Electronic Supplementary Information

Diastereoselective synthesis of CF_3-dihydrobenzofurans by [4+1] annulation of*in-situ* generated CF_3-*o*-quinone methides and sulfur ylides

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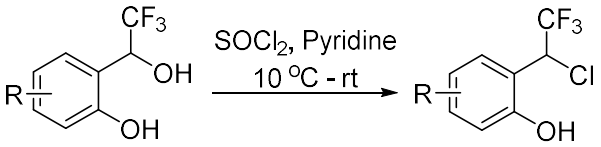
1. General information

All chemicals have been purchased from commercial sources and were used without further purification unless otherwise noted. All solvents are reagent grade or HPLC grade. Anhydrous acetonitrile (CH_3CN), dichloromethane (CH_2Cl_2) and N,N-dimethylformamide (DMF) were obtained from a dry solvent system. Dichloromethane was freshly distilled from CaH_2 and anhydrous tetrahydrofuran (THF) was freshly distilled from sodium-benzophenone. The synthetic transformations have been monitored by thin layer chromatography (TLC). TLC was performed on silica gel 60 F254 plates (glass plates). Concentration under reduced pressure was performed by rotary evaporation below 45 °C. Column chromatography was performed using silica gel (100-200 mesh) packed in glass columns. Yields refer to spectroscopically pure compounds after isolation. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded in $CDCl_3$ using 300, 400 or 500 MHz (^{1}H), 75, 100 or 125 MHz (^{13}C) and 377 MHz (19F). Chemical shifts (δ-values) are reported in ppm, spectra were calibrated related to solvents' residual proton chemical shifts ($CDCl_3$, δ = 7.26) and solvents' residual carbon chemical shifts ($CDCl_3$, δ = 77.16 ppm), multiplicity is reported as follows: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet or unresolved and coupling constant *J* in Hz. Melting points (mp) were determined in open capillaries and are uncorrected. Infrared spectra (IR) were recorded in a chlorofom. High-resolution mass spectra (HRMS) and APCI were obtained by electrospray ionization using a Q-TOF mass spectrometer in positive and negative ion mode as indicated.

2. General experimental procedure for the synthesis of 2-(1-chloro-2,2,2-trifluoroethyl)-phenols (1a-e)

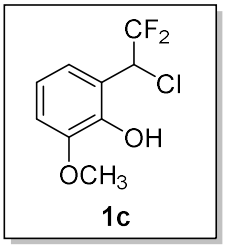


S1a-e **1a-e**

Prepared following the procedure reported in *J. Fluorine Chem.* 2003, **121**, 141-146. To a mixture of 2-(2,2,2-trifluoro-1-hydroxyethyl)phenols[1,2] **S1a-e** (10 mmol) and thionyl chloride (14 mmol) in dry toluene (15 ml) at –5 °C was added pyridine (10 mmol) slowly by maintaining the reaction temperature below 10 °C. Then reaction mixture was stirred at room temperature until completion of the starting material, complete consumption of starting material as monitored by TLC. Then reaction mixture was poured in to crushed ice and extracted with ethyl acetate (3 X 50 mL). The combined organic extracts were washed with diluted HCl (1 M) followed by water, and dried over sodium sulphate and concentrated in *vacuo* to give the desired 2-(1-chloro-2,2,2-trifluoroethyl)-phenols (**1a-e**) in good

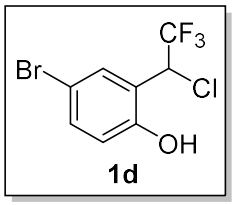
yields and used for further reactions without any purification (compounds are stored under inert atmosphere in a cool place).[1,2]

2-(1-Chloro-2,2,2-trifluoroethyl)-6-methoxyphenol (1c)



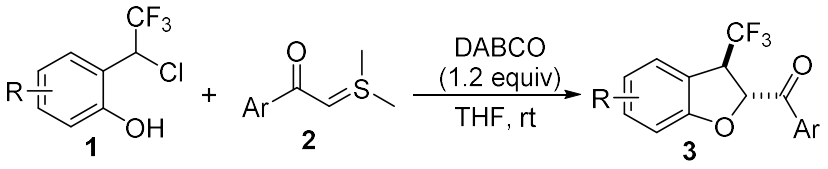
Following the general procedure, **1c** was obtained as brown liquid (yield: 69%);**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21–7.18 (m, 1H), 6.92 (t, *J* = 8.0 Hz, 1H), 6.89–6.86 (m, 1H), 6.00 (s, 1H), 5.79 (q, *J* = 7.0 Hz, 1H), 3.90 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ146.2, 143.9, 123.7 (q, *J* = 279.0 Hz), 121.0, 120.2, 118.2, 111.5, 56.2, 51.1 (q, *J* = 35.2 Hz); **^{19}F NMR** (376 MHz,$CDCl_3$) δ –73.28 (s, 3F); **IR ($CHCl_3$)ν_{max}** 3480, 2930, 2820, 1580, 1220, 740 cm^{-1}; APCI-MS: *m/z* calculated for $[M–F]^-$ $C_9H_8ClF_2O_2$ 221.0180, found 221.02**.**

4-Bromo-2-(1-chloro-2,2,2-trifluoroethyl)phenol (1d)



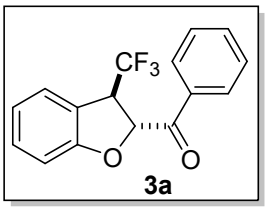
Following the general procedure, **1d** was obtained as brown liquid (yield: 72%);**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69–7.66 (s, 1H), 7.32 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.74 (d, *J* = 8.6 Hz, 1H), 5.71 (q, *J* = 6.9 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.6, 133.9, 132.6, 123.5 (q, *J* = 279.0 Hz), 121.3, 117.4, 113.2, 50.8 (q, *J* = 35.3 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ –73.13 (s, 3F); **IR ($CHCl_3$)ν_{max}** 3460, 2910, 1540, 1210, 770cm^{-1}; APCI-MS: *m/z* calculated for $[M–F]^-$ $C_8H_5BrClF_2O$ 268.9180, found 268.92**.**

3. Typical procedure for the synthesis of CF_3-dihydrobenzofurans (3)



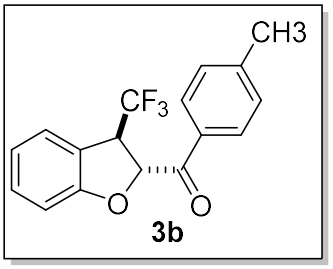
To a 10 mL single neck round bottom flask were added **1** (0.6 mmol) and THF (2 mL) followed by added the sulphur ylide **2a** (0.5 mmol) and DABCO (0.6 mmol) respectively at room temperature under nitrogen atmosphere. Then reaction mixture was stirred at room temperature for 8 h. The progress of reaction was monitored by TLC. After consumption of starting material, the reaction mixture was diluted with water and extracted with EtOAc (3 X 20 mL). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated in *vacuo*. The obtained crude mixture was purified by using column chromatography (using 1:9 EtOAc/hexane) to give desired product **3a** in good yield with excellent *dr* value (>20:1). The characterization data of **3a** is summarized below.

Phenyl(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone(3a)



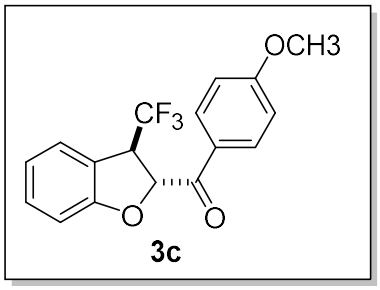
Following the general procedure, **3a** was obtained as white solid (136 mg, yield: 93%) m.p.= 89°C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17–8.11 (m, 2H), 7.69– 7.62 (m, 1H), 7.57–7.51 (m, 2H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.29–7.23 (m, 1H), 7.01–6.96 (m,1H), 6.87 (d, *J* = 8.2 Hz, 1H), 5.96 (d, *J* = 4.7 Hz, 1H), 4.89 (qd, *J* = 8.9, 4.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.0, 159.1, 134.2, 133.9, 130.6, 129.8, 128.8, 125.9,125.8 (q, *J* = 278.3 Hz), 121.9, 119.6, 110.4, 81.9, 47.4 (q, *J* = 30.1 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -70.47 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2880, 1715, 1580, 1255, 1180, 1085, 775cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{16}H_{12}O_2F_3$ $[M + H]^+$ 293.0790, found 293.0789**.**

***p*-Tolyl(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone(3b)**



Following the general procedure, **3b** was obtained as white solid (139 mg, yield: 91%), m.p.= 82 ^{o}C;**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05–8.01 (m, 2H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.28–7.22 (m, 1H), 6.99–6.94 (m, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 5.94 (d, *J* = 4.7 Hz, 1H), 4.88 (qd, *J* = 8.9, 4.7 Hz, 1H), 2.44 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.8, 159.6, 145.7, 131.7, 130.8, 130.2, 129.8, 126.1 (q, *J* = 278.3 Hz), 126.2, 122.1, 119.9, 110.6, 82.2, 47.3 (q, *J* = 30.1 Hz), 21.10; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.30 (s, 3F).**IR($CHCl_3$)ν_{max}** 2890, 1715, 1575, 1245, 1180, 1075, 765 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{17}H_{14}O_2F_3$ $[M+H]^+$ 307.0946, found 307.0946**.**

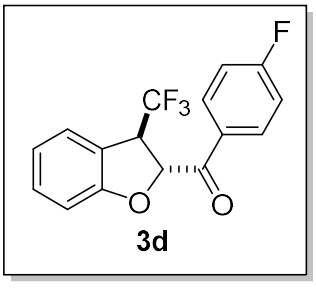
(4-Methoxyphenyl)(3-(trifluoromethyl)-2,3dihydrobenzofuran-2-yl)methanone (3c)



3c

Following the general procedure, **3c** was obtained as white solid (145 mg, yield: 90%), m.p.= 84^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16–8.10 (m, 2H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.28–7.23 (m, 1H), 7.04–6.94 (m, 3H), 6.87 (d, *J* = 8.1 Hz, 1H), 5.92 (d, *J* = 4.7 Hz, 1H), 4.90 (qd, *J* = 8.9, 4.7 Hz, 1H), 3.90 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.3, 164.4, 159.3, 132.2,130.6, 126.9, 125.9,125.9 (q, *J* = 278.2 Hz), 121.8, 119.7, 114.1, 110.3, 81.9, 55.6, 47.3 (q, *J* = 30.0 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.60 (s, 3F); **IR($CHCl_3$) ν_{max}** 2889, 1710, 1573, 1238, 1160, 1085, 760cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{17}H_{14}O_3F_3$ $[M+H]^+$ 323.0895, found 323.0895 **.**

(4-Fluorophenyl)(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3d)

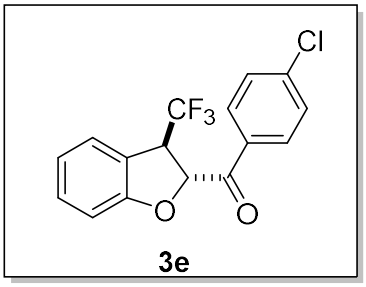


3d

Following the general procedure, **3d** was obtained as white solid (125.5 mg, yield: 81%), m.p.= 65 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.22–8.16 (m, 2H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.30–7.24 (m,

1H), 7.24 –7.19 (m, 2H), 7.02–6.96 (m, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 5.90 (d, *J* = 4.7 Hz, 1H), 4.91 (qd, *J* = 8.9, 4.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, CDCl3) δ 190.5, 166.4 (d, *J* = 257.0 Hz,), 159.0, 132.7 (d, *J* = 9.6 Hz), 130.7, 130.4, 126.0, 125.8 (d, *J* = 267.0 Hz), 122.0, 119.6, 116.1 (d, *J* = 22.0 Hz), 110.4, 82.1, 47.3 (q, *J* = 30.2 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.81(s, 3F), -102.74(s, 1F); **IR($CHCl_3$)** ν_{max} 2880, 1715, 1575, 1245, 1150, 1065, 755 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{16}H_{11}O_2F_4$ $[M + H]^+$: 311.0696, found 311.0695**.**

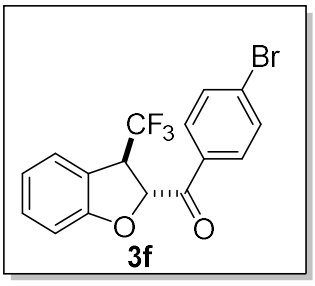
(4-Chlorophenyl)(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone(3e)



3e

Following the general procedure, **3e** was obtained as white solid (137 mg, yield: 84%), m.p.= 69 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11–8.06 (m, 2H), 7.54–7.49 (m, 2H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.30–7.24 (m, 1H), 6.99 (td, *J* = 7.5, 0.8 Hz, 1H), 6.86 (d, *J* = 8.2 Hz, 1H), 5.89 (d, *J* = 4.7 Hz, 1H), 4.90 (qd, *J* = 8.9, 4.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.9, 159.0, 132.7,132.2, 131.3, 130.7, 129.7, 125.9,125.7 (q, *J* = 278.3 Hz), 122.1, 119.5, 110.4, 82.1, 47.2 (q, *J* = 30.2 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.46 (s, 3F); **IR($CHCl_3$)** ν_{max} 2910, 1713, 1575, 1240, 1170, 1073, 770cm^{-1}; **HRMS(ESI)**: *m/z* calculated for $C_{16}H_{11}O_2F_3Cl$ $[M+H]^+$ 327.0400, found 327.0402.

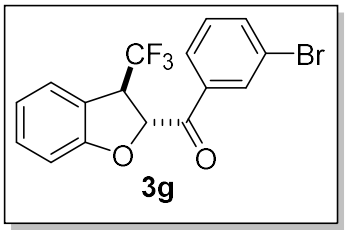
(4-Bromophenyl)(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3f)



3f

Following the general procedure, **3f** was obtained as white solid (157 mg, yield: 85%), m.p.= 63 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02–7.97 (m, 2H), 7.71–7.64 (m, 2H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.29 –7.23 (m, 1H), 6.98 (td, *J* = 7.5, 0.8 Hz, 1H), 6.86 (d, *J* = 8.2 Hz, 1H), 5.88 (d, *J* = 4.6 Hz, 1H),4.90 (qd, *J* = 8.8, 4.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ191.2, 159.0, 132.7, 132.2, 131.3, 130.7, 129.7, 125.9,125.8 (q, *J* = 278.3 Hz), 122.1, 119.5, 110.4, 82.1, 47.2 (q, *J* = 30.2 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.46 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2885, 1715, 1560, 1245, 1180, 1070, 773cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{16}H_{11}O_2F_3Br$ $[M+H]^+$ 370.9895, found 370.9896.

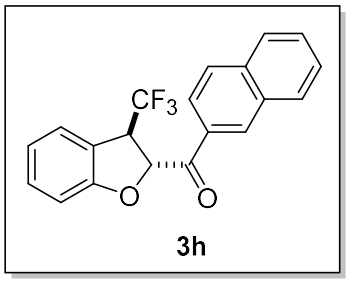
(3-Bromophenyl)(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3g)



3g

Following the general procedure, **3g** was obtained as white solid (144 mg, yield: 78%), m.p.= 64 °C;**^{1}H NMR** (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (t, *J* = 1.7 Hz, 1H), 8.09-8.06 (m, 1H), 7.80-7.76 (m, 1H), 7.45-7.37 (m, 2H), 7.30 –7.24 (m, 1H), 7.00 (td, *J* = 7.5, 0.9 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 5.88 (d, *J* = 4.6 Hz, 1H),4.89 (qd, *J* = 8.8, 4.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.9, 158.9, 137.1, 135.7, 132.7,130.4, 138.8, 128.4, 125.9, 125.7 (q, *J* = 278.3 Hz), 123.1, 122.1, 119.4, 110.5, 82.1, 47.2 (q, *J* = 30.3 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.40 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2880, 1710, 1570, 1235, 1170, 1065, 770 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{16}H_{11}O_2F_3Br$ $[M+H]^+$ 370.9895, found 370.9896.

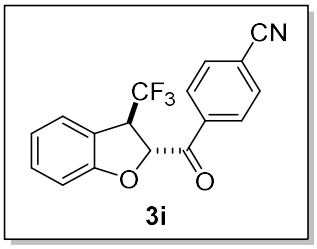
Naphthalen-2-yl(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3h)



3h

Following the general procedure, **3h** was obtained as white solid (126.6 mg, yield: 74%), m.p.= 105 °C;**^{1}H NMR** (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 1.0 Hz, 1H), 8.12 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.04 (d, *J* = 8.0, 0, 1H), 7.97–7.89 (m, 2H), 7.68–7.58 (m, 2H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.29–7.24 (m, 1H), 6.99 (td, *J* = 7.5, 0.9 Hz, 1H), 6.88 (d, *J* = 8.1 Hz, 1H), 6.11 (d, *J* = 4.6 Hz, 1H), 4.96 (qd, *J* = 8.9, 4.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.6, 159.4, 136.1, 132.45, 132.3, 131.3, 130.7, 129.9, 129.3, 128.8, 127.9, 127.1, 126.0,125.9 (q, *J* = 278.1 Hz), 124.6, 121.9, 119.7, 110.4, 82.1, 47.4 (q, *J* = 30.1 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.40 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2880, 1710, 1585, 1240, 1185, 770cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{20}H_{14}O_2F_3$ $[M+H]^+$ 343.0946, found 343.0947.

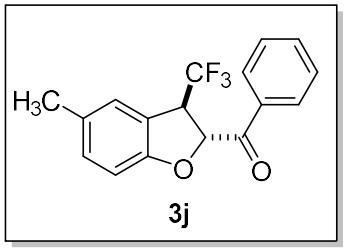
4-(3-(Trifluoromethyl)-2,3-dihydrobenzofuran-2-carbonyl)benzonitrile (3i)



3i

Following the general procedure, **3i** was obtained as white solid (117.3 mg, yield: 71%), m.p.= 102 °C;**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26–8.22 (m, 2H), 7.86–7.82 (m, 2H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.30–7.27 (m, 1H), 7.04–6.99 (m, 1H), 6.86 (d, *J* = 8.2 Hz, 1H), 5.89 (d, *J* = 4.6 Hz, 1H), 4.91 (qd, *J* = 8.7, 4.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.9, 158.6, 137.0, 132.6, 130.8, 130.3, 126.0,125.6 (q, *J* = 278.4 Hz), 122.3, 119.3, 117.7, 117.4, 110.5, 82.3, 47.2 (q, *J* = 30.3 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.44 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2885, 1714, 1580,1245, 1180, 1060, 780 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{17}H_9F_3NO_2$ $[M - H]^-$ 316.0579 , found 316.0569

(5-Methyl-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3j)

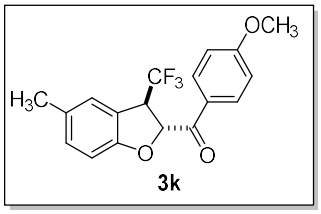


3j

Following the general procedure, **3j** was obtained as colorless oil (151 mg, yield: 82%);**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14–8.12 (m, 2H), 7.67–7.62 (m, 1H), 7.56–7.50 (m, 2H), 7.18 (s, 1H),

7.07–7.03 (m, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 5.93 (d, *J* = 4.6 Hz, 1H), 4.83 (qd, *J* = 8.9, 4.6 Hz, 1H), 2.31 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.4, 152.5, 129.5, 129.3, 126.7, 126.4, 125.0, 124.1, 121.5, 121.1 (q, *J* = 278.3 Hz), 114.8, 105.2, 77.3,42.6 (q, *J* = 30.0 Hz), 16.0; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.44 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2855, 1715, 1590, 1450, 1250, 1180, 785 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{17}H_{14}O_2F_3$ $[M+H]^+$ 307.0901, found 307.0912.

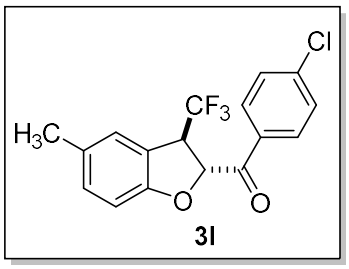
(4-Methoxyphenyl)(5-methyl-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3k)



3k

Following the general procedure, **3k** was obtained as colorless oil (161.3 mg, yield: 80%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14–8.09 (m, 2H), 7.18 (s, 1H), 7.07–7.03 (m, 1H), 7.02–6.98 (m, 2H), 6.75 (d, *J* = 8.2 Hz, 1H), 5.89 (d, *J* = 4.7 Hz, 1H), 4.84 (qd, *J* = 8.9, 4.7 Hz, 1H), 3.91 (s, 3H), 2.31 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.5, 164.4, 157.2, 132.2, 131.3, 130.9, 127.1, 126.3, 125.94 (q, *J* = 278.4 Hz), 119.7, 114.1, 109.8, 82.0, 55.4, 47.4 (q, *J* = 30.0 Hz), 20.8; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.44 (s, 3F); **IR($CHCl_3$)** ν_{max} 2957, 2847, 1715, 1455, 1417, 1245, 1165, 755cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{18}H_{16}O_3F_3$ $[M+H]^+$ 337.1007, found 337.1022.

(4-Chlorophenyl)(5-methyl-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3l)

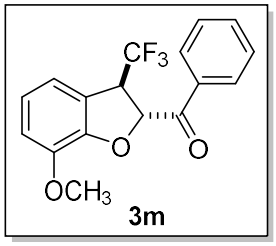


3l

Following the general procedure, **3l** was obtained as colorless oil (131 mg, yield: 77%);**^{1}H NMR** (400 MHz, $CDCl_3$) δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09–8.04 (m, 2H), 7.54–7.45 (m, 2H), 7.18 (s, 1H), 7.07–7.03 (m, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 5.86 (d, *J* = 4.6 Hz, 1H), 4.85 (qd, *J* = 8.9, 4.6 Hz, 1H), 2.30 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.2, 157.0, 140.8, 132.4, 131.6, 131.24, 131.21, 129.2, 126.3,125.8 (q, *J* = 278.3 Hz), 119.4, 109.9, 82.0, 47.3 (q, *J* = 30.1 Hz), 20.8; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.42 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2855, 1715, 1590, 1250,

1180, 785 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{17}H_{13}O_2F_3Cl$ $[M+H]^+$ 341.0556, found 341.0545.

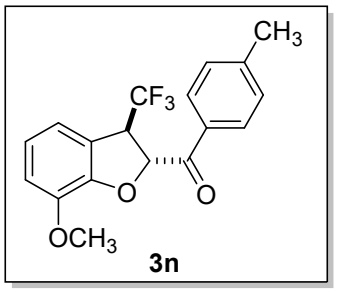
(7-Methoxy-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3m)



3m

Following the general procedure, **3m** was obtained as colorless oil (114 mg, yield: 71%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14–8.17 (m, 2H), 7.68–7.61 (m, 1H), 7.56–7.50 (m, 2H), 6.99 (dd, *J* = 7.5, 0.7 Hz, 1H), 6.94 (t, *J* = 7.8 Hz, 1H), 6.86 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.02 (d, *J* = 4.8 Hz, 1H),4.87 (qd, *J* = 8.8, 4.8 Hz, 1H), 3.83 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.7, 148.0, 144.8, 134.3, 133.9, 129.8, 128.9, 125.8 (q, *J* = 278.4 Hz), 122.7, 120.8, 117.7, 113.7, 82.3, 56.1, 48.0 (q, *J* = 30.2 Hz), 29.7; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.38 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2946, 2835, 1712, 1410, 1242, 1165, 755 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{17}H_{14}O_3F_3$ $[M+H]^+$ 323.0850, found 323.0863.

(7-Methoxy-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(p-tolyl)methanone (3n)

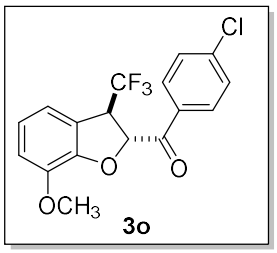


3n

Following the general procedure, **3n** was obtained as colorless oil (122.6 mg, yield: 73%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07–8.03 (m, *J* = 8.0 Hz, 2H), 7.35–7.32 (m, 2H), 6.99 (dd, *J* = 7.3 Hz, 1H), 6.93 (t, *J* = 7.7 Hz, 1H), 6.86 (dd, *J* = 7.8 Hz, 1H), 5.99 (d, *J* = 4.6 Hz, 1H), 4.86 (qd, *J* = 8.8, 4.8 Hz, 1H), 3.83 (s, 3H), 2.44 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.3, 148.1, 145.4, 144.8, 131.4, 129.9, 129.6, 125.8 (q, *J* = 278.4 Hz), 122.6,

120.9, 117.7, 113.7, 82.2, 56.2, 48.1 (q, J = 30.1 Hz), 21.8; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.37 (s, 3F); **IR($CHCl_3$)** ν_{max} 2947, 2837, 1710, 1465, 1415, 1240, 1155, 758 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{18}H_{16}O_3F_3$ $[M+H]^+$ 337.1007, found 337.1022.

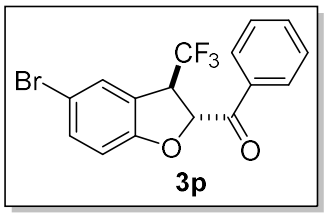
(4-Chlorophenyl)(7-methoxy-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3o)



3o

Following the general procedure, **3o** was obtained as colorless oil (135.3 mg, yield: 76%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04–7.98 (m, 2H), 7.45–7.36 (m, 2H), 6.90 (dd, J = 7.5, 0.8 Hz, 1H), 6.85 (t, J = 7.8 Hz, 1H), 6.77 (dd, J = 8.0, 1.0 Hz, 1H), 5.85 (d, J = 4.8 Hz, 1H), 4.81 (qd, J = 8.8, 4.8 Hz, 1H), 3.73 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.8, 147.8, 144.8, 140.9, 132.3, 131.2, 129.3, 125.72 (q, J = 278.4 Hz), 122.8, 120.7, 117.6, 113.6, 82.5, 56.1, 47.9 (q, J = 30.3 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -70.38 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2948, 2850, 1710, 1415, 1245, 1185, 758 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{17}H_{13}O_3F_3Cl$ $[M+H]^+$ 357.0505 , found 357.0509.

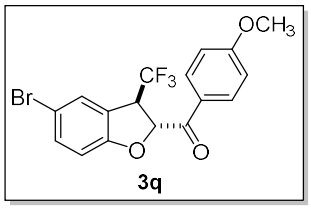
(5-Bromo-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3p)



3p

Following the general procedure, **3p** was obtained as colorless oil (146 mg, yield: 79%);**^{1}H NMR** (400 MHz, $CDCl_3$) δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15–8.10 (m, 2H), 7.69–7.65 (m, 1H), 7.57– 7.53 (m, 2H), 7.50 (s, 1H), 7.39–7.35 (m, 1H), 6.76 (d, J = 8.6 Hz, 1H), 5.98 (d, J = 4.7 Hz, 1H),4.88 (qd, J = 8.7, 4.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.4, 157.8, 134.5, 133.7, 130.7, 129.8, 128.9, 126.8, 126.0,125.5 (q, J = 274.8 Hz),121.4, 111.4, 82.5, 47.2 (q, J = 30.5 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -70.41 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2948, 1715, 1587, 1238, 1155, 748cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{16}H_{11}O_2F_3Br$ $[M+H]^+$ 370.9895, found 370.9896.

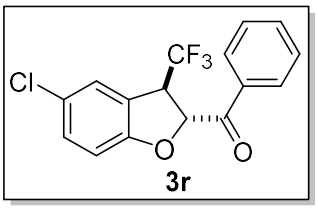
(5-Bromo-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(4-methoxyphenyl)methanone (3q)



3q

Following the general procedure, **3q** was obtained as colorless oil (150 mg, yield: 75%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 2H), 7.49 (s, 1H), 7.36 (d, *J* = 8.6 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 1H), 5.94 (d, *J* = 4.6 Hz, 1H), 4.95 – 4.84 (m, 1H), 3.91 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.7, 164.6, 158.4, 133.5, 132.2, 129.7, 128.9,125.4 (q, *J* = 254.1 Hz), 122.1, 114.2, 113.7, 111.9, 82.4, 55.7, 47.2 (q, *J* = 30.3 Hz); **^{19}F NMR** (377 MHz, $CDCl_3$) δ -70.34 (s, 3F); **IR ($CHCl_3$)** ν_{max} 2946, 2835, 1712, 1410, 1242, 1165, 755 cm^{-1}**; HRMS (ESI)**: *m/z* calculated for $C_{17}H_{13}O_3F_3Br$ $[M+H]^+$ 401.0000, found 400.9984.

(5-Chloro-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3r)

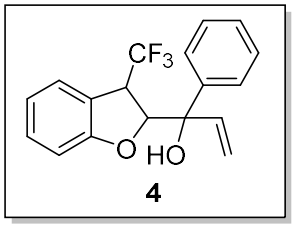


3r

Following the general procedure, **3r** was obtained as colorless oil (129 mg, yield: 79%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15–8.10 (m, 2H), 7.70–7.64 (m, 1H), 7.58– 7.52 (m, 2H), 7.37–7.33 (m, 1H), 7.25–7.21 (m, 1H), 6.80 (d, *J* = 8.6 Hz, 1H), 5.99 (d, *J* = 4.7 Hz, 1H), 4.88 (qd, *J* = 8.8, 4.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.0, 159.0, 140.9, 132.3, 131.2, 130.7, 129.2, 126.0, 125.8 (d, *J* = 278.4 Hz), 122.1, 119.5, 110.4, 82.1, 47.2 (q, *J* = 30.2 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -70.41 (s, 3F); **IR ($CHCl_3$)** 2950, 1710, 1585, 1236, 1165, 750 cm^{-1}; **HRMS (ESI)**: *m/z* calculated for $C_{16}H_{11}O_2F_3Cl$ $[M+H]^+$ 327.0400, found 327.0402.

4. Application:

Synthesis of 1-phenyl-1-(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)prop-2-en-1-ol (4)



4

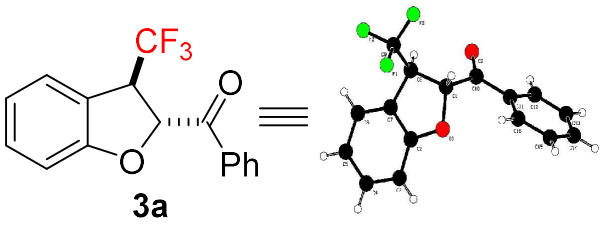
To a 25 mL two-necked round-bottomed flask were added **3a** (100 mg, 0.342 mmol) and THF (2 mL), where vinyl magnesium bromide (1.0 M THF solution, 0.684 mmol) was introduced slowly at 0 ºC, and the mixture was stirred for 1 h at the same temperature. Then, the reaction mixture was quenched with sat. aq.NH_4Cl and extracted with EtOAc (3 X 20 mL). After usual workup, the crude product was purified by column chromatography (hexane:EtOAc = 10:2) to give the desired product **4** as a colorless oil (84.26 mg, 0.263 mmol, 77%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55–7.50(m, 2H), 7.44–7.37 (m, 2H), 7.35–7.30 (m, 1H), 7.29–7.21 (m, 2H), 6.92 (td, *J* = 7.5, 0.9 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.34 (dd, *J* = 17.3, 10.8 Hz, 1H), 5.47 (dd, *J* = 17.3, 0.8 Hz, 1H), 5.33 (dd, *J* = 10.8, 0.8 Hz, 1H), 5.17 (d, *J* = 4.4 Hz, 1H),4.04 (qd, *J* = 8.8, 4.4 Hz, 1H), 2.15 (s, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.4, 140.3, 139.3, 130.3, 128.6, 128.0, 127.0, 126.2, 125.8, 124.2, 121.3, 116.1, 109.7, 86.4, 78.1, 47.7 (q, *J* = 29.4 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -70.97 (s, 3F); **IR ($CHCl_3$)** 3680, 2870,1675, 1580, 1265, 1180, 1085, 765 **cm^{-1}; HRMS (ESI)**: *m/z* calculated for $C_{18}H_{16}O_2F_3$ $[M+H]^+$ 321.1102, found 321.1100.

5. References:

1 Y.-F. Gong and K. Kato, *Synlett*, 2002, **431**.

2 Y.-F. Gong and K. Kato, *J. Fluorine Chem*., 2003, **121**, 141.

6. X-Ray crystallographic structure of Product 3a (CCDC 2023269):



3a

X-ray Crystallography.

X-ray data for the compound **3a** was collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 A) and a PHOTON-100 detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [1]. The structure was solved using intrinsic phasing method [2] and further refined with the SHELXL [2] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and U_{iso}(H) = 1.5U_{eq}(C) for methyl H or 1.2U_{eq}(C) for other H atoms].

Crystal structure determination of 3a

Crystal Data for $C_{16}H_{11}O_2F_3$ (M =292.26 g/mol): triclinic, space group P-1 (no. 2), a = 8.056(7) Å, b = 9.746(9) Å, c = 10.356(10) Å, α = 116.090(17)°, β = 91.310(17)°, γ = 108.693(16)°, V = 678.8(11) Å^3, Z = 2, T = 294.15 K, μ(Mo Kα) = 0.121 mm^{-1}, *Dcalc* = 1.4298 g/cm^3, 16052 reflections measured (4.46° ≤ 2Θ ≤ 61.12°), 4109 unique (R_{int} = 0.0317, R_{sigma} = 0.0355) which were used in all calculations. The final R_1 was 0.0538 (I>=2u(I)) and wR_2 was 0.1558 (all data). CCDC 2023269 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

1. Bruker (2016). APEX3, SAINT and SADABS. Bruker AXS, Inc., Madison, Wisconsin, USA.

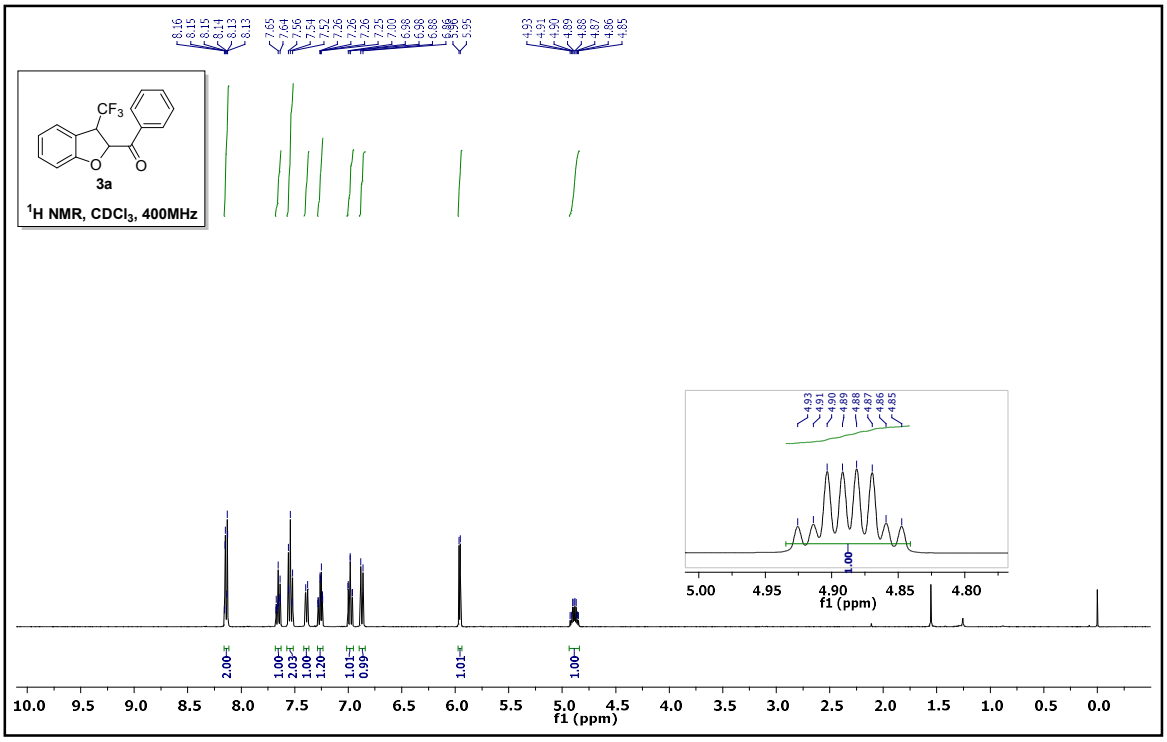
2. Sheldrick G. M. (2015) Acta Crystallogr C71: 3-8.

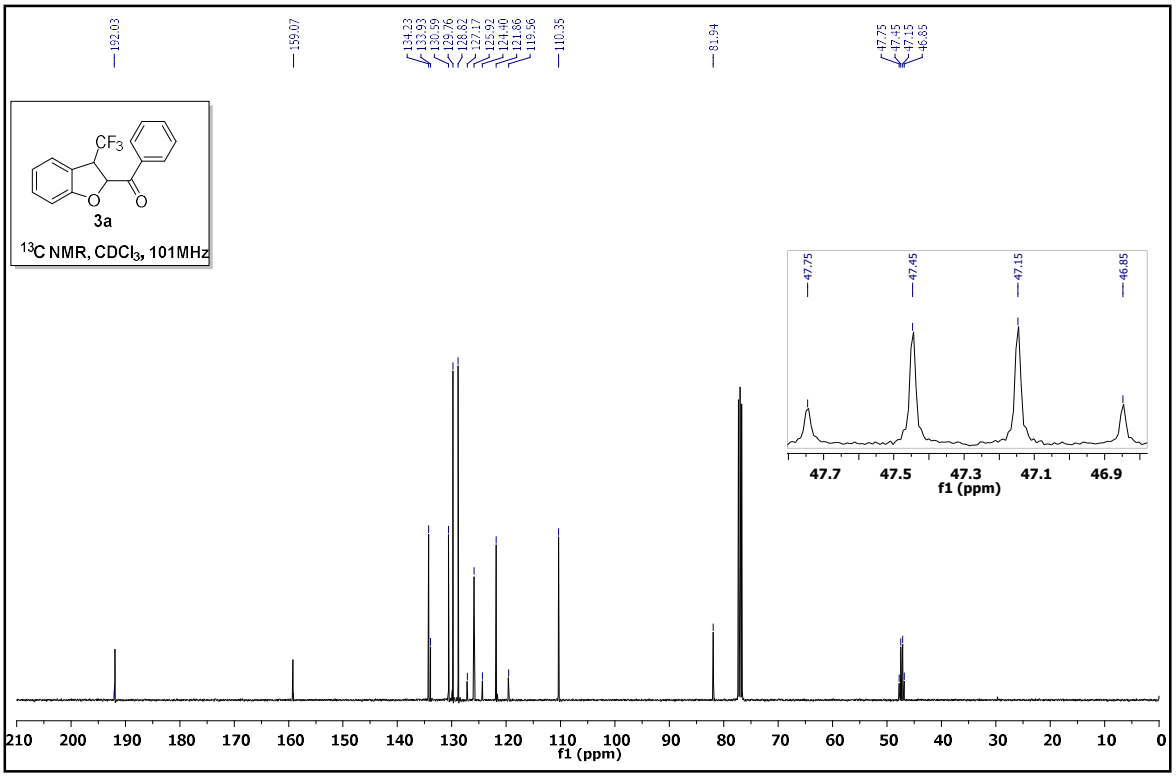
Figure Captions

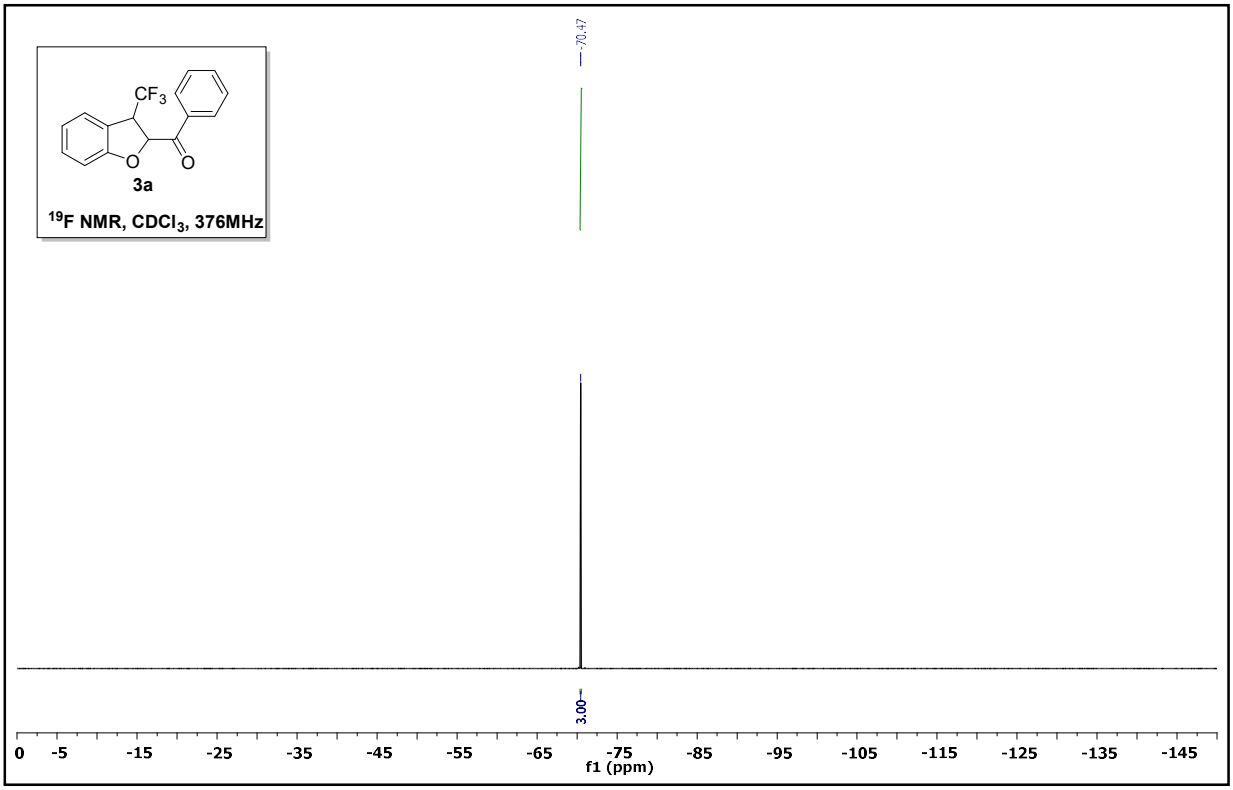
Fig.1. A view of **3a**, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii.

7. NMR Data (^{1}H, ^{13}C and ^{19}F)

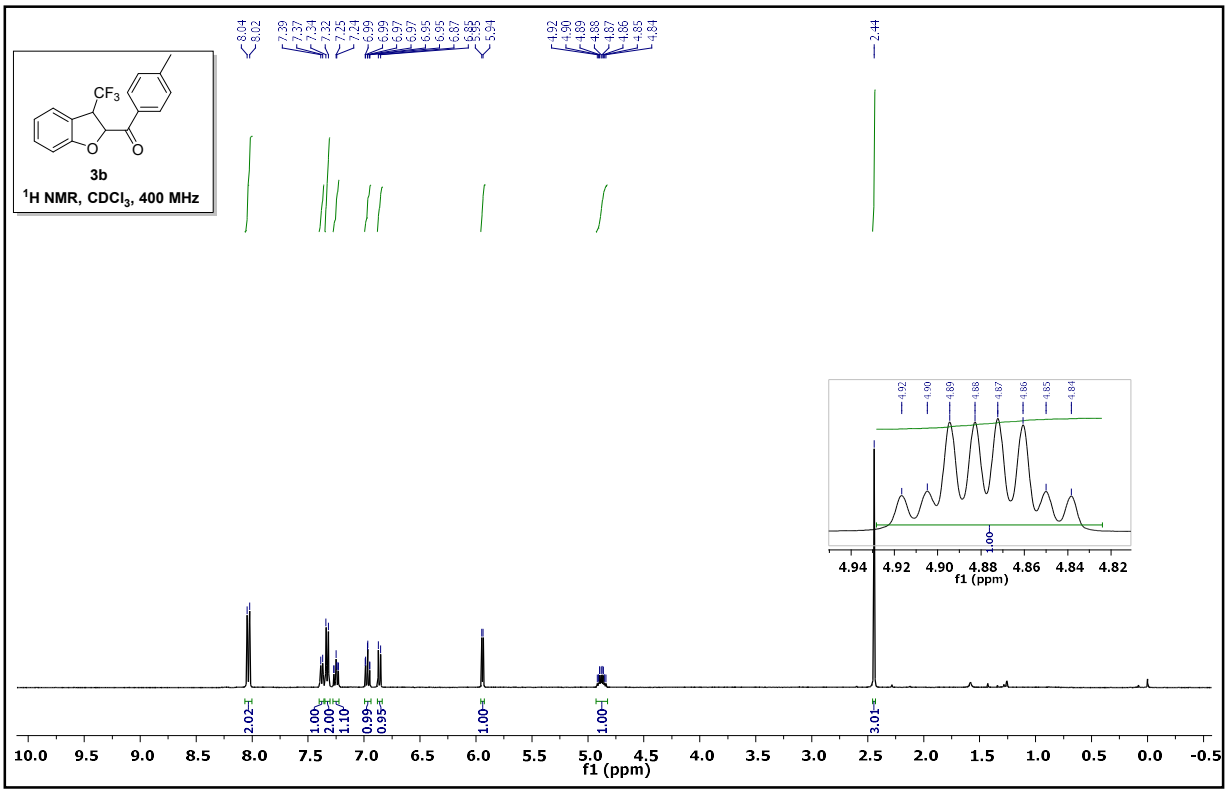
Phenyl(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3a):

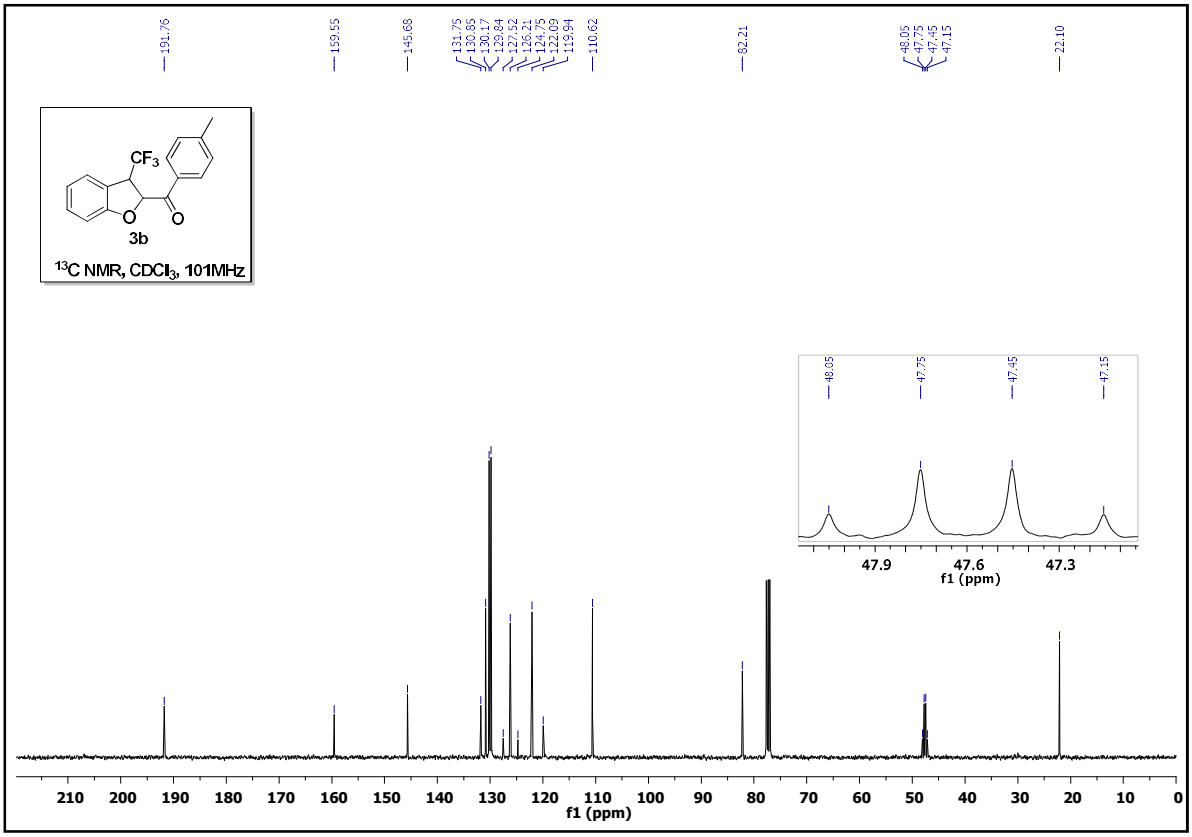


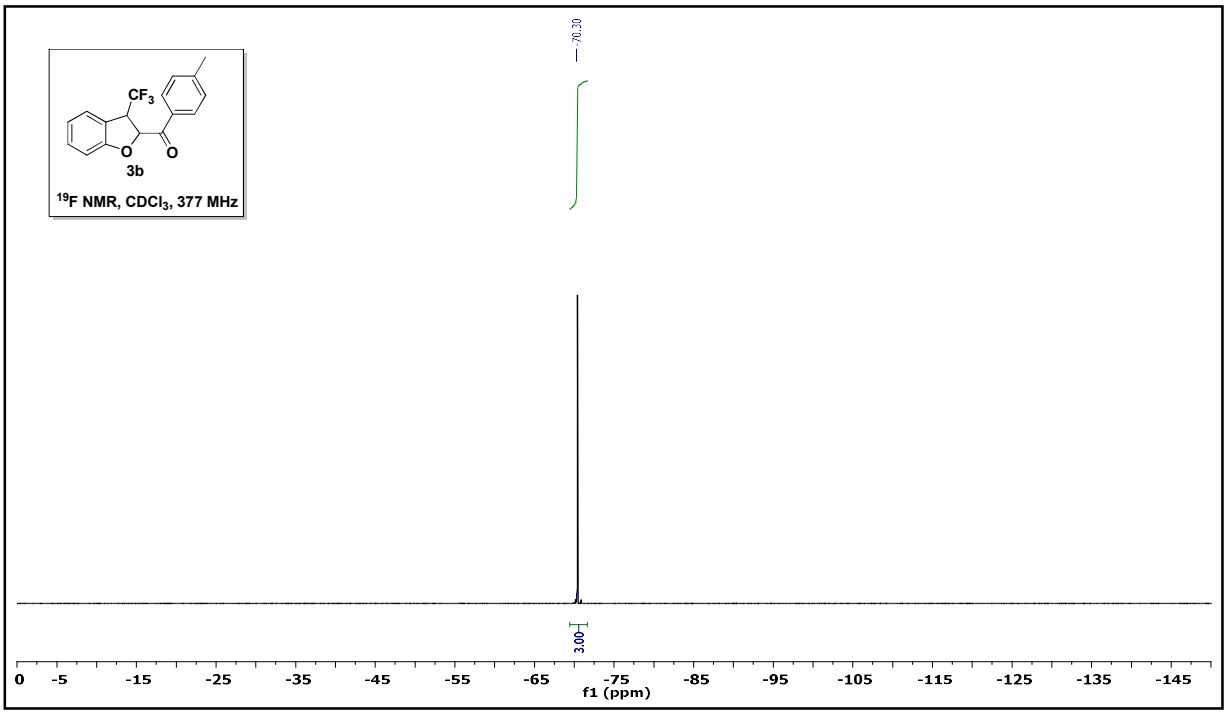




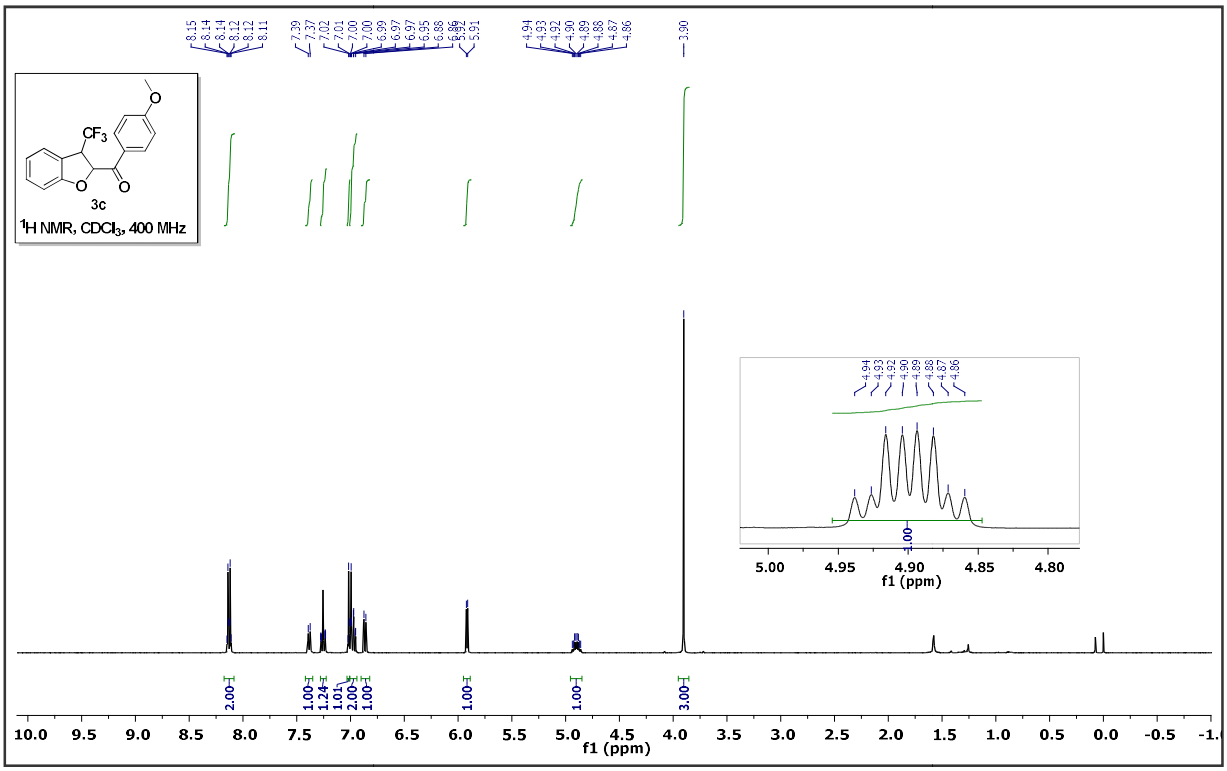
***p*-Tolyl(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3b):**

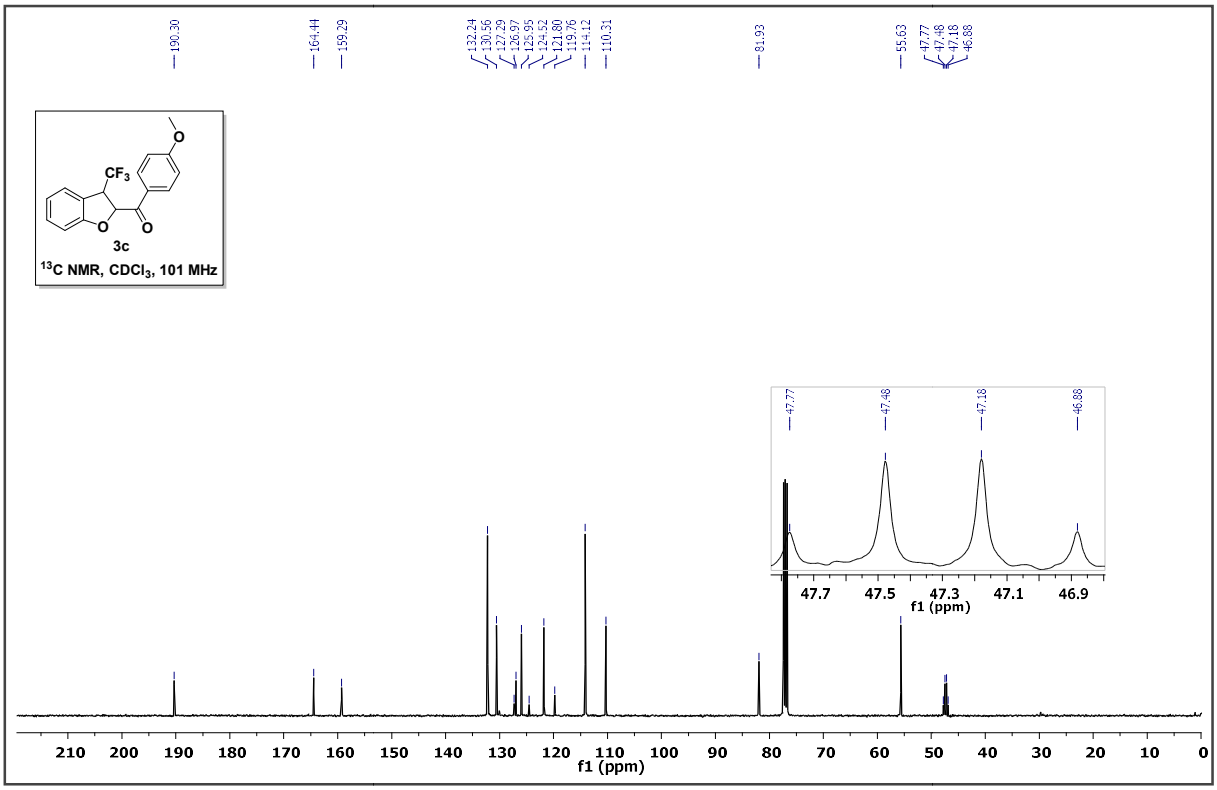


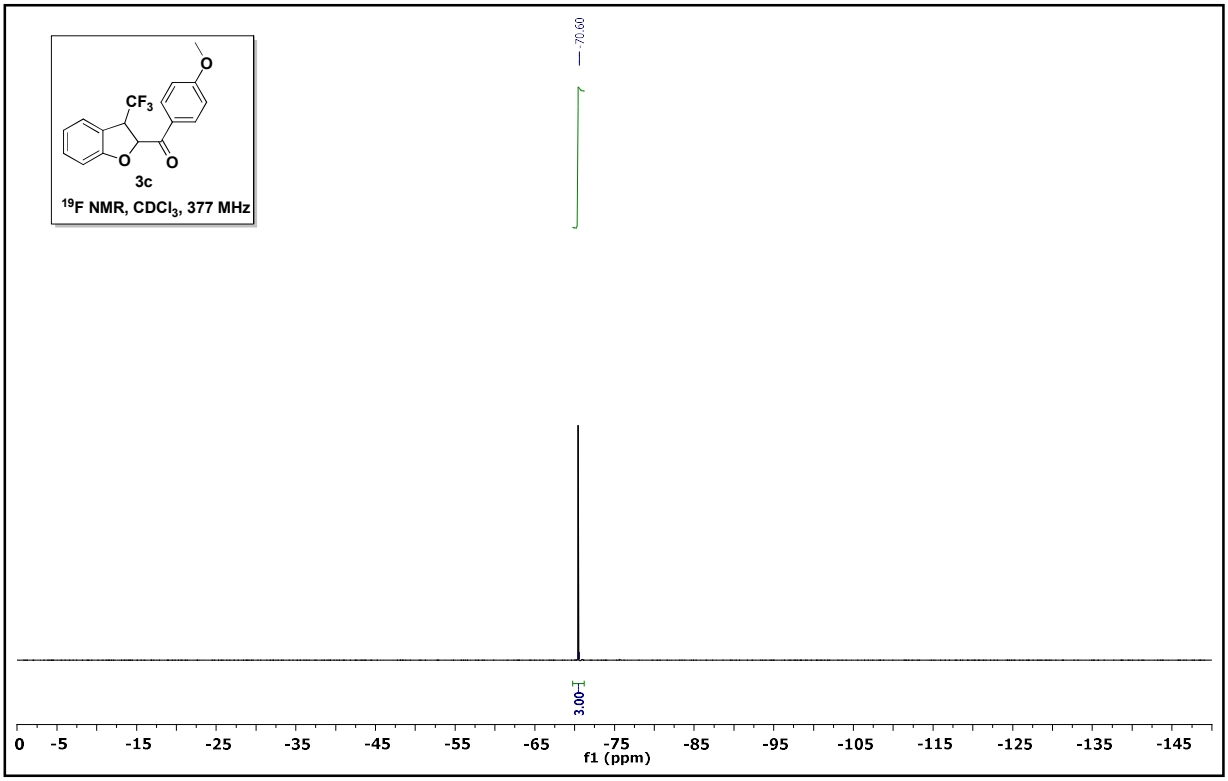

191.76
159.55
145.68
131.75
130.86
130.17
129.84
127.52
126.21
124.75
122.09
119.94
110.62
82.21
48.05
47.75
47.45
47.15
22.10
CF3
O
O
3b
13C NMR, CDCl3, 101MHz
47.9
47.6
47.3
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-70.30
CF3
O
O
3b
19F NMR, CDCl3, 377 MHz
3.00
0 -5 -15 -25 -35 -45 -55 -65 -75 -85 -95 -105 -115 -125 -135 -145
f1 (ppm)

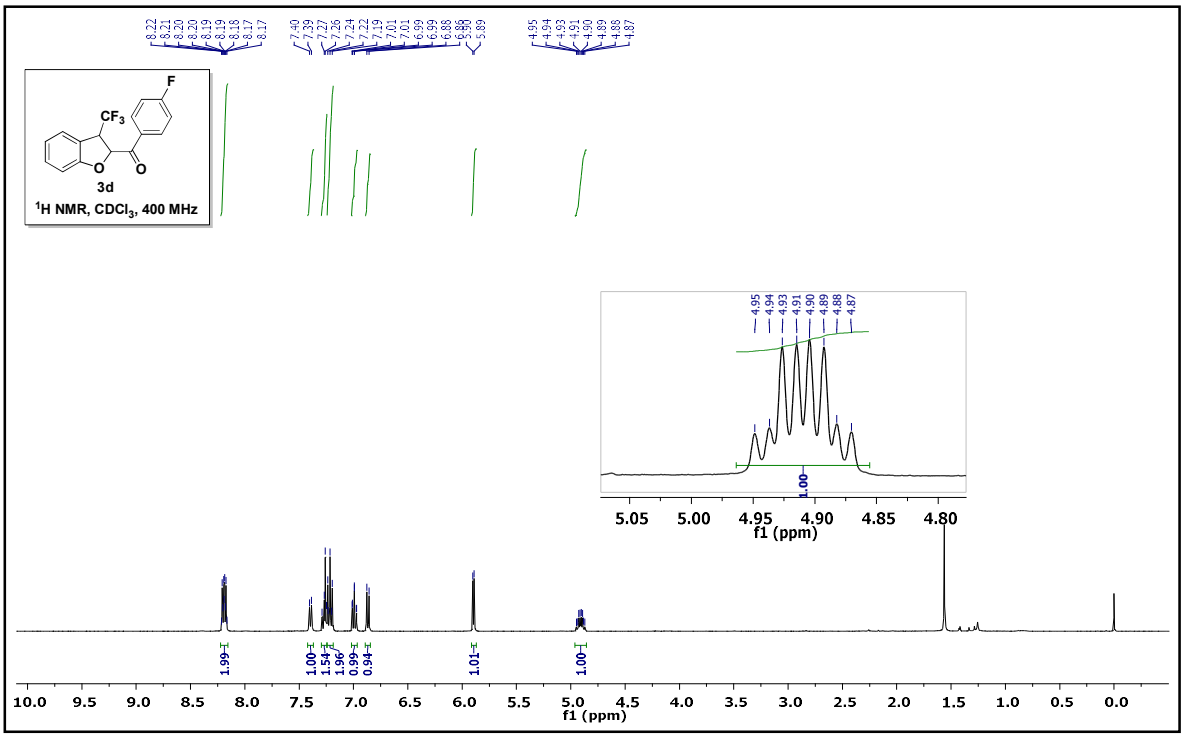
(4-Methoxyphenyl)(3-(trifluoromethyl)-2,3dihydrobenzofuran-2-yl)methanone (3c):

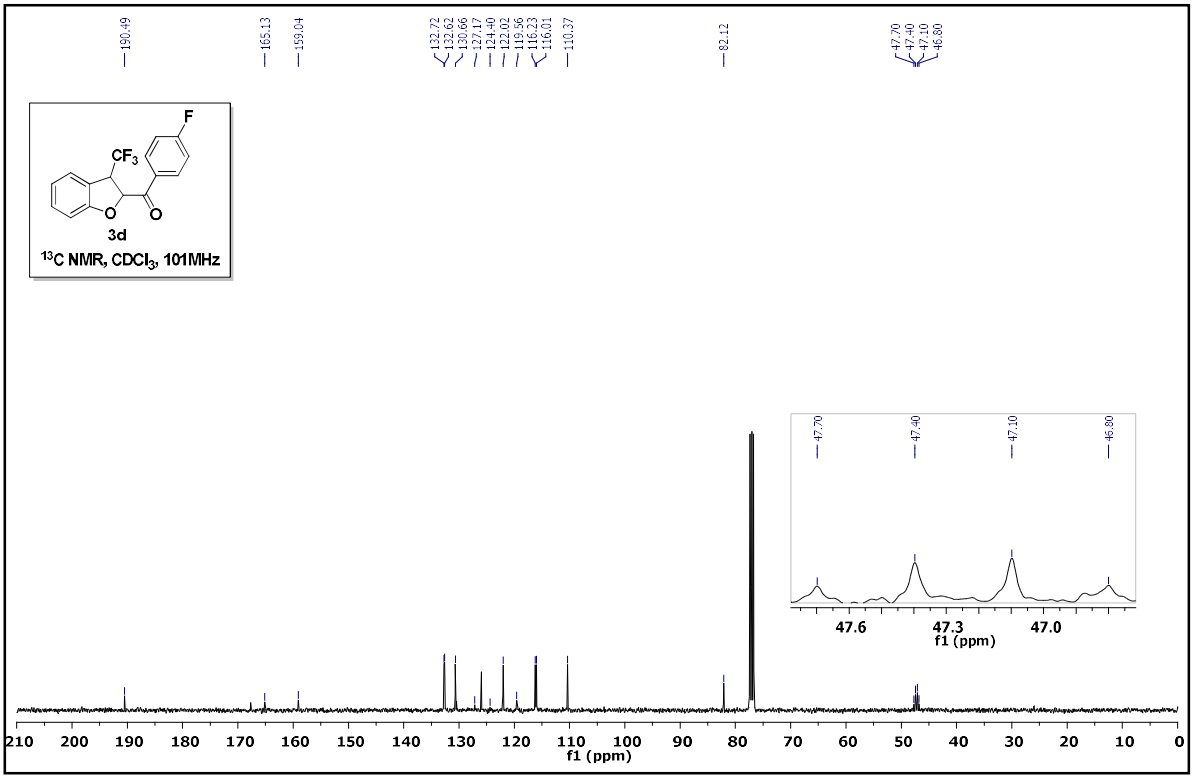


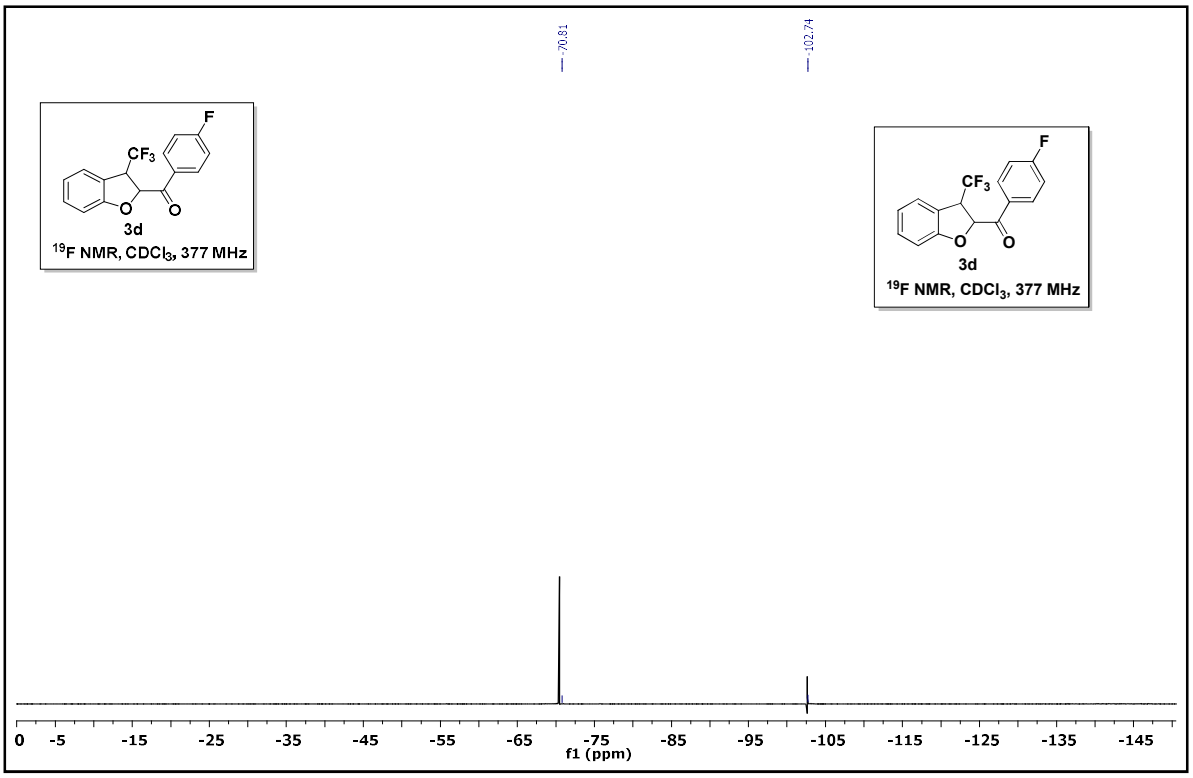




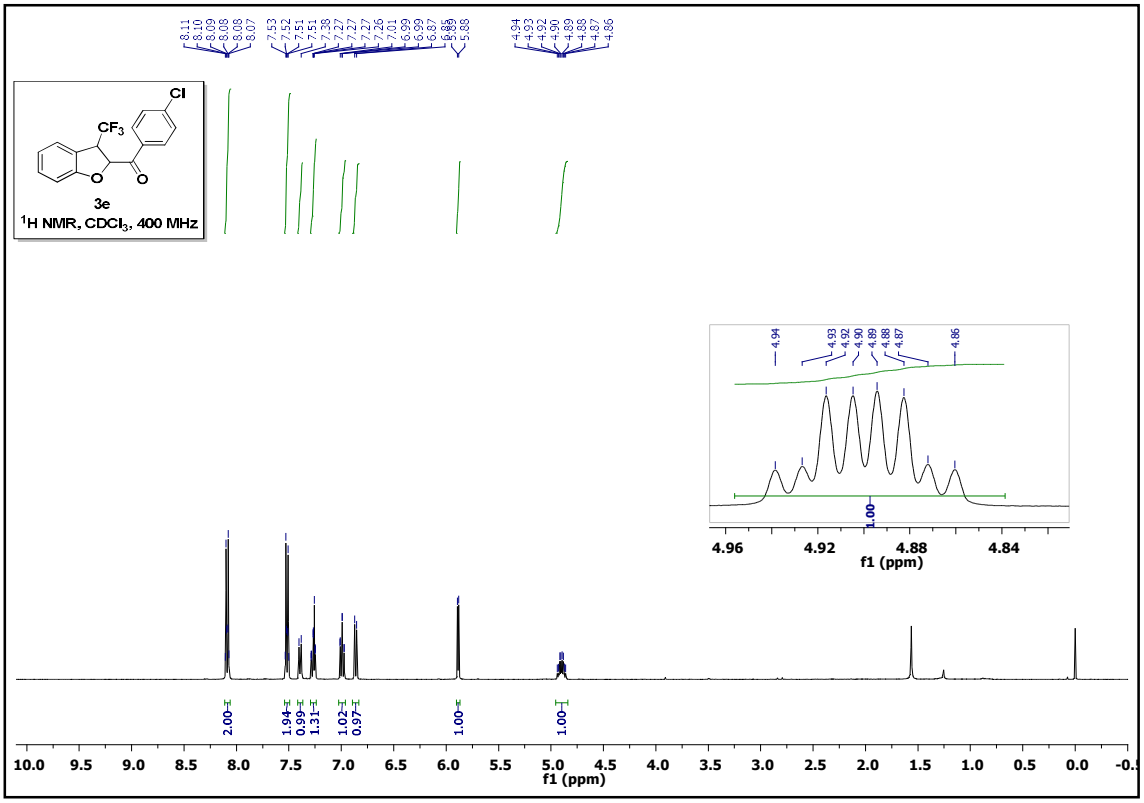
(4-Fluorophenyl)(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3d):

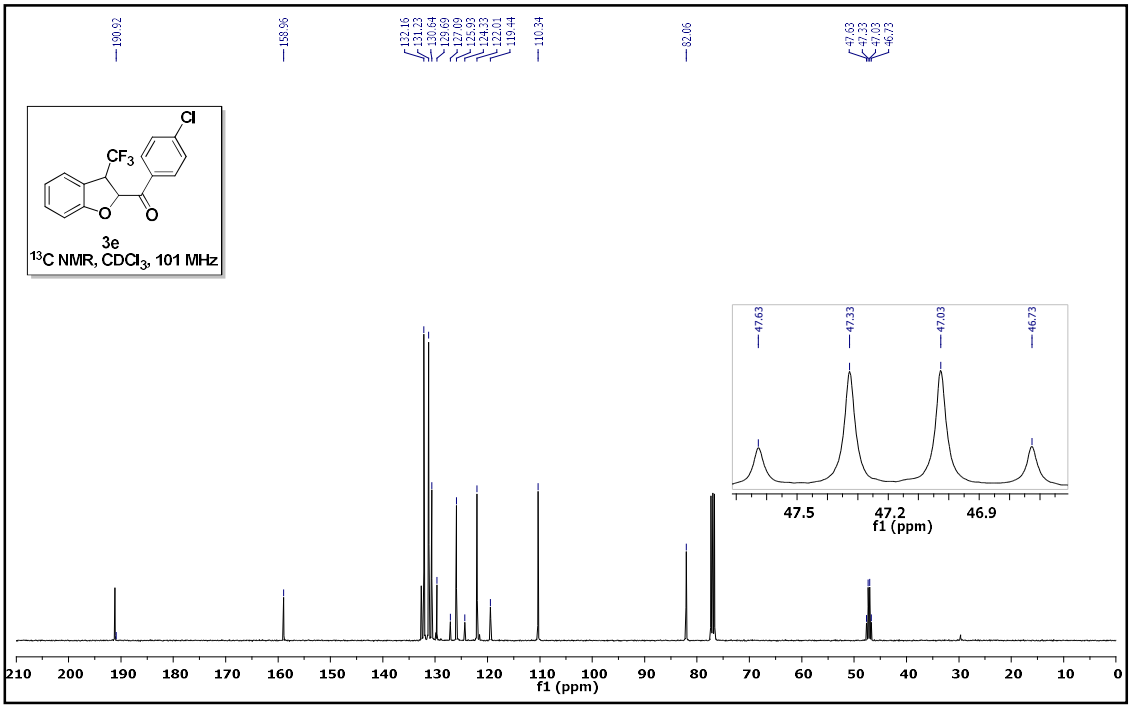


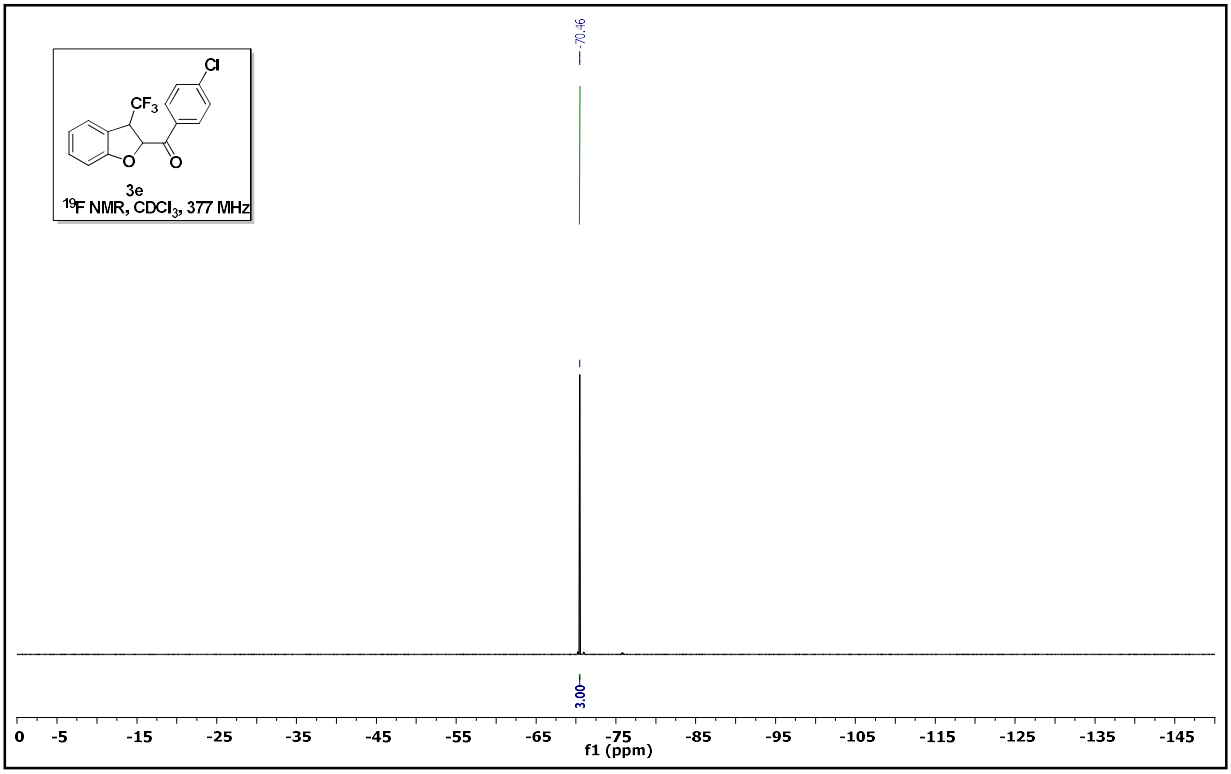




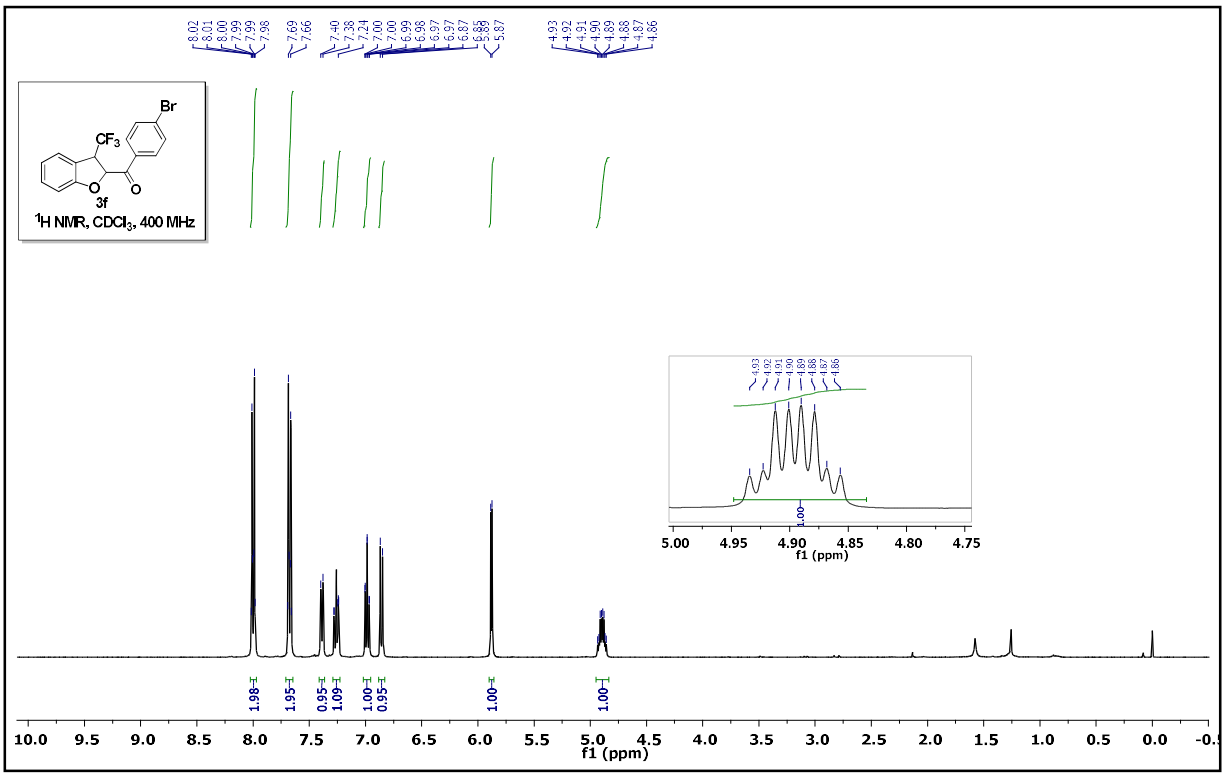
(4-Chlorophenyl)(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3e):

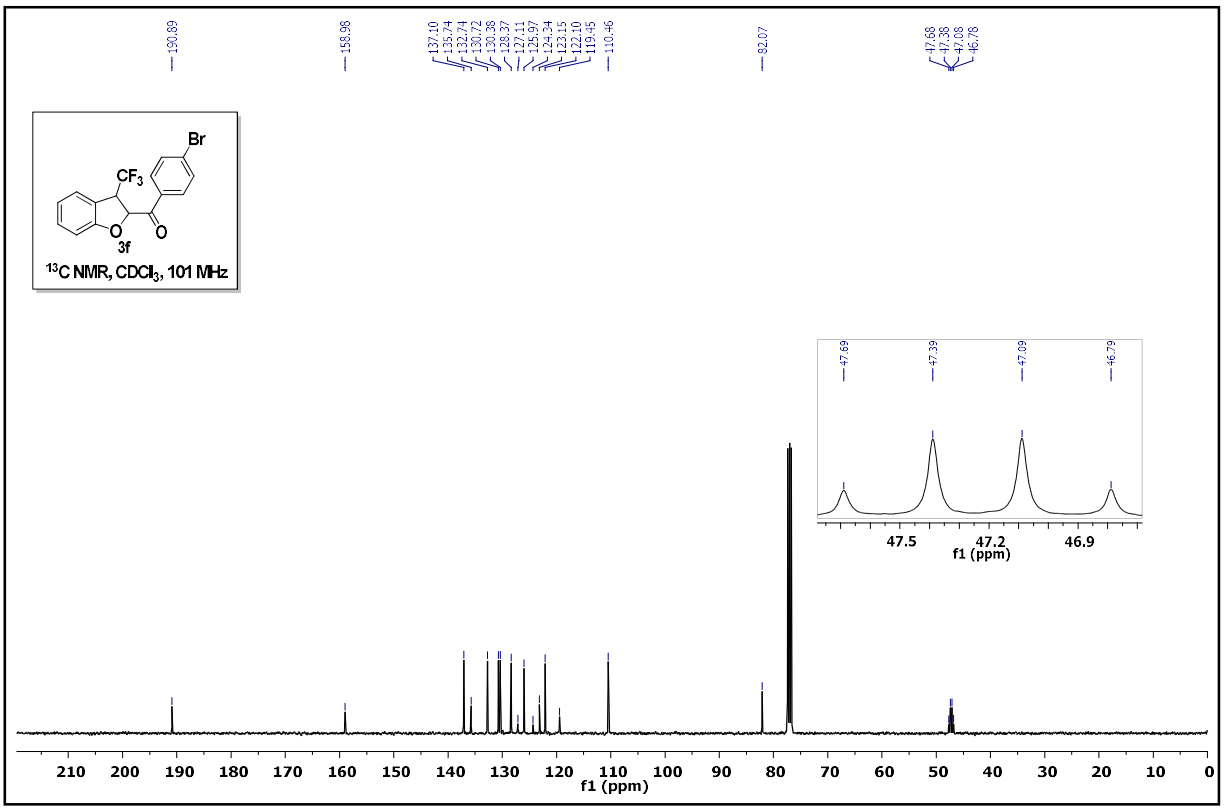

Cl
CF3
O
O
3e
1H NMR, CDCl3, 400 MHz
8.11
8.10
8.09
8.08
8.08
8.07
7.53
7.52
7.51
7.51
7.38
7.27
7.27
7.27
7.26
7.01
6.99
6.99
6.87
5.88
4.94
4.93
4.92
4.90
4.89
4.88
4.87
4.86
1.00
4.96
4.92
4.88
4.84
f1 (ppm)
2.00
1.94
0.99
1.31
1.02
0.97
1.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

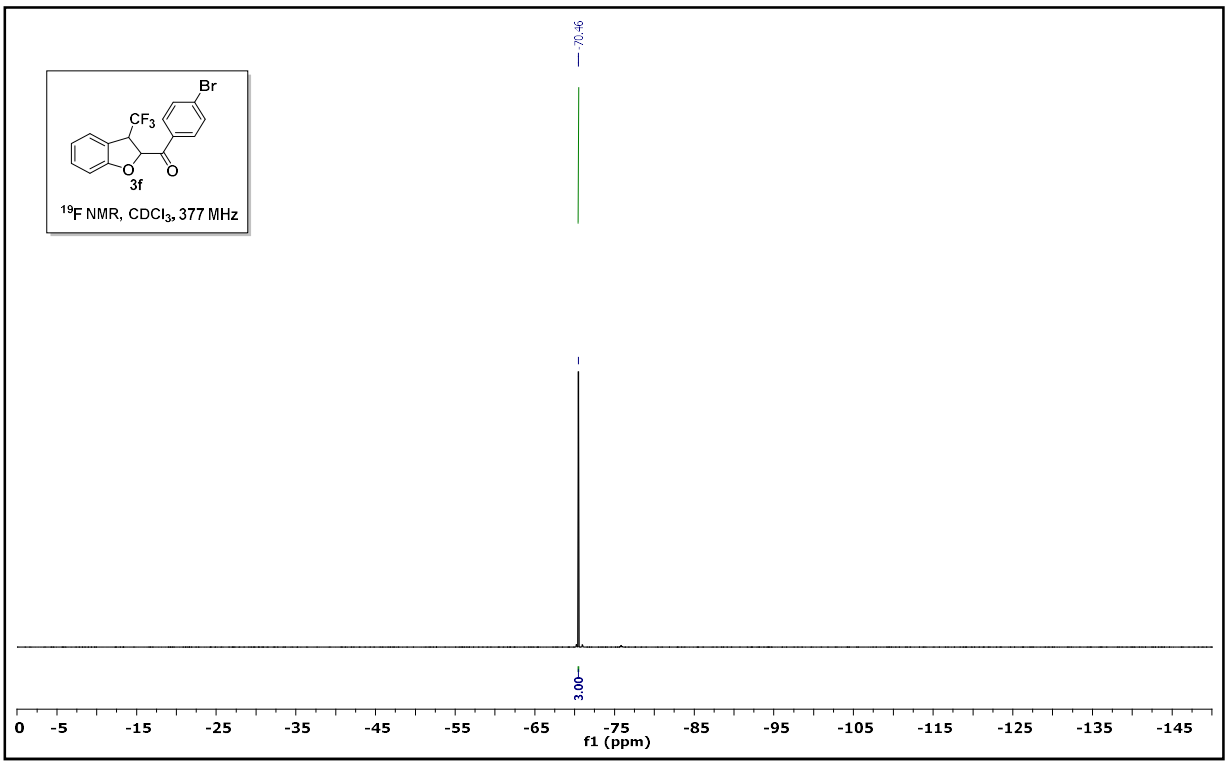

190.92
158.96
132.16
131.23
130.64
129.69
127.09
125.98
124.33
122.01
119.44
110.34
82.06
47.63
47.33
47.03
46.73
Cl
CF3
O
O
3e
13C NMR, CDCl3, 101 MHz
47.63
47.33
47.03
46.73
47.5
47.2
46.9
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



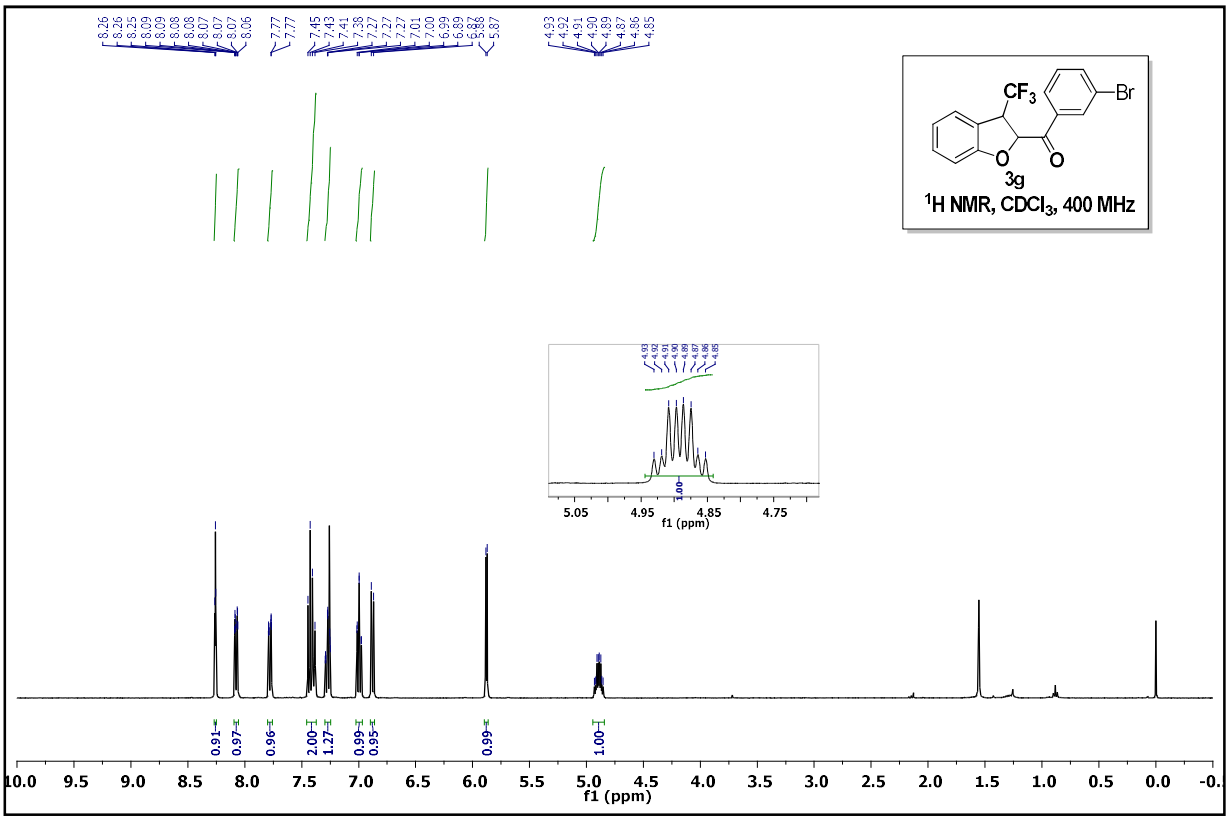
(4-Bromophenyl)(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3f):

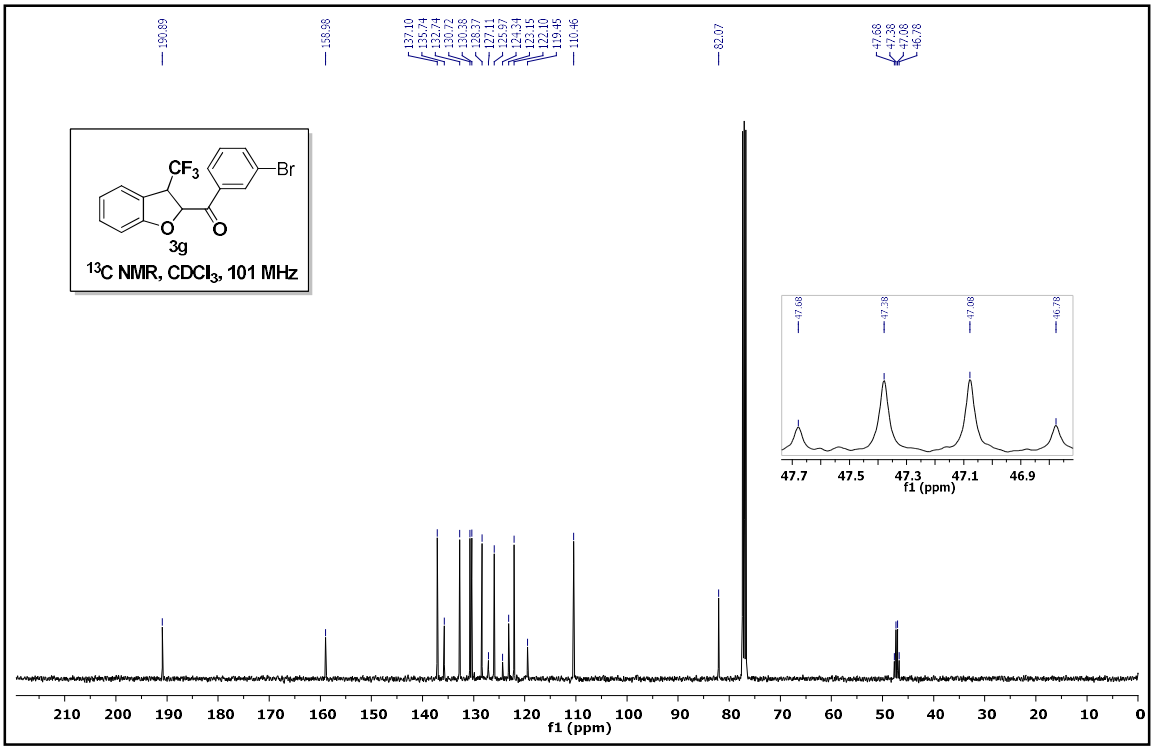


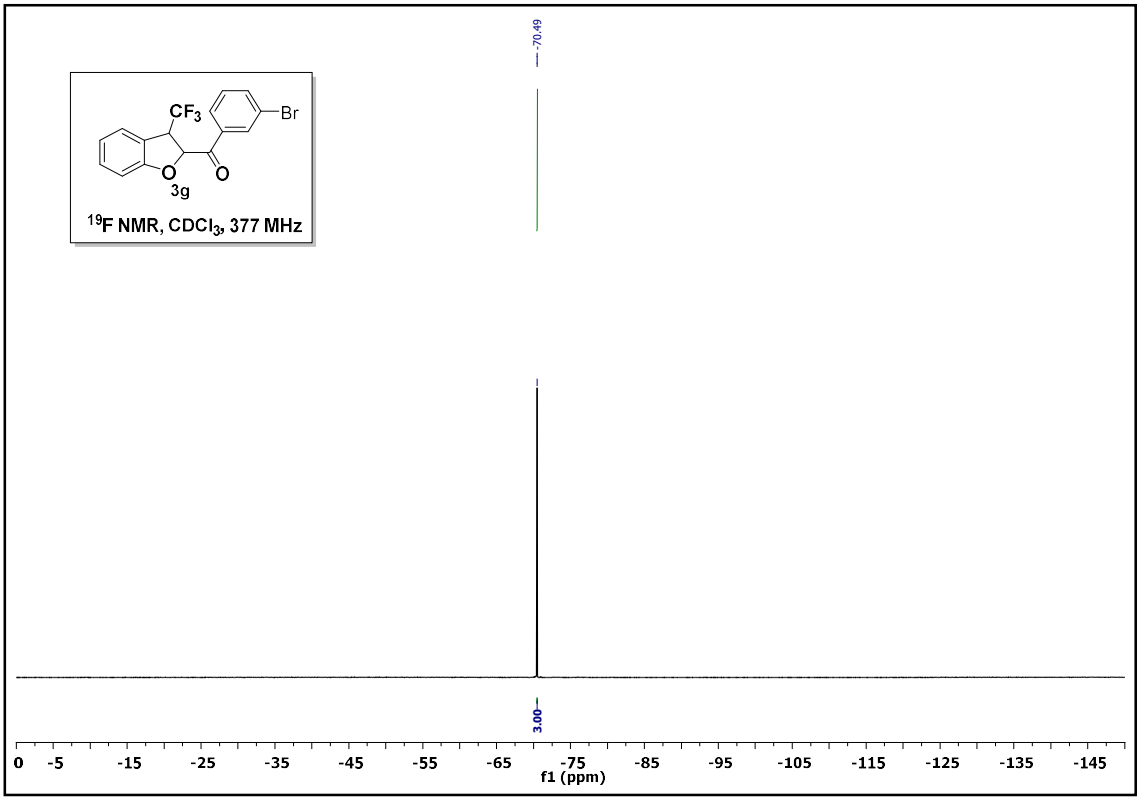

190.89
158.98
137.10
135.74
132.74
130.72
130.38
128.37
127.11
125.97
124.34
123.15
122.10
119.45
110.46
82.07
47.68
47.38
47.08
46.78
Br
CF3
O
O
3f
13C NMR, CDCl3, 101 MHz
47.69
47.39
47.09
46.79
47.5
47.2
46.9
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-70.46
Br
CF3
O
O
3f
19F NMR, CDCl3, 377 MHz
3.00
0 -5 -15 -25 -35 -45 -55 -65 -75 -85 -95 -105 -115 -125 -135 -145
f1 (ppm)

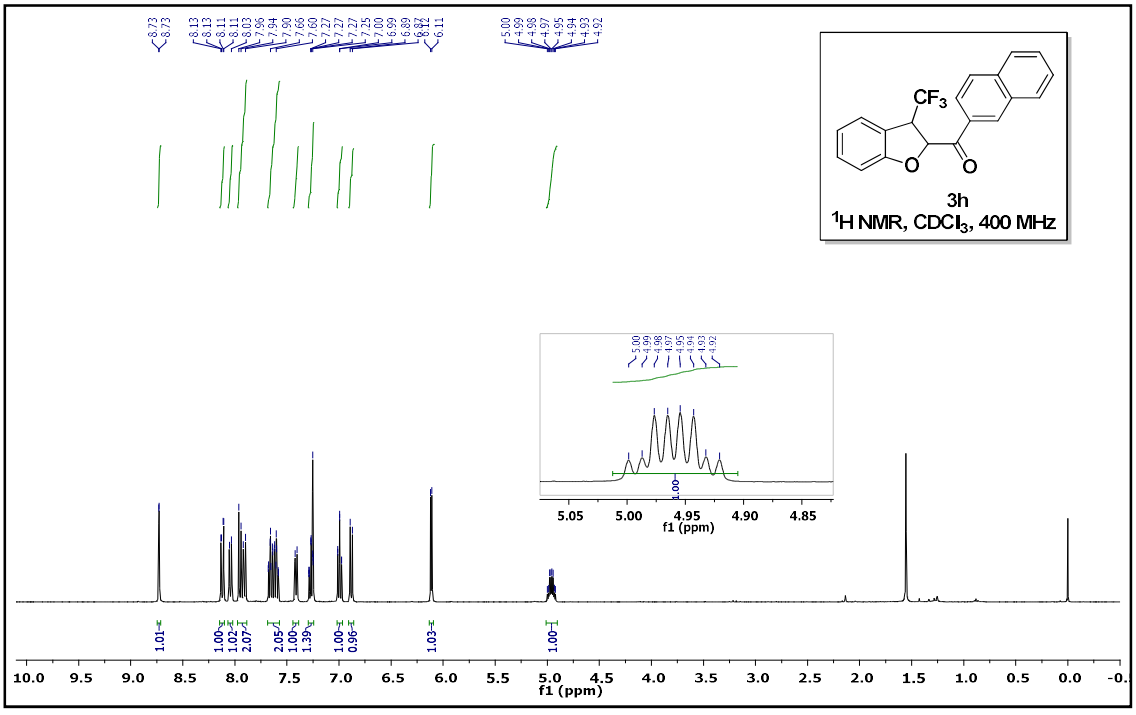
(3-Bromophenyl)(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3g):

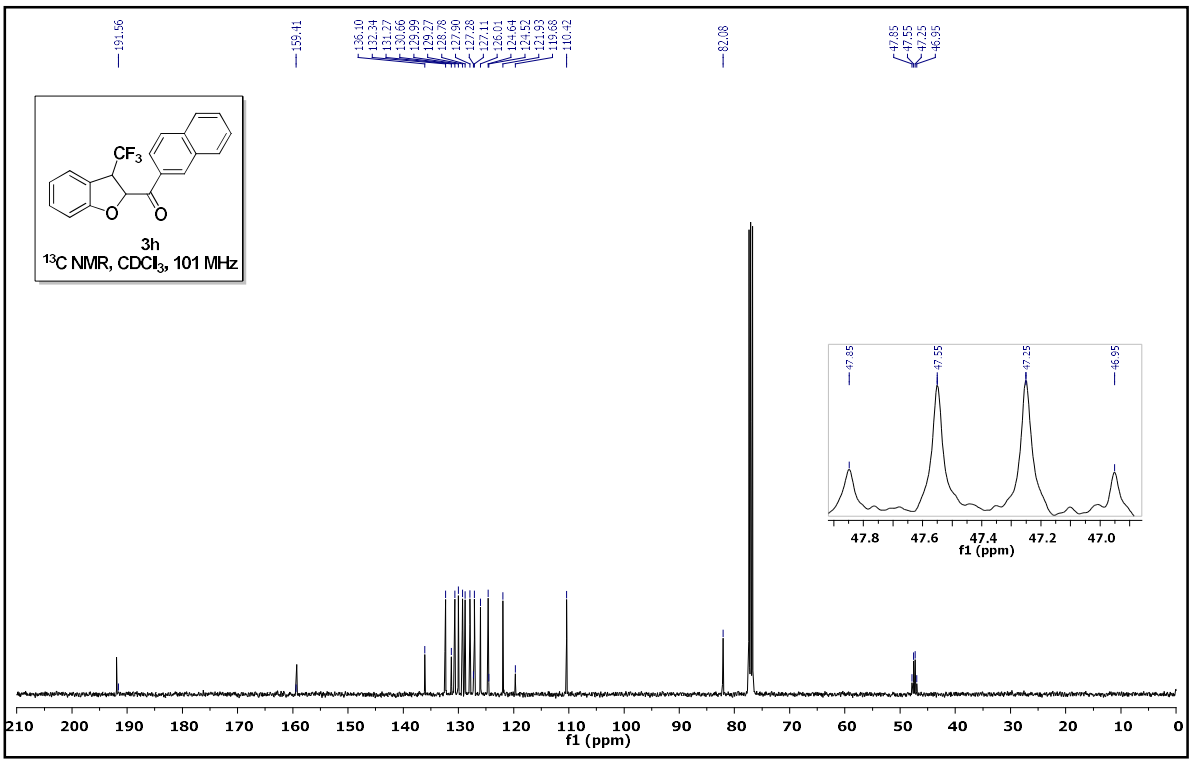


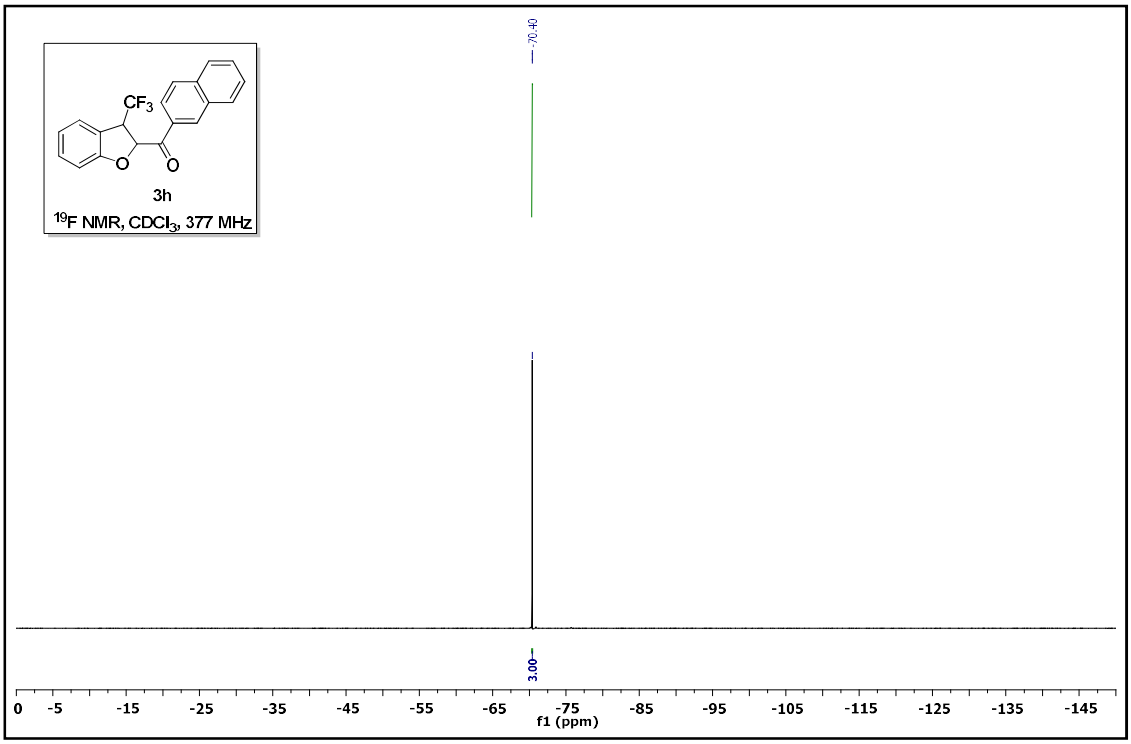




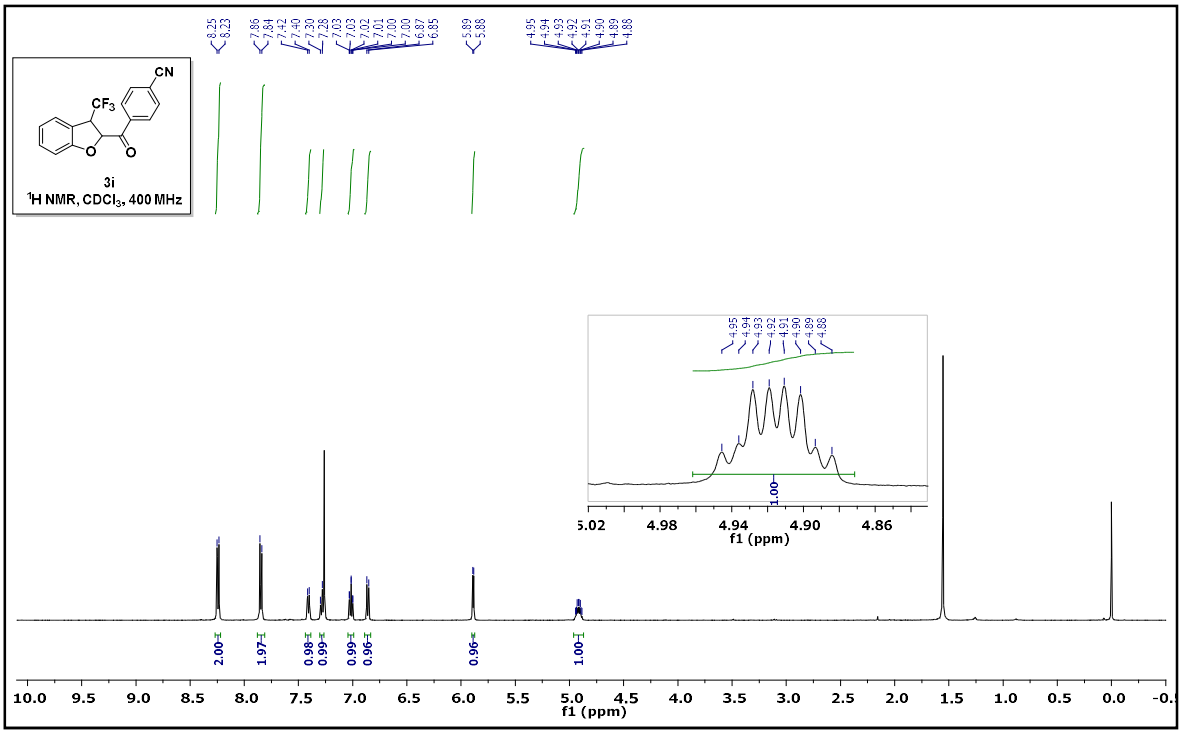
Naphthalen-2-yl(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3h):

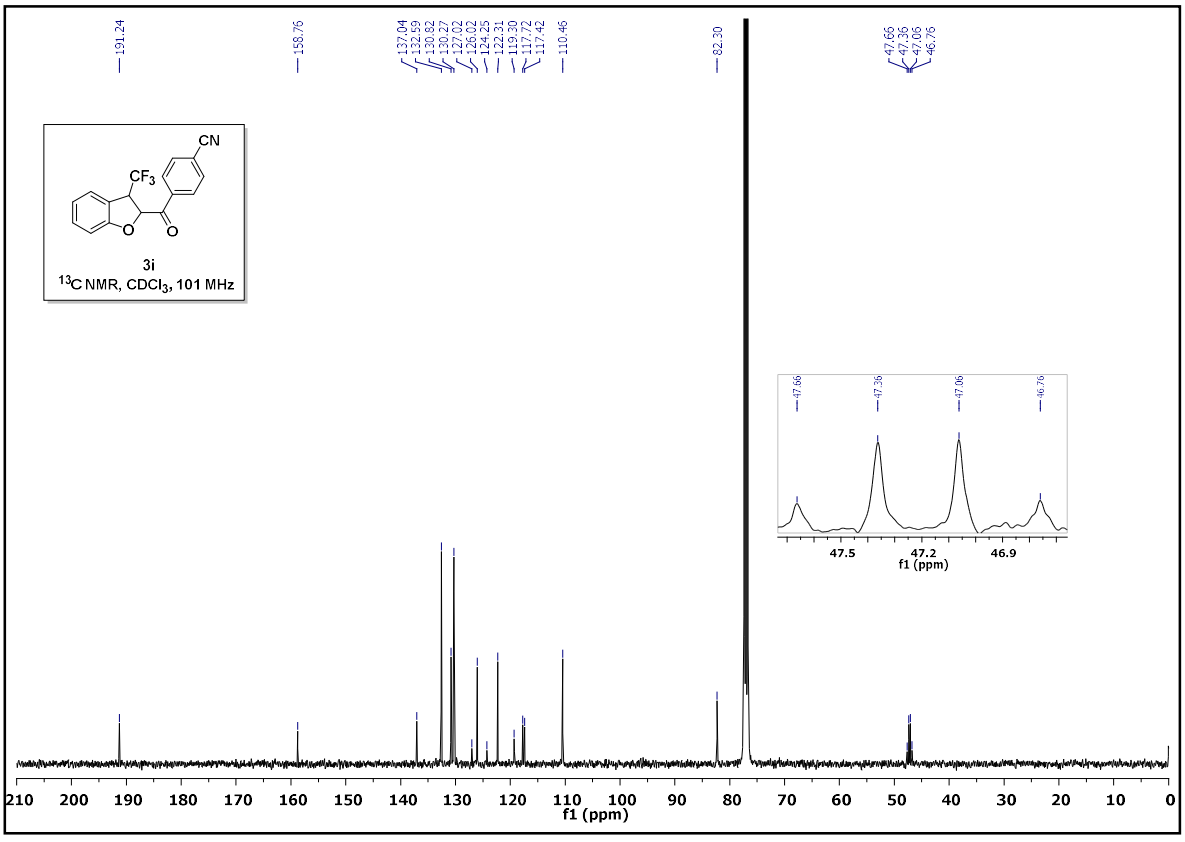


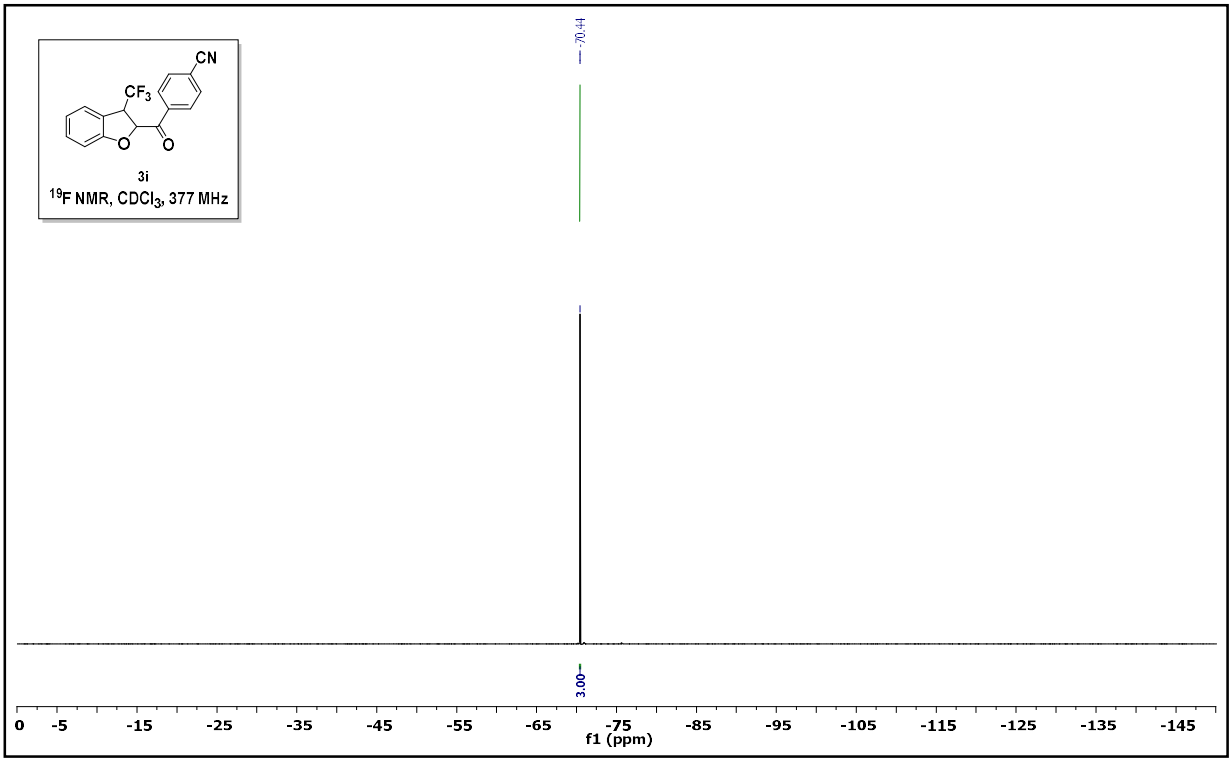

191.56
159.41
136.10
132.34
131.27
130.66
129.99
129.27
128.76
127.90
127.28
127.11
126.01
124.64
124.52
121.93
119.68
110.42
82.08
47.85
47.55
47.25
46.95
CF3
O
O
3h
13C NMR, CDCl3, 101 MHz
f1 (ppm)


-70.40
CF3
O
O
3h
19F NMR, CDCl3, 377 MHz
3.00
f1 (ppm)

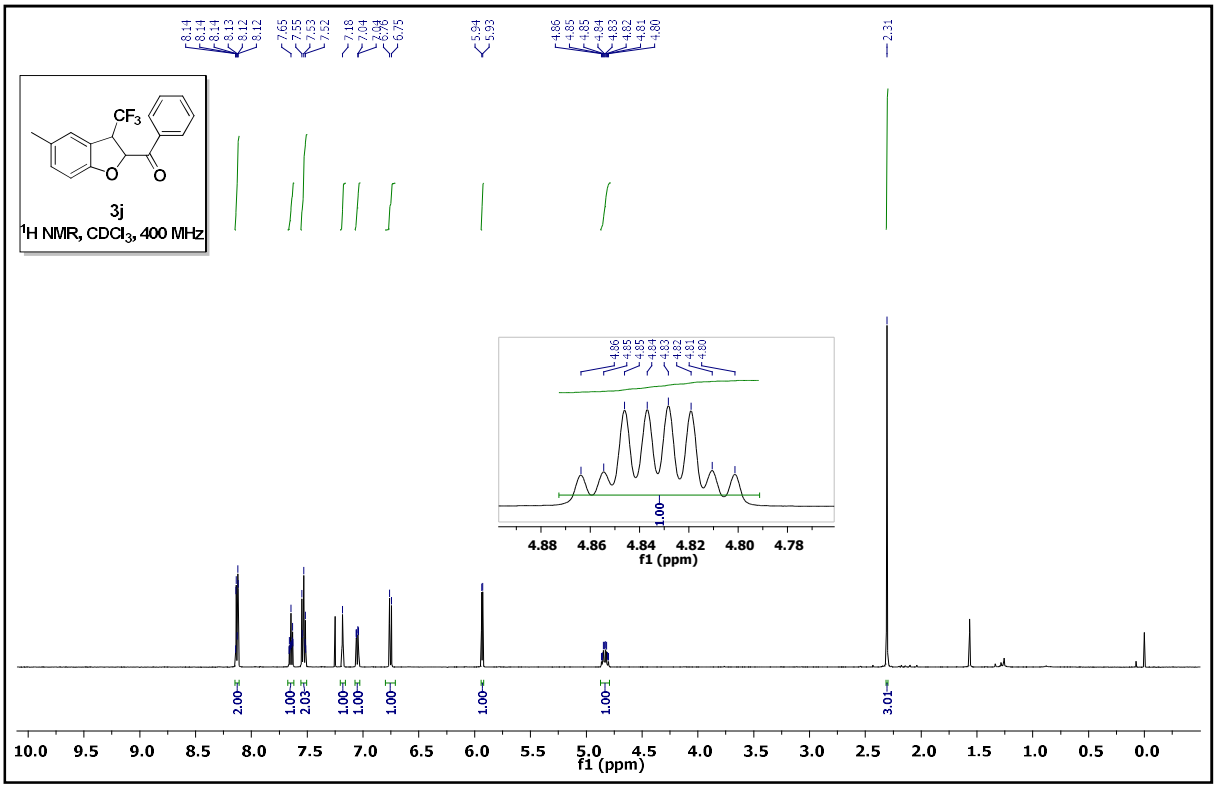
4-(3-(Trifluoromethyl)-2,3-dihydrobenzofuran-2-carbonyl)benzonitrile(3i):

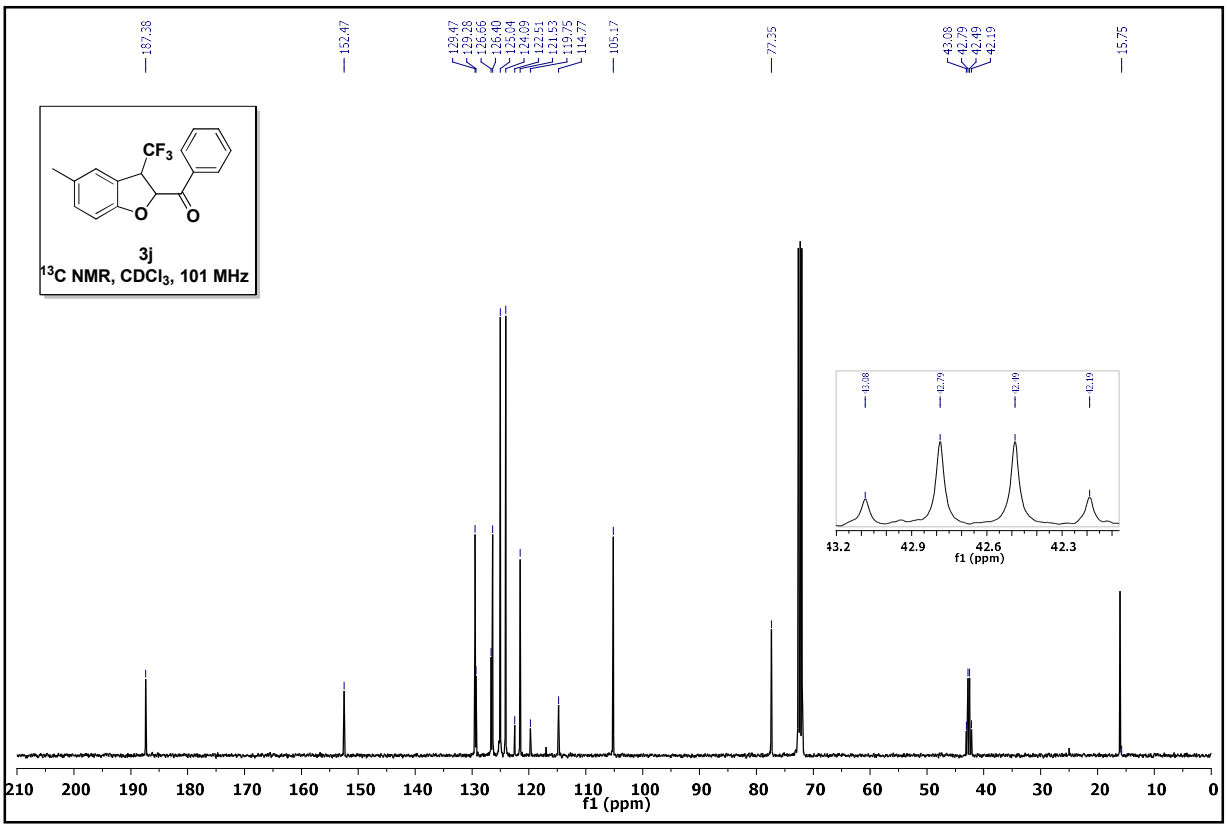


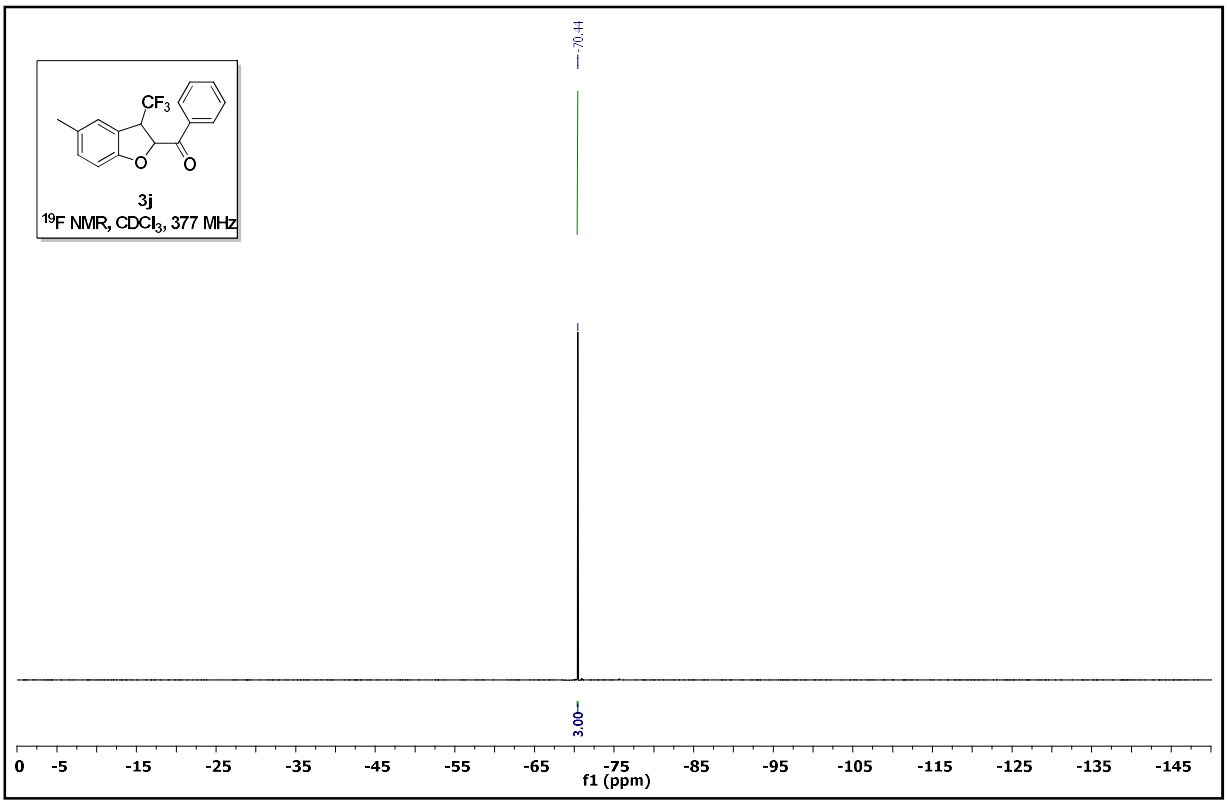




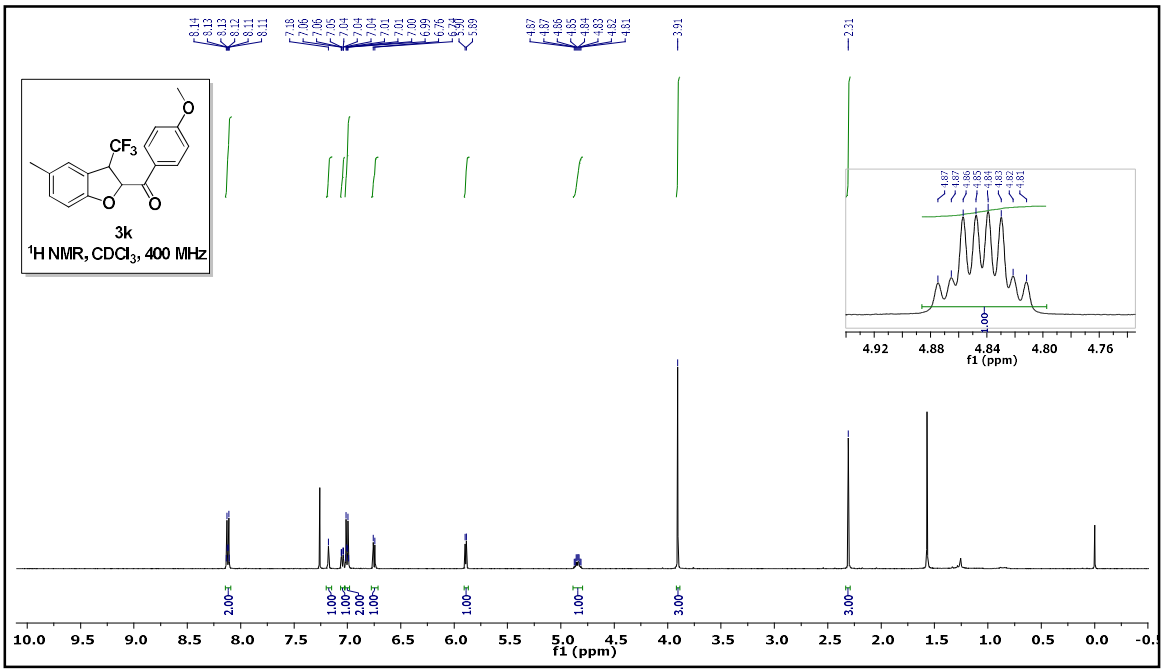
(5-Methyl-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3j):

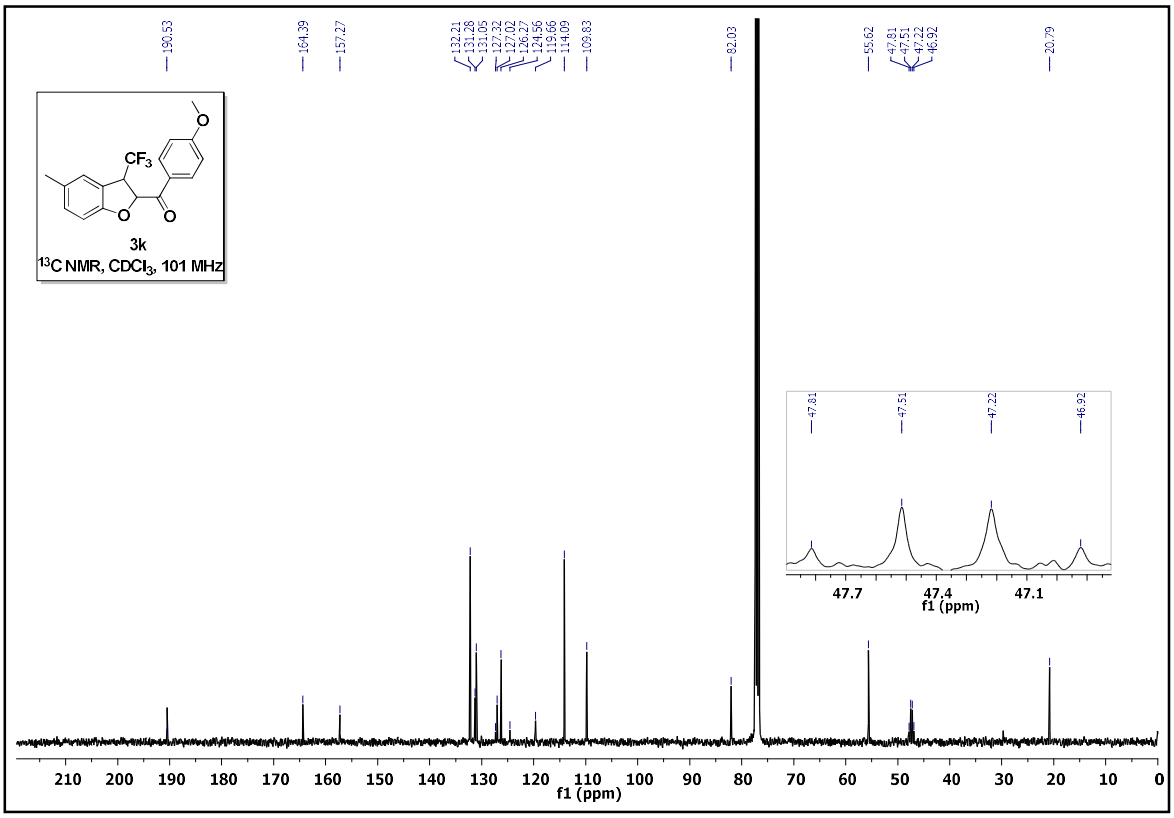


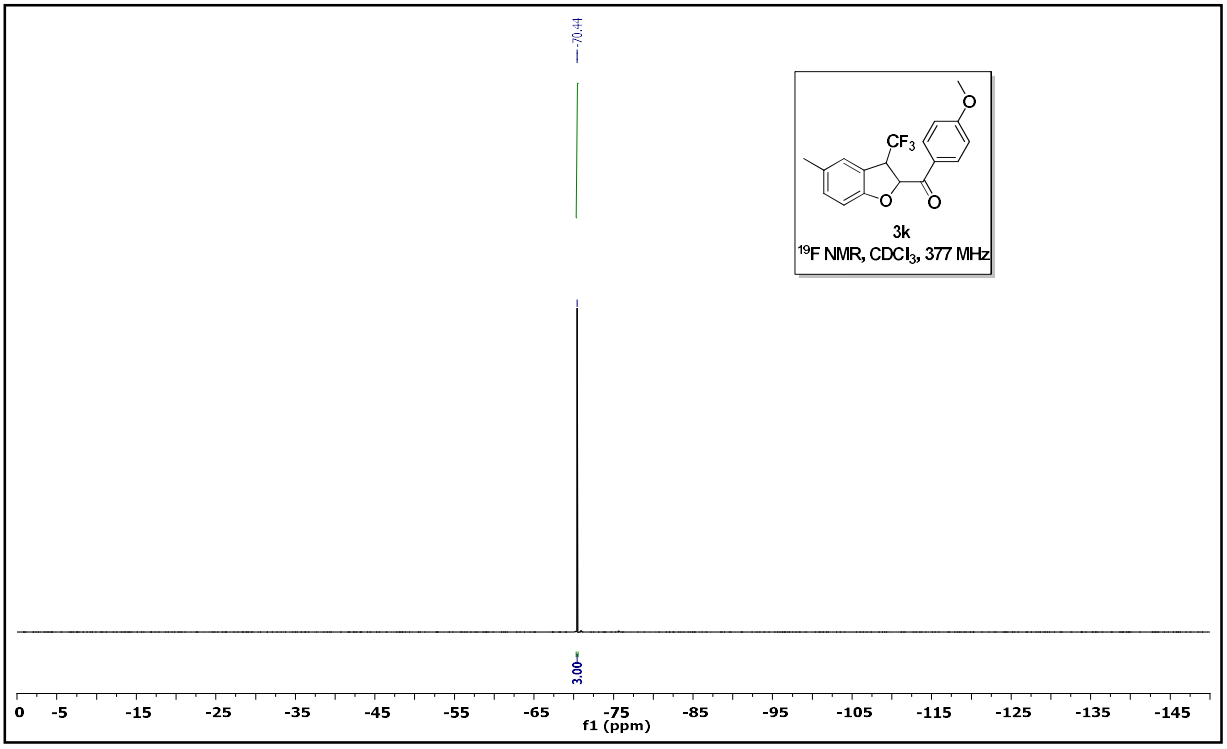

187.38
152.47
129.47
129.28
126.66
126.40
125.04
124.09
122.51
121.53
119.75
114.77
105.17
77.35
43.08
42.79
42.49
42.19
15.75
CF3
O
O
3j
13C NMR, CDCl3, 101 MHz
43.2
42.9
42.6
42.3
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-70.44
CF3
O
O
3j
19F NMR, CDCl3, 377 MHz
3.00
0
-5
-15
-25
-35
-45
-55
-65
-75
-85
-95
-105
-115
-125
-135
-145
f1 (ppm)

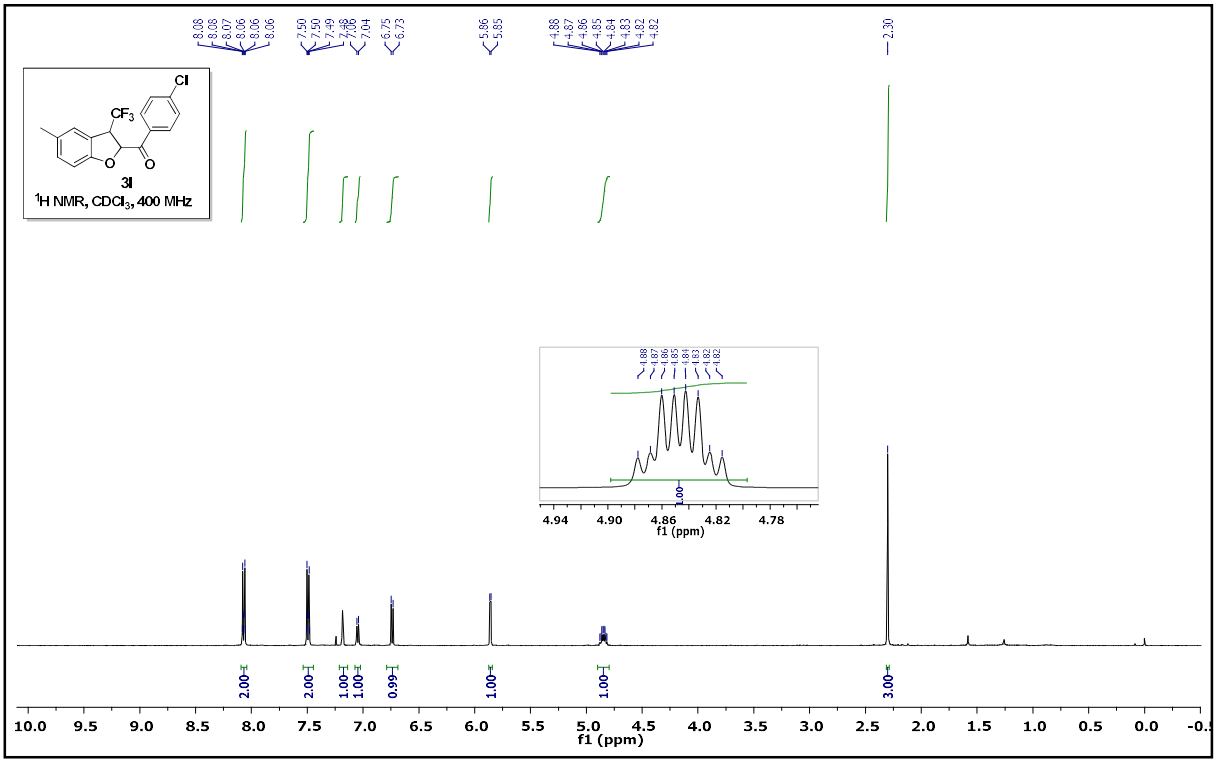
(4-Methoxyphenyl)(5-methyl-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3k):

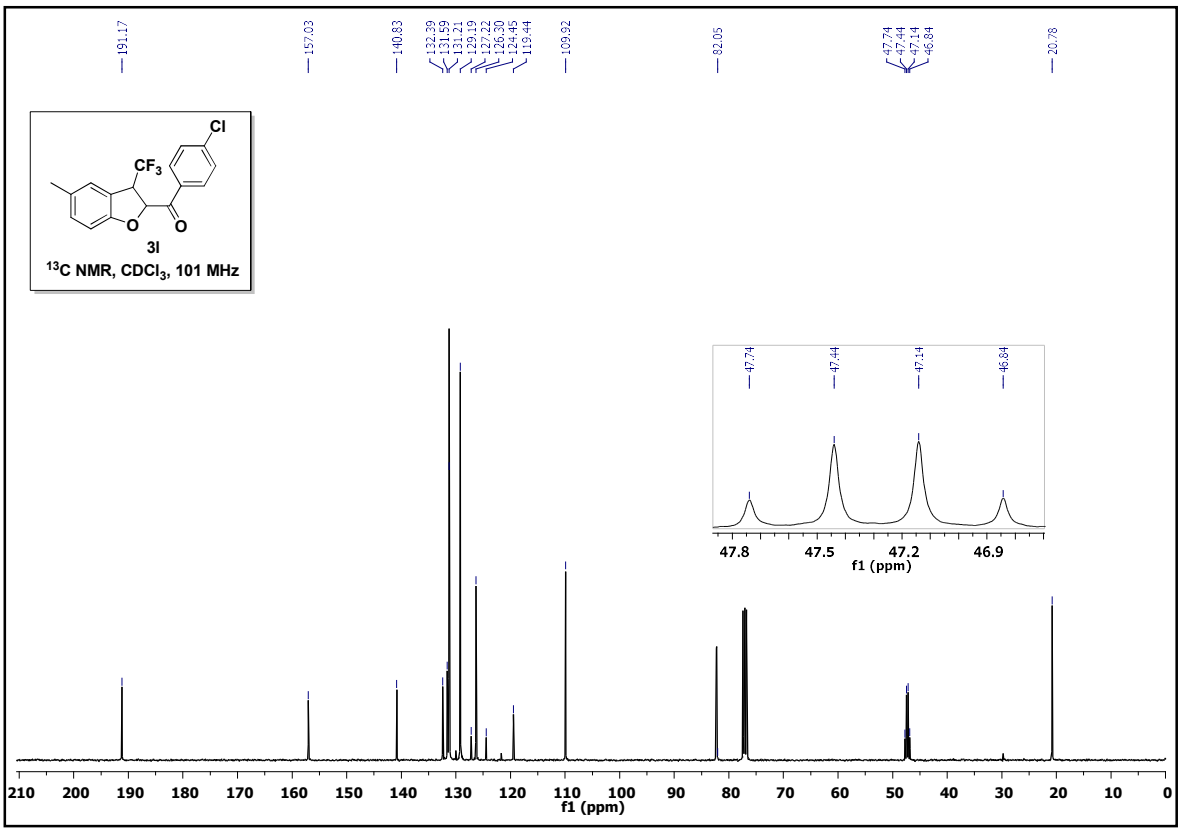


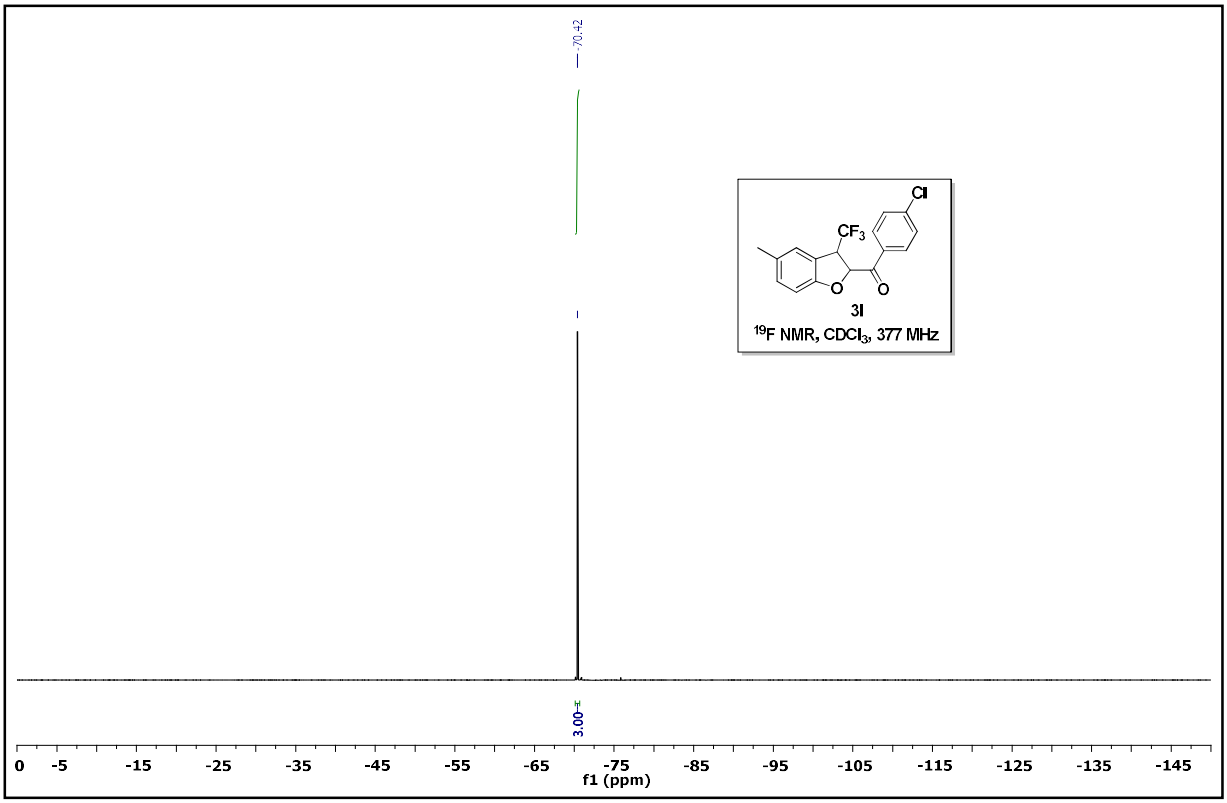




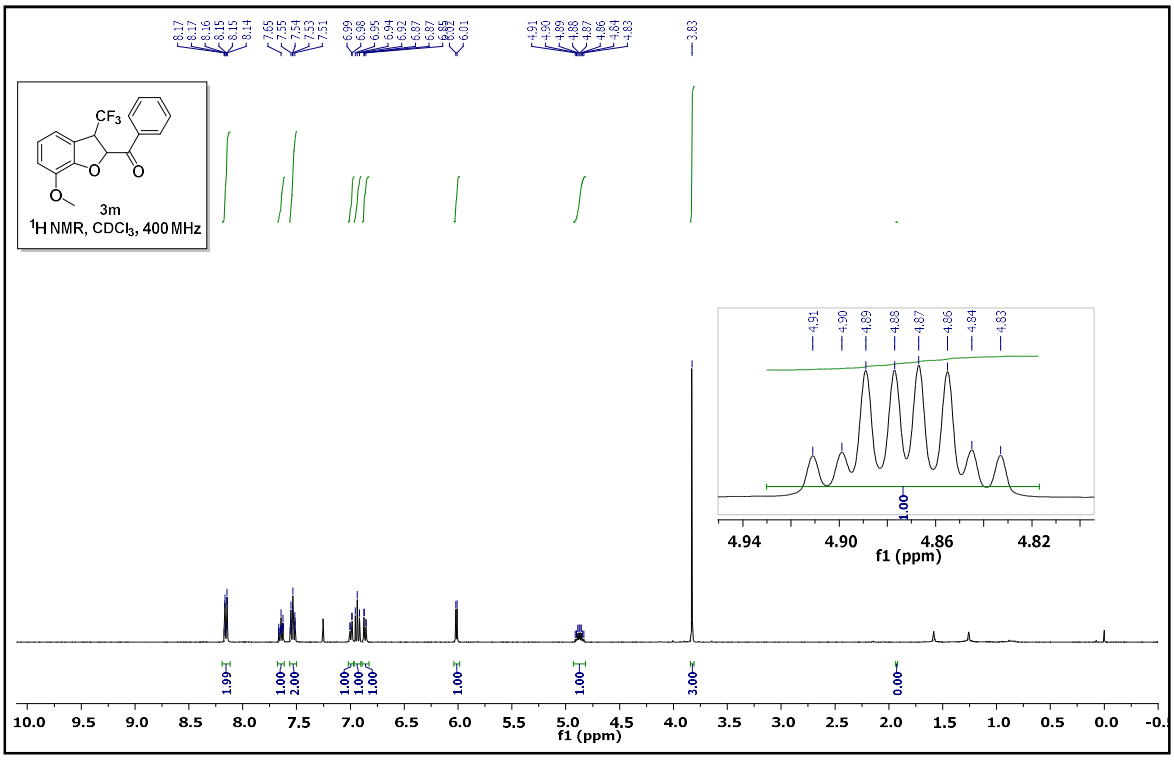
(4-Chlorophenyl)(5-methyl-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3l):

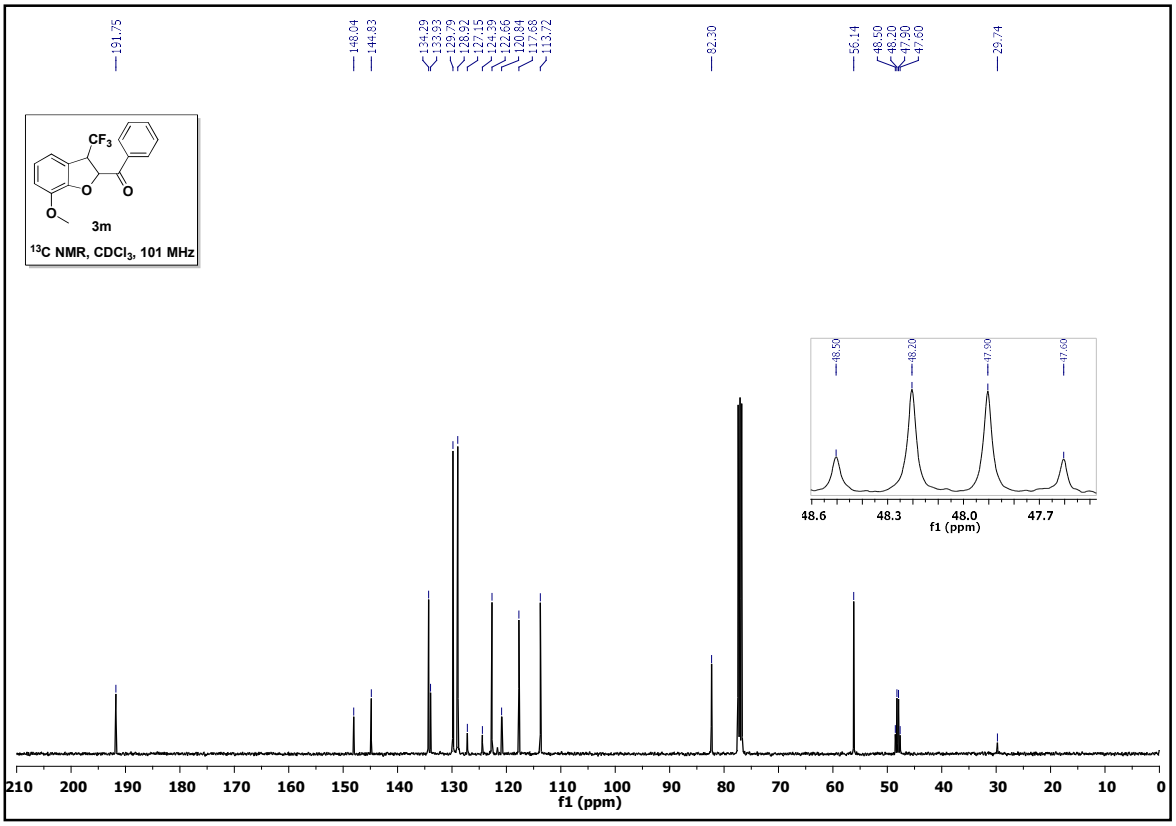


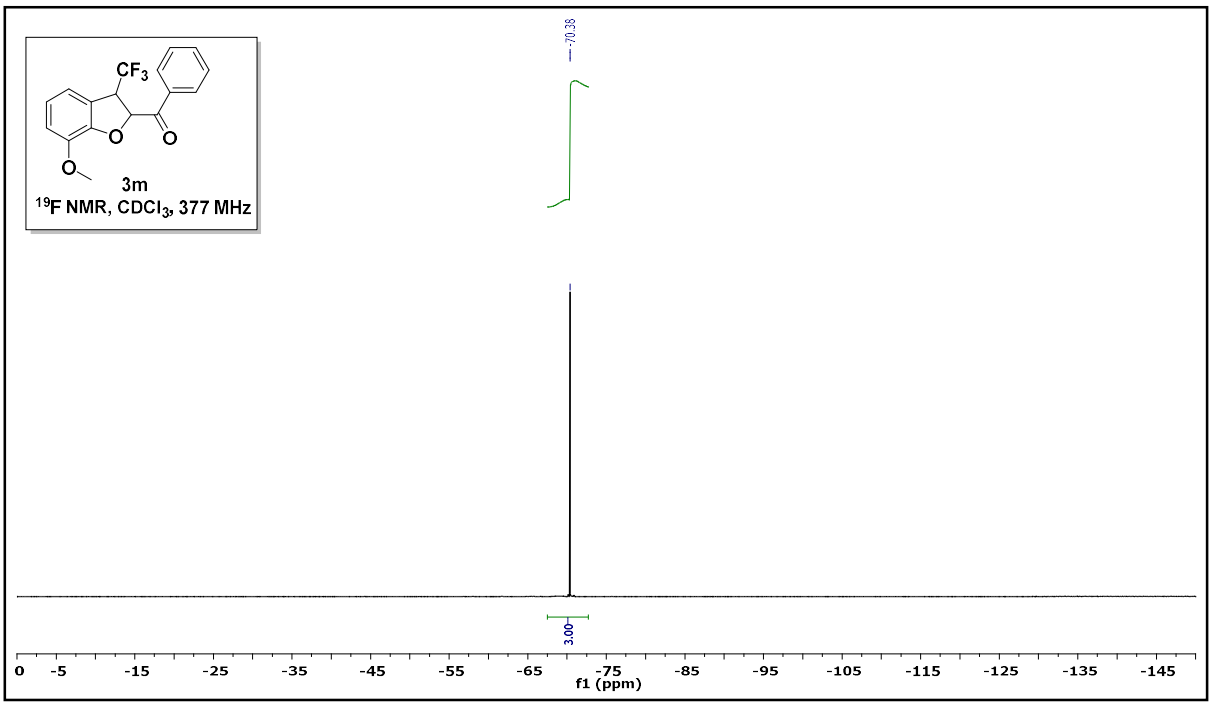

191.17
157.03
140.83
132.39
131.59
131.21
129.19
127.22
126.30
124.45
119.44
109.92
82.05
47.74
47.44
47.14
46.84
20.78
Cl
CF3
O
O
3l
13C NMR, CDCl3, 101 MHz
47.8
47.5
47.2
46.9
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-70.42
3.00
Cl
CF3
O
O
3l
19F NMR, CDCl3, 377 MHz
0 -5 -15 -25 -35 -45 -55 -65 -75 -85 -95 -105 -115 -125 -135 -145
f1 (ppm)

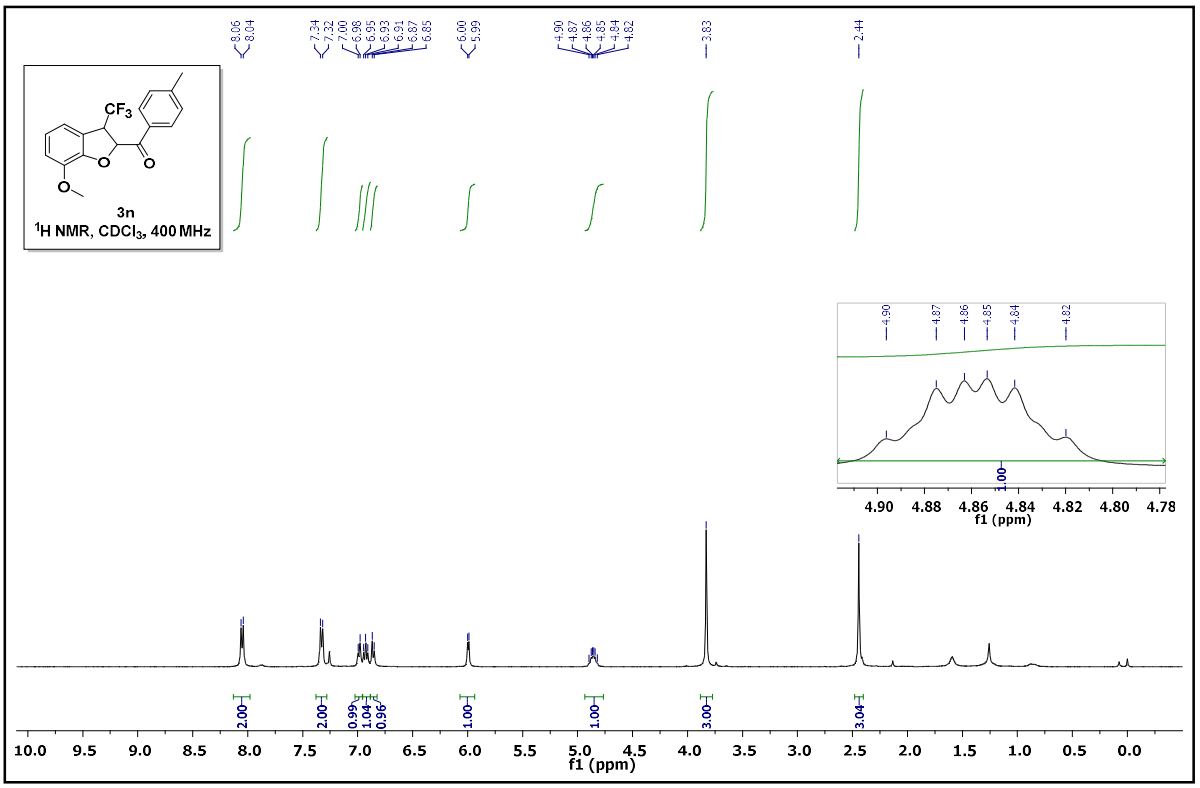
(7-Methoxy-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3m):

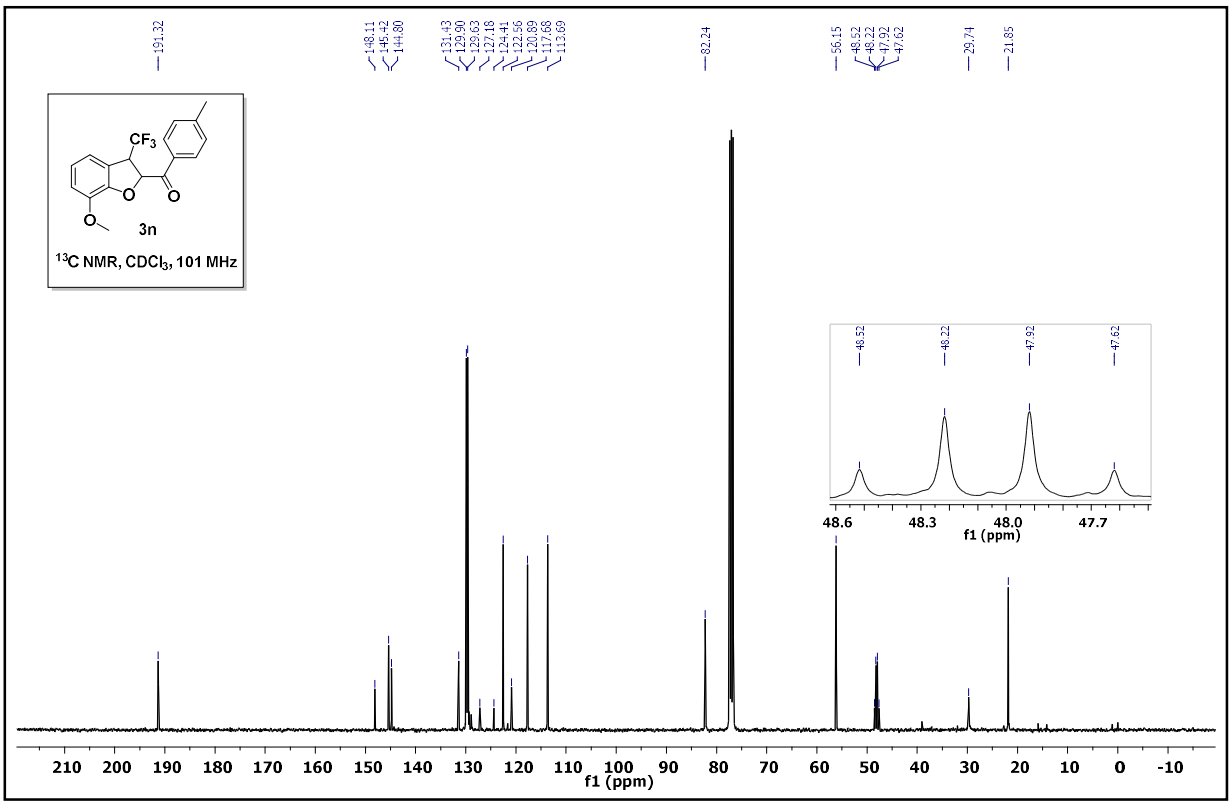


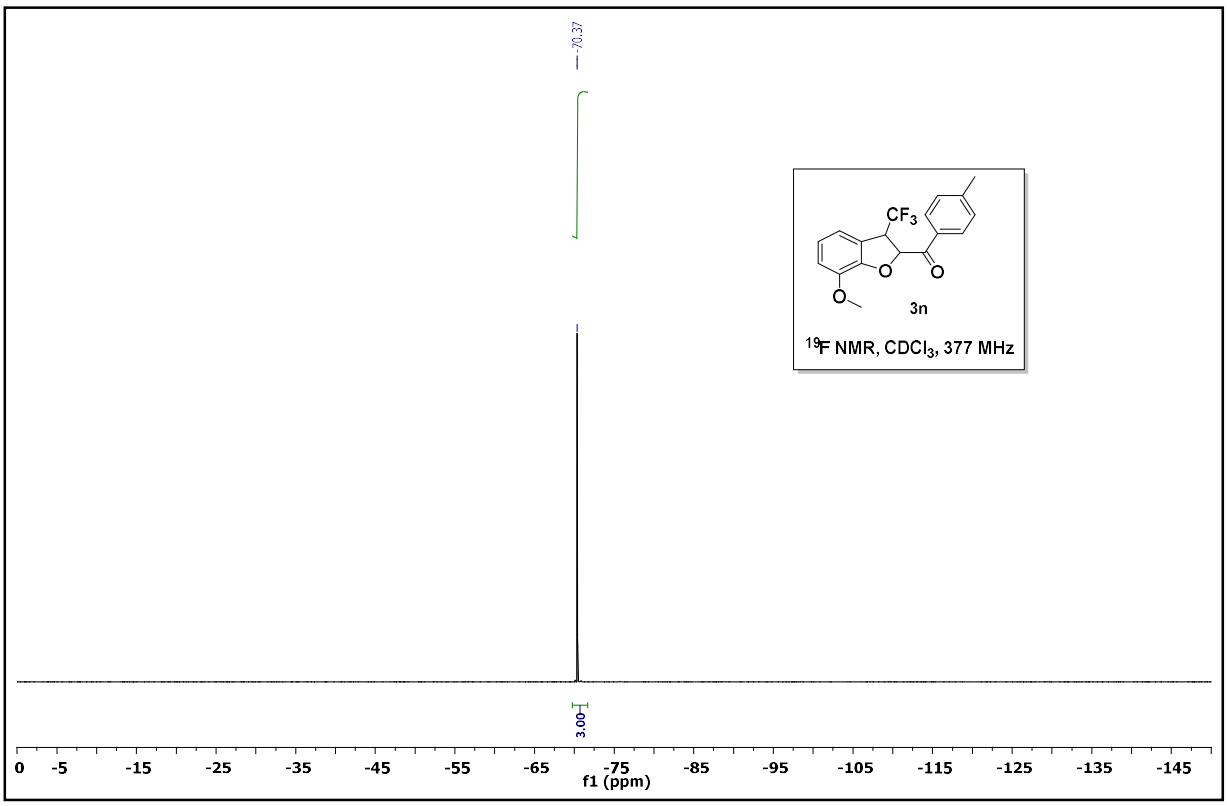




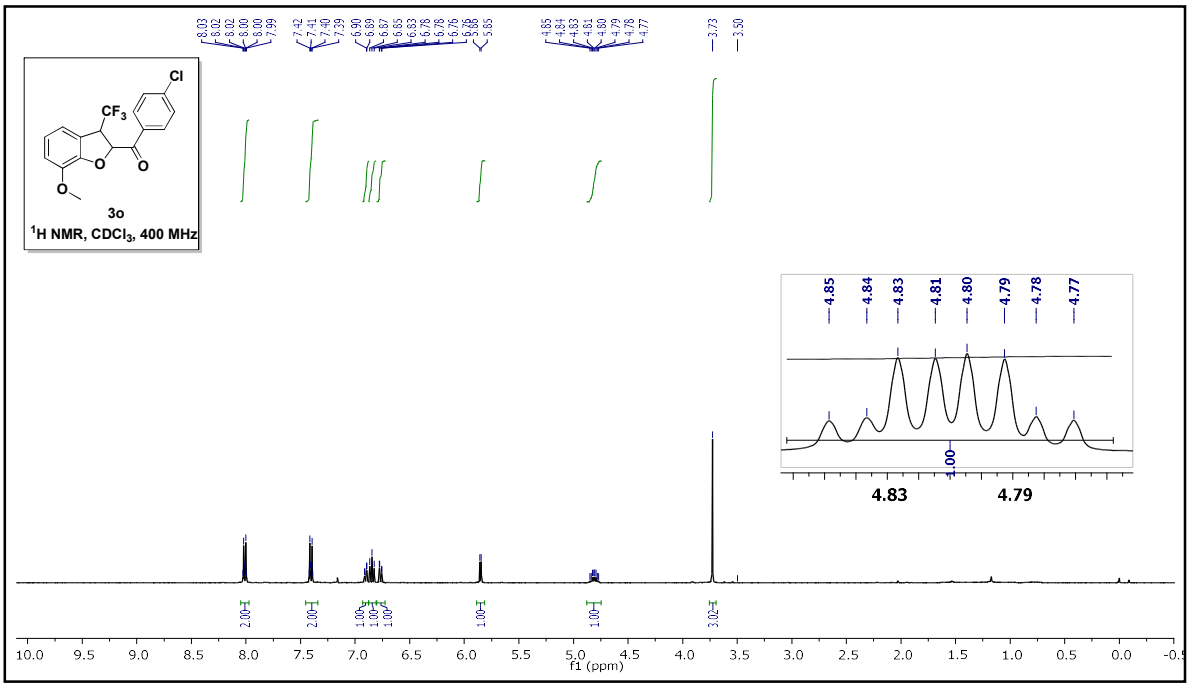
(7-Methoxy-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(p-tolyl)methanone(3n):

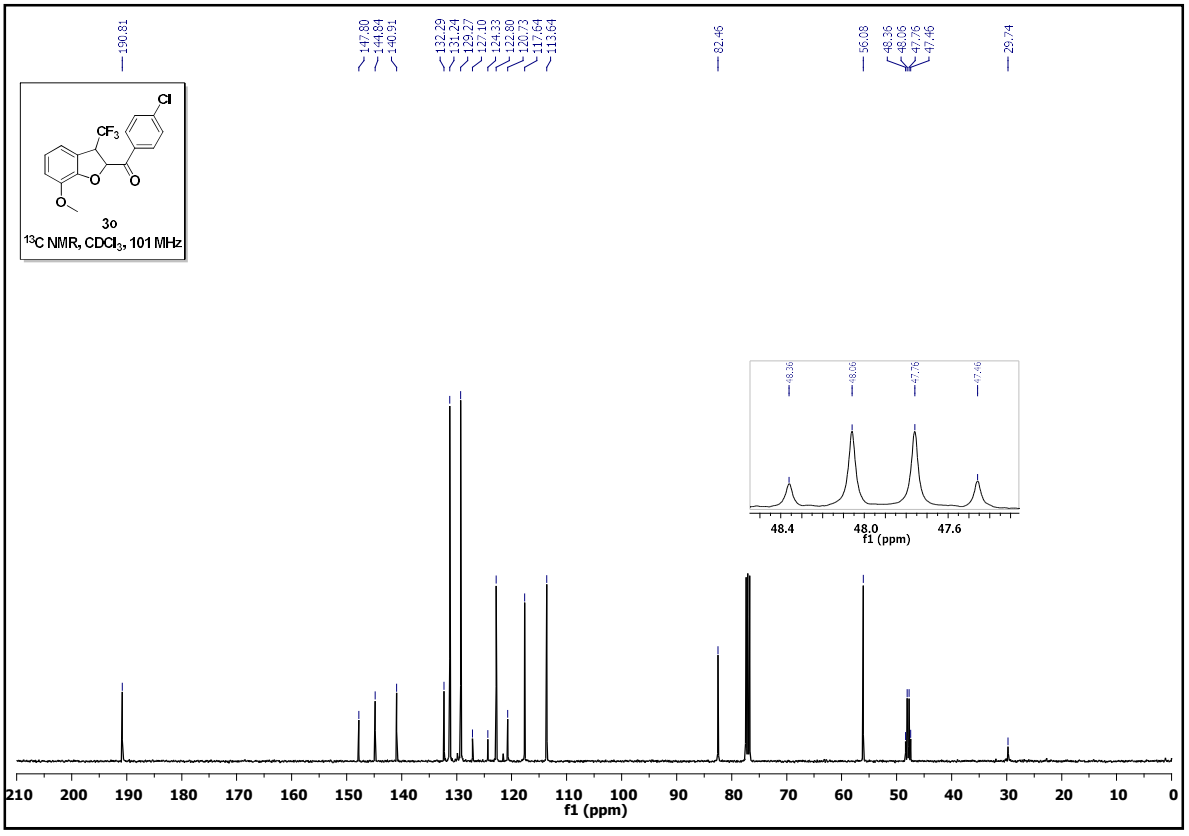


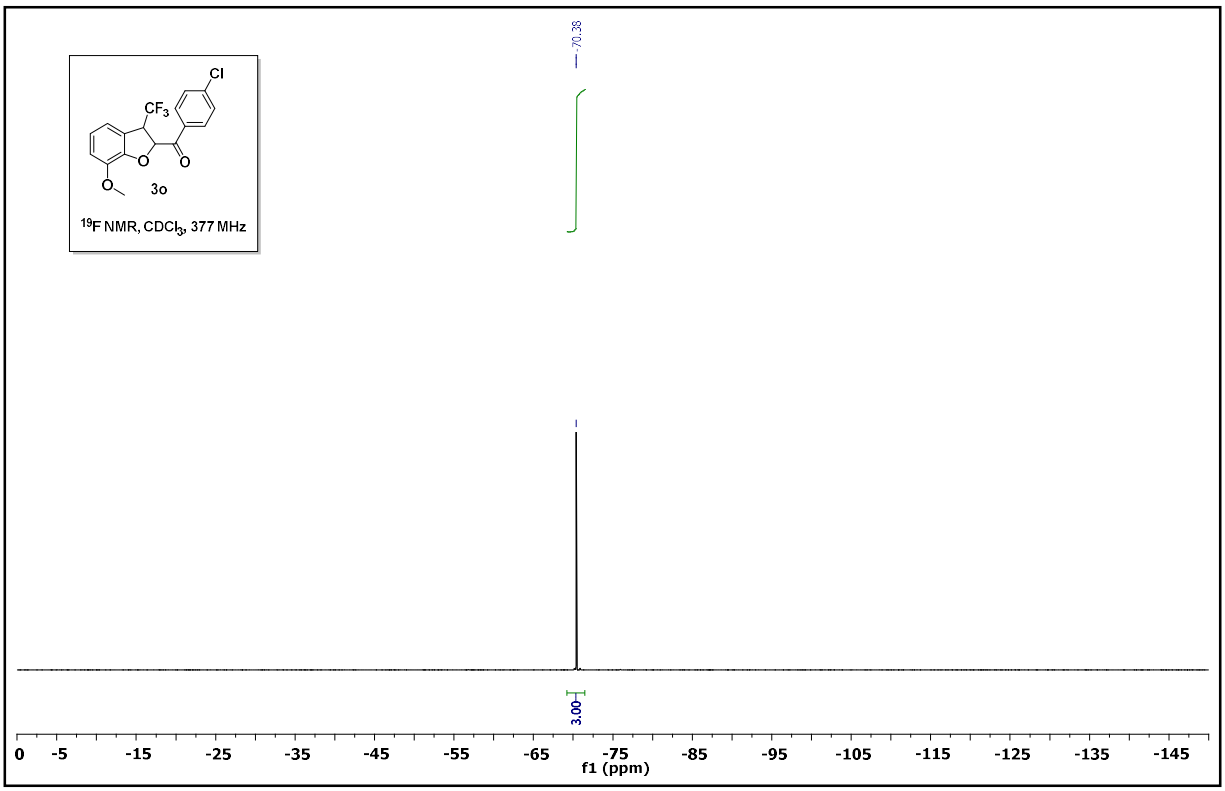

191.32
148.11
145.42
144.80
131.43
129.90
129.63
127.18
124.41
122.56
120.89
117.68
113.69
82.24
56.15
48.52
48.22
47.92
47.62
29.74
21.85
CF3
O
O
O
3n
13C NMR, CDCl3, 101 MHz
48.6
48.3
48.0
47.7
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-70.37
CF3
O
O
O
3n
19F NMR, CDCl3, 377 MHz
3.00
0 -5 -15 -25 -35 -45 -55 -65 -75 -85 -95 -105 -115 -125 -135 -145
f1 (ppm)

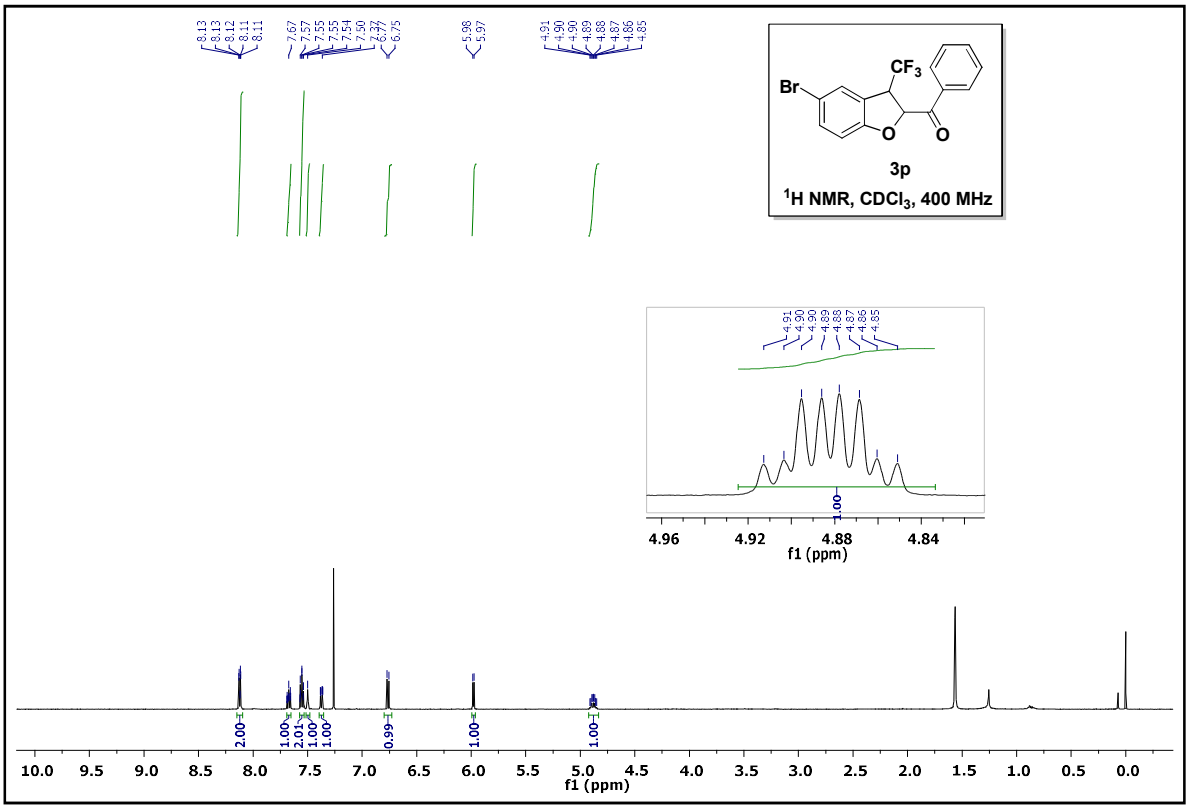
(4-Chlorophenyl)(7-methoxy-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)methanone (3o):

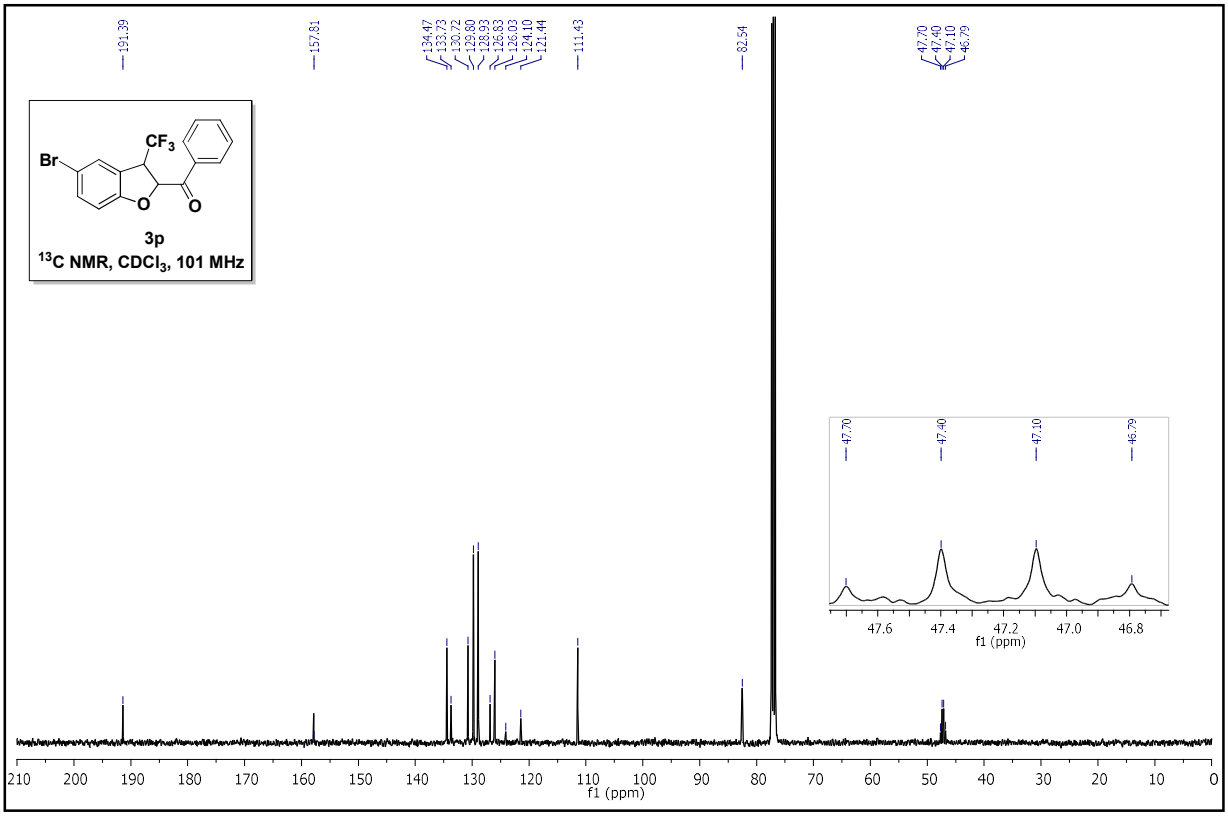


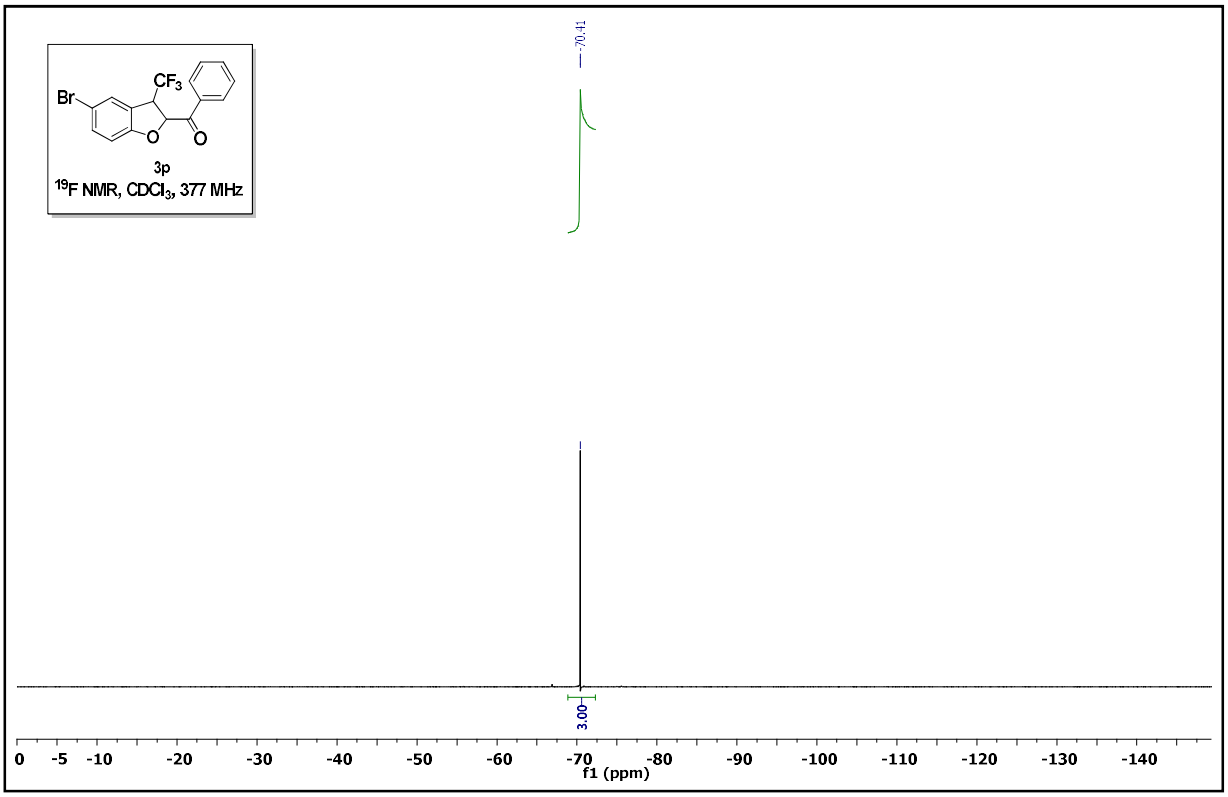




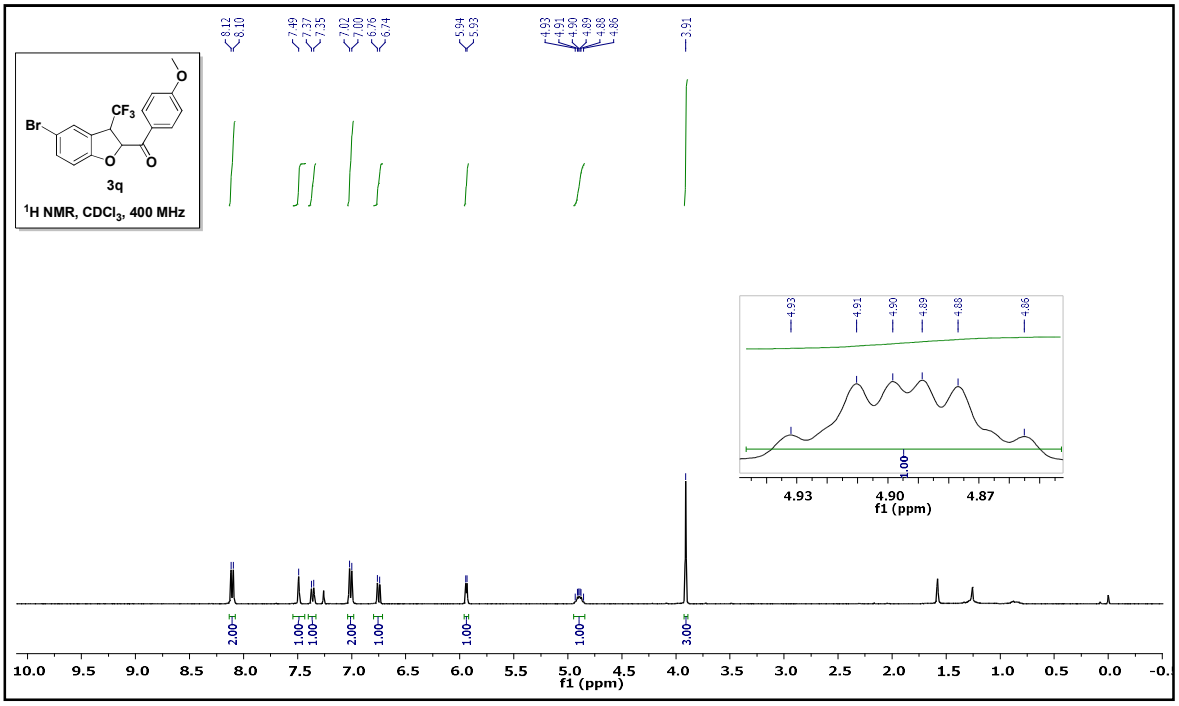
(5-Bromo-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3p):

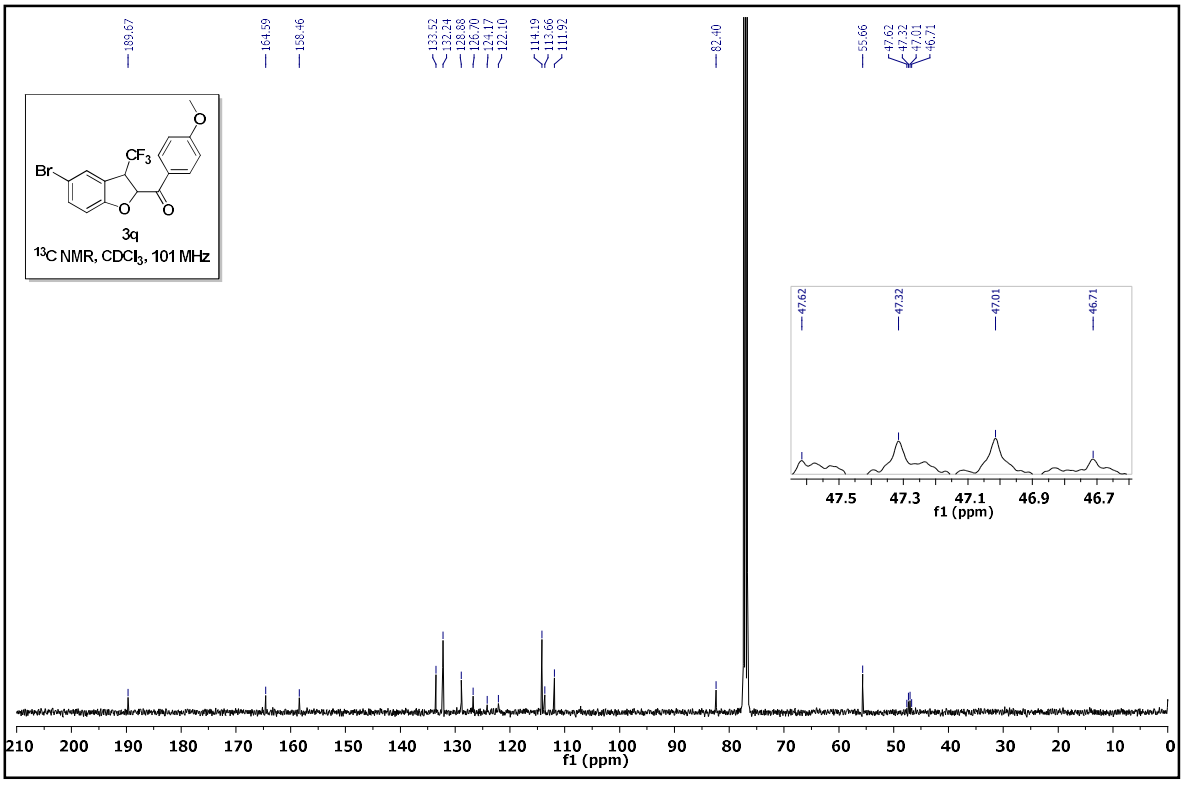


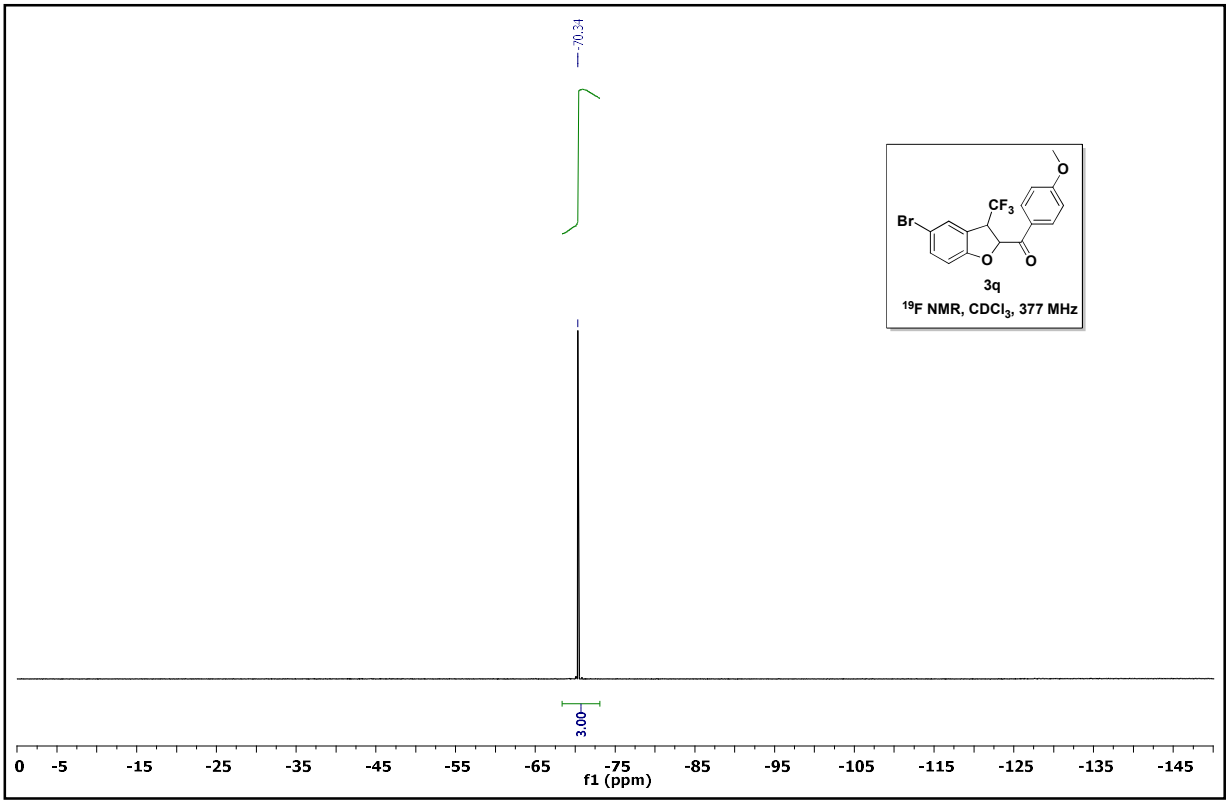

191.39
157.81
134.47
133.73
130.72
129.80
128.93
126.83
126.03
124.10
121.44
111.43
82.54
47.70
47.40
47.10
46.79
Br
CF3
O
O
3p
13C NMR, CDCl3, 101 MHz
f1 (ppm)


-70.41
Br
CF3
O
O
3p
19F NMR, CDCl3, 377 MHz
3.00
f1 (ppm)

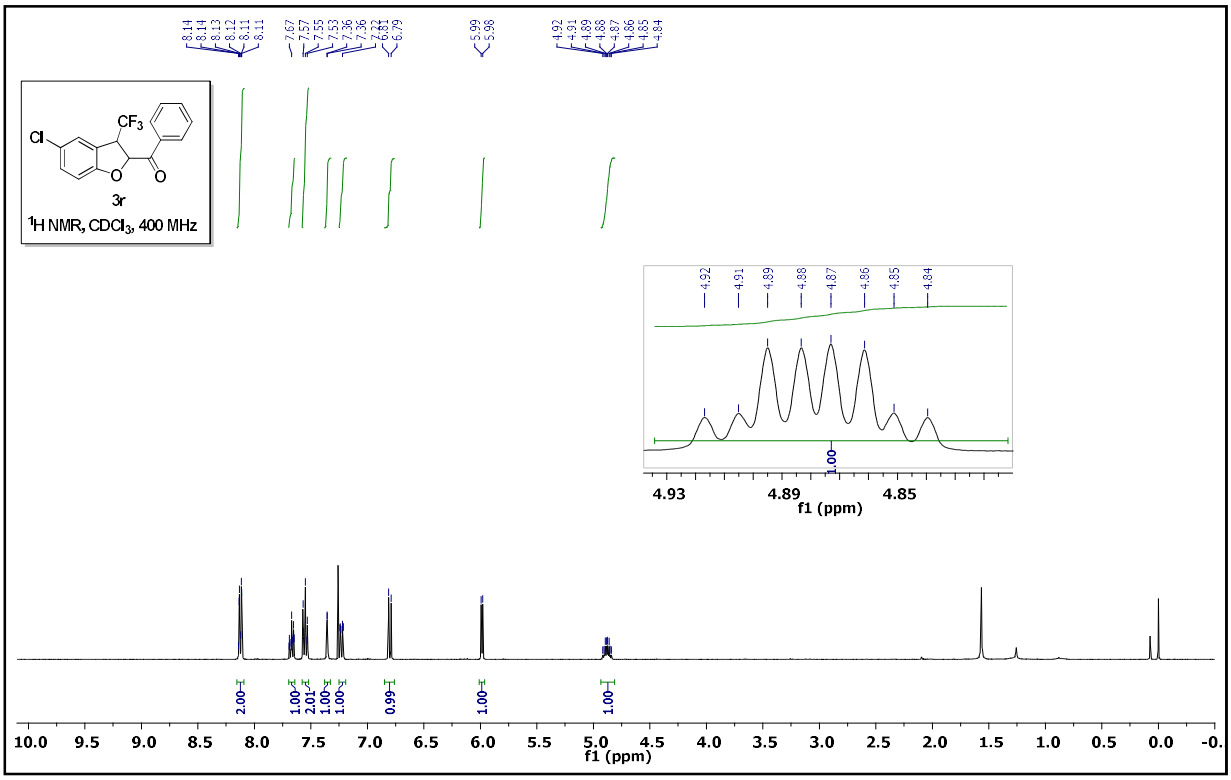
(5-Bromo-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(4-methoxyphenyl)methanone (3q):

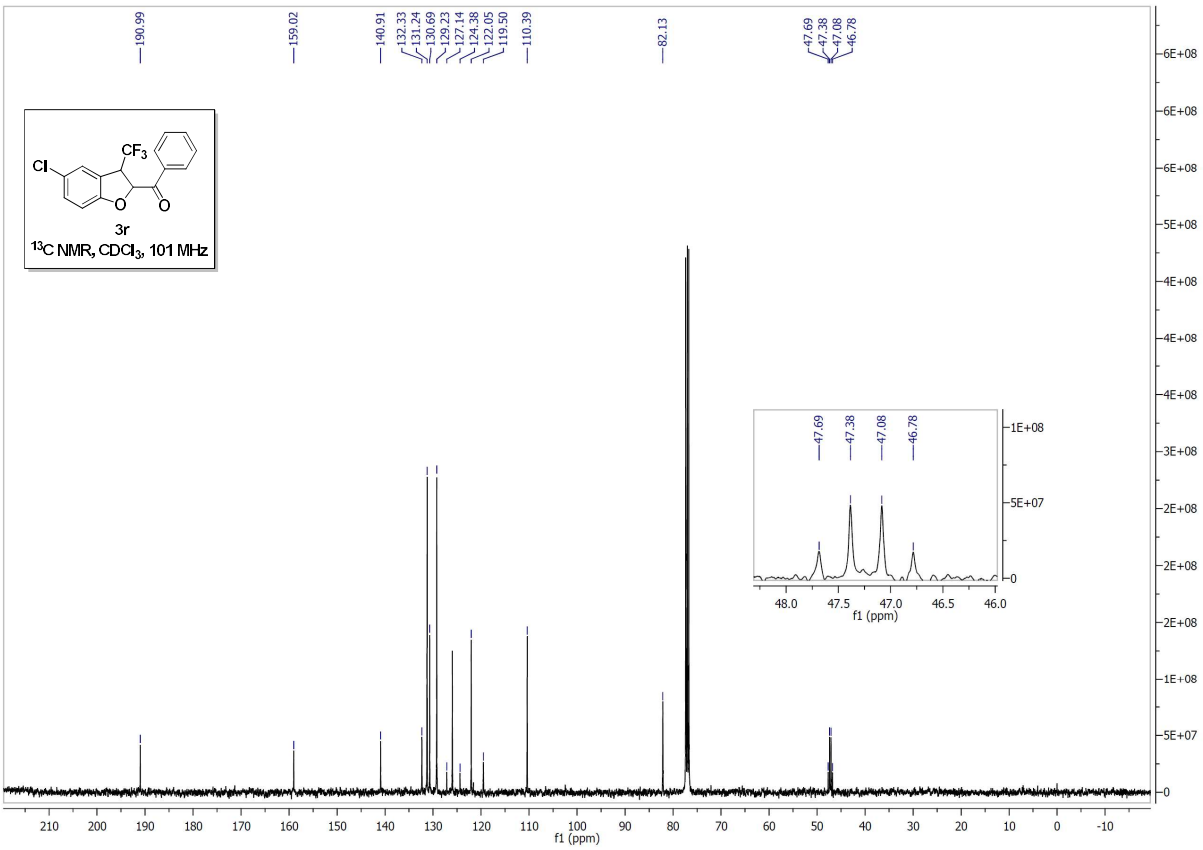


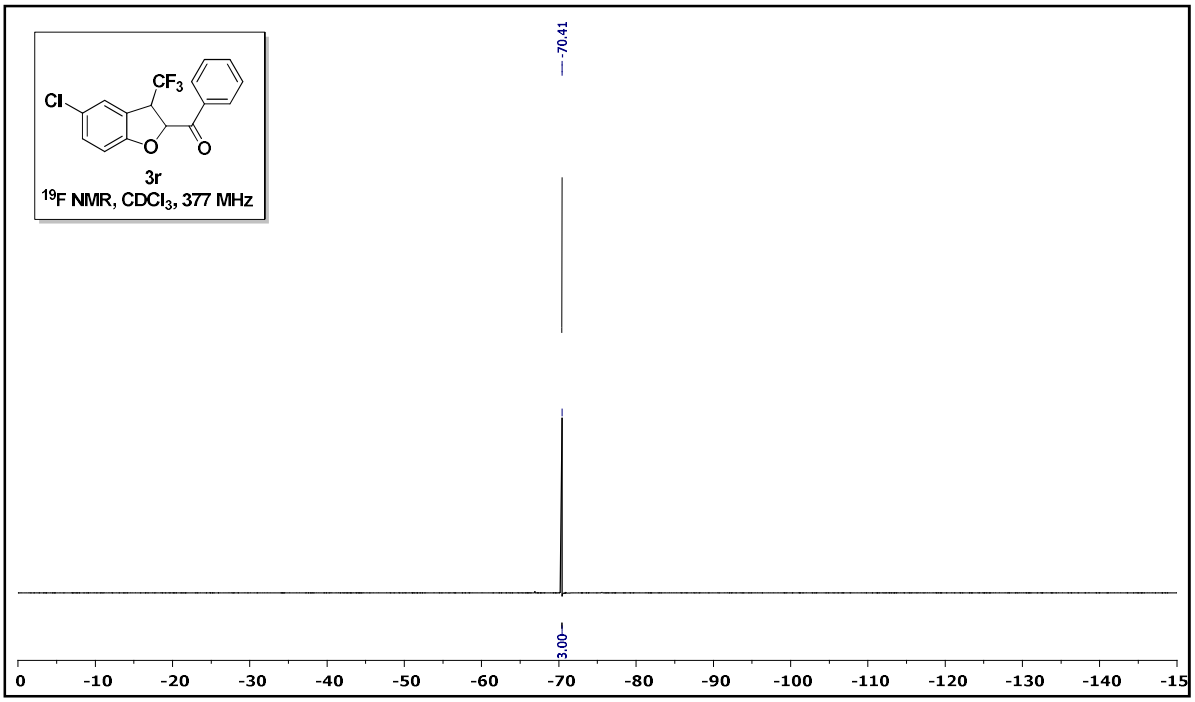




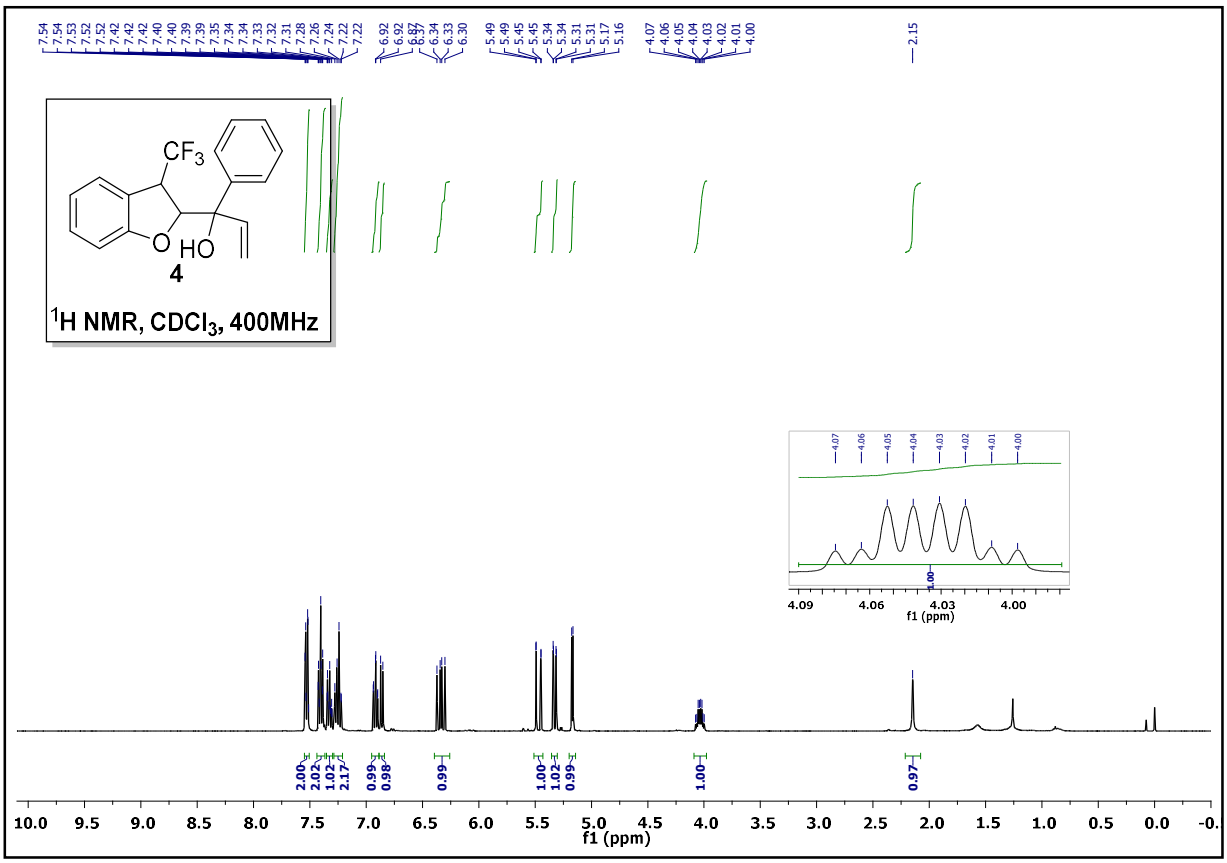
(5-Chloro-3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)(phenyl)methanone (3r):

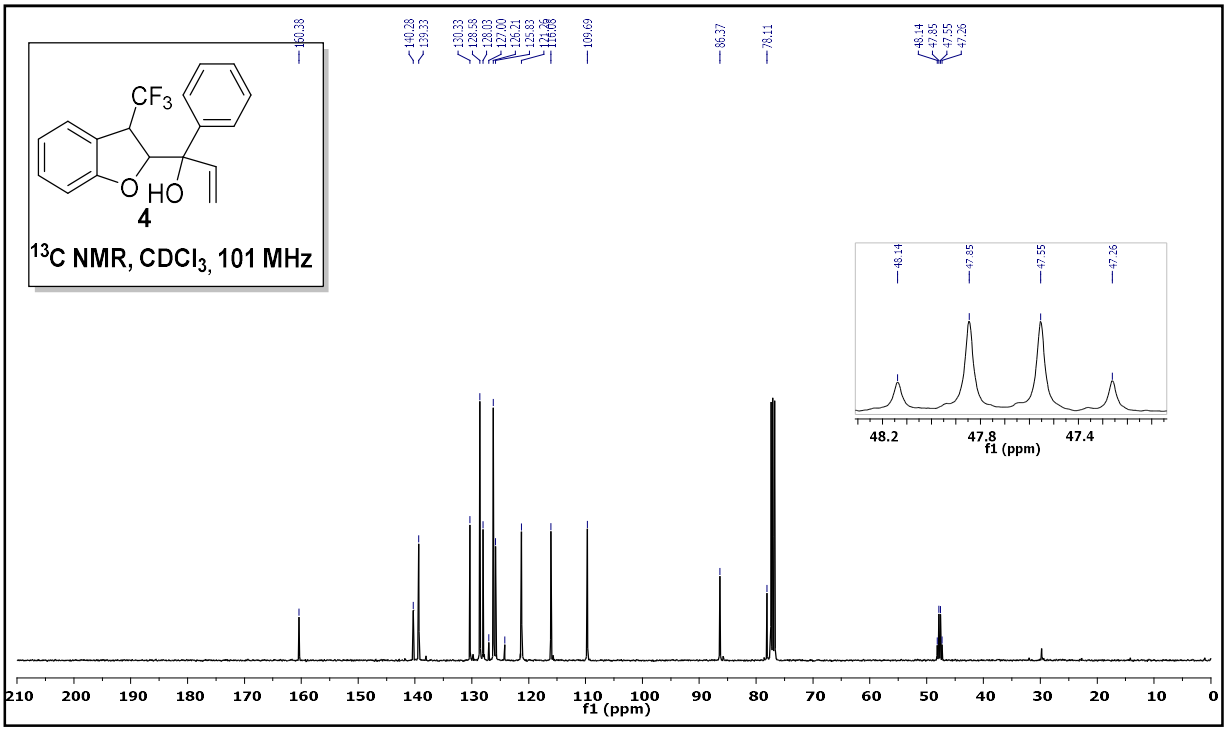


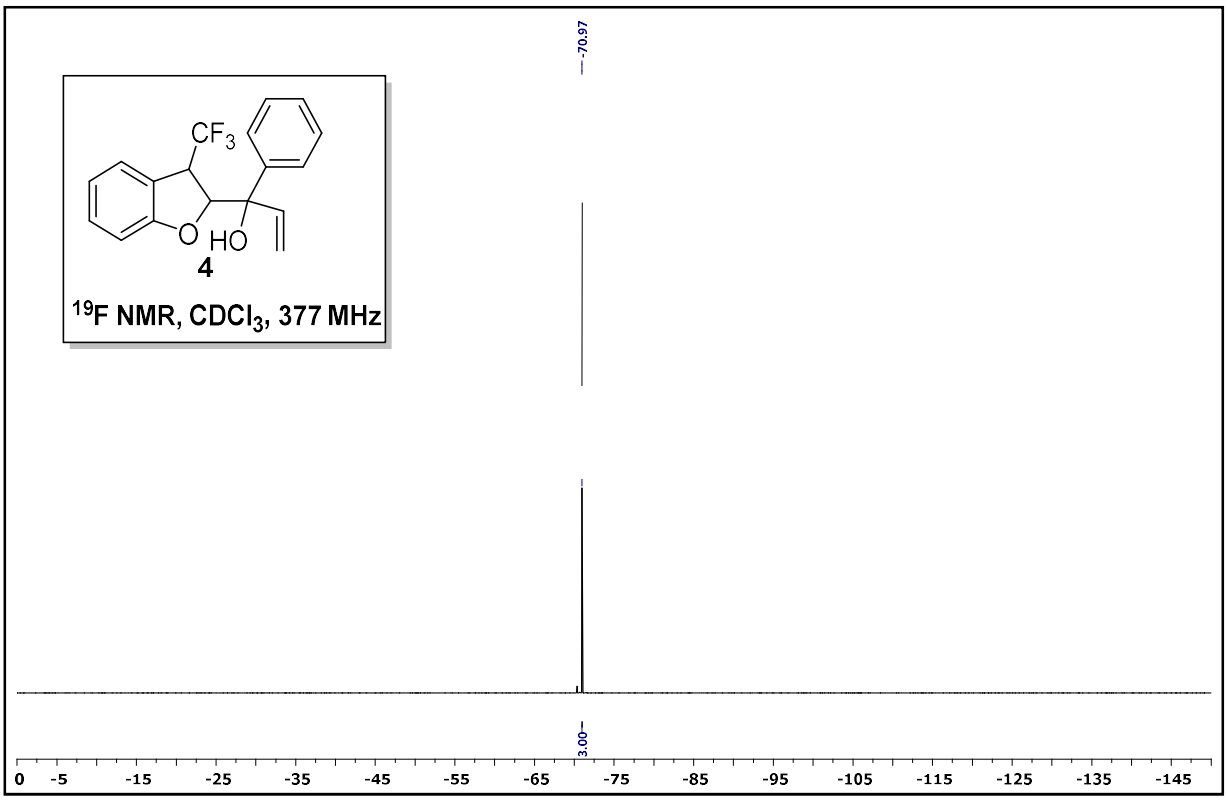




1-phenyl-1-(3-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)prop-2-en-1-ol (4)


CF3
O
HO
4
1H NMR, CDCl3, 400MHz
f1 (ppm)


CF3
O
HO
4
13C NMR, CDCl3, 101 MHz
f1 (ppm)


-70.97
CF3
O
HO
4
19F NMR, CDCl3, 377 MHz
3.00
0 -5 -15 -25 -35 -45 -55 -65 -75 -85 -95 -105 -115 -125 -135 -145