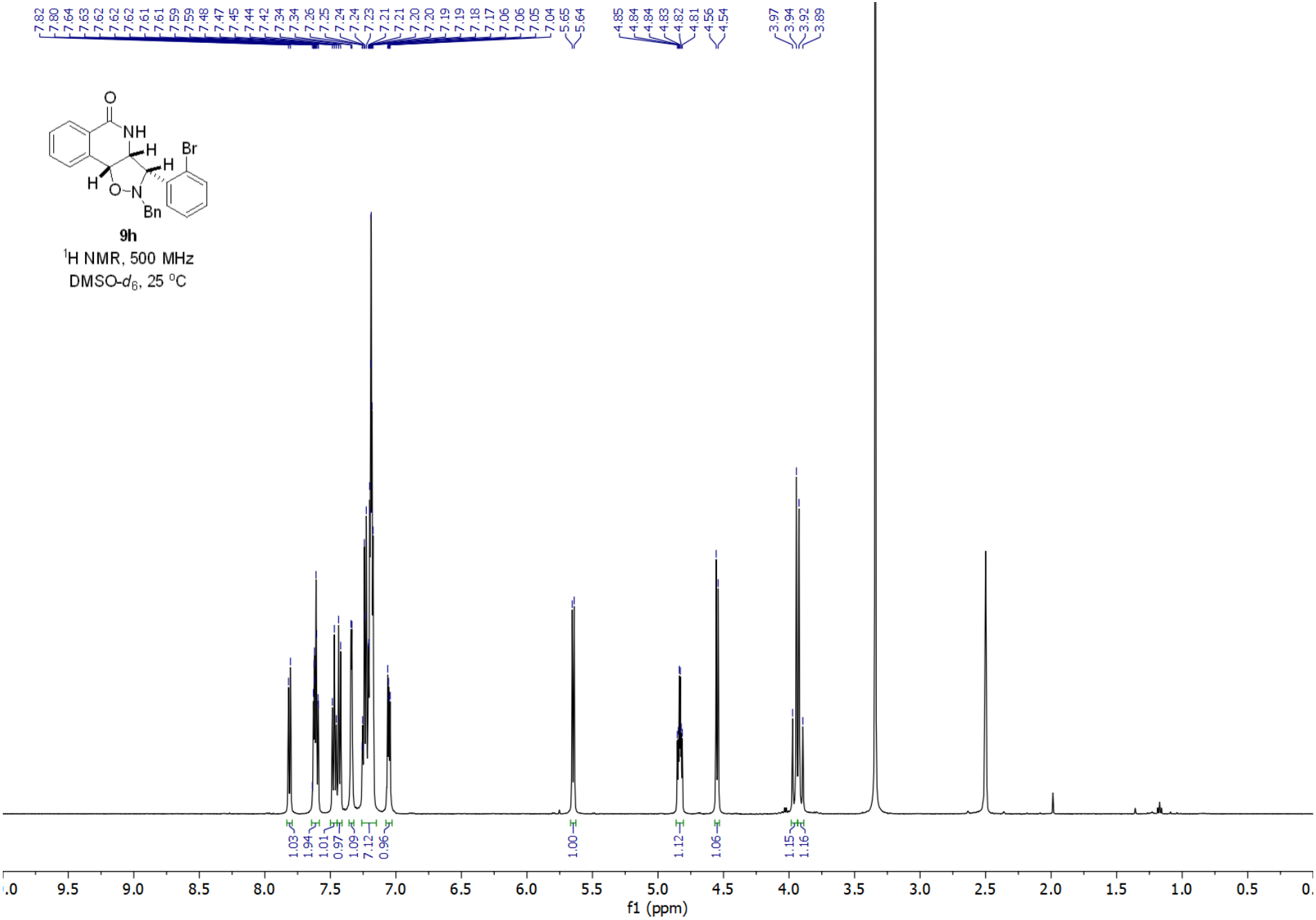

149.87
136.19
135.08
132.41
132.10
131.14
131.13
131.12
129.62
128.88
128.24
128.04
128.02
127.88
127.40
127.25
126.28
126.23
126.19
126.14
125.22
124.92
123.05
120.66
119.51
74.66
70.80
63.63
59.09
N–N
N
N
H
H
H
O–N
Bn
CF3
10g
13C NMR, 125 MHz
CDCl3, 25 °C
126.3 126.0
f1 (ppm)
126
124
122
f1 (ppm)
f1 (ppm)

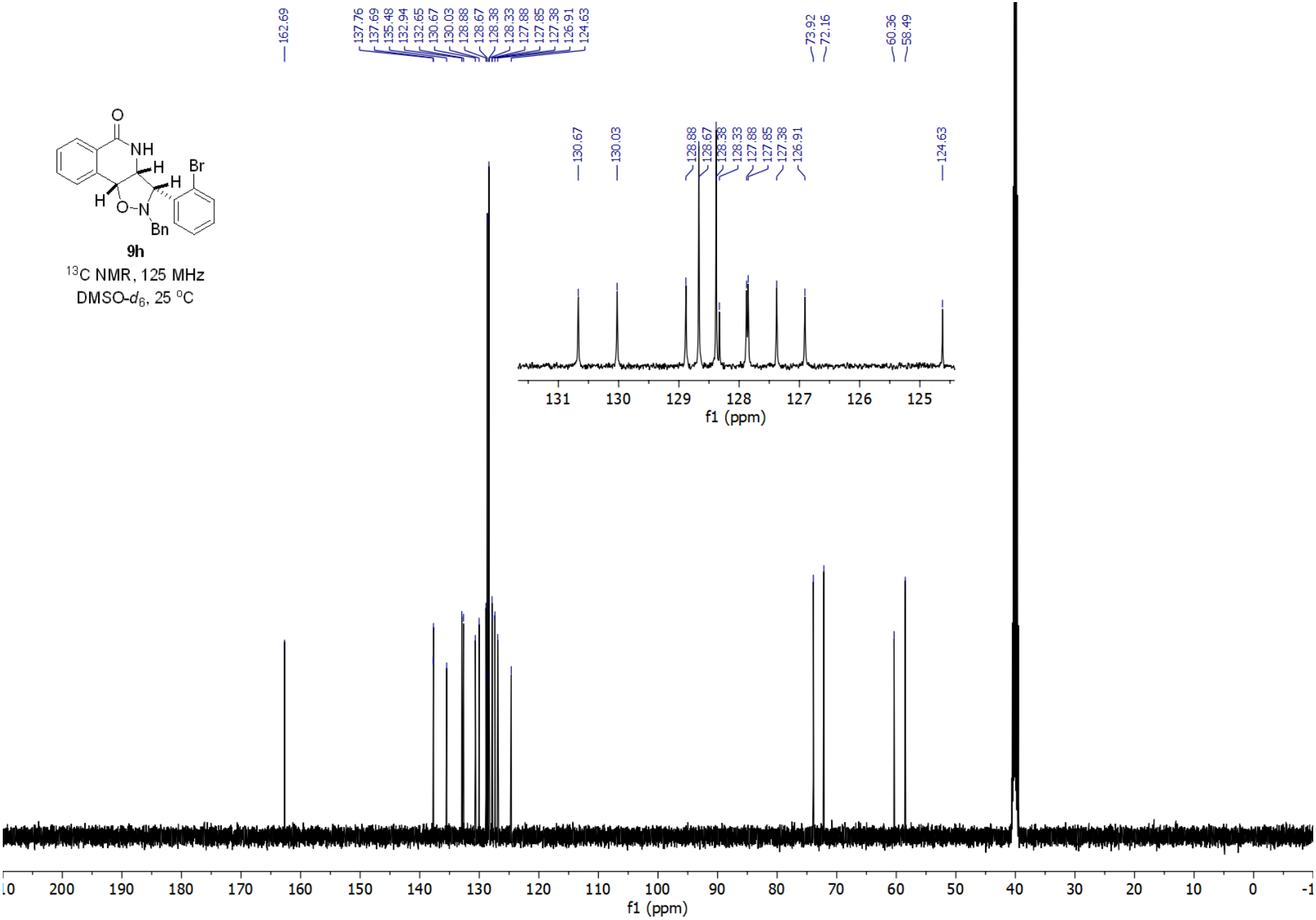
10g

^{19}F NMR, 470 MHz

$CDCl_3$, 25 ^{o}C



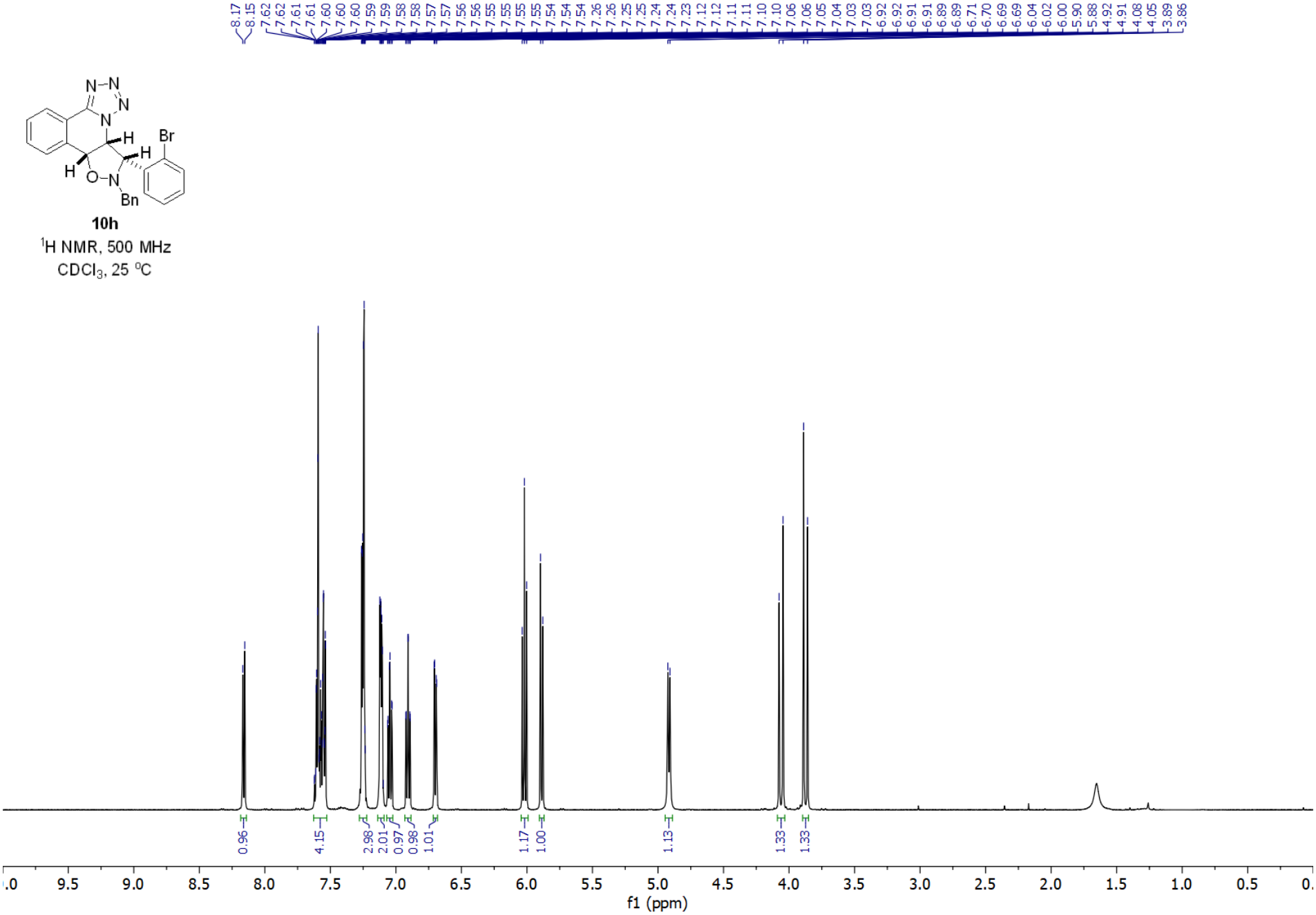

7.82 7.80 7.64 7.63 7.62 7.62 7.62 7.61 7.61 7.59 7.59 7.48 7.47 7.45 7.44 7.42 7.34 7.34 7.26 7.25 7.24 7.24 7.23 7.21 7.21 7.20 7.20 7.19 7.19 7.18 7.17 7.06 7.05 7.04 5.65 5.64 4.85 4.84 4.84 4.83 4.82 4.81 4.56 4.54 3.97 3.94 3.92 3.89
O
NH
H
H
H
O–N
Br
Bn
9h
^{1}H NMR, 500 MHz
DMSO-d_6, 25 °C
1.03 1.94 1.01 0.97 1.09 7.12 0.96 1.00 1.12 1.06 1.15 1.16
f1 (ppm)

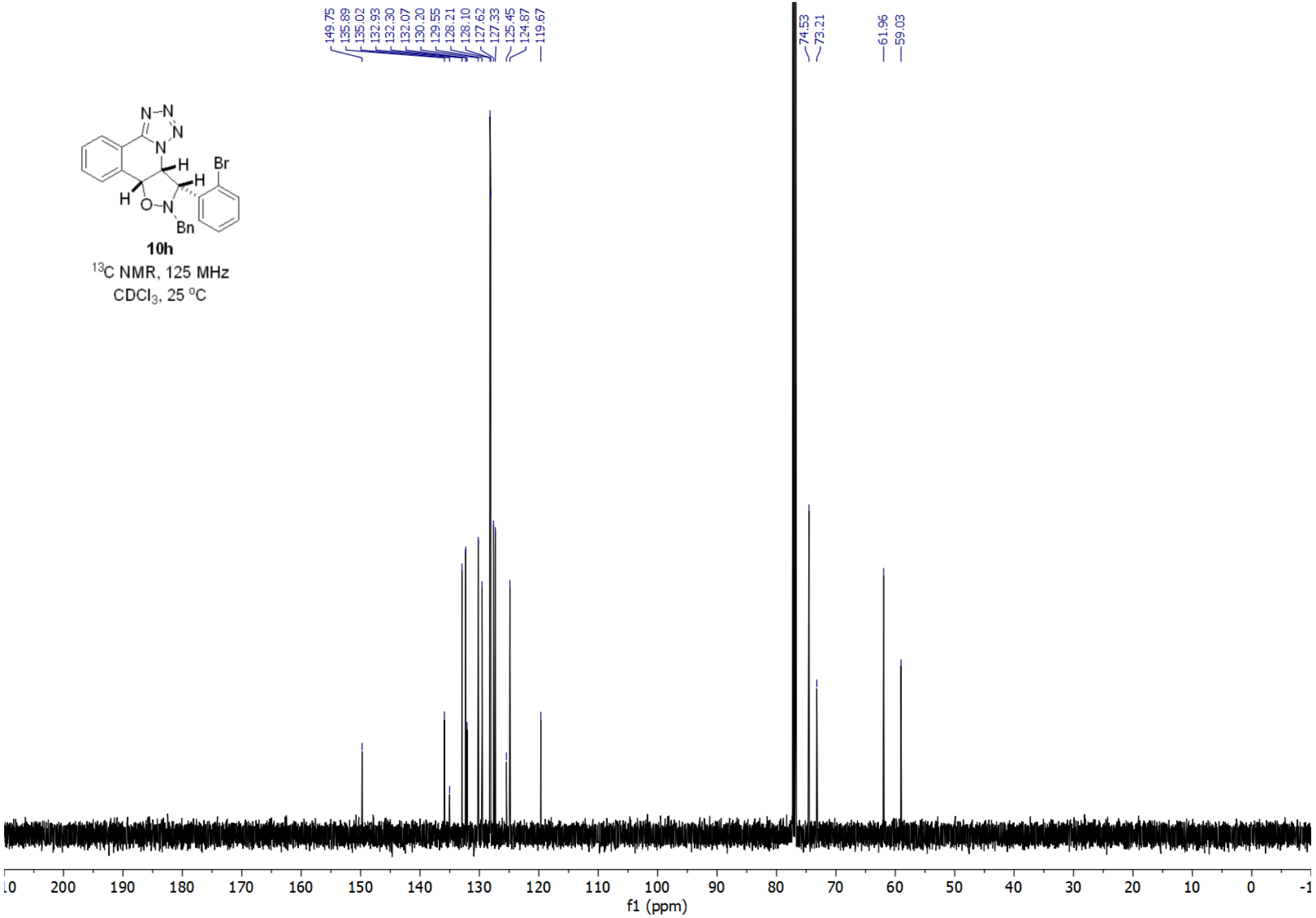

162.69
137.76
137.69
135.48
132.94
132.65
130.67
130.03
128.88
128.67
128.38
128.33
127.88
127.85
127.38
126.91
124.63
73.92
72.16
60.36
58.49
O
NH
H
H
Br
H
O
N
Bn
9h
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)
f1 (ppm)

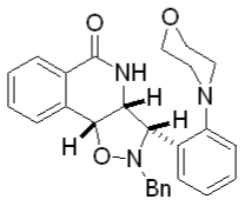
10h

^{1}H NMR, 500 MHz

$CDCl_3$, 25 ^oC



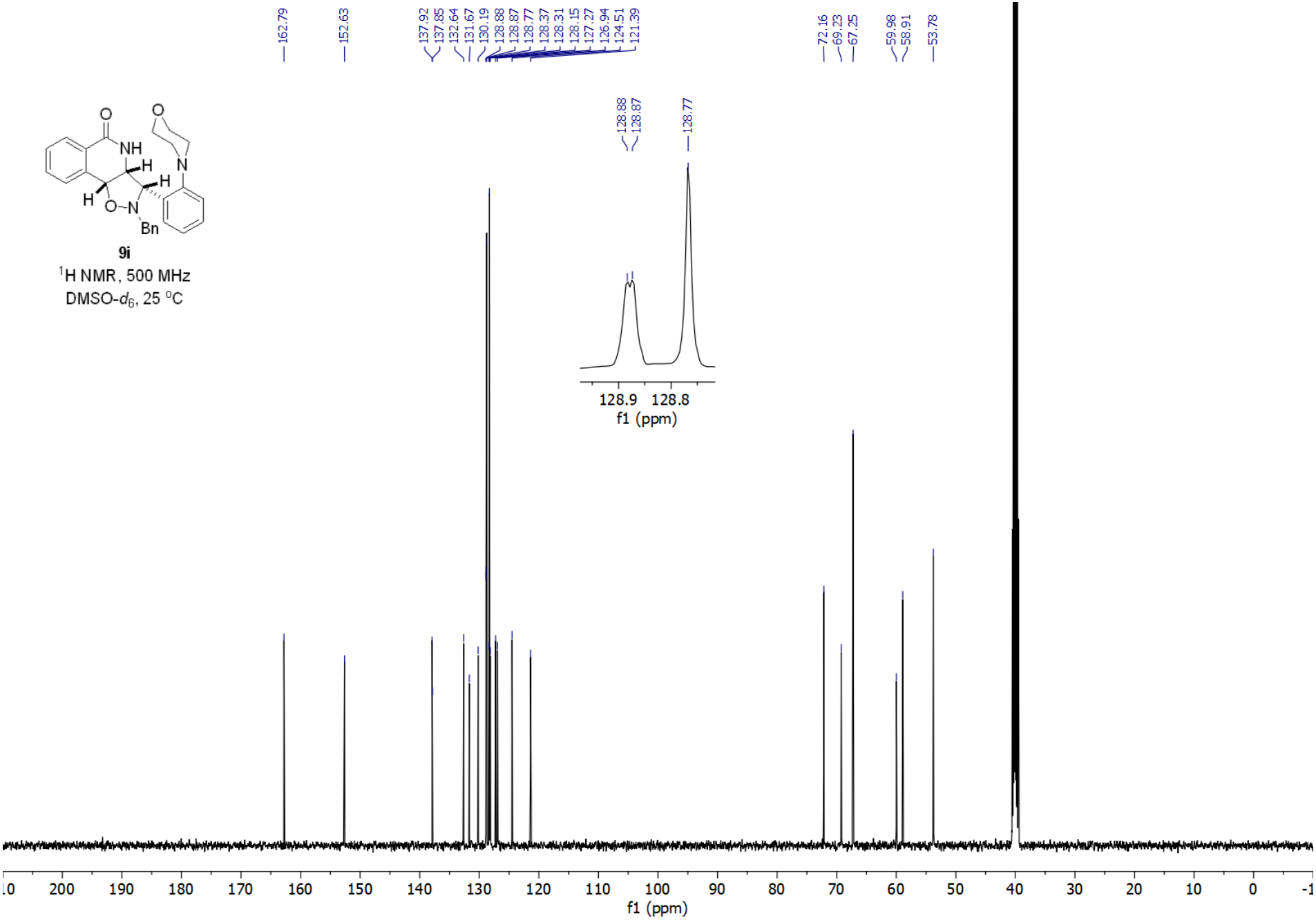

149.75
135.89
135.02
132.93
132.30
132.07
130.20
129.55
128.21
128.10
127.62
127.33
125.45
124.87
119.67
74.53
73.21
61.96
59.03
N
N
N
H
H
H
O
N
Br
Bn
10h
13C NMR, 125 MHz
CDCl3, 25 °C
f1 (ppm)

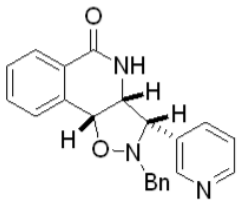


9i

^{1}H NMR, 500 MHz

DMSO-d_6, 25 ^{o}C

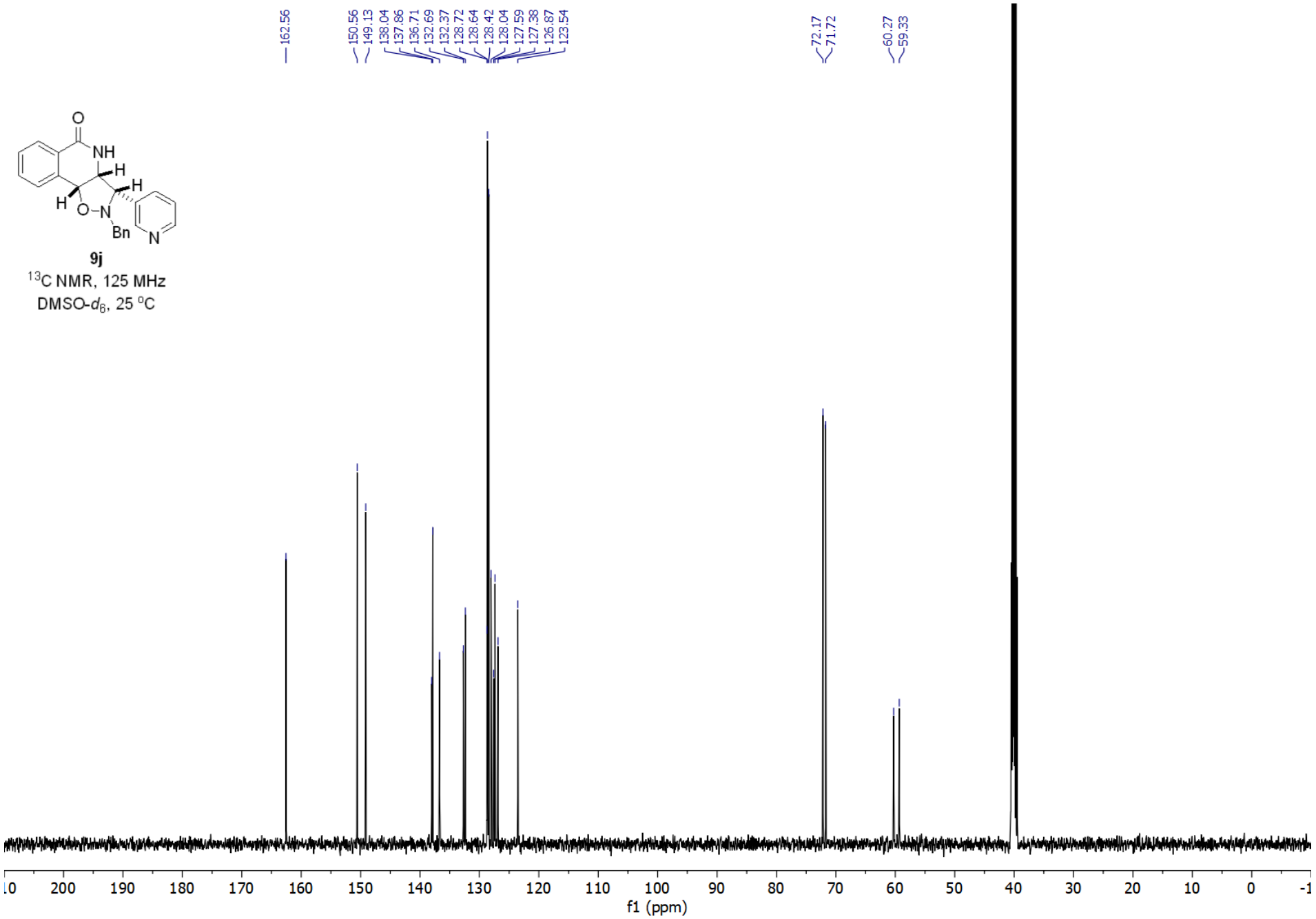

162.79
152.63
137.92
137.85
132.64
131.67
130.19
128.88
128.87
128.77
128.37
128.31
128.15
127.27
126.94
124.51
121.39
72.16
69.23
67.25
59.98
58.91
53.78
O
NH
H
H
H
O
N
O–N
Bn
9i
1H NMR, 500 MHz
DMSO-d6, 25 °C
128.9
128.8
f1 (ppm)
f1 (ppm)

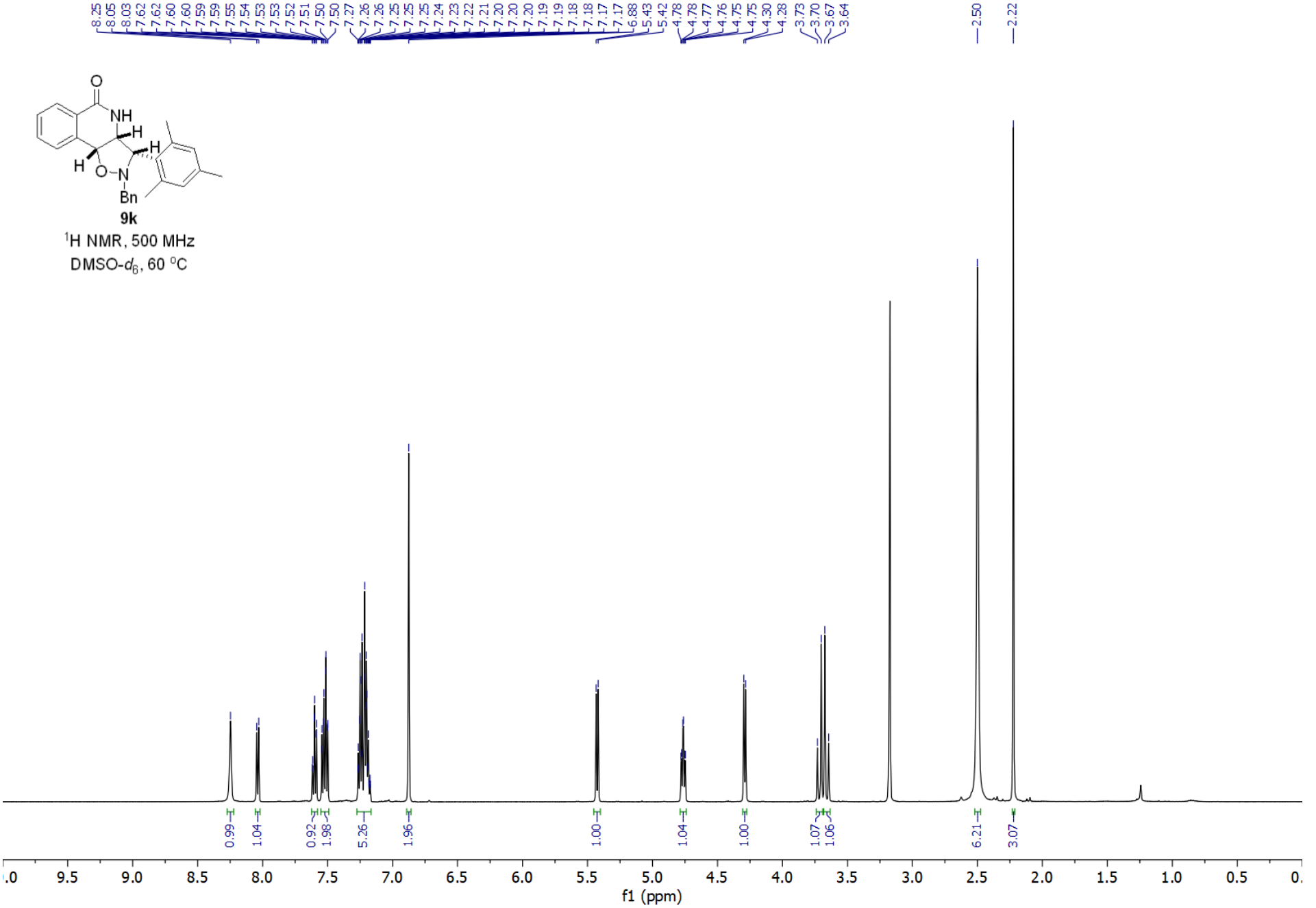


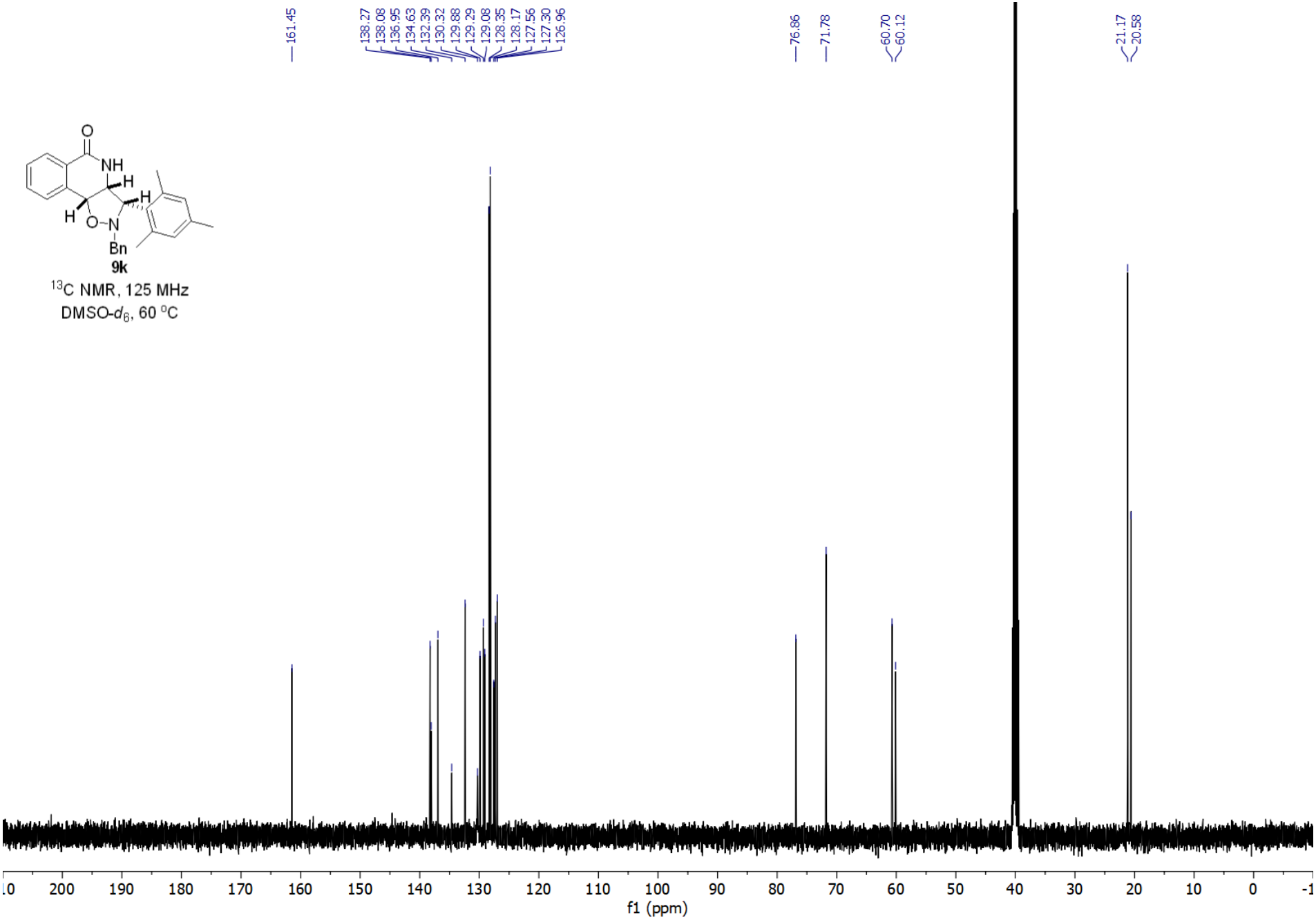
9j

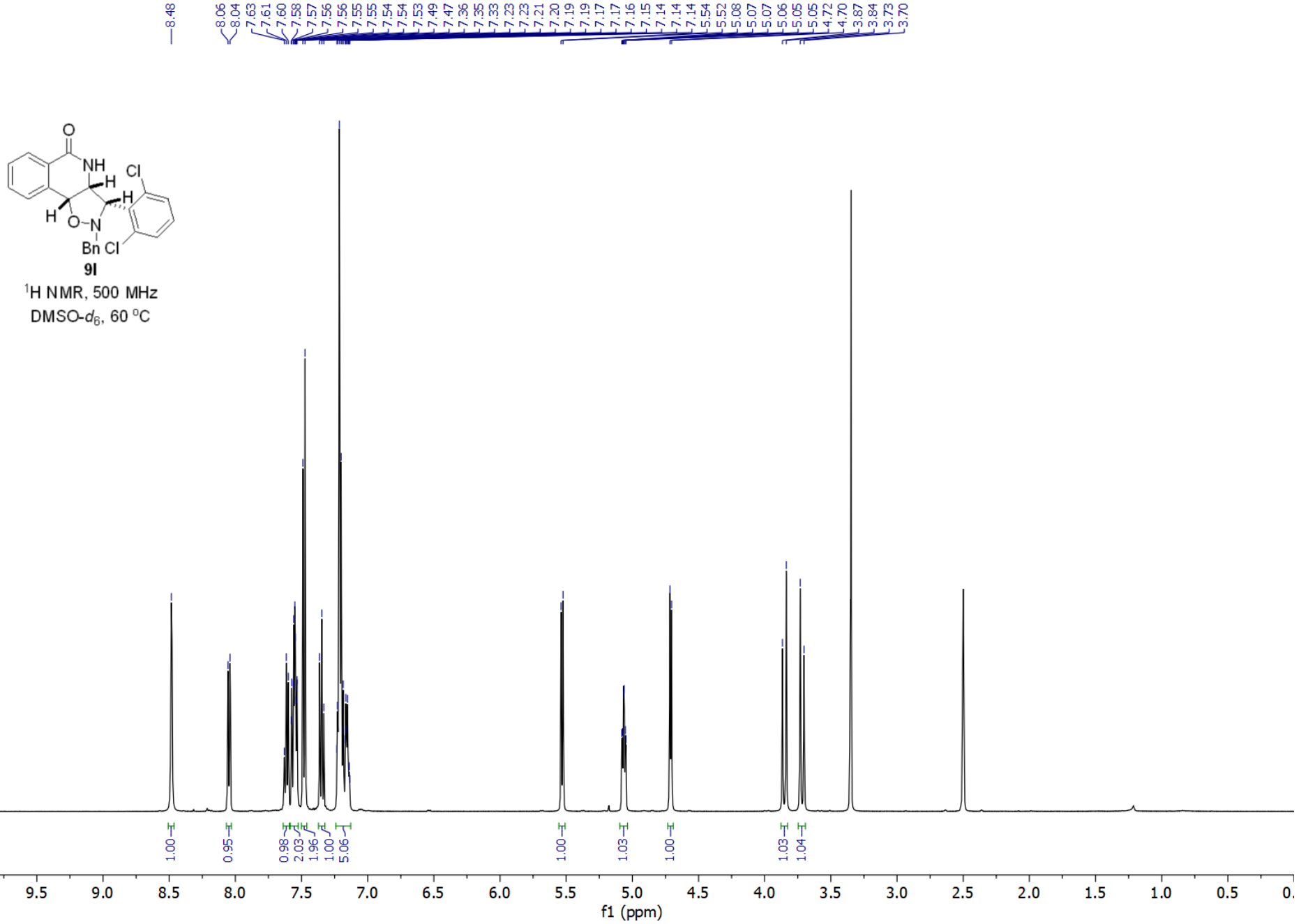
^{1}H NMR, 500 MHz

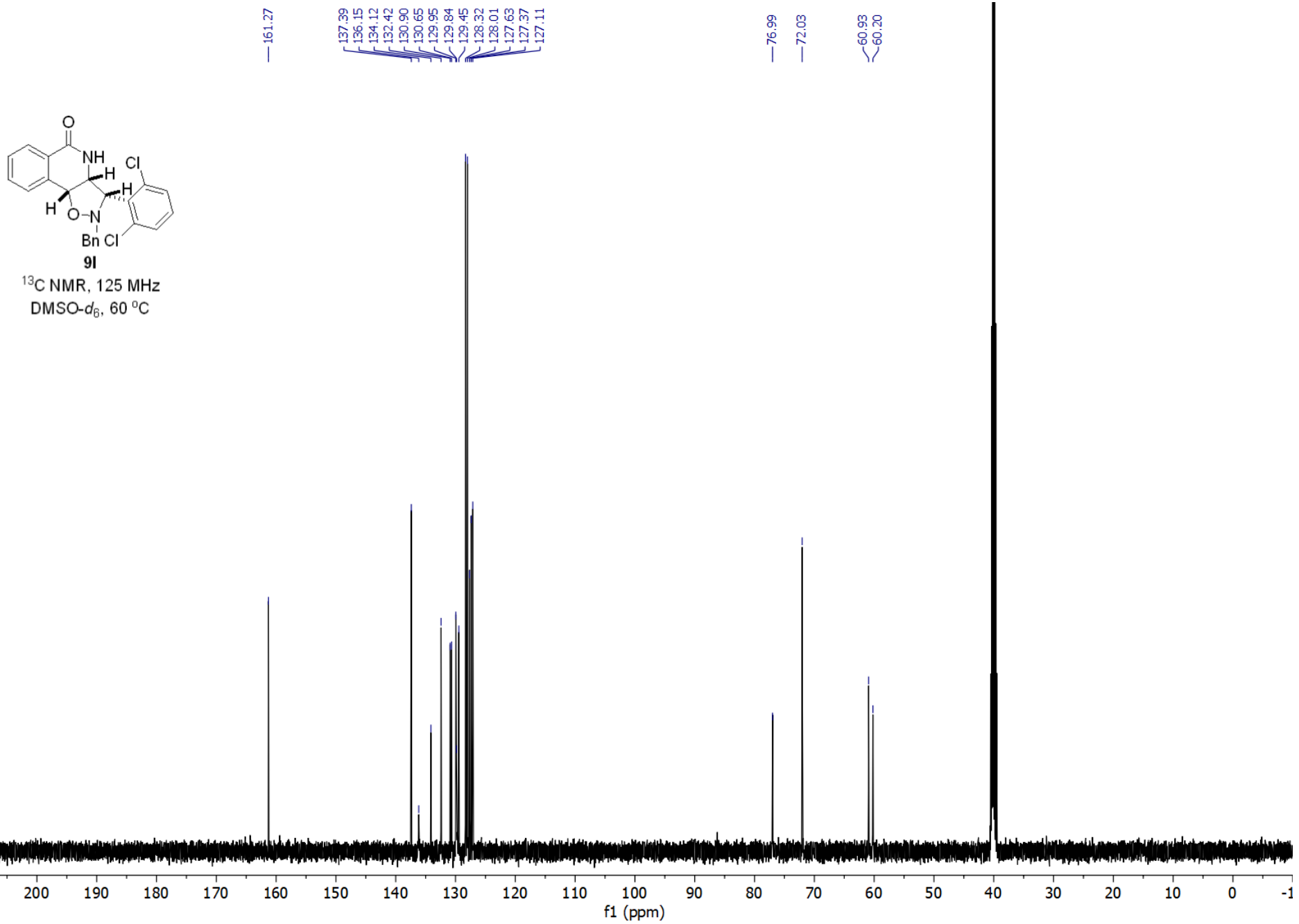
DMSO-d_6, 25 ^{o}C

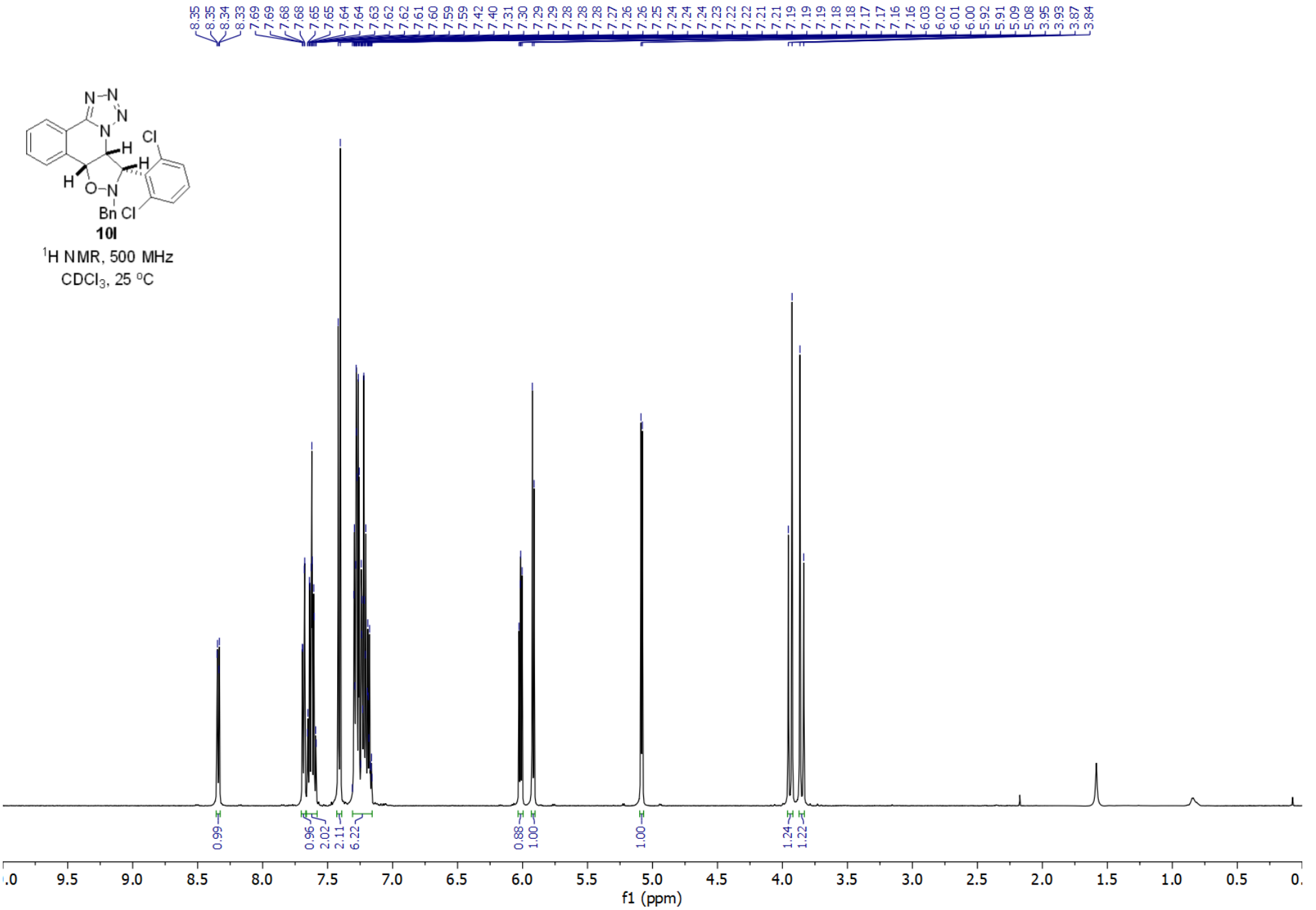

162.56
150.56
149.13
138.04
137.86
136.71
132.69
132.37
128.72
128.64
128.42
128.04
127.59
127.38
126.87
123.54
72.17
71.72
60.27
59.33
O
NH
H
H
H
O
N
Bn
N
9j
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

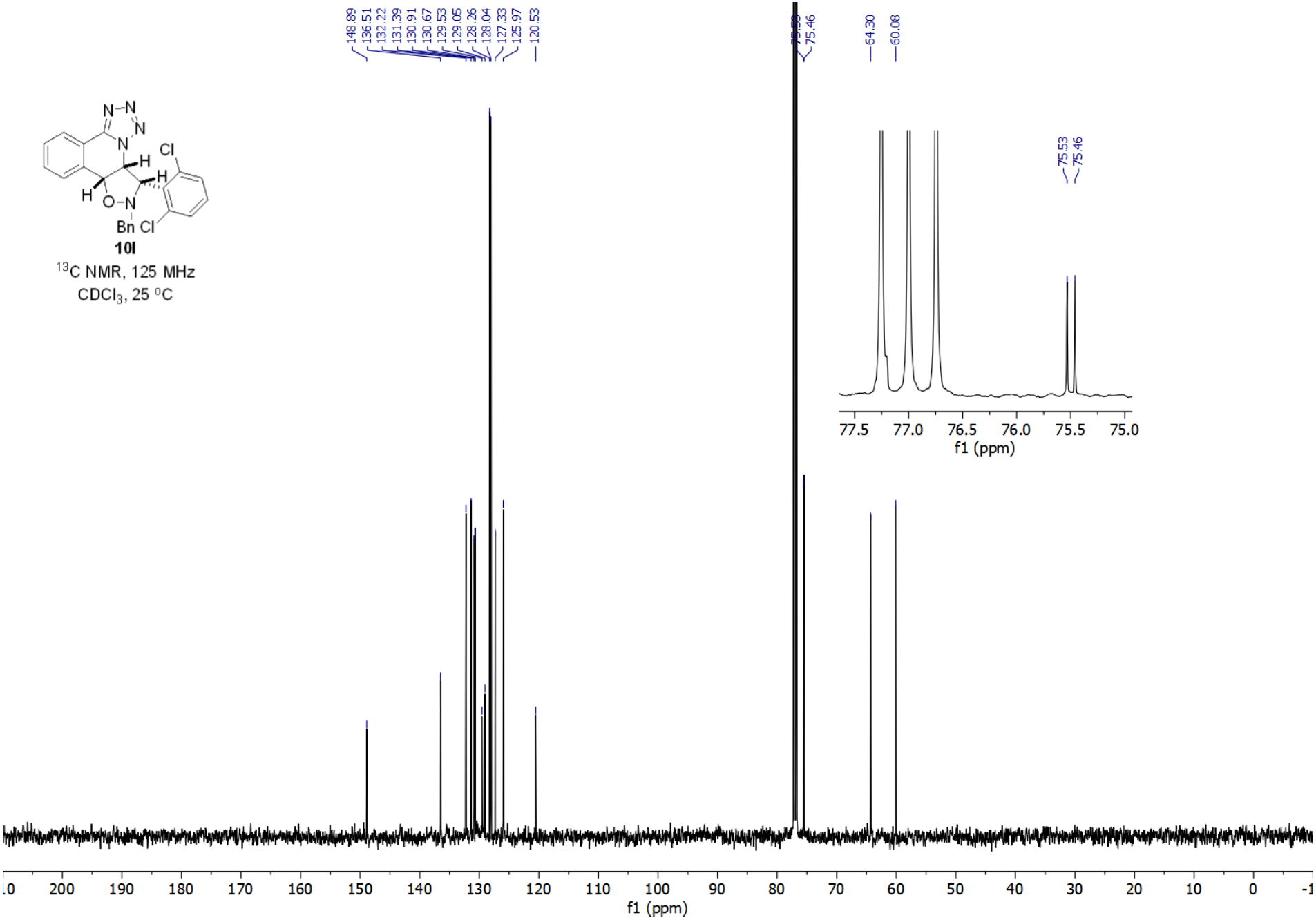

8.25 8.05 8.03 7.62 7.62 7.60 7.60 7.59 7.59 7.55 7.54 7.53 7.53 7.52 7.51 7.50 7.50 7.27 7.26 7.26 7.25 7.25 7.25 7.24 7.23 7.22 7.21 7.20 7.20 7.20 7.19 7.19 7.18 7.18 7.17 7.17 6.88 5.43 5.42 4.78 4.78 4.77 4.76 4.75 4.75 4.30 4.28 3.73 3.70 3.67 3.64 2.50 2.22
O
NH
H
H
H
O
N
Bn
9k
1H NMR, 500 MHz
DMSO-d6, 60 °C
0.99 1.04 0.92 1.98 5.26 1.96 1.00 1.04 1.00 1.07 1.06 6.21 3.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

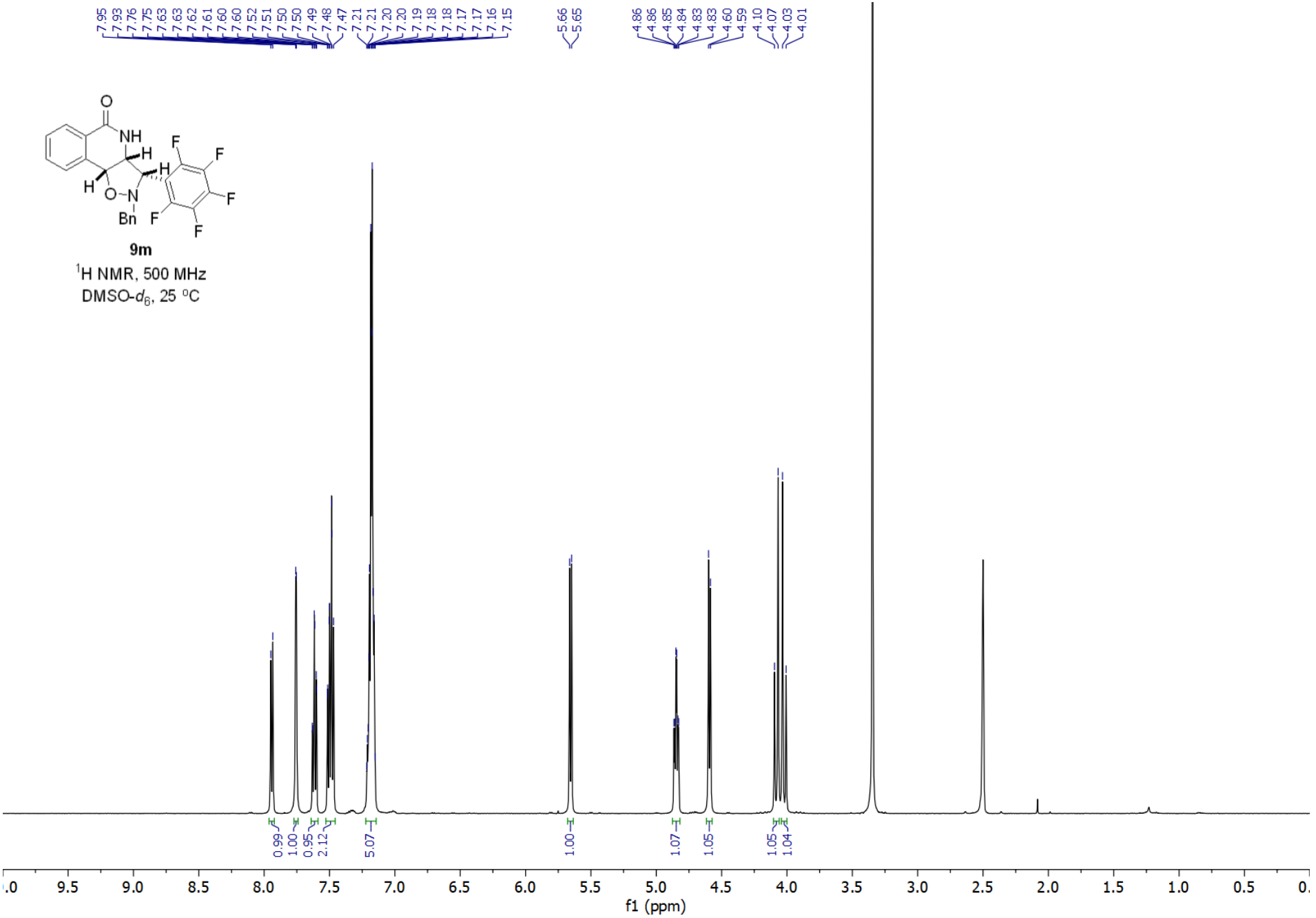

161.45
138.27
138.08
136.95
134.63
132.39
130.32
129.88
129.29
129.08
128.35
128.17
127.56
127.30
126.96
76.86
71.78
60.70
60.12
21.17
20.58
O
NH
H
H
H
O
N
Bn
9k
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)


8.48
8.06
8.04
7.63
7.61
7.60
7.58
7.57
7.56
7.56
7.55
7.55
7.54
7.54
7.53
7.49
7.47
7.36
7.35
7.33
7.23
7.23
7.21
7.20
7.19
7.19
7.17
7.17
7.16
7.15
7.14
7.14
7.14
5.54
5.52
5.08
5.07
5.07
5.06
5.05
5.05
4.72
4.70
3.87
3.84
3.73
3.70
O
NH
H
Cl
H
H
O
N
Bn
Cl
9l
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.00
0.95
0.98
2.03
1.96
1.00
5.06
1.00
1.03
1.00
1.03
1.04
f1 (ppm)


161.27
137.39
136.15
134.12
132.42
130.90
130.65
129.95
129.84
129.45
128.32
128.01
127.63
127.37
127.11
76.99
72.03
60.93
60.20
O
NH
H
Cl
H
H
O
N
Bn
Cl
9l
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)


8.35 8.35 8.34 8.33 7.69 7.69 7.68 7.68 7.65 7.65 7.64 7.64 7.63 7.62 7.62 7.61 7.60 7.59 7.59 7.42 7.40 7.31 7.30 7.29 7.29 7.28 7.28 7.28 7.27 7.26 7.26 7.25 7.24 7.24 7.24 7.23 7.22 7.22 7.21 7.21 7.19 7.19 7.19 7.18 7.18 7.17 7.17 7.16 7.16 6.03 6.02 6.01 6.00 5.92 5.91 5.09 5.08 3.95 3.93 3.87 3.84
N–N
N
N
H
H
H
O–N
Cl
Bn Cl
10l
1H NMR, 500 MHz
CDCl3, 25 °C
0.99
0.96
2.02
2.11
6.22
0.88
1.00
1.00
1.24
1.22
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

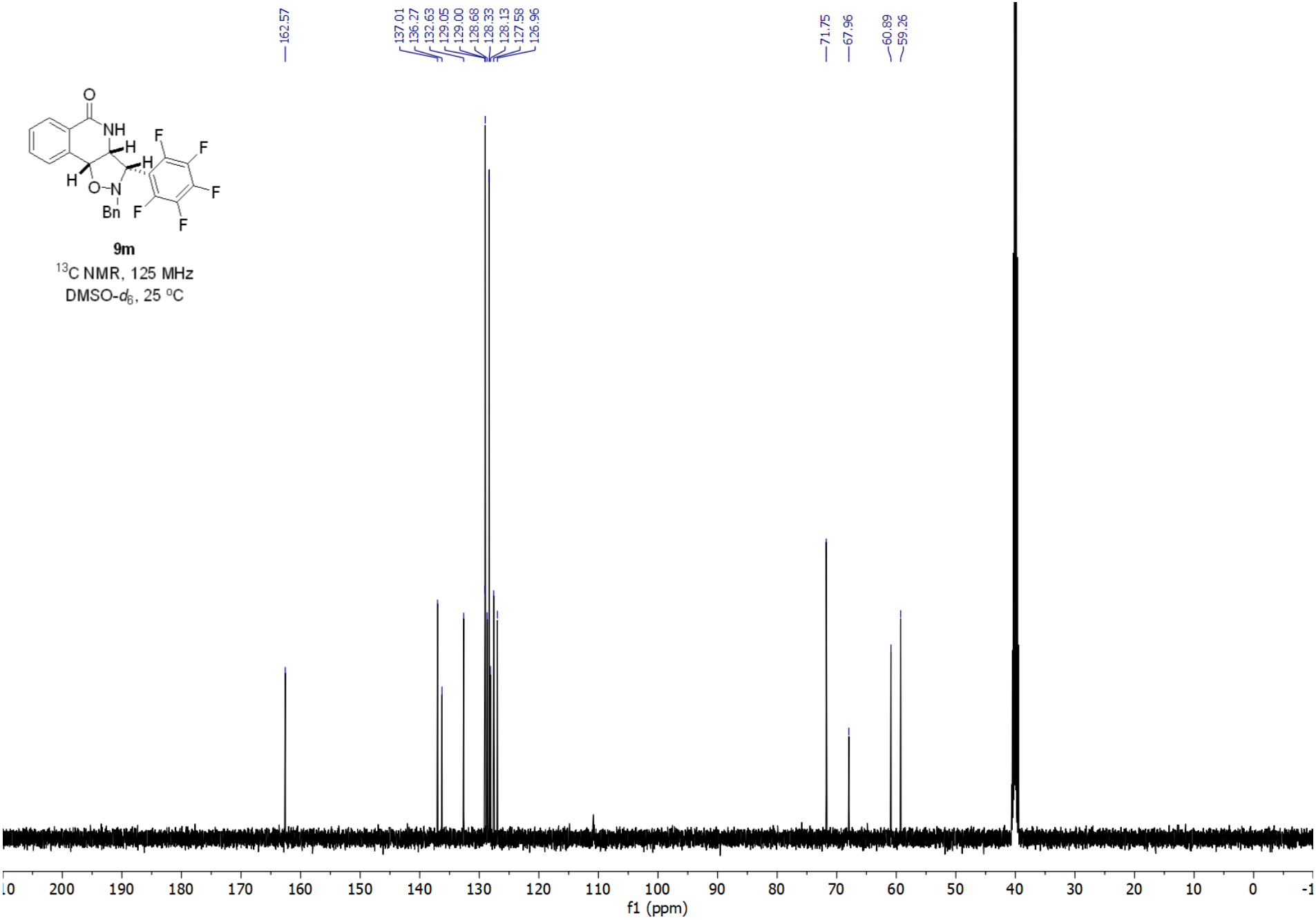

148.89
136.51
132.22
131.39
130.91
130.67
129.53
129.05
128.26
128.04
127.33
125.97
120.53
75.53
75.46
64.30
60.08
Cl
H
H
H
O
N
Bn Cl
10l
13C NMR, 125 MHz
CDCl3, 25 °C
77.5
77.0
76.5
76.0
75.5
75.0
f1 (ppm)
f1 (ppm)


7.95
7.93
7.76
7.75
7.63
7.63
7.62
7.61
7.60
7.60
7.52
7.51
7.50
7.50
7.49
7.48
7.47
7.21
7.21
7.20
7.20
7.19
7.18
7.18
7.17
7.17
7.16
7.15
5.66
5.65
4.86
4.86
4.85
4.84
4.83
4.83
4.60
4.59
4.10
4.07
4.03
4.01
O
NH
H
H
H
O
N
Bn
F
F
F
F
F
9m
1H NMR, 500 MHz
DMSO-d6, 25 °C
0.99
1.00
0.95
2.12
5.07
1.00
1.07
1.05
1.05
1.04
f1 (ppm)

9m

^{13}C NMR, 125 MHz

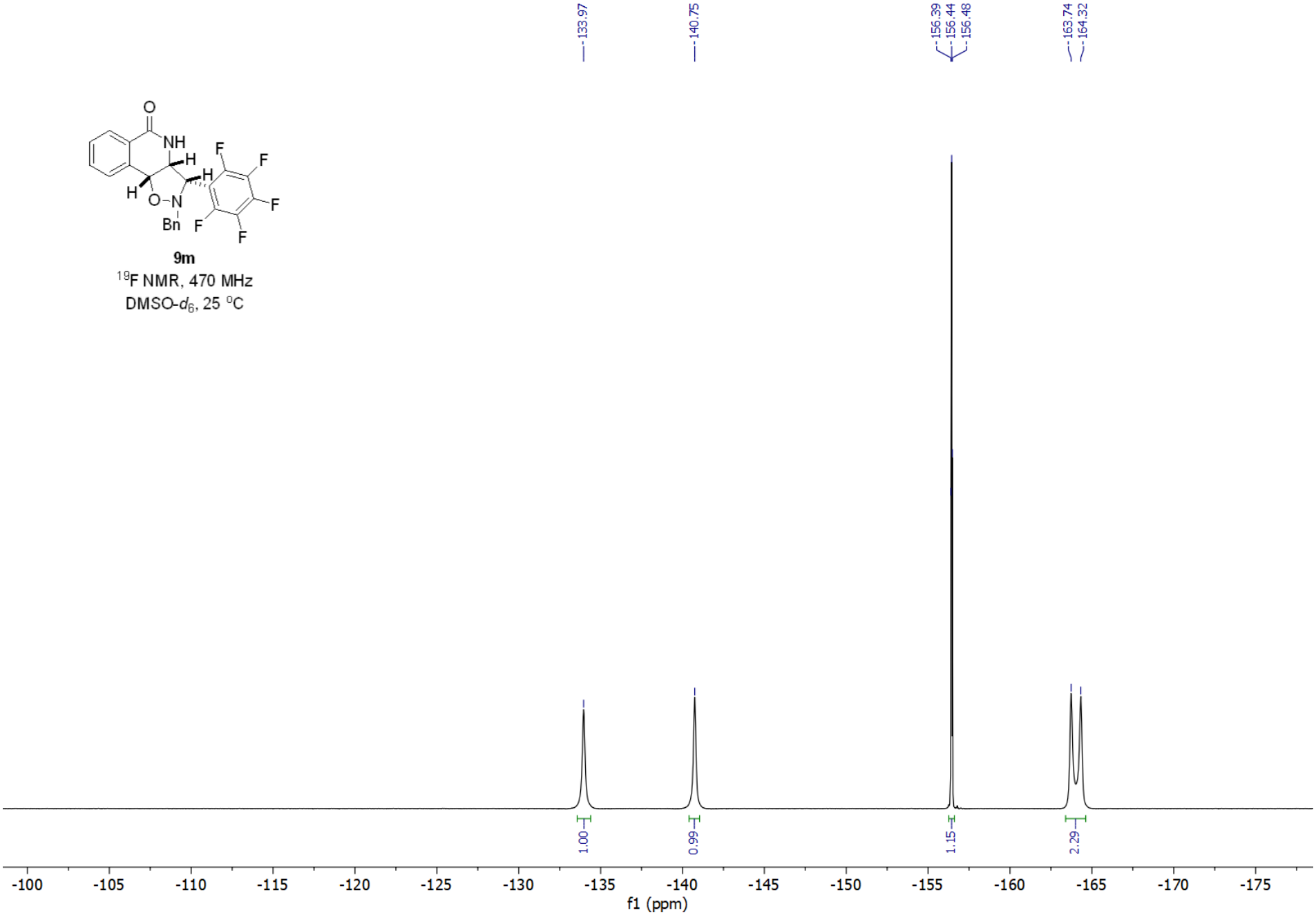
DMSO-d_6, 25 °C

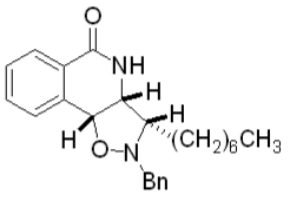


9m

^{19}F NMR, 470 MHz

DMSO-d_6, 25 ^{o}C

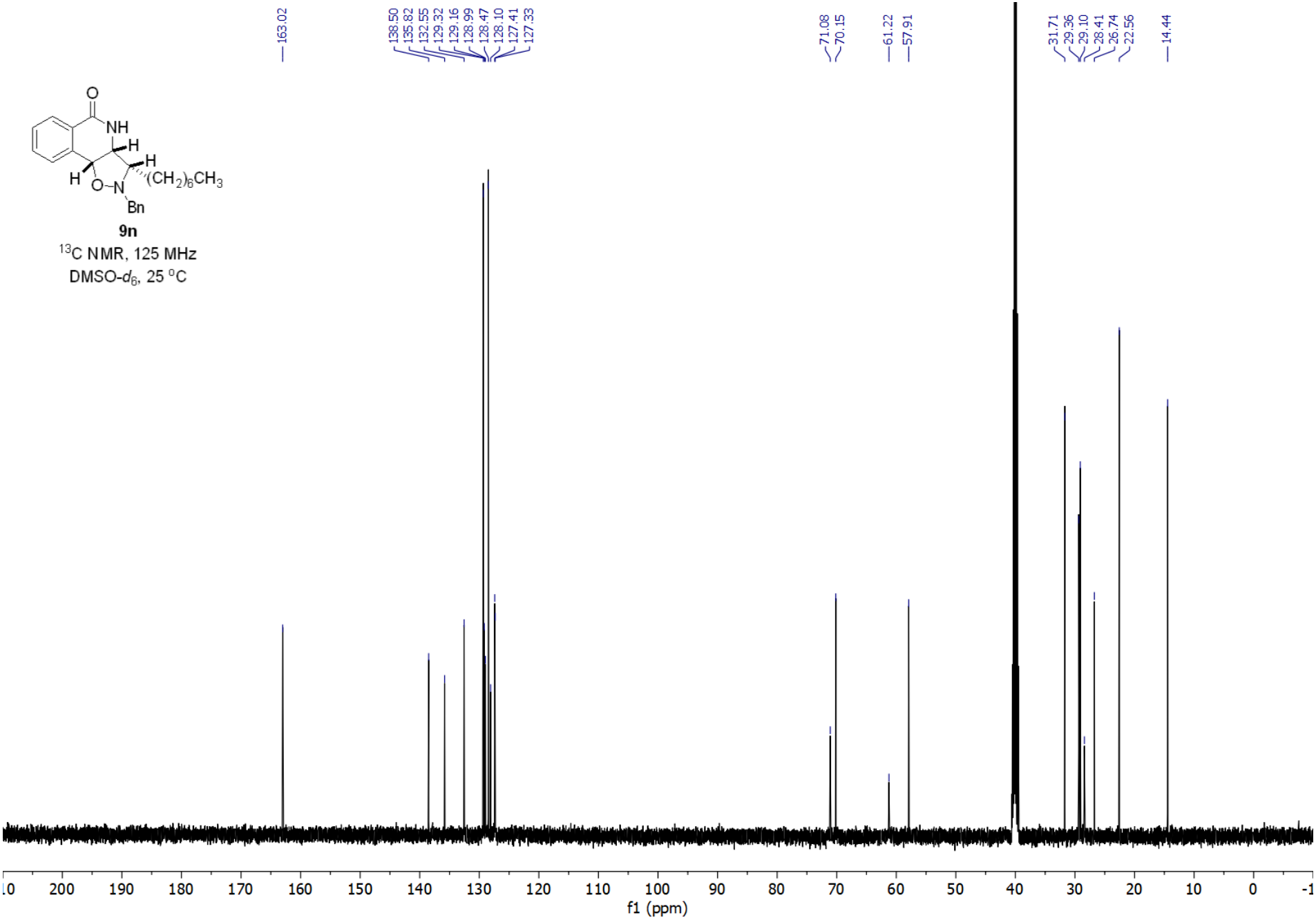


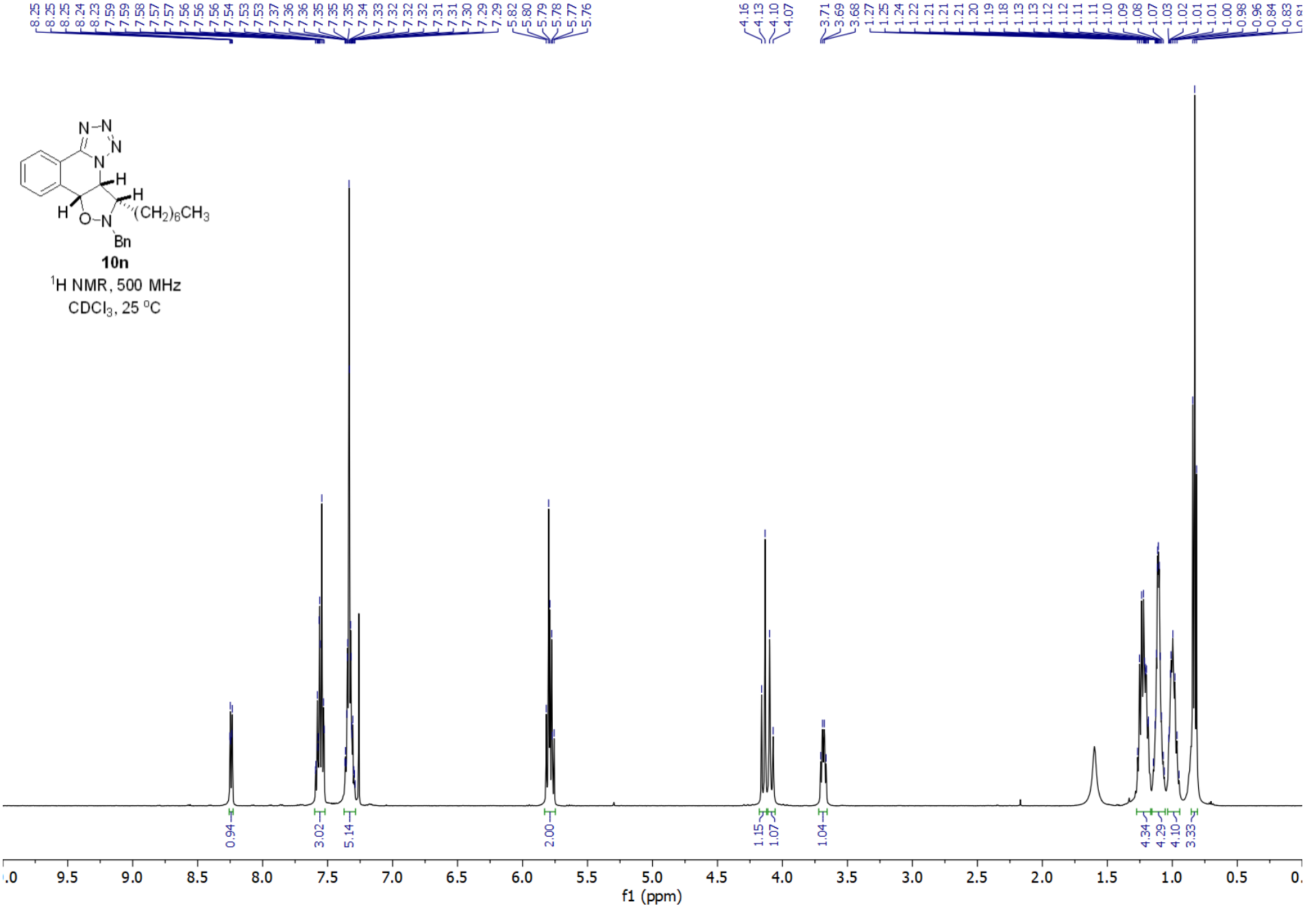


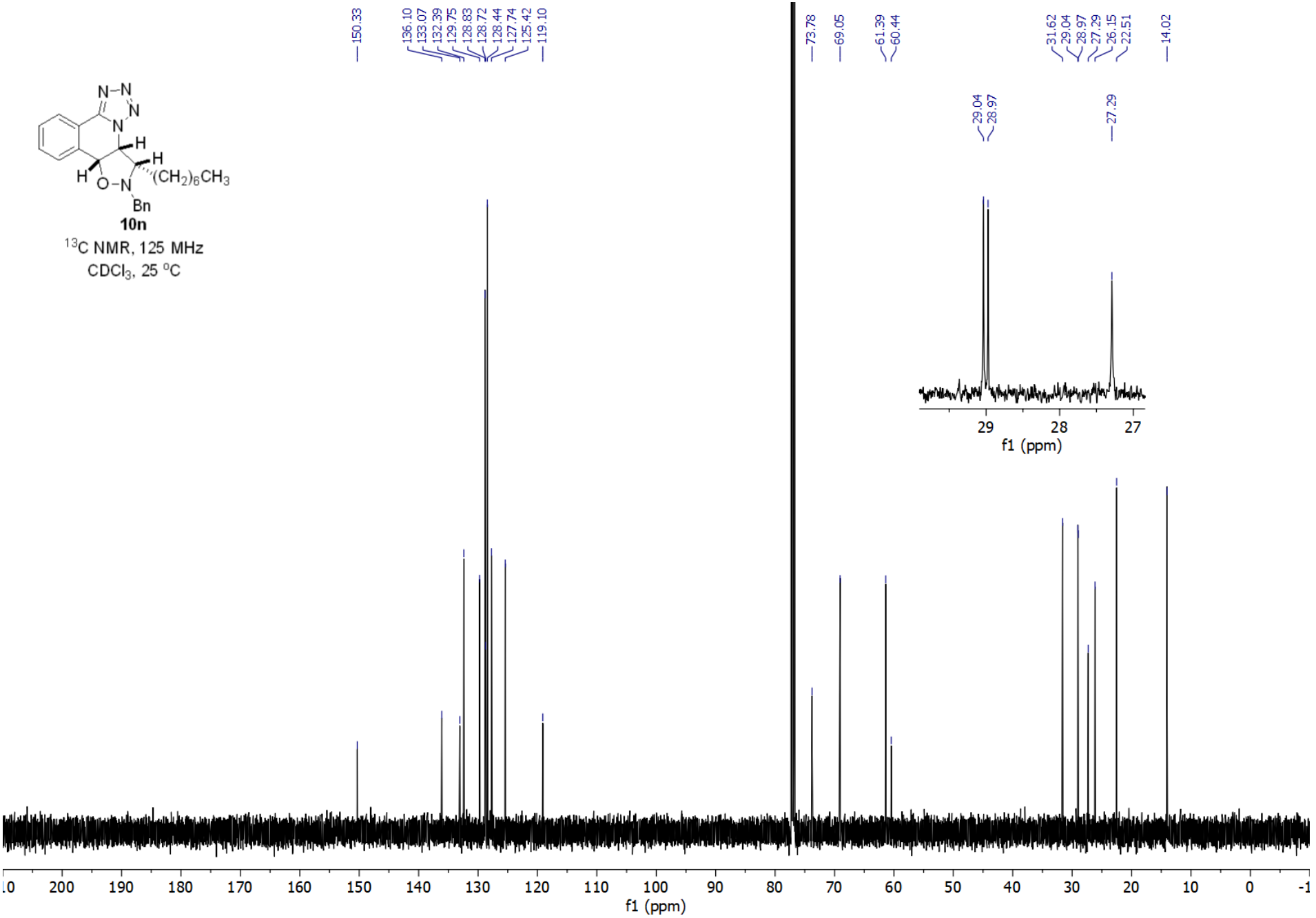
9n

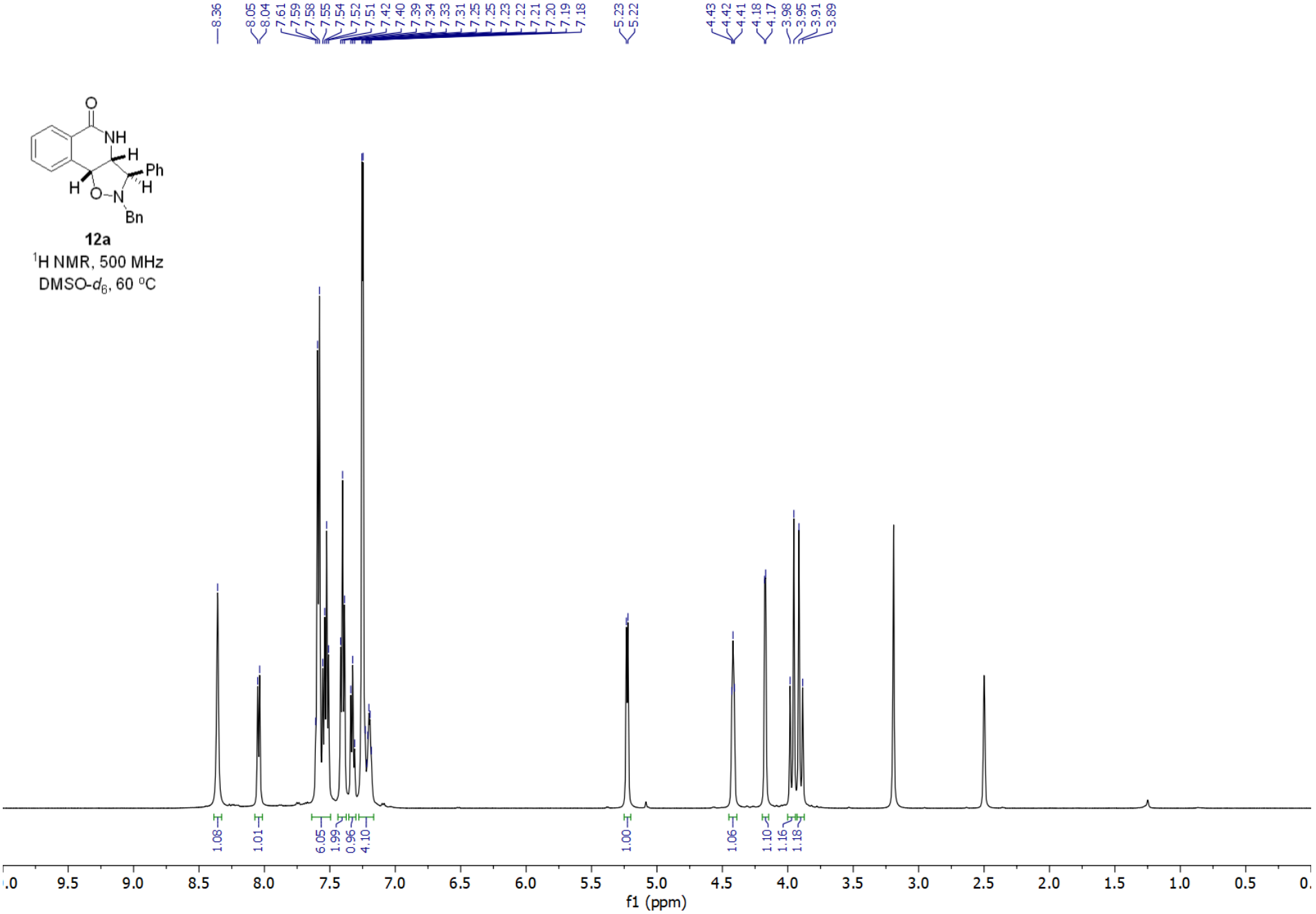
^{1}H NMR, 500 MHz

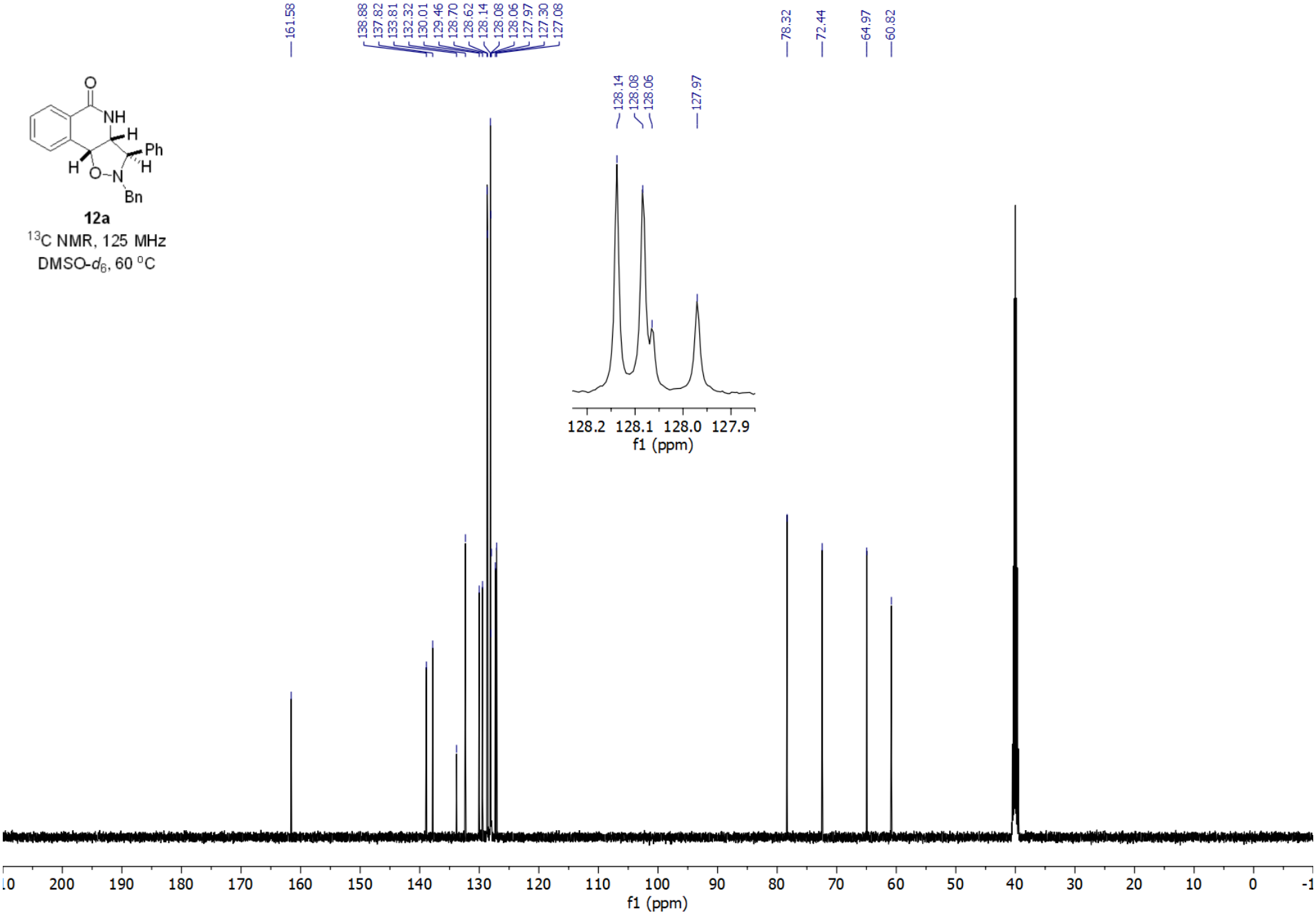
DMSO-d_6, 25 ^{o}C

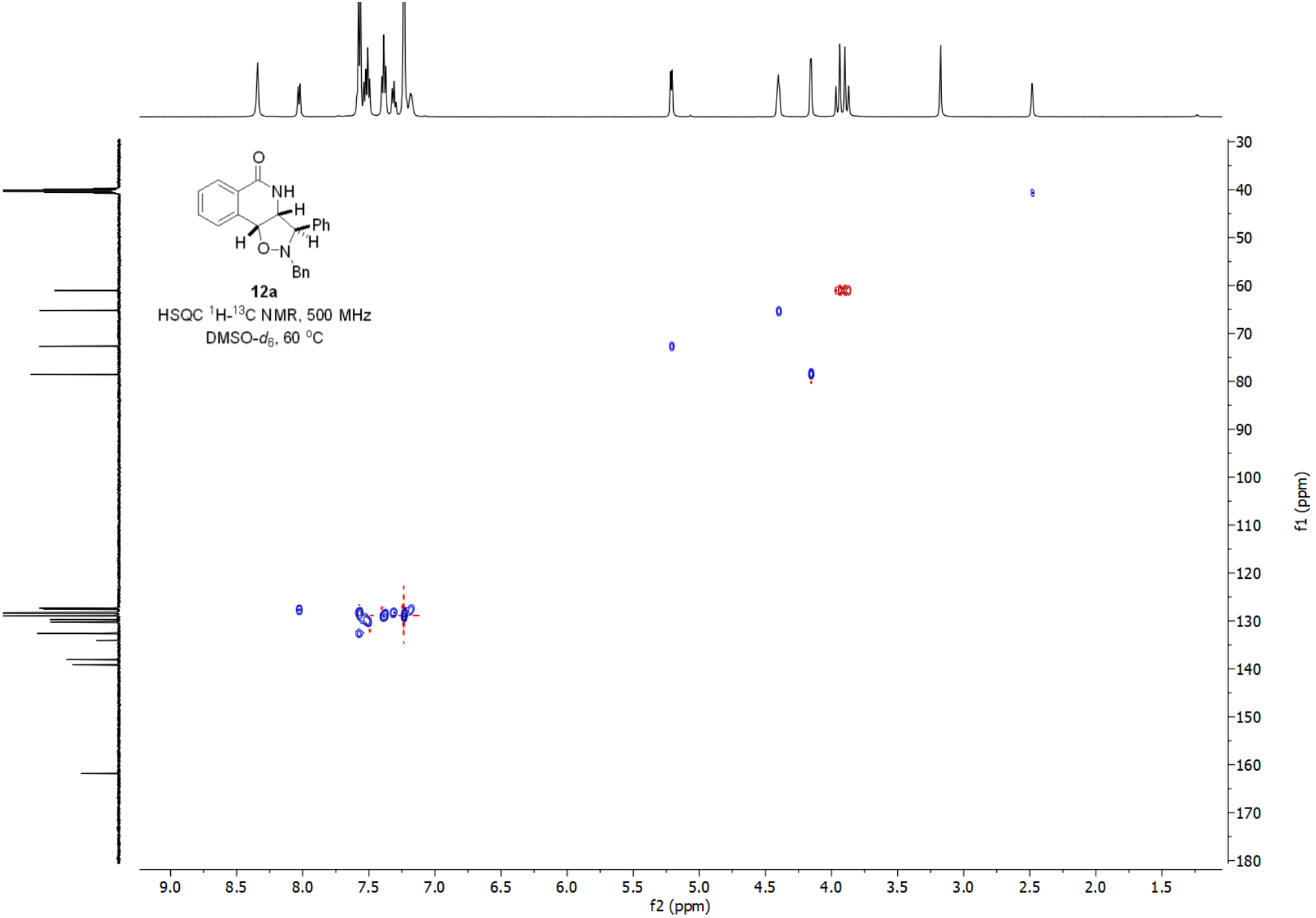

163.02
138.50
135.82
132.55
129.32
129.16
128.99
128.47
128.10
127.41
127.33
71.08
70.15
61.22
57.91
31.71
29.36
29.10
28.41
26.74
22.56
14.44
O
NH
H
H
H
O
N
(CH2)6CH3
Bn
9n
13C NMR, 125 MHz
DMSO-d6, 25 °C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

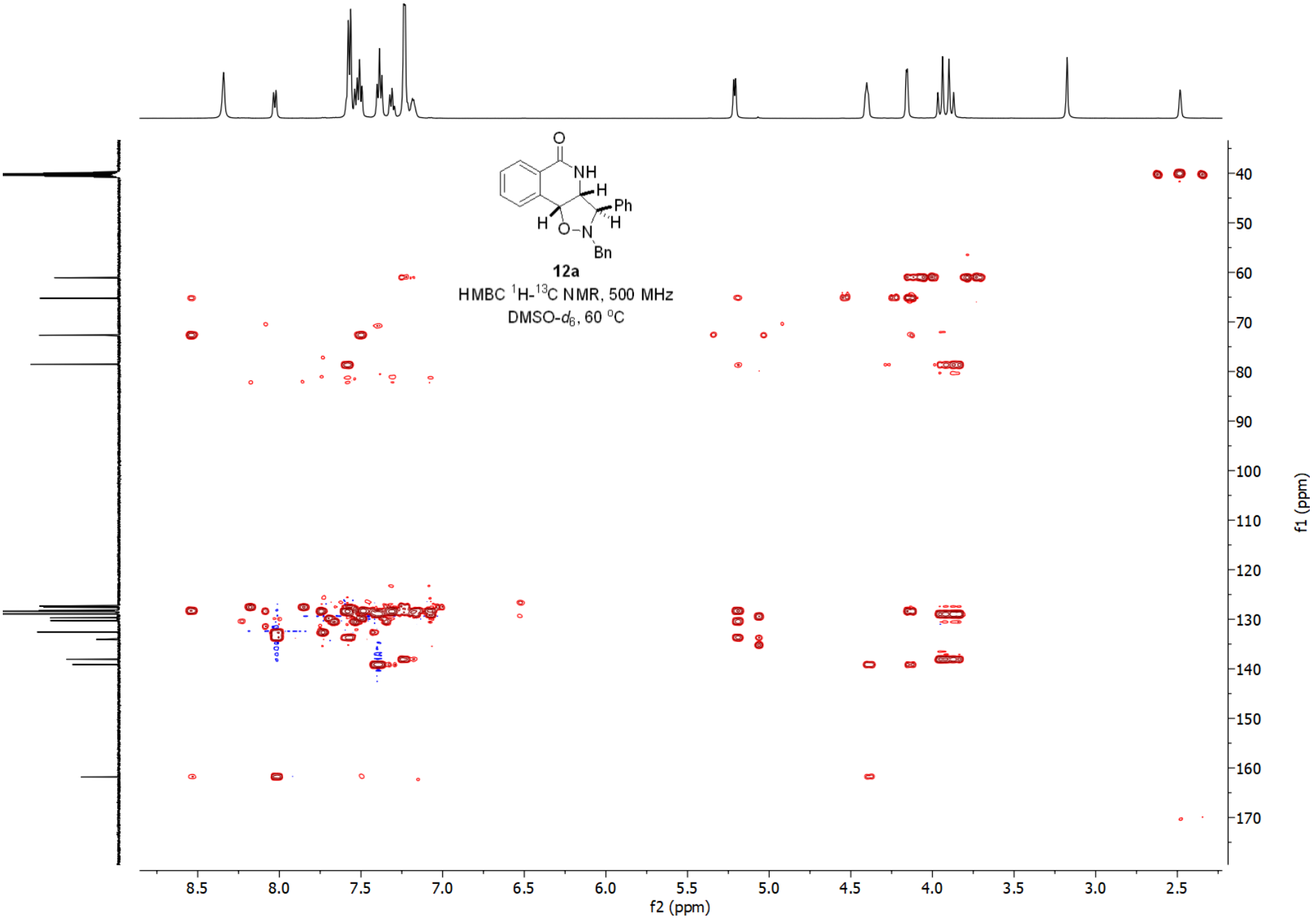

10n
1H NMR, 500 MHz
CDCl3, 25 °C
Bn
f1 (ppm)

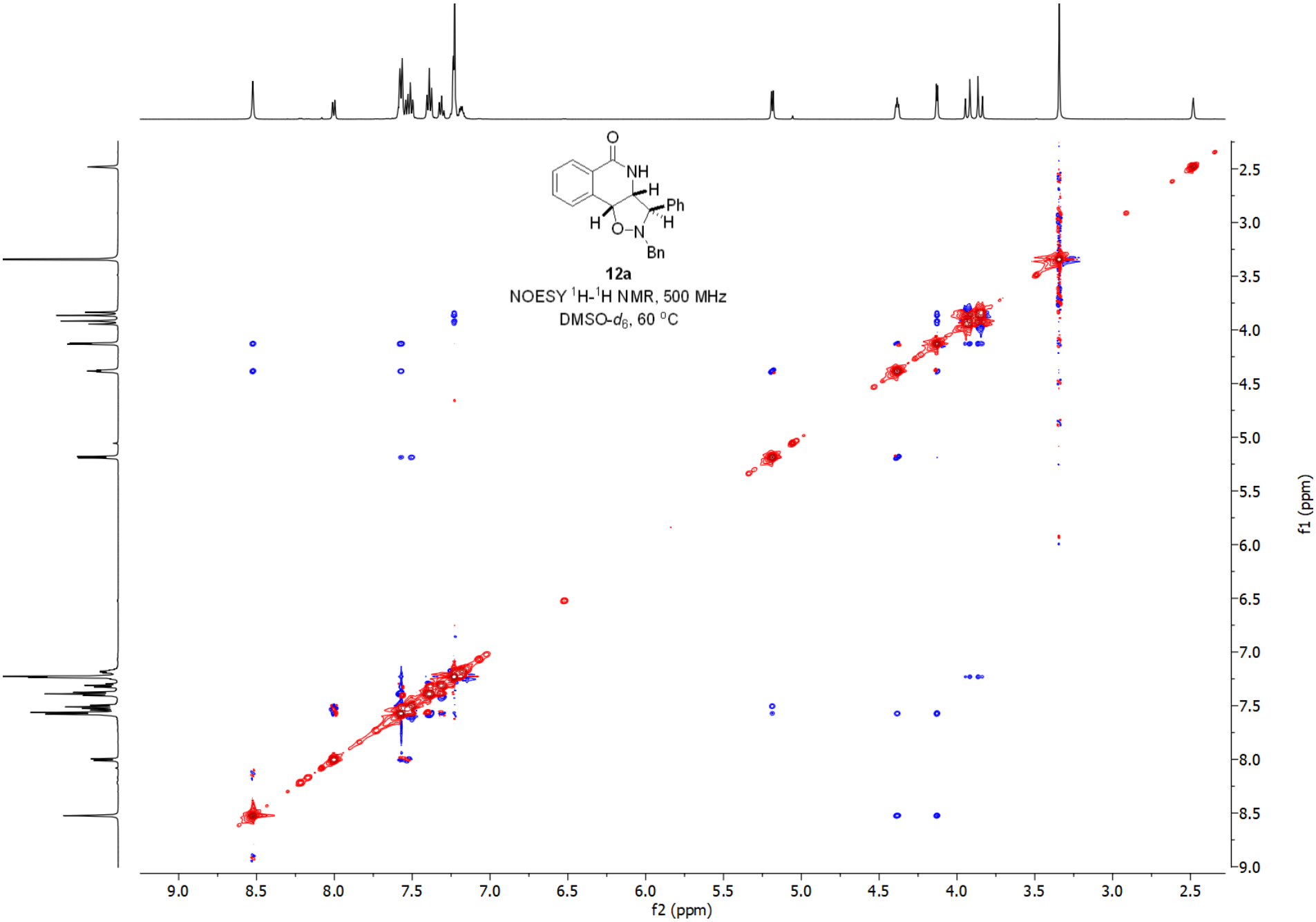

150.33
136.10
133.07
132.39
129.75
128.83
128.72
128.44
127.74
125.42
119.10
73.78
69.05
61.39
60.44
31.62
29.04
28.97
27.29
26.15
22.51
14.02
29.04
28.97
27.29
29
28
27
f1 (ppm)
N–N
N
N
H
H
H
O–N
(CH2)6CH3
Bn
10n
13C NMR, 125 MHz
CDCl3, 25 °C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

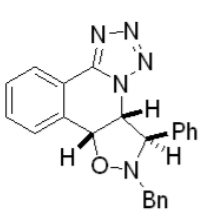

8.36
8.05
8.04
7.61
7.59
7.58
7.55
7.54
7.52
7.51
7.42
7.40
7.39
7.34
7.33
7.31
7.25
7.25
7.23
7.22
7.21
7.20
7.19
7.18
5.23
5.22
4.43
4.42
4.41
4.18
4.17
3.98
3.95
3.91
3.89
O
NH
H
Ph
H
H
O
N
Bn
12a
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.08
1.01
6.05
1.99
0.96
4.10
1.00
1.06
1.10
1.16
1.18
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


161.58
138.88
137.82
133.81
132.32
130.01
129.46
128.70
128.62
128.14
128.08
128.06
127.97
127.30
127.08
78.32
72.44
64.97
60.82
128.14
128.08
128.06
127.97
128.2 128.1 128.0 127.9
f1 (ppm)
O
NH
H
Ph
H
H
O
N
Bn
12a
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)


12a
HSQC ^{1}H-^{13}C NMR, 500 MHz
DMSO-d_6, 60 ^{o}C
f2 (ppm)
f1 (ppm)


O
NH
H
Ph
H
H
O
N
Bn
12a
HMBC ^{1}H-^{13}C NMR, 500 MHz
DMSO-d_6, 60 ^{o}C
f1 (ppm)
f2 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
40
50
60
70
80
90
100
110
120
130
140
150
160
170

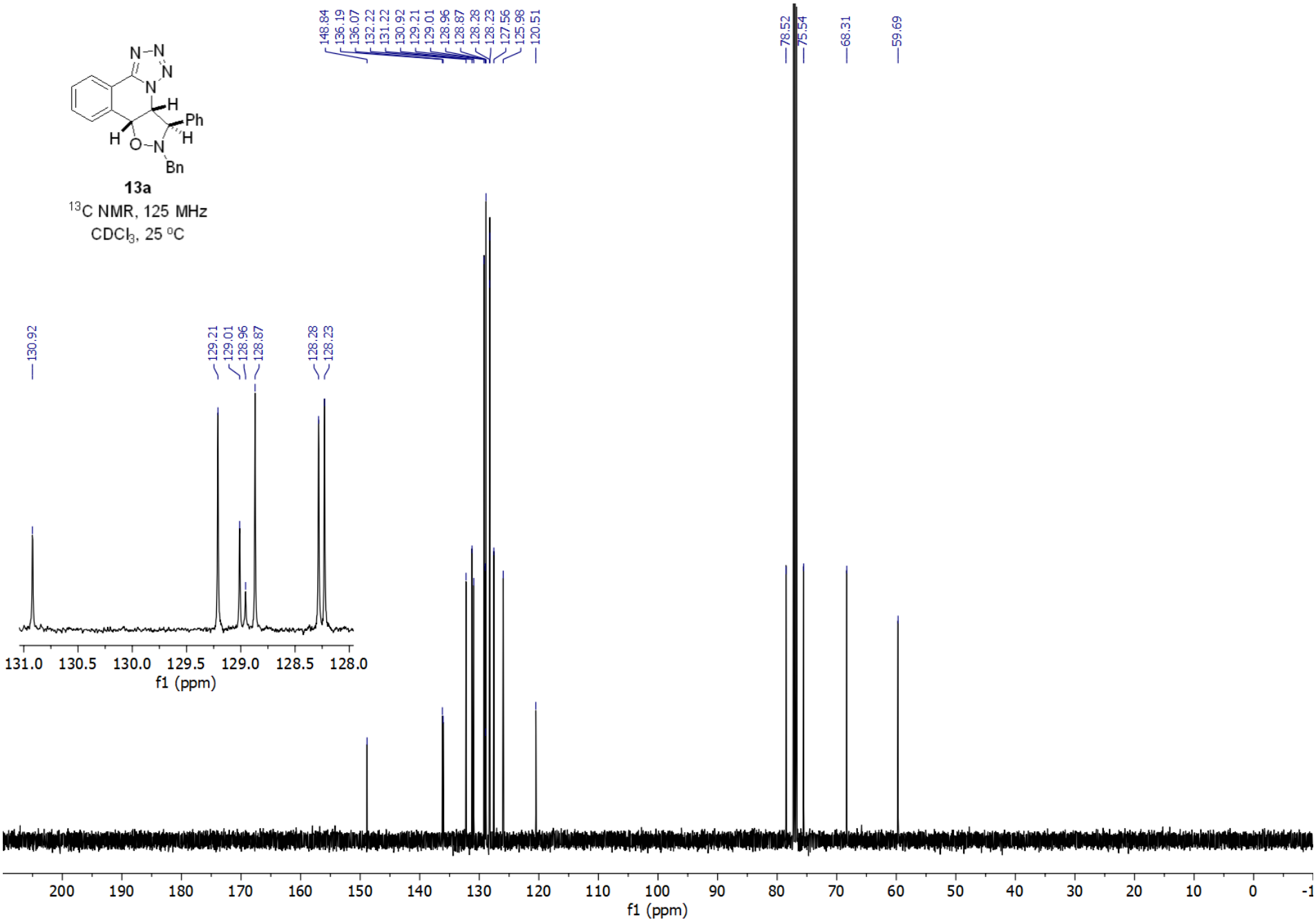

O
NH
H
Ph
H
H
O–N
Bn
12a
NOESY ^{1}H-^{1}H NMR, 500 MHz
DMSO-d_6, 60 °C
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
f2 (ppm)
f1 (ppm)

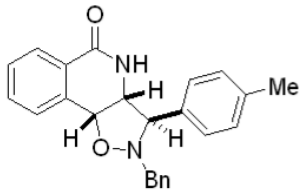


13a

^{1}H NMR, 500 MHz

$CDCl_3$, 25 ^{o}C

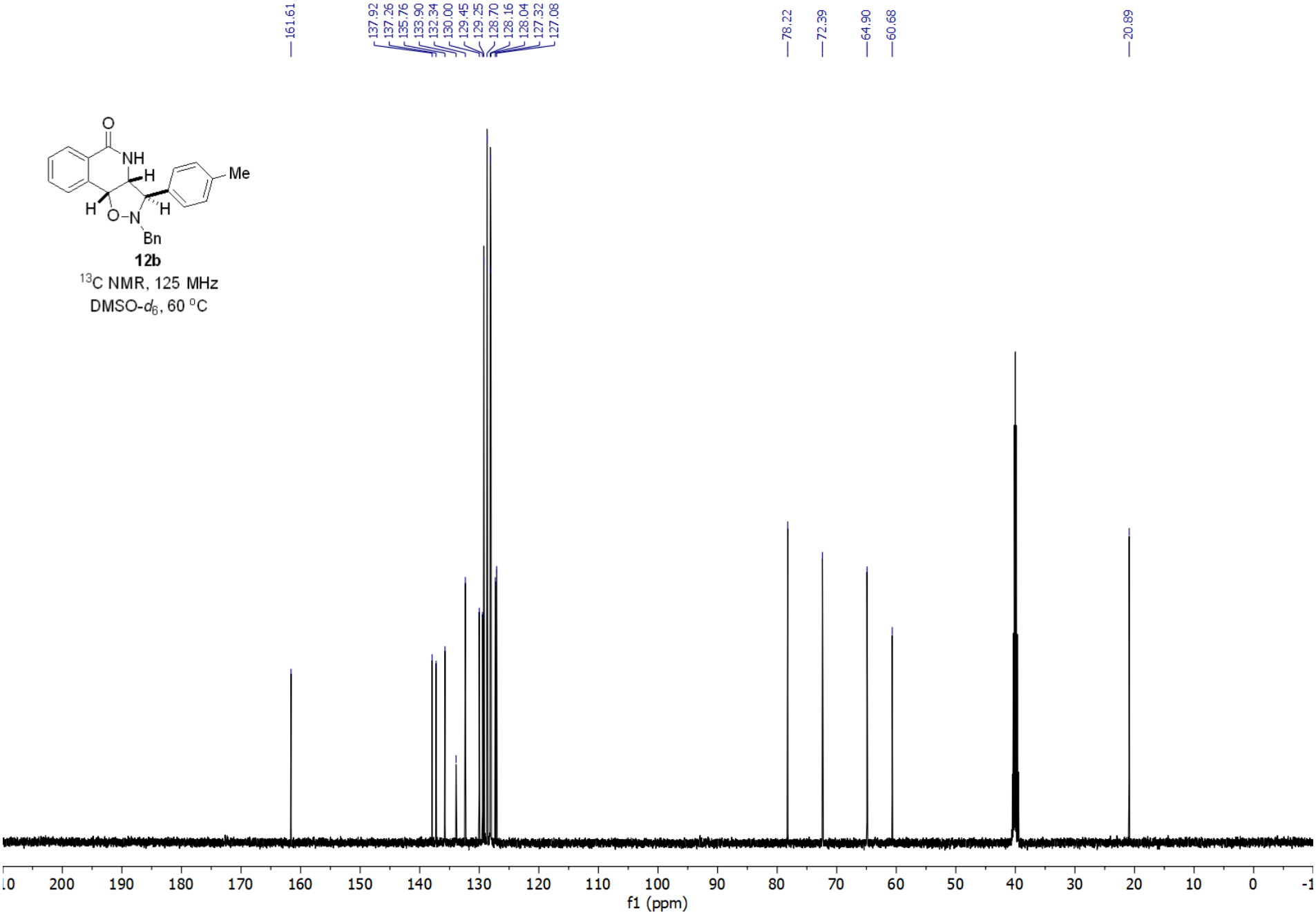

148.84
136.19
136.07
132.22
131.22
130.92
129.21
129.01
128.96
128.87
128.28
128.23
127.56
125.98
120.51
78.52
75.54
68.31
59.69
N
N
N
H
Ph
H
H
O
N
Bn
13a
13C NMR, 125 MHz
CDCl3, 25 °C
130.92
129.21
129.01
128.96
128.87
128.28
128.23
131.0 130.5 130.0 129.5 129.0 128.5 128.0
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

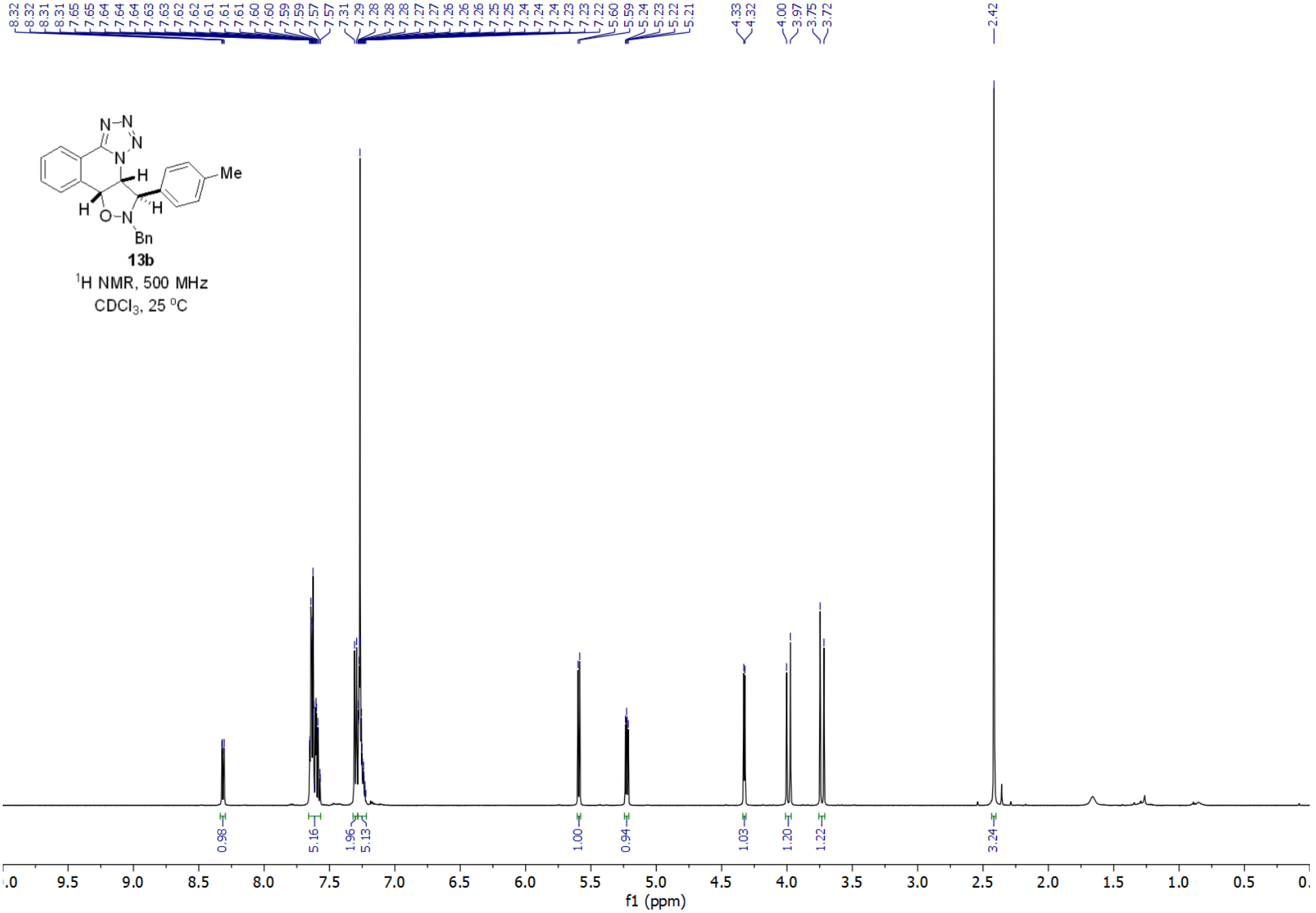


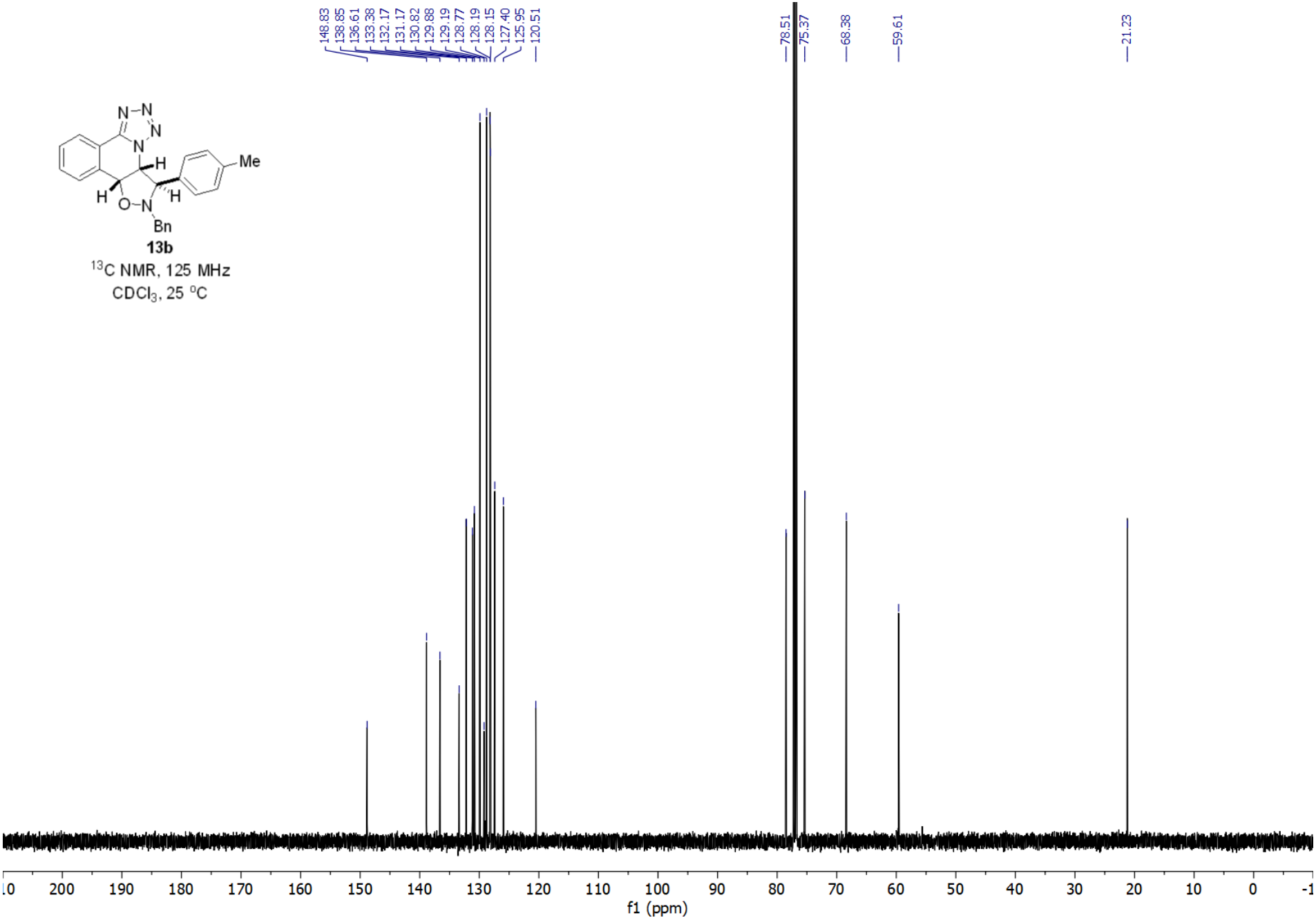
12b

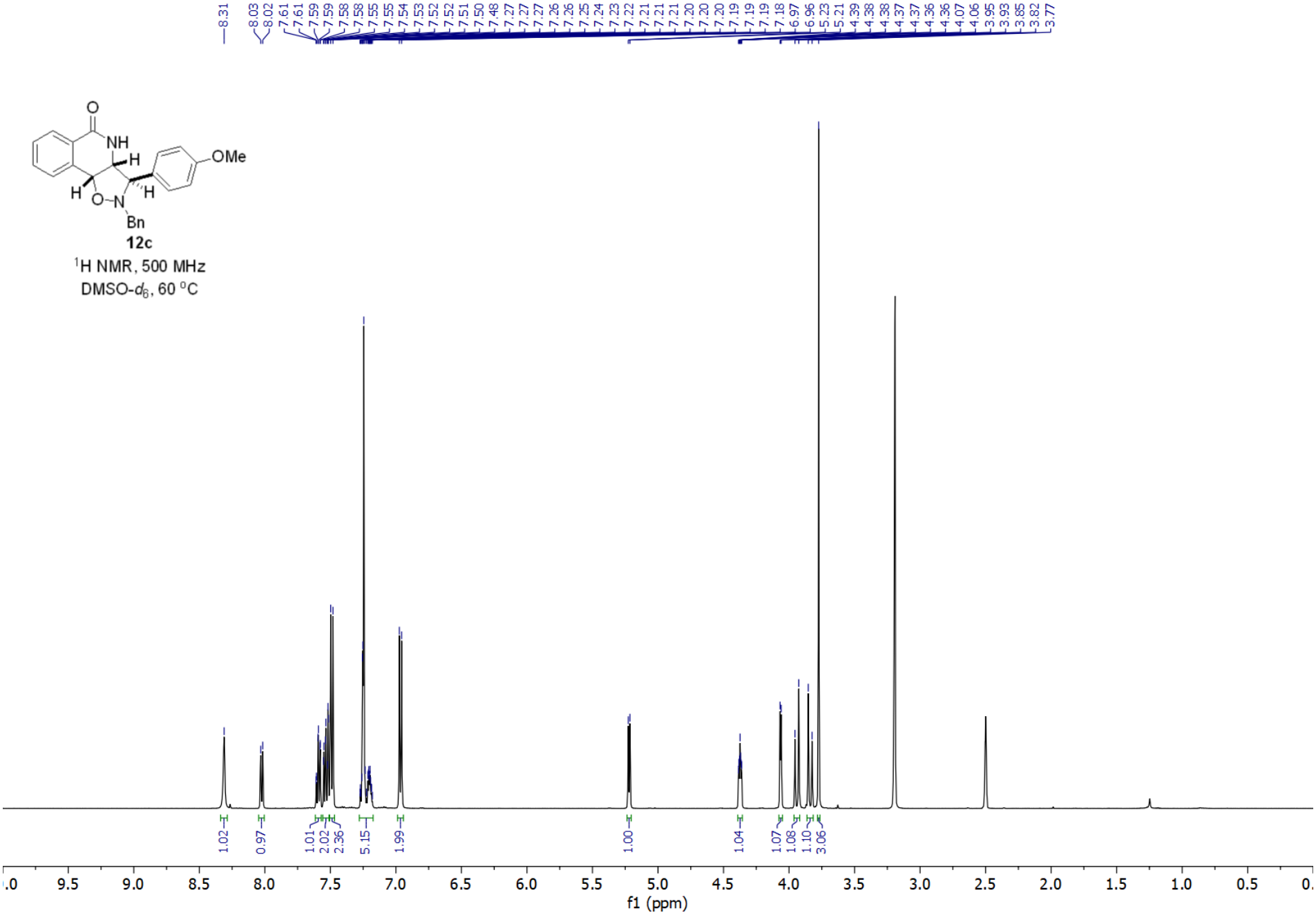
^{1}H NMR, 500 MHz

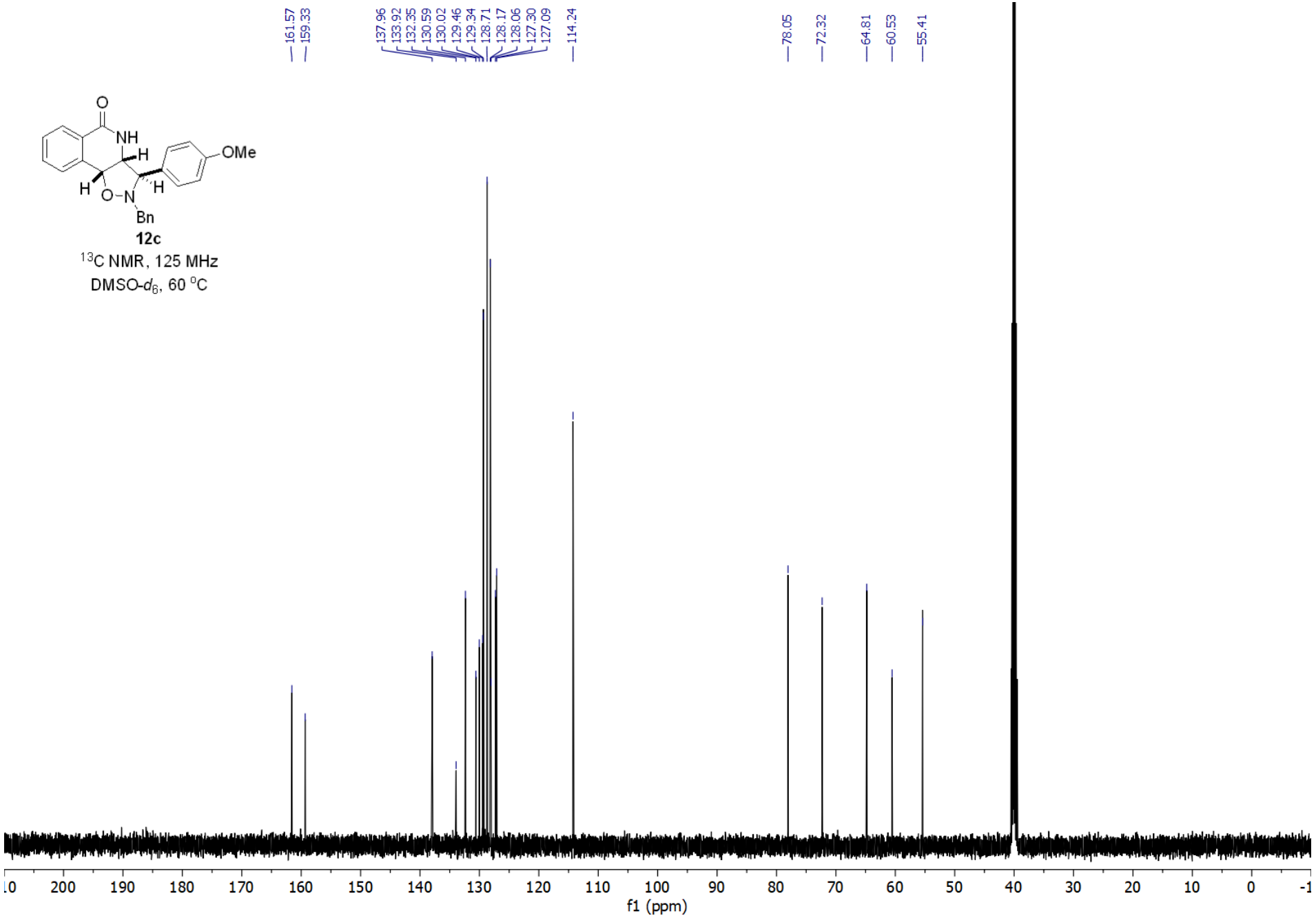
DMSO-d_6, 60 ^{0}C

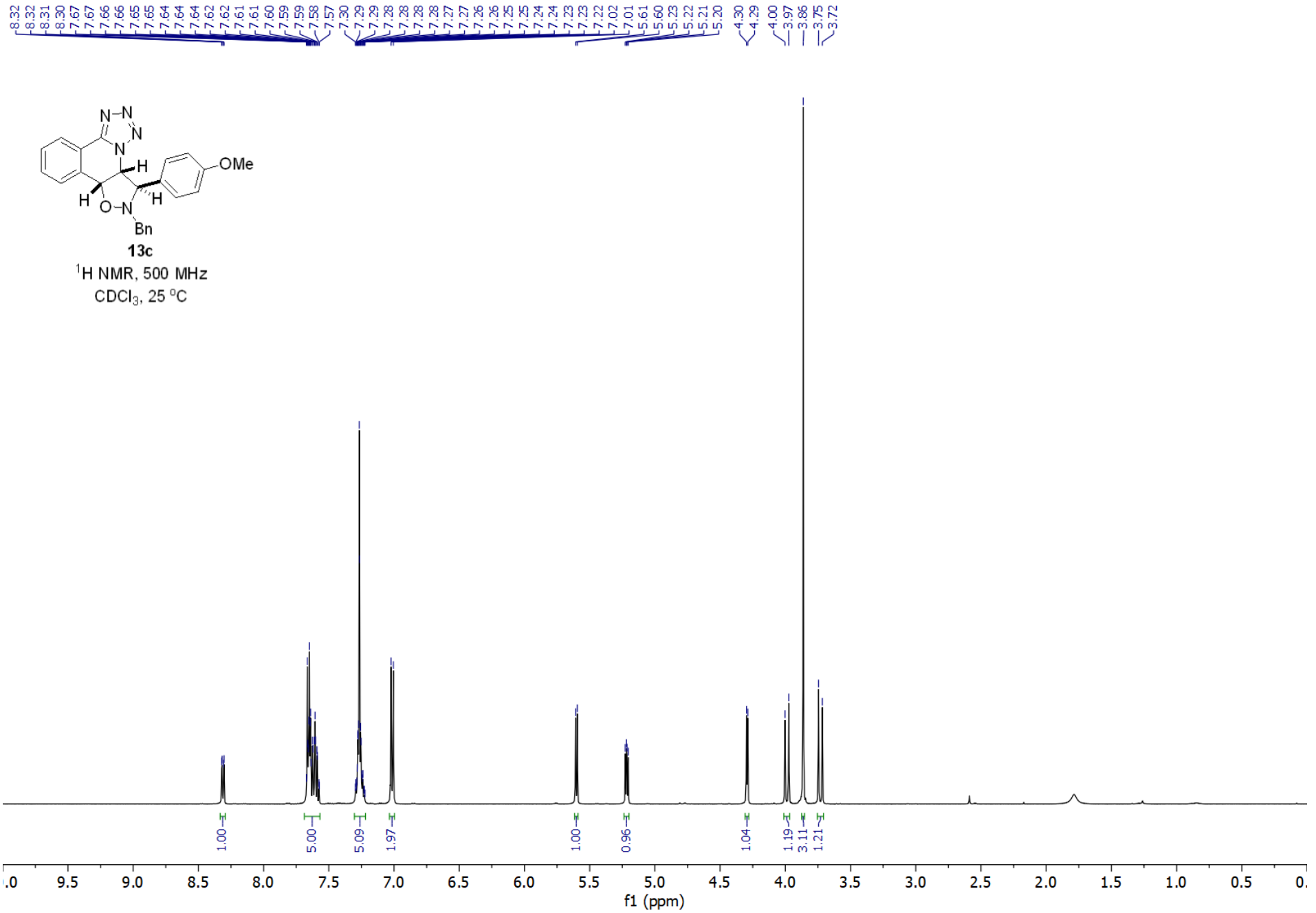

161.61
137.92
137.26
135.76
133.90
132.34
130.00
129.45
129.25
128.70
128.16
128.04
127.32
127.08
78.22
72.39
64.90
60.68
20.89
O
NH
H
Me
H
O–N
H
Bn
12b
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)


8.32 8.32 8.31 8.31 7.65 7.65 7.64 7.64 7.64 7.63 7.63 7.62 7.62 7.61 7.61 7.61 7.60 7.60 7.59 7.59 7.57 7.57 7.31 7.29 7.28 7.28 7.28 7.27 7.27 7.26 7.26 7.26 7.25 7.25 7.24 7.24 7.24 7.24 7.23 7.23 7.22 5.60 5.59 5.24 5.23 5.22 5.21 4.33 4.32 4.00 3.97 3.75 3.72 2.42
N
N
N
N
H
H
H
O
N
Me
Bn
13b
1H NMR, 500 MHz
CDCl3, 25 °C
0.98 5.16 1.96 5.13 1.00 0.94 1.03 1.20 1.22 3.24
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


148.83
138.85
136.61
133.38
132.17
131.17
130.82
129.88
129.19
128.77
128.19
128.15
127.40
125.95
120.51
78.51
75.37
68.38
59.61
21.23
N
N
N
H
H
H
O
N
Me
Bn
13b
13C NMR, 125 MHz
CDCl3, 25 °C
f1 (ppm)


8.31
8.03
8.02
7.61
7.61
7.59
7.59
7.59
7.58
7.58
7.55
7.55
7.54
7.53
7.52
7.52
7.51
7.50
7.48
7.27
7.27
7.27
7.26
7.26
7.25
7.24
7.23
7.22
7.21
7.21
7.21
7.20
7.20
7.20
7.19
7.19
7.19
7.18
6.97
6.96
5.23
5.21
4.39
4.38
4.38
4.37
4.37
4.36
4.36
4.07
4.06
3.95
3.93
3.85
3.82
3.77
O
NH
H
OMe
H
O
N
H
Bn
12c
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.02
0.97
1.01
2.02
2.36
5.15
1.99
1.00
1.04
1.07
1.08
1.10
3.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

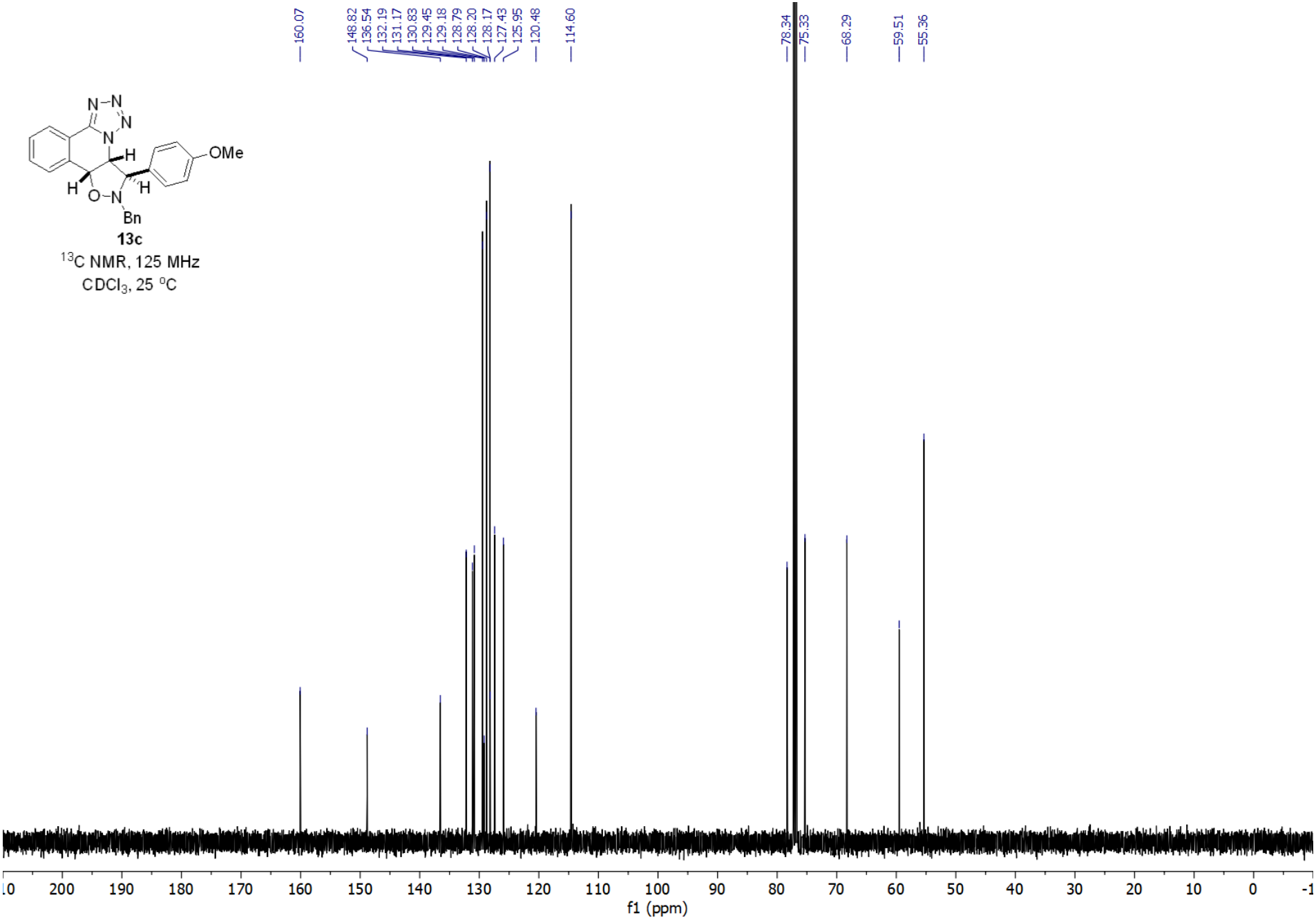

161.57
159.33
137.96
133.92
132.35
130.59
130.02
129.46
129.34
128.71
128.17
128.06
127.30
127.09
114.24
78.05
72.32
64.81
60.53
55.41
O
NH
H
OMe
H
O
N
H
Bn
12c
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

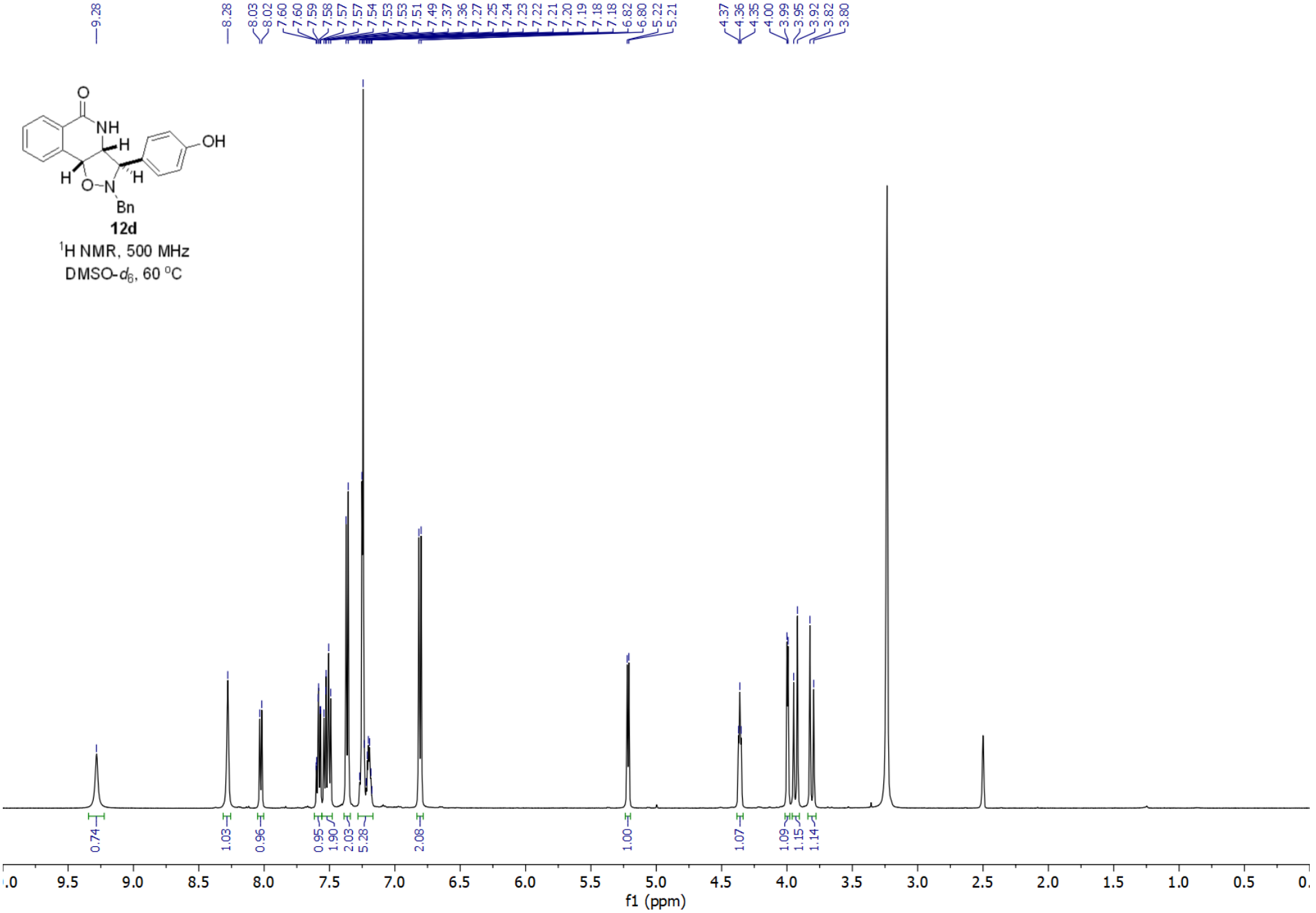

8.32 8.32 8.31 8.30 7.67 7.67 7.66 7.66 7.65 7.65 7.64 7.64 7.64 7.62 7.62 7.61 7.61 7.60 7.59 7.59 7.58 7.57 7.30 7.29 7.29 7.28 7.28 7.28 7.28 7.27 7.27 7.26 7.26 7.25 7.25 7.24 7.24 7.23 7.23 7.22 7.02 7.01 5.61 5.60 5.23 5.22 5.21 5.20 4.30 4.29 4.00 3.97 3.86 3.75 3.72
N
N
N
N
H
OMe
H
H
O
N
Bn
13c
1H NMR, 500 MHz
CDCl3, 25 °C
1.00 5.00 5.09 1.97 1.00 0.96 1.04 1.19 3.11 1.21
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

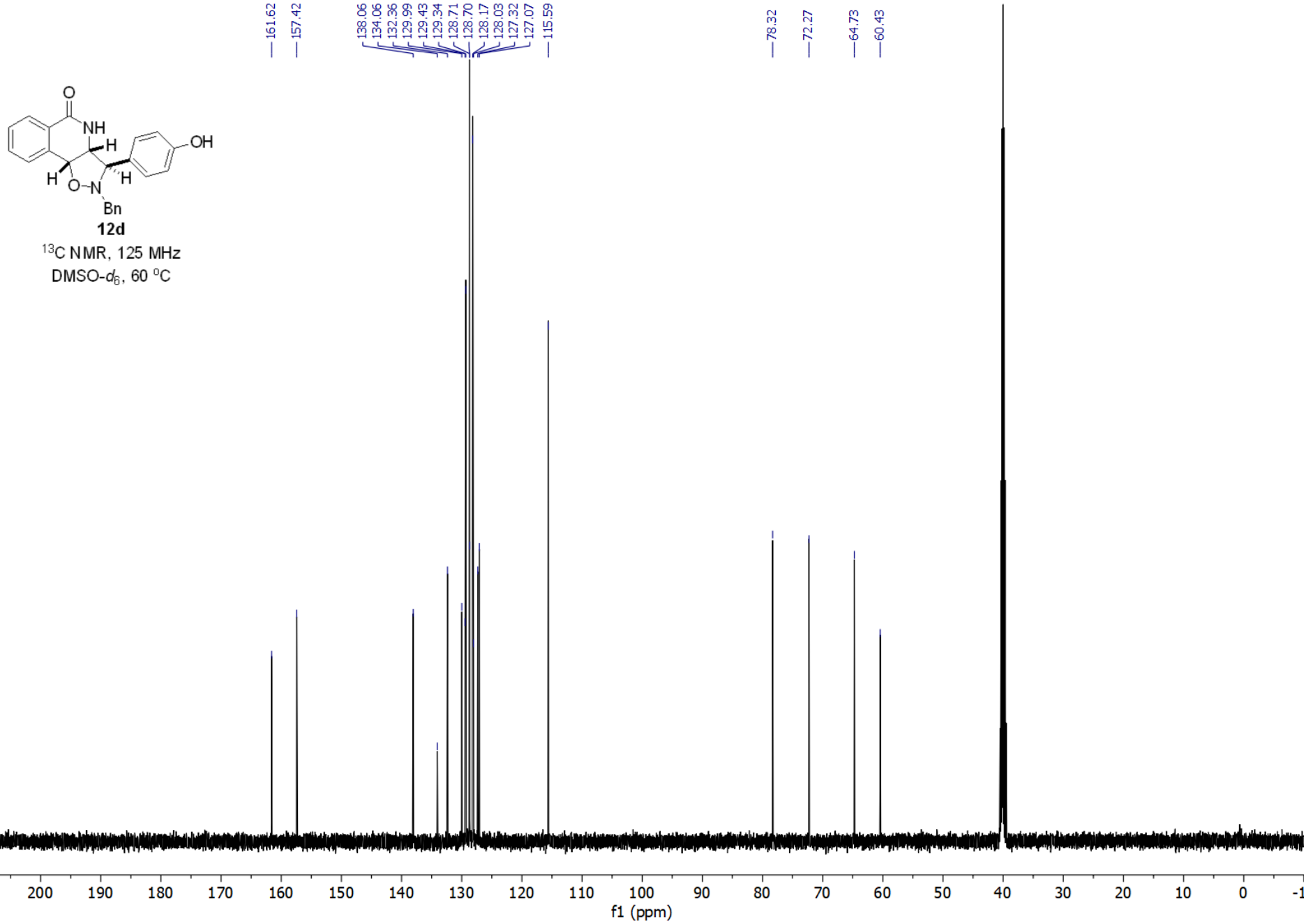
13c

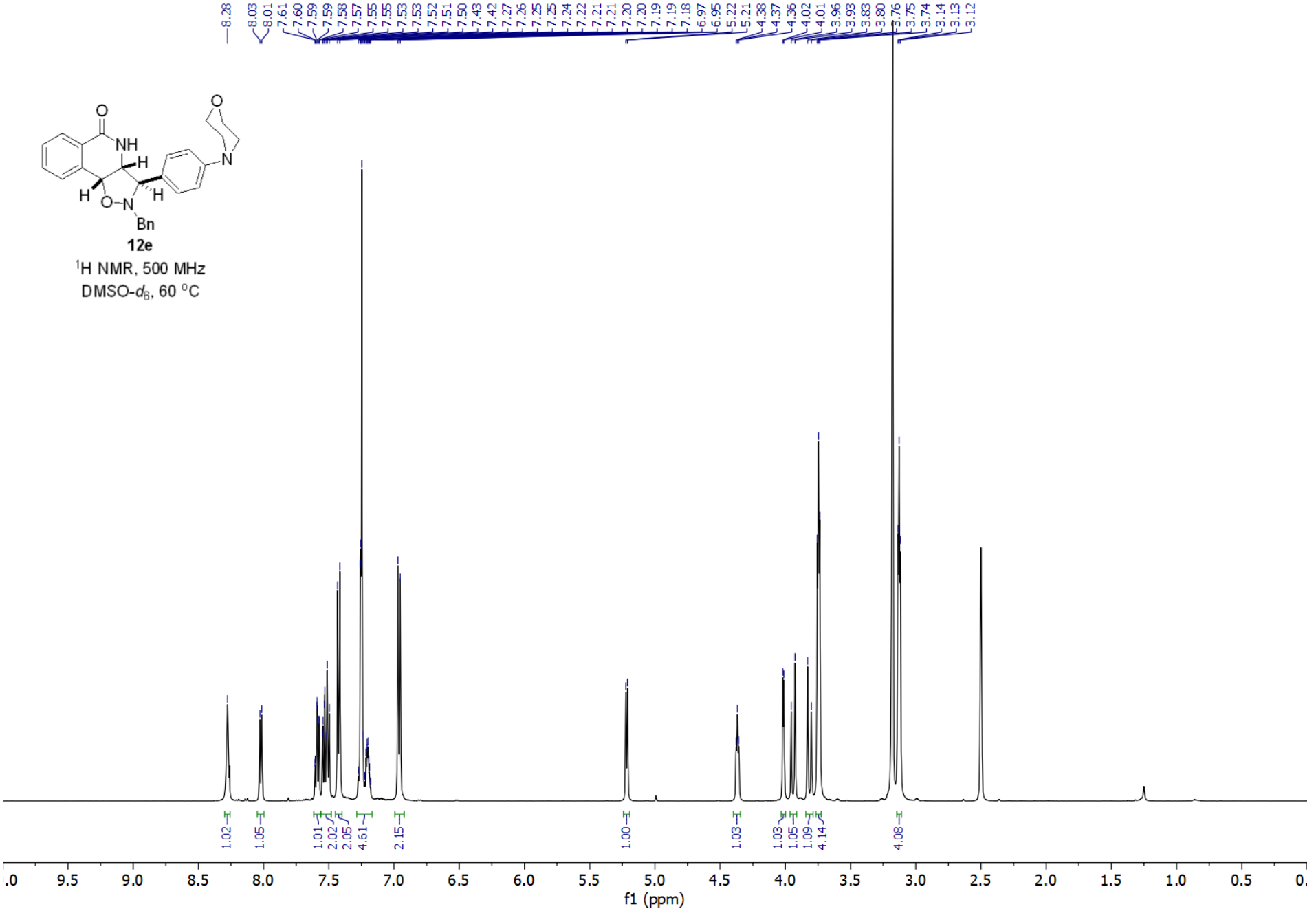
^{13}C NMR, 125 MHz

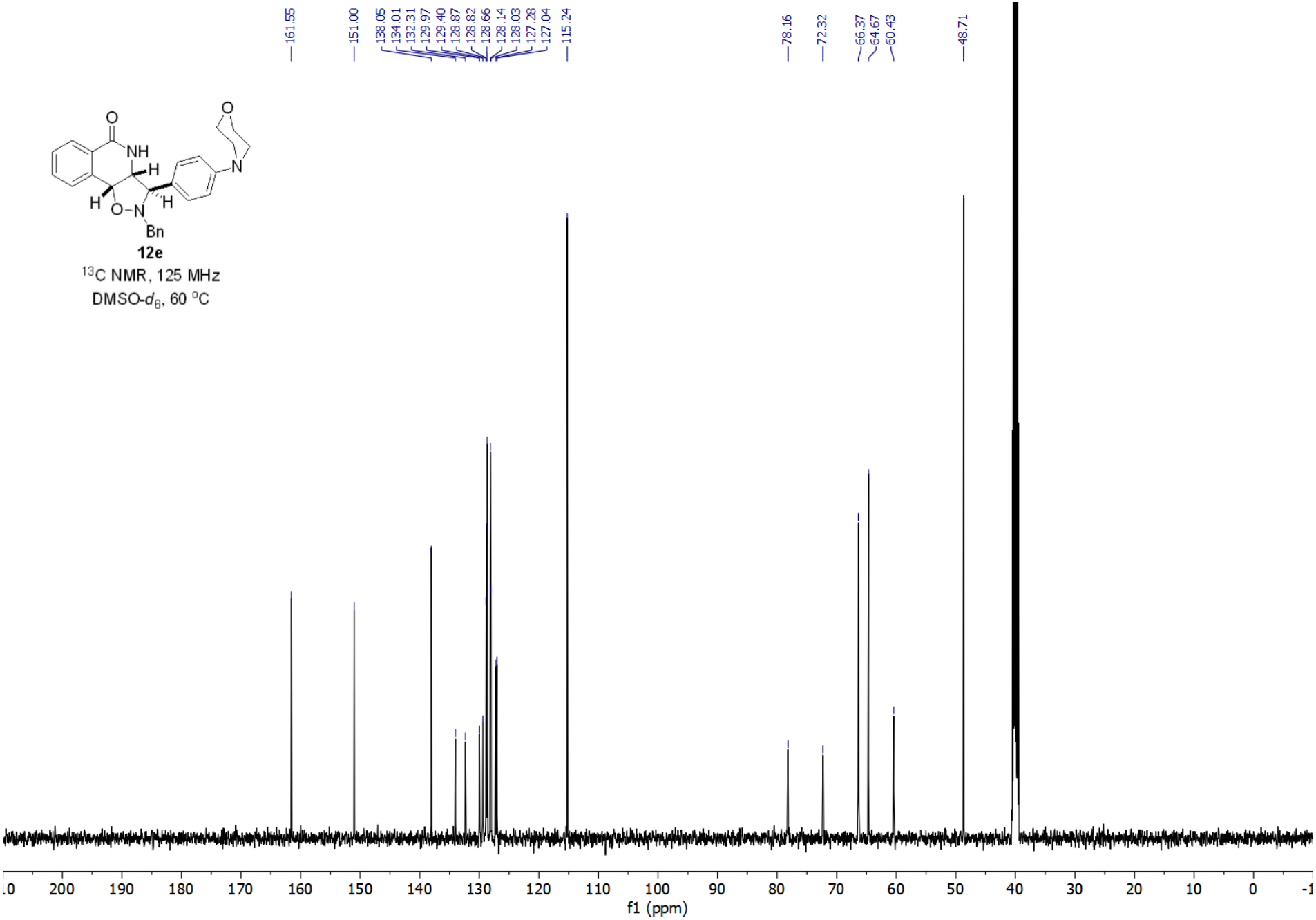
$CDCl_3$, 25 ^{o}C

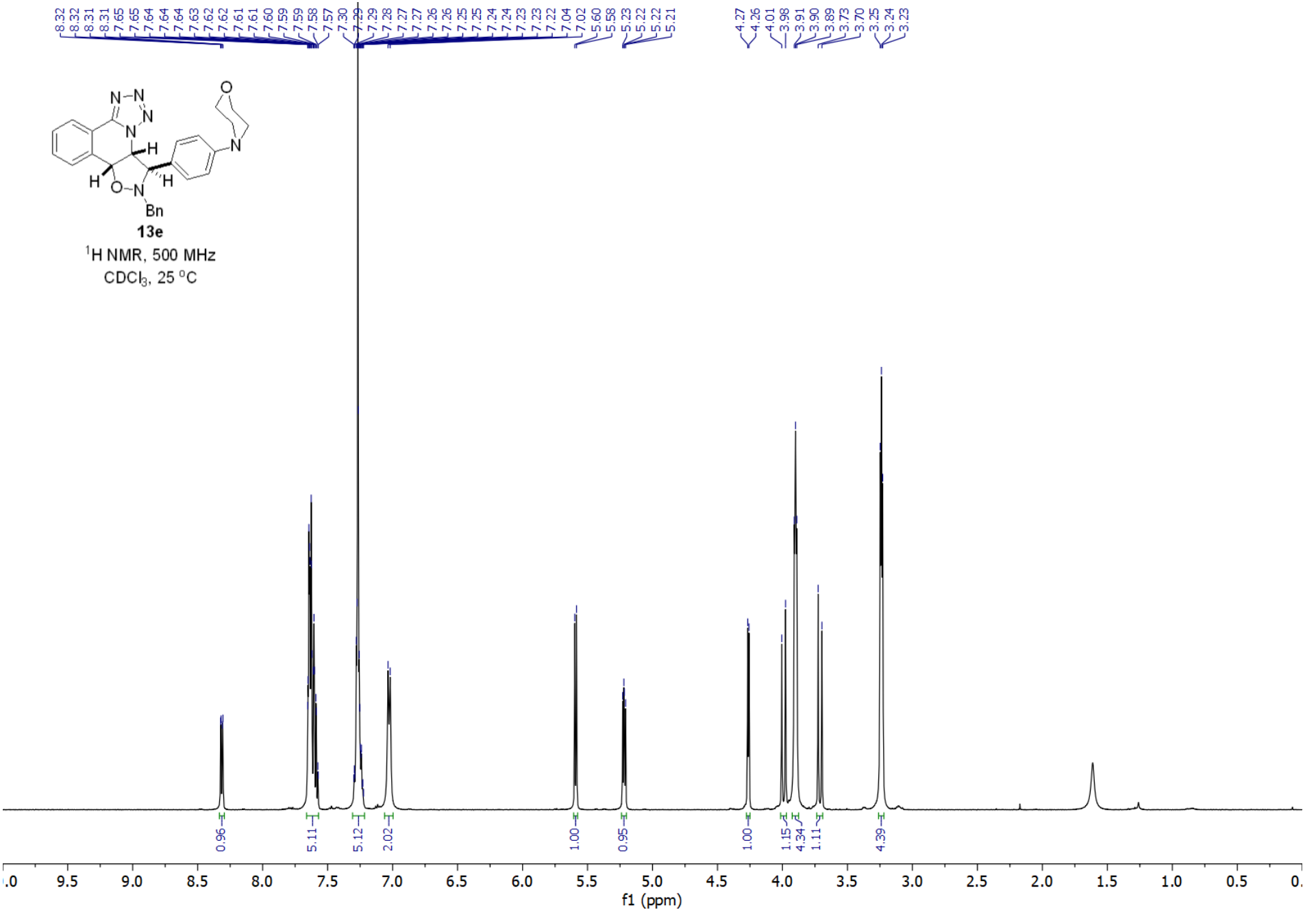



9.28
8.28
8.03
8.02
7.60
7.60
7.59
7.58
7.57
7.57
7.54
7.53
7.53
7.51
7.49
7.37
7.36
7.27
7.25
7.24
7.23
7.22
7.21
7.20
7.19
7.18
6.82
6.80
5.22
5.21
4.37
4.36
4.35
4.00
3.99
3.95
3.92
3.82
3.80
O
NH
H
OH
H
O
N
H
Bn
12d
1H NMR, 500 MHz
DMSO-d6, 60 °C
0.74
1.03
0.96
0.95
1.90
2.03
5.28
2.08
1.00
1.07
1.09
1.15
1.14
f1 (ppm)


161.62
157.42
138.06
134.06
132.36
129.99
129.43
129.34
128.71
128.70
128.17
128.03
127.32
127.07
115.59
78.32
72.27
64.73
60.43
O
NH
H
OH
H
O
N
H
Bn
12d
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)


8.28
8.03
8.01
7.61
7.60
7.59
7.59
7.58
7.57
7.55
7.55
7.53
7.53
7.52
7.51
7.50
7.43
7.42
7.27
7.26
7.25
7.25
7.24
7.22
7.21
7.21
7.20
7.20
7.19
7.19
7.18
6.97
6.95
5.22
5.21
4.38
4.37
4.36
4.02
4.01
3.96
3.93
3.83
3.80
3.76
3.75
3.74
3.14
3.13
3.12
O
NH
H
H
O
N
H
N
O
Bn
12e
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.02
1.05
1.01
2.02
2.05
4.61
2.15
1.00
1.03
1.03
1.05
1.09
4.14
4.08
f1 (ppm)

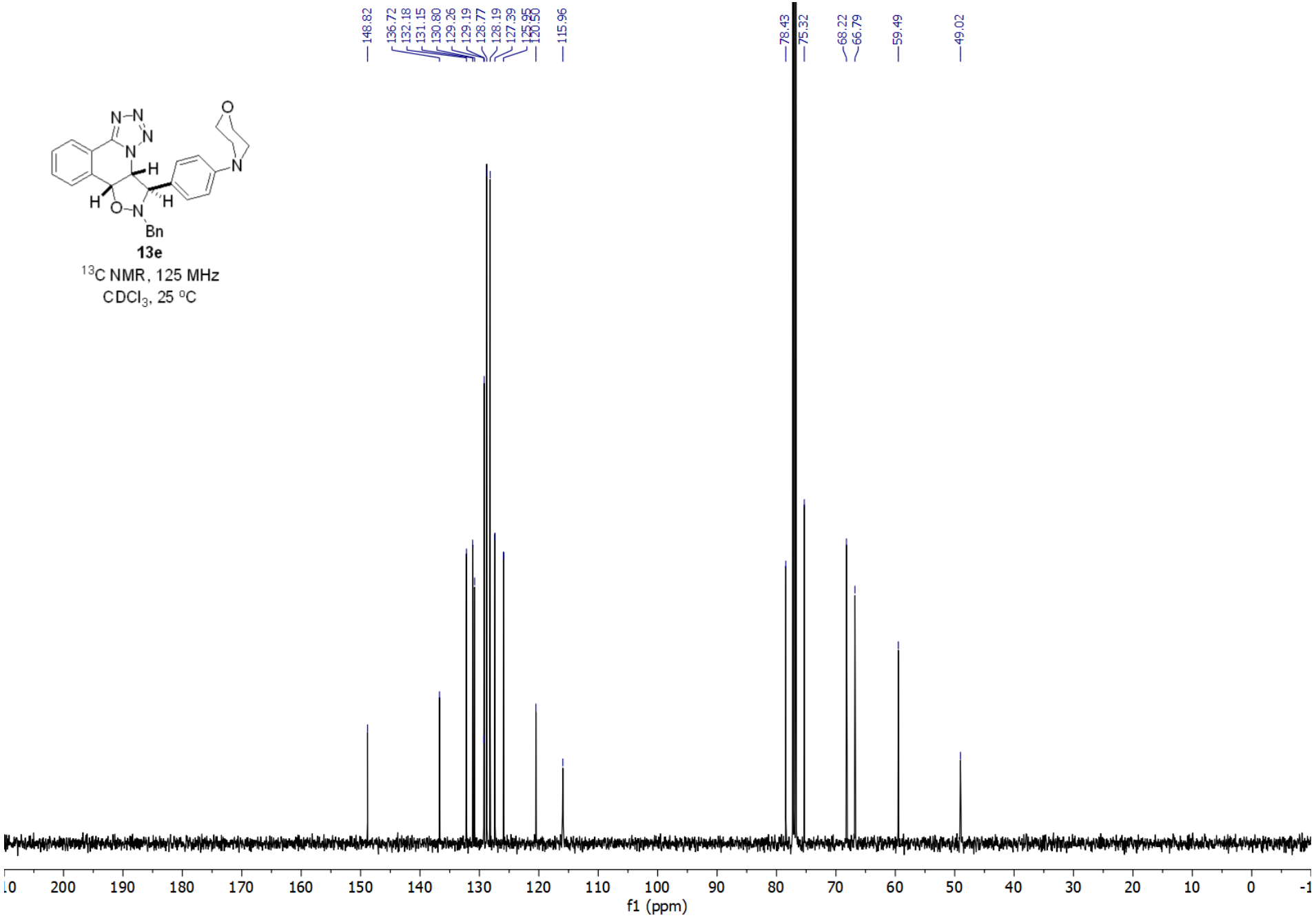

161.55
151.00
138.05
134.01
132.31
129.97
129.40
128.87
128.82
128.66
128.14
128.03
127.28
127.04
115.24
78.16
72.32
66.37
64.67
60.43
48.71
NH
H
H
H
O
N
Bn
O
N
12e
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

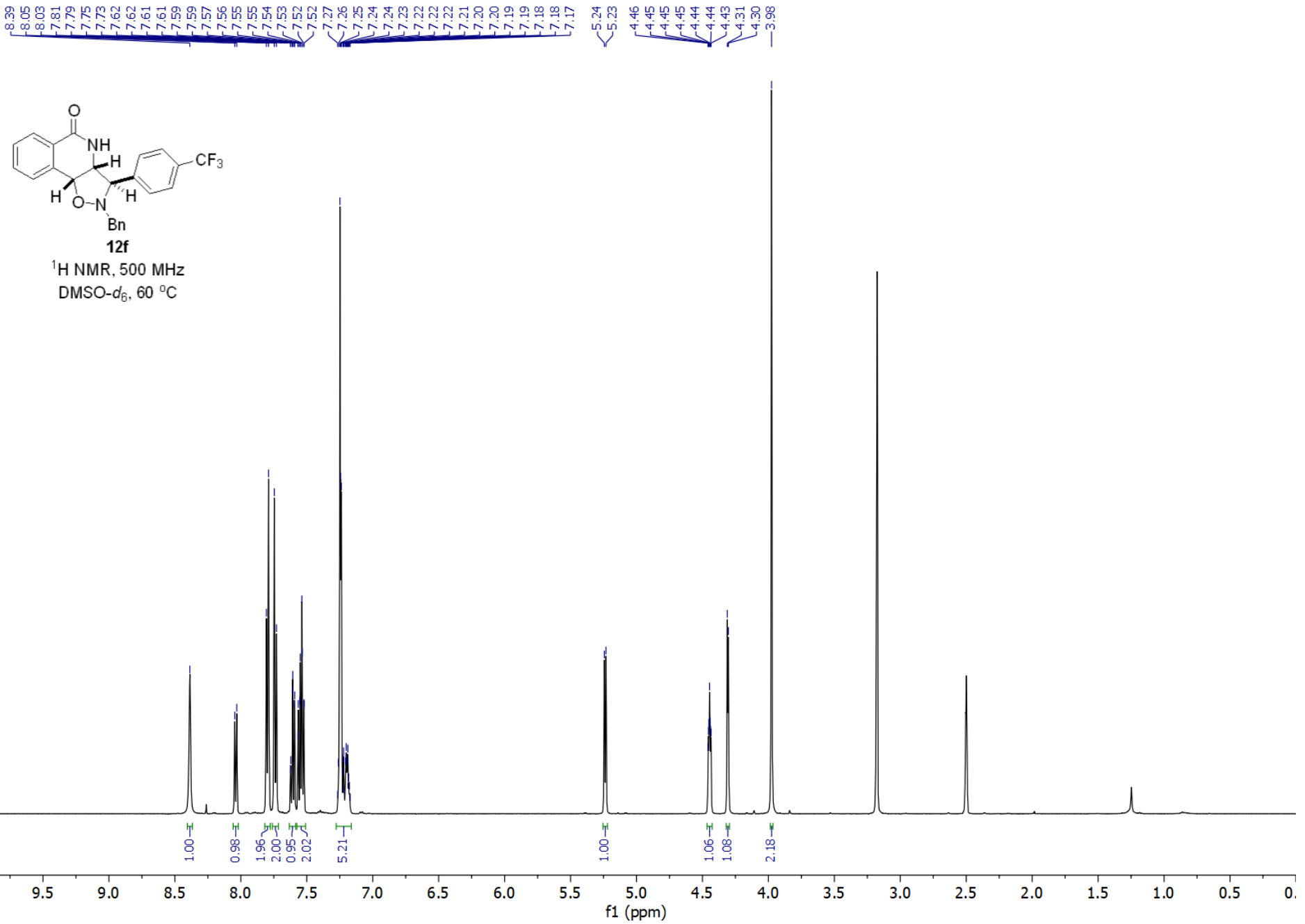

8.32 8.32 8.31 8.31 7.65 7.64 7.64 7.64 7.63 7.62 7.62 7.61 7.61 7.60 7.59 7.59 7.58 7.57 7.30 7.29 7.29 7.28 7.27 7.27 7.26 7.26 7.25 7.25 7.24 7.24 7.23 7.23 7.22 7.04 7.02 5.60 5.58 5.23 5.22 5.22 5.21 4.27 4.26 4.01 3.98 3.91 3.90 3.89 3.73 3.70 3.25 3.24 3.23
13e
1H NMR, 500 MHz
CDCl3, 25 °C
0.96 5.11 5.12 2.02 1.00 0.95 1.00 1.15 4.34 1.11 4.39
f1 (ppm)

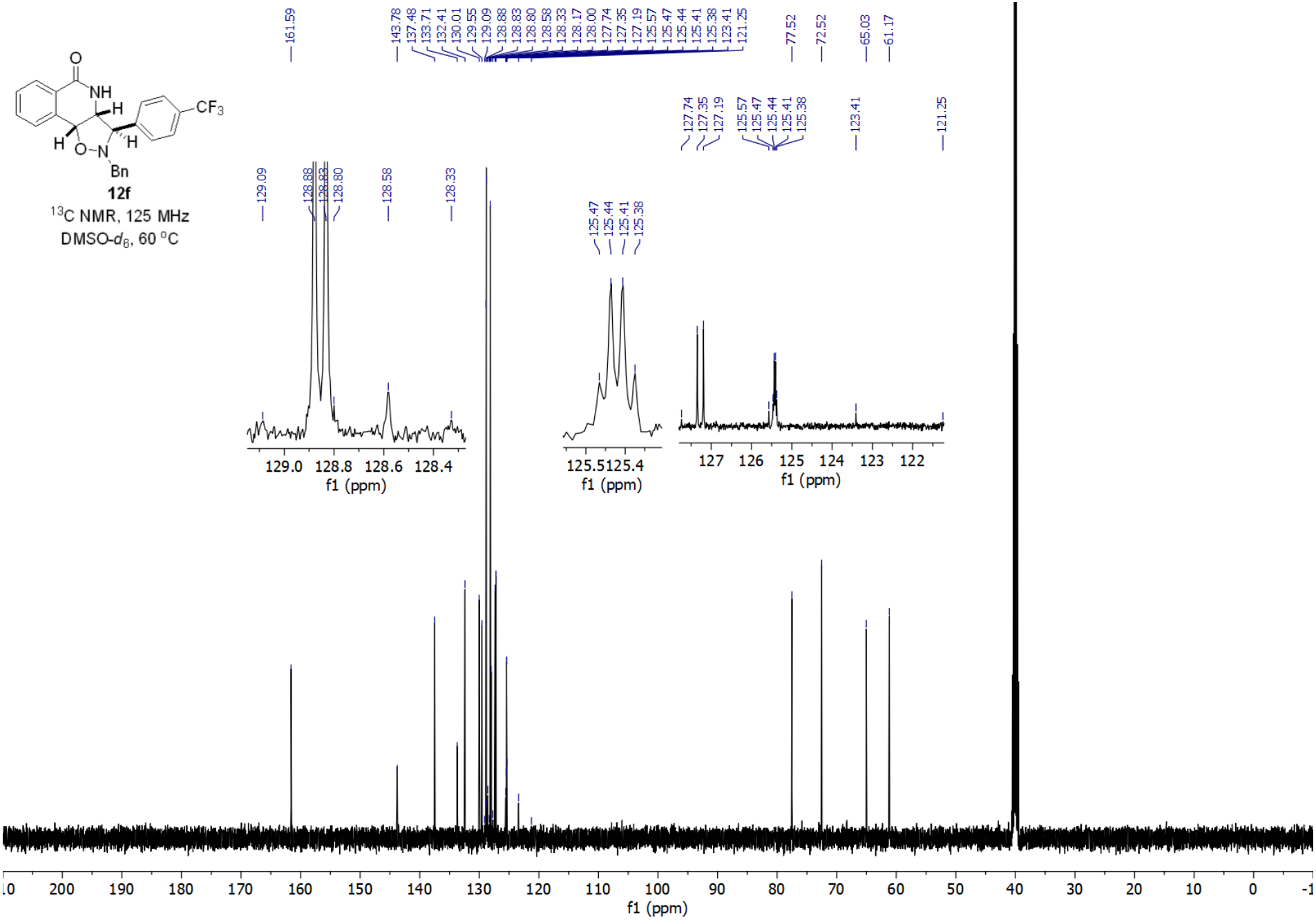
13e

^{13}C NMR, 125 MHz

$CDCl_3$, 25 °C



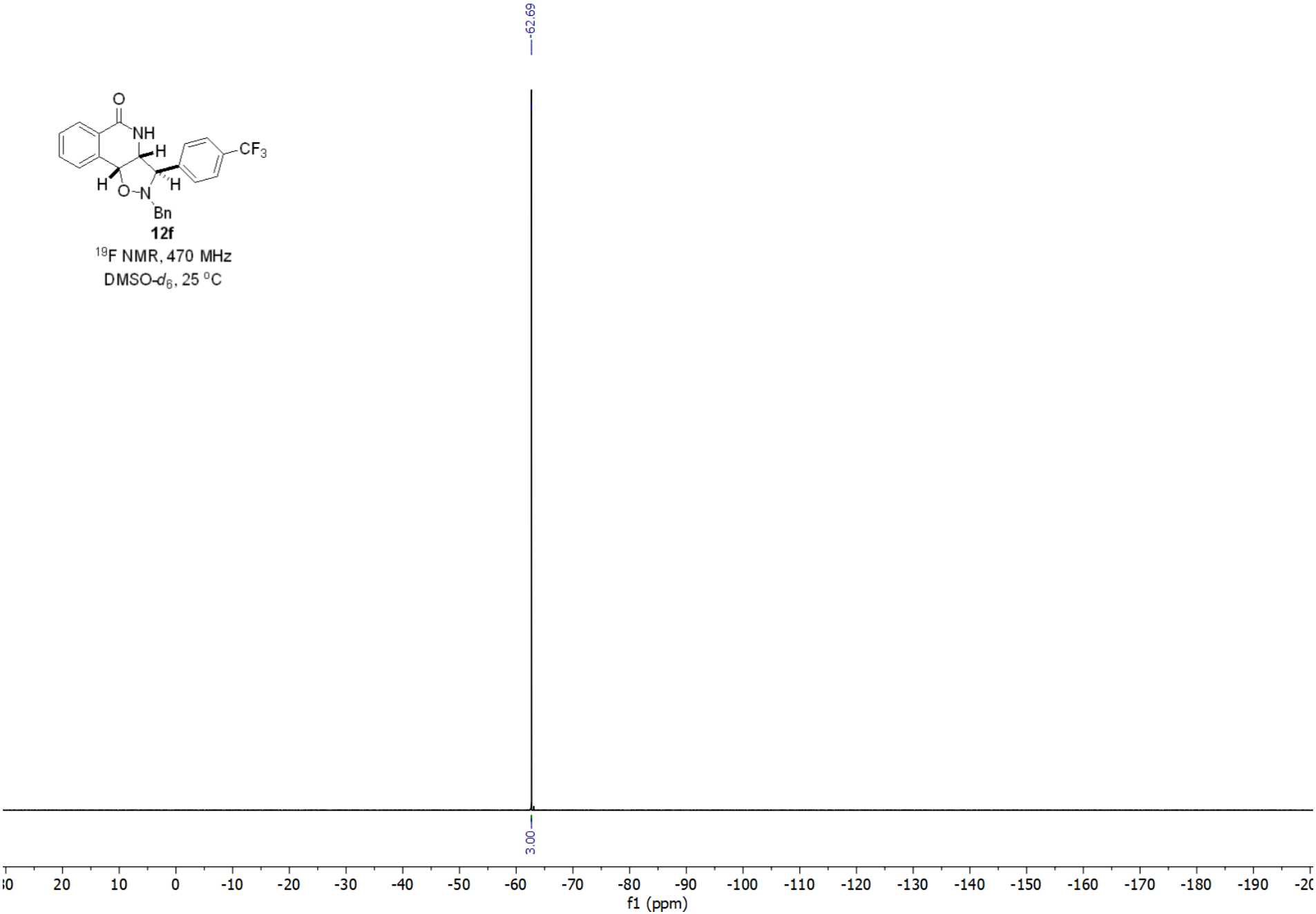

8.39
8.05
8.03
7.81
7.79
7.75
7.73
7.62
7.61
7.61
7.59
7.59
7.57
7.56
7.55
7.55
7.54
7.53
7.52
7.52
7.27
7.26
7.25
7.24
7.24
7.23
7.22
7.22
7.22
7.21
7.20
7.20
7.19
7.19
7.18
7.18
7.17
5.24
5.23
4.46
4.45
4.45
4.45
4.44
4.44
4.43
4.31
4.30
3.98
O
NH
H
CF3
H
O
N
H
Bn
12f
1H NMR, 500 MHz
DMSO-d6, 60 °C
1.00
0.98
1.96
2.00
0.95
2.02
5.21
1.00
1.06
1.08
2.18
f1 (ppm)

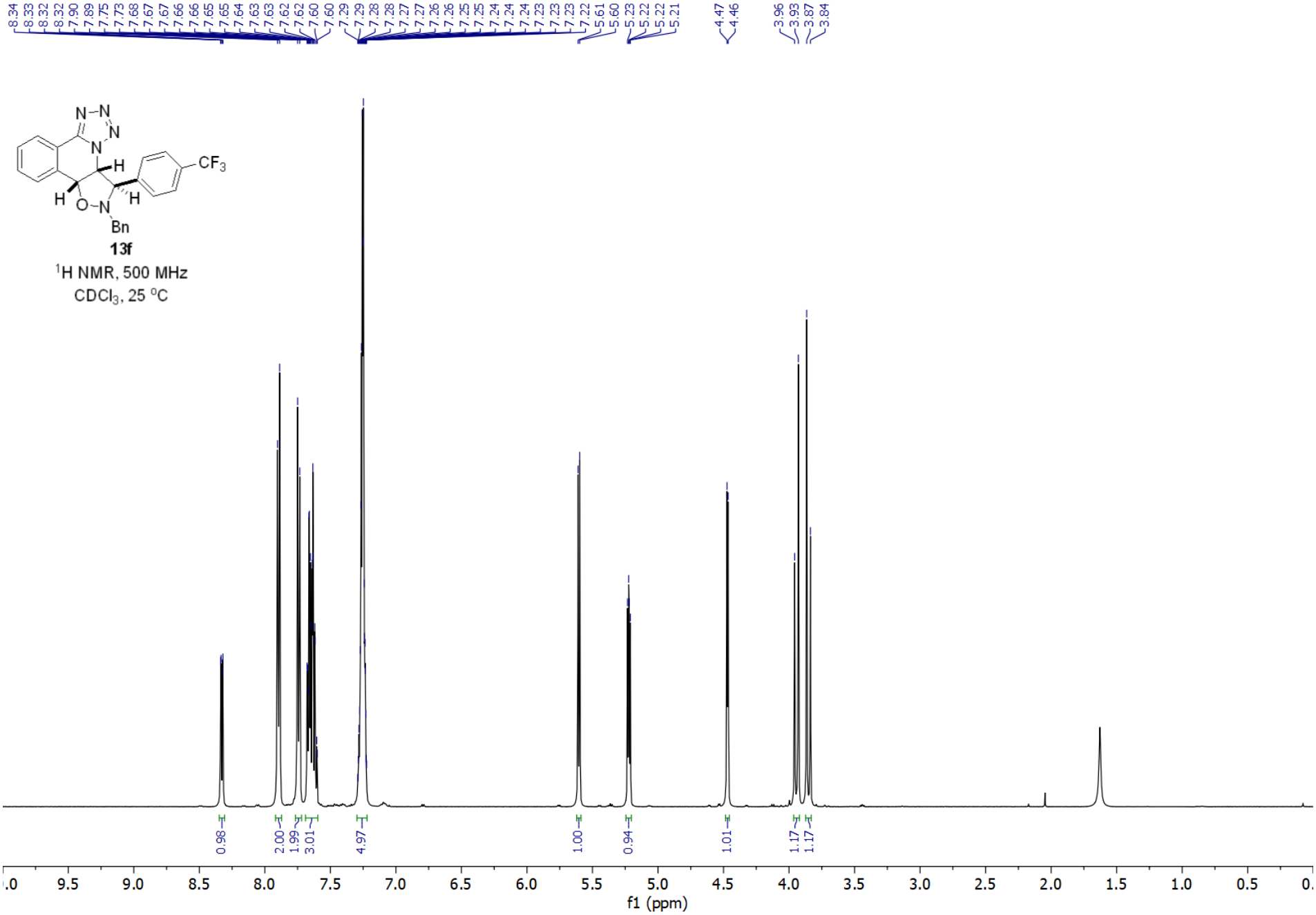

O
NH
H
CF3
H
O
N
H
Bn
12f
13C NMR, 125 MHz
DMSO-d6, 60 °C
161.59
143.78
137.48
133.71
132.41
130.01
129.55
129.09
128.88
128.83
128.80
128.58
128.33
128.17
128.00
127.74
127.35
127.19
125.57
125.47
125.44
125.41
125.38
123.41
121.25
77.52
72.52
65.03
61.17
129.0 128.8 128.6 128.4
f1 (ppm)
125.5125.4
f1 (ppm)
127 126 125 124 123 122
f1 (ppm)
f1 (ppm)

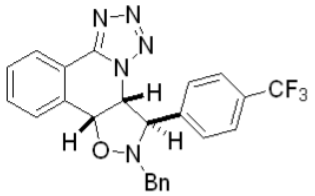
12f

^{19}F NMR, 470 MHz

DMSO-d_6, 25 ^{o}C




8.34
8.33
8.32
8.32
7.90
7.89
7.75
7.73
7.68
7.67
7.67
7.66
7.66
7.65
7.65
7.64
7.63
7.63
7.62
7.62
7.60
7.60
7.29
7.29
7.28
7.28
7.27
7.27
7.26
7.26
7.25
7.25
7.24
7.24
7.24
7.23
7.23
7.23
7.22
5.61
5.60
5.23
5.22
5.22
5.21
4.47
4.46
3.96
3.93
3.87
3.84
N–N
N
N
H
H
O–N
H
Bn
CF3
13f
1H NMR, 500 MHz
CDCl3, 25 °C
0.98
2.00
1.99
3.01
4.97
1.00
0.94
1.01
1.17
1.17
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



13f

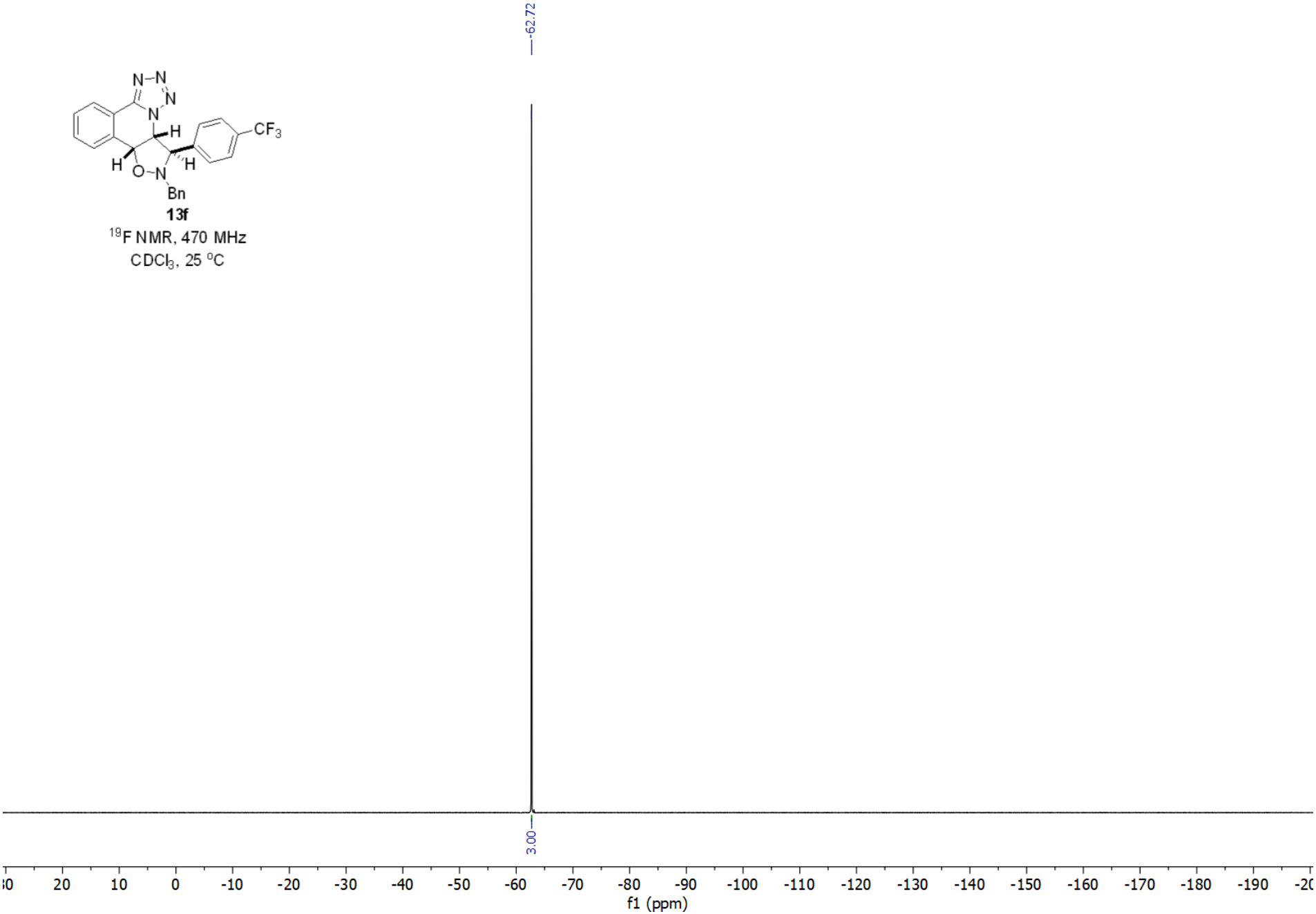
^{13}C NMR, 125 MHz

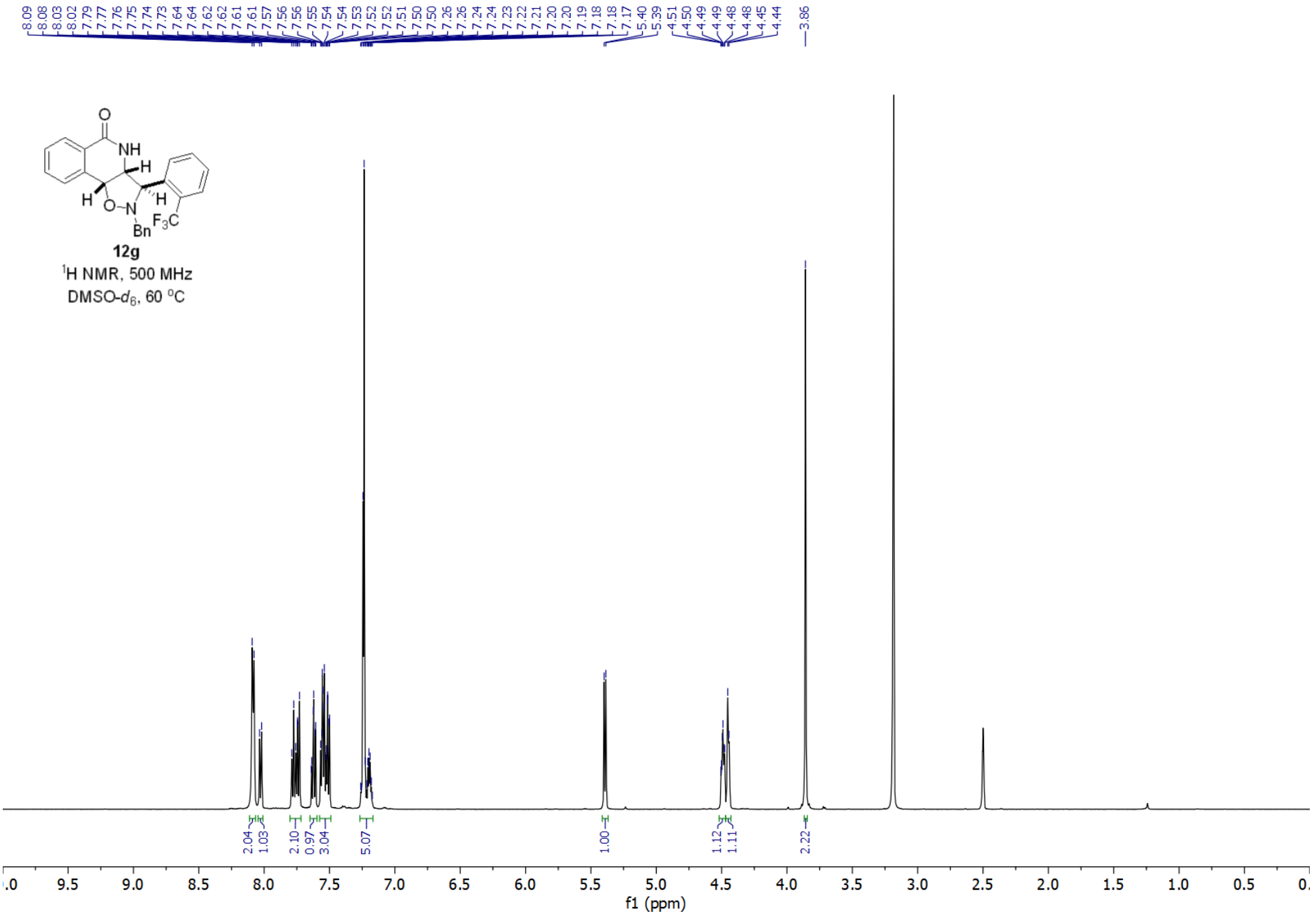
$CDCl_3$, 25 ^{o}C

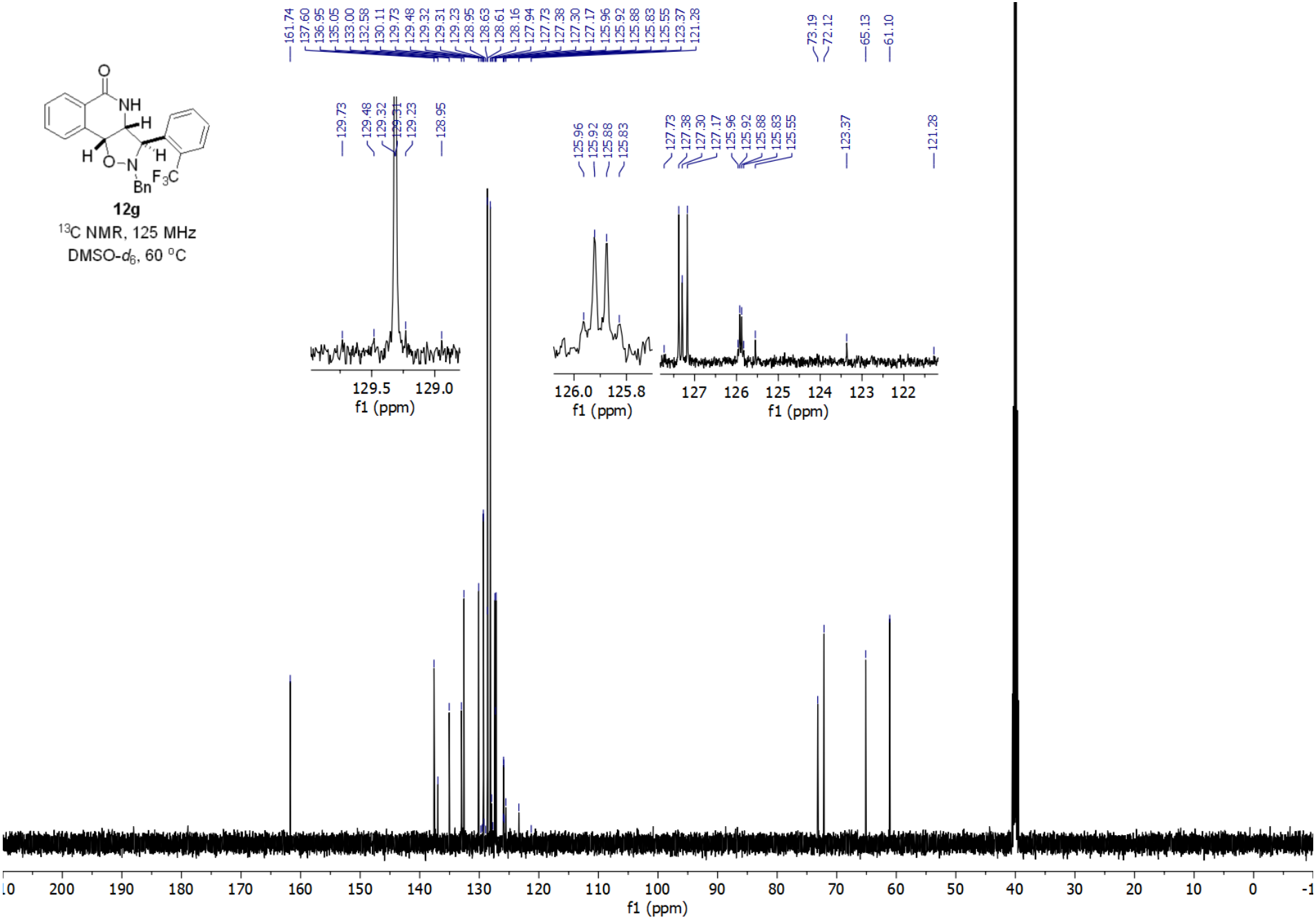
13f

^{19}F NMR, 470 MHz

$CDCl_3$, 25 °C



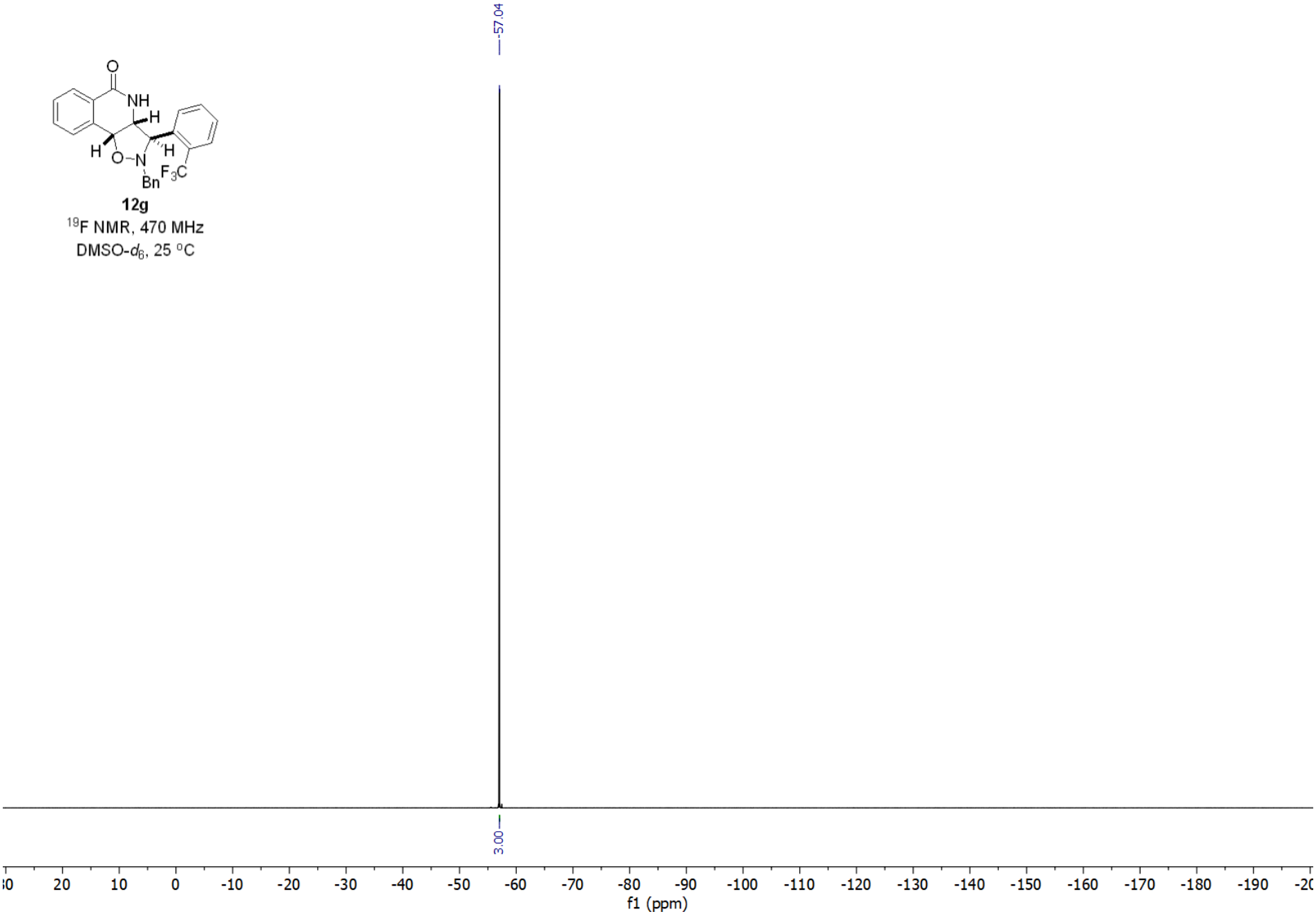

8.09 8.08 8.03 8.02 7.79 7.77 7.76 7.75 7.74 7.73 7.64 7.64 7.62 7.62 7.61 7.61 7.57 7.56 7.56 7.55 7.54 7.54 7.53 7.52 7.52 7.51 7.50 7.50 7.26 7.26 7.24 7.24 7.23 7.22 7.21 7.20 7.20 7.19 7.18 7.18 7.17 5.40 5.39 4.51 4.50 4.49 4.49 4.48 4.48 4.45 4.44 3.86
O
NH
H
H
O
N
H
Bn
F3C
12g
1H NMR, 500 MHz
DMSO-d6, 60 °C
2.04 1.03 2.10 0.97 3.04 5.07 1.00 1.12 1.11 2.22
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

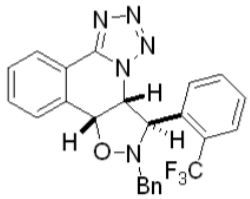

12g
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

12g

^{19}F NMR, 470 MHz

DMSO-d_6, 25 °C

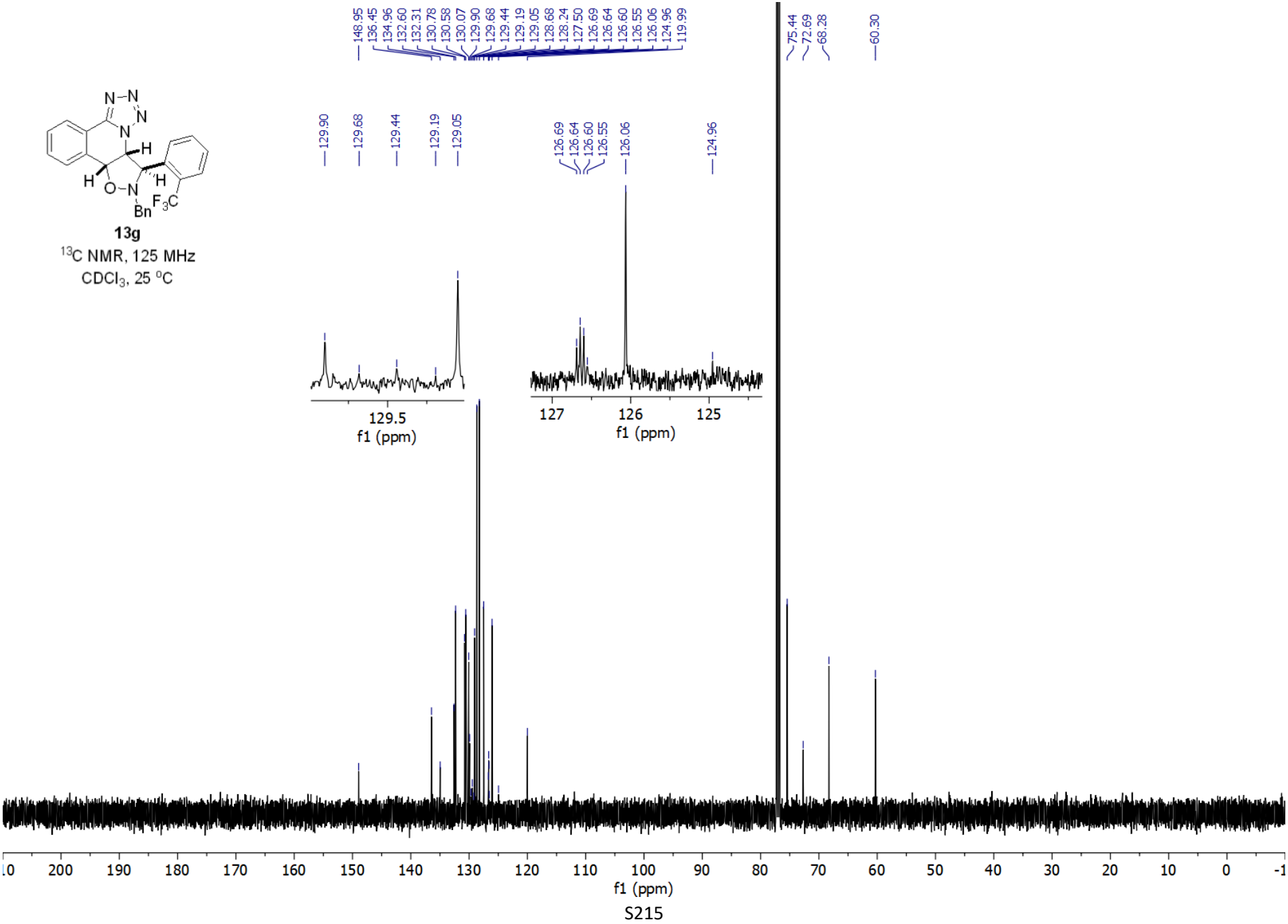




13g

^{1}H NMR, 500 MHz

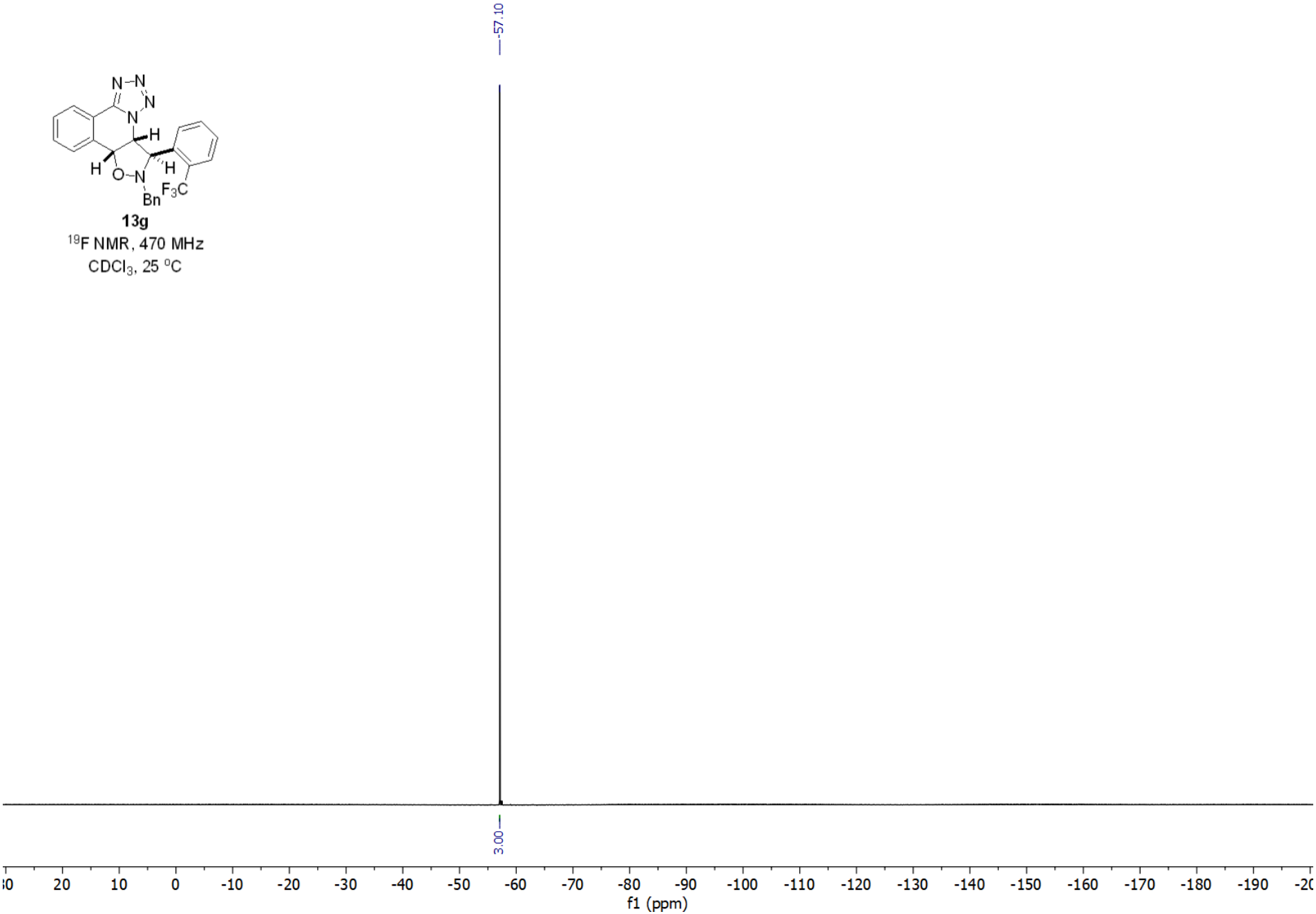
$CDCl_3$, 25 ^oC

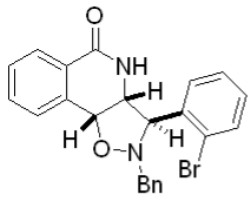

13g
13C NMR, 125 MHz
CDCl3, 25 °C
148.95
136.45
134.96
132.60
132.31
130.78
130.58
130.07
129.90
129.68
129.44
129.19
129.05
128.68
128.24
127.50
126.69
126.64
126.60
126.55
126.06
124.96
119.99
75.44
72.69
68.28
60.30
129.5
f1 (ppm)
127
126
125
f1 (ppm)
f1 (ppm)

13g

^{19}F NMR, 470 MHz

$CDCl_3$, 25 ^{o}C



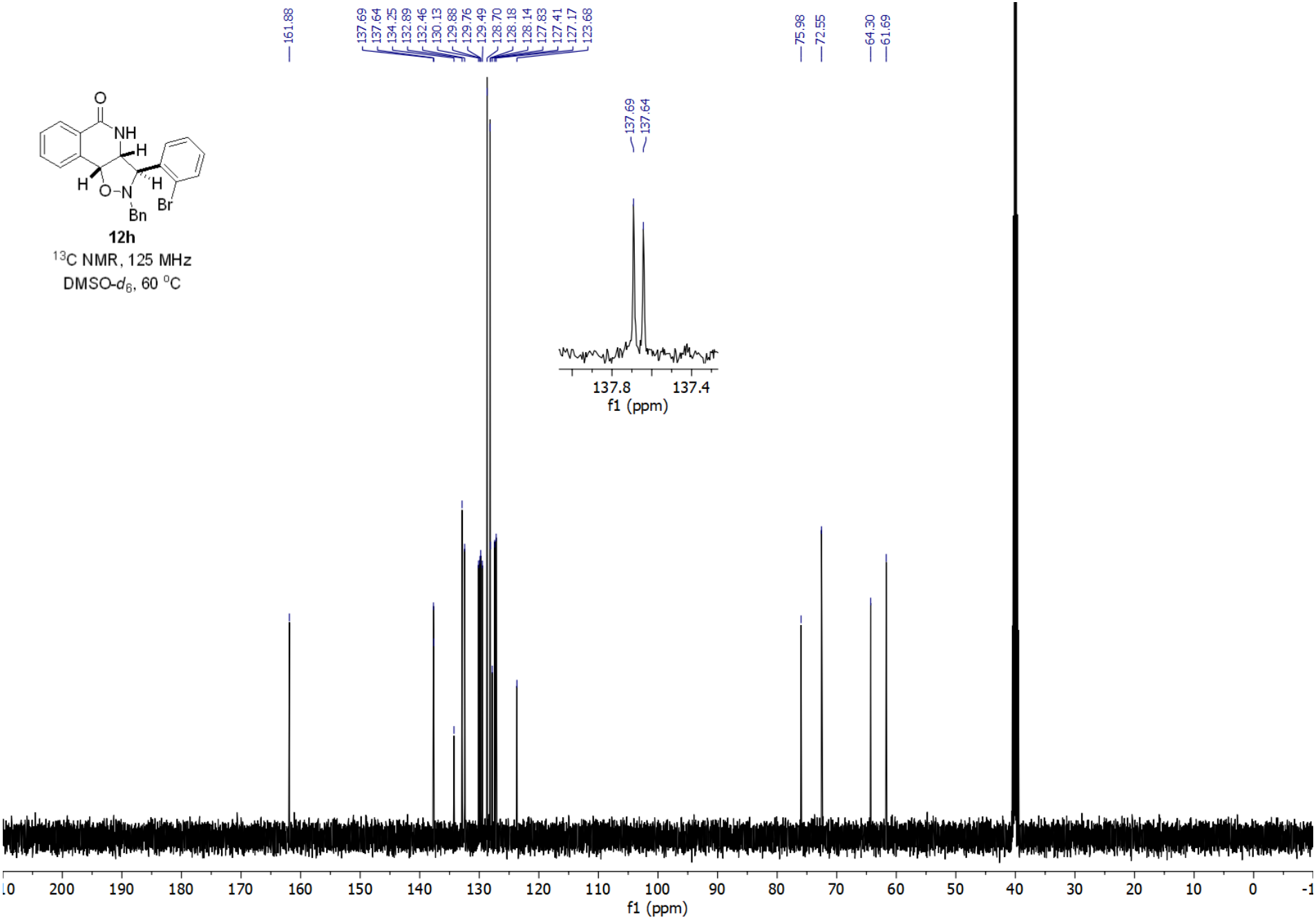


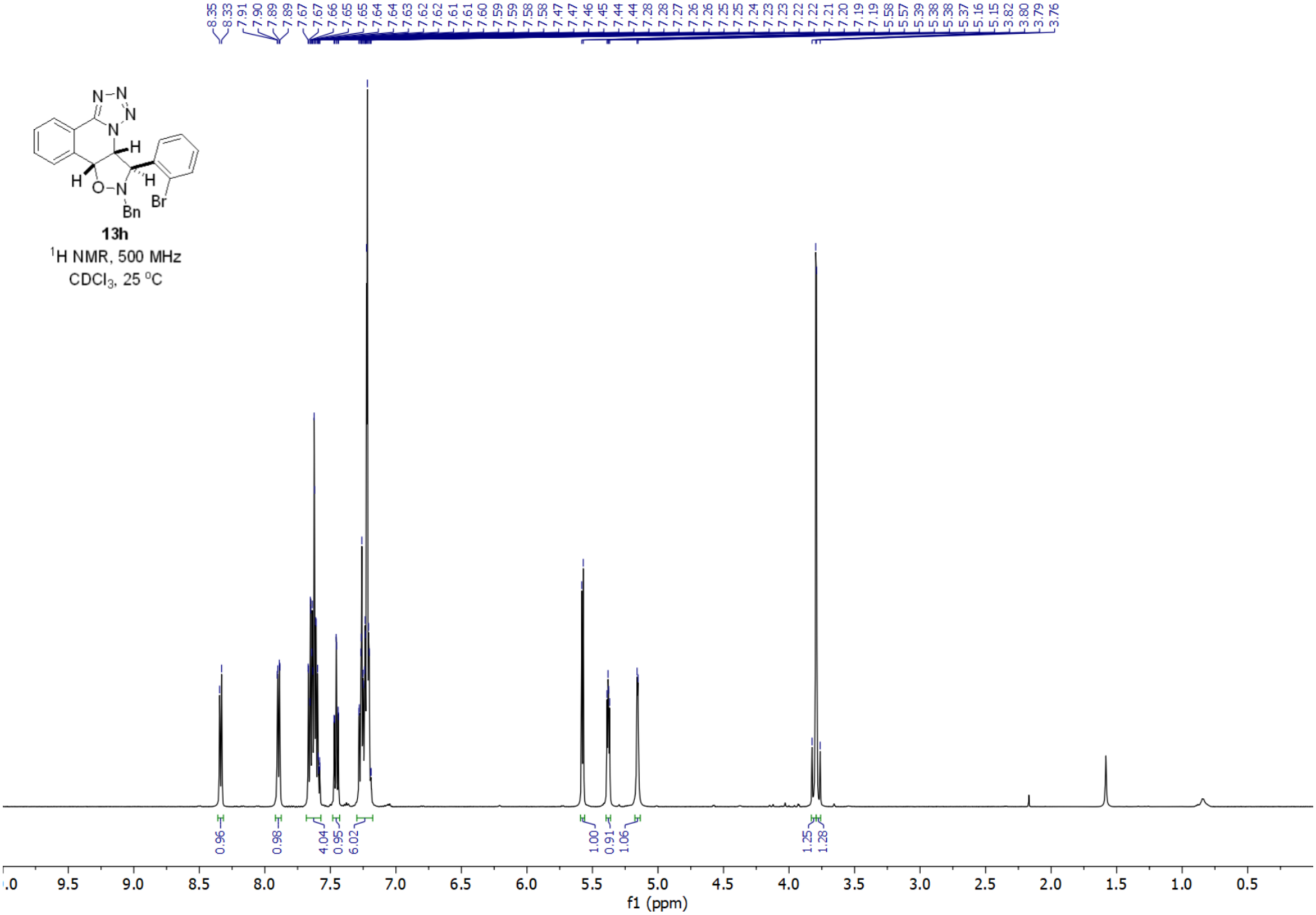
12h

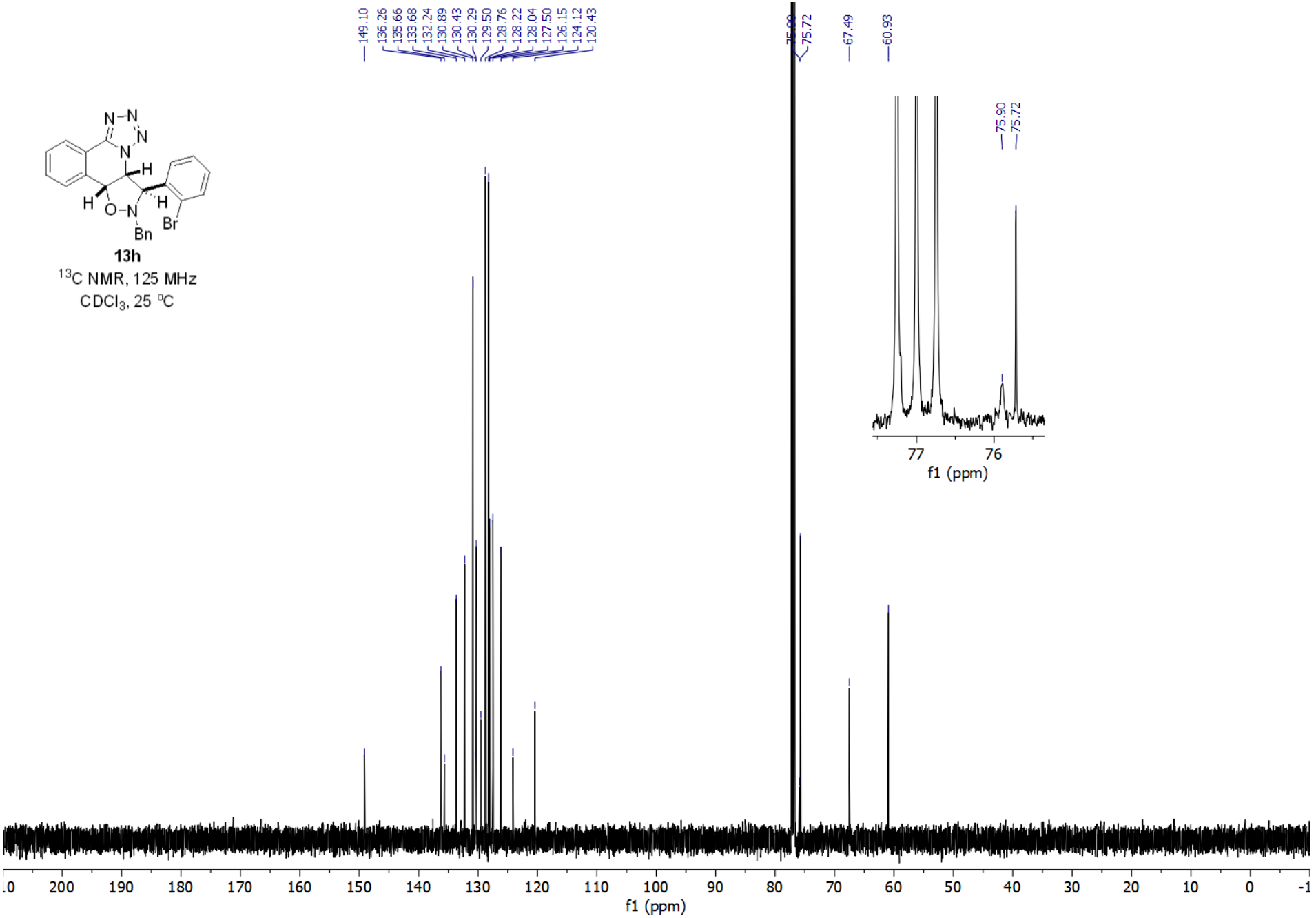
^{1}H NMR, 500 MHz

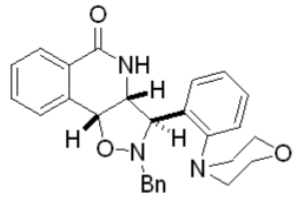
DMSO-d_6, 60 ^{o}C

f1 (ppm)


161.88
137.69
137.64
134.25
132.89
132.46
130.13
129.88
129.76
129.49
128.70
128.18
128.14
127.83
127.41
127.17
123.68
75.98
72.55
64.30
61.69
137.69
137.64
137.8
137.4
f1 (ppm)
O
NH
H
H
O–N
H
Bn
Br
12h
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)


8.35
8.33
7.91
7.90
7.89
7.89
7.67
7.67
7.66
7.65
7.65
7.64
7.64
7.63
7.62
7.62
7.61
7.61
7.60
7.59
7.59
7.58
7.58
7.47
7.47
7.46
7.45
7.44
7.44
7.28
7.28
7.27
7.26
7.26
7.25
7.25
7.24
7.23
7.23
7.22
7.22
7.21
7.20
7.19
7.19
5.58
5.57
5.39
5.38
5.38
5.37
5.16
5.15
3.82
3.80
3.79
3.76
N
N
N
H
H
O
N
H
Br
Bn
13h
1H NMR, 500 MHz
CDCl3, 25 °C
0.96
0.98
4.04
0.95
6.02
1.00
0.91
1.06
1.25
1.28
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

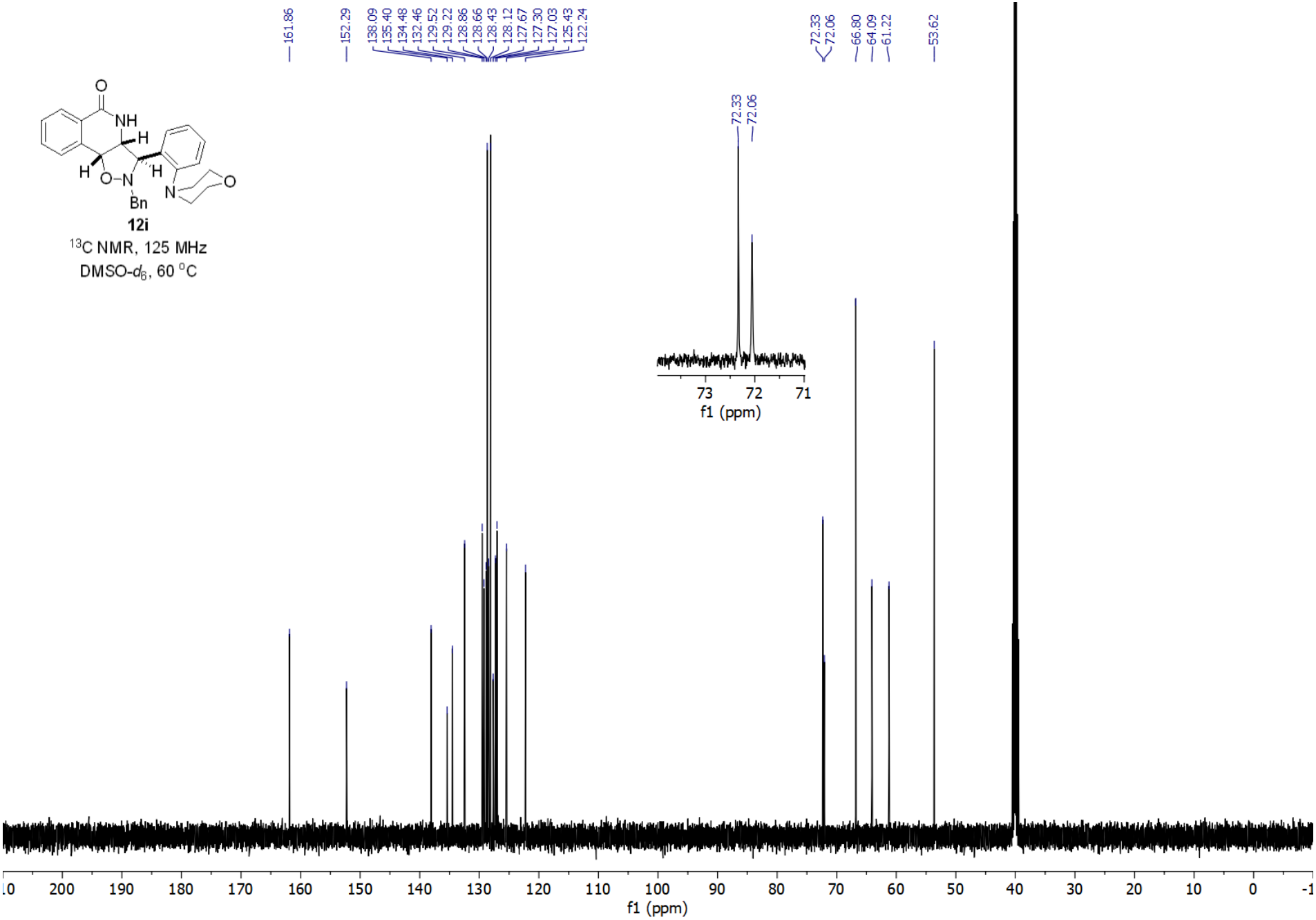

149.10
136.26
135.66
133.68
132.24
130.89
130.43
130.29
129.50
128.76
128.22
128.04
127.50
126.15
124.12
120.43
75.90
75.72
67.49
60.93
N–N
N
N
H
H
O–N
H
Bn
Br
13h
13C NMR, 125 MHz
CDCl3, 25 °C
75.90
75.72
77
76
f1 (ppm)
f1 (ppm)

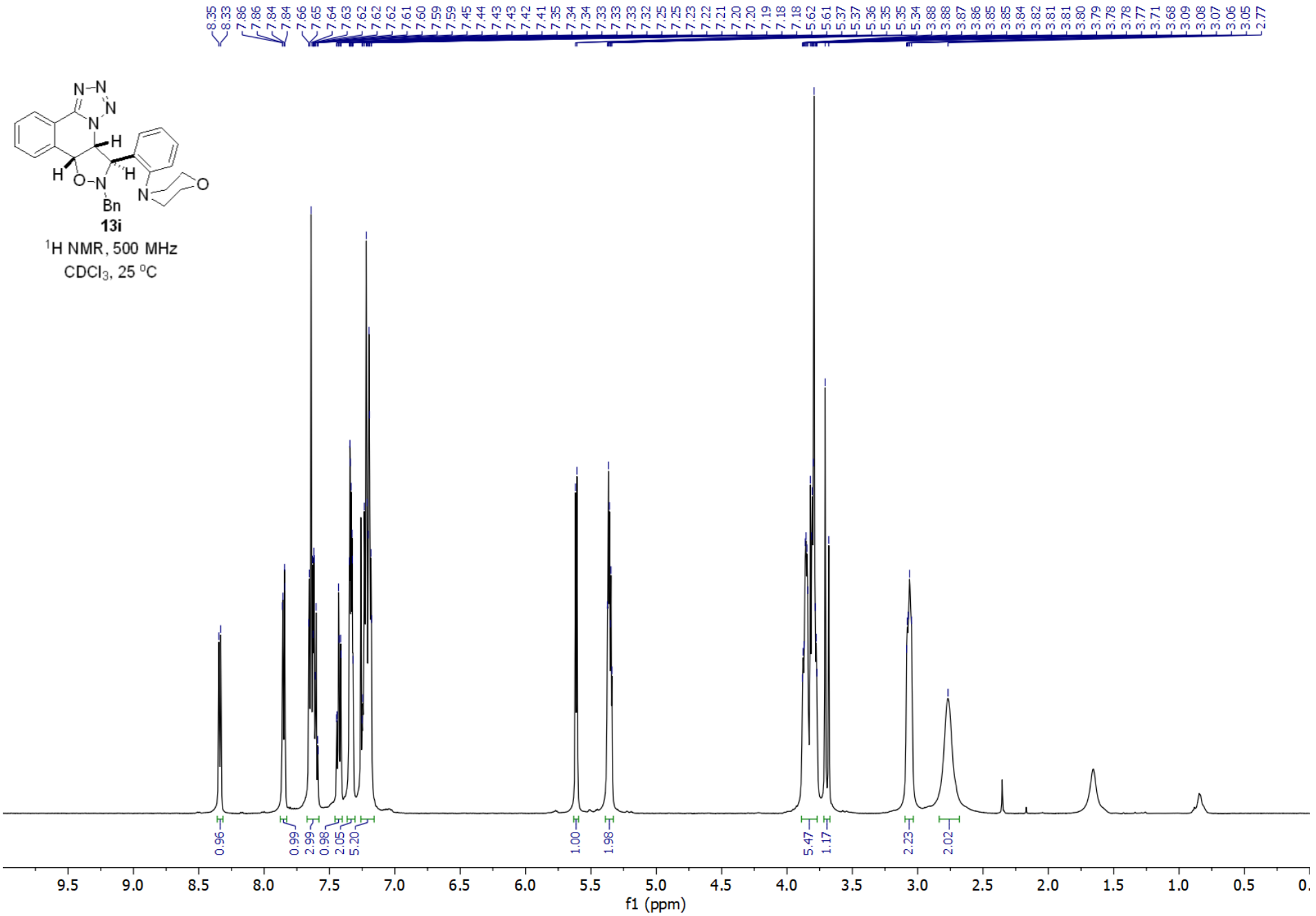


12i

^{1}H NMR, 500 MHz

DMSO-d_6, 60 ^{o}C

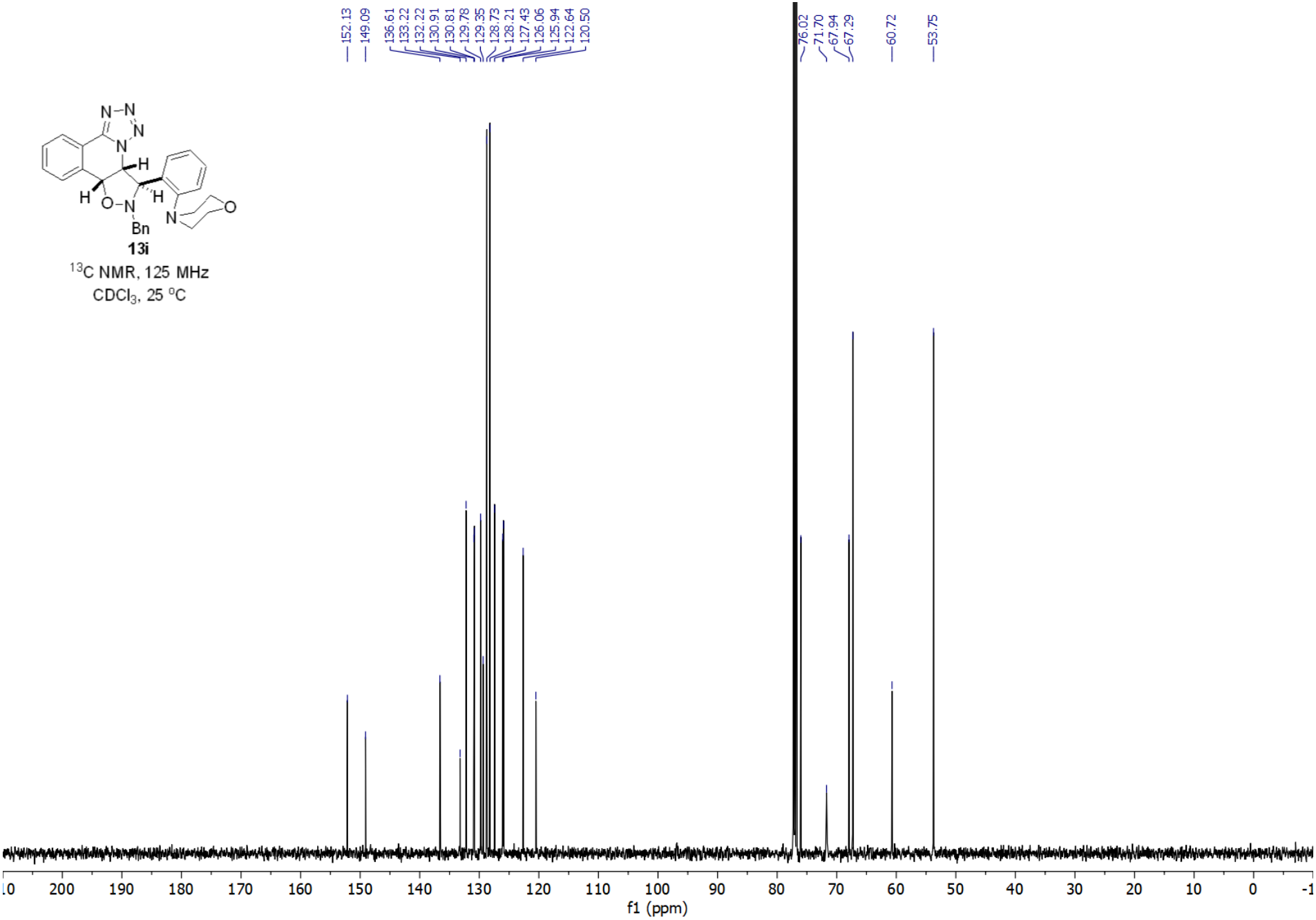

161.86
152.29
138.09
135.40
134.48
132.46
129.52
129.22
128.86
128.66
128.43
128.12
127.67
127.30
127.03
125.43
122.24
72.33
72.06
66.80
64.09
61.22
53.62
O
NH
H
H
O–N
H
N
O
Bn
12i
13C NMR, 125 MHz
DMSO-d6, 60 °C
73
72
71
f1 (ppm)
f1 (ppm)

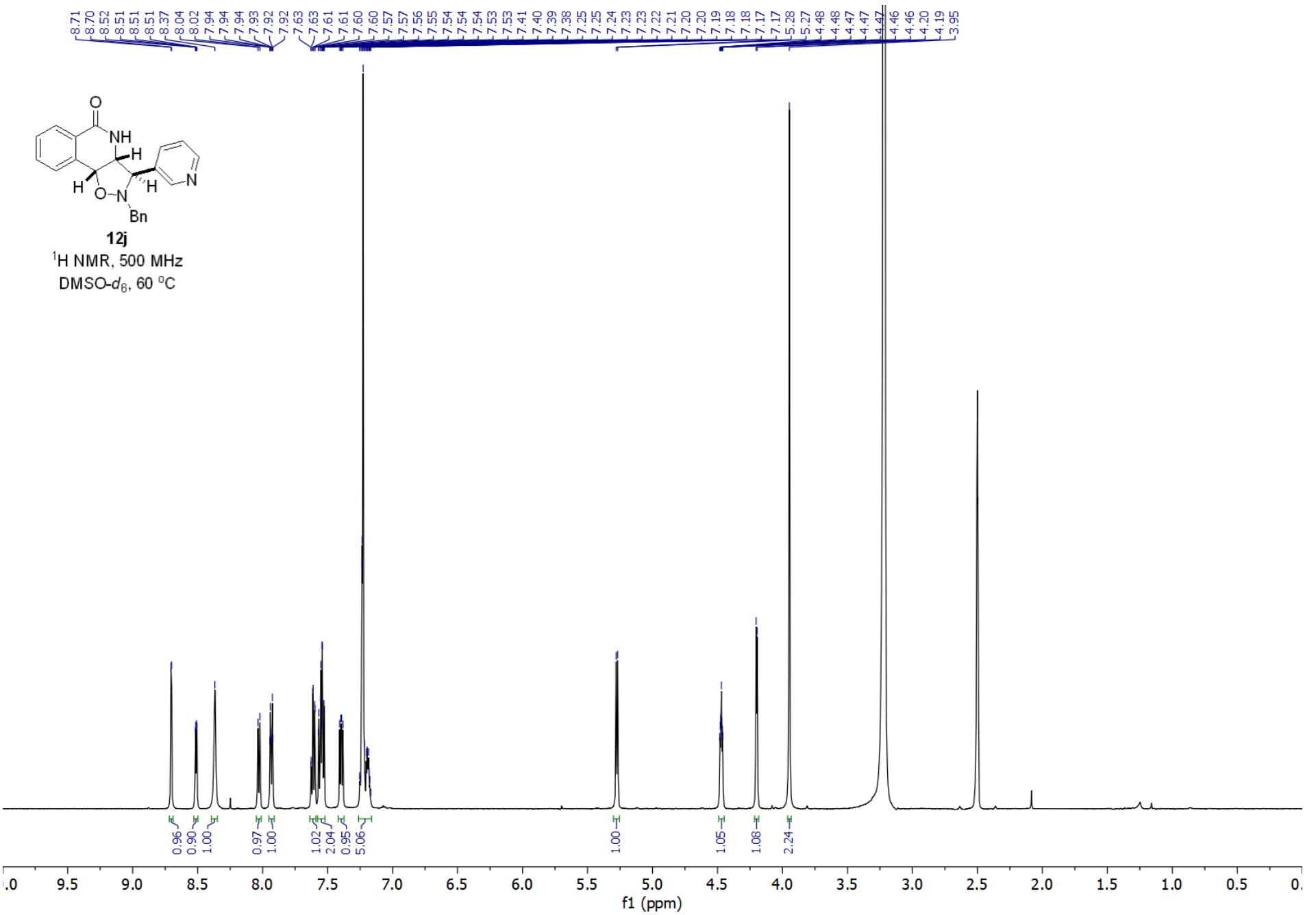

13i
1H NMR, 500 MHz
CDCl3, 25 °C
f1 (ppm)

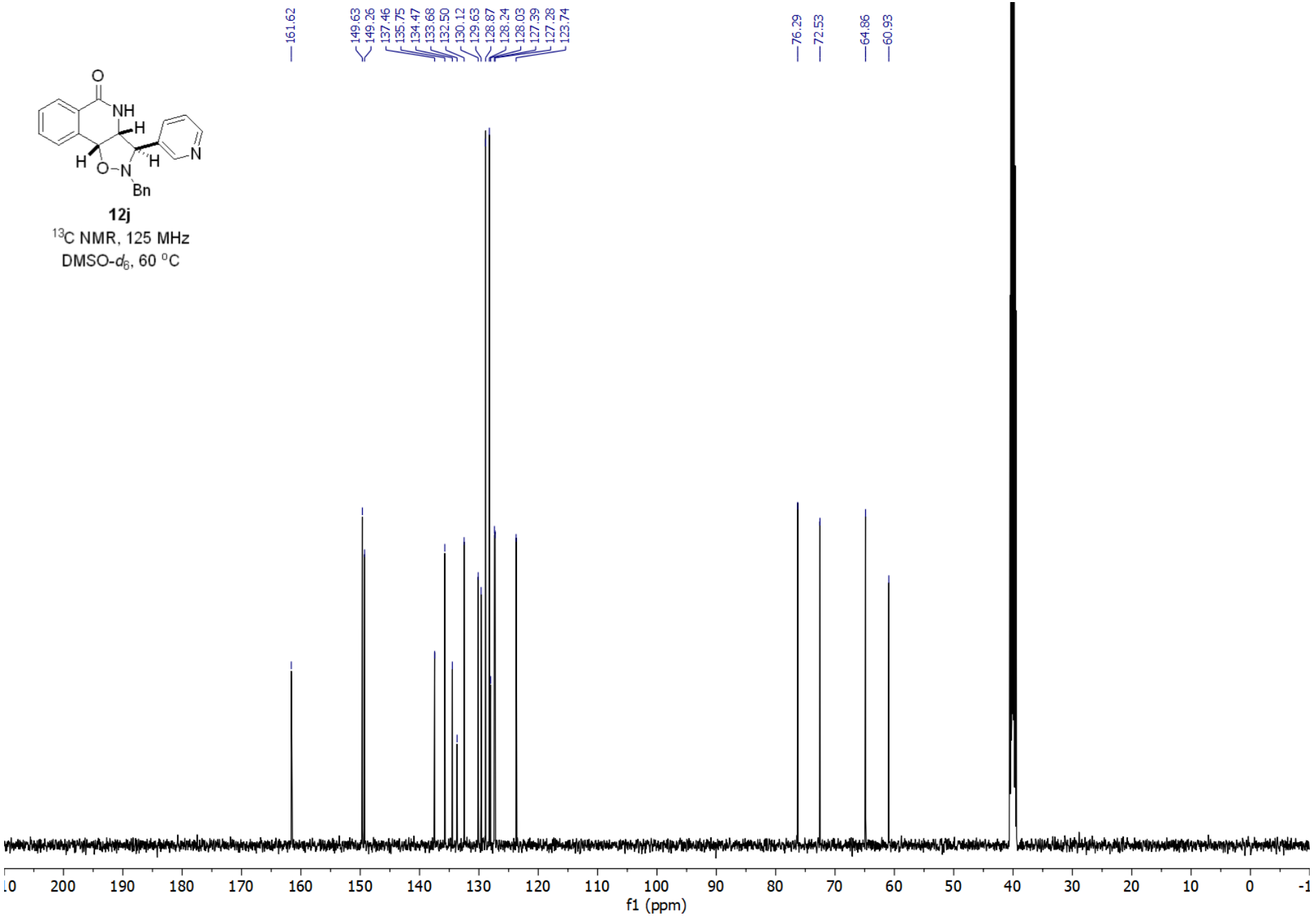
13i

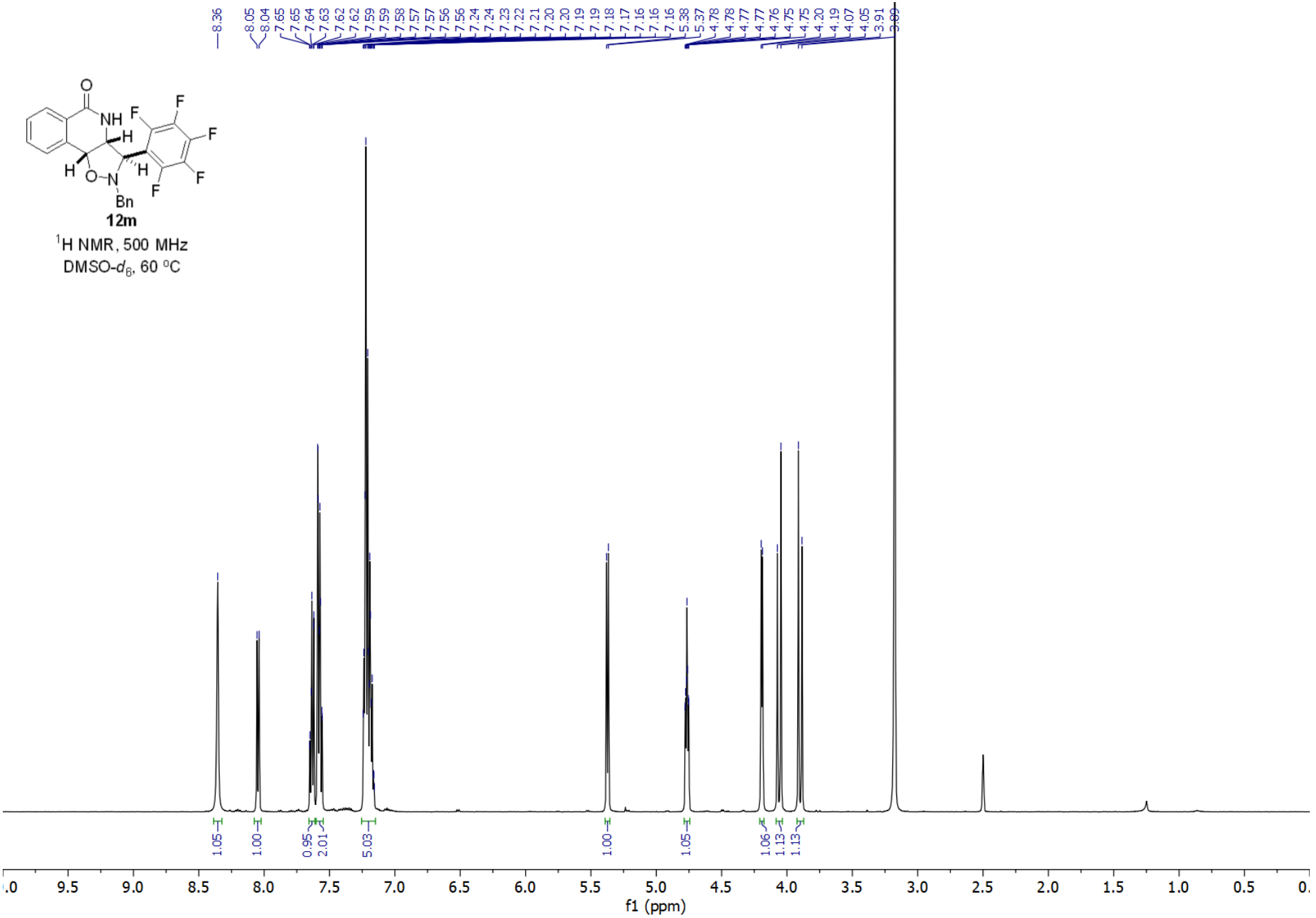
^{13}C NMR, 125 MHz

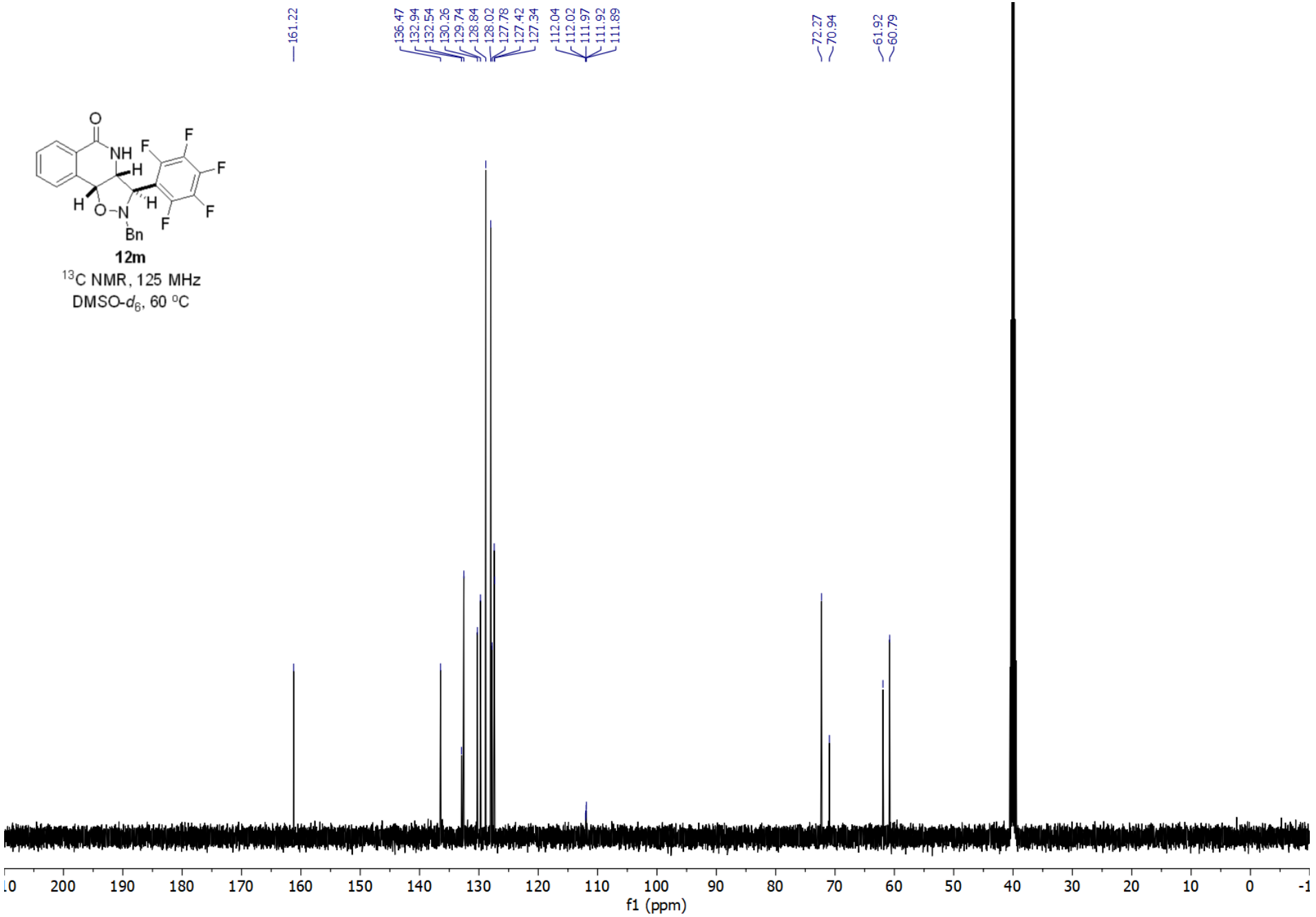
$CDCl_3$, 25 ^{o}C

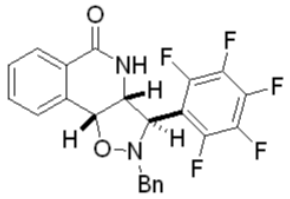



8.71 8.70 8.52 8.51 8.51 8.51 8.37 8.04 8.02 7.94 7.94 7.94 7.93 7.92 7.92 7.63 7.63 7.61 7.61 7.60 7.60 7.57 7.57 7.56 7.55 7.54 7.54 7.54 7.53 7.53 7.41 7.40 7.39 7.38 7.25 7.25 7.24 7.23 7.23 7.22 7.21 7.20 7.20 7.19 7.18 7.17 7.17 5.28 5.27 4.48 4.48 4.47 4.47 4.47 4.46 4.46 4.20 4.19 3.95
O
NH
H
H
O
N
H
N
Bn
12j
1H NMR, 500 MHz
DMSO-d6, 60 °C
0.96 0.90 1.00 0.97 1.00 1.02 2.04 0.95 5.06 1.00 1.05 1.08 2.24
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


161.62
149.63
149.26
137.46
135.75
134.47
133.68
132.50
130.12
129.63
128.87
128.24
128.03
127.39
127.28
123.74
76.29
72.53
64.86
60.93
O
NH
H
H
O
N
H
N
Bn
12j
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)


12m
1H NMR, 500 MHz
DMSO-d6, 60 °C
f1 (ppm)

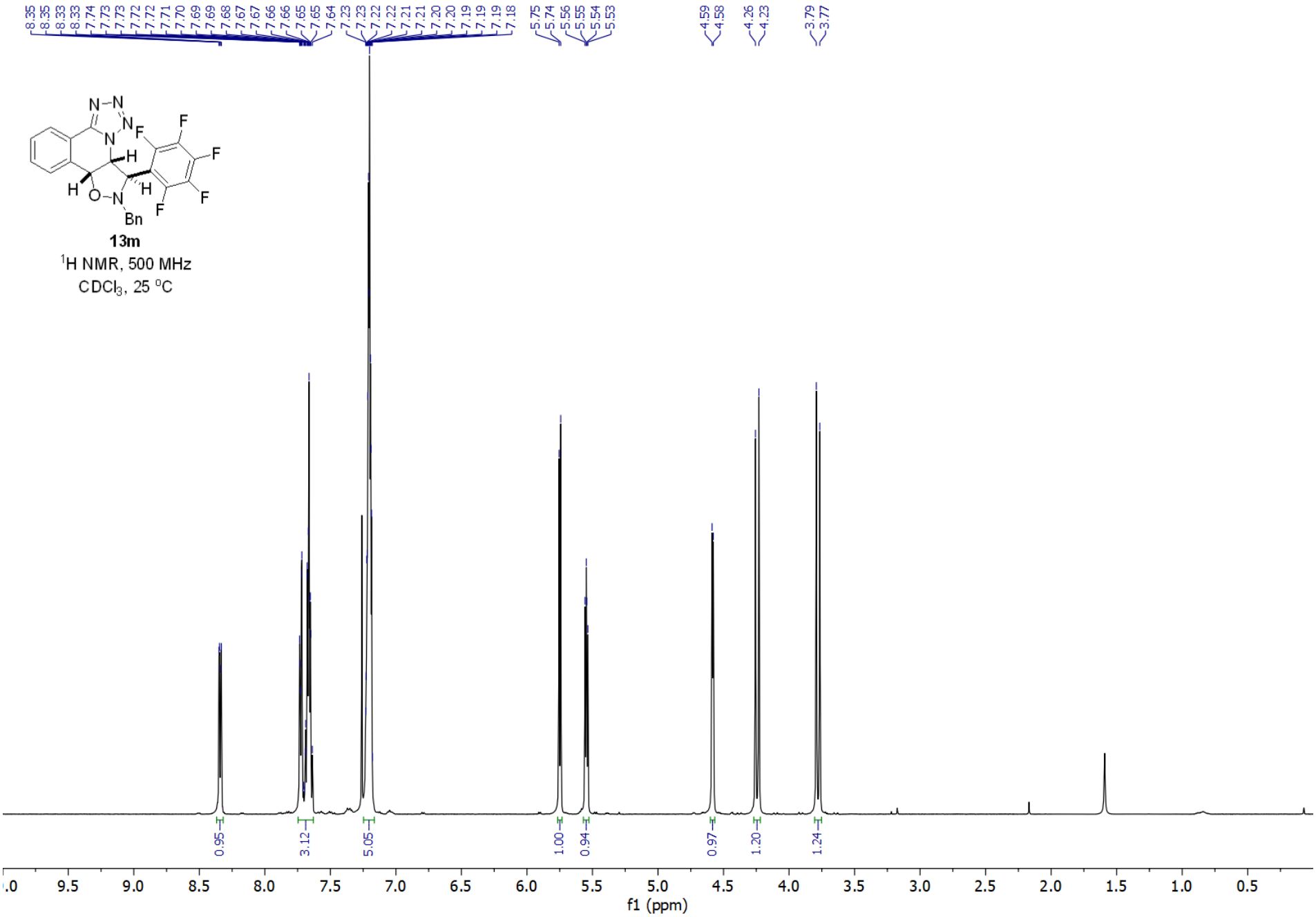

161.22
136.47
132.94
132.54
130.26
129.74
128.84
128.02
127.78
127.42
127.34
112.04
112.02
111.97
111.92
111.89
72.27
70.94
61.92
60.79
O
NH
H
F
F
F
F
F
H
O
N
H
Bn
12m
13C NMR, 125 MHz
DMSO-d6, 60 °C
f1 (ppm)

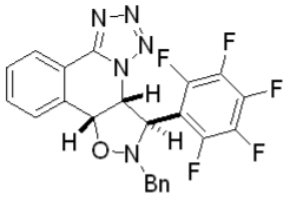


12m

^{19}F NMR, 470 MHz

DMSO-d_6, 25 °C


8.35
8.35
8.33
8.33
7.74
7.73
7.73
7.72
7.72
7.71
7.70
7.69
7.69
7.68
7.67
7.67
7.66
7.66
7.65
7.65
7.64
7.23
7.23
7.22
7.22
7.21
7.21
7.20
7.20
7.19
7.19
7.19
7.18
5.75
5.74
5.56
5.55
5.54
5.53
4.59
4.58
4.26
4.23
3.79
3.77
N
N
N
N
F
F
F
F
F
H
H
H
O
N
Bn
13m
1H NMR, 500 MHz
CDCl3, 25 °C
0.95
3.12
5.05
1.00
0.94
0.97
1.20
1.24
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



13m

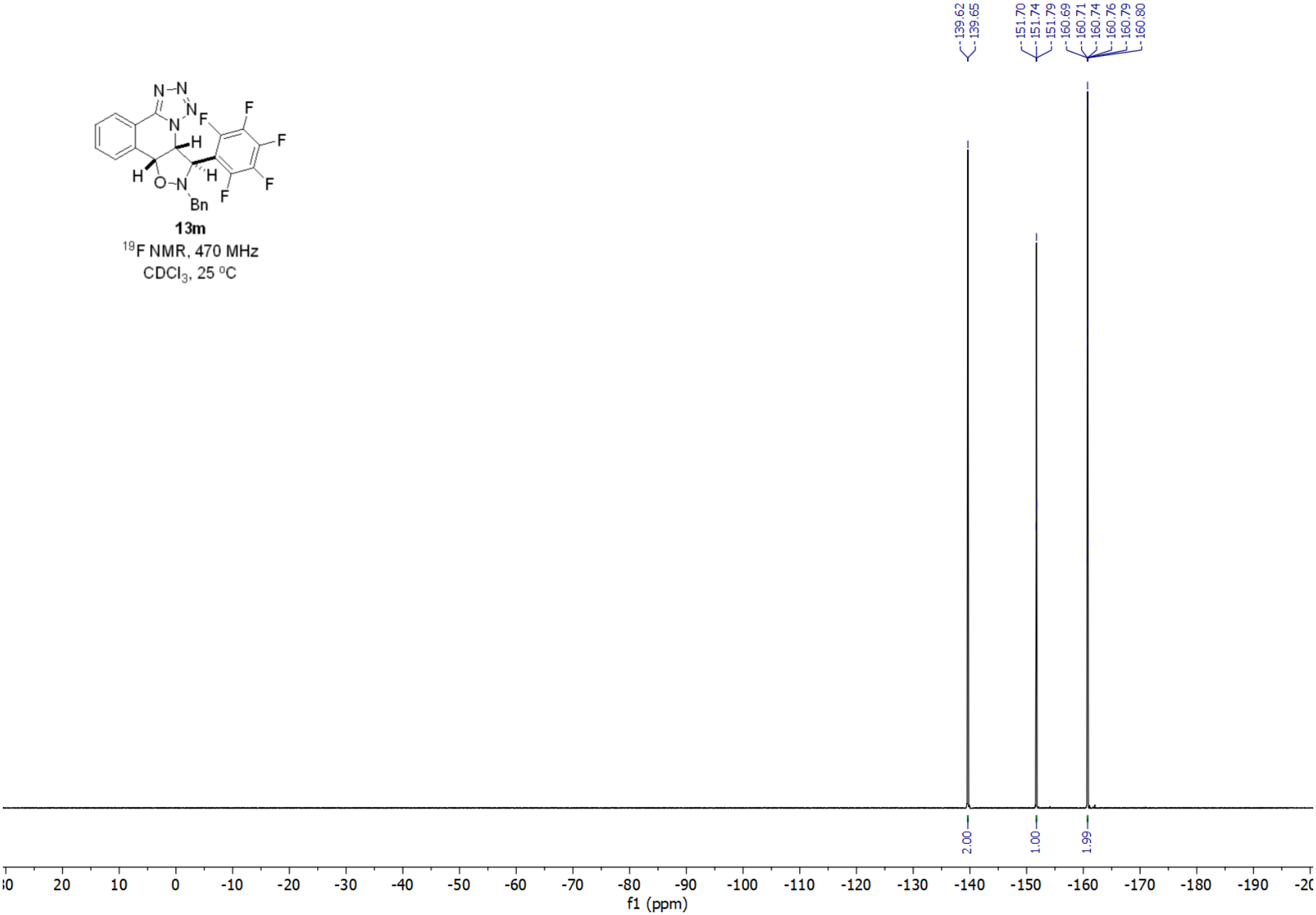
^{13}C NMR, 125 MHz

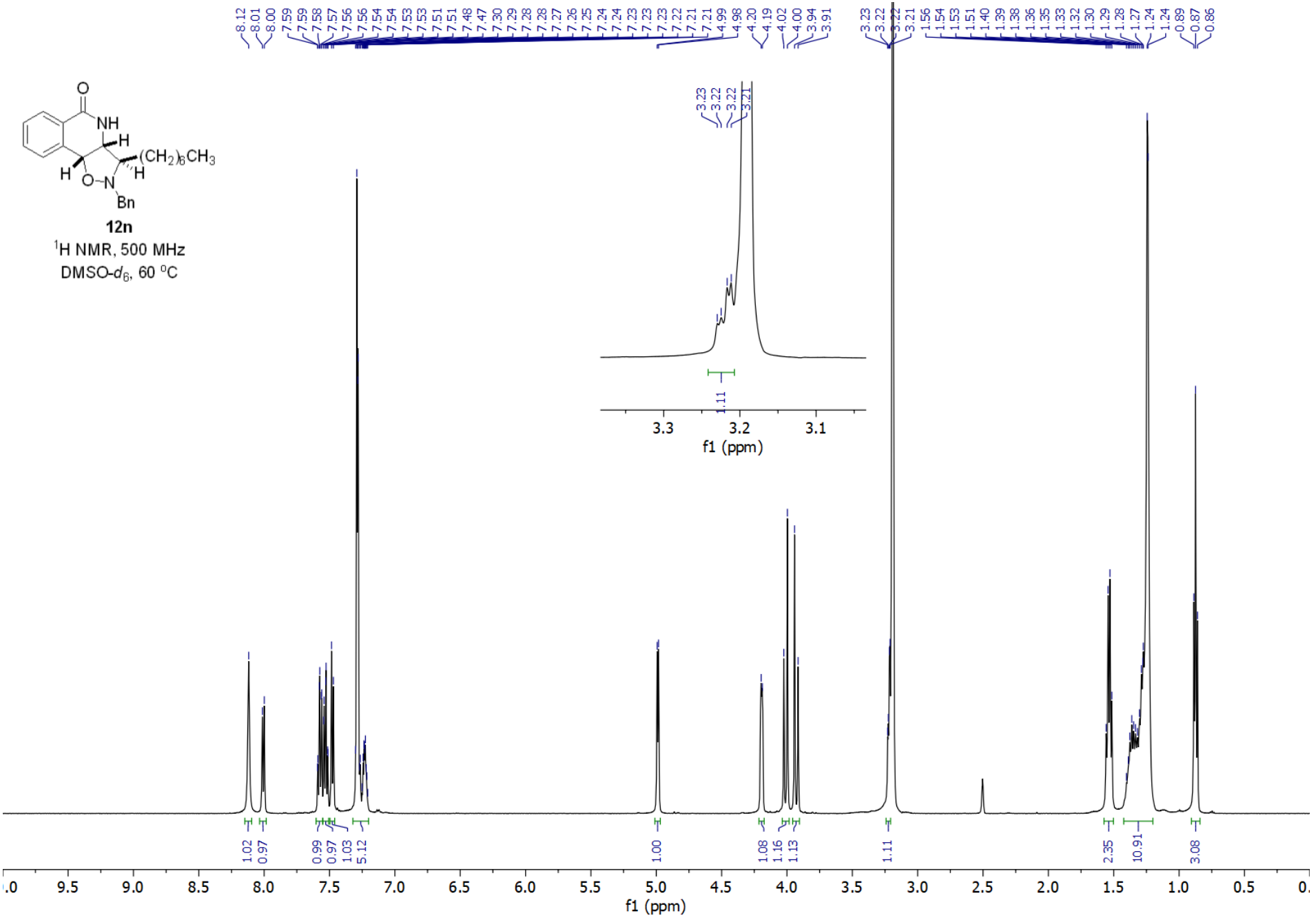
$CDCl_3$, 25 °C

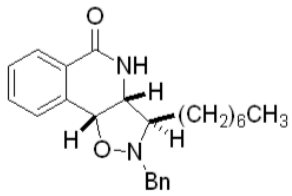
13m

^{19}F NMR, 470 MHz

$CDCl_3$, 25 °C



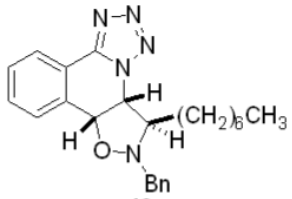

O
NH
H
(CH2)6CH3
H
H
O
N
Bn
12n
1H NMR, 500 MHz
DMSO-d6, 60 °C
f1 (ppm)



12n

^{13}C NMR, 125 MHz

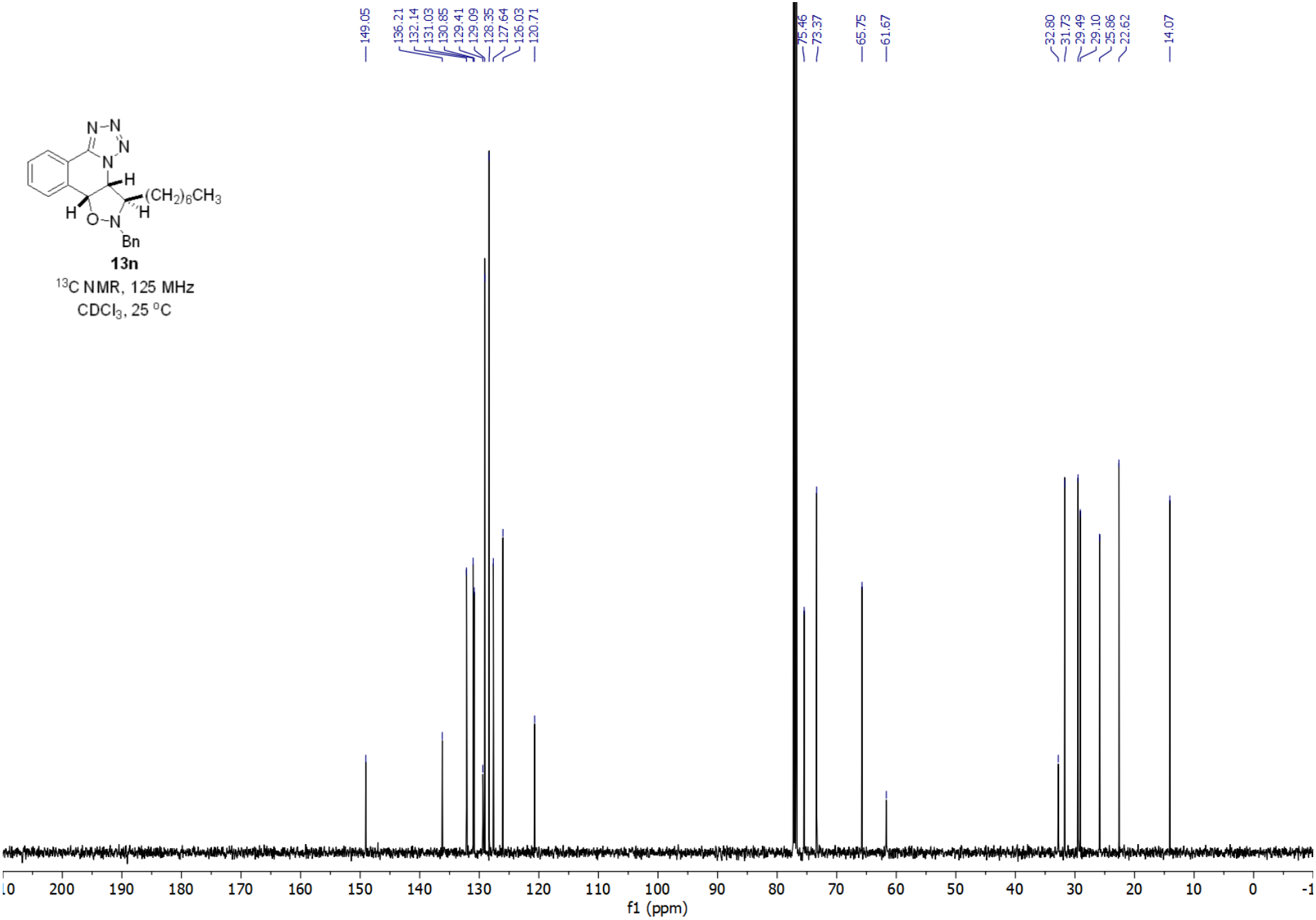
DMSO-d_6, 60 °C

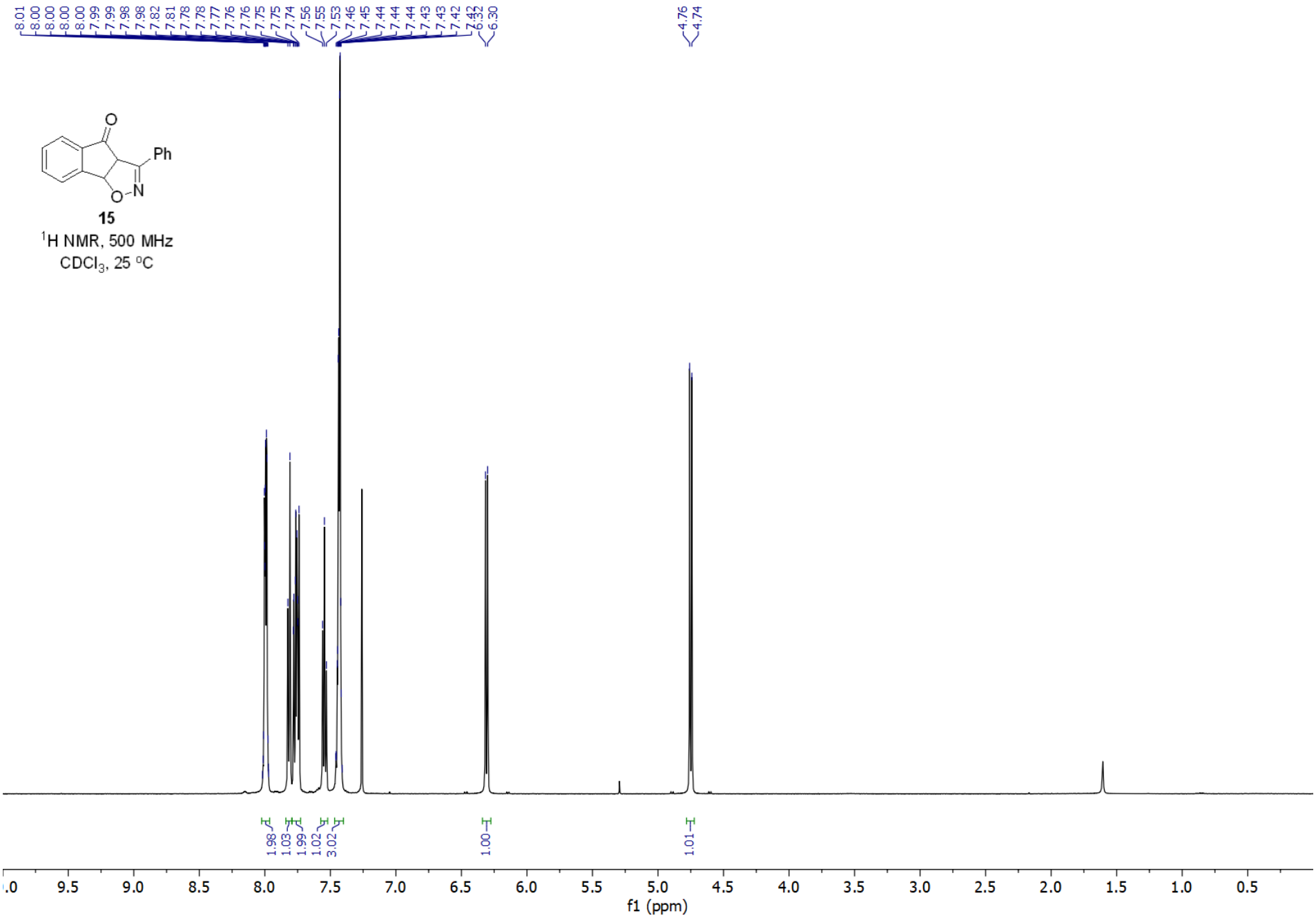


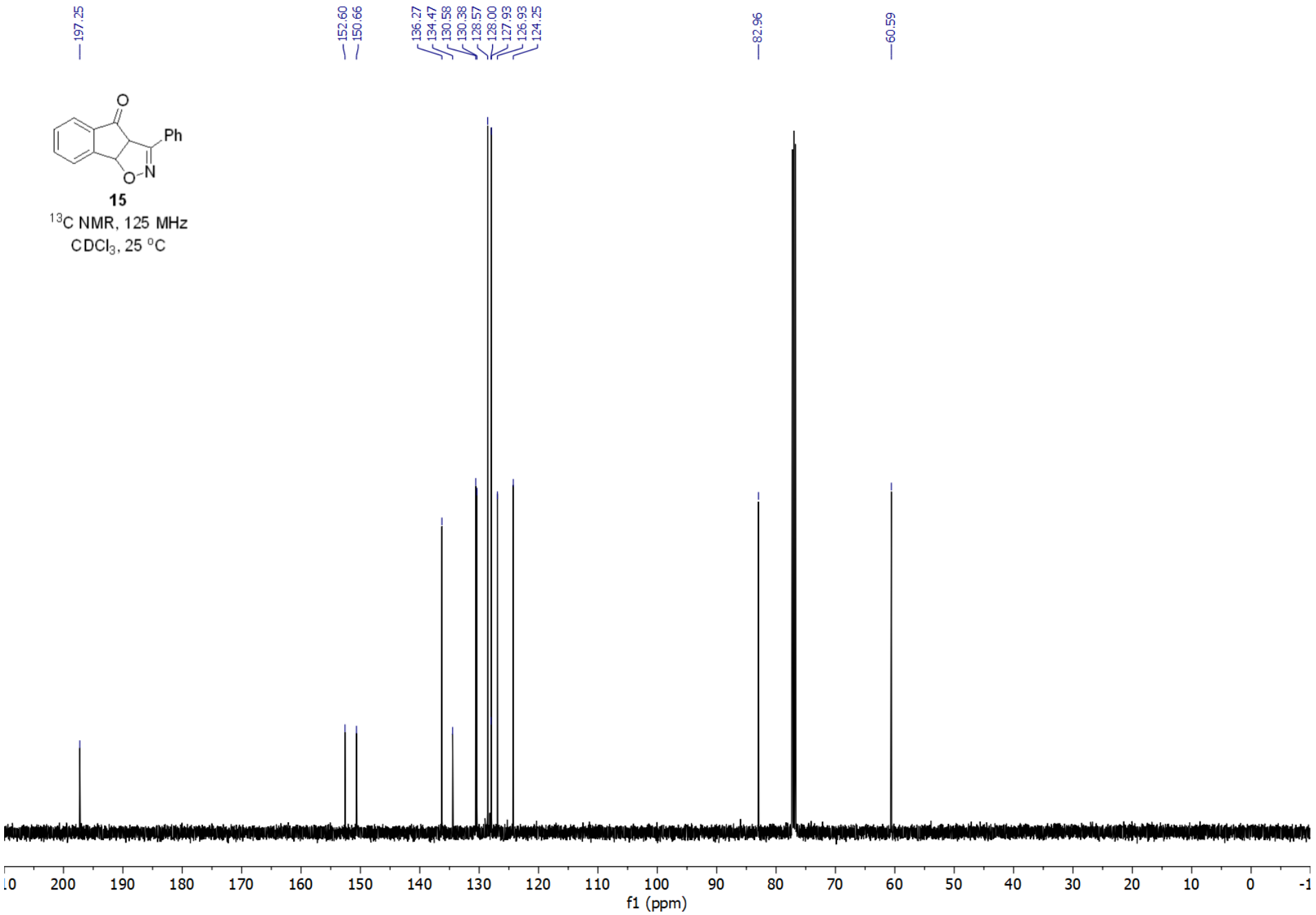
13n

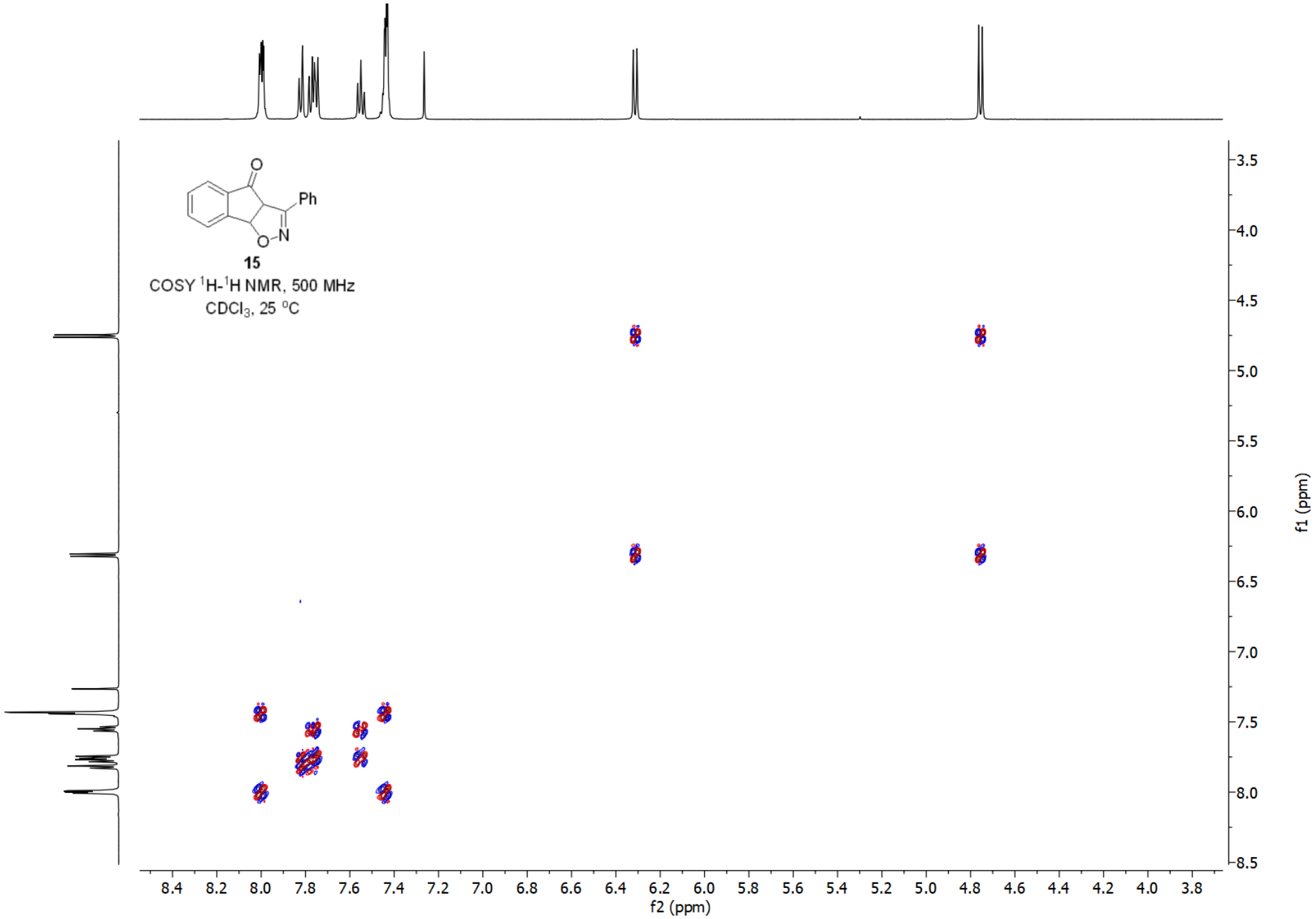
^{1}H NMR, 500 MHz

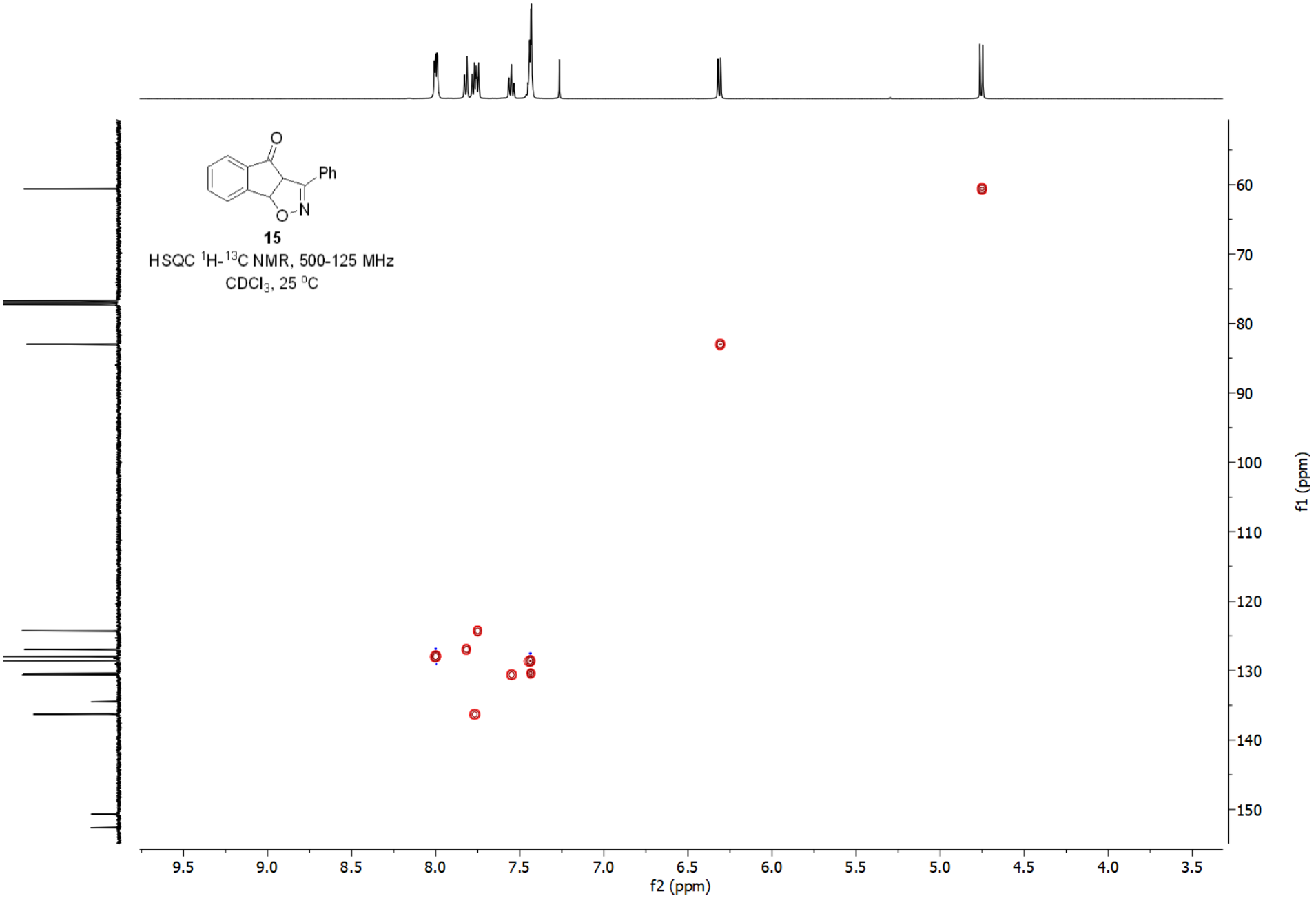
$CDCl_3$, 25 ^oC

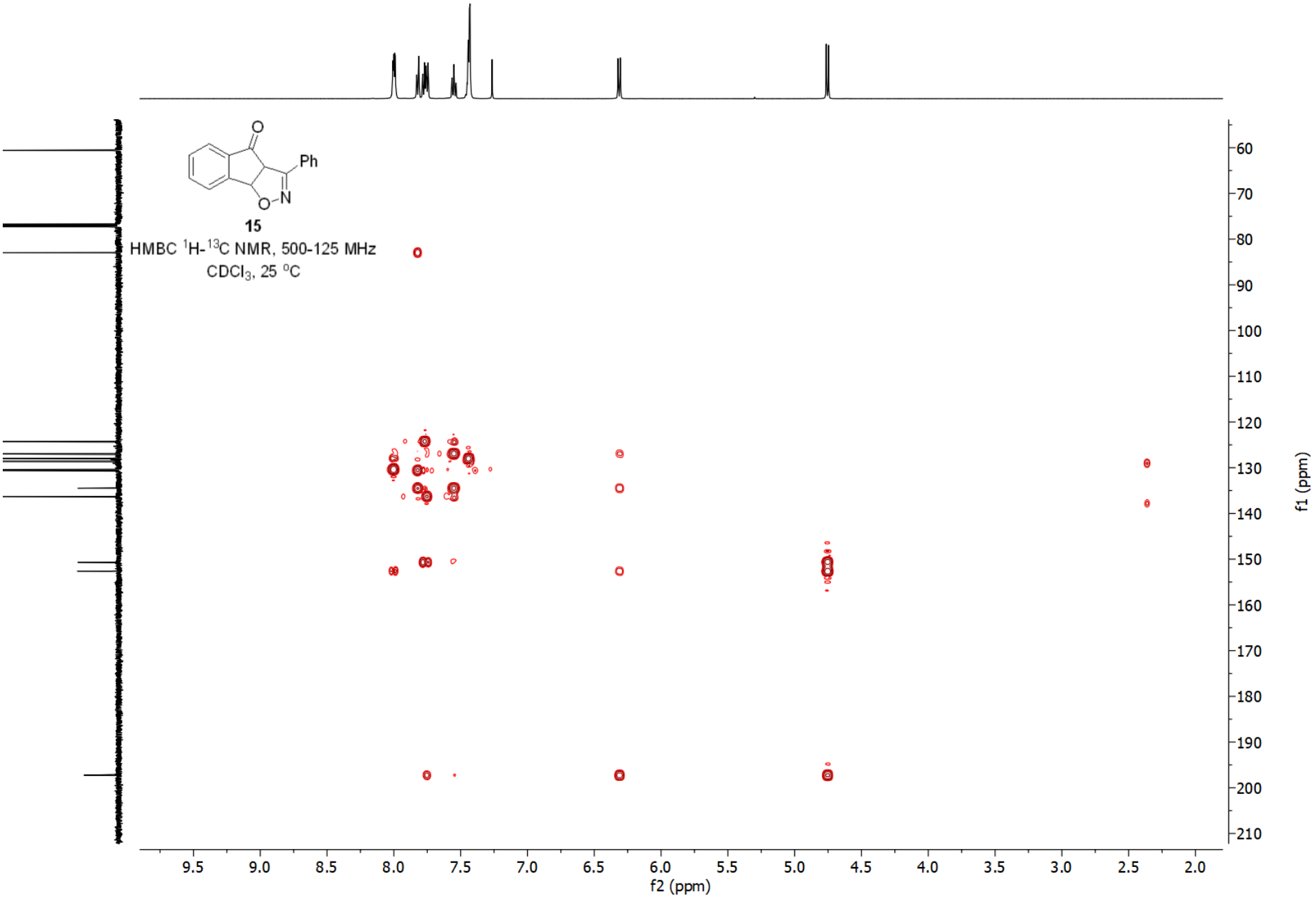

149.05
136.21
132.14
131.03
130.85
129.41
129.09
128.35
127.64
126.03
120.71
75.46
73.37
65.75
61.67
32.80
31.73
29.49
29.10
25.86
22.62
14.07
N–N
N
N
H
(CH2)6CH3
H
H
O–N
Bn
13n
13C NMR, 125 MHz
CDCl3, 25 °C
f1 (ppm)

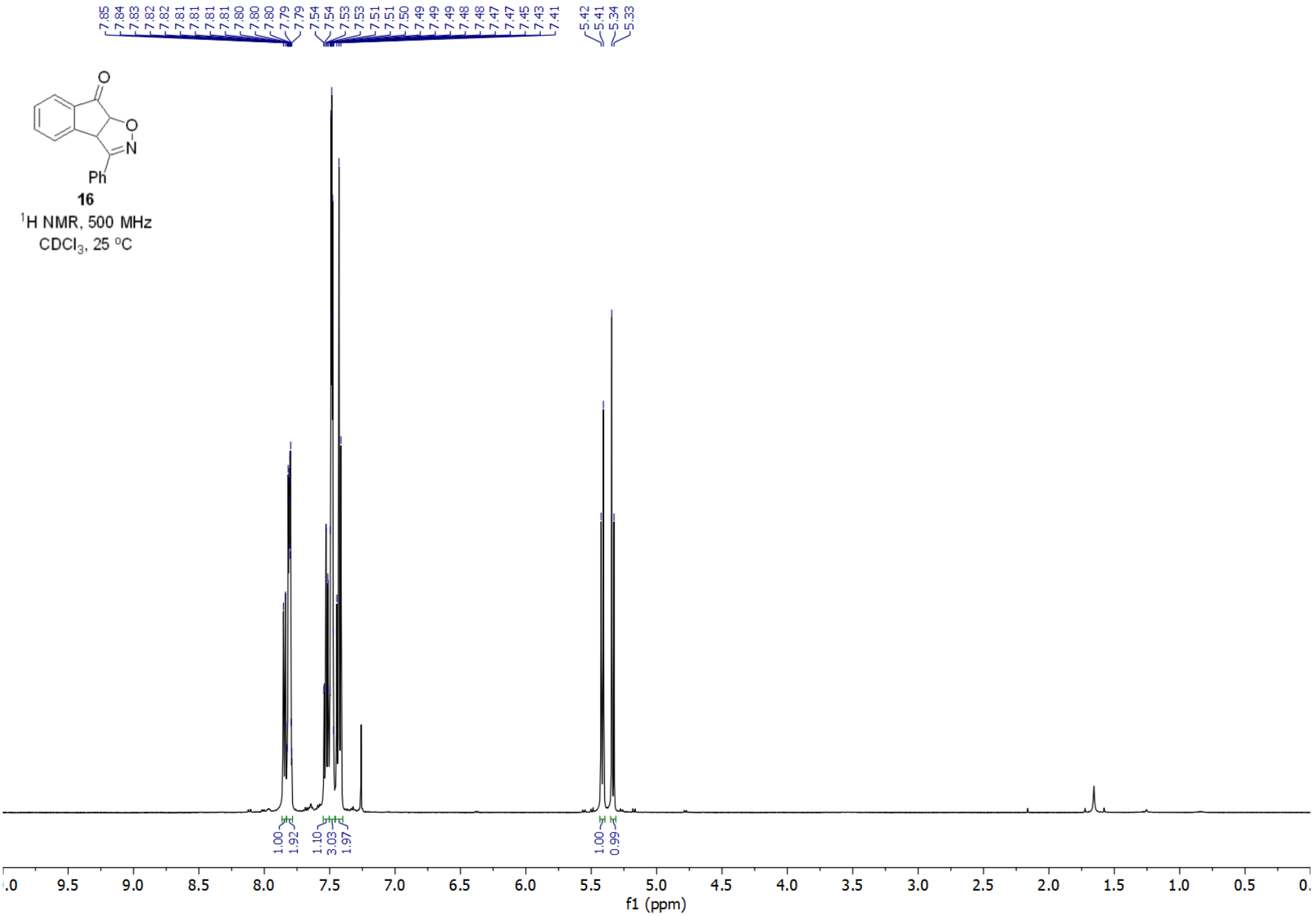

8.01
8.00
8.00
8.00
8.00
7.99
7.99
7.98
7.98
7.82
7.81
7.78
7.78
7.77
7.76
7.76
7.75
7.75
7.74
7.56
7.55
7.53
7.46
7.45
7.44
7.44
7.44
7.43
7.43
7.42
7.42
6.32
6.30
4.76
4.74
O
Ph
O
N
15
1H NMR, 500 MHz
CDCl3, 25 °C
1.98
1.03
1.99
1.02
3.02
1.00
1.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

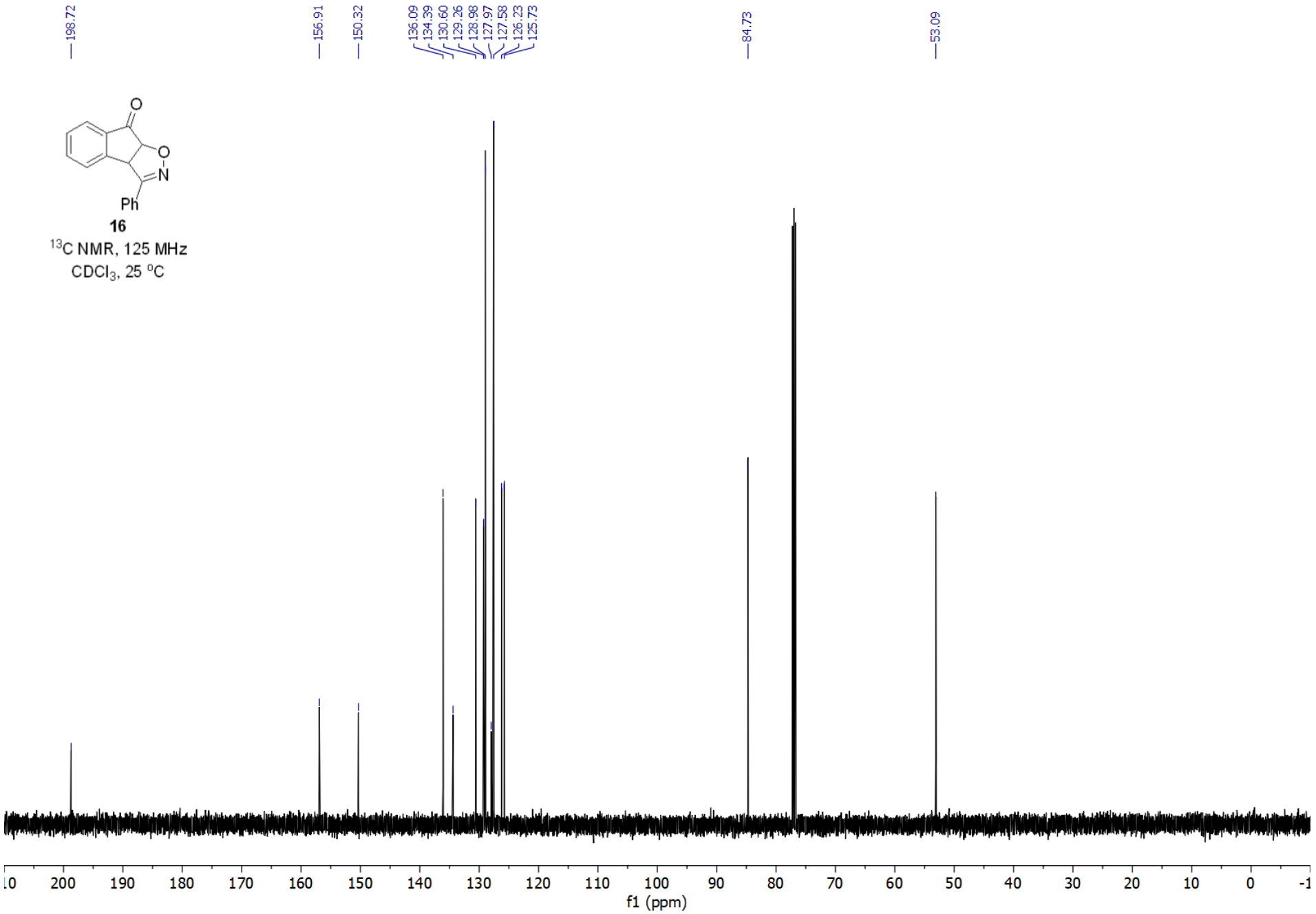

197.25
152.60
150.66
136.27
134.47
130.58
130.38
128.57
128.00
127.93
126.93
124.25
82.96
60.59
O
Ph
O
N
15
13C NMR, 125 MHz
CDCl3, 25 °C
f1 (ppm)

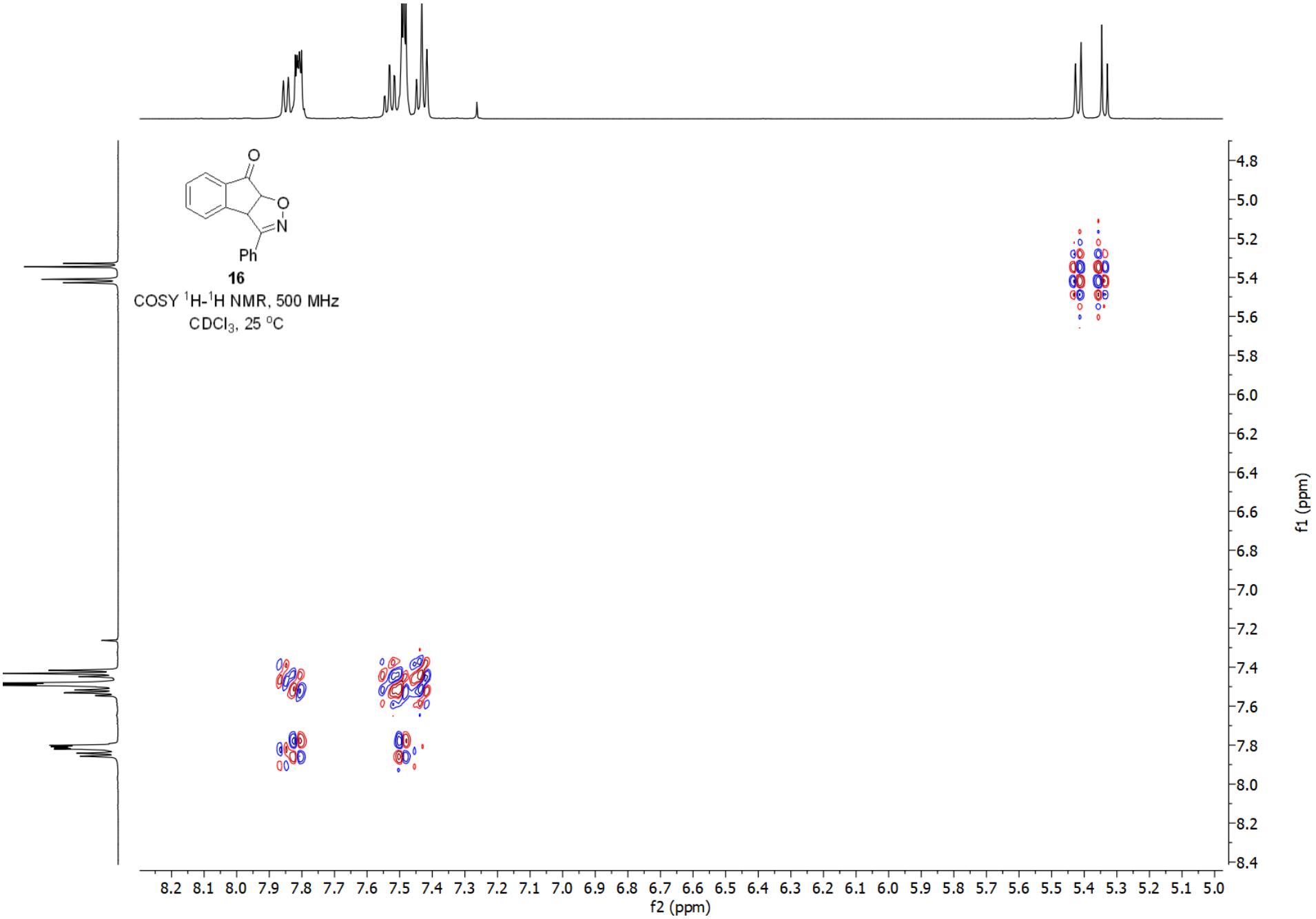

O
Ph
N
O
15
COSY ^{1}H-^{1}H NMR, 500 MHz
$CDCl_3$, 25 ^{o}C
f1 (ppm)
f2 (ppm)

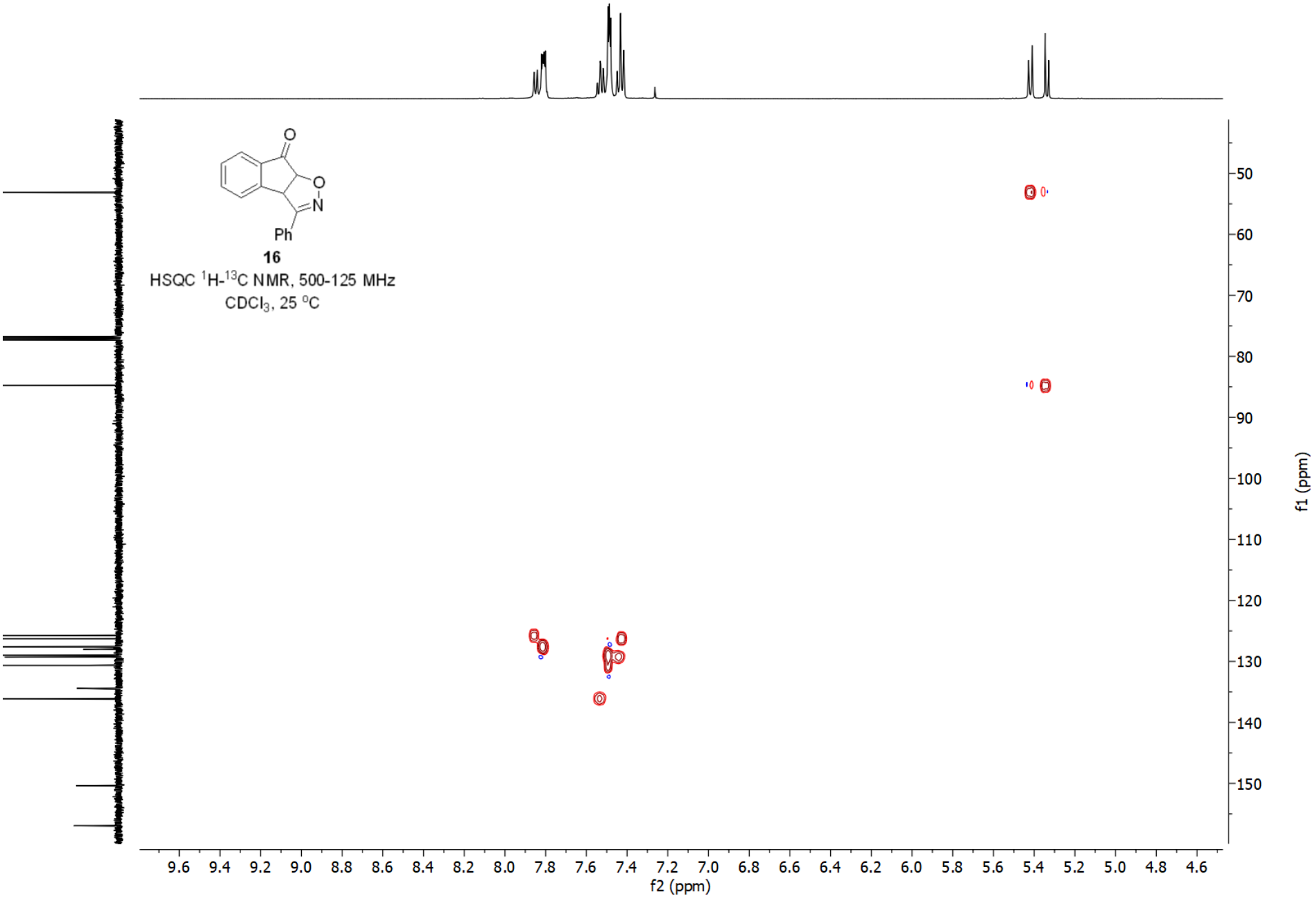

O
Ph
O
N
15
HSQC ^{1}H-^{13}C NMR, 500-125 MHz
$CDCl_3$, 25 ^{o}C
60
70
80
90
100
110
120
130
140
150
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
f2 (ppm)

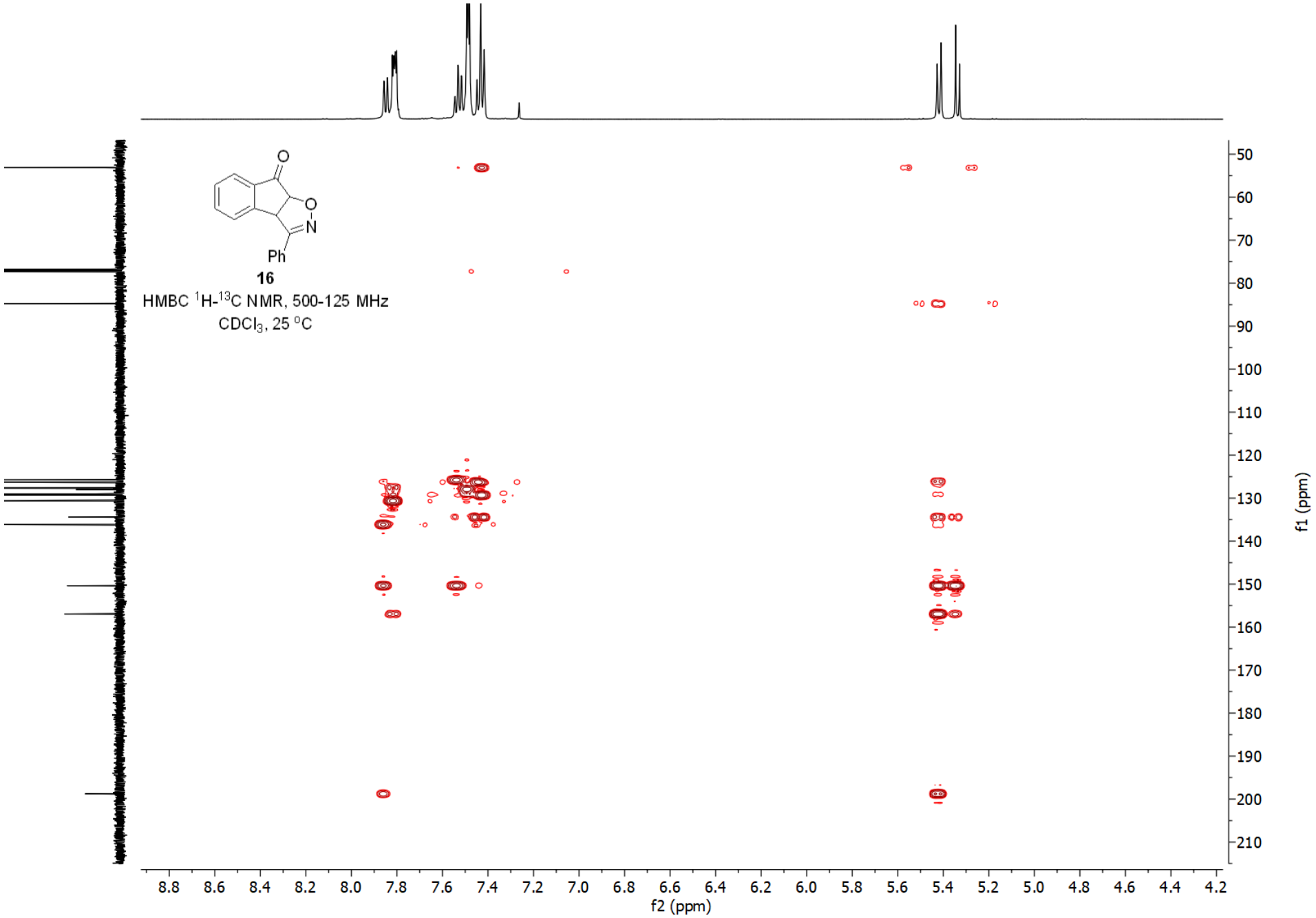

O
Ph
N
O
15
HMBC ^{1}H-^{13}C NMR, 500-125 MHz
$CDCl_3$, 25 ^{o}C
f2 (ppm)
f1 (ppm)

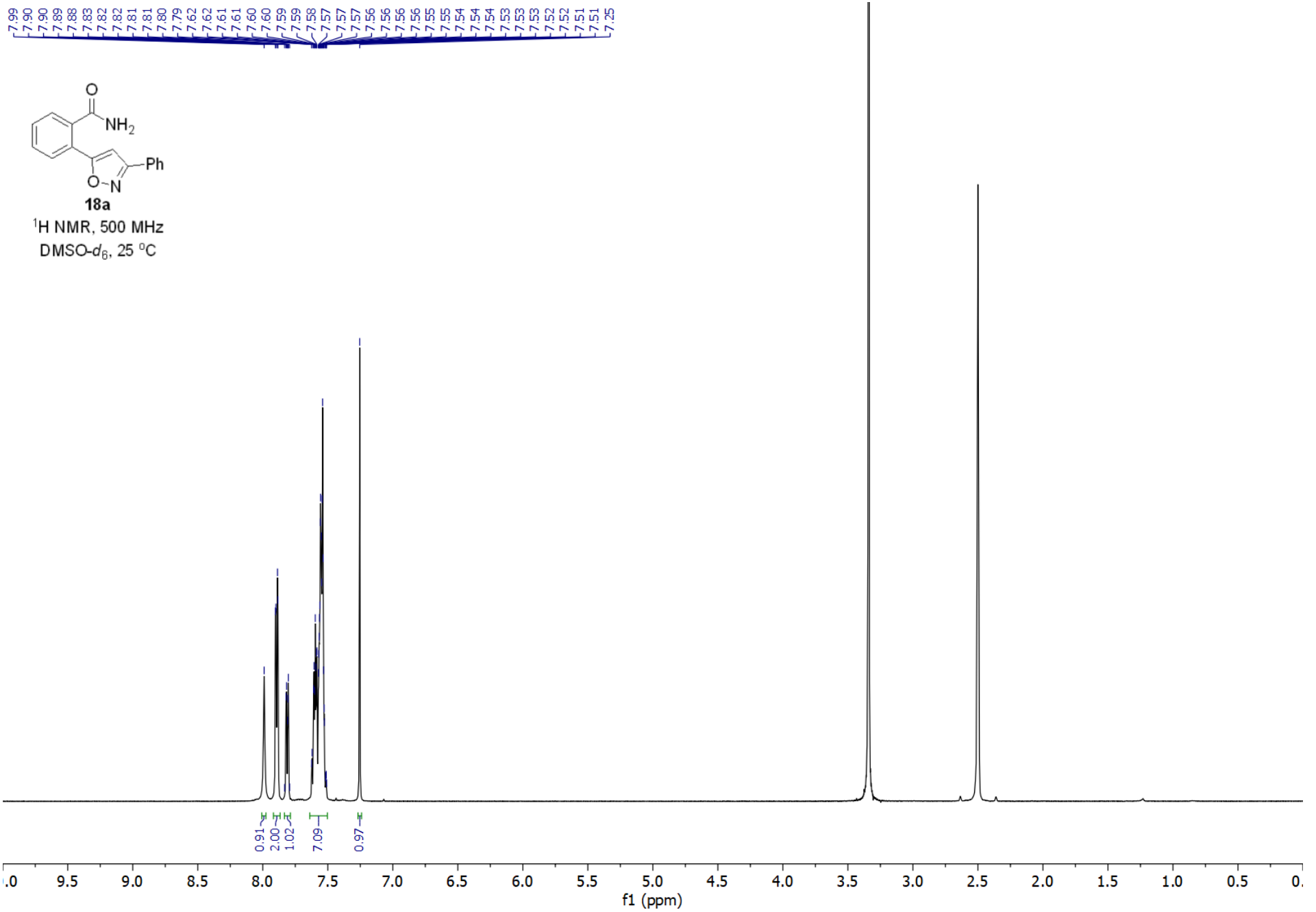

7.85
7.84
7.83
7.82
7.82
7.81
7.81
7.81
7.81
7.80
7.80
7.80
7.79
7.79
7.54
7.54
7.53
7.53
7.51
7.51
7.50
7.49
7.49
7.49
7.48
7.48
7.47
7.47
7.45
7.43
7.41
5.42
5.41
5.34
5.33
O
O
N
Ph
16
1H NMR, 500 MHz
CDCl3, 25 °C
1.00
1.92
1.10
3.03
1.97
1.00
0.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

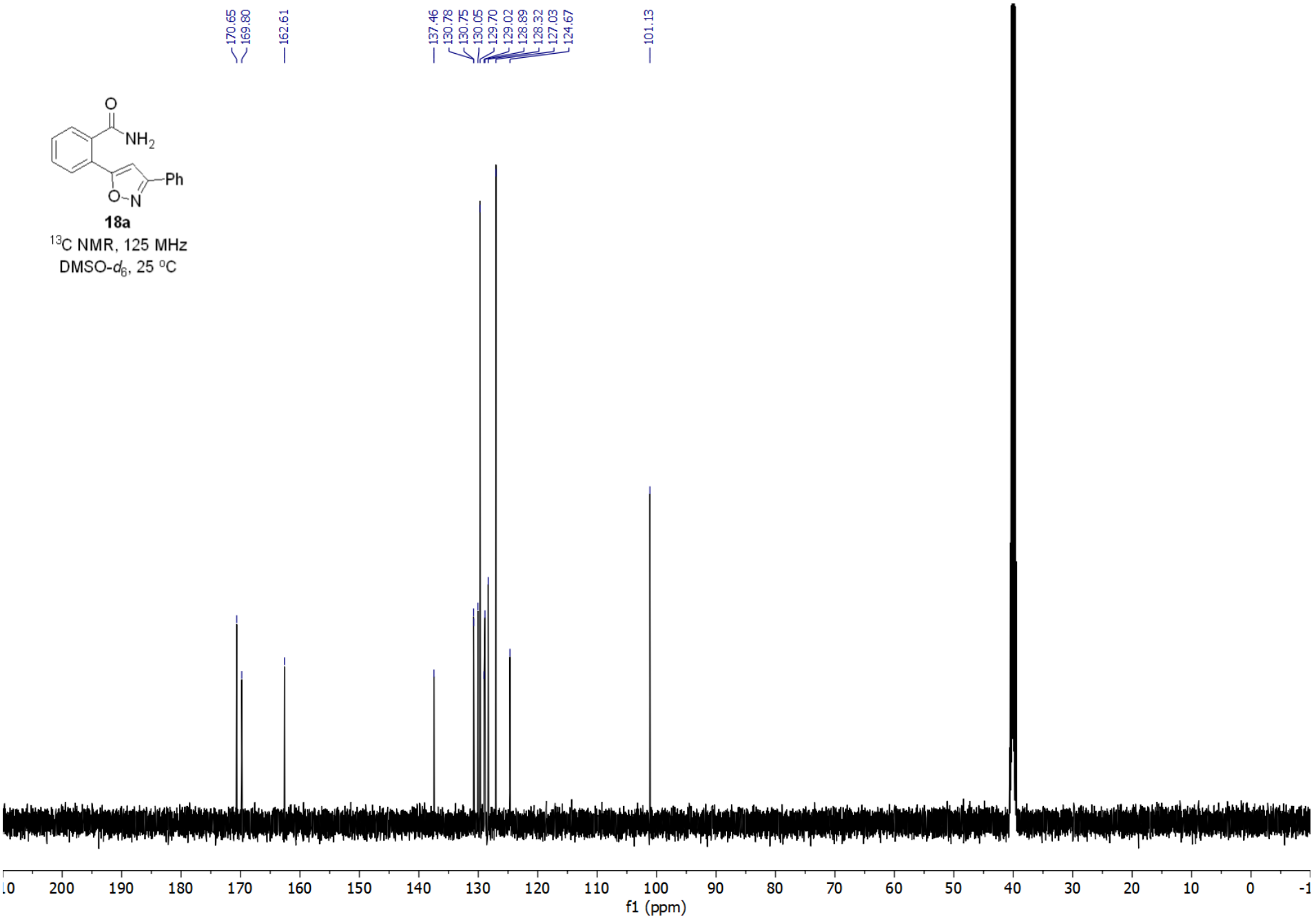

198.72
156.91
150.32
136.09
134.39
130.60
129.26
128.98
127.97
127.58
126.23
125.73
84.73
53.09
O
O
N
Ph
16
13C NMR, 125 MHz
CDCl3, 25 0C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

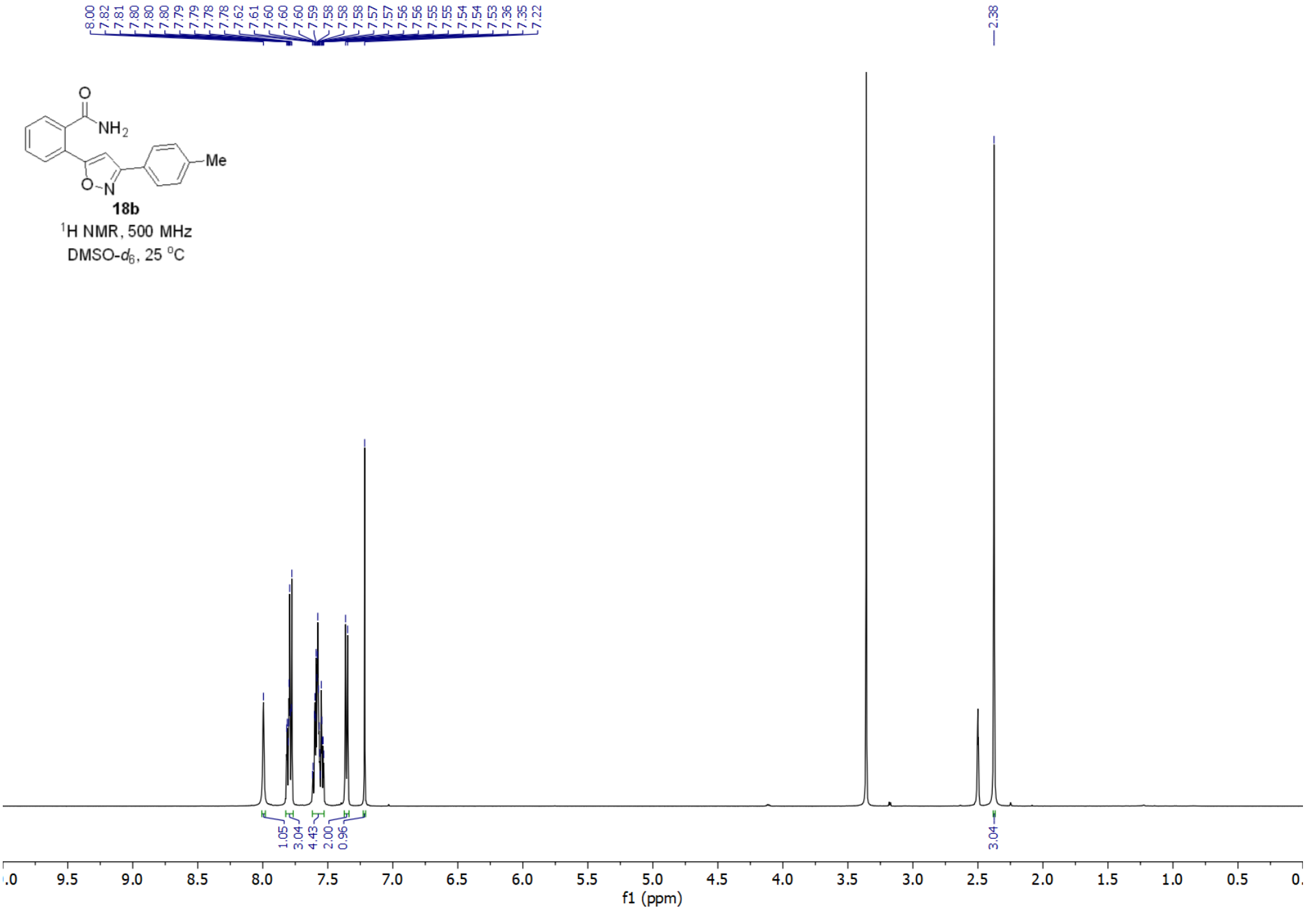

O
O
N
Ph
16
COSY ^{1}H-^{1}H NMR, 500 MHz
$CDCl_3$, 25 ^{0}C
f1 (ppm)
f2 (ppm)

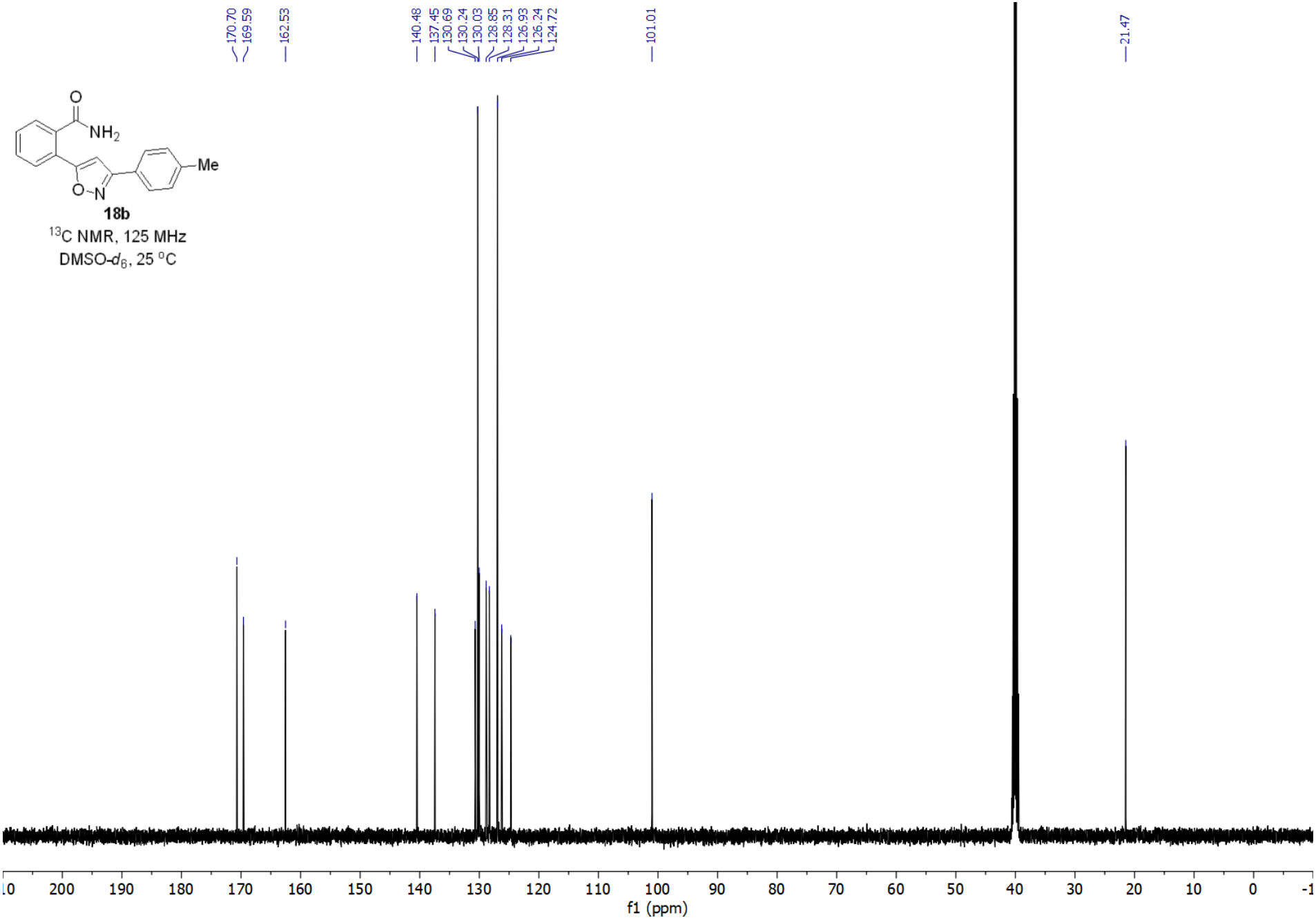

O
O
N
Ph
16
HSQC ^{1}H-^{13}C NMR, 500-125 MHz
$CDCl_3$, 25 ^{o}C
50
60
70
80
90
100
110
120
130
140
150
f1 (ppm)
9.6 9.4 9.2 9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6
f2 (ppm)

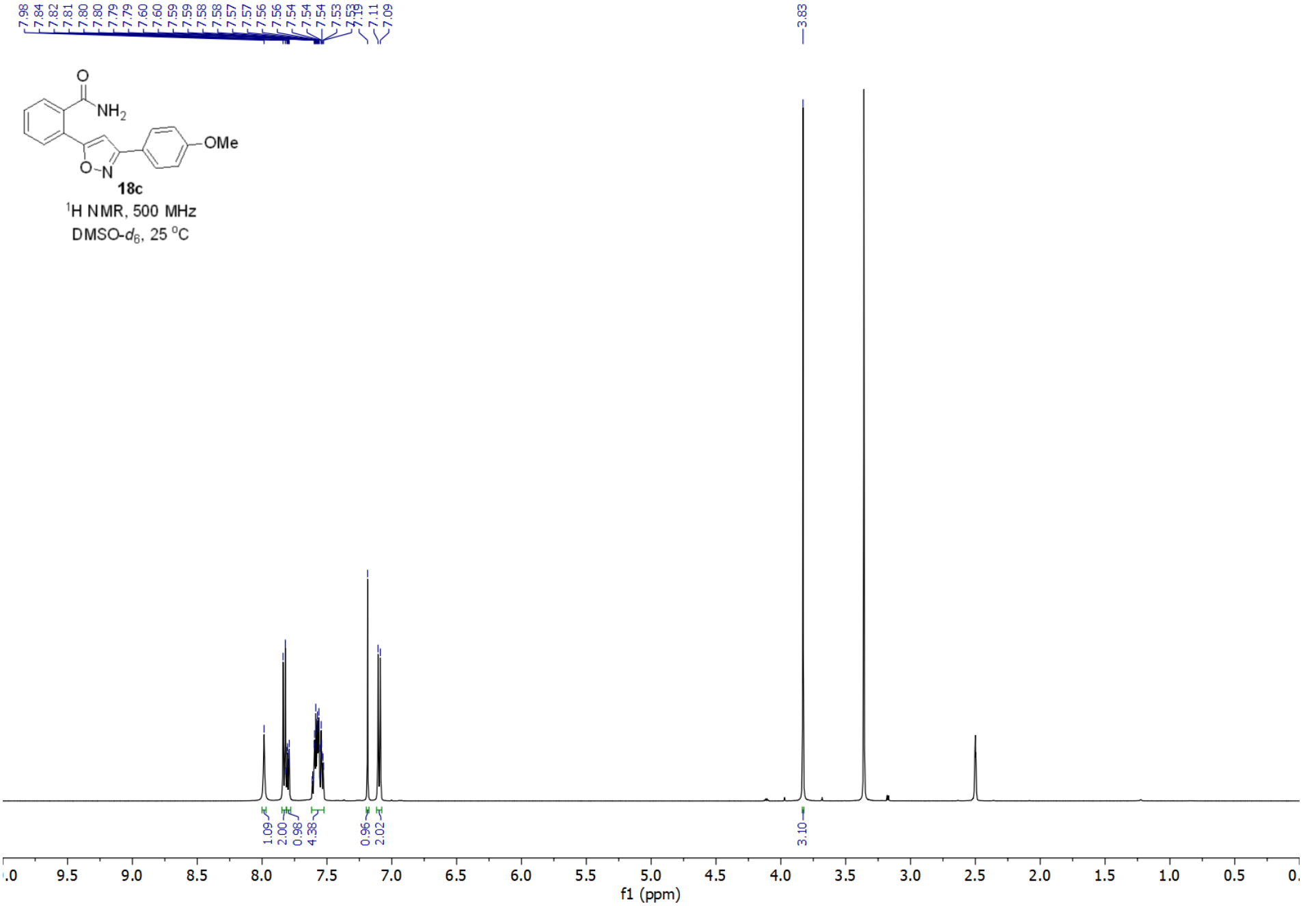

O
O
N
Ph
16
HMBC ^{1}H-^{13}C NMR, 500-125 MHz
$CDCl_3$, 25 °C
f2 (ppm)
f1 (ppm)

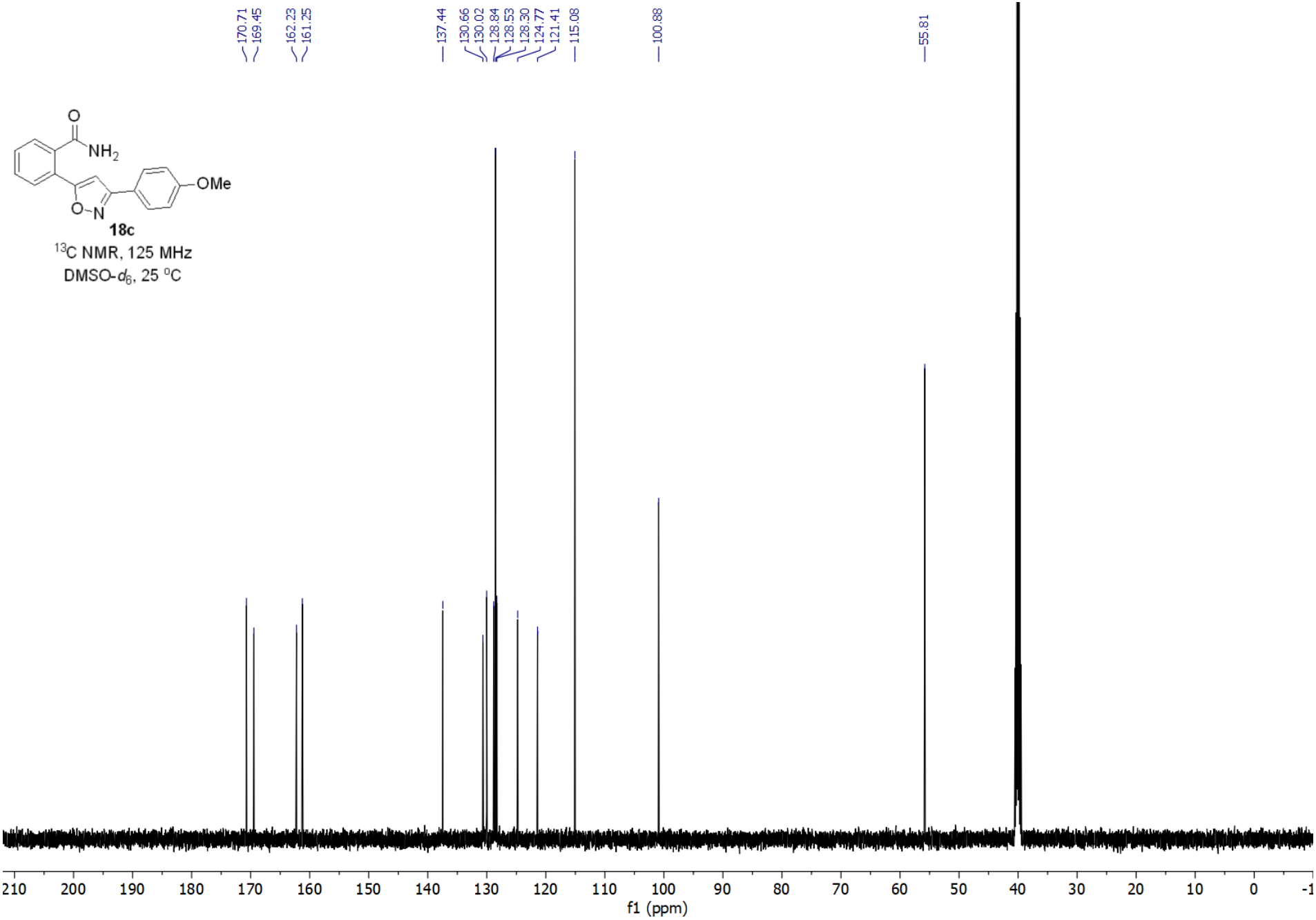

7.99 7.90 7.90 7.89 7.88 7.83 7.82 7.82 7.81 7.81 7.80 7.79 7.62 7.62 7.61 7.61 7.60 7.60 7.59 7.59 7.58 7.57 7.57 7.57 7.56 7.56 7.56 7.55 7.55 7.54 7.54 7.54 7.53 7.53 7.53 7.52 7.52 7.51 7.51 7.25
O
NH2
Ph
O
N
18a
1H NMR, 500 MHz
DMSO-d6, 25 °C
0.91
2.00
1.02
7.09
0.97
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

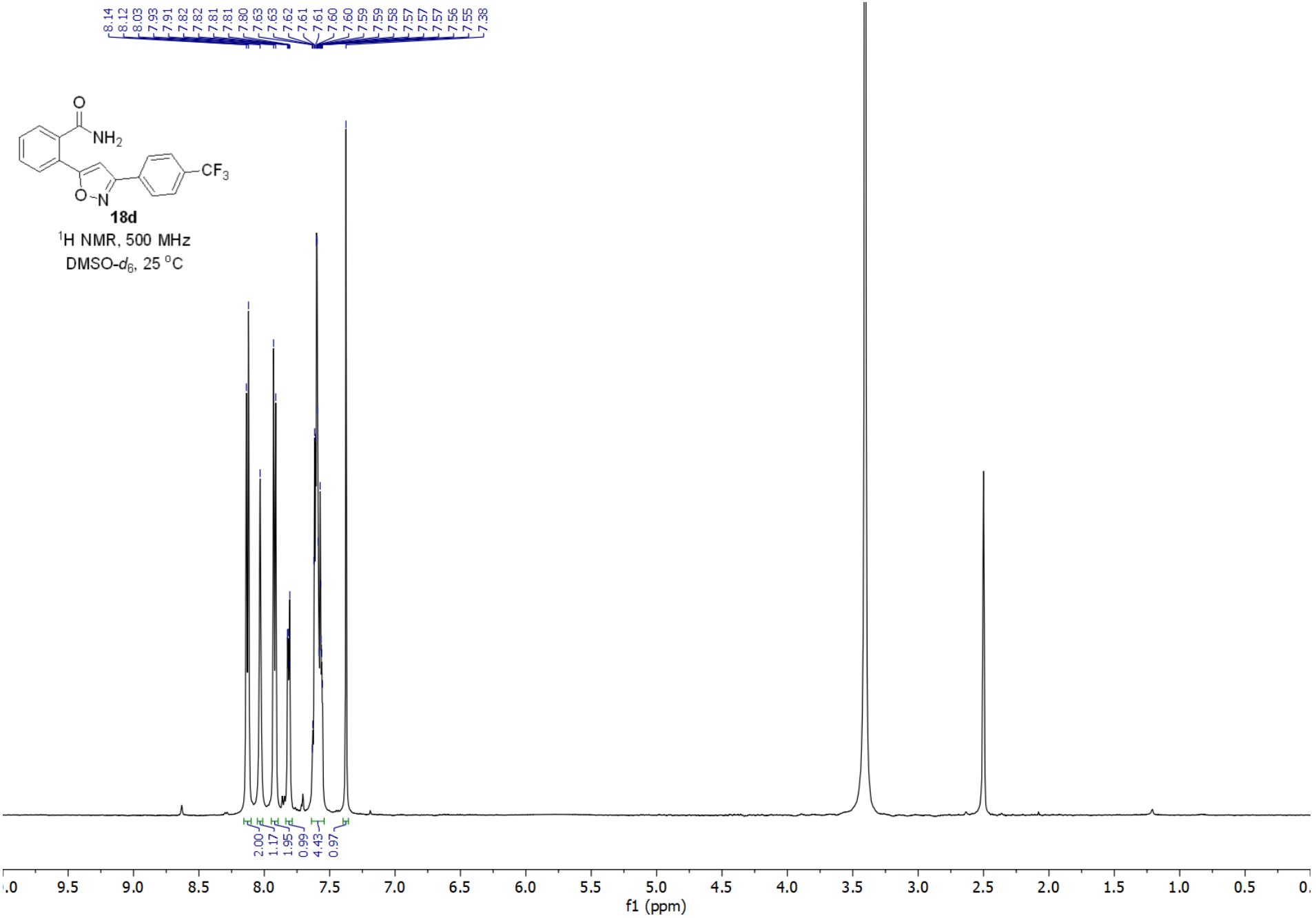

170.65
169.80
162.61
137.46
130.78
130.75
130.05
129.70
129.02
128.89
128.32
127.03
124.67
101.13
O
NH2
Ph
O
N
18a
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

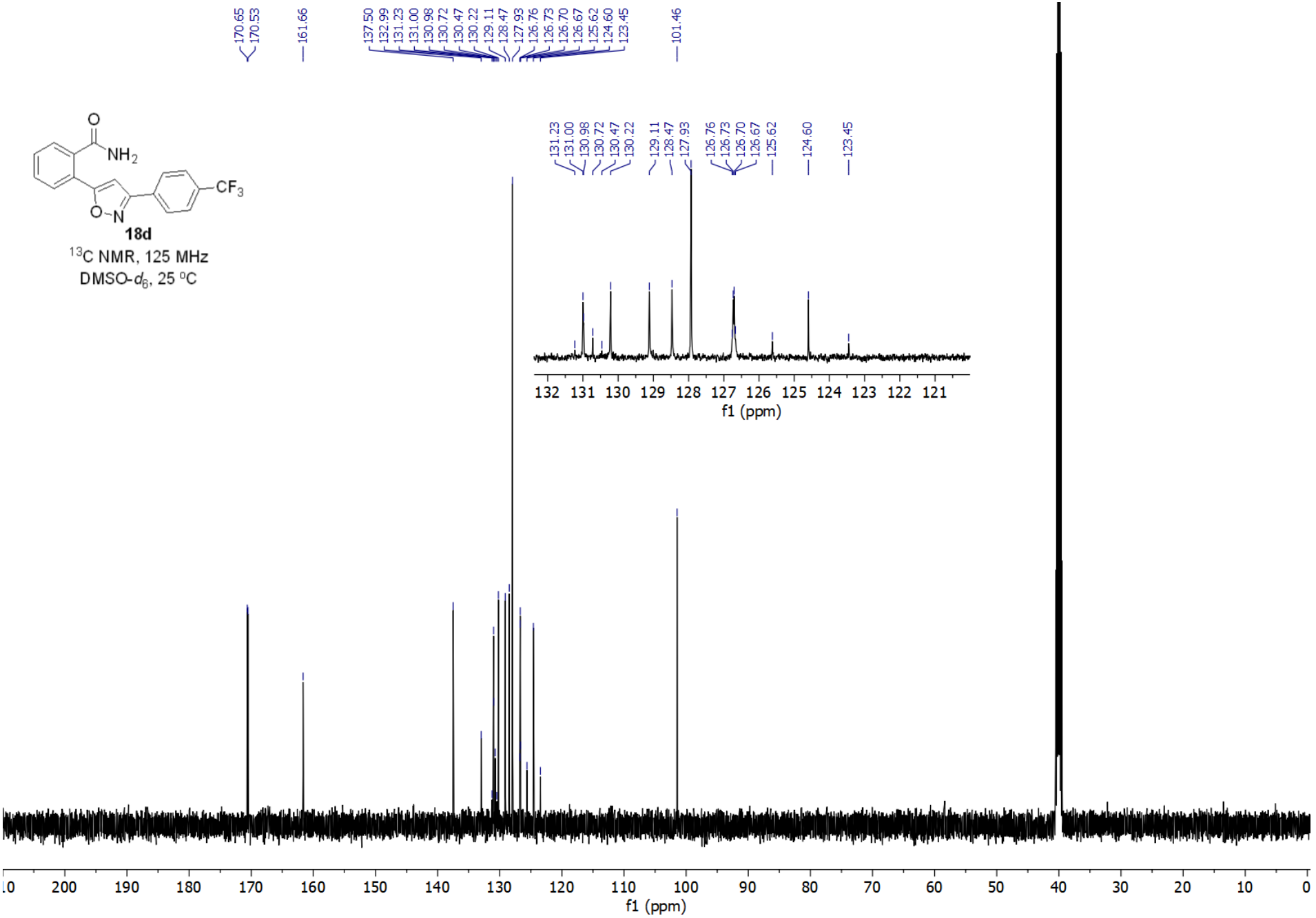

8.00
7.82
7.81
7.80
7.80
7.80
7.79
7.79
7.78
7.78
7.62
7.61
7.60
7.60
7.60
7.59
7.58
7.58
7.58
7.57
7.57
7.56
7.56
7.55
7.55
7.54
7.54
7.53
7.36
7.35
7.22
2.38
O
NH2
Me
O
N
18b
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.05
3.04
4.43
2.00
0.96
3.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


170.70
169.59
162.53
140.48
137.45
130.69
130.24
130.03
128.85
128.31
126.93
126.24
124.72
101.01
21.47
O
NH2
Me
O
N
18b
13C NMR, 125 MHz
DMSO-d6, 25 °C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


7.98
7.84
7.82
7.81
7.80
7.80
7.79
7.79
7.60
7.60
7.59
7.59
7.58
7.58
7.57
7.57
7.56
7.56
7.54
7.54
7.54
7.53
7.11
7.09
3.83
O
NH2
OMe
O
N
18c
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.09
2.00
0.98
4.38
0.96
2.02
3.10
f1 (ppm)


170.71
169.45
162.23
161.25
137.44
130.66
130.02
128.84
128.53
128.30
124.77
121.41
115.08
100.88
55.81
O
NH2
OMe
O
N
18c
13C NMR, 125 MHz
DMSO-d6, 25 °C
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

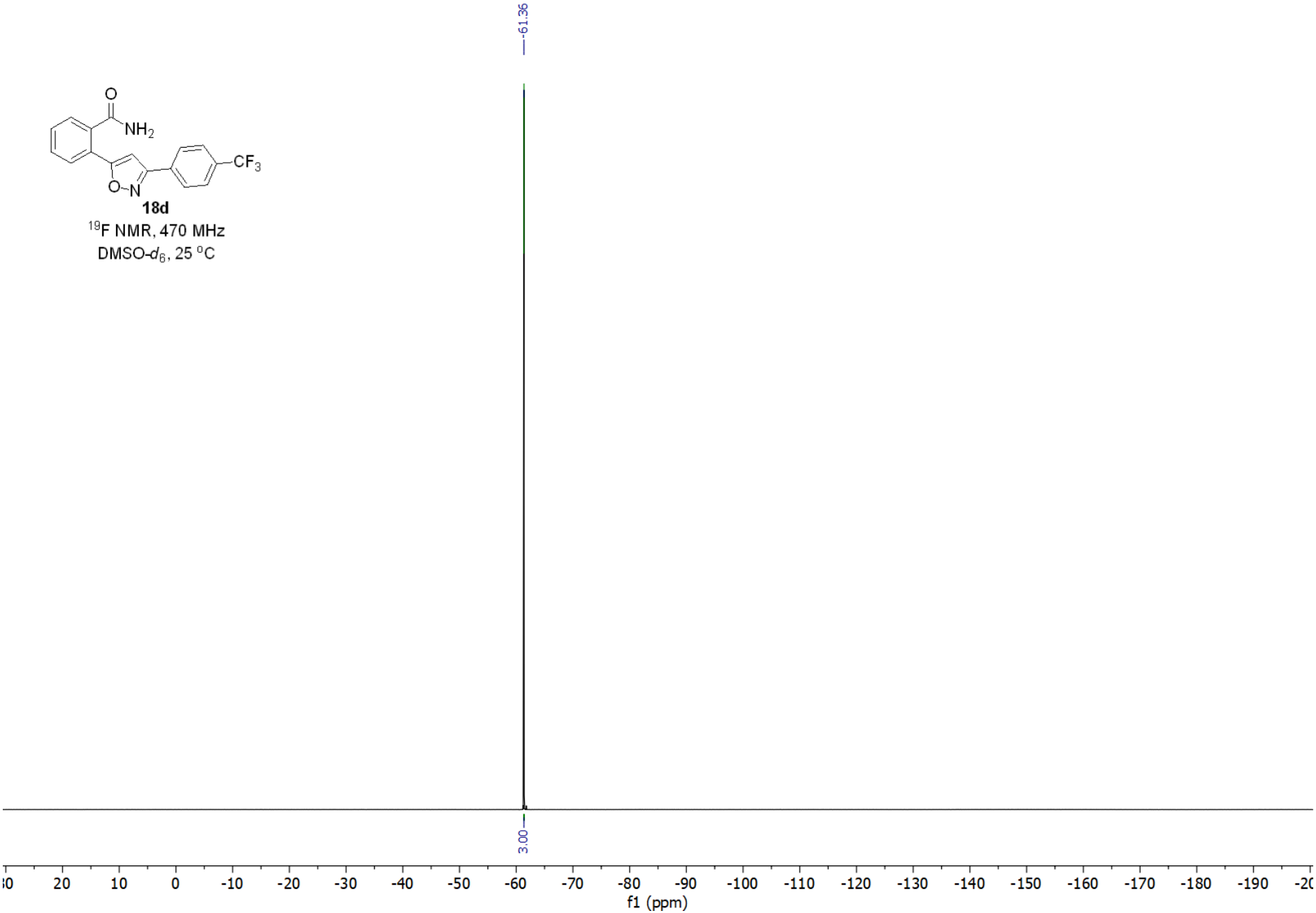

8.14
8.12
8.03
7.93
7.91
7.82
7.82
7.81
7.81
7.80
7.63
7.63
7.62
7.61
7.61
7.60
7.60
7.59
7.59
7.58
7.57
7.57
7.57
7.56
7.55
7.38
O
NH2
CF3
O
N
18d
1H NMR, 500 MHz
DMSO-d6, 25 °C
2.00
1.17
1.95
0.99
4.43
0.97
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

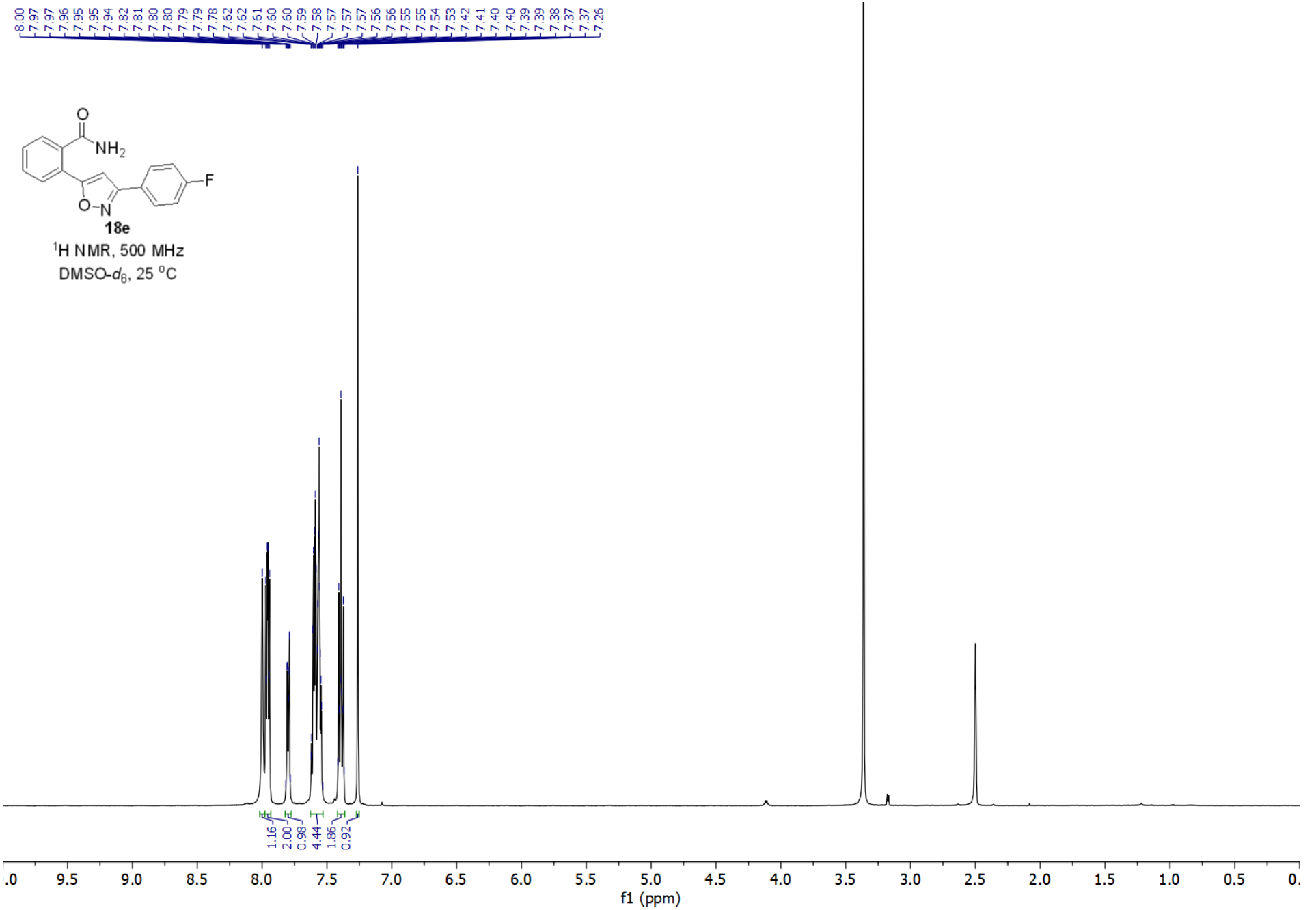

170.65
170.53
161.66
137.50
132.99
131.23
131.00
130.98
130.72
130.47
130.22
129.11
128.47
127.93
126.76
126.73
126.70
126.67
125.62
124.60
123.45
101.46
O
NH2
CF3
O
N
18d
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)
f1 (ppm)

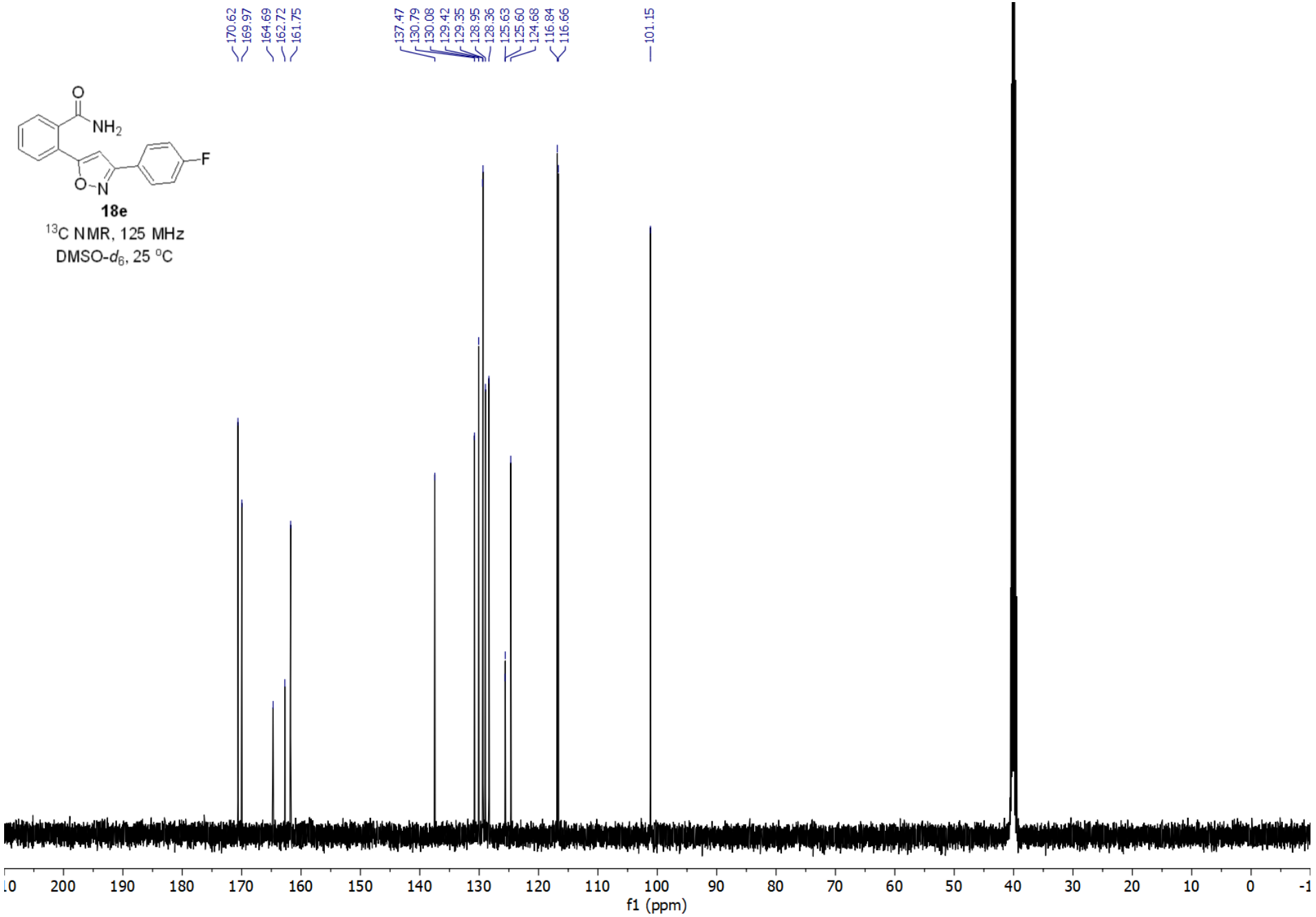
18d

^{19}F NMR, 470 MHz

DMSO-d_6, 25 °C



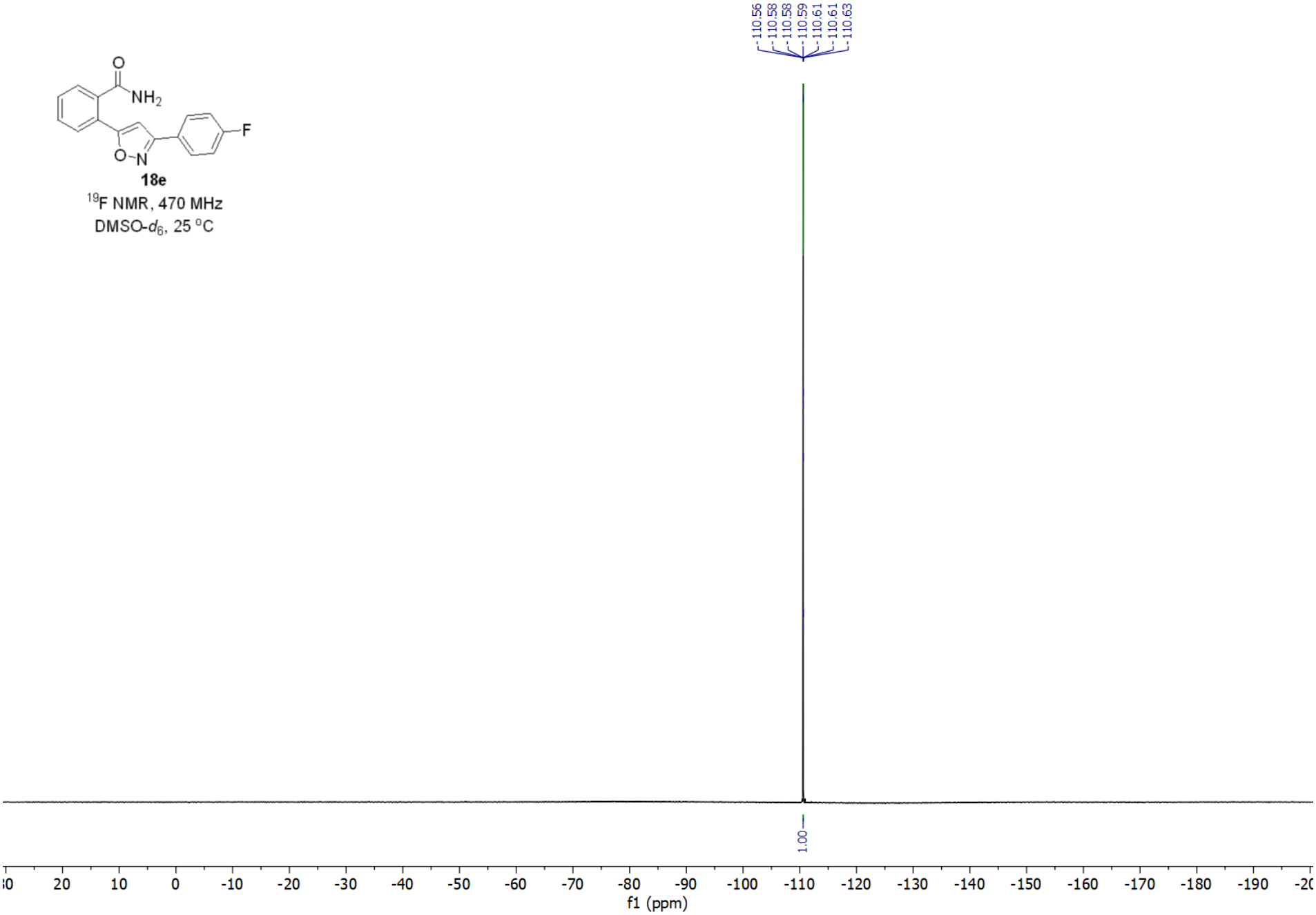

8.00 7.97 7.97 7.96 7.95 7.95 7.94 7.82 7.81 7.80 7.80 7.79 7.79 7.78 7.62 7.62 7.61 7.60 7.60 7.59 7.58 7.57 7.57 7.57 7.56 7.56 7.55 7.55 7.54 7.53 7.42 7.41 7.40 7.40 7.39 7.39 7.38 7.37 7.37 7.26
O
NH2
F
O
N
18e
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.16 2.00 0.98 4.44 1.86 0.92
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


170.62
169.97
164.69
162.72
161.75
137.47
130.79
130.08
129.42
129.35
128.95
128.36
125.63
125.60
124.68
116.84
116.66
101.15
O
NH2
F
O
N
18e
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

18e

^{19}F NMR, 470 MHz

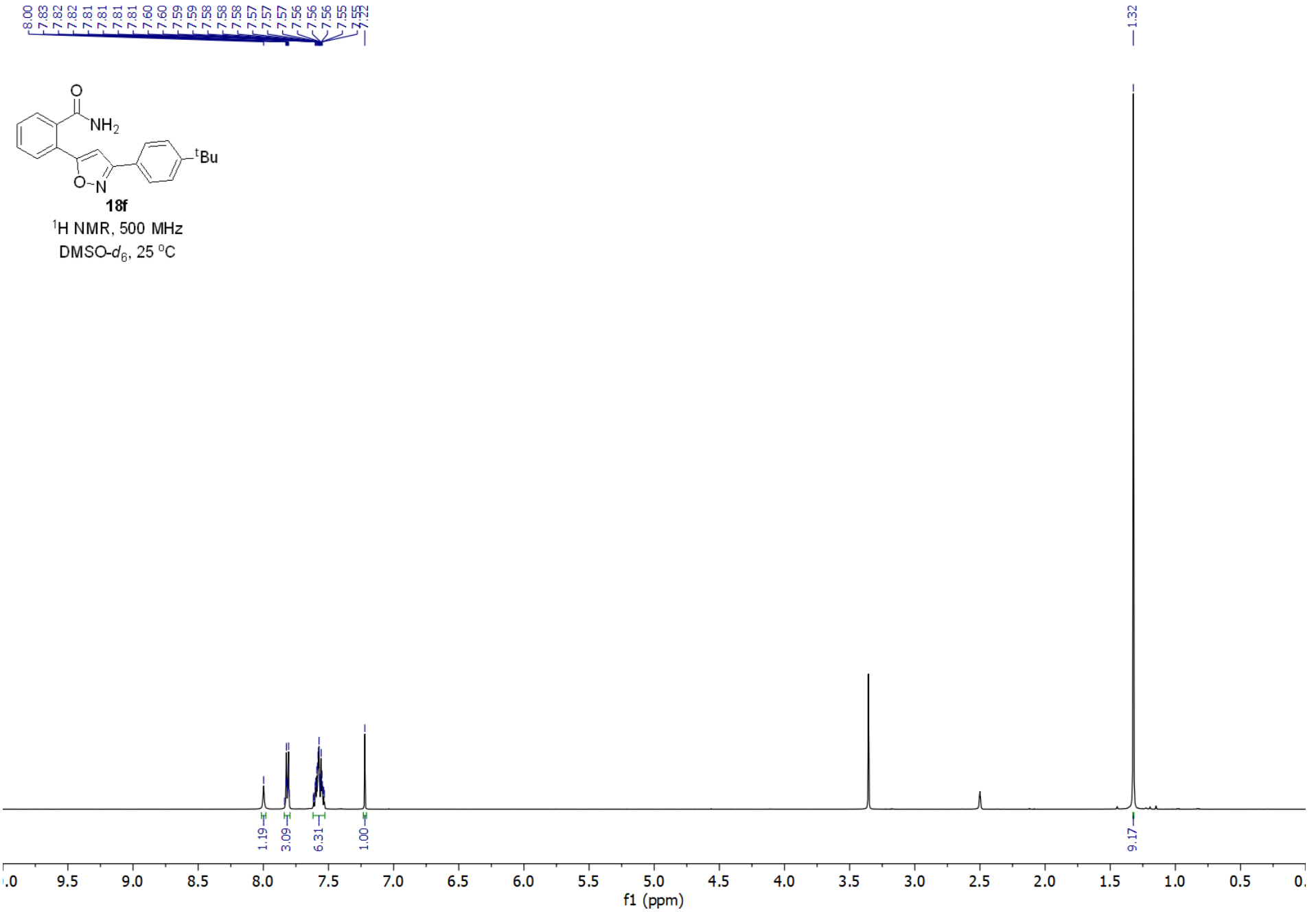
DMSO-d_6, 25 °C

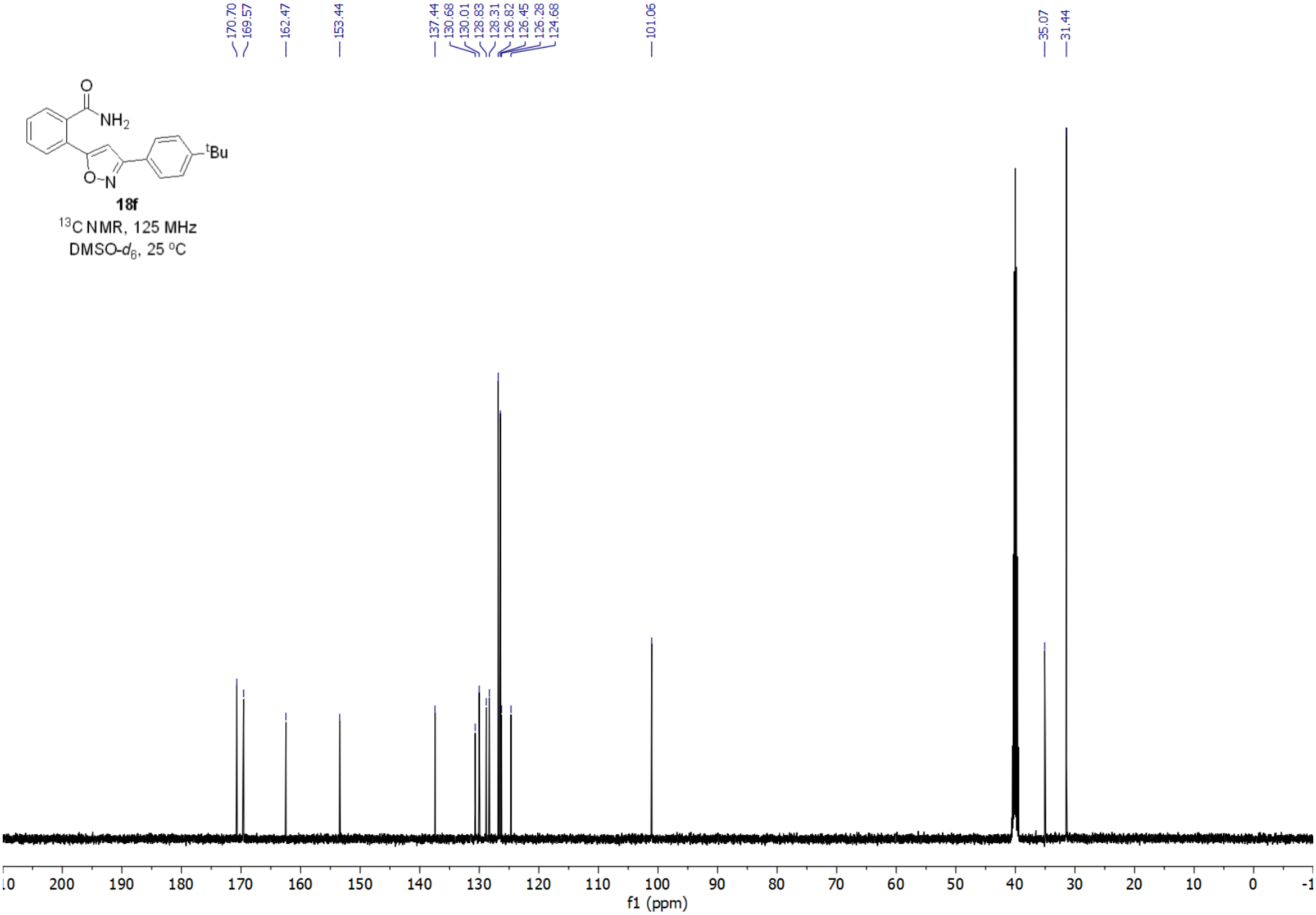


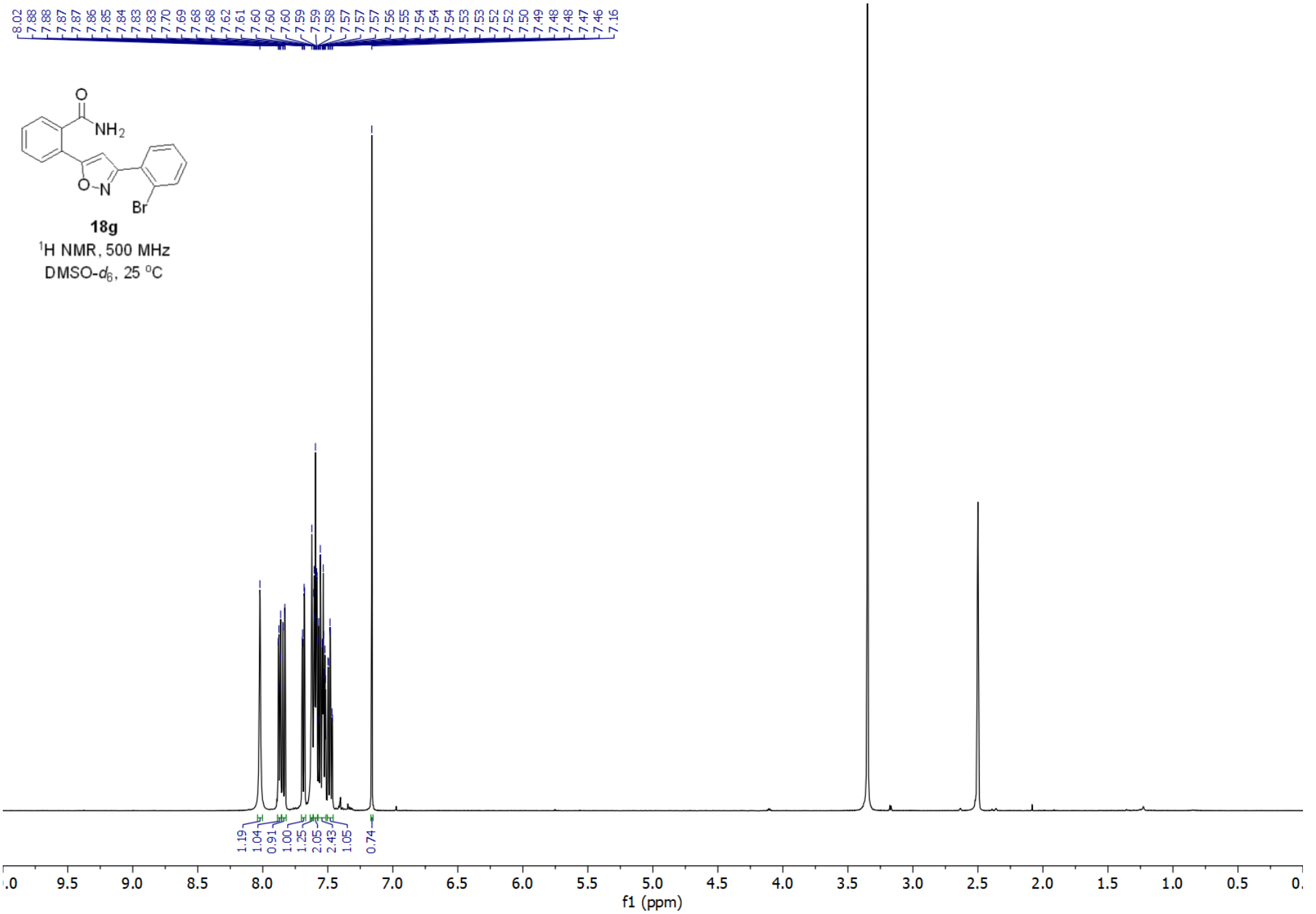
18f

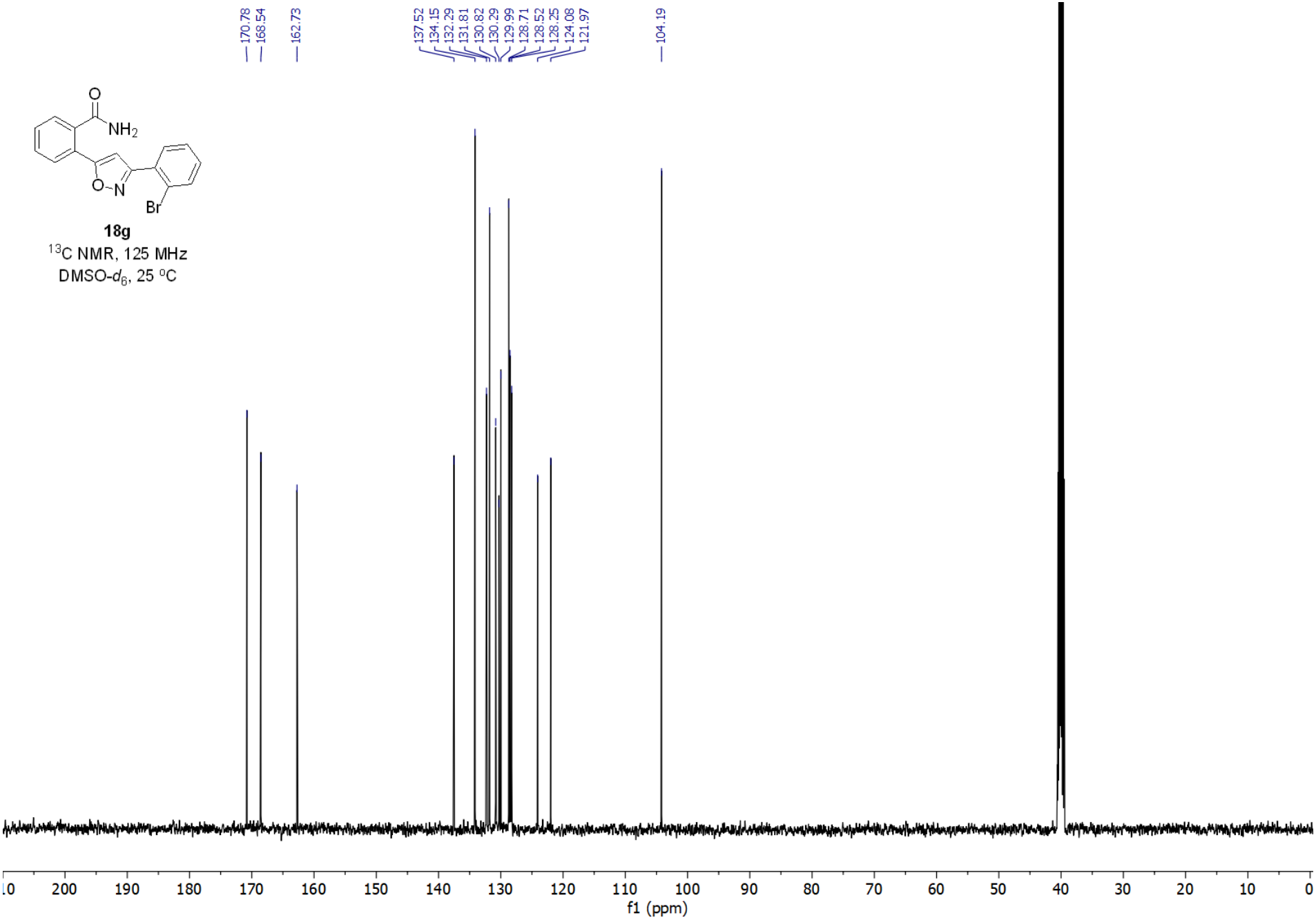
^{1}H NMR, 500 MHz

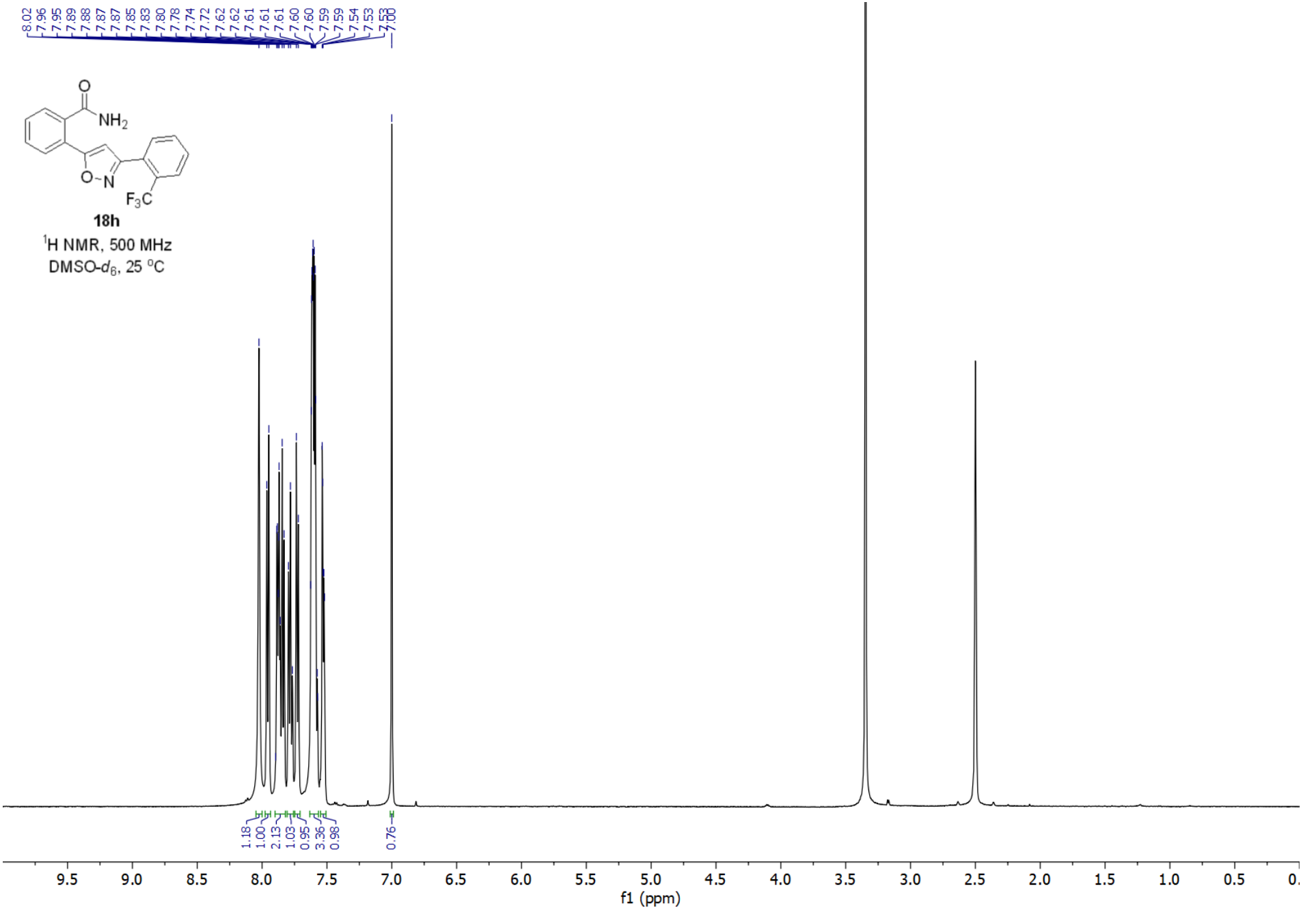
DMSO-d_6, 25 ^{o}C

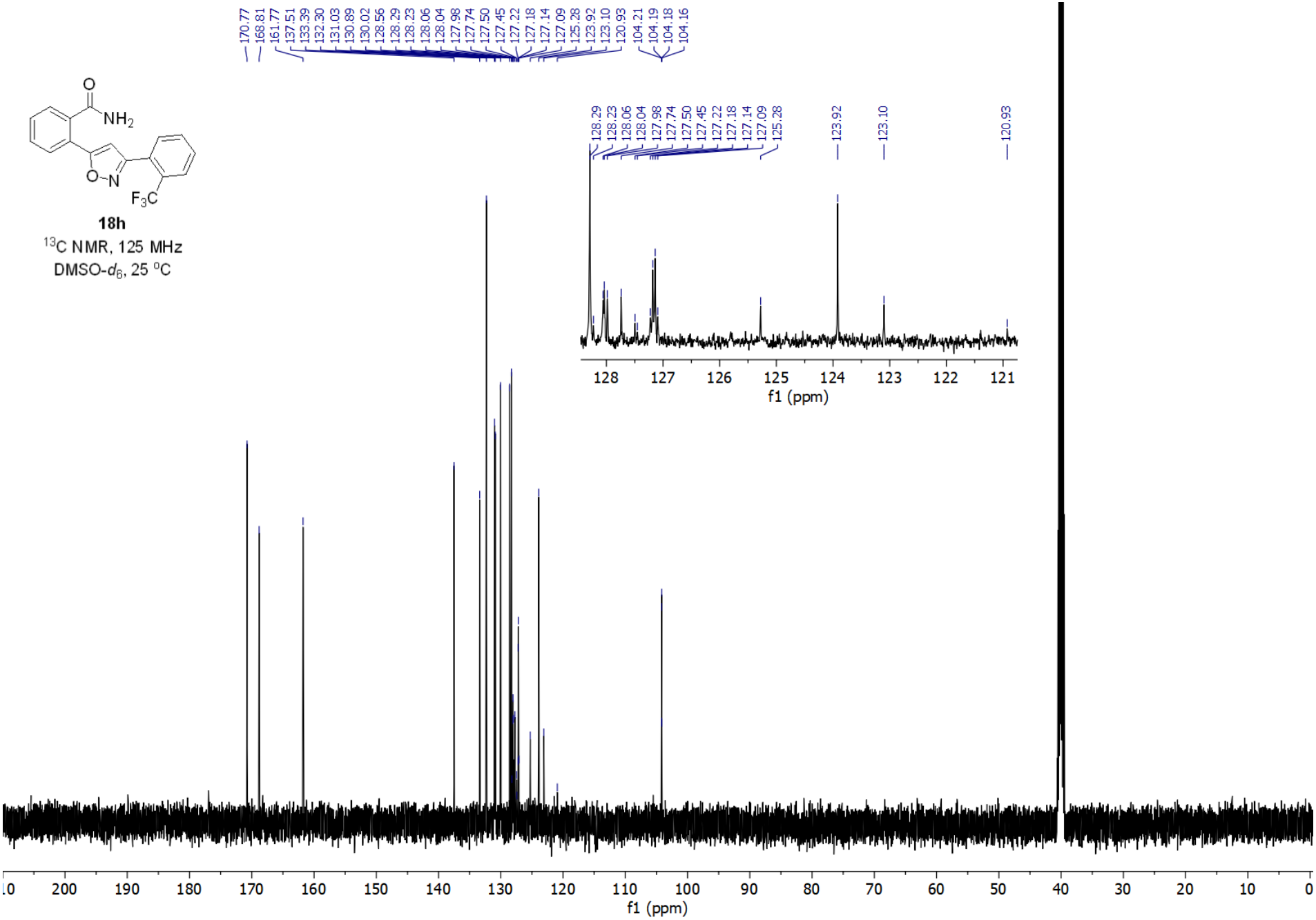



170.70
169.57
162.47
153.44
137.44
130.68
130.01
128.83
128.31
126.82
126.45
126.28
124.68
101.06
35.07
31.44
O
NH2
tBu
O
N
18f
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)


8.02 7.88 7.88 7.87 7.87 7.86 7.85 7.84 7.83 7.83 7.70 7.69 7.68 7.68 7.62 7.61 7.60 7.60 7.60 7.59 7.59 7.58 7.57 7.57 7.57 7.56 7.55 7.54 7.54 7.54 7.53 7.53 7.52 7.52 7.50 7.49 7.48 7.48 7.47 7.46 7.16
O
NH2
O
N
Br
18g
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.19 1.04 0.91 1.00 1.25 2.05 2.43 1.05 0.74
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


170.78
168.54
162.73
137.52
134.15
132.29
131.81
130.82
130.29
129.99
128.71
128.52
128.25
124.08
121.97
104.19
O
NH2
O
N
Br
18g
13C NMR, 125 MHz
DMSO-d6, 25 °C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

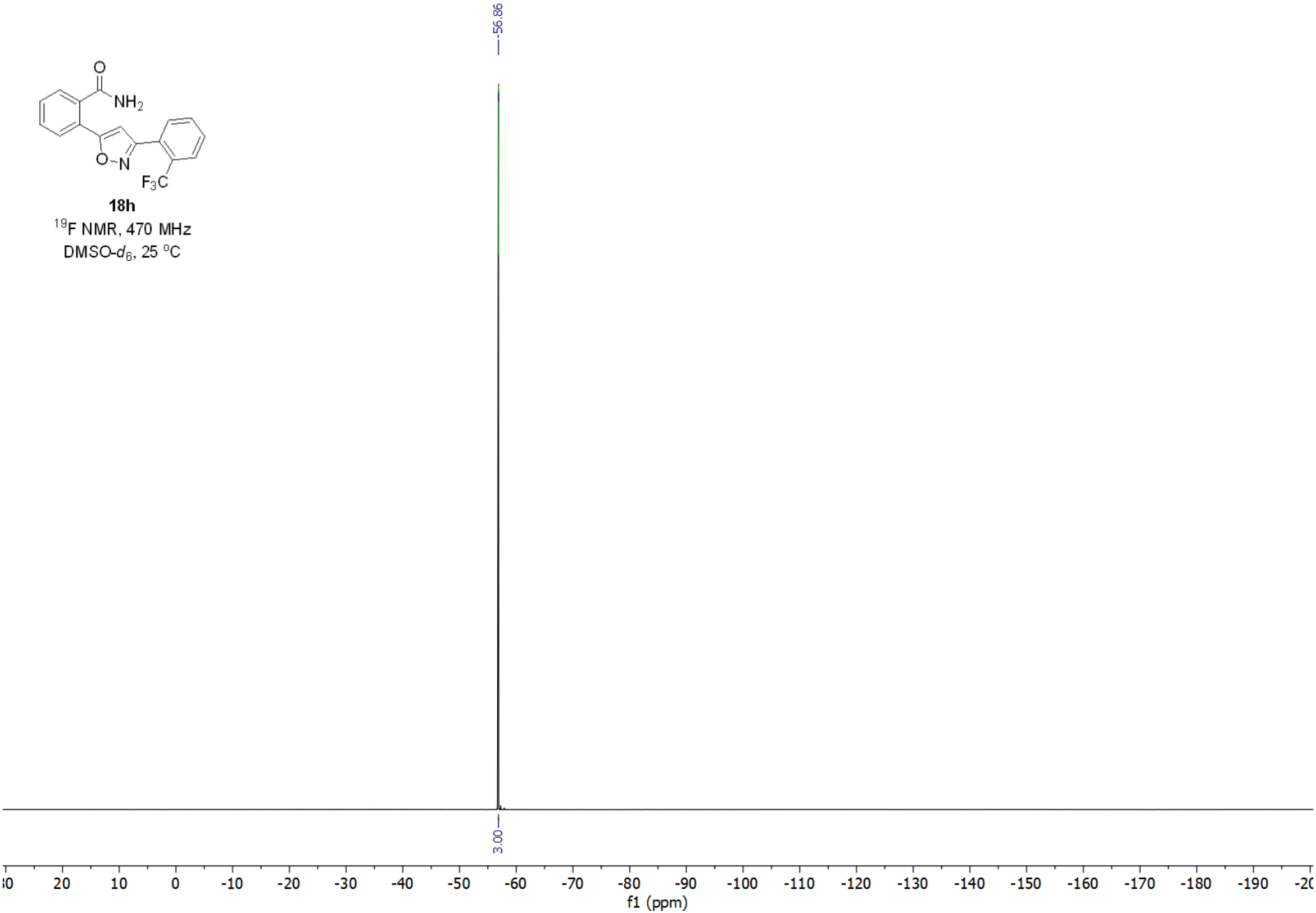

8.02
7.96
7.95
7.89
7.88
7.87
7.87
7.85
7.83
7.80
7.78
7.74
7.72
7.62
7.62
7.61
7.61
7.61
7.60
7.60
7.59
7.59
7.54
7.53
7.53
7.50
O
NH2
O
N
F3C
18h
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.18
1.00
2.13
1.03
0.95
3.36
0.98
0.76
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

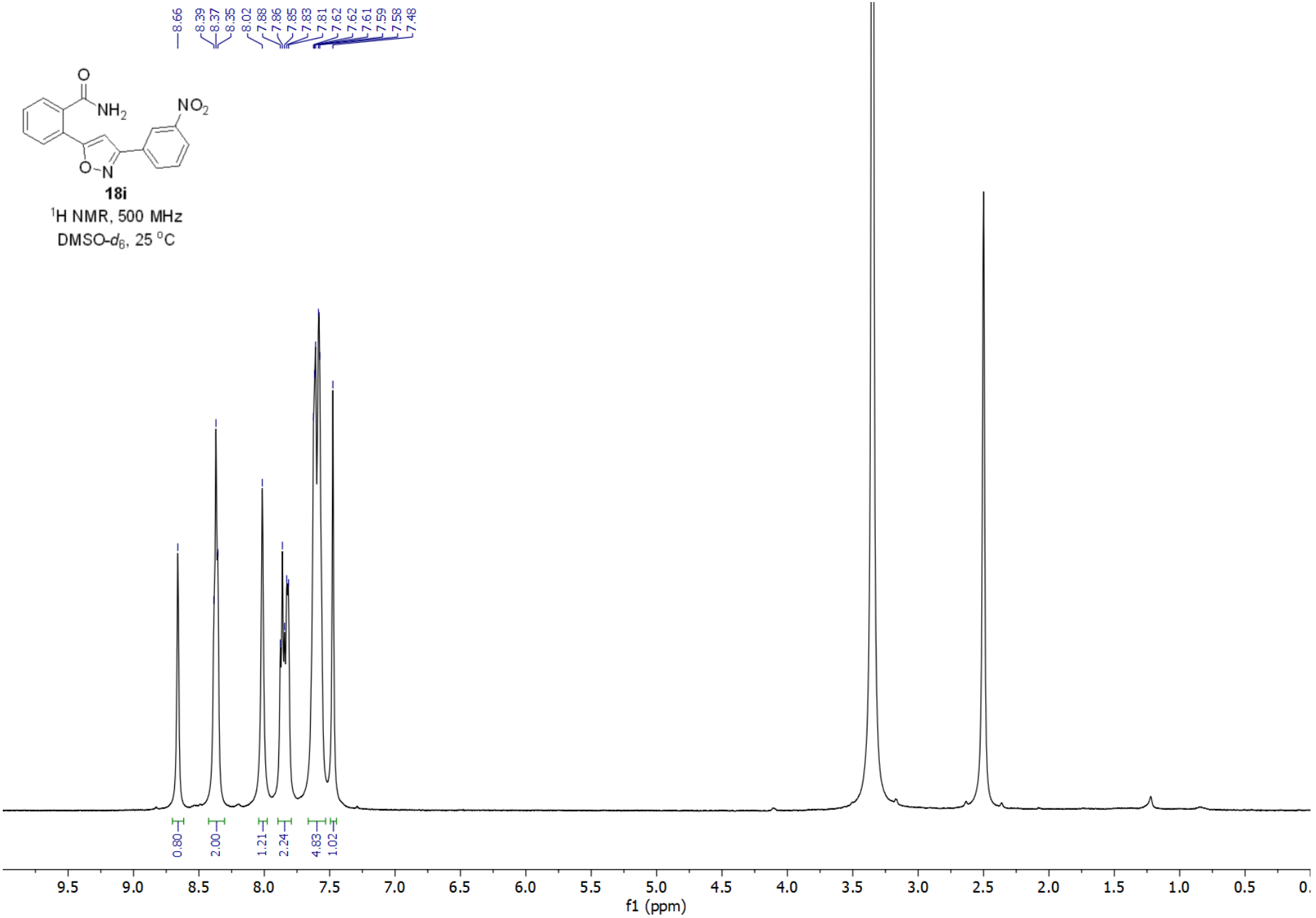

170.77
168.81
161.77
137.51
133.39
132.30
131.03
130.89
130.02
128.56
128.29
128.23
128.06
128.04
127.98
127.74
127.50
127.45
127.22
127.18
127.14
127.09
125.28
123.92
123.10
120.93
104.21
104.19
104.18
104.16
O
NH2
O
N
F3C
18h
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)
f1 (ppm)

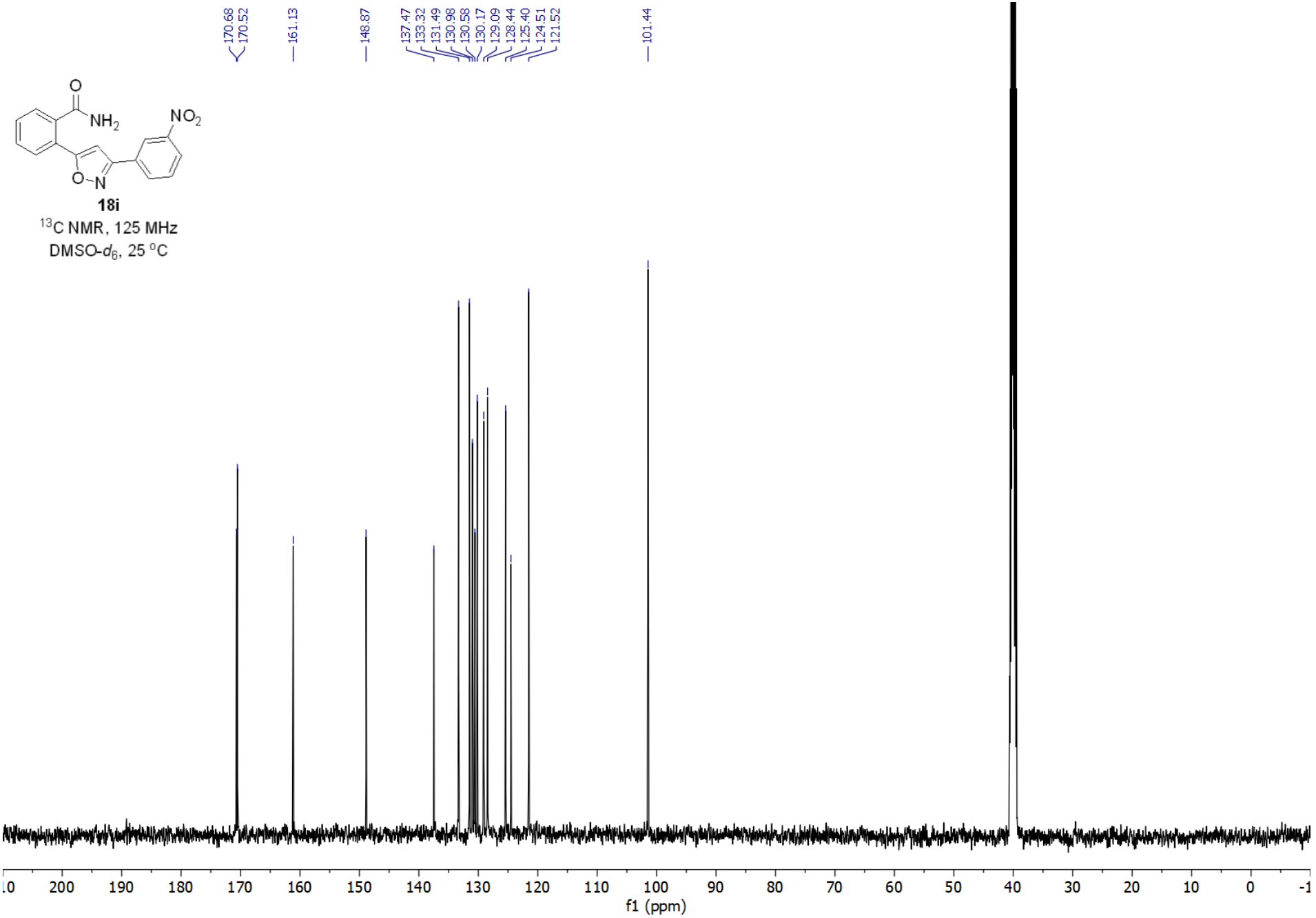
18h

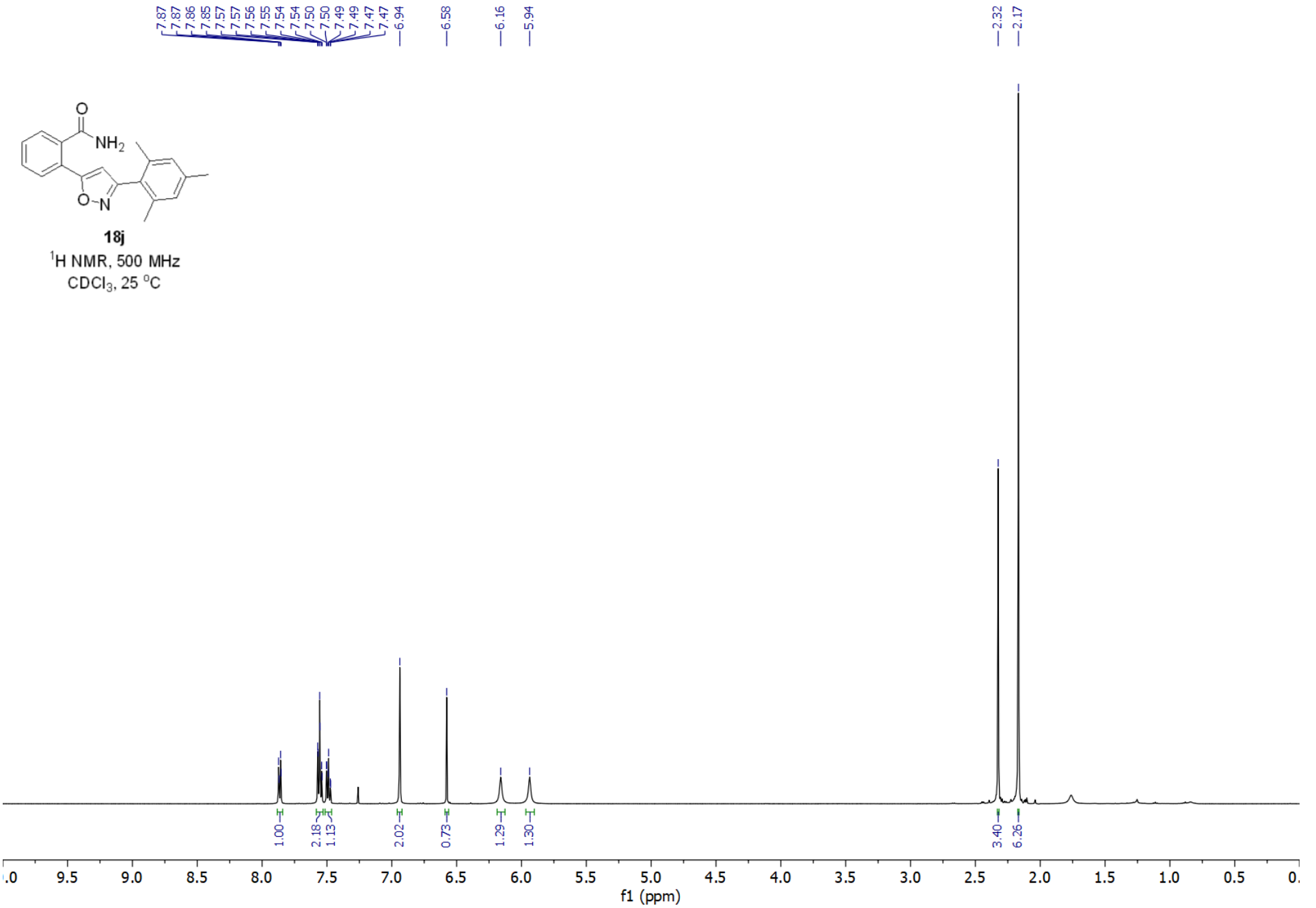
^{19}F NMR, 470 MHz

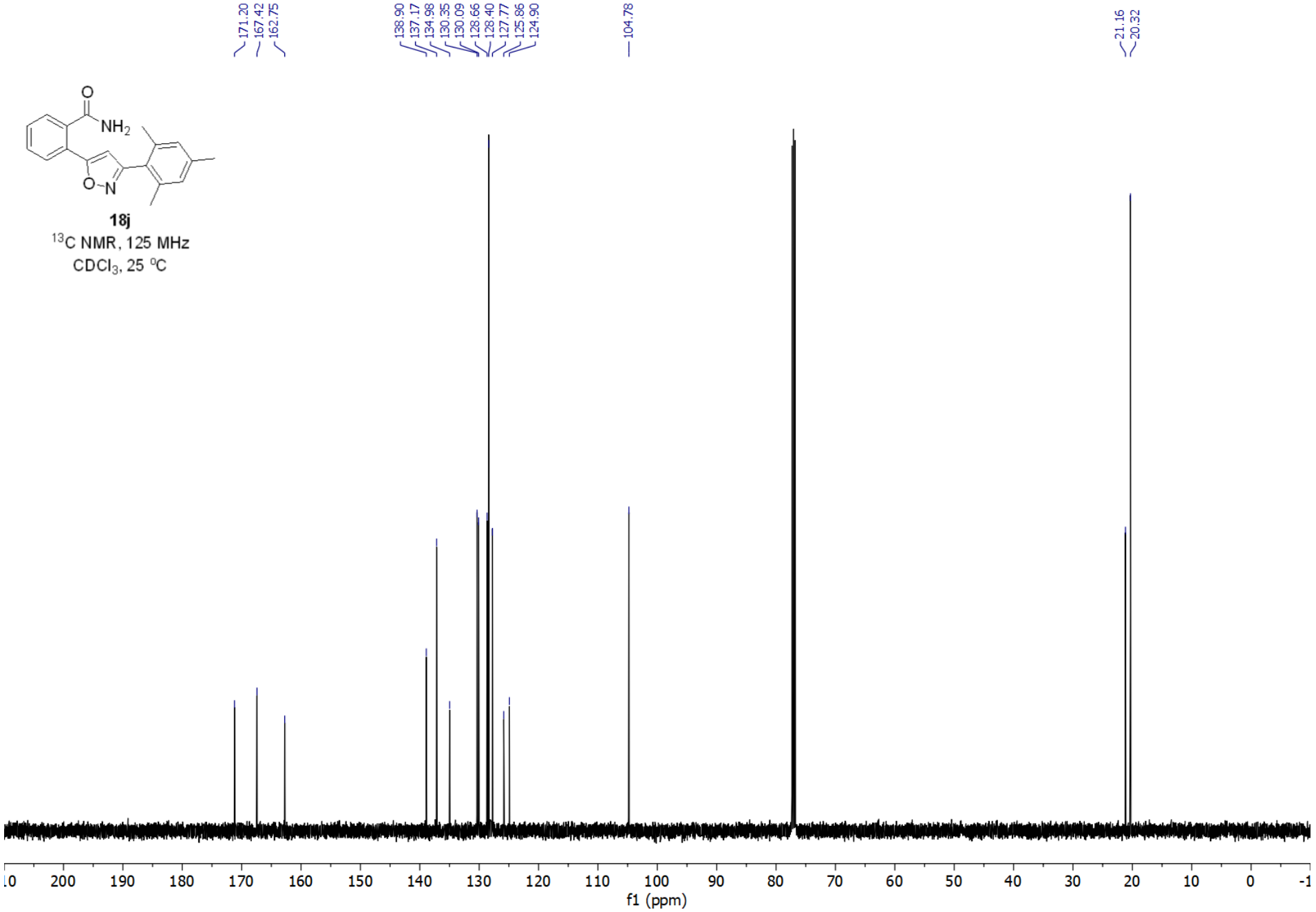
DMSO-d_6, 25 ^{o}C

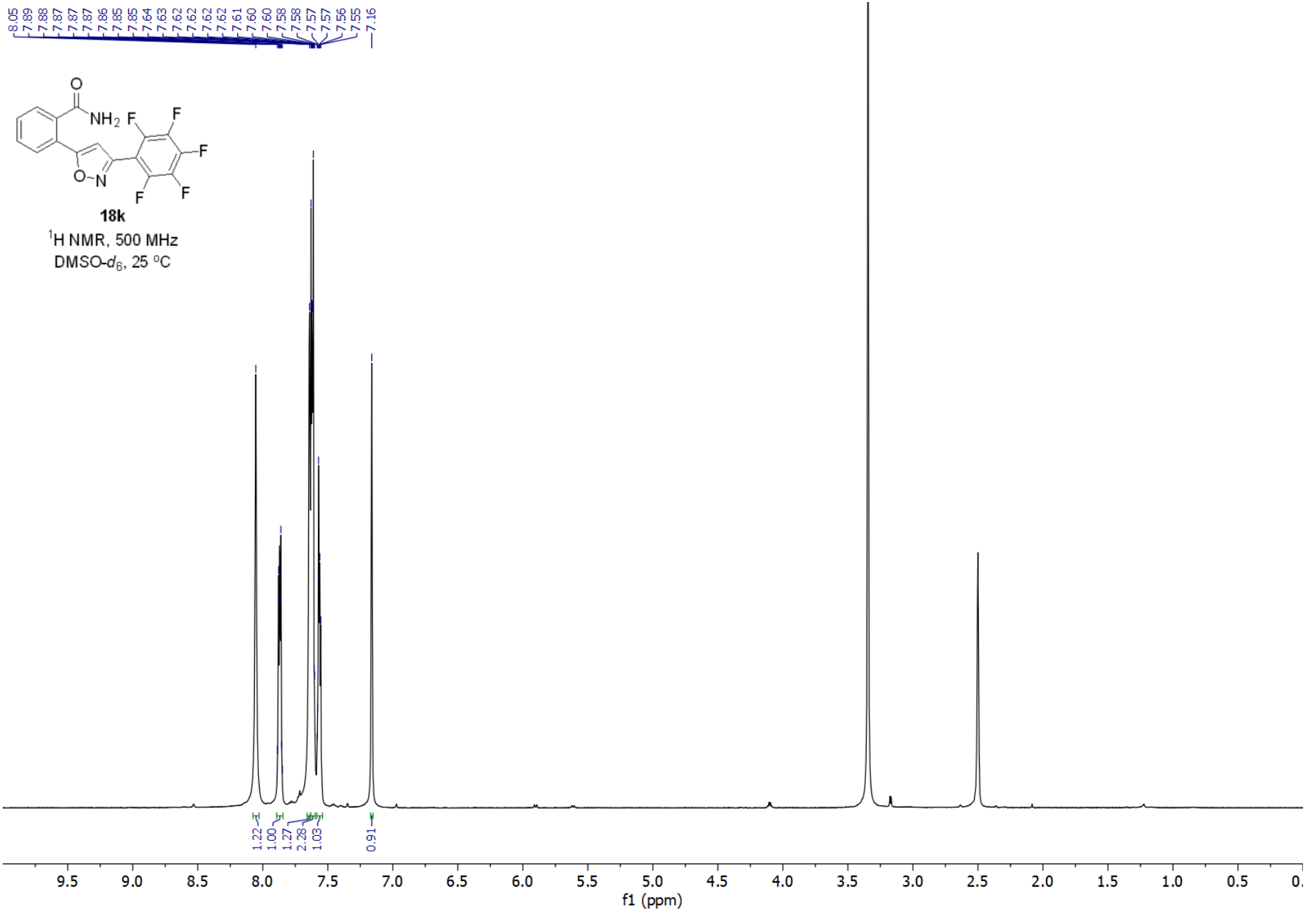


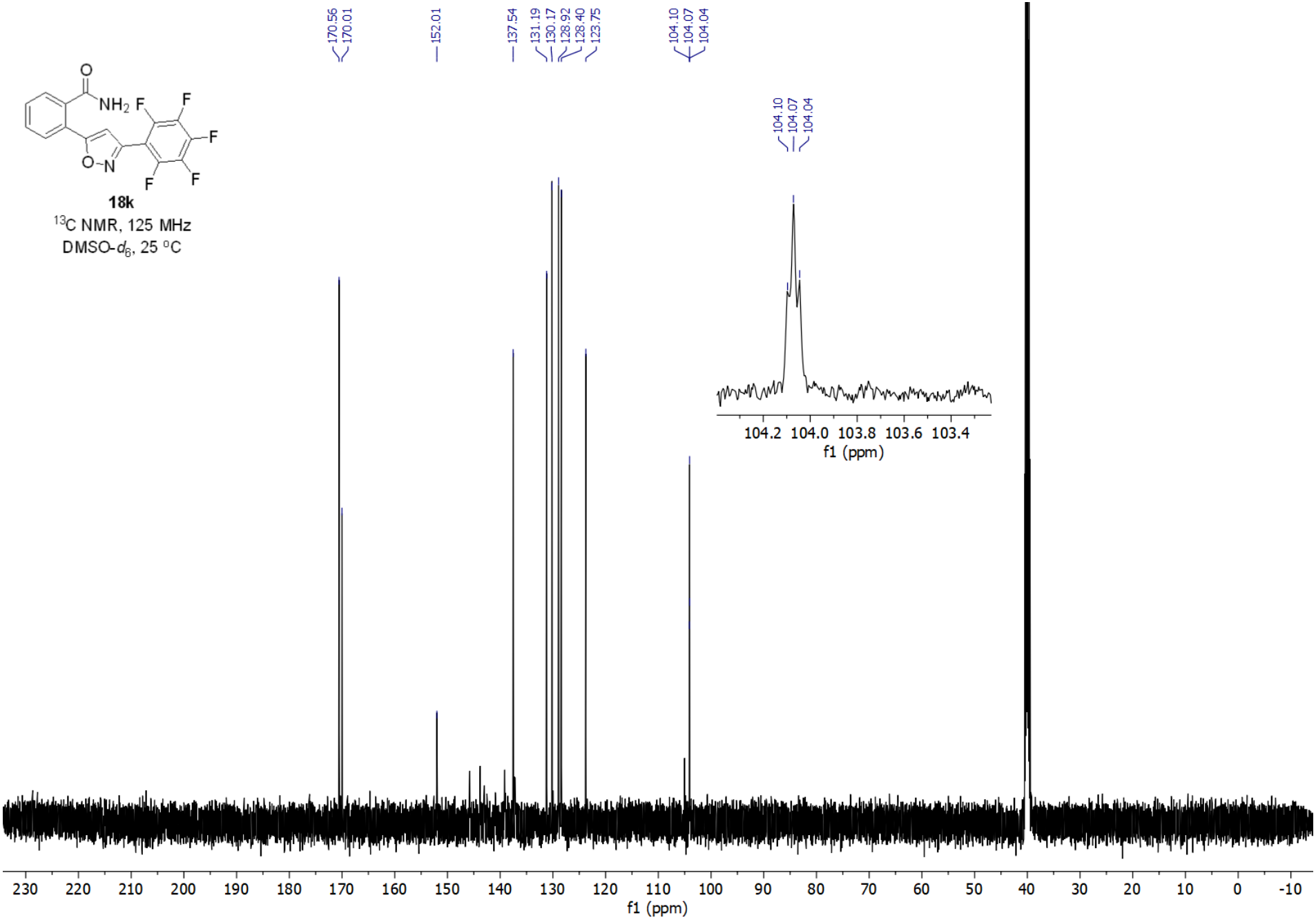

8.66
8.39
8.37
8.35
8.02
7.88
7.86
7.85
7.83
7.81
7.62
7.61
7.59
7.58
7.48
O
NH2
NO2
O
N
18i
1H NMR, 500 MHz
DMSO-d6, 25 °C
0.80
2.00
1.21
2.24
4.83
1.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


170.68
170.52
161.13
148.87
137.47
133.32
131.49
130.98
130.58
130.17
129.09
128.44
125.40
124.51
121.52
101.44
O
NH2
NO2
O
N
18i
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)


7.87
7.87
7.86
7.85
7.57
7.57
7.56
7.55
7.54
7.54
7.50
7.50
7.49
7.49
7.47
7.47
6.94
6.58
6.16
5.94
2.32
2.17
O
NH2
O
N
18j
1H NMR, 500 MHz
CDCl3, 25 °C
1.00
2.18
1.13
2.02
0.73
1.29
1.30
3.40
6.26
f1 (ppm)


171.20
167.42
162.75
138.90
137.17
134.98
130.35
130.09
128.66
128.40
127.77
125.86
124.90
104.78
21.16
20.32
O
NH2
O
N
18j
13C NMR, 125 MHz
CDCl3, 25 °C
f1 (ppm)

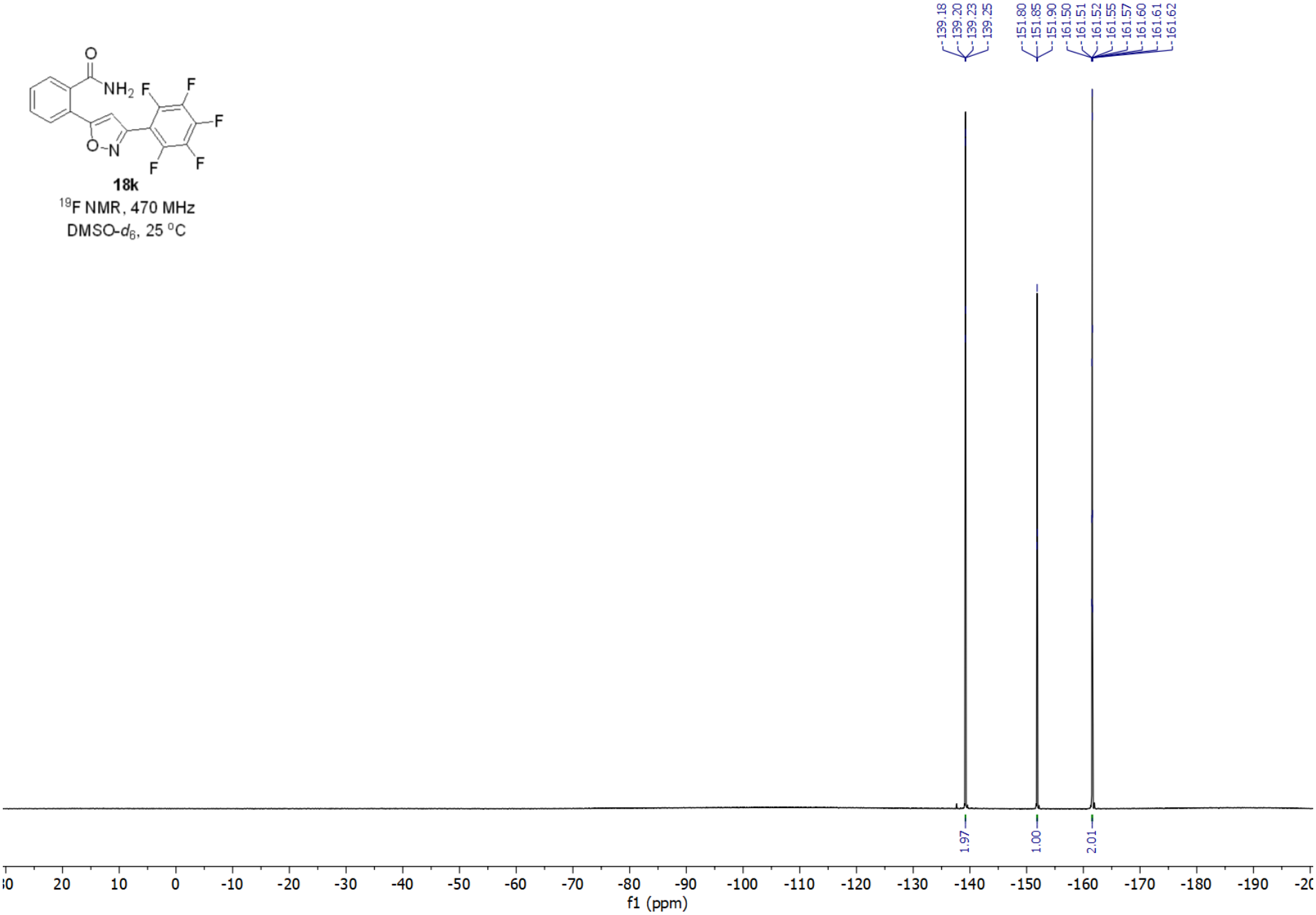

8.05
7.89
7.88
7.87
7.87
7.87
7.86
7.85
7.85
7.64
7.63
7.62
7.62
7.62
7.62
7.61
7.60
7.60
7.58
7.58
7.57
7.57
7.56
7.55
7.16
O
NH2
F
F
F
F
F
O
N
18k
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.22
1.00
1.27
2.28
1.03
0.91
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

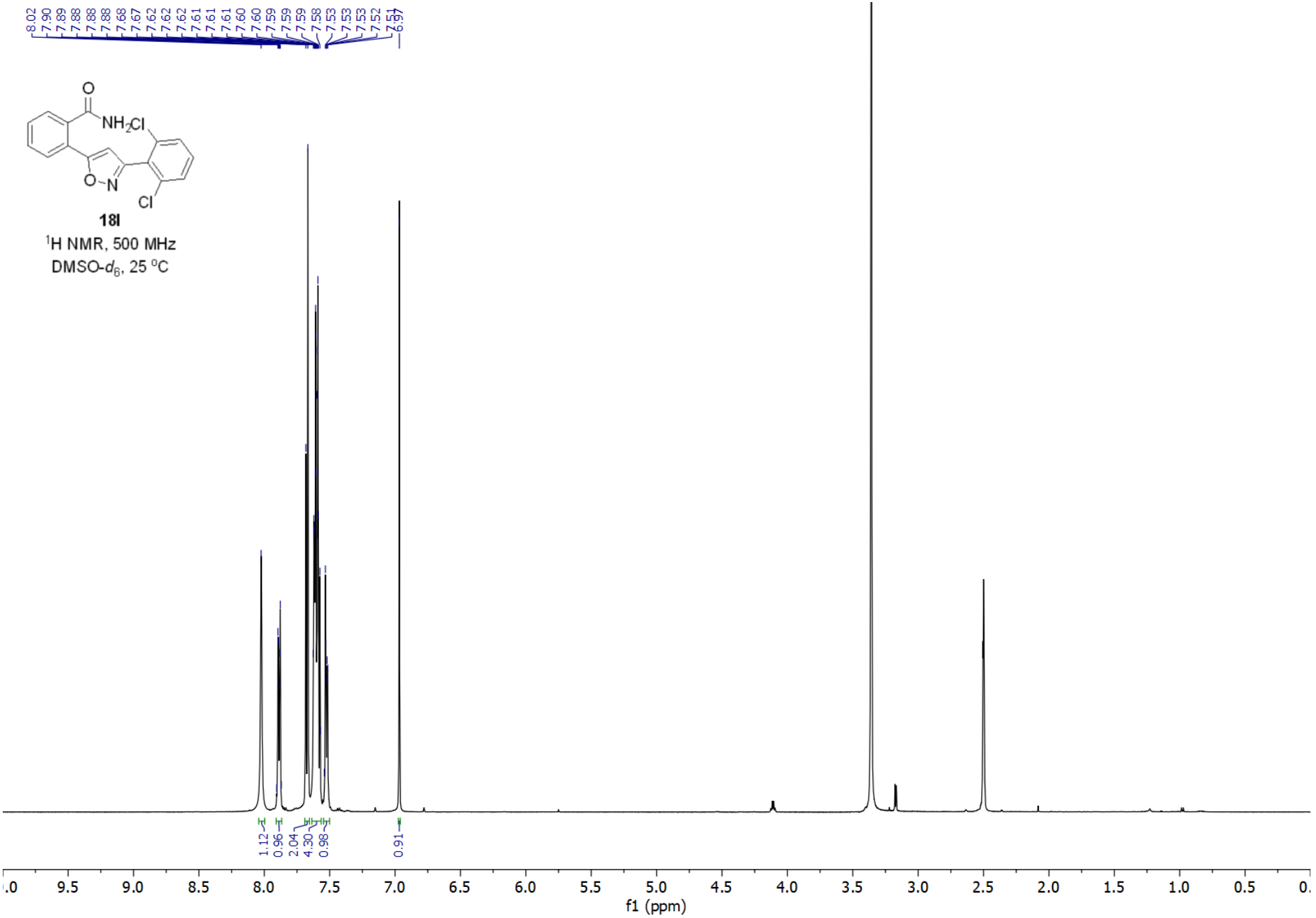

170.56
170.01
152.01
137.54
131.19
130.17
128.92
128.40
123.75
104.10
104.07
104.04
O
NH2
F
F
F
O
N
F
F
18k
13C NMR, 125 MHz
DMSO-d6, 25 °C
104.2 104.0 103.8 103.6 103.4
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

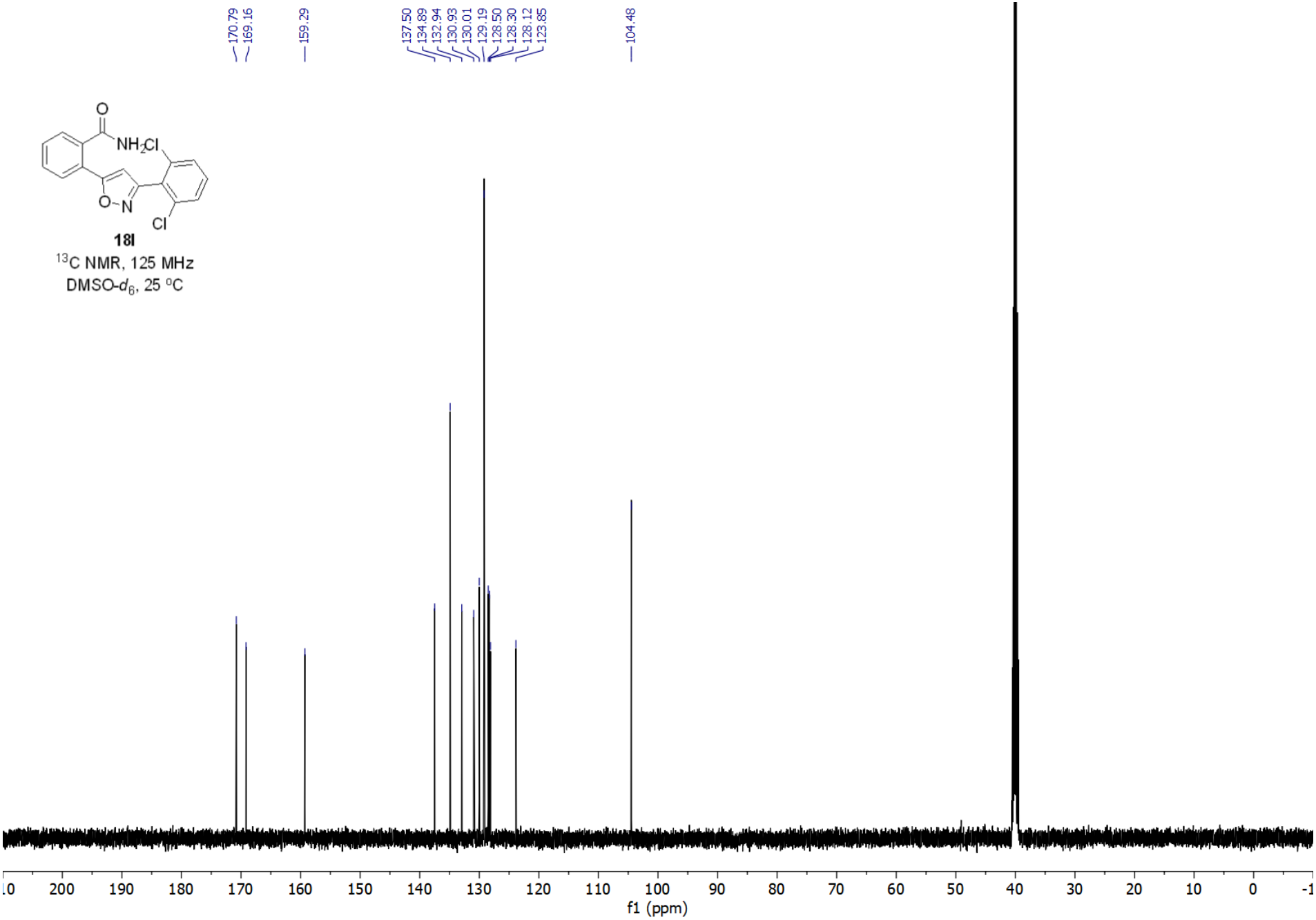
18k

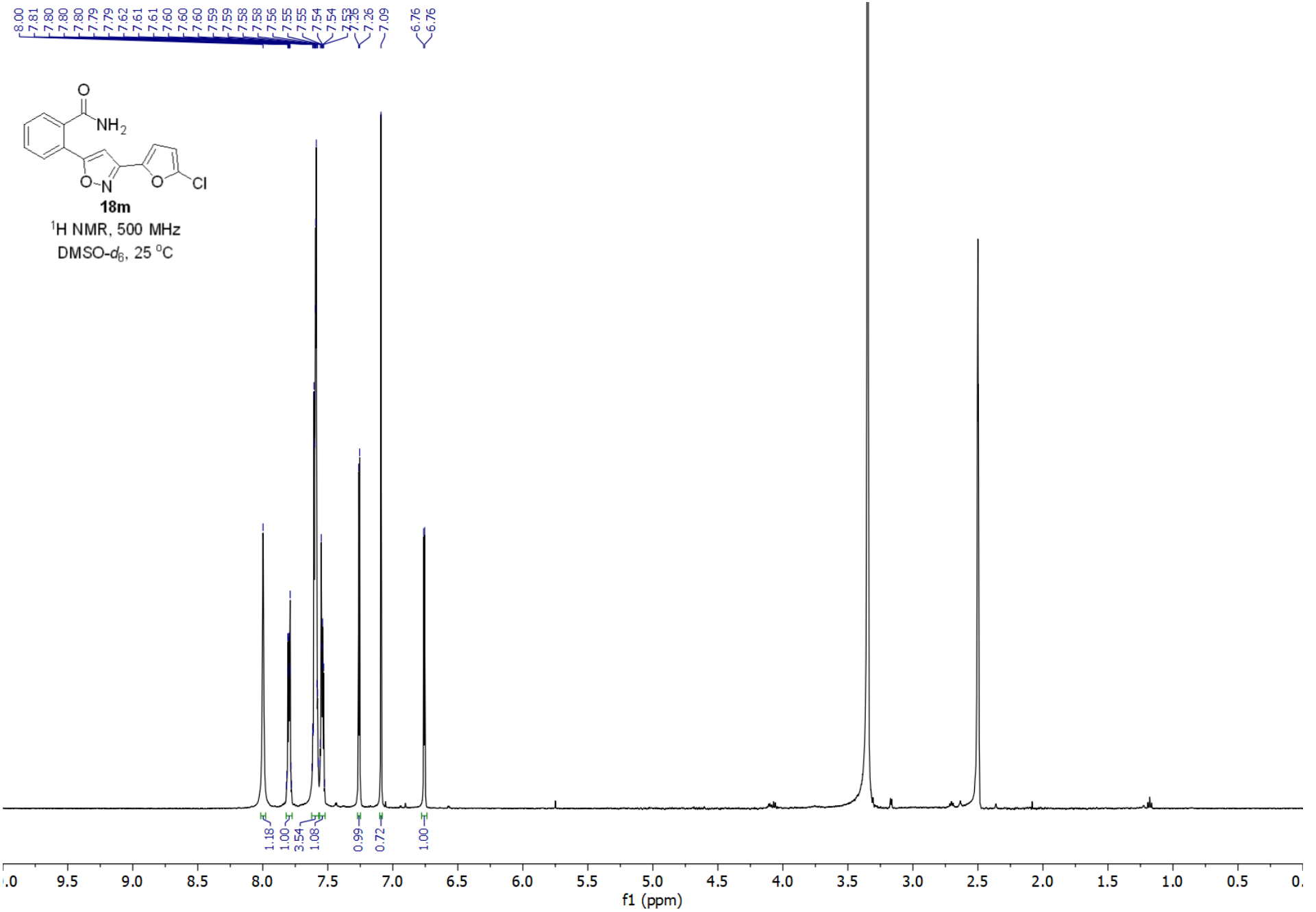
^{19}F NMR, 470 MHz

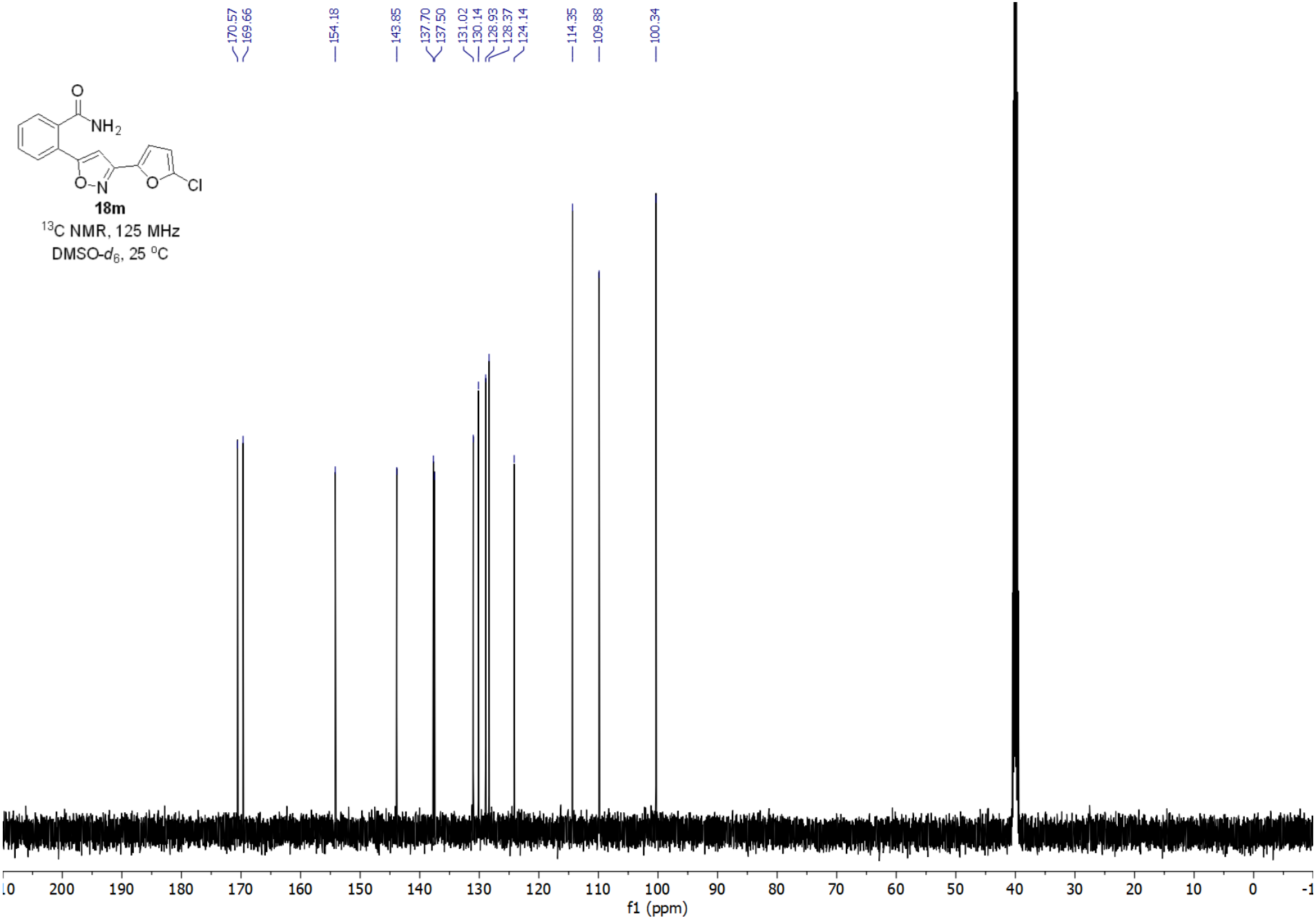
DMSO-d_6, 25 °C

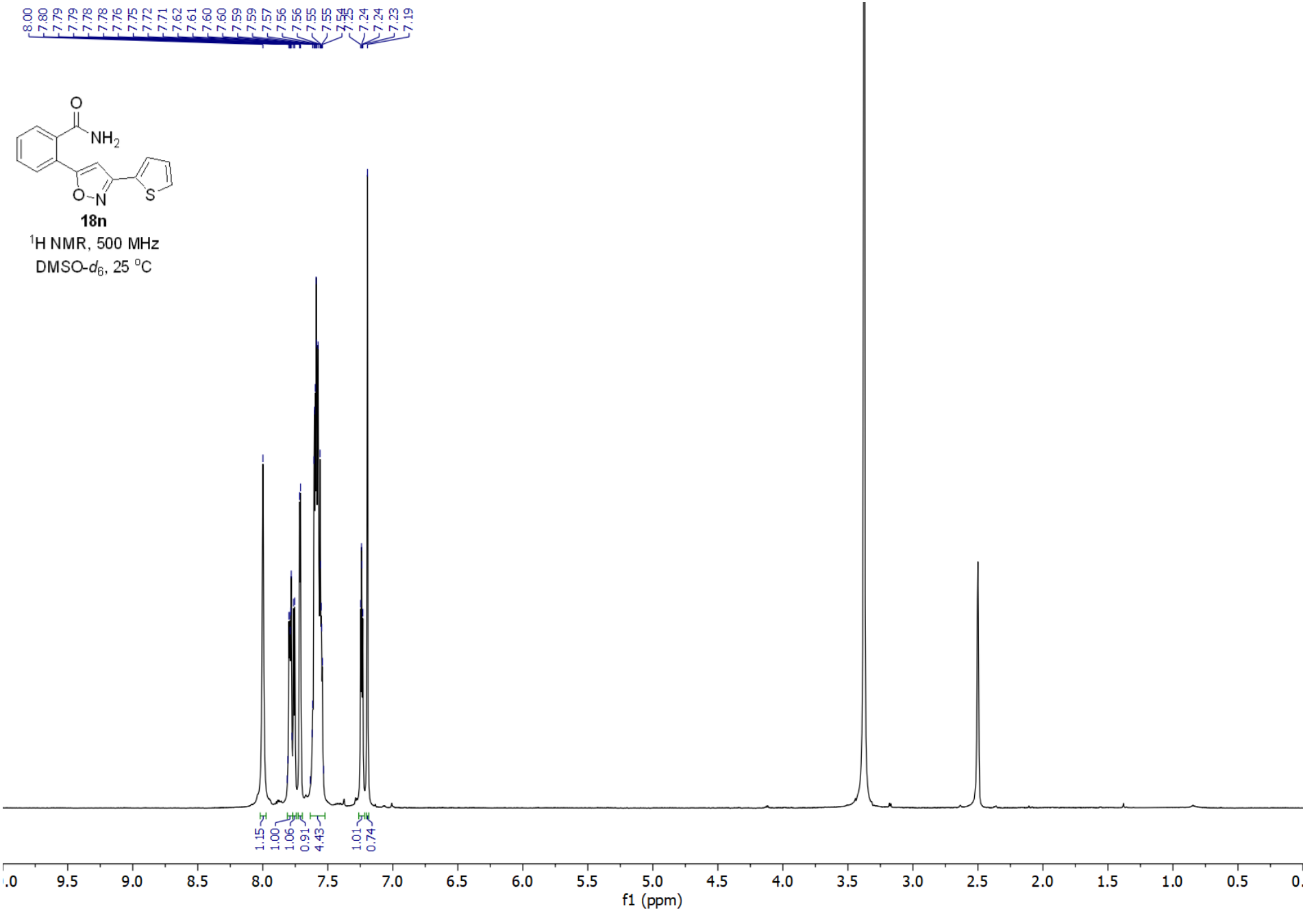


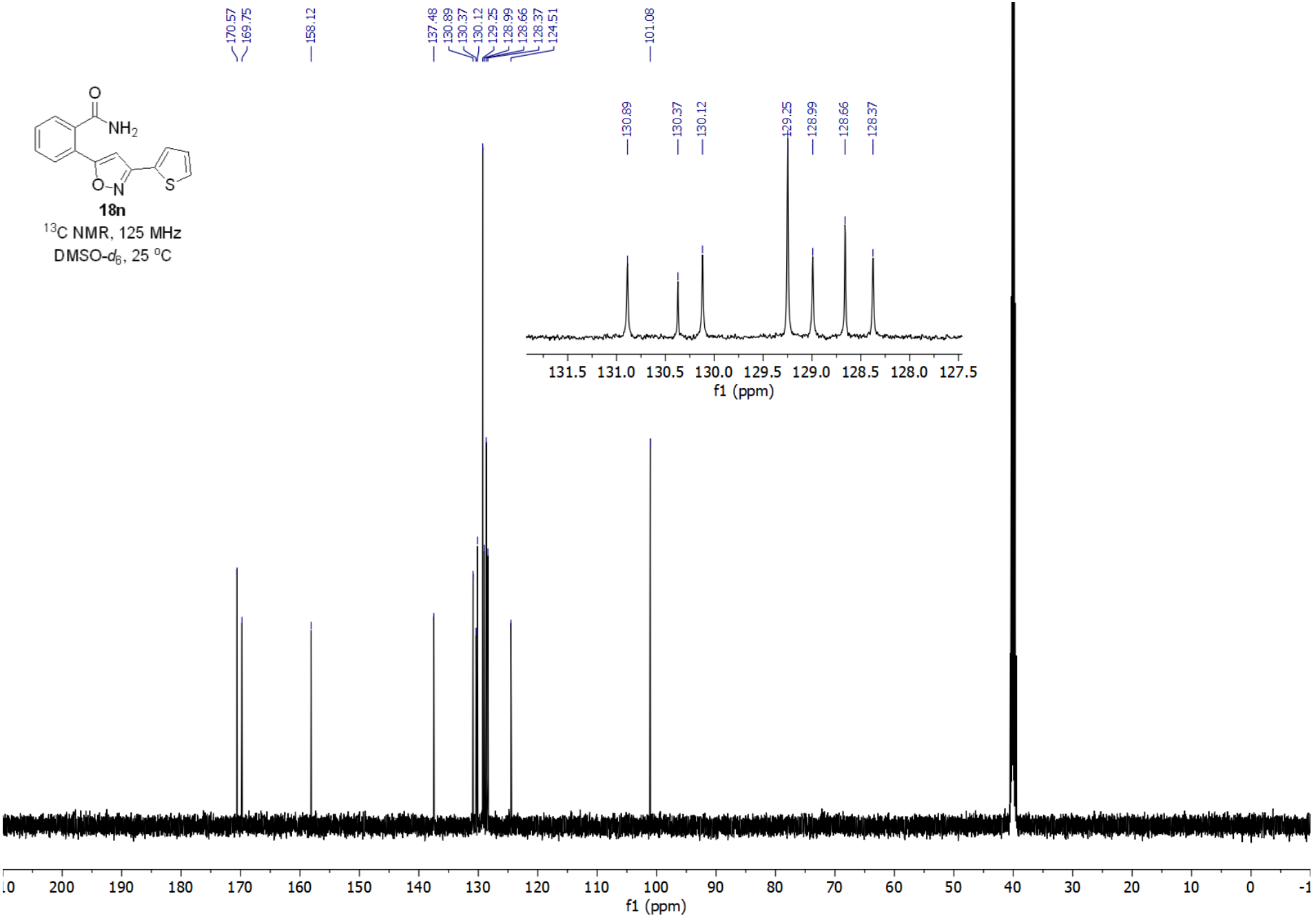

8.02
7.90
7.89
7.88
7.88
7.88
7.68
7.67
7.62
7.62
7.62
7.61
7.61
7.61
7.60
7.60
7.59
7.59
7.59
7.59
7.58
7.53
7.53
7.53
7.52
7.51
6.97
O
NH2
Cl
O
N
Cl
18l
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.12
0.96
2.04
4.30
0.98
0.91
f1 (ppm)

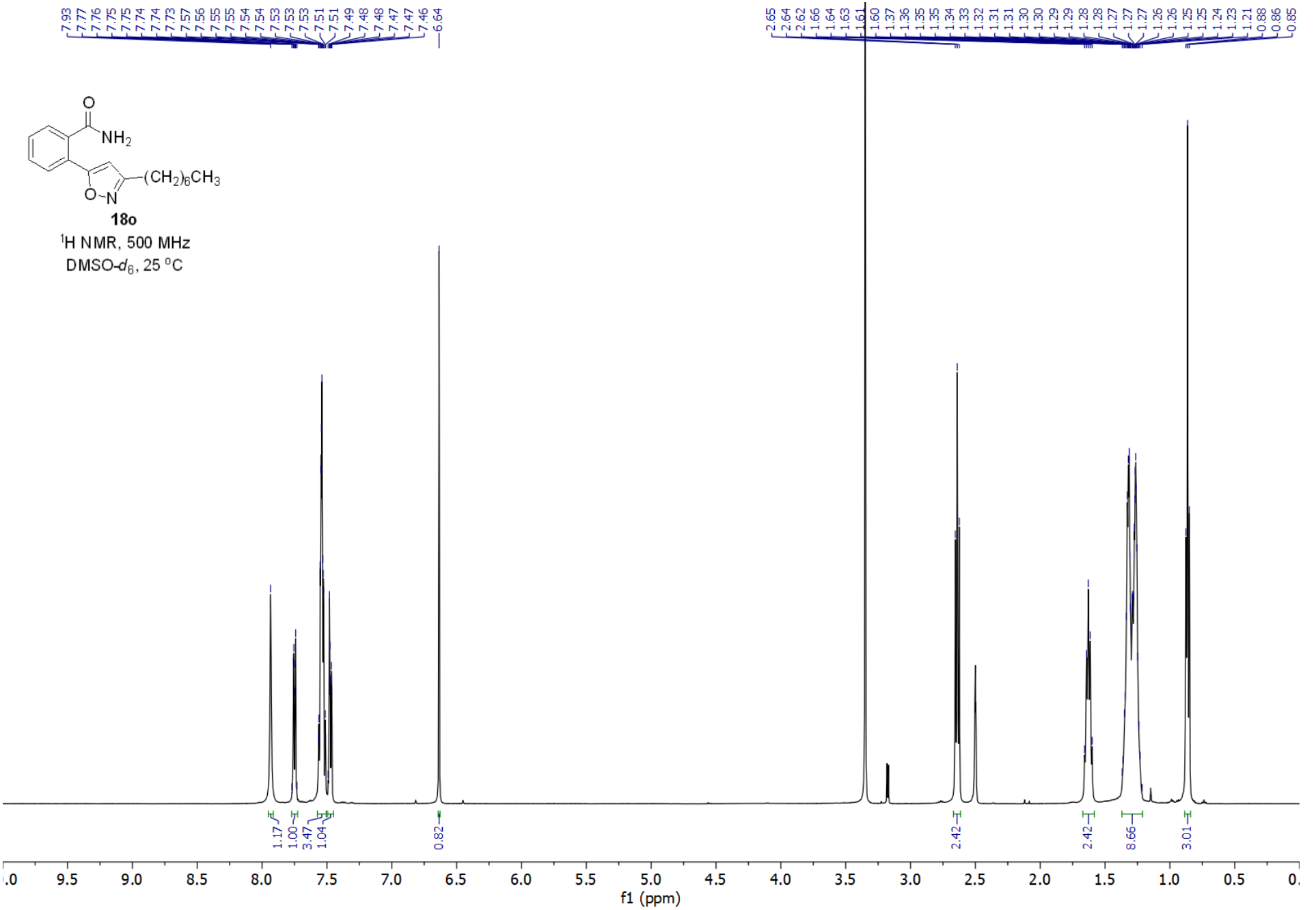

170.79
169.16
159.29
137.50
134.89
132.94
130.93
130.01
129.19
128.50
128.30
128.12
123.85
104.48
O
NH2
Cl
O
N
Cl
18l
13C NMR, 125 MHz
DMSO-d6, 25 °C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

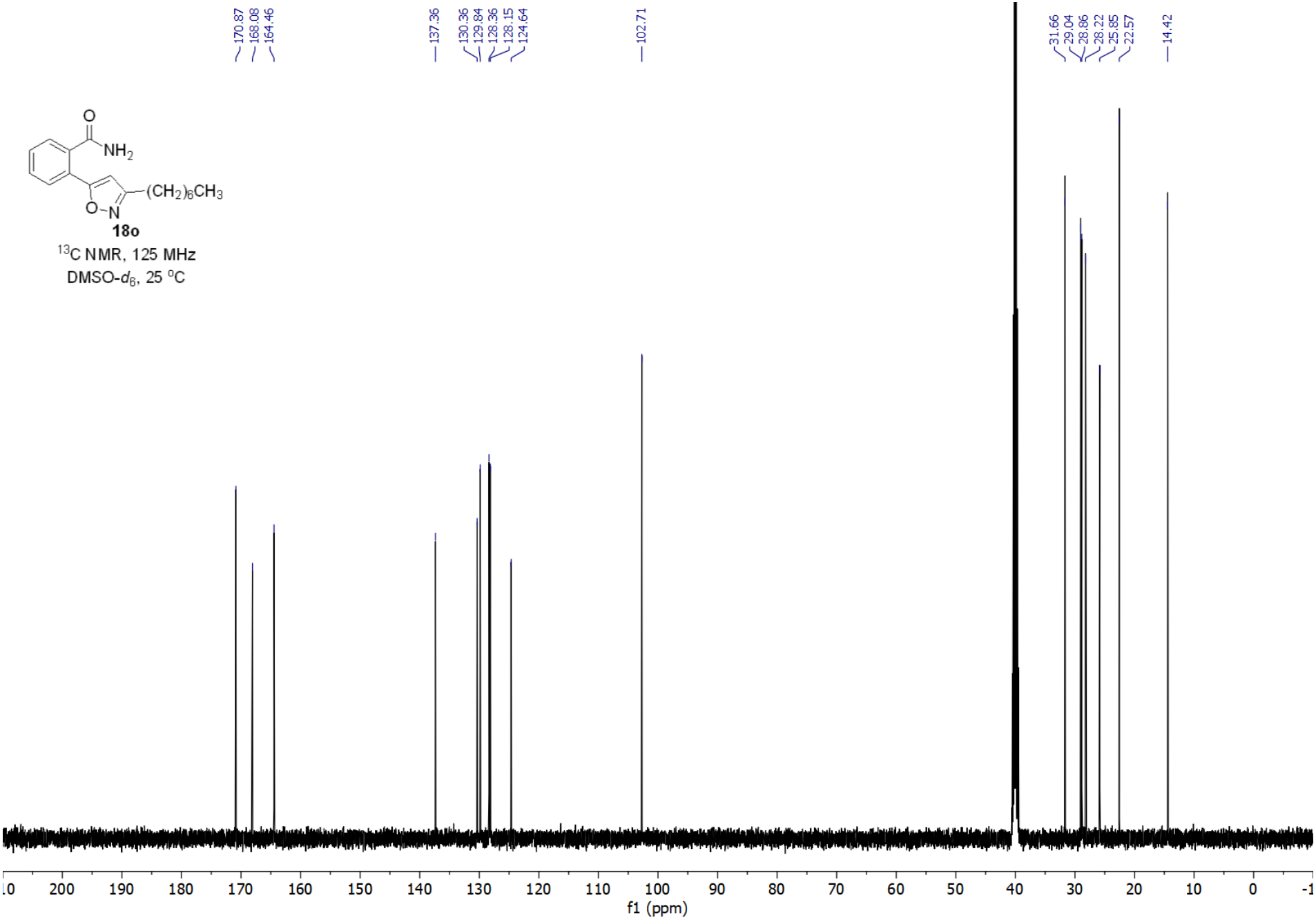

8.00
7.81
7.80
7.80
7.80
7.79
7.79
7.62
7.61
7.61
7.60
7.60
7.60
7.59
7.59
7.58
7.58
7.56
7.55
7.55
7.54
7.54
7.53
7.26
7.09
6.76
6.76
O
NH2
O
N
O
Cl
18m
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.18
1.00
3.54
1.08
0.99
0.72
1.00
f1 (ppm)

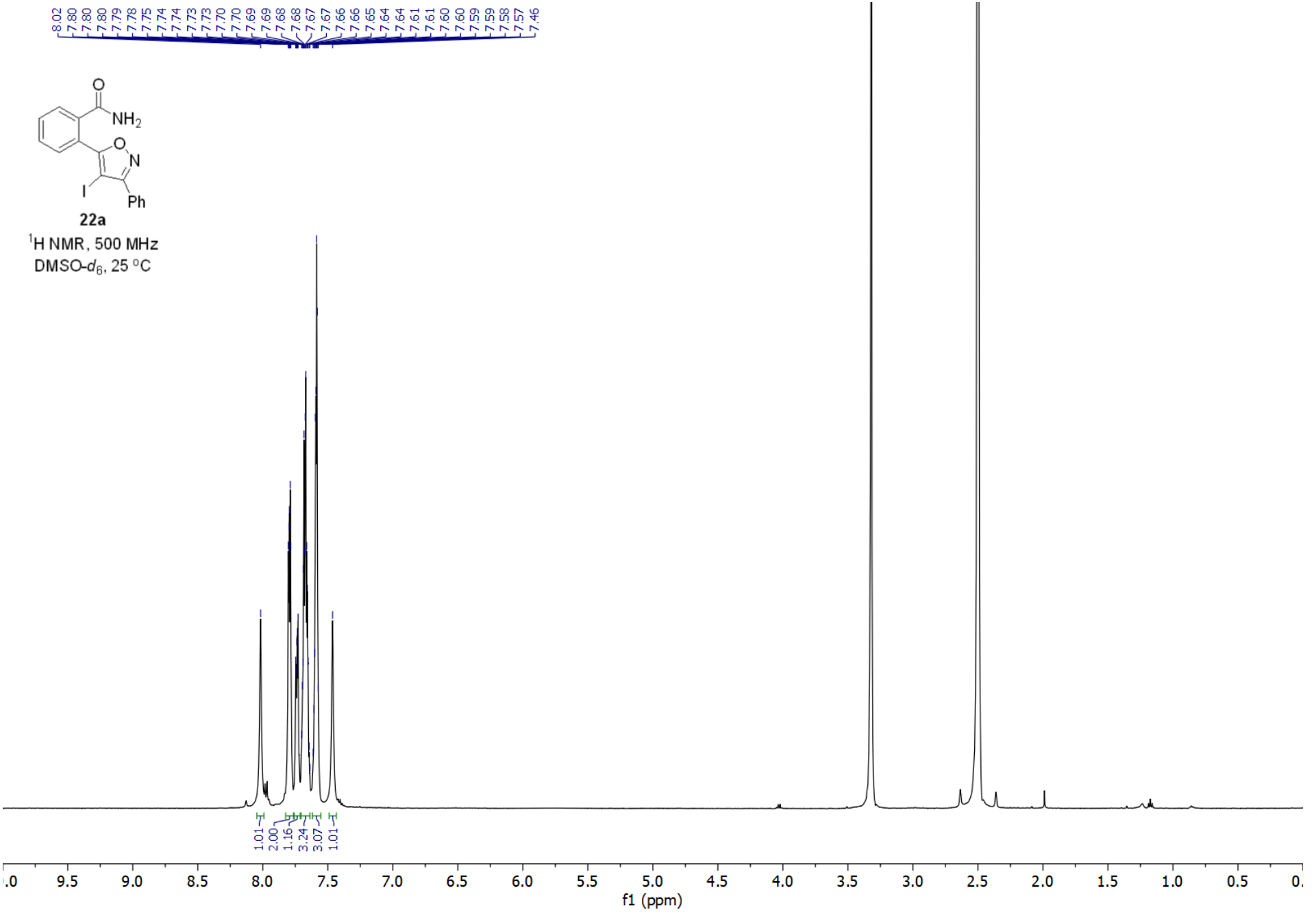

170.57
169.66
154.18
143.85
137.70
137.50
131.02
130.14
128.93
128.37
124.14
114.35
109.88
100.34
O
NH2
O
N
O
Cl
18m
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

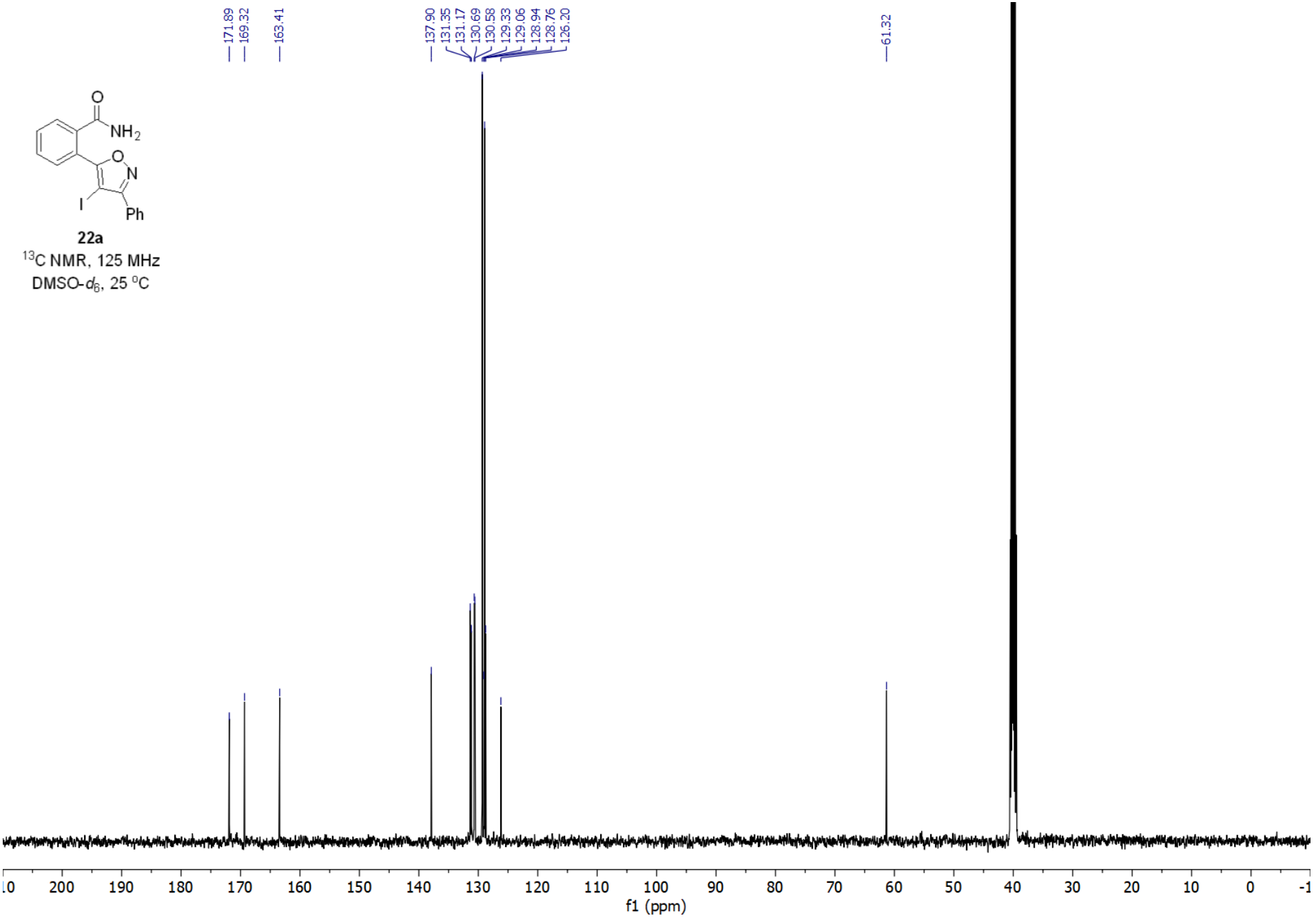

8.00
7.80
7.79
7.79
7.78
7.78
7.76
7.75
7.72
7.71
7.62
7.61
7.60
7.60
7.59
7.59
7.57
7.56
7.56
7.55
7.55
7.54
7.25
7.24
7.24
7.23
7.19
O
NH2
O
N
S
18n
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.15
1.00
1.06
0.91
4.43
1.01
0.74
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

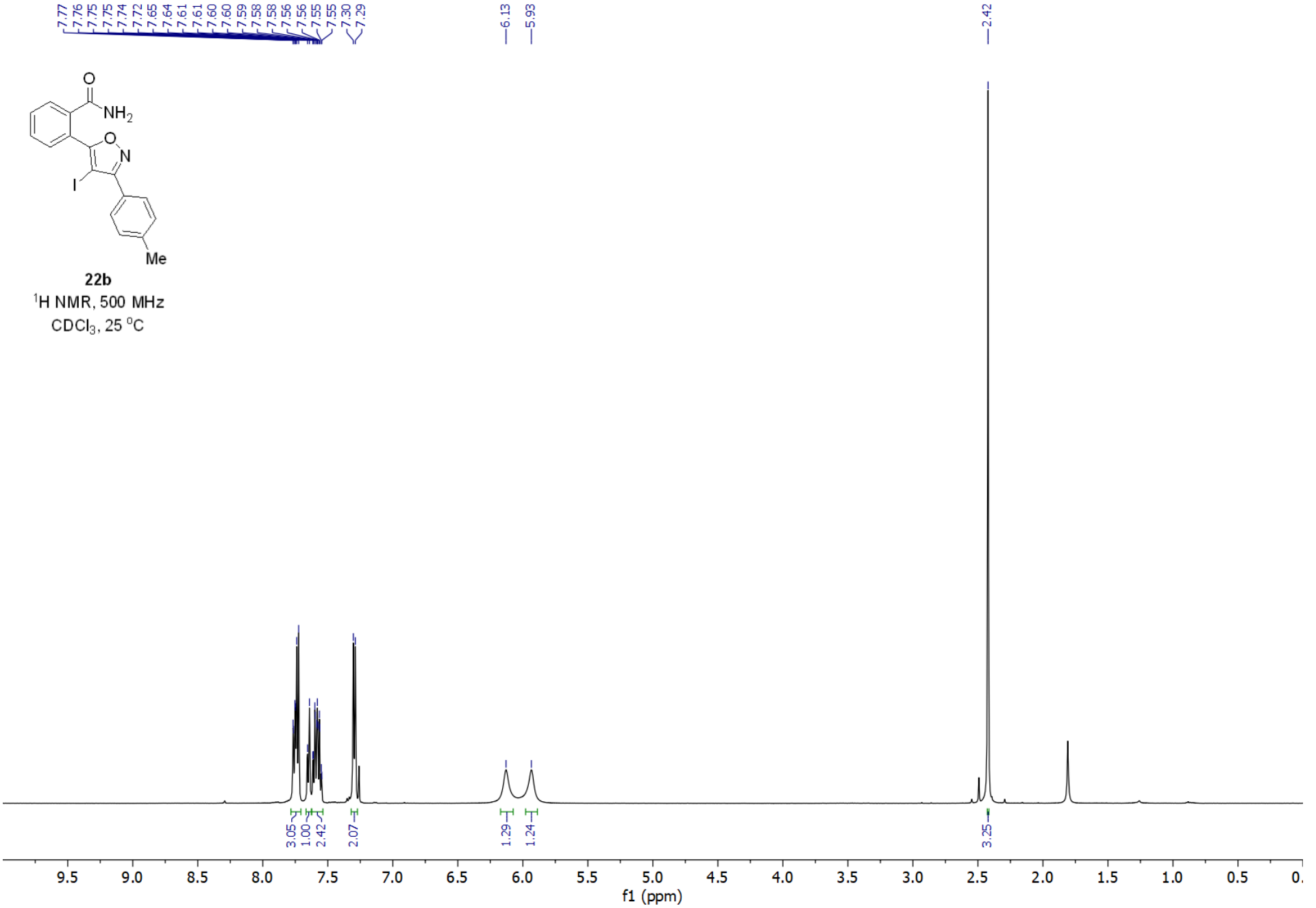

170.57
169.75
158.12
137.48
130.89
130.37
130.12
129.25
128.99
128.66
128.37
124.51
101.08
O
NH2
O
N
S
18n
13C NMR, 125 MHz
DMSO-d6, 25 °C
130.89
130.37
130.12
129.25
128.99
128.66
128.37
131.5 131.0 130.5 130.0 129.5 129.0 128.5 128.0 127.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

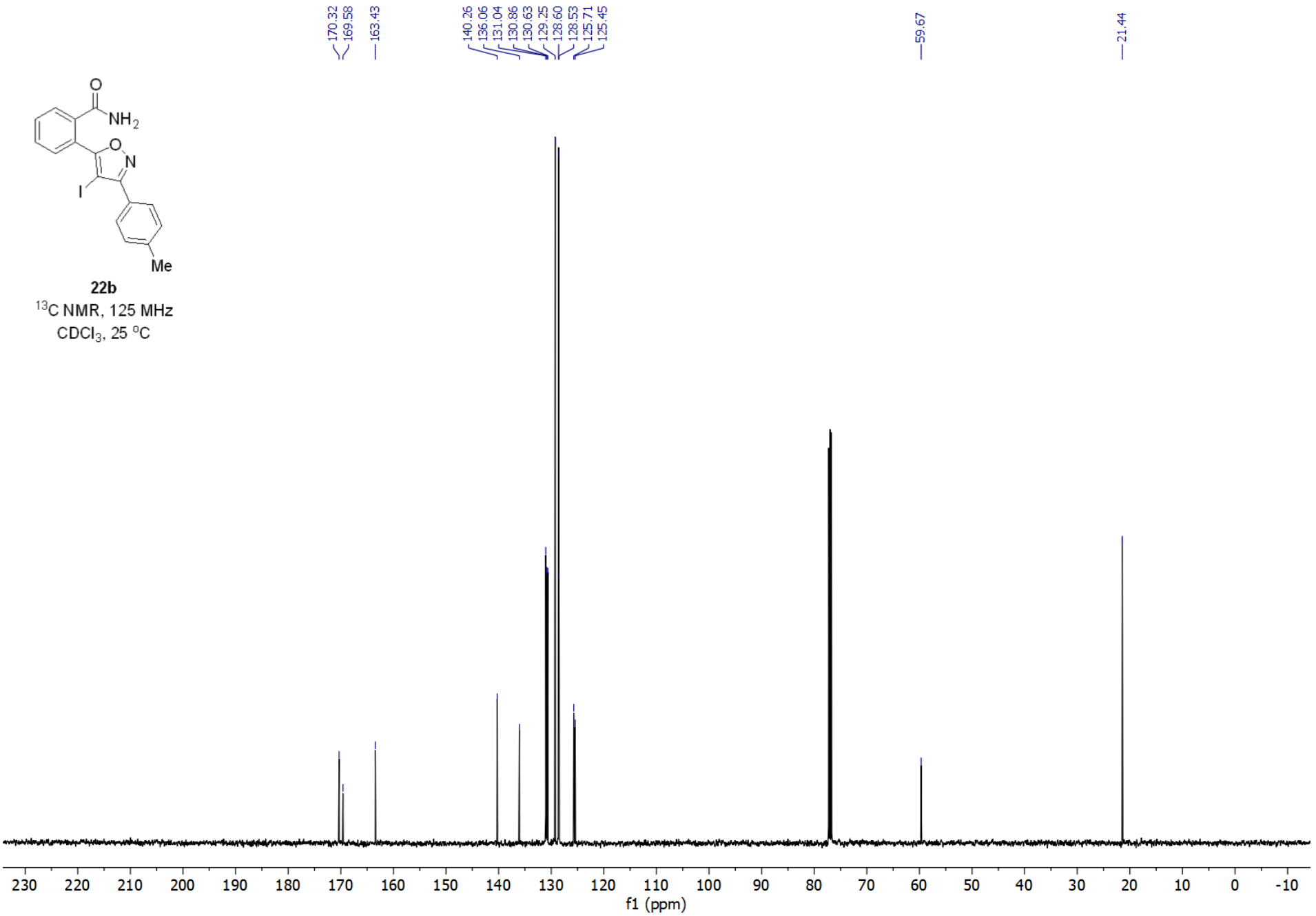

7.93 7.77 7.76 7.75 7.75 7.74 7.74 7.73 7.57 7.56 7.55 7.55 7.54 7.54 7.53 7.53 7.53 7.51 7.51 7.49 7.48 7.48 7.47 7.47 7.46 6.64
2.65 2.64 2.62 1.66 1.64 1.63 1.61 1.60 1.37 1.36 1.35 1.35 1.34 1.33 1.32 1.31 1.31 1.30 1.30 1.29 1.29 1.28 1.28 1.27 1.27 1.27 1.26 1.26 1.25 1.25 1.24 1.23 1.21 0.88 0.86 0.85
O
NH2
(CH2)6CH3
O
N
18o
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.17 1.00 3.47 1.04 0.82 2.42 2.42 8.66 3.01
f1 (ppm)

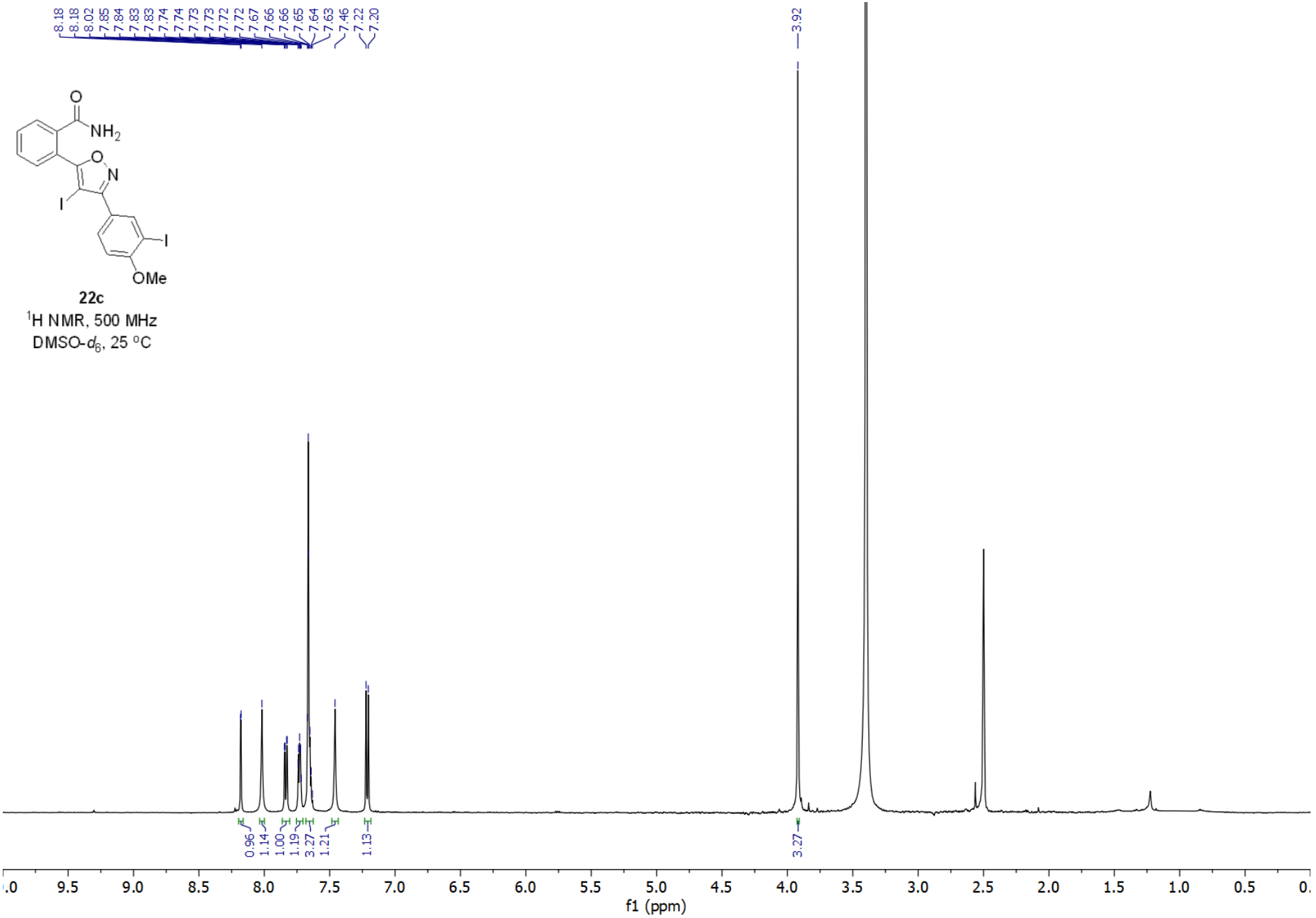

170.87
168.08
164.46
137.36
130.36
129.84
128.36
128.15
124.64
102.71
31.66
29.04
28.86
28.22
25.85
22.57
14.42
O
NH2
(CH2)6CH3
O
N
18o
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)


8.02
7.80
7.80
7.80
7.79
7.78
7.75
7.74
7.74
7.73
7.73
7.70
7.70
7.69
7.69
7.68
7.68
7.67
7.67
7.66
7.66
7.65
7.64
7.64
7.61
7.61
7.60
7.60
7.59
7.59
7.58
7.57
7.46
O
NH2
O
N
I
Ph
22a
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.01
2.00
1.16
3.24
3.07
1.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


171.89
169.32
163.41
137.90
131.35
131.17
130.69
130.58
129.33
129.06
128.94
128.76
126.20
61.32
O
NH2
O
N
I
Ph
22a
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)


7.77
7.76
7.75
7.75
7.74
7.72
7.65
7.64
7.61
7.61
7.60
7.60
7.59
7.58
7.58
7.56
7.56
7.55
7.55
7.30
7.29
6.13
5.93
2.42
O
NH2
O
N
I
Me
22b
1H NMR, 500 MHz
CDCl3, 25 °C
3.05
1.00
2.42
2.07
1.29
1.24
3.25
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

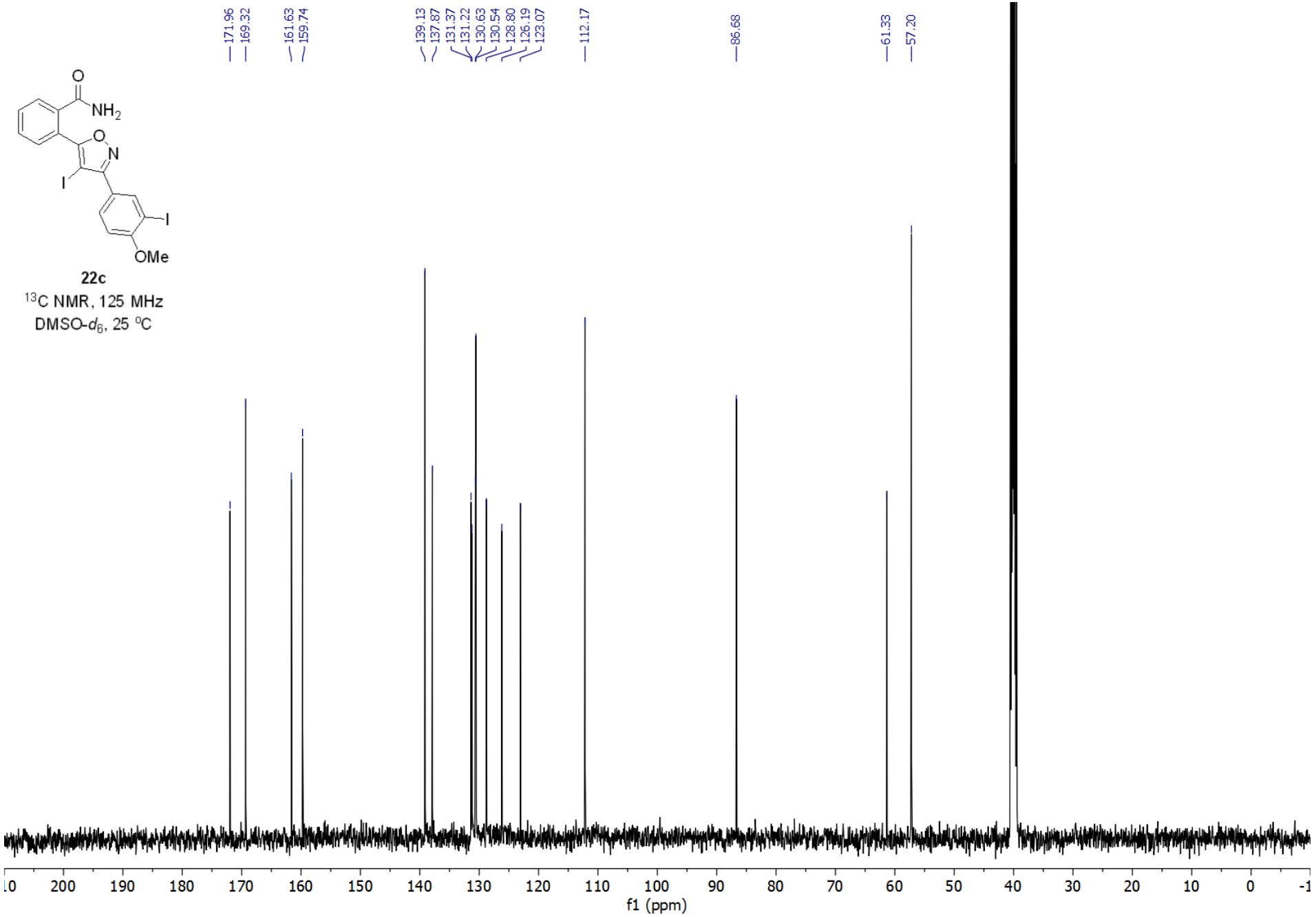

170.32
169.58
163.43
140.26
136.06
131.04
130.86
130.63
129.25
128.60
128.53
125.71
125.45
59.67
21.44
O
NH2
O
N
I
Me
22b
13C NMR, 125 MHz
CDCl3, 25 °C
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

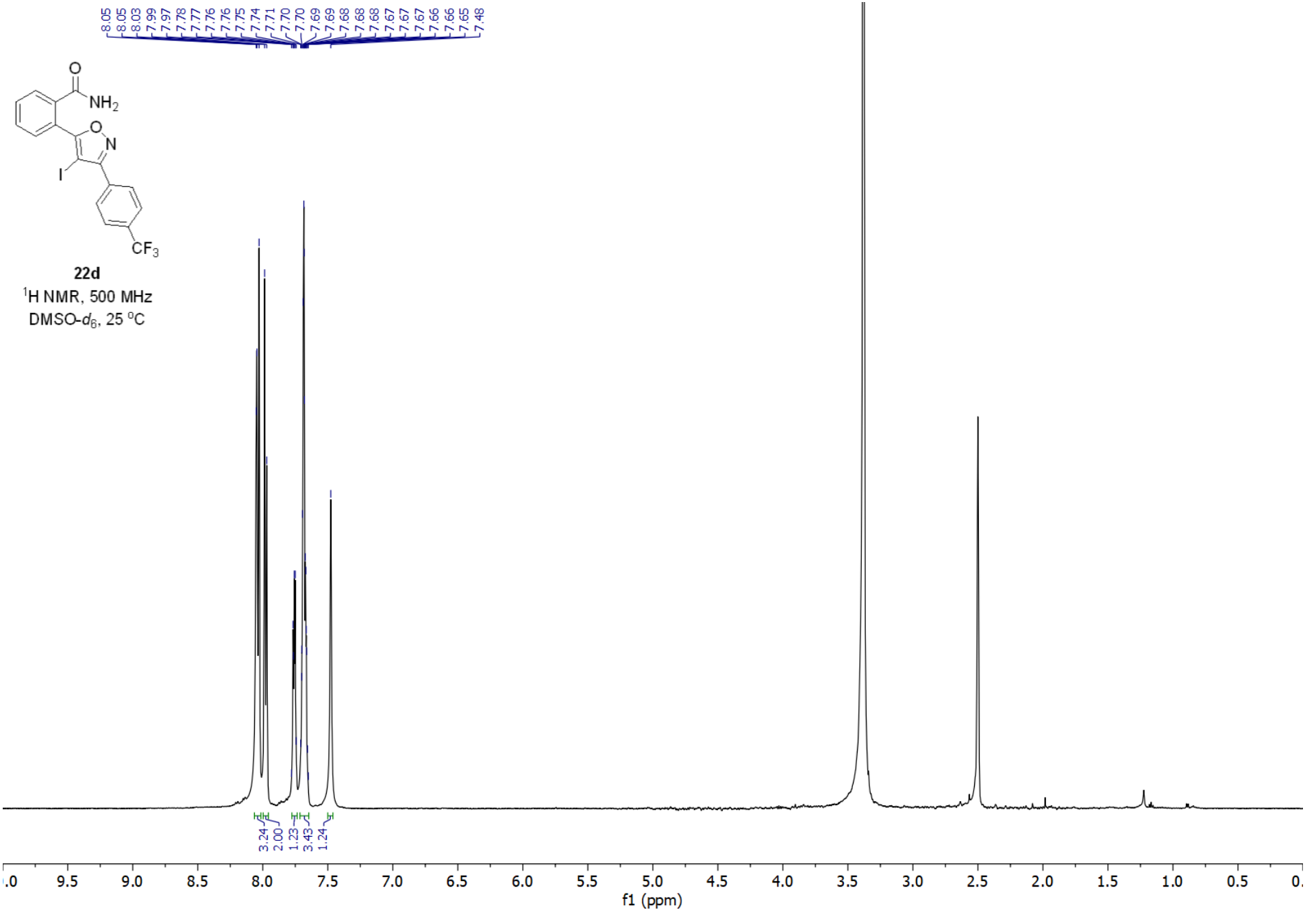


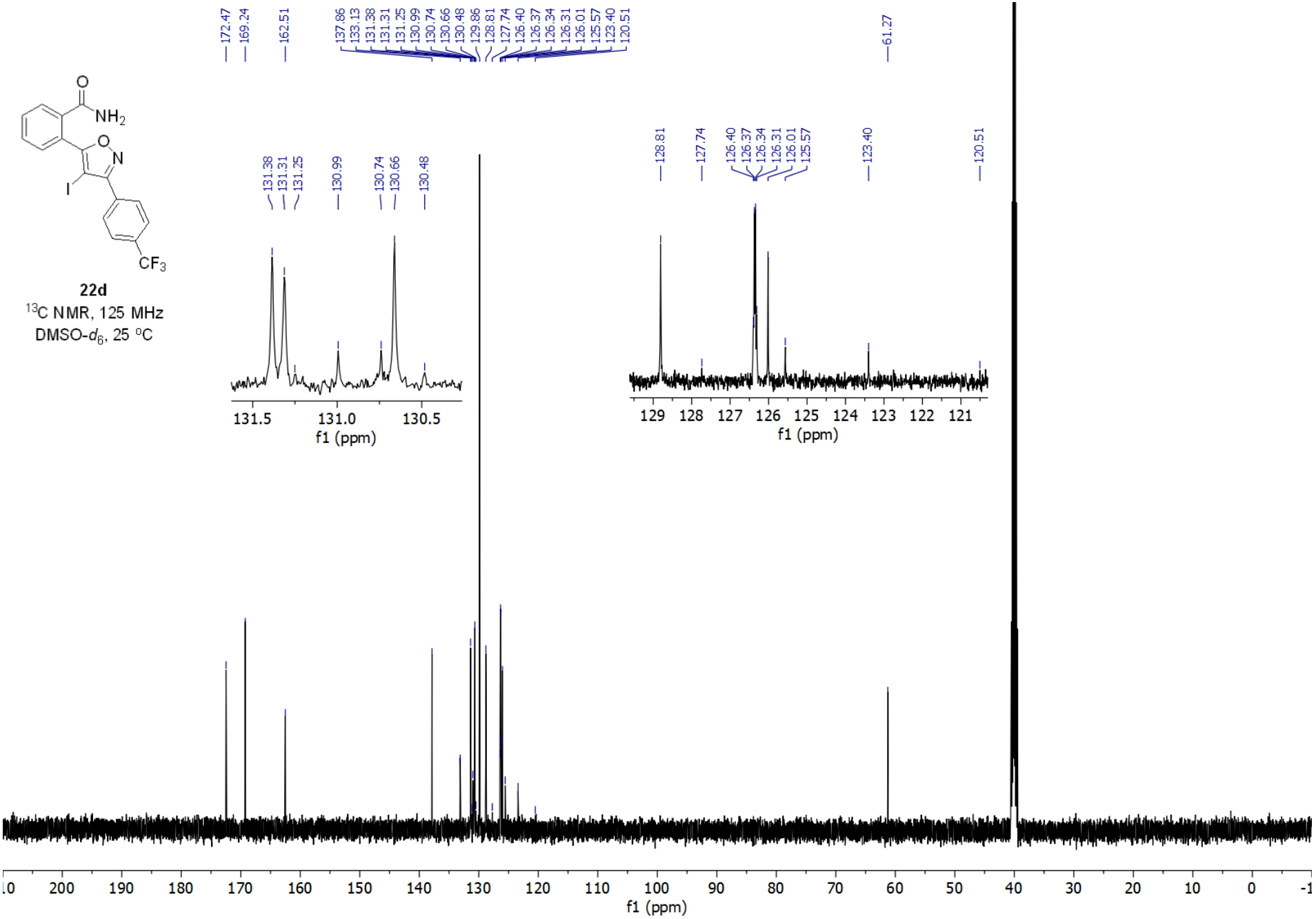
22c

^{1}H NMR, 500 MHz

DMSO-d_6, 25 °C


171.96
169.32
161.63
159.74
139.13
137.87
131.37
131.22
130.63
130.54
128.80
126.19
123.07
112.17
86.68
61.33
57.20
O
NH2
O
N
I
I
OMe
22c
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

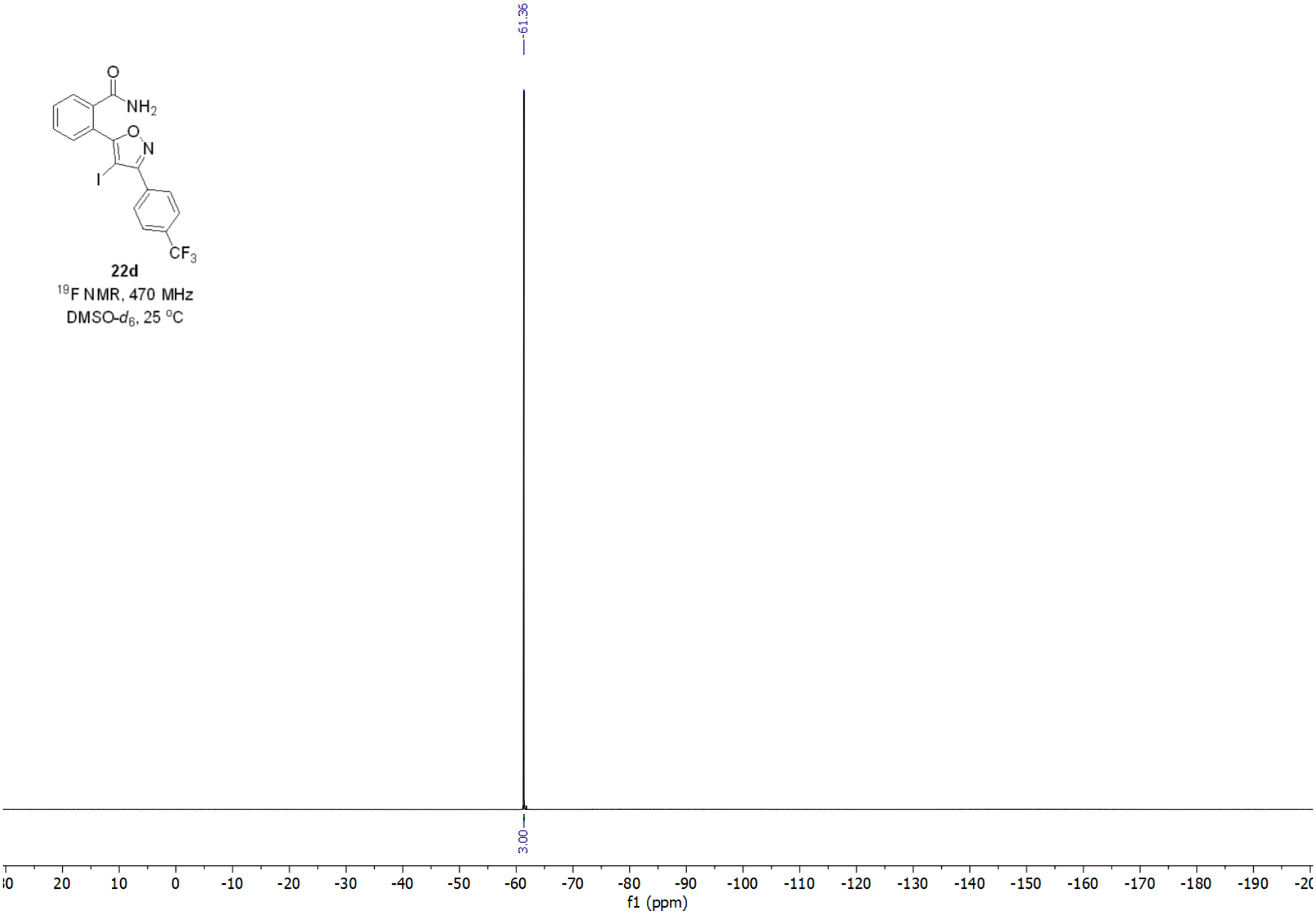

8.05
8.05
8.03
7.99
7.97
7.78
7.77
7.76
7.76
7.75
7.74
7.71
7.70
7.70
7.69
7.69
7.68
7.68
7.68
7.67
7.67
7.67
7.66
7.66
7.65
7.48
O
NH2
O
N
I
CF3
22d
1H NMR, 500 MHz
DMSO-d6, 25 °C
3.24
2.00
1.23
3.43
1.24
f1 (ppm)

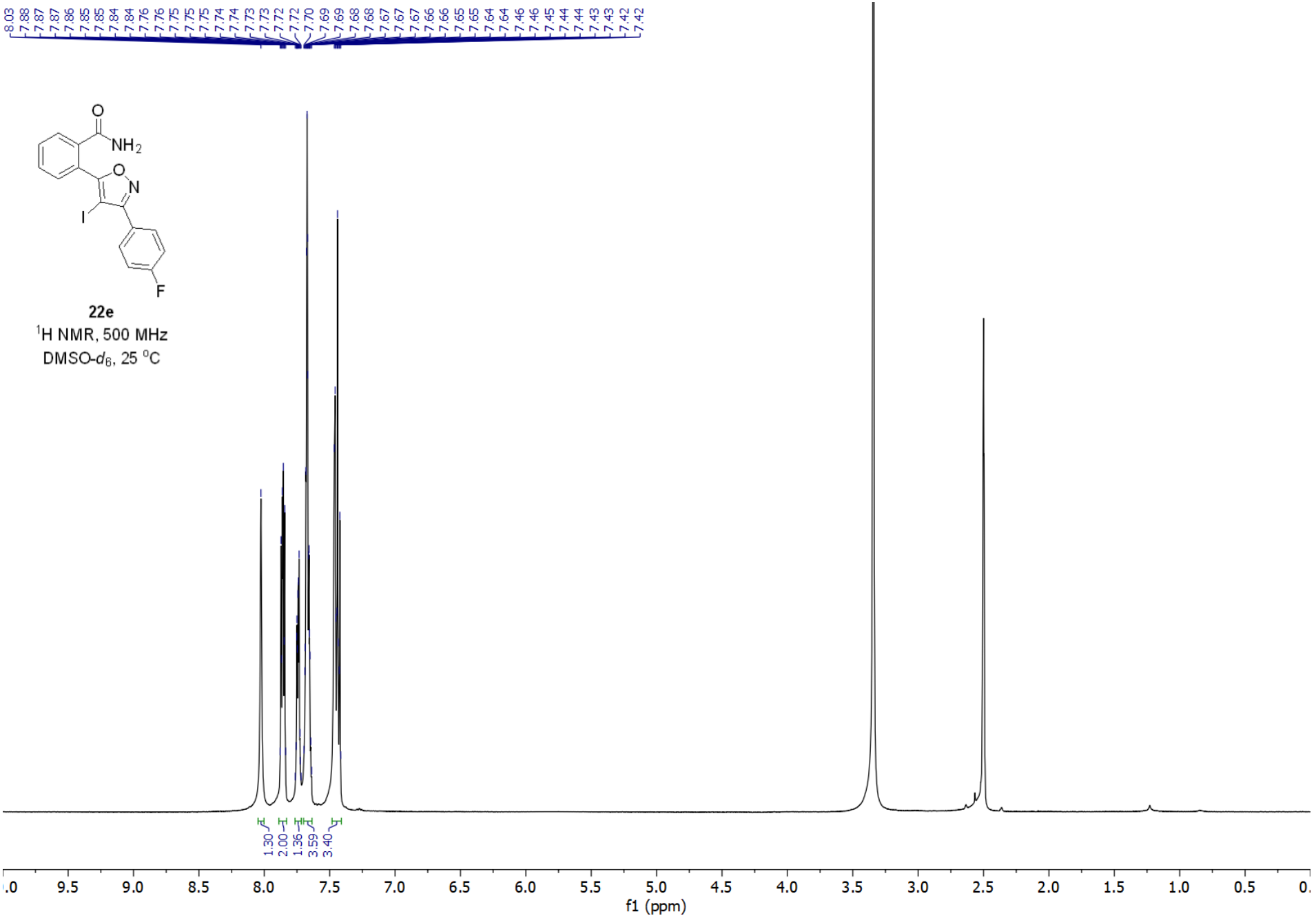

O
NH2
O
N
I
CF3
22d
13C NMR, 125 MHz
DMSO-d6, 25 °C
172.47
169.24
162.51
137.86
133.13
131.38
131.31
131.25
130.99
130.74
130.66
130.48
129.86
128.81
127.74
126.40
126.37
126.34
126.31
126.01
125.57
123.40
120.51
61.27
131.38
131.31
131.25
130.99
130.74
130.66
130.48
131.5
131.0
130.5
f1 (ppm)
128.81
127.74
126.40
126.37
126.34
126.31
126.01
125.57
123.40
120.51
129
128
127
126
125
124
123
122
121
f1 (ppm)
f1 (ppm)

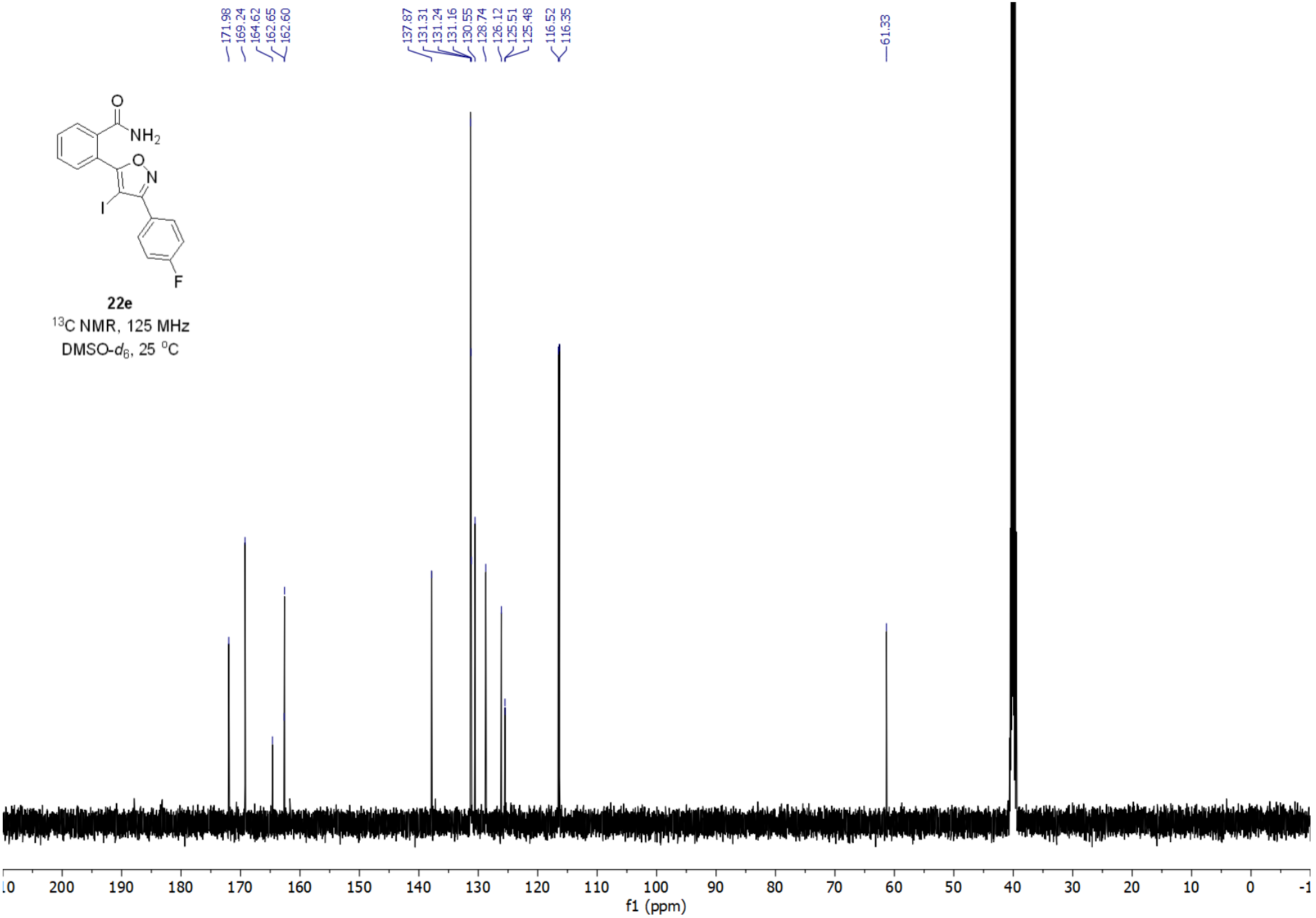
22d

^{19}F NMR, 470 MHz

DMSO-d_6, 25 ^{o}C



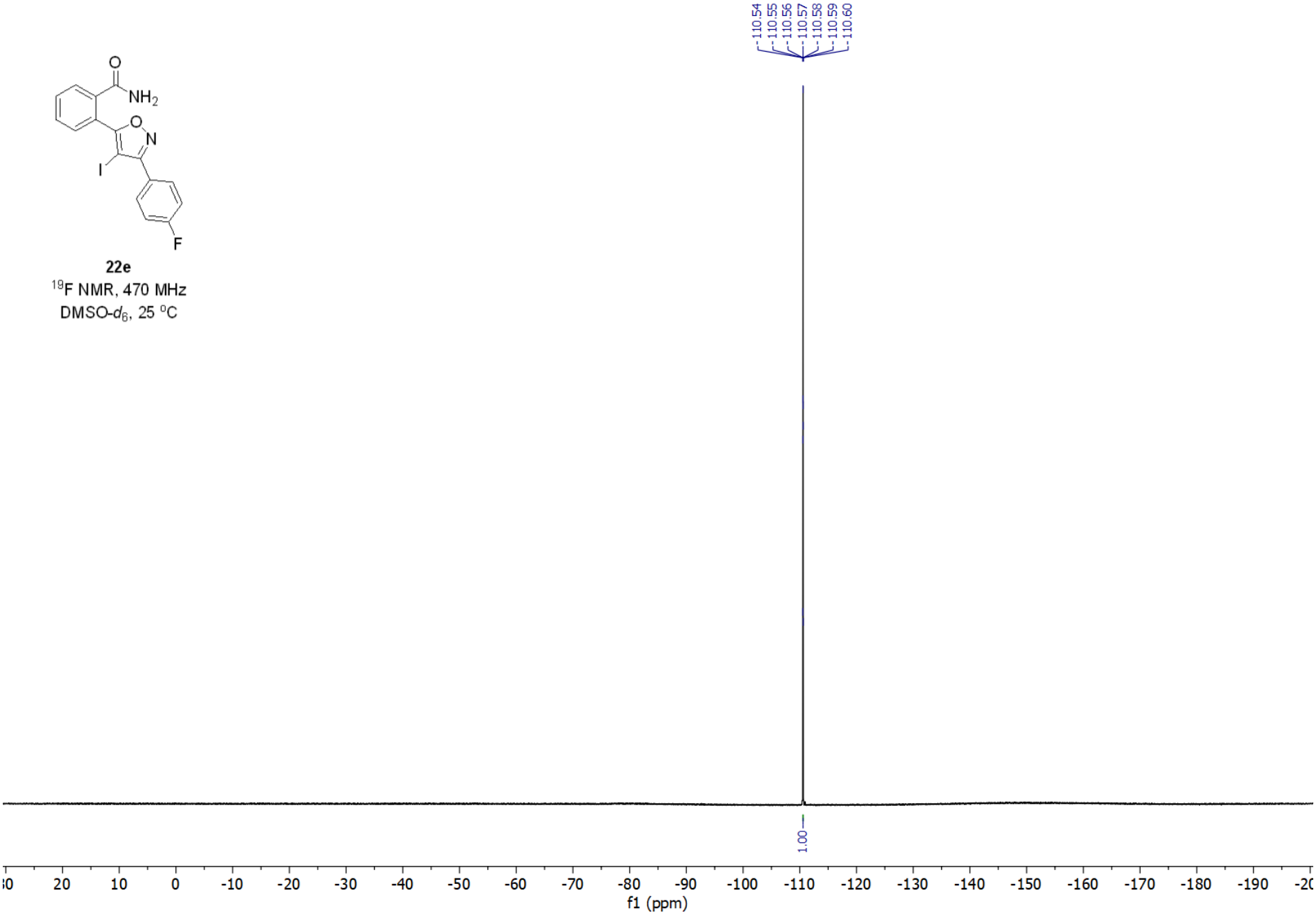

8.03
7.88
7.87
7.87
7.86
7.85
7.85
7.84
7.84
7.76
7.76
7.75
7.75
7.75
7.74
7.74
7.73
7.73
7.72
7.72
7.70
7.69
7.69
7.68
7.68
7.67
7.67
7.67
7.66
7.66
7.65
7.65
7.64
7.64
7.46
7.46
7.45
7.44
7.44
7.43
7.43
7.42
7.42
O
NH2
O
N
I
F
22e
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.30
2.00
1.36
3.59
3.40
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


171.98
169.24
164.62
162.65
162.60
137.87
131.31
131.24
131.16
130.55
128.74
126.12
125.51
125.48
116.52
116.35
61.33
O
NH2
O
N
I
F
22e
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

22e

^{19}F NMR, 470 MHz

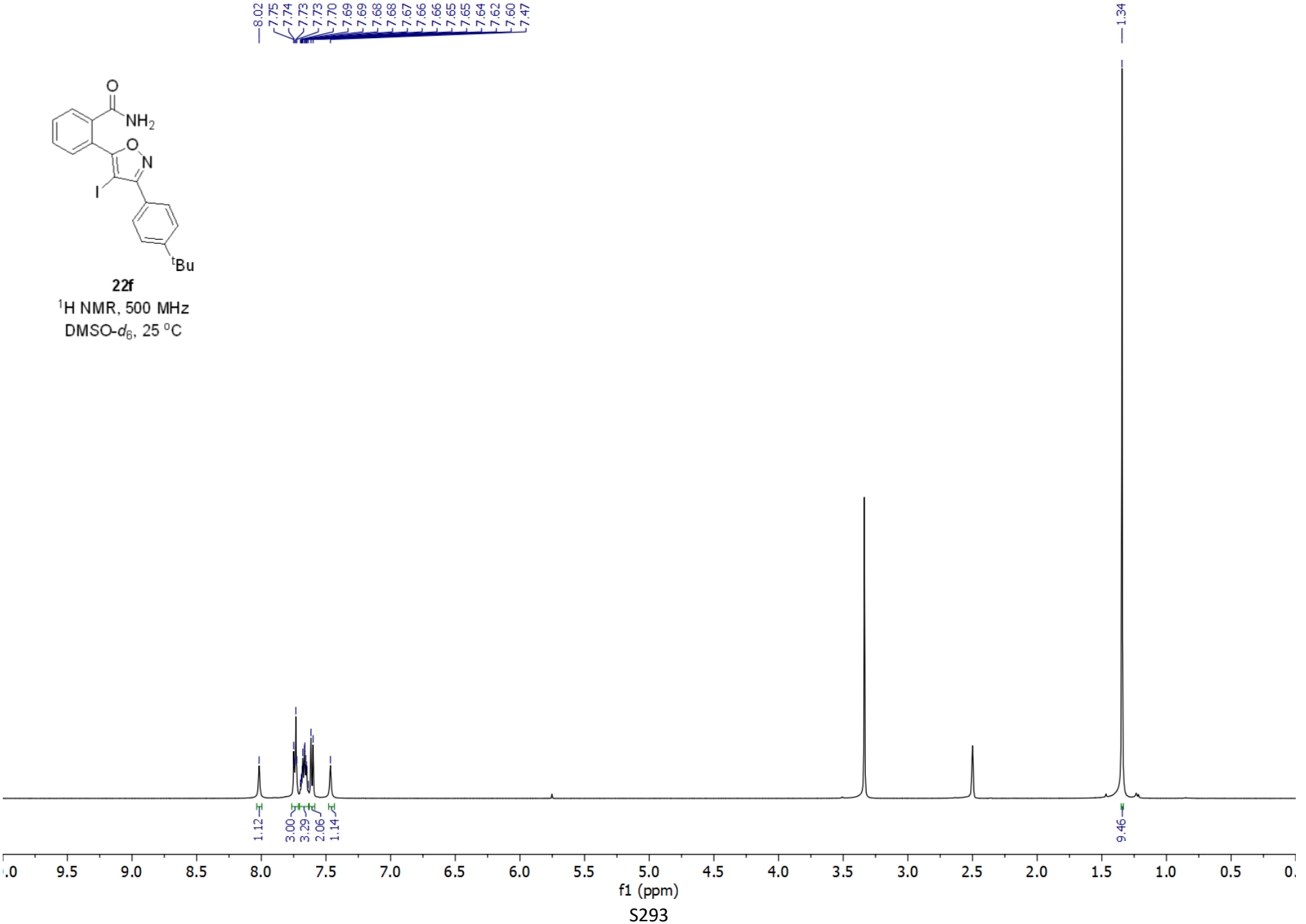
DMSO-d_6, 25 ^{0}C

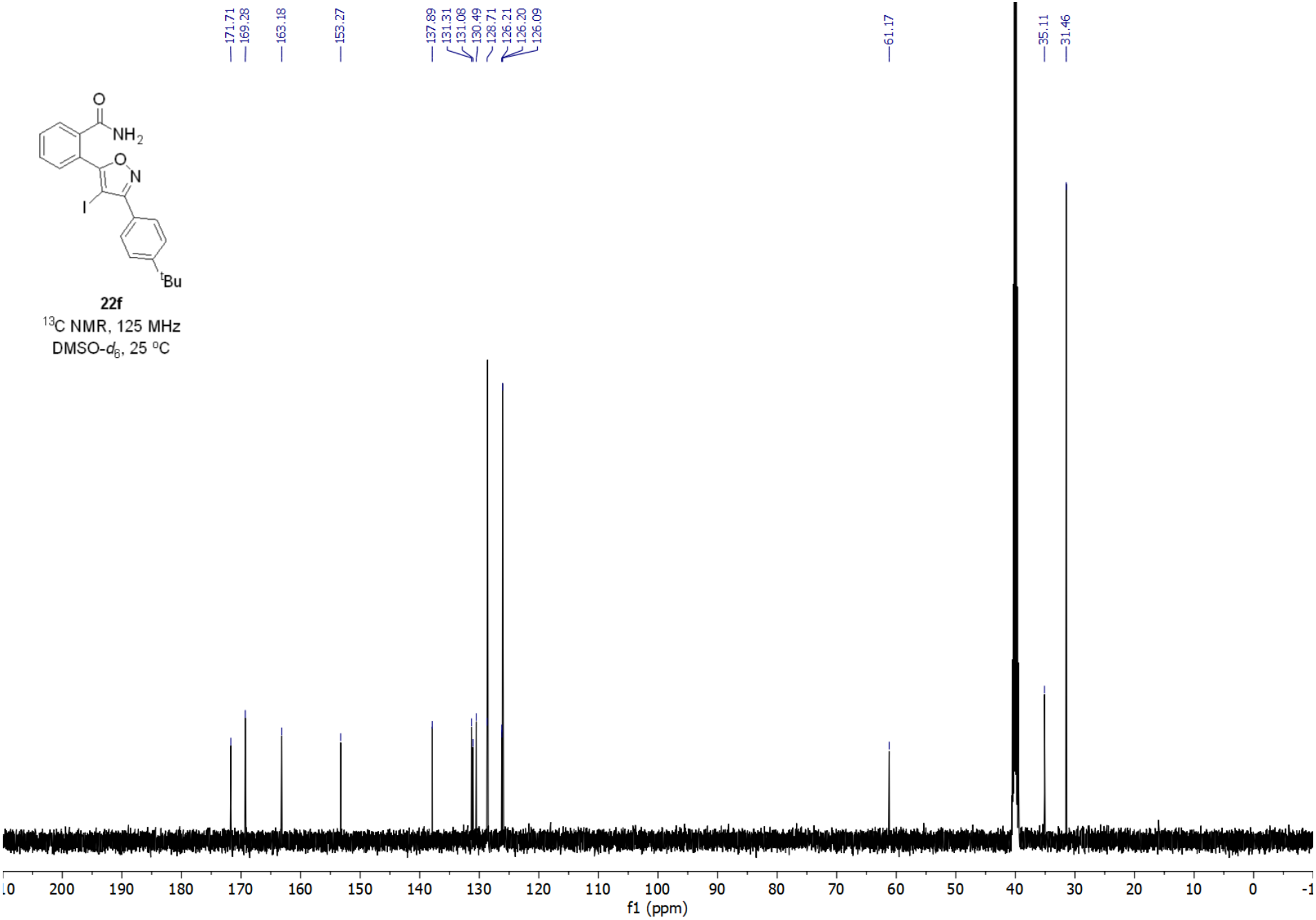


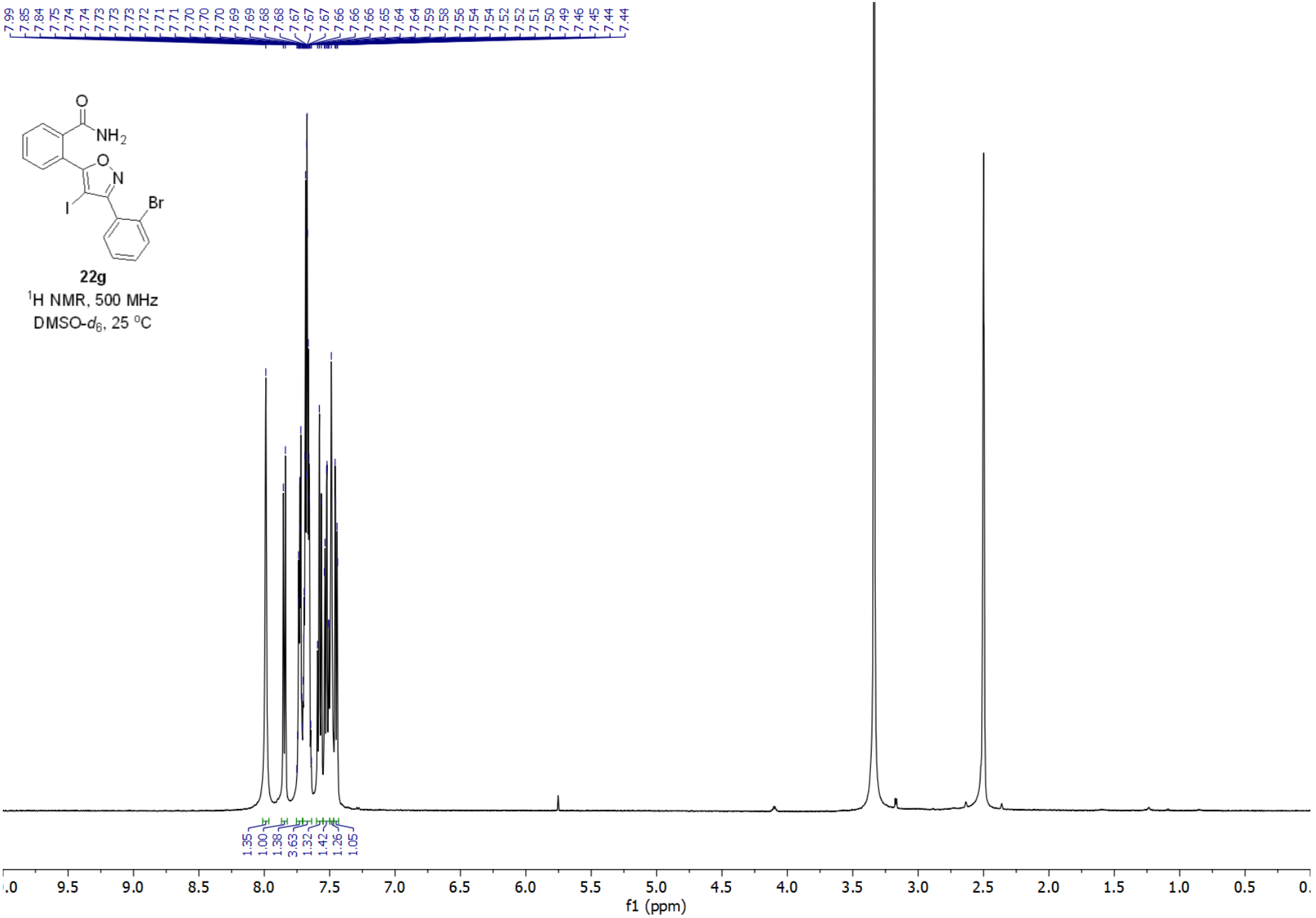
22f

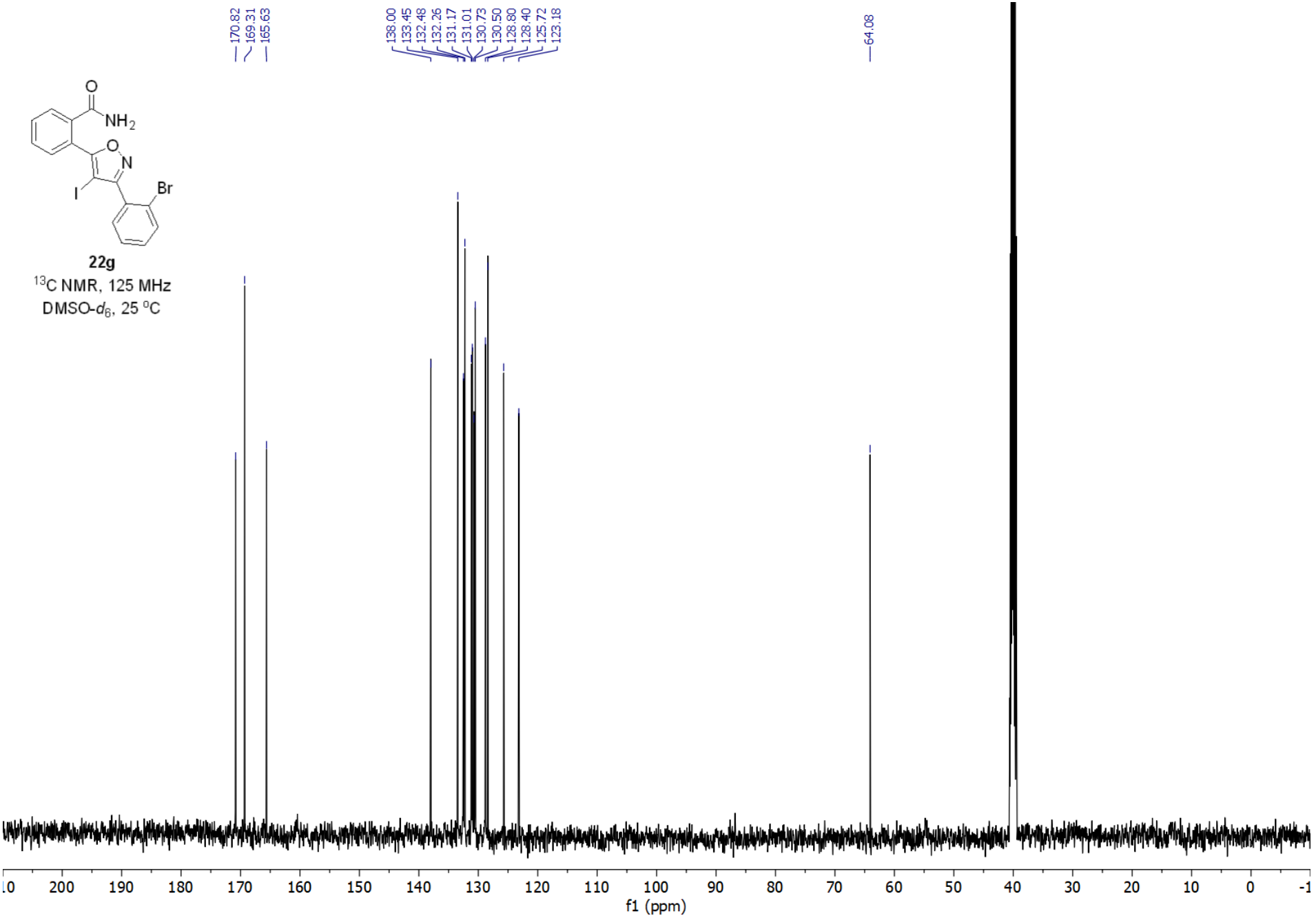
^{1}H NMR, 500 MHz

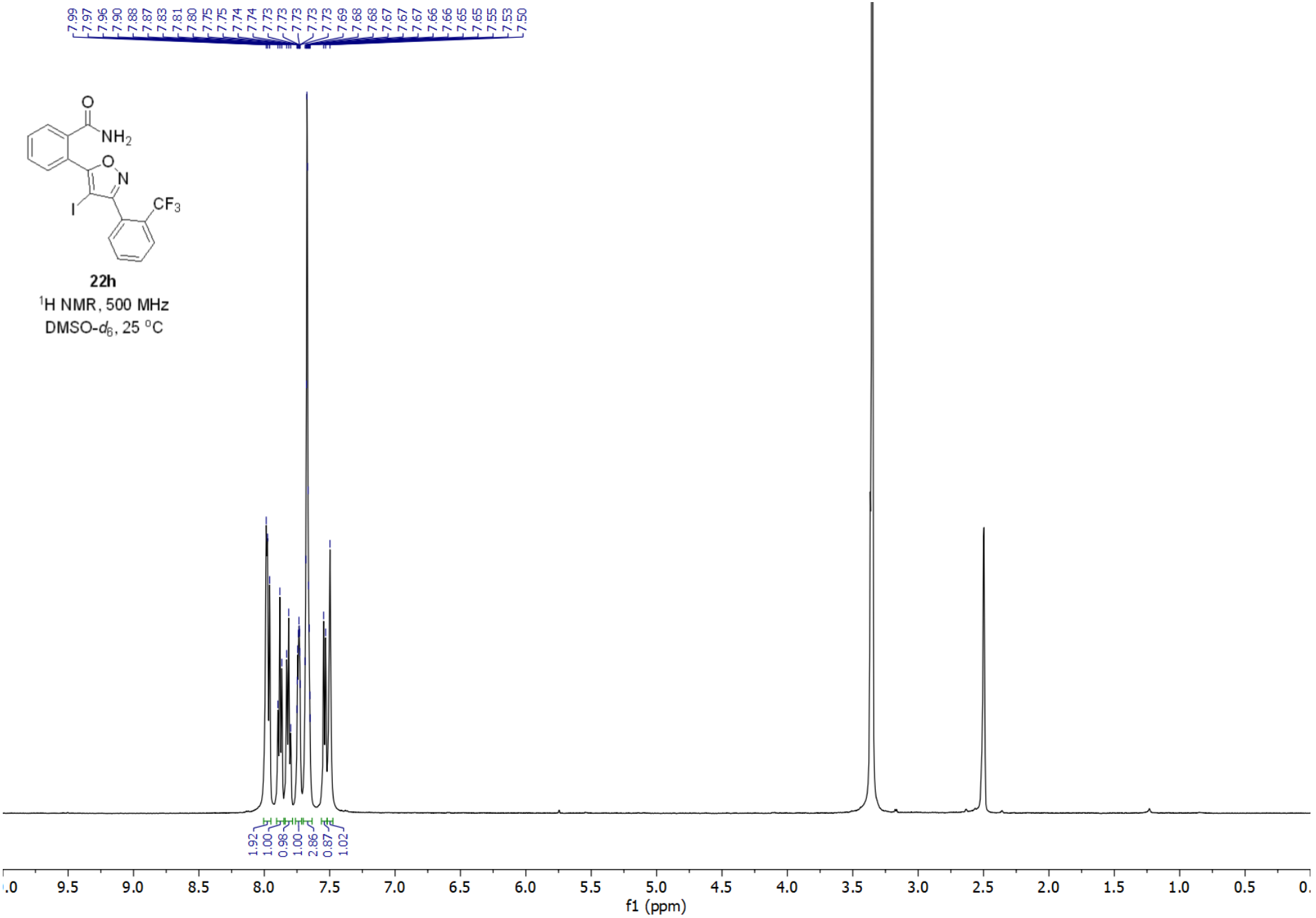
DMSO-d_6, 25 °C

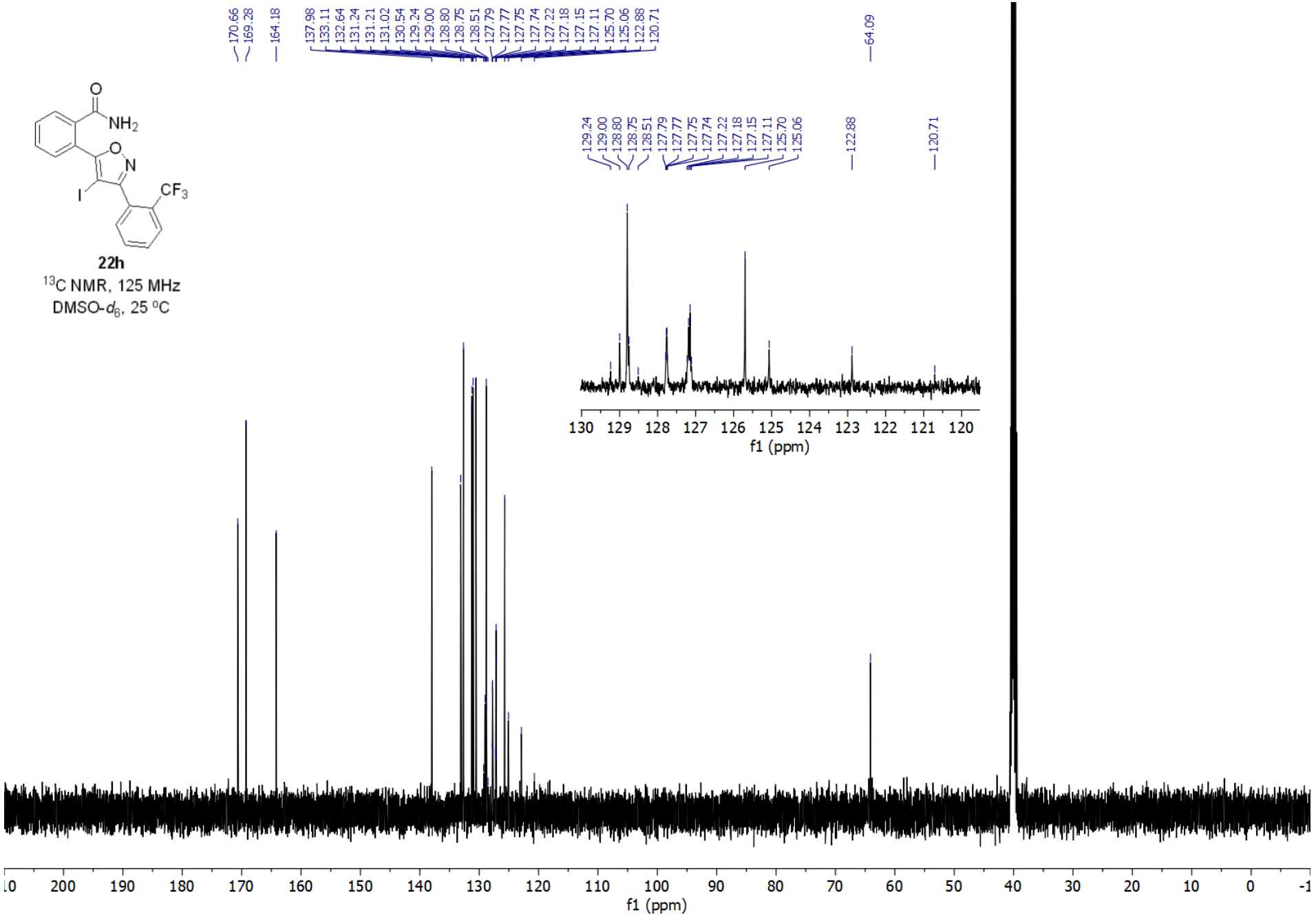



171.71
169.28
163.18
153.27
137.89
131.31
131.08
130.49
128.71
126.21
126.20
126.09
61.17
35.11
31.46
O
NH2
O
N
I
tBu
22f
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)


7.99
7.85
7.84
7.75
7.74
7.74
7.73
7.73
7.72
7.71
7.71
7.70
7.70
7.70
7.69
7.69
7.68
7.68
7.67
7.67
7.67
7.66
7.66
7.66
7.65
7.64
7.64
7.59
7.58
7.56
7.54
7.54
7.52
7.52
7.51
7.50
7.49
7.46
7.45
7.44
7.44
O
NH2
O
N
I
Br
22g
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.35
1.00
1.38
3.63
1.32
1.42
1.26
1.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


170.82
169.31
165.63
138.00
133.45
132.48
132.26
131.17
131.01
130.73
130.50
128.80
128.40
125.72
123.18
64.08
O
NH2
O
N
I
Br
22g
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

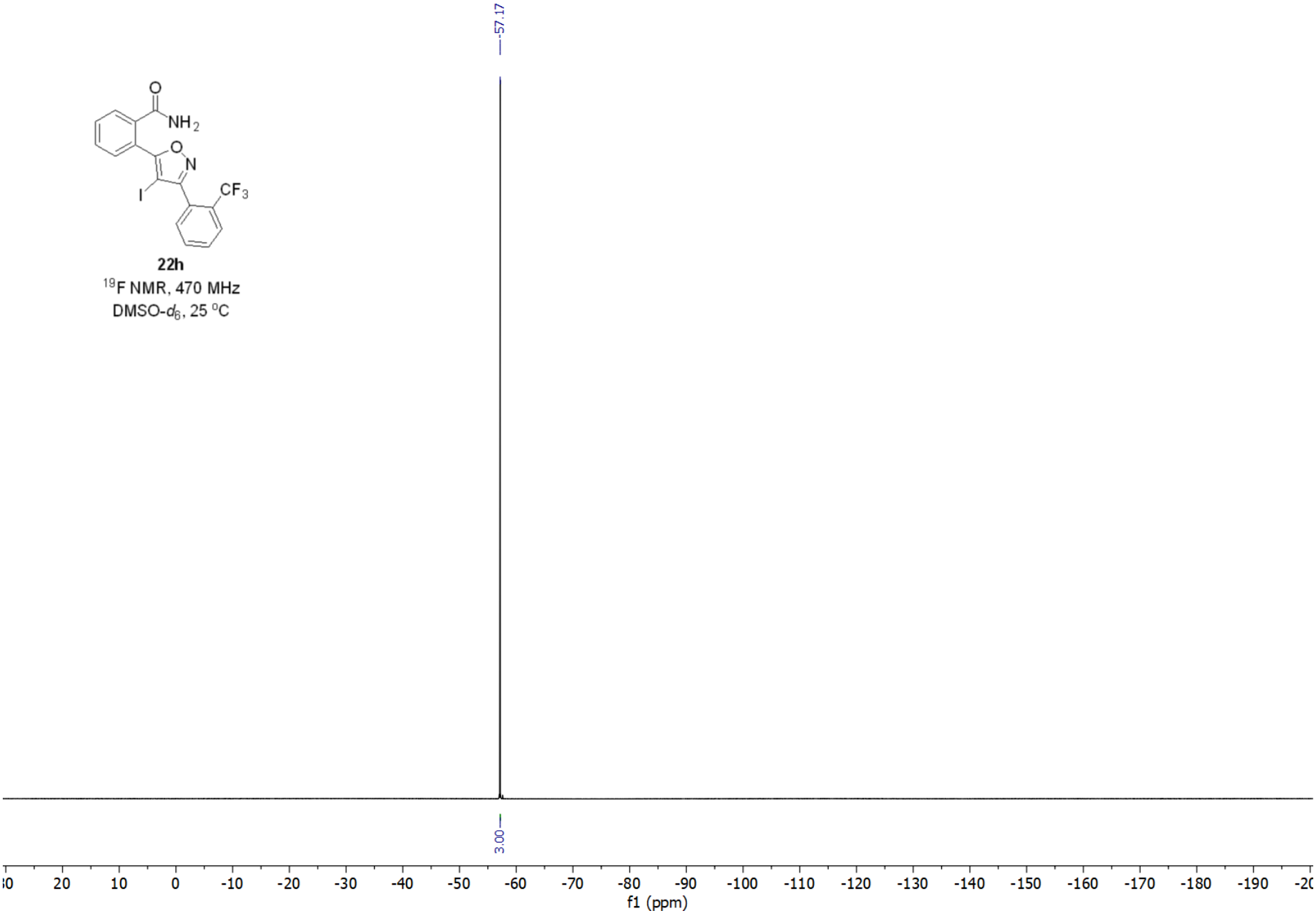

7.99
7.97
7.96
7.90
7.88
7.87
7.83
7.81
7.80
7.75
7.75
7.74
7.74
7.73
7.73
7.73
7.73
7.73
7.69
7.68
7.68
7.67
7.67
7.67
7.66
7.66
7.65
7.65
7.55
7.53
7.50
O
NH2
O
N
I
CF3
22h
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.92
1.00
0.98
1.00
2.86
0.87
1.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

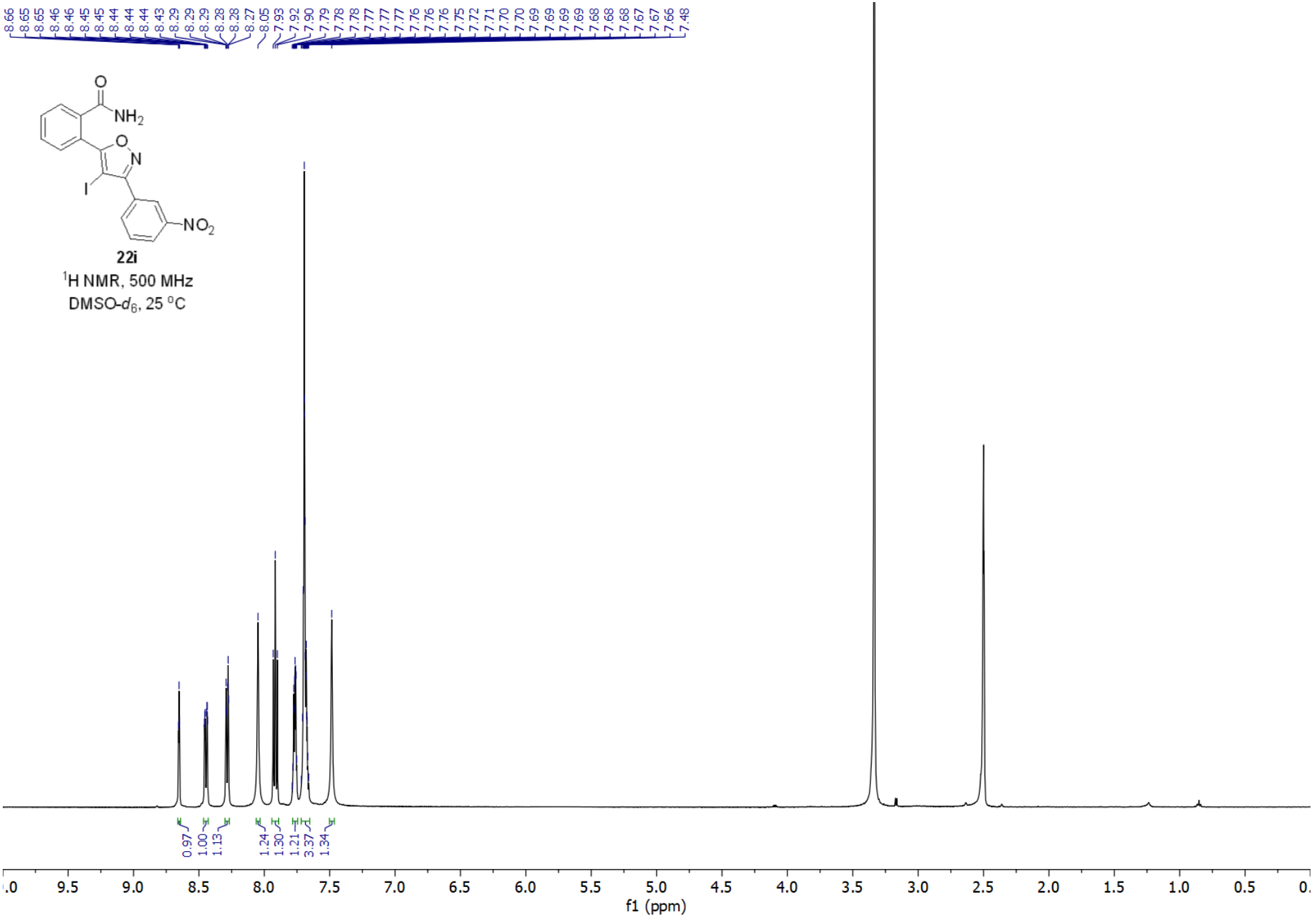

170.66
169.28
164.18
137.98
133.11
132.64
131.24
131.21
131.02
130.54
129.24
129.00
128.80
128.75
128.51
127.79
127.77
127.75
127.74
127.22
127.18
127.15
127.11
125.70
125.06
122.88
120.71
64.09
O
NH2
O
N
I
CF3
22h
13C NMR, 125 MHz
DMSO-d6, 25 °C
130 129 128 127 126 125 124 123 122 121 120
f1 (ppm)
f1 (ppm)

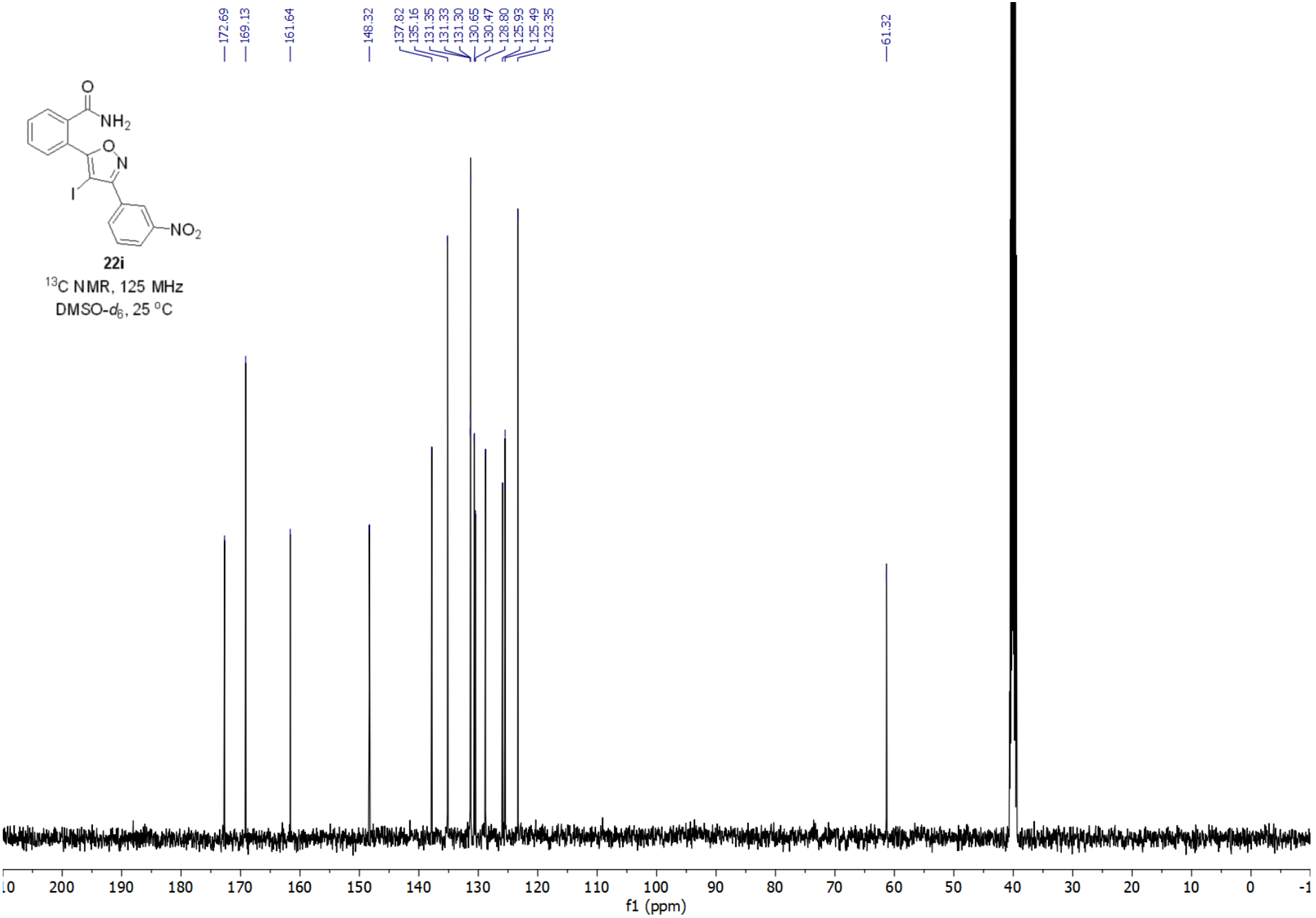
22h

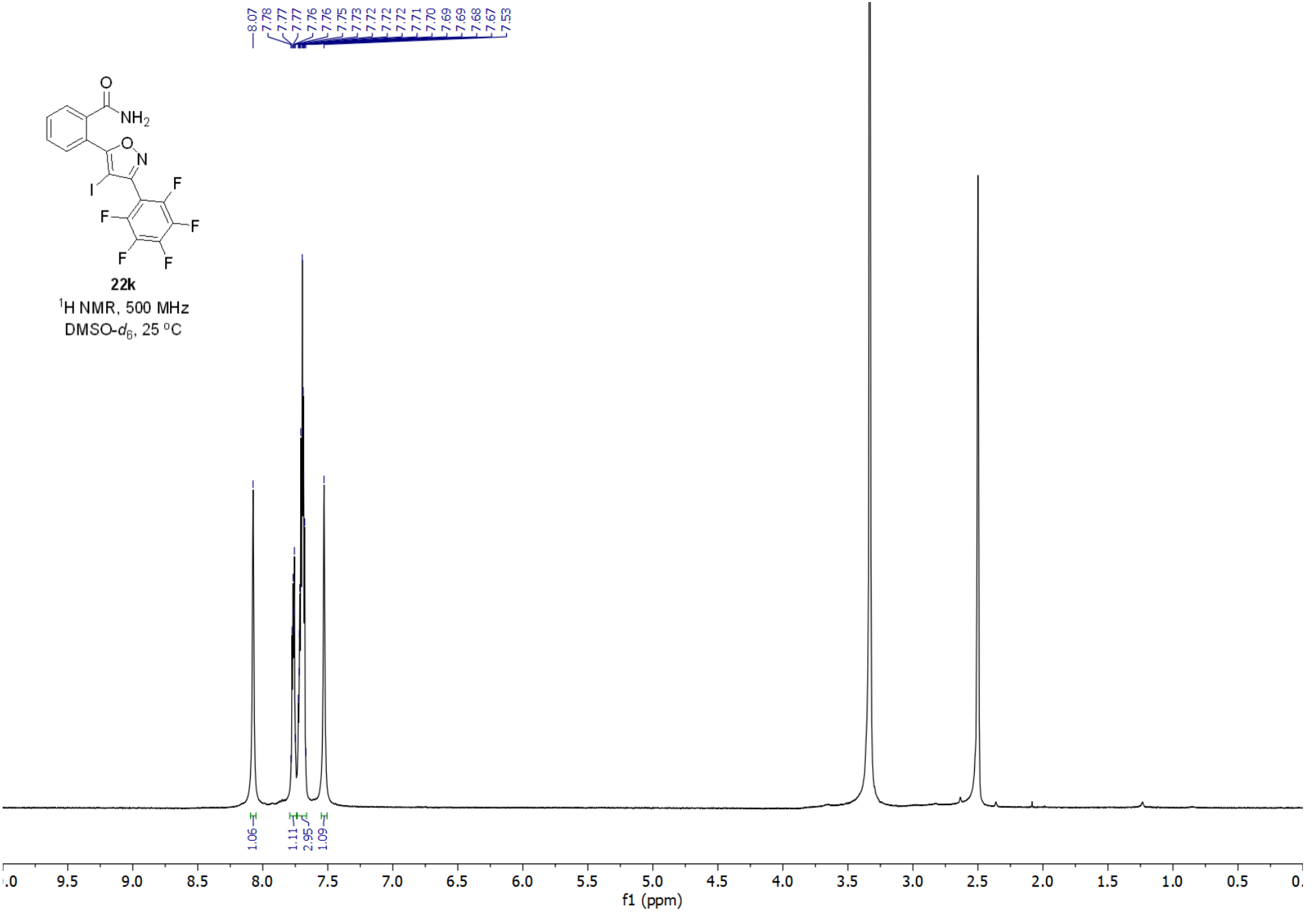
^{19}F NMR, 470 MHz

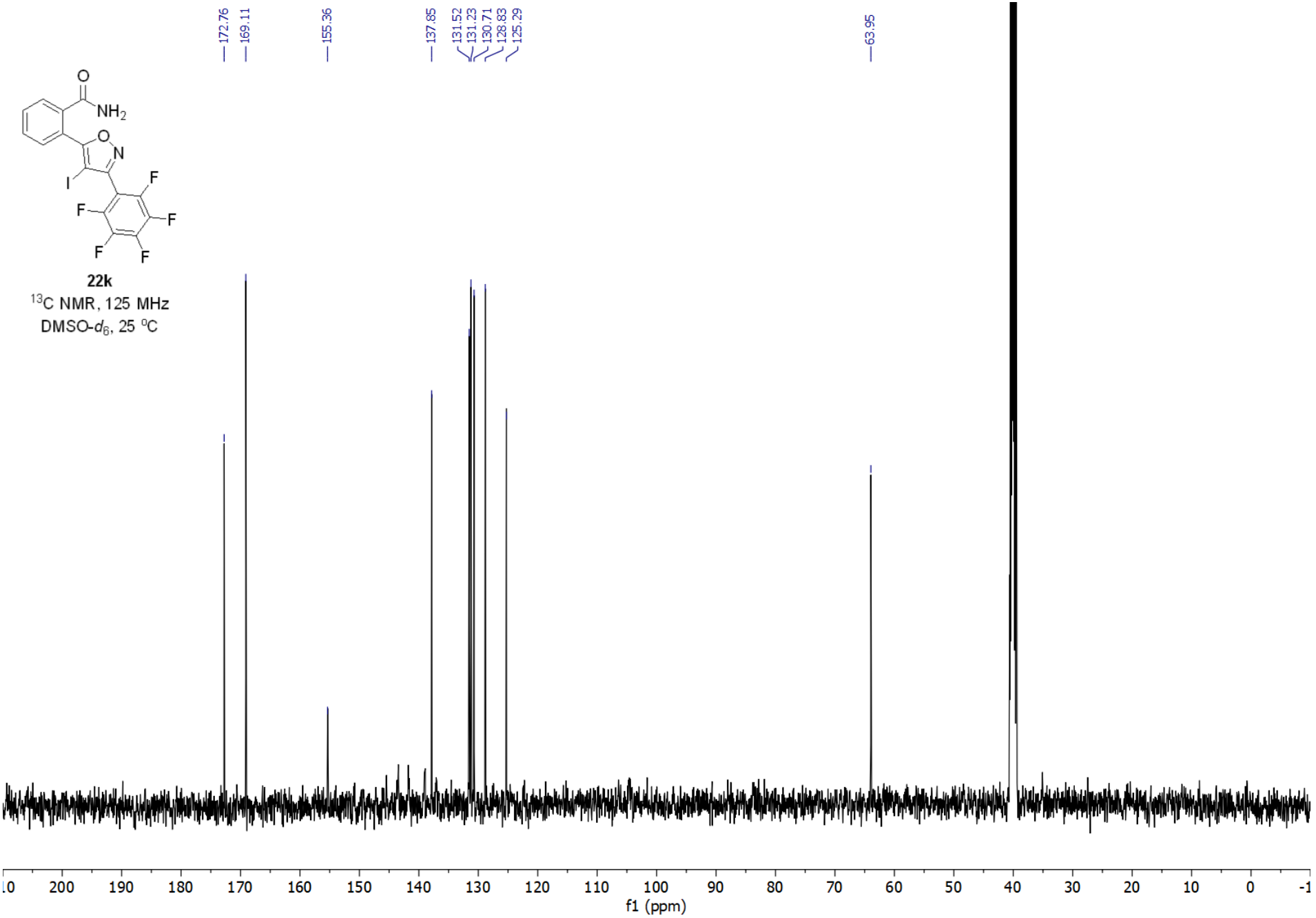
DMSO-d_6, 25 °C




8.66 8.65 8.65 8.46 8.46 8.45 8.45 8.44 8.44 8.44 8.43 8.29 8.29 8.29 8.28 8.28 8.27 8.05 7.93 7.92 7.90 7.79 7.78 7.78 7.77 7.77 7.77 7.76 7.76 7.76 7.75 7.72 7.71 7.70 7.70 7.69 7.69 7.69 7.69 7.68 7.68 7.68 7.67 7.67 7.66 7.48
O
NH2
O
N
I
NO2
22i
1H NMR, 500 MHz
DMSO-d6, 25 °C
0.97 1.00 1.13 1.24 1.30 1.21 3.37 1.34
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


172.69
169.13
161.64
148.32
137.82
135.16
131.35
131.33
131.30
130.65
130.47
128.80
125.93
125.49
123.35
61.32
O
NH2
O
N
I
NO2
22i
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

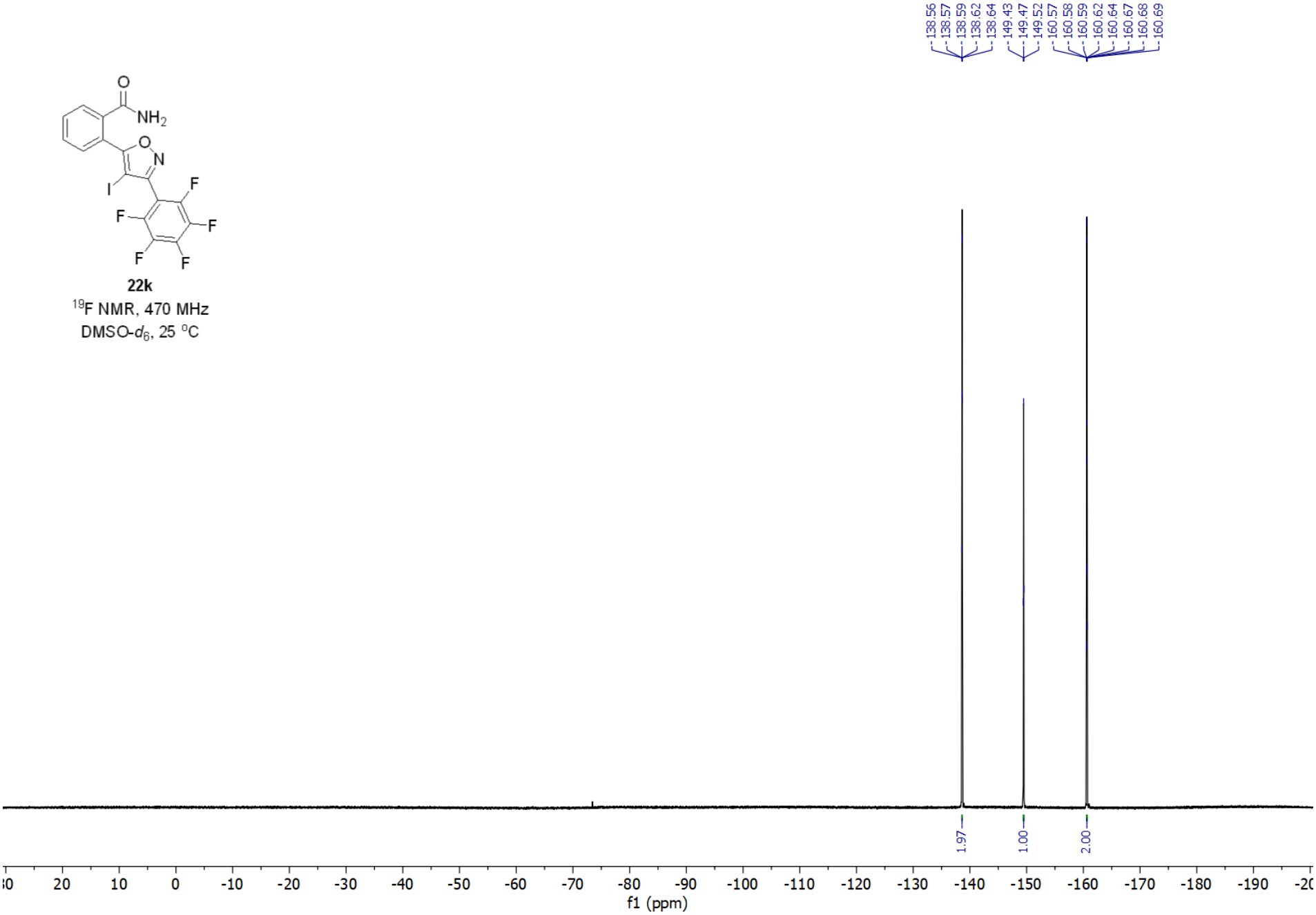

8.07
7.78
7.77
7.77
7.76
7.76
7.75
7.73
7.72
7.72
7.72
7.71
7.70
7.69
7.69
7.68
7.67
7.53
O
NH2
O
N
I
F
F
F
F
F
22k
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.06
1.11
2.95
1.09
f1 (ppm)

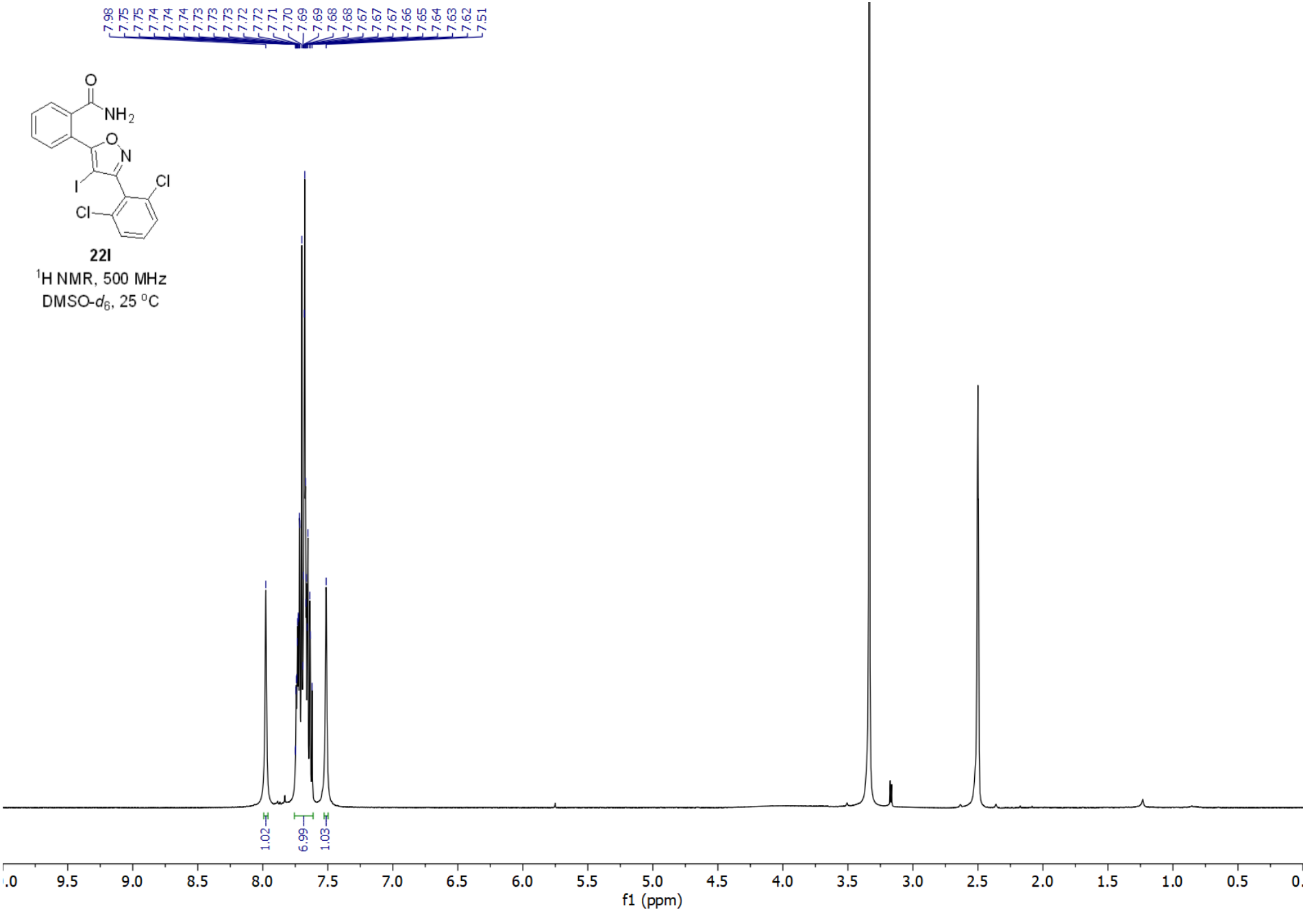

172.76
169.11
155.36
137.85
131.52
131.23
130.71
128.83
125.29
63.95
O
NH2
O
N
I
F
F
F
F
F
22k
13C NMR, 125 MHz
DMSO-d6, 25 °C
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

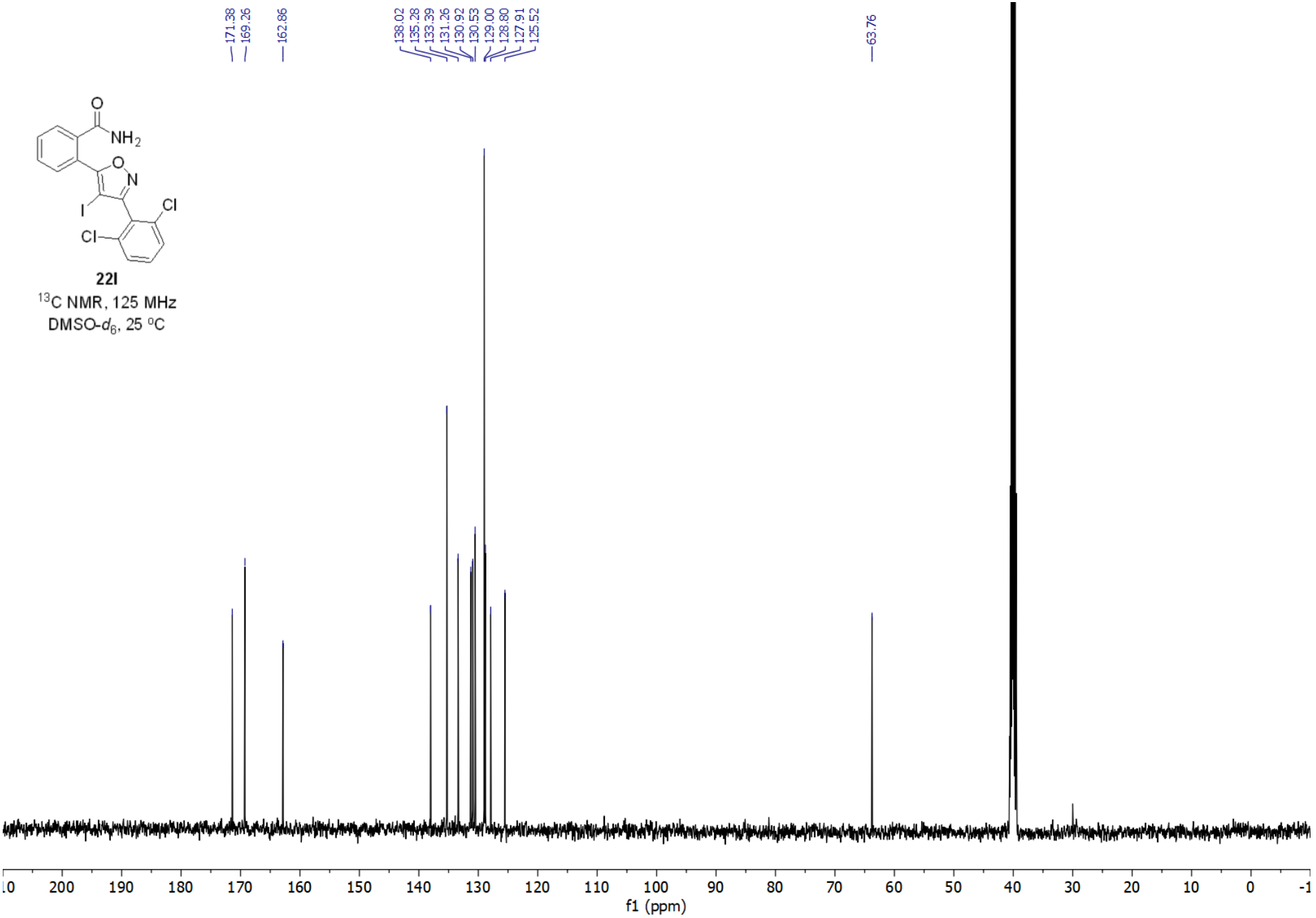
22k

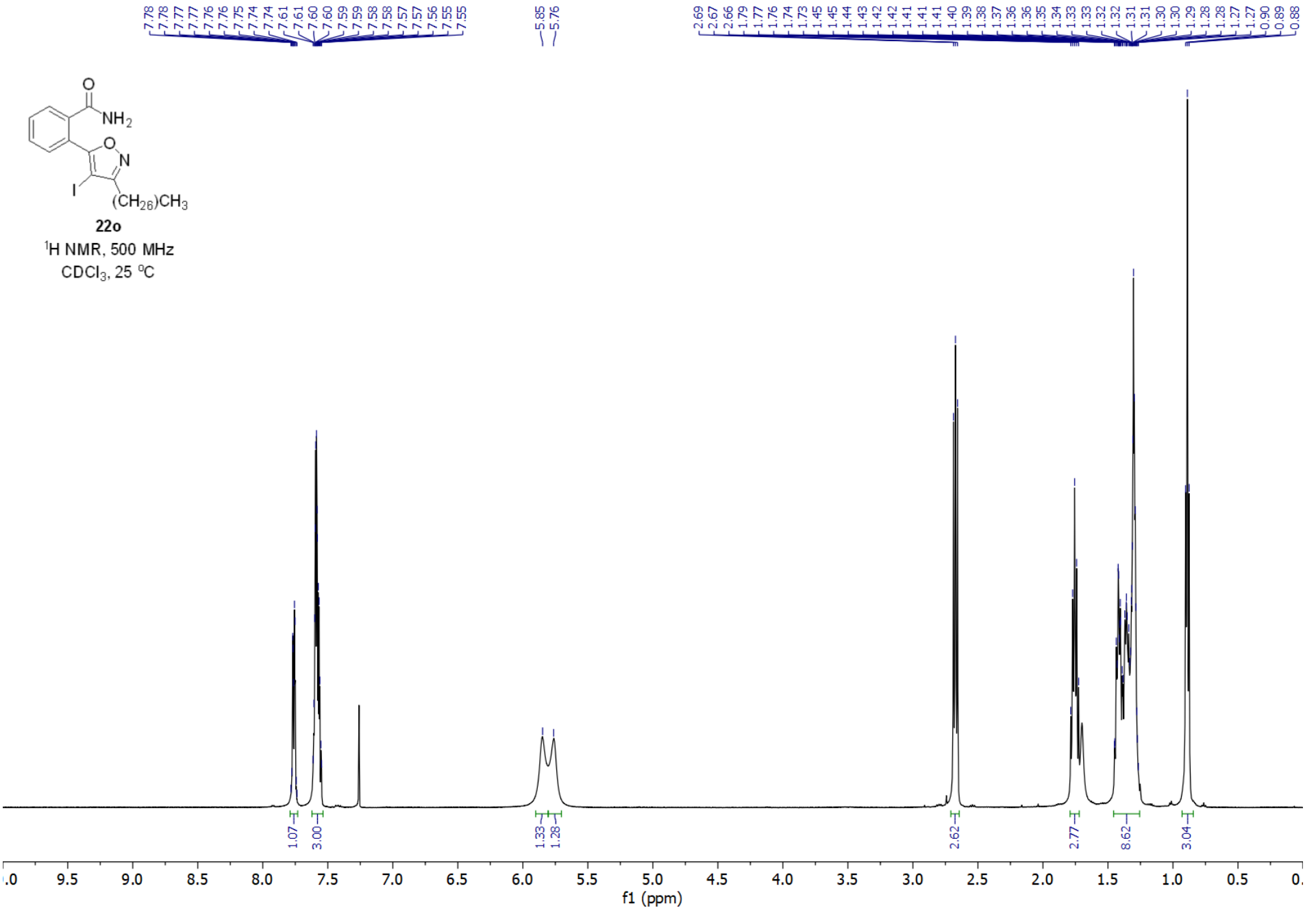
^{19}F NMR, 470 MHz

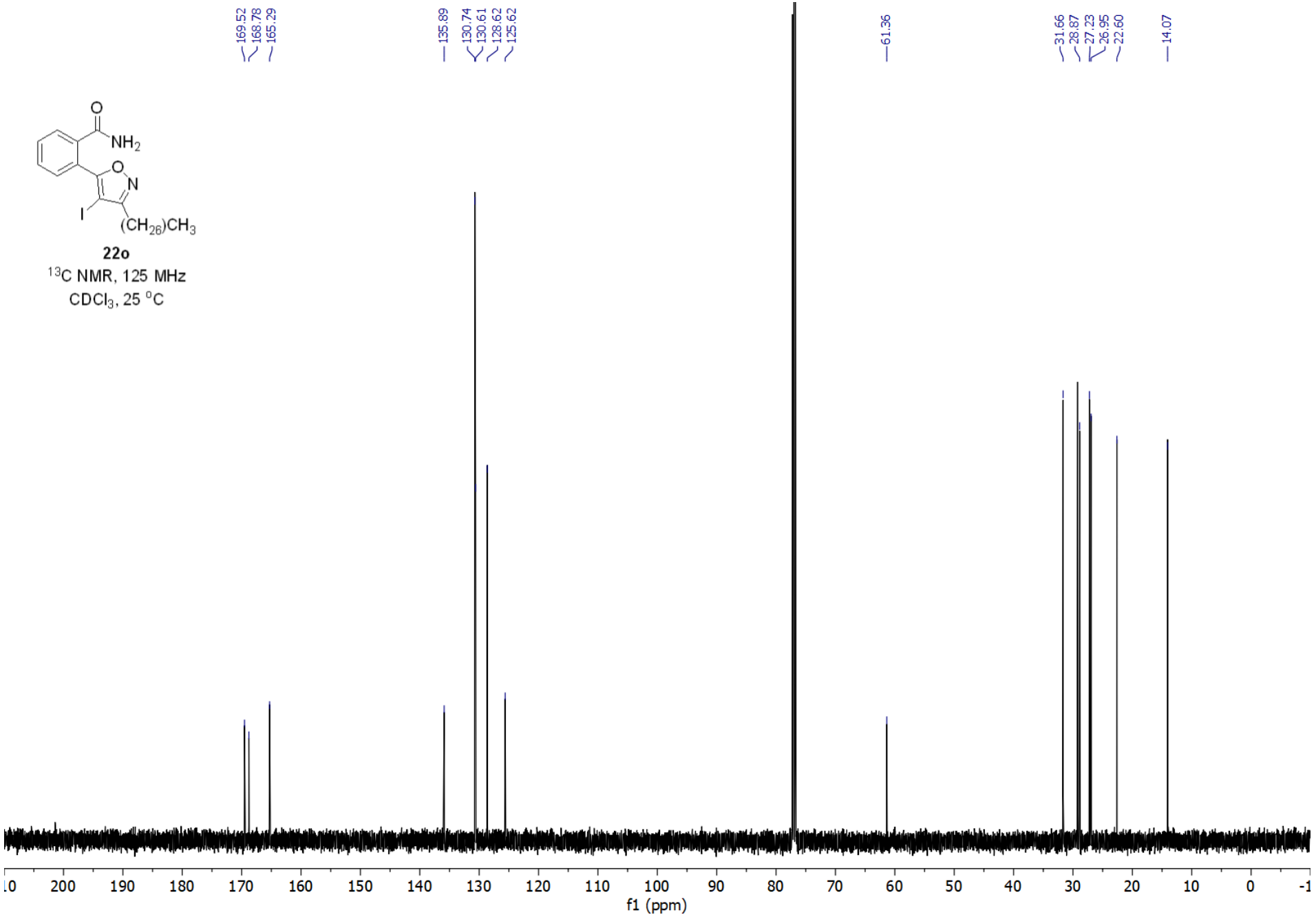
DMSO-d_6, 25 ^{0}C

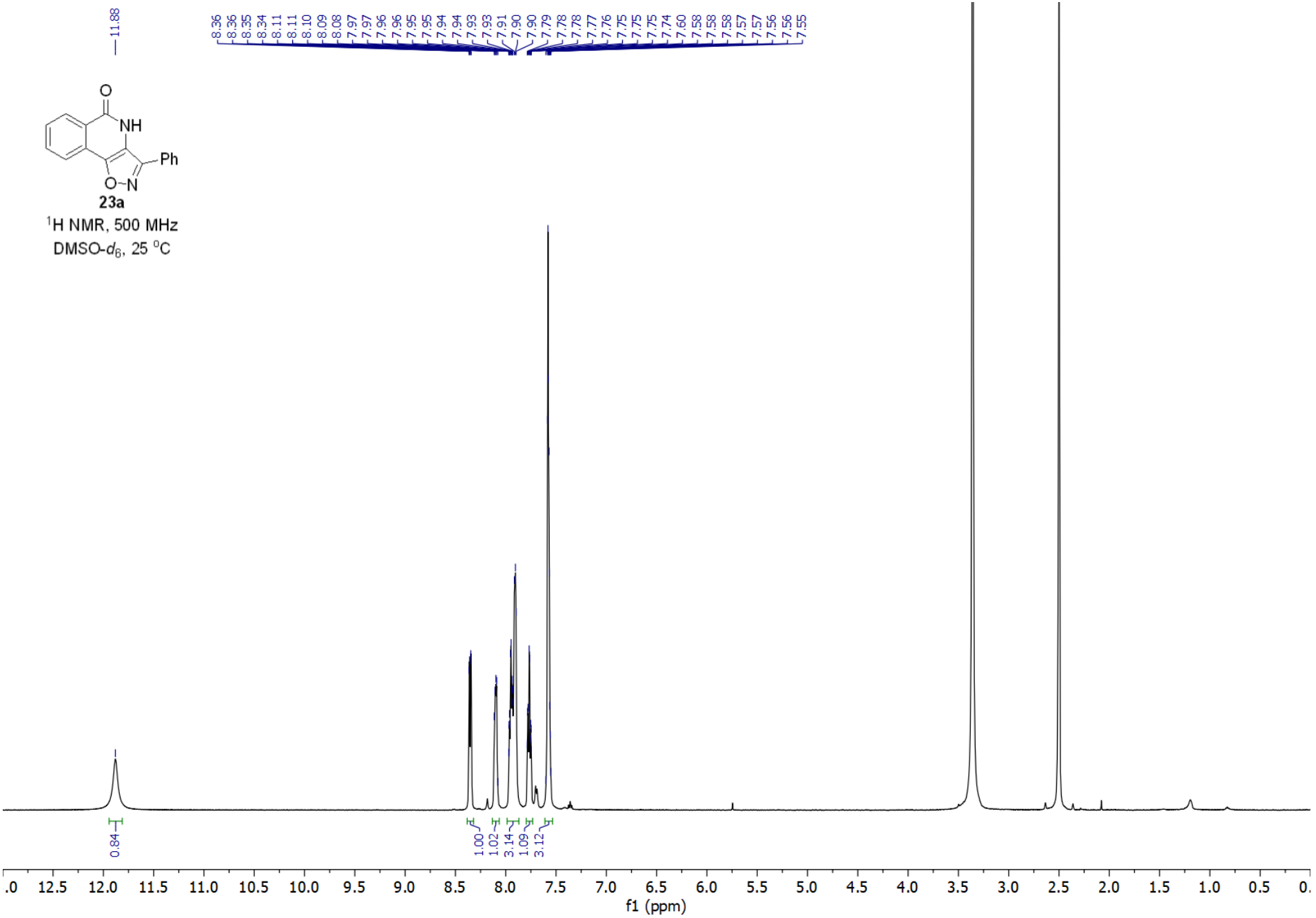


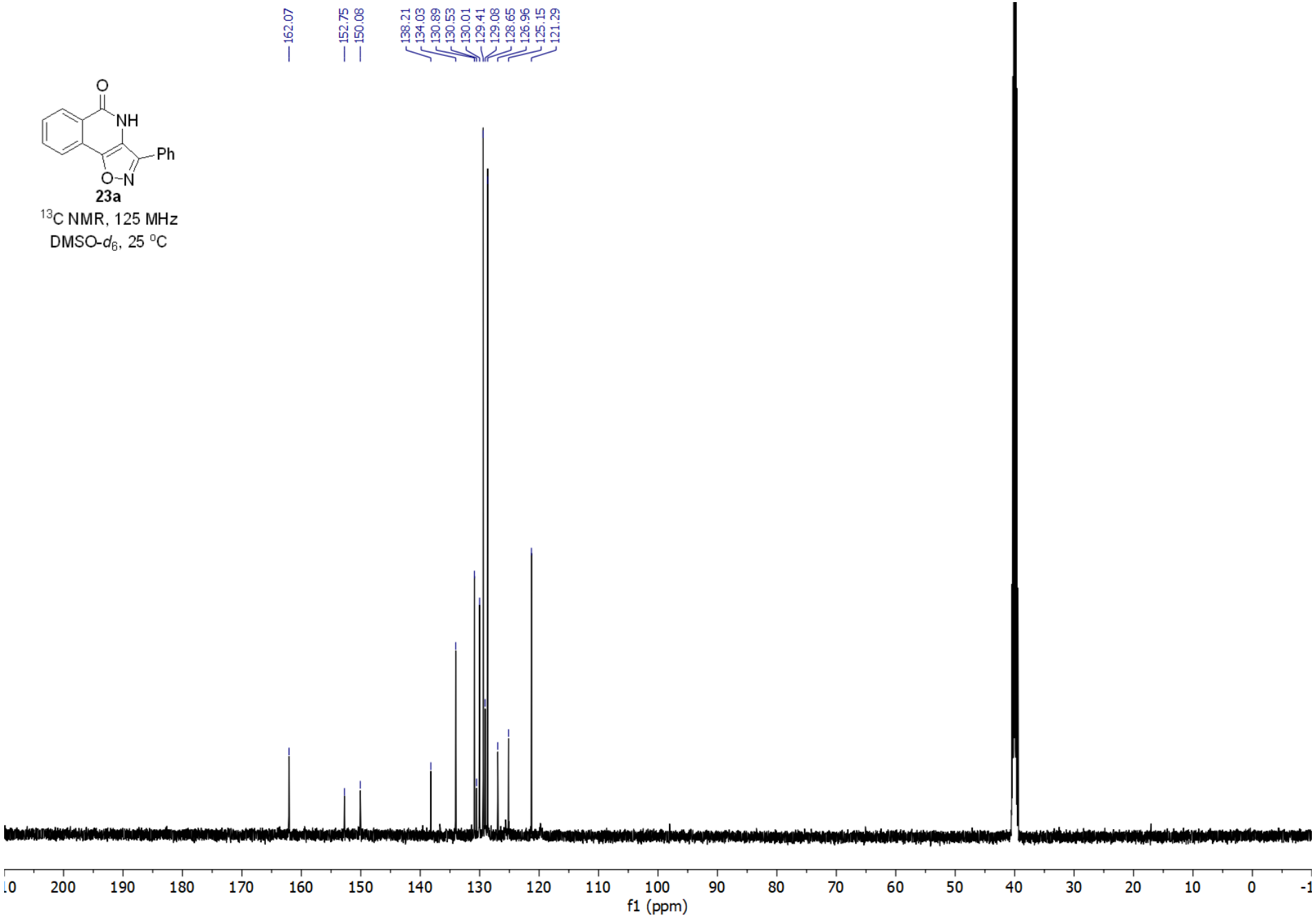

7.98
7.75
7.75
7.74
7.74
7.74
7.73
7.73
7.73
7.72
7.72
7.71
7.70
7.69
7.69
7.68
7.68
7.67
7.67
7.67
7.66
7.65
7.64
7.63
7.62
7.51
O
NH2
O
N
I
Cl
Cl
22l
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.02
6.99
1.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

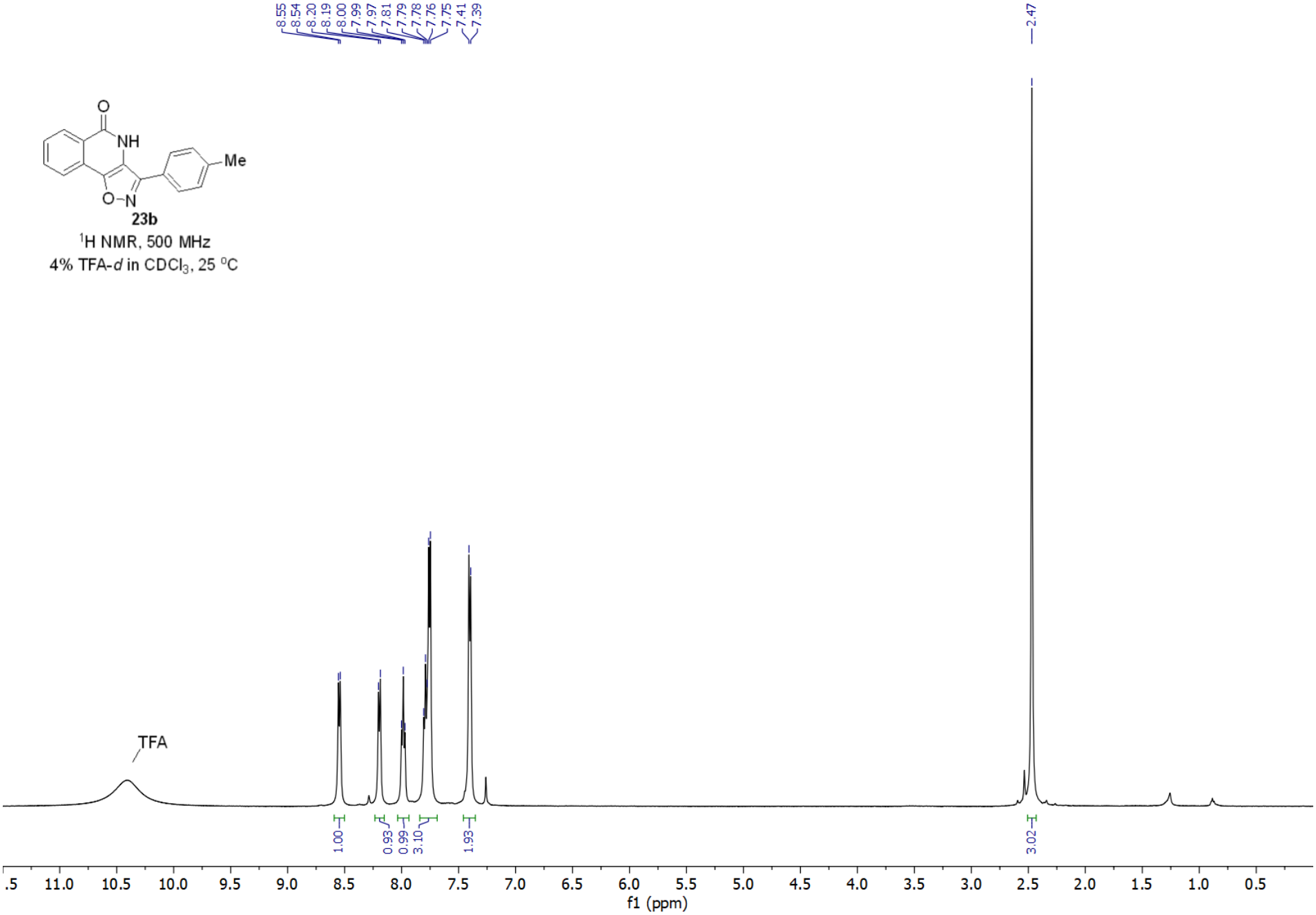

171.38
169.26
162.86
138.02
135.28
133.39
131.26
130.92
130.53
129.00
128.80
127.91
125.52
63.76
O
NH2
O
N
I
Cl
Cl
22l
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

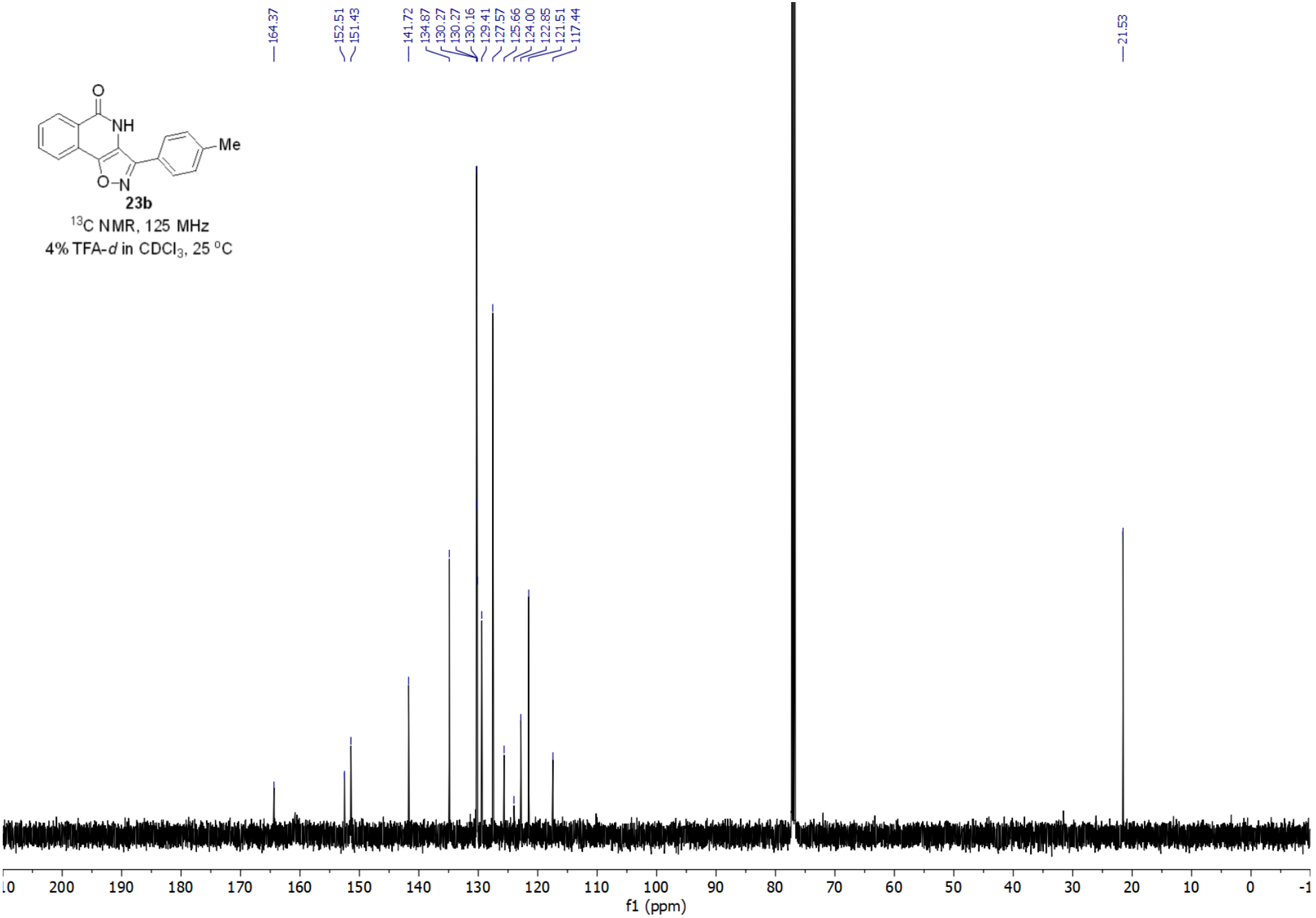

7.78 7.78 7.77 7.77 7.76 7.76 7.75 7.74 7.74 7.61 7.61 7.60 7.60 7.59 7.59 7.58 7.58 7.57 7.57 7.56 7.55 7.55
5.85 5.76
2.69 2.67 2.66 1.79 1.77 1.76 1.74 1.73 1.45 1.45 1.44 1.43 1.42 1.42 1.41 1.41 1.40 1.39 1.38 1.37 1.36 1.36 1.35 1.34 1.33 1.33 1.32 1.32 1.31 1.31 1.30 1.30 1.29 1.28 1.28 1.27 1.27 0.90 0.89 0.88
O
NH2
O
N
I
(CH26)CH3
22o
1H NMR, 500 MHz
CDCl3, 25 °C
1.07
3.00
1.33
1.28
2.62
2.77
8.62
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

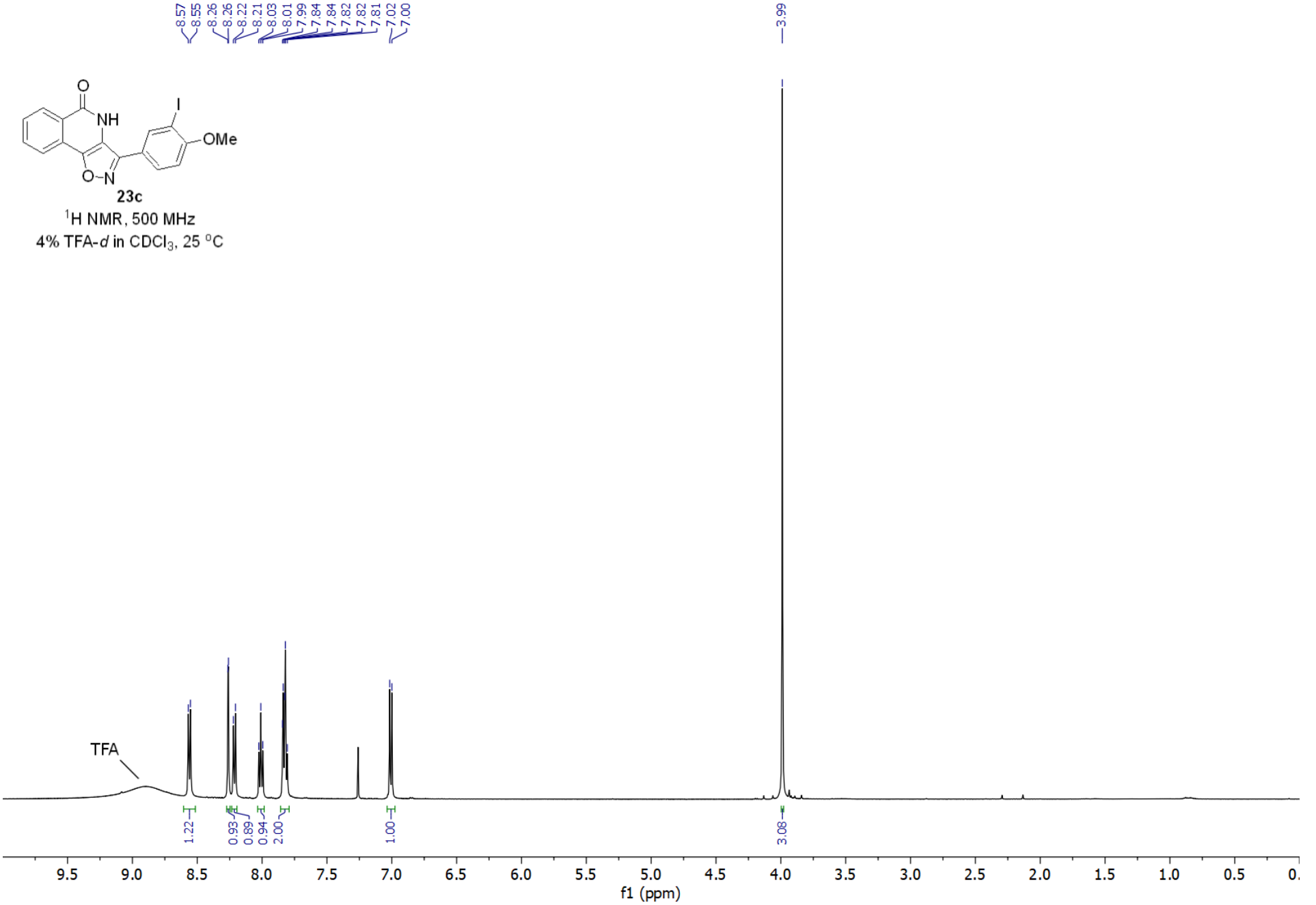

169.52
168.78
165.29
135.89
130.74
130.61
128.62
125.62
61.36
31.66
28.87
27.23
26.95
22.60
14.07
O
NH2
O
N
I
(CH26)CH3
22o
13C NMR, 125 MHz
CDCl3, 25 °C
f1 (ppm)

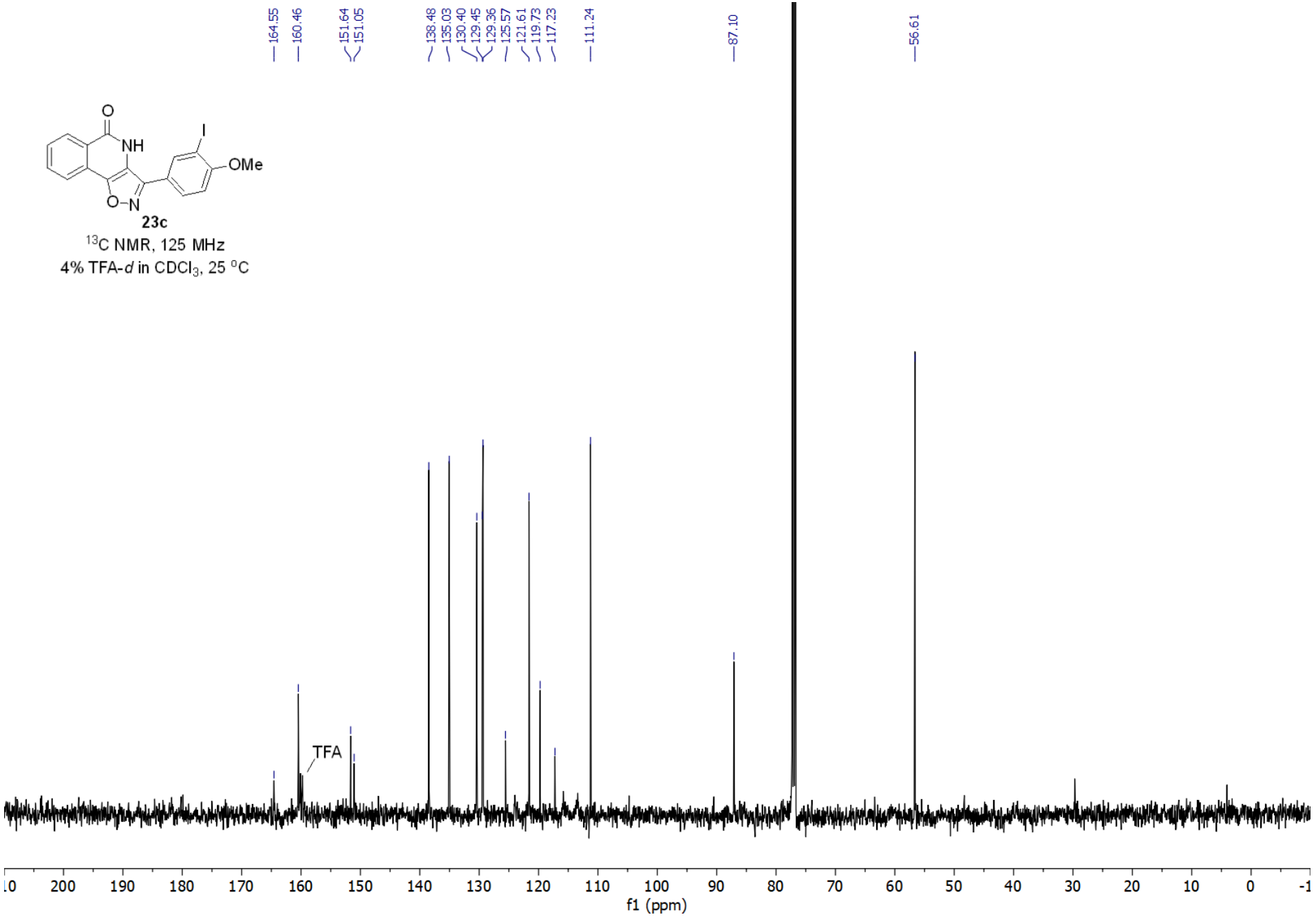

11.88
8.36
8.36
8.35
8.34
8.11
8.11
8.10
8.09
8.08
7.97
7.97
7.96
7.96
7.95
7.95
7.94
7.94
7.93
7.93
7.91
7.90
7.90
7.79
7.78
7.78
7.77
7.76
7.75
7.75
7.75
7.74
7.60
7.58
7.58
7.58
7.57
7.57
7.56
7.56
7.55
O
NH
Ph
O
N
23a
1H NMR, 500 MHz
DMSO-d6, 25 °C
0.84
1.00
1.02
3.14
1.09
3.12
.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

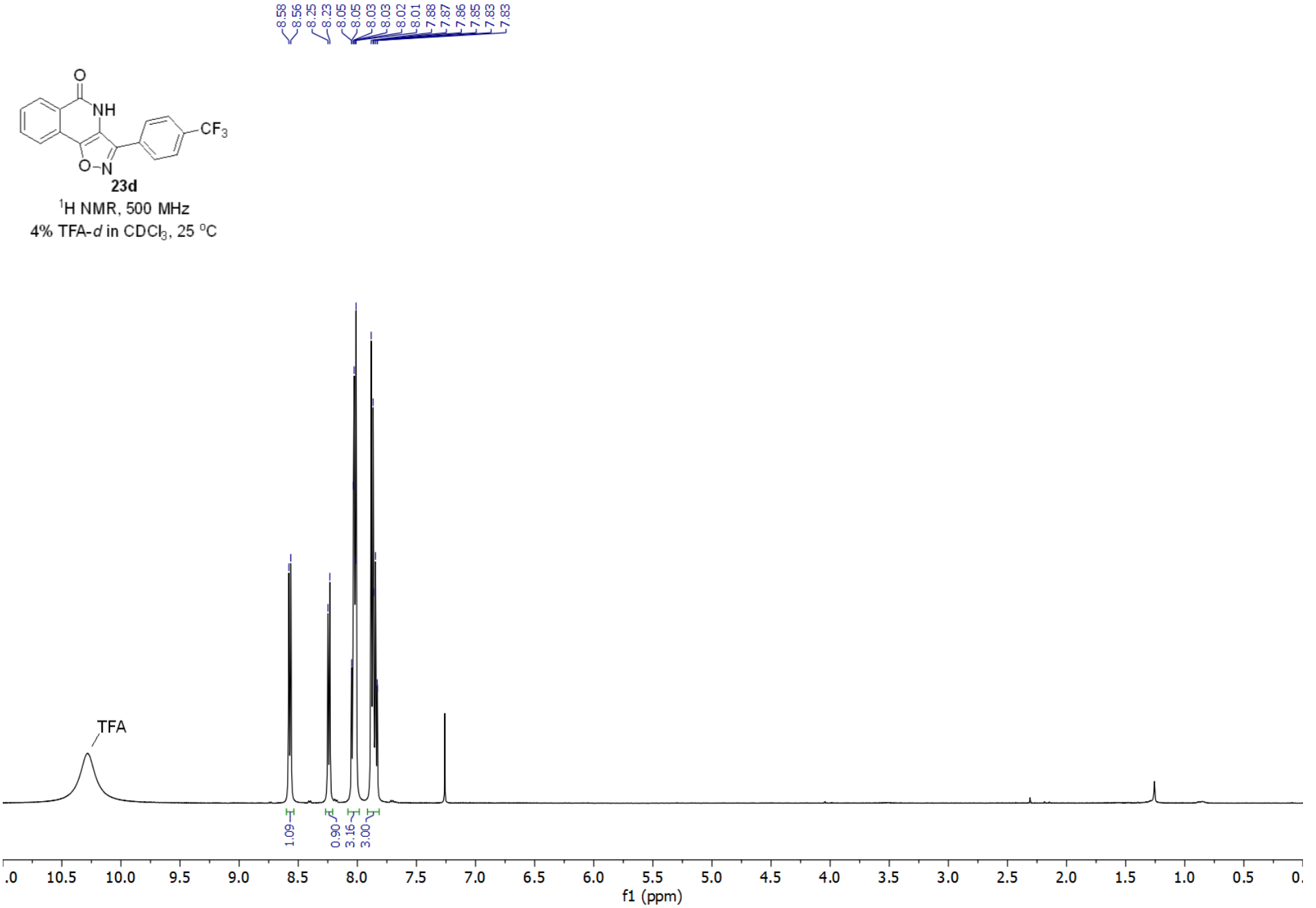

162.07
152.75
150.08
138.21
134.03
130.89
130.53
130.01
129.41
129.08
128.65
126.96
125.15
121.29
O
NH
Ph
O
N
23a
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

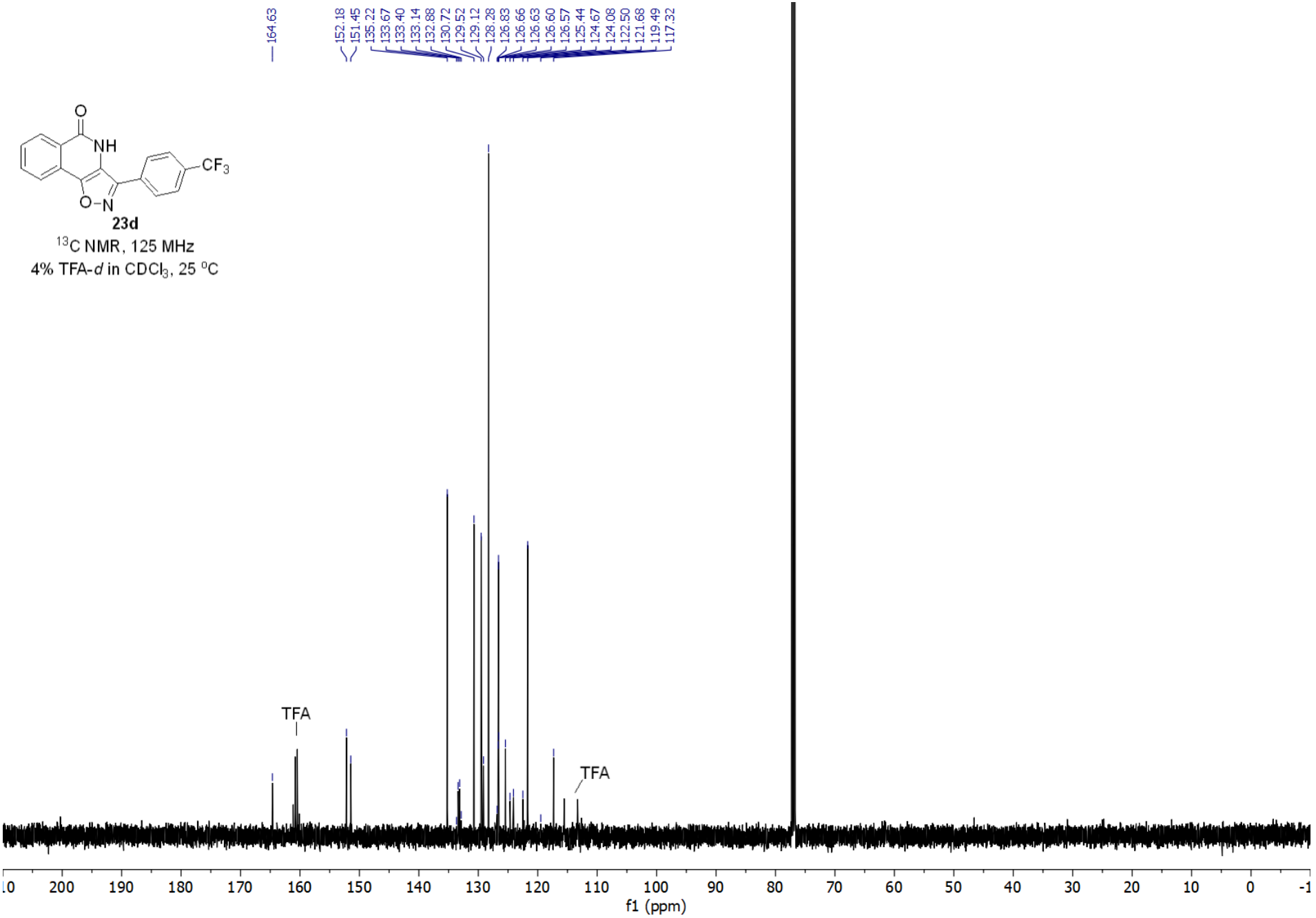

8.55
8.54
8.20
8.19
8.00
7.99
7.97
7.81
7.79
7.78
7.76
7.75
7.41
7.39
2.47
O
NH
Me
O
N
23b
1H NMR, 500 MHz
4% TFA-d in CDCl3, 25 °C
TFA
1.00
0.93
0.99
3.10
1.93
3.02
f1 (ppm)


164.37
152.51
151.43
141.72
134.87
130.27
130.27
130.16
129.41
127.57
125.66
124.00
122.85
121.51
117.44
21.53
O
NH
Me
O
N
23b
^{13}C NMR, 125 MHz
4% TFA-*d* in $CDCl_3$, 25 °C
f1 (ppm)


8.57
8.55
8.26
8.26
8.22
8.21
8.03
8.01
7.99
7.84
7.84
7.82
7.82
7.81
7.02
7.00
3.99
O
NH
I
OMe
O
N
23c
1H NMR, 500 MHz
4% TFA-d in CDCl3, 25 °C
TFA
1.22
0.93
0.89
0.94
2.00
1.00
3.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


164.55
160.46
151.64
151.05
138.48
135.03
130.40
129.45
129.36
125.57
121.61
119.73
117.23
111.24
87.10
56.61
O
NH
I
OMe
O–N
23c
13C NMR, 125 MHz
4% TFA-d in CDCl3, 25 °C
TFA
f1 (ppm)

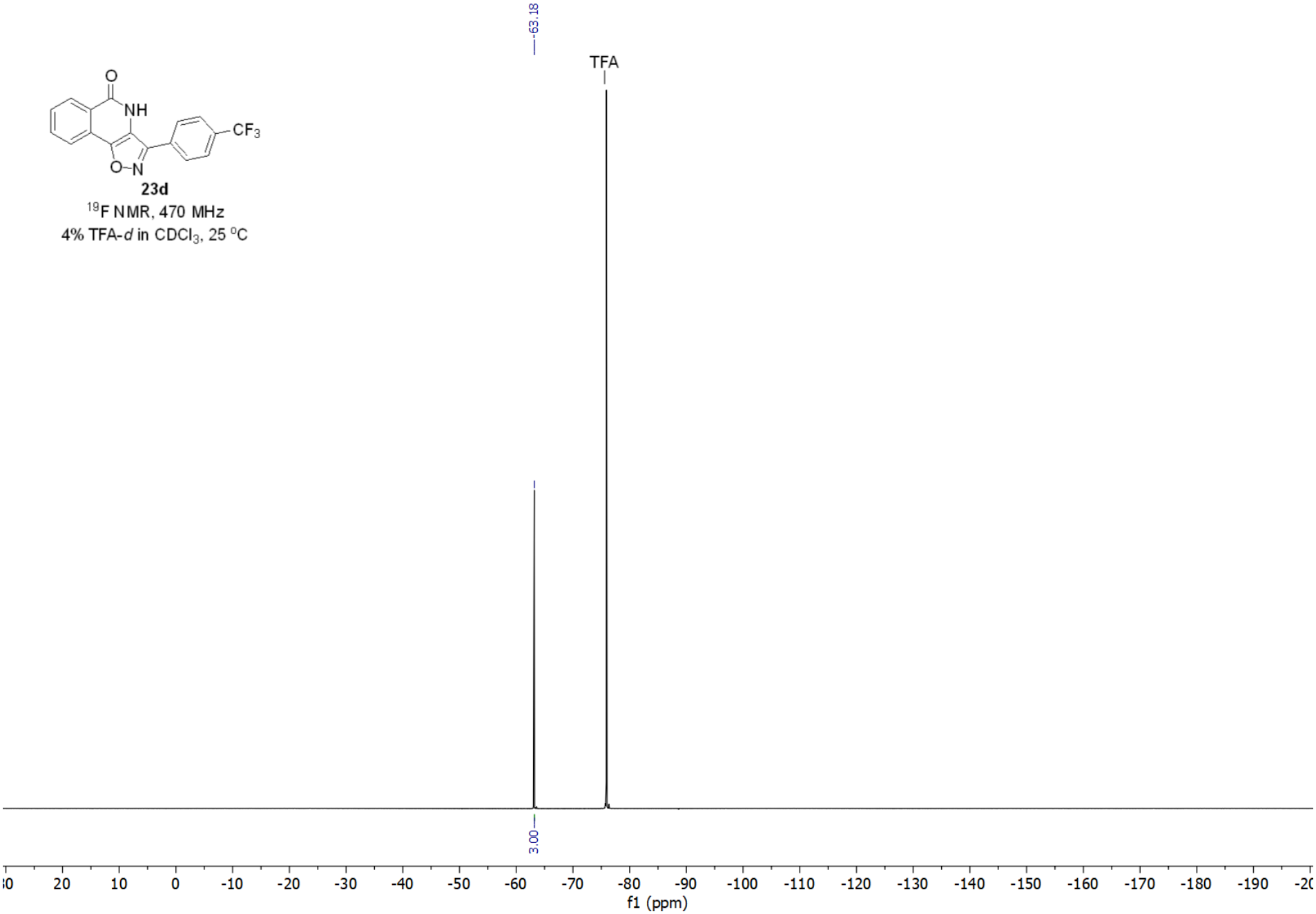

8.58
8.56
8.25
8.23
8.05
8.05
8.03
8.03
8.02
8.01
7.88
7.87
7.86
7.85
7.83
7.83
O
NH
CF3
O
N
23d
1H NMR, 500 MHz
4% TFA-d in CDCl3, 25 °C
TFA
1.09
0.90
3.16
3.00
f1 (ppm)

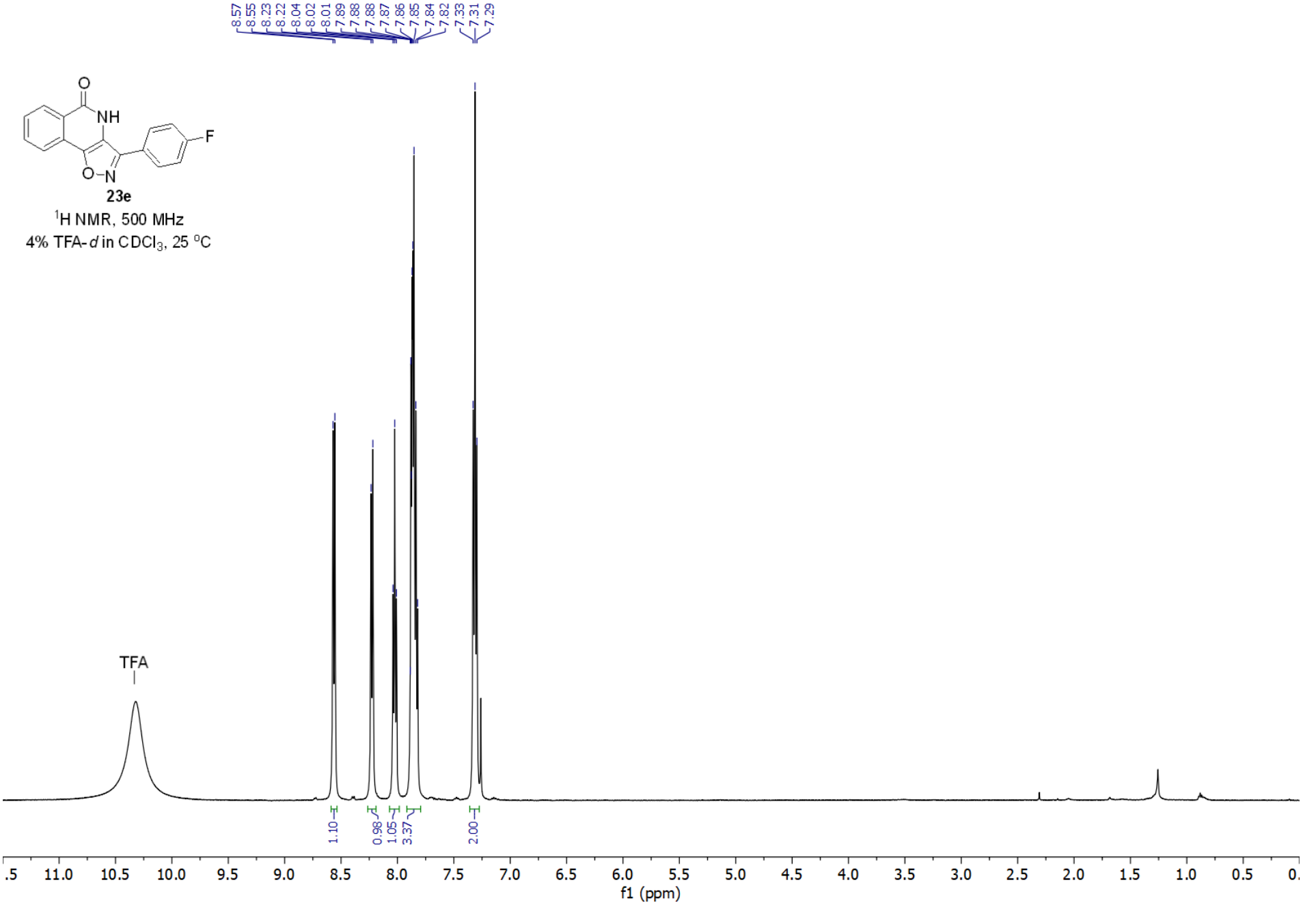

164.63
152.18
151.45
135.22
133.67
133.40
133.14
132.88
130.72
129.52
129.12
128.28
126.83
126.66
126.63
126.60
126.57
125.44
124.67
124.08
122.50
121.68
119.49
117.32
O
NH
CF3
O–N
23d
13C NMR, 125 MHz
4% TFA-d in CDCl3, 25 °C
TFA
TFA
f1 (ppm)

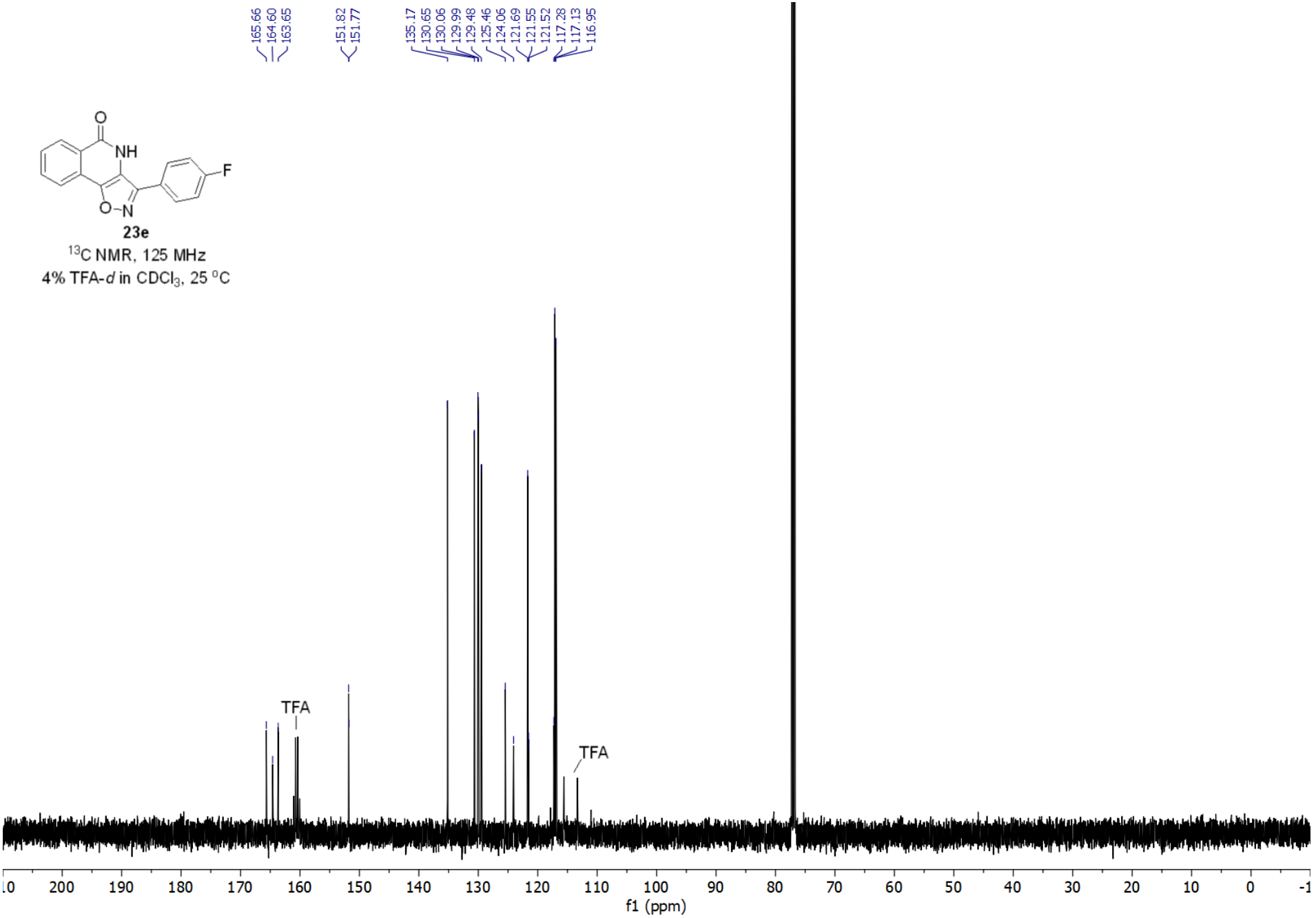
23d

^{19}F NMR, 470 MHz

4% TFA-*d* in $CDCl_3$, 25 ^{0}C




8.57
8.55
8.23
8.22
8.04
8.02
8.01
7.89
7.88
7.88
7.87
7.86
7.85
7.84
7.82
7.33
7.31
7.29
O
NH
F
O
N
23e
1H NMR, 500 MHz
4% TFA-d in CDCl3, 25 °C
TFA
1.10
0.98
1.05
3.37
2.00
f1 (ppm)



23e

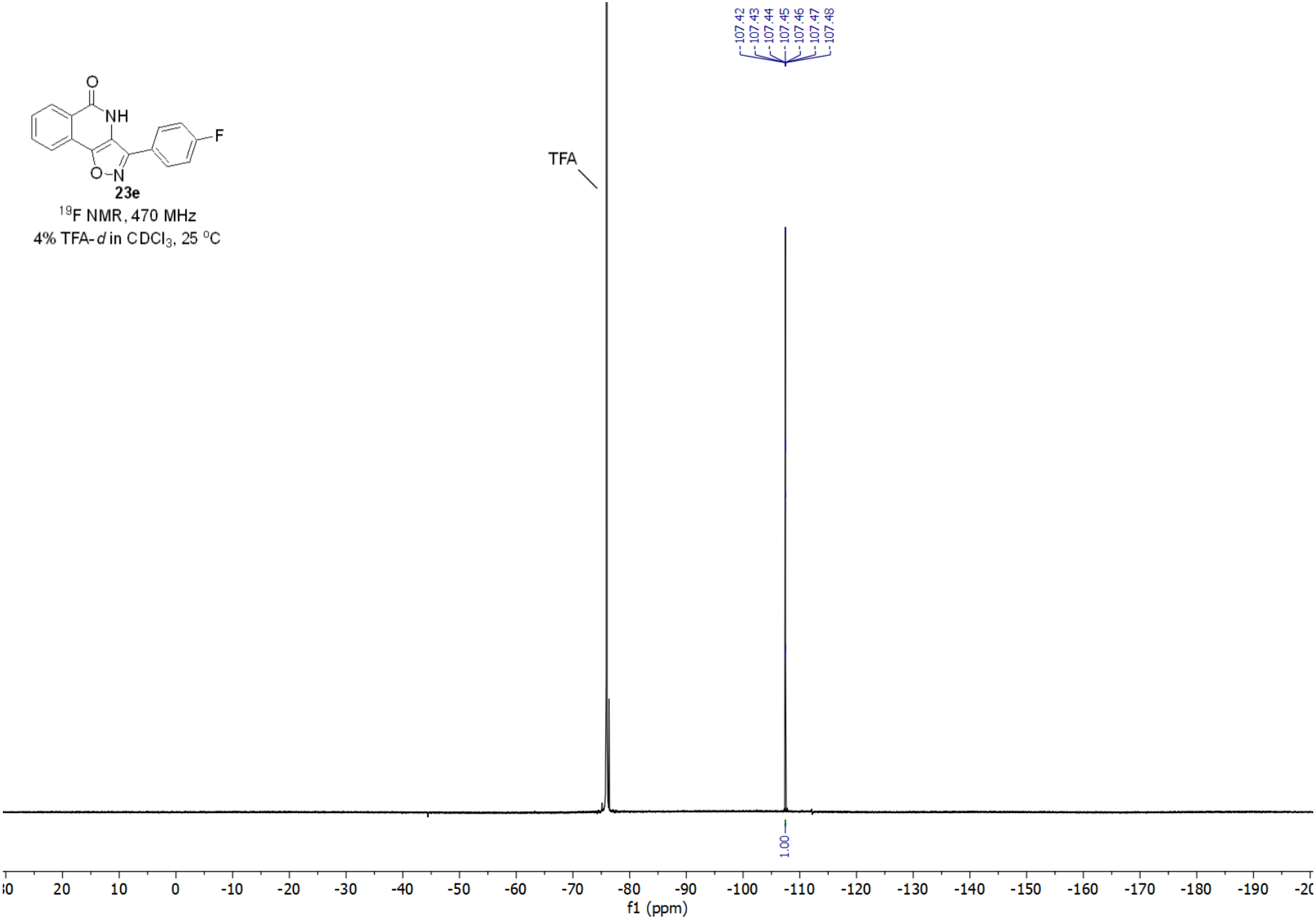
^{13}C NMR, 125 MHz

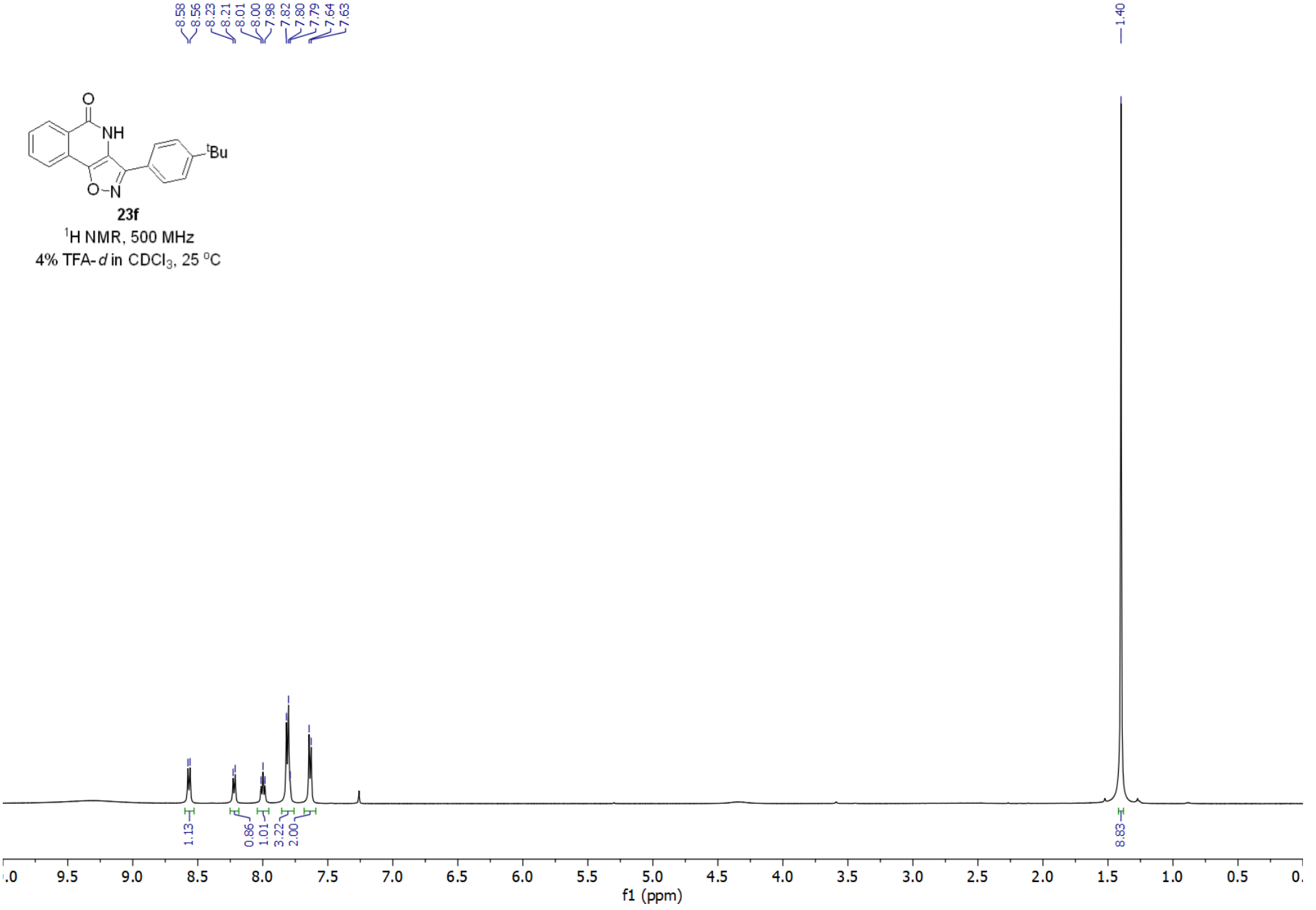
4% TFA-*d* in $CDCl_3$, 25 ^{0}C

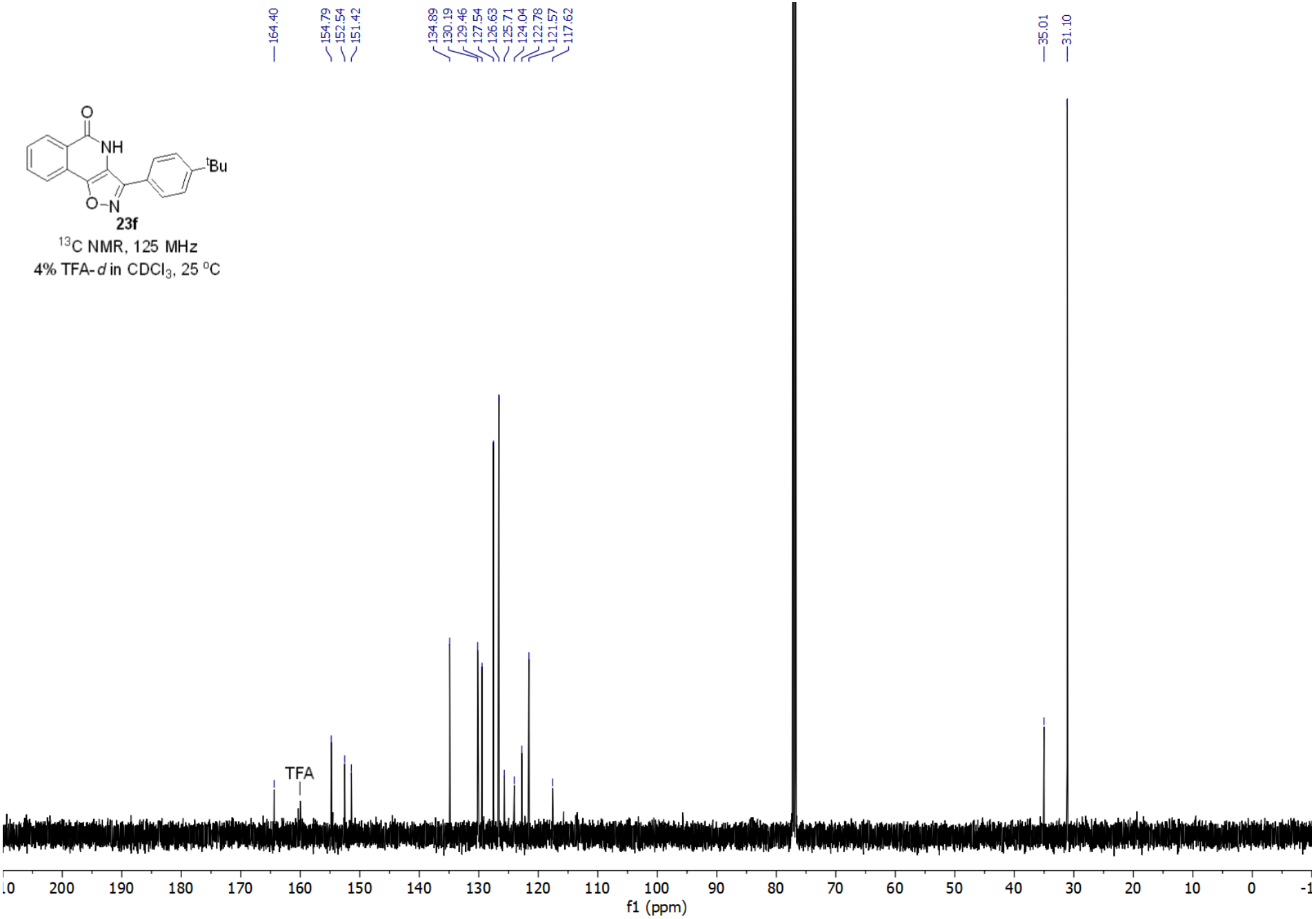
23e

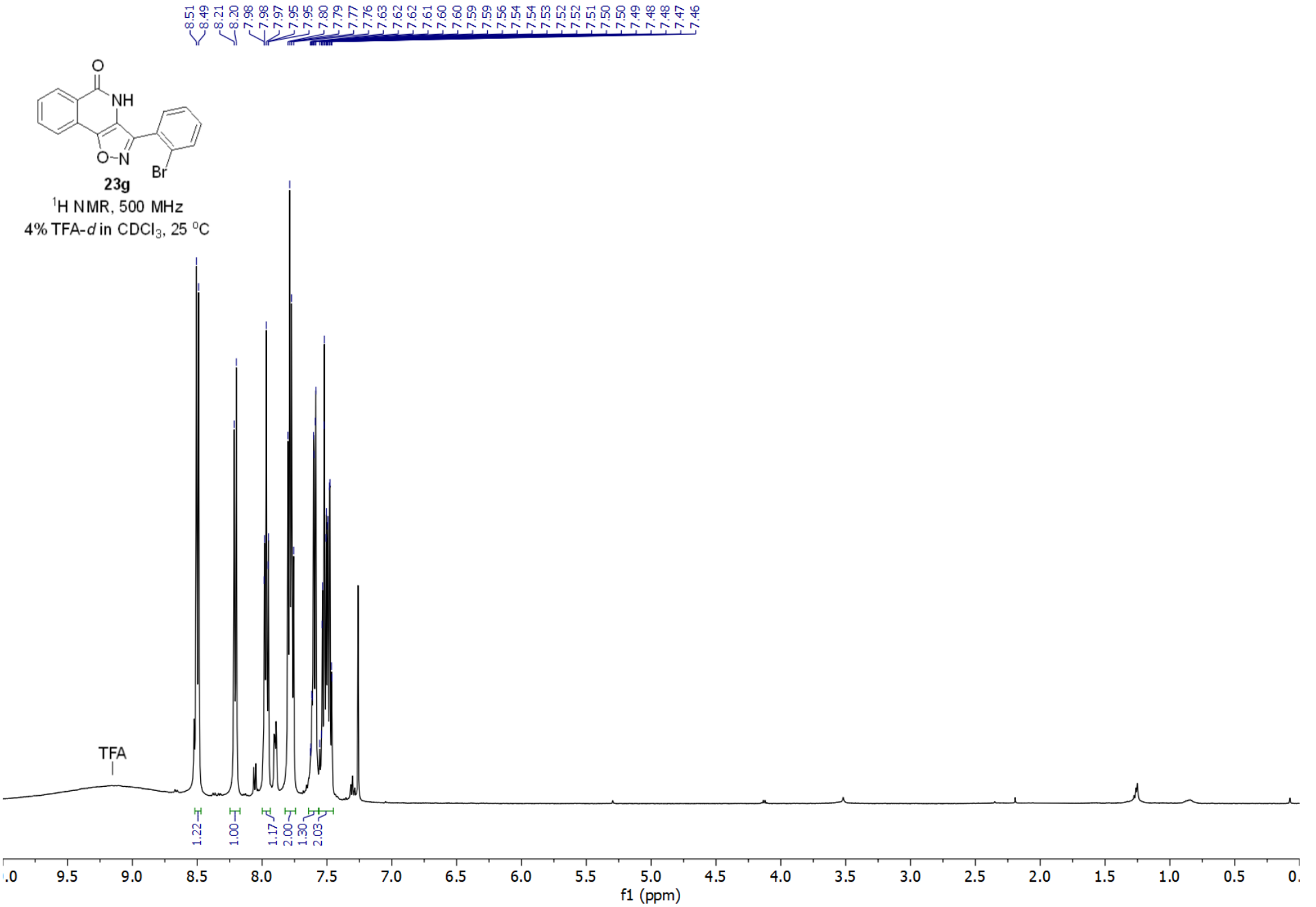
^{19}F NMR, 470 MHz

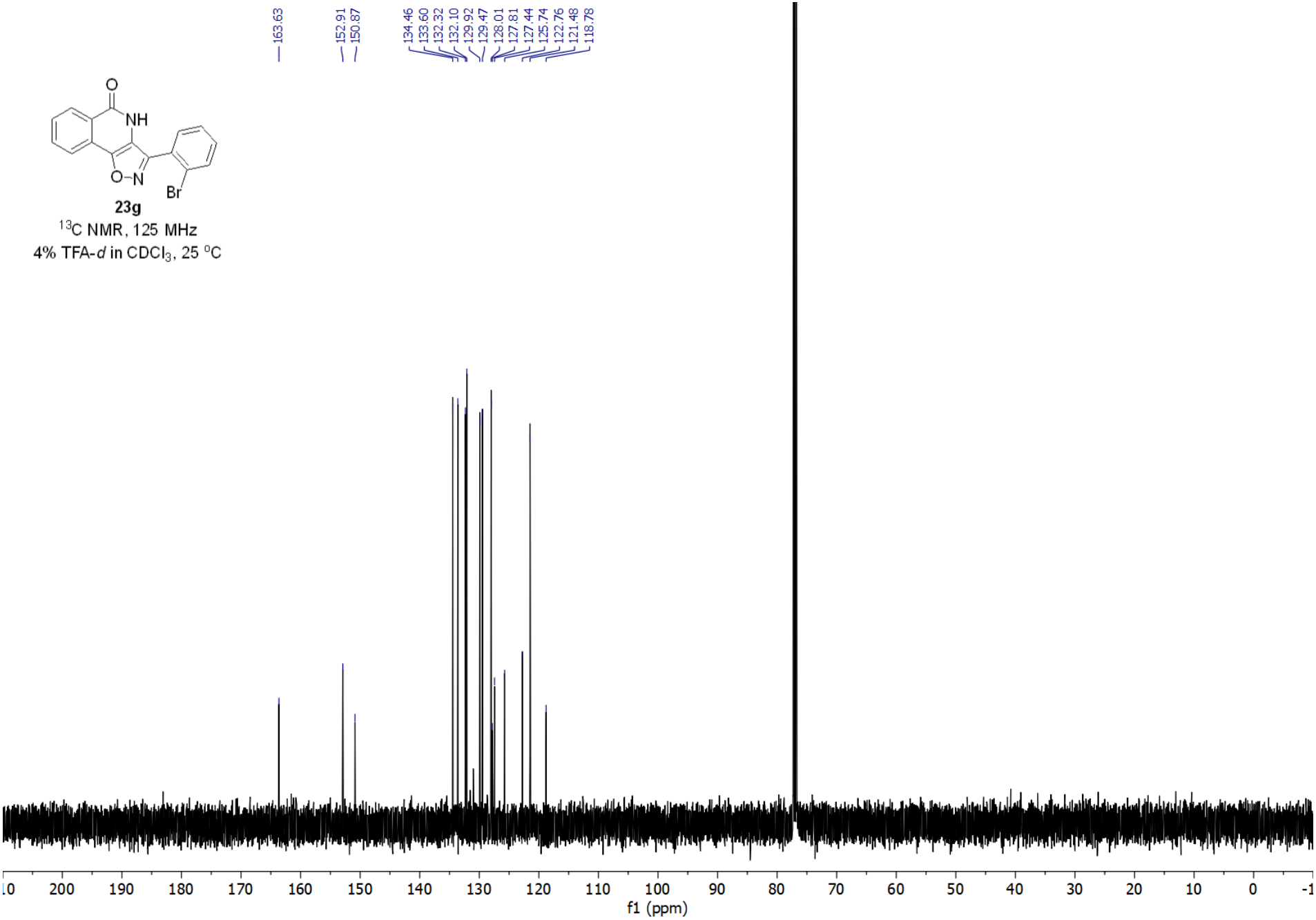
4% TFA-*d* in $CDCl_3$, 25 ^{0}C

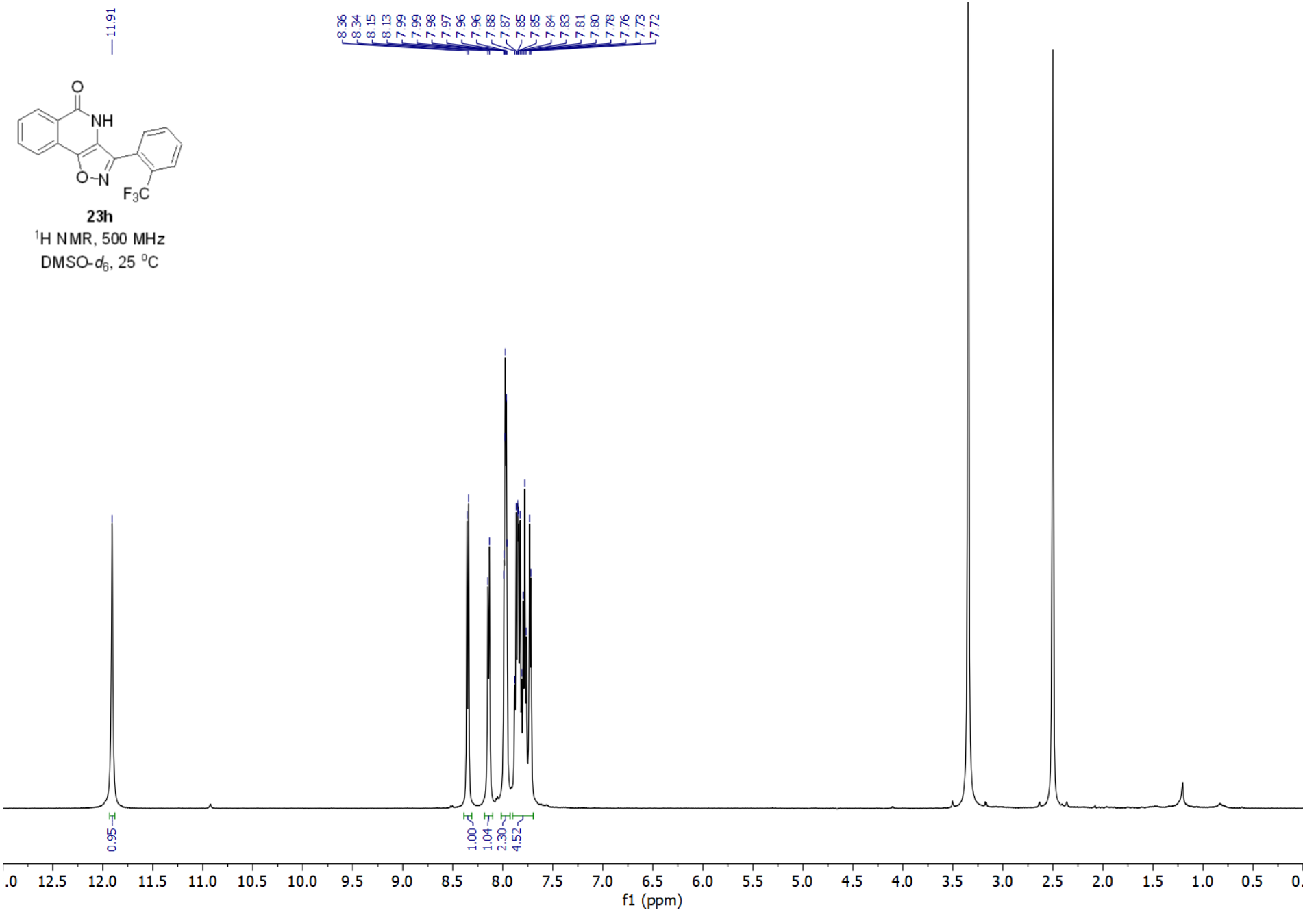


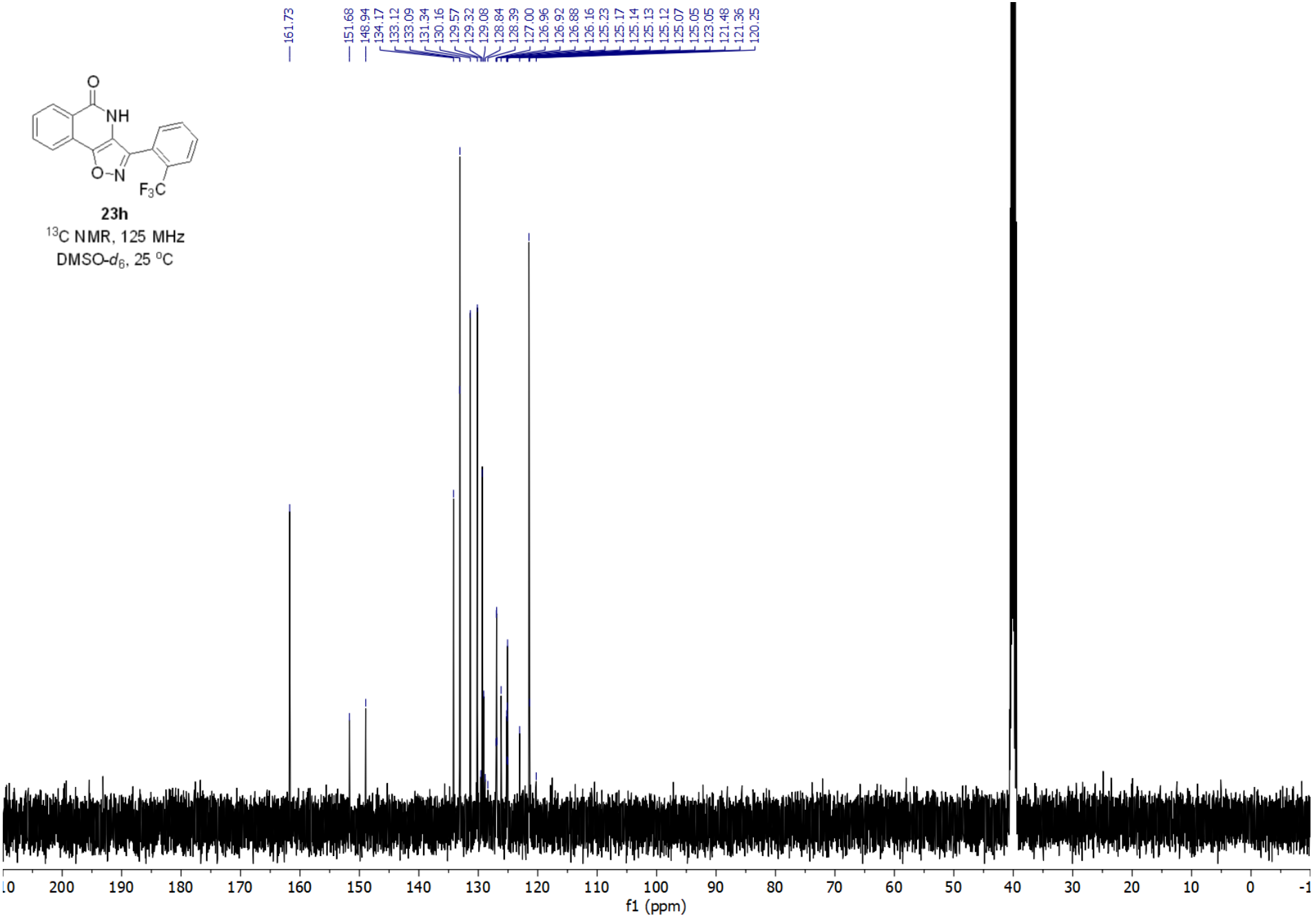

8.58
8.56
8.23
8.21
8.01
8.00
7.98
7.82
7.80
7.79
7.64
7.63
1.40
O
NH
O
N
tBu
23f
1H NMR, 500 MHz
4% TFA-d in CDCl3, 25 °C
1.13
0.86
1.01
3.22
2.00
8.83
f1 (ppm)


164.40
154.79
152.54
151.42
134.89
130.19
129.46
127.54
126.63
125.71
124.04
122.78
121.57
117.62
35.01
31.10
O
NH
tBu
O
N
23f
13C NMR, 125 MHz
4% TFA-d in CDCl3, 25 °C
TFA
f1 (ppm)


8.51
8.49
8.21
8.20
7.98
7.98
7.97
7.95
7.95
7.80
7.79
7.77
7.76
7.63
7.62
7.62
7.61
7.60
7.60
7.59
7.59
7.56
7.54
7.54
7.53
7.52
7.52
7.51
7.50
7.50
7.49
7.48
7.48
7.47
7.46
O
NH
O–N
Br
23g
1H NMR, 500 MHz
4% TFA-d in CDCl3, 25 °C
TFA
1.22
1.00
1.17
2.00
1.30
2.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


163.63
152.91
150.87
134.46
133.60
132.32
132.10
129.92
129.47
128.01
127.81
127.44
125.74
122.76
121.48
118.78
O
NH
O
N
Br
23g
13C NMR, 125 MHz
4% TFA-d in CDCl3, 25 °C
f1 (ppm)

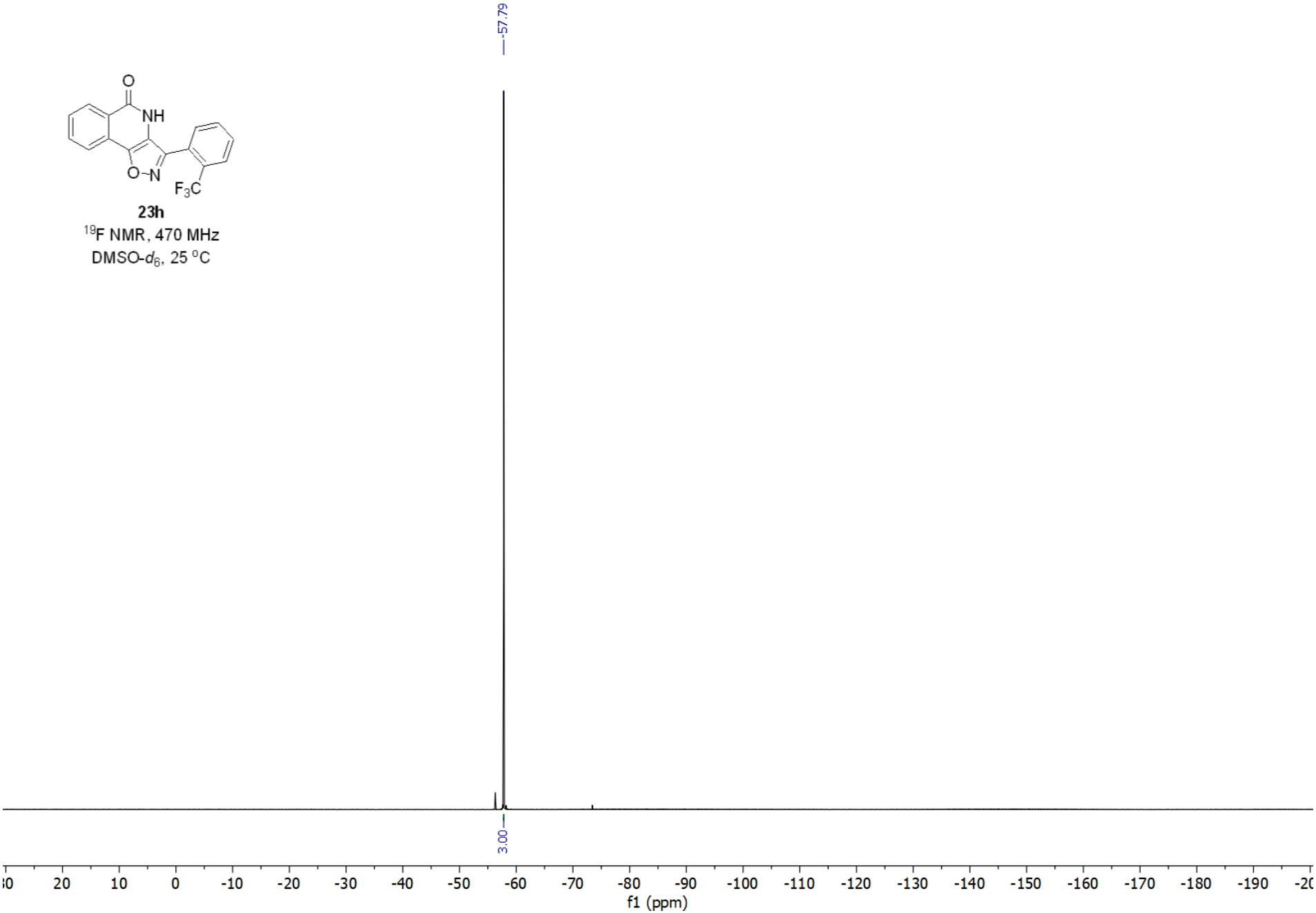

11.91
8.36
8.34
8.15
8.13
7.99
7.99
7.98
7.97
7.96
7.96
7.88
7.87
7.85
7.85
7.84
7.83
7.81
7.80
7.78
7.76
7.73
7.72
O
NH
O
N
F3C
23h
1H NMR, 500 MHz
DMSO-d6, 25 °C
0.95
1.00
1.04
2.30
4.52
f1 (ppm)

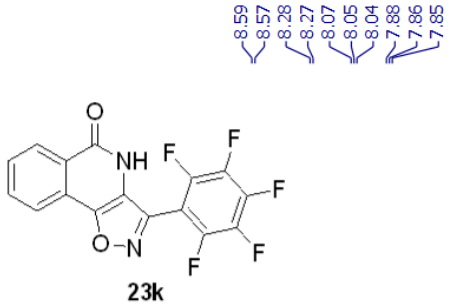

161.73
151.68
148.94
134.17
133.12
133.09
131.34
130.16
129.57
129.32
129.08
128.84
128.39
127.00
126.96
126.92
126.88
126.16
125.23
125.17
125.14
125.13
125.12
125.07
125.05
123.05
121.48
121.36
120.25
O
NH
O
N
F3C
23h
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)

23h

^{19}F NMR, 470 MHz

DMSO-d_6, 25 °C

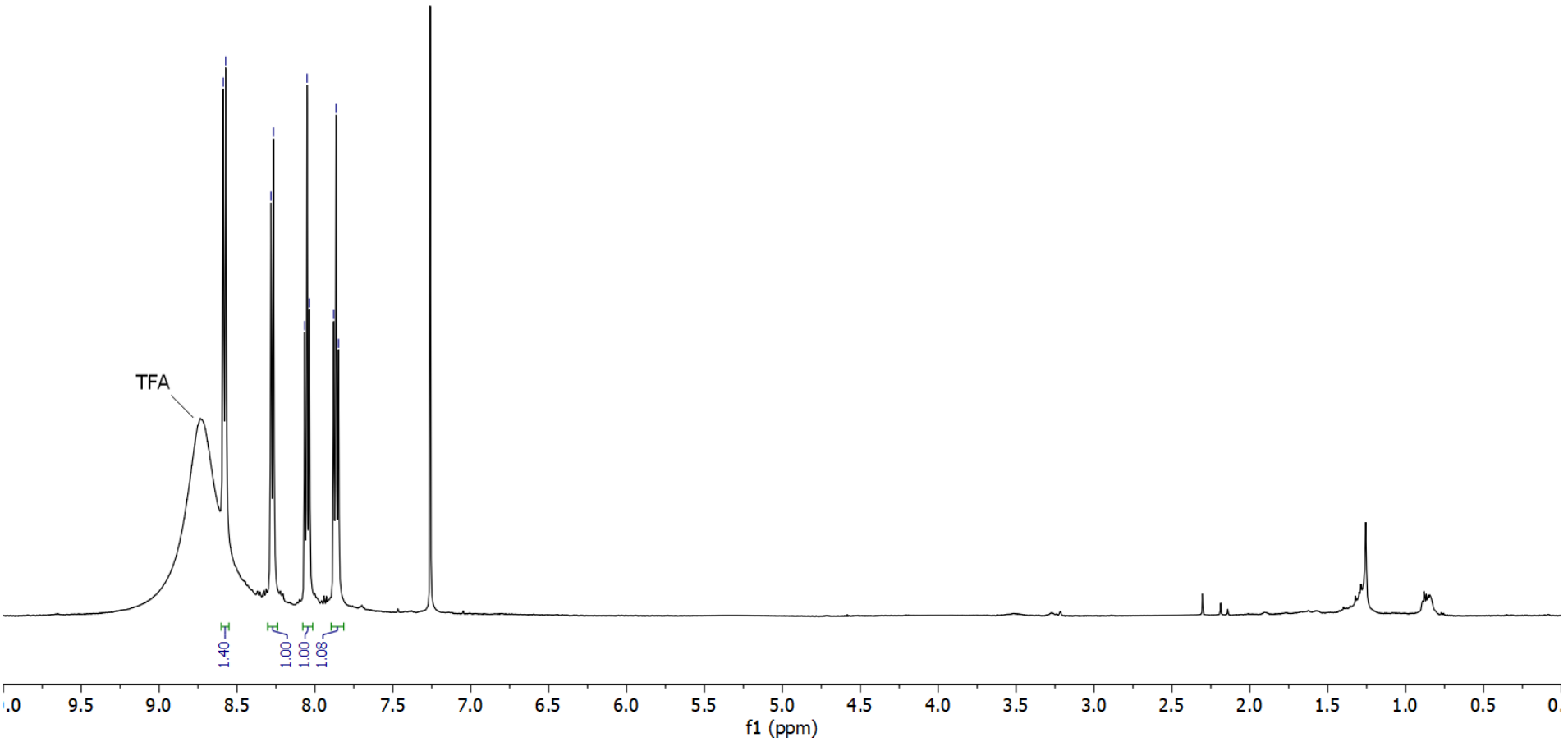


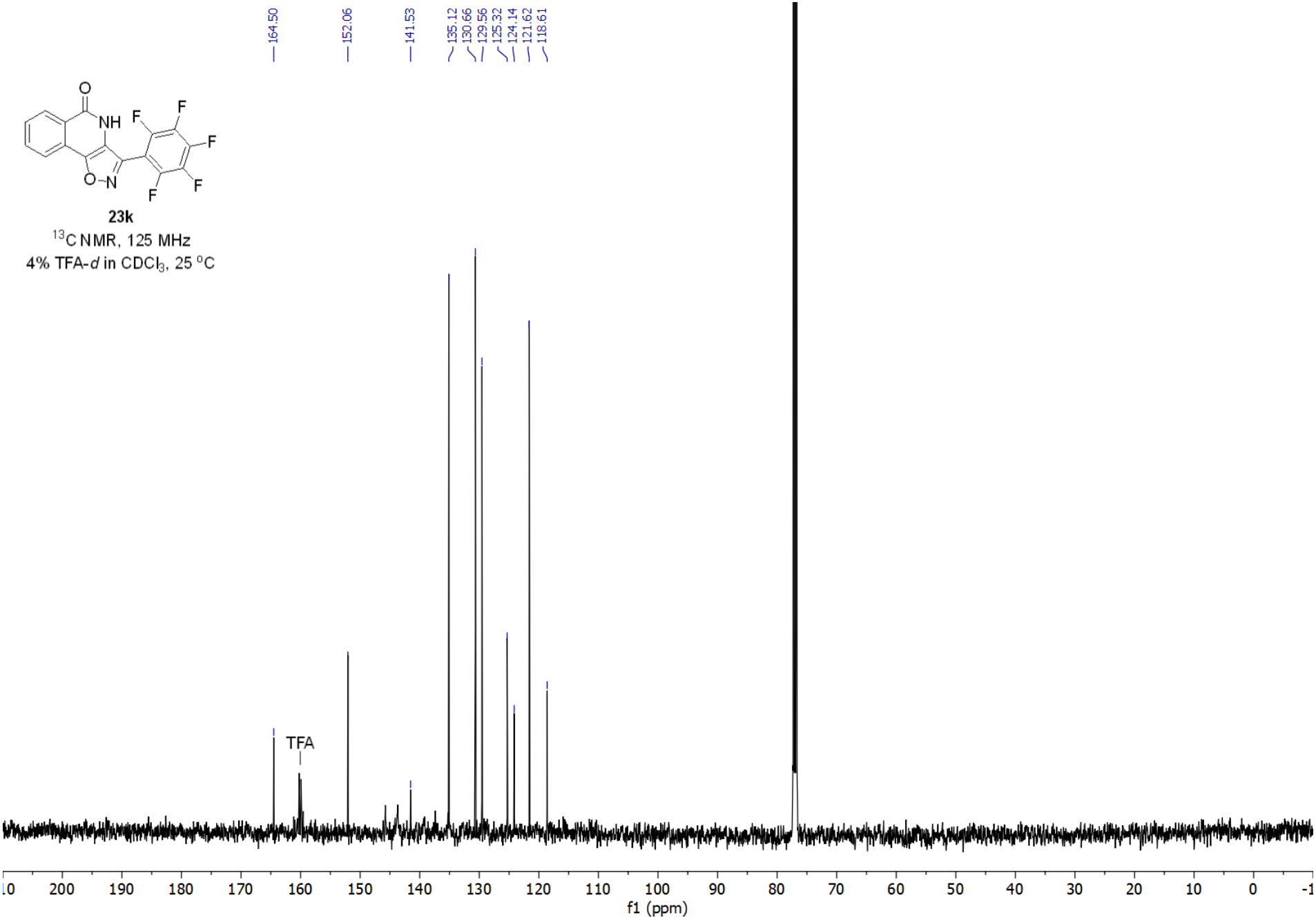


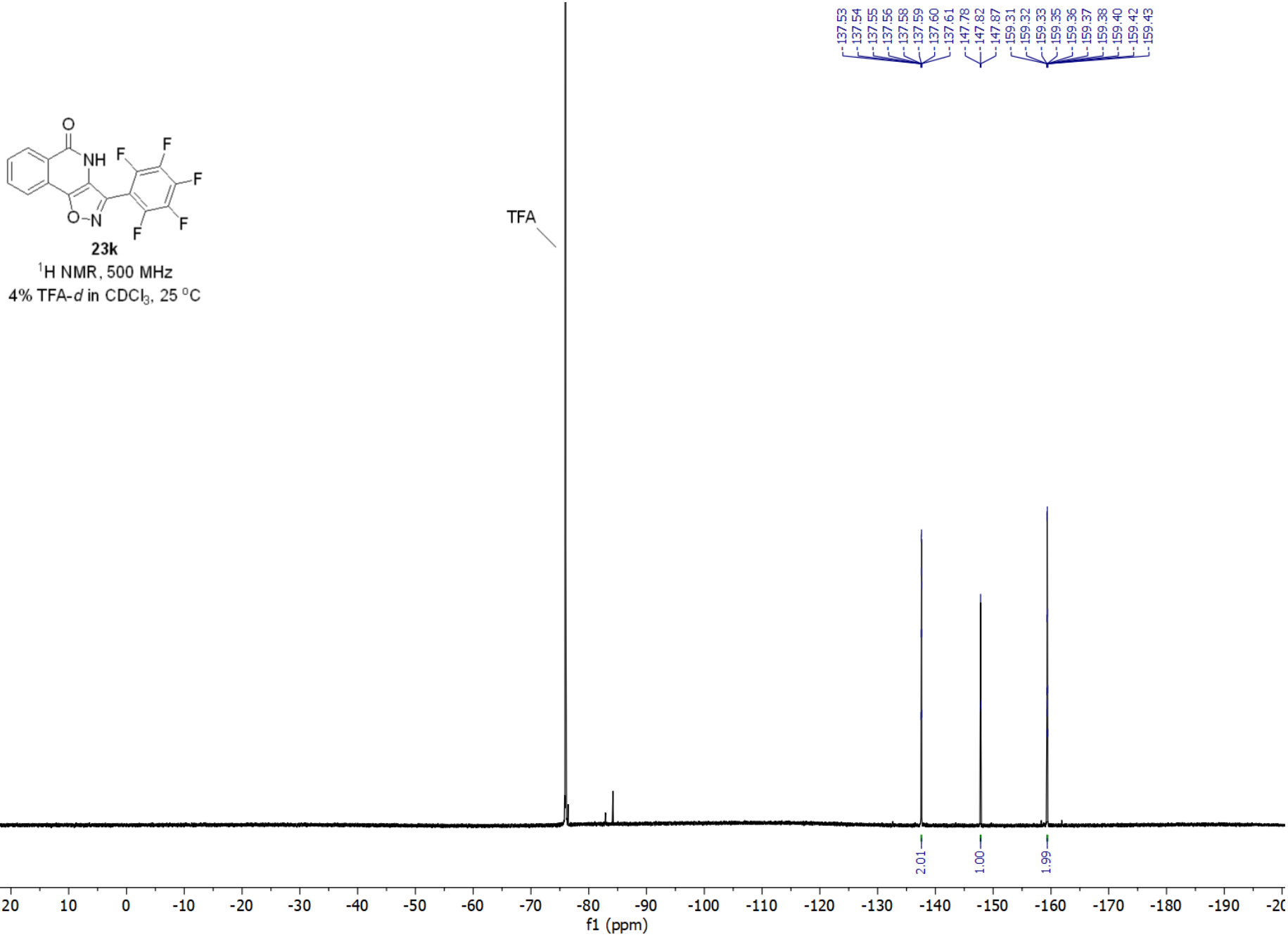
23k

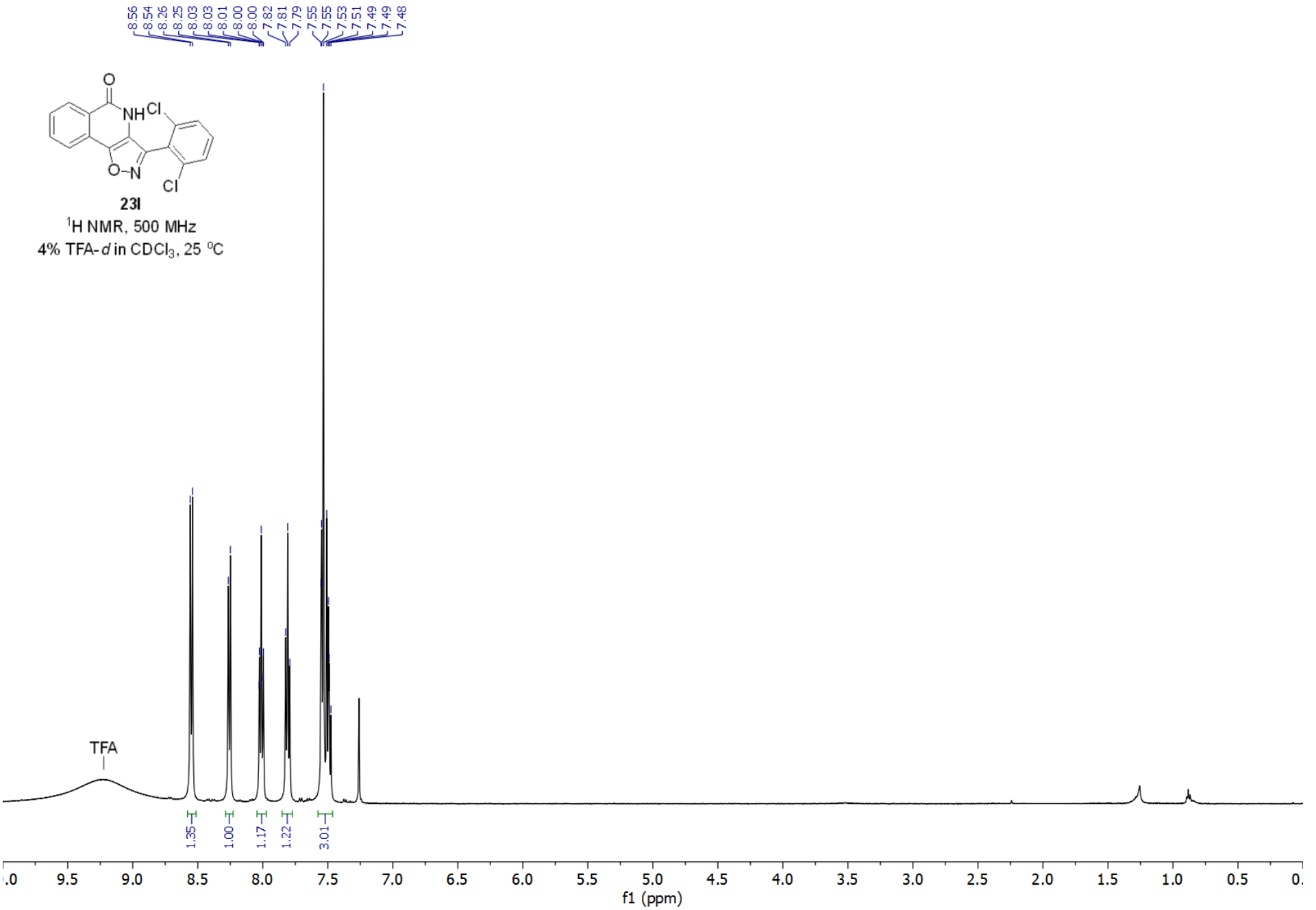
^{1}H NMR, 500 MHz

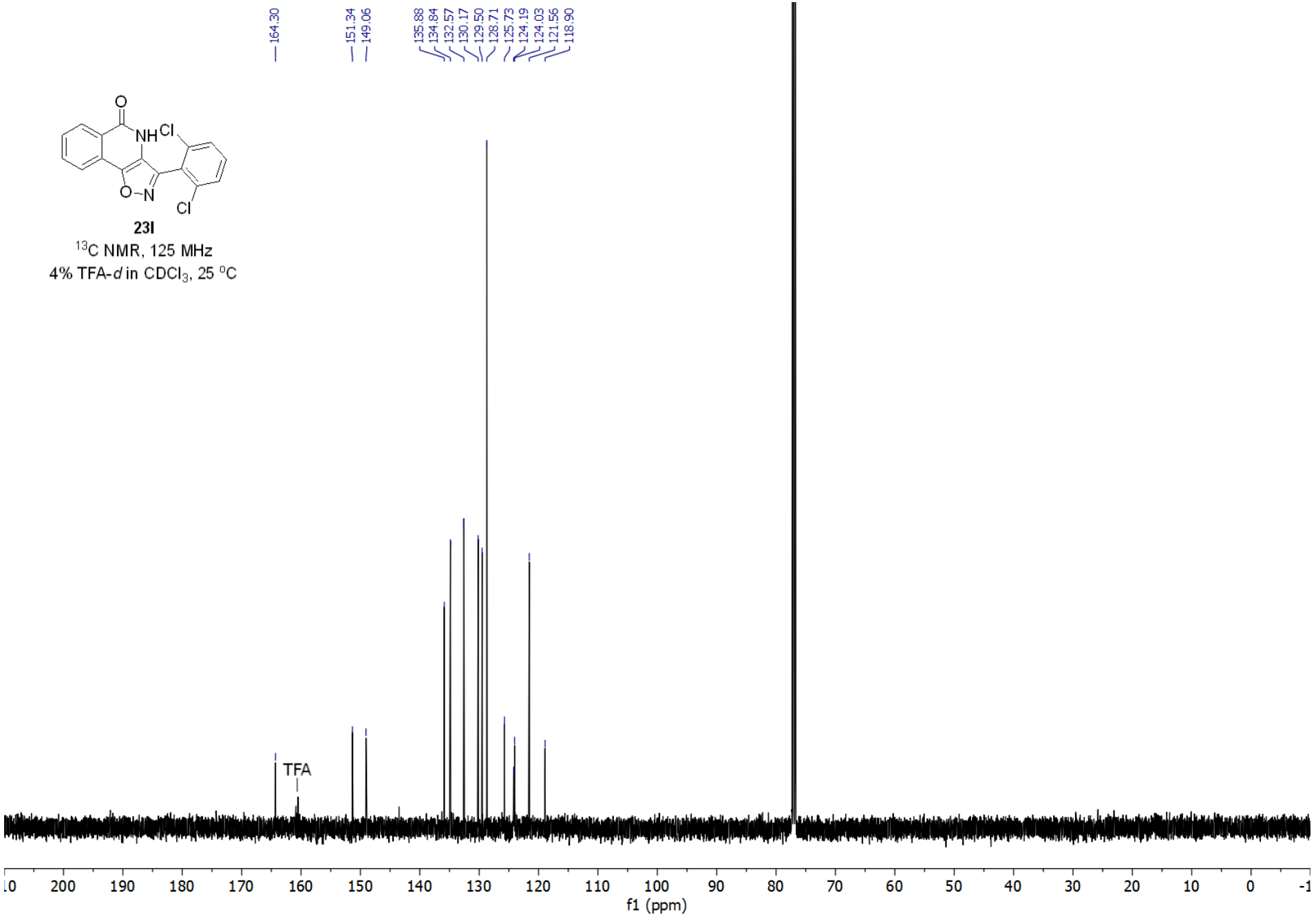
4% TFA-*d* in $CDCl_3$, 25 ^oC




164.50
152.06
141.53
135.12
130.66
129.56
125.32
124.14
121.62
118.61
O
NH
F
F
F
F
F
O
N
23k
13C NMR, 125 MHz
4% TFA-d in CDCl3, 25 °C
TFA
f1 (ppm)


O
NH
F
F
F
F
F
O
N
23k
1H NMR, 500 MHz
4% TFA-d in CDCl3, 25 °C
TFA
137.53
137.54
137.55
137.56
137.58
137.59
137.60
137.61
147.78
147.82
147.87
159.31
159.32
159.33
159.35
159.36
159.37
159.38
159.40
159.42
159.43
2.01
1.00
1.99
f1 (ppm)

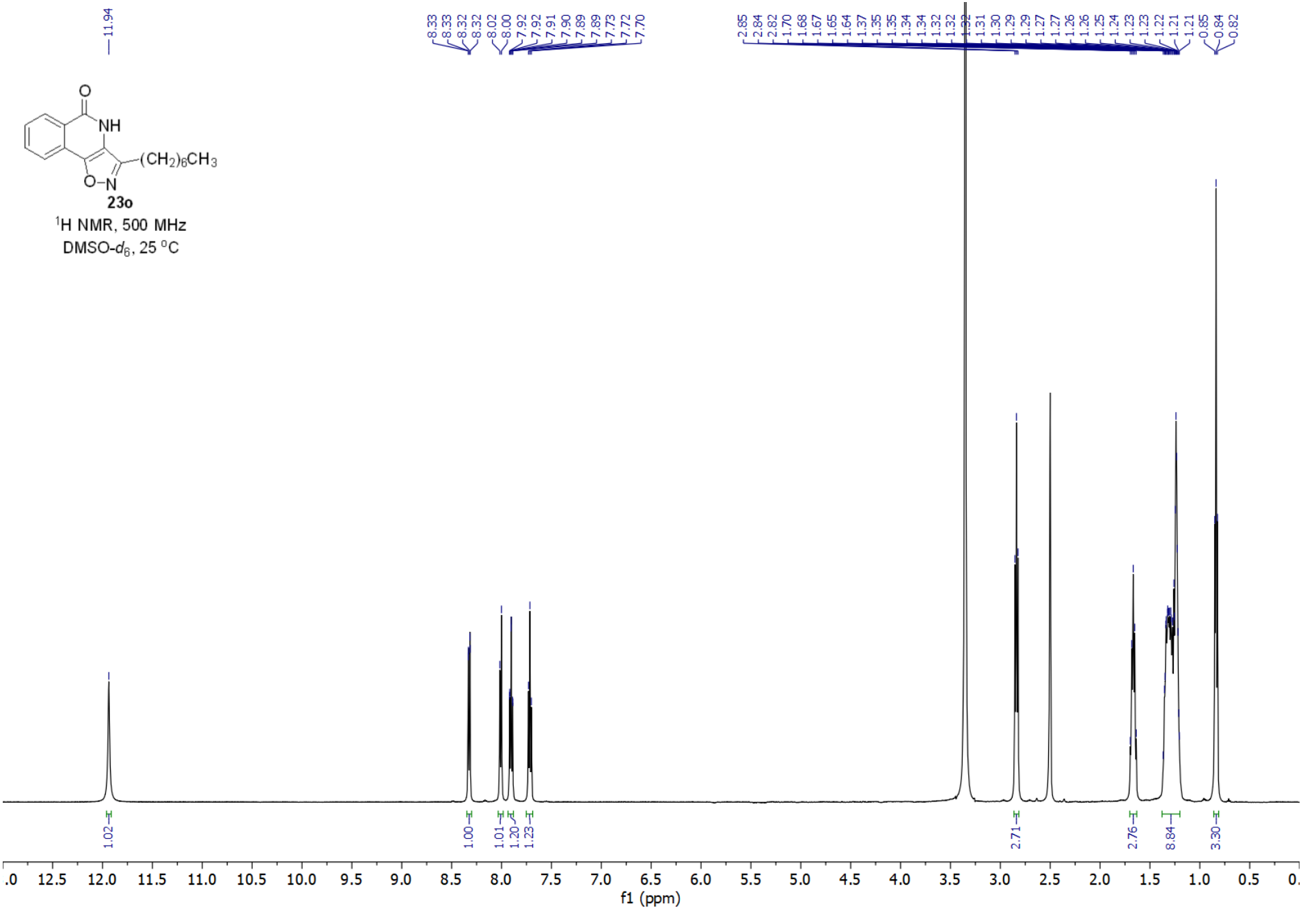

8.56
8.54
8.26
8.25
8.03
8.03
8.01
8.00
8.00
7.82
7.81
7.79
7.55
7.55
7.53
7.51
7.49
7.49
7.48
O
NH
Cl
O
N
Cl
23l
1H NMR, 500 MHz
4% TFA-d in CDCl3, 25 °C
TFA
1.35
1.00
1.17
1.22
3.01
f1 (ppm)

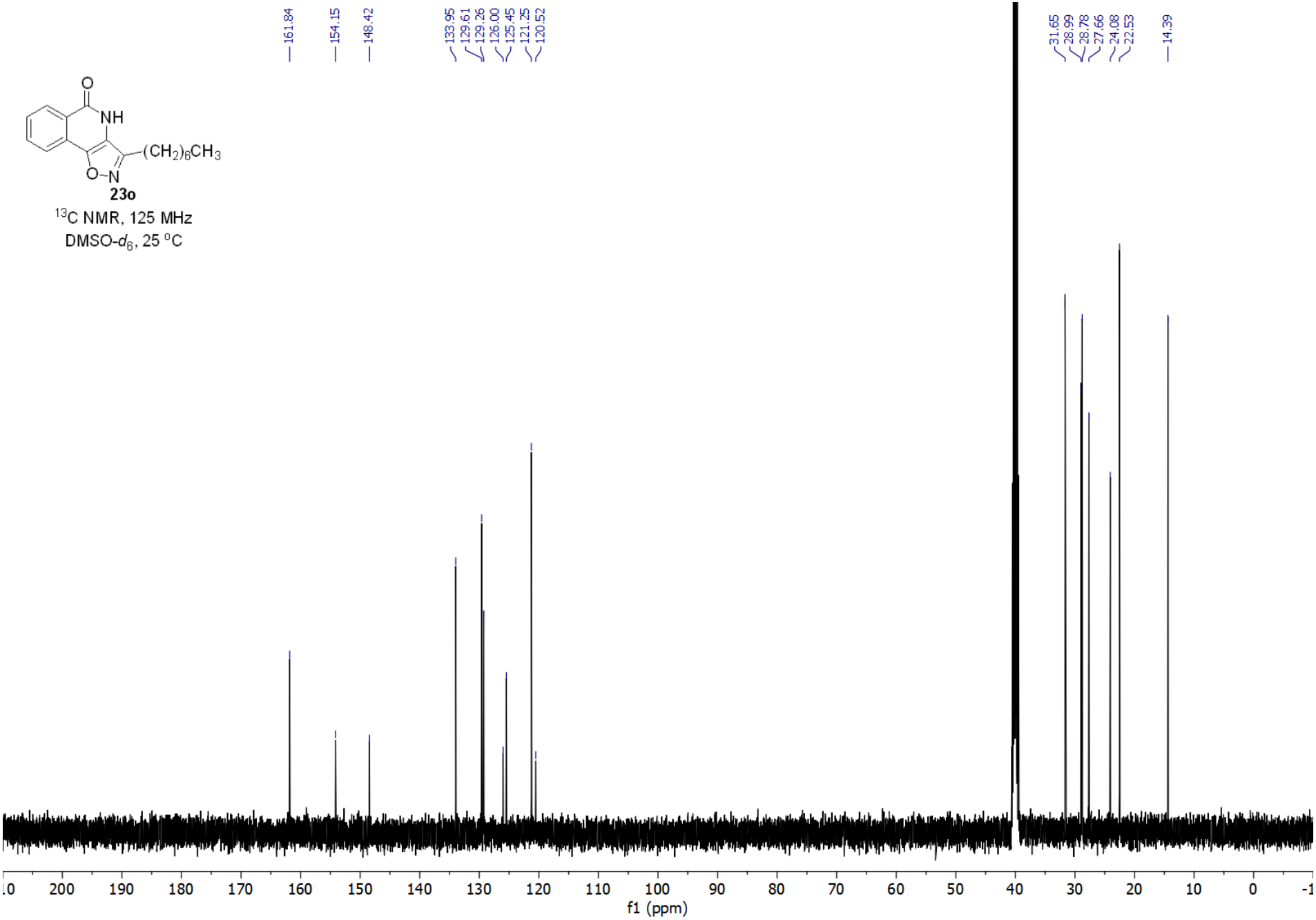


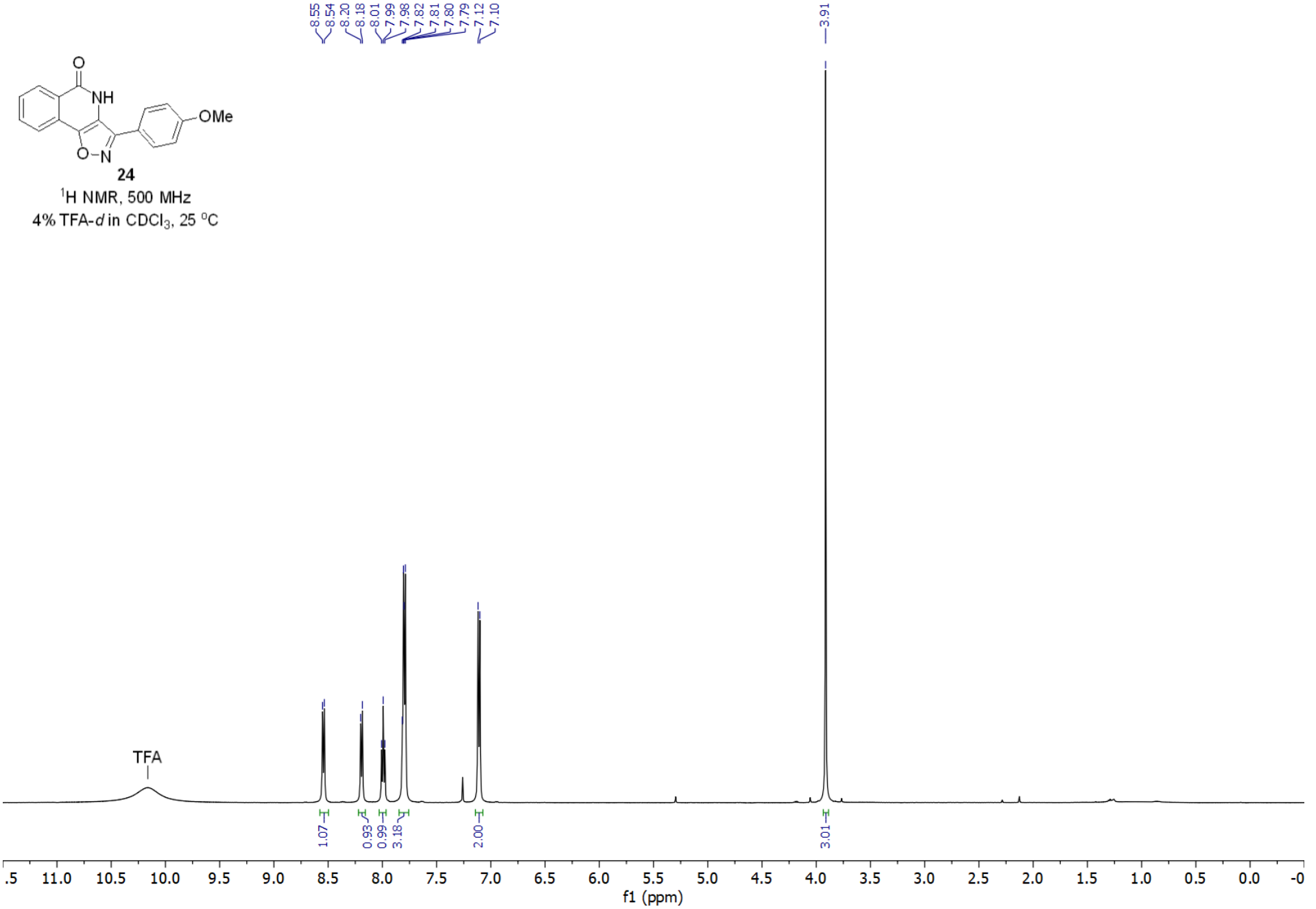
23l

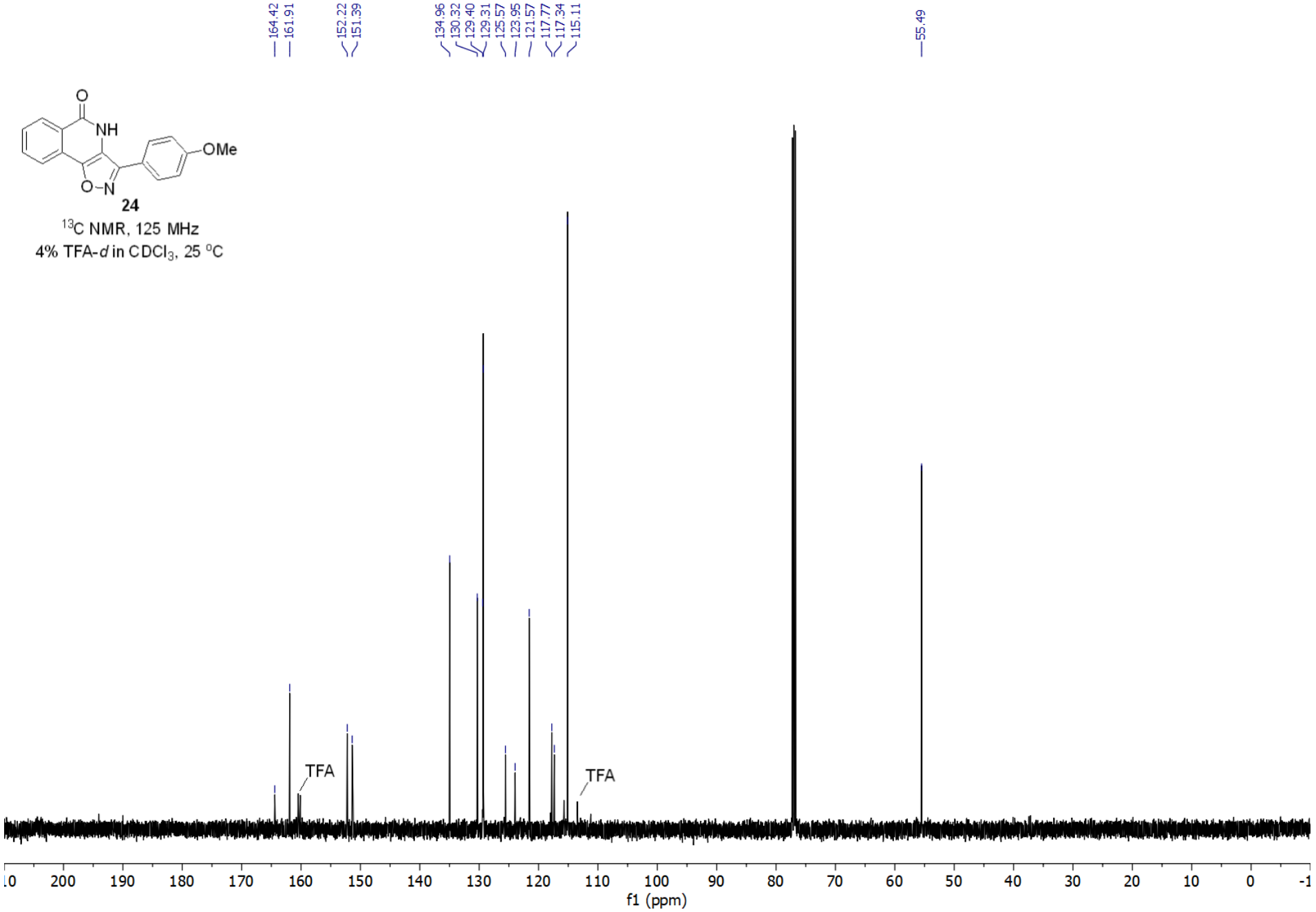
^{13}C NMR, 125 MHz

4% TFA-*d* in $CDCl_3$, 25 ^{0}C


11.94
8.33
8.33
8.32
8.32
8.02
8.00
7.92
7.92
7.91
7.90
7.89
7.89
7.73
7.72
7.70
2.85
2.84
2.82
1.70
1.68
1.67
1.65
1.64
1.37
1.35
1.35
1.34
1.34
1.32
1.32
1.32
1.31
1.30
1.29
1.29
1.27
1.27
1.26
1.26
1.25
1.24
1.23
1.23
1.22
1.21
1.21
0.85
0.84
0.82
O
NH
O–N
(CH2)6CH3
23o
1H NMR, 500 MHz
DMSO-d6, 25 °C
1.02
1.00
1.01
1.20
1.23
2.71
2.76
8.84
3.30
f1 (ppm)


161.84
154.15
148.42
133.95
129.61
129.26
126.00
125.45
121.25
120.52
31.65
28.99
28.78
27.66
24.08
22.53
14.39
NH
O
O
N
(CH2)6CH3
23o
13C NMR, 125 MHz
DMSO-d6, 25 °C
f1 (ppm)


8.55
8.54
8.20
8.18
8.01
7.99
7.98
7.82
7.81
7.80
7.79
7.12
7.10
3.91
O
NH
OMe
O
N
24
1H NMR, 500 MHz
4% TFA-d in CDCl3, 25 °C
TFA
1.07
0.93
0.99
3.18
2.00
3.01
f1 (ppm)


164.42
161.91
152.22
151.39
134.96
130.32
129.40
129.31
125.57
123.95
121.57
117.77
117.34
115.11
55.49
O
NH
OMe
O–N
24
^{13}C NMR, 125 MHz
4% TFA-*d* in $CDCl_3$, 25 ^{o}C
TFA
TFA
f1 (ppm)