

SUPPORTING INFORMATION

Zephycandidine A and Synthetic Analogues – Synthesis and Evaluation of Biological Activity

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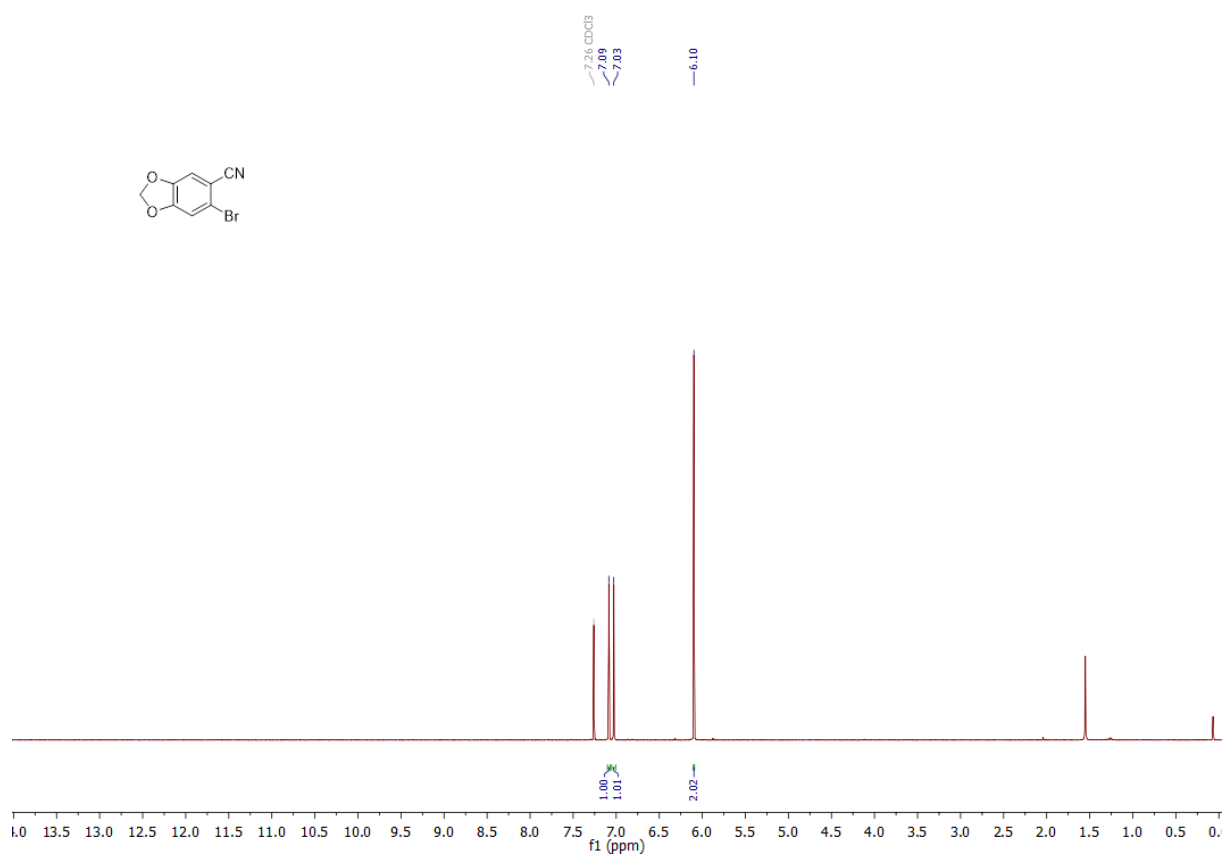
Department of Pharmacy – Center for Drug Research, Ludwig-Maximilians University,
Butenandtstr. 5-13, 81377 Munich, Germany

Content:

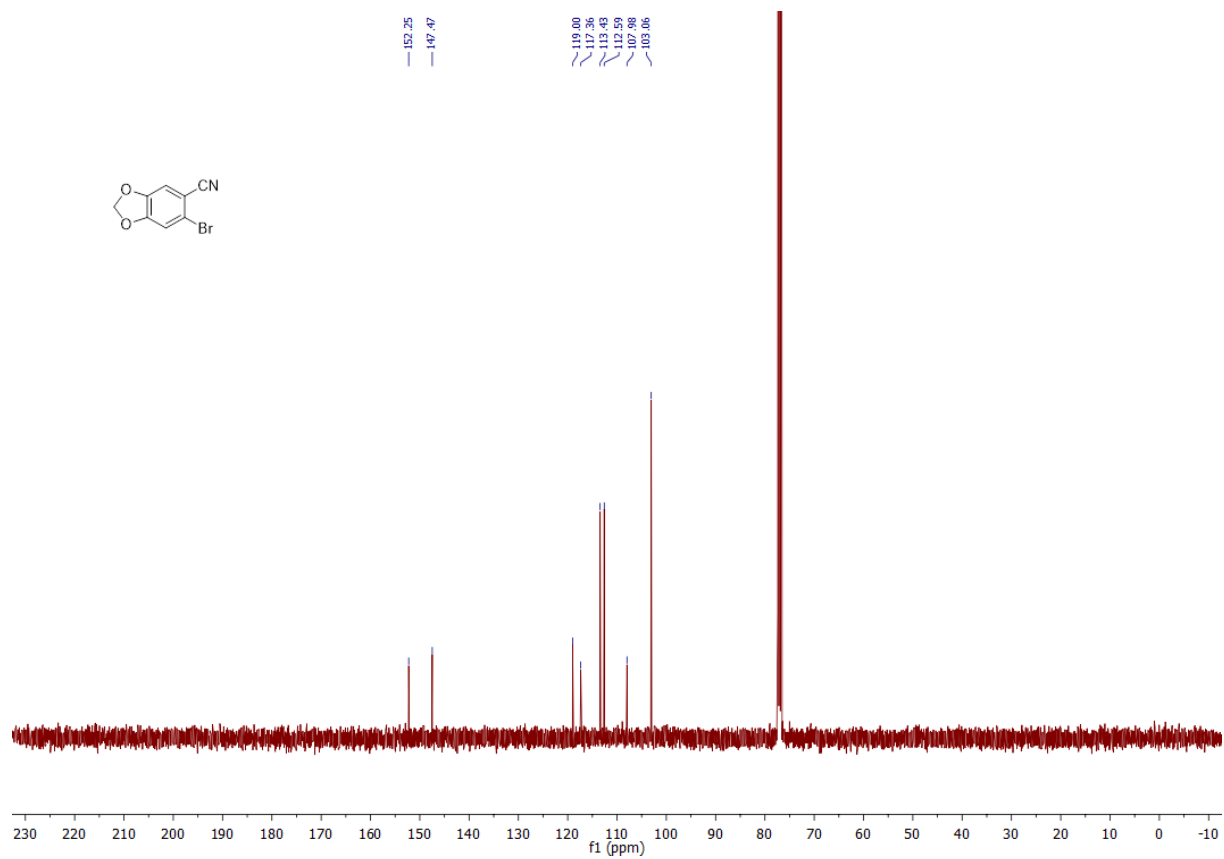
NMR data of the compounds 6a/b/d/e, 8a-e, 3, 9-15

Table S1: List of IC₅₀ values

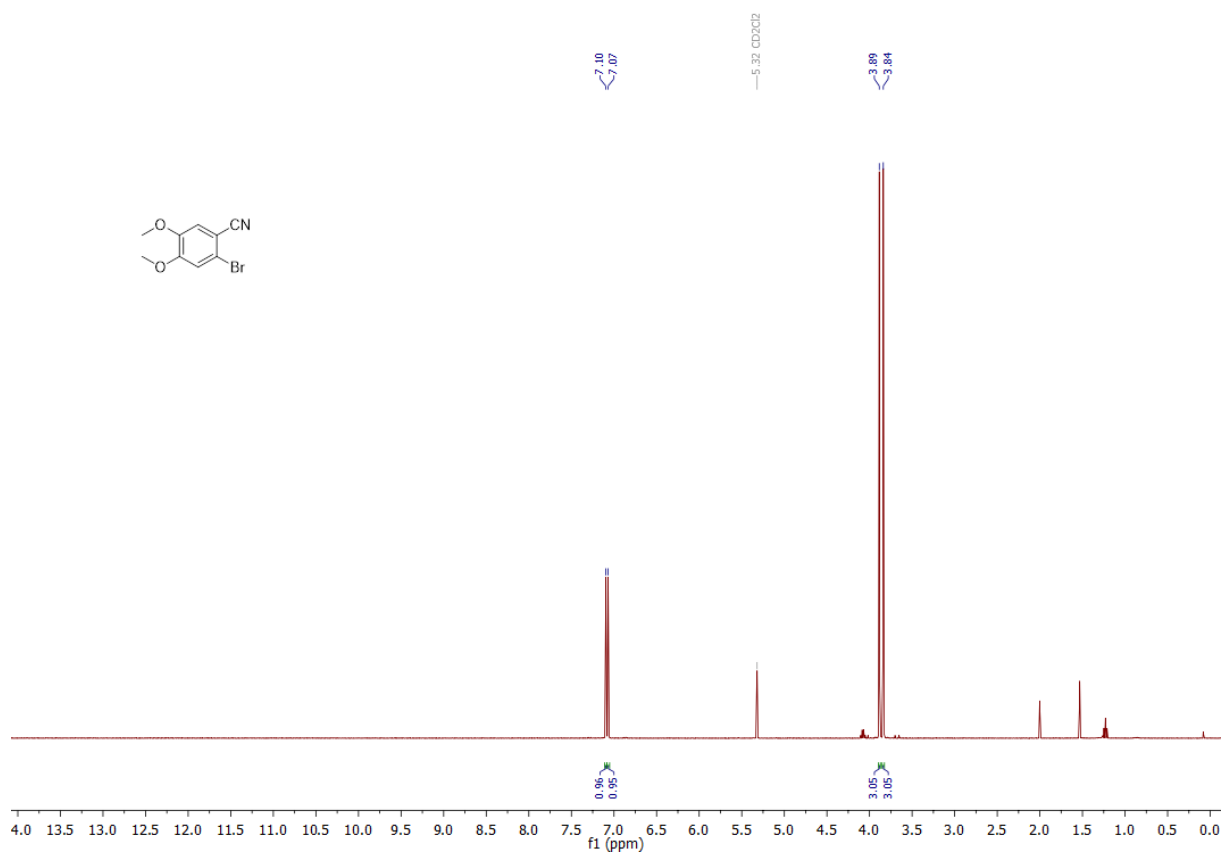
^1H NMR spectrum of compound 6a (400 MHz, CDCl_3)



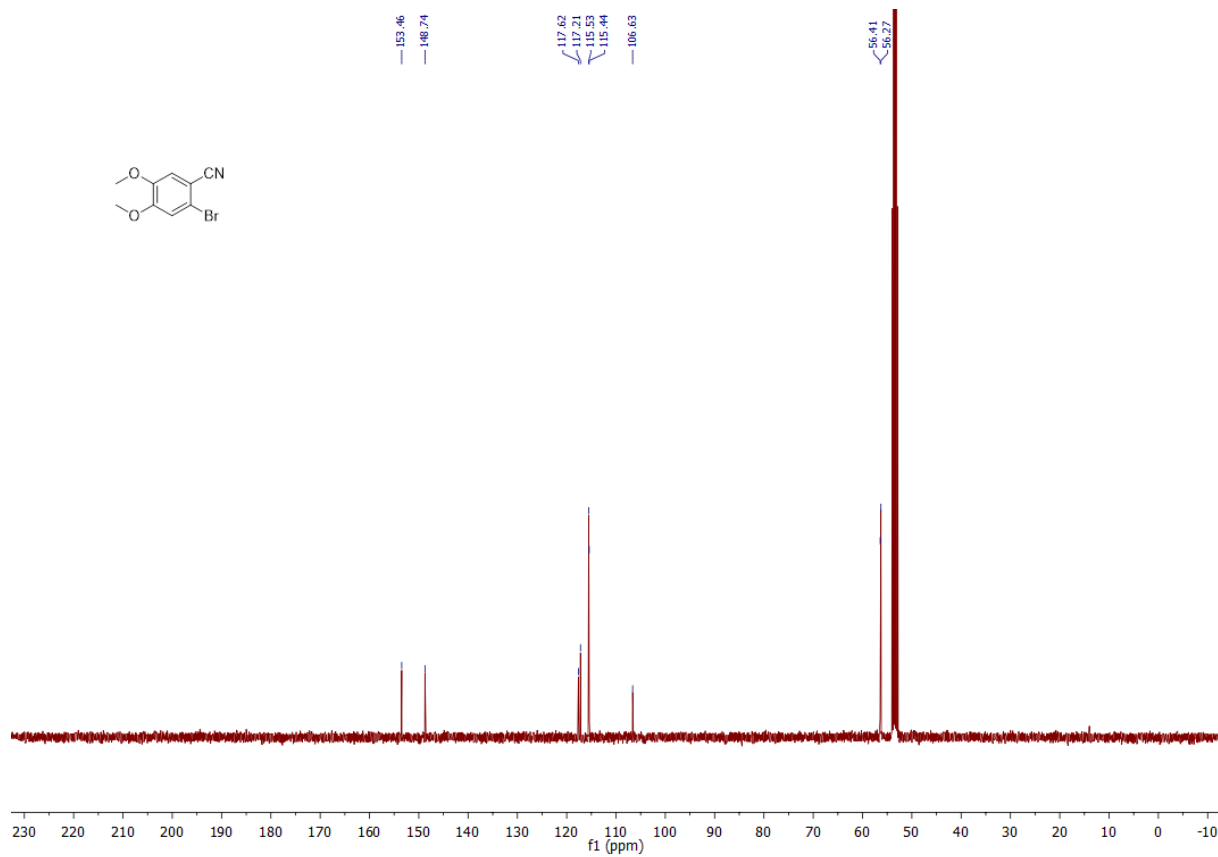
^{13}C NMR spectrum of compound 6a (101 MHz, CDCl_3)



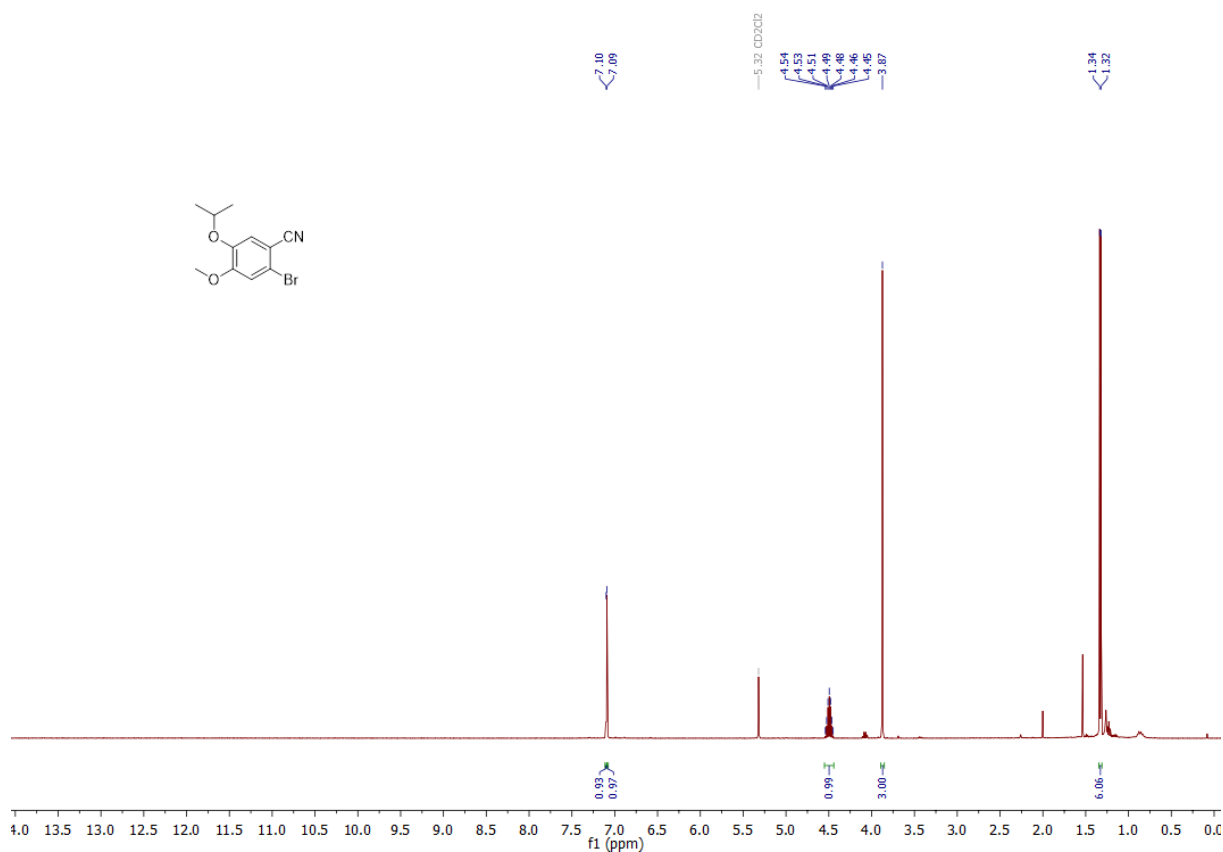
¹H NMR spectrum of compound 6b (400 MHz, methylene chloride-d₂)



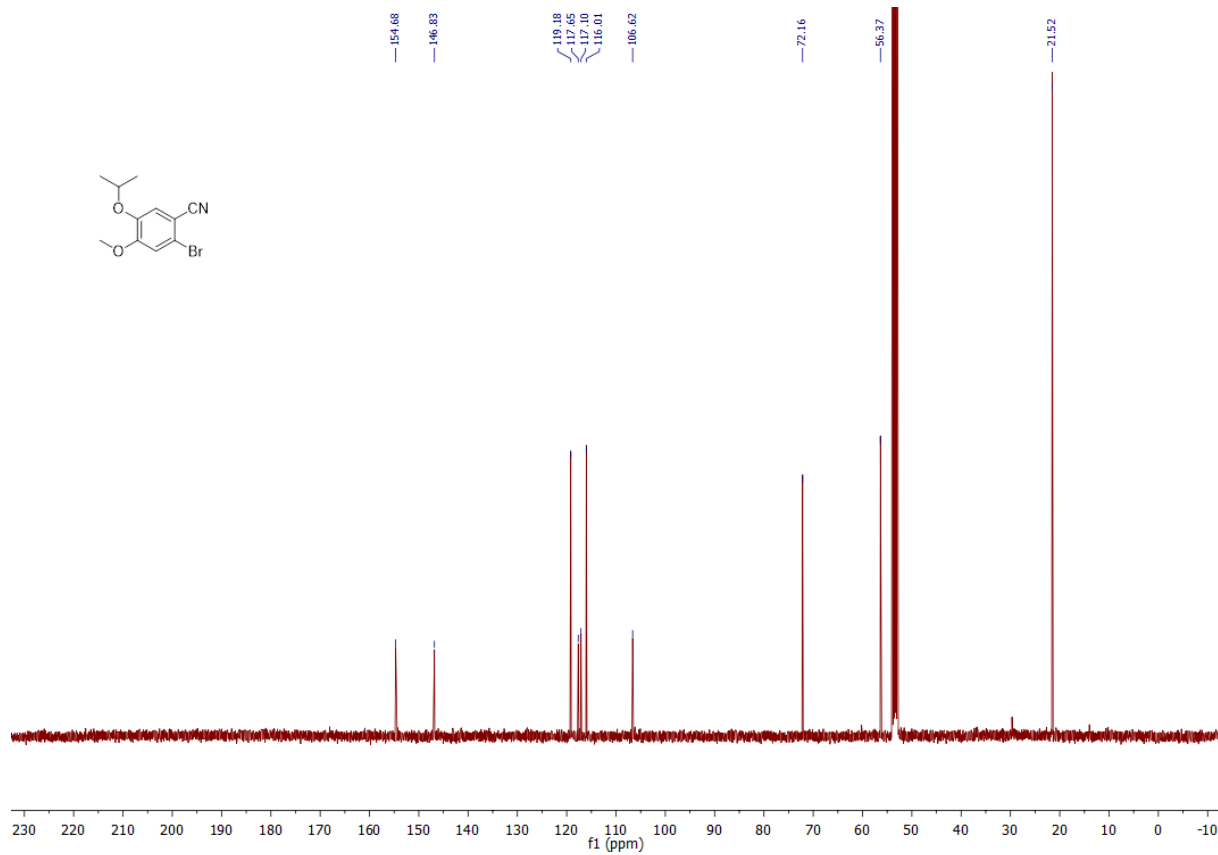
¹³C NMR spectrum of compound 6b (101 MHz, methylene chloride-d₂)



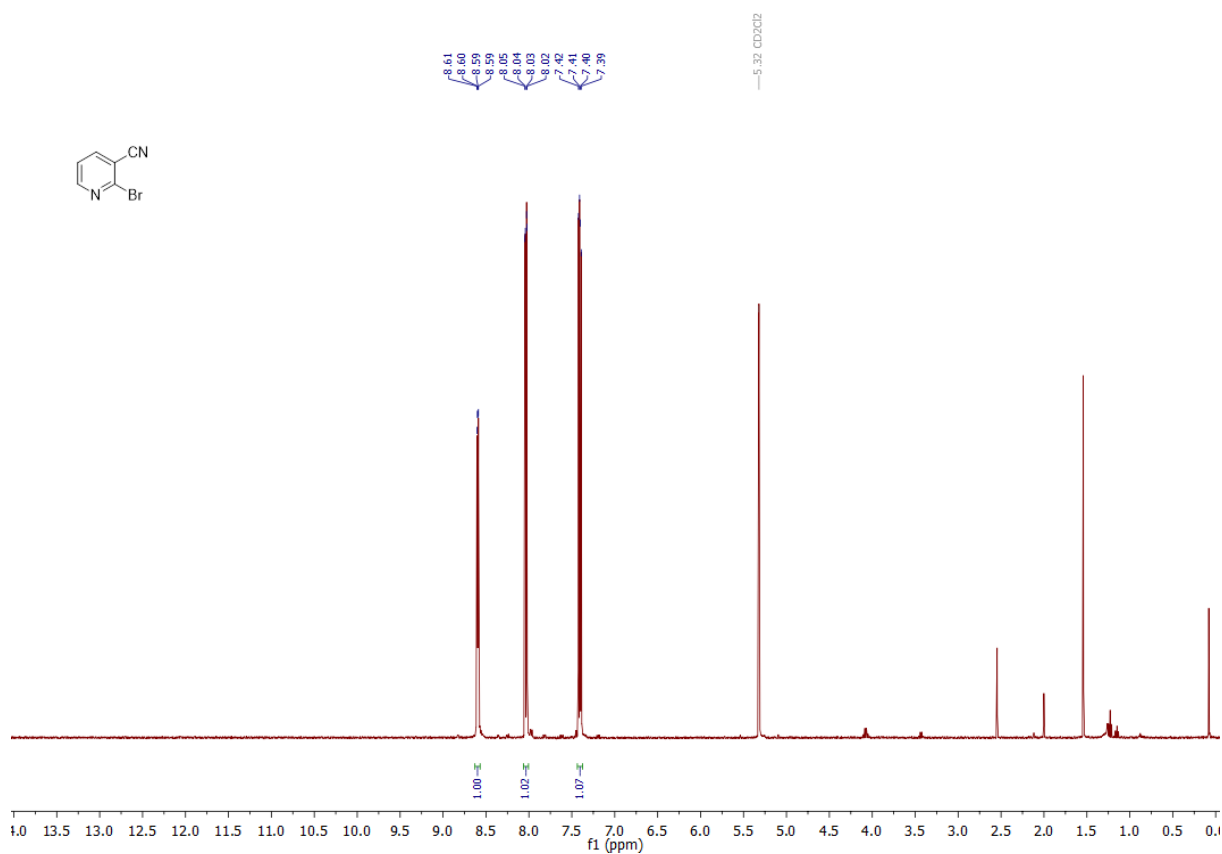
^1H NMR spectrum of compound 6d (400 MHz, methylene chloride- d_2)



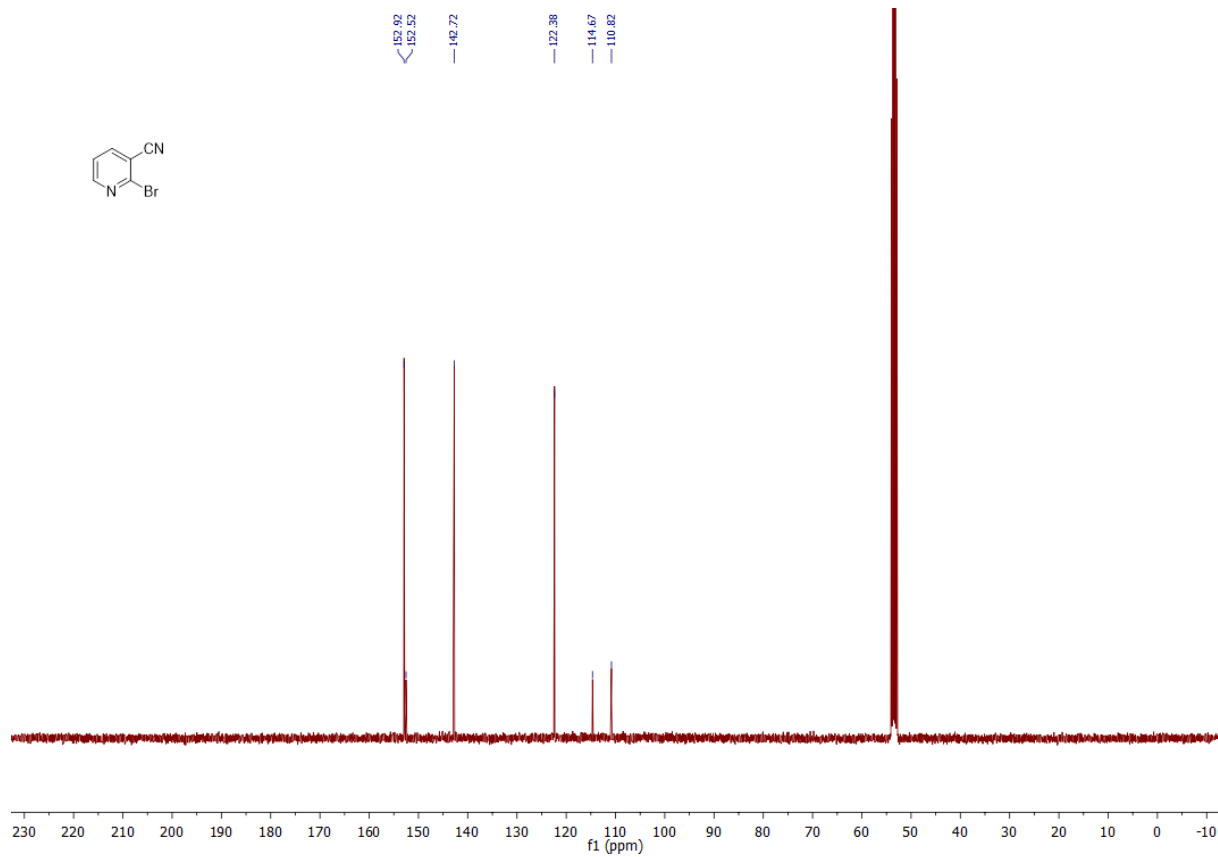
^{13}C NMR spectrum of compound 6d (101 MHz, methylene chloride- d_2)



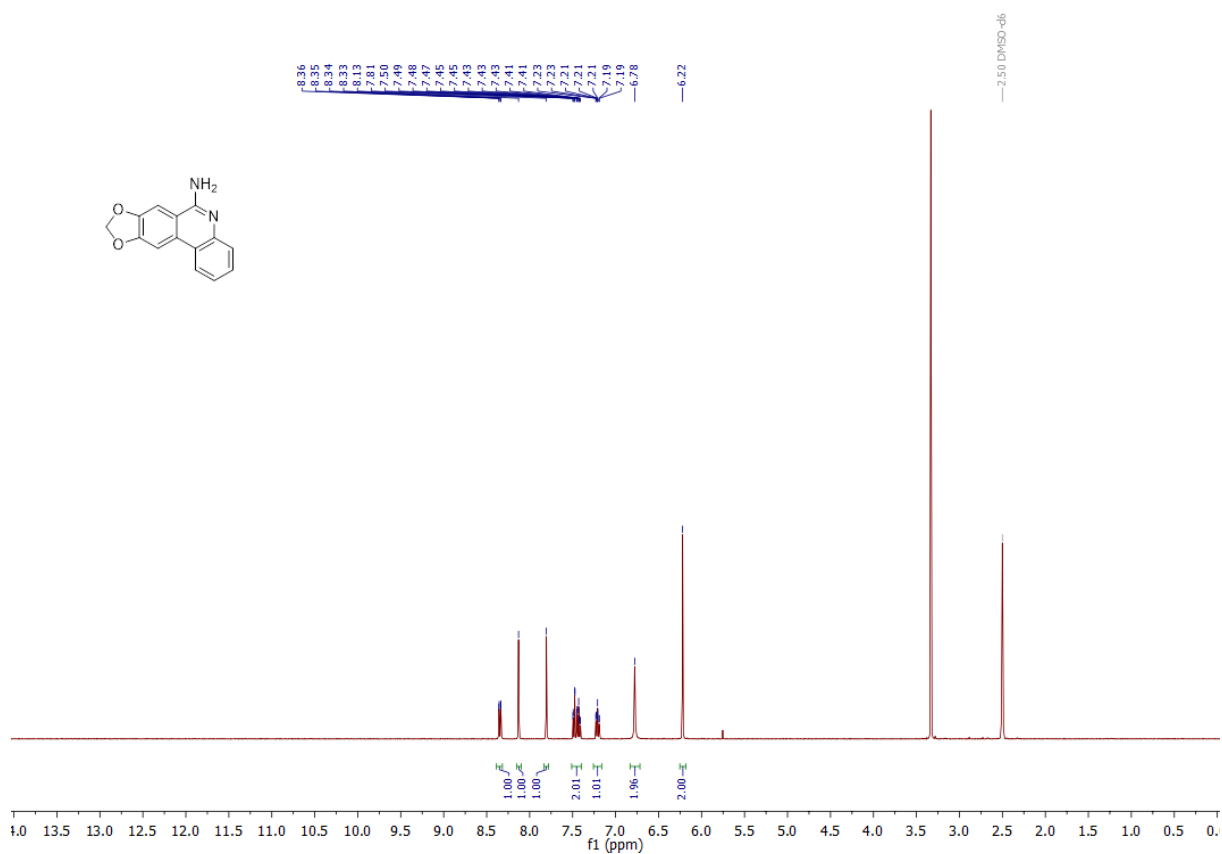
^1H NMR spectrum of compound 6e (400 MHz, methylene chloride- d_2)



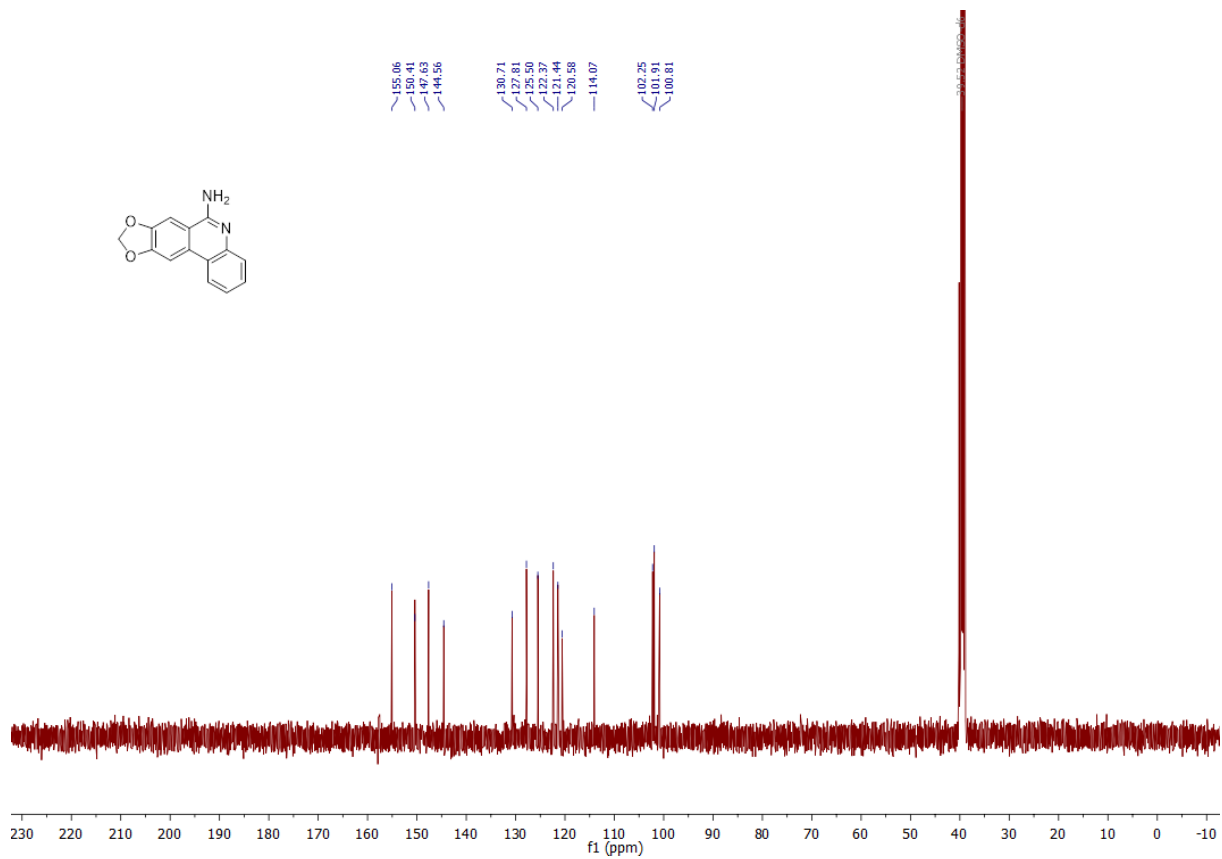
^{13}C NMR spectrum of compound 6e (101 MHz, methylene chloride- d_2)



^1H NMR spectrum of compound 8a (400 MHz, $\text{DMSO}-d_6$)



^{13}C NMR spectrum of compound 8a (101 MHz, $\text{DMSO}-d_6$)



COc1cc(OC)c2cc(N)nc2c1

Chemical structure: COc1cc(OC)c2cc(N)nc2c1

¹H NMR spectrum (ppm):

- 8.30, 8.28, 8.26, 8.24, 7.86, 7.67, 7.65, 7.65, 7.54, 7.53, 7.52, 7.52, 7.50, 7.50, 7.38, 7.38, 7.37, 7.37, 7.35, 7.35, 7.20, 5.32, 5.17, 4.08, 4.00

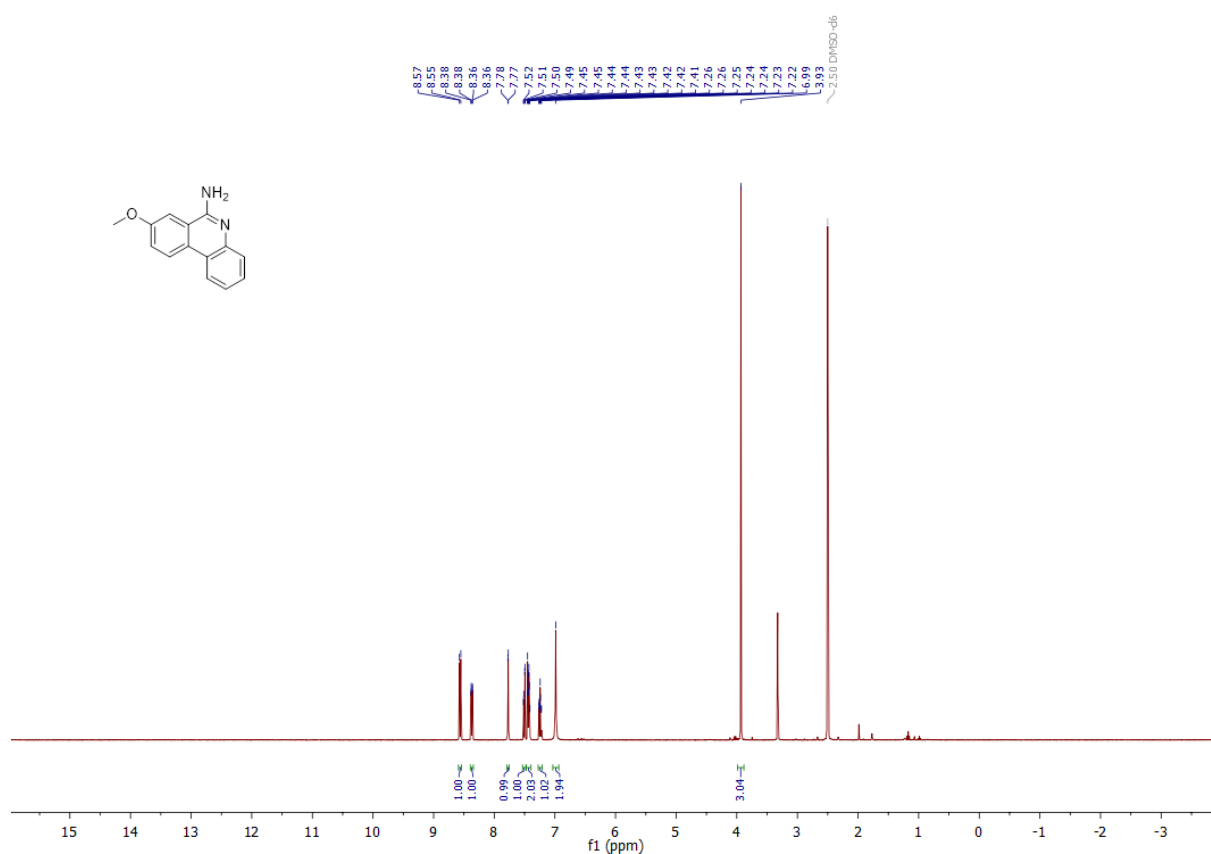
Integration values:

- 1.00, 1.00, 0.97, 0.99, 1.00, 1.94, 3.05, 2.99

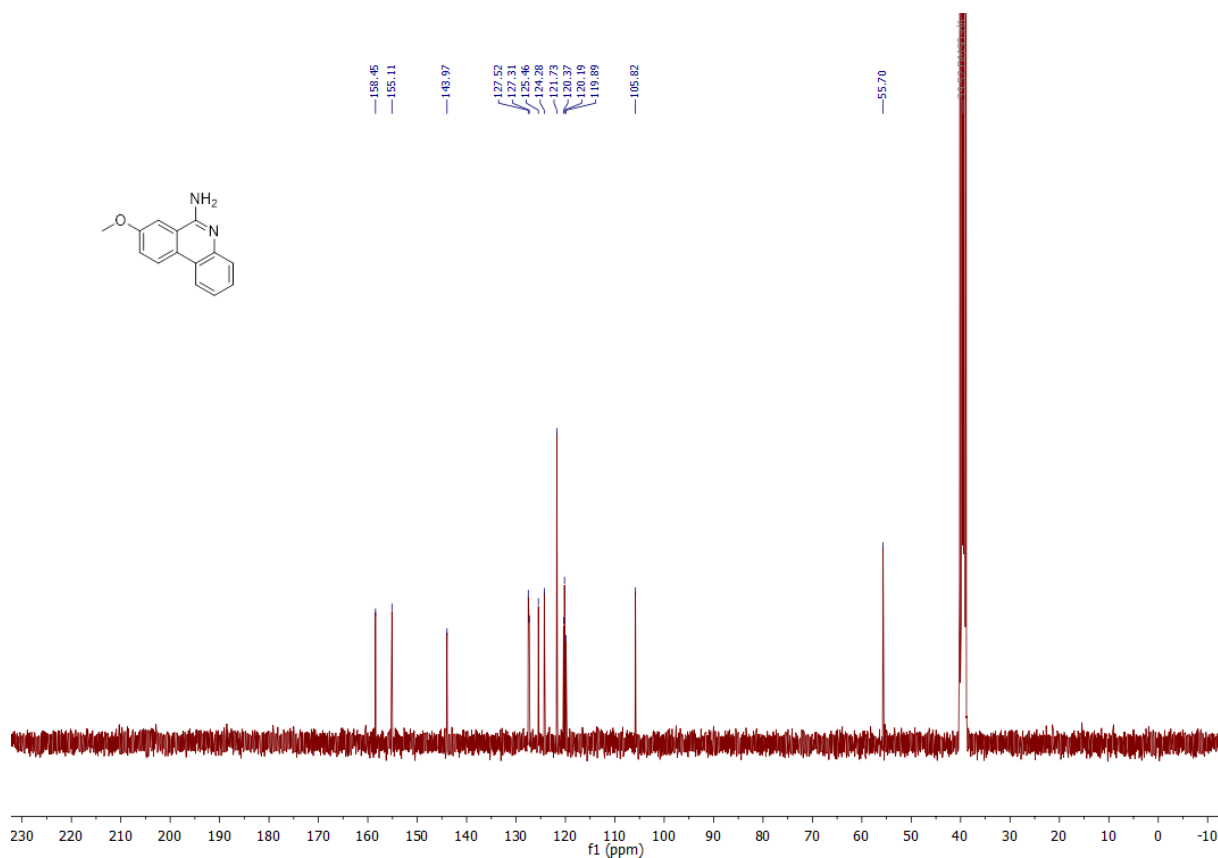
COc1cc(OC)ccc2c1nc(N)c3ccccc23

¹³C NMR spectrum (CDCl₃) of 6,7-dimethoxy-1-aminonaphthalene. The x-axis represents the chemical shift in ppm, ranging from -10 to 230. The spectrum shows several peaks corresponding to the structure, with the following labeled chemical shifts (ppm): 154.57, 153.15, 150.29, 144.57, 130.00, 128.47, 127.00, 123.30, 122.07, 121.89, 113.56, 104.27, 103.57, 56.59, 56.51, and 54.68. A solvent triplet for CDCl₃ is visible around 77 ppm.

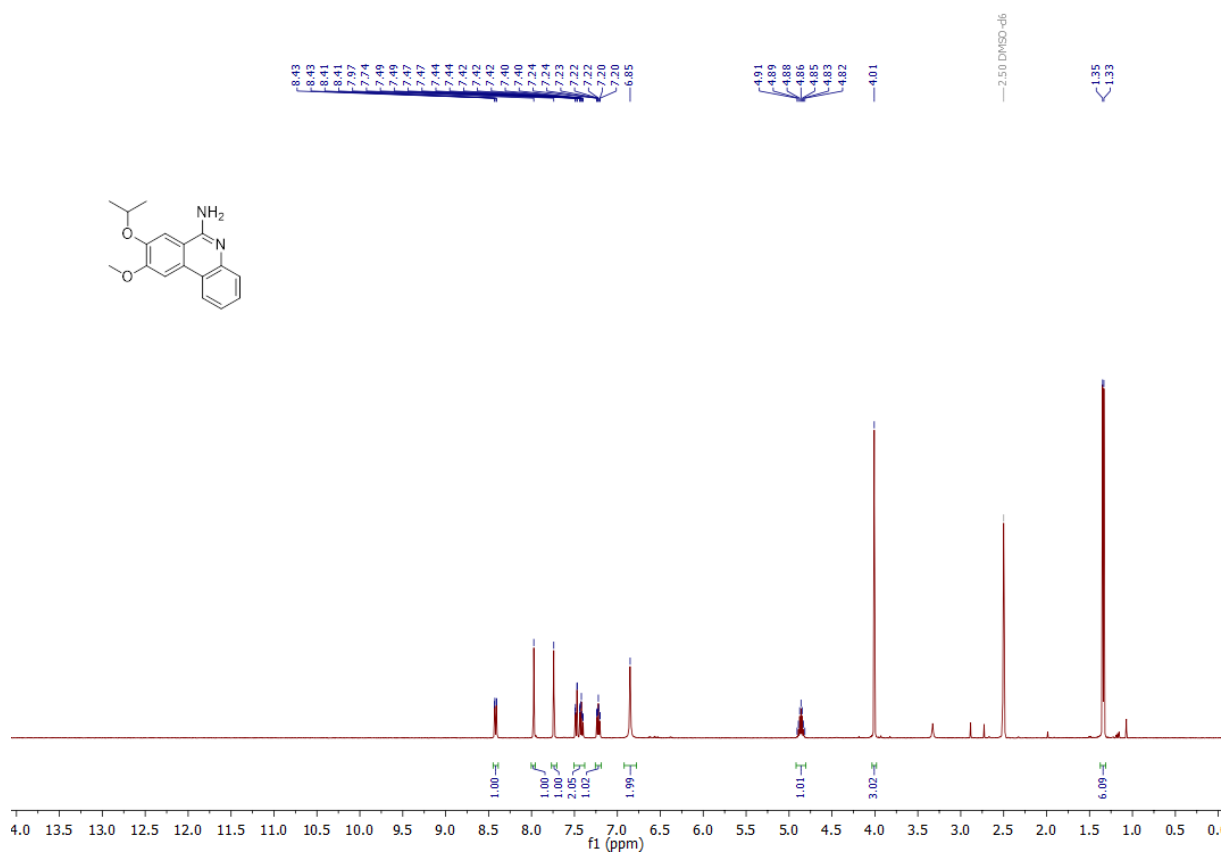
^1H NMR spectrum of compound 8c (400 MHz, DMSO- d_6)



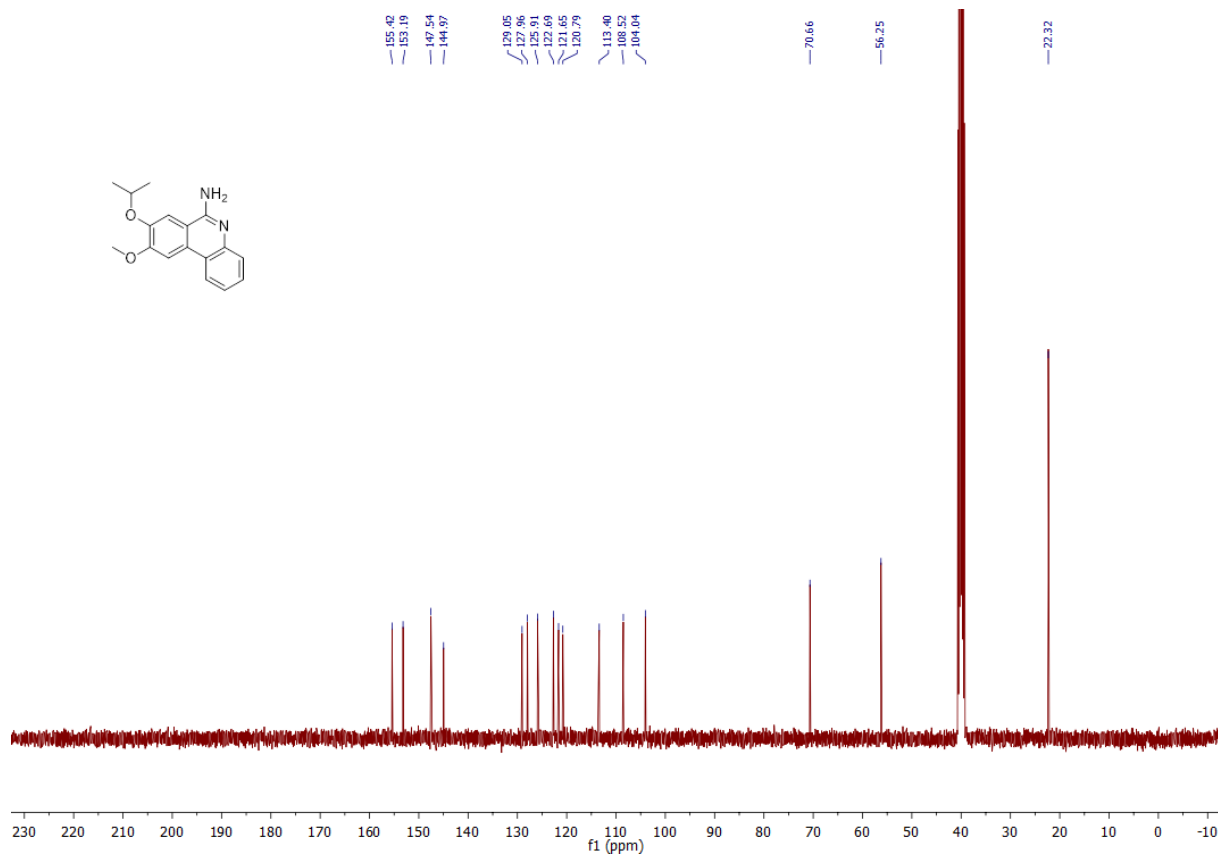
^{13}C NMR spectrum of compound 8c (101 MHz, DMSO- d_6)



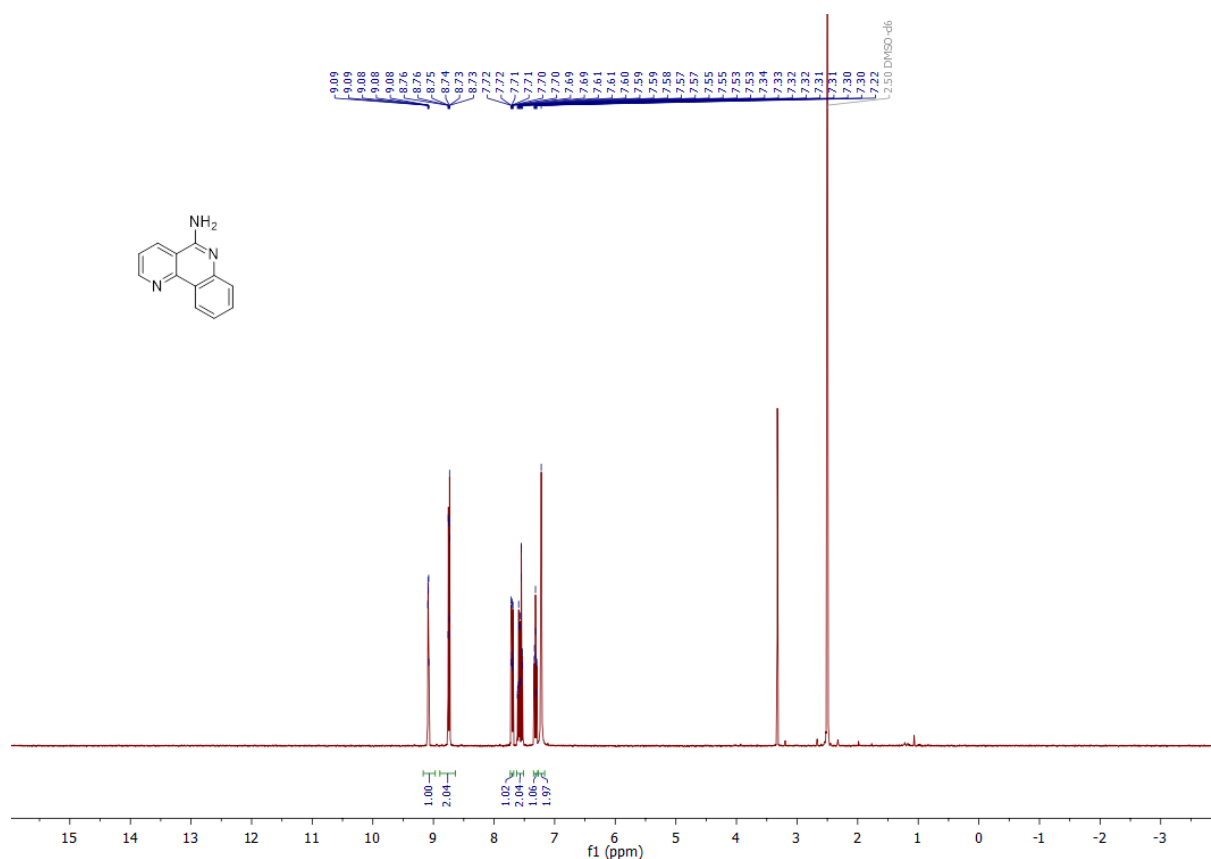
^1H NMR spectrum of compound 8d (400 MHz, DMSO- d_6)



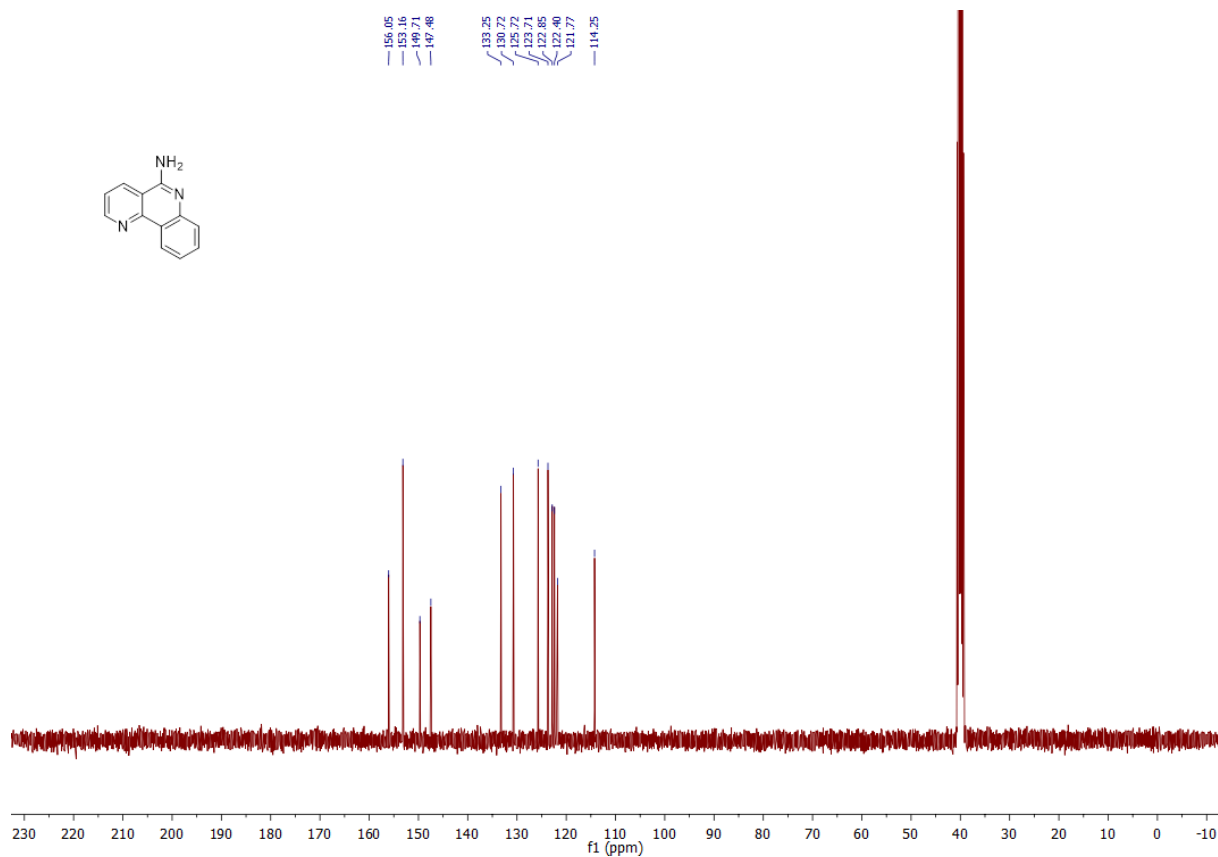
^{13}C NMR spectrum of compound 8d (101 MHz, DMSO- d_6)



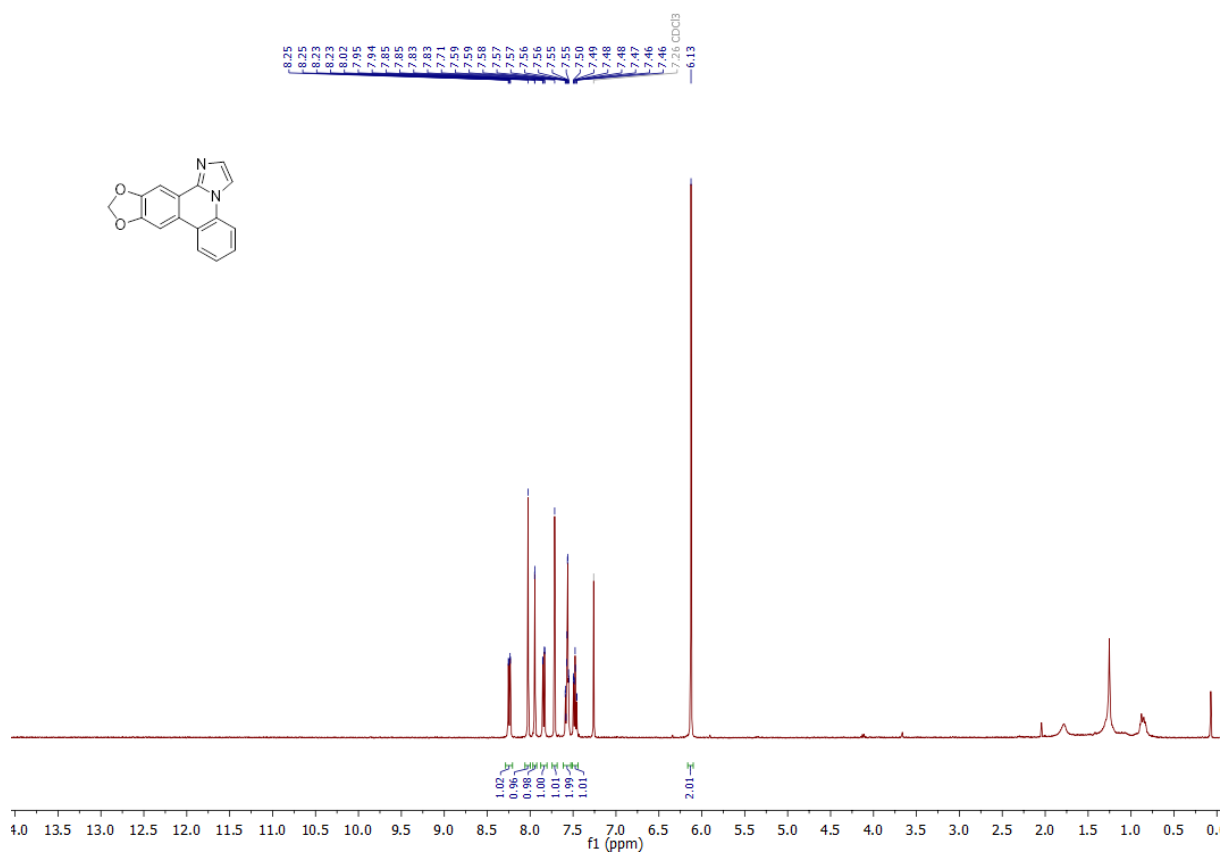
¹H NMR spectrum of compound 8e (400 MHz, DMSO-*d*₆)



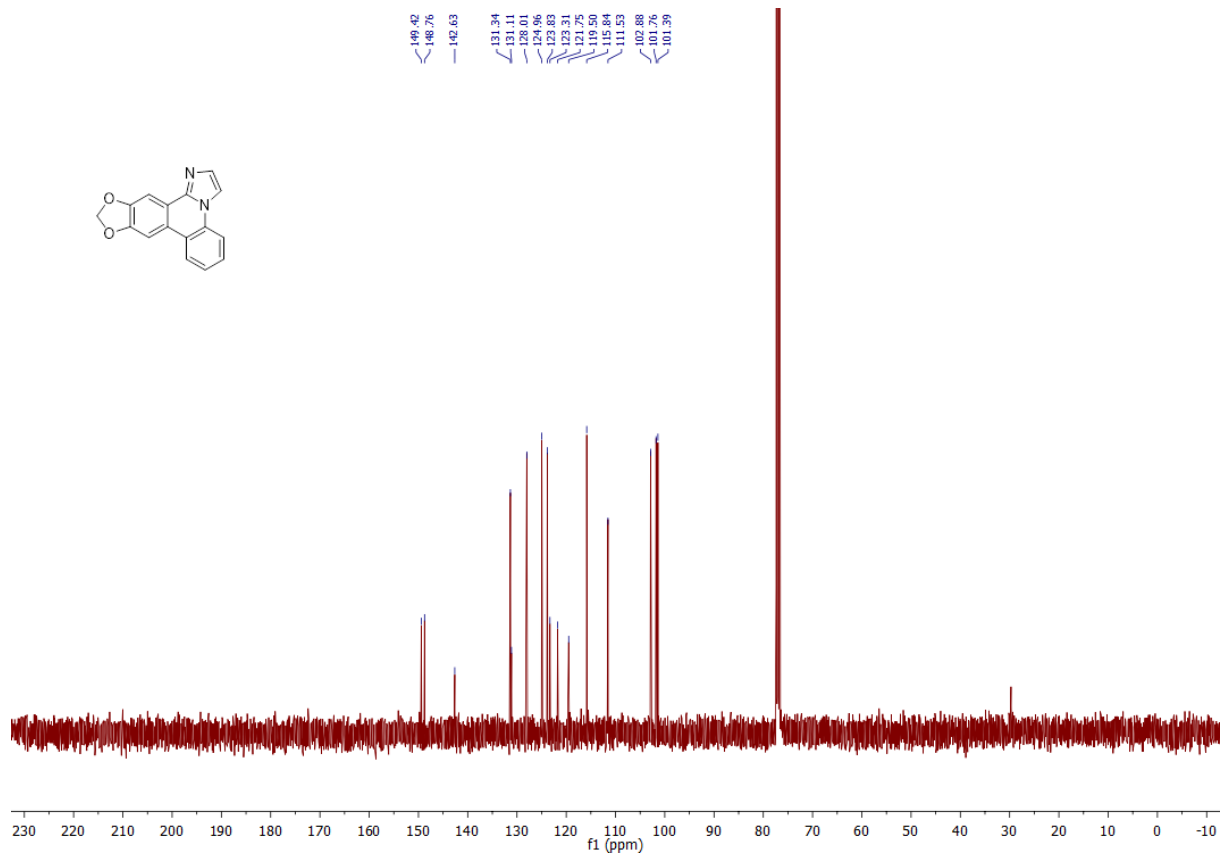
¹³C NMR spectrum of compound 8e (101 MHz, DMSO-*d*₆)



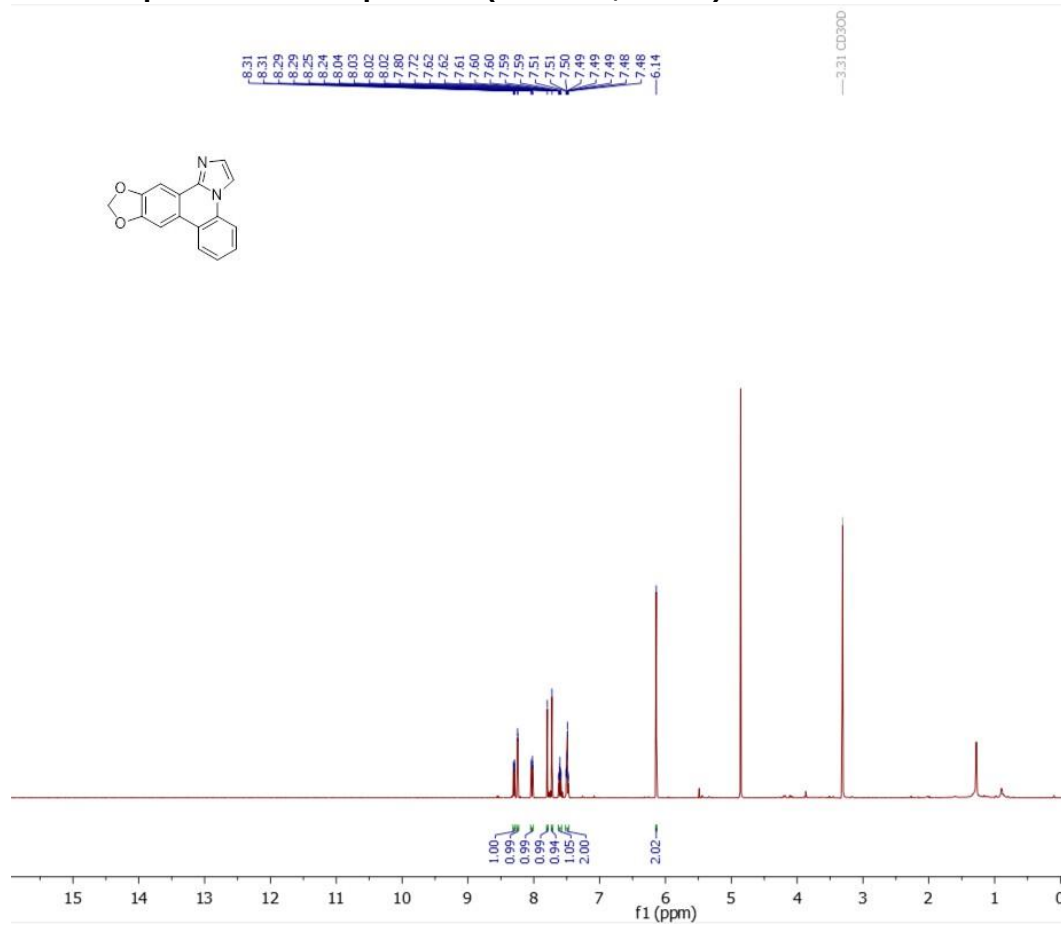
¹H NMR spectrum of compound 3 (400 MHz, CDCl₃)



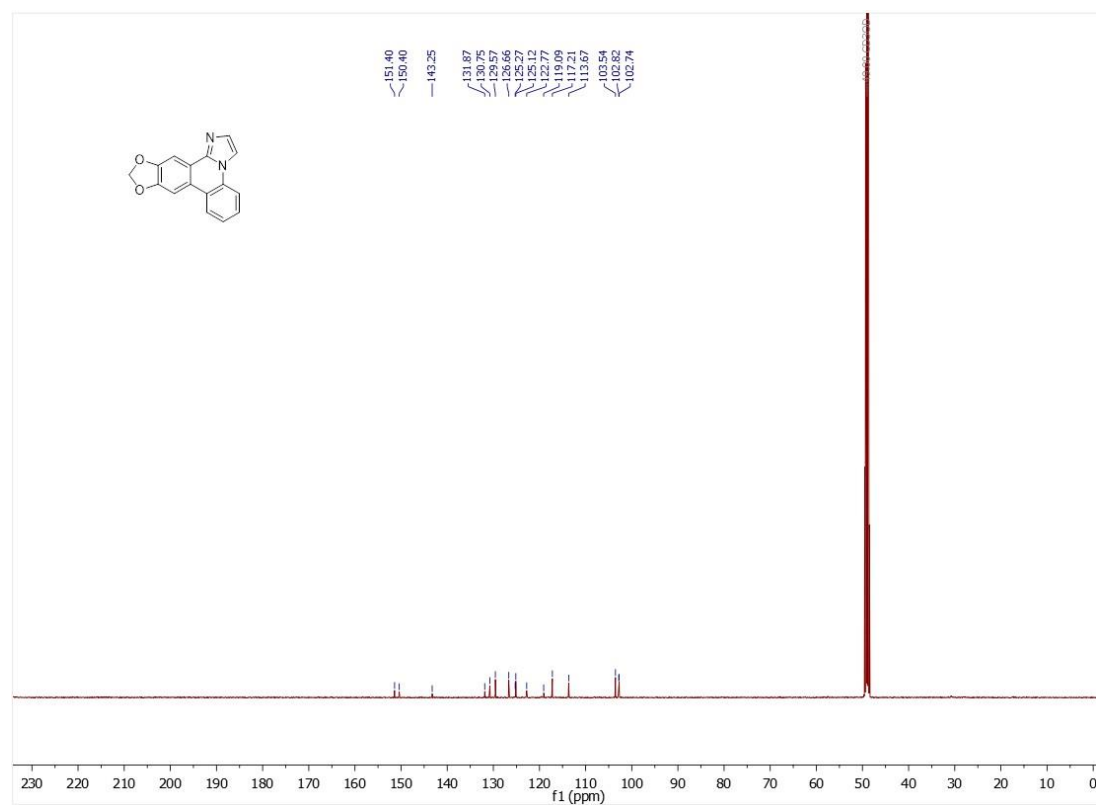
¹³C NMR spectrum of compound 3 (101 MHz, CDCl₃)



¹H NMR spectrum of compound 3 (400 MHz, MeOD)



¹³C NMR spectrum of compound 3 (101 MHz, MeOD)



COc1cc2c(c1)c1ccccc1n2C#N

¹H NMR spectrum (CDCl₃) of 6,7-dimethoxy-1H-benzotriazole. The spectrum displays aromatic signals between 7.4 and 8.4 ppm and methoxy singlets at 3.8 ppm. Integration values are shown below the peaks.

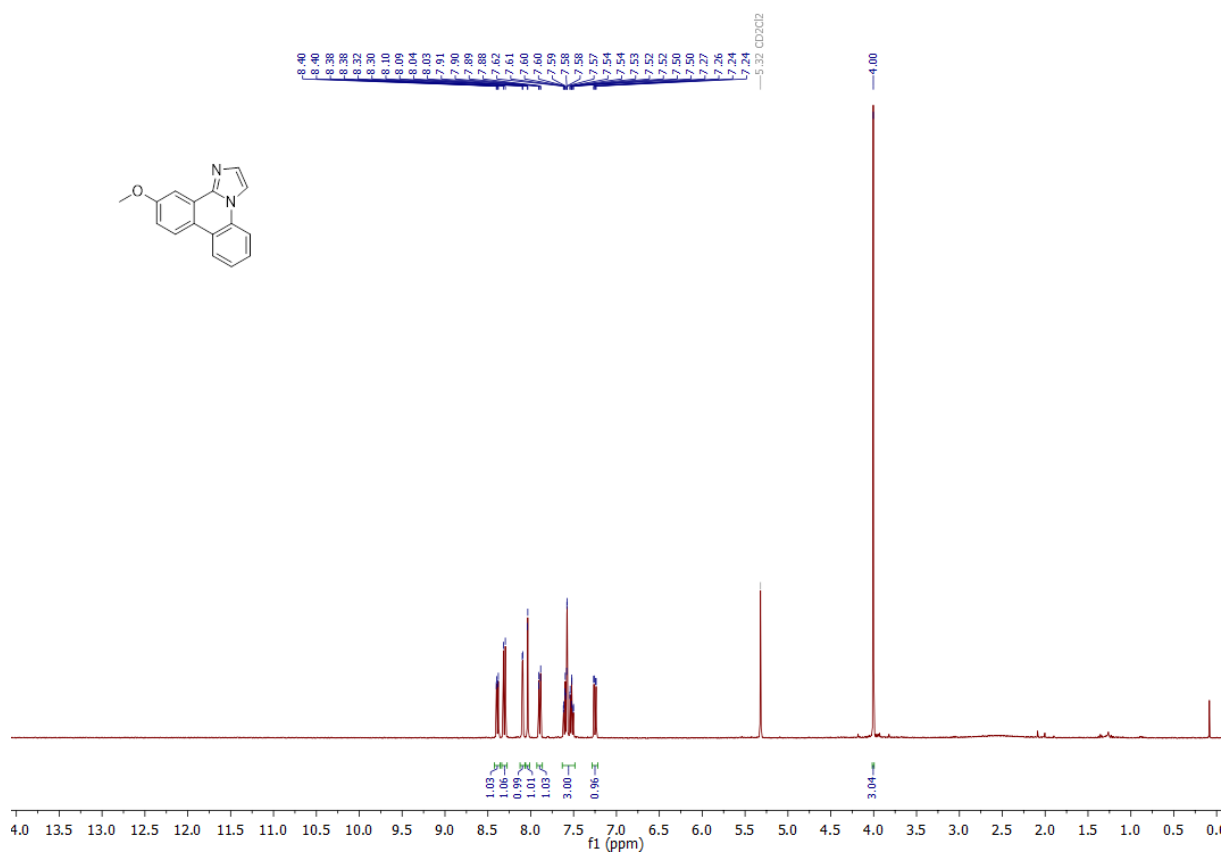
Chemical Shift (ppm)	Integration
8.35, 8.33, 8.32	1.02
8.00	2.00
7.89, 7.88, 7.87, 7.71, 7.61, 7.60, 7.59, 7.58, 7.57, 7.53, 7.51, 7.51, 7.51, 7.49, 7.49	1.02, 1.01, 1.01, 1.94
3.82, 3.81, 3.80, 3.79, 3.78, 3.77, 3.76, 3.75, 3.74, 3.73, 3.72, 3.71, 3.70, 3.69, 3.68, 3.67, 3.66, 3.65, 3.64, 3.63, 3.62, 3.61, 3.60, 3.59, 3.58, 3.57, 3.56, 3.55, 3.54, 3.53, 3.52, 3.51, 3.50, 3.49, 3.48, 3.47, 3.46, 3.45, 3.44, 3.43, 3.42, 3.41, 3.40, 3.39, 3.38, 3.37, 3.36, 3.35, 3.34, 3.33, 3.32, 3.31, 3.30, 3.29, 3.28, 3.27, 3.26, 3.25, 3.24, 3.23, 3.22, 3.21, 3.20, 3.19, 3.18, 3.17, 3.16, 3.15, 3.14, 3.13, 3.12, 3.11, 3.10, 3.09, 3.08, 3.07, 3.06, 3.05, 3.04, 3.03, 3.02, 3.01, 3.00, 2.99, 2.98, 2.97, 2.96, 2.95, 2.94, 2.93, 2.92, 2.91, 2.90, 2.89, 2.88, 2.87, 2.86, 2.85, 2.84, 2.83, 2.82, 2.81, 2.80, 2.79, 2.78, 2.77, 2.76, 2.75, 2.74, 2.73, 2.72, 2.71, 2.70, 2.69, 2.68, 2.67, 2.66, 2.65, 2.64, 2.63, 2.62, 2.61, 2.60, 2.59, 2.58, 2.57, 2.56, 2.55, 2.54, 2.53, 2.52, 2.51, 2.50, 2.49, 2.48, 2.47, 2.46, 2.45, 2.44, 2.43, 2.42, 2.41, 2.40, 2.39, 2.38, 2.37, 2.36, 2.35, 2.34, 2.33, 2.32, 2.31, 2.30, 2.29, 2.28, 2.27, 2.26, 2.25, 2.24, 2.23, 2.22, 2.21, 2.20, 2.19, 2.18, 2.17, 2.16, 2.15, 2.14, 2.13, 2.12, 2.11, 2.10, 2.09, 2.08, 2.07, 2.06, 2.05, 2.04, 2.03, 2.02, 2.01, 2.00, 1.99, 1.98, 1.97, 1.96, 1.95, 1.94, 1.93, 1.92, 1.91, 1.90, 1.89, 1.88, 1.87, 1.86, 1.85, 1.84, 1.83, 1.82, 1.81, 1.80, 1.79, 1.78, 1.77, 1.76, 1.75, 1.74, 1.73, 1.72, 1.71, 1.70, 1.69, 1.68, 1.67, 1.66, 1.65, 1.64, 1.63, 1.62, 1.61, 1.60, 1.59, 1.58, 1.57, 1.56, 1.55, 1.54, 1.53, 1.52, 1.51, 1.50, 1.49, 1.48, 1.47, 1.46, 1.45, 1.44, 1.43, 1.42, 1.41, 1.40, 1.39, 1.38, 1.37, 1.36, 1.35, 1.34, 1.33, 1.32, 1.31, 1.30, 1.29, 1.28, 1.27, 1.26, 1.25, 1.24, 1.23, 1.22, 1.21, 1.20, 1.19, 1.18, 1.17, 1.16, 1.15, 1.14, 1.13, 1.12, 1.11, 1.10, 1.09, 1.08, 1.07, 1.06, 1.05, 1.04, 1.03, 1.02, 1.01, 1.00, 0.99, 0.98, 0.97, 0.96, 0.95, 0.94, 0.93, 0.92, 0.91, 0.90, 0.89, 0.88, 0.87, 0.86, 0.85, 0.84, 0.83, 0.82, 0.81, 0.80, 0.79, 0.78, 0.77, 0.76, 0.75, 0.74, 0.73, 0.72, 0.71, 0.70, 0.69, 0.68, 0.67, 0.66, 0.65, 0.64, 0.63, 0.62, 0.61, 0.60, 0.59, 0.58, 0.57, 0.56, 0.55, 0.54, 0.53, 0.52, 0.51, 0.50, 0.49, 0.48, 0.47, 0.46, 0.45, 0.44, 0.43, 0.42, 0.41, 0.40, 0.39, 0.38, 0.37, 0.36, 0.35, 0.34, 0.33, 0.32, 0.31, 0.30, 0.29, 0.28, 0.27, 0.26, 0.25, 0.24, 0.23, 0.22, 0.21, 0.20, 0.19, 0.18, 0.17, 0.16, 0.15, 0.14, 0.13, 0.12, 0.11, 0.10, 0.09, 0.08, 0.07, 0.06, 0.05, 0.04, 0.03, 0.02, 0.01, 0.00	6.04

Chemical structure: COC1=CC=C2C(=C1)N=CN=C2

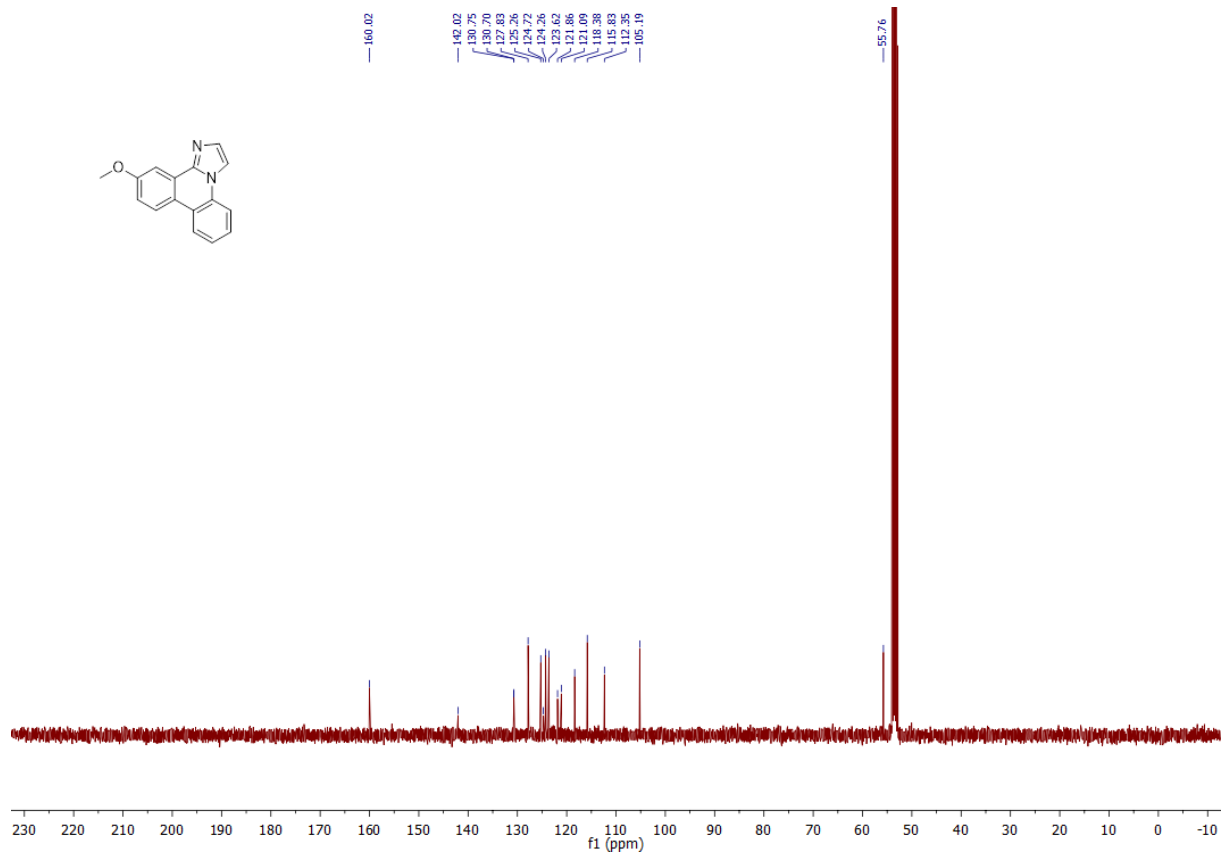
¹³C NMR spectrum (DMSO-d₆) peaks (ppm):

Peak (ppm)
151.22
151.20
142.94
131.84
131.59
128.36
125.36
124.15
122.22
121.99
118.61
116.48
112.23
105.40
104.50
56.64
56.53
50.00

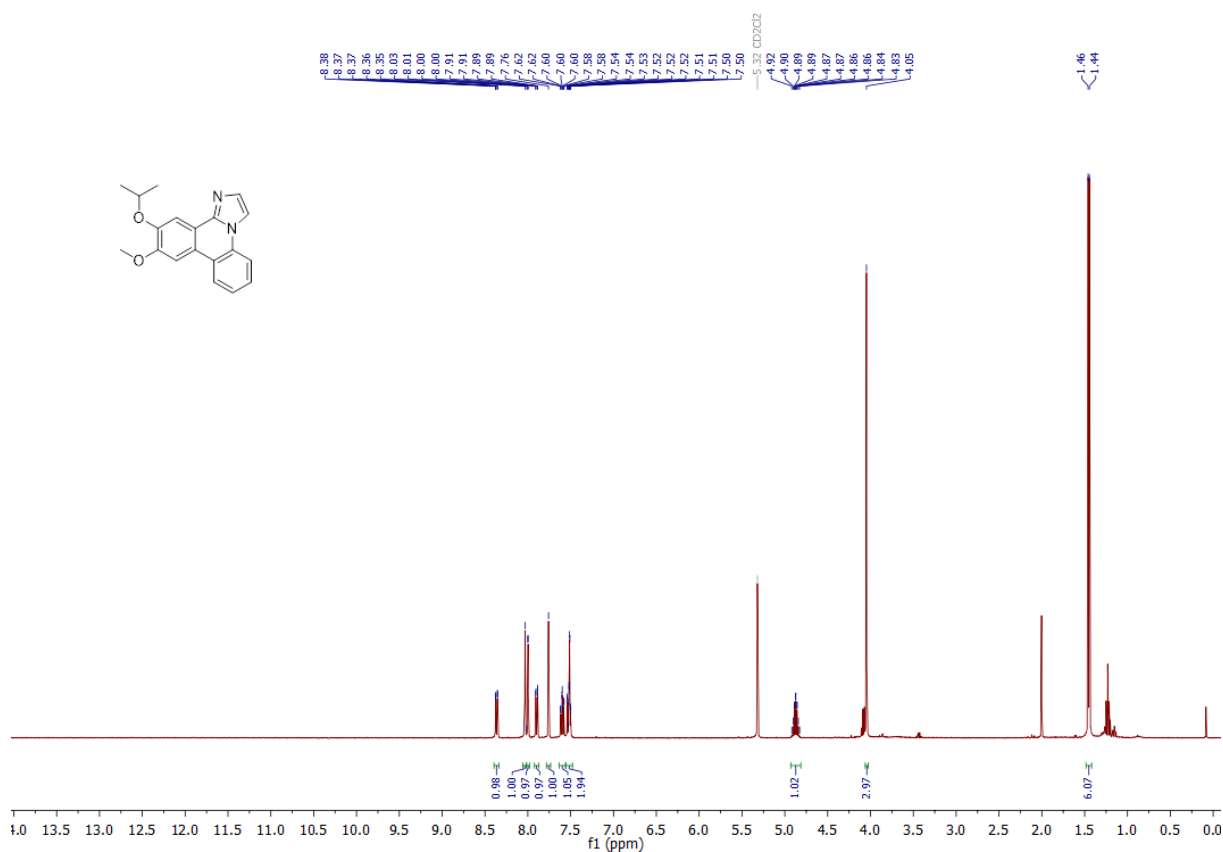
^1H NMR spectrum of compound 10 (400 MHz, methylene chloride- d_2)



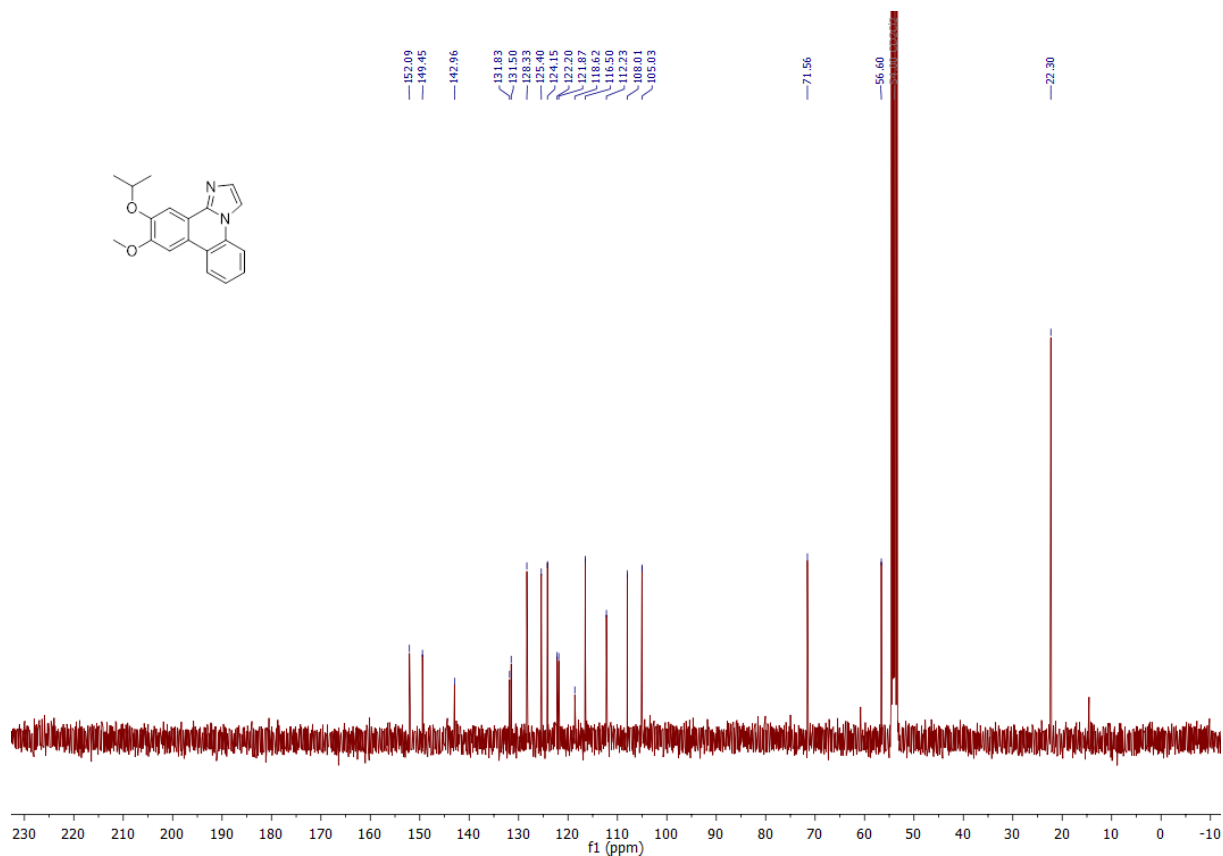
^{13}C NMR spectrum of compound 10 (101 MHz, methylene chloride- d_2)



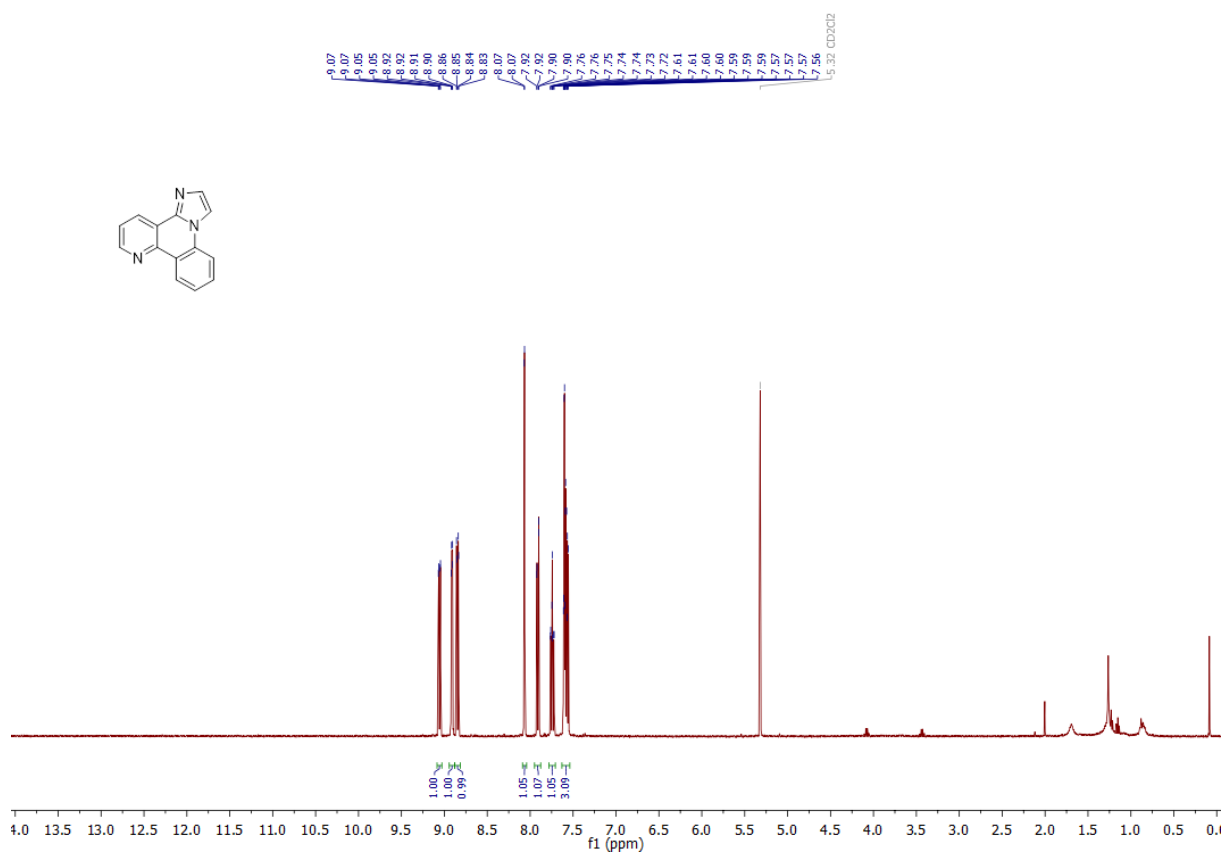
^1H NMR spectrum of compound 11 (400 MHz, methylene chloride- d_2)



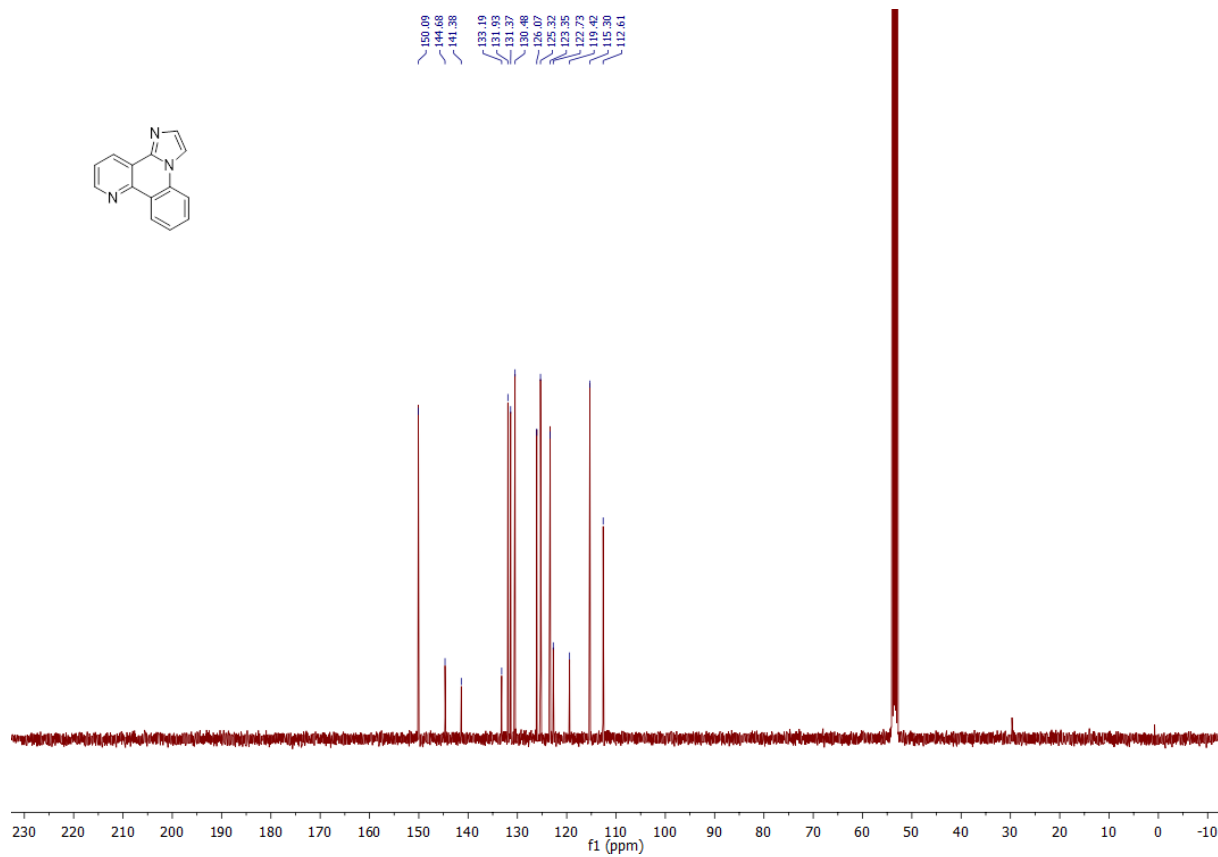
^{13}C NMR spectrum of compound 11 (101 MHz, methylene chloride- d_2)



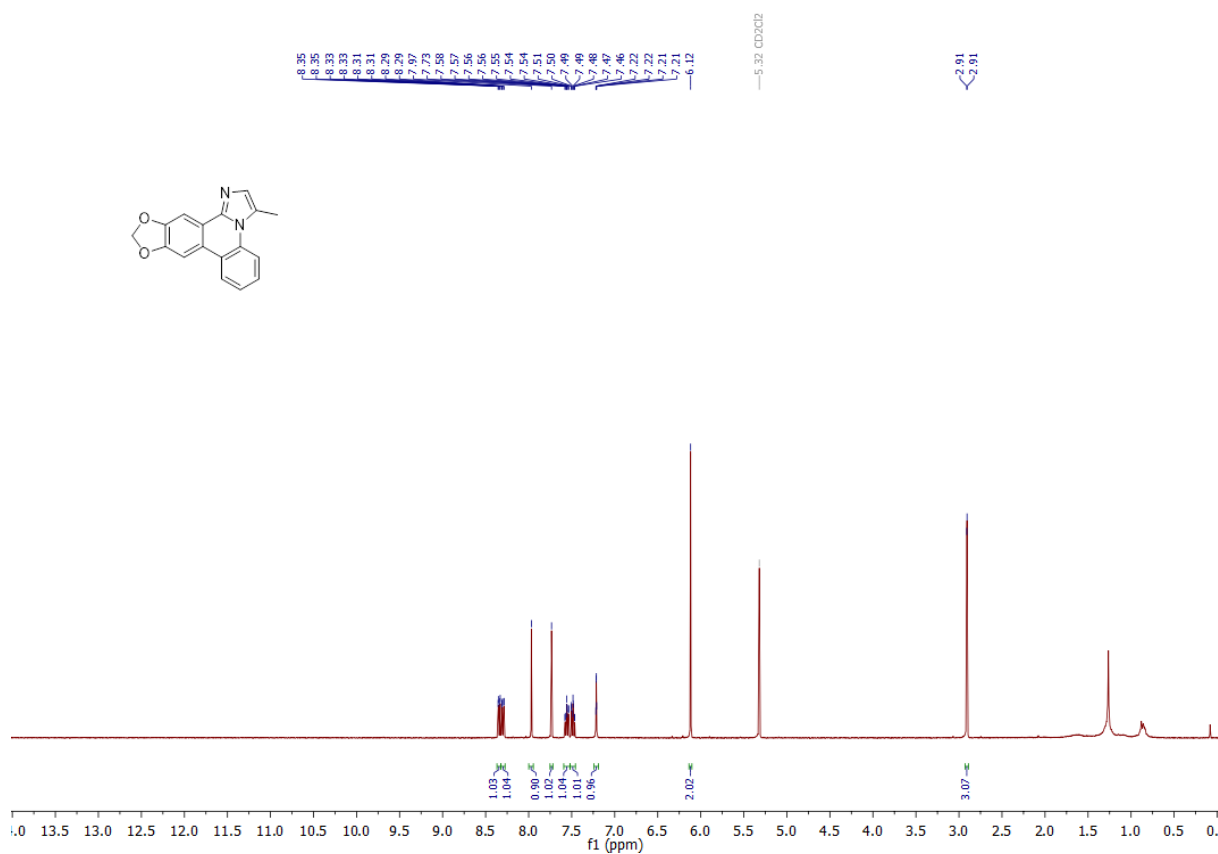
¹H NMR spectrum of compound 12 (400 MHz, methylene chloride-d₂)



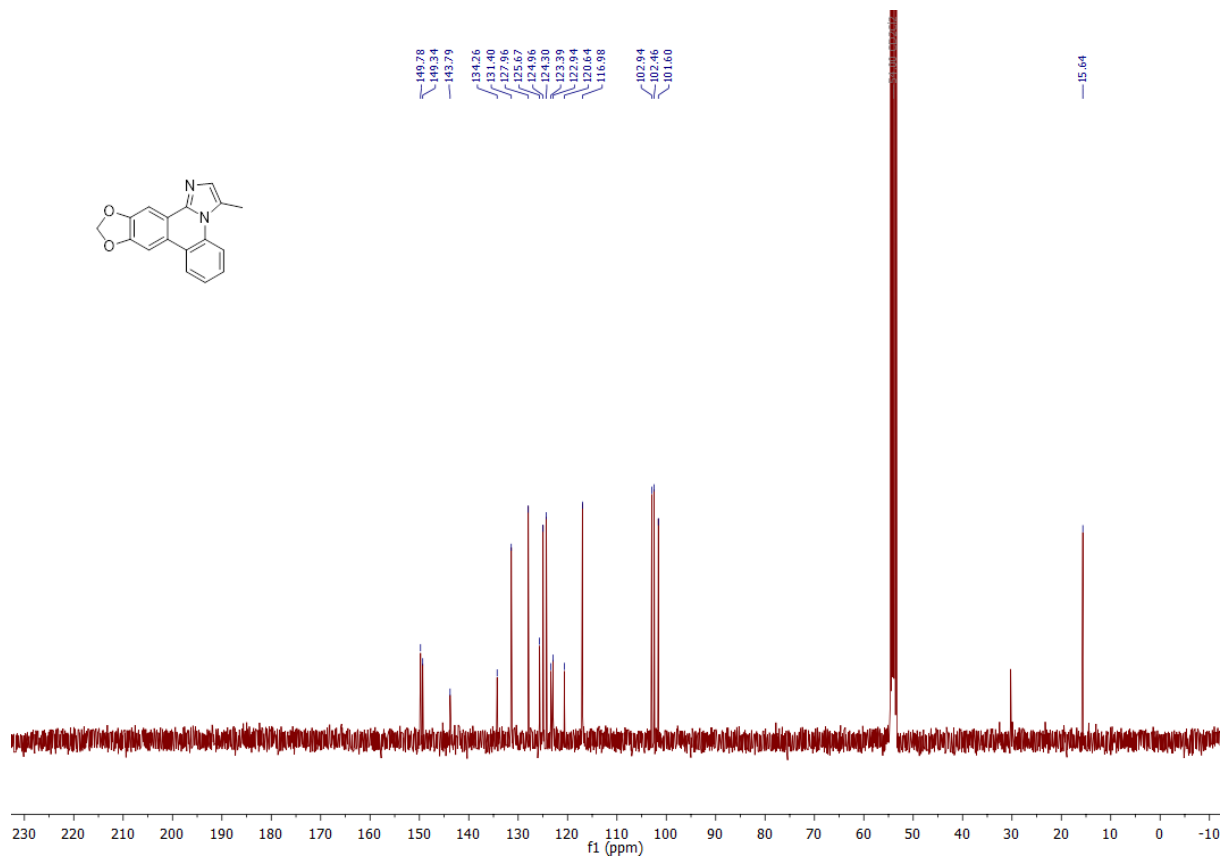
¹³C NMR spectrum of compound 12 (101 MHz, methylene chloride-d₂)



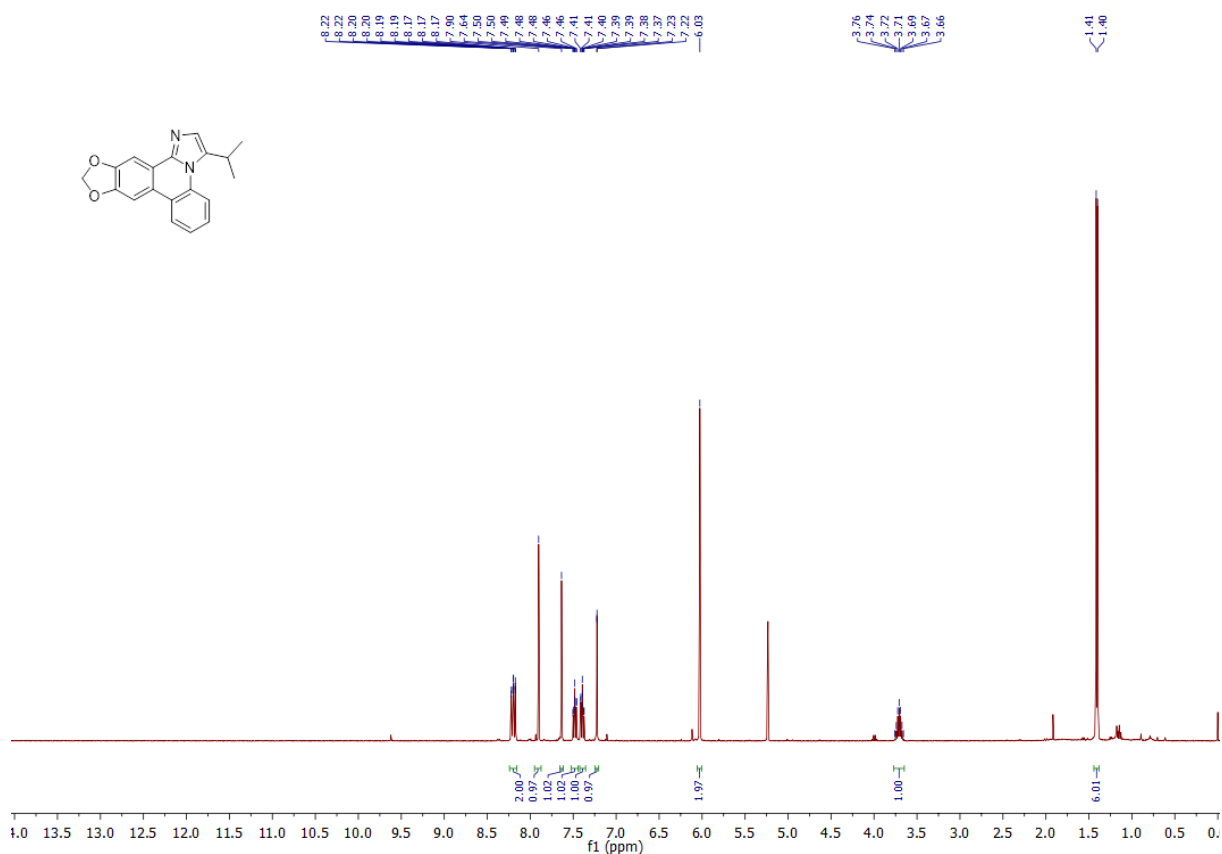
^1H NMR spectrum of compound 13 (400 MHz, methylene chloride- d_2)



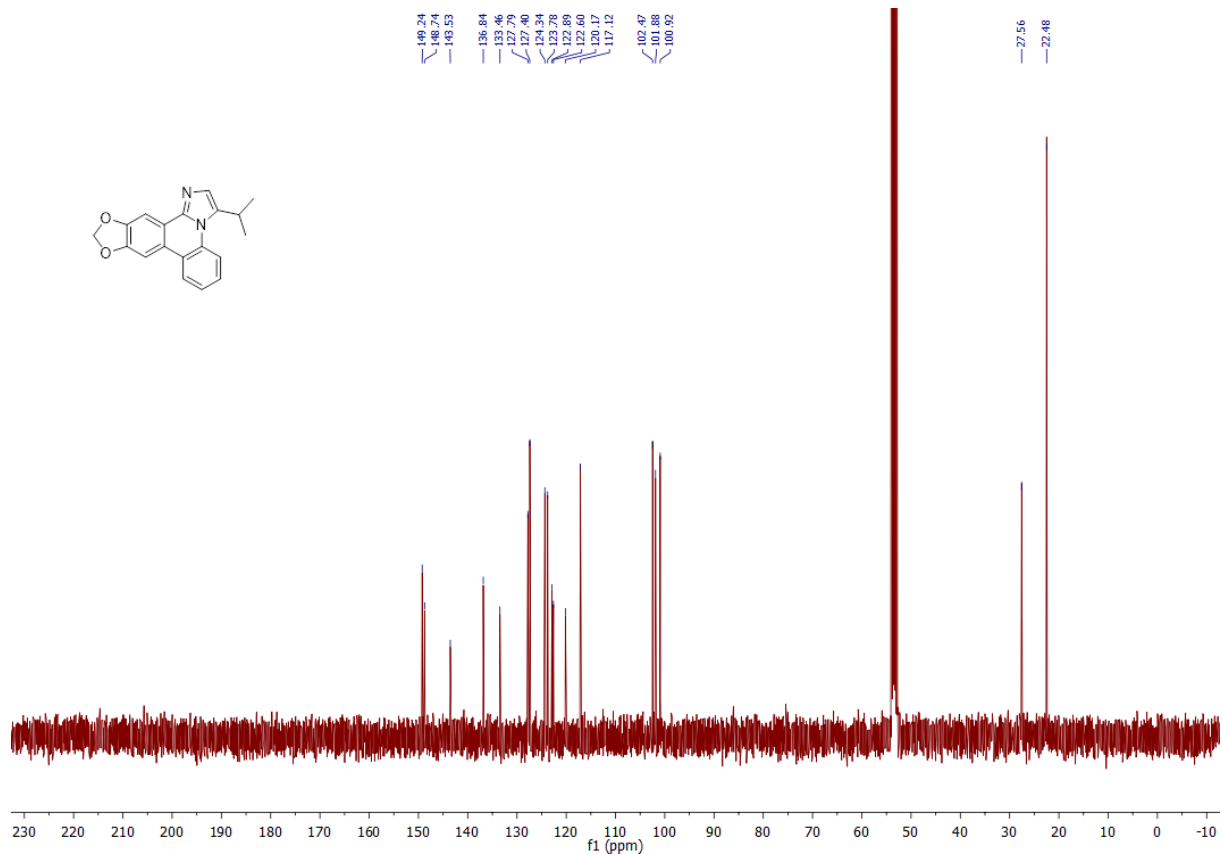
^{13}C NMR spectrum of compound 13 (101 MHz, methylene chloride- d_2)



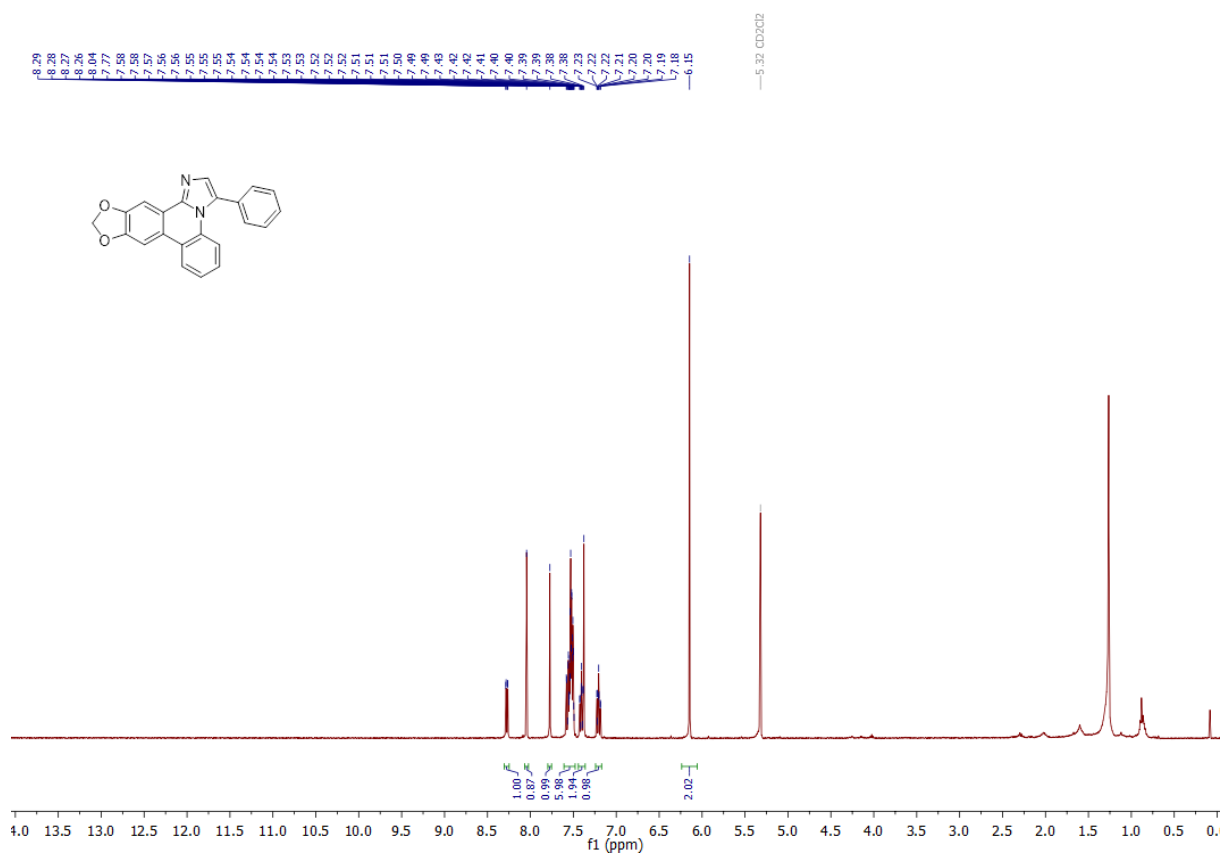
^1H NMR spectrum of compound 14 (400 MHz, methylene chloride- d_2)



^{13}C NMR spectrum of compound 14 (101 MHz, methylene chloride- d_2)



¹H NMR spectrum of compound 15 (400 MHz, methylene chloride-d₂)



¹³C NMR spectrum of compound 15 (101 MHz, methylene chloride-d₂)

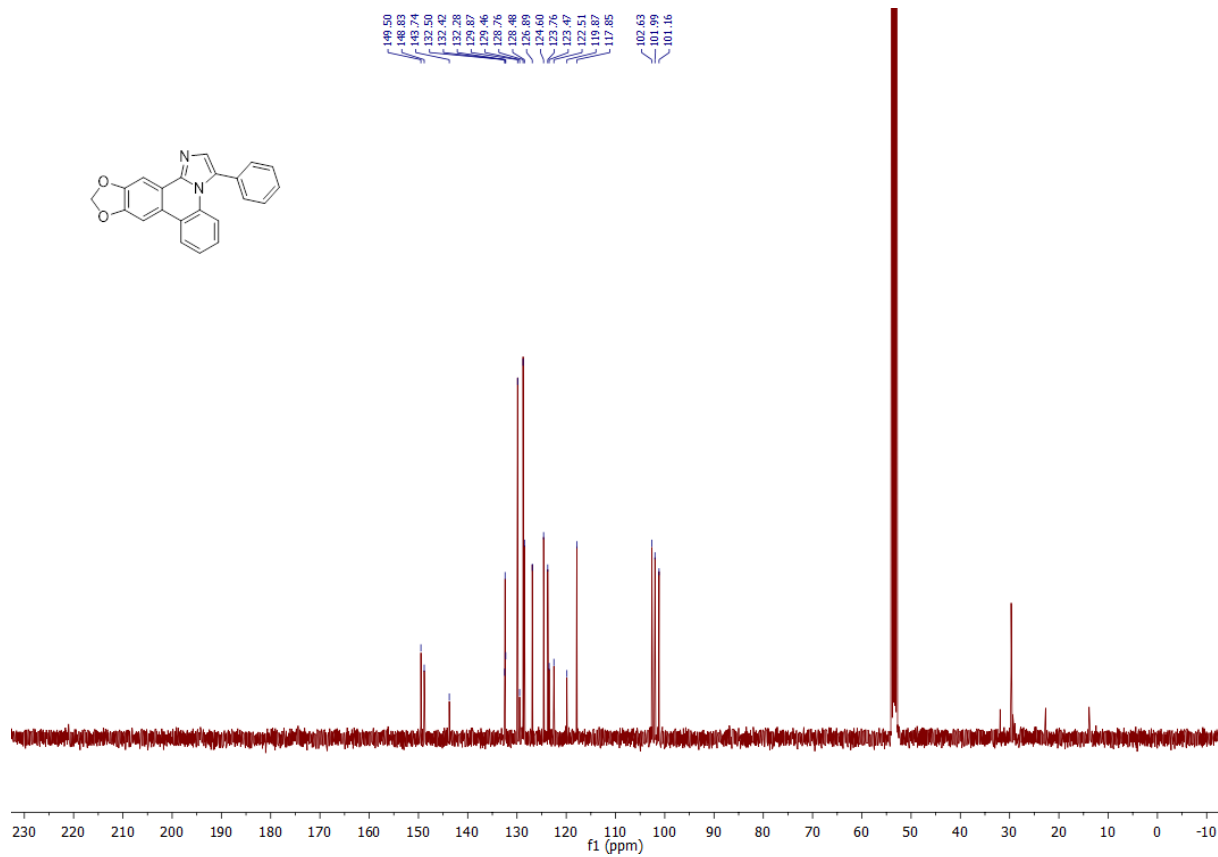


Table S1: List of IC₅₀ values

Compound #	IC₅₀ (Jurkat) [μM]	IC₅₀ (MCF7) [μM]	IC₅₀ (HL-60) [μM]	IC₅₀ (CEM) [μM]	IC₅₀ (HUVEC) [μM]
Zephycandidine A	11.7	145	n.a.	19.5	50.4
15	26.8	79.4	/	/	/
14	19.3	58.8	/	/	/
13	9.6	32.7	27.3	12.6	72.6
12	41.06	69.4	55.8	51.3	56.6
11	11.8	33.7	14.2	10.3	67.1
10	28.2	120	/	/	/
9	13.4	47.5	/	/	/

n.a. = no activity; / = not tested