

Supplementary Material

***N,N*-Dialkyl-*N'*-Chlorosulfonyl Chloroformamidines in Heterocyclic Synthesis.**

Part XIV. Synthesis and Reactivity of the New Benzo[4,5]imidazo[1,2-b][1,2,6]thiadiazine Ring System

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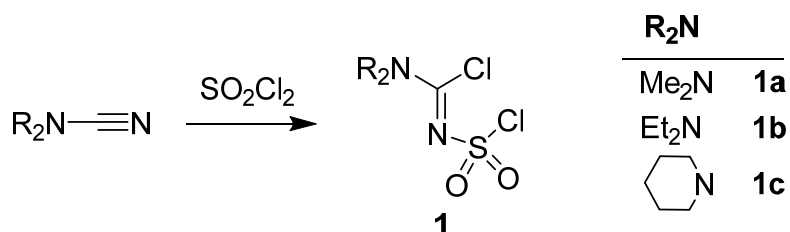
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Synthesis of dichlorides 1a-c

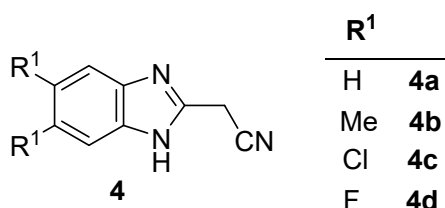
The dichlorides **1a-c** were prepared from sulfuryl chloride and the corresponding dialkyl cyanamide as previously described (Scheme S1).^[6]



Scheme S1

Synthesis of benzimidazole derivatives 4.

5,6-Dimethylbenzimidazole **4b**^[7] was prepared following published procedures,^[7,8] in which 4,5-dimethyl-1,2-diaminobenzene **5b** was heated with ethyl cyanoacetate. However, attempts to employ this procedure for preparation of the 5,6-dihalogenated derivatives **4c** and **4d**^[9] were unsuccessful, requiring the use of the relatively more reactive 2-cyanoacetimidic acid ethyl ester.^[10]



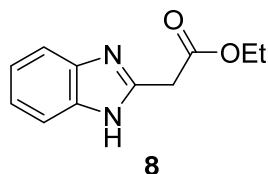
2-(5,6-Dichloro-1H-benzo[d]imidazol-2-yl)acetonitrile **4c**

A stirred mixture of 4,5-dichlorobenzene-1,2-diamine **5c** (1.0 g, 5.7 mmol) and 2-cyanoacetimidic acid ethyl ester hydrochloride^[9] (1.1 g, 7.6 mmol) in CH₂Cl₂ (30 mL) was heated at reflux overnight. The reaction mixture was cooled to room temperature and the precipitate was collected, washed with water and purified by column chromatography. Elution with 60% EtOAc in hexanes provided the *title compound* **4c** (0.63 g, 49%) as a white solid; mp 200 °C dec.; (Found: [M + H]⁺ 225.9935; C₉H₆Cl₂N₃, requires [M + H]⁺ 225.9939); ¹H NMR (600 MHz, DMSO-*d*₆ + 1 drop conc. HCl) 7.98 (2H, s, ArH), 4.64 (2H, s, CH₂). ¹³C NMR (150 MHz, DMSO-*d*₆ + 1 drop conc. HCl) 147.63, 134.85, 126.92, 116.46, 115.31, 18.20.

2-(5,6-Difluoro-1H-benzo[d]imidazol-2-yl)acetonitrile **4d**^[9]

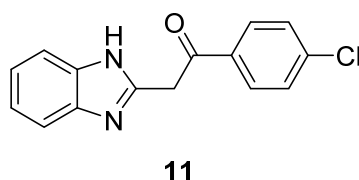
A mixture of 4,5-difluorobenzene-1,2-diamine **5d** (195 mg, 1.4 mmol) and 2-cyanoacetimidic acid ethyl ester hydrochloride^[10] (250 mg, 1.7 mmol) in CH₂Cl₂ (7 mL) was stirred at 40 °C overnight. After cooling, the precipitate was collected, washed with water and with CH₂Cl₂ (3 × 10 mL) to give the *title*

compound **4d** (184 mg, 70%) as a tan solid; mp 202–203 °C (lit.^[9] 210–212 °C); (Found: [M + H]⁺ 194.0525; C₉H₆N₃F₂ requires [M + H]⁺ 194.0530); ¹H NMR (400 MHz, DMSO-*d*₆) 7.62 (2H, t, *J* 10.9 Hz, Ar*H*), 4.37 (2H, s, CH₂); ¹³C NMR (150 MHz, DMSO-*d*₆ + 1 drop conc. HCl) 149.56 (d, *J* 17.0 Hz), 147.93 (d, *J* 17.0 Hz), 146.54, 128.86 (t, *J* 6.1 Hz), 114.76, 103.37 (dd, *J* 17.0, 7.2 Hz), 17.94.



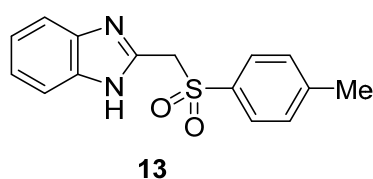
Ethyl 2-(1H-benzo[d]imidazol-2-yl)acetate **8**^[8]

Prepared by a literature procedure.^[11] Thus, acetyl chloride (1 mL, 14 mmol) was added dropwise to a stirred solution of benzimidazole acetonitrile **4a** (500 mg, 3.18 mmol) in EtOH (8 mL) at 0 °C. The reaction mixture was heated at reflux for 2 h, cooled to room temperature and the remaining solvent removed *in vacuo*. The hydrochloride salt was dissolved in water and neutralised with a saturated solution of NaHCO₃. Extraction with CH₂Cl₂ (3 × 20 mL) provided the *title compound* **8** (605 mg, 93%) as a brown solid; mp 106–108 °C (lit.^[8] 128.5–129.5 °C); ¹H NMR (600 MHz, DMSO-*d*₆) 7.56–7.48 (2H, m, Ar*H*), 7.20–7.12 (2H, m, Ar*H*), 4.13 (2H, q, *J* 7.1 Hz, CH₂CH₃), 3.97 (2H, s, ArCH₂), 1.20 (3H, t, *J* 7.1 Hz, CH₂CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) 168.72, 147.75, 138.71, 121.54, 114.75, 60.81, 35.10, 14.03.



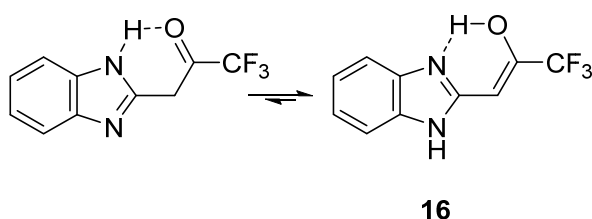
2-(1H-benzo[d]imidazol-2-yl)-1-(4-chlorophenyl)ethan-1-one **11**^[12]

Prepared by a literature procedure^[12] using acetonitrile as solvent in the first step with the modification of heating the tri-benzoylated intermediate in *n*-BuOH at 110 °C for 2 h rather than in 2-propanol at reflux. The *title compound* **11** (60% yield) was obtained as a bright yellow solid; mp 225–228 °C (lit.^[12] 226–228 °C). ¹H NMR (600 MHz, DMSO-*d*₆) 12.32 and 12.24 (1H, 2 x br s, NH), 8.09 (0.30H, d, *J* 8.5 Hz, Ar*H*), 7.87 (1.6H, d, *J* 8.5 Hz, Ar*H*), 7.64 (0.32H, d, *J* 8.6 Hz, Ar*H*), 7.51 (1.6H, d, *J* 8.6 Hz, Ar*H*), 7.56 and 7.37 (2H, 2 x m, H-4,7), 7.15–7.18 (2H, m, H-5,6), 6.03 (1H, s, C=CH-C=O), 4.67 (0.41H, s, CH₂).



2-Tosylmethyl-1H-benzo[d]imidazole **13**^[13,14]

A solution of 2-chloromethylbenzimidazole (0.57 g, 3.4 mmol) and sodium *p*-toluenesulfinate (1.6 g, 9 mmol) in freshly distilled DMSO (20 mL) was stirred at room temperature overnight. The reaction mixture was diluted with EtOAc (100 mL) and washed with brine (4 × 50 mL) to remove the DMSO and excess sulfinate salts. The organic phase was dried (Na₂SO₄), and the solvent was removed *in vacuo* to provide the *title compound* **13** (0.81 g, 83%) as a tan solid; mp 206–208 °C (lit.^[13] 202 °C); ¹H NMR (600 MHz, DMSO-*d*₆) 12.63 (1H, br. s, NH), 7.65 (2H, d, *J* 8.0 Hz, ArH), 7.53 (2H, dd, *J* 6.2, 2.9 Hz, ArH), 7.40 (2H, d, *J* 8.0 Hz, ArH), 7.18 (2H, dd, *J* 6.2, 2.9 Hz, ArH), 4.94 (2H, s, CH₂), 2.39 (3H, s, CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) 144.68, 142.52, 135.80, 129.75, 127.93, 122.09, 55.84, 21.09.



3-(1H-Benzo[d]imidazol-2-yl)-1,1,1-trifluoropropan-2-one (*3-(1,3-dihydro-2H-benzimidazol-2-ylidene)-1,1,1-trifluoropropan-2-one*) **16**

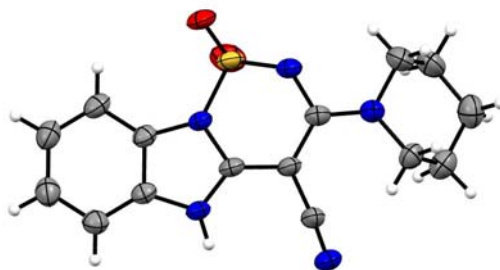
Prepared by a literature procedure.^[15] The *title compound* **16** (300 mg, 44%) was obtained as a white powder; mp 280–282 °C (lit.^[15] 279–280 °C dec.); ¹H NMR (600 MHz, DMSO-*d*₆) 12.68 (2H, br s, 2 x NH), 7.51 (2H, br s, ArH), 7.25–7.22 (2H, m, ArH), 5.41 (1H, s, C=CHCOCF₃); ¹³C NMR (150 MHz, DMSO-*d*₆) 167.96 (q, *J* 30.5 Hz), 151.94, 130.30, 123.13, 118.83 (q, *J* 288.9 Hz), 111.70 (m), 71.69; ¹⁹F (565 MHz, DMSO-*d*₆) –74.48.

References

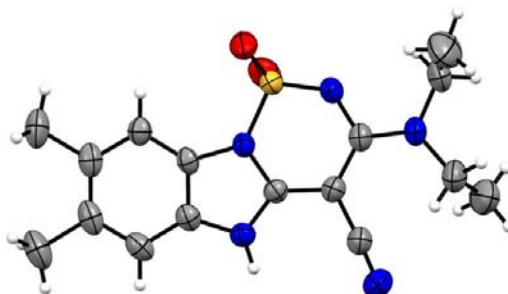
- [6] C. M. Forsyth, C. L. Francis, S. Jahangiri, A. J. Liepa, M. V. Perkins, A. P. Young, *Aust. J. Chem.* **2010**, *63*, 659–668. doi: 10.1071/CH09581
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Additional Crystal Structures

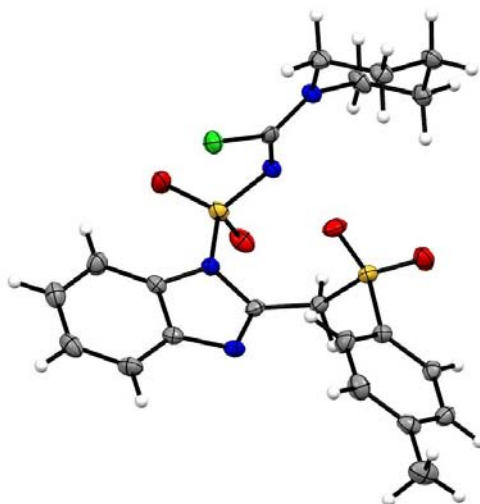


6c



6d

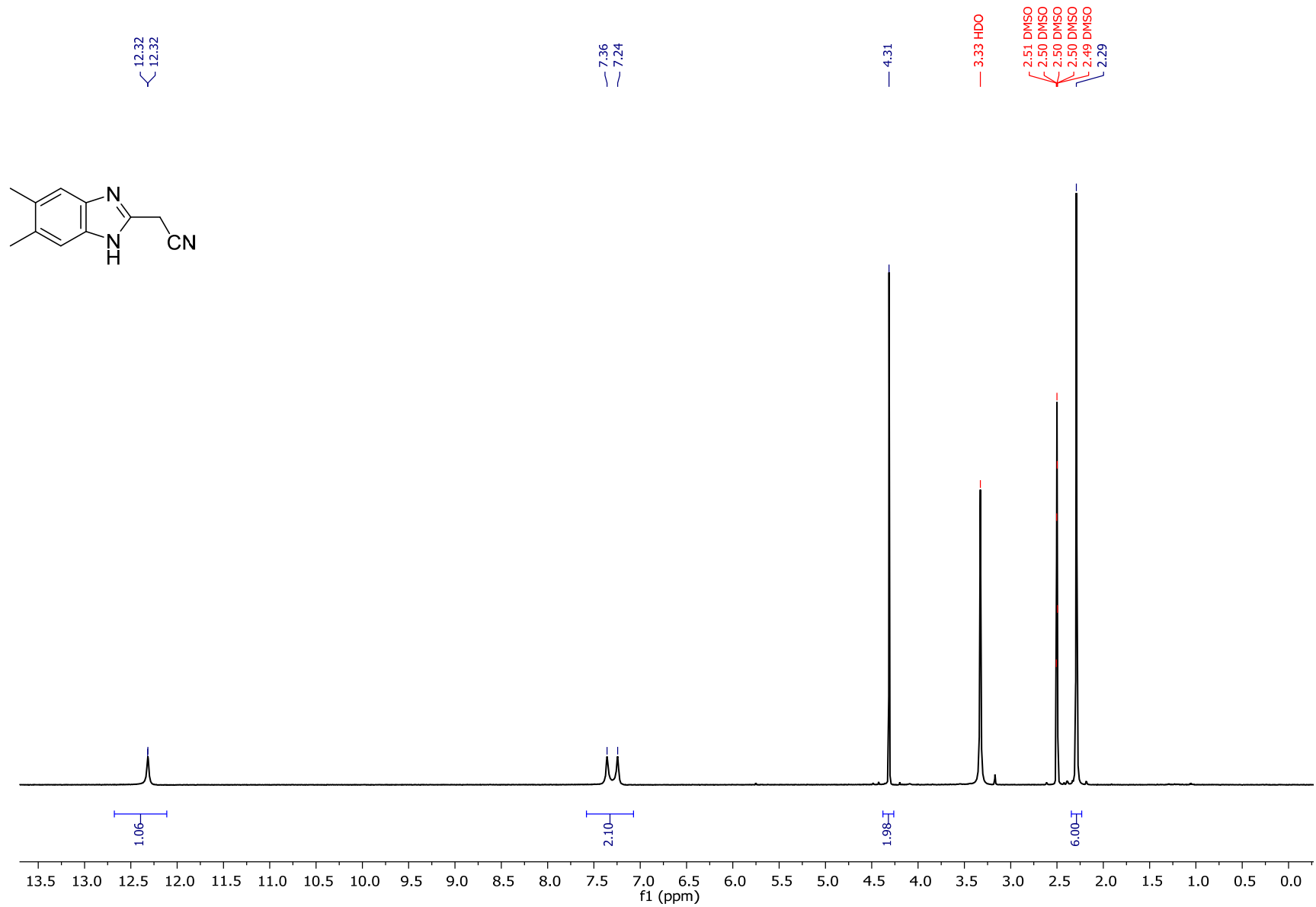
Figure S1. ORTEP diagrams of **6c** and **6d**. A molecule of DMSO is omitted from the crystal structure of **6d** for clarity.



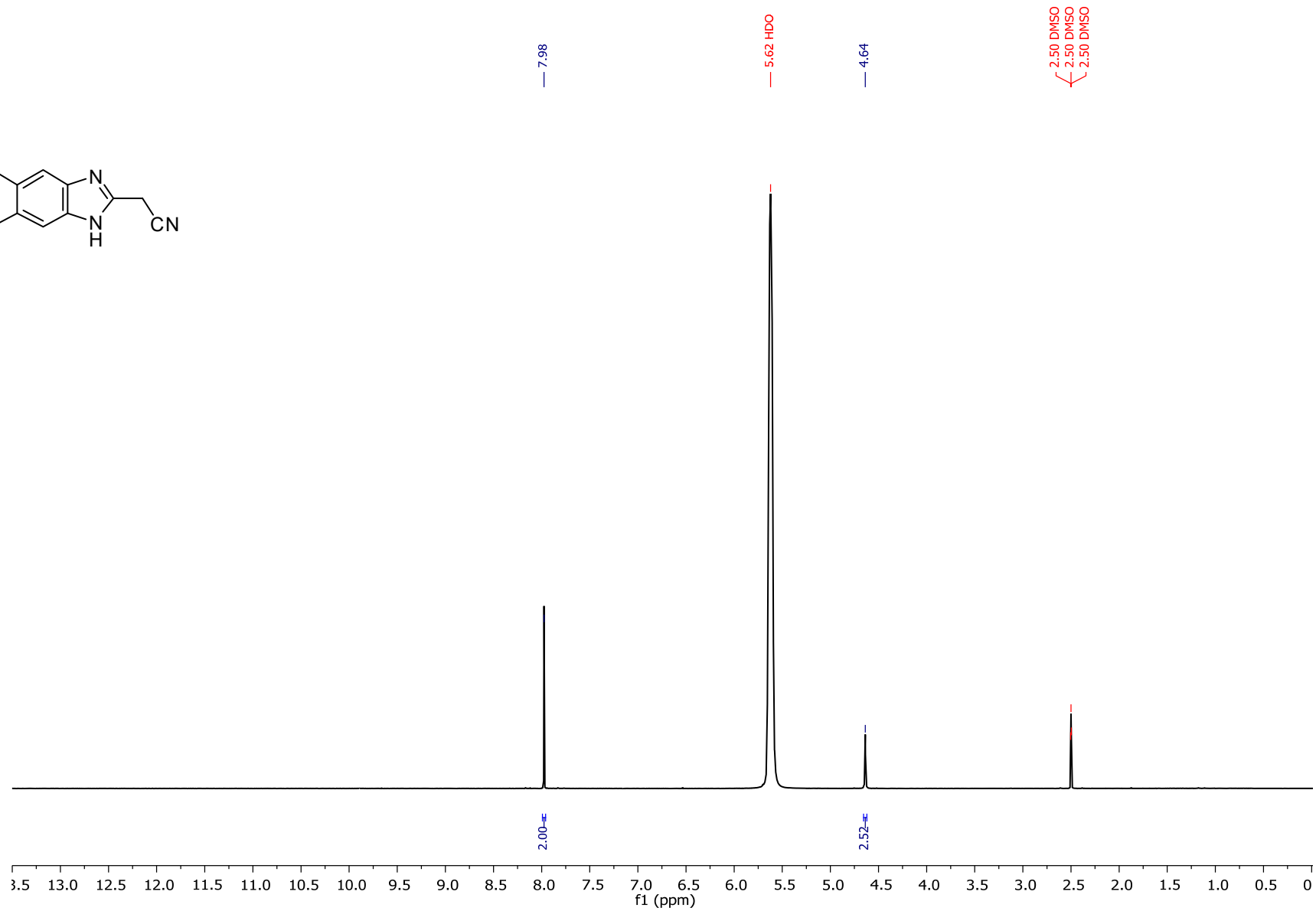
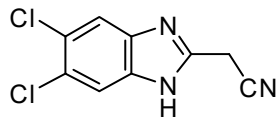
15b

Figure S2. ORTEP diagram of **15b**.

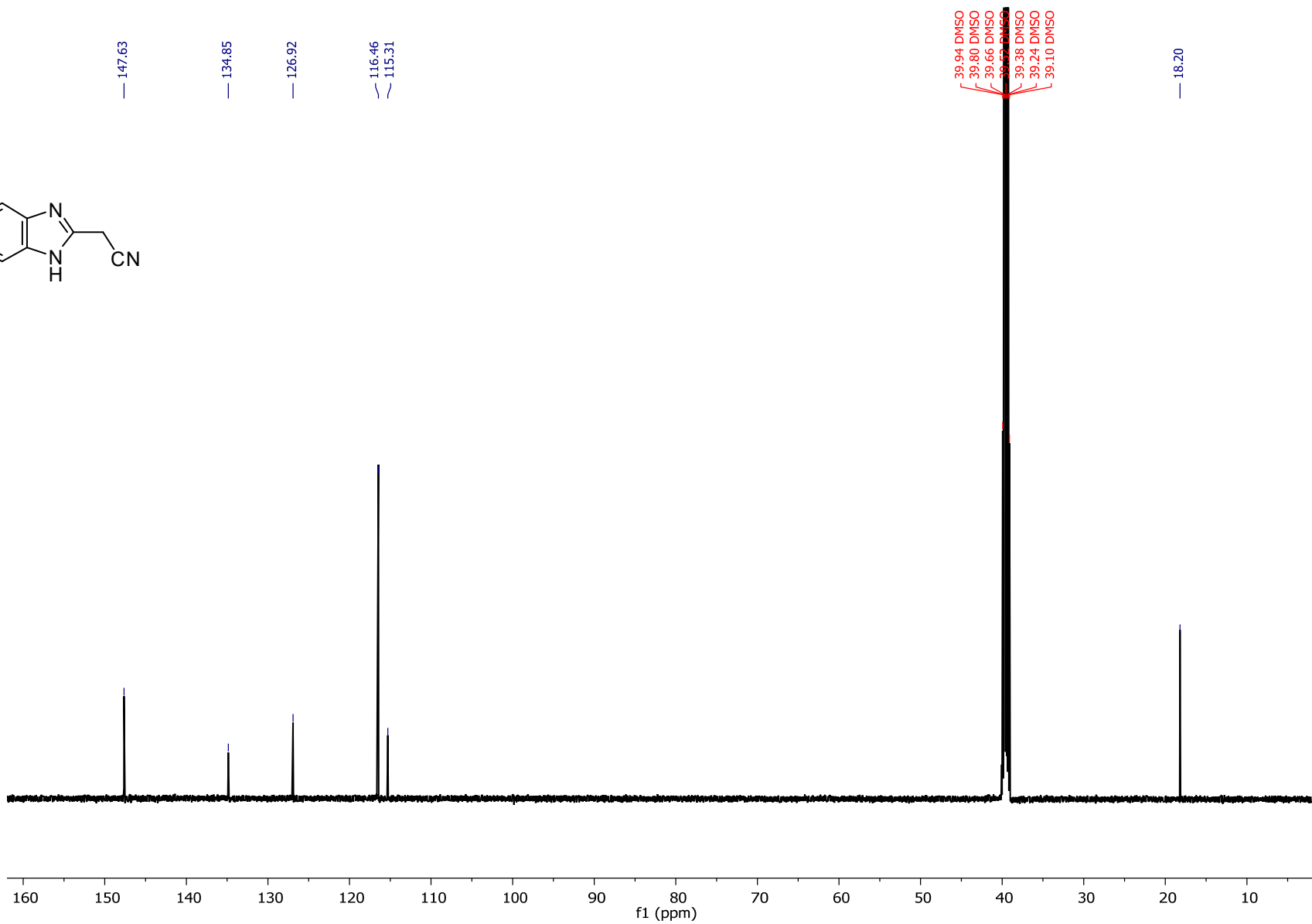
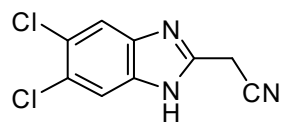
¹H NMR spectrum for **4b** (600 MHz; DMSO-*d*₆)



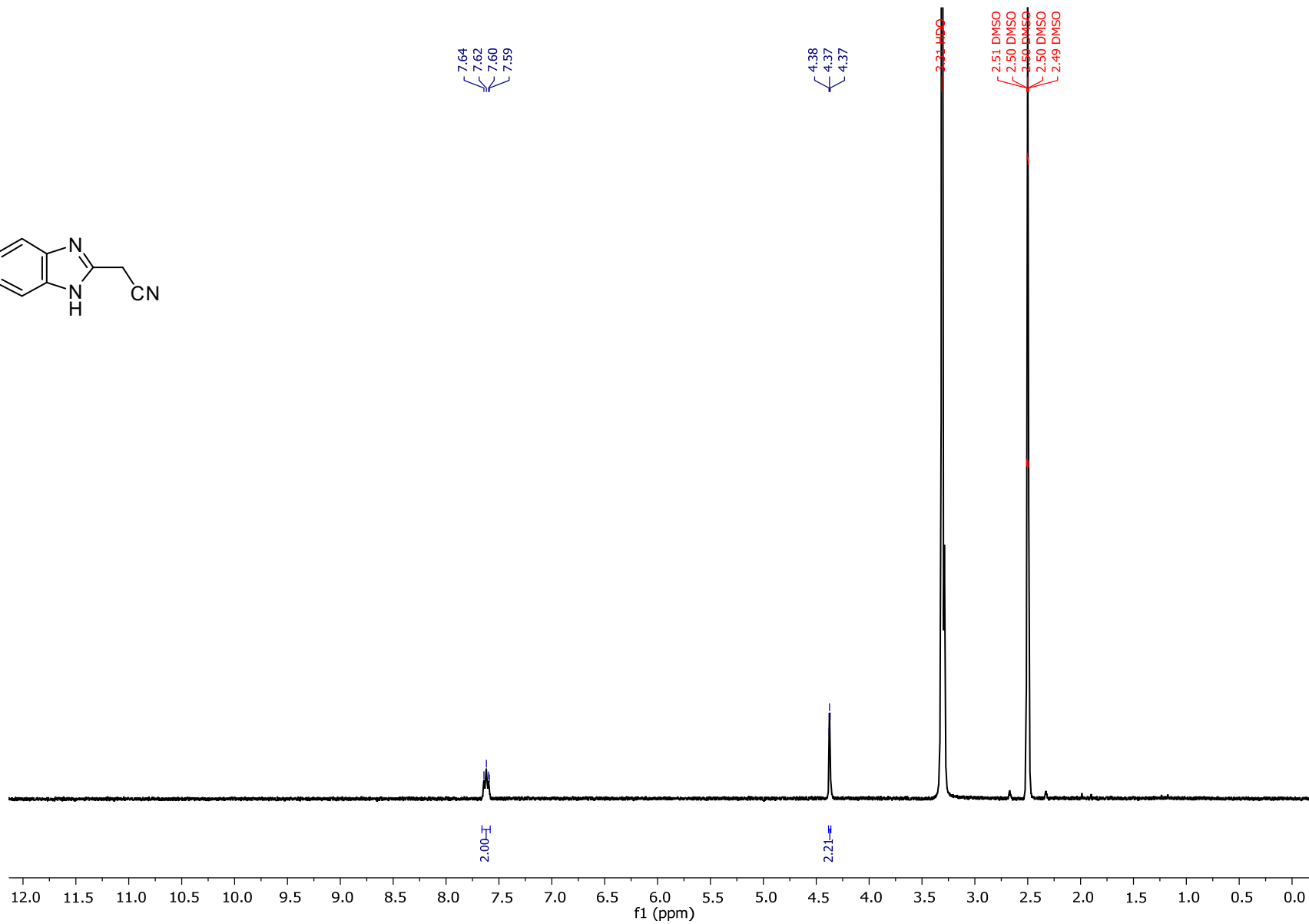
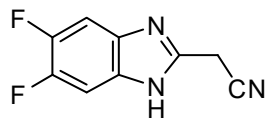
¹H NMR spectrum for **4c** (600 MHz; DMSO-*d*₆ + 1 drop conc. HCl)



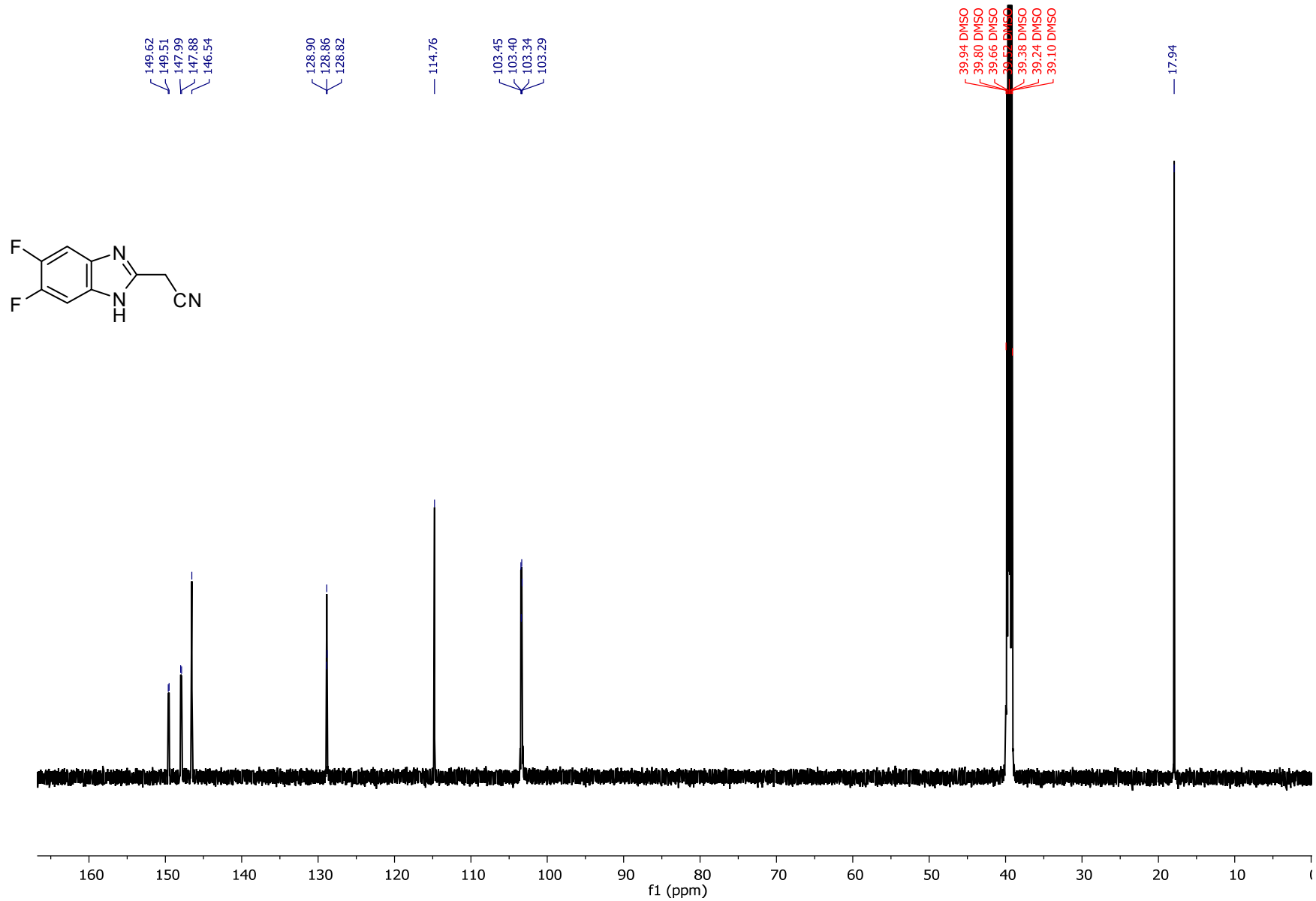
¹³C NMR spectrum for **4c** (150 MHz; DMSO-*d*₆ + 1 drop conc. HCl)



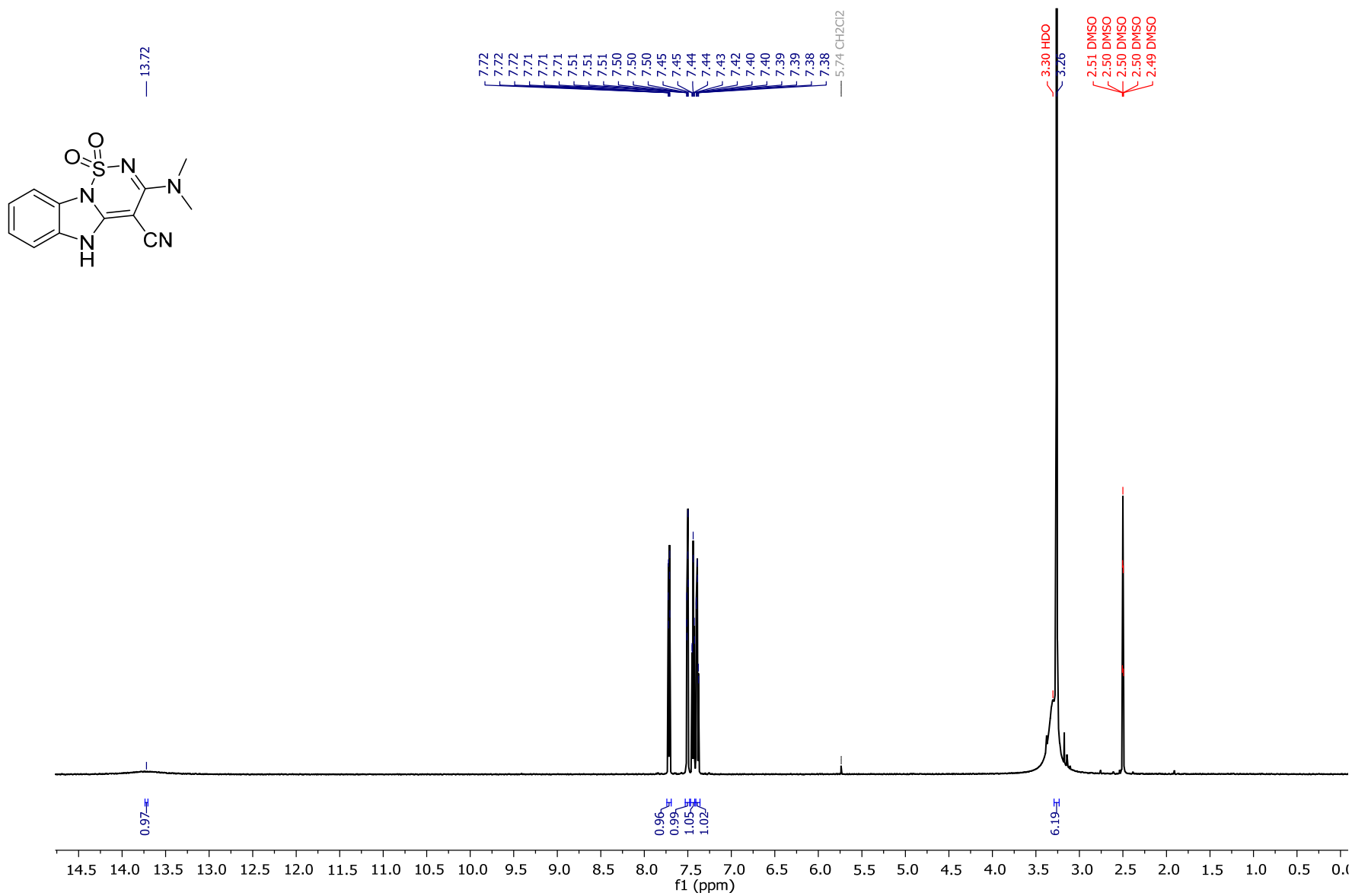
¹H NMR spectrum for **4d** (400 MHz; DMSO-*d*₆)



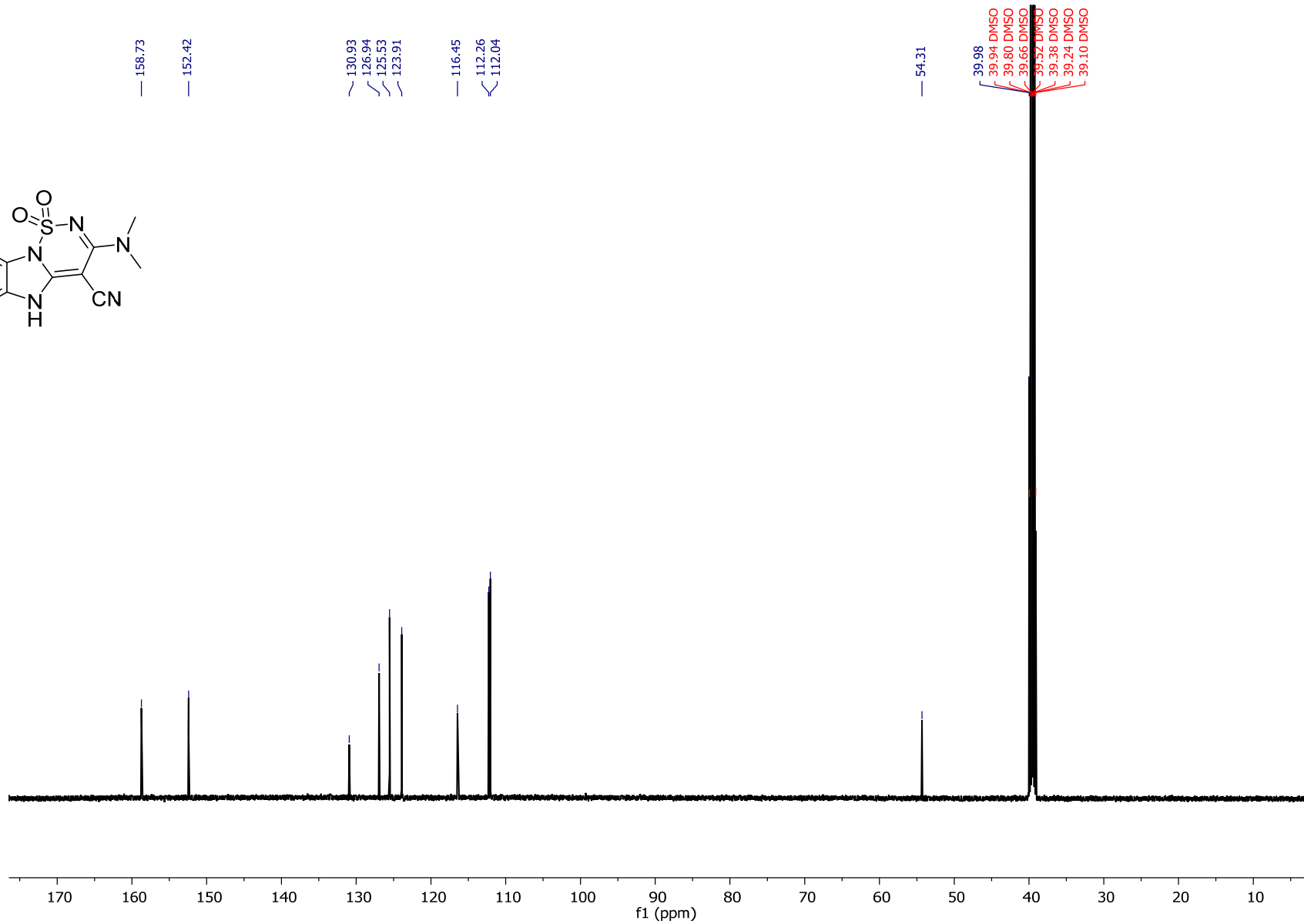
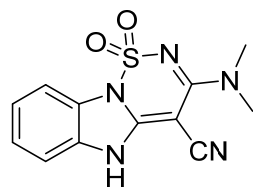
¹³C NMR spectrum for **4d** (150 MHz; DMSO-*d*₆ + 1 drop conc. HCl)



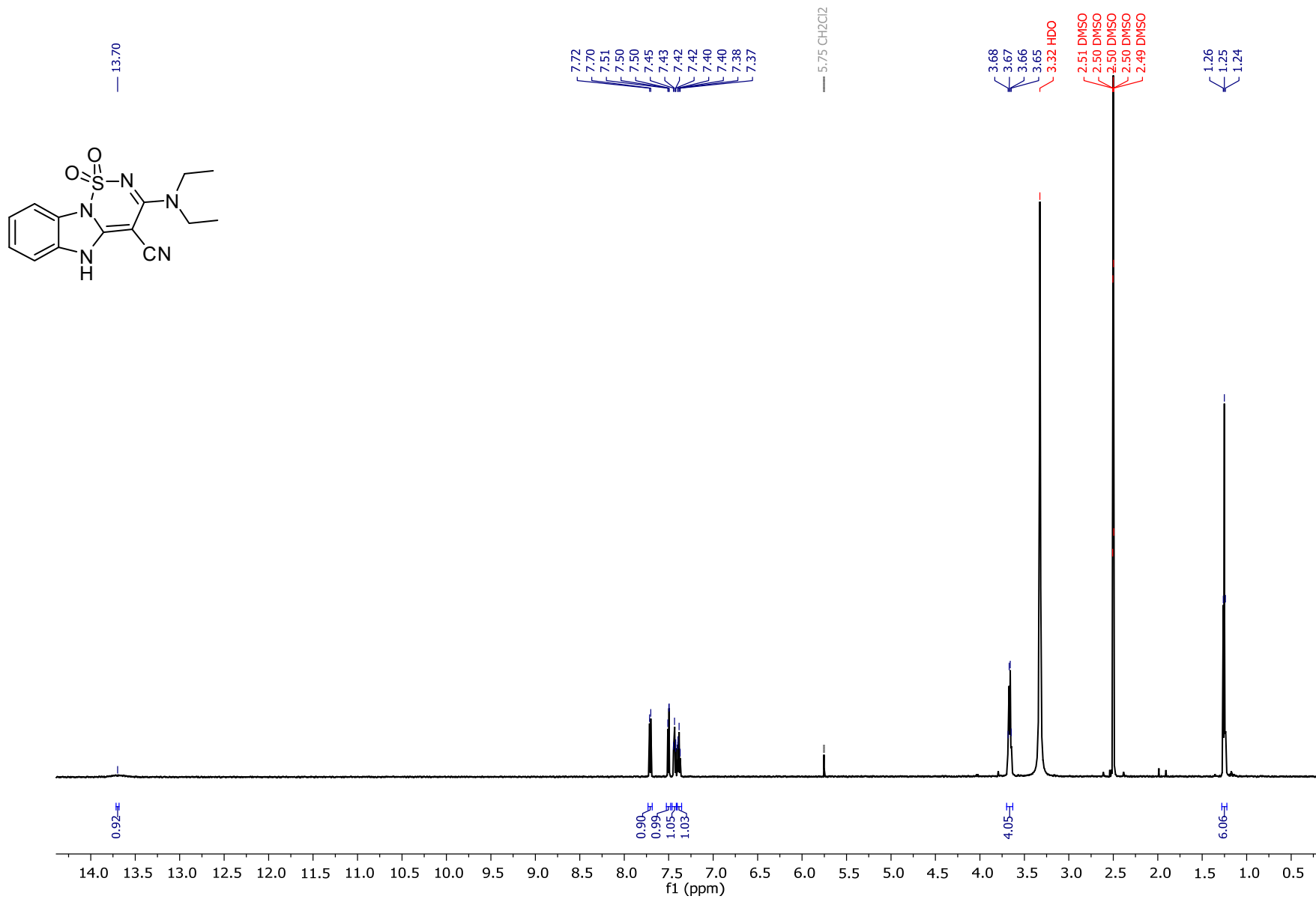
¹H NMR spectrum for **6a** (600 MHz; DMSO-*d*₆)



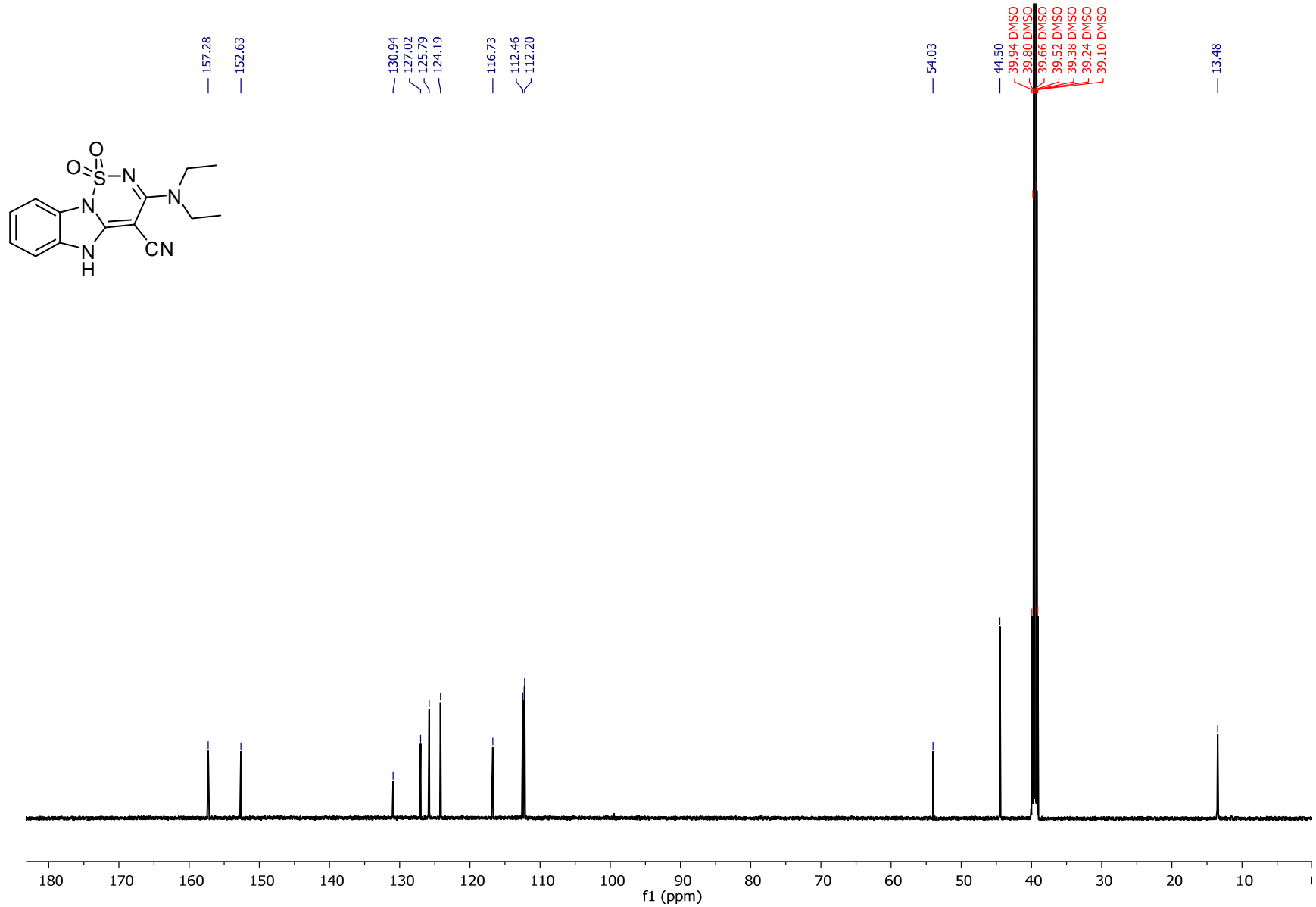
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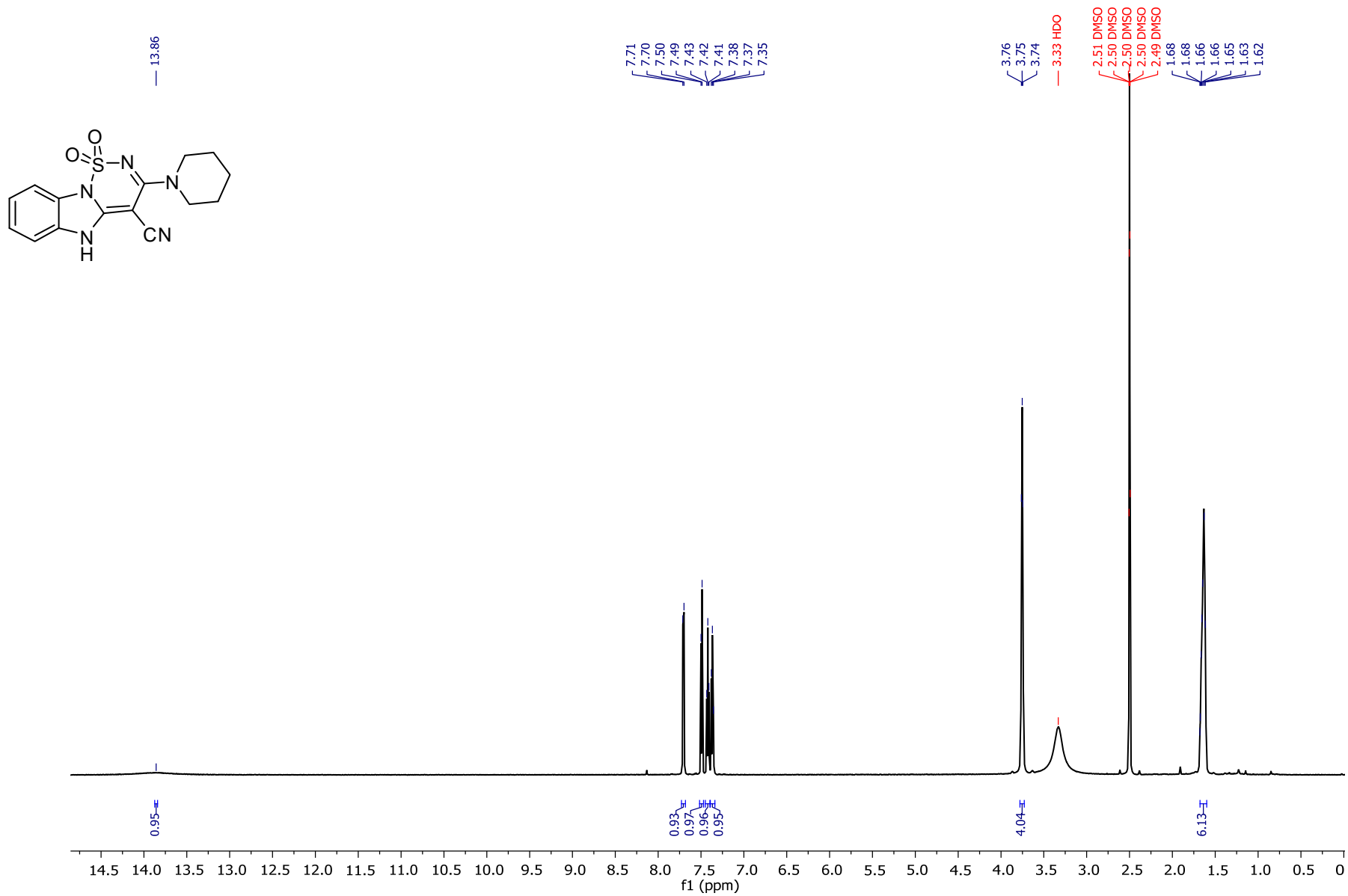
¹H NMR spectrum for **6b** (600 MHz; DMSO-*d*₆)



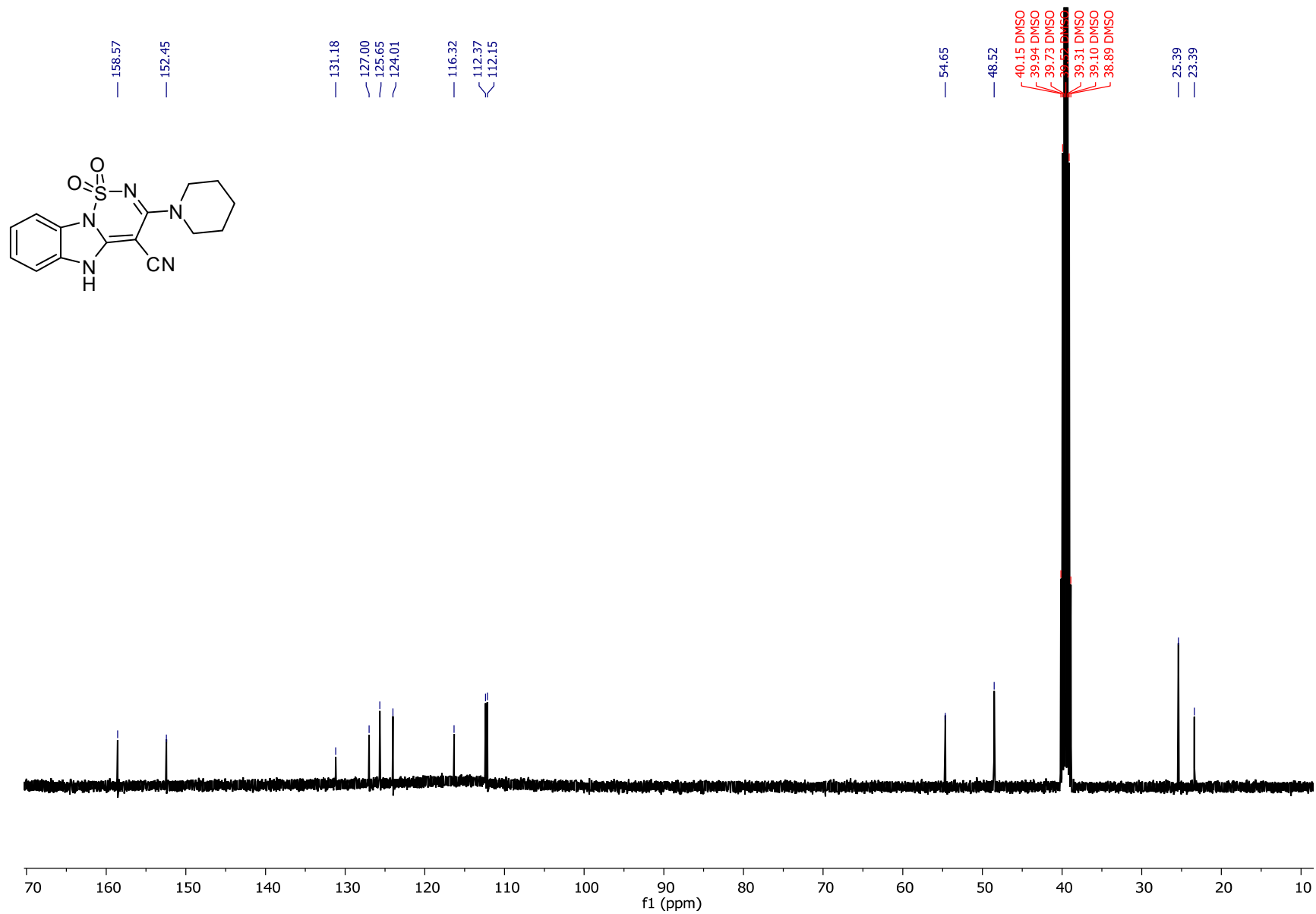
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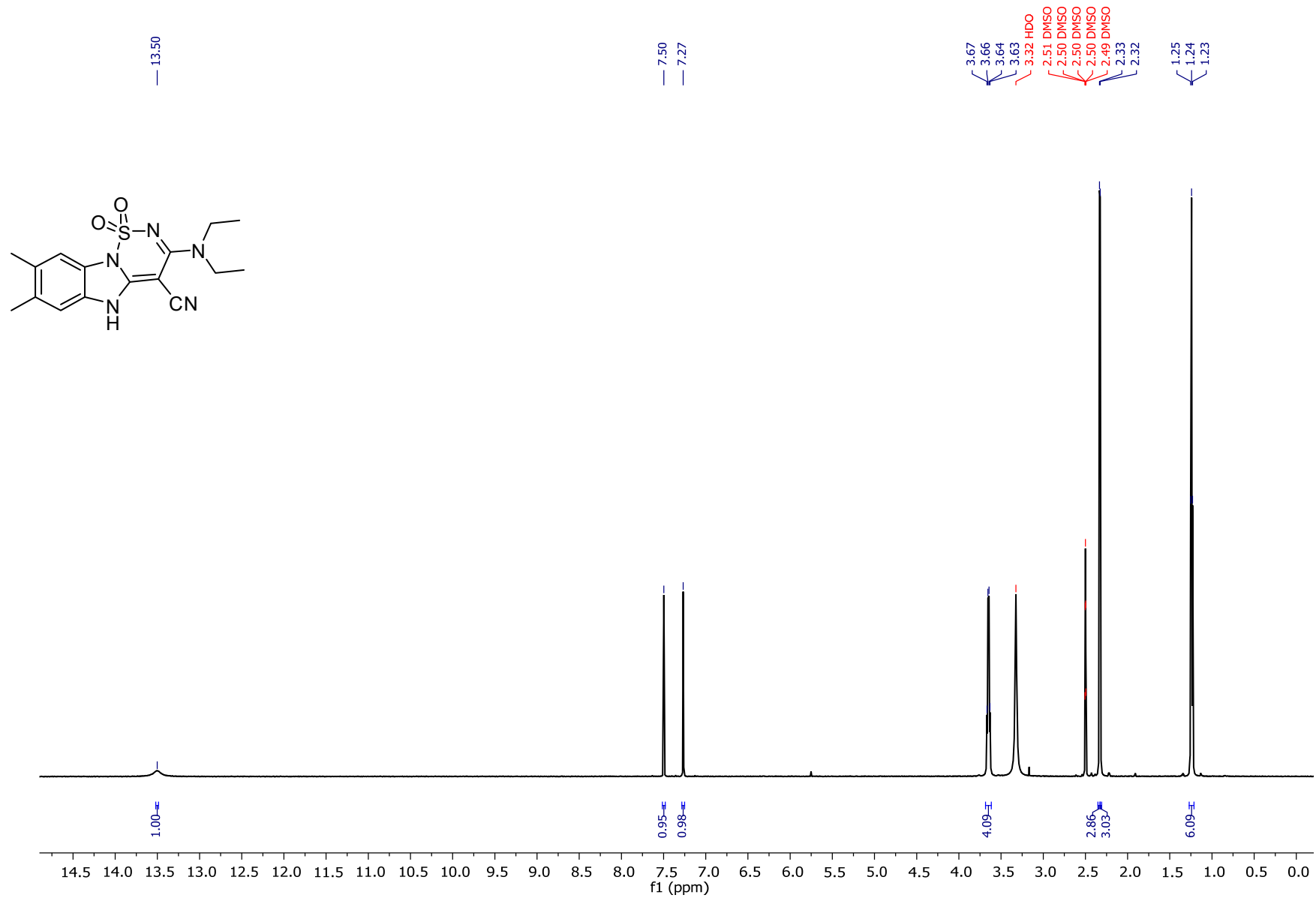
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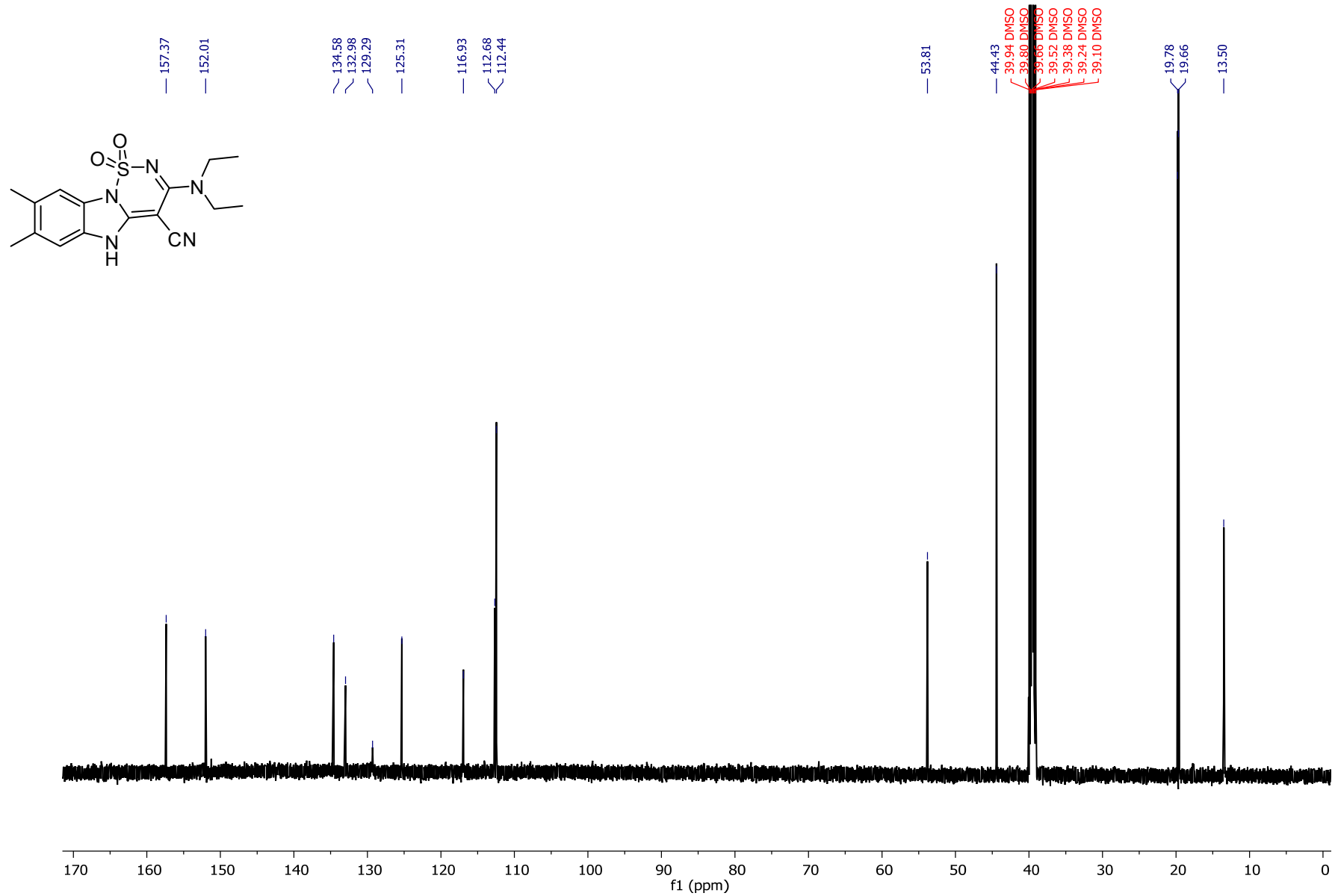
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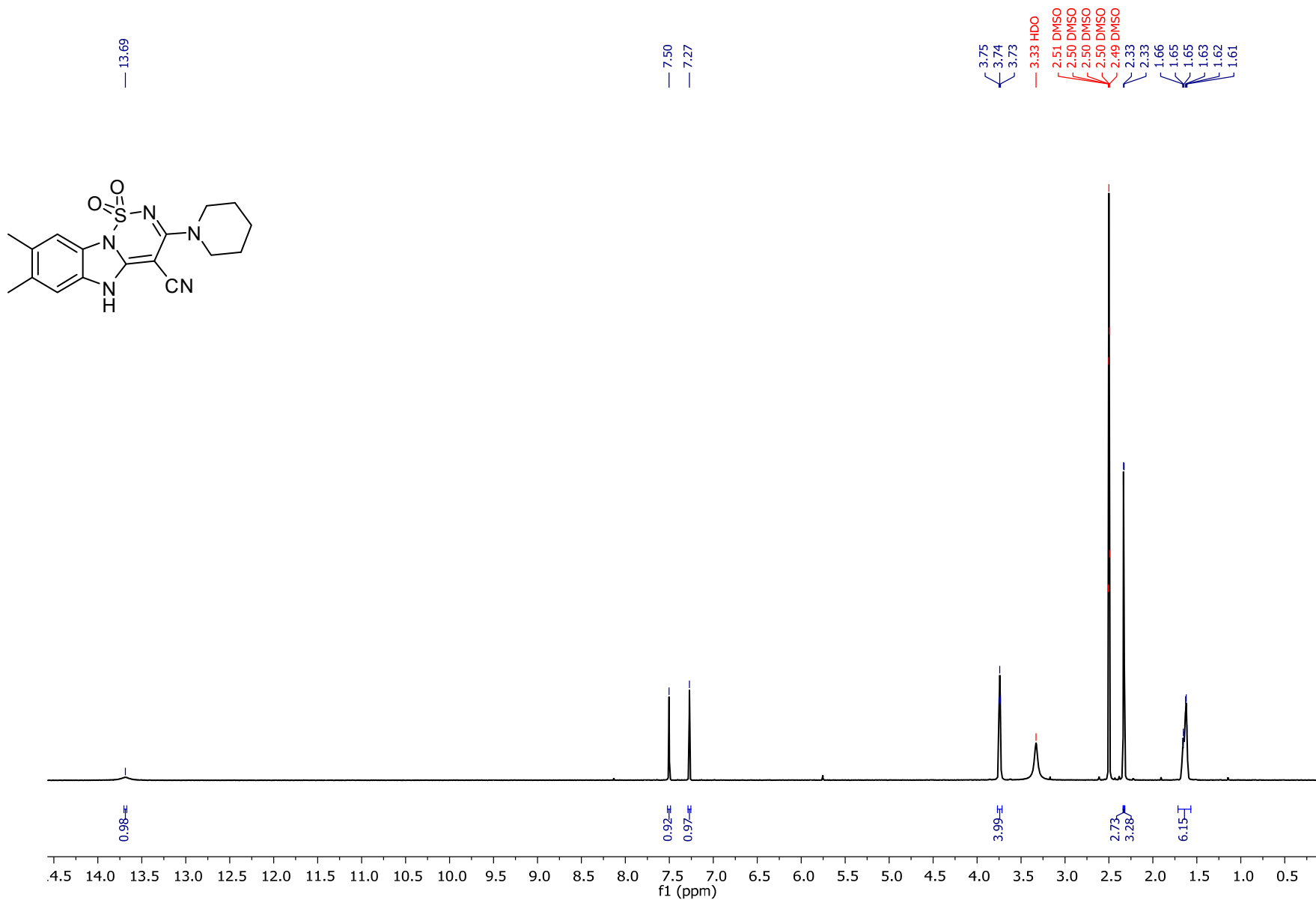
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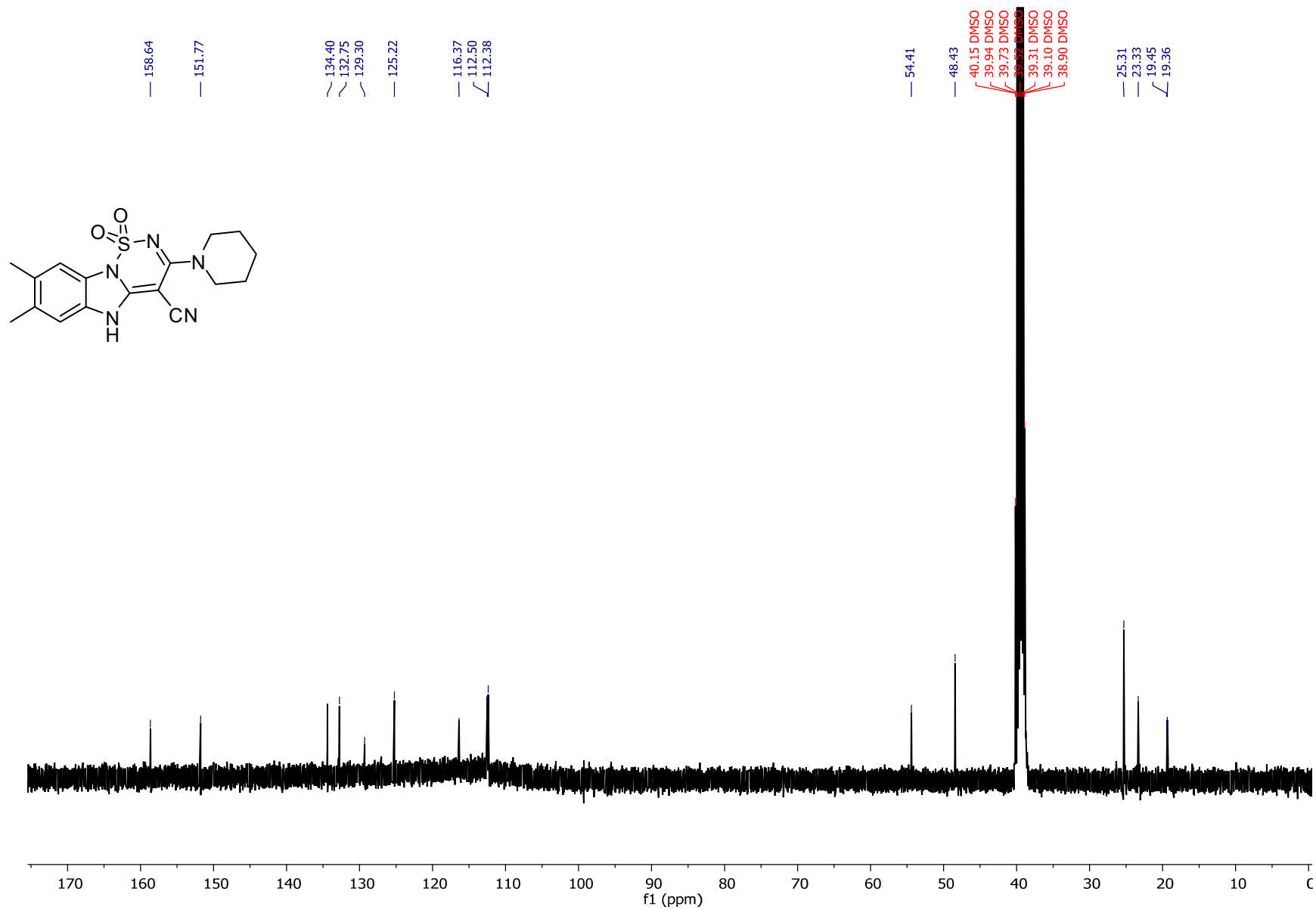
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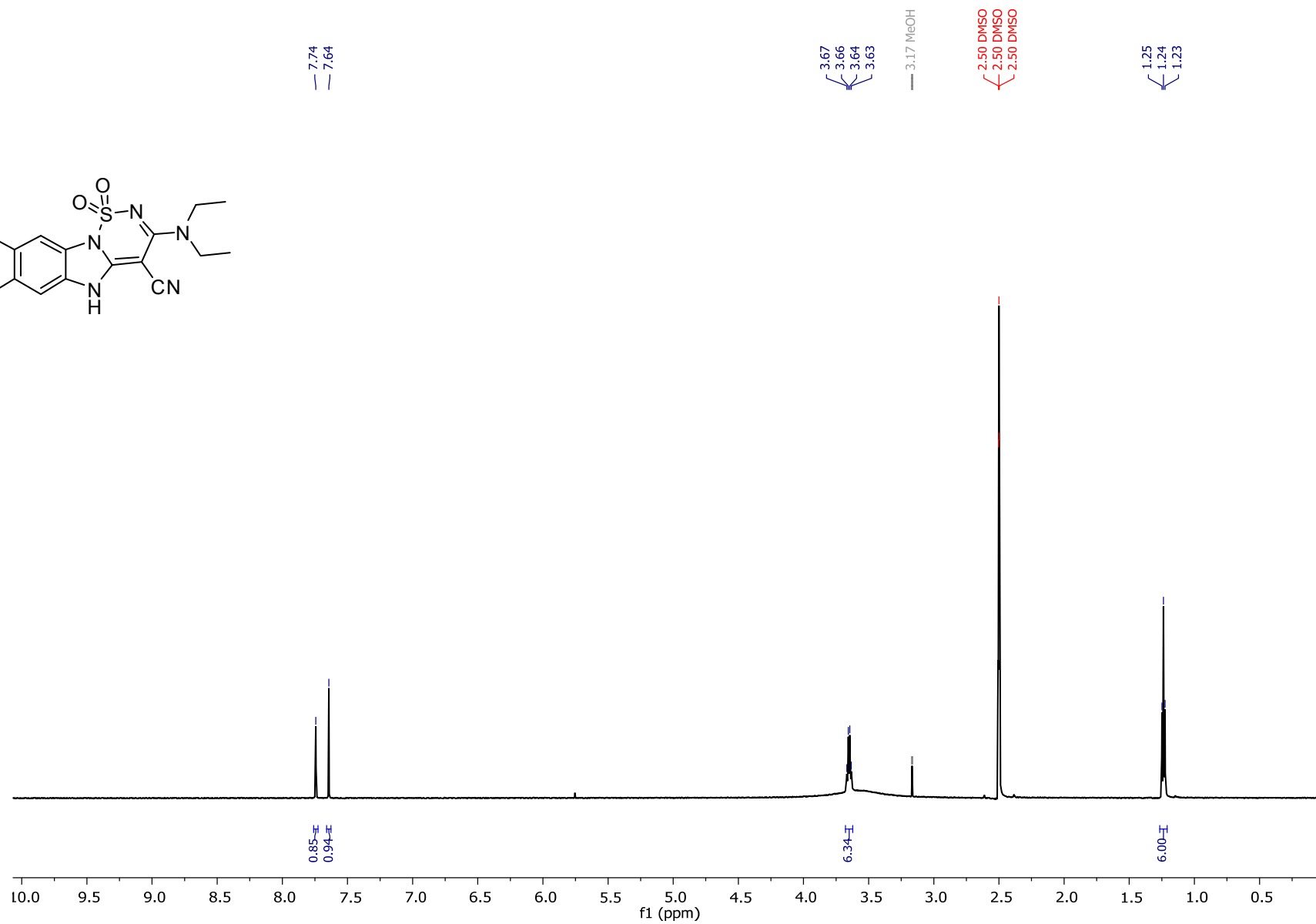
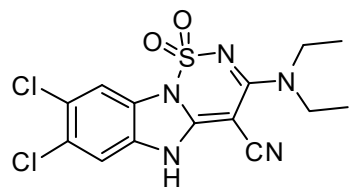
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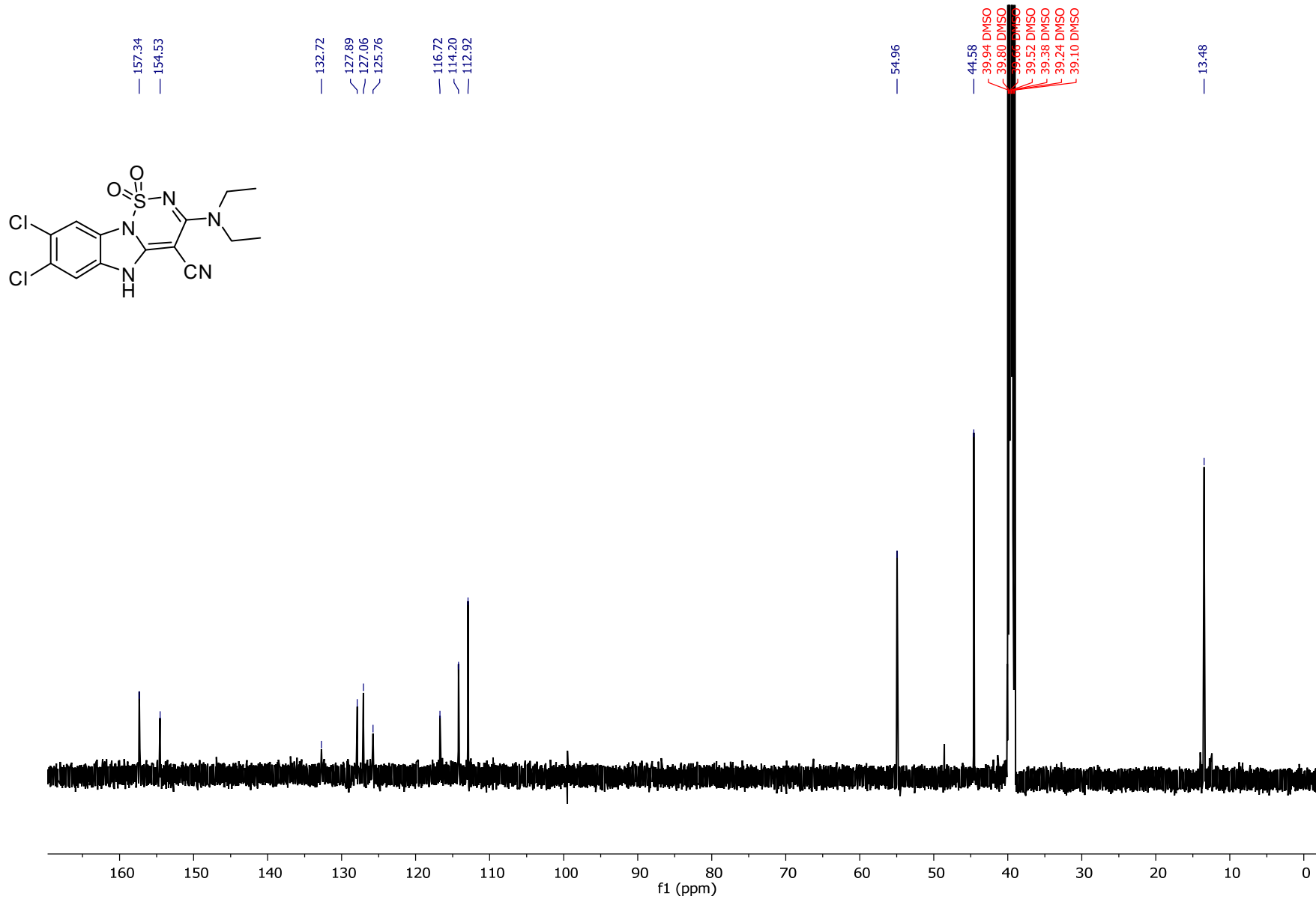
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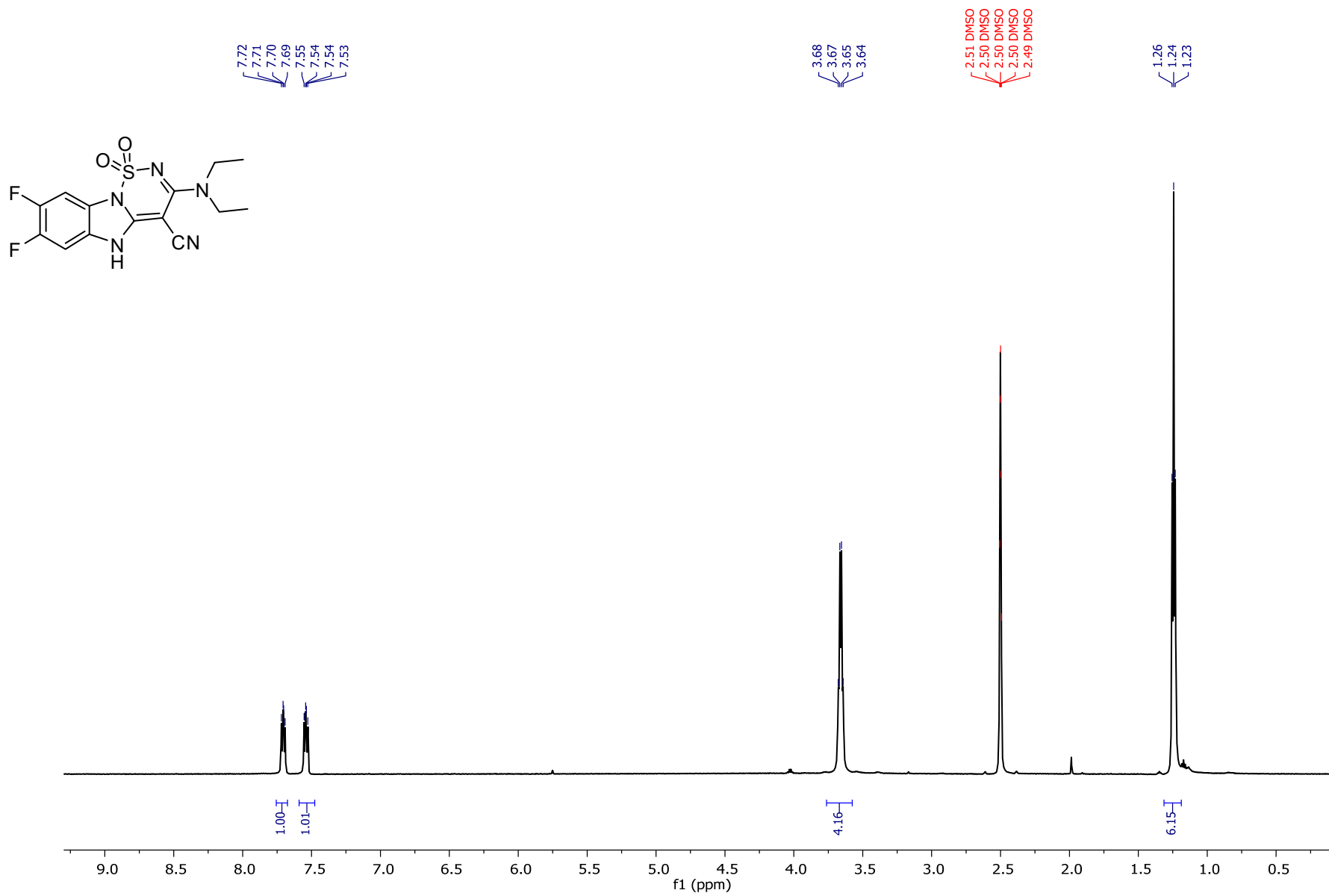
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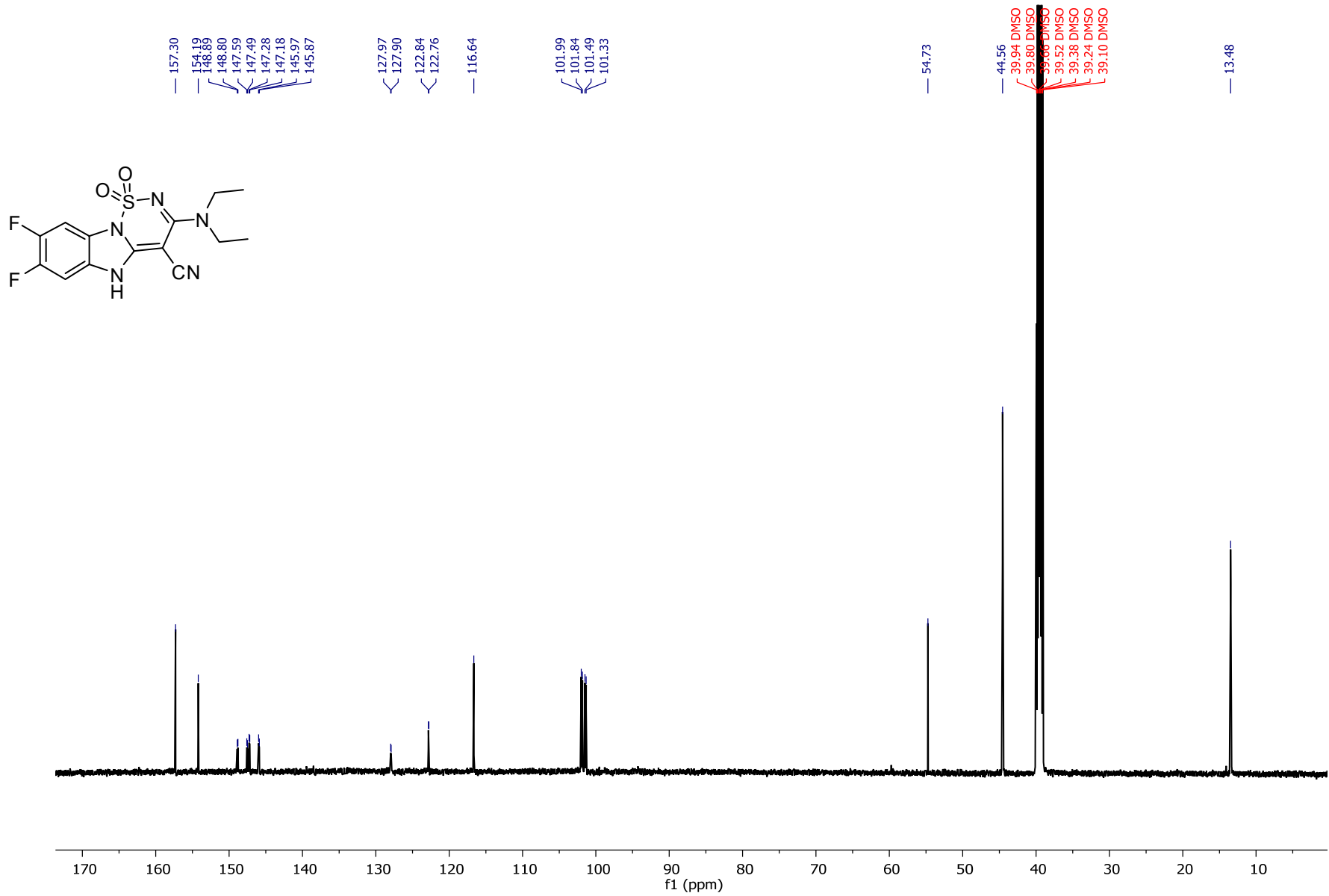
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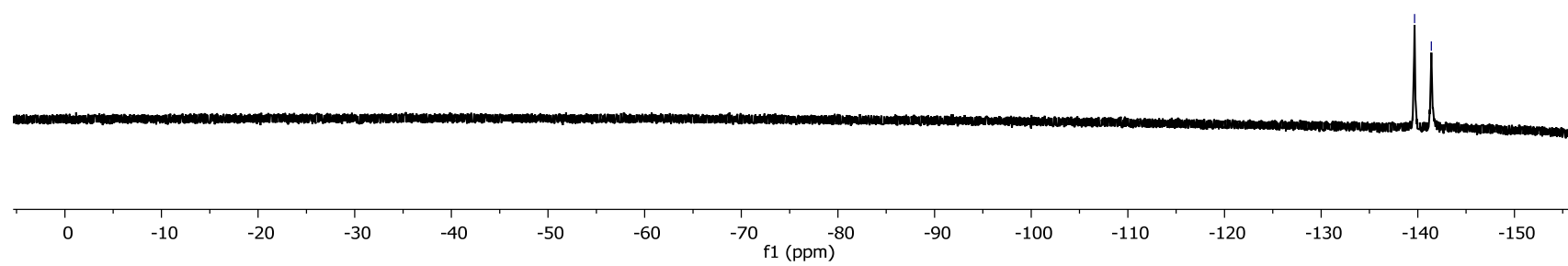
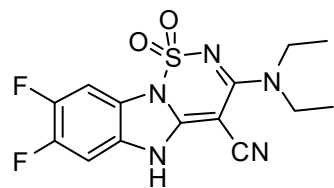
¹H NMR spectrum for **6g** (600 MHz; DMSO-*d*₆)



¹³C NMR spectrum for **6g** (150 MHz; DMSO-*d*₆)

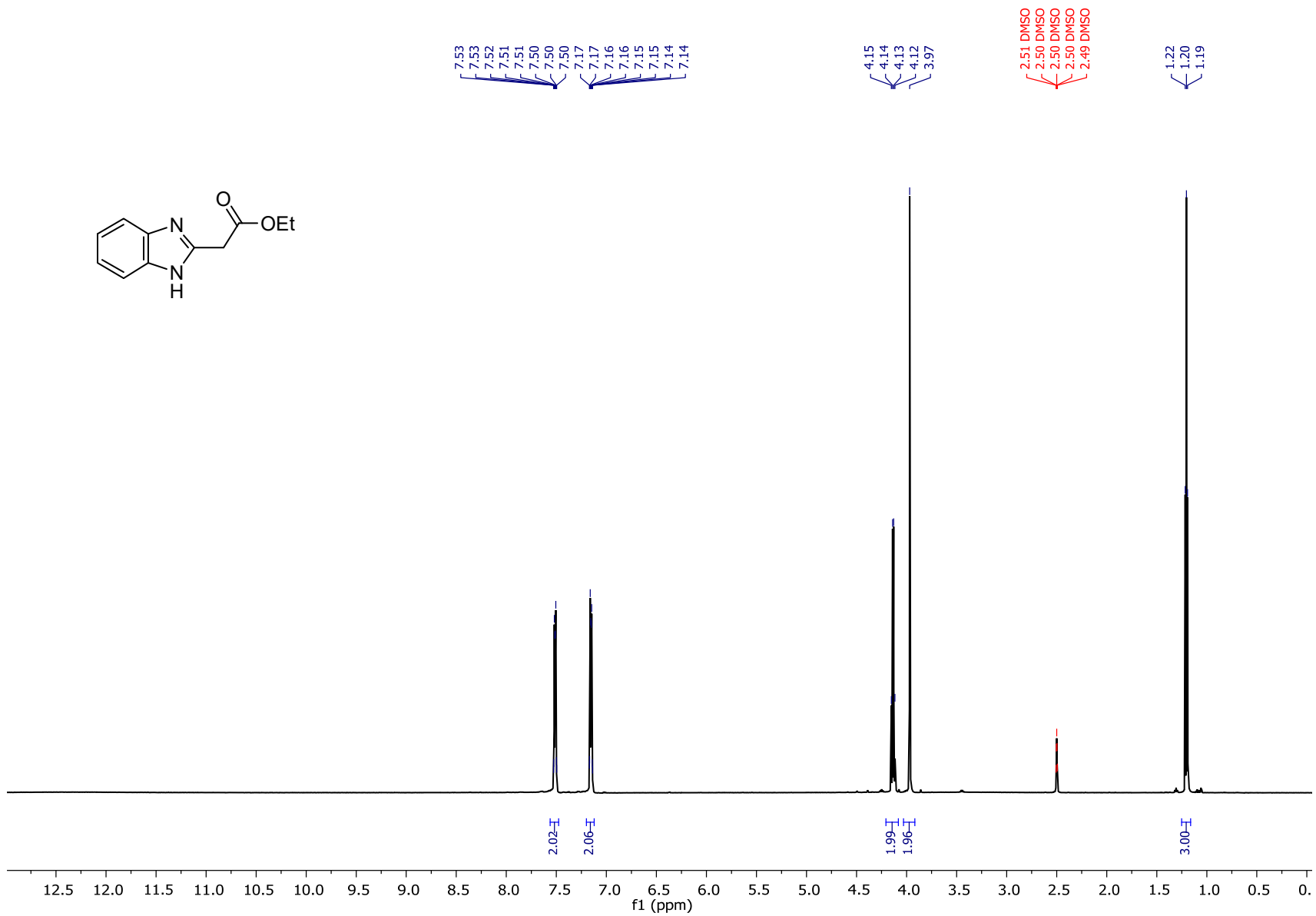
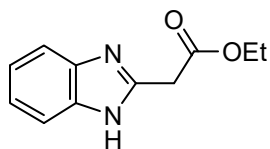


^{19}F NMR spectrum for **6g** (565 MHz, $\text{DMSO-}d_6$)

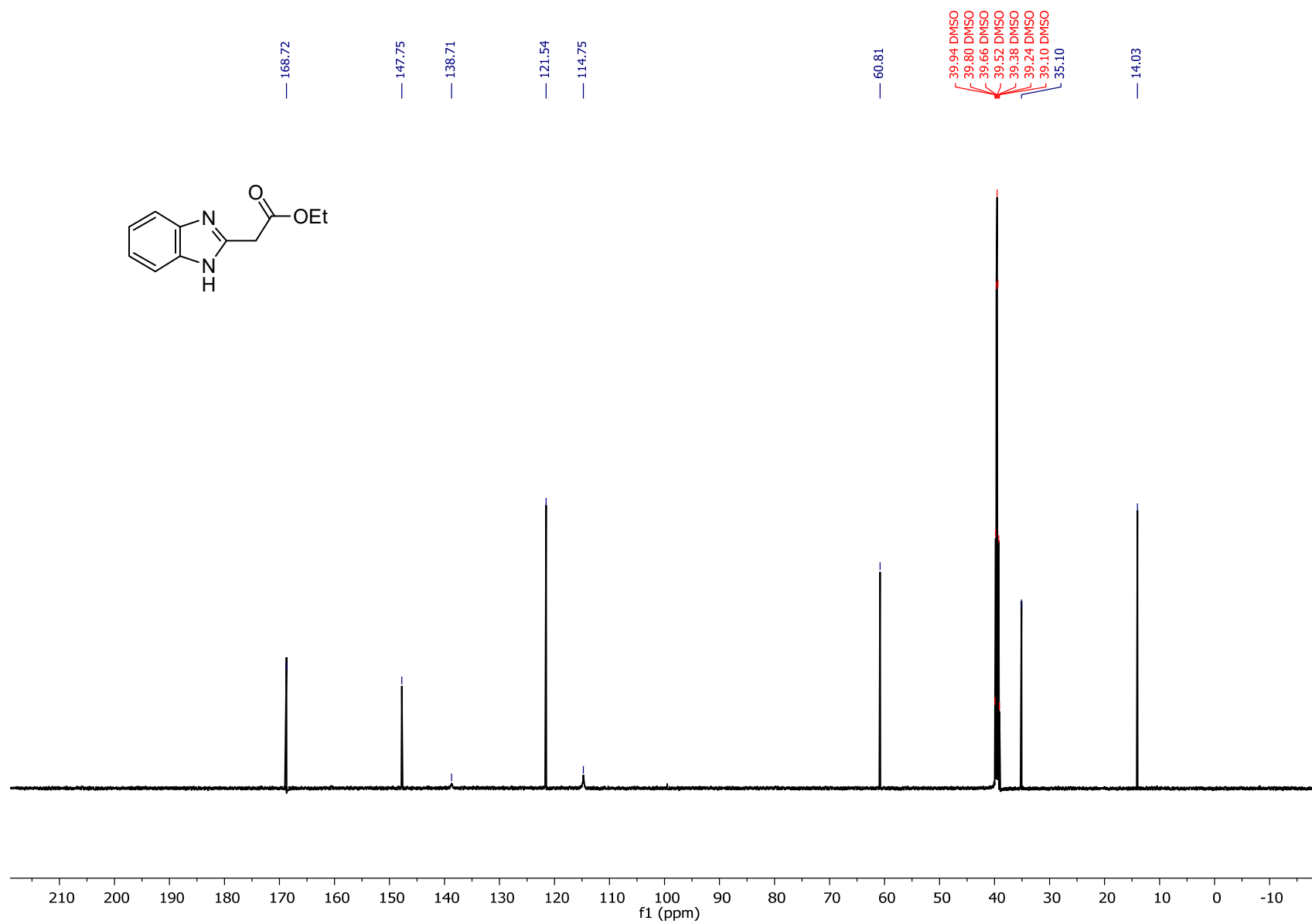


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-141.41

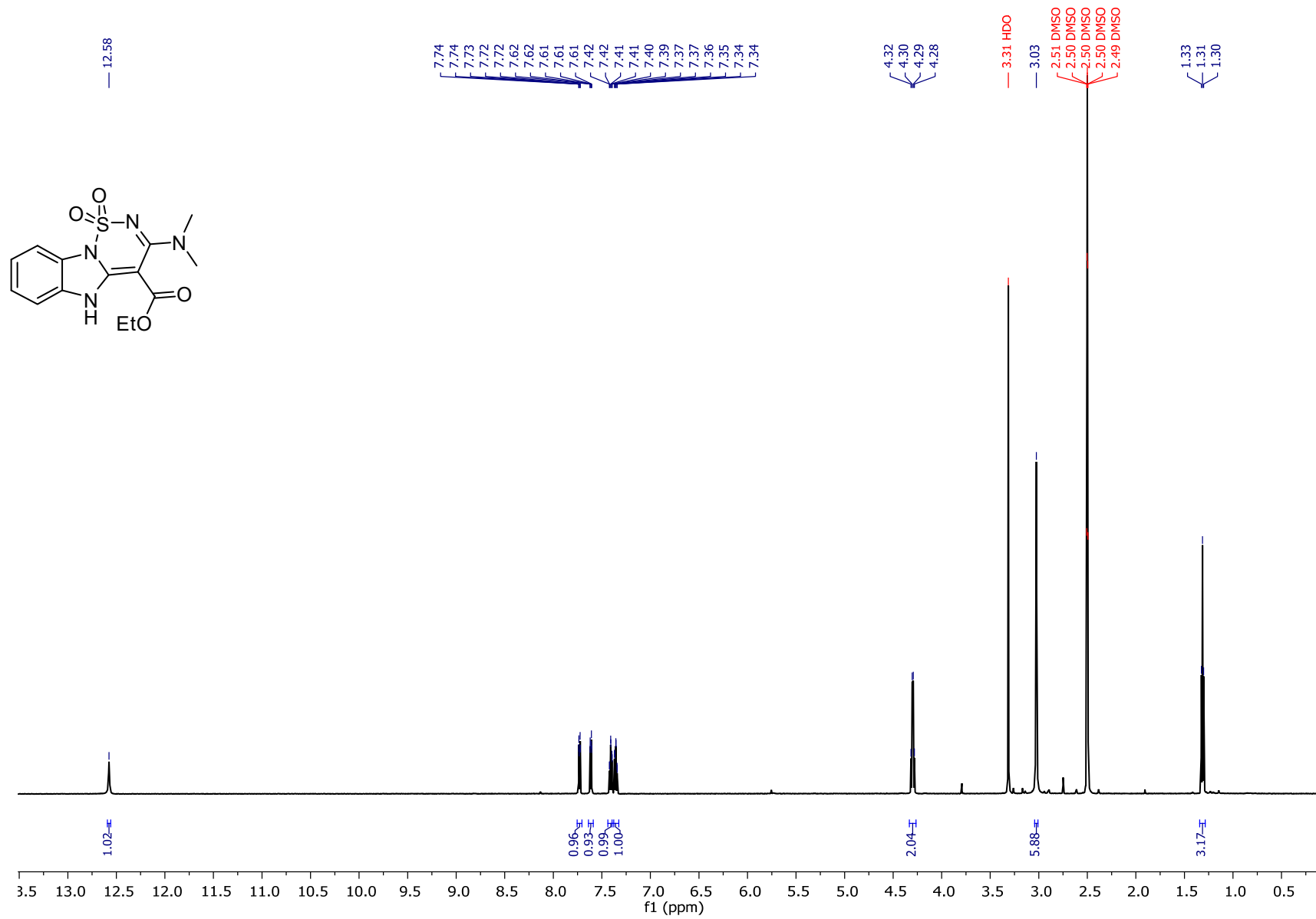
¹H NMR spectrum for **8** (600 MHz; DMSO-*d*₆)



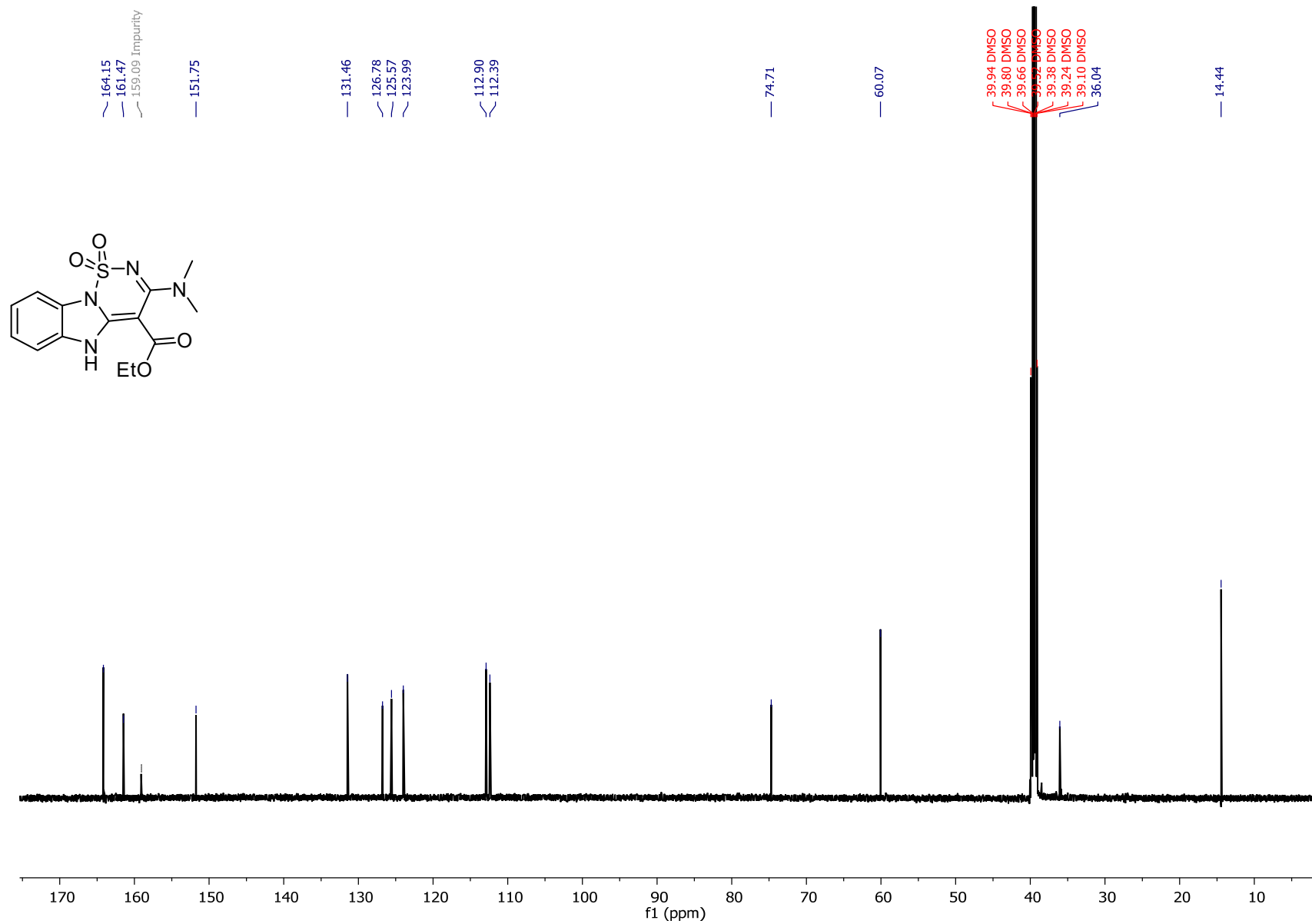
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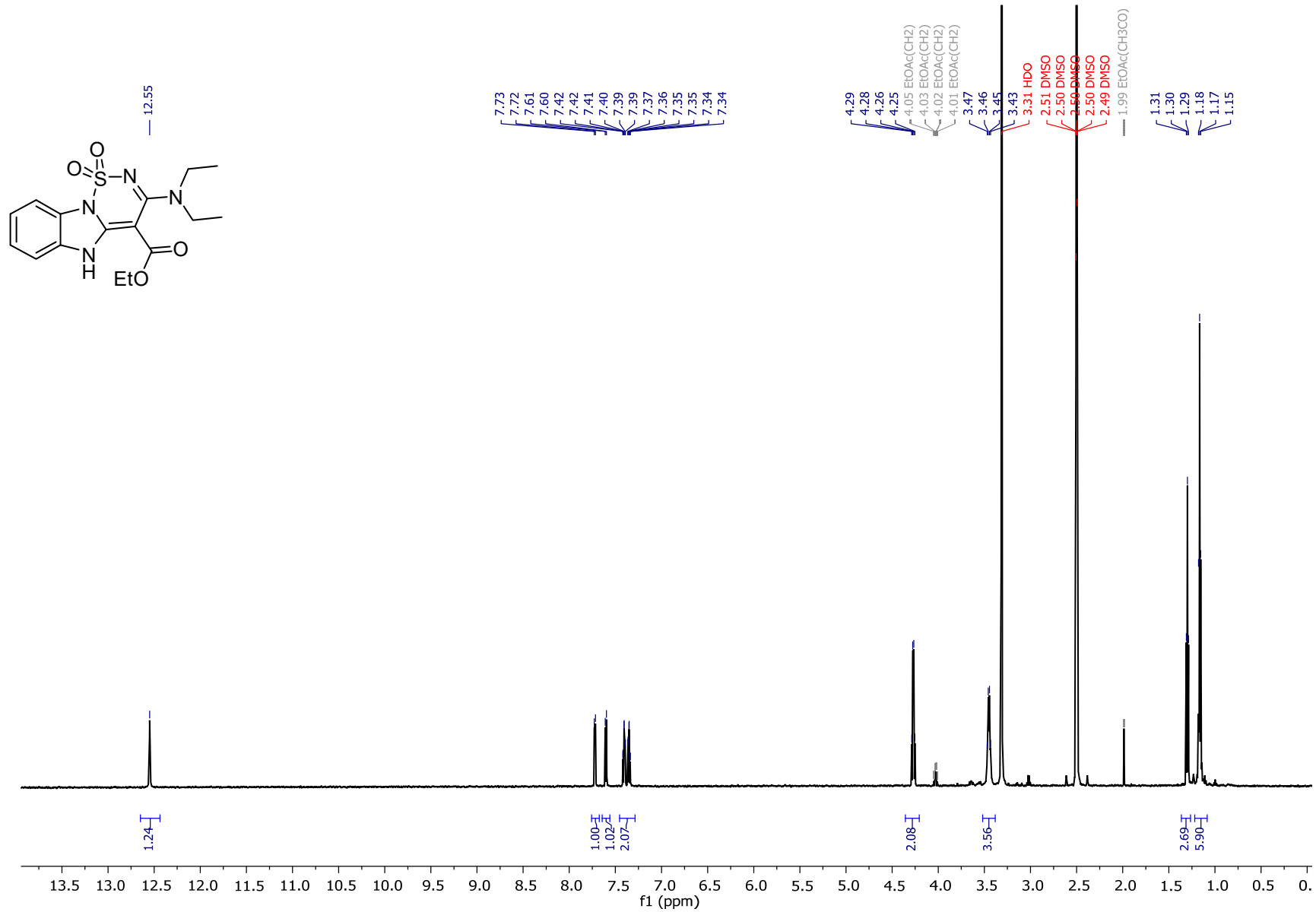
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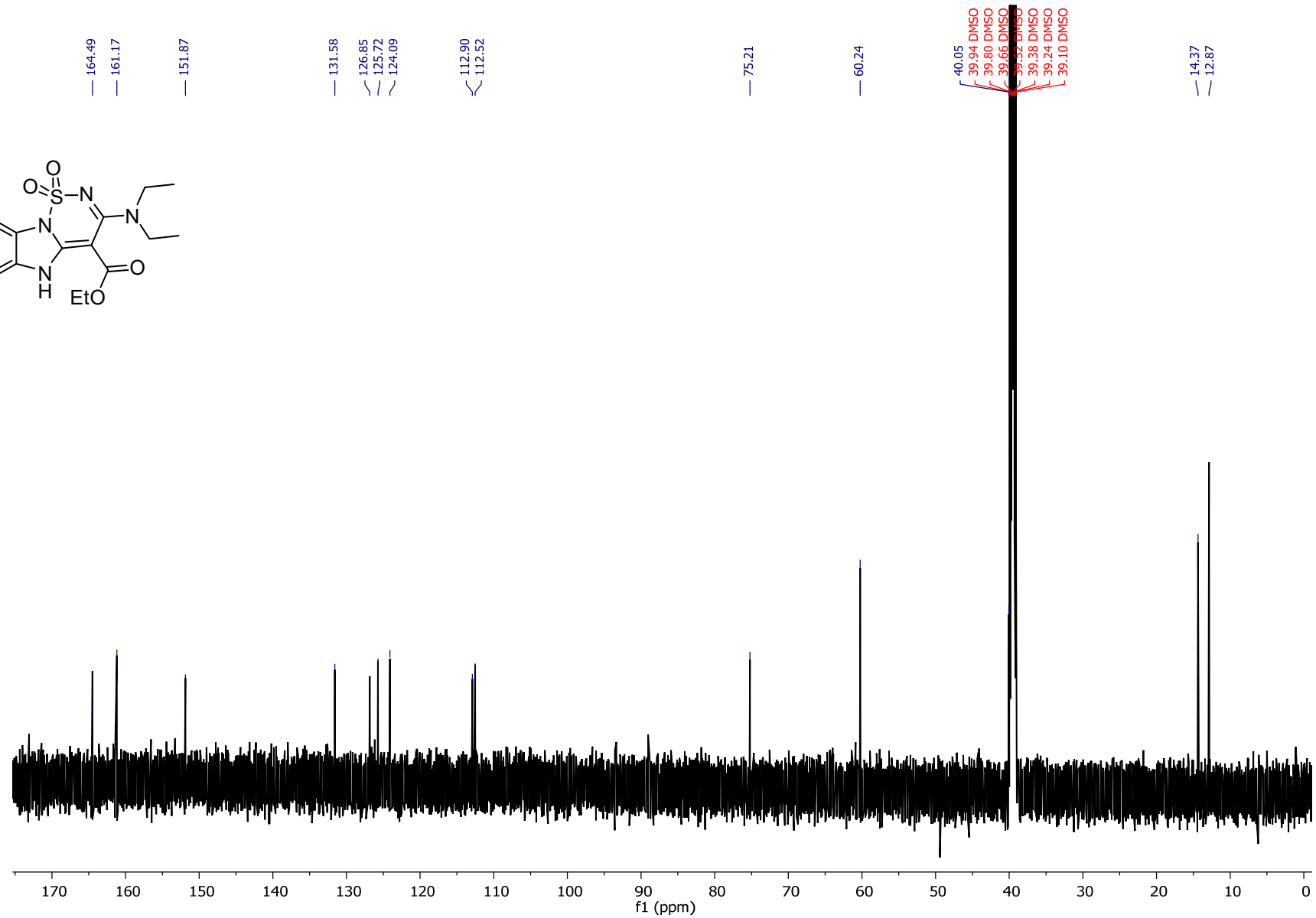
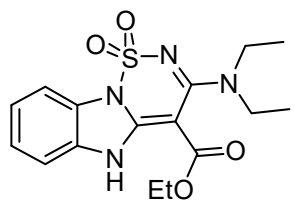
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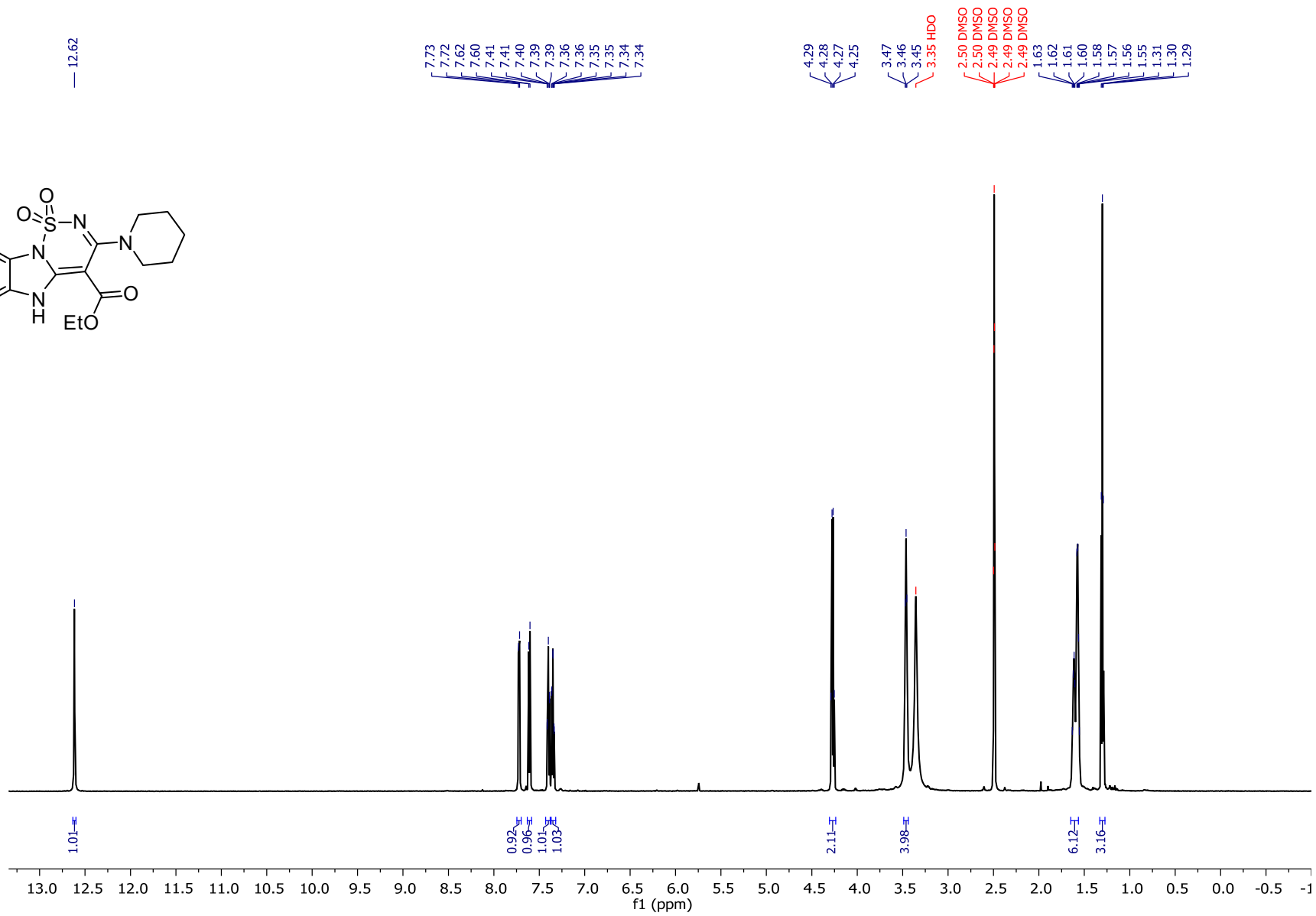
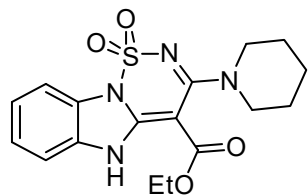
¹H NMR spectrum for **9b** (600 MHz; DMSO-*d*₆)



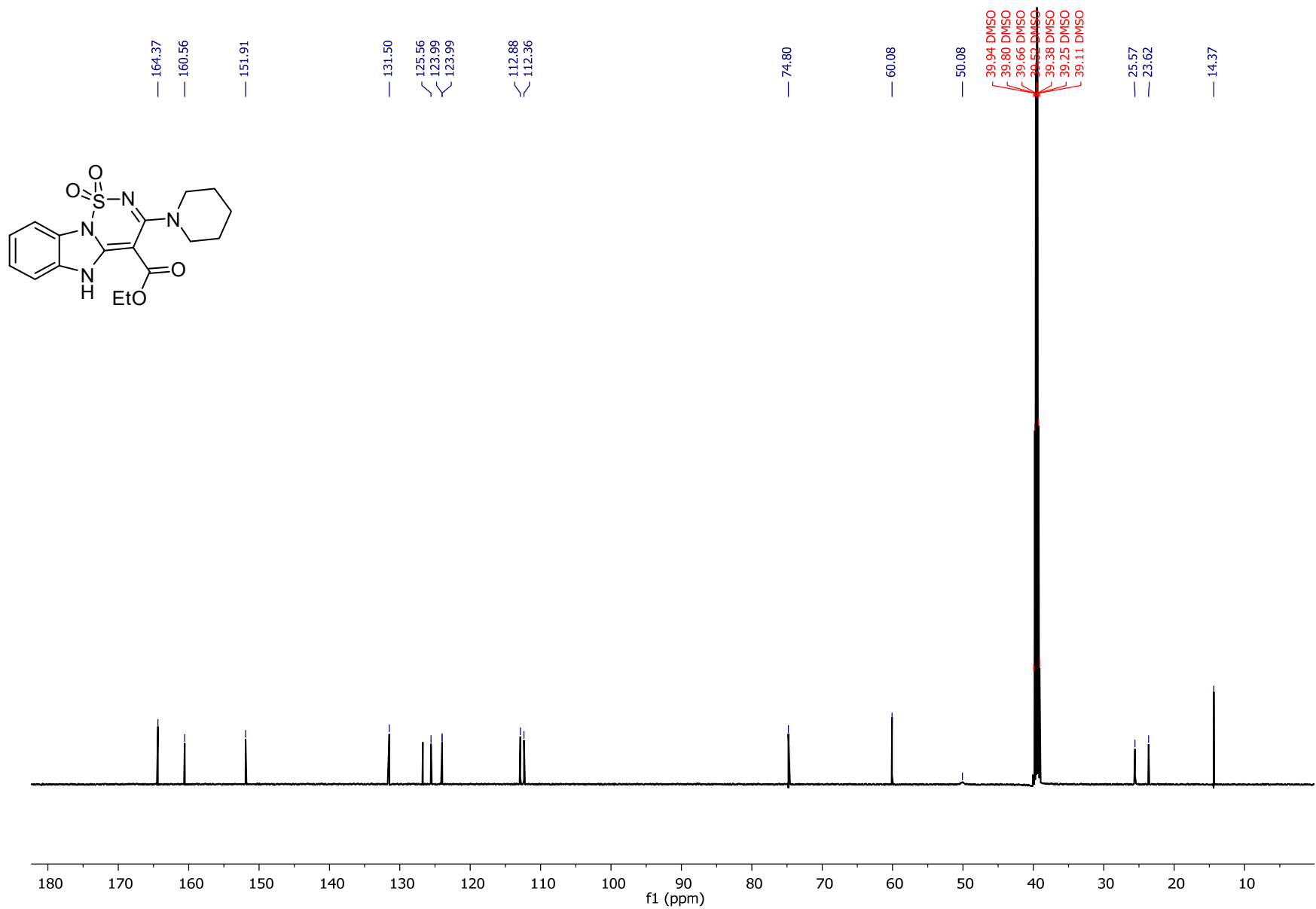
¹³C NMR for spectrum **9b** (150 MHz; DMSO-*d*₆)



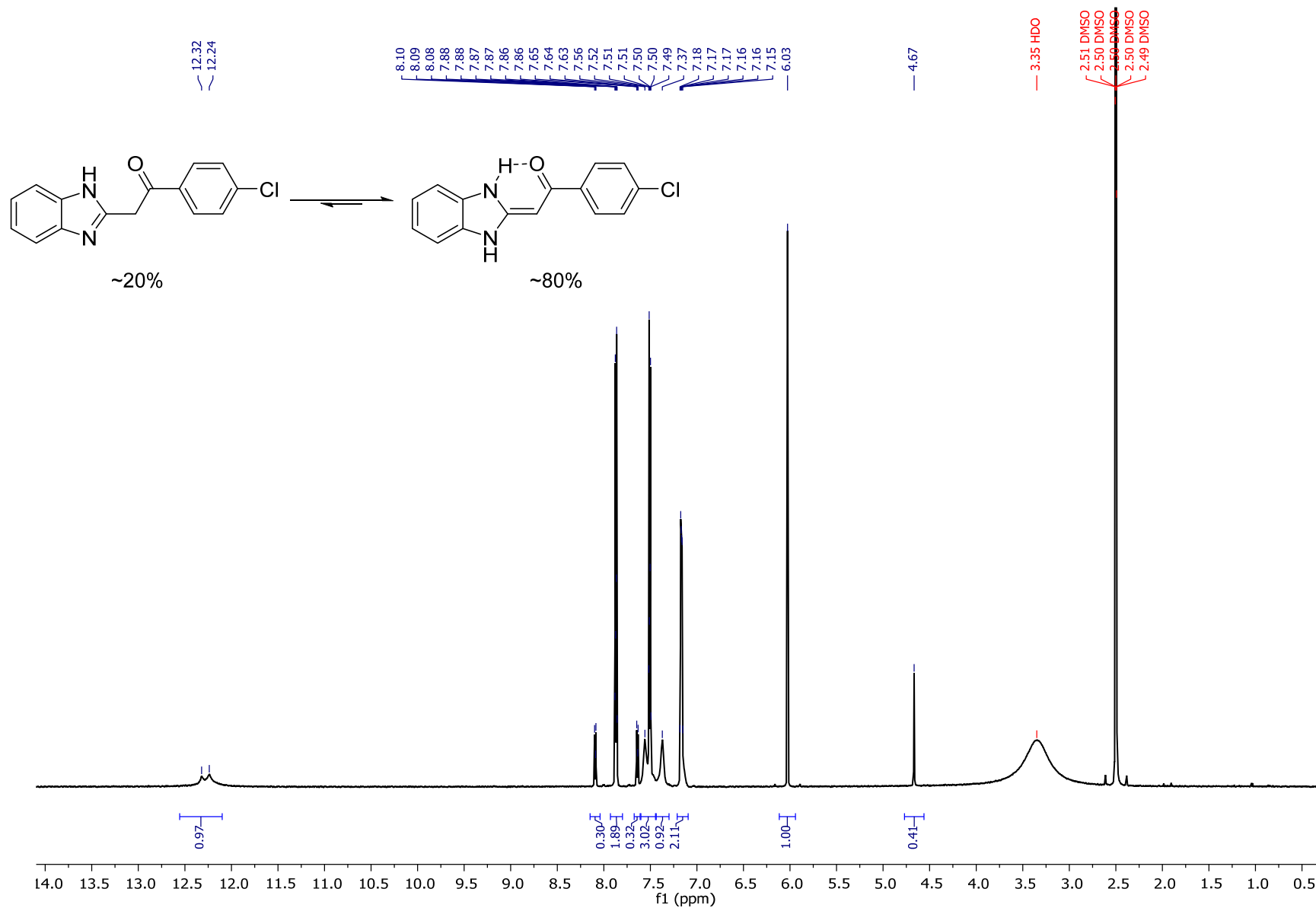
¹H NMR spectrum for **9c** (600 MHz; DMSO-*d*₆)



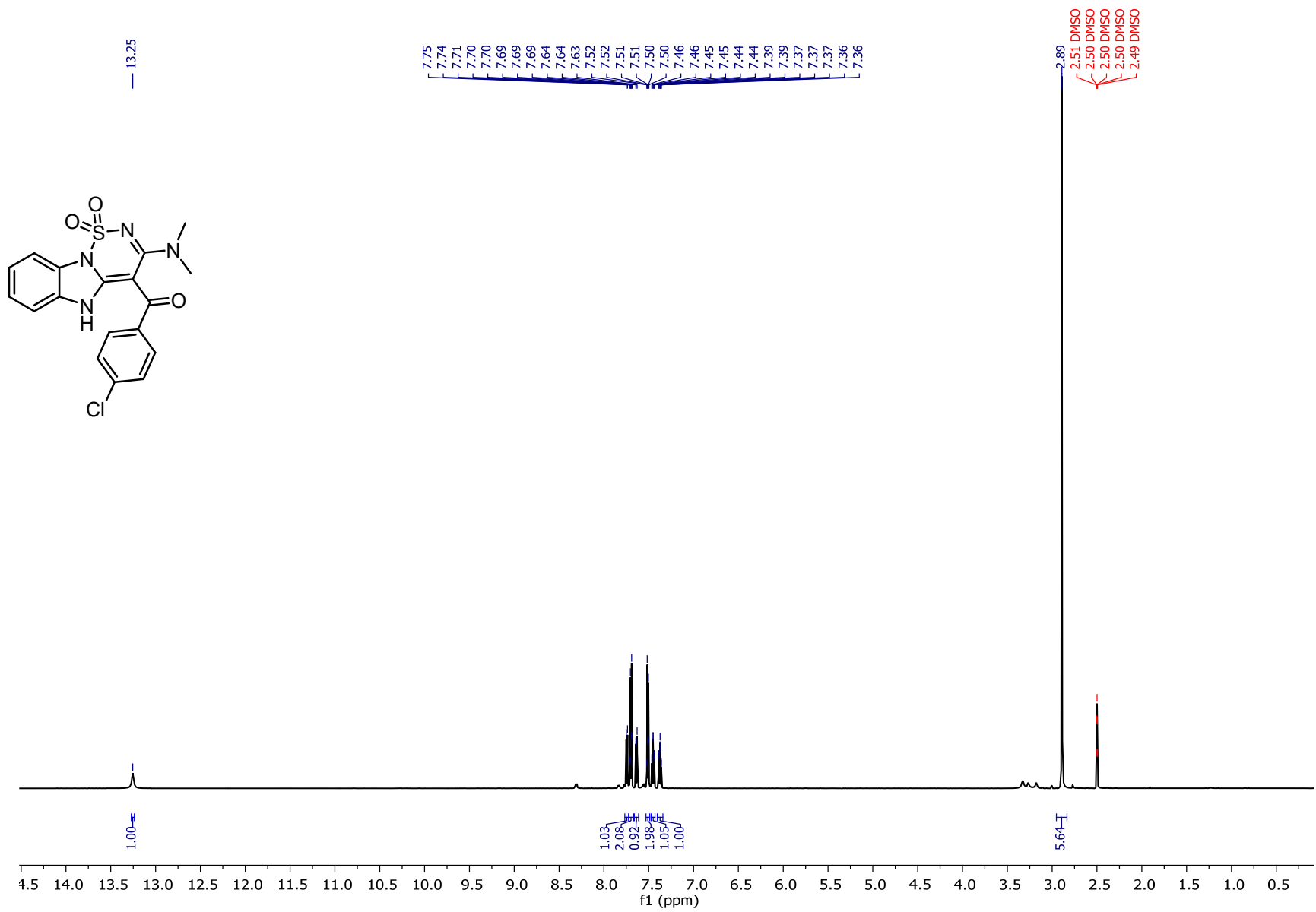
¹³C NMR spectrum for **9c** (150 MHz; DMSO-*d*₆)



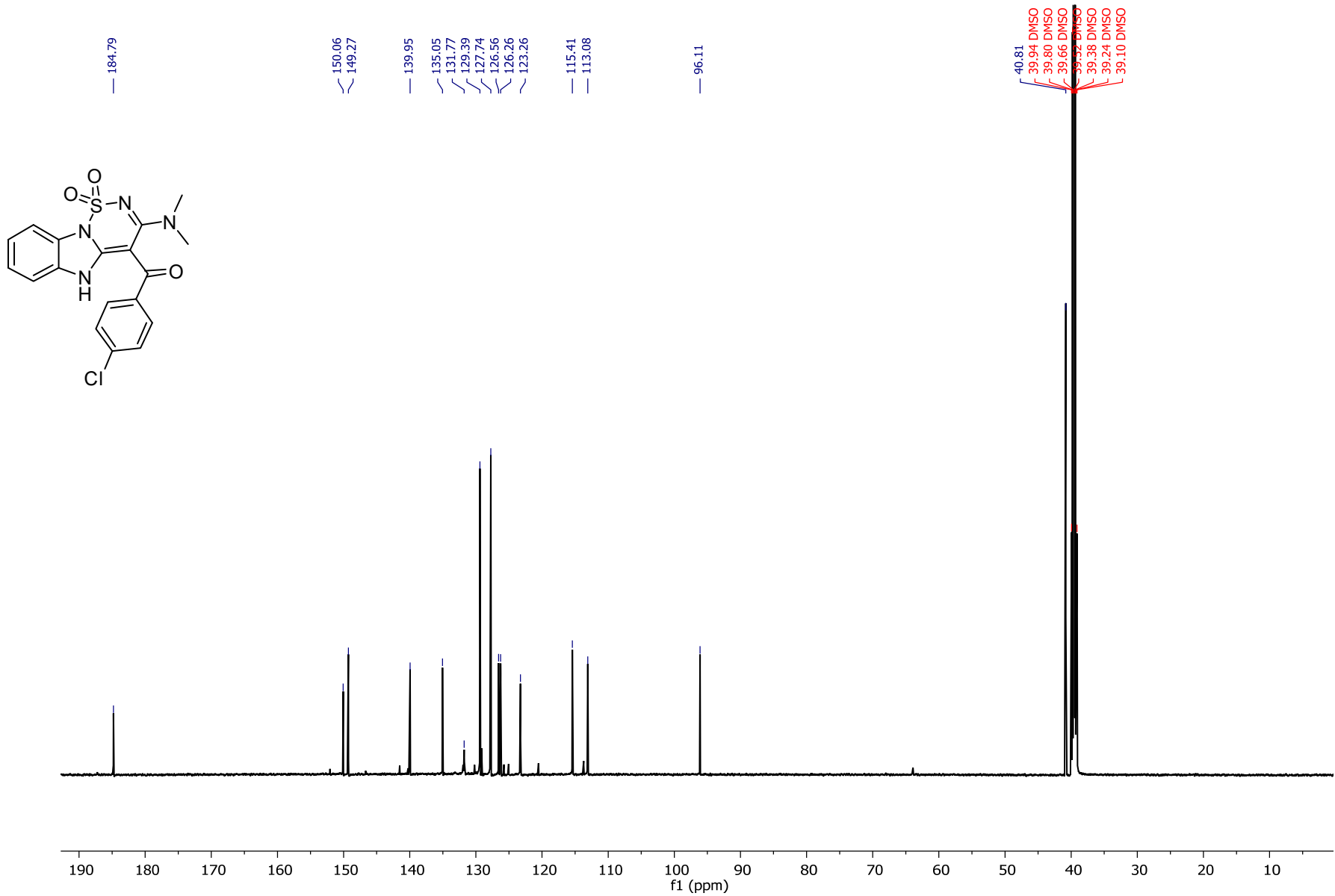
¹H NMR spectrum for **11** (600 MHz; DMSO-*d*₆)



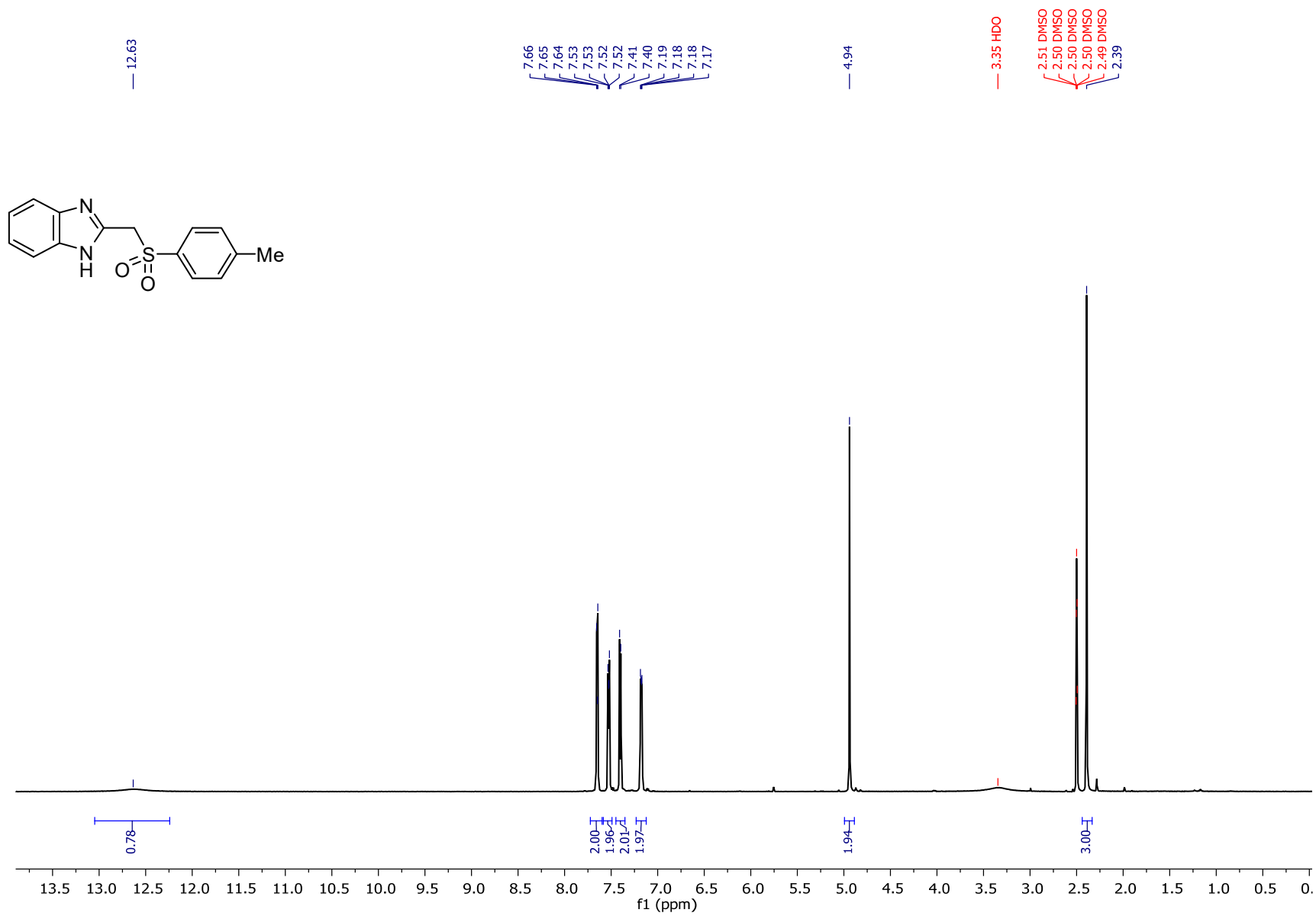
¹H NMR spectrum for **12** (600 MHz; DMSO-*d*₆)



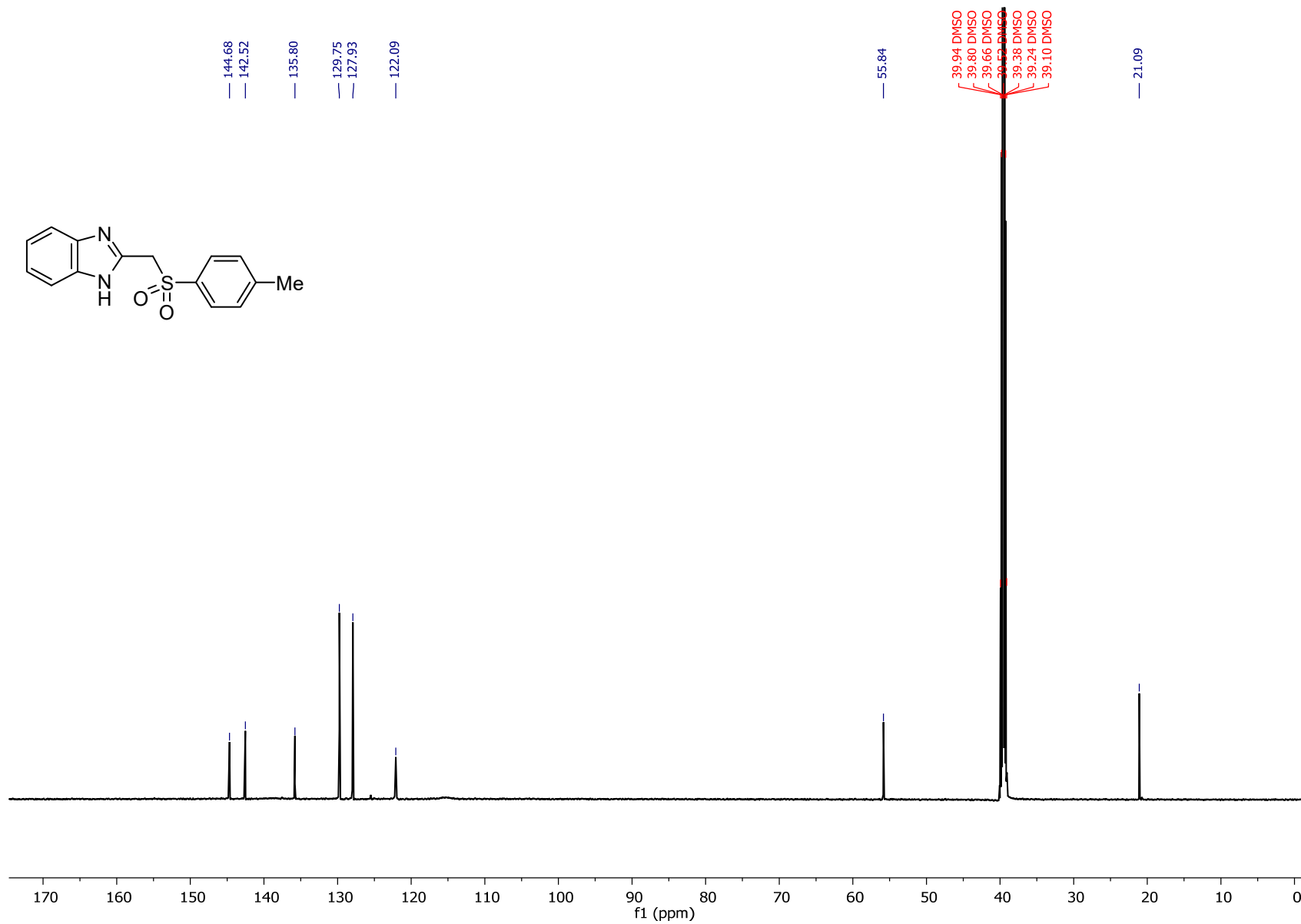
¹³C NMR spectrum for **12** (150 MHz; DMSO-*d*₆)



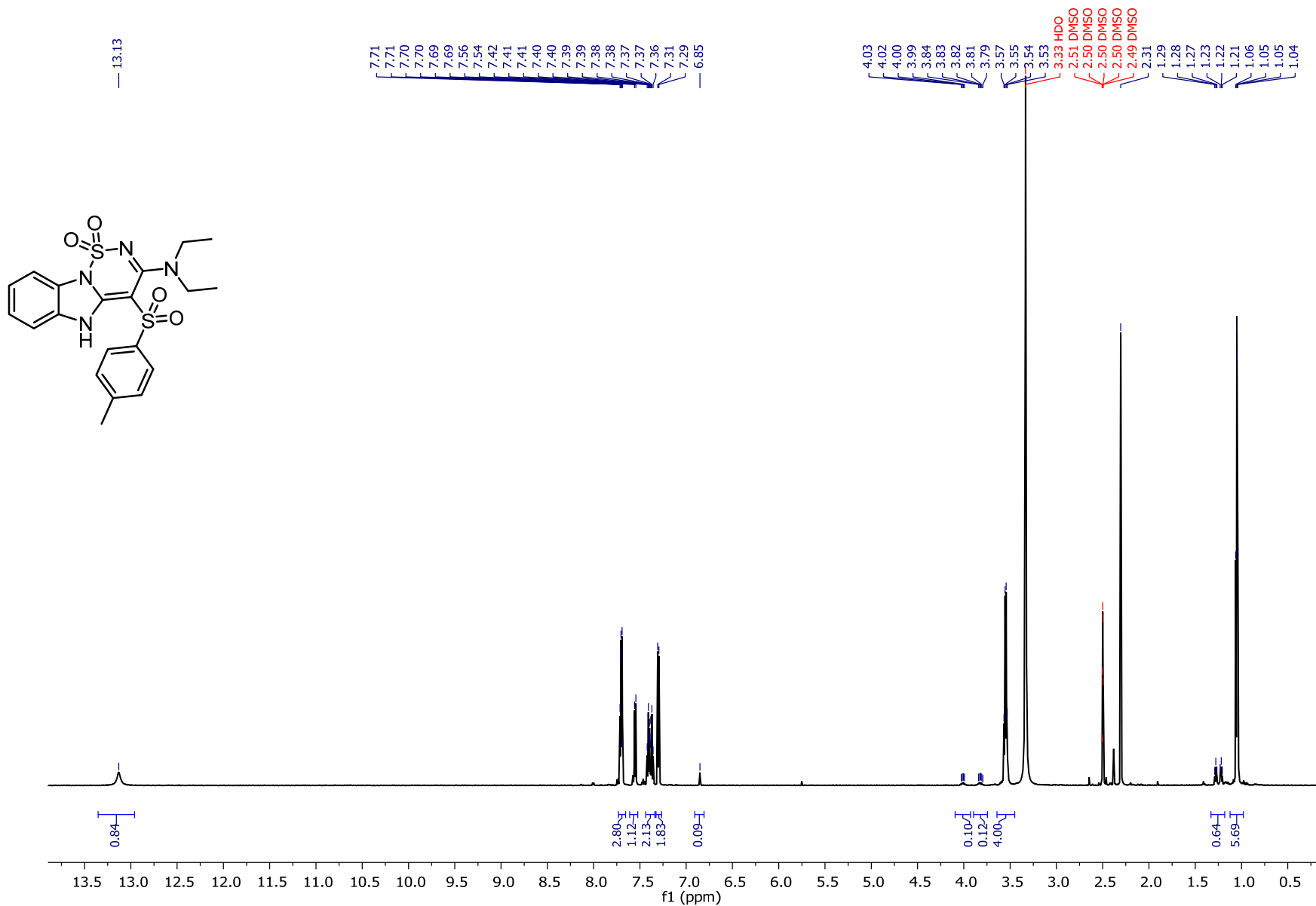
¹H NMR spectrum for **13** (600 MHz; DMSO-*d*₆)



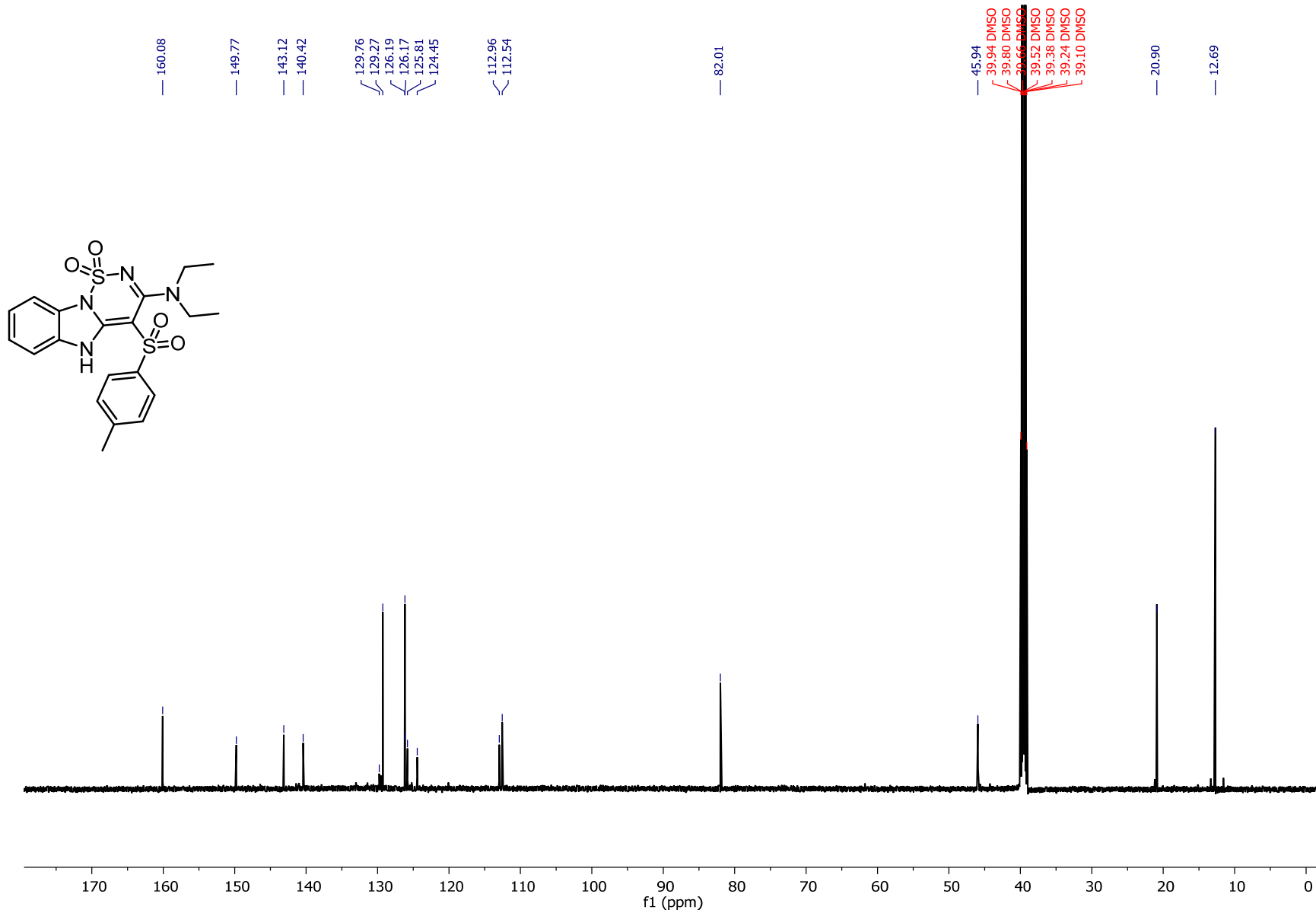
¹³C NMR spectrum for **13** (150 MHz; DMSO-*d*₆)



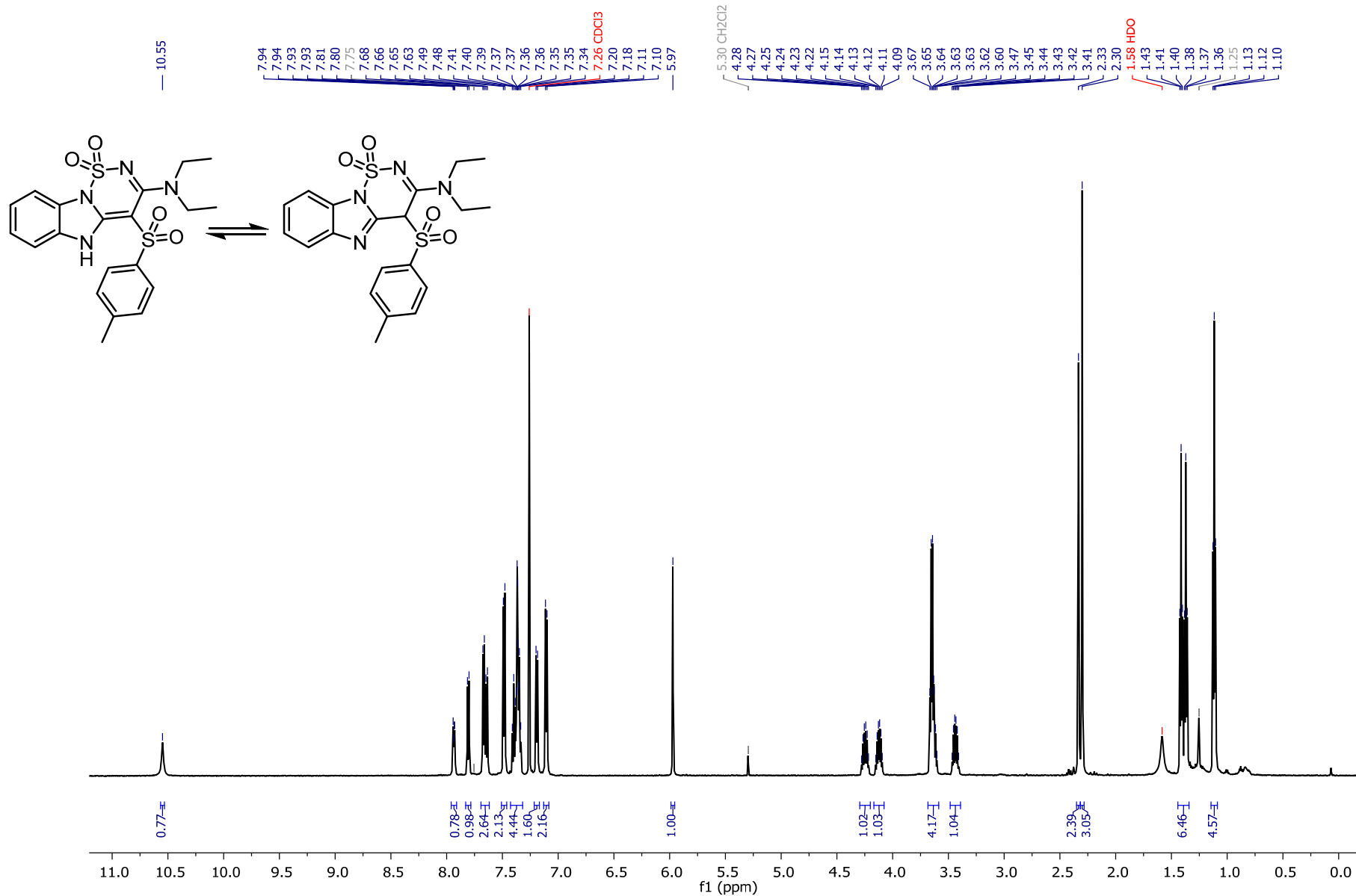
¹H NMR spectrum for **14a** (600 MHz; DMSO-*d*₆)



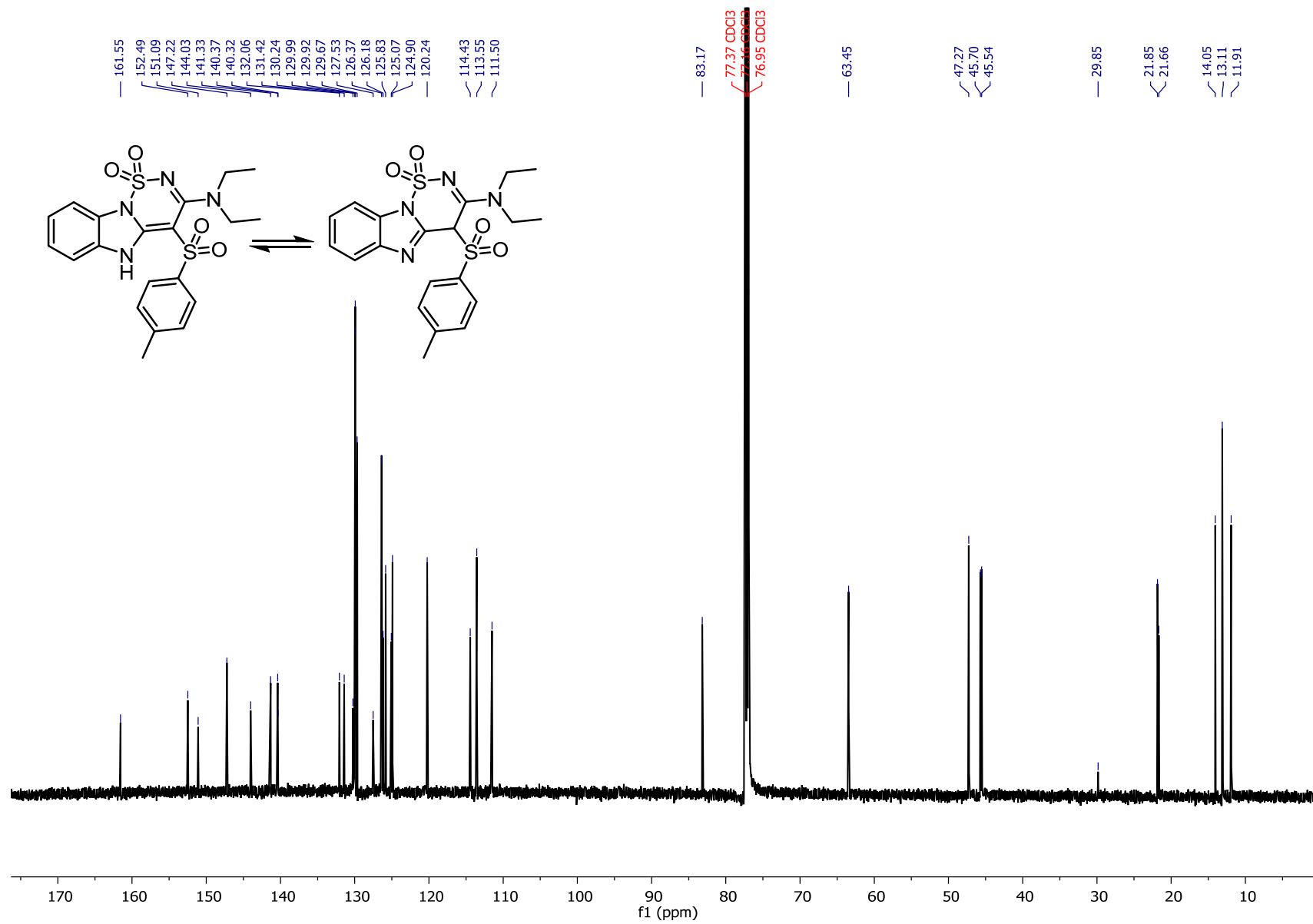
¹³C NMR spectrum for **14a** (150 MHz; DMSO-*d*₆)



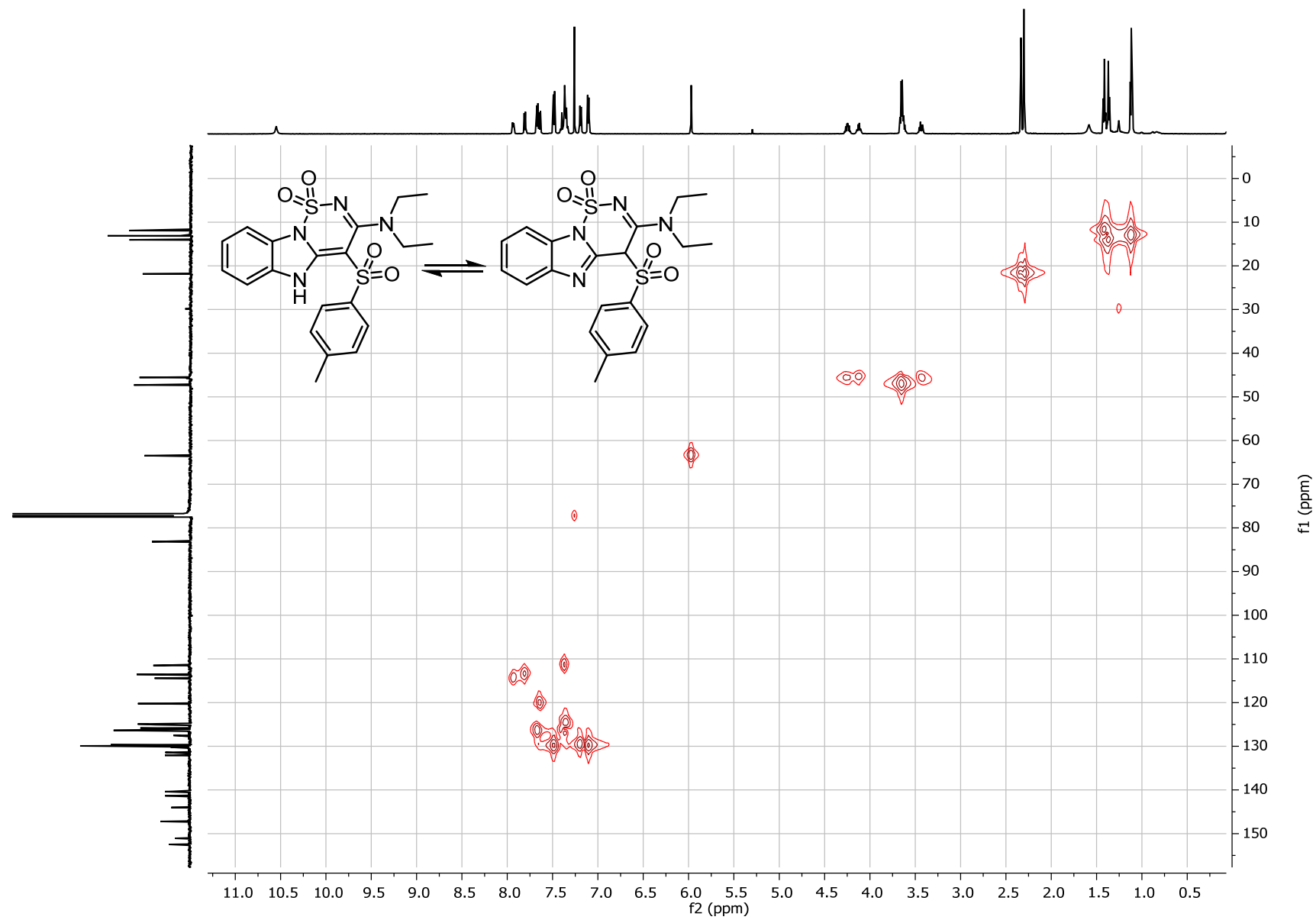
¹H NMR spectrum for **14a** (600 MHz; CDCl₃)



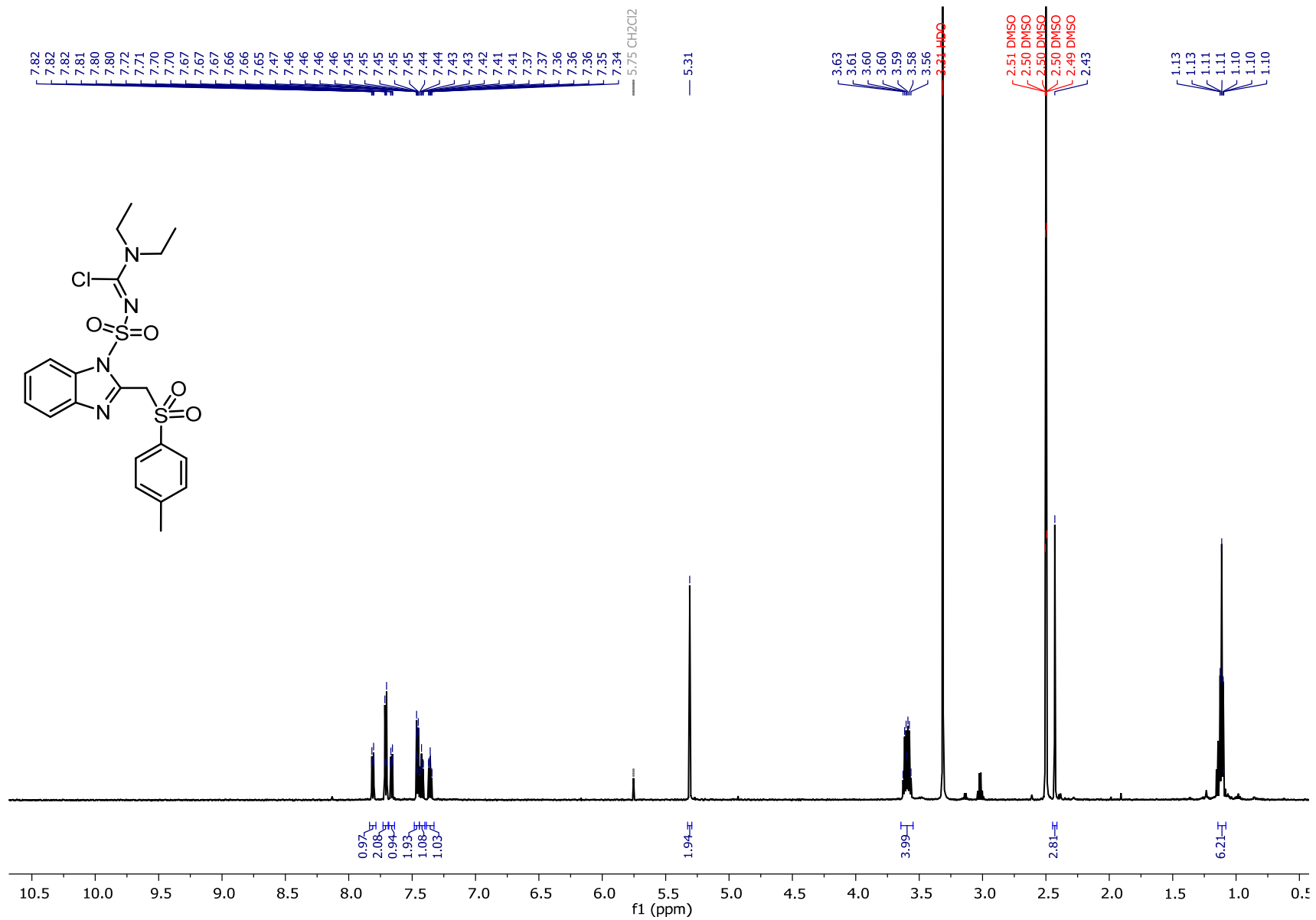
¹³C NMR spectrum for **14a** (150 MHz; CDCl₃)



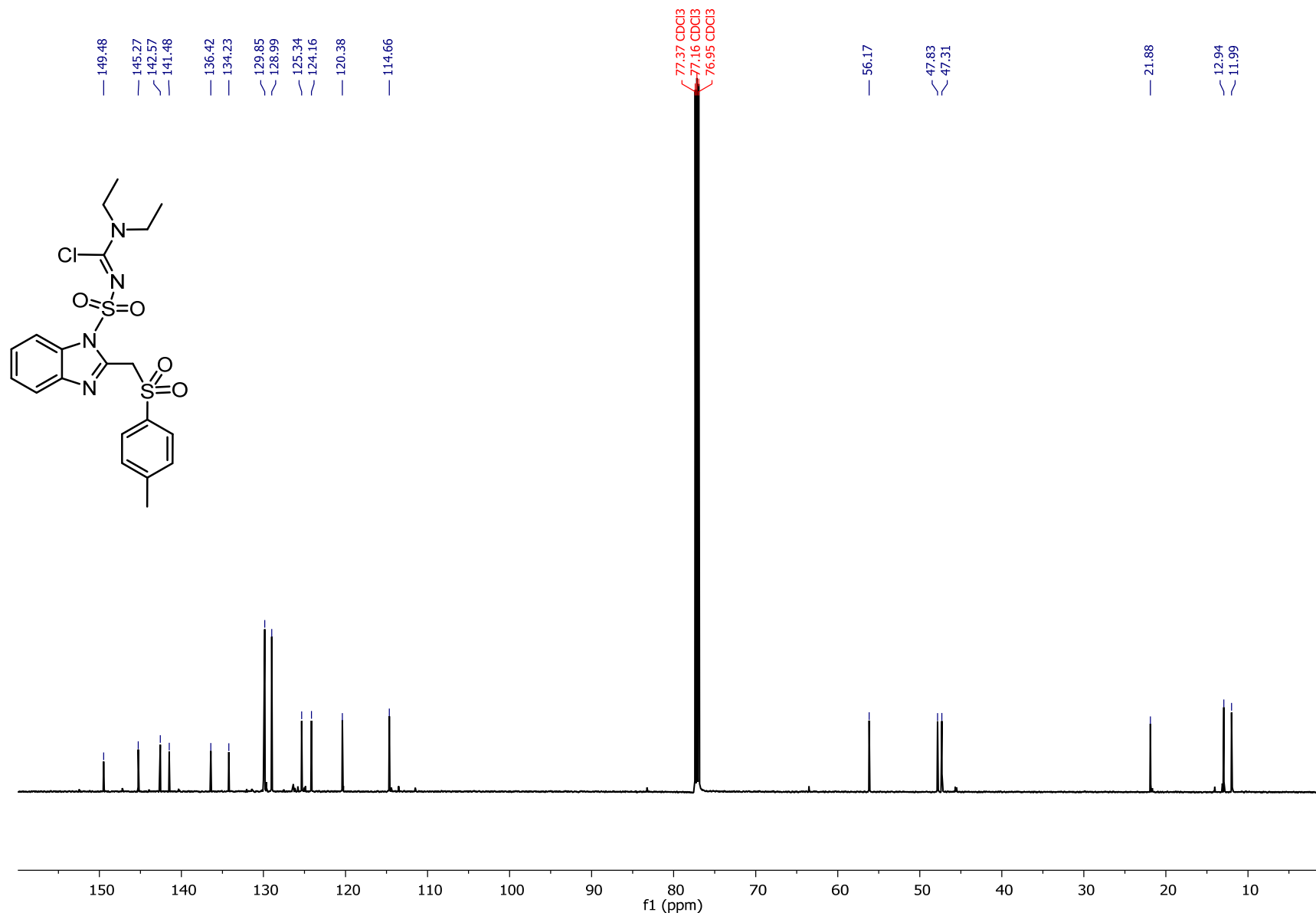
HMQC NMR spectrum for **14a** (600 × 150 MHz; CDCl₃)



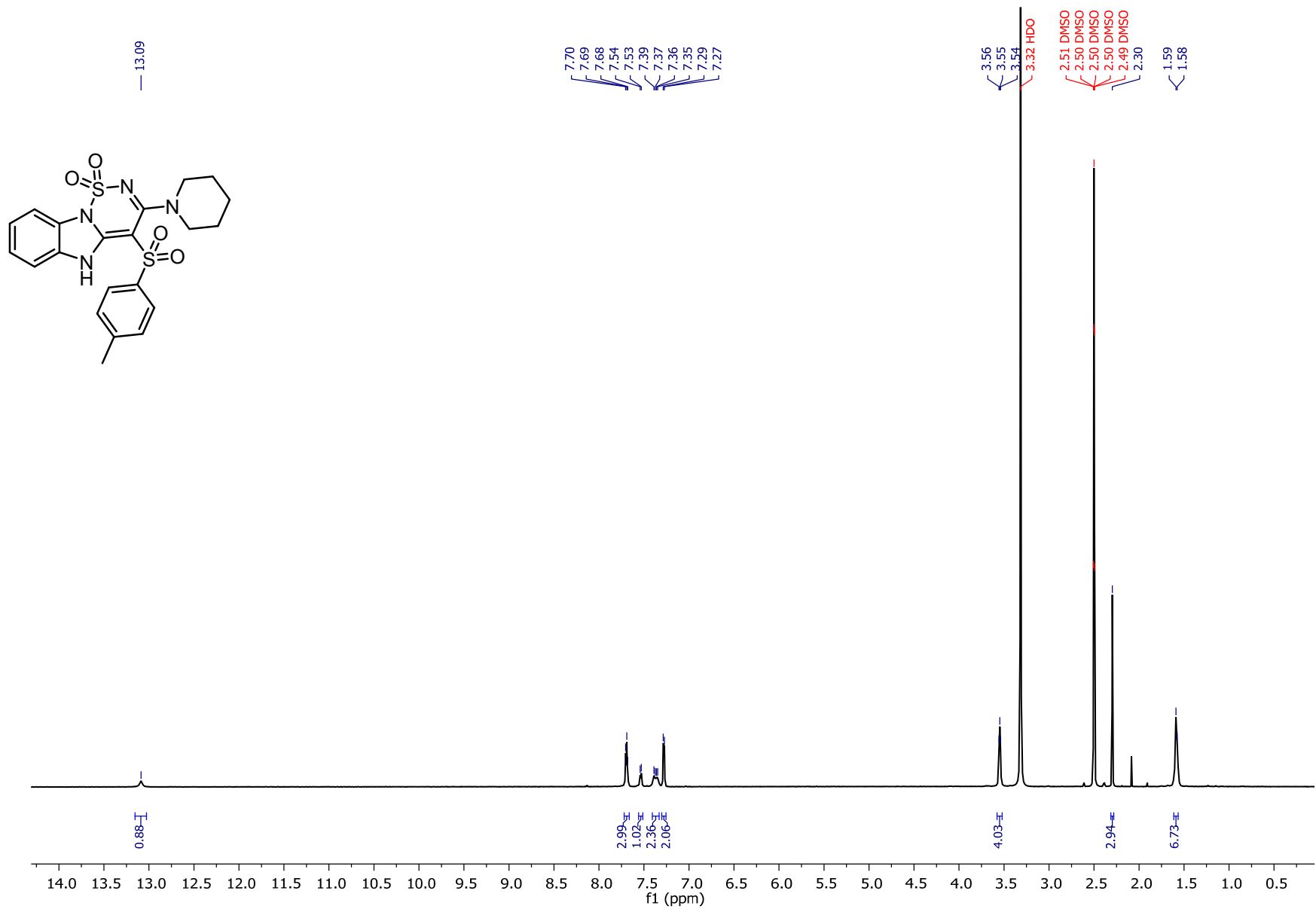
¹H NMR spectrum for **15a** (600 MHz; DMSO-*d*₆)



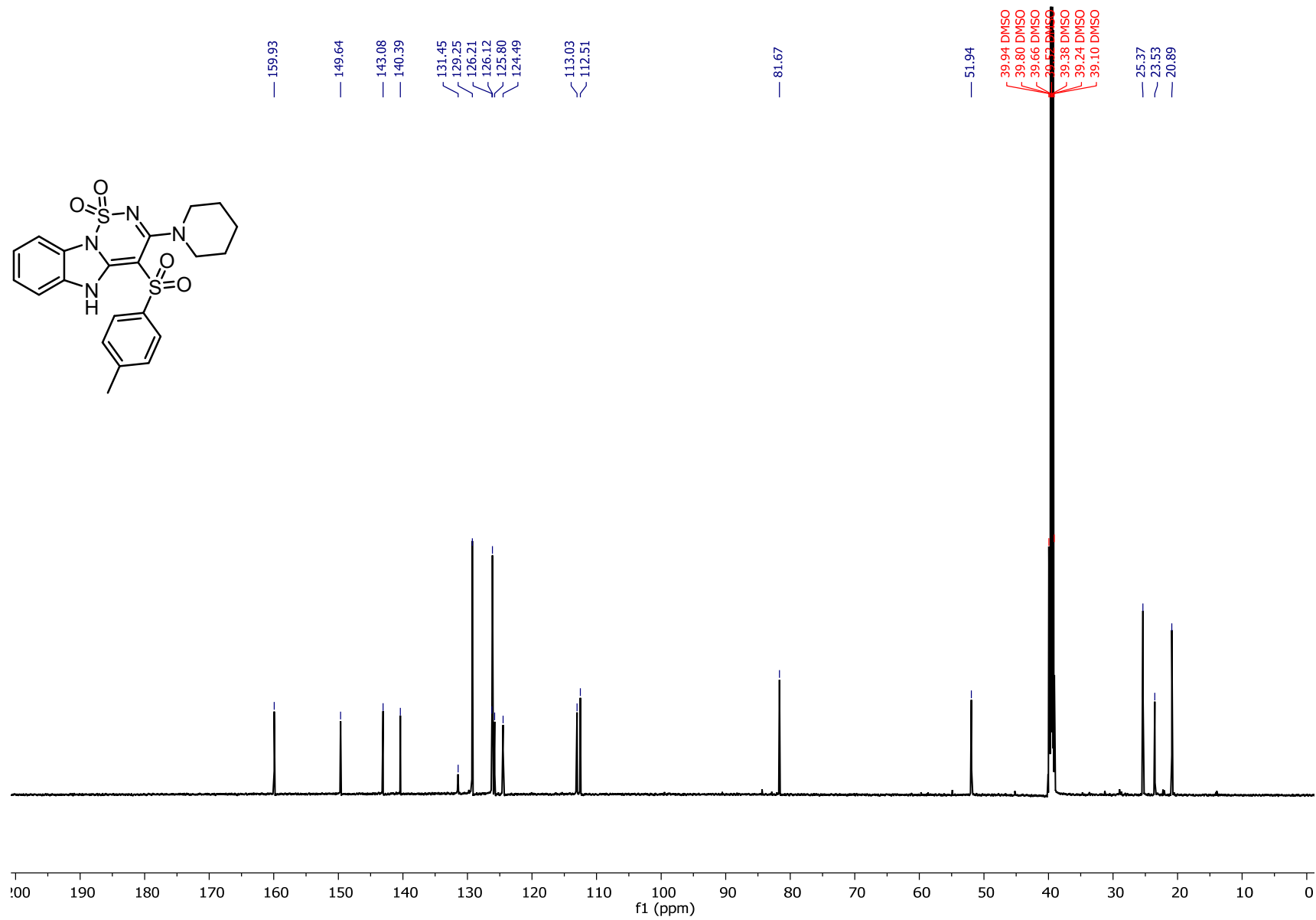
¹³C NMR spectrum for **15a** (150 MHz; DMSO-*d*₆)



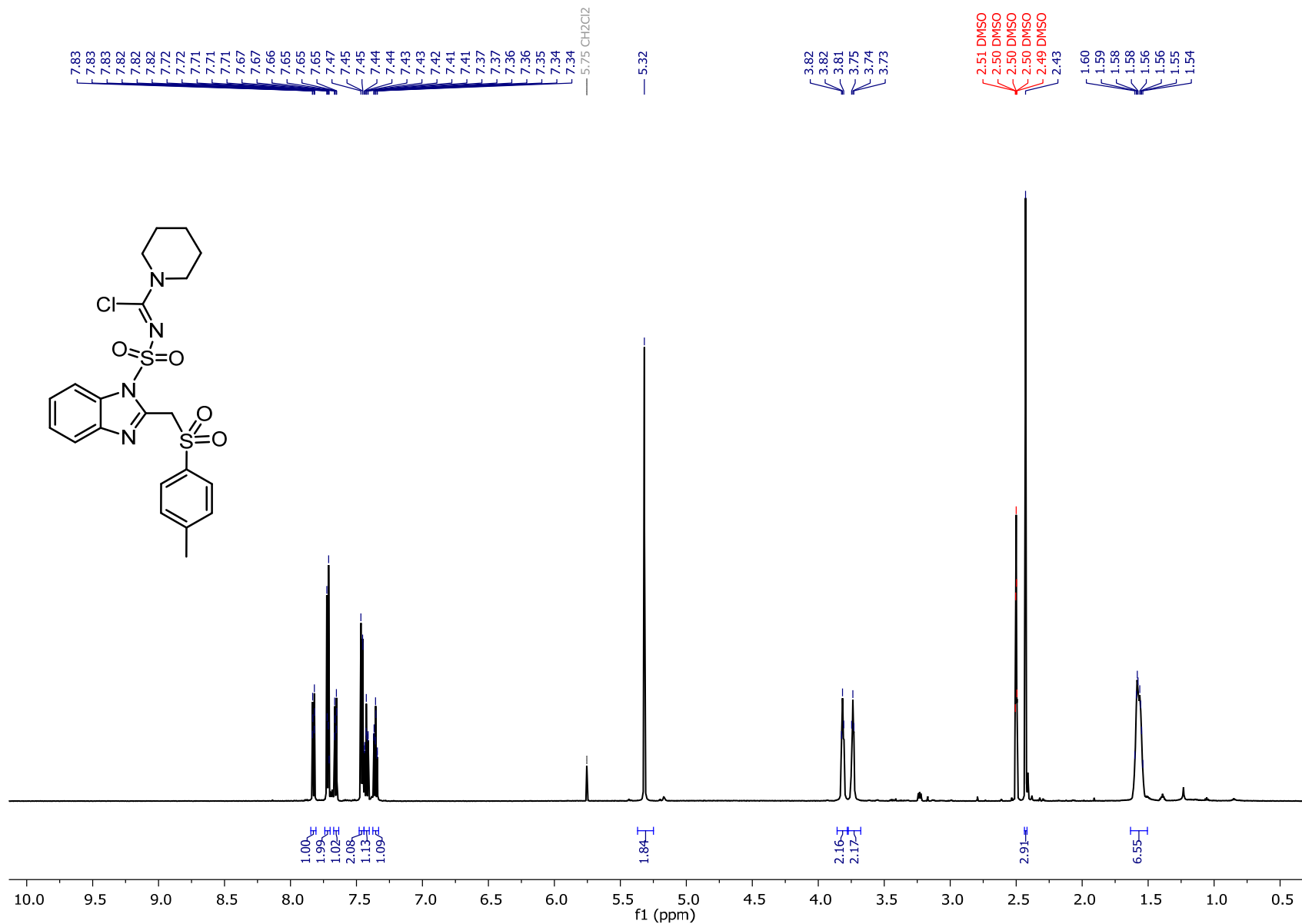
¹H NMR spectrum for **14b** (600 MHz; DMSO-*d*₆)



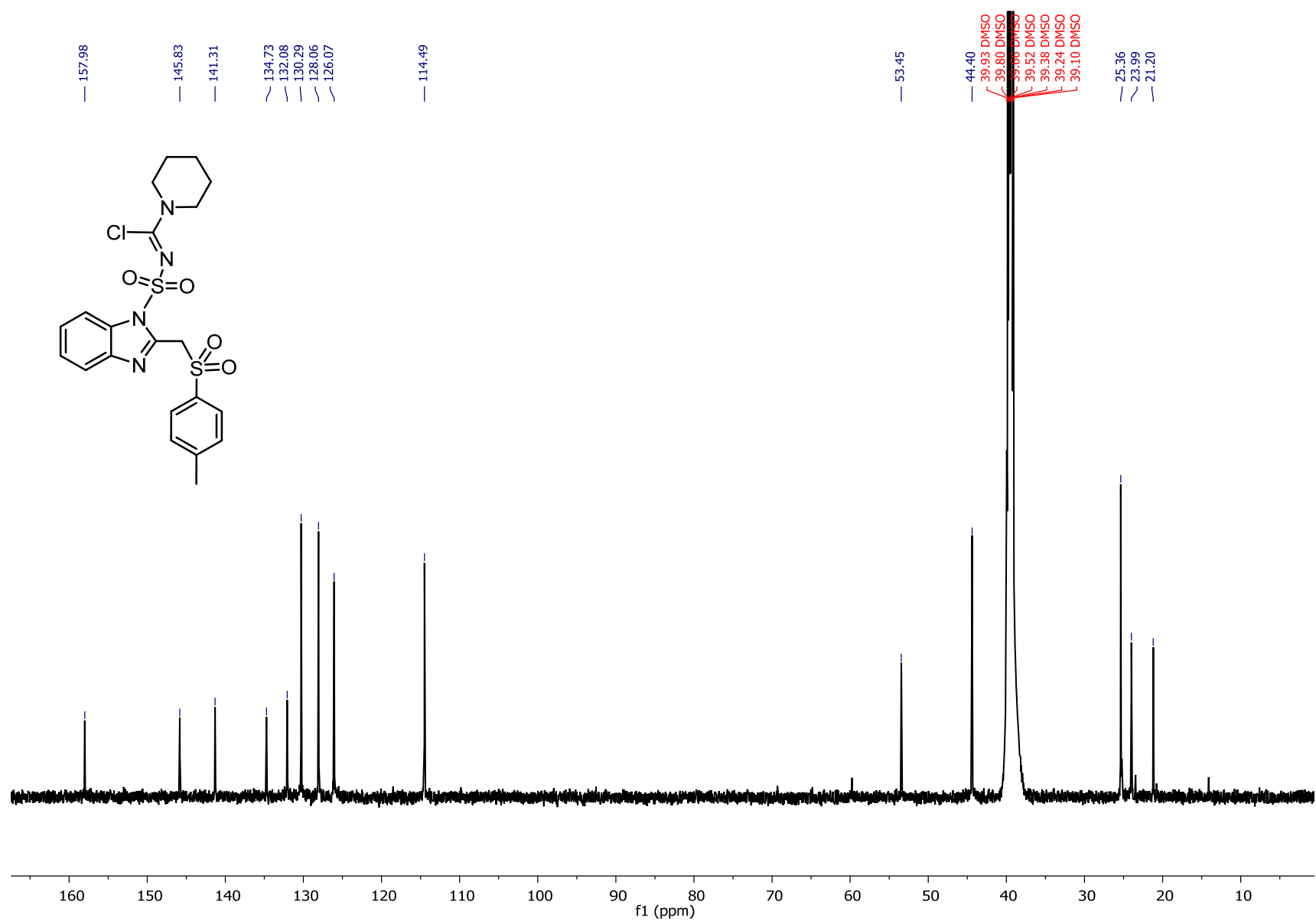
¹³C NMR spectrum for **14b** (150 MHz; DMSO-*d*₆)



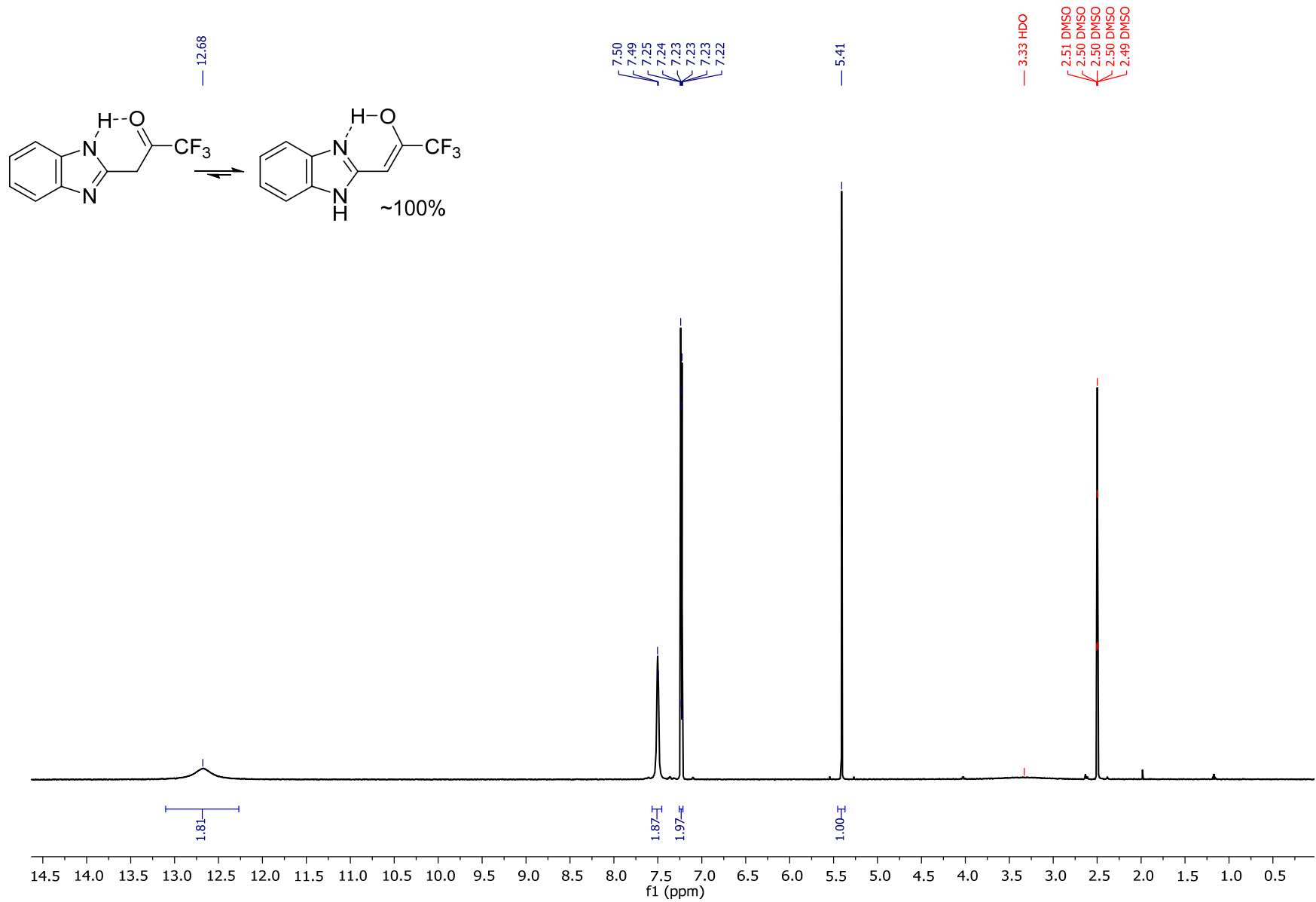
¹H NMR spectrum for **15b** (600 MHz; DMSO-*d*₆)



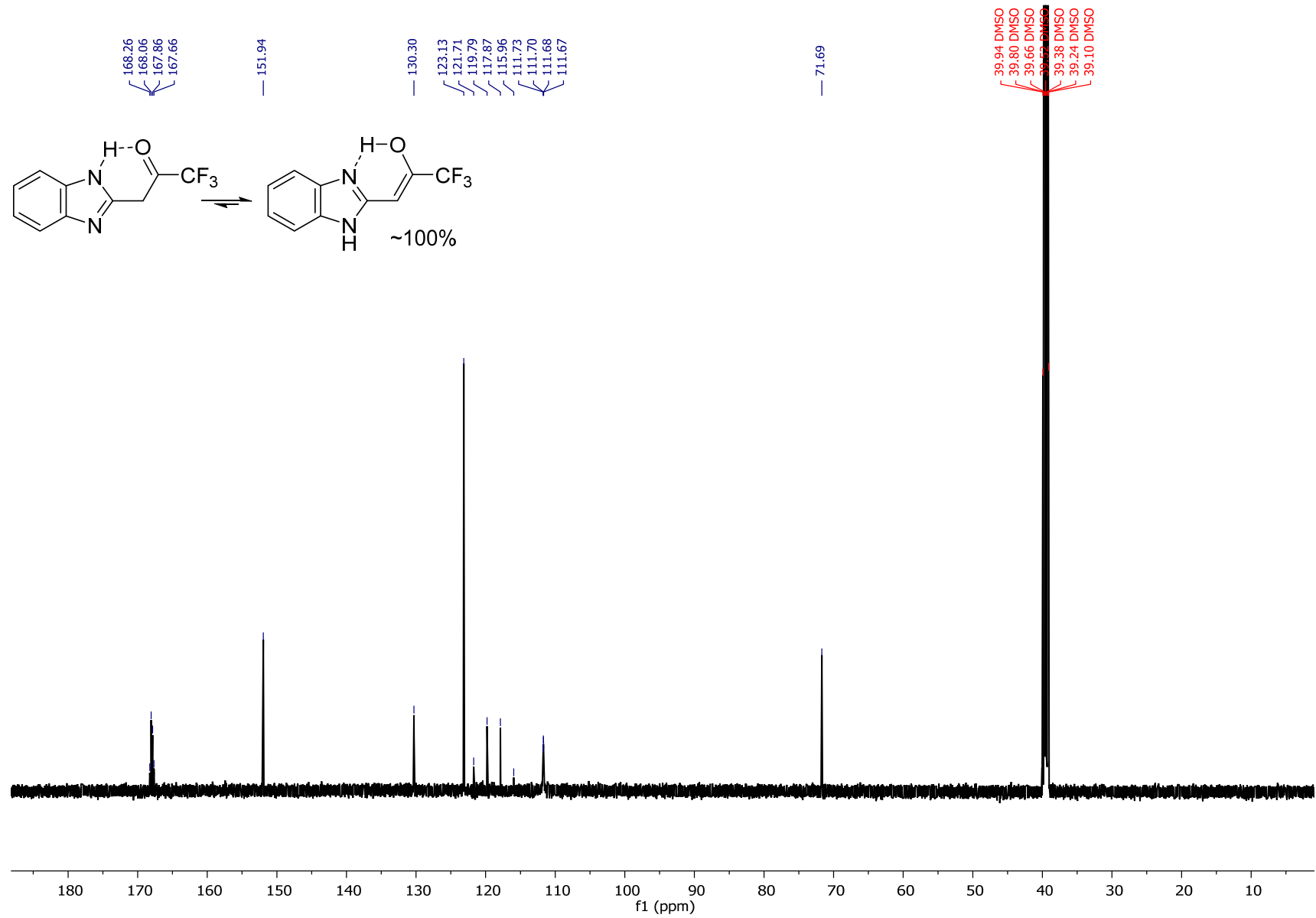
¹³C NMR spectrum for **15b** (150 MHz; DMSO-*d*₆)



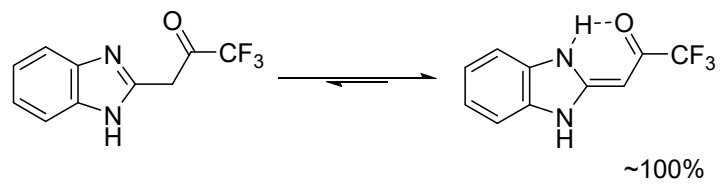
¹H NMR spectrum for **16** (600 MHz; DMSO-*d*₆)



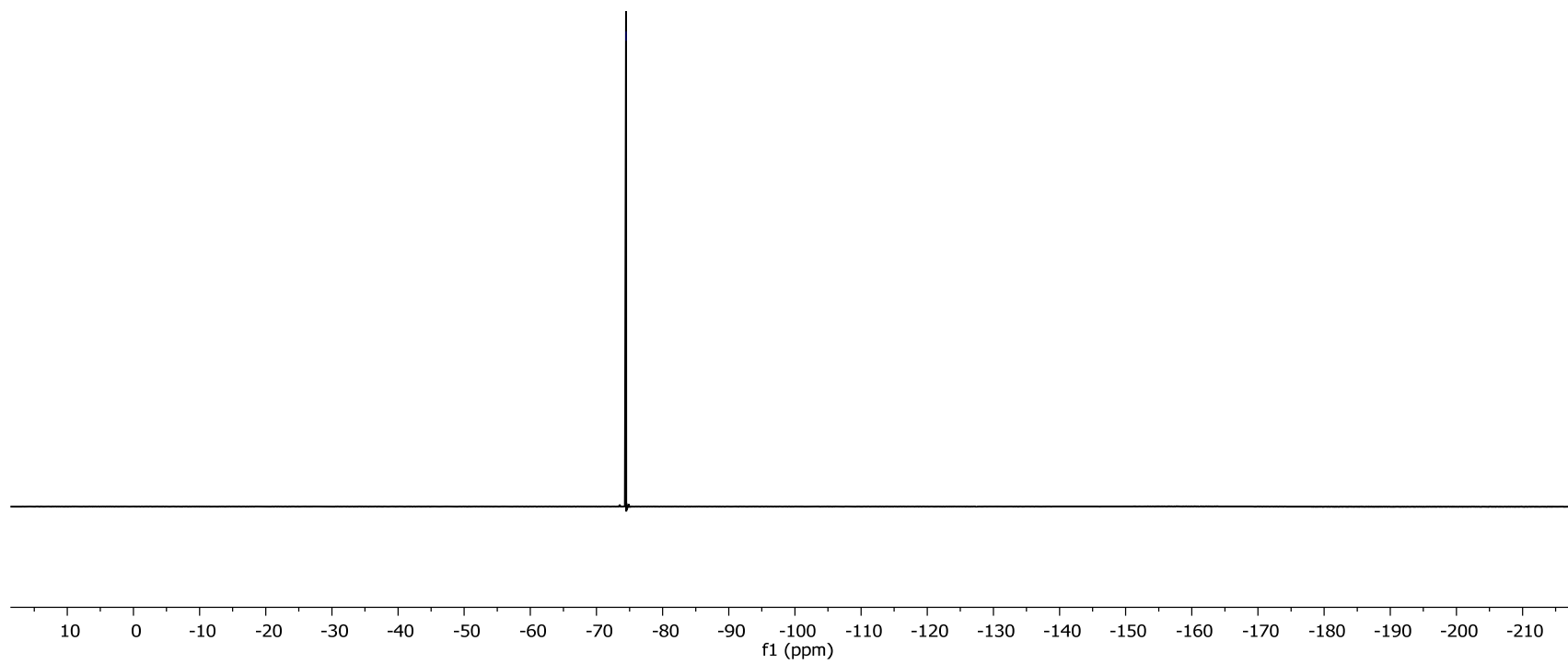
¹³C NMR spectrum for **16** (150 MHz; DMSO-*d*₆)



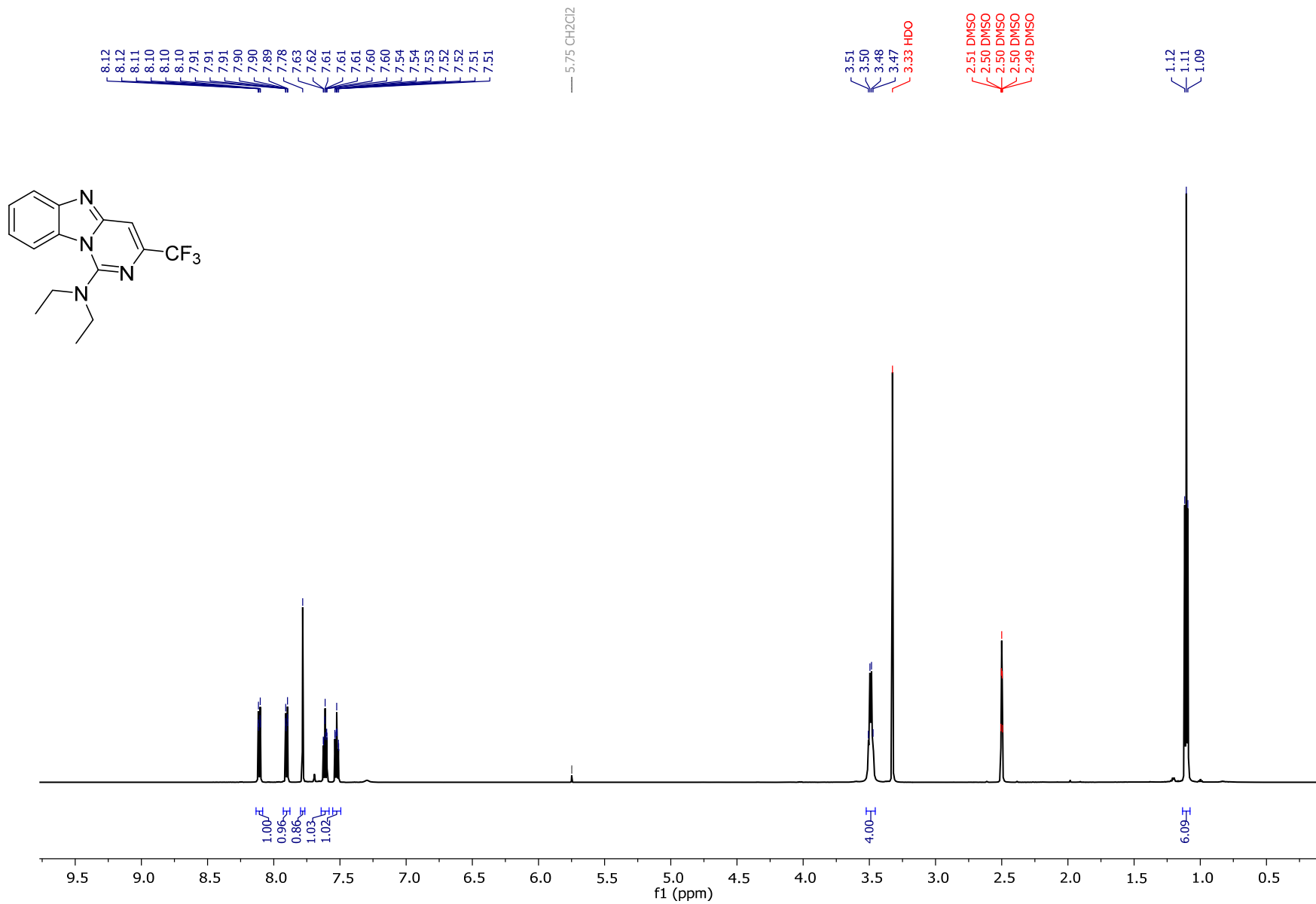
^{19}F NMR spectrum for **16** (565 MHz; $\text{DMSO-}d_6$)



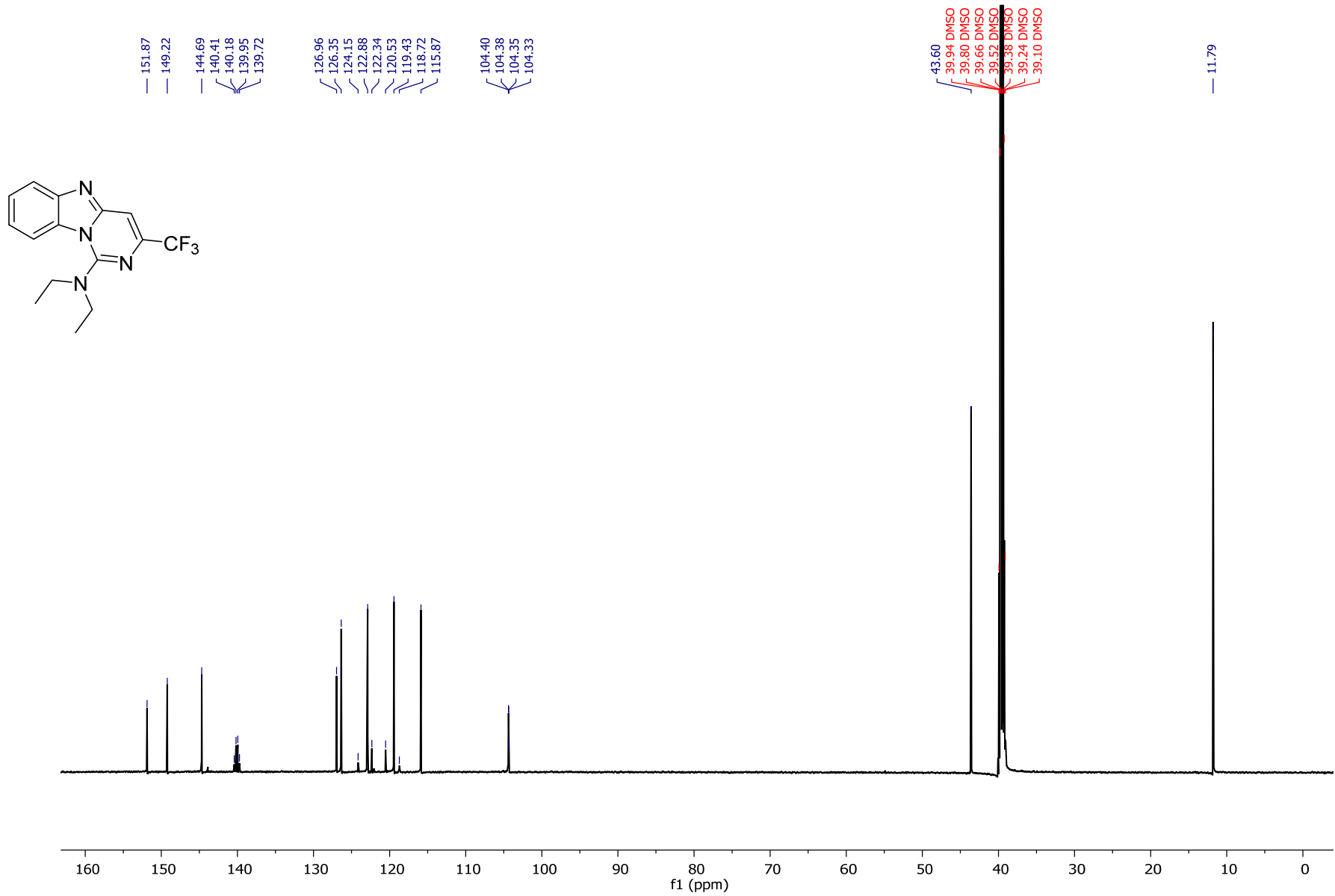
-74.48



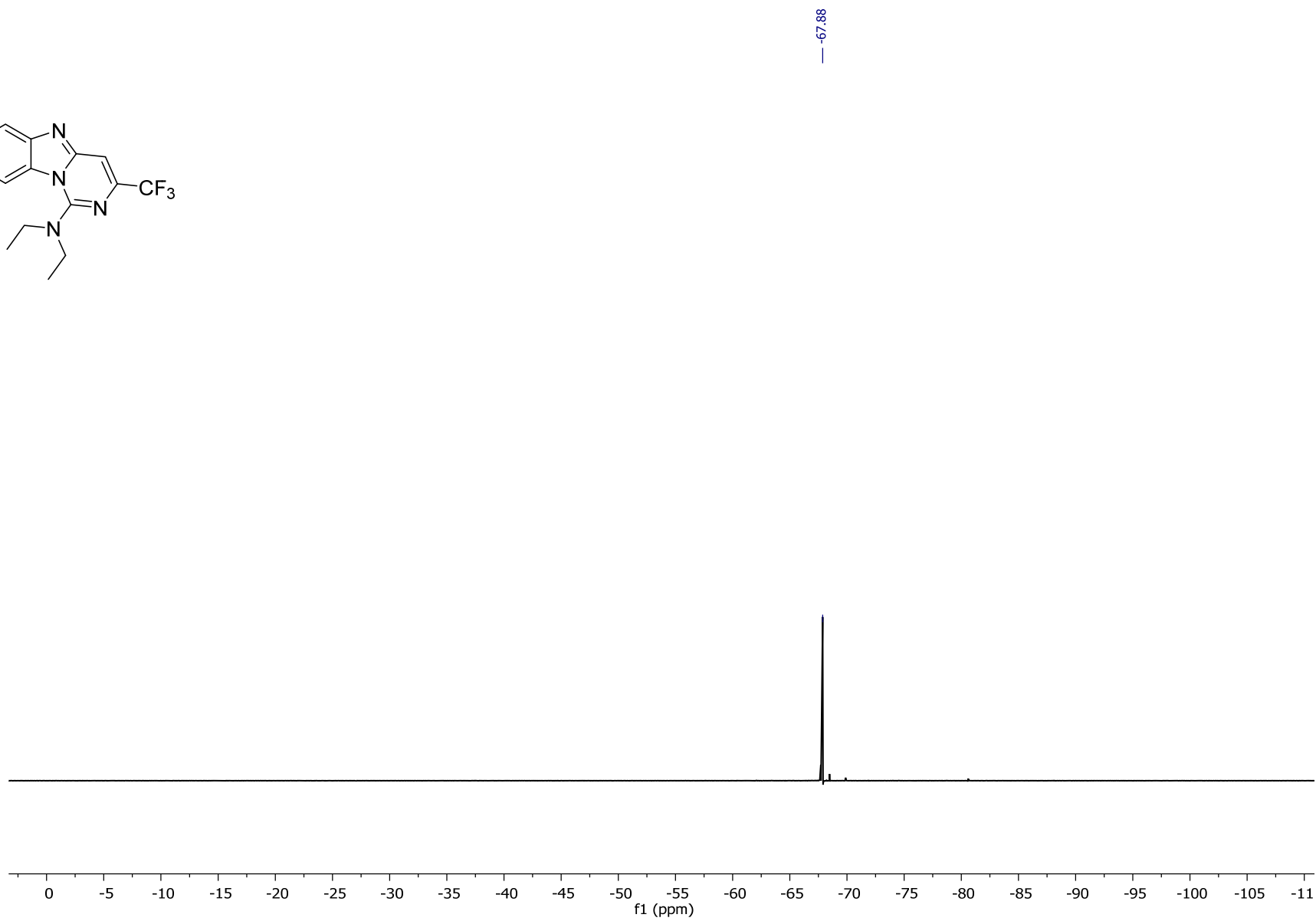
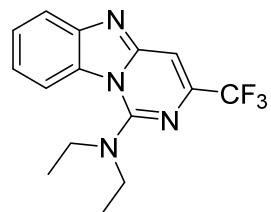
¹H NMR spectrum for **19** (600 MHz; DMSO-*d*₆)



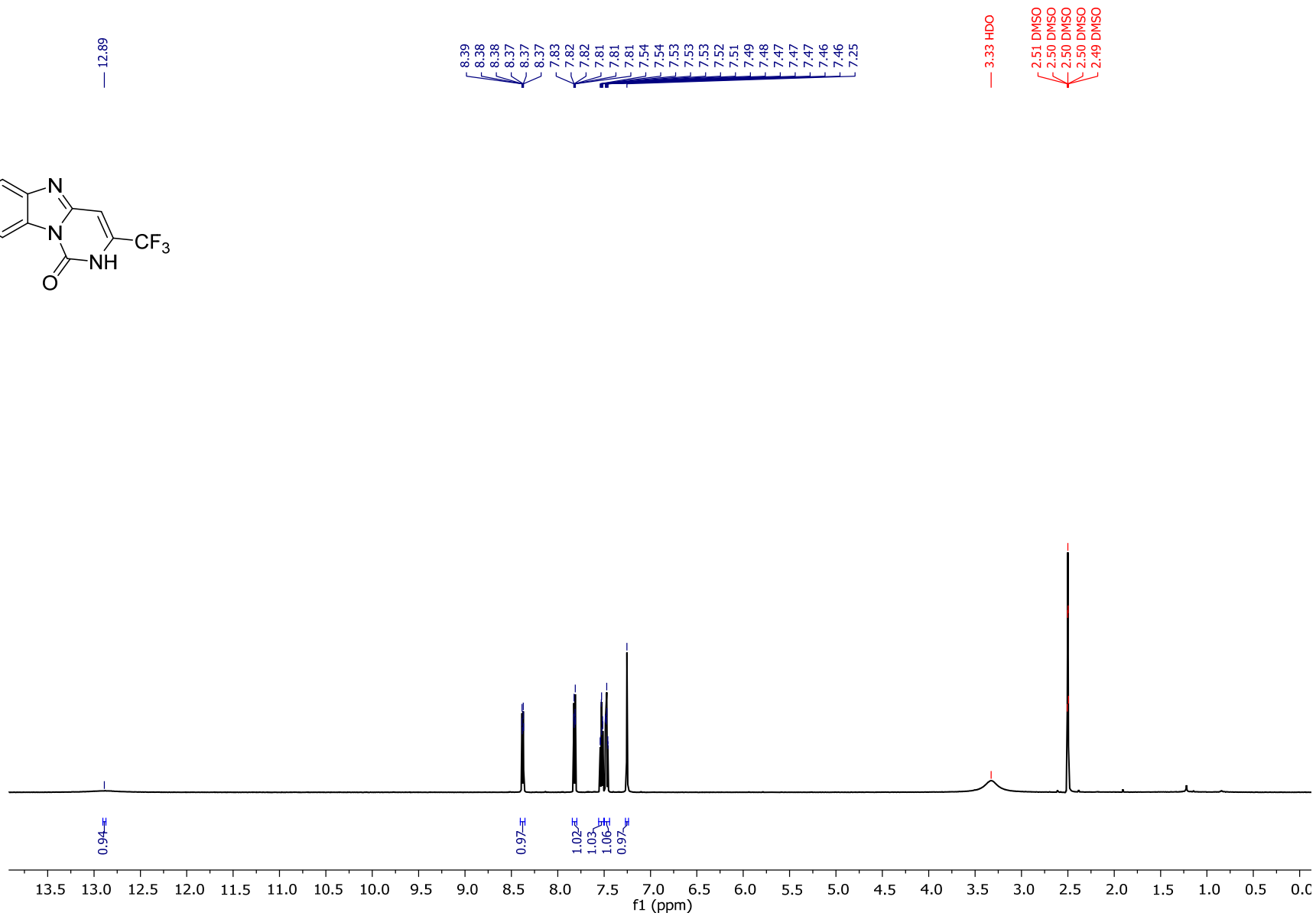
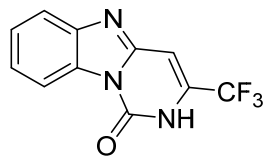
¹³C NMR spectrum for **19** (150 MHz; DMSO-*d*₆)



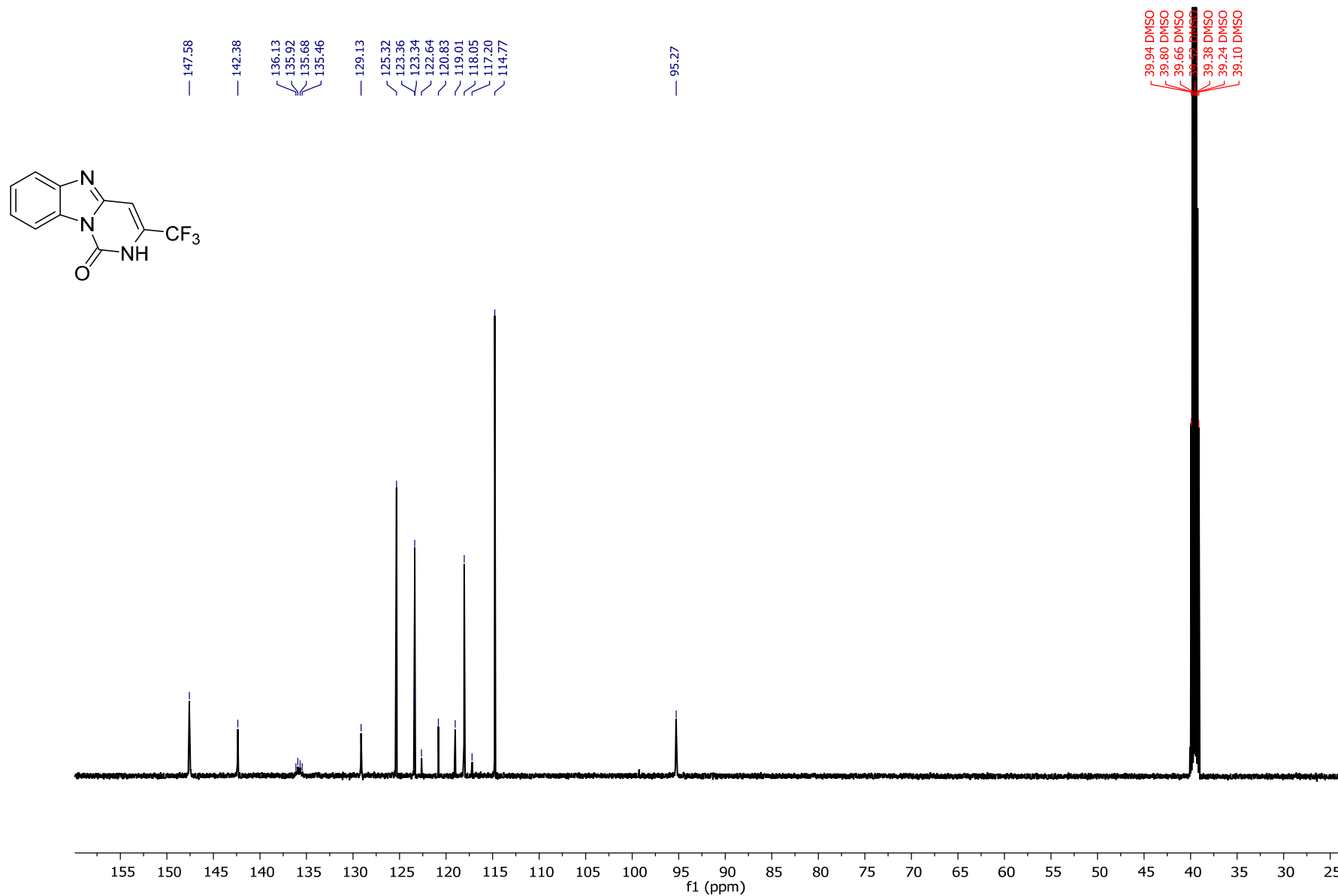
^{19}F NMR spectrum for **19** (565 MHz, $\text{DMSO-}d_6$)



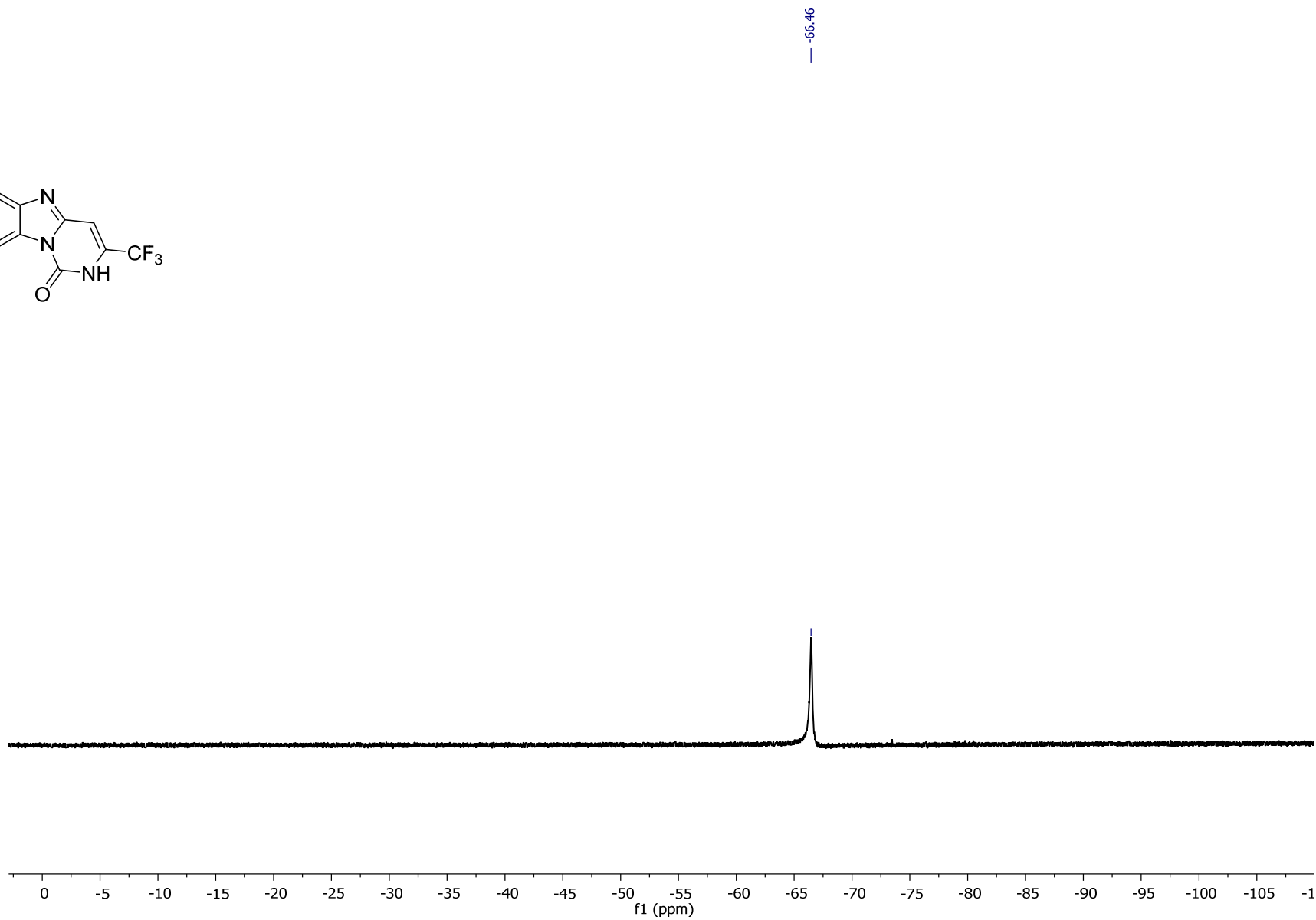
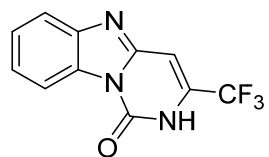
¹H NMR spectrum for **20** (600 MHz; DMSO-*d*₆)



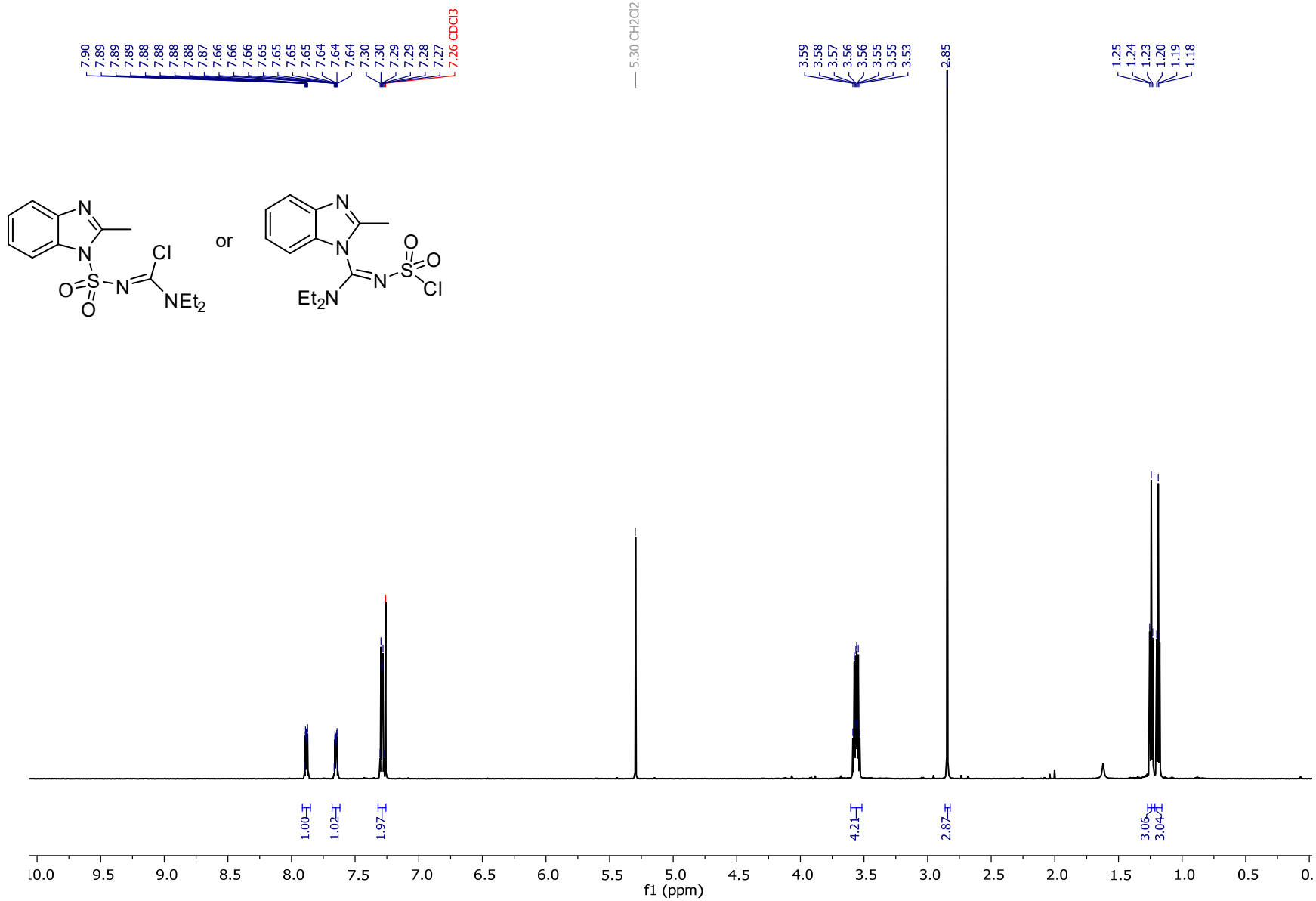
^{13}C NMR spectrum for **20** (150 MHz; 60 °C; D1 = 5s; DMSO- d_6)



^{19}F NMR spectrum for **20** (565 MHz, $\text{DMSO-}d_6$)



¹H NMR spectrum for **22/23** (600 MHz; CDCl₃)



7.90
7.89
7.89
7.88
7.88
7.88
7.87
7.66
7.66
7.65
7.65
7.65
7.64
7.64
7.30
7.30
7.29
7.29
7.28
7.27
7.26 CDCl₃

5.30 CH₂Cl₂

3.59
3.58
3.57
3.56
3.56
3.55
3.55
3.53

2.85

1.25
1.24
1.23
1.20
1.19
1.18

1.00
1.02
1.97

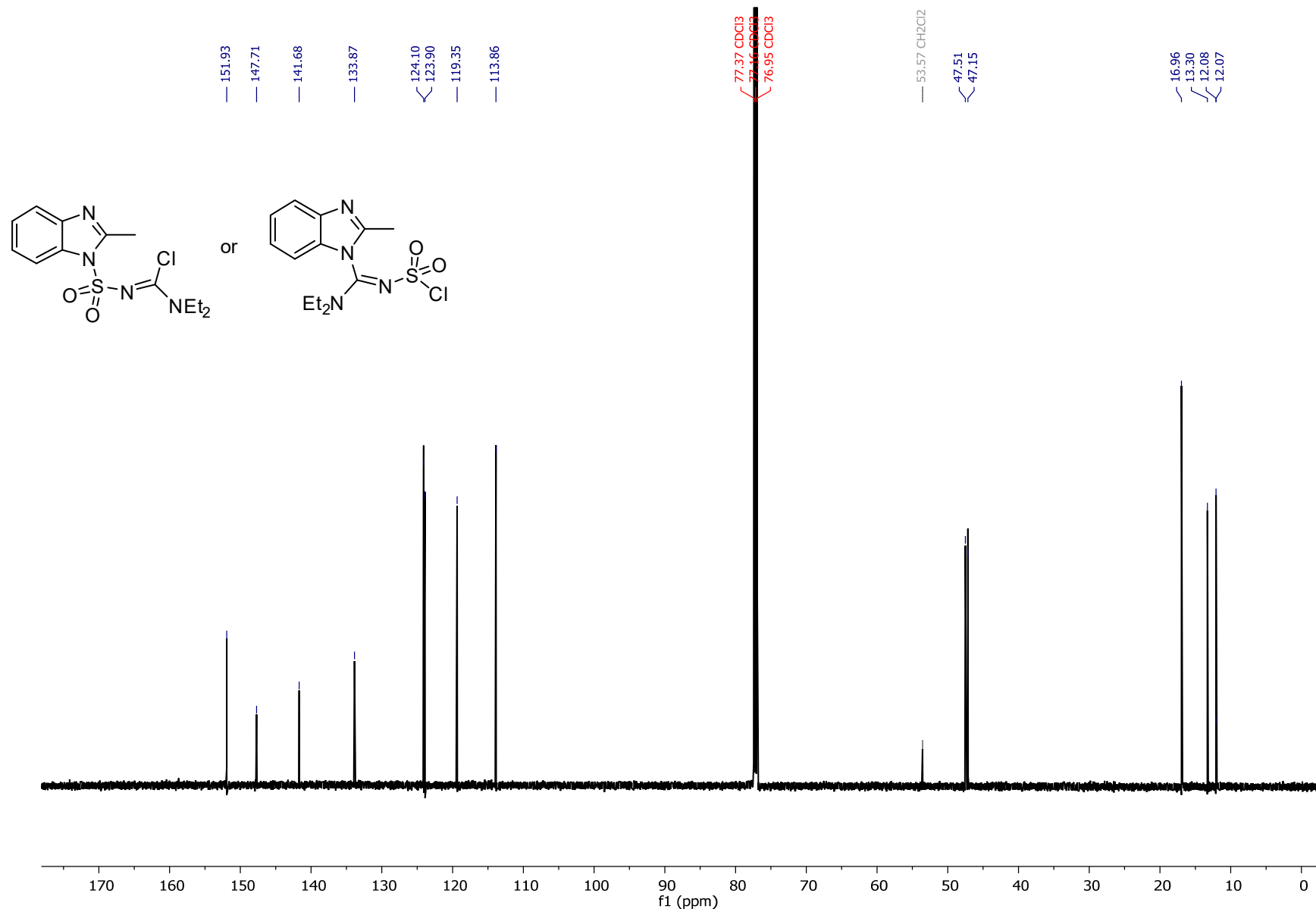
4.21

2.87

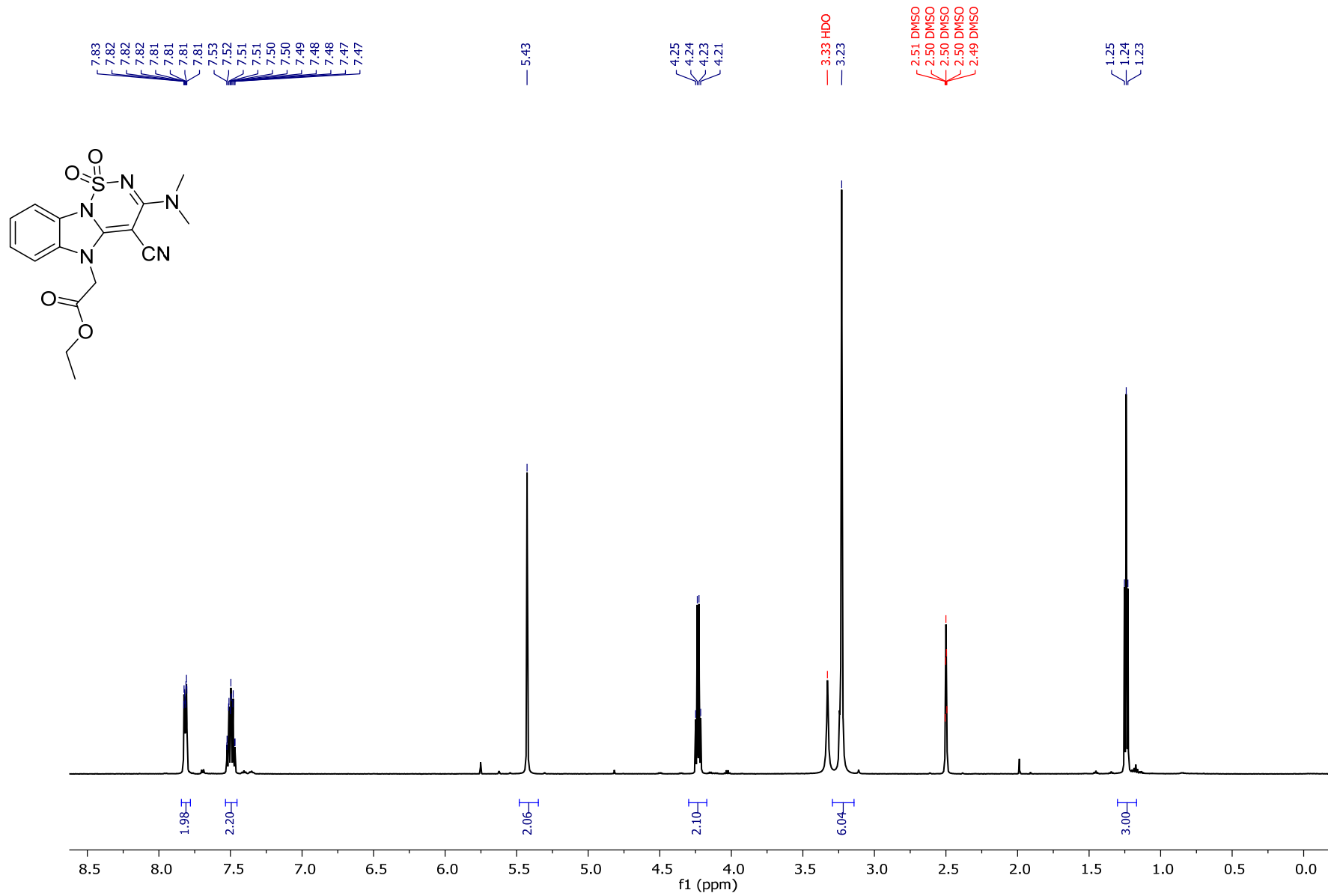
3.06
3.04

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.

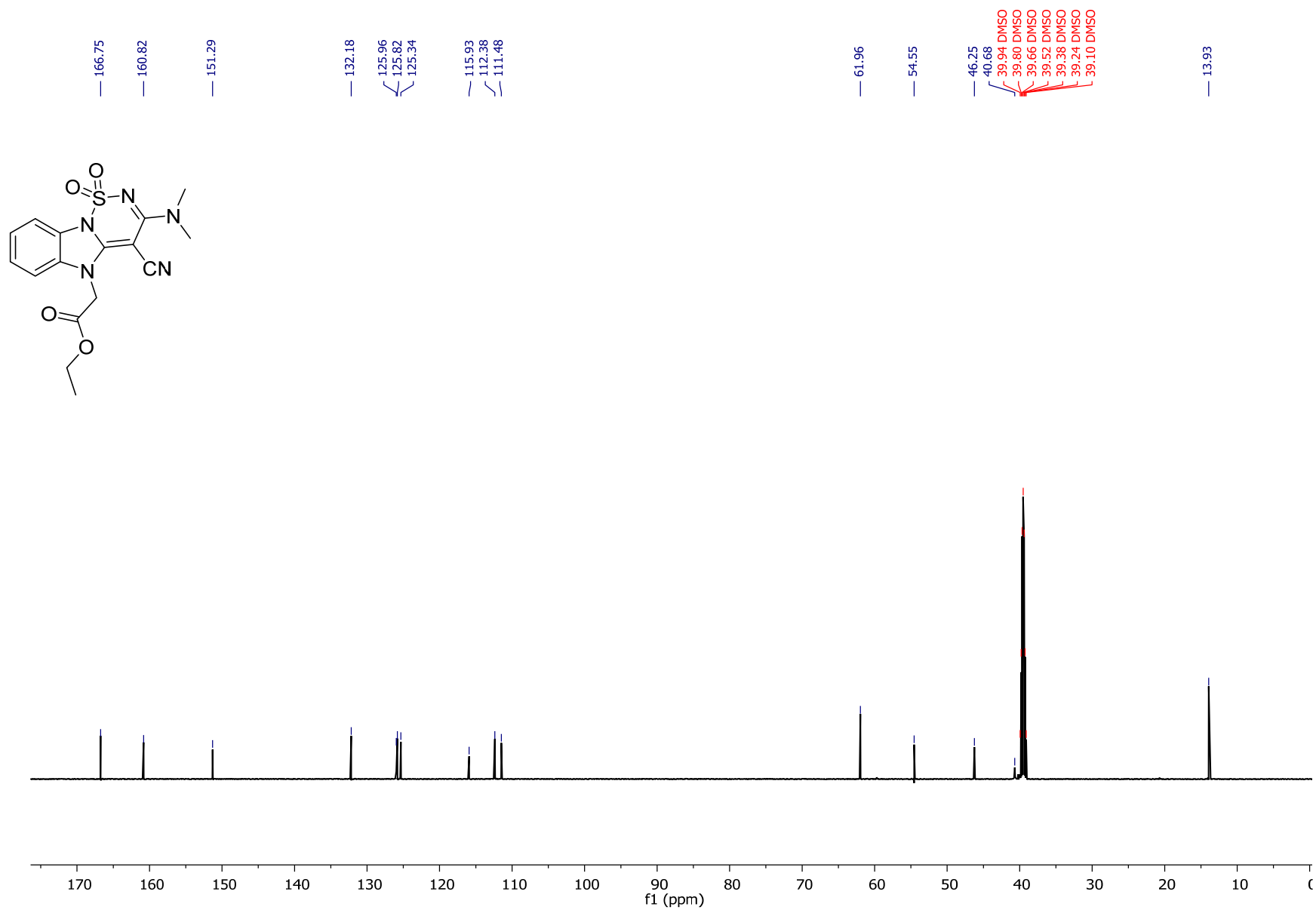
^{13}C NMR spectrum for **22/23** (150 MHz; CDCl_3)



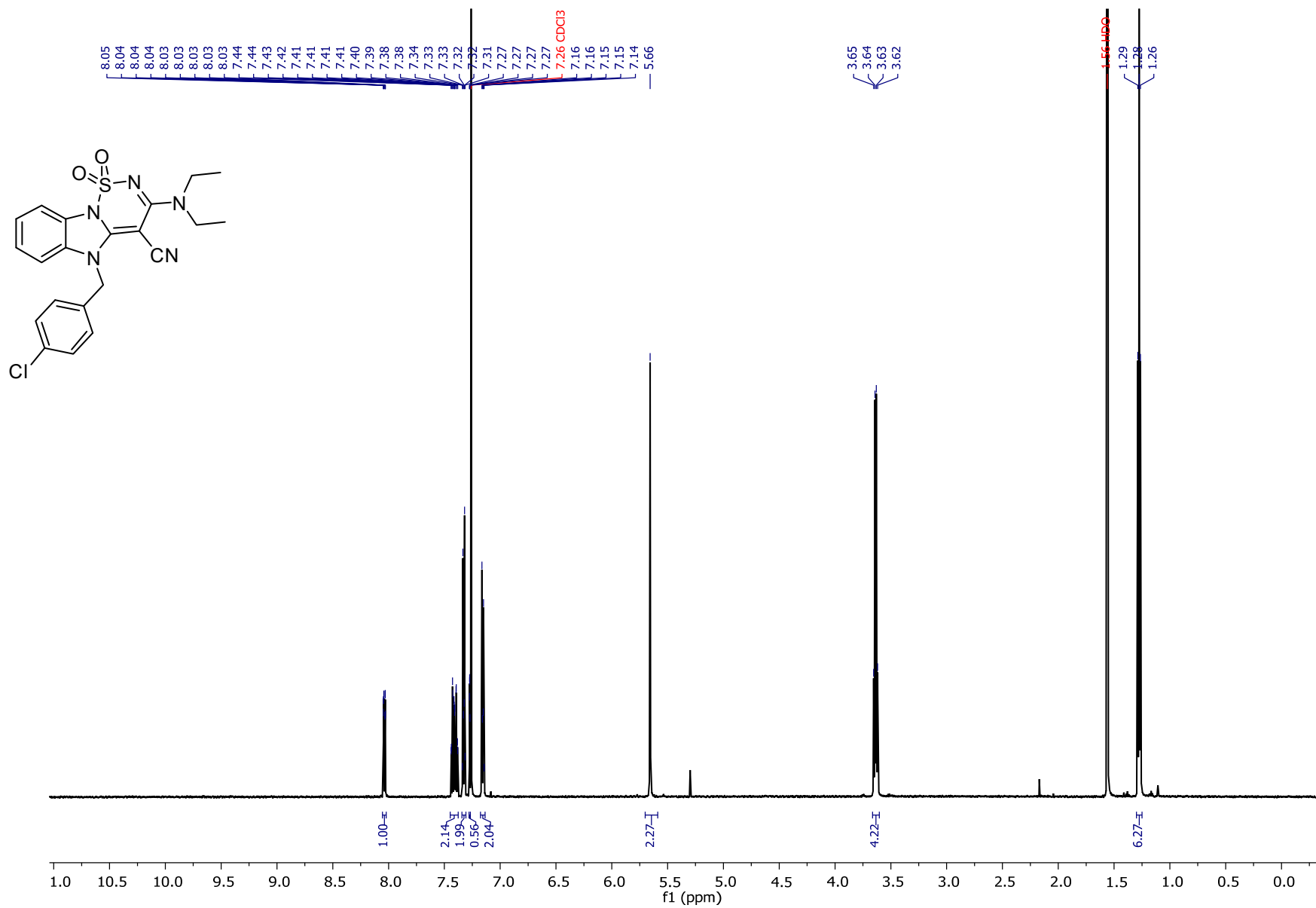
¹H NMR spectrum for **26a** (600 MHz; DMSO-*d*₆)



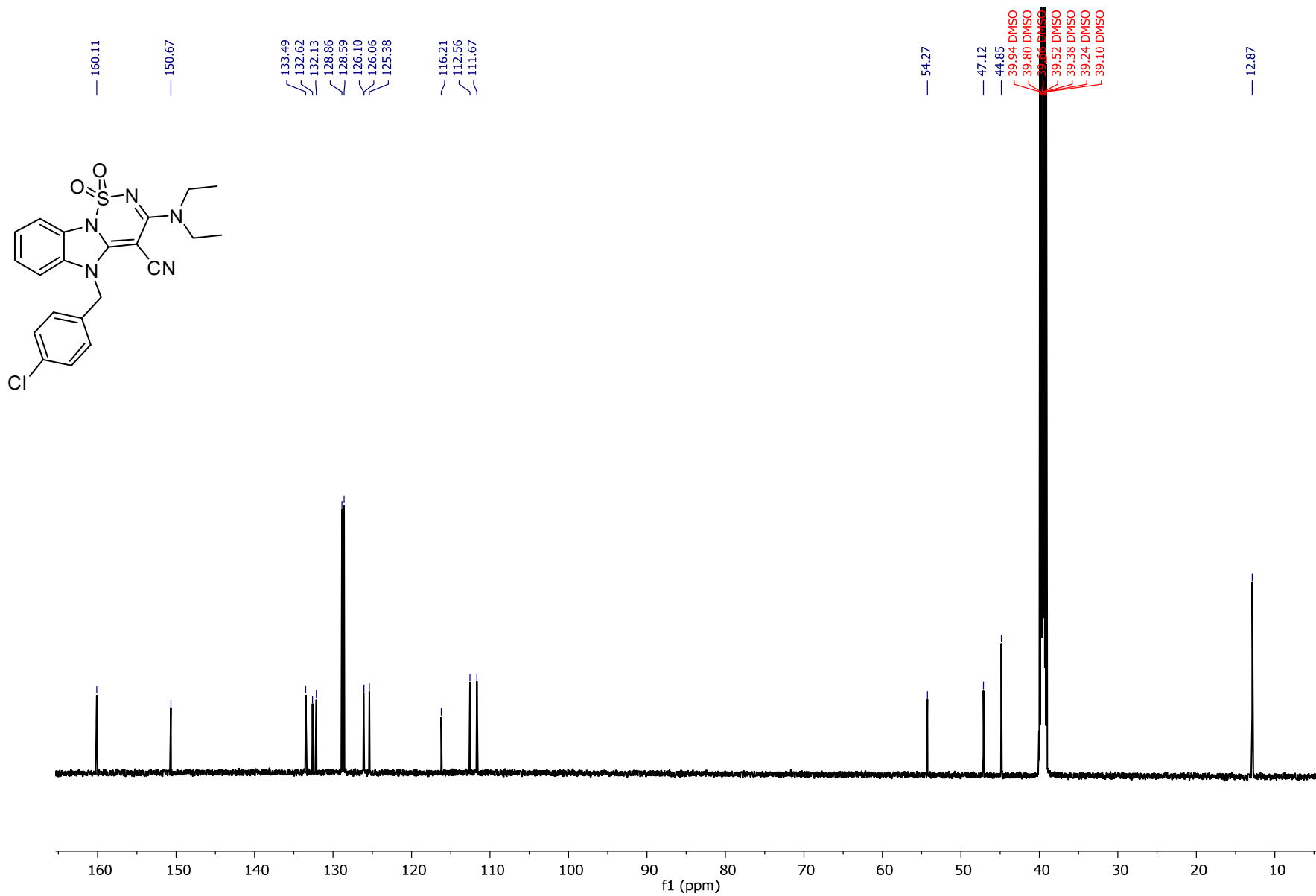
¹³C NMR spectrum for **26a** (150 MHz; DMSO-*d*₆)



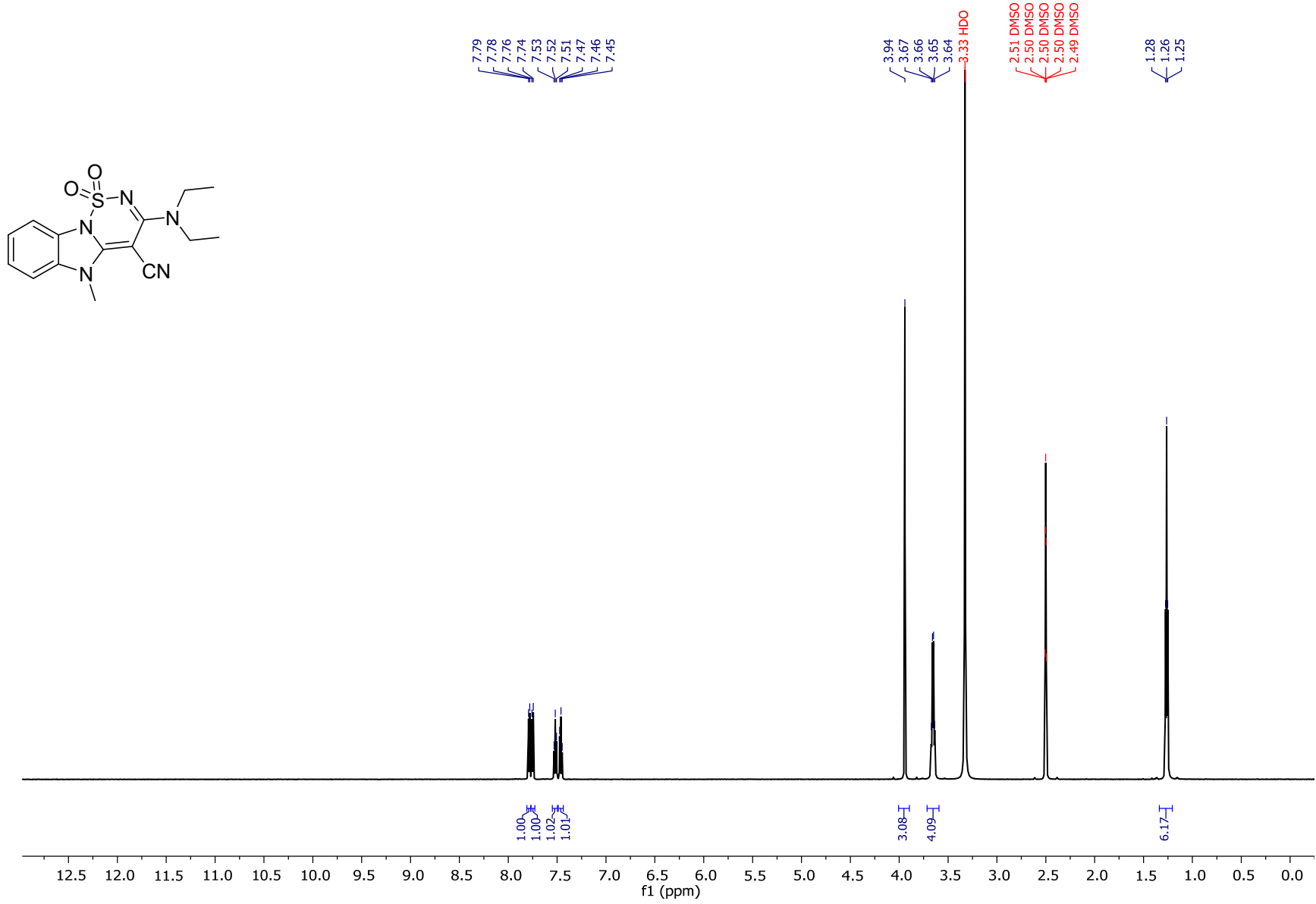
¹H NMR spectrum for **26b** (600 MHz; CDCl₃)



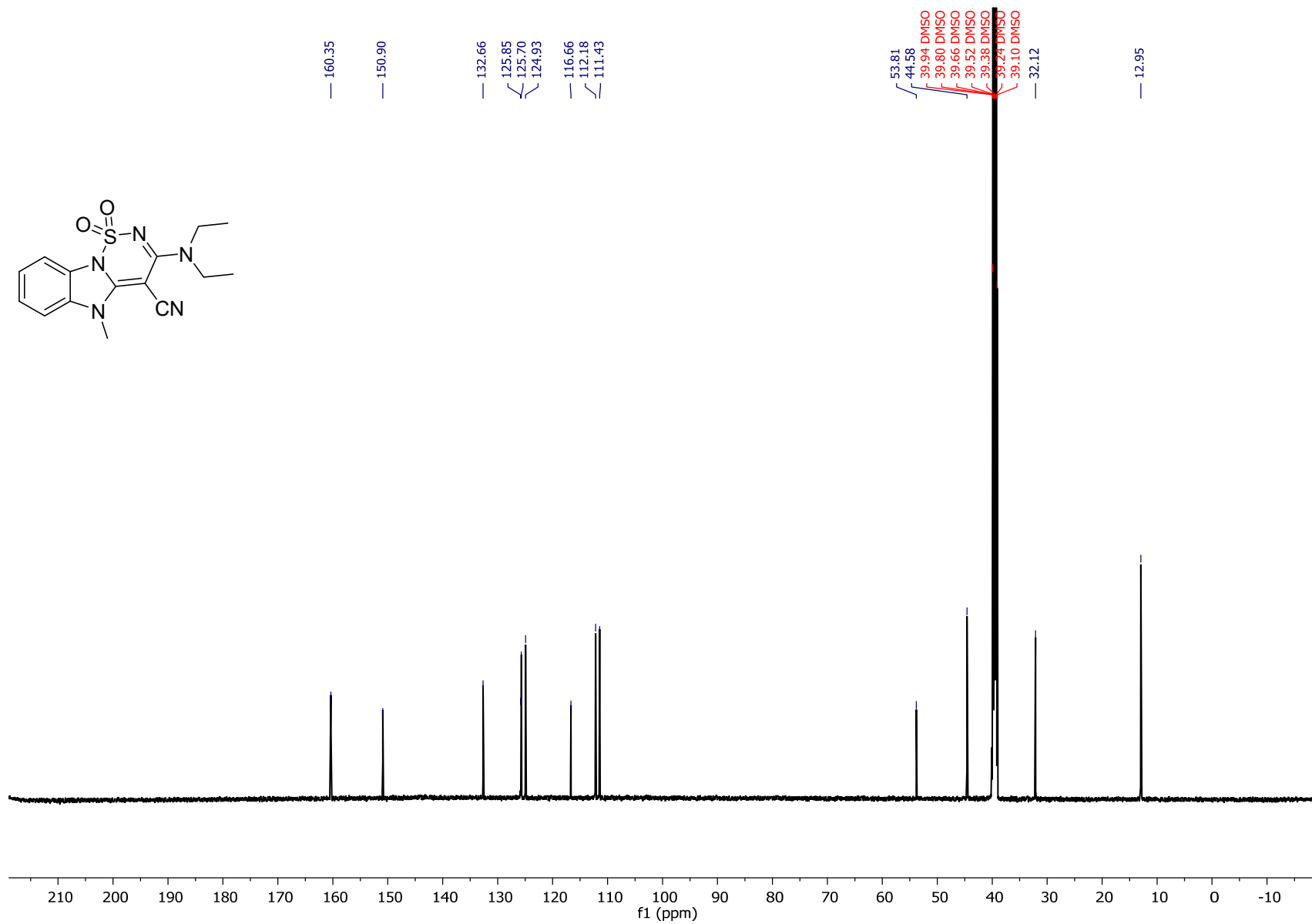
¹³C NMR spectrum for **26b** (150 MHz; DMSO-*d*₆)



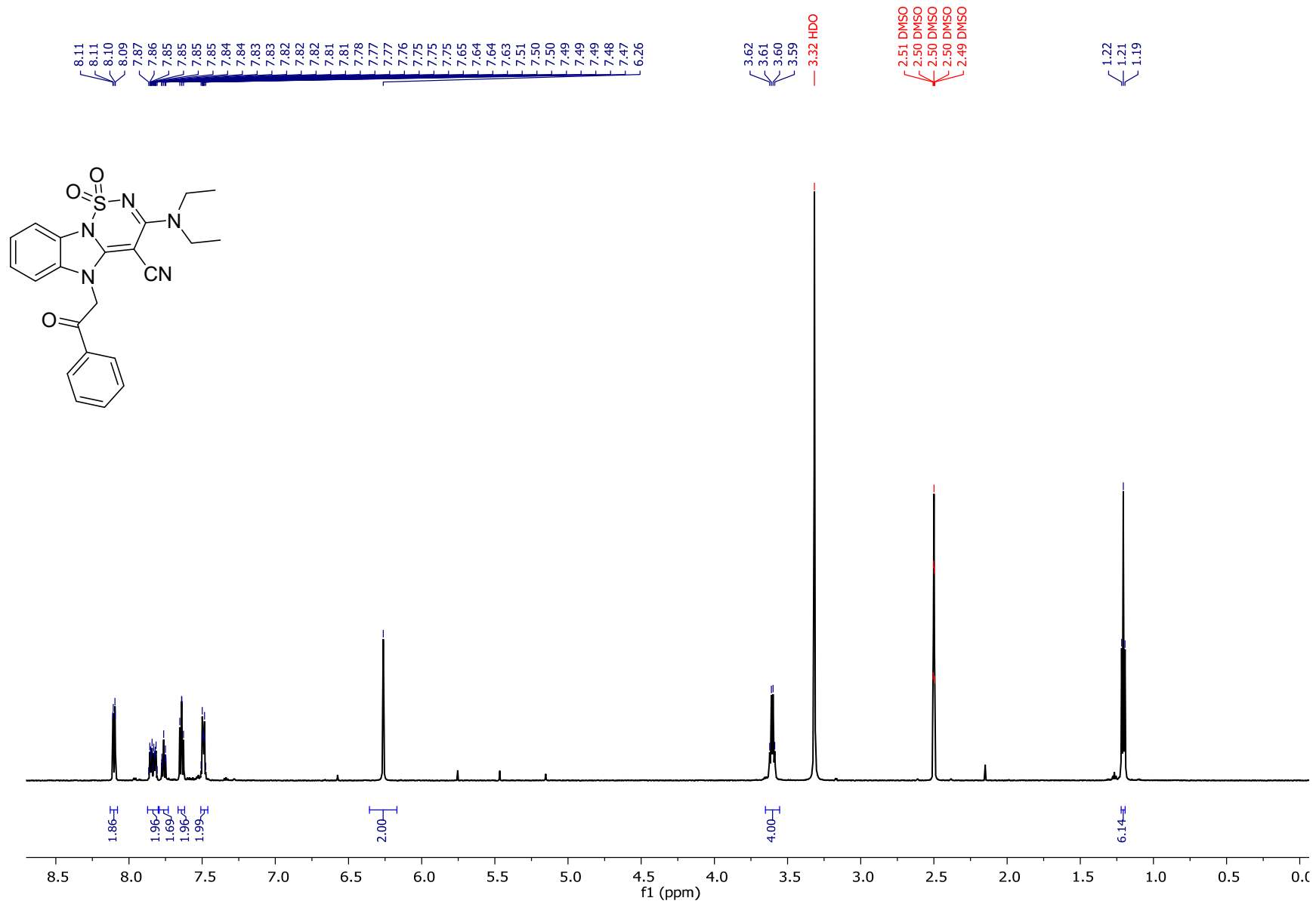
¹H NMR spectrum for **26c** (600 MHz; DMSO-*d*₆)



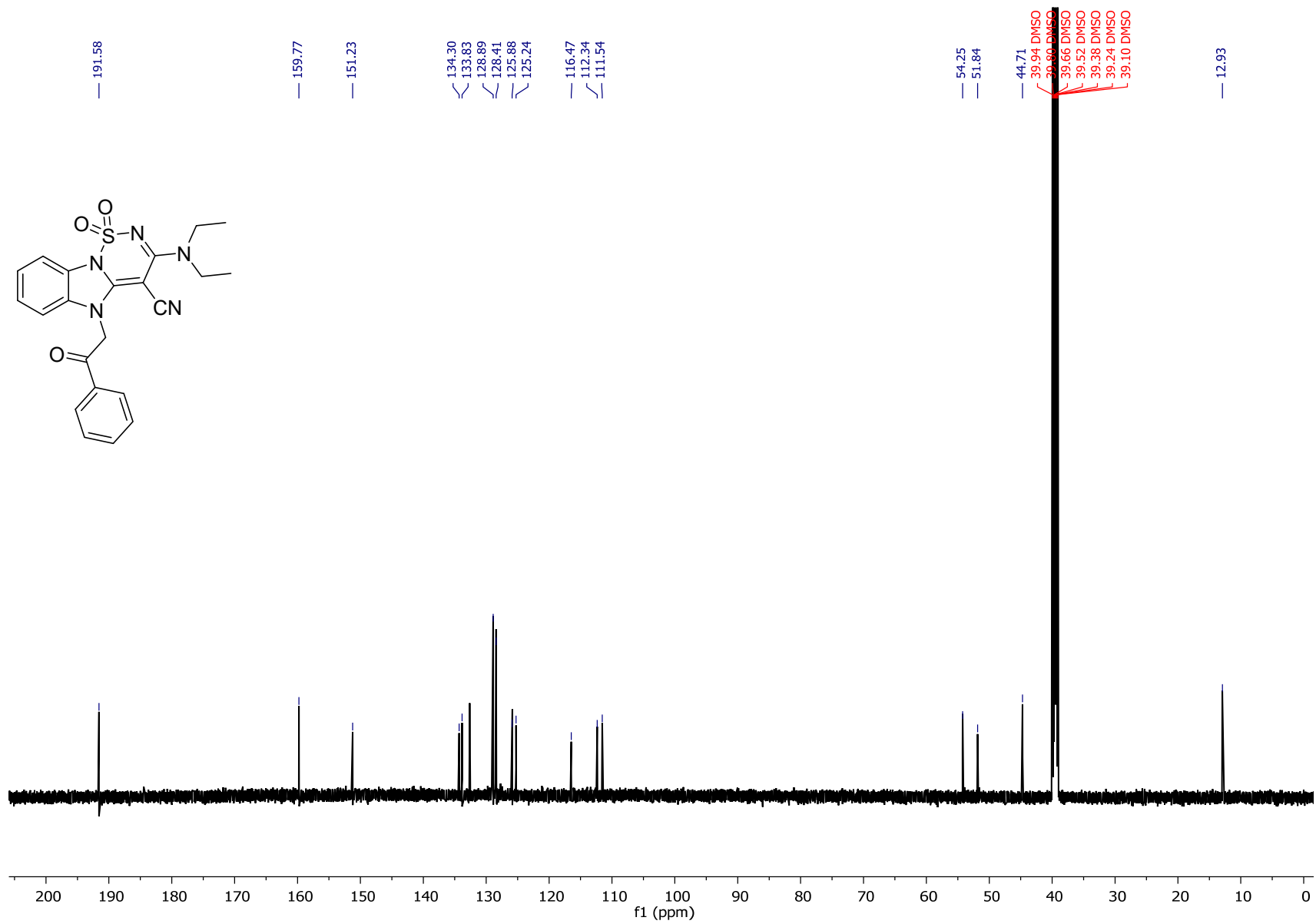
¹³C NMR spectrum for **26c** (150 MHz; DMSO-*d*₆)



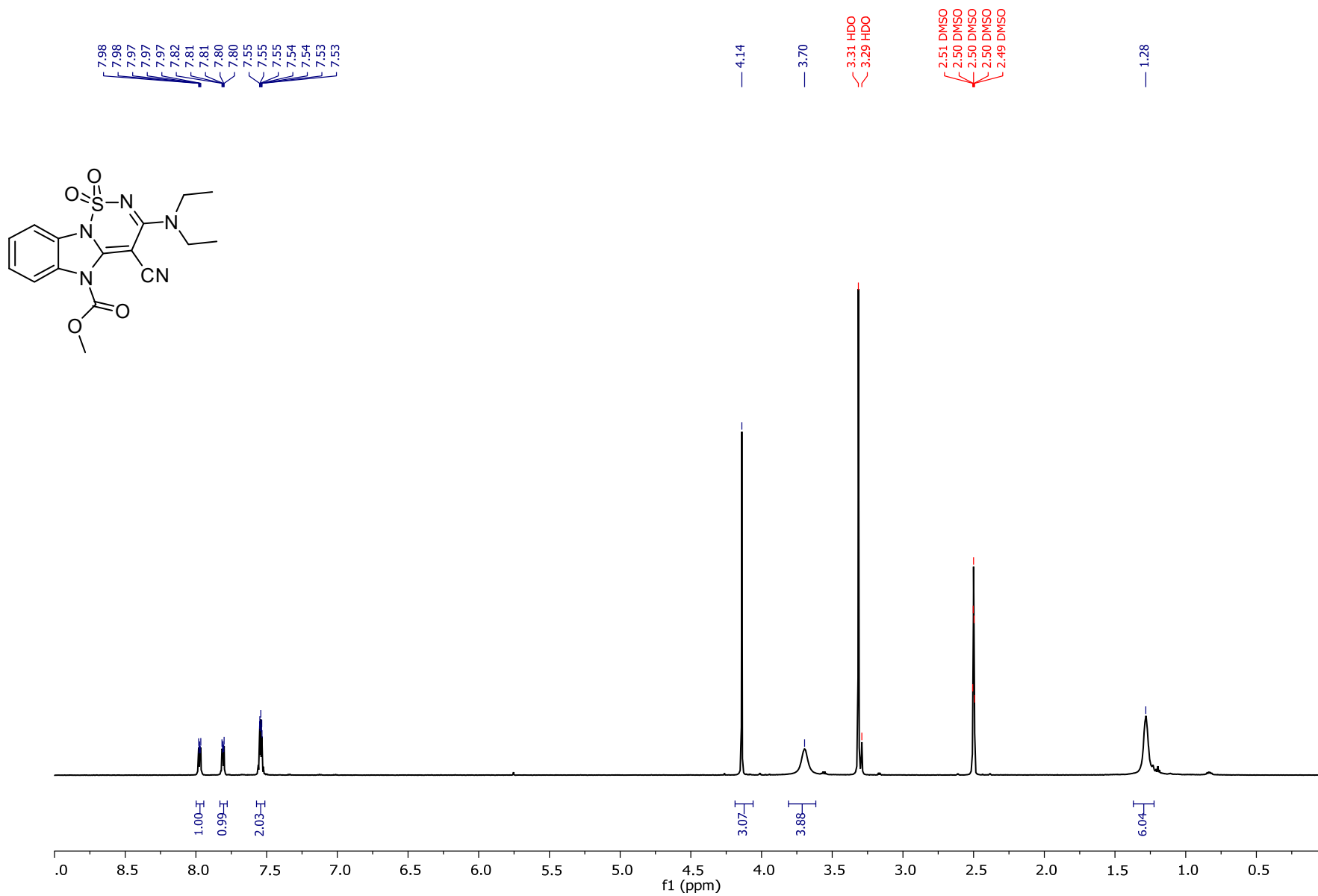
¹H NMR spectrum for **26d** (600 MHz; DMSO-*d*₆)



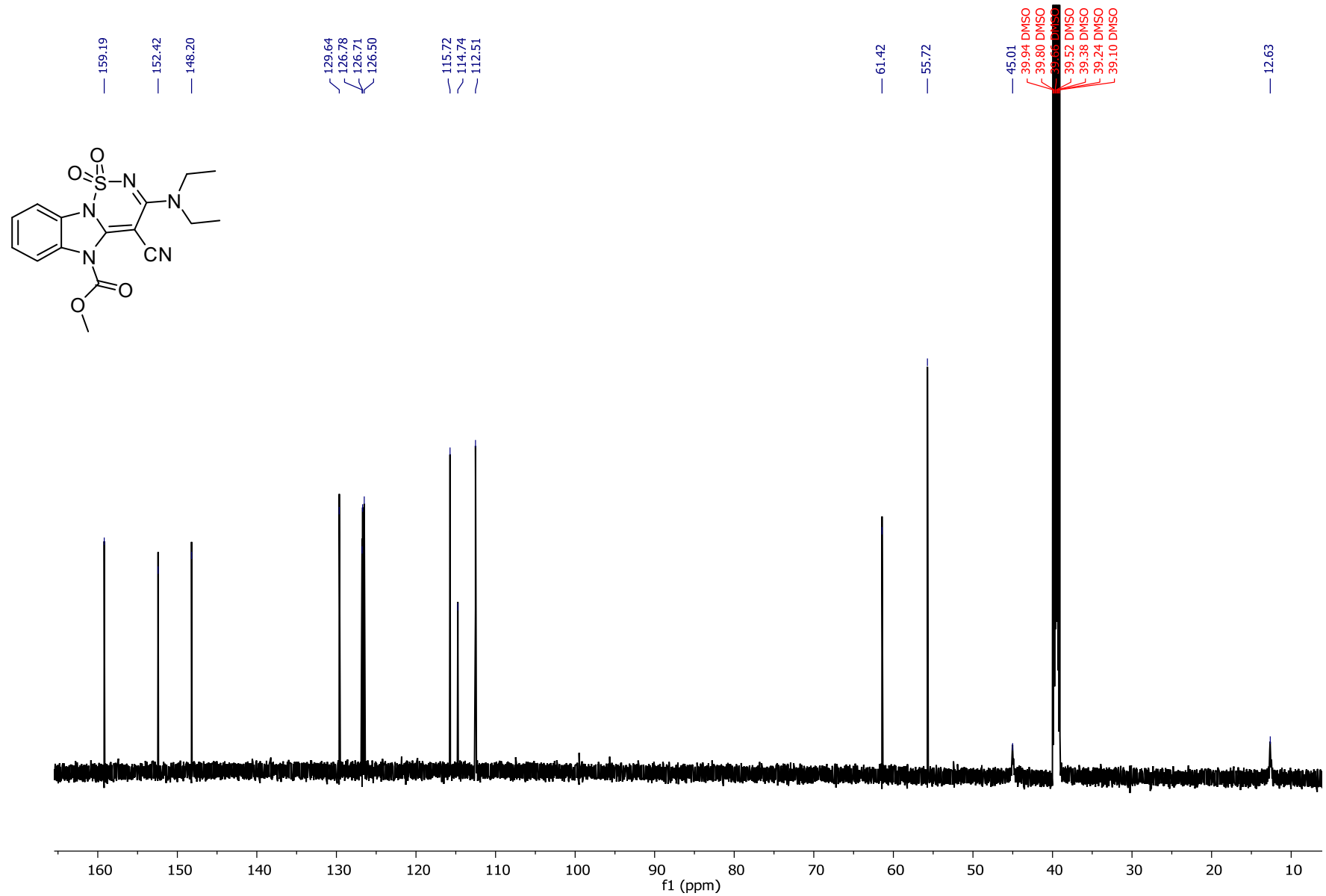
¹³C NMR spectrum for **26d** (150 MHz; DMSO-*d*₆)



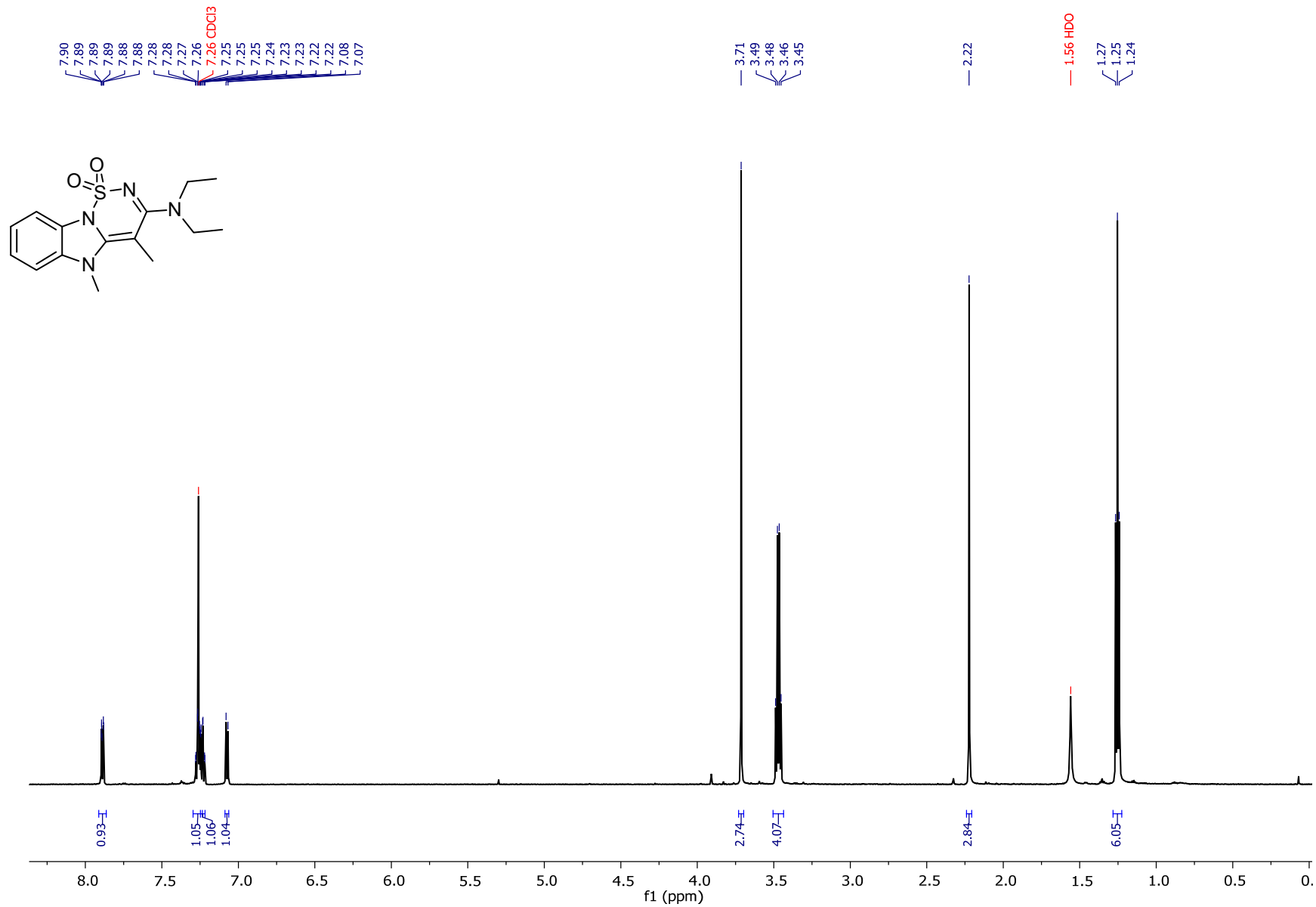
¹H NMR spectrum for **28** (600 MHz; DMSO-*d*₆)



¹³C NMR spectrum for **28** (150 MHz; DMSO-*d*₆)



¹H NMR spectrum for **29** (600 MHz; CDCl₃)



¹³C NMR spectrum for **29** (150 MHz; CDCl₃)

