Selective oxidative β-C−H bond sulfenylation of tetrahydroisoquinolines with elemental sulfur

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Supplementary Information

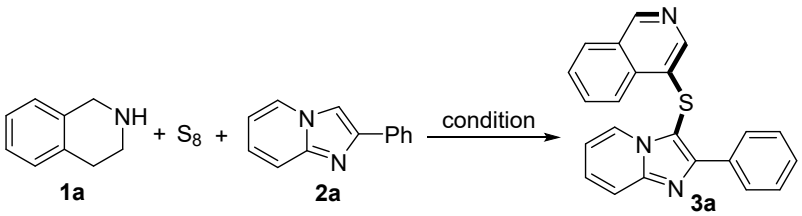
Table of Content

1 General Experimental

Unless otherwise mentioned, all materials were commercially obtained and used without further purification. imidazoheterocycles (**2**),[1] sulfide (**7**)[2] and disulfide (**8**)[2] were synthesized according to previously described methods. The ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded at 500 MHz, 126 MHz, 471 MHz, respectively, on a Bruker AM500 MHz with chemical shift values in ppm relative to TMS (δH 0.00 and δC 0.0) as internal standard. The coupling constants *J*, are reported in Hertz (Hz). All melting points were determined on a SGW X-4A melting point instrument without correction. High-resolution mass spectra (HRMS) were recorded on Q-Exactive plus Orbitrap (ESI). Infrared spectra (IR) were recorded on Spectrum TWO. Reactions were monitored by thin layer chromatography (TLC), on glass plates coated with silica gel with Fluorescent indicator (Huanghai, HSGF254) and visualized with UV light at 254 nm. Flash chromatography was performed on silica gel (Huanghai, 300-400) using petroleum ether (PE)-ethyl acetate (EA) as eluent. The structure of product **3l** (CCDC file number 2168420) was further confirmed by X-ray diffraction collected on a diffractometer with graphite-monochromated Cu Kα radiation.

2 Experimental section

2.1 Impact of reaction parameters

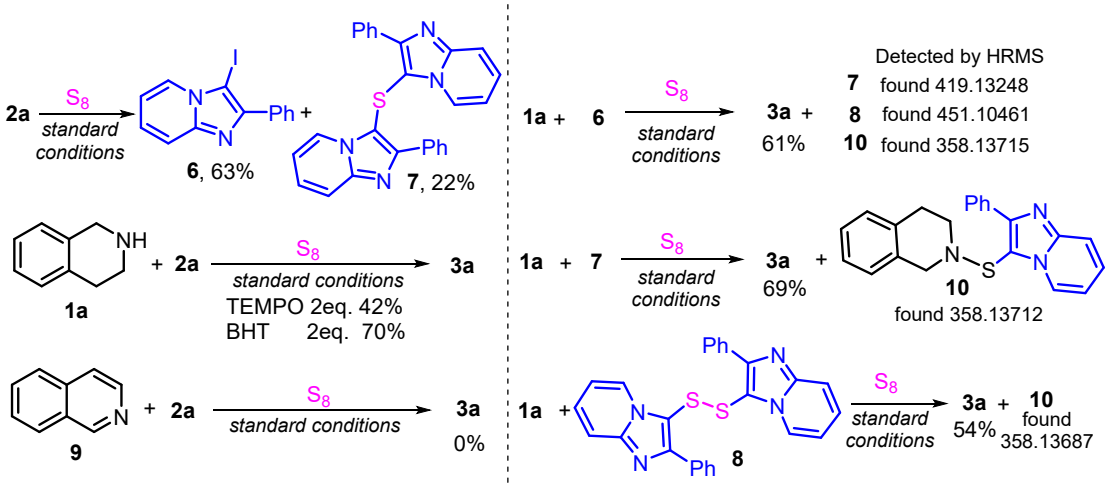


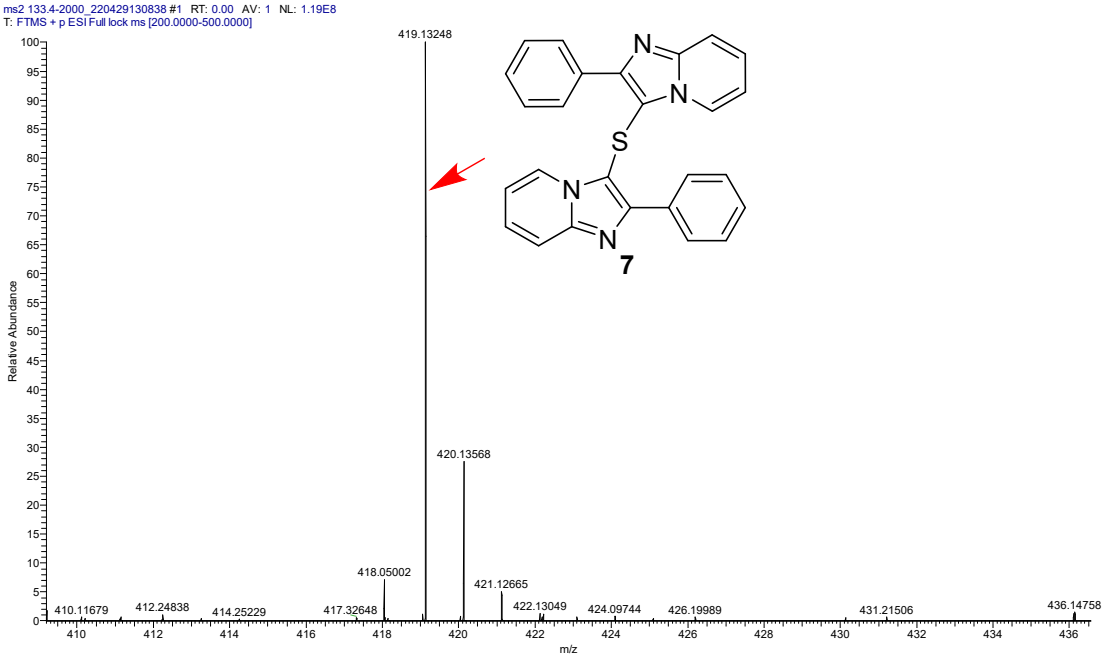
Entry[a]	Oxidant (eq.)	Additive (eq.)	Solvent (0.1 M)	Temperature (°C)	Yield (%)[b]
1	--	--	DMF	100	0
2	$Cu(OAc)_2$ (2)	--	DMF	100	0
3	Ag_2CO_3 (2)	--	DMF	100	0
4	KIO_3 (2)	--	DMF	100	27
5	KIO_4 (2)	--	DMF	100	Trace
6	KIO_3 (2)	--	DMAc	100	Trace
7	KIO_3 (2)	--	Xylene	100	0
8	KIO_3 (2)	--	NMP	100	Trace
9	KIO_3 (2)	--	DMSO	100	56
10	KIO_3 (2)	--	DMSO	90	33
11	**KIO_3 (2)**	**--**	**DMSO**	**110**	**78**

12	KIO_3 (2)	--	DMSO	120	62
13	KIO_3 (1)	--	DMSO	110	39
14	KIO_3 (3)	--	DMSO	110	73
15	KIO_3 (2)	I_2 (0.5)	DMSO	110	70
16	KIO_3 (2)	TBAI (0.5)	DMSO	110	68
17	KIO_3 (2)	$FeCl_3$ (0.2)	DMSO	110	30
18[c]	KIO_3 (2)	--	DMSO	110	76
19[d]	KIO_3 (2)	--	DMSO	110	45
20[e]	KIO_3 (2)	--	DMSO	110	75
21	KIO_3 (2)	--	DMSO (0.2M)	110	66
22	KIO_3 (2)	--	DMSO (0.05M)	110	55
23[f]	KIO_3 (2)	--	DMSO	110	59
24[g]	KIO_3 (2)	--	DMSO	110	61
25	DDQ (2)	--	DMSO	110	0
26	DTBP (2)	--	DMSO	110	57
27	TBHP (2)	--	DMSO	110	34

[a] Reaction conditions: **1a** (0.8 mmol), S_8 (0.6 mmol), **2a** (0.2 mmol), oxidant, additive, and solvent in air reacted for 10 h. [b] Isolated yield. [c] Reaction time: 24 h. [d] Under N_2. [e] Under O_2. [f] **1a** (0.6 mmol) was used. [g] S_8 (0.4 mmol) was used.

2.2 Control experiments

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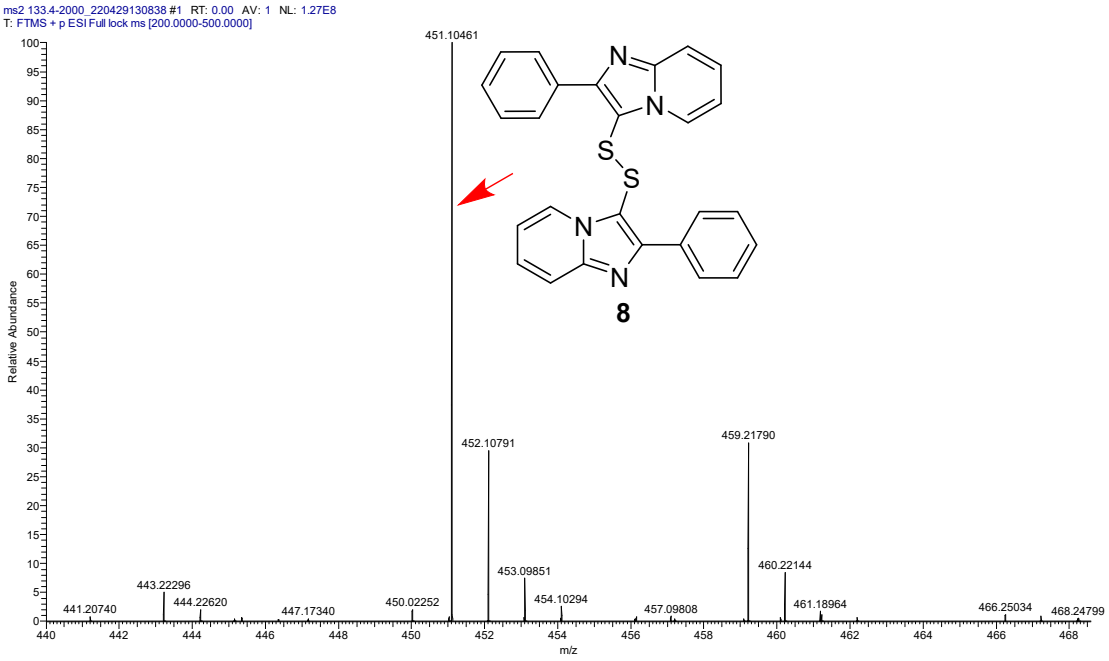
431.21506
436.14758
Relative Abundance
m/z
7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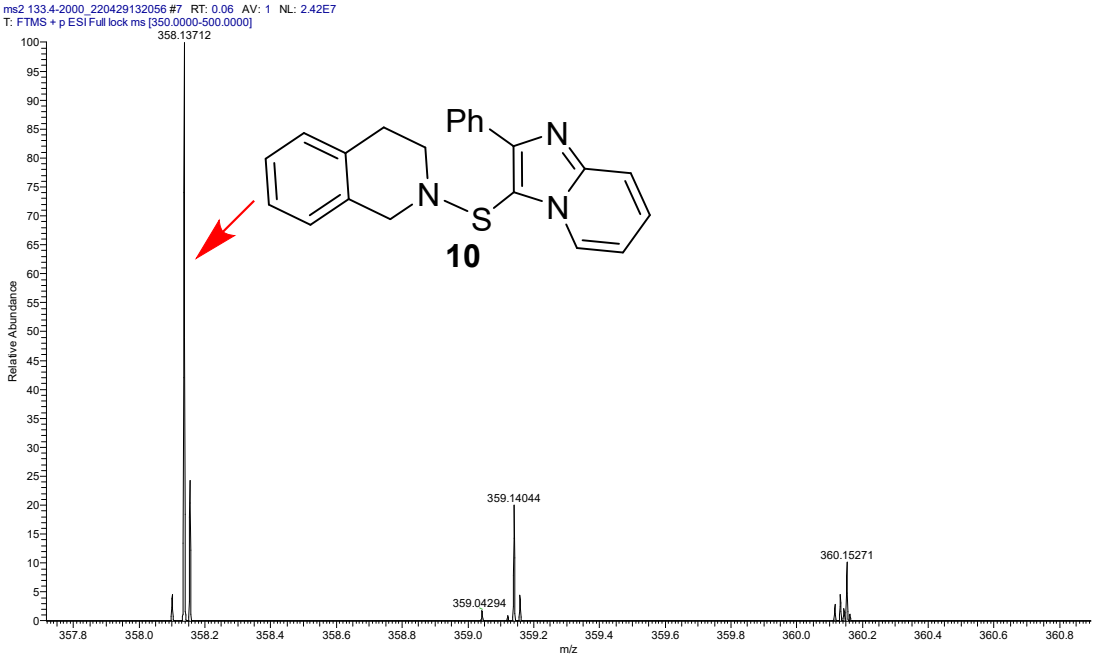
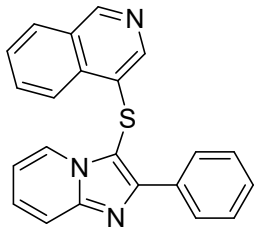
Relative Abundance
m/z
8



2.3 General procedure for synthesis of desired products 3 and 5

2 mL DMSO, 1,2,3,4-tetrahydroisoquinolines (**1**, 0.8 mmol), imidazoheterocycles (**2**, 0.2 mmol), S_8 (19.2 mg, 0.6 mmol) and KIO_3 (85.6 mg, 0.4 mmol), were added into the dry thick-walled glass pressure tube. The mixture was stirred in a preheated oil bath at 110 °C for in air 10 h. Then the reaction was cooled down to room temperature, diluted with 20 mL ethyl acetate and washed with 10 mL H_2O. The aqueous layer was extracted twice with ethyl acetate (5 mL) and the combined organic phase was dried over Na_2SO_4. After evaporation of the solvents the residue was purified by flash column chromatography (silica gel, PE–EtOAc, 4 : 1 to 1 : 1) to afford the desired products **3** and **5**.



4-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)isoquinoline

3a was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

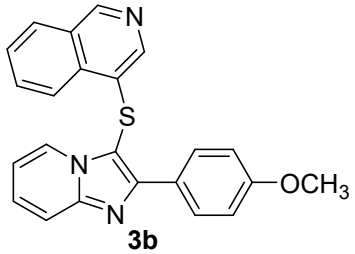
Yellow solid (55.1 mg, 78% yield), mp 146-148 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.24 – 8.19 (m, 4H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.77 – 7.73 (m, 3H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.44 – 7.41 (m, 2H), 7.38 – 7.35 (m, 1H), 7.32 – 7.28 (m, 1H), 6.82 (td, *J* = 7.0, 1.0 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.1, 151.0, 147.5, 139.6, 133.6, 133.3, 130.9, 128.8, 128.5, 128.4, 128.3, 128.0, 126.9, 126.8, 124.4, 122.9, 117.9, 113.4, 103.7

IR (KBr) 1632, 1559, 1442, 1345, 1226, 1153, 975, 748, 690 cm^{-1}

HRMS for $C_{22}H_{16}N_3S^+$ $(M+H)^+$: calcd. 354.10594, found 354.10590



3b

4-((2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)thio)isoquinoline

3b was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

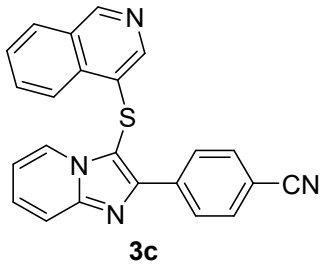
Yellow solid (46.9 mg, 61% yield), mp 175-177 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.23 (d, *J* = 7.0 Hz, 1H), 8.16 (d, *J* = 9.0 Hz, 2H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.82 – 7.68 (m, 4H), 7.35 – 7.31 (m, 1H), 6.98 – 6.95 (m, 2H), 6.84 (t, *J* = 7.0 Hz, 1H), 3.83 (s, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.2, 152.2, 151.1, 147.6, 139.6, 133.7, 131.0, 129.9, 128.6, 128.4, 128.1, 127.0, 126.9, 125.9, 124.4, 123.1, 117.8, 114.0, 113.3, 102.7, 55.4

IR (KBr) 2927, 1724, 1609, 1454, 1339, 1245, 1175, 1036, 834, 752 cm^{-1}

HRMS for $C_{23}H_{18}N_3OS^+$ $(M+H)^+$: calcd. 384.11651, found 384.11630



3c

4-(3-(isoquinolin-4-ylthio)imidazo[1,2-a]pyridin-2-yl)benzonitrile

3c was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

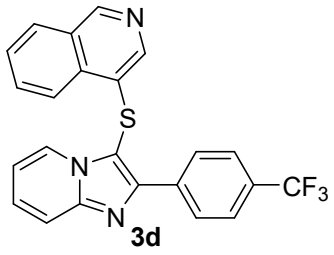
Yellow solid (60.2 mg, 80% yield), mp 214-216 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.36 (d, *J* = 8.5 Hz, 2H), 8.28 – 8.26 (m, 2H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.85 (t, *J* = 9.0 Hz, 1H), 7.78 – 7.70 (m, 5H), 7.42 – 7.39 (m, 1H), 6.92 (t, *J* = 6.5 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.4, 149.8, 147.8, 139. 5, 137.8, 133.63, 132.4, 131.3, 128.9, 128.6, 128.6, 128.4, 127.7, 126.3, 124.6, 122.8, 119.0, 118.3, 114.1, 112.1, 105.2

IR (KBr) 2921, 2852, 2226, 1561, 1464, 1343, 1234, 1154, 845, 759, 738 cm^{-1}

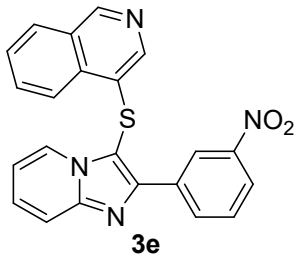
HRMS for $C_{23}H_{15}N_4S^+$ $(M+H)^+$: calcd. 379.10119, found 379.10129



3d

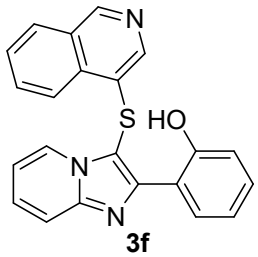
4-((2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridin-3-yl)thio)isoquinoline

3d was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
White solid (56.3 mg, 67% yield), mp 168-170 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.34 (d, *J* = 8.5 Hz, 2H), 8.26 (t, *J* = 7.5 Hz, 2H), 8.00(d, *J* = 8.5 Hz, 1H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.74 – 7.68 (m, 4H), 7.40 -7.36 (m, 1H), 6.90 (t, *J* = 6.5 Hz, 1H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 151.3, 150.5, 147.7, 139.5, 136.8, 133.6, 131.2, 130.7 (q, *J* = 32.3 Hz), 128.7, 128.6, 128.5, 128.2, 127.4, 126.5, 125.5 (q, *J* = 3.5 Hz), 124.6, 124.2 (q, *J* = 270.3.4 Hz), 122.9, 118.2, 113.9, 104.8
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.6
IR (KBr) 2920, 2850, 1619, 1565, 1492, 1323, 1166, 1097, 1066, 843, 744 cm^{-1}
HRMS for $C_{23}H_{15}F_3N_3S^+$ $(M+H)^+$: calcd. 422.09333, found 422.09344



3e

4-((2-(3-nitrophenyl)imidazo[1,2-a]pyridin-3-yl)thio)isoquinoline
3e was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
Yellow solid (55.8 mg, 70% yield), mp 196-197 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.15 (t, *J* = 2.0 Hz, 1H), 9.04 (s, 1H), 8.58 – 8.56 (m, 1H), 8.30 – 8.28 (m, 2H), 8.21 – 8.19 (m, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.85 – 7.82 (m, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.73 – 7.70 (m, 2H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.42 – 7.39 (m, 1H), 6.93 (t, *J* = 7.0 Hz, 1H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 151.4, 149.2, 148.5, 147.6, 139.6, 135.1, 134.2, 133.6, 131.3, 129.5, 128.6, 128.5, 128.3, 127.6, 126.4, 124.6, 123.3, 122.8, 118.2, 114.0, 105.1
IR (KBr) 2919, 1538, 1491, 1342, 1229, 1087, 820, 745, 703 cm^{-1}
HRMS for $C_{22}H_{15}N_4O_2S^+$ $(M+H)^+$: calcd. 399.09102, found 399.09106



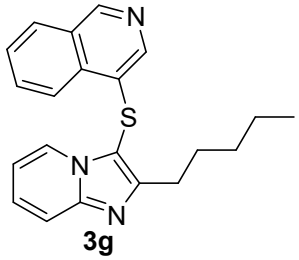
3f

2-(3-(isoquinolin-4-ylthio)imidazo[1,2-a]pyridin-2-yl)phenol
3f was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
Yellow solid (25.2 mg, 34% yield), mp 172-174 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 13.0 (s, 1H), 9.03 (s, 1H), 8.57 (d, *J* = 8.0 Hz, 1H), 8.32 – 8.29 (m, 2H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 1H), 7.76 – 7.69 (m, 3H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.08 (d, *J* = 8.5 Hz, 1H), 6.91 (t, *J* = 7.0 Hz, 1H), 6.81 (t, *J* = 7.5 Hz, 1H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 158.5, 151.2, 150.2, 145.2, 139.4, 133.7, 131.2, 130.9, 129.6, 128.6,

128.5, 128.2, 127.8, 126.2, 124.2, 122.9, 119.0, 117.9, 117.0, 116.0, 114.2, 102.6

IR (KBr) 2923, 2854, 1722, 1568, 1455, 1348, 1250, 1152, 736 cm^{-1}

HRMS for $C_{22}H_{16}N_3OS^+$ (M+H)$^+$: calcd. 370.10086, found 370.10114



3g

4-((2-pentylimidazo[1,2-a]pyridin-3-yl)thio)isoquinoline

3g was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

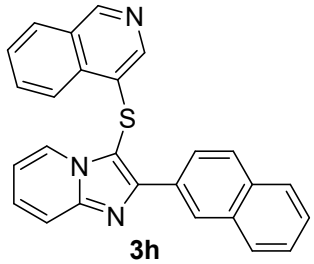
Yellow oil (31.2 mg, 45% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.34 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 7.0 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.72 – 7.62 (m, 3H), 7.31 – 7.28 (m, 1H), 6.82 (t, *J* = 7.0 Hz, 1H), 2.97 (t, *J* = 8.0 Hz, 2H), 1.84 – 1.78 (m, 2H), 1.38 – 1.29 (m, 4H), 0.83 (t, *J* = 7.5 Hz, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.4, 150.8, 147.6, 139.5, 133.6, 131.0, 128.5, 128.4, 128.0, 127.5, 126.3, 124.3, 123.0, 117.5, 113.0, 104.2, 31.8, 29.5, 28.3, 22.5, 14.1

IR (KBr) 2920, 2850, 1630, 1554, 1493, 1382, 1336, 1226, 975, 752, 737 cm^{-1}

HRMS for $C_{21}H_{22}N_3S^+$ (M+H)$^+$: calcd. 348.15289, found 348.15268



3h

4-((2-(naphthalen-2-yl)imidazo[1,2-a]pyridin-3-yl)thio)isoquinoline

3h was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

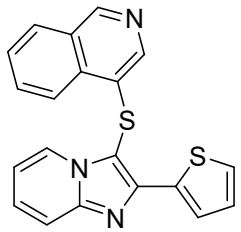
Yellow solid (45.7 mg, 57% yield), mp 184-186 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.71 (s, 1H), 8.35 (dd, *J* = 8.5, 1.5 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 2H), 7.99 (d, *J* = 9.0 Hz, 1H), 7.90 – 7.76 (m, 6H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.48 – 7.45 (m, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 7.0 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.1, 151.2, 147.7, 140.0, 133.8, 133.5, 133.4, 131.1, 130.8, 128.8, 128.6, 128.4, 128.2, 128.1, 127.7, 127.1, 126.9, 126.6, 126.2, 126.1, 124.5, 123.1, 118.0, 113.5, 104.3

IR (KBr) 2922, 2852, 1567, 1487, 1334, 1225, 1139, 825, 738 cm^{-1}

HRMS for $C_{26}H_{18}N_3S^+$ (M+H)$^+$: calcd. 404.12159, found 404.12158



3i

4-((2-(thiophen-2-yl)imidazo[1,2-a]pyridin-3-yl)thio)isoquinoline

3i was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

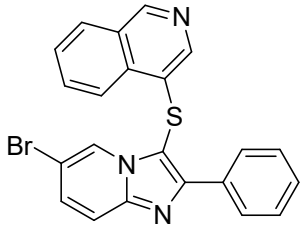
Yellow solid (53.8 mg, 75% yield), mp 186-188 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.21 (d, *J* = 6.5 Hz, 1H), 8.00 – 7.99 (m, 2H), 7.85 – 7.80 (m, 2H), 7.73 – 7.68 (m, 2H), 7.37 (d, *J* = 5.0 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.08 (t, *J* = 4.5 Hz, 1H), 6.84 (t, *J* = 7.0 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.1, 147.6, 147.4, 139.8, 136.1, 133.8, 131.1, 128.6, 128.4, 128.1, 127.9, 127.2, 126.9, 126.5, 124.3, 122.9, 117.7, 113.5, 102.8

IR (KBr) 2921, 2852, 1558, 1490, 1375, 1341, 1214, 1141, 976, 751, 697 cm^{-1}

HRMS for $C_{20}H_{14}N_3S_2^+$ $(M+H)^+$: calcd. 360.06237, found 360.06223



3j

4-((6-bromo-2-phenylimidazo[1,2-a]pyridin-3-yl)thio)isoquinoline

3j was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

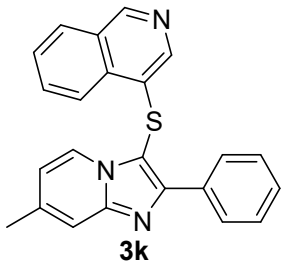
White solid (70.6 mg, 82% yield), mp 142-143 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.37 (s, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 8.17 (d, *J* = 7.0 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.79 – 7.75 (m, 2H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 9.5 Hz, 1H), 7.44 – 7.36 (m, 4H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.7, 151.2, 145.9, 139.3, 133.5, 132.8, 131.0, 130.4, 129.1, 128.6, 128.5, 128.5, 128.4, 128.1, 126.4, 124.6, 122.9, 118.5, 108.4, 104.3

IR (KBr) 2920, 1561, 1490, 1332, 1221, 1162, 1067, 811, 771, 686 cm^{-1}

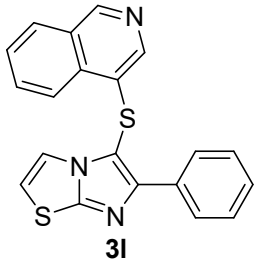
HRMS for $C_{22}H_{15}BrN_3S^+$ $(M+H)^+$: calcd. 432.01646, found 432.01669



3k

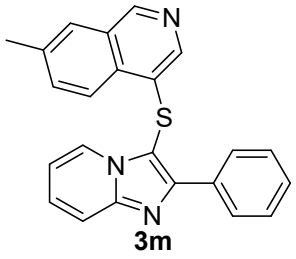
4-((7-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)thio)isoquinoline

3k was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
Yellow solid (58.9 mg, 80% yield), mp 146-148 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.18 – 8.16 (m, 2H), 8.09 (d, *J* = 7.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.79 – 7.76 (m, 2H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.50 (s, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.38 – 7.35 (m, 1H), 6.67 (dd, *J* = 7.0, 1.5 Hz, 1H), 2.42 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 152.2, 151.0, 148.0, 139.6, 138.2, 133.7, 133.5, 130.9, 128.7, 128.5, 128.3, 128.0, 127.1, 123.6, 123.0, 116.5, 116.0, 102.8, 21.5
IR (KBr) 2919, 1644, 1551, 1441, 1354, 1235, 1170, 1071, 881, 770, 688 cm^{-1}
HRMS for $C_{23}H_{18}N_3S^+$ $(M+H)^+$: calcd. 368.12159, found 368.12167



3l

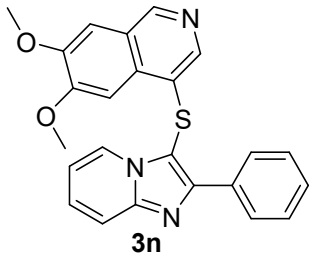
5-(isoquinolin-4-ylthio)-6-phenylimidazo[2,1-b]thiazole
3l was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
White solid (35.8 mg, 50% yield), mp 114-116 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 2H), 8.02 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.42 – 7.38 (m, 3H), 7.33 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 4.5 Hz, 1H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 153.3, 152.0, 151.3, 140.7, 133.7, 133.4, 131.0, 128.5, 128.4, 128.3, 128.1, 127.8, 127.5, 123.1, 117.9, 113.4, 105.4
IR (KBr) 2920, 2850, 1538, 1469, 1435, 1372, 1245, 1130, 974, 743, 696 cm^{-1}
HRMS for $C_{20}H_{14}N_3S_2^+$ $(M+H)^+$: calcd. 360.06237, found 360.06235



3m

6-methyl-4-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)isoquinoline
3m was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
Yellow solid (56.3 mg, 77% yield), mp 137-138 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.22 – 8.19 (m, 3H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.74 – 7.71 (m, 3H), 7.58 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.32 – 7.28 (m, 1H), 6.82 (t, *J* = 6.5 Hz, 1H), 2.54 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 152.0, 150.5, 147.4, 139.0, 138.2, 133.3, 133.2, 132.0, 128.8, 128.7, 128.5, 128.5, 127.1, 126.8, 126.5, 124.4, 122.8, 117.9, 113.3, 103.9, 21.7
IR (KBr) 2921, 2852, 1629, 1558, 1454, 1335, 1233, 978, 759, 695 cm^{-1}

HRMS for $C_{23}H_{18}N_3S^+$ (M+H)$^+$: calcd. 368.12159, found 368.12131



3n

6,7-dimethoxy-4-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)isoquinoline

3n was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

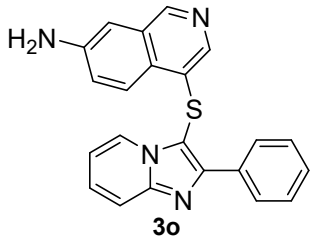
Yellow solid (48.0 mg, 58% yield), mp 211-213 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.30 (d, *J* = 7.5 Hz, 3H), 8.04 (s, 1H), 7.70 (d, *J* = 7.0 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.41 – 7.38 (m, 2H), 7.30 (t, *J* = 8.0 Hz, 1H), 7.17 (s, 1H), 6.84 (t, *J* = 6.5 Hz, 1H), 4.00 (s, 3H), 3.76 (s, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.7, 151.1, 150.8, 149.4, 147.3, 141.2, 133.5, 131.3, 128.9, 128.7, 128.7, 126.7, 124.9, 124.6, 123.9, 117.9, 113.3, 105.9, 105.0, 102.0, 56.2, 56.1

IR (KBr) 2921, 1619, 1502, 1463, 1340, 1253, 1150, 873, 723 cm^{-1}

HRMS for $C_{24}H_{20}N_3O_2S^+$ (M+H)$^+$: calcd. 414.12707, found 414.12701



3o

4-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)isoquinolin-7-amine

3o was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

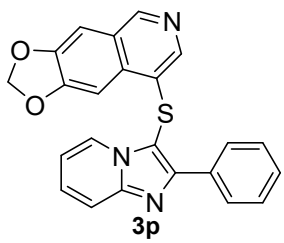
Yellow solid (39.2 mg, 53% yield), mp 217-219 °C.

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.05 (s, 1H), 8.46 (d, *J* = 7.0 Hz, 1H), 8.30 (d, *J* = 7.5 Hz, 2H), 8.11 (s, 1H), 7.70 – 7.65 (m, 4H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 4.5 Hz, 1H), 7.36 – 7.32 (m, 2H), 7.00 (t, *J* = 7.0 Hz, 1H), 6.61 (s, 2H)

^{13}C NMR (126 MHz, DMSO-d_6) δ 150.2, 148.5, 146.8, 145.5, 139.3, 133.5, 130.3, 129.6, 128.7, 128.7, 128.5, 126.4, 125.2, 122.8, 120.7, 117.3, 113.2, 109.5, 99.4

IR (KBr) 2920, 2851, 1632, 1448, 1349, 1225, 1150, 835, 754, 689 cm^{-1}

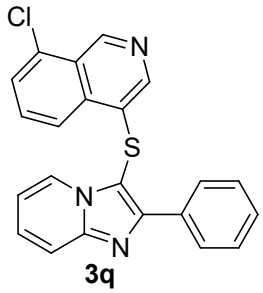
HRMS for $C_{22}H_{17}N_4S^+$ (M+H)$^+$: calcd. 369.11684, found 369.11679



3p

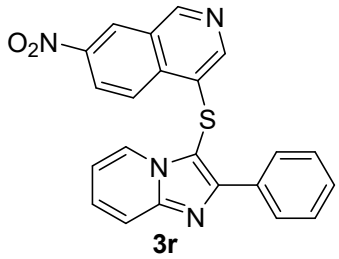
8-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)-[1,3]dioxolo[4,5-g]isoquinoline

3p was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
Brown solid (37.4 mg, 47% yield), mp 201-203 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.25 (d, *J* = 7.0 Hz, 1H), 8.18 (d, *J* = 7.5 Hz, 2H), 7.75 – 7.73 (m, 2H), 7.51 (s, 1H), 7.45(t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.0 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.19 (s, 1H), 6.86 (t, *J* = 7.0 Hz, 1H), 6.14 (s, 2H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 152.1, 151.7, 149.2, 148.9, 147.5, 140.0, 133.4, 132.4, 128.9, 128.7, 128.6, 126.9, 126.1, 125.7, 124.5, 118.0, 113.4, 104.4, 103.8, 102.1, 99.9
IR (KBr) 2921, 1577, 1452, 1343, 1231, 1037, 962, 759, 706 cm^{-1}
HRMS for $C_{23}H_{16}N_3O_2S^+$ $(M+H)^+$: calcd. 398.09577, found 398.09570



3q

8-chloro-4-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)isoquinoline
3q was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
White solid (64.7 mg, 84% yield), mp 208-209 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.44 (s, 1H), 8.21 (d, *J* = 6.5 Hz, 1H), 8.18 – 8.15 (m, 3H), 7.84 (s, 1H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.68 – 7.62 (m, 2H), 7.43 (d, *J* = 7.5 Hz, 2H), 7.39 – 7.32 (m, 2H), 6.85 (t, *J* = 6.5 Hz, 1H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 152.3, 147.9, 147.6, 140.5, 134.9, 133.3, 133.1, 130.8, 128.9, 128.6, 128.5, 128.4, 127.0, 127.0, 125.8, 124.3, 122.1, 118.0, 113.5, 103.2
IR (KBr) 2919, 1609, 1563, 1464, 1441, 1344, 1226, 889, 800, 745cm^{-1}
HRMS for $C_{22}H_{15}ClN_3S^+$ $(M+H)^+$: calcd. 388.06697, found 388.06705

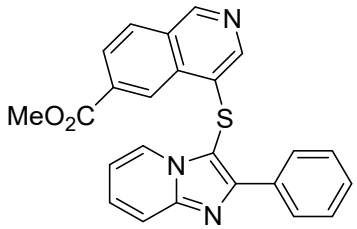


3r

7-nitro-4-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)isoquinoline
3r was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
Yellow solid (52.6 mg, 66% yield), mp 177-179 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.92 (d, *J* = 2.0 Hz, 1H), 8.51 (dd, *J* = 9.0, 2.0 Hz, 1H), 8.40 (d, *J* = 9.0 Hz, 1H), 8.26 (d, *J* = 6.5 Hz, 1H), 8.15 (d, *J* = 7.0 Hz, 2H), 7.97 (s, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.46 – 7.37 (m, 4H), 6.92 (t, *J* = 6.0 Hz, 1H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6, 152.5, 147.7, 146.6, 143.2, 136.2, 133.0, 129.1, 128.7, 128.6, 127.8, 127.5, 127.4, 125.4, 124.8, 124.3, 124.2, 118.2, 113.8, 102.6

IR (KBr) 2922, 1620, 1522, 1465, 1340, 1232, 1086, 794, 731, 692 cm^{-1}

HRMS for $C_{22}H_{15}N_4O_2S^+$ $(M+H)^+$: calcd. 399.09102, found 399.09128



3s

methyl 4-((2-phenylimidazo[1,2-a]pyridin-3-yl)thio)isoquinoline-6-carboxylate

3s was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

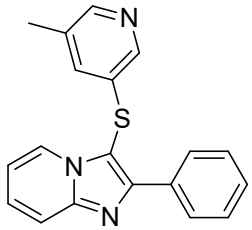
Yellow solid (60.2 mg, 73% yield), mp 80-82 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.88 (s, 1H), 8.64 (s, 1H), 8.23 (dd, *J* = 8.5, 1.0 Hz, 1H), 8.13 (d, *J* = 7.5 Hz, 2H), 8.08 (d, *J* = 7.0 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.62 (d, *J* = 9.0 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.38 (t, *J* = 7.0 Hz, 1H), 7.24 – 7.21 (m, 1H), 6.91 (t, *J* = 6.5 Hz, 1H), 4.02 (s, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 151.1, 143.8, 142.8, 139.8, 133.1, 132.6, 132.6, 130.8, 129.4, 128.6, 128.3, 128.2, 127.8, 127.6, 126.1, 124.9, 122.7, 117.7, 113.0, 105.7, 52.8

IR (KBr) 2956, 1717, 1574, 1352, 1278, 1208, 1103, 993, 755, 697 cm^{-1}

HRMS for $C_{24}H_{18}N_3O_2S^+$ $(M+H)^+$: calcd. 412.11142, found 412.11133



3t

3-((5-methylpyridin-3-yl)thio)-2-phenylimidazo[1,2-a]pyridine

3t was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

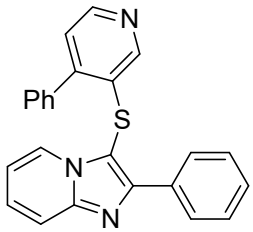
Yellow oil (30.9 mg, 49% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 6.5 Hz, 1H), 8.21 – 8.17 (m, 4H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.41 – 7.36 (m, 2H), 7.03 (s, 1H), 6.92 (t, *J* = 7.0 Hz, 1H), 2.19 (s, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.9, 148.2, 147.4, 144.3, 133.7, 133.2, 128.9, 128.7, 128.6, 128.5, 128.5, 127.1, 124.4, 118.0, 113.5, 104.8, 18.5

IR (KBr) 2923, 2852, 1631, 1578, 1496, 1465, 1341, 1230, 1161, 755, 793 cm^{-1}

HRMS for $C_{19}H_{16}N_3S^+$ $(M+H)^+$: calcd. 318.10594, found 318.10583



3u

2-phenyl-3-((4-phenylpyridin-3-yl)thio)imidazo[1,2-a]pyridine

3u was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

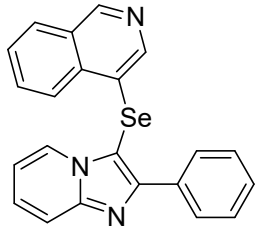
Yellow oil (42.4 mg, 56% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 5.0 Hz, 1H), 8.14 (d, *J* = 7.0 Hz, 2H), 8.08 (d, *J* = 7.0 Hz, 1H), 7.81 (s, 1H), 7.71 (d, *J* = 9.0 Hz, 1H), 7.55 – 7.48 (m, 5H), 7.44 (t, *J* = 7.0 Hz, 2H), 7.39 – 7.36 (m, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 5.0 Hz, 1H), 6.84 (t, *J* = 7.0 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.9, 148.1, 147.4, 146.9, 137.4, 133.2, 130.7, 129.1, 128.8, 128.8, 128.8, 128.5, 128.5, 126.9, 124.6, 124.3, 118.0, 113.4, 104.9

IR (KBr) 2919, 1571, 1495, 1441, 1341, 1233, 1032, 733, 693 cm^{-1}

HRMS for $C_{24}H_{18}N_3S^+$ $(M+H)^+$: calcd. 380.12159, found 380.12173



3v

4-((2-phenylimidazo[1,2-a]pyridin-3-yl)selanyl)isoquinoline

3v was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

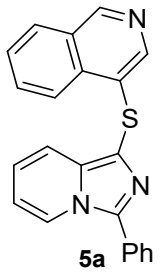
Yellow oil (51.5 mg, 64% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.37 (d, *J* = 7.0 Hz, 1H), 8.12 (d, *J* = 7.5 Hz, 2H), 8.08 (s, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.72 – 7.68 (m, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.48 – 7.45 (m, 2H), 7.42 – 7.39 (m, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 6.5 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6, 152.2, 148.1, 143.3, 135.5, 133.9, 131.2, 129.2, 129.1, 128.8, 128.5, 128.5, 128.1, 126.7, 125.6, 125.0, 124.1, 117.9, 113.4, 100.9

IR (KBr) 2919, 1630, 1565, 1464, 1340, 1232, 1148, 1073, 743, 703 cm^{-1}

HRMS for $C_{22}H_{16}N_3Se^+$ $(M+H)^+$: calcd. 402.05040, found 402.05020



5a

4-((3-phenylimidazo[1,5-a]pyridin-1-yl)thio)isoquinoline

5a was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 2:1).

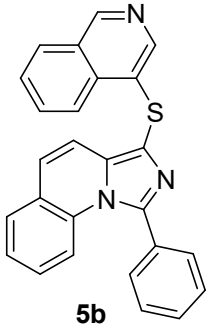
Yellow solid (51.3 mg, 73% yield), mp 80-81 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.53 (d, *J* = 8.5 Hz, 1H), 8.29 (d, *J* = 7.0 Hz, 1H), 8.23 (s, 1H), 7.92 (d, *J* = 7.0 Hz, 1H), 7.82 – 7.77 (m, 3H), 7.66 – 7.60 (m, 2H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 6.87 – 6. 84 (m, 1H), 6.64 (t, *J* = 7.0 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.6, 142.3, 139.6, 135.3, 134.4, 130.7, 130.3, 129.5, 129.3, 129.1, 128.4, 128.3, 128.0, 127.6, 124.0, 122.3, 121.5, 118.2, 114.0

IR (KBr) 2923, 1726, 1668, 1562, 1459, 1368, 1263, 1020, 733, 693 cm^{-1}

HRMS for $C_{22}H_{16}N_3S^+$ $(M+H)^+$: calcd. 354.10594, found 354.10577



5b

3-(isoquinolin-4-ylthio)-1-phenylimidazo[1,5-a]quinolone

5b was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 2:1).

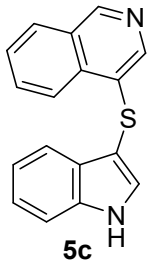
Yellow solid (51.6 mg, 64% yield), mp 150-152 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.52 (d, *J* = 8.5 Hz, 1H), 8.32 (s, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.82 – 7.78 (m, 1H), 7.68 – 7.62 (m, 4H), 7.59 – 7. 52 (m, 5H), 7.37 – 7.34 (m, 1H), 7.24 – 7.21 (m, 1H), 7.17 (d, *J* = 9.5 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.7, 143.4, 142.4, 134.6, 134.4, 133.0, 132.5, 130.8, 130.2, 129.9, 129.8, 129.6, 129.0, 129.0, 128.4, 128.1, 127.8, 125.8, 125.6, 124.1, 120.9, 117.5, 116.2

IR (KBr) 2923, 2853, 1722, 1616, 1561, 1457, 1353, 1256, 1099, 747, 700 cm^{-1}

HRMS for $C_{26}H_{18}N_3S^+$ $(M+H)^+$: : calcd. 404.12159, found 404.12125



5c

4-((1H-indol-3-yl)thio)isoquinoline

5c was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

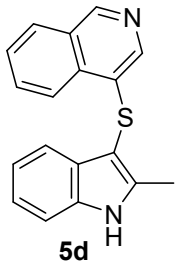
Yellow oil (36.5 mg, 66% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.8 (s, 1H), 9.08 (s, 1H), 8.39 (d, *J* = 8.0 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.94 – 7.90 (m, 3H), 7.78 – 7.75 (m, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.22 – 7.19 (m, 1H), 7.09 – 7.05 (m, 1H)

^{13}C NMR (126 MHz, DMSO-d_6) δ 150.3, 140.8, 137.2, 133.3, 133.1, 131.6, 130.7, 128.9, 128.8, 128.5, 128.2, 123.2, 122.8, 120.8, 118.7, 113.0, 98.1

IR (KBr) 2921, 2852, 1618, 1571, 1490, 1454, 1378, 1228, 1098, 741 cm^{-1}

HRMS for $C_{17}H_{13}N_2S^+$ $(M+H)^+$: calcd. 277.07940, found 277.07928



5d

4-((2-methyl-1H-indol-3-yl)thio)isoquinoline

5d was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

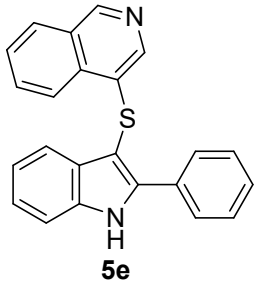
Yellow solid (33.3 mg, 57% yield), mp 244-246 °C.

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.81 (s, 1H), 9.07 (s, 1H), 8.35 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.93 (t, *J* = 7.5 Hz, 1H), 7.78 (t, *J* = 8.5 Hz, 1H), 7.70 (s, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 2.34 (s, 3H)

^{13}C NMR (126 MHz, DMSO-d_6) δ 149.8, 143.0, 139.6, 136.3, 133.1, 131.5, 130.8, 129.8, 128.8, 128.5, 128.2, 123.1, 122.1, 120.6, 118.0, 112.0, 94.4, 12.2

IR (KBr) 2920, 2851, 1619, 1572, 1449, 1375, 1227, 1074, 772, 728 cm^{-1}

HRMS for $C_{18}H_{15}N_2S^+$ (M+H)$^+$: calcd. 291.09505, found 291.09509



5e

4-((2-phenyl-1H-indol-3-yl)thio)isoquinoline

5e was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

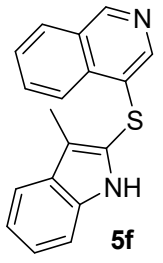
Yellow solid (49.8 mg, 71% yield), mp 238-240 °C.

^{1}H NMR (500 MHz, DMSO-d_6) δ 12.3 (s, 1H), 9.1 (s, 1H), 8.26 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 2H), 7.87 (t, *J* = 7.5 Hz, 1H), 7.77 – 7.74 (m, 2H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.51 – 7.46 (m, 3H), 7.42 (t, *J* = 7.0 Hz, 1H), 7.26 (t, *J* = 7.5 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H)

^{13}C NMR (126 MHz, DMSO-d_6) δ 150.0, 143.1, 139.4, 136.9, 133.0, 131.5, 131.5, 130.6, 130.6, 129.2, 128.8, 128.7, 128.6, 128.2, 123.4, 123.0, 121.2, 119.0, 112.7, 94.7

IR (KBr) 2920, 2851, 1736, 1573, 1445, 1376, 1225, 1041, 747, 692 cm^{-1}

HRMS for $C_{23}H_{17}N_2S^+$ (M+H)$^+$: calcd. 353.11070, found 353.11041



5f

4-((3-methyl-1H-indol-2-yl)thio)isoquinoline

5f was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

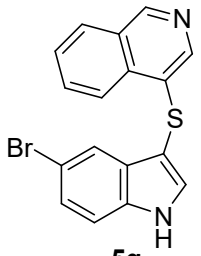
Yellow solid (27.8 mg, 48% yield), mp 144-146 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.45 (s, 1H), 8.27 (d, *J* = 8.5 Hz, 1H), 8.12 (s, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.77 (t, *J* = 7.5 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.27 – 7.20 (m, 2H), 7.14 (t, *J* = 7.0 Hz, 1H), 2.48 (s, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.1, 142.5, 137.2, 134.2, 131.0, 128.5, 128.5, 128.4, 128.2, 127.8, 123.5, 123.4, 120.1, 119.7, 119.4, 119.3, 110.9, 9.6

IR (KBr) 2919, 1518, 1572, 1444, 1379, 1255, 1164, 980, 729 cm^{-1}

HRMS for $C_{18}H_{15}N_2S^+$ $(M+H)^+$: calcd. 291.09505, found 291.09497



5g

4-((5-bromo-1H-indol-3-yl)thio)isoquinoline

5g was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

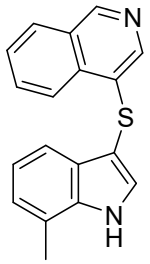
Brown solid (44.5 mg, 63% yield), mp 196-198 °C.

^{1}H NMR (500 MHz, DMSO-d_6) δ 12.05 (s, 1H), 9.13 (s, 1H), 8.39 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 2.5 Hz, 1H), 7.96 – 7.93 (m, 2H), 7.79 (t, *J* = 7.5 Hz, 1H), 7.58 (s, 1H), 7.53 (d, *J* = 8.5 Hz, 1H), 7.34 (d, *J* = 9.5 Hz, 1H)

^{13}C NMR (126 MHz, DMSO-d_6) δ 150.6, 140.8, 136.0, 134.8, 133.3, 131.7, 130.8, 130.3, 128.8, 128.6, 128.3, 125.4, 123.2, 120.8, 115.2, 113.6, 97.9

IR (KBr) 2920, 2851, 1573, 1452, 1377, 1257, 1102, 879, 742 cm^{-1}

HRMS for $C_{17}H_{12}BrN_2S^+$ $(M+H)^+$: calcd. 354.98991, found 354.98993



5h

4-((7-methyl-1H-indol-3-yl)thio)isoquinoline

5h was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

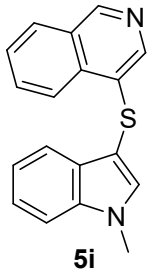
Yellow solid (30.3 mg, 52% yield), mp 188-190 °C

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.8 (s, 1H), 9.09 (s, 1H), 8.39 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.95 – 7.90 (m, 3H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 7.0 Hz, 1H), 7.02 – 6.97 (m, 2H), 2.53 (s, 3H)

^{13}C NMR (126 MHz, DMSO-d_6) δ 150.3, 140.8, 136.8, 133.3, 132.8, 131.6, 130.7, 128.8, 128.6, 128.5, 128.2, 123.3, 123.2, 122.3, 121.0, 116.3, 98.4, 17.1

IR (KBr) 2919, 2851, 1613, 1573, 1435, 1379, 1227, 1123, 1022, 779, 741 cm^{-1}

HRMS for $C_{18}H_{15}N_2S^+$ $(M+H)^+$: calcd. 291.09505, found 291.09503



5i

4-((1-methyl-1H-indol-3-yl)thio)isoquinoline

5i was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 2:1).

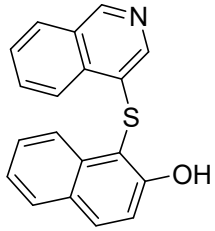
Yellow solid (36.0 mg, 62% yield), mp 129-130 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.40 (d, *J* = 8.5 Hz, 1H), 8.01 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.78 (t, *J* = 8.0 Hz, 1H), 7.64 – 7.60 (m, 2H), 7.39 – 7.37 (m, 2H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 3.84 (s, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.7, 140.9, 137.7, 135.2, 133.7, 131.3, 130.5, 129.6, 128.1, 128.1, 127.6, 123.4, 122.8, 120.8, 119.6, 110.0, 98.6, 33.3

IR (KBr) 2920, 1569, 1511, 1458, 1334, 1240, 1154, 737 cm^{-1}

HRMS for $C_{18}H_{15}N_2S^+$ $(M+H)^+$: calcd. 291.09505, found 291.09473



5j

1-(isoquinolin-4-ylthio)naphthalen-2-ol

5j was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

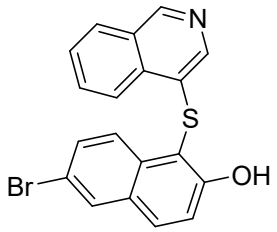
Yellow solid (36.3 mg, 60% yield), mp 198-200 °C.

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.63 (s, 1H), 9.07 (s, 1H), 8.40 (d, *J* = 8.5 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 7.5 Hz, 1H), 7.97 – 7.92 (m, 2H), 7.77 (t, *J* = 7.0 Hz, 1H), 7.63 (s, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 9.0 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H)

^{13}C NMR (126 MHz, DMSO-d_6) δ 159.1, 149.9, 139.7, 136.1, 133.4, 133.0, 131.5, 129.7, 129.2, 128.8, 128.5, 128.4, 128.3, 124.2, 123.9, 123.3, 119.0, 106.2

IR (KBr) 2921, 1617, 1502, 1435, 1345, 1272, 1211, 1152, 813, 744 cm^{-1}

HRMS for $C_{19}H_{14}NOS^+$ $(M+H)^+$: calcd. 304.07906, found 304.07901



5k

6-bromo-1-(isoquinolin-4-ylthio)naphthalen-2-ol

5k was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

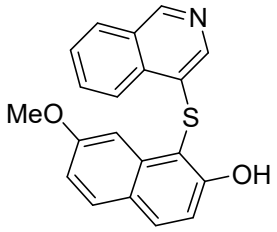
Yellow solid (54.1 mg, 71% yield), mp 221-223 °C.

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.8 (s, 1H), 9.1 (s, 1H), 8.36 (d, *J* = 8.5 Hz, 1H), 8.21 – 8.16 (m, 3H), 8.01 (d, *J* = 9.0 Hz, 1H), 7.93 (td, *J* = 7.0, 1.0 Hz, 1H), 7.78 (t, *J* = 8.0 Hz, 1H), 7.62 – 7.59 (m, 2H), 7.42 (d, *J* = 9.0 Hz, 1H)

^{13}C NMR (126 MHz, DMSO-d_6) δ 159.1, 149.7, 139.4, 134.4, 133.0, 131.6, 131.1, 130.7, 130.4, 130.0, 128.9, 128.3, 128.1, 127.9, 126.2, 122.8, 119.8, 116.3, 106.3

IR (KBr) 2921, 2852, 1725, 1615, 1589, 1485, 1380, 1340, 1189, 807, 745 cm^{-1}

HRMS for $C_{19}H_{13}BrNOS^+$ (M+H)$^+$: calcd. 381.98957, found 381.98965



5l

1-(isoquinolin-4-ylthio)-7-methoxynaphthalen-2-ol

5l was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).

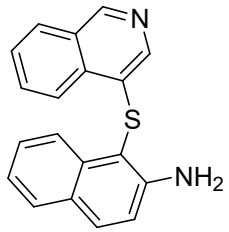
Yellow solid (43.5 mg, 65% yield), mp 178-180 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.43 (d, *J* = 8.5 Hz, 1H), 7.99 (d, *J* = 8.5 Hz, 1H), 7.87 – 7.82 (m, 2H), 7.74 – 7.68 (m, 3H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.31 (s, 1H), 7.19 (d, *J* = 8.5 Hz, 1H), 7.01 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.69 (s, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.8, 157.8, 150.4, 140.2, 137.2, 134.0, 132.9, 130.9, 130.4, 128.4, 128.2, 127.9, 127.4, 124.8, 122.9, 116.1, 114.5, 105.2, 103.6, 55.3

IR (KBr) 2919, 1616, 1512, 1462, 1418, 1377, 1139, 1091, 838, 750 cm^{-1}

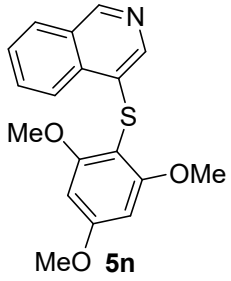
HRMS for $C_{20}H_{16}NO_2S^+$ (M+H)$^+$: calcd. 334.08963, found 334.08960



5m

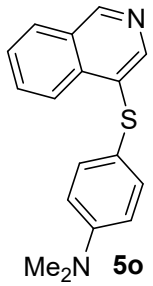
1-(isoquinolin-4-ylthio)naphthalen-2-amine

5m was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 1:1).
Yellow solid (40.6 mg, 67% yield), mp 185-187 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.41 (d, *J* = 8.0 Hz, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.84 – 7.81 (m, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 – 7.65 (m, 2H), 7.41 – 7.38 (m, 1H), 7.27 – 7.24 (m, 1H), 7.06 (d, *J* = 8.5 Hz, 1H), 4.76 (s, 2H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.7, 148.9, 139.2, 136.6, 133.9, 132.4, 130.6, 128.7, 128.7, 128.3, 128.1, 127.7, 124.0, 123.2, 122.9, 117.8, 102.0
IR (KBr) 2920, 1615, 1473, 1379, 1215, 1055, 978, 816, 746cm^{-1}
HRMS for $C_{19}H_{15}N_2S^+$ (M+H)$^+$: calcd. 303.09505, found 303.09503



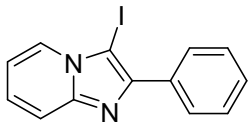
5n

4-((2,4,6-trimethoxyphenyl)thio)isoquinoline
5n was purified by silica gel chromatography (petroleum ether/ethyl acetate = 5:1 to 2:1).
Yellow solid (49.6 mg, 76% yield), mp 111-113 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 7.89 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 6.14 (s, 2H), 3.78 (s, 3H), 3.72 (s, 6H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 163.3, 162.5, 149.5, 140.6, 134.2, 130.3, 130.2, 128.3, 127.9, 127.4, 124.0, 97.0, 91.4, 56.3, 55.6
IR (KBr) 2922, 1569, 1412, 1338, 1225, 1122, 1028, 816, 741 cm^{-1}
HRMS for $C_{18}H_{18}NO_3S^+$ (M+H)$^+$: calcd. 328.10019, found 328.10007



5o

4-(isoquinolin-4-ylthio)-N,N-dimethylaniline
5o was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1 to 2:1).
Yellow solid (43.8 mg, 78% yield), mp 132-134 °C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.30 (d, *J* = 8.5 Hz, 1H), 8.22 (s, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.75 – 7.72 (m, 1H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 9.0 Hz, 2H), 6.68 (d, *J* = 8.5 Hz, 2H), 2.96 (s, 6H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 150.8, 150.7, 143.3, 135.1, 134.6, 131.4, 130.7, 128.5, 128.1, 127.7, 124.0, 116.8, 113.3, 40.4
IR (KBr) 2919, 1588, 1504, 1360, 1226, 1192, 980, 811, 749 cm^{-1}
HRMS for $C_{17}H_{17}N_2S^+$ (M+H)$^+$: calcd. 281.11070, found 281.11069



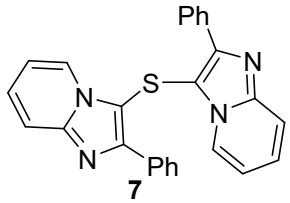
6

3-iodo-2-phenylimidazo[1,2-a]pyridine[3]

6 was purified by silica gel chromatography (petroleum ether/ethyl acetate = 8:1 to 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 – 8.11 (m, 3H), 7.65 (d, *J* = 9.5 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.26 (m, 1H), 6.94 (t, *J* = 7.0 Hz, 1H)

HRMS for $C_{13}H_{10}IN_2^+$ $(M+H)^+$: calcd. 320.98832, found 320.98831



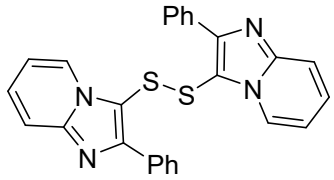
7

bis(2-phenylimidazo[1,2-a]pyridin-3-yl)sulfane[2]

7 was purified by silica gel chromatography (petroleum ether/ethyl acetate = 6:1 to 3:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.0 Hz, 4H), 7.62 (t, *J* = 7.5 Hz, 4H), 7.58 – 7.54 (m, 4H), 7.49 (d, *J* = 9.0 Hz, 2H), 7.11 (t, *J* = 8.0 Hz, 2H), 6.36 (t, *J* = 7.0 Hz, 2H)

HRMS for $C_{26}H_{19}N_4S^+$ $(M+H)^+$: calcd. 419.13249, found 419.13232



8

1,2-bis(2-phenylimidazo[1,2-a]pyridin-3-yl)disulfane[2]

8 was purified by silica gel chromatography (petroleum ether/ethyl acetate = 5:1 to 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 6.0 Hz, 2H), 7.63 (s, 4H), 7.35 (d, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 2H), 7.13 – 7.09 (m, 6H), 6.73 (t, *J* = 7.0 Hz, 2H)

HRMS for $C_{26}H_{19}N_4S_2^+$ $(M+H)^+$: calcd. 451.10456, found 451.10489

References

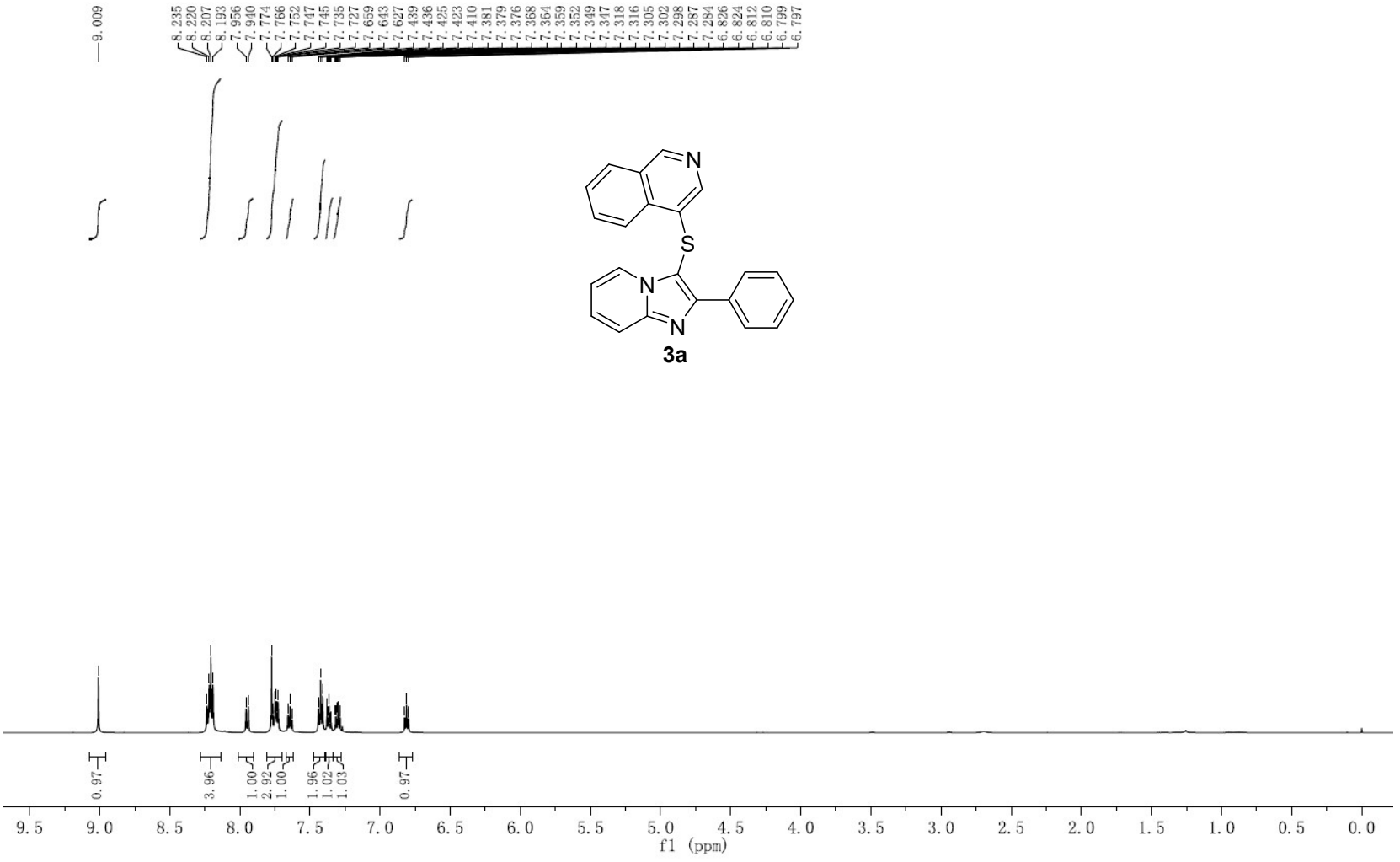
1. Semwal, R.; Ravi, C.; Kumar, R.; Meena, R.; Adimurthy, S. *J. Org. Chem*. **2019**, *84*, 792−805.
2. Reddy, R. J.; Shankar, A.; Kumar, J. J.; Sharadha, N. *New J. Chem*., **2022**, *46*, 4784–4791

Reference:

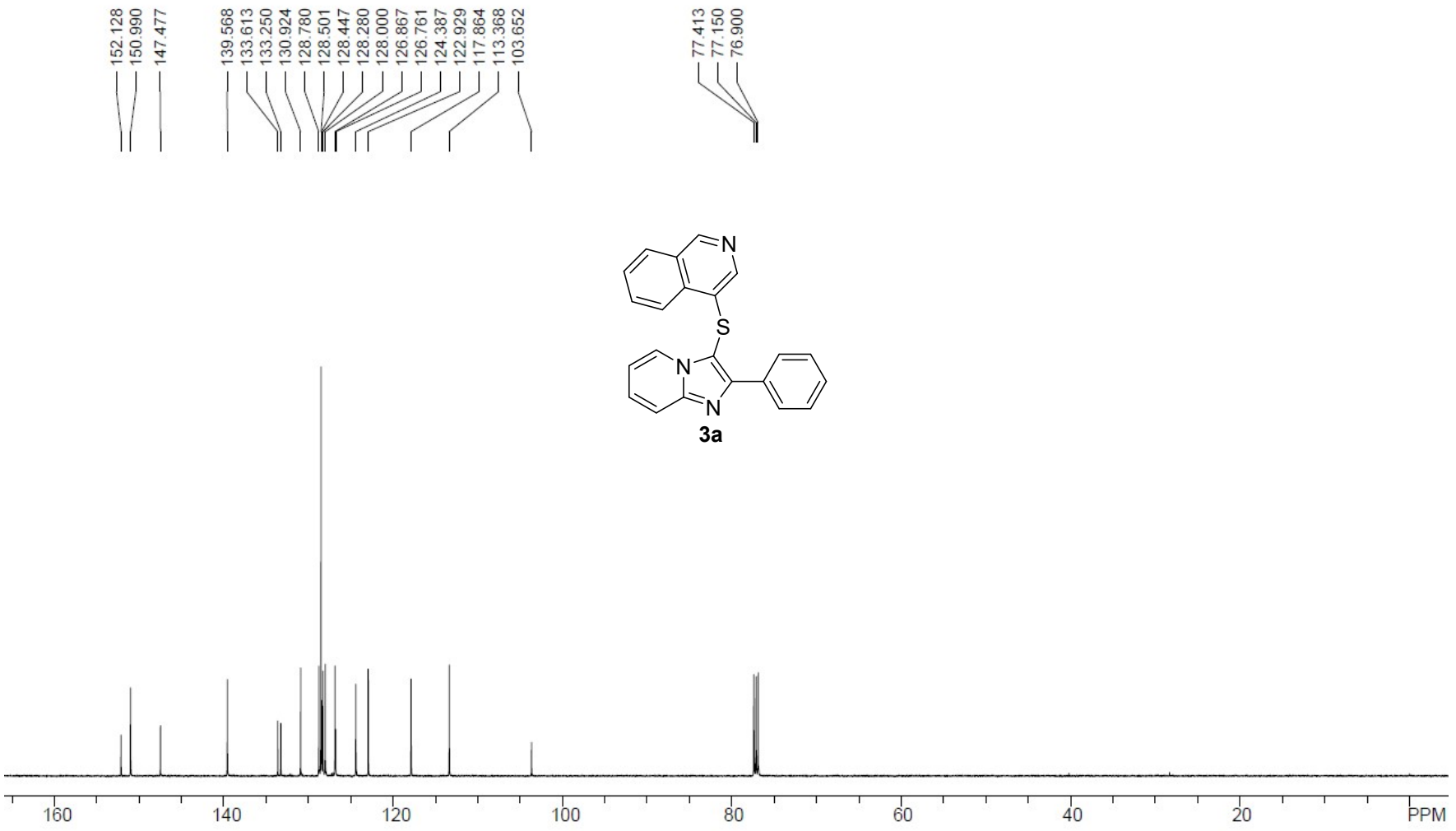
1. D. C. Mohan, R. R. Donthiri, S. N. Rao, S. Adimurthya, *Adv. Synth. Catal*. **2013**, *355*, 2217-2221.
2. R. J. Reddy, A. Shankar, J. J. Kumar, N. Sharadha, *New J. Chem*., **2022**, *46*, 4784-4791.
3. Semwal, R.; Ravi, C.; Kumar, R.; Meena, R.; Adimurthy, S. *J. Org. Chem*. **2019**, *84*, 792−805.

3 Copies of ^{1}H and ^{13}C NMR Spectra

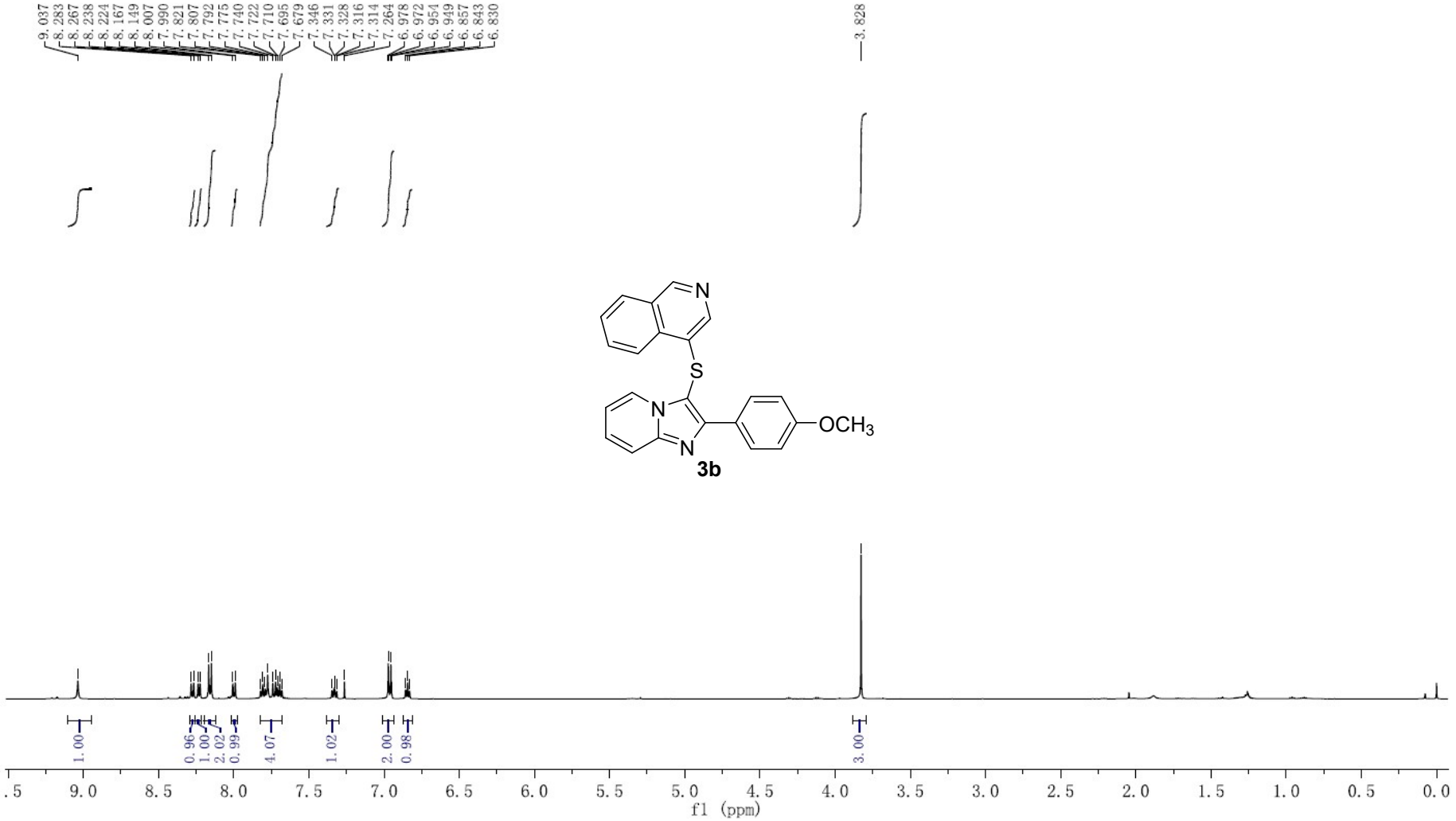
^{1}H NMR (500 MHz, $CDCl_3$) of **3a**



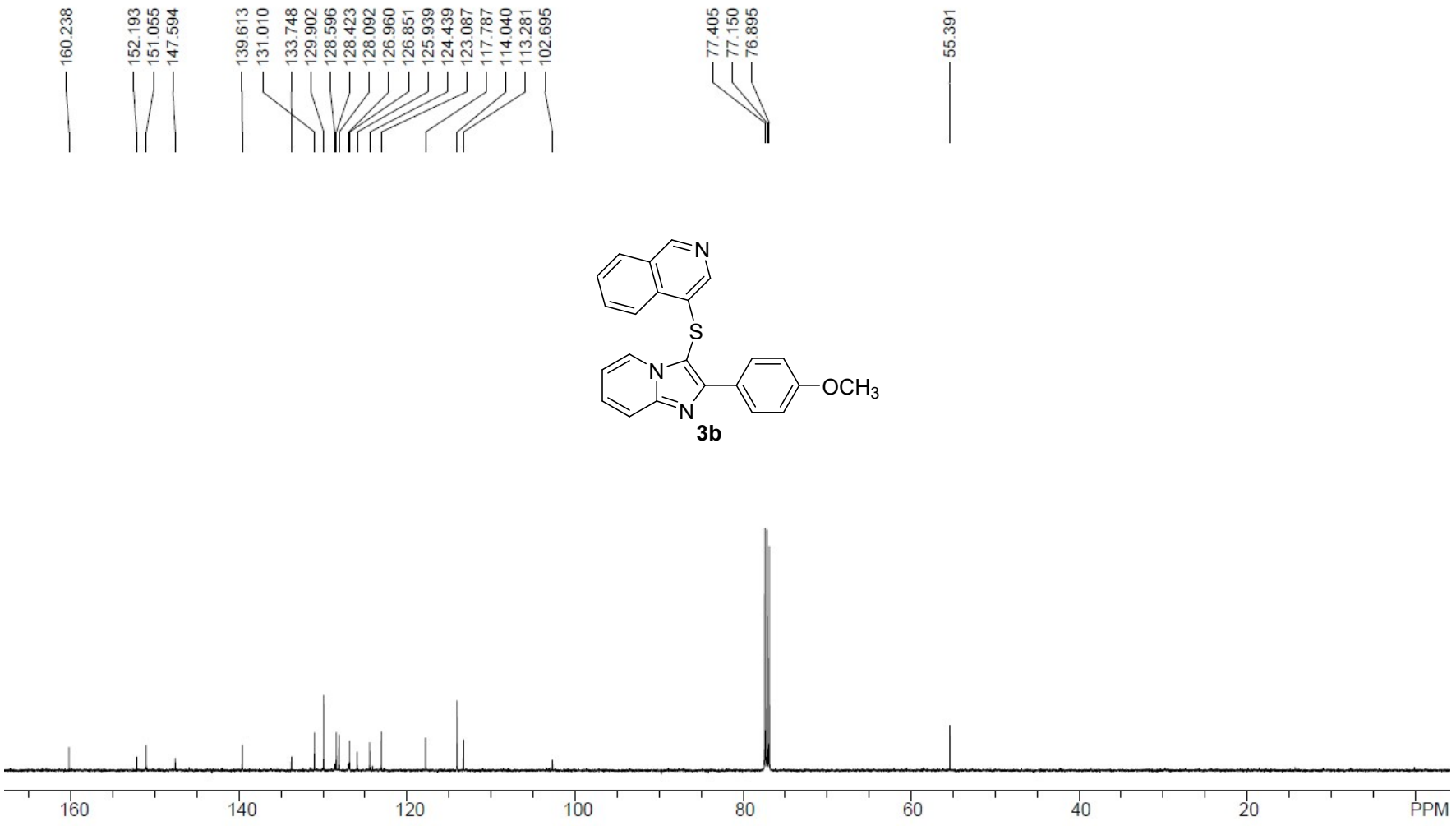
^{13}C NMR (126 MHz, $CDCl_3$) of **3a**



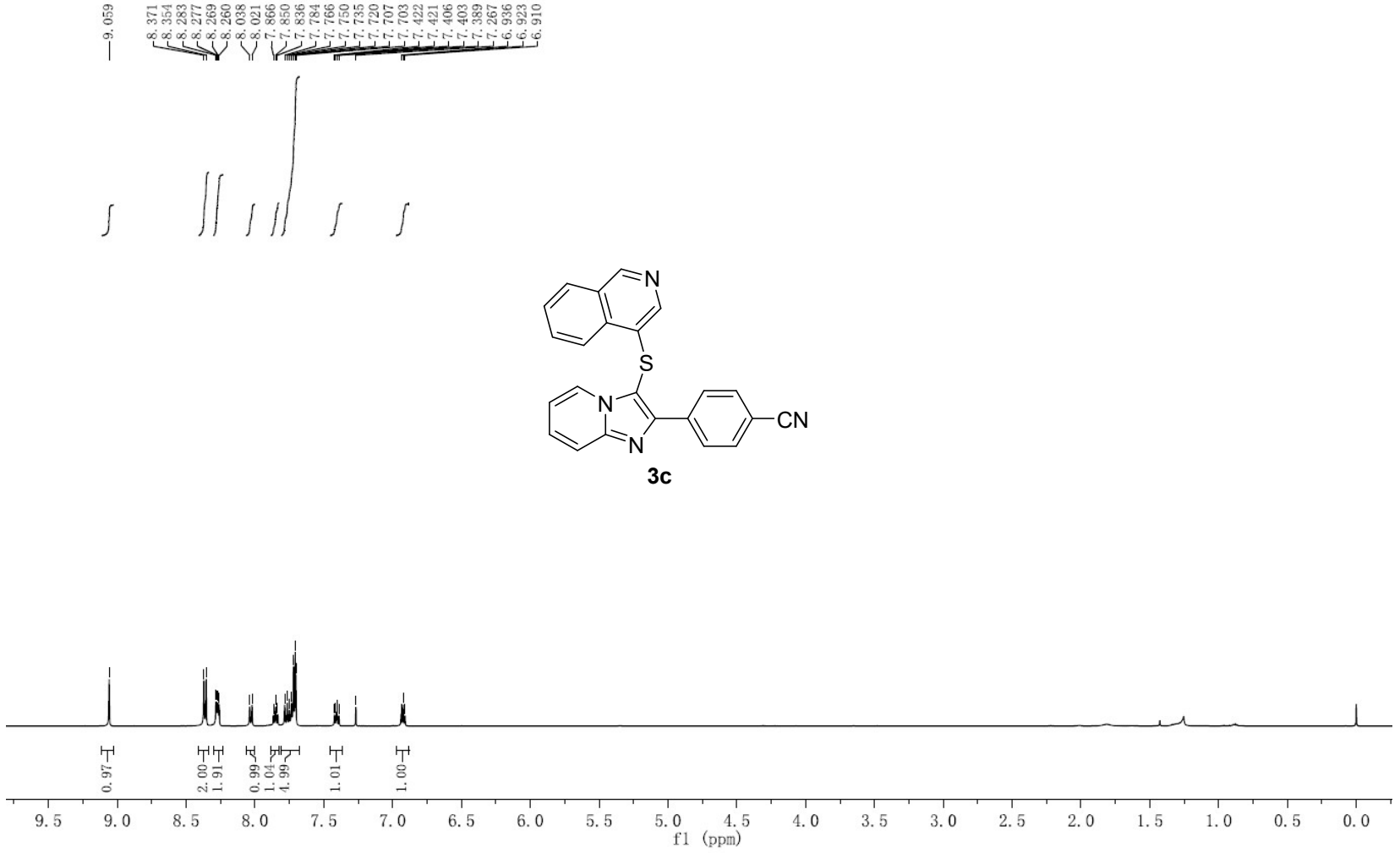
^{1}H NMR (500 MHz, $CDCl_3$) of **3b**



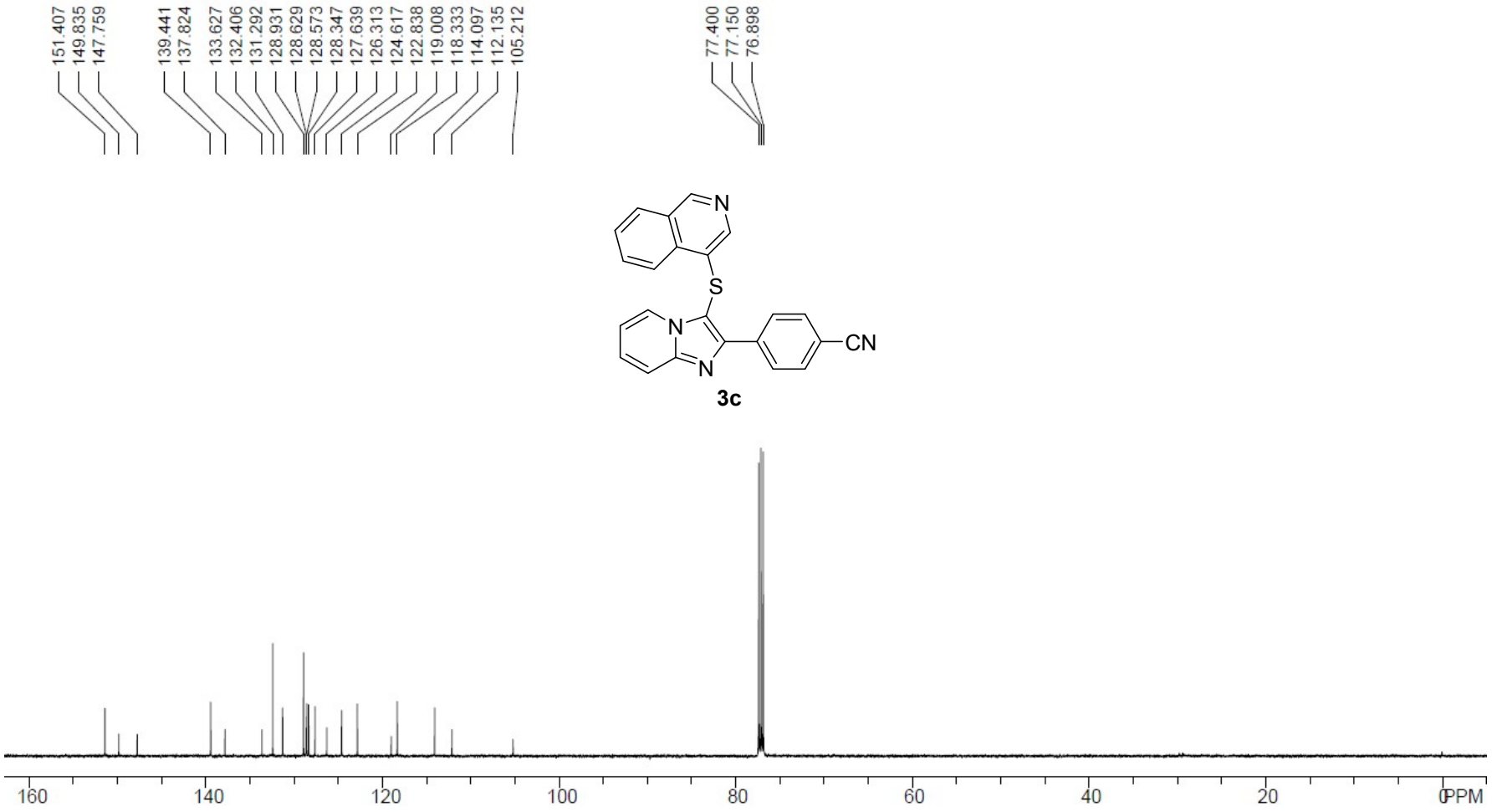
^{13}C NMR (126 MHz, $CDCl_3$) of **3a**



^{1}H NMR (500 MHz, $CDCl_3$) of **3c**

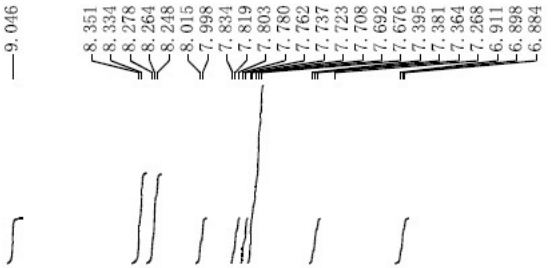


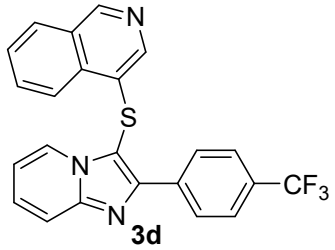
^{13}C NMR (126 MHz, $CDCl_3$) of **3c**



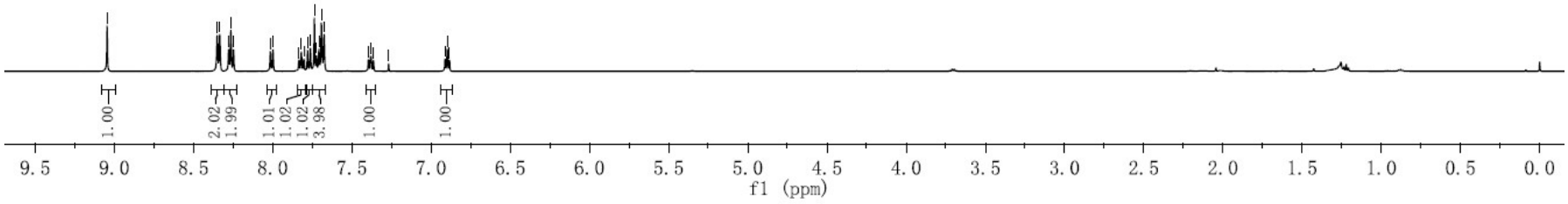
3c

^{1}H NMR (500 MHz, $CDCl_3$) of **3d**

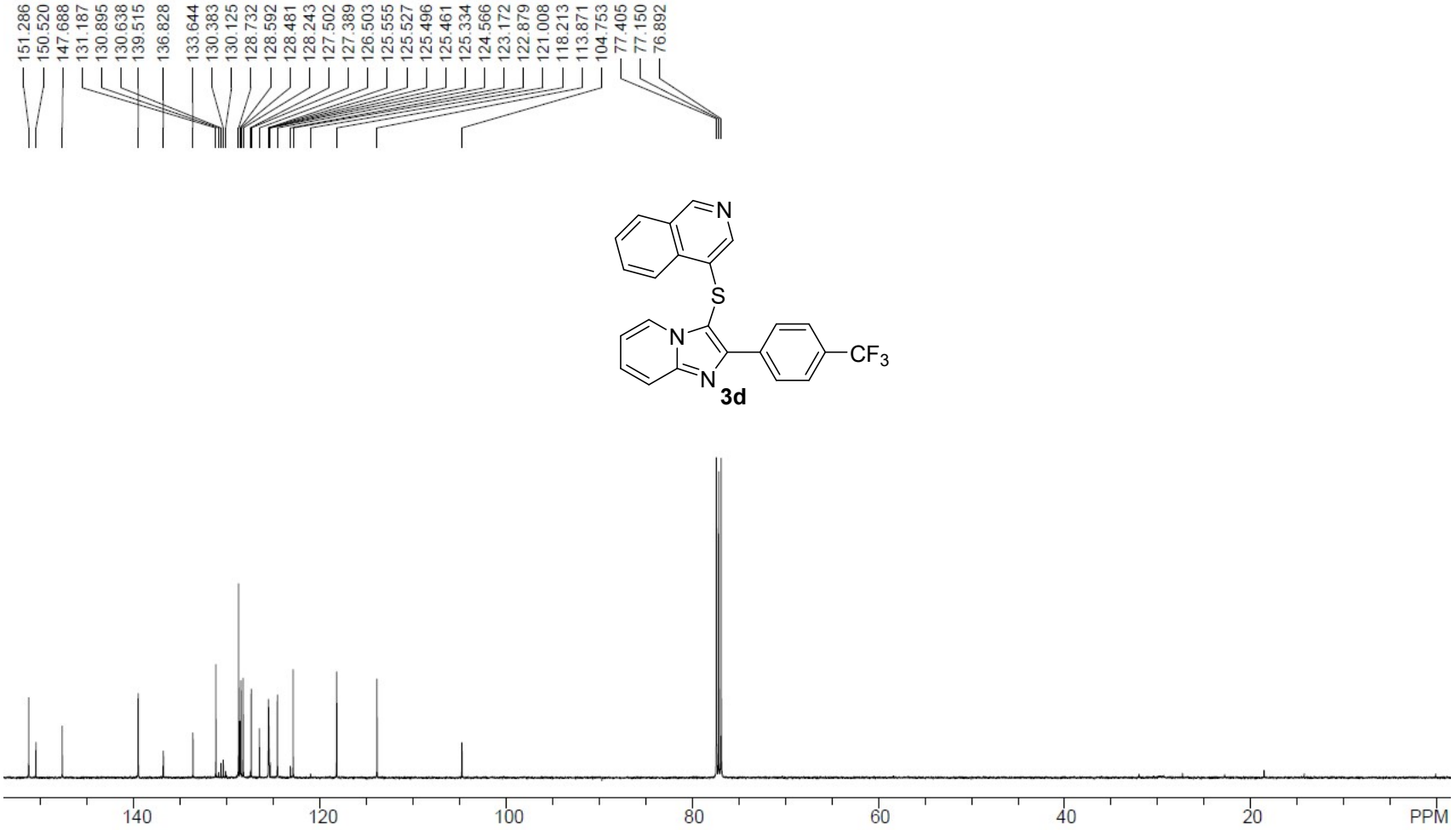




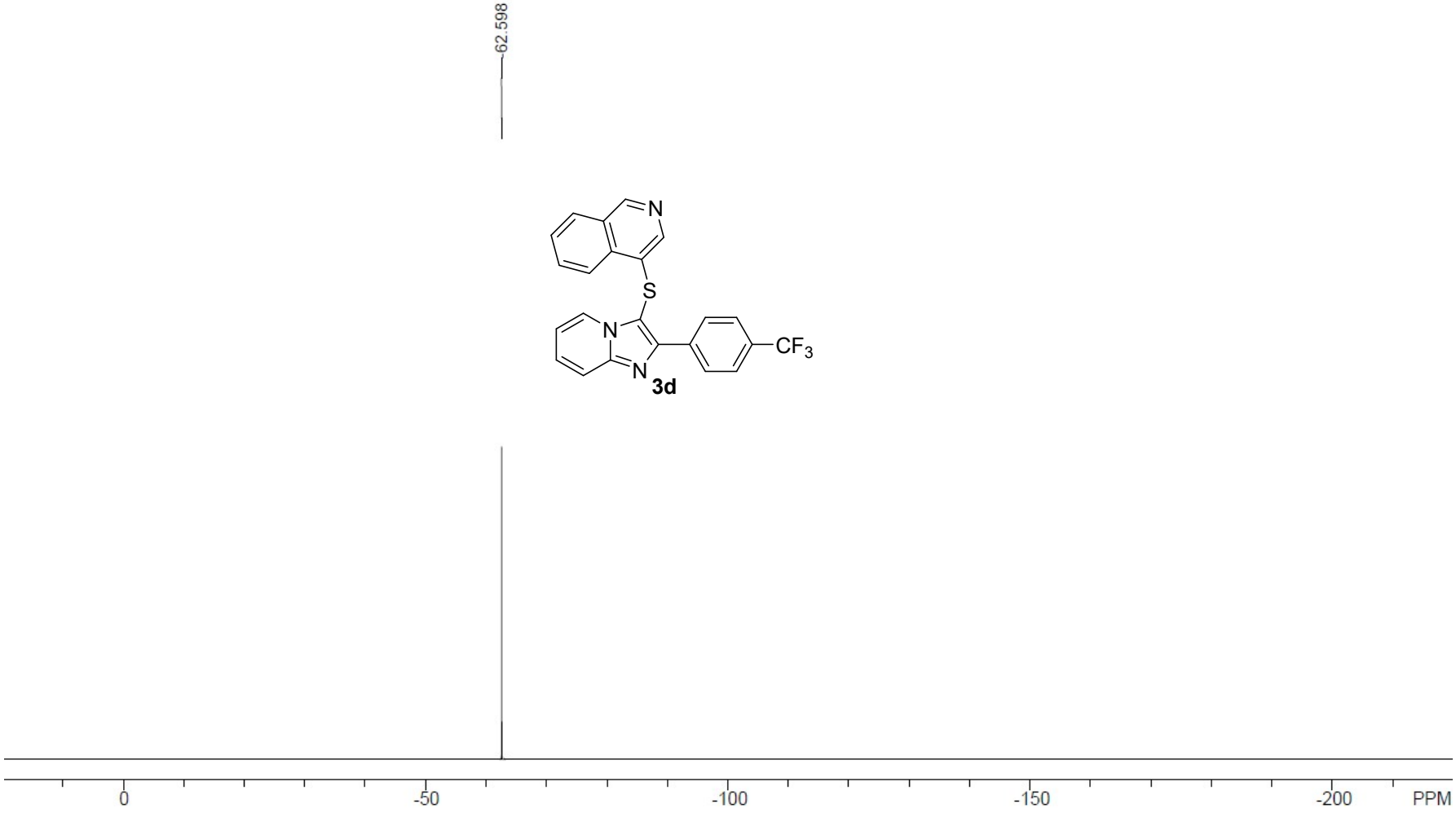
3d



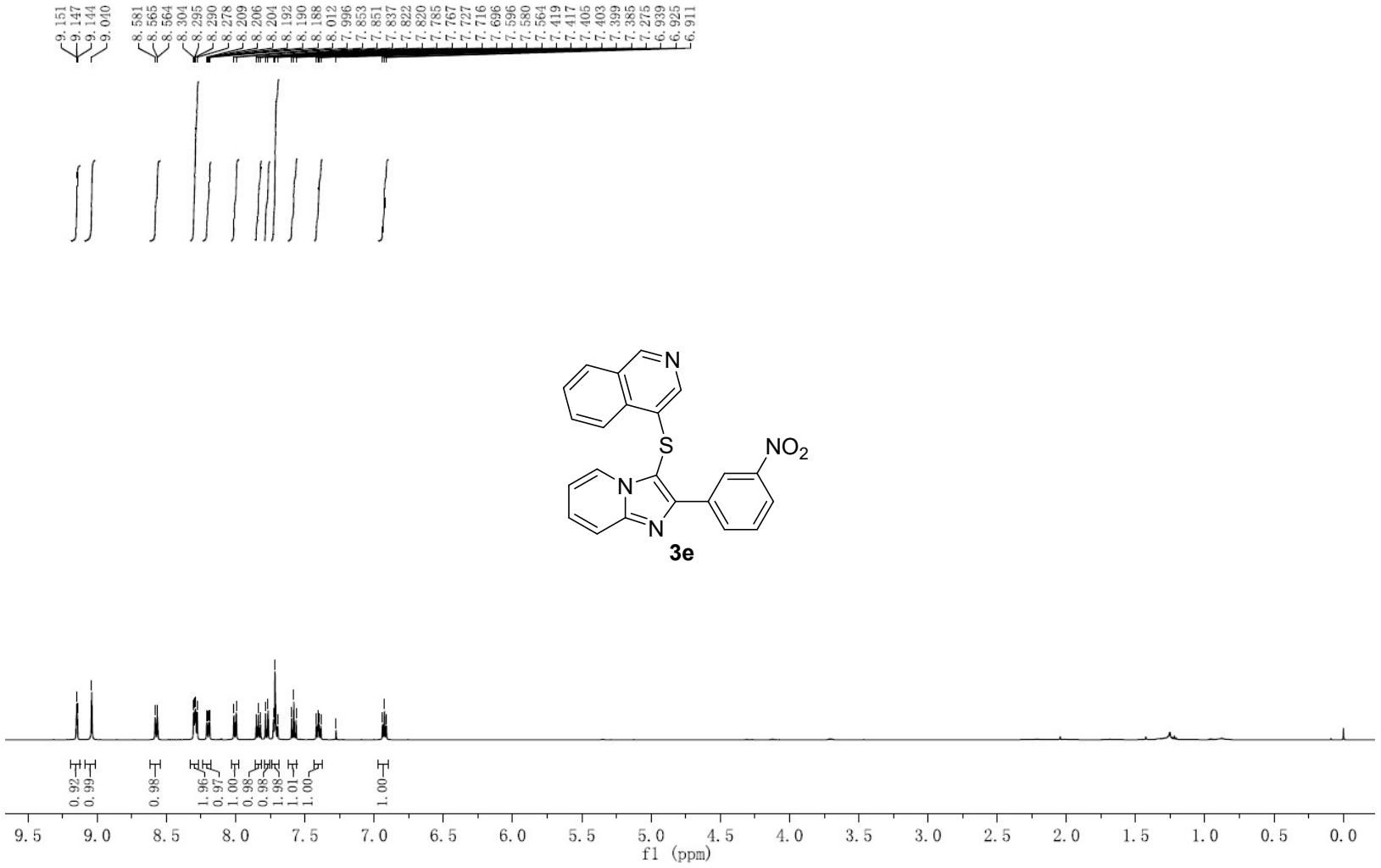
^{13}C NMR (126 MHz, $CDCl_3$) of **3d**



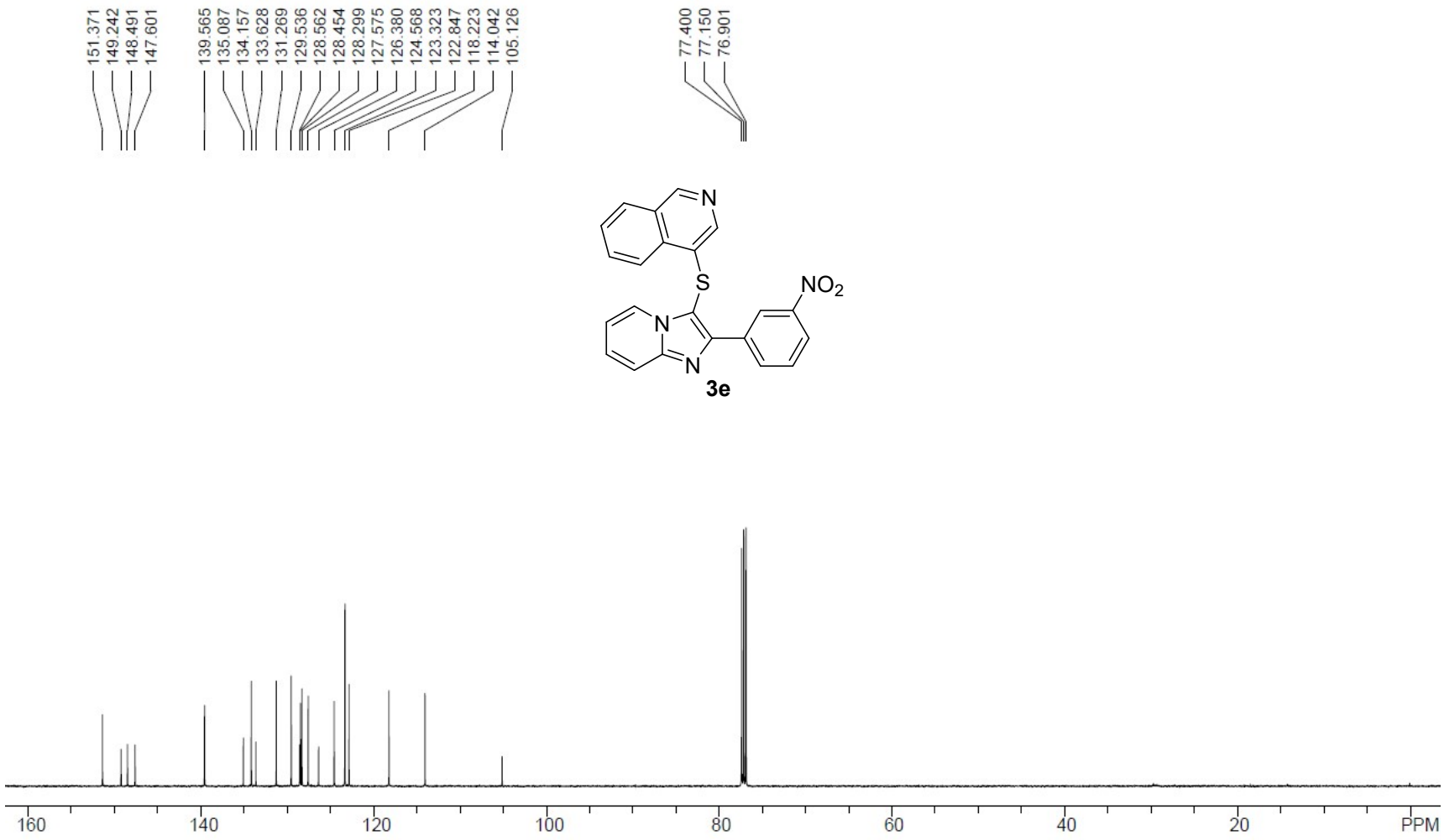
^{19}F NMR (471 MHz, $CDCl_3$) of **3d**



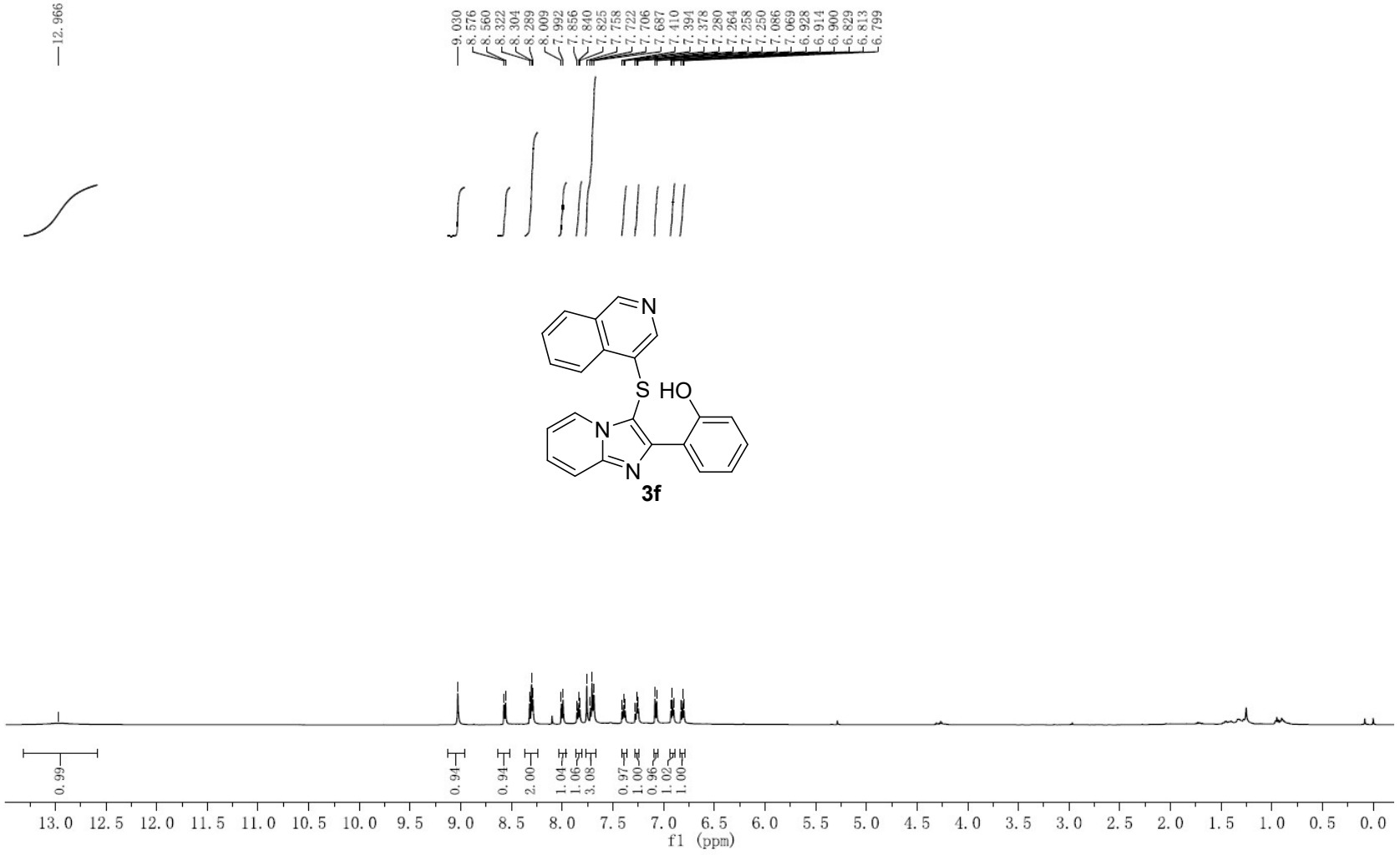
^{1}H NMR (500 MHz, $CDCl_3$) of **3e**



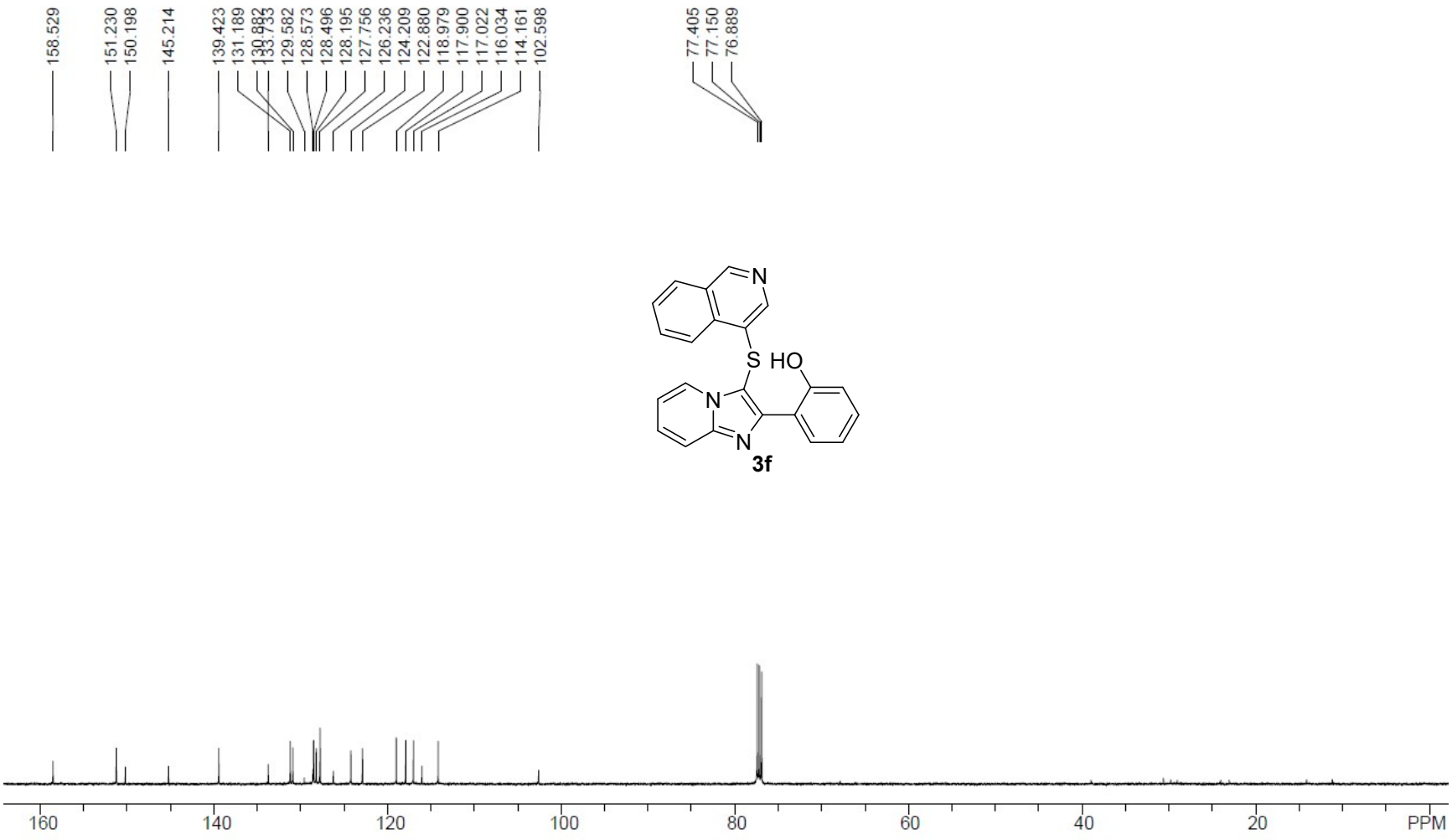
^{13}C NMR (126 MHz, $CDCl_3$) of **3e**



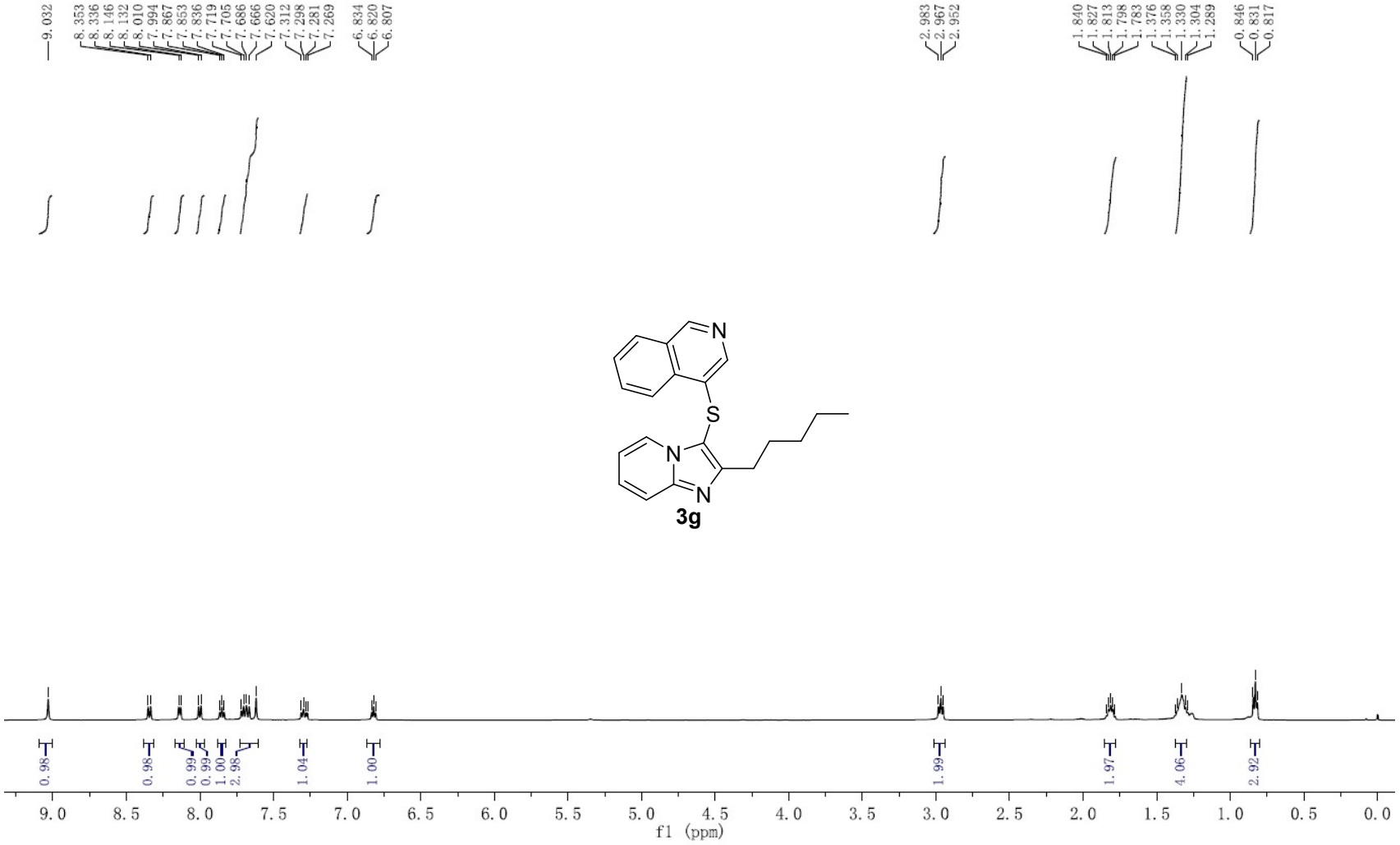
^{1}H NMR (500 MHz, $CDCl_3$) of **3f**



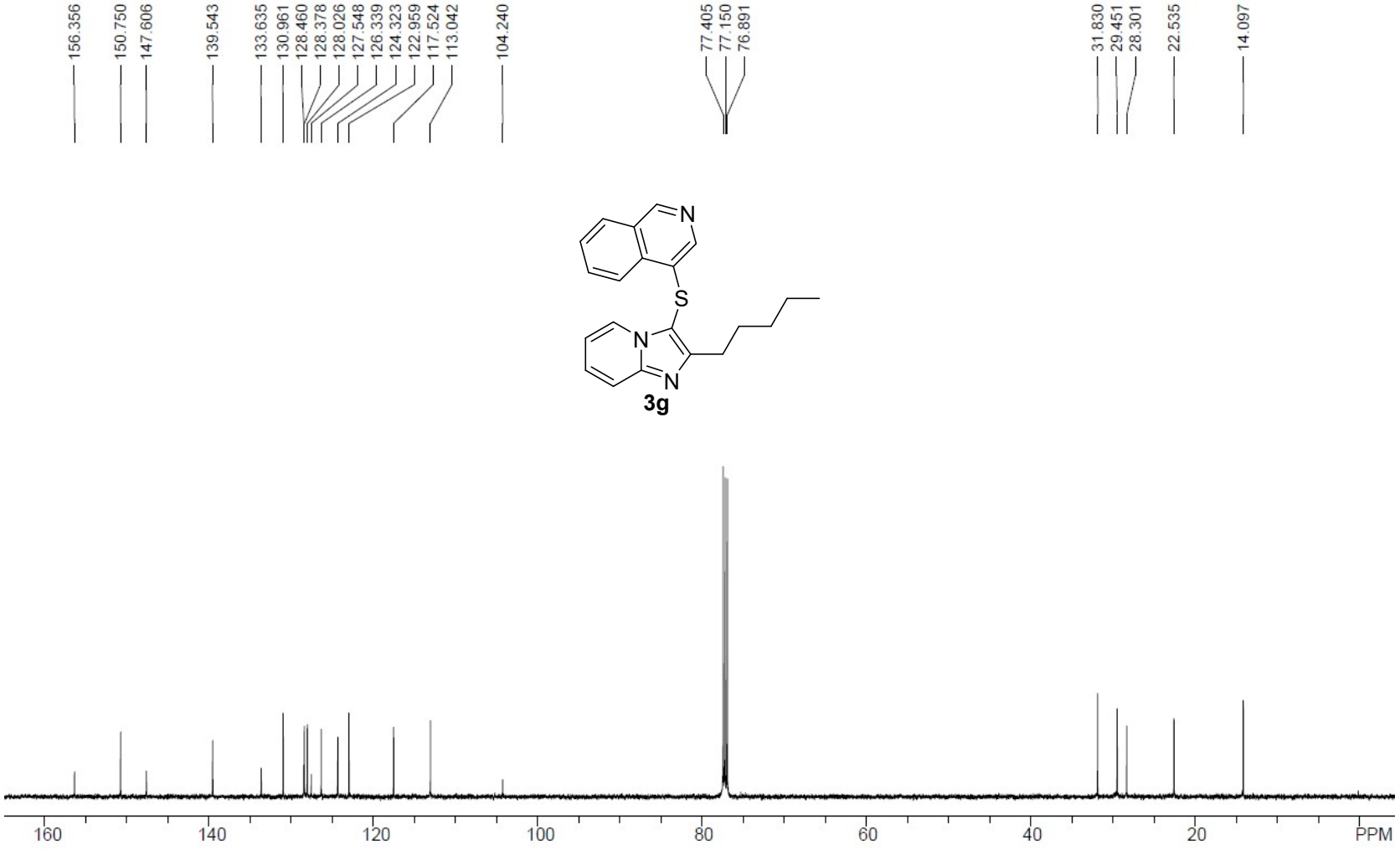
^{13}C NMR (126 MHz, $CDCl_3$) of **3f**



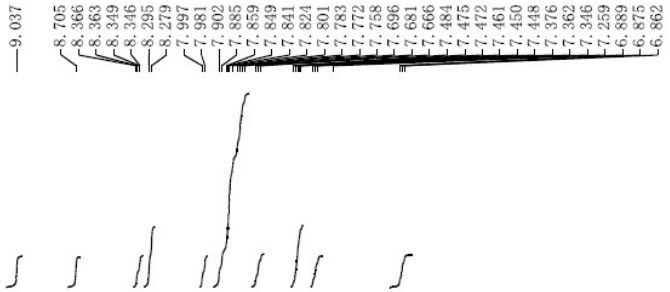
^{1}H NMR (500 MHz, $CDCl_3$) of **3g**

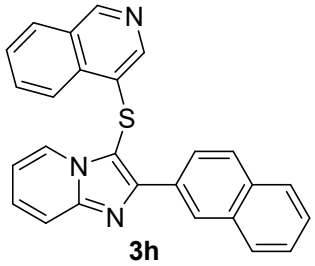


^{13}C NMR (126 MHz, $CDCl_3$) of **3g**

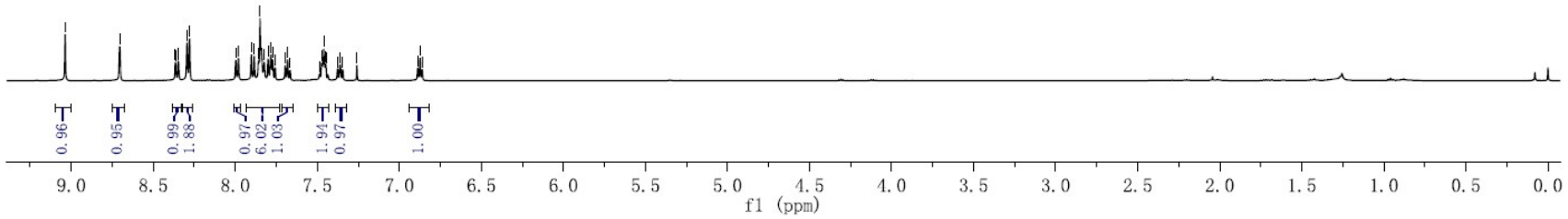


^{1}H NMR (500 MHz, $CDCl_3$) of **3h**

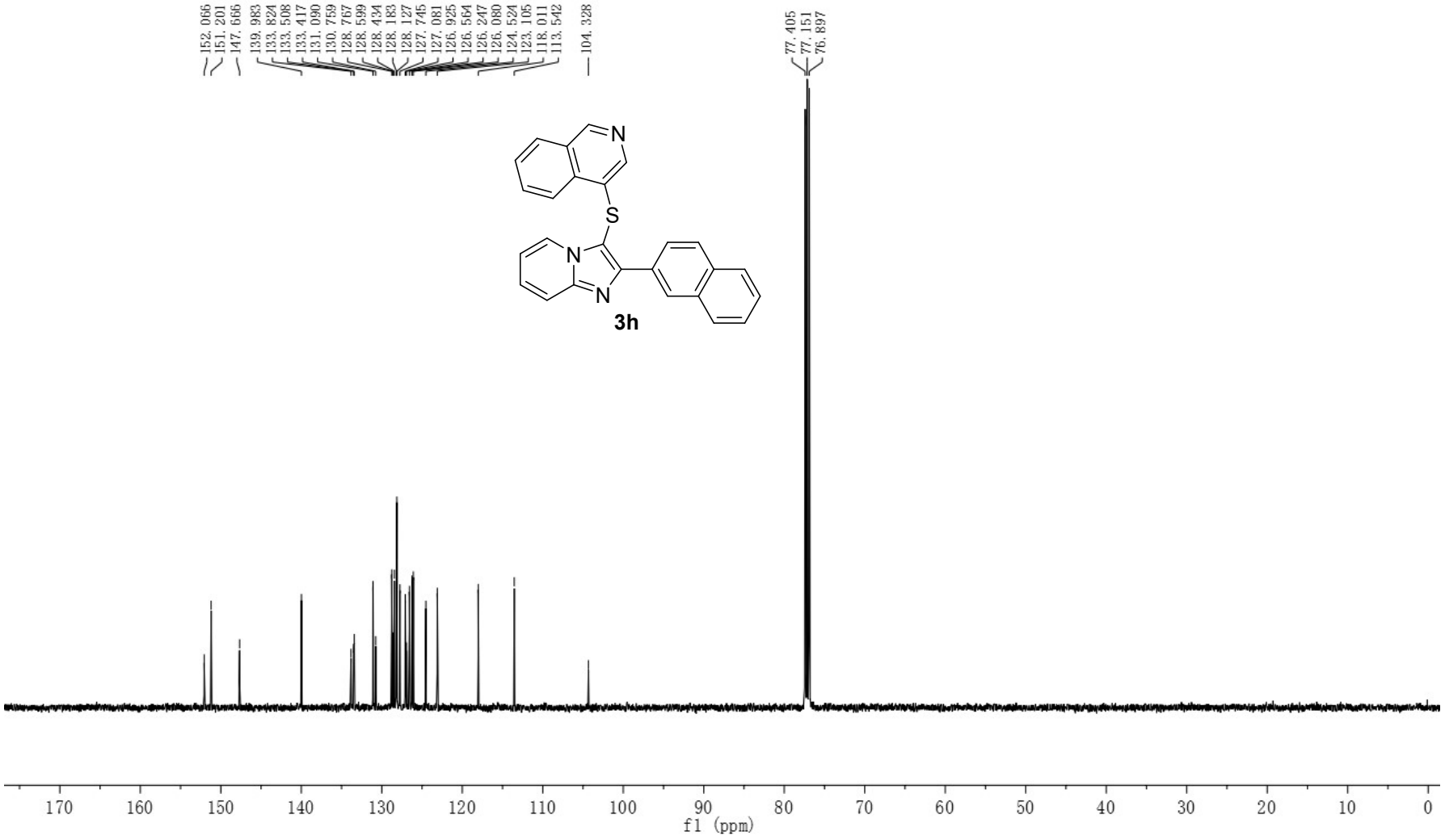




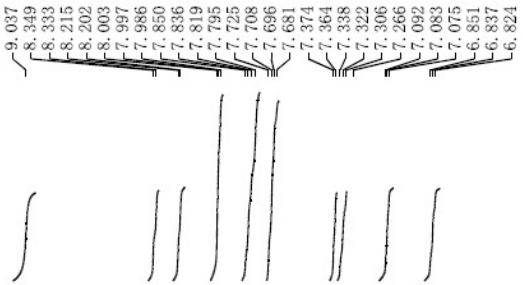
3h

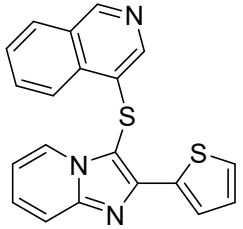


^{13}C NMR (126 MHz, $CDCl_3$) of **3h**

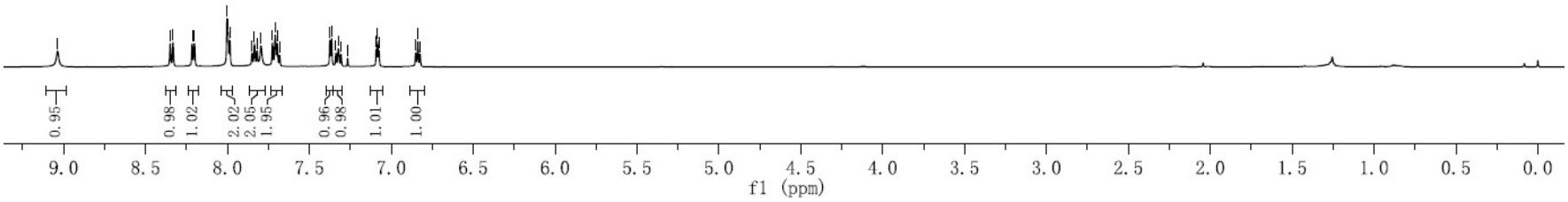


^{1}H NMR (500 MHz, $CDCl_3$) of **3i**

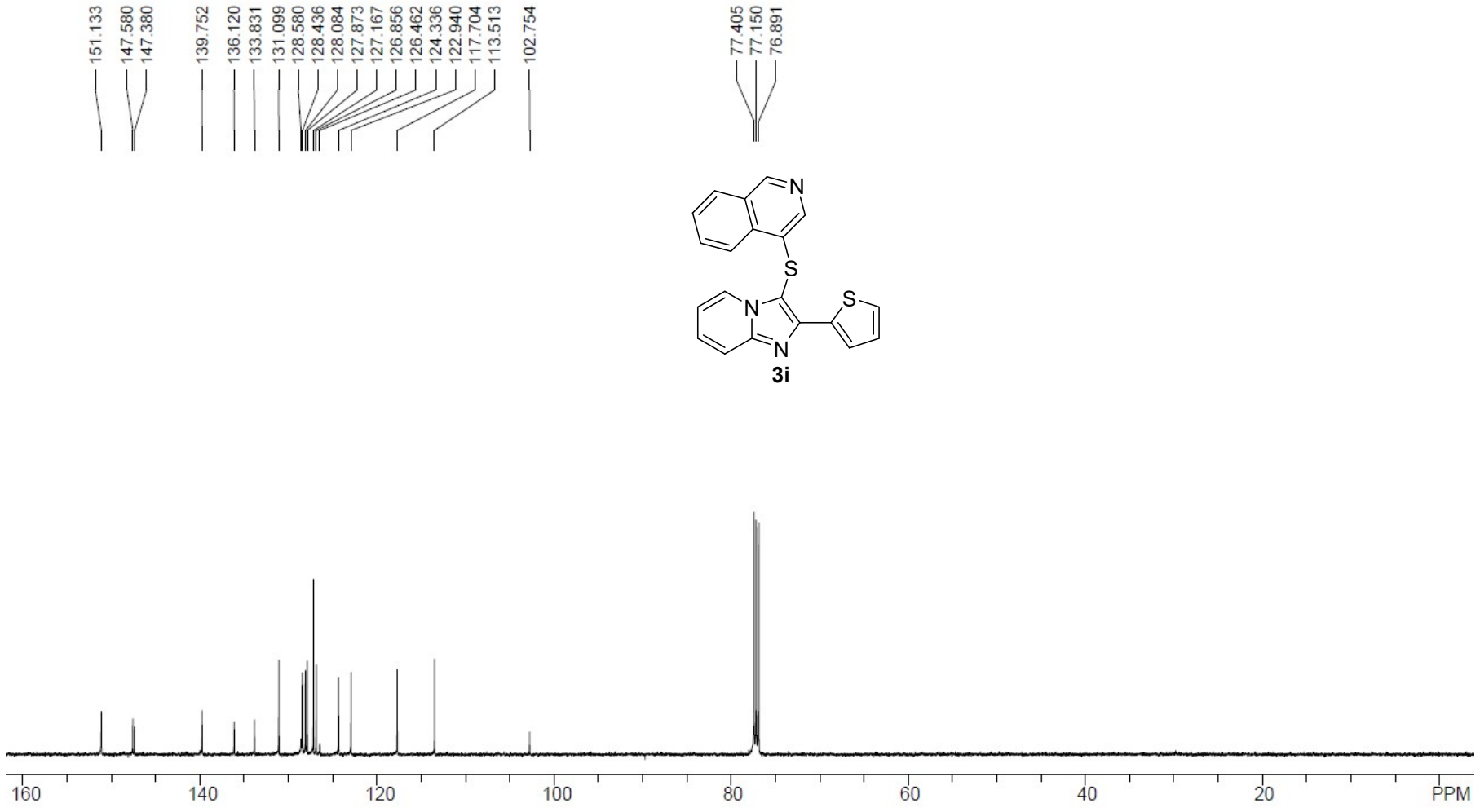




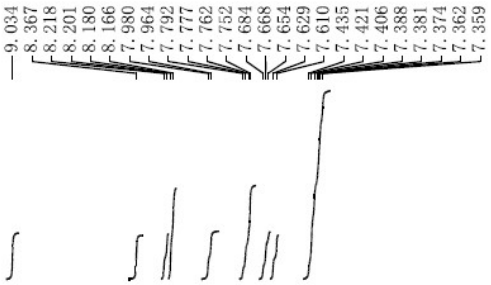
3i

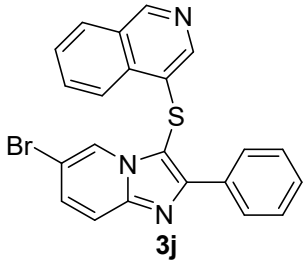


^{13}C NMR (126 MHz, $CDCl_3$) of **3i**

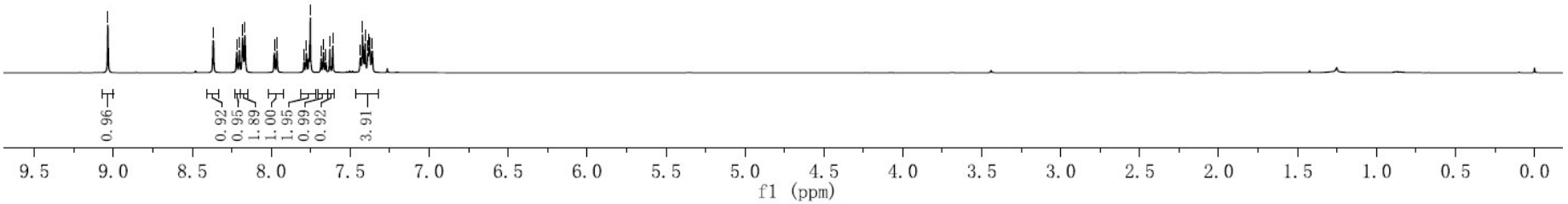


^{1}H NMR (500 MHz, $CDCl_3$) of **3j**

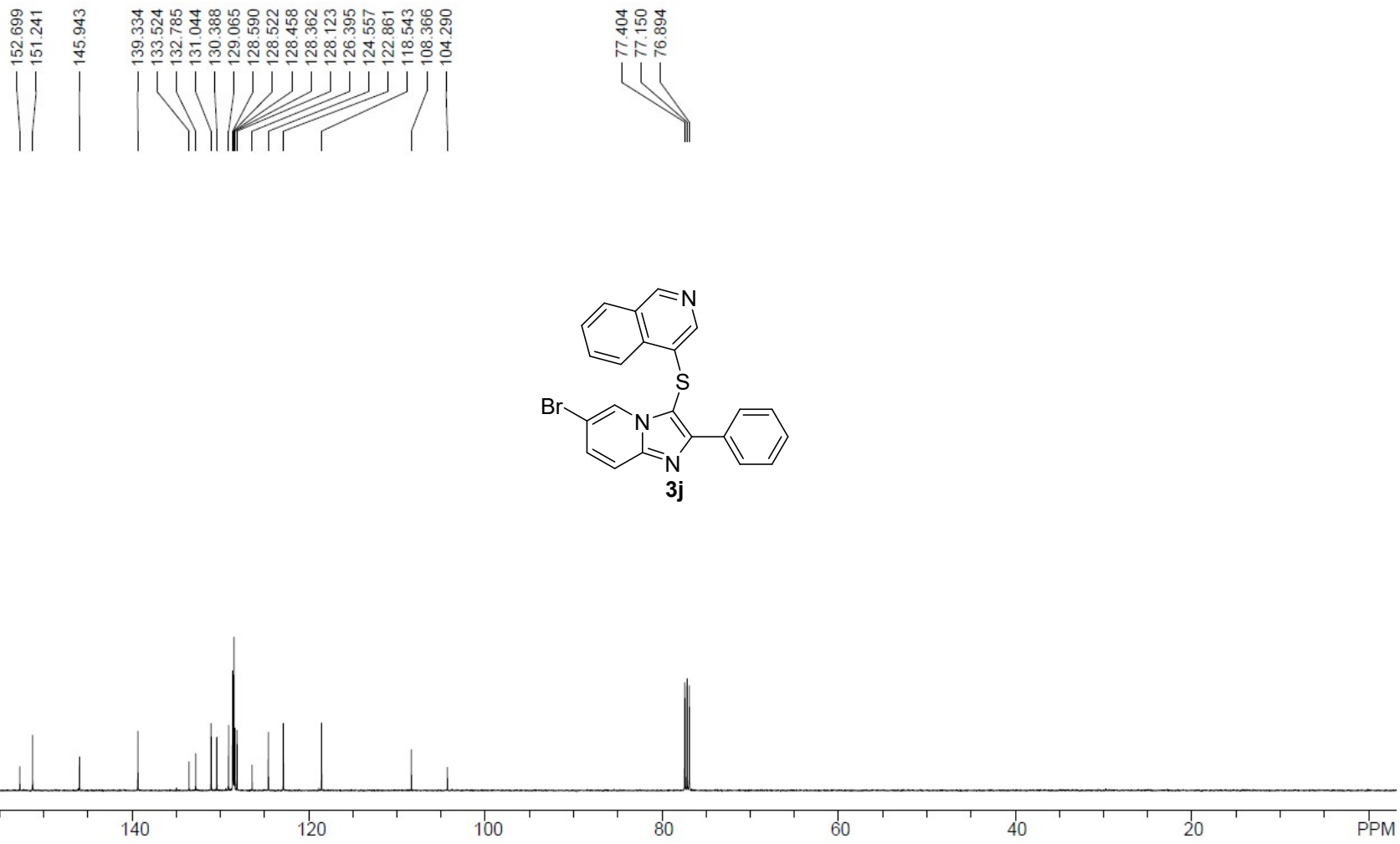




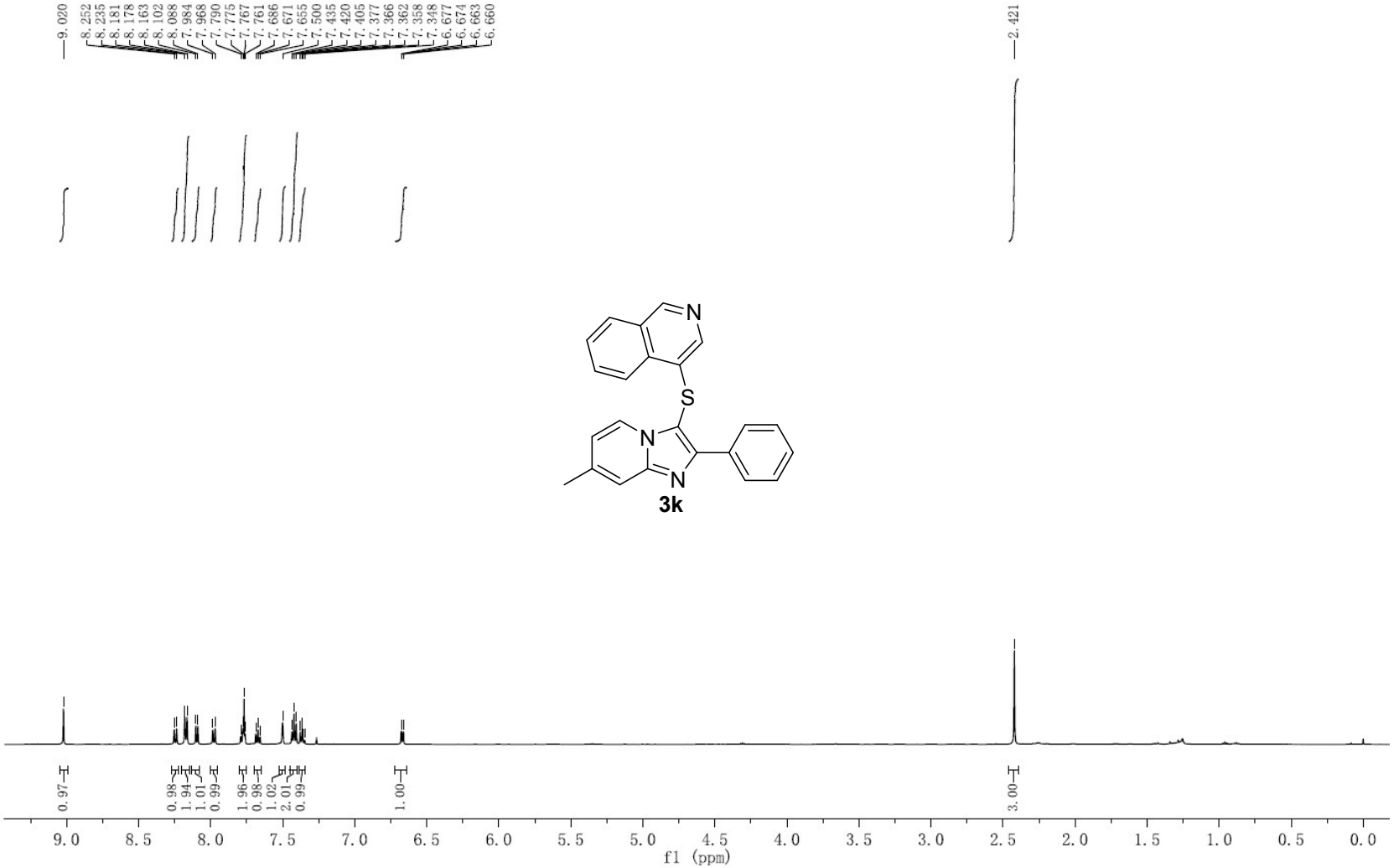
3j



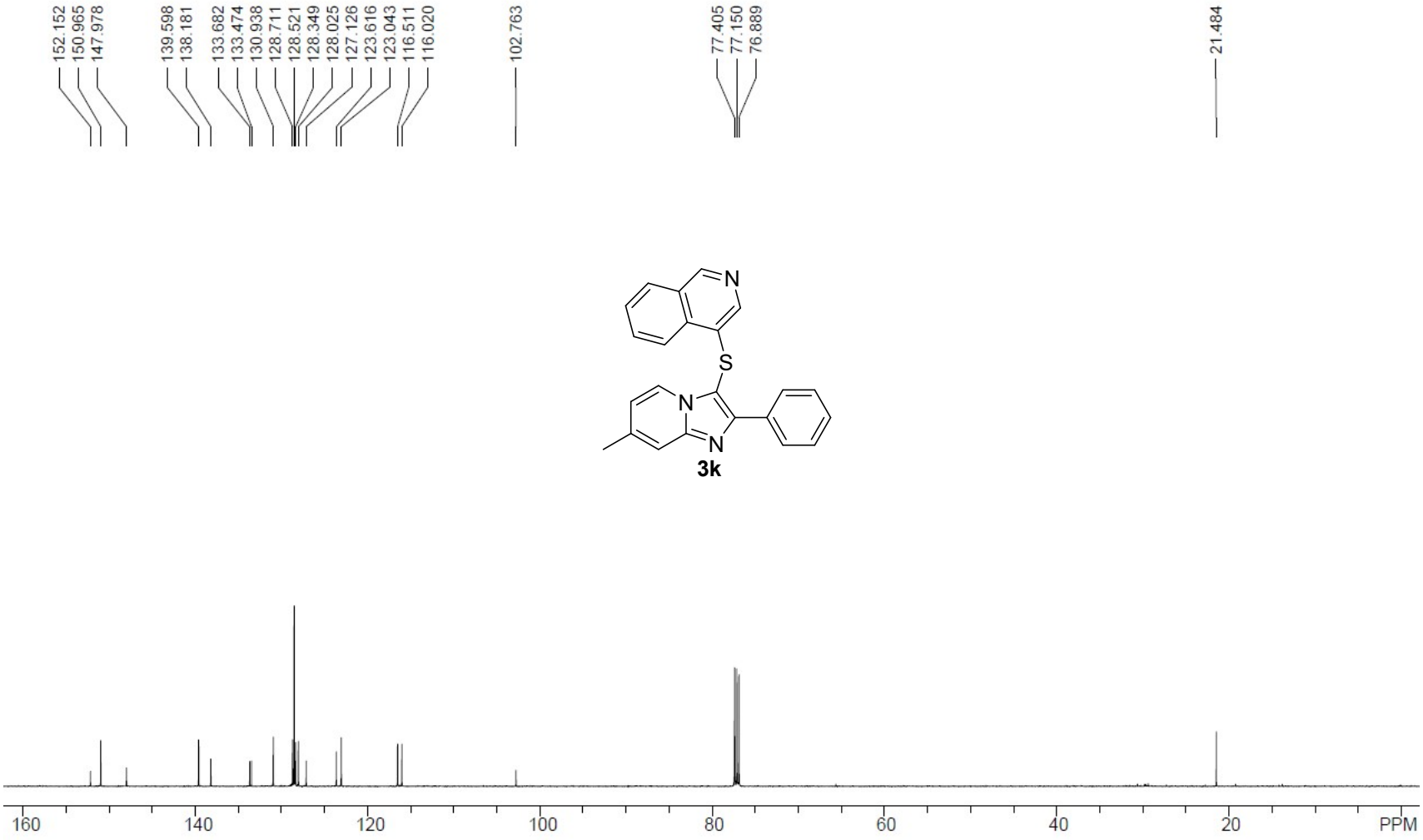
^{13}C NMR (126 MHz, $CDCl_3$) of **3j**



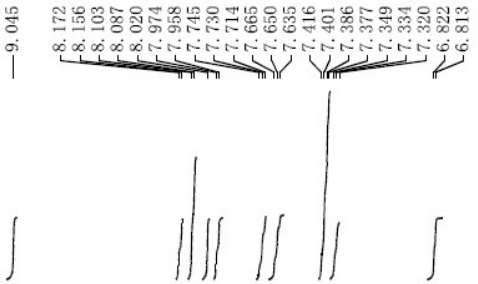
^{1}H NMR (500 MHz, $CDCl_3$) of **3k**

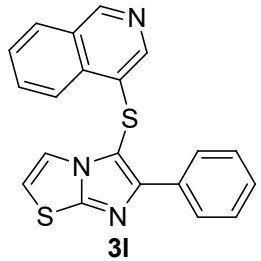


^{13}C NMR (126 MHz, $CDCl_3$) of **3k**

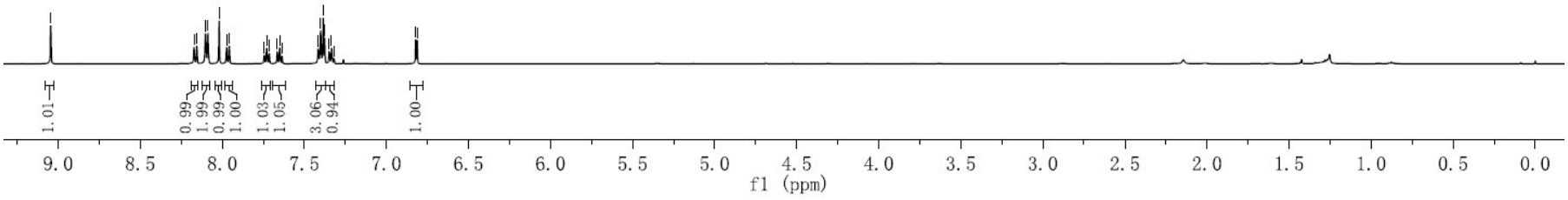


^{1}H NMR (500 MHz, $CDCl_3$) of **3l**

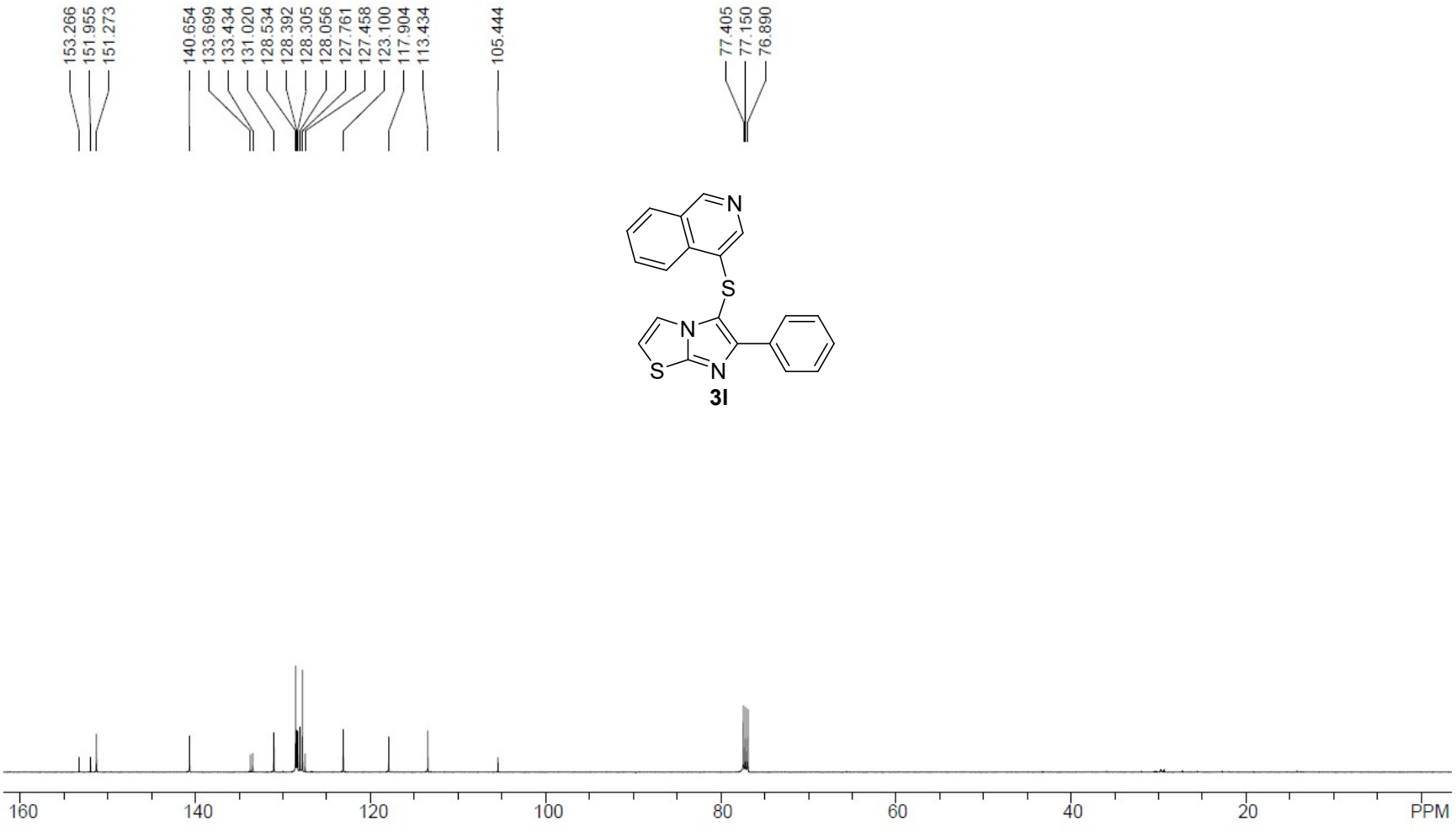




3l



^{13}C NMR (126 MHz, $CDCl_3$) of **3l**



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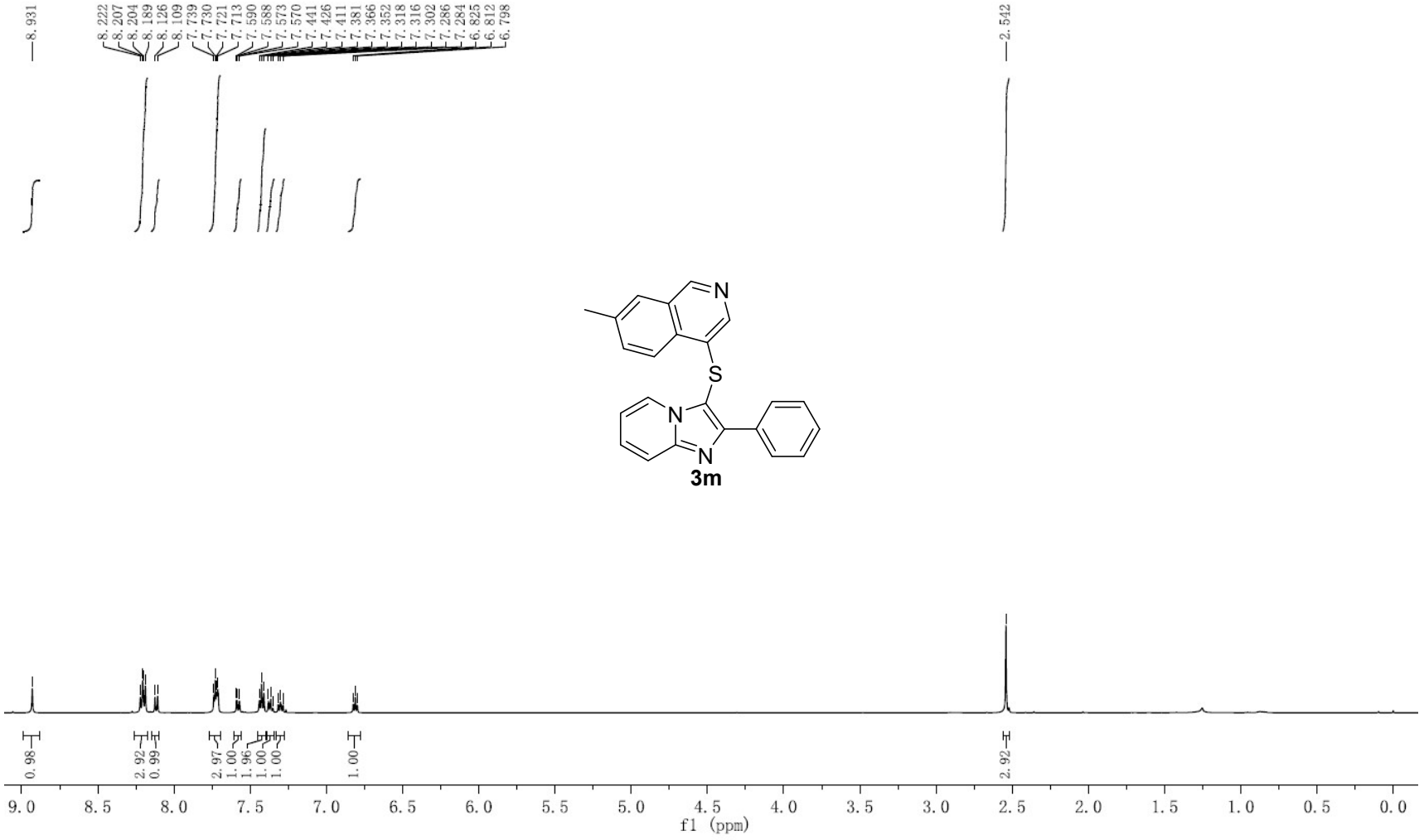
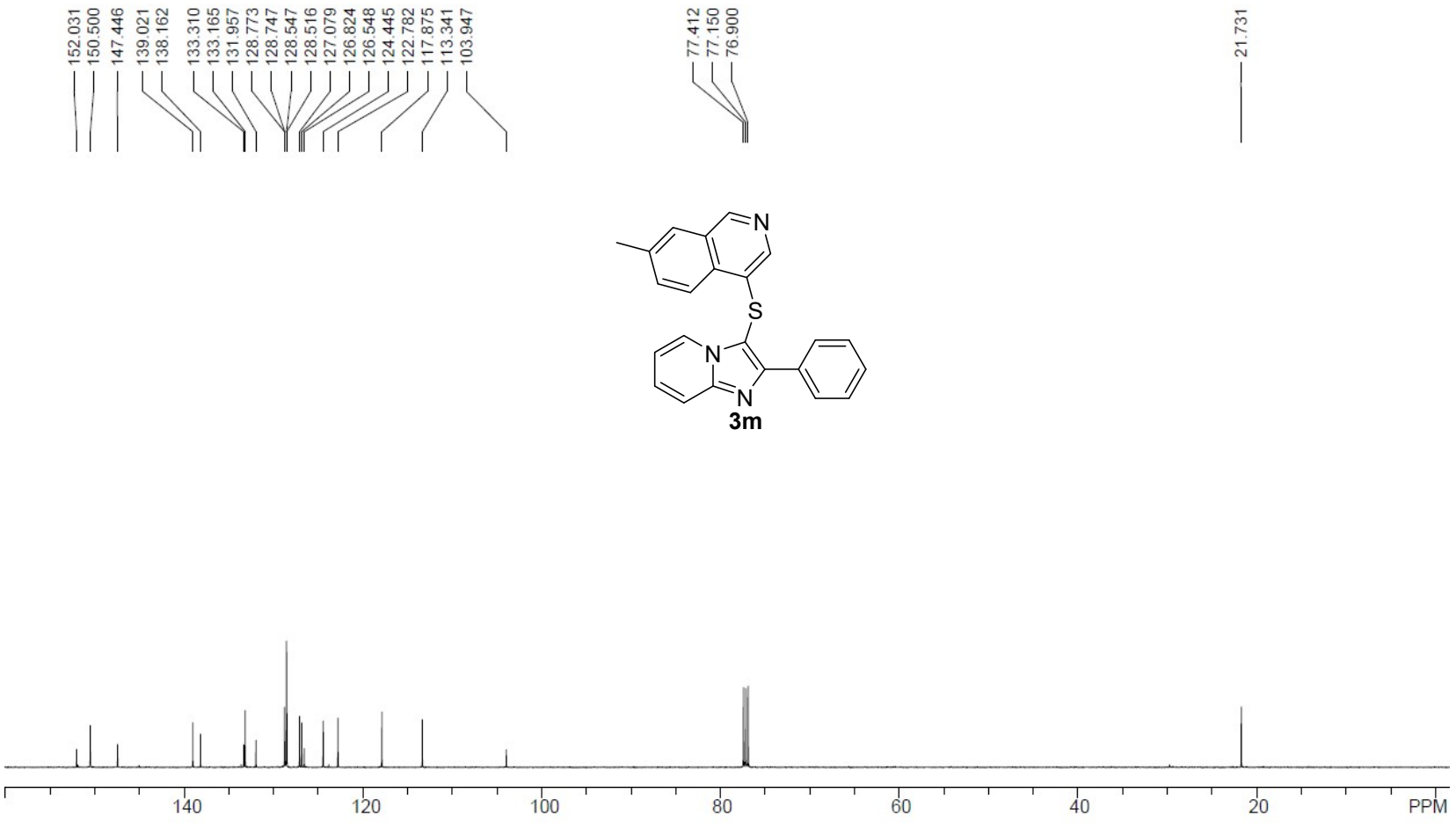


^{13}C NMR (126 MHz, $CDCl_3$) of **3m**



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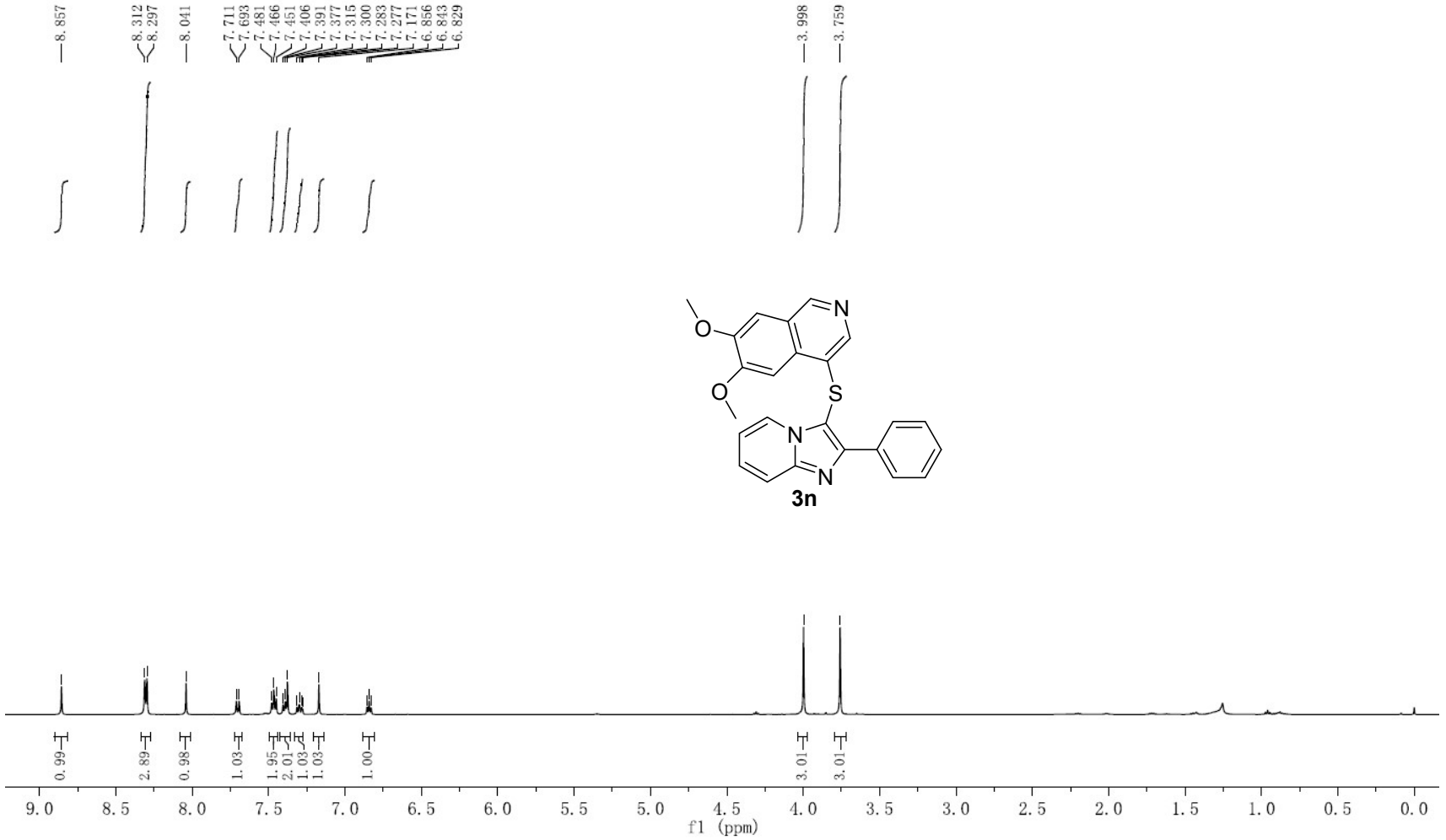
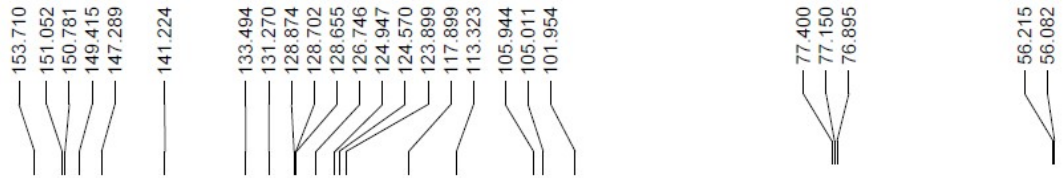
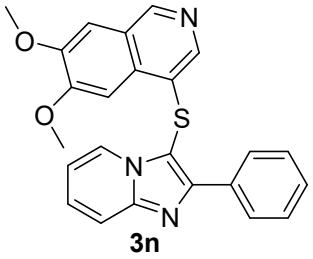
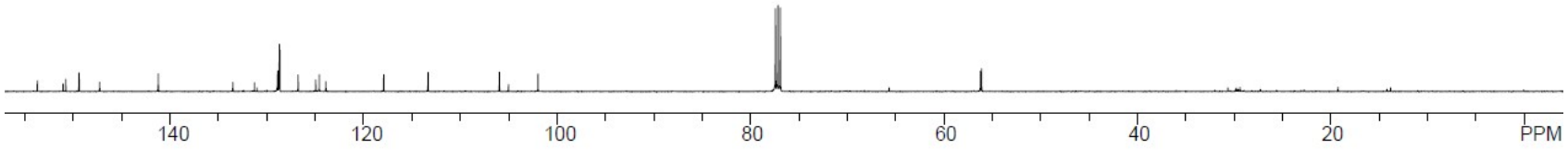


^{13}C NMR (126 MHz, $CDCl_3$) of **3n**

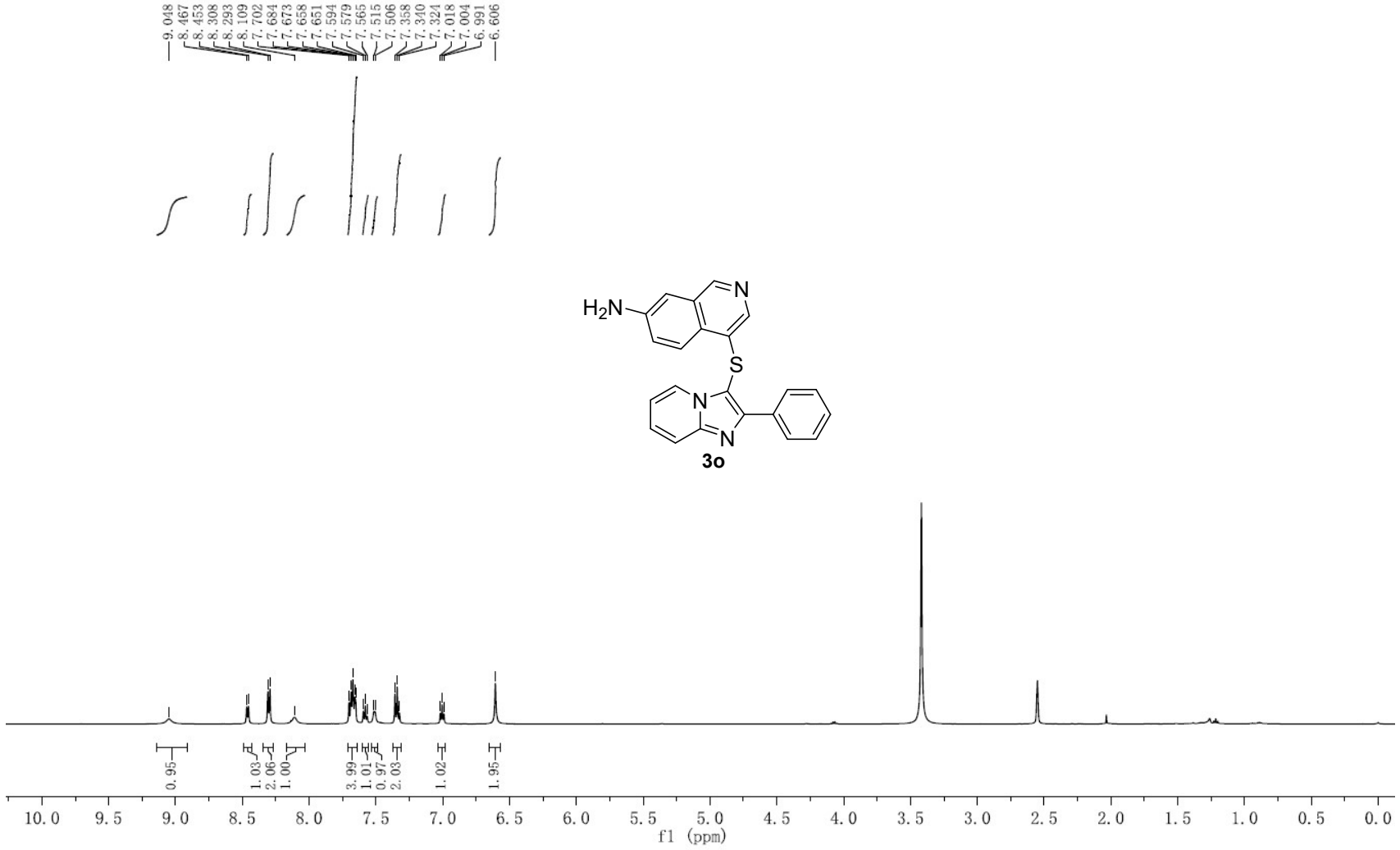




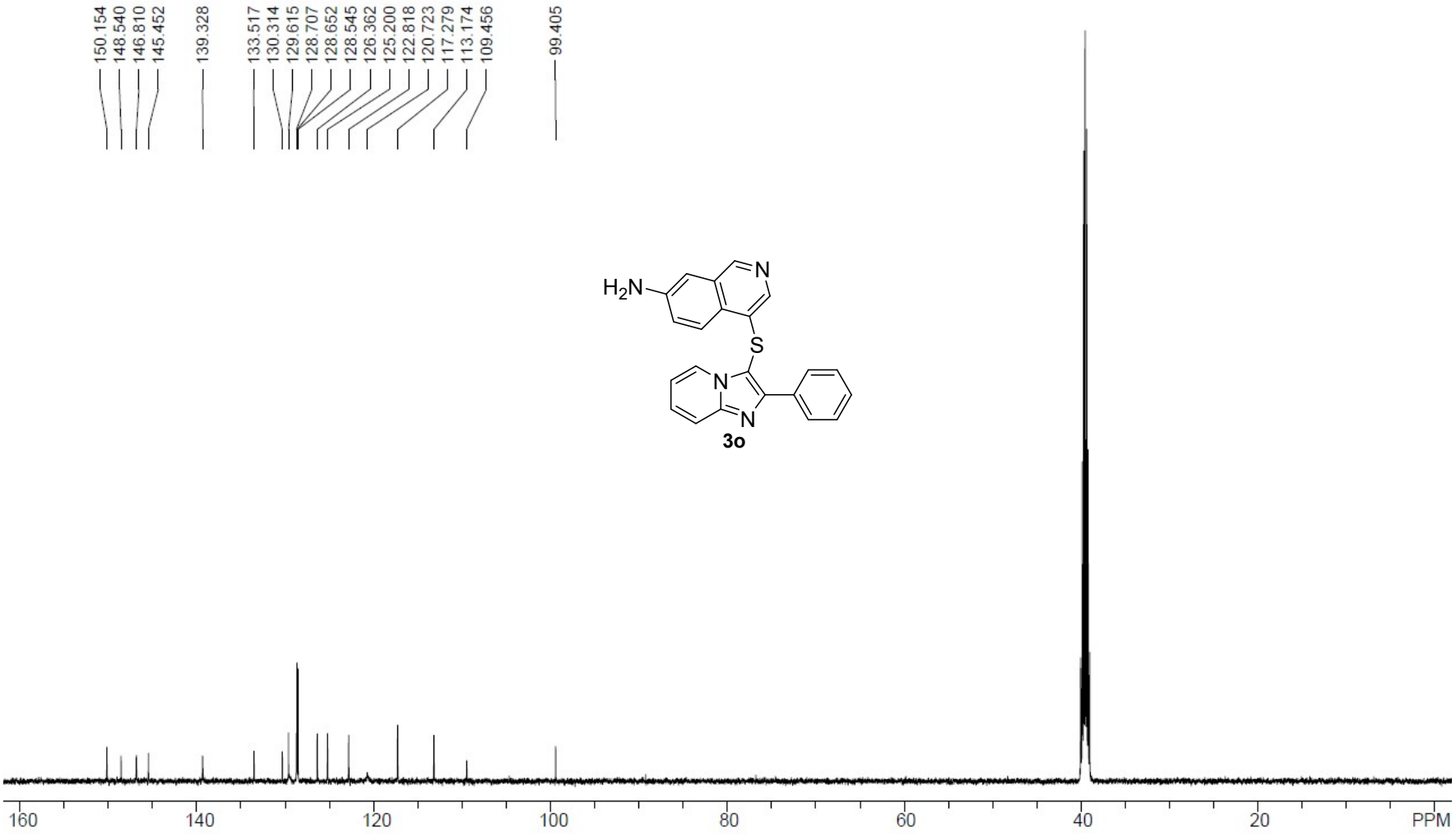
3n



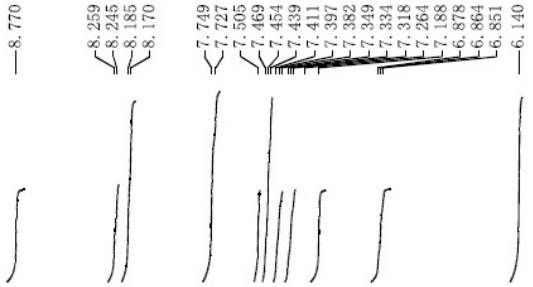
^{1}H NMR (500 MHz, DMSO-d_6) of **3o**

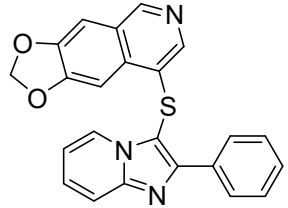


^{13}C NMR (126 MHz, DMSO-d_6) of **3o**



^{1}H NMR (500 MHz, $CDCl_3$) of **3p**





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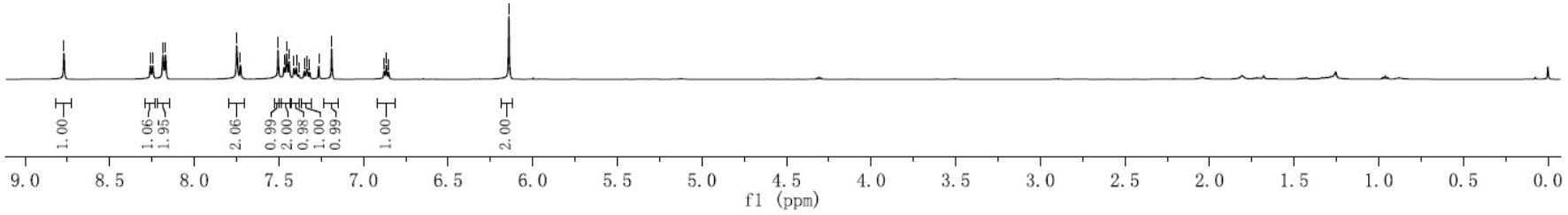
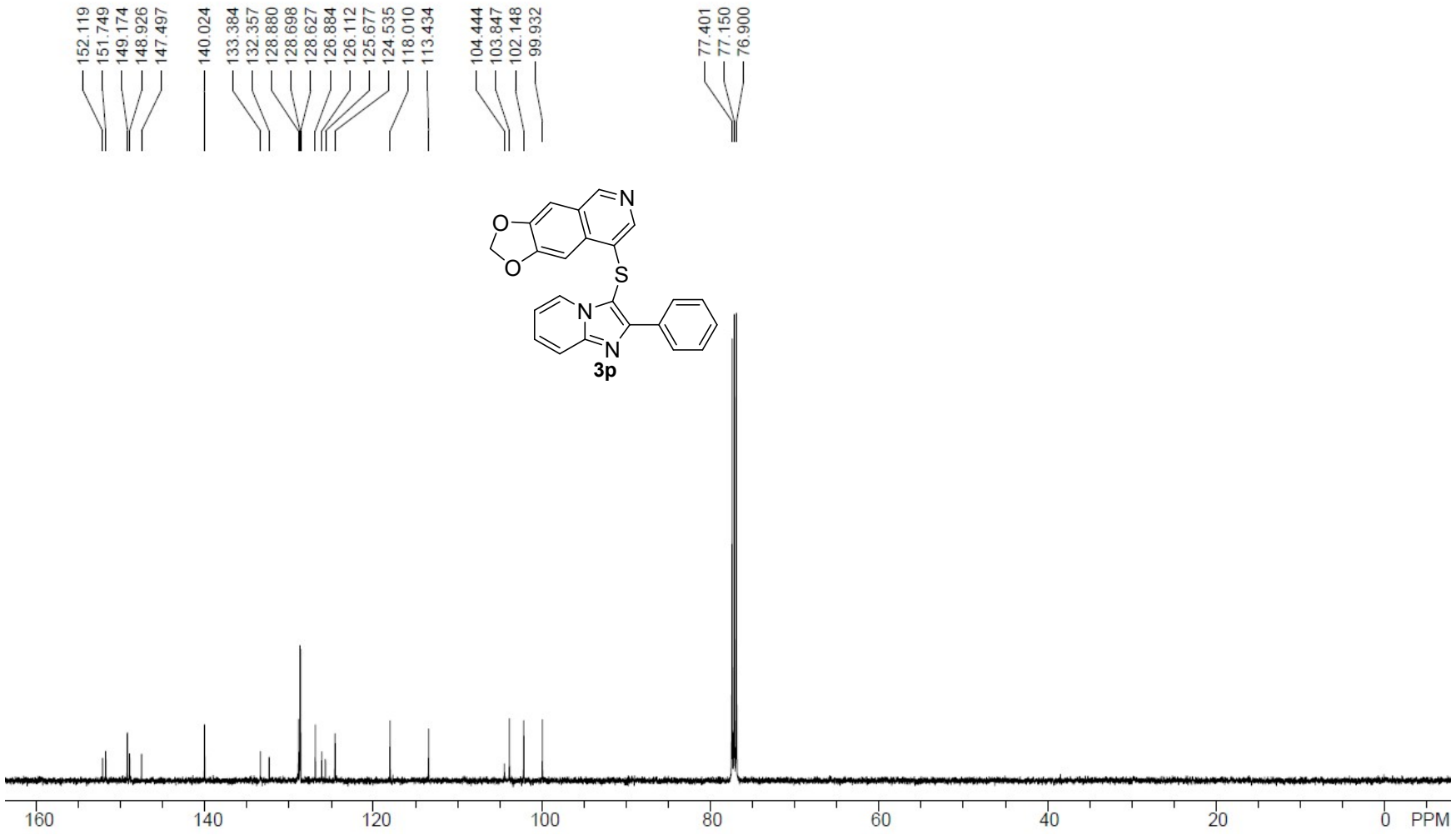
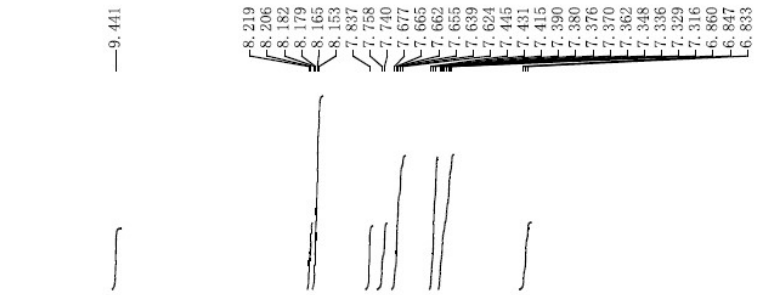
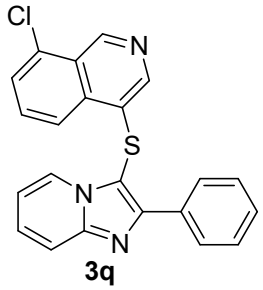


^{13}C NMR (126 MHz, $CDCl_3$) of **3p**

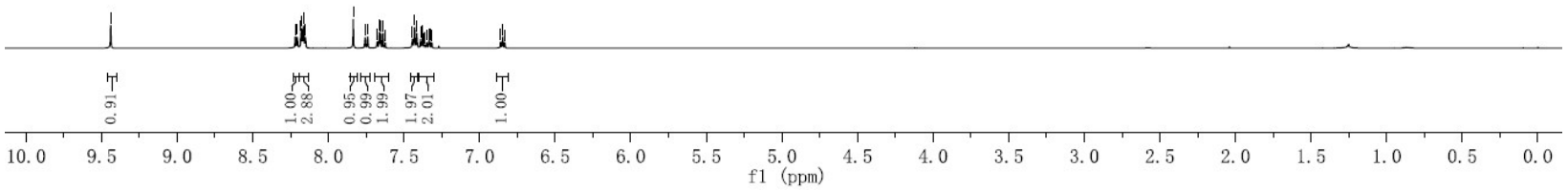


^{1}H NMR (500 MHz, $CDCl_3$) of **3q**

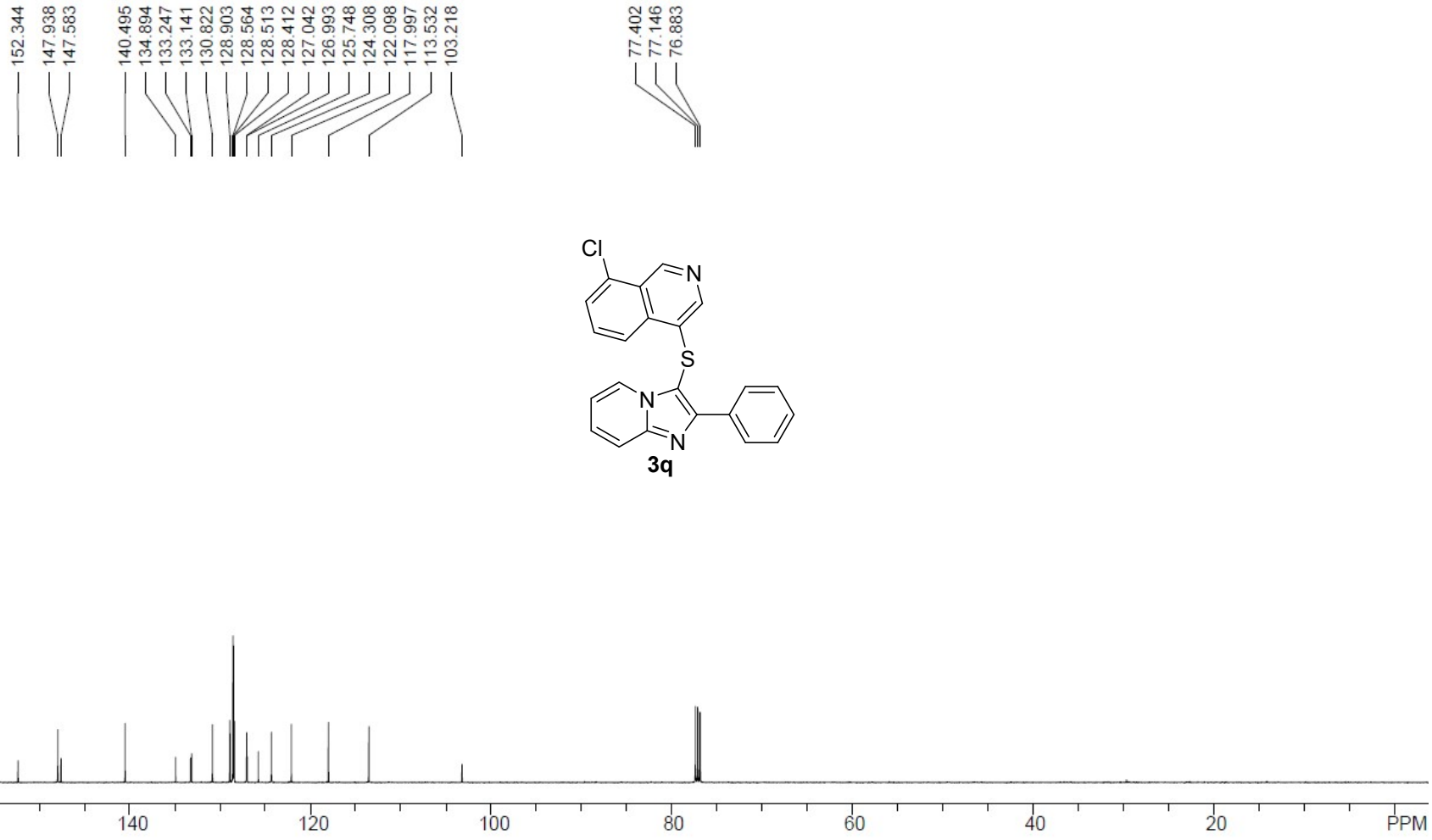




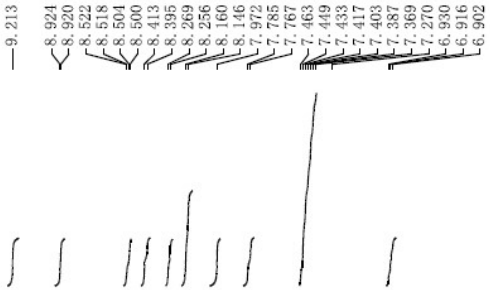
3q

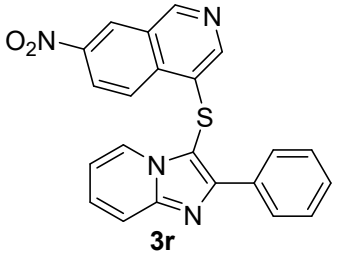


^{13}C NMR (126 MHz, $CDCl_3$) of **3q**

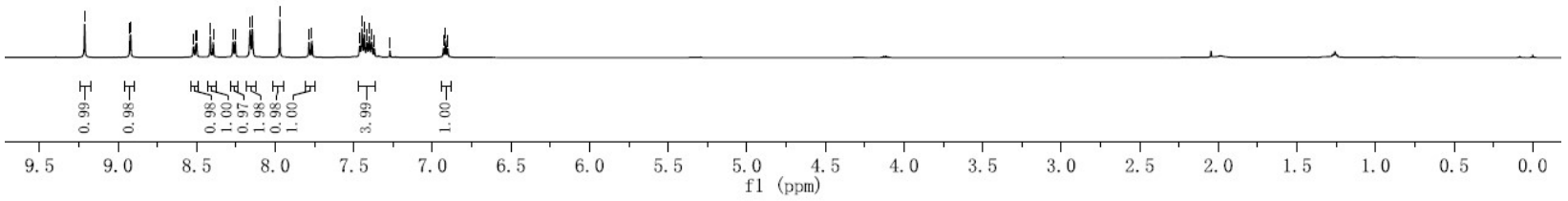


^{1}H NMR (500 MHz, $CDCl_3$) of **3r**

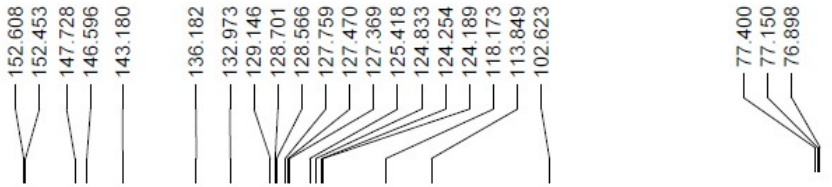


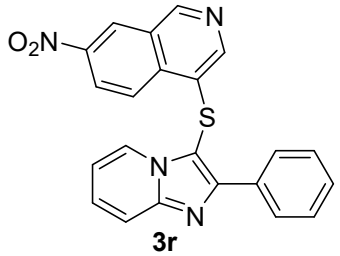


3r

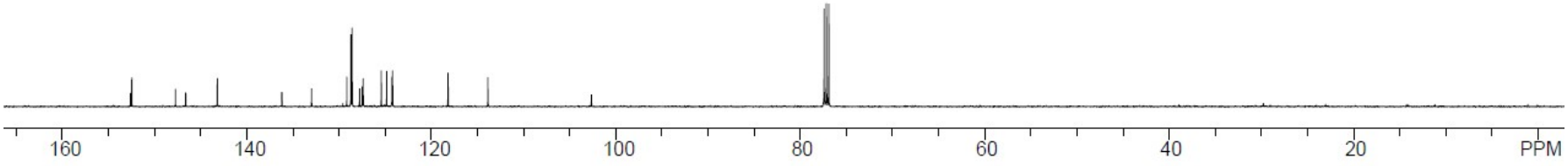


^{13}C NMR (126 MHz, $CDCl_3$) of **3r**

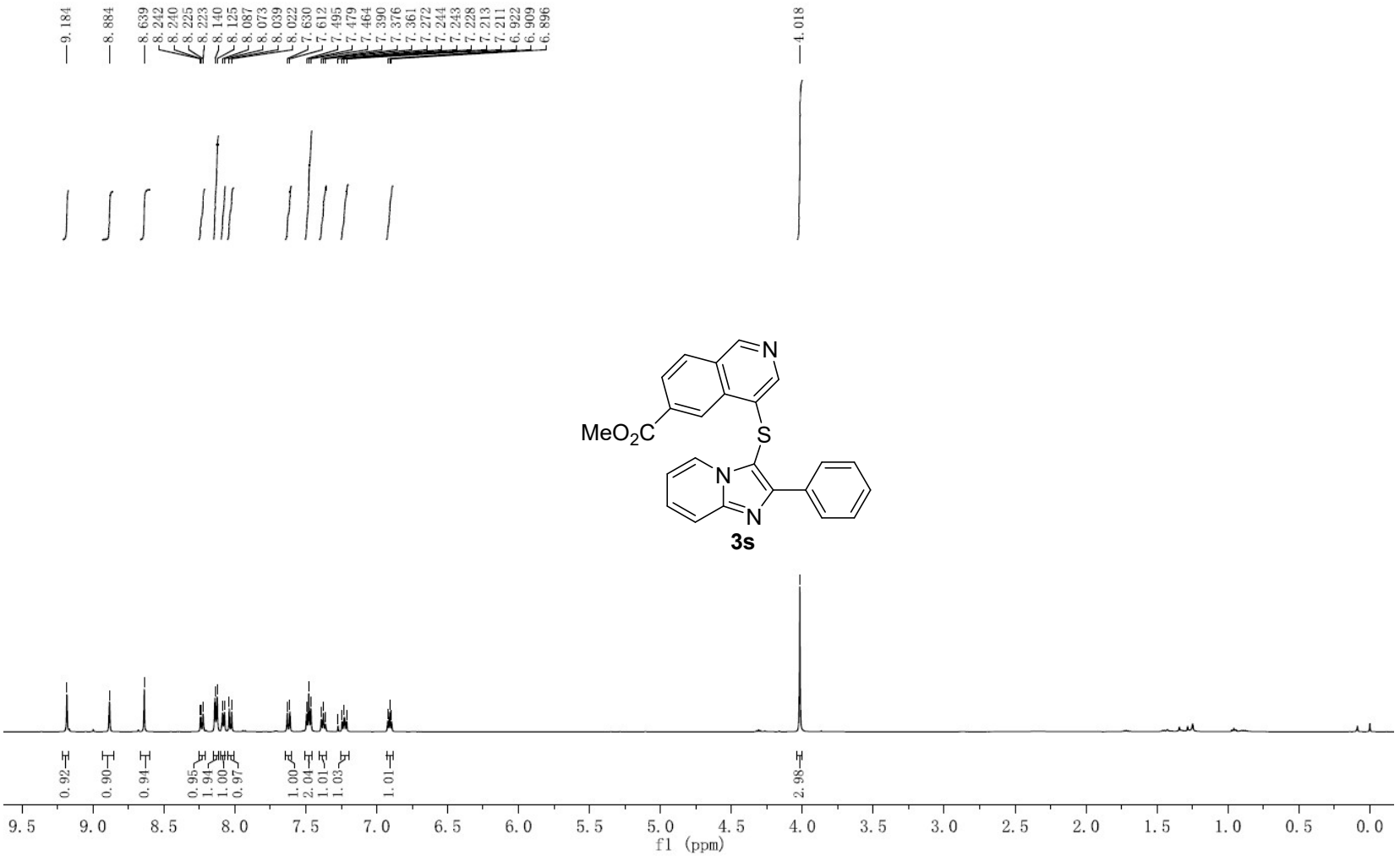




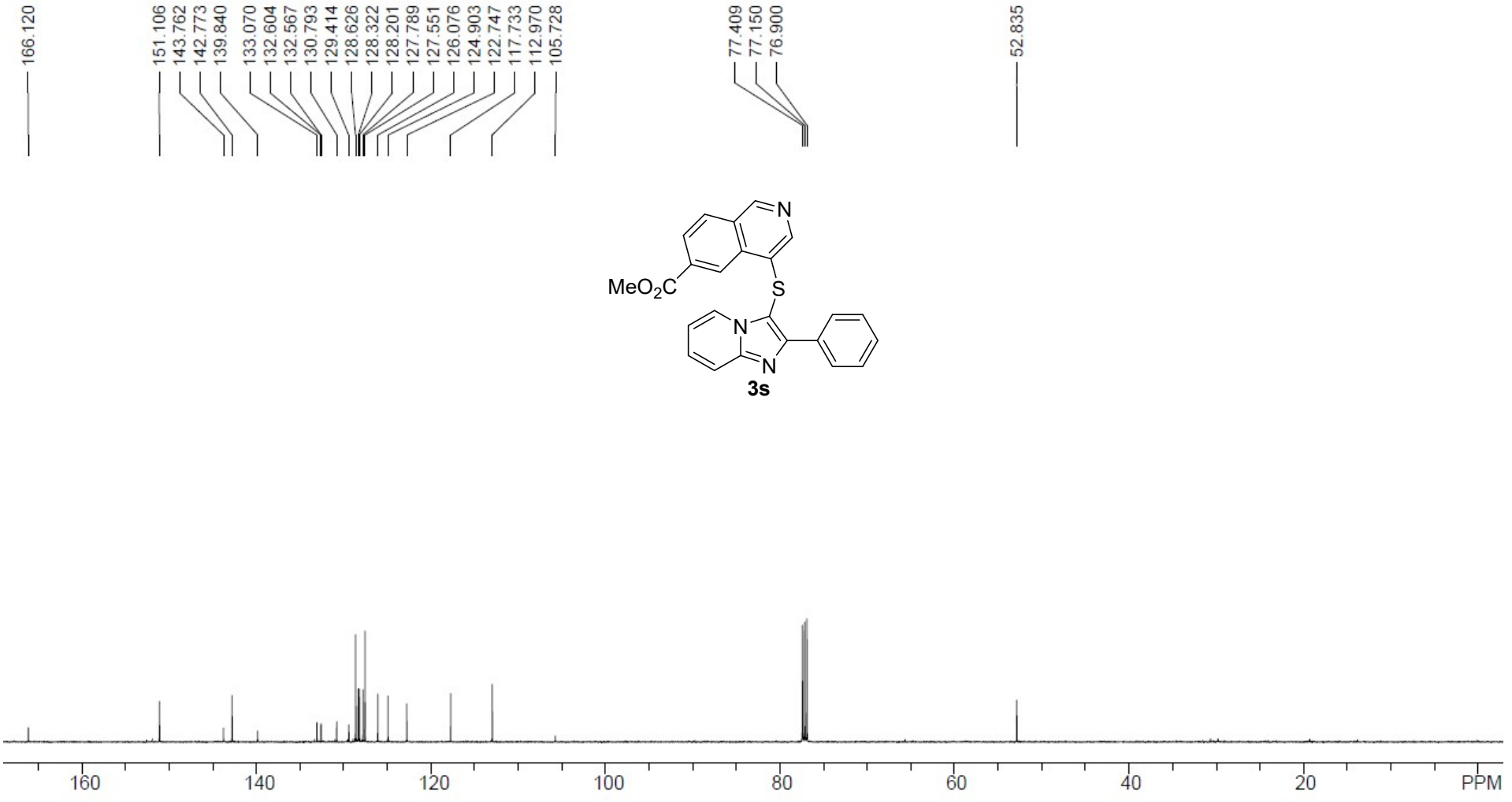
3r



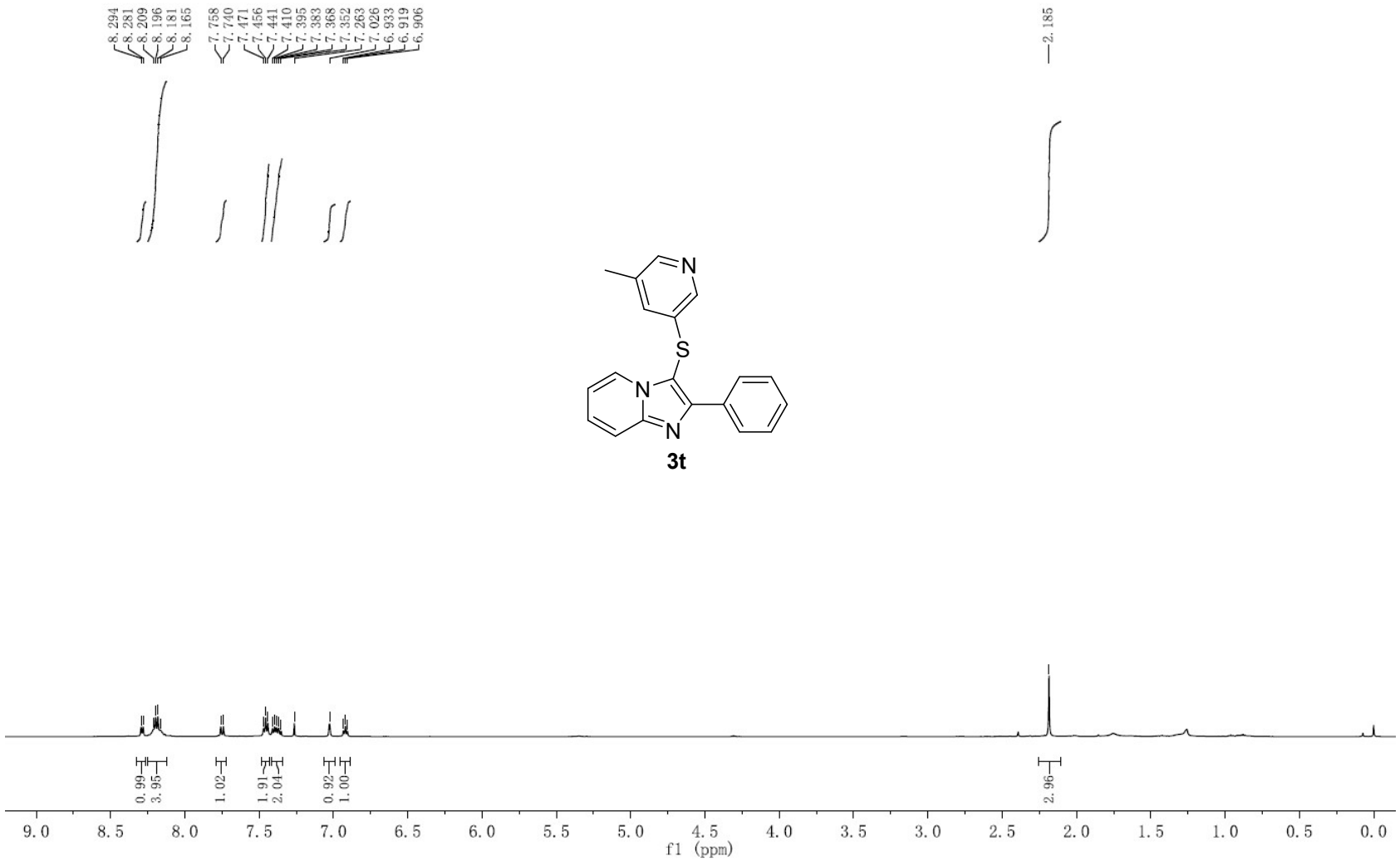
^{1}H NMR (500 MHz, $CDCl_3$) of **3s**



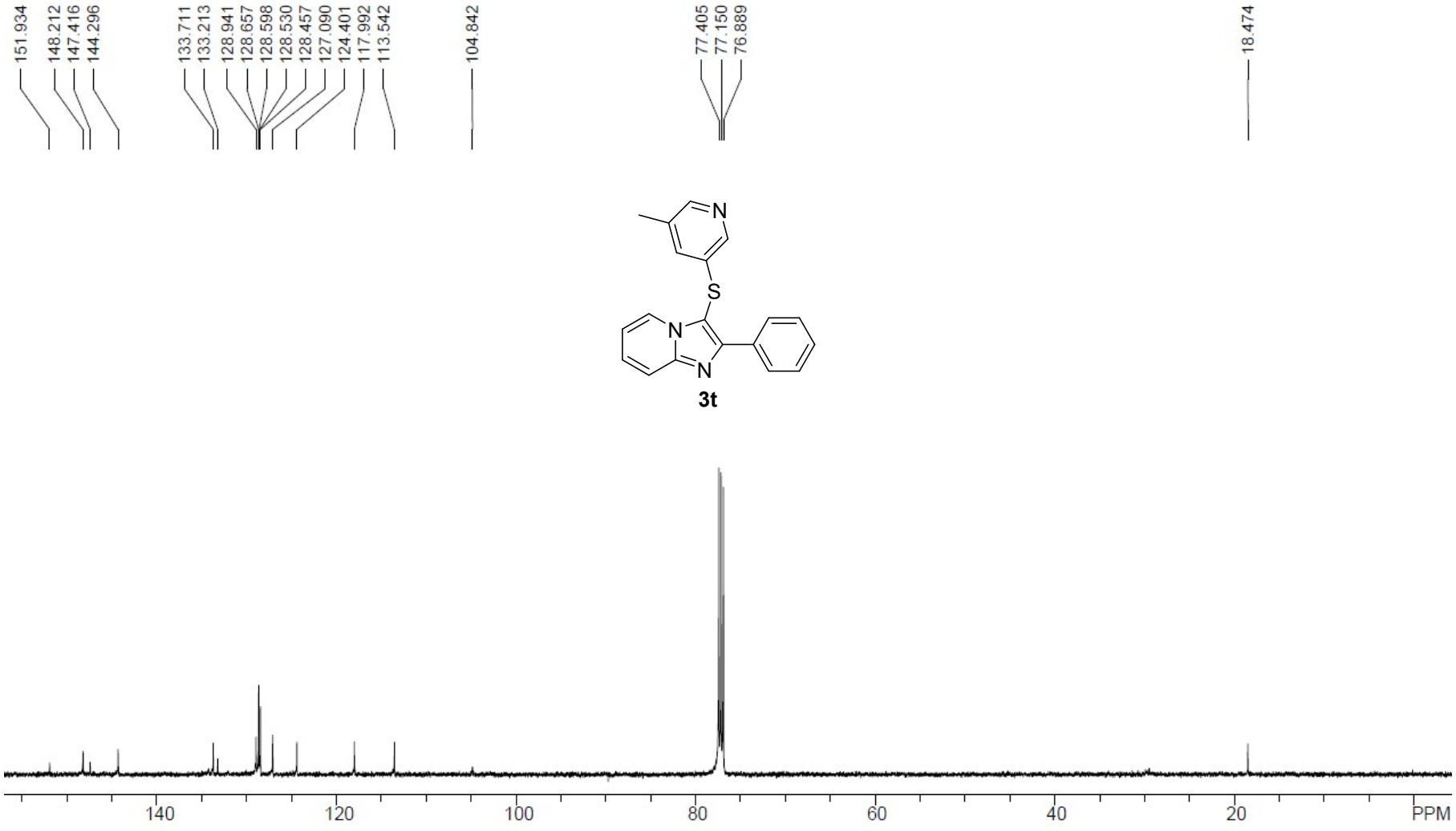
^{13}C NMR (126 MHz, $CDCl_3$) of **3s**



^{1}H NMR (500 MHz, $CDCl_3$) of **3t**

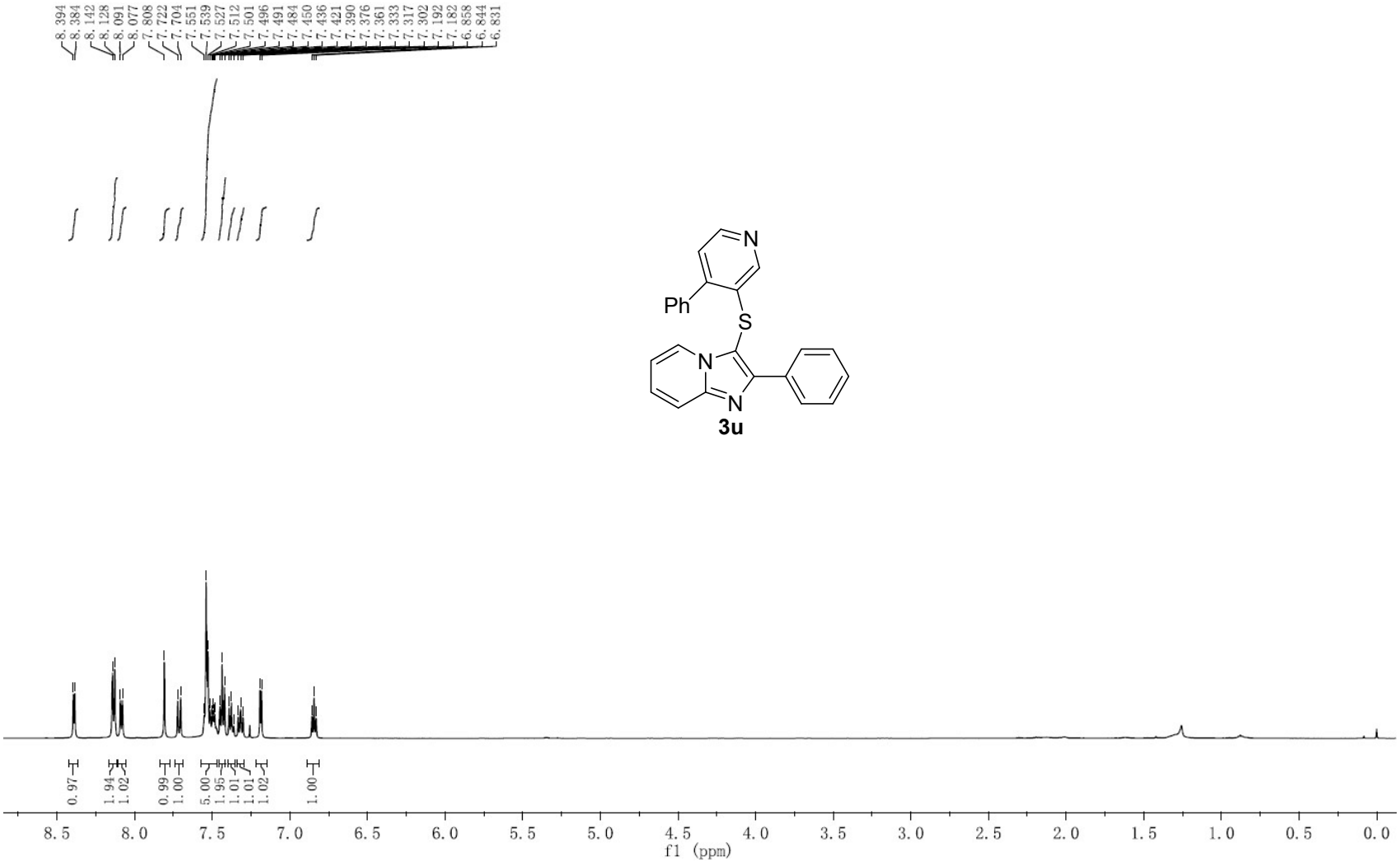


^{13}C NMR (126 MHz, $CDCl_3$) of **3t**



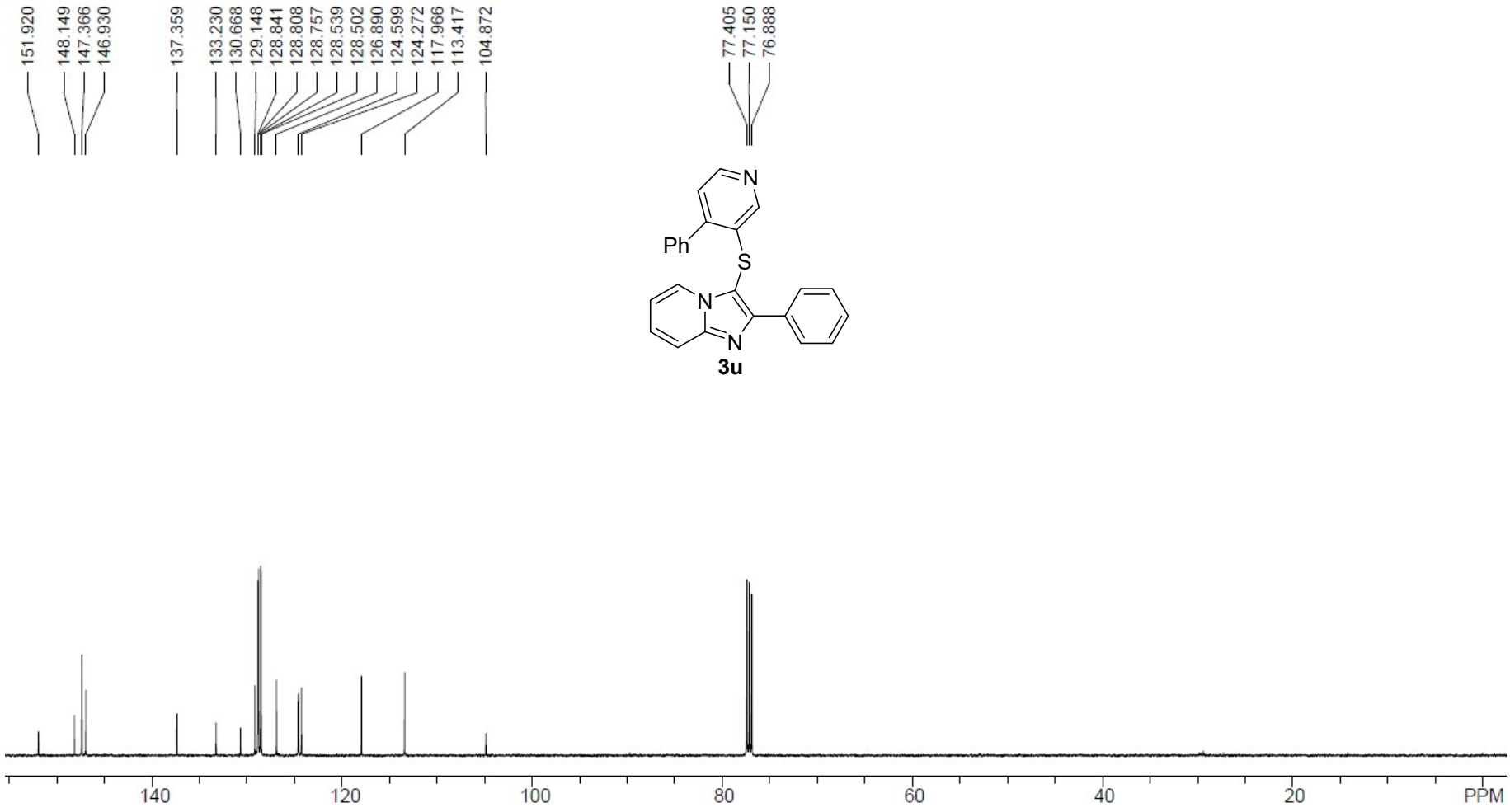
3t

^{1}H NMR (500 MHz, $CDCl_3$) of **3u**

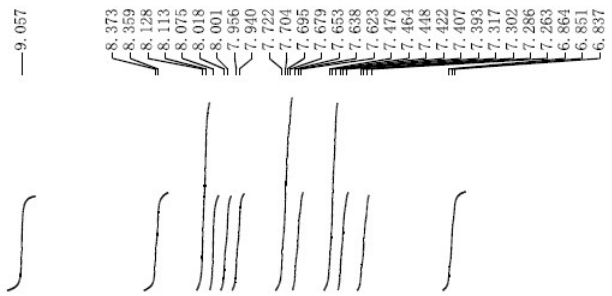


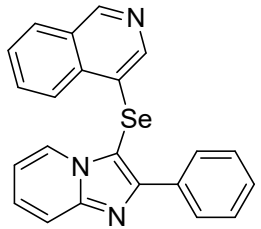
3u

^{13}C NMR (126 MHz, $CDCl_3$) of **3u**

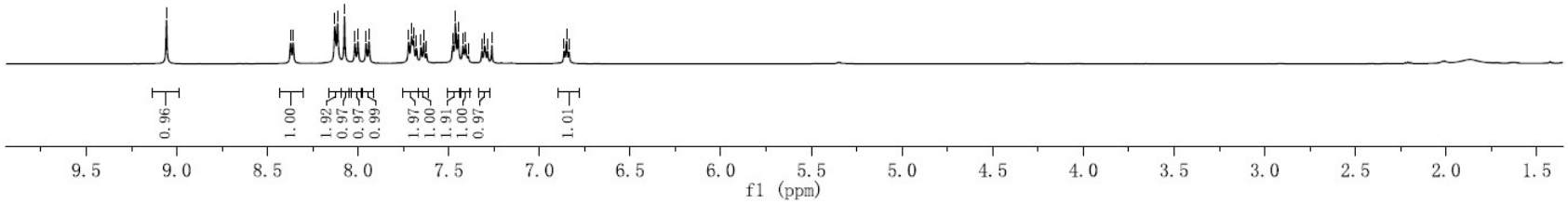


^{1}H NMR (500 MHz, $CDCl_3$) of **3v**

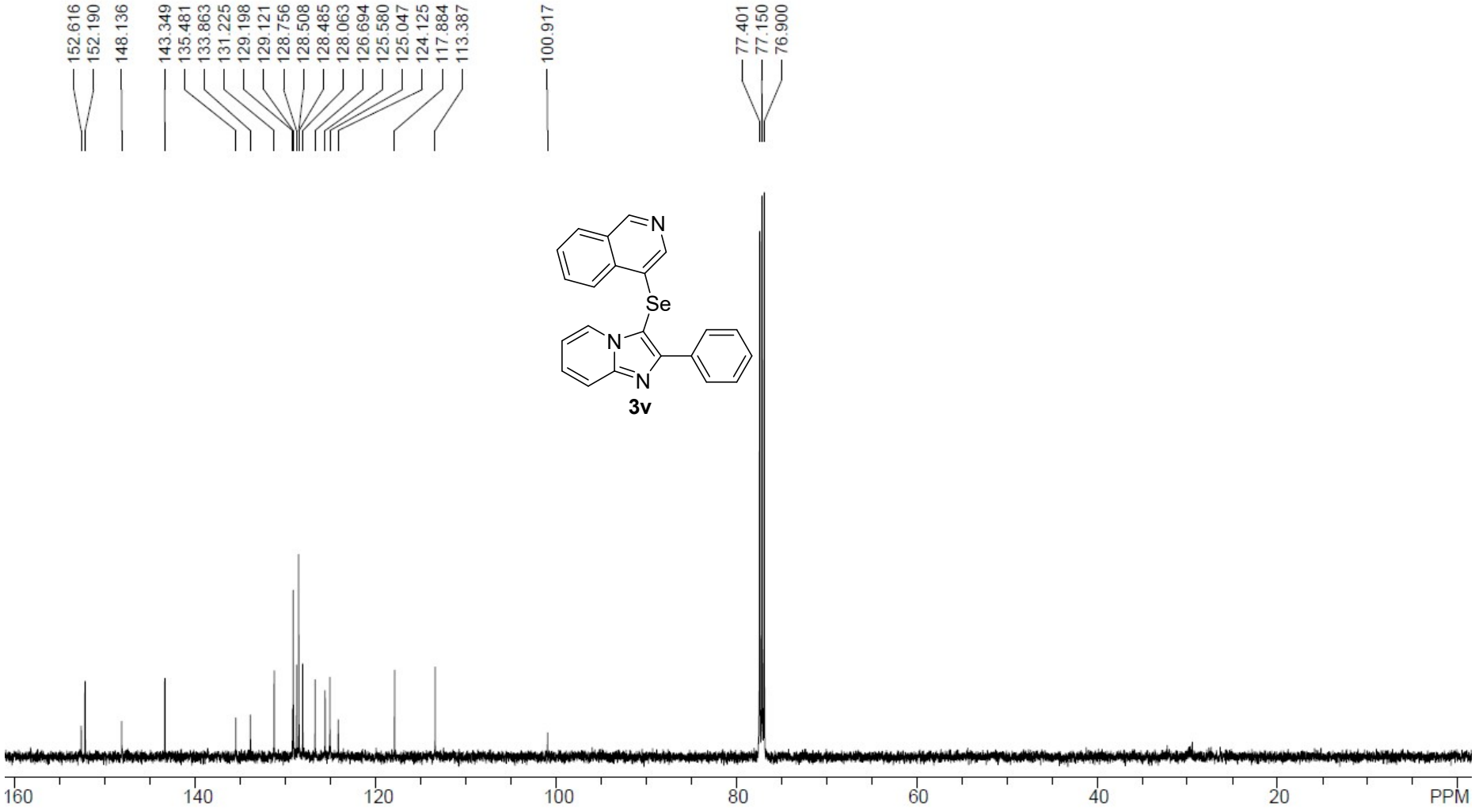




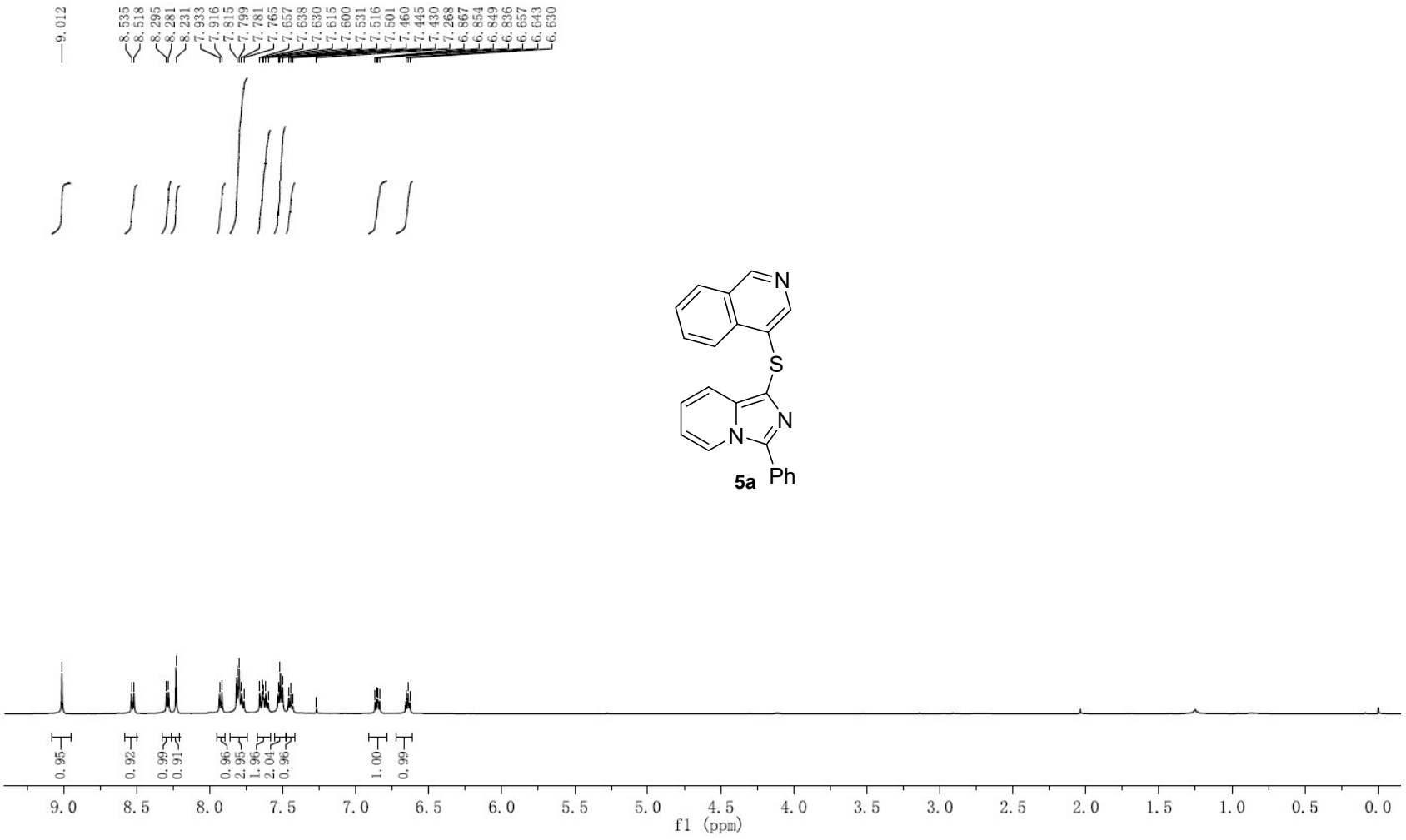
3v



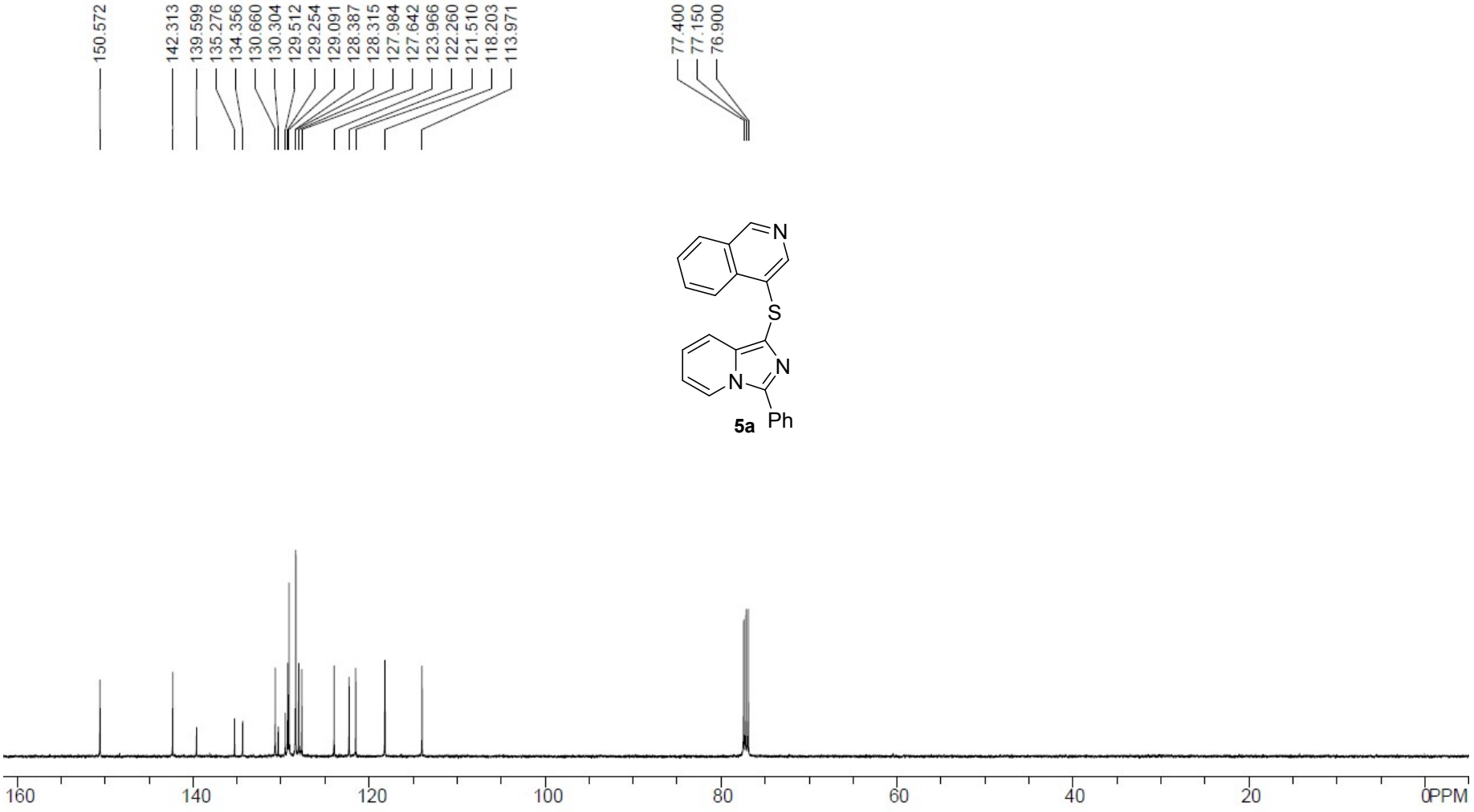
^{13}C NMR (126 MHz, $CDCl_3$) of **3v**



^{1}H NMR (500 MHz, $CDCl_3$) of **5a**

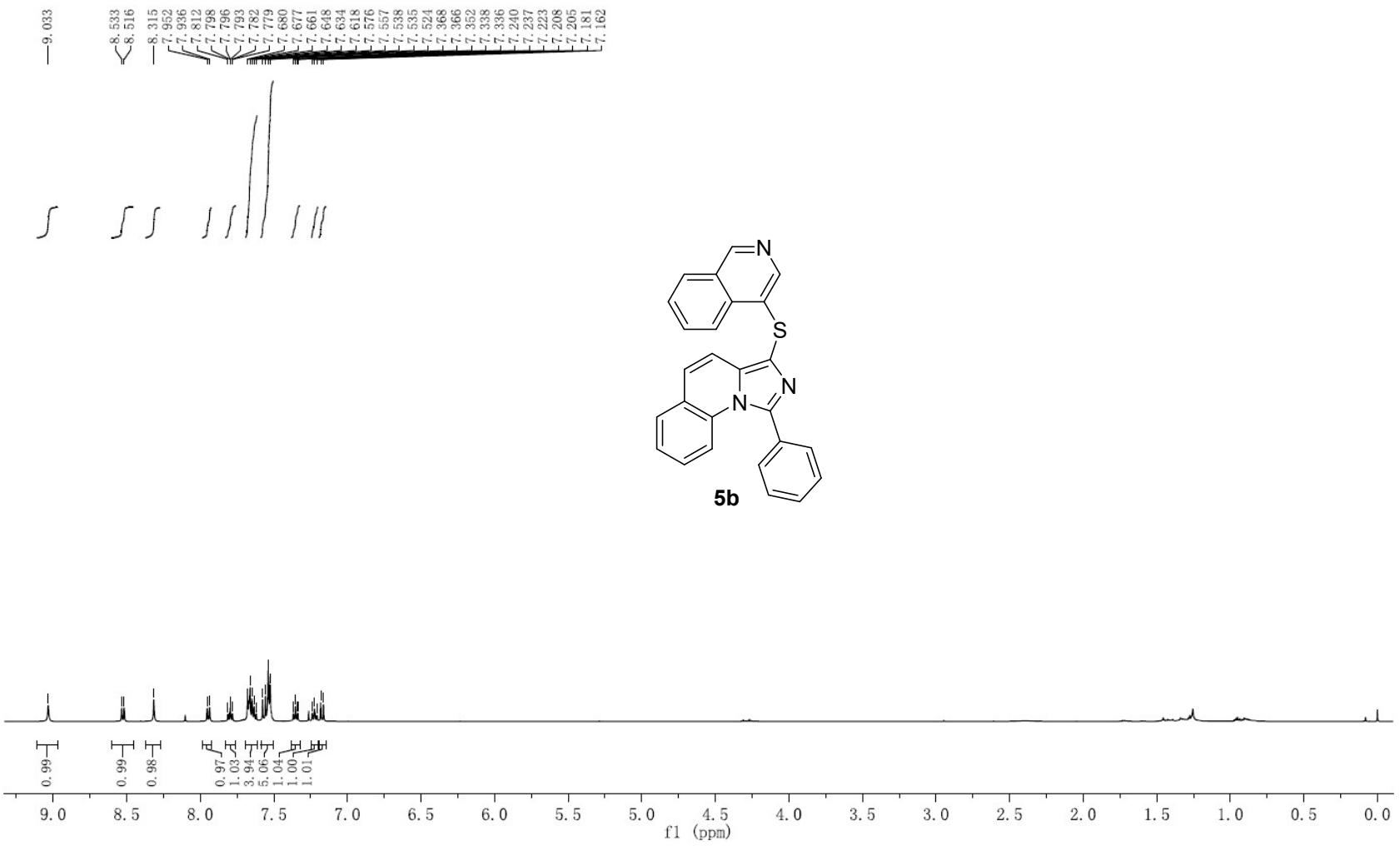


^{13}C NMR (126 MHz, $CDCl_3$) of **5a**



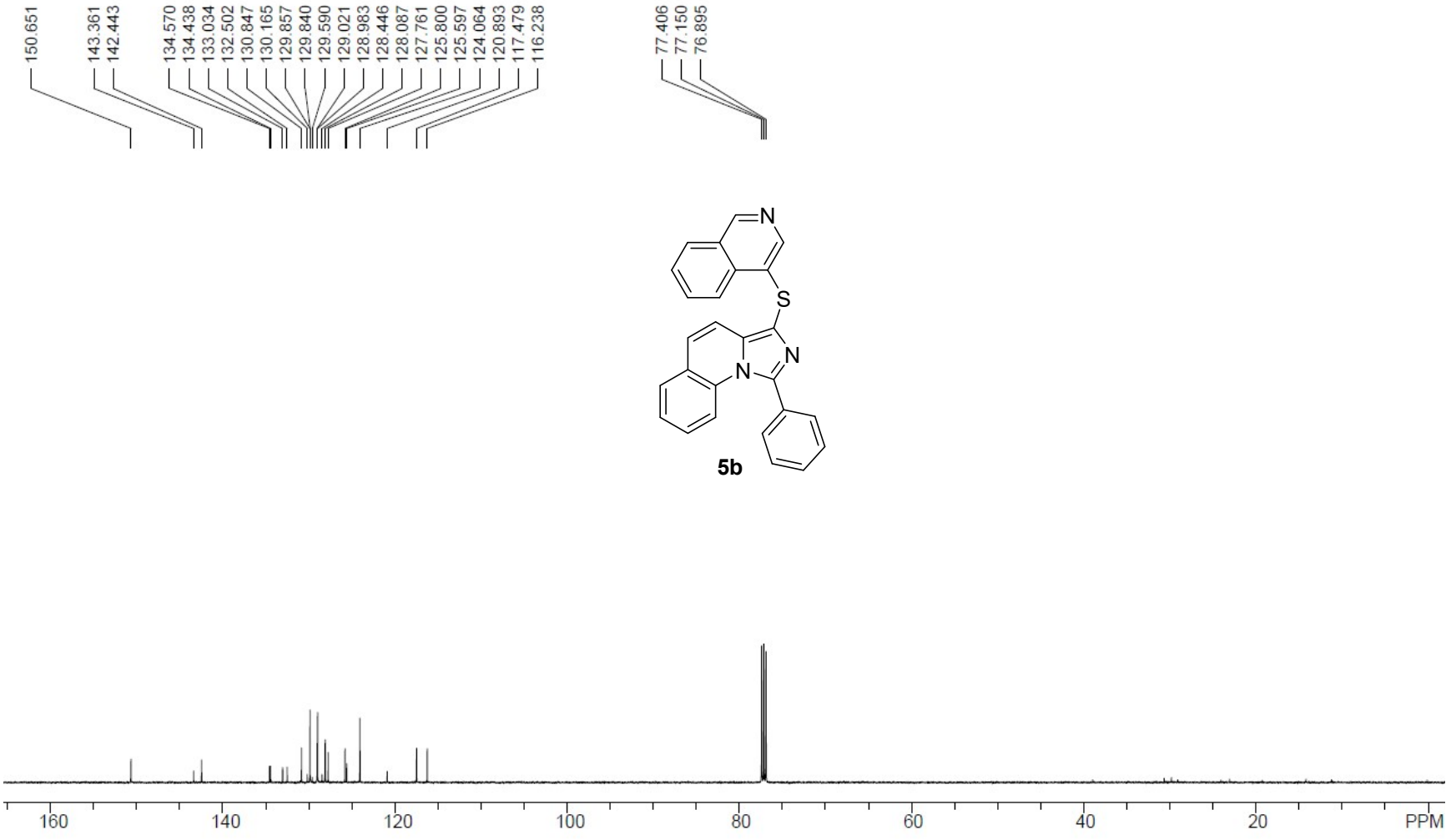
5a

^{1}H NMR (500 MHz, $CDCl_3$) of **5b**

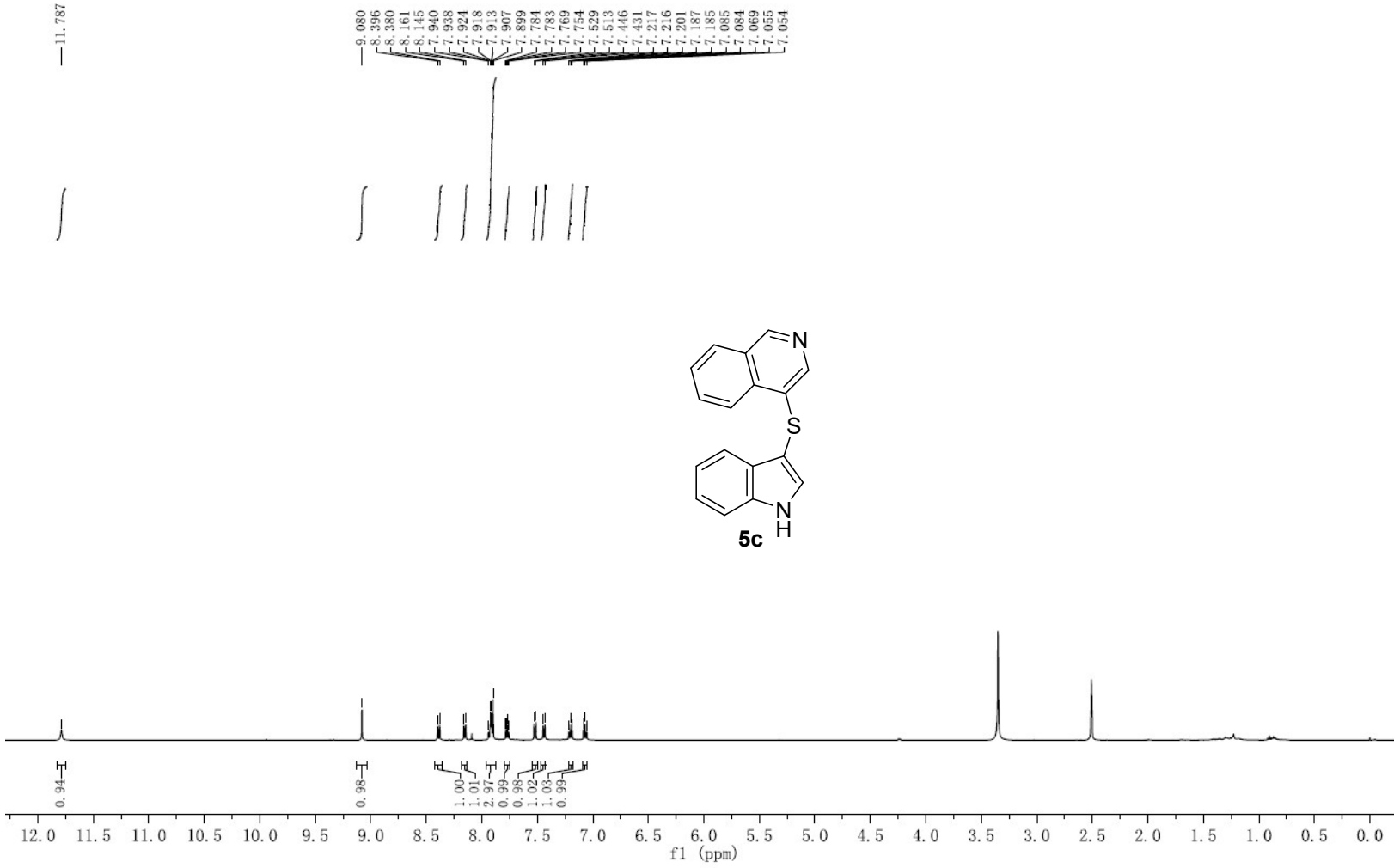


5b

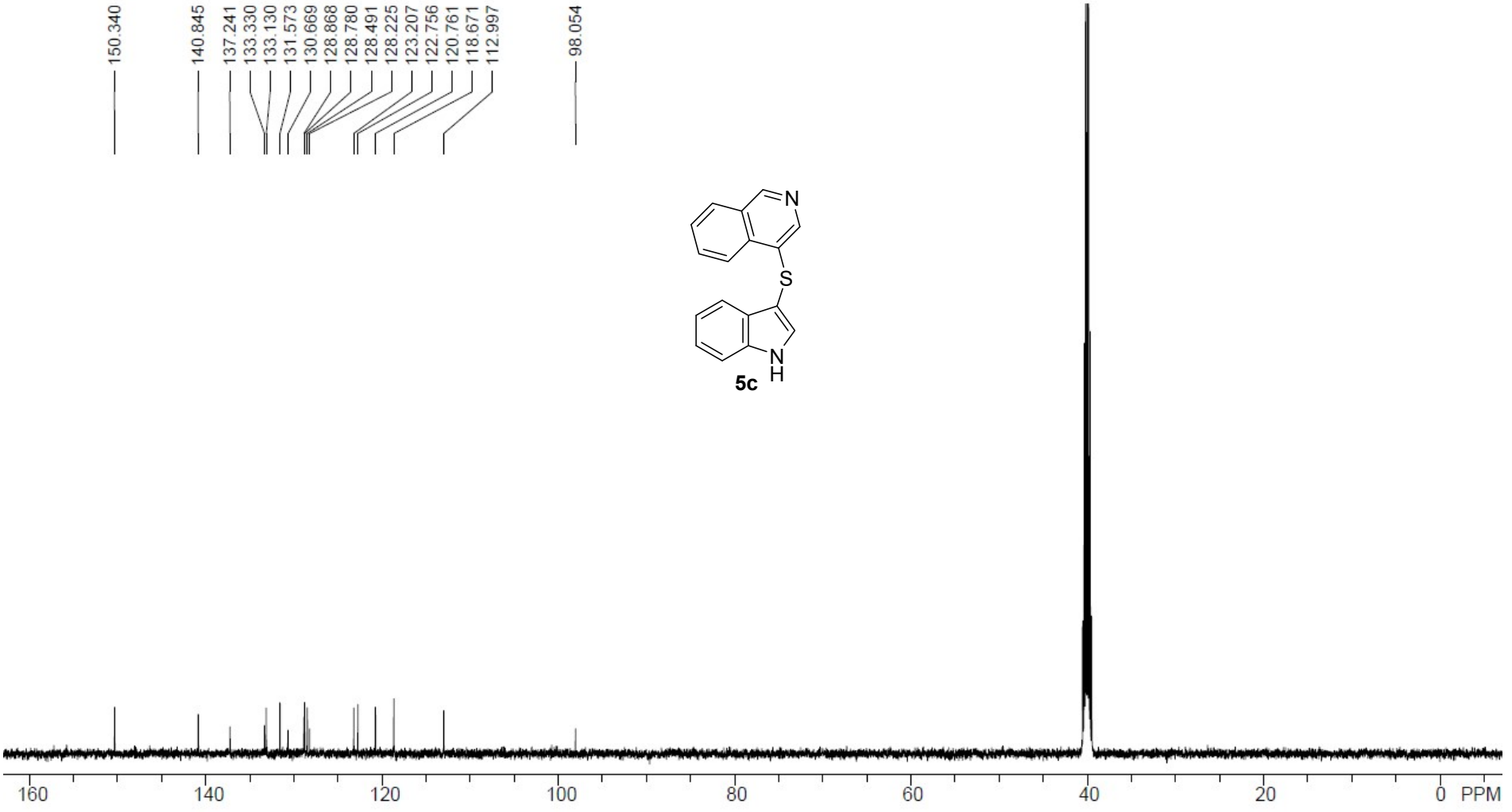
^{13}C NMR (126 MHz, $CDCl_3$) of **5b**



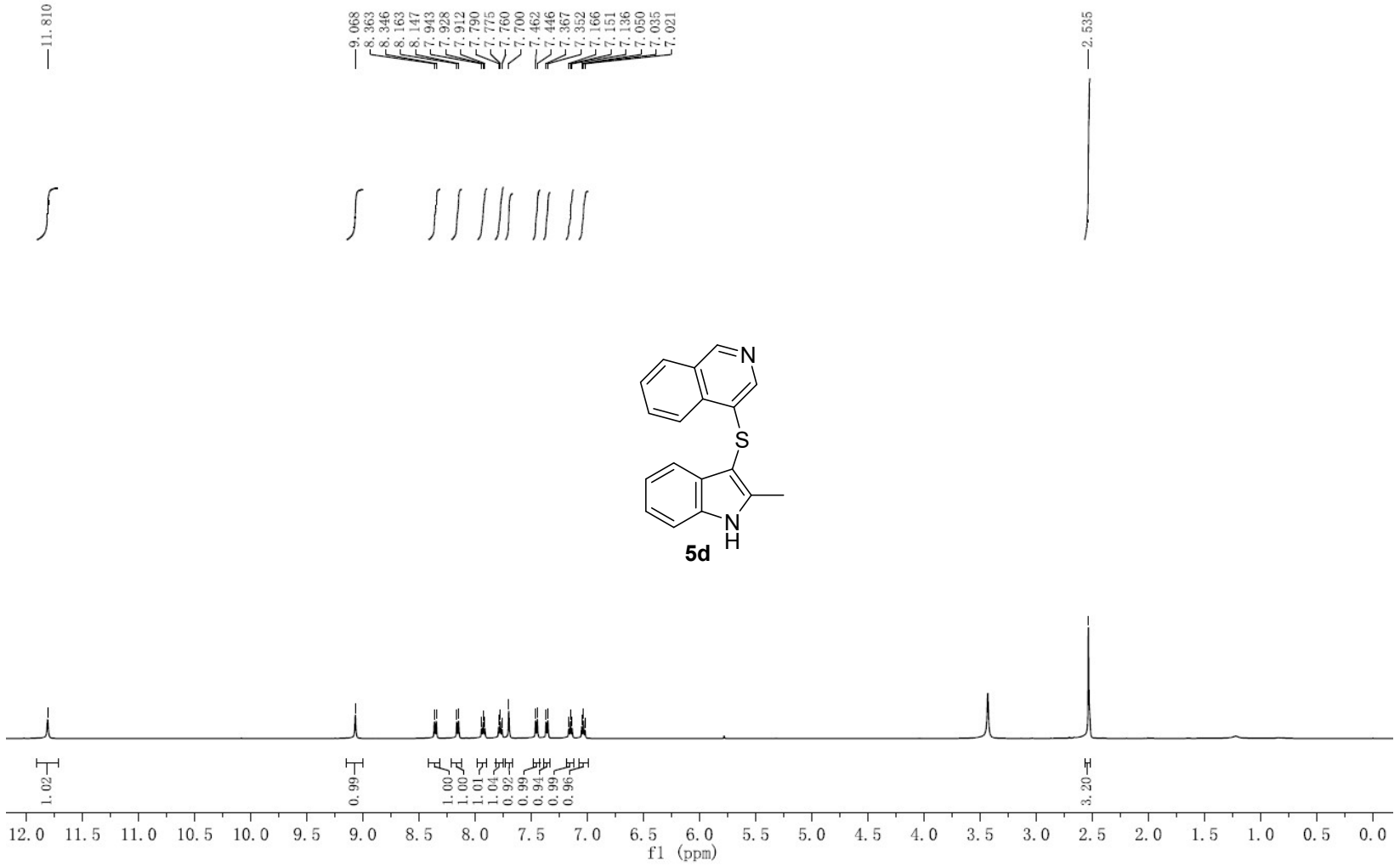
^{1}H NMR (500 MHz, DMSO-d_6) of **5c**



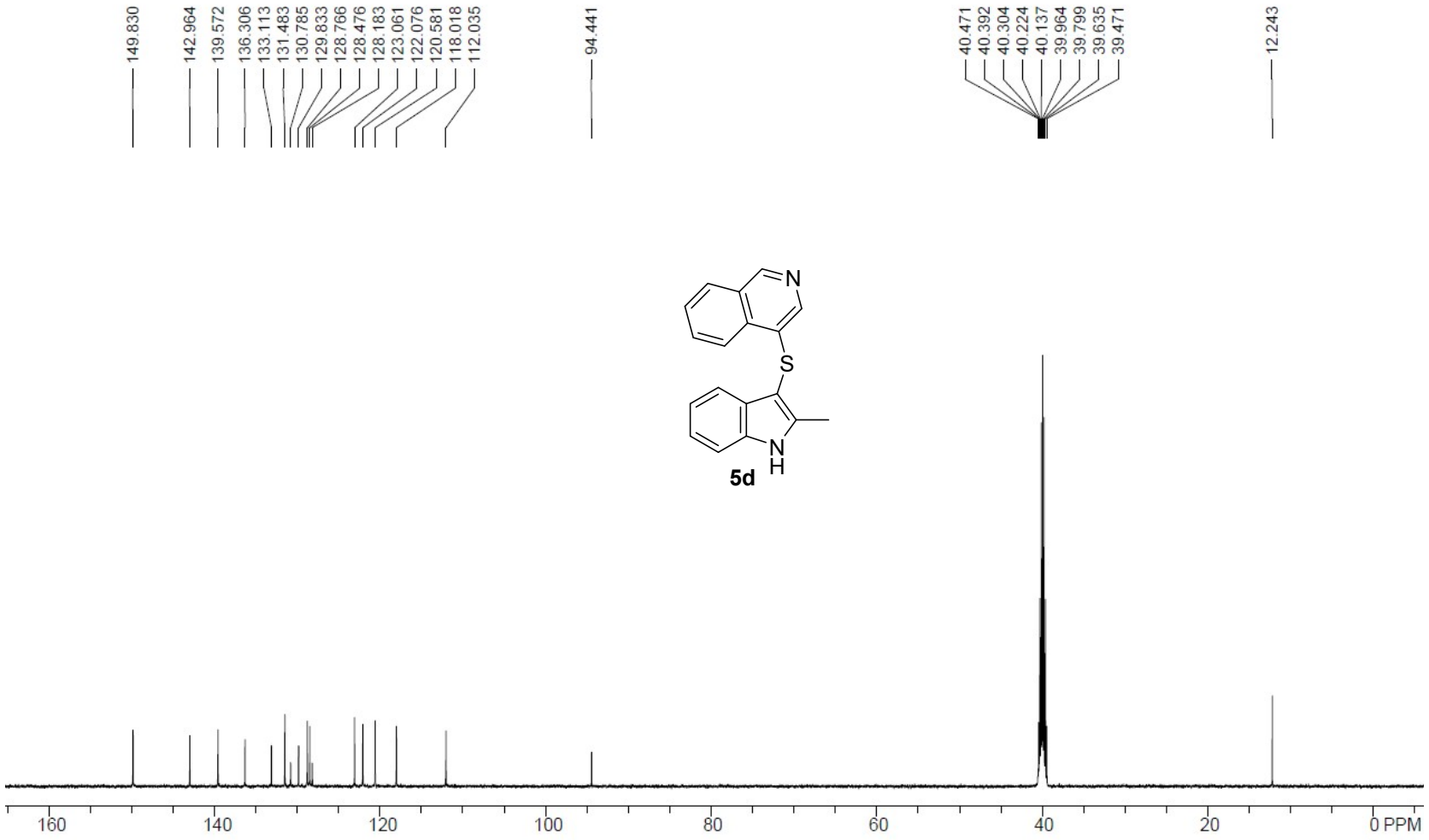
^{13}C NMR (126 MHz, DMSO-d_6) of **5c**



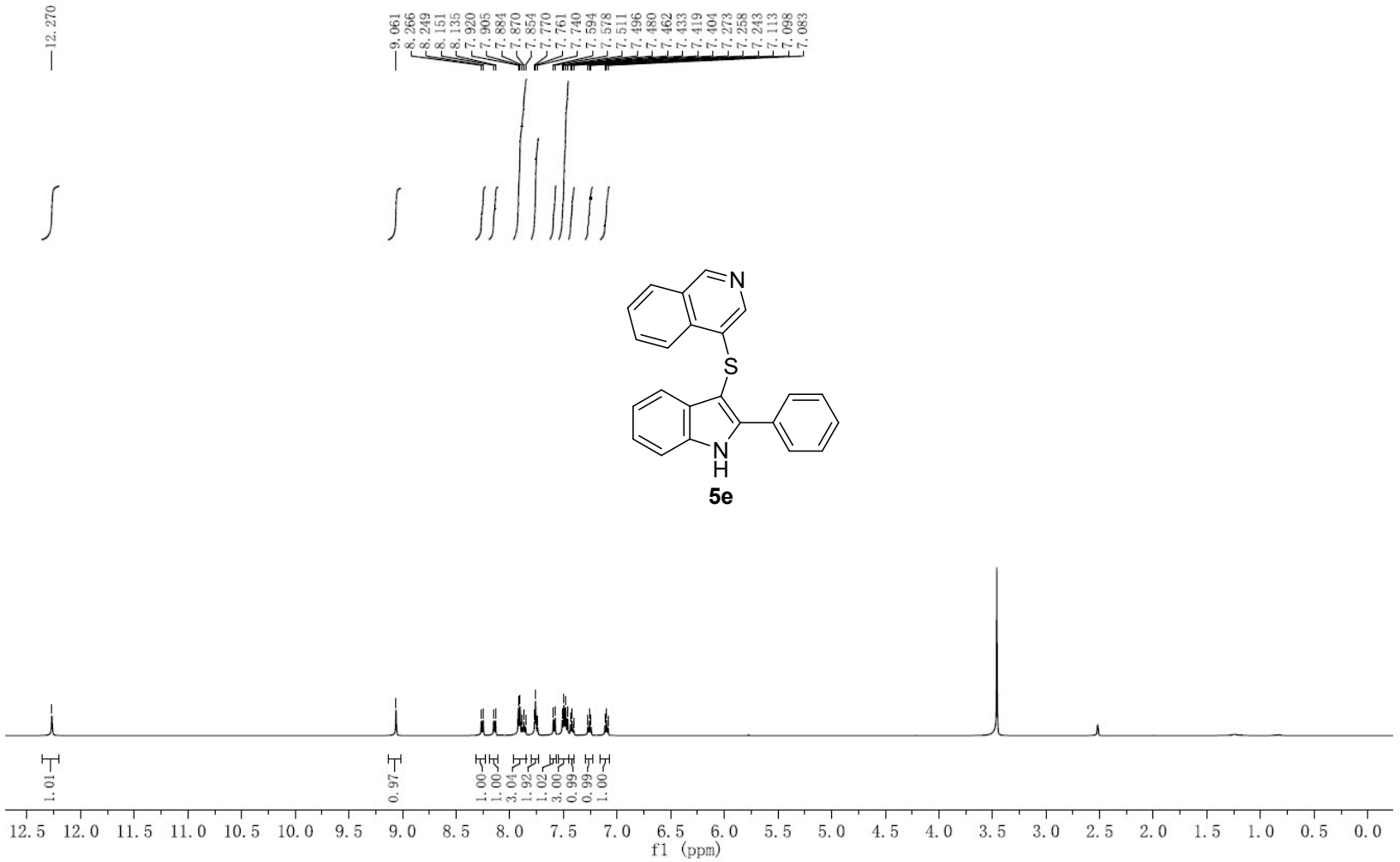
^{1}H NMR (500 MHz, DMSO-d_6) of **5d**



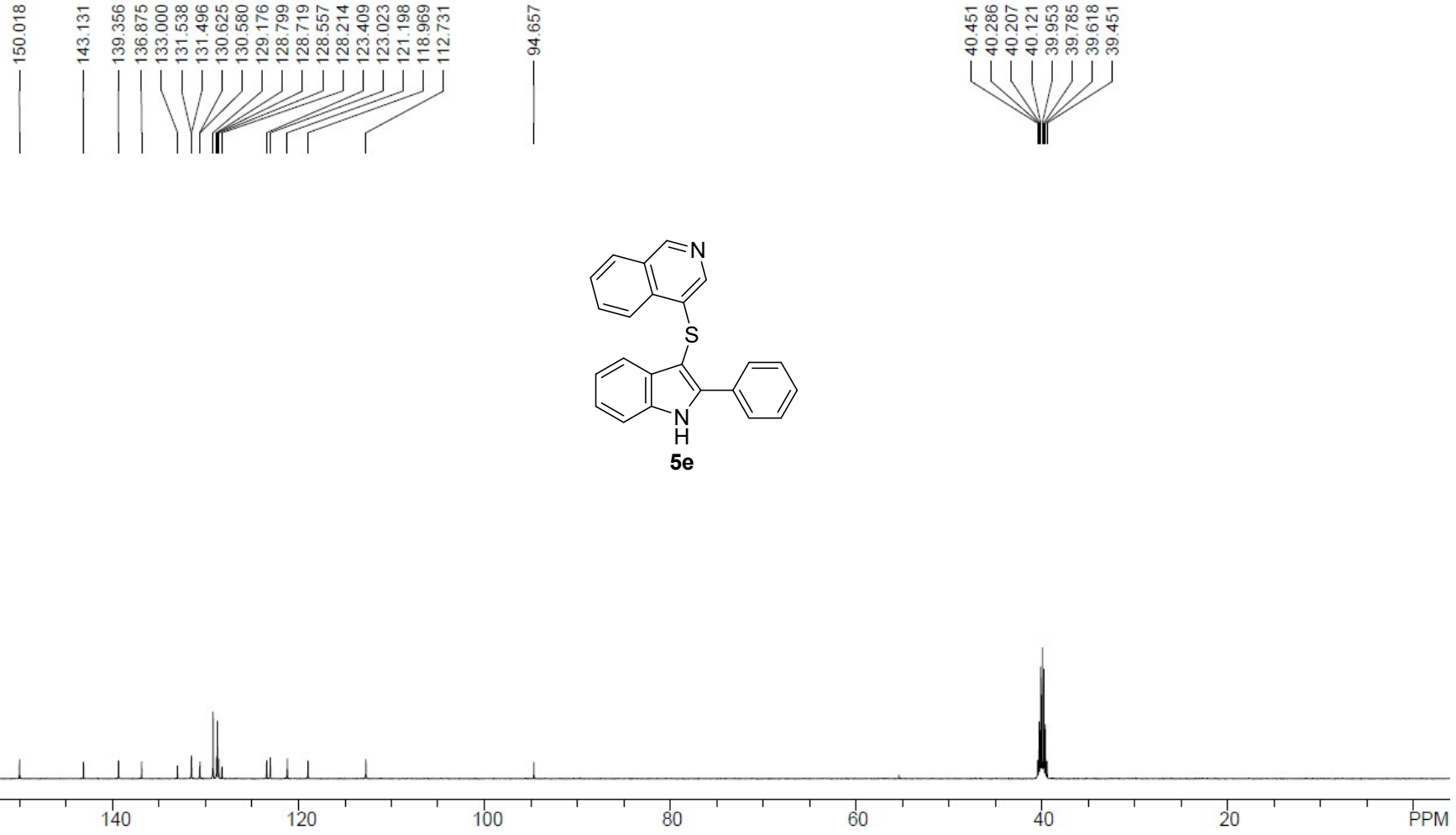
^{13}C NMR (126 MHz, DMSO-d_6) of **5d**



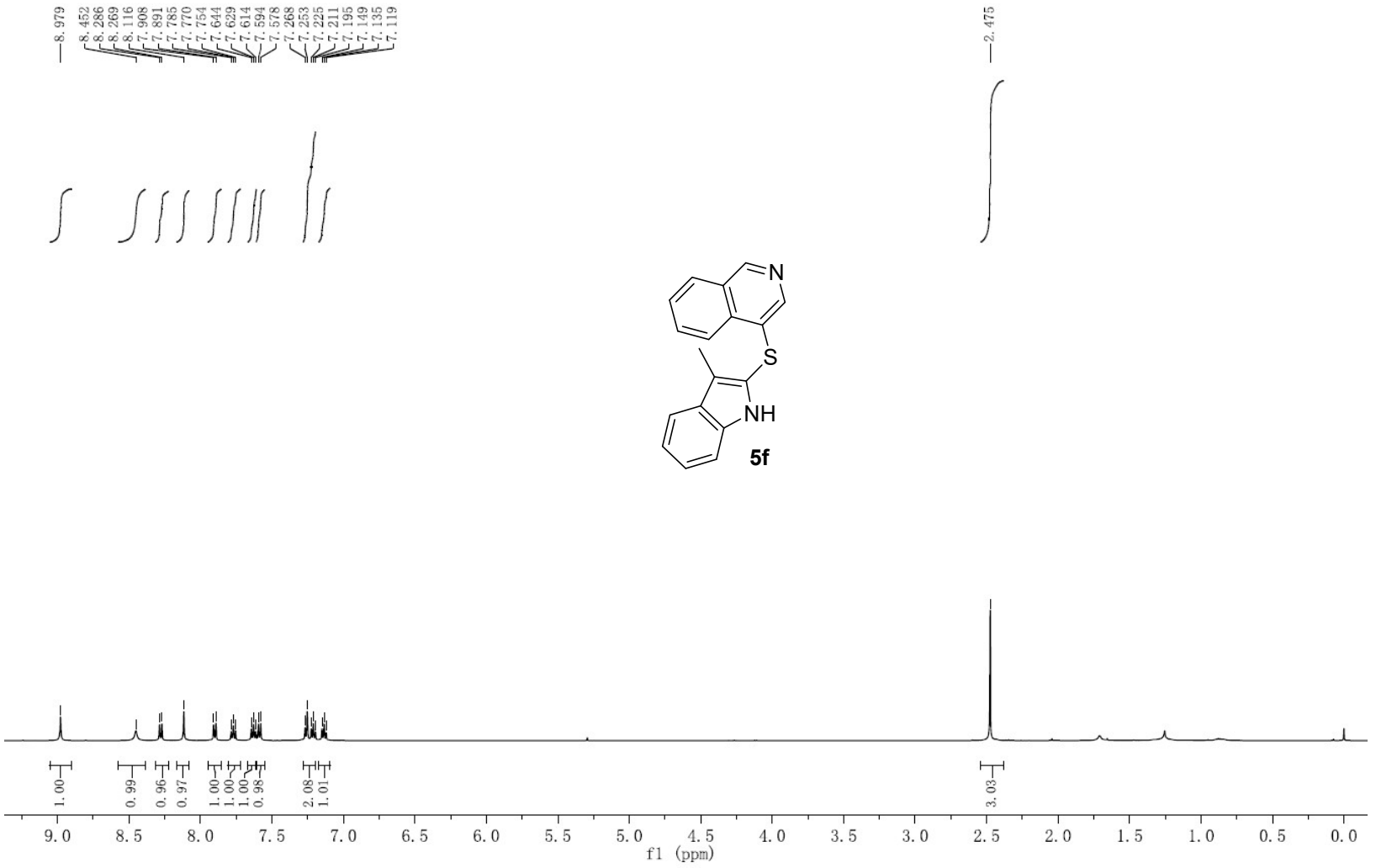
^{1}H NMR (500 MHz, DMSO-d_6) of **5e**



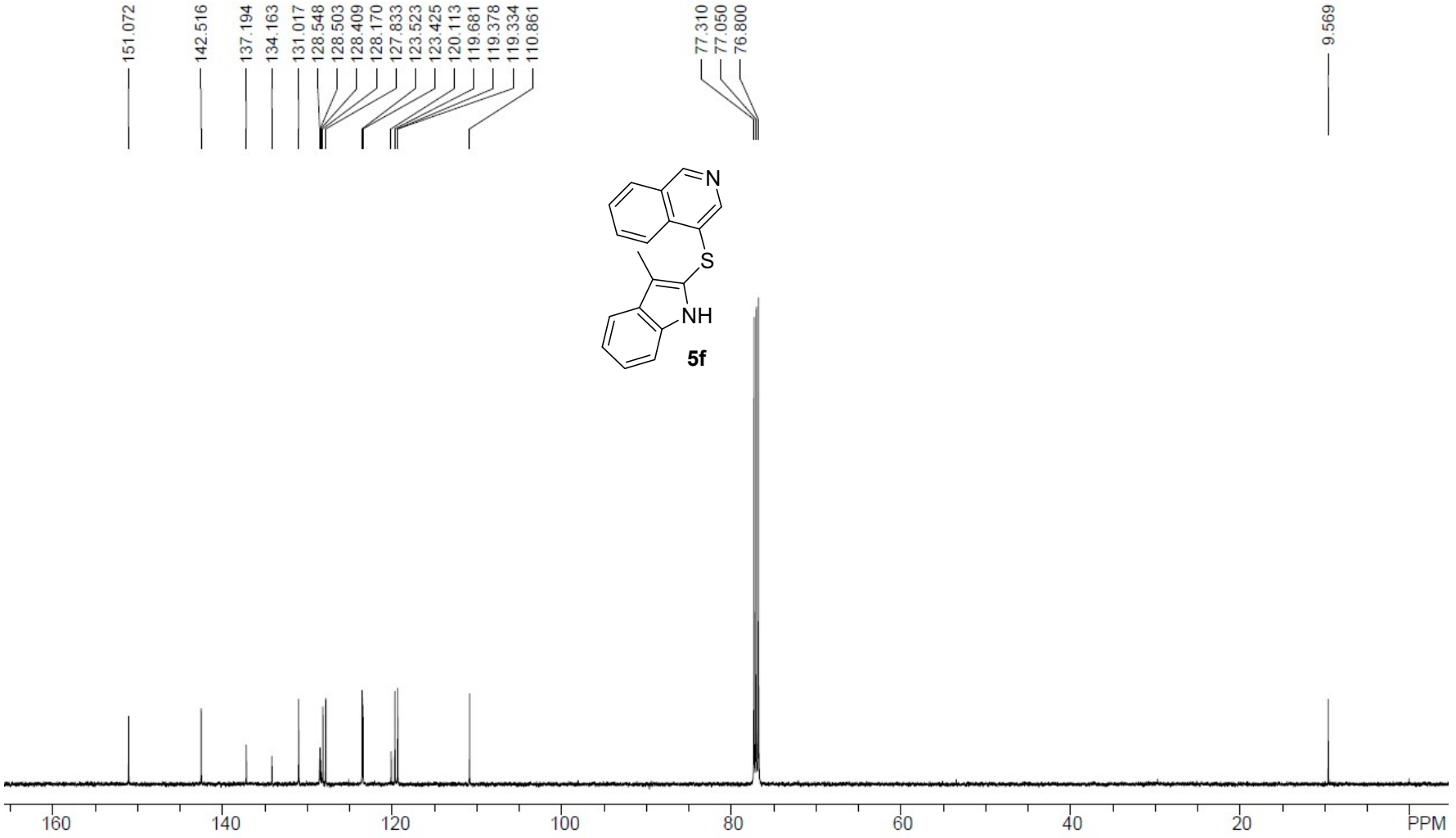
^{13}C NMR (126 MHz, DMSO-d_6) of **5e**



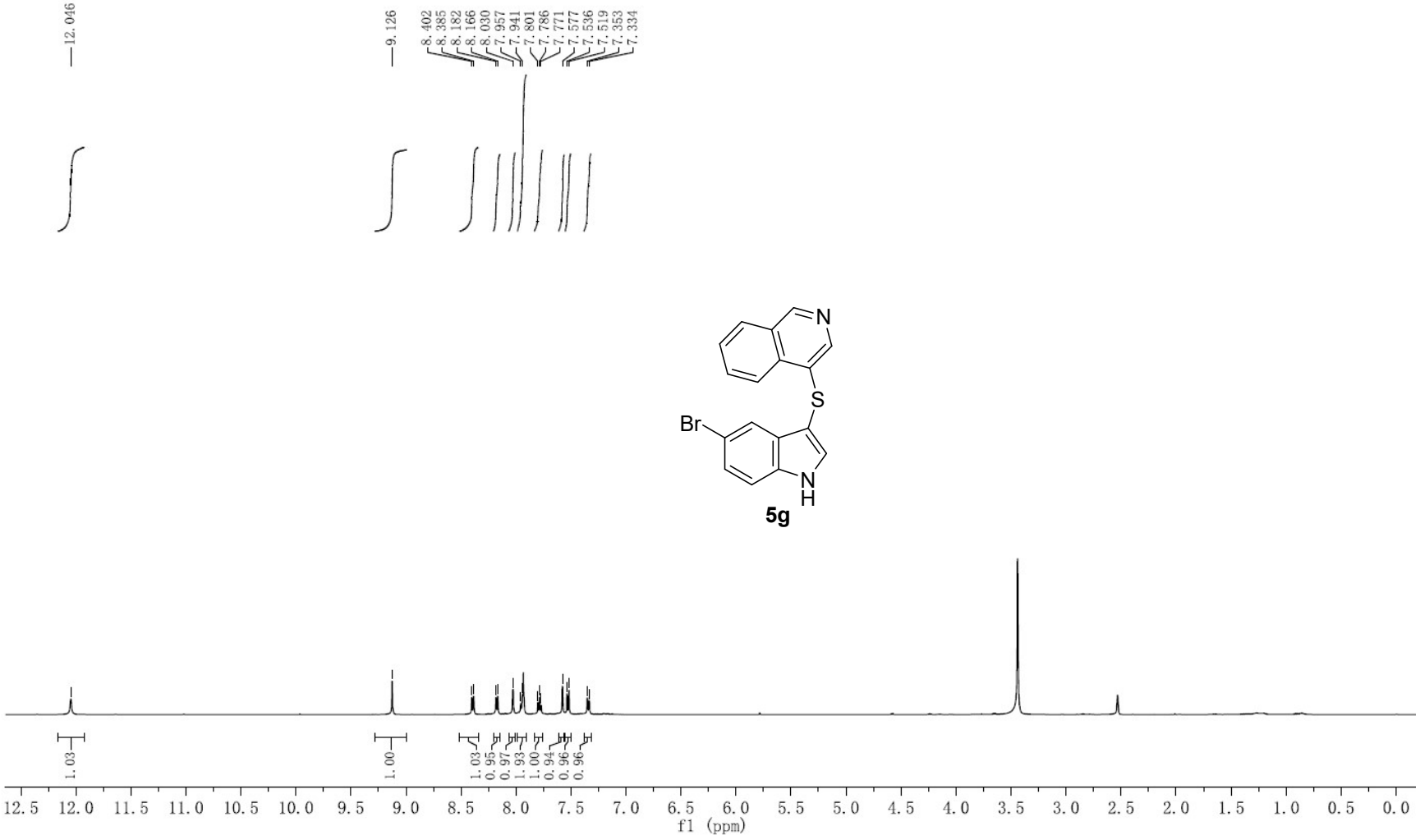
^{1}H NMR (500 MHz, $CDCl_3$) of **5f**



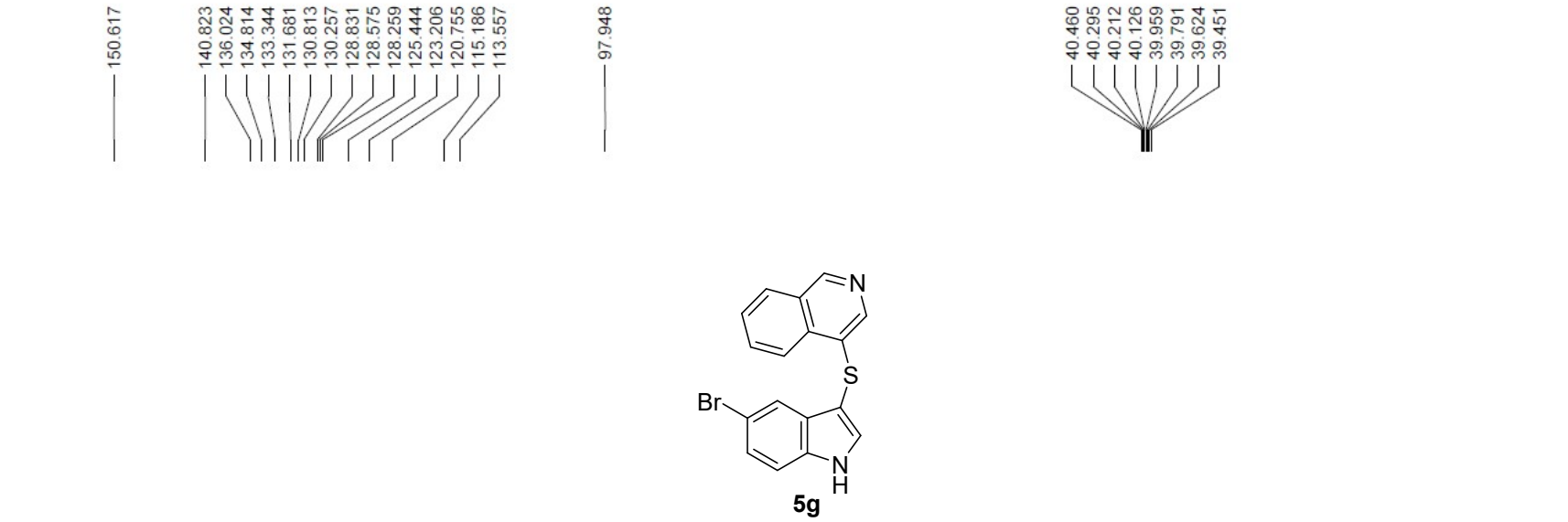
^{13}C NMR (126 MHz, $CDCl_3$) of **5f**

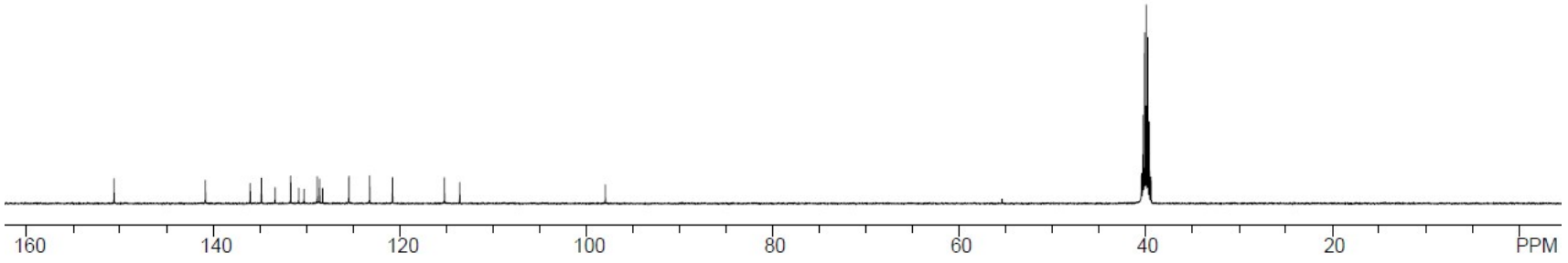


^{1}H NMR (500 MHz, DMSO-d_6) of **5g**

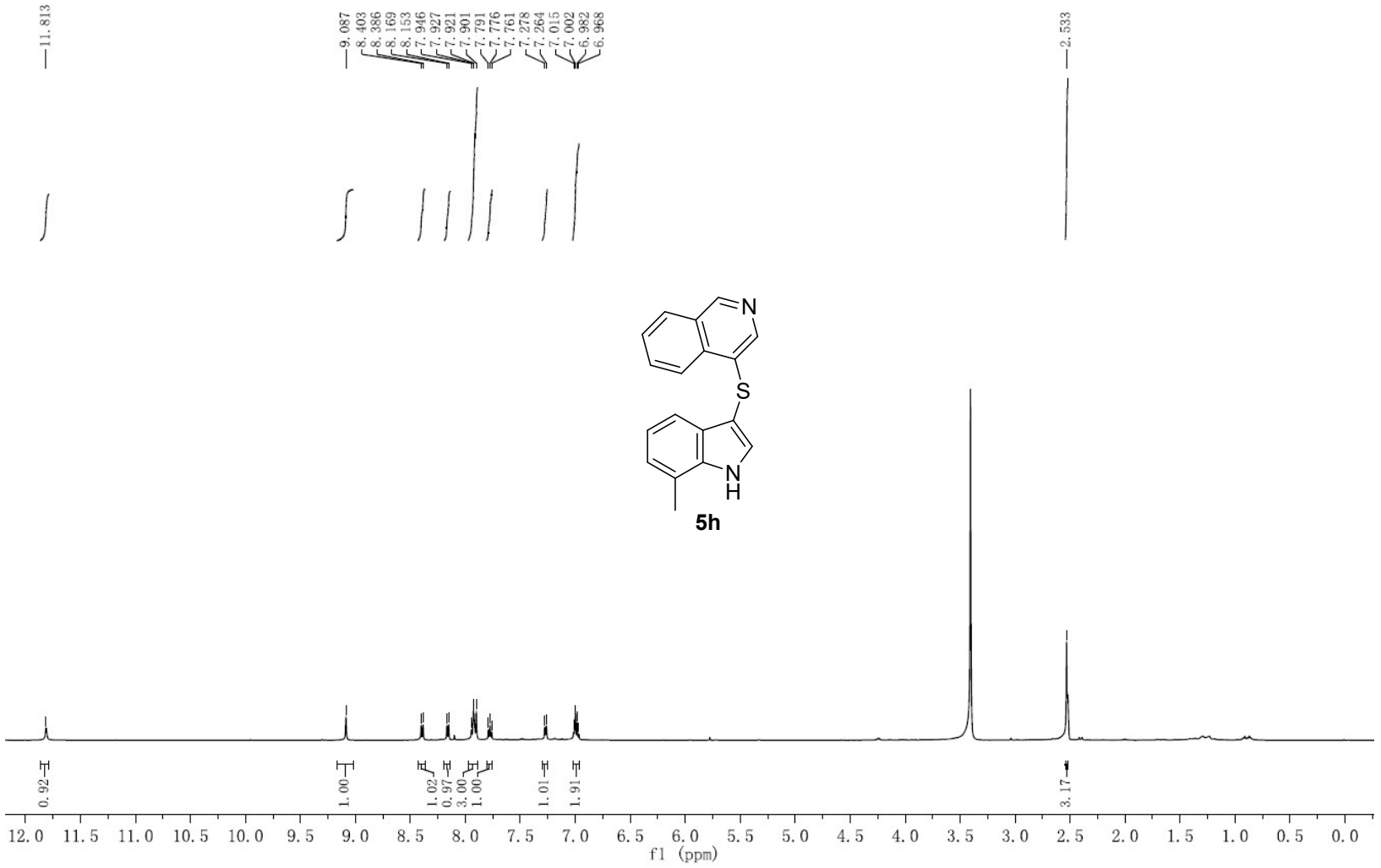


^{13}C NMR (126 MHz, DMSO-d_6) of **5g**

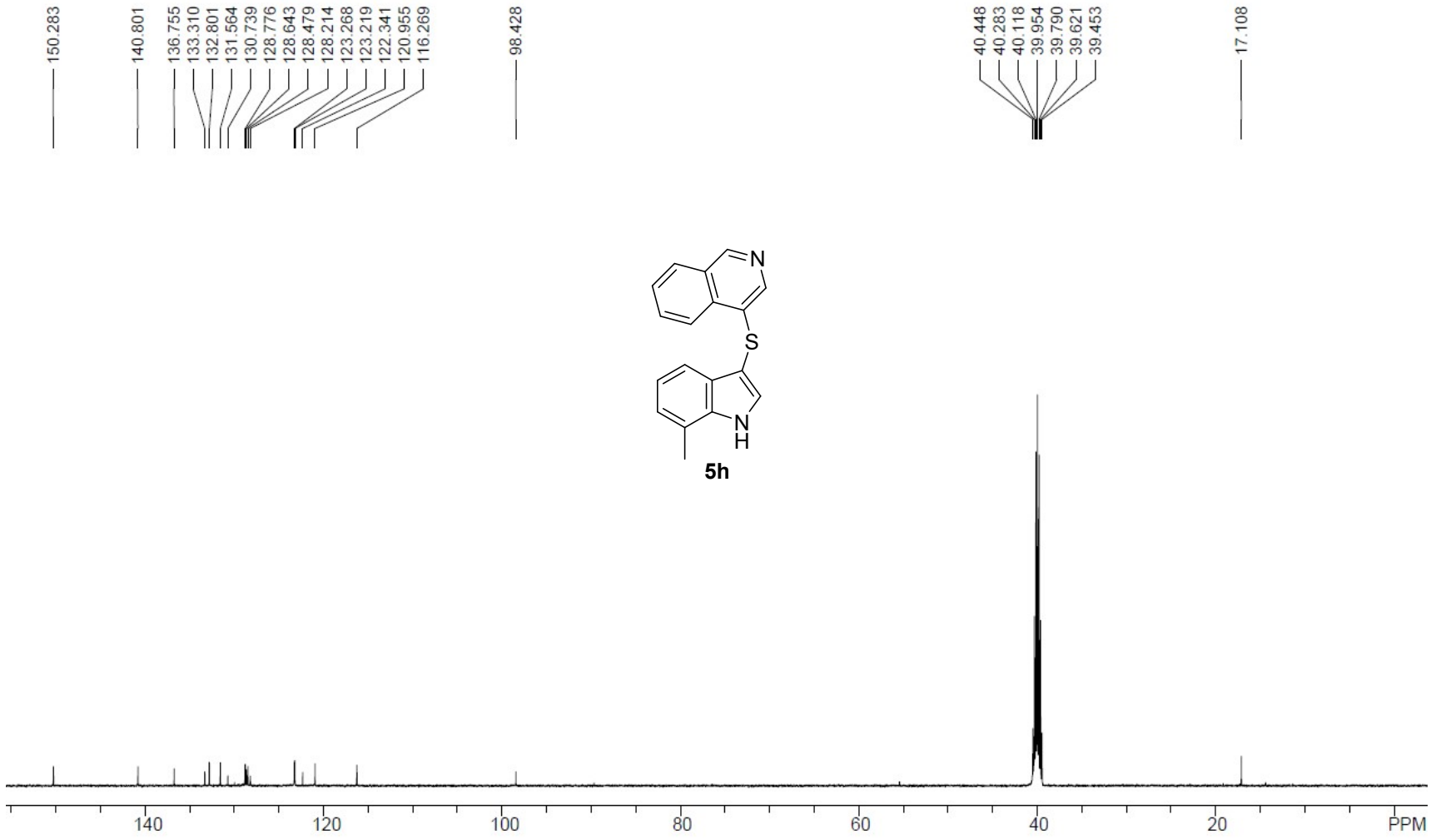




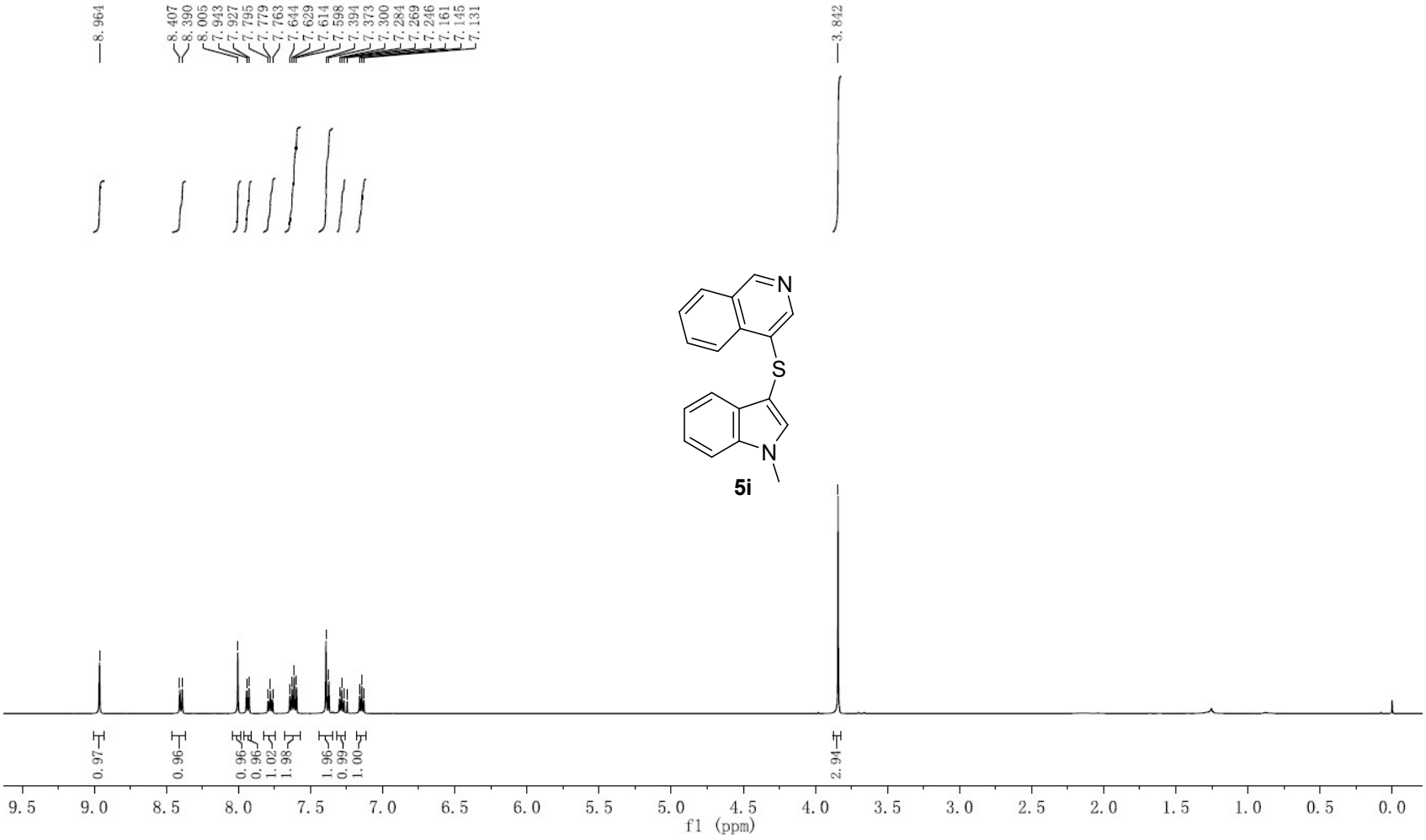
^{1}H NMR (500 MHz, DMSO-d_6) of **5h**



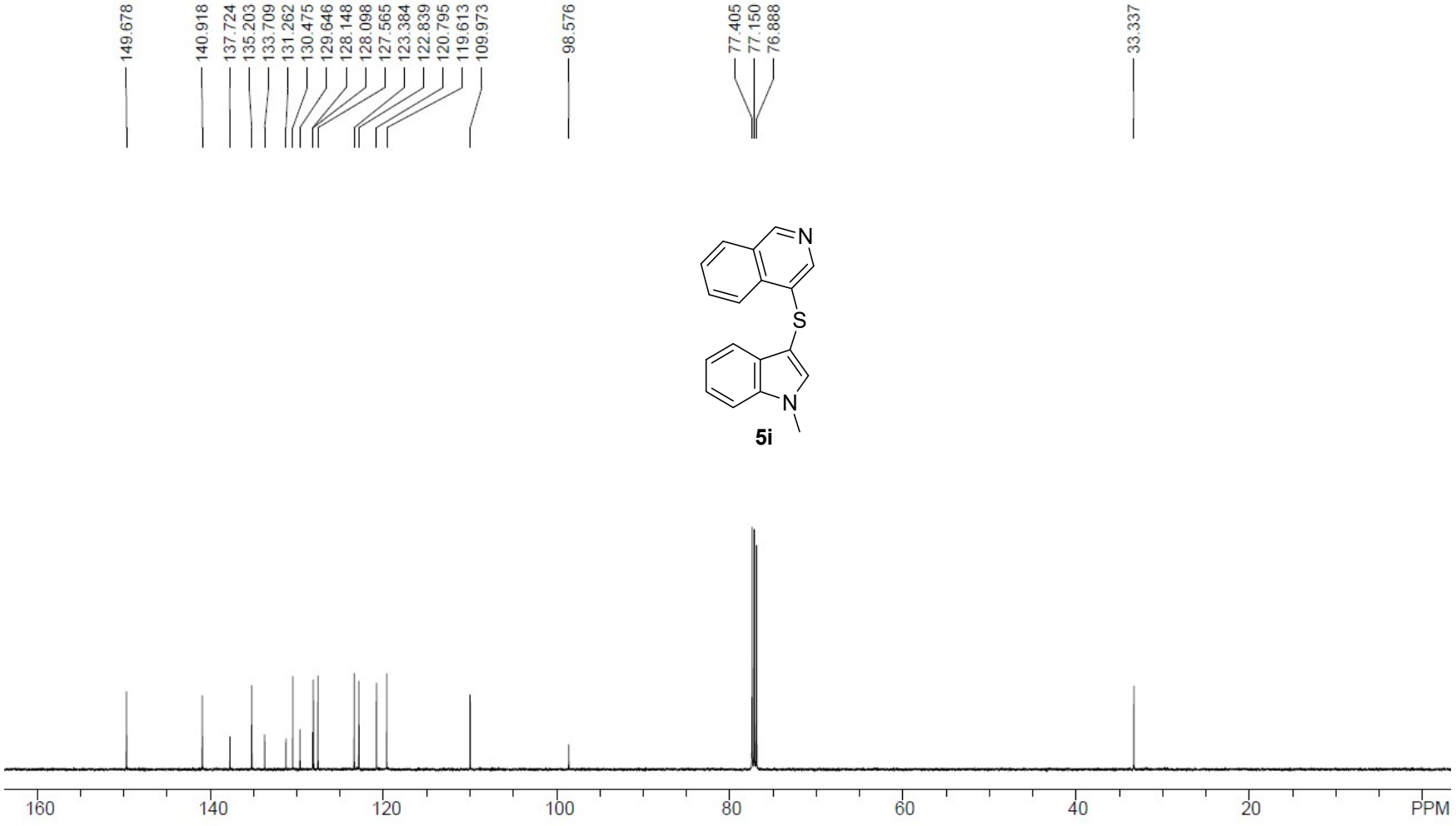
^{13}C NMR (126 MHz, DMSO-d_6) of **5h**



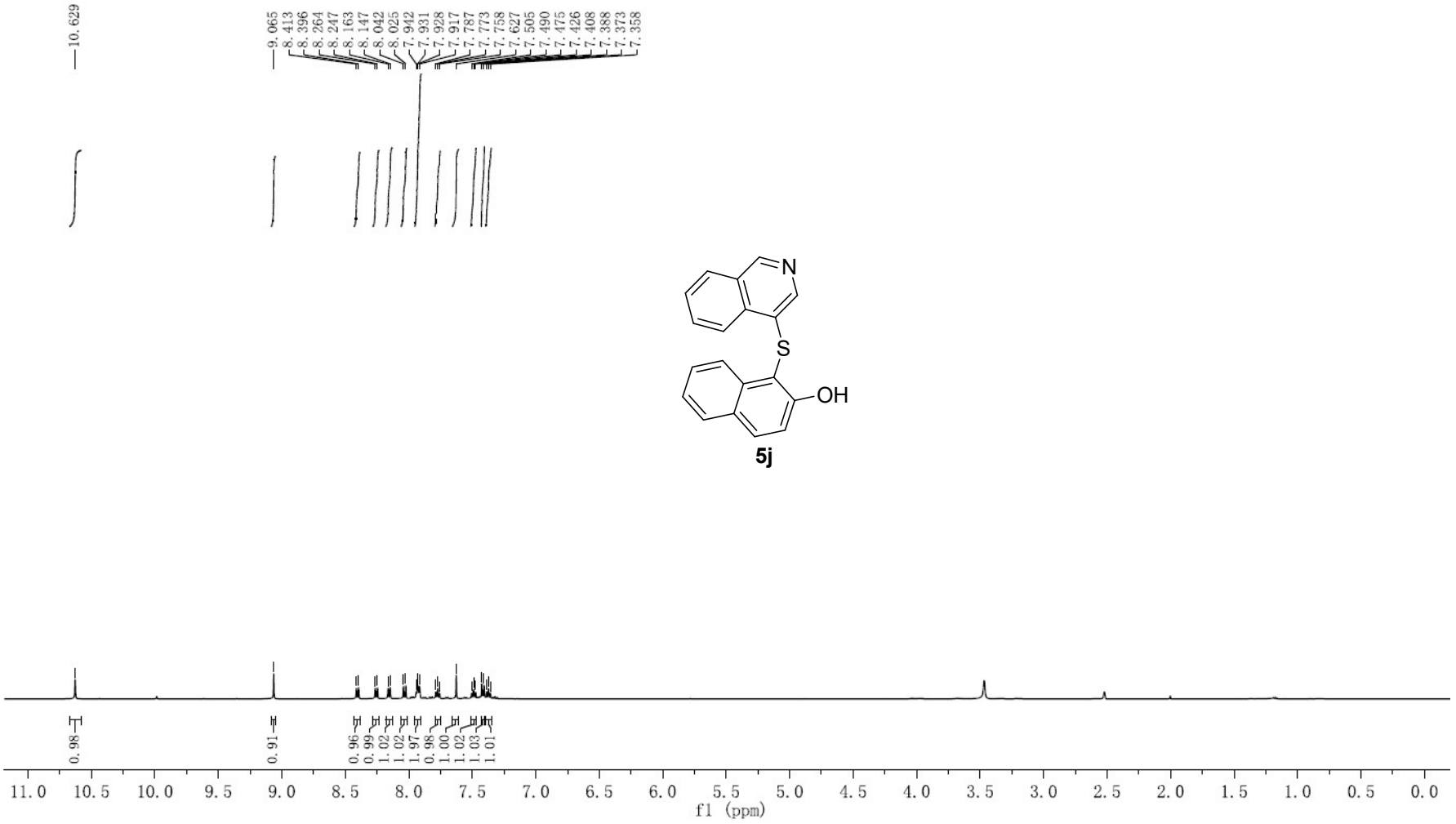
^{1}H NMR (500 MHz, $CDCl_3$) of **5i**



^{13}C NMR (126 MHz, $CDCl_3$) of **5i**

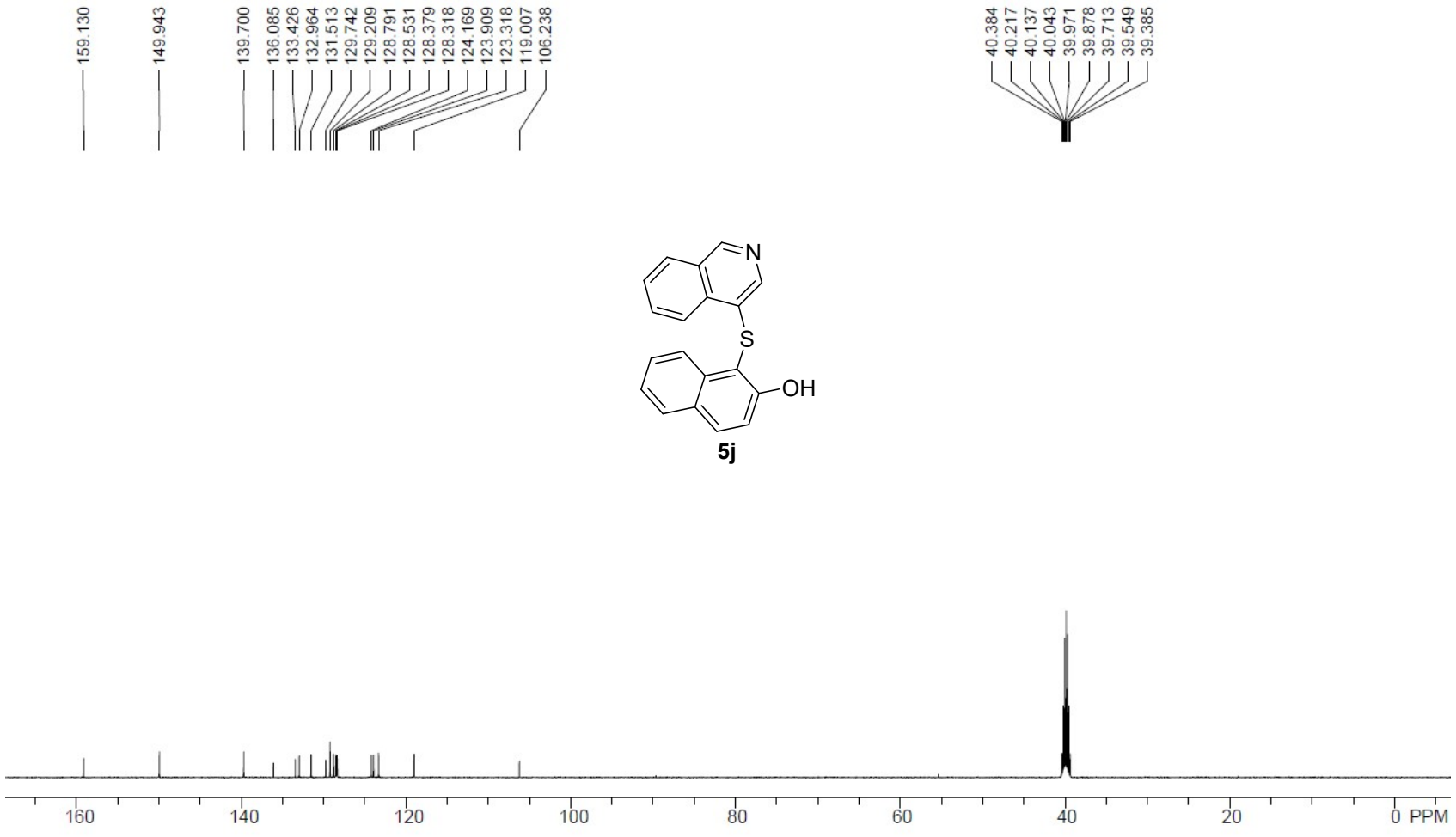


^{1}H NMR (500 MHz, DMSO-d_6) of **5j**



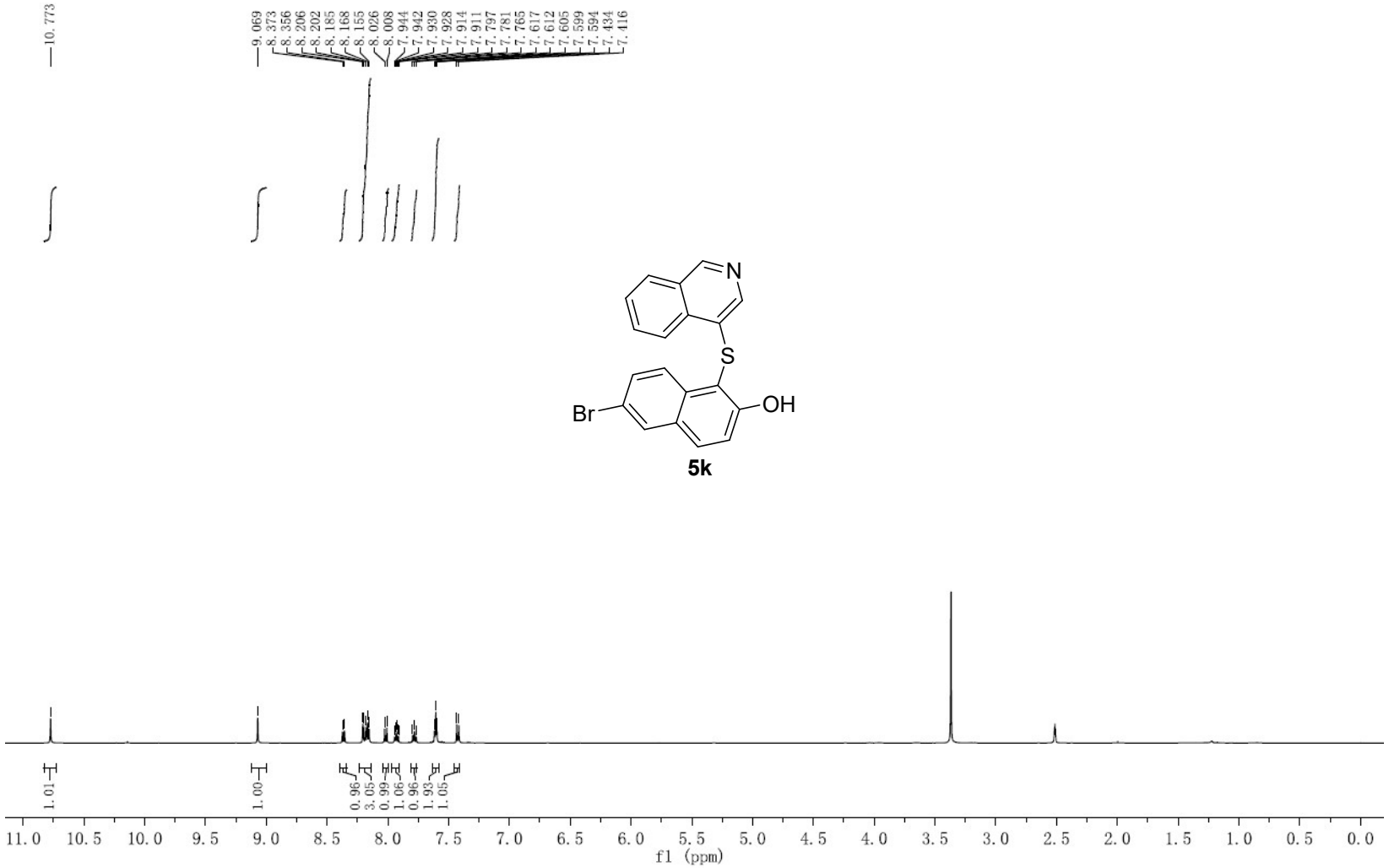
5j

^{13}C NMR (126 MHz, DMSO-d_6) of **5j**

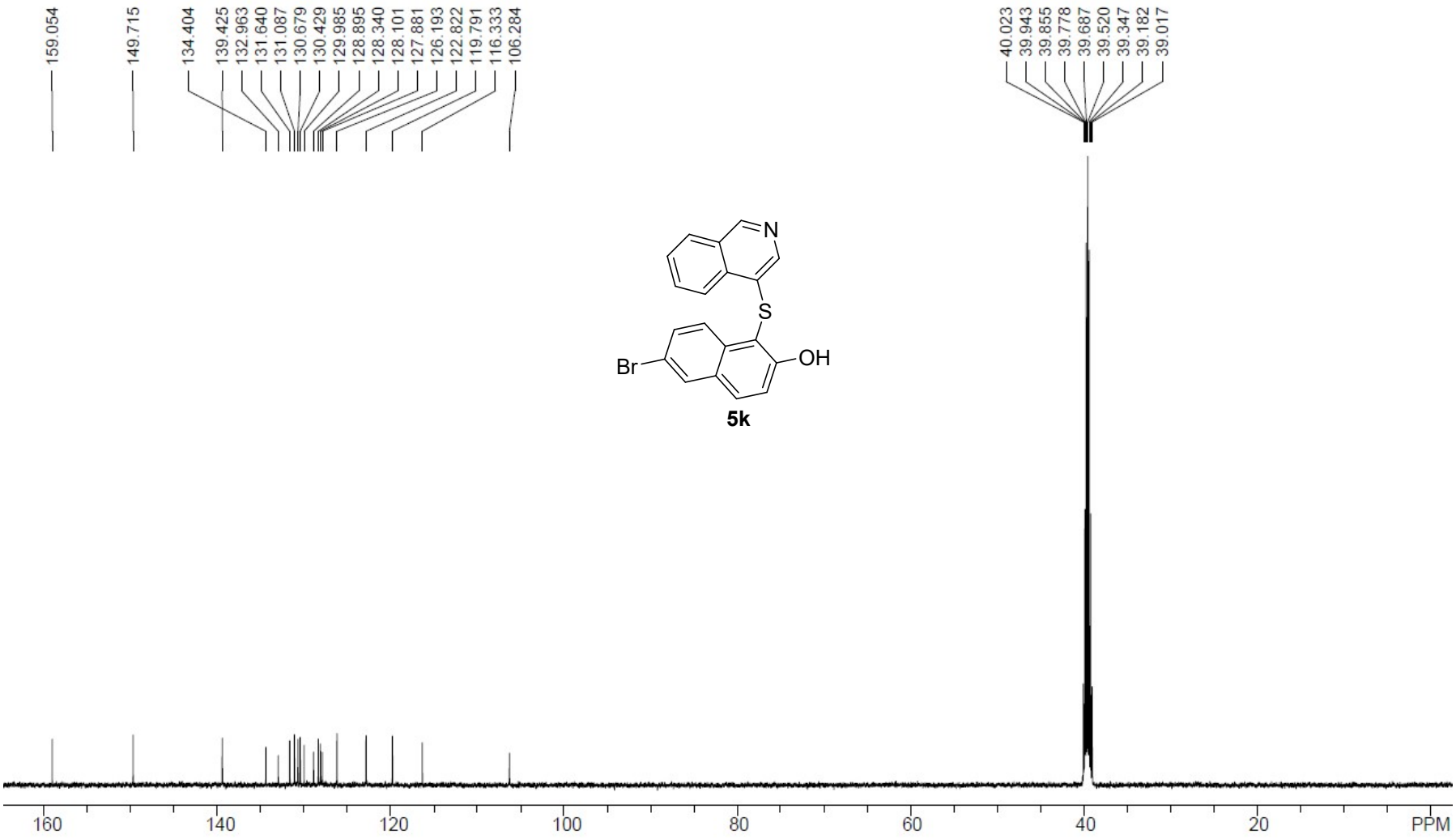


5j

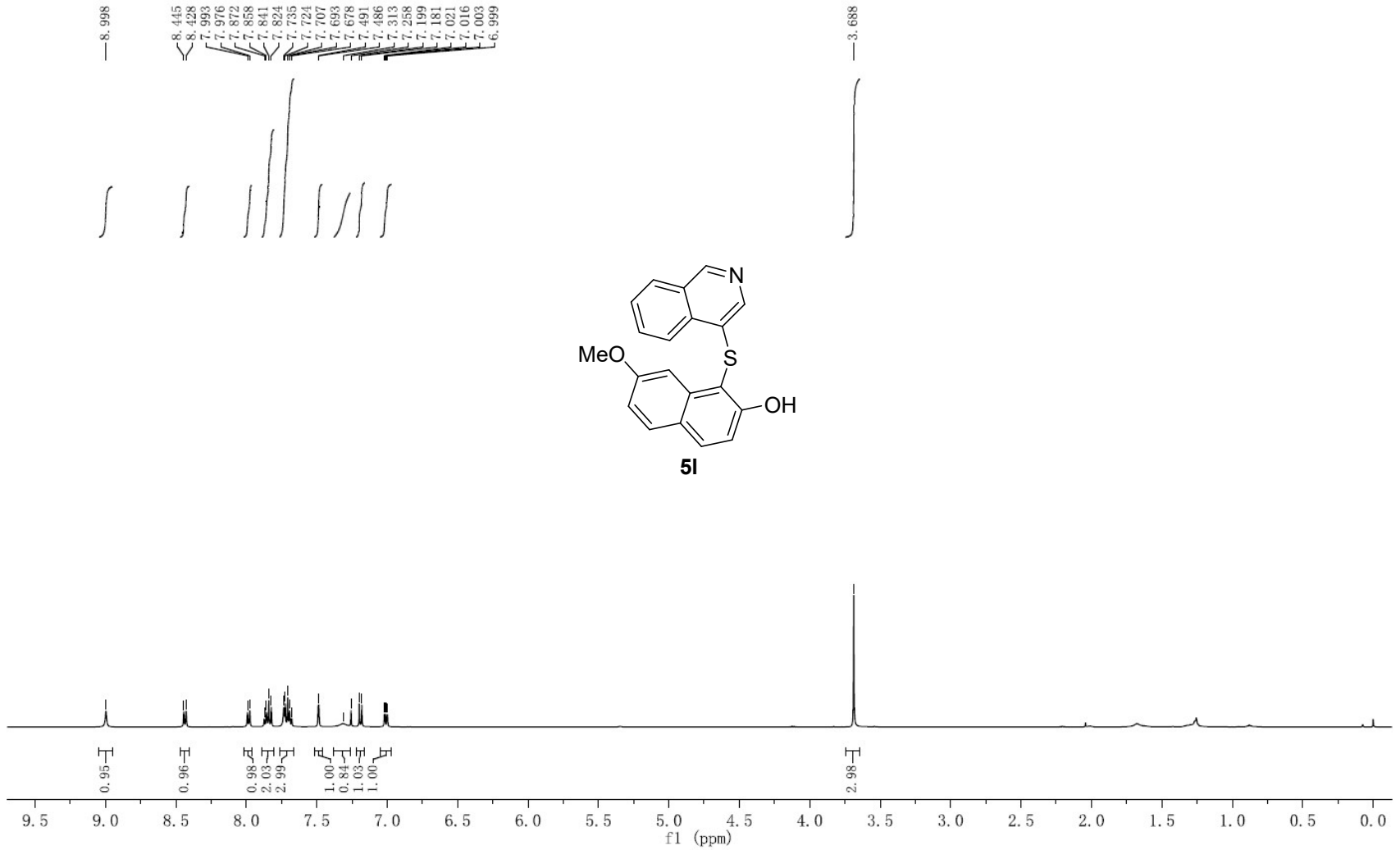
^{1}H NMR (500 MHz, DMSO-d_6) of **5k**



^{13}C NMR (126 MHz, DMSO-d_6) of **5k**

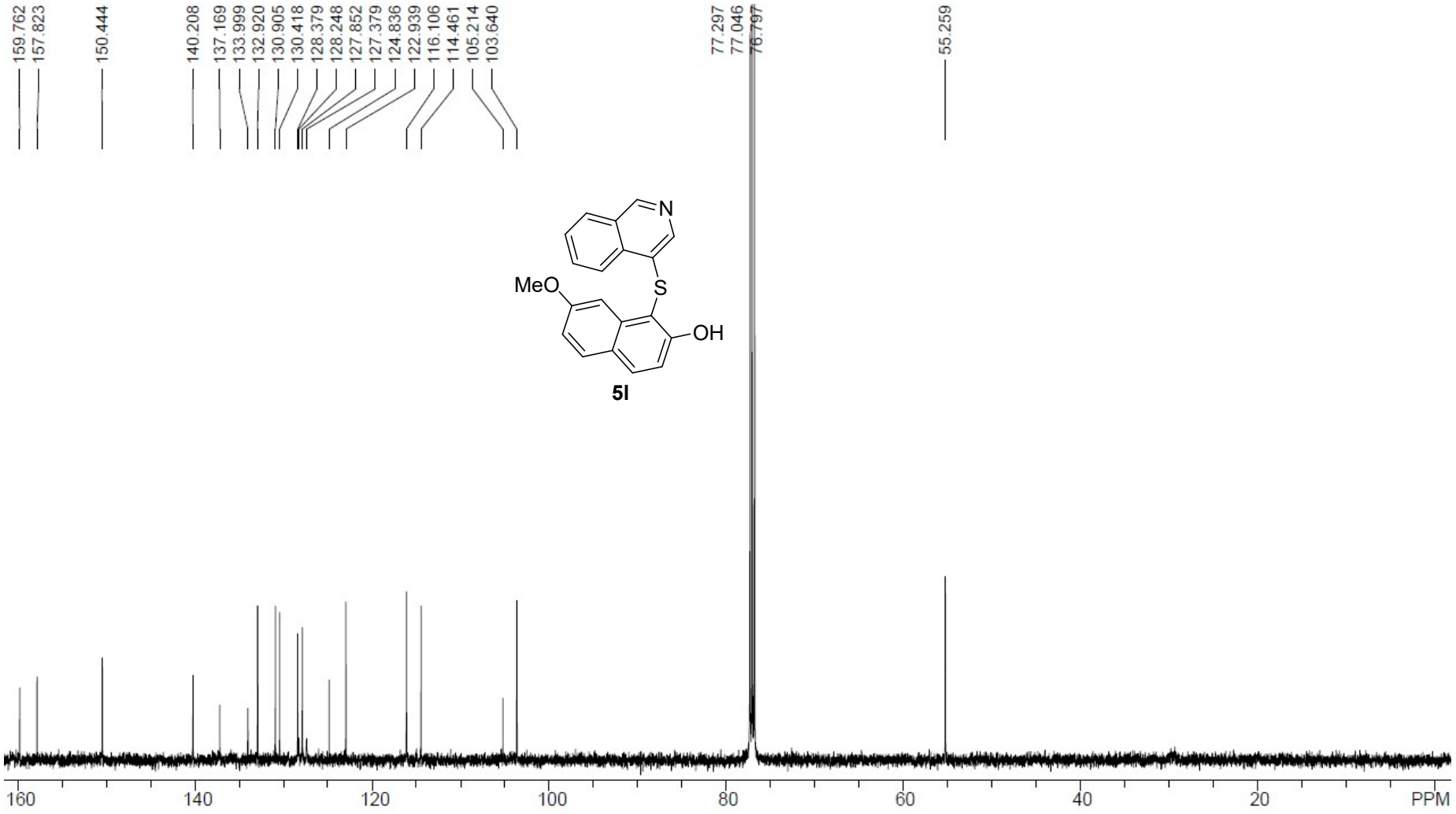


^{1}H NMR (500 MHz, $CDCl_3$) of **5l**



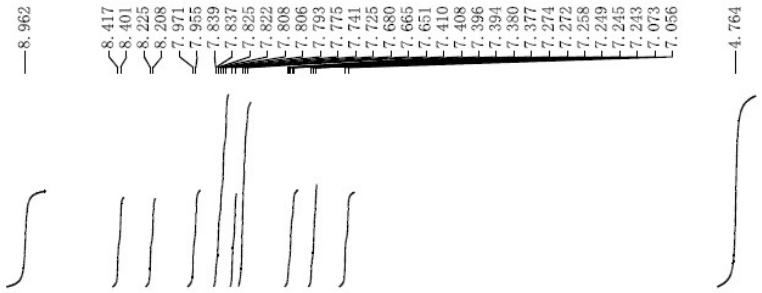
5l

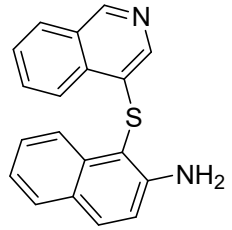
^{13}C NMR (126 MHz, $CDCl_3$) of **5l**



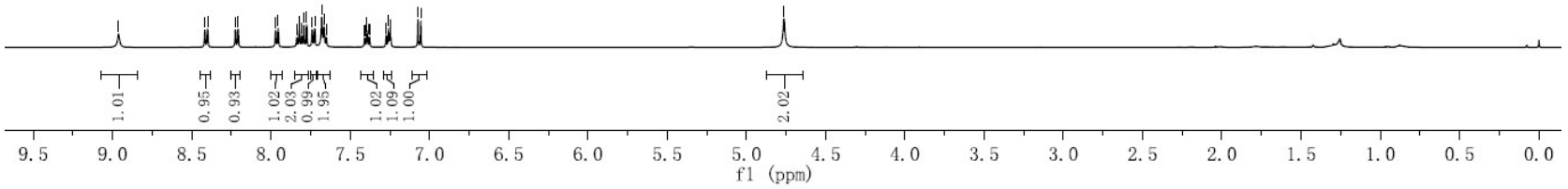
5l

^{1}H NMR (500 MHz, $CDCl_3$) of **5m**

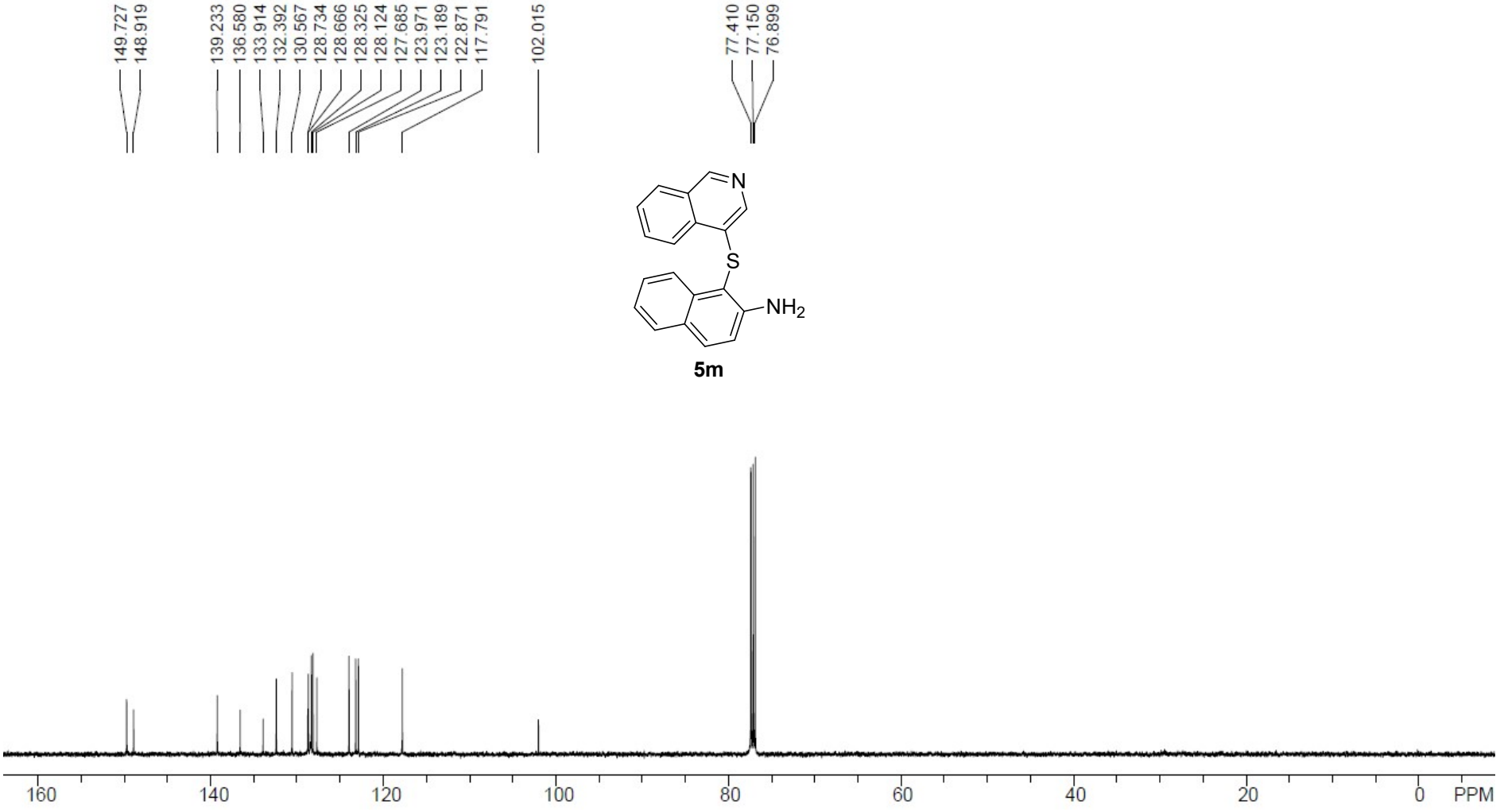




5m

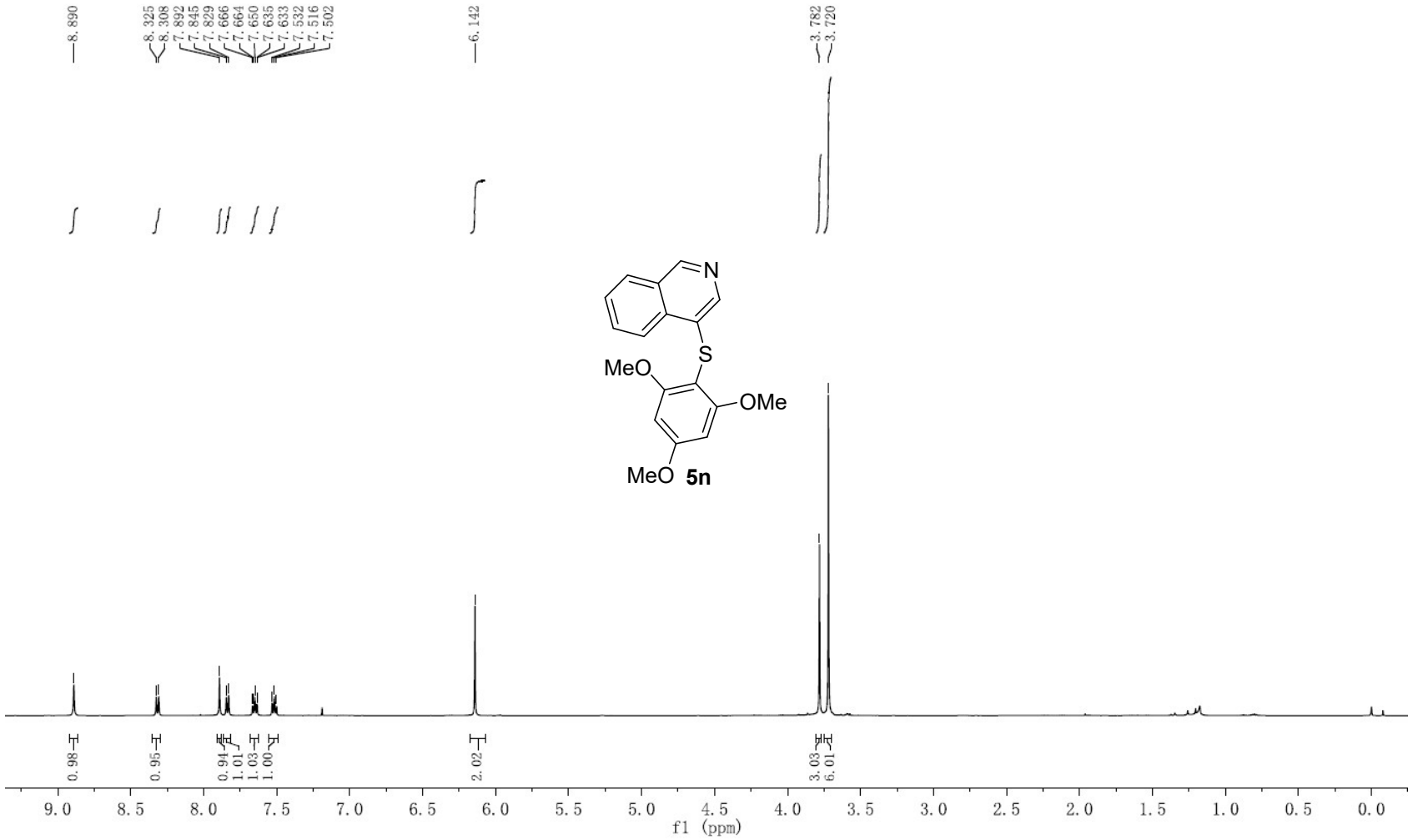


^{13}C NMR (126 MHz, $CDCl_3$) of **5m**

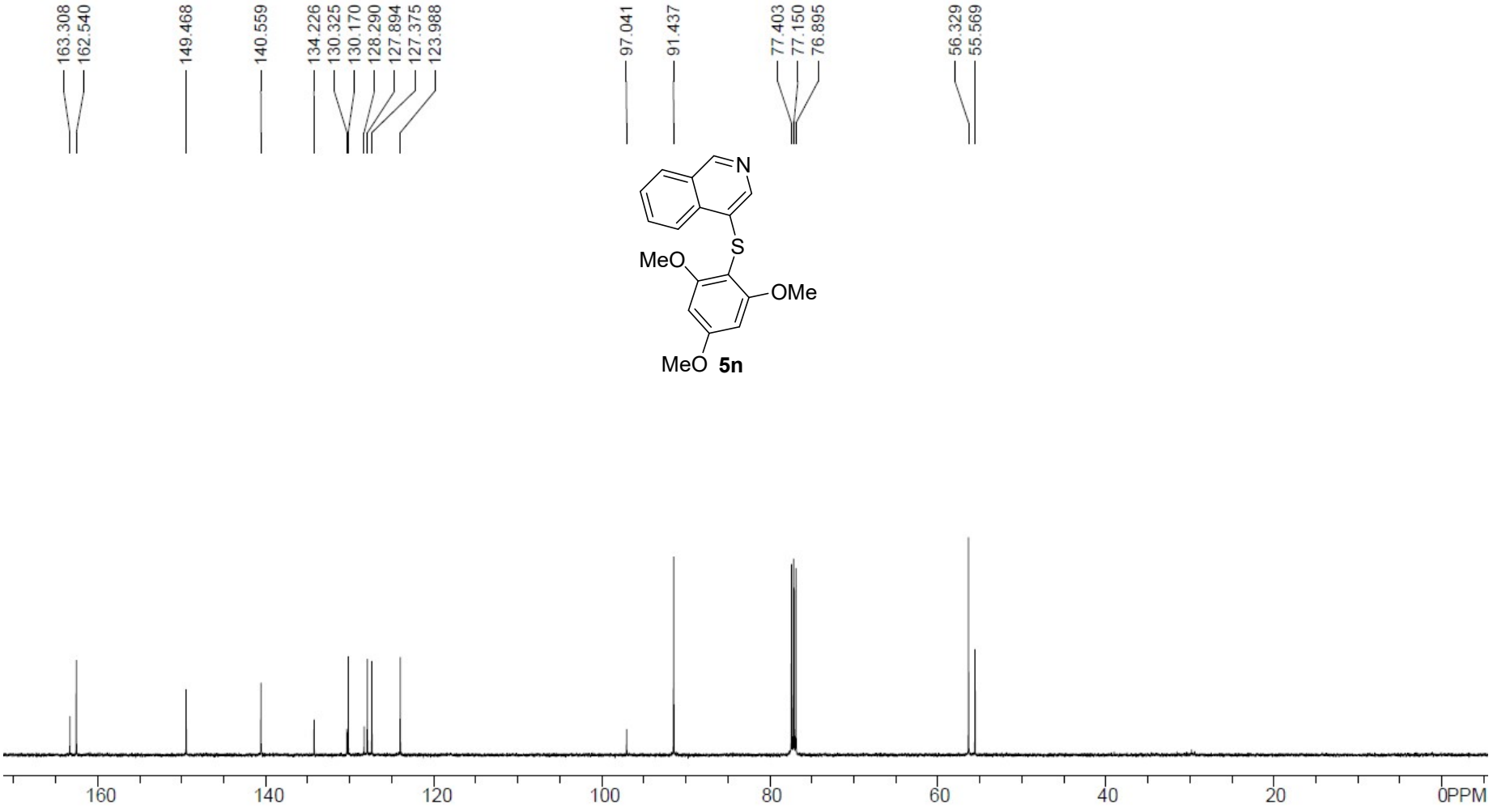


5m

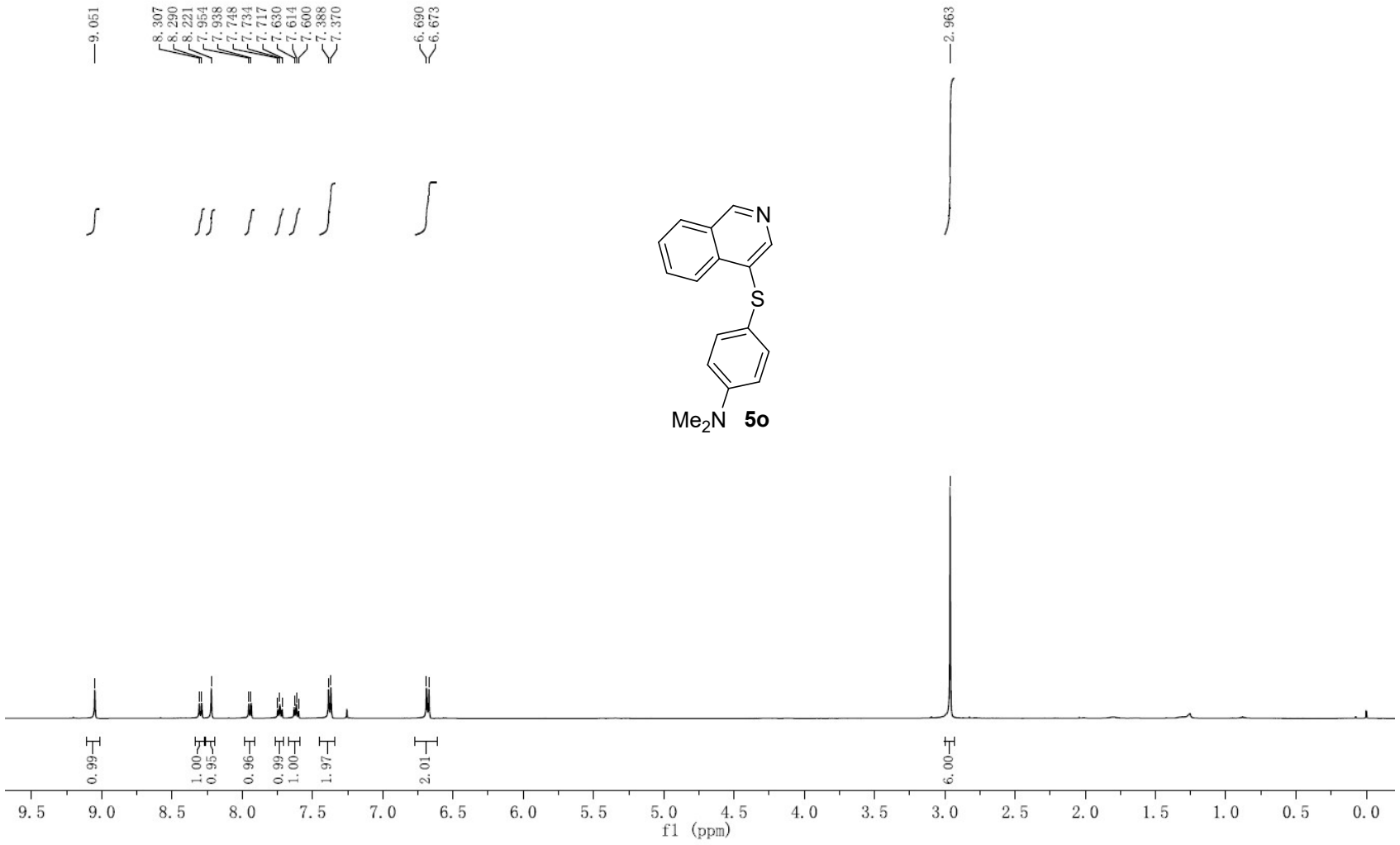
^{1}H NMR (500 MHz, $CDCl_3$) of **5n**



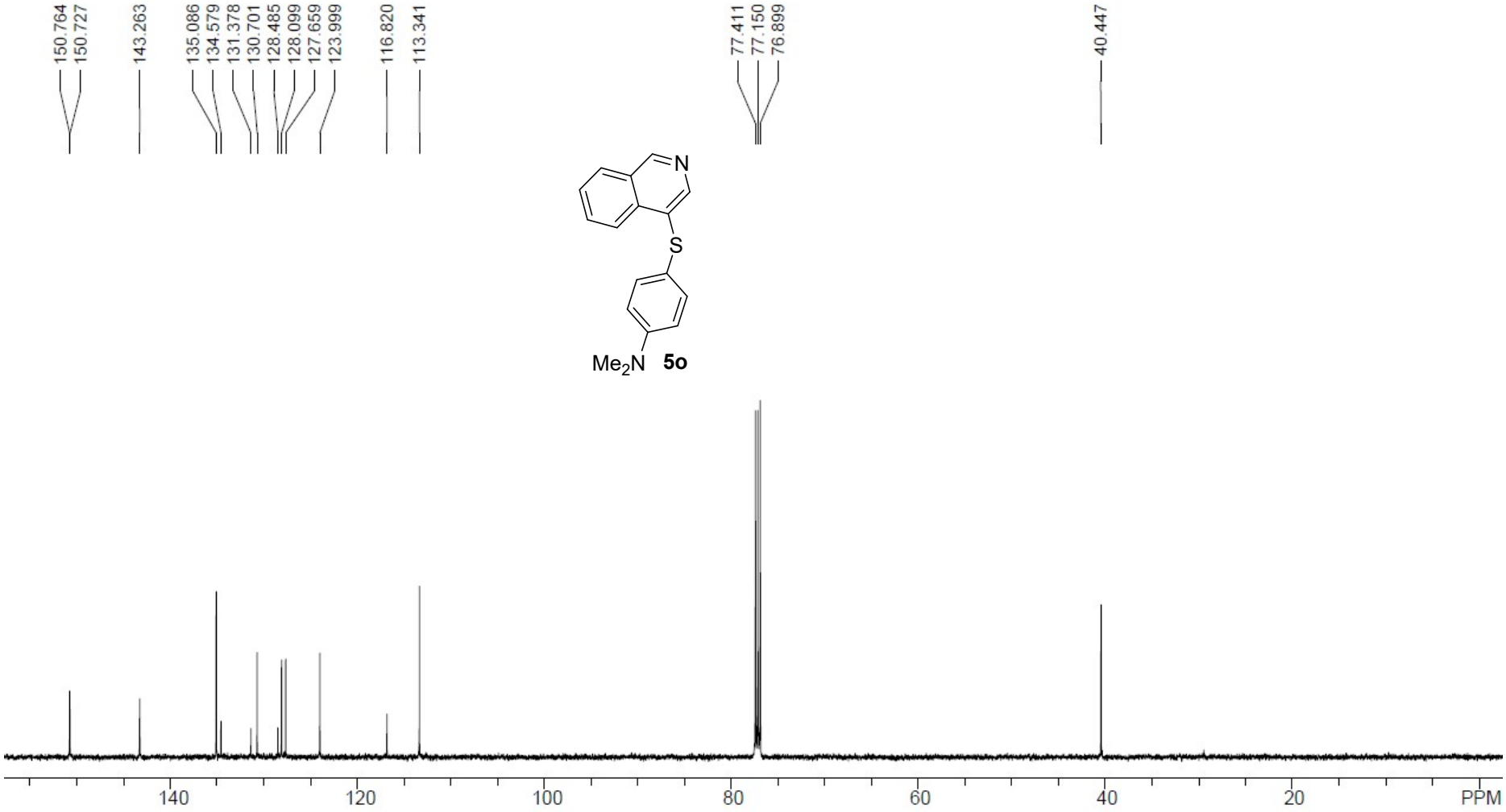
^{13}C NMR (126 MHz, $CDCl_3$) of **5n**



^{1}H NMR (500 MHz, $CDCl_3$) of **5o**



^{13}C NMR (126 MHz, $CDCl_3$) of **5o**



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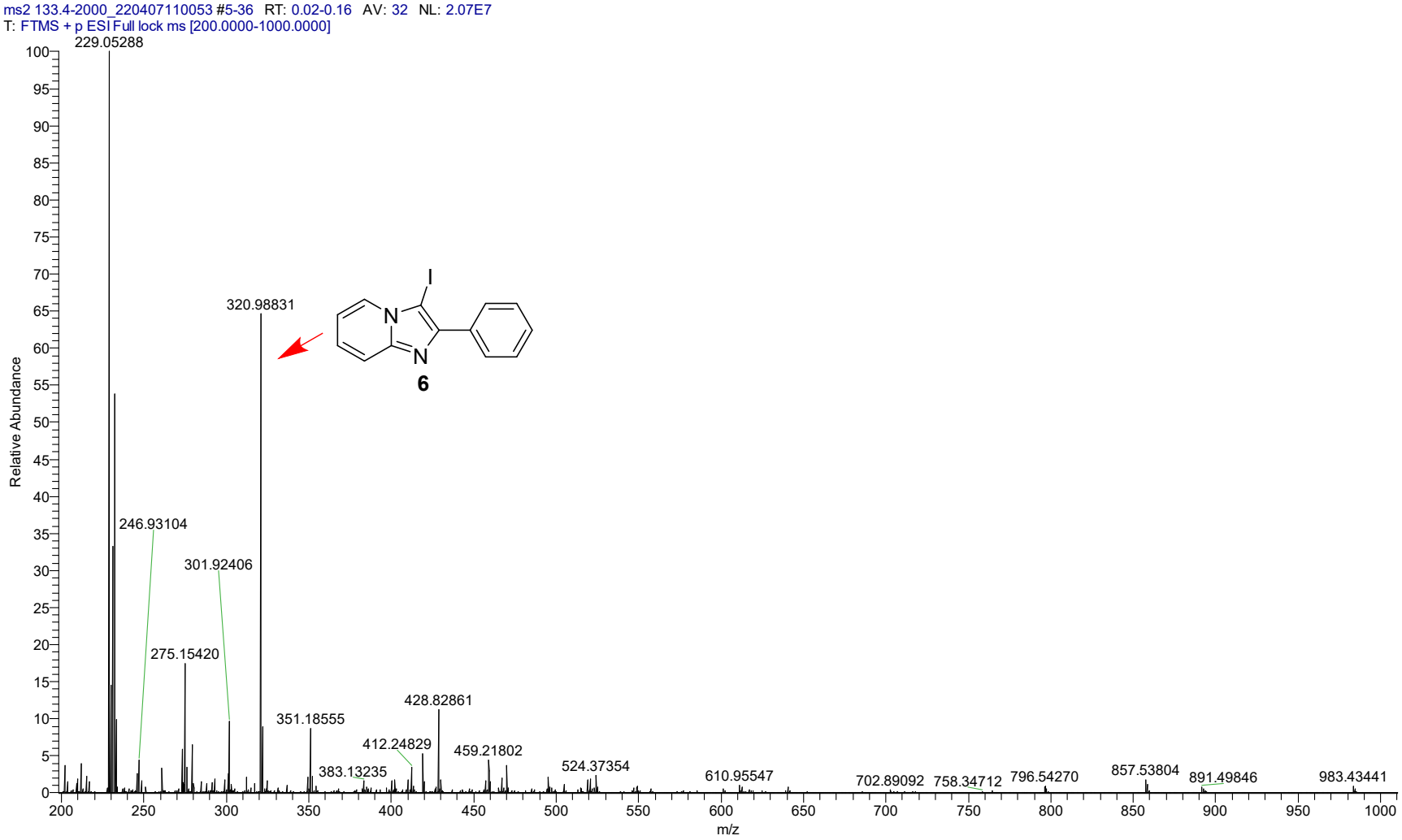
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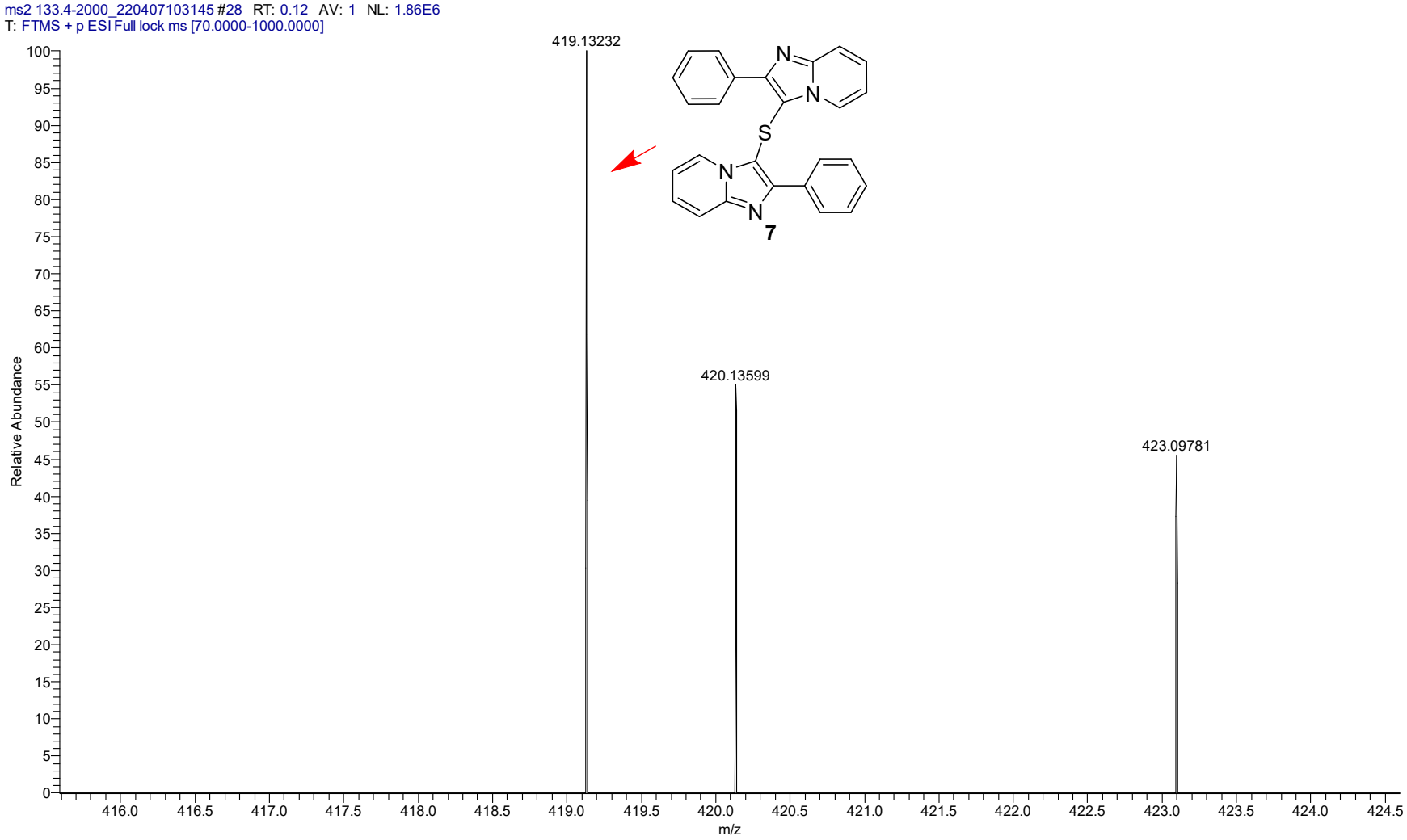
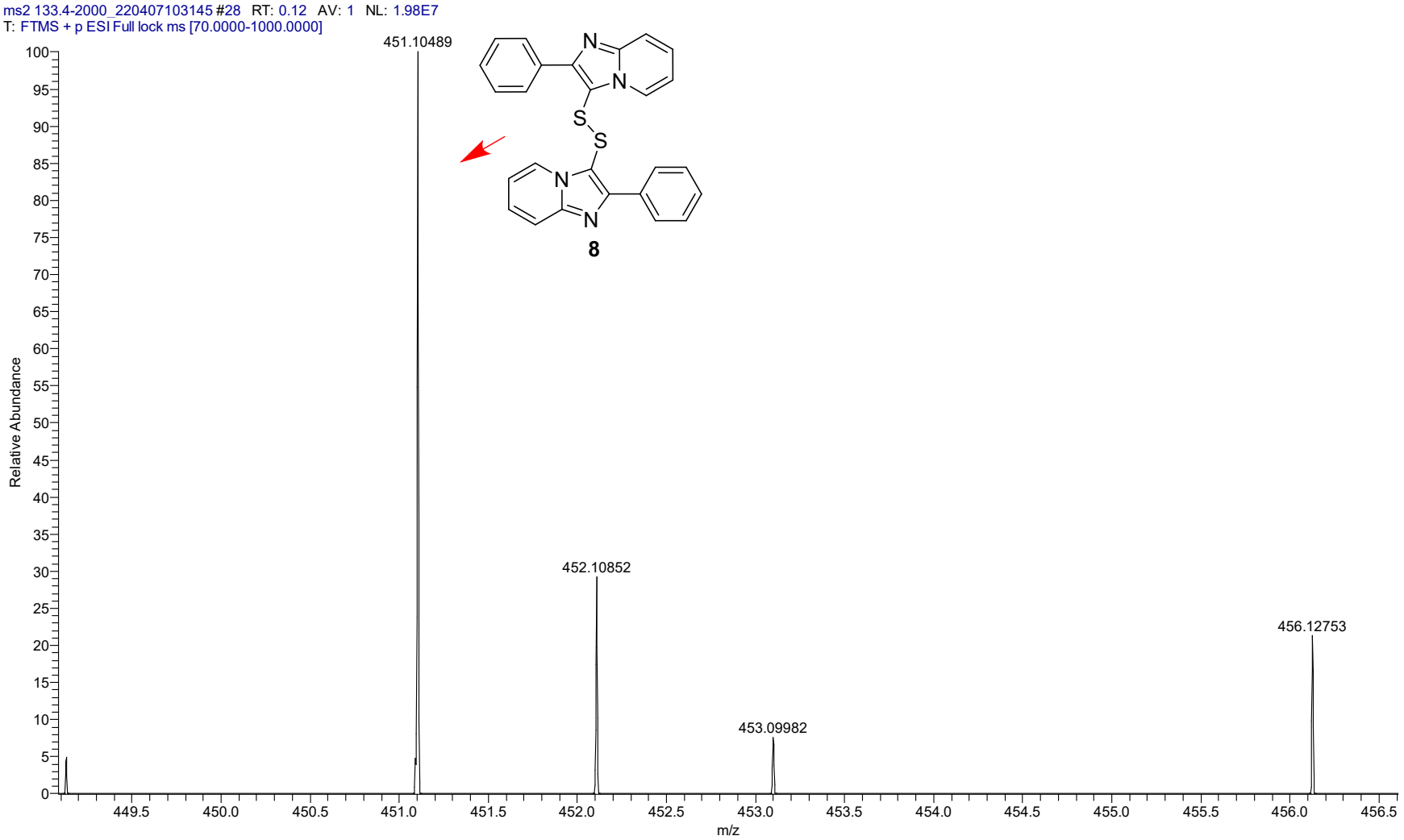
I
N
N
6

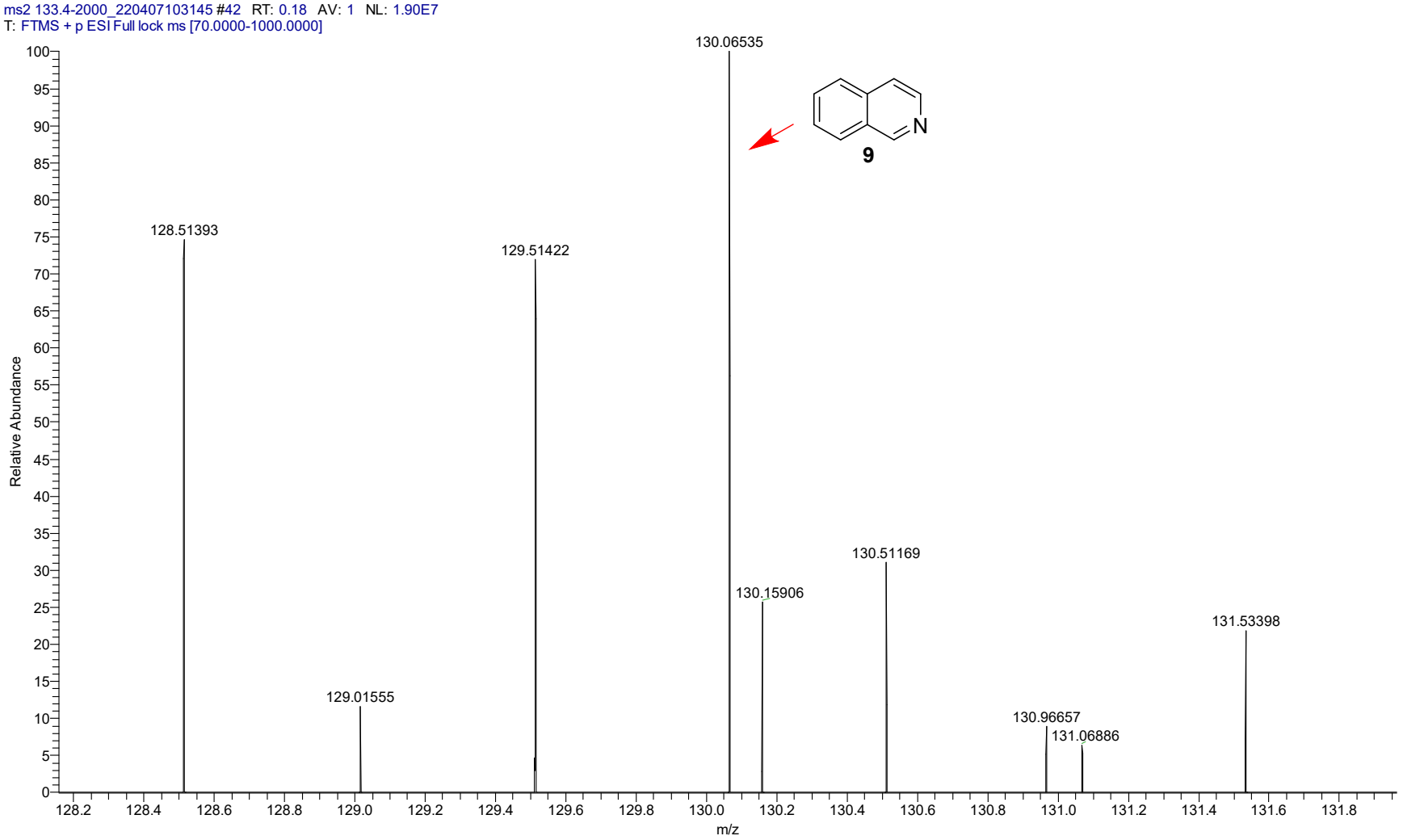
HRMS (ESI) of **7**


ms2 133.4-2000_220407103145 #28 RT: 0.12 AV: 1 NL: 1.86E6
T: FTMS + p ESI Full lock ms [70.0000-1000.0000]
419.13232
420.13599
423.09781
Relative Abundance
m/z
7

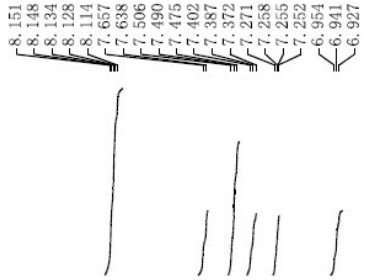
HRMS (ESI) of **8**

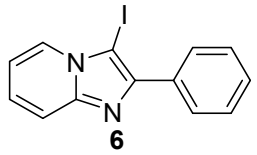

ms2 133.4-2000_220407103145 #28 RT: 0.12 AV: 1 NL: 1.98E7
T: FTMS + p ESI Full lock ms [70.0000-1000.0000]
451.10489
452.10852
453.09982
456.12753
Relative Abundance
m/z
8

HRMS (ESI) of **9**

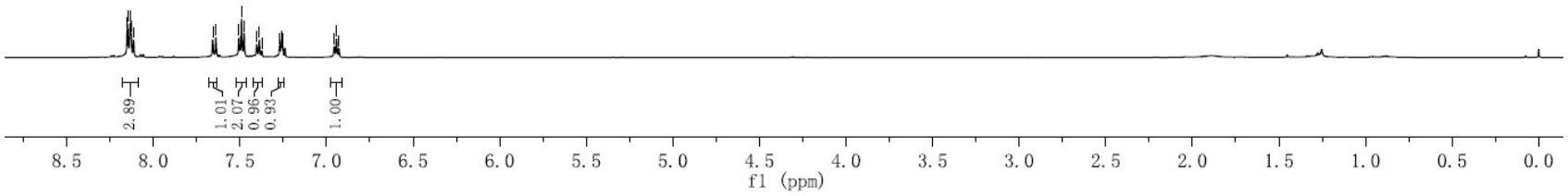

ms2 133.4-2000_220407103145 #42 RT: 0.18 AV: 1 NL: 1.90E7
T: FTMS + p ESI Full lock ms [70.0000-1000.0000]
130.06535
128.51393
129.51422
129.01555
130.15906
130.51169
131.53398
130.96657
131.06886
9
Relative Abundance
m/z

^{1}H NMR (500 MHz, $CDCl_3$) of **6**

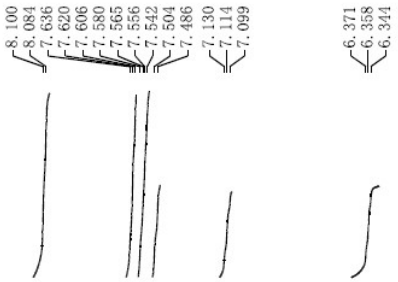


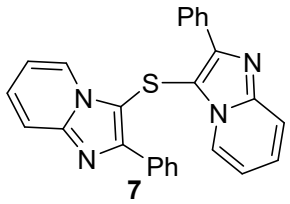


6

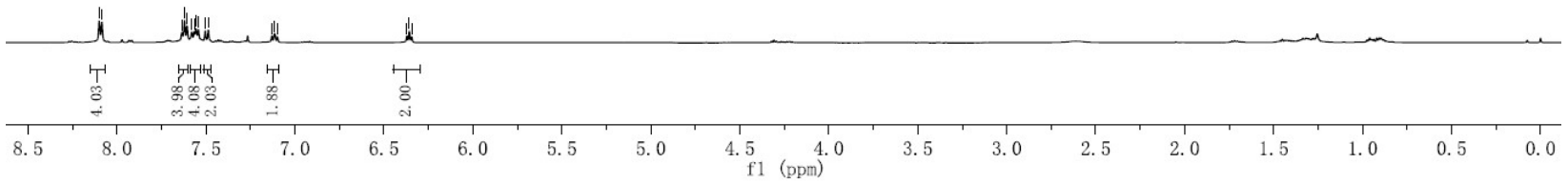


^{1}H NMR (500 MHz, $CDCl_3$) of **7**

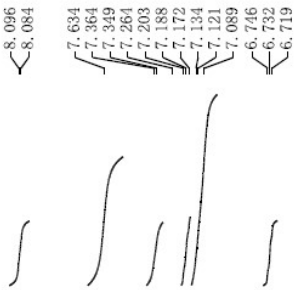


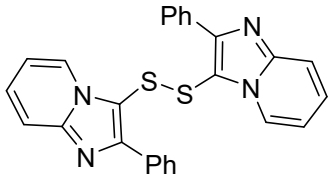


7



^{1}H NMR (500 MHz, $CDCl_3$) of **8**





8