Mechanoredox Radical Annulation for the Solvent-Free Synthesis of 2-Substituted Benzothiophenes

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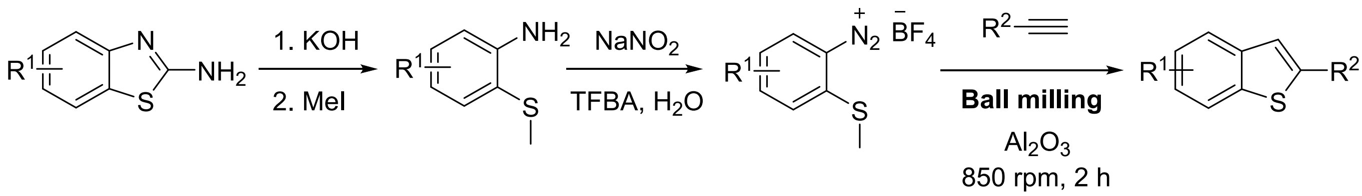
General methods

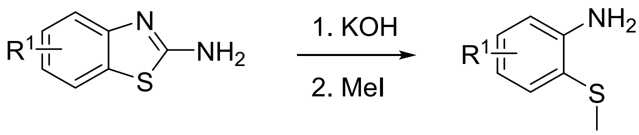
Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F_{254} glass plates precoated with a 0.2 mm thickness of silica gel. The TLC plates were visualized by shortwave (254 nm). Purification was performed by medium-pressure liquid chromatography (MPLC) using silica gel (Kieselgel 60, particle size 0.040–0.063 mm, Merck). The separations were carried out on a Combiflash NextGen 300 system equipped with a UV detector. Melting points: Barnstead / Elecrothermal 9300, measurements were performed in open glass capillaries without corrections. NMR spectra: Bruker AV 400 MHz (^{1}H–NMR: 400 MHz, ^{13}C–NMR: 100 MHz), the spectra were recorded in DMSO, $CDCl_3$ using TMS as internal standard and H_2O and are reported in ppm. ^{1}H NMR data are reported as: (s = singlet, d = doublet, dd = doublet of doublet, ddd = doublet of doublet of doublet, dt = doublet of triplet, t = triplet, td = triplet of doublet, q = quartet, m = multiplet; coupling constant(s) in Hz; integration, proton assignment). High resolution mass spectra (HRMS) was performed at JEOL JMS-700 (FAB). All solvents were purified using column filter solvent purification system before use unless otherwise indicated. Reagents were purchased and used without further purification.

Safety note: Aryl diazonium tetrafluoroborate salts should be handled with appropriate care. Although these materials are substantially more thermally stable than diazonium chloride or nitrate salts, they should not be heated or subjected to friction in the dry state in large quantities. All milling experiments described herein were performed on a small scale (≤2.1 mmol of diazonium salt), using a sealed ZrO_2 milling jar at ambient temperature with the standard cooling cycle (1 h milling, 1 h rest, 1 h milling). Appropriate personal protective equipment (safety glasses, laboratory coat, and gloves) was worn at all times. No exothermic events or decomposition were observed during any experiment.

Experimental sections

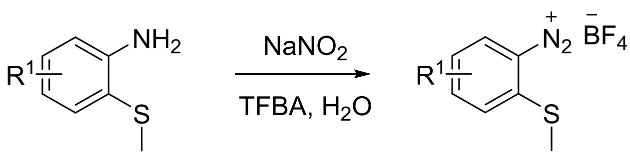


Method A. Synthesis of ortho-S-methyl aniline derivatives



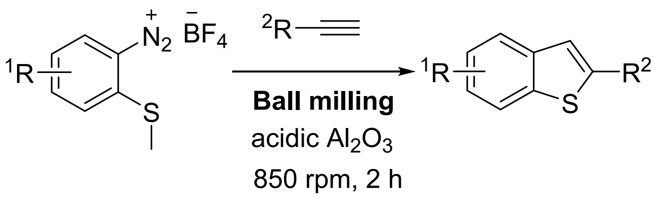
To a stirred solution of the thiazole starting material (3.0 g) in water (25 mL), potassium hydroxide (15.0 g, excess, approximately ≥2.0 equiv relative to the substrate) was added portionwise at 0 °C. After complete addition, the reaction mixture was heated to 110 °C and stirred for 20 h. After cooling to room temperature, methyl iodide (1.0 equiv relative to the starting material) was added dropwise, and the reaction mixture was stirred at room temperature for an additional 2 h. Reaction progress was monitored by TLC and confirmed to be complete. The reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with brine (3×), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by medium-pressure liquid chromatography (MPLC) using hexane/ethyl acetate (10:1) as the eluent to afford the desired compound.

Method B. Synthesis of diazonium salt derivatives (1aa-1ah)



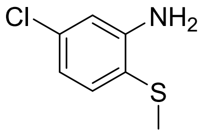
The ortho-S-methyl aniline derivative was dissolved in a precooled solvent mixture of tetrafluoroboric acid (48% min, w/w, aqueous solution) and water (1:3, v/v). The total solvent volume was adjusted proportionally (e.g., 6 mL of HBF_4 solution and 18 mL of water per 2.5 g of substrate). The reaction medium was maintained at 5–10 °C or below throughout the setup. The resulting suspension was stirred at 0 °C for 10 min. Separately, sodium nitrite (1.05 equiv relative to the starting material) was dissolved in the minimum amount of water, and the resulting solution was added dropwise to the reaction mixture at 0 °C with careful temperature control. After complete addition, the reaction mixture was stirred for an additional 30 min at the same temperature. Cold diethyl ether was then added directly to the reaction flask, and the resulting mixture was immediately filtered. The solid residue was washed with cold diethyl ether. Care was taken to ensure that the diethyl ether remained sufficiently cooled, as elevated temperatures may lead to partial dissolution of the product. The filtered solid was dried to afford the corresponding diazonium tetrafluoroborate salt.

Method C. Synthesis of benzothiophene derivatives (3aa-3ah)



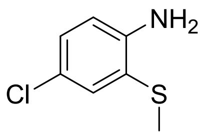
Five 10 mm diameter zirconium oxide balls were placed into a 20 mL zirconium oxide jar (50 mm diameter). Subsequently, methylthio arenediazonium tetrafluoroborate (1 equiv), aluminum oxide (acidic, 10 equiv), and alkyne (10 equiv) were added sequentially to the jar. The jar was then tightly sealed and mounted onto a Planetary Micro Mill. Milling was performed at 850 rpm for one hour, followed by a one-hour cooling period. After cooling, milling was continued for another hour. The resulting mixture was then transferred to a beaker using dichloromethane and ethyl acetate. This mixture was subsequently filtered through a celite bed. The obtained filtrate was then concentrated under reduced pressure. Finally, the crude compound was purified by flash column chromatography using a hexane/ethyl acetate (50:1) mixture as the eluent.

5-chloro-2-(methylthio)aniline



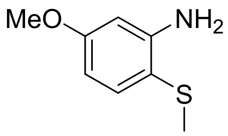
The target compounds were synthesized following the procedures described in Method A. 53% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

4-chloro-2-(methylthio)aniline



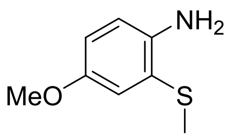
The target compounds were synthesized following the procedures described in Method A. 47% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

5-methoxy-2-(methylthio)aniline



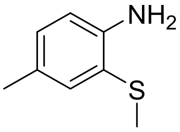
The target compounds were synthesized following the procedures described in Method A. 59% yield. The spectroscopic data are consistent with the reported values (lit.[2]).

4-methoxy-2-(methylthio)aniline



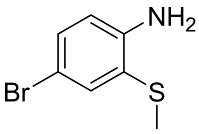
The target compounds were synthesized following the procedures described in Method A. 65% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

4-methyl-2-(methylthio)aniline



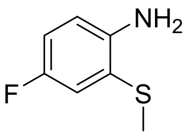
The target compounds were synthesized following the procedures described in Method A. 75% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

4-bromo-2-(methylthio)aniline



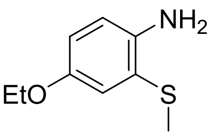
The target compounds were synthesized following the procedures described in Method A. 79% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

4-fluoro-2-(methylthio)aniline



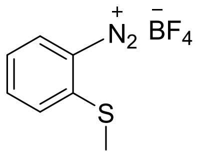
The target compounds were synthesized following the procedures described in Method A. 70% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

4-ethoxy-2-(methylthio)aniline



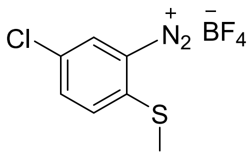
The target compounds were synthesized following the procedures described in Method A. 73% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

1-(2-(methylthio)phenyl)diazonium tetrafluoroborate (1a)



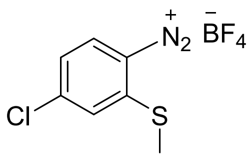
The target compounds were synthesized following the procedures described in Method B. 85% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

1-(5-chloro-2-(methylthio)phenyl)diazonium tetrafluoroborate (1aa)



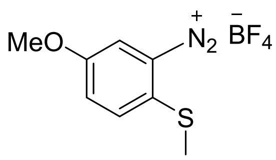
The target compounds were synthesized following the procedures described in Method B. 86% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

1-(4-chloro-2-(methylthio)phenyl)diazonium tetrafluoroborate (1ab)



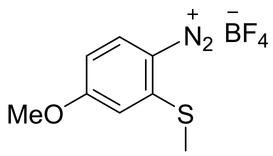
The target compounds were synthesized following the procedures described in Method B. 83% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

1-(5-methoxy-2-(methylthio)phenyl)diazonium tetrafluoroborate (1ac)



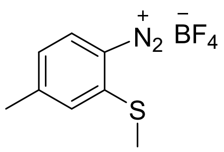
The target compounds were synthesized following the procedures described in Method B. 89% yield. This compound has been previously reported and is associated with a registered CAS number (CAS No. 101219-43-6); however, its ^{1}H and ^{13}C NMR spectroscopic data have not been reported. The NMR data are therefore provided below. ^{1}H NMR (400 MHz, DMSO) : δ 8.32 (m, 1H), 7.97 (m, 1H), 7.82 (m, 1H), 3.89 (s, 3H), 2.76 (s, 3H)., ^{13}C NMR (100 MHz, DMSO) : δ 157.8, 137.7, 132.6, 129.0, 115.6, 115.1, 56.9, 17.2.

1-(4-methoxy-2-(methylthio)phenyl)diazonium tetrafluoroborate (1ad)



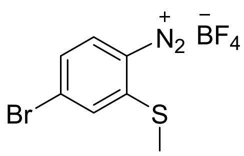
The target compounds were synthesized following the procedures described in Method B. 80% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

1-(4-methyl-2-(methylthio)phenyl)diazonium tetrafluoroborate (1ae)



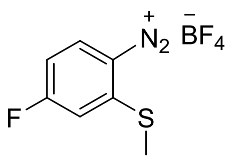
The target compounds were synthesized following the procedures described in Method B. 85% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

1-(4-bromo-2-(methylthio)phenyl)diazonium tetrafluoroborate (1af)



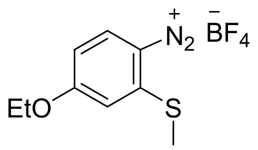
The target compounds were synthesized following the procedures described in Method B. 88% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

1-(4-fluoro-2-(methylthio)phenyl)diazonium tetrafluoroborate (1ag)



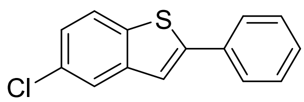
The target compounds were synthesized following the procedures described in Method B. 83% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

1-(4-ethoxy-2-(methylthio)phenyl)diazonium tetrafluoroborate (1ah)



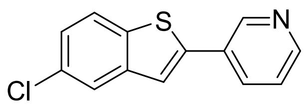
The target compounds were synthesized following the procedures described in Method B. 82% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

5-chloro-2-phenylbenzo[b]thiophene (3aa)



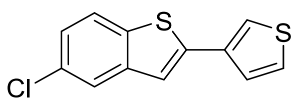
The target compounds were synthesized following the procedures described in Method C. 33% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

3-(5-chlorobenzo[b]thiophen-2-yl)pyridine (3ba)



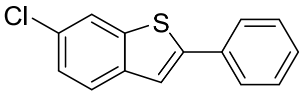
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (51% yield).: mp 128–129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.96 (d, J = 2.4 Hz, 1H), 8.59 (dd, J = 4.8, 1.6 Hz, 1H), 7.94 (ddd, J = 8.0, 2.4, 1.6 Hz, 1H), 7.77 (d, J = 2.0 Hz, 1H), 7.75 (d, J = 8.6 Hz, 1H), 7.50 (s, 1H), 7.36 (dd, J = 7.5, 4.8 Hz, 1H), 7.30 (dd, J = 8.6, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 149.7, 147.6, 142.5, 141.6, 137.9, 133.7, 131.2, 130.0, 125.4, 123.9, 123.5, 123.4, 120.0.; HRMS (FAB$^+$) m/z [M + H]$^+$ calcd for $C_{13}H_9ClNS$ 246.0144, found 246.0148

5-chloro-2-(thiophen-3-yl)benzo[b]thiophene (3ca)



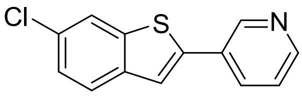
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (42% yield).; mp 181–184 °C.; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.73 – 7.71 (m, 2H), 7.55 (t, J = 2.2 Hz, 1H), 7.43 (s, 1H), 7.42 (s, 1H), 7.35 (s, 1H), 7.29 (dd, J = 8.5, 2.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 141.8, 141.1, 137.2, 135.4, 130.9, 126.9, 126.2, 124.8, 123.3, 123.0, 122.0, 118.7.; HRMS (FAB$^+$) m/z [M + H]$^+$ calcd for $C_{12}H_8ClS_2$ 250.9756; found 250.9750

6-chloro-2-phenylbenzo[b]thiophene (3ab)



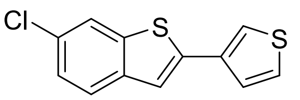
The target compounds were synthesized following the procedures described in Method C. 35% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

3-(6-chlorobenzo[b]thiophen-2-yl)pyridine (3bb)



The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light purple solid (25% yield).; mp 136–139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.96 (d, J = 2.5 Hz, 1H), 8.59 (dd, J = 4.8, 1.6 Hz, 1H), 7.93 (ddd, J = 8.0, 2.4, 1.6 Hz, 1H), 7.82 (d, J = 2.5 Hz, 1H), 7.71 (d, J = 8.5 Hz, 1H), 7.55 (s, 1H), 7.38 – 7.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 149.5, 147.5, 141.0, 140.8, 138.9, 133.7, 131.1, 130.1, 125.8, 124.7, 123.9, 122.1, 120.3.; HRMS (FAB$^+$) m/z [M + H]$^+$ calcd for for $C_{13}H_9ClNS$ 246.0144; found 246.0140

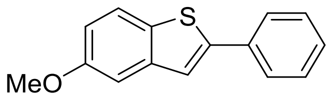
6-chloro-2-(thiophen-3-yl)benzo[b]thiophene (3cb)



The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (39% yield).: mp 207–208 °C,; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.76 (s, 1H), 7.63 (d, J = 8.5 Hz, 1H), 7.50 (s, 1H), 7.40 (s, 1H), 7.39 (s, 1H), 7.36 (s, 1H), 7.30 (dd, J = 8.4, 1.9

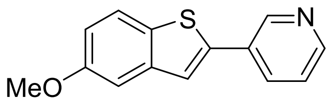
Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 140.2, 139.7, 139.1, 135.4, 130.3, 126.9, 126.1, 125.5, 124.3, 121.9, 121.7, 119.0.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{12}H_8ClS_2$ 250.9756; found 250.9738

5-methoxy-2-phenylbenzo[b]thiophene (3ac)



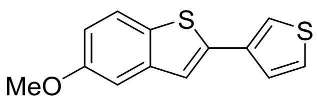
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (25% yield).; mp 126–128 °C; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.71 – 7.66 (m, 3H), 7.46 (s, 1H), 7.43 – 7.39 (m, 2H), 7.87 – 7.79 (m, 2H), 7.35 – 7.31 (m, 1H), 7.23 (d, J = 2.5 Hz, 1H), 6.96 (dd, J = 8.8, 2.6 Hz, 1H), 3.87 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.8, 145.6, 141.8, 134.5, 132.1, 129.1, 128.4, 126.5, 123.1, 119.4, 105.8, 55.7.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{15}H_{13}OS$ 241.0687; found 241.0689

3-(5-methoxybenzo[b]thiophen-2-yl)pyridine (3bc)



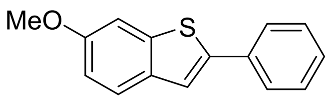
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (39% yield).; mp 128–129 °C; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.97 (d, J = 1.6 Hz, 1H), 8.56 (dd, J = 4.8, 1.6 Hz, 1H), 7.93 (ddd, J = 7.9, 2.4, 1.6 Hz, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.34 (ddd, J = 8.0, 4.8, 0.9 Hz, 1H), 7.25 (d, J = 2.4 Hz, 1H), 7.00 (dd, J = 8.8, 2.5 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.0, 149.3, 147.5, 141.6, 141.6, 133.6, 132.3, 130.6, 123.8, 123.2, 120.7, 115.3, 106.0, 55.7.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for for $C_{14}H_{12}NOS$ 242.0640; found 242.0641

5-methoxy-2-(thiophen-3-yl)benzo[b]thiophene (3cc)



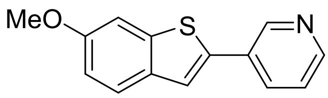
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (20% yield).; mp 148–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.65 (d, J = 8.9 Hz, 1H), 7.49 (dd, J = 2.8, 1.5 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.33 (s, 1H), 7.20 (d, J = 2.5 Hz, 1H), 6.95 (dd, J = 8.8, 2.5 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.8, 141.6, 140.3, 136.0, 131.5, 126.7, 126.2, 123.0, 121.3, 119.4, 114.5, 105.8, 55.7.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{13}H_{11}OS_2$ 247.0251; found 247.0248

6-methoxy-2-phenylbenzo[b]thiophene (3ad)



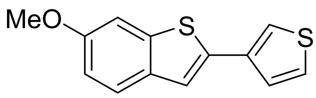
The target compounds were synthesized following the procedures described in Method C. 42% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

3-(6-methoxybenzo[b]thiophen-2-yl)pyridine (3bd)



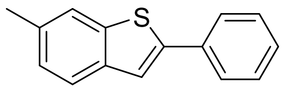
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (49% yield).; mp 118–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.94 (d, J = 2.4 Hz, 1H), 8.53 (dd, J = 4.8, 1.6 Hz, 1H), 7.90 (ddd, J = 8.0, 2.4, 1.6 Hz, 1H), 7.67 (d, J = 8.7 Hz, 1H), 7.50 (s, 1H), 7.34 – 7.30 (m, 2H), 7.00 (dd, J = 8.7, 2.4 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.0, 148.8, 147.3, 141.4, 137.6, 134.5, 133.3, 130.7, 124.6, 123.8, 120.4, 115.0, 104.9, 55.7.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{14}H_{12}NOS$ 242.0640; found 242.0630

6-methoxy-2-(thiophen-3-yl)benzo[b]thiophene (3cd)



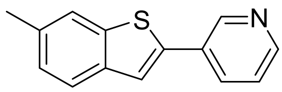
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (41% yield).; mp 159–161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.61 (d, J = 8.7 Hz, 1H), 7.42 (dd, J = 2.7, 1.6 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.31 (s, 1H), 7.27 (d, J = 2.4 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.6, 140.6, 136.6, 136.0, 134.6, 126.6, 126.1, 124.2, 120.6, 119.1, 114.6, 105.0, 55.7.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{13}H_{11}OS_2$ 247.0251; found 247.0254

6-methyl-2-phenylbenzo[b]thiophene (3ae)



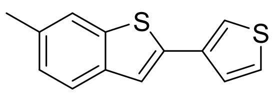
The target compounds were synthesized following the procedures described in Method C. 42% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

3-(6-methylbenzo[b]thiophen-2-yl)pyridine (3be)



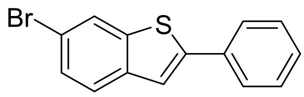
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (36% yield).; mp 172–175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.96 (d, J = 2.4 Hz, 1H), 8.55 (dd, J = 4.8, 1.6 Hz, 1H), 7.93 (ddd, J = 8.0, 2.4, 1.6 Hz, 1H), 7.68 (d, J = 8.2 Hz, 1H), 7.64 (s, 1H), 7.54 (s, 1H), 7.33 (dd, J = 7.9, 4.8 Hz, 1H), 7.19 (d, J = 8.1 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 149.0, 147.5, 140.2, 139.1, 138.3, 135.1, 133.5, 130.7, 126.7, 123.8, 123.6, 122.3, 120.7, 21.8.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{14}H_{12}NS$ 226.0690; found 226.0685

6-methyl-2-(thiophen-3-yl)benzo[b]thiophene (3ce)



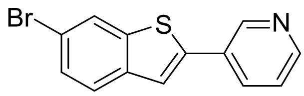
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (33% yield).; mp 196–199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.61 (d, J = 8.1 Hz, 1H), 7.58 (d, J = 0.8 Hz, 1H), 7.46(dd, J = 2.9, 1.4 Hz, 1H), 7.39 – 7.35 (m, 3H), 7.15 (dd, J = 8.2, 1.6 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 139.5, 138.4, 137.9, 136.0, 134.4, 126.6, 126.4, 126.2, 123.2, 122.2, 121.0, 119.3, 21.7.; HRMS (FAB^{+}) m/z [M + H]$^{+}$ calcd for $C_{13}H_{11}S_2$ 231.0302; found 231.0305

6-bromo-2-phenylbenzo[b]thiophene (3af)



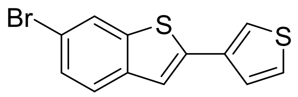
The target compounds were synthesized following the procedures described in Method C. 39% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

3-(6-bromobenzo[b]thiophen-2-yl)pyridine (3bf)



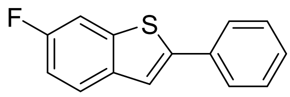
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light purple solid (20% yield).; mp 146–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.96 (d, J = 1.5 Hz, 1H), 8.59 (dd, J = 4.8, 1.6 Hz, 1H), 7.98 (d, J = 2.0 Hz, 1H), 7.94 (ddd, J = 8.0, 2.5, 1.6 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.55 (s, 1H), 7.48 (dd, J = 8.4, 1.8 Hz, 1H), 7.36 (ddd, J = 7.9, 4.8, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 149.6, 147.5, 141.2, 141.1, 139.2, 133.7, 130.0, 128.5, 125.02, 124.99, 123.9, 120.4, 118.9.; HRMS (FAB^{+}) m/z [M + H]$^{+}$ calcd for $C_{13}H_9BrNS$ 289.9639; found 289.9639

6-bromo-2-(thiophen-3-yl)benzo[b]thiophene (3cf)



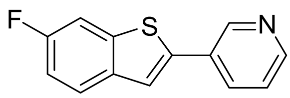
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (37% yield).; mp 194–196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.92 (d, J = 1.8 Hz, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.51 (t, J = 2.1 Hz, 1H), 7.44 (dd, J = 8.4, 1.8 Hz, 1H), 7.40 (s, 1H), 7.39 (s, 1H), 7.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 140.6, 139.7, 139.4, 135.3, 128.1, 127.0, 126.1, 124.8, 124.6, 121.8, 119.0, 118.1.; HRMS (FAB$^+$) m/z [M + H]$^+$ calcd for $C_{12}H_8BrS_2$ 294.9251; found 294.9228

6-fluoro-2-phenylbenzo[b]thiophene (3ag)



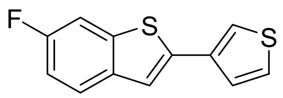
The target compounds were synthesized following the procedures described in Method C. 40% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

3-(6-fluorobenzo[b]thiophen-2-yl)pyridine (3bg)



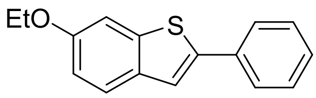
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light purple solid (27% yield). mp 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.95 (d, J = 1.5 Hz, 1H), 8.57 (dd, J = 4.8, 1.6 Hz, 1H), 7.92 (ddd, J = 8.0, 2.4, 1.6 Hz, 1H), 7.74 (dd, J = 8.8, 5.1 Hz, 1H), 7.55(s, 1H), 7.53 (dd, J = 8.8, 2.4 Hz, 1H), 7.35 (ddd, J = 7.9, 4.8, 0.9 Hz, 1H), 7.13 (dt, J = 8.8, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.9 (d, J = 244.1 Hz), 149.3, 147.5, 140.8 (d, J = 10.4 Hz), 140.1 (d, J = 3.8 Hz), 137.0 (d, J = 1.8 Hz), 133.6, 130.2, 125.0 (d, J = 9.1 Hz), 123.8, 120.3, 114.0 (d, J = 24.2 Hz), 108.7 (d, J = 25.4 Hz).; HRMS (FAB$^+$) m/z [M + H]$^+$ calcd for $C_{13}H_9FNS$ 230.0440; found 230.0424

6-fluoro-2-(thiophen-3-yl)benzo[b]thiophene (3cg)



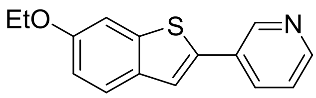
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (38% yield).; mp 189–193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66 (dd, J = 8.7, 5.1 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.39 (s, 1H), 7.38 (s, 1H), 7.35 (s, 1H), 7.08 (dd, J = 8.9, 2.4 Hz, 1H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.6 (d, J = 242.7 Hz), 140.1 (d, J = 10.3 Hz), 138.8 (d, J = 4.0 Hz), 137.1 (d, J = 1.7 Hz), 126.8, 126.1, 124.5 (d, J = 9.0 Hz), 121.4, 118.9, 113.6 (d, J = 23.9 Hz), 108.5 (d, J = 25.4 Hz).; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{12}H_8FS_2$ 235.0051; found 235.0047

6-ethoxy-2-phenylbenzo[b]thiophene (3ah)



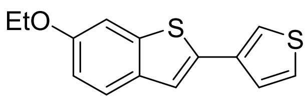
The target compounds were synthesized following the procedures described in Method C. 85% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

3-(6-ethoxybenzo[b]thiophen-2-yl)pyridine (3bh)



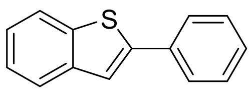
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (38% yield).; mp 103–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.94 (d, J = 1.5 Hz, 1H), 8.53 (dd, J = 4.8, 1.6 Hz, 1H), 7.91 (ddd, J = 8.0, 2.4, 1.6 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.50 (s, 1H), 7.33 (ddd, J = 8.0, 4.9, 0.9 Hz, 1H) 7.30 (d, J = 2.3 Hz, 1H), 7.00 (dd, J = 8.7, 2.3 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 1.46 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 157.3, 148.8, 147.3, 141.4, 137.6, 134.5, 133.3, 130.7, 124.6, 123.8, 120.5, 115.5, 105.7, 64.0, 15.0.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{15}H_{14}NOS$ 256.0796; found 256.0780

6-ethoxy-2-(thiophen-3-yl)benzo[b]thiophene (3ch)



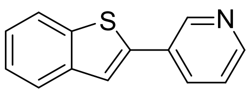
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (28% yield).; mp 134–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.60 (d, J = 8.7 Hz, 1H), 7.42 (dd, J = 2.6, 1.5 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.31 (s, 1H), 7.26 (d, J = 2.3 Hz, 1H), 6.96 (dd, J = 8.6, 2.3 Hz, 1H), 4.09 (q, J = 6.9 Hz, 2H), 1.45 (t, J = 7.0 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 156.9, 140.6, 136.5, 136.0, 134.5, 126.6, 126.1, 124.2, 120.6, 119.1, 115.0, 105.8, 64.0, 15.0.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{14}H_{13}OS_2$ 261.0408; found 261.0419

2-Phenylbenzo[b]thiophene (3a)



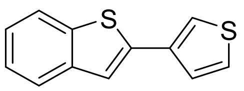
The target compounds were synthesized following the procedures described in Method C. 53% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

3-(benzo[b]thiophen-2-yl)pyridine (3b)



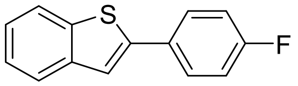
The target compounds were synthesized following the procedures described in Method C. The crude residue was purified by column chromatography to afford the desired compound as a light brown solid (48% yield).; mp 130–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.99 (d, J = 2.4 Hz, 1H), 8.58 (dd, J = 4.8, 1.6 Hz, 1H), 7.97 (td, J = 8.0, 2.4, 1.6 Hz, 1H), 7.87 – 7.79 (m, 2H), 7.60 (s, 1H), 7.37 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 149.3, 147.6, 140.5, 140.4, 139.8, 133.7, 130.5, 125.0, 124.9, 124.0, 123.8, 122.5, 120.9.; HRMS (FAB^+) m/z $[M + H]^+$ calcd for $C_{13}H_{10}NS$ 212.0534; found 212.0544

2-(Thiophen-3-yl)benzo[b]thiophene (3c)



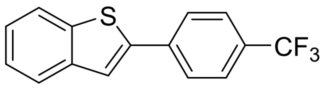
The target compounds were synthesized following the procedures described in Method C. 38% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

2-(4-Fluorophenyl)benzo[b]thiophene (3d):



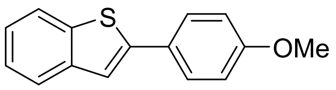
The target compounds were synthesized following the procedures described in Method C. 27% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

2-(4-(trifluoromethyl)phenyl)benzo[b]thiophene (3e)



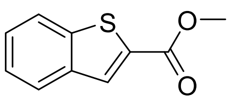
The target compounds were synthesized following the procedures described in Method C. 24% yield. The spectroscopic data are consistent with the reported values (lit.[4]).

2-(4-Methoxyphenyl)benzo[b]thiophene (3f)



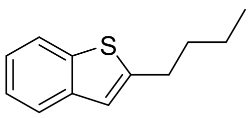
The target compounds were synthesized following the procedures described in Method C. 28% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

Methyl benzo[b]thiophene-2-carboxylate (3g)



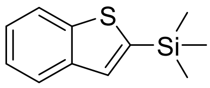
The target compounds were synthesized following the procedures described in Method C. 31% yield. The spectroscopic data are consistent with the reported values (lit.[1]).

2-butylbenzo[b]thiophene (3h)



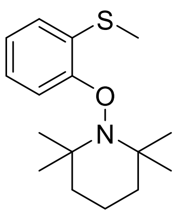
The target compounds were synthesized following the procedures described in Method C. Due to its volatility, the yield (13%) could not be reliably determined. The spectroscopic data are consistent with the reported values (lit.[1]).

benzo[b]thiophen-2-yltrimethylsilane (3i)



The target compounds were synthesized following the procedures described in Method C. Due to its volatility, the yield (8%) could not be reliably determined. The spectroscopic data are consistent with the reported values (lit.[1]).

2,2,6,6-Tetramethyl-1-[2-(methylthio)phenoxy]piperidine (4)

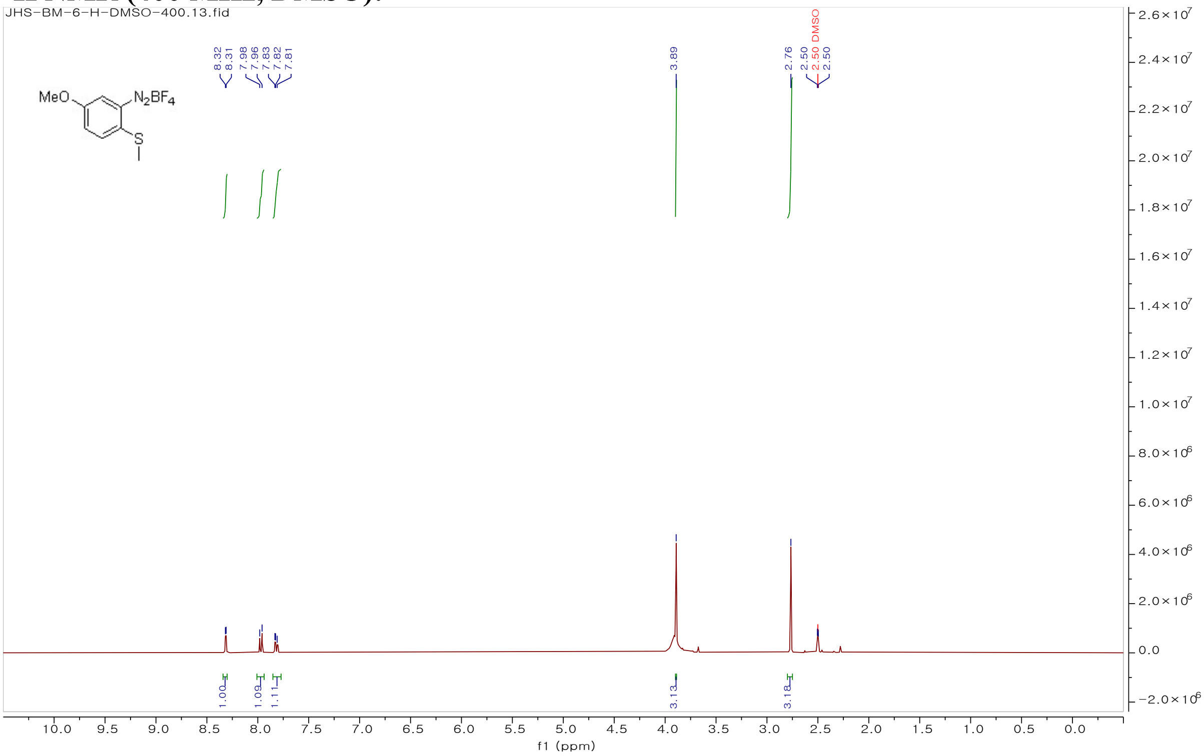


1-(2-(methylthio)phenyl)diazonium tetrafluoroborate (500 mg, 1.0 equiv), TEMPO (5.0 equiv), and phenylacetylene (5.0 equiv) were placed in a ZrO_2 milling jar together with five zirconium oxide balls (10 mm diameter). The reaction mixture was subjected to ball milling for 1 h, followed by a resting period of 1 h, and then milled again for an additional 1 h, giving a total milling time of 2 h. After completion of the reaction, the crude mixture was purified by column chromatography on silica gel. 80% yield. The spectroscopic data are consistent with the reported values (lit.[5]).

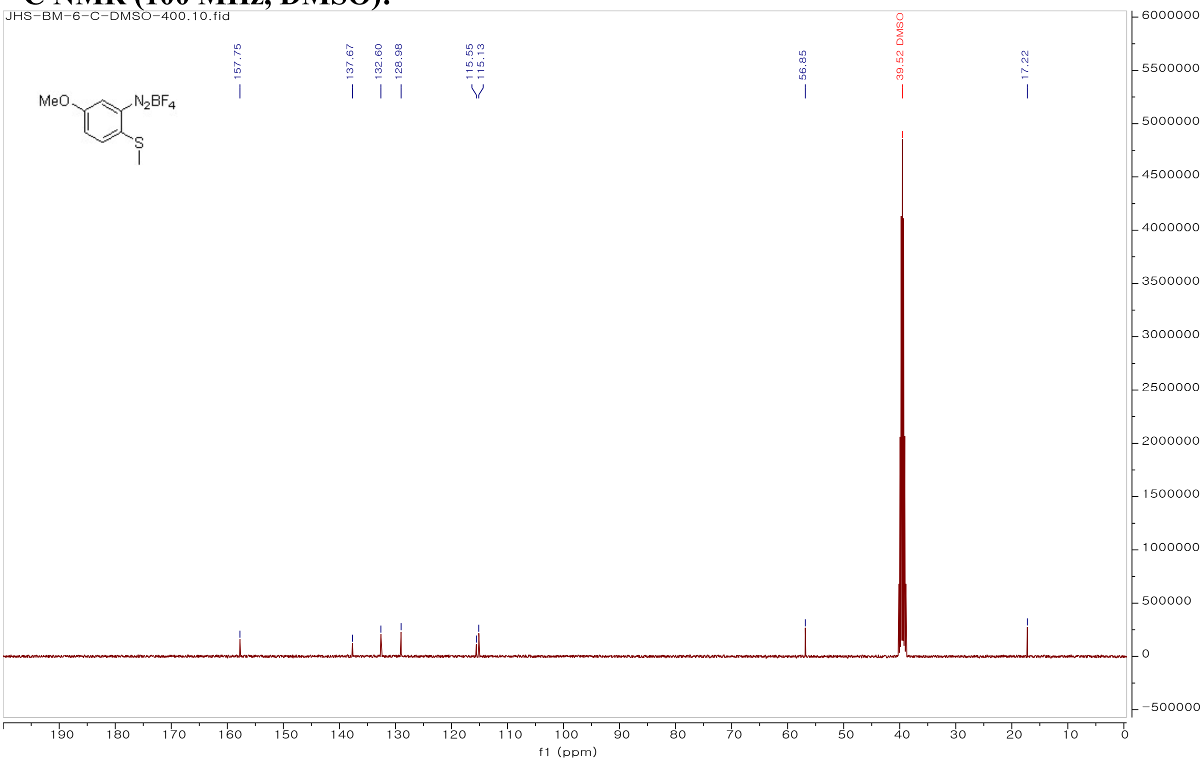
NMR spectroscopic Data of Synthesized Compounds

1-(5-methoxy-2-(methylthio)phenyl)-2-(tetrafluoro-l5-boraneyl)diazene (1ac)

^{1}H NMR (400 MHz, DMSO):

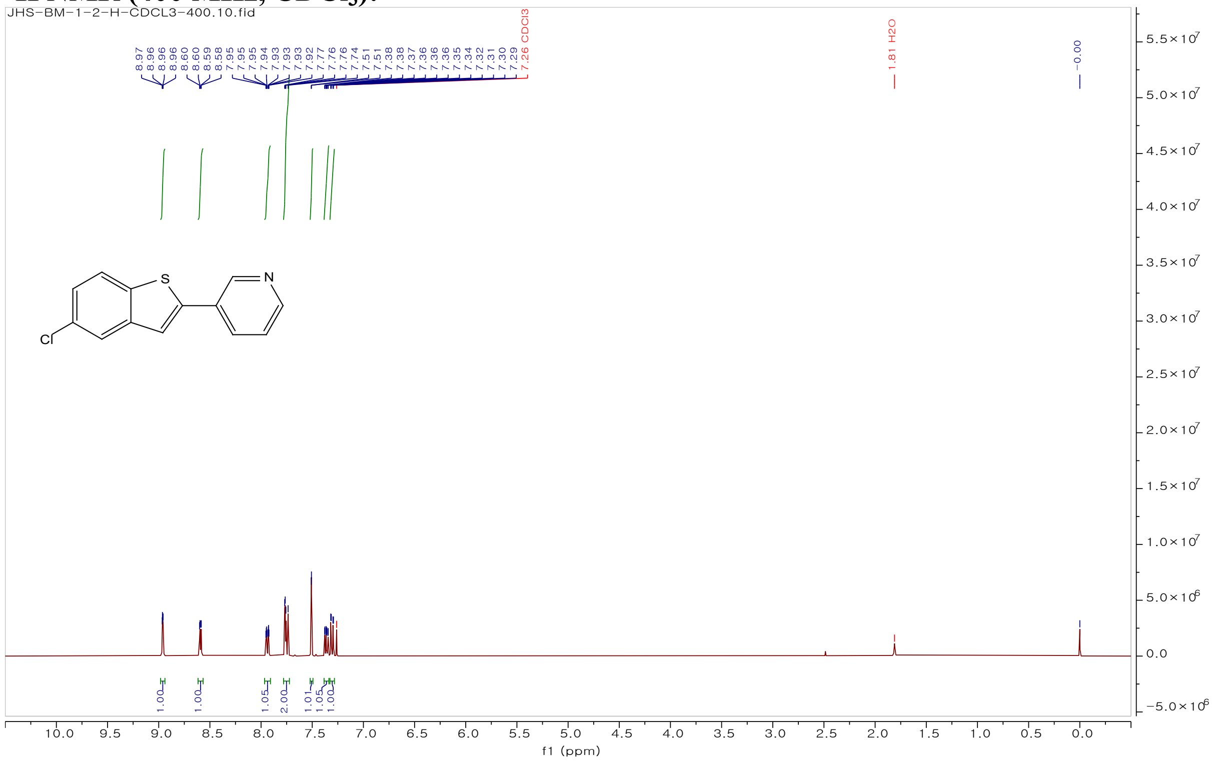


^{13}C NMR (100 MHz, DMSO):

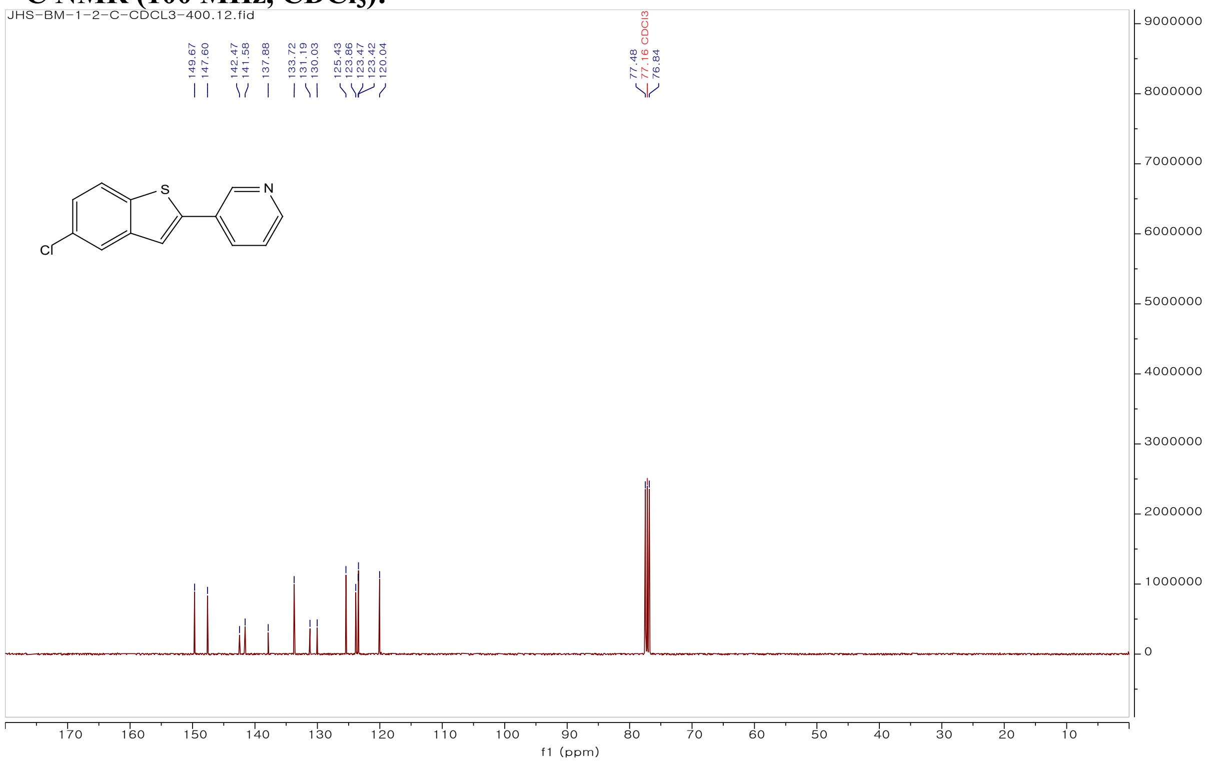


3-(5-chlorobenzo[b]thiophen-2-yl)pyridine (3ba)

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

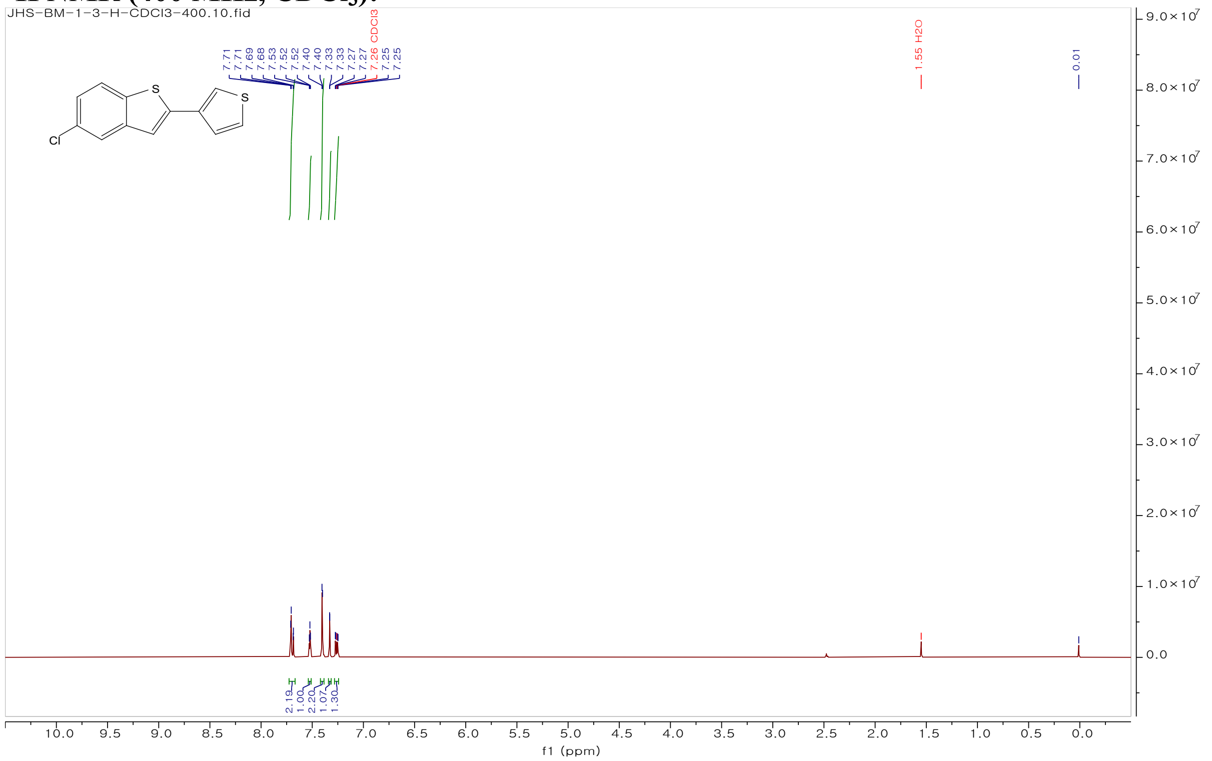


^{13}C NMR (100 MHz, $CDCl_3$):

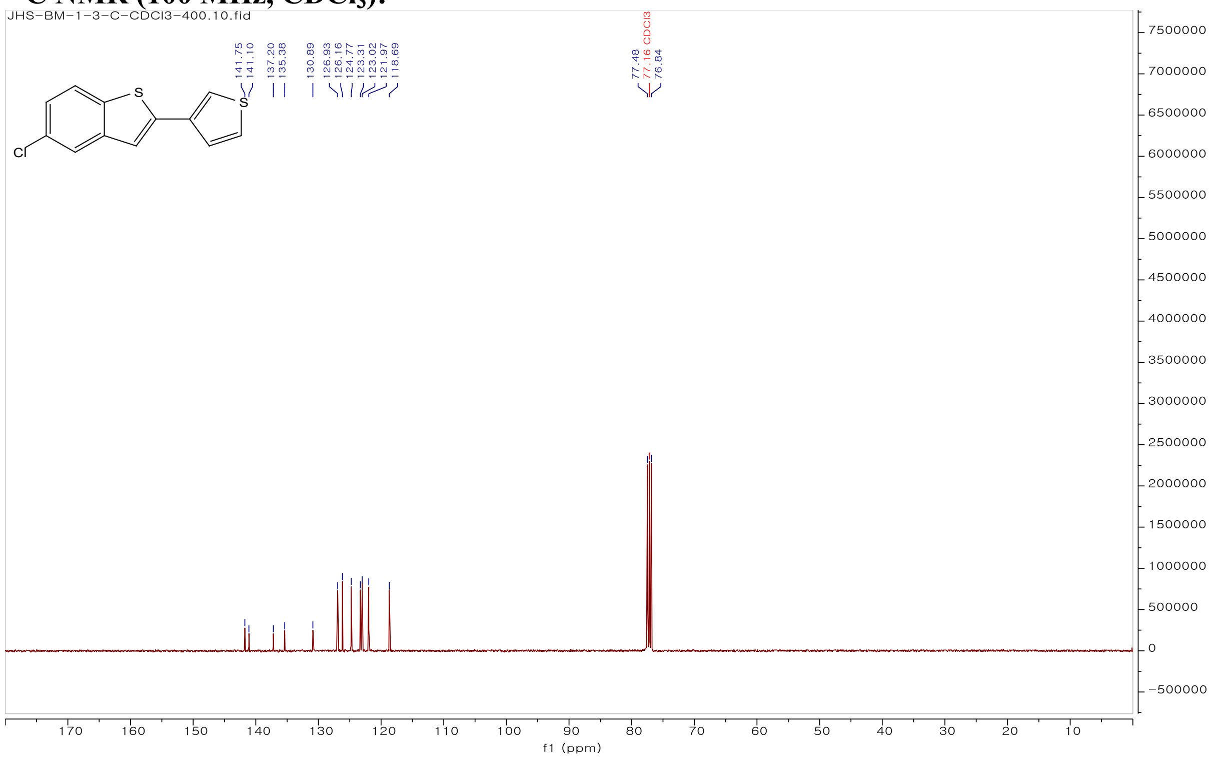


5-chloro-2-(thiophen-3-yl)benzo[b]thiophene (3ca)

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

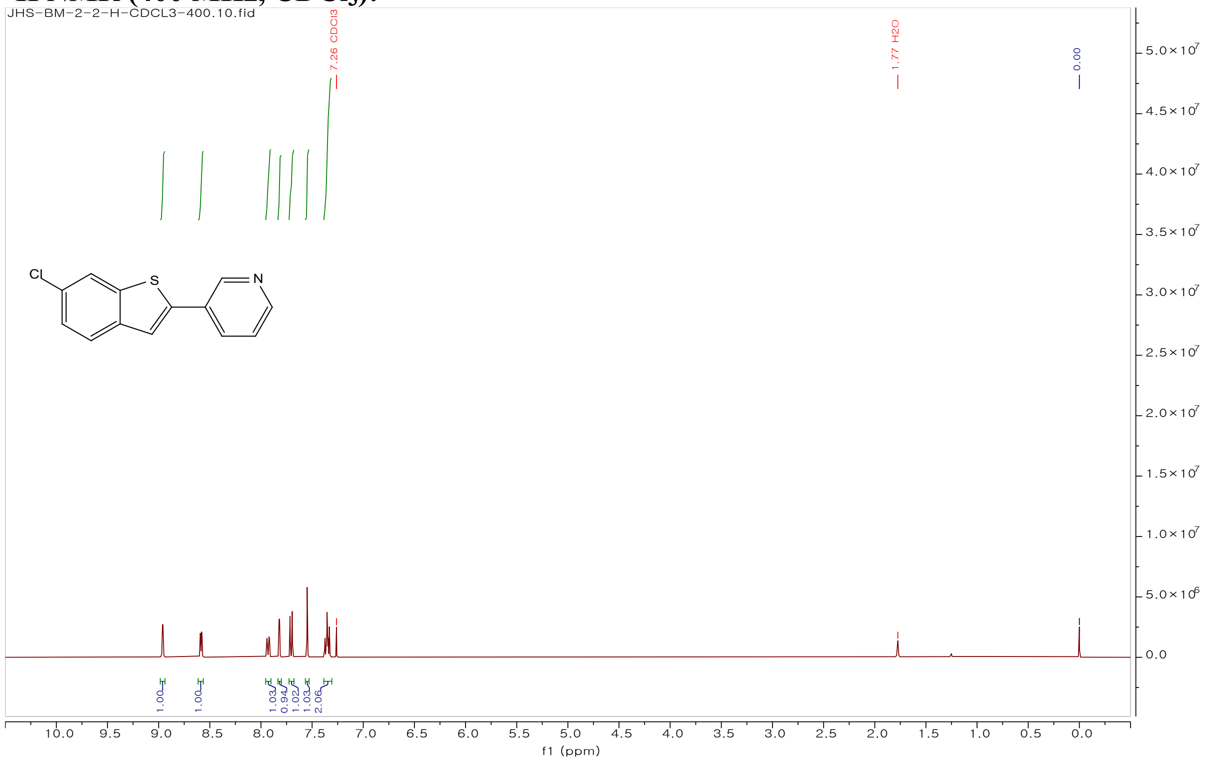


^{13}C NMR (100 MHz, $CDCl_3$):

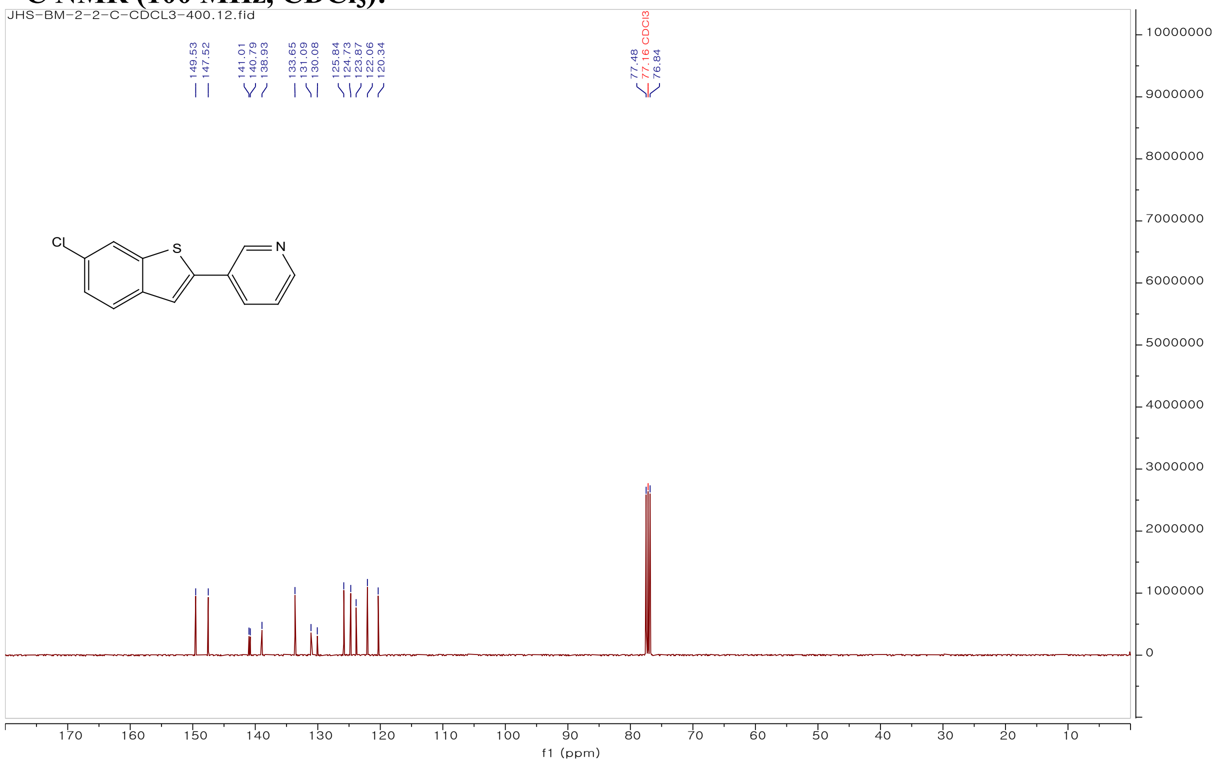


3-(6-chlorobenzo[b]thiophen-2-yl)pyridine (3bb)

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

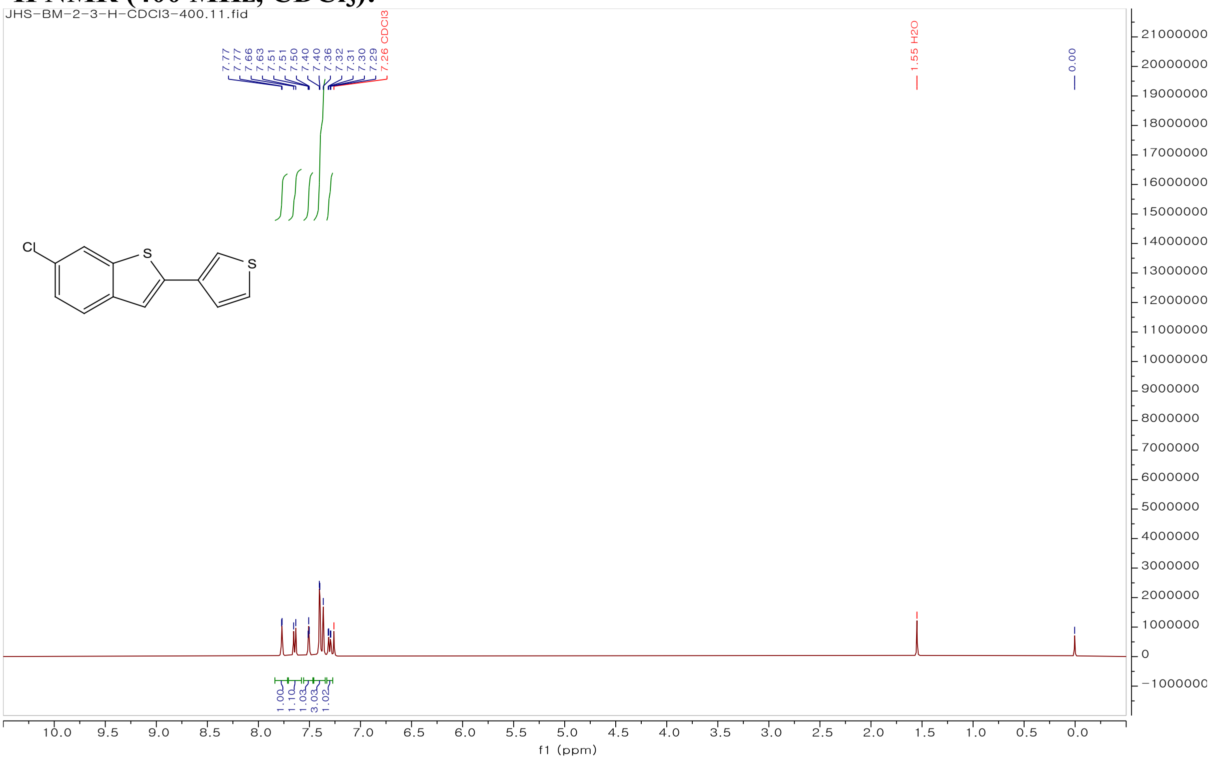


^{13}C NMR (100 MHz, $CDCl_3$):

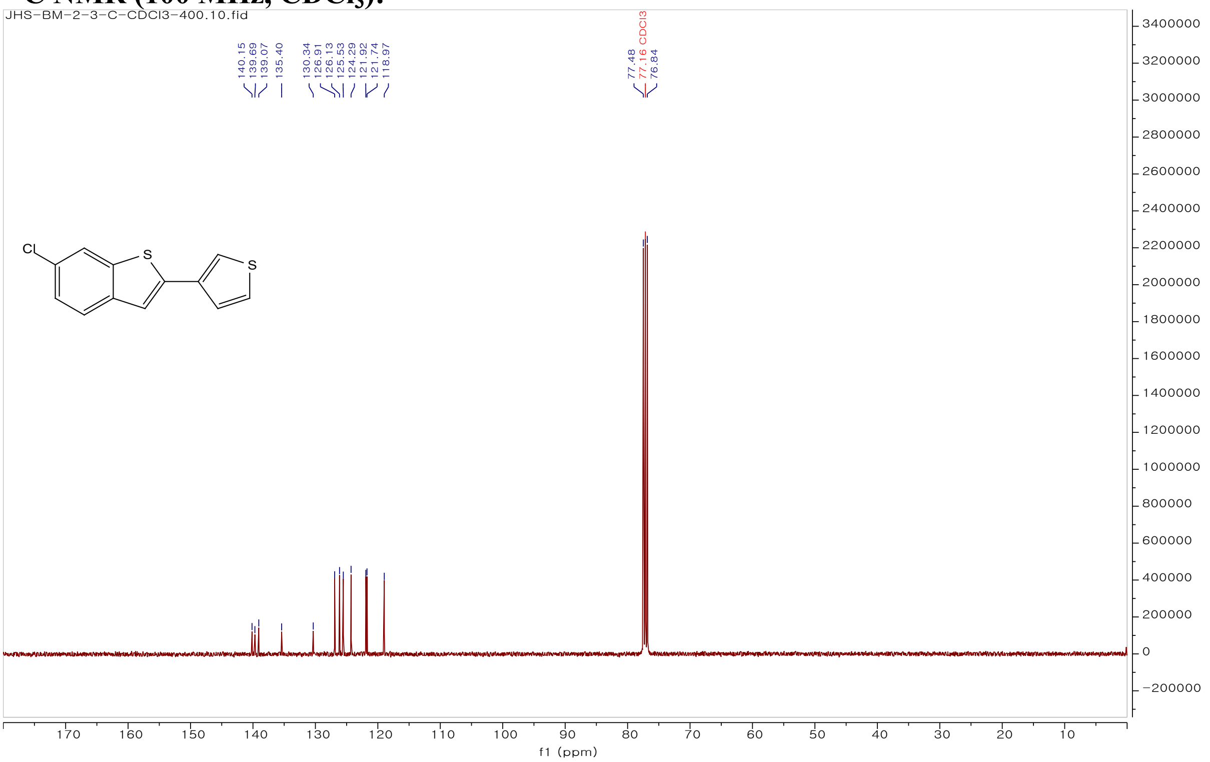


6-chloro-2-(thiophen-3-yl)benzo[b]thiophene (3cb)

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

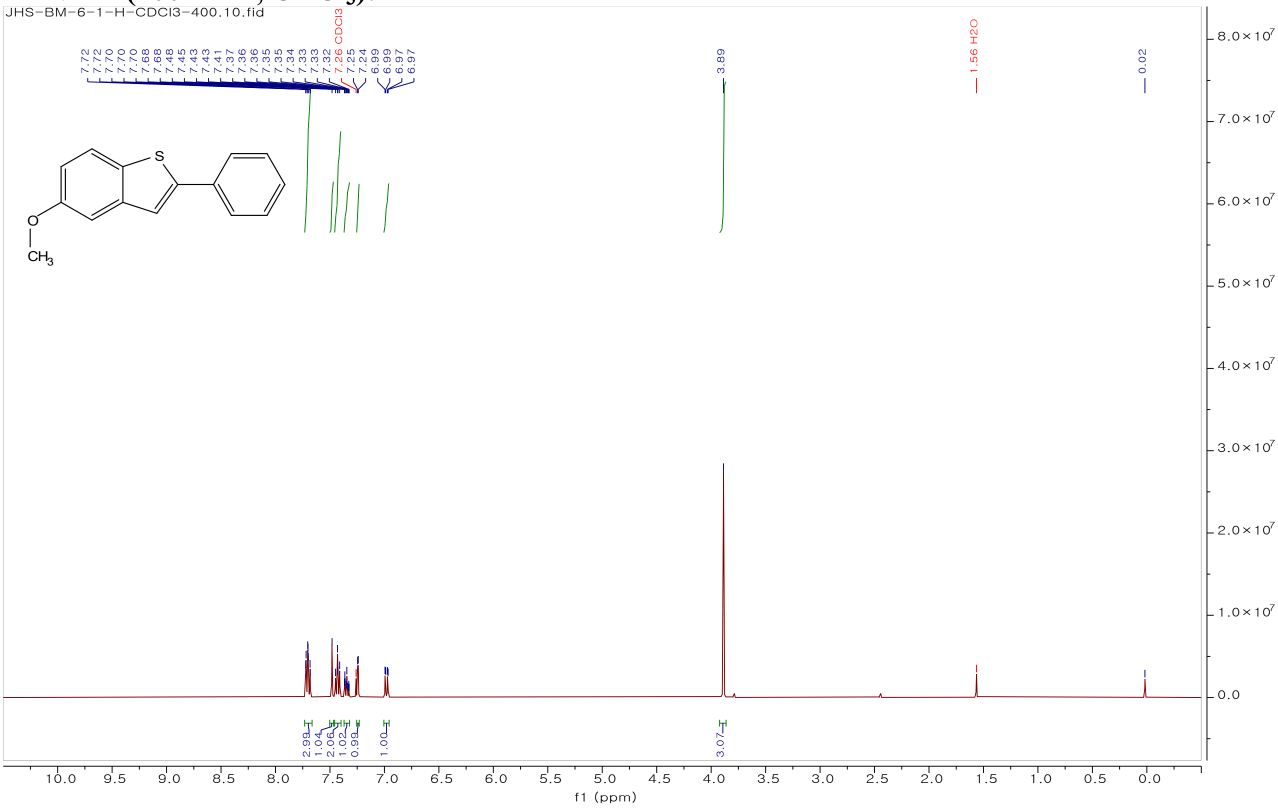


^{13}C NMR (100 MHz, $CDCl_3$):

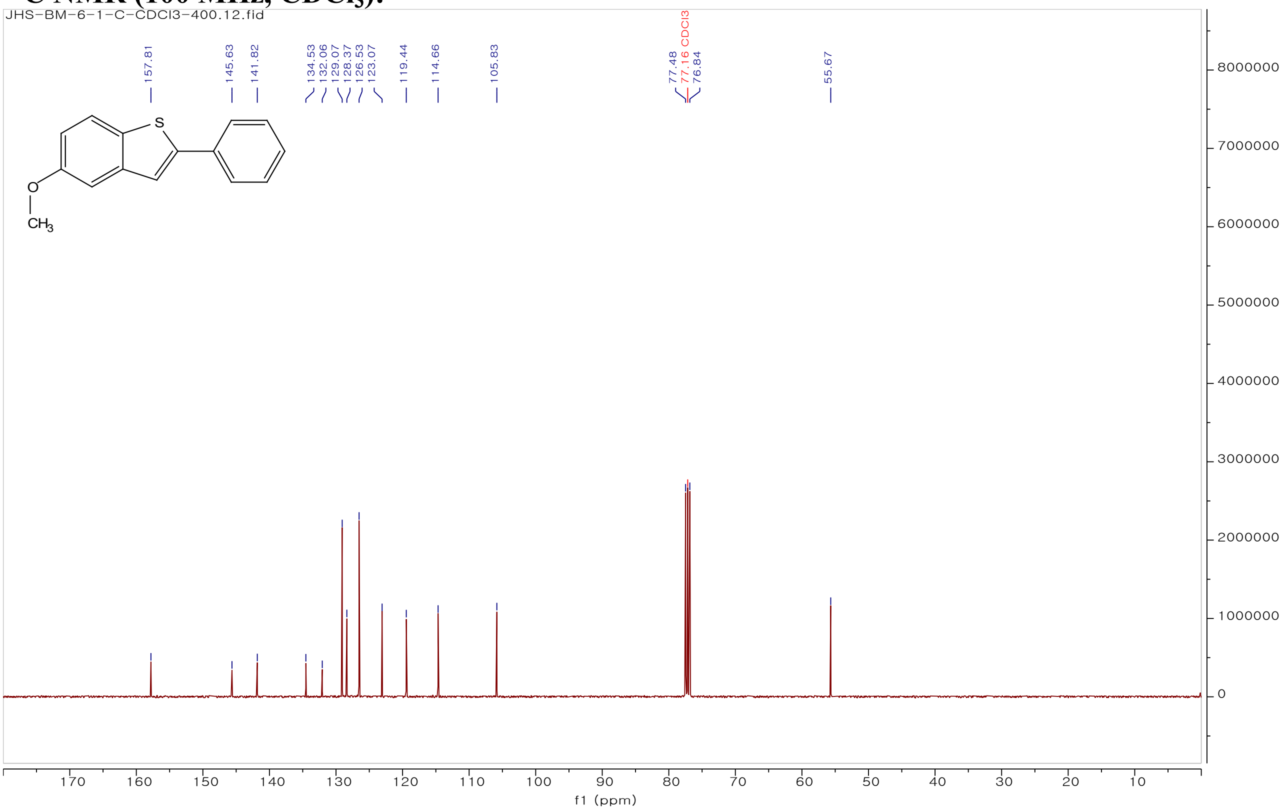


5-methoxy-2-phenylbenzo[b]thiophene (3ac)

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

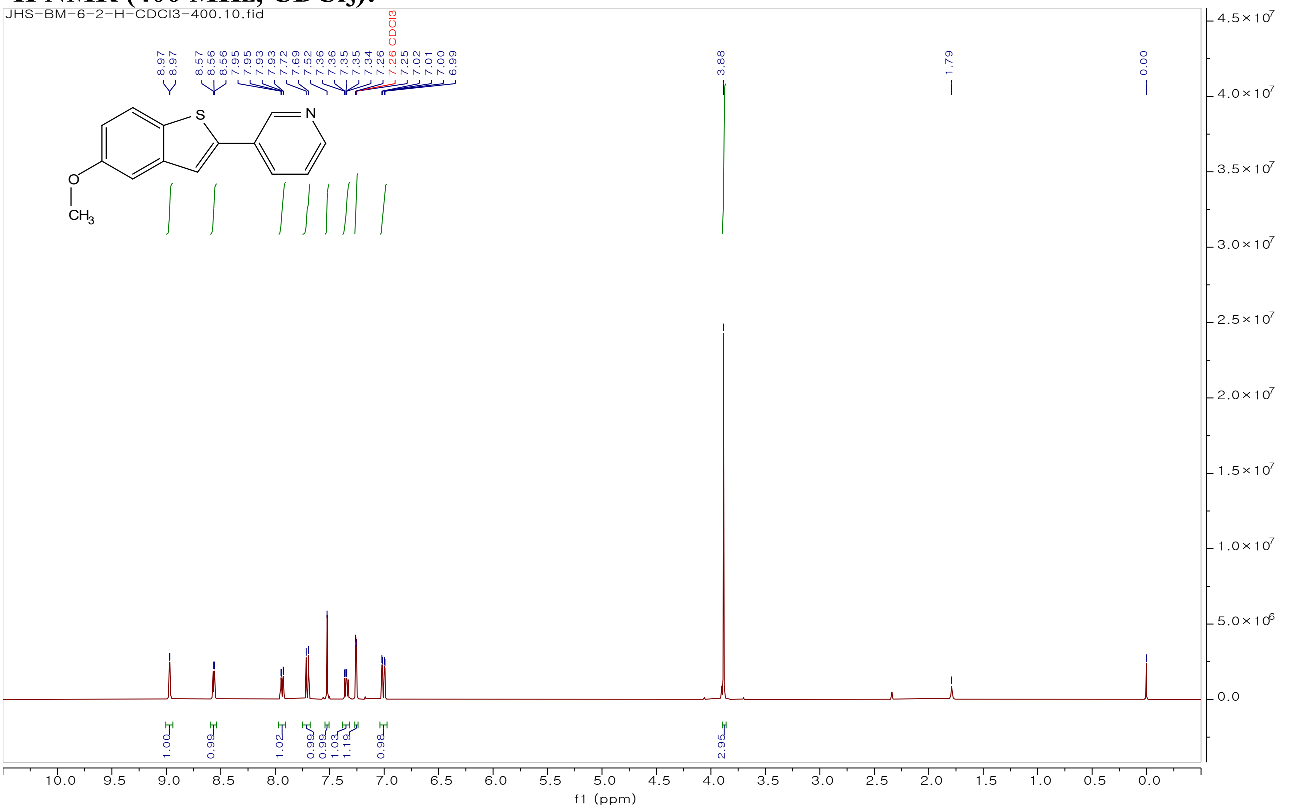


^{13}C NMR (100 MHz, $CDCl_3$):

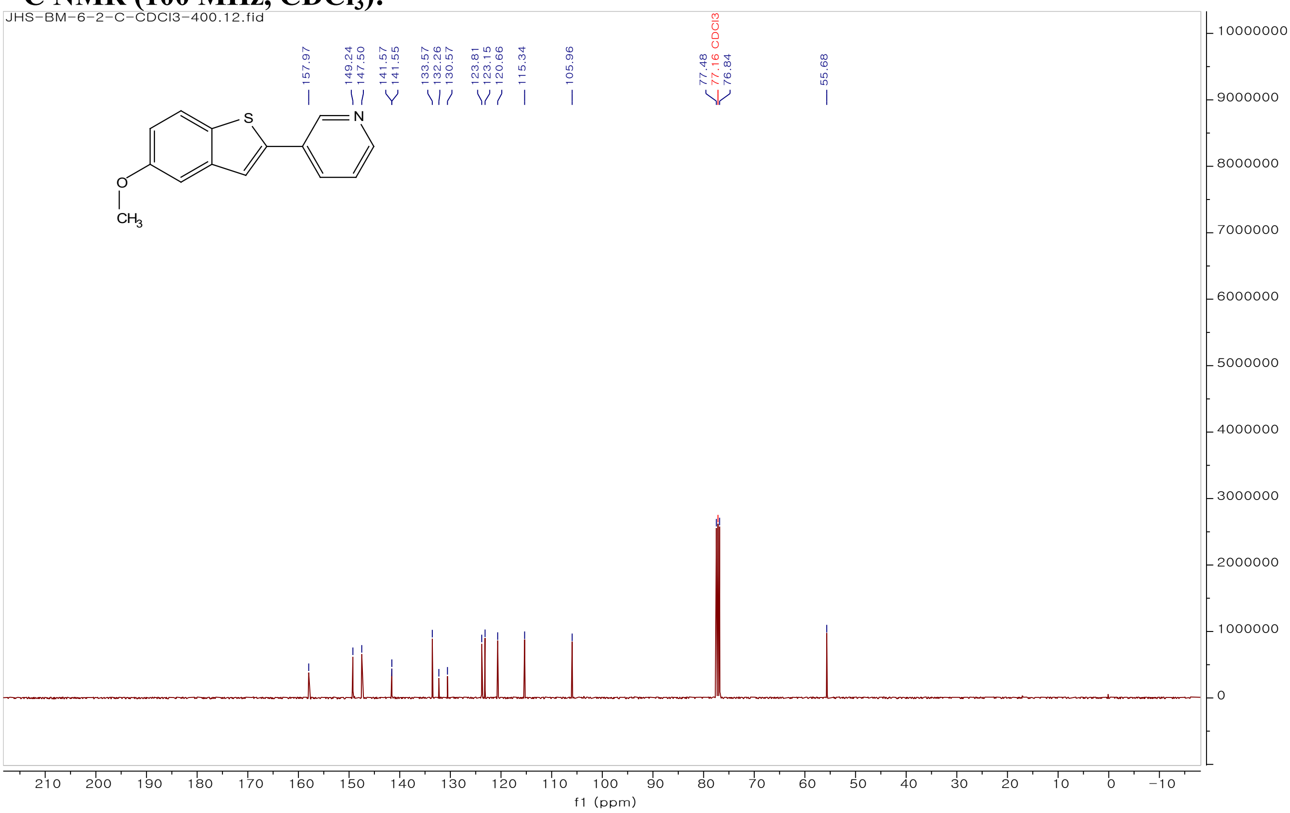


3-(5-methoxybenzo[b]thiophen-2-yl)pyridine (3bc)

^{1}H NMR (400 MHz, CDCl$_3$):

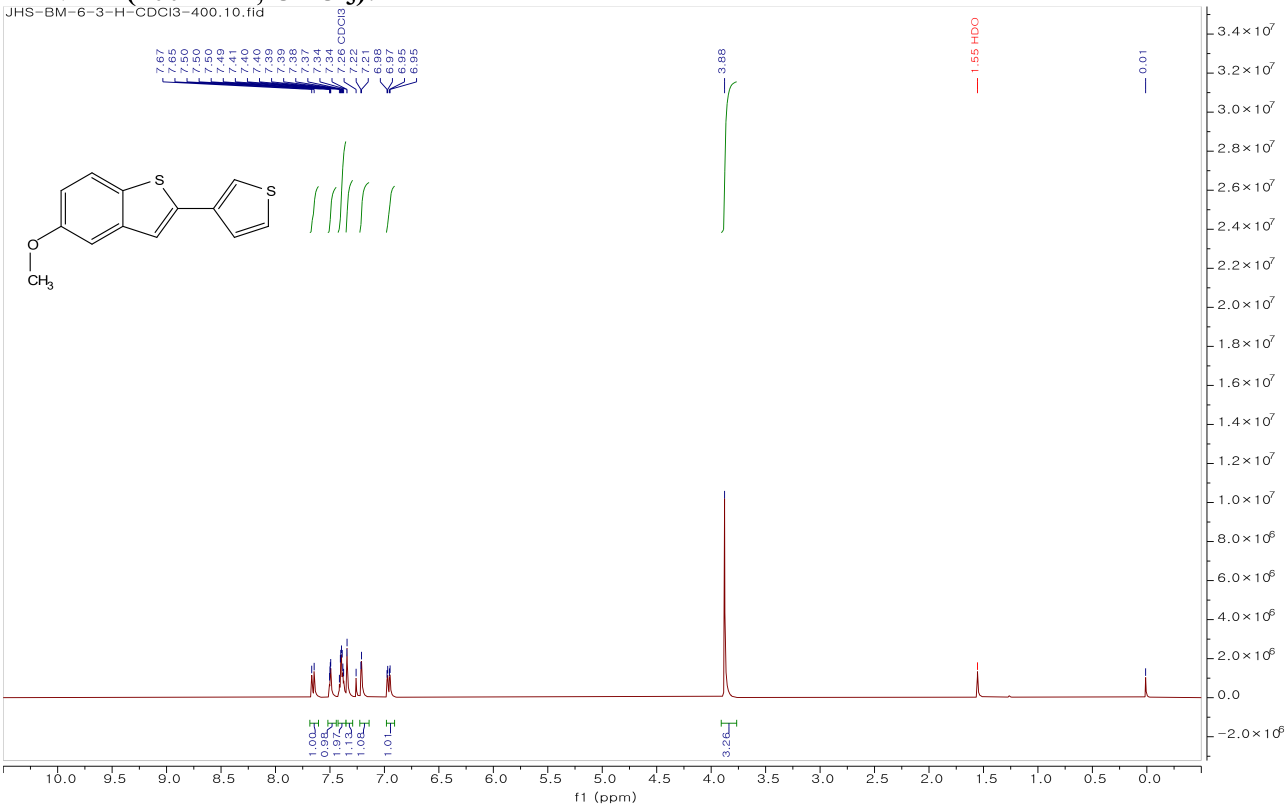


^{13}C NMR (100 MHz, CDCl$_3$):

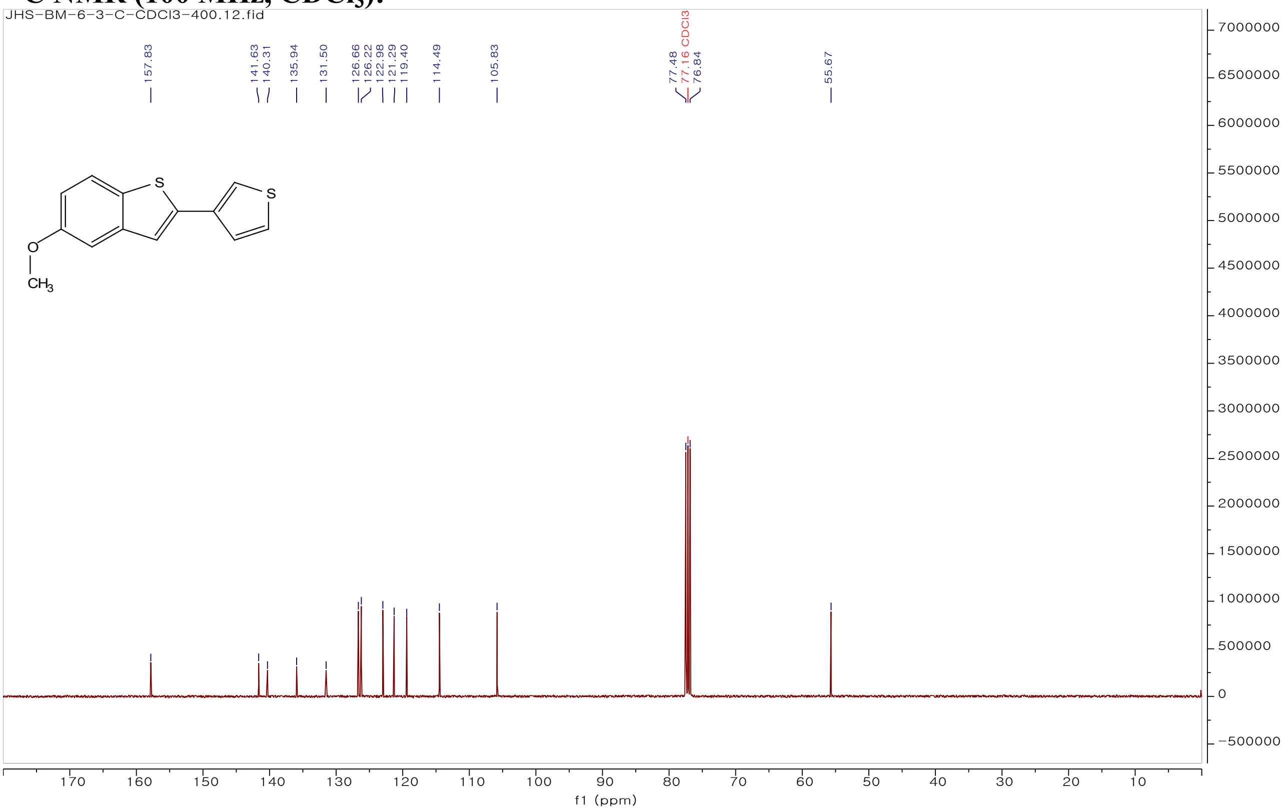


5-methoxy-2-(thiophen-3-yl)benzo[b]thiophene (3cc)

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

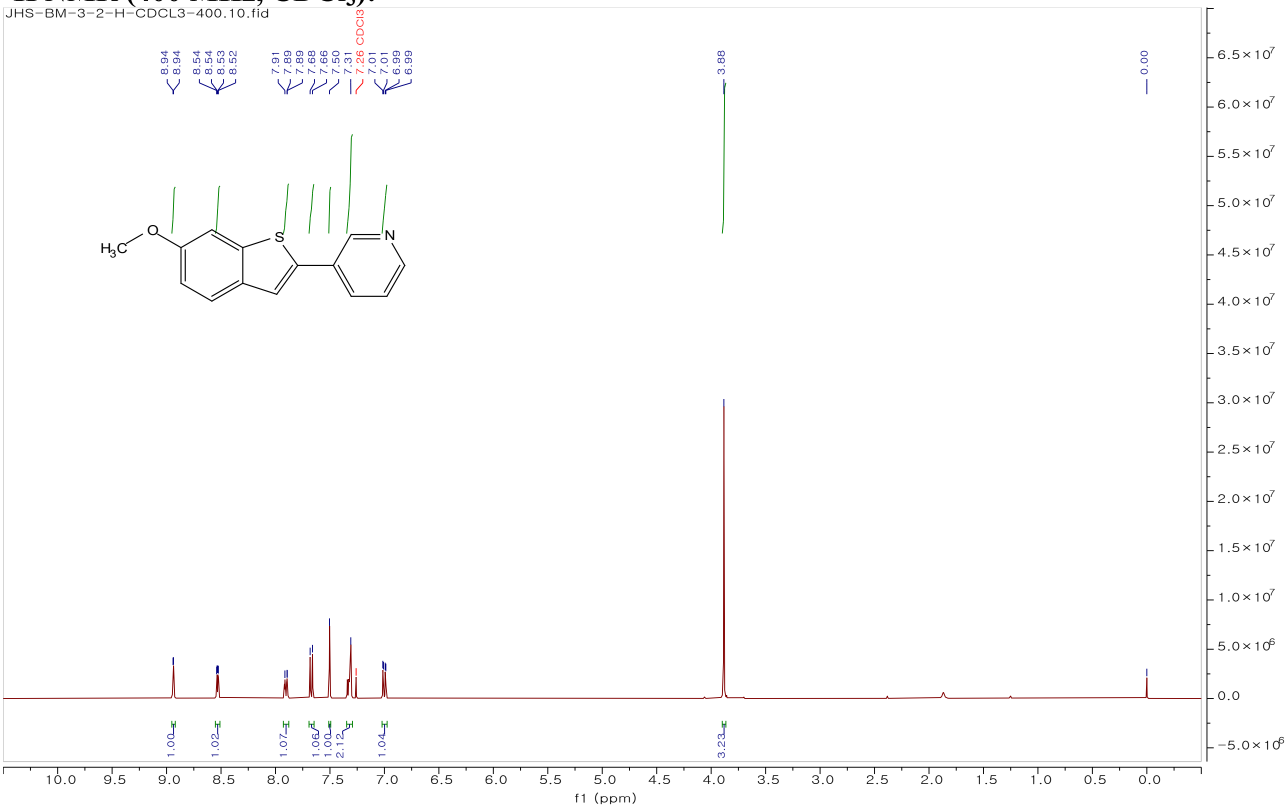


^{13}C NMR (100 MHz, $CDCl_3$):

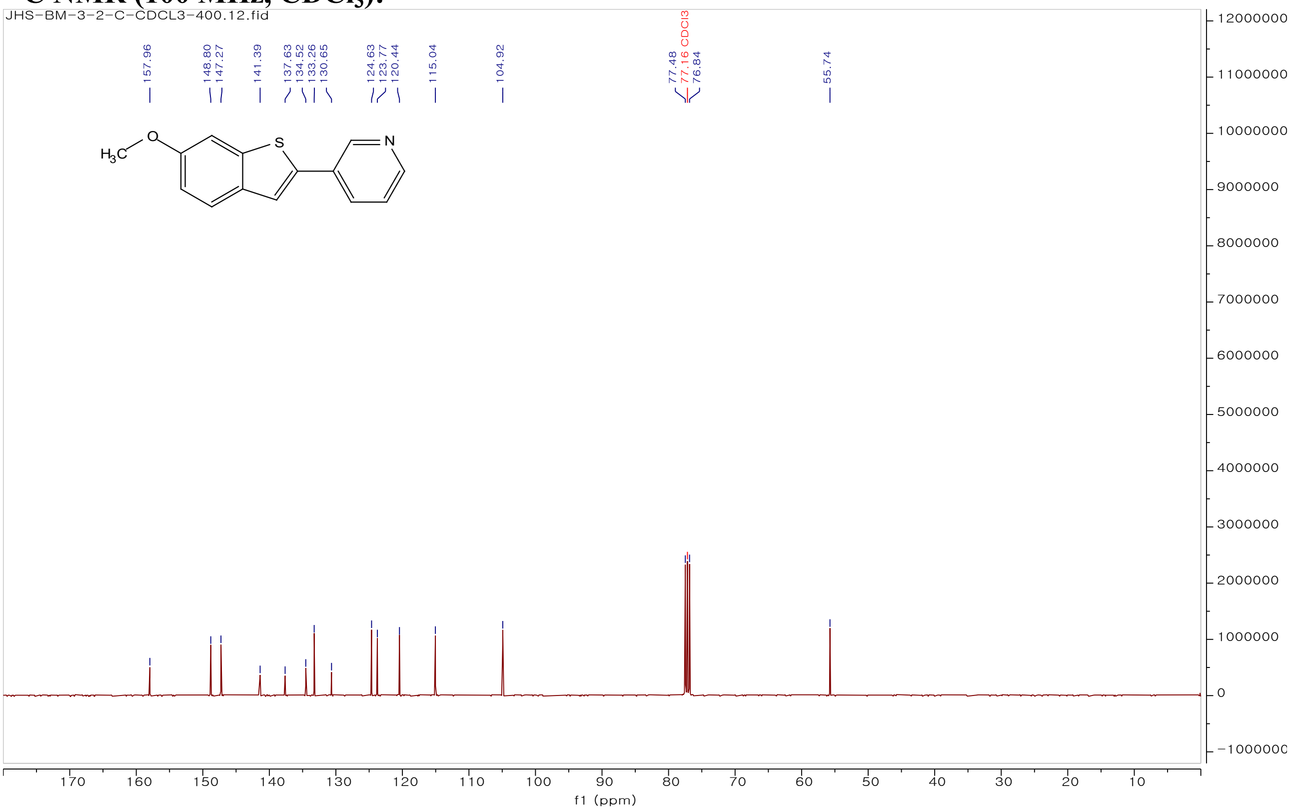


3-(6-methoxybenzo[b]thiophen-2-yl)pyridine (3bd)

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

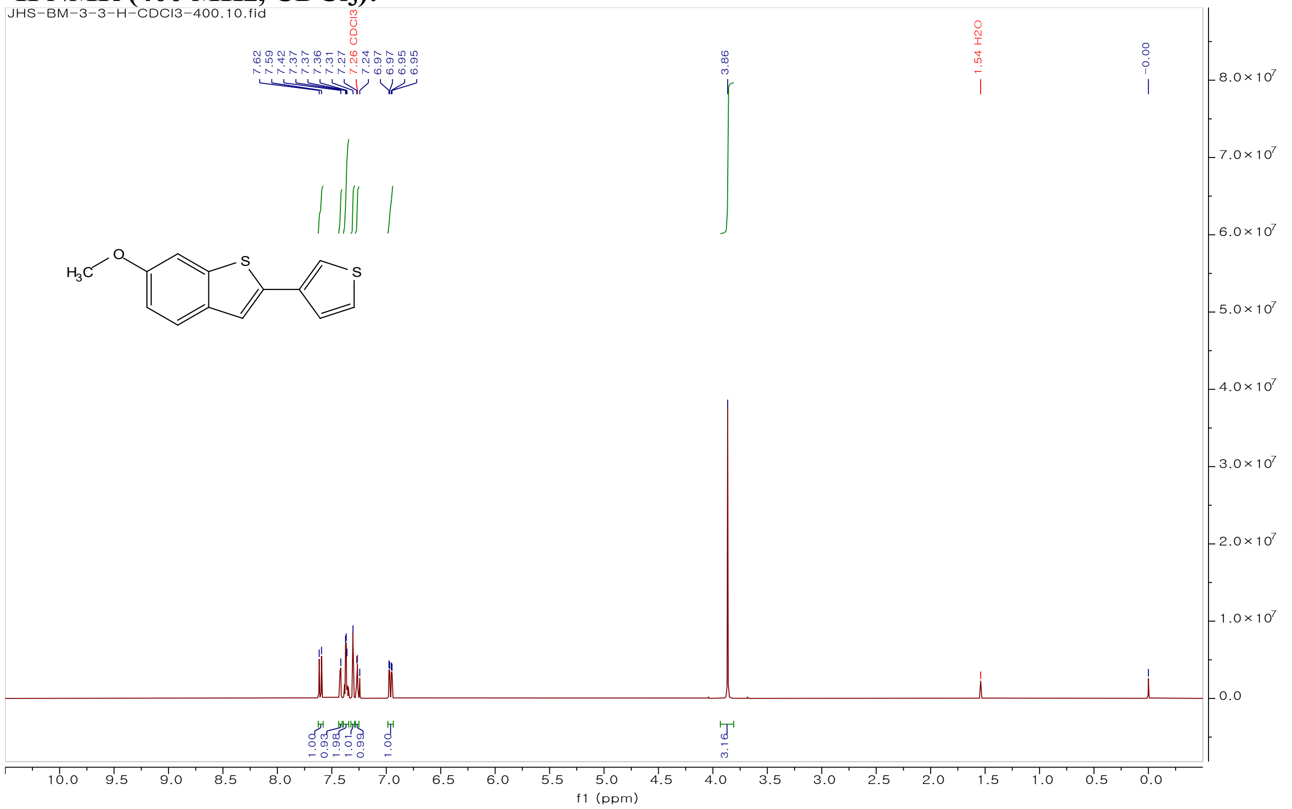


^{13}C NMR (100 MHz, $CDCl_3$):

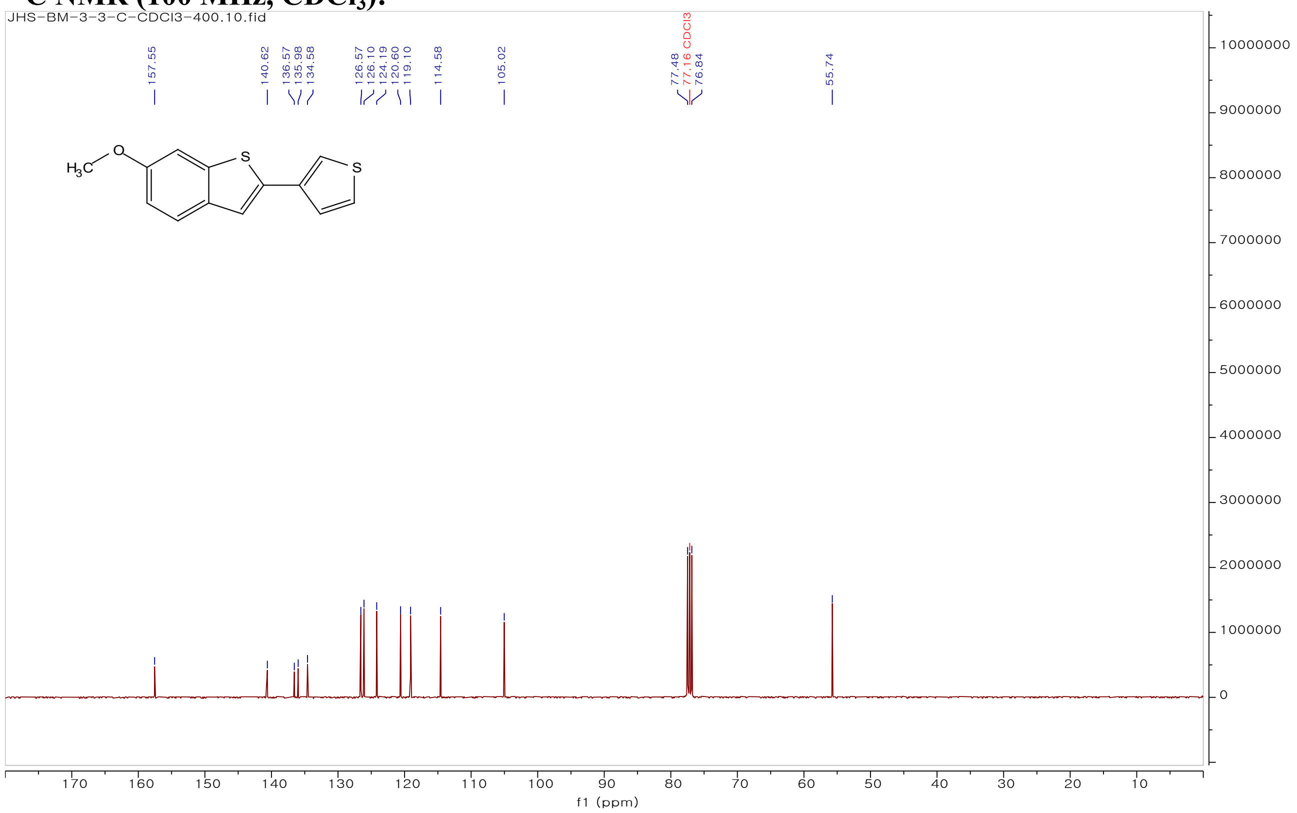


6-methoxy-2-(thiophen-3-yl)benzo[b]thiophene (3cd)

[1]H NMR (400 MHz, $CDCl_3$):

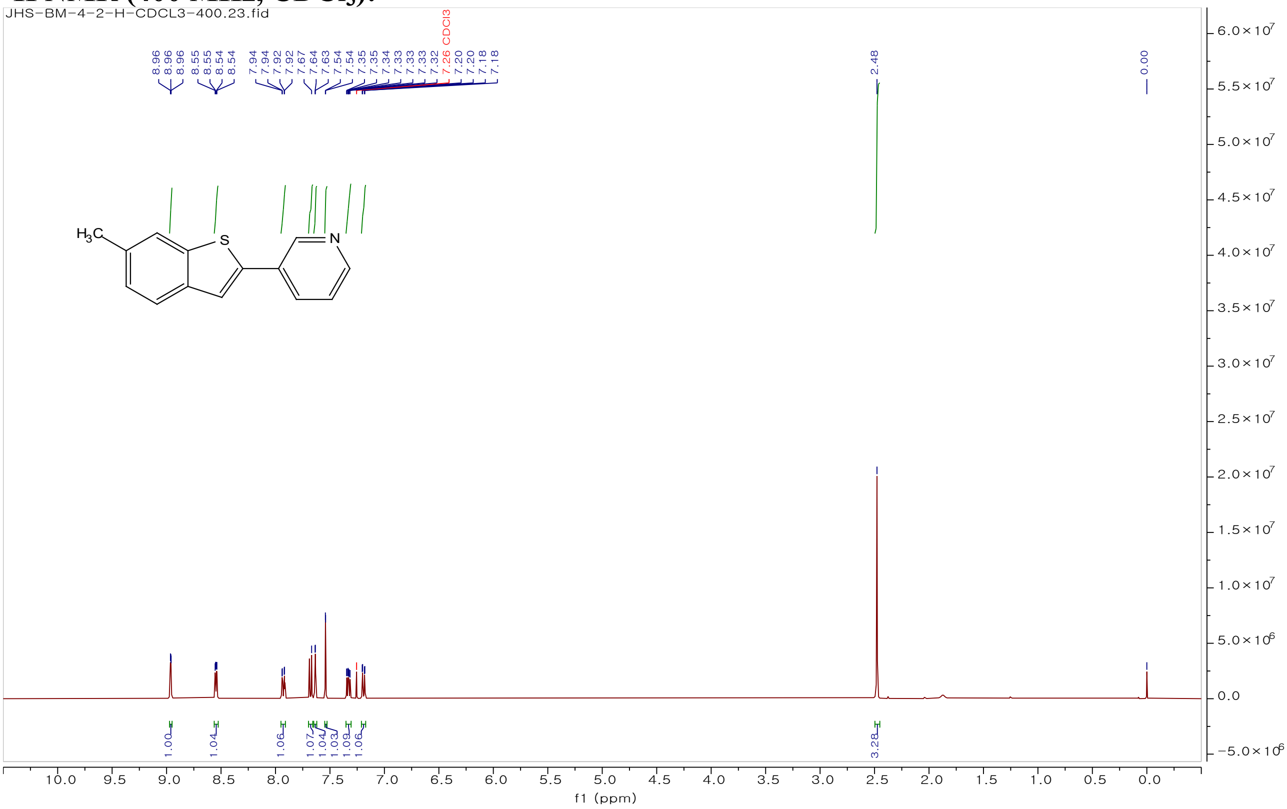


[13]C NMR (100 MHz, $CDCl_3$):

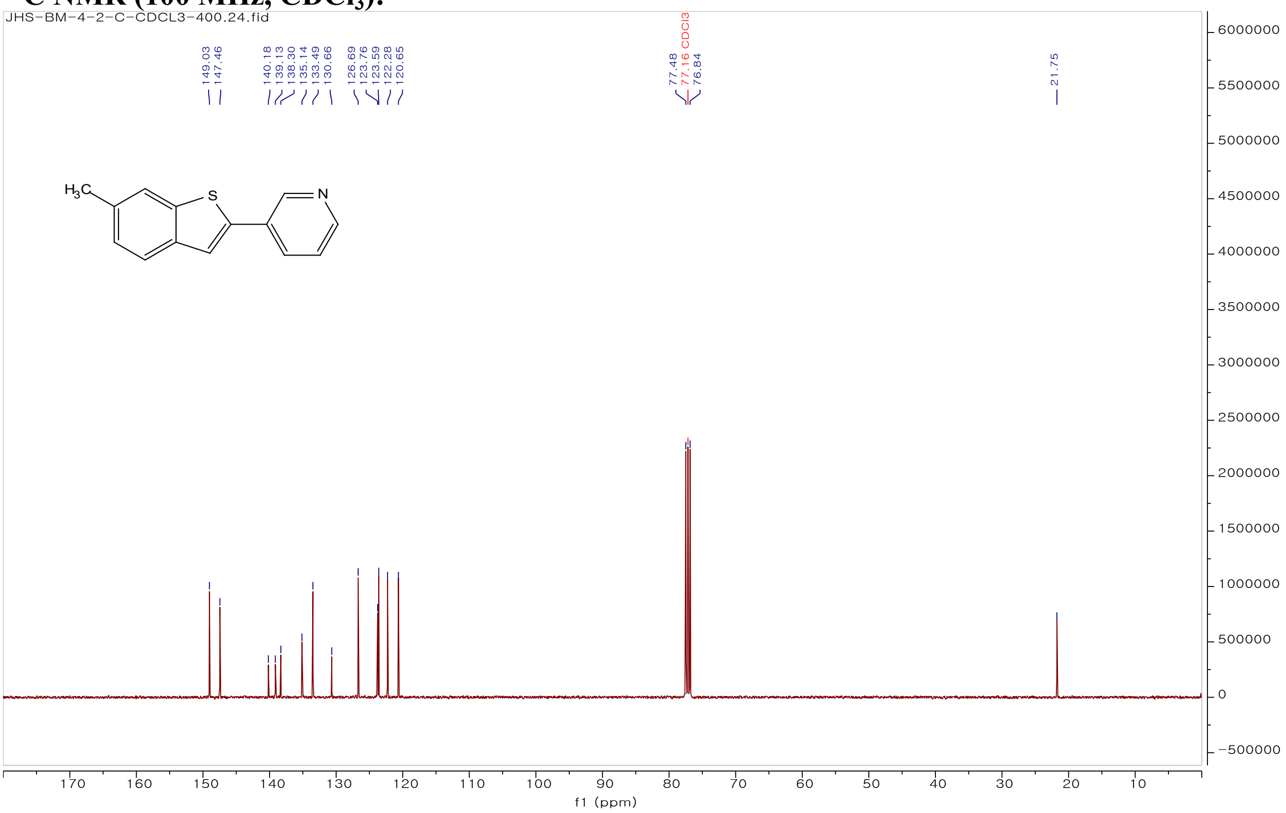


3-(6-methylbenzo[b]thiophen-2-yl)pyridine (3be)

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

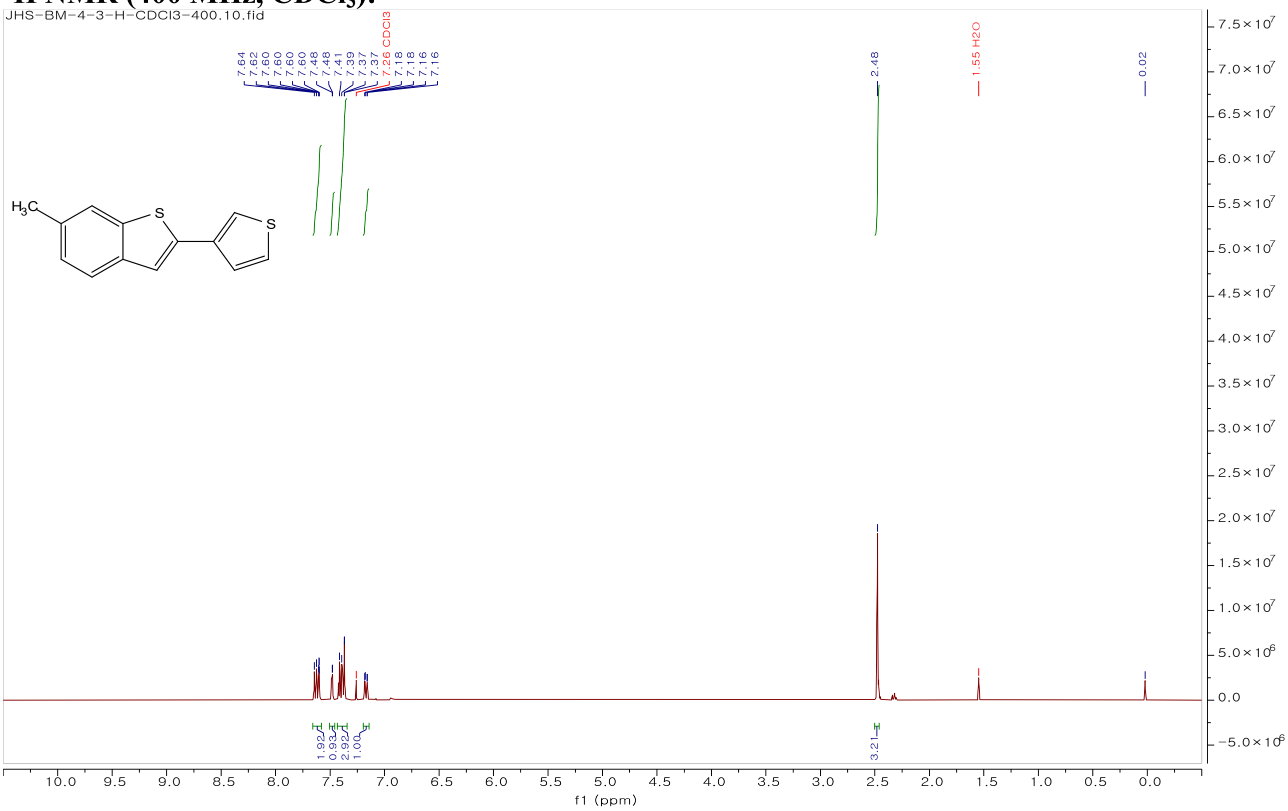


^{13}C NMR (100 MHz, $CDCl_3$):

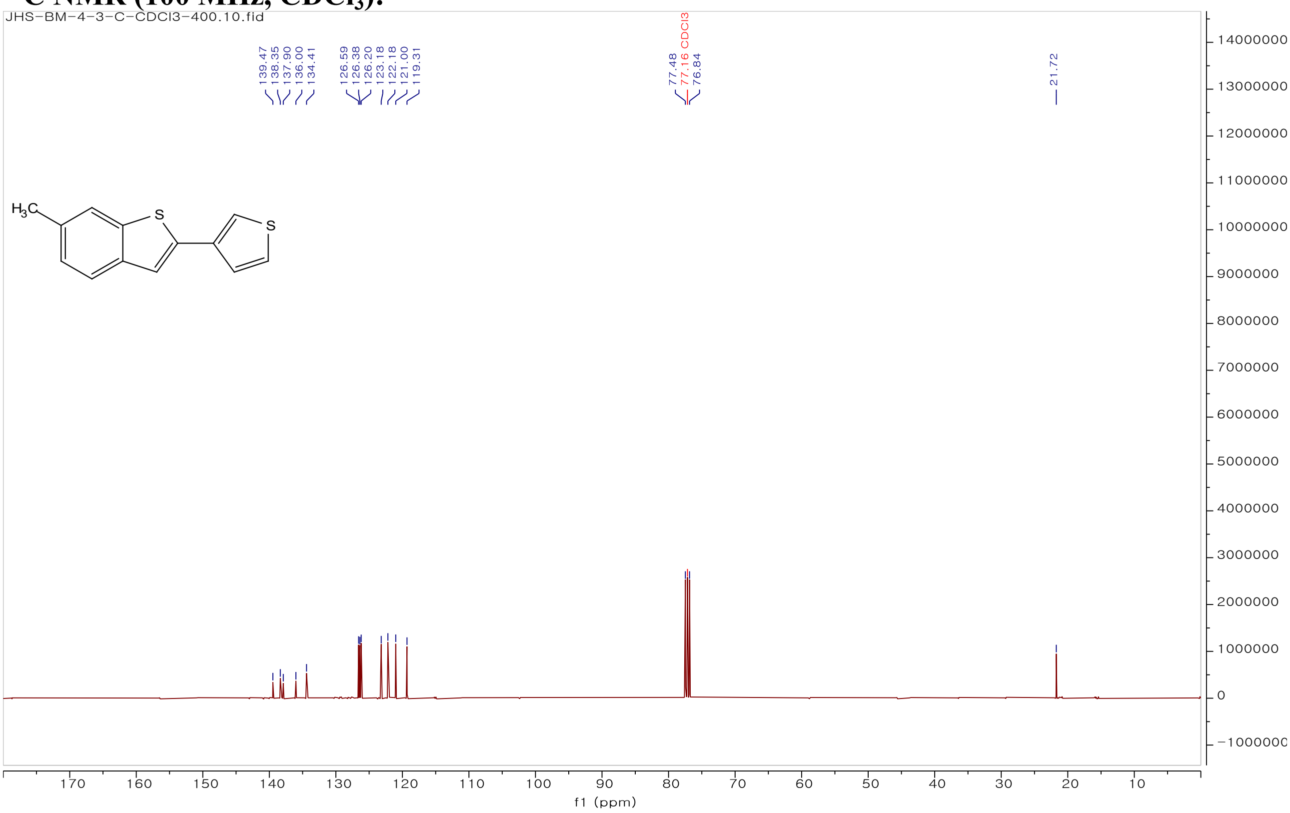


6-methyl-2-(thiophen-3-yl)benzo[b]thiophene (3ce)

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

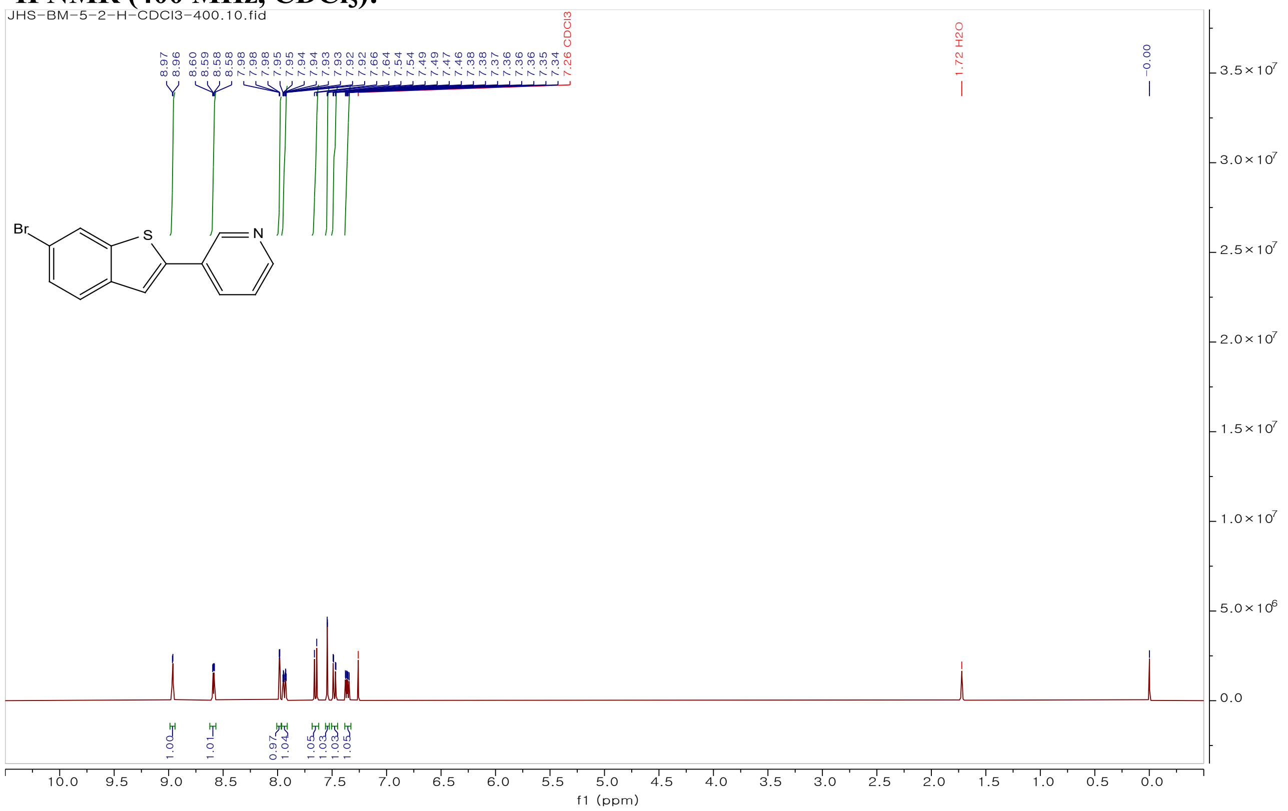


^{13}C NMR (100 MHz, $CDCl_3$):

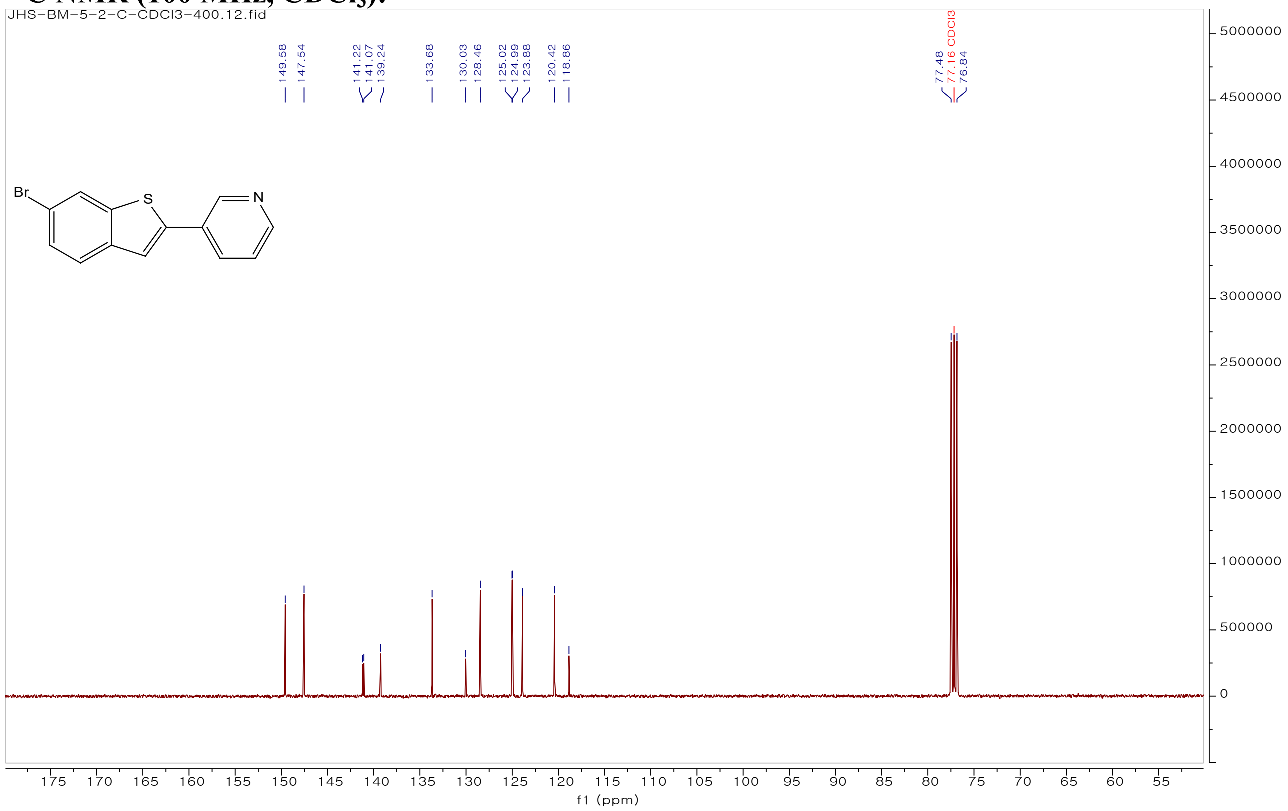


3-(6-bromobenzo[b]thiophen-2-yl)pyridine (3bf)

^{1}H NMR (400 MHz, CDCl$_3$):

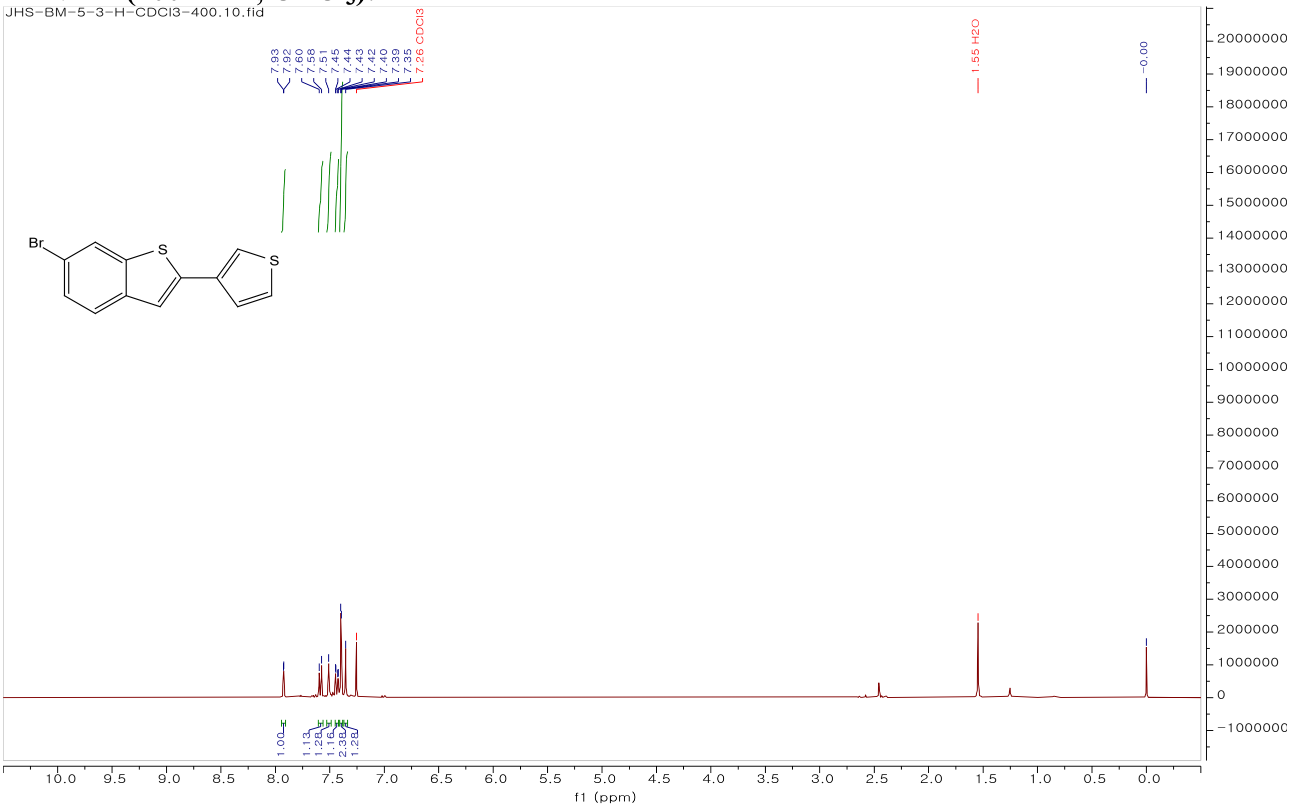


^{13}C NMR (100 MHz, CDCl$_3$):

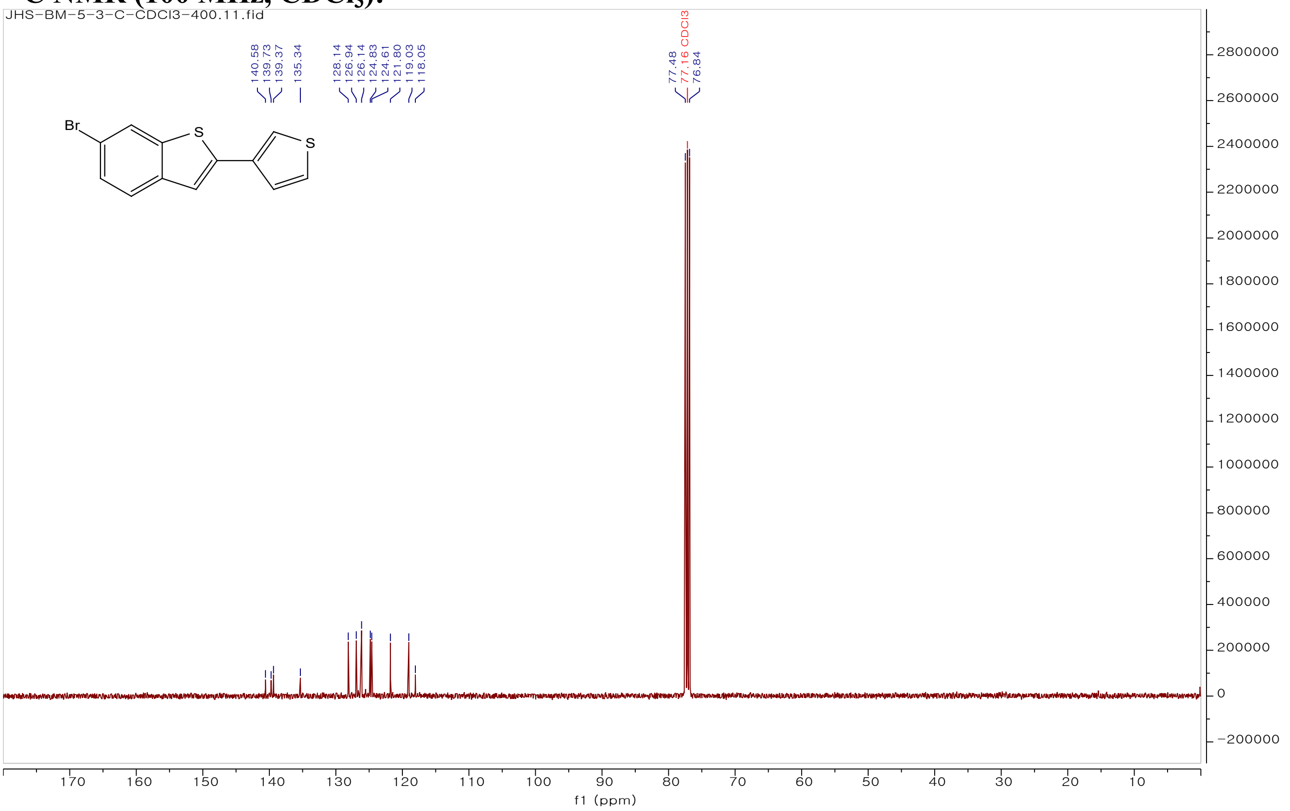


6-bromo-2-(thiophen-3-yl)benzo[b]thiophene (3cf)

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

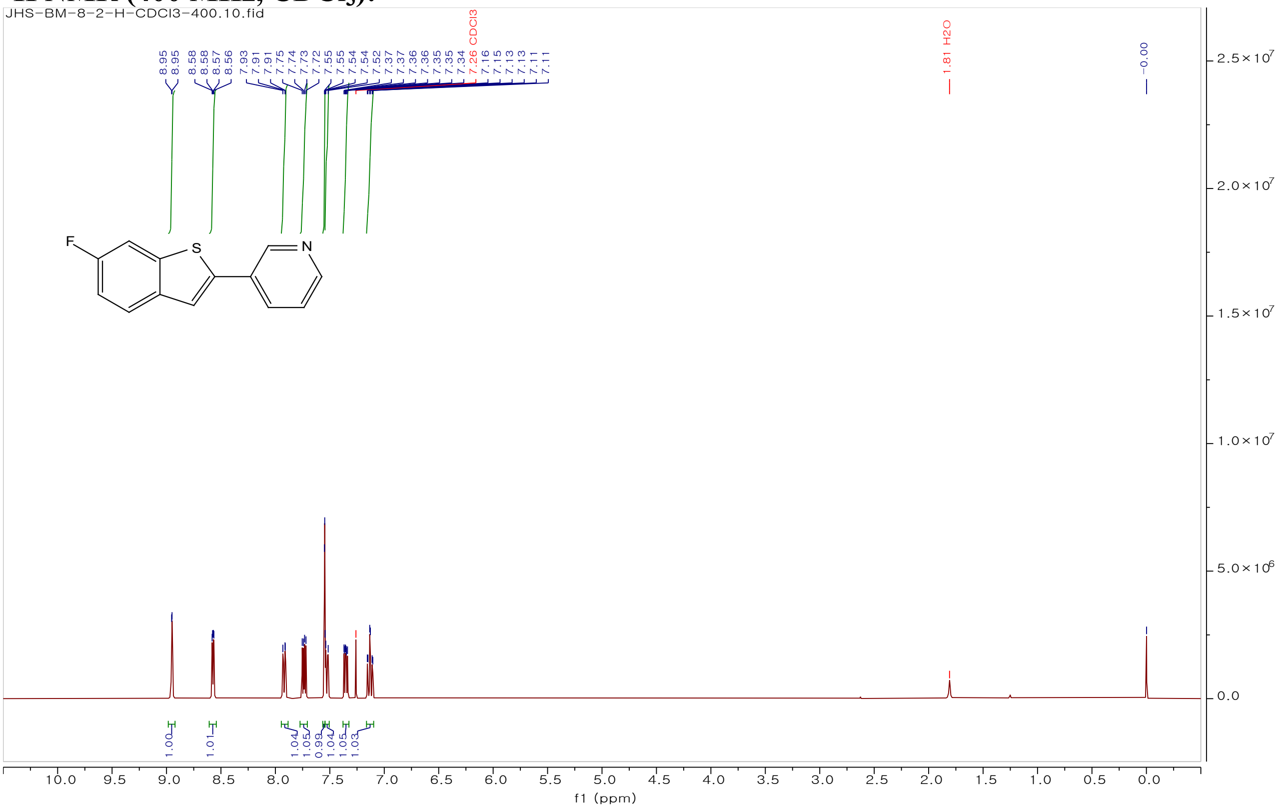


^{13}C NMR (100 MHz, $CDCl_3$):

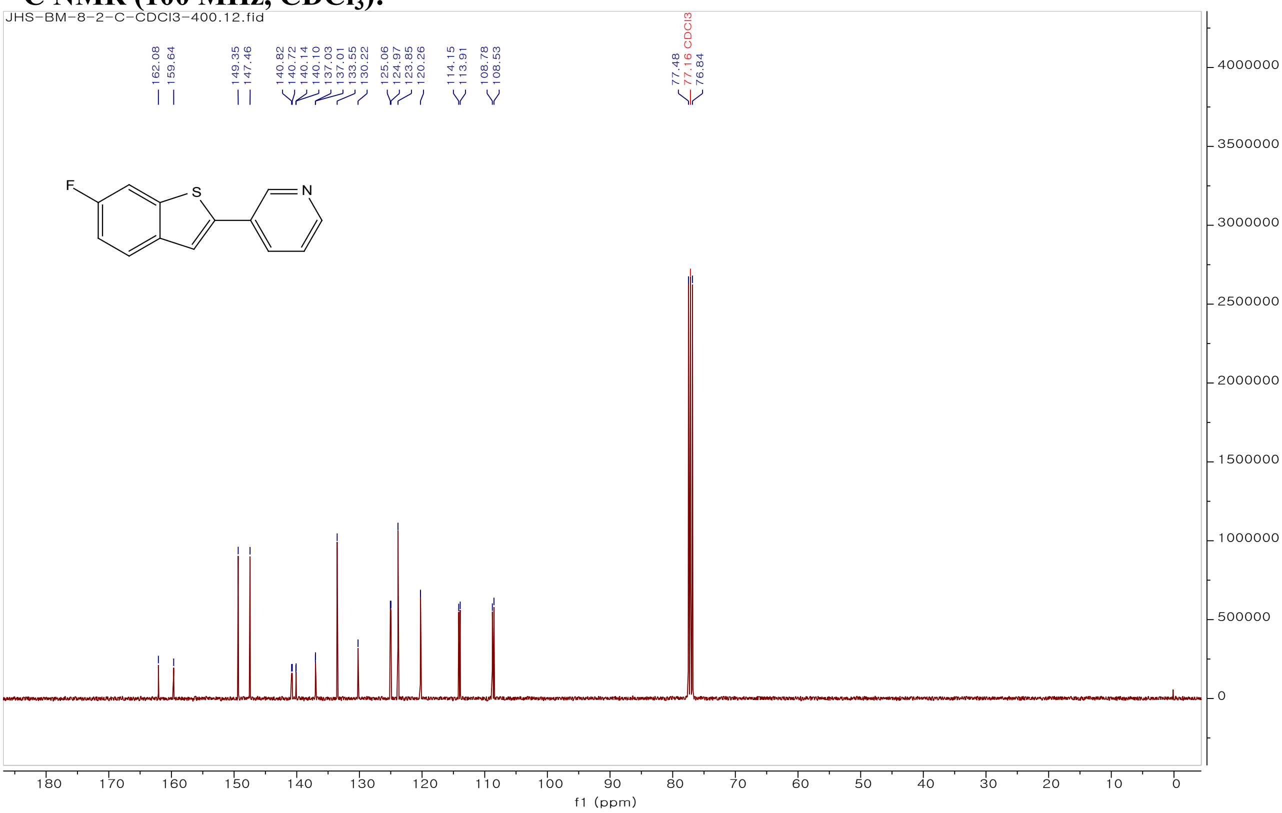


3-(6-fluorobenzo[b]thiophen-2-yl)pyridine (3bg)

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

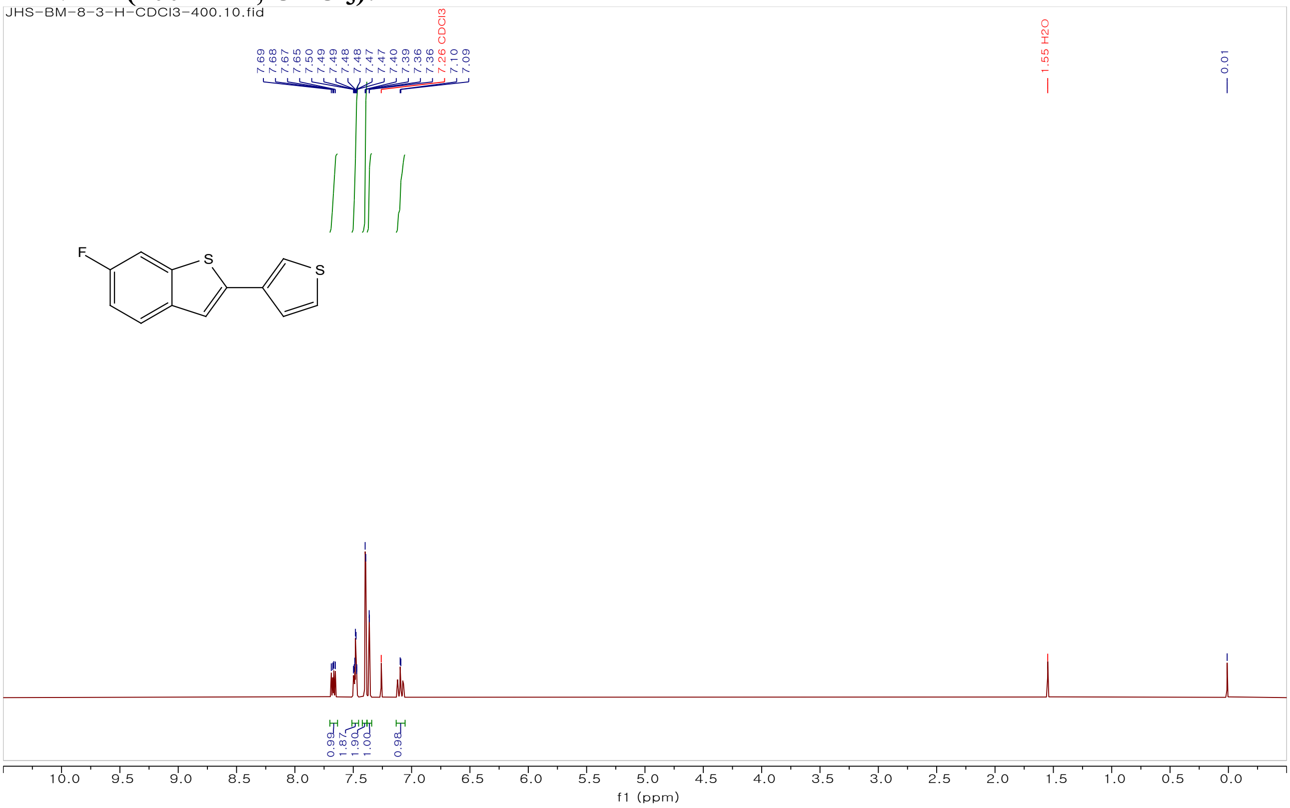


^{13}C NMR (100 MHz, $CDCl_3$):

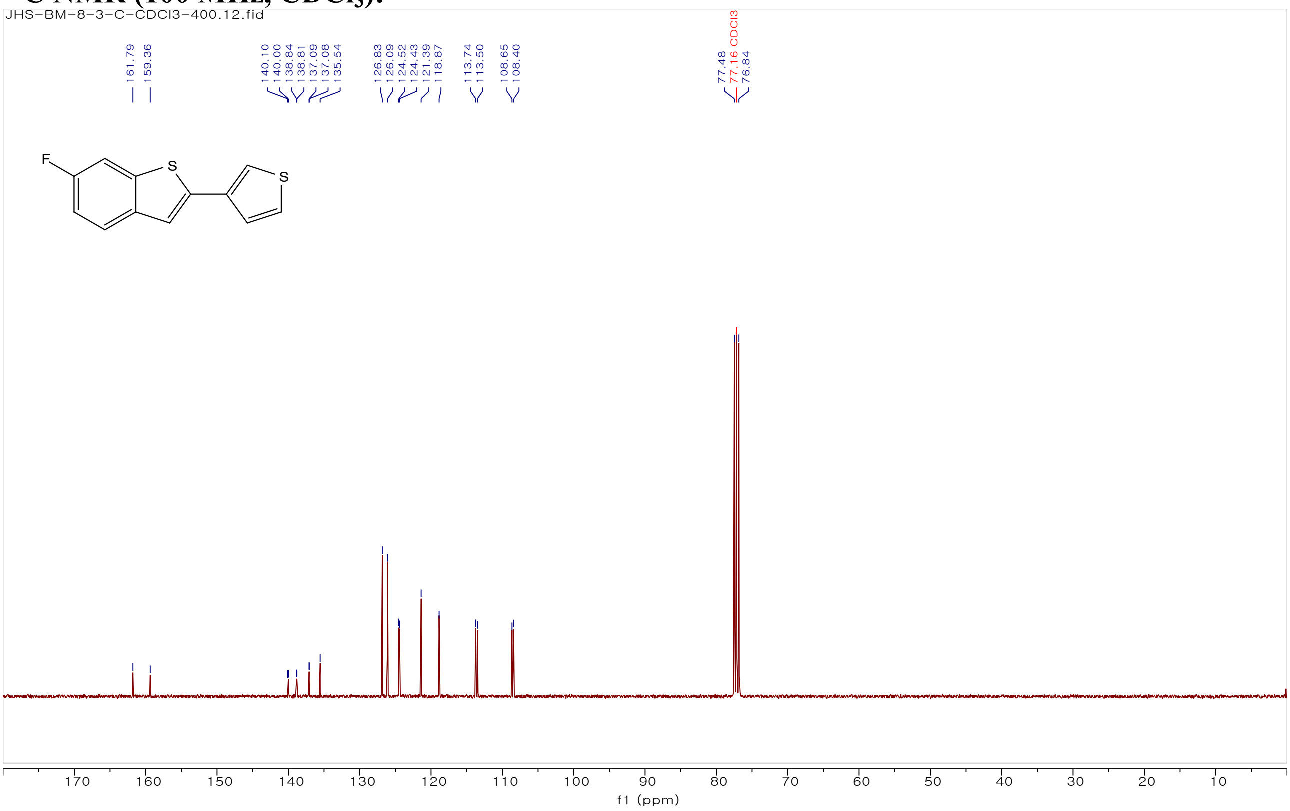


6-fluoro-2-(thiophen-3-yl)benzo[b]thiophene (3cg)

^{1}H NMR (400 MHz, CDCl$_3$):

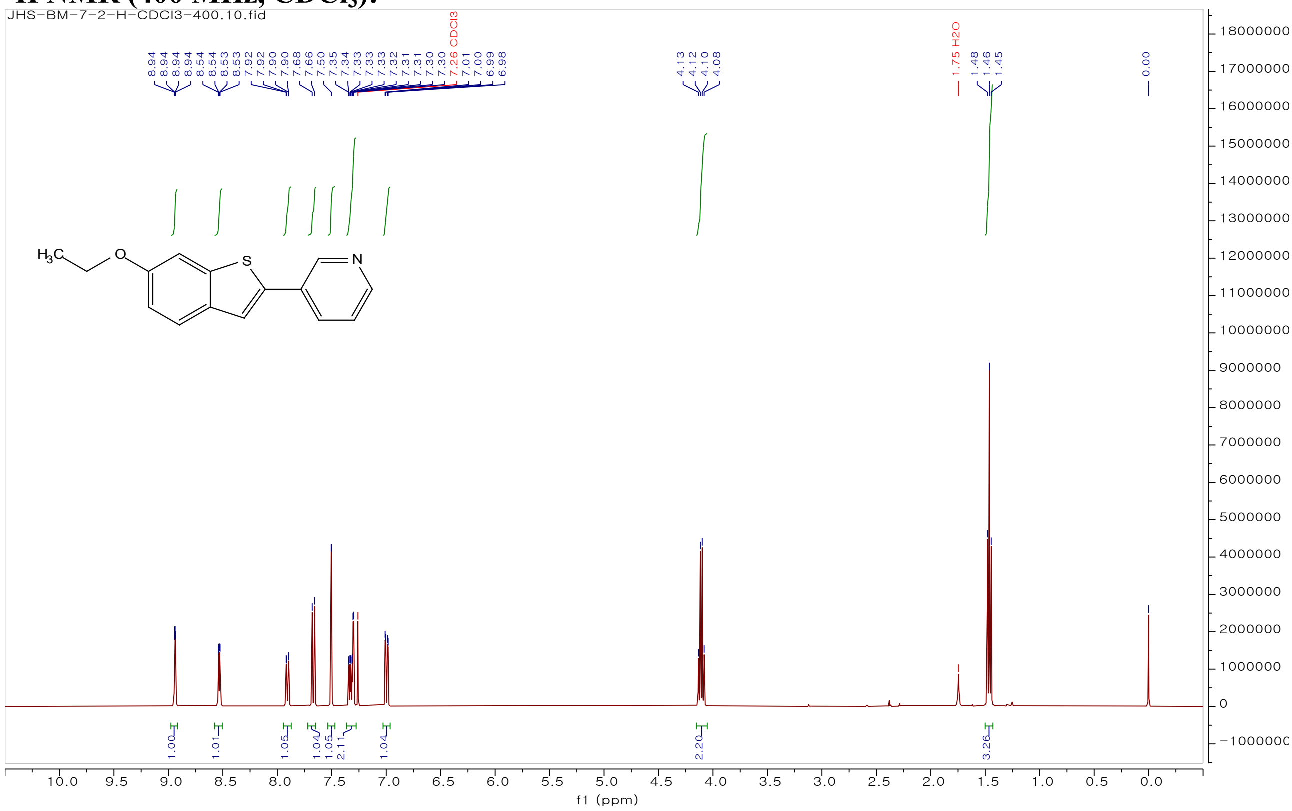


^{13}C NMR (100 MHz, CDCl$_3$):

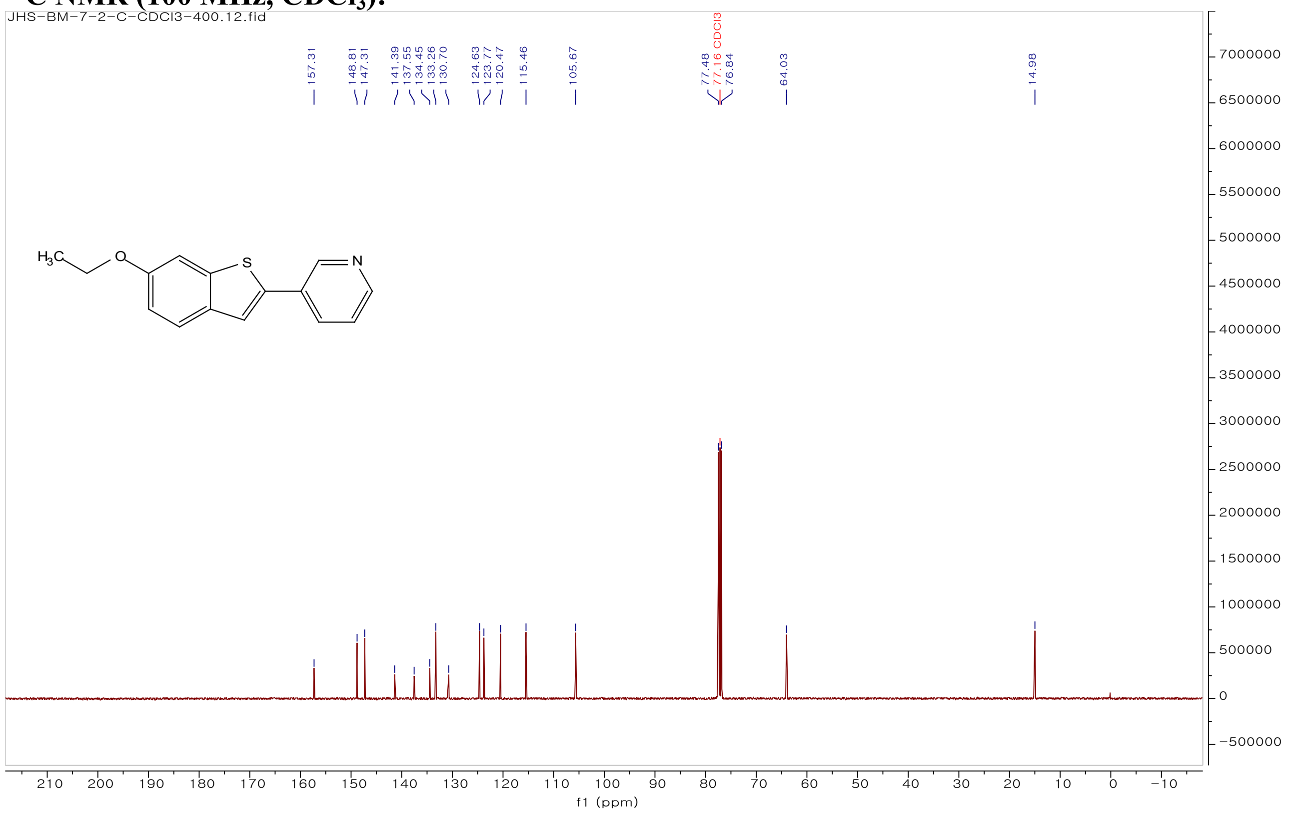


3-(6-ethoxybenzo[b]thiophen-2-yl)pyridine (3bh)

^{1}H NMR (400 MHz, CDCl$_3$):

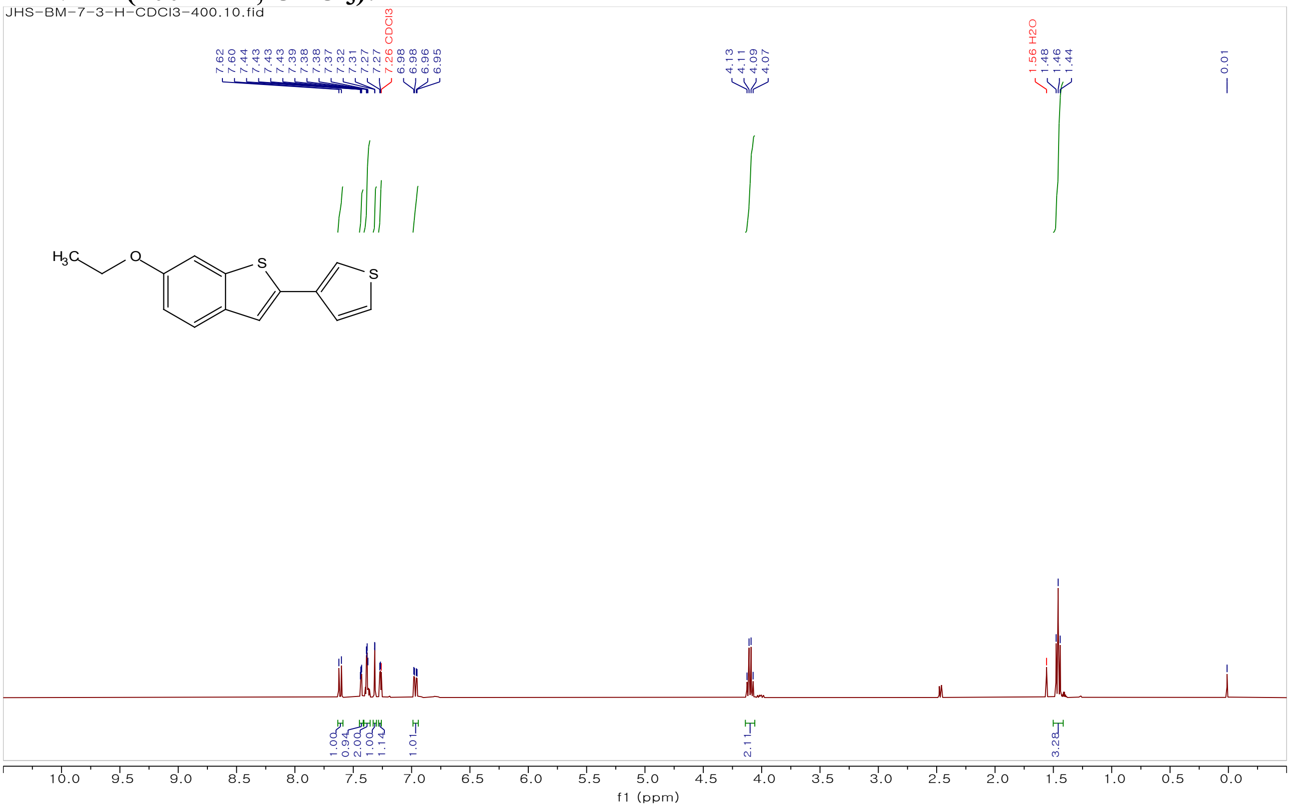


^{13}C NMR (100 MHz, CDCl$_3$):

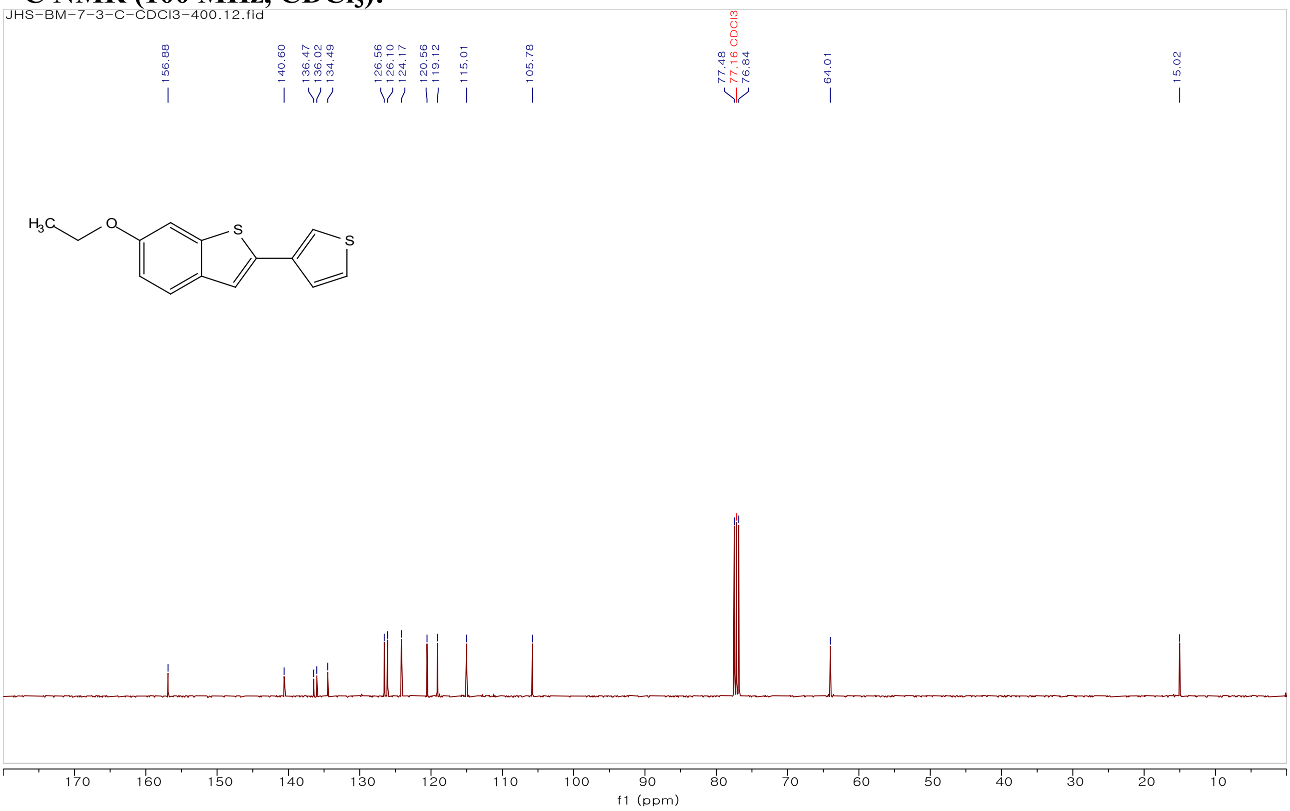


6-ethoxy-2-(thiophen-3-yl)benzo[b]thiophene (3ch)

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

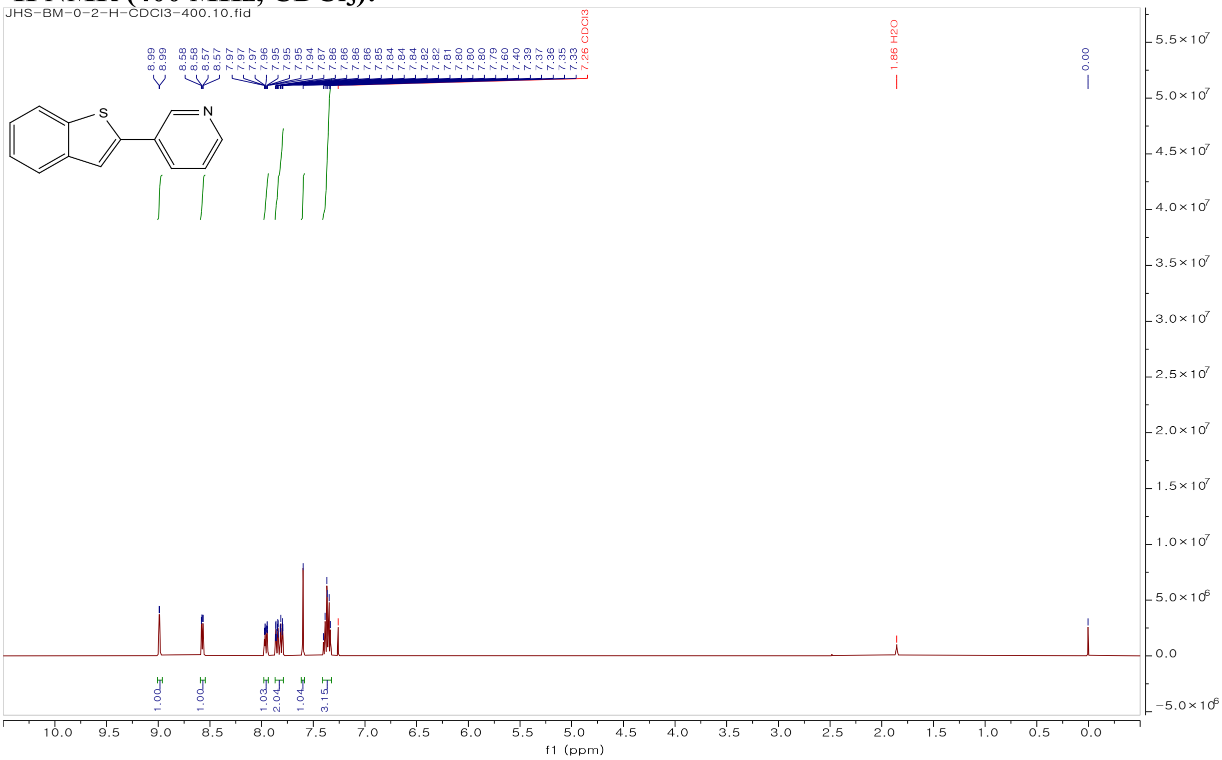


^{13}C NMR (100 MHz, $CDCl_3$):

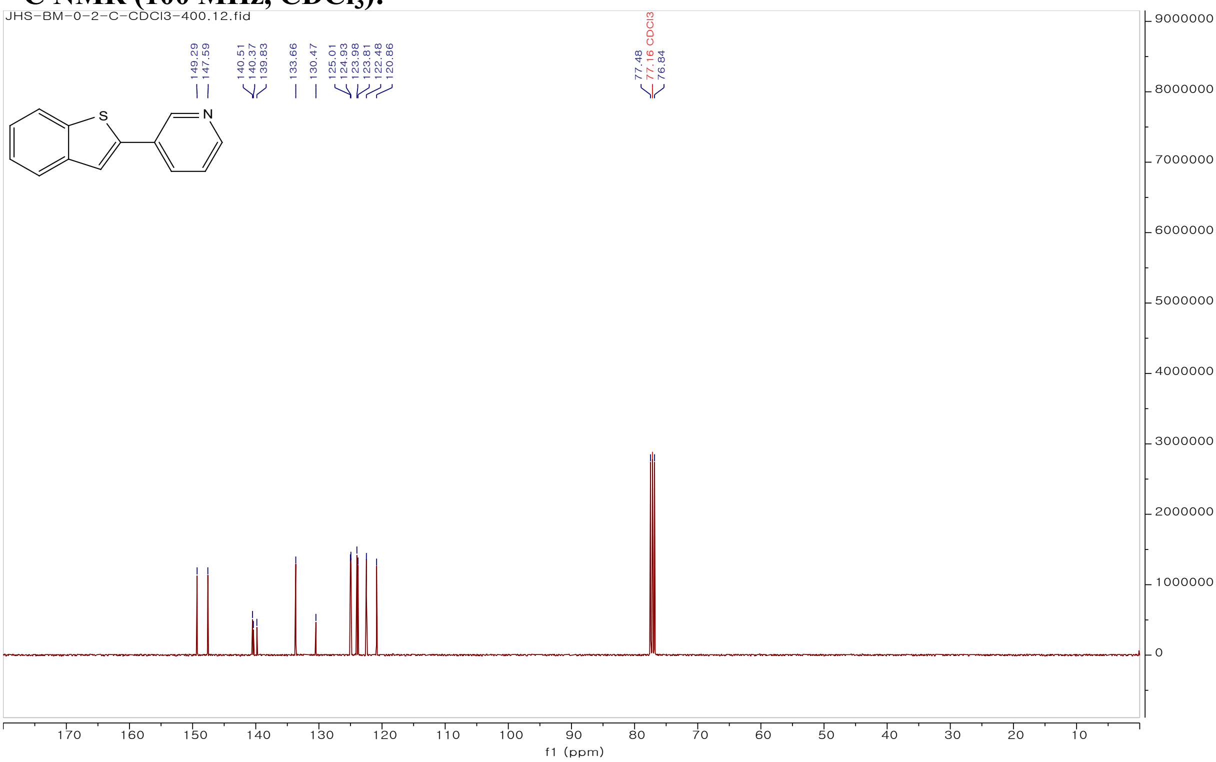


3-(benzo[b]thiophen-2-yl)pyridine (3b)

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

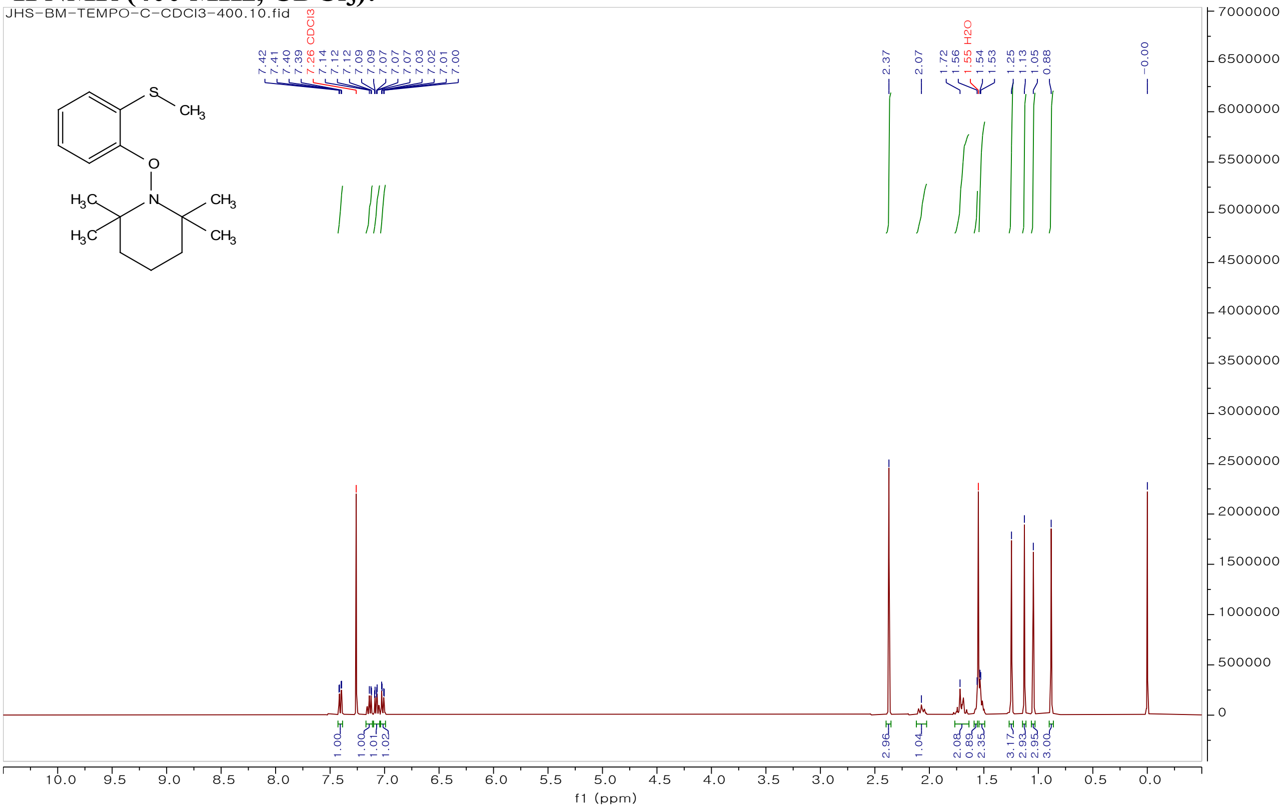


^{13}C NMR (100 MHz, $CDCl_3$):

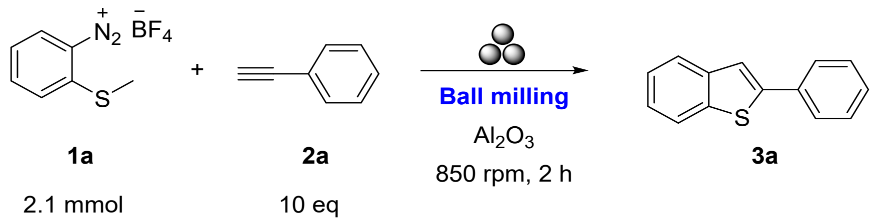


2,2,6,6-Tetramethyl-1-[2-(methylthio)phenoxy]piperidine (4)

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



An optimization study of the number of ZrO_2 balls



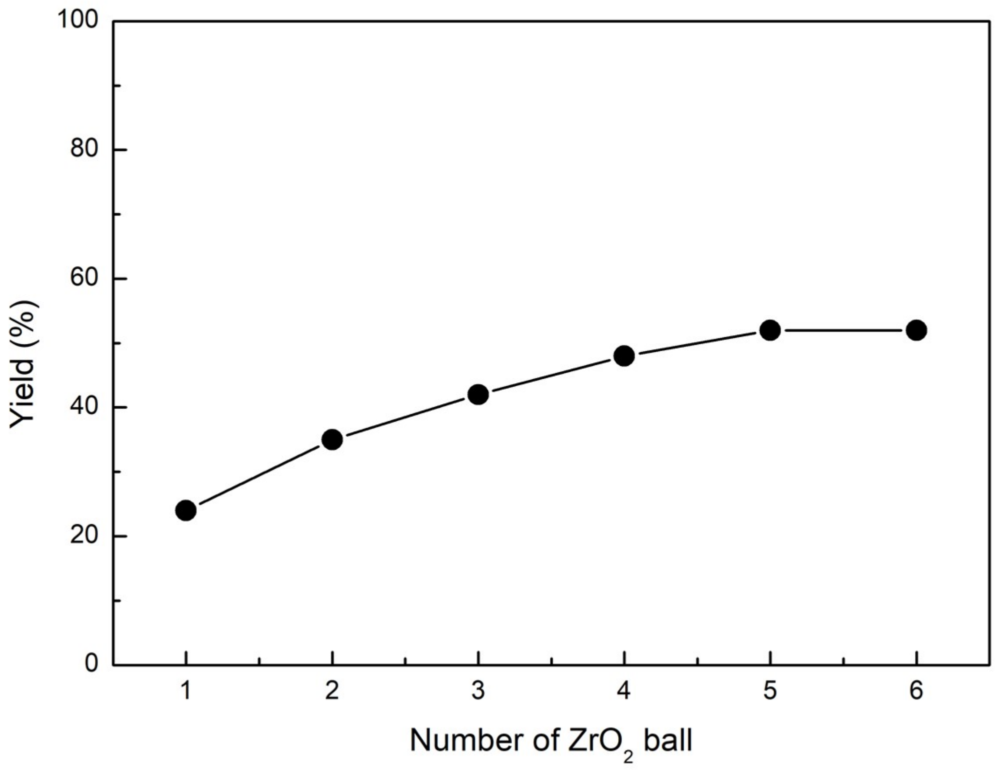
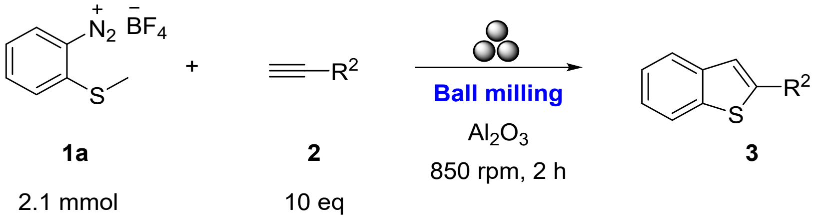
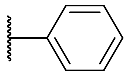
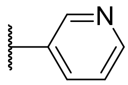
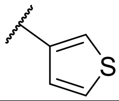
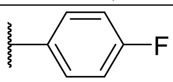
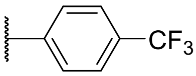
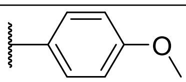
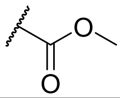
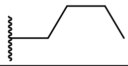
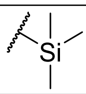


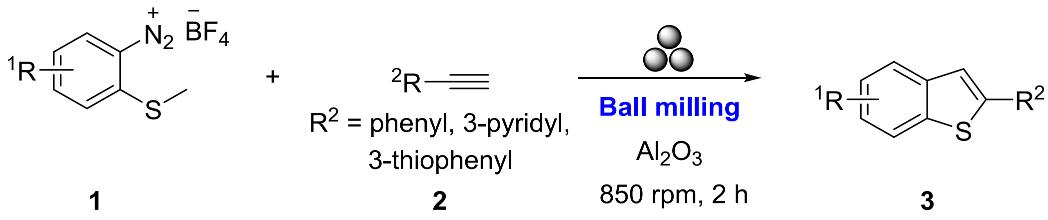
Table S1. An examination of a broad range of ethynyl compounds, including aryl-, heterocyclic-, and alkyl-substituted ethynes (2)



Entry	R^2	**3** (Yield (%))[a]
1		**3a** (53)
2		**3b** (48)
3		**3c** (38)
4		**3d** (27)
5		**3e** (24)
6		**3f** (28)
7		**3g** (31)
8		**3h** (13)[b]
9		**3i** (8)[b]

[a]After column chromatography, [b]Due to its volatility, the yield could not be reliably determined.

Table S2. Comparison of yields obtained in this work with those reported by Koenig and co-workers (photoredox) and Zeng and co-workers (electrochemical) for directly comparable substrates.



Comp. No.	R¹	R²	Yield (%)[a]	Yield (%)[a]	Yield (%)[a]	Notes
			This work (mechano-redox)	Koenig (photo-redox)[b]	Zeng (electro-chem.)[c]	
Aryl-substituted alkynes (R^2 = aryl)						
3a	H	Ph	**53**	75	65	Aryl alkyne; all three methods applicable
3aa	5-Cl	Ph	**33**	65	—	Electron-withdrawing R^1
3ab	6-Cl	Ph	**35**	70	—	Electron-withdrawing R^1
3ac	5-OMe	Ph	**42**	—	—	Electron-donating R^1
3ad	6-OMe	Ph	**25**	63	—	Electron-donating R^1
3ae	6-Me	Ph	**42**	72	—	Electron-donating R^1
3af	6-Br	Ph	**39**	72	—	Halogen substituent
3ag	6-F	Ph	**40**	62	—	Halogen substituent
3ah	6-OEt	Ph	**33**	76	—	Electron-donating R^1
Hetero–heterocyclic products (R^2 = 3-pyridyl)						
3b	H	3-Pyr	**48**	—	35	Hetero–hetero
3ba	5-Cl	3-Pyr	**51**	—	—	Hetero–hetero;

Comp. No.	R¹	R²	Yield (%)[a]	Yield (%)[a]	Yield (%)[a]	Notes
			This work (mechano-redox)	Koenig (photo-redox)[b]	Zeng (electro-chem.)[c]	
						best yield in this work
3bb	6-Cl	3-Pyr	**25**	—	—	Hetero–hetero
3bc	5-OMe	3-Pyr	**49**	—	—	Hetero–hetero
3bd	6-OMe	3-Pyr	**39**	—	—	Hetero–hetero
3be	6-Me	3-Pyr	**36**	—	—	Hetero–hetero
3bf	6-Br	3-Pyr	**20**	—	—	Hetero–hetero
3bg	6-F	3-Pyr	**27**	—	—	Hetero–hetero
3bh	6-OEt	3-Pyr	**38**	—	—	Hetero–hetero
Hetero–heterocyclic products (R² = 3-thienyl)						
3c	H	3-Thio	**38**	62	34	Hetero–hetero
3ca	5-Cl	3-Thio	**42**	—	—	Hetero–hetero
3cb	6-Cl	3-Thio	**39**	—	—	Hetero–hetero
3cc	5-OMe	3-Thio	**20**	—	—	Hetero–hetero
3cd	6-OMe	3-Thio	**41**	—	—	Hetero–hetero
3ce	6-Me	3-Thio	**33**	—	—	Hetero–hetero
3cf	6-Br	3-Thio	**37**	—	—	Hetero–hetero
3cg	6-F	3-Thio	**38**	—	—	Hetero–hetero
3ch	6-OEt	3-Thio	**28**	—	—	Hetero–hetero
Other alkyne substrates						
3d	H	4-F-Ph	**27**	64	—	EW aryl alkyne
3e	H	4-CF_3-Ph	**24**	—	44	Strong EW group
3f	H	4-OMe-Ph	**28**	72	—	ED aryl alkyne

Comp. No.	R¹	R²	Yield (%)[a]	Yield (%)[a]	Yield (%)[a]	Notes
			This work (mechano-redox)	Koenig (photo-redox)[b]	Zeng (electro-chem.)[c]	
3g	H	CO_2Me	**31**	60	—	Electron-poor alkyne
3h	H	*n*-Bu	**13**	30	—	Alkyl alkyne; volatile product
3i	H	TMS	**8**	45	—	Silyl alkyne; volatile product

[a] Isolated yield after column chromatography. Values for this work are from the present manuscript; photoredox yields ([b]) from Hari, Hering, and König, *Org. Lett.* 2012, **14**, 5334–5337; electrochemical yields ([c]) from Lan, Jiang, Little, and Zeng, *J. Electrochem.* 2024, **30**, 2313002.

[b] Photoredox conditions: eosin Y (cat.), DMSO, LED 530 nm, 14 h, 20 °C.

[c] Electrochemical conditions: C felt anode, Ni plate cathode, $n\text{-}Bu_4NBF_4$ (0.3 mmol), DMSO, 25 °C, J = 4 mA/cm².

— = not reported for this substrate combination in the cited reference. EW = electron-withdrawing; ED = electron-donating.

Color key: Green = this work (mechanoredox); Blue = Koenig photoredox; Orange = Zeng electrochemical; — = not reported.

Reference

1. Hari, Durga Prasad; *Organic Letters*, 2012, **14(20)**, 5334-5337.
2. Hodson, Stephen J.; *Journal of Medicinal Chemistry*, 2002, **45(11)**, 2229-2239
3. R. Leardini, G. F. Pedulli et al., *J. Chem. Soc., Chem. Commun.*, 1985, **20**, 1390–1391
4. Lapointe, David; *Journal of Organic Chemistry*, 2011, **76(3)**, 749-759
5. Zang, Hao et al., *Advanced Synthesis & Catalysis*, 2016, **358(11)**, 1746-1752