

-Supporting Information-

8-Aminoimidazo[1,2-*a*]pyridine (AIP) Directed Pd(II) Catalysis: Site-Selective *Ortho*-C(sp²)-H Arylation in Aqueous Medium

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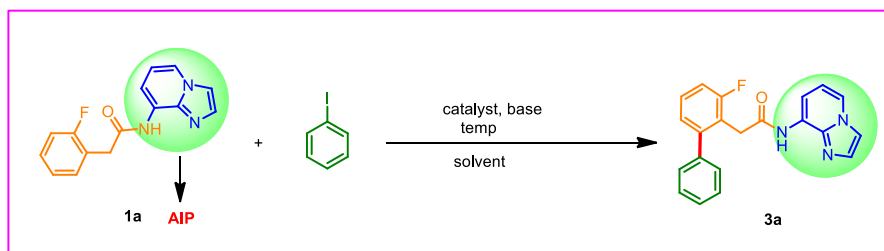
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Experimental

General Considerations:

Unless stated otherwise, all reagents such as various iodobenzene, carboxylic acids, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, imidazo[1,2-*a*]pyridine-8-amine and solvents were used as received from commercial suppliers. NMR spectra were recorded on 400 MHz spectrometer at 298 K with calibration done on the basis of solvent residual peak. Products were purified using Combiflash column chromatography on silica gel (230-400 mesh). Ethyl acetate and hexane were used as eluents. Progress of reaction was monitored using silica gel TLC.

Optimization studies



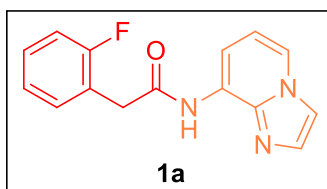
entry	catalyst (mol%)	base (equiv)	temp (°C)	time (h)	yield (%) ^b
1.	Pd(OAc) ₂ (20)	K ₂ CO ₃ (2.5)	140	24	65
2.	Pd(OAc) ₂ (20)	K ₂ CO ₃ (2.5)	120	15	70
3.	Pd(OAc)₂ (15)	K₂CO₃ (2.5)	120	15	71
4.	Pd(OAc) ₂ (10)	K ₂ CO ₃ (2.5)	120	24	65
5.	Pd(OAc) ₂ (5)	K ₂ CO ₃ (2.5)	120	15	34
6.	Pd(PPh ₃) ₄ (15)	K ₂ CO ₃ (2.5)	120	15	38
7.	PdCl ₂ (15)	K ₂ CO ₃ (2.5)	120	15	46
8.	Cu(OAc) ₂ (15)	K ₂ CO ₃ (2.5)	120	15	NR
9.	Ni(OAc) ₂ (15)	K ₂ CO ₃ (2.5)	120	15	NR
10.	Pd(OAc) ₂ (15)	Cs ₂ CO ₃ (2.5)	120	15	54
11.	Pd(OAc) ₂ (15)	AgOAc (2.5)	120	15	52
12.	Pd(OAc) ₂ (15)	Ag ₂ CO ₃ (2.5)	120	15	43
13.	Pd(OAc) ₂ (15)	K ₂ CO ₃ (2.5)	100	15	36
14.	Pd(OAc) ₂ (15)	K ₂ CO ₃ (2.5)	120	8	37
15.	-	K ₂ CO ₃ (2.5)	120	15	NR
16	Pd(OAc) ₂ (15)	-	120	15	NR
17 ^c .	Pd(OAc) ₂ (15)	K ₂ CO ₃ (2.5)	120	15	56
18.	Pd(OAc) ₂ (15)	K ₂ CO ₃ (1.5)	120	15	47
19.	Pd(OAc) ₂ (15)	K ₂ CO ₃ (3)	120	15	54
20 ^d .	Pd(OAc) ₂ (15)	K ₂ CO ₃ (2.5)	120	15	52
21 ^e .	Pd(OAc) ₂ (15)	K ₂ CO ₃ (2.5)	120	15	65
22.	Pd(OAc) ₂ (15)	K ₂ CO ₃ (2.5)	120	24	68

^aReaction conditions: 2-(2-fluorophenyl)-*N*-(imidazo[1,2-*a*]pyridin-8-yl)-acetamide (0.20 mmol), iodobenzene (2 equiv), water (4 ml), air. ^bIsolated Yields. ^cReaction run under N₂ atmosphere. ^d1.0 equiv PhI was used; ^e3 equiv. PhI was used.

General Experimental Procedure for Preparation of 8-AIP substituted Amides (A):

To the stirred mixture of carboxylic acid (2 mmol, 1 equiv) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (3 mmol, 1.5 equiv) in pyridine (5 ml) at 25° C was added imidazo[1,2-*a*]pyridin-8-amine (2 mmol, 1 equiv) and mixture was stirred at 40° C for 15 h. The reaction mixture was concentrated under reduced pressure and the residue was taken up in ethyl acetate. The organic layer was washed with water, dried over sodium sulphate, filtered and concentrated under reduced pressure. The crude product was purified by Combiflash chromatography using silica gel column by using ethyl acetate/hexane as an eluent.

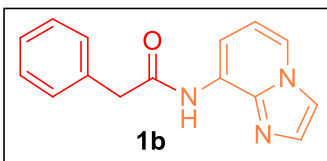
2-(2-fluorophenyl)-*N*-(imidazo[1,2-*a*]pyridin-8-yl)acetamide (1a): Following the general procedure A, **1a** was



obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane) as a off white solid: mp 80–82 °C; yield 91% (490 mg); $R_f = 0.4$ (ethyl acetate/hexane (40/60)); $^1\text{H NMR}$ (400 MHz, DMSO- d_6 , ppm): δ 4.00 (s, 2H), 6.83 (t, $J = 7.1$ Hz, 1H), 7.14-7.20 (m, 2H), 7.29-

7.34 (m, 1H), 7.42 (dt, $J = 7.7$ Hz, 1.4 Hz, 1H), 7.57 (d, $J = 0.7$ Hz, 1H), 7.95 (d, $J = 7.5$ Hz, 1H), 7.97 (d, $J = 0.8$ Hz, 1H), 8.25 (dd, $J = 6.5$ Hz, 0.6 Hz, 1H), 10.18 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, DMSO- d_6 , ppm): δ 36.3, 110.5, 112.1, 114.3, 115.0 ($J_{C-F} = 21.7$ Hz), 121.5, 122.8 ($J_{C-F} = 16.0$ Hz), 124.2 ($J_{C-F} = 2.9$ Hz), 127.2, 128.8 ($J_{C-F} = 7.8$ Hz), 131.6, 131.9 ($J_{C-F} = 4.3$ Hz), 138.6, 160.7 ($J_{C-F} = 242.9$ Hz), 169.3; $^{19}\text{F NMR}$ (400 MHz, DMSO- d_6 , ppm): δ -117.0; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{12}\text{FN}_3\text{ONa}$ 292.0861, found 292.0859.

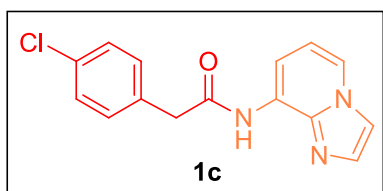
***N*-(imidazo[1,2-*a*]pyridin-8-yl)-2-phenylacetamide (1b):** Following the general procedure A, **1b** was obtained after



purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane) as a off white solid: mp 96–98 °C; yield 81% (407 mg); $R_f = 0.4$ (ethyl acetate/hexane (40/60)); $^1\text{H NMR}$ (400 MHz, DMSO- d_6 , ppm) δ 3.89 (s, 2H), 6.82 (t, $J = 7.1$ Hz, 1H), 7.25-7.39 (m, 5H), 7.56 (s, 1H), 7.94 (d, J

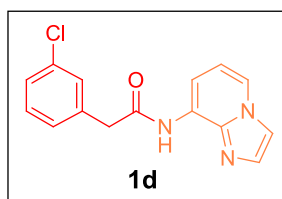
= 7.4 Hz, 1H), 7.97 (s, 1H), 8.25 (d, $J = 6.6$ Hz, 1H), 10.10 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, DMSO- d_6 , ppm) δ 42.8, 110.5, 112.1, 114.3, 121.5, 126.5, 127.2, 128.2, 129.2, 131.5, 135.8, 138.6, 170.4; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{ONa}$ 274.0956, found 274.0949

2-(4-chlorophenyl)-*N*-(imidazo[1,2-*a*]pyridin-8-yl)acetamide (1c): Following the general procedure A, **1c** was



obtained after purification by Combiflash column chromatography using silica gel column (10-30% ethyl acetate/hexane) as a off white solid: mp 88– 90 °C; yield 84% (480 mg); $R_f = 0.3$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.91 (s, 2H), 6.82 (t, $J = 7.1$ Hz, 1H), 7.39 (m, 4H), 7.56 (s, 1H), 7.92 (d, $J = 7.4$ Hz, 1H), 7.97 (s, 1H), 8.25 (d, $J = 6.6$ Hz, 1H), 10.17 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 41.9, 110.6, 112.1, 114.3, 121.6, 127.2, 128.2, 131.1, 131.3, 131.6, 134.8, 138.6, 170.1; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{13}\text{ClN}_3\text{O}$ 286.0747, found 286.0739.

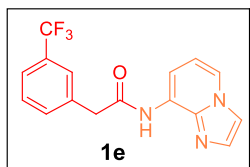
2-(3-chlorophenyl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (1d): Following the general procedure A, **1d** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl



acetate/hexane) as a light grey solid: mp 118– 120 °C; yield 81% (463 mg); $R_f = 0.3$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.92 (s, 2H), 6.83 (t, $J = 7.2$ Hz, 1H), 7.33-7.39 (m, 3H), 7.47 (s, 1H), 7.57 (s, 1H), 7.93 (d, $J = 7.5$ Hz, 1H), 7.98 (s, 1H), 8.26 (d, $J = 6.6$ Hz, 1H), 10.23 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 42.2, 110.7, 112.1, 114.4, 121.6, 126.5, 127.2, 128.0, 129.1, 130.1, 131.6, 132.8, 138.3, 138.6,

169.9; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{12}\text{ClN}_3\text{ONa}$ 308.0566, found 308.0564.

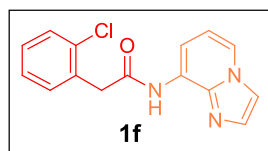
N-(imidazo[1,2-a]pyridin-8-yl)-2-(3-(trifluoromethyl)phenyl)acetamide (1e) : Following the general procedure A, **1e** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl



acetate/hexane) as a light grey solid: mp 106– 108 °C; yield 85% (542 mg); $R_f = 0.3$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 4.03 (s, 2H), 6.83 (t, $J = 7.1$ Hz, 1H), 7.56-7.64 (m, 3H), 7.68 (d, $J = 6.8$ Hz, 1H), 7.77 (s, 1H), 7.93 (d, $J = 7.5$ Hz, 1H), 7.98 (s, 1H), 8.26 (d, $J = 6.7$ Hz, 1H), 10.30 (s, 1H); ^{13}C NMR (100 MHz, DMSO-

d_6 , ppm): δ 42.2, 110.7, 112.1, 114.3, 121.6, 122.8, 123.3 ($J_{\text{C-F}} = 3.7$ Hz), 125.5, 125.8 ($J_{\text{C-F}} = 3.9$ Hz), 127.2, 128.7, 129.0, 129.2, 131.6, 133.4, 137.2, 138.6, 169.9; ^{19}F NMR (376.5 MHz, DMSO- d_6): δ -61.0 (3F); HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{12}\text{F}_3\text{N}_3\text{ONa}$ 342.0829, found 342.0827.

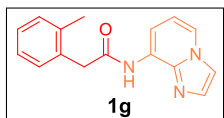
2-(2-chlorophenyl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (1f) : Following the general procedure A, **1f** was obtained after purification by Combiflash column chromatography using silica gel column (10-30% ethyl



acetate/hexane) as a off white solid: mp 106-108 °C; yield 77% (440 mg); $R_f = 0.3$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 4.08 (s, 2H),

6.83 (t, $J = 7.1$ Hz, 1H), 7.31-7.33 (m, 2H), 7.45-7.47 (m, 2H), 7.57 (s, 1H), 7.93 (d, $J = 7.1$ Hz, 1H), 7.98 (s, 1H), 8.26 (d, $J = 6.4$ Hz, 1H), 10.12 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 41.4, 110.9, 112.7, 114.9, 122.0, 127.6, 127.8, 129.1, 129.5, 132.1, 132.7, 134.2, 134.3, 139.1, 169.7; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{12}\text{ClN}_3\text{ONa}$ 308.0566, found 308.0561.

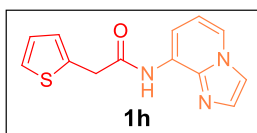
***N*-(imidazo[1,2-*a*]pyridin-8-yl)-2-(*o*-tolyl)acetamide (1g)** : Following the general procedure A, **1g** was obtained



after purification by Combiflash column chromatography using silica gel column (10-30% ethyl acetate/hexane) as a off white solid: mp 98-100° C; yield 84% (446 mg); $R_f = 0.4$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.30 (s, 3H), 3.93 (s,

2H), 6.83 (t, $J = 7.1$ Hz, 1H), 7.17-7.29 (m, 4H), 7.55 (s, 1H), 7.94 (d, $J = 7.6$ Hz, 1H), 7.97 (s, 1H), 8.25 (d, $J = 6.3$ Hz, 1H), 9.95 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 19.8, 41.4, 110.8, 112.7, 114.9, 122.0, 126.3, 127.3, 127.8, 130.4, 130.6, 132.1, 135.0, 137.3, 139.1, 170.8; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{15}\text{N}_3\text{ONa}$ 288.1112 found 288.1111.

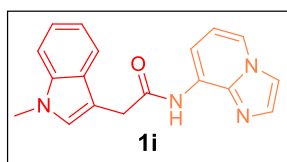
***N*-(imidazo[1,2-*a*]pyridin-8-yl)-2-(thiophen-2-yl)acetamide (1h)** : Following the general procedure A, **1h** was



obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane) as a light grey solid: mp 68-70 °C; yield 83% (427 mg); $R_f = 0.3$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 ,

ppm): δ 4.14 (s, 2H), 6.84 (t, $J = 7.1$ Hz, 1H), 6.98-7.03 (m, 2H), 7.40 (d, $J = 5.1$ Hz, 1H), 7.56 (s, 1H), 7.95 (d, $J = 7.5$ Hz, 1H) 7.98 (s, 1H), 8.27 (d, $J = 6.7$ Hz, 1H), 10.19 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 37.1, 110.6, 112.1, 114.4, 121.7, 125.2, 126.6, 126.7, 127.2, 131.6, 136.9, 138.5, 169.4; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{11}\text{N}_3\text{OSNa}$ 280.0520, found 280.0512.

***N*-(imidazo[1,2-*a*]pyridin-8-yl)-2-(1-methyl-1H-indol-3-yl)acetamide (1i)** : Following the general procedure A, **1i** was obtained after purification by Combiflash column chromatography using silica gel column (20-60% ethyl

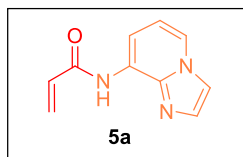


acetate/hexane) as a light yellow solid: mp 133– 135 °C; yield 71% (432 mg); $R_f = 0.3$ (ethyl acetate/hexane (50/50); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.77 (s, 3H), 3.97 (s, 2H), 6.81 (t, $J = 7.1$ Hz, 1H), 7.02 (t, $J = 7.4$ Hz, 1H), 7.14 (t, $J = 7.4$ Hz,

1H), 7.32 (s, 1H), 7.40 (d, $J = 8.2$ Hz, 1H), 7.52 (s, 1H), 7.64 (d, $J = 7.8$ Hz, 1H), 7.94-7.96 (m, 2H), 8.22 (d, $J = 6.7$ Hz, 1H), 9.87 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 32.2, 33.3, 107.5, 109.5, 110.0, 112.2, 114.3,

118.5, 118.9, 121.1, 121.3, 127.3, 127.5, 128.4, 131.5, 136.5, 138.5, 170.9; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{18}H_{16}N_4ONa$ 327.1221, found 307.1219.

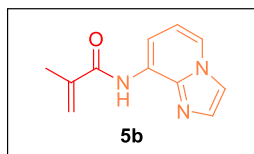
N-(imidazo[1,2-*a*]pyridin-8-yl)acrylamides (**5a**) : Following the general procedure A, **5a** was obtained after



purification by Combiflash column chromatography using silica gel column (20-30% ethyl acetate/hexane) as a gummy solid: mp 101–103 °C; yield 83% (311 mg); R_f = 0.35 (ethyl acetate/hexane (40/60)); 1H NMR (400 MHz, DMSO- d_6 , ppm): δ 5.77 (dd, J = 10.2 Hz, 1.6 Hz, 1H), 6.29 (dd, J = 17.0 Hz, 1.6 Hz, 1H), 6.85-6.96 (m, 2H), 7.57 (s, 1H), 7.98 (s, 1H),

8.07 (d, J = 7.5 Hz, 1H), 8.29 (d, J = 6.7 Hz, 1H), 10.26 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 111.2, 112.1, 114.4, 121.8, 127.2, 127.3, 128.1, 131.5, 131.6, 164.2; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{10}H_9N_3ONa$ 210.0643, found 210.0639.

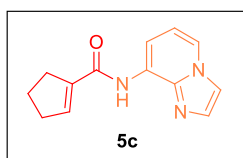
N-(imidazo[1,2-*a*]pyridin-8-yl)methacrylamide (**5b**) : Following the general procedure A, **5b** was obtained after



purification by Combiflash column chromatography using silica gel column (20-30% ethyl acetate/hexane) as a gummy solid: mp 105-107 °C; yield 86% (346 mg); R_f = 0.35 (ethyl acetate/hexane (40/60)); 1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.04 (s, 3H), 5.61 (s, 1H), 5.96 (s, 1H), 6.89 (t, J = 7.1 Hz, 1H), 7.56 (s, 1H), 7.88 (d, J = 7.4 Hz, 1H), 7.99

(s, 1H), 8.30 (d, J = 6.7 Hz, 1H), 9.26 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 18.2, 110.8, 112.1, 114.5, 121.3, 121.9, 126.6, 131.7, 138.9, 139.4, 166.2; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{11}H_{11}N_3ONa$ 224.0800, found 224.0795.

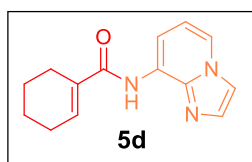
N-(imidazo[1,2-*a*]pyridin-8-yl)cyclopent-1-ene-1-carboxamide (**5c**) : Following the general procedure A, **5c** was



obtained after purification by Combiflash column chromatography using silica gel column (20-30% ethyl acetate/hexane) as a gummy solid: mp 102-104 °C; yield 84% (382 mg); R_f = 0.3 (ethyl acetate/hexane (40/60)); 1H NMR (400 MHz, DMSO- d_6 , ppm): δ 1.93-2.00 (m, 2H), 2.45 (m, 1H), 2.53 (m, 1H), 2.63-2.65 (m, 2H), 6.81 (s, 1H), 6.88 (t, J = 7.1 Hz, 1H),

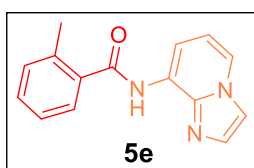
7.56 (s, 1H), 7.88 (d, J = 7.3 Hz, 1H), 7.99 (s, 1H), 8.29 (d, J = 6.6 Hz, 1H), 9.08 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 23.2, 31.4, 33.4, 110.1, 113.2, 113.6, 120.1, 127.4, 131.6, 139.1, 139.4, 140.0, 164.1; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{13}H_{13}N_3ONa$ 250.0956, found 250.0954.

N-(imidazo[1,2-*a*]pyridin-8-yl)cyclohex-1-ene-1-carboxamide (**5d**) : Following the general procedure A, **5d** was obtained after purification by Combiflash column chromatography using silica gel column (20-30% ethyl



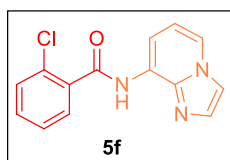
acetate/hexane) as a gummy solid: mp 107–109 °C; yield 80% (386 mg); R_f = 0.3 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 1.69-1.65 (m, 2H), 1.62-1.58 (m, 2H), 2.23-2.22 (m, 2H), 2.34-2.33 (m, 2H), 6.89-6.84 (m, 2H), 7.55 (s, 1H), 7.89 (d, J = 7.4 Hz, 1H), 7.98 (s, 1H), 8.27 (d, J = 6.8 Hz, 1H), 9.04 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 21.5, 22.1, 24.2, 25.5, 110.6, 112.8, 115.0, 122.0, 127.3, 132.2, 133.4, 135.5, 139.3, 166.7; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{15}\text{N}_3\text{ONa}$ 264.1112, found 264.1111.

N-(imidazo[1,2-*a*]pyridin-8-yl)-2-methylbenzamide (**5e**) : Following the general procedure A, **5e** was obtained after



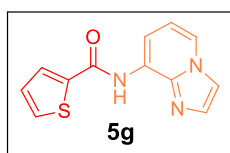
purification by Combiflash column chromatography using silica gel column (20-50% ethyl acetate/hexane) as a off white solid: mp 76-78 °C; yield 76% (382 mg); R_f = 0.3 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.44 (s, 3H), 6.89 (t, J = 7.0 Hz, 1H), 7.25-7.30 (m, 2H), 7.38 (t, J = 7.5 Hz, 1H), 7.52-7.56 (m, 2H), 7.92 (d, J = 7.0 Hz, 1H), 7.97 (s, 1H), 8.31 (d, J = 6.6Hz, 1H), 9.73 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 19.5, 111.9, 112.0, 114.4, 122.3, 125.7, 126.8, 127.1, 130.0, 130.7, 131.8, 135.6, 135.9, 139.1, 168.0; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{ONa}$ 274.0956, found 274.0950.

2-chloro-*N*-(imidazo[1,2-*a*]pyridin-8-yl)benzamide (**5f**) : Following the general procedure A, **5f** was obtained after



purification by Combiflash column chromatography using silica gel column (20-50% ethyl acetate/hexane) as a off white solid: mp 126-128 °C; yield 81% (440 mg); R_f = 0.3 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 6.92 (t, J = 7.0 Hz, 1H), 7.44-7.47 (m, 1H), 7.51-7.56 (m, 3H), 7.66 (d, J = 7.4 Hz, 1H), 8.01 (m, 2H), 8.35 (d, J = 6.7 Hz, 1H), 10.30 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 112.0, 114.4, 122.5, 126.7, 127.1, 129.3, 129.6 (2C), 129.9, 131.3, 131.9, 135.8, 138.9, 165.5; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{10}\text{ClN}_3\text{ONa}$ 294.0409, found 294.0406.

N-(imidazo[1,2-*a*]pyridin-8-yl)thiophene-2-carboxamide (**5g**) : Following the general procedure A, **5g** was



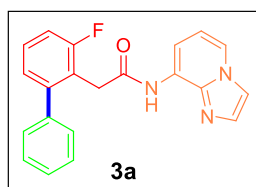
obtained after purification by Combiflash column chromatography using silica gel column (20-50% ethyl acetate/hexane) as a light grey solid: mp 78– 80 °C; yield 74% (360 mg); R_f = 0.3 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 6.92 (t, J = 7.1

Hz, 1H), 7.25 (t, $J = 4.6$ Hz, 1H), 7.59 (s, 1H), 7.78 (d, $J = 7.2$ Hz, 1H), 7.92 (d, $J = 4.9$ Hz, 1H), 8.02 (s, 1H), 8.11 (d, $J = 3.3$ Hz, 1H), 8.36 (d, $J = 6.7$ Hz, 1H), 9.96 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 112.0, 113.4, 114.4, 122.6, 126.4, 128.3, 129.7, 131.9, 132.3, 138.8, 139.4, 160.0; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_9\text{N}_3\text{OSNa}$ 266.0363, found 266.0358.

General Procedure for the Pd (II) Catalysed Arylation of Amide Derivatives in Water (B):

A screw cap vial was charged with an appropriate amide (0.20 mmol, 1 equiv) in water (4 mL), (Het)iodo arene (0.40 mmol, 2 equiv) and K_2CO_3 (0.50 mmol, 2.5 equiv) at room temperature followed by the addition of $\text{Pd}(\text{OAc})_2$ (15 mol %). The resulting suspension was heated at 120° C in an oil bath for 15 h. After completion, the reaction mixture was cooled to room temperature and filtered through celite bed and bed was washed with ethyl acetate. Then, aqueous layer was extracted with ethyl acetate. Combined organic layer was washed with brine solution, dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure to obtain crude product. The crude material was purified by Combiflash column chromatography (silica gel) using hexane/ethyl acetate mixture as an eluent to afford the desired arylated product.

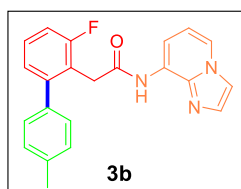
2-(3-fluoro-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3a) : Following the general procedure B, **3a** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl



acetate/hexane) as a off white solid: mp 136-138 °C; yield 71% (49.0 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.87 (s, 2H), 6.83 (t, $J = 7.1$ Hz, 1H), 7.14 (d, $J = 7.6$ Hz, 1H), 7.24 (t, $J = 9.0$ Hz, 1H), 7.34-7.46 (m, 6H), 7.55 (s, 1H), 7.91 (d, $J = 7.4$ Hz, 1H), 7.97 (s, 1H), 8.26 (d, $J = 6.6$ Hz, 1H), 10.11 (s, 1H); ^{13}C

NMR (100 MHz, DMSO- d_6 , ppm): δ 34.4, 110.5, 112.1, 113.8 ($J_{\text{C-F}} = 22.2$ Hz), 114.3, 120.7 ($J_{\text{C-F}} = 16.0$ Hz), 121.5, 125.5, 127.2, 127.5, 128.3, 128.4 (2C), 128.7, 131.5, 138.5, 139.4, 144.4 ($J_{\text{C-F}} = 3.8$ Hz), 161.2 ($J_{\text{C-F}} = 242.6$ Hz), 169.7; ^{19}F NMR (400 MHz, DMSO- d_6): δ -114.6; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{16}\text{FN}_3\text{ONa}$ 368.1174, found 368.1171.

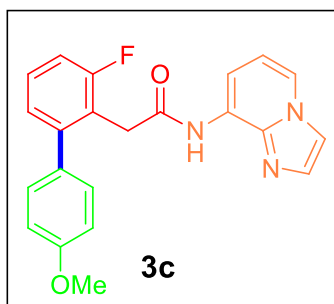
2-(3-fluoro-4'-methyl-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3b) : Following the general procedure B, **3b** was obtained after purification by Combiflash column chromatography



using silica gel column (10-40% ethyl acetate/hexane) as a off white solid: mp 113–115 °C; yield 74% (53.2 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.31 (s, 3H), 3.86 (s, 2H), 6.83 (t, $J = 7.1$ Hz, 1H), 7.12 (d, $J = 7.6$ Hz,

1H), 7.19-7.24 (m, 5H), 7.38-7.40 (m, 1H), 7.55 (s, 1H), 7.91 (d, $J = 7.3$ Hz, 1H), 7.97 (s, 1H), 8.26 (d, $J = 6.8$ Hz, 1H), 10.09 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 20.6, 34.4, 110.4, 112.1, 113.6 ($J_{\text{C-F}} = 22.1$ Hz), 114.3, 120.7 ($J_{\text{C-F}} = 16.0$ Hz), 121.5, 125.5, 127.2, 128.3 ($J_{\text{C-F}} = 9.3$ Hz), 128.6, 128.9, 131.5, 136.5 ($J_{\text{C-F}} = 2.3$ Hz), 136.8, 138.5, 144.4 ($J_{\text{C-F}} = 4.1$ Hz), 161.2 ($J_{\text{C-F}} = 242.5$ Hz), 169.7; ^{19}F NMR (400 MHz, DMSO- d_6 , ppm): δ -114.6; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{18}\text{FN}_3\text{ONa}$ 382.1331, found 382.1327.

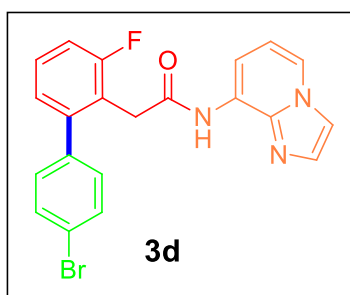
2-(3-fluoro-4'-methoxy-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3c) : Following the general procedure B, **3c** was obtained after purification by Combiflash column chromatography using silica gel column (10-



40% ethyl acetate/hexane) as a off white solid: mp 128-130 °C; yield 61% (45.8 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.75 (s, 3H), 3.87 (s, 2H), 6.84 (t, $J = 7.2$ Hz, 1H), 6.99 (d, $J = 8.4$ Hz, 2H), 7.12 (d, $J = 7.6$ Hz, 1H), 7.20 (t, $J = 8.9$ Hz, 1H), 7.29 (d, $J = 8.2$ Hz, 2H), 7.35-7.41 (m, 1H), 7.55 (s, 1H), 7.92 (d, $J = 7.5$ Hz, 1H), 7.97 (s, 1H), 8.26 (d, $J = 6.5$ Hz, 1H), 10.11 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 34.5, 55.0,

110.5, 112.1, 113.5 ($J_{\text{C-F}} = 22.1$ Hz), 113.8, 114.3, 120.7 ($J_{\text{C-F}} = 16.0$ Hz), 121.5, 125.6, 127.2, 128.2 ($J_{\text{C-F}} = 9.6$ Hz), 129.9, 131.5, 131.6 ($J_{\text{C-F}} = 8.3$ Hz), 138.5, 144.1, 158.7, 161.3 ($J_{\text{C-F}} = 244.0$ Hz), 169.8; ^{19}F NMR (400 MHz, DMSO- d_6 , ppm): δ -114.6; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{18}\text{FN}_3\text{O}_2\text{Na}$ 398.1280, found 398.1280.

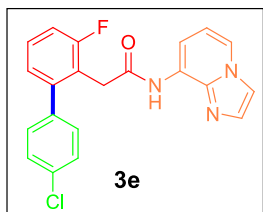
2-(4'-bromo-3-fluoro-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3d) : Following the general procedure B, **3d** was obtained after purification by Combiflash column chromatography using silica gel column (10-



40% ethyl acetate/hexane) as a off white solid: mp 137-139 °C; yield 57% (48.4 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.86 (s, 2H), 6.95 (bs, 1H), 7.14 (d, $J = 7.7$ Hz, 1H), 7.26 (t, $J = 8.9$ Hz, 1H), 7.32 (d, $J = 8.4$ Hz, 2H), 7.39-7.43 (m, 1H), 7.62-7.65 (m, 3H), 7.93 (d, $J = 7.3$ Hz, 1H), 8.05 (s, 1H), 8.34 (m, 1H), 10.25 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 34.1, 111.6, 112.6, 114.2 (d, $J_{\text{C-F}} = 22.2$ Hz), 114.5, 120.7

(d, $J_{\text{C-F}} = 16.4$ Hz), 121.2, 121.9, 125.4, 126.9, 128.5 (d, $J_{\text{C-F}} = 9.3$ Hz), 130.6, 130.9, 131.3, 138.0, 138.6 (d, $J_{\text{C-F}} = 2.3$ Hz), 143.1 (d, $J_{\text{C-F}} = 4.17$ Hz), 161.2 (d, $J_{\text{C-F}} = 242.76$ Hz), 169.6; ^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): δ -114.4; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{15}\text{BrFN}_3\text{ONa}$ 446.0280, found 446.0274.

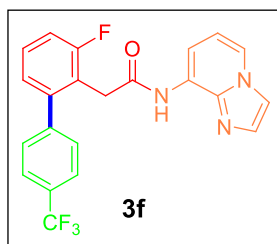
2-(4'-chloro-3-fluoro-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3e) : Following the general



procedure B, **3e** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane) as a off white solid: mp 150-152 °C; yield 63% (47.8 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); $^1\text{H NMR}$ (400 MHz, DMSO- d_6 , ppm): δ 3.87 (s, 2H), 6.83 (t, $J = 7.0$ Hz, 1H), 7.14 (d, $J = 7.6$ Hz, 1H), 7.26 (t, $J = 8.9$ Hz, 1H), 7.37-7.44 (m, 3H), 7.49-7.51 (m, 2H), 7.55 (s, 1H), 7.89 (d, $J = 7.3$

Hz, 1H), 7.97 (s, 1H), 8.26 (d, $J = 6.7$ Hz, 1H), 10.13 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, DMSO- d_6 , ppm): δ 34.2, 110.6, 112.1, 114.1, 114.3 ($J_{C-F} = 3.5$ Hz), 120.8 ($J_{C-F} = 16.1$ Hz), 121.5, 125.5 ($J_{C-F} = 2.3$ Hz), 127.2, 128.4, 128.5, 130.6, 131.6, 132.5, 138.2 ($J_{C-F} = 2.1$ Hz), 138.5, 143.1 ($J_{C-F} = 3.9$ Hz), 161.2 ($J_{C-F} = 242.9$ Hz), 169.6; $^{19}\text{F NMR}$ (400 MHz, DMSO- d_6 , ppm): δ -114.4; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{15}\text{ClFN}_3\text{ONa}$ 402.0785, found 402.0780.

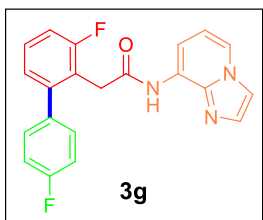
2-(3-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3f) : Following the general procedure B, **3f** was obtained after purification by Combiflash column chromatography using silica gel



column (10-40% ethyl acetate/hexane) as a off white solid: mp 158-160 °C; yield 66% (54.6 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); $^1\text{H NMR}$ (400 MHz, DMSO- d_6 , ppm): δ 3.88 (s, 2H), 6.82 (t, $J = 7.1$ Hz, 1H), 7.18 (d, $J = 7.6$ Hz, 1H), 7.30 (t, $J = 9.0$ Hz, 1H), 7.42-7.48 (m, 1H), 7.54 (s, 1H), 7.59 (d, $J = 8.0$ Hz, 2H), 7.80 (d, $J = 8.0$ Hz, 2H), 7.88 (d, $J = 7.4$ Hz, 1H), 7.97 (s, 1H), 8.26 (d, $J = 6.6$ Hz, 1H), 10.15 (s, 1H); ^{13}C

NMR (100 MHz, DMSO- d_6 , ppm): δ 34.1, 110.6, 112.1, 114.3, 114.6 ($J_{C-F} = 22.3$ Hz), 120.9 ($J_{C-F} = 16.5$ Hz), 121.6, 122.8, 125.3 ($J_{C-F} = 3.7$ Hz), 125.5, 127.1, 127.6, 127.9, 128.2, 128.6 ($J_{C-F} = 9.3$ Hz), 129.7, 131.5, 138.5, 142.9 ($J_{C-F} = 4.2$ Hz), 143.5, 161.2 ($J_{C-F} = 242.9$ Hz), 169.5; $^{19}\text{F NMR}$ (100 MHz, DMSO- d_6 , ppm): δ -61.1, -114.4; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{15}\text{F}_4\text{N}_3\text{ONa}$ 436.1048, found 436.1045.

2-(3,4'-difluoro-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3g) : Following the general procedure B, **3g** was obtained after purification by Combiflash column chromatography using silica gel column (10-

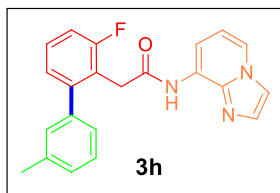


40% ethyl acetate/hexane) as a off white solid: mp 148-150 °C; yield 72% (52.3 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); $^1\text{H NMR}$ (400 MHz, DMSO- d_6 , ppm): δ 3.86 (s, 2H), 6.83 (t, $J = 7.1$ Hz, 1H), 7.14 (d, $J = 7.5$ Hz, 1H), 7.22-7.29 (m, 3H), 7.39-7.41 (m, 3H), 7.55 (s, 1H), 7.90 (d, $J = 7.4$ Hz, 1H), 7.97 (s, 1H), 8.26 (d, $J = 6.7$ Hz, 1H), 10.12

(s, 1H); $^{13}\text{C NMR}$ (100 MHz, DMSO- d_6 , ppm): δ 34.2, 110.5, 112.1, 114.0 ($J_{C-F} = 22.1$ Hz), 114.3, 115.2 ($J_{C-F} =$

21.0 Hz), 120.9 ($J_{C-F} = 16.3$ Hz), 121.5, 125.6, 127.2, 128.4 ($J_{C-F} = 9.2$ Hz), 130.8 ($J_{C-F} = 8.4$ Hz), 131.6, 135.7, 138.5, 143.3 ($J_{C-F} = 3.9$ Hz), 161.2 ($J_{C-F} = 242.5$ Hz), 161.7 ($J_{C-F} = 242.9$ Hz), 169.6; ^{19}F NMR (100 MHz, DMSO- d_6 , ppm): δ -114.5, -114.8; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{15}\text{F}_2\text{N}_3\text{ONa}$ 386.1080, found 386.1077.

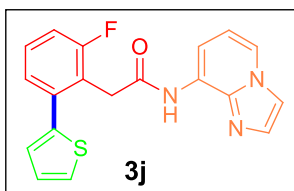
2-(3-fluoro-3'-methyl-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3h) (CR211-12061-51-P):



Following the general procedure B, **3h** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane) as a off white solid: mp 116-118 °C; yield 73% (52.5 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.26 (s, 3H), 3.87 (s, 2H), 6.83 (t, $J =$

7.1 Hz, 1H), 7.11-7.24 (m, 5H), 7.31 (t, $J = 7.7$ Hz, 1H), 7.36-7.41 (m, 1H), 7.55 (s, 1H), 7.93 (d, $J = 7.3$ Hz, 1H), 7.97 (s, 1H), 8.26 (d, $J = 6.7$ Hz, 1H), 10.13 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 20.9, 34.4, 110.5, 112.1, 113.8 ($J_{C-F} = 22.0$ Hz), 114.3, 120.7 ($J_{C-F} = 16.0$ Hz), 121.5, 125.5, 125.8, 127.3, 128.1, 128.2, 128.3 ($J_{C-F} = 11.7$ Hz), 129.4, 131.5, 137.5, 138.5, 139.4, 144.5 ($J_{C-F} = 4.0$ Hz), 161.2 ($J_{C-F} = 242.3$ Hz), 169.8; ^{19}F NMR (400 MHz, DMSO- d_6 , ppm): δ -114.6; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{18}\text{FN}_3\text{ONa}$ 382.1331, found 382.1331

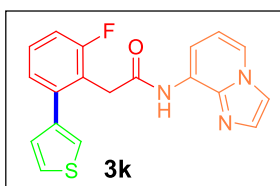
2-(2-fluoro-6-(thiophen-2-yl)phenyl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3j) : Following the general



procedure B, **3j** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane) as a off white solid: mp 120-122 °C; yield 68% (47.8 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 4.05 (s, 2H), 6.84 (t, $J = 7.1$ Hz,

1H), 7.12-7.16 (m, 2H), 7.23-7.33 (m, 2H), 7.37-7.43 (m, 1H), 7.57 (s, 1H), 7.62 (d, $J = 4.9$ Hz, 1H), 7.93 (d, $J = 7.4$ Hz, 1H), 7.98 (s, 1H), 8.26 (d, $J = 6.6$ Hz, 1H), 10.26 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 34.4, 110.5, 112.2, 114.3, 114.6 ($J_{C-F} = 22.8$ Hz), 121.2 ($J_{C-F} = 16.1$ Hz), 121.5, 126.3, 127.1, 127.2, 127.3, 127.7, 128.5 ($J_{C-F} = 9.3$ Hz), 131.6, 136.8 ($J_{C-F} = 4.2$ Hz), 138.5, 140.1 ($J_{C-F} = 2.6$ Hz), 161.4 ($J_{C-F} = 242.3$ Hz), 169.5; ^{19}F NMR (400 MHz, DMSO- d_6 , ppm): δ -114.0; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{14}\text{FN}_3\text{OSNa}$ 374.0739, found 374.0734.

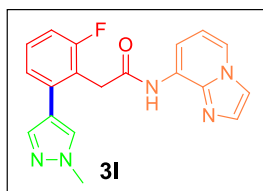
2-(2-fluoro-6-(thiophen-3-yl)phenyl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3k) : Following the general procedure B, **3k** was obtained after purification by Combiflash column chromatography using silica gel column (10-



40% ethyl acetate/hexane) as a off white solid: mp 159-161 °C; yield 70% (49.2 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.95 (s, 2H), 6.83 (t, $J = 7.2$ Hz, 1H), 7.19-7.22 (m, 3H), 7.35-7.41 (m, 1H), 7.56 (s, 2H), 7.

64 (t, $J = 3.8$ Hz, 1H), 7.91 (d, $J = 7.4$ Hz, 1H), 7.98 (s, 1H), 8.26 (d, $J = 6.8$ Hz, 1H), 10.17 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 34.3, 110.5, 112.1, 113.8 ($J_{\text{C-F}} = 22.2$ Hz), 114.3, 120.8 ($J_{\text{C-F}} = 16.0$ Hz), 121.5, 123.8, 125.5, 126.5, 127.2, 128.3 ($J_{\text{C-F}} = 9.2$ Hz), 128.5, 131.6, 139.2 ($J_{\text{C-F}} = 4.4$ Hz), 139.7 ($J_{\text{C-F}} = 2.4$ Hz), 161.3 ($J_{\text{C-F}} = 242.3$ Hz), 169.7; ^{19}F NMR (400 MHz, DMSO- d_6 , ppm): δ -114.5; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{14}\text{FN}_3\text{OSNa}$ 374.0739, found 374.0734

2-(2-fluoro-6-(1-methyl-1H-pyrazol-4-yl)phenyl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (3I) : Following the general procedure B, **3I** was obtained after purification by Combiflash column chromatography using silica gel



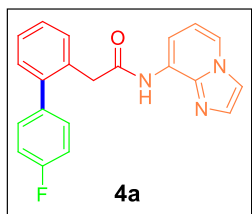
column (10-40% ethyl acetate/hexane) as a off white solid: mp 172–174 °C; yield 49%

(34.2 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm):

δ 3.85 (s, 3H), 4.01 (s, 2H), 6.87 (m, 1H), 7.13 (t, $J = 9.0$ Hz, 1H), 7.21 (d, $J = 7.6$ Hz, 1H), 7.33-7.35 (m, 1H), 7.56 (s, 1H), 7.61 (s, 1H), 7.90 (m, 2H), 8.01 (s, 1H), 8.29 (d, J

= 5.7 Hz, 1H), 10.17 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 29.4, 34.7, 111.9, 113.1, 113.5 ($J_{\text{C-F}} = 13.6$ Hz), 113.6, 115.0, 120.0 ($J_{\text{C-F}} = 2.5$ Hz), 120.8 ($J_{\text{C-F}} = 16.0$ Hz), 122.5, 125.7, 127.4, 128.9 ($J_{\text{C-F}} = 9.5$ Hz), 130.2, 131.4, 136.2 ($J_{\text{C-F}} = 4.5$ Hz), 138.4, 138.8, 162.0 ($J_{\text{C-F}} = 241.4$ Hz), 170.2; ^{19}F NMR (400 MHz, DMSO- d_6 , ppm): δ -114.6; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{FN}_5\text{ONa}$ 372.1236, found 372.1232.

2-(4'-fluoro-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (4a) : Following the general procedure



B, **4a** was obtained after purification by Combiflash column chromatography using silica

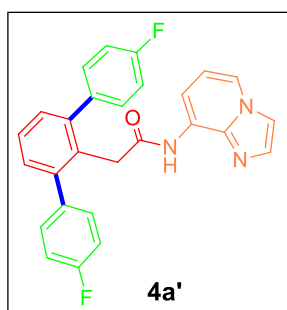
gel column (10-40% ethyl acetate/hexane). **4a**: Off white solid: mp 95–97 °C; yield 75%

(51.8 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm):

δ 3.86 (s, 2H), 6.82 (t, $J = 7.1$ Hz, 1H), 7.16-7.26 (m, 3H), 7.33-7.48 (m, 5H), 7.54 (s,

1H), 7.88 (d, $J = 7.4$ Hz, 1H), 7.96 (s, 1H), 8.25 (d, $J = 6.7$ Hz, 1H), 9.89 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 40.6, 110.5, 112.1, 114.3, 114.9 ($J_{\text{C-F}} = 21.2$ Hz), 121.5, 126.8, 127.1, 127.5, 129.8, 130.5, 130.9 ($J_{\text{C-F}} = 8.0$ Hz), 131.5, 133.1, 137.0 ($J_{\text{C-F}} = 3.1$ Hz), 138.5, 140.9, 161.4 ($J_{\text{C-F}} = 242.3$ Hz), 170.5; ^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): δ -115.7; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{16}\text{FN}_3\text{ONa}$ 368.1174, found 368.1170.

2-(4,4''-difluoro-[1,1':3',1''-terphenyl]-2'-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (4a') : Following the



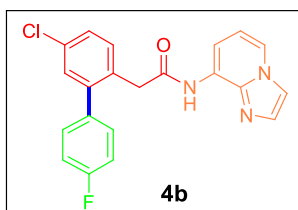
general procedure B, **4a'** was obtained after purification by Combiflash column

chromatography using silica gel column (10-40% ethyl acetate/hexane). Off white

solid: mp 181–183 °C; yield 19% (16.7 mg); $R_f = 0.6$ (ethyl acetate/hexane (40/60));

^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.67 (s, 2H), 6.81 (t, J = 7.1 Hz, 1H), 7.18 (t, J = 8.8 Hz, 4H), 7.26 (d, J = 7.6 Hz, 2H), 7.36-7.44 (m, 5H), 7.48 (s, 1H), 7.79 (d, J = 7.5 Hz, 1H), 7.93 (s, 1H), 8.22 (d, J = 6.6 Hz, 1H), 9.53 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 40.0, 110.3, 112.1, 114.2, 114.9 ($J_{\text{C-F}}$ = 21.3 Hz), 121.4, 126.7, 127.1, 129.2, 130.8 ($J_{\text{C-F}}$ = 7.7 Hz), 131.1, 131.5, 137.5, 138.4, 142.2, 161.4 ($J_{\text{C-F}}$ = 242.2 Hz), 170.8; ^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): δ -115.5; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{19}\text{F}_2\text{N}_3\text{ONa}$ 462.1393, found 462.1391.

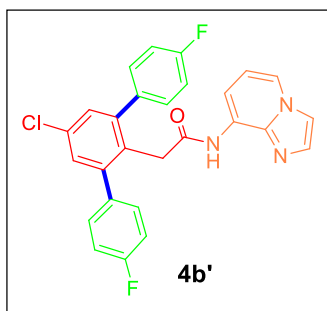
2-(5-chloro-4'-fluoro-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (4b) : Following the general procedure B, **4b** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane). Off white solid: mp 136–138 °C; yield 73% (55.4 mg); R_f = 0.5 (ethyl acetate/hexane



(40/60); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.85 (s, 2H), 6.81 (t, J = 7.08 Hz, 1H), 7.23 (t, J = 8.70 Hz, 2H), 7.30 (s, 1H), 7.39-7.47 (m, 4H), 7.55 (s, 1H), 7.87 (d, J = 7.36 Hz, 1H), 7.96 (s, 1H), 8.25 (d, J = 6.68 Hz, 1H), 10.01 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 40.1, 110.6, 112.1, 114.3, 115.1 (d, J_{CF} = 21.2 Hz),

121.6, 127.1, 127.3, 129.2, 130.9 ($J_{\text{C-F}}$ = 8.2 Hz), 131.2, 131.6, 132.4, 132.5, 135.6 ($J_{\text{C-F}}$ = 3.1 Hz), 138.5, 142.8, 161.6 ($J_{\text{C-F}}$ = 243.0 Hz), 170.2; ^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): δ -114.9 (1F); HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{15}\text{ClFN}_3\text{ONa}$ 402.0785, found 402.0779.

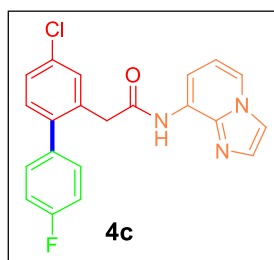
2-(5'-chloro-4,4''-difluoro-[1,1':3',1''-terphenyl]-2'-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (4b'): Following



the general procedure B, **4b'** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane). **4b'**: Off white solid: mp 229–231 °C; yield 16% (15.1 mg); R_f = 0.6 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.65 (s, 2H), 6.80 (t, J = 7.1 Hz, 1H), 7.20 (t, J = 8.8 Hz, 4H), 7.33 (s, 2H), 7.38-7.42 (m, 4H), 7.48 (s, 1H), 7.77 (d, J = 7.0 Hz, 1H), 7.93 (s, 1H), 8.23 (d, J = 6.7 Hz, 1H),

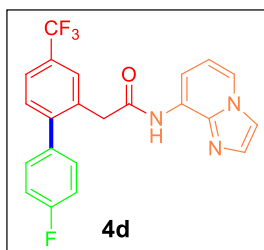
9.64 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 38.5, 110.6, 112.0, 114.1, 114.9, 115.2, 115.1 ($J_{\text{C-F}}$ = 21.4 Hz, 4C), 121.5, 127.0, 128.6, 130.6, 130.7, 130.8, 130.9, 131.5, 136.1 ($J_{\text{C-F}}$ = 2.6 Hz), 138.4, 144.1, 161.6 ($J_{\text{C-F}}$ = 242.8 Hz), 170.5; ^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): δ -114.7; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{18}\text{ClF}_2\text{N}_3\text{ONa}$ 496.1003, found 496.0999.

2-(4-chloro-4'-fluoro-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (4c) : Following the general procedure B, **4c** was obtained after purification by Combiflash column chromatography using silica gel column (10-



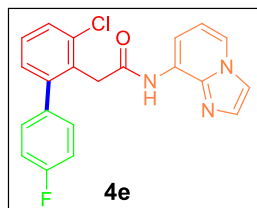
40% ethyl acetate/hexane) as a off white solid: mp 136–138 °C; yield 85% (64.6 mg); R_f = 0.5 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.87 (s, 2H), 6.82 (t, J = 5.9 Hz, 1H), 7.21-7.39 (m, 6H), 7.54 (d, J = 9.6 Hz, 2H), 7.86 (d, J = 7.0 Hz, 1H), 7.97 (s, 1H), 8.26 (d, J = 6.6 Hz, 1H), 10.04 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 40.2, 110.7, 112.1, 114.3, 114.9, 115.2, 121.6, 126.7, 127.1, 130.3, 130.9 (J_{C-F} = 7.8 Hz), 131.5, 131.9, 135.6, 135.8, 138.5, 139.8, 161.5 (J_{C-F} = 242.6 Hz), 170.0; ^{19}F NMR (400 MHz, DMSO- d_6 , ppm): δ -115.2; HRMS (ESI) m/z $[M+Na]^+$ calcd for $\text{C}_{21}\text{H}_{15}\text{ClFN}_3\text{ONa}$ 402.0785, found 402.0778.

2-(4'-fluoro-4-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (4d) : Following



the general procedure B, **4d** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane) as a off white solid: mp 128–130 °C; yield 69% (57.0 mg); R_f = 0.5 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.98 (s, 2H), 6.81 (t, J = 7.1 Hz, 1H), 7.26 (t, J = 8.8 Hz, 2H), 7.42-7.49 (m, 3H), 7.55 (s, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.84-7.86 (m, 2H), 7.97 (s, 1H), 8.26 (d, J = 6.4 Hz, 1H), 10.10 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 40.2, 110.8, 112.1, 114.3, 115.2 (d, J_{C-F} = 21.2 Hz), 121.6, 123.5 (q, J_{C-F} = 3.6 Hz), 127.1, 127.5 (q, J_{C-F} = 3.9 Hz), 128.2 (q, J_{CF} = 17.4 Hz), 130.8, 130.9 (J_{C-F} = 8.28 Hz), 131.6, 134.8, 135.7 (J_{C-F} = 3.0 Hz), 138.6, 161.7 (d, J_{C-F} = 243.2 Hz), 170.1; ^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): δ -60.9 (s, 3F)-114.7 (s, 1F); HRMS (ESI) m/z $[M+Na]^+$ calcd for $\text{C}_{22}\text{H}_{15}\text{F}_4\text{N}_3\text{ONa}$ 436.1048, found 436.1043.

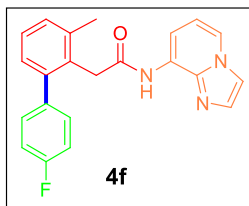
2-(3-chloro-4'-fluoro-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (4e) : Following the general procedure B, **4e** was obtained after purification by Combiflash column chromatography



using silica gel column (10-40% ethyl acetate/hexane) as a off white solid: mp 153–155 °C; yield 62% (47.1 mg); R_f = 0.5 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.94 (s, 2H), 6.83 (t, J = 7.0 Hz, 1H), 7.25-7.29 (m, 3H), 7.39-7.40 (m, 3H), 7.52 (d, J = 8.24 Hz, 1H), 7.55 (s, 1H), 7.91 (d, J = 7.0 Hz, 1H), 7.97 (s, 1H), 8.26 (d, J = 6.4 Hz, 1H), 10.15 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 40.1, 110.5, 112.1, 114.3, 115.1,

115.3, 121.5, 127.2, 128.2, 128.3, 128.6, 130.7 ($J_{C-F} = 8.4$ Hz), 131.5 ($J_{C-F} = 3.0$ Hz), 135.0, 136.5 ($J_{C-F} = 2.7$ Hz), 138.5, 143.6, 161.6 ($J_{C-F} = 243.1$ Hz), 169.5; ^{19}F NMR (400 MHz, DMSO- d_6 , ppm): δ -114.8; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{15}\text{ClFN}_3\text{ONa}$ 402.0785, found 402.0782.

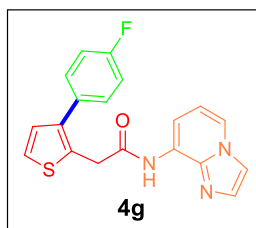
2-(4'-fluoro-3-methyl-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (4f) : Following the general



procedure B, **4f** was obtained after purification by Combiflash column chromatography using silica gel column (10-40% ethyl acetate/hexane) as a off white solid: mp 122-124 °C; yield 83% (59.7 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.30 (s, 3H), 3.84 (s, 2H), 6.84 (t, $J = 7.0$ Hz, 1H), 7.08-7.09 (m, 1H),

7.21-7.25 (m, 4H), 7.37 (t, $J = 6.8$ Hz, 2H), 7.54 (s, 1H), 7.92 (d, $J = 7.2$ Hz, 1H), 7.97 (s, 1H), 8.26 (d, $J = 6.5$ Hz, 1H), 9.96 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 19.8, 38.3, 110.7, 112.2, 114.4, 115.0 ($J_{C-F} = 21.4$ Hz) 121.6, 126.2, 126.6, 127.2, 127.5, 129.3, 130.8 ($J_{C-F} = 7.7$ Hz), 131.5, 131.9, 137.8, 138.5, 141.8, 161.4 ($J_{C-F} = 242.3$ Hz), 170.5; ^{19}F NMR (400 MHz, DMSO- d_6 , ppm): δ -115.7; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{18}\text{FN}_3\text{ONa}$ 382.1331, found 382.1326.

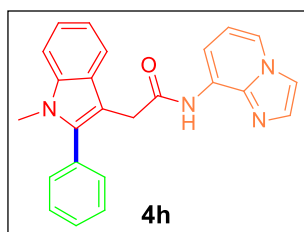
2-(3-(4-fluorophenyl)thiophen-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (4g) : Following the general procedure B, **4g** was obtained after purification by Combiflash column chromatography using silica gel column (10-



40% ethyl acetate/hexane) as a off white solid: mp 148-150 °C; yield 53% (37.2 mg); $R_f = 0.5$ (ethyl acetate/hexane (50/50)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 4.16 (s, 2H), 6.84 (t, $J = 7.1$ Hz, 1H), 7.12 (d, $J = 5.2$ Hz, 1H), 7.27 (t, $J = 8.9$ Hz, 2H), 7.50 (d, $J = 5.2$ Hz, 1H) 7.52-7.56 (m, 3H), 7.94 (d, $J = 7.5$ Hz, 1H), 7.98 (s, 1H), 8.28 (d, $J = 6.7$ Hz,

1H), 10.28 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 35.5, 110.9, 112.1, 114.3, 115.3 ($J_{C-F} = 21.2$ Hz), 121.8, 124.4, 127.1, 128.7, 130.4 ($J_{C-F} = 8.2$ Hz), 131.6, 131.7, 132.2 ($J_{C-F} = 3.1$ Hz), 138.6, 138.8, 161.3 ($J_{C-F} = 242.3$ Hz), 169.6; ^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): δ -115.5; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{14}\text{FN}_3\text{OSNa}$ 374.0739, found 374.0730.

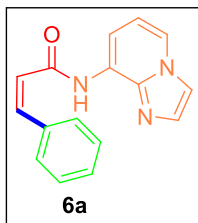
N-(imidazo[1,2-a]pyridin-8-yl)-2-(1-methyl-2-phenyl-1H-indol-3-yl)acetamide (4h) : Following the general procedure B, **4h** was obtained after purification by Combiflash column chromatography using silica gel column (20-



60% ethyl acetate/hexane) as a off white solid: mp 123-125 °C; yield 64% (48.7 mg); $R_f = 0.4$ (ethyl acetate/hexane (50/50)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 3.64 (s, 3H), 3.89 (s, 2H), 6.81 (t, $J = 7.1$ Hz, 1H), 7.06 (t, $J = 7.4$ Hz, 1H), 7.20 (t, $J =$

7.5 Hz, 1H), 7.46-7.56 (m, 5H), 7.59-7.61 (m, 2H), 7.65 (d, $J = 8.0$ Hz, 1H), 7.91 (d, $J = 7.2$ Hz, 1H), 7.96 (s, 1H), 8.24 (d, $J = 6.6$ Hz, 1H), 9.89 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 30.8, 32.7, 106.2, 109.8, 110.1, 112.1, 114.3, 118.7, 119.2, 121.4, 121.6, 127.1, 127.2, 128.2, 128.5, 130.3, 130.7, 131.6, 136.8, 138.5, 139.0, 170.8; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{20}\text{N}_4\text{ONa}$ 403.1534, found 403.1530.

N-(imidazo[1,2-*a*]pyridin-8-yl)-3-phenylacrylamide (**6a**) : Following the general procedure B, **6a** was obtained after purification by Combiflash column chromatography using silica gel column (20-40% ethyl acetate/hexane) as a

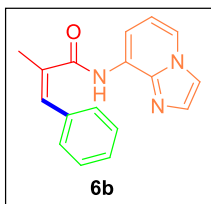


gummy solid: mp 104–106 °C; yield 52% (27.4 mg); $R_f = 0.5$ (ethyl acetate/hexane (40/60));

^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 6.55 (d, $J = 12.8$ Hz, 1H), 6.86 (d, $J = 7.1$ Hz, 1H), 6.91 (d, $J = 12.7$ Hz, 1H), 7.29-7.37 (m, 3H), 7.57 (s, 1H), 7.72 (d, $J = 7.0$ Hz, 2H), 7.98-8.01 (m, 2H), 8.29 (d, $J = 6.6$ Hz, 1H), 10.11 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ

110.8, 113.2, 113.6, 120.4, 122.9, 127.4, 128.2, 128.9, 129.5, 131.5, 134.7, 138.9, 140.4, 165.3; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{13}\text{N}_3\text{ONa}$ 286.0956, found 286.0955.

N-(imidazo[1,2-*a*]pyridin-8-yl)-2-methyl-3-phenylacrylamide (**6b**) : Following the general procedure B, **6b** was



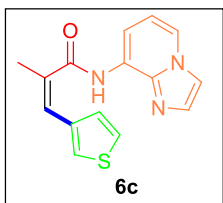
obtained after purification by Combiflash column chromatography using silica gel column

(20-40% ethyl acetate/hexane) as a gummy solid: mp 107–109 °C; yield 47% (26.0 mg); $R_f =$

0.5 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.14 (s, 3H), 6.58 (s, 1H), 6.87 (t, $J = 6.9$ Hz, 1H), 7.16 (t, $J = 7.2$ Hz, 1H), 7.24 (t, $J = 7.5$ Hz, 2H), 7.34 (d, J

$= 7.3$ Hz, 2H), 7.45 (s, 1H), 7.93 (s, 2H), 8.27 (d, $J = 6.6$ Hz, 1H), 9.52 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 21.9, 110.0, 112.1, 114.3, 122.0, 126.7, 127.4, 127.7 (2C), 128.3 (2C), 128.6, 131.7, 134.2, 135.6, 138.5, 169.7; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{ONa}$ 300.1113, found 300.1111.

N-(imidazo[1,2-*a*]pyridin-8-yl)-2-methyl-3-(thiophen-3-yl)acrylamide (**6c**) : Following the general procedure B, **6c** was obtained after purification by Combiflash column chromatography using silica gel column (20-40% ethyl

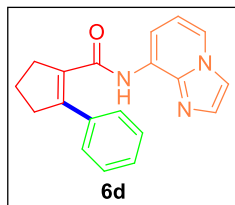


acetate/hexane) as a gummy solid, yield 53% (30.0 mg); $R_f = 0.5$ (ethyl acetate/hexane

(40/60); ^1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.10 (s, 3H), 6.53 (s, 1H), 6.89 (t, $J = 7.0$ Hz, 1H), 7.09 (d, $J = 4.7$ Hz, 1H), 7.40-7.42 (m, 1H), 7.49 (m, 2H), 7.92-8.01 (m, 2H), 8.30 (d, $J = 6.3$ Hz, 1H), 9.71 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 21.6,

111.3, 112.1, 114.4, 122.1, 122.9, 124.4, 126.3, 126.6, 126.7, 131.7, 132.5, 137.0, 138.6, 169.8; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{15}H_{13}N_3OSNa$ 306.0676, found 306.0672.

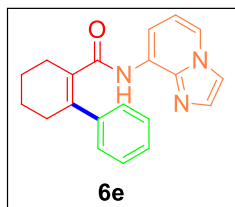
N-(imidazo[1,2-*a*]pyridin-8-yl)-2-phenylcyclopent-1-ene-1-carboxamide (**6d**) : Following the general procedure B, **6d** was obtained after purification by Combiflash column chromatography using silica gel column (20-40% ethyl



acetate/hexane) as a off white solid: mp 132–134 °C; yield 43% (26.1 mg); R_f = 0.5 (ethyl acetate/hexane (40/60)); 1H NMR (400 MHz, DMSO- d_6 , ppm): δ 1.99-2.02 (m, 2H), 2.88 (t, J = 7.48 Hz, 4H), 6.83 (t, J = 7.1 Hz, 1H), 7.22-7.32 (m, 3H), 7.40-7.42 (m, 3H), 7.91 (s, 2H), 8.23 (d, J = 6.7 Hz, 1H), 9.14 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 21.5,

35.8, 37.9, 110.0, 112.1, 114.3, 121.6, 126.7, 127.2, 127.8, 128.2, 131.5, 133.1, 135.7, 138.3, 144.7, 166.4; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{19}H_{17}N_3ONa$ 326.1269, found 326.1265.

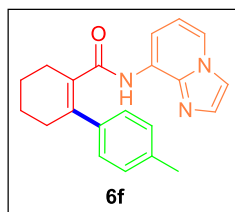
N-(imidazo[1,2-*a*]pyridin-8-yl)-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-carboxamide (**6e**) : Following the general procedure B, **6e** was obtained after purification by Combiflash column chromatography using silica gel column (20-



40% ethyl acetate/hexane) as a off white solid: mp 131-133 °C; yield 44% (27.9 mg); R_f = 0.5 (ethyl acetate/hexane (40/60)); 1H NMR (400 MHz, DMSO- d_6 , ppm): δ 1.74 (m, 4H), 2.42 (m, 4H), 6.76 (t, J = 7.0 Hz, 1H), 7.08-7.12 (m, 1H), 7.19-7.23 (m, 2H), 7.30-7.31 (m, 2H), 7.41 (s, 1H), 7.78 (d, J = 7.1 Hz, 1H), 7.86 (s, 1H), 8.15 (d, J = 6.4 Hz, 1H), 8.72 (s,

1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 21.4, 22.1, 26.8, 30.5, 109.3, 112.1, 114.2, 121.3, 126.7, 127.1, 127.2, 128.1, 131.5, 132.3, 138.1, 138.5, 141.4, 169.8, HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{20}H_{19}N_3ONa$ 340.1425, found 340.1420.

N-(imidazo[1,2-*a*]pyridin-8-yl)-4'-methyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-carboxamide (**6f**) : Following the general procedure B, **6f** was obtained after purification by Combiflash column

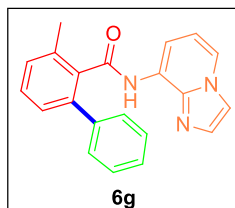


chromatography using silica gel column (20-40% ethyl acetate/hexane) as a off white solid: mp 106-108 °C; yield 47% (31.1 mg); R_f = 0.5 (ethyl acetate/hexane (40/60)); 1H NMR (400 MHz, DMSO- d_6 , ppm): δ 1.72 (m, 4H), 2.14 (s, 3H), 2.39-2.41 (m, 4H), 6.77

(t, J = 7.1 Hz, 1H), 7.02 (d, J = 7.7 Hz, 2H), 7.20 (d, J = 7.6 Hz, 2H), 7.42 (s, 1H), 7.80 (d, J = 7.3 Hz, 1H), 7.87 (s, 1H), 8.17 (d, J = 6.6 Hz, 1H), 8.72 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 20.6, 21.5, 22.1, 26.9, 30.6,

109.3, 112.2, 114.3, 121.3, 126.8, 127.0, 128.7, 131.5, 131.8, 136.4, 138.1, 138.3, 138.5, 170.1; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{21}H_{21}N_3ONa$ 354.1582, found 354.1577.

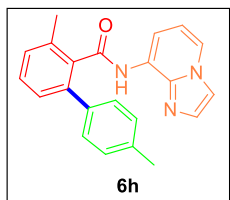
N-(imidazo[1,2-*a*]pyridin-8-yl)-3-methyl-[1,1'-biphenyl]-2-carboxamide (**6g**) : Following the general procedure B, **6g** was obtained after purification by Combiflash column chromatography using silica gel column (20-60% ethyl



acetate/hexane) as a off white solid: mp 94-96 °C; yield 55% (36.0 mg); R_f = 0.6 (ethyl acetate/hexane (40/60)); 1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.41 (s, 3H), 6.82 (t, J = 7.0 Hz, 1H), 7.25 (t, J = 7.4 Hz, 1H), 7.31-7.32 (m, 3H), 7.44 (t, J = 7.5 Hz, 1H), 7.50-7.51 (m, 3H), 7.65 (d, J = 7.0 Hz, 1H), 7.94 (s, 1H), 8.28 (d, J = 6.6 Hz, 1H), 9.93 (s, 1H); ^{13}C

NMR (100 MHz, DMSO- d_6 , ppm): δ 19.1, 111.8, 112.3, 114.1, 122.3, 126.5, 127.0, 127.1, 128.0, 128.4, 128.7, 128.8, 131.9, 134.4, 136.7, 138.7, 139.1, 140.2, 168.2; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{21}H_{17}N_3ONa$ 350.1269, found 350.1264.

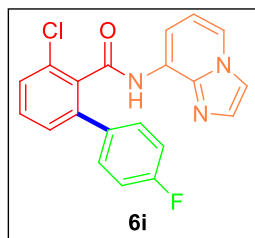
N-(imidazo[1,2-*a*]pyridin-8-yl)-3,4'-dimethyl-[1,1'-biphenyl]-2-carboxamide (**6h**) : Following the general procedure B, **6h** was obtained after purification by Combiflash column chromatography



using silica gel column (20-60% ethyl acetate/hexane) as a off white solid: mp 142-144 °C; yield 47% (32.1 mg); R_f = 0.6 (ethyl acetate/hexane (40/60)); 1H NMR (400 MHz, DMSO- d_6 , ppm): δ 2.24 (s, 3H), 2.39 (s, 3H), 6.84 (t, J = 7.1 Hz, 1H), 7.13 (d, J = 7.8 Hz, 2H), 7.21 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 7.40-7.43 (m, 3H), 7.50 (s, 1H), 7.71 (d, J =

7.4 Hz, 1H), 7.94 (s, 1H), 8.28 (d, J = 6.5 Hz, 1H), 9.93 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 19.1, 20.5, 111.9, 112.2, 114.1, 122.2, 126.5, 127.0, 128.2, 128.5, 128.6, 128.7, 131.8, 134.4, 136.3, 136.6, 137.3, 138.6, 139.0, 168.3; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{22}H_{19}N_3ONa$ 364.1425, found 364.1424.

3-chloro-4'-fluoro-*N*-(imidazo[1,2-*a*]pyridin-8-yl)-[1,1'-biphenyl]-2-carboxamide (**6i**) : Following the general procedure B, **6i** was obtained after purification by Combiflash column chromatography

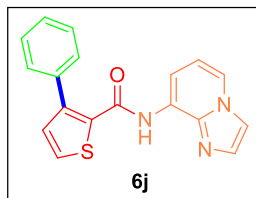


using silica gel column (20-60% ethyl acetate/hexane) as a off white solid: mp 130-132° C; yield 44% (32.2 mg); R_f = 0.6 (ethyl acetate/hexane (40/60)); 1H NMR (400 MHz, DMSO- d_6 , ppm): δ 6.83 (t, J = 7.1 Hz, 1H), 7.19 (t, J = 8.8 Hz, 2H), 7.36 (d, J = 7.1, 1H), 7.51-7.58 (m, 5H), 7.76 (d, J = 7.4 Hz, 1H), 7.96 (s, 1H), 8.29 (d, J = 6.6 Hz, 1H),

10.73 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 111.9, 112.1, 114.2, 114.9, 115.1, 122.3, 126.6, 127.9, 128.4, 130.1, 130.2, 130.5, 130.6, 131.8, 135.5 (J_{C-F} = 3.1Hz), 136.1, 138.8, 140.0, 161.7 (J_{C-F} = 243.1 Hz), 165.4;

^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): δ -114.7; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{13}\text{ClFN}_3\text{ONa}$ 388.0628, found 388.0621.

N-(imidazo[1,2-*a*]pyridin-8-yl)-3-phenylthiophene-2-carboxamide (**6j**) : Following the general procedure B, **6j** was



obtained after purification by Combiflash column chromatography using silica gel column (20-60% ethyl acetate/hexane) as a off white solid: mp 138-140 °C; yield 66%

(42.2 mg); R_f = 0.5 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm):

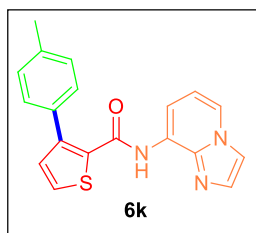
δ 6.85 (t, J = 7.1 Hz, 1H), 7.26 (t, J = 5.0 Hz, 1H), 7.35 (s, 1H), 7.39-7.47 (m, 3H), 7.54-

7.56 (m, 2H), 7.88-7.93 (m, 3H), 8.24 (d, J = 6.7 Hz, 1H), 9.05 (s, 1H); ^{13}C NMR (100

MHz, DMSO- d_6 , ppm): δ 110.0, 112.0, 114.3, 121.9, 126.3, 128.3, 128.8, 129.0, 130.0, 131.1, 131.7, 132.7, 134.3,

138.1, 143.2, 160.6; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{18}\text{H}_{13}\text{N}_3\text{OSNa}$ 342.0676, found 342.0671.

N-(imidazo[1,2-*a*]pyridin-8-yl)-3-(*p*-tolyl)thiophene-2-carboxamide (**6k**) : Following the general procedure B, **6k**



was obtained after purification by Combiflash column chromatography using silica gel

column (20-60% ethyl acetate/hexane) as a off white solid: mp 104–106 °C; yield 57%

(38.0 mg); R_f = 0.5 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6 , ppm):

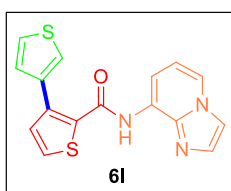
δ 2.35 (s, 3H), 6.85 (t, J = 7.0 Hz, 1H), 7.27-7.22 (m, 3H), 7.35 (s, 1H), 7.42 (d, J = 7.8

Hz, 2H), 7.88-7.91 (m, 3H), 8.24 (d, J = 6.6 Hz, 1H), 9.03 (s, 1H); ^{13}C NMR (100 MHz,

DMSO- d_6 , ppm): δ 20.8, 109.9, 112.1, 114.4, 121.9, 126.4, 128.6, 129.7, 130.1, 131.1, 131.3, 131.7, 132.5, 137.9,

138.1, 143.3, 160.7; HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{15}\text{N}_3\text{OSNa}$ 356.0832, found 356.0830.

N-(imidazo[1,2-*a*]pyridin-8-yl)-[3,3'-bithiophene]-2-carboxamide (**6l**) : Following the general procedure B, **6l** was



obtained after purification by Combiflash column chromatography using silica gel

column (20-60% ethyl acetate/hexane) as a grey solid: mp 159–161 °C; yield 63% (41.0

mg); R_f = 0.5 (ethyl acetate/hexane (40/60)); ^1H NMR (400 MHz, DMSO- d_6): δ 6.87 (t, J

= 7.1 Hz, 1H), 7.29 (d, J = 5.0 Hz, 1H), 7.34 (d, J = 4.8 Hz, 1H), 7.41 (s, 1H), 7.65-7.67 (m,

1H), 7.89-7.94 (m, 4H), 8.27 (d, J = 6.7 Hz, 1H), 9.29 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 110.2, 112.1,

114.4, 121.9, 125.3, 126.4, 127.5, 128.0, 129.9, 131.0, 131.8, 132.5, 134.3, 137.6, 138.3, 160.7; HRMS (ESI) m/z

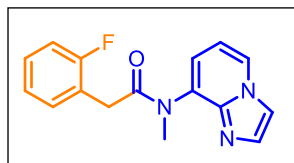
$[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{11}\text{N}_3\text{OS}_2\text{Na}$ 348.0240, found 348.0236.

Experimental procedure for the preparation of 2-(2-fluorophenyl)-*N*-(imidazo[1,2-*a*]pyridin-8-yl)-*N*-methylacetamide (7a**):** In 25 ml round bottomed flask, **1a** (1 mmol, 269 mg) was dissolved in dry DMF (5 ml) and

1.5 equiv of NaH was added into the reaction mixture. Afterwards, 2.5 equiv of MeI was added dropwise into the reaction mixture at 0° C and then stirred at room temperature for 2 hr. After the completion of the reaction via TLC chromatography, 20 ml water was added and the product was extracted with ethyl acetate (4 X 10 ml). Organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude product was then purified using column chromatography using 10-50% ethylacetate/hexane as eluent.

2-(2-fluorophenyl)-N-(imidazo[1,2-a]pyridin-8-yl)-N-methylacetamide: (7a)

Yield = 75% (212.5 mg), white brown solid, melting point: 103-105 °C; ¹H NMR (400 MHz, CDCl₃): δ 3.25 (s,



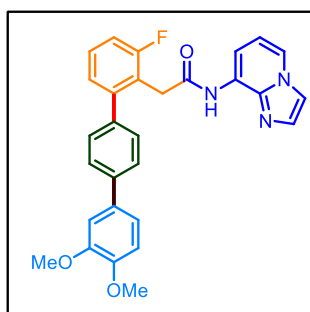
3H), 3.49-3.53 (m, 2H), 6.94 (t, *J* = 6.9Hz, 1H), 7.05-7.07 (m, 1H), 7.15 (s, 1H), 7.22 (d, *J* = 6.2Hz, 1H), 7.31 (d, *J* = 6.0Hz, 1H), 7.62 (s, 1H), 8.06 (s, 1H), 8.54 (d, *J* = 6.4Hz, 1H), ¹³C NMR (100MHz, CDCl₃) : δ 33.3, 36.0, 111.6, 114.4, 114.6, 114.8,

122.8 (*J*_{C-F} = 15.8 Hz), 123.2, 123.8 (2C), 126.8, 128.4 (*J*_{C-F} = 8.1Hz), 131.5, 131.6 (*J*_{C-F} = 4.4Hz), 133.1, 141.6, 160.4 (*J*_{C-F} = 242.7Hz), 169.2.

Experimental procedure for the preparation of 2-(3-fluoro-3',4"-dimethoxy-[1,1':4',1"-terphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)-acetamide (8d):

To a stirred solution of 2-(4'-bromo-3-fluoro-[1,1'-biphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (50 mg, 0.118 mmol) in THF (0.9 mL) and water (0.3 mL) in a sealed tube was degassed by vacuum/N₂ backfill cycle (repeated for two times). To this reaction mixture, Pd(dppf)Cl₂ (8.6 mg, 0.0118 mmol), K₂CO₃ (40.7 mg, 0.295 mmol) and (3,4-dimethoxyphenyl)boronic acid (32.2 mg, 0.177 mmol) was added and again degassed by vacuum/N₂ backfill cycle for two times. Then reaction mixture was heated at 90° C for 3 h. After completion of the reaction (monitored by TLC), reaction mixture was filtered through celite bed and bed was washed with ethyl acetate. Filtrate was concentrated under reduced pressure to obtain crude which was purified in Combiflash column chromatography using 4 gm silica gel column and ethyl acetate/hexane as eluent. Fraction eluted with 40% ethyl acetate/hexane was concentrated to obtain 2-(3-fluoro-3',4"-dimethoxy-[1,1':4',1"-terphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)acetamide (**8d**) as white solid (41.5 mg, 73%). R_f = 0.4 (hexane/ethyl acetate 70/30).

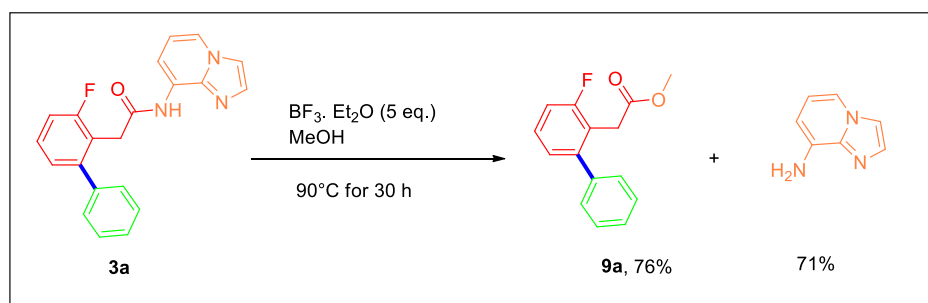
2-(3-fluoro-3',4"-dimethoxy-[1,1':4',1"-terphenyl]-2-yl)-N-(imidazo[1,2-a]pyridin-8-yl)-acetamide (8d):



melting point: 124-126; ¹H NMR (400 MHz, DMSO-d₆): δ 3.78 (s, 3H), 3.83 (s, 3H), 3.95 (s, 2H), 6.84 (t, *J* = 7.2Hz, 1H), 7.01 (d, *J* = 8.4Hz, 1H), 7.18-7.27 (m,

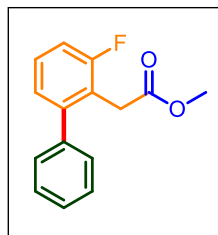
4H), 7.41-7.45 (m, 3H), 7.55 (s, 1H), 7.72 (d, $J = 8.2\text{Hz}$, 2H), 7.96 (s, 1H), 7.97 (d, $J = 8.0\text{Hz}$, 1H), 8.26 (d, $J = 6.5\text{Hz}$, 1H), 10.21 (s, 1H), ^{13}C NMR (100MHz, DMSO- d_6): δ 34.5, 55.4, 55.4, 110.2, 110.5, 112.1 ($J_{\text{C-F}} = 16.0\text{Hz}$), 113.9 ($J_{\text{C-F}} = 22.0\text{Hz}$), 114.4, 118.7, 120.8 ($J_{\text{C-F}} = 16.0\text{Hz}$), 121.5, 125.5, 126.1, 127.3, 128.4 ($J_{\text{C-F}} = 9.2\text{Hz}$), 129.2, 131.5, 132.1, 137.8 (2C), 138.5, 139.3, 144.0 (2C), 148.5, 149.0, 161.3 ($J_{\text{C-F}} = 242.6\text{Hz}$), 169.8. ^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): -114.4. HRMS (ESI) m/z $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{29}\text{H}_{24}\text{FN}_3\text{O}_3\text{Na}$ 504.1699, found 504.1695.

Experimental procedure for the removal of 8-AIP auxiliary:



To a stirred solution of 2-(3-fluoro-[1,1'-biphenyl]-2-yl)-*N*-(imidazo[1,2-*a*]pyridin-8-yl)acetamide (**3a**, 50 mg, 0.14 mmol, 1 equiv) in MeOH (1.5 mL) in a screw cap reaction vial was added $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (0.09 mL, 0.724 mmol, 5 equiv) at 25 °C and the reaction mixture was heated at 90 °C for 30 h. After completion of the reaction (monitored by TLC), the reaction mixture was neutralized with Et_3N and evaporated to obtain crude which was purified by Combiflash column chromatography using 4 gm silica gel column and ethyl acetate/hexane as eluent. Fraction eluted with 10% ethyl acetate/hexane was concentrated under reduced pressure to afford methyl 2-(3-fluoro-[1,1'-biphenyl]-2-yl)acetate as gummy liquid (26.0 mg, 76% yield): $R_f = 0.5$ (hexane/ethyl acetate 80/20) and fraction eluted with ethyl acetate was concentrated to obtain imidazo[1,2-*a*]pyridin-8-amine (13.7 mg, 71%) as light brown solid.

Methyl-2-(3-fluoro[1,1'-biphenyl]-2-yl)-acetate (**9a**):



Yield = 76% (26.9 mg), mp: ^1H NMR (400 MHz, CDCl_3): δ 3.61 (s, 2H), 3.65 (s, 3H), 7.05-7.10 (m, 2H), 7.25-7.32 (m, 3H), 7.36-7.42 (m, 3H), ^{13}C NMR (100MHz, CDCl_3): δ 32.2, 52.1, 114.0, 114.2, 119.8, 120.0, 125.5, 126.0, 127.6, 128.2, 128.3, 129.0, 139.7, 139.8, 144.6 (2C), 161.6 ($J_{\text{C-F}} = 240.\text{Hz}$), 171.5; ^{19}F NMR (376.5 MHz, DMSO- d_6 , ppm): -115.0.

Experimental procedure for intermolecular competition experiment:

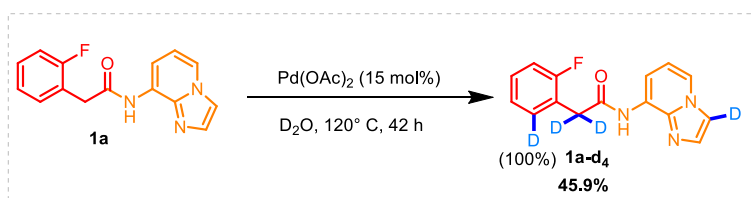
A screw cap vial was charged with an appropriate amide **1a** (0.20 mmol, 1 equiv) in water (4 mL), 4-iodo anisole and 4-iodo bromobenzene (0.4 mmol, 2 equiv), K_2CO_3 (0.5 mmol, 2.5 equiv) at room temperature followed by the addition of $Pd(OAc)_2$ (0.03 mmol, 15 mol %). The resulting suspension was heated at 120° C in an oil bath for 15 h. After completion, the reaction mixture was cooled to room temperature and filtered through celite bed and bed was washed with ethyl acetate. Then, aqueous layer was extracted with ethyl acetate. Combined organic layer was washed with brine solution, dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure to obtain crude product. The crude material was purified by Combiflash column chromatography (silica gel) using hexane/ethyl acetate mixture as an eluent to afford the desired arylated product **3c** (60%, 45.0 mg) and **3f** (40%, 33.0 mg) yields respectively.

Experimental procedure for radical quenching experiments:

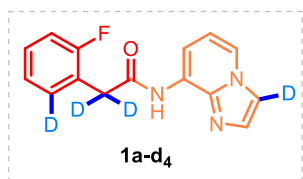
A screw cap vial was charged with an appropriate amide **1a** (0.20 mmol, 1 equiv) in water (4 mL), iodo arene (0.4 mmol, 2 equiv), K_2CO_3 (0.5 mmol, 2.5 equiv) at room temperature followed by the addition of $Pd(OAc)_2$ (0.03 mmol, 15 mol % equiv) and radical scavengers (BHT/ $Ph_2C=CH_2$, 3 equiv, 0.60 mmol). The resulting suspension was heated at 120° C in an oil bath for 18 h. After completion, the reaction mixture was cooled to room temperature and filtered through celite bed and bed was washed with ethyl acetate. Then, aqueous layer was extracted with ethyl acetate. Combined organic layer was washed with brine solution, dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure to obtain crude product. The crude material was purified by Combiflash column chromatography (silica gel) using hexane/ethyl acetate mixture as an eluent to afford the desired arylated product **3a** (67%, 46.2 mg) and (64%, 44.1 mg) yields respectively.

Experimental procedure for the preparation of **1a-d₄**:

H-D exchange study

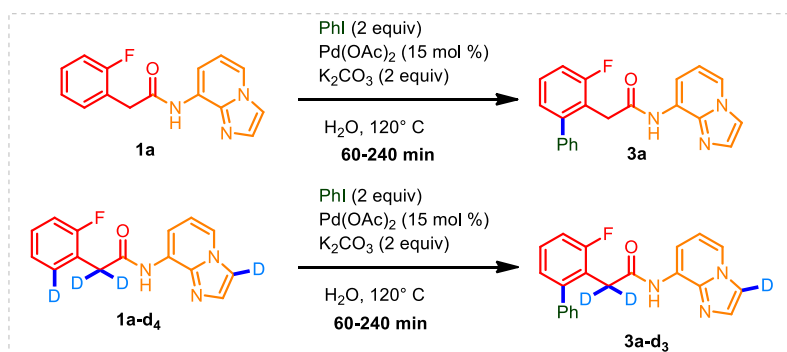


107.7 mg (0.4 mmol) starting amide (**1a**) and 13.5 mg, 0.06 mmol Pd(OAc)₂ and 4 mL D₂O was heated at 120° C in a sealed tube for 42 h. Then, the reaction mixture was cooled to room temperature and extracted with EtOAc. Afterwards, the organic layer was dried over Na₂SO₄, filtered and concentrated under reduced pressure to obtain crude product. The, crude reaction mixture was purified in Combiflash using EtOAc/Hexane as eluent. Pure fraction eluted with 30% EtOAc to obtain the desired 1a-d₄ product as off white solid, 64 mg (45.9%).



off white solid; melting point: 95-97° C, ¹H NMR (400 MHz, DMSO-d₆, ppm): δ 6.83 (t, *J* = 7.0 Hz, 1H), 7.16-7.21 (m, 2H), 7.30-7.35 (m, 1H), 7.57 (s, 1H), 7.92 (d, *J* = 7.4Hz, 1H), 8.26 (d, *J* = 6.6Hz, 1H), 10.16 (s, 1H); ¹⁹F NMR (376.5 MHz, DMSO-d₆, ppm): δ -117.0; HRMS (ESI) *m/z* [M+H]⁺calcd for C₁₅H₉D₄FN₃O 274.1293, found 274.1292.

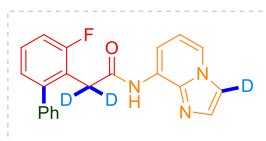
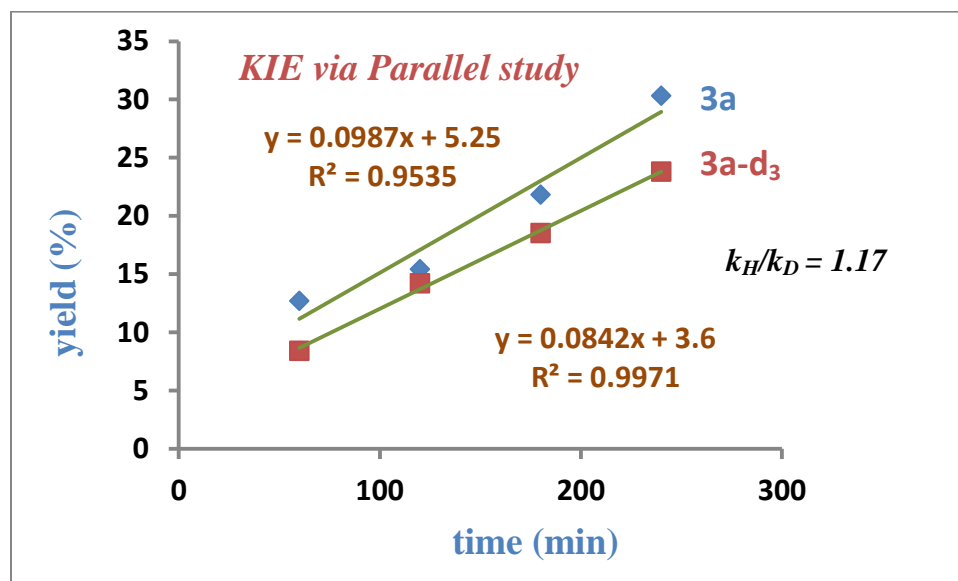
Kinetic Isotope effect *via* Parallel Study



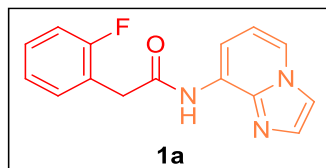
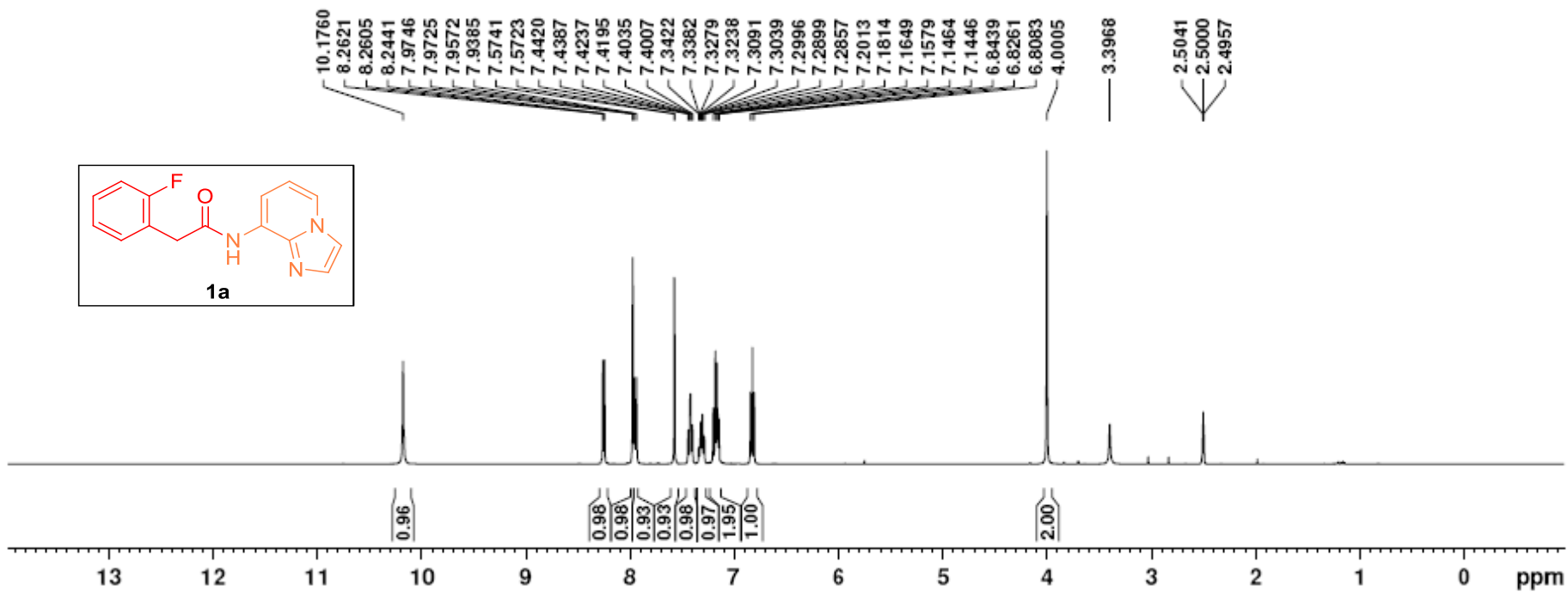
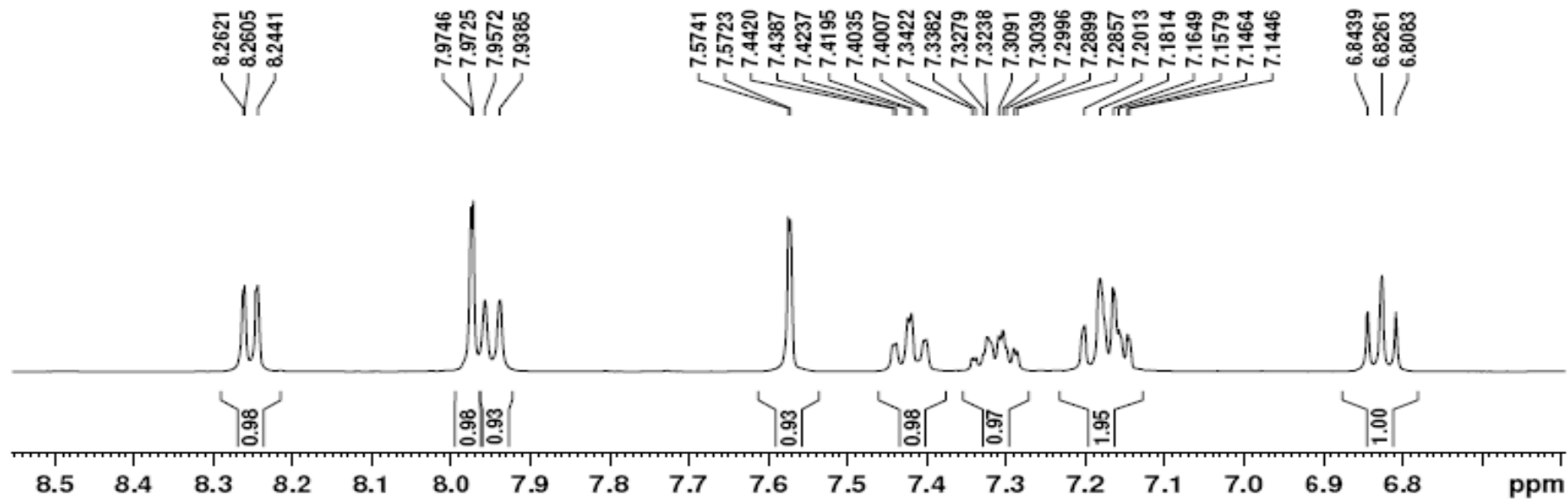
$$KIE = k_H/k_D = 1.17$$

8-AIP substituted amide (**1a**) and deuterated 8-AIP substituted amide (**1a-d₄**) were independently reacted with iodobenzene for four different time intervals (1-4 h) under the standard reaction conditions. The product distributions (**3a/ 3a-d₃**) were analyzed from the workup crude reaction mixture by LCMS analysis.

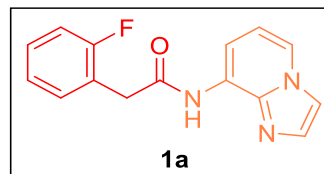
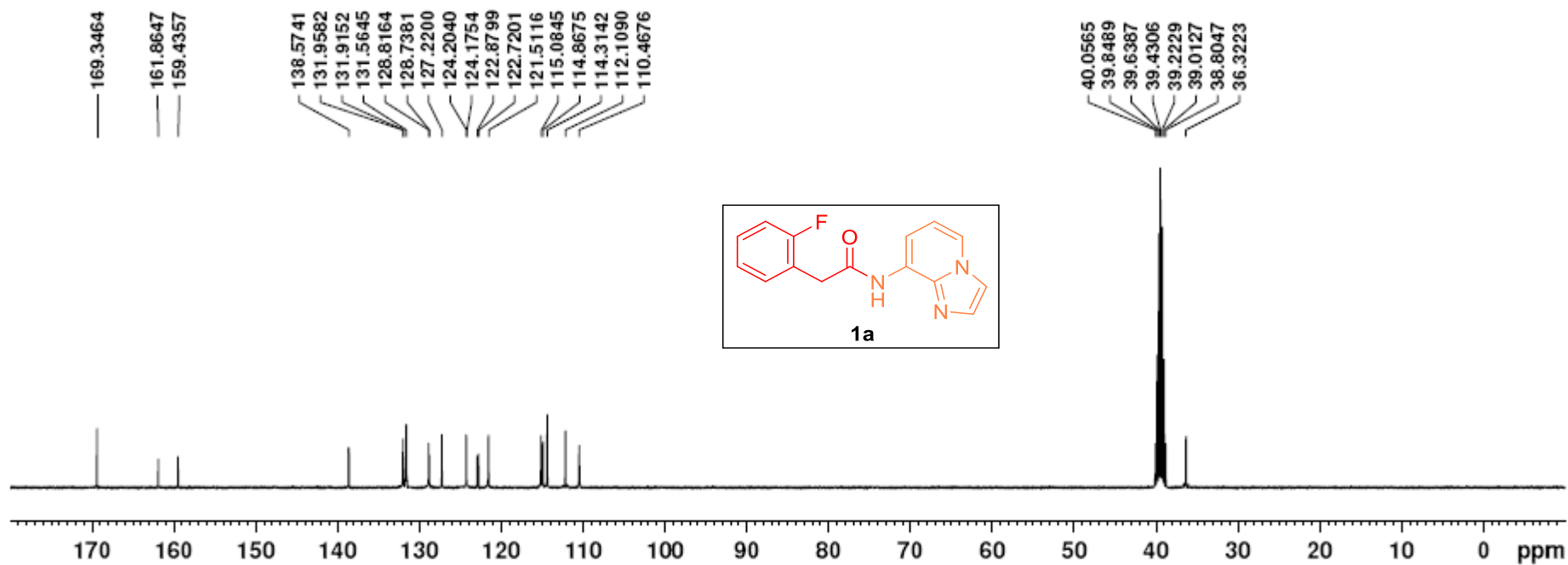
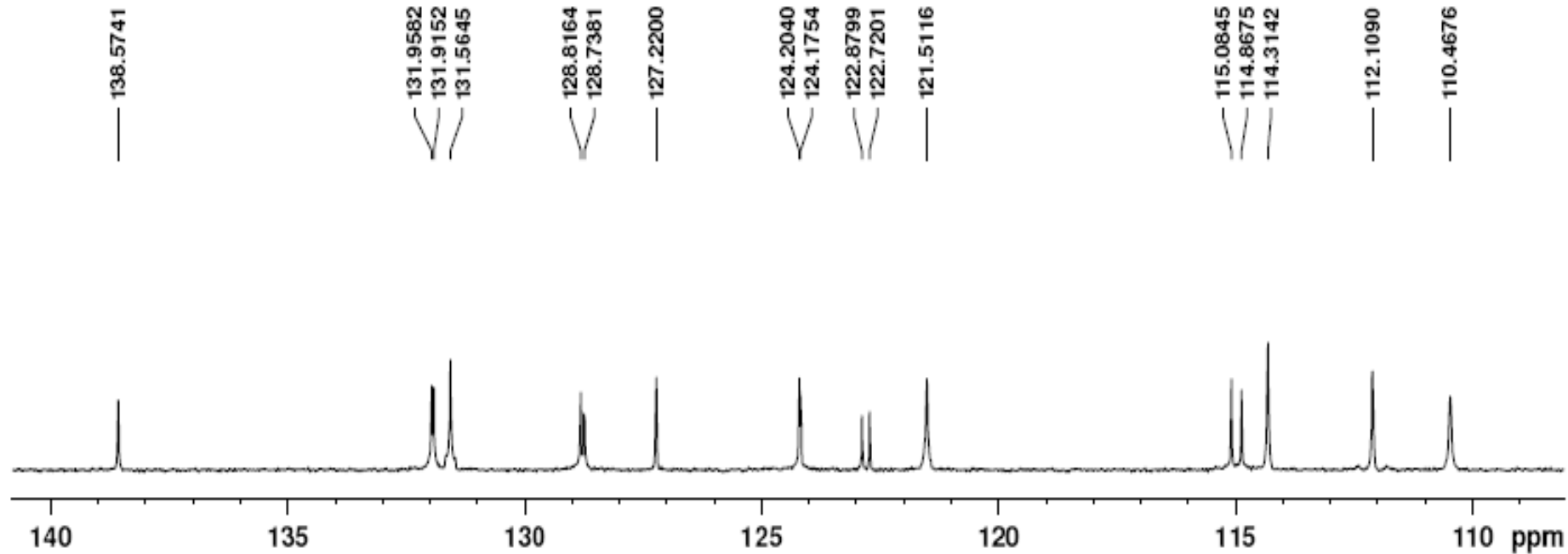
time (min)	60	120	180	240
3a (yield; %)	12.7	15.4	21.8	30.3
3a-d₃ (yield; %)	8.4	14.2	18.5	23.8



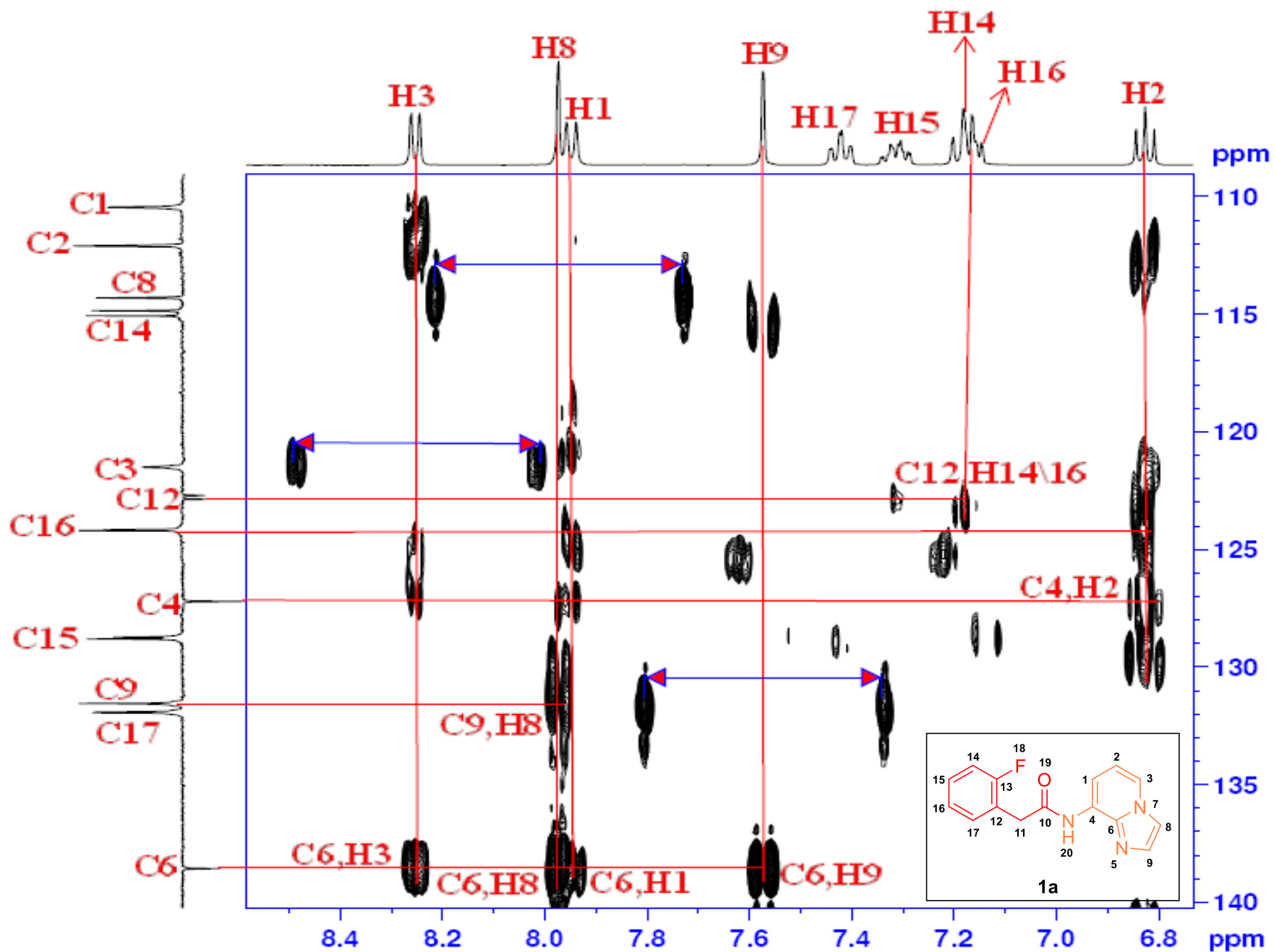
white solid; ¹H NMR (400 MHz, DMSO-d₆, ppm): δ 6.83 (t, *J* = 7.1 Hz, 1H), 7.13 (d, *J* = 8.8Hz, 1H), 7.23 (t, *J* = 9.1Hz, 1H), 7.36-7.45 (m, 6H), 7.55 (s, 1H), 7.93-7.94 (m, 1H), 8.25 (d, *J* = 6.7Hz, 1H), 10.17 (s, 1H); ¹⁹F NMR (376.5 MHz, DMSO-d₆, ppm): -114.5. HRMS (ESI) *m/z* [M+H]⁺calcd for C₂₁H₂₂D₃FN₃O 349.1544, found 349.1555.



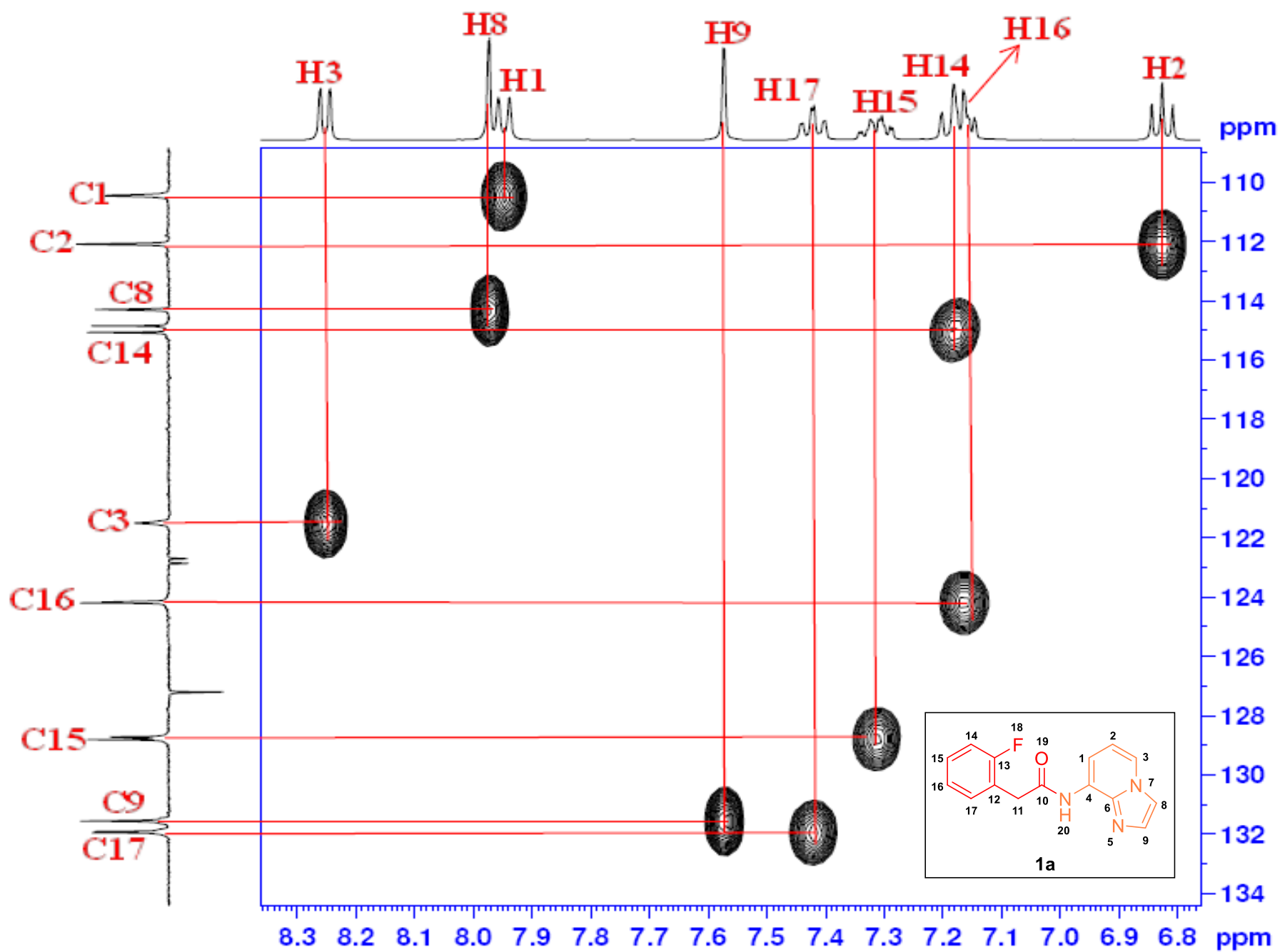
¹H NMR of **1a** in DMSO-d₆



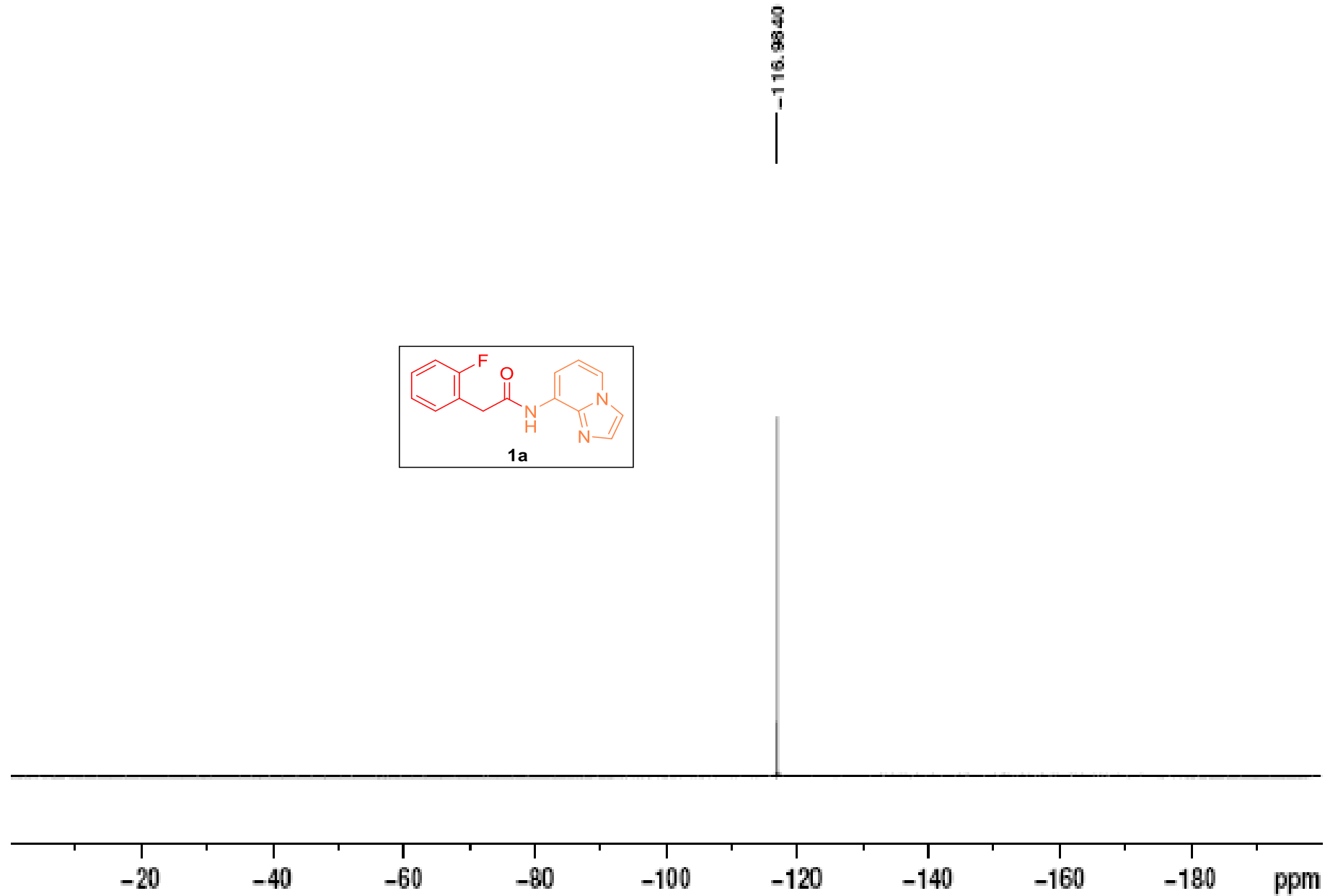
^{13}C NMR of **1a** in DMSO-d_6



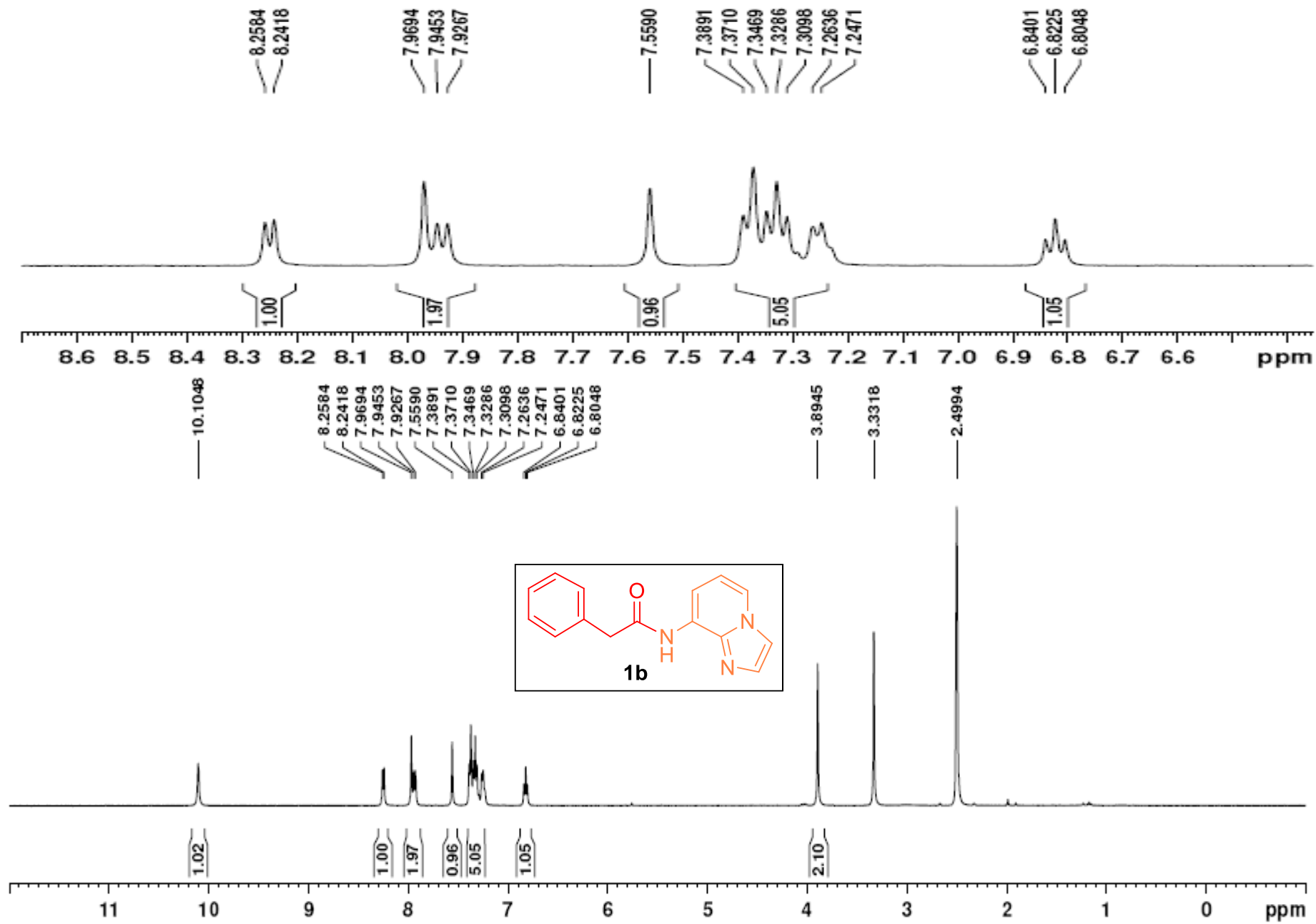
HMBC of **1a** in DMSO- d_6



HSQC of **1a** in DMSO-d₆



^{19}F NMR of **1a** in DMSO-d_6

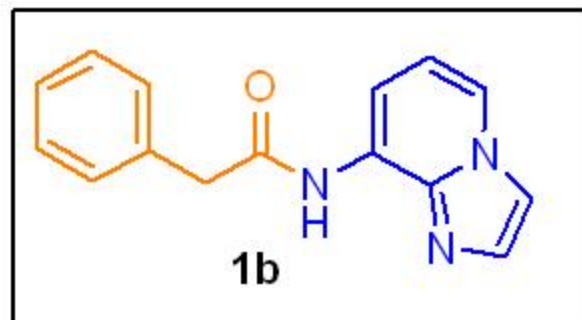


^1H NMR of **1b** in DMSO-d_6

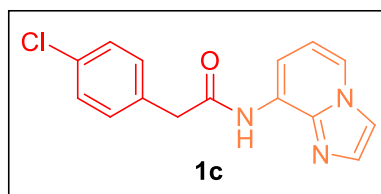
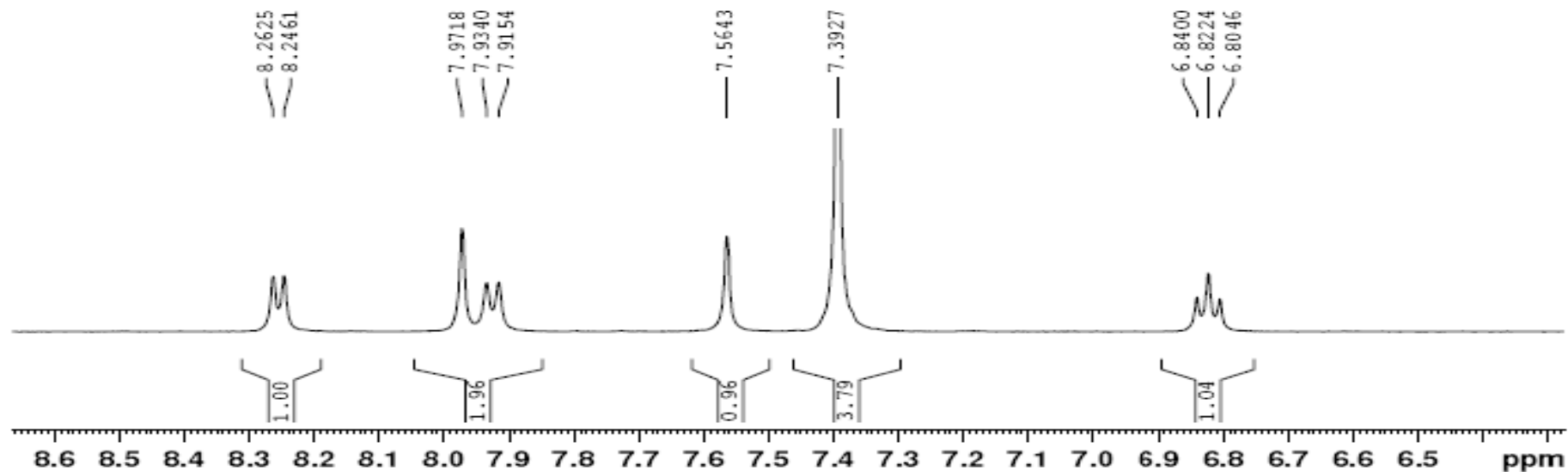
170.4142

138.5647
135.8069
131.5374
129.1714
128.2562
127.2486
126.5016
121.4880
114.3002
112.0983
110.4718

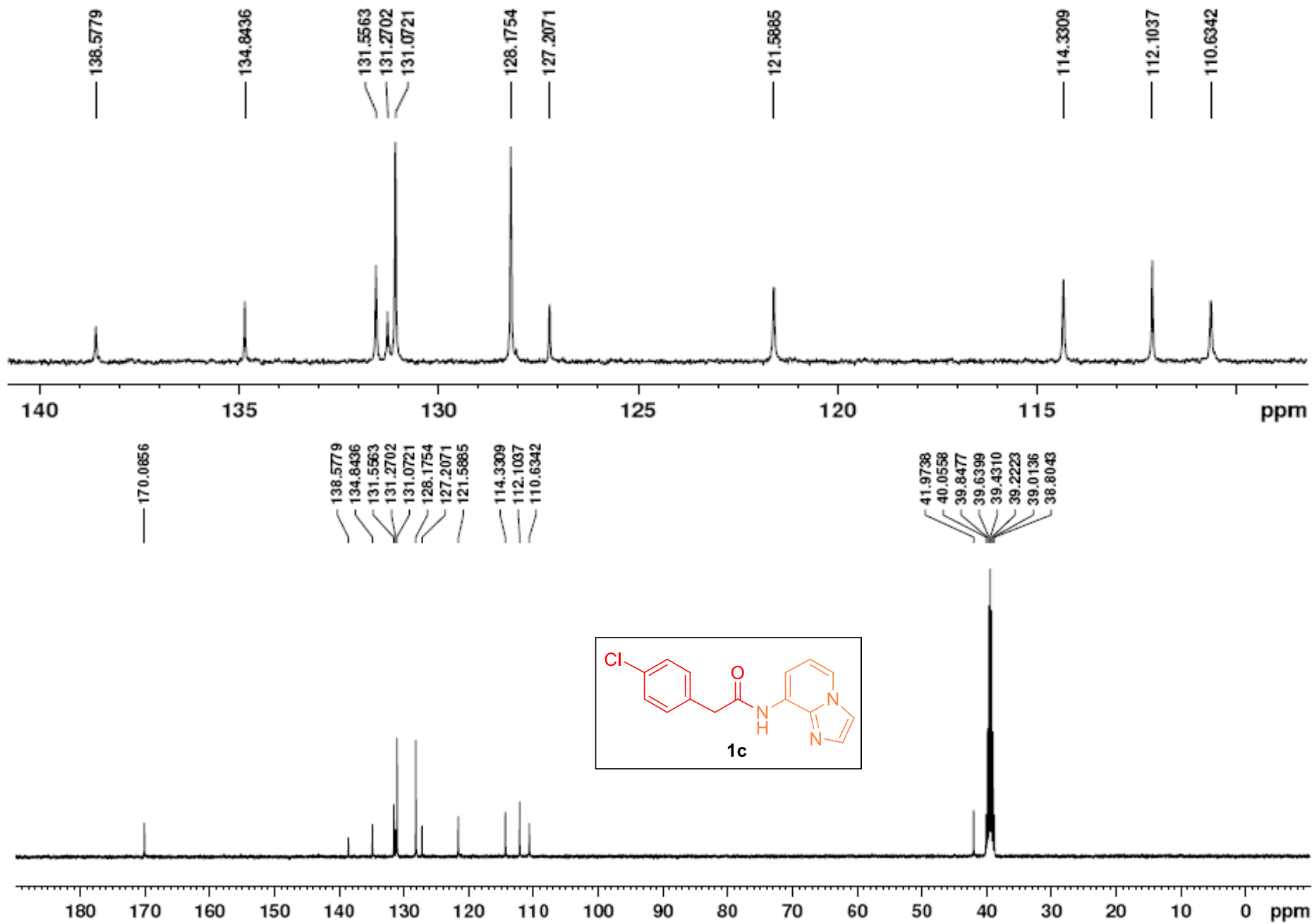
42.8474
40.0536
39.8451
39.6365
39.4279
39.2190
39.0105
38.8019



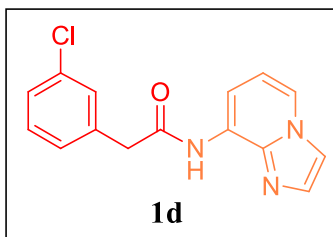
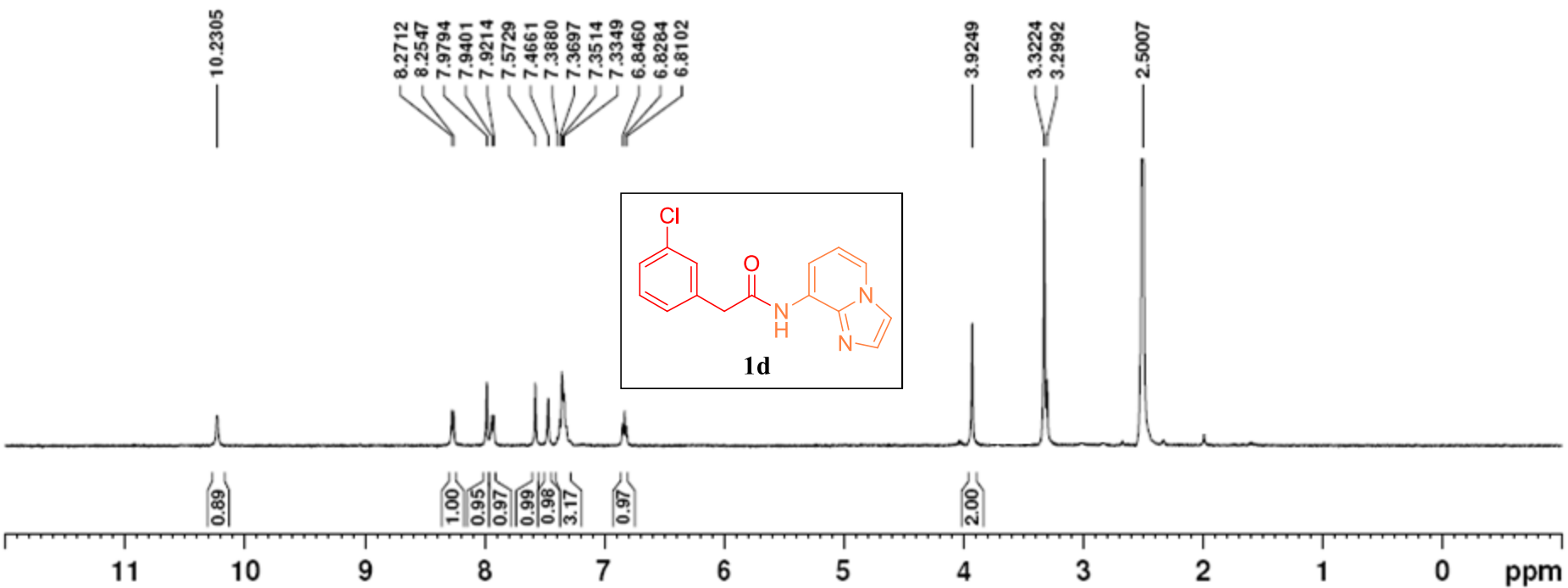
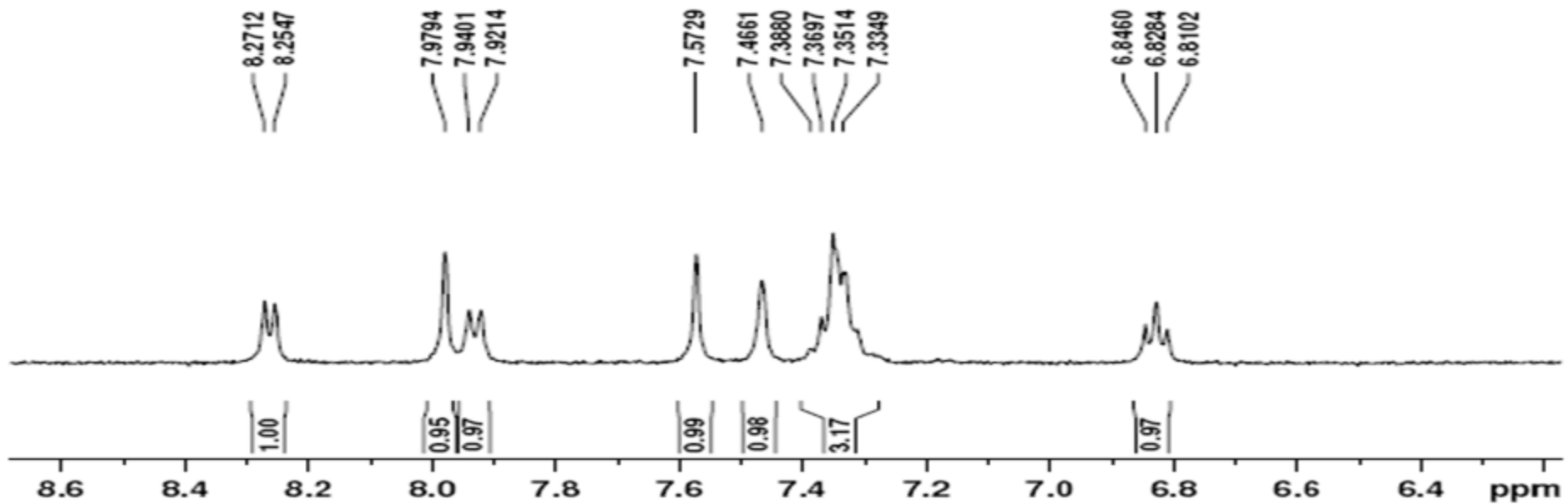
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



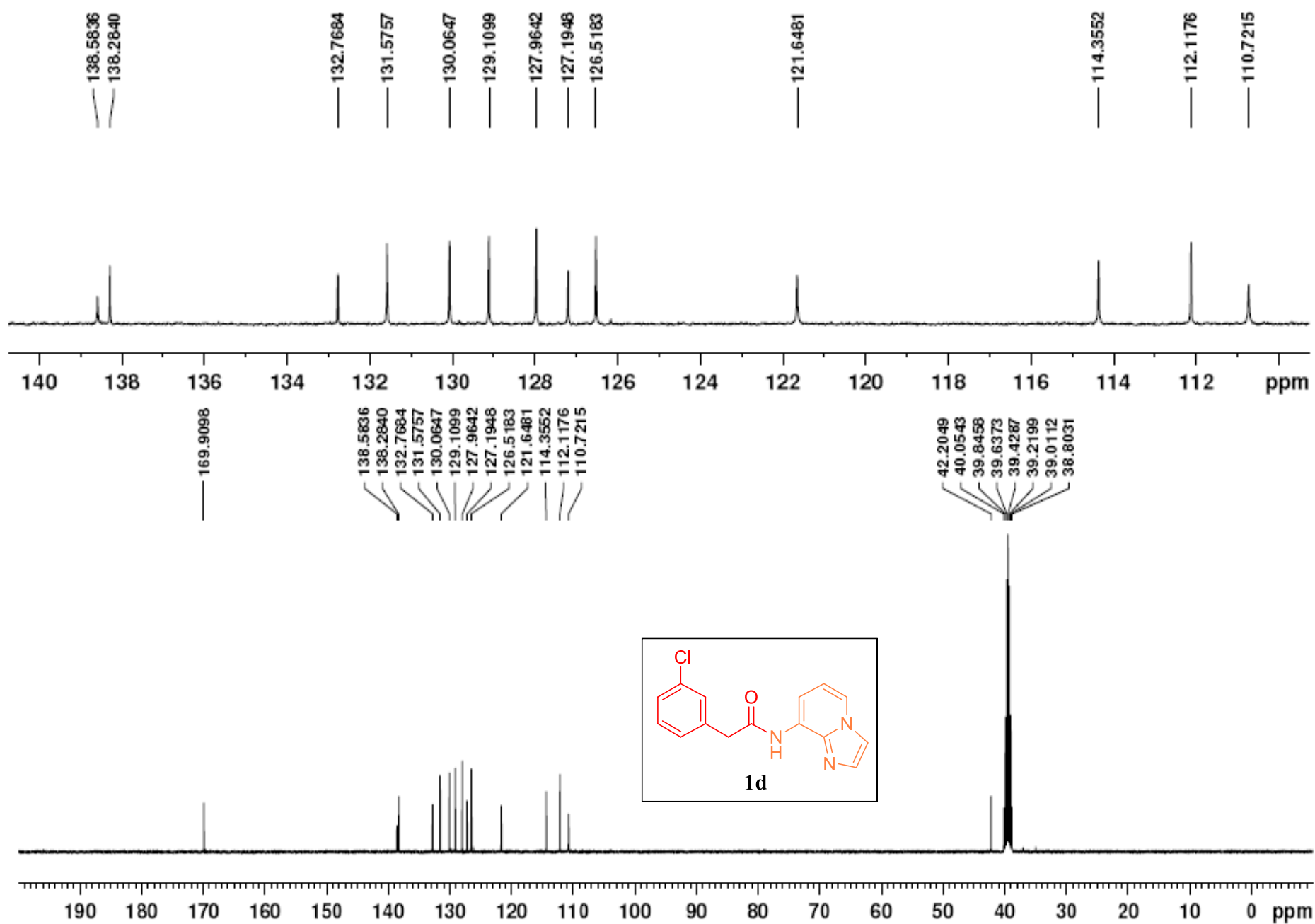
^1H NMR of **1c** in DMSO-d_6



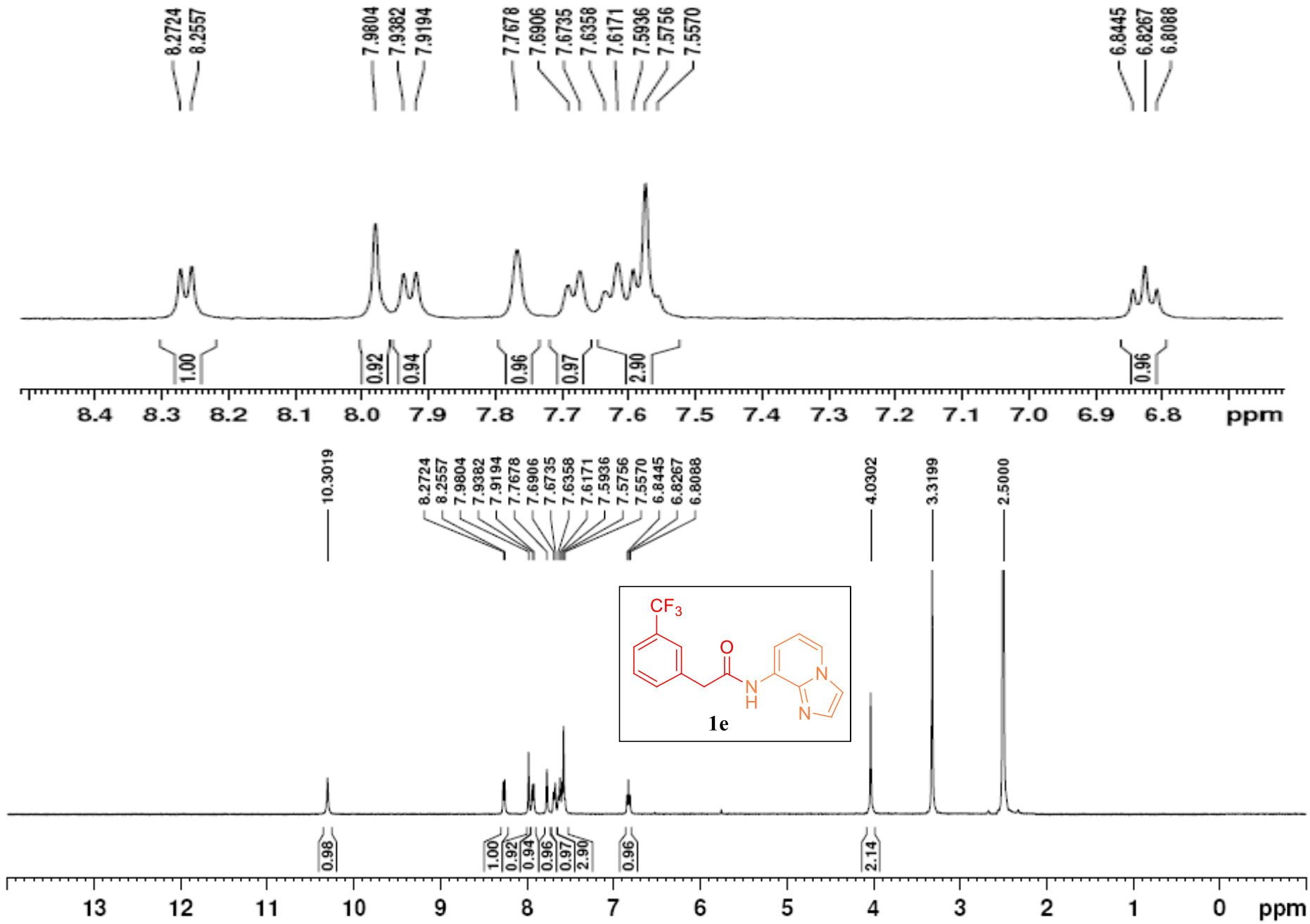
¹³C NMR of **1c** in DMSO-d₆



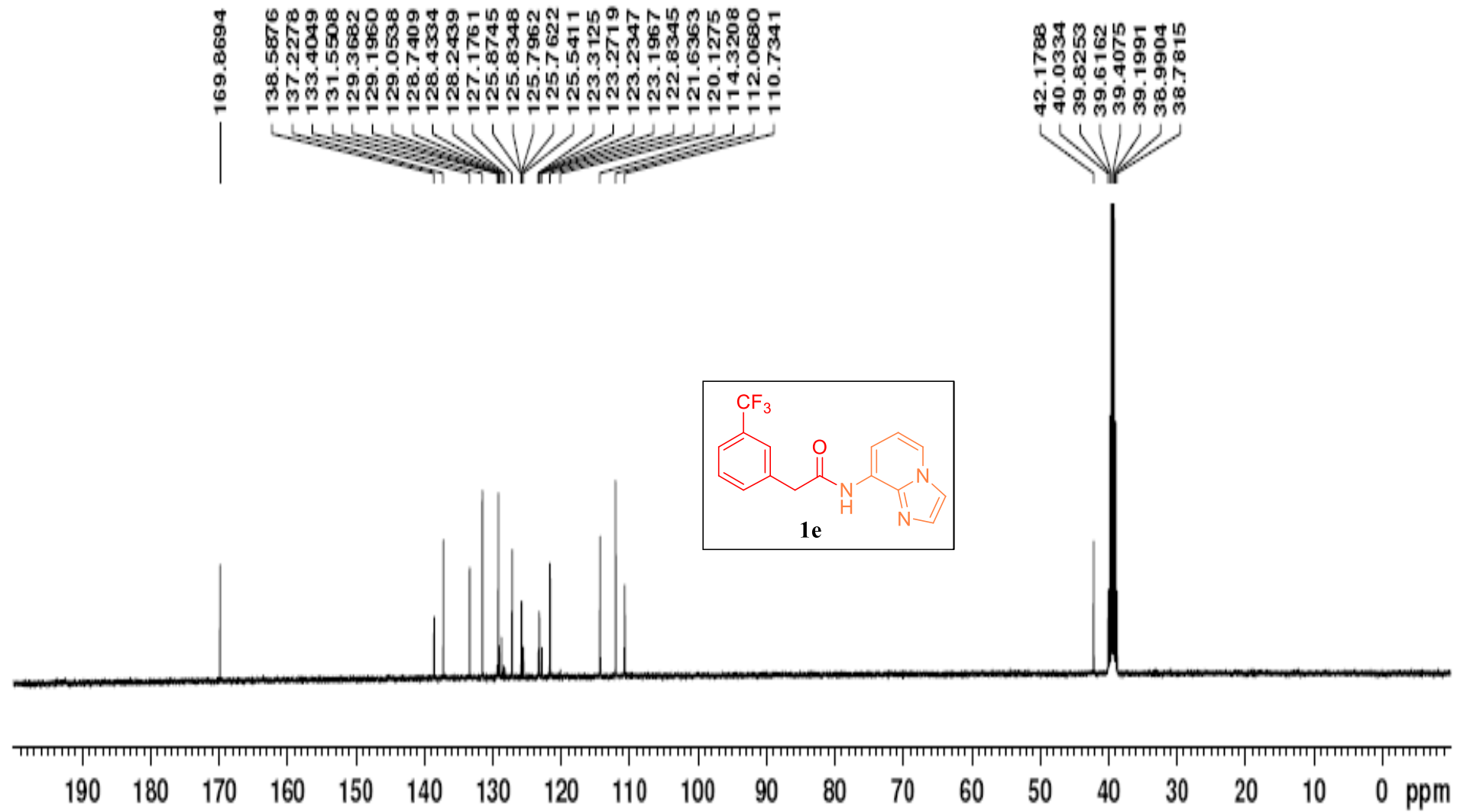
^1H NMR of **1d** in DMSO-d_6



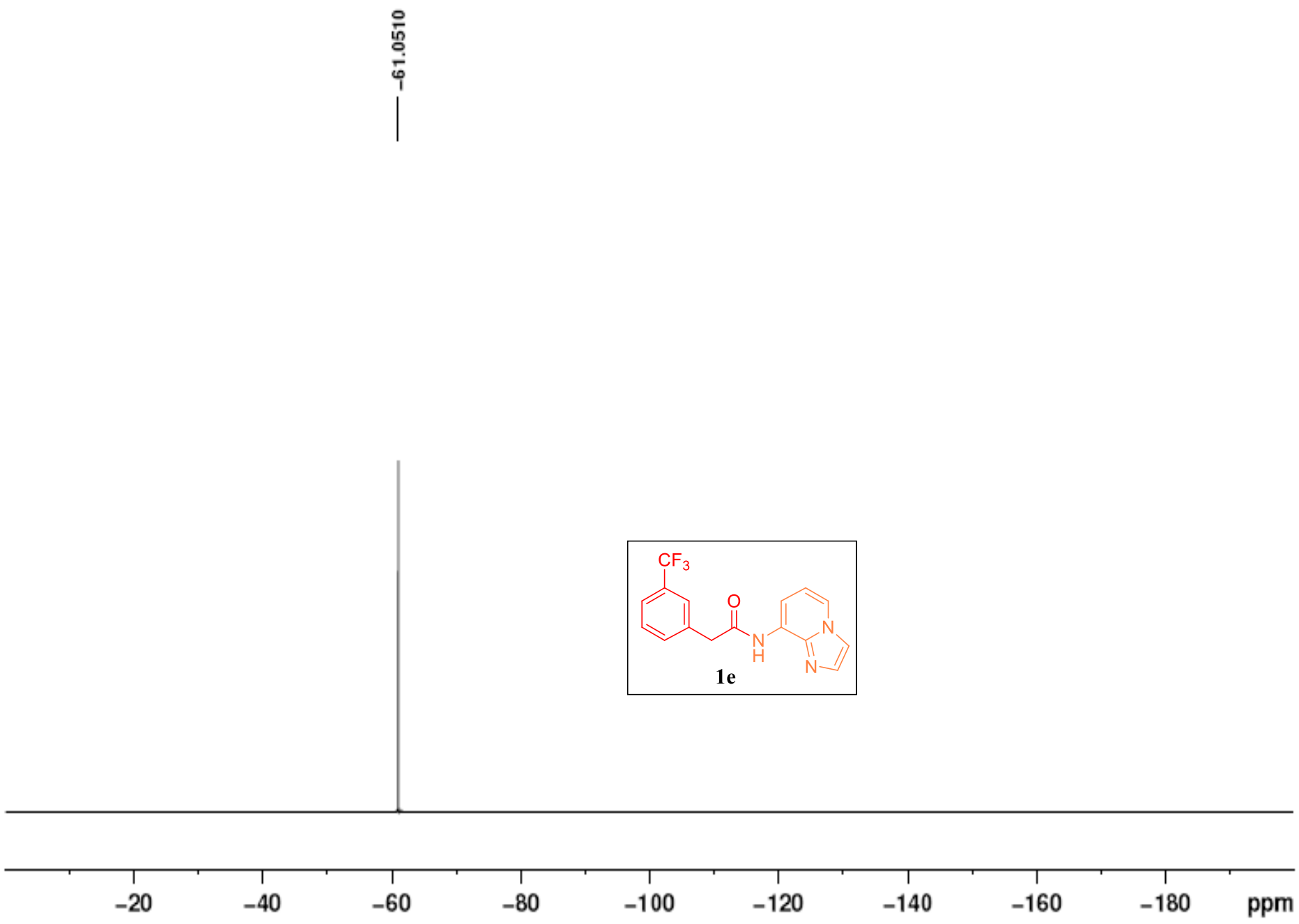
¹³C NMR of **1d** in DMSO-d₆



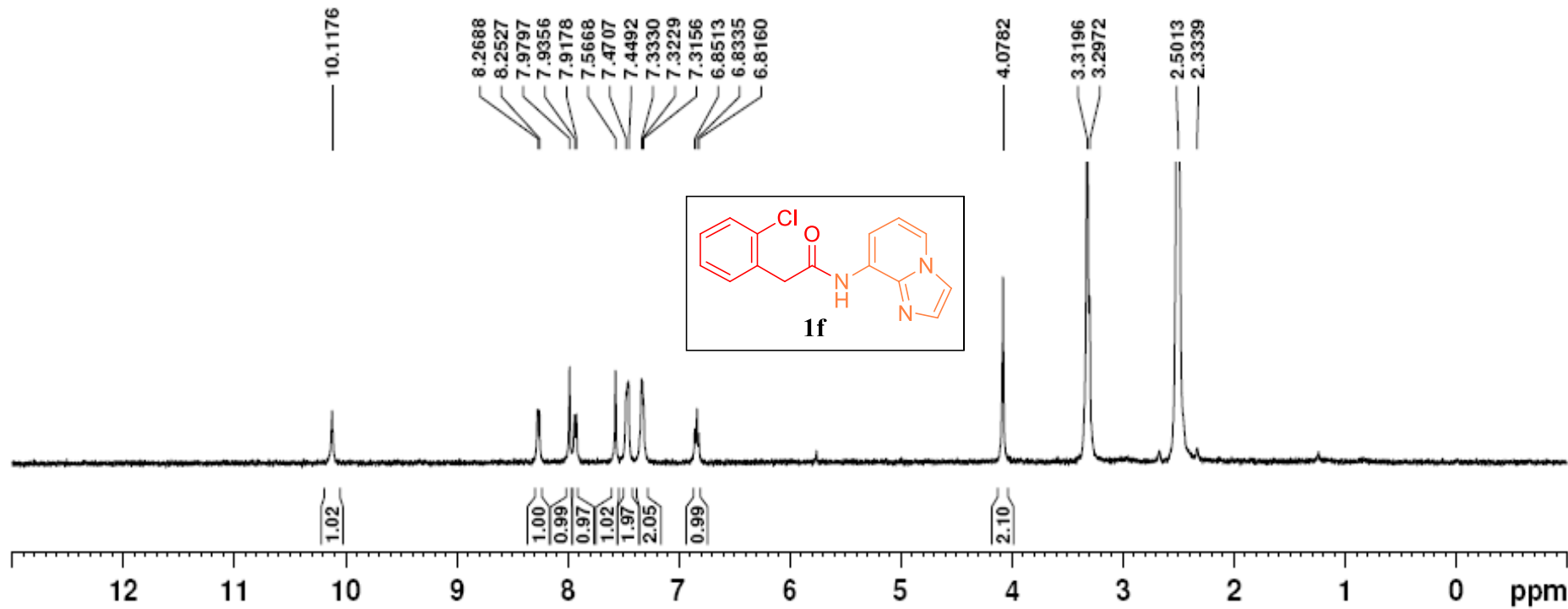
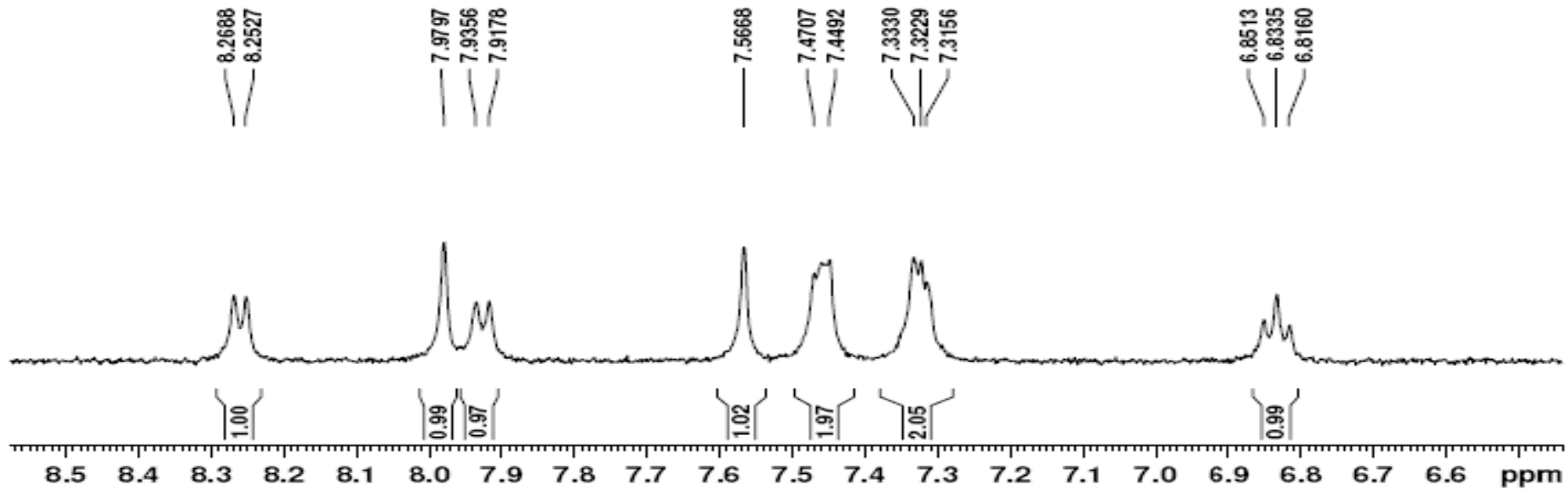
¹H NMR of **1e** in DMSO-d₆



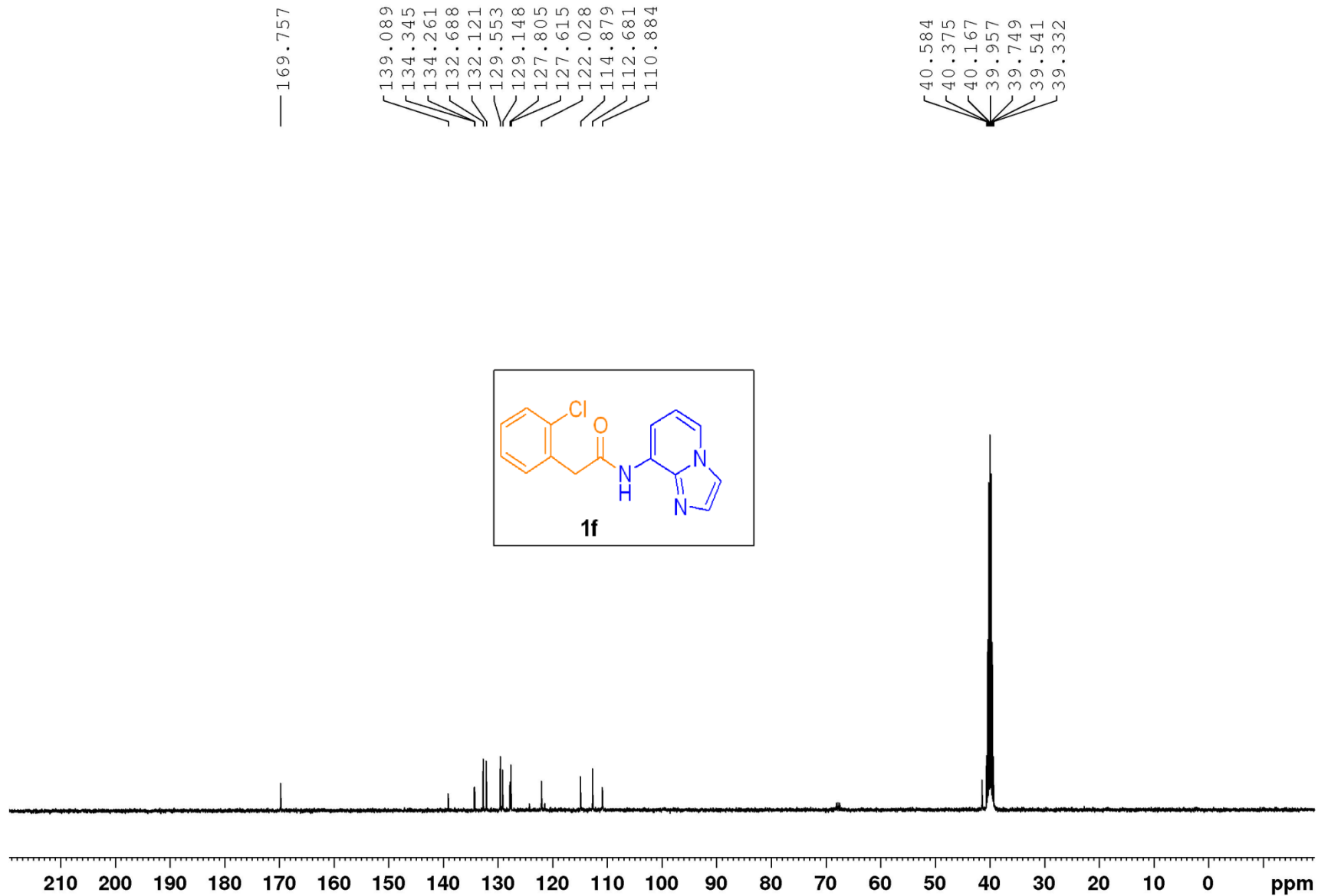
¹³C NMR of **1e** in DMSO-d₆



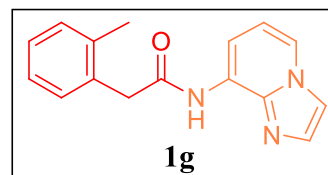
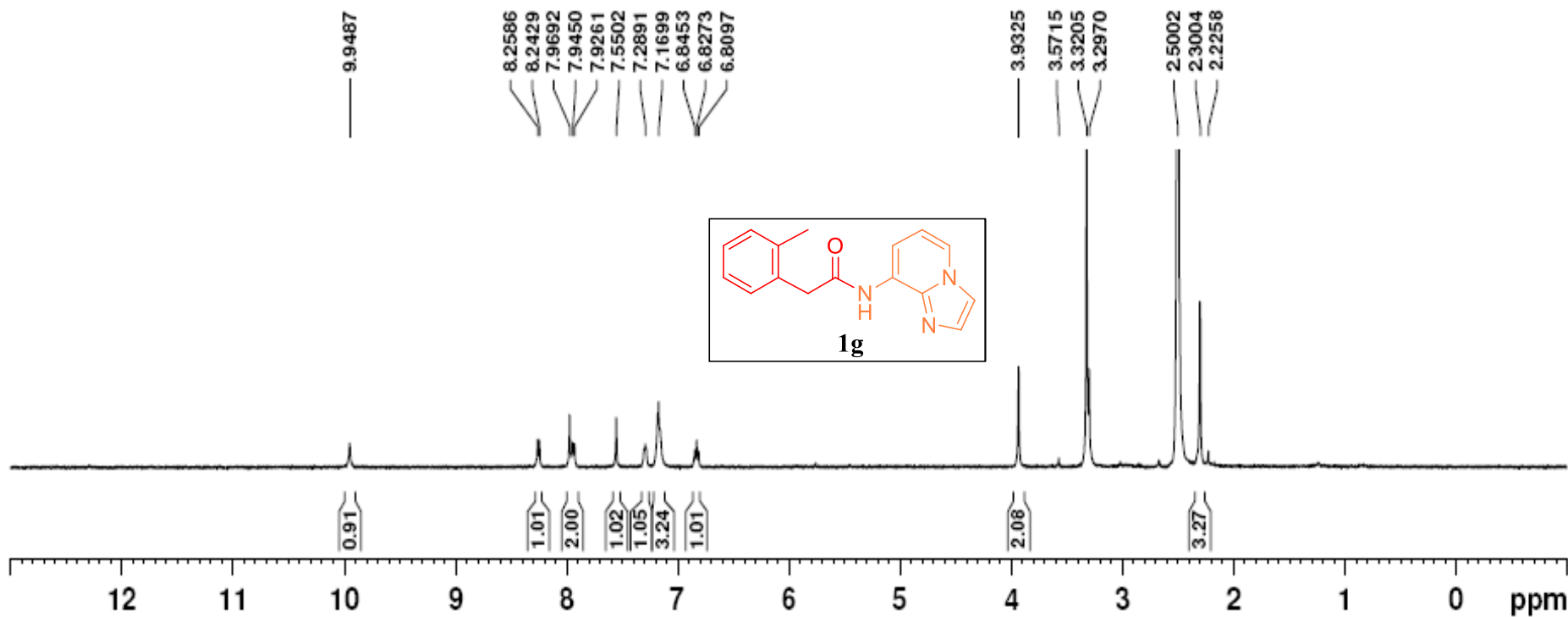
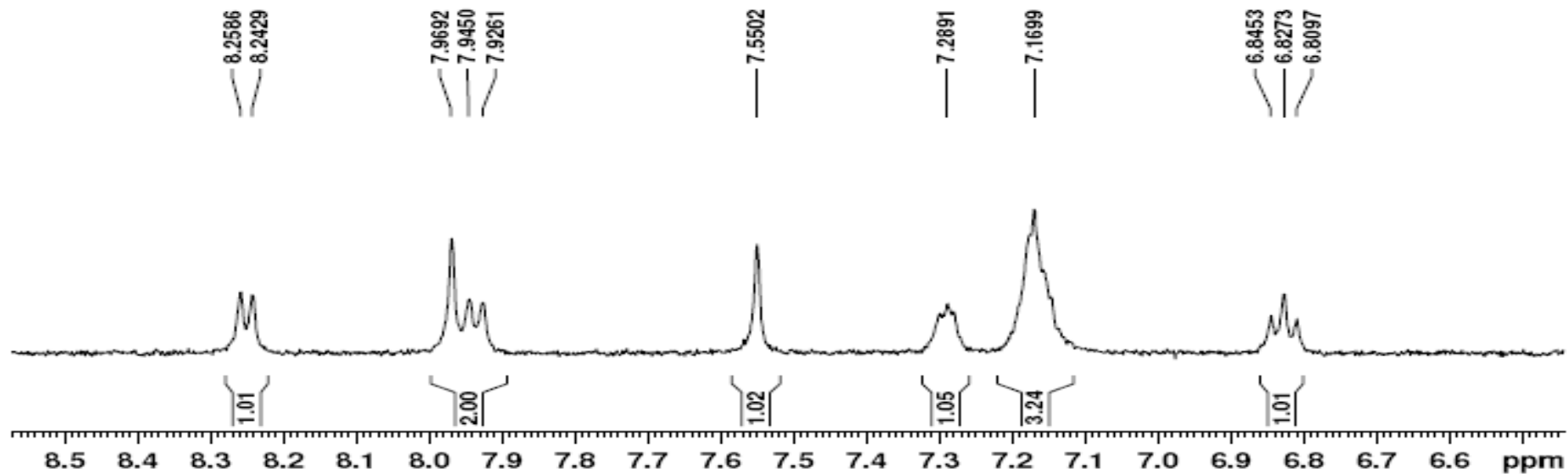
${}^{19}\text{F}$ NMR of **1e** in DMSO-d_6



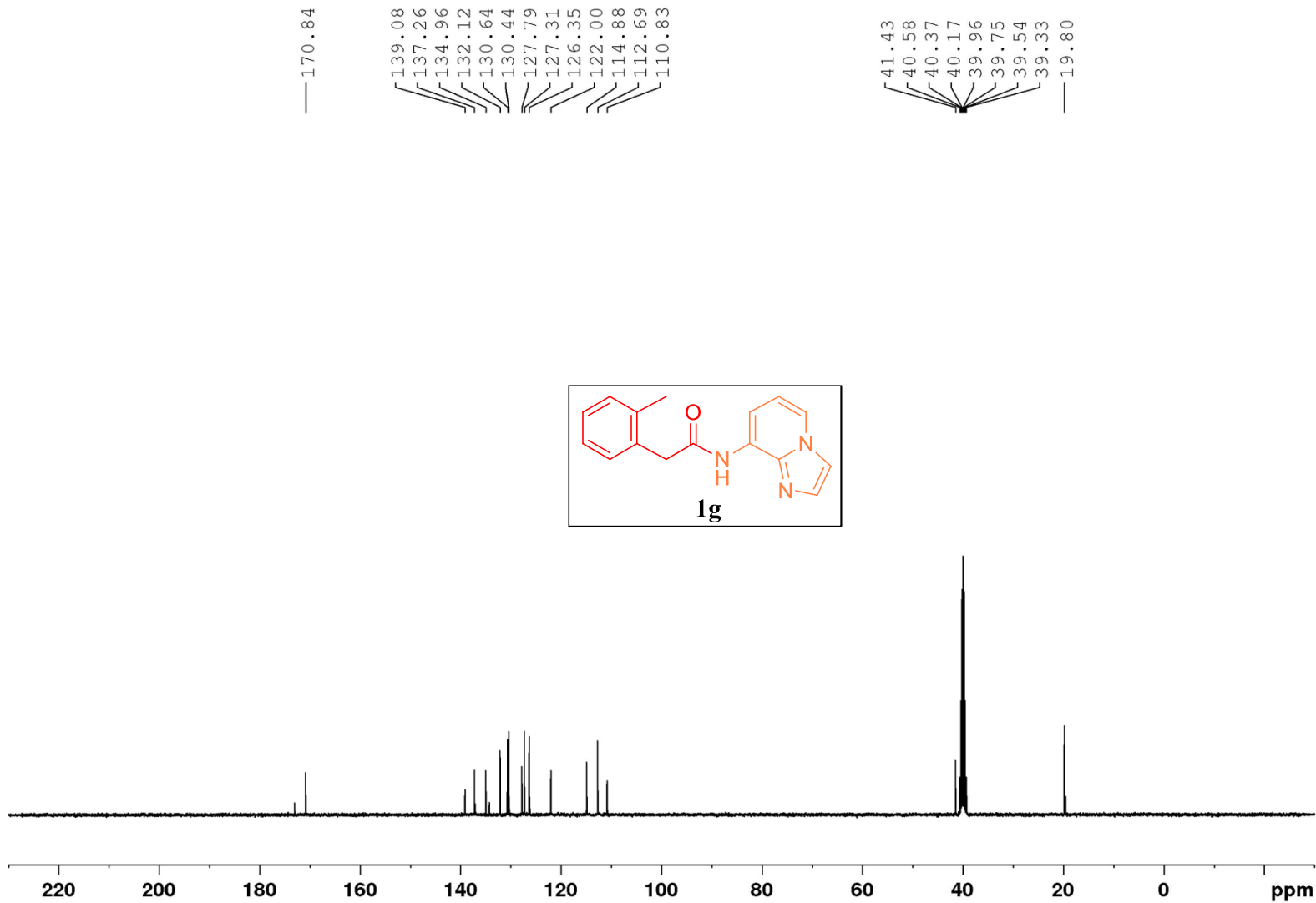
¹H NMR of **1f** in DMSO-d₆



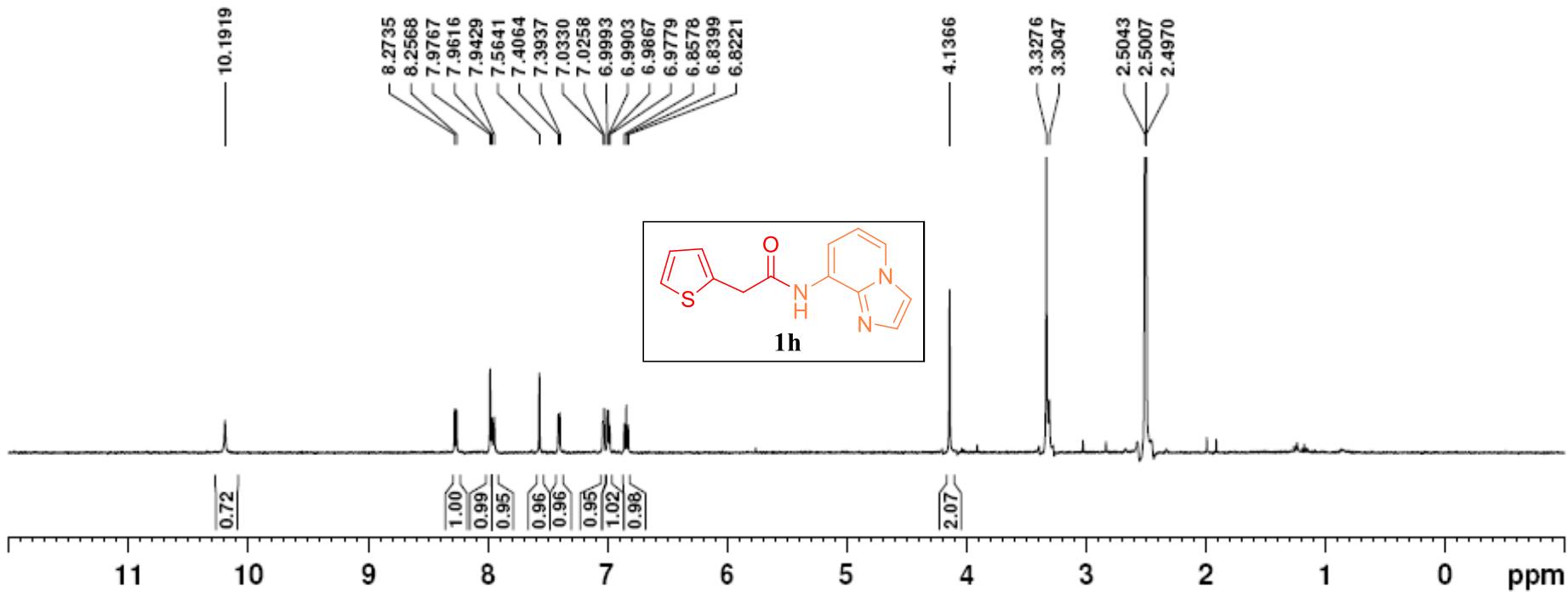
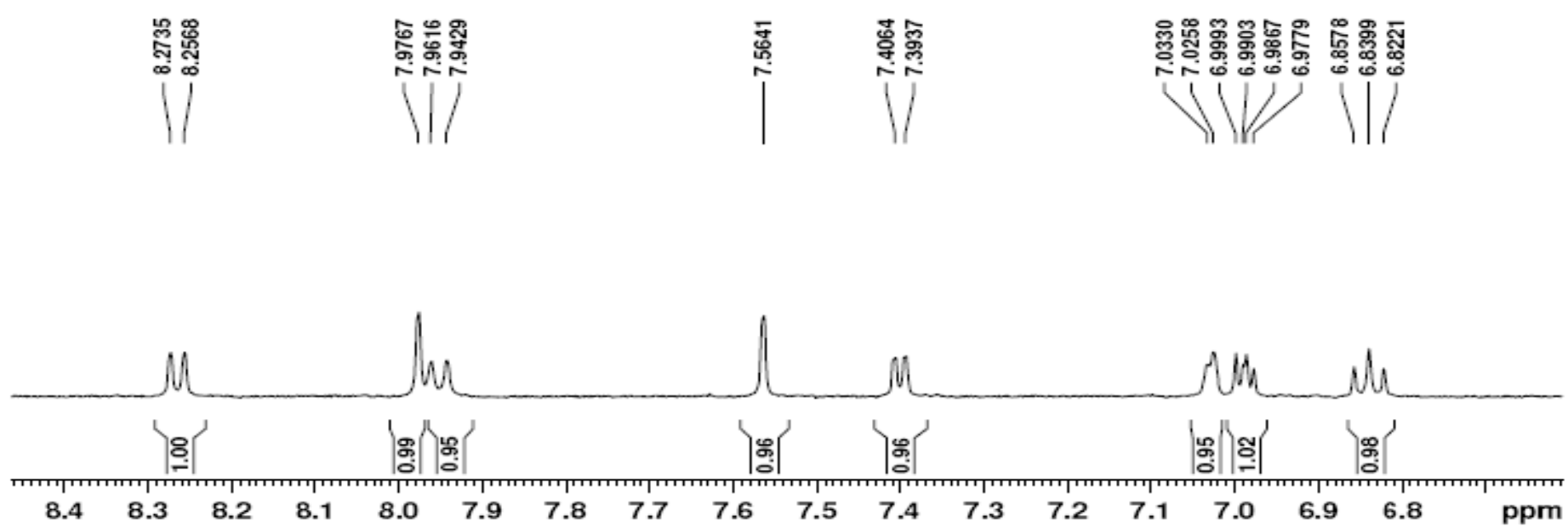
^{13}C NMR of **1f** in DMSO-d_6



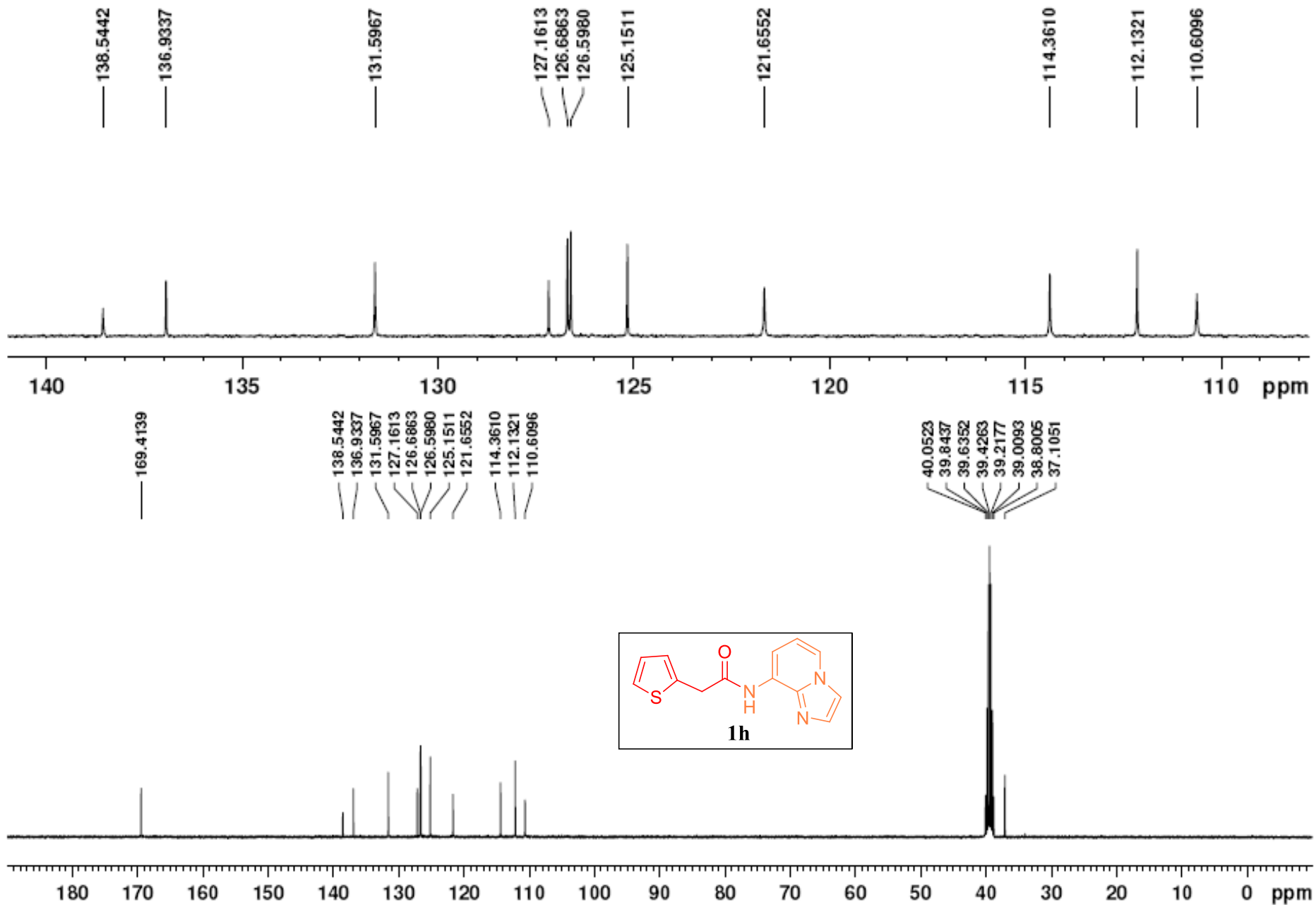
¹H NMR of **1g** in DMSO-d₆



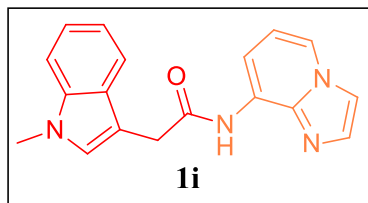
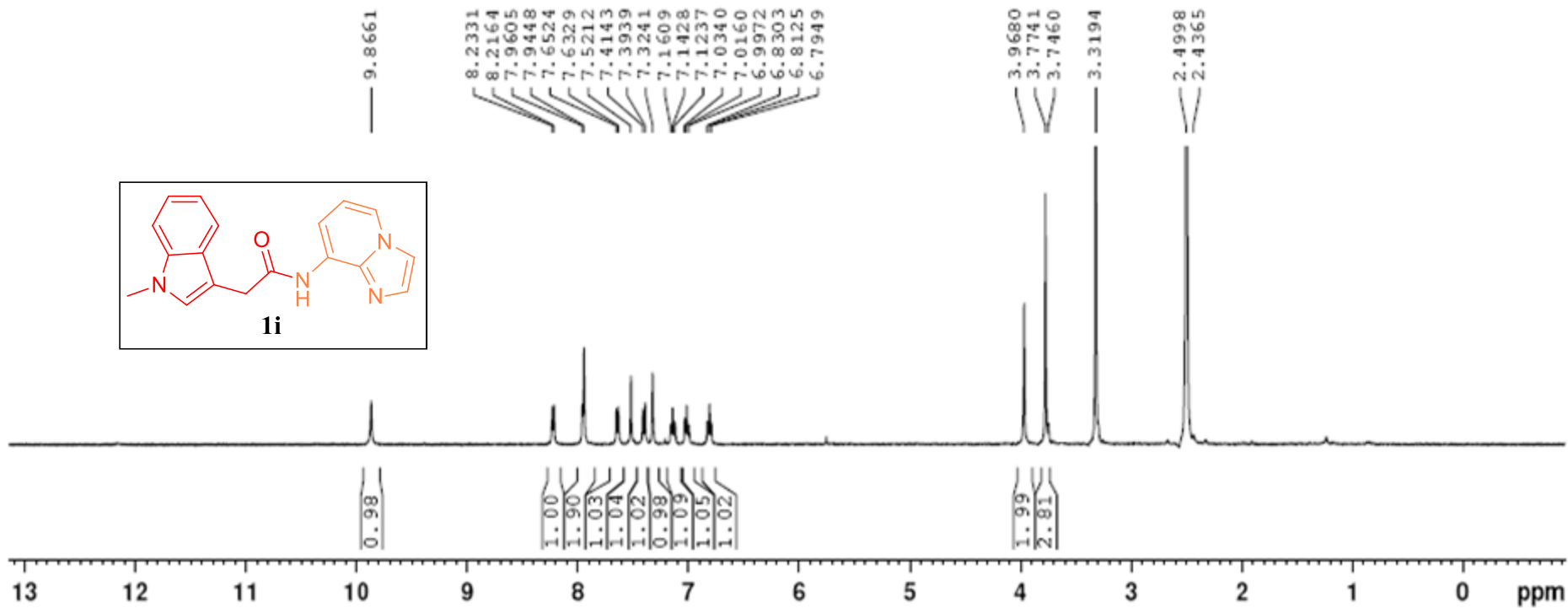
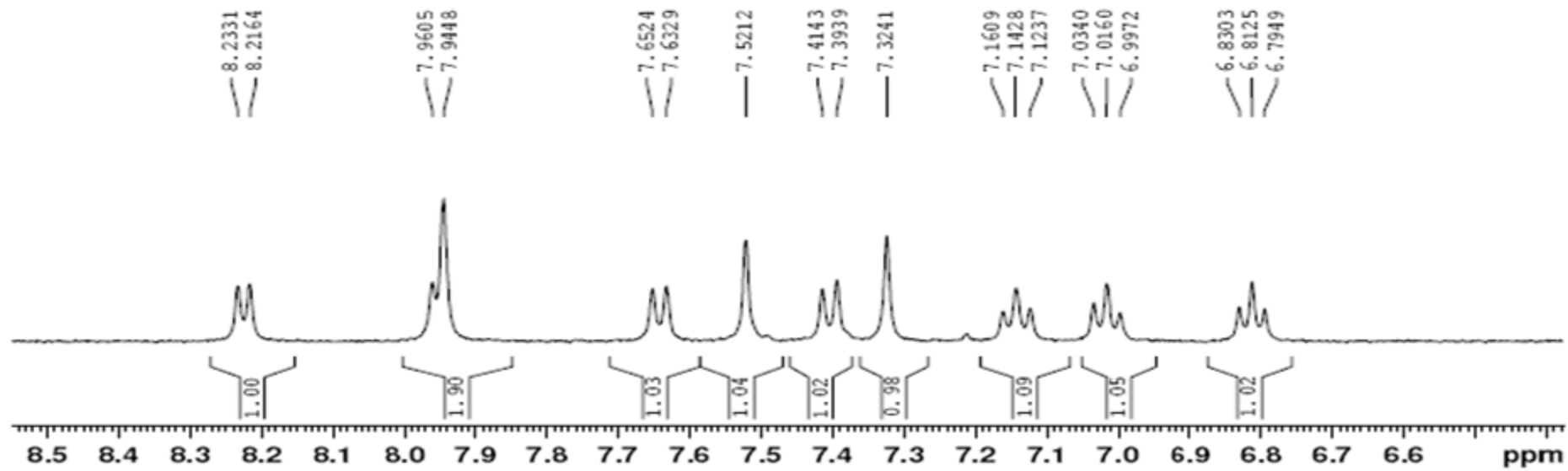
13C NMR of 1g in DMSO-d6



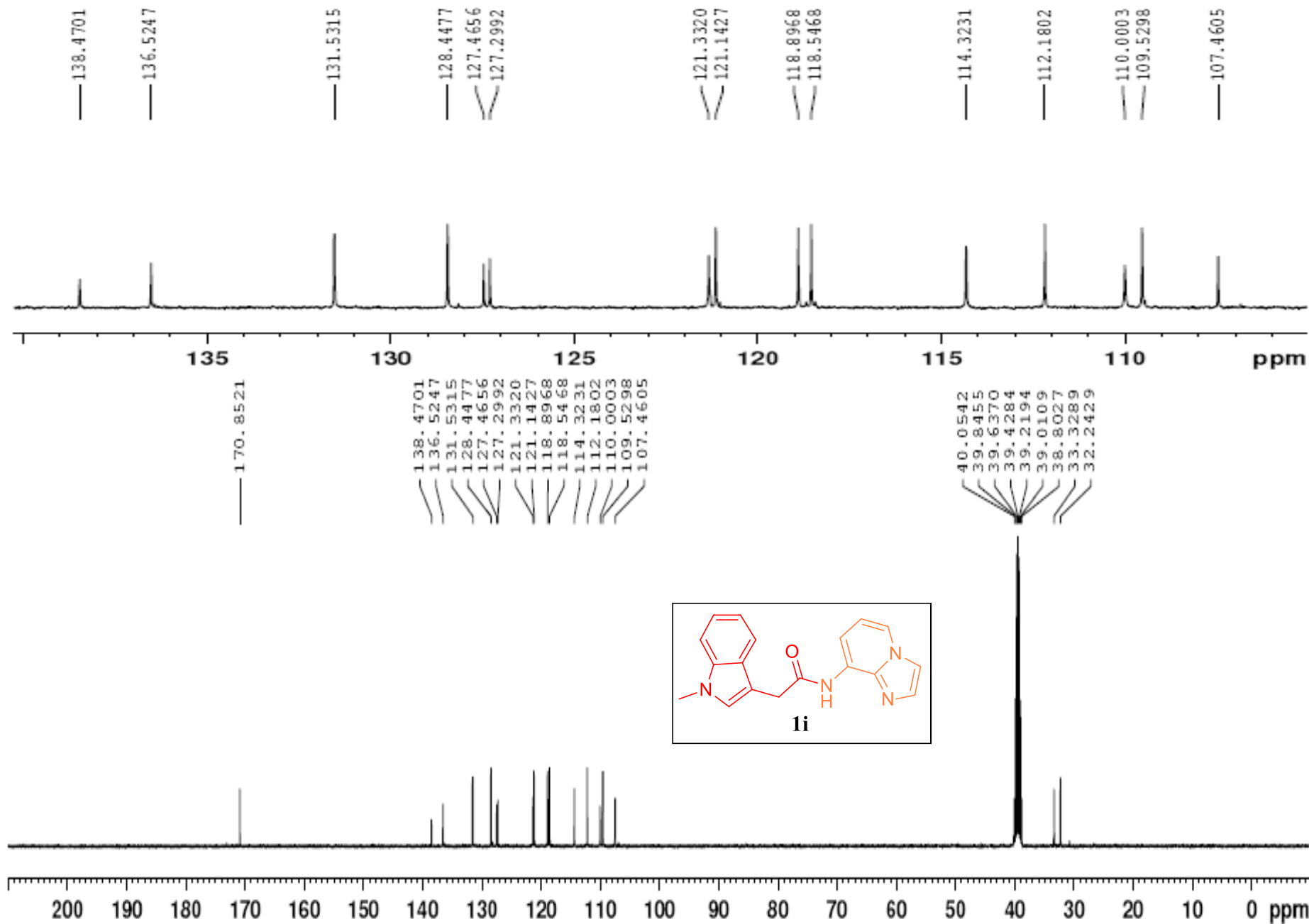
¹H NMR of **1h** in DMSO-d₆



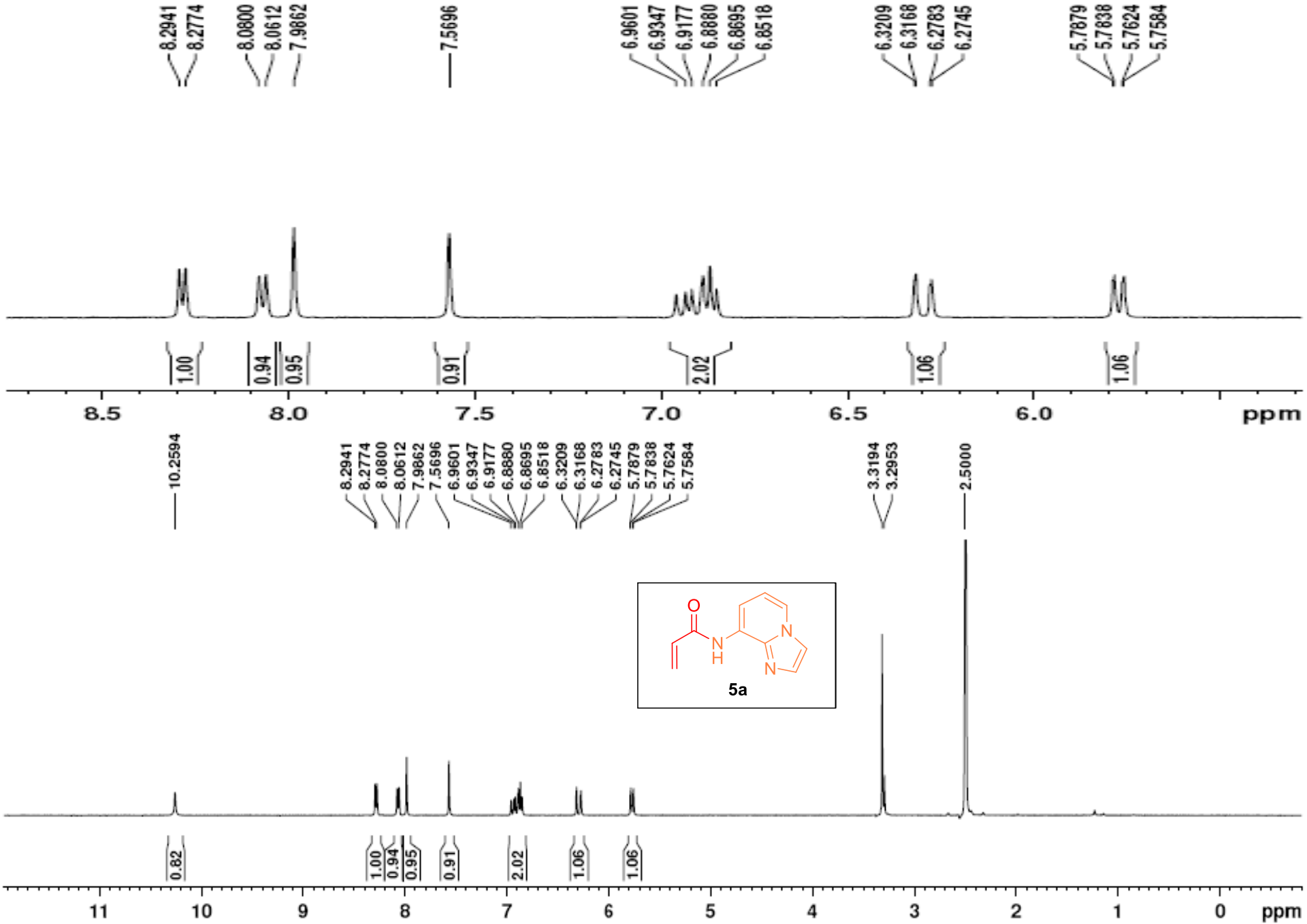
¹³C NMR of **1h** in DMSO-d₆



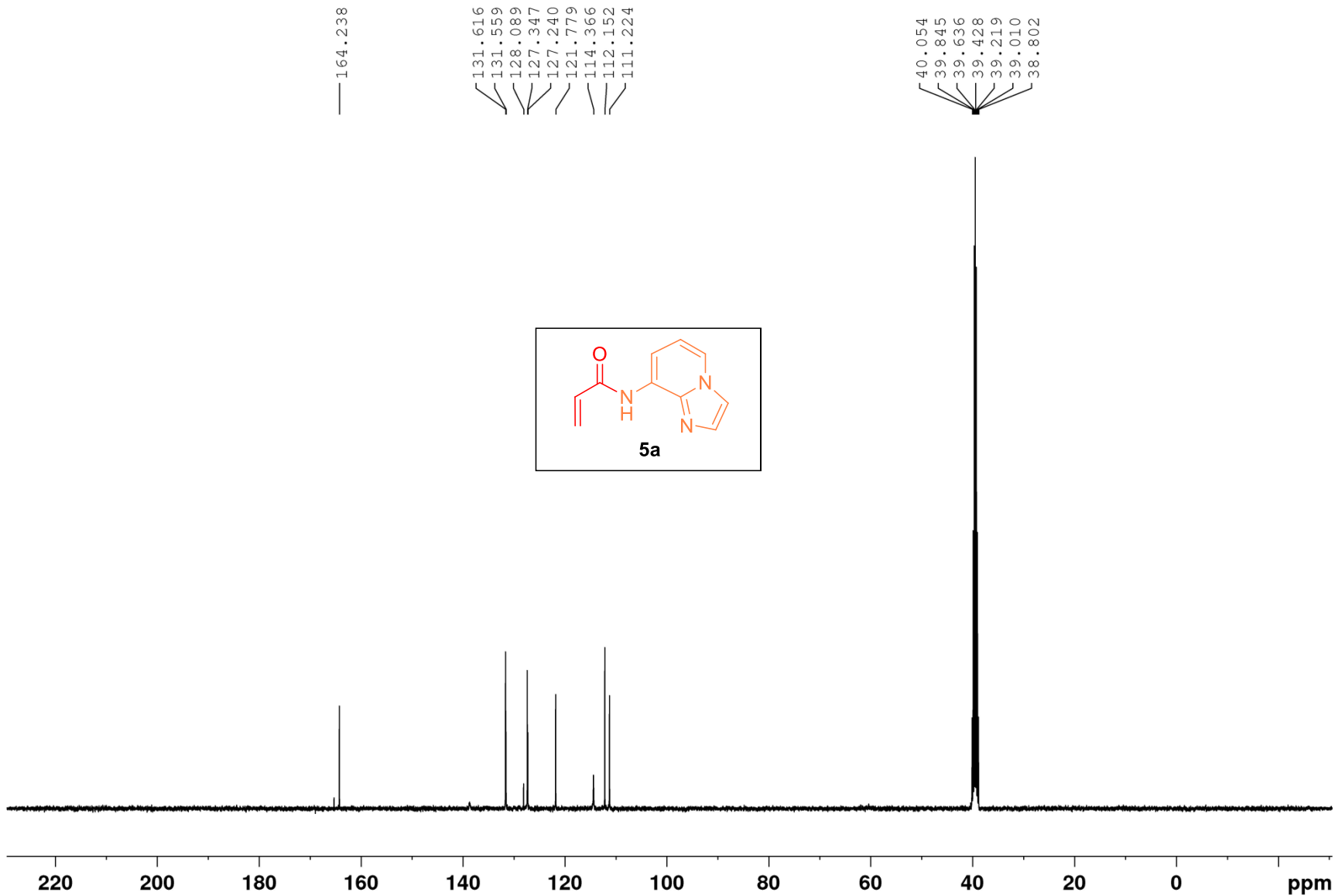
^1H NMR of **1i** in DMSO-d_6

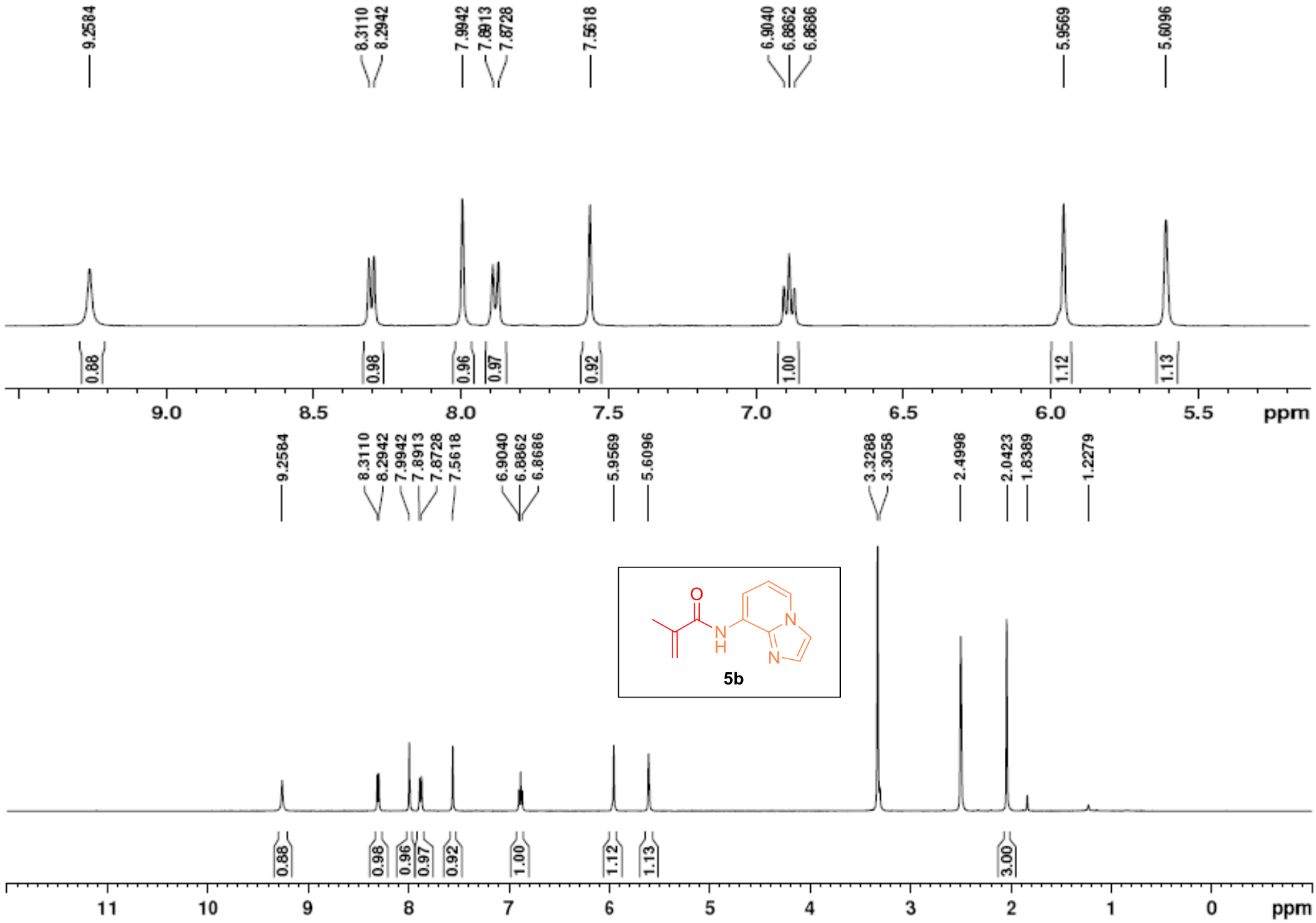


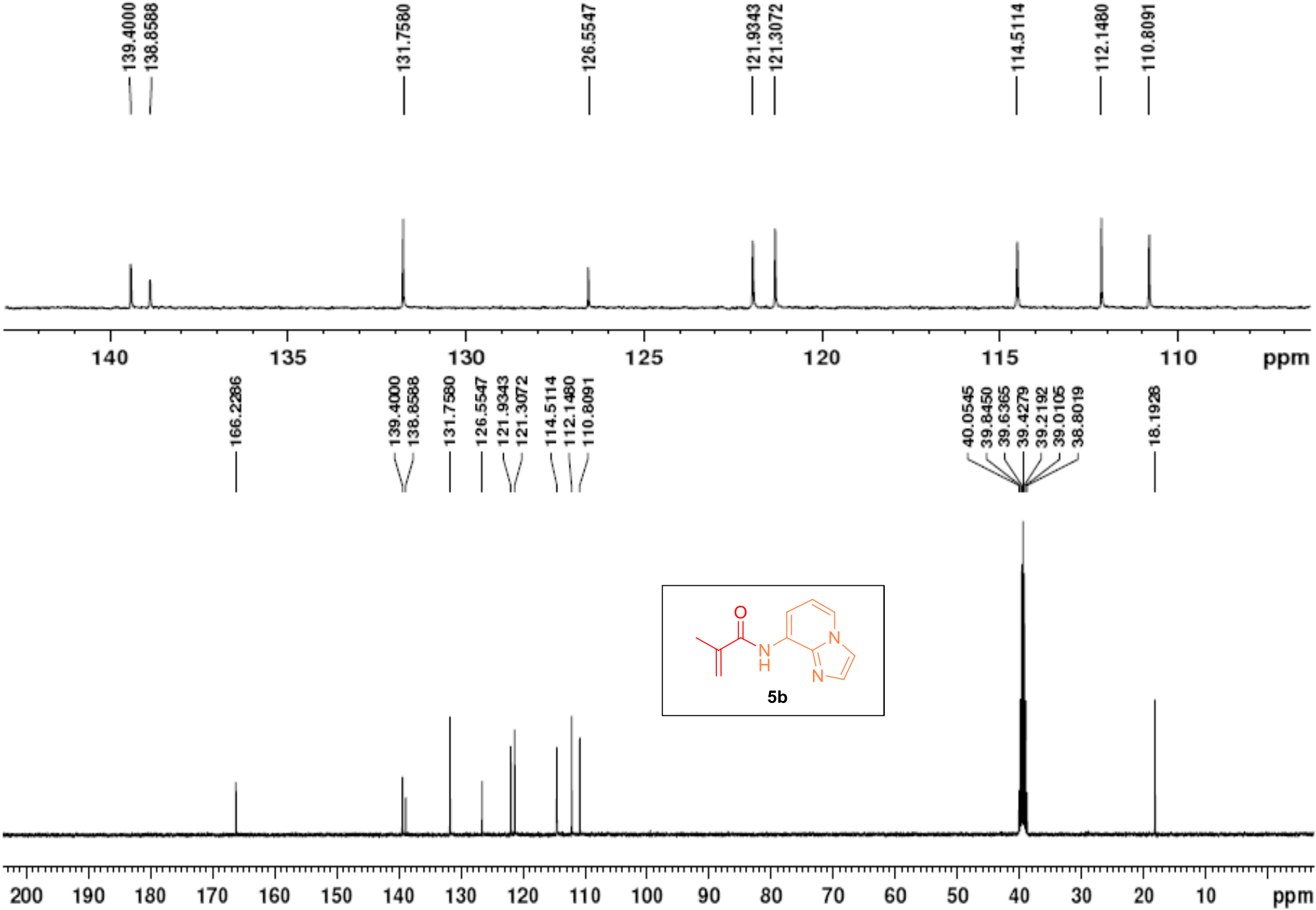
¹³C NMR of **1i** in DMSO-d₆

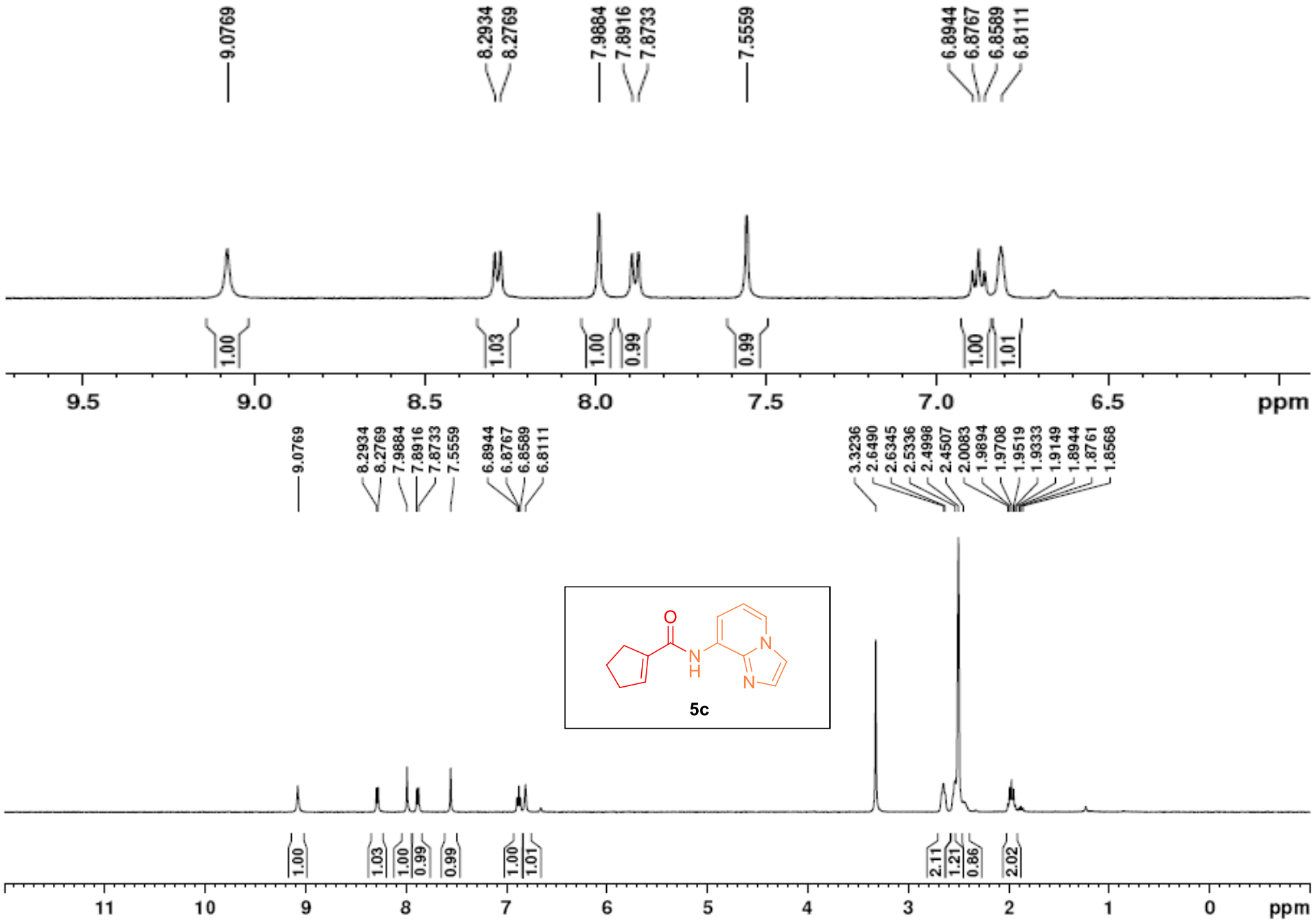


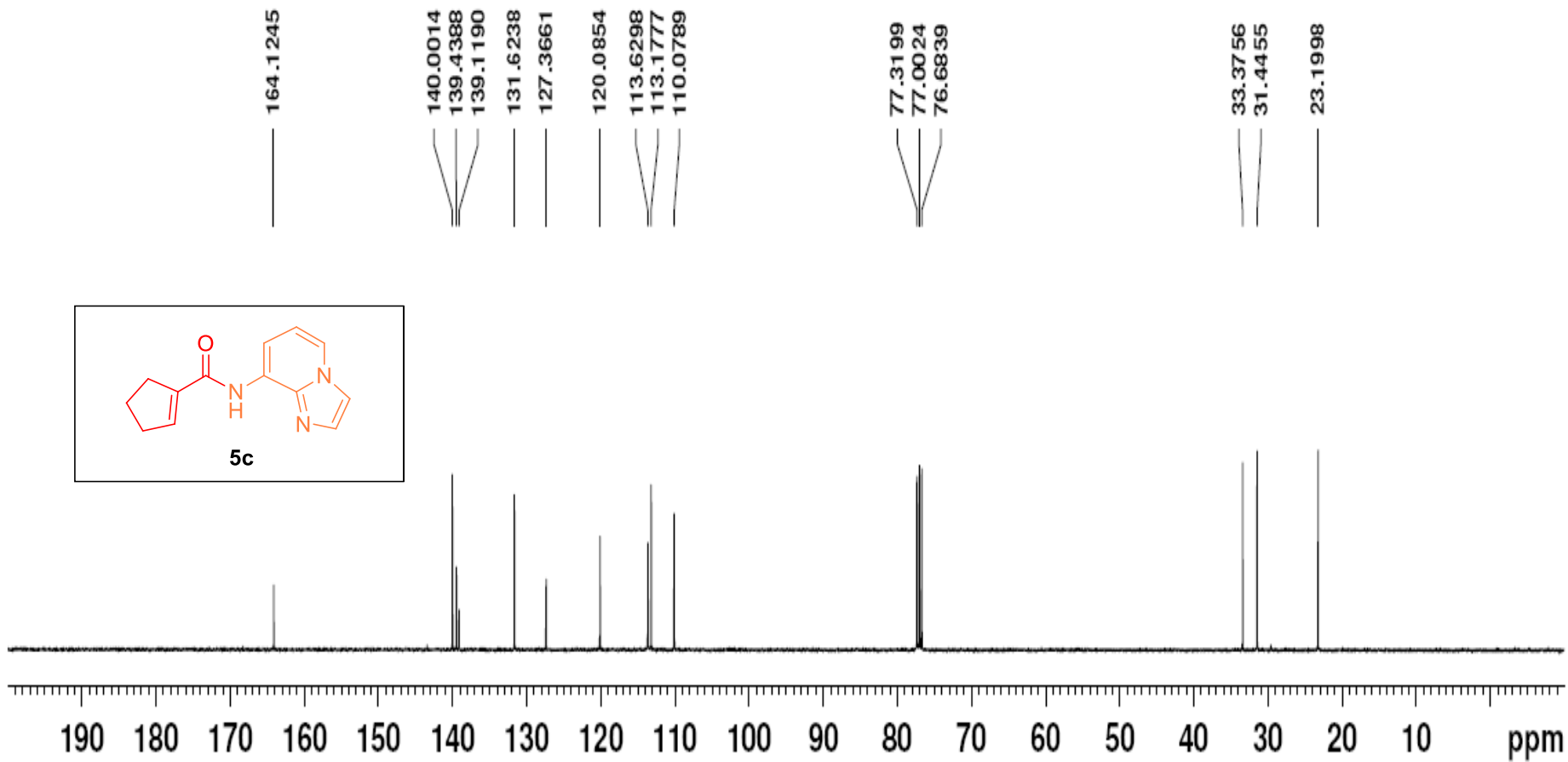
¹H NMR of 5a

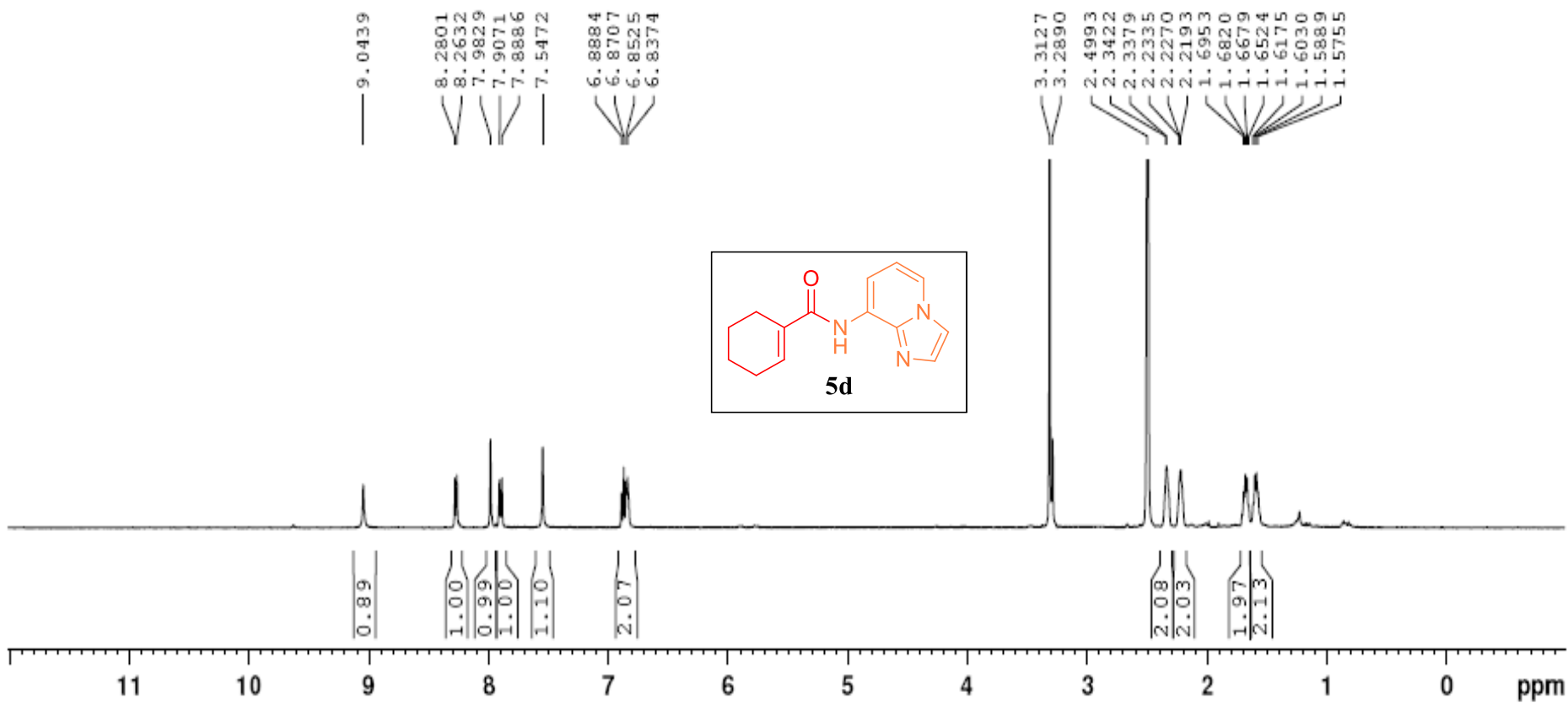
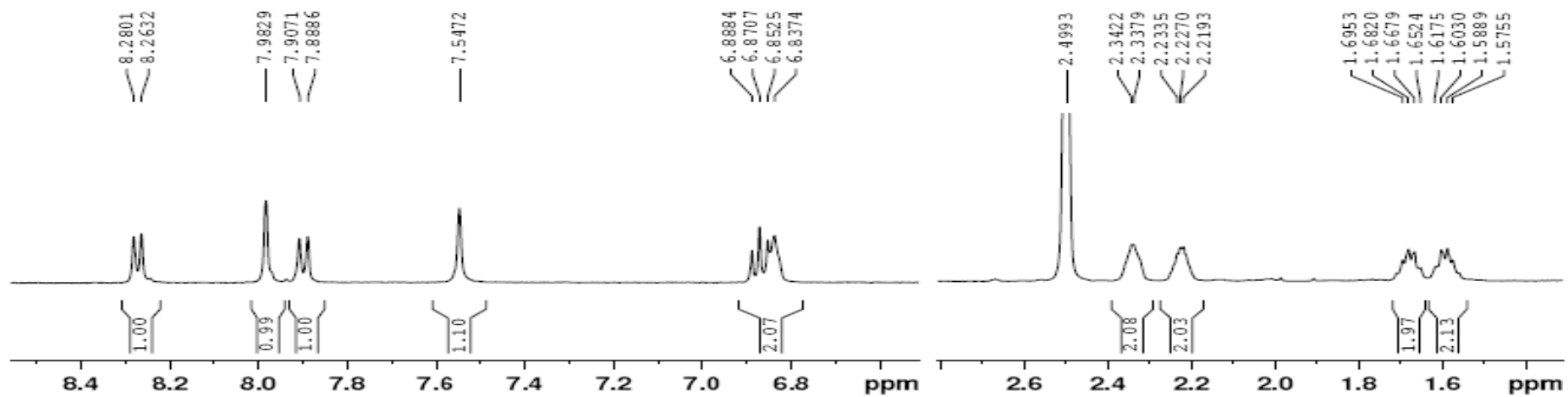




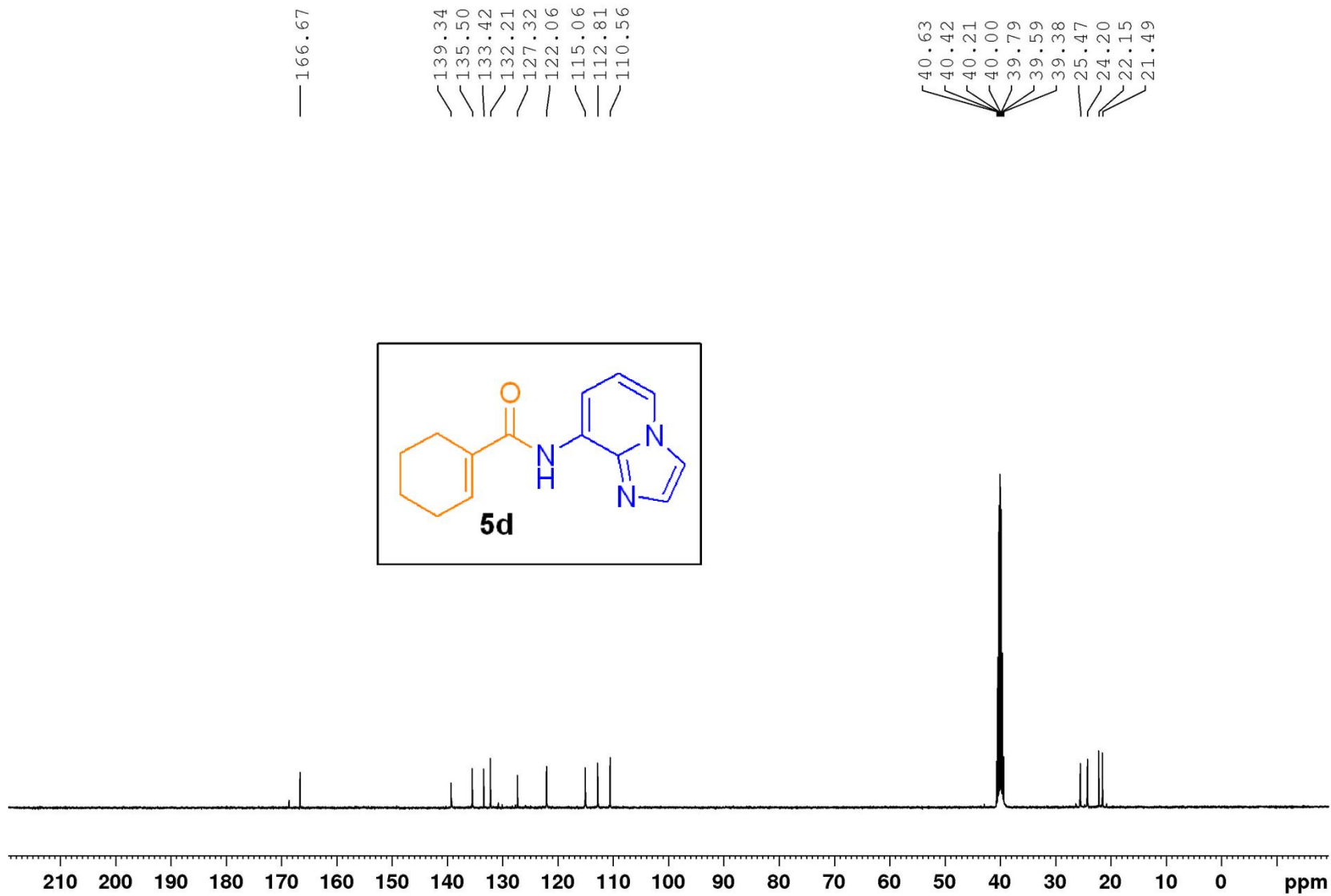




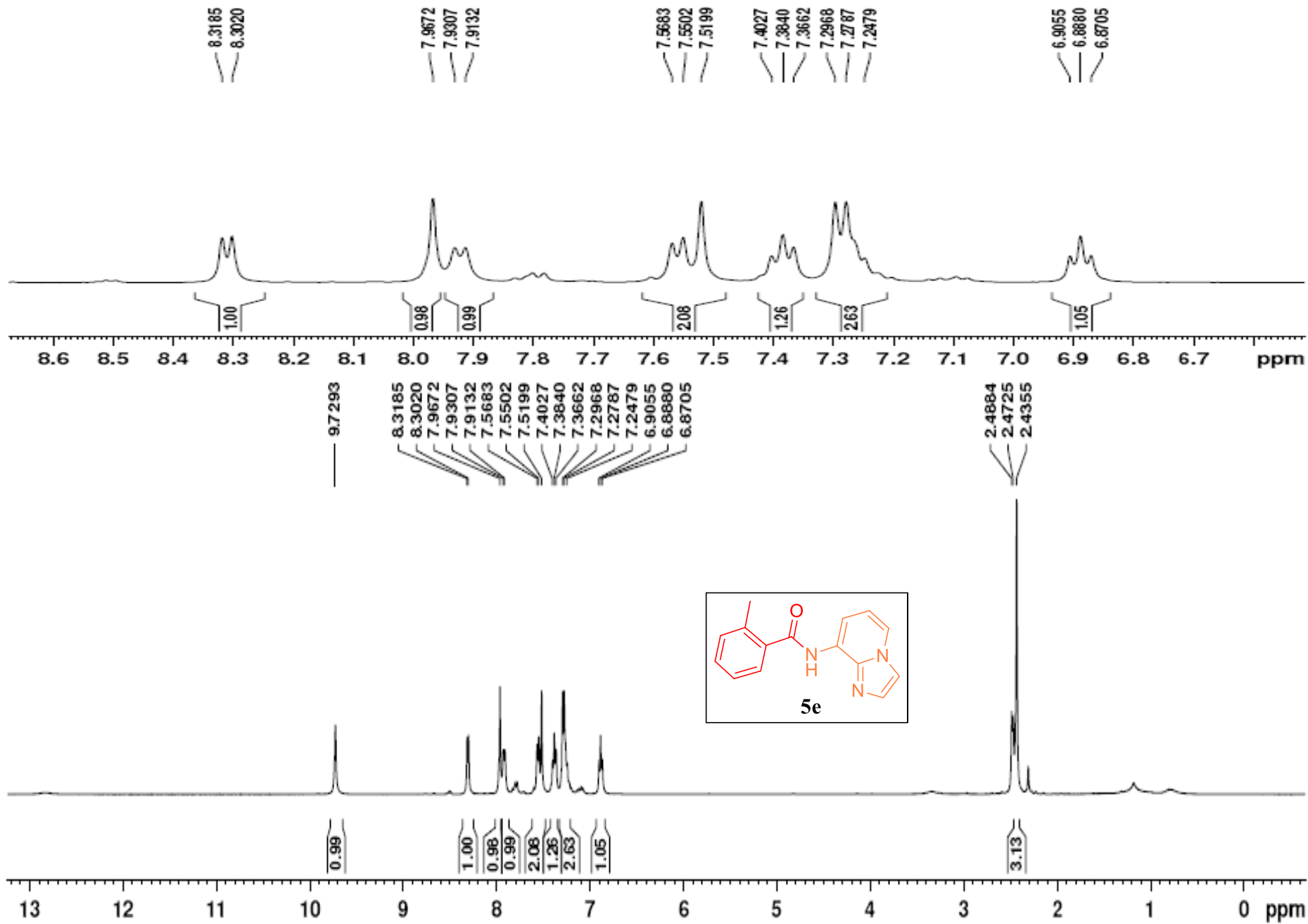




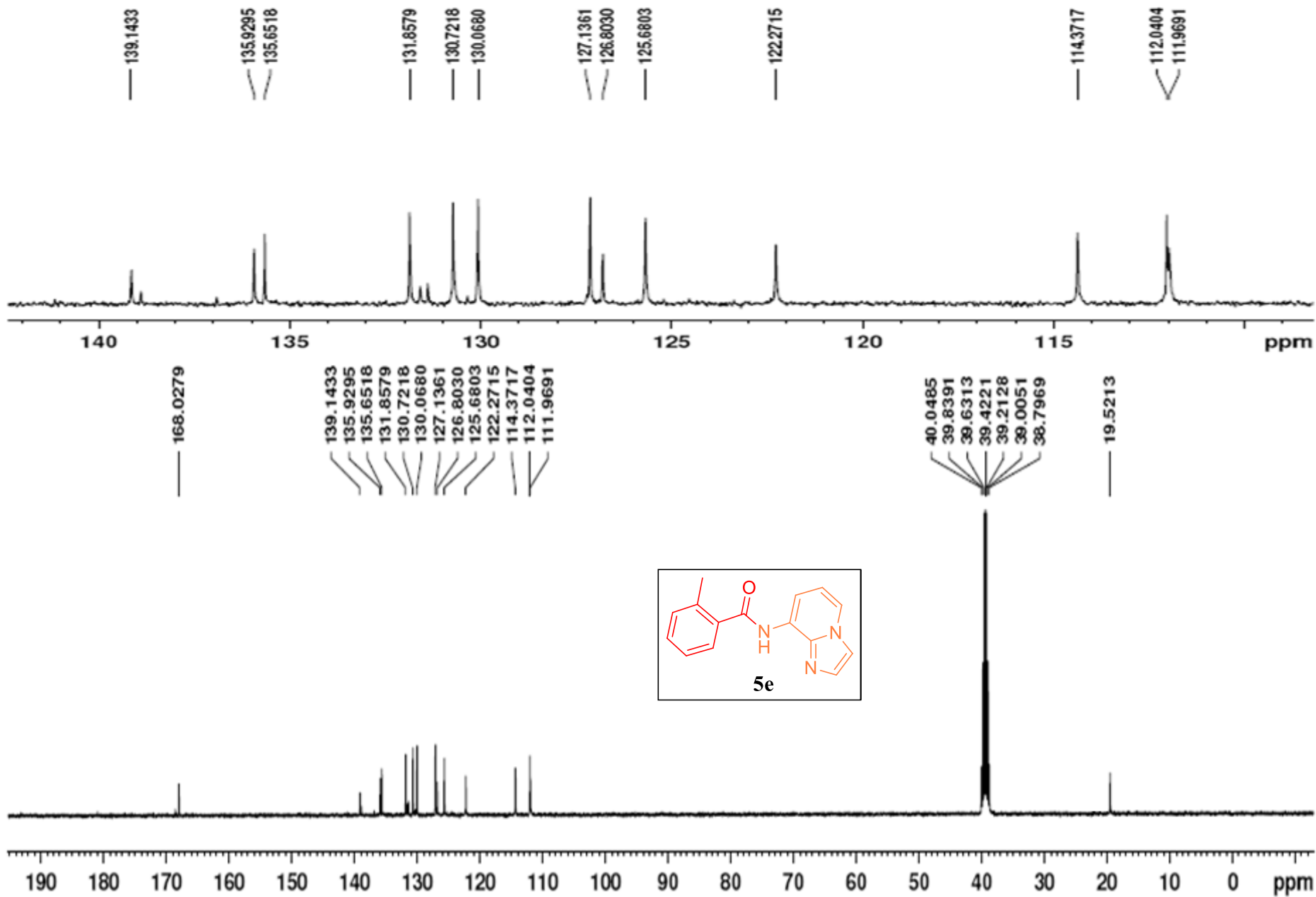
¹H NMR of **5d** in DMSO-d₆



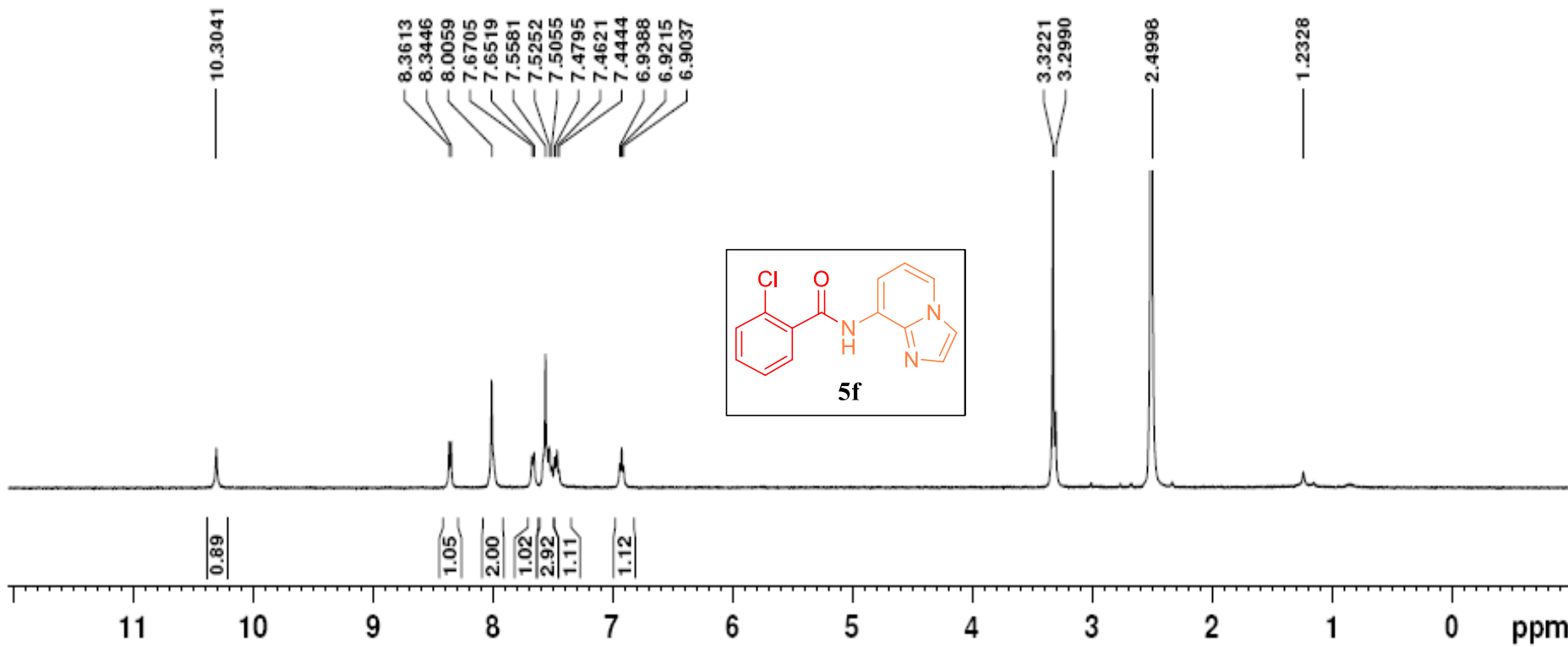
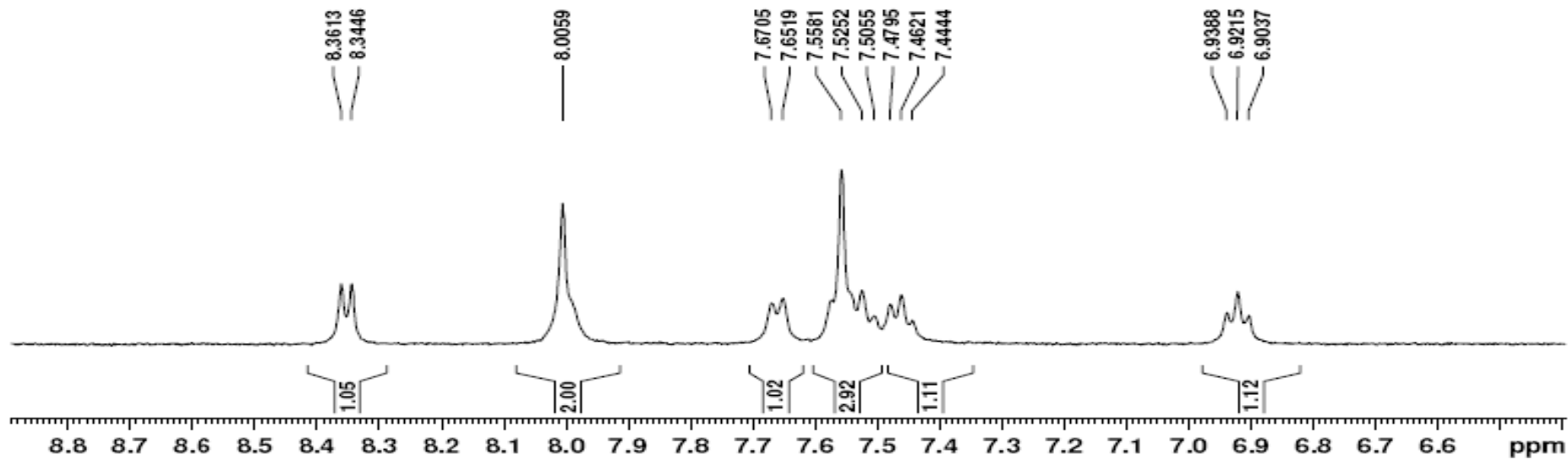
^{13}C NMR of **5d** in DMSO-d_6



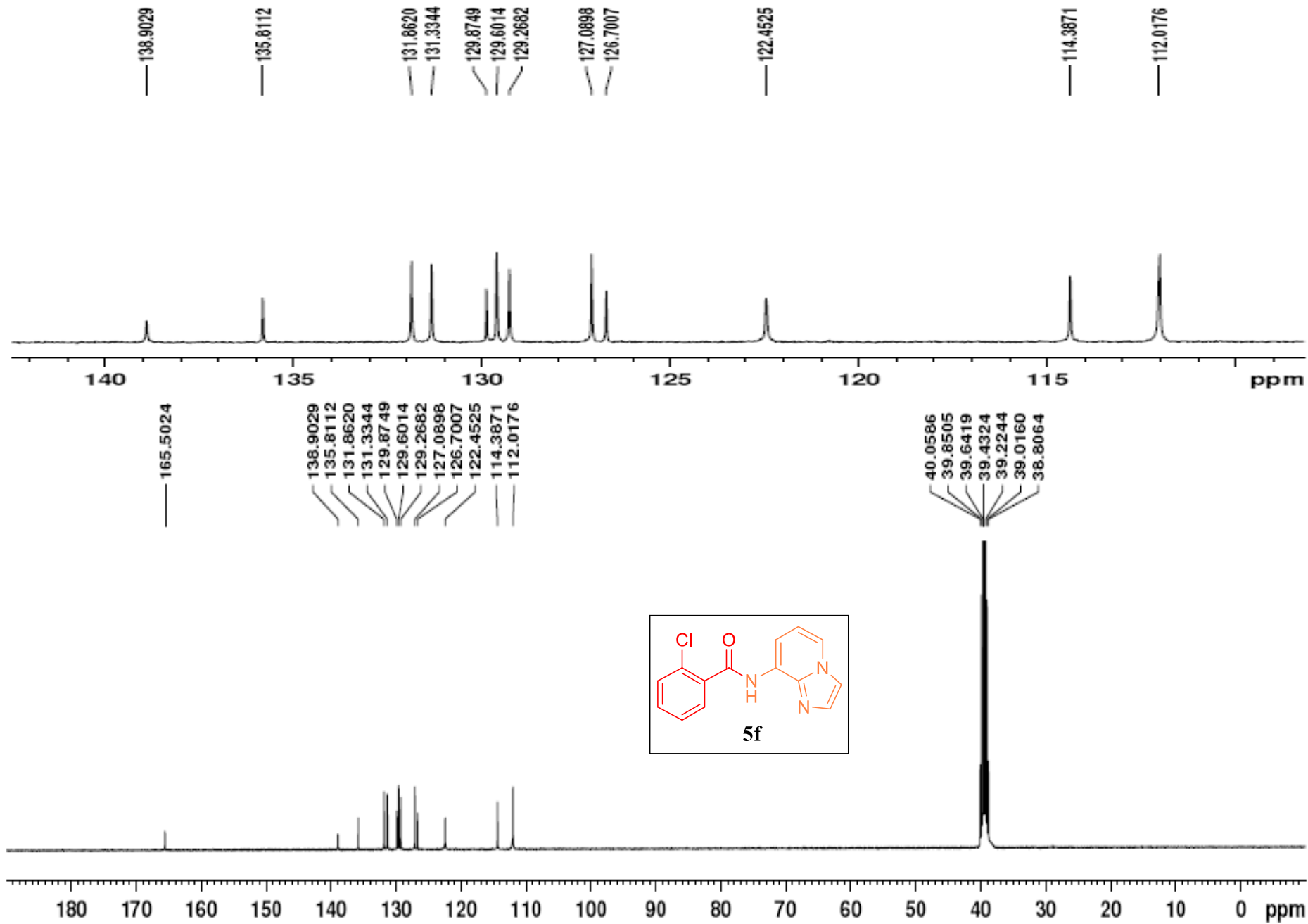
¹H NMR of **5e** in DMSO-d₆



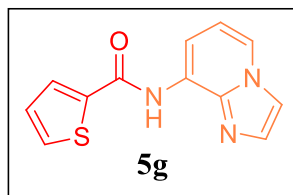
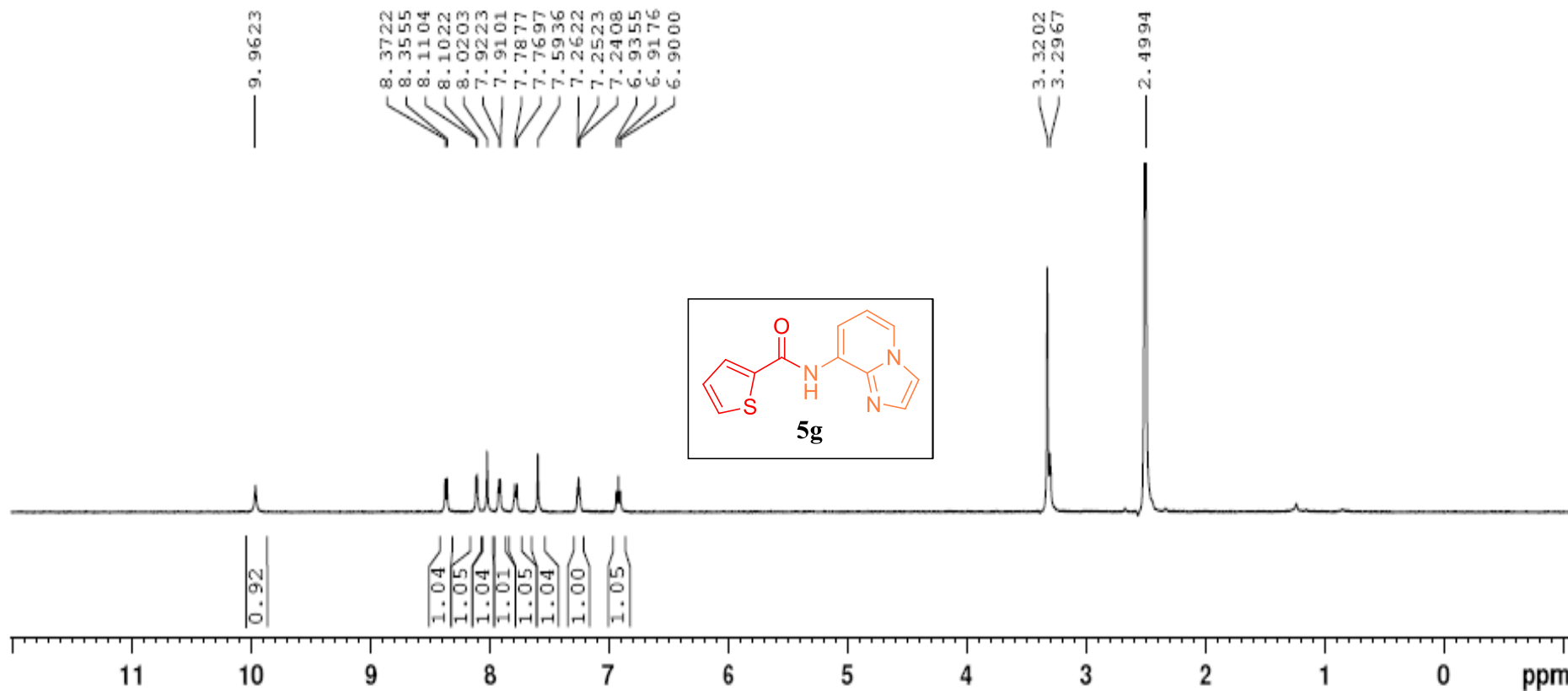
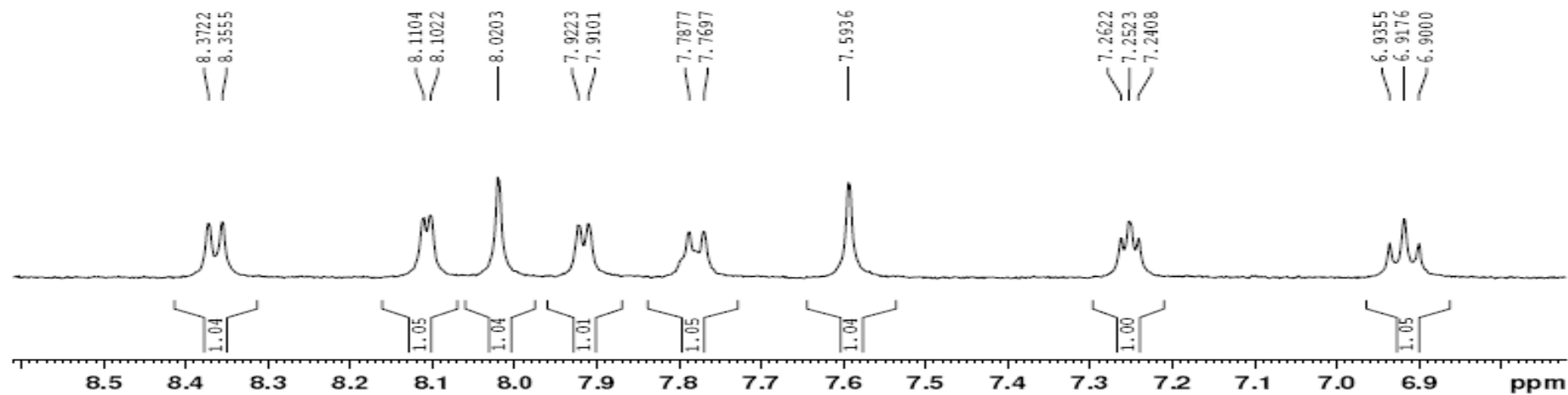
^{13}C NMR of **5e** in DMSO-d_6



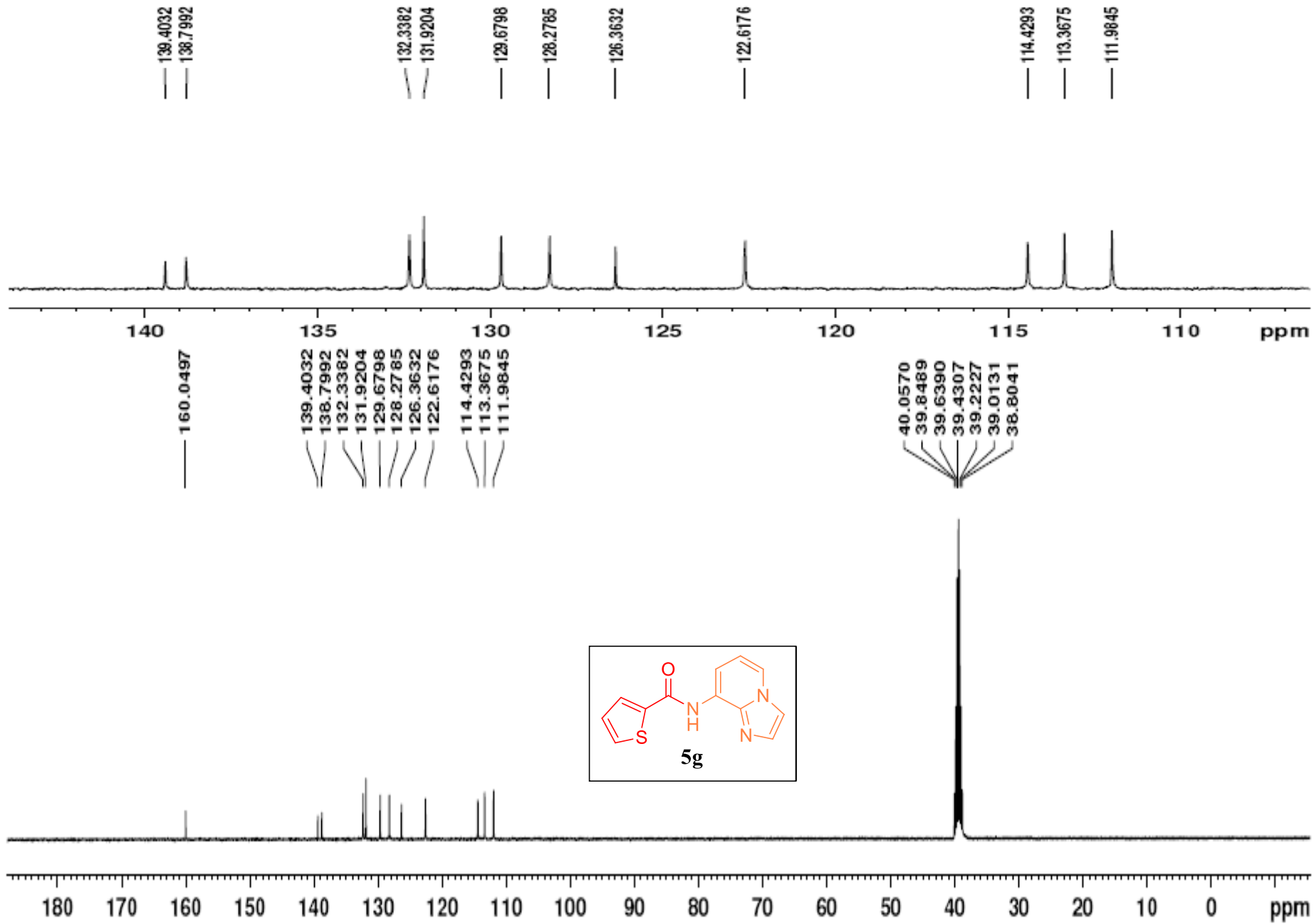
¹H NMR of **5f** in DMSO-d₆



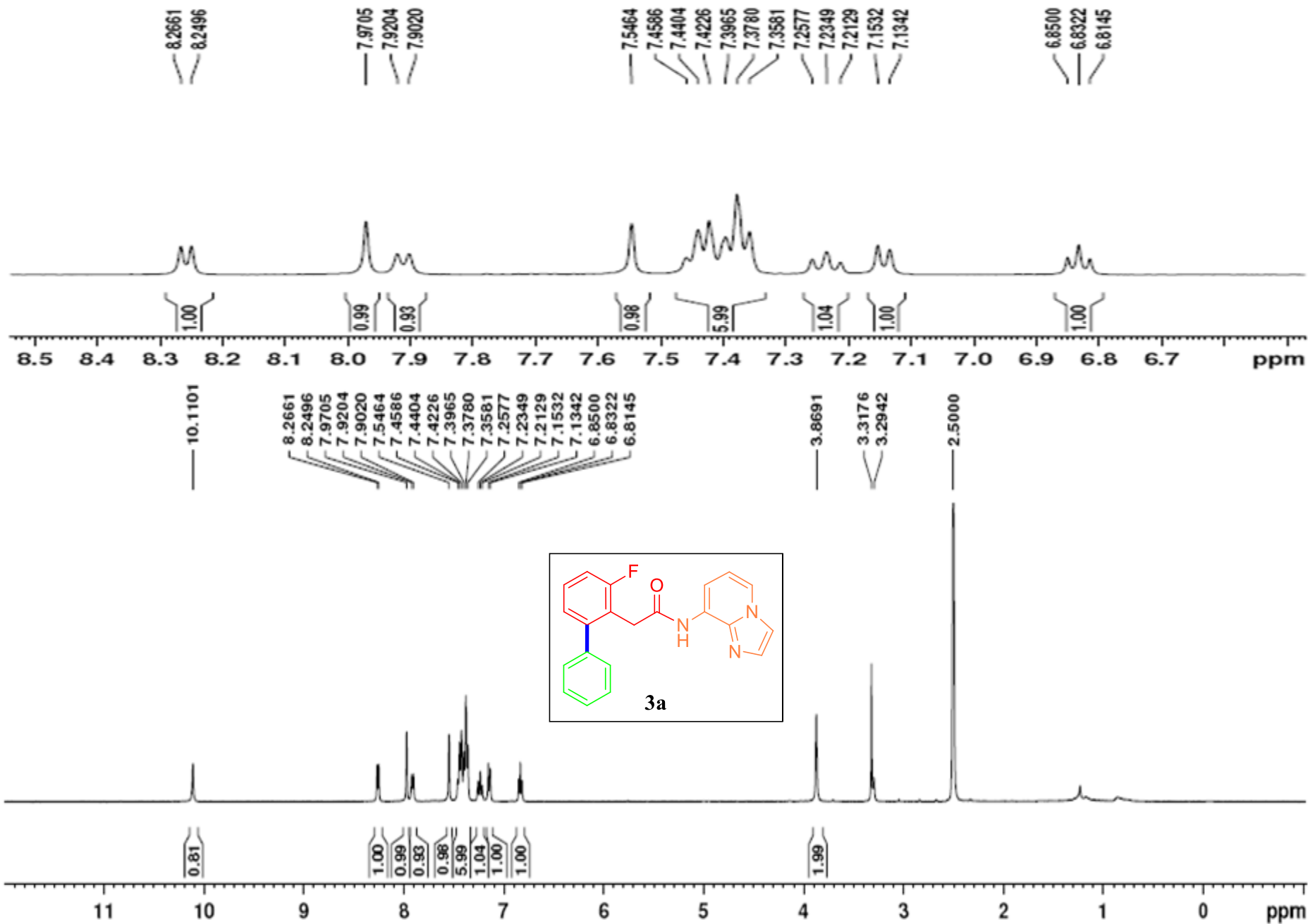
¹³C NMR of **5f** in DMSO-d₆



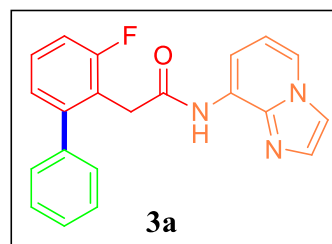
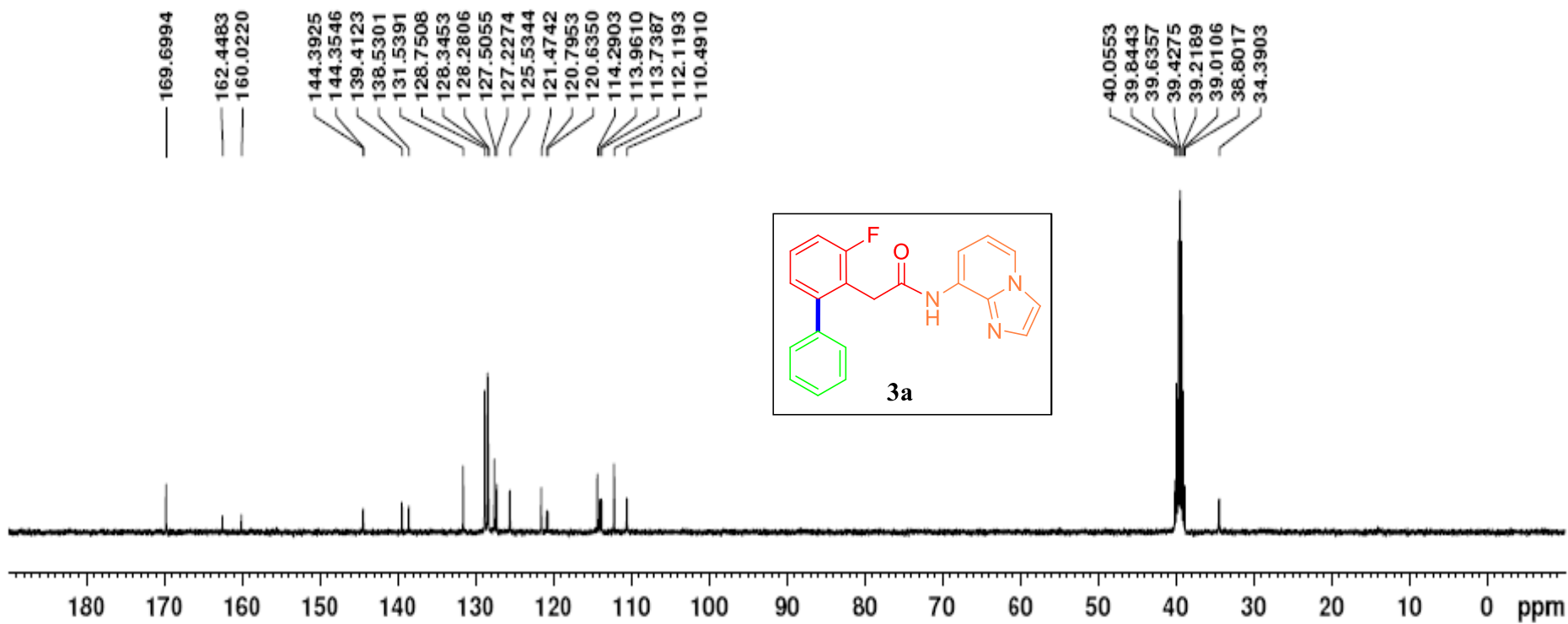
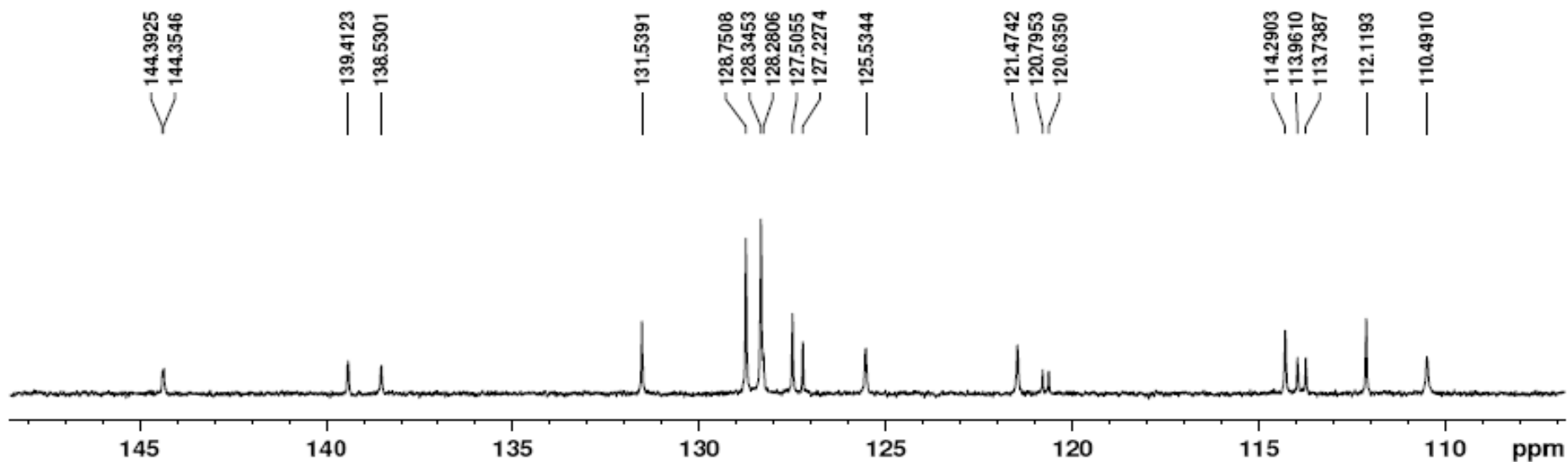
^1H NMR of **5g** in DMSO-d_6



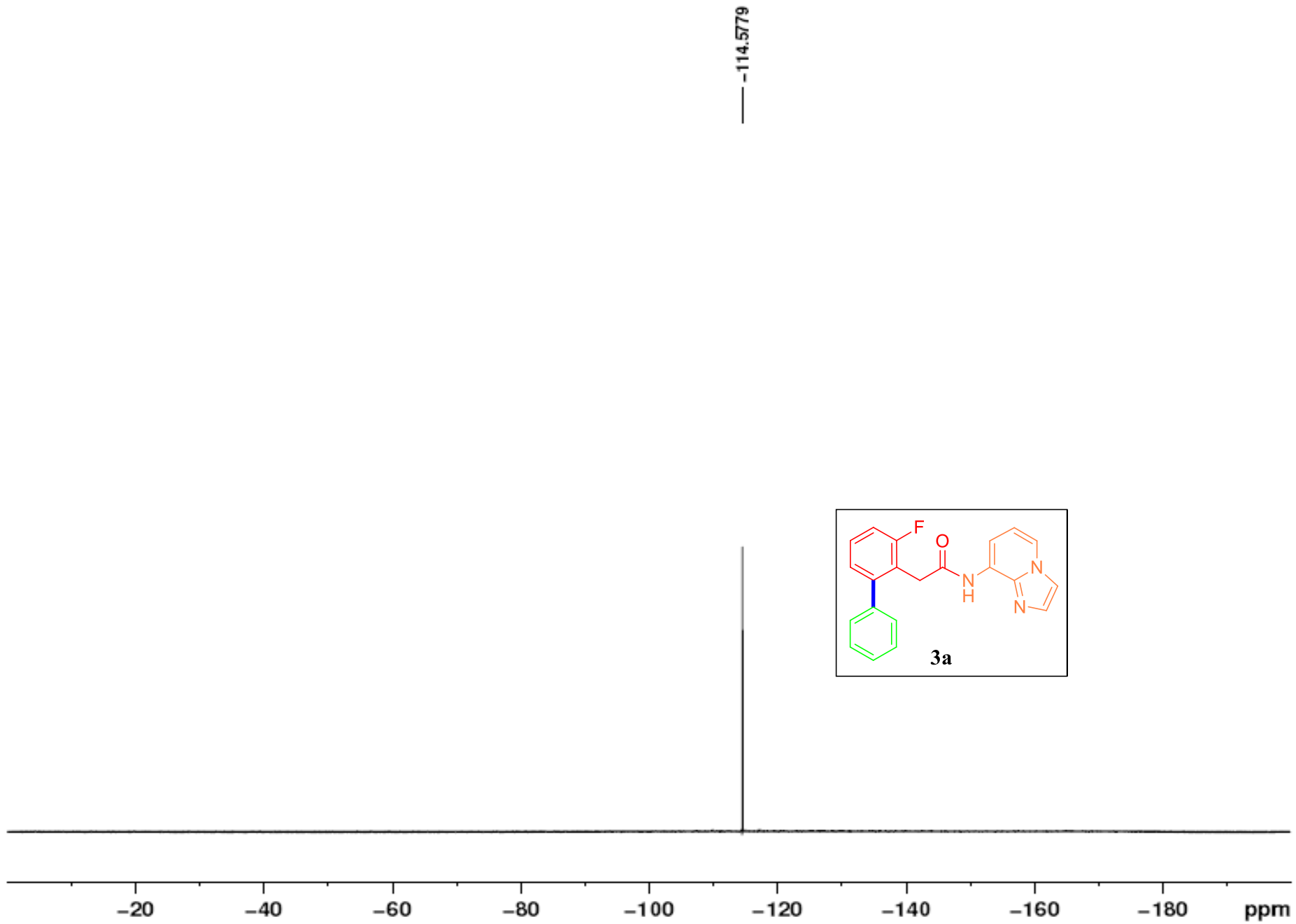
¹³C NMR of **5g** in DMSO-d₆



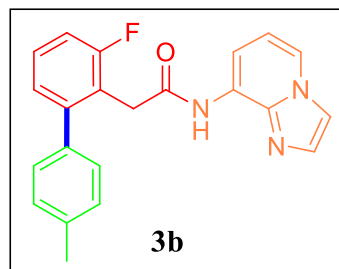
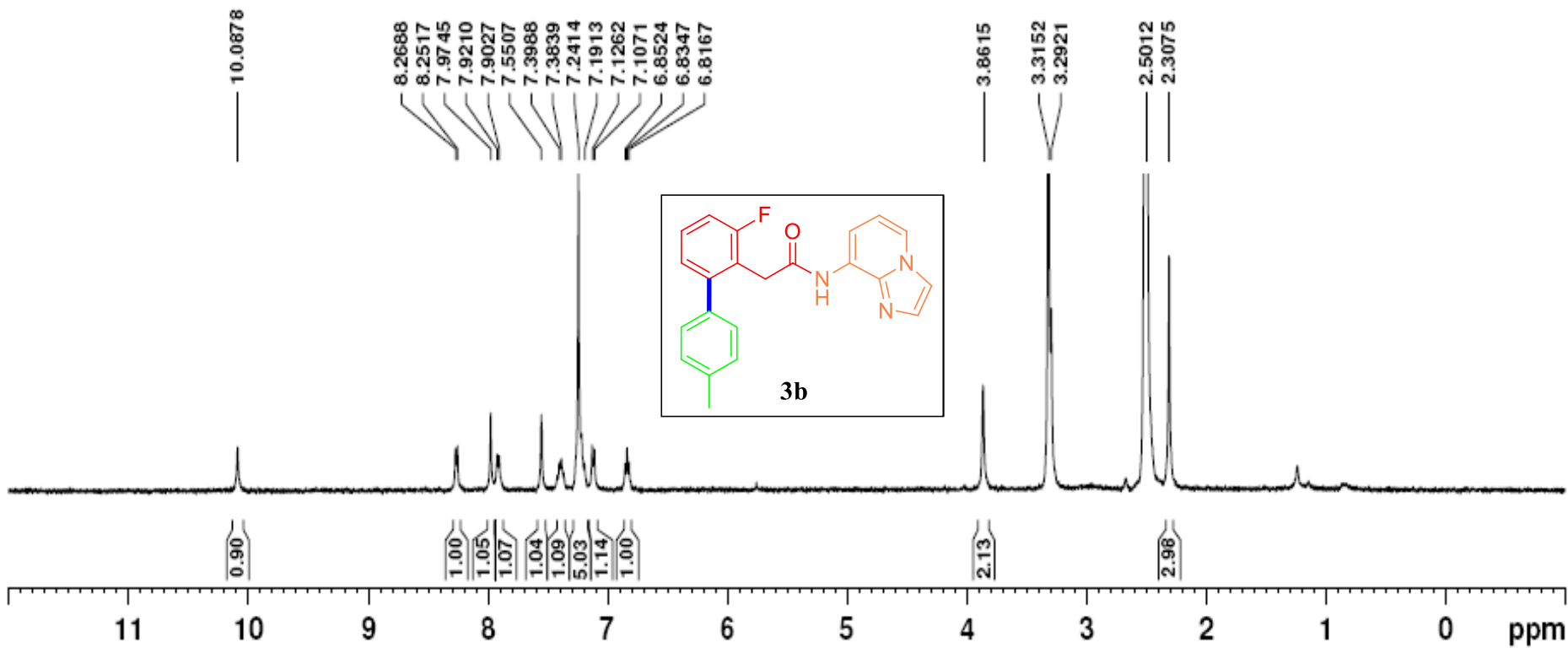
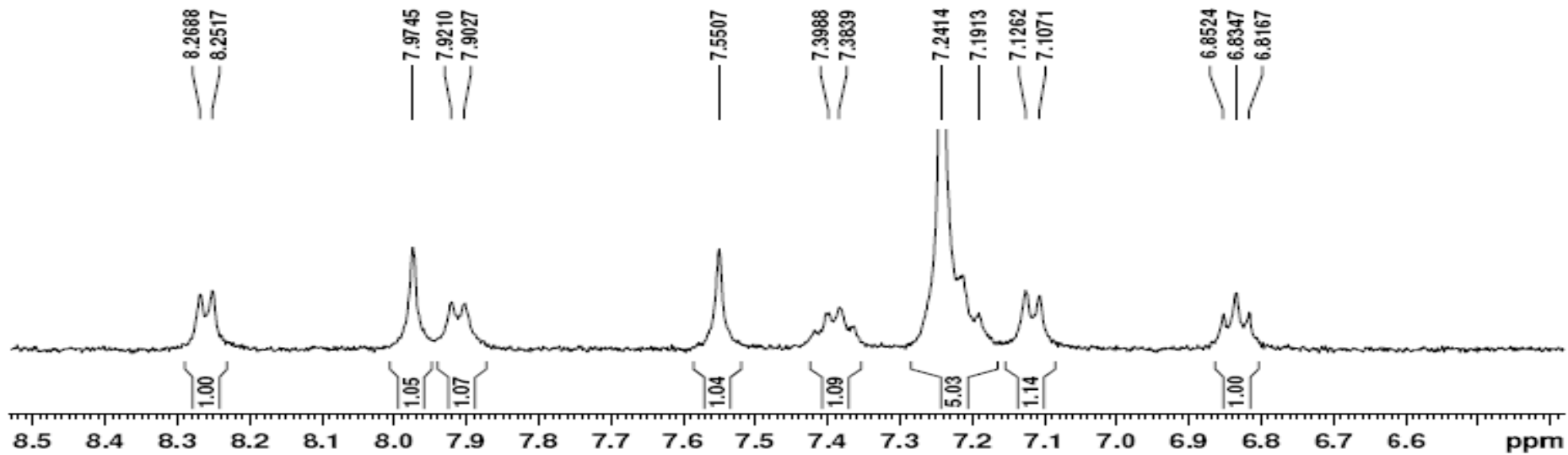
¹H NMR of **3a** in DMSO-d₆



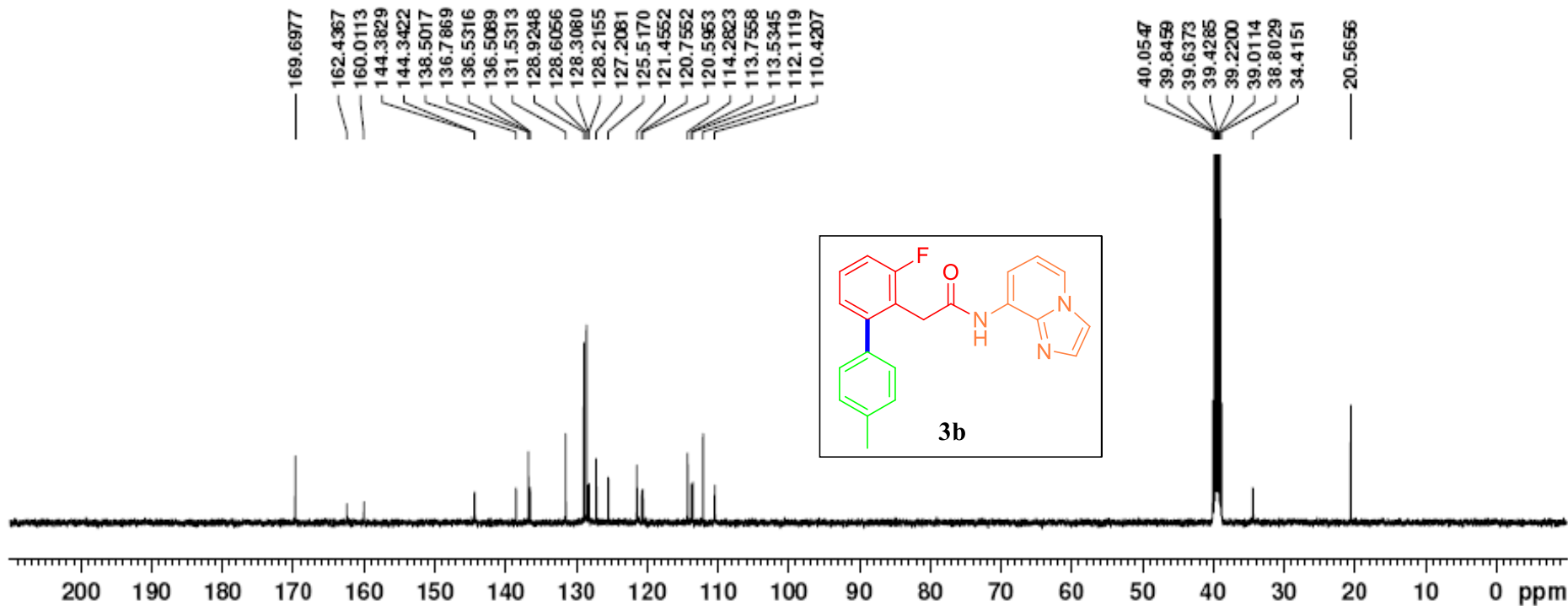
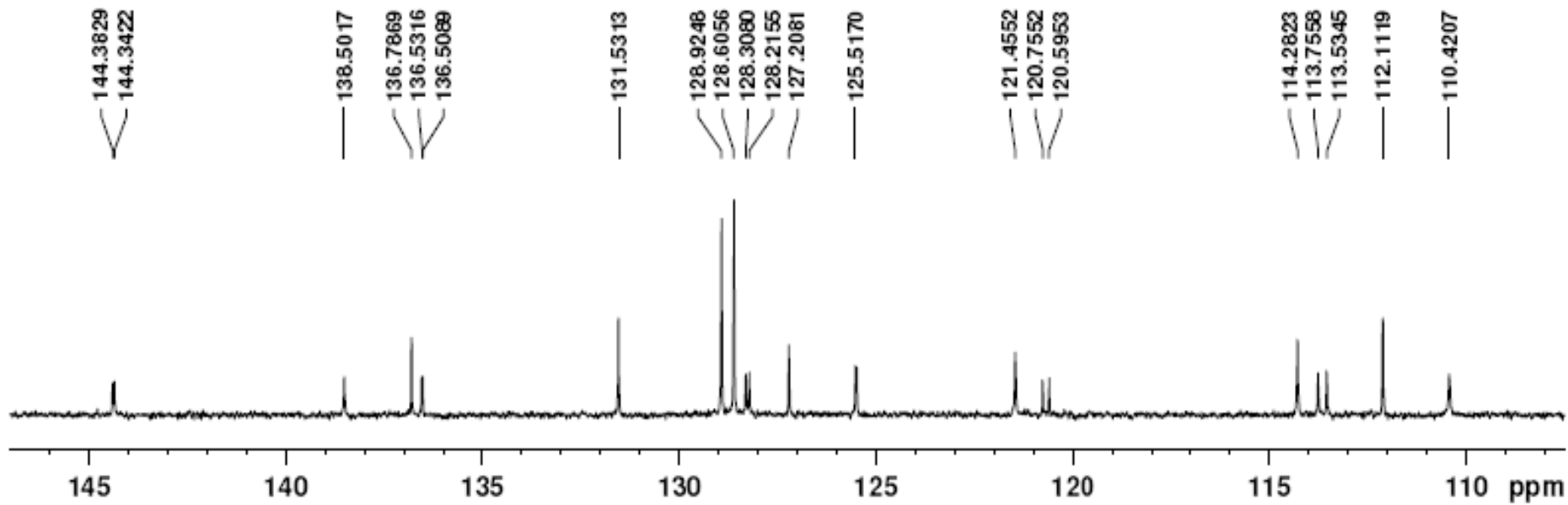
¹³C NMR of **3a** in DMSO-d₆



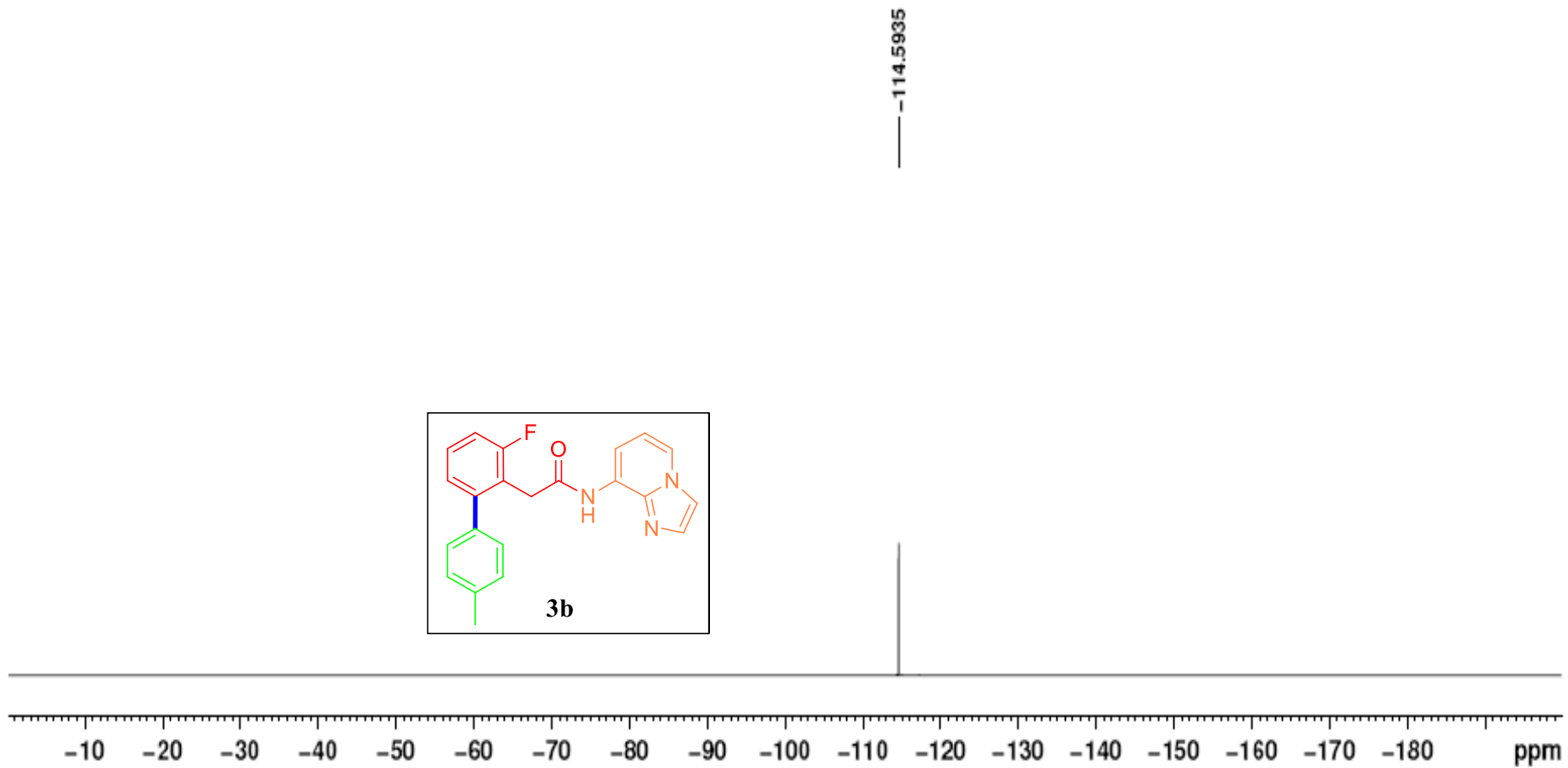
^{19}F NMR of **3a** in DMSO-d_6



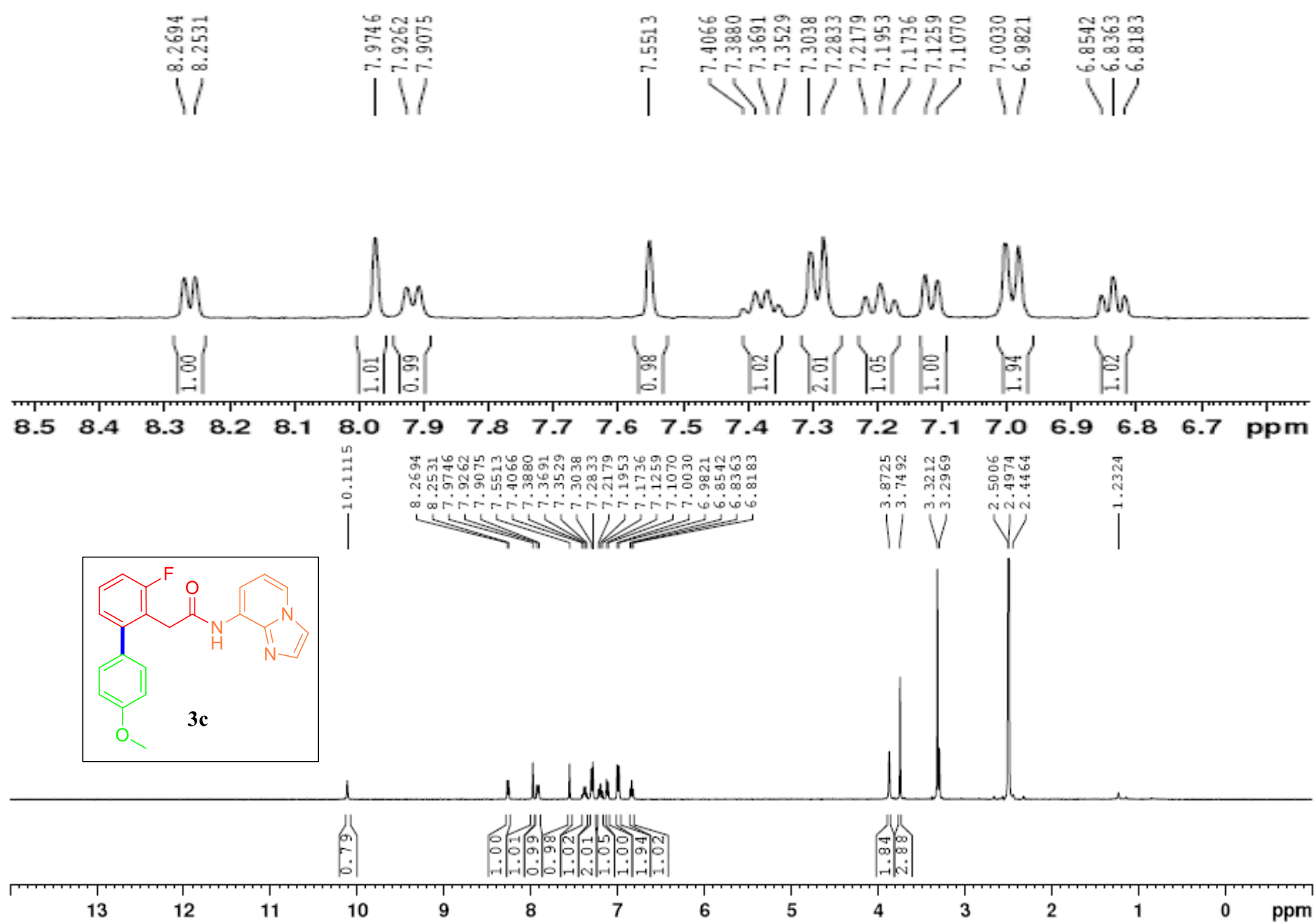
^1H NMR of **3b** in DMSO-d_6



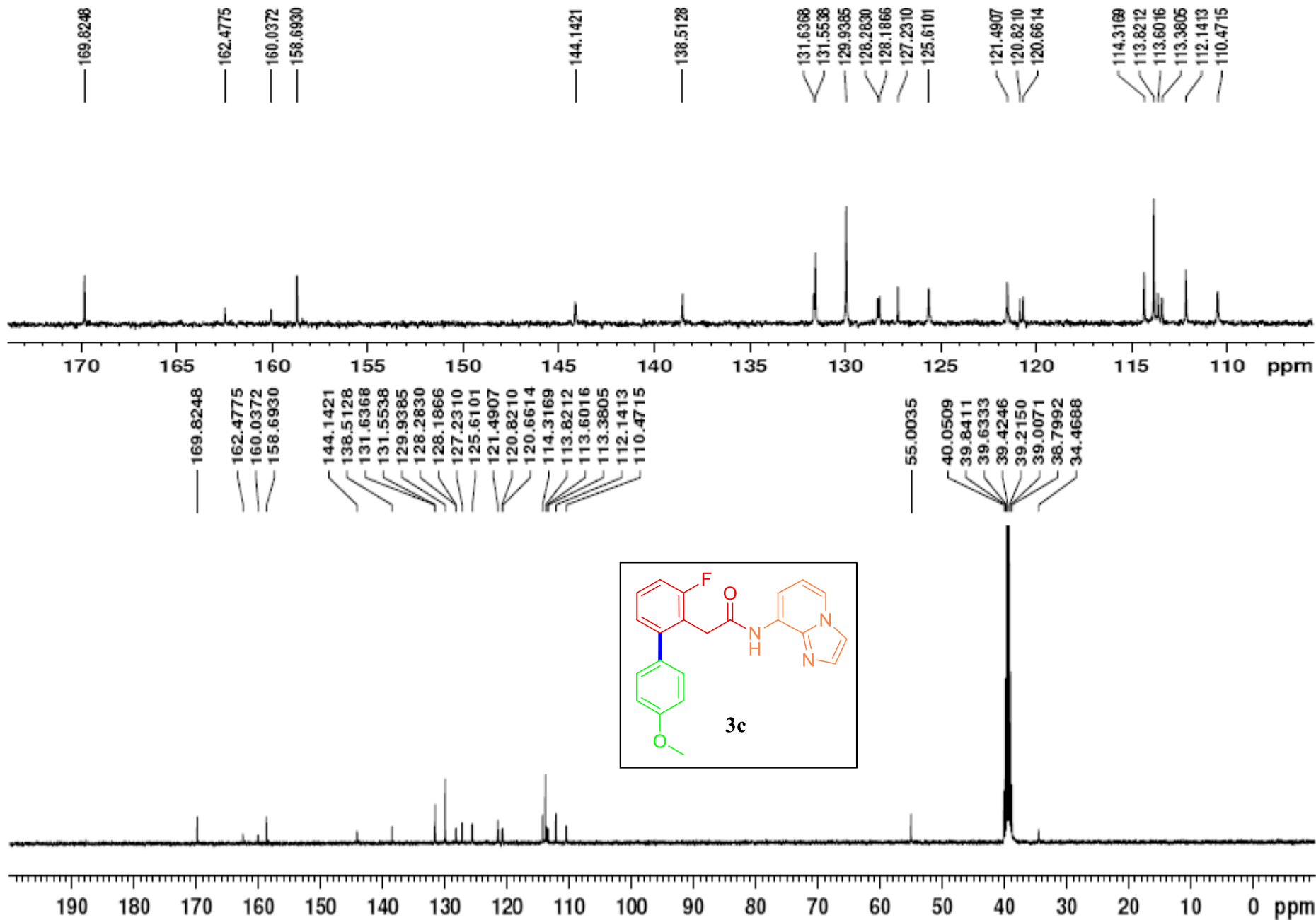
¹³C NMR of **3b** in DMSO-d₆



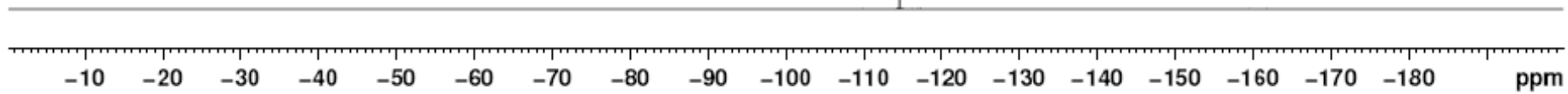
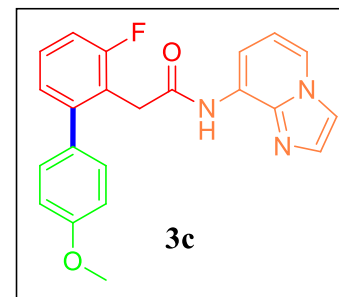
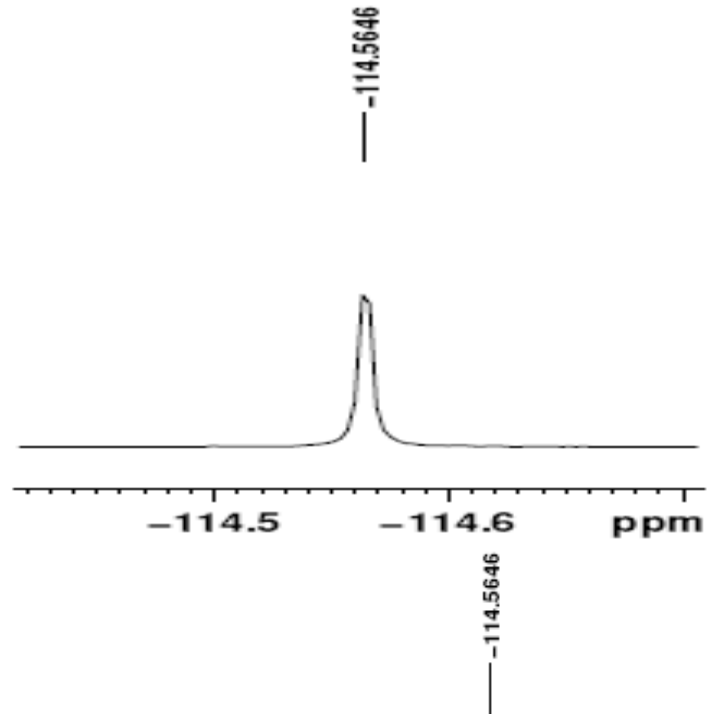
^{19}F NMR of **3b** in DMSO-d_6



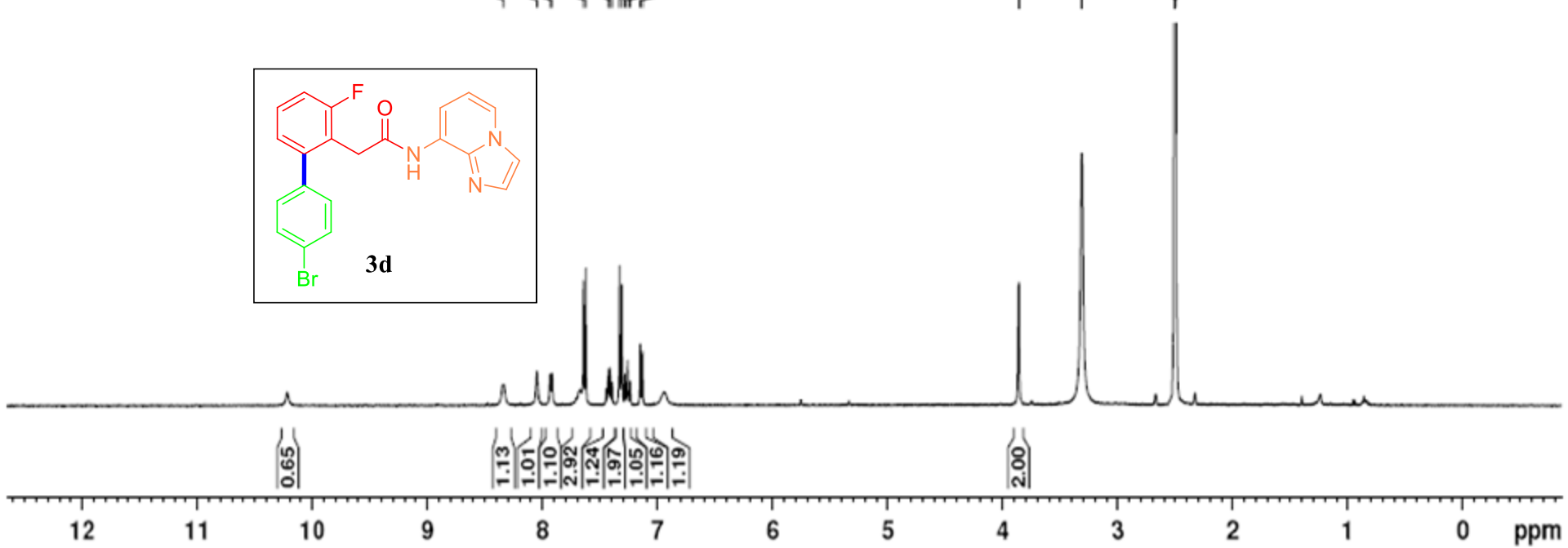
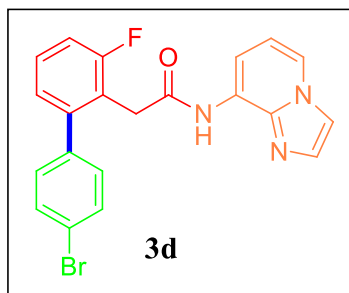
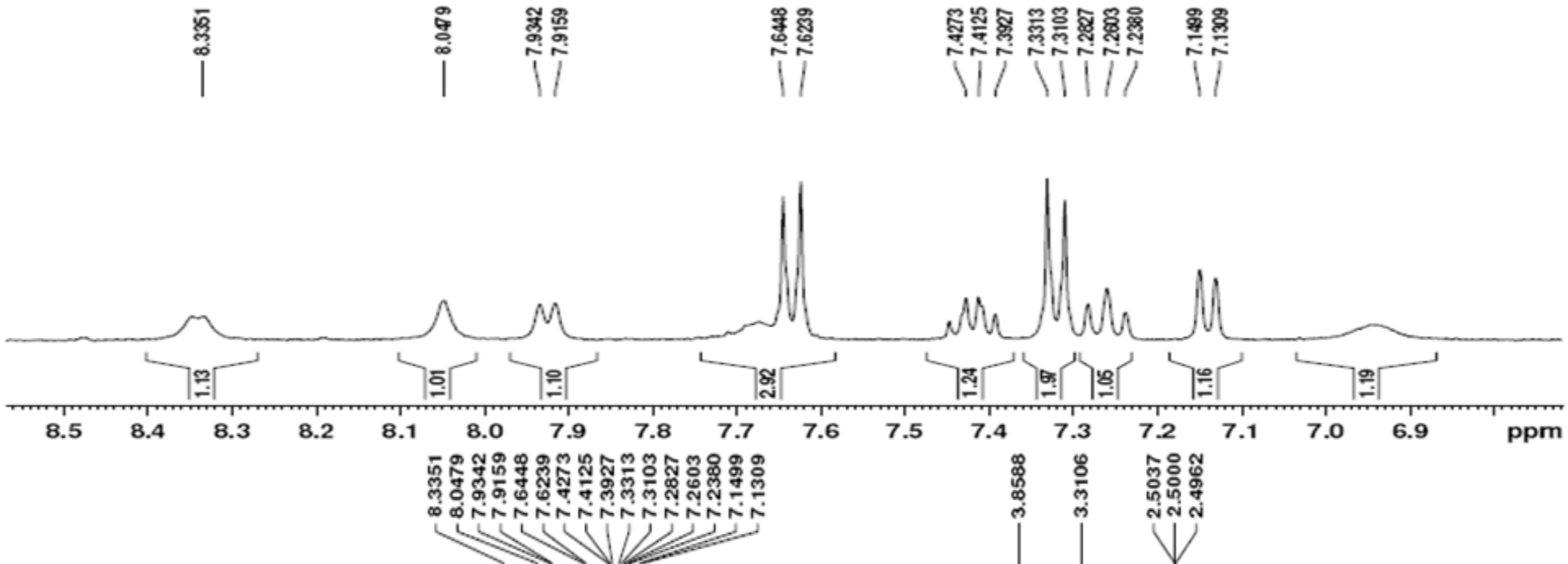
¹H NMR of **3c** in DMSO-d₆



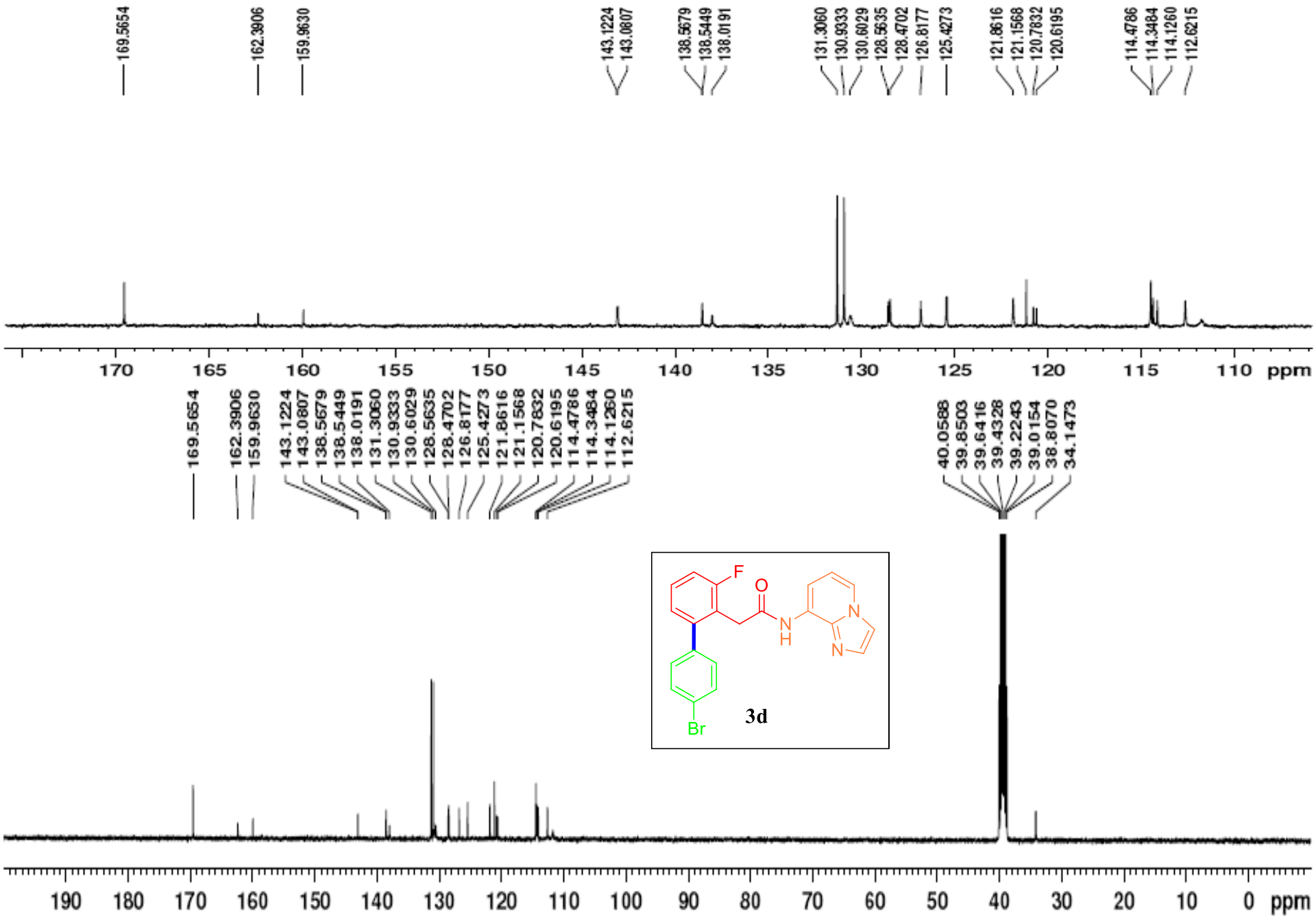
¹³C NMR of **3c** in DMSO-d₆



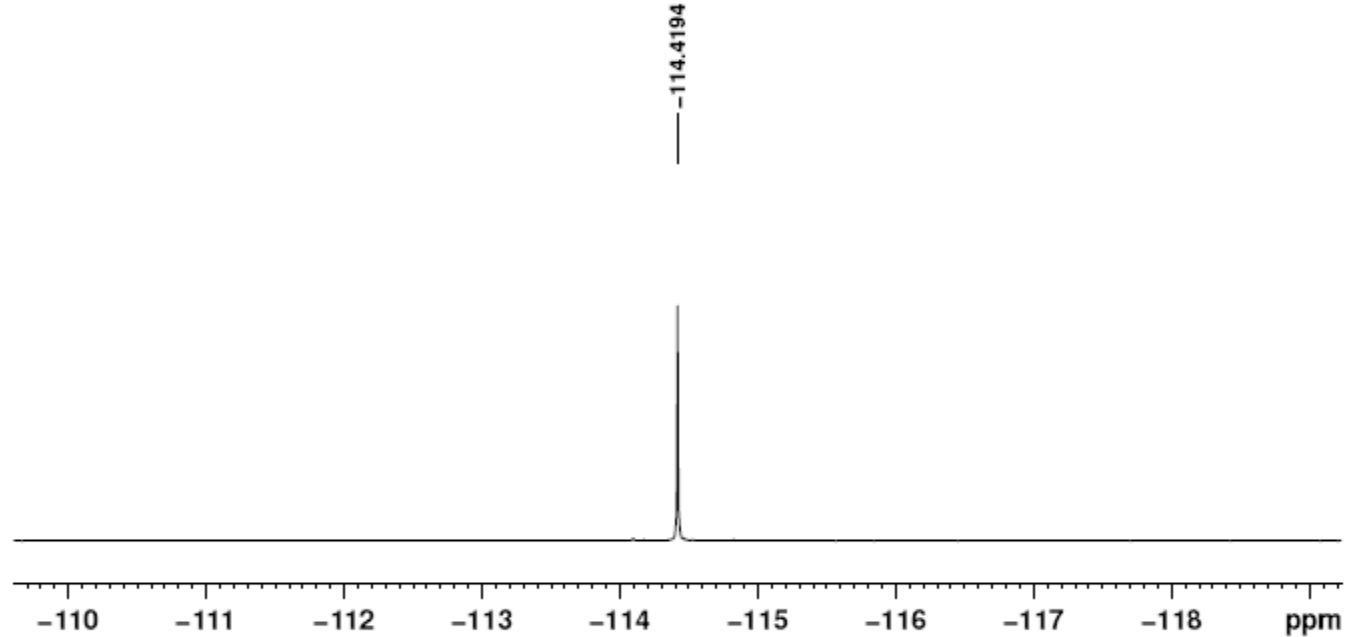
^{19}F NMR of **3c** in DMSO-d_6



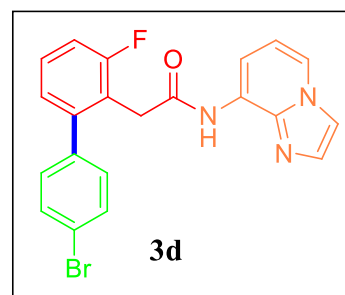
1H NMR of **3d**



¹³C NMR of **3d** in DMSO-d₆



-114.4194



-40

-60

-80

-100

-120

-140

-160

-180

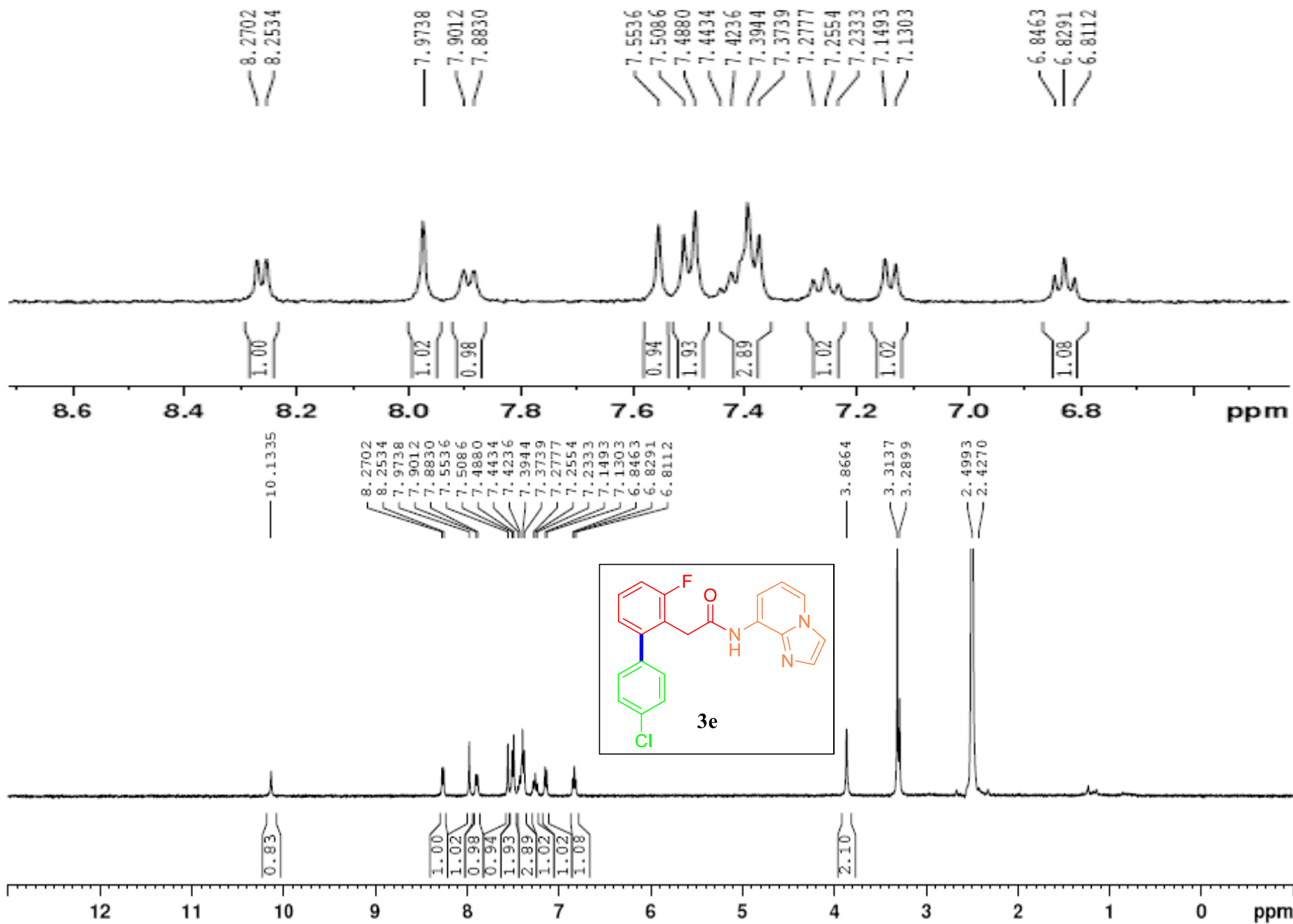
-200

-220

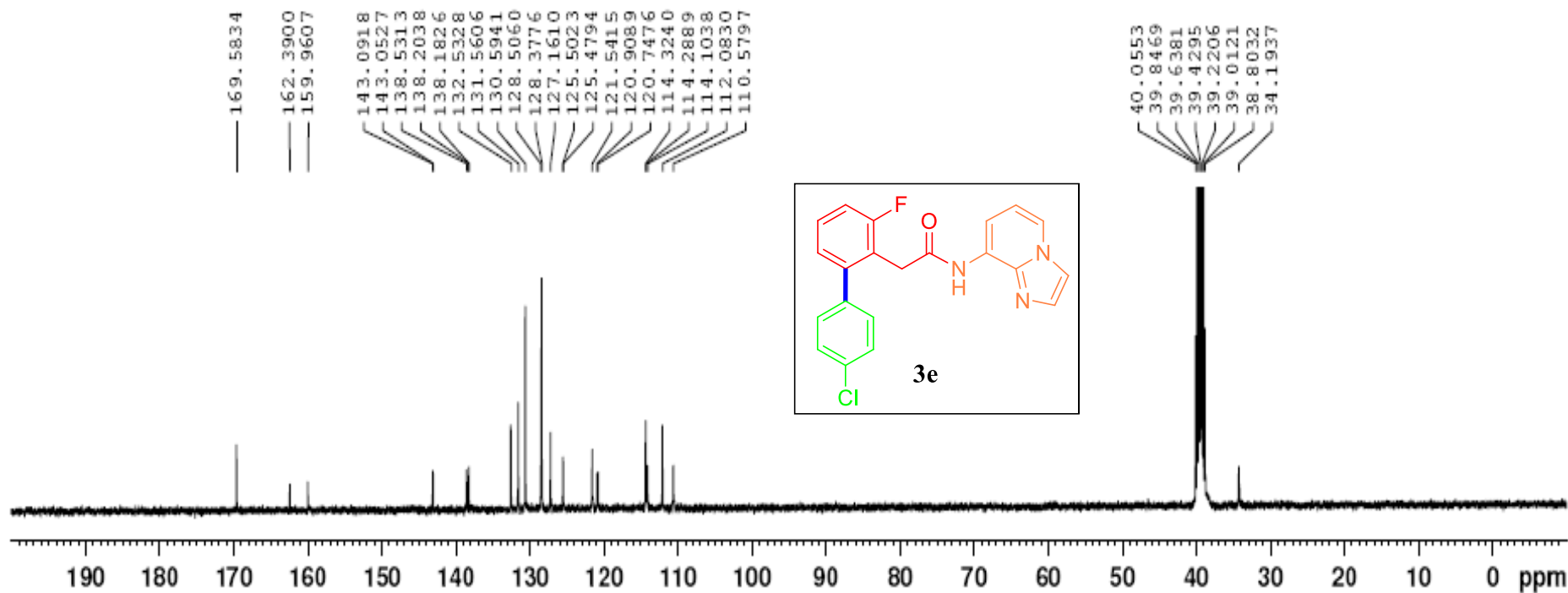
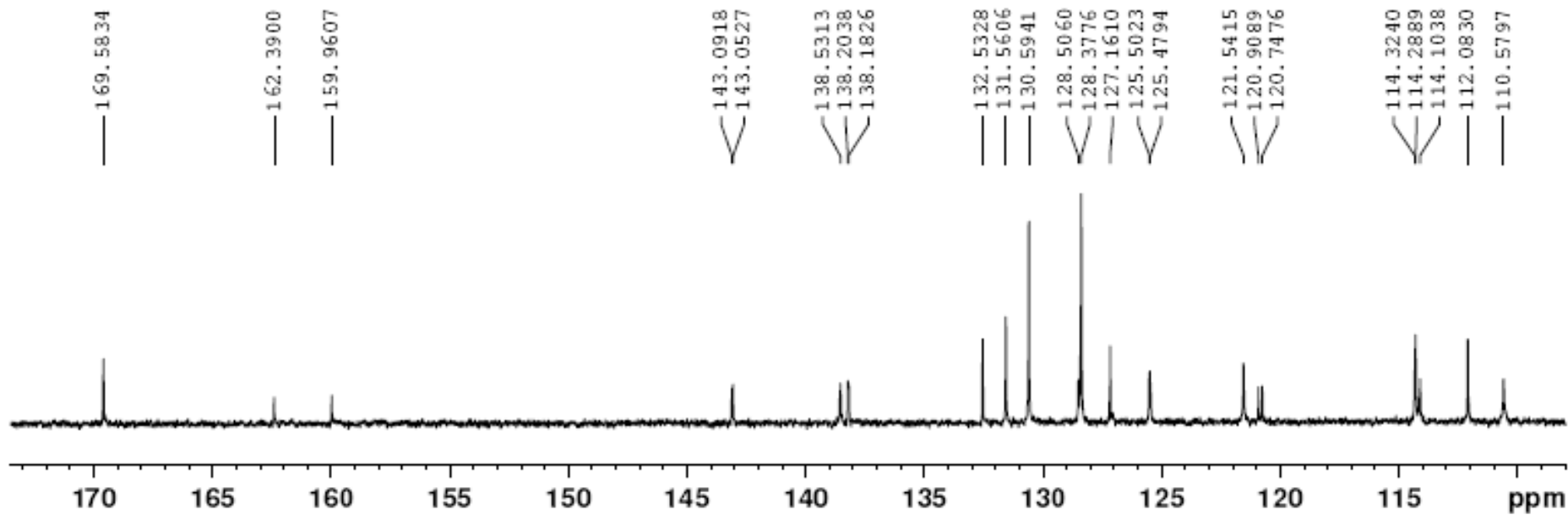
-240

ppm

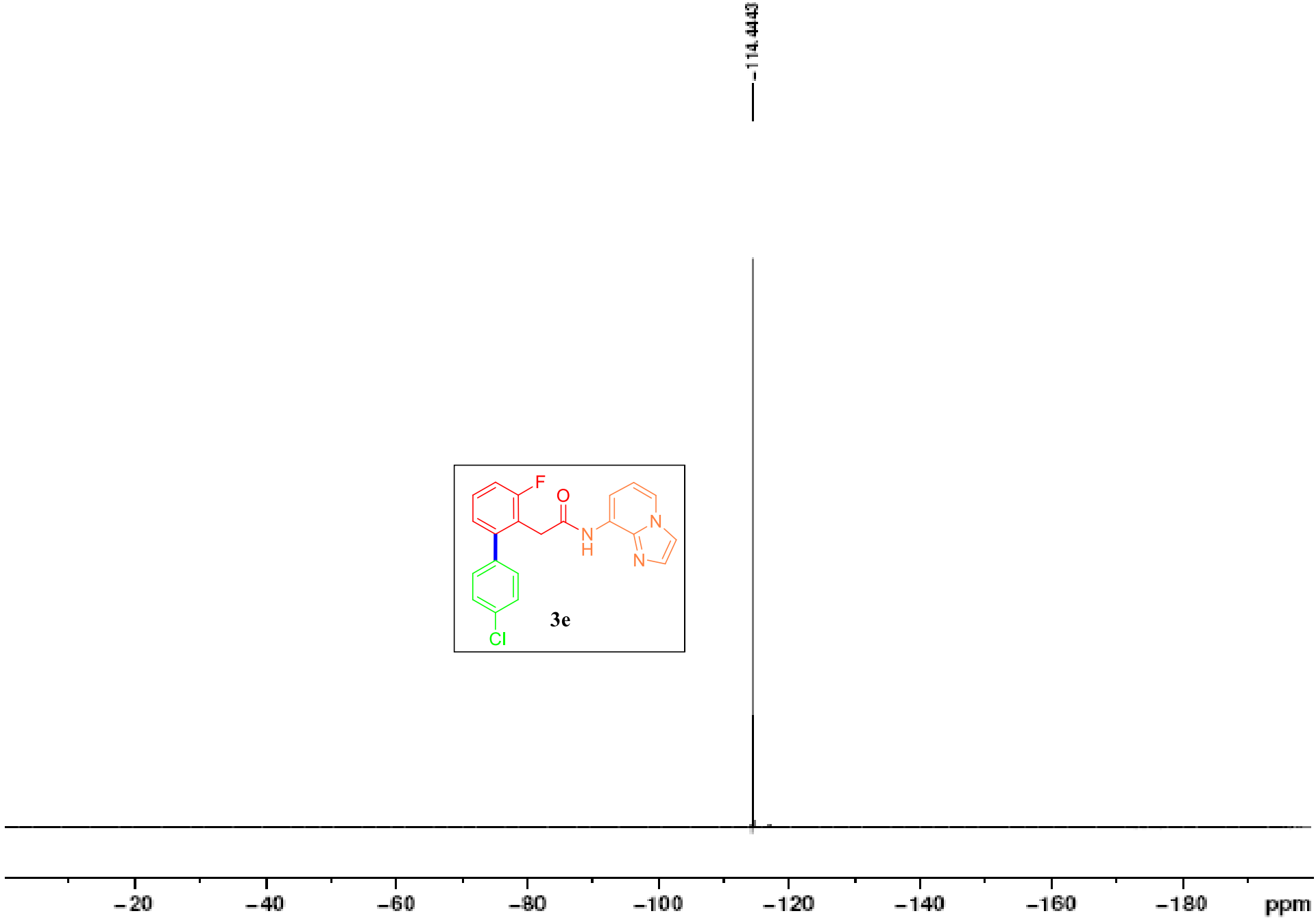
^{19}F NMR of **3d** in DMSO-d_6



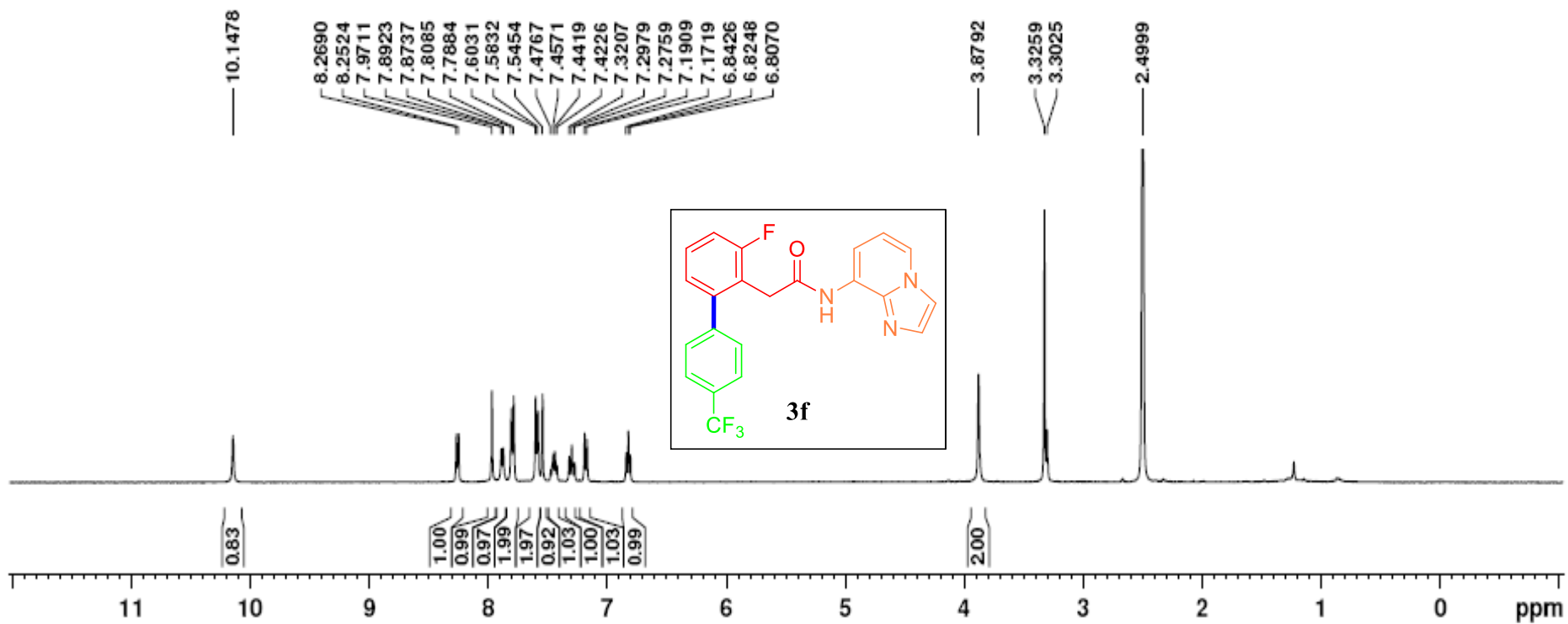
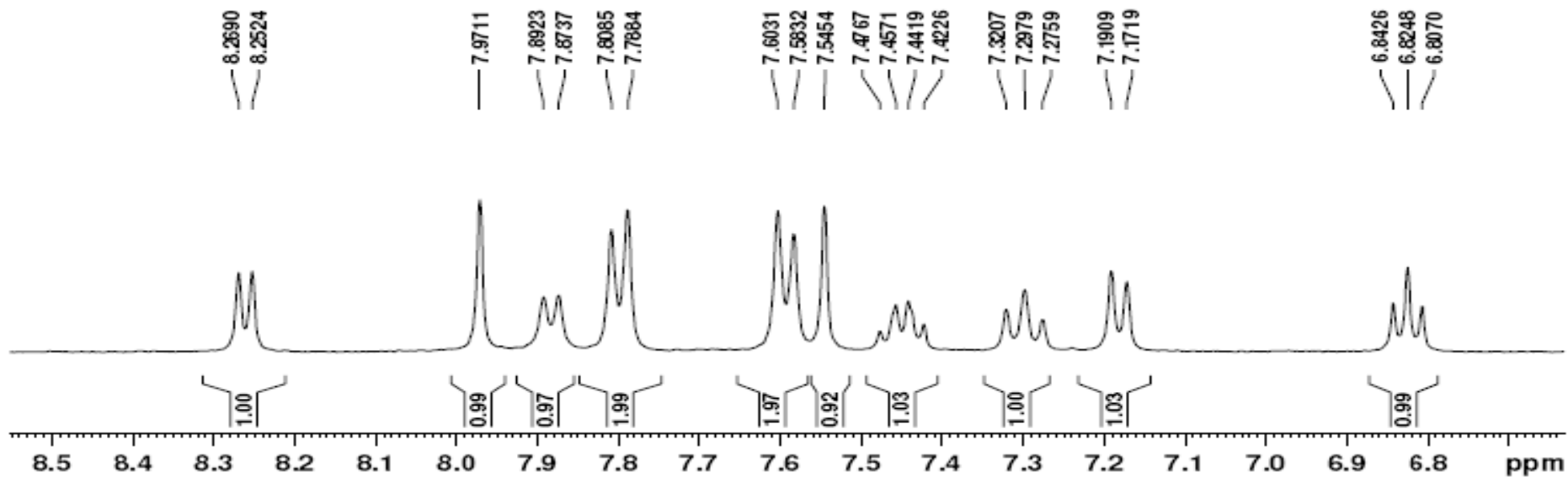
¹H NMR of **3e** in DMSO-d₆



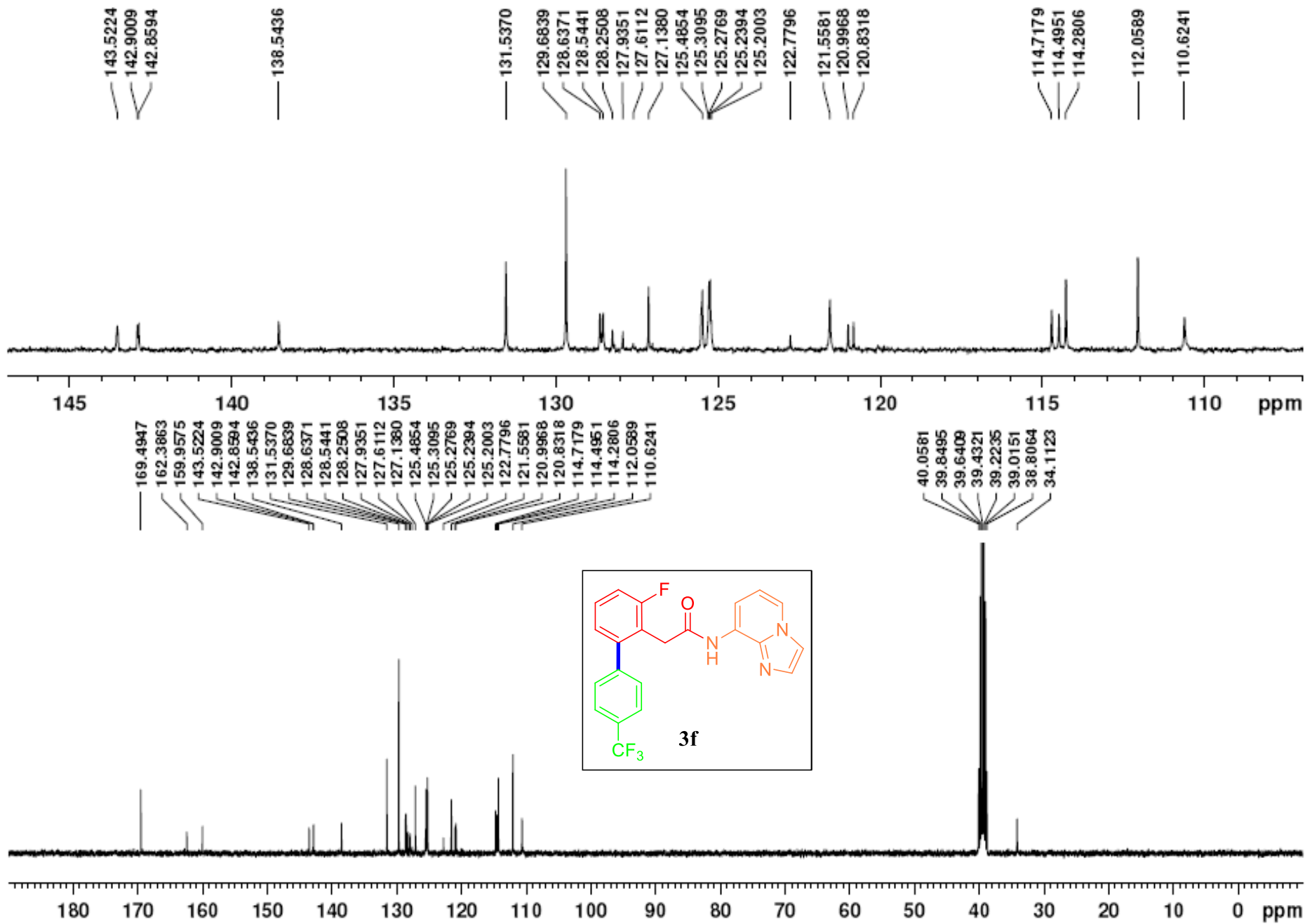
¹³C NMR of 3e in DMSO-d₆



^{19}F NMR of **3e** in DMSO-d_6



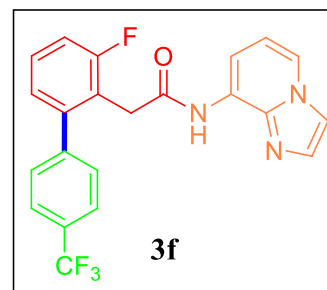
^1H NMR of **3f** in DMSO-d_6



¹³C NMR of **3f** in DMSO-d₆

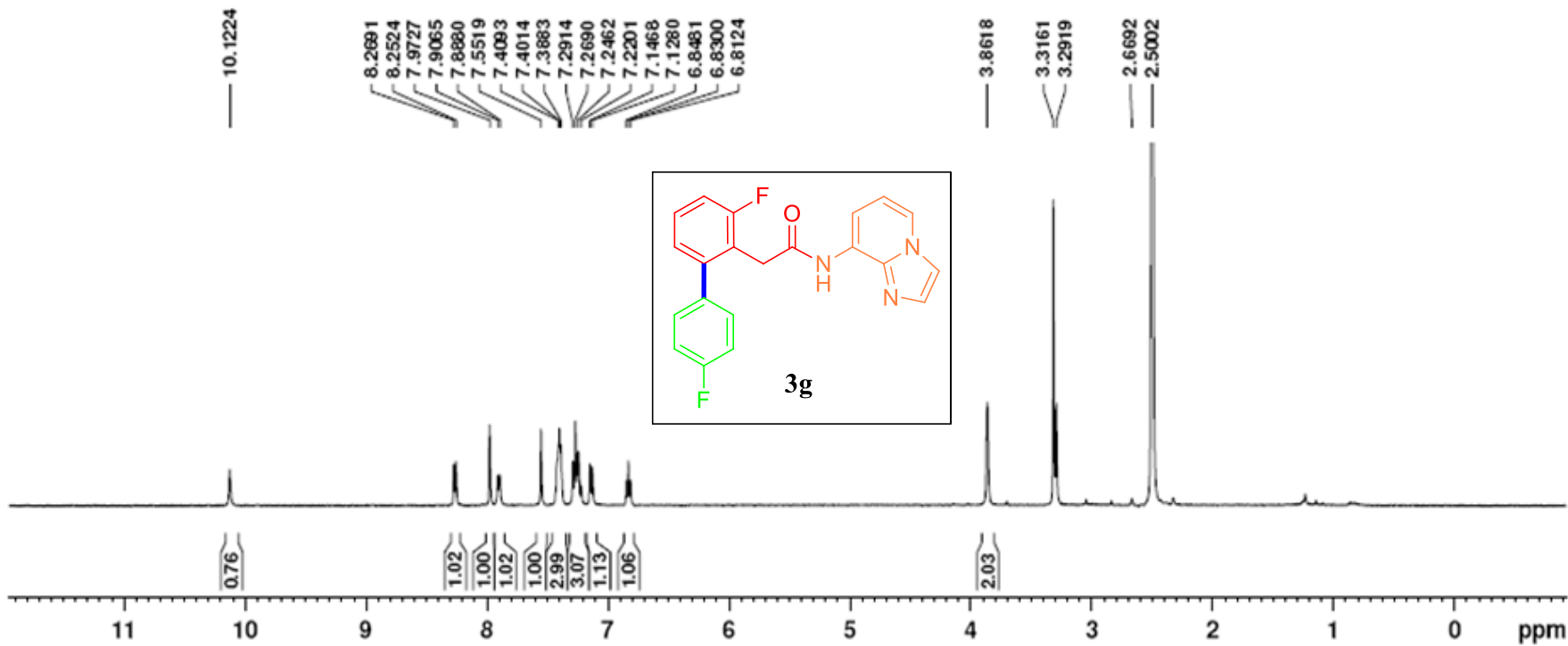
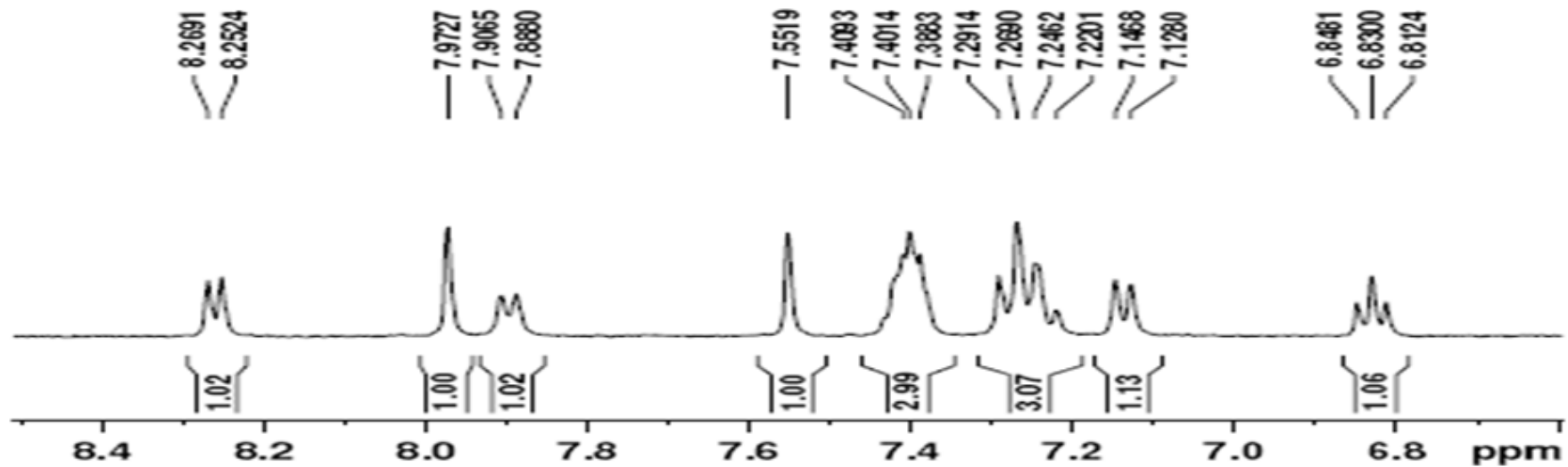
-61.0590

-114.4342

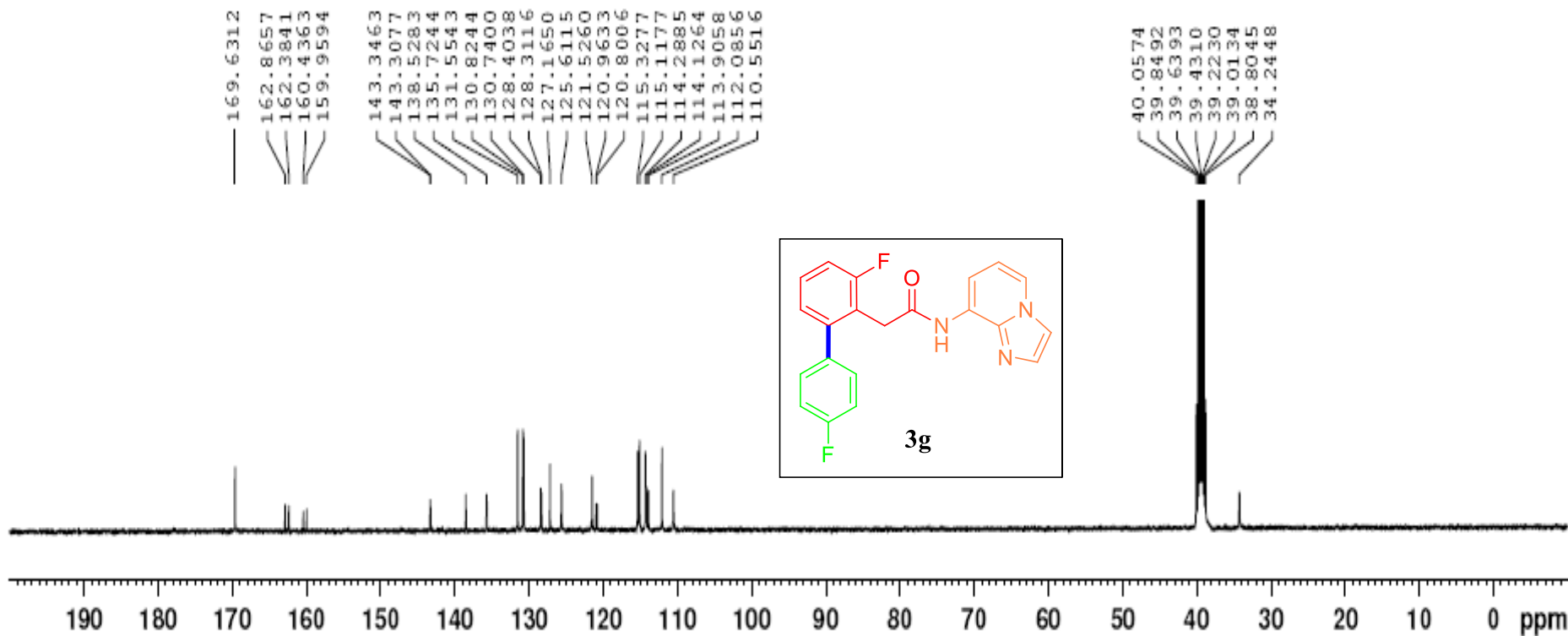
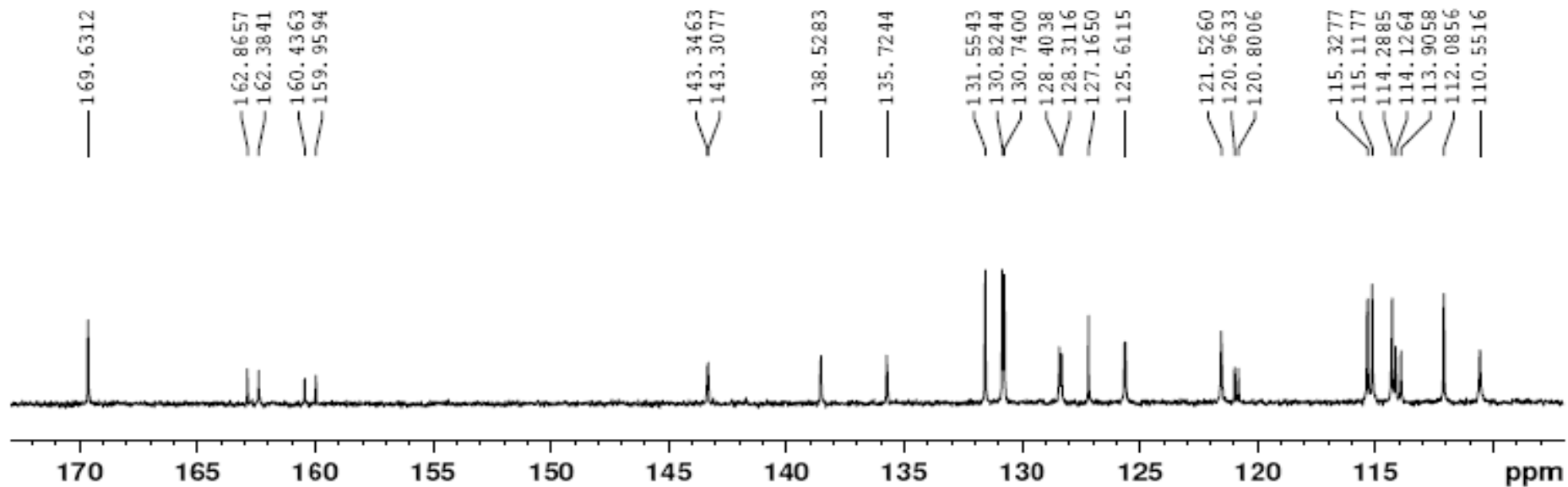


-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 ppm

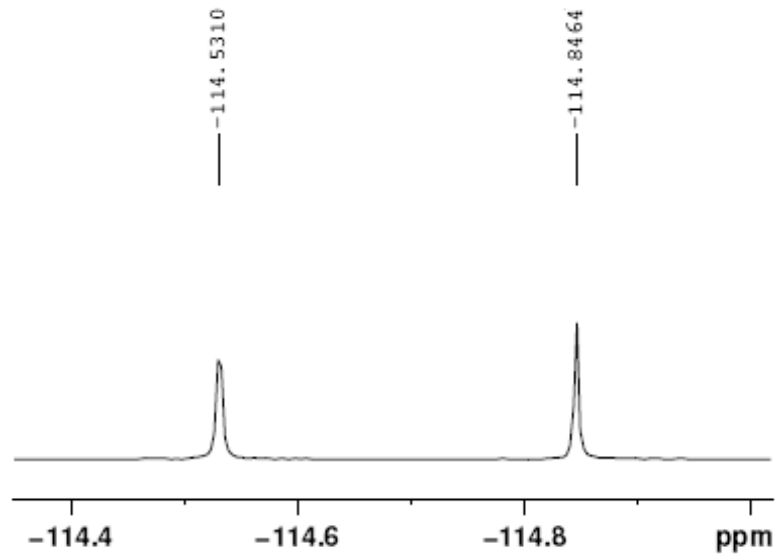
¹⁹F NMR of **3f** in DMSO-d₆



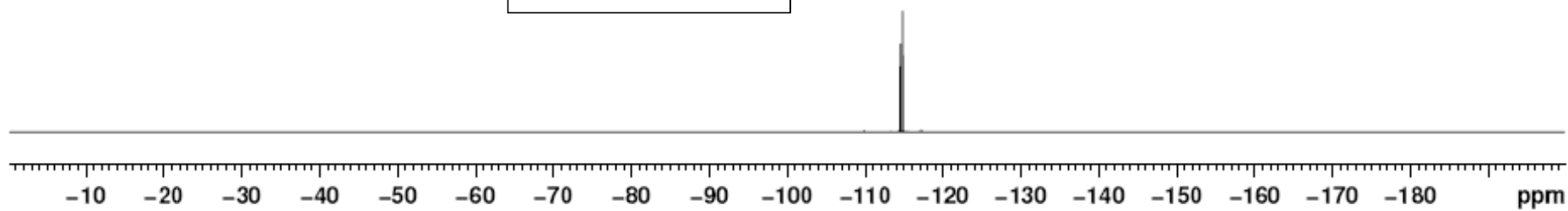
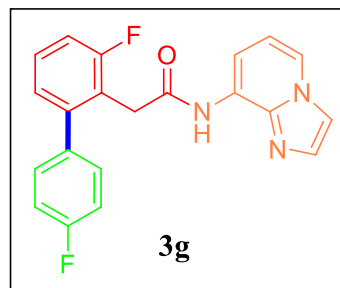
^1H NMR of **3g** in DMSO-d_6



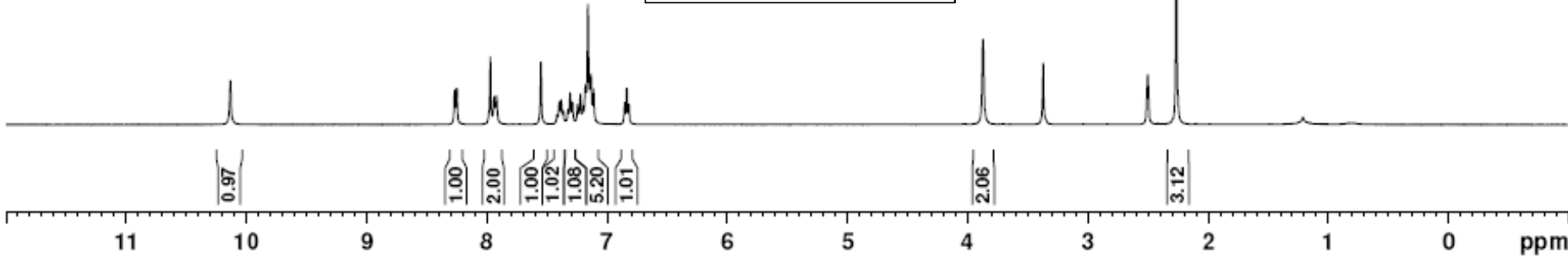
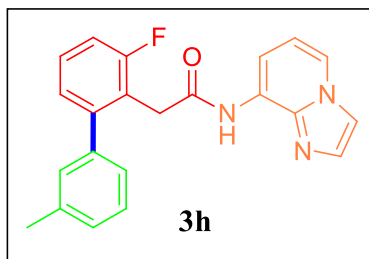
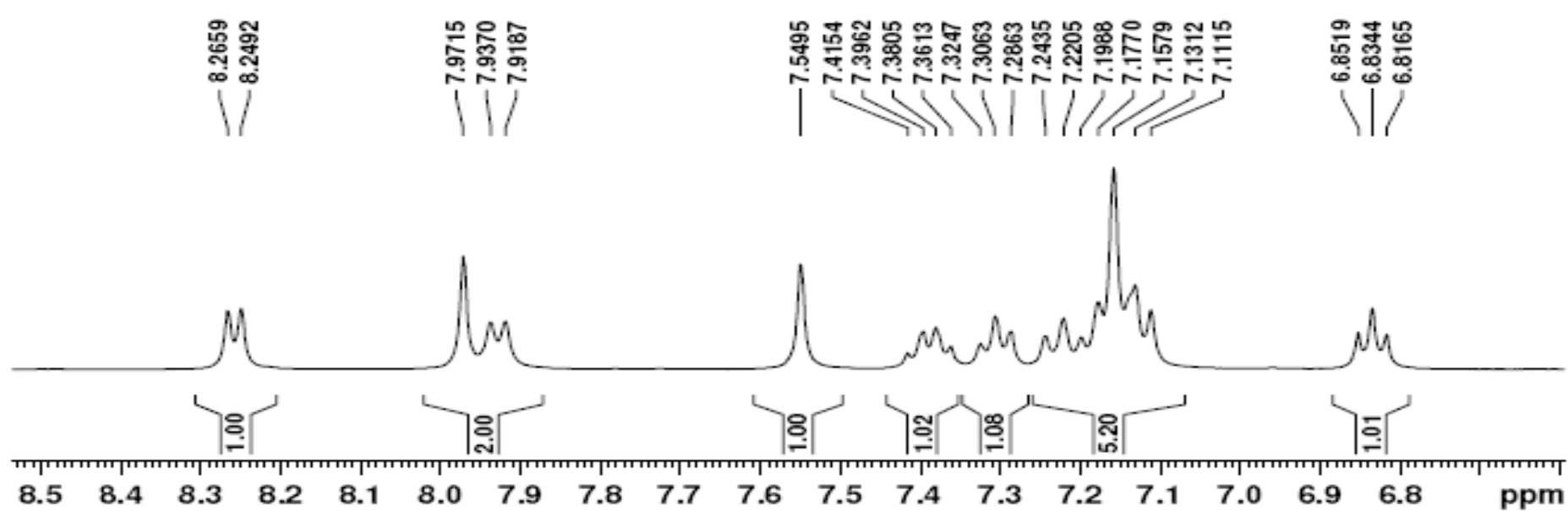
¹³C NMR of **3g** in DMSO-d₆



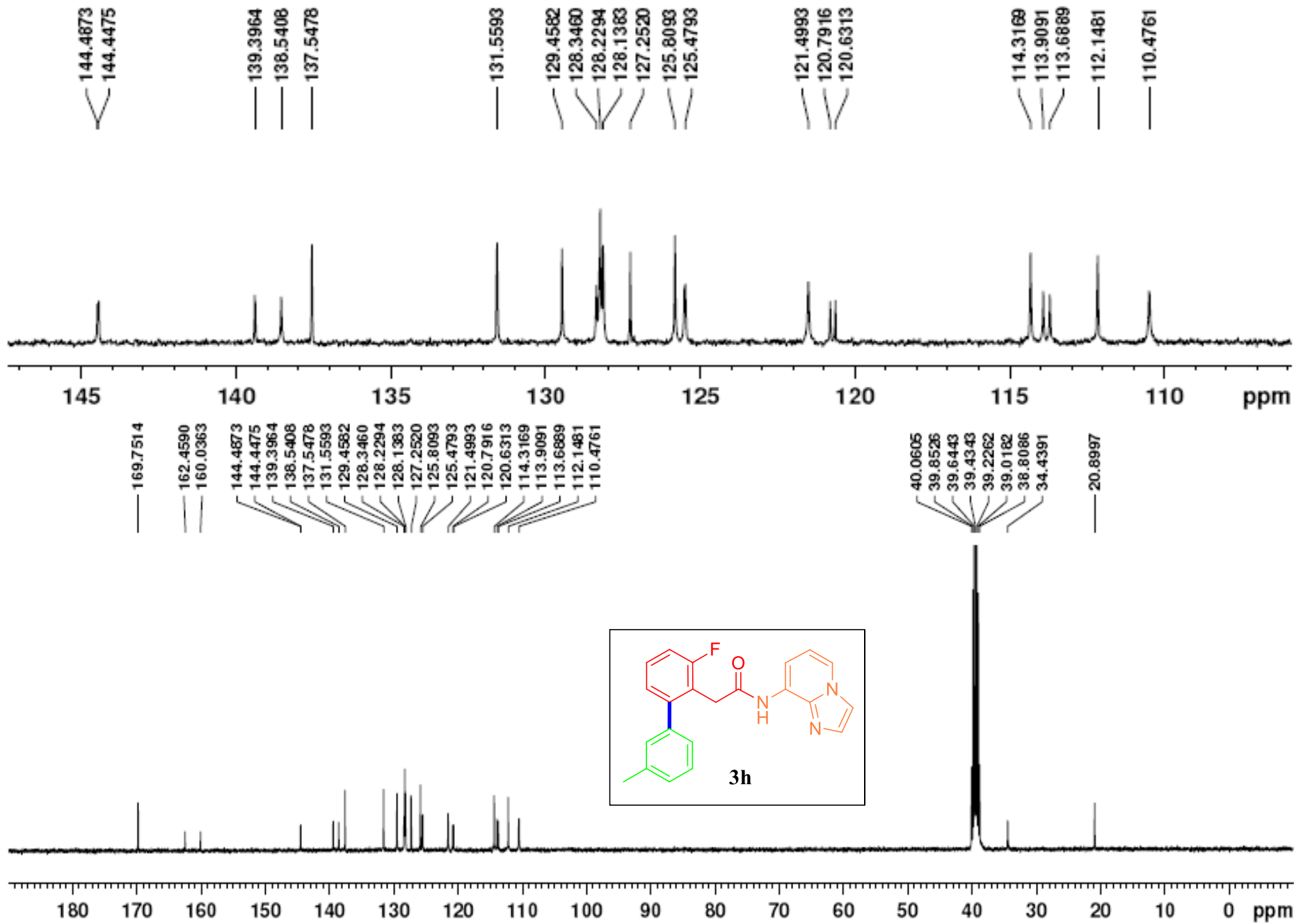
-114.5310
-114.8464



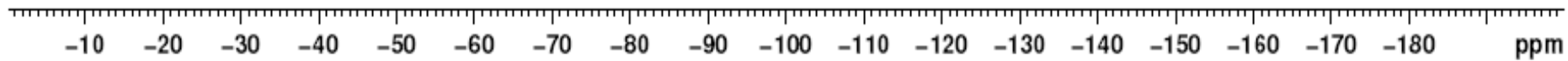
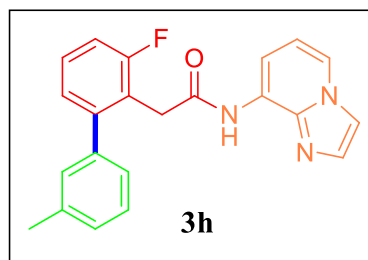
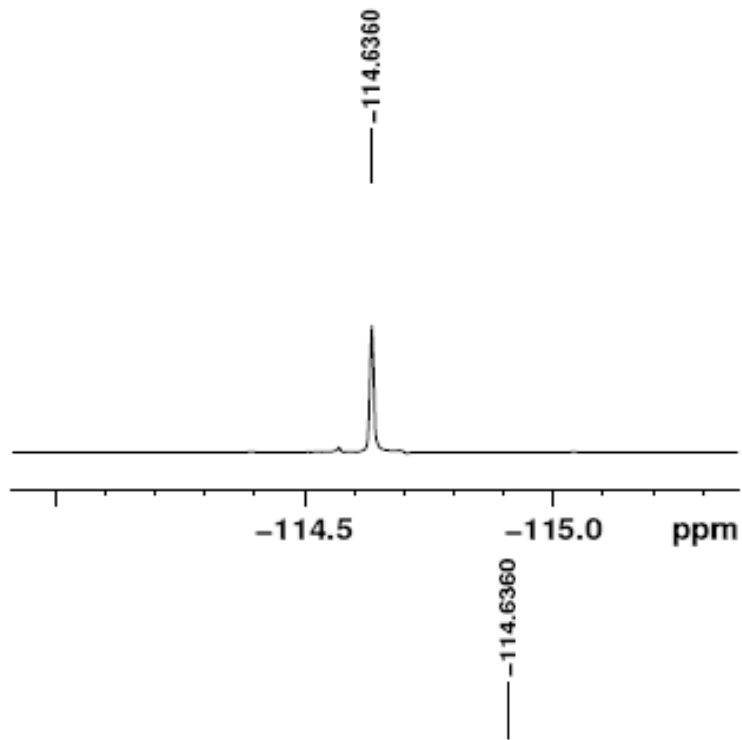
^{19}F NMR of **3g** in DMSO-d_6



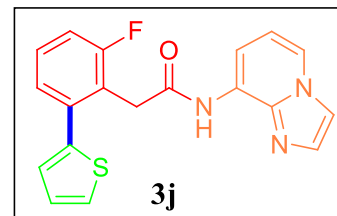
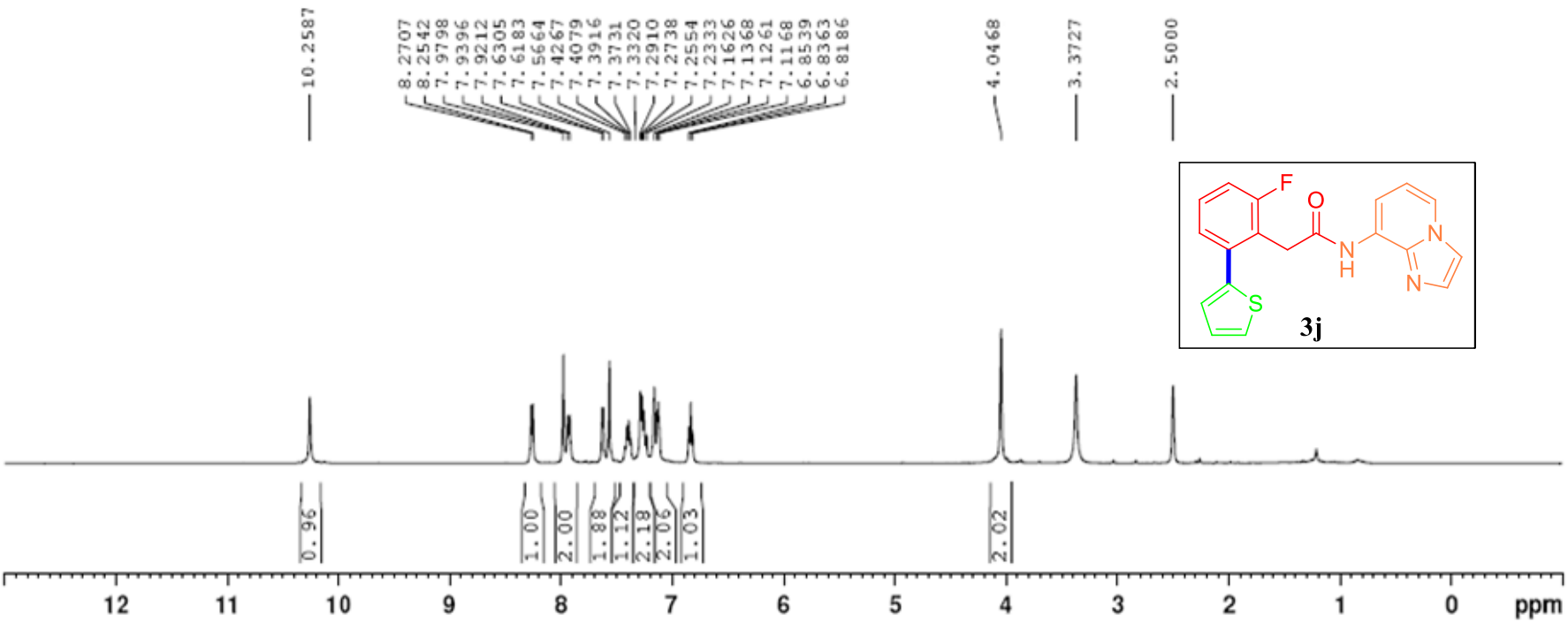
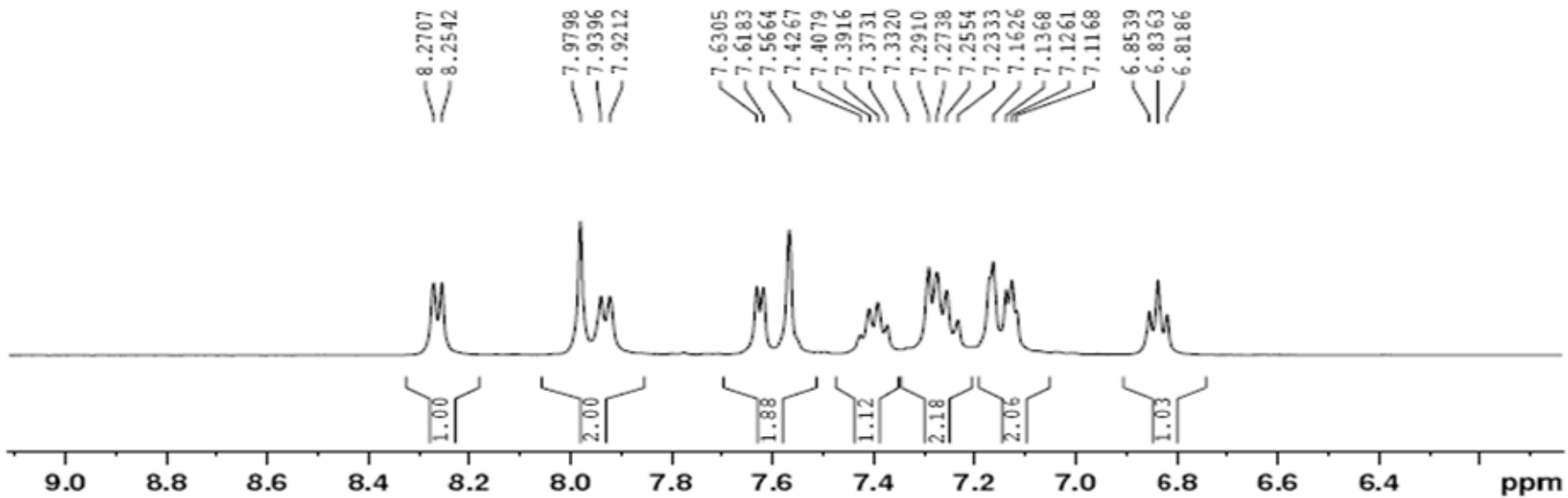
¹H NMR of **3h** in DMSO-d₆



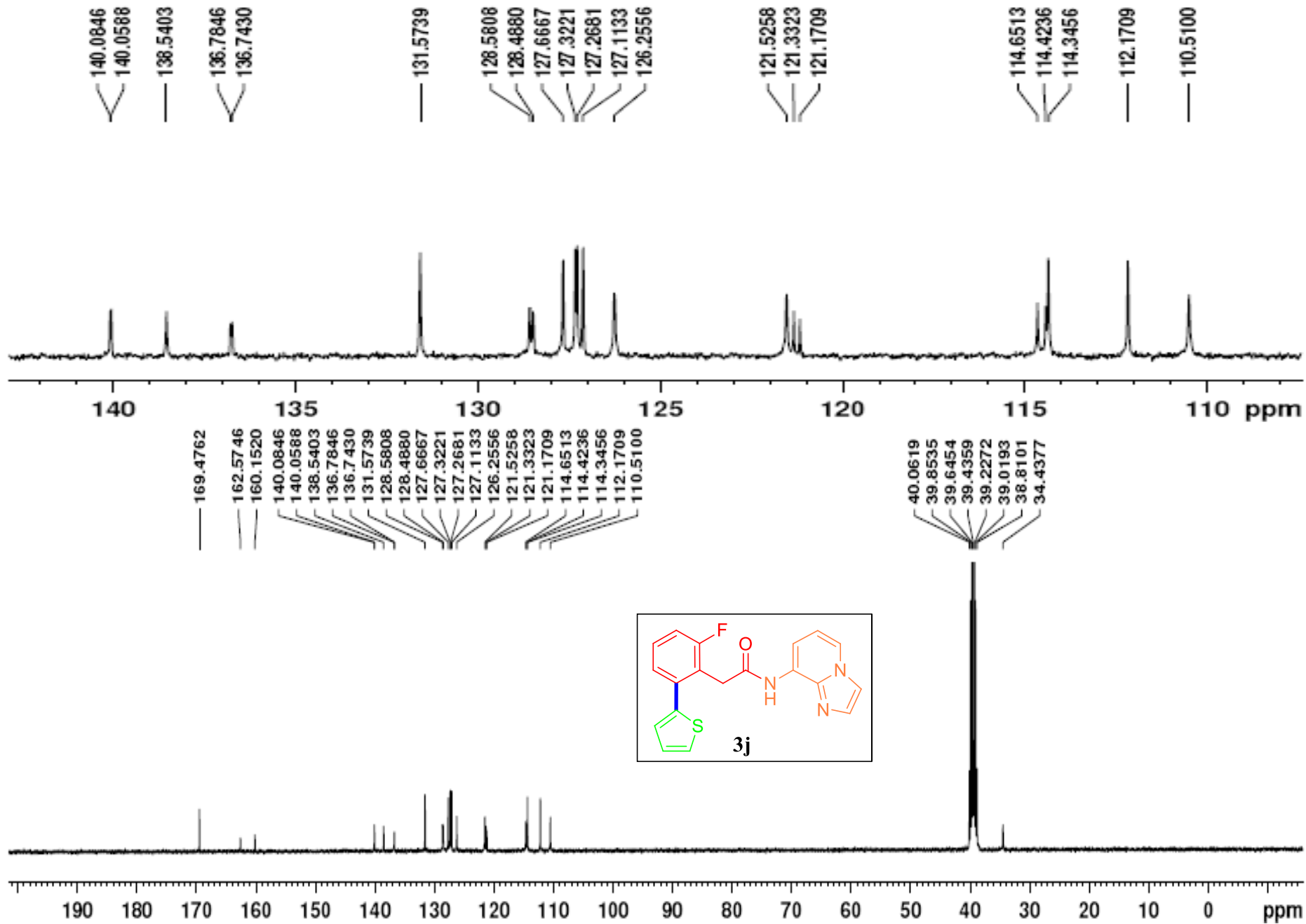
¹³C NMR of **3h** in DMSO-d₆



^{19}F NMR of **3h** in DMSO-d_6

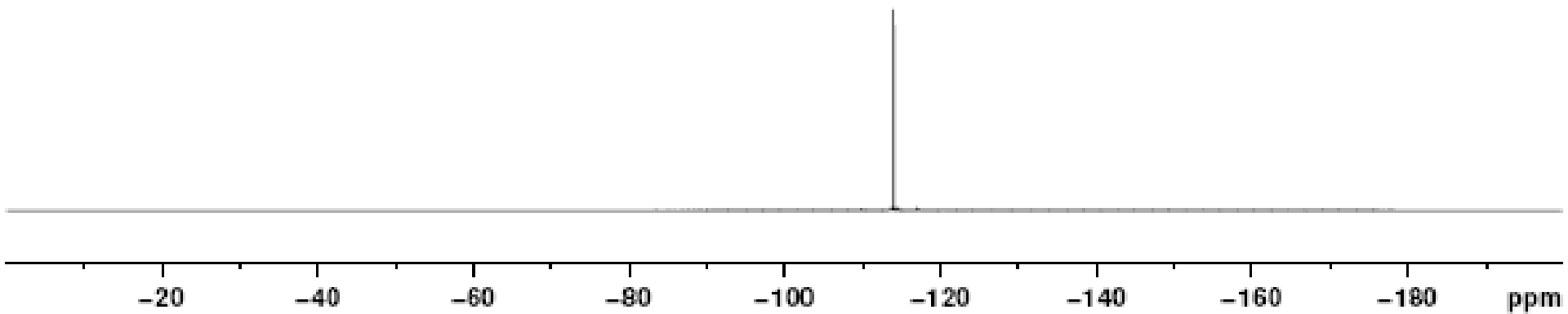
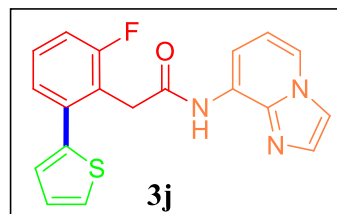


¹H NMR of 3j

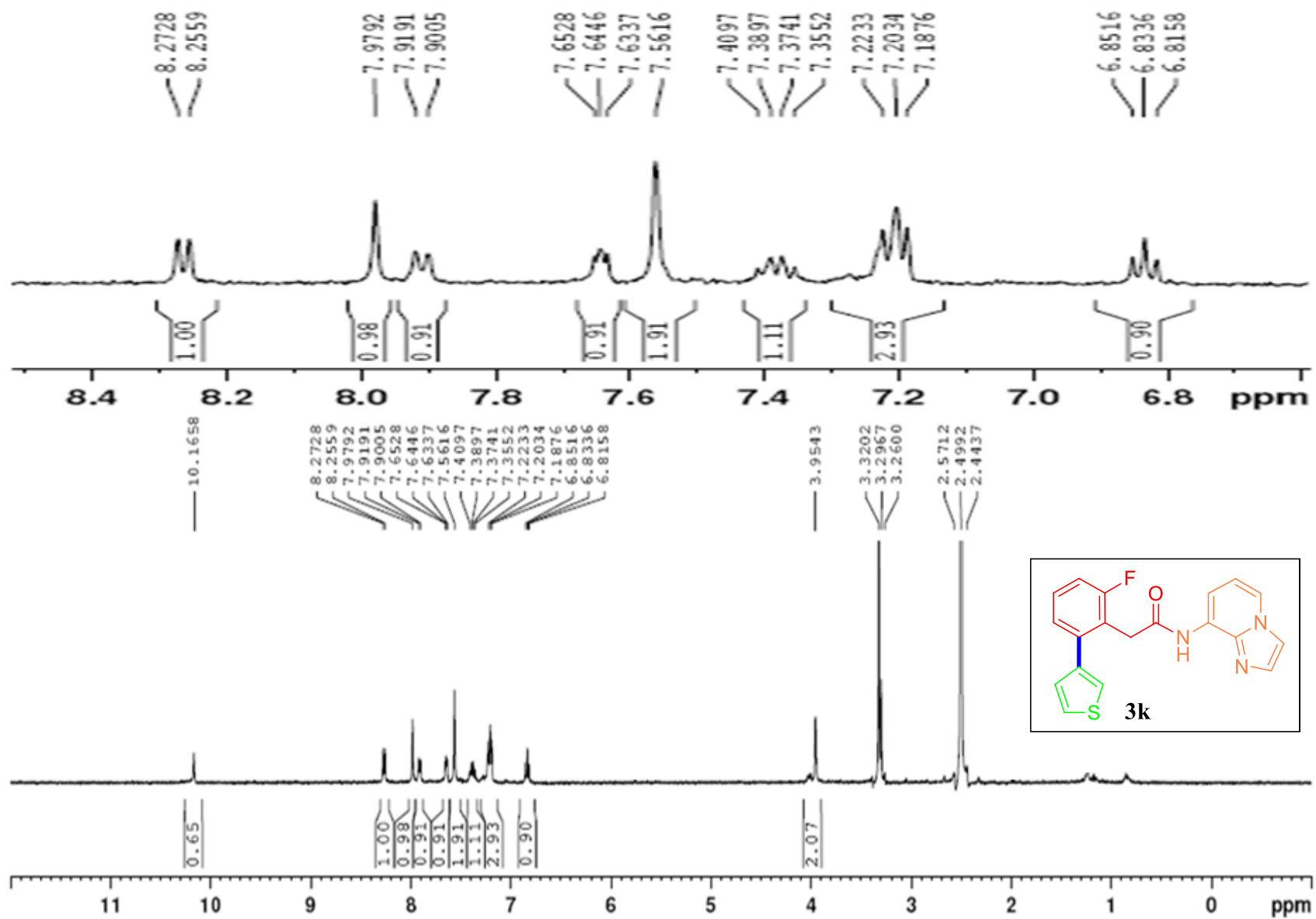


¹³C NMR of **3j** in DMSO-d₆

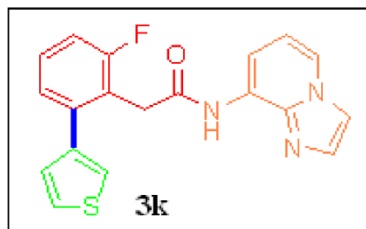
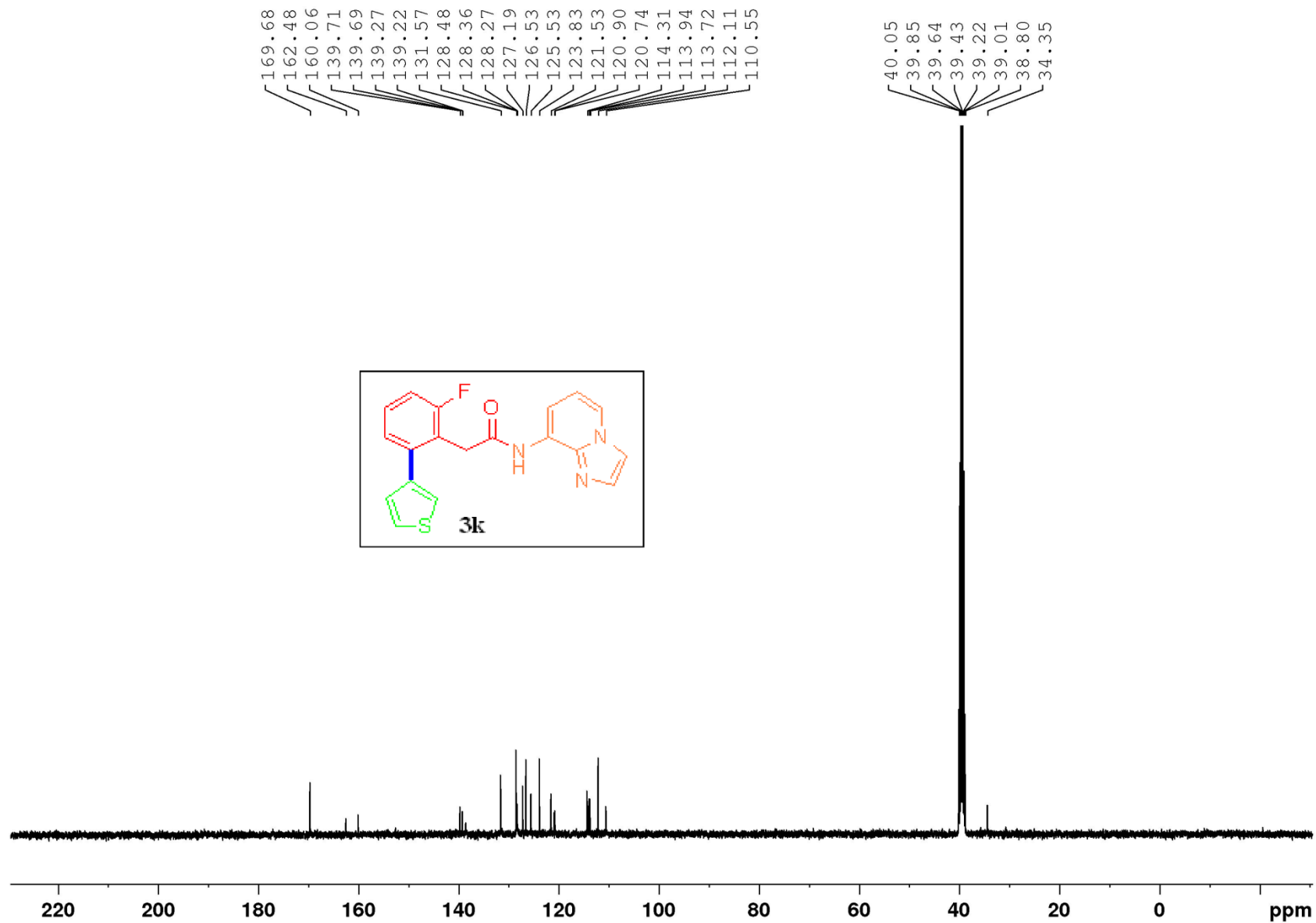
-113.9721



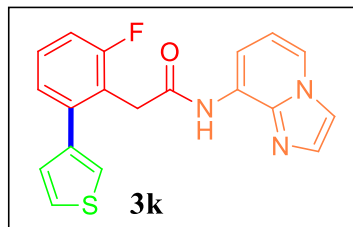
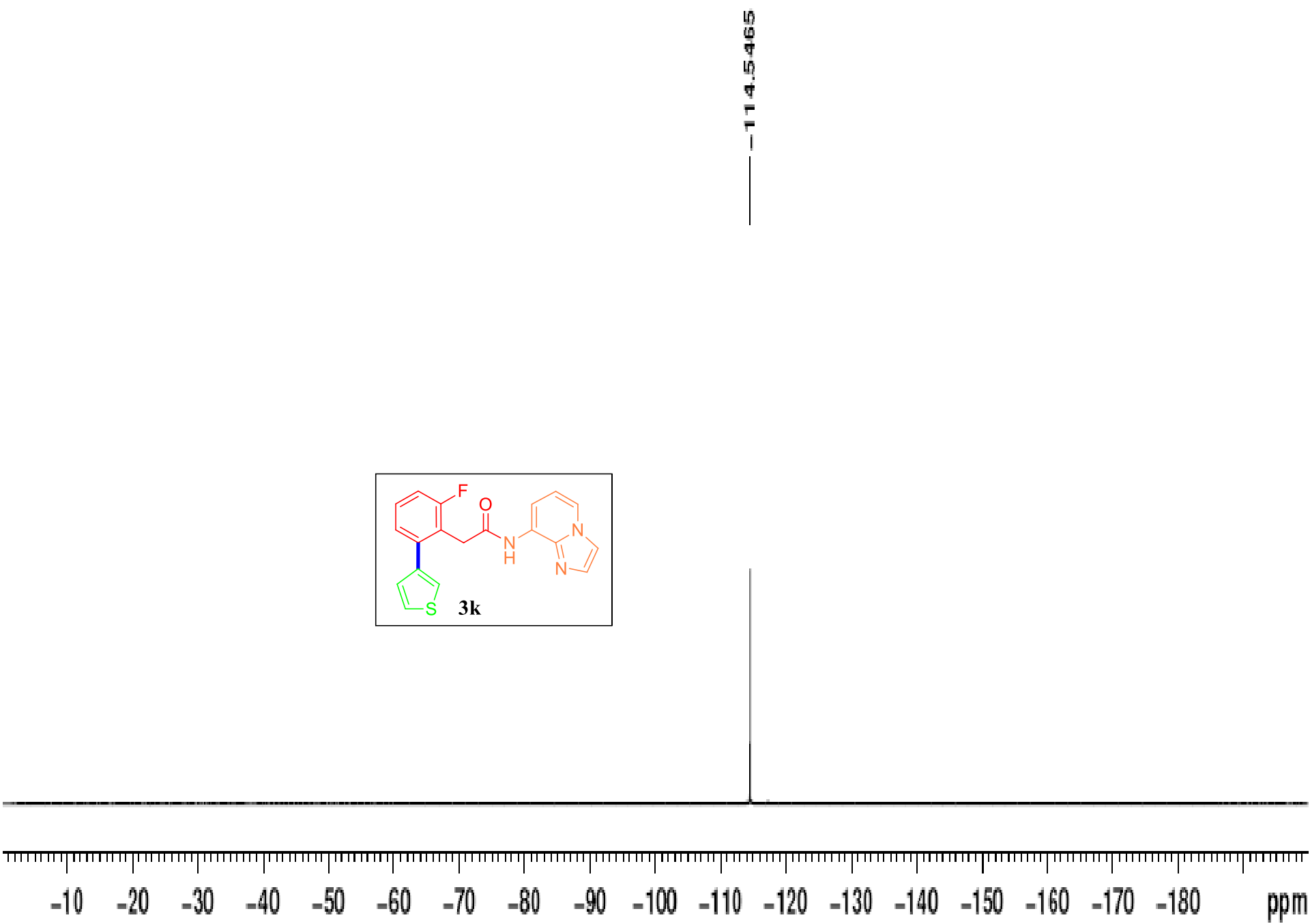
¹⁹F NMR of **3j** in DMSO-d₆



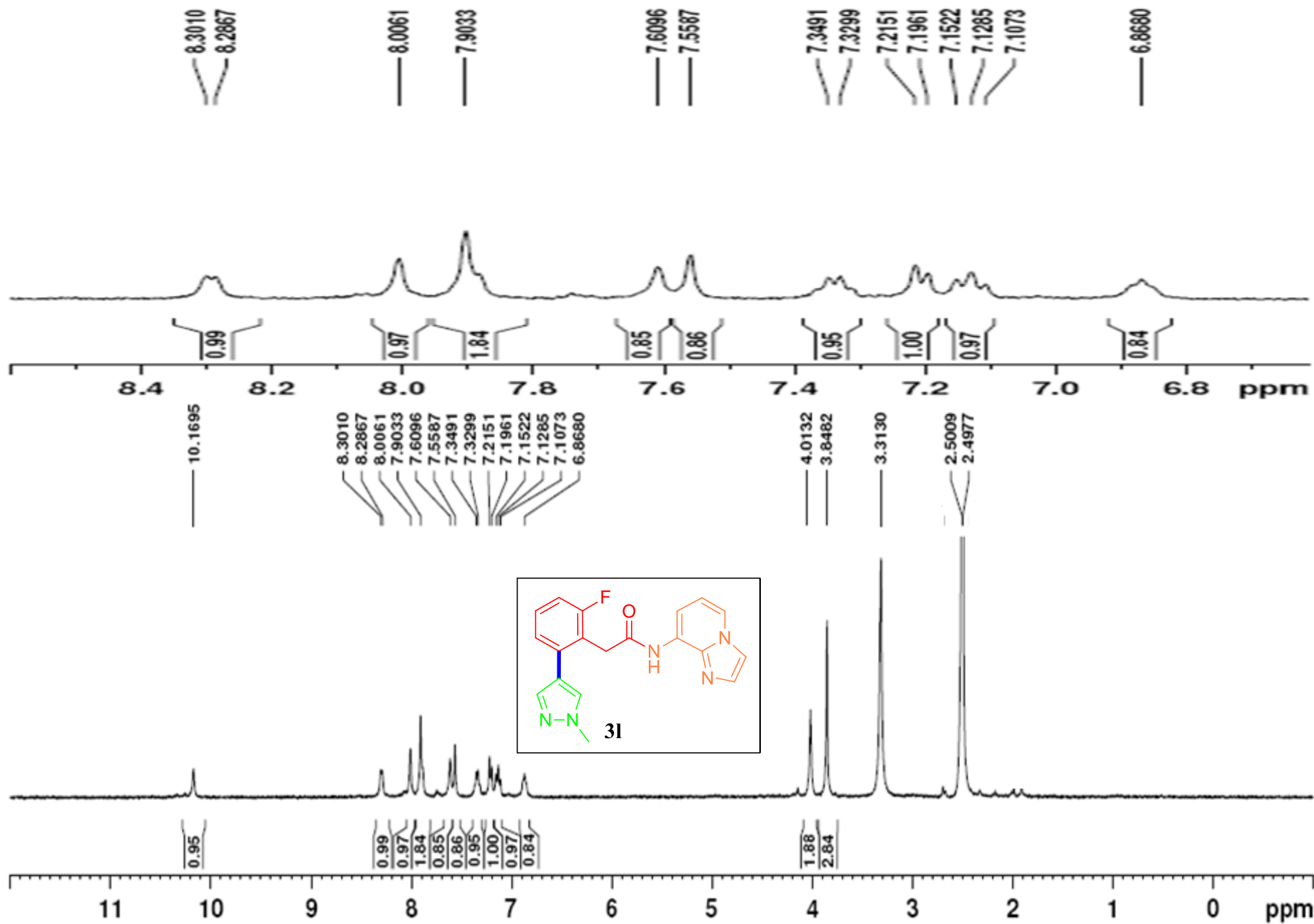
1H NMR of **3K**



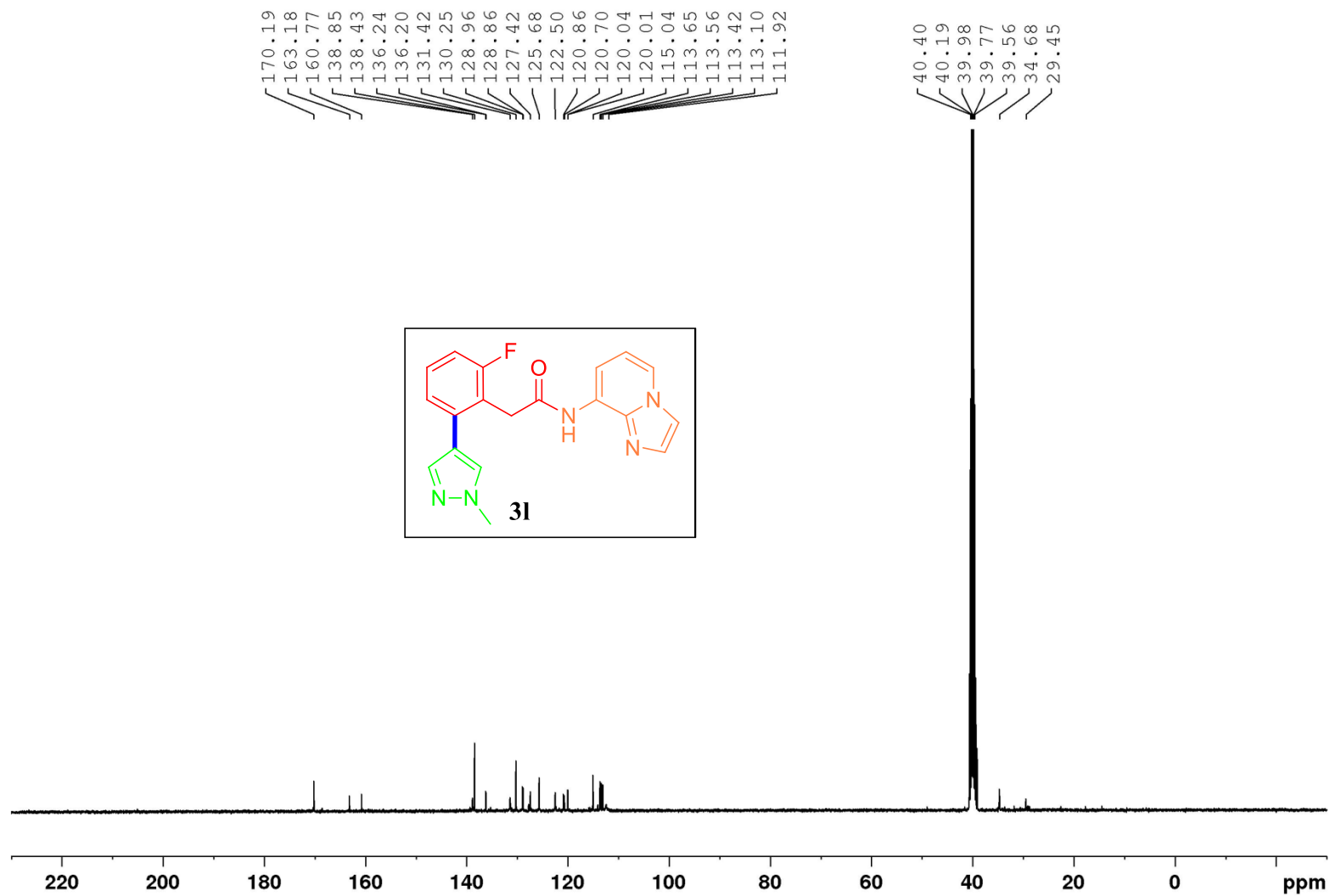
¹³C NMR of 3k



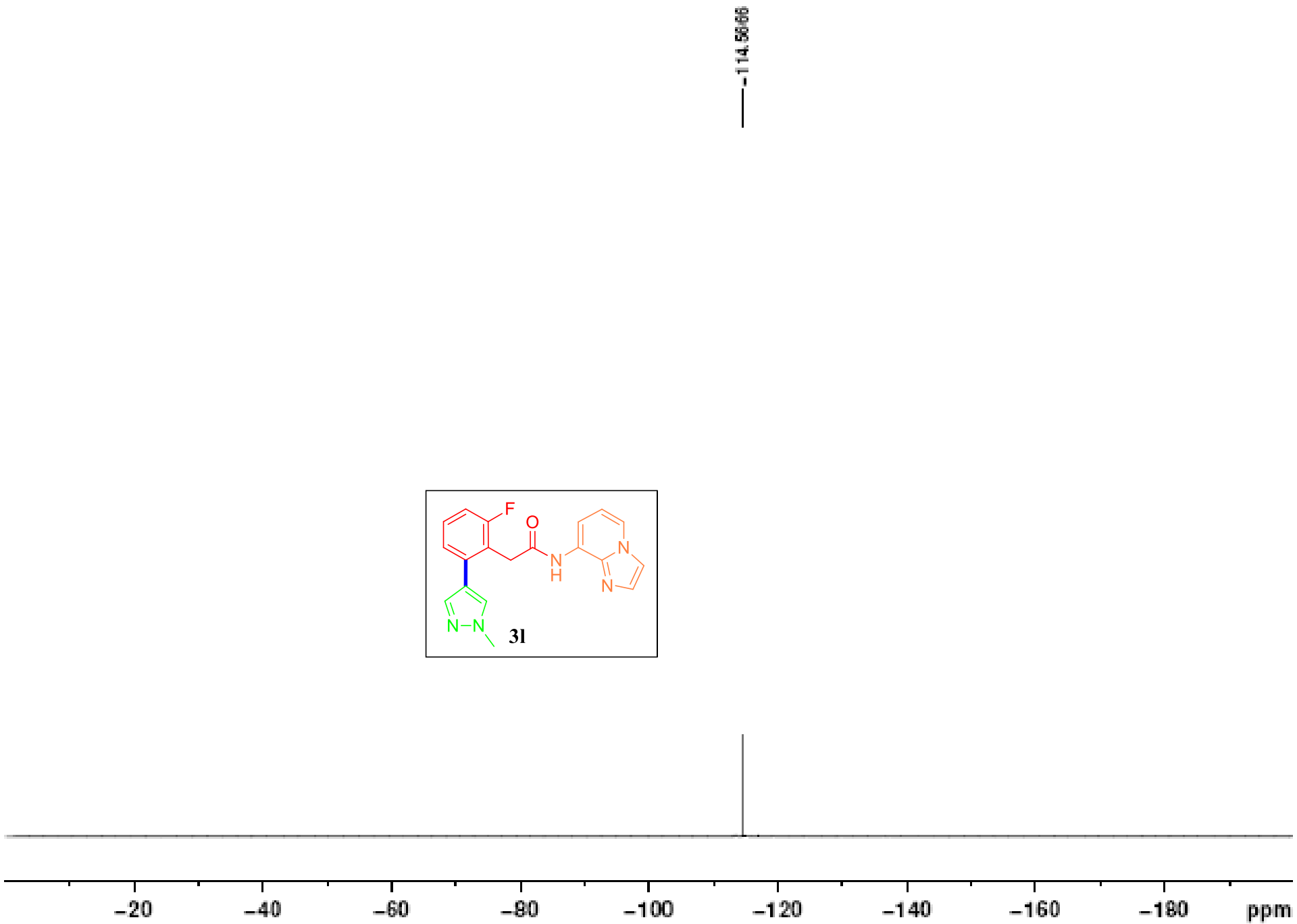
¹⁹F NMR of **3k** in DMSO-d₆



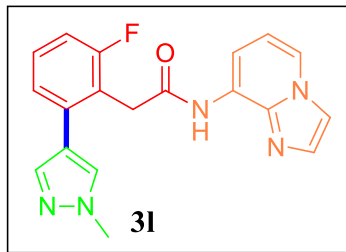
1H NMR of 3I



^{13}C NMR of **31**



-114.5666



-20

-40

-60

-80

-100

-120

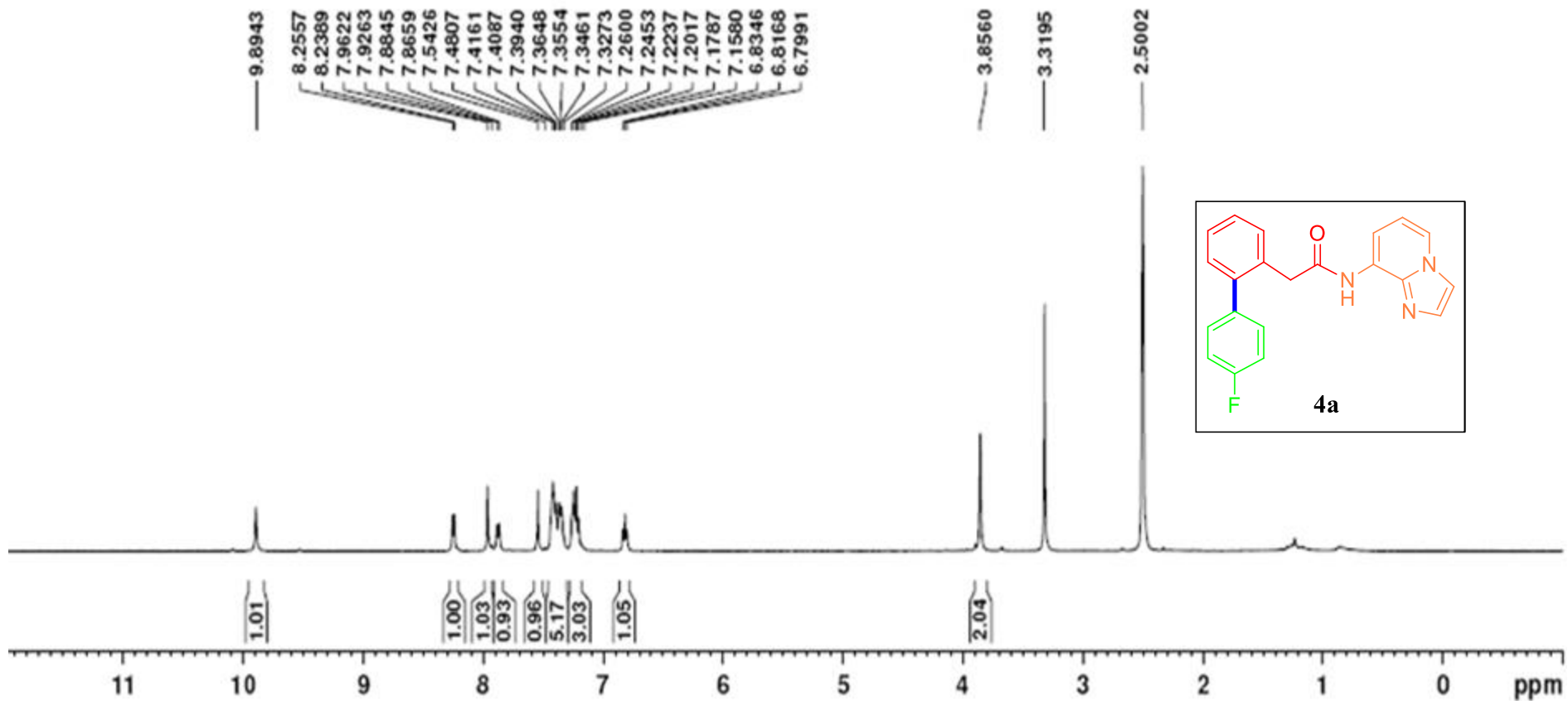
-140

-160

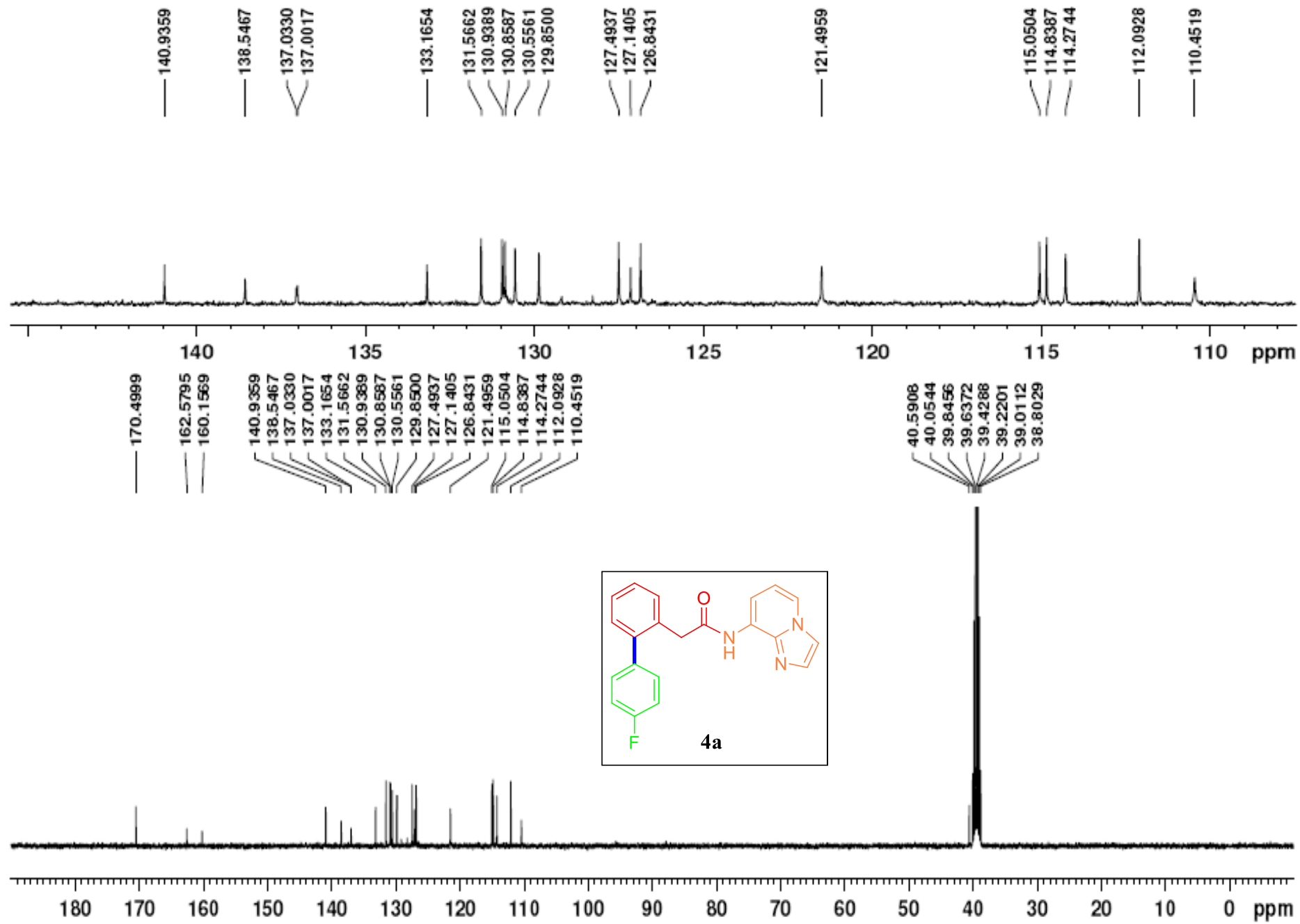
-180

ppm

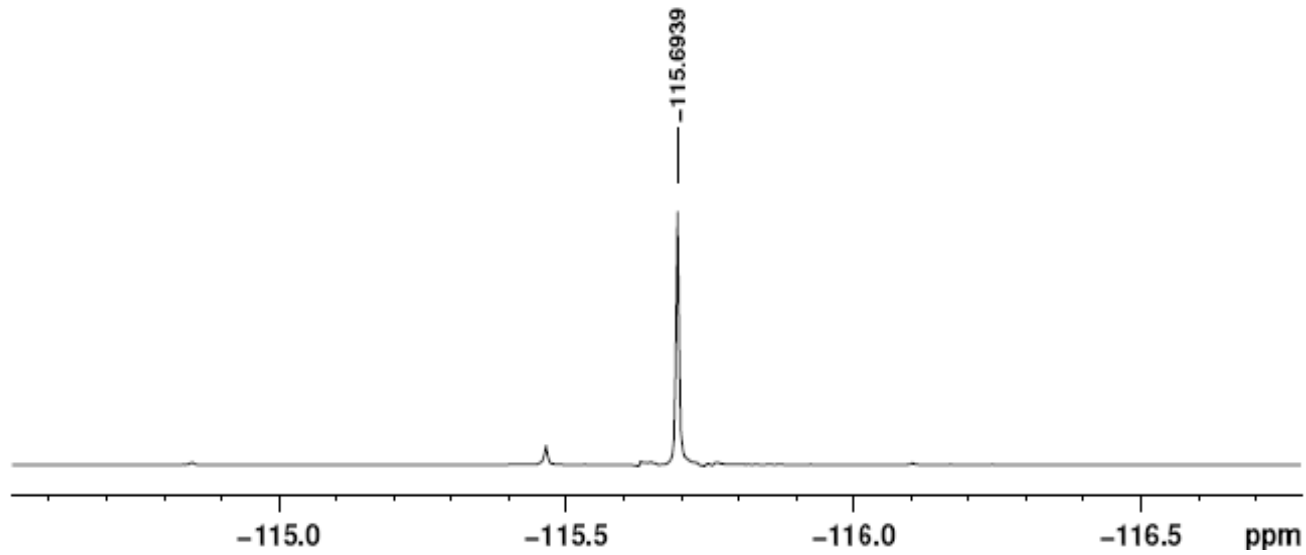
^{19}F NMR of **3l** in DMSO-d_6



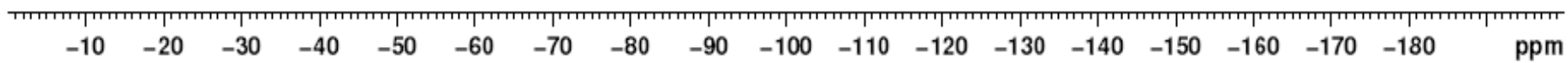
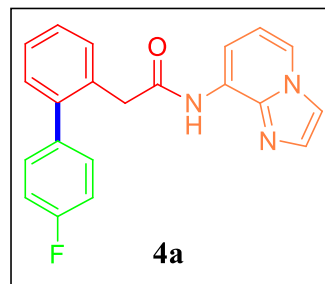
1H NMR of **4a**



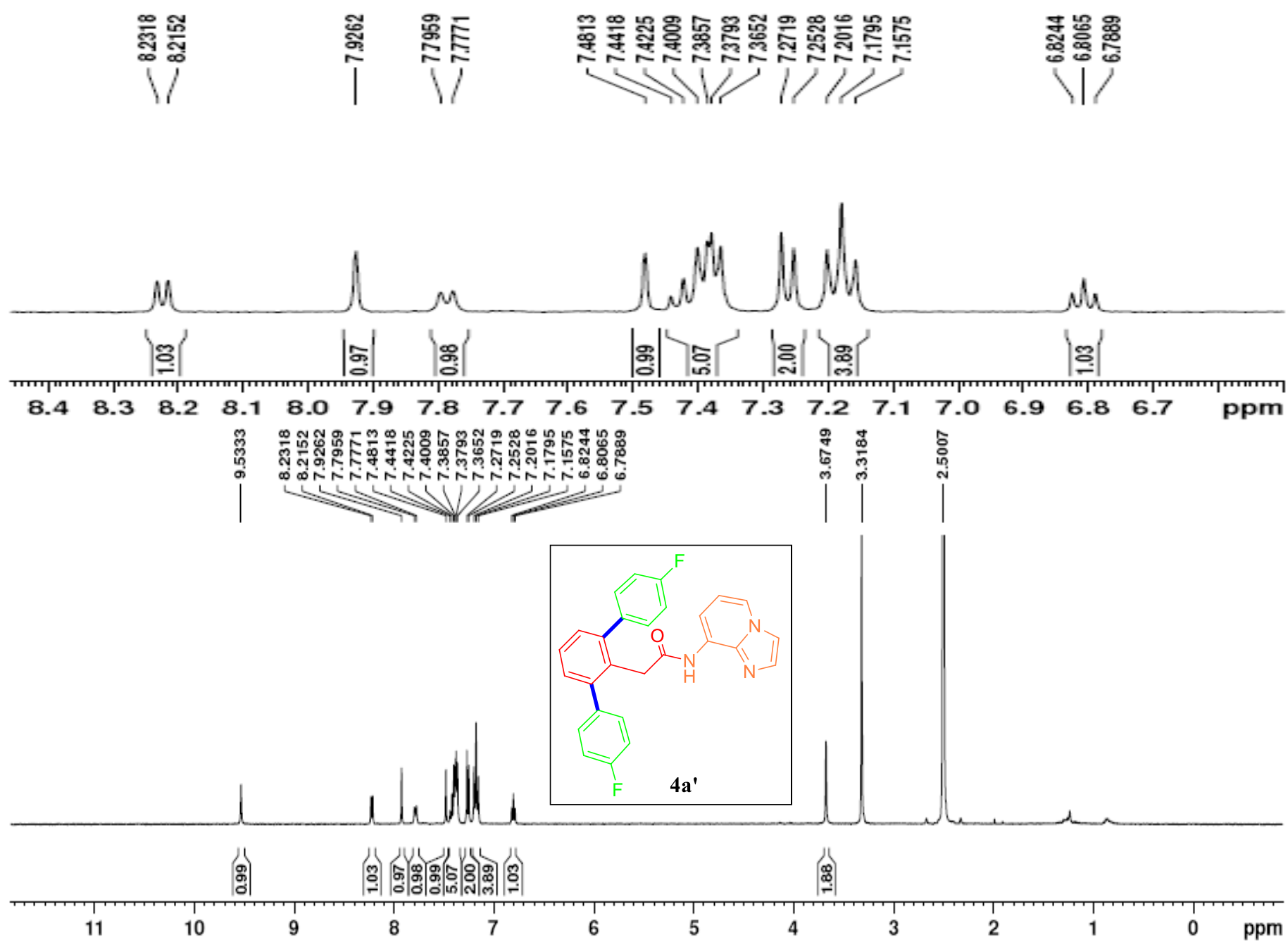
¹³C NMR of **4a** in DMSO-d₆



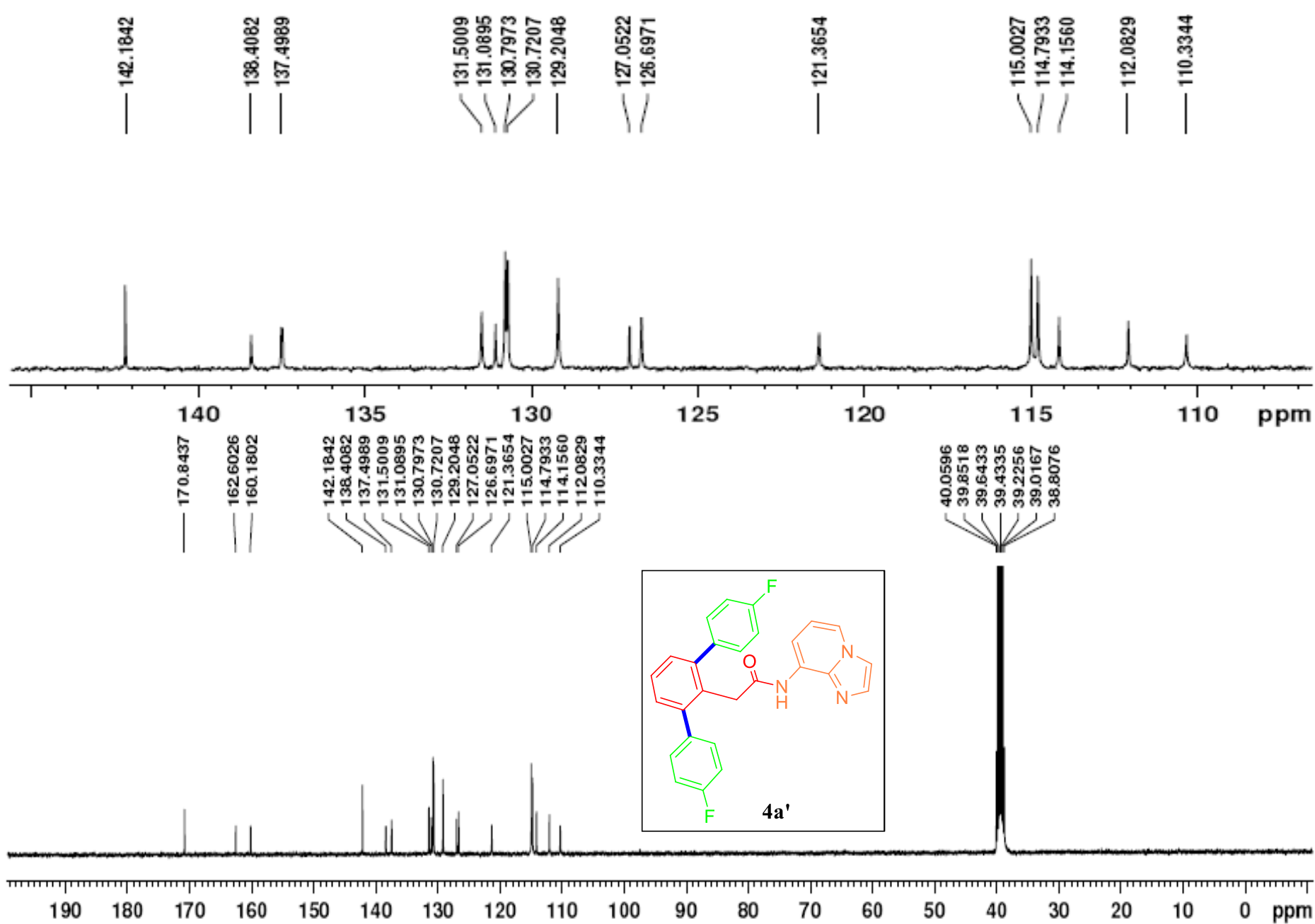
-115.6939



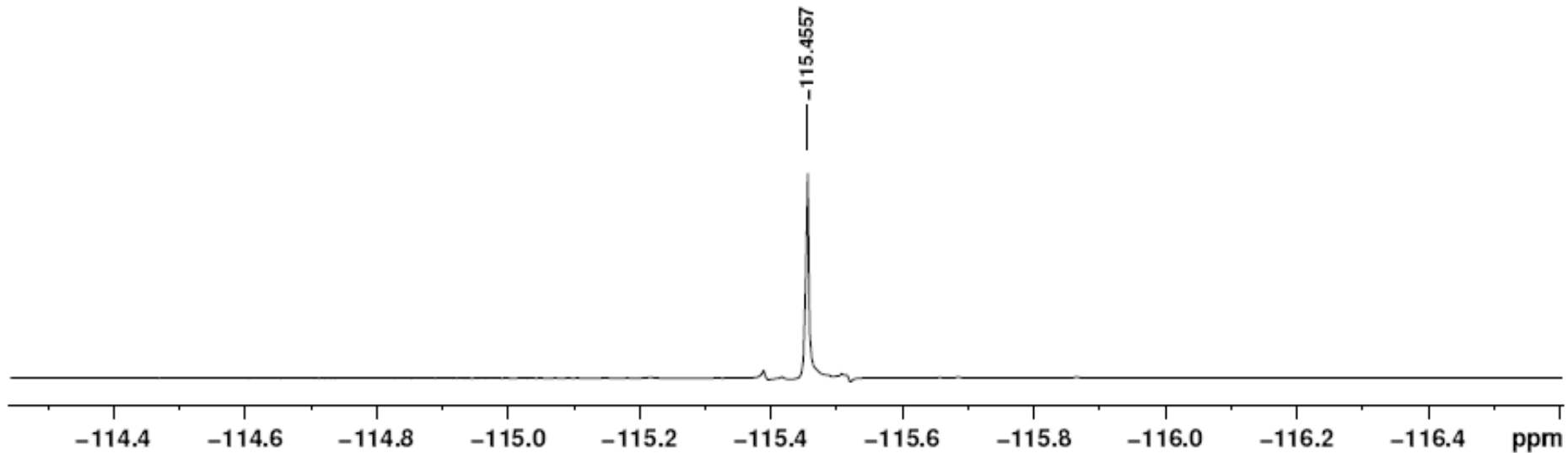
^{19}F NMR of **4a** in DMSO-d_6



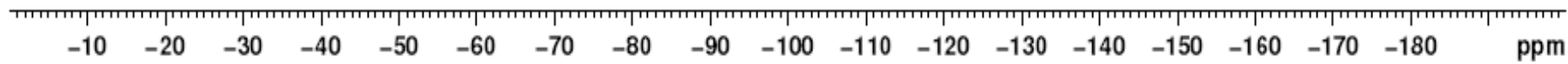
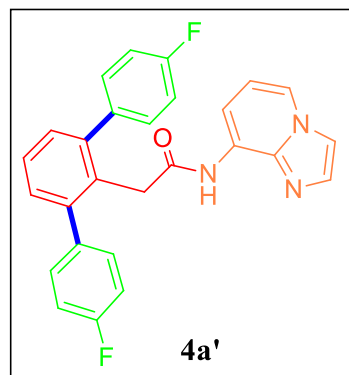
¹H NMR of **4a'** in DMSO-d₆



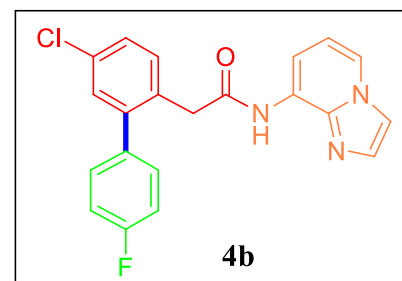
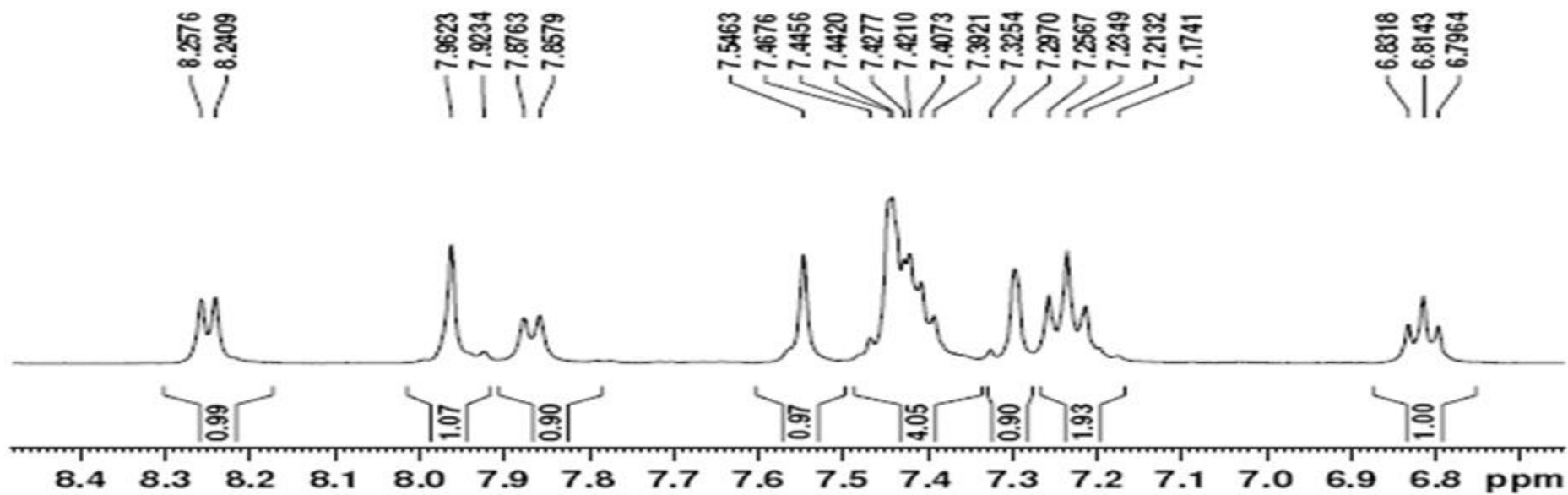
¹³C NMR of **4a'** in DMSO-d₆



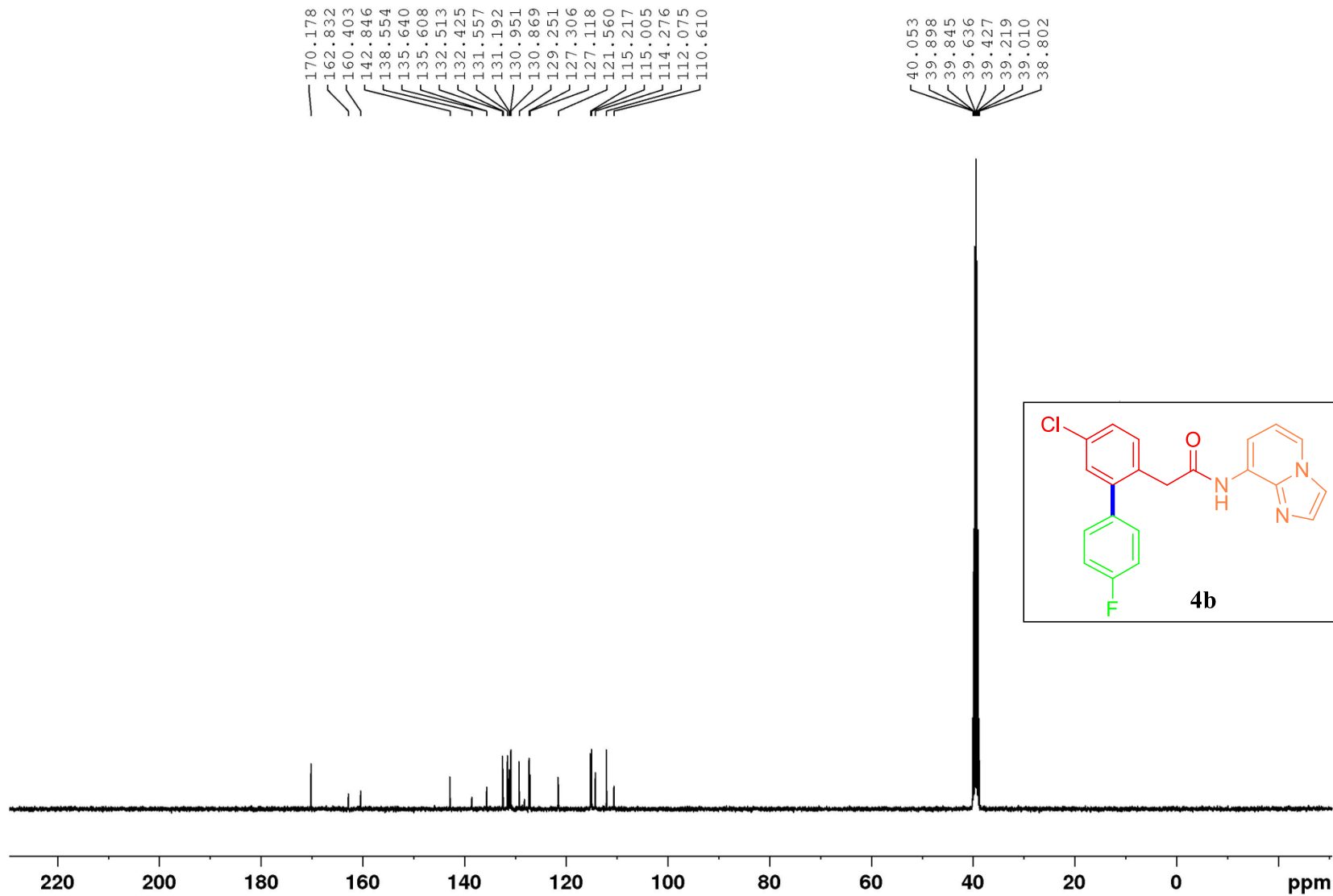
-115.4557



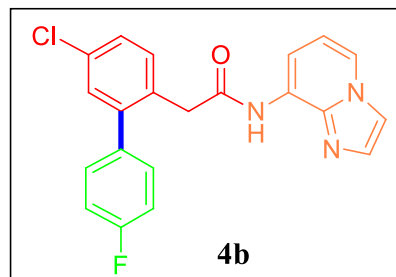
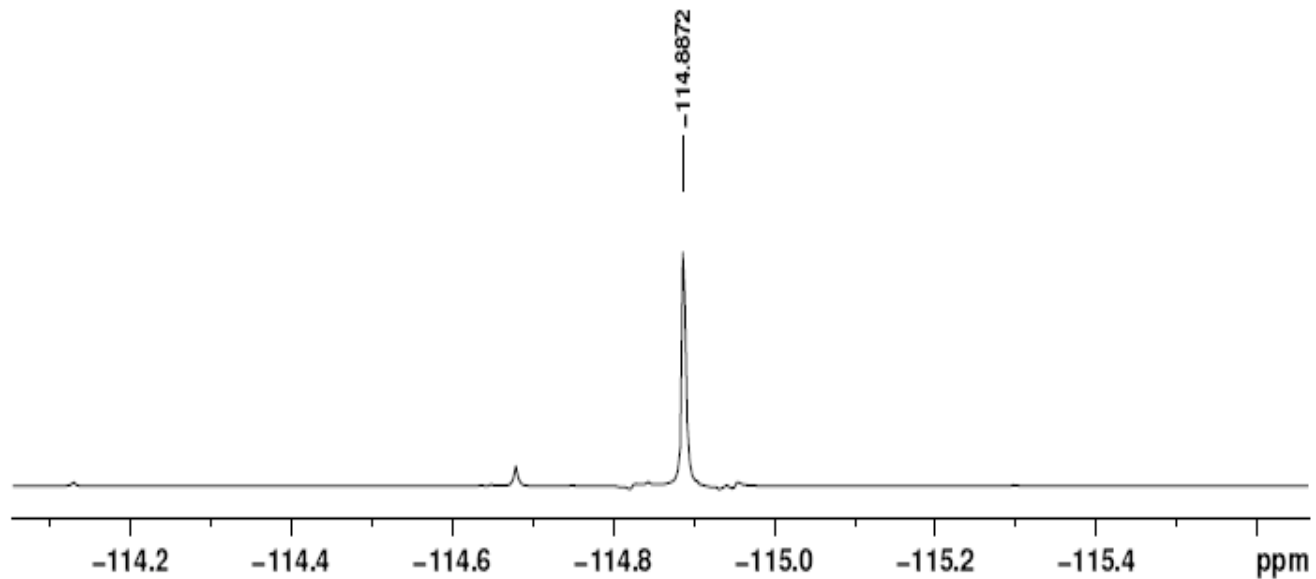
^{19}F NMR of **4a'** in DMSO-d_6



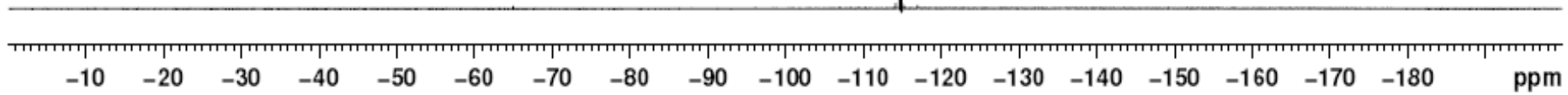
¹H NMR of **4b**



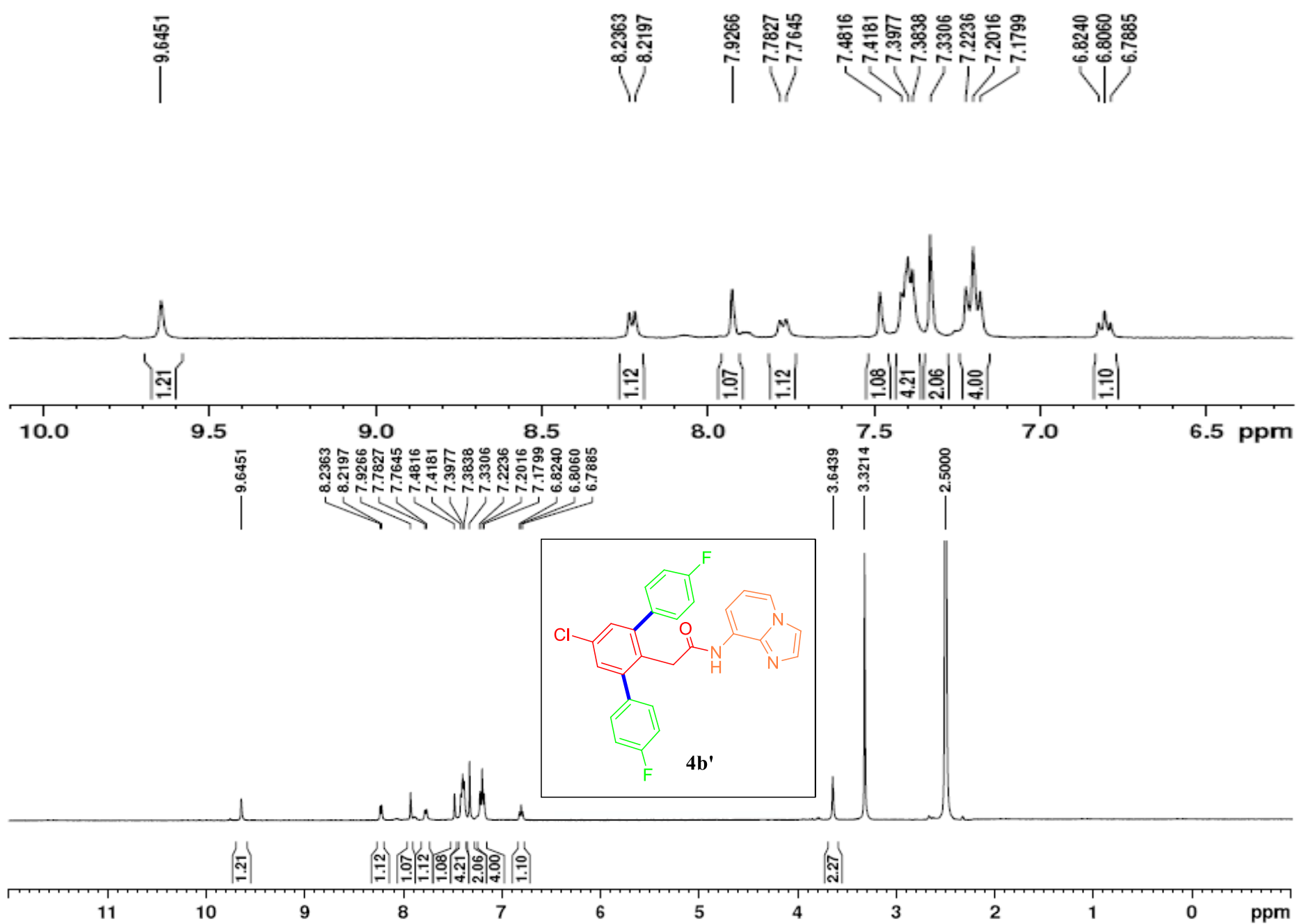
13C NMR of **4b**



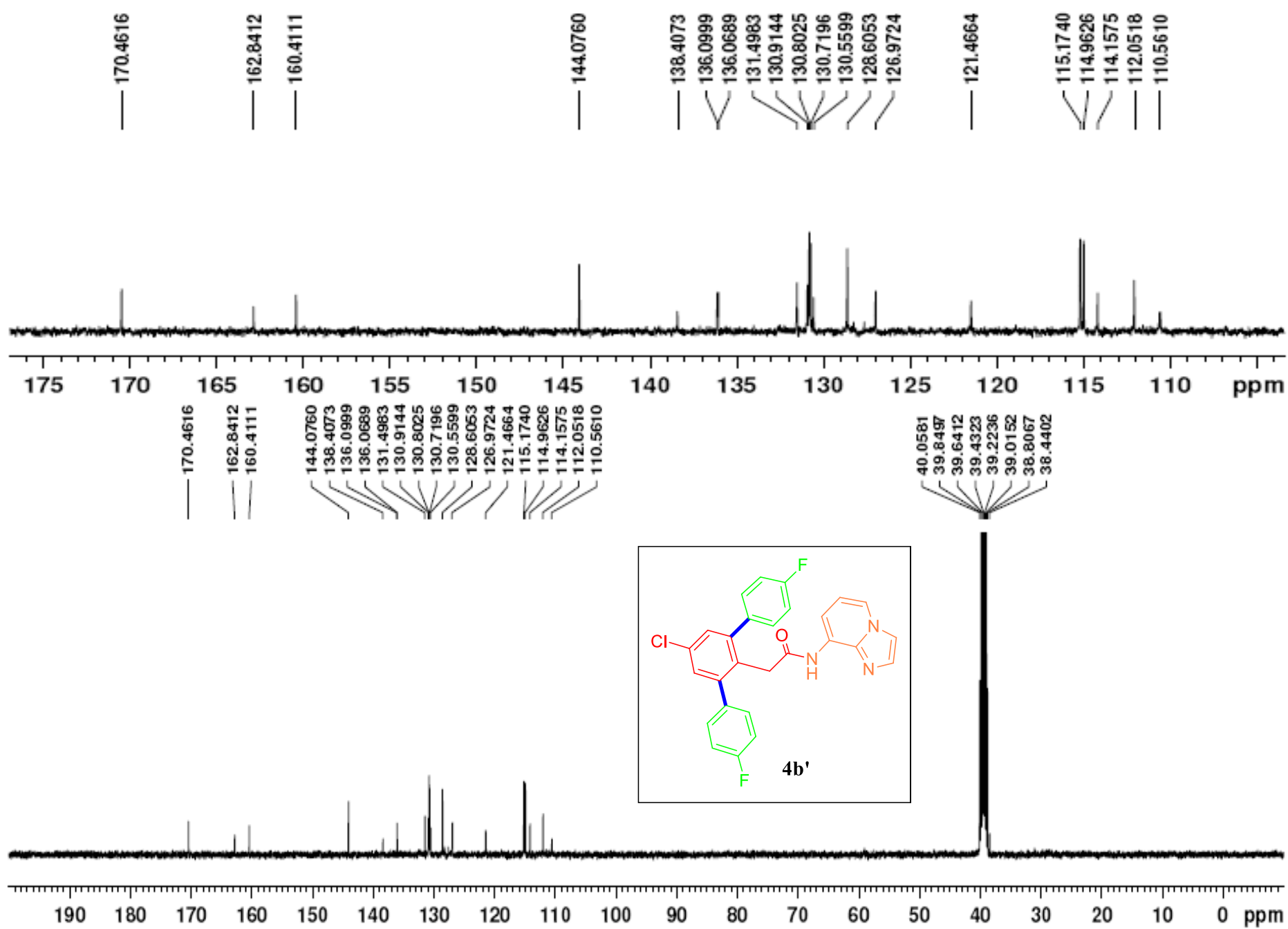
-114.8872



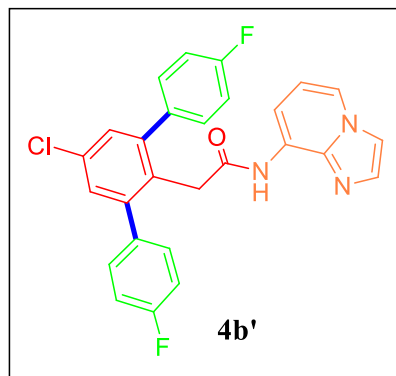
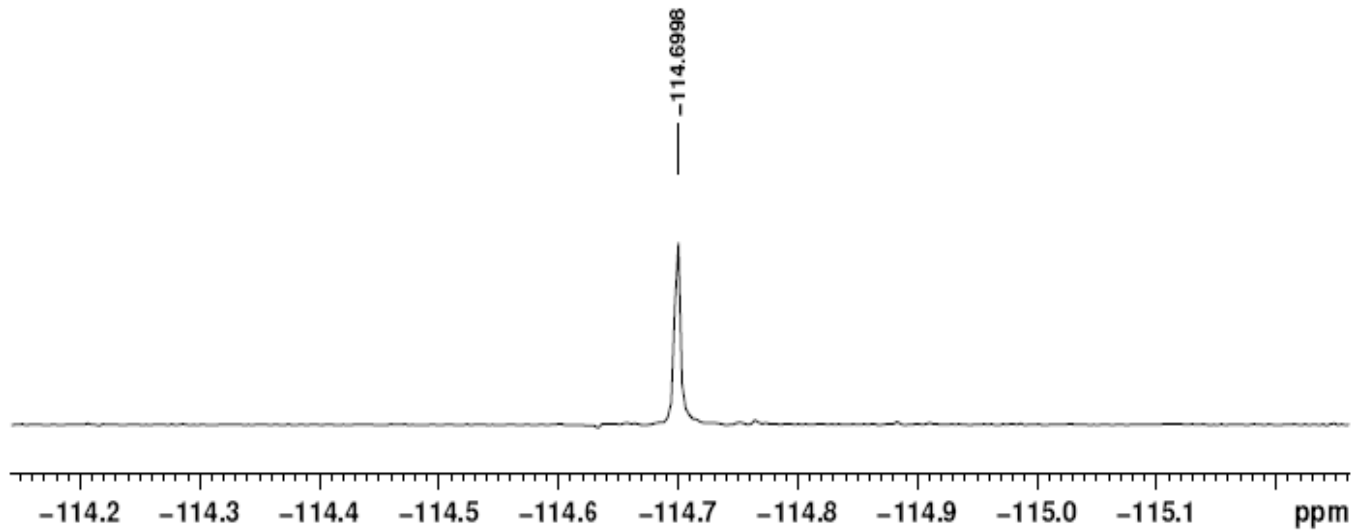
^{19}F NMR of **4b** in DMSO-d_6



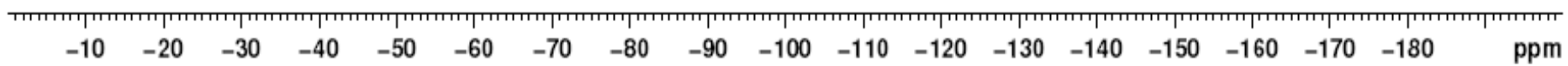
¹H NMR of 4b' in DMSO-d₆



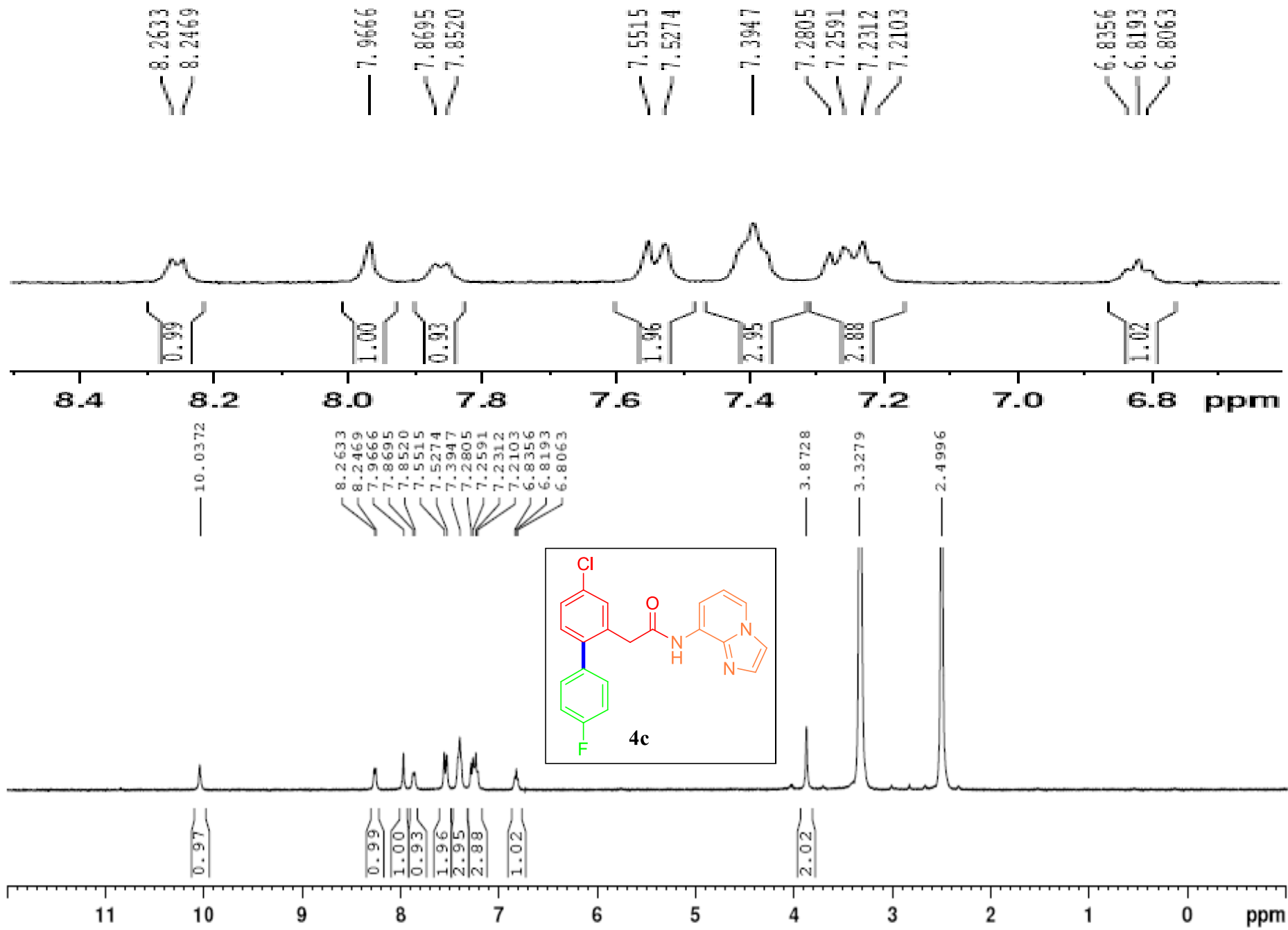
¹³C NMR of **4b'** in DMSO-d₆



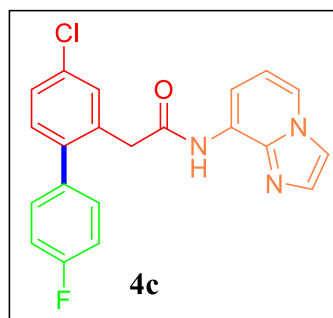
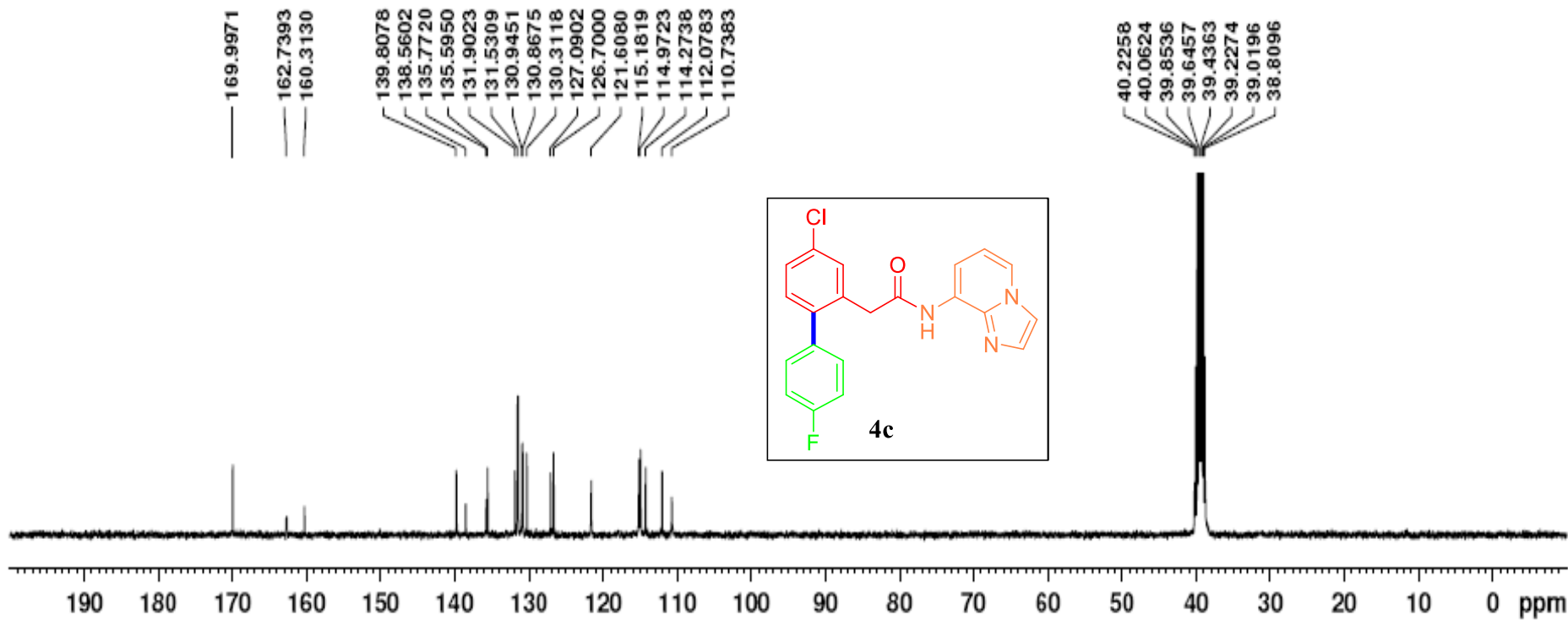
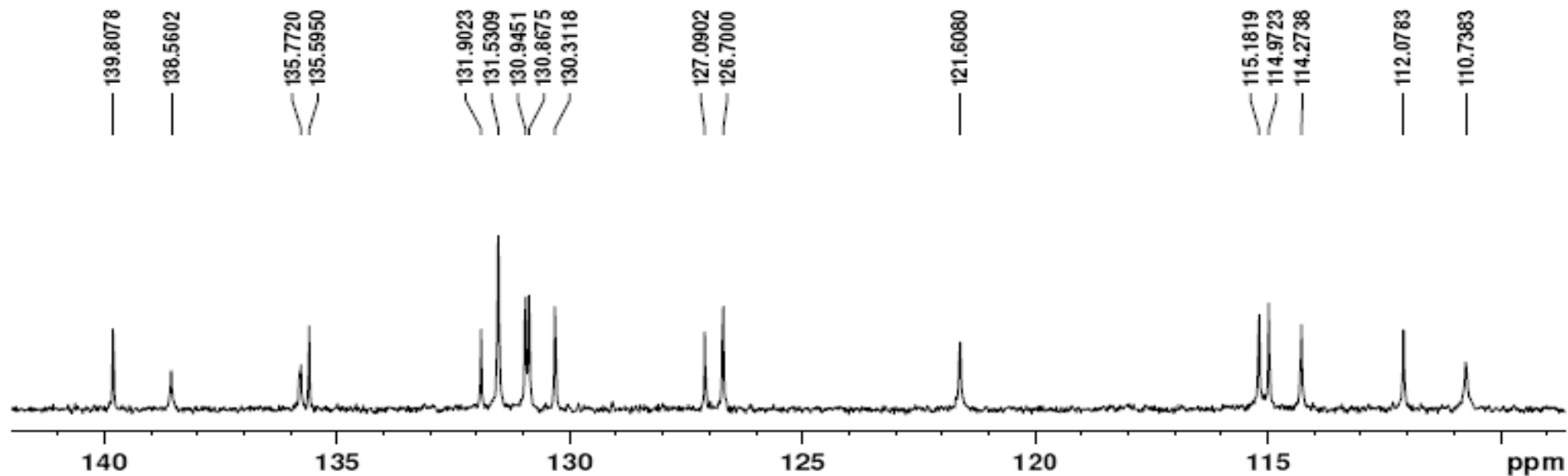
$^{-}114.6998$



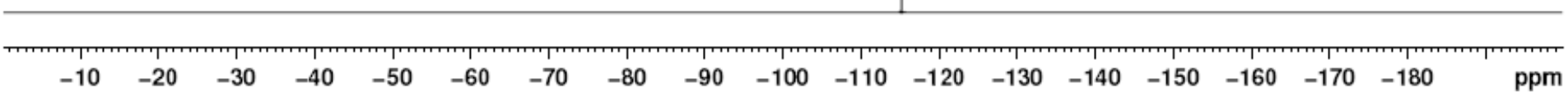
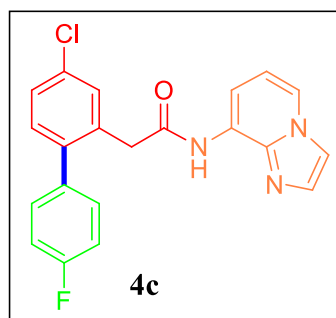
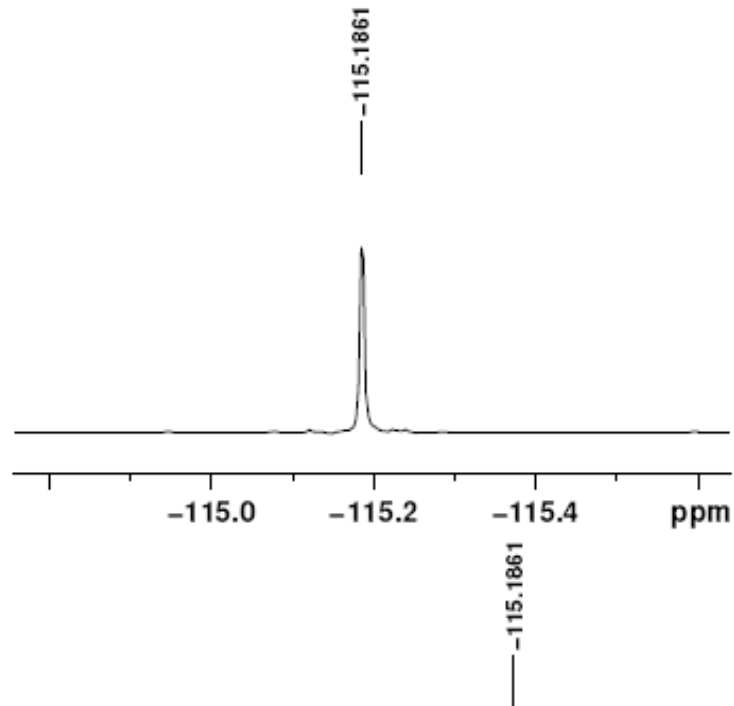
^{19}F NMR of **4b'** in DMSO-d_6



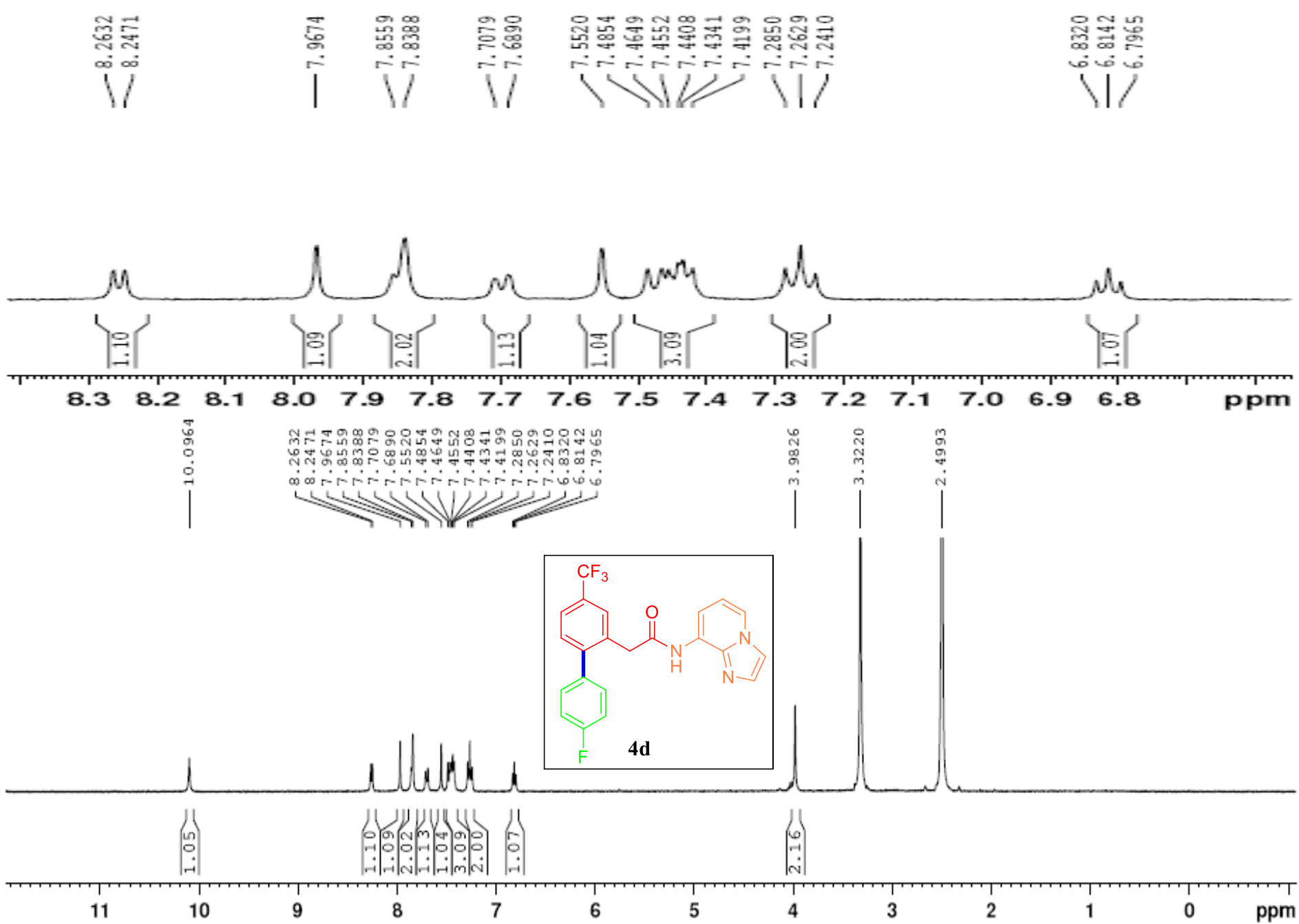
¹H NMR of **4c** in DMSO-d₆



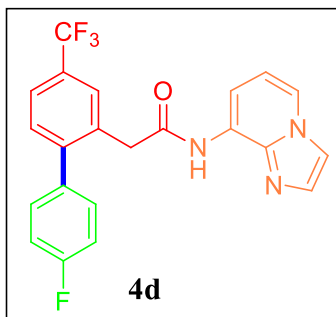
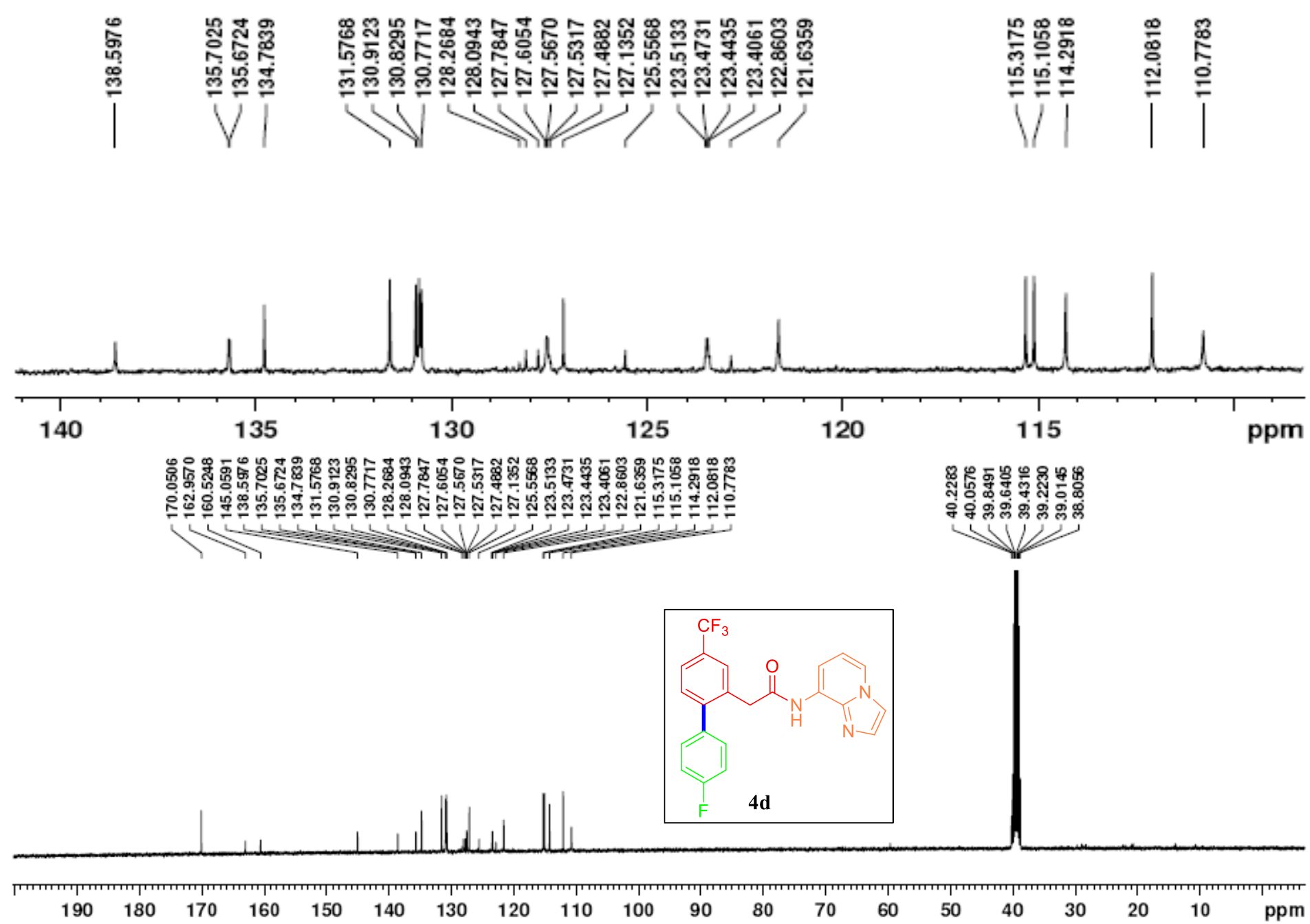
¹³C NMR of **4c** in DMSO-d₆



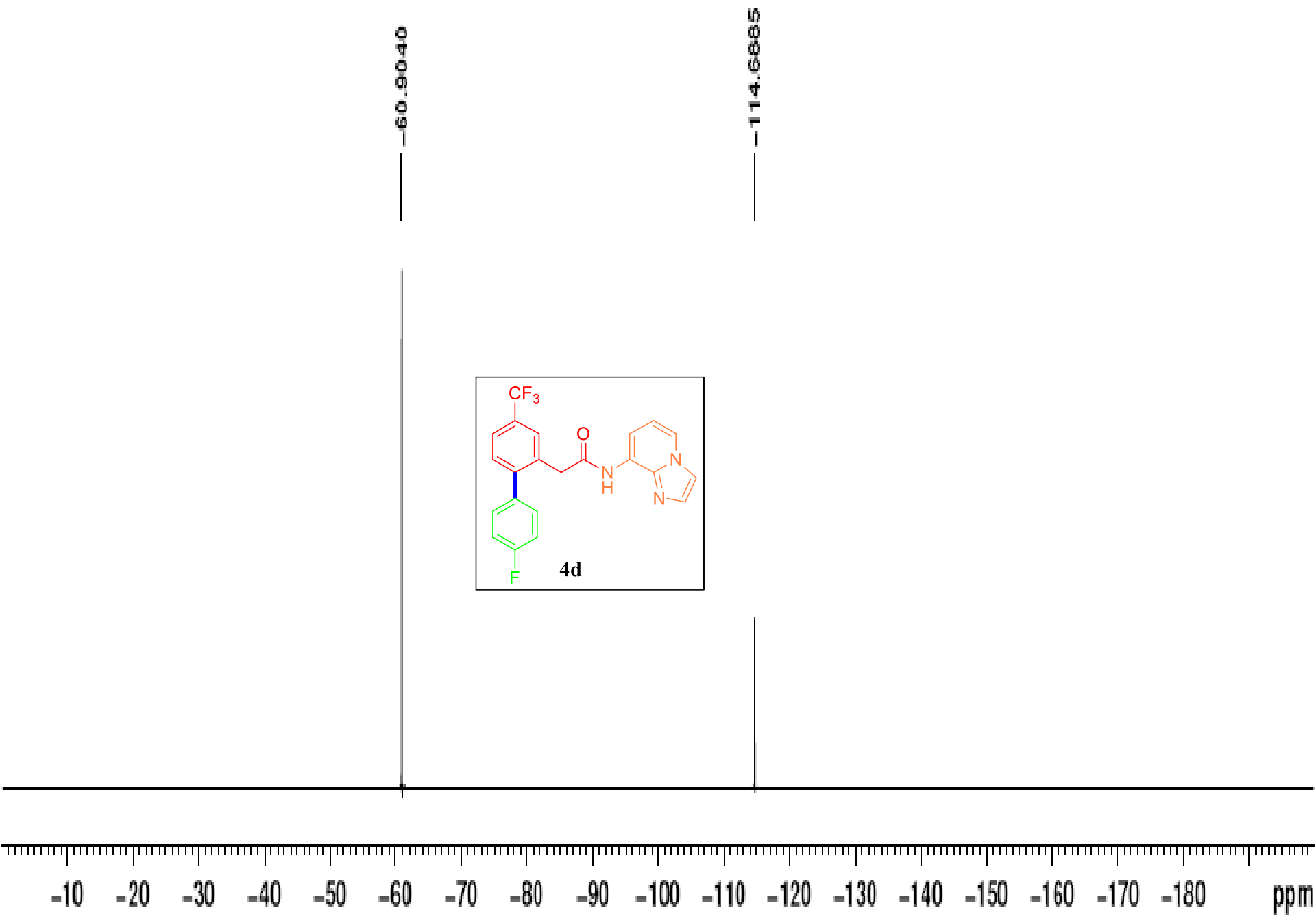
^{19}F NMR of **4c** in DMSO-d_6



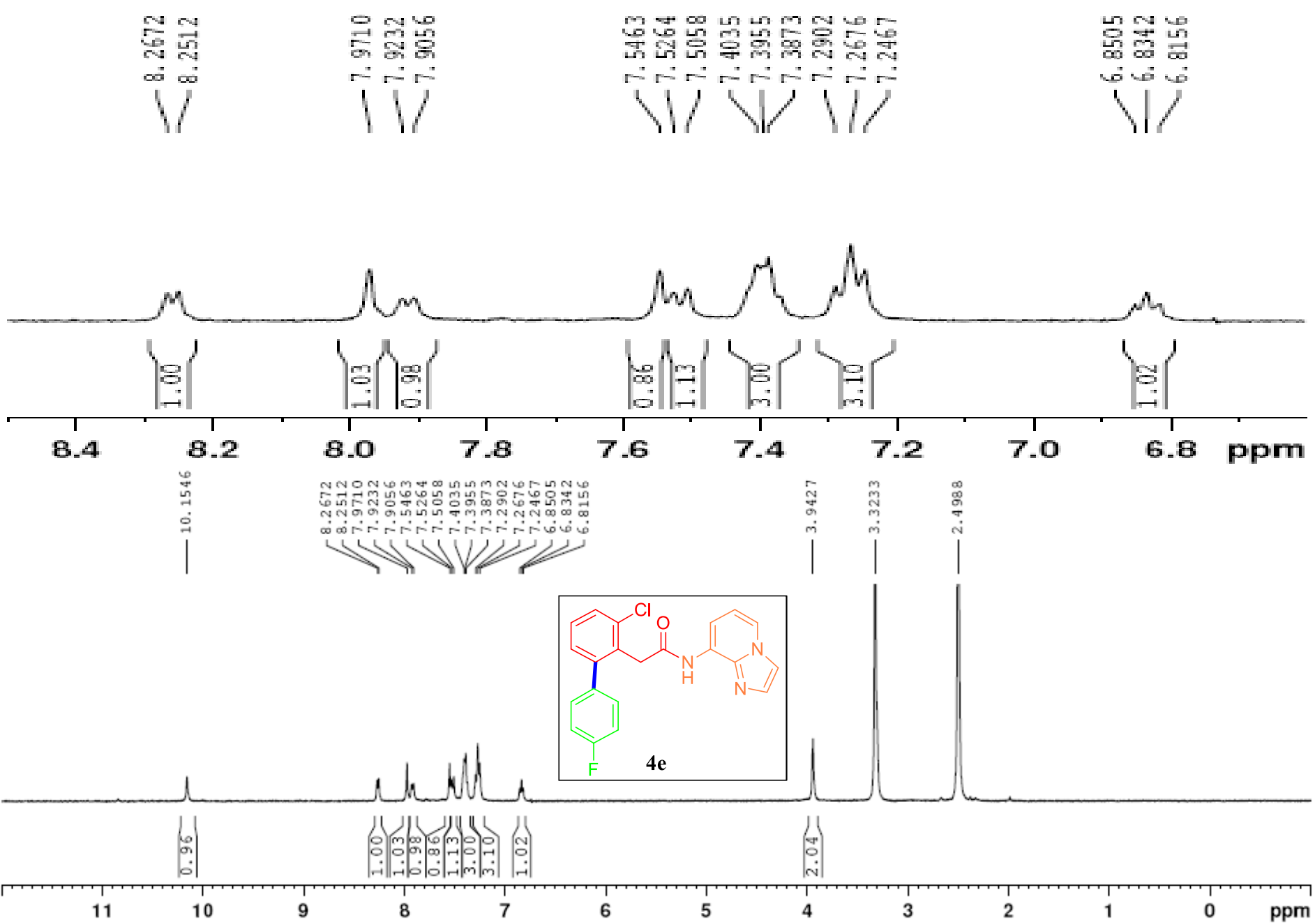
¹H NMR of **4d** in DMSO-d₆



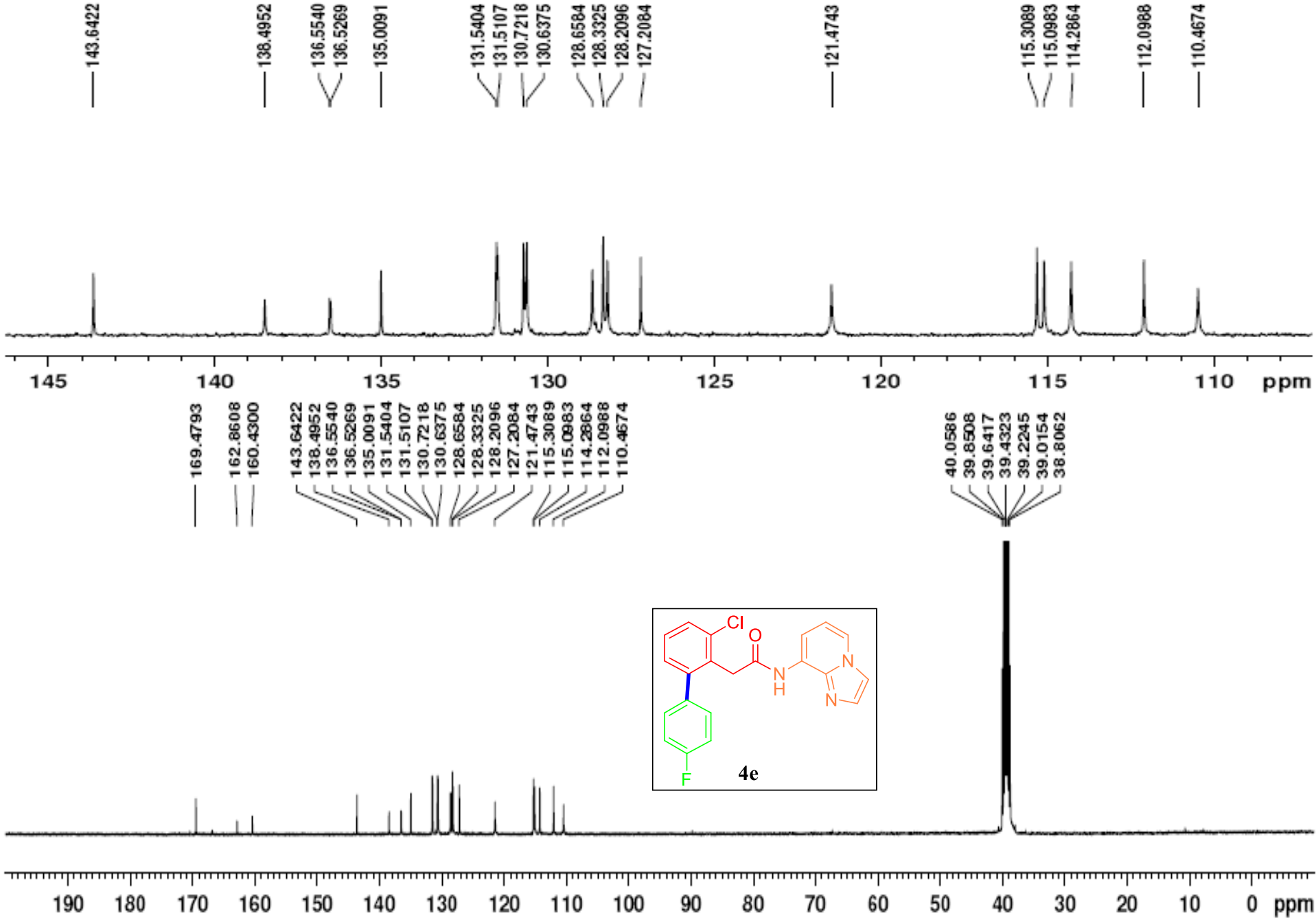
¹³C NMR of **4d** in DMSO-d₆



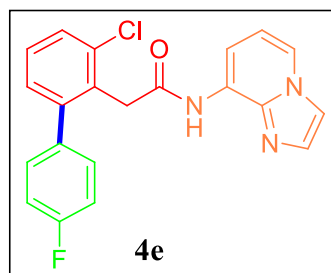
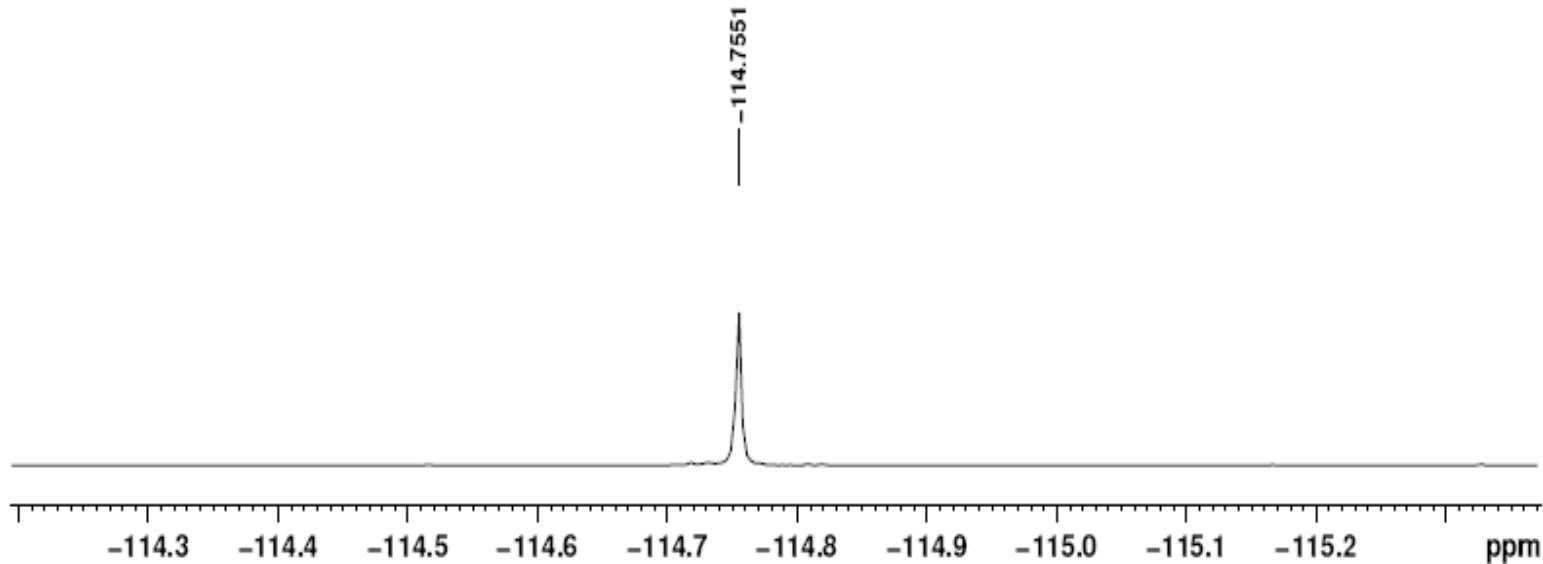
${}^{19}\text{F}$ NMR of **4d** in DMSO-d_6



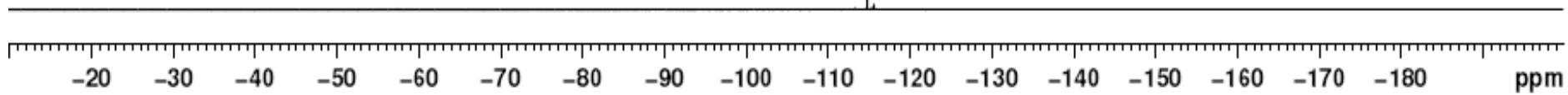
¹H NMR of **4e** in DMSO-d₆



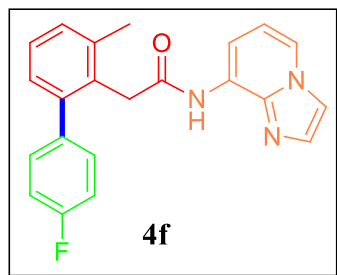
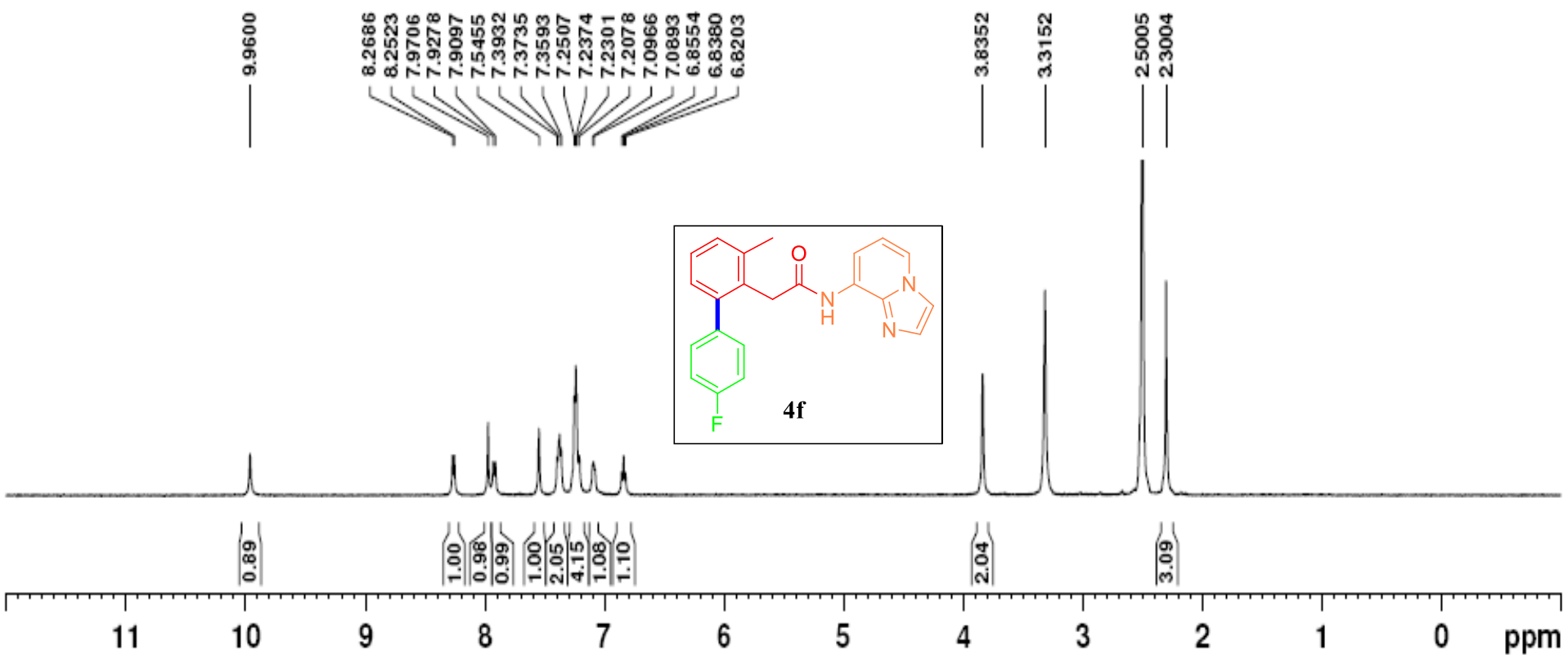
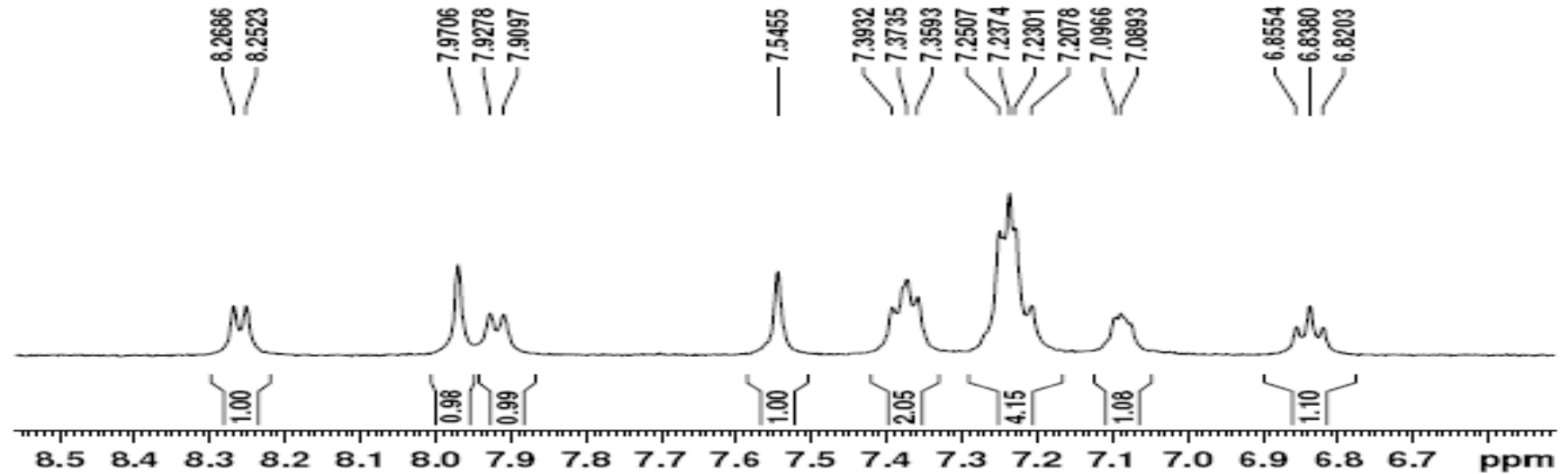
¹³C NMR of **4e** in DMSO-d₆

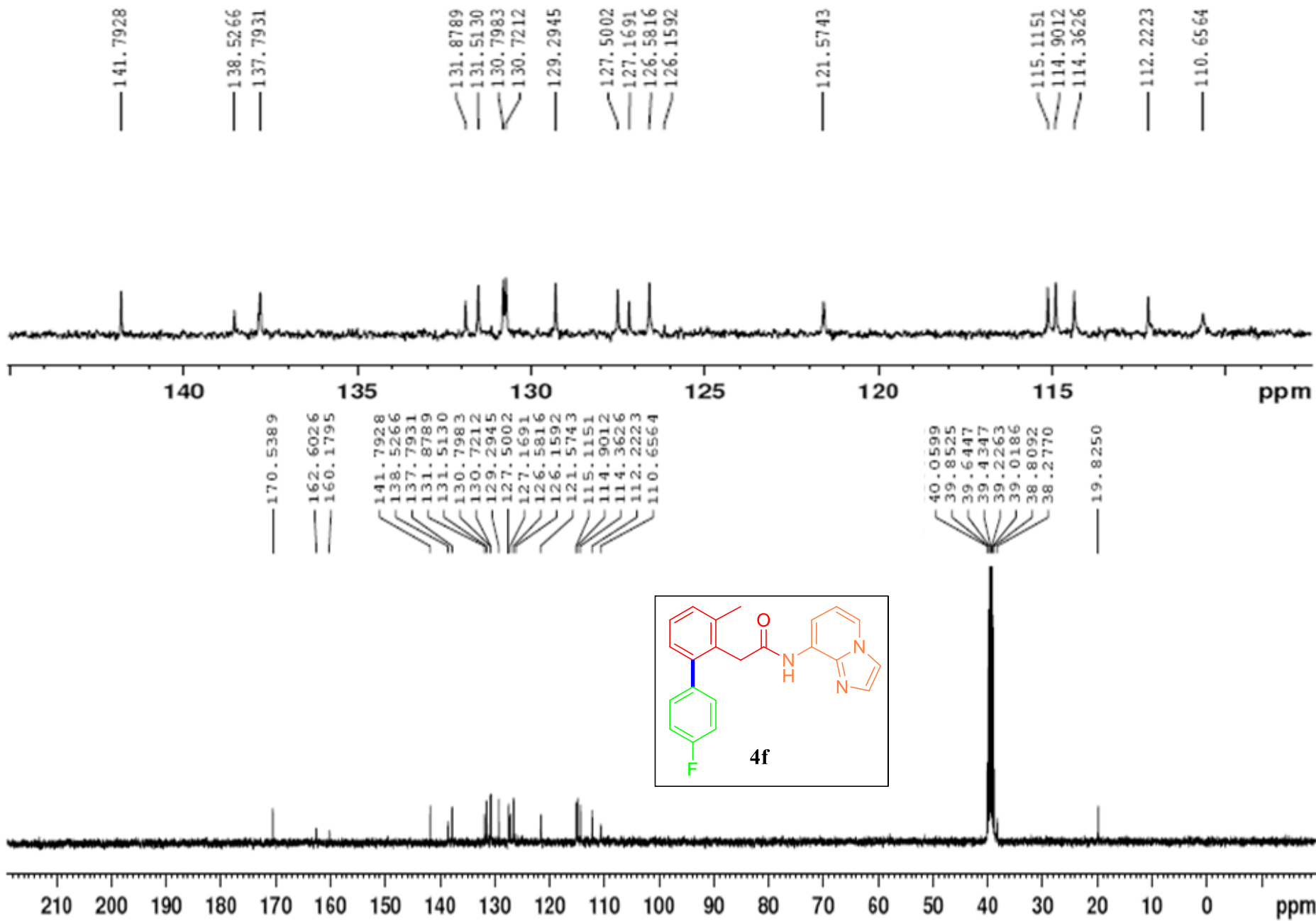


$^{-}114.7551$

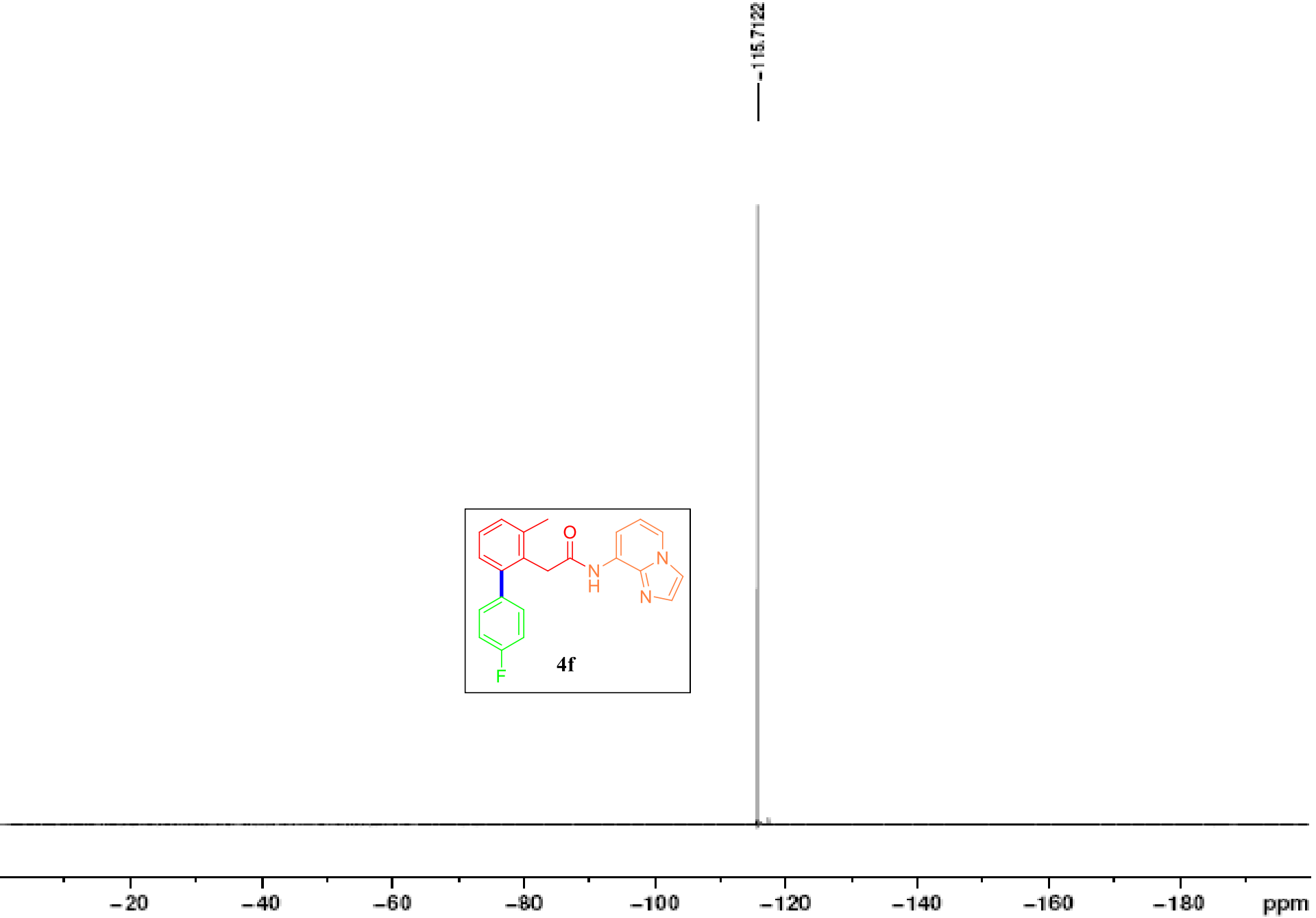


^{19}F NMR of **4e** in DMSO-d_6

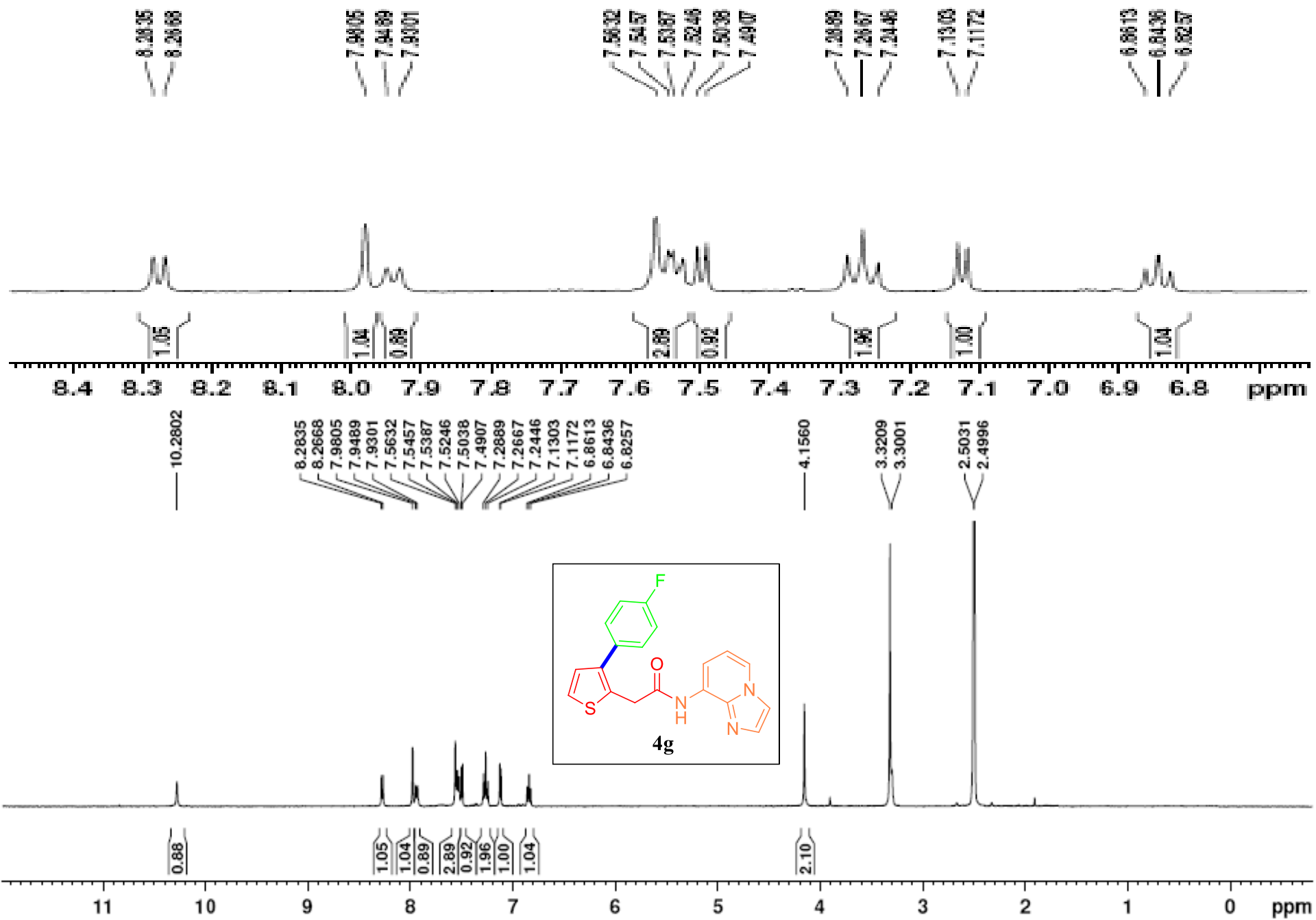




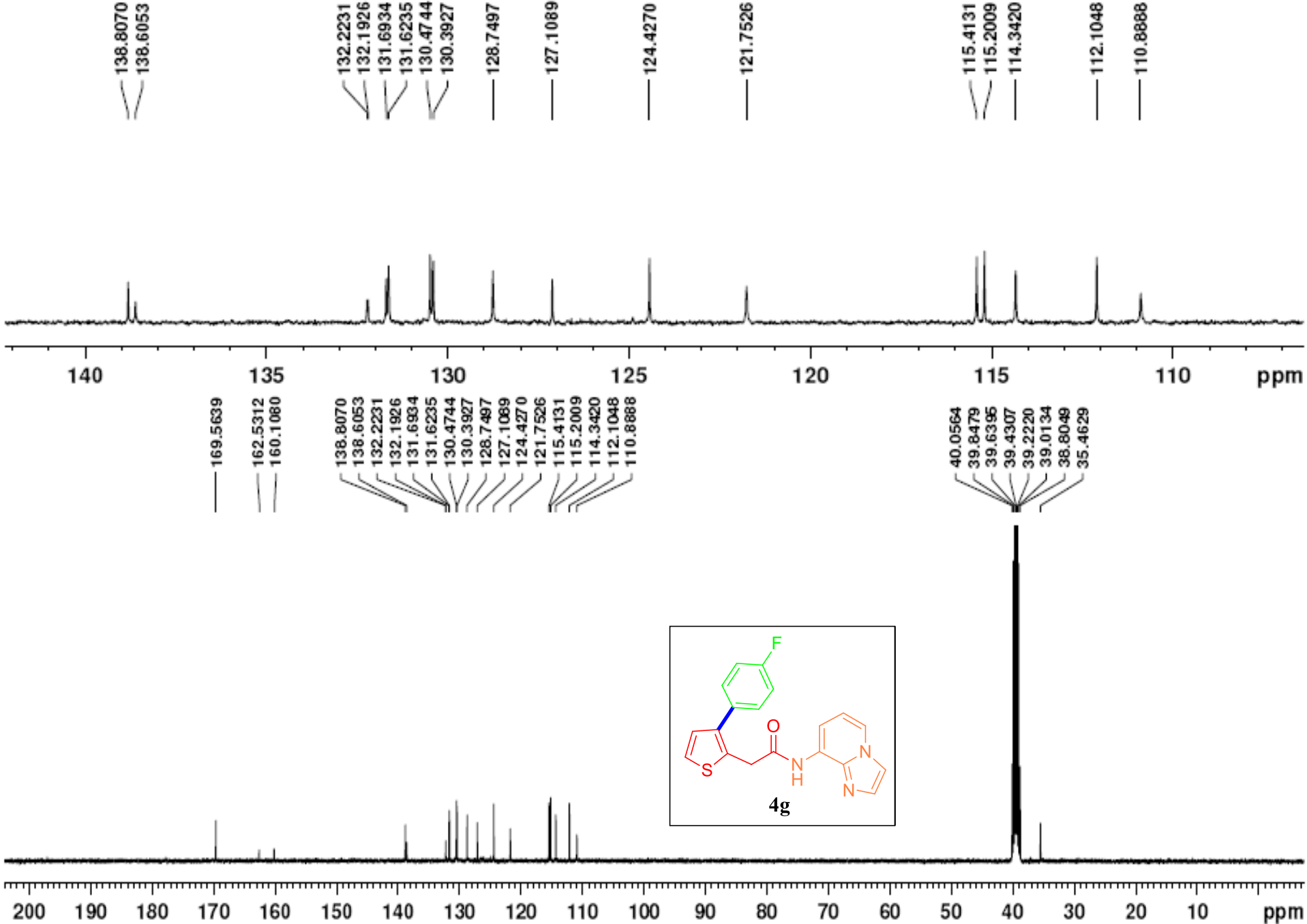
13C NMR of 4f



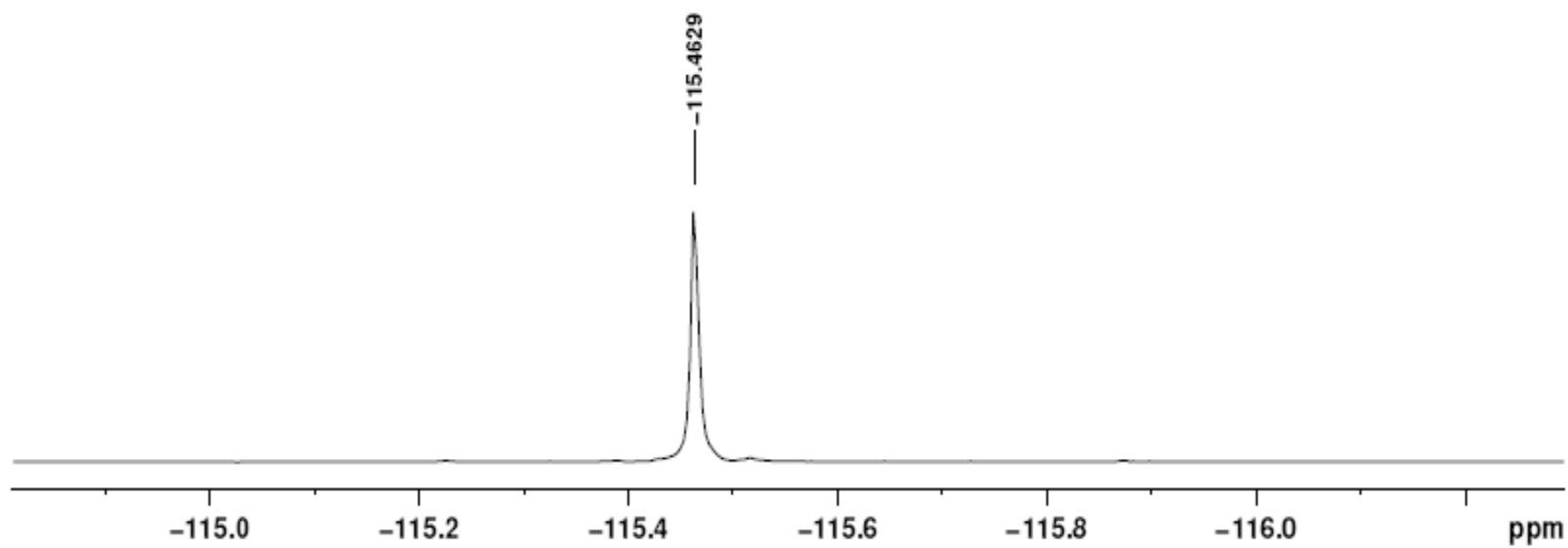
^{19}F NMR of **4f** in DMSO-d_6



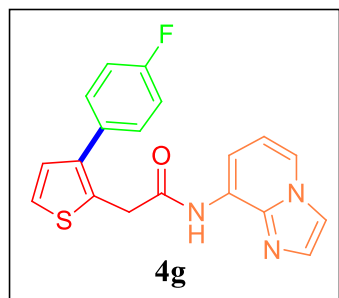
¹H NMR of **4g** in DMSO-d₆



¹³C NMR of 4g in DMSO-d₆

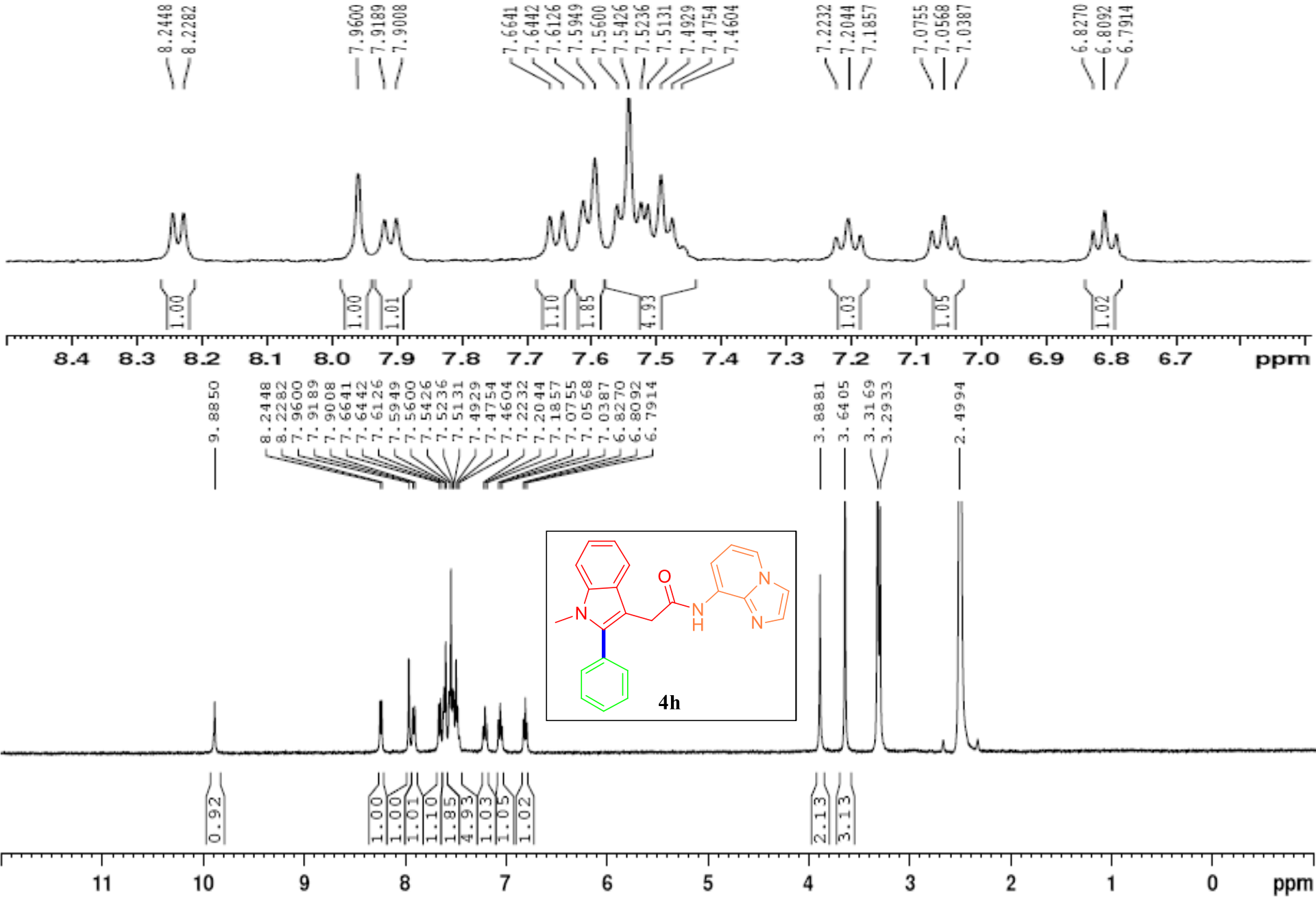


-115.4629

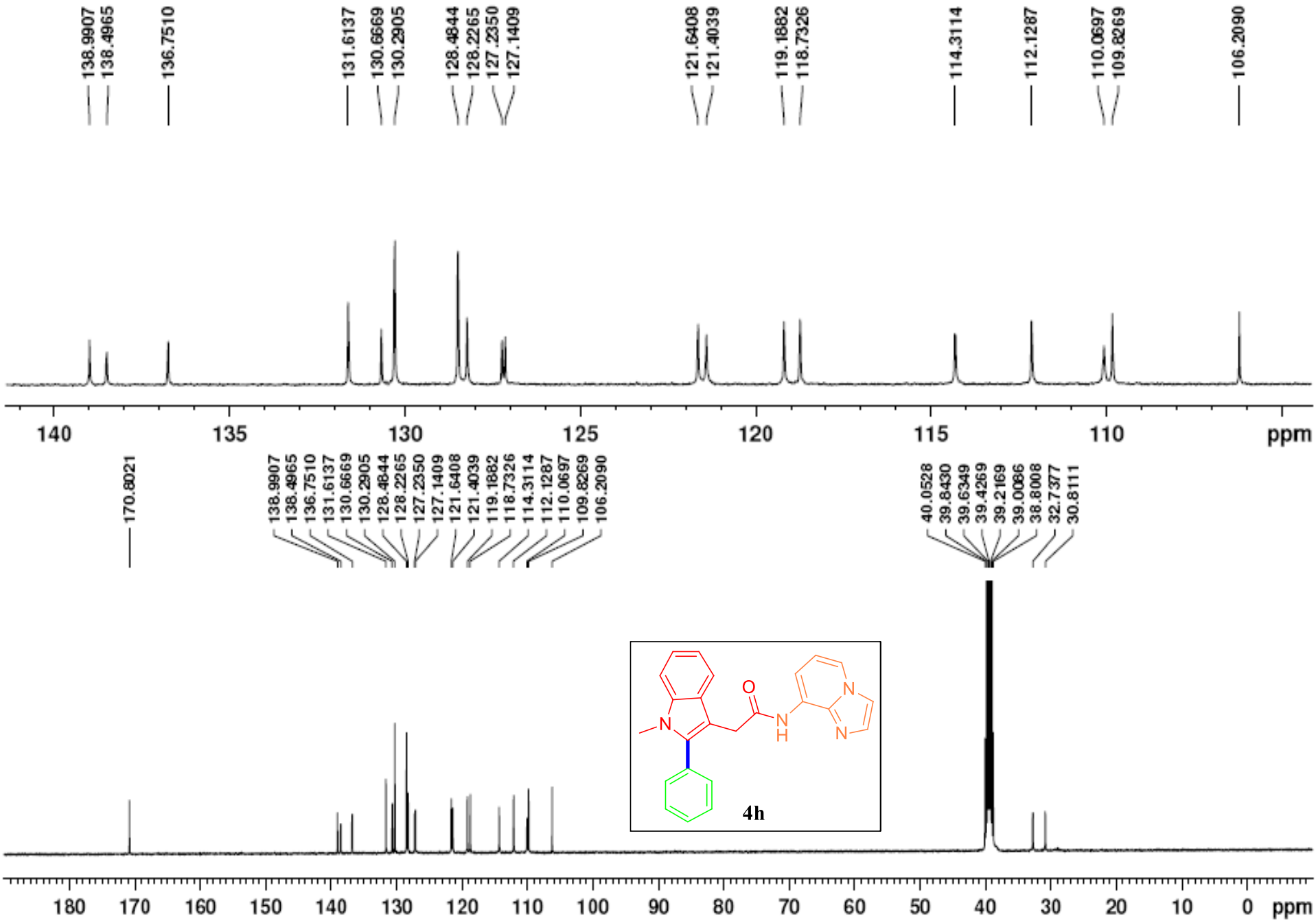


-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 ppm

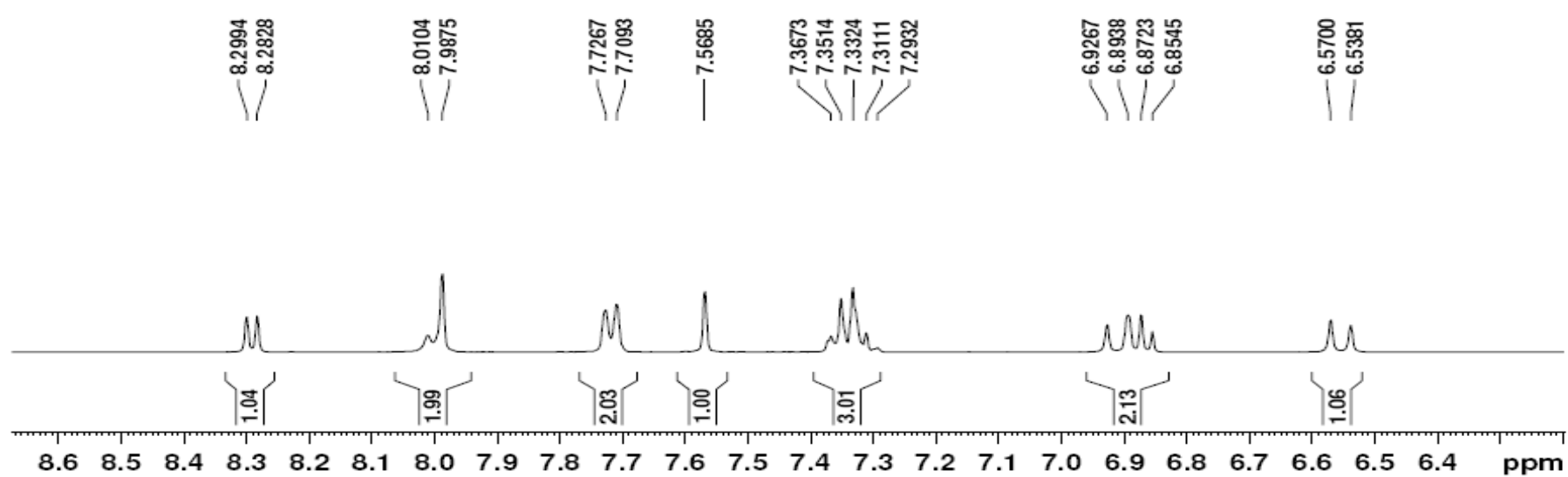
^{19}F NMR of **4g** in DMSO-d_6



¹H NMR of **4h** in DMSO-d₆



¹³C NMR of **4h** in DMSO-d₆

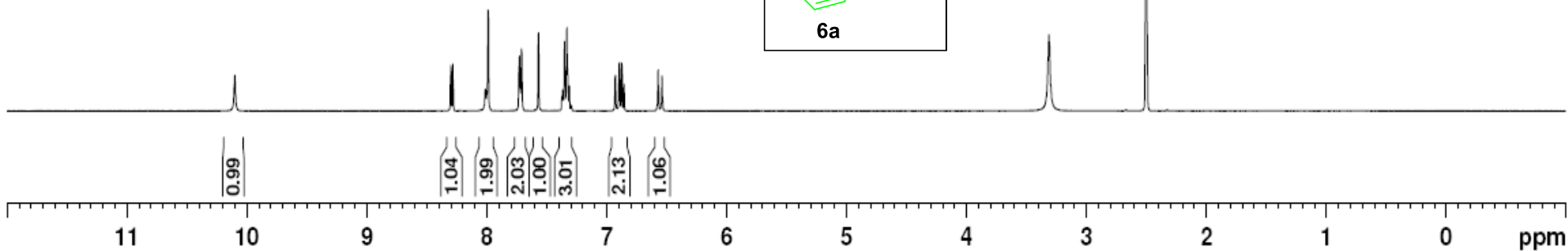
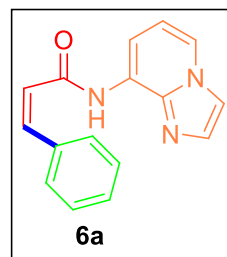


10.1004

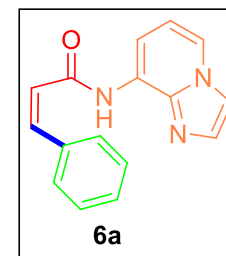
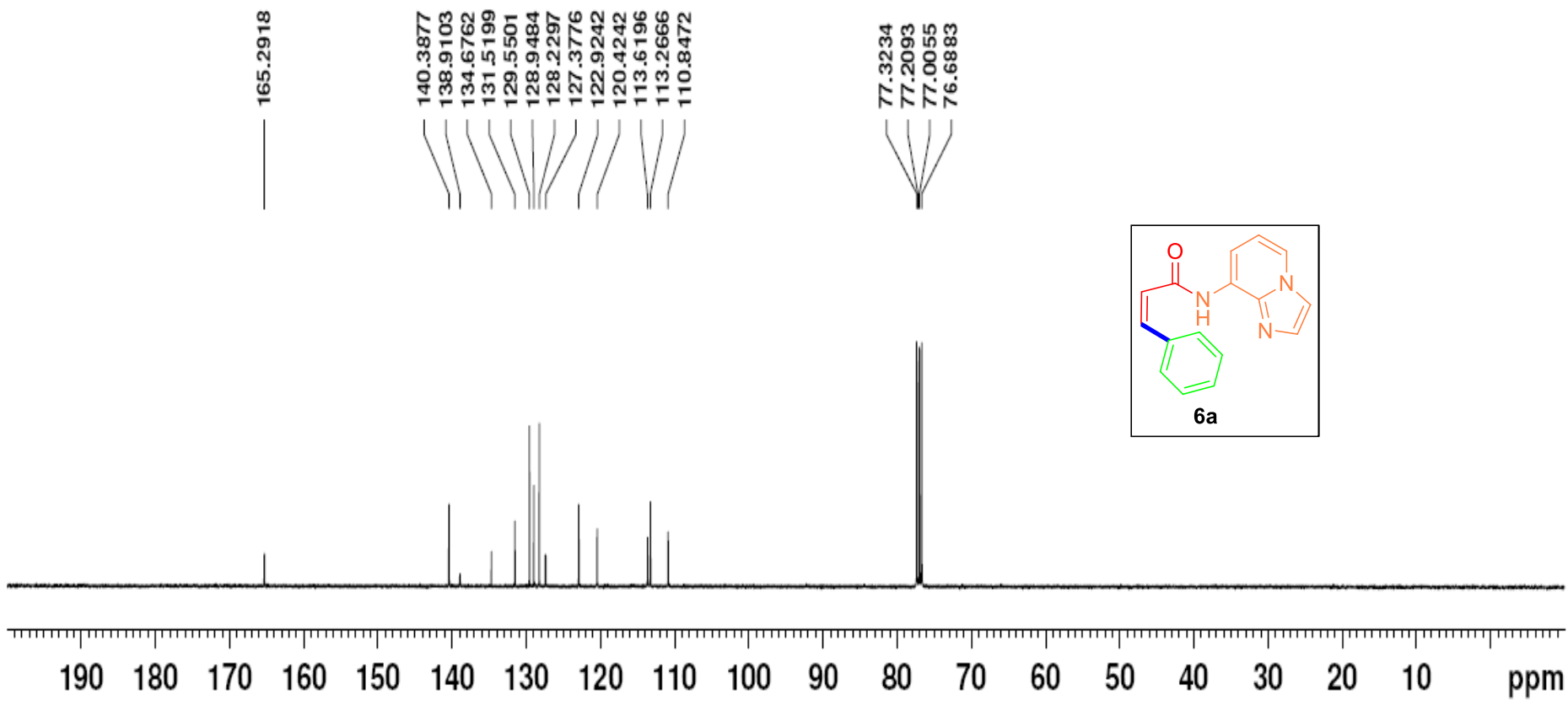
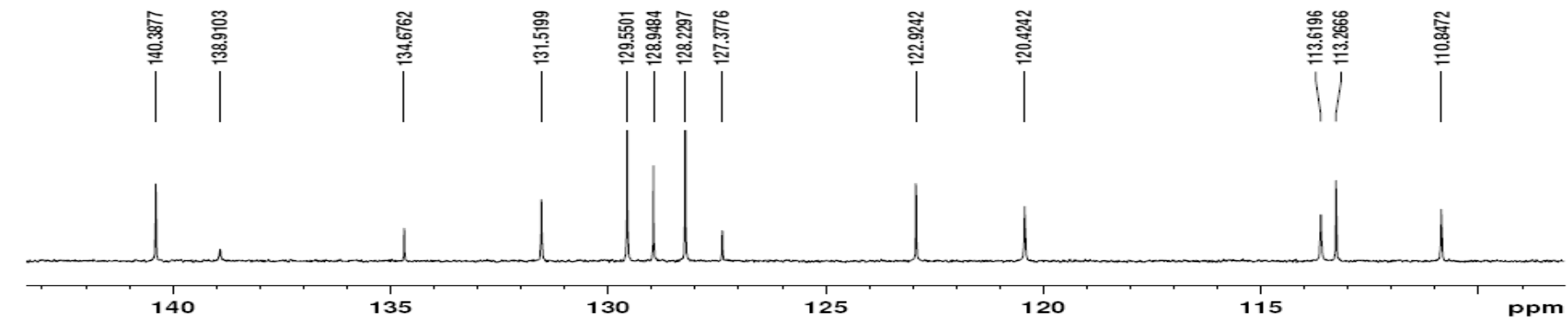
8.2994
8.2828
8.0104
7.9875
7.7267
7.7093
7.5685
7.3673
7.3514
7.3324
7.3111
7.2932
6.9267
6.8938
6.8723
6.8545
6.5700
6.5381

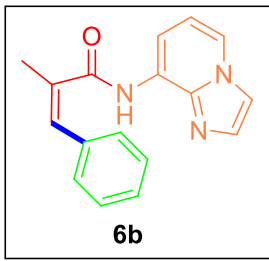
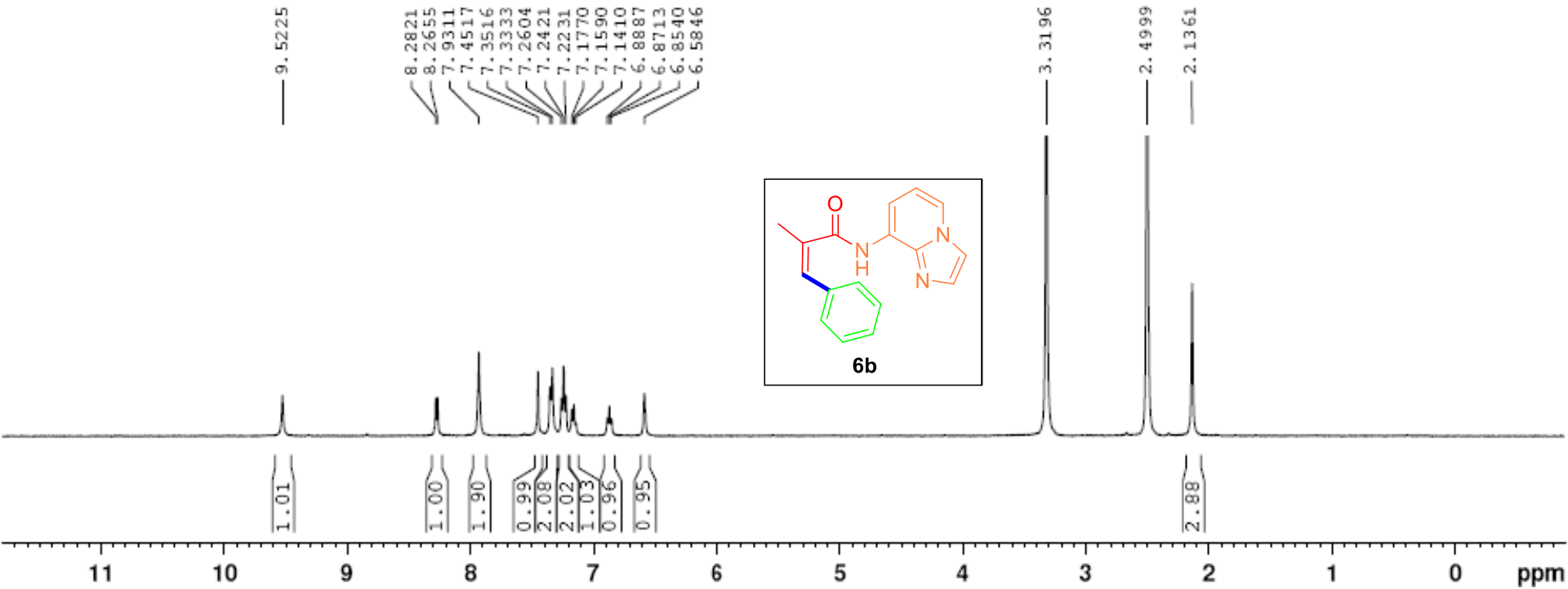
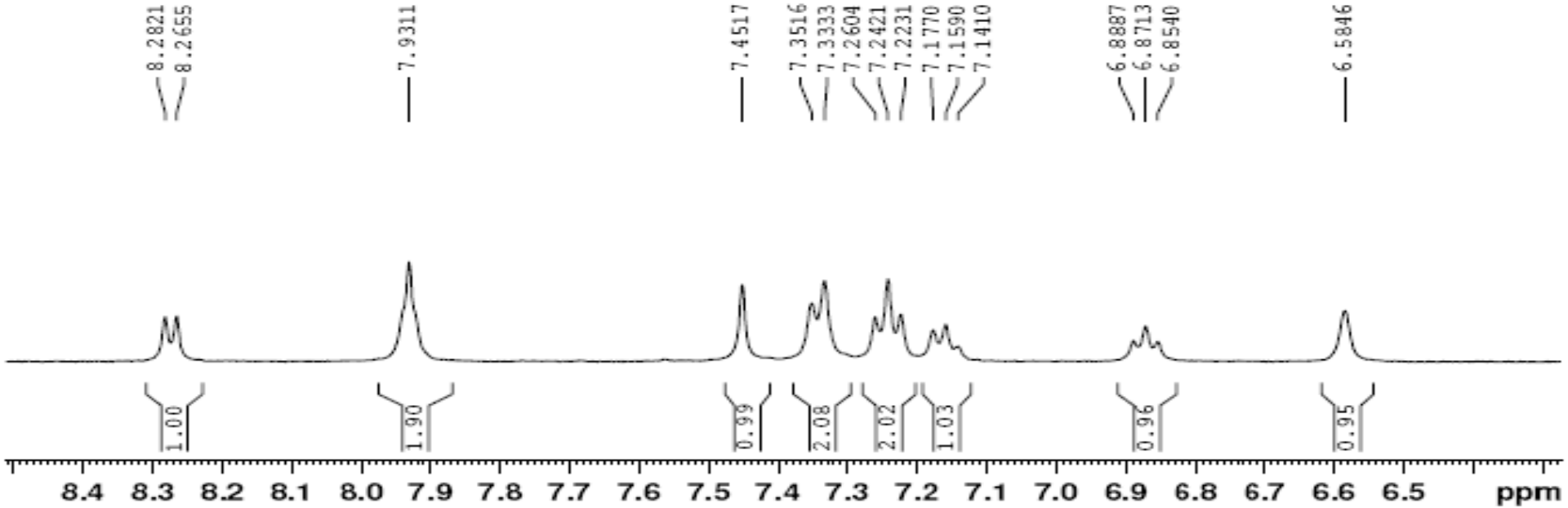
3.3115

2.5000

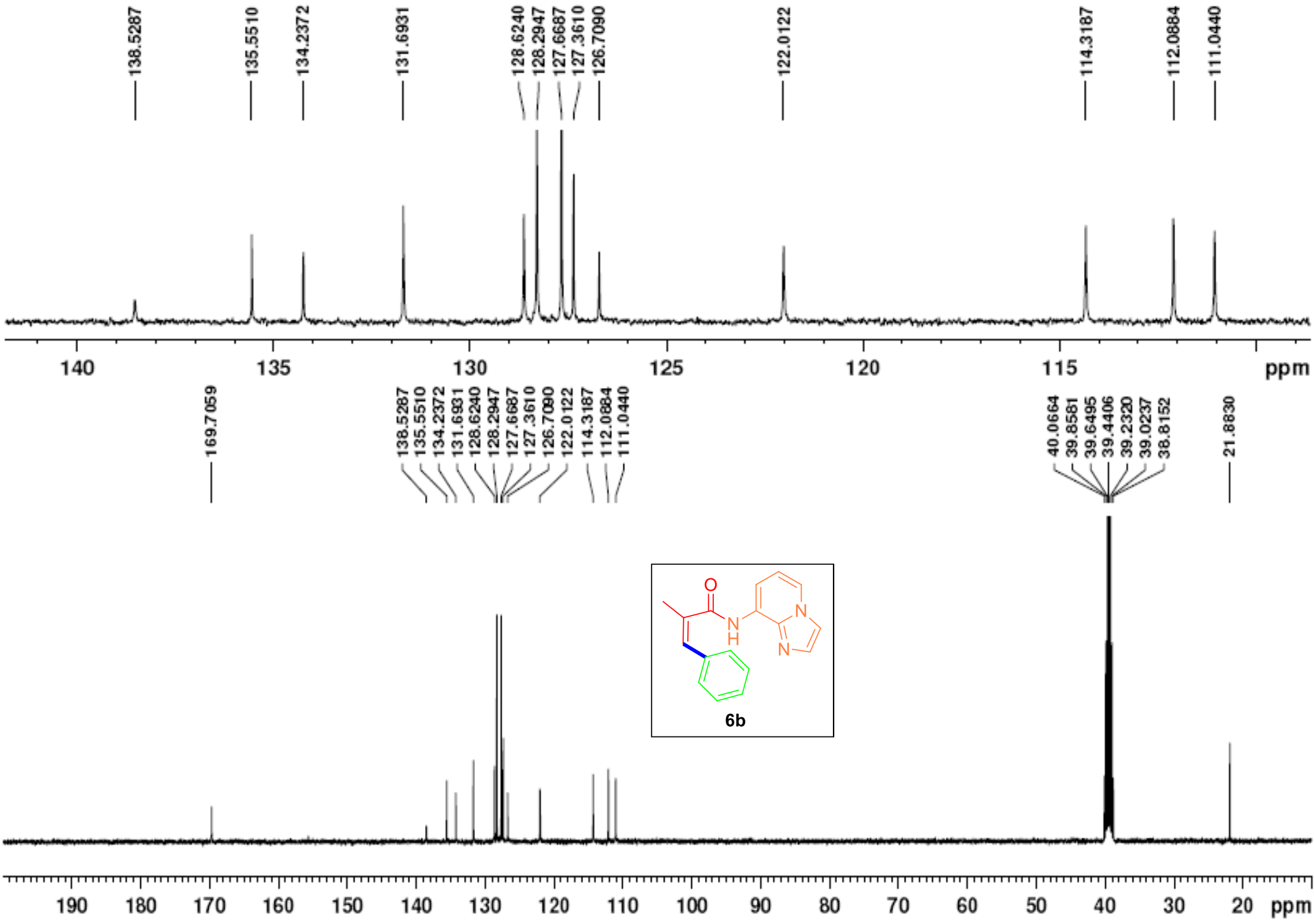


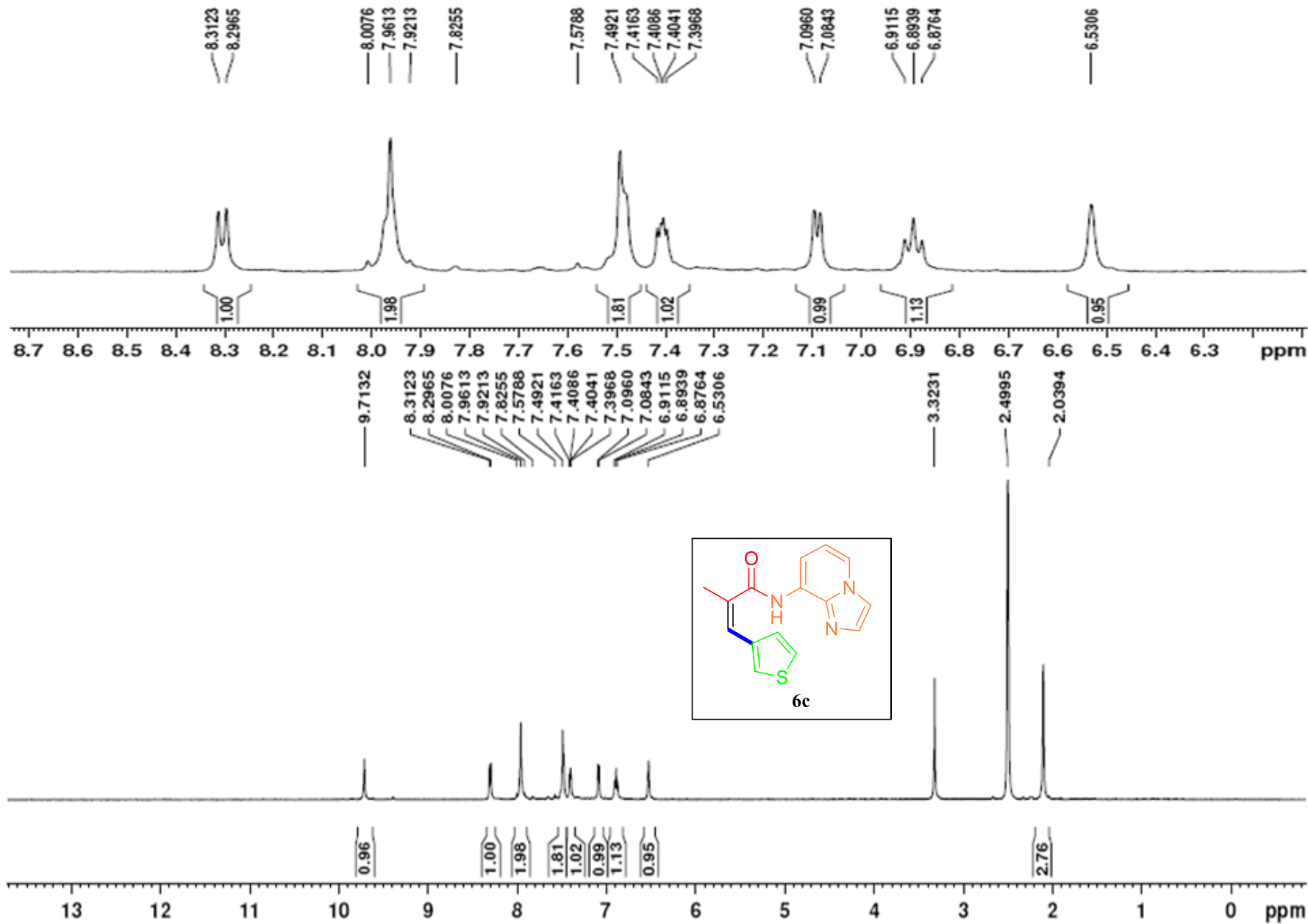
^1H NMR of 6a



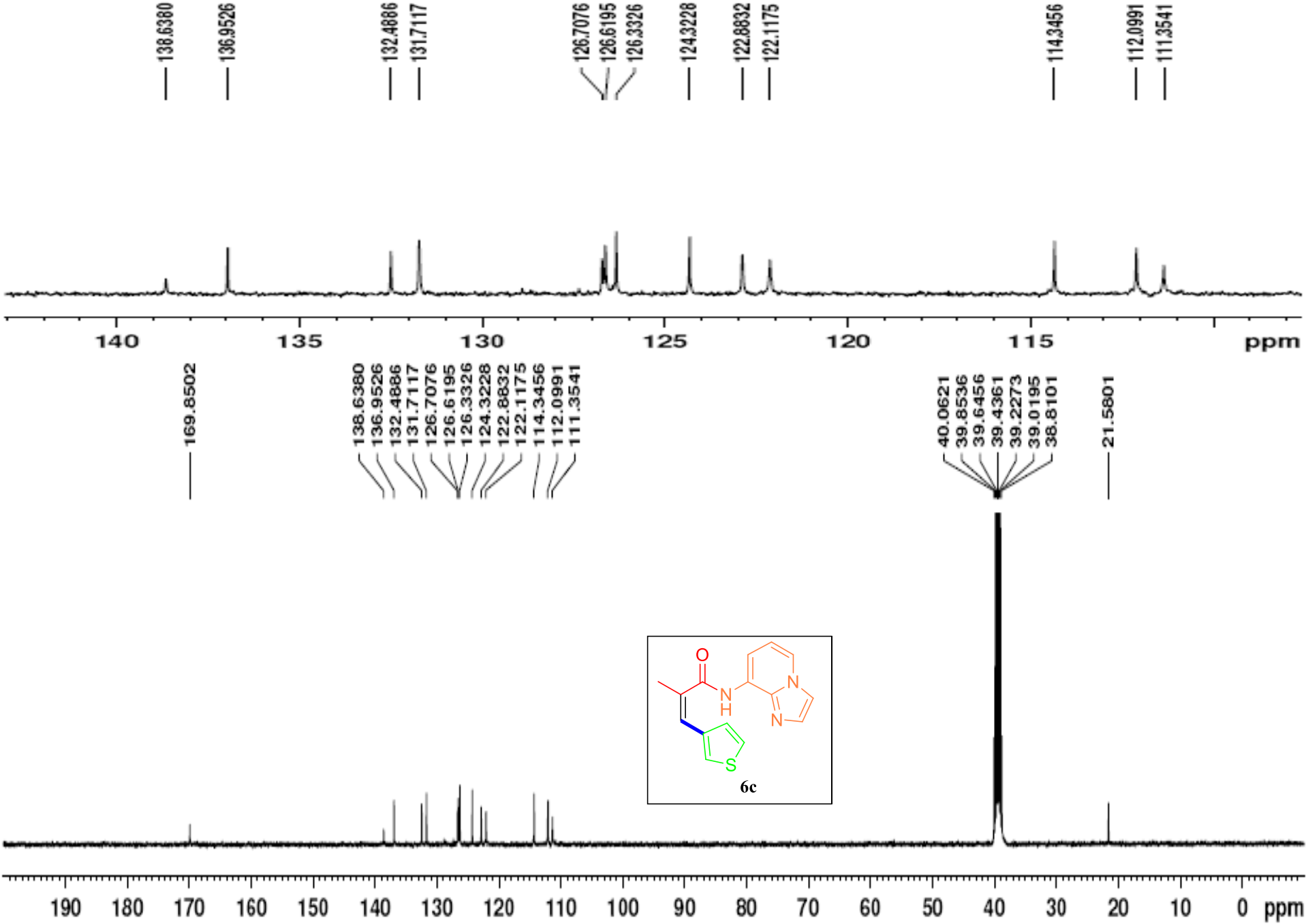


¹H NMR of **6b**

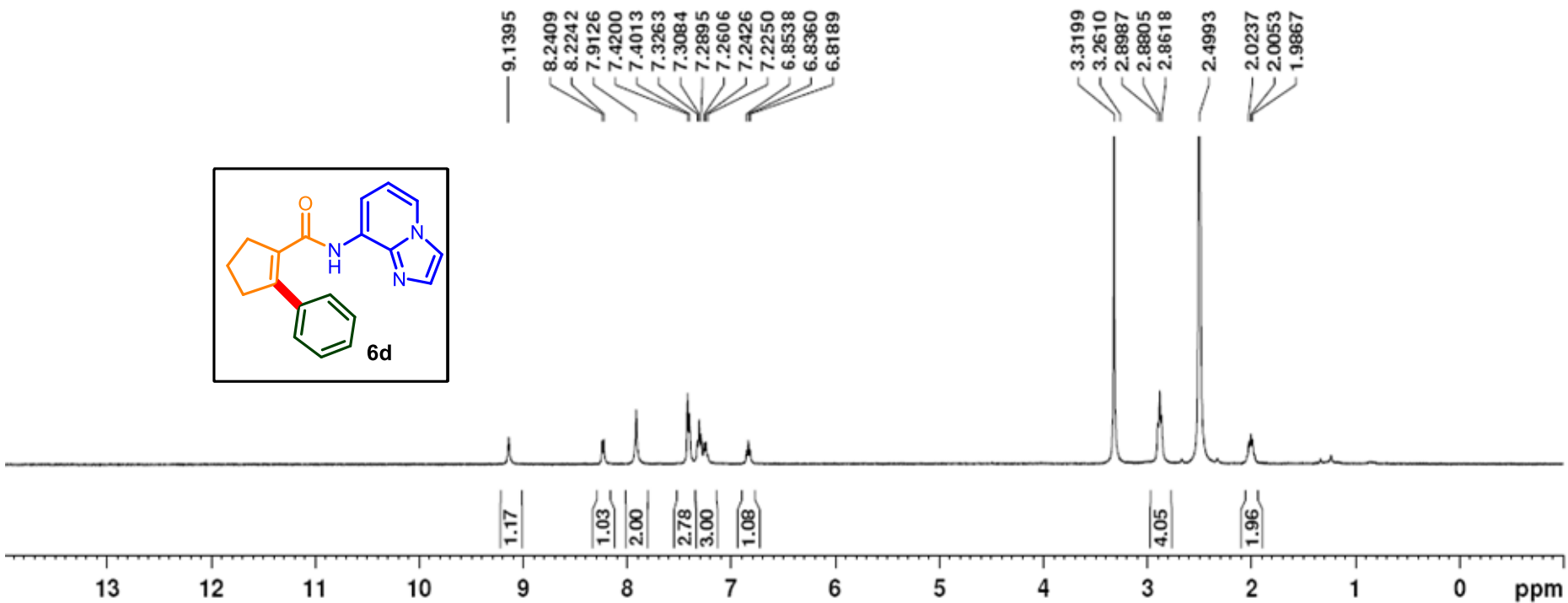
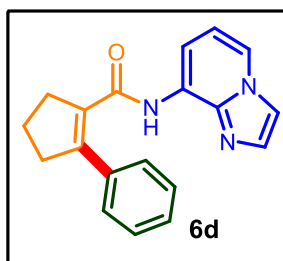
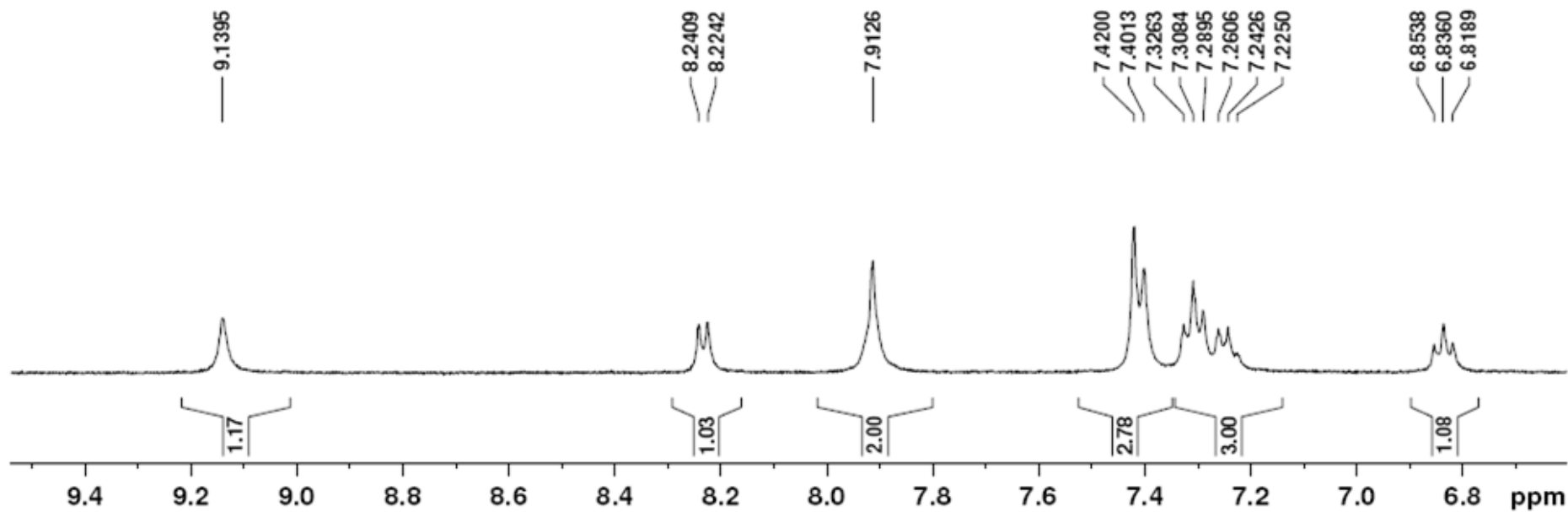




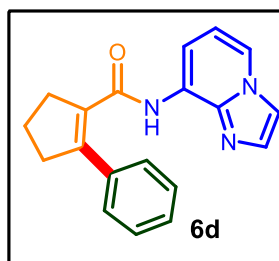
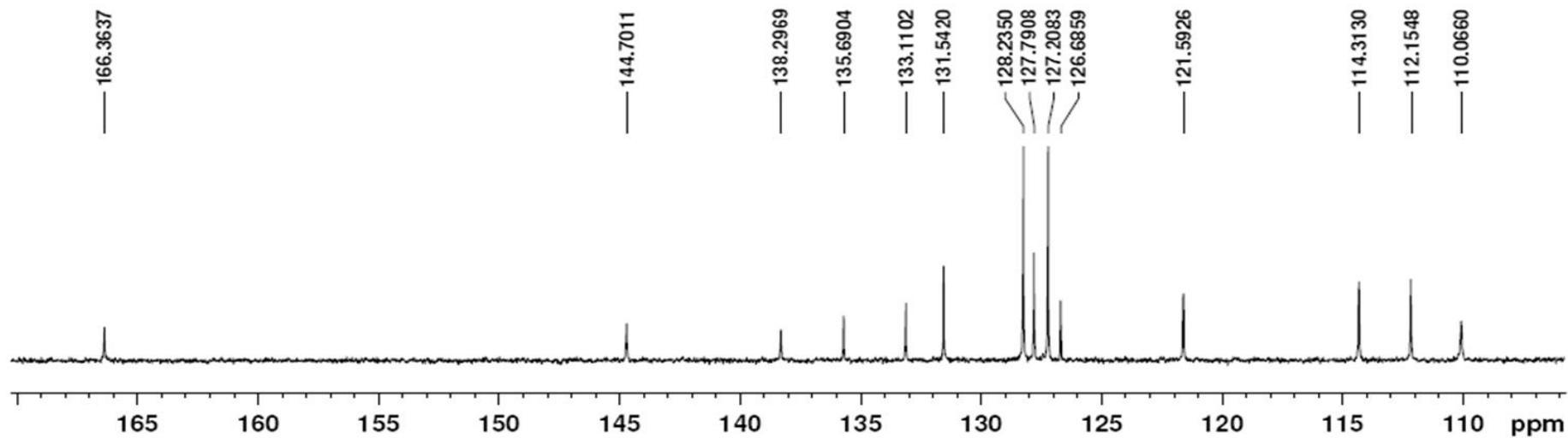
1H NMR of 6c

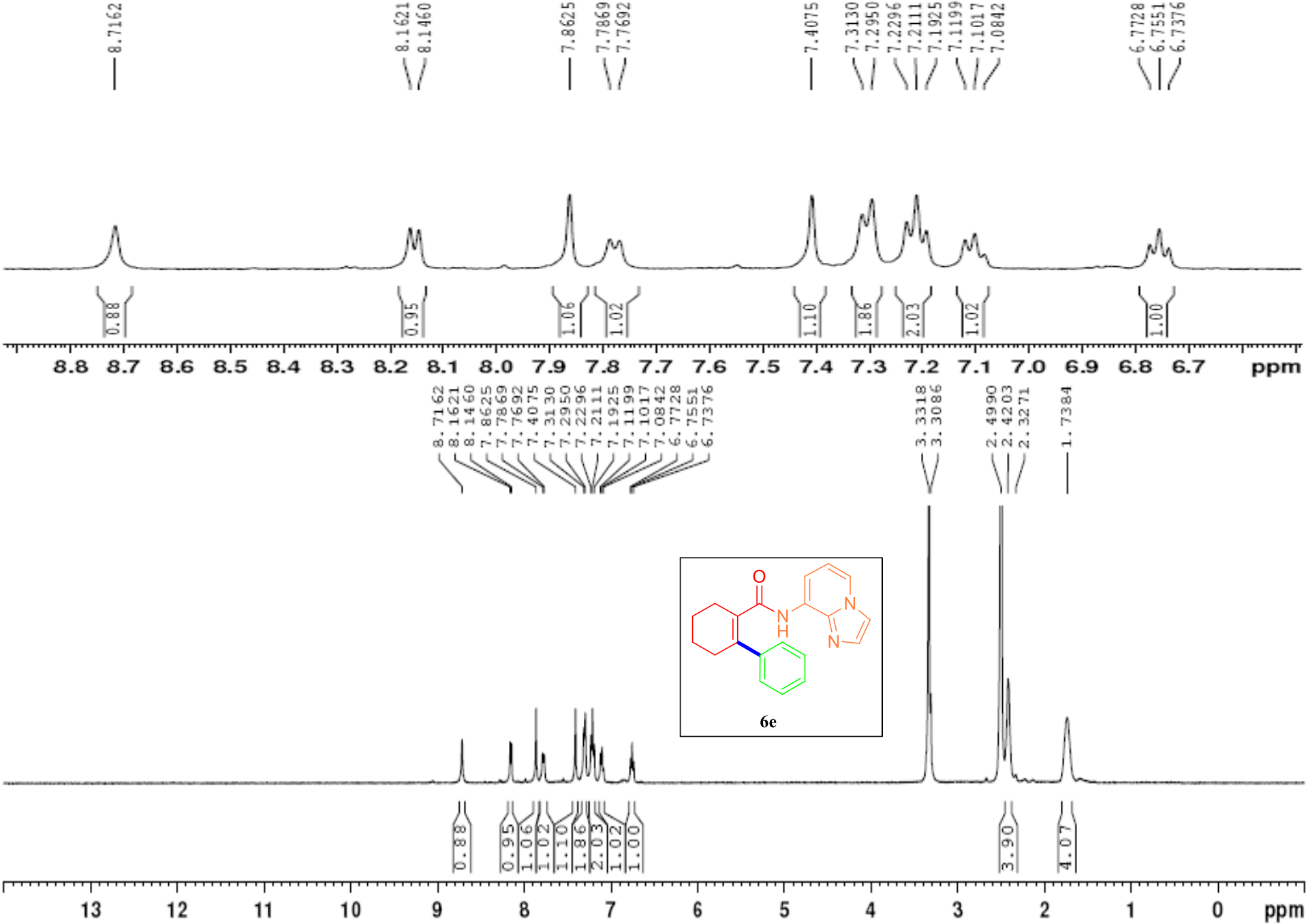


¹³C NMR of **6c** in DMSO-d₆

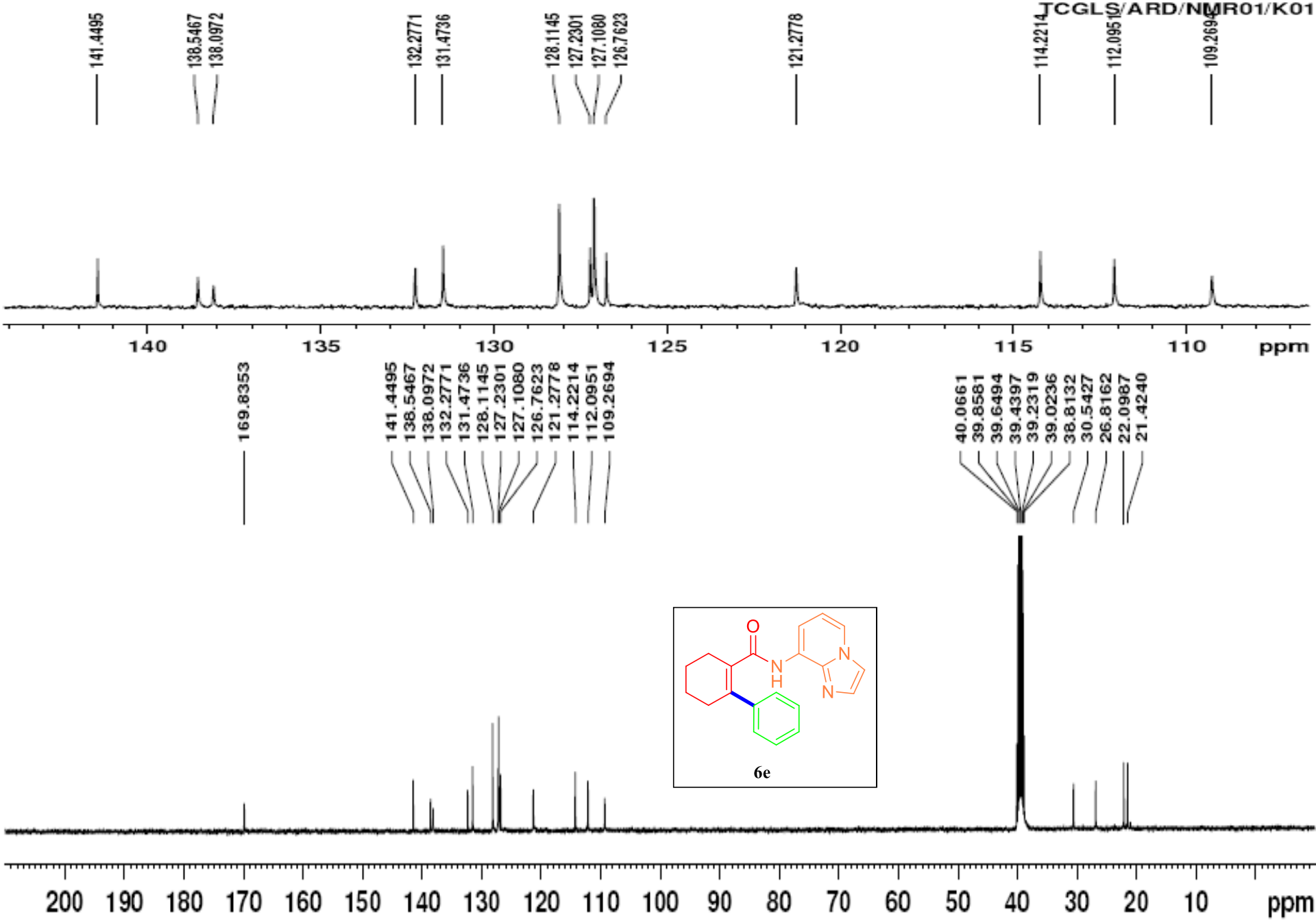


^1H NMR of **6d**

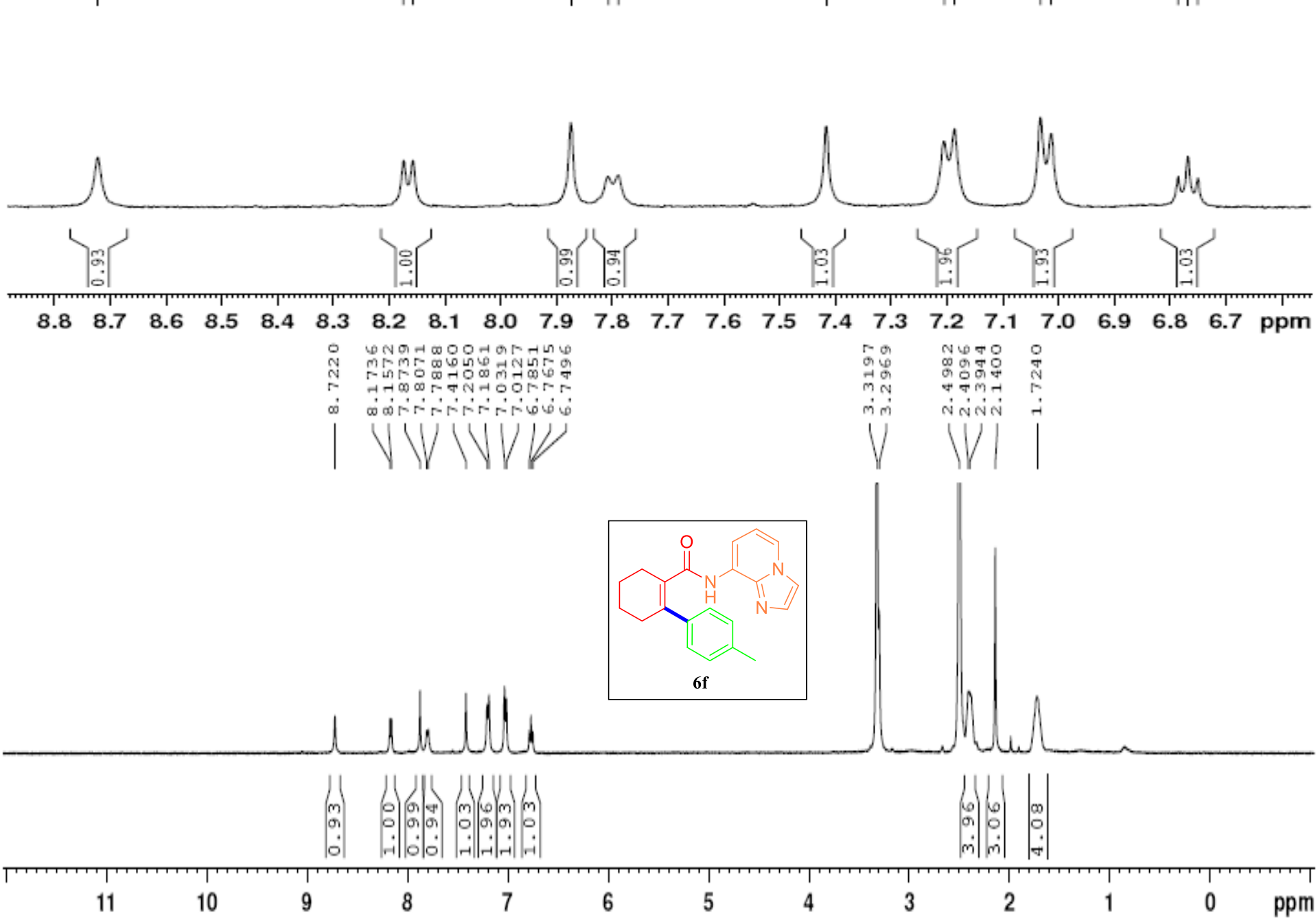




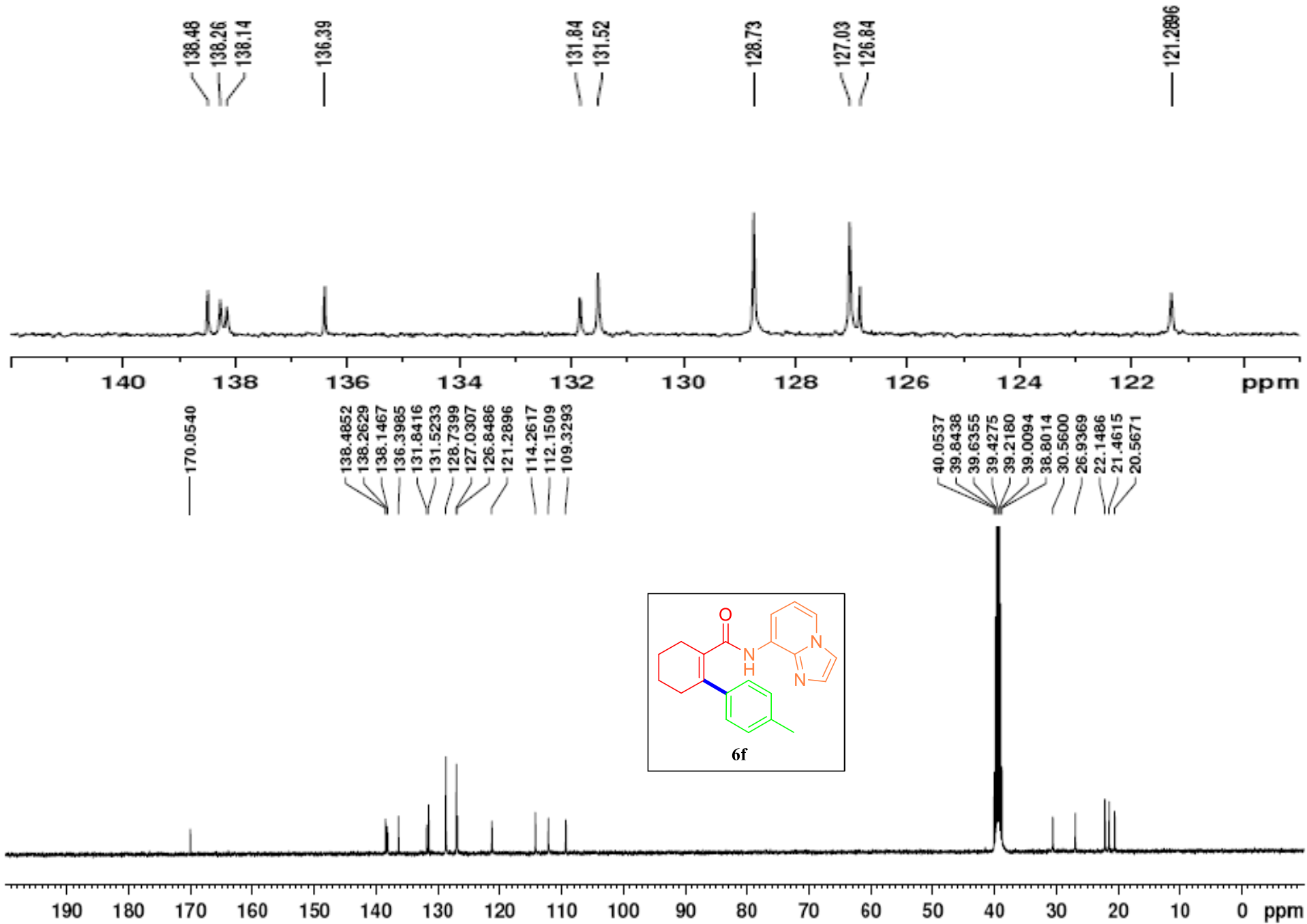
¹H NMR of **6e** in DMSO-d₆



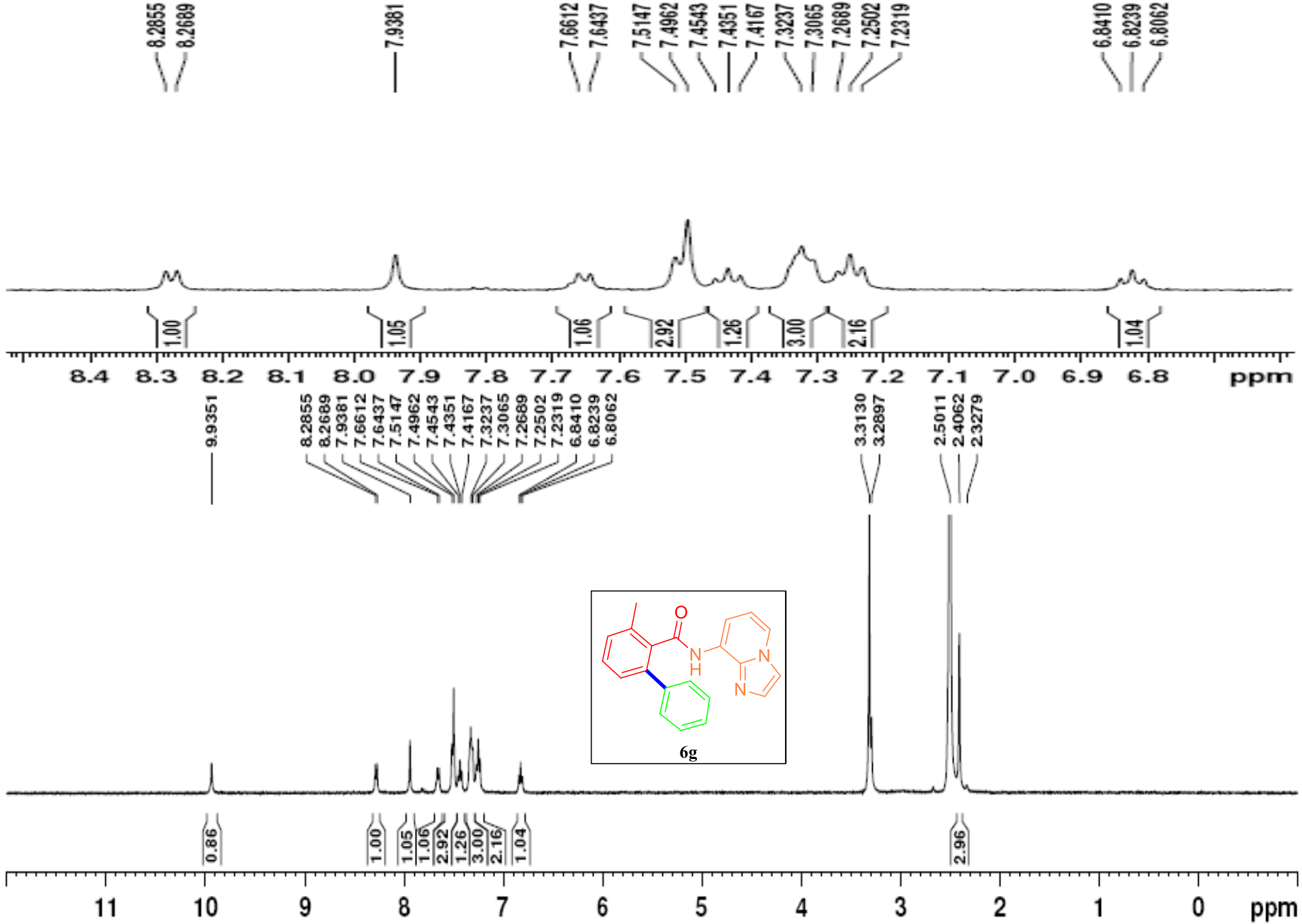
¹³C NMR of 6e in DMSO-d₆



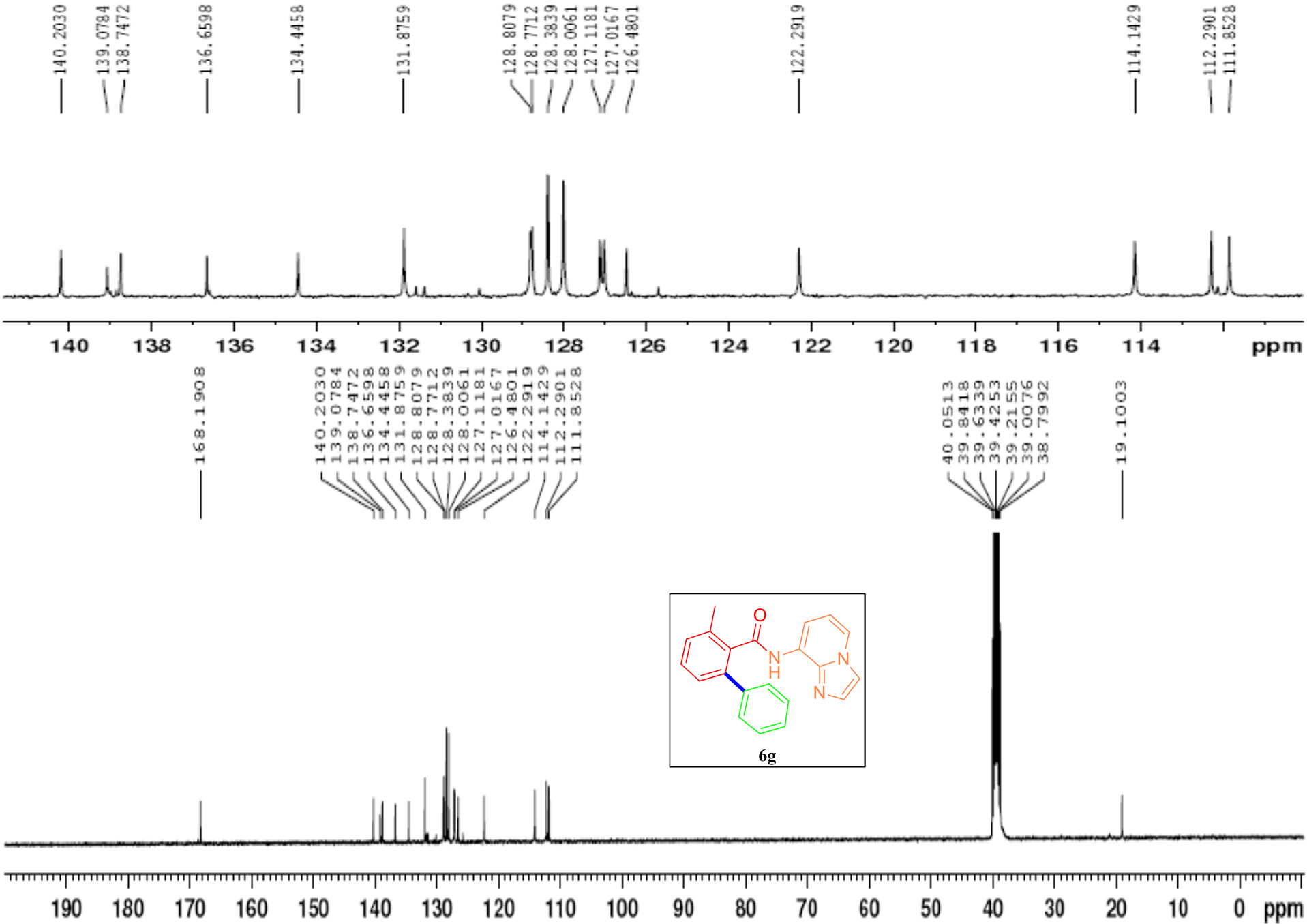
¹H NMR of **6f** in DMSO-d₆



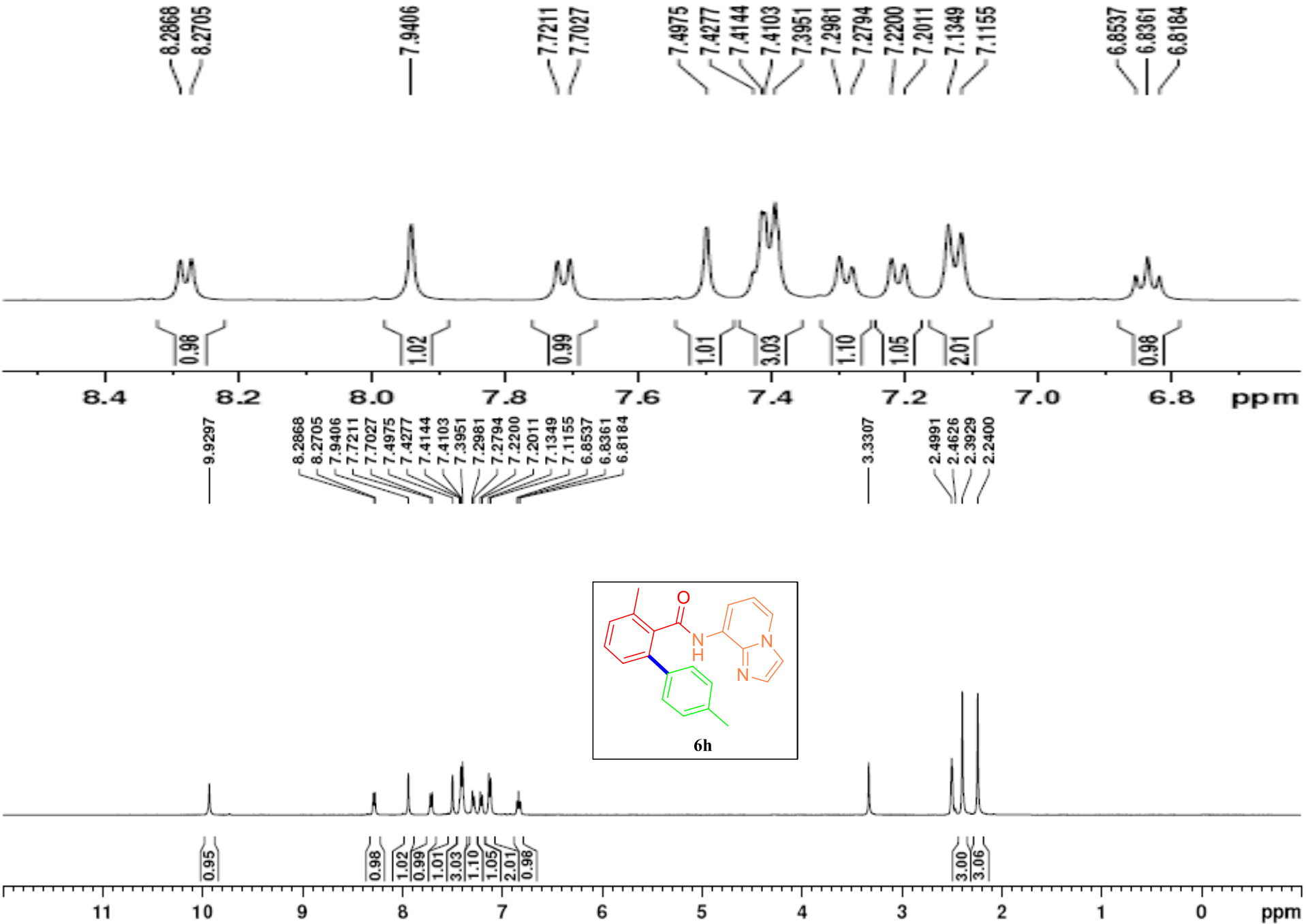
¹³C NMR of **6f** in DMSO-d₆



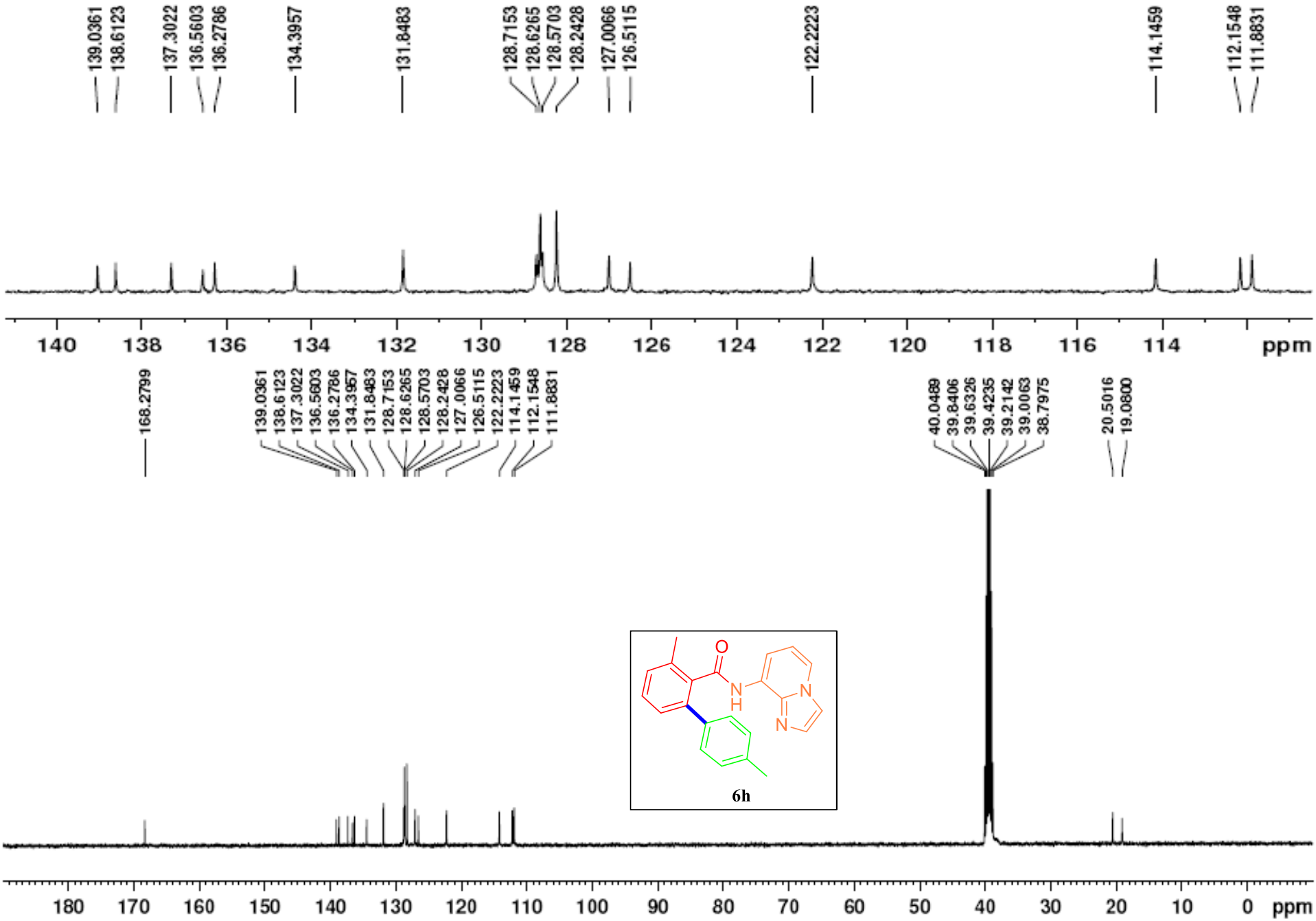
¹H NMR of **6g** in DMSO-d₆



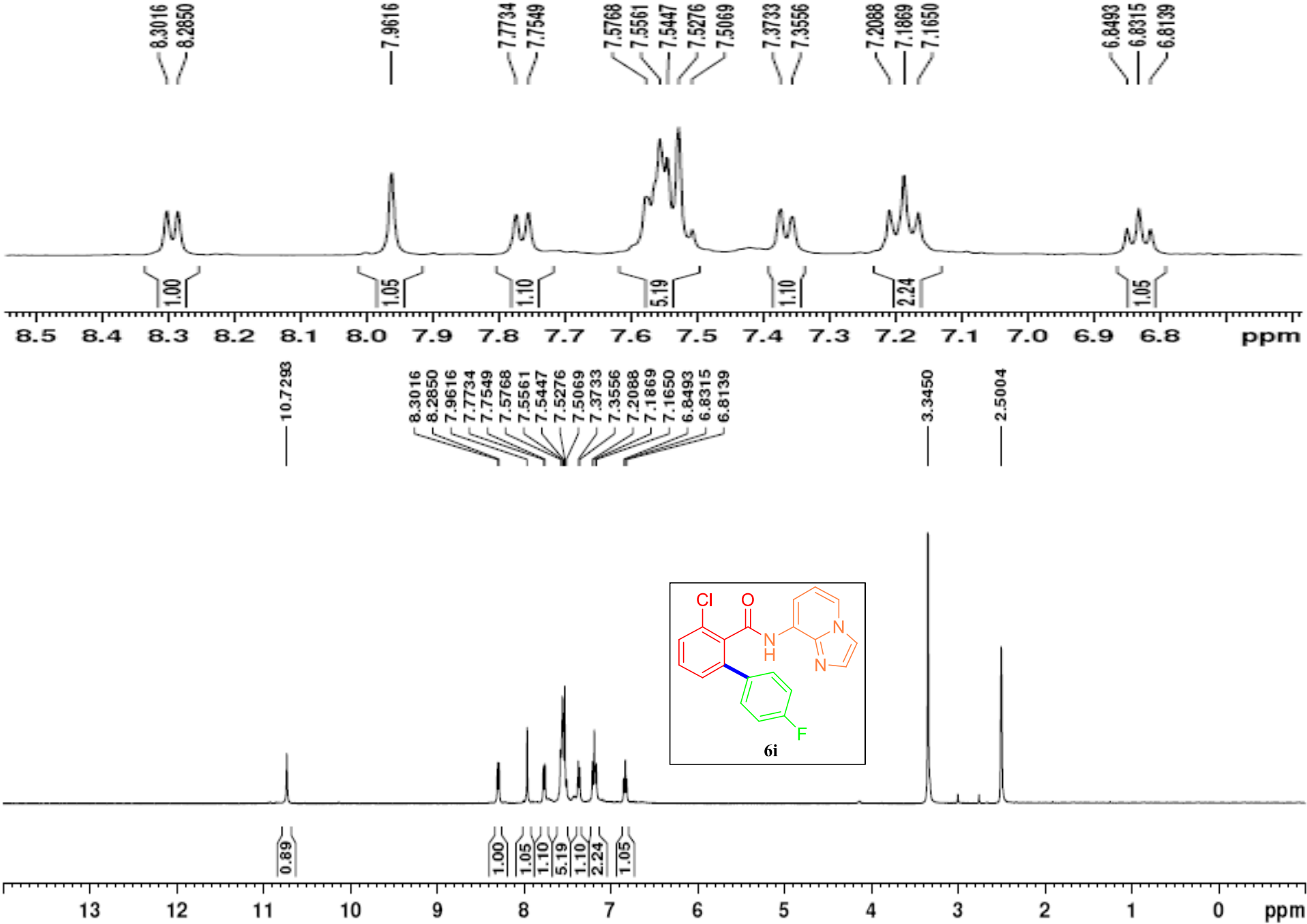
¹³C NMR of **6g** in DMSO-d₆



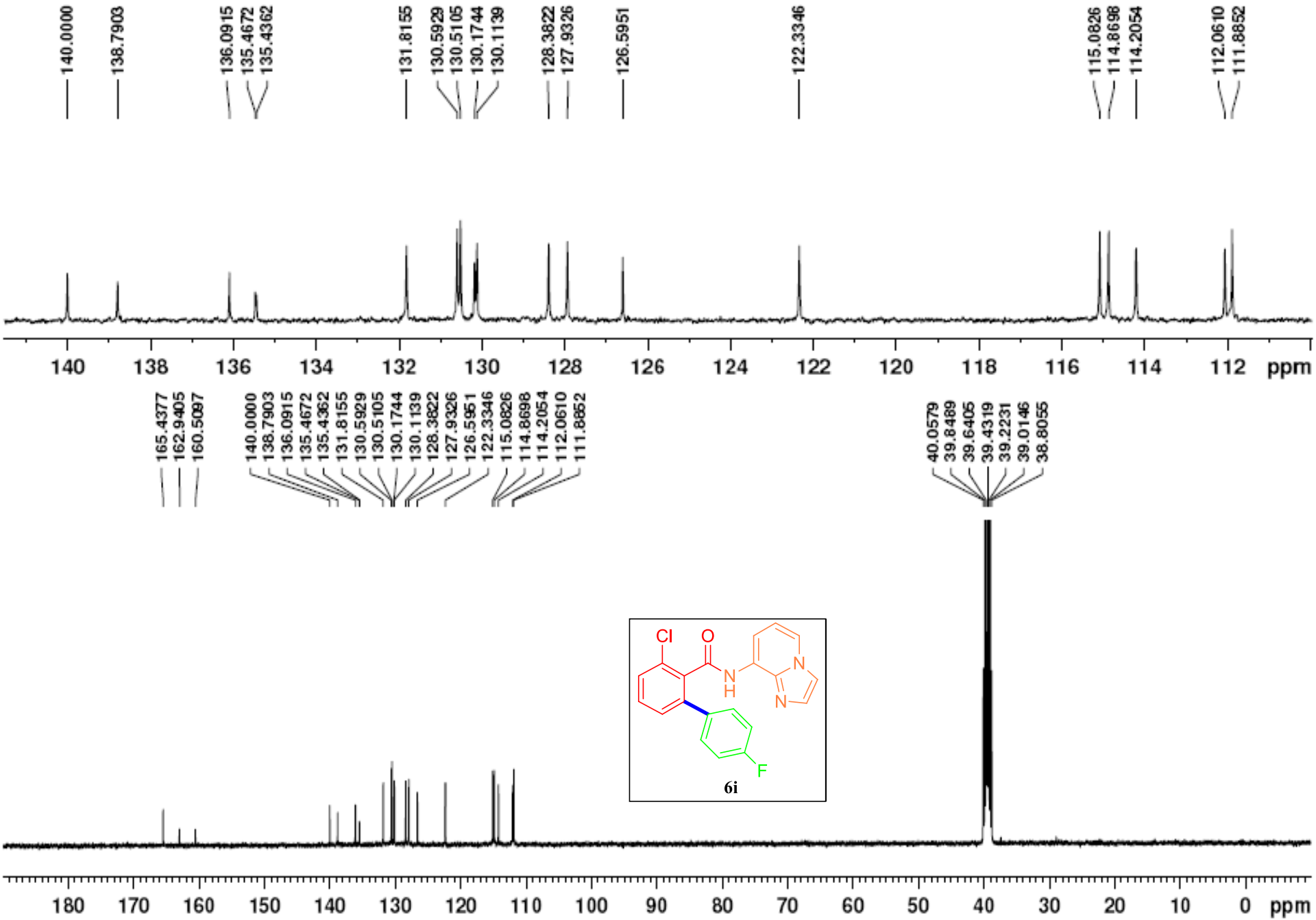
^1H NMR of **6h** in DMSO-d_6



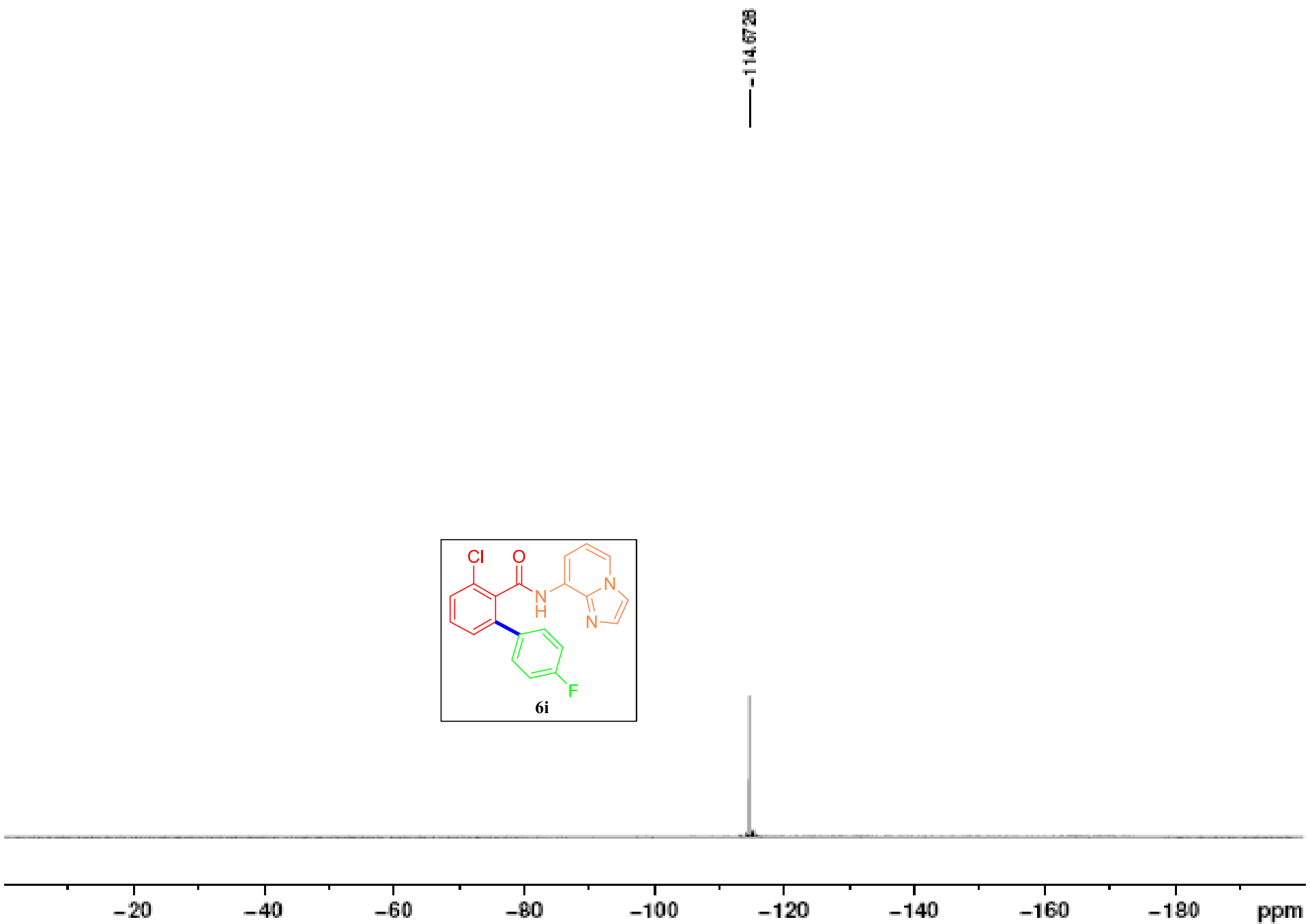
¹³C NMR of **6h** in DMSO-d₆



¹H NMR of **6i** in DMSO-*d*₆



¹³C NMR of **6i** in DMSO-d₆



-114.6726

-20

-40

-60

-80

-100

-120

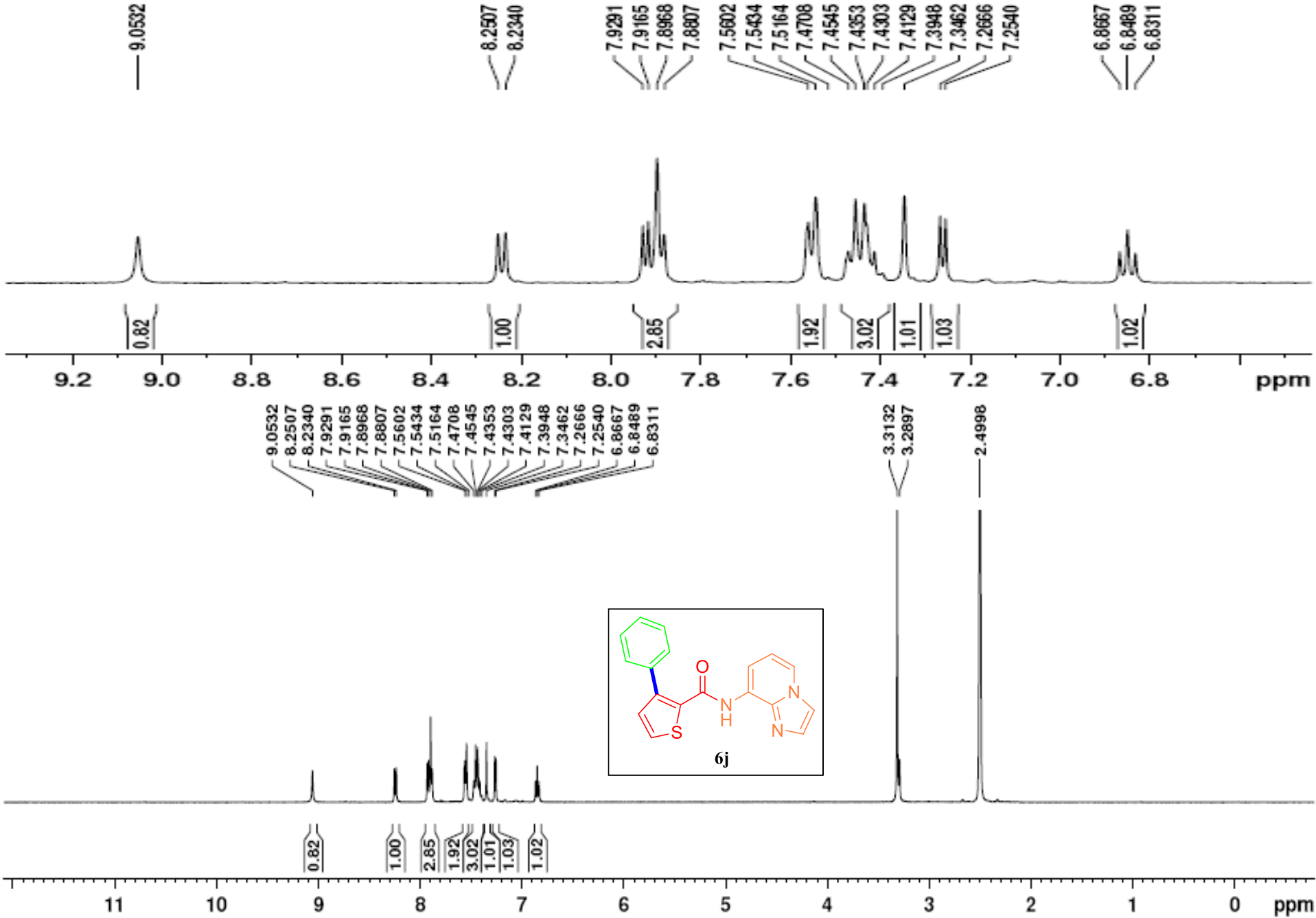
-140

-160

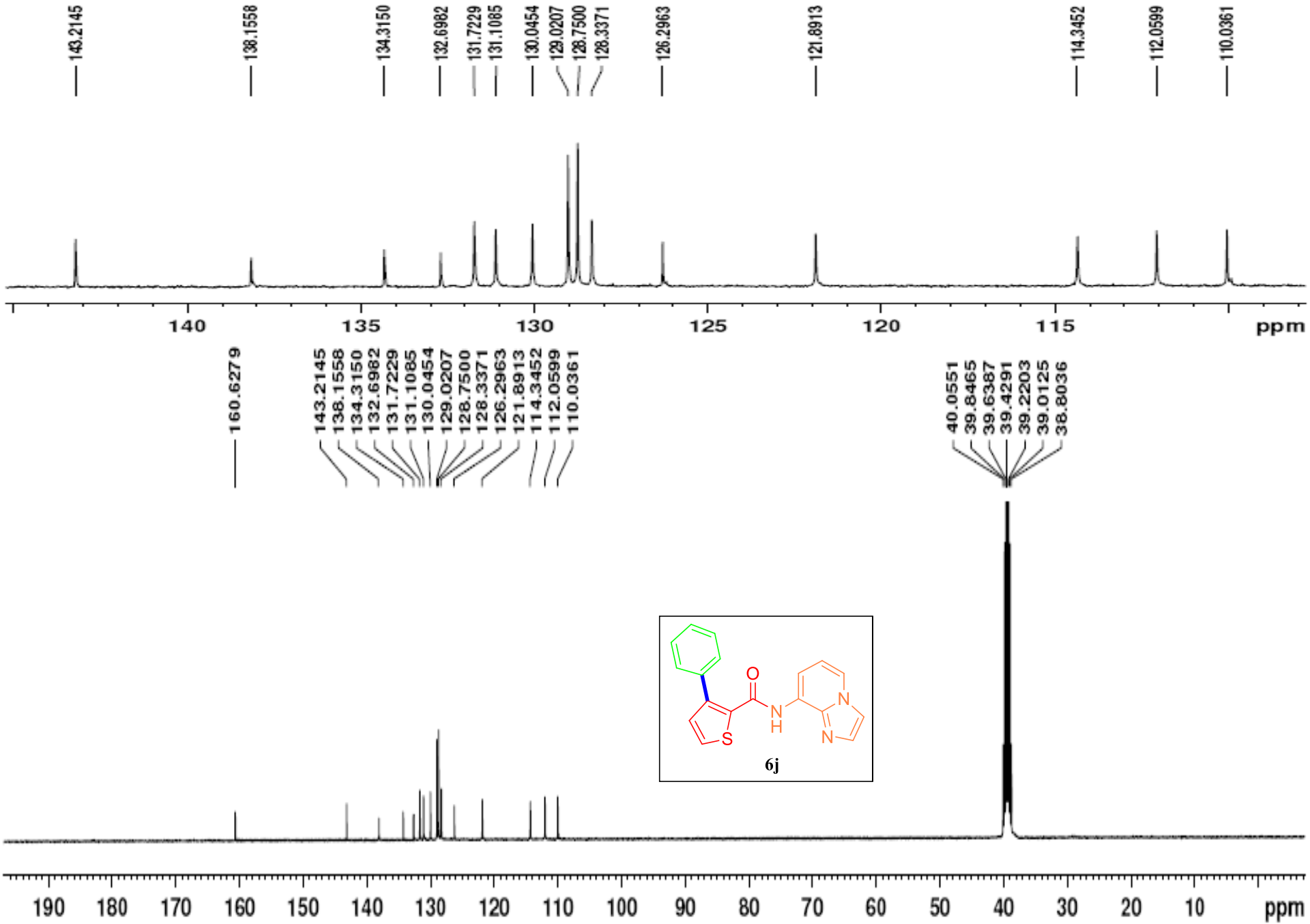
-180

ppm

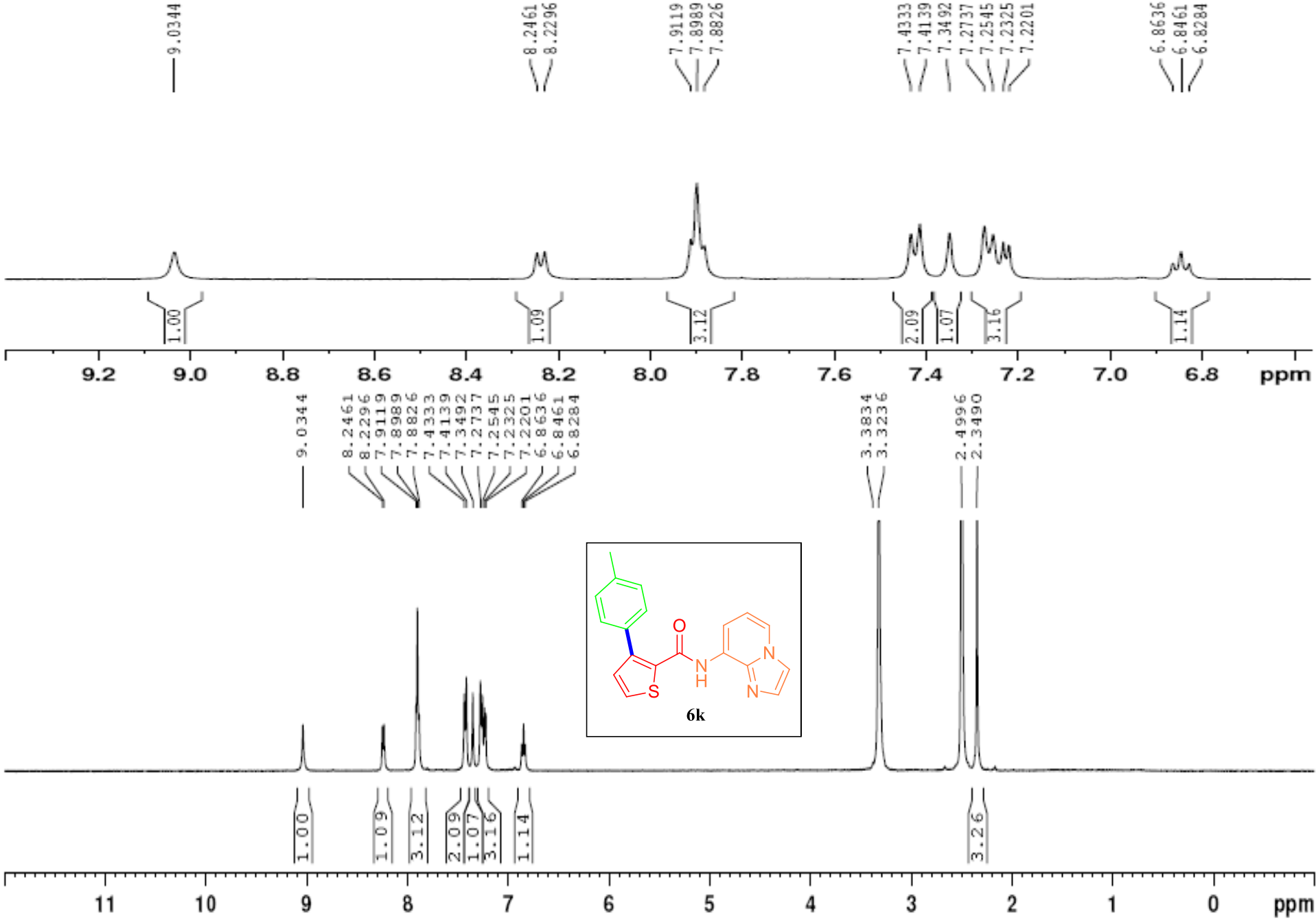
^{19}F NMR of **6i** in DMSO-d_6



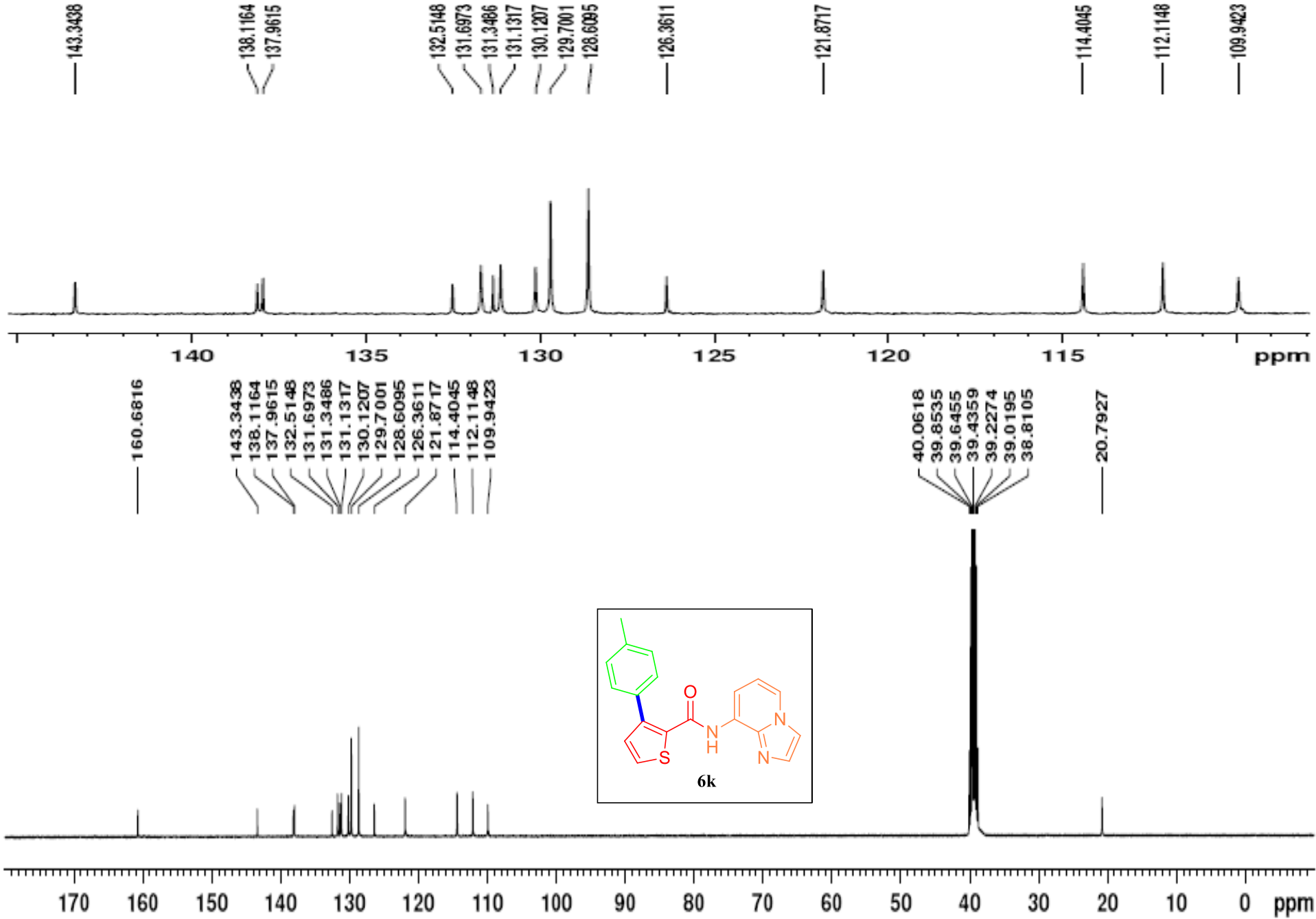
¹H NMR of **6j** in DMSO-d₆



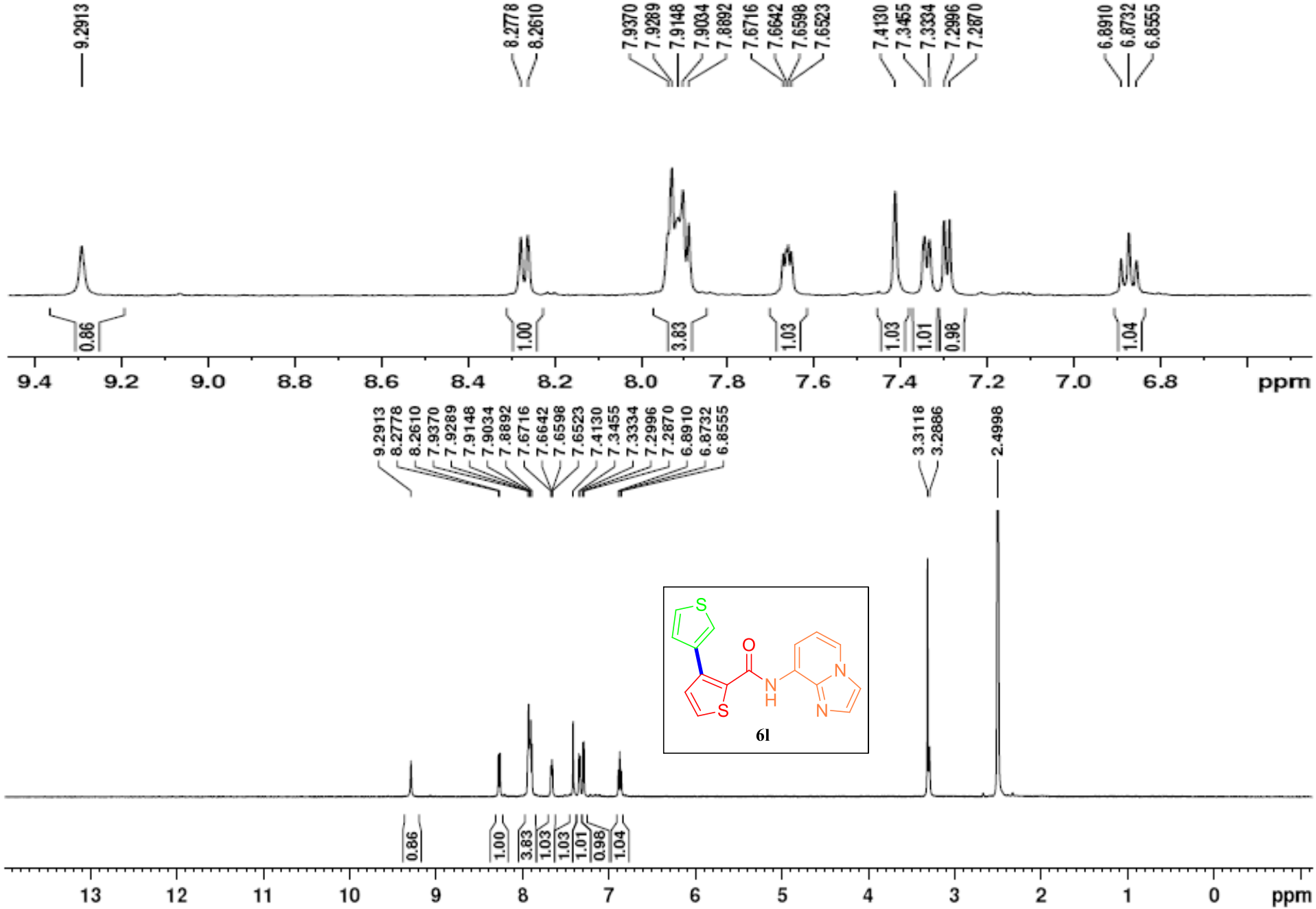
¹³C NMR of **6j** in DMSO-d₆



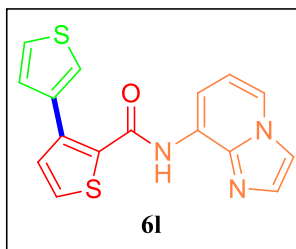
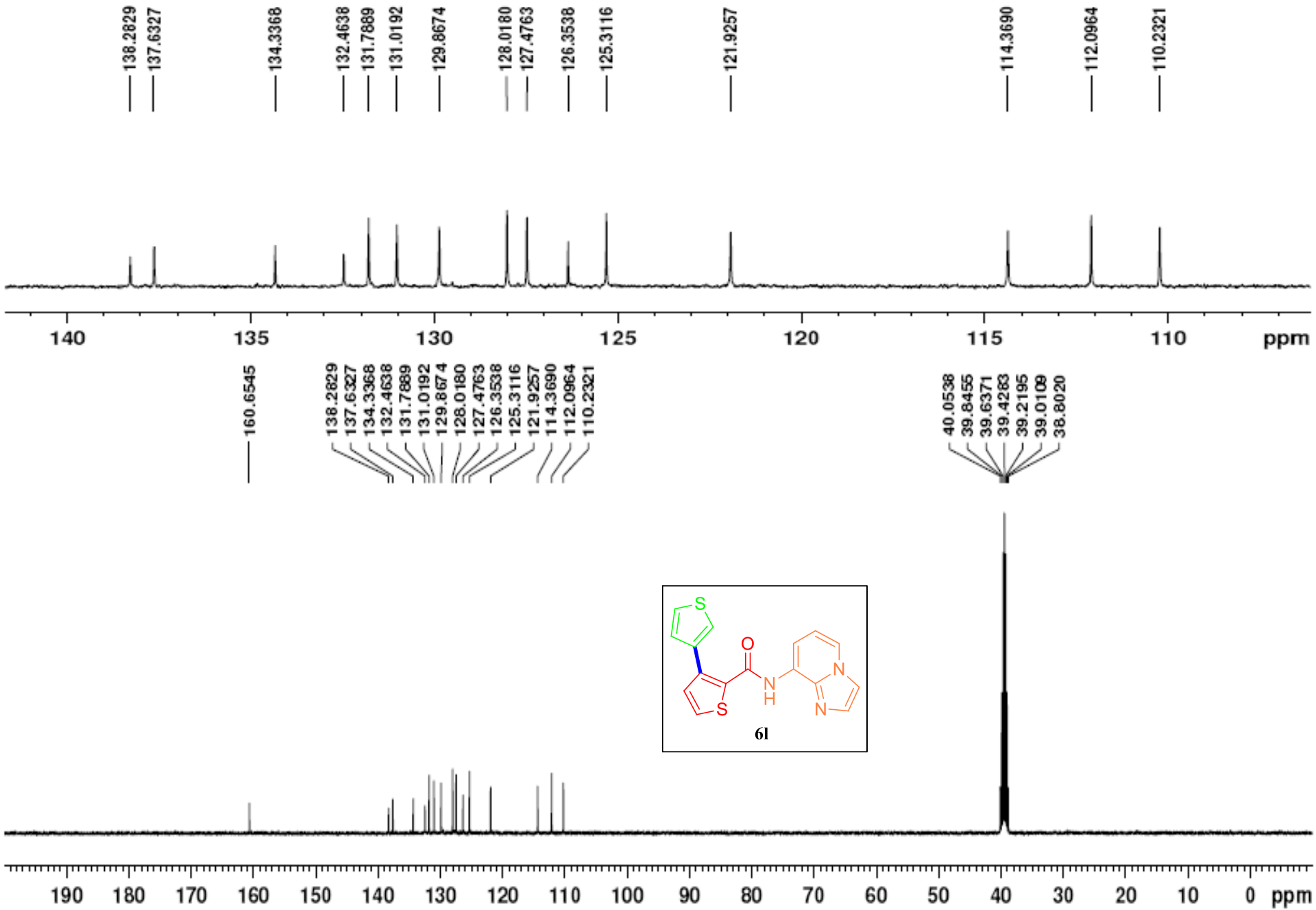
¹H NMR of **6k** in DMSO-d₆



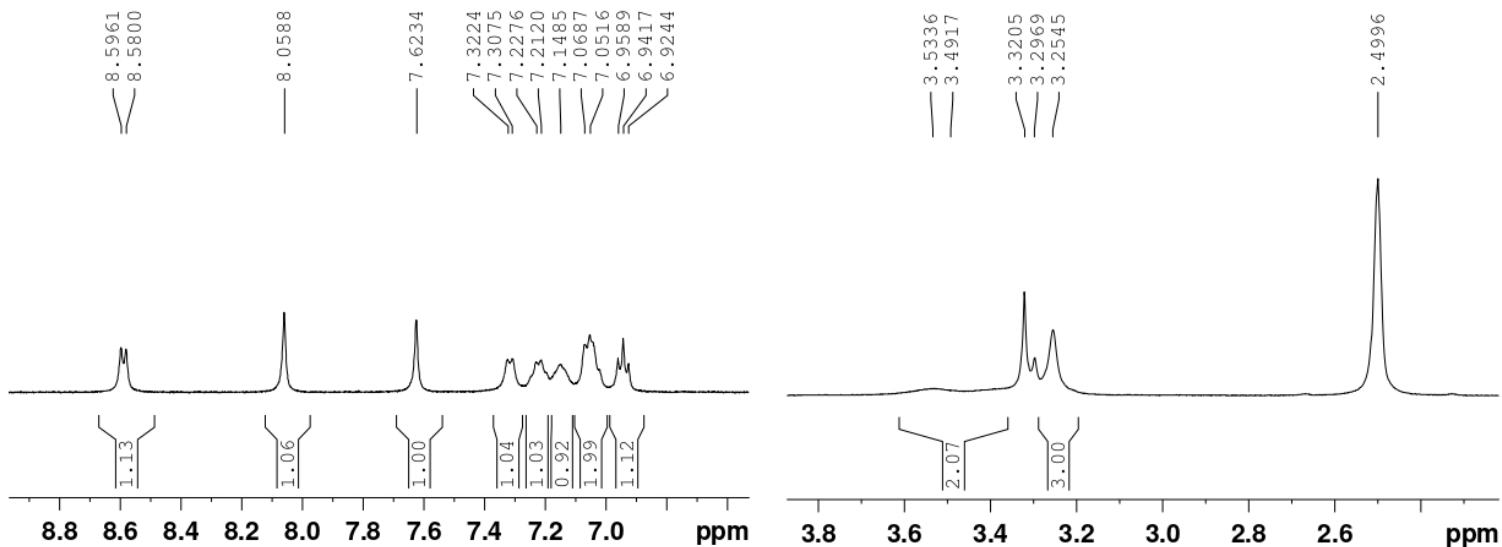
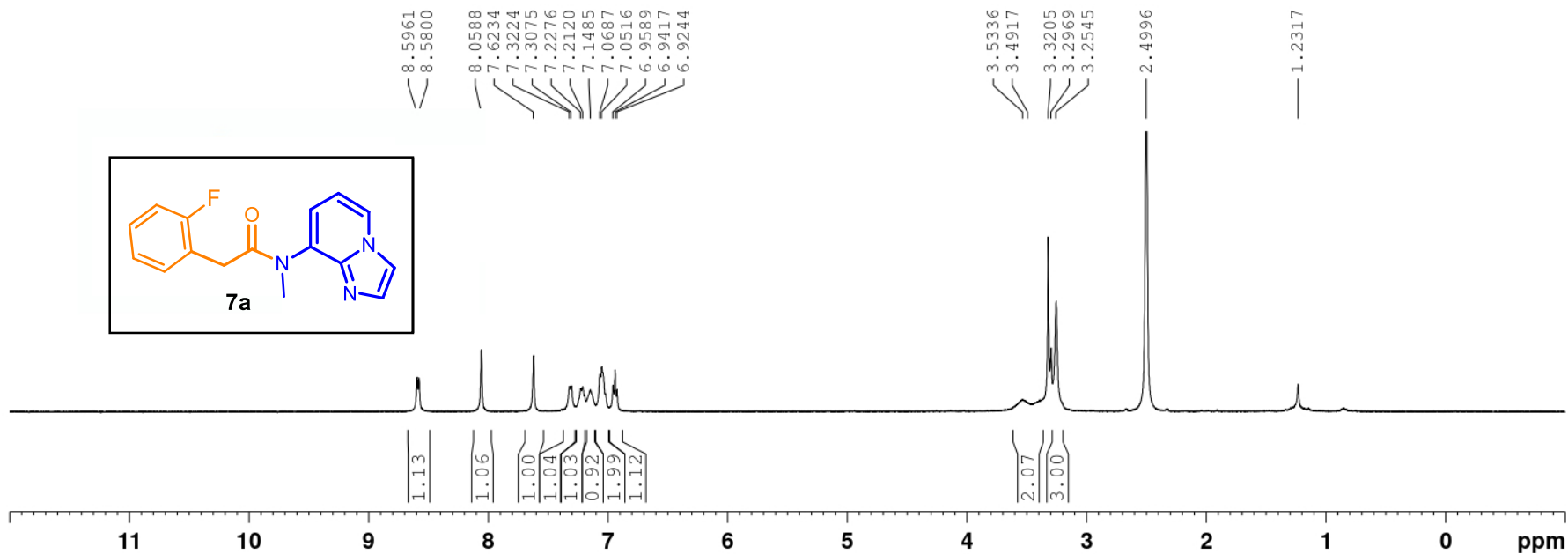
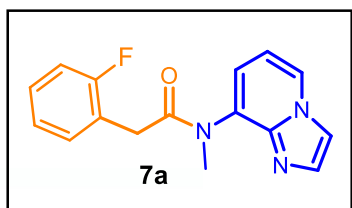
¹³C NMR of **6k** in DMSO-d₆

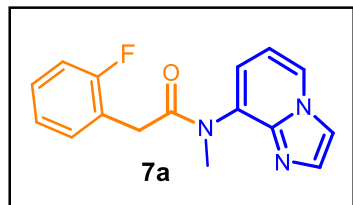
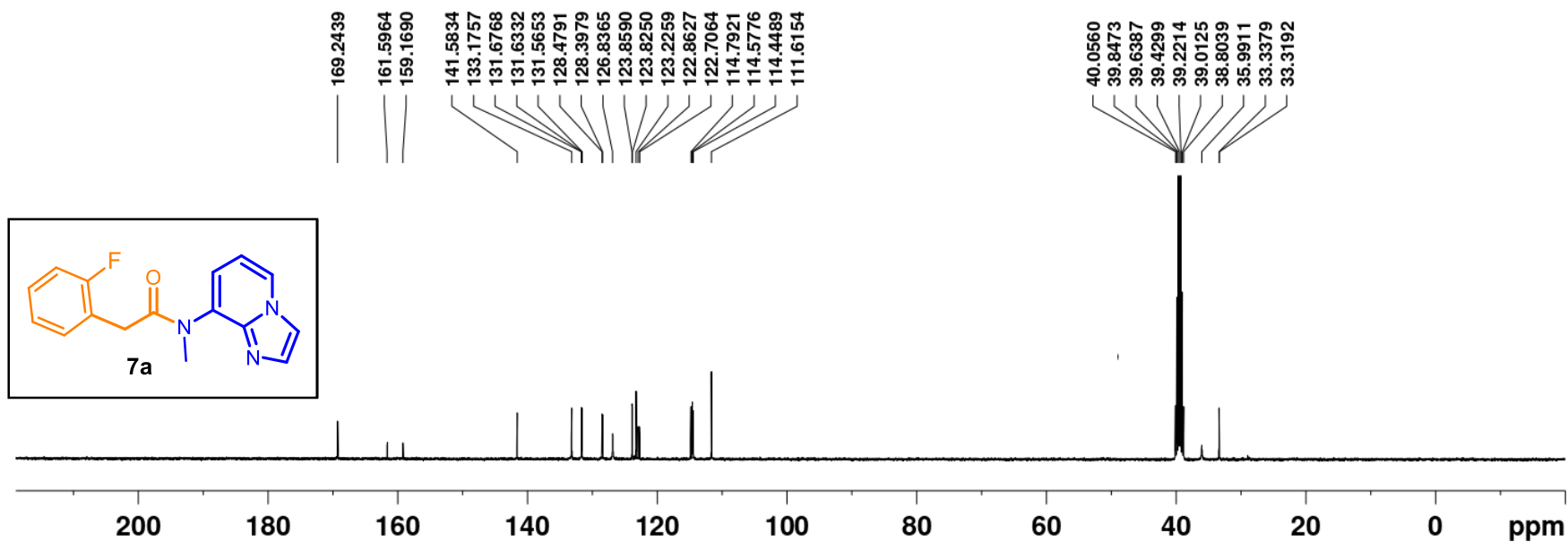
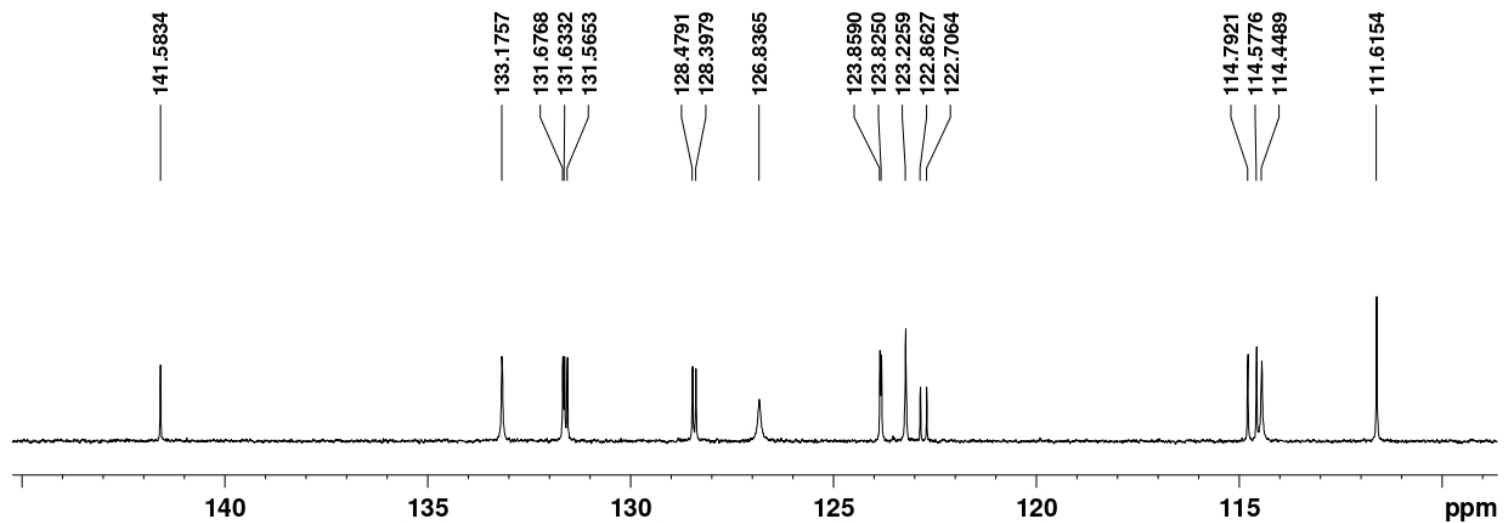


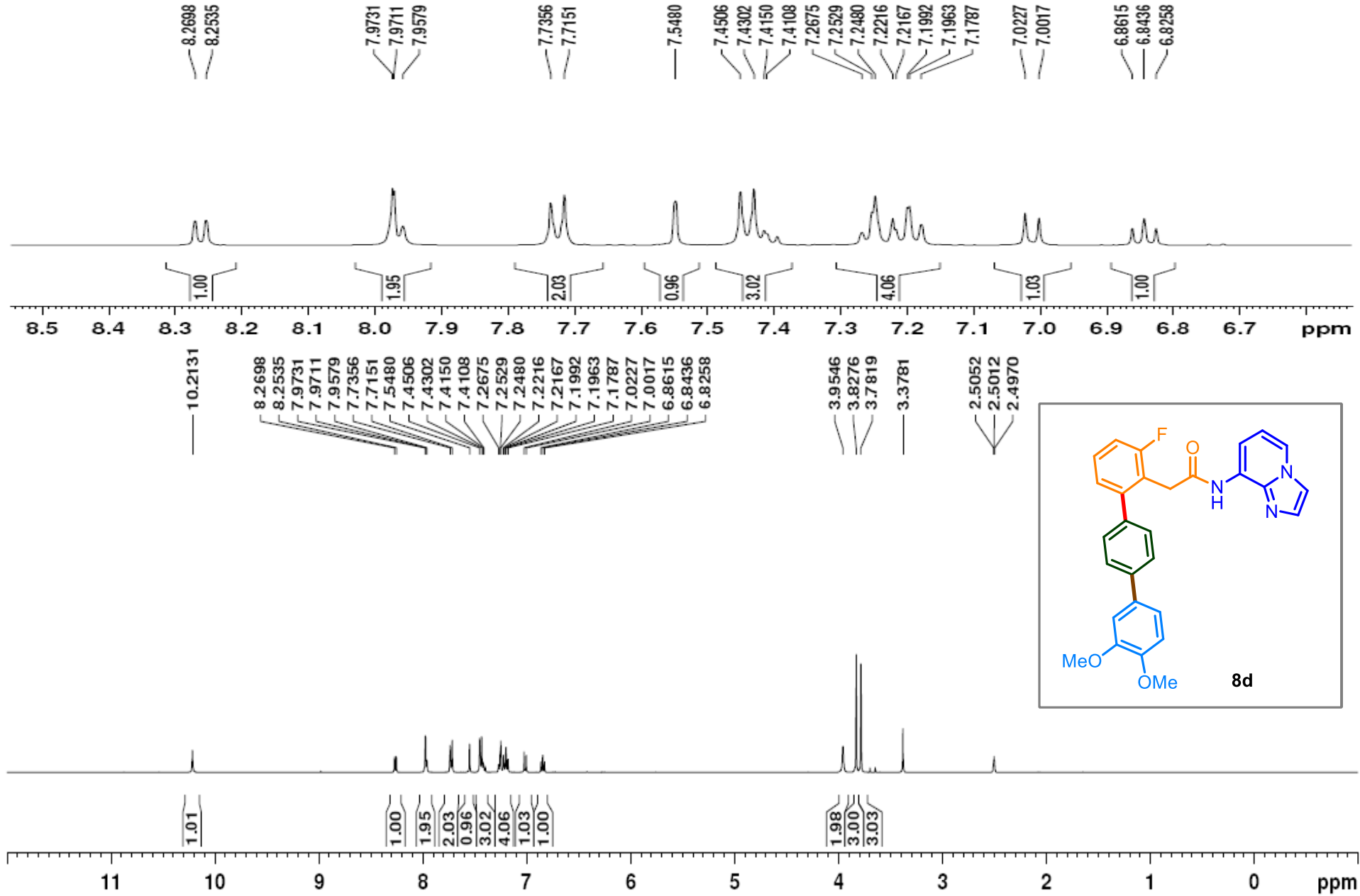
^1H NMR of **6l** in DMSO-d_6



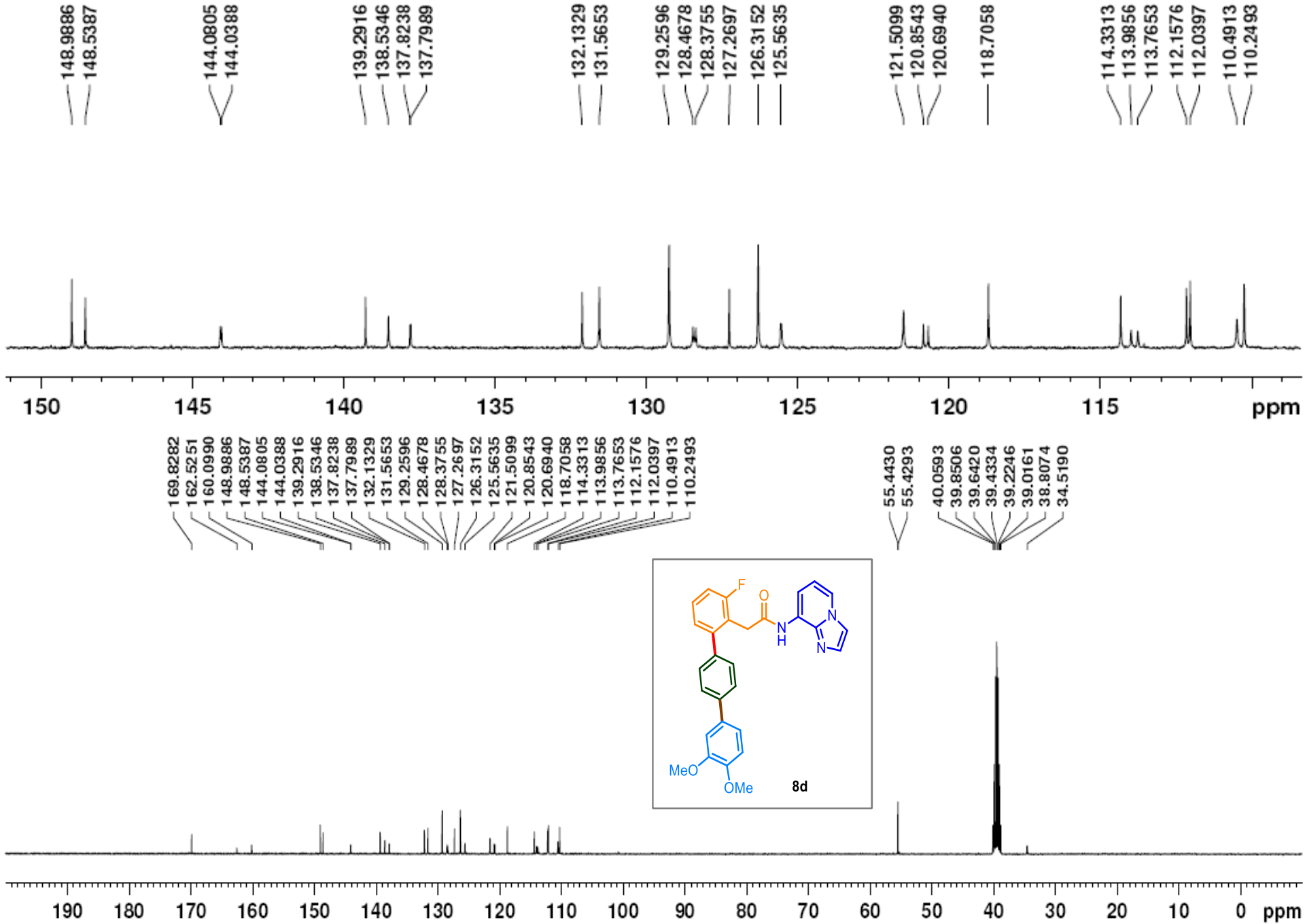
¹³C NMR of **6l** in DMSO-d₆



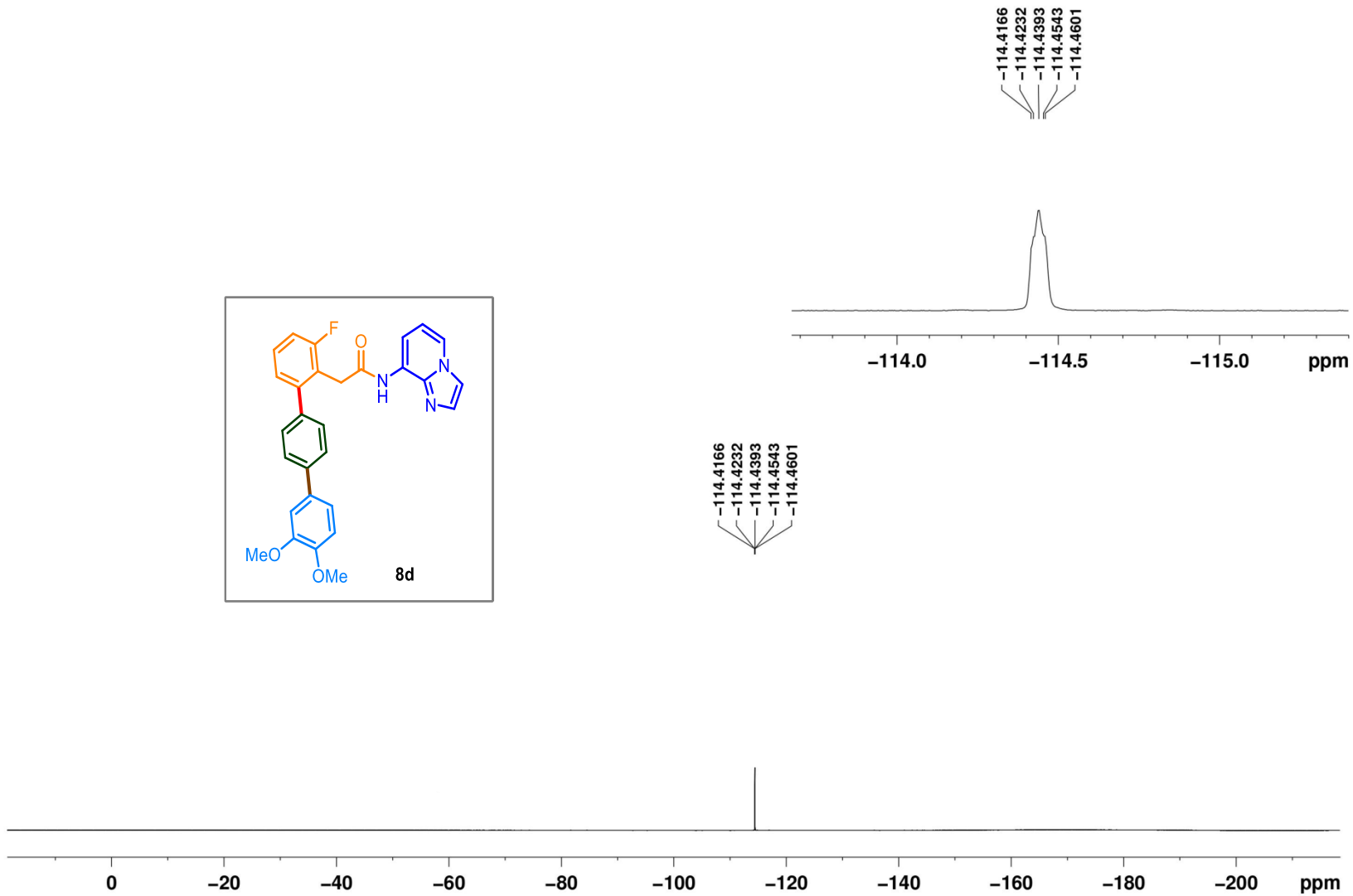
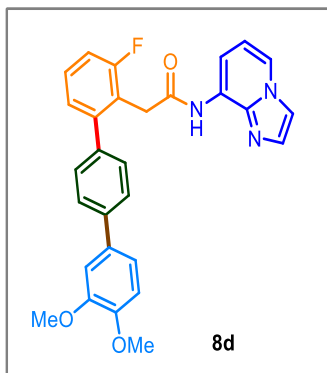




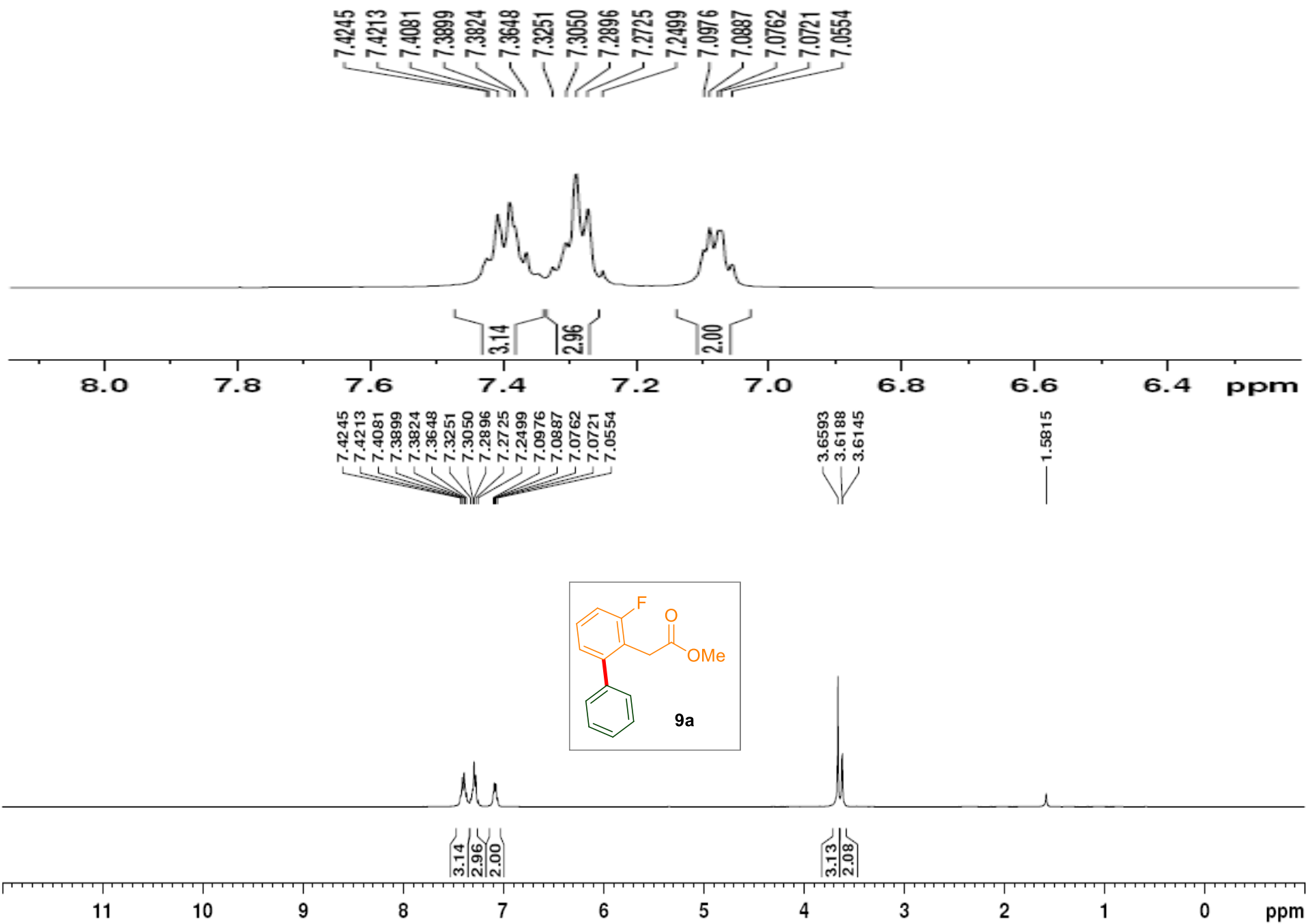
1H NMR of **8d**



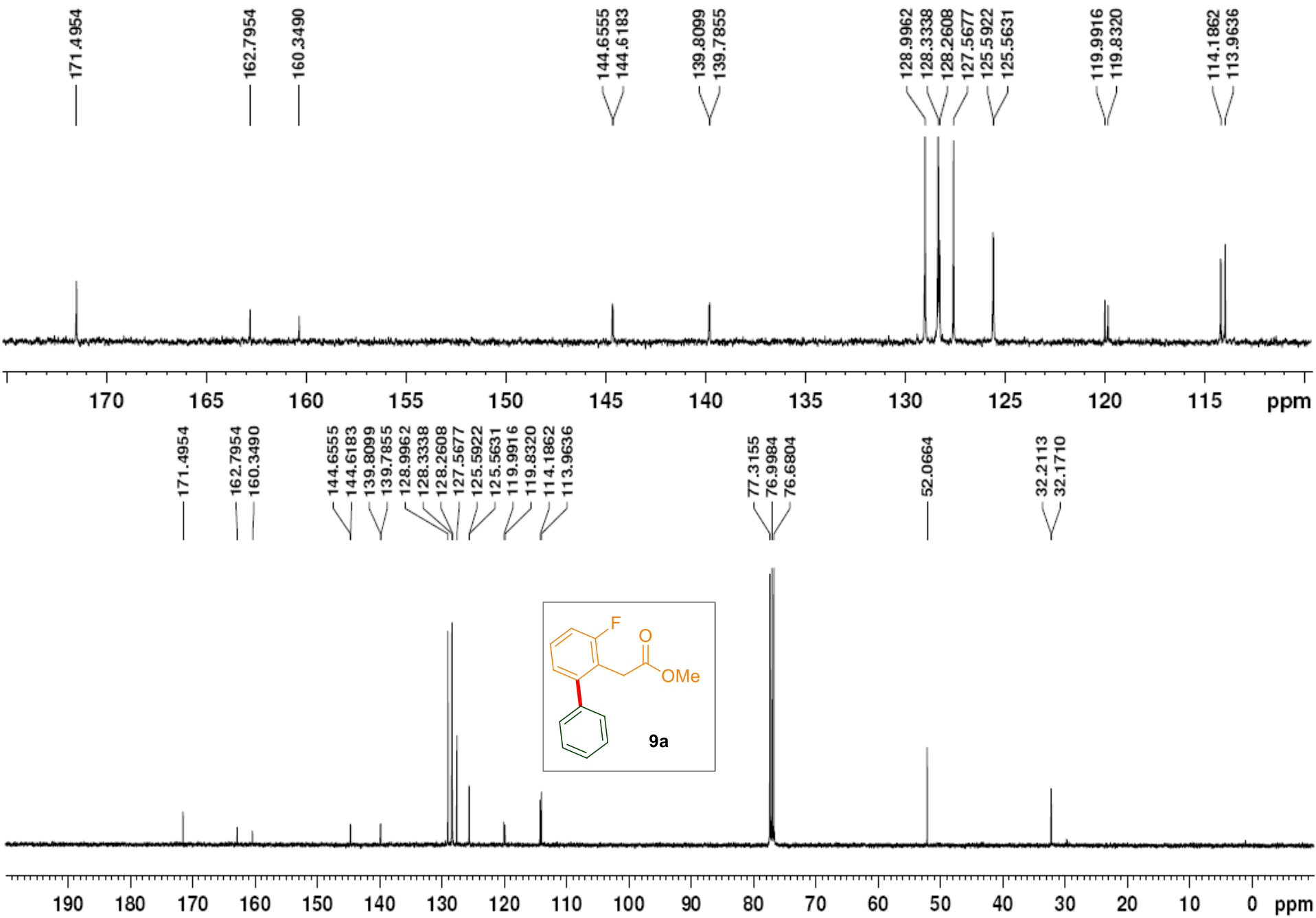
13C NMR of **8d**



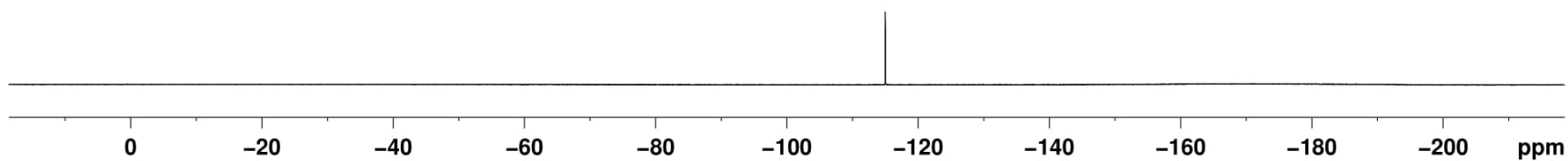
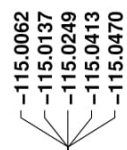
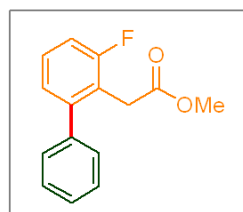
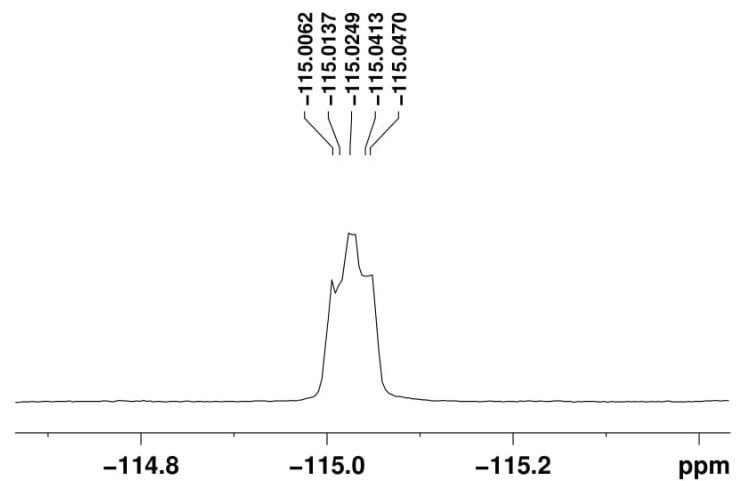
^{19}F NMR of **8d**



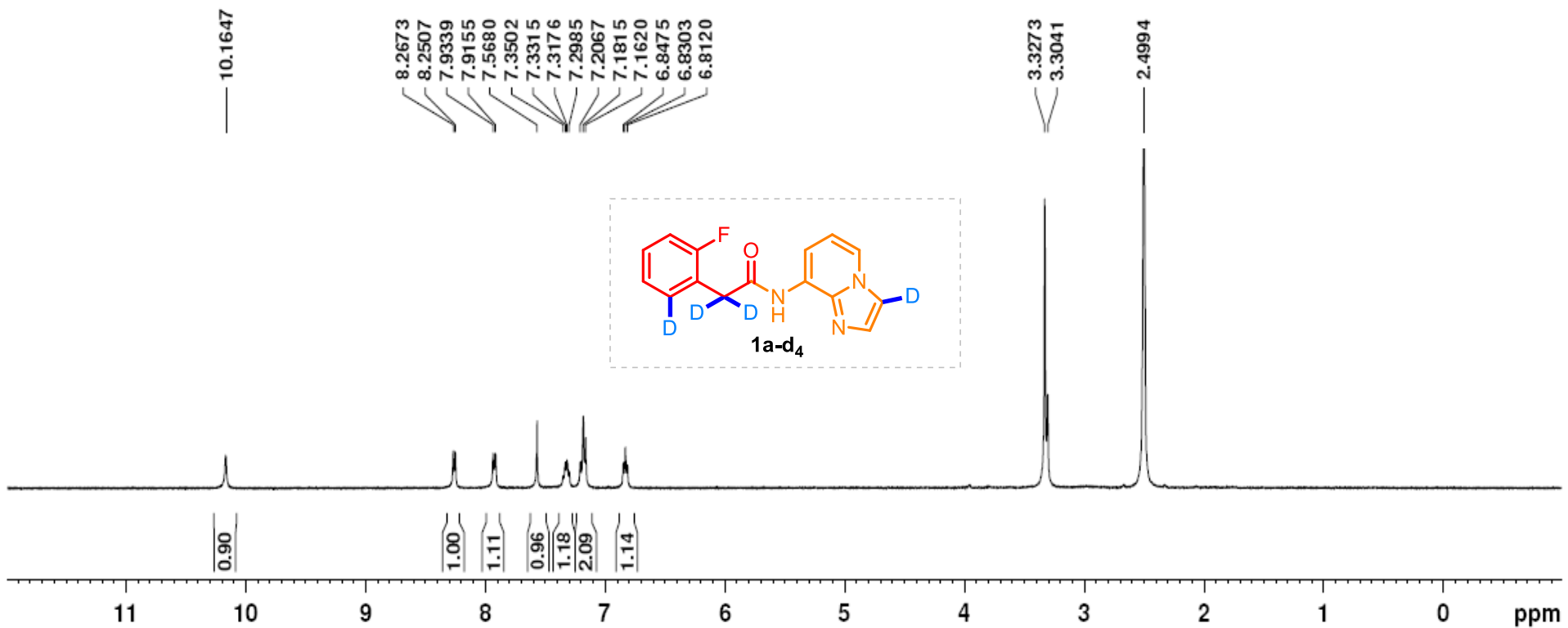
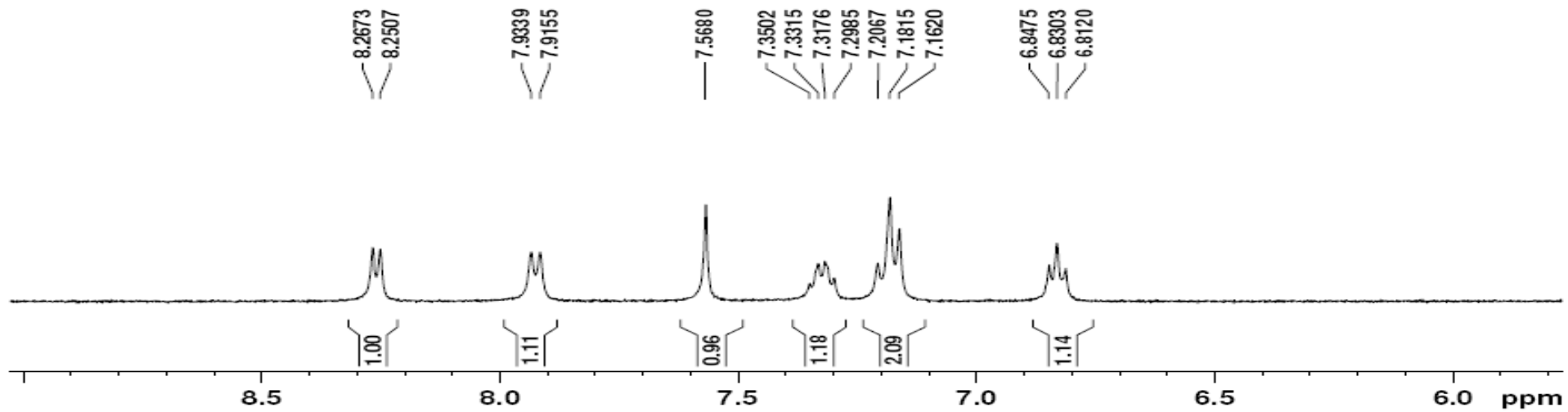
¹H NMR of 9a



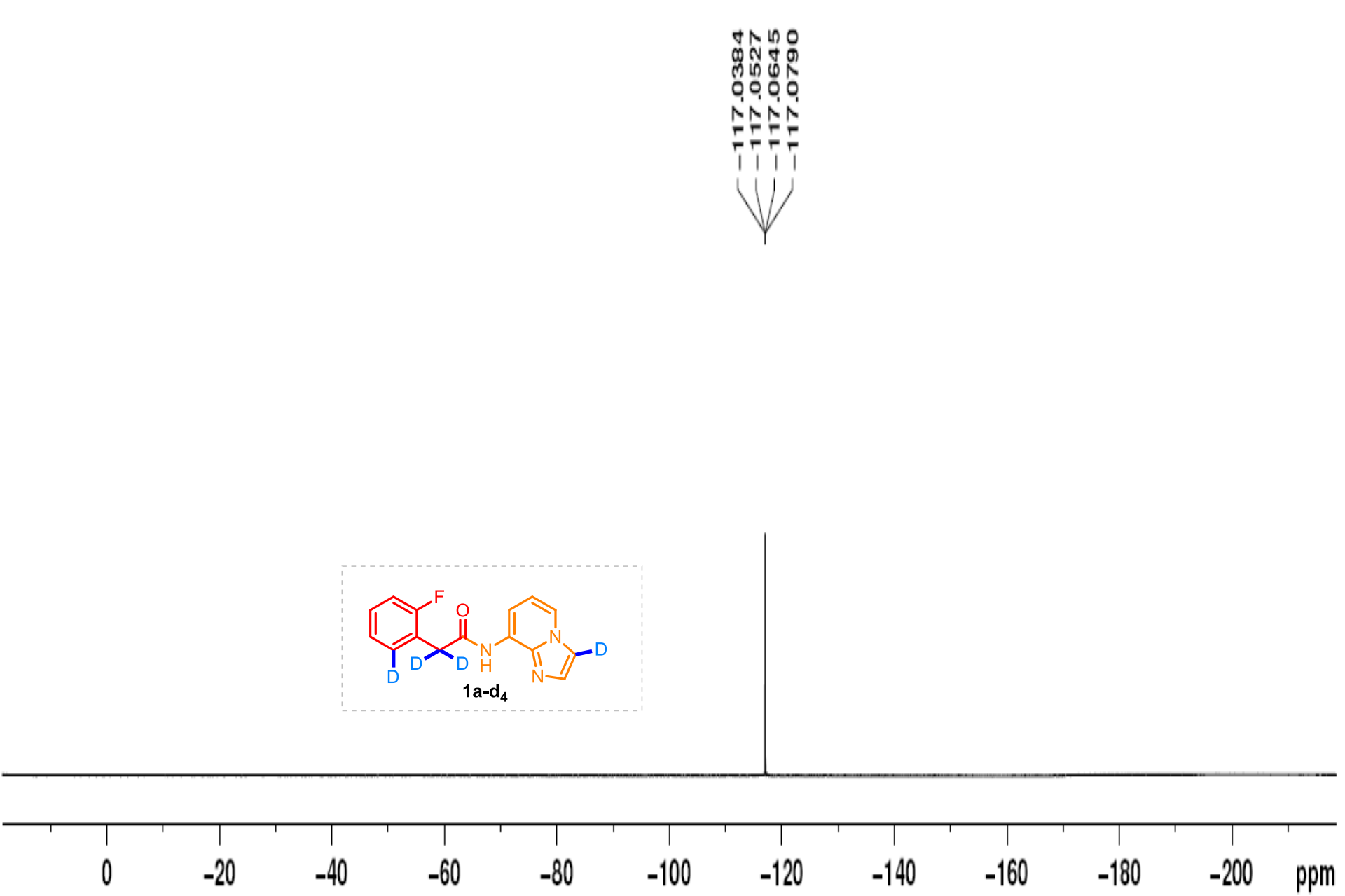
13C NMR of 9a



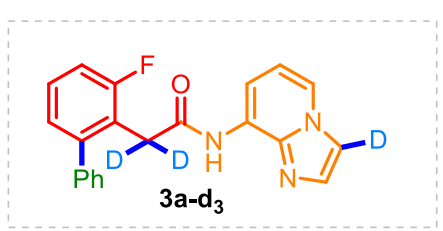
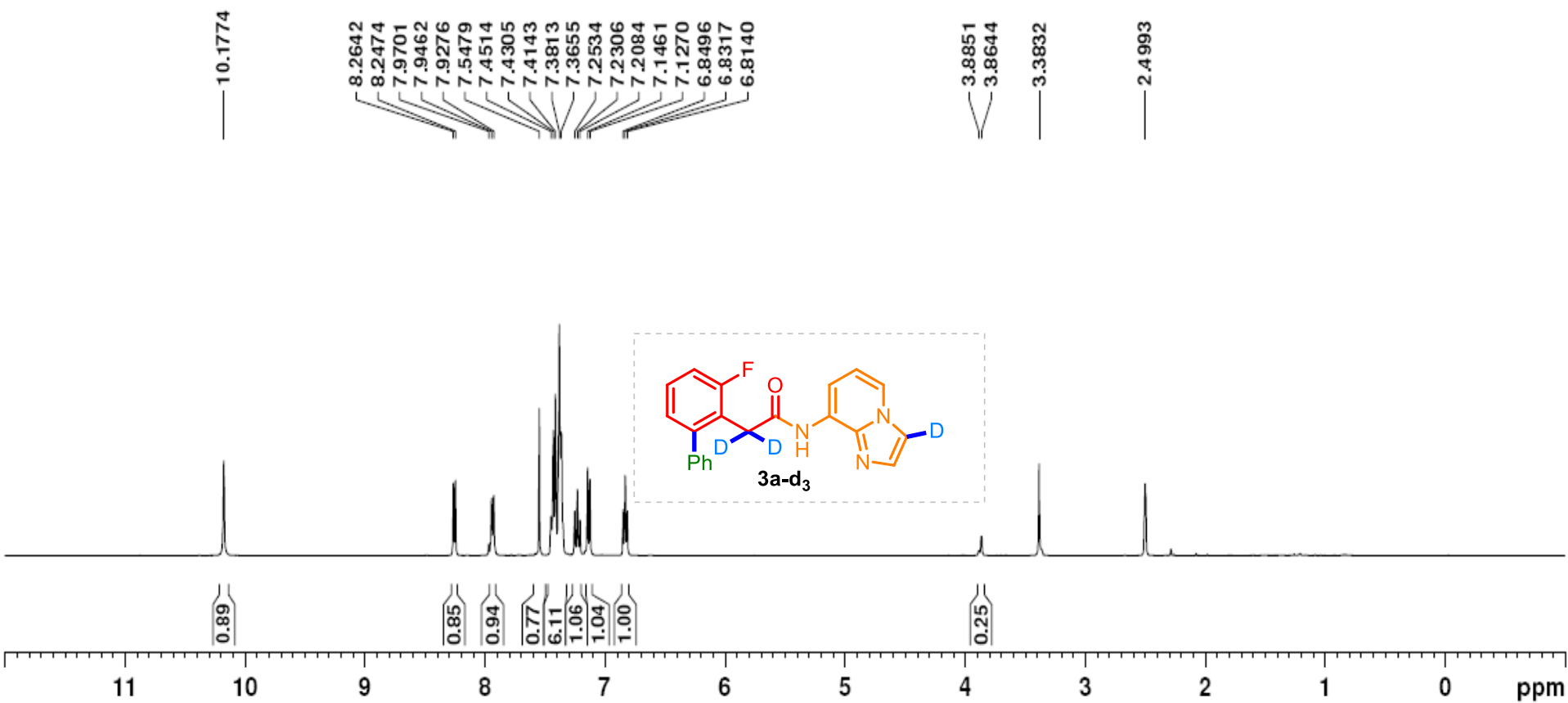
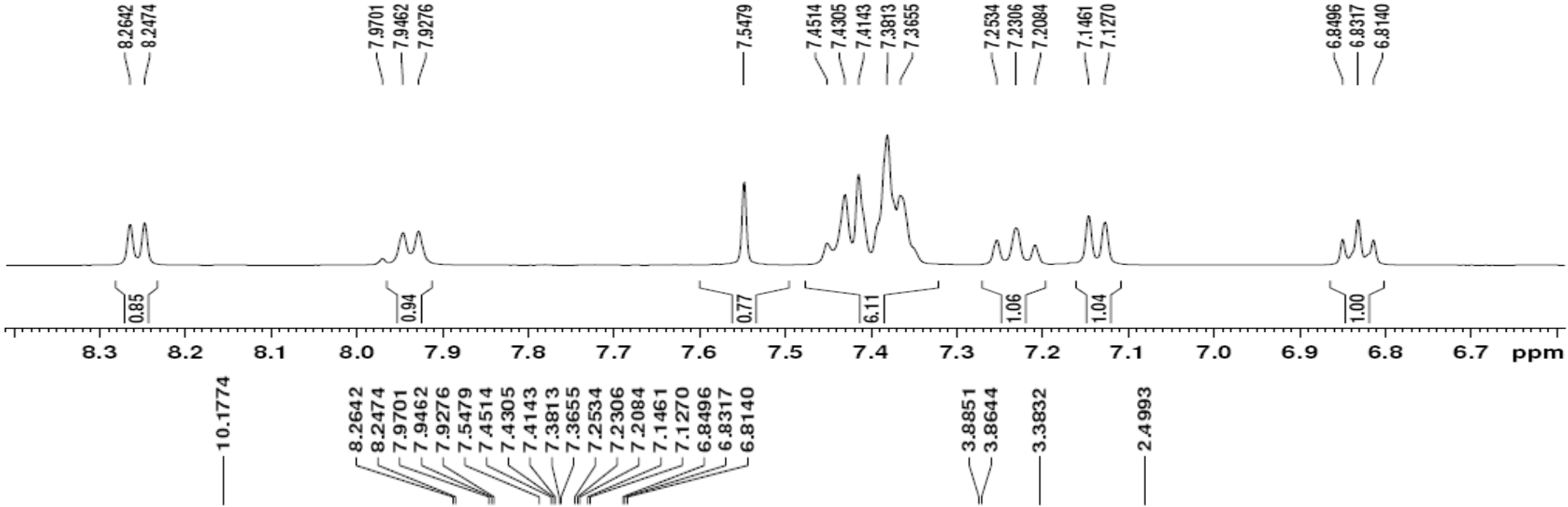
^{19}F NMR of 9a



1H NMR of **1a-d₄**

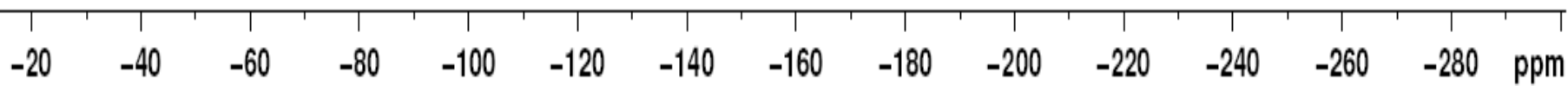
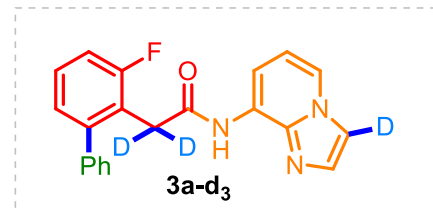


19F NMR of **1a-d₄**

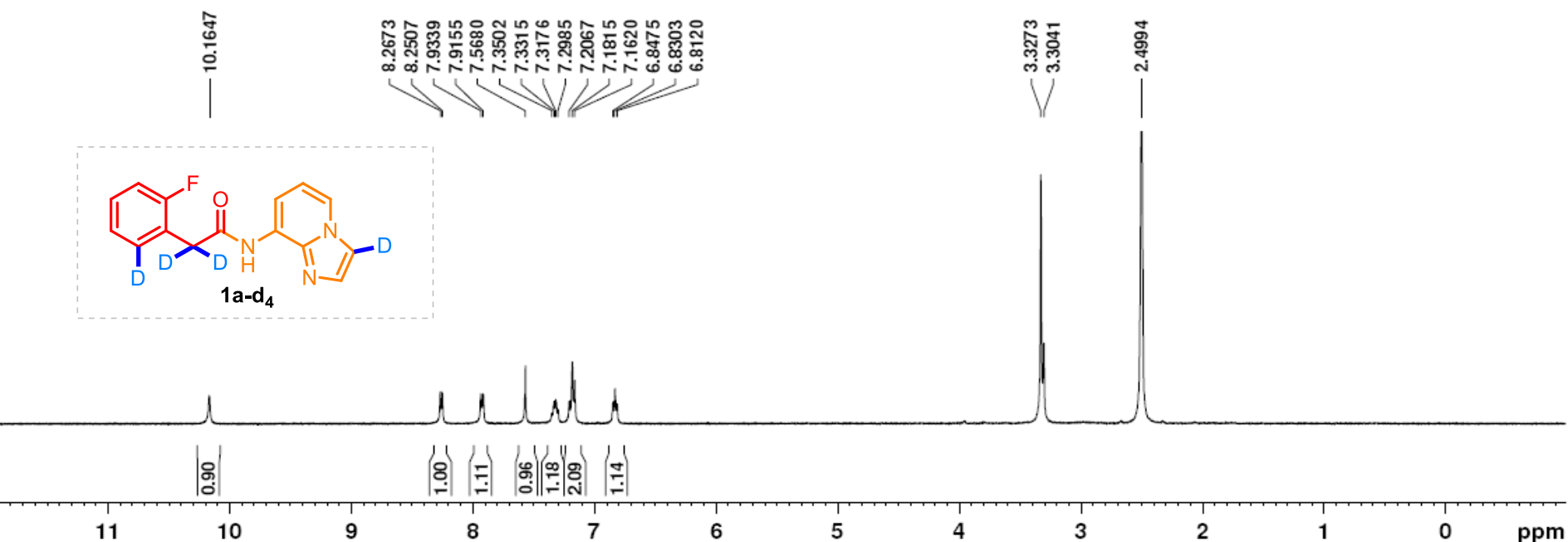
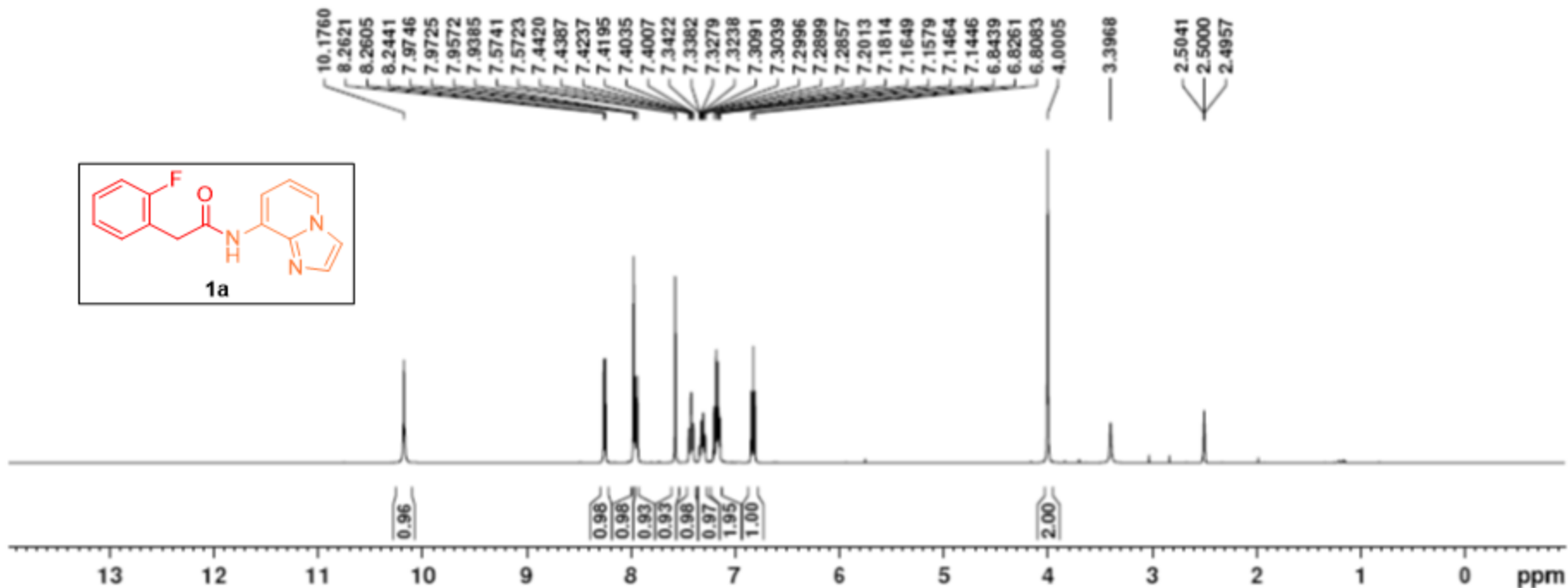


1H NMR of $3a-d_3$

114.5661
114.5811
114.5900
114.6076



19F NMR of 3a-d₃



Comparison between ¹H NMR of **1a** and **1a-d₄**