Supporting Information

Highly substituted benzo[*b*]furan synthesis through substituent migration

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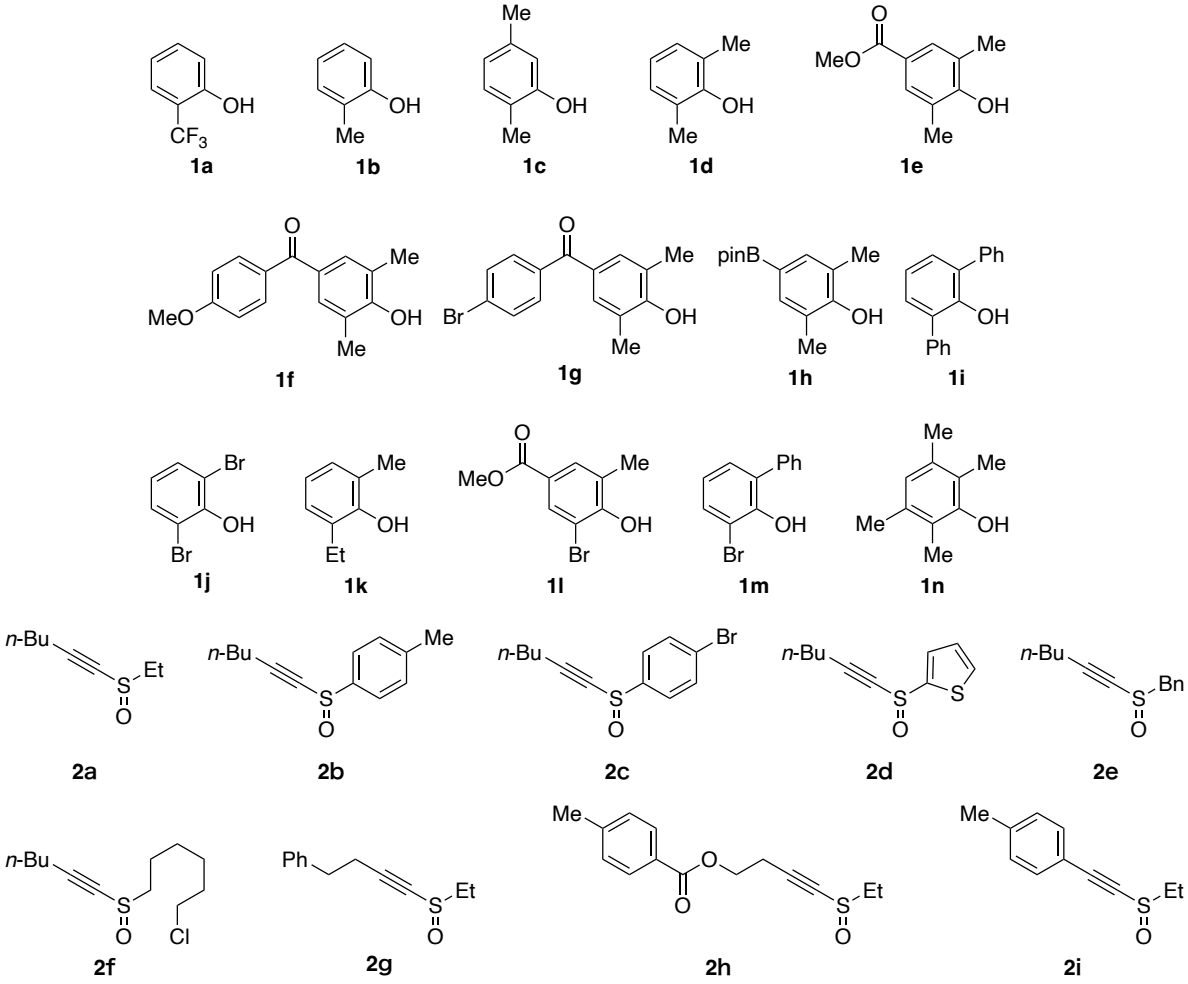
General Information

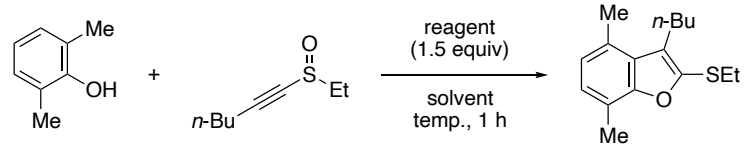
All reactions were performed with dry glassware under atmosphere of argon, unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed on precoated (0.25 mm) silica-gel plates (Merck Chemicals, Silica Gel 60 F254, Cat. No. 1.05715). Column chromatography was conducted using silica-gel (Kanto Chemical Co., Inc., Silica Gel 60N, spherical neutral, particle size 40–50 μm, Cat. No. 37562-85 or particle size 63–210 μm, Cat. No. 37565-85). Preparative TLC (PTLC) was performed on silica gel (Wako Pure Chemical Industries Ltd., Wakogel B-5F, Cat. No. 230-00043). Melting points (Mp) were measured on an OptiMelt MPA100 (Stanford Research Systems), and are uncorrected. ^{1}H NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 400 MHz. ^{13}C NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 101 MHz. ^{19}F NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 376 MHz. All NMR measurements were carried out at 25 ºC. $CDCl_3$, CD_2Cl_2, or DMSO-d_6 was used as a solvents for obtaining NMR spectra. Chemical shifts (δ) are given in parts per million (ppm) downfield from the solvent peak (δ 7.26 for ^{1}H NMR in $CDCl_3$, δ 77.0 for ^{13}C NMR in $CDCl_3$; δ 5.32 for ^{1}H NMR in CD_2Cl_2, δ 53.5 for ^{13}C NMR in CD_2Cl_2; δ 2.54 for ^{1}H NMR in DMSO-d_6, δ 40.5 for ^{13}C NMR in DMSO-d_6) as an internal reference with coupling constants (*J*) in hertz (Hz). The abbreviations s, d, t, q, and m signify singlet, doublet, triplet, quartet, and multiplet, respectively. High-resolution mass spectra (HRMS) were measured on a JEOL JMS-T100CS "AccuTOF CS" mass spectrometer under positive electrospray ionization (ESI^+) conditions or negative electrospray ionization (ESI^-) conditions, or JMS-700 (JEOL, Tokyo, Japan) mass spectrometer under electron impact ionization (EI) conditions or fast atom bombardment (FAB) conditions.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Methyl 4-hydroxy-3,5-dimethylbenzoate (**1e**),[S1] (4-hydroxy-3,5-dimethylphenyl)(4-methoxyphenyl)methanone (**1f**),[S2] (4-bromophenyl)(4-hydroxy-3,5-dimethylphenyl)methanone (**1g**),[S3] 2,6-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol,[S4] 3-bromo-[1,1'-biphenyl]-2-ol (**1m**),[S5] 2,3,5,6-tetramethylphenol (**1n**),[S6] 1-(ethylsulfinyl)hex-1-yne (**2a**),[S7] 1-(hex-1-yn-1-ylsulfinyl)-4-methylbenzene (**2b**),[S7] 1-bromo-4-(hex-1-yn-1-ylsulfinyl)benzene (**2c**),[S7] ((hex-1-yn-1-ylsulfinyl)methyl)benzene (**2e**),[S7] 1-((6-chlorohexyl)sulfinyl)hex-1-yne (**2f**),[S7] (4-(ethylsulfinyl)but-3-yn-1-yl)benzene (**2g**),[S7] 4-(ethylsulfinyl)but-3-yn-1-yl 4-methylbenzoate (**2h**),[S7] and 1-((ethylsulfinyl)ethynyl)-4-methylbenzene (**2i**)[S7] were prepared according to the reported methods.

Structures of Phenols 1 and Alkynyl Sulfoxides 2



Optimization of Reaction Conditions



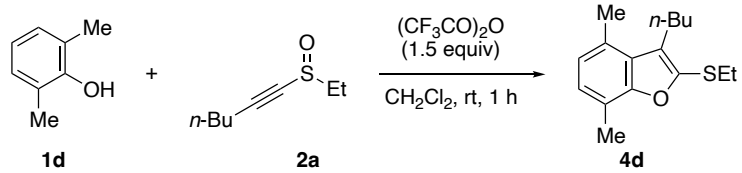
1d **2a** **4d**

entry	reagent	solvent	temp.	**4d** / %[a]
1	$(CF_3CO)_2O$	CH_2Cl_2	rt	64[b]
2	Tf_2O with 2,5-(*t*-Bu)$_2$pyridine (3.0 equiv.)	CH_2Cl_2	rt	56
3	$(CF_3CO)_2O$	$(CH_2Cl)_2$	rt	55
4	$(CF_3CO)_2O$	$CHCl_3$	rt	0
5	$(CF_3CO)_2O$	Et_2O	rt	59
6	$(CF_3CO)_2O$	$MeNO_2$	rt	31
7	$(CF_3CO)_2O$	MeCN	rt	43
8	$(CF_3CO)_2O$	CH_2Cl_2	40 °C	60
9	$(CF_3CO)_2O$	CH_2Cl_2	0 °C	62
10	$(CF_3CO)_2O$	CH_2Cl_2	–78 °C	40

[a] ^{1}H NMR yields. [b] Isolated yield.

Experimental Procedures

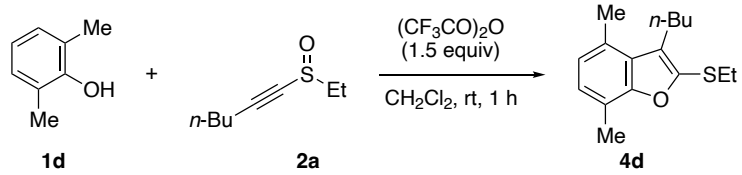
A typical procedure for the synthesis of benzo[b]furans



To a mixture of 2,6-dimethylphenol (**1d**) (24.4 mg, 0.200 mmol, 2.0 equiv) and 1-(ethylsulfinyl)hex-1-yne (**2a**) (15.9 mg, 0.100 mmol) in dichloromethane (1.0 mL) was added trifluoroacetic anhydride (20.9 μL, 0.150 mmol, 1.5 equiv) at room temperature. After stirring for 1 h at the same temperature, to the mixture was added an aqueous saturated solution of sodium bicarbonate (5 mL). The mixture was extracted with dichloromethane (15 mL × 3). The combined organic extract was washed with brine (20 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/CH_2Cl_2 = 10/1) to give 3-butyl-2-(ethylthio)-4,7-dimethylbenzo[*b*]furan (**4d**) (16.9 mg, 64.4 μmol, 64%) as a colorless oil.

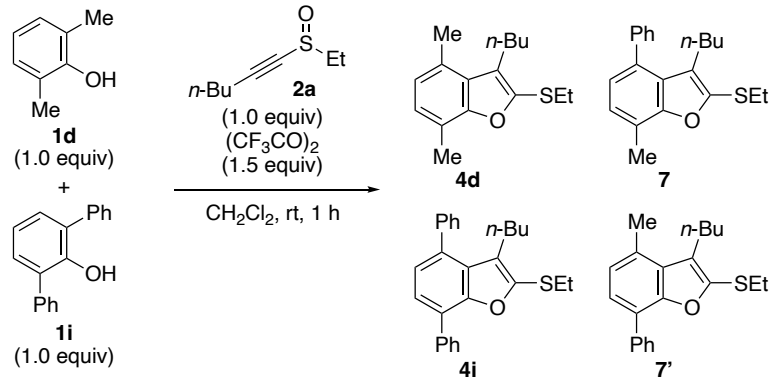
According to the procedure for preparing 3-butyl-2-(ethylthio)-7-(trifluoromethyl)benzofuran (**3a**), 3-butyl-2-(ethylthio)-7-methylbenzofuran (**3b**), 3-butyl-2-(ethylthio)-4-methylbenzofuran (**4b**), 3-butyl-2-(ethylthio)-4,6-dimethylbenzofuran (**3c**), 3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran (**4c**), 3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran (**4d**), methyl 3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-carboxylate (**4e**), (3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-yl)(4-methoxyphenyl)methanone (**4f**), (4-bromophenyl)(3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-yl)methanone (**4g**), 2-(3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4h**), 3-butyl-2-(ethylthio)-4,7-diphenylbenzofuran (**4i**), 4,7-dibromo-3-butyl-2-(ethylthio)benzofuran (**4j**), 3-butyl-7-ethyl-2-(ethylthio)-4-methylbenzofuran (**4k**), 3-butyl-4-ethyl-2-(ethylthio)-7-methylbenzofuran (**4k'**), methyl 7-bromo-3-butyl-2-(ethylthio)-4-methylbenzofuran-5-carboxylate (**4l**), methyl 3-butyl-4,7-dimethyl-2-(*p*-tolylthio)benzofuran-5-carboxylate (**4m**), methyl 2-((4-bromophenyl)thio)-3-butyl-4,7-dimethylbenzofuran-5-carboxylate (**4n**), 3-butyl-4,7-dimethyl-2-(thiophen-2-ylthio)benzofuran (**4o**), methyl 2-(benzylthio)-3-butyl-4,7-dimethylbenzofuran-5-carboxylate (**4p**), methyl 3-butyl-2-((6-chlorohexyl)thio)-4,7-dimethylbenzofuran-5-carboxylate (**4q**), methyl 2-(ethylthio)-4,7-dimethyl-3-phenethylbenzofuran-5-carboxylate (**4r**), methyl 2-(ethylthio)-4,7-dimethyl-3-(2-((4-methylbenzoyl)oxy)ethyl)benzofuran-5-carboxylate (**4s**), methyl 2-(ethylthio)-4,7-dimethyl-3-(p-tolyl)benzofuran-5-carboxylate (**4t**), and 3-butyl-7-(4-methoxyphenyl)-4-phenyl-2-(p-tolyl)benzofuran (**11**) were prepared from the corresponding phenols and alkynyl sulfoxides.

Synthesis of benzo[b]furans in 1 mmol scale



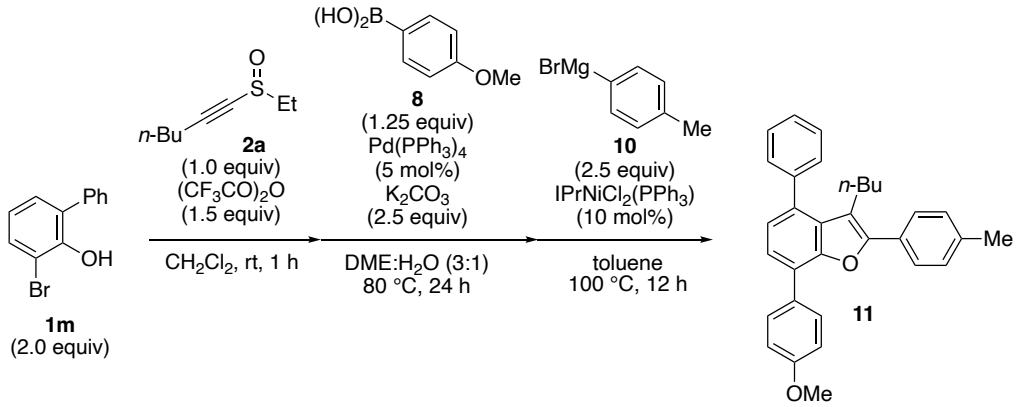
To a mixture of 2,6-dimethylphenol (**1d**) (244 mg, 2.00 mmol, 2.0 equiv) and 1-(ethylsulfinyl)hex-1-yne (**2a**) (159 mg, 1.00 mmol) in dichloromethane (10.0 mL) was added trifluoroacetic anhydride (209 μL, 1.50 mmol, 1.5 equiv) at room temperature. After stirring for 1 h at the same temperature, to the mixture was added an aqueous saturated solution of sodium bicarbonate (10 mL). The mixture was extracted with dichloromethane (15 mL × 3). The combined organic extract was washed with brine (20 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica-gel 12 g, *n*-hexane/CH_2Cl_2 = 10/1) to give 3-butyl-2-(ethylthio)-4,7-dimethylbenzo[*b*]furan (**4d**) (152 mg, 0.580 mmol, 58%) as a colorless oil.

*Crossover experiment for the reaction of alkynyl sulfoxide **2a** with 2,6-disubstituted phenols **1d** and **1i***



To a mixture of 2,6-dimethylphenol (**1d**) (18.4 mg, 0.151 mmol, 1.0 equiv), 2,6-diphenylphenol (**1i**) (37.1 mg, 0.151 mmol, 1.0 equiv) and 1-(ethylsulfinyl)hex-1-yne (**2a**) (23.9 mg, 0.151 mmol) in dichloromethane (1.5 mL) was added trifluoroacetic anhydride (31.3 μL, 0.225 mmol, 1.5 equiv) at room temperature. After stirring for 1 h at the same temperature, to the mixture was added an aqueous saturated solution of sodium bicarbonate (5 mL). The mixture was extracted with dichloromethane (15 mL × 3). The combined organic extract was washed with brine (20 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/CH_2Cl_2 = 5/1) to give 3-butyl-2-(ethylthio)-4,7-dimethylbenzo[*b*]furan (**4d**) (18.4 mg, 70.1 μmol, 46%) as a colorless oil and 3-butyl-2-(ethylthio)-4,7-diphenylbenzo[*b*]furan (**4i**) (4.9 mg, 13 μmol, 9%) as a pale yellow oil.

*Synthesis of 3-butyl-7-(4-methoxyphenyl)-4-phenyl-2-(4-tolyl)benzo[b]furan (**11**)*



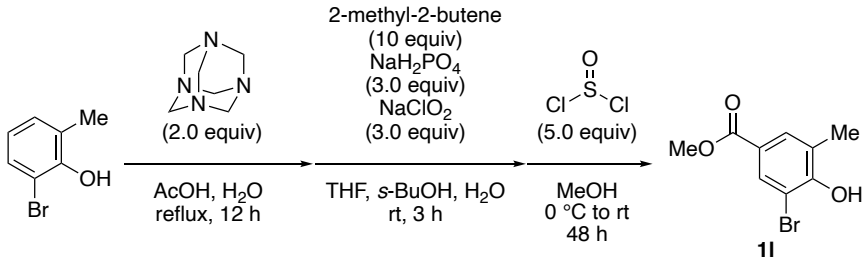
To a mixture of 3-bromo-[1,1'-biphenyl]-2-ol (**1m**) (150 mg, 0.602 mmol, 2.0 equiv) and 1-(ethylsulfinyl)hex-1-yne (**2a**) (47.8 mg, 0.302 mmol) in dichloromethane (3.0 mL) was added trifluoroacetic anhydride (62.5 μL, 0.450 mmol, 1.5 equiv) at room temperature. After stirring for 1 h at the same temperature, to the mixture was added an aqueous saturated solution of sodium bicarbonate (10 mL). The mixture was extracted with dichloromethane (15 mL × 3). The combined organic extract was washed with brine (20 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure and used for next reaction without further purification.

To the resulting mixture were added (4-methoxyphenyl)boronic acid (**8**) (57.0 mg, 0.375 mmol, 1.25 equiv), potassium carbonate (104 mg, 0.752 mmol, 2.50 equiv), and $Pd(PPh_3)_4$ (17.3 mg, 15.0 μmol, 5 mol%) dissolved in 1,2-dimethoxyethane (2.25 mL), and water (750 μL) at room temperature. After stirring for 24 h at 80 °C, to the mixture was added water (10 mL). The mixture was extracted with EtOAc (15 mL × 2). The combined organic extract was washed with brine (20 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/CH_2Cl_2 = 5/1) to give 3-butyl-2-(ethylthio)-7-(4-methoxyphenyl)-4-phenylbenzofuran (**9**) (49.1 mg, 118 μmol, 39% over two steps) as a colorless solid.

To a mixture of 3-butyl-2-(ethylthio)-7-(4-methoxyphenyl)-4-phenylbenzofuran (**9**) (21.6 mg, 51.8 μmol) and $IPrNiCl_2(PPh_3)$ (3.9 mg, 5.0 μmol, 10 mol%) in toluene (500 μL) was added 4-tolylmagnesium bromide (**10**) (120 μL, 126 μmol, 1.05 M in THF, 2.5 equiv) at room temperature. After stirring for 12 h at 100 °C, to the mixture

was added an aqueous 1 M HCl (10 mL). The mixture was extracted with EtOAc (15 mL × 2). The combined organic extract was washed with brine (20 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/toluene = 5/1) to give 3-butyl-7-(4-methoxyphenyl)-4-phenyl-2-(4-tolyl)benzo[*b*]furan (**11**) (16.4 mg, 36.7 μmol, 71%) as a colorless solid.

*A typical procedure for the synthesis of methyl 3-bromo-4-hydroxy-5-methylbenzoate (**1l**)*

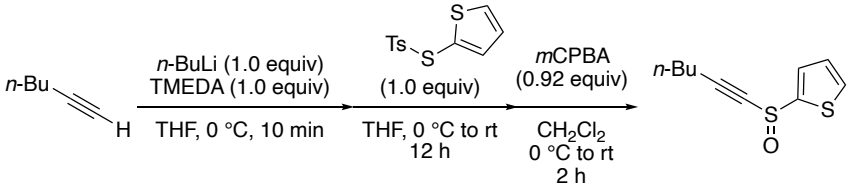


To a mixture of 2-bromo-6-methylphenol (1.87 g, 10.0 mmol) and hexamethylenetetramine (2.80 g, 20.0 mmol, 2.0 equiv) in acetic acid (17 mL) was added water (4.0 mL) at room temperature. After stirring for 12 h at reflux (bath temperature: 110 °C), the mixture was cooled to room temperature, and poured into ice water (30 mL). A precipitate formed was separated and recrystallized from toluene (30 mL) to give 3-bromo-4-hydroxy-5-methylbenzaldehyde (679 mg, 3.16 mmol, 32%) as a brown solid.

To a mixture of 3-bromo-4-hydroxy-5-methylbenzaldehyde (431 mg, 2.00 mmol), *s*-BuOH (800 μL), water (800 μL), and 2-methyl-2-butene (2.1 mL, 20.0 mmol, 10 equiv) dissolved in THF (3.2 mL) were added NaH_2PO_4 (720 mg, 6.00 mmol, 3.0 equiv) and $NaClO_2$ (ca. 80%, 678 mg, ca. 6.0 mmol, ca. 3.0 equiv) at room temperature. After stirring for 3 h at the same temperature, to the mixture was added an aqueous saturated NH_4Cl solution (10 mL). The mixture was extracted with EtOAc (15 mL × 2). The combined organic extract was washed with brine (20 mL), and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica-gel 20 g, *n*-hexane/EtOAc = 2/1) to give 3-bromo-4-hydroxy-5-methylbenzoic acid (290 mg, 1.26 mmol, 63%) as a colorless solid.

To a solution of 3-bromo-4-hydroxy-5-methylbenzoic acid (140 mg, 0.606 mmol) dissolved in methanol (2.5 mL) was added thionyl chloride (216 μL, 3.00 mmol, 5.0 equiv) at 0 °C. After stirring for 10 min at the same temperature, the mixture was allowed to warm to room temperature. After stirring for 48 h at room temperature, to the mixture was added solid sodium bicarbonate until gas evolution ceased. The suspension was concentrated under reduced pressure. To the resulting mixture was added water (10 mL). The residue was extracted with EtOAc (10 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure to give methyl 3-bromo-4-hydroxy-5-methylbenzoate (**1l**) (139 mg, 0.567 mmol, 93%) as a brown solid, which was used for next reaction without further purification.

*Synthesis of 2-(hex-1-yn-1-ylsulfinyl)thiophene (**2d**)*



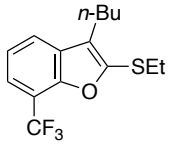
To a mixture of 1-hexyne (319 mg, 3.88 mmol) and *N,N,N',N'*-tetramethylethylenediamine (TMEDA) (451 mg, 3.88 mmol, 1.0 equiv) dissolved in THF (8.0 mL) was added *n*-BuLi (2.66 M in *n*-hexane, 1.45 mL, 3.88 mmol, 1.0 equiv) at 0 °C. After stirring for 10 min at the same temperature, to the mixture was added *S*-(thiophen-2-yl) 4-methylbenzenesulfonothioate (1.05 g, 3.88 mmol, 1.0 equiv) dissolved in THF (3.9 mL). After stirring for 10 min at the same temperature, the mixture was allowed to warm to room temperature. After stirring for 12 h at room temperature, the mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (30 mL). The mixture was washed with water (10 mL) and brine (10 mL), and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 35 g, *n*-hexane) to give 2-(hex-1-yn-1-ylthio)thiophene (492 mg, 2.51 mmol, 65%) as a pale yellow oil.

To a solution of 2-(hex-1-yn-1-ylthio)thiophene (320 mg, 1.63 mmol) in CH_2Cl_2 (7.5 mL) was slowly added *m*CPBA (ca. 77%, 340 mg, ca. 1.5 mmol, ca. 0.92 equiv) at 0 °C. After stirring for 10 min at the same temperature, the mixture was allowed to warm to room temperature. After stirring for 2 h at room temperature, to the mixture was added an aqueous saturated solution of potassium carbonate (5 mL) and an aqueous saturated solution of

sodium thiosulfate (5 mL). The mixture was extracted with CH_2Cl_2 (10 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 10 g, *n*-hexane/EtOAc = 4/1) to give 2-(hex-1-yn-1-ylsulfinyl)thiophene (**2d**) (239 mg, 1.13 mmol, 69%) as a colorless oil.

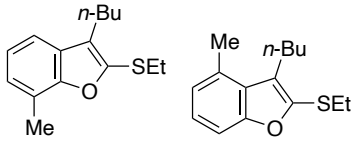
Characterization Data of New Compounds

3-Butyl-2-(ethylthio)-7-(trifluoromethyl)benzofuran (**3a**)



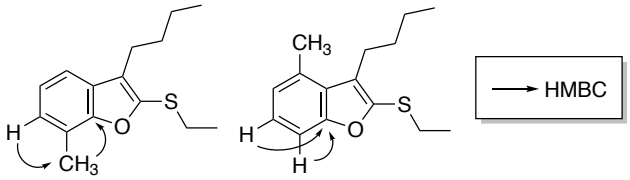
Yield: 85% (51.6 mg, 0.171 mmol); Colorless oil; TLC R_f 0.71 (*n*-hexane/CH_2Cl_2 = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.95 (t, 3H, *J* = 7.3 Hz), 1.28–1.45 (m, 5H), 1.59–1.69 (m, 2H), 2.76 (t, 2H, *J* = 7.6 Hz), 2.95 (q, 2H, *J* = 7.4 Hz), 7.28 (dd, 1H, *J* = 7.8, 7.8 Hz), 7.50 (d, 1H, *J* = 7.8 Hz), 7.66 (d, 1H, *J* = 7.8 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.9, 15.4, 22.5, 24.0, 29.2, 31.7, 114.2 (q, J_{C-F} = 34.0 Hz), 121.3 (q, J_{C-F} = 4.5 Hz), 121.9, 123.2, 123.3 (q, J_{C-F} = 271 Hz), 124.0, 130.7, 148.1, 151.3 (q, J_{C-F} = 1.6 Hz); ^{19}F NMR ($CDCl_3$, 377 MHz): δ –61.0 (s, 3F); IR (NaCl, cm^{-1}) 1059, 1099, 1132, 1150, 1168, 1225, 1319, 1427, 2932, 2960; HRMS (EI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{15}H_{17}F_3OS^{\cdot+}$ 302.0952; Found 302.0951.

3-Butyl-2-(ethylthio)-7-methylbenzofuran (**3b**)
3-Butyl-2-(ethylthio)-4-methylbenzofuran (**4b**)

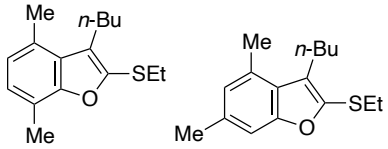


An inseparable mixture of **3b** and **4b** (65:35) was obtained. Yield: 82% (50.4 mg, 0.203 mmol); Colorless oil; TLC R_f 0.81 (*n*-hexane/CH_2Cl_2 = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz) for **3b**: δ 0.96 (t, 3H, *J* = 7.4 Hz), 1.31 (t, 3H, *J* = 7.4 Hz), 1.34–1.45 (m, 2H), 1.59–1.72 (m, 2H), 2.52 (s, 3H), 2.77 (t, 2H, *J* = 7.6 Hz), 2.91 (q, 2H, *J* = 7.4 Hz), 7.09 (d, 1H, *J* = 7.3 Hz), 7.13 (dd, 1H, *J* = 7.3, 7.3 Hz), 7.35 (d, 1H, *J* = 7.3 Hz); for **4b**: δ 0.98 (t, 3H, *J* = 7.2 Hz), 1.30 (t, 3H, *J* = 7.4 Hz), 1.39–1.52 (m, 2H), 1.54–1.66 (m, 2H), 2.64 (s, 3H), 2.86 (t, 2H, *J* = 8.0 Hz), 2.90 (q, 2H, *J* = 7.4 Hz), 6.97 (d, 1H, *J* = 7.7 Hz), 7.16 (dd, 1H, *J* = 7.7, 7.7 Hz), 7.27 (d, 1H, *J* = 7.7 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz) for **3b**: δ 13.9, 15.0, 15.3, 22.5, 24.4, 29.5, 31.9, 117.0, 121.2, 122.3, 125.4, 125.9, 128.4, 145.4, 154.7; for **4b**: δ 13.9, 15.3, 19.1, 22.5, 25.4, 29.3, 33.9, 108.7, 124.0, 124.3, 126.2, 127.1, 131.1, 145.7, 155.9; IR (NaCl, cm^{-1}) 1072, 1083, 1263, 1414, 1454, 2859, 2870, 2929, 2958; HRMS (EI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{15}H_{20}OS^{\cdot+}$ 248,1235; Found 248,1237.

The regiochemistries of **3b** and **4b** were determined by the HMBC experiments.

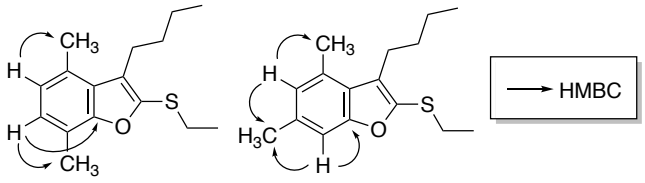


3-Butyl-2-(ethylthio)-4,6-dimethylbenzofuran (**3c**)
3-Butyl-2-(ethylthio)-4,7-dimethylbenzofuran (**4c**)

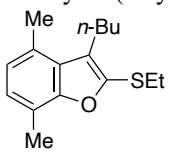


An inseparable mixture of **3c** and **4c** (35:65) was obtained. Yield: 70% (46.5 mg, 0.177 mmol); Colorless oil; TLC R_f 0.80 (*n*-hexane/CH_2Cl_2 = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz) for **3c**: δ 0.97 (t, 3H, *J* = 7.3 Hz), 1.31 (t, 3H, *J* = 7.4 Hz), 1.38–1.51 (m, 2H), 1.53–1.64 (m, 2H), 2.47 (s, 3H), 2.60 (s, 3H), 2.78–2.94 (m, 4H), 6.87 (d, 1H, *J* = 7.4 Hz), 6.96 (d, 1H, *J* = 7.4 Hz); for **4c**: δ 0.97 (t, 3H, *J* = 7.3 Hz), 1.28 (t, 3H, *J* = 7.4 Hz), 1.38–1.51 (m, 2H), 1.53–1.64 (m, 2H), 2.41 (s, 3H), 2.59 (s, 3H), 2.78–2.94 (m, 4H), 6.81 (s, 1H), 7.08 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz) for **3c**: δ 14.0, 14.8, 15.4, 18.9, 22.6, 25.5, 29.5, 34.0, 118.8, 124.0, 125.2, 126.59, 126.61, 128.4, 145.4, 154.9; for **4c**: δ 14.0, 15.3, 19.1, 21.5, 22.6, 25.5, 29.5, 34.0, 109.0, 124.7, 125.6, 126.4, 130.6, 134.7, 144.8, 156.4; IR (NaCl, cm^{-1}) 837, 1059, 1085, 1261, 1378, 1455, 2860, 2870, 2928, 2958; HRMS (EI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{16}H_{22}OS^{\cdot+}$ 262.1391; Found 262.1392.

The regiochemistries of **3c** and **4c** were determined by the HMBC experiments.

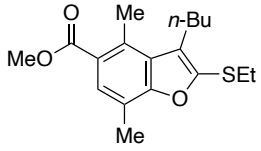


3-Butyl-2-(ethylthio)-4,7-dimethylbenzofuran (**4d** (= **3c**))



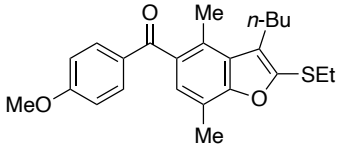
Yield: 64% (16.9 mg, 64.4 μmol); Colorless oil; TLC R_f 0.62 (*n*-hexane/CH_2Cl_2 = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.97 (t, 3H, *J* = 7.3 Hz), 1.31 (t, 3H, *J* = 7.4 Hz), 1.39–1.51 (m, 2H), 1.52–1.64 (m, 2H), 2.47 (s, 3H), 2.60 (s, 3H), 2.80–2.94 (m, 4H), 6.87 (d, 1H, *J* = 7.4 Hz), 6.96 (d, 1H, *J* = 7.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 14.0, 14.8, 15.3, 18.9, 22.6, 25.4, 29.4, 34.0, 118.7, 123.9, 125.1, 126.5, 126.6, 128.4, 145.3, 154.8; IR (NaCl, cm^{-1}) 803, 960, 1067, 1097, 1262, 1381, 1455, 1504, 2870, 2928, 2956; HRMS (FAB) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{16}H_{22}OS^{\cdot+}$ 262.1391; Found 262.1391.

Methyl 3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-carboxylate (**4e**)



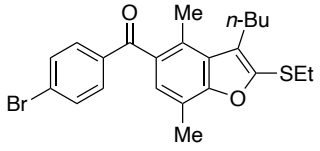
Yield: 79% (38.2 mg, 0.119 mmol); Colorless oil; TLC R_f 0.74 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.96 (t, 3H, *J* = 7.3 Hz), 1.30 (t, 3H, *J* = 7.4 Hz), 1.37–1.49 (m, 2H), 1.51–1.63 (m, 2H), 2.46 (s, 3H), 2.80 (s, 3H), 2.84–2.97 (m, 4H), 3.90 (s, 3H), 7.60 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.9, 14.7, 15.3, 16.2, 22.5, 25.8, 29.3, 33.6, 51.8, 118.5, 124.8, 127.0, 127.4, 127.7, 131.9, 147.0, 156.3, 168.8; IR (NaCl, cm^{-1}) 1045, 1159, 1195, 1245, 1275, 1342, 1434, 1721, 2930, 2955; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{24}NaO_3S^+$ 343.1344; Found 343.1344.

(3-Butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-yl)(4-methoxyphenyl)methanone (**4f**)



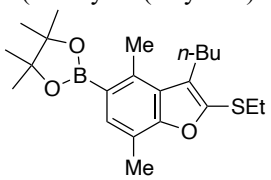
Yield: 86% (51.9 mg, 0.131 mmol); Colorless solid; Mp 80–82 °C; TLC R_f 0.18 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.95 (t, 3H, *J* = 7.3 Hz), 1.32 (t, 3H, *J* = 7.4 Hz), 1.37–1.49 (m, 2H), 1.51–1.63 (m, 2H), 2.46 (s, 3H), 2.50 (s, 3H), 2.86 (t, 2H, *J* = 7.8 Hz), 2.92 (q, 2H, *J* = 7.4 Hz), 3.87 (s, 3H), 6.87–6.96 (AA'BB', 2H), 6.99 (s, 1H), 7.75–7.87 (AA'BB', 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.9, 14.7, 15.3, 16.0, 22.5, 25.5, 29.3, 33.8, 55.5, 113.6, 118.2, 125.4, 126.8, 127.1, 127.2, 131.1, 132.5, 134.4, 146.8, 155.2, 163.5, 197.9; IR (NaCl, cm^{-1}) 1079, 1166, 1262, 1346, 1455, 1601, 1647; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{24}H_{28}NaO_3S^+$ 419.1657; Found 419.1651.

(4-Bromophenyl)(3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-yl)methanone (**4g**)



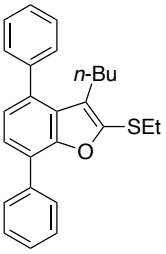
Yield: 81% (55.2 mg, 0.124 mmol); Colorless solid; Mp 58–60 °C; TLC R_f 0.34 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.95 (t, 3H, *J* = 7.3 Hz), 1.32 (t, 3H, *J* = 7.4 Hz), 1.37–1.49 (m, 2H), 1.51–1.63 (m, 2H), 2.46 (s, 3H), 2.52 (s, 3H), 2.86 (t, 2H, *J* = 7.9 Hz), 2.93 (q, 2H, *J* = 7.4 Hz), 6.98 (s, 1H), 7.54–7.64 (AA'BB', 2H), 7.64–7.72 (AA'BB', 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.9, 14.7, 15.3, 16.1, 22.5, 25.5, 29.3, 33.8, 118.4, 125.8, 126.7, 127.3, 128.1, 128.2, 131.6, 131.7, 133.3, 137.2, 147.2, 155.5, 198.0; IR (NaCl, cm^{-1}) 1077, 1170, 1258, 1283, 1324, 1341, 1584, 1648; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{25}{}^{79}BrNaO_2S^+$ 467.0656; Found 467.0652.

2-(3-Butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4h**)



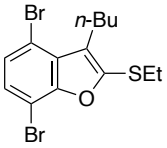
Yield: 68% (38.7 mg, 99.6 μmol); Colorless oil; TLC R_f 0.76 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.96 (t, 3H, *J* = 7.2 Hz), 1.29 (t, 3H, *J* = 7.3 Hz), 1.37 (s, 12H), 1.40–1.50 (m, 2H), 1.52–1.63 (m, 2H), 2.45 (s, 3H), 2.82 (s, 3H), 2.84–2.92 (m, 4H), 7.49 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.9, 14.6, 15.3, 17.7, 22.6, 24.9, 25.8, 29.4, 33.8, 83.3, 117.9, 126.8, 127.0, 133.0, 136.7, 145.3, 156.6 (the signal for the carbon which is attached to the boron atom was not observed); IR (NaCl, cm^{-1}) 1146, 1169, 1272, 1306, 1332, 1366, 1392, 1409, 2929, 2959; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{33}BNaO_3S^+$ 411.2141; Found 411.2142.

3-Butyl-2-(ethylthio)-4,7-diphenylbenzofuran (**4i**)



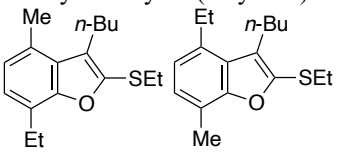
Yield: 54% (31.1 mg, 80.5 μmol); Pale yellow oil; TLC R_f 0.61 (*n*-hexane/CH_2Cl_2 = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.63 (t, 3H, *J* = 6.8 Hz), 0.84–1.02 (m, 4H), 1.31 (t, 3H, *J* = 7.4 Hz), 2.45 (q, 2H, *J* = 7.0 Hz), 2.92 (q, 2H, *J* = 7.4 Hz), 7.20 (d, 1H, *J* = 7.7 Hz), 7.36–7.49 (m, 7H), 7.49–7.58 (m, 2H), 7.86–7.97 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.6, 15.4, 22.5, 25.3, 29.2, 32.4, 123.6, 123.9, 124.8, 125.4, 126.7, 127.3, 127.5, 127.8, 128.5, 128.7, 129.4, 135.4, 136.4, 140.2, 146.9, 153.0; IR (NaCl, cm^{-1}) 1089, 1369, 1448, 1478, 2859, 2870, 2928, 2956; HRMS (FAB) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{26}H_{26}OS^{\cdot+}$ 386.1704; Found 386.1704.

4,7-Dibromo-3-butyl-2-(ethylthio)benzofuran (**4j**)



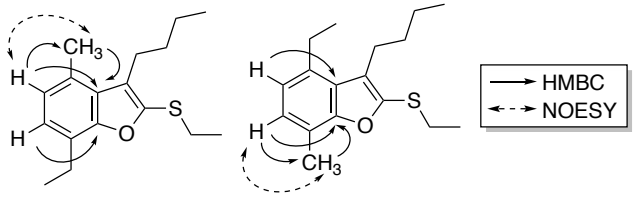
Yield: 29% (16.6 mg, 42.3 μmol); Colorless oil; TLC R_f 0.67 (*n*-hexane/CH_2Cl_2 = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.96 (t, 3H, *J* = 7.3 Hz), 1.33 (t, 3H, *J* = 7.4 Hz), 1.37–1.49 (m, 2H), 1.54–1.67 (m, 2H), 2.88 (t, 2H, *J* = 7.8 Hz), 2.97 (q, 2H, *J* = 7.4 Hz), 7.21–7.27 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ. 13.9, 15.4, 22.5, 24.4, 29.1, 33.6, 103.2, 112.5, 126.1, 127.90, 127.91, 128.7, 149.2, 153.2; IR (NaCl, cm^{-1}) 895, 914, 1080, 1110, 1371, 1454, 2859, 2929, 2958; HRMS (FAB) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{14}H_{16}{}^{79}Br_2OS^{\cdot+}$ 389.9289; Found 389.9288.

3-Butyl-7-ethyl-2-(ethylthio)-4-methylbenzofuran (**4k**)
3-Butyl-4-ethyl-2-(ethylthio)-7-methylbenzofuran (**4k'**)

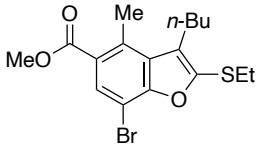


An inseparable mixture of **4k** and **4k'** (63:37) was obtained. Yield: 37% (25.8 mg, 93.3 μmol); Colorless oil; TLC R_f 0.65 (*n*-hexane/CH_2Cl_2 = 10/1); ^{1}H NMR (CD_2Cl_2, 400 MHz) for **4k**: δ 0.96 (t, 3H, *J* = 7.3 Hz), 1.24–1.33 (m, 6H), 1.38–1.50 (m, 2H), 1.52–1.63 (m, 2H), 2.58 (s, 3H), 2.79–2.96 (m, 6H), 6.88 (d, 1H, *J* = 7.4 Hz), 6.97 (d, 1H, *J* = 7.4 Hz); for **4k'**: δ 0.96 (t, 3H, *J* = 7.3 Hz), 1.24–1.33 (m, 6H), 1.38–1.50 (m, 2H), 1.52–1.63 (m, 2H), 2.44 (s, 3H), 2.79–2.96 (m, 6H), 6.92 (d, 1H, *J* = 7.5 Hz), 7.00 (d, 1H, *J* = 7.5 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz) for **4k**: δ 13.8, 14.1, 15.3, 18.7, 22.60, 22.65, 25.4, 29.5, 34.1, 123.5, 124.1, 125.0, 126.5, 126.7, 128.6, 145.4, 154.4; for **4k'**: δ 13.7, 14.5, 15.3, 16.0, 22.7, 25.0, 25.6, 29.4, 33.9, 118.5, 122.0, 125.3, 125.6, 126.1, 135.3, 145.7, 154.9; IR (NaCl, cm^{-1}) 814, 1055, 1077, 1100, 1261, 1385, 1455, 2872, 2930, 2962; HRMS (EI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{17}H_{24}OS^{\cdot+}$ 276.1548; Found 276.1548

The regiochemistries of **4k** and **4k'** were determined by the HMBC and NOESY experiments.



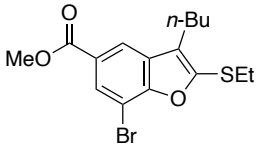
Methyl 7-bromo-3-butyl-2-(ethylthio)-4-methylbenzofuran-5-carboxylate (**4l**)



An inseparable mixture of **4l** and methyl 7-bromo-3-butyl-2-(ethylthio)benzofuran-5-carboxylate (94:6) was obtained. Yield: 53% (21.2 mg; **4l**: 20.4 mg, 52.9 μmol); Colorless oil; TLC R_f 0.50 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.96 (t, 3H, *J* = 7.3 Hz), 1.32 (t, 3H, *J* = 7.4 Hz), 1.36–1.49 (m, 2H), 1.51–1.61 (m, 2H), 2.79 (s, 3H), 2.87 (t, 2H, *J* = 7.6 Hz), 2.95 (q, 2H, *J* = 7.4 Hz), 3.91 (s, 3H), 7.96 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.9, 15.3, 16.2, 22.5, 25.9, 29.2, 33.4, 52.1, 101.0, 126.2, 127.0, 129.1, 129.6, 133.9, 148.7, 154.2, 167.4; IR (NaCl, cm^{-1}) 1060, 1129, 1239, 1273, 1321, 1335, 1434, 1461, 1724, 2930, 2956; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{21}{}^{79}BrNaO_3S^+$ 407.0293; Found 407.0293.

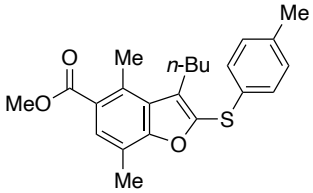
An authentic sample of methyl 7-bromo-3-butyl-2-(ethylthio)benzofuran-5-carboxylate was prepared from 1-(ethylsulfinyl)hex-1-yne (**2a**) and 2-bromo-4-(methoxycarbonyl)phenol in 47% yield according to our previous report.[S7]

Methyl 7-bromo-3-butyl-2-(ethylthio)benzofuran-5-carboxylate



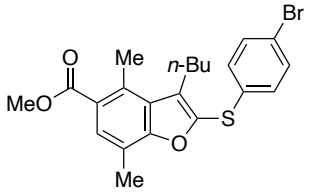
Yield: 47% (35.8 mg, 96.4 μmol); Yellow oil; TLC R_f 0.57 (*n*-hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.94 (t, 3H, *J* = 7.3 Hz), 1.28–1.44 (m, 5H), 1.57–1.68 (m, 2H), 2.74 (t, 2H, *J* = 7.7 Hz), 2.96 (q, 2H, *J* = 7.4 Hz), 3.95 (s, 3H), 8.11–8.18 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.9, 15.4, 22.5, 24.3, 29.3, 31.8, 52.4, 103.8, 120.9, 126.1, 126.4, 128.9, 130.1, 149.1, 155.3, 166.2; IR (NaCl, cm^{-1}) 808, 1110, 1132, 1258, 1285, 1435, 1491, 1727, 2952; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{20}{}^{79}BrO_3S^+$ 371.0311; Found 371.0315.

Methyl 3-butyl-4,7-dimethyl-2-(p-tolylthio)benzofuran-5-carboxylate (**4m**)



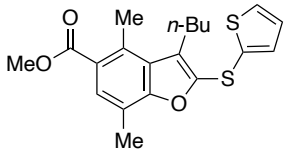
Yield: 78% (45.3 mg, 0.118 mmol); Colorless solid; Mp 75–77 °C; TLC R_f 0.42 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.93 (t, 3H, *J* = 7.3 Hz), 1.38–1.48 (m, 2H), 1.51–1.61 (m, 2H), 2.30 (s, 3H), 2.45 (s, 3H), 2.83 (s, 3H), 2.96 (t, 2H, *J* = 7.7 Hz), 3.91 (s, 3H), 6.99–7.12 (AA'BB', 2H), 7.12–7.20 (AA'BB', 2H), 7.65 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.8, 14.7, 16.2, 20.9, 22.5, 26.0, 33.4, 51.9, 118.9, 125.0, 127.2, 128.3 (two signals overlapped), 129.6, 129.9, 131.5, 132.4, 136.6, 144.8, 156.6, 168.7; IR (NaCl, cm^{-1}) 1160, 1248, 1340, 1439, 1492, 1716; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{26}NaO_3S^+$ 405.1500; Found 405.1502.

Methyl 2-((4-bromophenyl)thio)-3-butyl-4,7-dimethylbenzofuran-5-carboxylate (**4n**)



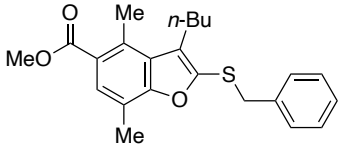
Yield: 82% (36.3 mg, 81.1 μmol); Colorless solid; Mp 82–84 °C; TLC R_f 0.42 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.92 (t, 3H, *J* = 7.3 Hz), 1.34–1.46 (m, 2H), 1.50–1.61 (m, 2H), 2.44 (s, 3H), 2.83 (s, 3H), 2.94 (t, 2H, *J* = 7.7 Hz), 3.91 (s, 3H), 7.00–7.10 (AA'BB', 2H), 7.33–7.41 (AA'BB', 2H), 7.66 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.8, 14.7, 16.2, 22.5, 26.0, 33.4, 52.0, 119.1, 120.3, 125.2, 127.0, 128.6, 129.0, 130.7, 132.1, 132.6, 134.6, 143.3, 156.8, 168.6; IR (NaCl, cm^{-1}) 1073, 1159, 1199, 1246, 1342, 1455, 1468, 1716, 1723; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{23}{}^{79}BrNaO_3S^+$ 469.0449; Found 469.0444.

3-Butyl-4,7-dimethyl-2-(thiophen-2-ylthio)benzofuran (**4o**)



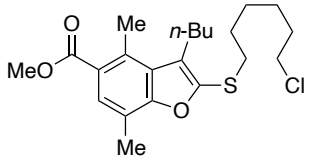
Yield: 27% (19.7 mg, 52.6 μmol); Colorless solid; Mp 58–60 °C; TLC R_f 0.32 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.98 (t, 3H, *J* = 7.2 Hz), 1.38–1.53 (m, 2H), 1.53–1.65 (m, 2H), 2.45 (s, 3H), 2.79 (s, 3H), 3.00 (t, 2H, *J* = 7.6 Hz), 3.89 (s, 3H), 6.97 (dd, 1H, *J* = 5.4, 3.6 Hz), 7.28 (dd, 1H, *J* = 3.6, 1.3 Hz), 7.33 (dd, 1H, *J* = 5.4, 1.3 Hz), 7.61 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 14.0, 14.7, 16.2, 22.6, 26.0, 33.4, 51.9, 118.9, 125.0, 127.1, 127.5 (two signals overlapped), 128.3, 129.7, 131.3, 132.6, 133.4, 145.7, 156.4, 168.7; IR (NaCl, cm^{-1}) 1045, 1080, 1113, 1159, 1196, 1219, 1246, 1283, 1341, 1352, 1724; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{22}F_3NaO_3S_2^+$ 397.0908; Found 397.0906.

Methyl 2-(benzylthio)-3-butyl-4,7-dimethylbenzofuran-5-carboxylate (**4p**)



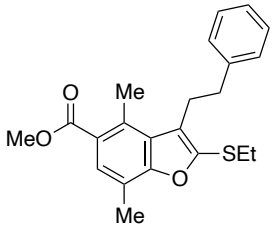
Yield: 79% (29.7 mg, 77.6 μmol); Colorless solid; Mp 52–54 °C; TLC R_f 0.47 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.87 (t, 3H, *J* = 6.4 Hz), 1.20–1.35 (m, 4H), 2.46 (s, 3H), 2.62 (t, 2H, *J* = 7.2 Hz), 2.74 (s, 3H), 3.90 (s, 3H), 4.06 (s, 2H), 7.10–7.18 (AA'BB'C, 2H), 7.18–7.28 (m, 3H), 7.60 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.8, 14.7, 16.1, 22.4, 25.5, 33.3, 39.6, 51.9, 118.5, 124.8, 127.2 (two signals overlapped), 127.8, 128.0, 128.4, 128.8, 132.0, 137.6, 146.1, 156.4, 168.8; IR (NaCl, cm^{-1}) 1158, 1202, 1243, 1328, 1346, 1455, 1724, 2726; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{26}NaO_3S^+$ 405.1500; Found 405.1500.

Methyl 3-butyl-2-((6-chlorohexyl)thio)-4,7-dimethylbenzofuran-5-carboxylate (**4q**)



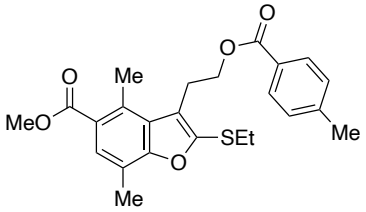
Yield: 75% (31.1 mg, 75.7 μmol); Yellow oil; TLC R_f 0.39 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.96 (t, 3H, *J* = 7.3 Hz), 1.36–1.51 (m, 6H), 1.51–1.70 (m, 4H), 1.70–1.83 (m, 2H), 2.46 (s, 3H), 2.79 (s, 3H), 2.83–2.93 (m, 4H), 3.52 (t, 2H, *J* = 6.6 Hz), 3.90 (s, 3H), 7.60 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 13.9, 14.7, 16.2, 22.5, 25.8, 26.4, 27.7, 29.7, 32.4, 33.6, 34.9, 44.9, 51.9, 118.4, 124.8, 126.7, 127.3, 127.7, 131.9, 147.0, 156.3, 168.8; IR (NaCl, cm^{-1}) 1159, 1195, 1245, 1275, 1342, 1434, 1455, 1462, 1721, 2859, 2932, 2952; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{31}{}^{35}ClNaO_3S^+$ 433.1580; Found 433.1581.

Methyl 2-(ethylthio)-4,7-dimethyl-3-phenethylbenzofuran-5-carboxylate (**4r**)



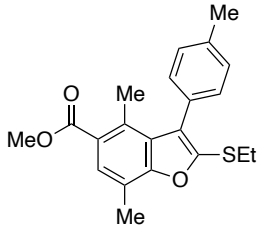
Yield: 81% (28.5 mg, 77.3 μmol); Colorless solid; Mp 69–71 °C; TLC R_f 0.36 (*n*-hexane/CH_2Cl_2 = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.27 (t, 3H, *J* = 7.4 Hz), 2.48 (s, 3H), 2.81 (q, 2H, *J* = 7.4 Hz), 2.85–2.94 (m, 5H), 3.21 (t, 2H, *J* = 7.8 Hz), 3.92 (s, 3H), 7.16–7.28 (m, 3H), 7.28–7.36 (AA'BB'C, 2H), 7.64 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 14.7, 15.3, 16.3, 28.4, 29.2, 37.7, 51.9, 118.6, 124.9, 125.7, 126.1, 127.2, 127.8, 128.4, 128.5, 131.7, 141.1, 147.7, 156.3, 168.8; IR (NaCl, cm^{-1}) 1080, 1109, 1162, 1188, 1242, 1261, 1435, 1453; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{24}NaO_3S^+$ 391.1344; Found 391.1345.

Methyl 2-(ethylthio)-4,7-dimethyl-3-(2-((4-methylbenzoyl)oxy)ethyl)benzofuran-5-carboxylate (**4s**)



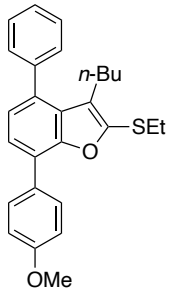
Yield: 83% (34.7 mg, 81.4 μmol); Colorless solid; Mp 84–86 °C; TLC R_f 0.49 (*n*-hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.30 (t, 3H, *J* = 7.4 Hz), 2.40 (s, 3H), 2.47 (s, 3H), 2.87 (s, 3H), 2.94 (q, 2H, *J* = 7.4 Hz), 3.41 (t, 2H, *J* = 7.2 Hz), 3.91 (s, 3H), 4.49 (t, 2H, *J* = 7.2 Hz), 7.19–7.25 (AA'BB', 2H), 7.62 (s, 1H), 7.88–7.95 (AA'BB', 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 14.7, 15.3, 16.4, 21.6, 25.7, 29.2, 51.9, 64.4, 118.6, 121.7, 125.2, 127.16, 127.21, 127.8, 129.0, 129.6, 131.4, 143.6, 148.9, 156.3, 166.6, 168.7; IR (NaCl, cm^{-1}) 1103, 1156, 1246, 1272, 1285, 1701, 1718; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{24}H_{26}NaO_5S^+$ 449.1399; Found 449.1393.

Methyl 2-(ethylthio)-4,7-dimethyl-3-(p-tolyl)benzofuran-5-carboxylate (**4t**)



Yield: 81% (28.8 mg, 81.3 μmol); Colorless solid; Mp 73–75 °C; TLC R_f 0.57 (*n*-hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.25 (t, 3H, *J* = 7.4 Hz), 2.29 (s, 3H), 2.43 (s, 3H), 2.53 (s, 3H), 2.89 (q, 2H, *J* = 7.4 Hz), 3.87 (s, 3H), 7.19–7.30 (m, 4H), 7.65 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 15.2, 14.7, 17.0, 21.4, 28.8, 51.8, 118.4, 125.1, 127.0, 127.8 (two signals overlapped), 128.8, 130.2, 130.4, 132.4, 137.6, 148.1, 155.9, 168.6; IR (NaCl, cm^{-1}) 1106, 1173, 1186, 1256, 1278, 1346, 1432, 1720; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{22}NaO_3S^+$ 377.1187; Found 377.1186.

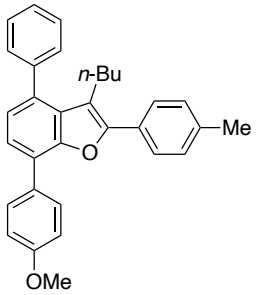
3-Butyl-2-(ethylthio)-7-(4-methoxyphenyl)-4-phenylbenzofuran (**9**)



Yield: 39% (two steps) (49.1 mg, 0.118 mmol); Colorless solid; Mp 88–90 °C; TLC R_f 0.26 (*n*-hexane/CH_2Cl_2 = 2/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.61 (t, 3H, *J* = 7.1 Hz), 0.80–1.00 (m, 4H), 1.30 (t, 3H, *J* = 7.4 Hz), 2.43 (t, 2H, *J* = 7.0 Hz), 2.92 (q, 2H, *J* = 7.4 Hz), 3.89 (s, 3H), 7.02–7.09 (AA'BB', 2H), 7.16 (d, 1H, *J* = 7.7 Hz), 7.36–

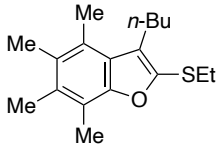
7.48 (m, 6H), 7.80–7.90 (AA'BB', 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 101 MHz): δ 13.6, 15.4, 22.5, 25.3, 29.2, 32.4, 55.3, 114.0, 123.1, 123.6, 124.7, 125.5, 126.6, 127.3, 127.7, 128.8, 129.4, 129.8, 134.8, 140.3, 146.8, 152.9, 159.1; IR (NaCl, cm^{-1}) 820, 830, 840, 914, 1026, 1086, 1251, 1272, 1295, 1306, 1611, 2726; (EI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{27}H_{28}O_2S^{\cdot+}$ 416.1810; Found 416.1809.

3-Butyl-7-(4-methoxyphenyl)-4-phenyl-2-(*p*-tolyl)benzofuran (**11**)



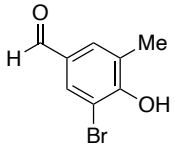
Yield: 71% (16.4 mg, 36.7 μmol); Colorless solid; Mp 120–122 °C; TLC R_f 0.17 (*n*-hexane/toluene = 5/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.59 (t, 3H, *J* = 7.4 Hz), 0.79–0.91 (m, 2H), 1.02–1.13 (m, 2H), 2.40 (s, 3H), 2.53 (t, 2H, *J* = 8.2 Hz), 3.89 (s, 3H), 7.02–7.09 (AA'BB', 2H), 7.15 (d, 1H, *J* = 7.6 Hz), 7.23–7.29 (AA'BB', 2H), 7.37–7.52 (m, 6H), 7.58–7.65 (AA'BB', 2H), 7.86–7.94 (AA'BB', 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 101 MHz): δ 13.5, 21.3, 22.6, 24.5, 32.3, 55.3, 114.0, 116.7, 122.7, 123.7, 124.9, 127.2, 127.3, 127.7, 127.9, 128.6, 129.1, 129.3, 129.5, 129.8, 135.2, 138.0, 140.7, 151.2, 151.5, 159.1; IR (NaCl, cm^{-1}) 820, 1029, 1102, 1176, 1186, 1249, 1292, 1504, 2676, 2727; HRMS (FAB) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{32}H_{30}O_2^{\cdot+}$ 446.2246; Found 446.2247.

3-Butyl-2-(ethylthio)-4,5,6,7-tetramethylbenzofuran (**12**)



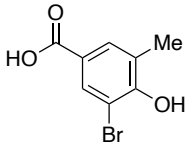
Yield: 25% (14.6 mg, 50.3 μmol); Pale yellow oil; TLC R_f 0.35 (*n*-hexane/CH_2Cl_2 = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.95 (t, 3H, *J* = 7.3 Hz), 1.27 (t, 3H, *J* = 7.3 Hz) 1.37–1.48 (m, 2H), 1.51–1.63 (m, 2H), 2.26 (s, 3H), 2.29 (s, 3H), 2.42 (s, 3H), 2.51 (s, 3H), 2.80–2.92 (m, 4H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 101 MHz): δ 12.3, 14.0, 15.3, 15.7, 15.8, 16.1, 22.5, 26.0, 29.5, 33.5, 116.8, 124.0, 125.6, 126.4, 129.4, 131.9, 144.5, 153.5; IR (NaCl, cm^{-1}) 1053, 1092, 1119, 1259, 1378, 1454, 2870, 2929, 2956; HRMS (FAB) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{18}H_{26}OS^{\cdot+}$ 290.1704; Found 290.1705.

3-Bromo-4-hydroxy-5-methylbenzaldehyde



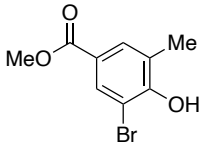
Yield: 32% (679 mg, 3.16 mmol); Brown solid; Mp 116–118 °C; TLC R_f 0.30 (*n*-hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.36 (s, 3H), 6.15 (br s, 1H), 7.62 (d, 1H, *J* = 1.9 Hz), 7.87 (d, 1H, *J* = 1.9 Hz), 9.79 (s, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 101 MHz): δ 16.6, 110.8, 126.6, 130.4, 131.6, 132.0, 155.6, 189.7; IR (NaCl, cm^{-1}) 828, 866, 1106, 1245, 1335, 1455, 1594, 1678, 3373; HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_8H_6{}^{79}BrO_2^-$ 212.9551; Found 212.9550.

3-Bromo-4-hydroxy-5-methylbenzoic acid



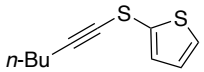
Yield: 63% (290 mg, 1.26 mmol); Colorless solid; Mp 238–240 °C; TLC R_f 0.14 (*n*-hexane/AcOEt = 2/1); ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.25 (s, 3H), 7.68 (d, 1H, *J* = 2.0 Hz), 7.86 (d, 1H, *J* = 2.0 Hz), 9.91 (br s, 1H), 12.76 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 101 MHz): δ 17.3, 110.4, 123.2, 126.7, 131.5, 131.9, 156.1, 166.3; IR (NaCl, cm^{-1}) 900, 1304, 1455, 1601, 1660, 3451; HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_8H_6{}^{79}BrO_3^-$ 228.9500; Found 228.9501.

Methyl 3-bromo-4-hydroxy-5-methylbenzoate (**1l**)



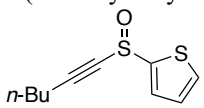
Yield: 93% (139 mg, 0.568 mmol); Brown solid; Mp 122–124 °C; TLC R_f 0.23 (*n*-hexane/CH_2Cl_2 = 1/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.32 (s, 3H), 3.88 (s, 3H), 5.94 (s, 1H), 7.78 (d, 1H, *J* = 2.0 Hz), 8.02 (d, 1H, *J* = 2.0 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 16.6, 52.1, 109.9, 123.2, 125.7, 131.3, 131.9, 154.3, 165.8; IR (NaCl, cm^{-1}) 909, 992, 1014, 1132, 1203, 1259, 1278, 1308, 1444, 1650, 1694, 3405; HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_9H_8{}^{79}BrO_3^-$ 242.9657; Found 242.9657.

2-(Hex-1-yn-1-ylthio)thiophene



Yield: 65% (492 mg, 2.51 mmol); Pale yellow oil; TLC R_f 0.56 (*n*-hexane); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.91 (t, 3H, *J* = 7.3 Hz), 1.35–1.47 (m, 2H), 1.47–1.59 (m, 2H), 2.33 (t, 2H, *J* = 7.0 Hz), 6.97 (dd, 1H, *J* = 5.3, 3.6 Hz), 7.13 (dd, 1H, *J* = 3.6, 1.3 Hz), 7.35 (dd, 1H, *J* = 5.3, 1.3 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 13.5, 19.8, 21.9, 30.5, 66.8, 96.5, 127.5, 128.5, 130.3, 131.5; IR (NaCl, cm^{-1}) 847, 1219, 1409, 1459, 1465, 2863, 2871, 2932, 2958; HRMS (EI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{10}H_{12}S_2^{\cdot+}$ 196.0380; Found 196.0370.

2-(Hex-1-yn-1-ylsulfinyl)thiophene (**2d**)



Yield: 69% (239 mg, 1.13 mmol); Colorless oil; TLC R_f 0.31 (*n*-hexane/EtOAc = 4/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.92 (t, 3H, *J* = 7.3 Hz), 1.38–1.50 (m, 2H), 1.54–1.66 (m, 2H), 2.48 (t, 2H, *J* = 7.0 Hz), 7.11 (dd, 1H, *J* = 5.0, 3.7 Hz), 7.61 (dd, 1H, *J* = 3.7, 1.2 Hz), 7.68 (dd, 1H, *J* = 5.0, 1.2 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 101 MHz): δ 13.4, 19.4, 21.9, 29.4, 77.7, 106.3, 127.5, 131.7, 132.4, 146.1; IR (NaCl, cm^{-1}) 853, 1000, 1072, 1090, 1223, 1402, 1465, 2182, 2872, 2932, 2958; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{10}H_{12}NaOS_2^+$ 235.0227; Found 235.0224.

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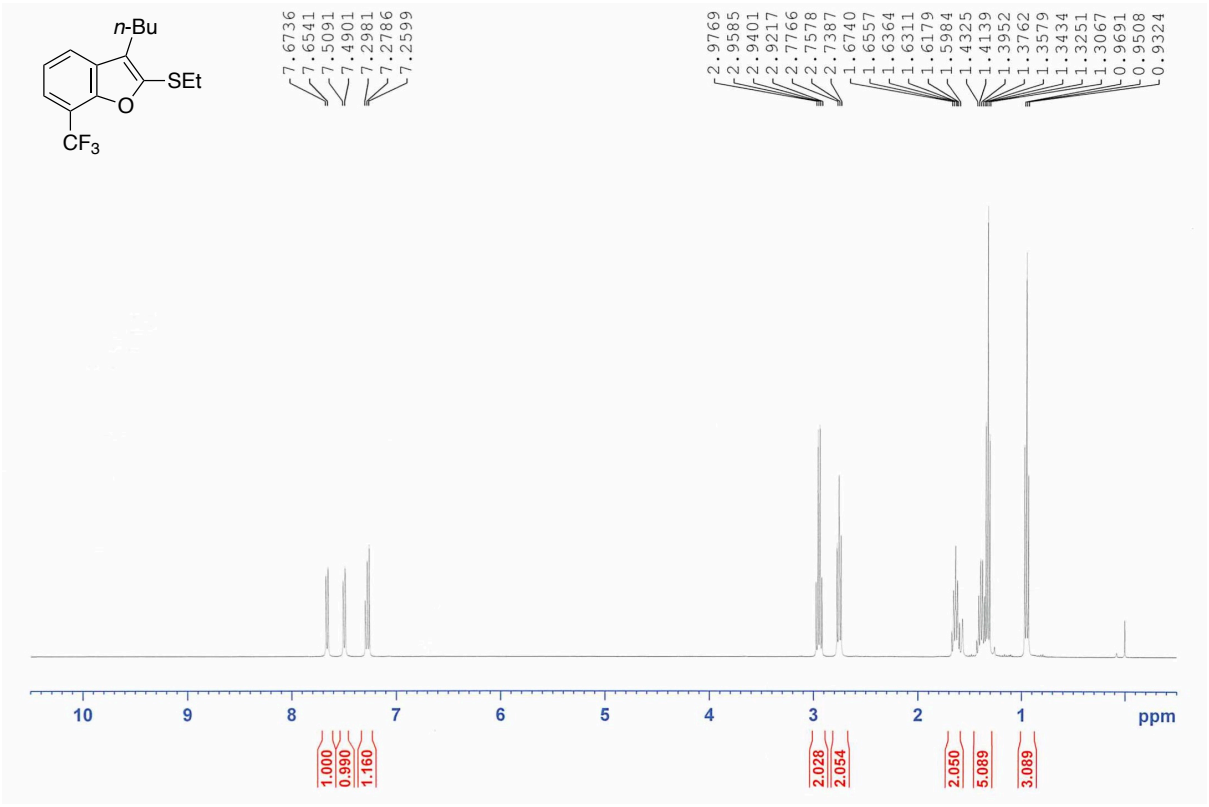
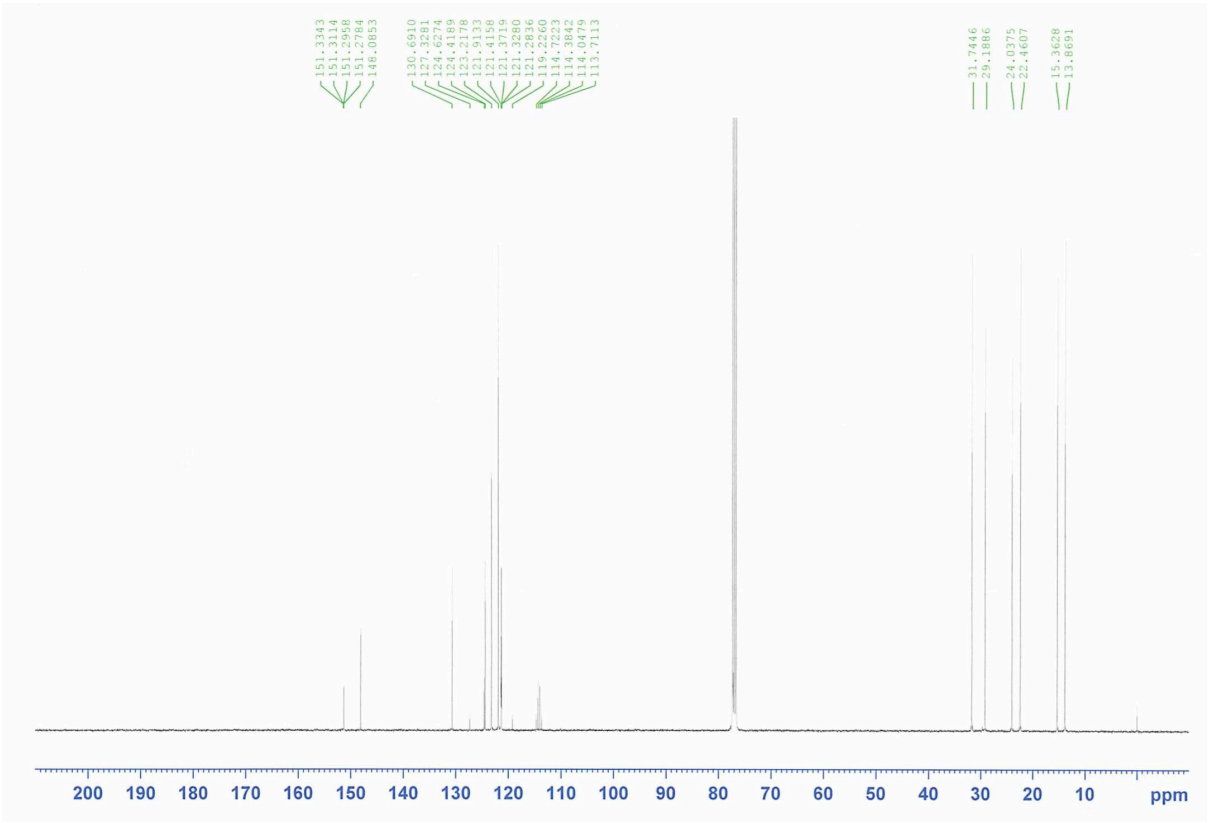
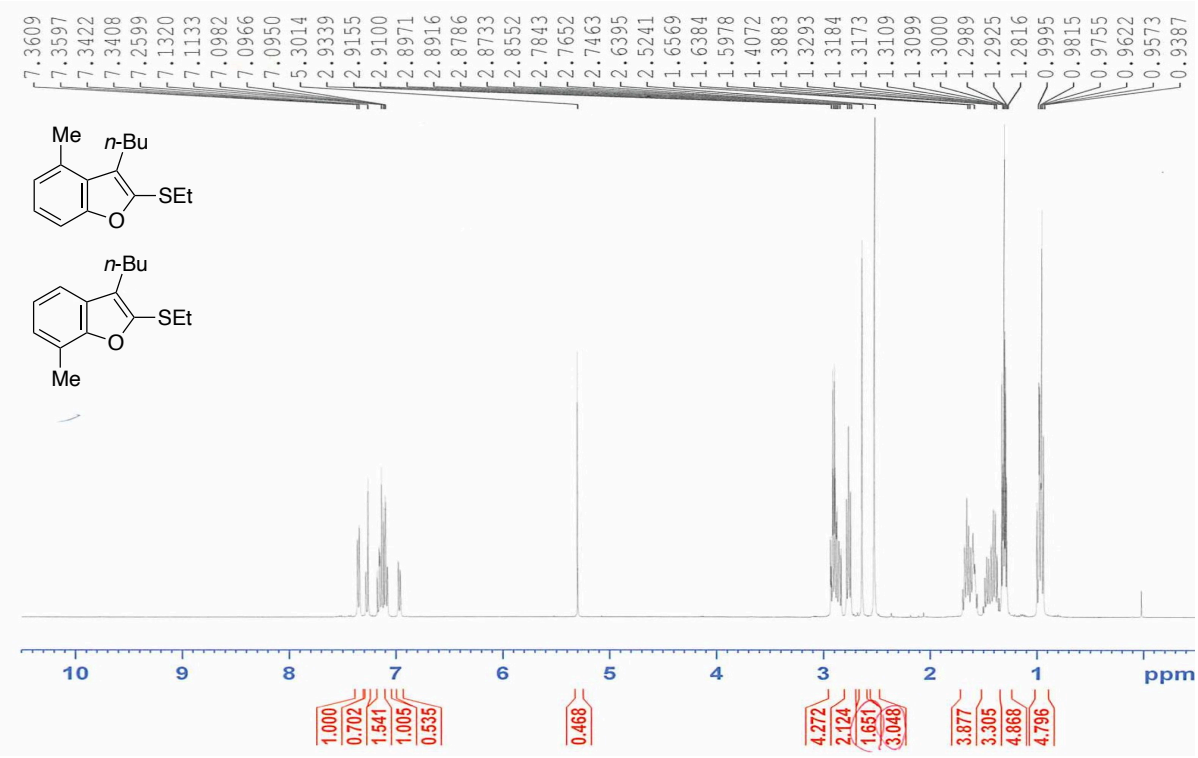
^{1}H and ^{13}C NMR Spectra of Compounds

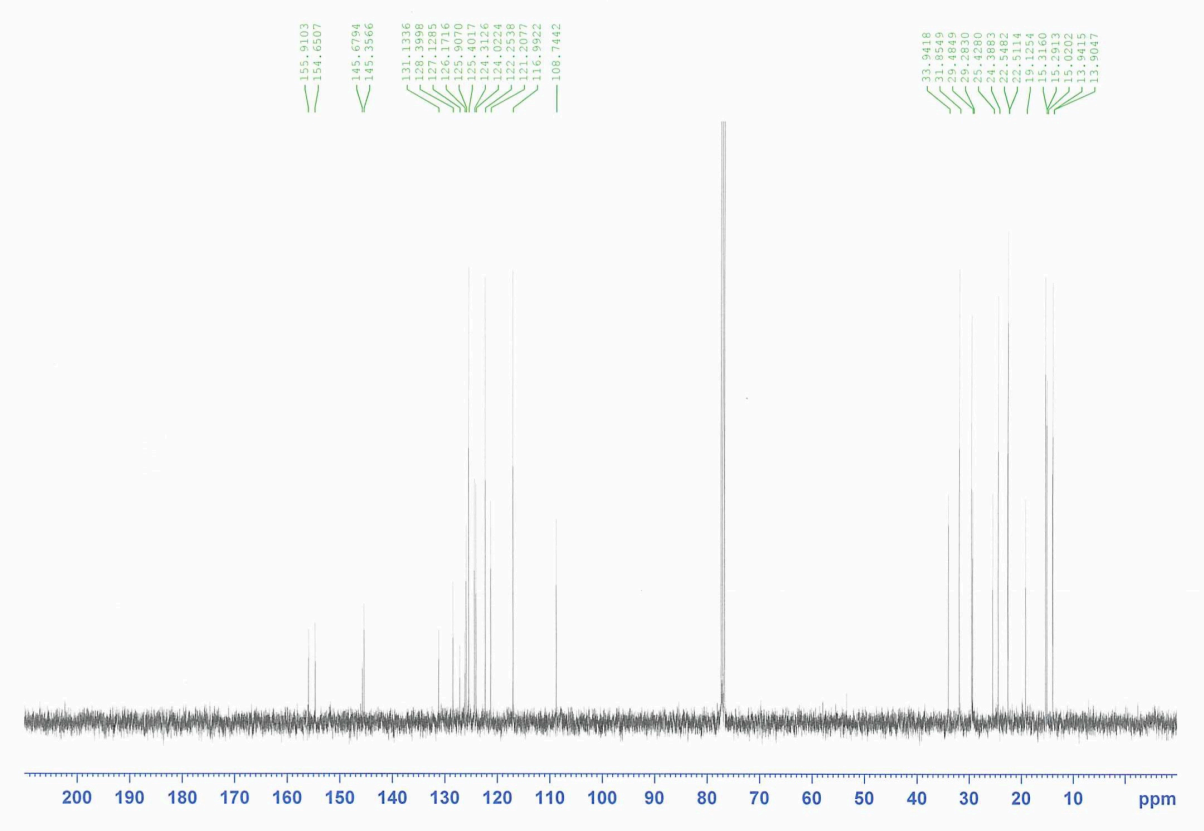
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-butyl-2-(ethylthio)-7-(trifluoromethyl)benzofuran (**3a**) ($CDCl_3$)

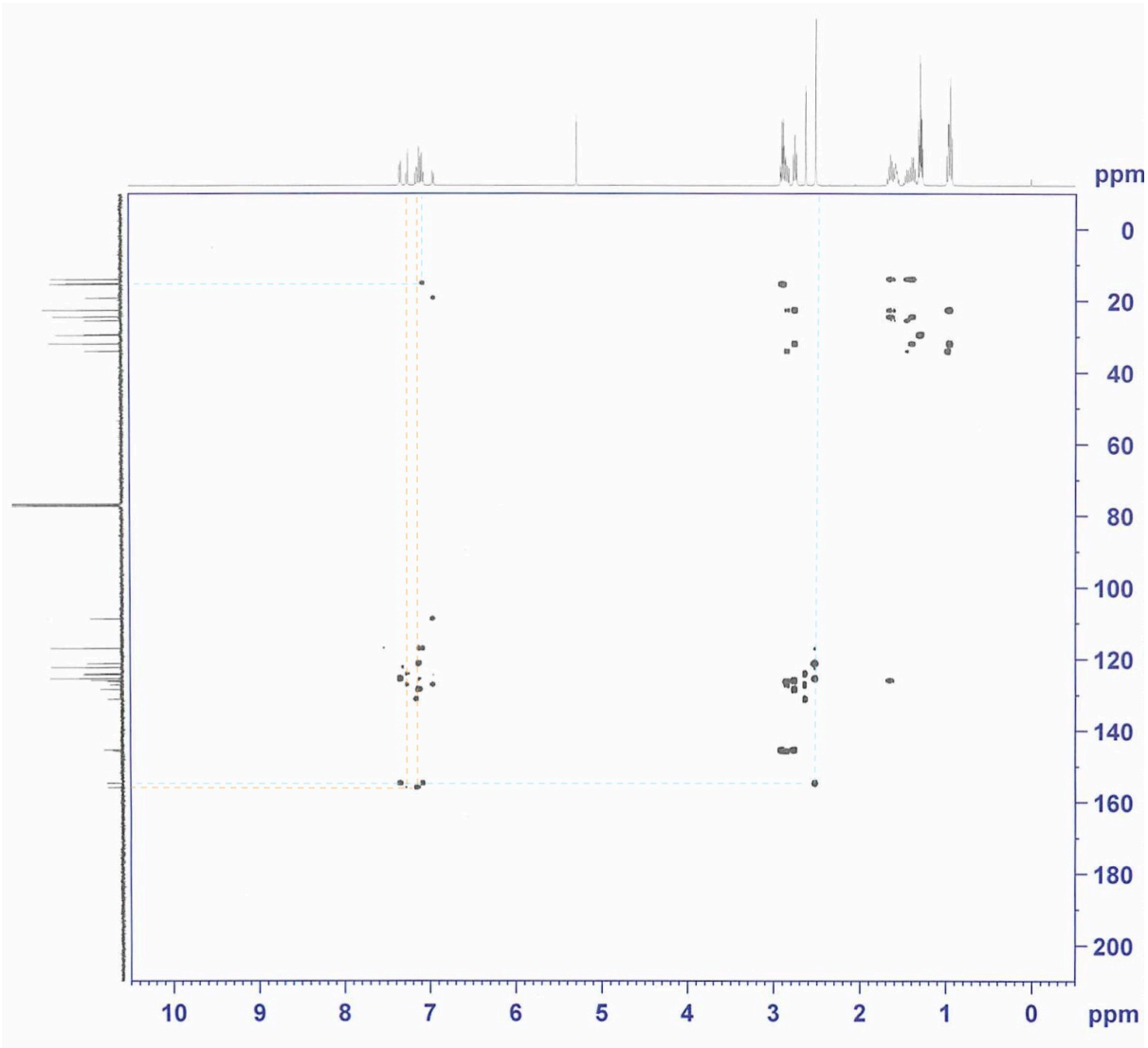




^{1}H NMR (400 MHz),^{13}C NMR (101 MHz), and HMBC spectra of a mixture of 3-butyl-2-(ethylthio)-7-methylbenzofuran (**3b**) and 3-butyl-2-(ethylthio)-4-methylbenzofuran (**4b**) ($CDCl_3$)



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180
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10
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8
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6
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2
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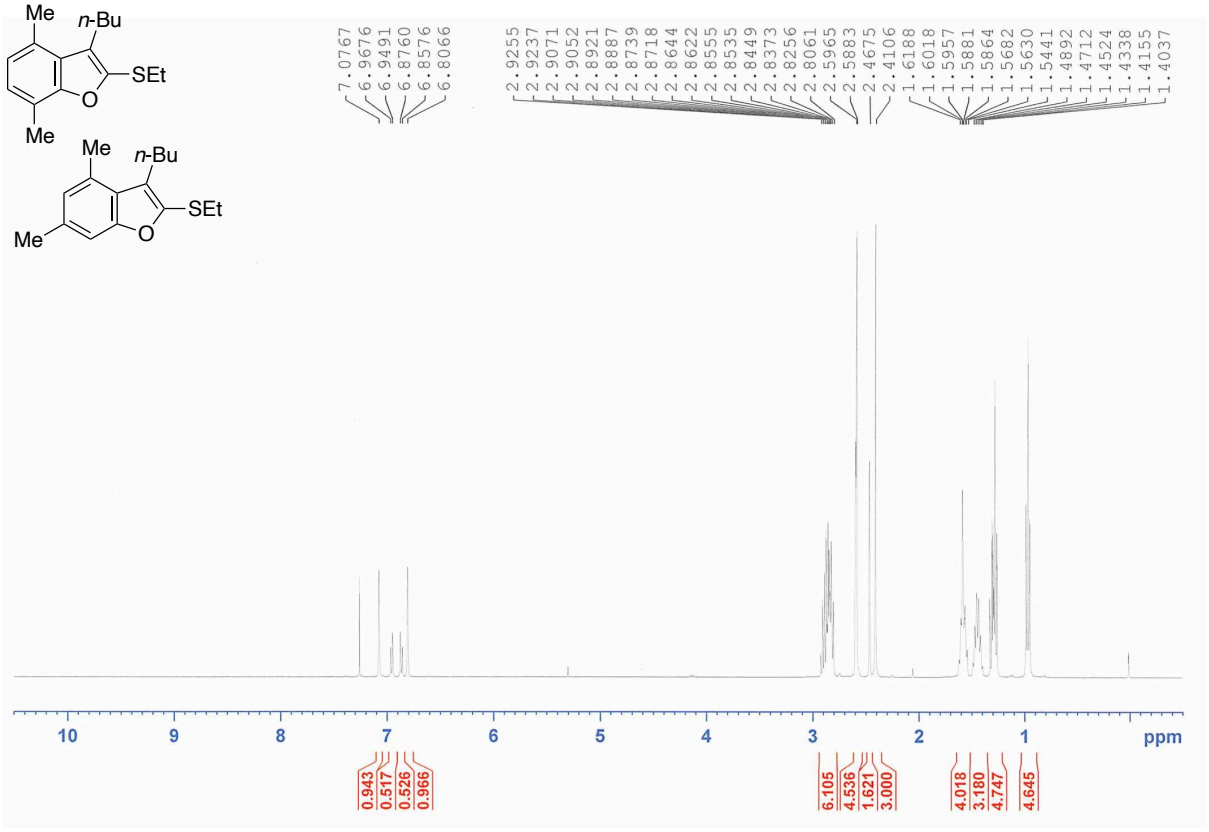
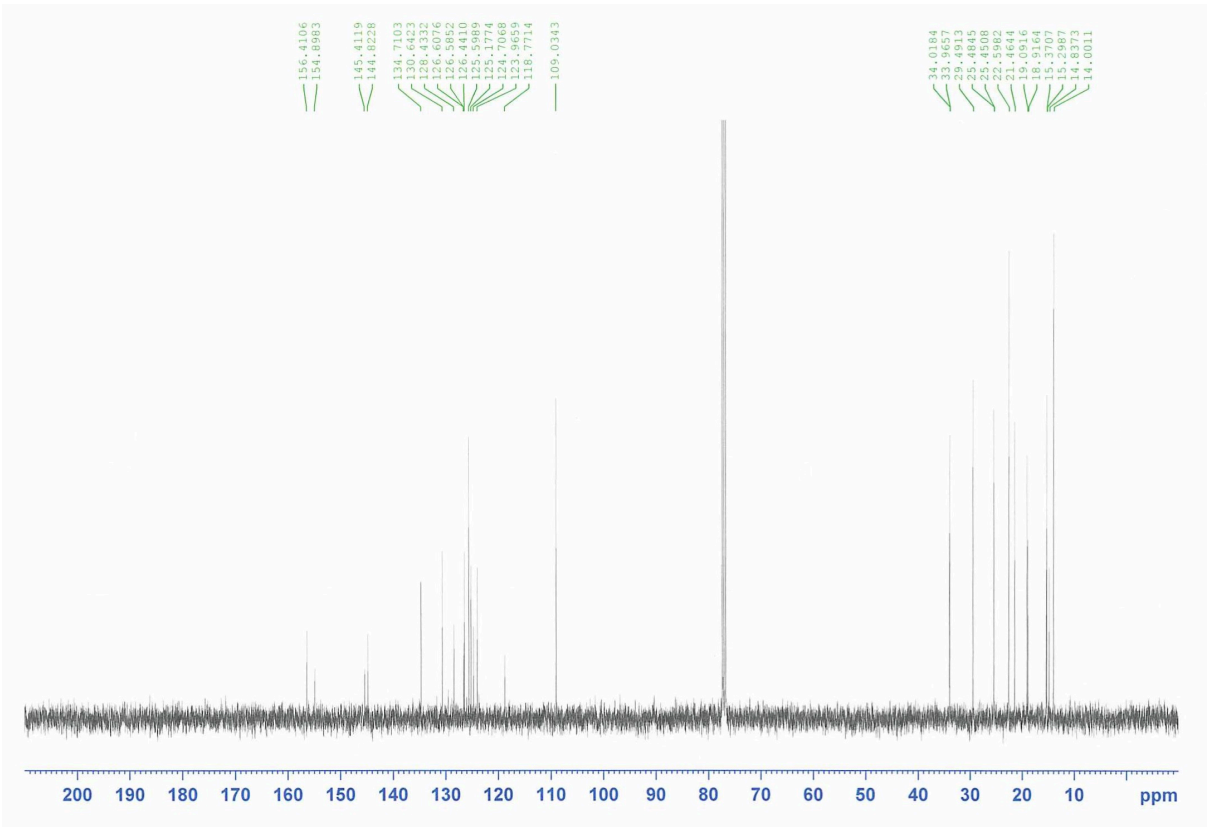
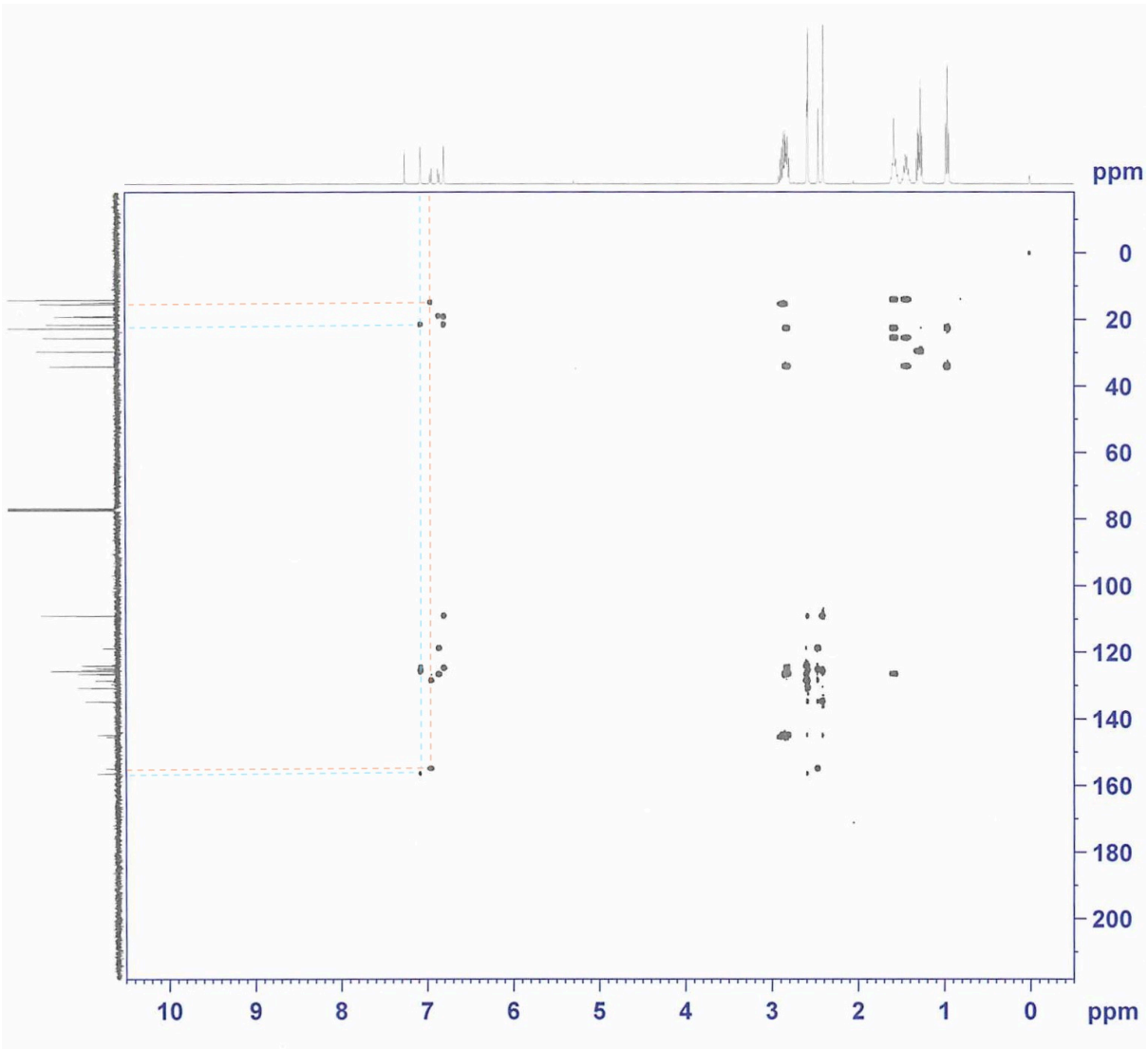
0
ppm

^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), and HMBC spectra of a mixture of 3-butyl-2-(ethylthio)-4,6-dimethylbenzofuran (**3c**) and 3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran (**4c**) ($CDCl_3$)



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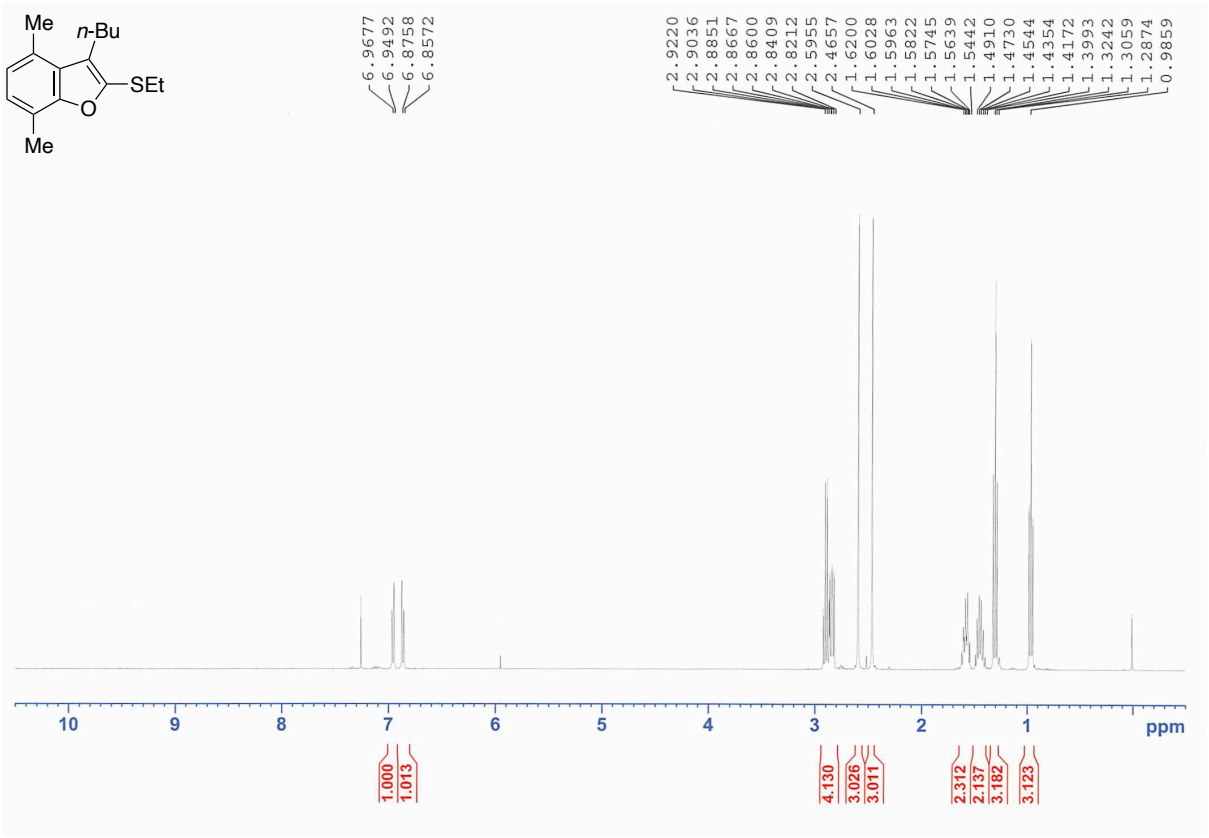
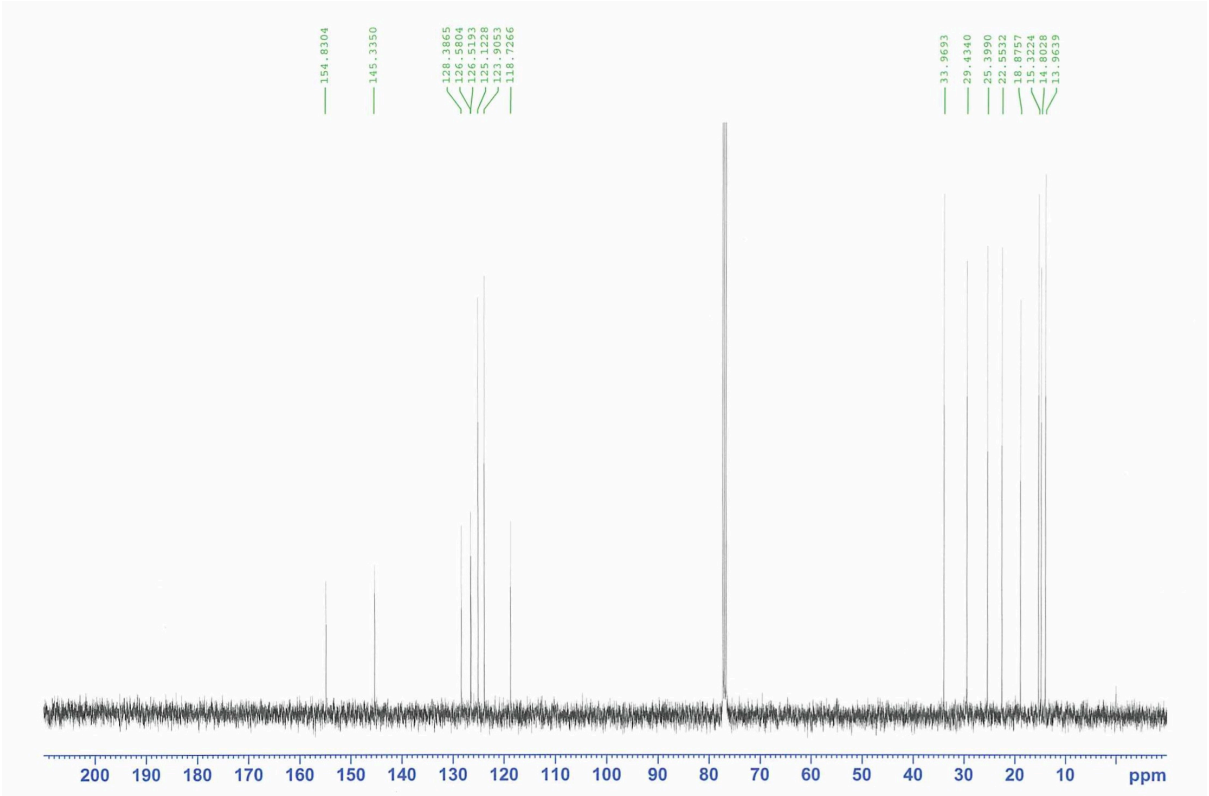
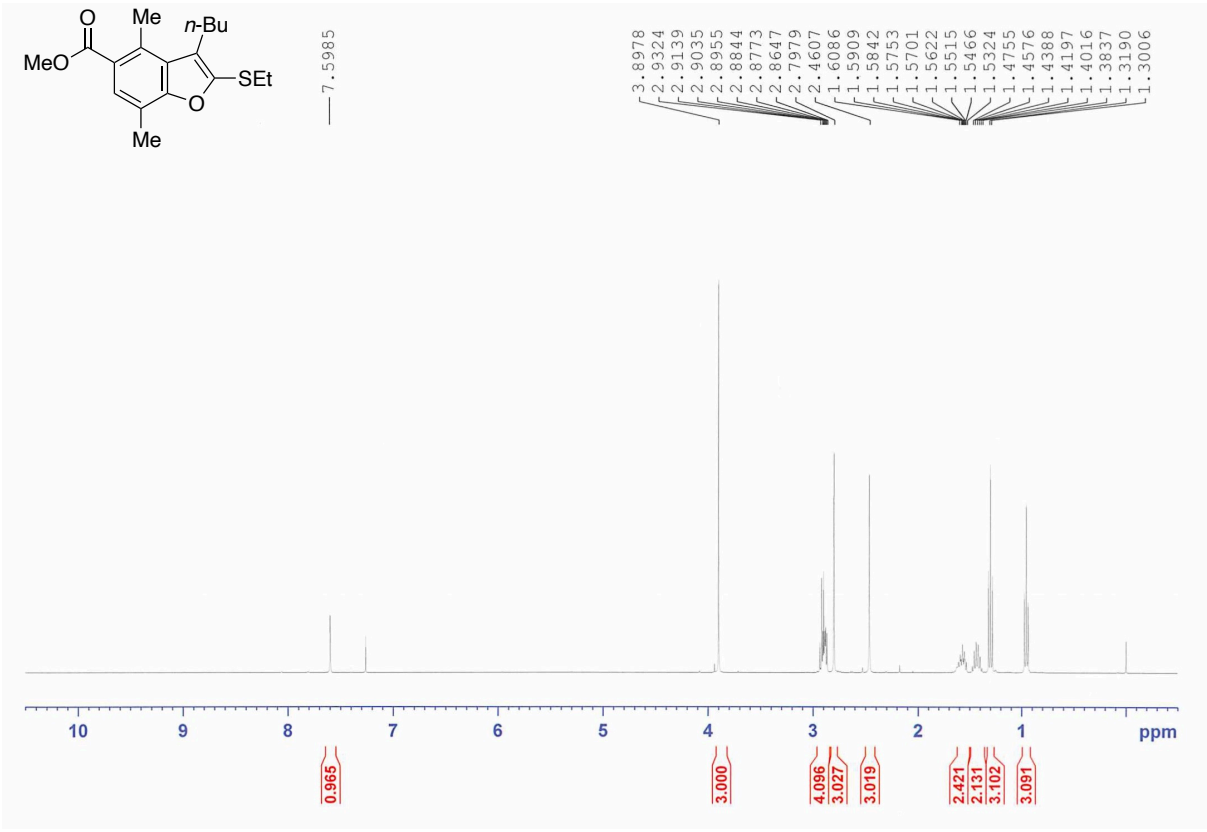
ppm

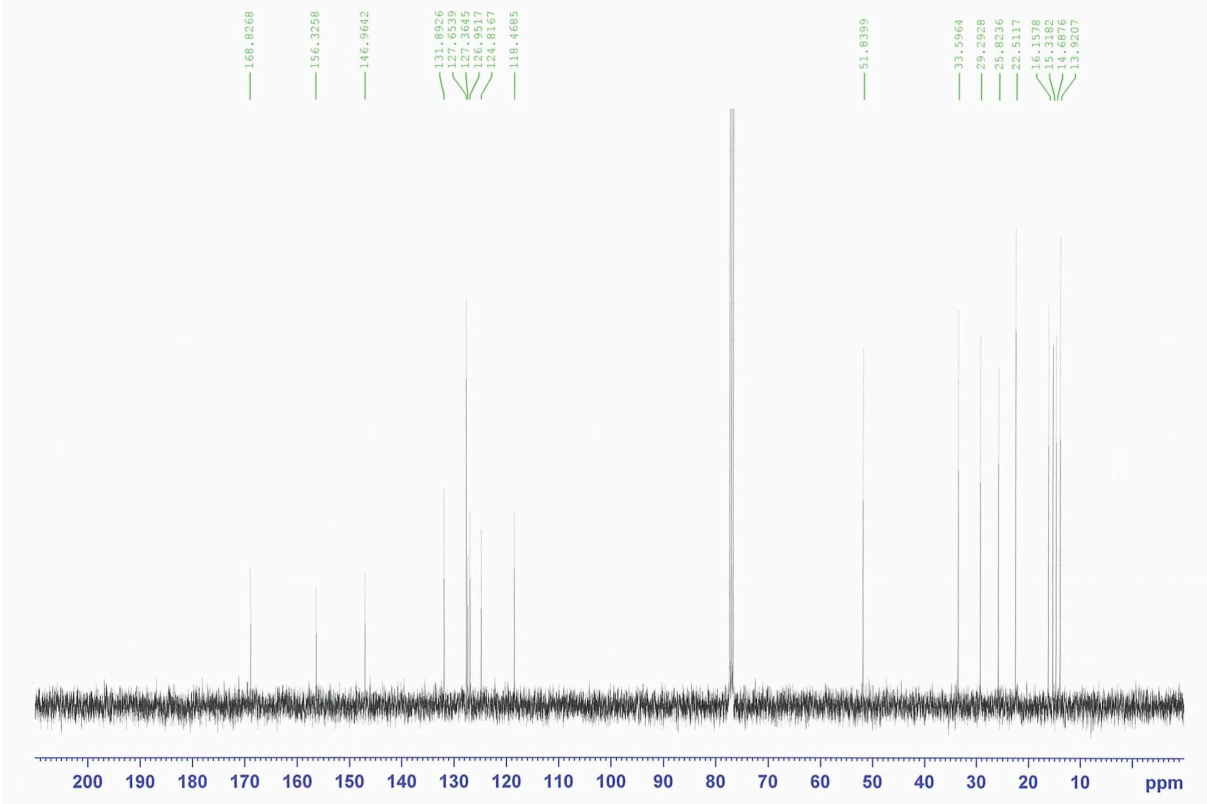
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran (**4d** (= **3c**)) ($CDCl_3$)



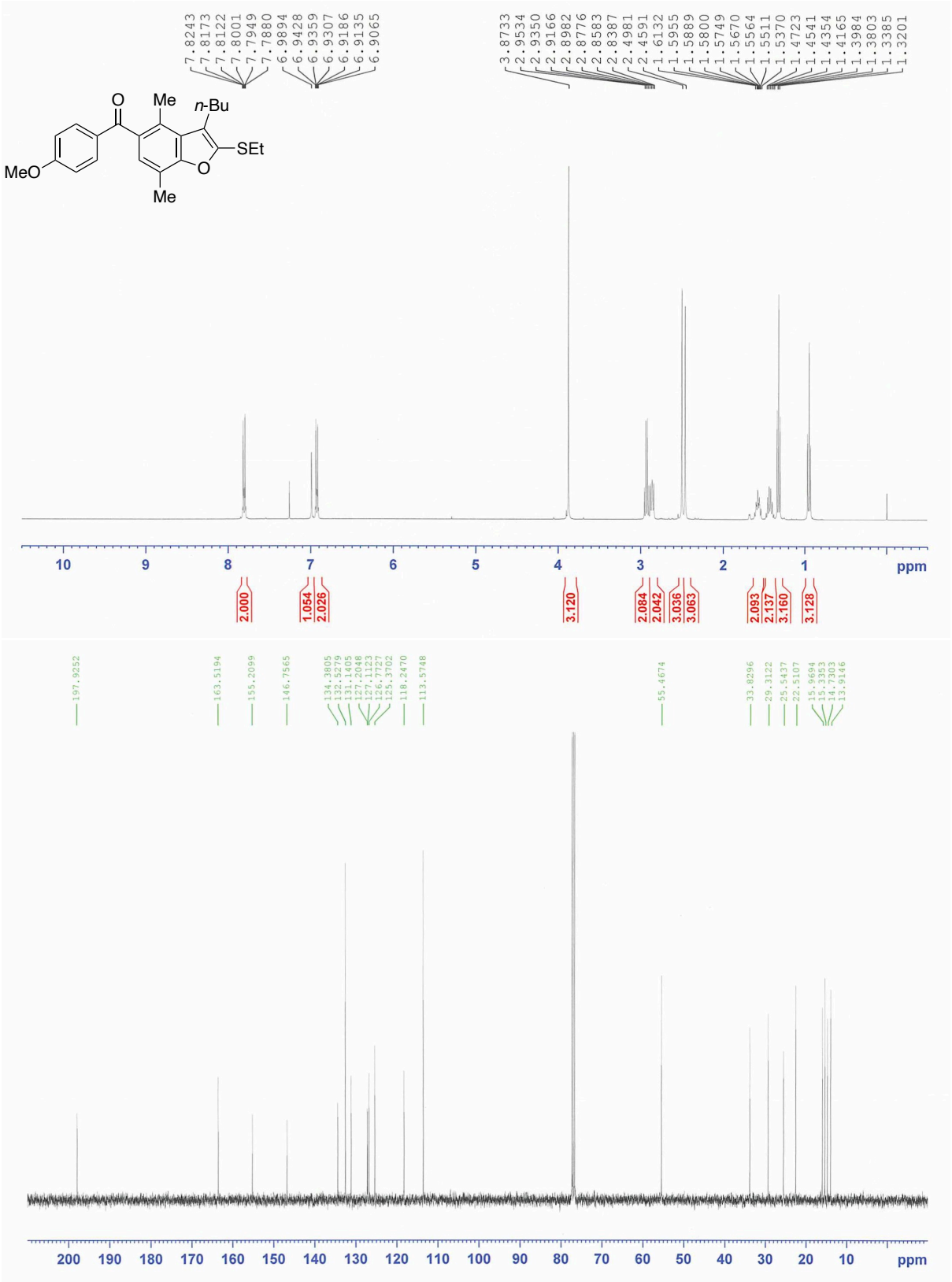


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-carboxylate (**4e**) ($CDCl_3$)

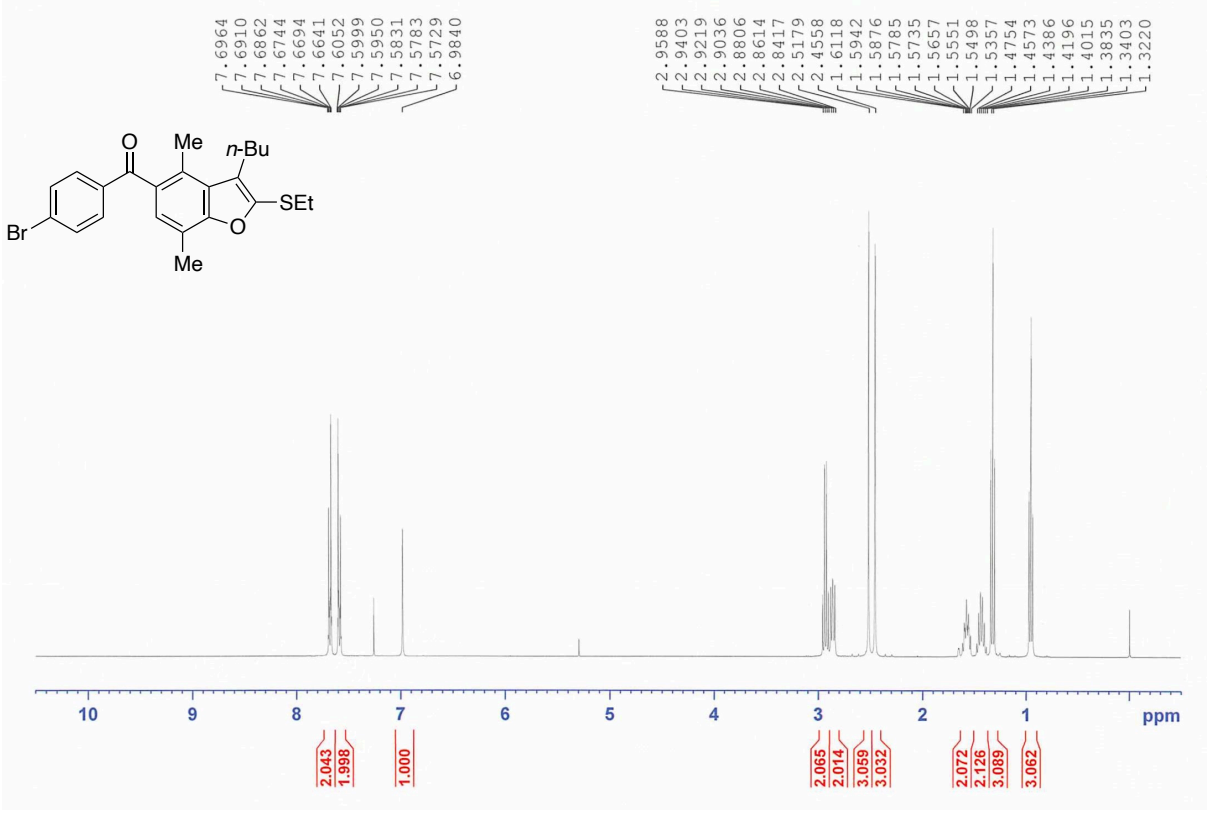


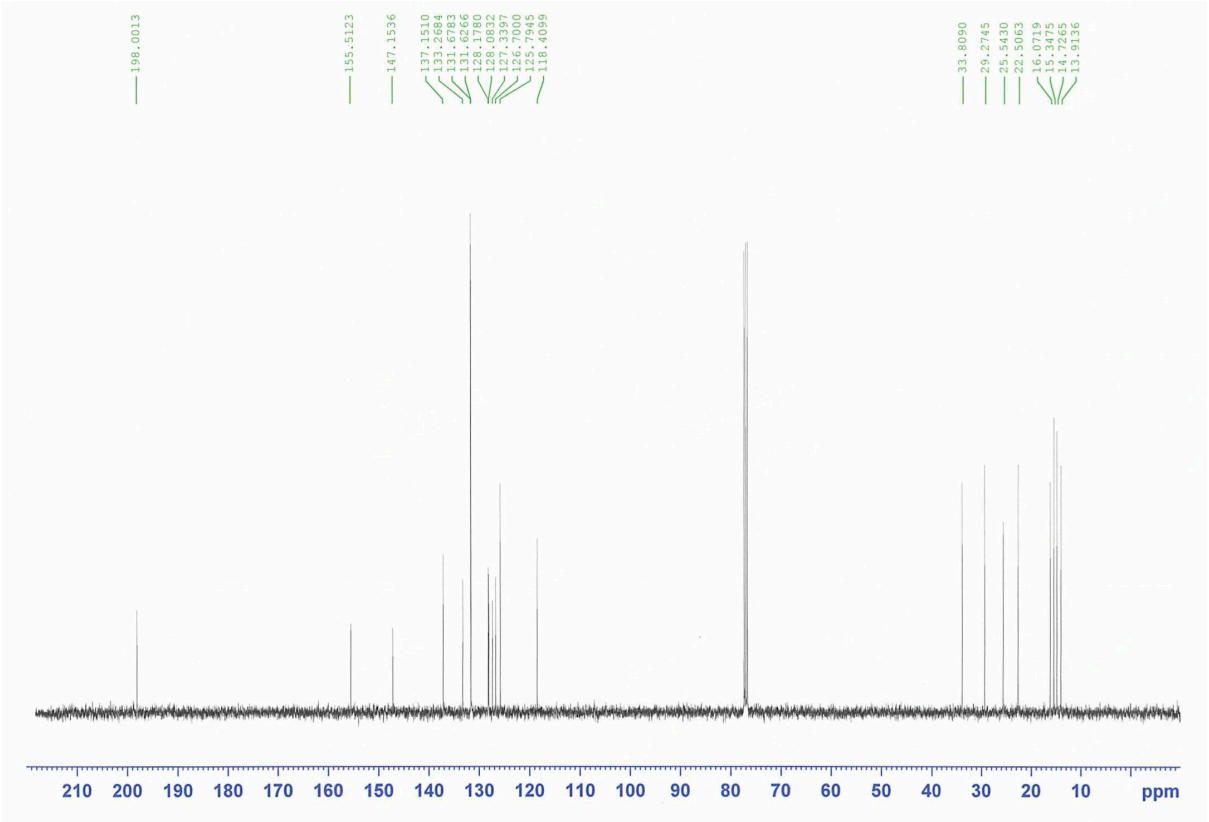


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of (3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-yl)(4-methoxyphenyl)methanone (**4f**) ($CDCl_3$)

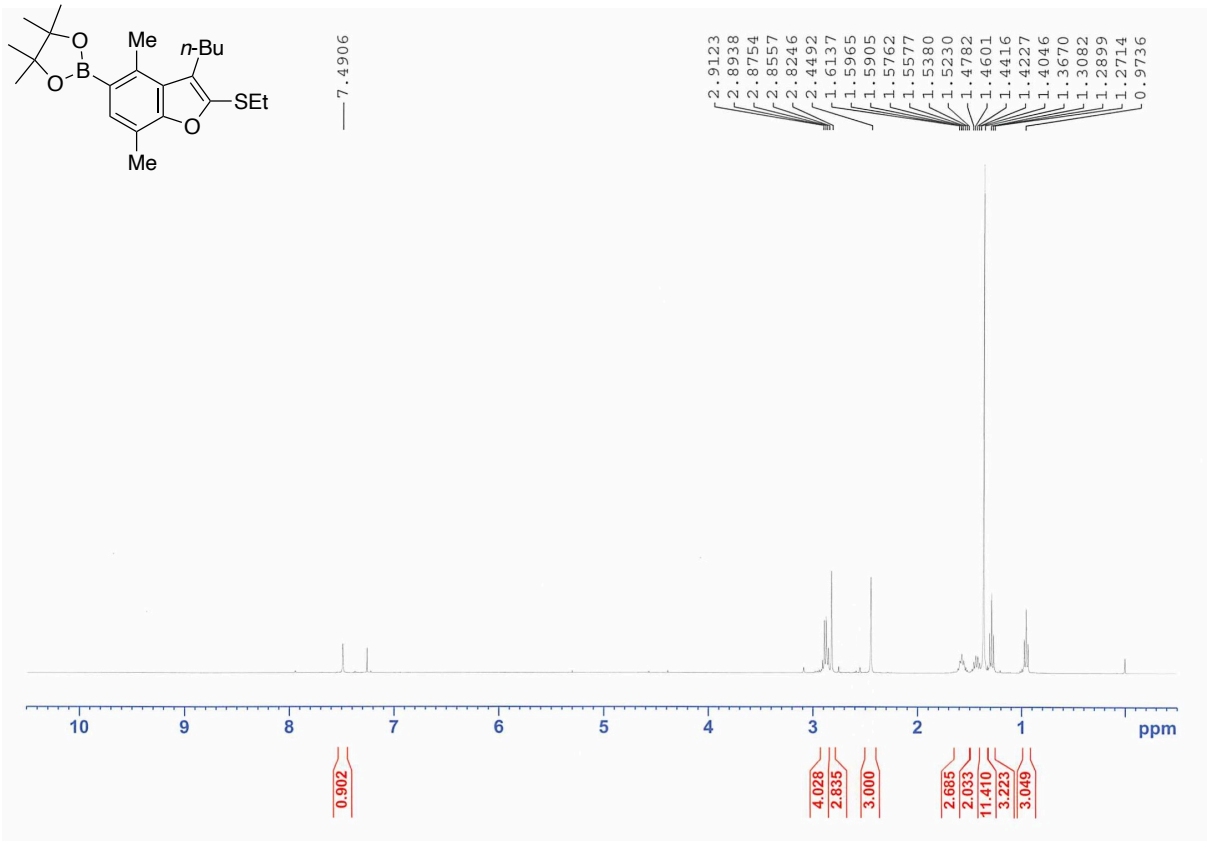


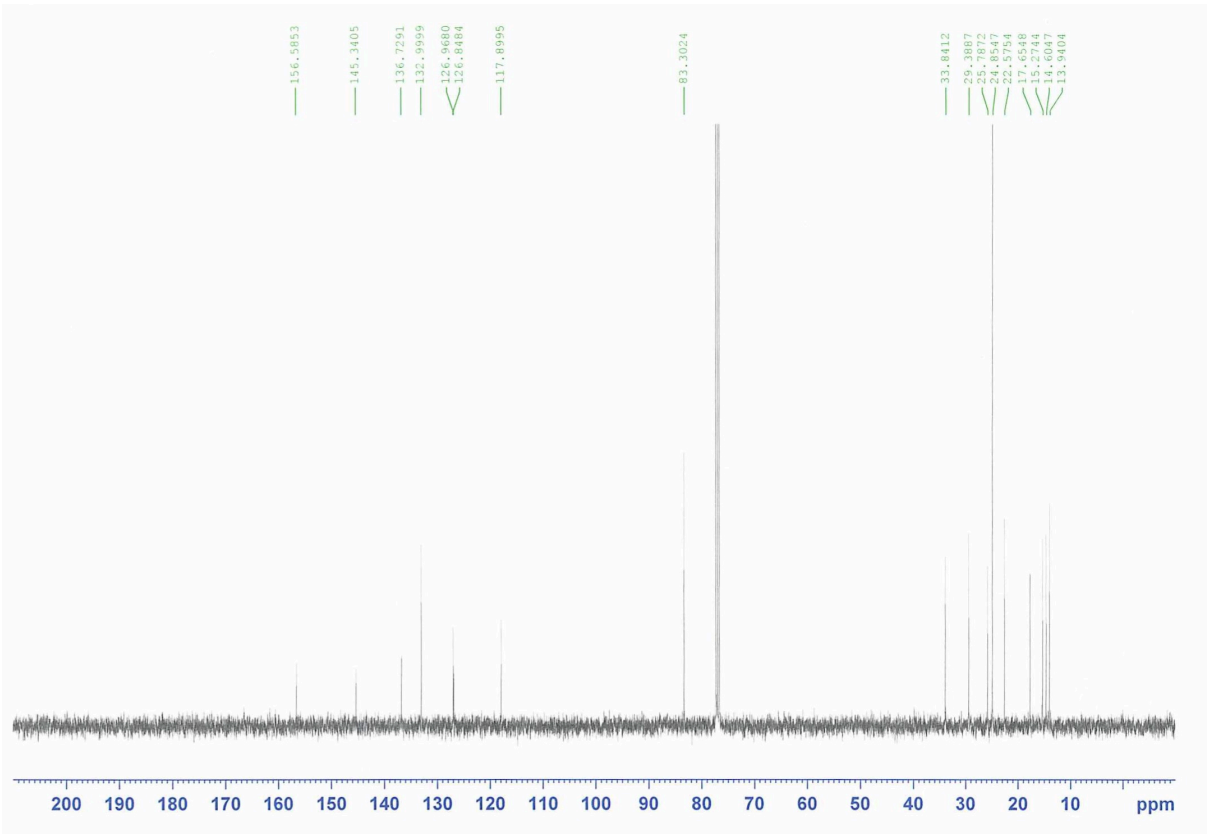
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of (4-bromophenyl)(3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-yl)methanone (**4g**) ($CDCl_3$)



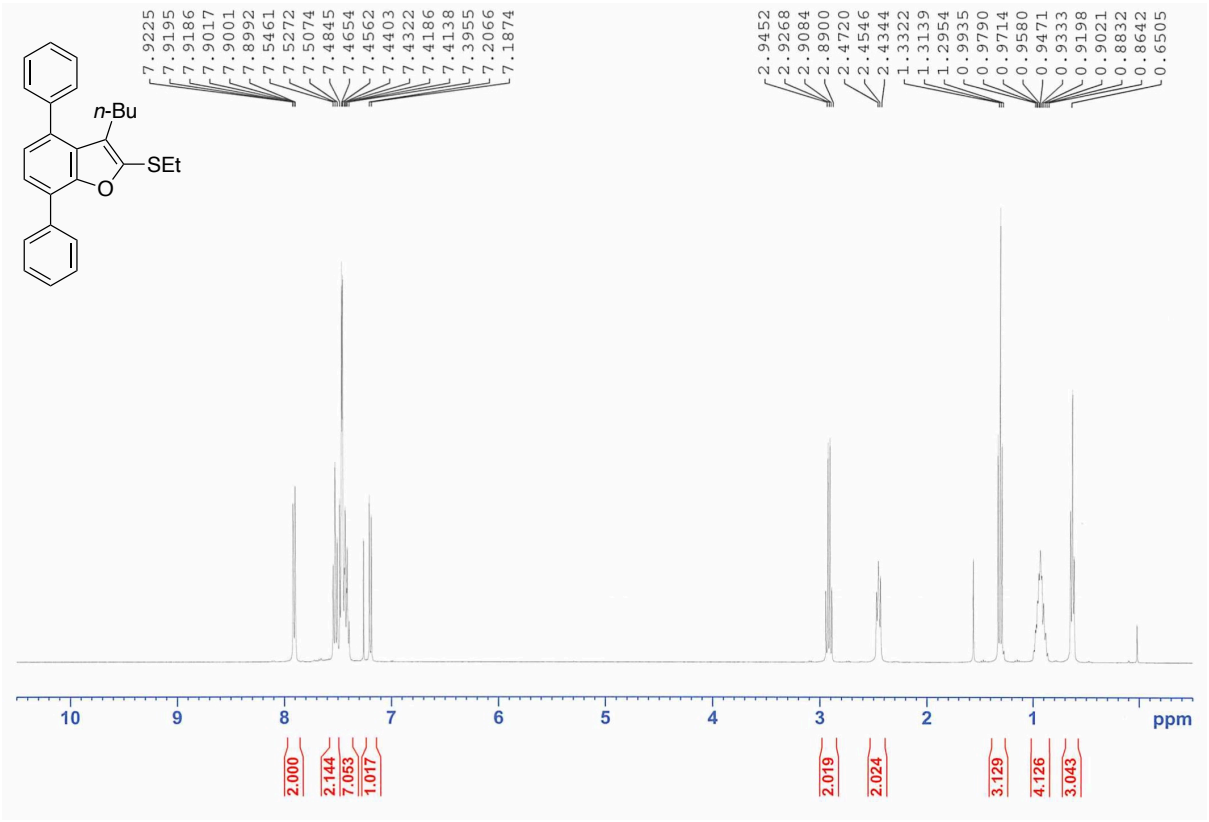


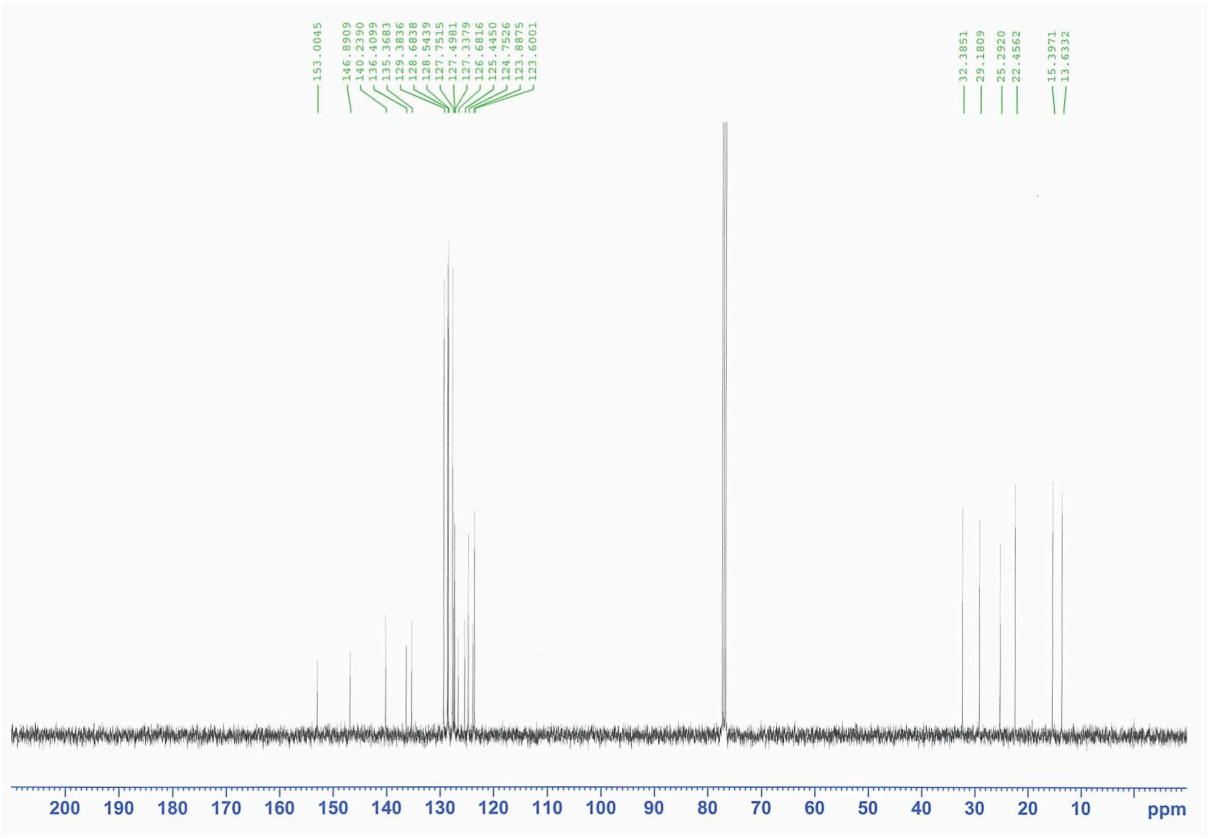
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-(3-butyl-2-(ethylthio)-4,7-dimethylbenzofuran-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4h**) ($CDCl_3$)



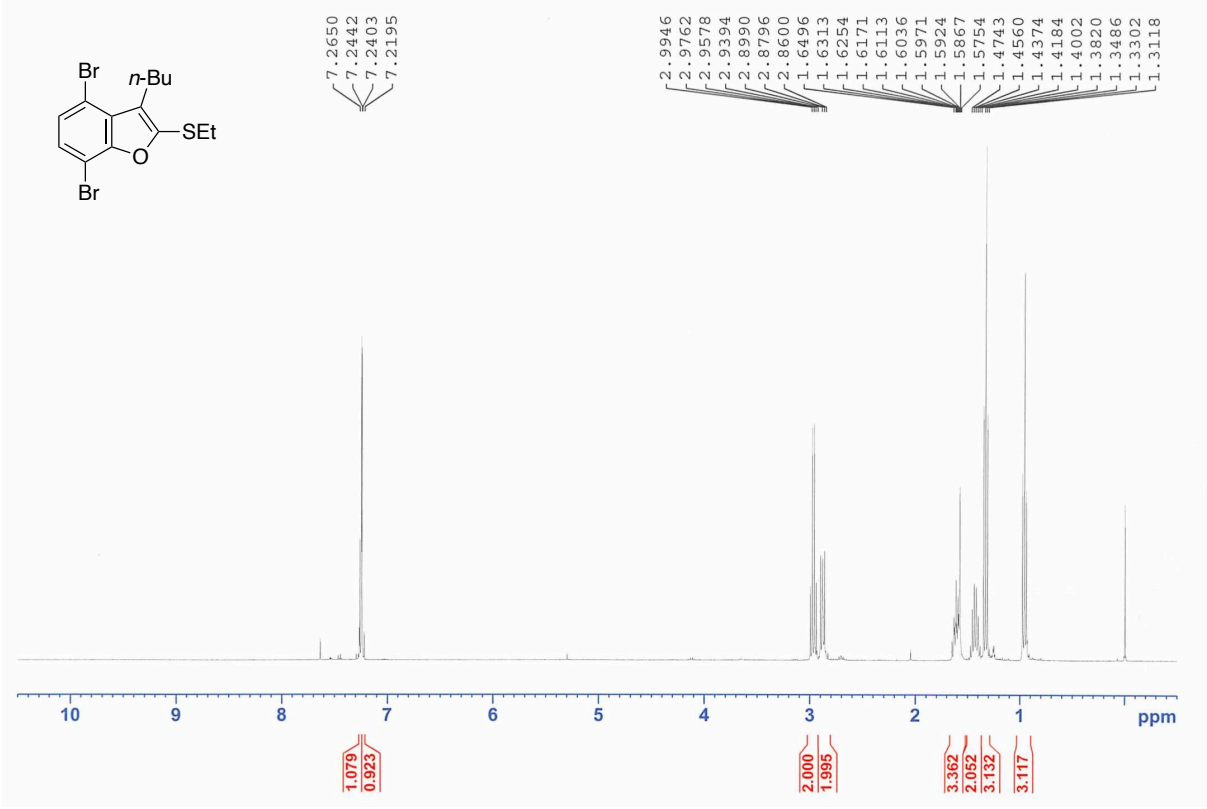


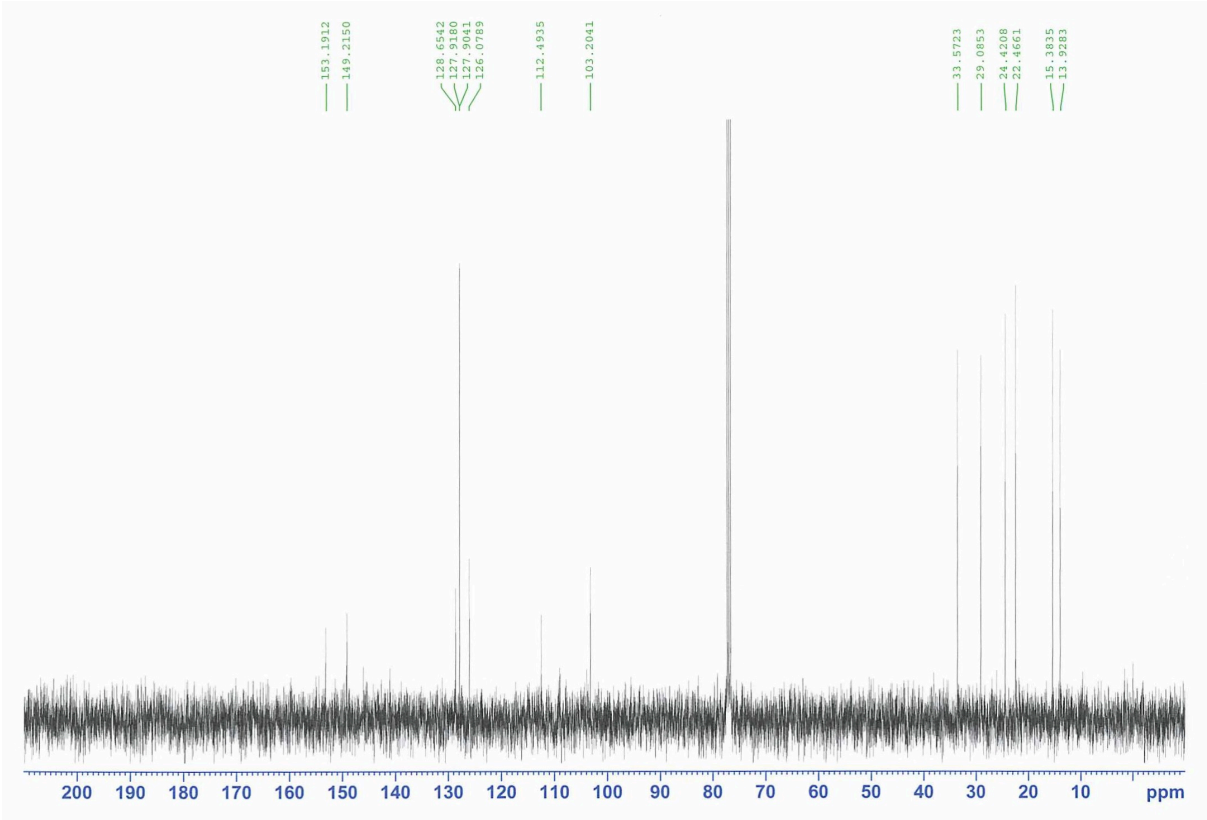
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-butyl-2-(ethylthio)-4,7-diphenylbenzofuran (**4i**) ($CDCl_3$)



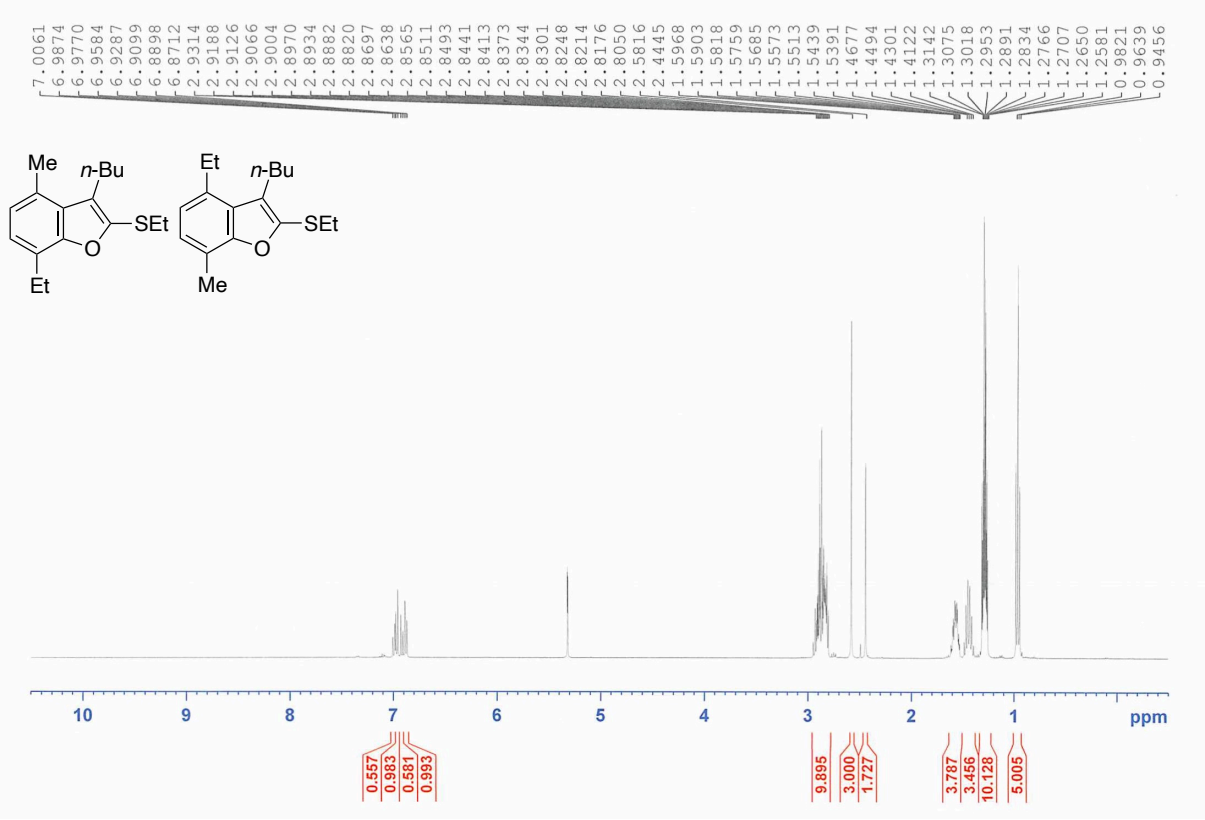


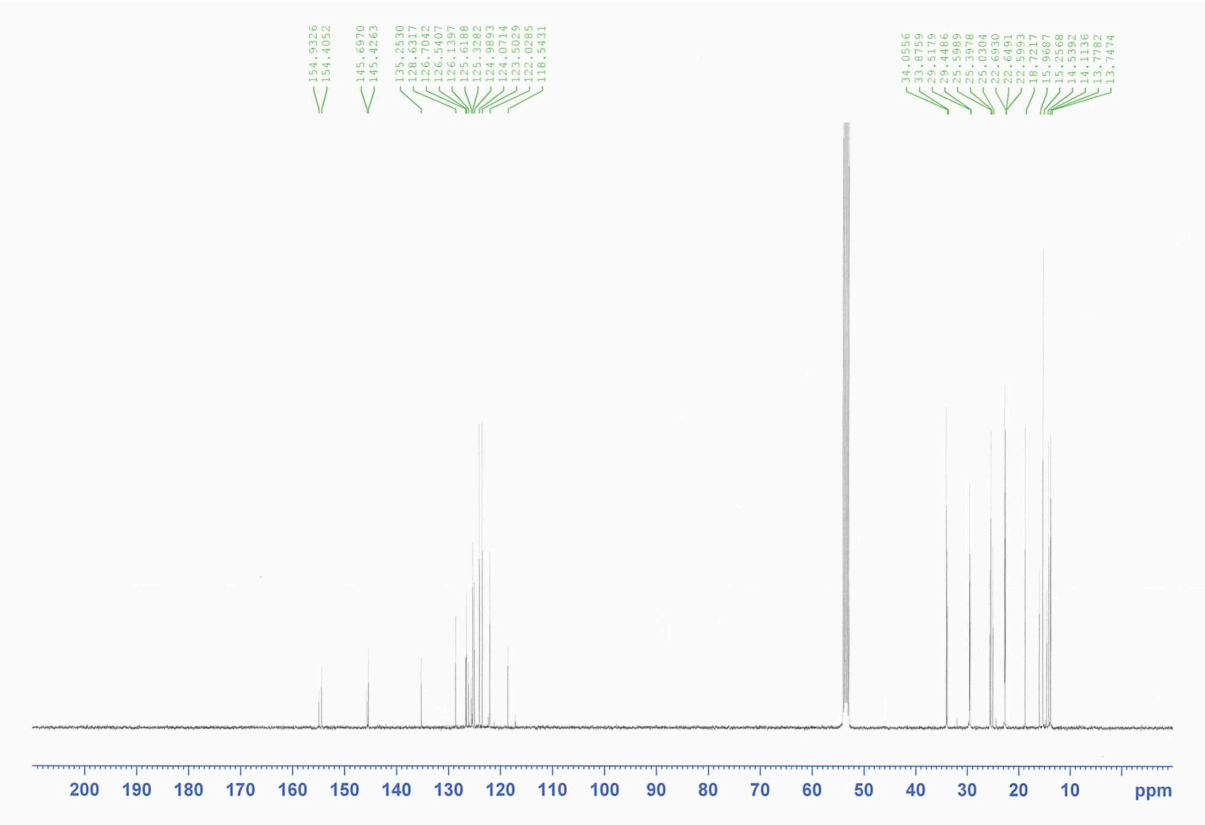
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4,7-dibromo-3-butyl-2-(ethylthio)benzofuran (**4j**) ($CDCl_3$)

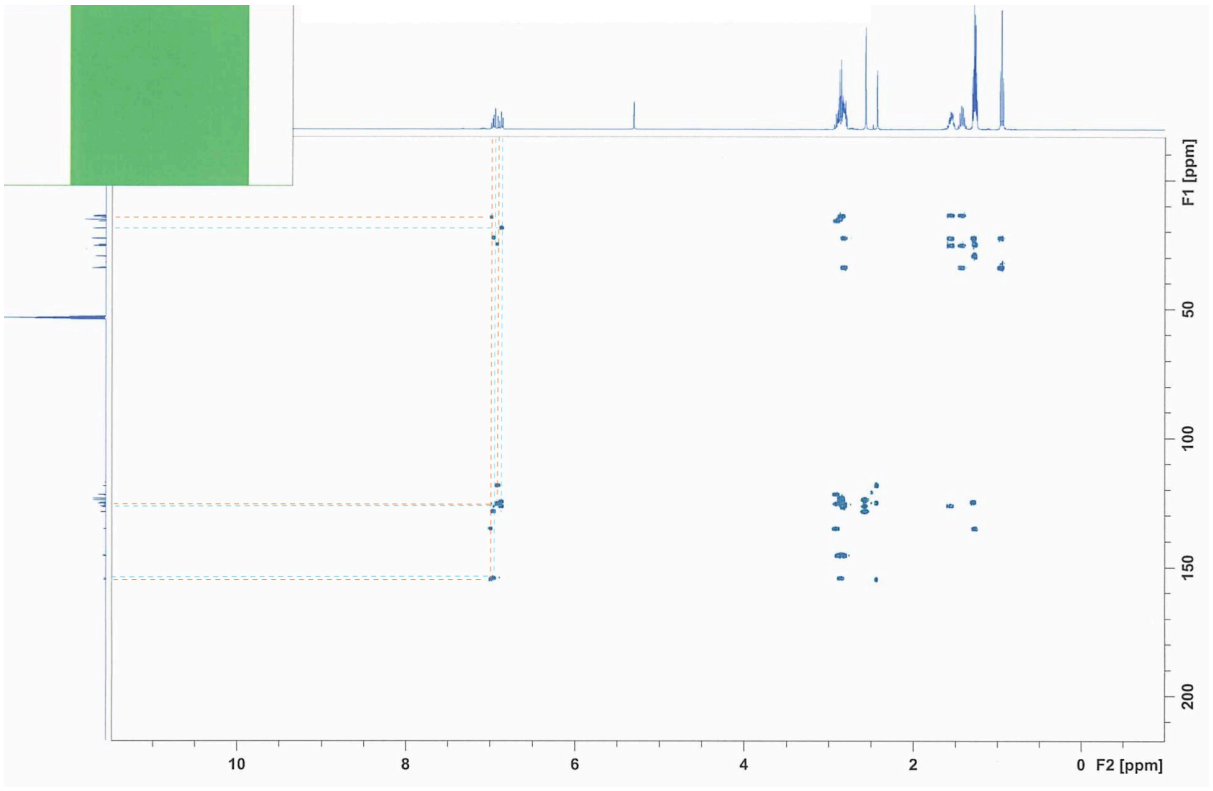




^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), and HMBC spectra of a mixture of 3-butyl-7-ethyl-2-(ethylthio)-4-methylbenzofuran (**4k**) and 3-butyl-4-ethyl-2-(ethylthio)-7-methylbenzofuran (**4k'**) (CD_2Cl_2)






F1 [ppm]
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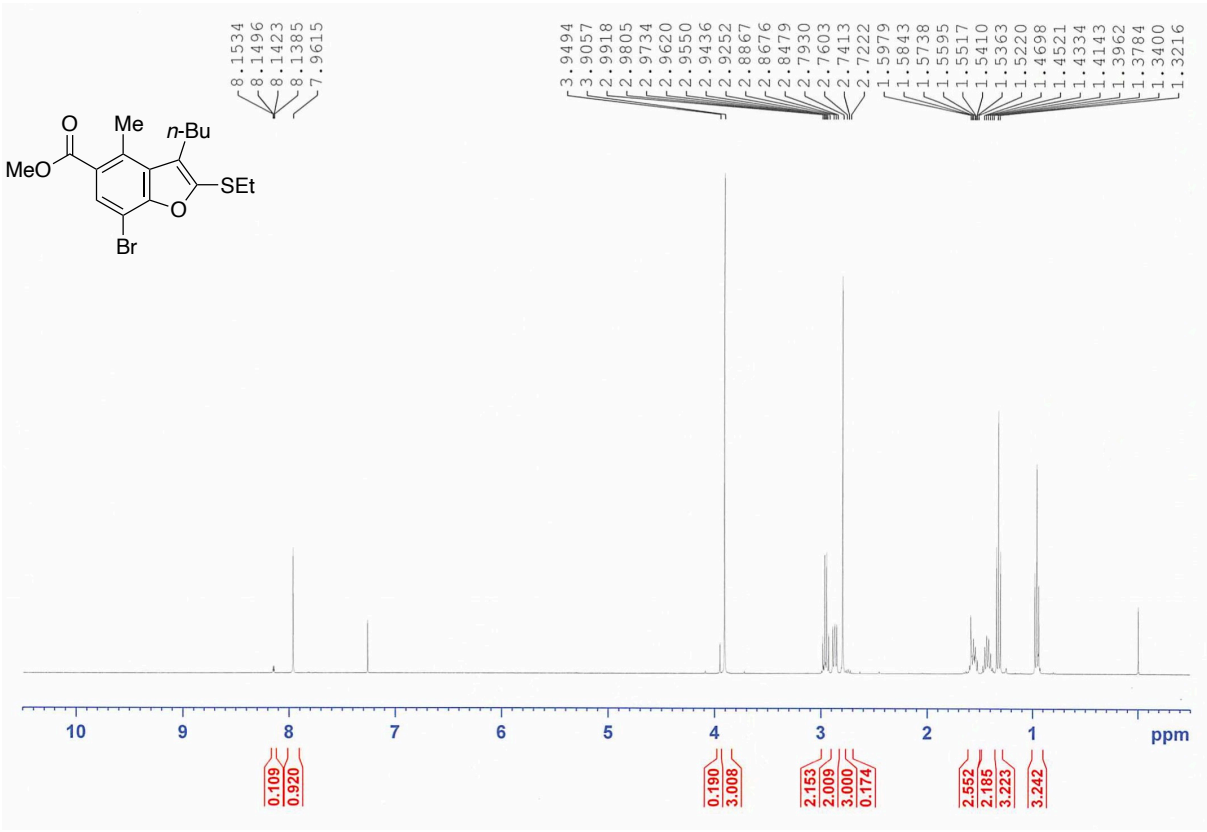
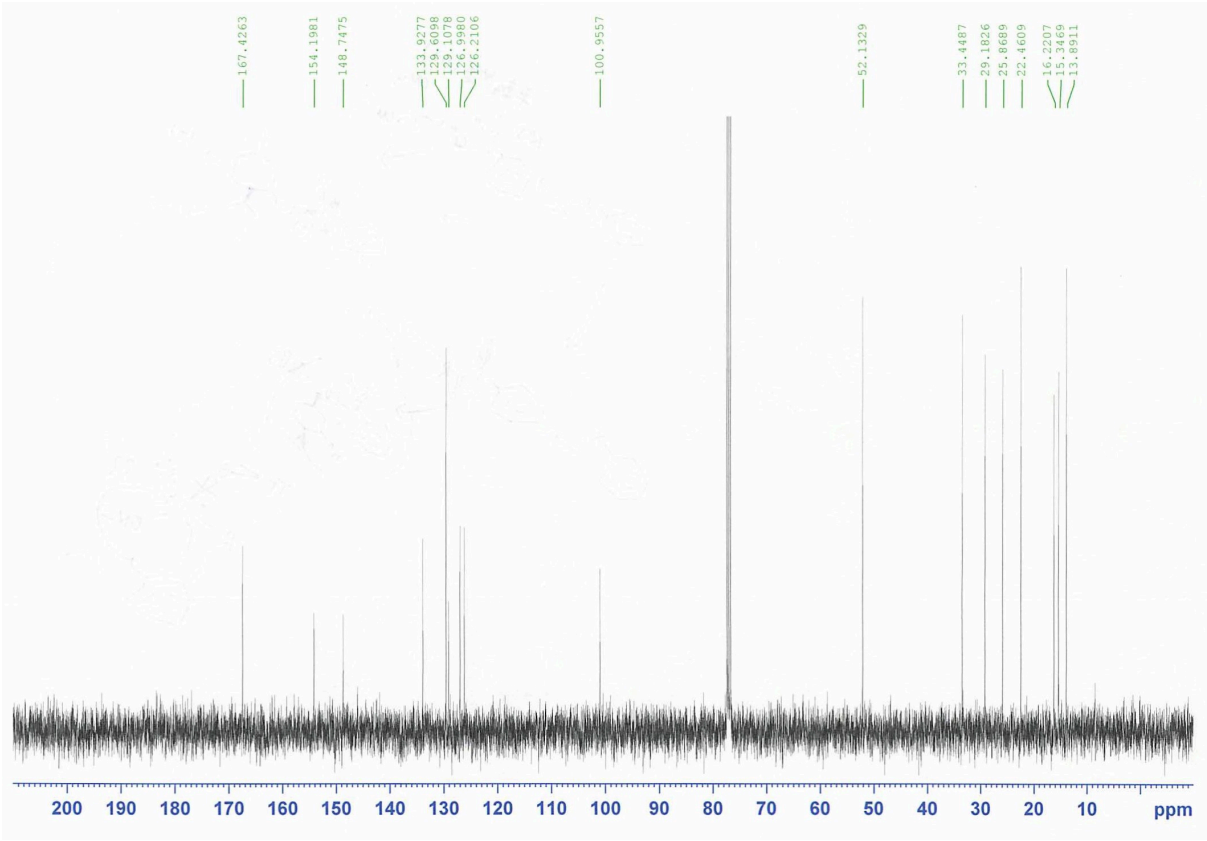
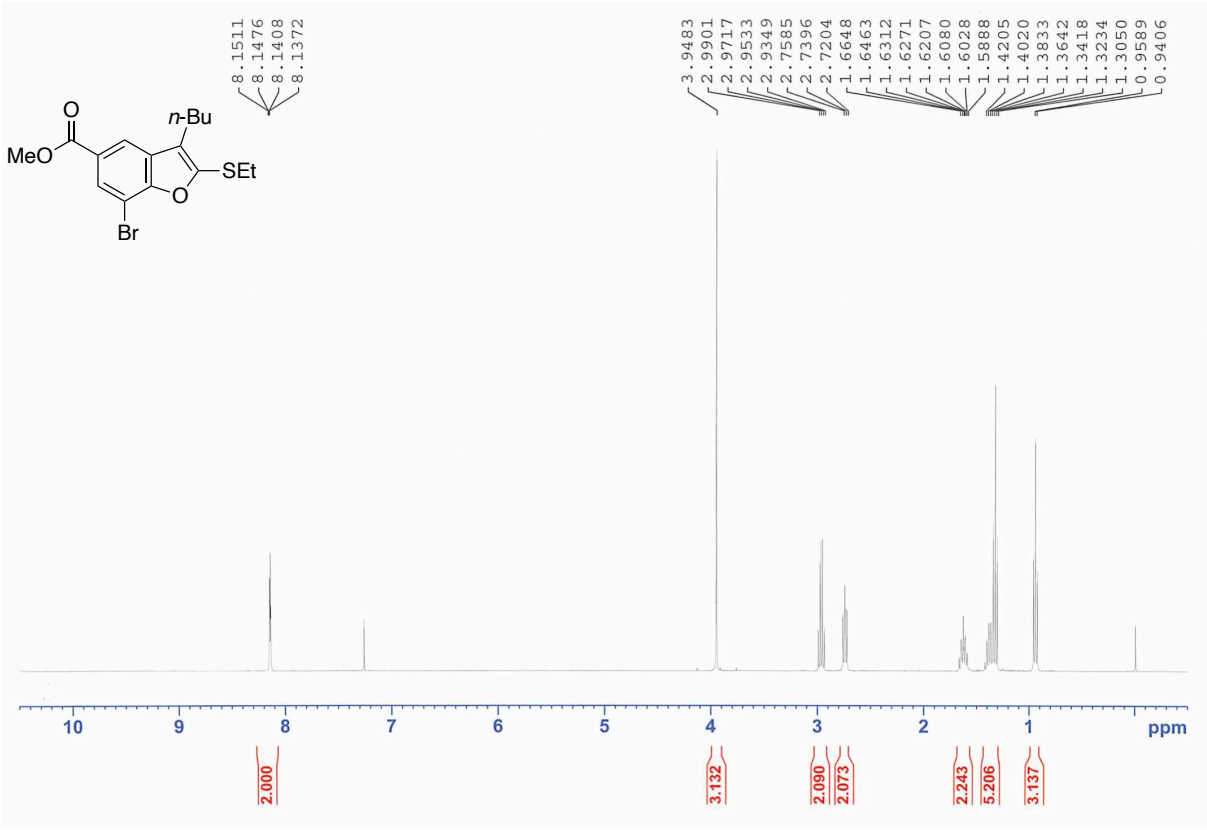
150
200
10
8
6
4
2
0 F2 [ppm]

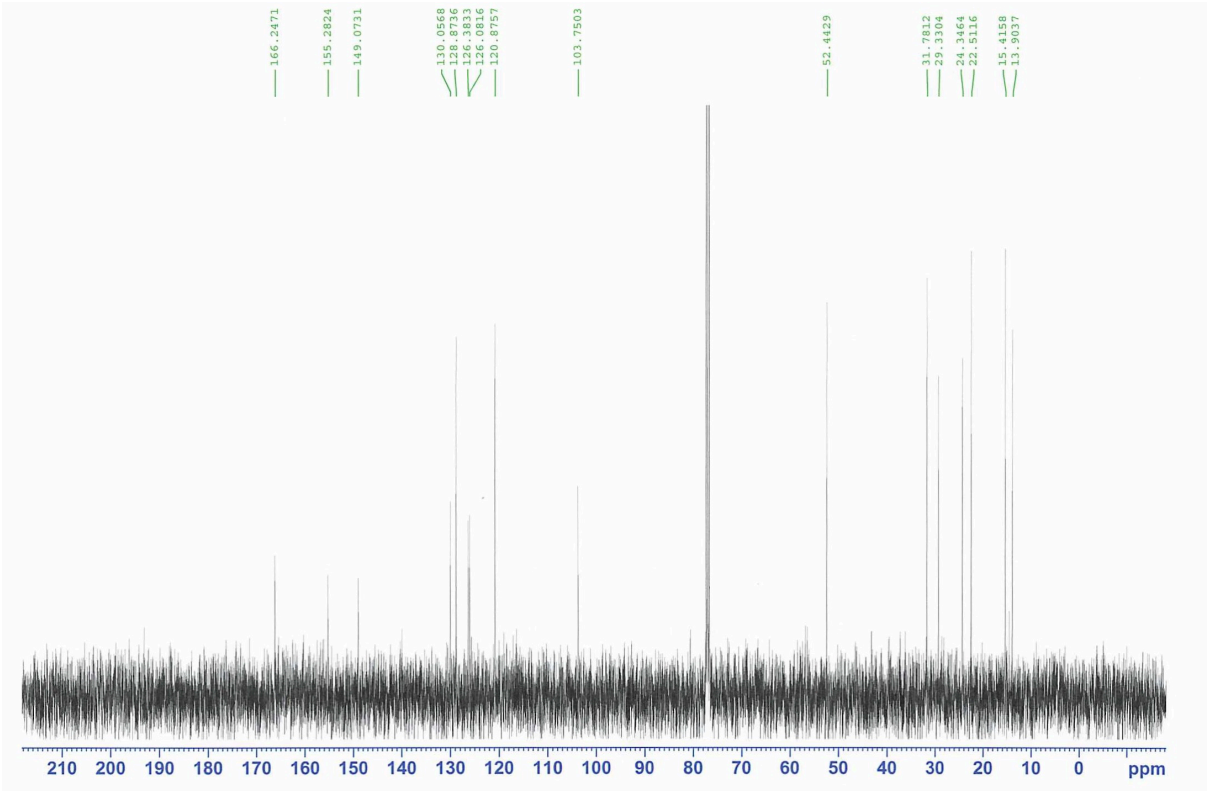
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 7-bromo-3-butyl-2-(ethylthio)-4-methylbenzofuran-5-carboxylate (**4l**) ($CDCl_3$)



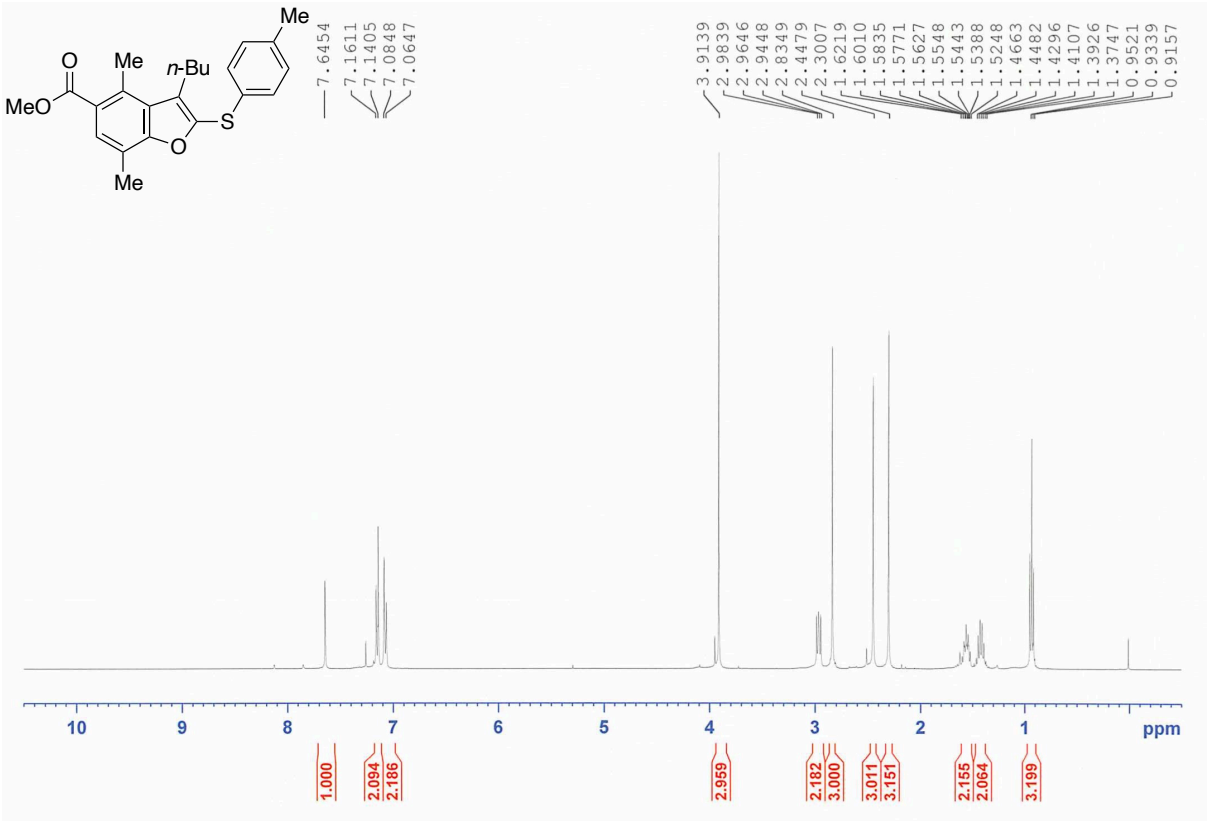


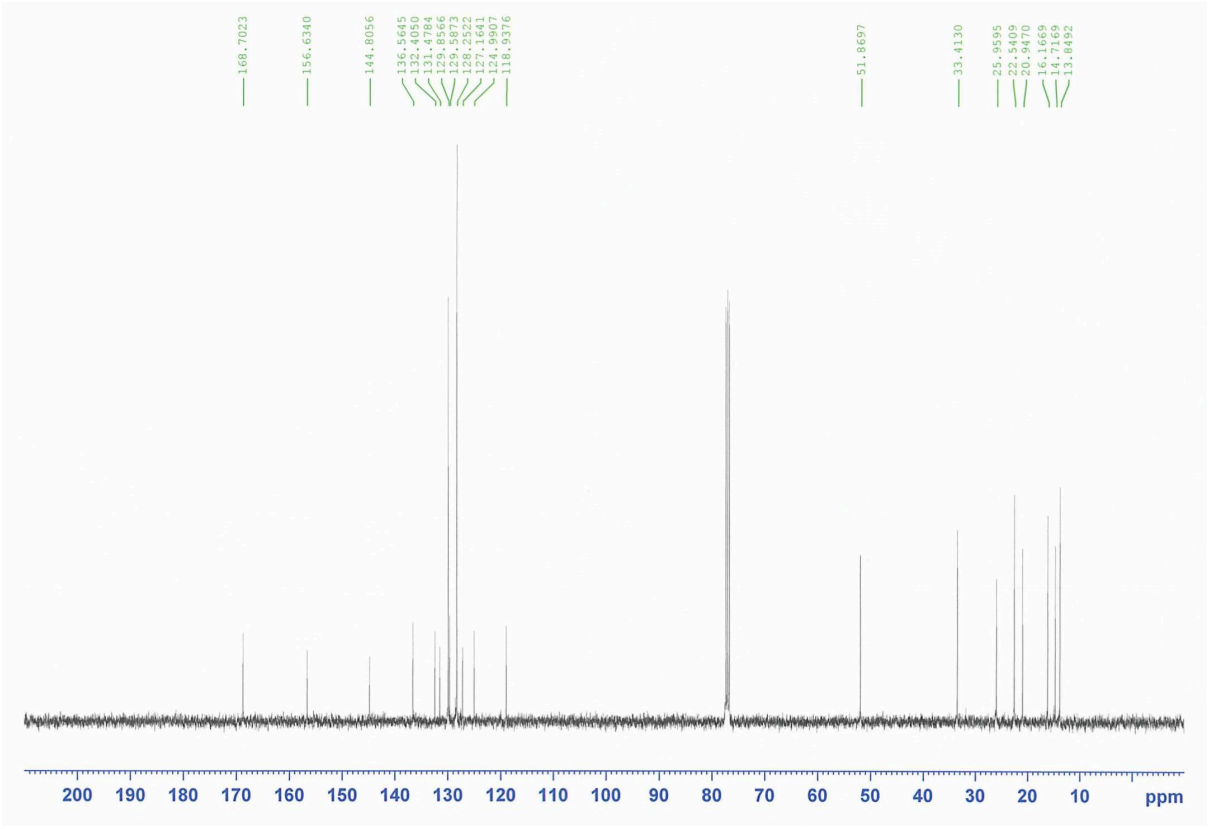
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 7-bromo-3-butyl-2-(ethylthio)benzofuran-5-carboxylate ($CDCl_3$)



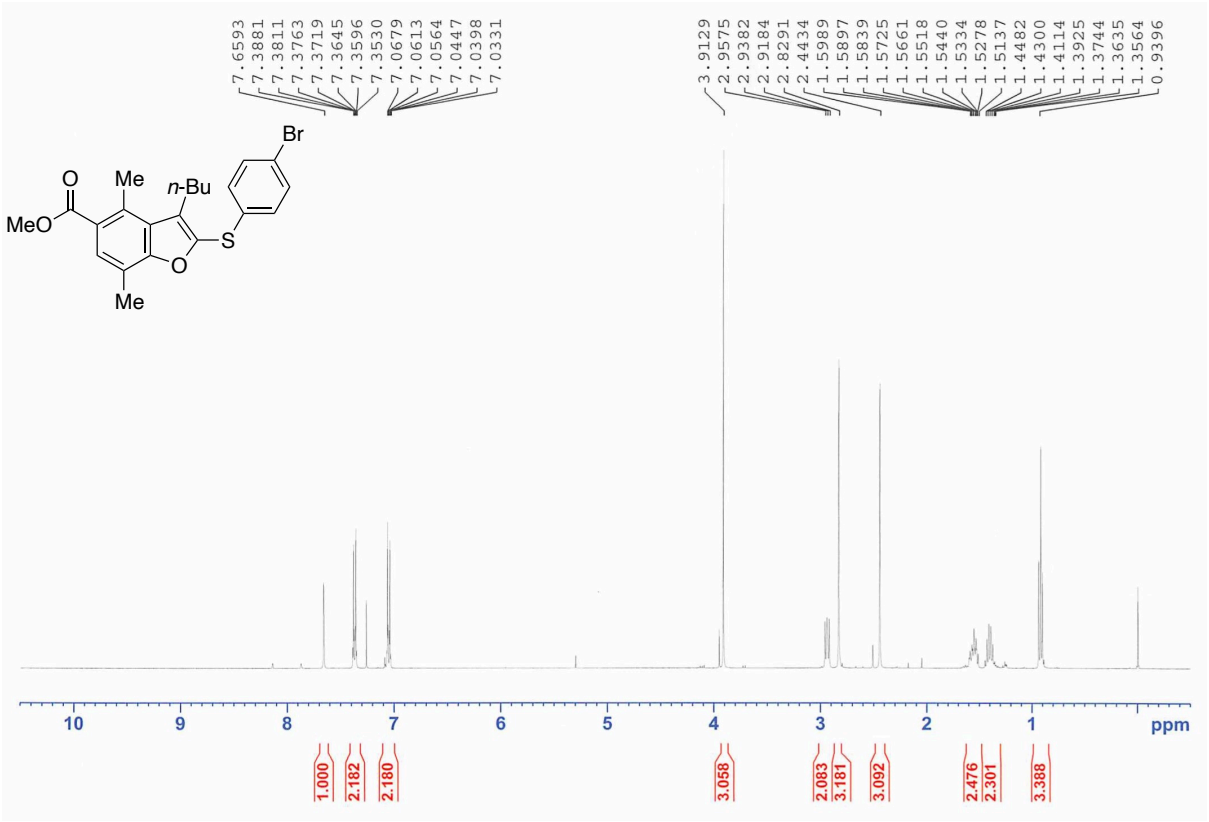


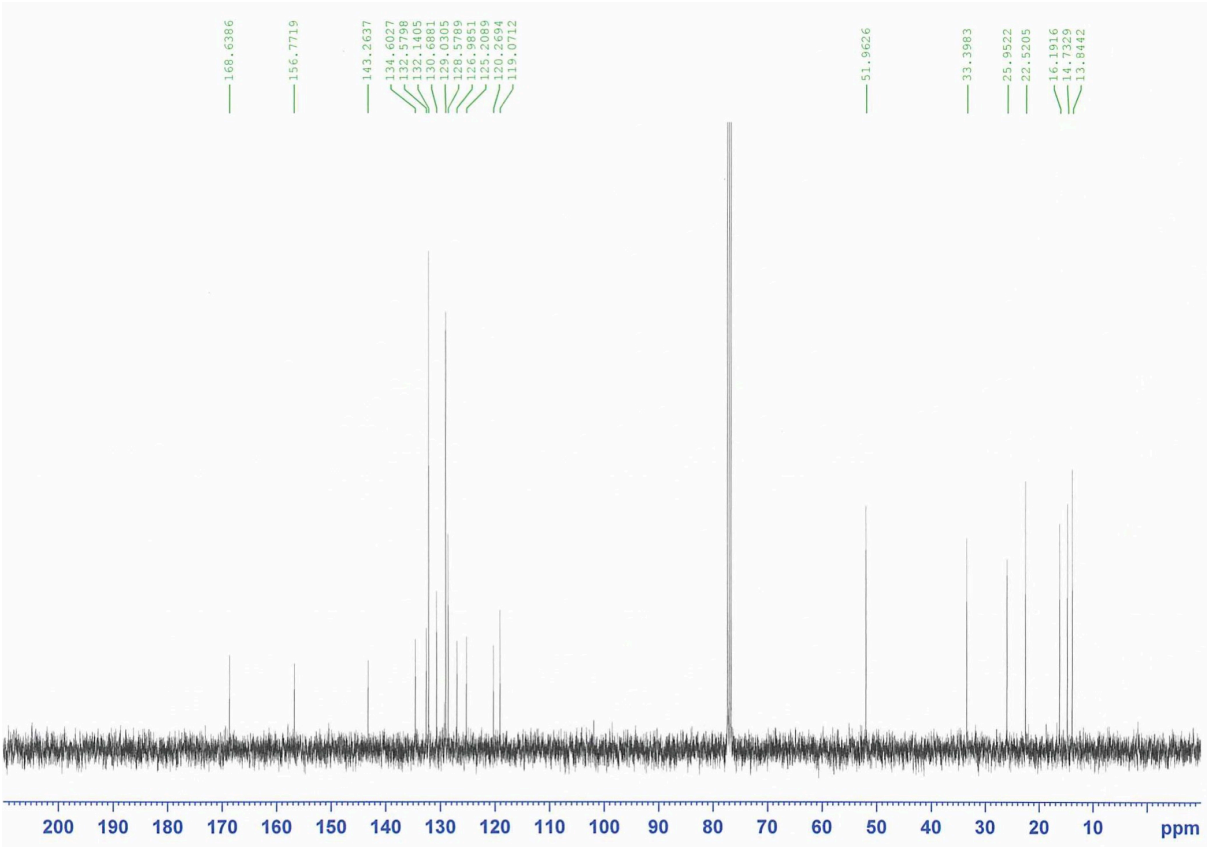
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 3-butyl-4,7-dimethyl-2-(p-tolylthio)benzofuran-5-carboxylate (**4m**) ($CDCl_3$)



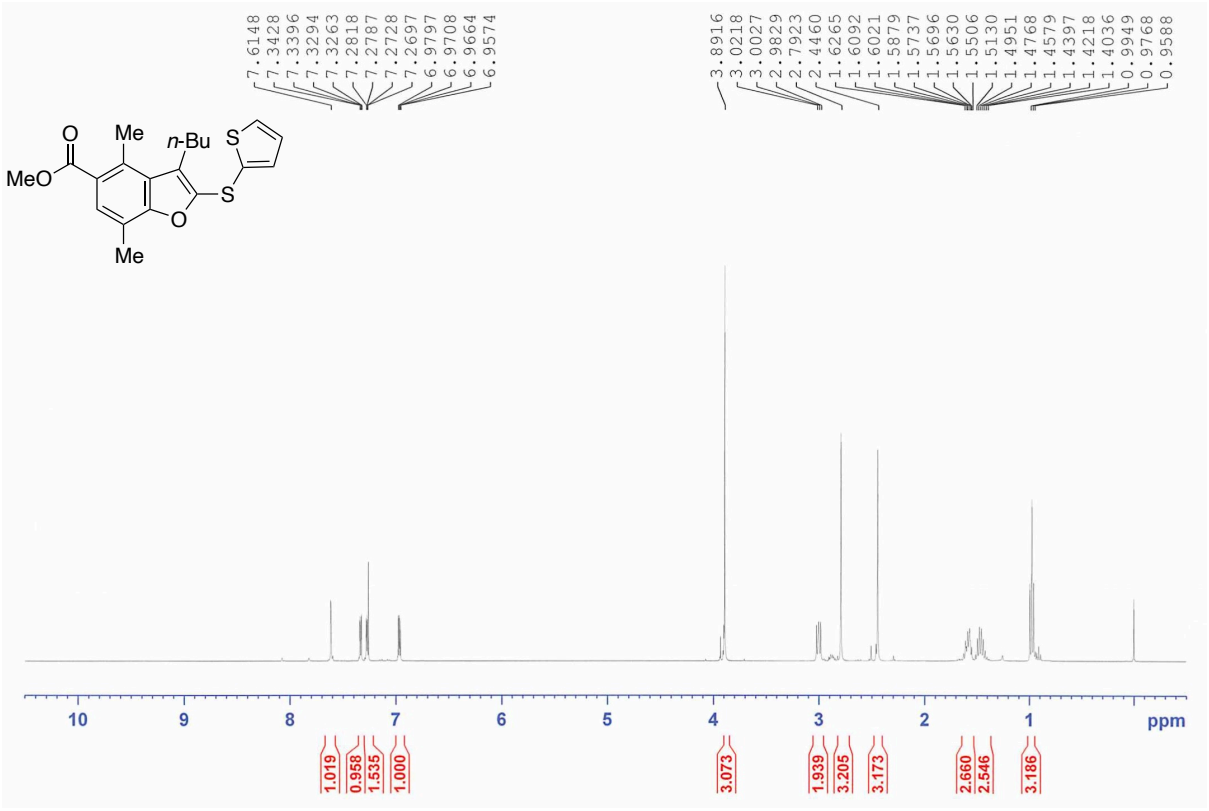


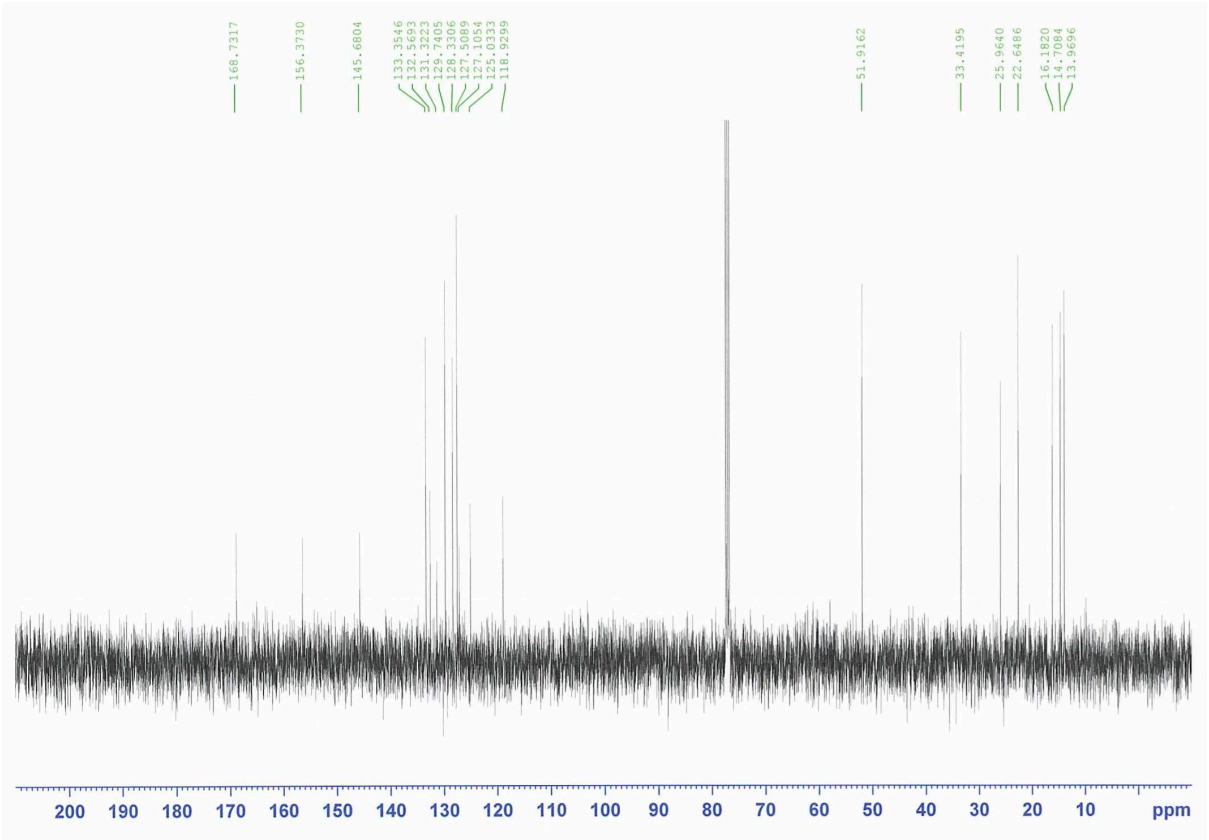
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 2-((4-bromophenyl)thio)-3-butyl-4,7-dimethylbenzofuran-5-carboxylate (**4n**) ($CDCl_3$)



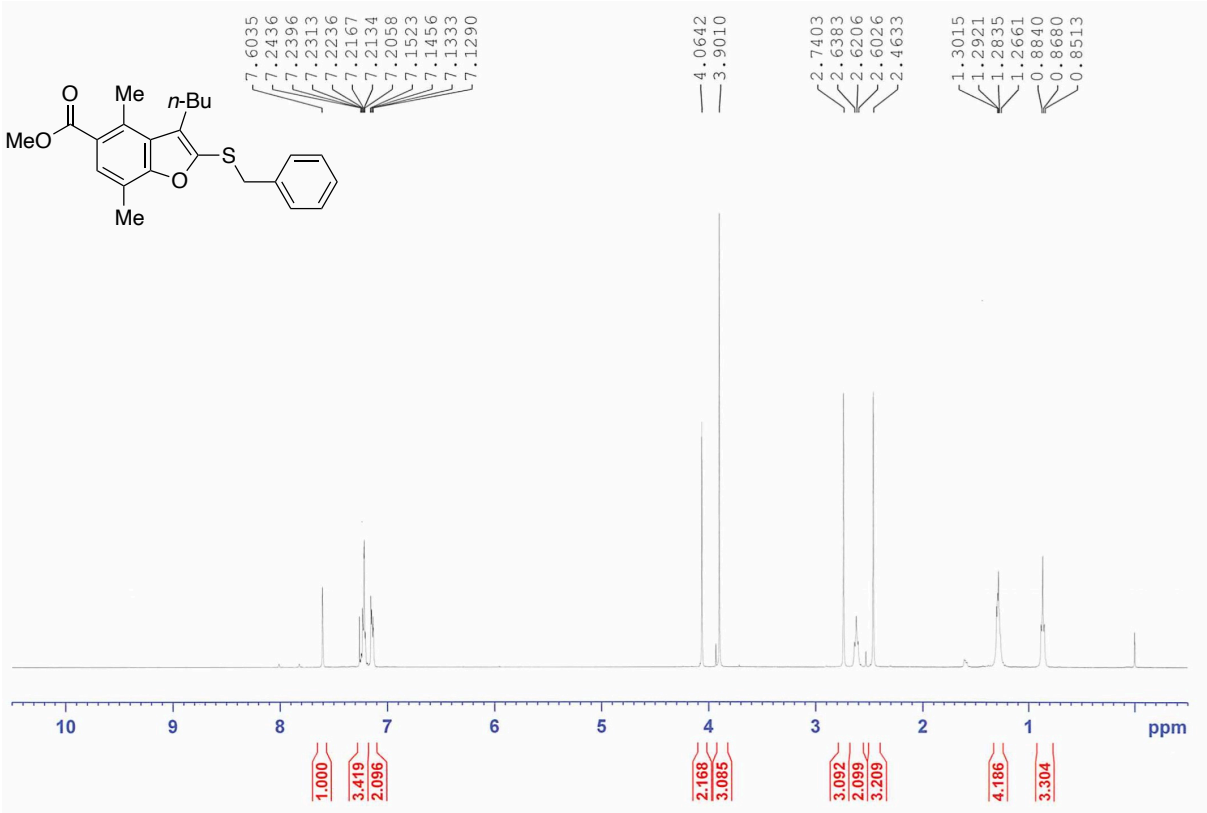


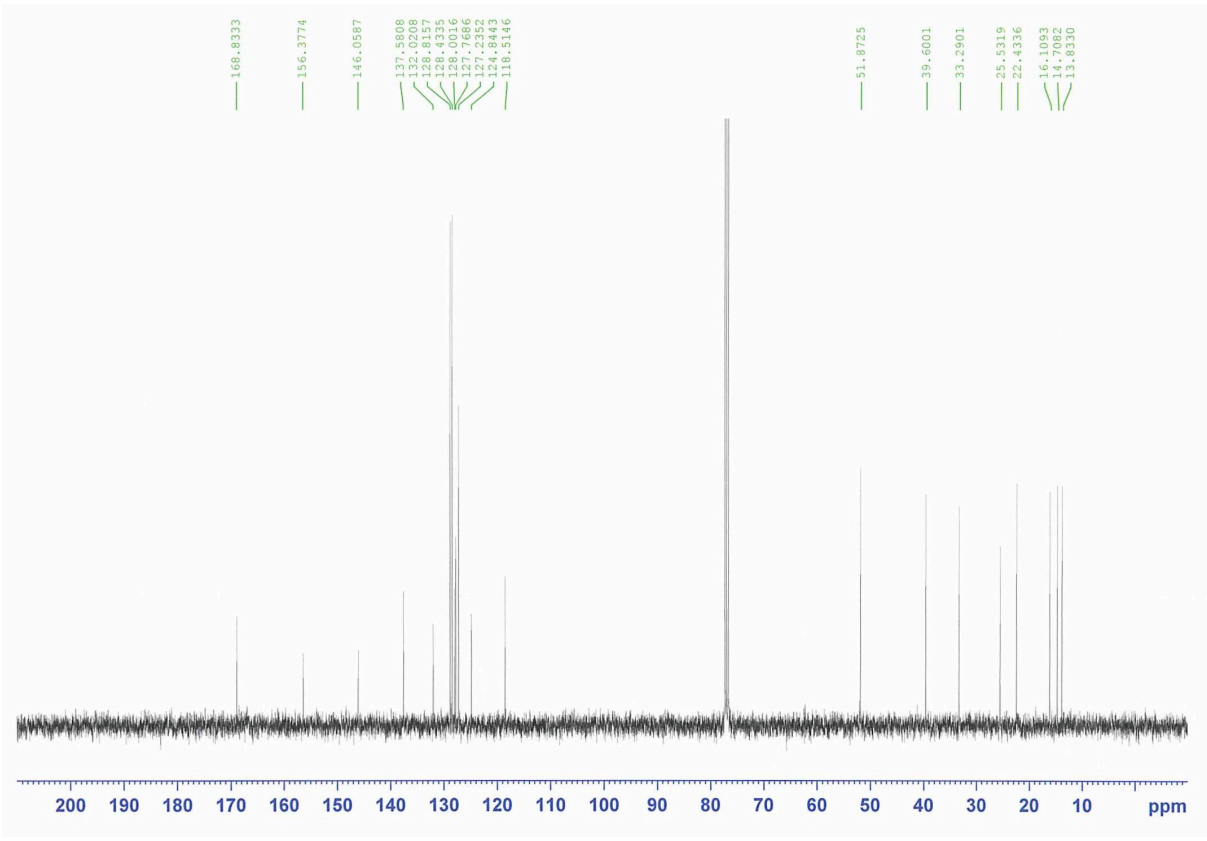
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-butyl-4,7-dimethyl-2-(thiophen-2-ylthio)benzofuran (**4o**) ($CDCl_3$)



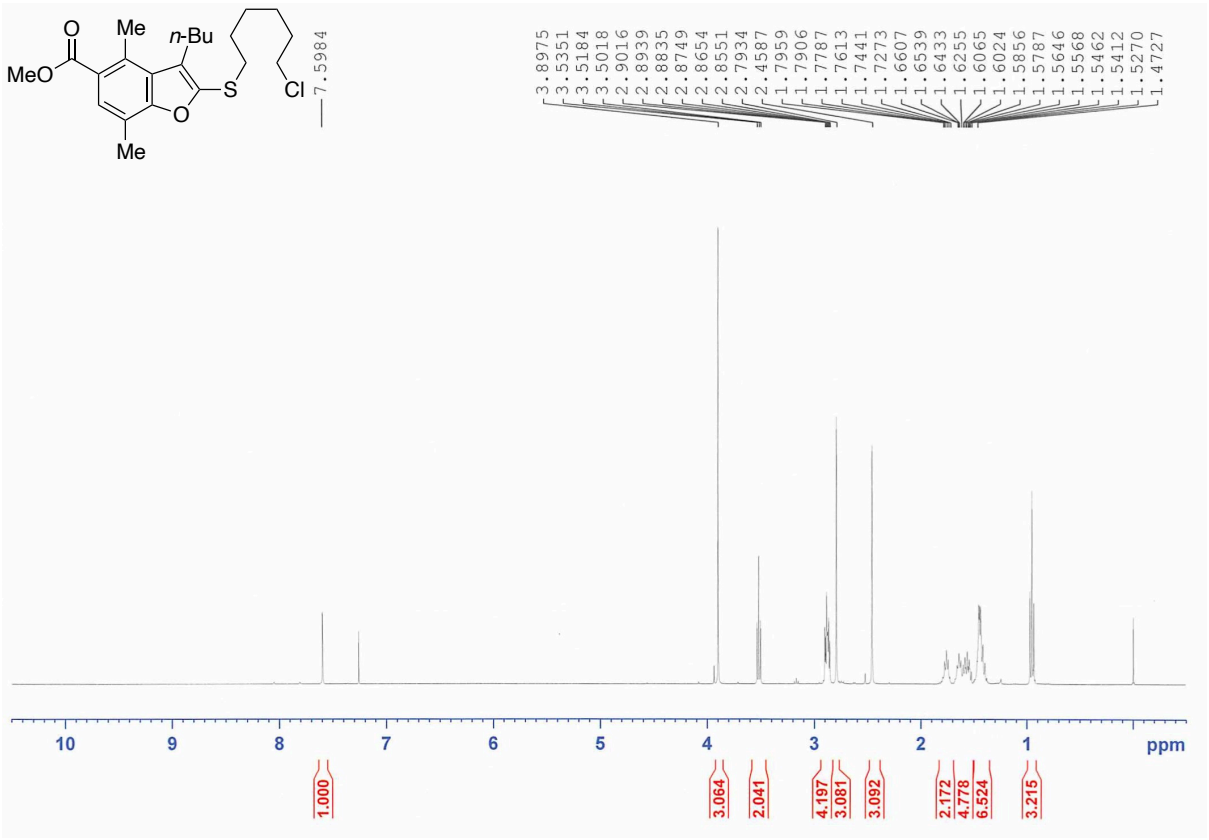


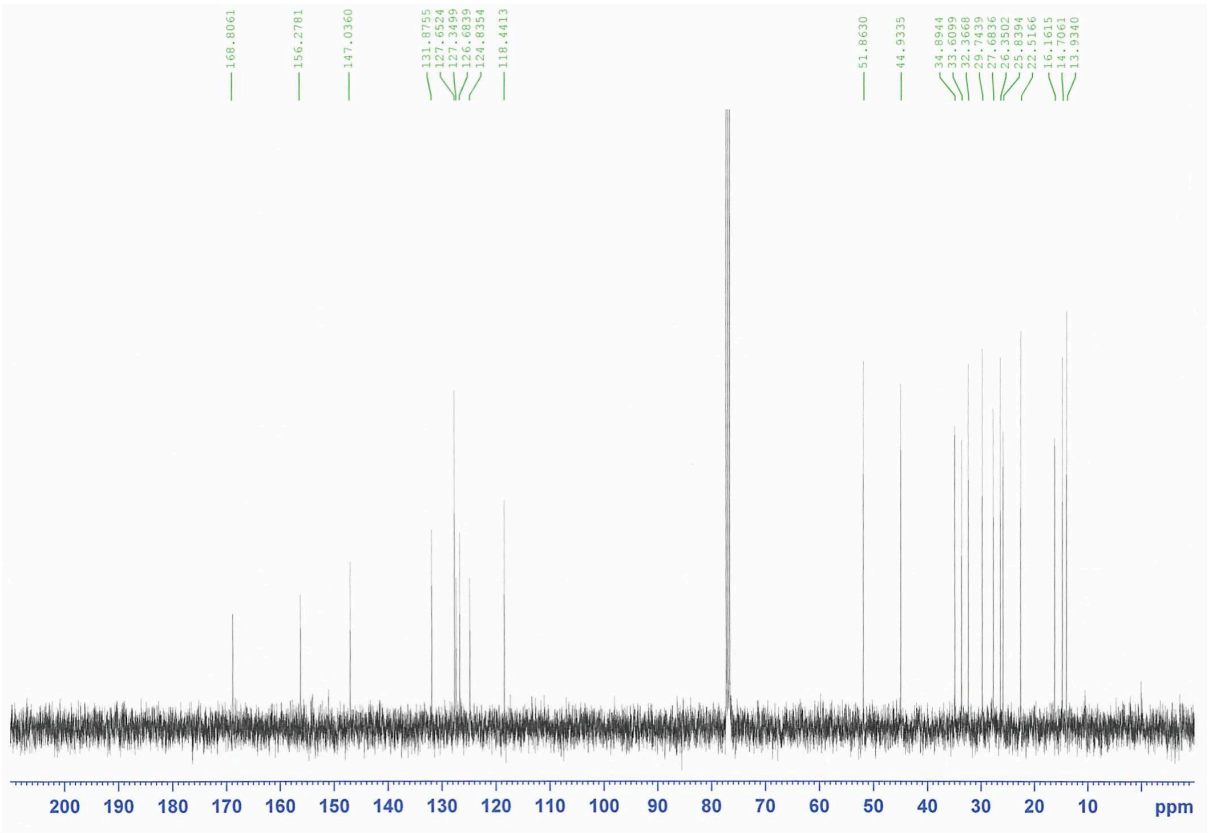
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 2-(benzylthio)-3-butyl-4,7-dimethylbenzofuran-5-carboxylate (**4p**) ($CDCl_3$)



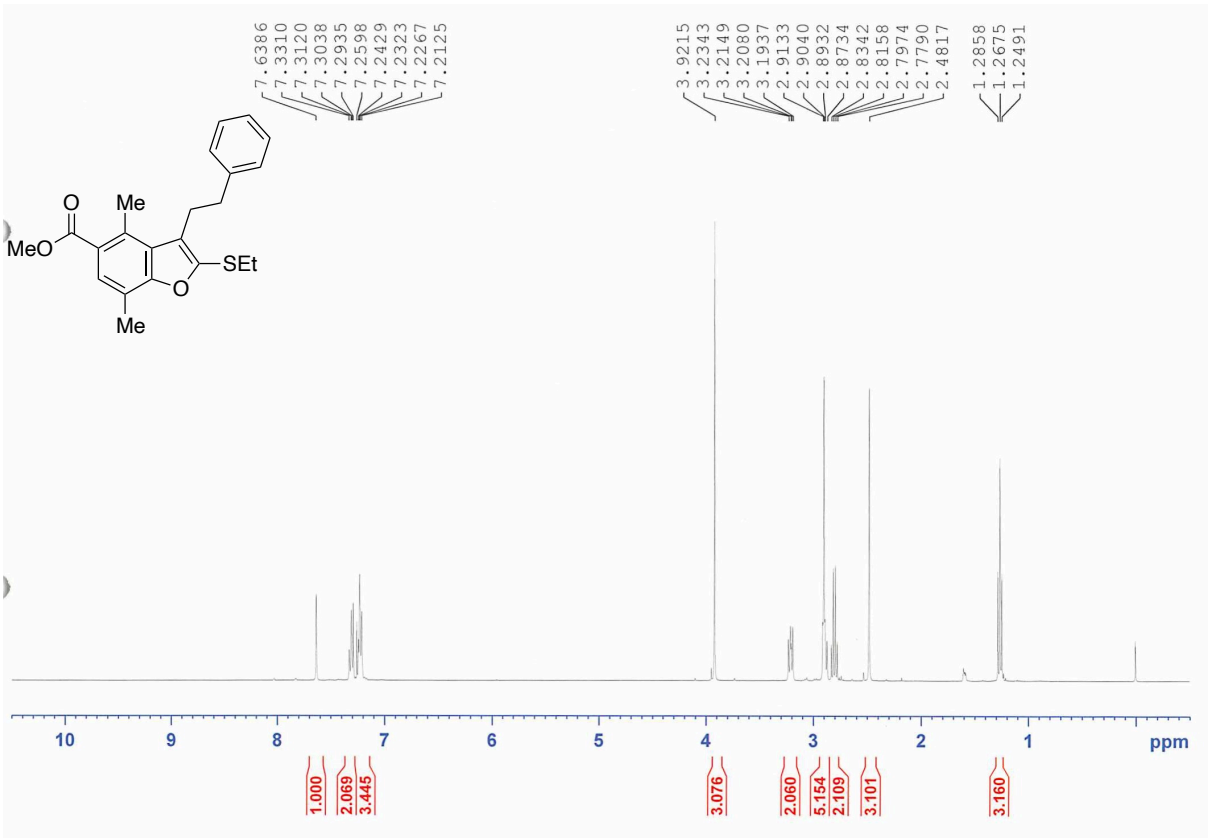


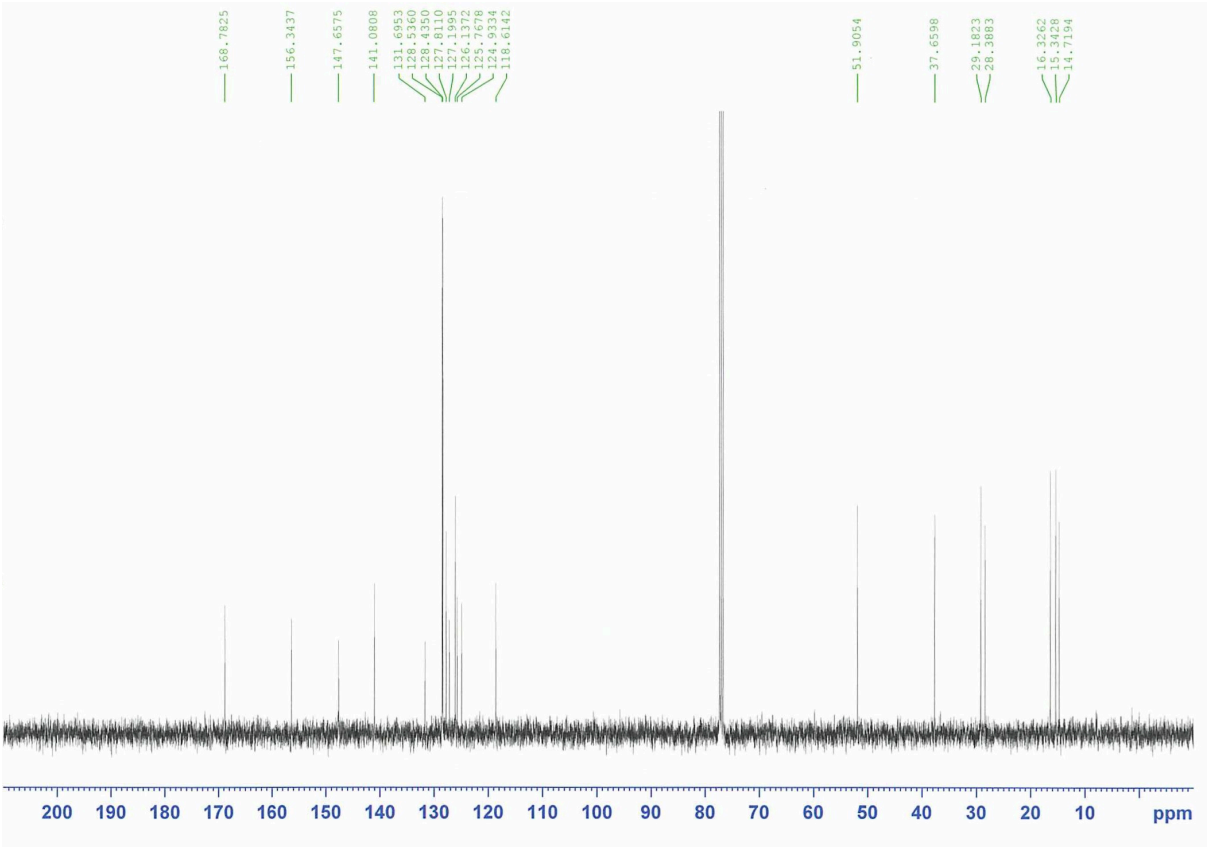
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 3-butyl-2-((6-chlorohexyl)thio)-4,7-dimethylbenzofuran-5-carboxylate (**4q**) ($CDCl_3$)



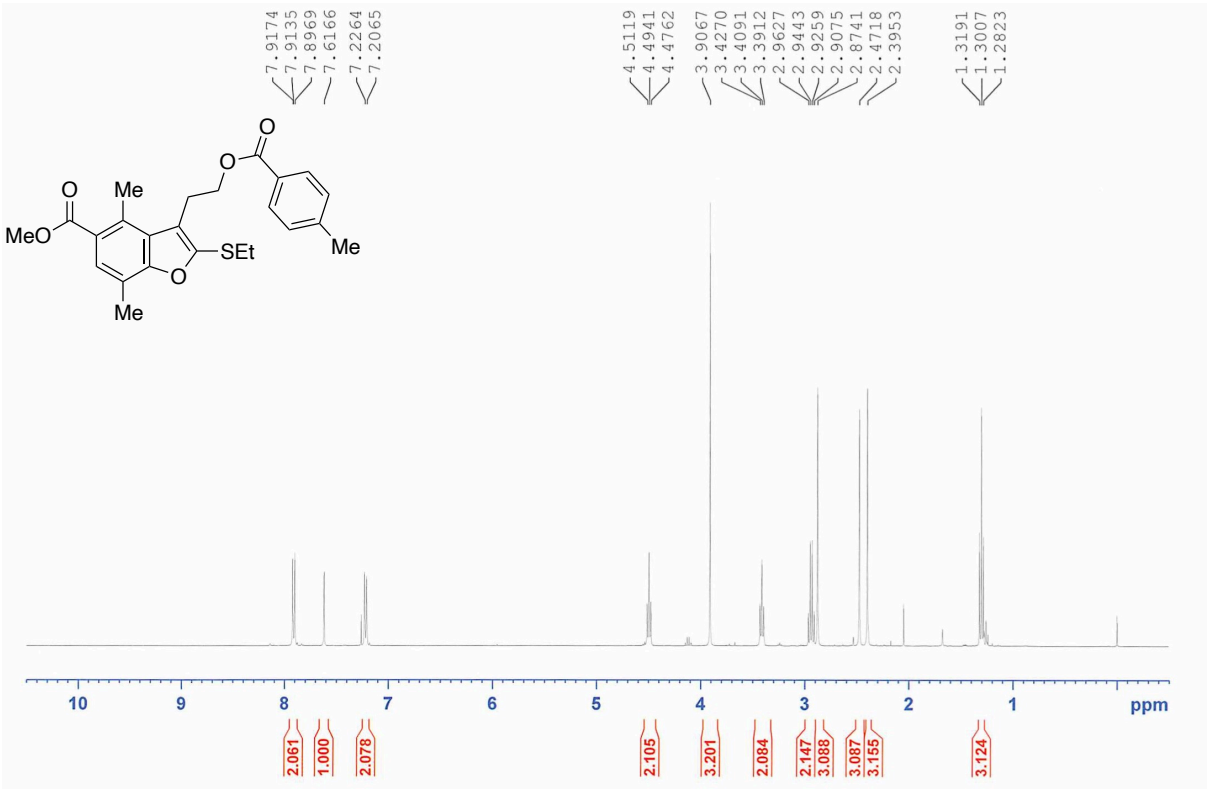


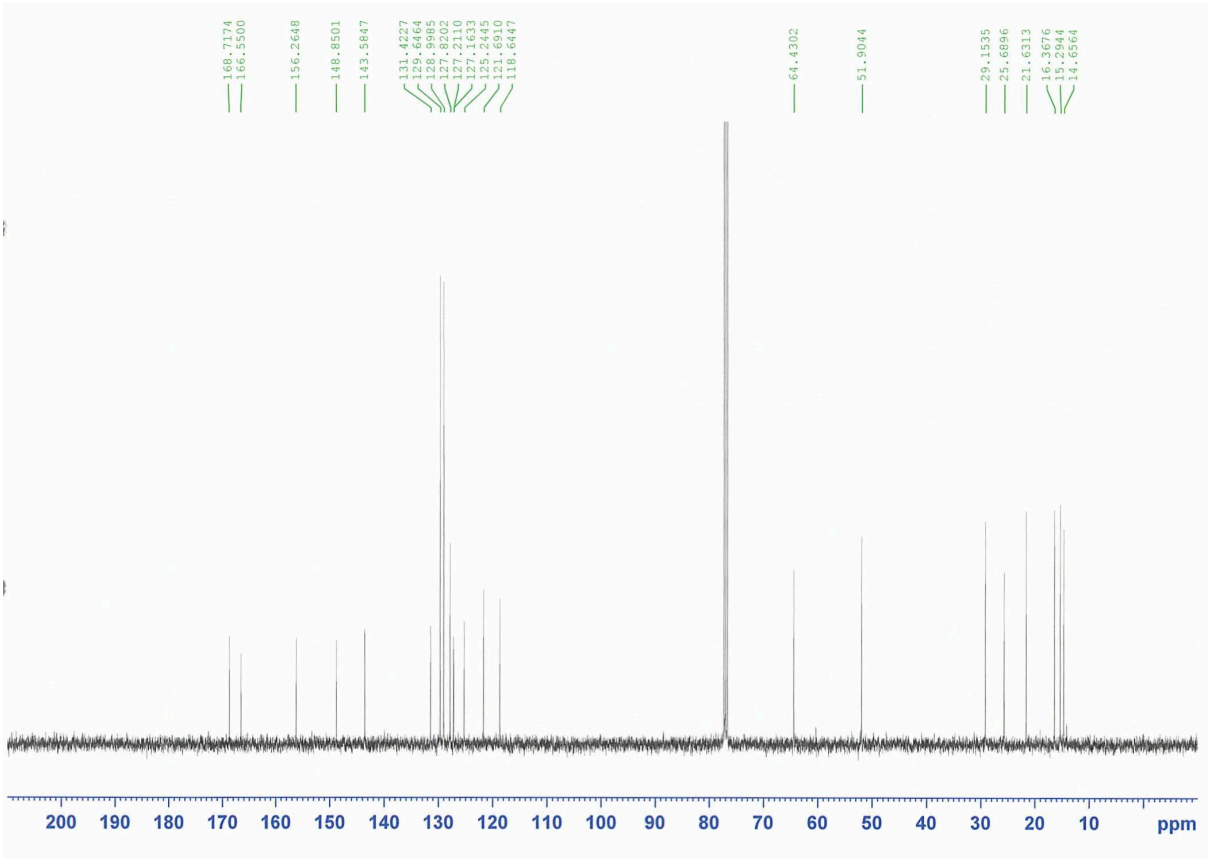
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 2-(ethylthio)-4,7-dimethyl-3-phenethylbenzofuran-5-carboxylate (**4r**) ($CDCl_3$)



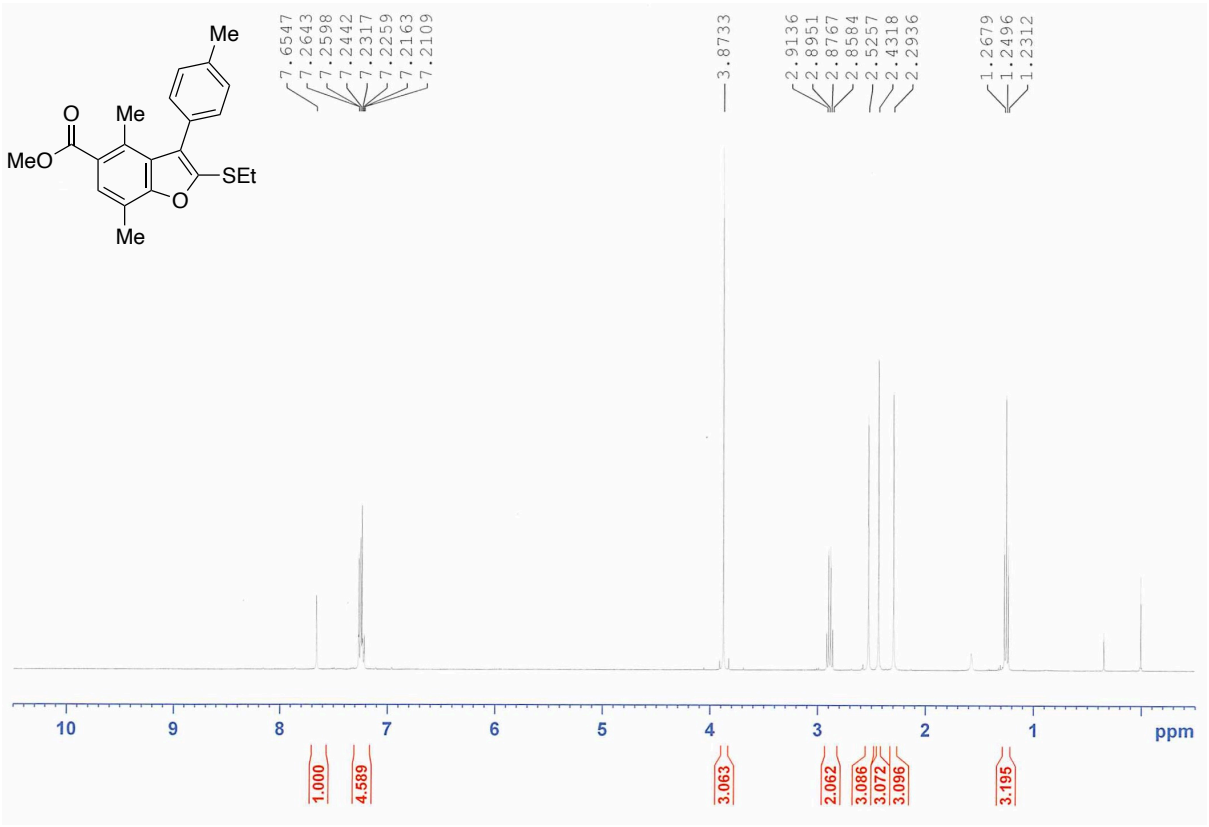


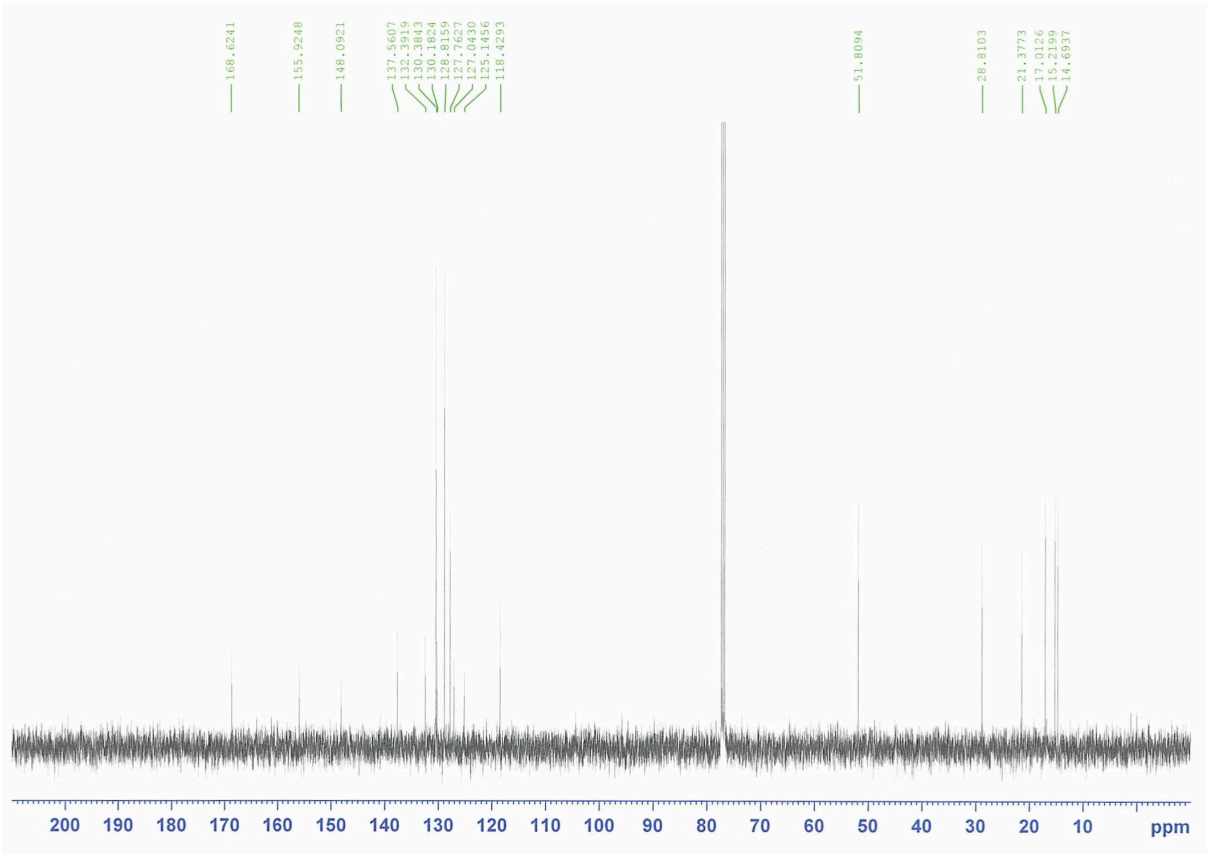
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 2-(ethylthio)-4,7-dimethyl-3-(2-((4-methylbenzoyl)oxy)ethyl)benzofuran-5-carboxylate (**4s**) ($CDCl_3$)



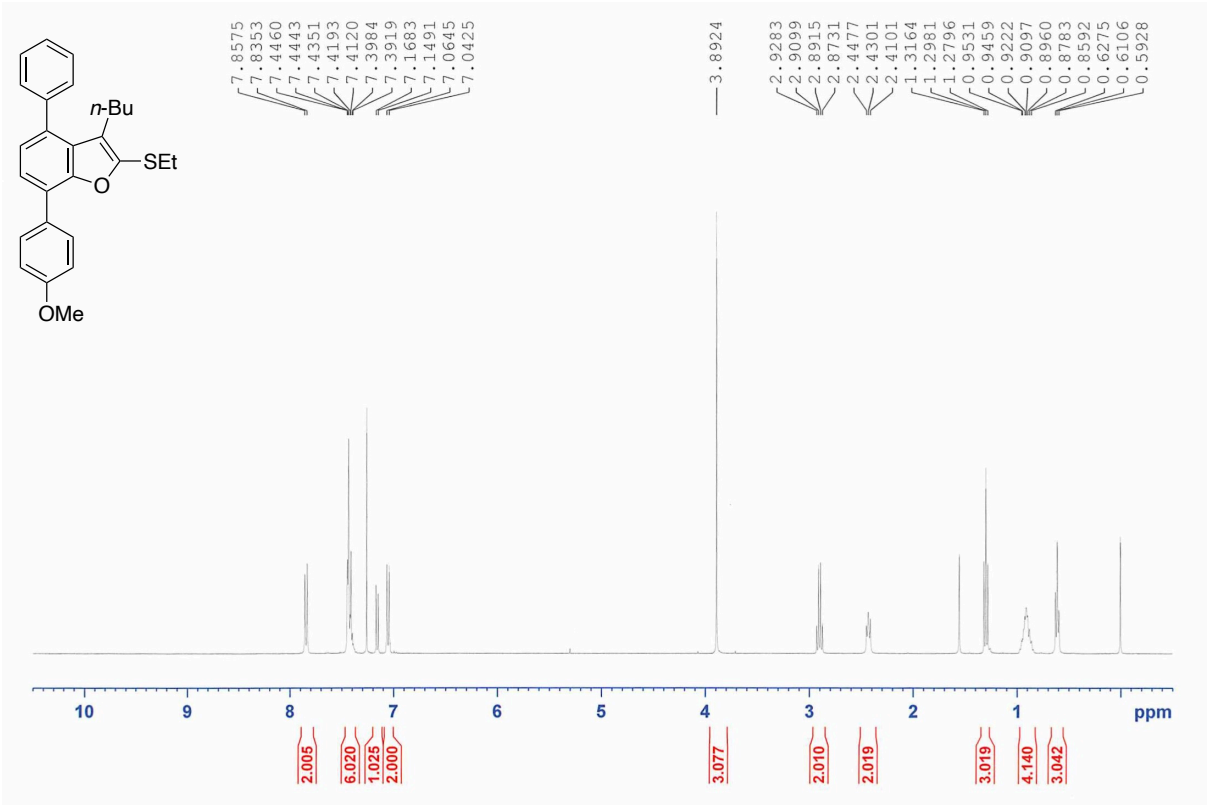


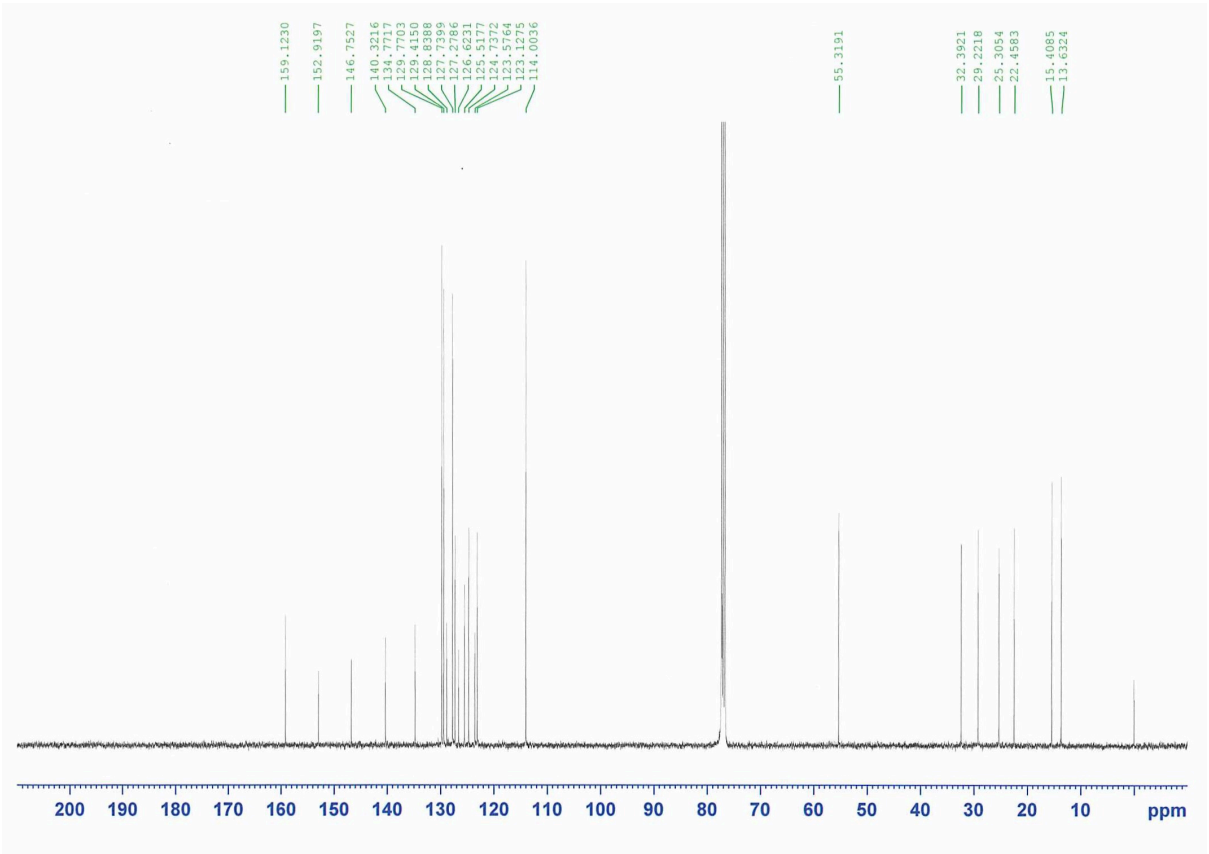
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 2-(ethylthio)-4,7-dimethyl-3-(p-tolyl)benzofuran-5-carboxylate (**4t**) ($CDCl_3$)



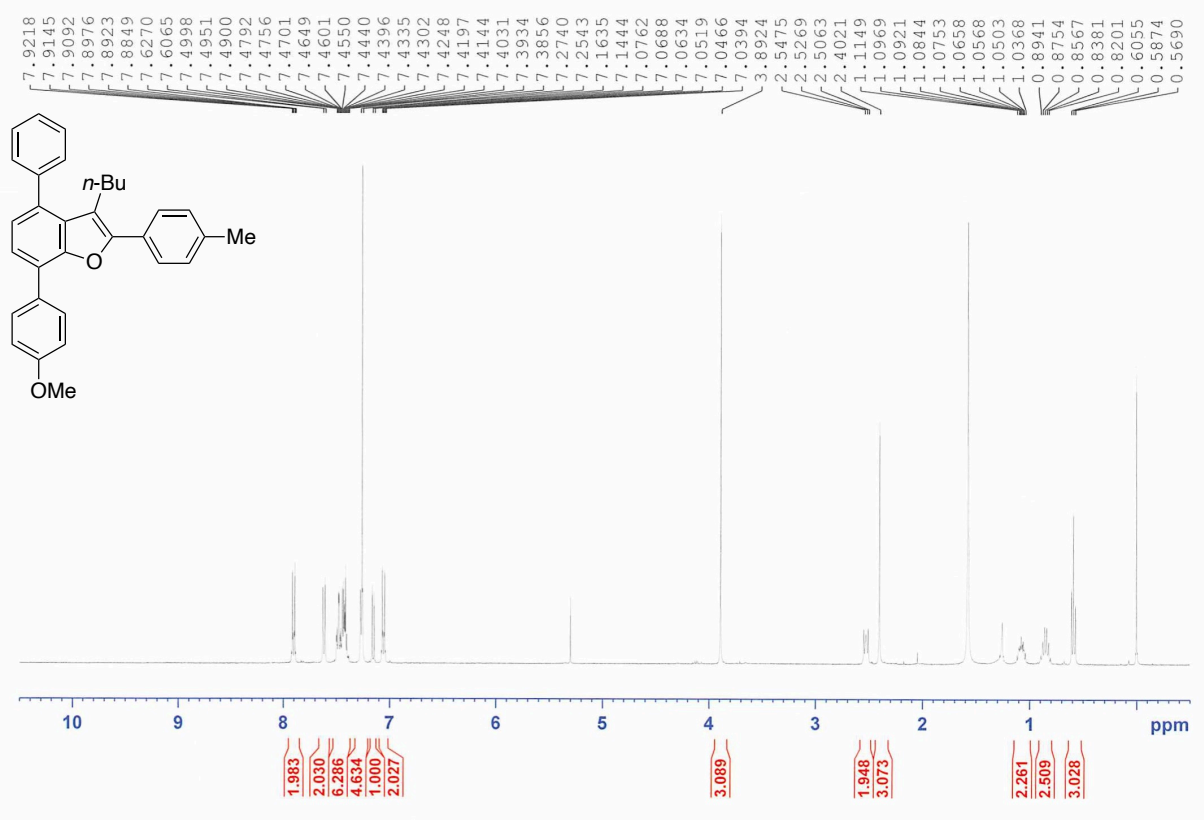


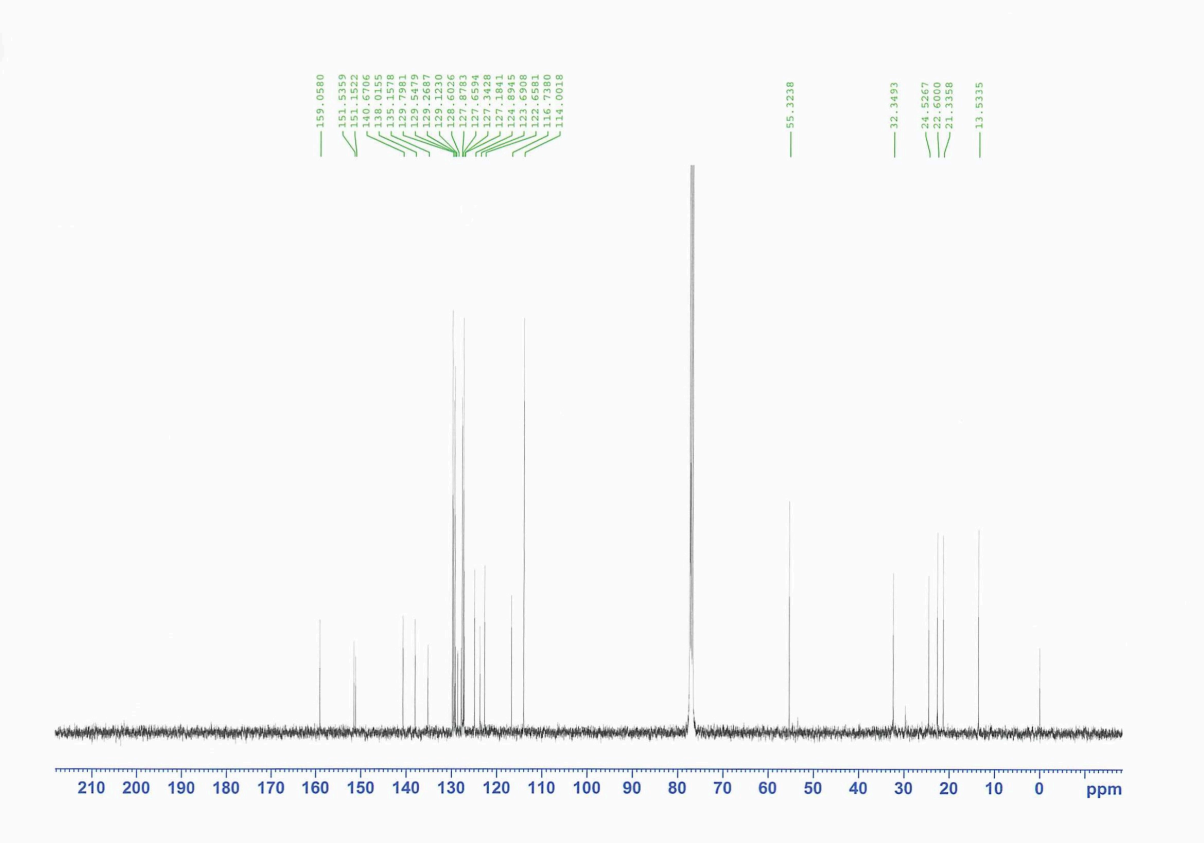
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-butyl-2-(ethylthio)-7-(4-methoxyphenyl)-4-phenylbenzofuran (**9**) ($CDCl_3$)



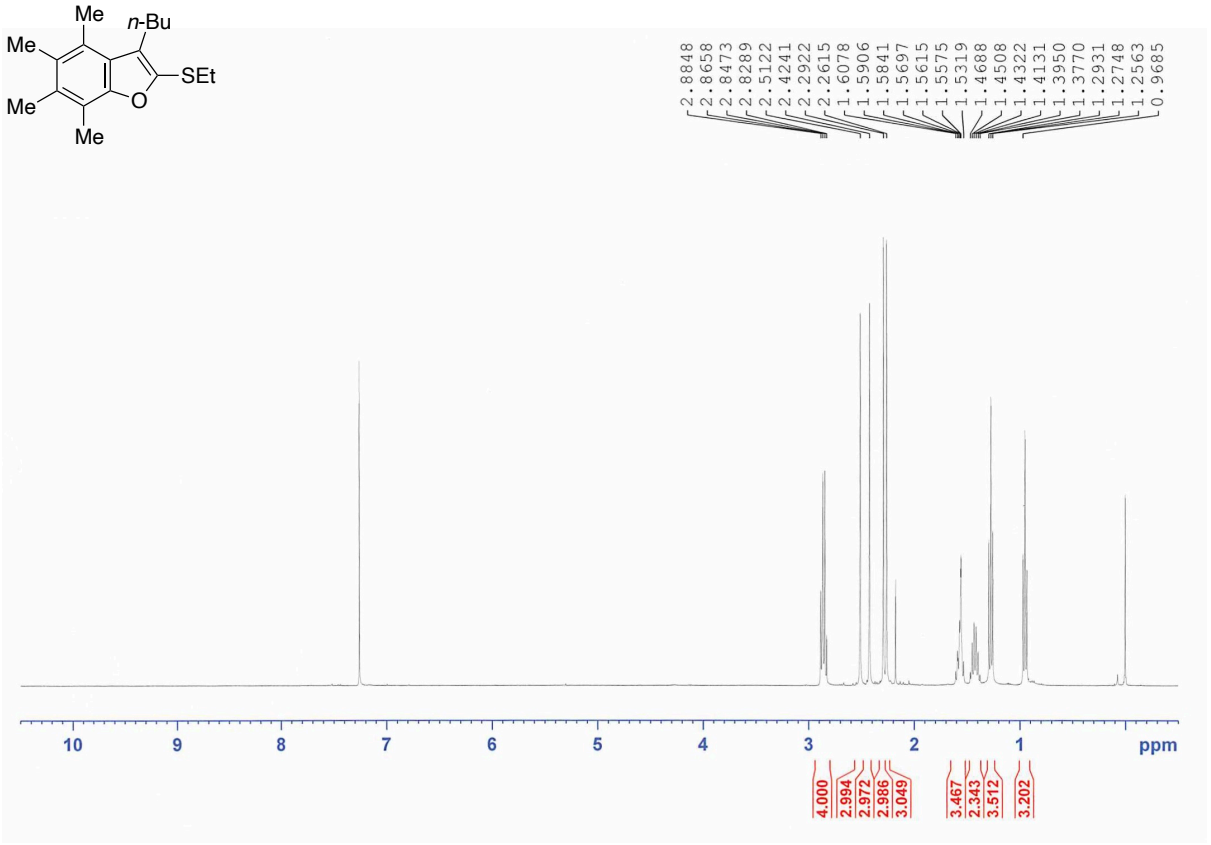


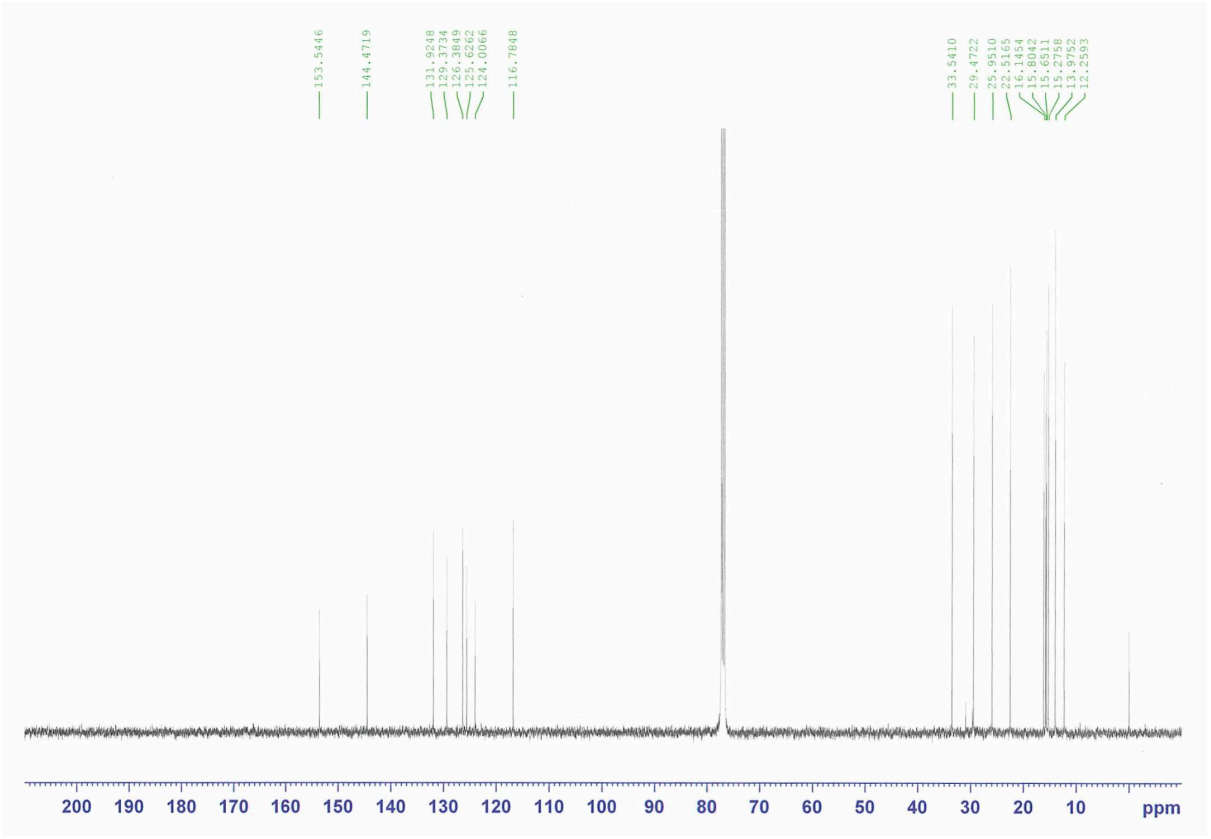
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-butyl-7-(4-methoxyphenyl)-4-phenyl-2-(*p*-tolyl)benzofuran (**11**) ($CDCl_3$)



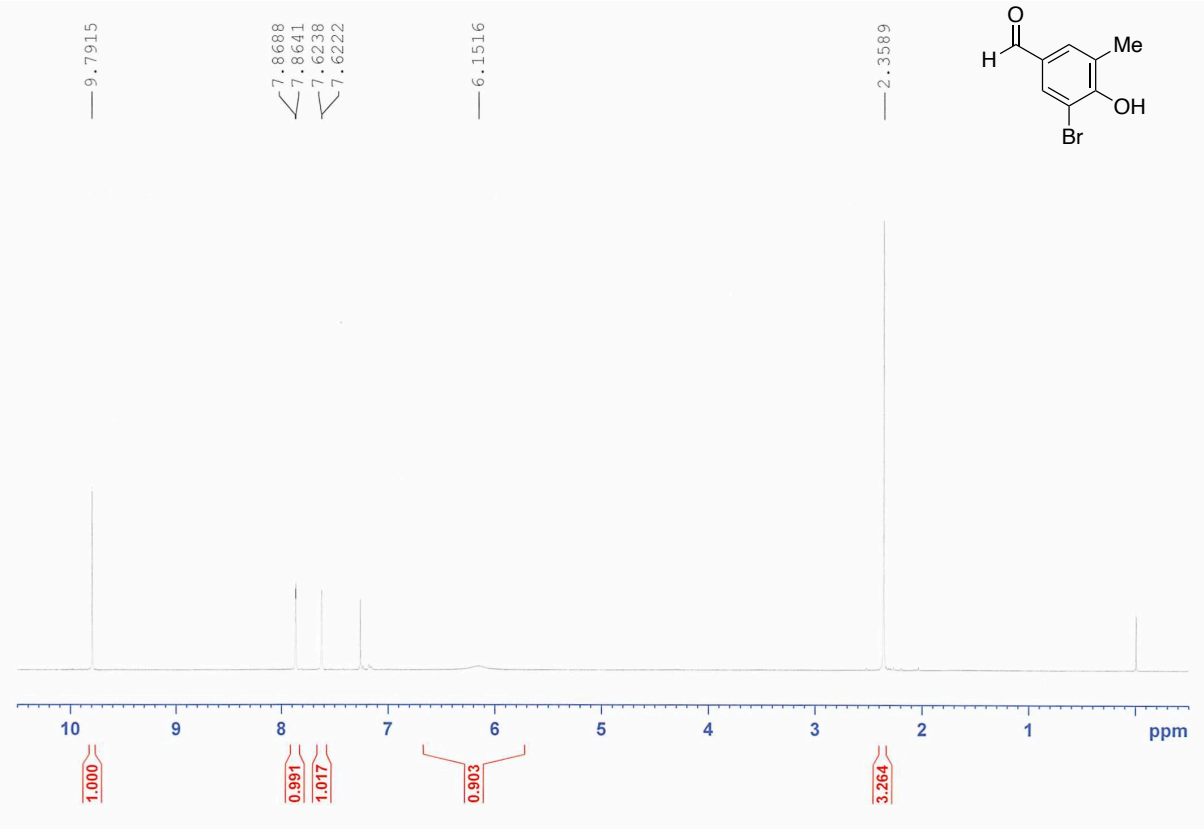


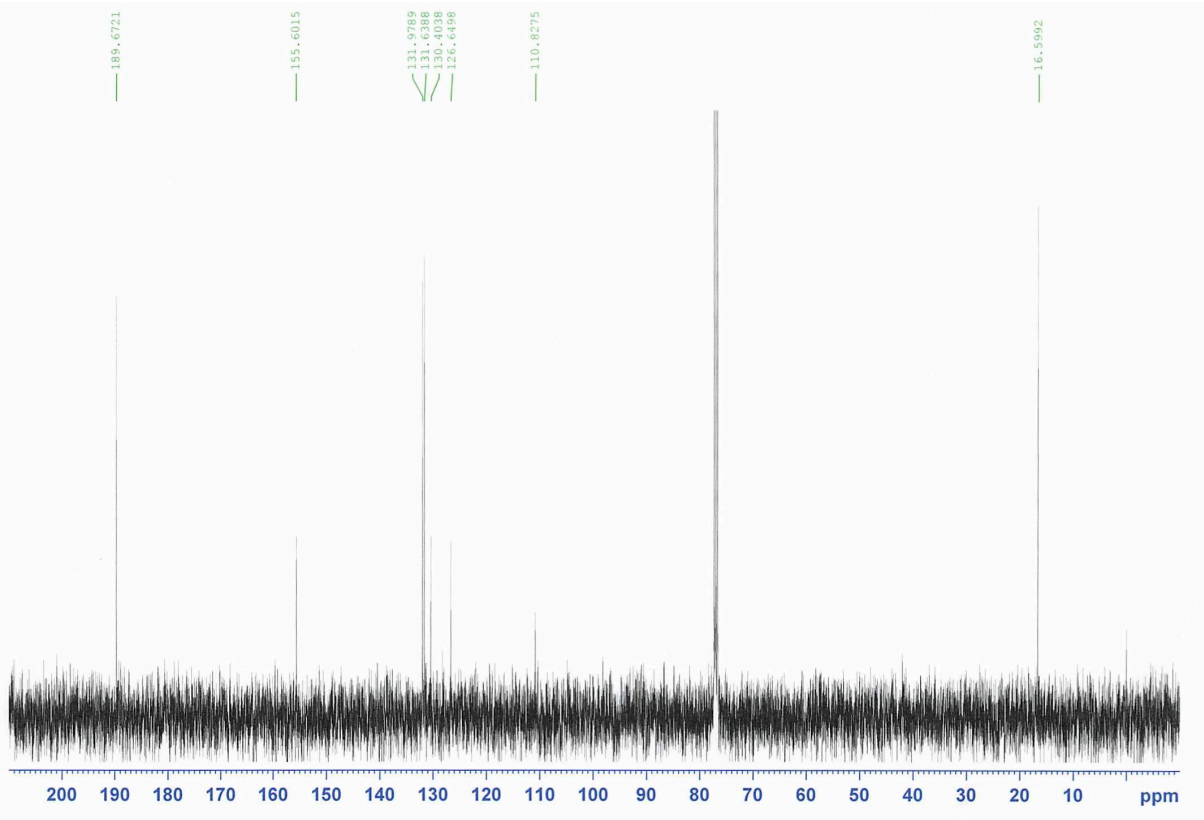
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-butyl-2-(ethylthio)-4,5,6,7-tetramethylbenzofuran (**12**) ($CDCl_3$)



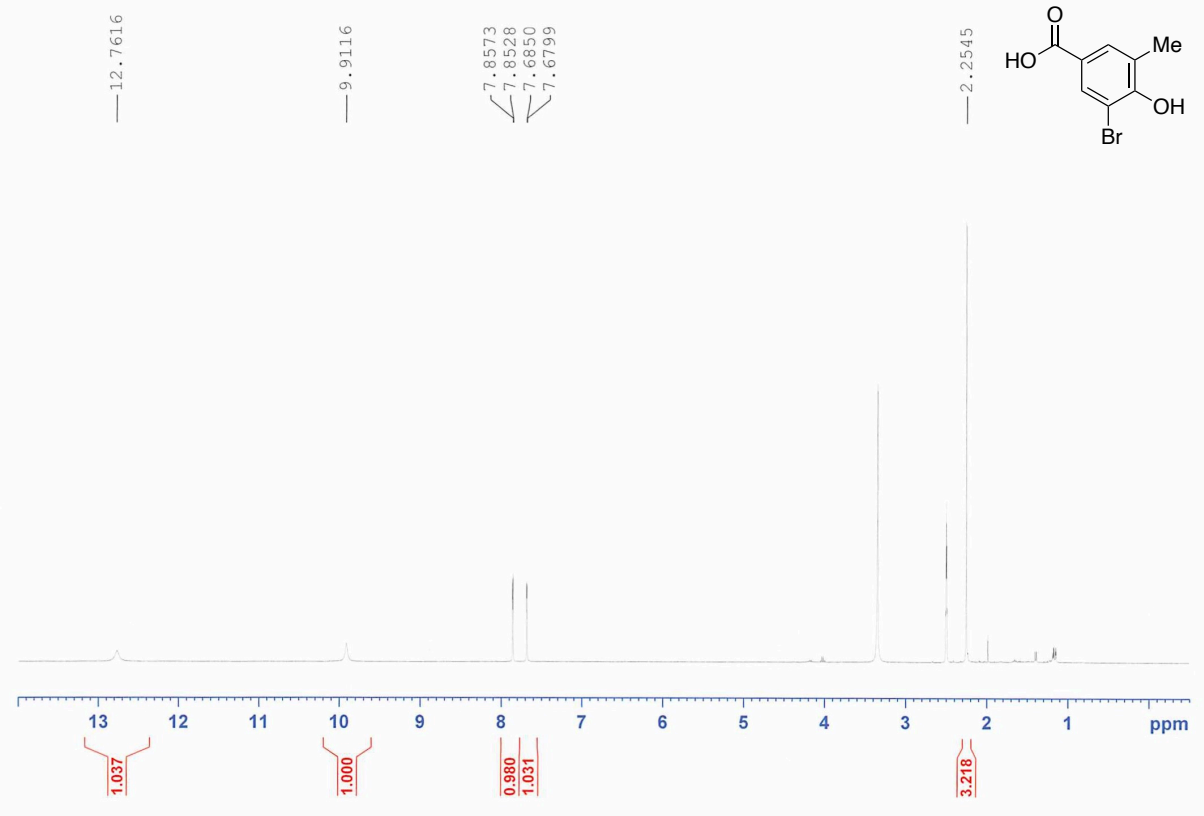


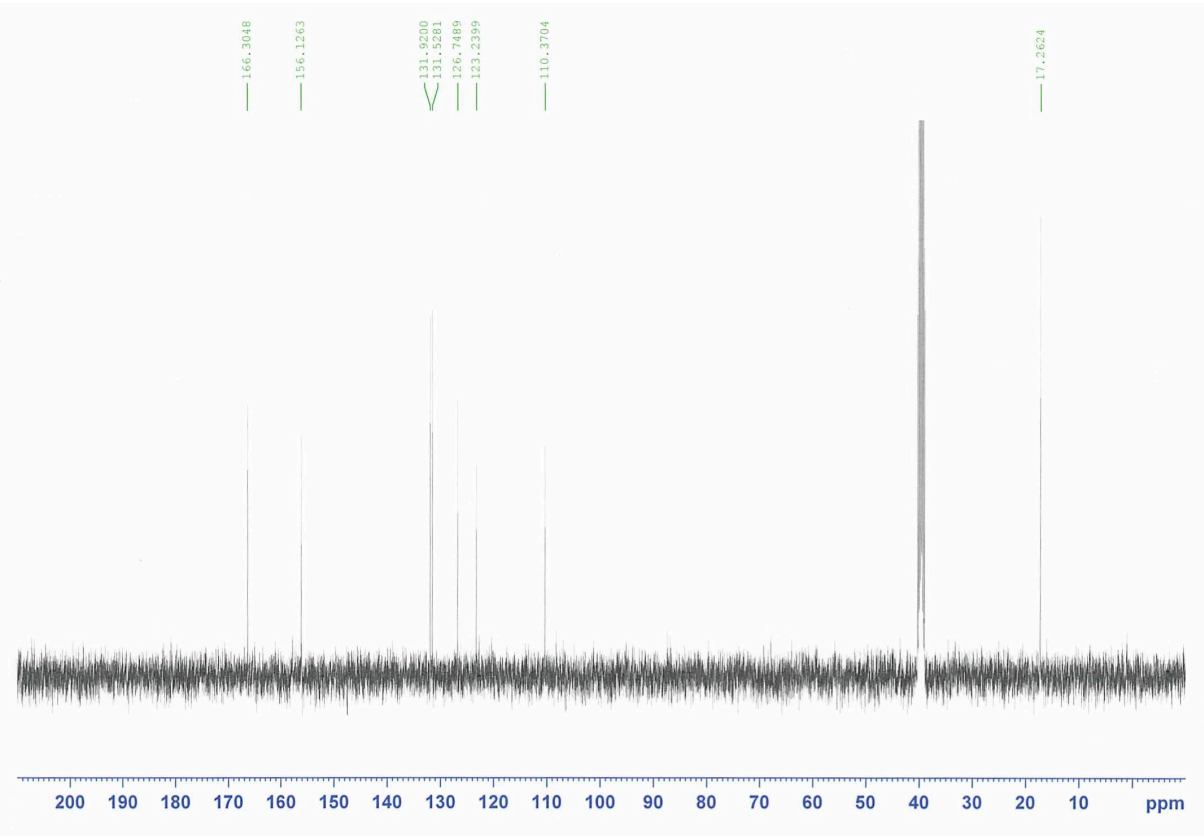
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-bromo-4-hydroxy-5-methylbenzaldehyde ($CDCl_3$)



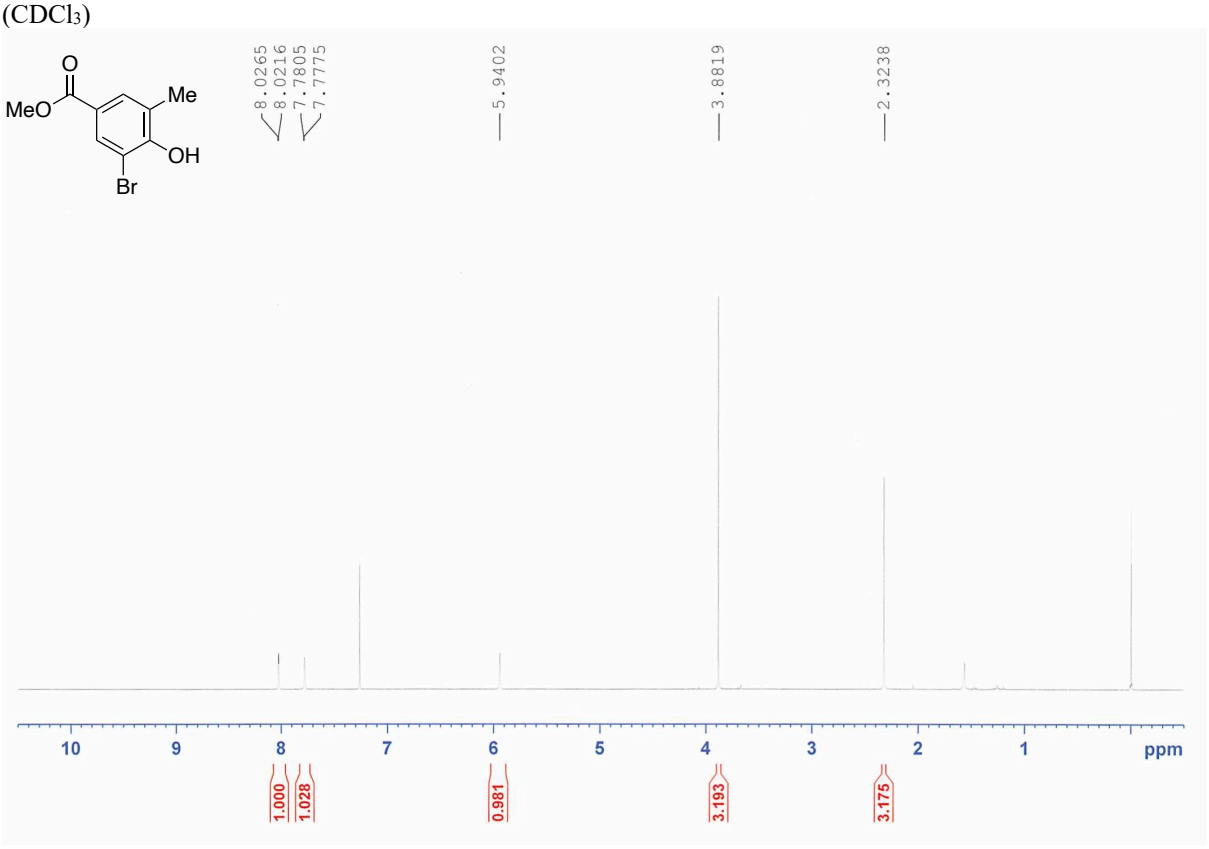


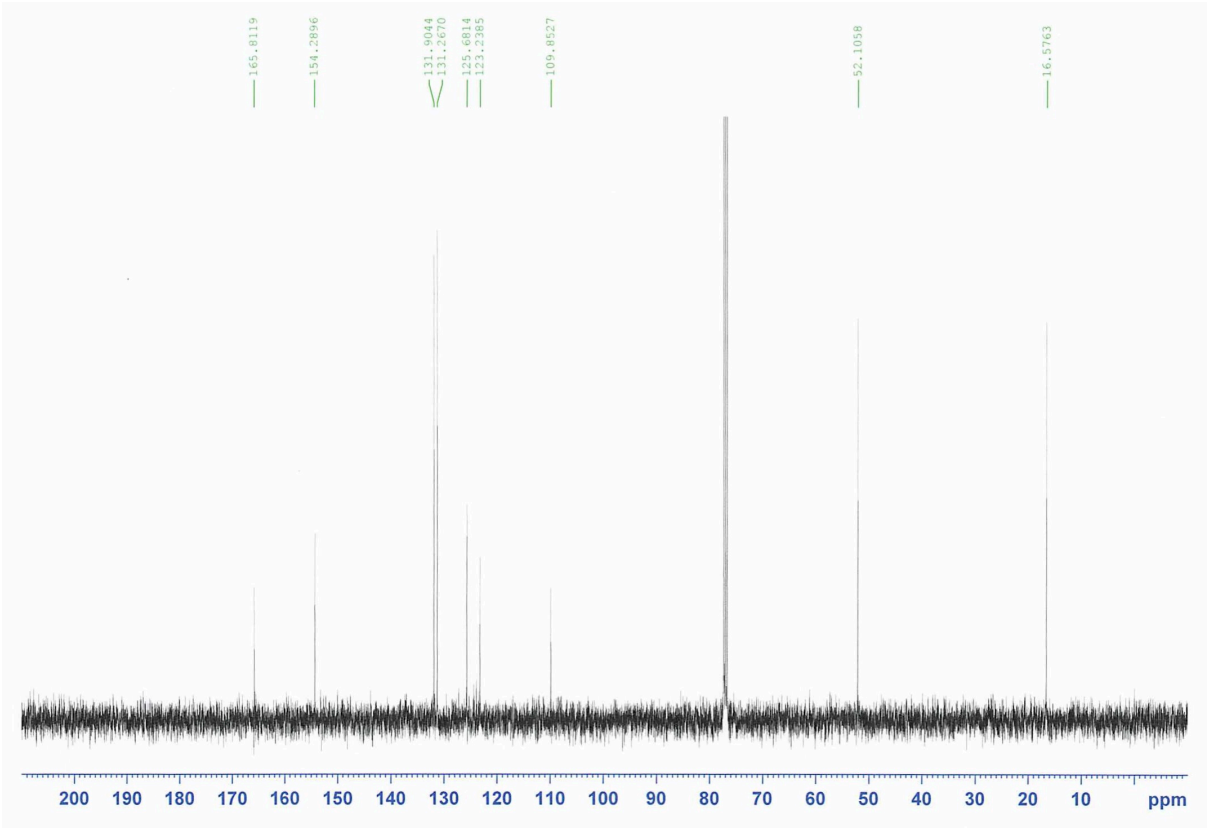
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-bromo-4-hydroxy-5-methylbenzoic acid (DMSO-d_6)



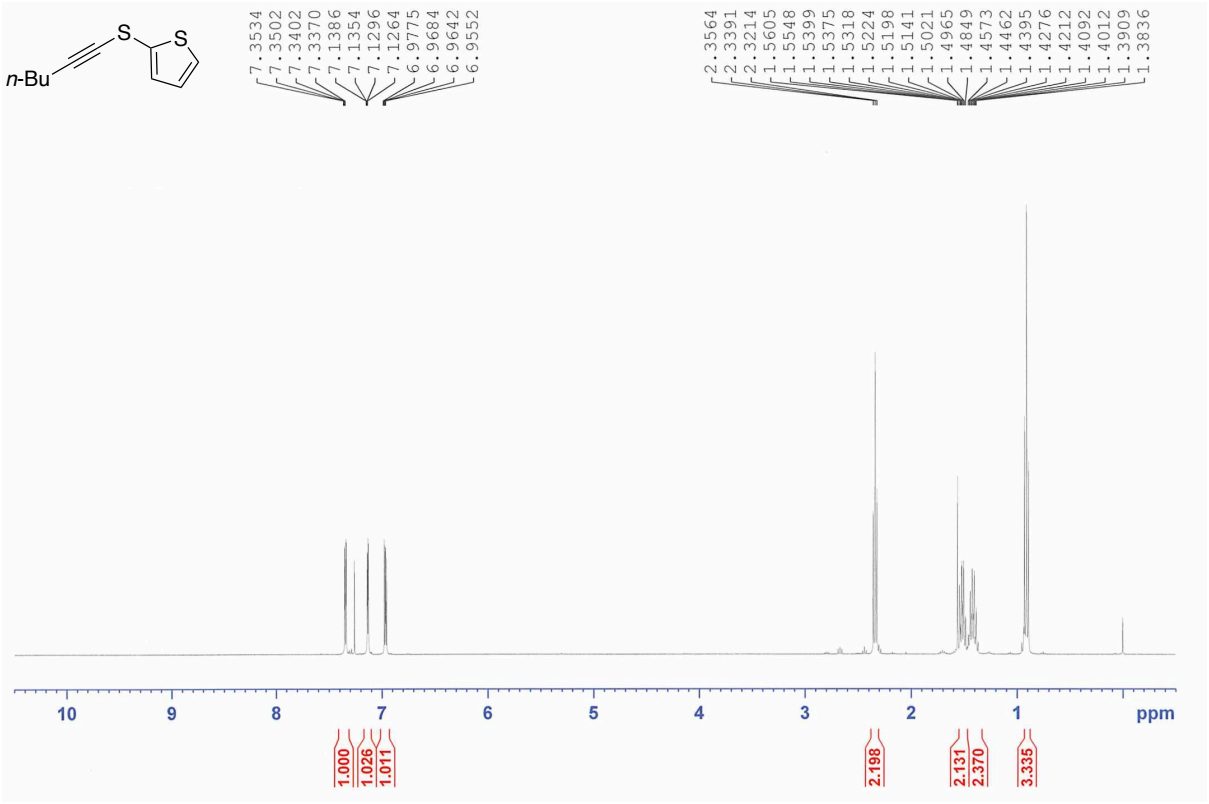


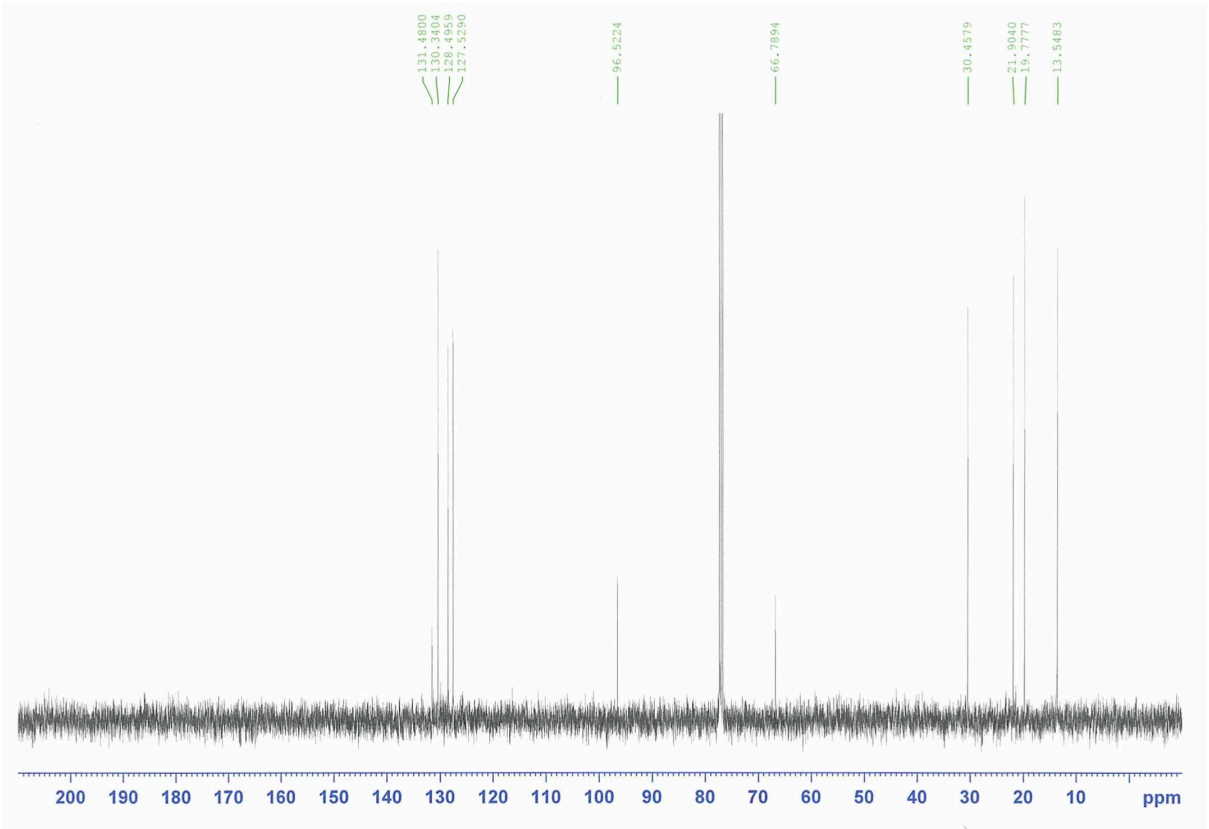
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl 3-bromo-4-hydroxy-5-methylbenzoate (**1l**) ($CDCl_3$)





^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-(hex-1-yn-1-ylthio)thiophene ($CDCl_3$)





^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-(hex-1-yn-1-ylsulfinyl)thiophene (**2d**) ($CDCl_3$)