BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY

Supporting Information

for

Nickel-catalyzed cross-coupling of 2-fluorobenzofurans with arylboronic acids via aromatic C–F bond activation

Takeshi Fujita, Haruna Yabuki, Ryutaro Morioka, Kohei Fuchibe and Junji Ichikawa

Beilstein J. Org. Chem. **2025,** *21,* 146–154. doi:10.3762/bjoc.21.8

Detailed experimental procedures and spectral data

1. General statement

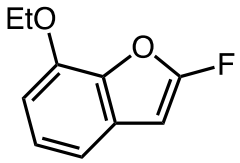
^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and ^{31}P NMR were recorded on a Bruker Avance 500 or a JEOL ECS-400 spectrometer. Chemical shift values are given in ppm relative to internal Me_4Si (for ^{1}H NMR: δ = 0.00 ppm), $CDCl_3$ (for ^{13}C NMR: δ = 77.0 ppm), C_6F_6 (for ^{19}F NMR: δ = 0.0 ppm), and H_3PO_4 (for ^{31}P NMR: δ = 0.0 ppm). IR spectra were recorded on a Horiba FT-730 spectrometer. Mass spectra were measured on a JEOL JMS-T100GCV or a JEOL JMS-T200GC spectrometer.

Column chromatography was conducted on silica gel (Silica Gel 60 N, Kanto Chemical Co., Inc.). Toluene and *N*,*N*-dimethylformamide (DMF) were purified by a solvent-purification system (GlassContour) equipped with columns of activated alumina and supported-copper catalyst (Q-5) before use. 1,4-Dioxane and methanol were distilled from sodium, and stored over molecular sieves 4 Å. Unless otherwise noted, materials were obtained from commercial sources and used directly without further purifications.

2. Preparation of 2-fluorobenzofurans

2-Fluorobenzofuran (**1a**) [1], 2-fluoronaphtho[2,1-*b*]furan (**1b**) [1], 2-fluoro-7-methoxybenzofuran (**1c**) [1], 2-fluorobenzo[*b*]thiophene (**4**) [2], 5-bromo-2-fluorobenzofuran (**1e**) [1], 2-chlorobenzofuran (**1a-Cl**) [3], 2-bromobenzofuran (**1a-Br**) [4], and 2-iodobenzofuran (**1a-I**) [5] were prepared according to the literature procedures, and their spectral data showed good agreement with the literature data.

7-Ethoxy-2-benzofuran (1d)

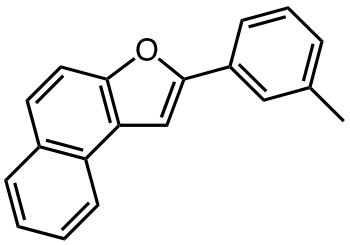


To a DMF (415 mL) solution of 2-(2,2-difluorovinyl)-6-ethoxyphenol (2.75 g, 13.7 mmol) was added DBU (2.46 mL, 16.5 mmol). After stirring at 100 °C for 2 h, water (250 mL) was added to the mixture. Organic materials were extracted with diethyl ether three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (pentane/diethyl ether = 10:1) to give **1d** (1.65 g, 67%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13 (dd, J = 8.1, 7.8 Hz, 1H), 7.04 (dd, J = 7.8, 1.0 Hz, 1H), 6.77 (d, J = 8.1 Hz, 1H), 5.83 (d, J_{HF} = 6.7 Hz, 1H), 4.23 (q, J = 7.0 Hz, 2H), 1.50 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 160.2 (d, J_{CF} = 280 Hz), 144.1, 136.8, 129.6, 124.2, 112.9 (d, J_{CF} = 5 Hz), 107.3, 78.7 (d, J_{CF} = 13 Hz), 64.6, 14.9. ^{19}F NMR (470 MHz, $CDCl_3$): δ 49.5 (d, J_{FH} = 7 Hz, 1F). IR (neat): 3136, 3060, 2983, 2933, 1643, 1496, 1439, 1396, 1340, 1296, 1196, 1082, 1018, 978, 893, 783, 727, 658, 607, 555 cm^{-1}. HRMS (EI): *m/z* Calcd for $C_{10}H_9FO_2$ $[M]^+$: 180.0587; Found: 180.0592.

3. Synthesis of 2-Arylbenzofurans

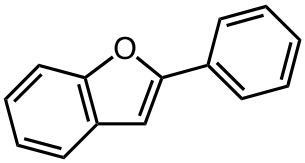
2-(3-Methylphenyl)naphtho[2,1-*b*]furan (3bb)



To the mixture of 2-fluoronaphtho[2,1-*b*]furan (**1b**, 56 mg, 0.30 mmol), (3-methylphenyl)boronic acid (**2b**, 41 mg, 0.30 mmol), $Ni(cod)_2$ (4.2 mg, 0.015 mmol), PCy_3 (8.2 mg, 0.029 mmol), 1,5-cyclooctadiene (1.8 μL, 0.015 mmol), and K_2CO_3 (50 mg, 0.36 mmol) were added toluene (3.0 mL) and H_2O (0.6 mL). After stirring at room temperature for 13 h, the reaction mixture was diluted with H_2O. Organic materials were extracted with diethyl ether three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to give **3bb** (76 mg, 98%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.75–7.67 (m, 4H), 7.58 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.49–7.46 (m, 2H), 7.35 (dd, *J* = 7.7, 7.6 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.6, 152.3, 138.5, 130.5, 130.4, 129.1, 128.8, 128.7, 127.6, 126.2, 125.3, 125.1, 124.6, 124.5, 123.4, 121.9, 112.3, 100.3, 21.5. IR (KBr): 3051, 1606, 1487, 1387, 1280, 1255, 1163, 1053, 991, 935, 789, 690 cm^{-1}. HRMS (EI): *m/z* Calcd for $C_{19}H_{14}O$ $[M]^+$: 258.1045; Found: 258.1035.

2-Phenylbenzofuran (3aa)



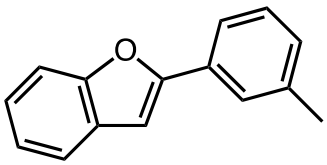
Compound **3aa** was synthesized by the method described for compound **3bb** using 2-fluorobenzofuran (**1a**, 28 mg, 0.20 mmol), phenylboronic acid (**2a**, 29 mg, 0.24 mmol), $Ni(cod)_2$ (2.8 mg, 0.010 mmol), PCy_3 (5.6 mg, 0.020 mmol), 1,5-cyclooctadiene (1.2 μL, 0.010 mmol), K_2CO_3 (55 mg, 0.40 mmol), toluene (2.0 mL), and H_2O (0.4 mL).

A white solid, 31 mg, 77% yield.

^1H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, *J* = 7.8 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.43 (dd, *J* = 7.8, 7.5 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.29–7.20 (m, 2H), 7.00 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.9, 154.8, 130.4, 129.2, 128.8, 128.5, 124.9, 124.2, 122.9, 120.9, 111.1, 101.3.

Spectral data for this compound showed good agreement with literature data [6].

2-(3-Methylphenyl)benzofuran (3ab)



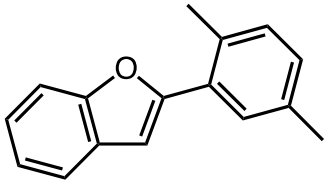
Compound **3ab** was synthesized by the method described for compound **3bb** using 2-fluorobenzofuran (**1a**, 28 mg, 0.20 mmol), (3-methylphenyl)boronic acid (**2b**, 33 mg, 0.24 mmol), $Ni(cod)_2$ (2.8 mg, 0.010 mmol), PCy_3 (5.6 mg, 0.020 mmol), 1,5-cyclooctadiene (1.2 μL, 0.010 mmol), K_2CO_3 (55 mg, 0.40 mmol), toluene (2.0 mL), and H_2O (0.4 mL).

A white solid, 41 mg, 96% yield.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (s, 1H), 7.67 (d, *J* = 7.9 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.33 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.29–7.21 (m, 2H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.00 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.1, 154.8, 138.4, 130.3, 129.3, 129.2, 128.7, 125.5, 124.1, 122.9, 122.1, 120.8, 111.1, 101.2, 21.5.

Spectral data for this compound showed good agreement with literature data [7].

2-(2,5-Dimethylphenyl)benzofuran (3ac)



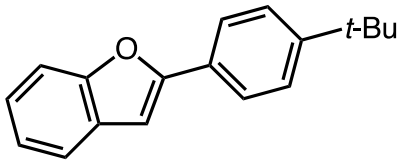
Compound **3ac** was synthesized by the method described for compound **3bb** using 2-fluorobenzofuran (**1a**, 27 mg, 0.20 mmol), (2,5-dimethylphenyl)boronic acid (**2c**, 36 mg, 0.24 mmol), $Ni(cod)_2$ (2.8 mg, 0.010 mmol), PCy_3 (5.6 mg, 0.020 mmol), 1,5-cyclooctadiene (1.2 μL, 0.010 mmol), K_2CO_3 (55 mg, 0.40 mmol), toluene (2.0 mL), and H_2O (0.4 mL).

A white solid, 37 mg, 83% yield.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (s, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.30–7.22 (m, 2H), 7.17 (d, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 1H), 6.87 (s, 1H), 2.53 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.8, 154.3, 135.5, 132.7, 131.2, 129.6, 129.3, 129.2, 128.6, 124.1, 122.7, 120.8, 111.0, 104.9, 21.4, 21.0.

Spectral data for this compound showed good agreement with literature data [6].

2-[4-(*tert*-Butyl)phenyl]benzofuran (3ad)



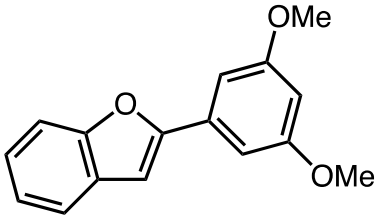
Compound **3ad** was synthesized by the method described for compound **3bb** using 2-fluorobenzofuran (**1a**, 29 mg, 0.21 mmol), [4-(*tert*-butyl)phenyl]boronic acid (**2d**, 43 mg, 0.24 mmol), $Ni(cod)_2$ (2.8 mg, 0.010 mmol), PCy_3 (5.6 mg, 0.020 mmol), 1,5-cyclooctadiene (1.2 μL, 0.010 mmol), K_2CO_3 (57 mg, 0.41 mmol), toluene (2.0 mL), and H_2O (0.4 mL).

A white solid, 53 mg, 99% yield.

^1H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.27–7.19 (m, 2H), 6.96 (s, 1H), 1.35 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.1, 154.8, 151.8, 129.3, 127.7, 125.7, 124.7, 124.0, 122.8, 120.7, 111.1, 100.7, 34.7, 31.2.

Spectral data for this compound showed good agreement with literature data [8].

2-(3,5-Dimethoxyphenyl)benzofuran (3ae)



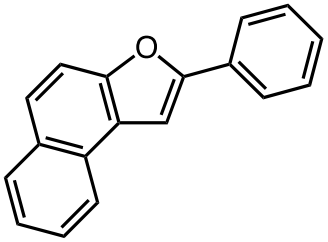
Compound **3ae** was synthesized by the method described for compound **3bb** using 2-fluorobenzofuran (**1a**, 28 mg, 0.20 mmol), (3,5-dimethoxyphenyl)boronic acid (**2e**, 44 mg, 0.24 mmol), $Ni(cod)_2$ (5.5 mg, 0.020 mmol), PCy_3 (11 mg, 0.040 mmol), 1,5-cyclooctadiene (2.5 μL, 0.020 mmol), K_2CO_3 (55 mg, 0.40 mmol), toluene (2.0 mL), and H_2O (0.4 mL).

A colorless oil, 38 mg, 73% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 7.6 Hz, 1H) 7.52 (d, *J* = 8.1 Hz, 1H), 7.30–7.23 (m, 2H), 7.04–7.02 (m, 3H), 6.48 (t, *J* = 2.2 Hz, 1H), 3.88 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 161.0, 155.6, 154.7, 132.1, 129.0, 124.3, 122.9, 120.9, 111.1, 102.9, 101.8, 101.0, 55.4.

Spectral data for this compound showed good agreement with literature data [8].

2-Phenylnaphtho[2,1-*b*]furan (3ba)

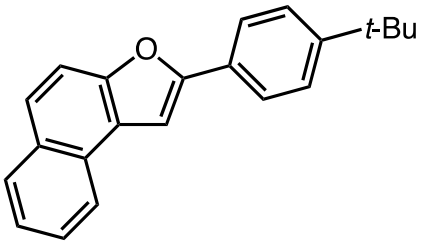


Compound **3ba** was synthesized by the method described for compound **3bb** using 2-fluoronaphtho[2,1-*b*]furan (**1b**, 56 mg, 0.30 mmol), phenylboronic acid (**2a**, 38 mg, 0.31 mmol), $Ni(cod)_2$ (4.2 mg, 0.015 mmol), PCy_3 (8.4 mg, 0.030 mmol), 1,5-cyclooctadiene (1.8 µL, 0.015 mmol), K_2CO_3 (50 mg, 0.36 mmol), toluene (3.0 mL), and H_2O (0.6 mL). A white solid, 71 mg, 96% yield.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.2 Hz, 1H) 7.95–7.91 (m, 3H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 7.59 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.51–7.45 (m, 4H), 7.35 (t, *J* = 7.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.3, 152.3, 130.6, 130.4, 128.80, 128.76, 128.2, 127.6, 126.2, 125.1, 124.6, 124.52, 124.48, 123.4, 112.2, 100.4.

Spectral data for this compound showed good agreement with literature data [8].

2-[4-(*tert*-Butyl)phenyl]naphtho[2,1-*b*]furan (3bd)



Compound **3bd** was synthesized by the method described for compound **3bb** using 2-fluoronaphtho[2,1-*b*]furan (**1b**, 55 mg, 0.30 mmol), [4-(*tert*-butyl)phenyl]boronic acid (**2d**, 54 mg, 0.30 mmol), $Ni(cod)_2$ (4.3 mg, 0.016 mmol), PCy_3 (8.2 mg, 0.029 mmol), 1,5-cyclooctadiene (1.8 μL, 0.015 mmol), K_2CO_3 (51 mg, 0.37 mmol), toluene (3.0 mL), and H_2O (0.6 mL).

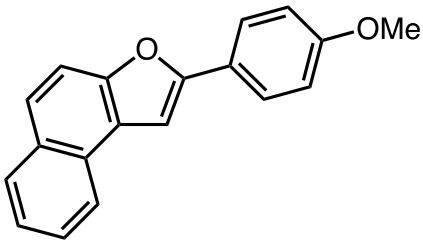
A white solid, 84 mg, 94% yield.

^1H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.86–7.84 (m, 2H), 7.68–7.66 (m, 2H), 7.57–7.55 (m, 1H), 7.49–7.46 (m, 4H), 1.36 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6, 152.2, 151.5, 130.4, 128.8, 127.9, 127.6, 127.4, 126.1, 125.8, 124.8, 124.6, 124.5, 123.5, 112.3, 99.8, 34.7, 31.3.

Spectral data for this compound showed good agreement with literature data [9].

2-(4-Methoxyphenyl)naphtho[2,1-*b*]furan (3bf)



Compound **3bf** was synthesized by the method described for compound **3bb** using 2-fluoronaphtho[2,1-*b*]furan (**1b**, 39 mg, 0.21 mmol), (4-methoxyphenyl)boronic acid (**2f**, 38 mg, 0.25 mmol), $Ni(cod)_2$ (2.8 mg, 0.010 mmol), PCy_3 (5.6 mg, 0.020 mmol), 1,5-

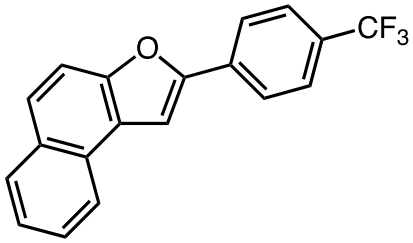
cyclooctadiene (1.2 μL, 0.010 mmol), K_2CO_3 (55 mg, 0.40 mmol), toluene (2.0 mL), and H_2O (0.4 mL).

A white solid, 54 mg, 94% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.70–7.65 (m, 2H), 7.59–7.47 (m, 2H), 7.36 (s, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 159.8, 155.5, 152.0, 130.4, 128.7, 127.5, 126.12, 126.06, 124.7, 124.5, 124.4, 123.52, 123.45, 114.3, 112.2, 98.8, 55.3.

Spectral data for this compound showed good agreement with literature data [10].

2-[4-(Trifluoromethyl)phenyl]naphtho[2,1-*b*]furan (3bg)



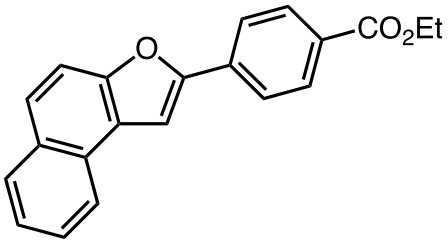
Compound **3bg** was synthesized by the method described for compound **3bb** using 2-fluoronaphtho[2,1-*b*]furan (**1b**, 56 mg, 0.30 mmol), [4-(trifluoromethyl)phenyl]boronic acid (**2g**, 57 mg, 0.30 mmol), $Ni(cod)_2$ (17 mg, 0.060 mmol), PCy_3 (34 mg, 0.12 mmol), 1,5-cyclooctadiene (7.4 μL, 0.060 mmol), K_3PO_4 (76 mg, 0.36 mmol), toluene (3.0 mL), and H_2O (0.6 mL).

A white solid, 74 mg, 78% yield.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 2H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.78–7.69 (m, 4H), 7.63–7.61 (m, 2H), 7.52 (dd, *J* = 8.0, 7.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.6, 152.8, 133.8, 130.5, 129.8 (q, J_{CF} = 32 Hz), 128.9, 127.6, 126.6, 126.2, 125.9 (q, J_{CF} = 4 Hz), 124.9, 124.6, 124.3, 124.1 (q, J_{CF} = 271 Hz), 123.4, 112.3, 102.4. ^{19}F NMR (470 MHz, $CDCl_3$): δ 100.3 (s). IR (KBr): 3066,

2929, 1616, 1412, 1325, 1169, 1128, 1072, 1012, 922, 841, 802, 750, 675, 594 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{19}H_{11}F_3O$ $[M]^+$: 312.0762; Found: 312.0770.

Ethyl 4-(naphtho[2,1-*b*]furan-2-yl)benzoate (3bh)

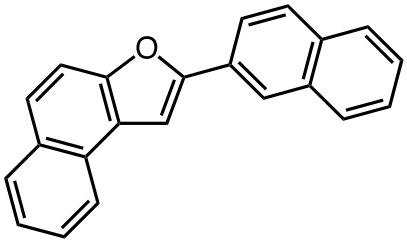


Compound **3bh** was synthesized by the method described for compound **3bb** using 2-fluoronaphtho[2,1-*b*]furan (**1b**, 38 mg, 0.20 mmol), [4-(ethoxycarbonyl)phenyl]boronic acid (**2h**, 47 mg, 0.24 mmol), $Ni(cod)_2$ (2.9 mg, 0.011 mmol), PCy_3 (5.7 mg, 0.020 mmol), 1,5-cyclooctadiene (1.2 μL, 0.010 mmol), K_2CO_3 (57 mg, 0.41 mmol), toluene (2.0 mL), and H_2O (0.4 mL).

A white solid, 35 mg, 54% yield.

^1H NMR (400 MHz, $CDCl_3$): δ 8.19–8.13 (m, 3H), 7.99–7.95 (m, 3H), 7.77 (d, *J* = 9.4 Hz, 1H), 7.70 (d, *J* = 9.4 Hz, 1H), 7.65 (s, 1H), 7.62 (ddd, *J* = 8.4, 6.8, 0.8 Hz, 1H), 7.51 (ddd, *J* = 8.2, 6.8, 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 154.2, 152.9, 134.5, 130.5, 130.2, 129.8, 128.9, 127.6, 126.6, 126.1, 124.8, 124.4, 124.3, 123.4, 112.3, 102.5, 61.1, 14.4. IR (KBr): 3057, 2981, 1712, 1608, 1410, 1367, 1279, 1178, 1105, 1022, 989, 856, 810, 768, 690 cm^{-1}. HRMS (FD): *m*/*z* Calcd for $C_{21}H_{16}O_3$ $[M]^+$: 316.1099; Found: 316.1105.

2-(Naphthalen-2-yl)naphtho[2,1-*b*]furan (3bi)



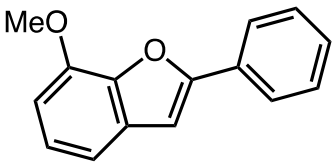
Compound **3bi** was synthesized by the method described for compound **3bb** using 2-fluoronaphtho[2,1-*b*]furan (**1b**, 56 mg, 0.30 mmol), 2-naphthylboronic acid (**2i**, 51 mg, 0.30 mmol), $Ni(cod)_2$ (4.1 mg, 0.015 mmol), PCy_3 (8.5 mg, 0.030 mmol), 1,5-cyclooctadiene (1.8 μL, 0.015 mmol), K_2CO_3 (50 mg, 0.36 mmol), toluene (3.0 mL), methanol (0.6 mL), and H_2O (0.6 mL).

A white solid, 62 mg, 70% yield.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (s, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 8.01–7.92 (m, 4H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 1H), 7.74 (d, *J* = 9.0 Hz, 1H), 7.65 (s, 1H), 7.62 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.55–7.51 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.4, 152.5, 133.5, 133.1, 130.5, 128.8, 128.6, 128.4, 127.9, 127.8, 127.6, 126.7, 126.4, 126.3, 125.4, 124.63, 124.61, 123.5, 123.4, 122.7, 112.3, 101.1.

Spectral data for this compound showed good agreement with literature data [11].

7-Methoxy-2-phenylbenzofuran (3ca)



Compound **3ca** was synthesized by the method described for compound **3bb** using 2-fluoro-7-methoxybenzofuran (**1c**, 56 mg, 0.33 mmol), phenylboronic acid (**2a**, 37 mg, 0.31 mmol), $Ni(cod)_2$ (4.1 mg, 0.015 mmol), PCy_3 (8.1 mg, 0.029 mmol), 1,5-

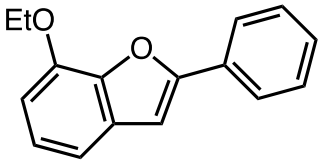
cyclooctadiene (1.8 μL, 0.015 mmol), K_2CO_3 (50 mg, 0.36 mmol), toluene (3.0 mL), and H_2O (0.6 mL).

A white solid, 46 mg, 67% yield.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 7.4 Hz, 2H), 7.44 (dd, *J* = 7.9, 7.4 Hz, 2H), 7.36–7.33 (m, 1H), 7.19–7.13 (m, 2H), 7.01 (s, 1H), 6.80 (d, *J* = 6.7 Hz, 1H), 4.05 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.0, 145.3, 144.1, 130.9, 130.3, 128.7, 128.5, 125.0, 123.6, 113.3, 106.6, 101.6, 56.1.

Spectral data for this compound showed good agreement with literature data [12].

7-Ethoxy-2-phenylbenzofuran (3da)



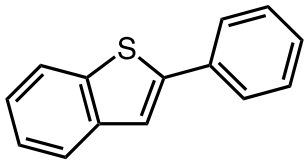
Compound **3da** was synthesized by the method described for compound **3bb** using 7-ethoxy-2-fluorobenzofuran (**1d**, 54 mg, 0.30 mmol), phenylboronic acid (**2a**, 37 mg, 0.31 mmol), $Ni(cod)_2$ (4.1 mg, 0.015 mmol), PCy_3 (8.1 mg, 0.029 mmol), 1,5-cyclooctadiene (1.8 μL, 0.015 mmol), K_2CO_3 (50 mg, 0.36 mmol), toluene (3.0 mL), and H_2O (0.6 mL).

A colorless oil, 46 mg, 65% yield.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.0 Hz, 2H), 7.44 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.12 (dd, *J* = 7.8, 7.6 Hz, 1H), 7.00 (s, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 4.32 (q, *J* = 7.0 Hz, 2H), 1.54 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.9, 144.5, 144.3, 131.0, 130.4, 128.7, 128.5, 125.0, 123.5, 113.2, 108.1, 101.6, 64.7, 15.0.

Spectral data for this compound showed good agreement with literature data [12].

2-Phenylbenzo[*b*]thiophene (5)



Compound **5** was synthesized by the method described for compound **3bb** using 2-fluorobenzo[*b*]thiophene (**4**, 45 mg, 0.29 mmol), phenylboronic acid (**2a**, 37 mg, 0.30 mmol), $Ni(cod)_2$ (17 mg, 0.060 mmol), PCy_3 (34 mg, 0.12 mmol), K_2CO_3 (50 mg, 0.36 mmol), toluene (3.0 mL), and H_2O (0.6 mL).

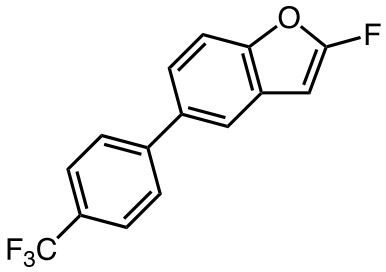
A white solid, 29 mg, 48% yield.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 2H), 7.54 (s, 1H), 7.42 (dd, *J* = 7.9, 7.5 Hz, 2H), 7.36–7.29 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 144.2, 140.7, 139.5, 134.3, 128.9, 128.2, 126.5, 124.5, 124.3, 123.5, 122.2, 119.4.

Spectral data for this compound showed good agreement with literature data [13].

4. Orthogonal coupling reactions of aromatic C–F and C–Br bonds

2-Fluoro-5-[4-(trifluoromethyl)phenyl]benzofuran (1f)

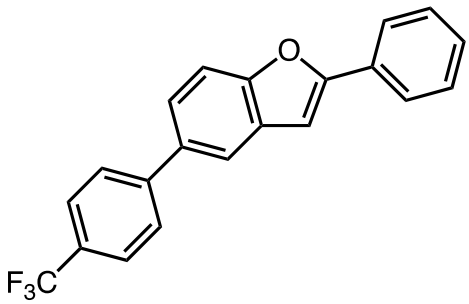


To the mixture of 5-bromo-2-fluorobenzofuran (**1e**, 357 mg, 1.66 mmol), [4-(trifluoromethyl)phenyl)]boronic acid (**2g**, 453 mg, 2.39 mmol), $Pd(PPh_3)_4$ (92 mg, 0.080 mmol), K_3PO_4 (1.27 g, 5.98 mmol), and H_2O (0.18 mL, 10 mmol) was added 1,4-dioxane (5.3 mL). After stirring at 80 °C for 12 h, the reaction mixture was diluted with

H_2O. Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane) to give **1f** (444 mg, 95%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73–7.65 (m, 5H), 7.47–7.43 (m, 2H), 5.91 (d, J_{HF} = 6.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 160.9 (d, J_{CF} = 281 Hz), 147.7, 144.9, 135.9, 129.2 (q, J_{CF} = 32 Hz), 128.6 (d, J_{CF} = 3 Hz), 127.6, 125.7 (q, J_{CF} = 4 Hz), 124.3 (q, J_{CF} = 272 Hz), 123.0 (d, J_{CF} = 4 Hz), 119.5 (d, J_{CF} = 6 Hz), 111.3, 78.6 (d, J_{CF} = 14 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ 100.5 (s, 3F), 52.3 (d, J_{FH} = 7 Hz, 1F). IR (KBr): 3149, 1637, 1468, 1323, 1165, 1124, 1068, 976, 843, 810, 777, 671 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{15}H_8F_4O$ $[M]^+$: 280.0511; Found: 280.0522.

2-Phenyl-5-[4-(trifluoromethyl)phenyl]benzofuran (3fa)



Compound **3fa** was synthesized by the method described for compound **3bb** using 2-fluoro-5-[4-(trifluoromethyl)phenyl]benzofuran (**1f**, 85 mg, 0.30 mmol), phenylboronic acid (**2a**, 38 mg, 0.31 mmol), $Ni(cod)_2$ (4.2 mg, 0.015 mmol), PCy_3 (8.2 mg, 0.029 mmol), 1,5-cyclooctadiene (1.8 μL, 0.015 mmol), K_2CO_3 (50 mg, 0.36 mmol), toluene (3.0 mL), and H_2O (0.6 mL).

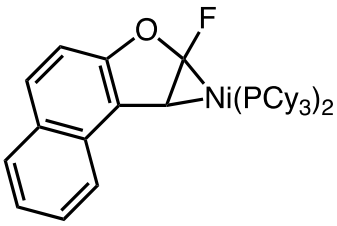
A white solid, 83 mg, 81% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 6.8 Hz, 2H), 7.78 (d, *J* = 1.6 Hz, 1H), 7.75–7.69 (m, 4H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.52–7.45 (m, 3H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.08

(s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 154.9, 145.2, 135.1, 130.2, 129.9, 129.0 (q, J_{CF} = 32 Hz), 128.85, 128.85, 127.6, 125.7 (q, J_{CF} = 4 Hz), 125.0, 124.5 (q, J_{CF} = 270 Hz), 123.9, 119.6, 111.5, 101.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ 99.4 (s).

Spectral data for this compound showed good agreement with literature data [14].

5. Formation of nickelacyclopropane E_b



To the mixture of 2-fluoronaphtho[2,1-*b*]furan (**1b**, 18 mg, 0.098 mmol), $Ni(cod)_2$ (28 mg, 0.10 mmol), PCy_3 (56 mg, 0.20 mmol), 1,5-cyclooctadiene (12 μL, 0.098 mmol), and K_2CO_3 (17 mg, 0.12 mmol) were added toluene (1.0 mL) and H_2O (0.2 mL). After stirring at room temperature for 13 h, the formation of nickelacyclopropane **E_b** was confirmed by ^{19}F and ^{31}P NMR measurement and HRMS analysis.

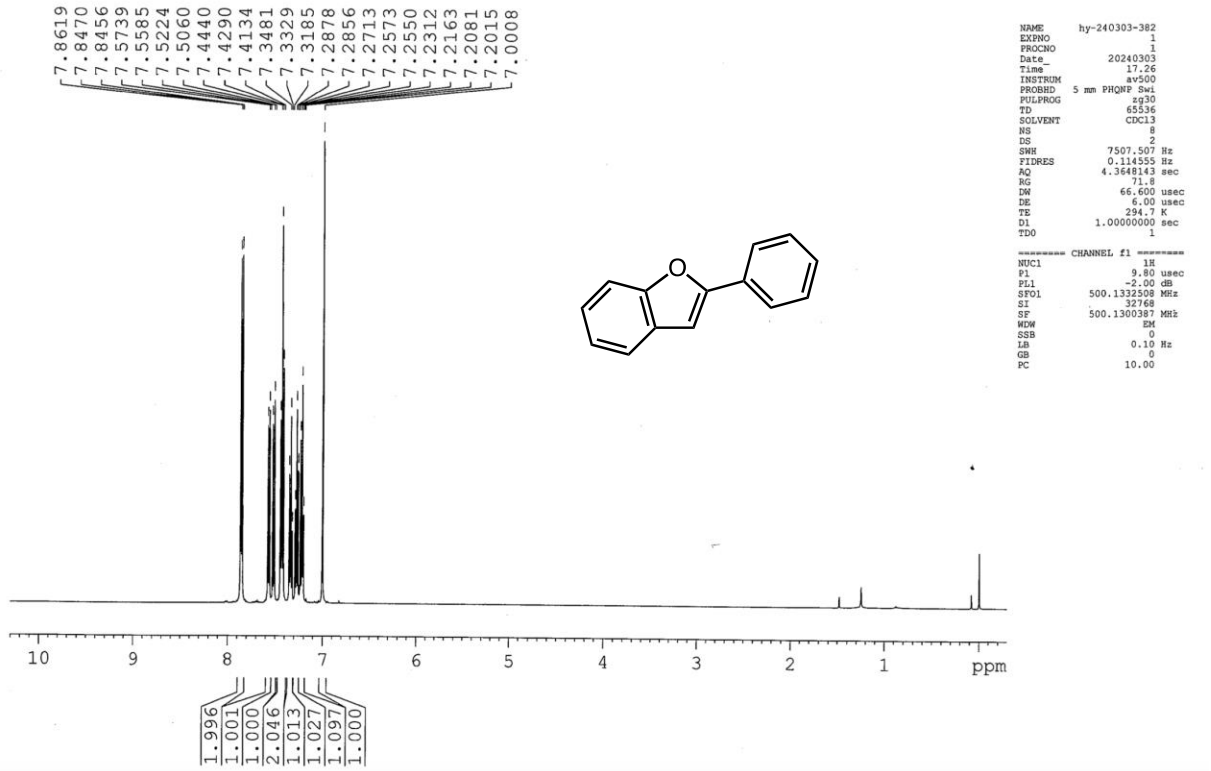
^{19}F NMR (470 MHz, $CDCl_3$): δ 55.0 (br dd, J_{FP} = 53, 42 Hz). ^{31}P NMR (202 MHz, $CDCl_3$): δ 40.5–38.6 (br s, 1P), 33.4–32.0 (br s, 1P). HRMS (FD): *m/z* Calcd for $C_{48}H_{73}FNiOP_2$ $[M]^+$: 804.4474; Found: 804.4449.

6. References

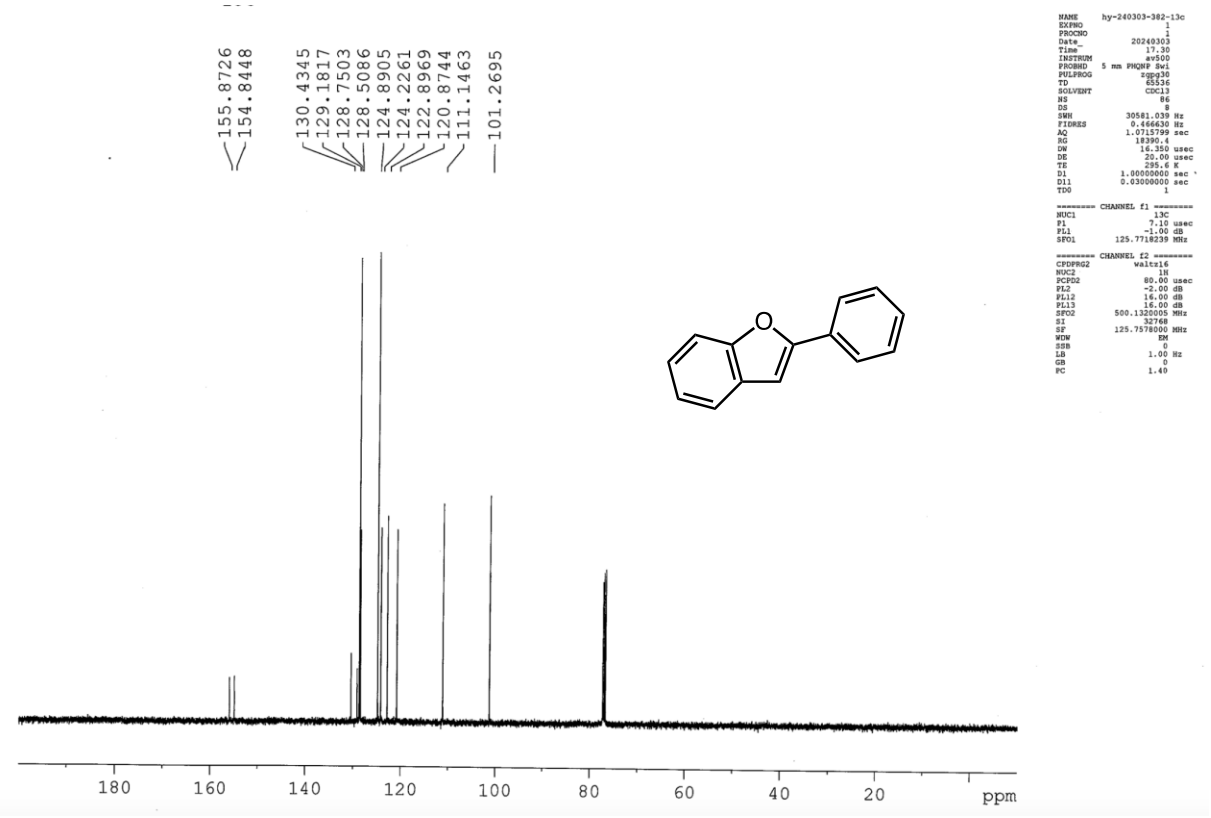
1. Morioka, R.; Fujita, T.; Ichikawa, J. *Helv. Chim. Acta* **2020**, *103*, e2000159.
2. Hofsäß, R.; Rombach, D.; Wagenknecht, H.-A. *Synlett* **2017**, *28*, 1422–1426.
3. Liégault, B.; Petrov, I.; Gorelsky, S. I.; Fagnou, K. *J. Org. Chem.* **2010**, *75*, 1047–1060.
4. Chen, W.; Zhang, Y.; Zhang, L.; Wang, M.; Wang, L. *Chem. Commun.* **2011**, *47*, 10476–10478.
5. Tong, Z.; Garry, O. L.; Smith, P. J.; Jiang, Y.; Mansfield, S. J.; Anderson, E. A. *Org. Lett.* **2021**, *23*, 4888–4892.
6. Dwight, T. A.; Rue, N. R.; Charyk, D.; Josselyn, R.; DeBoef, B. *Org. Lett.* **2007**, *9*, 3137–3139.
7. Csékei, M.; Novák, Z.; Kotschy, A. *Tetrahedron* **2008**, *64*, 8992–8996.
8. Moure, M. J.; SanMartin, R.; Domínguez, E. *Adv. Synth. Catal.* **2014**, *356*, 2070–2080.
9. Liu, L.; Li, X.; Dong, J.; Zhou, Y.; Yin, S.-F. *Org. Lett.* **2016**, *18*, 3138–3141.
10. Pan, C.; Yu, J.; Zhou, Y.; Wang, Z.; Zhou, M.-M. *Synlett* **2006**, 1657–1662.
11. Gao, H.; Xu, Q.-L.; Keene, C.; Kürti, L. *Chem. Eur. J.* **2014**, *20*, 8883–8887.
12. Liu, J.; Chen, W.; Ji, Y.; Wang, L. *Adv. Synth. Catal.* **2012**, *354*, 1585–1592.
13. Kashiki, T.; Shinamura, S.; Kohara, M.; Miyazaki, E.; Takimiya, K.; Ikeda, M.; Kuwabara, H. *Org. Lett.* **2009**, *11*, 2473–2475.
14. Yamaguchi, M.; Katsumata, H.; Manabe, K. *J. Org. Chem.* **2013**, *78*, 9270–9281.

7. ^{1}H, ^{13}C, and ^{19}F NMR charts

2-Phenylbenzofuran (3aa)

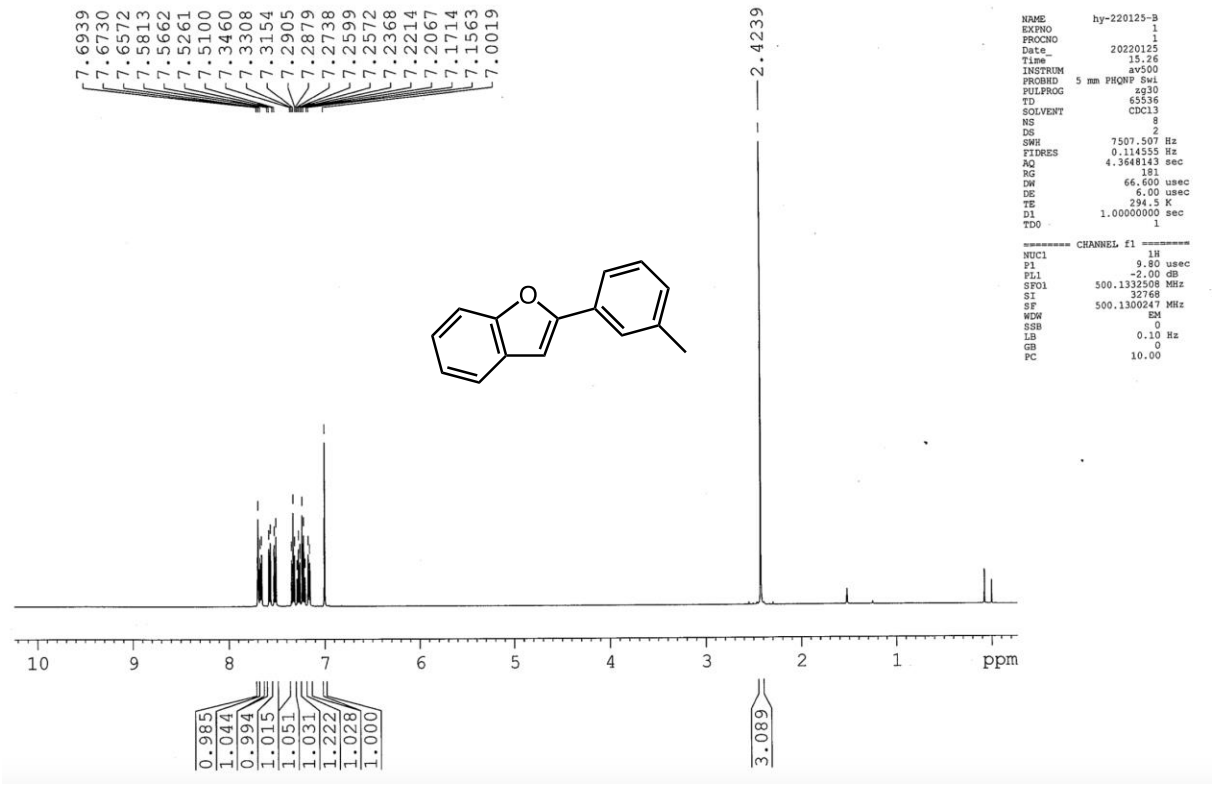


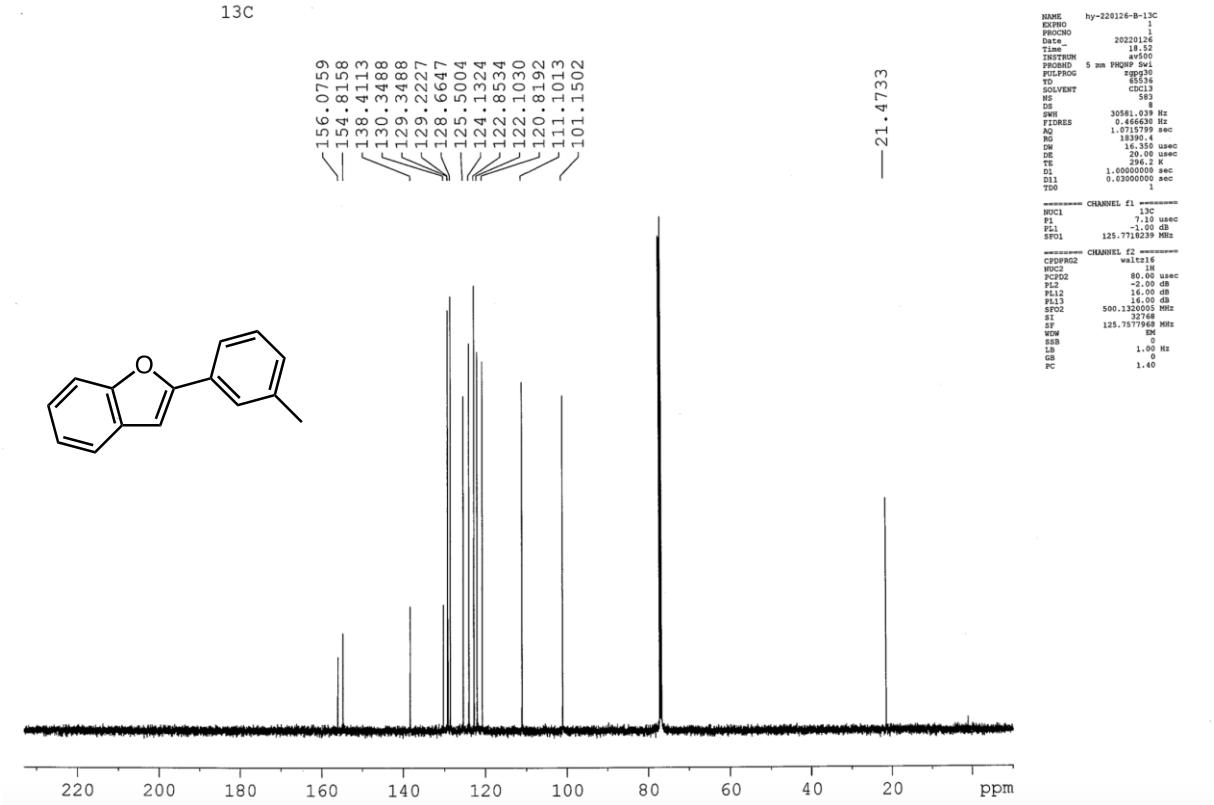

```
NAME          hy-240303-382
EXPNO                     1
PROCNO                    1
Date_              20240303
Time                  17.26
INSTRUM                av500
PROBHD  5 mm PHQNP Swi
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                        8
DS                        2
SWH               7507.507 Hz
FIDRES            0.114555 Hz
AQ                4.3648143 sec
RG                      71.8
DW                 66.600 usec
DE                  6.00 usec
TE                  294.7 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     9.80 usec
PL1                   -2.00 dB
SFO1          500.1332508 MHz
SI                    32768
SF            500.1300387 MHz
WDW                      EM
SSB                       0
LB                     0.10 Hz
GB                        0
PC                    10.00
```



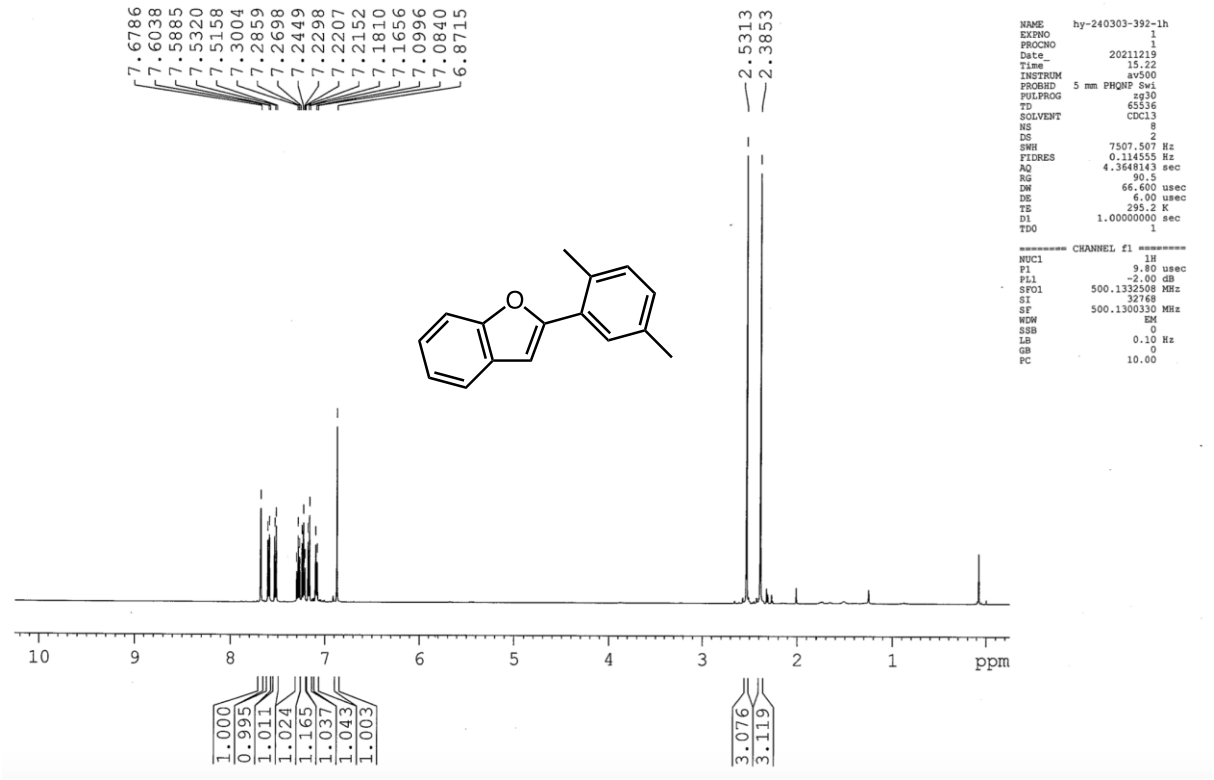

```
NAME          hy-240303-382-13c
EXPNO                     1
PROCNO                    1
Date_              20240303
Time                  17.30
INSTRUM                av500
PROBHD  5 mm PHQNP Swi
PULPROG               zgpg30
TD                    65536
SOLVENT               CDCl3
NS                       86
DS                        9
SWH              30581.039 Hz
FIDRES            0.466630 Hz
AQ                1.0715799 sec
RG                   18390.4
DW                 16.350 usec
DE                  20.00 usec
TE                  295.6 K
D1                1.00000000 sec
D11               0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                     7.10 usec
PL1                   -1.00 dB
SFO1          125.7718239 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                 80.00 usec
PL2                   -2.00 dB
PL12                  16.00 dB
PL13                  16.00 dB
SFO2          500.1320005 MHz
SI                    32768
SF            125.7578000 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                    1.40
```

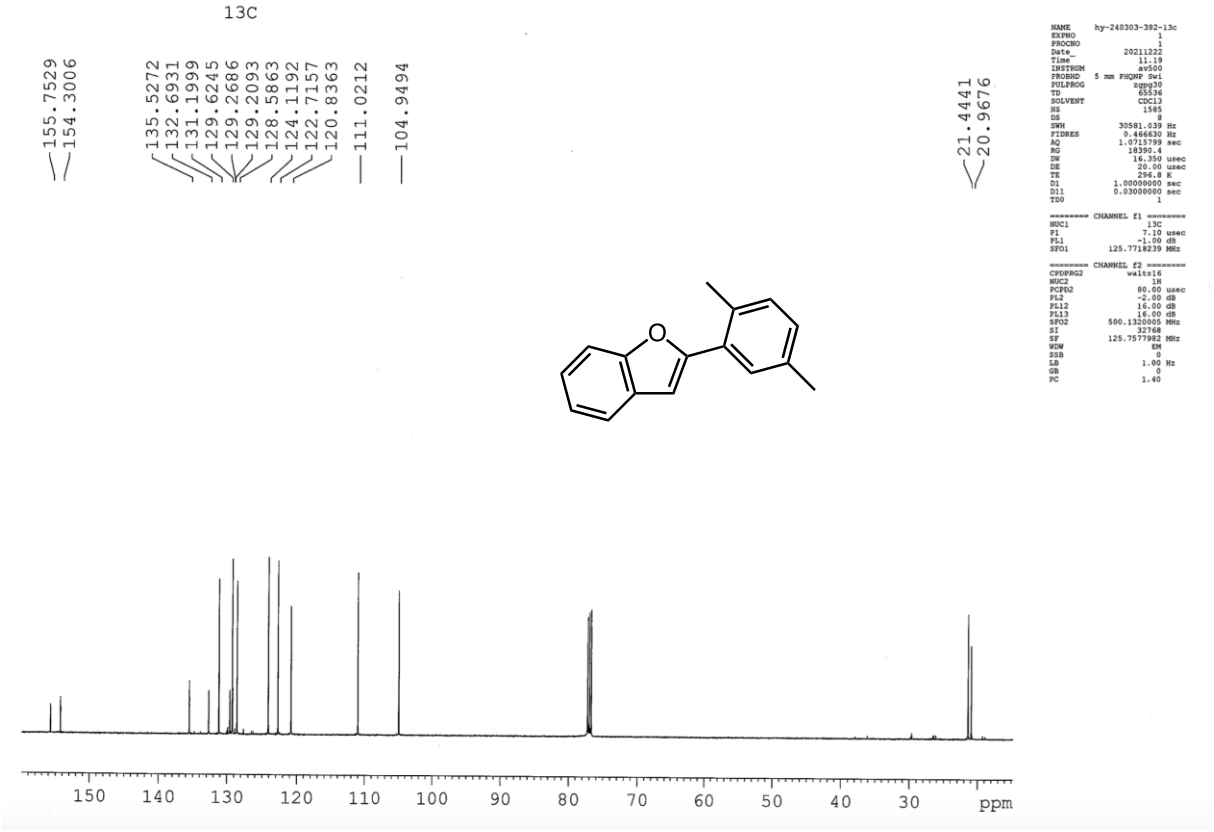
2-(3-Methylphenyl)benzofuran (3ab)



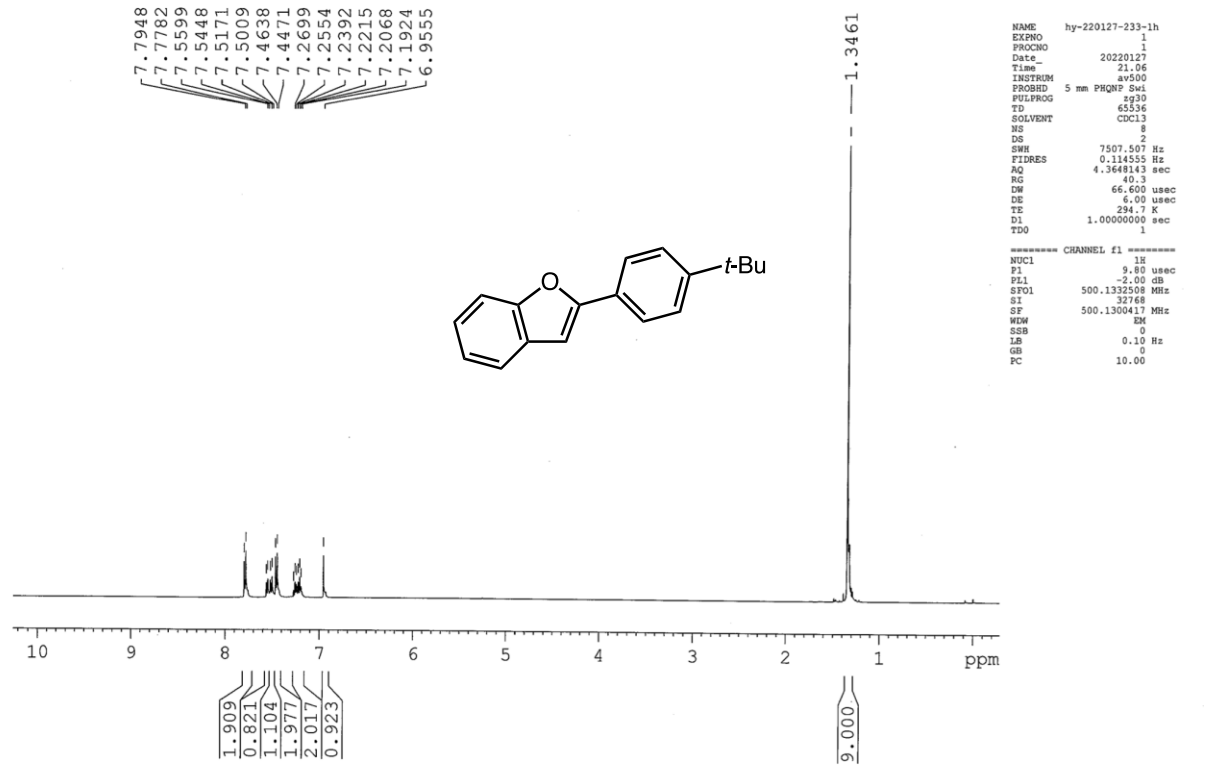


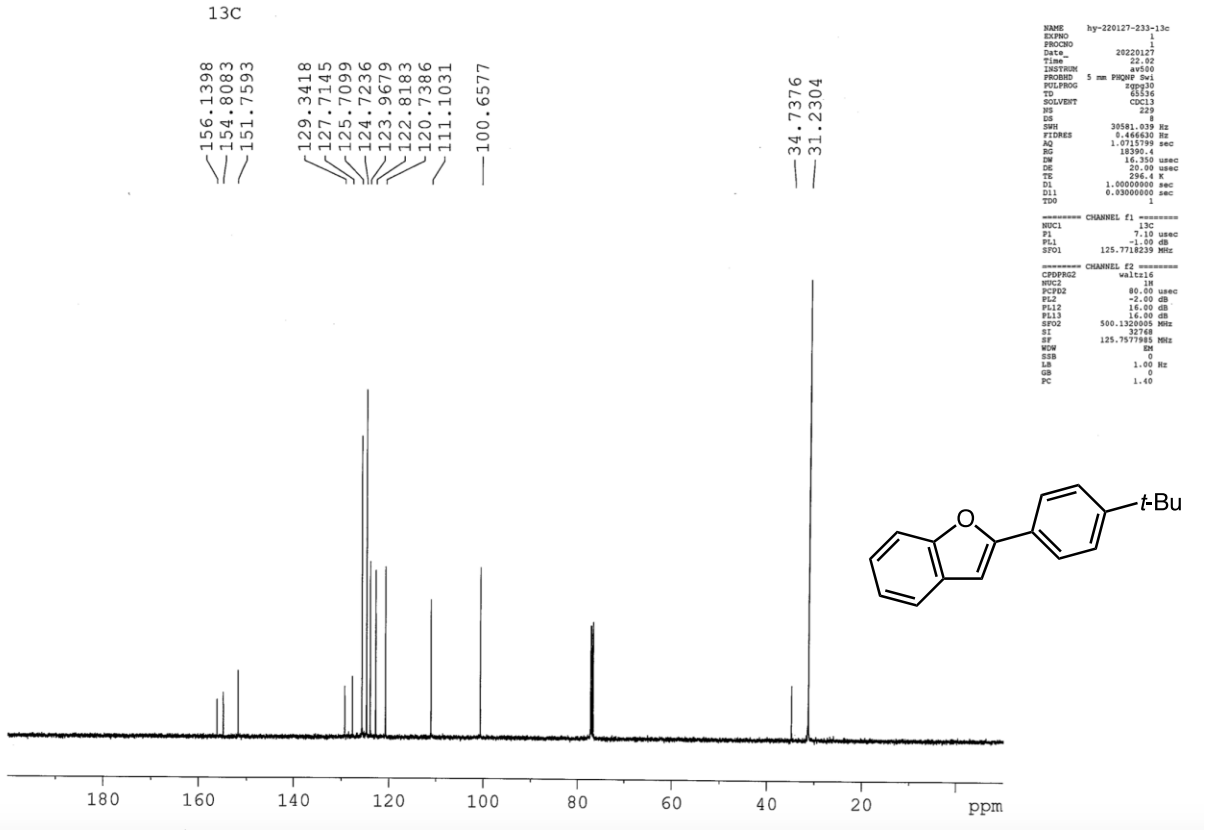
2-(2,5-Dimethylphenyl)benzofuran (3ac)



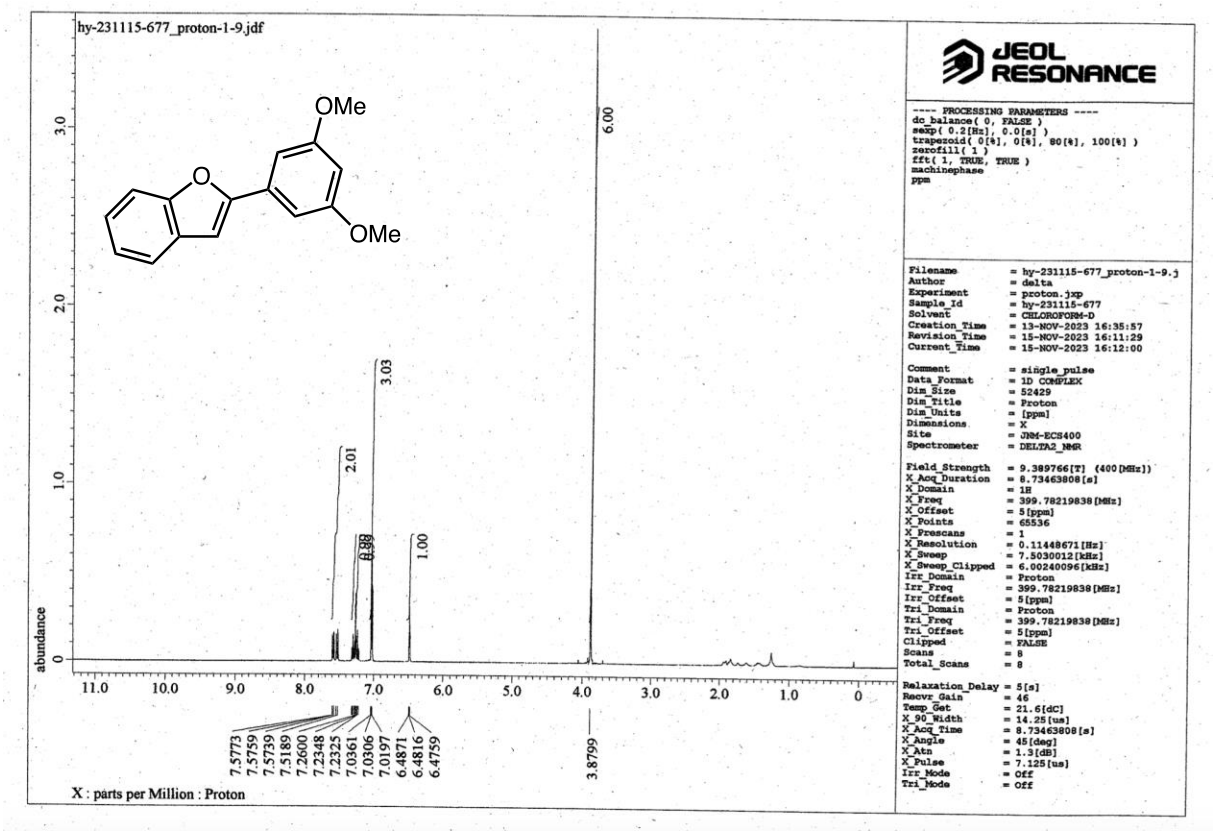


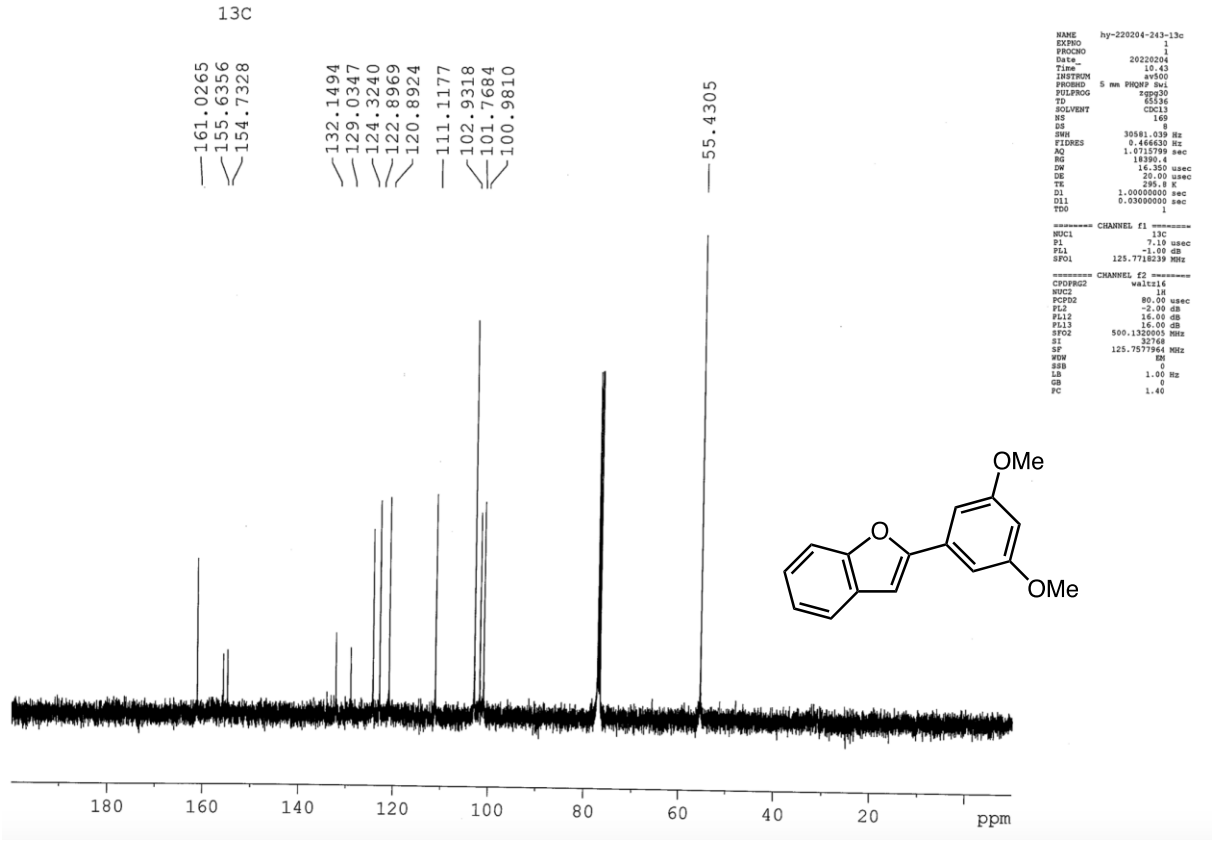
2-[4-(*tert*-Butyl)phenyl]benzofuran (3ad)



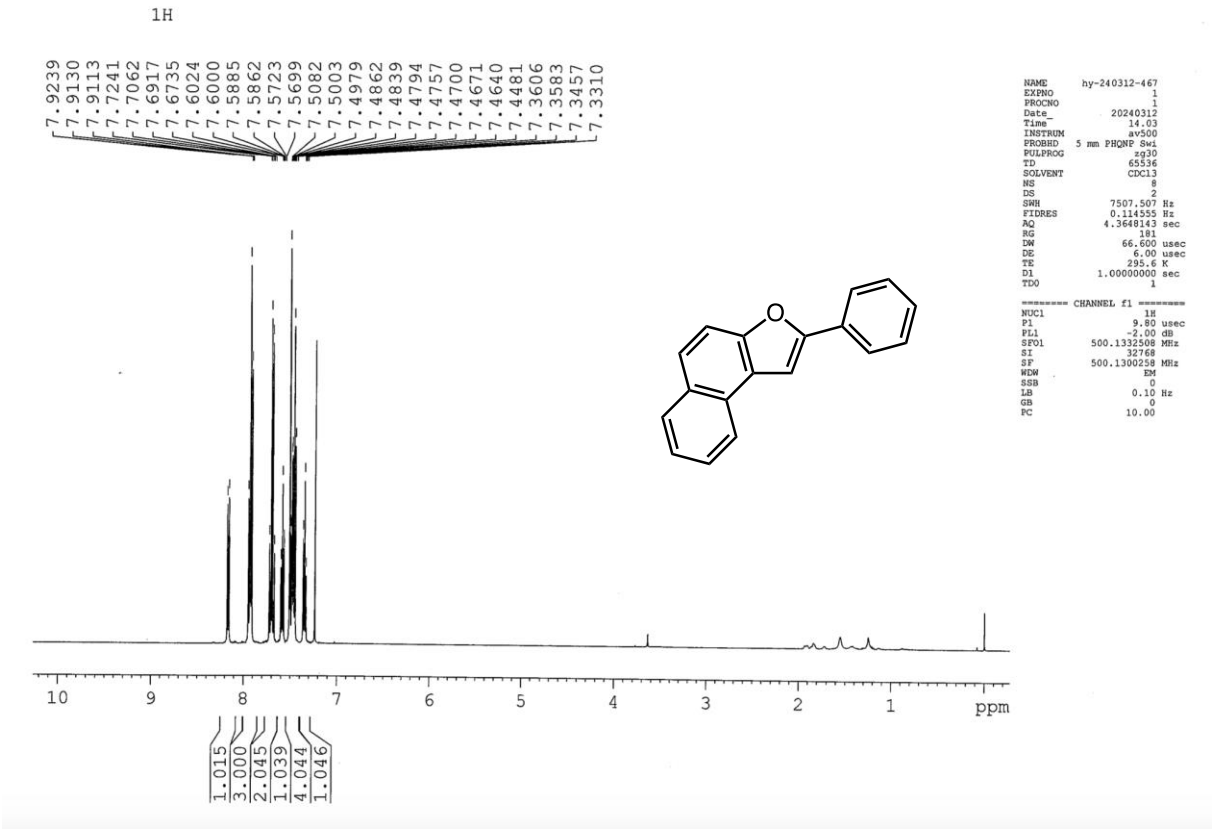


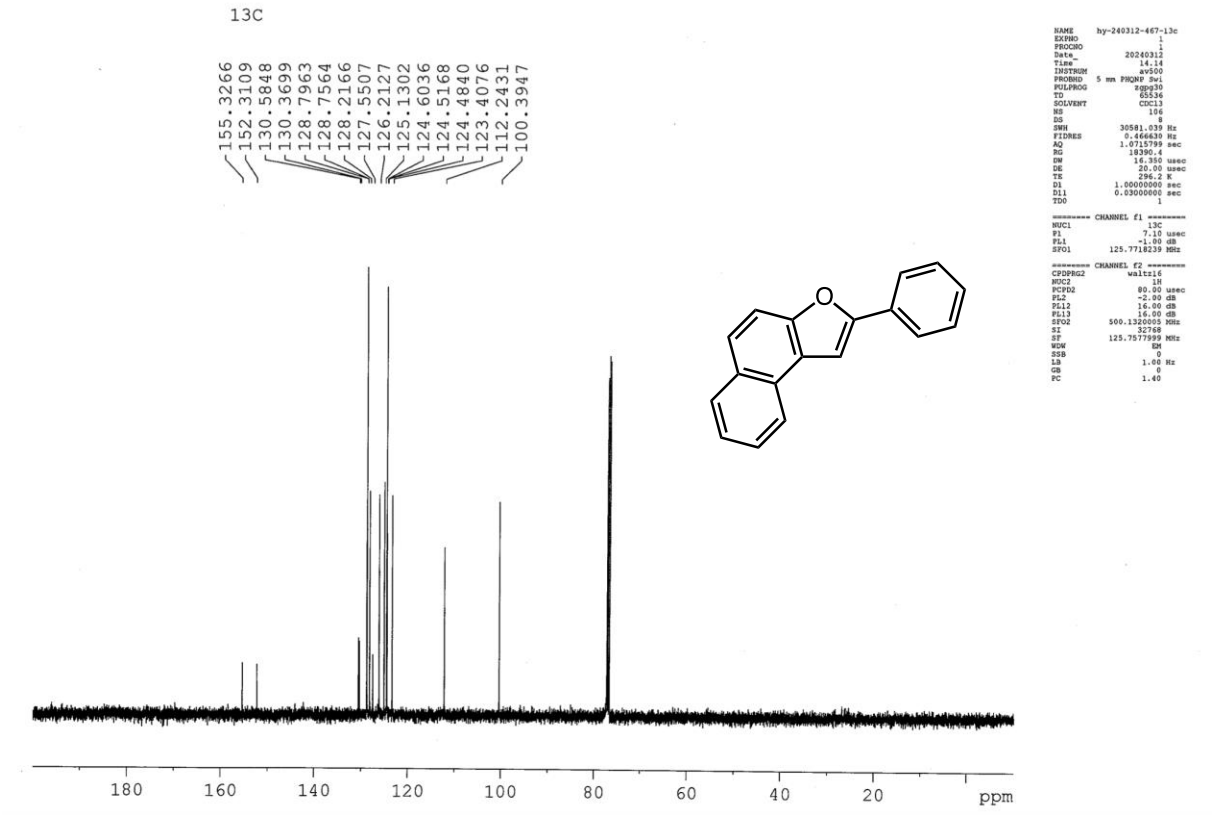
2-(3,5-Dimethoxyphenyl)benzofuran (3ae)



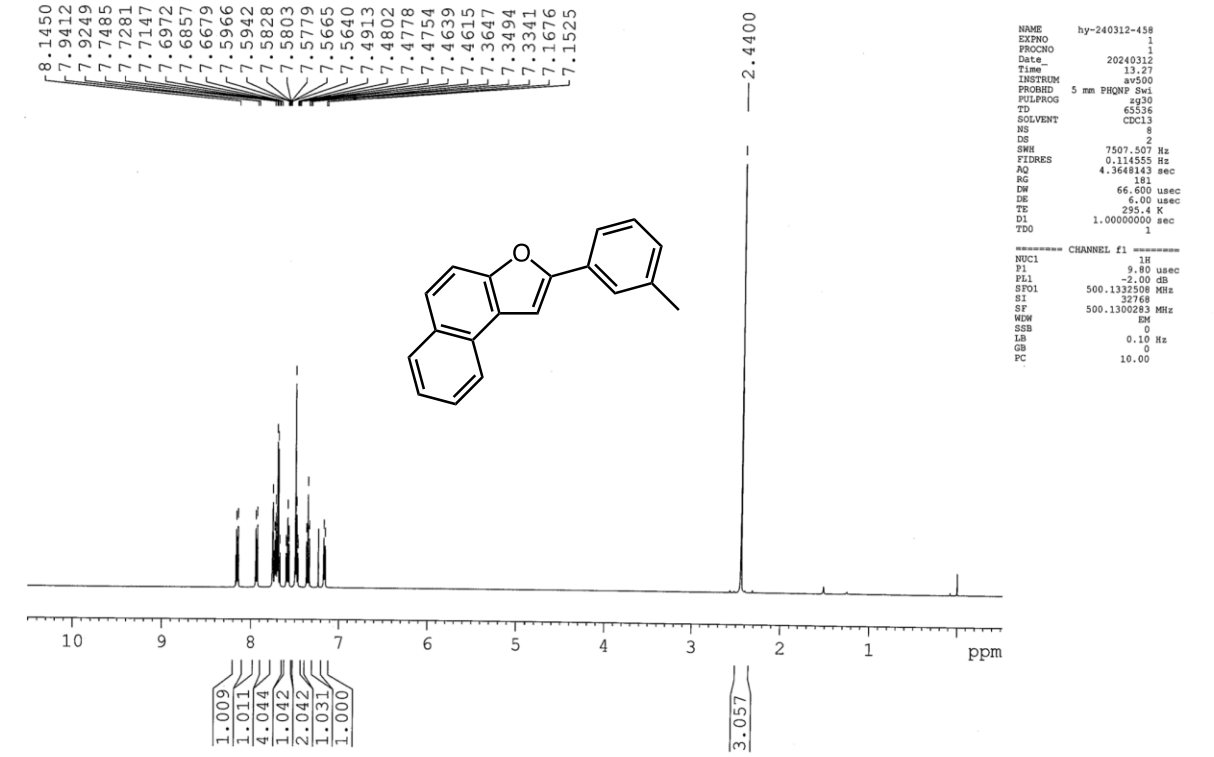


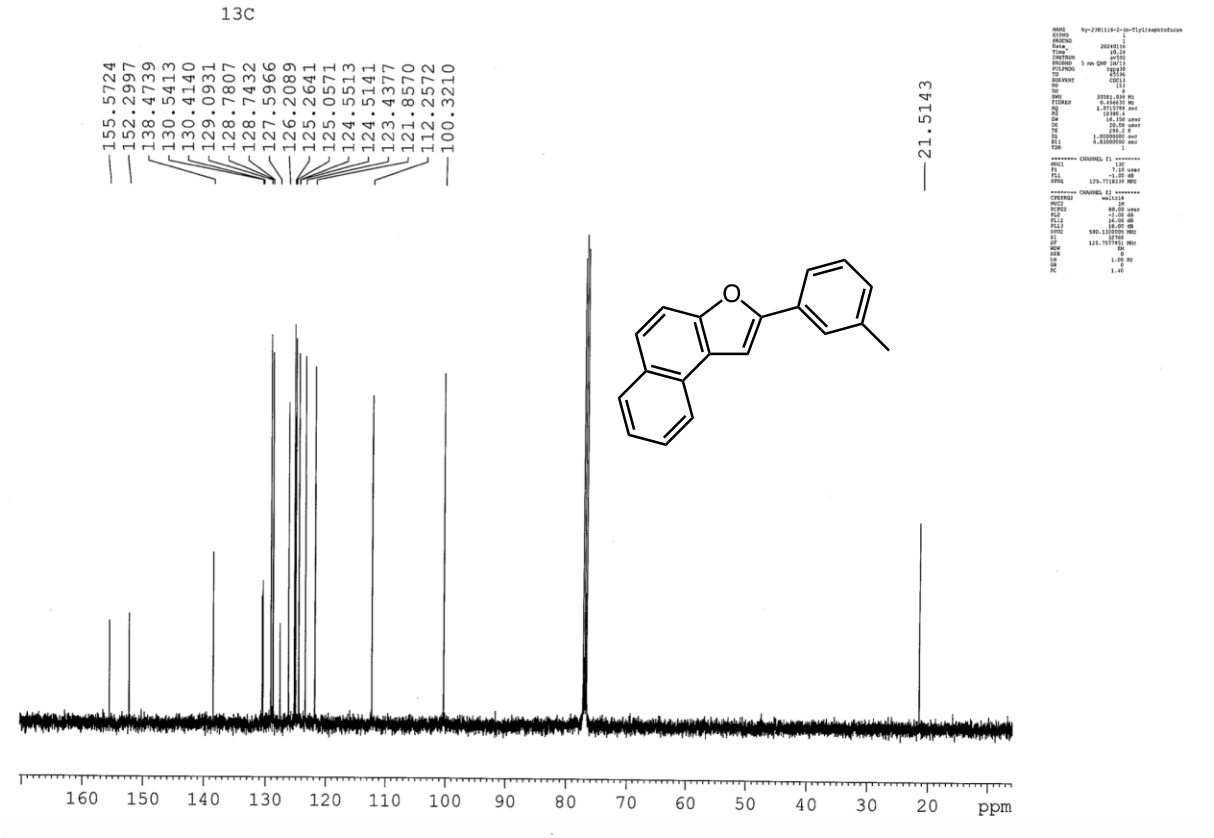
2-Phenylnaphtho[2,1-*b*]furan (3ba)



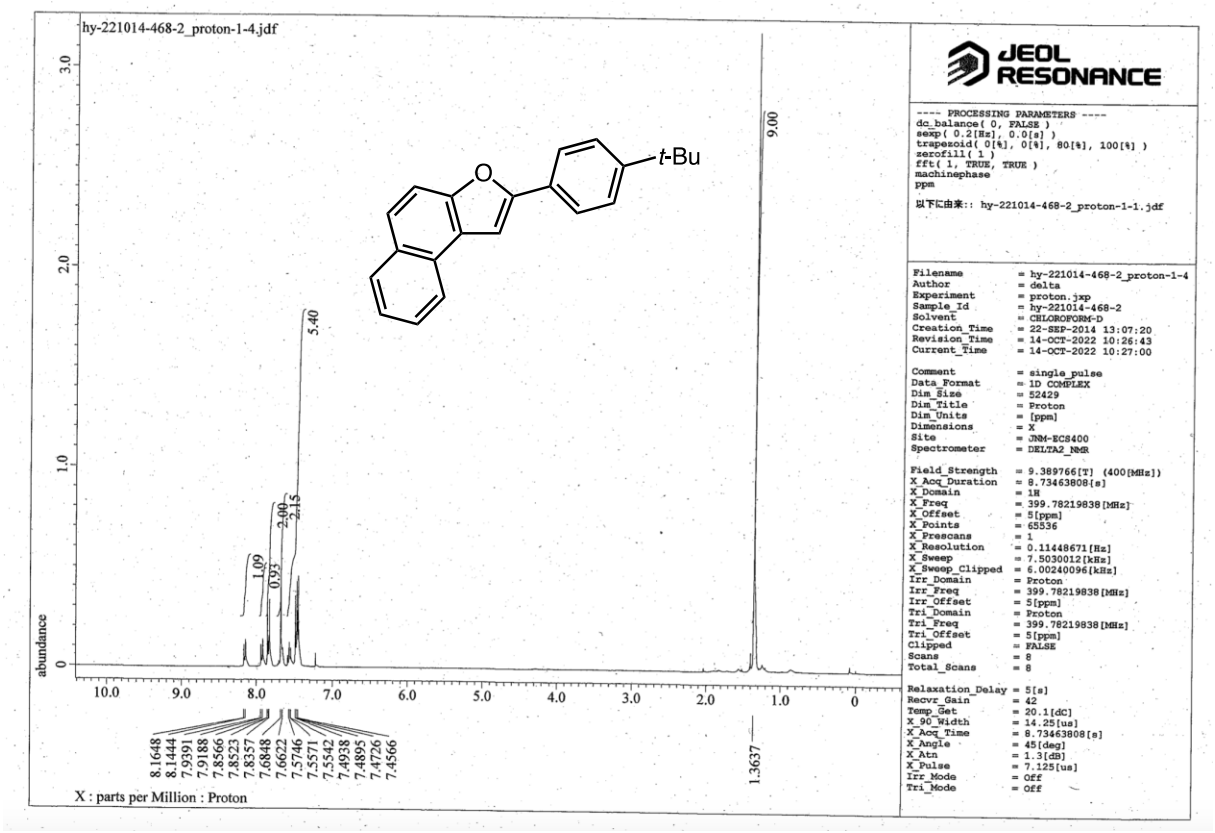


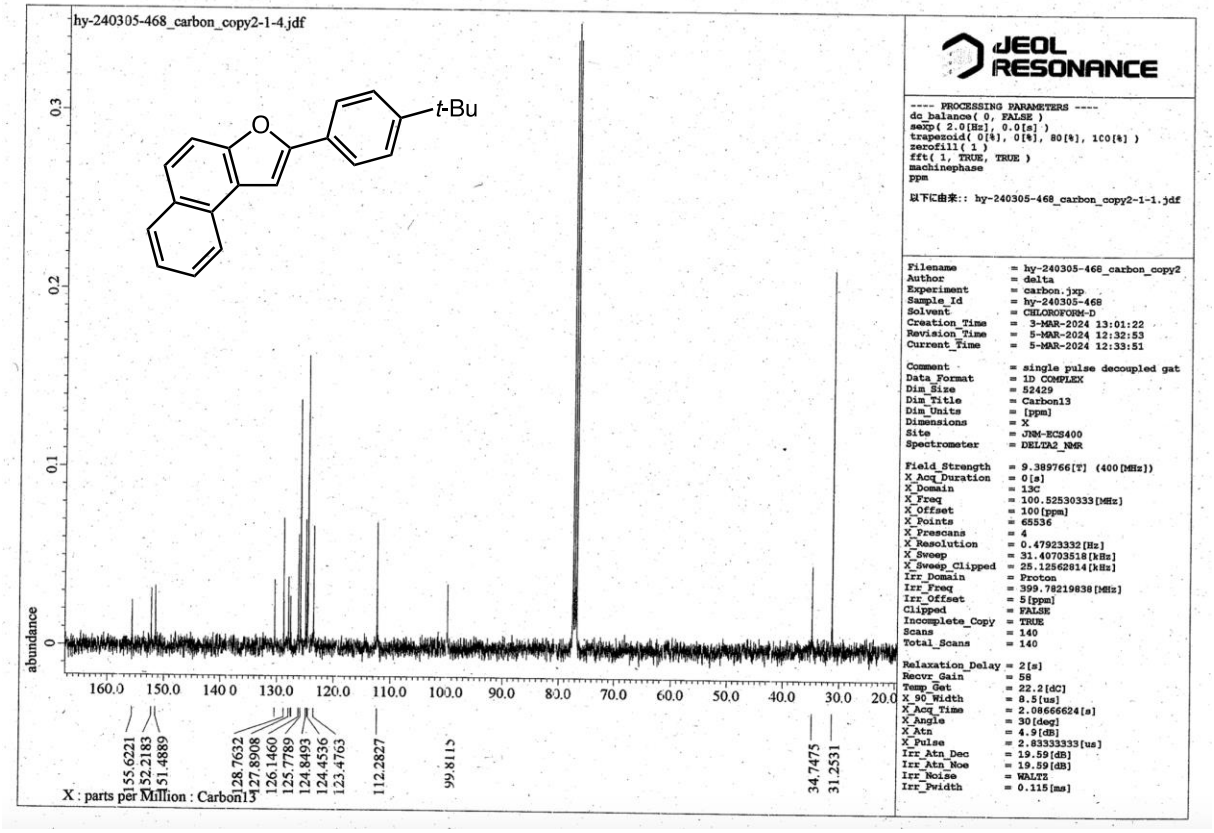
2-(3-Methylphenyl)naphtho[2,1-*b*]furan (3bb)



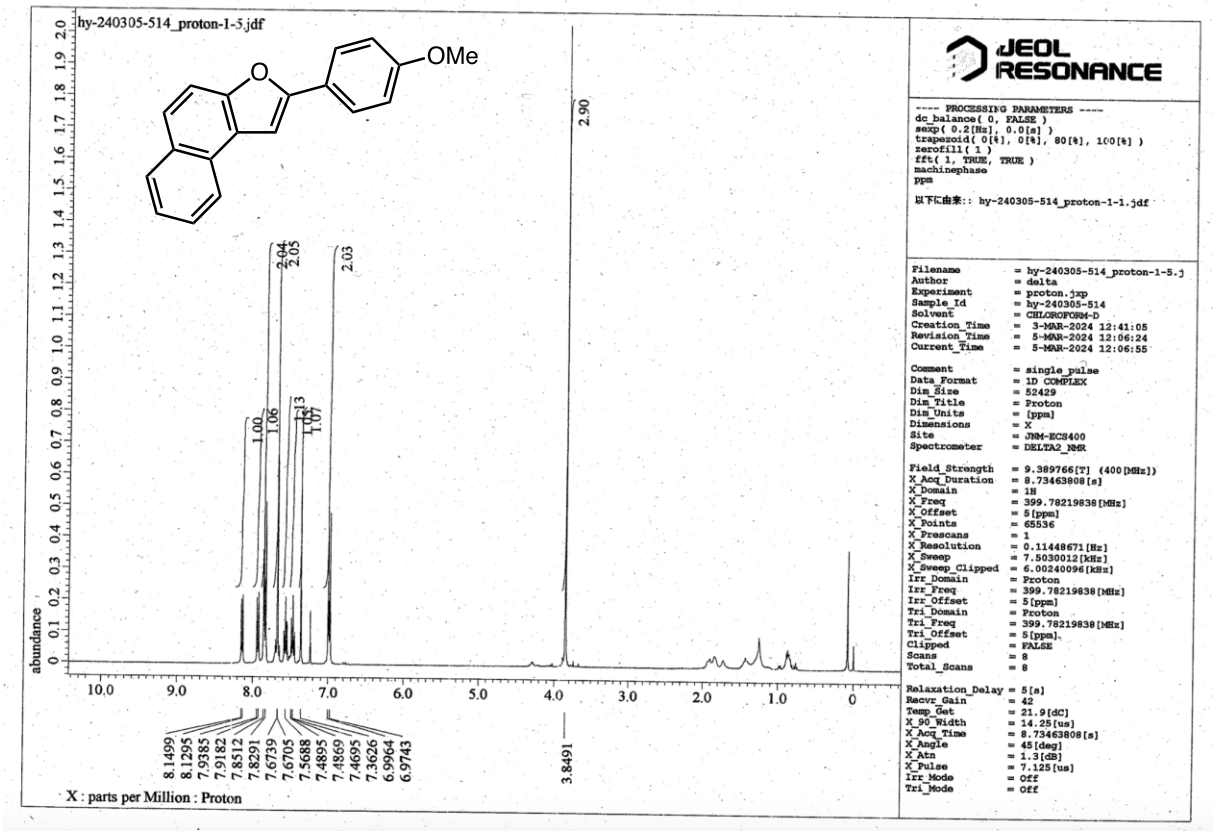


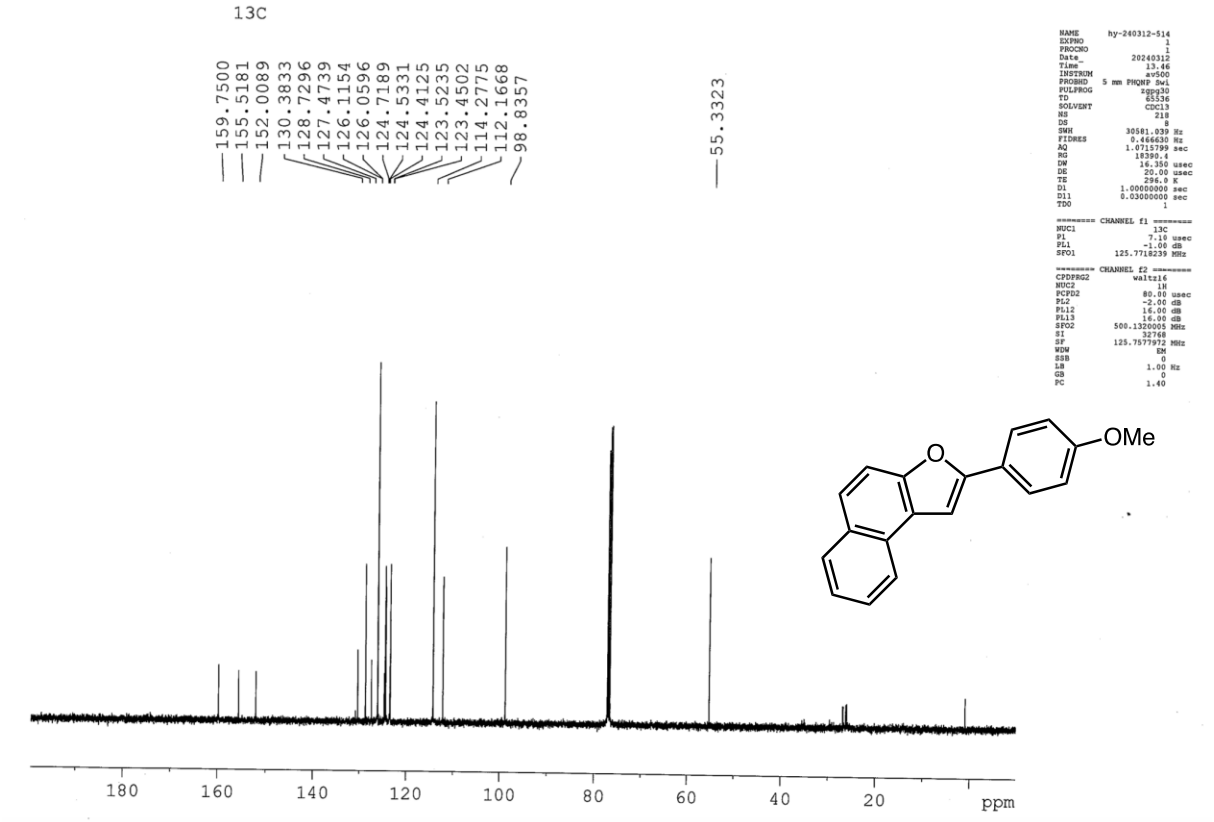
2-[4-(*tert*-Butyl)phenyl]naphtho[2,1-*b*]furan (3bd)



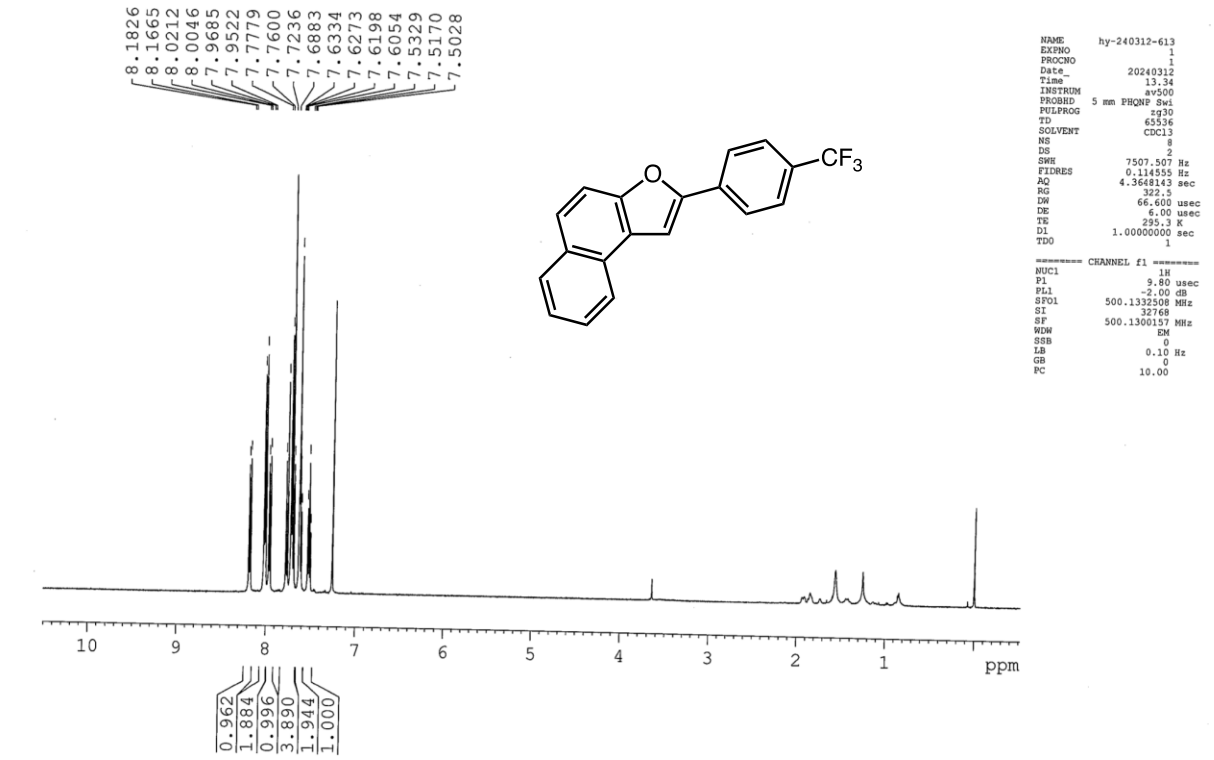


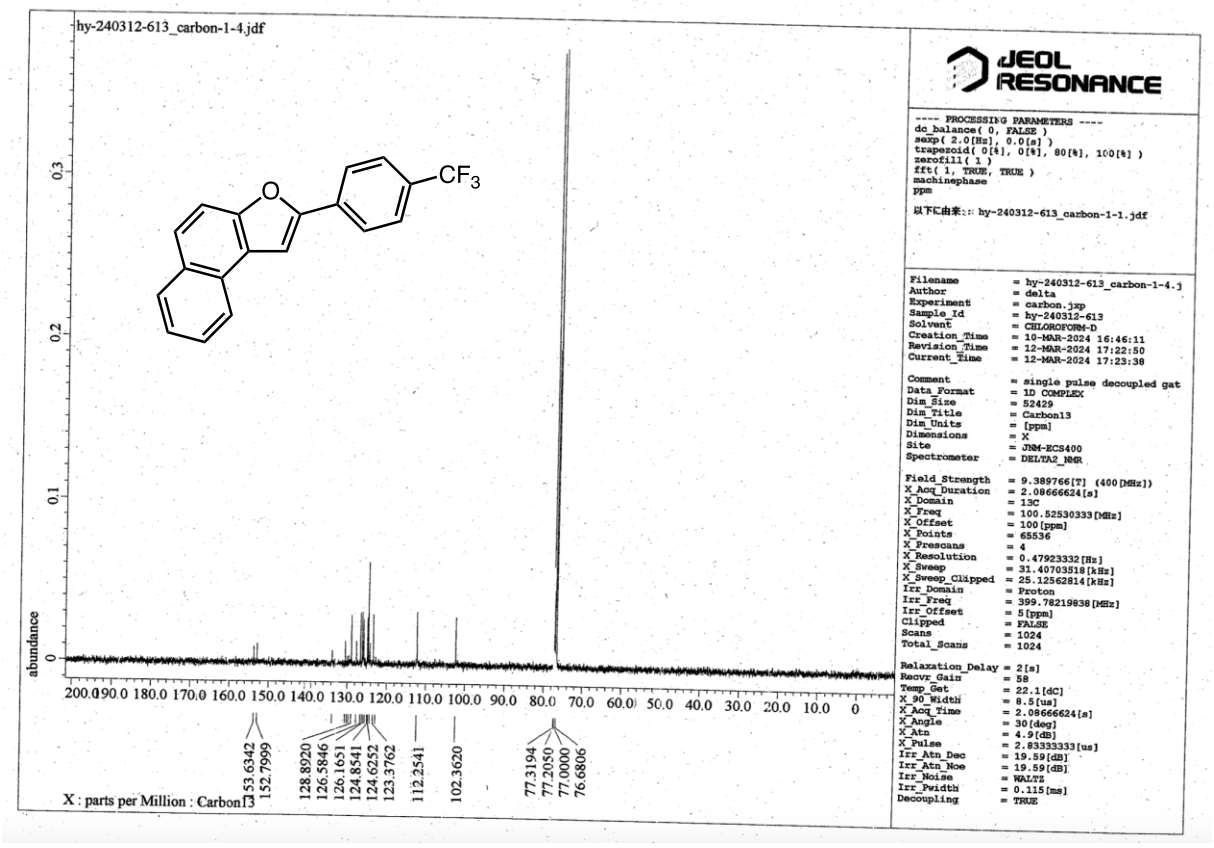
2-(4-Methoxyphenyl)naphtho[2,1-*b*]furan (3bf)

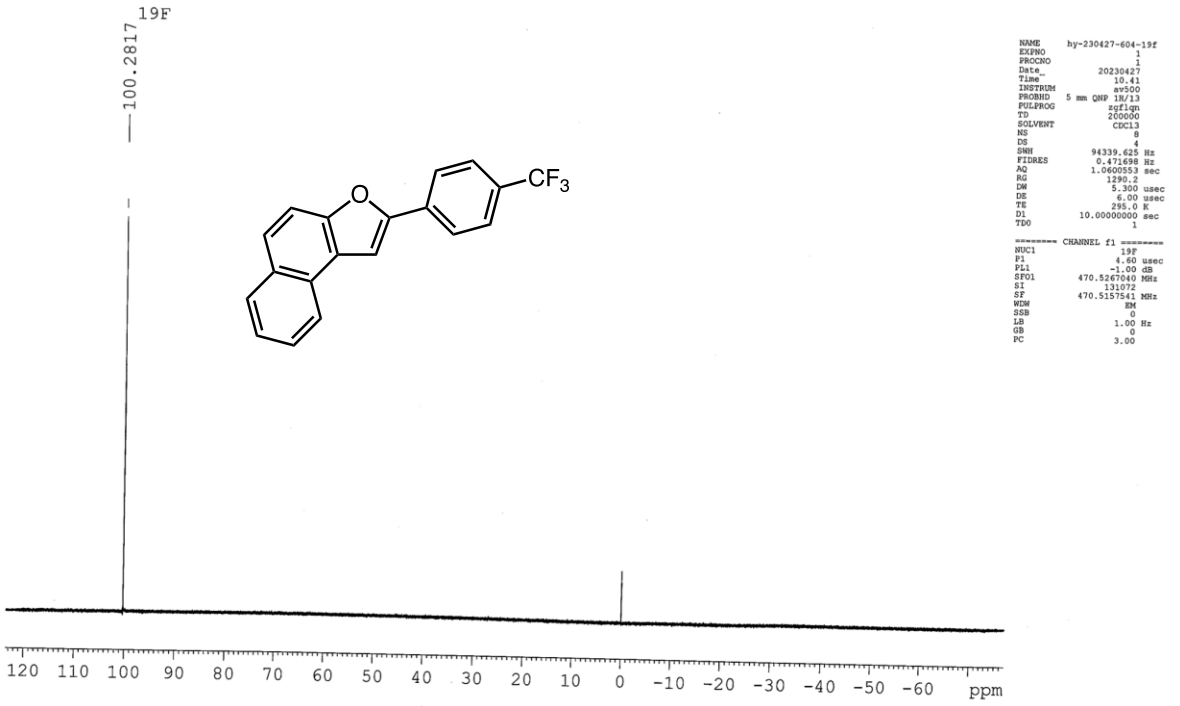




2-[4-(Trifluoromethyl)phenyl]naphtho[2,1-*b*]furan (3bg)

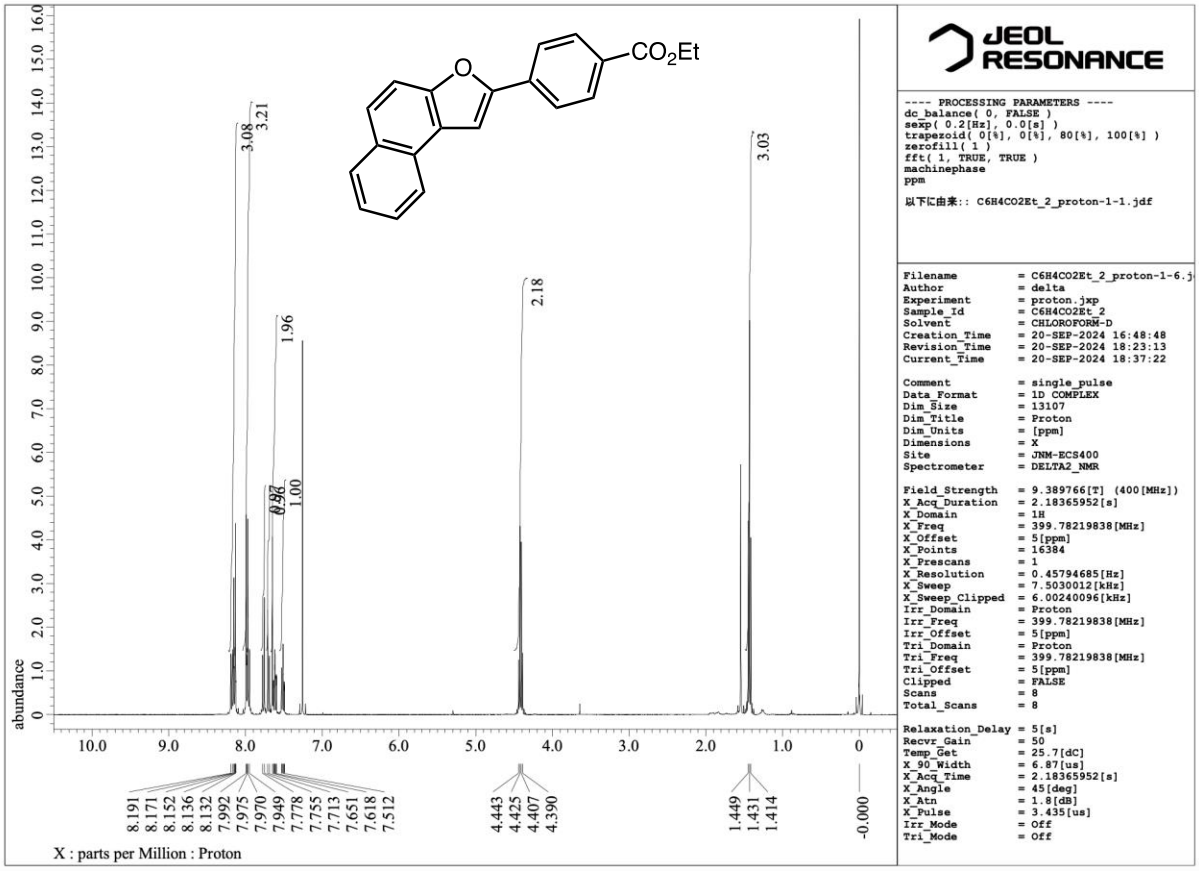


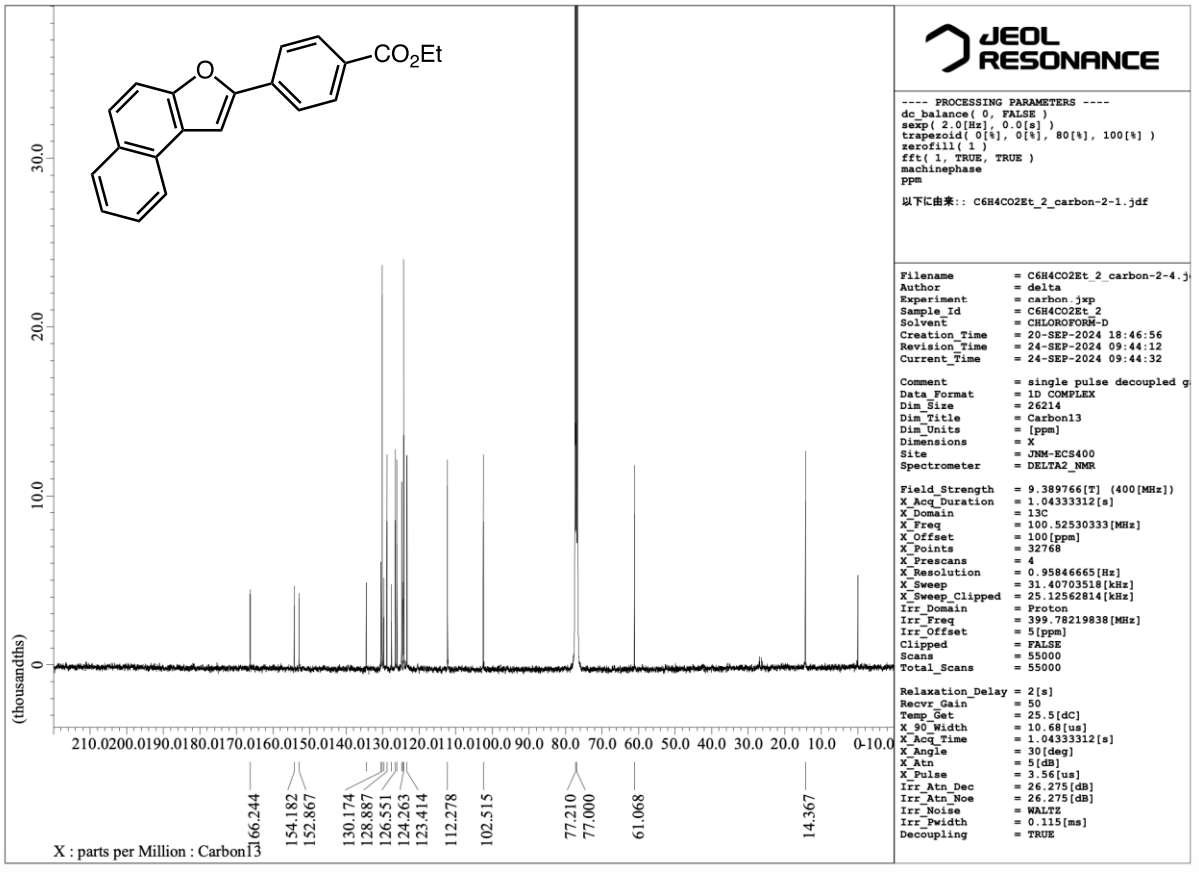




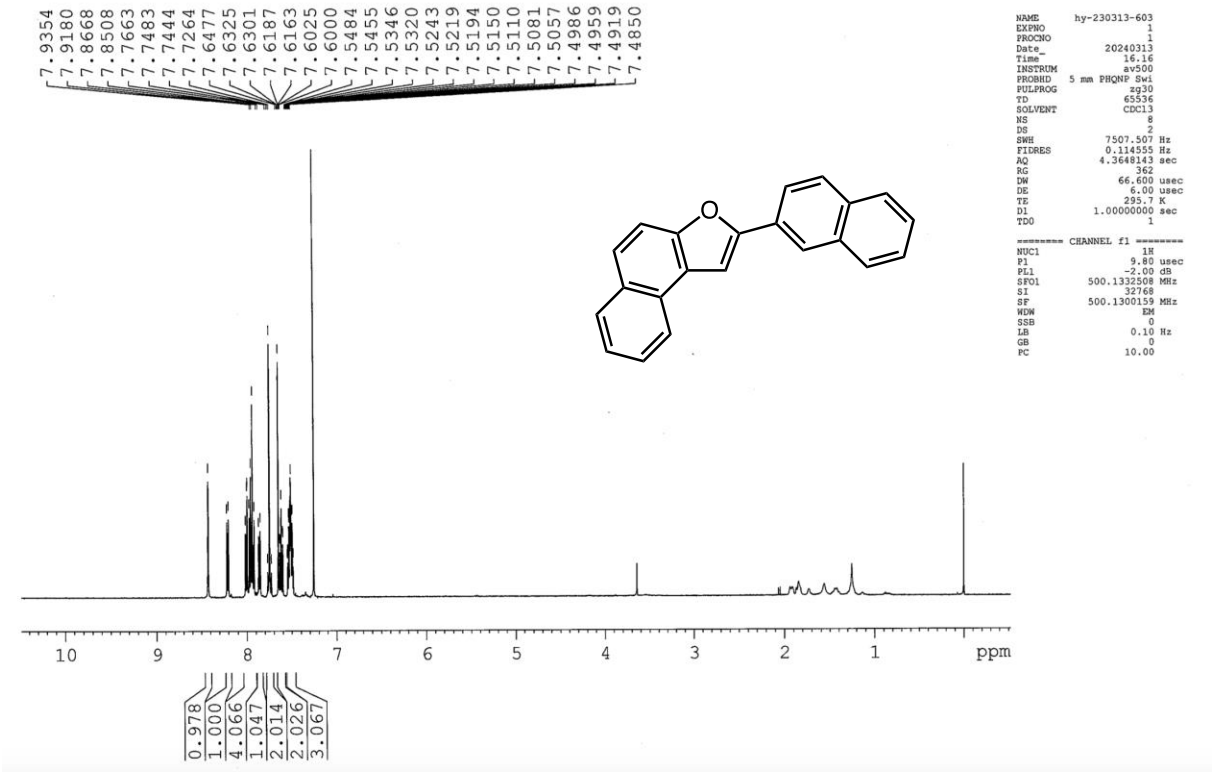
NAME	hy-230427-604-19f
EXPNO	1
PROCNO	1
Date_	20230427
Time	10.41
INSTRUM	av500
PROBHD	5 mm QNP 1H/13
PULPROG	zgflqn
TD	200000
SOLVENT	CDCl3
NS	8
DS	4
SWH	94339.625 Hz
FIDRES	0.471698 Hz
AQ	1.0600553 sec
RG	1290.2
DW	5.300 usec
DE	6.00 usec
TE	295.0 K
D1	10.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	19F
P1	4.60 usec
PL1	-1.00 dB
SFO1	470.5267040 MHz
SI	131072
SF	470.5157541 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	3.00

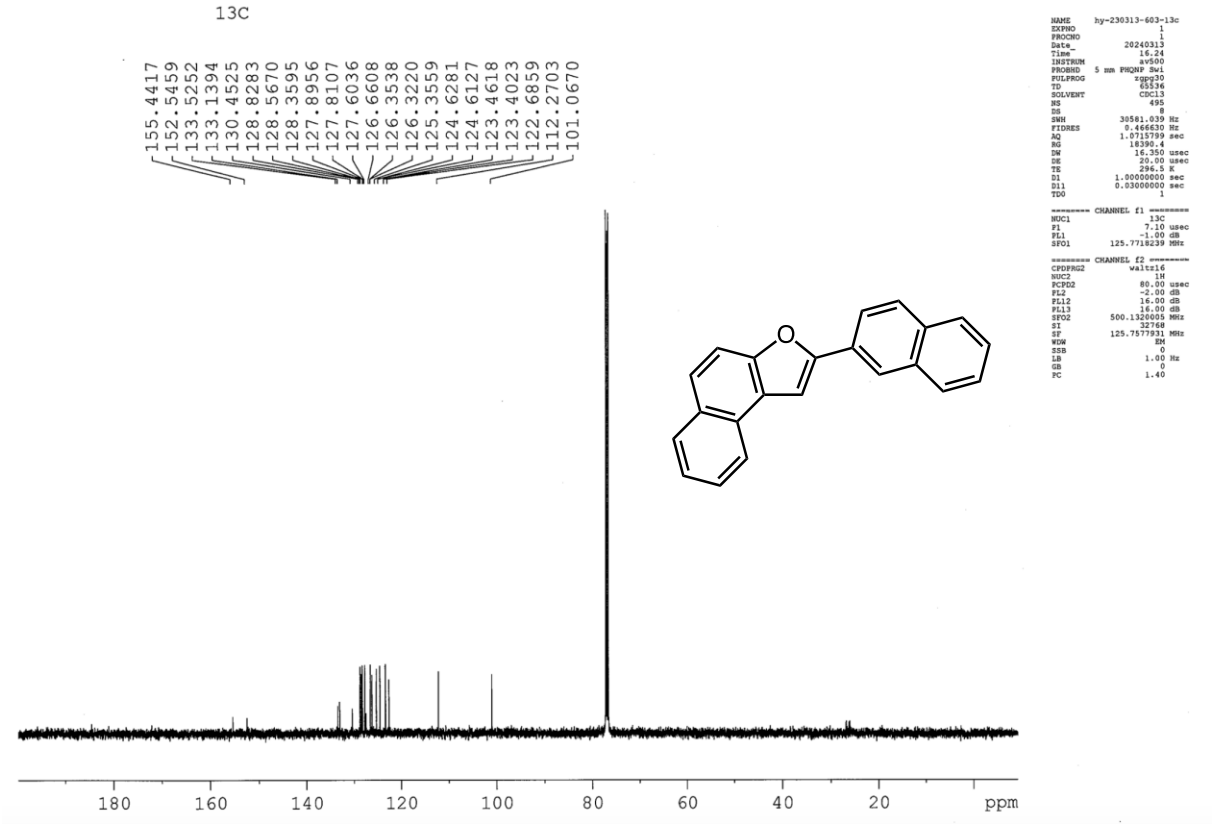
Ethyl 4-(naphtho[2,1-*b*]furan-2-yl)benzoate (3bh)



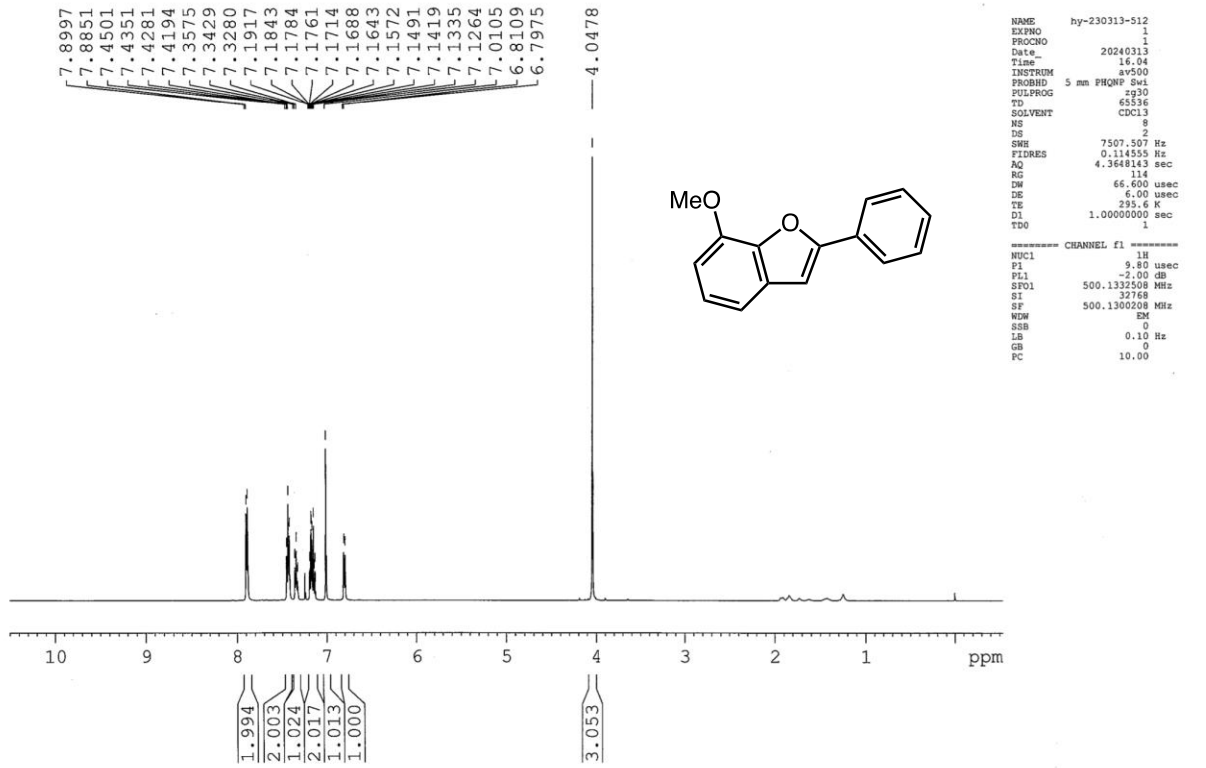


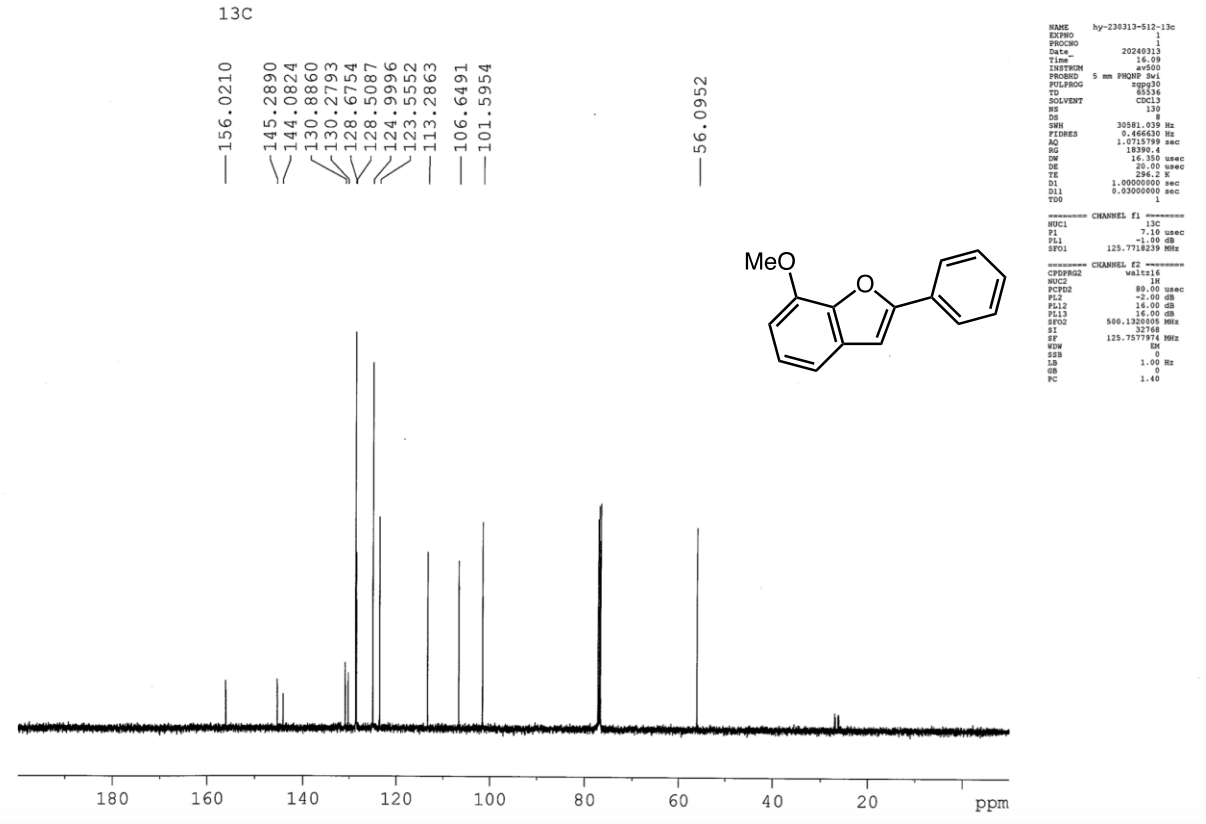
2-(Naphthalen-2-yl)naphtho[2,1-*b*]furan (3bi)



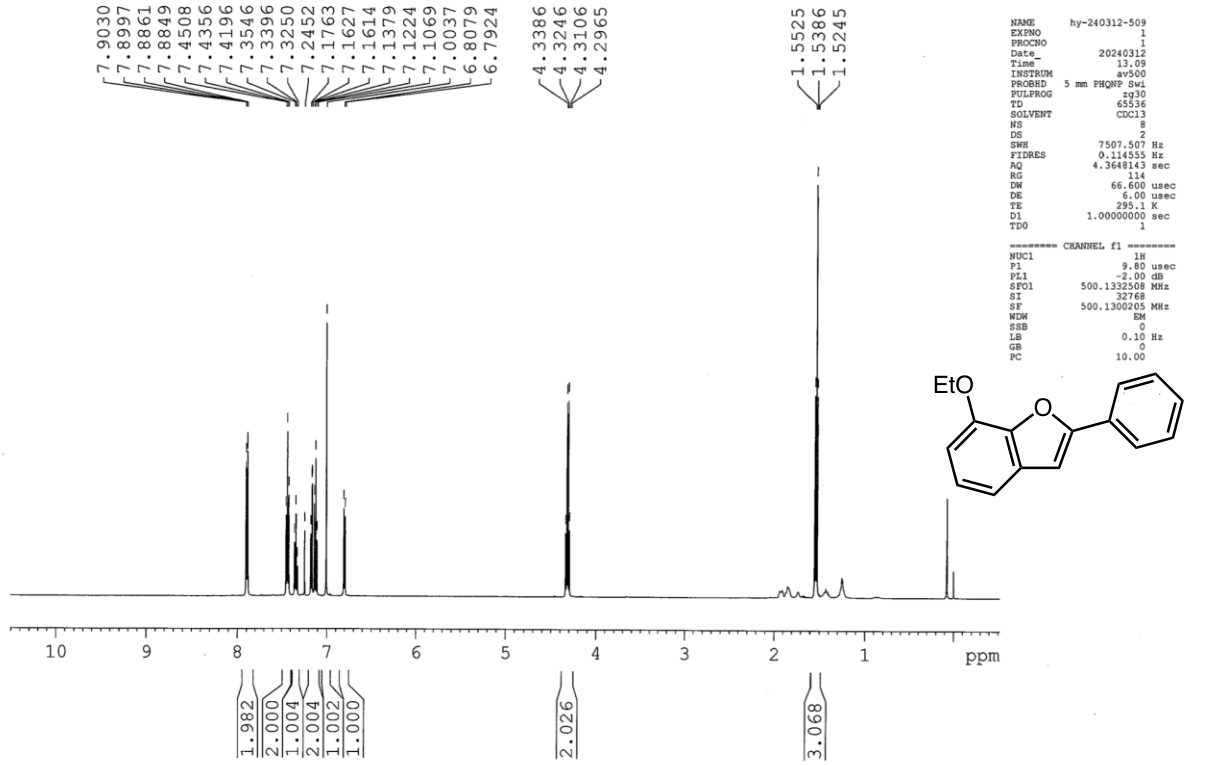


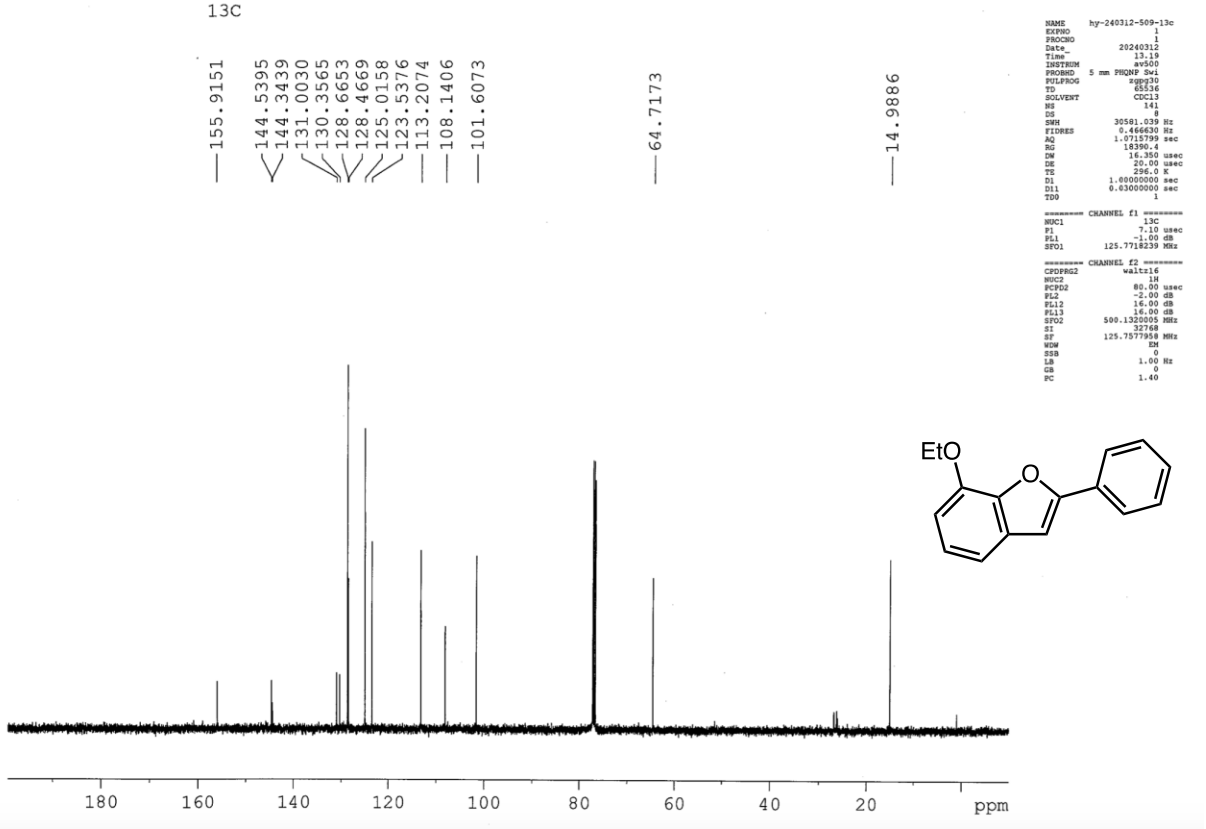
7-Methoxy-2-phenylbenzofuran (3ca)



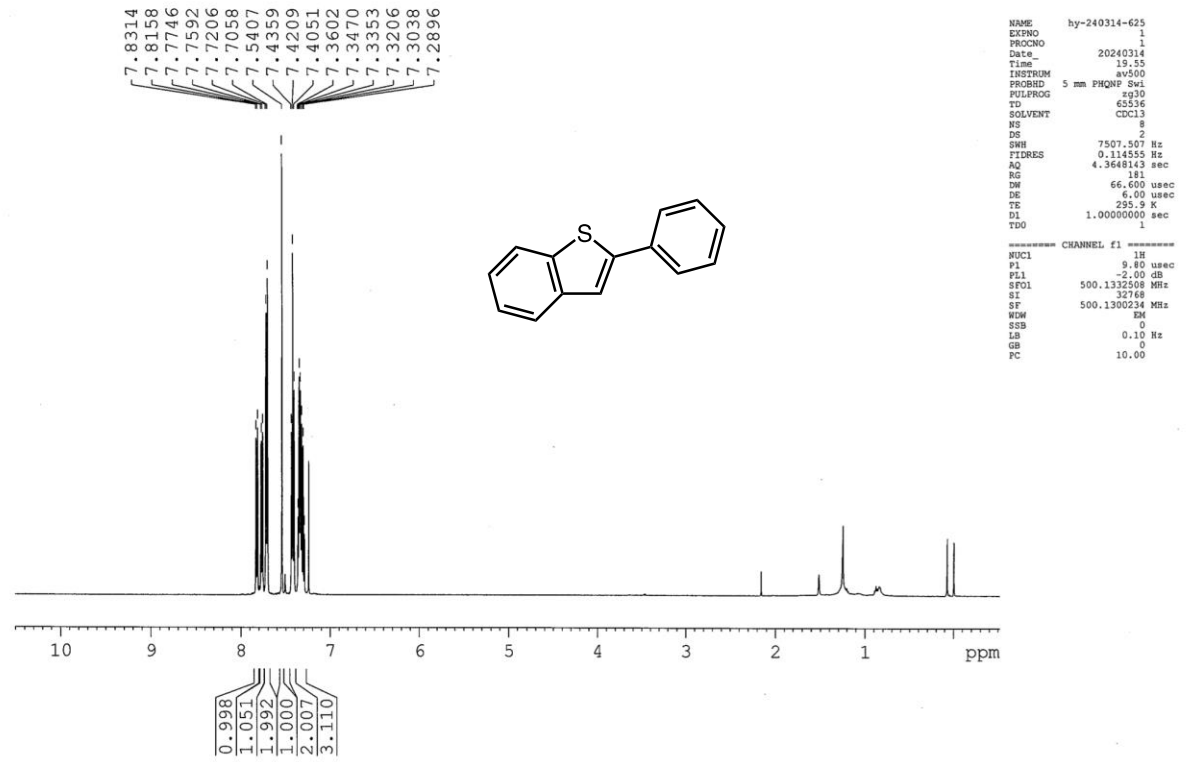


7-Ethoxy-2-phenylbenzofuran (3da)

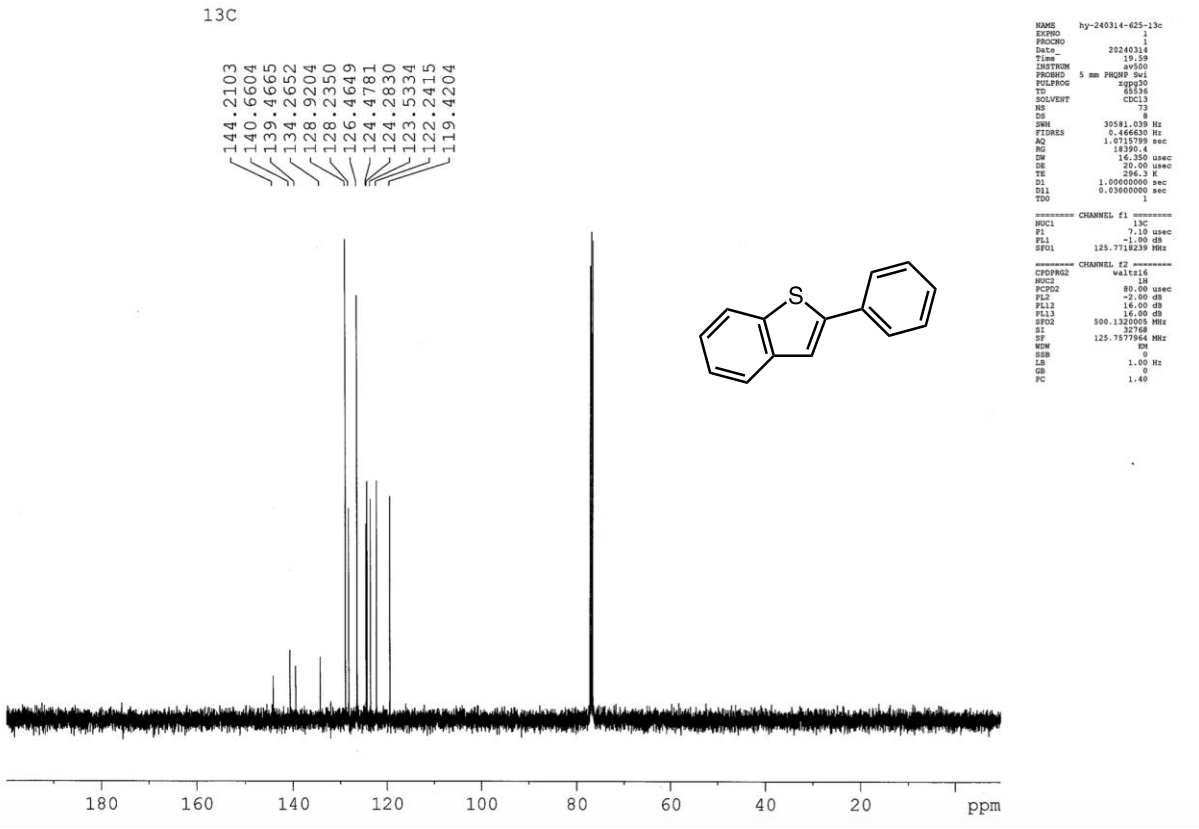




2-Phenylbenzo[*b*]thiophene (5)

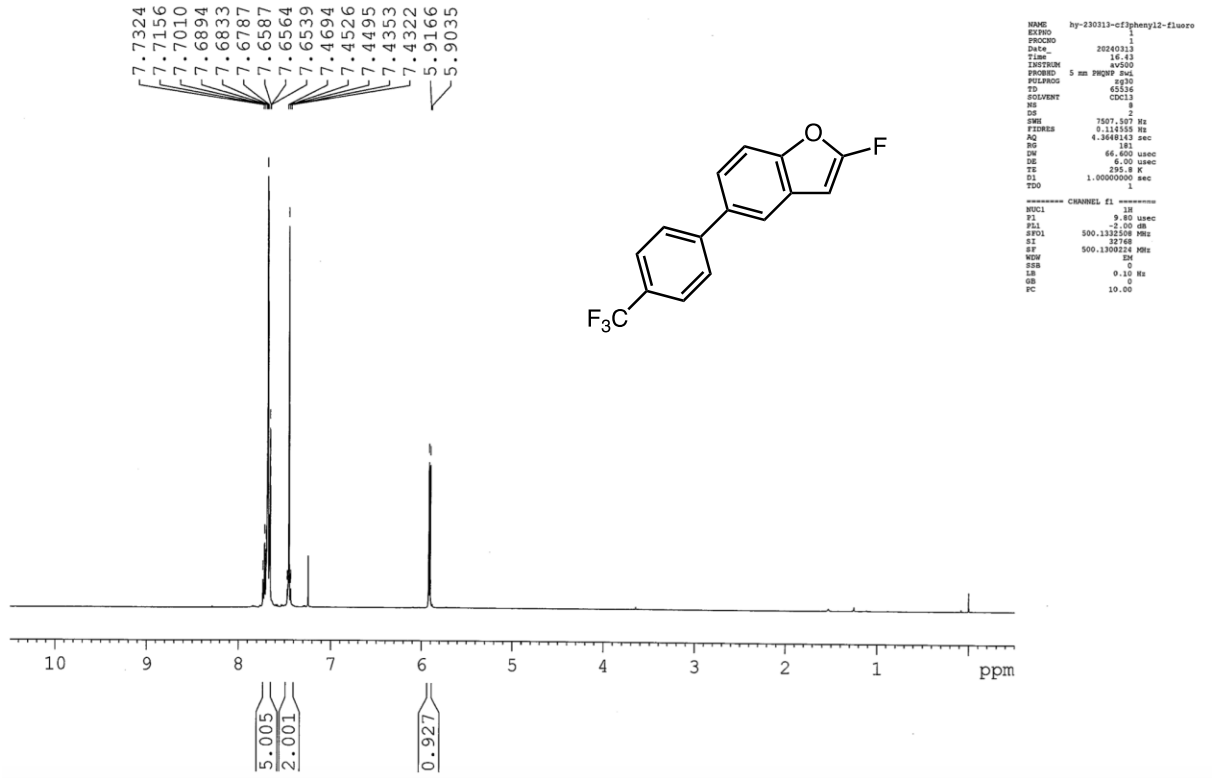


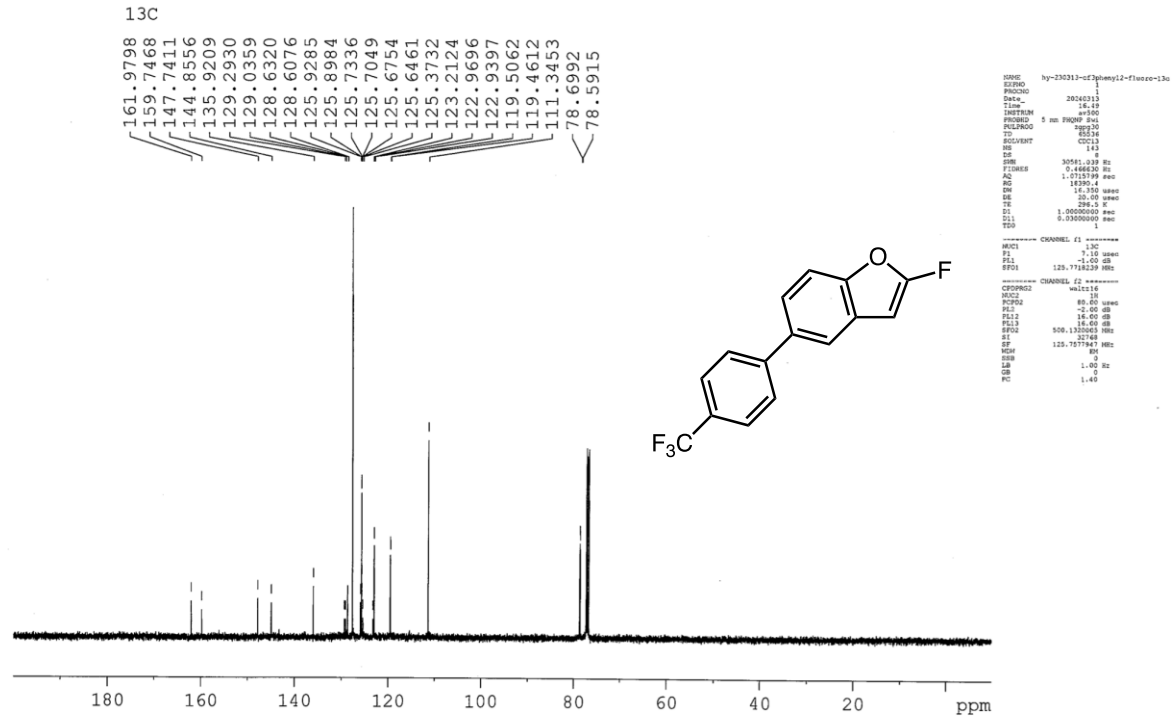

```
NAME          hy-240314-625
EXPNO                 1
PROCNO                1
Date_          20240314
Time              19.55
INSTRUM           av500
PROBHD   5 mm PHQNP Swi
PULPROG           zg30
TD                65536
SOLVENT           CDCl3
NS                    8
DS                    2
SWH           7507.507 Hz
FIDRES        0.114555 Hz
AQ            4.3648143 sec
RG                  181
DW             66.600 usec
DE              6.00 usec
TE              295.9 K
D1          1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                1H
P1               9.80 usec
PL1             -2.00 dB
SFO1       500.1332508 MHz
SI                32768
SF         500.1300234 MHz
WDW                EM
SSB                   0
LB             0.10 Hz
GB                    0
PC                10.00
```

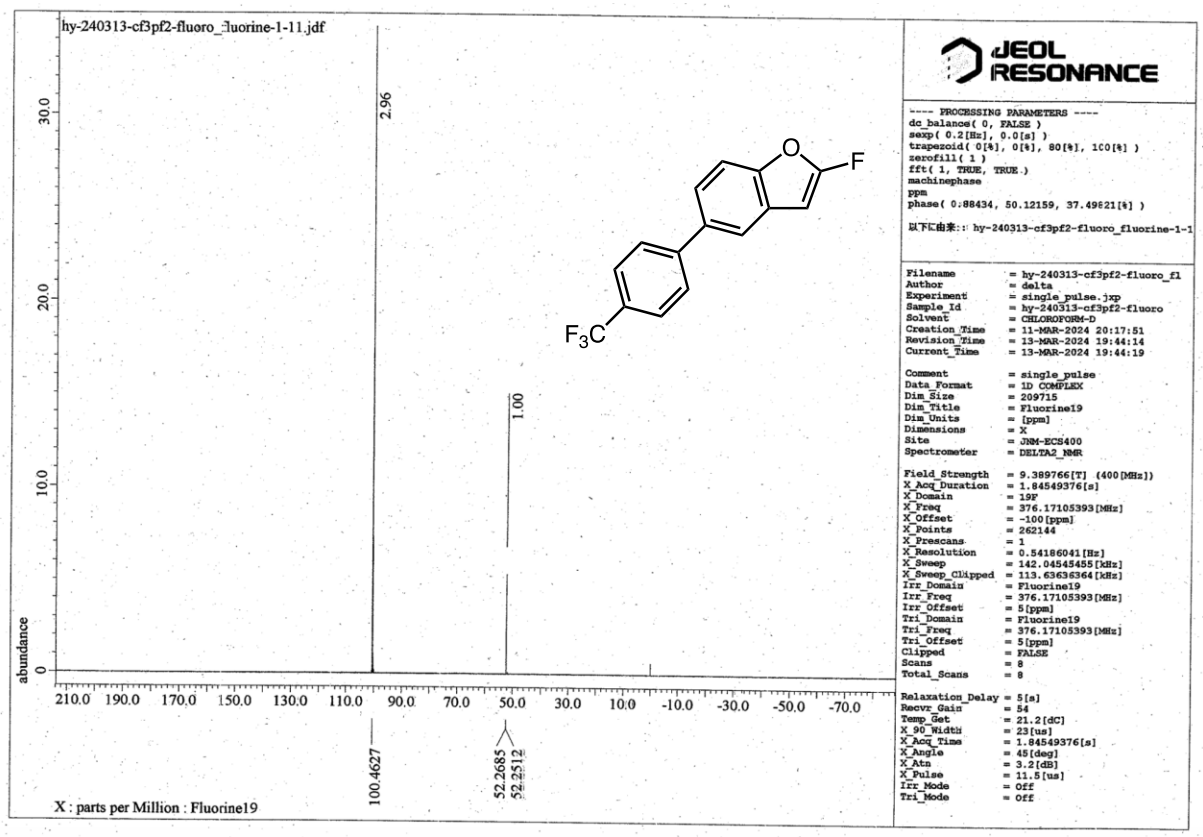



```
NAME          hy-240314-625-13c
EXPNO                 1
PROCNO                1
Date_          20240314
Time              19.59
INSTRUM           av500
PROBHD   5 mm PHQNP Swi
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                   72
DS                    8
SWH          30581.039 Hz
FIDRES        0.466630 Hz
AQ            1.0715799 sec
RG               18390.4
DW             16.350 usec
DE             20.00 usec
TE              296.3 K
D1          1.00000000 sec
D11         0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1               7.10 usec
PL1             -1.00 dB
SFO1       125.7718239 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2           80.00 usec
PL2             -2.00 dB
PL12            16.00 dB
PL13            16.00 dB
SFO2       500.1320005 MHz
SI                32768
SF         125.7577964 MHz
WDW                EM
SSB                   0
LB             1.00 Hz
GB                    0
PC                1.40
```

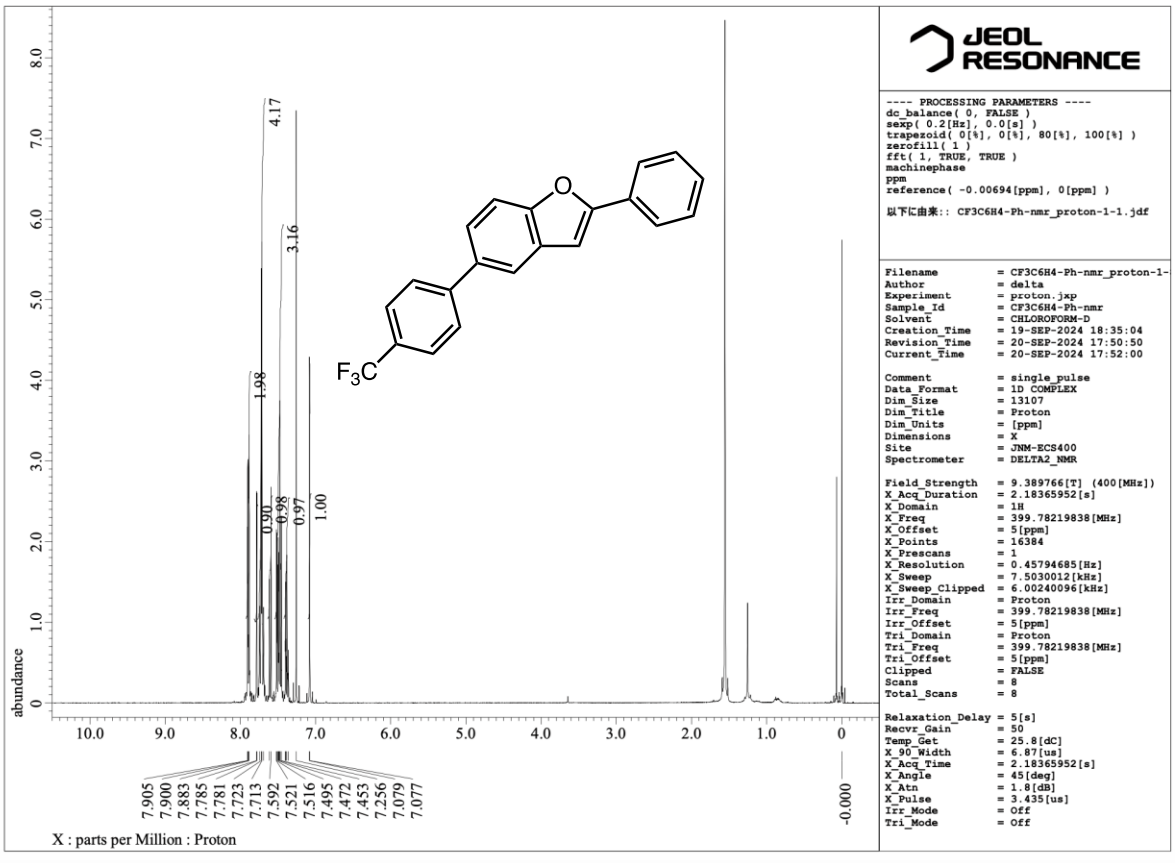
2-Fluoro-5-[4-(trifluoromethyl)phenyl]benzofuran (1f)

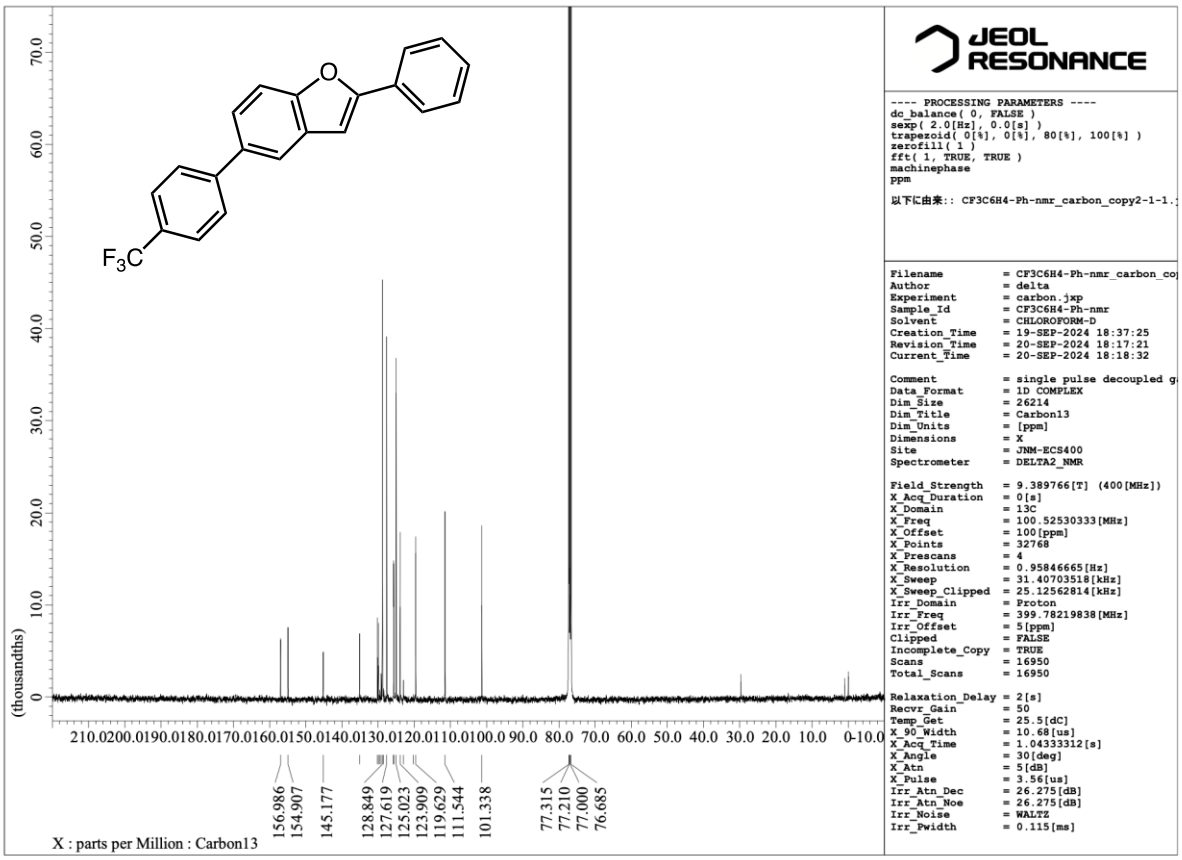


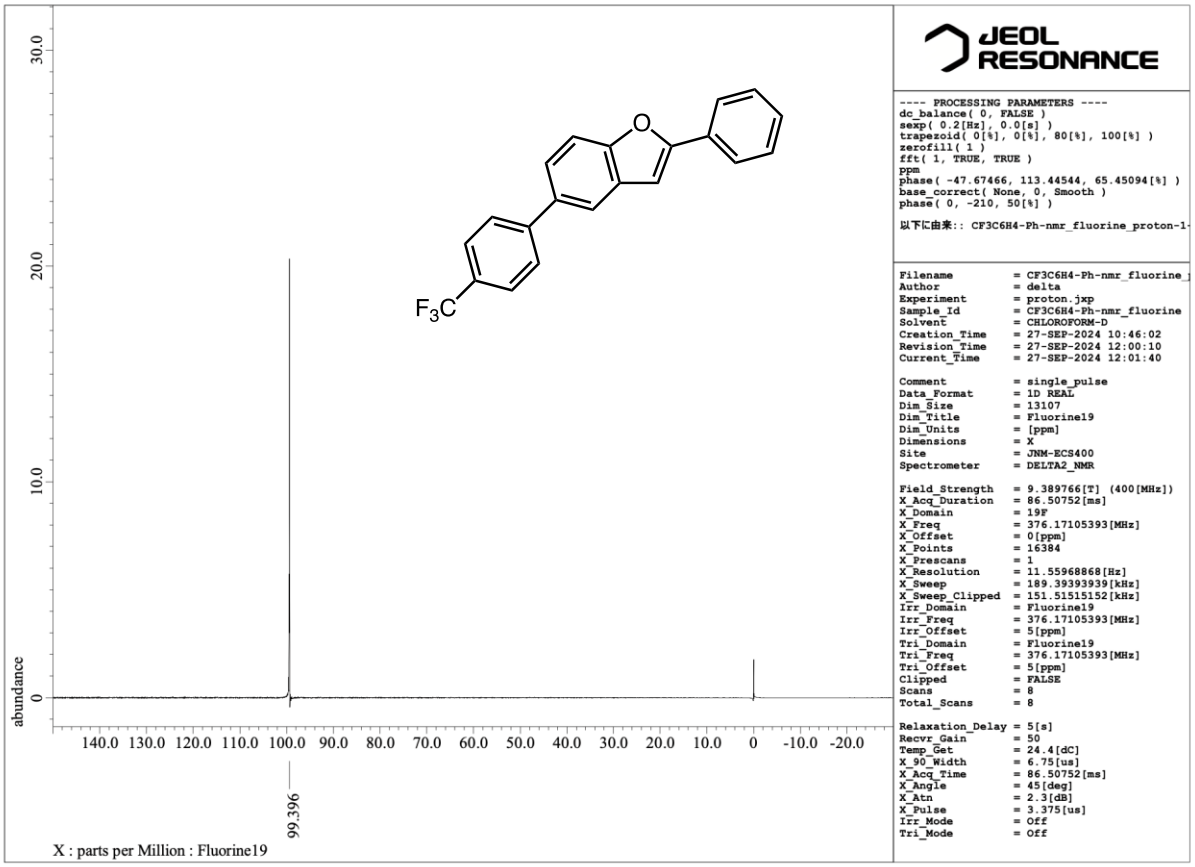



hy-240313-cf3pf2-fluoro_fluorine-1-11.jdf
2.96
1.00
100.4627
52.2685
52.2512
X : parts per Million : Fluorine19
JEOL RESONANCE
---- PROCESSING PARAMETERS ----
dc_balance(0, FALSE)
sexp(0.2[Hz], 0.0[s])
trapezoid(0[%], 0[%], 80[%], 100[%])
zerofill(1)
fft(1, TRUE, TRUE)
machinephase
ppm
phase(0.88434, 50.12159, 37.49621[%])
以下に由来:: hy-240313-cf3pf2-fluoro_fluorine-1-1
Filename = hy-240313-cf3pf2-fluoro_fl
Author = delta
Experiment = single_pulse.jxp
Sample_Id = hy-240313-cf3pf2-fluoro
Solvent = CHLOROFORM-D
Creation_Time = 11-MAR-2024 20:17:51
Revision_Time = 13-MAR-2024 19:44:14
Current_Time = 13-MAR-2024 19:44:19
Comment = single_pulse
Data_Format = 1D COMPLEX
Dim_Size = 209715
Dim_Title = Fluorine19
Dim_Units = [ppm]
Dimensions = X
Site = JNM-ECS400
Spectrometer = DELTA2_NMR
Field_Strength = 9.389766[T] (400[MHz])
X_Acq_Duration = 1.84549376[s]
X_Domain = 19F
X_Freq = 376.17105393[MHz]
X_Offset = -100[ppm]
X_Points = 262144
X_Prescans = 1
X_Resolution = 0.54186041[Hz]
X_Sweep = 142.04545455[kHz]
X_Sweep_Clipped = 113.63636364[kHz]
Irr_Domain = Fluorine19
Irr_Freq = 376.17105393[MHz]
Irr_Offset = 5[ppm]
Tri_Domain = Fluorine19
Tri_Freq = 376.17105393[MHz]
Tri_Offset = 5[ppm]
Clipped = FALSE
Scans = 8
Total_Scans = 8
Relaxation_Delay = 5[s]
Recvr_Gain = 54
Temp_Get = 21.2[dC]
X_90_Width = 23[us]
X_Acq_Time = 1.84549376[s]
X_Angle = 45[deg]
X_Atn = 3.2[dB]
X_Pulse = 11.5[us]
Irr_Mode = Off
Tri_Mode = Off

2-Phenyl-5-[4-(trifluoromethyl)phenyl]benzofuran (3fa)

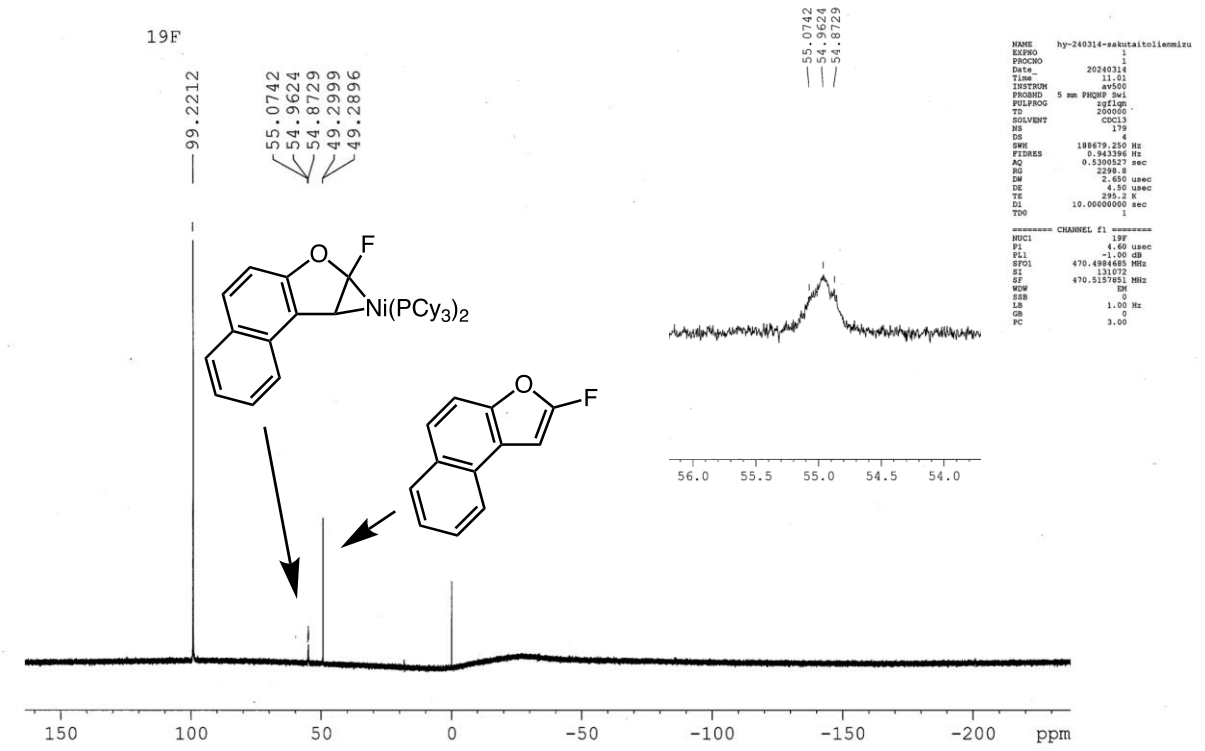




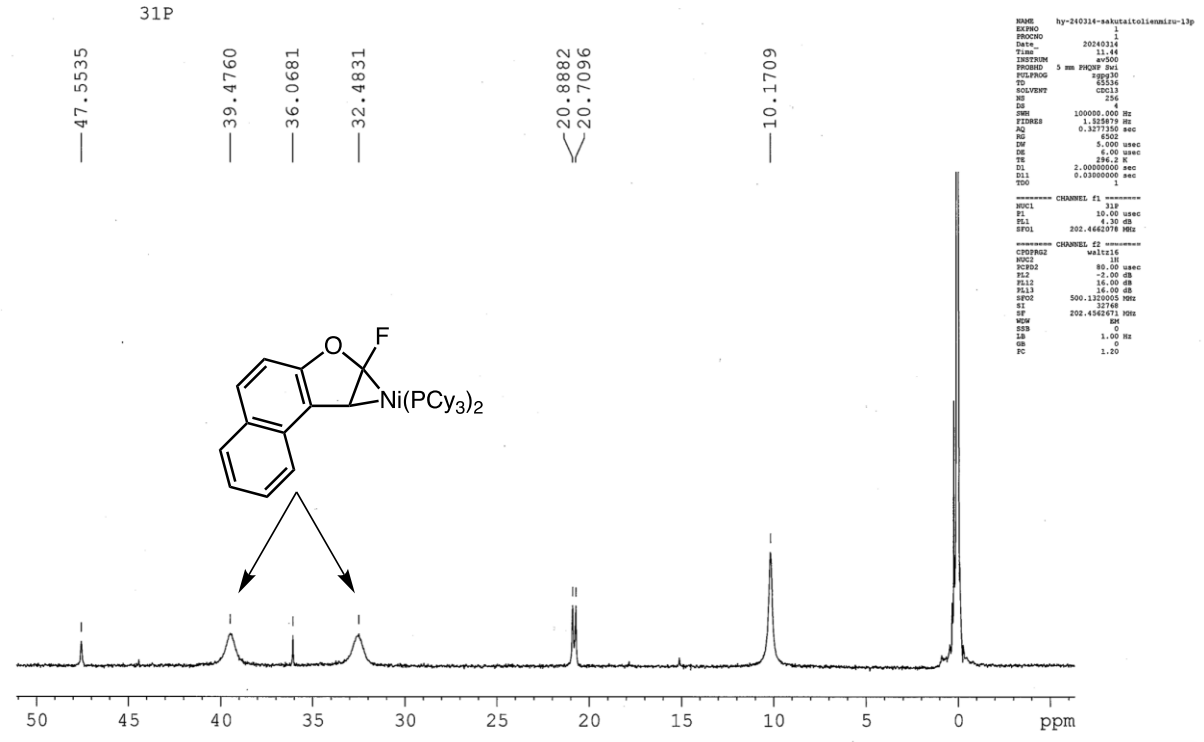

30.0
20.0
10.0
0
abundance
O
F3C
140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
99.396
X : parts per Million : Fluorine19
JEOL RESONANCE
---- PROCESSING PARAMETERS ----
dc_balance(0, FALSE)
sexp(0.2[Hz], 0.0[s])
trapezoid(0[%], 0[%], 80[%], 100[%])
zerofill(1)
fft(1, TRUE, TRUE)
ppm
phase(-47.67466, 113.44544, 65.45094[%])
base_correct(None, 0, Smooth)
phase(0, -210, 50[%])
以下に由来:: CF3C6H4-Ph-nmr_fluorine_proton-1-
Filename = CF3C6H4-Ph-nmr_fluorine_
Author = delta
Experiment = proton.jxp
Sample_Id = CF3C6H4-Ph-nmr_fluorine
Solvent = CHLOROFORM-D
Creation_Time = 27-SEP-2024 10:46:02
Revision_Time = 27-SEP-2024 12:00:10
Current_Time = 27-SEP-2024 12:01:40
Comment = single_pulse
Data_Format = 1D REAL
Dim_Size = 13107
Dim_Title = Fluorine19
Dim_Units = [ppm]
Dimensions = X
Site = JNM-ECS400
Spectrometer = DELTA2_NMR
Field_Strength = 9.389766[T] (400[MHz])
X_Acq_Duration = 86.50752[ms]
X_Domain = 19F
X_Freq = 376.17105393[MHz]
X_Offset = 0[ppm]
X_Points = 16384
X_Prescans = 1
X_Resolution = 11.55968868[Hz]
X_Sweep = 189.39393939[kHz]
X_Sweep_Clipped = 151.51515152[kHz]
Irr_Domain = Fluorine19
Irr_Freq = 376.17105393[MHz]
Irr_Offset = 5[ppm]
Tri_Domain = Fluorine19
Tri_Freq = 376.17105393[MHz]
Tri_Offset = 5[ppm]
Clipped = FALSE
Scans = 8
Total_Scans = 8
Relaxation_Delay = 5[s]
Recvr_Gain = 50
Temp_Get = 24.4[dC]
X_90_Width = 6.75[us]
X_Acq_Time = 86.50752[ms]
X_Angle = 45[deg]
X_Atn = 2.3[dB]
X_Pulse = 3.375[us]
Irr_Mode = Off
Tri_Mode = Off

8. NMR and HRMS charts of nickelacyclopropane E_b

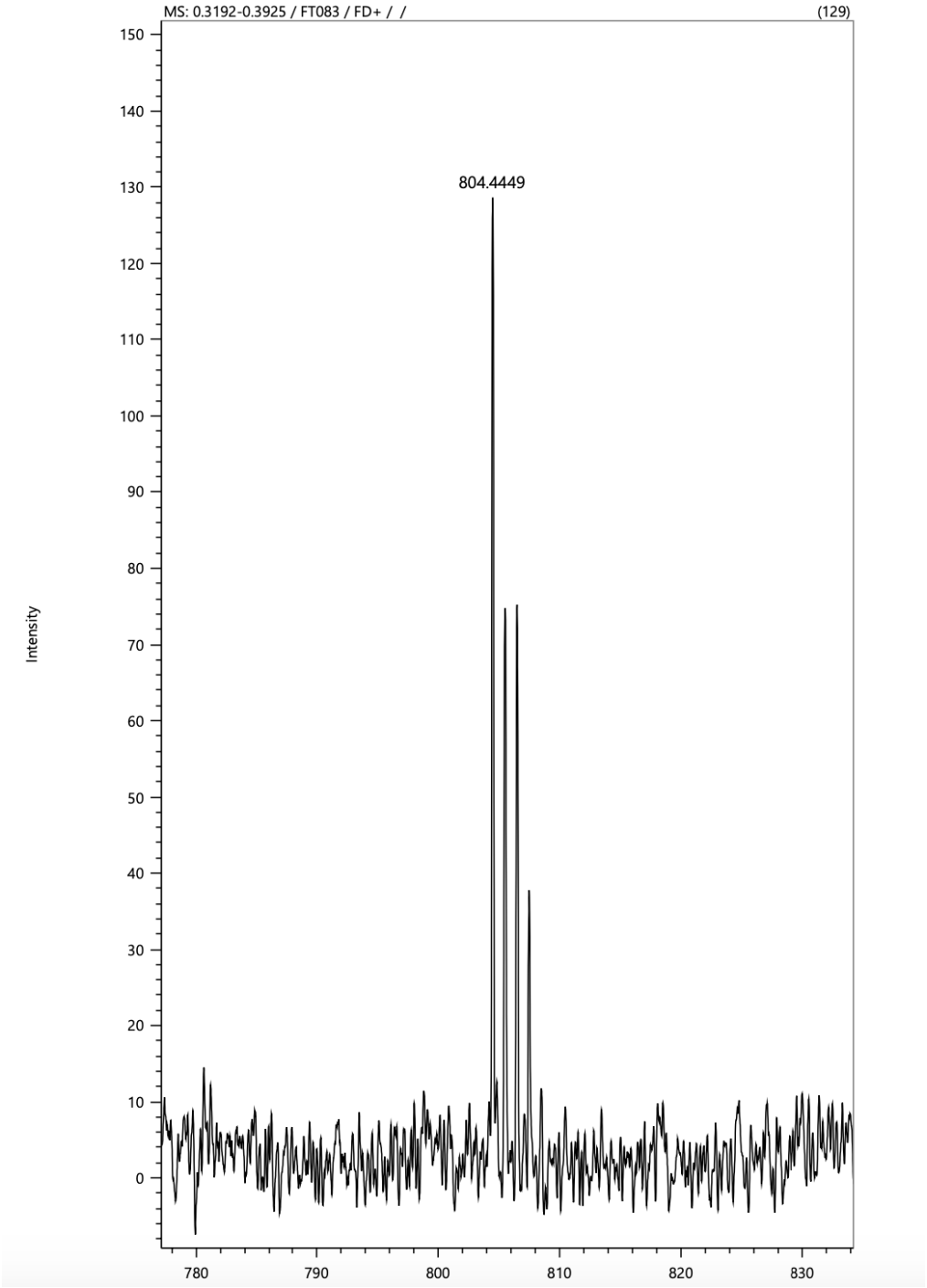
^{19}F NMR



^{31}P NMR



HRMS


MS: 0.3192-0.3925 / FT083 / FD+ / /
(129)
804.4449
Intensity
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
780
790
800
810
820
830