Synthesis of heteroaryl containing sulfides via enaminone ligand assisted, copper-catalyzed C-S coupling reactions of heteroaryl thiols and aryl halides

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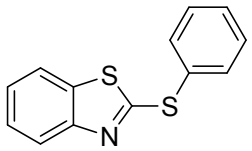
Genearal experimental information

All experiments were carried out at open atmosphere. All chemicals and solvents used in the experiments were obtained from commercial sources and used directly without further treatment. Solvents have been distilled before used in experiments. ^{1}H and ^{13}C NMR were recorded in 400 MHz apparatus. The frequency for ^{1}H NMR and ^{13}C NMR test are 400 MHz and 100 MHz, respectively. The chemical shifts were reported in ppm using TMS as internal standard. Melting points were tested in X-4A instrument without correcting temperature, and the HRMS were tested in Agilent 6210 LC/TOF instrument under EI model.

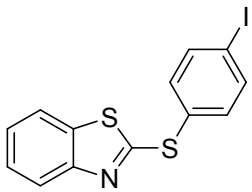
General procedure for the synthesis of heteroaryl sulfides 5. To a 25 mL round bottom flask were located heteroayrl thiol **4** (0.5 mmol), aryl halide **2** (0.6 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.05 mmol), ligand **L3** (0.05 mmol), Cs_2CO_3 (1.0 mmol) and DMSO (2 mL). The resulting mixture was stirred at 100 ^{o}C for 12 h (TLC). Upon completion, the mixture was allowed to cool down to room temperature. Subsequently, 10 mL water was added, and the resulting mixture was extracted with ethyl acetate (3 × 10 mL). The organic phase was combined and dried with anhydrous Na_2SO_4. After filtering the solid away, the solvent was removed in vacuum, and the residue was

subjected to column chromatography to give pure products using mixed petroleum and ethyl acetate as eluent.

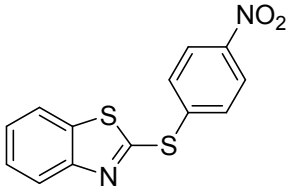
Characterization data



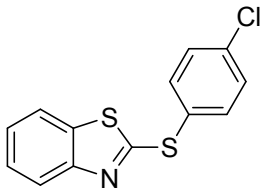
2-(Phenylthio)benzo[d]thiazole (**5a**).[1] Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, 1 H, *J* = 8.0 Hz), 7.61 (dd, 2 H, *J1* = 8.0 Hz, *J*2 = 1.2 Hz), 7.51 (d, 1 H, *J* = 8.0 Hz), 7.36-7.33 (m, 3 H), 7.28 (t,1 H, *J* = 8.0 Hz), 7.13 (t, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 154.0, 135.5, 135.4, 130.6, 130.0, 129.9, 126.2, 124.4, 122.0, 120.9.



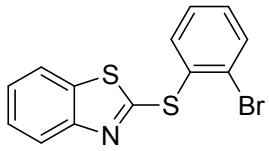
2-(4-Iodophenylthio)benzo[d]thiazole (**5b**). Light yellow solid; mp 72-73 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, 1 H, *J* = 8.0 Hz), 7.70 (d, 2 H, *J* = 8.0 Hz), 7.58 (d, 1 H, *J* = 8.0 Hz), 7.33 (d, 3 H, *J* = 8.0 Hz), 7.18 (q, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 153.8, 139.1, 136.5, 135.7, 129.9, 126.3, 124.6, 122.1, 120.8, 97.0. HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_8INS_2$: 368.9143; found: 368.9152.



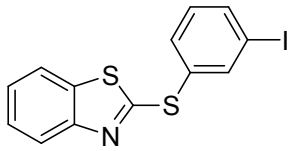
2-(4-Nitrophenylthio)benzo[d]thiazole (**5c**).[1] Yellow solid; mp 95-96 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (d, 2 H, *J* = 8.0 Hz), 7.87 (d, 1 H, *J* = 8.0 Hz), 7.68 (d, 3 H, *J* = 8.0 Hz), 7.38 (t, 1 H, *J* = 6.0 Hz), 7.29 (t, 1 H, *J* = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8, 153.6, 148.1, 140.3, 136.2, 132.7, 126.8, 125.6, 124.5, 122.8, 121.2.



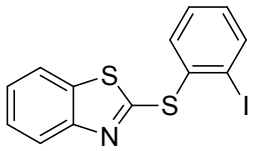
2-(4-Chlorophenylthio)benzo[d]thiazole (**5d**).[2] Light yellow solid; mp 60-61 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, 1 H, *J* = 8.0 Hz), 7.55 (t, 3 H, *J* = 8.0 Hz), 7.31 (q, 3 H, *J* = 8.0 Hz), 7.17 (t, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 153.8, 137.0, 136.5, 135.5, 130.2, 128.4, 126.3, 124.6, 122.1, 120.9.



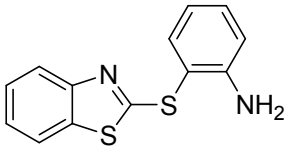
2-(2-Bromophenylthio)benzo[d]thiazole (**5e**). Light yellow solid; mp 66-67 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, 1 H, *J* = 8.0 Hz), 7.72 (d, 1 H, *J* = 8.0Hz), 7.68 (d, 1 H, *J* = 8.0 Hz), 7.61 (d, 1 H, *J* = 8.0 Hz), 7.35 (d, 1 H, *J* = 8.0 Hz), 7.31 (d, 1 H, *J* = 8.0 Hz), 7.26 (d, 1 H, *J* = 8.0 Hz), 7.20 (t, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.1, 153.9, 137.0, 135.8, 134.3, 131.8, 131.75, 129.9, 128.7, 126.3, 124.6, 122.2, 120.9. HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_8BrNS_2$: 320.9282; found: 320.9294.



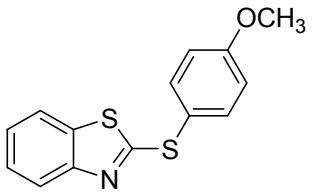
2-(3-Iodophenylthio)benzo[d]thiazole (**5f**). Light yellow solid; mp 47-49 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (s, 1 H), 7.79 (d, 1 H, *J* = 8.0 Hz), 7.72 (d, 1 H, *J* = 8.0 Hz), 7.59 (d, 2 H, *J* = 8.0 Hz), 7.32 (d, 1 H, *J* = 8.0 Hz), 7.20 (t, 1 H, *J* = 8.0 Hz), 7.09 (t, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.9, 153.9, 143.1, 139.3, 135.7, 134.1, 132.2, 131.3, 126.4, 124.7, 122.2, 120.9, 94.9. HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_8INS_2$: 368.9143; found: 368.9154.



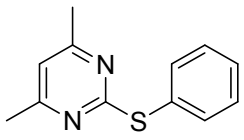
2-(2-Iodophenylthio)benzo[d]thiazole (**5g**).[3] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ =7.94 (d, 1 H, *J* = 8.0 Hz), 7.83 (d, 1 H, *J* = 8.0 Hz), 7.76 (d, 1 H, *J* = 8.0 Hz), 7.60 (d, 1 H, *J* =8.0 Hz), 7.35 (q, 2 H, *J* = 8.0 Hz), 7.20 (t, 1 H, *J* = 8.0 Hz), 7.08 (t, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.7, 153.9, 140.9, 136.3, 135.8, 135.8, 131.7, 129.7, 126.3, 124.6, 122.2, 121.0, 107.5.



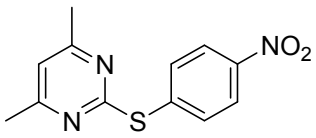
2-(Benzo[d]thiazol-2-ylthio)aniline (**5h**).[4] Brown solid; mp 121-123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, 1 H, *J* = 8.0 Hz), 7.60 (d, 1 H, *J* = 8.0 Hz), 7.47 (d, 2 H, *J* = 8.0 Hz), 7.36 (t, 1 H, *J* = 8.0 Hz), 7.22 (q, 1 H, *J* = 8.0 Hz), 6.71 (d, 2 H, *J* = 8.0Hz), 4.01 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.6, 154.3, 149.2, 137.7, 137.6, 135.4, 126.1, 123.9, 121.6, 121.6, 120.8, 116.4, 115.9.



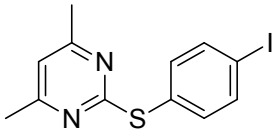
2-(4-Methoxyphenylthio)benzo[d]thiazole (**5i**).[1] Light brown solid; mp 63-64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, 1 H, *J* = 8.0 Hz), 7.58 (q, 3 H, *J* = 8.0 Hz), 7.32 (t,1 H, *J* = 8.0 Hz), 7.18 (d, 1 H, J = 8.0 Hz), 6.94 (d, 2 H, J = 8.0 Hz), 3.81 (s,3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1, 161.7, 154.1, 137.7, 135.4, 126.1, 124.0, 121.8, 120.7, 120.1, 115.5, 55.5.



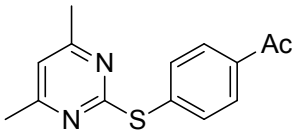
4,6-Dimethyl-2-(phenylthio)pyrimidine (**5j**).[5] Brown solid; mp 61-62 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64-7.62 (m, 2 H), 7.39-7.38 (m, 3 H), 6.69 (s, 1 H), 2.33 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 167.3, 134.8, 130.3, 128.8, 116.4, 116.3, 23.9.



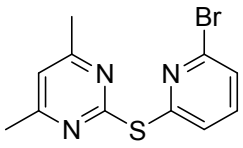
4,6-Dimethyl-2-(4-nitrophenylthio)pyrimidine (**5k**).[6] Pale yellow solid; mp 118-120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, 2 H, *J* = 8.0 Hz), 7.74 (d, 2 H, *J* = 8.0 Hz), 6.73 (s, 1 H), 2.31 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.1, 167.8, 147.4, 139.8, 134.0, 123.6, 117.3, 23.8.



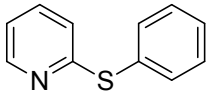
2-(4-Iodophenylthio)-4,6-dimethylpyrimidine (**5l**). Pale red oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, 2 H, *J* = 8.0 Hz), 7.35 (d, 2 H, *J* = 8.0 Hz), 7.62 (s, 1 H), 2.35 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 167.7, 138.2, 136.6, 130.6, 116.8, 95.1, 24.1. HRMS (EI): m/z $[M]^+$ calcd for $C_{12}H_{11}IN_2S$: 341.9688; found: 341.9697.



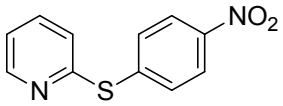
1-(4-(4,6-Dimethylpyrimidin-2-ylthio)phenyl)ethanone (**5m**). Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, 2 H, *J* = 8.0 Hz), 7.93 (d, 2 H, *J* = 8.0 Hz), 6.76 (s, 1 H), 2.62 (s, 3 H), 2.36 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 169.9, 167.6, 137.0, 136.5, 133.8, 128.5, 116.9, 26.7, 23.8. HRMS (EI): m/z $[M]^+$ calcd for $C_{14}H_{14}N_2OS$: 258.0821; found: 258.0827.



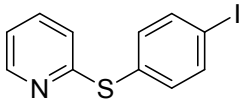
2-(6-Bromopyridin-2-ylthio)-4,6-dimethylpyrimidine (**5n**). Yellow solid; mp 110-112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, 1 H, *J* = 8.0 Hz), 7.55 (t, 1 H, *J* = 8.0 Hz), 7.40 (d, 1 H, *J* = 8.0 Hz), 6.80 (s, 1 H), 2.39 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 167.6, 155.7, 141.1, 138.7, 127.3, 126.7, 117.3, 23.8. HRMS (EI): m/z $[M]^+$ calcd for $C_{11}H_{10}BrN_3S$: 294.9773; found: 294.9776.



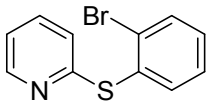
2-(Phenylthio)pyridine (**5o**).[7] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (d, 1 H, *J* = 4.0 Hz), 7.52-7.49 (m, 2 H), 7.38-7.32 (m, 4 H), 6.90 (q, 1 H, *J* = 8.0 Hz), 6,79 (d, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.5, 149.6, 136.8, 135.0, 131.0, 129.7, 129.1, 121.3, 119.9.



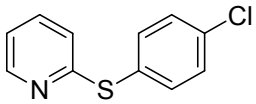
2-(4-Nitrophenylthio)pyridine (**5p**).[8] Pale yellow solid; mp 84-85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (d, 1 H, *J* = 4.0 Hz), 8.10 (d, 2 H, *J* = 8.0 Hz), 7.58-7.51 (m, 3 H), 7.23 (d, 1 H, *J* = 8.0 Hz), 7.11 (t, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6, 150.5, 146.9, 142.5, 137.5, 131.9, 124.9, 124.2, 122.1.



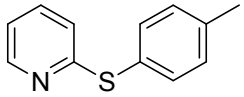
2-(4-Iodophenylthio)pyridine (**5q**). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (d, 1 H, *J* = 4.0 Hz), 7.73 (d, 2 H, *J* = 8.0 Hz), 7.48 (t, 1 H, *J* = 8.0 Hz), 7.30 (d, 2 H, *J* = 8.0 Hz), 7.03 (t, 1 H, *J* = 8.0 Hz), 6.96 (d, 2 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 149.7, 138.7, 136.9, 136.2, 131.3, 121.9, 120.3, 95.2. HRMS (EI): m/z $[M]^+$ calcd for $C_{11}H_8INS$: 312.9422; found: 312.9424.



2-(2-Bromophenylthio)pyridine (**5r**).[9] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.38 (d, 1 H, *J* = 4.0 Hz), 7.64 (d, 1 H, *J* = 8.0 Hz), 7.58 (d, 1 H, *J* = 8.0 Hz), 7.43 (t, 1 H, *J* = 8.0 Hz), 7.27 (t, 1 H, *J* = 8.0 Hz), 7.19 (t, 1 H, *J* = 8.0 Hz), 6.97 (q, 1 H, *J* = 4.0 Hz), 6.86 (d, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 150.0, 136.8, 136.5, 133.9, 132.9, 130.5, 129.5, 128.3, 122.1, 120.4.



2-(4-Chlorophenylthio)pyridine (**5s**).[9] Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (s, 1 H), 7.42 (q, 3 H, *J* = 8.0 Hz), 7.31 (d, 2 H, *J* = 8.0 Hz), 6.94 (t, 1 H, *J* = 6.0 Hz), 6.86 (d, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.5, 149.8, 149.7, 136.9, 136.1, 135.4, 129.6, 121.6, 120.3.



2-(*p*-Tolylthio)pyridine (**5t**).[8] Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (s,1 H), 7.48 (d, 2 H, *J* = 8.0 Hz), 7.41 (t, 1 H, *J* = 4.0 Hz), 7.23 (d, 2 H, *J* = 8.0 Hz), 6.96 (t, 1 H, *J* = 8.0 Hz), 6.82 (d, 1 H, *J* = 8.0 Hz), 2.38 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.2, 149.5, 139.5, 136.7, 135.3, 130.5, 127.2, 120.9, 119.6, 21.3.

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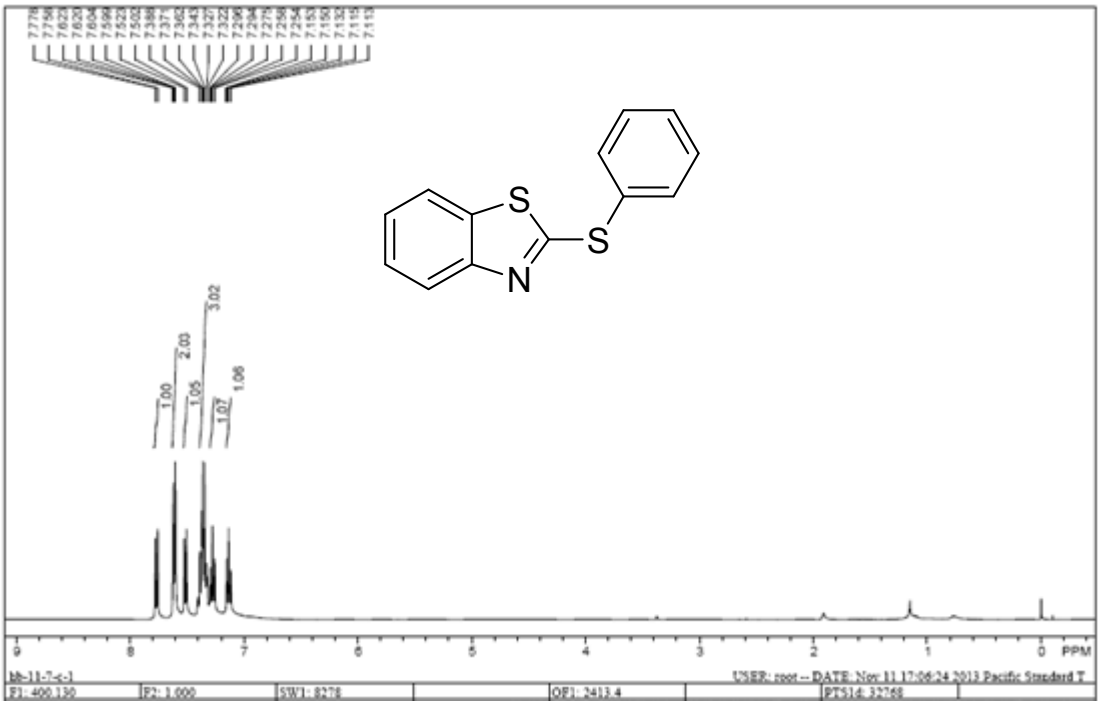
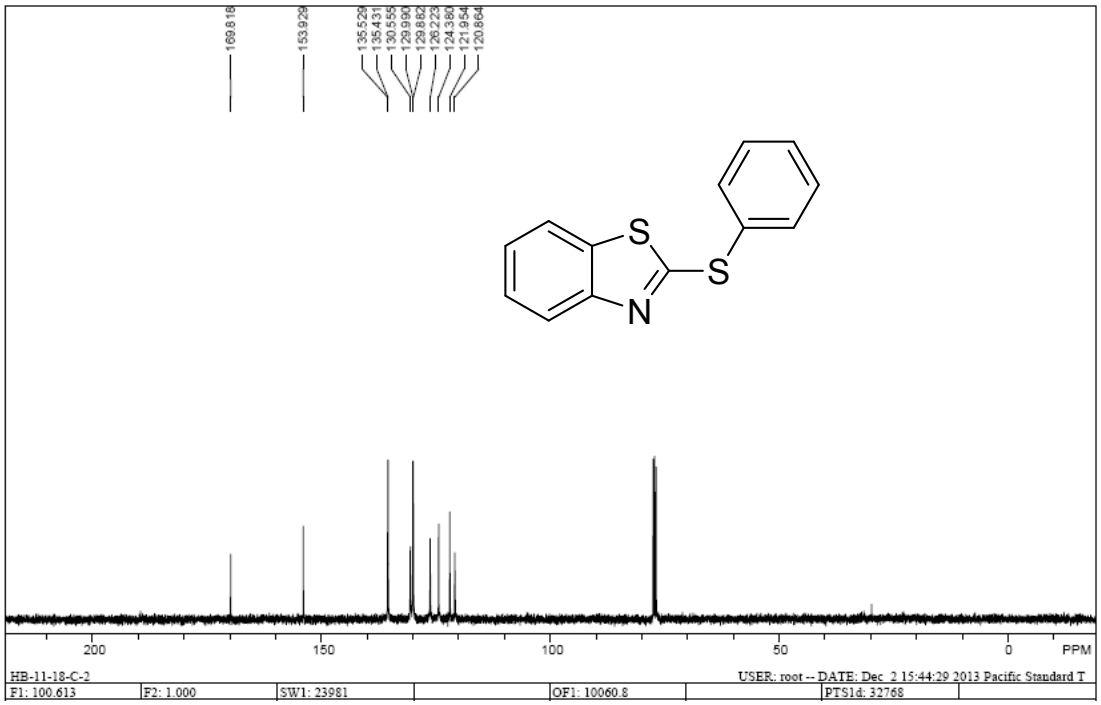
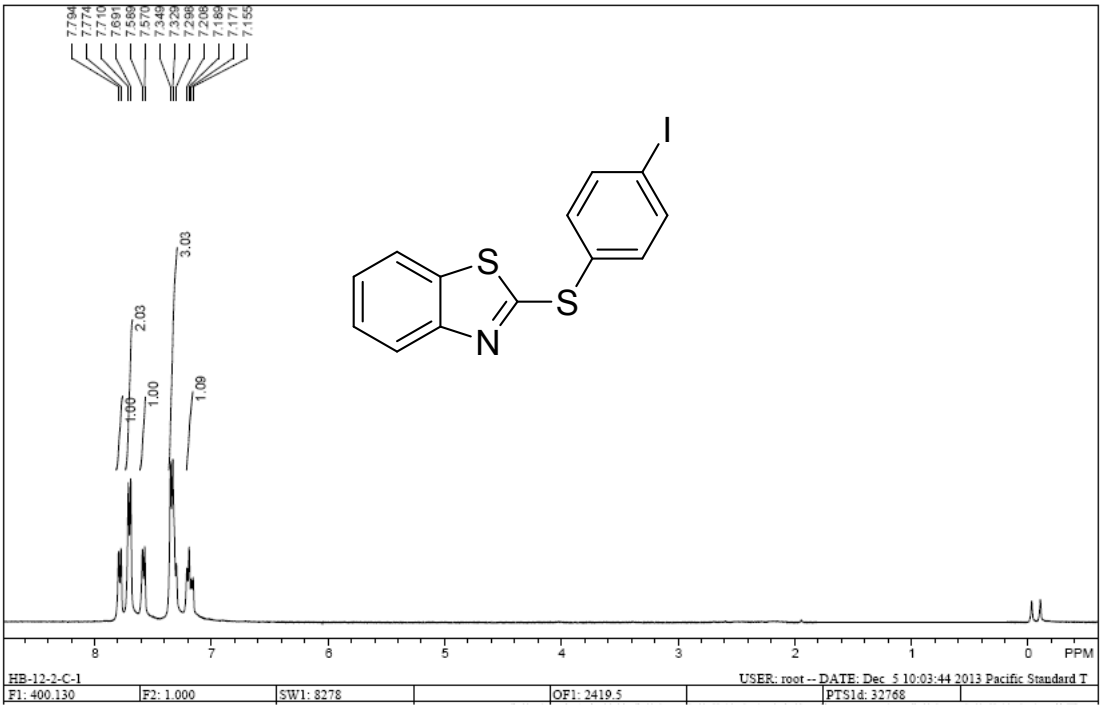
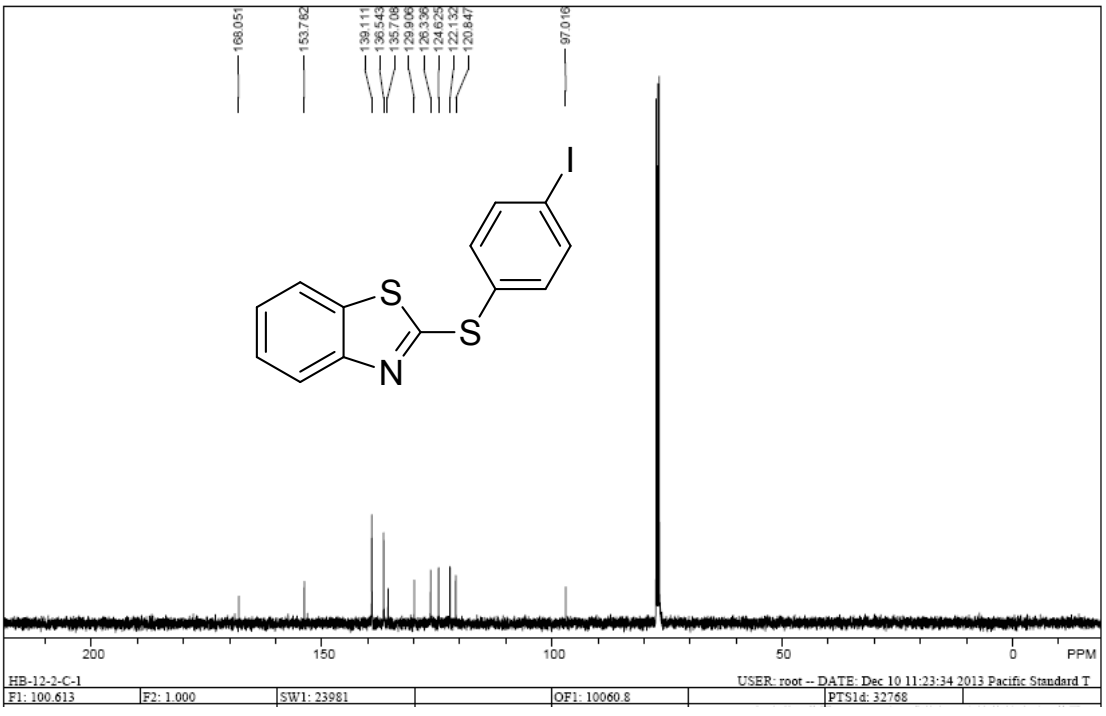
^{1}H and ^{13}C NMR of **5a**



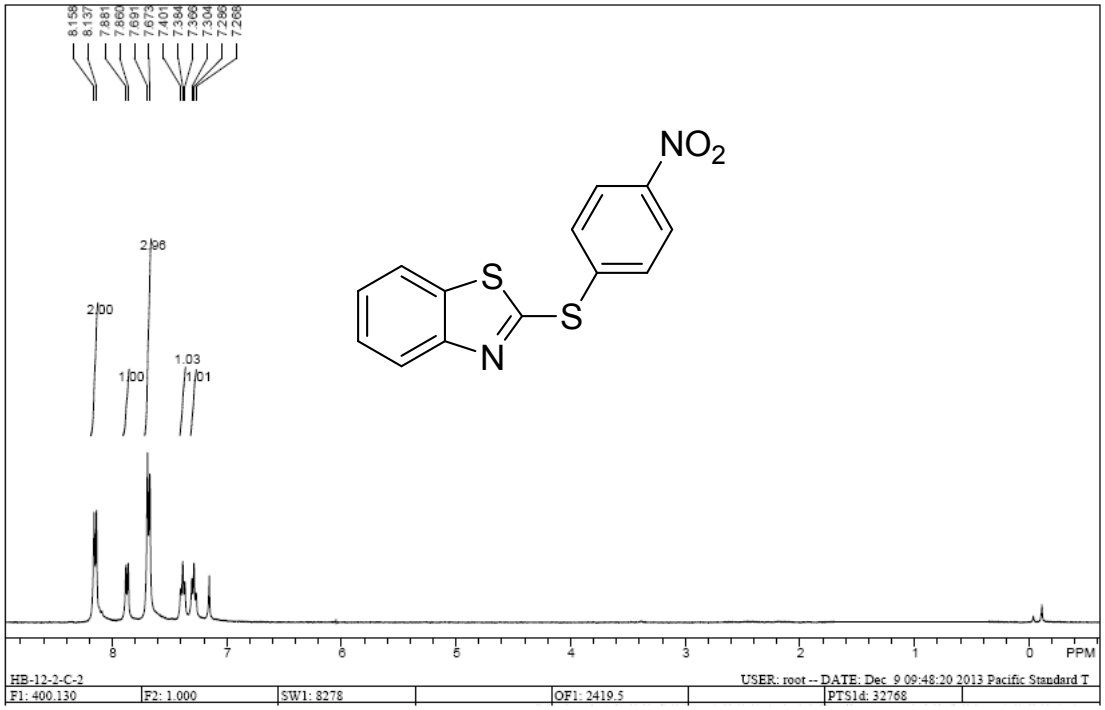


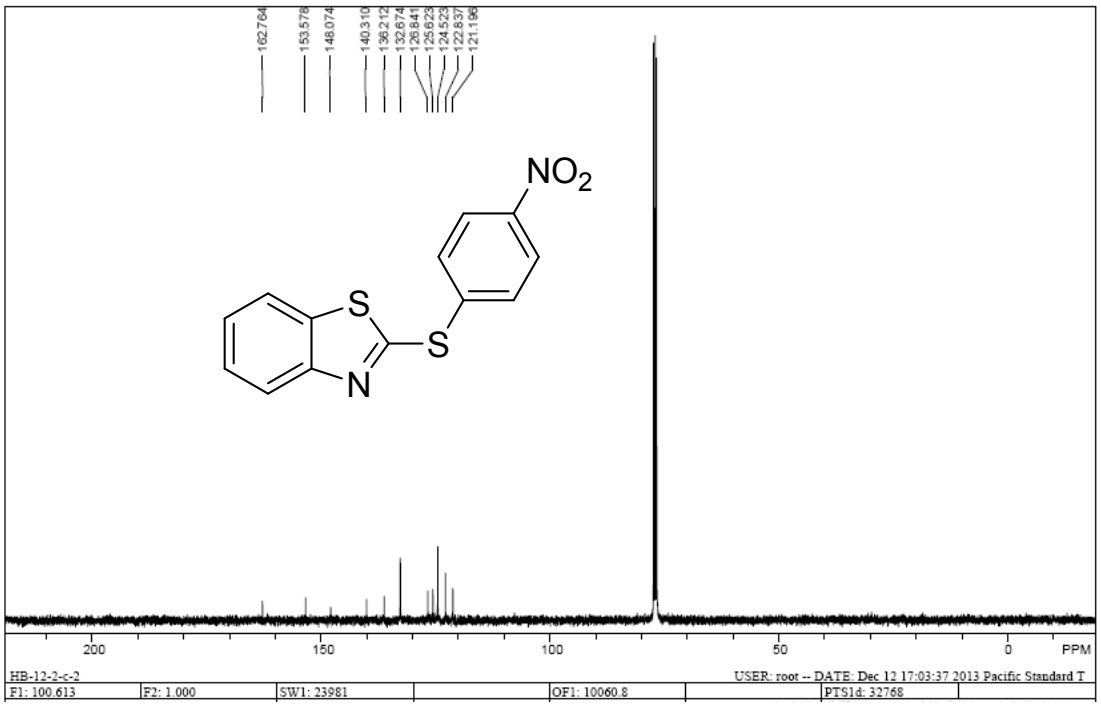
^{1}H and ^{13}C NMR of **5b**



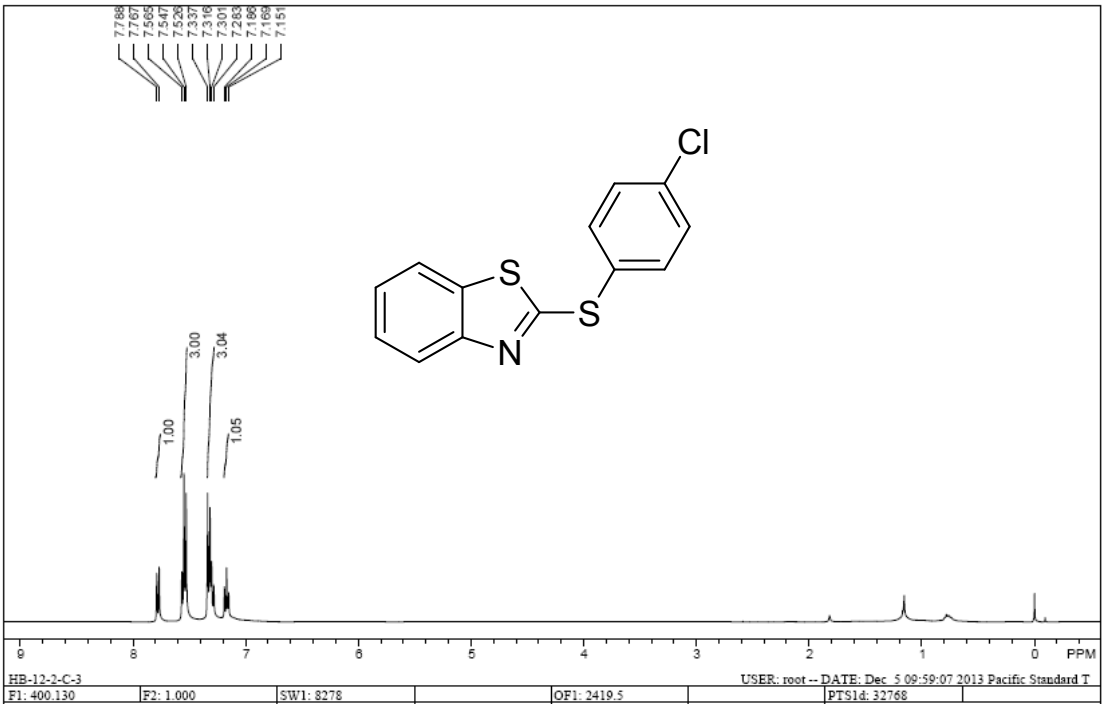


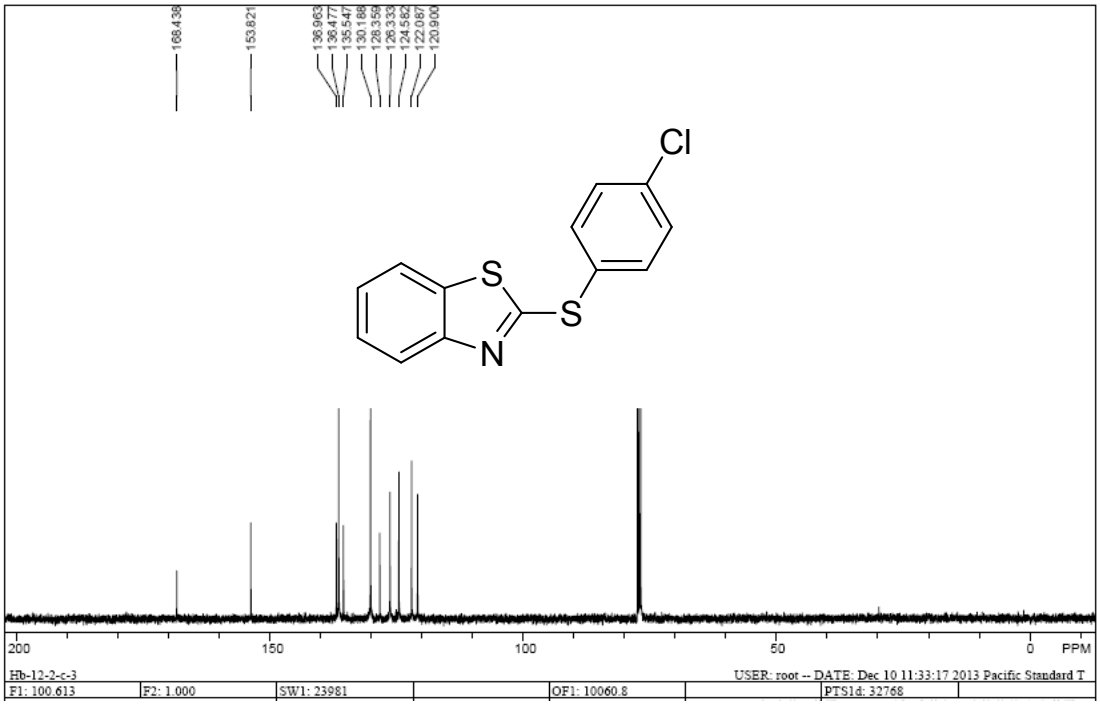
^{1}H and ^{13}C NMR of **5c**



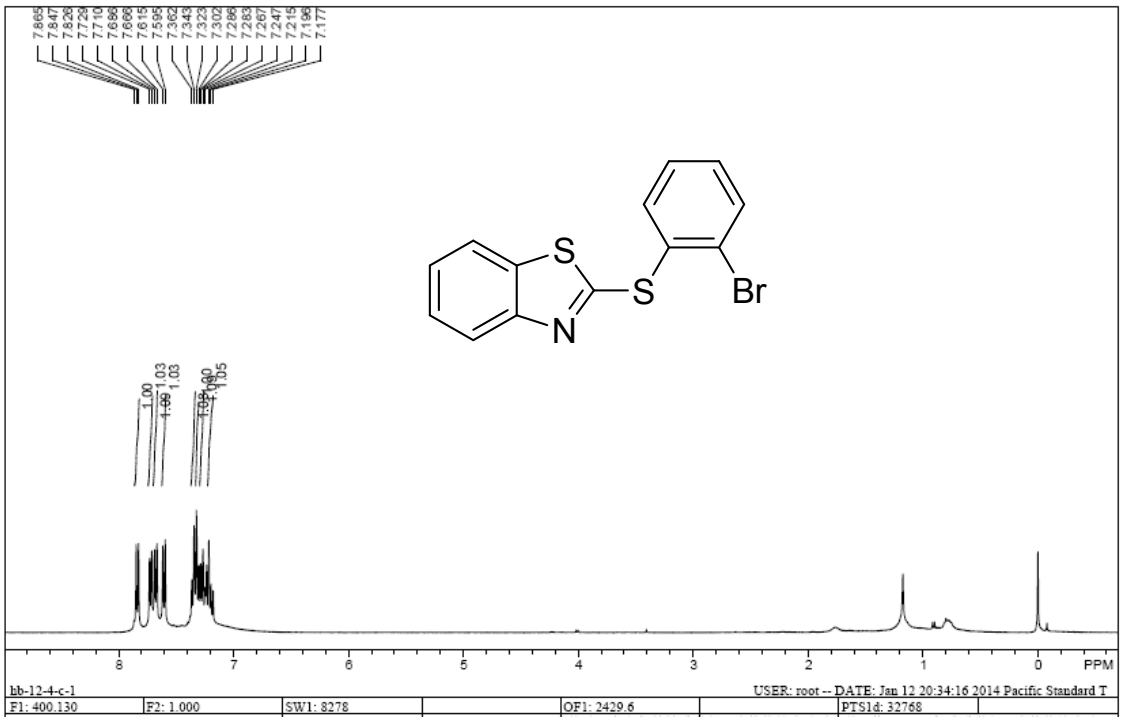


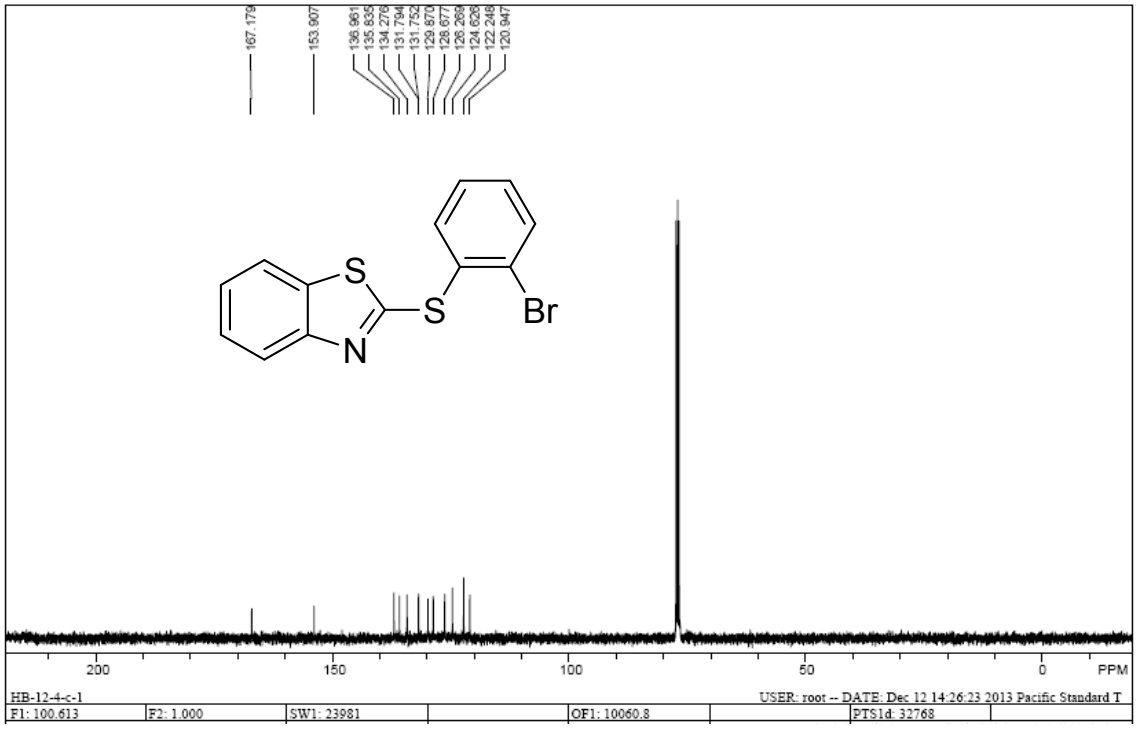
^{1}H and ^{13}C NMR of **5d**



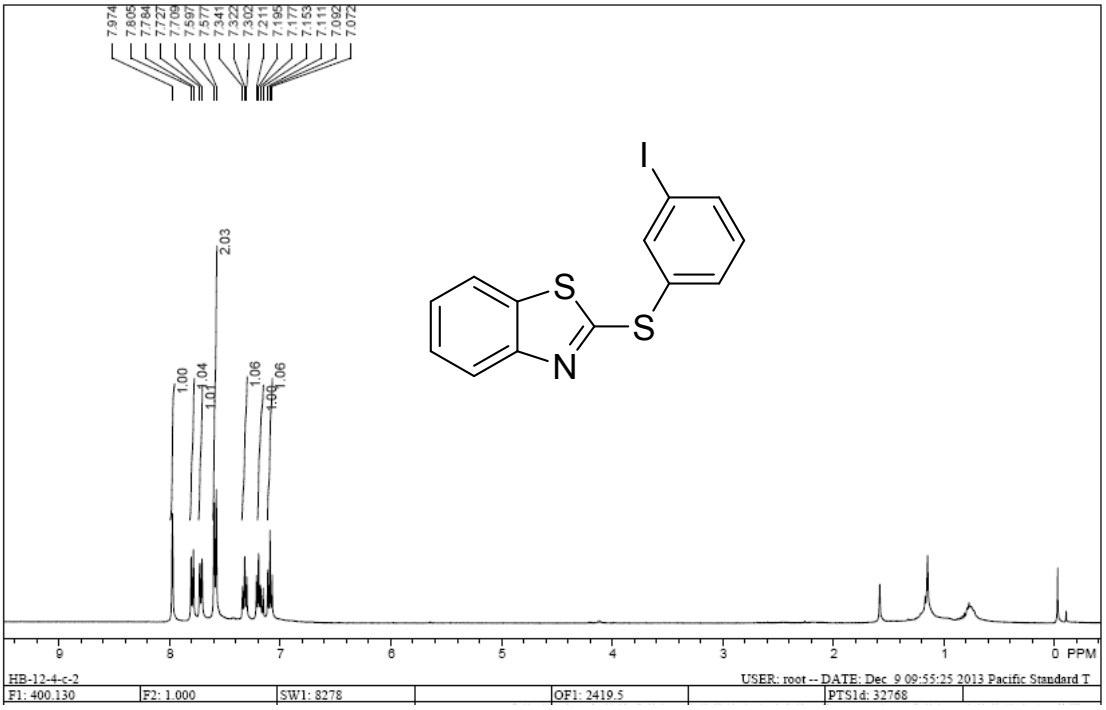


^{1}H and ^{13}C NMR of **5e**

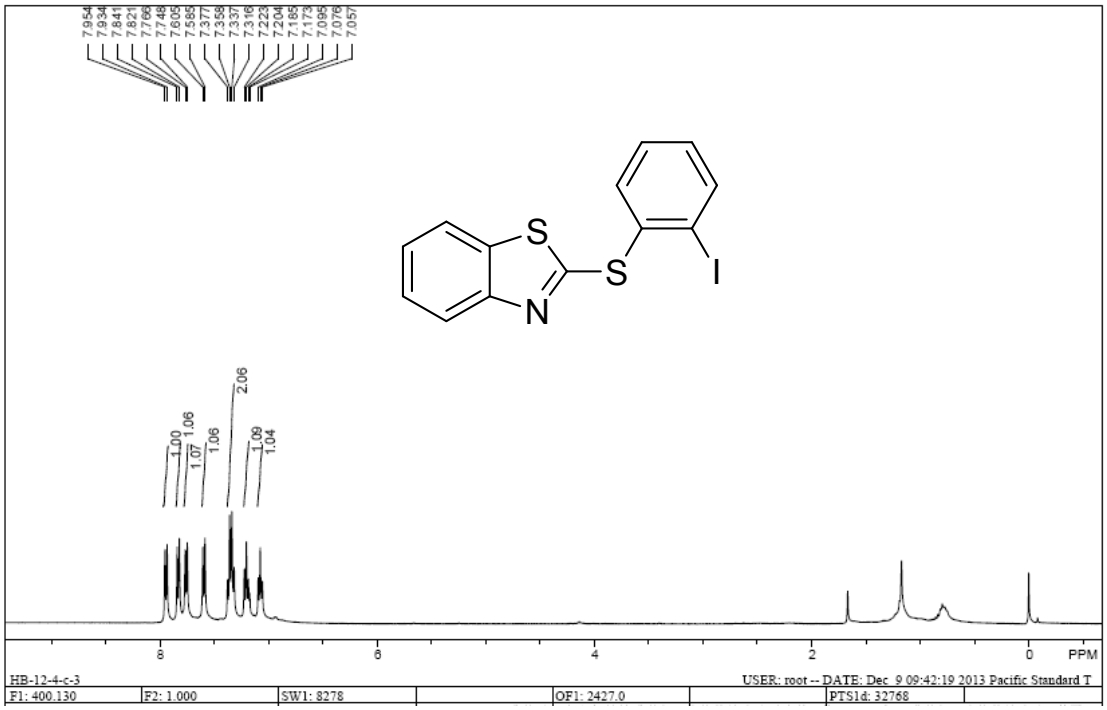


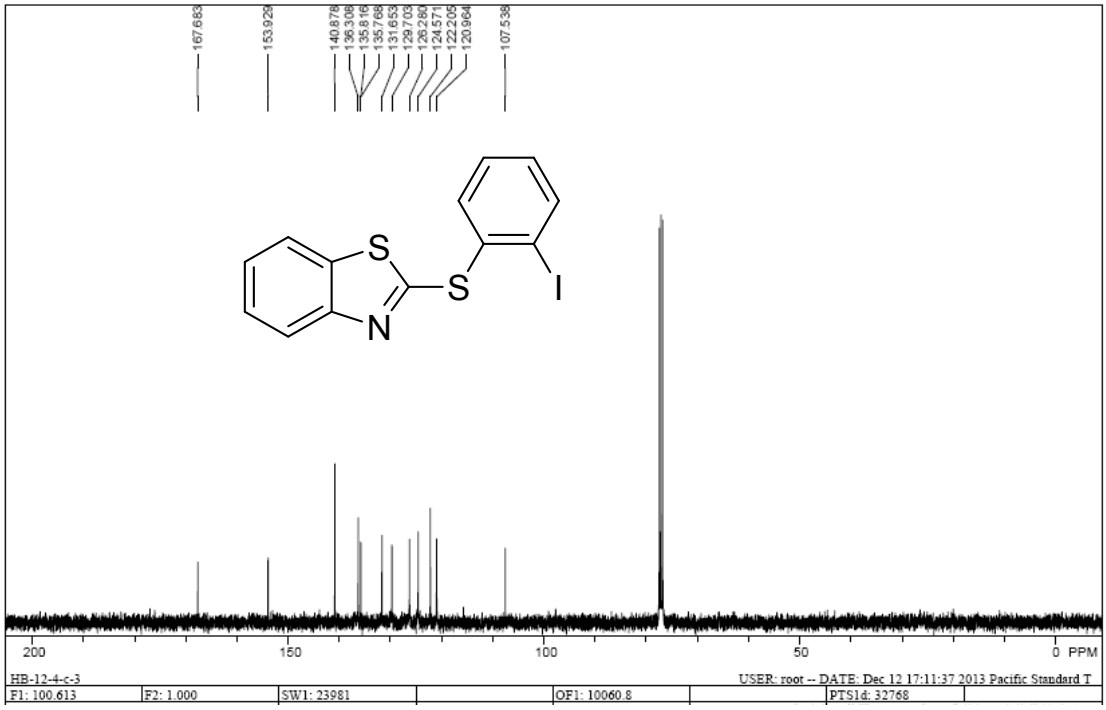


^{1}H and ^{13}C NMR of **5f**

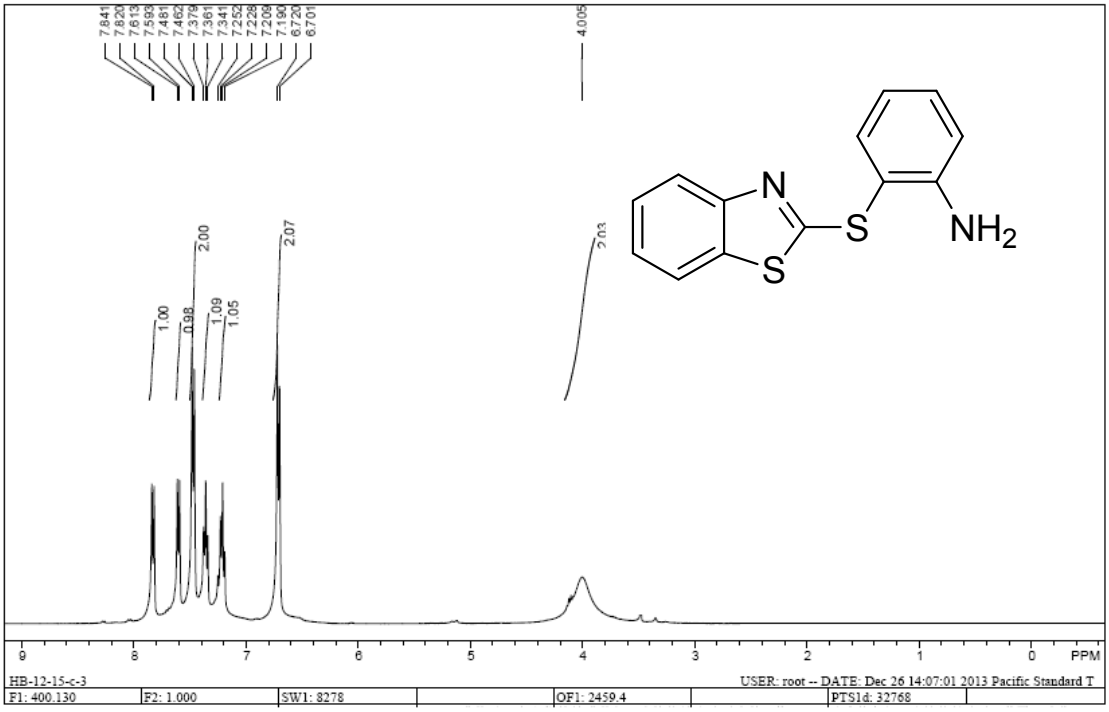


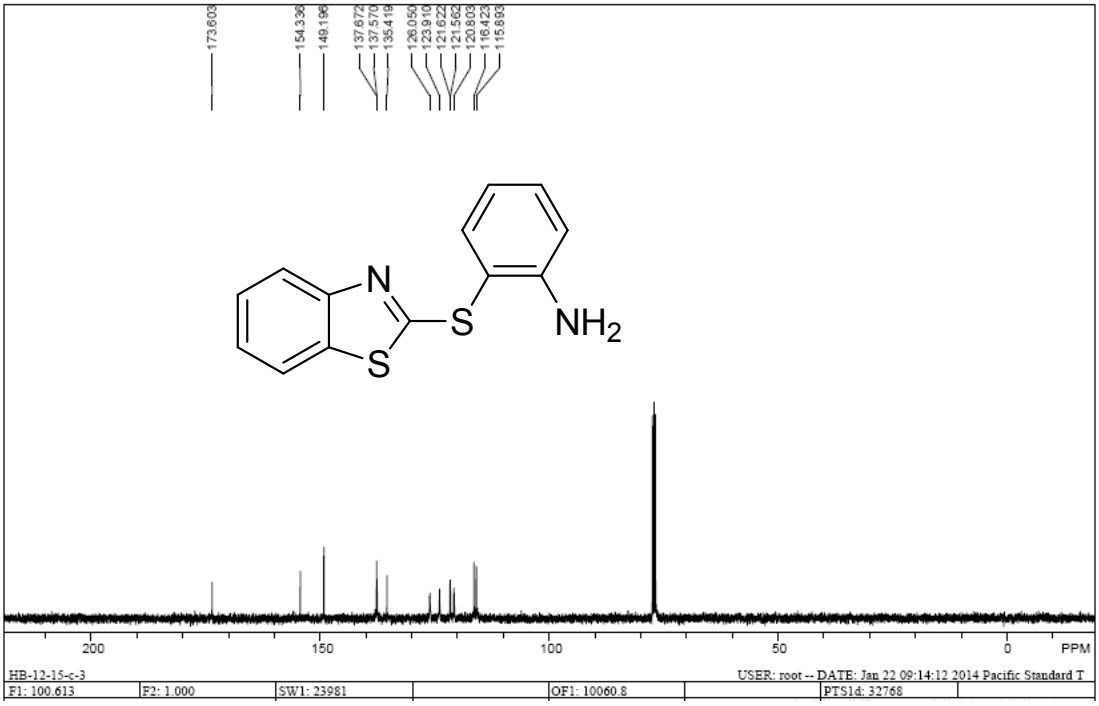
^{1}H and ^{13}C NMR of **5g**



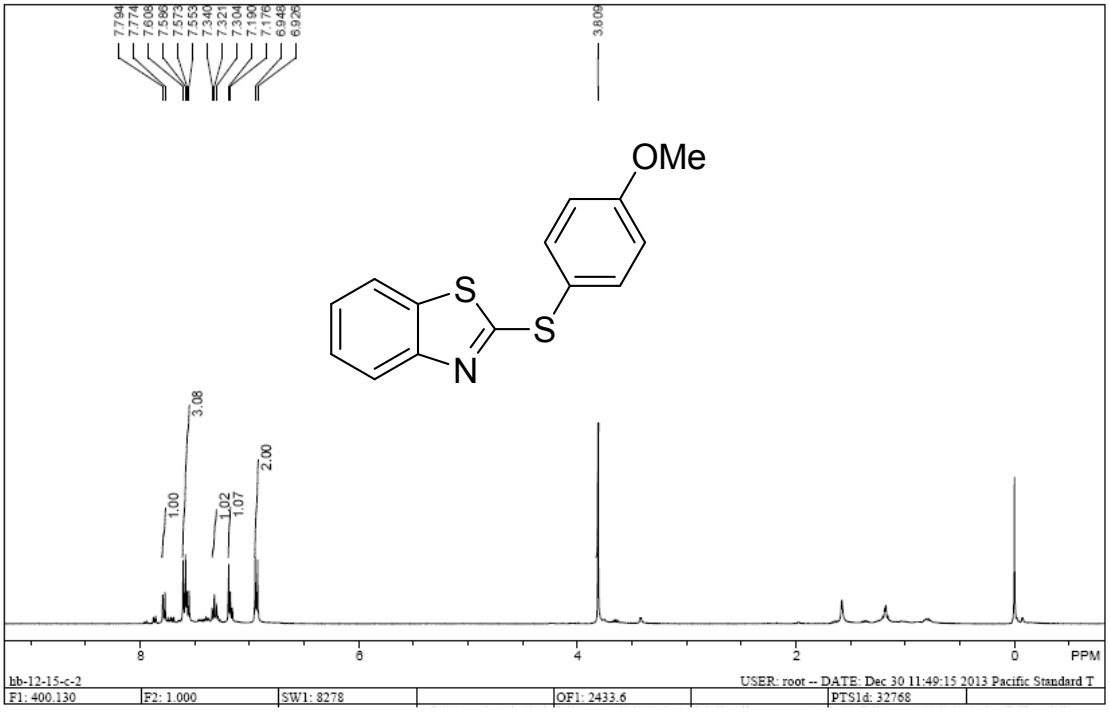


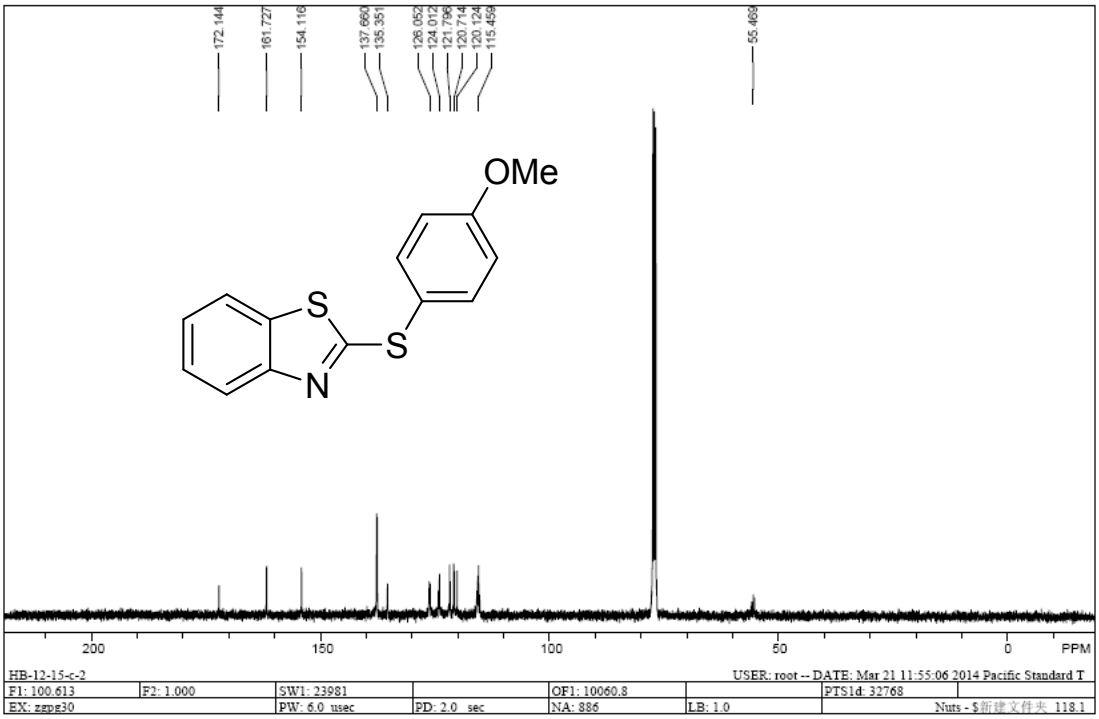
^{1}H and ^{13}C NMR of **5h**



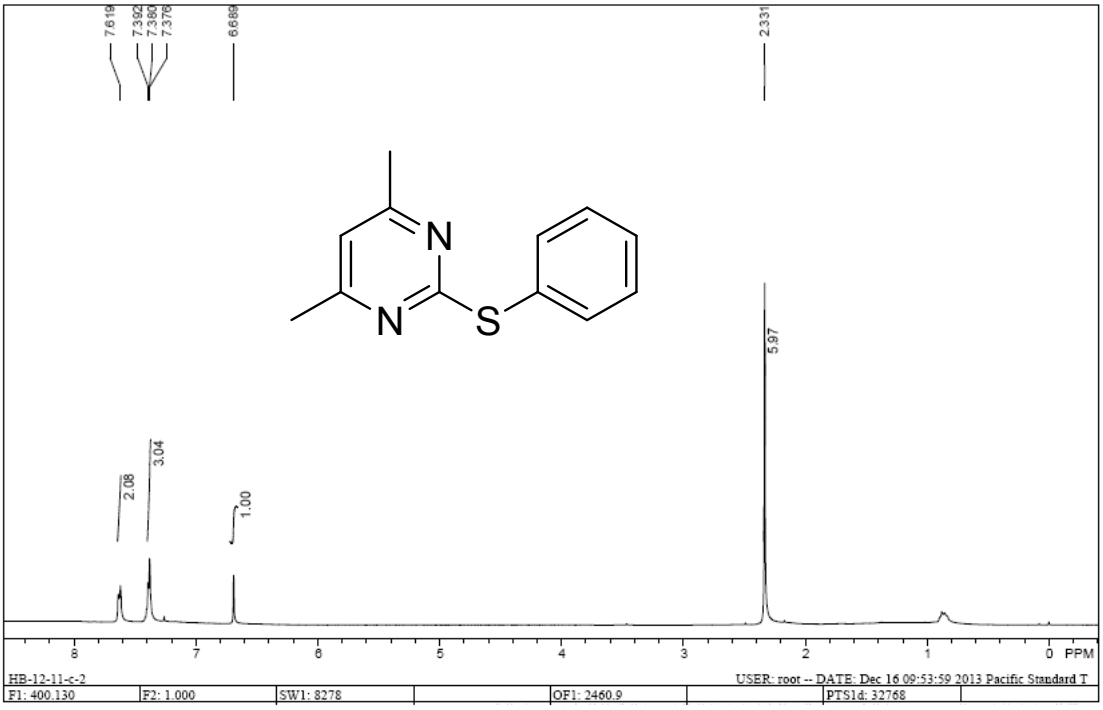


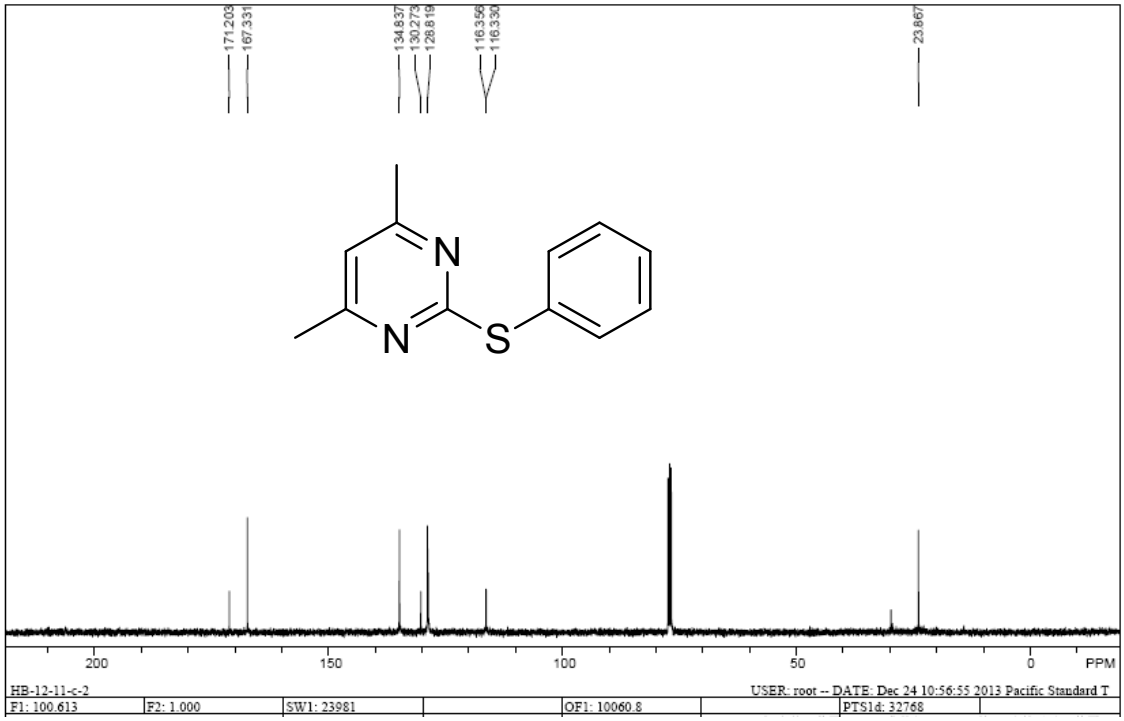
^{1}H and ^{13}C NMR of **5i**



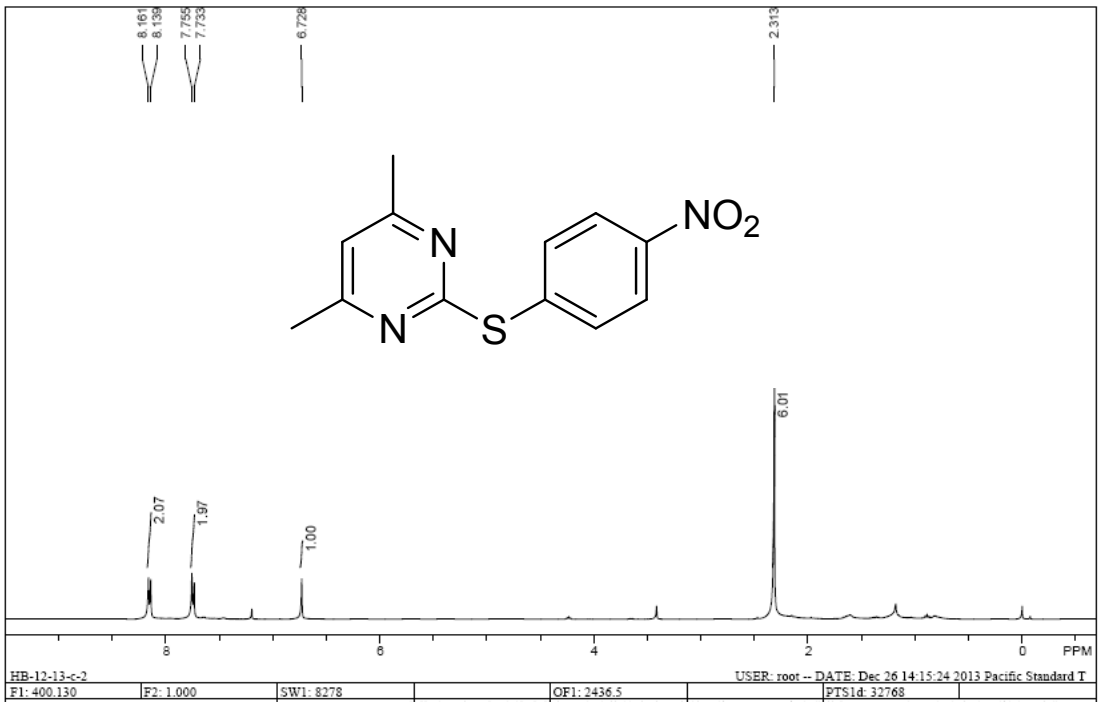


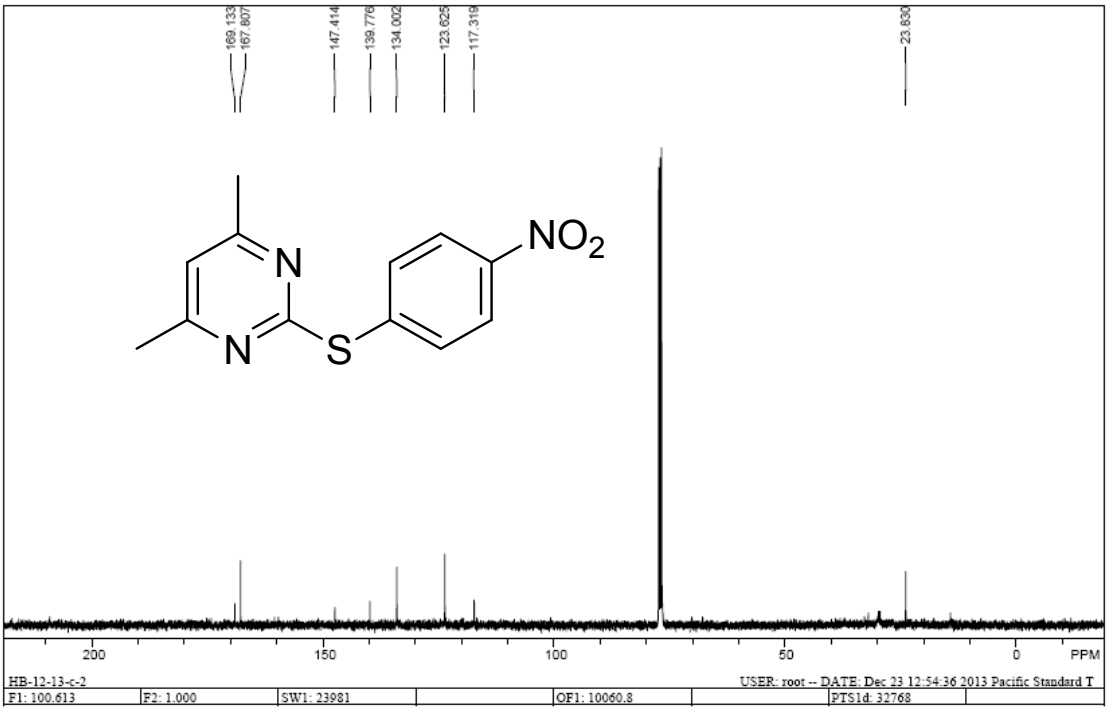
^{1}H and ^{13}C NMR of **5j**



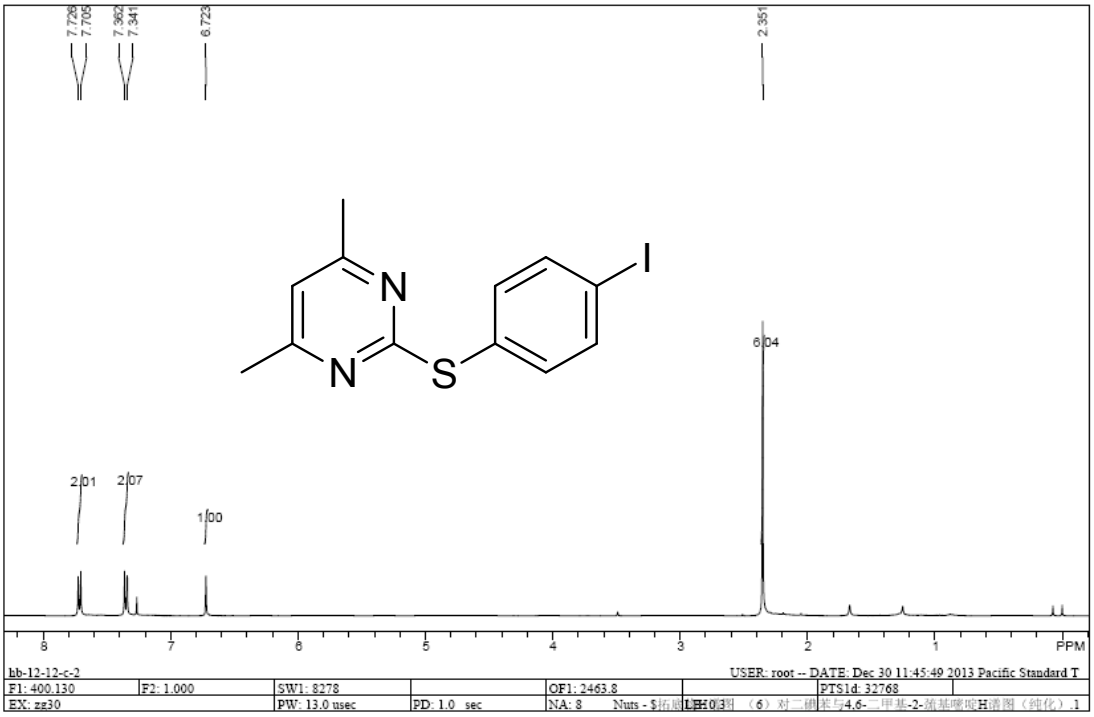


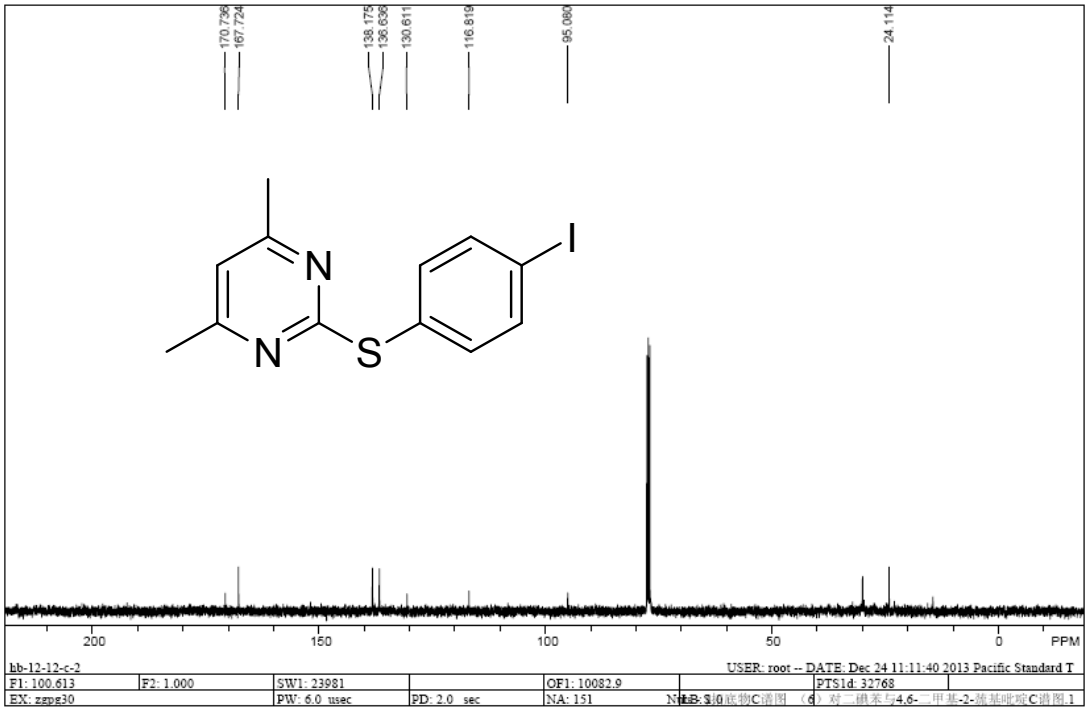
^{1}H and ^{13}C NMR of **5k**



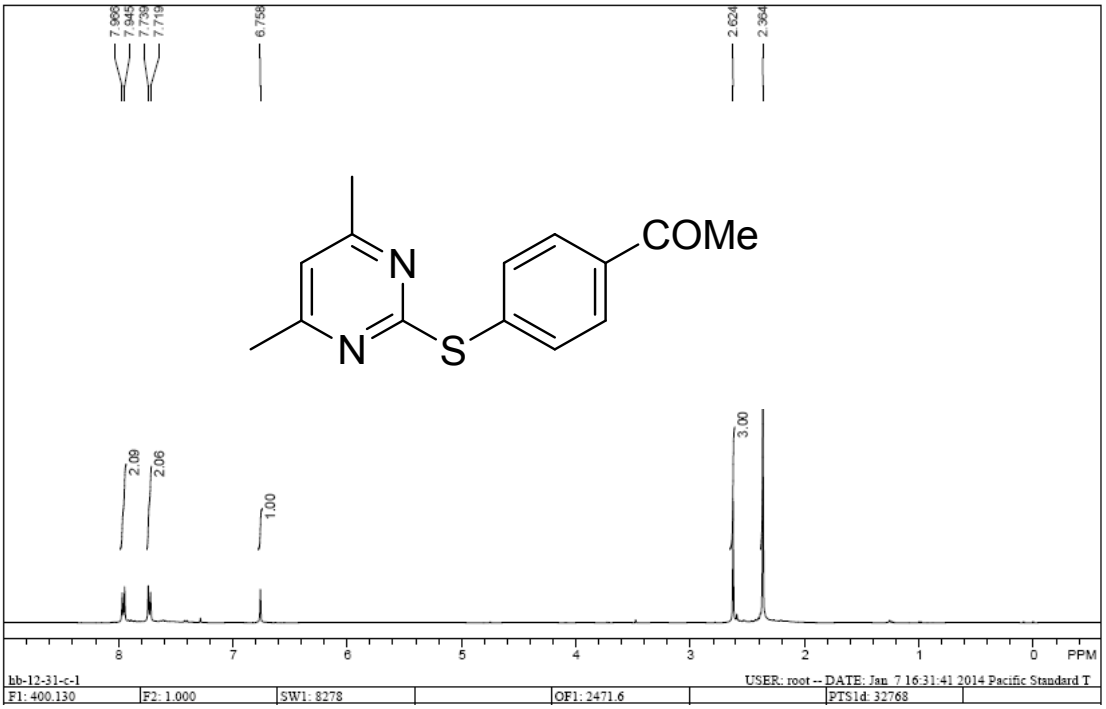


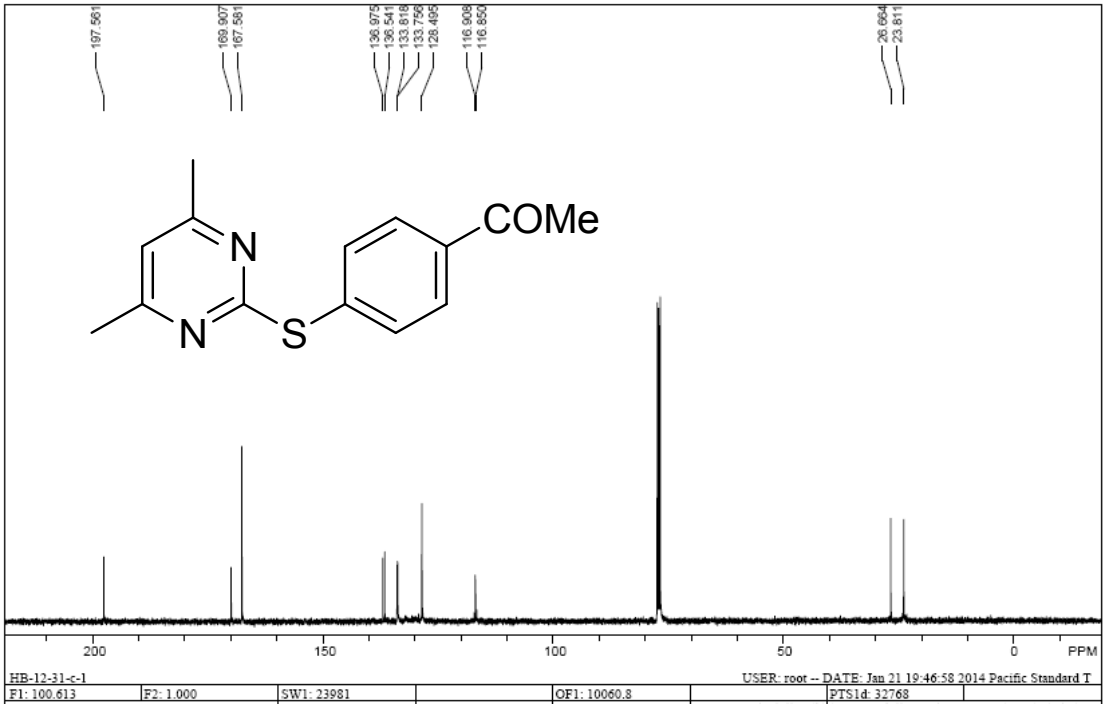
^{1}H and ^{13}C NMR of **5l**



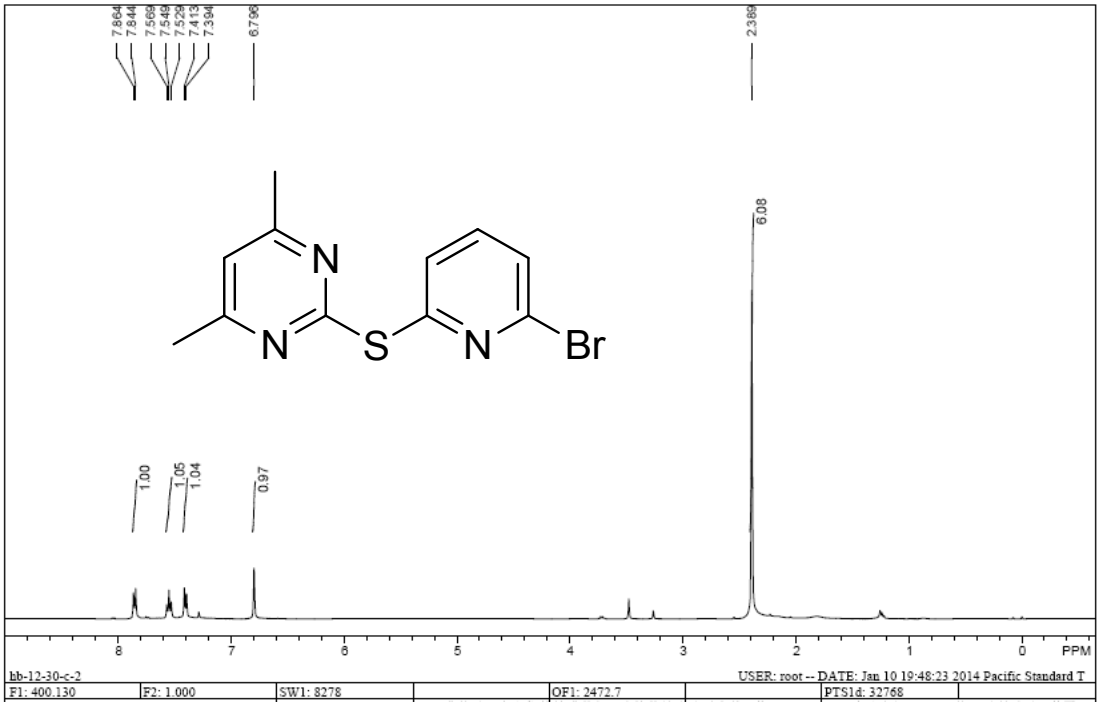


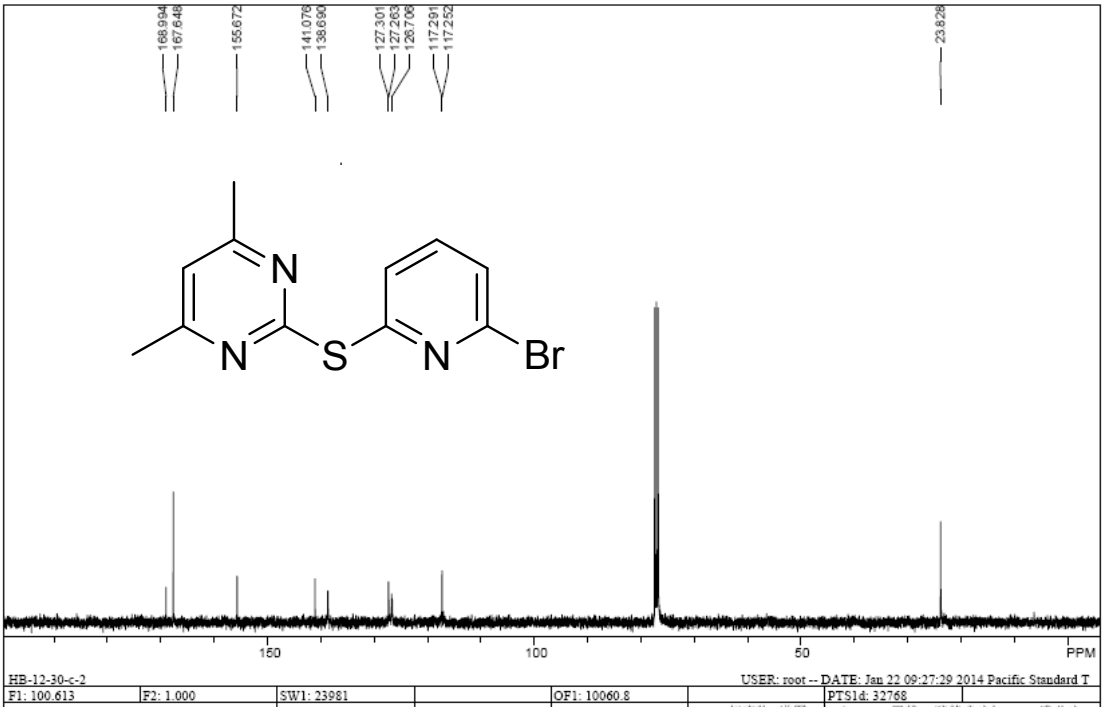
^{1}H and ^{13}C NMR of **5m**



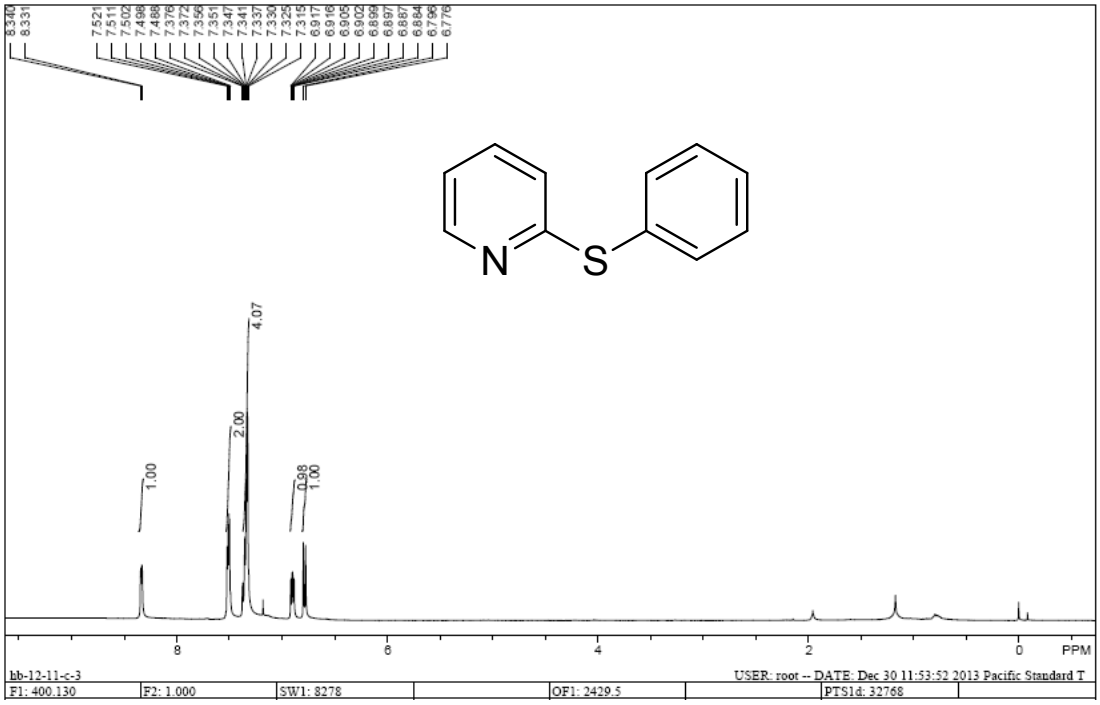


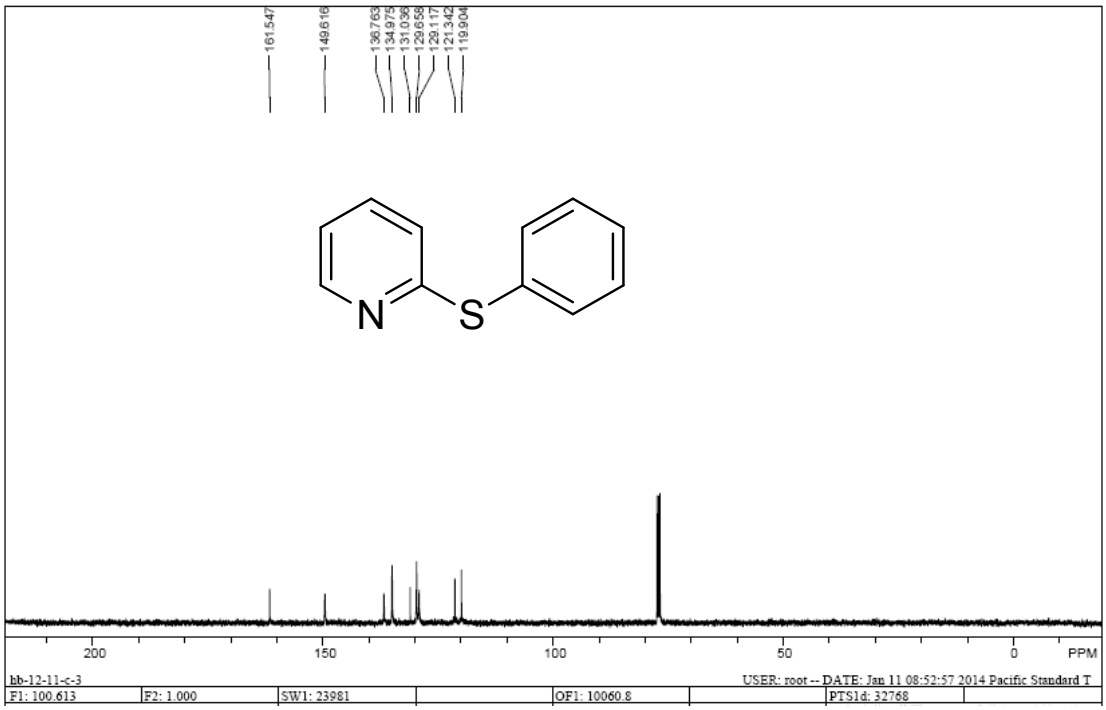
^{1}H and ^{13}C NMR of **5n**



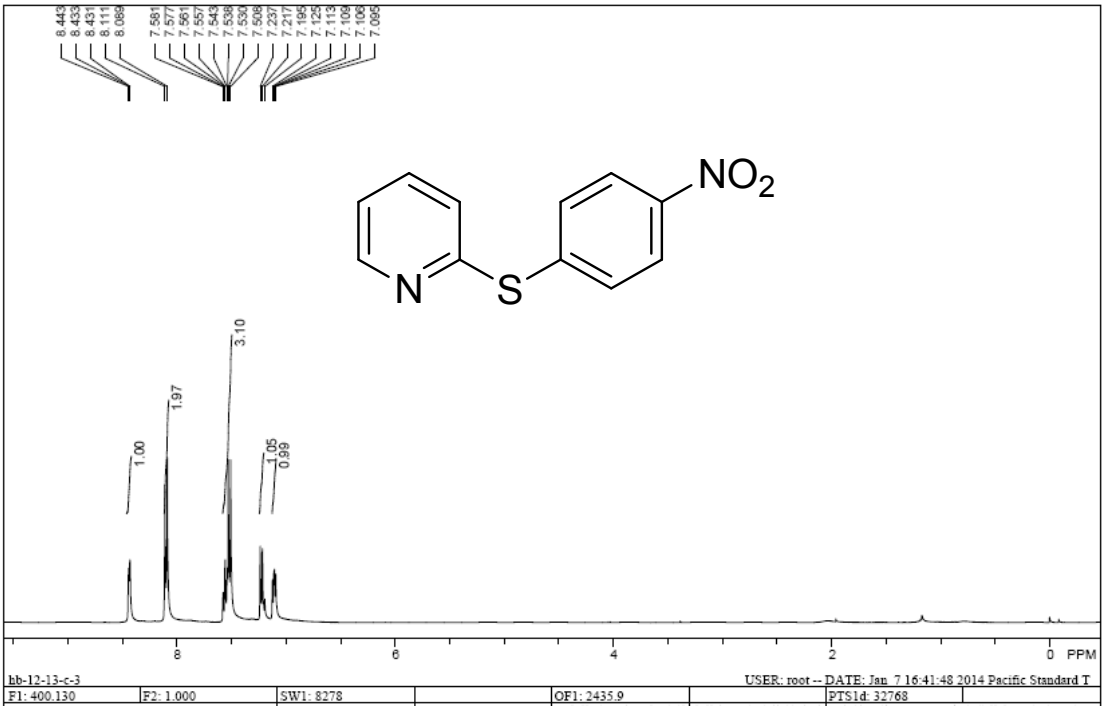


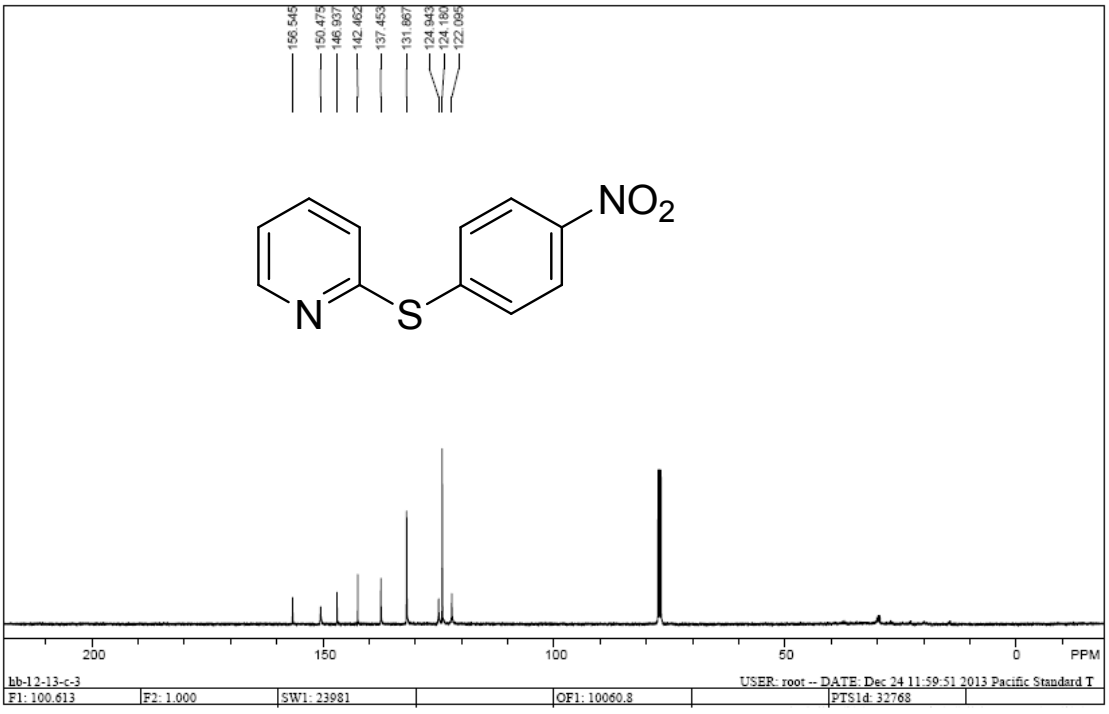
^{1}H and ^{13}C NMR of **5o**



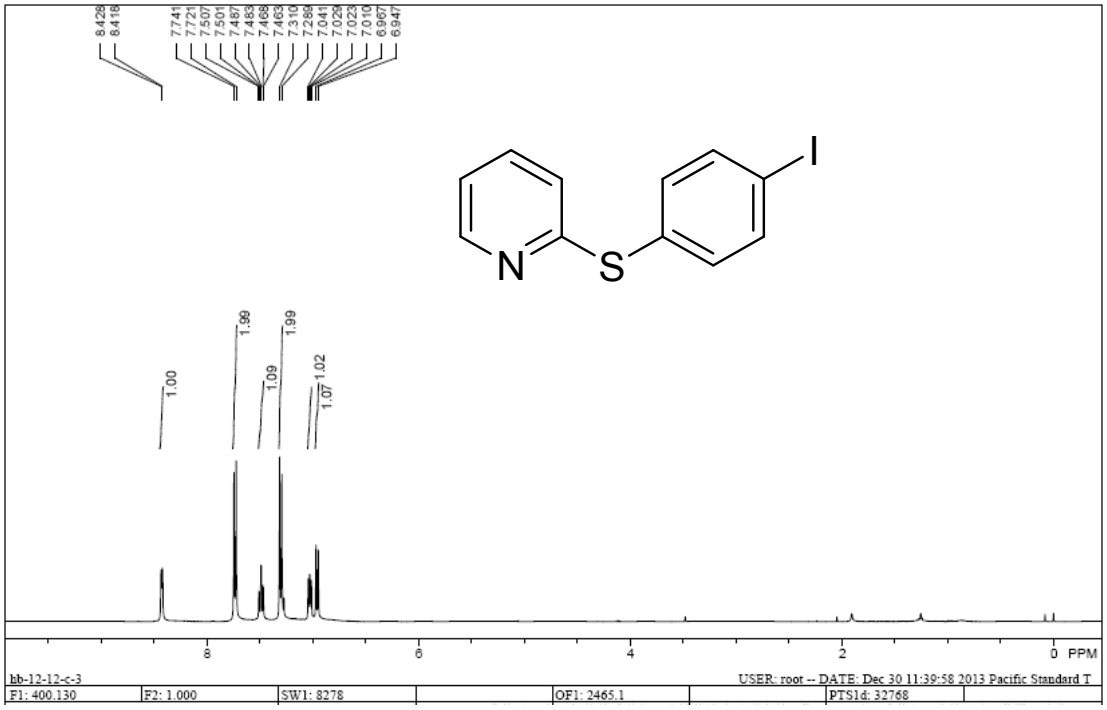


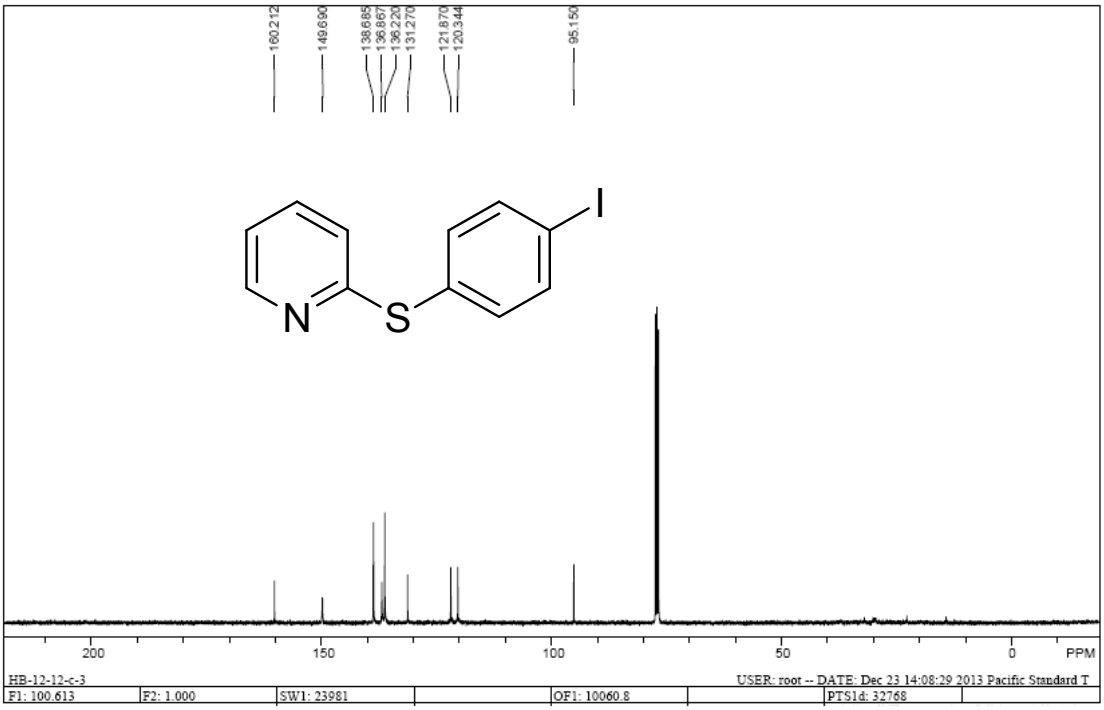
^{1}H and ^{13}C NMR of **5p**



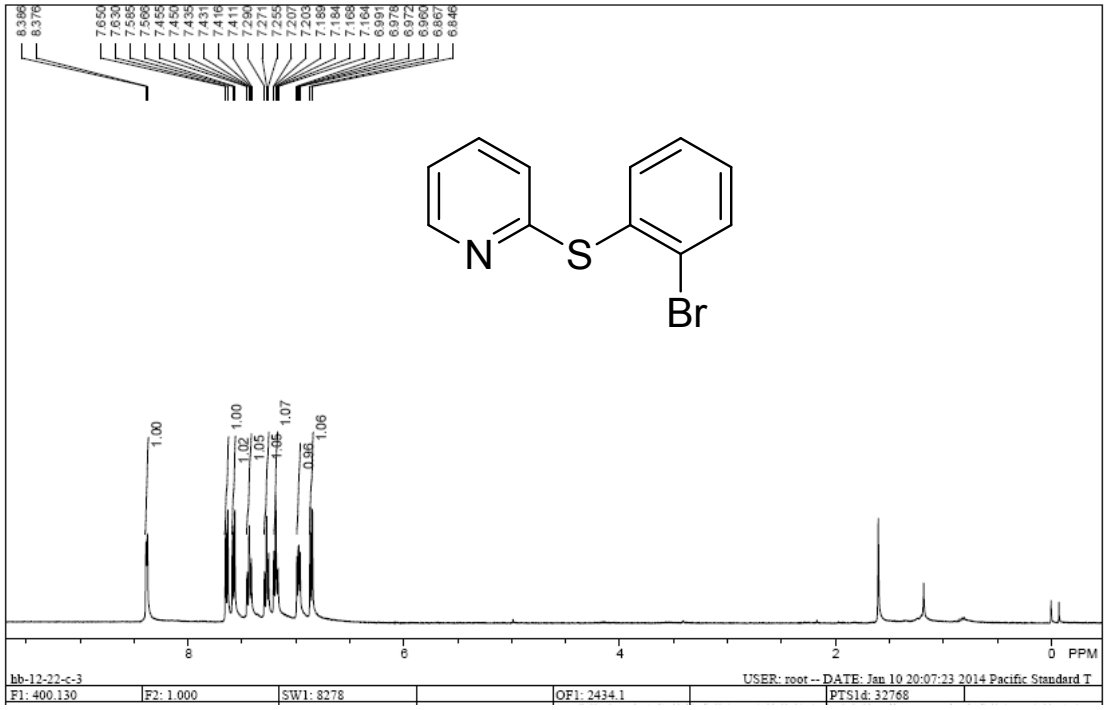


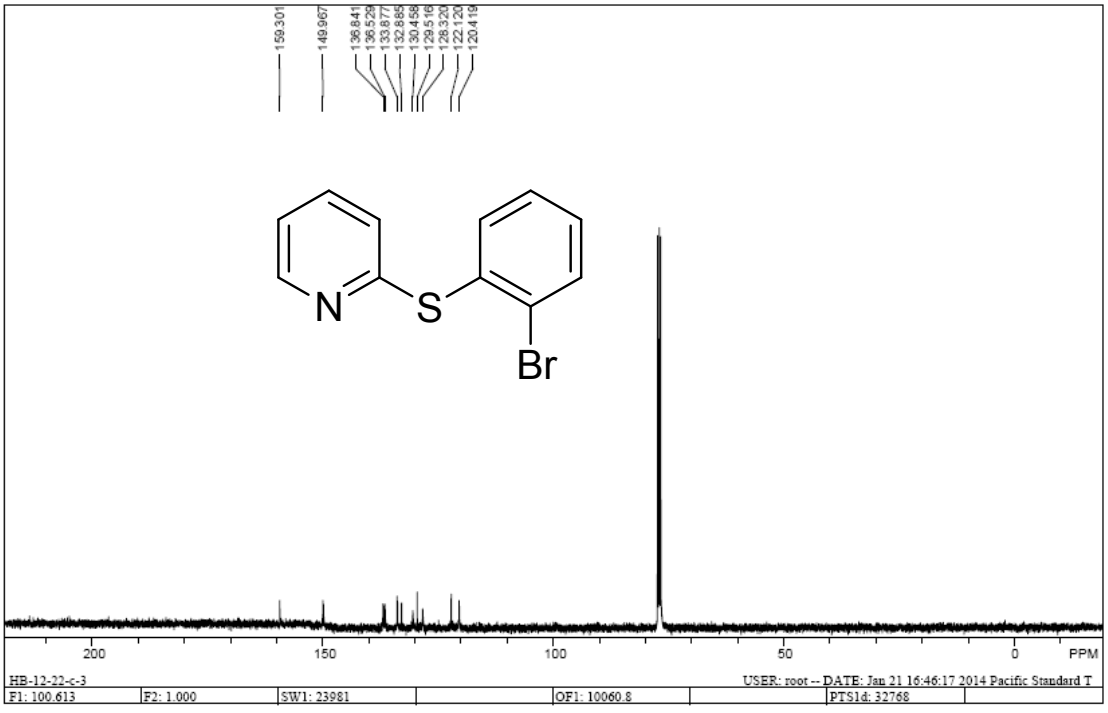
^{1}H and ^{13}C NMR of **5q**



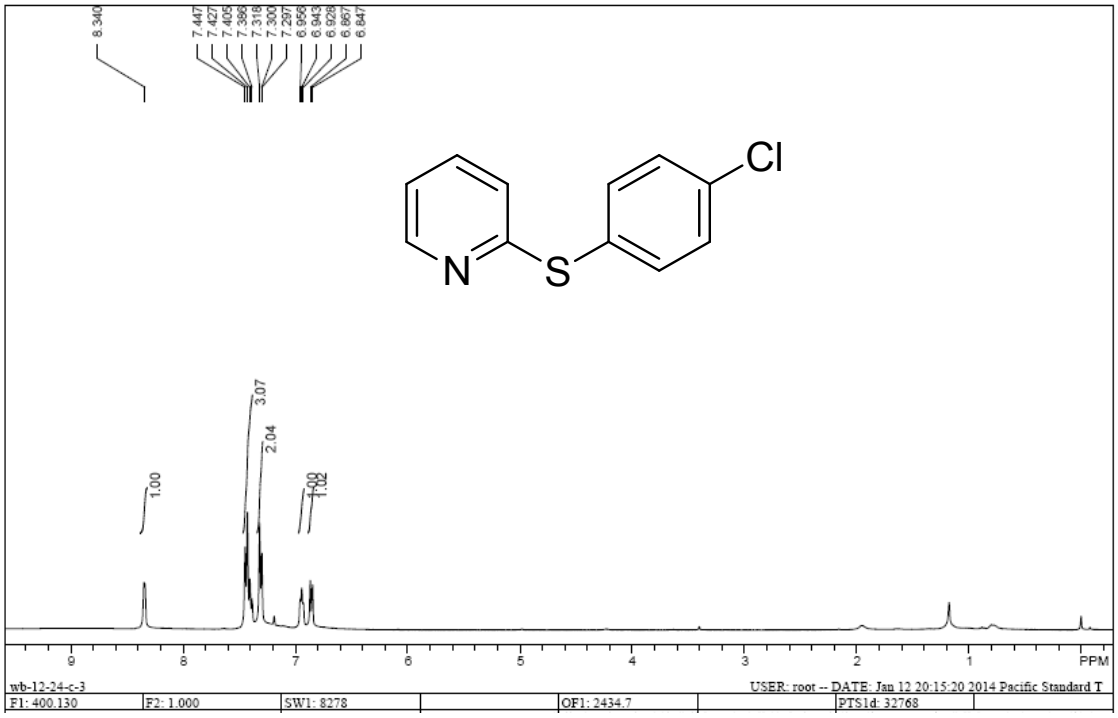


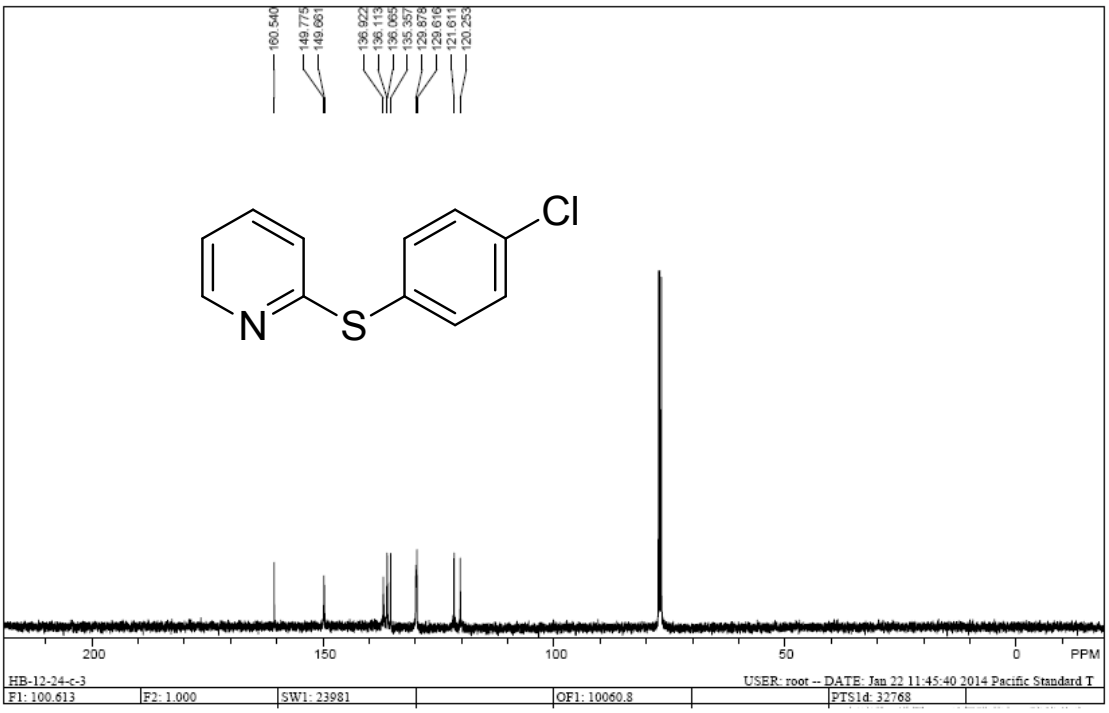
^{1}H and ^{13}C NMR of **5r**





^{1}H and ^{13}C NMR of **5s**





^{1}H and ^{13}C NMR of **5t**