

Decarboxylative biaryl synthesis in a continuous flow reactor

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Experimental procedures and data

General Methods. Reactions were performed in a vapourtec R2+/R4 reactor employing a stainless steel reactor coil (10 mL). All reactions were monitored by GC using *n*-tetradecane as an internal standard. Response factors of the products with regard to *n*-tetradecane were obtained experimentally by analyzing known quantities of the substances. GC analyses were carried out using a Phenomenex ZB-5MS column and a time program beginning with 0.5 min at 50 °C followed by 45 °C/min ramp to 320 °C. Column chromatography was performed using a Combi Flash Companion-Chromatography-System (Isco-Systems) and RediSep packed columns (4 g and 12 g). NMR spectra were obtained on a Varian 400 MHz NMR system using MeOH-*d*₄ or CDCl₃, as solvent, with proton and carbon resonances at 400 MHz and 101 MHz, respectively. Mass spectral data were acquired on a Micromass GCT Mass Spectrometer. Melting points were determined with a Mettler FP61 melting point apparatus.

All compounds are commercially available and were used without further purification.

General procedure for the synthesis and characterization of tetraethyl ammonium carboxylate salts. A 100 mL, two-necked, round-bottomed flask was charged with the carboxylic acid (10.0 mmol) and methanol (20.0 mL). To this, an aqueous solution of tetraethylammonium hydroxide (35% in H₂O, 4.11 mL, 10.0 mmol) was added dropwise. After complete addition, the reaction mixture was stirred for another 1 h at room temperature. The volatiles were removed in vacuo using a water bath temperature of 60 °C. The resulting solid was triturated with *tert*-butylmethyl ether (25 mL) and ethyl acetate (25 mL) and dried at 10 mbar to provide the corresponding tetraethyl ammonium carboxylate salts 78-99% yield.

Tetraethyl ammonium 2-nitrobenzoate (5a). Compound **5a** was prepared from 2-nitrobenzoic acid (1.76 g, 10.0 mmol) yielding **5a** as a white solid (3.00 g, 95%). ¹H NMR (400 MHz, METHANOL-*d*₄) δ = 1.25 (tt, *J*=7.18, 1.61 Hz, 12 H), 3.26 (q, *J*=7.29 Hz, 8 H), 7.43 - 7.51 (m, 1 H), 7.55 - 7.68 (m, 2 H), 7.86 (d, *J*=8.20 Hz, 1 H) ppm. ¹³C NMR (101 MHz, METHANOL-*d*₄) δ = 7.73, 53.34, 124.52, 129.67, 129.81, 134.28, 138.66, 148.32, 173.31 ppm.

Tetraethyl ammonium benzothiophene-2-carboxylate (5b). Compound **5b** was prepared from benzothiophene-2-carboxylic acid (1.78 g, 10.00 mmol) yielding **5b** as an off-white solid (3.39 g, 99%). ¹H NMR (400 MHz, METHANOL-*d*₄) δ = 1.18 (tt, *J*=7.27, 1.90 Hz, 12 H), 3.16 (q, *J*=7.22 Hz, 8 H), 7.32 - 7.39 (m, 2 H), 7.79 (s, 1 H), 7.83 (td, *J*=3.47, 2.44 Hz, 2 H) ppm. ¹³C NMR (101 MHz, METHANOL-*d*₄) δ = 7.65, 53.31, 123.64, 125.51, 125.84, 126.64, 127.23, 141.34, 142.90, 145.58, 169.75 ppm.

Tetraethyl ammonium 4,5-dimethoxy-2-nitrobenzoate (5e). Compound **5e** was prepared from 4,5-dimethoxy-2-nitrobenzoic acid (2.27 g, 10.0 mmol) yielding **5e** as a yellow solid (3.05 g, 86%). ¹H NMR (400 MHz, METHANOL-*d*₄) δ = 1.34 (tt, *J*=7.30, 1.78 Hz, 12 H), 3.30 - 3.39 (m, 8 H), 3.95 (s, 3 H), 3.99 (s, 3 H), 7.08 (s, 1 H), 7.59 (s, 1 H) ppm. ¹³C NMR (101 MHz, METHANOL-*d*₄) δ = 7.72, 53.41, 56.99, 57.01, 108.10, 111.29, 126.46, 129.37, 130.08, 133.76, 139.92, 149.53, 154.82, 173.98 ppm.

Tetraethyl ammonium 2-methylsulphonylbenzoate (5g). Compound **5g** was prepared from 2-methylsulphonylbenzoic acid (1.00 g, 5.00 mmol) yielding **5g** as an off-white solid (1.29 g, 78%). ¹H NMR (400 MHz, METHANOL-*d*₄) δ = 1.32 (tt, *J*=7.27, 1.90 Hz, 12 H), 3.29 - 3.38 (m, 8 H), 3.43 (s, 3 H), 7.52 - 7.58 (m, 1 H), 7.62 (dd, *J*=7.61, 1.37 Hz, 1 H), 7.70 (td, *J*=7.47, 1.27 Hz, 1 H) 8.00 (dd, *J*=7.91, 0.88 Hz, 1 H) ppm. ¹³C NMR (101 MHz, METHANOL-*d*₄) δ = 7.73, 45.10, 53.40, 128.96, 129.57, 129.65, 134.78, 137.73, 144.48, 175.14 ppm.

Tetraethyl ammonium 2,4-dimethylthiazole-5-carboxylate (5h). Compound **5h** was prepared from 2,4-dimethylthiazole-5-carboxylic acid (1.57 g, 10.00 mmol) yielding **5h** as an off-white solid (2.32 g, 81%). ¹H NMR (400 MHz, METHANOL-*d*₄) δ = 1.32 (tt, *J*=7.27, 1.90 Hz, 12 H), 2.62 (s, 3 H), 2.63 (s, 3 H), 3.20 - 3.42 (m, 8 H) ppm. ¹³C NMR (101 MHz, METHANOL-*d*₄) δ = 7.73, 16.65, 18.85, 53.41, 133.29, 154.25, 167.61, 169.13 ppm.

Tetraethyl ammonium benzofuran-2-carboxylate (5i). Compound **5i** was prepared from benzofuran-2-carboxylic acid (1.62 g, 10.00 mmol) yielding **5i** as an off-white solid (3.29 g, 99%). ¹H

NMR (400 MHz, METHANOL-*d*4) δ = 1.19 (tt, $J=7.30$, 1.88 Hz, 12 H), 3.17 (q, $J=7.29$ Hz, 8 H) 7.20 - 7.29 (m, 2 H), 7.32 - 7.39 (m, 1 H), 7.53 (dd, $J=8.30$, 0.68 Hz, 1 H), 7.64 (d, $J=7.81$ Hz, 1 H) ppm. ^{13}C NMR (101 MHz, METHANOL-*d*4) δ = 7.65, 53.31, 110.20, 112.78, 123.34, 124.29, 127.02, 129.60, 154.15, 156.30, 166.73 ppm.

Tetraethyl ammonium 5-methoxy-2-nitrobenzoate (5k). Compound **5k** was prepared from 5-methoxy-2-nitrobenzoic acid (1.97 g, 10.0 mmol) yielding **5k** as a yellow solid (3.11 g, 95%). ^1H NMR (400 MHz, METHANOL-*d*4) δ = 1.31 (tt, $J=7.27$, 1.81 Hz, 12 H), 3.32 (q, $J=7.35$ Hz, 8 H), 3.93 (s, 3 H), 6.94 - 7.06 (m, 2 H), 8.02 (d, $J=9.76$ Hz, 1 H) ppm. ^{13}C NMR (101 MHz, METHANOL-*d*4) δ = 7.74, 53.40, 56.76, 113.97, 114.10, 127.36, 140.20, 142.17, 165.21, 173.70 ppm.

Tetraethyl ammonium 4-methylbenzoylformate (5n). Compound **5n** was prepared from 4-methylbenzoylformic acid (1.64 g, 10.00 mmol) yielding **5n** as a pale yellow solid (2.51 g, 86%). ^1H NMR (400 MHz, METHANOL-*d*4) δ = 1.30 (tt, $J=7.27$, 1.90 Hz, 12 H), 2.46 (s, 3 H), 3.30 (q, $J=7.35$ Hz, 8 H), 7.34 - 7.42 (m, 2 H), 7.89 - 7.97 (m, 2 H) ppm. ^{13}C NMR (101 MHz, METHANOL-*d*4) δ = 7.72, 21.88, 53.36, 130.52, 130.82, 132.70, 146.09, 173.90, 197.01 ppm.

General procedure for decarboxylative cross-coupling reactions in a flow reactor (Table 2). The carboxylic acid (0.48 mmol) and potassium *tert*-butoxide (0.48 mmol, 56.1 mg) or the tetraethylammonium carboxylate (0.48 mmol), $\text{CuNO}_3(\text{phen})(\text{PPh}_3)_2$ (0.02 mmol, 18.7 mg) and palladium acetate (0.008 mmol, 1.8 mg) are weighed in a screw-cap vial directly prior to the experiment (*in the presence of KO^tBu the mixture of solids changes colour upon standing*). A solution of triflate (0.40 mmol) in 2 mL of anhydrous NMP is added and the resulting suspension sonicated until complete dissolution of all material is observed. This mixture is subjected to a 2 mL sample loop on the vapourtec R2+ unit via syringe preceded by a small (1 cm) air bubble to avoid dispersion. A single flow channel was used to deliver either the system solvent or the reaction mixture via a selection valve directly to the reactor. At a reactor temperature of 170 °C, the sample loop is emptied at a flow-rate of 0.167 mL/min (60 min residence time) using fresh, commercial (Aldrich), anhydrous NMP from the solvent reservoir

(it is not recommended to use commercial NMP that has been open to air for an extended period of time, as it is hygroscopic and high amounts of water will lead to increased protodecarboxylation and a decrease in yield). After 60 min the collection of reactor output is started for approximately 30 min (5 mL dark brown solution).

Work-up: The solution is collected into a beaker containing 50 mL 2 N HCl and 50 mL dichloromethane. While collecting the two phases are stirred vigorously. After collection is complete the mixture is stirred for further 30 min. After the phases have separated, the bottom organic layer is pumped at a flow-rate of 2 mL/min through an Omnifit column filled with 1 g of Arbocel and 10 g of silica gel. After all the material has been passed through the column, pure dichloromethane is pumped through the purification unit until TLC indicates that all material has been washed off. This solution is transferred into a 250 mL separating funnel and washed with aqueous bicarbonate solution (25 mL) and brine (25 mL), dried over magnesium sulfate, filtered and the volatiles evaporated *in vacuo*. The residue is purified by column chromatography (heptane:ethyl acetate / 4:1) to afford the products.

Synthesis of 4'-methyl-2-nitrobiphenyl under continuous flow conditions. A solution of tetraethylammonium 2-nitrobenzoate (12.0 mmol, 3.56 g), 4-tolyl triflate (10.0 mmol, 2.40 g), CuNO₃(phen)(PPh₃)₂ (0.5 mmol, 468 mg) and palladium acetate (0.2 mmol, 45.0 mg) in anhydrous NMP (50 mL) is aspirated through a single flow channel and pumped through the reactor coil at 170 °C for 6 h. The collected reaction mixture is transferred to a separating funnel and diluted with 250 mL ethyl acetate, extracted twice with 2 N HCl (250 mL), aqueous bicarbonate solution (250 mL) and brine (100 mL). The organic layer is dried (MgSO₄), filtered and the volatiles evaporated *in vacuo*. The residue is purified by column chromatography (heptane:ethyl acetate / 4:1) to afford 4'-methyl-2-nitrobiphenyl as a yellow oil (1.20 g, 56%).

Synthesis of 4'-methyl-2-nitrobiphenyl (3aa). Compound **3aa** was prepared either from 2-nitrobenzoic acid (0.48 mmol, 84.4 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) or tetraethyl ammonium 2-nitrobenzoate (0.48 mmol, 151 mg) and 4-methylphenyl triflate (0.40mmol, 99.1 mg)

yielding **3aa** as a yellow oil (60.5 mg, 71%). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 4'-methyl-2-nitrobiphenyl [CAS: 70680-21-6].

Synthesis of 2-(4'-methylphenyl)-benzothiophene (3ba). Compound **3ba** was prepared from tetraethyl ammonium benzothiophene-2-carboxylate (0.48 mmol, 148 mg) and 4-methylphenyl triflate (0.40 mmol, 99.1 mg) yielding **3ba** as a white solid (62.8 mg, 70%, m.p. 169-170 °C). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 2-(4'-methylphenyl)-benzothiophene [CAS: 25664-47-5].

Synthesis of 4'-methyl-5-fluoro-2-nitrobiphenyl (3ca). Compound **3ca** was prepared from 5-fluoro-2-nitrobenzoic acid (0.48 mmol, 88.9 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) and 4-methylphenyl triflate (0.40mmol, 99.1 mg) yielding **3ca** as a yellow solid (43.2 mg, 46%, m.p. 59-61 °C). This compound is unknown.

¹H NMR (400 MHz, *CHLOROFORM-D*) δ ppm 7.94 (dd, *J*=8.9, 5.1 Hz, 1 H) 7.22 - 7.31 (m, 4 H) 7.14 - 7.21 (m, 2 H) 2.45 (s, 3 H). ¹³C NMR (101 MHz, *CHLOROFORM-D*) δ ppm 163.8 (d, *J*=255.2 Hz), 145.3, 139.5 (d, *J*=9.25 Hz), 138.7, 133.5, 129.5, 127.5, 126.8 (d, *J*=10.2 Hz), 118.7, 114.8 (d, *J*=23.1 Hz), 21.2. Anal. Calcd. for C₁₃H₁₀FNO₂: C, 67.5; H, 4.4; N, 6.1. Found: C, 67.1; H, 4.3; N, 6.2. MS (TOF CI⁺): *m/z* = 249 ([M-NH₄⁺]).

Synthesis of 4',5-dimethyl-2-nitrobiphenyl (3da). Compound **3da** was prepared from 5-methyl-2-nitrobenzoic acid (0.48 mmol, 87.0 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) and 4-methylphenyl triflate (0.40mmol, 99.1 mg) yielding **3da** as a yellow oil (65.5 mg, 72%). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 4',5-dimethyl-2-nitrobiphenyl [CAS: 70689-98-4].

Synthesis of 4'-methyl-4,5-dimethoxy-2-nitrobiphenyl (3ea). Compound **3ea** was prepared from tetraethyl ammonium 4,5-dimethoxy-2-nitrobenzoate (0.48 mmol, 171 mg) and 4-methylphenyl triflate (0.40mmol, 99.1 mg) yielding **3ea** as a yellow solid (71.1 mg, 65%, m.p. 107-109 °C). This compound is unknown.

^1H NMR (400 MHz, *CHLOROFORM-D*) δ ppm 7.52 (s, 1 H) 7.16 - 7.24 (m, 4 H) 6.77 (s, 1 H) 3.97 (s, 3 H) 3.94 (s, 3 H) 2.40 (s, 3 H). ^{13}C NMR (101 MHz, *CHLOROFORM-D*) δ ppm 152.1, 147.8, 141.1, 137.7, 135.3, 131.3, 129.2, 127.8, 113.6, 107.7, 56.4, 56.4, 21.2. Anal. Calcd. for $\text{C}_{15}\text{H}_{15}\text{NO}_4$: C, 65.9; H, 5.5; N, 5.1. Found: C, 66.2; H, 5.7; N, 5.2. MS (TOF CI^+): $m/z = 291$ ($[\text{M}-\text{NH}_4^+]$), 274 ($[\text{M}-\text{H}^+]$).

Synthesis of 4'-methyl-2,3,4,5,6-pentafluorobiphenyl (3fa). Compound **3fa** was prepared from pentafluorobenzoic acid (0.48 mmol, 102 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) and 4-methylphenyl triflate (0.40 mmol, 99.1 mg) yielding **3fa** as a white solid (43.4 mg, 42%, m.p. 117-118 °C). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 4'-methyl-2,3,4,5,6-pentafluorobiphenyl [CAS: 14621-04-6].

Synthesis of 4'-methyl-2-methylsulphonylbiphenyl (3ga). Compound **3ga** was prepared either from 2-methylsulphonylbenzoic acid (0.48 mmol, 96.1 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) or tetraethyl ammonium 2-methylsulphonylbenzoate (0.48 mmol, 158 mg) and 4-methylphenyl triflate (0.40 mmol, 99.1 mg) yielding **3ga** as a white solid (36.5 mg, 37% or 39.4 mg, 40%, m.p. 128-130 °C). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 4'-methyl-2-methylsulphonylbiphenyl [CAS: 632339-04-9].

Synthesis of 5-(4'-methylphenyl)-2,4-dimethyl-1,3-thiazole (3ha). Compound **3ha** was prepared either from 2,4-dimethylthiazole-5-carboxylic acid (0.48 mmol, 75.5 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) or tetraethyl ammonium 2,4-dimethylthiazole-5-carboxylate (0.48 mmol, 138 mg) and 4-methylphenyl triflate (0.40 mmol, 99.1 mg) yielding **3ha** as a colorless oil (43.1 mg, 53% or 48.8 mg, 60%). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 5-(4'-methylphenyl)-2,4-dimethyl-1,3-thiazole [CAS: 1227469-89-7].

Synthesis of 2-(4'-methylphenyl)-benzofuran (3ia). Compound **3ia** was prepared from tetraethyl ammonium benzofuran-2-carboxylate (0.48 mmol, 140 mg) and 4-methylphenyl triflate (0.40 mmol, 99.1 mg) yielding **3ia** as a white solid (50.0 mg, 60%, m.p. 125-126 °C). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 2-(4'-methylphenyl)-benzofuran [CAS: 25664-48-6].

Synthesis of 2-(4'-methylphenyl)-3-methyl-benzofuran (3ja). Compound **3ja** was prepared from 3-methylbenzofuran-2-carboxylic acid (0.48 mmol, 84.6 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) and 4-methylphenyl triflate (0.40 mmol, 99.1 mg) yielding **3ja** as a white solid (59.6 mg, 67%, m.p. 60-62 °C). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 2-(4'-methylphenyl)-3-methyl-benzofuran [CAS: 204908-14-5].

Synthesis of 4'-methyl-5-methoxy-2-nitrobiphenyl (3ka). Compound **3ka** was prepared either from 5-methoxy-2-nitrobenzoic acid (0.48 mmol, 94.6 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) or tetraethyl ammonium 5-methoxy-2-nitrobenzoate (0.48 mmol, 157 mg) and 4-methylphenyl triflate (0.40 mmol, 99.1 mg) yielding **3ka** as a yellow oil (69.0 mg, 71% or 70.1 mg, 72%). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 4'-methyl-5-methoxy-2-nitrobiphenyl [CAS: 1071850-24-2].

Synthesis of 2-(4'-methylphenyl)-3-methyl-benzothiophene (3la). Compound **3la** was prepared from 3-methylbenzothiophene-2-carboxylic acid (0.48 mmol, 92.3 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) and 4-methylphenyl triflate (0.40 mmol, 99.1 mg) yielding **3la** as a white solid (78.2 mg, 82%, m.p. 81-82 °C). This compound is unknown.

¹H NMR (400 MHz, *CHLOROFORM-D*) δ ppm 7.83 (d, *J*=7.8 Hz, 1 H) 7.72 (d, *J*=8.2 Hz, 1 H) 7.45 (t, *J*=7.4 Hz, 2 H) 7.40 (d, *J*=7.0 Hz, 1 H) 7.34 (t, *J*=7.0 Hz, 1 H) 7.28 (d, *J*=7.8 Hz, 2 H) 2.47 (s, 3 H) 2.43 (s, 3 H). ¹³C NMR (101 MHz, *CHLOROFORM-D*) δ ppm 141.3 (s) 138.8 (s) 138.1 (s) 137.7 (s) 131.8 (s) 129.5 (s) 129.2 (s) 127.0 (s) 124.1 (s) 124.1 (s) 122.1 (s) 122.0 (s) 21.3 (s) 12.6 (s). Anal. Calcd. for C₁₆H₁₄S: C, 80.6; H, 5.9; S, 13.5. Found: C, 80.9; H, 5.8; N, 13.2. MS (TOF CI⁺): *m/z* = 239 ([M-H⁺]).

Synthesis of 2-nitrobiphenyl (3ab). Compound **3ab** was prepared from 2-nitrobenzoic acid (84.4 mg, 0.48 mmol), potassium tert-butoxide (56.1 mg, 0.48 mmol) and phenyl trifluoromethanesulfonate (90.5 mg, 0.40 mmol) yielding **3ab** as a yellow oil (49.4 mg, 62%). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 2-nitrobiphenyl [CAS: 86-00-0].

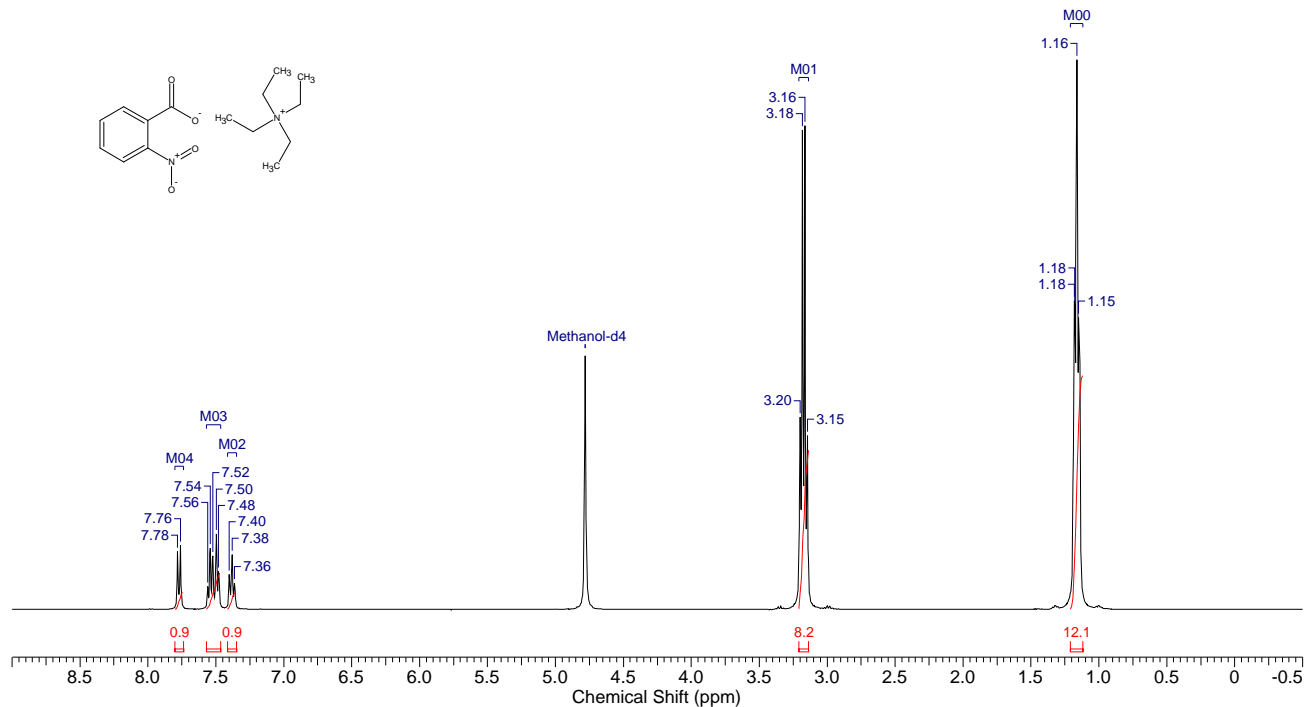
Synthesis of 2-(2-nitrophenyl)naphthalene (3ac). Compound **3ac** was prepared from 2-nitrobenzoic acid (84.4 mg, 0.48 mmol), potassium tert-butoxide (56.1 mg, 0.48 mmol) and 2-naphthyl trifluoromethanesulfonate (111 mg, 0.40 mmol) yielding **3ac** as a yellow solid (72.8 mg, 73%, m.p. 98-100 °C). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 2-(2-nitrophenyl)naphthalene [CAS: 94064-83-2].

Synthesis of 4-acyl-2'-nitrobiphenyl (3ad). Compound **3ad** was prepared from 2-nitrobenzoic acid (0.48 mmol, 84.4 mg), potassium tert-butoxide (0.48 mmol, 56.1 mg) and 4-acylphenyl trifluoromethanesulfonate (0.40 mmol, 107 mg) yielding **3ad** as a yellow solid (52.1 mg, 54%, m.p. 100-102 °C). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 4-acyl-2'-nitrobiphenyl [CAS: 5730-96-1].

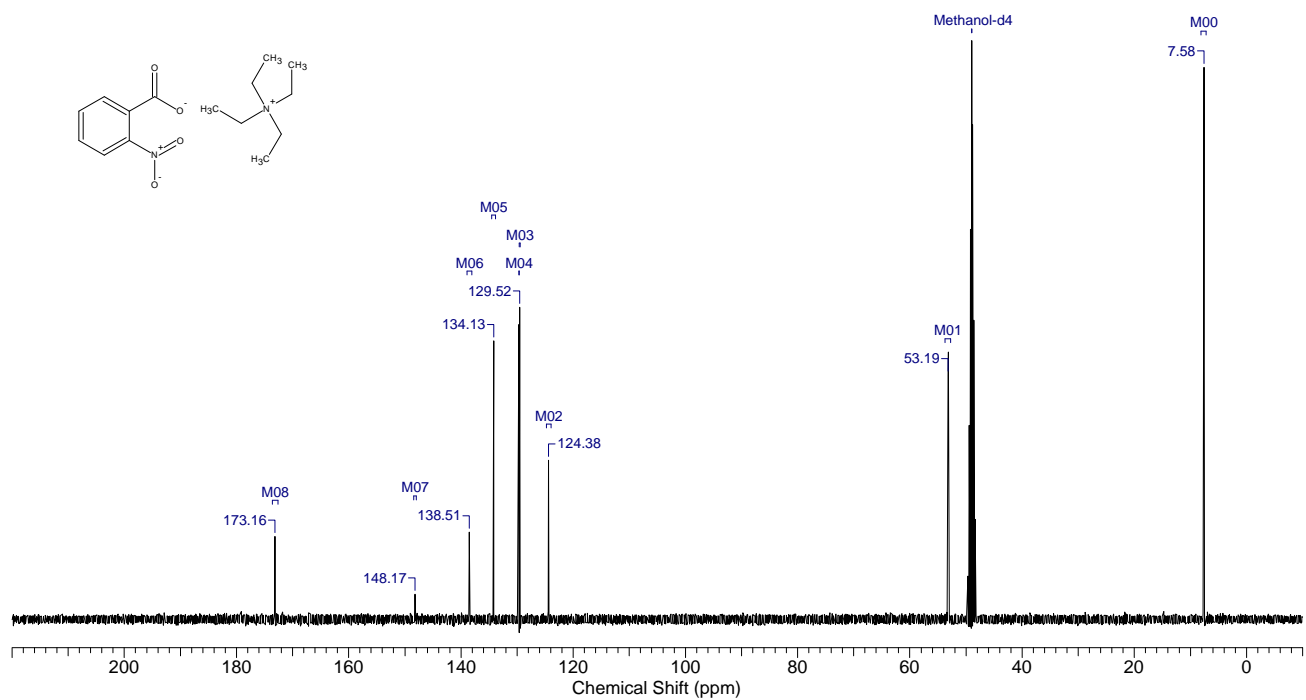
Synthesis of 4,4'-dimethylbenzophenone (3na). Compound **3na** was prepared from tetraethyl ammonium 4-methylbenzoylformate (0.48 mmol, 141 mg) and 4-methylphenyl trifluoromethanesulfonate (0.40 mmol, 99.1 mg) yielding **3na** as a light yellow solid (12.6 mg, 15%, m.p. 67-68 °C). The spectroscopic data (NMR, GC-MS) matched those reported in the literature for 4,4'-dimethylbenzophenone [CAS: 611-97-2].

tetraethyl ammonium 2-nitrobenzoate (**4a**)

$^1\text{H NMR}$ (400 MHz, $\text{METHANOL-}D_4$) δ ppm 7.77 (d, $J=8.2$ Hz, 1 H) 7.47 - 7.57 (m, 2 H) 7.38 (t, $J=7.6$ Hz, 1 H) 3.17 (q, $J=7.3$ Hz, 8 H) 1.12 - 1.21 (m, 12 H)

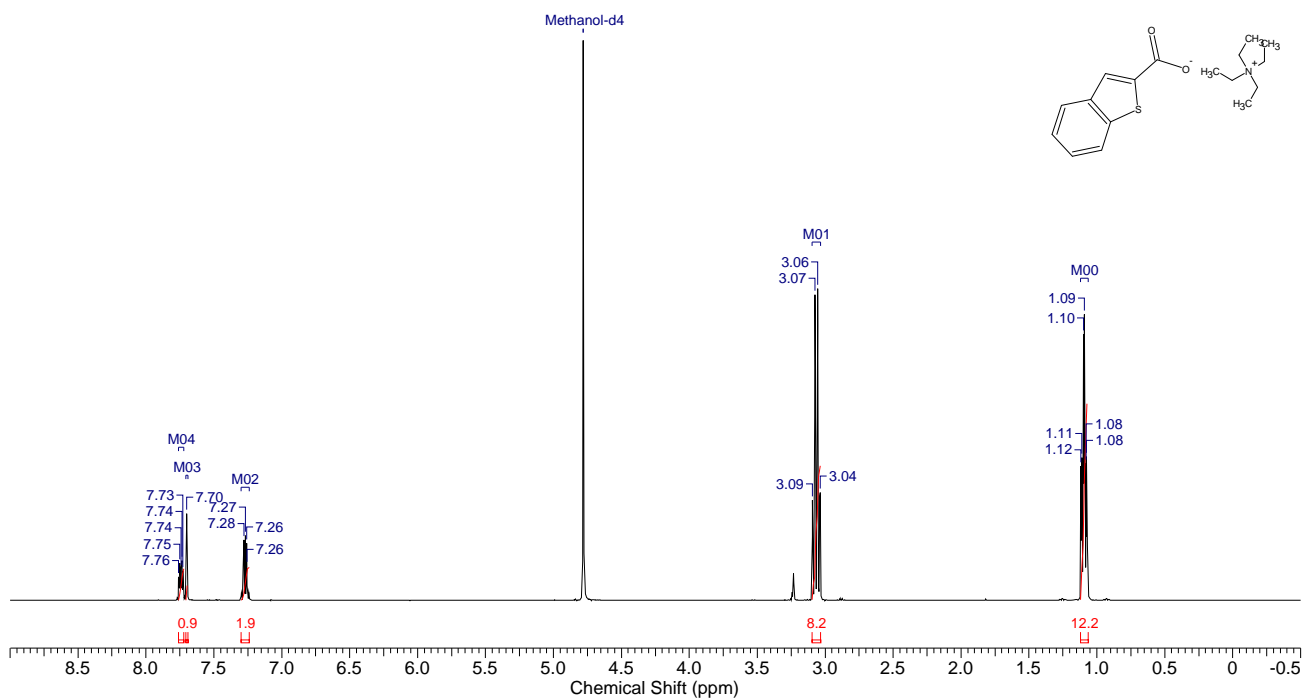


$^{13}\text{C NMR}$ (101 MHz, $\text{METHANOL-}D_4$) δ ppm 173.2 (s) 148.2 (s) 138.5 (s) 134.1 (s) 129.7 (s) 129.5 (s) 124.4 (s) 53.3 (s) 53.2 (s) 53.2 (s) 7.6 (s)

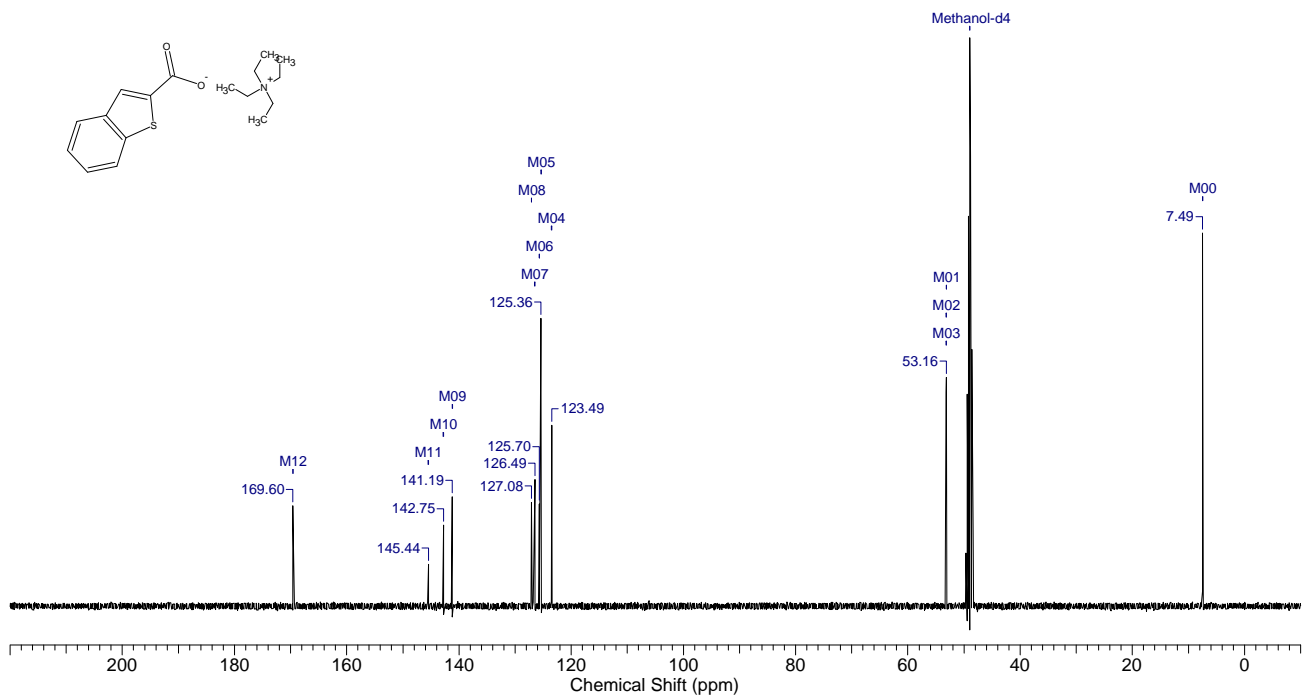


tetraethyl ammonium benzo[*b*]thiophene-2-carboxylate (4b)

¹H NMR (400 MHz, METHANOL-D₄) δ ppm 7.72 - 7.76 (m, 2 H) 7.70 (s, 1 H) 7.24 - 7.30 (m, 2 H) 3.07 (q, *J*=7.2 Hz, 8 H) 1.09 (tt, *J*=7.3, 1.9 Hz, 12 H)

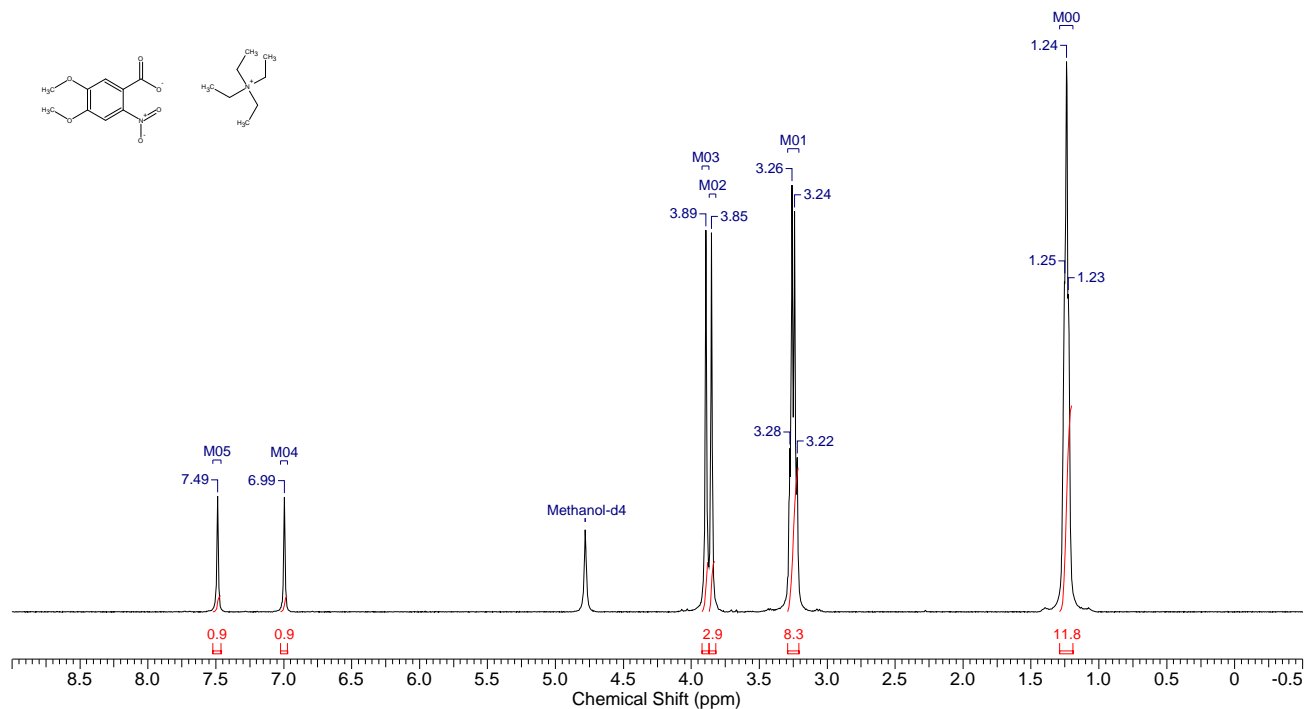


¹³C NMR (101 MHz, METHANOL-D₄) δ ppm 169.6 (s) 145.4 (s) 142.8 (s) 141.2 (s) 127.1 (s) 126.5 (s) 125.7 (s) 125.4 (s) 123.5 (s) 53.2 (s) 53.2 (s) 53.1 (s) 7.5 (s)

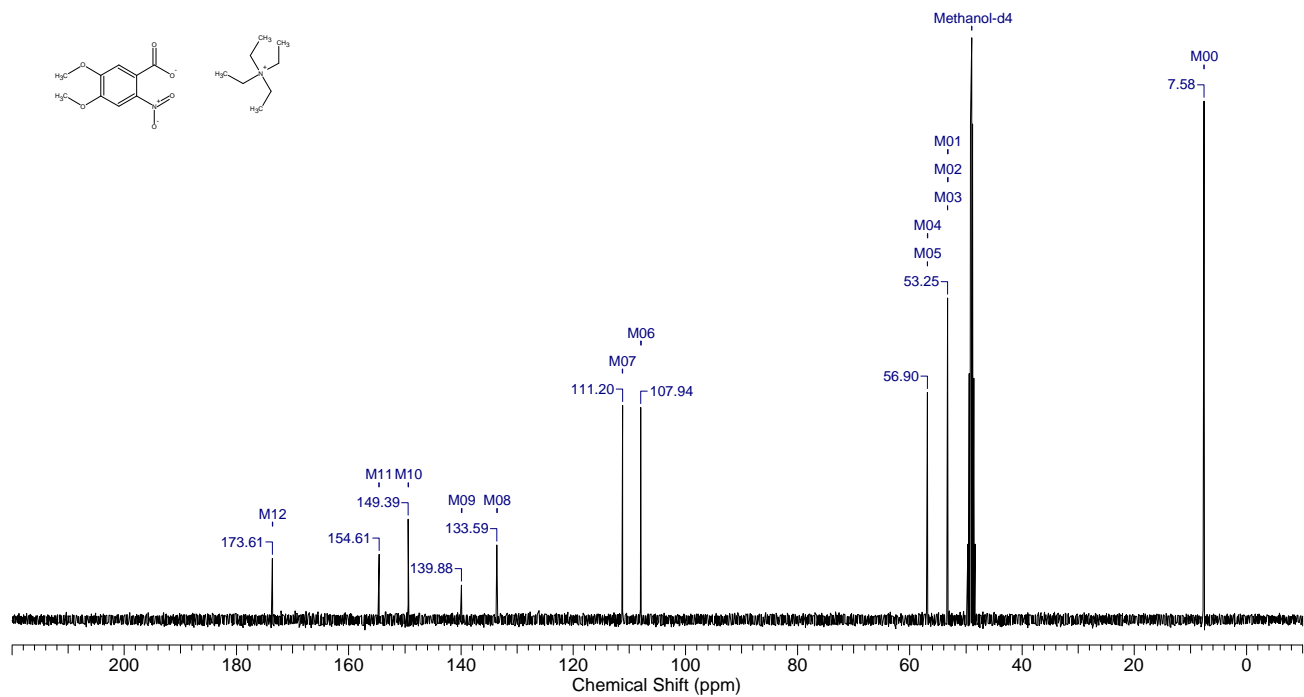


tetraethyl ammonium 4,5-dimethoxy-2-nitrobenzoate (4e)

$^1\text{H NMR}$ (400 MHz, *METHANOL-D4*) δ ppm 7.49 (s, 1 H) 6.99 (s, 1 H) 3.89 (s, 3 H) 3.85 (s, 3 H) 3.25 (q, $J=7.2$ Hz, 8 H) 1.24 (t, $J=5.5$ Hz, 12 H)

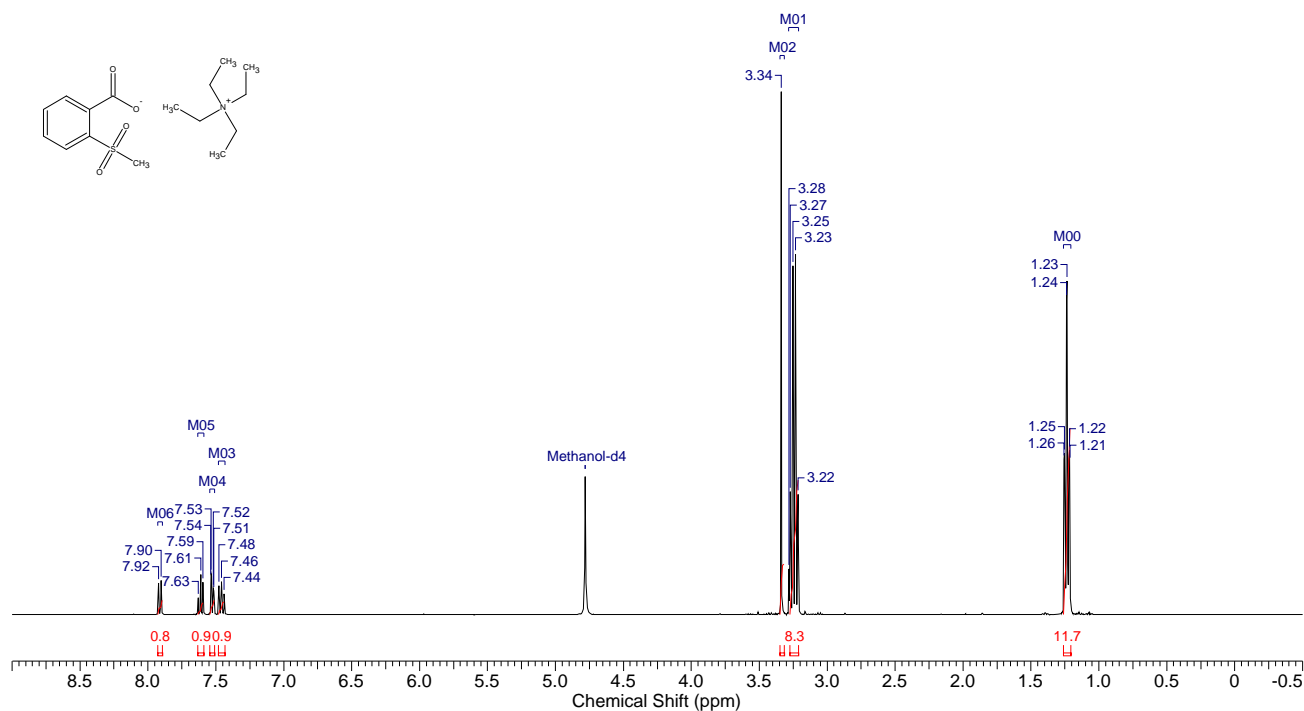


$^{13}\text{C NMR}$ (101 MHz, *METHANOL-D4*) δ ppm 173.6 (s) 154.6 (s) 149.4 (s) 139.9 (s) 133.6 (s) 111.2 (s) 107.9 (s) 56.9 (s) 56.9 (s) 53.3 (s) 53.2 (s) 53.2 (s) 7.6 (s)

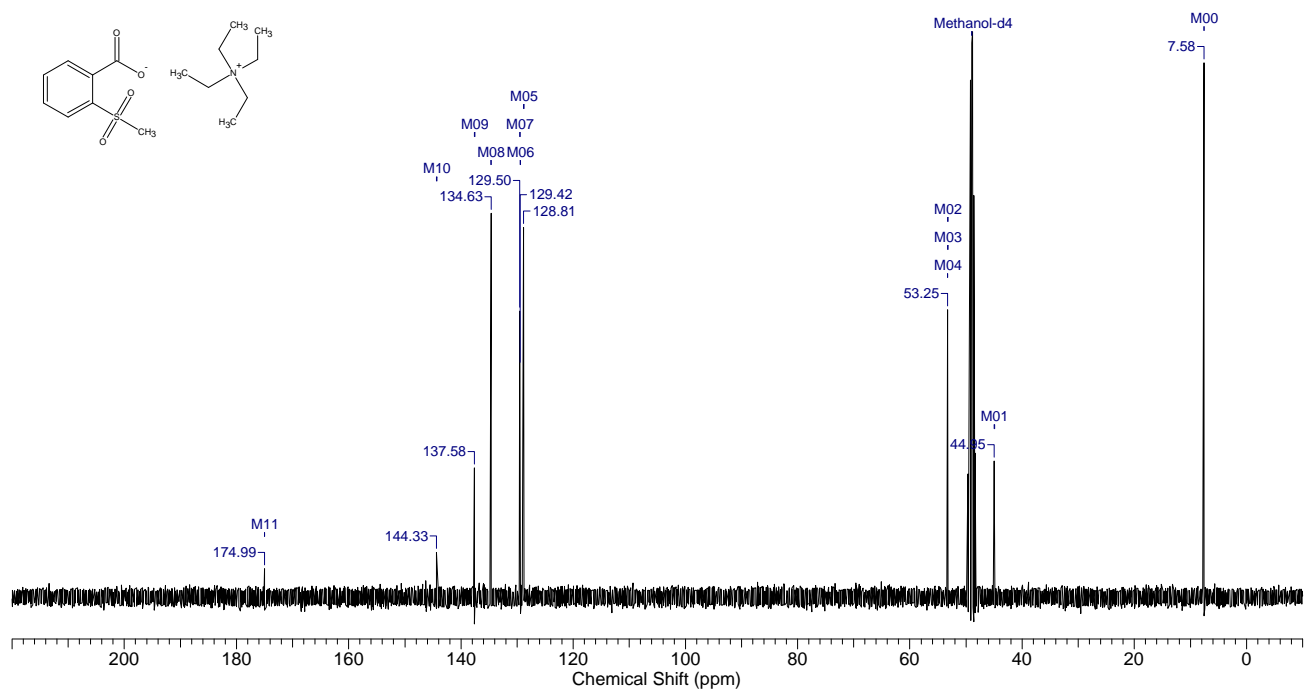


tetraethyl ammonium 2-methylsulphonylbenzoate (4g)

¹H NMR (400 MHz, METHANOL-D₄) δ ppm 7.91 (dd, *J*=7.9, 0.9 Hz, 1 H) 7.61 (td, *J*=7.5, 1.3 Hz, 1 H) 7.51 - 7.54 (m, 1 H) 7.46 (td, *J*=7.6, 1.6 Hz, 1 H) 3.34 (s, 3 H) 3.21 - 3.28 (m, 8 H) 1.23 (tt, *J*=7.3, 1.9 Hz, 12 H)

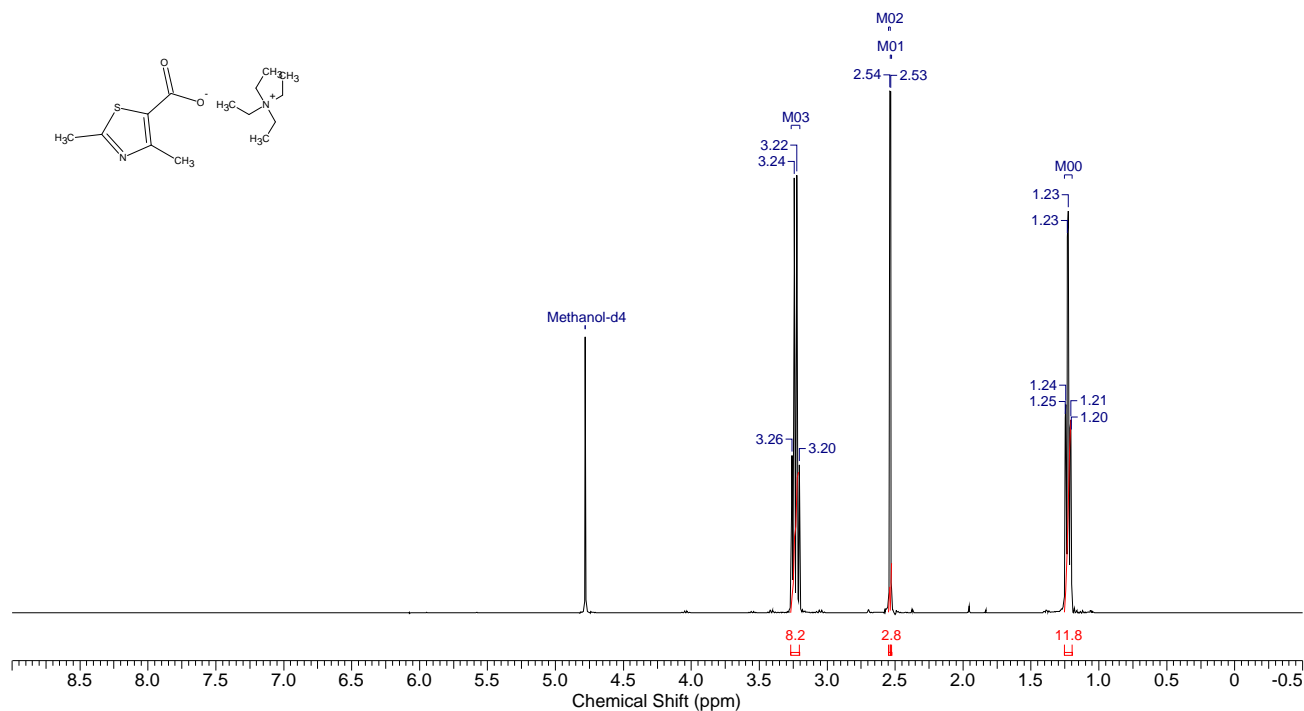


¹³C NMR (101 MHz, METHANOL-D₄) δ ppm 175.0 (s) 144.3 (s) 137.6 (s) 134.6 (s) 129.5 (s) 129.4 (s) 128.8 (s) 53.3 (s) 53.2 (s) 53.2 (s) 44.9 (s) 7.6 (s)

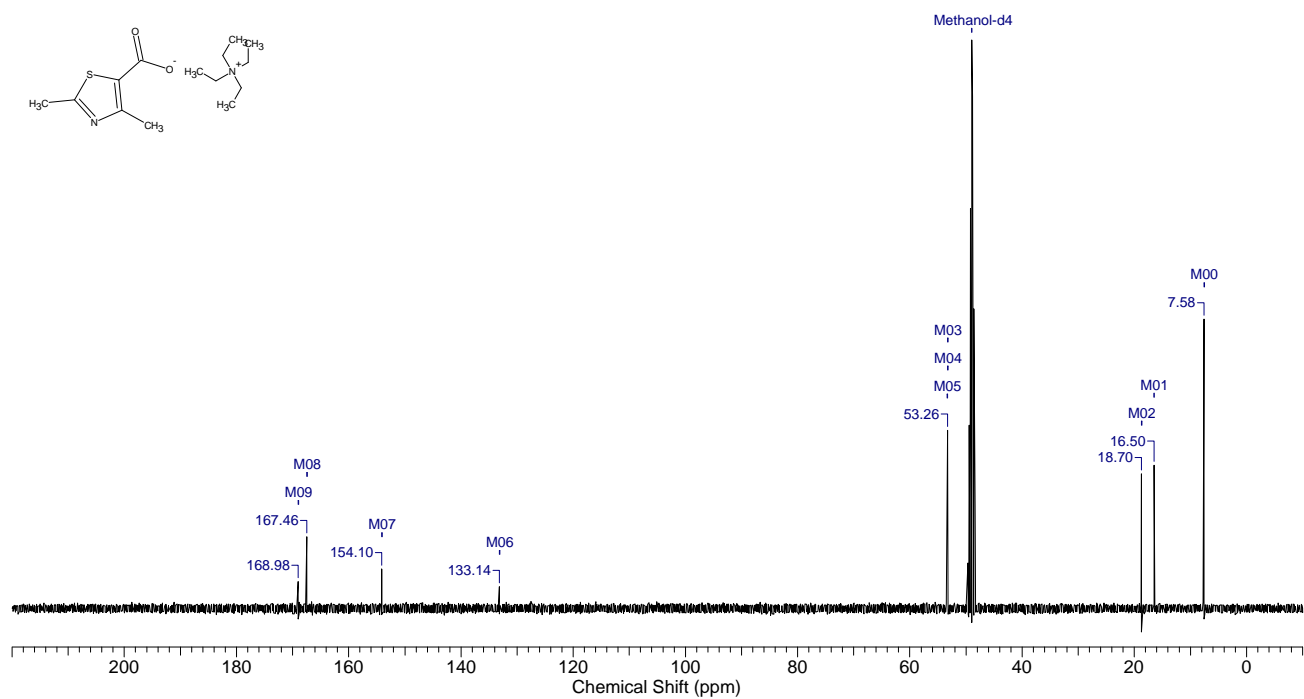


tetraethyl ammonium 2,4-dimethylthiazole-5-carboxylate (4h)

¹H NMR (400 MHz, METHANOL-D₄) δ ppm 3.23 (q, *J*=7.2 Hz, 8 H) 2.54 (s, 3 H) 2.53 (s, 3 H) 1.23 (tt, *J*=7.3, 1.9 Hz, 12 H)

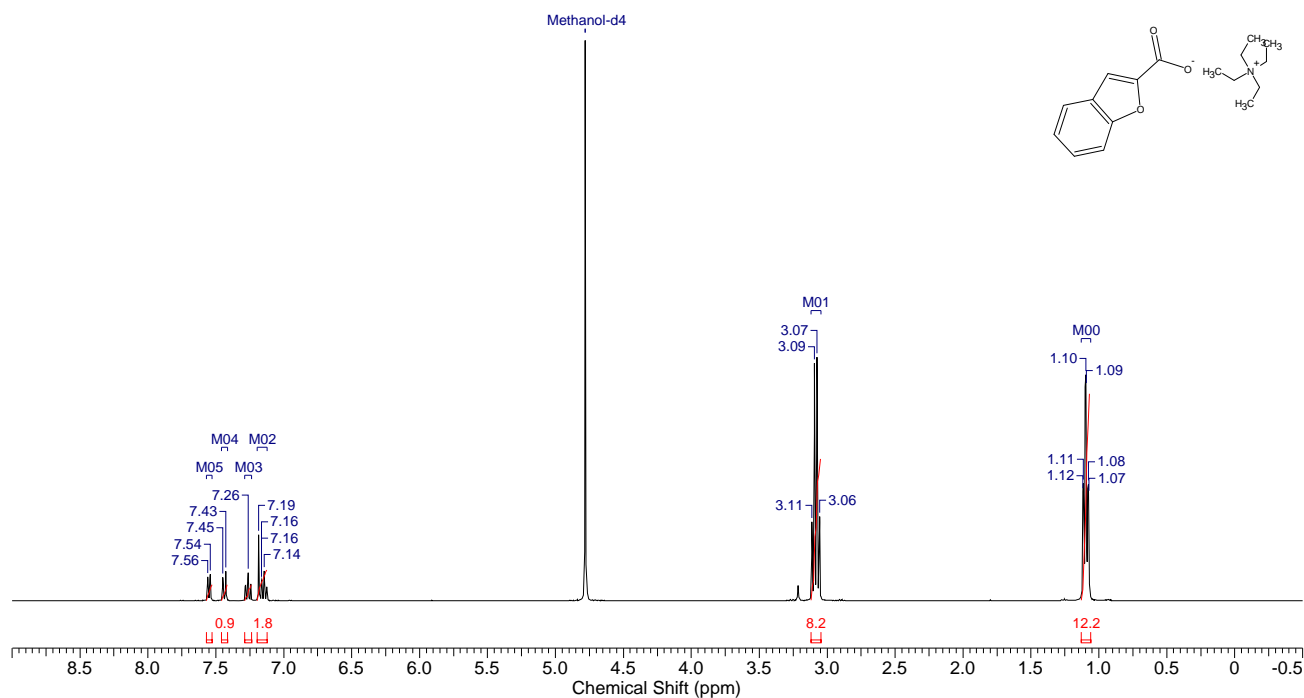


¹³C NMR (101 MHz, METHANOL-D₄) δ ppm 169.0 (s) 167.5 (s) 154.1 (s) 133.1 (s) 53.3 (s) 53.3 (s) 53.2 (s) 18.7 (s) 16.5 (s) 7.6 (s)

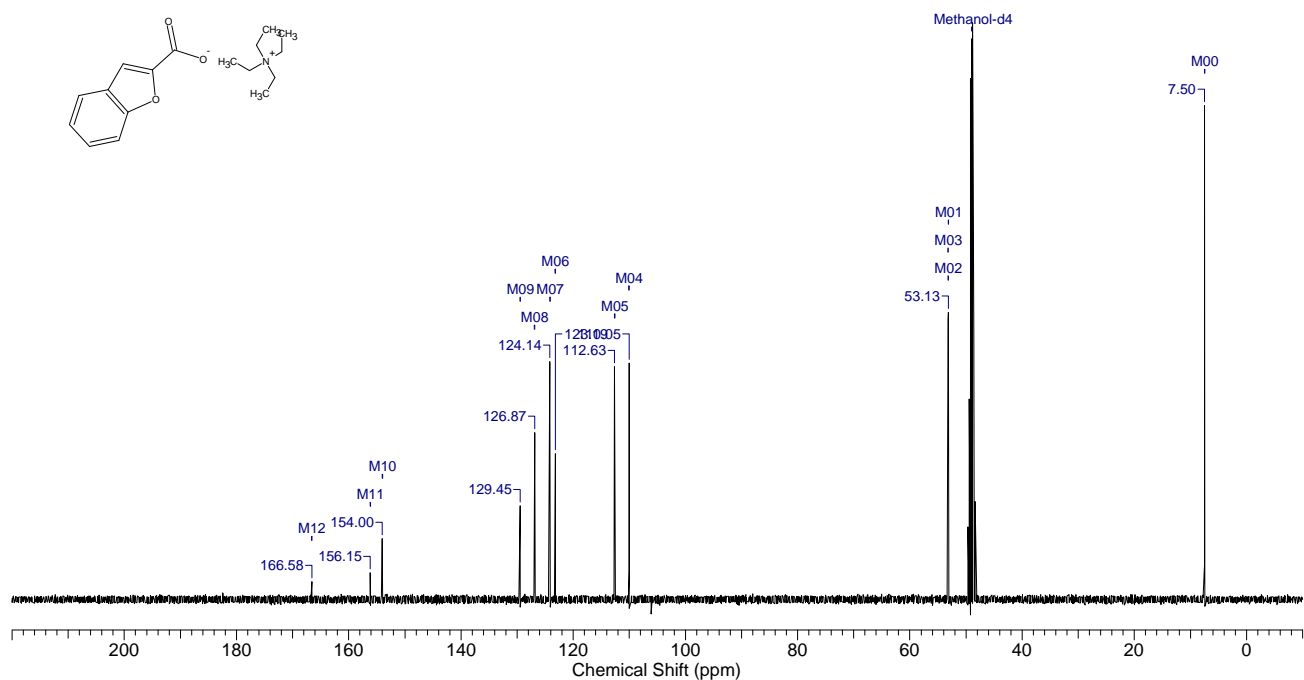


tetraethyl ammonium benzofuran-2-carboxylate (4i)

^1H NMR (400 MHz, *METHANOL-D4*) δ ppm 7.55 (d, $J=7.8$ Hz, 1 H) 7.41 - 7.46 (m, 1 H) 7.26 (d, $J=1.2$ Hz, 1 H) 7.12 - 7.19 (m, 2 H) 3.08 (q, $J=7.3$ Hz, 8 H) 1.10 (tt, $J=7.3, 1.9$ Hz, 12 H)

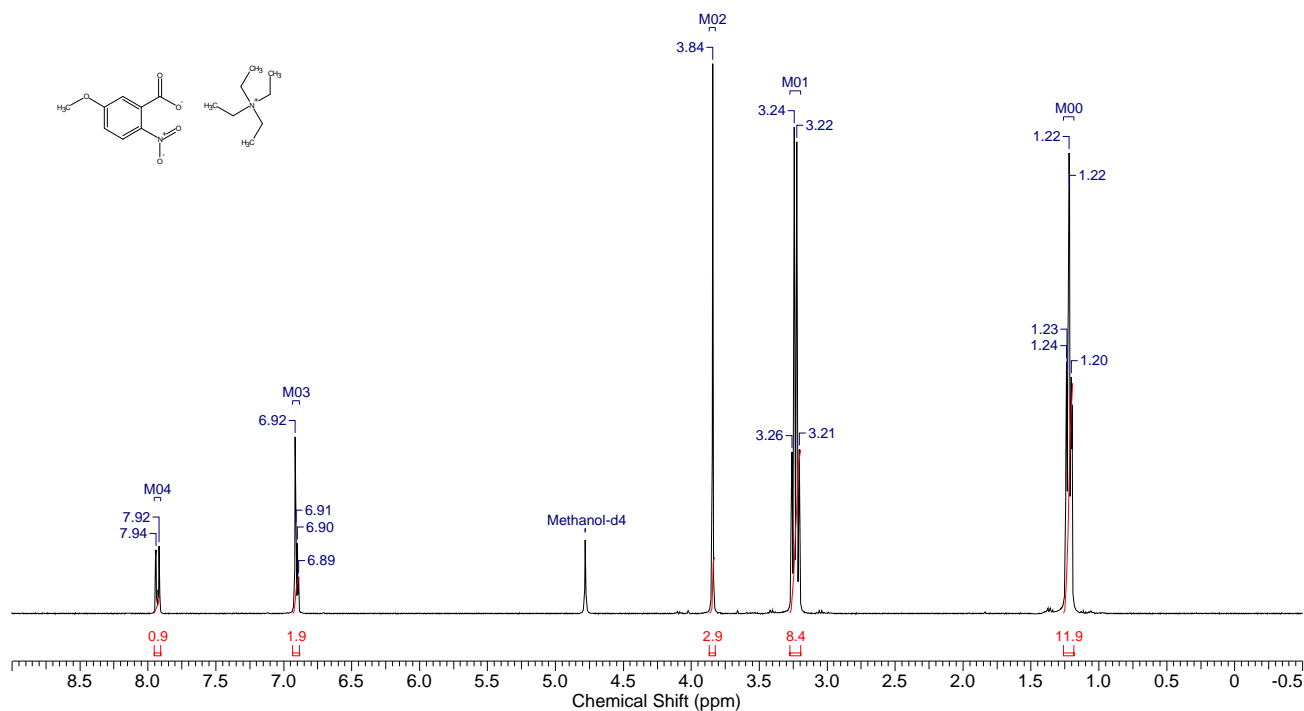


^{13}C NMR (101 MHz, *METHANOL-D4*) δ ppm 166.6 (s) 156.2 (s) 154.0 (s) 129.5 (s) 126.9 (s) 124.1 (s) 123.2 (s) 112.6 (s) 110.0 (s) 53.2 (s) 53.2 (s) 53.1 (s) 7.5 (s)

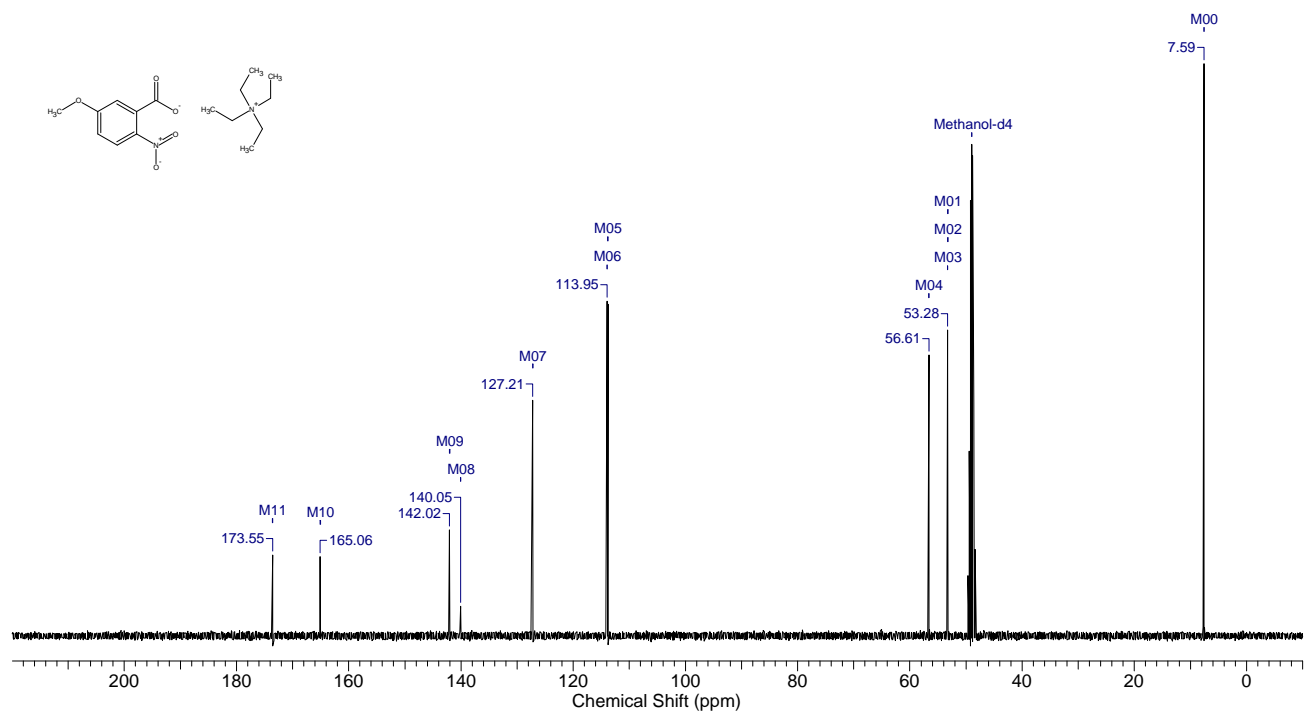


tetraethyl ammonium 5-methoxy-2-nitrobenzoate (4k)

$^1\text{H NMR}$ (400 MHz, *METHANOL-D4*) δ ppm 7.93 (d, $J=9.8$ Hz, 1 H) 6.88 - 6.94 (m, 2 H) 3.84 (s, 3 H) 3.23 (q, $J=7.4$ Hz, 8 H) 1.22 (tt, $J=7.3$, 1.8 Hz, 12 H)

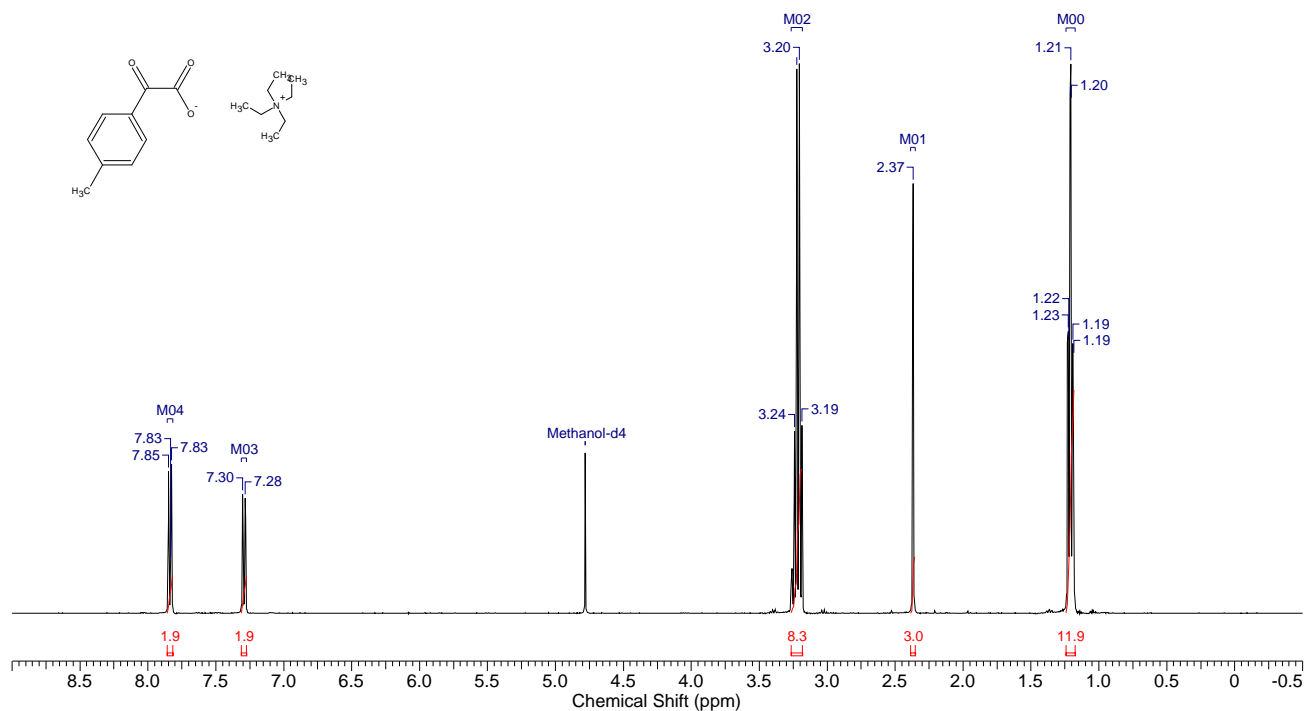


$^{13}\text{C NMR}$ (101 MHz, *METHANOL-D4*) δ ppm 173.5 (s) 165.1 (s) 142.0 (s) 140.1 (s) 127.2 (s) 114.0 (s) 113.8 (s) 56.6 (s) 53.3 (s) 53.2 (s) 53.2 (s) 7.6 (s)

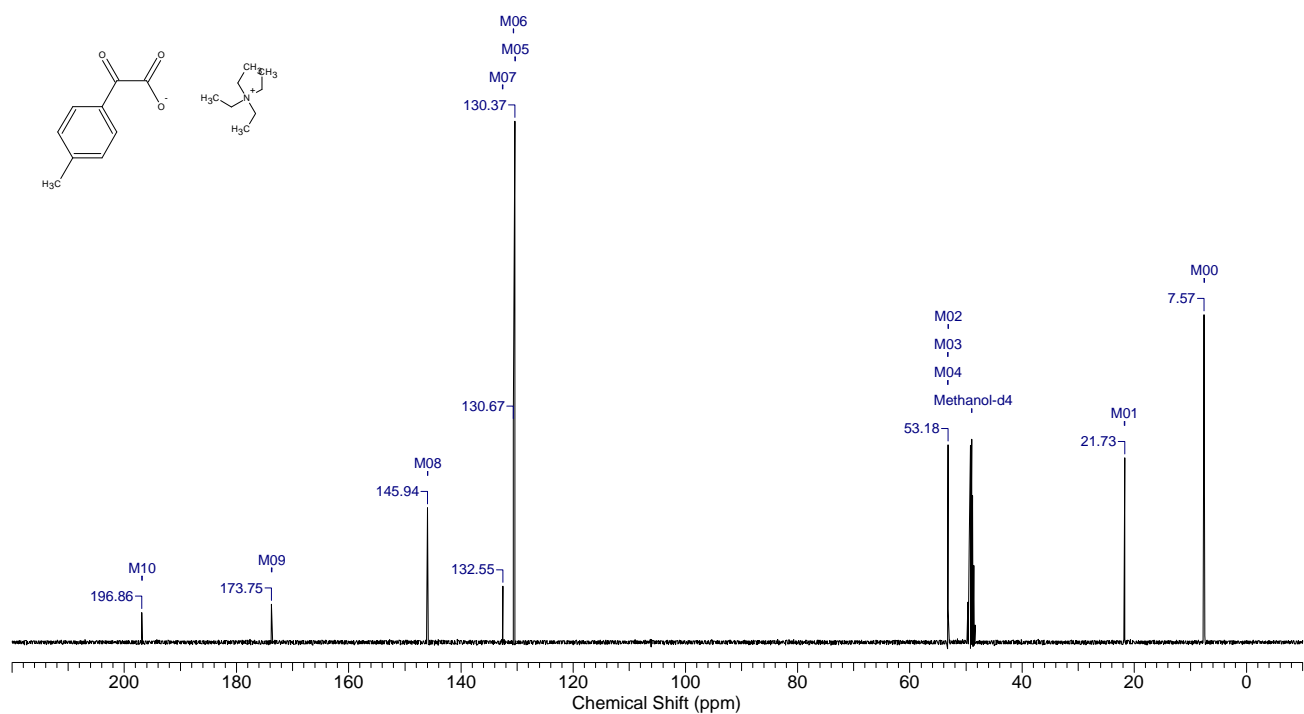


tetraethyl ammonium 4-methylbenzoylformate (4n)

¹H NMR (400 MHz, METHANOL-D₄) δ ppm 7.82 - 7.86 (m, 2 H) 7.29 (d, *J*=8.0 Hz, 2 H) 3.21 (q, *J*=7.4 Hz, 8 H) 2.37 (s, 3 H) 1.21 (tt, *J*=7.3, 1.9 Hz, 12 H)

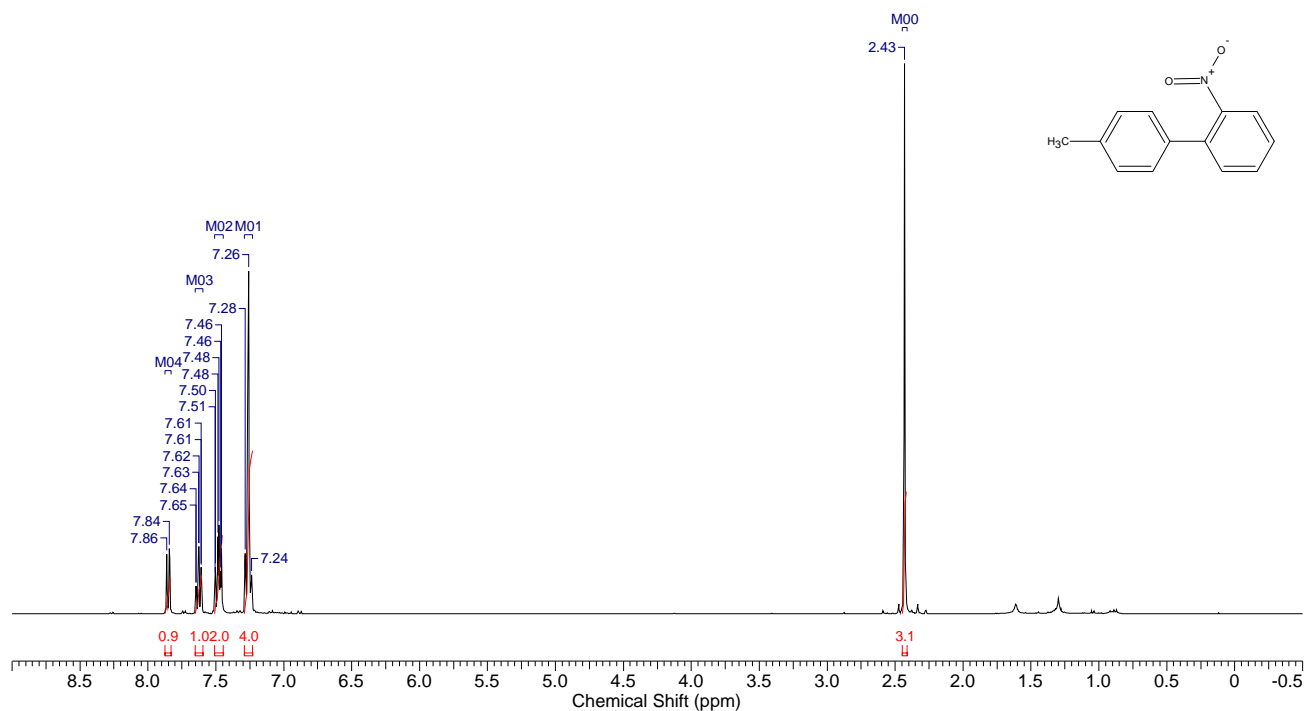


¹³C NMR (101 MHz, METHANOL-D₄) δ ppm 196.9 (s) 173.7 (s) 145.9 (s) 132.5 (s) 130.7 (s) 130.4 (s) 53.2 (s) 53.2 (s) 53.2 (s) 21.7 (s) 7.6 (s)

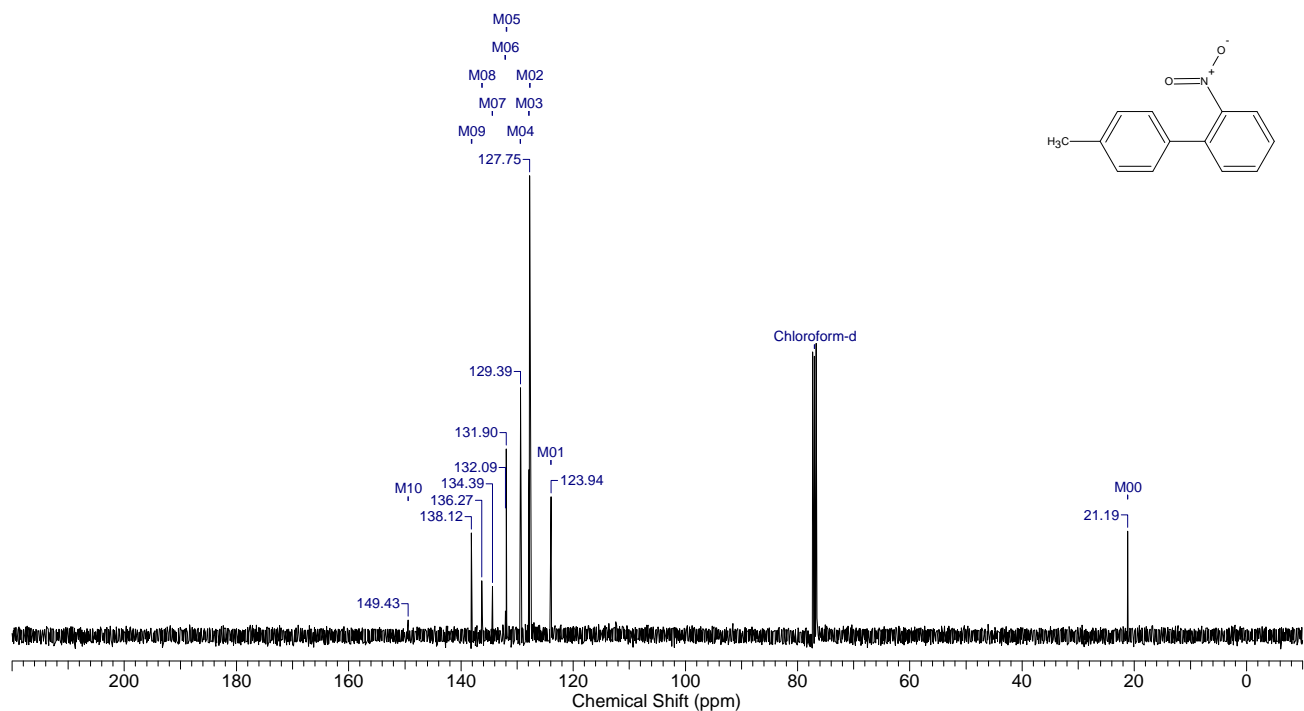


4'-methyl-2-nitrophenyl (3aa)

$^1\text{H NMR}$ (400 MHz, *CHLOROFORM-D*) δ ppm 7.85 (d, $J=8.2$ Hz, 1 H) 7.63 (td, $J=7.6, 1.2$ Hz, 1 H) 7.44 - 7.51 (m, 2 H) 7.23 - 7.29 (m, 4 H) 2.43 (s, 3 H)

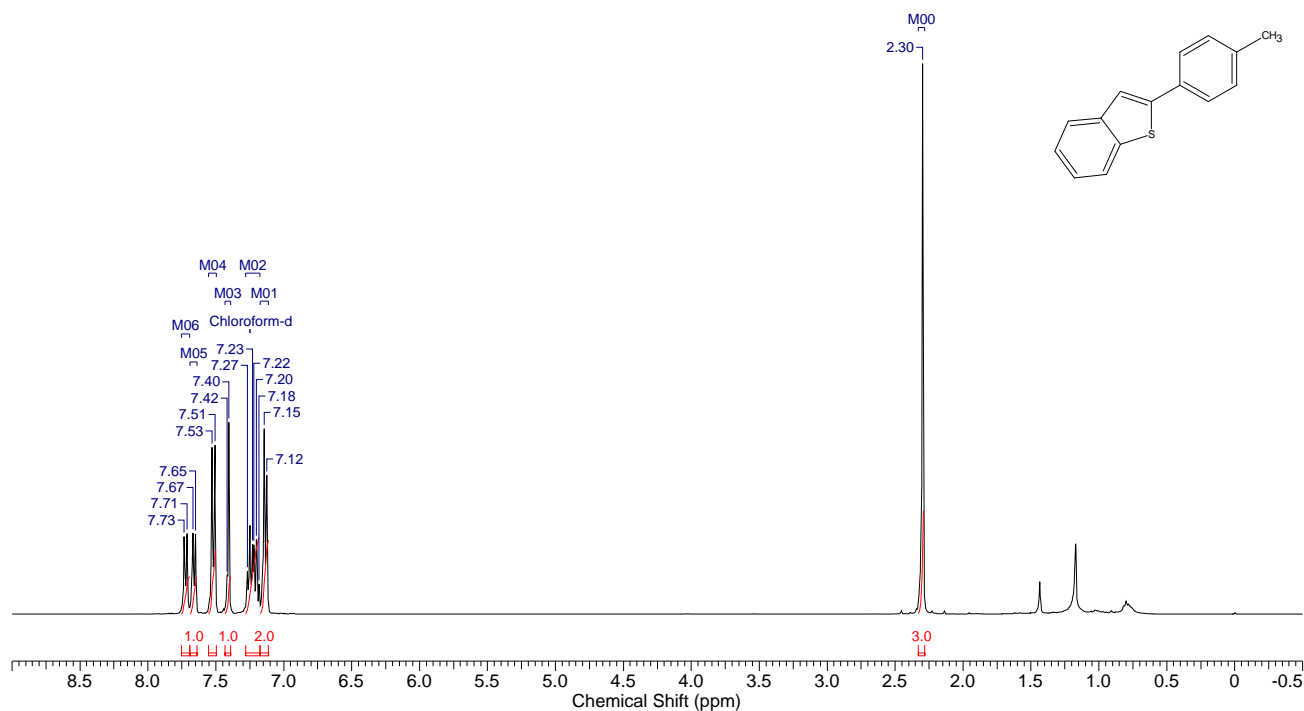


$^{13}\text{C NMR}$ (101 MHz, *CHLOROFORM-D*) δ ppm 149.4 (s) 138.1 (s) 136.3 (s) 134.4 (s) 132.1 (s) 131.9 (s) 129.4 (s) 127.9 (s) 127.7 (s) 123.9 (s) 21.2 (s)

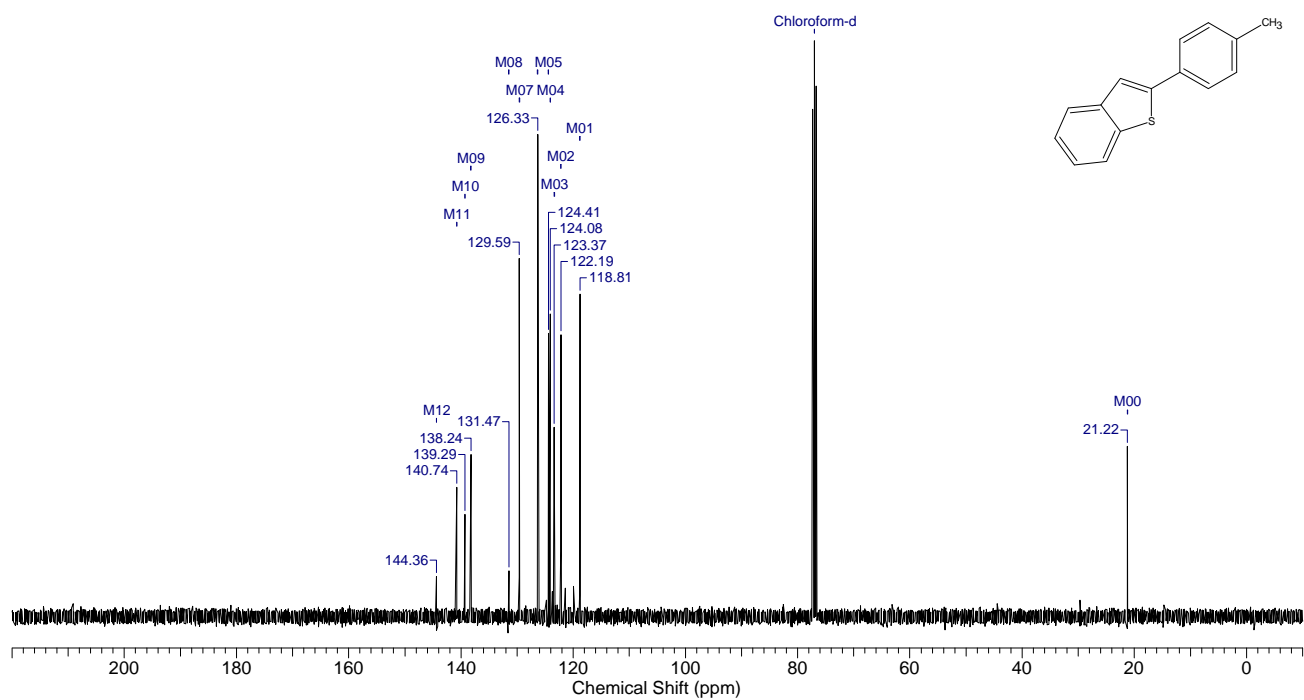


2-(4'-methylphenyl)-benzothiophene (3ba)

¹H NMR (400 MHz, CHLOROFORM-D) δ ppm 7.72 (d, $J=7.8$ Hz, 1 H) 7.66 (d, $J=7.8$ Hz, 1 H) 7.52 (d, $J=8.2$ Hz, 2 H) 7.39 - 7.43 (m, 1 H) 7.18 - 7.28 (m, 2 H) 7.14 (d, $J=8.2$ Hz, 2 H) 2.30 (s, 3 H)

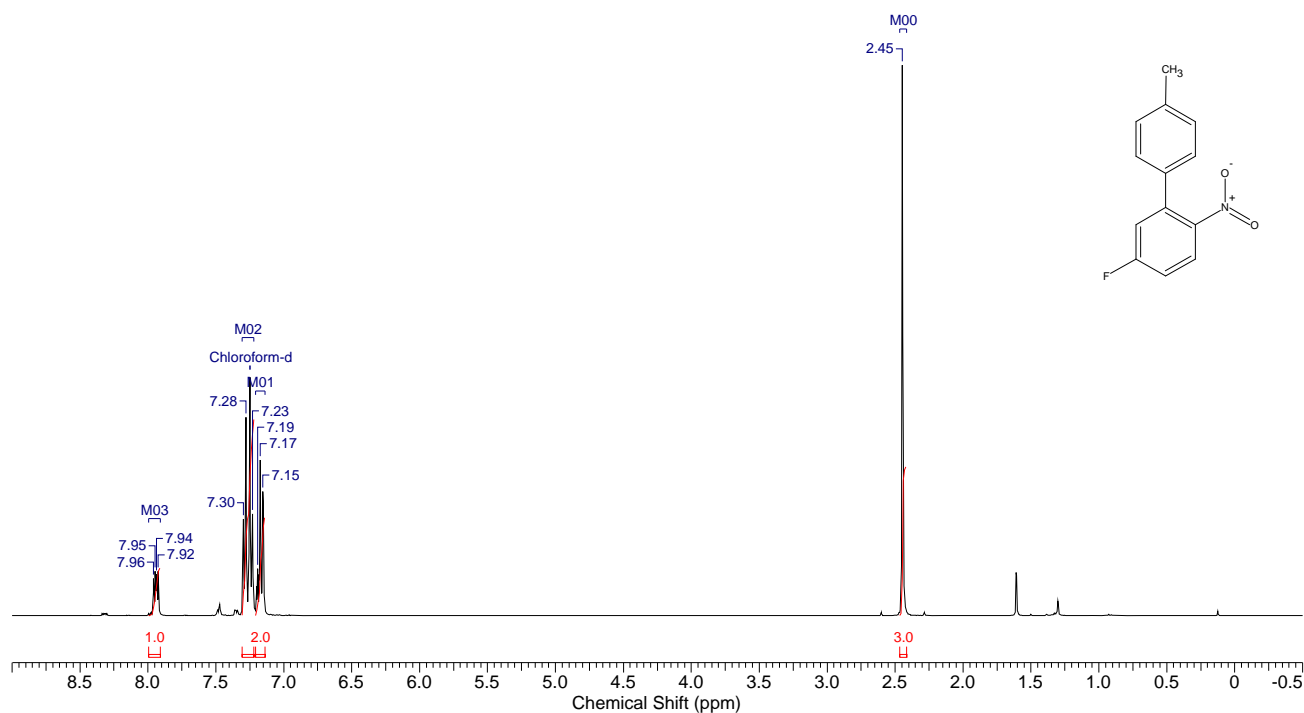


¹³C NMR (101 MHz, CHLOROFORM-D) δ ppm 144.4 (s) 140.7 (s) 139.3 (s) 138.2 (s) 131.5 (s) 129.6 (s) 126.3 (s) 124.4 (s) 124.1 (s) 123.4 (s) 122.2 (s) 118.8 (s) 21.2 (s)

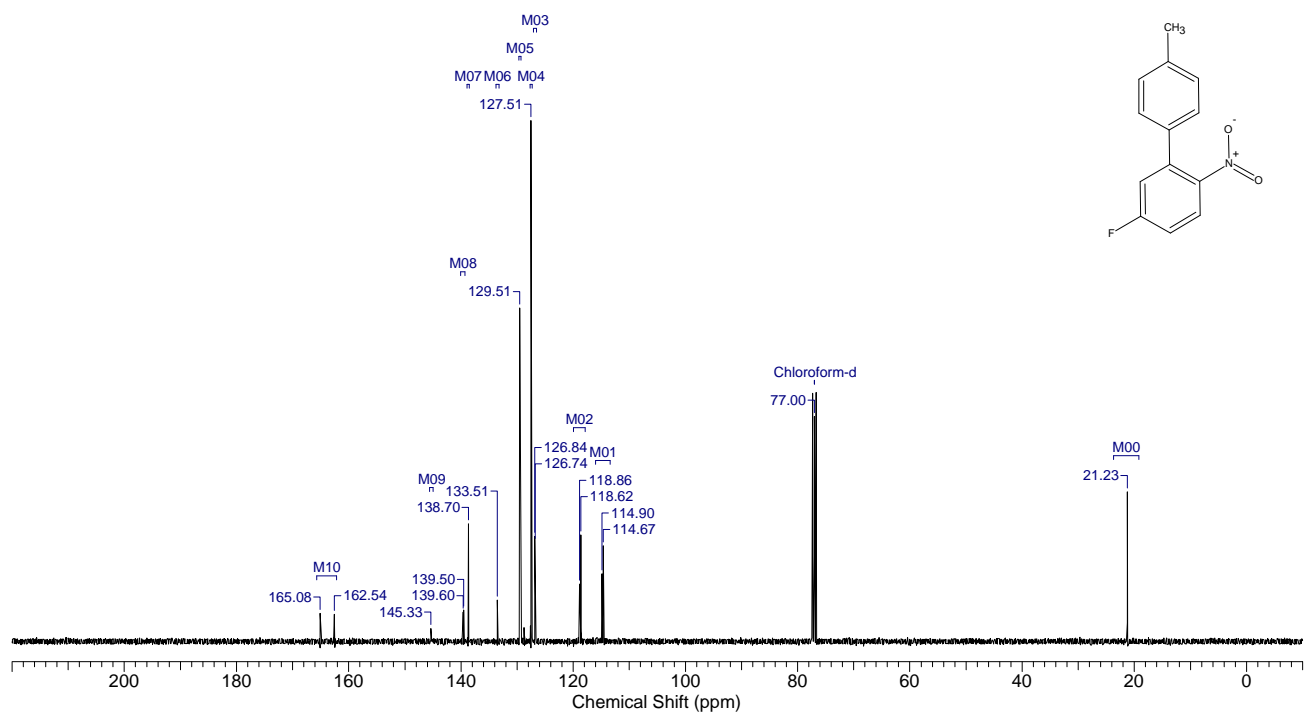


4'-methyl-5-fluoro-2-nitrophenyl (3ca)

¹H NMR (400 MHz, CHLOROFORM-D) δ ppm 7.94 (dd, *J*=8.9, 5.1 Hz, 1 H) 7.22 - 7.31 (m, 4 H) 7.14 - 7.21 (m, 2 H) 2.45 (s, 3 H)

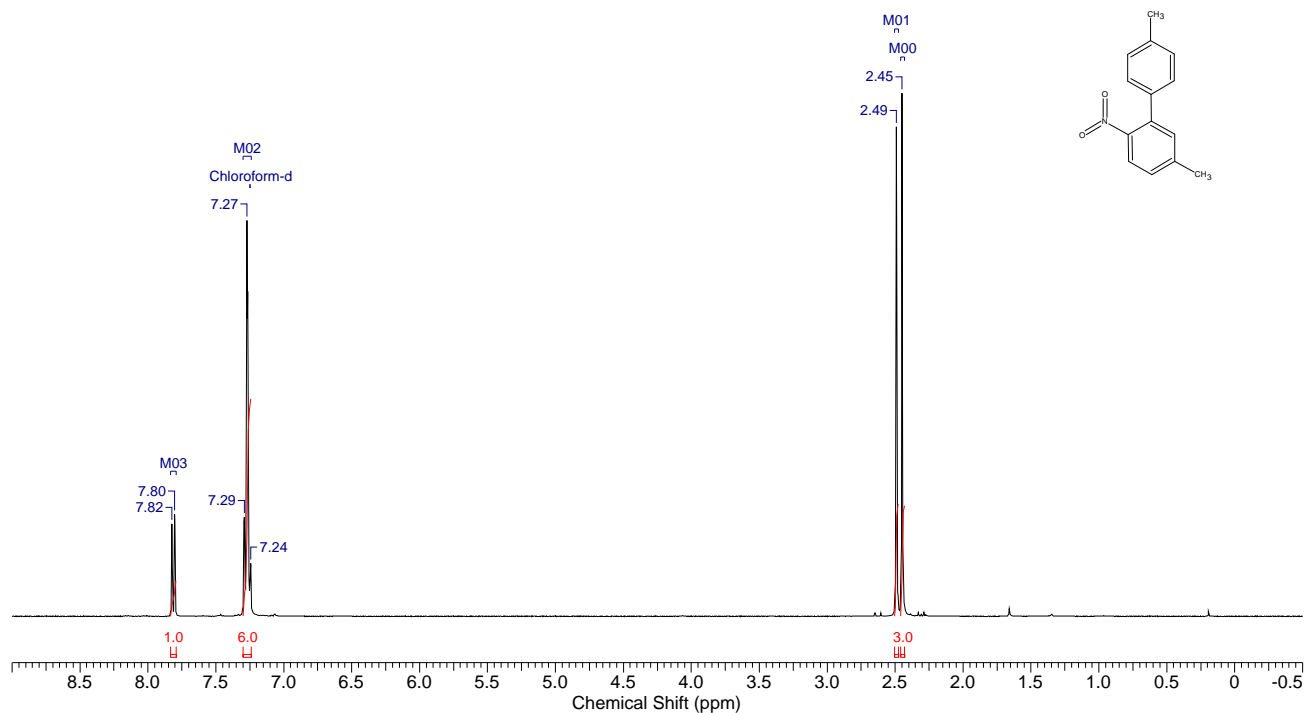


¹³C NMR (101 MHz, CHLOROFORM-D) δ ppm 163.8 (d) 145.3 (s) 139.5 (d) 138.7 (s) 133.5 (s) 129.5 (s) 127.5 (s) 126.8 (d) 118.7 (d) 114.8 (d) 21.2 (s)

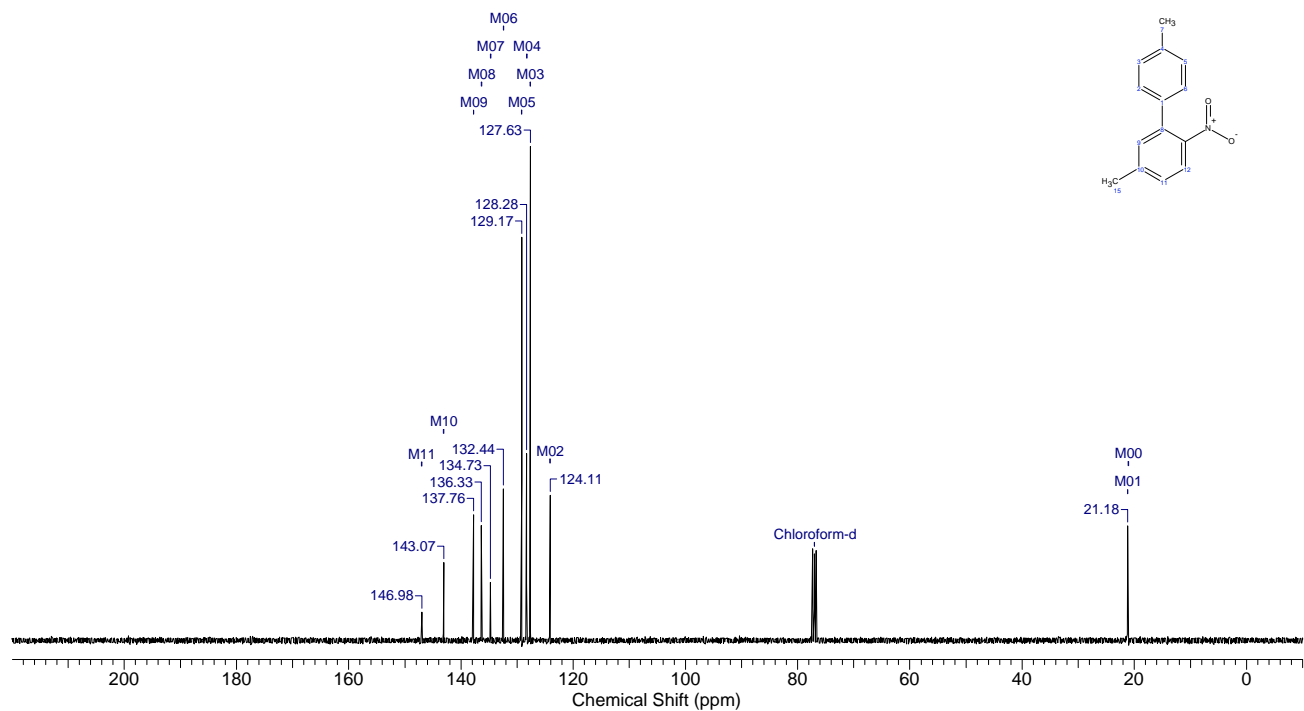


4',5-dimethyl-2-nitrobiphenyl (3da)

$^1\text{H NMR}$ (400 MHz, CHLOROFORM-D) δ ppm 7.81 (d, $J=8.2$ Hz, 1 H) 7.24 - 7.30 (m, 6 H) 2.49 (s, 3 H) 2.45 (s, 3 H)

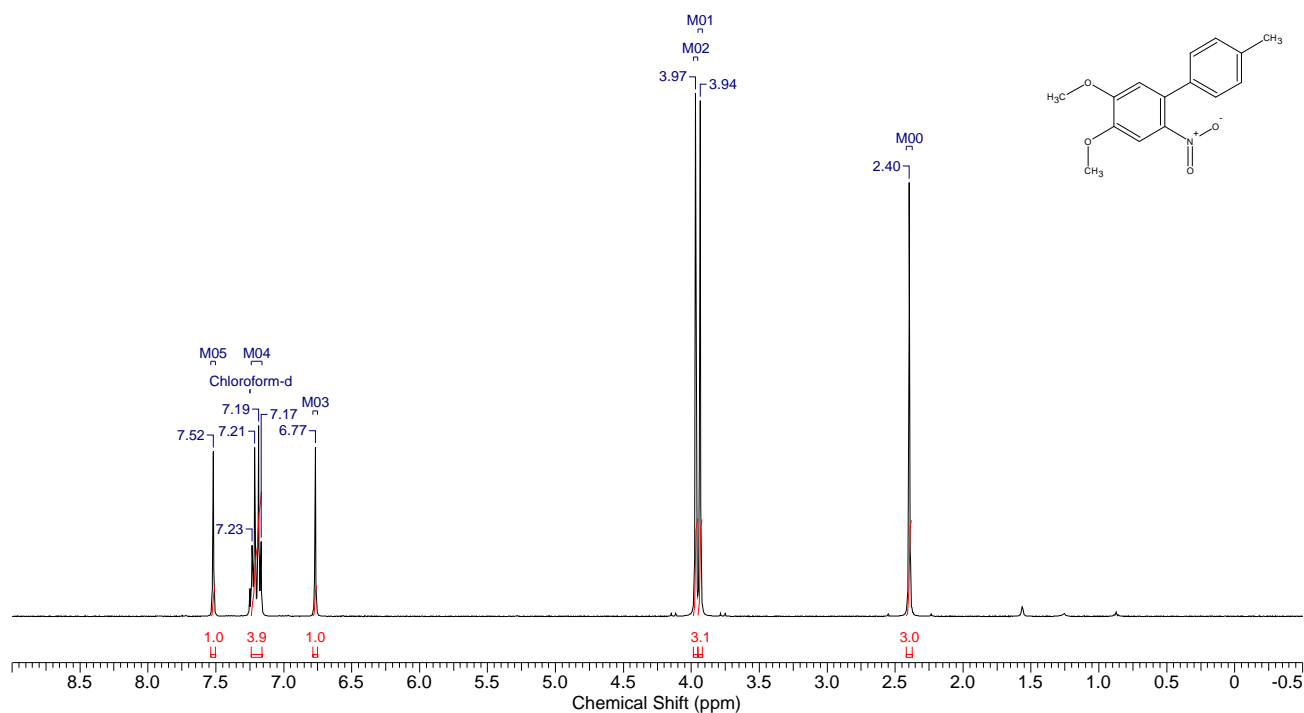


$^{13}\text{C NMR}$ (101 MHz, CHLOROFORM-D) δ ppm 147.0 (s) 143.1 (s) 137.8 (s) 136.3 (s) 134.7 (s) 132.4 (s) 129.2 (s) 128.3 (s) 127.6 (s) 124.1 (s) 21.2 (s) 21.1 (s)

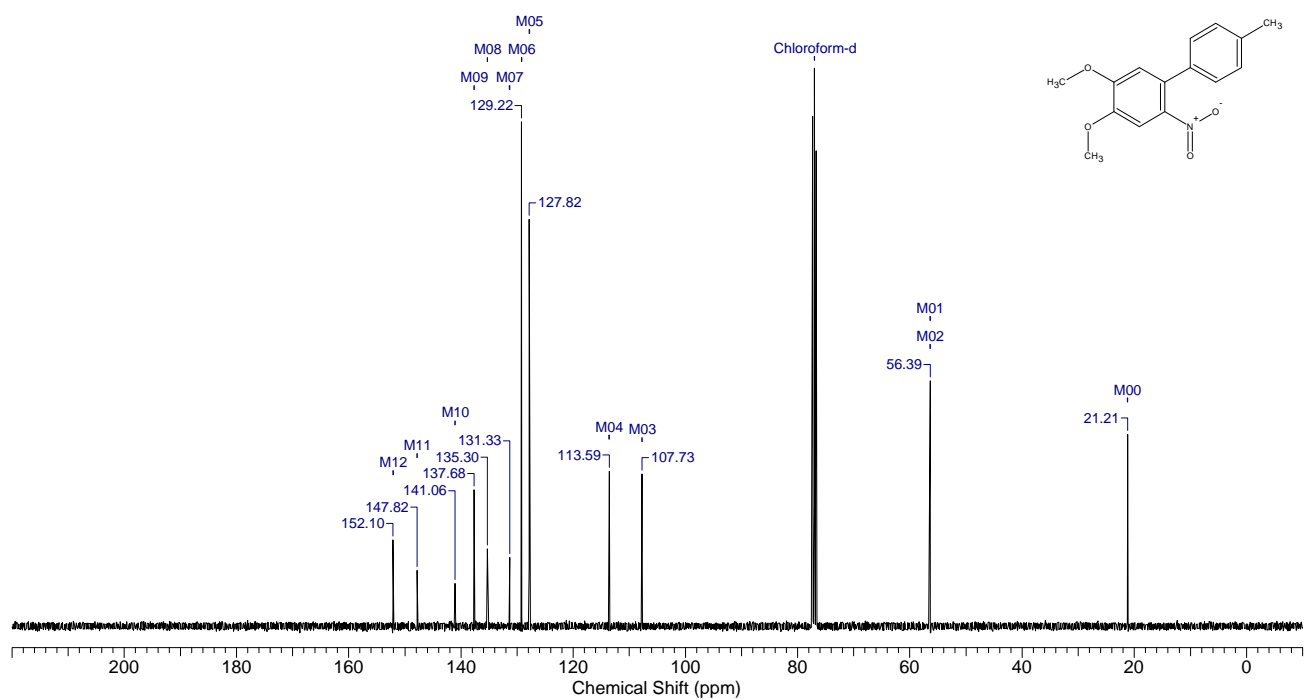


4'-methyl-4,5-dimethoxy-2-nitrophenyl (3ea)

¹H NMR (400 MHz, CHLOROFORM-D) δ ppm 7.52 (s, 1 H) 7.16 - 7.24 (m, 4 H) 6.77 (s, 1 H) 3.97 (s, 3 H) 3.94 (s, 3 H) 2.40 (s, 3 H)

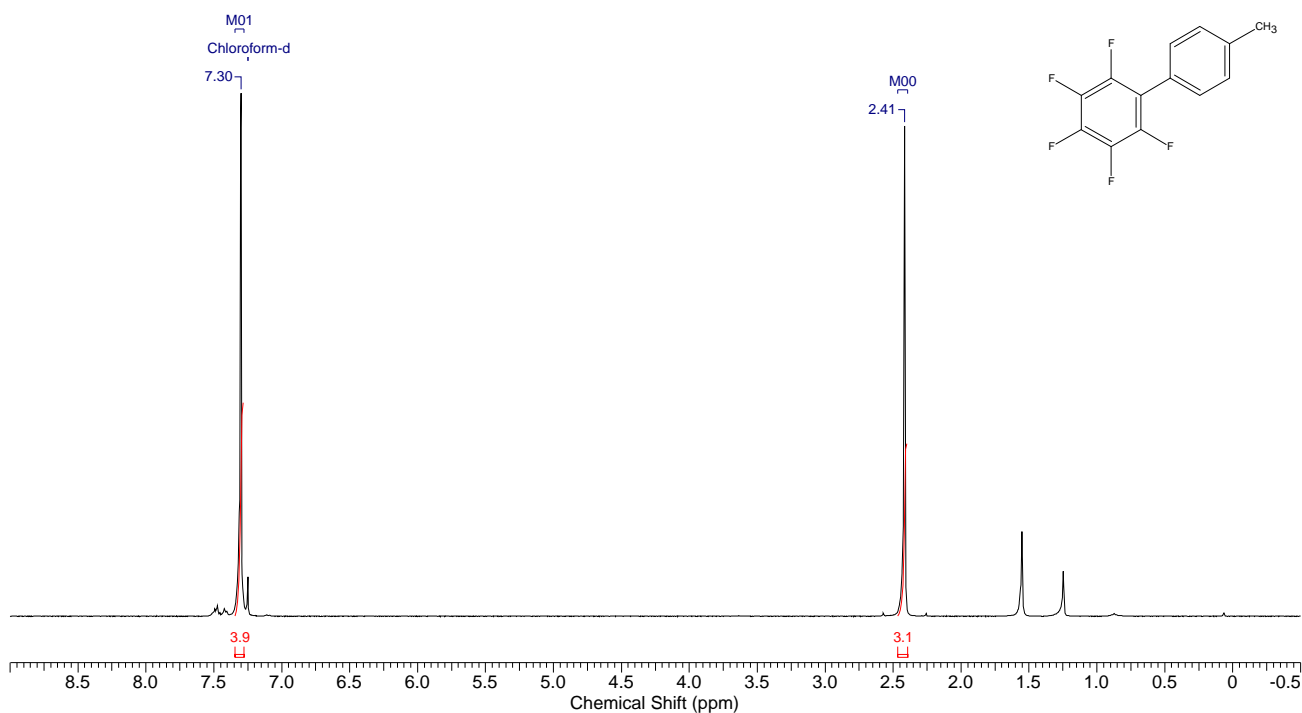


¹³C NMR (101 MHz, CHLOROFORM-D) δ ppm 152.1 (s) 147.8 (s) 141.1 (s) 137.7 (s) 135.3 (s) 131.3 (s) 129.2 (s) 127.8 (s) 113.6 (s) 107.7 (s) 56.4 (s) 56.4 (s) 21.2 (s)

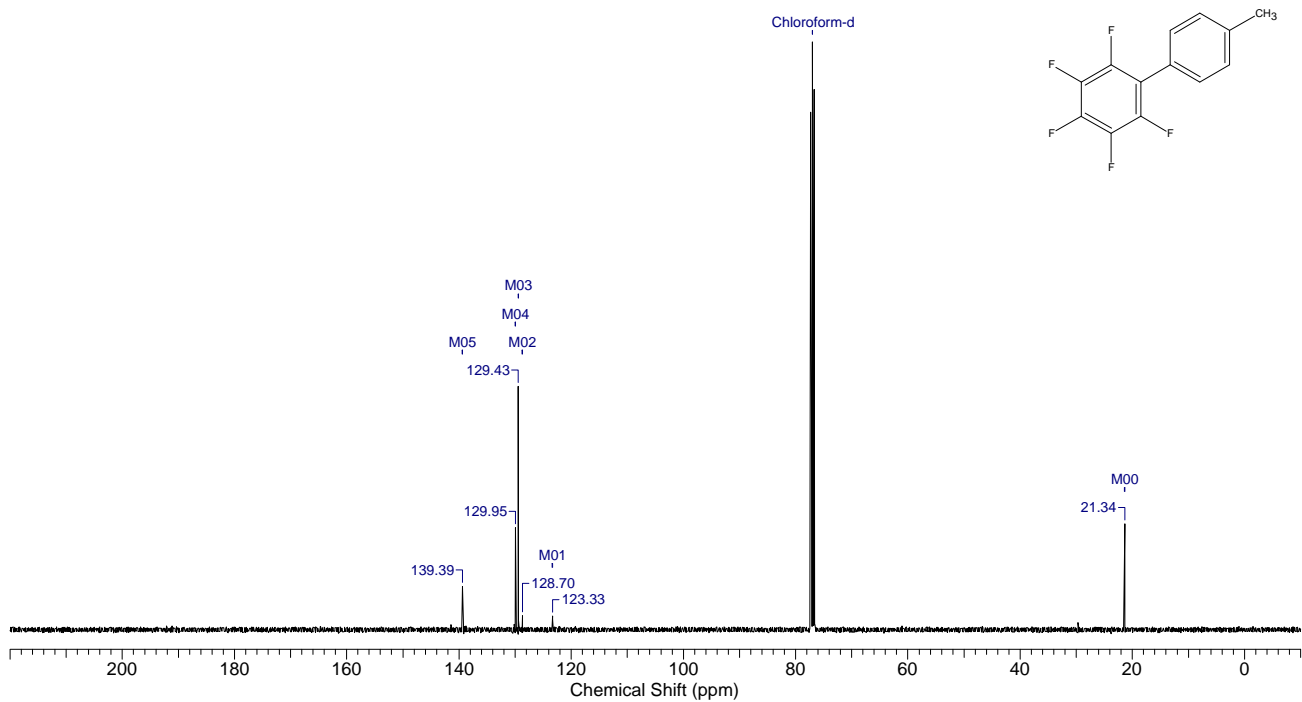


4'-methyl-2,3,4,5,6-pentafluorobiphenyl (3f)

$^1\text{H NMR}$ (400 MHz, *CHLOROFORM-D*) δ ppm 7.30 (s, 4 H) 2.41 (s, 3 H)

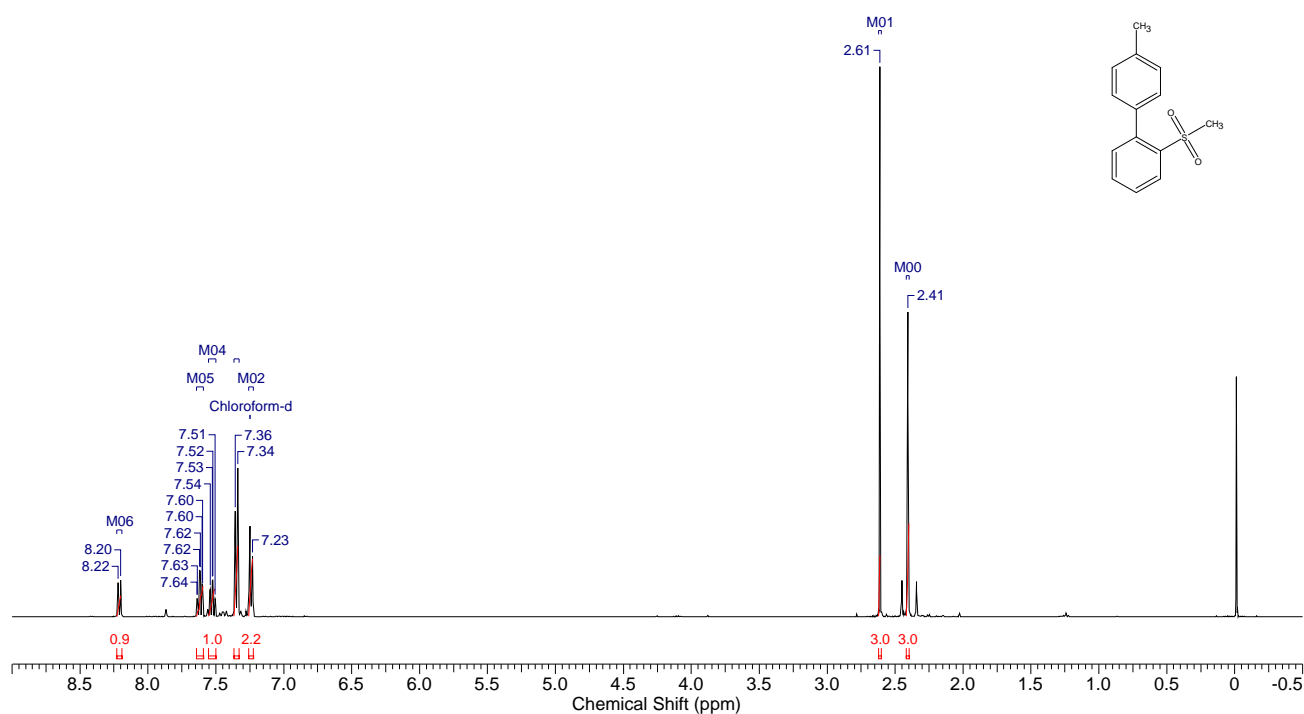


$^{13}\text{C NMR}$ (101 MHz, *CHLOROFORM-D*) δ ppm 139.4 (s) 130.0 (s) 129.4 (s) 128.7 (s) 123.3 (s) 21.3 (s)

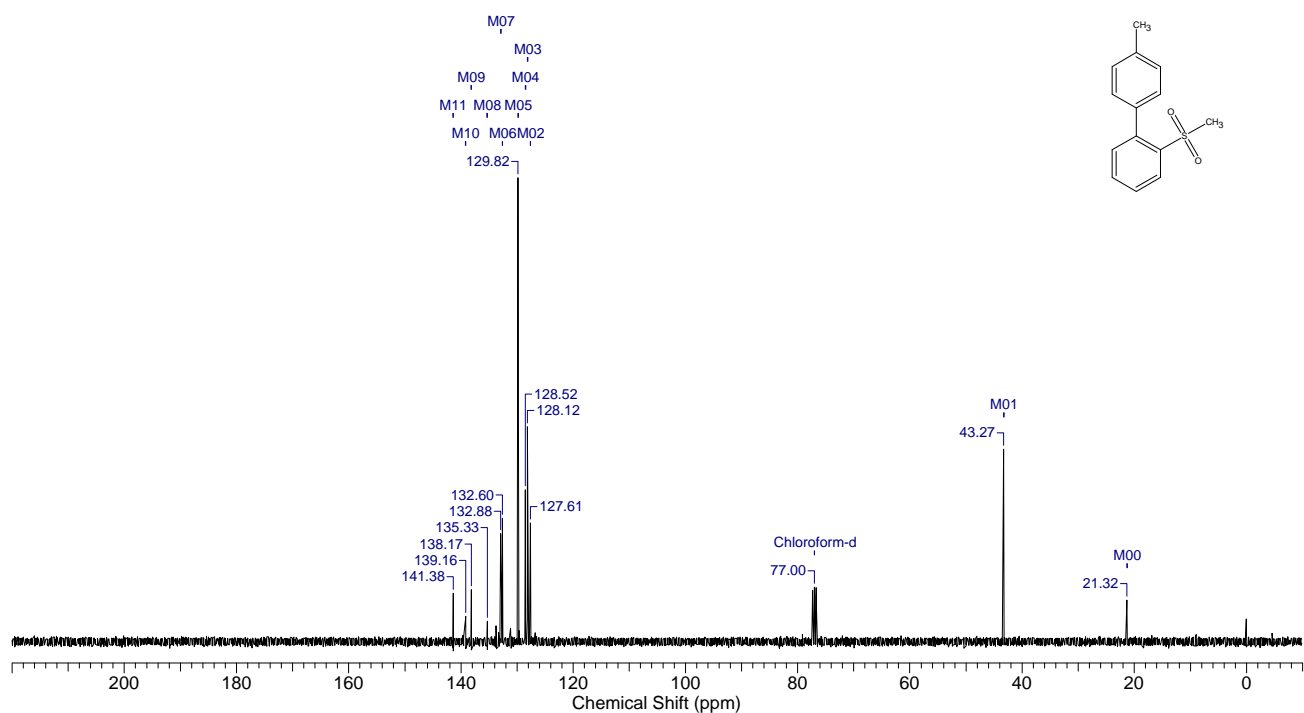


4'-methyl-2-methylsulphonylbiphenyl (3ga)

¹H NMR (400 MHz, CHLOROFORM-D) δ ppm 8.21 (dd, $J=8.0, 1.4$ Hz, 1 H) 7.62 (td, $J=7.6, 1.4$ Hz, 1 H) 7.50 - 7.55 (m, 1 H) 7.33 - 7.37 (m, 3 H) 7.23 (s, 2 H) 2.61 (s, 3 H) 2.41 (s, 3 H)

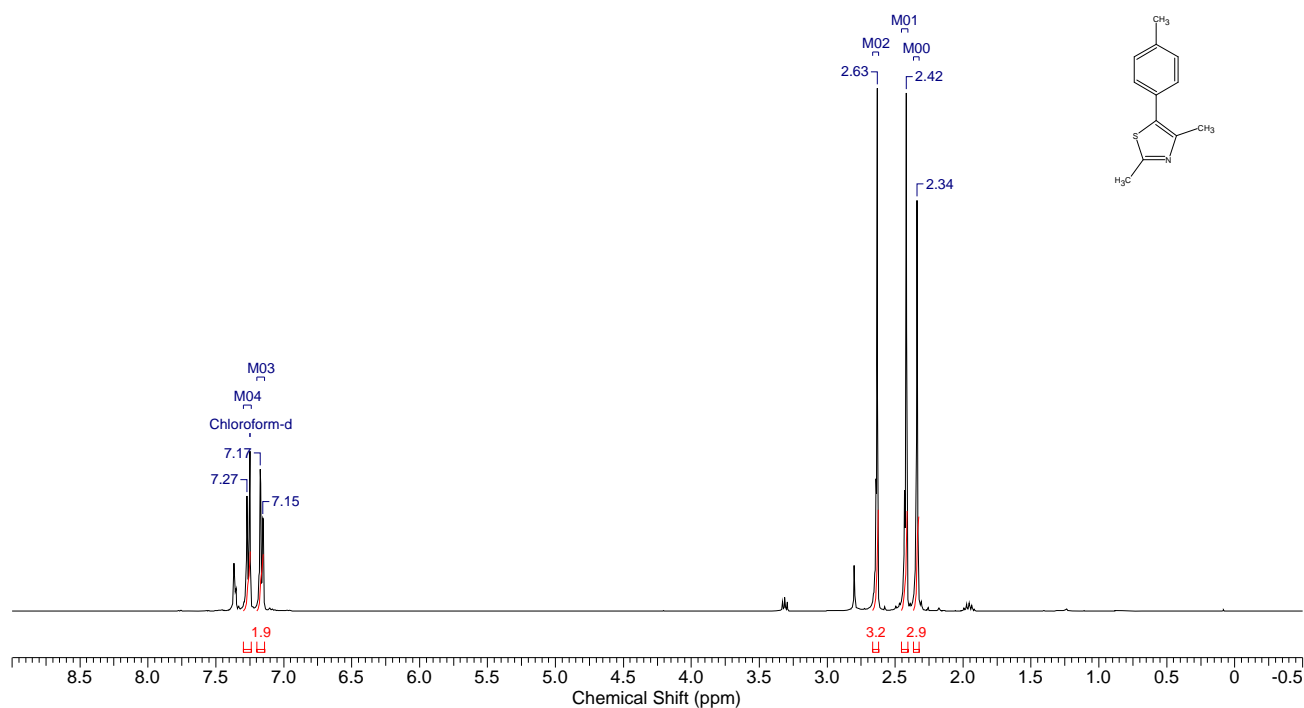


¹³C NMR (101 MHz, CHLOROFORM-D) δ ppm 141.4 (s) 139.2 (s) 138.2 (s) 135.3 (s) 132.9 (s) 132.6 (s) 129.8 (s) 128.5 (s) 128.1 (s) 127.6 (s) 43.3 (s) 21.3 (s)

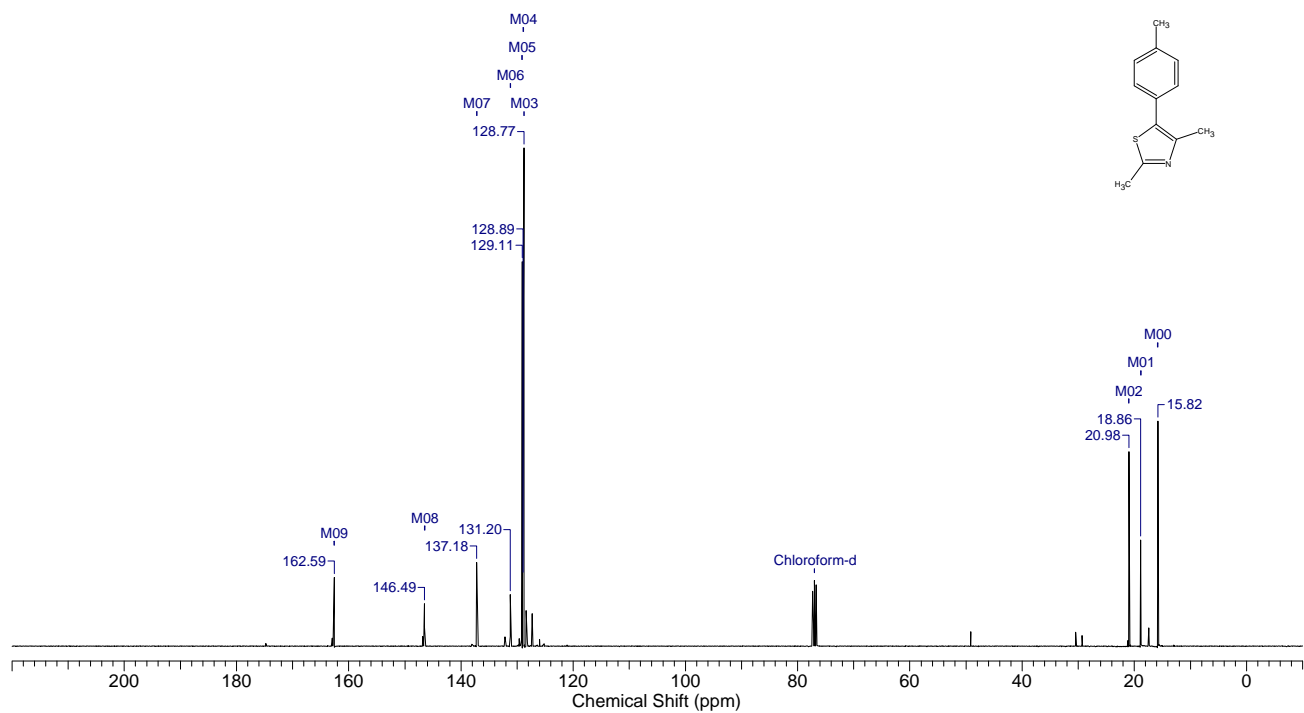


5-(4'-methylphenyl)-2,4-dimethyl-1,3-thiazole (3ha)

¹H NMR (400 MHz, CHLOROFORM-D) δ ppm 7.27 (s, 2 H) 7.14 - 7.20 (m, 2 H) 2.63 (s, 3 H) 2.42 (s, 3 H) 2.34 (s, 3 H)

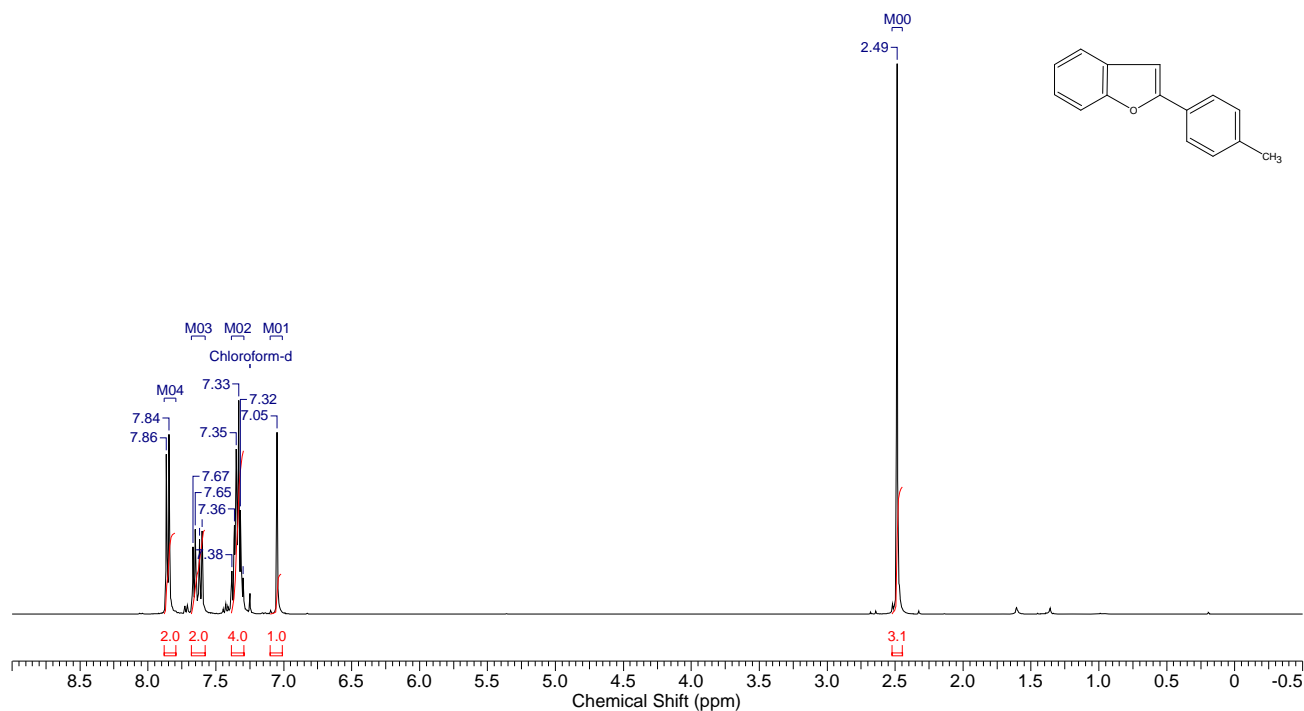


¹³C NMR (101 MHz, CHLOROFORM-D) δ ppm 162.6 (s) 146.5 (s) 137.2 (s) 131.2 (s) 129.1 (s) 128.9 (s) 128.8 (s) 21.0 (s) 18.9 (s) 15.8 (s)

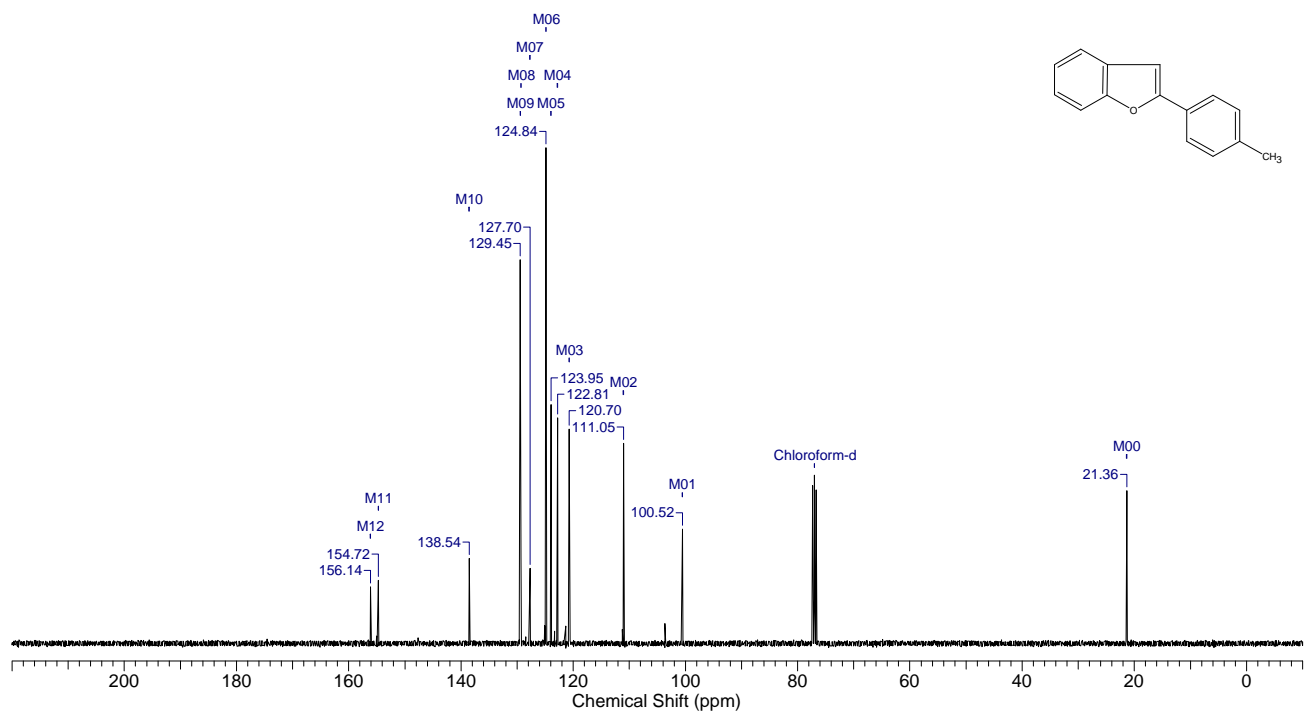


2-(4'-methylphenyl)-benzofuran (3ia)

$^1\text{H NMR}$ (400 MHz, CHLOROFORM-D) δ ppm 7.85 (d, $J=7.8$ Hz, 2 H) 7.63 (dd, $J=19.6, 7.4$ Hz, 2 H) 7.34 (td, $J=12.9, 7.4$ Hz, 4 H) 7.05 (s, 1 H) 2.49 (s, 3 H)

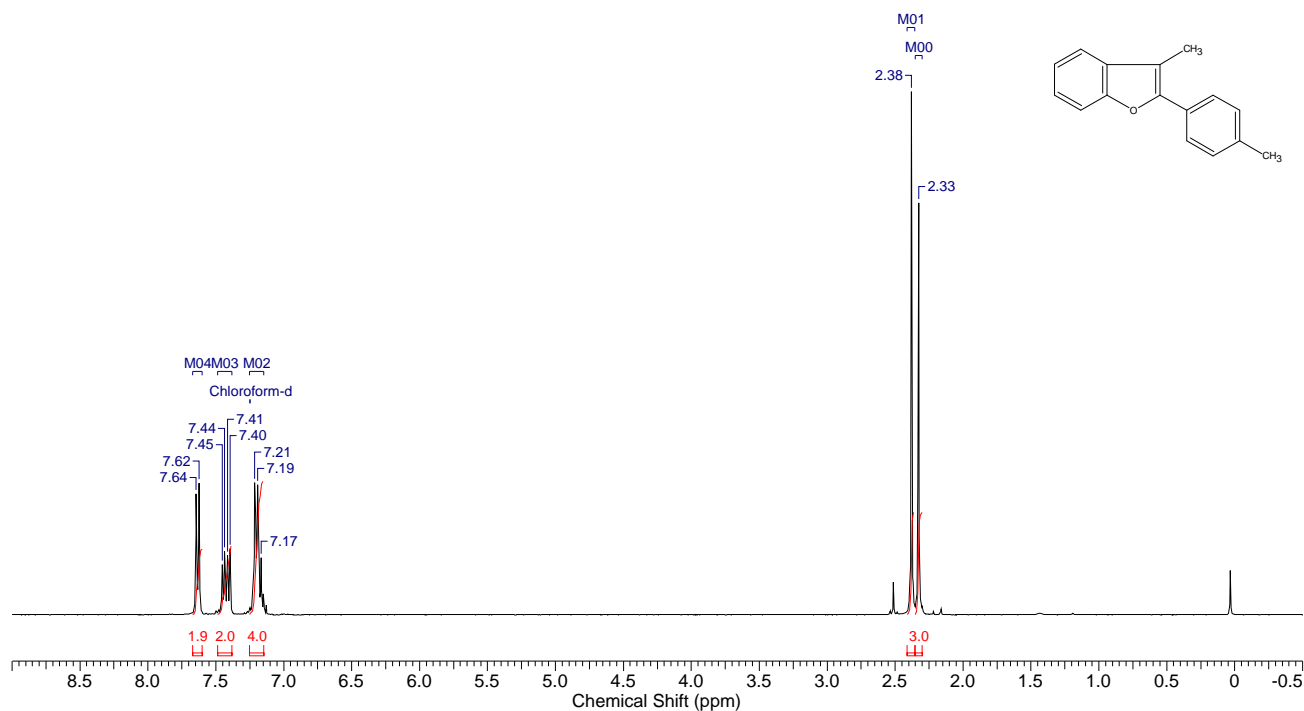


$^{13}\text{C NMR}$ (101 MHz, CHLOROFORM-D) δ ppm 156.1 (s) 154.7 (s) 138.5 (s) 129.4 (s) 129.3 (s) 127.7 (s) 124.8 (s) 124.0 (s) 122.8 (s) 120.7 (s) 111.1 (s) 100.5 (s) 21.4 (s)

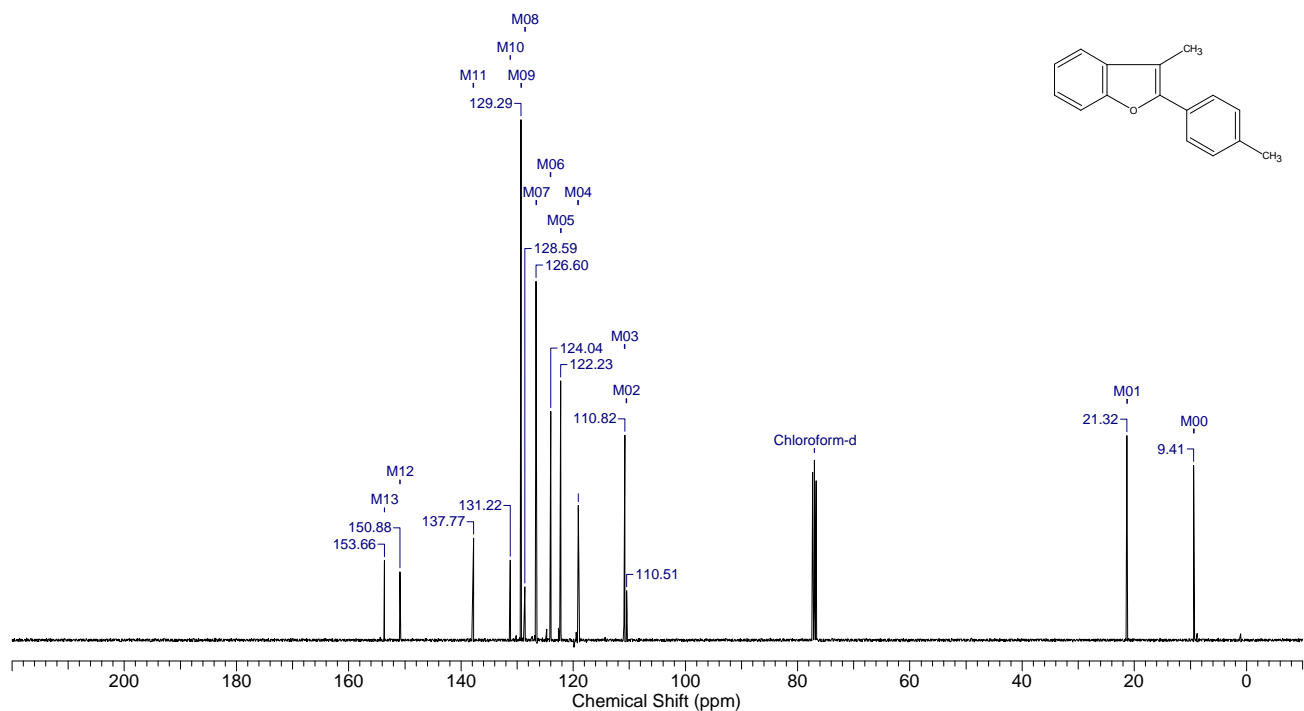


2-(4'-methylphenyl)-3-methyl-benzofuran (3ja)

$^1\text{H NMR}$ (400 MHz, CHLOROFORM-D) δ ppm 7.63 (d, $J=8.2$ Hz, 2 H) 7.43 (dd, $J=16.0, 7.0$ Hz, 2 H) 7.15 - 7.25 (m, 4 H) 2.38 (s, 3 H) 2.33 (s, 3 H)

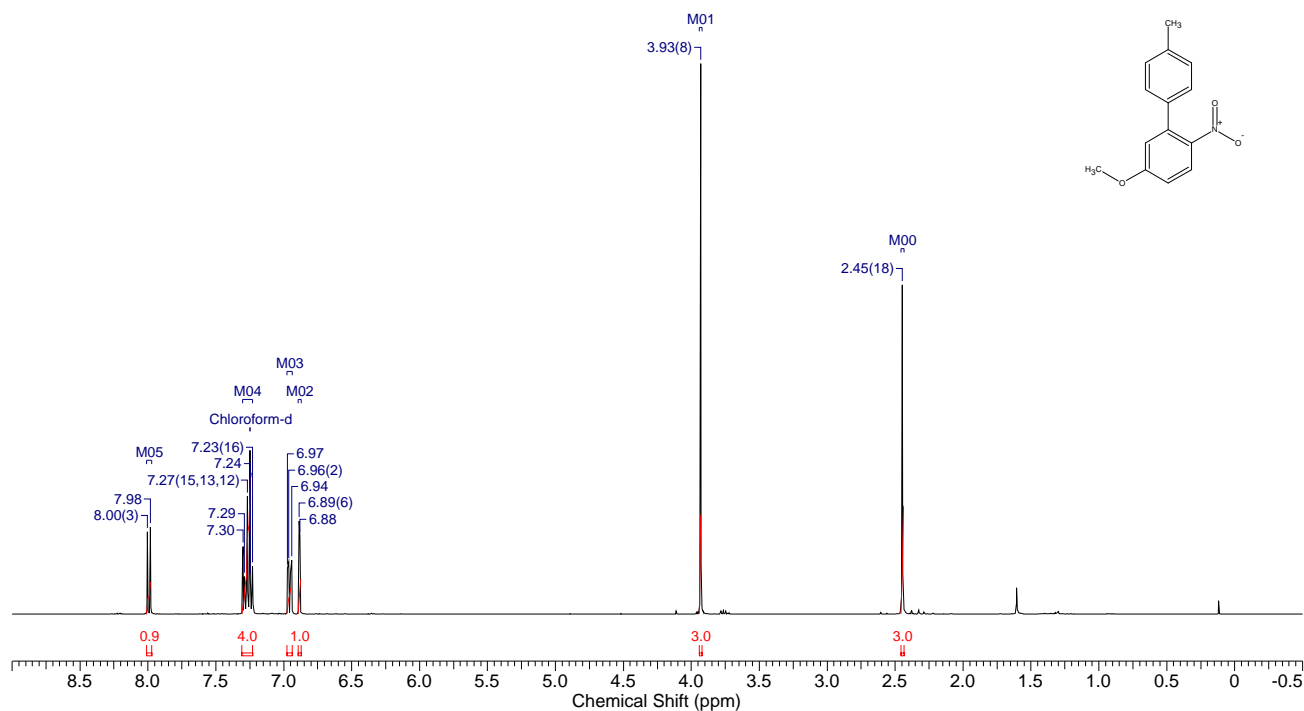


$^{13}\text{C NMR}$ (101 MHz, CHLOROFORM-D) δ ppm 153.7 (s) 150.9 (s) 137.8 (s) 131.2 (s) 129.3 (s) 128.6 (s) 126.6 (s) 124.0 (s) 122.2 (s) 119.1 (s) 110.8 (s) 110.5 (s) 21.3 (s) 9.4 (s)

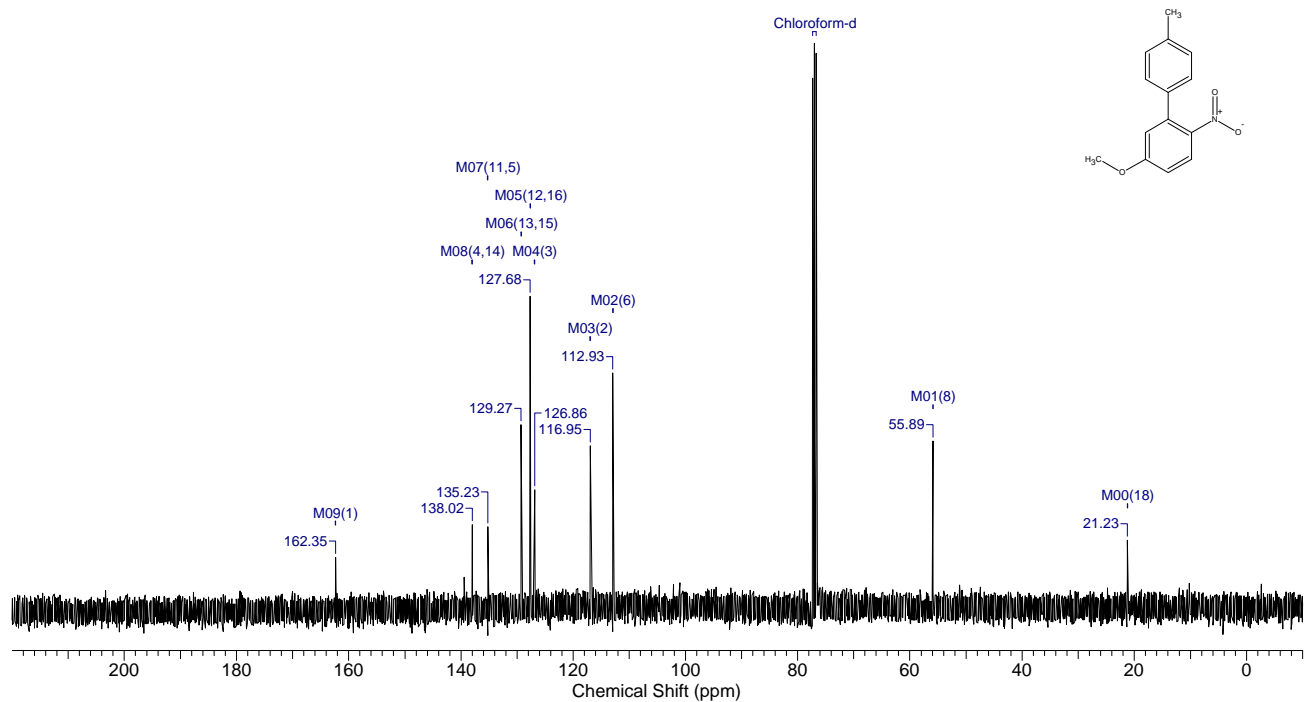


4'-methyl-5-methoxy-2-nitrophenyl (3ka)

¹H NMR (400 MHz, CHLOROFORM-D) δ ppm 7.99 (d, *J*=9.2 Hz, 1 H) 7.23 - 7.30 (m, 4 H) 6.96 (dd, *J*=8.9, 2.9 Hz, 1 H) 6.88 (d, *J*=2.9 Hz, 1 H) 3.93 (s, 3 H) 2.45 (s, 3 H)

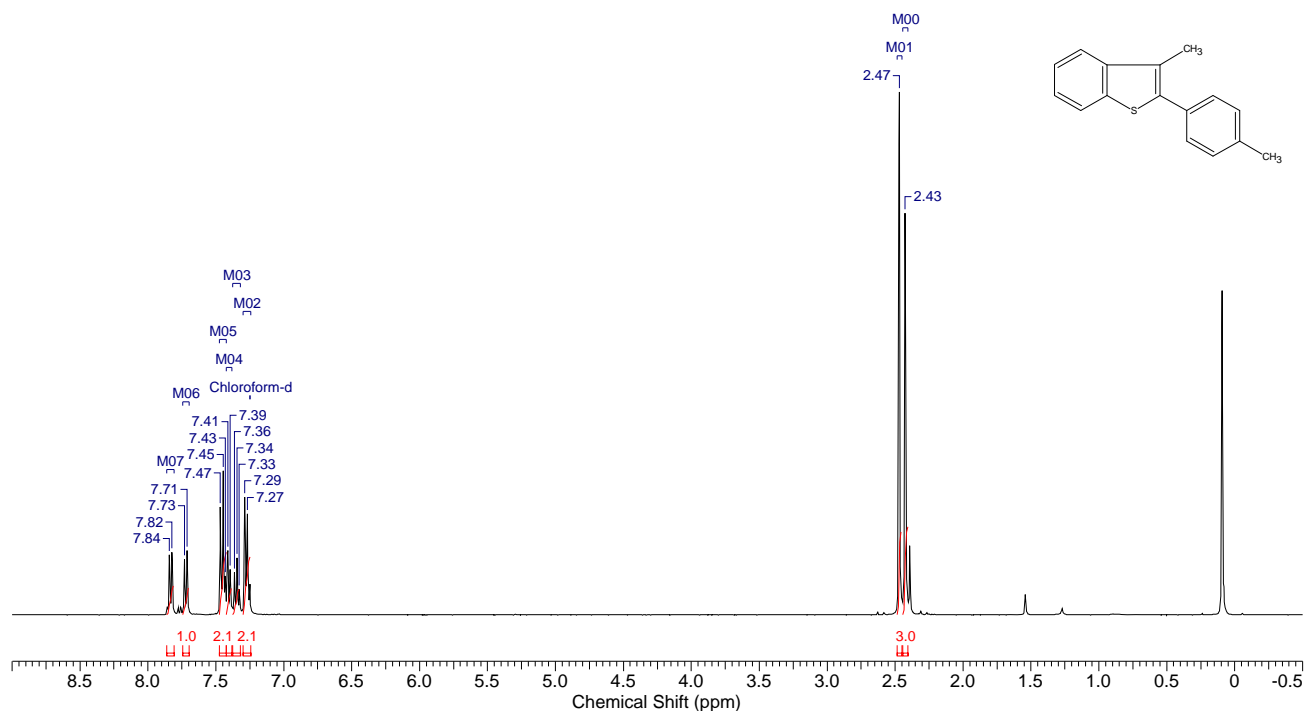


¹³C NMR (101 MHz, CHLOROFORM-D) δ ppm 162.4 (s) 138.0 (s) 135.2 (s) 129.3 (s) 127.7 (s) 126.9 (s) 117.0 (s) 112.9 (s) 55.9 (s) 21.2 (s)

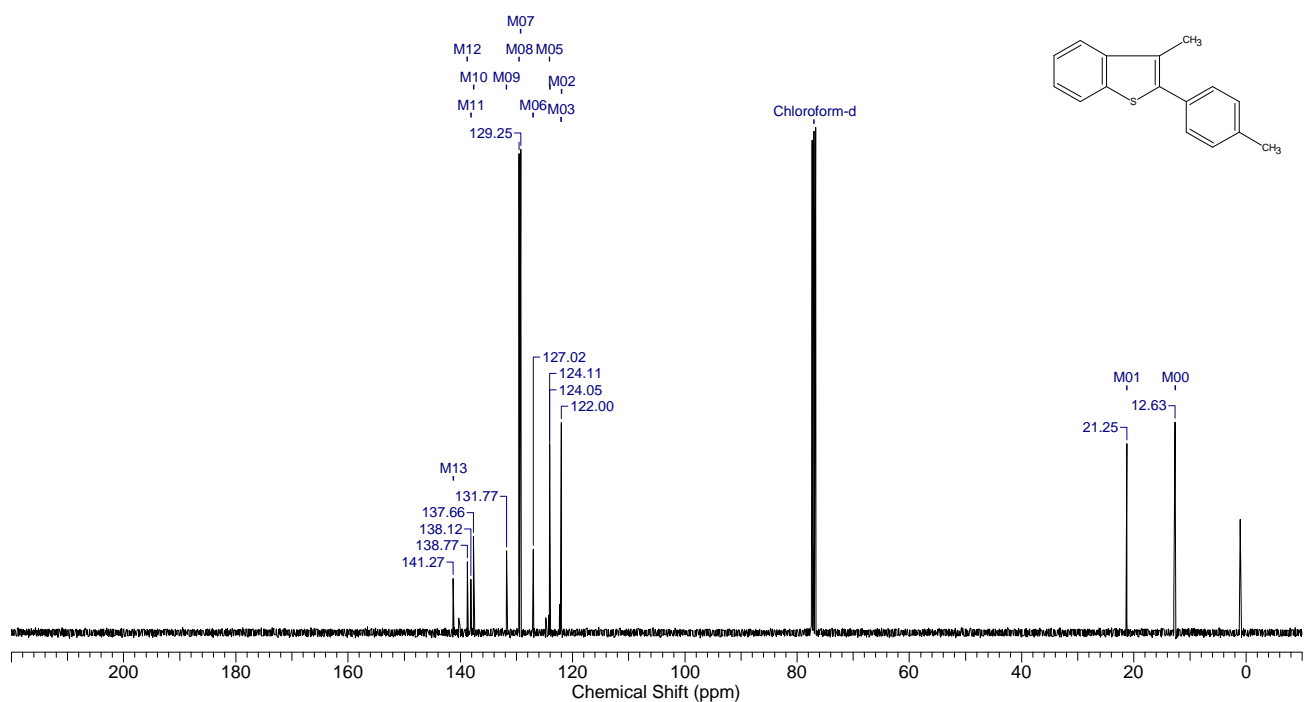


2-(4'-methylphenyl)-3-methyl-benzothiophene (3la)

$^1\text{H NMR}$ (400 MHz, *CHLOROFORM-D*) δ ppm 7.83 (d, $J=7.8$ Hz, 1 H) 7.72 (d, $J=8.2$ Hz, 1 H) 7.45 (t, $J=7.4$ Hz, 2 H) 7.40 (d, $J=7.0$ Hz, 1 H) 7.34 (t, $J=7.0$ Hz, 1 H) 7.28 (d, $J=7.8$ Hz, 2 H) 2.47 (s, 3 H) 2.43 (s, 3 H)

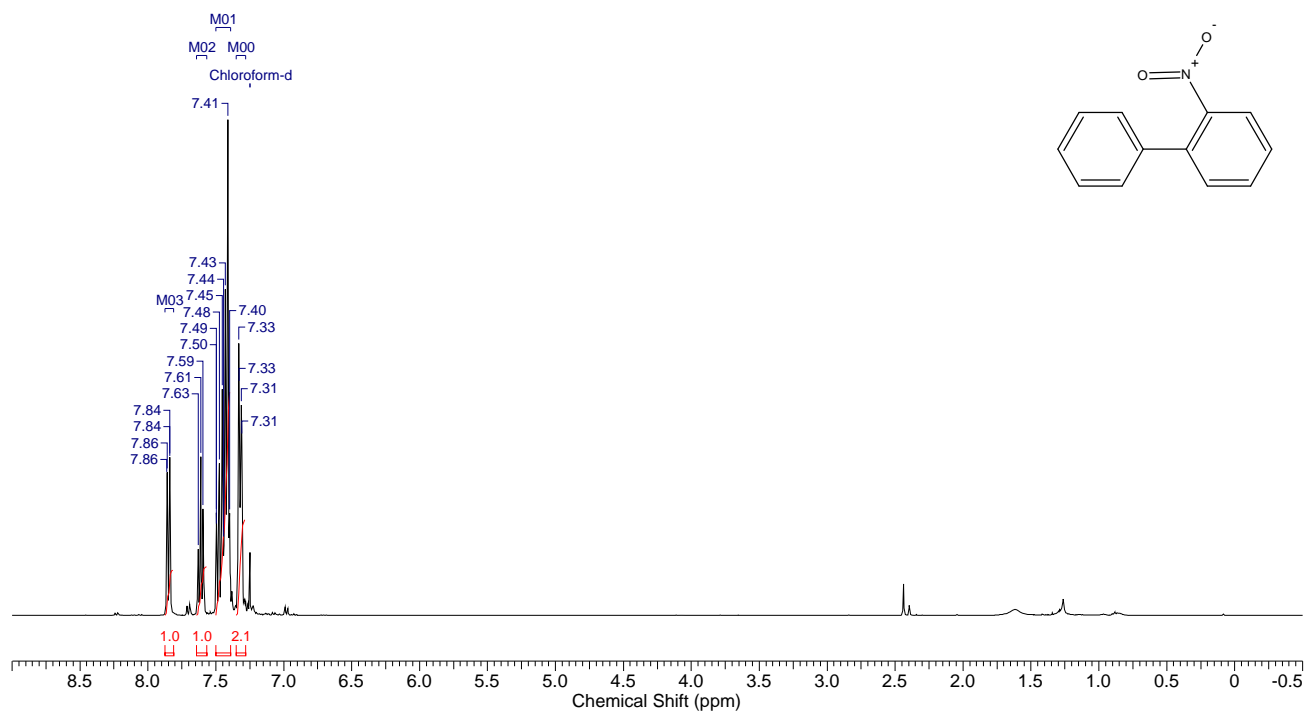


$^{13}\text{C NMR}$ (101 MHz, *CHLOROFORM-D*) δ ppm 141.3 (s) 138.8 (s) 138.1 (s) 137.7 (s) 131.8 (s) 129.5 (s) 129.2 (s) 127.0 (s) 124.1 (s) 124.1 (s) 122.1 (s) 122.0 (s) 21.3 (s) 12.6 (s)

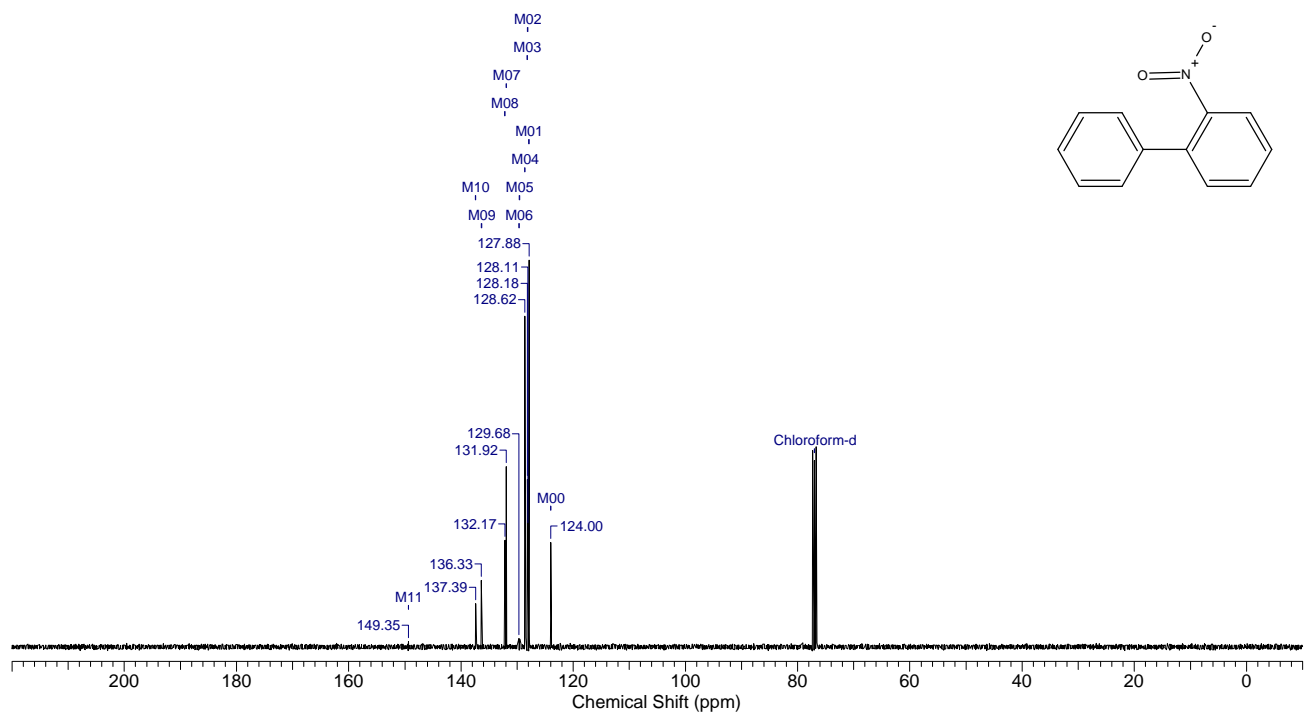


2-nitrobiphenyl (3ab)

^1H NMR (400 MHz, *CHLOROFORM-D*) δ ppm 7.85 (dd, $J=8.0, 1.0$ Hz, 1 H) 7.61 (td, $J=7.5, 1.2$ Hz, 1 H) 7.39 - 7.50 (m, 5 H) 7.32 (dd, $J=7.5, 1.9$ Hz, 2 H)

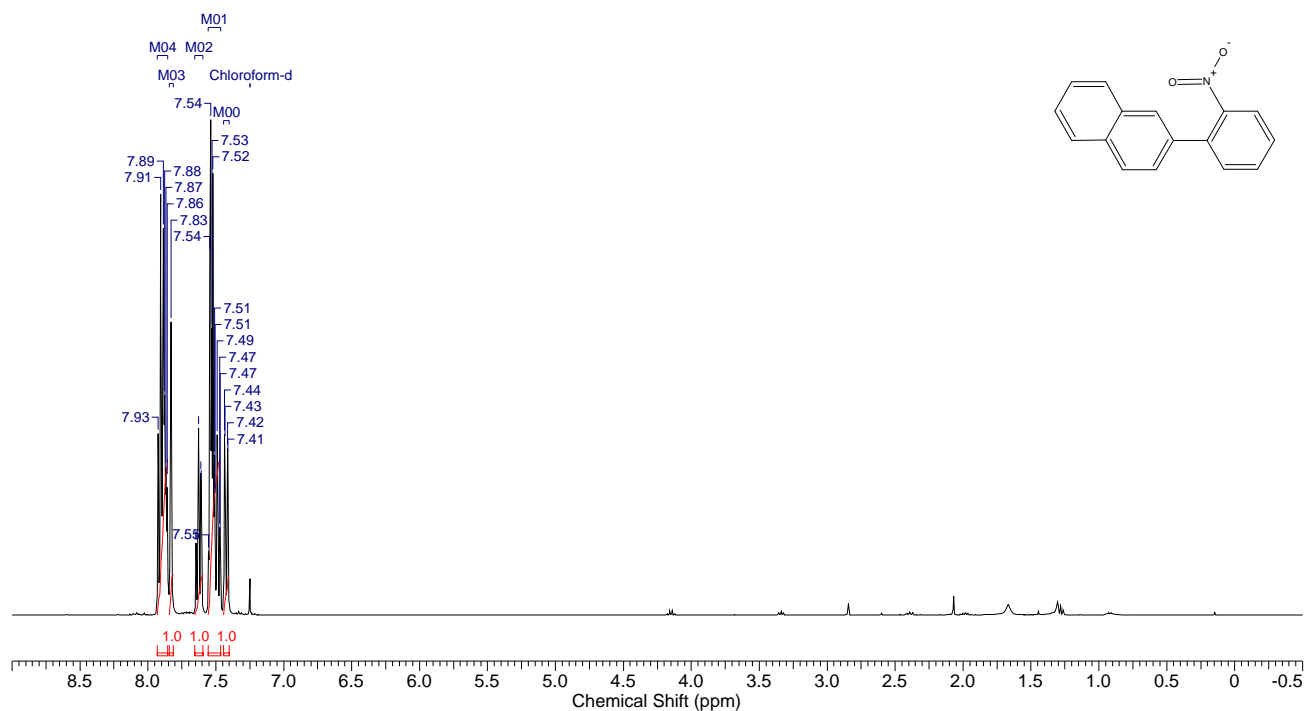


^{13}C NMR (101 MHz, *CHLOROFORM-D*) δ ppm 149.3 (s) 137.4 (s) 136.3 (s) 132.2 (s) 131.9 (s) 129.7 (s) 129.6 (s) 128.6 (s) 128.2 (s) 128.1 (s) 127.9 (s) 124.0 (s)

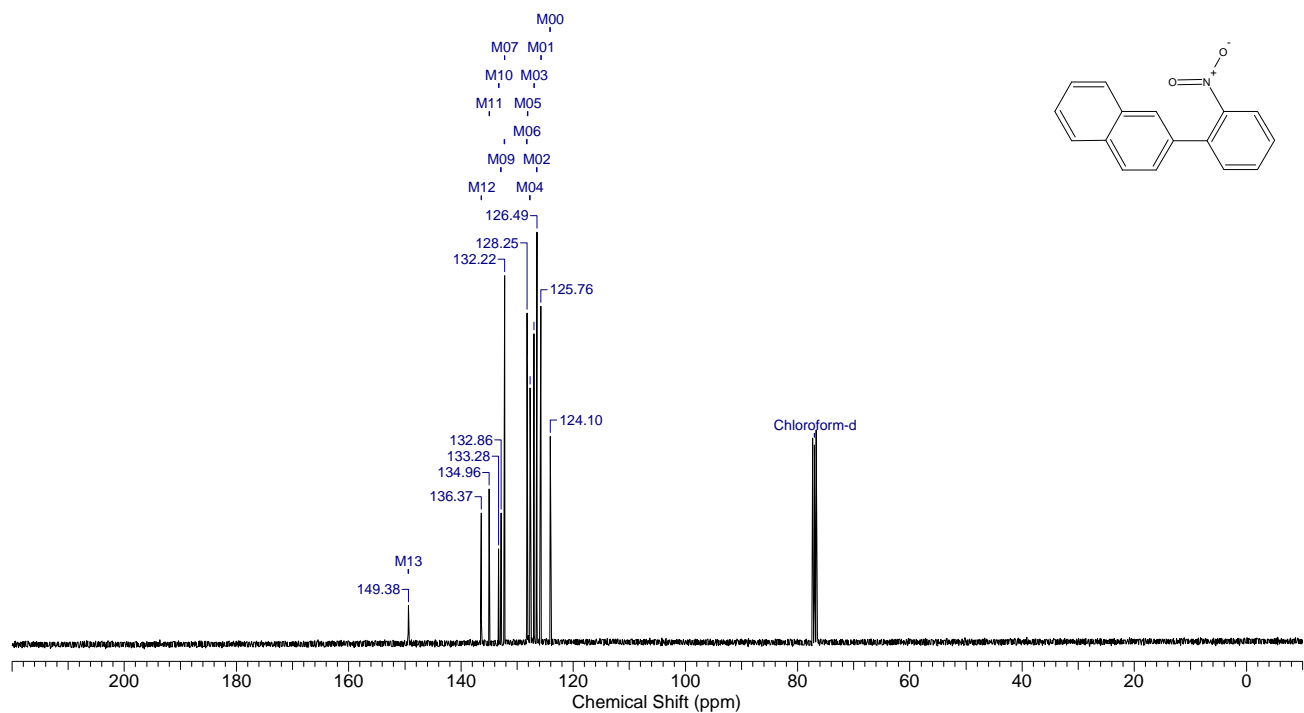


2-(2-nitrophenyl)naphthalene (3ac)

^1H NMR (400 MHz, *CHLOROFORM-D*) δ ppm 7.85 - 7.93 (m, 4 H) 7.83 (s, 1 H) 7.59 - 7.65 (m, 1 H) 7.47 - 7.56 (m, 4 H) 7.42 (dd, $J=8.4, 1.8$ Hz, 1 H)

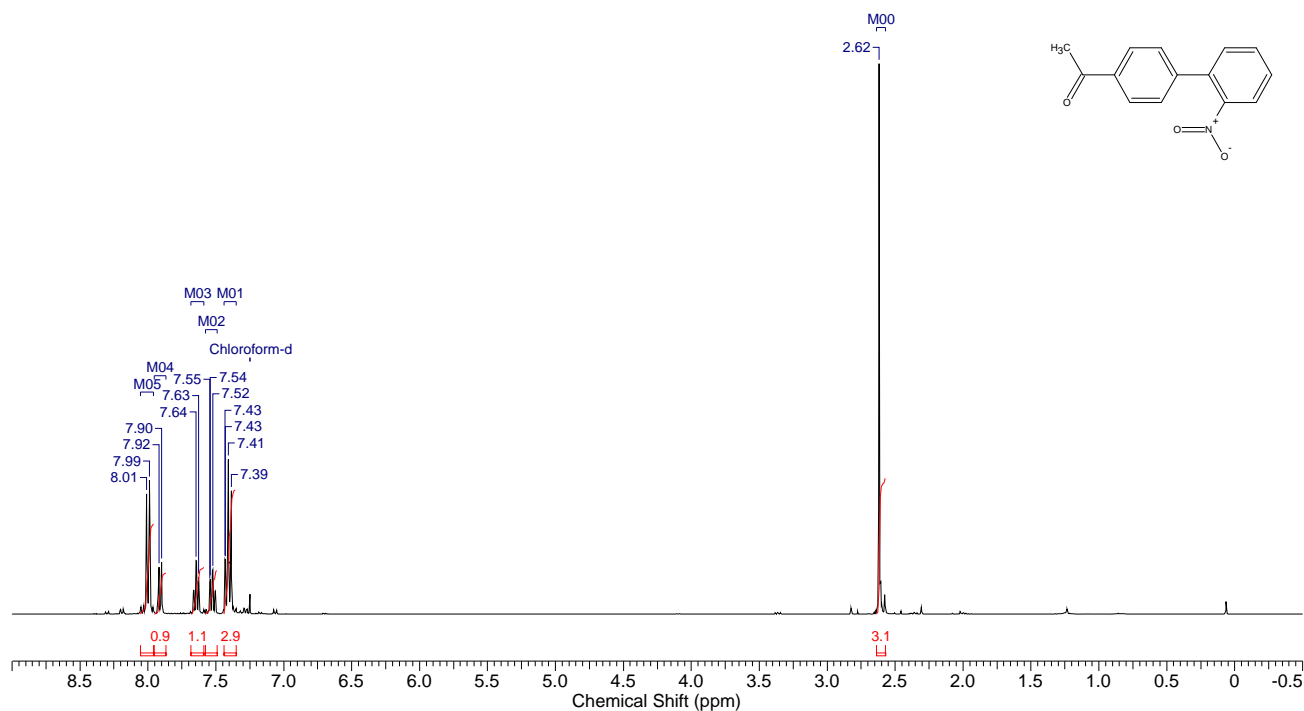


^{13}C NMR (101 MHz, *CHLOROFORM-D*) δ ppm 149.4 (s) 136.4 (s) 135.0 (s) 133.3 (s) 132.9 (s) 132.3 (s) 132.2 (s) 128.3 (s) 128.1 (s) 127.7 (s) 127.0 (s) 126.5 (s) 125.8 (s) 124.1 (s)

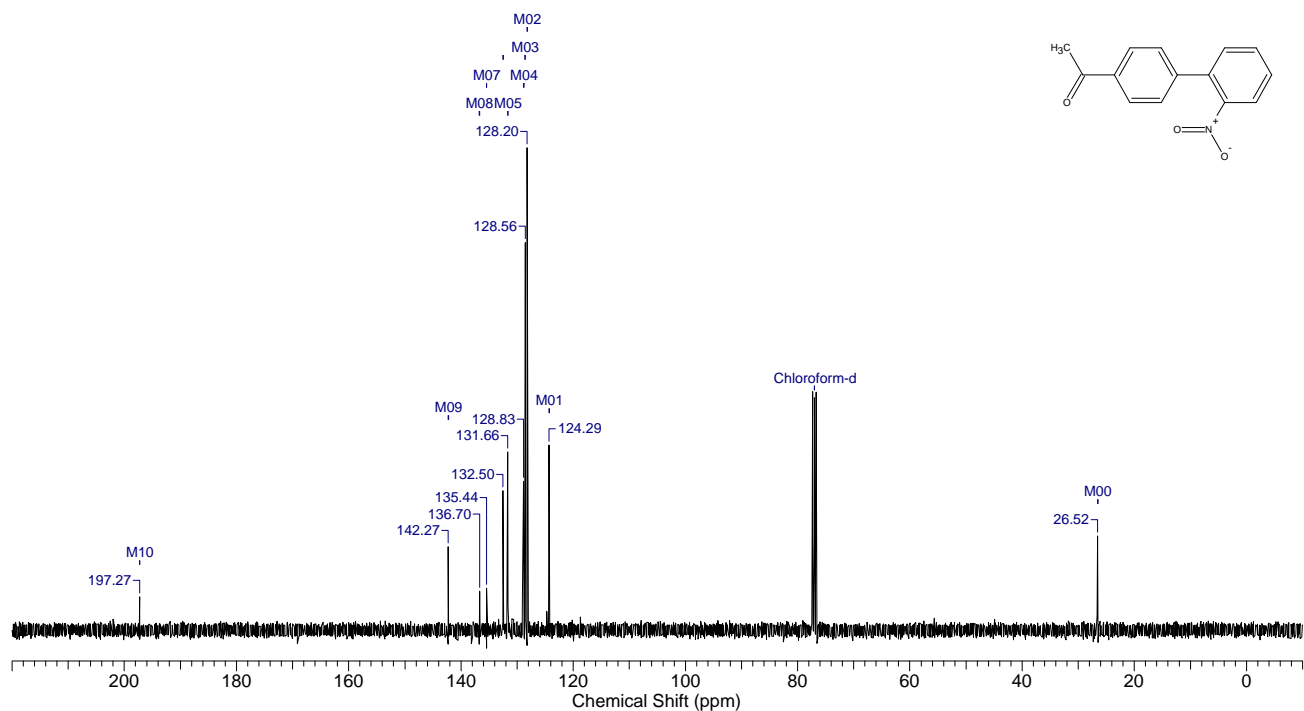


4-acyl-2'-nitrobiphenyl (3ad)

$^1\text{H NMR}$ (400 MHz, *CHLOROFORM-D*) δ ppm 8.00 (d, $J=8.5$ Hz, 2 H) 7.87 - 7.95 (m, 1 H) 7.59 - 7.68 (m, 1 H) 7.49 - 7.58 (m, 1 H) 7.35 - 7.44 (m, 3 H) 2.62 (s, 3 H)

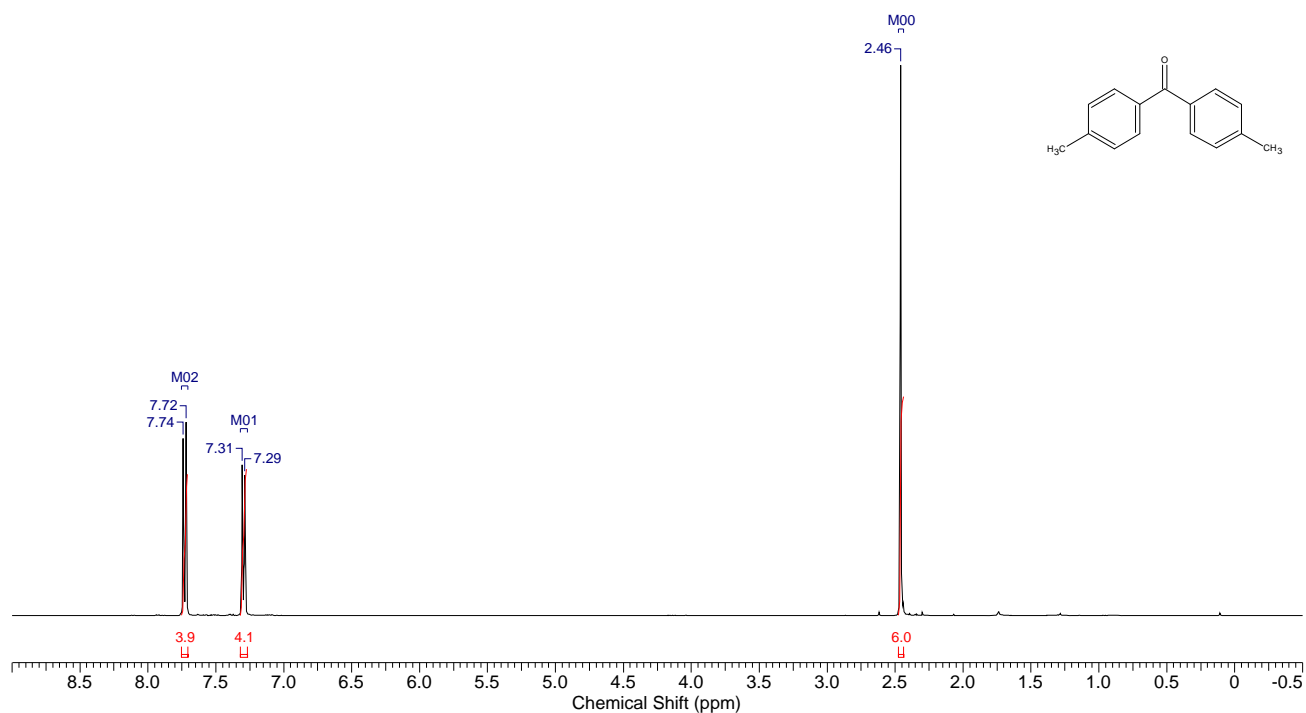


$^{13}\text{C NMR}$ (101 MHz, *CHLOROFORM-D*) δ ppm 197.3 (s) 142.3 (s) 136.7 (s) 135.4 (s) 132.5 (s) 131.7 (s) 128.8 (s) 128.6 (s) 128.2 (s) 124.3 (s) 26.5 (s)



4,4'-dimethylbiphenyl-2-one (3na)

$^1\text{H NMR}$ (400 MHz, CHLOROFORM-D) δ ppm 7.73 (d, $J=8.0$ Hz, 4 H) 7.30 (d, $J=8.0$ Hz, 4 H) 2.46 (s, 6 H)



$^{13}\text{C NMR}$ (101 MHz, CHLOROFORM-D) δ ppm 196.1 (s) 142.8 (s) 135.3 (s) 130.1 (s) 128.9 (s) 21.5 (s)

