Electronic Supplementary Material (ESI) for ChemComm.

Dioxygen-Triggered Oxidative Cleavage of C-S Bond towards C-N Bond Formation

Zongchao Lv,[a, †] Huamin Wang,[a, †] Zhicong Quan,[a] Yuan Gao,[a] and Aiwen Lei*[a,b]

[a]The Institute for Advanced Studies (IAS), College of Chemistry and Molecular Sciences, Wuhan University, Wuhan 430072, Hubei, People's Republic of China

[b]National Research Center for Carbohydrate Synthesis, Jiangxi Normal University, Nanchang 330022, Jiangxi, People's Republic of China

[†]These authors contributed equally

***corresponding author,**

E-mail: aiwenlei@whu.edu.cn

Supporting Information

Table of Contents

1. General Considerations

All manipulations were carried out by standard schlenk techniques. Unless otherwise stated, analytical grade solvents and commercially available reagents were used to conduct the reactions. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum ether (bp. 60-90 ^{o}C). Gradient flash chromatography was conducted eluting with a continuous gradient from petroleum ether to the ethyl acetate. All new compounds were characterized by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS. The known compounds were characterized by ^{1}H NMR and ^{13}C NMR. The ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer using TMS as an internal standard. The chemical shifts (δ) were given in part per million relative to $CDCl_3$ (7.26 ppm for ^{1}H NMR), $CDCl_3$ (77.16 ppm for ^{13}C NMR), DMSO (2.50 ppm for ^{1}H NMR), DMSO (39.52 ppm for ^{13}C NMR). Melting points (uncorrected) were determined on a micro melting point apparatus. Infrared (IR) spectra were recorded on an Agilent Technologies Cary 630 FTIR system, with samples loaded as solids. Frequencies are given in reciprocal centimeters (cm^{-1}) and only selected absorbance is reported. High resolution mass spectra (HRMS) were measured with a Bruker UltiMate3000 & Compact instrument and accurate masses were reported for the molecular ion + Hydrogen $(M+H)^{+}$.

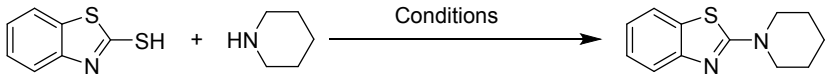
2. Experimental Procedures

2.1 General Procedure for Conditions Screening

A solution of 2-mercaptobenzothiazole **1a** (0.3 mmol, 1 equivalent, 50.2 mg), piperidine **2a** (0.9 mmol, 3 equivalent, 76.6 mg, or 1.2 mmol, 4 equivalent, 102.2 mg) and additive {I_2 (0.075 mmol, 0.25 equivalent, 19 mg), NH_4Cl (0.15 mmol, 0.5 equivalent, 8 mg), NaOAc (0.15 mmol, 0.5 equivalent, 12.3 mg), or Et_3N (0.15 mmol, 0.5 equivalent, 15.2 mg)} in solvent {DMA (2.0 mL), DMSO (2.0 mL), DMF (2.0 mL), or NMP (2.0 mL)} was stirred under an oxygen atmosphere at 95-120 ^{o}C for 12-30 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (5 mL). The aqueous solution was extracted with ethyl acetate (3 × 10 mL) and the combined extracts were dried with anhydrous Na_2SO_4. The solvent was removed

under reduced pressure by rotary evaporation. Then, the pure product was obtained by flash column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 5:1).

Table S1 The investigation of reaction condition[a].



1a **2a** **3aa**

Entry	**1a:2a**	Additive (x mol%)	Solvent	T (^{o}C)	Time (h)	Yield (%)[b]
1	1:3	I_2 (25)	DMA (2 mL)	95	12	23
2	1:3	I_2 (25)	DMA (2 mL)	100	12	37
3	1:3	I_2 (25)	DMA (2 mL)	110	12	55
4	1:3	I_2 (25)	DMA (2 mL)	120	12	40
5	1:3	I_2 (25)	DMSO (2 mL)	110	12	32
6	1:3	I_2 (25)	DMF (2 mL)	110	12	23
7	1:3	I_2 (25)	NMP (2 mL)	110	12	trace
8	1:3	NH_4Cl (50)	DMA (2 mL)	110	12	55
9	1:3	NaOAc (50)	DMA (2 mL)	110	12	62
10	1:3	Et_3N (50)	DMA (2 mL)	110	12	53
11	1:3	–	DMA (2 mL)	110	12	65
12	1:3	–	DMA (2 mL)	110	24	63
13	1:4	–	DMA (2 mL)	110	24	94 (86)[e]
14	1:4	–	DMA (2 mL)	110	30	91
15	1:4	–	DMA (2 mL)	110	12	67
16	1:4	–	DMA (2 mL)	110	15	75
17[c]	1:4	–	DMA (2 mL)	110	24	29
18[d]	1:4	–	DMA (2 mL)	110	24	17

[a] Reaction conditions(unless otherwise stated): **1a** (0.3 mmol), **2a** (1.2 mmol), 110 ^{o}C, 24 h, in DMA (2 mL) under a dioxygen atmosphere; [b] GC yield by using biphenyl as internal standard; [c] in air; [d] in N_2; [e] Isolated yield.

2.2 General Procedure for Substrate Scope

A solution of thiol **1** (0.3 mmol, 1 equivalent) and amine **2** (1.2 mmol, 4 equivalent) in DMA (2.0 mL) was stirred under an oxygen atmosphere at 110 ^{o}C for 24 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (5 mL). The aqueous solution was extracted with ethyl acetate (3 × 10 mL) and the combined extracts were dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure by rotary evaporation. Then, the pure product was obtained by flash column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 5:1 to 1:1).

3. Mechanism Studies

3.1 The radical inhibition experiment

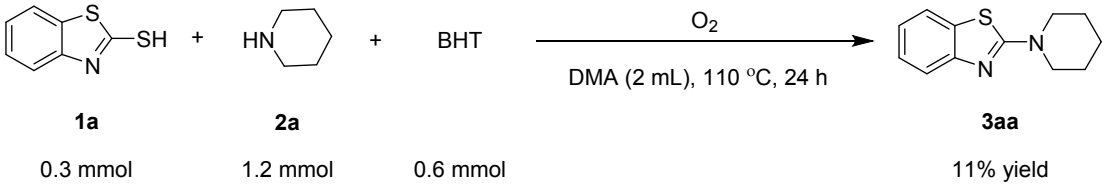


Figure S1 The radical inhibition experiment

A solution of 2-mercaptobenzothiazole **1a** (0.3 mmol, 1 equivalent, 50.2 mg), piperidine **2a** (1.2 mmol, 4 equivalent, 102.2 mg) and BHT (0.6 mmol, 2 equivalent, 132.2 mg) in DMA (2.0 mL) was stirred under an oxygen atmosphere at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (5 mL). The aqueous solution was extracted with ethyl acetate (3 × 10 mL) and the combined extracts were dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure by rotary evaporation. Then, the pure product **3aa** was obtained in 11% yield by flash column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 5:1).

3.2 The intermediate experiments

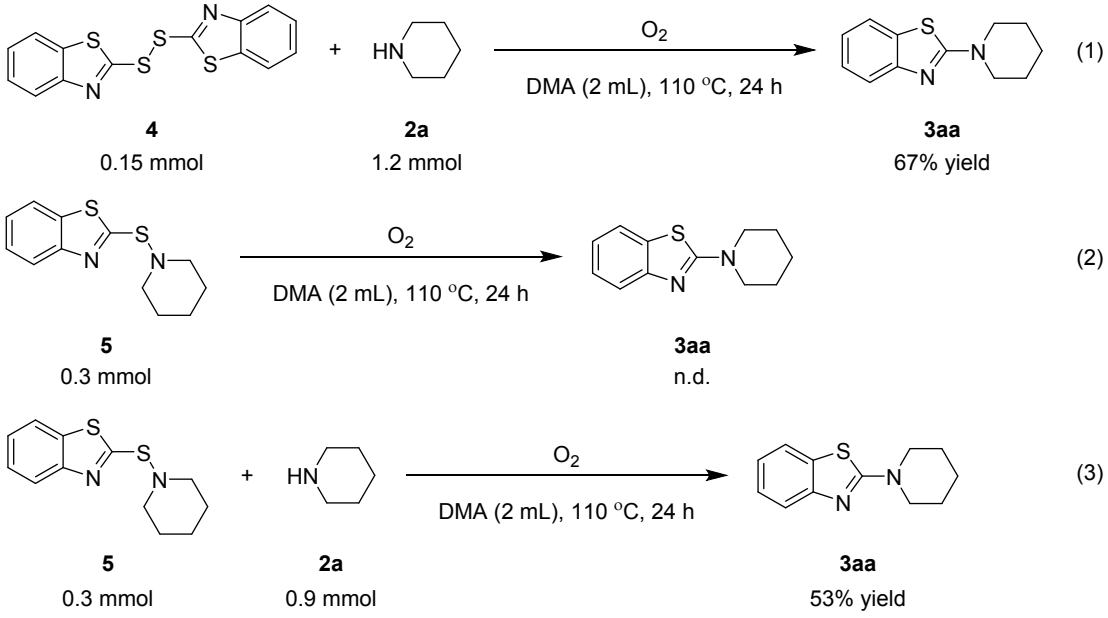


Figure S2 The intermediate experiments.

(1) A solution of 1,2-bis(benzo[d]thiazol-2-yl)disulfane **4** (0.15 mmol, 1 equivalent, 49.9 mg), Piperidine **2a** (1.2 mmol, 8 equivalent, 102.2 mg) in DMA (2.0 mL) was stirred under an oxygen atmosphere at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (5 mL). The aqueous solution was extracted with ethyl

acetate (3 × 10 mL) and the combined extracts were dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure by rotary evaporation. Then, the pure product **3aa** was obtained in 67% yield by flash column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 5:1).

(2) A solution of 2-(piperidin-1-ylthio)benzo[d]thiazole **5** (0.3 mmol, 1 equivalent, 75.1 mg) in DMA (2.0 mL) was stirred under an oxygen atmosphere at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (5 mL) and ethyl acetate (10 mL). No desired product was detected by TLC and GC-MS.

(3) A solution of 2-(piperidin-1-ylthio)benzo[d]thiazole **5** (0.3 mmol, 1 equivalent, 75.1 mg), Piperidine **2a** (0.9 mmol, 3 equivalent, 76.64 mg) in DMA (2.0 mL) was stirred under an oxygen atmosphere at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (5 mL). The aqueous solution was extracted with ethyl acetate (3 × 10 mL) and the combined extracts were dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure by rotary evaporation. Then, the pure product **3aa** was obtained in 53% yield by flash column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 5:1).

4. Procedure for Gram-Scale Reaction

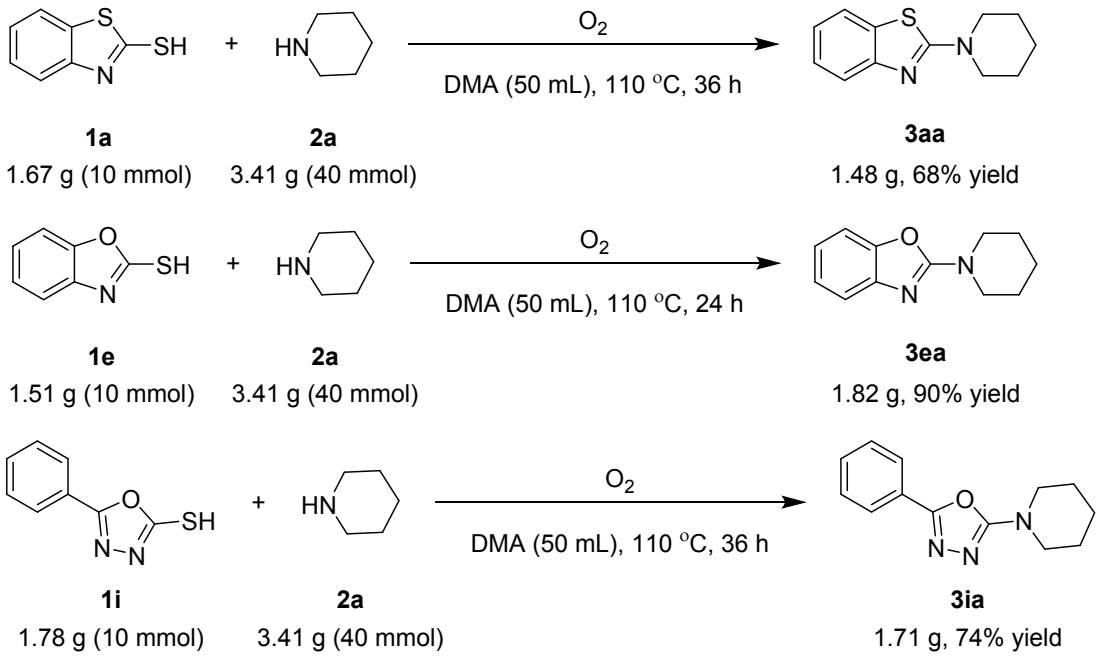


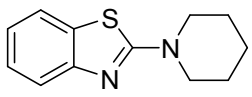
Figure S3 The gram-scale reactions.

(1) A solution of 2-mercaptobenzothiazole **1a** (10 mmol, 1 equivalent, 1.67 g), piperidine **2a** (40 mmol, 4 equivalent, 3.41 g) in DMA (50 mL) was stirred under an oxygen atmosphere at 110 °C for 36 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (100 mL). The aqueous solution was extracted with ethyl acetate (3 × 100 mL) and the combined extracts were dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure by rotary evaporation. Then, the pure product **3aa** was obtained in 68% yield by flash column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 5:1).

(2) A solution of 2-mercatobenzoxazole **1e** (10 mmol, 1 equivalent, 1.51 g), piperidine **2a** (40 mmol, 4 equivalent, 3.41 g) in DMA (50 mL) was stirred under an oxygen atmosphere at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (100 mL). The aqueous solution was extracted with ethyl acetate (3 × 100 mL) and the combined extracts were dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure by rotary evaporation. Then, the pure product **3ea** was obtained in 90% yield by flash column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 5:1).

(3) A solution of 5-phenyl-1,3,4-oxadiazole-2-thiol **1i** (10 mmol, 1 equivalent, 1.78 g), Piperidine **2a** (40 mmol, 4 equivalent, 3.41 g) in DMA (50 mL) was stirred under an oxygen atmosphere at 110 °C for 36 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (100 mL). The aqueous solution was extracted with ethyl acetate (3 × 100 mL) and the combined extracts were dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure by rotary evaporation. Then, the pure product **3ia** was obtained in 74% yield by flash column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 5:1).

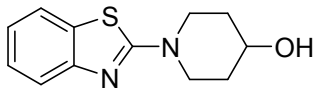
5. Characterization of Products



3aa

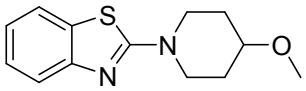
2-(Piperidin-1-yl)benzo[d]thiazole (3aa)[1]: 56.2 mg white solid was obtained in 86% isolated yield. m.p. 86-89 °C. IR (ATR): υ 2937, 2847, 1621, 1587, 1520, 1438, 1379, 1330, 1285, 1256, 1211, 1118, 1006, 931, 902, 849, 812, 756, 689 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (td, *J* = 8.0, 0.1 Hz, 1H),

7.53 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.04 (td, *J* = 8.0, 4.0 Hz, 1H), 3.60 – 3.58 (m, 4H), 1.70 – 1.68 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.99, 153.04, 130.74, 125.96, 121.12, 120.67, 118.84, 49.71, 25.41, 24.35.



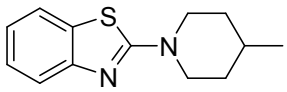
3ab

1-(Benzo[d]thiazol-2-yl)piperidin-4-ol (3ab): 53.4 mg white solid was obtained in 76% isolated yield. m.p. 113-116 °C. IR (ATR): υ 3354, 3198, 2922, 2851, 1654, 1591, 1524, 1446, 1375, 1330, 1285, 1252, 1215, 1084, 1017, 972, 816, 749, 723, 667 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.53 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.28 (td, *J* = 8.0, 0.1 Hz, 1H), 7.06 (td, *J* = 8.0, 0.1 Hz, 1H), 3.97 – 3.91 (m, 3H), 3.39 – 3.32 (m, 2H), 2.53 (s, 1H), 2.00 – 1.94 (m, 2H), 1.69 – 1.60 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.68, 152.72, 130.75, 126.09, 121.45, 120.76, 118.88, 66.93, 46.09, 33.53. **HRMS (ESI)** calcd for $C_{12}H_{15}N_2OS^+$, $[M+H]^+$, 235.0900, found 235.0901.



3ac

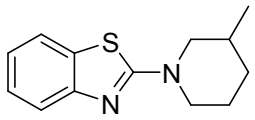
2-(4-Methoxypiperidin-1-yl)benzo[d]thiazole (3ac): 62.8 mg white solid was obtained in 84% isolated yield. m.p. 74-77 °C. IR (ATR): υ 3056, 2974, 2944, 2851, 2814, 1528, 1446, 1375, 1289, 1222, 1125, 1092, 1017, 935, 816, 752 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.53 (dd, *J* = 4.0, 0.1 Hz, 1H), 7.27 (td, *J* = 8.0, 0.1 Hz, 1H), 7.04 (td, *J* = 8.0, 0.1 Hz, 1H), 3.88 – 3.82 (m, 2H), 3.48 – 3.39 (m, 3H), 3.36 (s, 3H), 1.98 – 1.92 (m, 2H), 1.75 – 1.67 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.52, 152.87, 130.82, 125.95, 121.25, 120.65, 118.88, 75.13, 55.79, 45.78, 29.94. **HRMS (ESI)** calcd for $C_{13}H_{17}N_2OS^+$, $[M+H]^+$, 249.1056, found 249.1055.



3ad

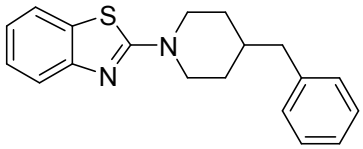
2-(4-Methylpiperidin-1-yl)benzo[d]thiazole (3ad): 42.8 mg white solid was obtained in 62% isolated yield. m.p. 71-74 °C. IR (ATR): υ 2952, 2922, 2847, 1528, 1446, 1382, 1285, 1226, 1155, 1125, 1088, 1017, 965, 790, 753 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.54 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.28 (td, *J* = 8.0, 4.0 Hz, 1H), 7.05 (td, *J* = 8.0, 4.0 Hz, 1H), 4.13 – 4.08 (m, 2H), 3.13 – 3.06 (m, 2H), 1.77 – 1.73 (m, 2H), 1.66 – 1.60 (m, 1H), 1.35 – 1.25 (m, 2H), 0.98 (d, *J* = 8.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.87, 153.05, 130.79, 125.96, 121.14, 120.67, 118.86, 49.10, 33.55, 30.91, 21.87. **HRMS (ESI)** calcd for $C_{13}H_{17}N_2S^+$, $[M+H]^+$, 233.1107, found 233.1111.



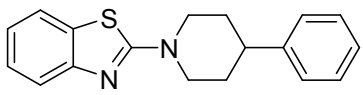
3ae

2-(3-Methylpiperidin-1-yl)benzo[d]thiazole (3ae): 47.5 mg white solid was obtained in 68% isolated yield. m.p. 82-85 °C. IR (ATR): υ 2922, 2855, 1729, 1595, 1535, 1442, 1390, 1282, 1226, 1125, 1073, 969, 924, 887, 849, 752 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.54 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.27 (td, *J* = 8.0, 4.0 Hz, 1H), 7.04 (td, *J* = 8.0, 0.1 Hz, 1H), 4.06 – 4.01 (m, 2H), 3.07 (td, *J* = 12.0, 4.0 Hz, 1H), 2.76 – 2.70 (m, 1H), 1.88 – 1.83 (m, 1H), 1.80 – 1.73 (m, 2H), 1.70 – 1.60 (m, 1H), 1.21 – 1.11 (m, 1H), 0.97 (d, *J* = 8.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.90, 153.06, 130.72, 125.98, 121.13, 120.67, 118.84, 56.14, 49.24, 32.92, 30.85, 24.95, 19.10. **HRMS (ESI)** calcd for $C_{13}H_{17}N_2S^+$, $[M+H]^+$, 233.1107, found 233.1106.



3af

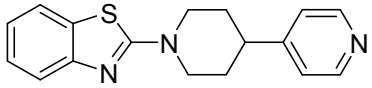
2-(4-Benzylpiperidin-1-yl)benzo[d]thiazole (3af): 73.1 mg white solid was obtained in 79% isolated yield. m.p. 106-109 °C. IR (ATR): υ 3063, 3022, 2922, 2851, 1535, 1442, 1386, 1274, 1237, 1170, 1107, 1054, 961, 920, 834, 749, 697 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 – 7.53 (m, 2H), 7.33 – 7.21 (m, 4H), 7.17 – 7.15 (m, 2H), 7.08 – 7.04 (m, 1H), 4.13 (d, *J* = 16.0 Hz, 2H), 3.10 – 3.04 (m, 2H), 2.59 – 2.58 (m, 2H), 1.82 – 1.79 (m, 3H), 1.42 – 1.33 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.82, 152.98, 140.00, 130.79, 129.23, 128.45, 126.21, 126.03, 121.25, 120.72, 118.91, 49.10, 43.09, 38.11, 31.56. **HRMS (ESI)** calcd for $C_{19}H_{21}N_2S^+$, $[M+H]^+$, 309.1420, found 309.1419.



3ag

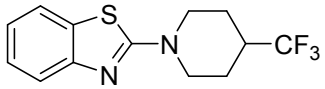
2-(4-Phenylpiperidin-1-yl)benzo[d]thiazole (3ag): 78.6 mg white solid was obtained in 89% isolated yield. m.p. 129-132 °C. IR (ATR): υ 3060, 3026, 2944, 2851, 1528, 1438, 1379, 1341, 1259, 1211, 1095, 1069, 917, 805, 749, 697 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 2H), 7.37 – 7.31 (m, 3H),

7.27 – 7.23 (m, 3H), 7.12 – 7.08 (m, 1H), 4.33 – 4.29 (m, 2H), 3.28 – 3.21 (m, 2H), 2.83 – 2.75 (m, 1H), 2.01 – 1.97 (m, 2H), 1.92 – 1.82 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.78, 152.97, 145.19, 130.84, 128.67, 126.83, 126.63, 126.04, 121.33, 120.74, 118.99, 49.40, 42.51, 32.72. **HRMS (ESI)** calcd for $C_{18}H_{19}N_2S^+$, $[M+H]^+$, 295.1263, found 295.1263.



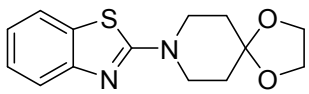
3ah

2-(4-(Pyridin-4-yl)piperidin-1-yl)benzo[d]thiazole (3ah): 71.4 mg white solid was obtained in 81% isolated yield. m.p. 157-160 °C. IR (ATR): υ 3056, 3015, 2952, 2907, 2858, 1528, 1438, 1416, 1386, 1338, 1282, 1244, 1215, 1002, 917, 879, 838, 760, 697 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.52 – 8.50 (m, 2H), 7.60 – 7.58 (m, 1H), 7.56 – 7.54 (m, 1H), 7.30 – 7.26 (m, 1H), 7.11 – 7.04 (m, 3H), 4.29 – 4.25 (m, 2H), 3.23 – 3.16 (m, 2H), 2.77 – 2.71 (m, 1H), 1.95 – 1.92 (m, 2H), 1.81 – 1.74 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.58, 153.63, 152.80, 150.10, 130.80, 126.07, 122.19, 121.46, 120.74, 119.05, 48.96, 41.70, 31.73. **HRMS (ESI)** calcd for $C_{17}H_{18}N_3S^+$, $[M+H]^+$, 296.1216, found 296.1214.



3ai

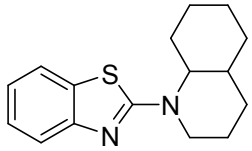
2-(4-(Trifluoromethyl)piperidin-1-yl)benzo[d]thiazole (3ai): 55.7 mg white solid was obtained in 65% isolated yield. m.p. 165-168 °C. IR (ATR): υ 3056, 2955, 2922, 2847, 1517, 1446, 1386, 1326, 1285, 1252, 1189, 1129, 1080, 1002, 861, 812, 756, 693 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (dd, J = 8.0, 0.1 Hz, 1H), 7.57 (dd, J = 8.0, 0.1 Hz, 1H), 7.31 (td, J = 8.0, 0.1 Hz, 1H), 7.19 (td, J = 8.0, 0.1 Hz, 1H), 4.27 – 4.23 (m, 2H), 3.13 – 3.05 (m, 2H), 2.34 – 2.22 (m, 1H), 2.01 – 1.97 (m, 2H), 1.76 – 1.65 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.46, 152.72, 130.89, 127.02 (q, $^1J_{C\text{-}F}$ = 279.0 Hz), 126.19, 121.71, 120.83, 119.28, 47.56, 40.50 (q, $^2J_{C\text{-}F}$ = 27.9 Hz), 24.10 (q, $^3J_{C\text{-}F}$ = 3.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -73.75. **HRMS (ESI)** calcd for $C_{13}H_{14}F_3N_2S^+$, $[M+H]^+$, 287.0824, found 287.0825.



3aj

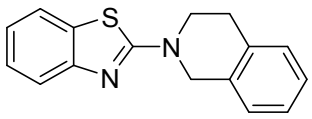
8-(Benzo[d]thiazol-2-yl)-1,4-dioxa-8-azaspiro[4.5]decane (3aj)[2]: 59.8 mg white solid was obtained in 72% isolated yield. m.p. 117-120 °C. IR (ATR): υ 2922, 2866, 1543, 1438, 1386, 1356, 1289, 1233, 1196, 1133, 1099, 1066, 943, 890, 838, 749 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 8.0, 0.1

Hz, 1H), 7.54 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.28 (td, *J* = 8.0, 0.1 Hz, 1H), 7.06 (td, *J* = 8.0, 0.1 Hz, 1H), 3.98 (s, 4H), 3.74 (t, *J* = 8.0 Hz, 4H), 1.83 (t, *J* = 8.0 Hz, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.30, 152.91, 130.99, 126.02, 121.38, 120.72, 118.97, 106.93, 64.56, 46.84, 34.43.



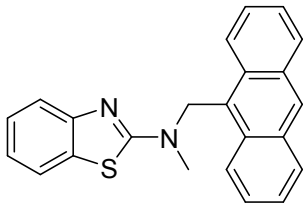
3ak

2-(Octahydroquinolin-1(2H)-yl)benzo[d]thiazole (3ak): 45.9 mg white solid was obtained in 56% isolated yield. m.p. 73-76 °C. IR (ATR): υ 2922, 2851, 1595, 1531, 1446, 1390, 1341, 1315, 1233, 1129, 1017, 957, 931, 887, 834, 797, 749 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.54 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.27 (td, *J* = 8.0, 0.1 Hz, 1H), 7.04 (td, *J* = 8.0, 0.1 Hz, 1H), 3.87 – 3.81 (m, 1H), 3.58 – 3.51 (m, 1H), 3.23 – 3.17 (m, 1H), 2.42 – 2.38 (m, 1H), 1.97 – 1.92 (m, 1H), 1.86 – 1.84 (m, 1H), 1.78 – 1.65 (m, 5H), 1.51 – 1.40 (m, 2H), 1.35 – 1.28 (m, 1H), 1.26 – 1.09 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.29, 152.90, 130.54, 125.79, 120.90, 120.50, 118.78, 65.92, 44.85, 38.54, 33.15, 30.36, 27.07, 26.16, 25.46, 22.63. **HRMS (ESI)** calcd for $C_{16}H_{21}N_2S^+$, $[M+H]^+$, 273.1420, found 273.1421.



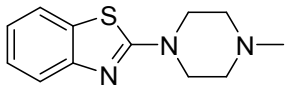
3al

2-(3,4-Dihydroisoquinolin-2(1H)-yl)benzo[d]thiazole (3al)[2]: 58.6 mg white solid was obtained in 73% isolated yield. m.p. 139-142 °C. IR (ATR): υ 3056, 3026, 2952, 2918, 2847, 1733, 1662, 1595, 1531, 1490, 1442, 1401, 1334, 1282, 1230, 1189, 1155, 1047, 969, 928, 890, 816, 741, 701 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (t, *J* = 8.0 Hz, 2H), 7.34 – 7.30 (m, 1H), 7.25 – 7.18 (m, 4H), 7.11 – 7.07 (m, 1H), 4.83 (s, 2H), 3.88 (t, *J* = 8.0 Hz, 2H), 3.03 (t, *J* = 8.0 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.25, 152.91, 134.43, 132.66, 130.59, 128.71, 126.98, 126.71, 126.54, 126.16, 121.34, 120.84, 119.10, 49.73, 46.31, 28.93.



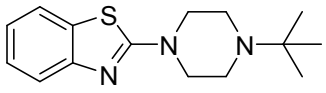
3am

N-(anthracen-9-ylmethyl)-N-methylbenzo[d]thiazol-2-amine (3am): 31.3 mg off-white solid was obtained in 30% isolated yield. m.p. 75-78 ^{o}C. IR (ATR): υ 3052, 2955, 2922, 2792, 1945, 1722, 1669, 1625, 1576, 1524, 1453, 1423, 1379, 1330, 1282,1252, 1159, 1121, 1047, 998, 961, 931, 887, 842, 808, 756, 730, 693 cm^{-1}.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.34 (d, *J* = 12.0 Hz, 2H), 8.07 – 8.05 (m, 2H), 7.74 – 7.68 (m, 2H), 7.54 – 7.48 (m, 4H), 7.42 – 7.37 (m, 1H), 7.15 (td, *J* = 8.0, 1.0 Hz, 1H), 5.82 (s, 2H), 2.74 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.84, 153.31, 131.58, 131.50, 131.08, 129.42, 128.87, 127.01, 126.68, 126.22, 125.33, 124.10, 121.27, 120.92, 119.22, 46.88, 36.00. **HRMS (ESI)** calcd for $C_{23}H_{19}N_2S^+$, $[M+H]^+$, 355.1263, found 355.1266.



3an

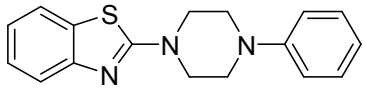
2-(4-Methylpiperazin-1-yl)benzo[d]thiazole (3an)[3]: 27.6 mg white solid was obtained in 40% isolated yield. m.p. 82-85 ^{o}C. IR (ATR): υ 3052, 2937, 2885, 2844, 2691, 1654, 1524, 1446, 1338, 1297, 1263, 1211, 1166, 1140, 1069, 1039, 954, 834, 786, 749 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.54 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.28 (td, *J* = 8.0, 0.1 Hz, 1H), 7.06 (td, *J* = 8.0, 0.1 Hz, 1H), 3.65 (t, *J* = 8.0 Hz, 4H), 2.53 (t, *J* = 4.0 Hz, 4H), 2.34 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.82, 152.73, 130.78, 126.08, 121.53, 120.78, 119.15, 54.32, 48.30, 46.22.



3ao

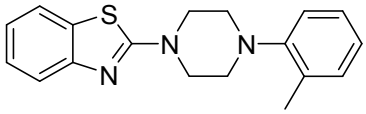
2-(4-(Tert-butyl)piperazin-1-yl)benzo[d]thiazole (3ao): 49.8 mg white solid was obtained in 60% isolated yield. m.p. 132-135 ^{o}C. IR (ATR): υ 2967, 2922, 2851, 2810, 2750, 1647, 1595, 1535, 1438, 1386, 1345, 1200, 1140, 1110, 1013, 958, 917, 838, 805, 745, 719 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.54 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.27 (td, *J* = 8.0, 4.0 Hz, 1H), 7.05 (td, *J* = 8.0, 0.1 Hz, 1H), 3.62 (t, *J* = 4.0 Hz, 4H), 2.68 (t, *J* = 4.0 Hz, 4H), 1.08 (s, 9H). **^{13}C NMR** (101 MHz,

$CDCl_3$) δ 168.79, 152.85, 130.73, 126.02, 121.35, 120.74, 119.04, 54.12, 49.15, 45.39, 26.00. **HRMS (ESI)** calcd for $C_{15}H_{22}N_3S^+$, $[M+H]^+$, 276.1529, found 276.1532.



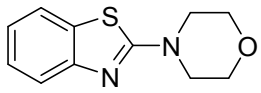
3ap

2-(4-Phenylpiperazin-1-yl)benzo[d]thiazole (3ap)[2]: 68.8 mg white solid was obtained in 78% isolated yield. m.p. 150-153 °C. IR (ATR): υ 3052, 2952, 2914, 2844, 1539, 1442, 1382, 1345, 1293, 1230, 1155, 1069, 1025, 991, 935, 752, 685 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.35 – 7.30 (m, 3H), 7.12 (td, *J* = 8.0, 4.0 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.94 (td, *J* = 8.0, 1.0 Hz, 1H), 3.82 (t, *J* = 4.0 Hz, 4H), 3.34 (t, *J* = 4.0 Hz, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.79, 152.70, 151.03, 130.82, 129.36, 126.17, 121.68, 120.85, 120.77, 119.28, 116.95, 49.20, 48.40.



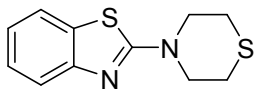
3aq

2-(4-(*o*-Tolyl)piperazin-1-yl)benzo[d]thiazole (3aq): 63.9 mg white solid was obtained in 69% isolated yield. m.p. 117-120 °C. IR (ATR): υ 3056, 3019, 2959, 2918, 2840, 1591, 1520, 1442, 1375, 1323, 1293, 1230, 1148, 1073, 1025, 853, 749, 719 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 2H), 7.35 – 7.31 (m, 1H), 7.25 – 7.19 (m, 2H), 7.12 – 7.09 (m, 1H), 7.07 – 7.03 (m, 2H), 3.80 (t, *J* = 4.0 Hz, 4H), 3.06 (t, *J* = 4.0 Hz, 4H), 2.38 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.01, 152.77, 150.97, 132.81, 131.29, 130.78, 126.80, 126.13, 123.89, 121.57, 120.82, 119.27, 119.22, 51.37, 49.01, 17.96. **HRMS (ESI)** calcd for $C_{18}H_{20}N_3S^+$, $[M+H]^+$, 310.1372, found 310.1371.



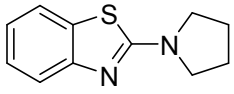
3ar

4-(Benzo[d]thiazol-2-yl)morpholine (3ar)[2]: 30.8 mg white solid was obtained in 48% isolated yield. m.p. 125-128 °C. IR (ATR): υ 2955, 2914, 2851, 1733, 1531, 1461, 1379, 1338, 1289, 1226, 1181, 1110, 1066, 1017, 972, 943, 857, 823, 752, 697 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.32 (td, *J* = 8.0, 0.1 Hz, 1H), 7.11 (td, *J* = 8.0, 0.1 Hz, 1H), 3.85 (t, *J* = 4.0 Hz, 4H), 3.64 (t, *J* = 4.0 Hz, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.17, 152.60, 130.69, 126.25, 121.83, 120.93, 119.43, 66.39, 48.61.



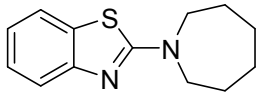
3as

2-Thiomorpholinobenzo[d]thiazole (3as)[1]: 30.4 mg white solid was obtained in 43% isolated yield. m.p. 88-91 °C. IR (ATR): υ 2963, 2914, 2847, 1543, 1431, 1356, 1293, 1230, 1189, 1095, 1017, 950, 797, 749, 723, 674 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.54 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.30 (td, *J* = 8.0, 0.1 Hz, 1H), 7.08 (td, *J* = 8.0, 0.1 Hz, 1H), 3.96 (t, *J* = 4.0 Hz, 4H), 2.74 (t, *J* = 4.0 Hz, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.17, 152.69, 130.73, 126.18, 121.62, 120.80, 119.19, 51.30, 26.66.



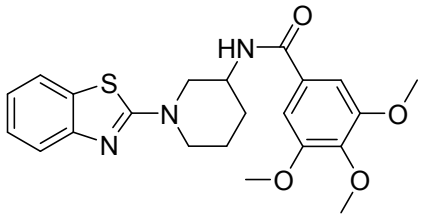
3at

2-(Pyrrolidin-1-yl)benzo[d]thiazole (3at)[4]: 25.6 mg off-white solid was obtained in 42% isolated yield. m.p. 96-99 °C. IR (ATR): υ 2952, 2918, 2847, 1743, 1599, 1543, 1446, 1364, 1315, 1274, 1218, 1177, 1121, 1058, 1017, 969, 857, 820, 749, 719, 670 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 – 7.59 (m, 1H), 7.58 – 7.57 (m, 1H), 7.30 – 7.28 (m, 1H), 7.04 (td, *J* = 8.0, 0.1 Hz, 1H), 3.57 (t, *J* = 4.0 Hz, 4H), 2.08 – 2.05 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.44, 153.39, 130.80, 126.00, 120.78, 120.74, 118.73, 49.58, 25.77.



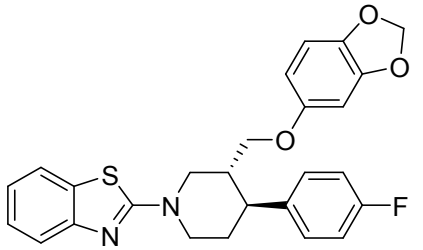
3au

2-(Azepan-1-yl)benzo[d]thiazole (3au): 23.0 mg off-white solid was obtained in 33% isolated yield. m.p. 82-85 °C. IR (ATR): υ 2922, 2851, 1595, 1535, 1442, 1386, 1360, 1300, 1252, 1192, 1155, 1125, 1066, 1013, 902, 849, 823, 749, 685 cm^{-1}. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.71 (dd, *J* = 8.0, 0.1 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.24 (td, *J* = 8.0, 4.0 Hz, 1H), 7.01 (td, *J* = 8.0, 4.0 Hz, 1H), 3.62 (t, *J* = 4.0 Hz, 4H), 1.79 – 1.77 (m, 4H), 1.54 – 1.51 (m, 4H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 167.13, 153.07, 130.20, 125.85, 120.98, 120.49, 118.04, 50.27, 27.25, 26.89. **HRMS (ESI)** calcd for $C_{13}H_{17}N_2S^+$, $[M+H]^+$, 233.1107, found 233.1105.



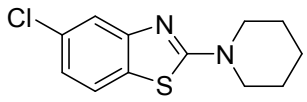
3av

N-(1-(benzo[d]thiazol-2-yl)piperidin-3-yl)-3,4,5-trimethoxybenzamide (3av): 73.2 mg white solid was obtained in 57% isolated yield. m.p. 158-161 °C. IR (ATR): υ 3265, 2937, 2847, 1628, 1584, 1535, 1498, 1446, 1412, 1379, 1341, 1259, 1233, 1185, 1129, 991, 857, 775, 749, 708, 678 cm^{-1}. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.36 – 8.35 (m, 1H), 7.75 – 7.73 (m, 1H), 7.45 – 7.43 (m, 1H), 7.28 – 7.25 (m, 1H), 7.17 (s, 2H), 7.07 – 7.04 (m, 1H), 4.17 – 4.14 (m, 1H), 3.99 – 3.90 (m, 2H), 3.81 (s, 6H), 3.70 (s, 3H), 3.23 – 3.10 (m, 2H), 1.99 – 1.89 (m, 2H), 1.71 – 1.63 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 167.94, 165.72, 152.58, 152.56, 139.97, 130.49, 129.63, 126.00, 121.17 (d, J = 2.0 Hz), 118.50, 104.95, 60.12, 56.01, 52.57, 48.41, 46.00, 29.62, 23.30. **HRMS (ESI)** calcd for $C_{22}H_{26}N_3O_4S^+$, $[M+H]^+$, 428.1639, found 428.1638.



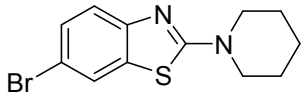
3aw

2-((3R,4S)-3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)piperidin-1-yl)benzo[d]thiazole (3aw): 99.7 mg white solid was obtained in 72% isolated yield. m.p. 76-79 °C. IR (ATR): υ 3056, 2918, 2773, 1893, 1684, 1632, 1595, 1531, 1446, 1386, 1271, 1218, 1177, 1125, 1103, 1036, 969, 931, 831, 782, 752, 723, 671 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 2H), 7.35 – 7.30 (m, 1H), 7.14 – 7.08 (m, 3H), 7.01 – 6.97 (m, 2H), 6.67 – 6.65 (m, 1H), 6.43 – 6.42 (m, 1H), 6.20 – 6.18 (m, 1H), 5.90 (s, 2H), 4.47 – 4.43 (m, 1H), 4.34 – 4.30 (m, 1H), 3.69 – 3.66 (m, 1H), 3.54 – 3.50 (m, 1H), 3.27 – 3.20 (m, 2H), 2.85 – 2.78 (m, 1H), 2.26 – 2.19 (m, 1H), 1.96 – 1.90 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.67, 161.70 (d, $^{1}J_{C\text{-}F}$ = 245.4 Hz), 154.14, 152.89, 148.24, 141.83, 138.56 (d, $^{4}J_{C\text{-}F}$ = 3.0 Hz), 130.92, 128.84 (d, $^{3}J_{C\text{-}F}$ = 7.1 Hz), 126.10, 121.47, 120.78, 119.08, 115.66 (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 107.93, 105.63, 101.20, 98.09, 68.55, 52.16, 49.16, 43.80, 41.60, 33.29. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.64. **HRMS (ESI)** calcd for $C_{26}H_{24}FN_2O_3S^+$, $[M+H]^+$, 463.1486, found 463.1492.



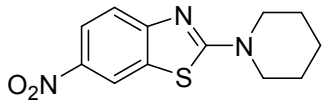
3ba

5-Chloro-2-(piperidin-1-yl)benzo[d]thiazole (3ba): 45.7 mg white solid was obtained in 61% isolated yield. m.p. 78-81 °C. IR (ATR): υ 2922, 2851, 1520, 1438, 1326, 1244, 1211, 1121, 1062, 1010, 905, 857, 820, 790, 730, 670 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (m, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.00 (dd, *J* = 8.0, 0.1 Hz, 1H), 3.59 – 3.58 (m, 4H), 1.69 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.95, 154.21, 131.80, 129.02, 121.26, 121.17, 118.78, 49.75, 25.42, 24.31. **HRMS (ESI)** calcd for $C_{12}H_{14}ClN_2S^+$, $[M+H]^+$, 253.0561, found 253.0561.



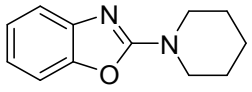
3ca

6-Bromo-2-(piperidin-1-yl)benzo[d]thiazole (3ca): 40.9 mg white solid was obtained in 46% isolated yield. m.p. 119-122 °C. IR (ATR): υ 2926, 2847, 1528, 1438, 1379, 1330, 1241, 1207, 1121, 1084, 1047, 1010, 957, 931, 898, 868, 812, 693 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.66 (m, 1H), 7.35 (m, 2H), 3.57 – 3.56 (m, 4H), 1.70 – 1.68 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.98, 152.09, 132.46, 129.14, 123.13, 119.92, 113.27, 49.74, 25.40, 24.27. **HRMS (ESI)** calcd for $C_{12}H_{14}BrN_2S^+$, $[M+H]^+$, 297.0056, found 297.0056.



3da

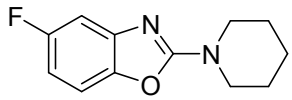
6-Nitro-2-(piperidin-1-yl)benzo[d]thiazole (3da)[1]: 26.8 mg white solid was obtained in 34% isolated yield. m.p. 164-167 °C. IR (ATR): υ 2937, 2855, 1532, 1498, 1438, 1297, 1252, 1118, 1010, 879, 831, 749 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.0 Hz, 1H), 8.17 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 3.67 (m, 4H), 1.73 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.87, 158.59, 141.42, 130.93, 122.70, 117.77, 117.25, 50.05, 25.47, 24.16.



3ea

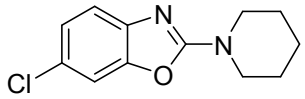
2-(Piperidin-1-yl)benzo[d]oxazole (3ea)[4]: 56.4 mg off-white solid was obtained in 93% isolated yield. m.p. 67-70 °C. IR (ATR): υ 2922, 2851, 1625, 1573, 1453, 1394, 1356, 1274, 1174, 1136, 1054, 1025,

917, 883, 790, 741, 667 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.13 (td, *J* = 8.0, 0.1 Hz, 1H), 6.98 (td, *J* = 8.0, 0.1 Hz, 1H), 3.64 – 3.63 (m, 4H), 1.66 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.49, 148.72, 143.39, 123.90, 120.34, 116.02, 108.63, 46.66, 25.30, 24.13.



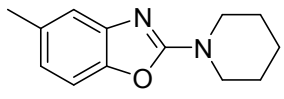
3fa

5-Fluoro-2-(piperidin-1-yl)benzo[d]oxazole (3fa): 64.1 mg white solid was obtained in 96% isolated yield. m.p. 79-82 °C. IR (ATR): υ 2922, 2855, 1636, 1576, 1468, 1442, 1394, 1282, 1256, 1177, 1125, 1025, 976, 950, 890, 834, 797, 667 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.10 – 7.07 (m, 1H), 6.99 (dd, *J* = 8.0, 0.1 Hz, 1H), 6.65 (td, *J* = 8.0, 0.1 Hz, 1H), 3.62 (m, 4H), 1.65 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.57, 160.11 (d, $^{1}J_{C\text{-}F}$ = 238.0 Hz), 144.93, 144.60 (d, $^{3}J_{C\text{-}F}$ = 52.0 Hz), 108.38 (d, $^{3}J_{C\text{-}F}$ = 40.0 Hz), 106.60 (d, $^{2}J_{C\text{-}F}$ = 104.0 Hz), 103.08 (d, $^{2}J_{C\text{-}F}$ = 104.0 Hz), 46.55, 25.28, 24.04. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -119.40. **HRMS (ESI)** calcd for $C_{12}H_{14}FN_2O^+$, $[M+H]^+$, 221.1085, found 221.1085.



3ga

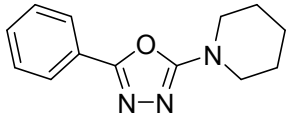
6-Chloro-2-(piperidin-1-yl)benzo[d]oxazole (3ga): 64.6 mg white solid was obtained in 91% isolated yield. m.p. 68-71 °C. IR (ATR): υ 2993, 2944, 2855, 1640, 1580, 1461, 1397, 1349, 1289, 1125, 1095, 1047, 1013, 957, 913, 801, 719 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 – 7.19 (m, 2H), 7.10 (dd, *J* = 8.0, 4.0 Hz, 1H), 3.63 (m, 4H), 1.67 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.80, 148.90, 142.33, 125.33, 124.21, 116.27, 109.48, 46.70, 25.32, 24.09. **HRMS (ESI)** calcd for $C_{12}H_{14}ClN_2O^+$, $[M+H]^+$, 237.0789, found 237.0792.



3ha

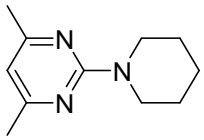
5-Methyl-2-(piperidin-1-yl)benzo[d]oxazole (3ha)[5]: 51.1 mg white solid was obtained in 79% isolated yield. m.p. 92-95 °C. IR (ATR): υ 2940, 2855, 1640, 1584, 1438, 1397, 1289, 1256, 1181, 1151, 1121, 1017, 958, 887, 790 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 (s, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.78 (dd,

J = 8.0, 0.1 Hz, 1H), 3.63 – 3.62 (m, 4H), 2.37 (s, 3H), 1.66 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.72, 146.90, 143.55, 133.51, 120.97, 116.47, 107.98, 46.66, 25.32, 24.17, 21.65.



3ia

2-Phenyl-5-(piperidin-1-yl)-1,3,4-oxadiazole (3ia)[6]: 49.6 mg white solid was obtained in 72% isolated yield. m.p. 98-101 °C. IR (ATR): υ 2937, 2855, 1617, 1487, 1442, 1379, 1301, 1271, 1129, 1058, 1025, 958, 902, 857, 801, 723, 678 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 – 7.89 (m, 2H), 7.45 – 7.43 (m, 3H), 3.55 – 3.54 (m, 4H), 1.69 – 1.68 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.49, 159.08, 130.41, 128.89, 125.80, 124.86, 47.22, 25.04, 23.92.



3ja

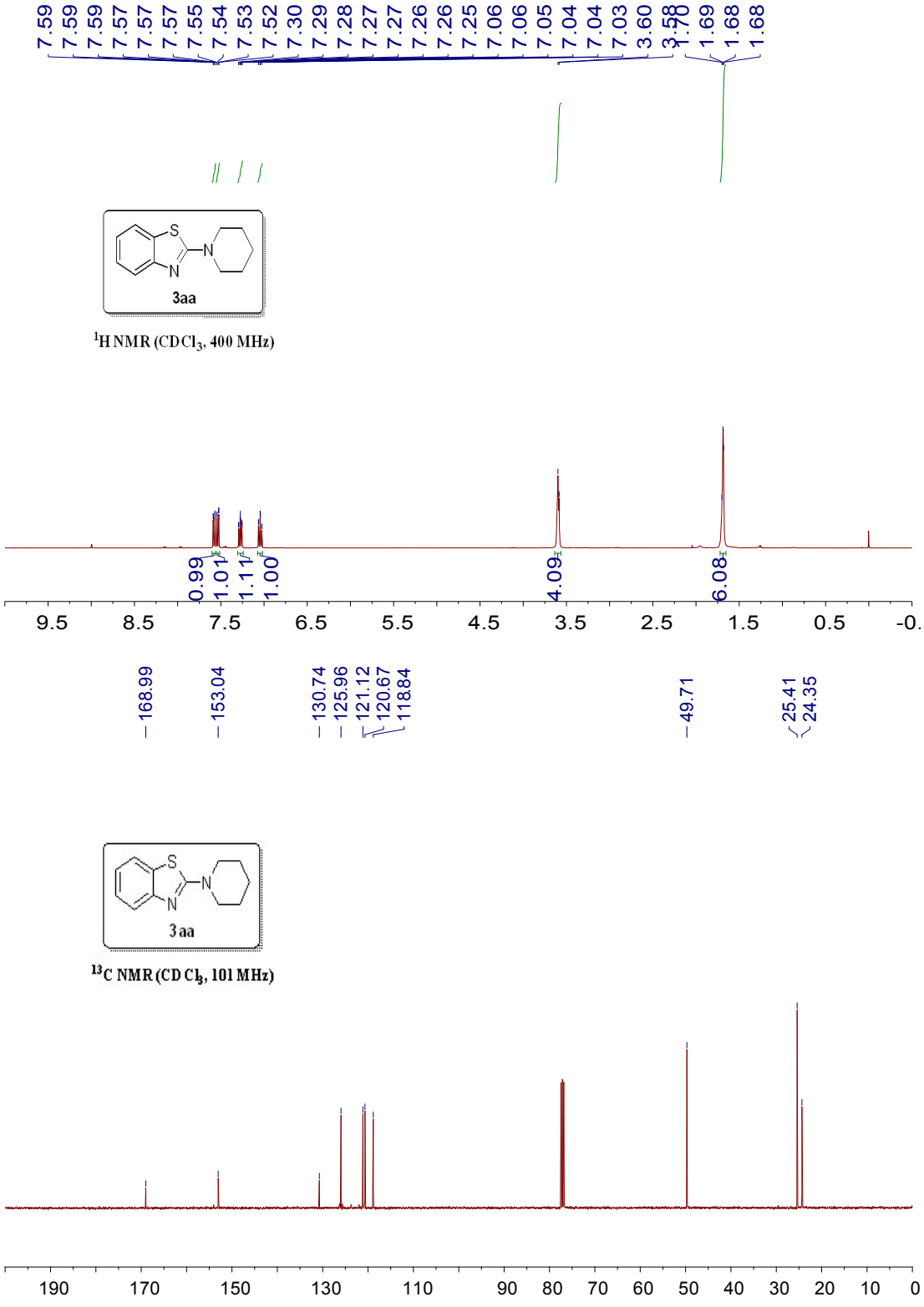
4,6-Dimethyl-2-(piperidin-1-yl)pyrimidine (3ja): 17.0 mg white solid was obtained in 30% isolated yield. m.p. 62-65 °C. IR (ATR): υ 2956, 2914, 1729, 1461, 1379, 1259, 1192, 1155, 1080, 1021, 905, 849, 797, 693 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.21 (s, 1H), 3.79 – 3.77 (m, 4H), 2.27 (s, 6H), 1.64 – 1.56 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.04, 108.39, 44.80, 26.00, 25.09, 24.28, 1.17. **HRMS (ESI)** calcd for $C_{11}H_{18}N_3^+$, $[M+H]^+$, 192.1495, found 192.1499.

6. References

1. D. W. Ma, X. Lu, L. Shi, H. Zhang, Y. W. Jiang and X. Q. Liu. *Angew. Chem. Int. Ed.*, 2011, **50**, 1118-1121.
2. L. L. Joyce and R. A. Batey. *Org. Lett.*, 2009, **11**, 2792-2795,
3. M. W. Hooper, M. Utsunomiya and J. F. Hartwig. *J. Org. Chem.*, 2003, **68**, 2861-2873.
4. A. El-Faham, M. Chebbo, M. Abdul-Ghani and G. Younes. *J. Heterocyclic Chem.*, 2006, **43**, 599-606.
5. J. Y. Kim, S. H. Cho, J. Joseph and S. Chang. *Angew. Chem. Int. Ed.*, 2010, **49**, 9899-9903.

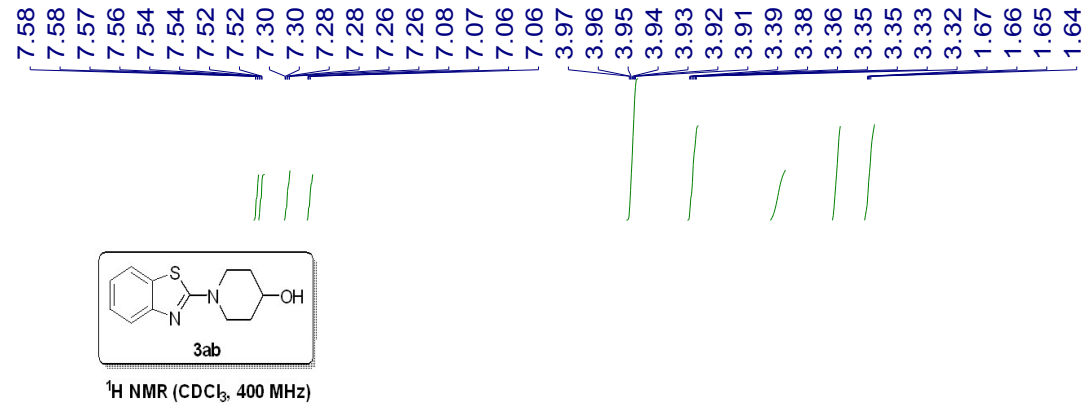
6. J. Joseph, J. Y. Kim and S. Chang. *Chem. Eur. J.*, 2011, **17**, 8294-8298.

7. NMR Spectra of Products

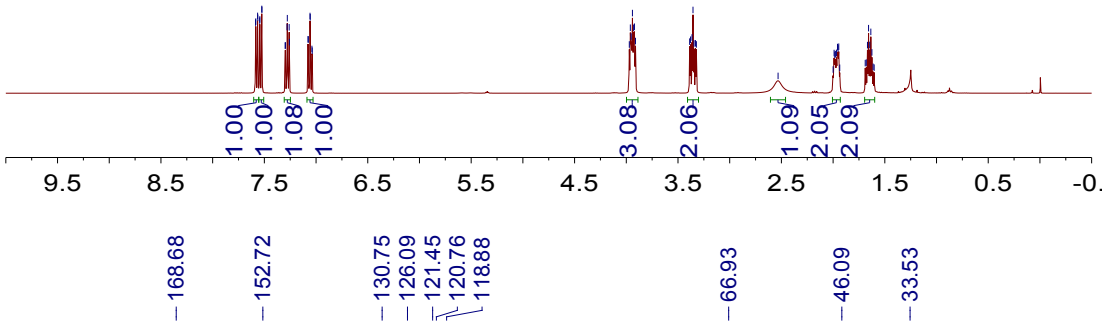


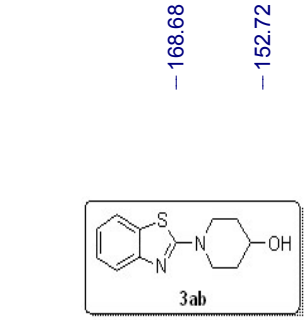
^{1}H NMR ($CDCl_3$, 400 MHz)

^{13}C NMR ($CDCl_3$, 101 MHz)

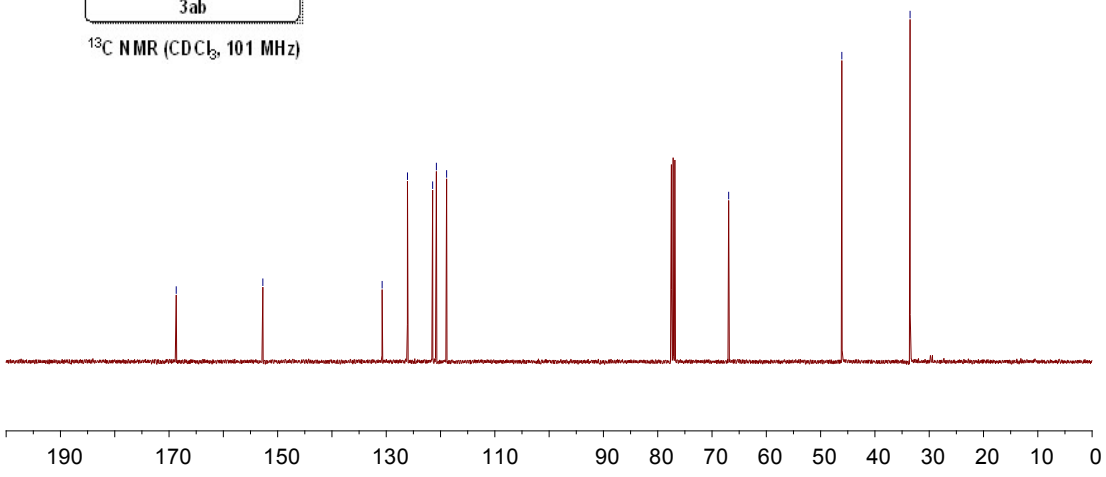


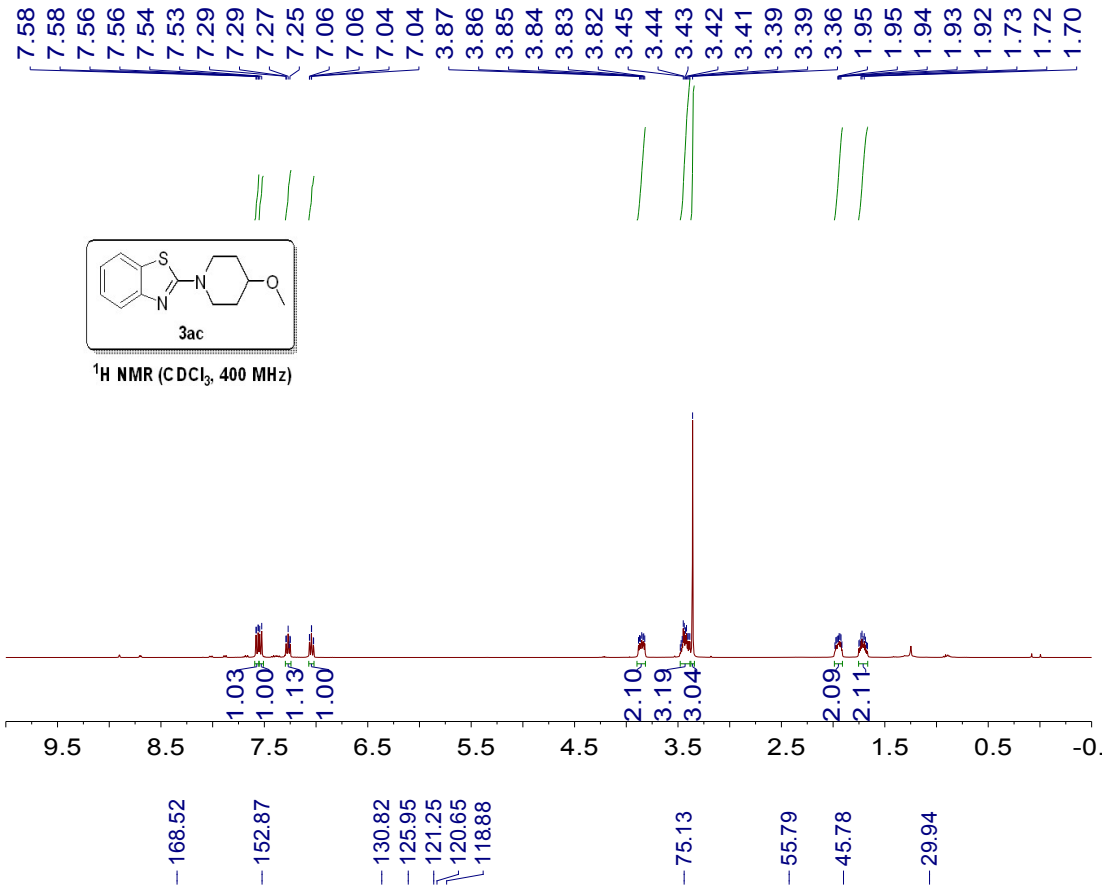
^{1}H NMR ($CDCl_3$, 400 MHz)

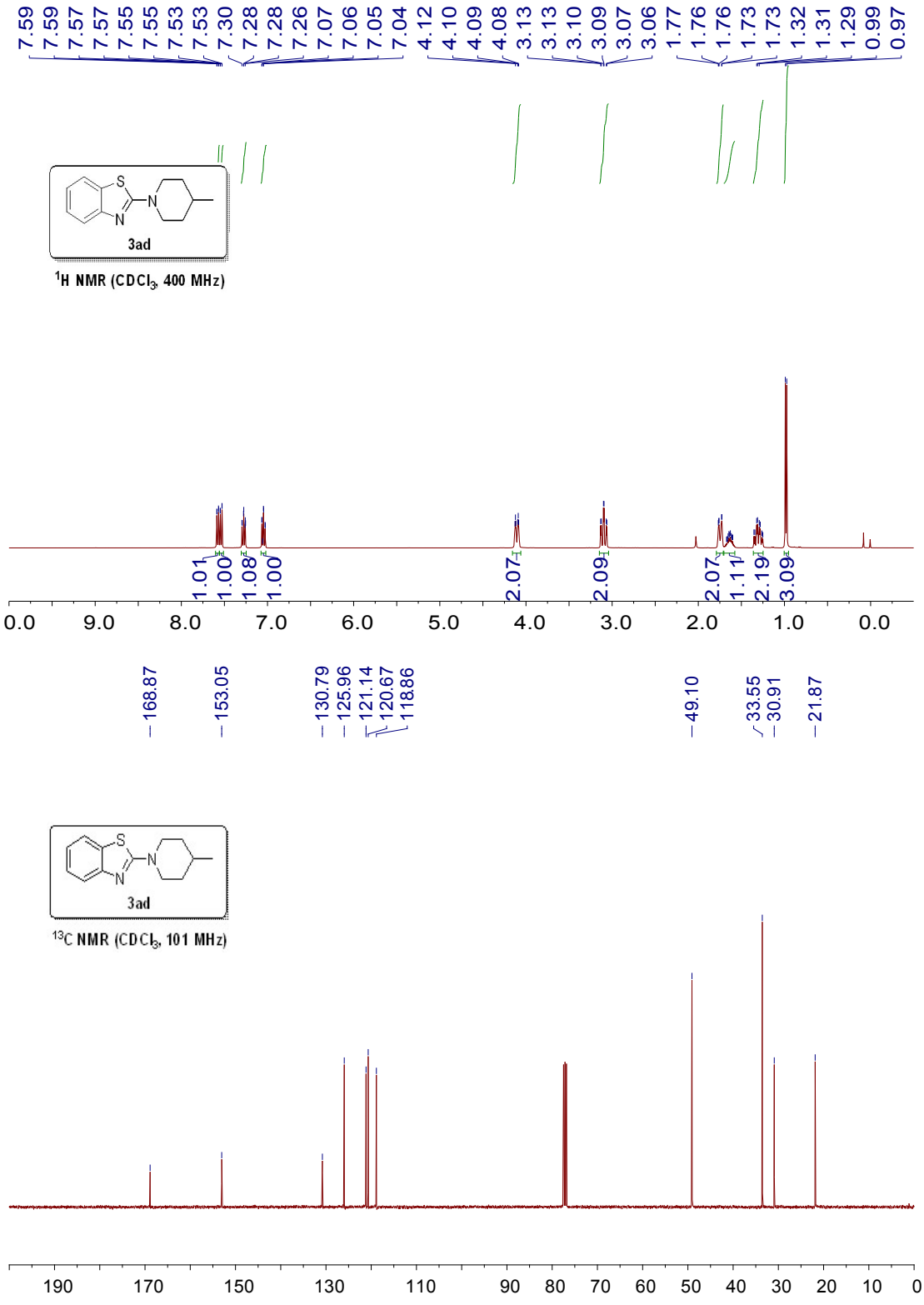


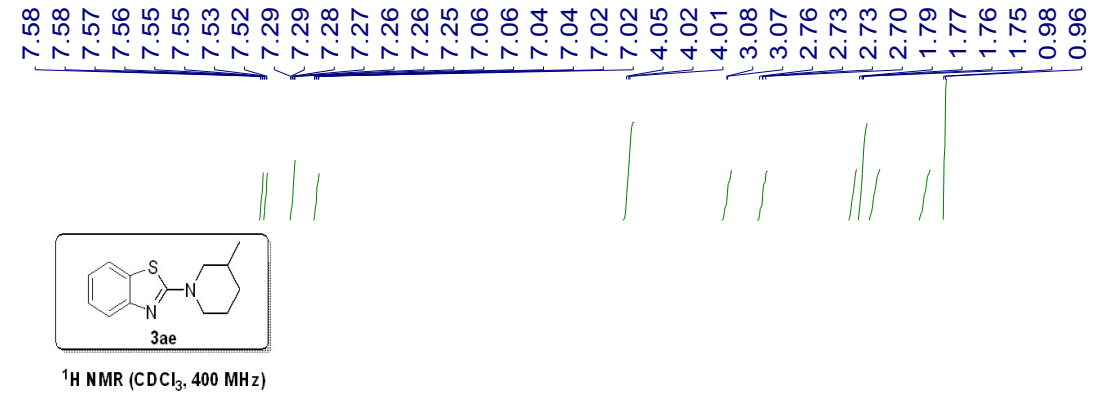


^{13}C NMR ($CDCl_3$, 101 MHz)



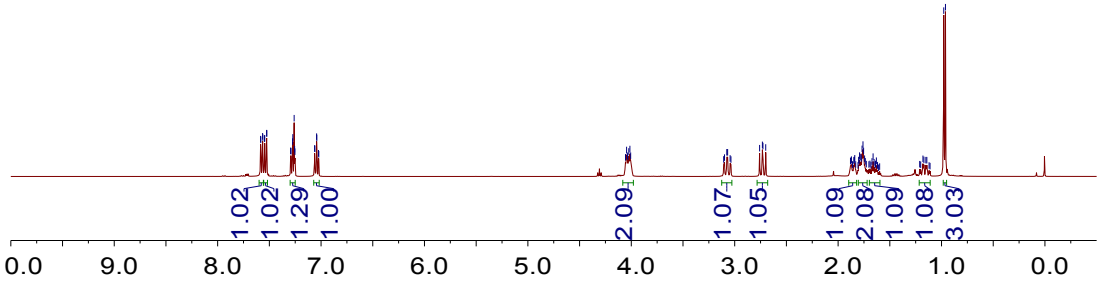

7.58
7.58
7.56
7.56
7.54
7.53
7.29
7.29
7.27
7.25
7.06
7.06
7.04
7.04
3.87
3.86
3.85
3.84
3.83
3.82
3.45
3.44
3.43
3.42
3.41
3.39
3.39
3.36
1.95
1.95
1.94
1.93
1.92
1.73
1.72
1.70
3ac
1H NMR (CDCl3, 400 MHz)
1.03
1.00
1.13
1.00
2.10
3.19
3.04
2.09
2.11
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.
168.52
152.87
130.82
125.95
121.25
120.65
118.88
75.13
55.79
45.78
29.94
3ac
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

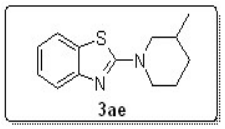

7.59
7.59
7.57
7.57
7.55
7.55
7.53
7.53
7.30
7.28
7.28
7.26
7.07
7.06
7.05
7.04
4.12
4.10
4.09
4.08
3.13
3.13
3.10
3.09
3.07
3.06
1.77
1.76
1.76
1.73
1.73
1.32
1.31
1.29
0.99
0.97
3ad
1H NMR (CDCl3, 400 MHz)
1.01
1.00
1.08
1.00
2.07
2.09
2.07
1.11
2.19
3.09
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
168.87
153.05
130.79
125.96
121.14
120.67
118.86
49.10
33.55
30.91
21.87
3ad
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0



3ae

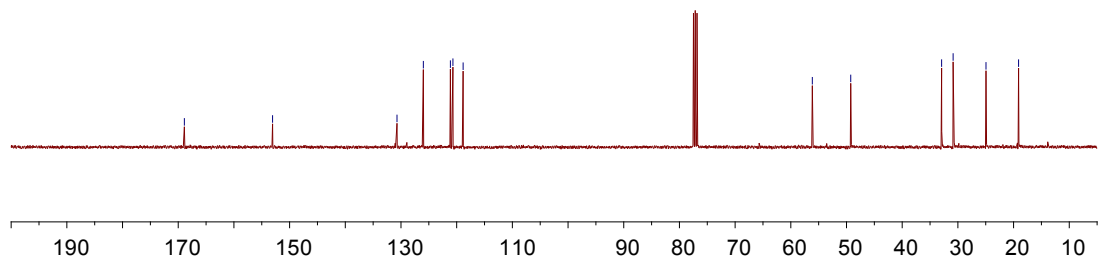
^{1}H NMR ($CDCl_3$, 400 MHz)

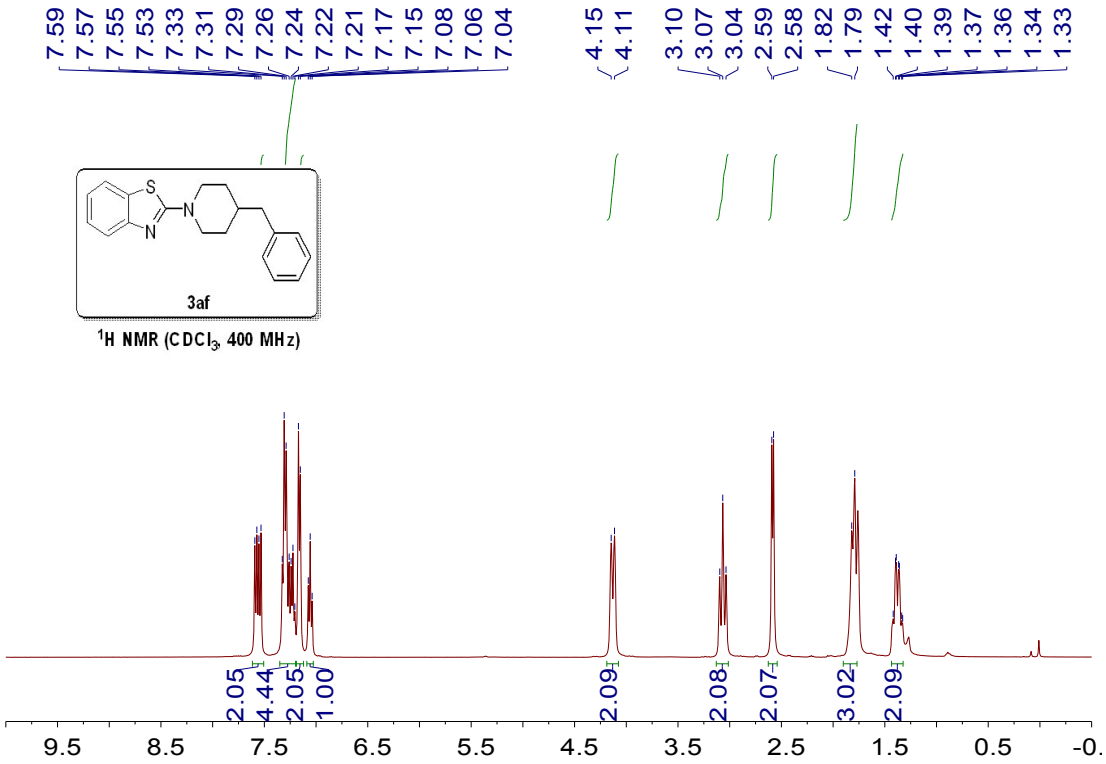


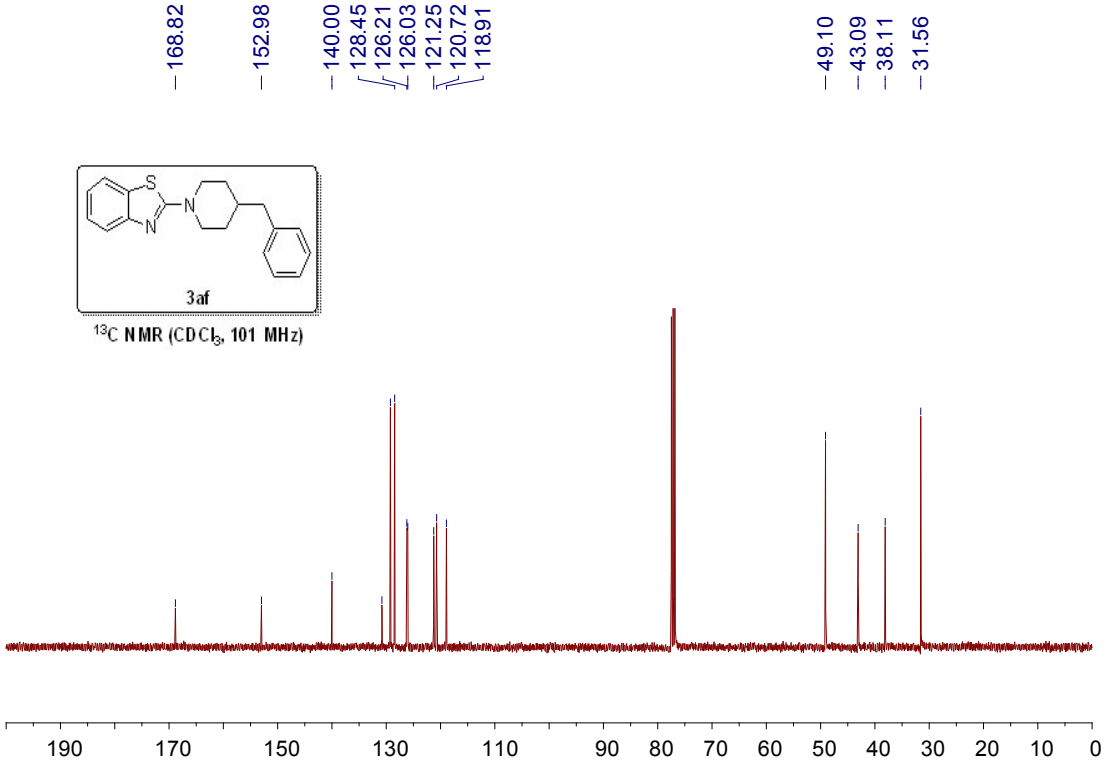


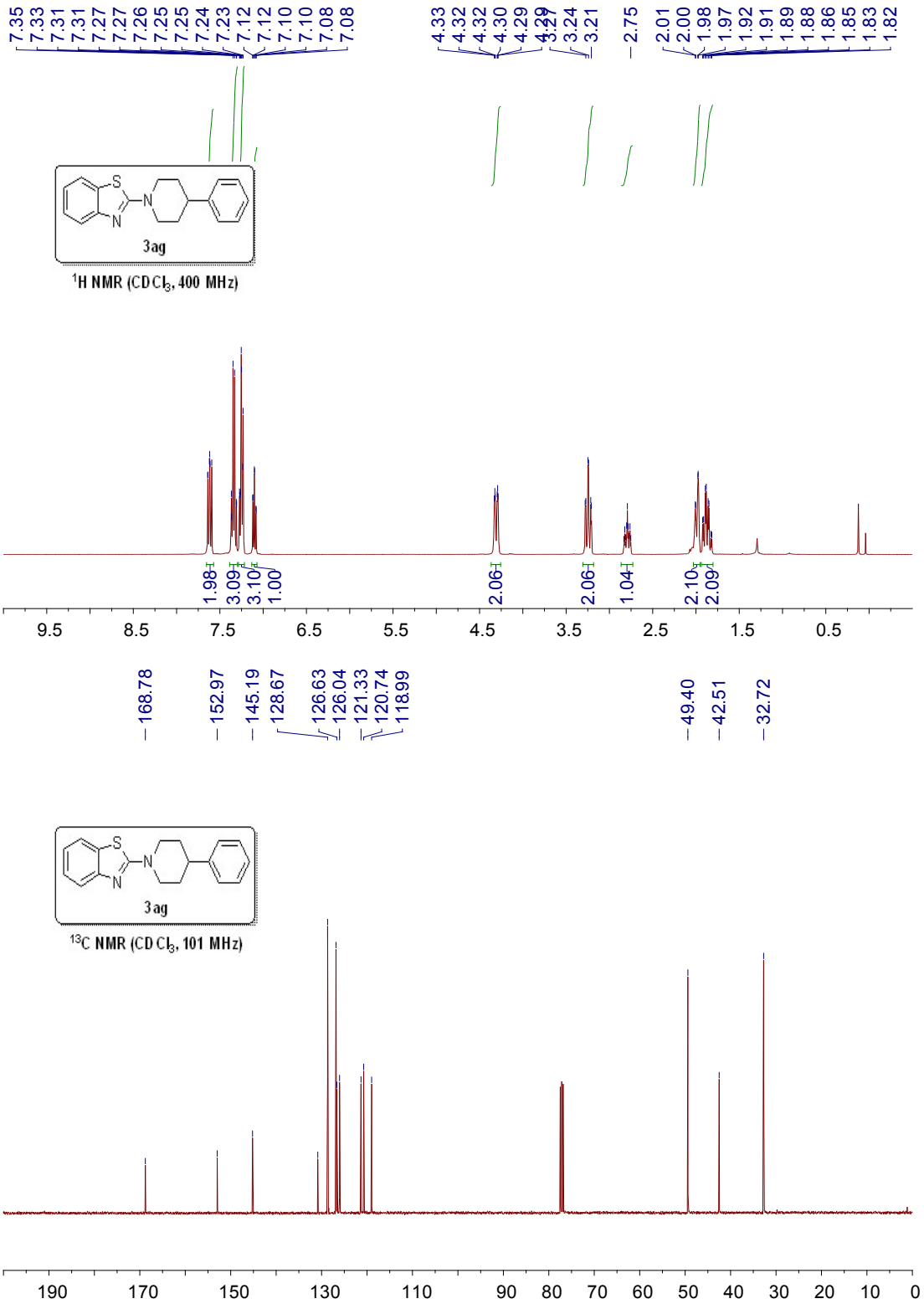
3ae

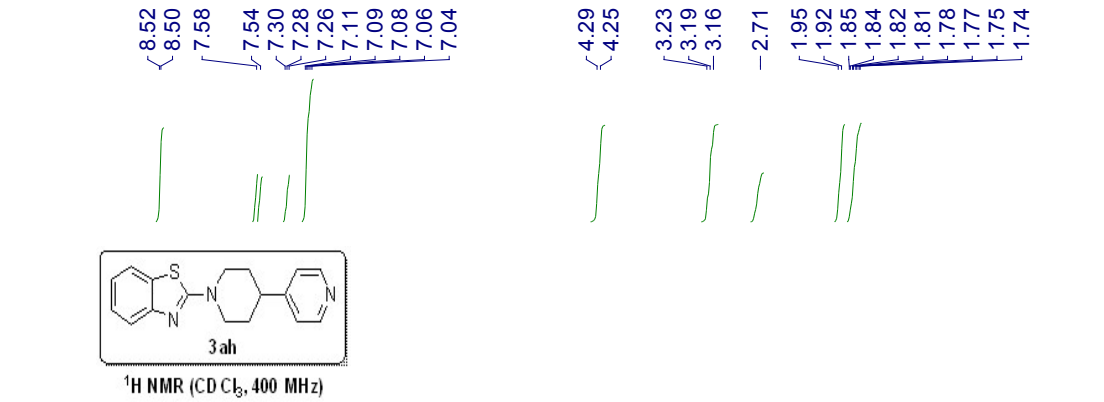
^{13}C NMR ($CDCl_3$, 101 MHz)

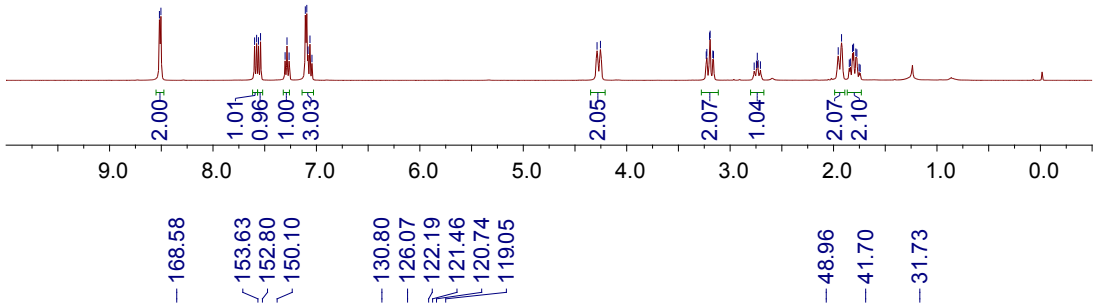



7.59
7.57
7.55
7.53
7.33
7.31
7.29
7.26
7.24
7.22
7.21
7.17
7.15
7.08
7.06
7.04
4.15
4.11
3.10
3.07
3.04
2.59
2.58
1.82
1.79
1.42
1.40
1.39
1.37
1.36
1.34
1.33
3af
1H NMR (CDCl3, 400 MHz)
2.05
4.44
2.05
1.00
2.09
2.08
2.07
3.02
2.09
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5

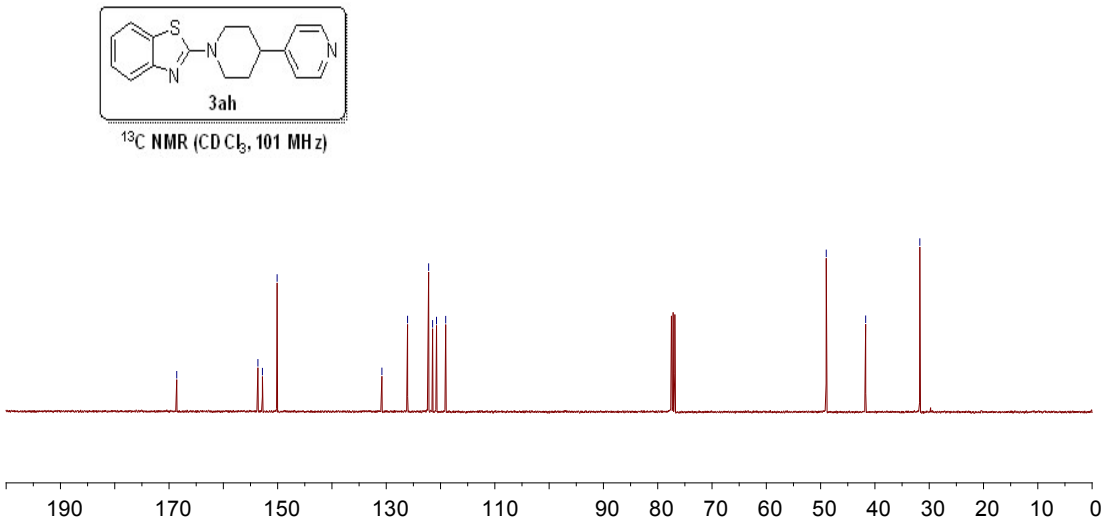

168.82
152.98
140.00
128.45
126.21
126.03
121.25
120.72
118.91
49.10
43.09
38.11
31.56
3af
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

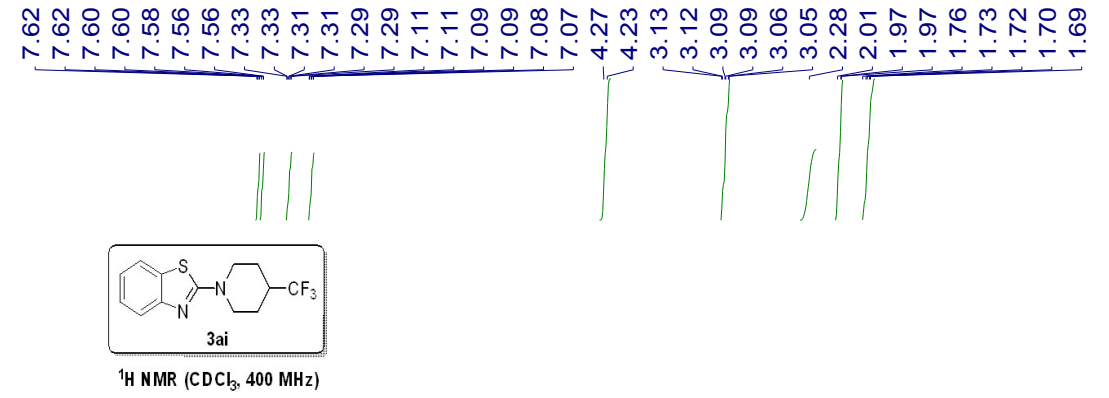

7.35
7.33
7.31
7.31
7.27
7.27
7.26
7.25
7.25
7.24
7.23
7.12
7.12
7.10
7.10
7.08
7.08
4.33
4.32
4.32
4.30
4.29
3.24
3.21
2.75
2.01
2.00
1.98
1.97
1.92
1.91
1.89
1.88
1.86
1.85
1.83
1.82
3ag
1H NMR (CDCl3, 400 MHz)
1.98
3.09
3.10
1.00
2.06
2.06
1.04
2.10
2.09
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
168.78
152.97
145.19
128.67
126.63
126.04
121.33
120.74
118.99
49.40
42.51
32.72
3ag
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0


8.52
8.50
7.58
7.54
7.30
7.28
7.26
7.11
7.09
7.08
7.06
7.04
4.29
4.25
3.23
3.19
3.16
2.71
1.95
1.92
1.85
1.84
1.82
1.81
1.78
1.77
1.75
1.74
3ah
^{1}H NMR (CDCl$_3$, 400 MHz)


2.00
1.01
0.96
1.00
3.03
2.05
2.07
1.04
2.07
2.10
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

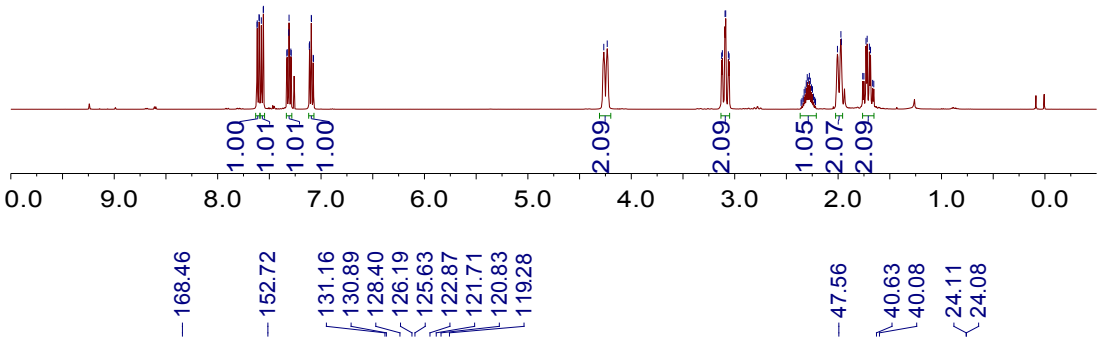
168.58
153.63
152.80
150.10
130.80
126.07
122.19
121.46
120.74
119.05
48.96
41.70
31.73

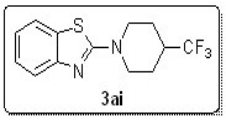

3ah
^{13}C NMR (CDCl$_3$, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0



3ai

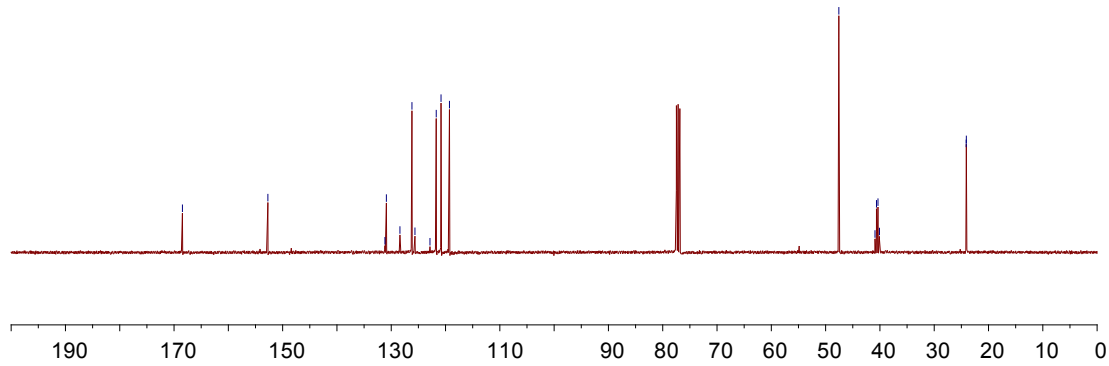
^{1}H NMR ($CDCl_3$, 400 MHz)

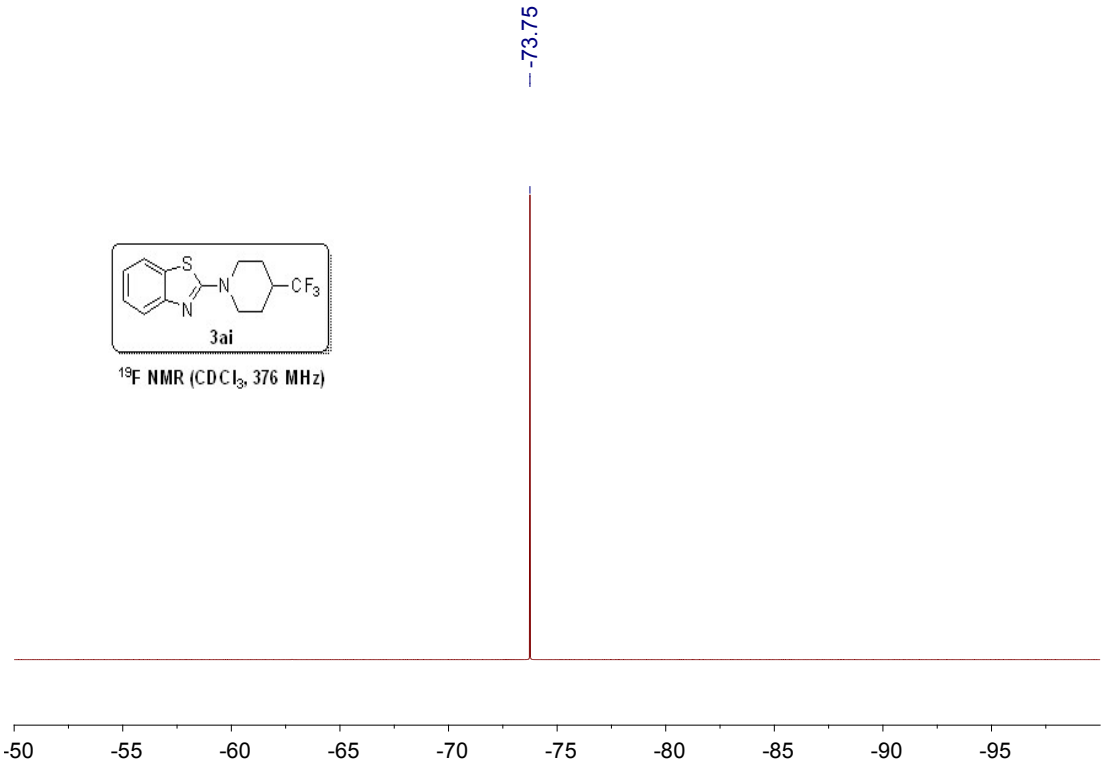




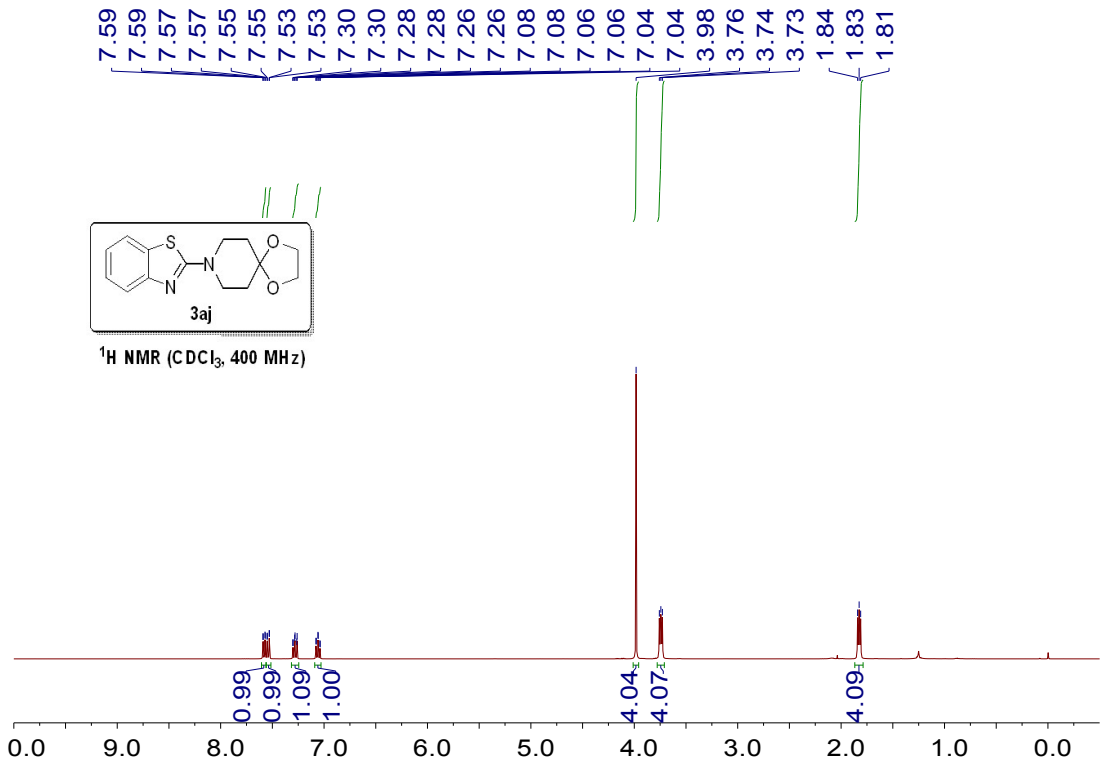
3ai

^{13}C NMR ($CDCl_3$, 101 MHz)

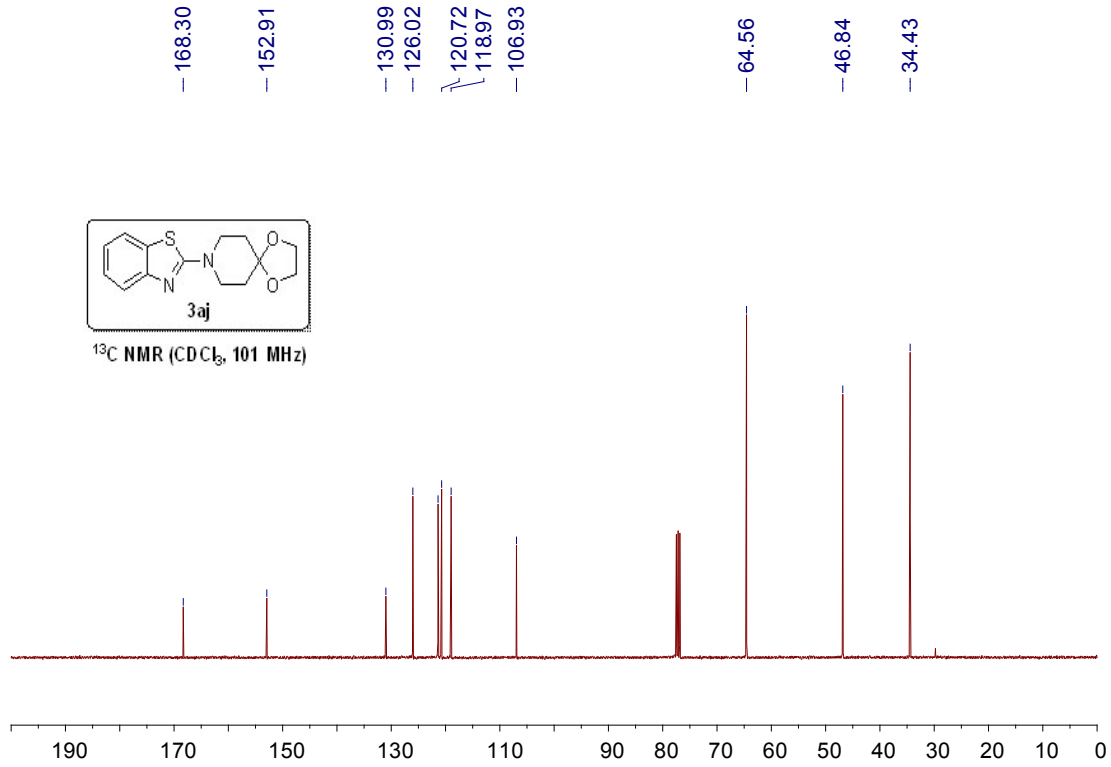


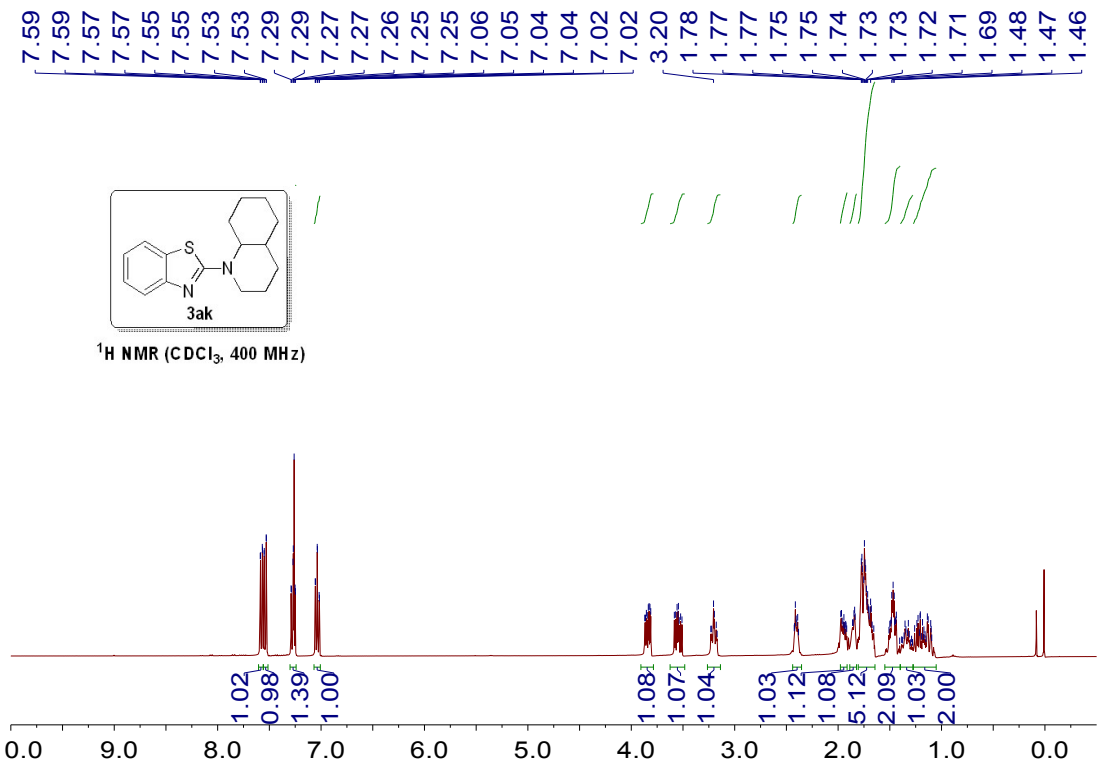


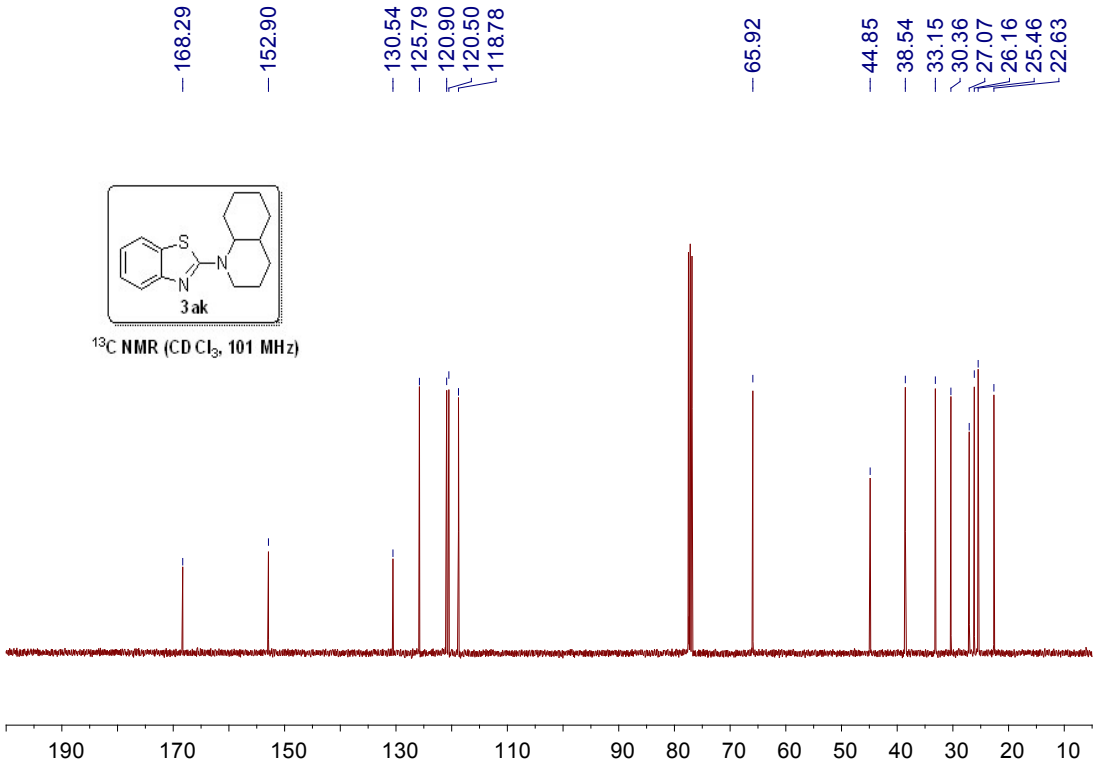
^{19}F NMR ($CDCl_3$, 376 MHz)

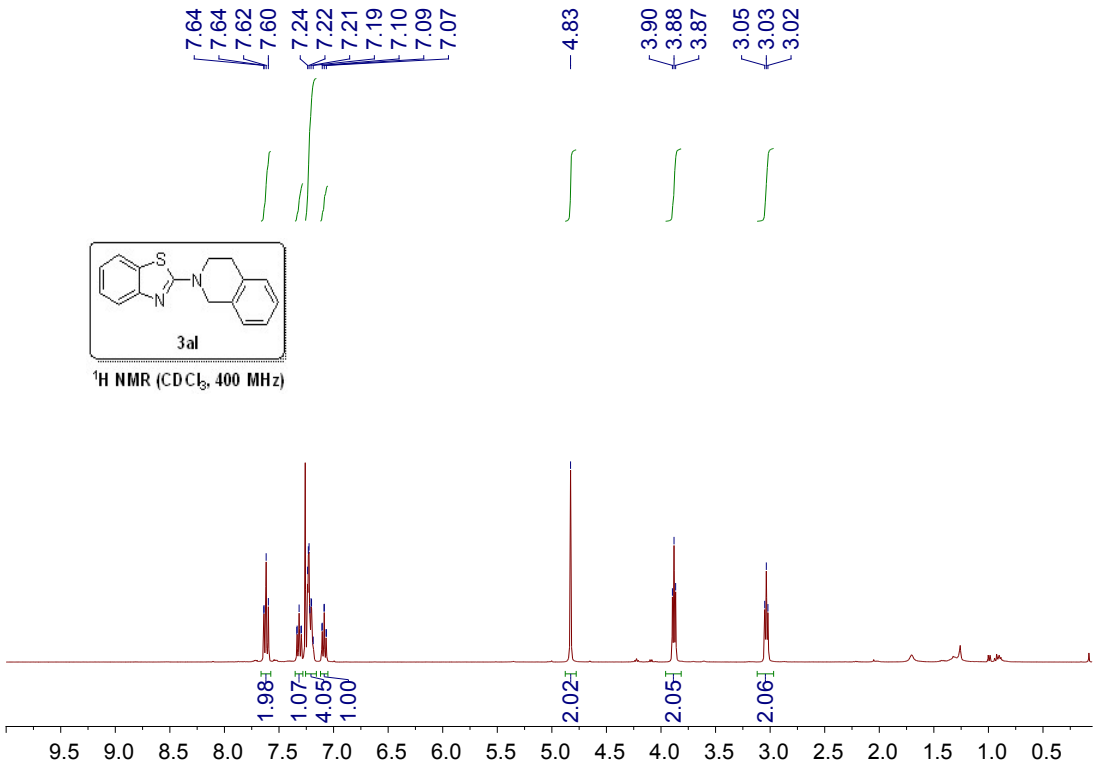


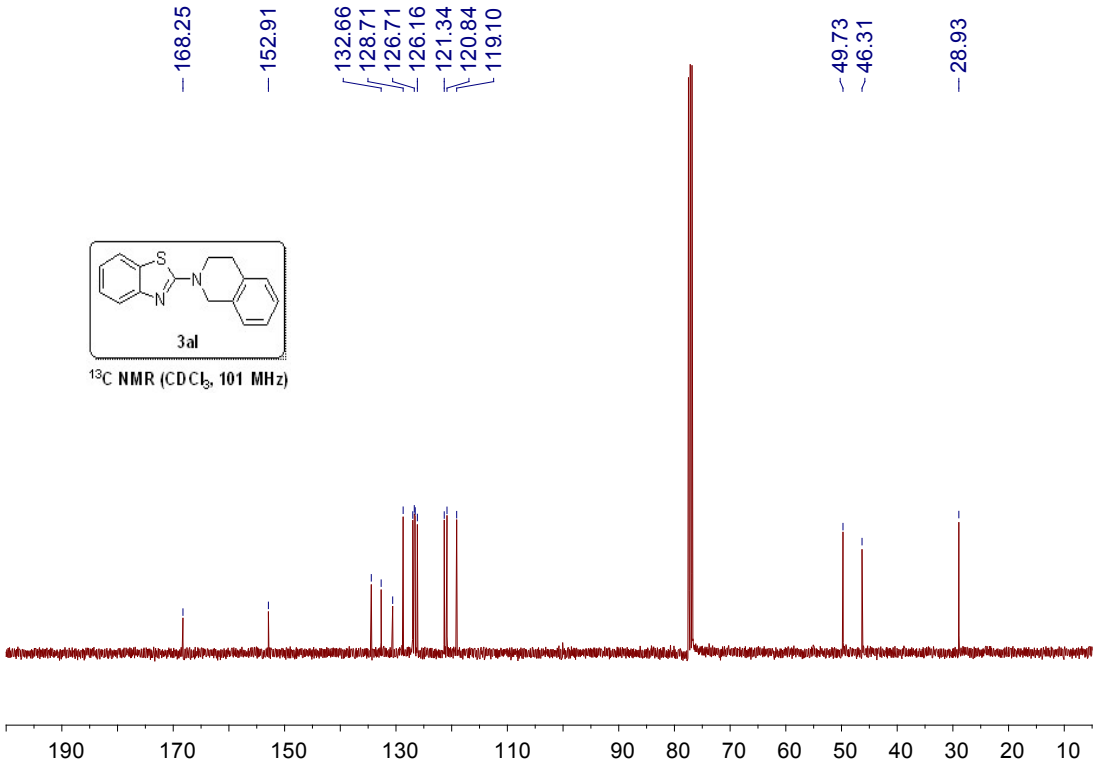
^{1}H NMR ($CDCl_3$, 400 MHz)

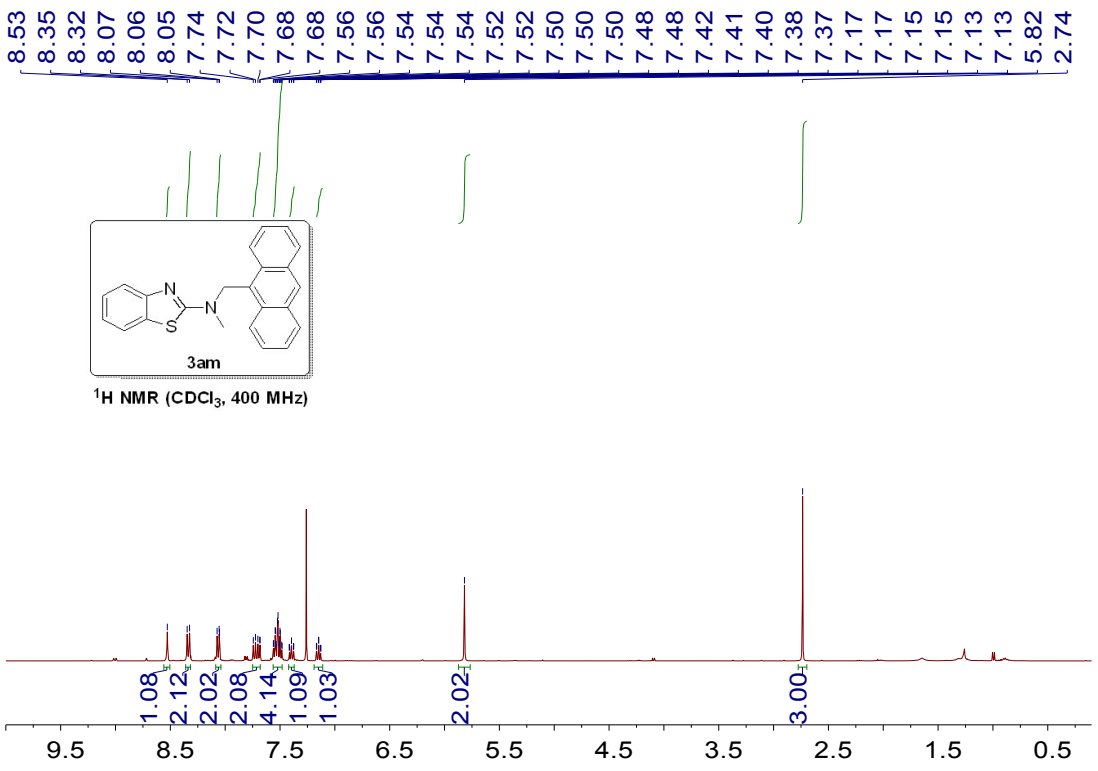

168.30
152.91
130.99
126.02
120.72
118.97
106.93
64.56
46.84
34.43
3aj
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

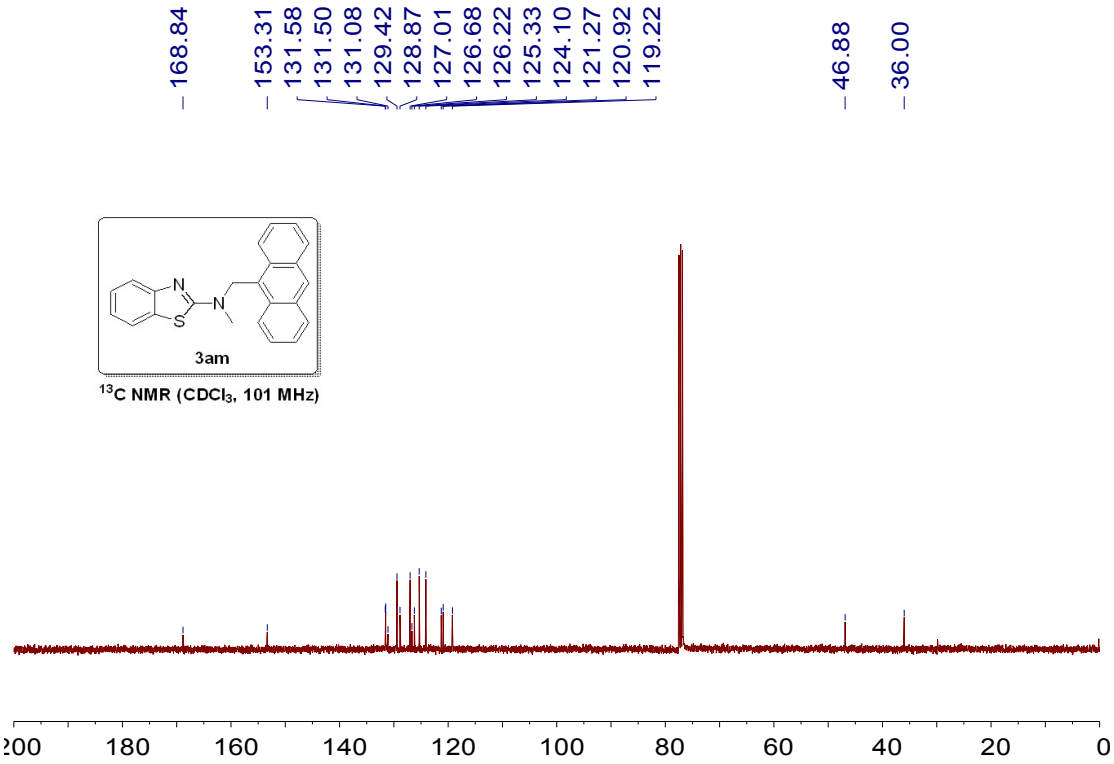

7.59
7.59
7.57
7.57
7.55
7.55
7.53
7.53
7.29
7.29
7.27
7.27
7.26
7.25
7.25
7.06
7.05
7.04
7.04
7.02
7.02
3.20
1.78
1.77
1.77
1.75
1.75
1.74
1.73
1.73
1.72
1.71
1.69
1.48
1.47
1.46
3ak
1H NMR (CDCl3, 400 MHz)
1.02
0.98
1.39
1.00
1.08
1.07
1.04
1.03
1.12
1.08
5.12
2.09
1.03
2.00
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

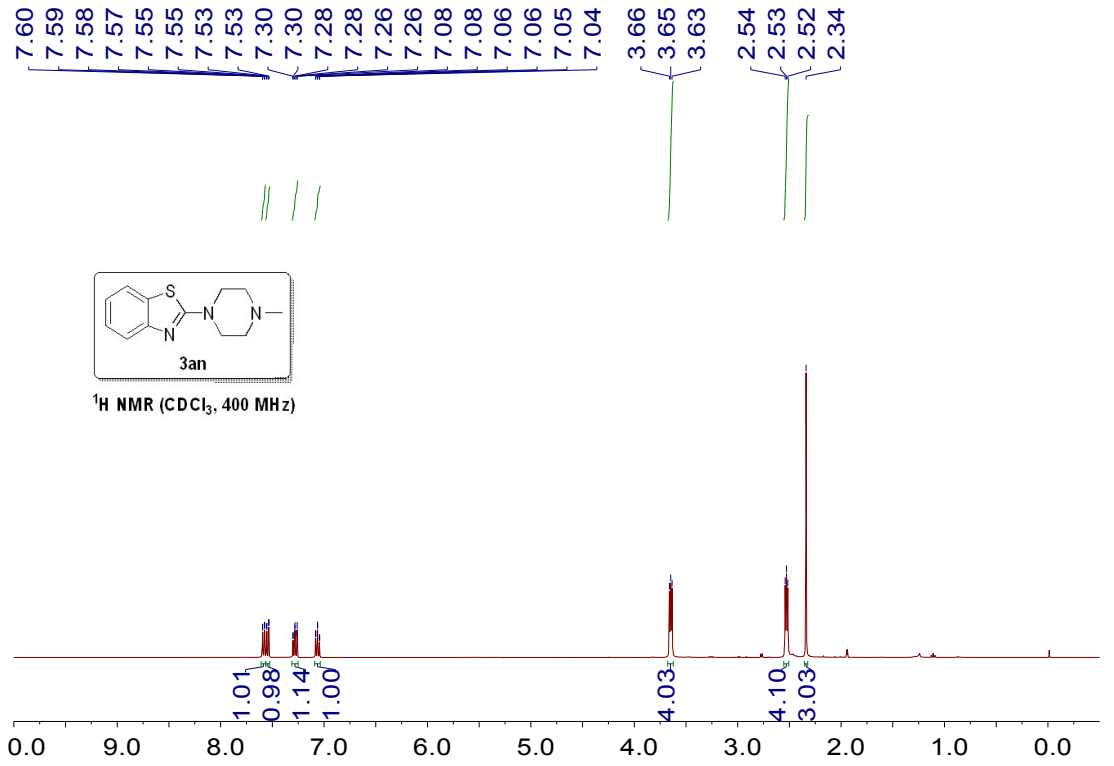

168.29
152.90
130.54
125.79
120.90
120.50
118.78
65.92
44.85
38.54
33.15
30.36
27.07
26.16
25.46
22.63
3ak
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10

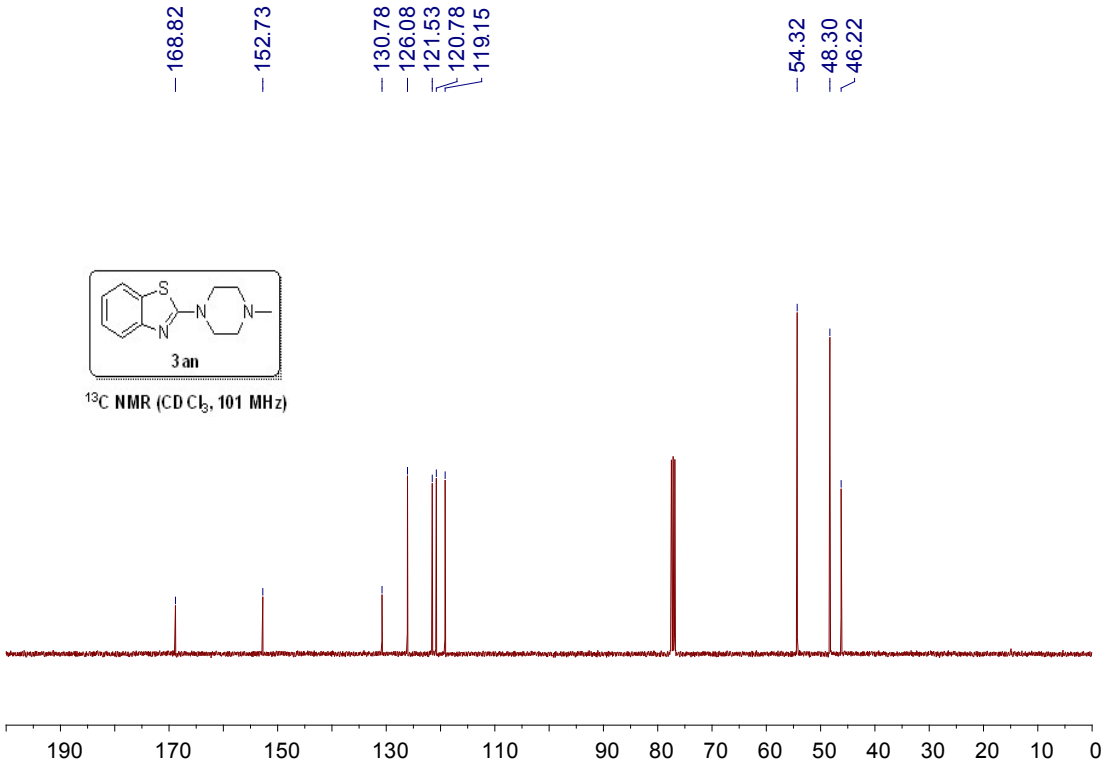

7.64
7.64
7.62
7.60
7.24
7.22
7.21
7.19
7.10
7.09
7.07
4.83
3.90
3.88
3.87
3.05
3.03
3.02
3al
1H NMR (CDCl3, 400 MHz)
1.98
1.07
4.05
1.00
2.02
2.05
2.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

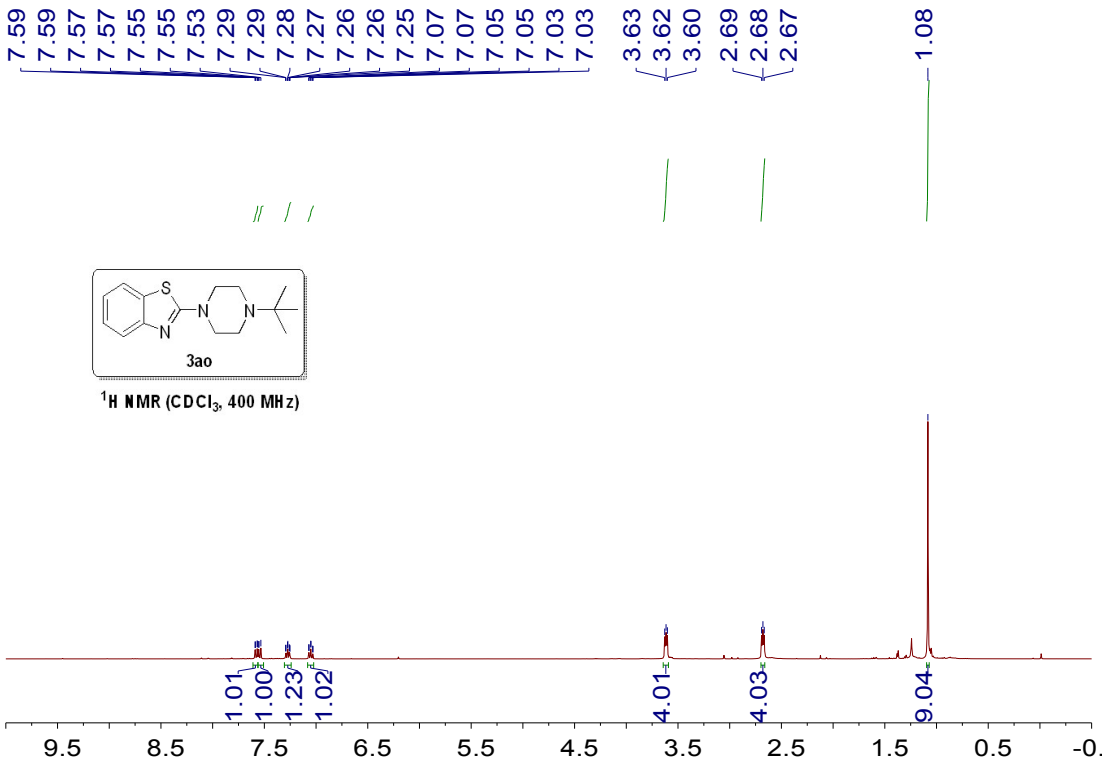

168.25
152.91
132.66
128.71
126.71
126.16
121.34
120.84
119.10
49.73
46.31
28.93
3al
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10

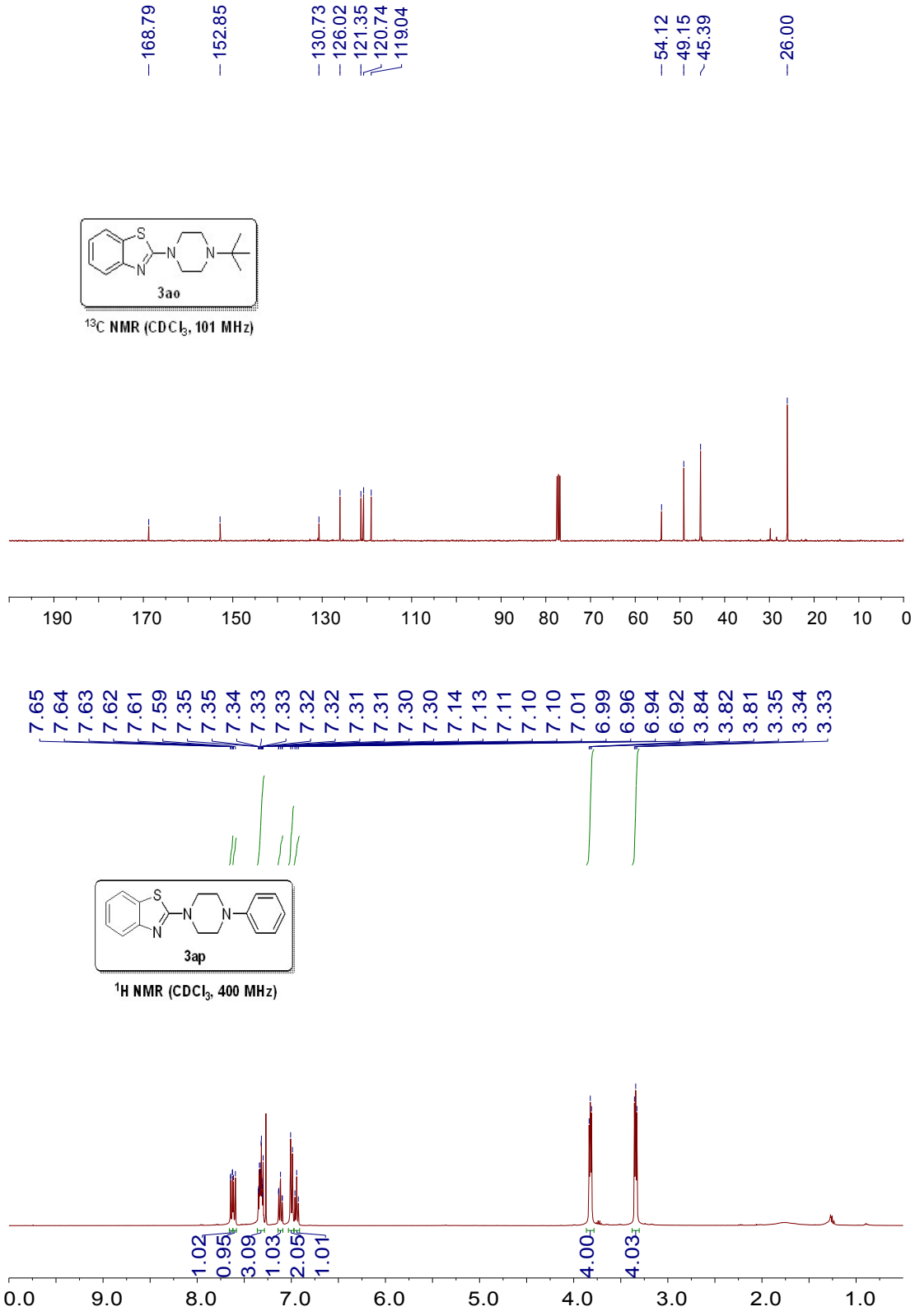

8.53
8.35
8.32
8.07
8.06
8.05
7.74
7.72
7.70
7.68
7.68
7.56
7.56
7.54
7.54
7.54
7.52
7.52
7.50
7.50
7.50
7.48
7.48
7.42
7.41
7.40
7.38
7.37
7.17
7.17
7.15
7.15
7.13
7.13
5.82
2.74
3am
1H NMR (CDCl3, 400 MHz)
1.08
2.12
2.02
2.08
4.14
1.09
1.03
2.02
3.00
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5

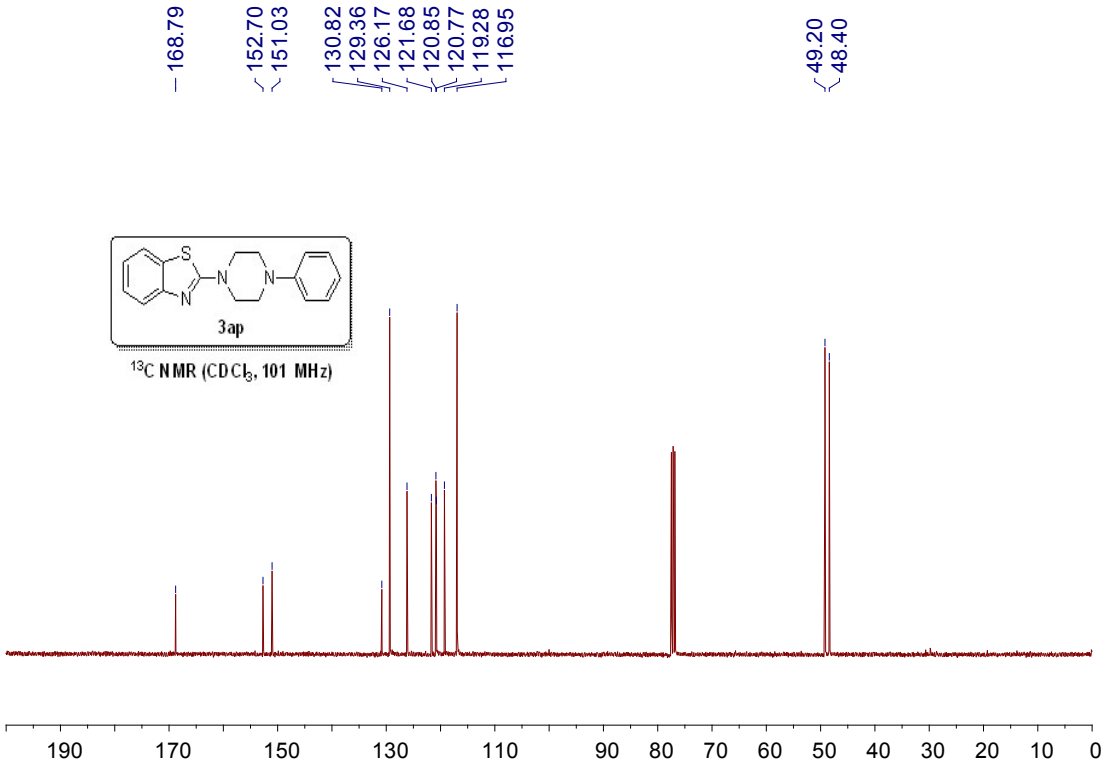

168.84
153.31
131.58
131.50
131.08
129.42
128.87
127.01
126.68
126.22
125.33
124.10
121.27
120.92
119.22
46.88
36.00
3am
13C NMR (CDCl3, 101 MHz)
200
180
160
140
120
100
80
60
40
20
0

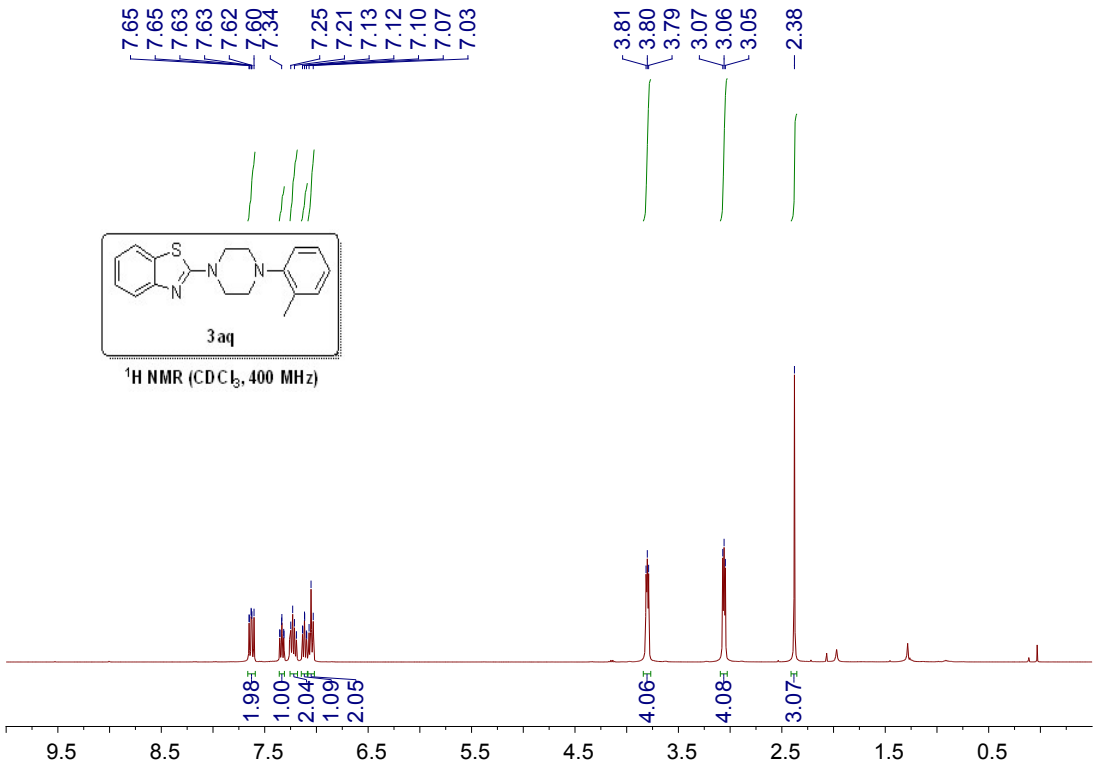

7.60
7.59
7.58
7.57
7.55
7.55
7.53
7.53
7.30
7.30
7.28
7.28
7.26
7.26
7.08
7.08
7.06
7.06
7.05
7.04
3.66
3.65
3.63
2.54
2.53
2.52
2.34
3an
1H NMR (CDCl3, 400 MHz)
1.01
0.98
1.14
1.00
4.03
4.10
3.03
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

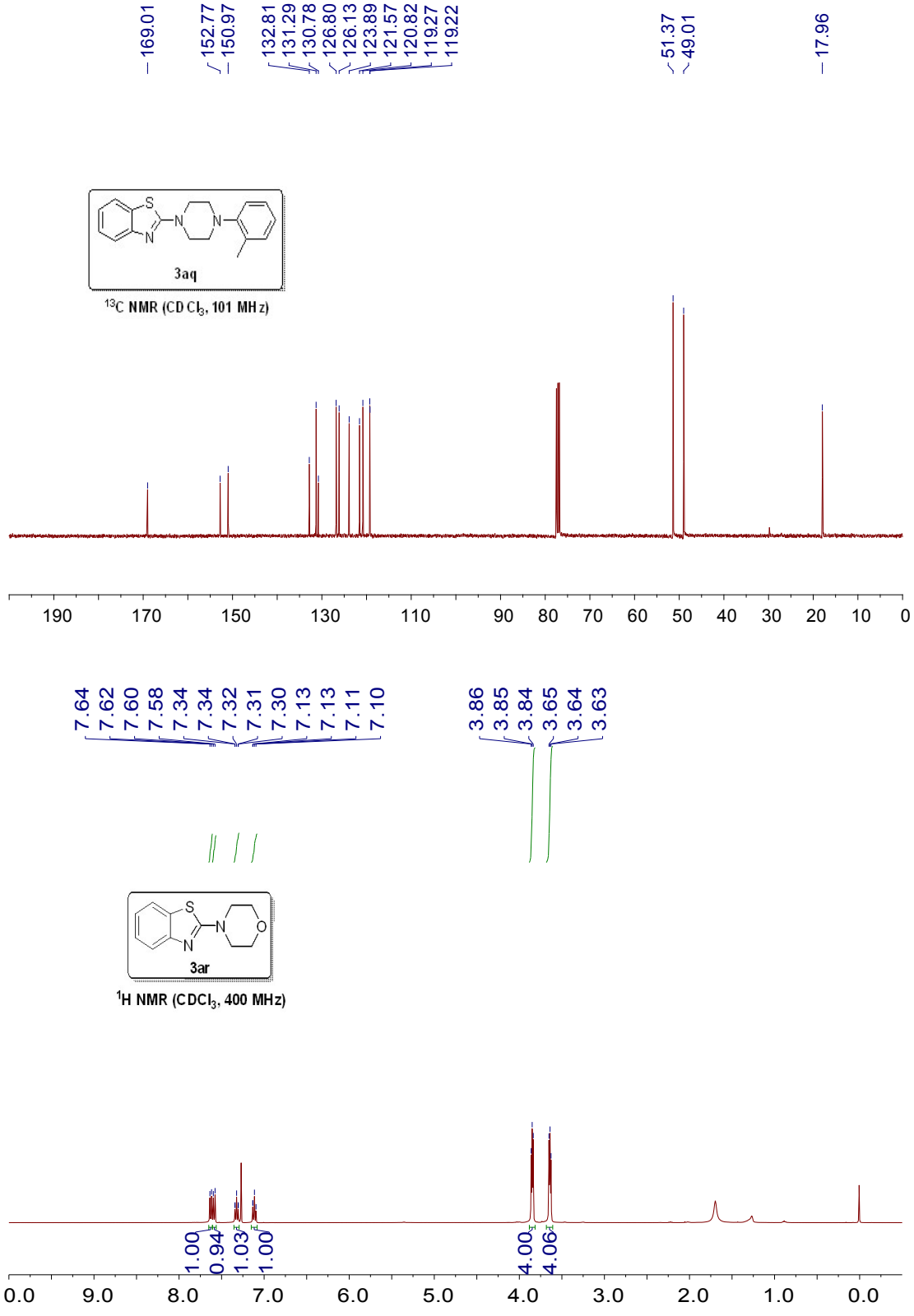

168.82
152.73
130.78
126.08
121.53
120.78
119.15
54.32
48.30
46.22
3an
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

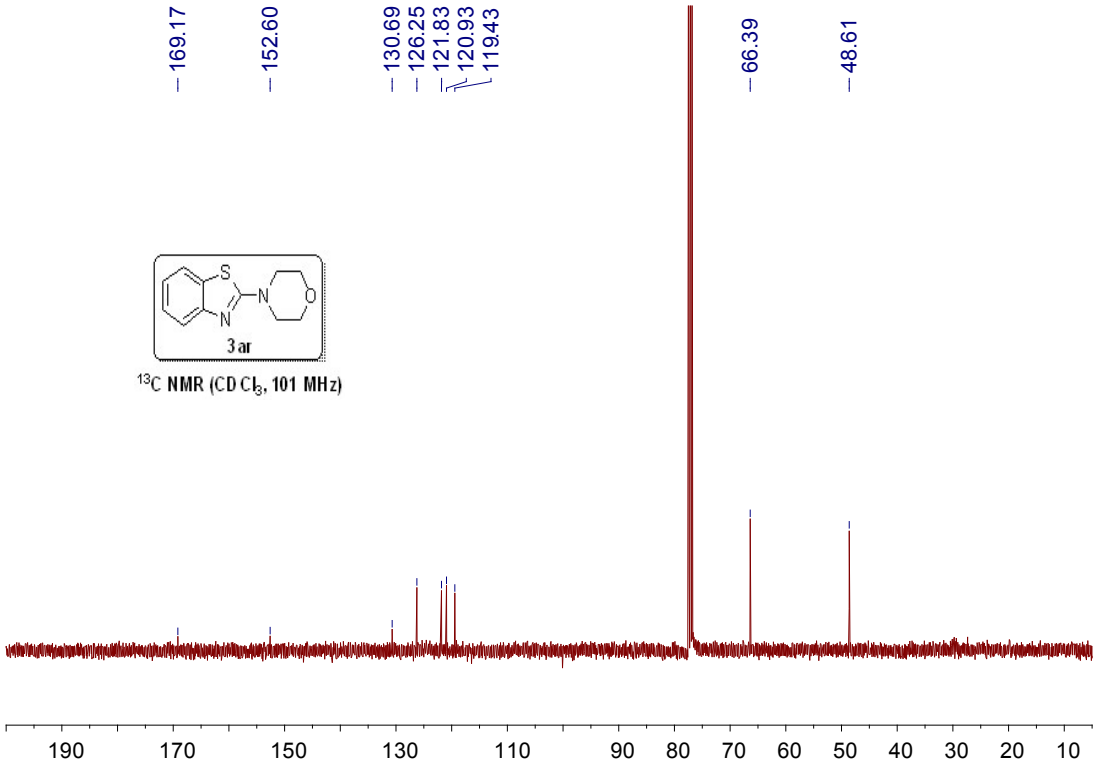

7.59
7.59
7.57
7.57
7.55
7.55
7.53
7.29
7.29
7.28
7.27
7.26
7.26
7.25
7.07
7.07
7.05
7.05
7.03
7.03
3.63
3.62
3.60
2.69
2.68
2.67
1.08
3ao
1H NMR (CDCl3, 400 MHz)
1.01
1.00
1.23
1.02
4.01
4.03
9.04
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.


168.79
152.85
130.73
126.02
121.35
120.74
119.04
54.12
49.15
45.39
26.00
3ao
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
7.65
7.64
7.63
7.62
7.61
7.59
7.35
7.35
7.34
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.30
7.14
7.13
7.11
7.10
7.10
7.01
6.99
6.96
6.94
6.92
3.84
3.82
3.81
3.35
3.34
3.33
3ap
1H NMR (CDCl3, 400 MHz)
1.02
0.95
3.09
1.03
2.05
1.01
4.00
4.03
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

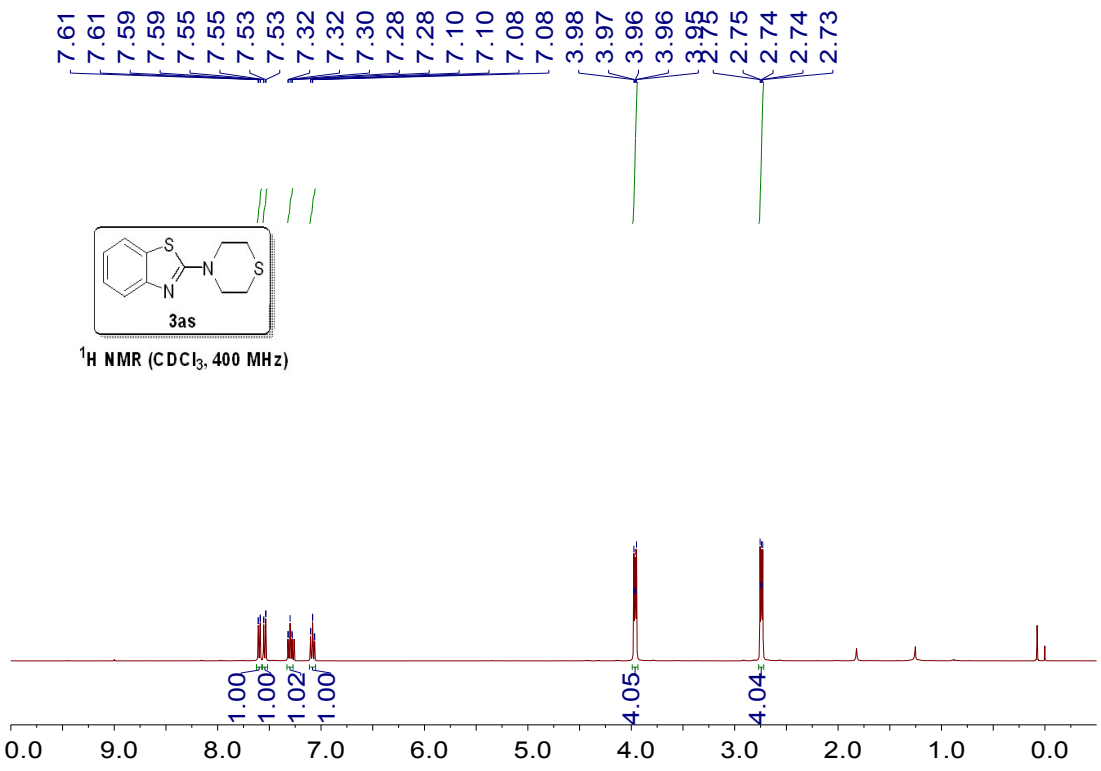

168.79
152.70
151.03
130.82
129.36
126.17
121.68
120.85
120.77
119.28
116.95
49.20
48.40
3ap
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0


7.65
7.65
7.63
7.63
7.62
7.60
7.34
7.25
7.21
7.13
7.12
7.10
7.07
7.03
3.81
3.80
3.79
3.07
3.06
3.05
2.38
3aq
1H NMR (CDCl3, 400 MHz)
1.98
1.00
2.04
1.09
2.05
4.06
4.08
3.07
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5

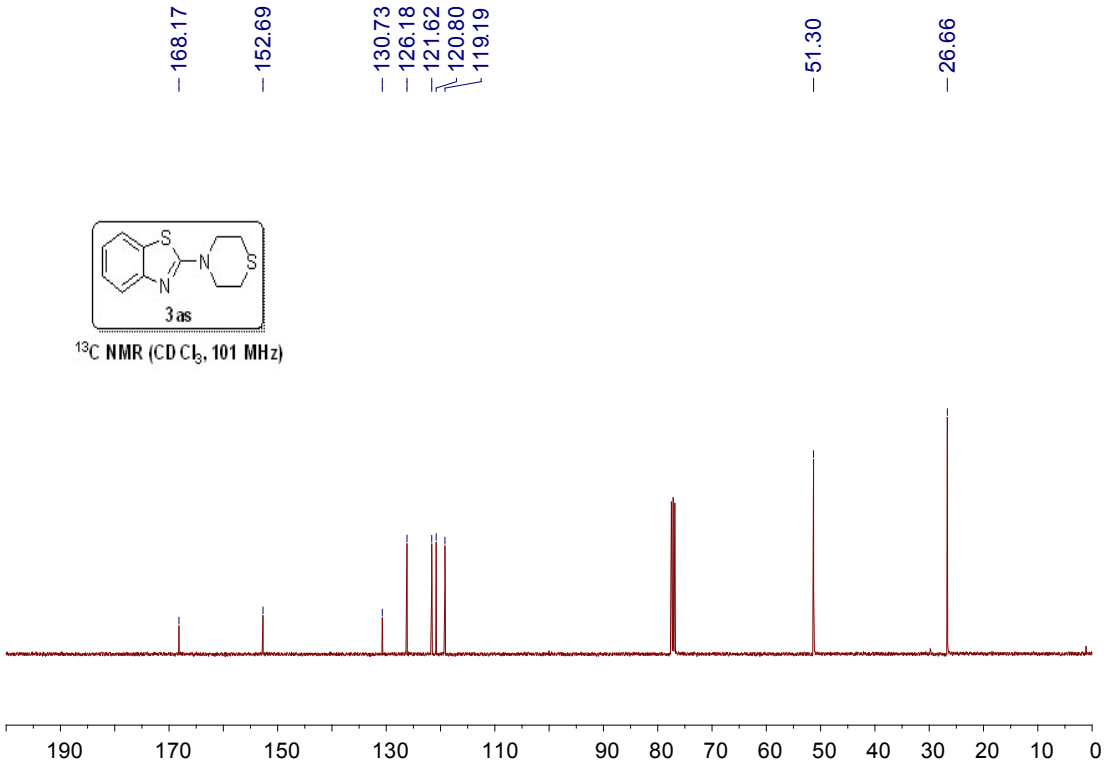

169.01
152.77
150.97
132.81
131.29
130.78
126.80
126.13
123.89
121.57
120.82
119.27
119.22
51.37
49.01
17.96
3aq
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
7.64
7.62
7.60
7.58
7.34
7.34
7.32
7.31
7.30
7.13
7.13
7.11
7.10
3.86
3.85
3.84
3.65
3.64
3.63
3ar
1H NMR (CDCl3, 400 MHz)
1.00
0.94
1.03
1.00
4.00
4.06
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0



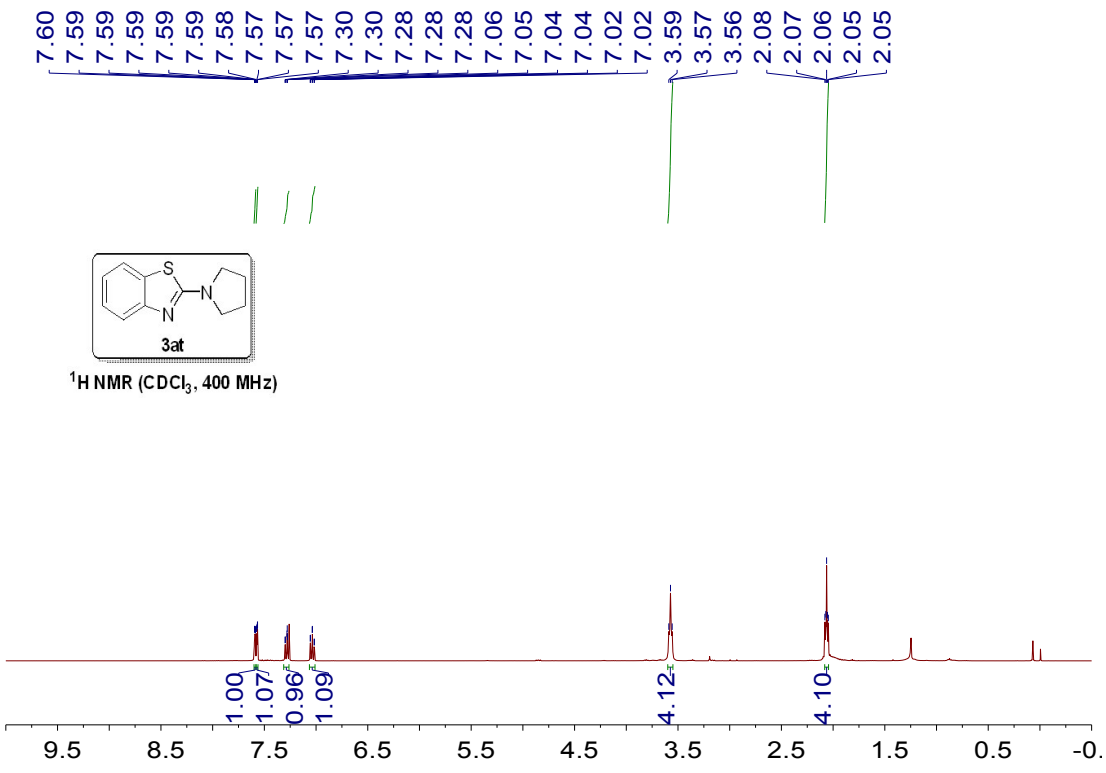
^{13}C NMR ($CDCl_3$, 101 MHz)



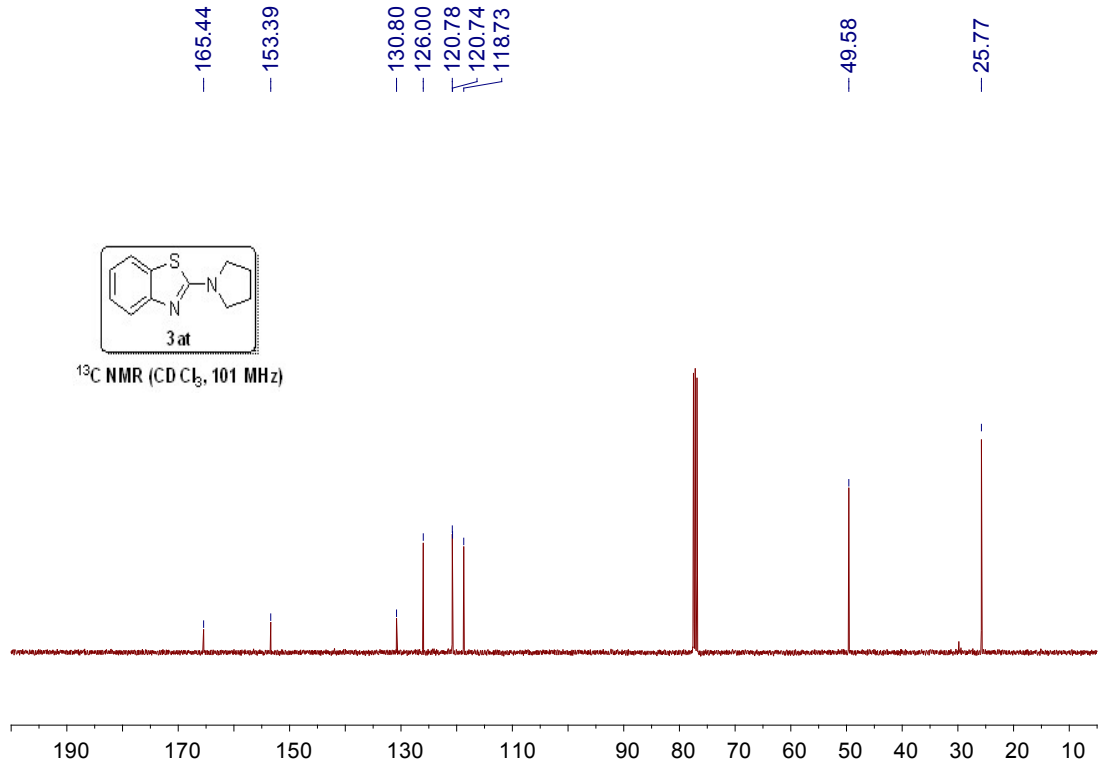
^{1}H NMR ($CDCl_3$, 400 MHz)

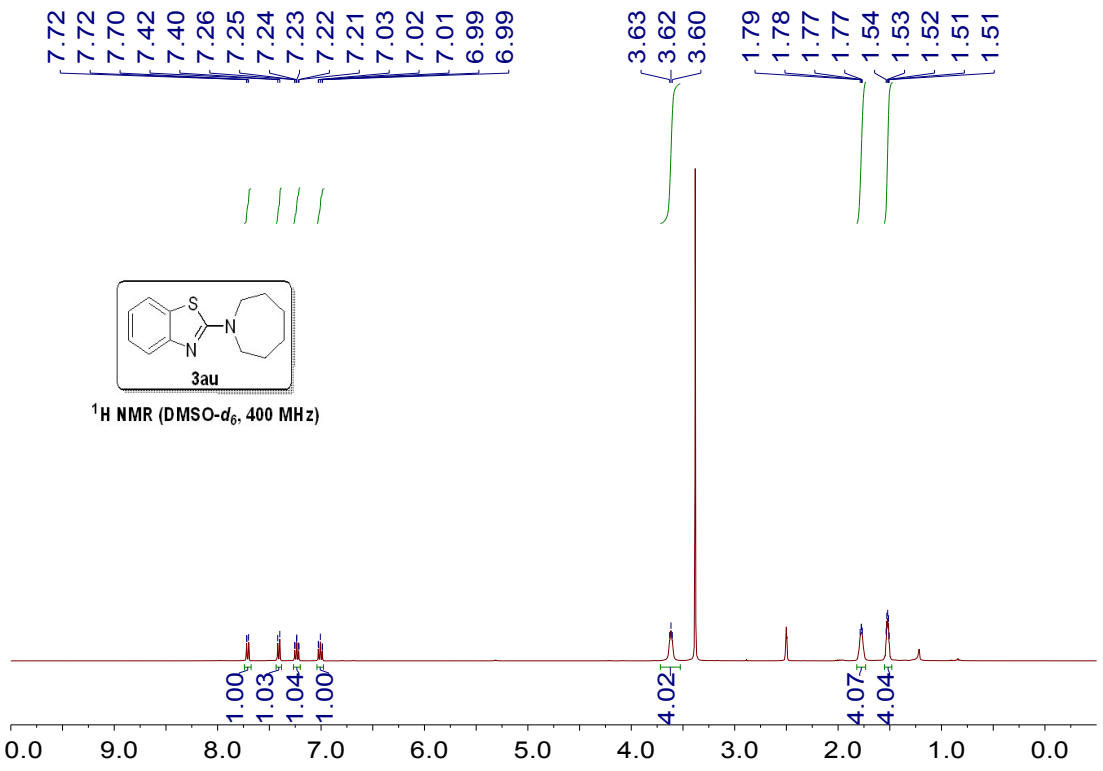


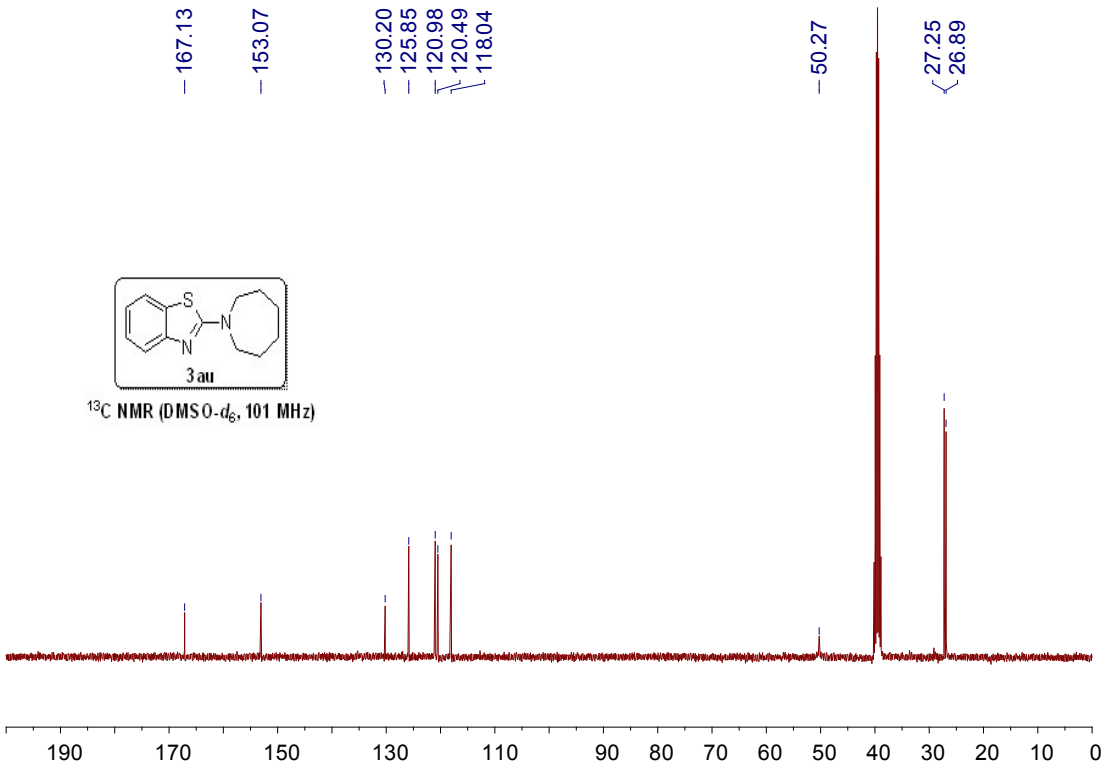
^{13}C NMR ($CDCl_3$, 101 MHz)

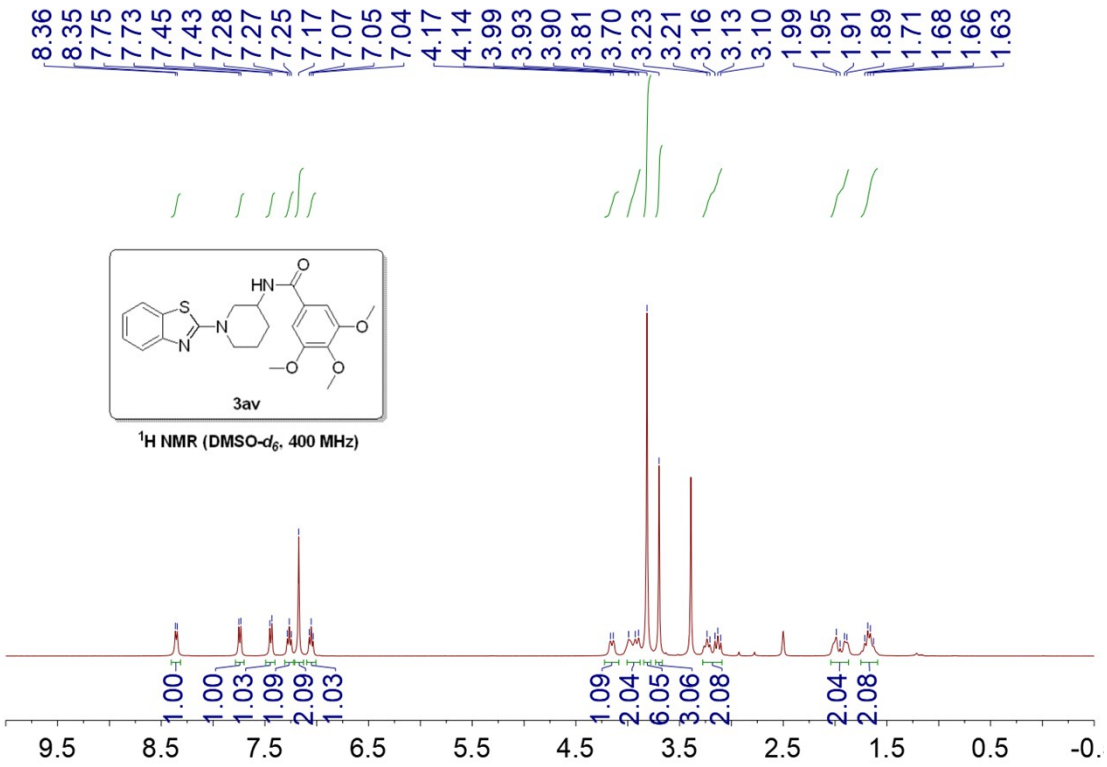


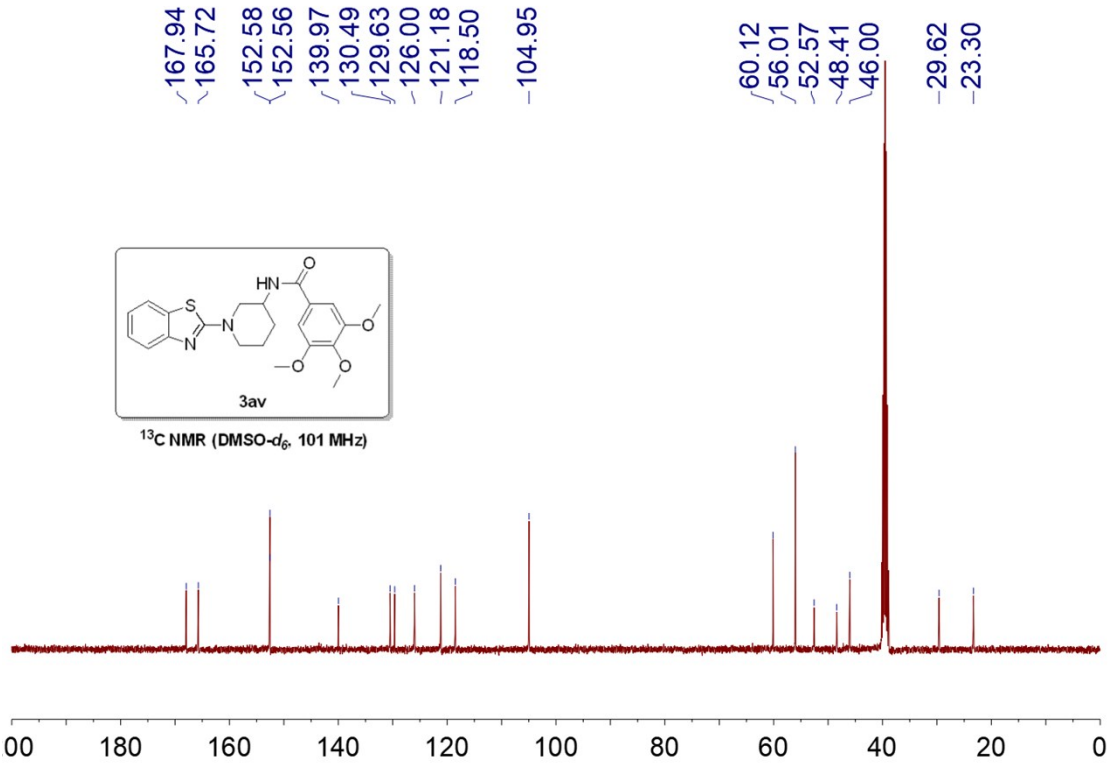
^{1}H NMR ($CDCl_3$, 400 MHz)


165.44
153.39
130.80
126.00
120.78
120.74
118.73
49.58
25.77
3at
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10

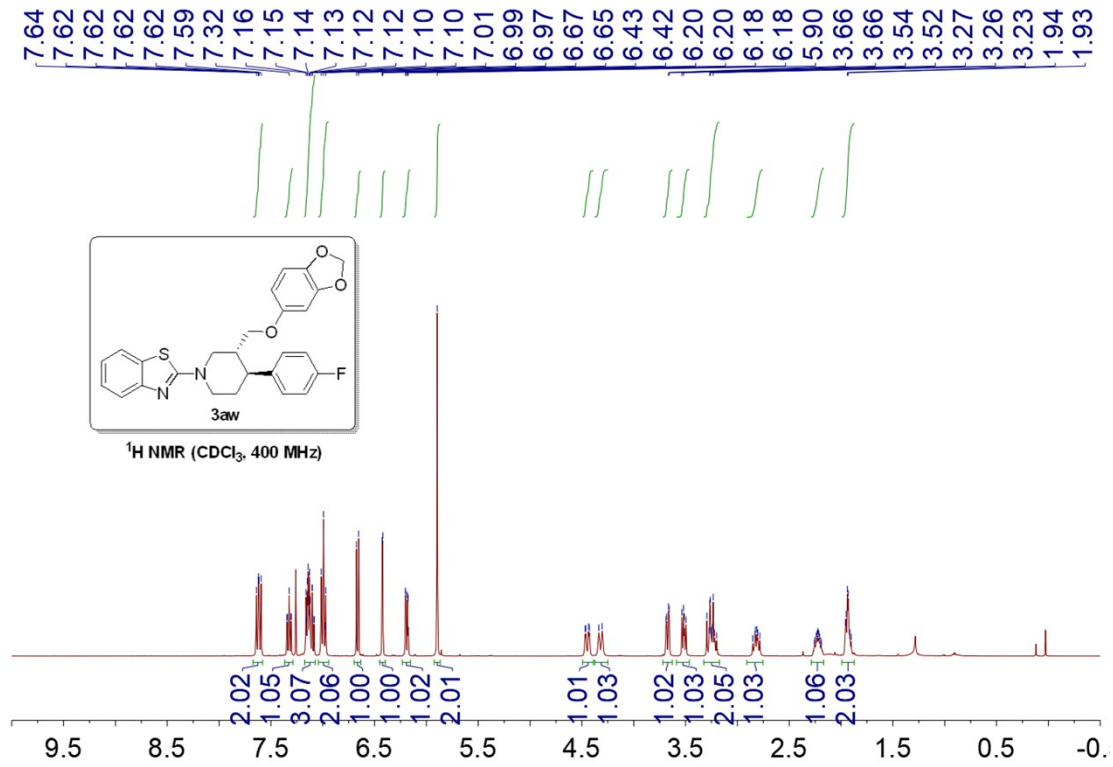

7.72
7.72
7.70
7.42
7.40
7.26
7.25
7.24
7.23
7.22
7.21
7.03
7.02
7.01
6.99
6.99
3.63
3.62
3.60
1.79
1.78
1.77
1.77
1.54
1.53
1.52
1.51
1.51
3au
1H NMR (DMSO-d6, 400 MHz)
1.00
1.03
1.04
1.00
4.02
4.07
4.04
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


167.13
153.07
130.20
125.85
120.98
120.49
118.04
50.27
27.25
26.89
3au
13C NMR (DMSO-d6, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

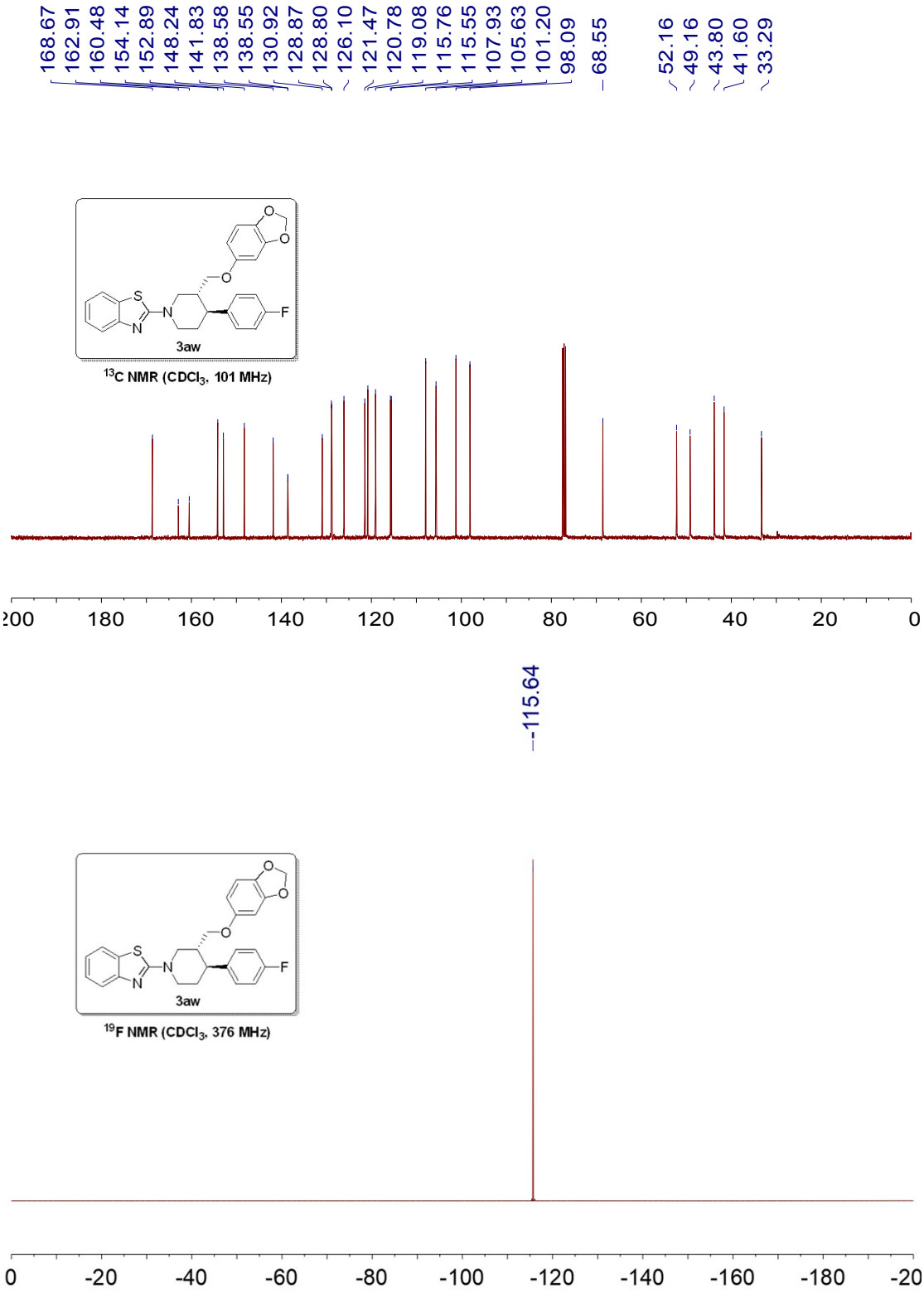

8.36
8.35
7.75
7.73
7.45
7.43
7.28
7.27
7.25
7.17
7.07
7.05
7.04
4.17
4.14
3.99
3.93
3.90
3.81
3.70
3.23
3.21
3.16
3.13
3.10
1.99
1.95
1.91
1.89
1.71
1.68
1.66
1.63
3av
1H NMR (DMSO-d6, 400 MHz)
1.00
1.00
1.03
1.09
2.09
1.03
1.09
2.04
6.05
3.06
2.08
2.04
2.08
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5

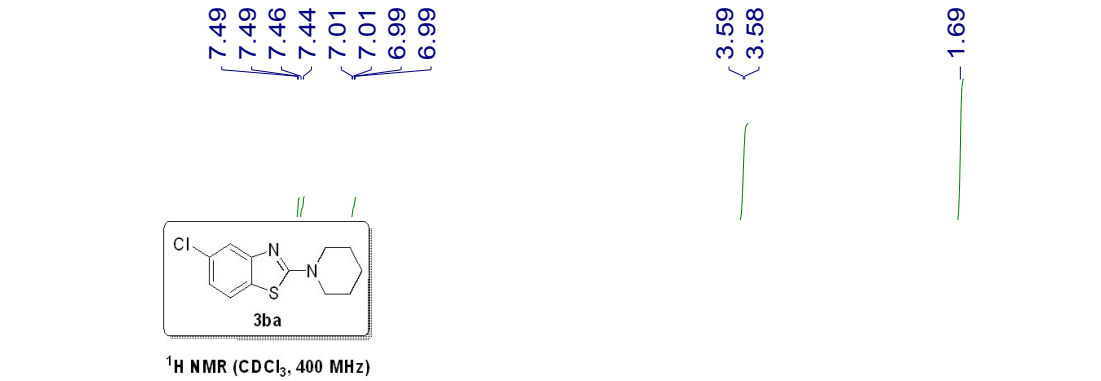


^{13}C NMR (DMSO-d_6, 101 MHz)

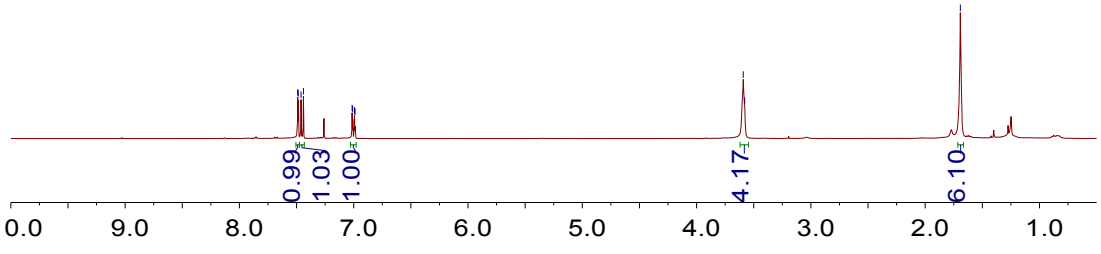


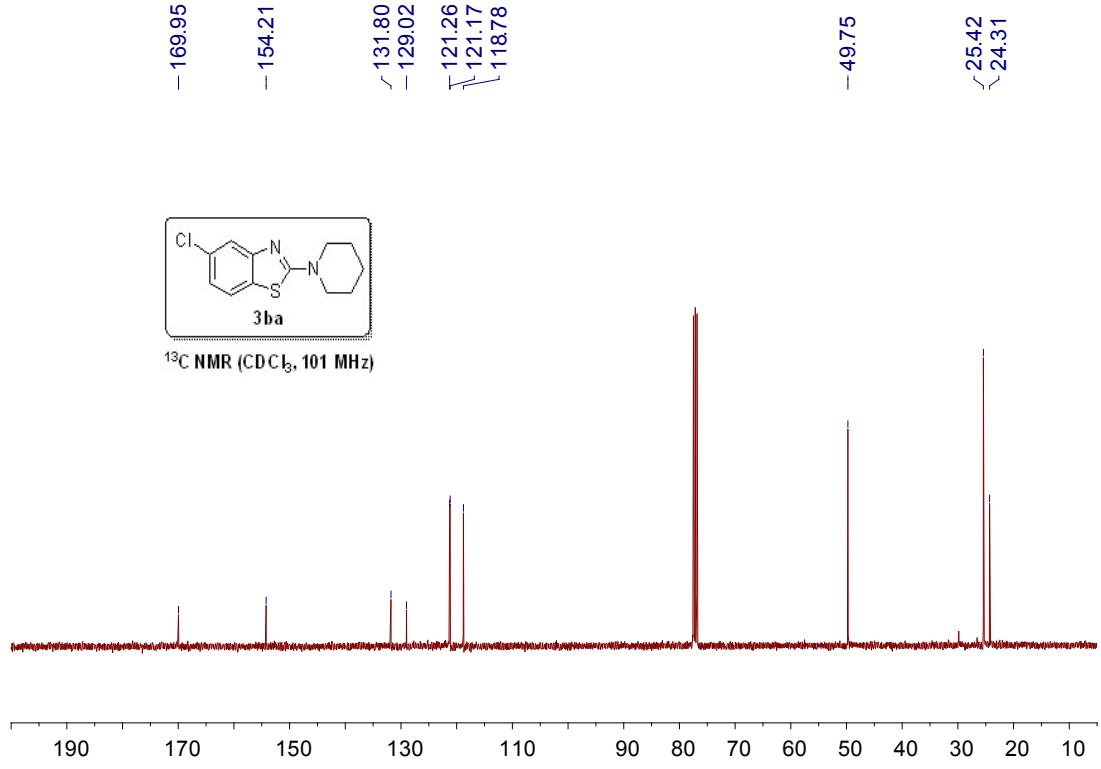
^{1}H NMR ($CDCl_3$, 400 MHz)


168.67
162.91
160.48
154.14
152.89
148.24
141.83
138.58
138.55
130.92
128.87
128.80
126.10
121.47
120.78
119.08
115.76
115.55
107.93
105.63
101.20
98.09
68.55
52.16
49.16
43.80
41.60
33.29
3aw
13C NMR (CDCl3, 101 MHz)
200
180
160
140
120
100
80
60
40
20
0
-115.64
3aw
19F NMR (CDCl3, 376 MHz)
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-20

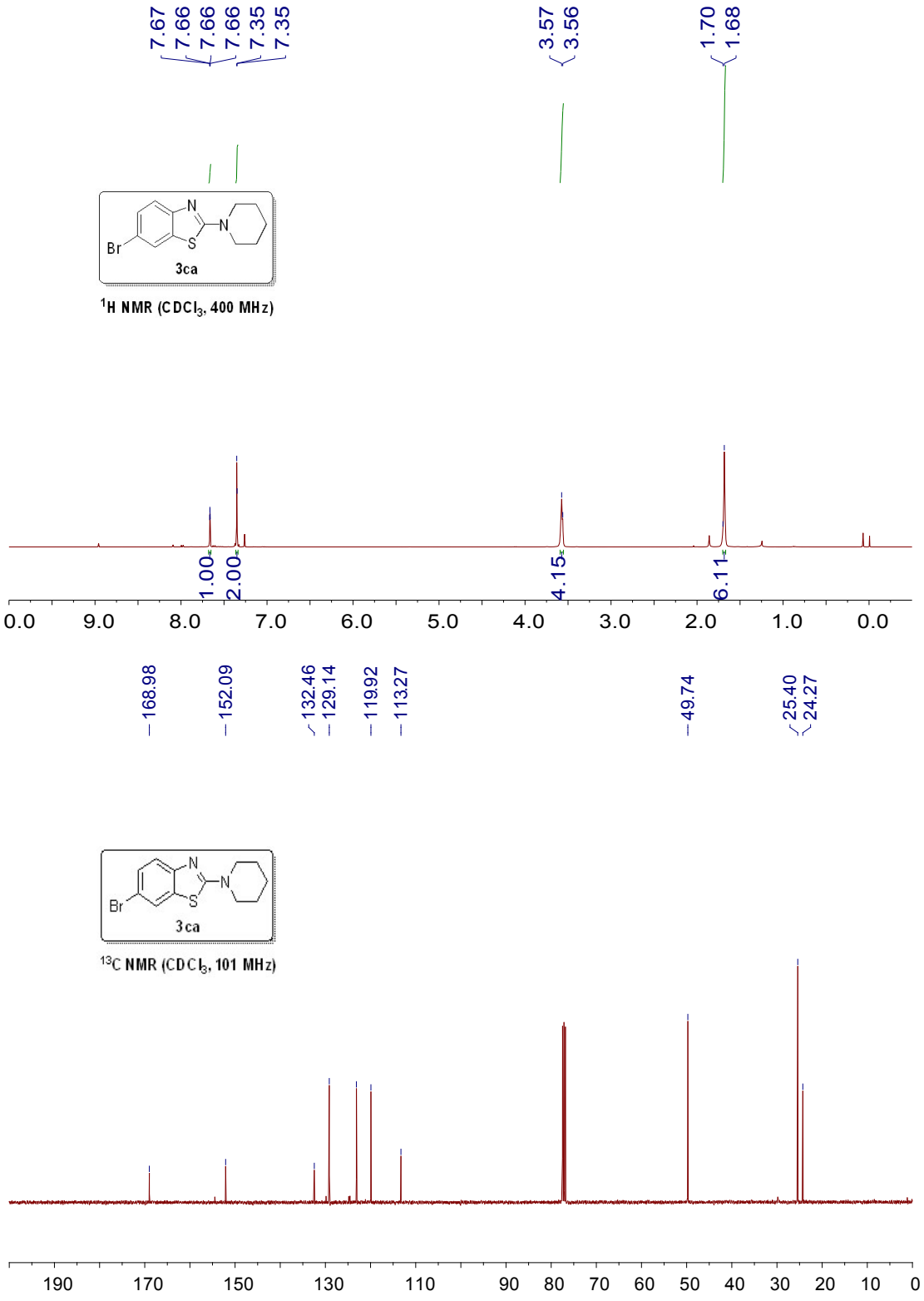


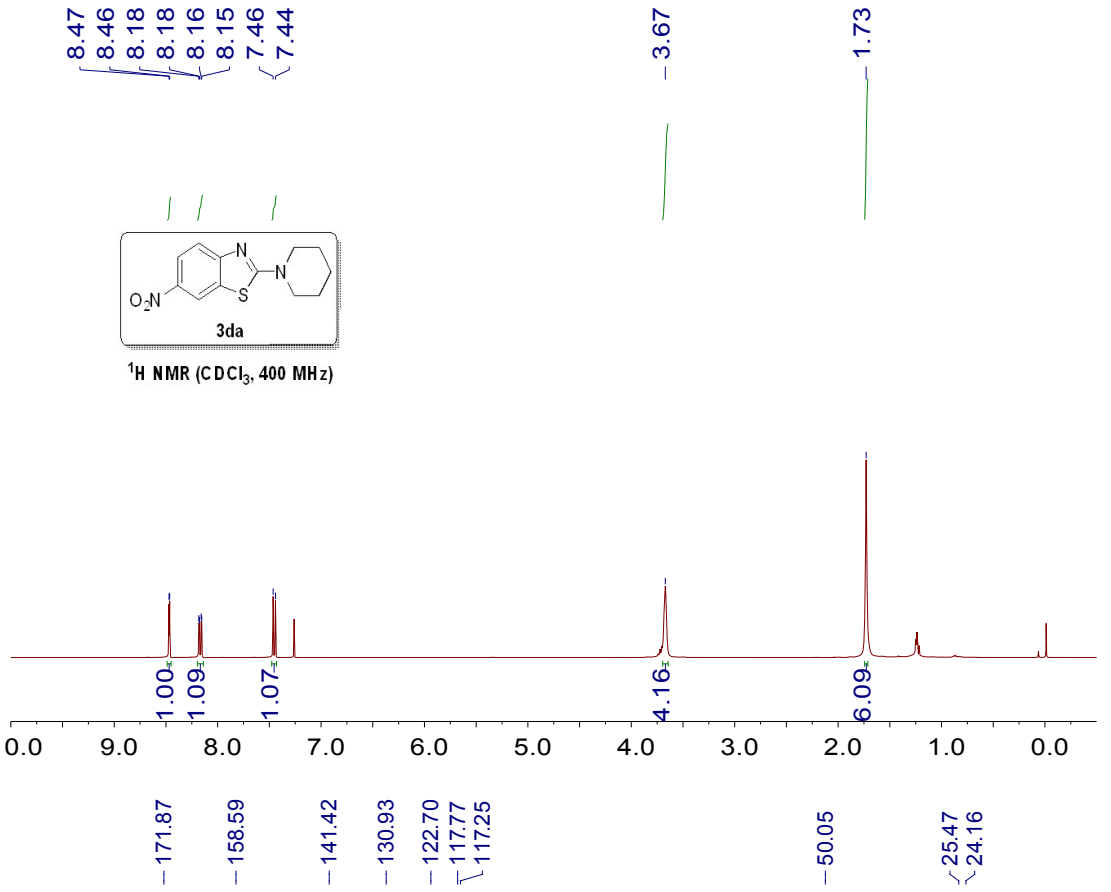
^{1}H NMR ($CDCl_3$, 400 MHz)



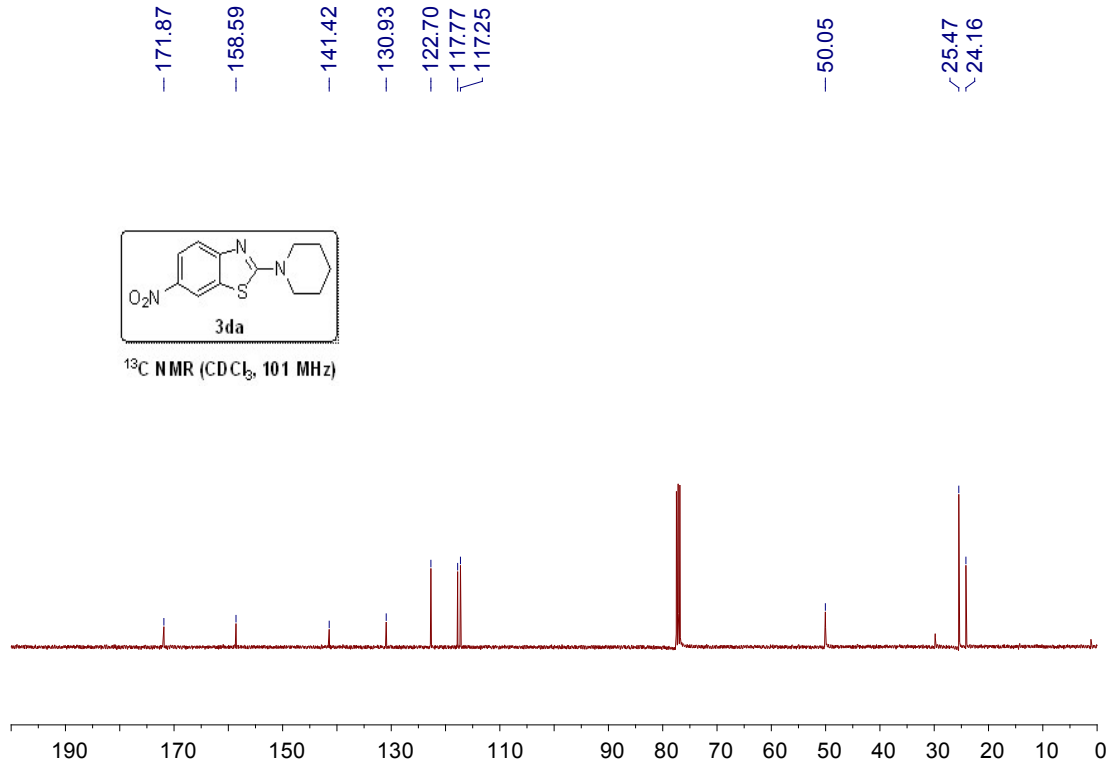


^{13}C NMR ($CDCl_3$, 101 MHz)

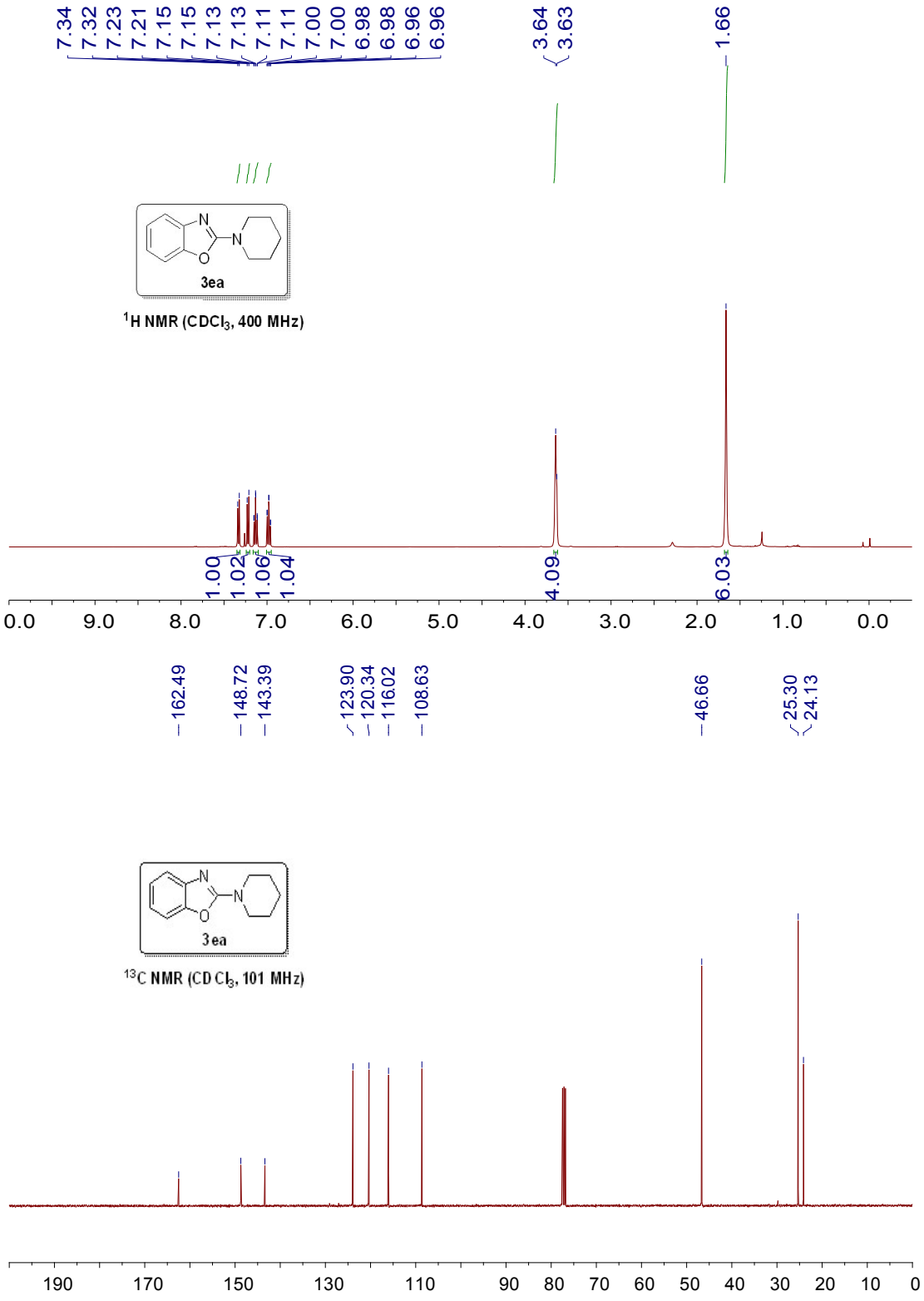

7.67
7.66
7.66
7.66
7.35
7.35
3.57
3.56
1.70
1.68
Br
N
S
N
3ca
1H NMR (CDCl3, 400 MHz)
1.00
2.00
4.15
6.11
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
168.98
152.09
132.46
129.14
119.92
113.27
49.74
25.40
24.27
Br
N
S
N
3ca
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

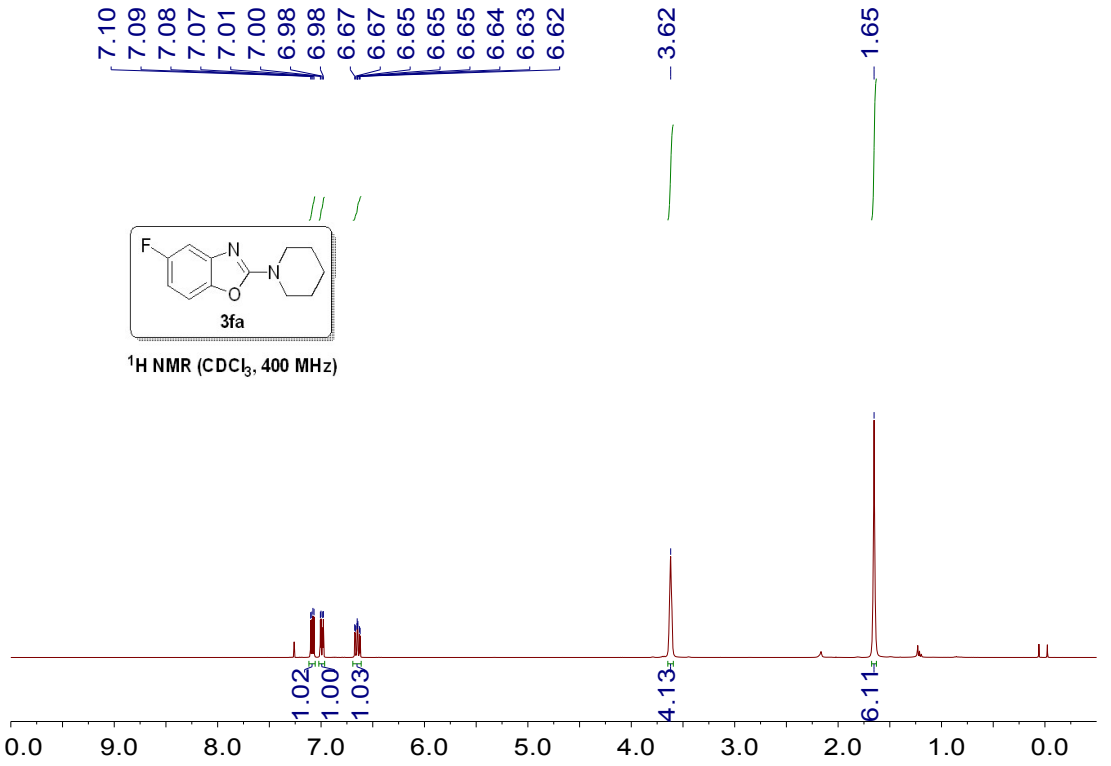


^{1}H NMR ($CDCl_3$, 400 MHz)

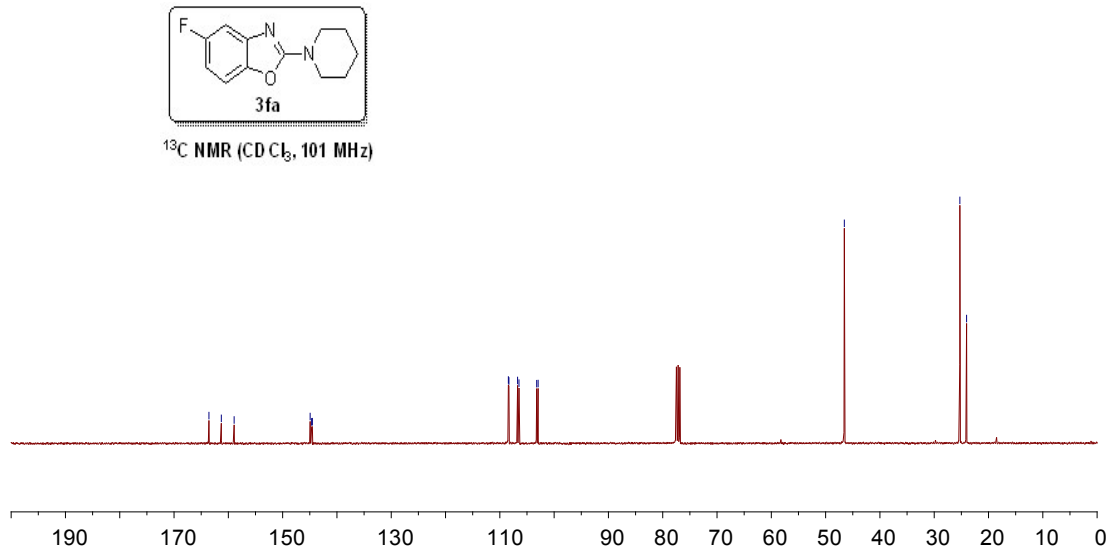


^{13}C NMR ($CDCl_3$, 101 MHz)

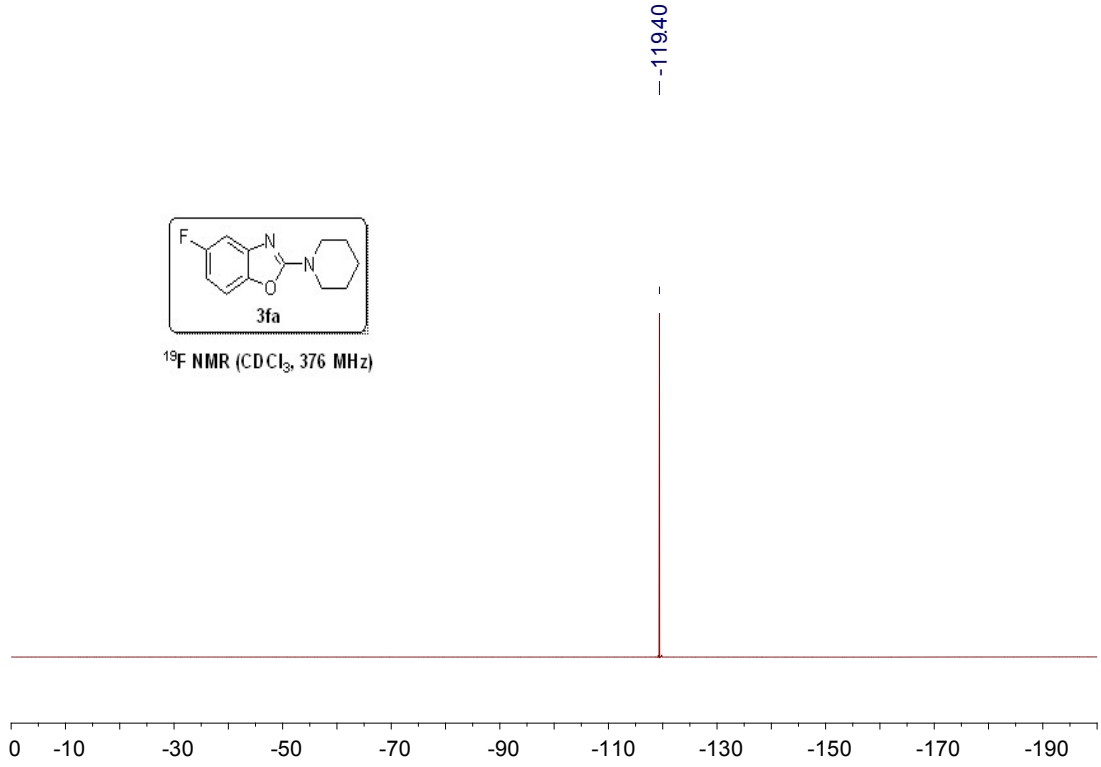

7.34
7.32
7.23
7.21
7.15
7.15
7.13
7.13
7.11
7.11
7.00
7.00
6.98
6.98
6.96
6.96
3.64
3.63
1.66
3ea
1H NMR (CDCl3, 400 MHz)
1.00
1.02
1.06
1.04
4.09
6.03
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
162.49
148.72
143.39
123.90
120.34
116.02
108.63
46.66
25.30
24.13
3ea
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

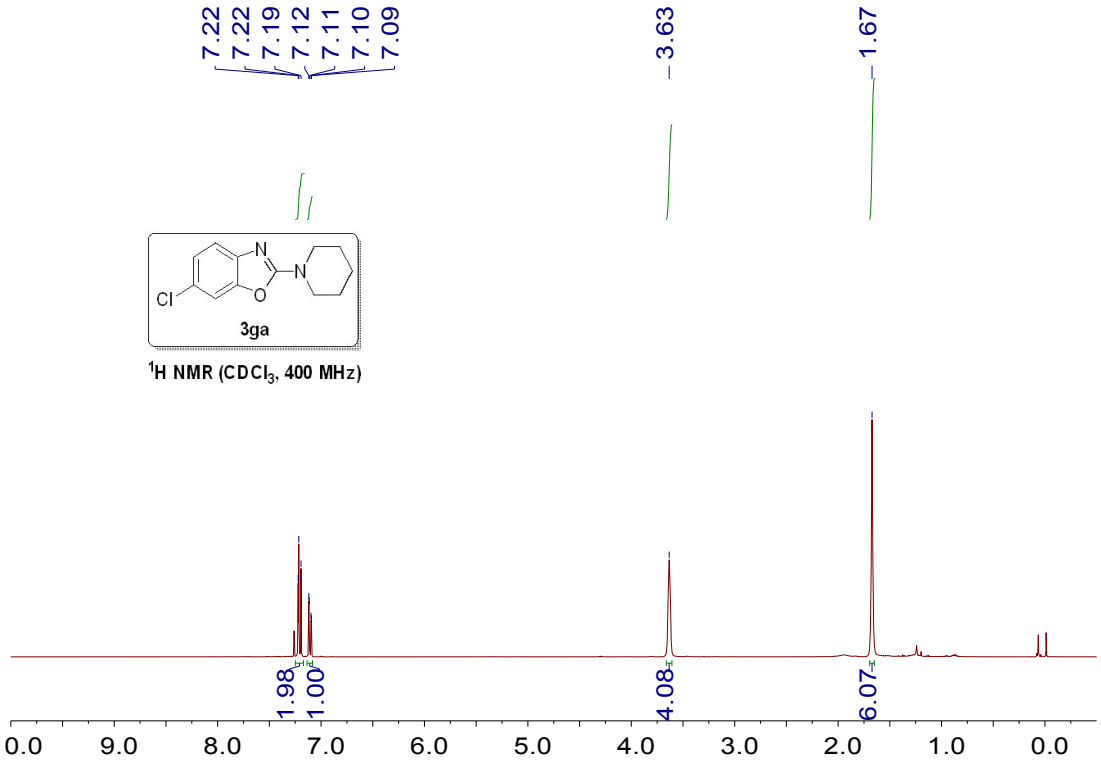


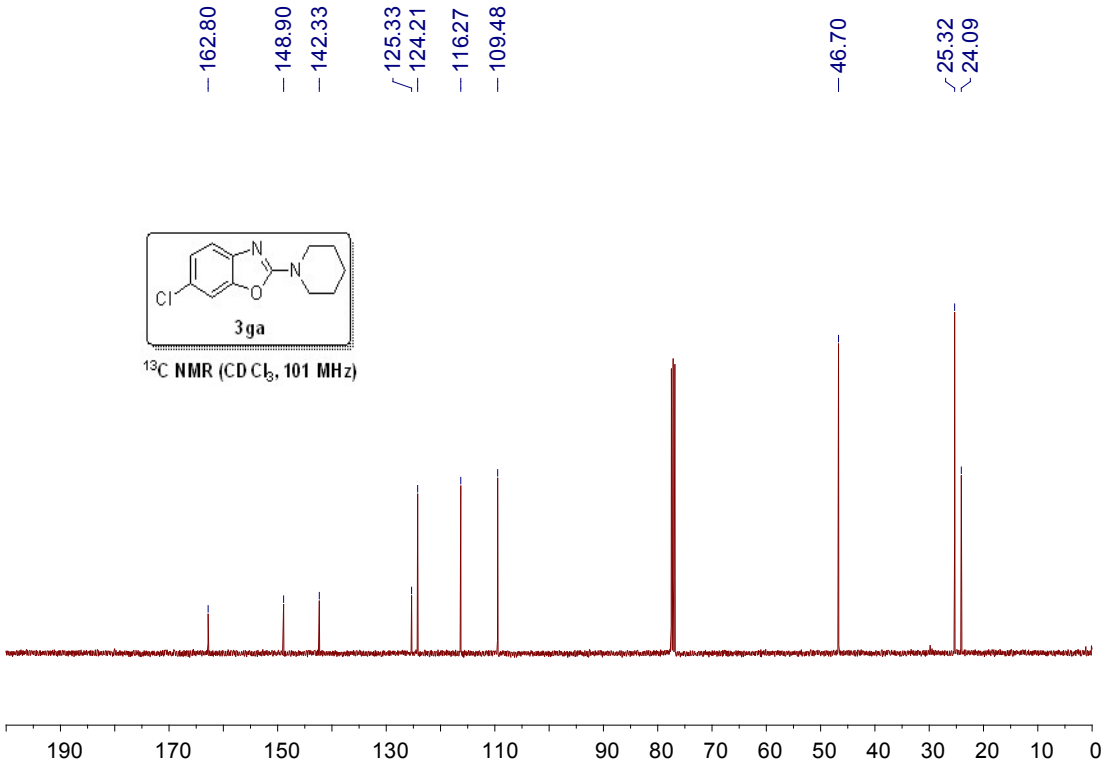
^{1}H NMR ($CDCl_3$, 400 MHz)

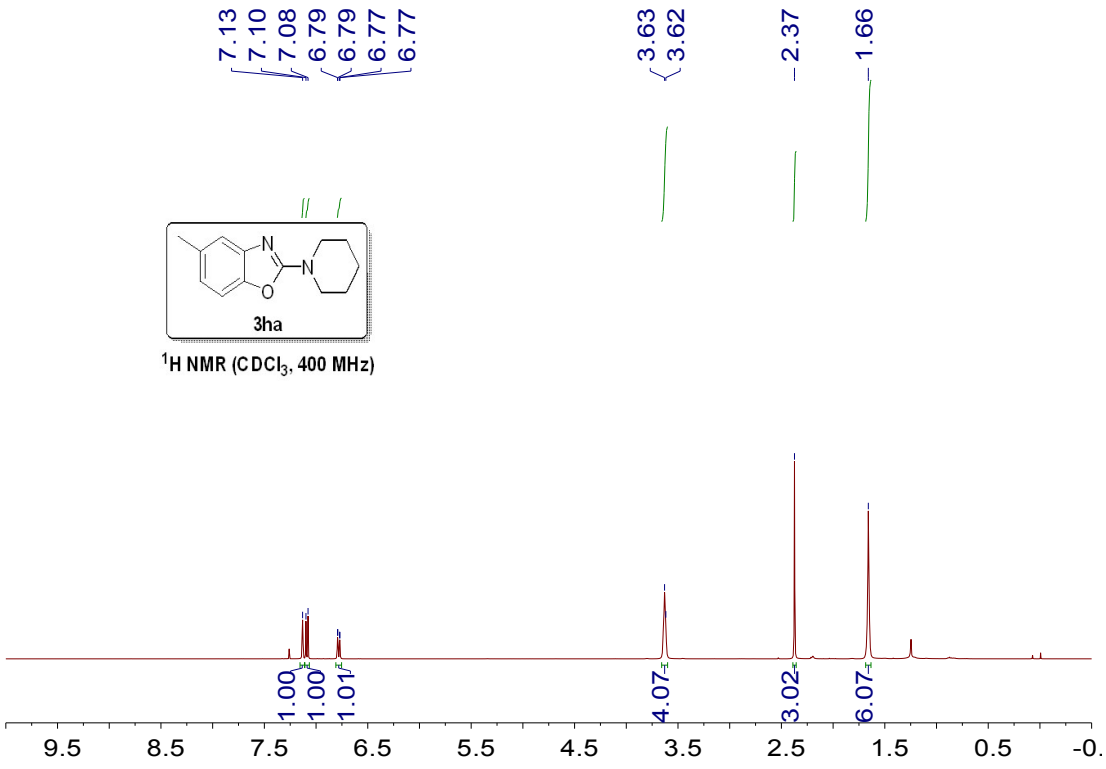


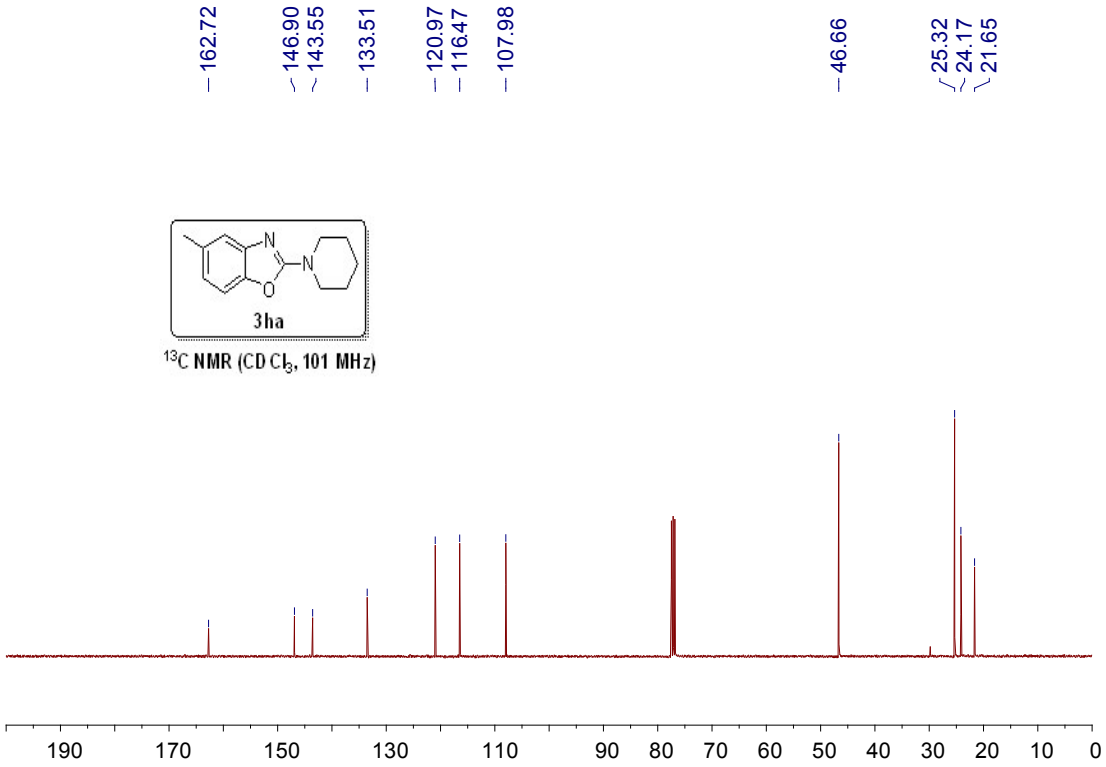
^{13}C NMR ($CDCl_3$, 101 MHz)

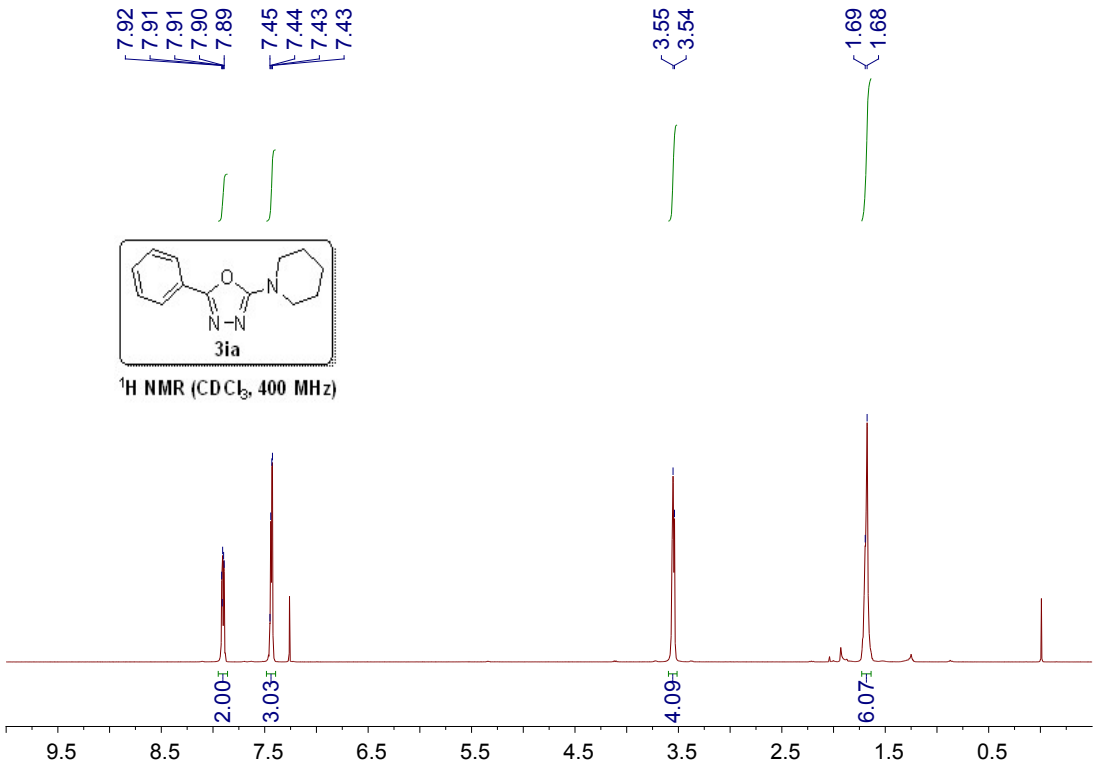

-119.40
F
N
O
N
3fa
^{19}F NMR ($CDCl_3$, 376 MHz)
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190

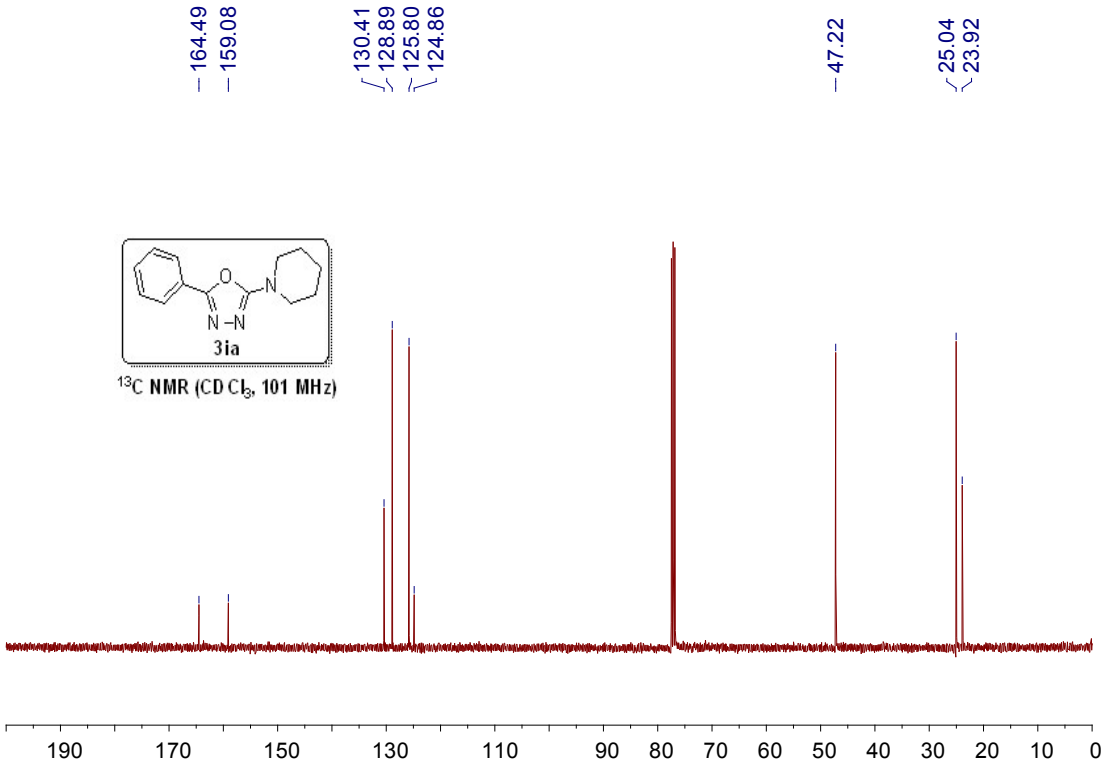

7.22
7.22
7.19
7.12
7.11
7.10
7.09
3.63
1.67
N
O
N
Cl
3ga
^{1}H NMR ($CDCl_3$, 400 MHz)
1.98
1.00
4.08
6.07
0.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

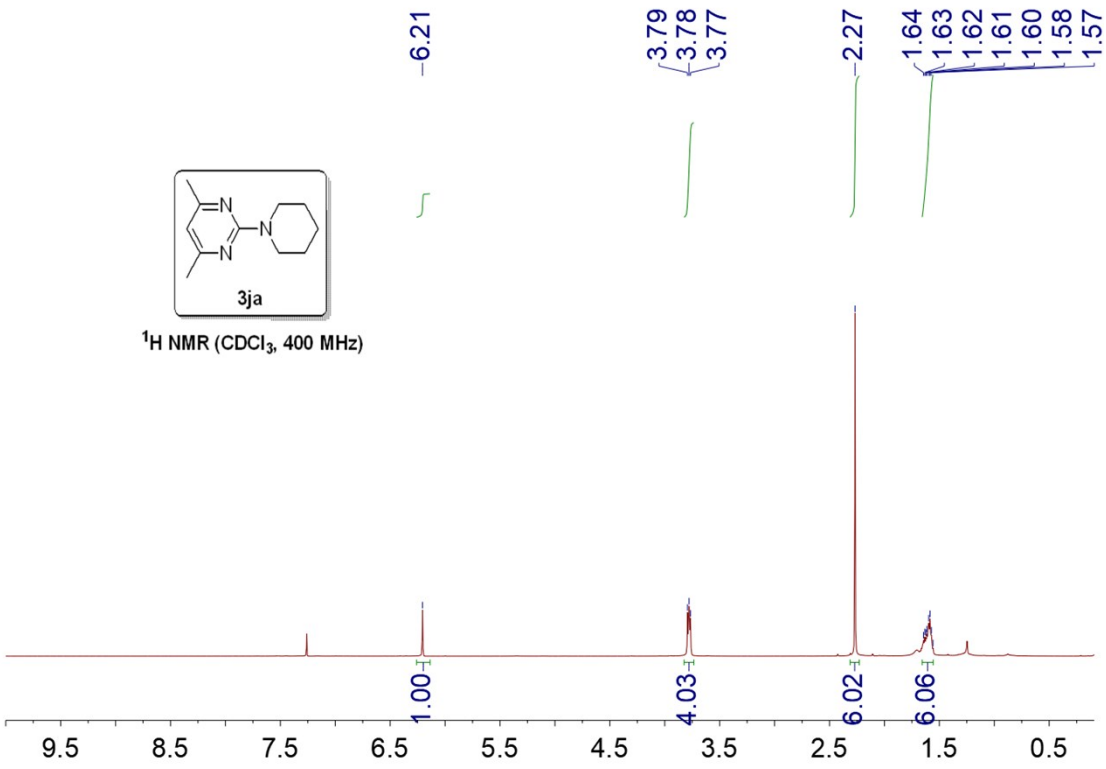

162.80
148.90
142.33
125.33
124.21
116.27
109.48
46.70
25.32
24.09
3ga
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

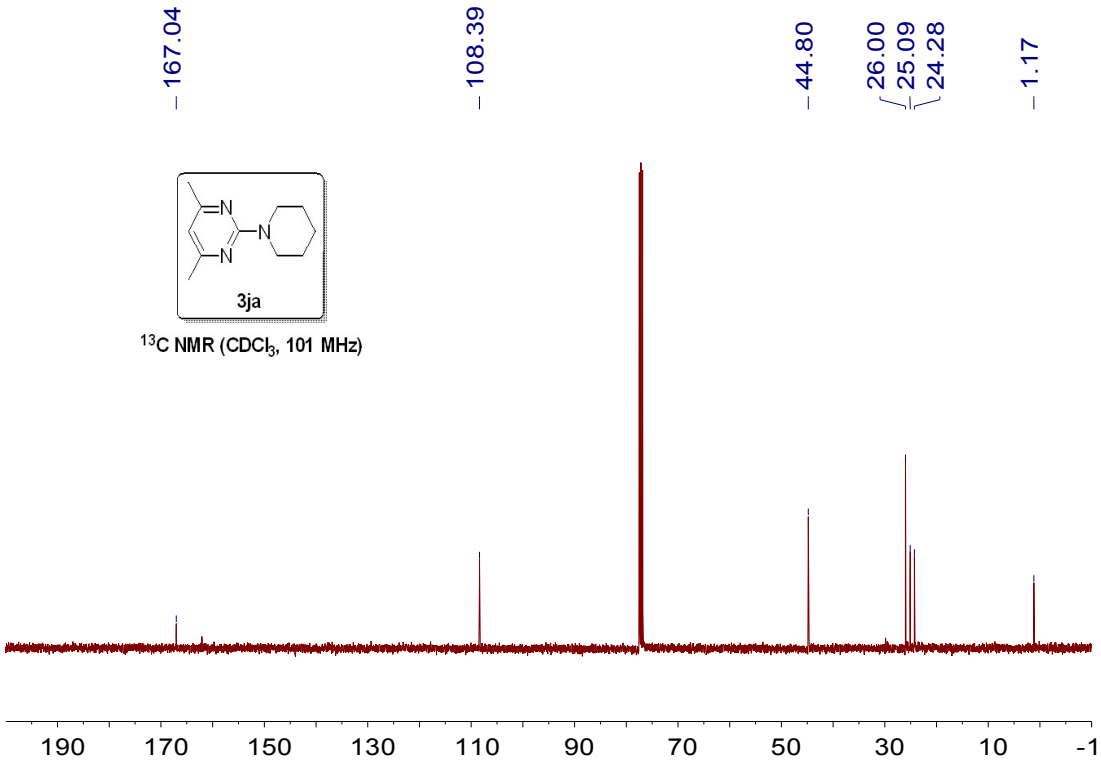

7.13
7.10
7.08
6.79
6.79
6.77
6.77
3.63
3.62
2.37
1.66
3ha
1H NMR (CDCl3, 400 MHz)
1.00
1.00
1.01
4.07
3.02
6.07
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.


162.72
146.90
143.55
133.51
120.97
116.47
107.98
46.66
25.32
24.17
21.65
3ha
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0


7.92
7.91
7.91
7.90
7.89
7.45
7.44
7.43
7.43
3.55
3.54
1.69
1.68
3ia
1H NMR (CDCl3, 400 MHz)
2.00
3.03
4.09
6.07
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5


164.49
159.08
130.41
128.89
125.80
124.86
47.22
25.04
23.92
3ia
13C NMR (CDCl3, 101 MHz)
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0


6.21
3.79
3.78
3.77
2.27
1.64
1.63
1.62
1.61
1.60
1.58
1.57
3ja
1H NMR (CDCl3, 400 MHz)
1.00
4.03
6.02
6.06
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5



^{13}C NMR ($CDCl_3$, 101 MHz)