Supporting Information

Selective Methylation of Amides, N-heterocycles, Thiols and Alcohols with Tetramethylammonium Fluoride (TMAF)

Hong-Gang Cheng, Maoping Pu, Gourab Kundu, and Franziska Schoenebeck*

Institute of Organic Chemistry, RWTH Aachen University Landoltweg 1, 52074 Aachen (Germany)
E-mail: franziska.schoenebeck@rwth-aachen.de

Contents

1. General Experimental Details

All reagents and starting materials were commercially available and used as received. Anhydrous toluene was dried using an Innovative Technology PS-MD-5 solvent purification system. Solvents used in work up and purification were distilled prior to use. Thin layer chromatography (TLC) was performed on Merck Kieselgel 60 F254 aluminium plates with unmodified silica and visualized either under UV light or stained with potassium permanganate. Flash column chromatography was performed with Merck silica gel 60 (35 – 70 mesh).

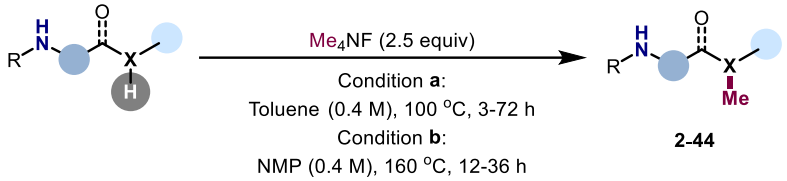
All ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Varian VNMRS 600 or Varian VNMRS 400 spectrometers at ambient temperature. Chemical shifts (δ) are reported in parts per million (ppm), relative to solvent residual peaks. Coupling constants (*J*) are given in Hertz (Hz). Signals are described as br = broad, s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, and m = multiplet.

Gas chromatography coupled with mass spectrometry (GC-MS) was performed on an Agilent Technologies 5975 series MSD mass spectrometer under electrospray ionization (EI) mode coupled with an Agilent Technologies 7820A gas chromatograph employing an Agilent 19091s-433 HP-5MS column (30 m x 0.250 μm x 0.250 μm).

High-resolution mass spectrometry (HRMS) was performed using a Thermo Scientific LTQ Orbitrap XL spectrometer.

2. General Procedures

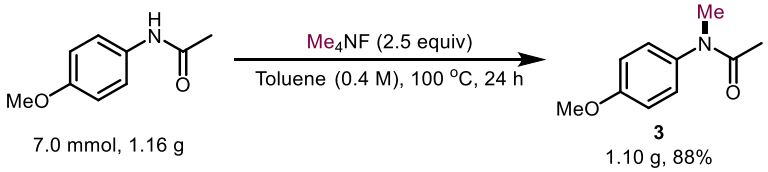
General procedure for the methylation with tetramethylammonium fluoride (TMAF)



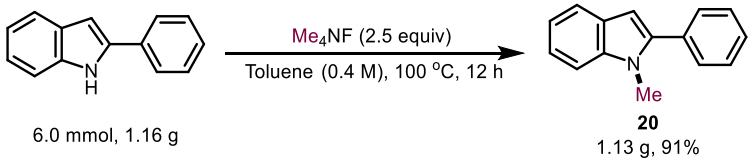
Procedure **a** (standard procedure): To a 4 mL reaction vial equipped with a magnetic stirring bar was added substrate (0.40 mmol), TMAF (93.1 mg, 1.0 mmol), and toluene (1.0 mL). Then, the reaction was stirred at 100 °C in a heating block for 3-72 h. After the completion of the reaction (monitored by TLC), the resulting reaction mixture was cooled to room temperature. Purification by procedure A: filtration through a small pad of silica and washing with ethyl acetate (20 mL), or procedure B: washing with water (15 mL) and extracting with ethyl acetate (15 mL*3), or procedure C: flash column chromatography, to give the corresponding methylation products.

Procedure **b**: To a 4 mL reaction vial equipped with a magnetic stirring bar was added substrate (0.40 mmol), TMAF (93.1 mg, 1.0 mmol), and NMP (1.0 mL). Then, the reaction was stirred at 160 °C in a heating block for 12-36 h. After the completion of the reaction (monitored by TLC), the resulting reaction mixture was cooled to room temperature, washed with water (15 mL) and extracted with methyl *tert*-butyl ether (MTBE) (15 mL*3), dried over Na_2SO_4, and concentrated under vacuum to give the corresponding methylation products.

3. Gram-Scale Reactions

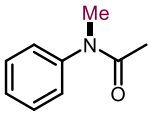


To a 50 mL flask equipped with a magnetic stirring bar was added *N*-(4-methoxyphenyl)acetamide (7.0 mmol, 1.16 g), TMAF (1.63 g, 17.5 mmol), and toluene (17.5 mL). After 24 h of stirring at 100 °C in a heating block, the reaction mixture was cooled to room temperature, and purified by filtration through a small pad of silica and washing with ethyl acetate (40 mL) to give the desired product **3** as a white solid in 88% yield (1.10 g).

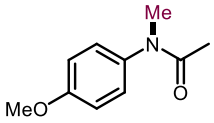


To a 50 mL flask equipped with a magnetic stirring bar was added 2-phenyl-1*H*-indole (6.0 mmol, 1.16 g), TMAF (1.4 g, 15 mmol), and toluene (15 mL). After 12 h of stirring at 100 °C in a heating block, the reaction mixture was cooled to room temperature, and purified by filtration through a small pad of silica and washing with ethyl acetate (40 mL) to give the desired product **20** as a white solid in 91% yield (1.13 g).

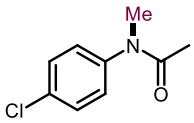
4. Compound Characterization Data



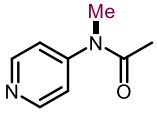
***N*-methyl-*N*-phenylacetamide** (**2**) (**CAS: 579-10-2**): Prepared, following the general procedure from *N*-phenylacetamide and TMAF after 12 h. The title product was obtained by purification procedure A as a white powder (54.9 mg, 92%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.42 – 7.39 (m, 2H), 7.32 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 2H), 3.25 (s, 3H), 1.86 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.7, 144.7, 129.8, 127.8, 127.2, 37.3, 22.5. These data are in agreement with those reported previously in the literature.[1]



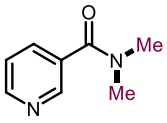
***N*-(4-methoxyphenyl)-*N*-methylacetamide** (**3**) (**CAS: 35813-38-8**): Prepared, following the general procedure from *N*-(4-methoxyphenyl)acetamide and TMAF after 12 h. The title product was obtained by purification procedure A as a white solid (67.4 mg, 94%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.08 (d, *J* = 8.3 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 3.81 (s, 3H), 3.21 (s, 3H), 1.83 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.0, 158.9, 137.6, 128.2, 114.9, 55.6, 37.4, 22.4. These data are in agreement with those reported previously in the literature.[2]



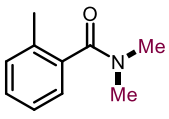
***N*-(4-chlorophenyl)-*N*-methylacetamide** (**4**) (**CAS: 10219-10-0**): Prepared, following the general procedure from *N*-(4-chlorophenyl)acetamide and TMAF after 12 h. The title product was obtained by purification procedure A as a light yellow solid (69.8 mg, 95%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 3.22 (s, 3H), 1.85 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.4, 143.2, 133.6, 130.0, 128.6, 37.2, 22.5. These data are in agreement with those reported previously in the literature.[3]



***N*-methyl-*N*-(pyridin-4-yl)acetamide** (**5**) (**CAS: 53209-33-9**): Prepared, following the general procedure from *N*-(pyridin-4-yl)acetamide and TMAF after 48 h. The title product was obtained after purification by column chromatography (DCM/MeOH 10:1) as a white solid (42.1 mg, 70%). R_f = 0.39 (DCM/MeOH 10:1). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.63 (d, *J* = 6.4 Hz, 2H), 7.15 (d, *J* = 5.8 Hz, 2H), 3.30 (s, 3H), 2.04 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 170.0, 151.7, 151.4, 121.0, 36.9, 22.8. These data are in agreement with those reported previously in the literature.[2]

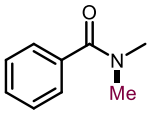


***N,N*-dimethylnicotinamide** (**6**) (**CAS: 6972-69-6**): Prepared, following the general procedure from nicotinamide and TMAF after 48 h. The title product was obtained by purification procedure B as a light yellow oil (54.6 mg, 91%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.66 – 8.62 (m, 2H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.33 (dd, *J* = 7.8, 4.9 Hz, 1H), 3.11 (s, 3H), 2.99 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 169.0, 150.7, 148.1, 135.0, 132.2, 123.4, 39.6, 35.5. These data are in agreement with those reported previously in the literature.[4]

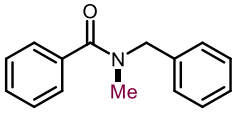


***N,N*,2-trimethylbenzamide** (**7**) (**CAS: 6639-19-6**): Prepared, following the general procedure from 2-methylbenzamide and TMAF after 12 h. The title product was obtained by purification procedure A as a colorless oil (60.7 mg, 93%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.33 – 7.29 (m, 1H), 7.25 – 7.20 (m, 3H), 3.18 (s, 3H), 2.87 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ =

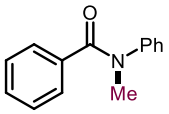
171.6, 136.8, 134.1, 130.4, 128.8, 126.0, 125.9, 38.5, 34.6, 19.0. These data are in agreement with those reported previously in the literature.[5]



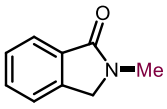
***N,N*-dimethylbenzamide** (**8**) (**CAS: 611-74-5**): Prepared, following the general procedure from *N*-methylbenzamide and TMAF after 12 h. The title product was obtained by purification procedure A as a white solid (53.7 mg, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.40 – 7.35 (m, 5H), 3.09 (s, 3H), 2.95 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.7, 136.4, 129.5, 128.4, 127.1, 39.6, 35.4. These data are in agreement with those reported previously in the literature.[1]



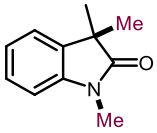
***N*-benzyl-*N*-methylbenzamide** (**9**) (**CAS: 61802-83-3**): Prepared, following the general procedure from *N*-benzylbenzamide and TMAF after 12 h. The title product was obtained by purification procedure A as a colorless oil (83.8 mg, 93%). **^{1}H NMR** (400 MHz, $CDCl_3$) (1:1 mixture of rotamers): δ = 7.37 – 7.35 (m, 2H), 7.31 – 7.24 (m, 6H), 7.21 – 7.18 (m, 1H), 7.10 – 7.04 (m, 1H), 4.66 (s, 1H), 4.41 (s, 1H), 2.93 (s, 1.5H), 2.76 (s, 1.5H). **^{13}C NMR** (101 MHz, $CDCl_3$) (rotamers): δ = 172.3, 171.6, 137.1, 136.6, 136.3, 129.6, 128.84, 128.77, 128.5, 128.2, 127.6, 127.0, 126.8, 55.2, 50.8, 37.0, 33.2. These data are in agreement with those reported previously in the literature.[6]



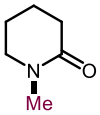
***N*-methyl-*N*-phenylbenzamide** (**10**) (**CAS: 1934-92-5**): Prepared, following the general procedure from *N*-phenylbenzamide and TMAF after 48 h. The title product was obtained after purification by column chromatography (Hexane/EtOAc 3:1) as a yellow oil (80.3 mg, 95%). R_f = 0.30 (Hexane/EtOAc 3:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 7.4 Hz, 2H), 7.23 – 7.20 (m, 3H), 7.17 – 7.11 (m, 3H), 7.03 (d, *J* = 7.7 Hz, 2H), 3.50 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.8, 145.0, 136.0, 129.7, 129.2, 128.8, 127.8, 127.0, 126.6, 38.5. These data are in agreement with those reported previously in the literature.[7]



2-methylisoindolin-1-one (**11**) (**CAS: 5342-91-6**): Prepared, following the general procedure from isoindolin-1-one and TMAF after 12 h. The title product was obtained by purification procedure A as a white solid (57.7 mg, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 7.4 Hz, 1H), 7.50 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.45 – 7.40 (m, 2H), 4.35 (s, 2H), 3.18 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 168.7, 141.1, 133.0, 131.2, 128.1, 123.6, 122.7, 52.1, 29.5. These data are in agreement with those reported previously in the literature.[8]

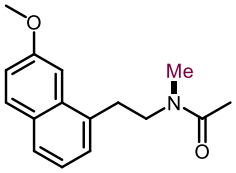


1,3,3-trimethylindolin-2-one (**12**) (**CAS: 20200-86-6**): Prepared, following the general procedure from 3-methylindolin-2-one and TMAF after 12 h. The title product was obtained by purification procedure A as a colorless oil (68.7 mg, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.28 – 7.20 (m, 1H), 7.21 (d, *J* = 7.3 Hz, 1H), 7.06 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 3.22 (s, 3H), 1.37 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 181.5, 142.8, 136.0, 127.8, 122.6, 122.4, 108.1, 44.3, 26.3, 24.5. These data are in agreement with those reported previously in the literature.[9]

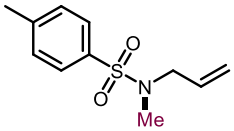


1-methylpiperidin-2-one (**13**) (**CAS: 931-20-4**): Prepared, following the general procedure from piperidin-2-one and TMAF after 12 h. The title product was obtained by purification procedure A as a brown oil (36.2 mg, 80%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.20 (t, *J* = 5.6 Hz, 2H),

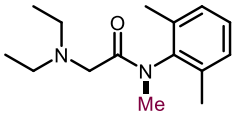
2.86 (s, 3H), 2.28 (t, *J* = 6.0 Hz, 2H), 1.75 – 1.69 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 169.9, 49.9, 34.6, 32.2, 23.1, 21.5. These data are in agreement with those reported previously in the literature.[10]



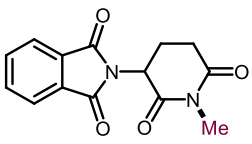
***N*-(2-(7-methoxynaphthalen-1-yl)ethyl)-*N*-methylacetamide** (**14**): Prepared, following the general procedure from *N*-(2-(7-methoxynaphthalen-1-yl)ethyl)acetamide and TMAF after 12 h. The title product was obtained by purification procedure A as a colorless oil (87.5 mg, 85%). **IR** (neat): 2936, 1628, 1508, 1469, 1406, 1357, 1253, 1213, 1134, 1028, 911, 830, 752, 698 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) (2:1 mixture of rotamers): δ = 7.71 (dd, *J* = 19.5, 8.9 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.26 – 7.17 (m, 2H), 7.15 – 7.08 (m, 1H), 3.97 (s, 2H), 3.89 (s, 1H), 3.63 – 3.57 (m, 2H), 3.21 (t, *J* = 7.8 Hz, 2H), 2.94 (s, 1H), 2.85 (s, 2H), 2.05 (s, 2H), 1.78 (s, 1H). **^{1}H NMR** (400 MHz, DMSO-d_6, 140 °C): δ = 7.81 (d, *J* = 8.9 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.54 (s, 1H), 7.34 (d, *J* = 7.0 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.18 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.96 (s, 3H), 3.64 (t, *J* = 7.5 Hz, 2H), 3.25 (t, *J* = 7.4 Hz, 2H), 2.92 (s, 3H), 1.92 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) (rotamers): δ = 170.7, 170.6, 158.14, 158.09, 134.1, 133.5, 132.8, 130.8, 130.2, 129.3, 127.7, 127.5, 127.2, 127.0, 123.5, 123.2, 118.6, 118.1, 102.6, 101.9, 55.7, 55.4, 51.4, 49.7, 37.3, 33.7, 32.1, 31.5, 22.2, 21.0. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{16}H_{19}NO_2$: 280.13080; found: 280.13062.



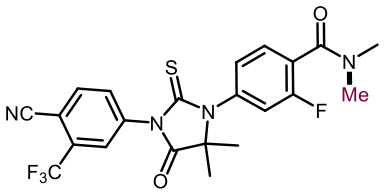
***N*-allyl-*N*,4-dimethylbenzenesulfonamide** (**15**) (**CAS: 112497-43-5**): Prepared, following the general procedure from *N*-allyl-4-methylbenzenesulfonamide and TMAF after 24 h. The title product was obtained after purification by column chromatography (Hexane/EtOAc 2:1) as a colorless oil (40.6 mg, 45%). R_f = 0.21 (Hexane/EtOAc 2:1). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.74 – 5.67 (m, 1H), 5.20 – 5.19 (m, 1H), 5.17 (t, *J* = 1.4 Hz, 1H), 3.62 (d, *J* = 6.3 Hz, 2H), 2.66 (s, 3H), 2.43 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 143.5, 134.6, 132.8, 129.8, 127.6, 119.2, 53.2, 34.3, 21.7. These data are in agreement with those reported previously in the literature.[11]



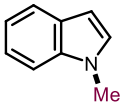
2-(diethylamino)-*N*-(2,6-dimethylphenyl)-*N*-methylacetamide (**16**) (**CAS: 31058-85-2**): Prepared, following the general procedure from lidocaine and TMAF after 12 h. The title product was obtained after purification by column chromatography (EtOAc) as a colorless oil (43.5 mg, 88%). R_f = 0.20 (EtOAc). **IR** (neat): 2965, 1659, 1465, 1377, 1281, 1162, 1082, 906, 774 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.15 – 7.05 (m, 3H), 3.10 (s, 3H), 2.80 (s, 2H), 2.52 (q, *J* = 7.2 Hz, 4H), 2.19 (s, 6H), 0.87 (t, *J* = 7.2 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.0, 140.7, 135.8, 129.0, 128.2, 54.3, 47.5, 34.4, 17.7, 12.0. **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{15}H_{25}N_2O$: 249.19614; found: 249.19658.



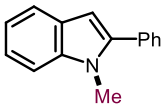
2-(1-methyl-2,6-dioxopiperidin-3-yl)isoindoline-1,3-dione (**17**) (**CAS: 42472-93-5**): Prepared, following the general procedure from thalidomide and TMAF using NMP as solvent after 12 h. The title product was obtained after purification by column chromatography (Hexane/EtOAc 2:1) as a white solid (50.0 mg, 92%). R_f = 0.50 (Hexane/EtOAc 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.88 – 7.86 (m, 2H), 7.77 – 7.74 (m, 2H), 5.01 – 4.97 (m, 1H), 3.20 (s, 3H), 3.00 – 2.96 (m, 1H), 2.86 – 2.72 (m, 2H), 2.13 (dt, *J* = 12.7, 6.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.2, 168.8, 167.5, 134.5, 131.9, 123.9, 50.2, 32.0, 27.4, 22.1. These data are in agreement with those reported previously in the literature.[12]



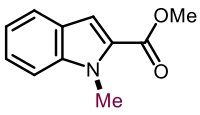
4-(3-(4-cyano-3-(trifluoromethyl)phenyl)-5,5-dimethyl-4-oxo-2-thioxoimidazolidin-1-yl)-2-fluoro-N,N-dimethylbenzamide (**18**): Prepared, following the general procedure from enzalutamide and TMAF after 12 h. The title product was obtained after purification by column chromatography (Hexane/EtOAc 1:2) as a yellow oil (50.7 mg, 53%). R_f = 0.41 (Hexane/EtOAc 1:4). **IR** (neat): 2935, 2234, 1758, 1635, 1497, 1412, 1309, 1220, 1174, 1131, 1060, 907, 814, 731 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.99 – 7.95 (m, 2H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.58 – 7.54 (m, 1H), 7.17 (d, *J* = 8.1 Hz, 1H), 7.10 (d, *J* = 9.3 Hz, 1H), 3.15 (s, 3H), 3.00 (s, 3H), 1.59 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 179.8, 174.6, 165.5, 158.3 (d, *J* = 251.5 Hz), 137.4 (d, *J* = 9.5 Hz), 137.0, 135.4, 133.6 (q, *J* = 33.5 Hz), 132.3, 130.4 (d, *J* = 5.1 Hz), 127.2 (q, *J* = 4.7 Hz), 126.4 – 126.2 (m), 123.3, 120.6, 117.8 (d, *J* = 23.3 Hz), 114.8, 110.4, 66.7, 38.6, 38.5, 35.2, 23.8. **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -61.99, -111.50. **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{19}F_4N_4O_2S$: 479.11594; found: 479.11594.



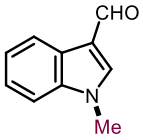
1-methyl-1*H*-indole (**19**) (**CAS: 603-76-9**): Prepared, following the general procedure from 1*H*-indole and TMAF after 3 h. The title product was obtained by purification procedure A as a colorless oil (47.2 mg, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.29 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.17 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.09 (d, *J* = 3.1 Hz, 1H), 6.55 (d, *J* = 3.1 Hz, 1H), 3.82 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 136.8, 128.9, 128.6, 121.6, 121.0, 119.4, 109.3, 101.0, 32.9. These data are in agreement with those reported previously in the literature.[13]



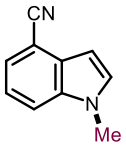
1-methyl-2-phenyl-1*H*-indole (**20**) (**CAS: 3558-24-5**): Prepared, following the general procedure from 2-phenyl-1*H*-indole and TMAF after 6 h. The title product was obtained by purification procedure A as a white solid (81.3 mg, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 7.2 Hz, 2H), 7.57 – 7.53 (m, 2H), 7.50 – 7.44 (m, 2H), 7.36 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.26 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.68 (s, 1H), 3.81 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 141.6, 138.5, 132.9, 129.5, 128.6, 128.1, 127.9, 121.8, 120.6, 120.0, 109.7, 101.8, 31.2. These data are in agreement with those reported previously in the literature.[14]



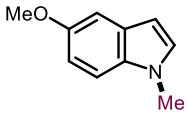
methyl 1-methyl-1*H*-indole-2-carboxylate (**21**) (**CAS: 37493-34-8**): Prepared, following the general procedure from methyl 1*H*-indole-2-carboxylate and TMAF after 6 h. The title product was obtained by purification procedure A as a white solid (72.7 mg, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.0 Hz, 1H), 7.41 – 7.31 (m, 3H), 7.16 (dd, *J* = 7.0, 7.0 Hz, 1H), 4.09 (s, 3H), 3.92 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 162.8, 139.8, 127.8, 126.0, 125.1, 122.7, 120.7, 110.4, 51.8, 31.7. These data are in agreement with those reported previously in the literature.[15]



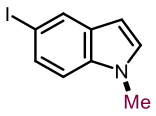
1-methyl-1*H*-indole-3-carbaldehyde (**22**) (**CAS: 19012-03-4**): Prepared, following the general procedure from 1*H*-indole-3-carbaldehyde and TMAF after 6 h. The title product was obtained by purification procedure A as a white solid (57.3 mg, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 9.96 (s, 1H), 8.30 (d, *J* = 6.6 Hz, 1H), 7.62 (s, 1H), 7.37 – 7.30 (m, 3H), 3.83 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 184.5, 139.4, 137.9, 125.3, 124.1, 123.0, 122.1, 118.1, 110.0, 33.7. These data are in agreement with those reported previously in the literature.[16]



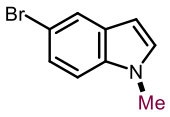
1-methyl-1*H*-indole-4-carbonitrile (**23**) (**CAS: 628711-58-0**): Prepared, following the general procedure from 1*H*-indole-4-carbonitrile and TMAF after 6 h. The title product was obtained by filtration through a small pad of silica and washing with hexane/ethyl acetate (4:1, 20 mL) as a white solid (53.4 mg, 85%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 8.3 Hz, 1H), 7.46 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.26 – 7.22 (m, 2H), 6.68 (dd, *J* = 3.1, 0.9 Hz, 1H), 3.84 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 136.4, 131.5, 129.7, 124.9, 121.1, 118.9, 114.1, 103.1, 100.1, 33.2. These data are in agreement with those reported previously in the literature.[17]



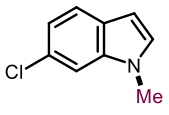
5-methoxy-1-methyl-1*H*-indole (**24**) (**CAS: 2521-13-3**): Prepared, following the general procedure from 5-methoxy-1*H*-indole and TMAF after 6 h. The title product was obtained by purification procedure A as a white solid (62.6 mg, 97%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.8 Hz, 1H), 7.16 (d, *J* = 2.4 Hz, 1H), 7.05 (d, *J* = 3.0 Hz, 1H), 6.95 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.46 (d, *J* = 3.0 Hz, 1H), 3.90 (s, 3H), 3.77 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 154.1, 132.2, 129.4, 128.9, 111.9, 110.0, 102.6, 100.5, 56.0, 33.0. These data are in agreement with those reported previously in the literature.[17]



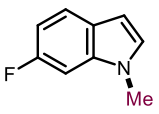
5-iodo-1-methyl-1*H*-indole (**25**) (**CAS: 280563-07-7**): Prepared, following the general procedure from 5-iodo-1*H*-indole and TMAF after 6 h. The title product was obtained by purification procedure A as a colorless solid (99.7 mg, 97%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 1.8 Hz, 1H), 7.48 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.10 (ddd, *J* = 8.6, 8.6, 0.7 Hz, 1H), 7.01 (d, *J* = 3.1 Hz, 1H), 6.43 (dd, *J* = 3.1, 0.9 Hz, 1H), 3.75 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 135.8, 131.1, 129.8, 129.7, 129.7, 111.3, 100.3, 82.9, 33.0. These data are in agreement with those reported previously in the literature.[18]



5-bromo-1-methyl-1*H*-indole (**26**) (**CAS: 10075-52-2**): Prepared, following the general procedure from 5-bromo-1*H*-indole and TMAF after 6 h. The title product was obtained by purification procedure A as a white solid (80.6 mg, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 1.8 Hz, 1H), 7.30 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 7.05 (d, *J* = 3.1 Hz, 1H), 6.42 (dd, *J* = 3.1, 0.9 Hz, 1H), 3.78 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 135.5, 130.2, 130.1, 124.4, 123.4, 112.8, 110.8, 100.6, 33.1. These data are in agreement with those reported previously in the literature.[17]

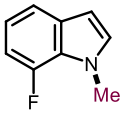


6-chloro-1-methyl-1*H*-indole (**27**) (**CAS: 155868-51-2**): Prepared, following the general procedure from 6-chloro-1*H*-indole and TMAF after 6 h. The title product was obtained by filtration through a small pad of silica and washing with hexane/ethyl acetate (10:1, 20 mL) as a yellow oil (57.7 mg, 87%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.4 Hz, 1H), 7.32 (s, 1H), 7.08 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.04 (d, *J* = 3.1 Hz, 1H), 6.46 (d, *J* = 3.1 Hz, 1H), 3.76 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 137.2, 129.6, 127.7, 127.1, 121.8, 120.1, 109.4, 101.3, 33.0. These data are in agreement with those reported previously in the literature.[13]

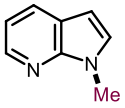


6-fluoro-1-methyl-1*H*-indole (**28**) (**CAS: 441715-92-0**): Prepared, following the general procedure from 6-fluoro-1*H*-indole and TMAF after 6 h. The title product was obtained by purification procedure A as a yellow oil (55.5 mg, 93%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.54

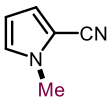
(dd, *J* = 8.6, 5.3 Hz, 1H), 7.04 – 6.99 (m, 2H), 6.89 (ddd, *J* = 9.1, 2.3, 2.3 Hz, 1H), 6.48 (d, *J* = 3.1 Hz, 1H), 3.75 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 159.9 (d, *J* = 236.7 Hz), 136.8 (d, *J* = 11.8 Hz), 129.3 (d, *J* = 3.7 Hz), 125.0, 121.7 (d, *J* = 10.2 Hz), 108.1 (d, *J* = 24.5 Hz), 101.2, 95.7 (d, *J* = 26.2 Hz), 33.0. **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -121.24 – -121.30 (m). These data are in agreement with those reported previously in the literature.[13]



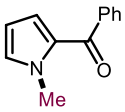
7-fluoro-1-methyl-1*H*-indole (**29**): Prepared, following the general procedure from 7-fluoro-1*H*-indole and TMAF after 6 h. The title product was obtained by purification procedure A as a yellow oil (56.7 mg, 95%). **IR** (neat): 2924, 1630, 1572, 1494, 1458, 1307, 1237, 1215, 1122, 1034, 845, 781, 715 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 7.9 Hz, 1H), 7.04 – 6.99 (m, 2H), 6.91 (dd, *J* = 12.8, 7.8 Hz, 1H), 6.52 (dd, *J* = 2.7, 2.7 Hz, 1H), 4.02 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 150.6 (d, *J* = 243.3 Hz), 132.8 (d, *J* = 5.6 Hz), 130.4, 124.8 (d, *J* = 9.6 Hz), 119.6 (d, *J* = 6.4 Hz), 116.8 (d, *J* = 3.6 Hz), 107.0 (d, *J* = 17.7 Hz), 101.8 (d, *J* = 1.7 Hz), 35.8 (d, *J* = 5.3 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -137.05 (d, *J* = 12.4 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for C_9H_8FN: 150.07135; found: 150.07118.



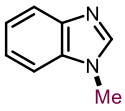
1-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (**30**) (**CAS: 27257-15-4**): Prepared, following the general procedure from 1*H*-pyrrolo[2,3-*b*]pyridine and TMAF after 6 h. The title product was obtained by purification procedure A as a yellow oil (48.7 mg, 92%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.33 (dd, *J* = 4.6, 1.6 Hz, 1H), 7.88 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.15 (d, *J* = 3.4 Hz, 1H), 7.03 (dd, *J* = 7.8, 4.7 Hz, 1H), 6.43 (d, *J* = 3.4 Hz, 1H), 3.87 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 147.9, 142.9, 129.0, 128.7, 120.6, 115.5, 99.3, 31.3. These data are in agreement with those reported previously in the literature.[19]



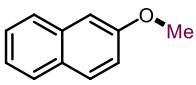
1-methyl-1*H*-pyrrole-2-carbonitrile (**31**) (**CAS: 34884-10-1**): Prepared, following the general procedure from 1*H*-pyrrole-2-carbonitrile and TMAF after 6 h. The title product was obtained by purification procedure A as a colorless oil (38.2 mg, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 6.80 – 6.76 (m, 2H), 6.15 (dd, *J* = 3.3, 3.3 Hz, 1H), 3.77 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 127.6, 120.0, 113.9, 109.5, 104.5, 35.4. These data are in agreement with those reported previously in the literature.[20]



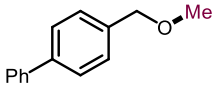
(1-methyl-1*H*-pyrrol-2-yl)(phenyl)methanone (**32**) (**CAS: 37496-06-3**): Prepared, following the general procedure from phenyl(1*H*-pyrrol-2-yl)methanone and TMAF after 6 h. The title product was obtained by purification procedure A as a yellow oil (71.1 mg, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.82 – 7.79 (m, 2H), 7.55 – 7.51 (m, 1H), 7.47 – 7.43 (m, 2H), 6.93 – 6.92 (m, 1H), 6.74 (dd, *J* = 4.1, 1.7 Hz, 1H), 6.16 (dd, *J* = 4.0, 2.5 Hz, 1H), 4.04 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 186.3, 140.0, 131.6, 131.5, 130.6, 129.3, 128.1, 123.0, 108.2, 37.5. These data are in agreement with those reported previously in the literature.[21]



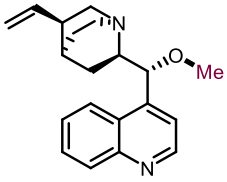
1-methyl-1*H*-benzo[*d*]imidazole (**33**) (**CAS: 1632-83-3**): Prepared, following the general procedure from 1*H*-benzo[*d*]imidazole and TMAF after 6 h. The title product was obtained by purification procedure A as a yellow solid (46.6 mg, 88%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.80 – 7.77 (m, 2H), 7.35 (d, *J* = 7.2 Hz, 1H), 7.31 – 7.24 (m, 2H), 3.77 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 143.7, 143.5, 134.6, 122.9, 122.1, 120.2, 109.4, 31.0. These data are in agreement with those reported previously in the literature.[22]



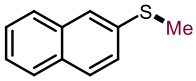
2-methoxynaphthalene (**34**) (**CAS: 93-04-9**): Prepared, following the general procedure from naphthalen-2-ol and TMAF after 6 h. The title product was obtained by purification procedure A as a pale yellow oil (60.1 mg, 95%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.79 – 7.74 (m, 3H), 7.47 – 7.43 (m, 1H), 7.37 – 7.33 (m, 1H), 7.18 – 7.15 (m, 2H), 3.94 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 157.7, 134.7, 129.5, 129.1, 127.8, 126.9, 126.5, 123.7, 118.8, 105.9, 55.4. These data are in agreement with those reported previously in the literature.[23]



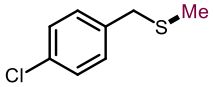
4-(methoxymethyl)-1,1'-biphenyl (**35**) (**CAS: 86130-05-4**): Prepared, following the general procedure from [1,1'-biphenyl]-4-ylmethanol and TMAF after 6 h. The title product was obtained by purification procedure A as a colorless oil (72.2 mg, 91%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.64 – 7.61 (m, 4H), 7.49 – 7.43 (m, 4H), 7.37 (dd, *J* = 7.4, 7.4 Hz, 1H), 4.53 (s, 2H), 3.45 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 141.0, 140.7, 137.4, 128.9, 128.3, 127.4, 127.3, 127.2, 74.5, 58.3. These data are in agreement with those reported previously in the literature.[24]



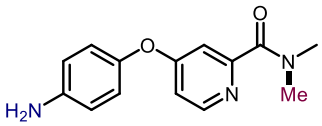
(1*S*,2*R*,4*S*,5*R*)-2-((*R*)-methoxy(quinolin-4-yl)methyl)-5-vinylquinuclidine (**36**): Prepared, following the general procedure from cinchonidine and TMAF after 6 h. The title product was obtained by purification procedure B as a colorless solid (115.9 mg, 94%). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.89 (d, *J* = 4.4 Hz, 1H), 8.15 – 8.09 (m, 2H), 7.71 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.56 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.46 (d, *J* = 4.4 Hz, 1H), 5.73 – 5.67 (m, 1H), 5.05 (s, 1H), 4.93 – 4.86 (m, 2H), 3.40 – 3.34 (m, 1H), 3.29 (s, 3H), 3.09 – 3.04 (m, 2H), 2.71 – 2.66 (m, 1H), 2.62 – 2.58 (m, 1H), 2.26 – 2.22 (m, 1H), 1.78 – 1.71 (m, 3H), 1.55 – 1.47 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 150.3, 148.6, 146.4, 142.0, 130.6, 129.1, 126.74, 126.66, 123.2, 118.5, 114.3, 83.3, 60.7, 57.3, 57.2, 43.3, 40.2, 28.0, 27.8, 22.2. These data are in agreement with those reported previously in the literature.[25]



methyl(naphthalen-2-yl)sulfane (**37**) (**CAS: 7433-79-6**): Prepared, following the general procedure from naphthalene-2-thiol and TMAF after 6 h. The title product was obtained by purification procedure A as a colorless solid (66.2 mg, 95%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.50 – 7.39 (m, 3H), 2.60 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 136.2, 134.0, 131.4, 128.3, 127.8, 126.9, 126.7, 125.8, 125.3, 123.5, 15.9. These data are in agreement with those reported previously in the literature.[26]

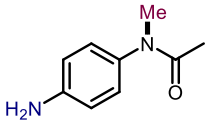


(4-chlorobenzyl)(methyl)sulfane (**38**) (**CAS: 5925-82-6**): Prepared, following the general procedure from (4-chlorophenyl)methanethiol and TMAF after 6 h. The title product was obtained by purification procedure A as a colorless oil (63.6 mg, 92%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 2H), 3.64 (s, 2H), 1.98 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 136.9, 132.8, 130.3, 128.7, 37.8, 15.0. These data are in agreement with those reported previously in the literature.[27]

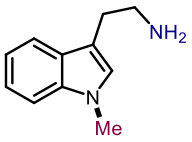


4-(4-aminophenoxy)-*N*,*N*-dimethylpicolinamide (**39**) (**CAS: 284462-86-8**): Prepared, following the general procedure from 4-(4-aminophenoxy)-*N*-methylpicolinamide and TMAF after 12 h. The title product was obtained after purification by column chromatography (EtOAc) as a brown solid (66.9 mg,

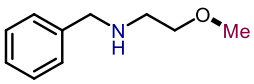
65%). Alternatively, following procedure **b** after 12 h, the title product was obtained in 90% yield (92.6 mg). R_f = 0.28 (EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.36 (s, 1H), 7.05 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.82 – 6.81 (m, 1H), 6.67 (d, *J* = 8.4 Hz, 2H), 3.72 (brs, 2H), 3.07 (s, 3H), 3.02 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 168.8, 166.7, 156.3, 149.9, 145.3, 144.5, 122.0, 116.3, 112.3, 111.0, 39.0, 35.7. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{14}H_{15}N_3O_2$:280.10565; found: 280.10495. These data are in agreement with those reported previously in the literature.[28]



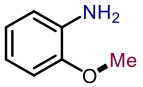
***N*-(4-aminophenyl)-*N*-methylacetamide** (**40**) (**CAS: 119-63-1**): Prepared, following the procedure **b** after 36 h from *N*-(4-aminophenyl)acetamide and TMAF. The title product was obtained as a grey solid (57.8 mg, 88%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 6.93 (d, *J* = 8.2 Hz, 2H), 6.66 (d, *J* = 8.2 Hz, 2H), 3.81 (brs, 2H), 3.19 (s, 3H), 1.84 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.3, 146.1, 135.5, 128.0, 115.7, 37.4, 22.4. These data are in agreement with those reported previously in the literature.[29]



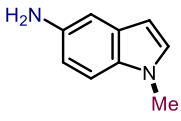
2-(1-methyl-1*H*-indol-3-yl)ethan-1-amine (**41**) (**CAS: 7518-21-0**): Prepared, following the general procedure from 2-(1*H*-indol-3-yl)ethan-1-amine and TMAF after 12 h. The title product was obtained by purification procedure B as a yellow oil (62.7 mg, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 7.9 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.23 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.11 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.88 (s, 1H), 3.74 (s, 3H), 3.06 – 2.99 (m, 2H), 2.93 – 2.86 (m, 2H), 1.47 (brs, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 137.2, 128.0, 126.9, 121.6, 119.1, 118.8, 112.3, 109.3, 42.6, 32.7, 29.5. These data are in agreement with those reported previously in the literature.[30]



***N*-benzyl-2-methoxyethan-1-amine** (**42**) (**CAS: 51353-26-5**): Prepared, following the general procedure from 2-(benzylamino)ethan-1-ol and TMAF after 8 h. The title product was obtained by purification procedure A as a colorless oil (50.2 mg, 76%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.34 – 7.30 (m, 4H), 7.26 – 7.21 (m, 1H), 3.82 (s, 2H), 3.51 (t, *J* = 5.2 Hz, 2H), 3.35 (s, 3H), 2.80 (t, *J* = 5.1 Hz, 2H), 1.72 (brs, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 140.4, 128.5, 128.3, 127.0, 72.2, 59.0, 54.1, 48.9. These data are in agreement with those reported previously in the literature.[31]



2-methoxyaniline (**43**) (**CAS: 90-04-0**): Prepared, following the general procedure from 2-aminophenol and TMAF after 12 h. The title product was obtained by purification procedure A as a colorless oil (44.4 mg, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 6.82 – 6.79 (m, 2H), 6.76 – 6.72 (m, 2H), 3.86 (s, 3H), 3.79 (brs, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 147.5, 136.3, 121.2, 118.6, 115.2, 110.6, 55.6. These data are in agreement with those reported previously in the literature.[32]



1-methyl-1*H*-indol-5-amine (**44**) (**CAS: 102308-97-4**): Prepared, following the general procedure from 1*H*-indol-5-amine and TMAF after 72 h. The title product was obtained after purification by column chromatography (Hexane/EtOAc 1:1) as a brown solid (42.1 mg, 72%). Alternatively, following procedure **b** after 24 h, the title product was obtained in 95% yield (55.5 mg). R_f = 0.30 (Hexane/EtOAc 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$): 7.13 (d, *J* = 8.6 Hz, 1H), 6.97 – 6.93 (m, 2H), 6.70 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.30 (d, *J* = 3.0 Hz, 1H), 3.73 (s, 3H), 3.44 (brs, 2H). **^{13}C NMR** (101 MHz,

$CDCl_3$): δ = 139.3, 132.0, 129.4, 129.3, 112.6, 109.8, 105.9, 99.6, 33.0. These data are in agreement with those reported previously in the literature.[33]

5. Computational Details

Software: DFT calculations were performed using Gaussian 09, Revision D.01.[34] A grid size of 99,590 (UltraFine option) was used for all calculations. Geometry optimization was conducted in the gas-phase at the M06-2X/6-31G(d,p) level of theory. Frequencies were calculated at the same level of theory and used to verify the nature of all stationary points as either minima (no imaginary frequencies) or transition states (one imaginary frequency). Additionally, transition states were confirmed by following the intrinsic reaction coordinate (IRC) to their corresponding intermediates. Single point energies were calculated at the M06-2X/def2-TZVP level of theory employing the SMD solvation model for toluene. All energies were corrected to 1M standard state (addition of 1.89 kcal/mol to every species). Images were created using the CYLview software.[35]

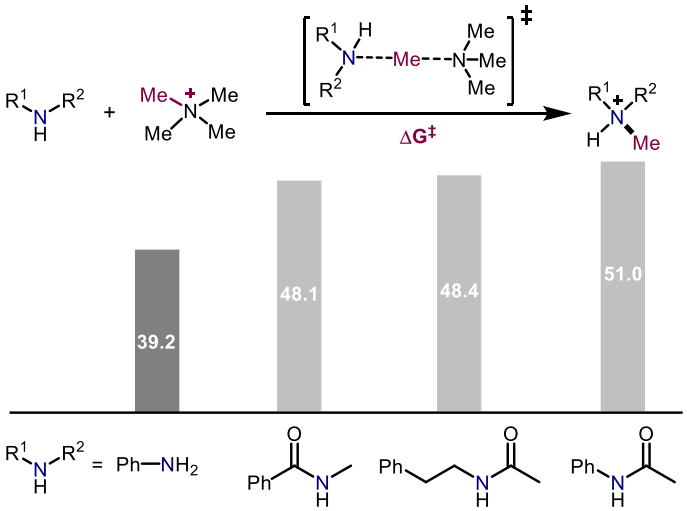


Figure S1. The direct methyl cation transfer from NMe_4^+ to aniline and amides. Energies refer to Gibbs free energy activation barriers (in kcal/mol), calculated at the SMD (toluene) M06-2X/def2-TZVP//M06-2X/6-31G(d,p) level of theory.

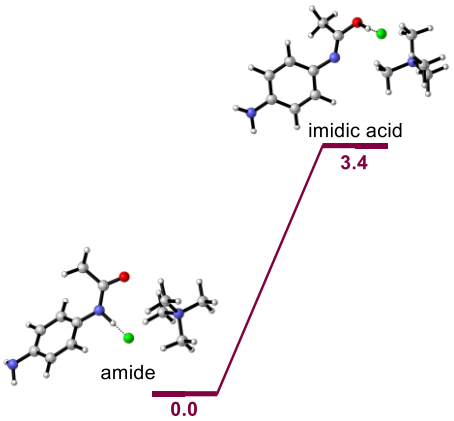


Figure S2. Tautomerization of the amide to the imidic acid. Energies refer to Gibbs free energy activation barriers (in kcal/mol), calculated at the SMD (toluene) M06-2X/def2-TZVP//M06-2X/6-31G(d,p) level of theory.

Coordinates

Me_4N^+

C	1.800934	-0.142910	-0.194549
H	1.355464	0.018769	0.787327
H	1.899385	0.805615	-0.723131
H	1.190082	-0.834758	-0.775042
C	3.793184	-0.964123	-1.356125
H	4.784268	-1.394811	-1.211371
H	3.165041	-1.649267	-1.926011
H	3.870873	-0.007125	-1.872810
C	4.017948	0.200705	0.785388
H	3.550383	0.359366	1.757453
H	5.005523	-0.243598	0.911678
H	4.097421	1.146114	0.248003
C	3.047793	-2.045793	0.709703
H	2.589570	-1.868230	1.682943
H	2.426495	-2.719339	0.118791
H	4.045067	-2.468155	0.835219
N	3.164909	-0.738051	-0.013868

Thermal correction to Gibbs Free Energy= 0.136586

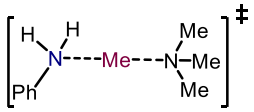
SCF energy (smd(toluene)M062x/Def2-TZVP)= -214.1856706

$PhNH_2$

C	-1.520166	-0.093317	-0.260385
C	-2.609042	-0.102485	-1.141147
C	-3.694224	-0.938448	-0.909382
C	-3.720491	-1.780906	0.199087
C	-2.638439	-1.774653	1.075454
H	-2.594659	0.548188	-2.011519
H	-4.528667	-0.928780	-1.604037
H	-4.569912	-2.430915	0.376876
H	-2.640484	-2.423766	1.945851
C	-1.548346	-0.942422	0.852940
H	-0.705791	-0.948125	1.539391
N	-0.403981	0.703348	-0.518587
H	-0.591515	1.517919	-1.085295
H	0.144327	0.935054	0.297214

Thermal correction to Gibbs Free Energy= 0.08911

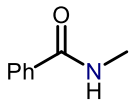
SCF energy (smd(toluene)M062x/Def2-TZVP)= -287.594282



C	-1.666340	0.832322	-0.000594
C	-2.156322	0.355444	-1.212911
C	-3.166186	-0.601652	-1.205545
C	-3.670676	-1.080048	0.001228
C	-3.166044	-0.599505	1.207087
H	-1.767400	0.738458	-2.153175
H	-3.562195	-0.968568	-2.146014
H	-4.461396	-1.821969	0.001933
H	-3.561945	-0.964739	2.148255
C	1.070632	0.800373	-0.000759
H	1.694218	1.686000	-0.001585
H	0.819836	0.308054	-0.932518
H	0.819970	0.309695	0.931902
C	3.554502	0.036940	-1.209191
H	4.490410	-0.532145	-1.267975
H	2.951747	-0.189920	-2.092416
H	3.793887	1.103556	-1.204347
C	3.554576	0.038981	1.208770
H	2.951877	-0.186388	2.092414
H	4.490488	-0.530002	1.268455
H	3.793956	1.105587	1.202106
C	2.409648	-1.715698	0.001300
H	1.811331	-1.929687	0.890792
H	1.811314	-1.931188	-0.887818
H	3.288431	-2.371956	0.001845
N	2.799968	-0.303071	0.000101
N	-0.562531	1.760365	-0.001485
H	-0.586433	2.361814	-0.824732
C	-2.156179	0.357603	1.212627
H	-1.767150	0.742297	2.152162
H	-0.586317	2.363257	0.820708

Thermal correction to Gibbs Free Energy= 0.242741

SCF energy (smd(toluene)M062x/Def2-TZVP)= -501.7315655

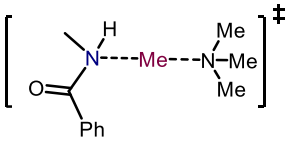


C	-0.074800	-0.260040	-0.095880
C	-0.990320	-1.190200	0.399040
C	-2.337440	-0.862150	0.491400
C	-2.781260	0.387770	0.063160
C	-1.876150	1.307310	-0.460390
H	-0.624060	-2.166680	0.698190
H	-3.044690	-1.583030	0.888510
H	-3.834730	0.641190	0.127760
H	-2.223890	2.271990	-0.815330
C	1.355900	-0.699920	-0.218680
N	2.335970	0.242630	-0.055830

O	1.633130	-1.857790	-0.485330
H	3.255450	-0.156470	-0.186990
C	2.255230	1.496000	0.673350
H	2.286030	2.365740	0.007880
H	1.332180	1.537200	1.252490
H	3.094250	1.568060	1.369740
C	-0.524050	0.986290	-0.536540
H	0.179930	1.695570	-0.961600

Thermal correction to Gibbs Free Energy= 0.123961

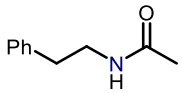
SCF energy (smd(toluene)M062x/Def2-TZVP)= -440.2475647



C	1.878760	0.192220	0.377130
C	1.957620	-1.130900	0.832390
C	2.914490	-1.989670	0.308690
C	3.817760	-1.524120	-0.645050
C	3.767770	-0.198880	-1.071390
H	1.267970	-1.467260	1.600070
H	2.966310	-3.016210	0.654310
H	4.572670	-2.192090	-1.045950
H	4.492150	0.170590	-1.788640
C	-1.513280	0.709560	-0.008390
H	-2.116850	1.436930	-0.538900
H	-1.651320	0.559630	1.055850
H	-0.953480	-0.021760	-0.581450
C	-4.299280	-0.014350	0.443240
H	-5.177520	-0.669820	0.383870
H	-4.059860	0.153160	1.496790
H	-4.547630	0.943640	-0.021440
C	-3.397260	-0.778900	-1.666180
H	-2.500160	-1.172620	-2.151980
H	-4.225880	-1.475930	-1.845700
H	-3.650580	0.185510	-2.114840
C	-2.745930	-1.865110	0.392540
H	-1.849630	-2.253600	-0.099710
H	-2.523640	-1.693650	1.449390
H	-3.540210	-2.618830	0.319090
N	-3.143550	-0.603770	-0.235530
C	0.840130	1.024040	1.033830
N	-0.058270	1.847420	0.221360
O	0.541590	0.942290	2.196620
H	-0.419890	2.566400	0.850790
C	0.317130	2.410390	-1.087360
H	1.116400	3.146810	-0.992640
H	0.629450	1.603740	-1.750710
H	-0.563300	2.899600	-1.507670
C	2.797580	0.661290	-0.569710
H	2.802060	1.698550	-0.882740

Thermal correction to Gibbs Free Energy= 0.274612

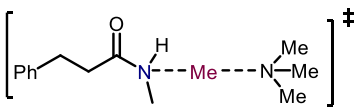
SCF energy (smd(toluene)M062x/Def2-TZVP)= -654.3676598



C	-2.249910	-1.238850	-0.143410
C	-3.562860	-0.911090	0.183350
C	-3.948740	0.423680	0.267740
C	-3.015440	1.428130	0.023100
H	-1.952430	-2.282540	-0.211820
H	-4.286200	-1.698920	0.368470
H	-4.972740	0.680210	0.519210
H	-3.309790	2.471210	0.082650
H	2.661620	-1.809620	0.246840
C	2.965630	1.523020	0.160880
H	2.092650	1.765930	-0.451980
H	2.731490	1.784230	1.196960
H	3.819920	2.107770	-0.174320
C	-1.704860	1.095270	-0.303640
H	-0.978230	1.881350	-0.498690
N	2.374690	-0.850810	0.391580
C	3.342340	0.057270	0.050500
O	4.454250	-0.302200	-0.288670
C	-1.306310	-0.240750	-0.393940
C	0.132250	-0.586020	-0.682290
C	0.970030	-0.576760	0.607680
H	0.564050	0.132160	-1.388910
H	0.206280	-1.575070	-1.147430
H	0.864140	0.393110	1.102480
H	0.569820	-1.319890	1.304980

Thermal correction to Gibbs Free Energy= 0.175564

SCF energy (smd(toluene)M062x/Def2-TZVP)= -518.8713589

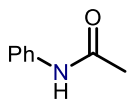


C	-3.455200	-1.000110	-1.106570
C	-4.523060	-1.784170	-0.682340
C	-5.191650	-1.468890	0.497810
C	-4.790610	-0.367940	1.250180

H	-2.943070	-1.240300	-2.035650
H	-4.838200	-2.635460	-1.276290
H	-6.029160	-2.074920	0.826200
H	-5.315750	-0.113260	2.164620
C	2.175420	-0.073630	-0.250990
H	1.987420	-0.079700	0.816220
H	2.867240	0.645410	-0.673670
H	1.842180	-0.918660	-0.841300
C	4.486890	-1.616490	-1.079750
H	5.391560	-2.214920	-0.913120
H	3.782710	-2.208620	-1.670340
H	4.759430	-0.720270	-1.643000
C	4.764490	-0.397690	0.988520
H	4.255460	-0.080690	1.902880
H	5.673740	-0.945390	1.266360
H	5.051720	0.487810	0.415560
C	3.419310	-2.405700	0.940280
H	2.925190	-2.087000	1.862260
H	2.711900	-2.981870	0.337730
H	4.263740	-3.054720	1.204620
N	3.863070	-1.230060	0.188270
H	0.714630	1.021270	-1.683560
C	0.510570	2.640420	1.213900
H	-0.580480	2.644810	1.281320
H	0.886210	1.909240	1.936910
H	0.894950	3.628380	1.460230
C	-3.720990	0.414490	0.824090
H	-3.418940	1.281530	1.407870
N	0.669190	0.960220	-0.663380
C	0.969240	2.300650	-0.174580
O	1.640810	2.999300	-0.881060
C	-3.047190	0.105550	-0.358330
C	-1.845640	0.909600	-0.796060
C	-0.572550	0.283040	-0.223340
H	-1.937370	1.950700	-0.465890
H	-1.777520	0.924040	-1.890170
H	-0.592710	0.284040	0.870400
H	-0.501300	-0.761740	-0.542870

Thermal correction to Gibbs Free Energy= 0.329117

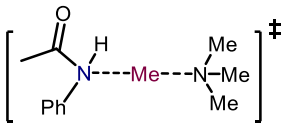
SCF energy (smd(toluene)M062x/Def2-TZVP)= -732.9938216



C	0.256640	-0.348590	-0.205180
C	1.178900	-1.310010	0.218020
C	2.519530	-0.976230	0.367910
C	2.953810	0.322520	0.115280
C	2.037510	1.278980	-0.311760
H	0.832280	-2.315430	0.438430
H	3.224690	-1.732860	0.696650
H	3.998720	0.583950	0.242600
H	2.367390	2.289480	-0.530510
H	-1.270160	-1.657320	-0.734800
C	-2.139770	1.239200	0.722850
H	-1.249380	1.307060	1.349650
H	-2.115460	2.057000	-0.002450
H	-3.040420	1.349480	1.325460
C	0.698930	0.945620	-0.490510
H	-0.001580	1.679780	-0.872170
N	-1.091030	-0.726540	-0.380010
C	-2.252760	-0.088410	0.005190
O	-3.328200	-0.606730	-0.222950

Thermal correction to Gibbs Free Energy= 0.122431

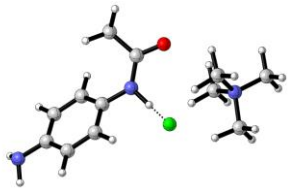
SCF energy (smd(toluene)M062x/Def2-TZVP)= -440.255018



C	-1.611080	-0.027560	-0.300270
C	-2.637590	-0.152420	-1.232520
C	-3.680910	-1.038750	-0.984410
C	-3.696950	-1.788550	0.188770
C	-2.664710	-1.657270	1.114200
H	-2.626430	0.439720	-2.143810
H	-4.480670	-1.139960	-1.709470
H	-4.511900	-2.477470	0.380900
H	-2.673140	-2.242990	2.026660
C	1.161770	0.145240	-0.294030
H	1.116520	0.160890	0.787270
H	1.680390	0.950340	-0.799920
H	0.924910	-0.777500	-0.809200
C	3.671590	-0.906500	-1.353740
H	4.672350	-1.353230	-1.290640
H	3.029480	-1.572300	-1.936740
H	3.751630	0.053430	-1.870760
C	3.890360	0.242170	0.759360
H	3.418470	0.402980	1.732470
H	4.908850	-0.132890	0.923990
H	3.950700	1.198300	0.232640
C	2.926650	-1.973500	0.680590
H	2.456250	-1.796970	1.651950
H	2.288430	-2.639150	0.093000
H	3.891410	-2.470490	0.846100

N	3.092160	-0.702110	-0.024630
H	-0.466730	1.075760	-1.583270
C	-1.267610	2.406440	1.317480
H	-2.326690	2.203270	1.140020
H	-0.928220	1.713830	2.092890
H	-1.126060	3.432350	1.651710
C	-1.611920	-0.780150	0.871810
H	-0.807610	-0.690330	1.595330
N	-0.518270	0.887600	-0.579880
C	-0.478510	2.220370	0.059970
O	0.229280	3.028360	-0.467860

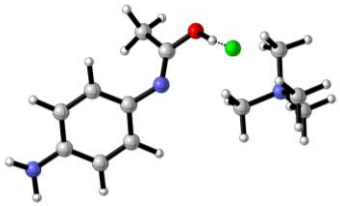
Thermal correction to Gibbs Free Energy= 0.275253
SCF energy (smd(toluene)M062x/Def2-TZVP)= -654.3726765



Amide.TMAF

C	4.37935	-0.73922	0.15209
C	3.99367	0.44710	0.77467
C	2.68163	0.90620	0.69604
C	1.71919	0.20396	-0.03298
C	2.10127	-1.00867	-0.62838
C	3.40500	-1.46771	-0.54299
H	4.72559	1.01577	1.34336
H	2.40802	1.80864	1.23139
H	1.33169	-1.58155	-1.13817
H	3.68096	-2.40271	-1.02447
N	0.36186	0.56130	-0.14350
H	-0.28882	-0.35351	-0.36751
C	-0.15583	1.79587	-0.30198
O	-1.38077	1.98004	-0.36563
C	0.75536	3.00765	-0.42003
H	0.93387	3.44918	0.56498
H	1.72011	2.77360	-0.87253
H	0.22192	3.74316	-1.02242
N	5.71702	-1.17256	0.17519
H	6.23378	-0.81652	0.97104
H	5.80721	-2.17970	0.12675
C	-3.45265	0.01025	-1.11786
H	-2.46169	-0.38531	-1.35947
H	-4.22685	-0.33406	-1.80584
H	-3.41166	1.09615	-1.05317
C	-5.15005	-0.10596	0.64017
H	-5.86763	-0.47742	-0.09350
H	-5.38001	-0.51153	1.62669
H	-5.17519	0.98379	0.66870
C	-3.70568	-2.03170	0.18062
H	-2.67612	-2.26262	-0.11378
H	-3.94997	-2.43386	1.16542
H	-4.42882	-2.38599	-0.55710
C	-2.78566	-0.05019	1.25280
H	-2.78859	1.03820	1.24549
H	-3.07628	-0.45905	2.22355
H	-1.81374	-0.41603	0.92130
N	-3.78672	-0.53873	0.24283
F	-1.02560	-1.38939	-0.62117

SCF Energy= -809.49448
ZPE correction= 0.3404
Thermal correction to Energy = 0.359689
Thermal correction to Enthalpy = 0.360633
Thermal correction to Gibbs Free Energy = 0.292813
SCF energy (smd(toluene)M062x/Def2-TZVP) = -809.8278804

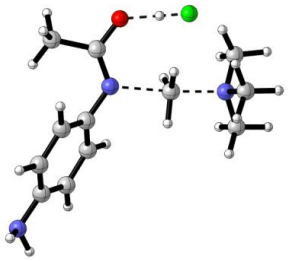


Imidic Acid.TMAF

C	-4.549845	-0.480114	0.215582
C	-3.559309	-1.427149	-0.063433
C	-2.214317	-1.095747	0.028430
C	-1.795110	0.194473	0.380727
C	-2.796895	1.130686	0.675098
C	-4.145029	0.803884	0.589419
H	-3.851777	-2.433564	-0.354029
H	-1.453688	-1.844071	-0.177567
H	-2.503024	2.126924	0.993403
H	-4.897115	1.554315	0.821655
N	-0.428469	0.462106	0.511236
H	1.897169	1.320866	1.105787
C	0.117189	1.485518	-0.066605
O	1.362736	1.799790	0.133140
C	-0.562790	2.399117	-1.071736
H	-1.485267	1.978373	-1.471739
H	-0.788876	3.360420	-0.601154
H	0.147344	2.596918	-1.877479

N	-5.913800	-0.797515	0.071666
H	-6.111251	-1.775259	0.239289
H	-6.513678	-0.221481	0.647381
C	4.052197	-1.564796	1.176863
H	3.739191	-2.563117	1.486943
H	5.138292	-1.526089	1.073715
H	3.681125	-0.794252	1.858061
C	3.866969	0.102414	-0.584107
H	4.940210	0.072772	-0.781960
H	3.311770	0.376099	-1.481172
H	3.614409	0.776883	0.233882
C	3.879413	-2.272745	-1.163966
H	3.565882	-3.265363	-0.837678
H	3.415726	-2.032257	-2.121529
H	4.966061	-2.235121	-1.255115
C	1.942562	-1.316083	-0.011919
H	1.653407	-0.625769	0.778075
H	1.490258	-1.003389	-0.953315
H	1.659943	-2.343116	0.228363
N	3.439820	-1.272885	-0.158008
F	2.554731	0.838807	1.885126

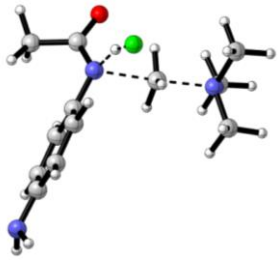
SCF Energy= -809.48201
ZPE correction= 0.33872
Thermal correction to Energy= 0.358270
Thermal correction to Enthalpy= 0.359215
Thermal correction to Gibbs Free Energy= 0.289762
SCF energy (smd(toluene)M062x/Def2-TZVP)= -809.8193391



Imidic Acid-TS2

C	-4.01881	-0.95767	0.15429
C	-3.09766	-1.41011	-0.79617
C	-1.85521	-0.80261	-0.92715
C	-1.48049	0.27874	-0.11843
C	-2.40215	0.71109	0.84659
C	-3.64968	0.11587	0.97243
H	-3.36629	-2.23937	-1.44588
H	-1.15626	-1.15503	-1.68097
H	-2.12226	1.52556	1.50867
H	-4.34937	0.48162	1.71981
N	-0.19266	0.81359	-0.22654
H	2.36214	2.09105	0.34068
C	0.07047	2.09773	-0.35908
O	1.24697	2.56874	-0.30889
C	-1.01601	3.12285	-0.63953
H	-1.96134	2.67913	-0.95052
H	-1.18202	3.72691	0.25713
H	-0.63752	3.79263	-1.41354
N	-5.29750	-1.52500	0.24556
H	-5.34181	-2.48433	-0.06911
H	-5.72282	-1.42608	1.15705
C	3.44901	-1.36393	1.43375
H	2.66734	-1.83512	2.03532
H	4.39374	-1.90009	1.58323
H	3.55796	-0.31667	1.72587
C	4.03663	-0.68033	-0.80531
H	5.03000	-1.12909	-0.68793
H	3.73775	-0.74495	-1.85452
H	4.04244	0.36352	-0.48226
C	2.83666	-2.76549	-0.45608
H	2.09713	-3.25818	0.17988
H	2.45864	-2.73262	-1.48100
H	3.76971	-3.34147	-0.43465
C	1.45834	-0.41067	-0.10751
H	1.79366	0.29563	0.62951
H	1.59661	-0.17610	-1.15411
H	0.78192	-1.21331	0.16673
N	3.05020	-1.39845	0.01925
F	3.18534	1.73362	0.81856

SCF Energy= -809.45314
ZPE correction= 0.3377
Thermal correction to Energy= 0.357479
Thermal correction to Enthalpy= 0.358423
Thermal correction to Gibbs Free Energy= 0.288008
SCF energy (smd(toluene)M062x/Def2-TZVP)= -809.7819152

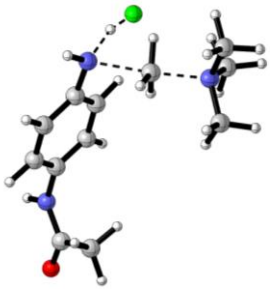


Amide-TS1

C	-3.58565	-1.14416	-0.16942
C	-3.03562	-0.45496	-1.25438
C	-1.87933	0.30136	-1.10321
C	-1.24388	0.41999	0.14060
C	-1.78703	-0.29410	1.21841
C	-2.93602	-1.05661	1.06755
H	-3.51879	-0.51666	-2.22652
H	-1.45703	0.81169	-1.96529
H	-1.28184	-0.23492	2.17748
H	-3.34696	-1.58752	1.92290
N	-0.03106	1.11161	0.32183
H	0.50990	0.90389	1.79887
C	0.18718	2.35895	-0.19911
O	1.32647	2.81326	-0.29993
C	-0.99055	3.23588	-0.61057
H	-1.09924	3.22558	-1.69907
H	-1.93485	2.92221	-0.16503
H	-0.74856	4.25769	-0.31581
N	-4.78529	-1.85783	-0.30222
H	-4.96432	-2.18558	-1.24128
H	-4.88854	-2.60836	0.36664
C	4.01431	-0.81953	0.73197
H	3.49236	-0.94942	1.68325
H	4.90847	-1.45318	0.70560
H	4.30734	0.22839	0.64175
C	3.67448	-0.81506	-1.66950
H	4.60358	-1.36946	-1.84912
H	2.95329	-1.05801	-2.45333
H	3.87837	0.25762	-1.69870
C	2.68692	-2.55960	-0.30589
H	2.23210	-2.75505	0.66773
H	1.94567	-2.74909	-1.08578
H	3.54382	-3.22906	-0.44793
C	1.58535	-0.09206	-0.08611
H	2.12775	0.84719	-0.11947
H	1.05819	-0.43300	-0.97168
H	1.36436	-0.55554	0.86531
N	3.09893	-1.15529	-0.36596
F	0.84269	0.50607	2.63016

SCF Energy= -809.44011

ZPE correction= 0.3374
Thermal correction to Energy= 0.357603
Thermal correction to Enthalpy= 0.358547
Thermal correction to Gibbs Free Energy= 0.287590
SCF energy (smd(toluene)M062x/Def2-TZVP)= -809.7734884



Aniline-TS3

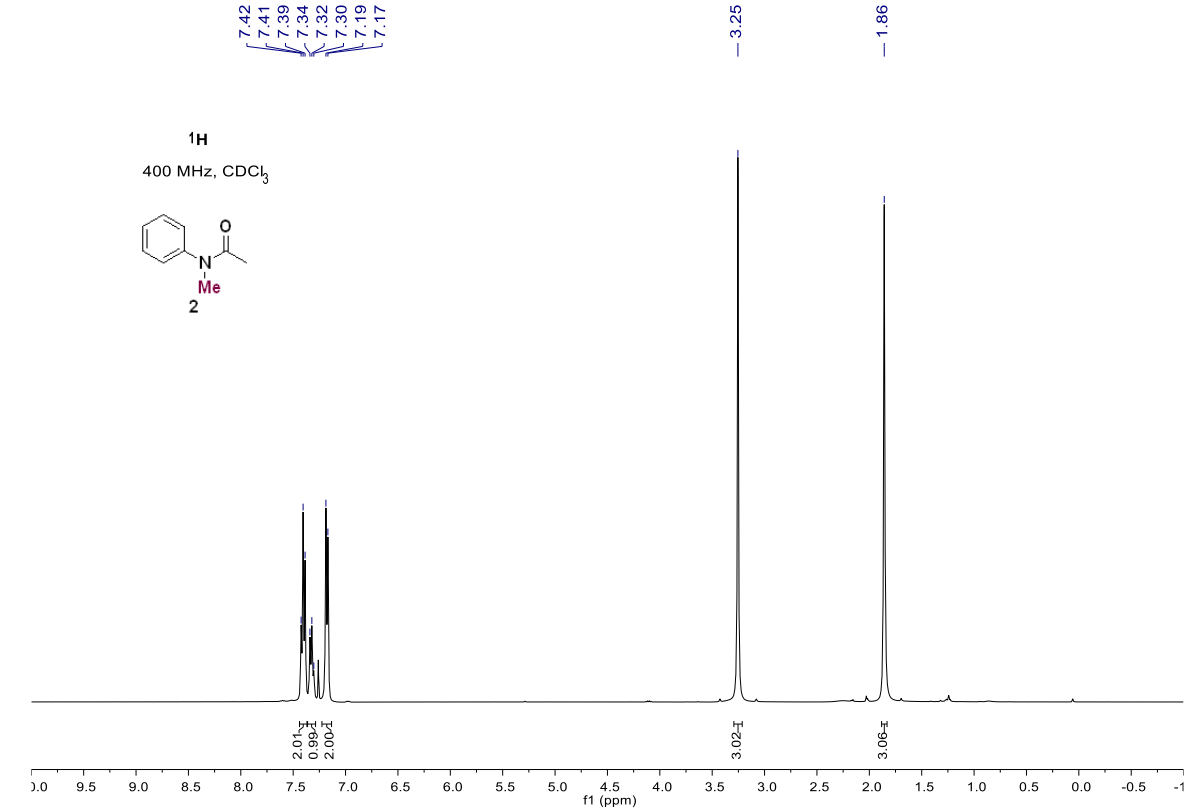
C	-0.00128	-1.55916	-0.51070
C	-0.33953	-1.15018	0.80118
C	-1.61608	-0.70171	1.10292
C	-2.60935	-0.65675	0.12234
C	-2.29515	-1.07747	-1.17179
C	-1.01630	-1.50928	-1.48944
H	0.42515	-1.24363	1.56793
H	-1.86594	-0.39310	2.11464
H	-3.07338	-1.05695	-1.93052
H	-0.78753	-1.82539	-2.50434
N	-3.92396	-0.20033	0.43875
H	-4.58189	-0.83129	0.87772
C	-4.42358	1.05463	0.21031
O	-5.56704	1.34942	0.50799
C	-3.46491	2.03894	-0.43076
H	-2.54047	2.11148	0.14784
H	-3.19129	1.70949	-1.43650
H	-3.96103	3.00655	-0.47942
N	1.30099	-1.92508	-0.75961
H	2.04698	-2.29066	0.44655
H	1.40311	-2.32975	-1.68661
C	3.54888	1.13617	1.41878
H	3.74092	0.10086	1.71460
H	4.29637	1.81262	1.84662
H	2.55830	1.41245	1.78637
C	2.96357	2.47346	-0.52940
H	3.51520	3.33865	-0.14358
H	2.98880	2.48846	-1.62143

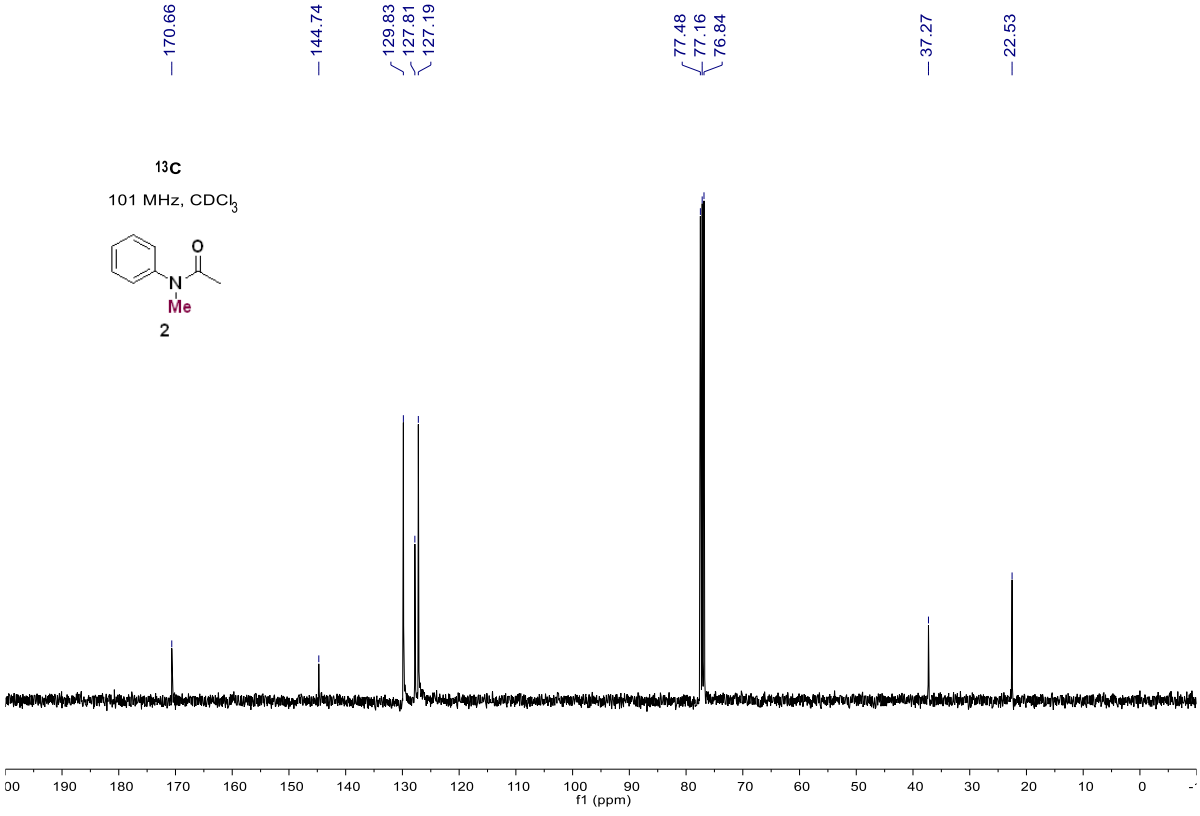
H	1.92413	2.52899	-0.19745
C	4.89594	1.00883	-0.59282
H	5.28849	0.06368	-0.21187
H	4.84111	0.95904	-1.68289
H	5.56677	1.82397	-0.29873
C	2.49368	-0.20990	-0.56202
H	1.67300	0.09635	0.07543
H	2.43751	0.01960	-1.62087
H	3.20821	-0.92928	-0.19673
N	3.54921	1.21765	-0.05210
F	2.59164	-2.23319	1.30759

SCF Energy= -809.43402
ZPE correction= 0.3382
Thermal correction to Energy=
0.357853
Thermal correction to Enthalpy=
0.358797
Thermal correction to Gibbs Free Energy=
0.288558
SCF energy (smd(toluene)M062x/Def2-
TZVP)= -809.7694882

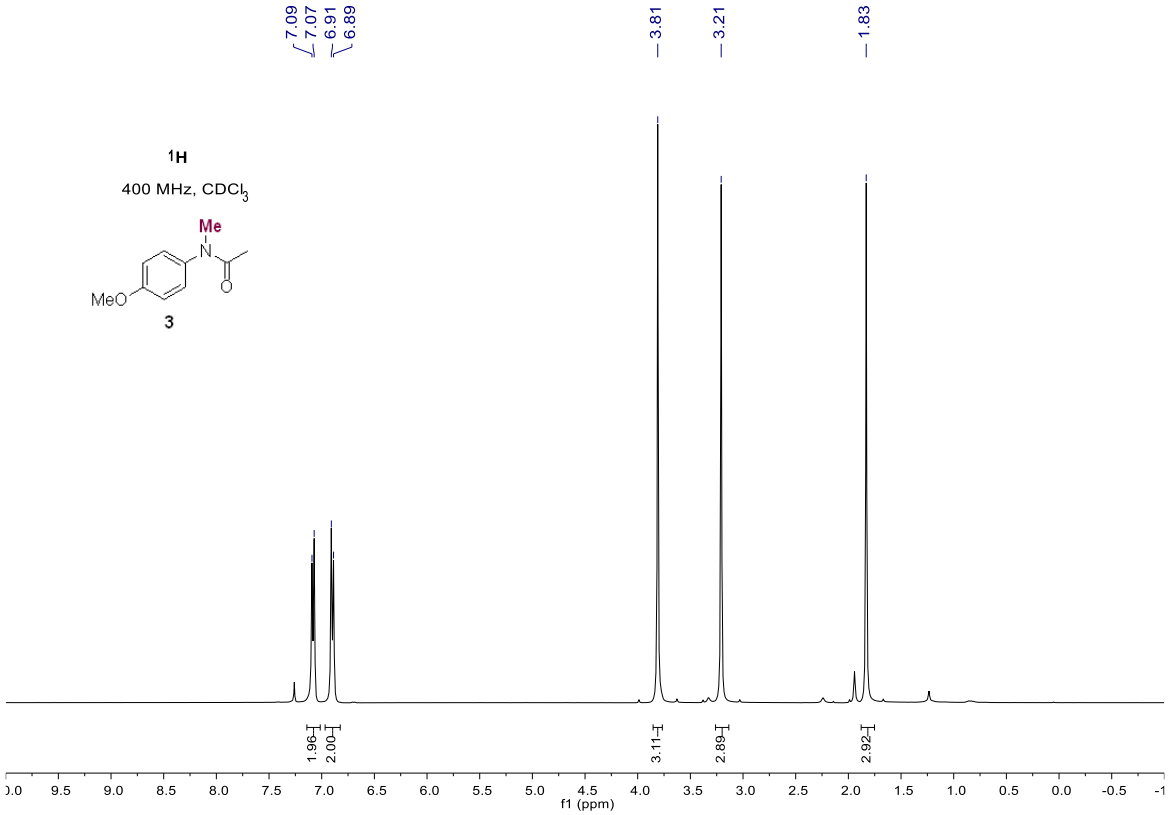
6. NMR Spectra

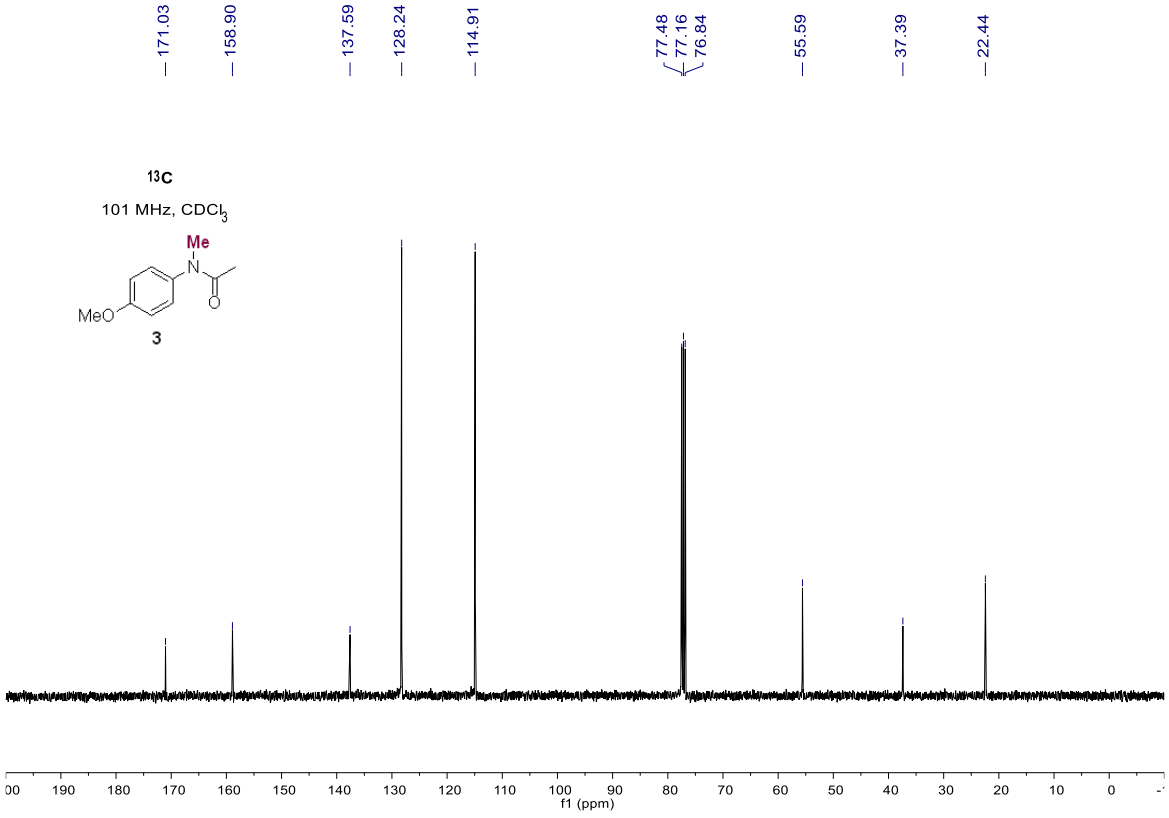
N-methyl-*N*-phenylacetamide (2)



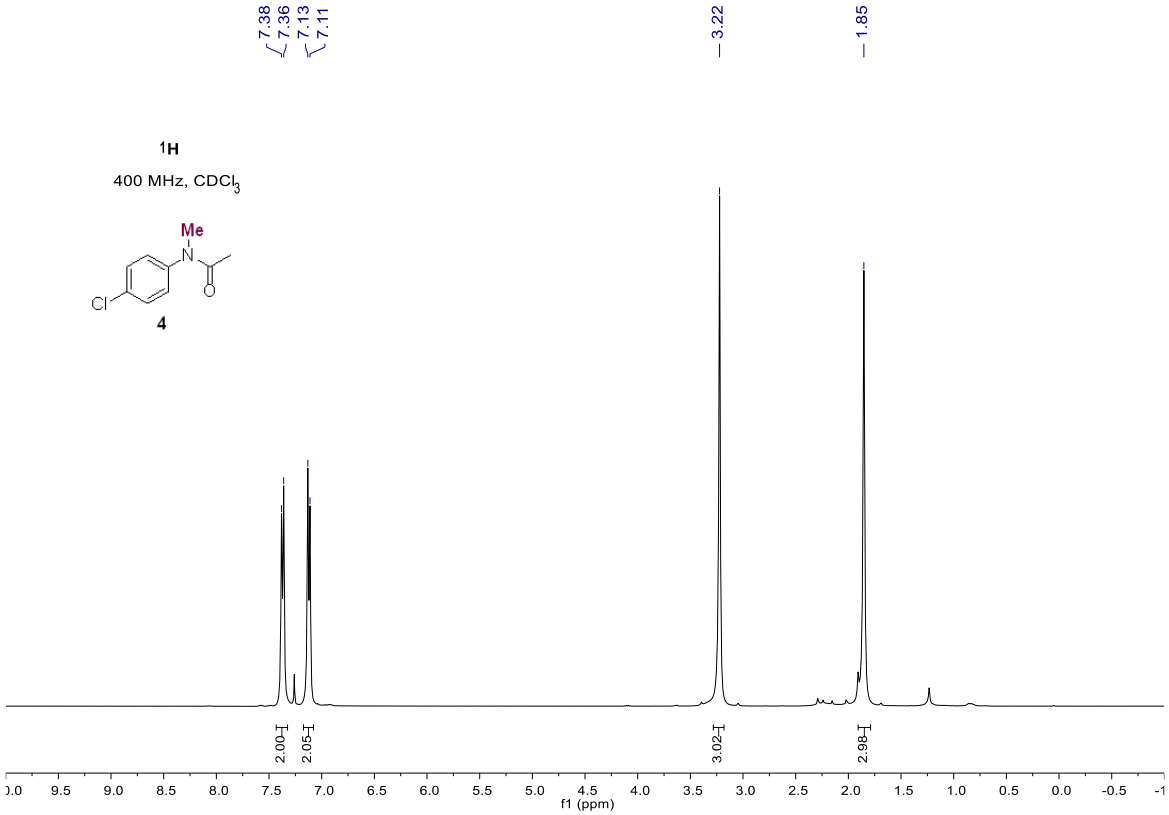


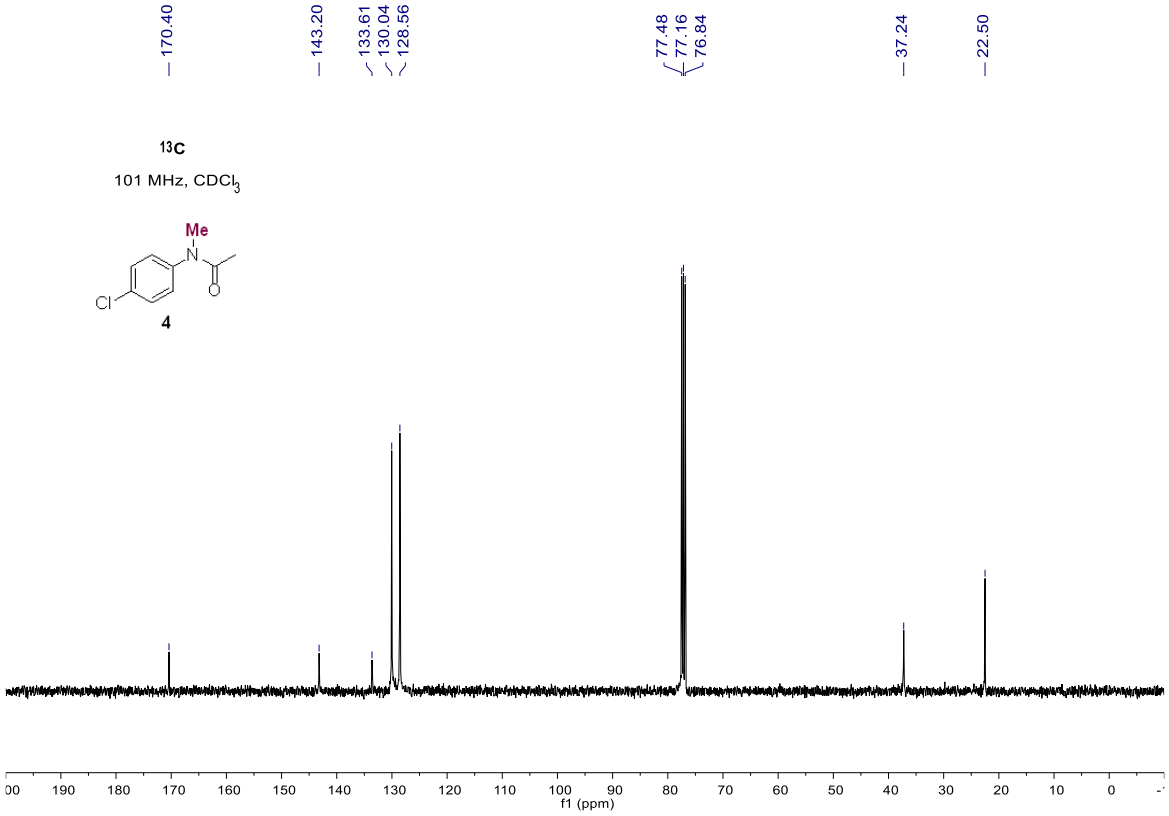
N-(4-methoxyphenyl)-*N*-methylacetamide (3)



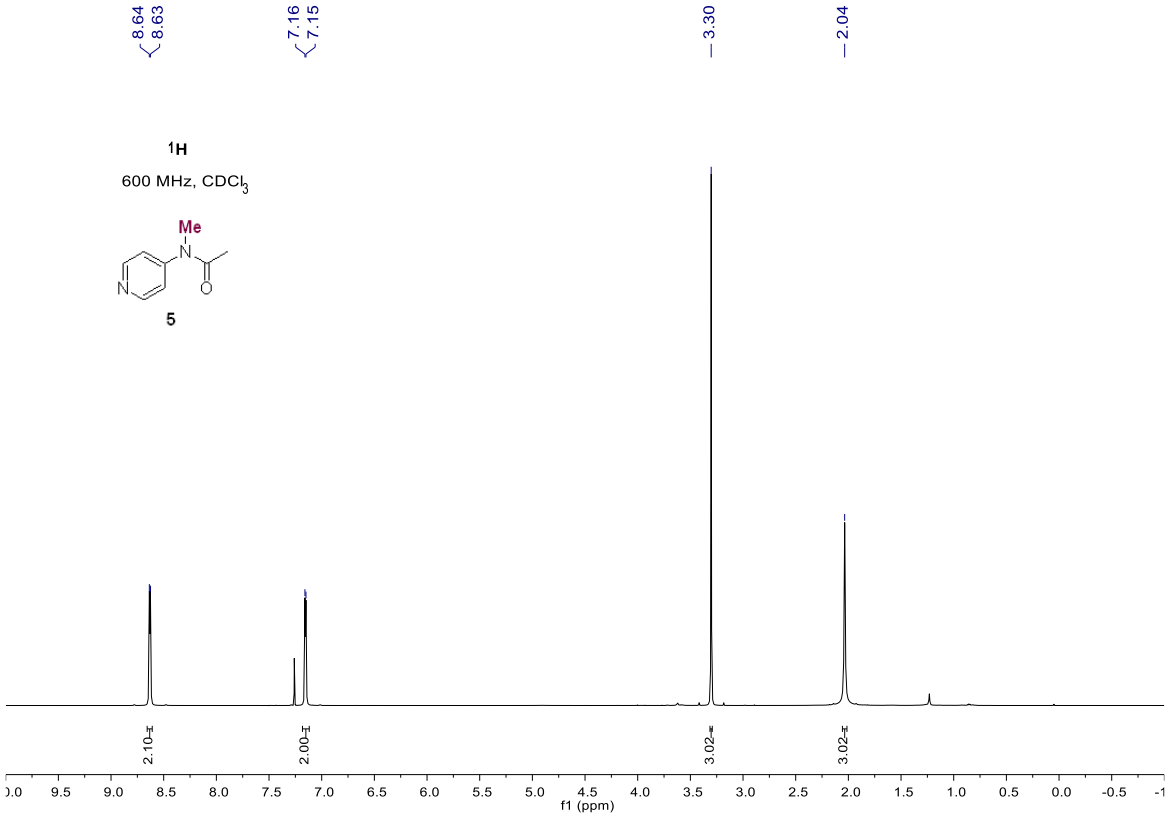


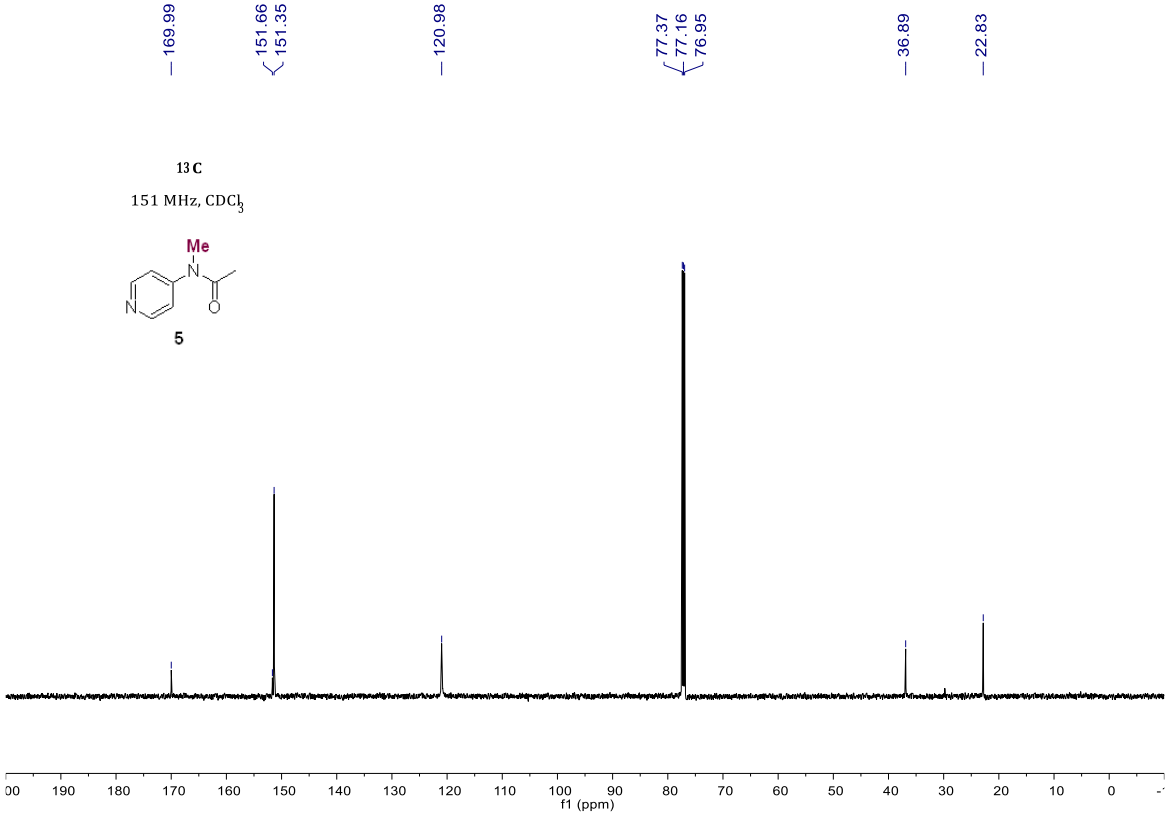
N-(4-chlorophenyl)-*N*-methylacetamide (4)



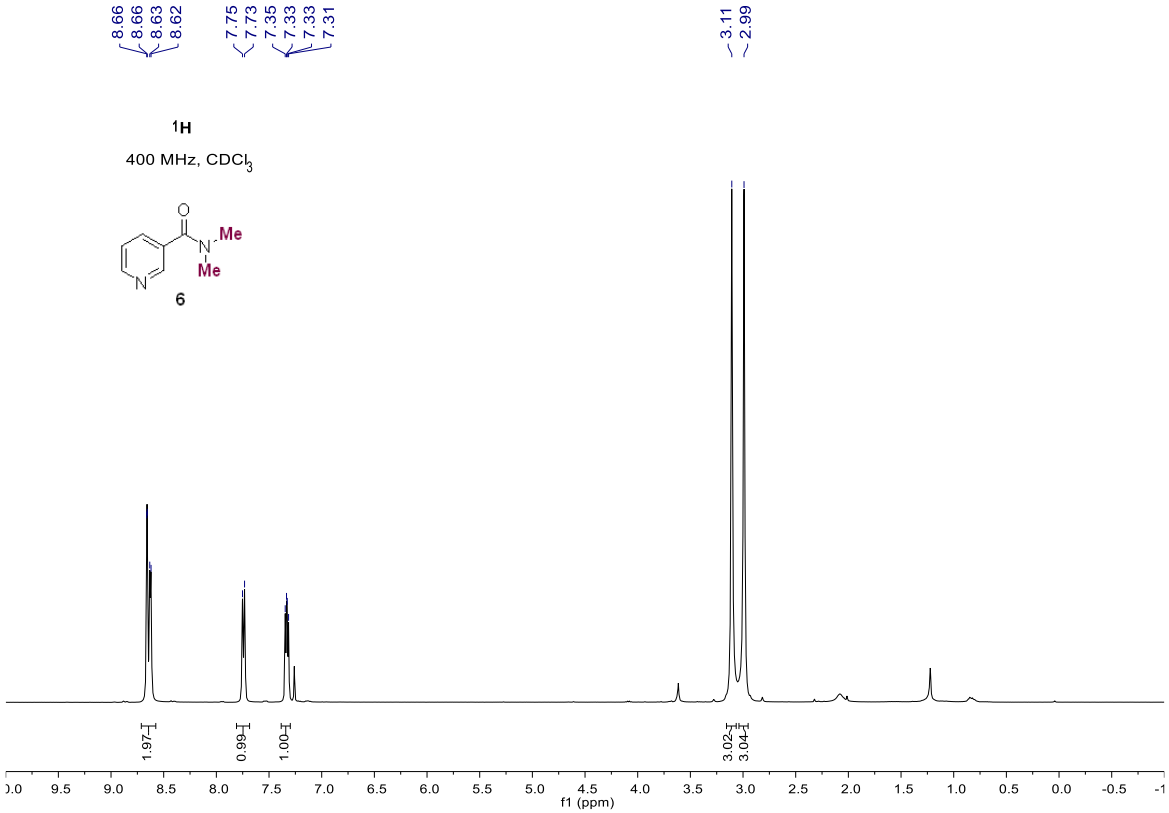


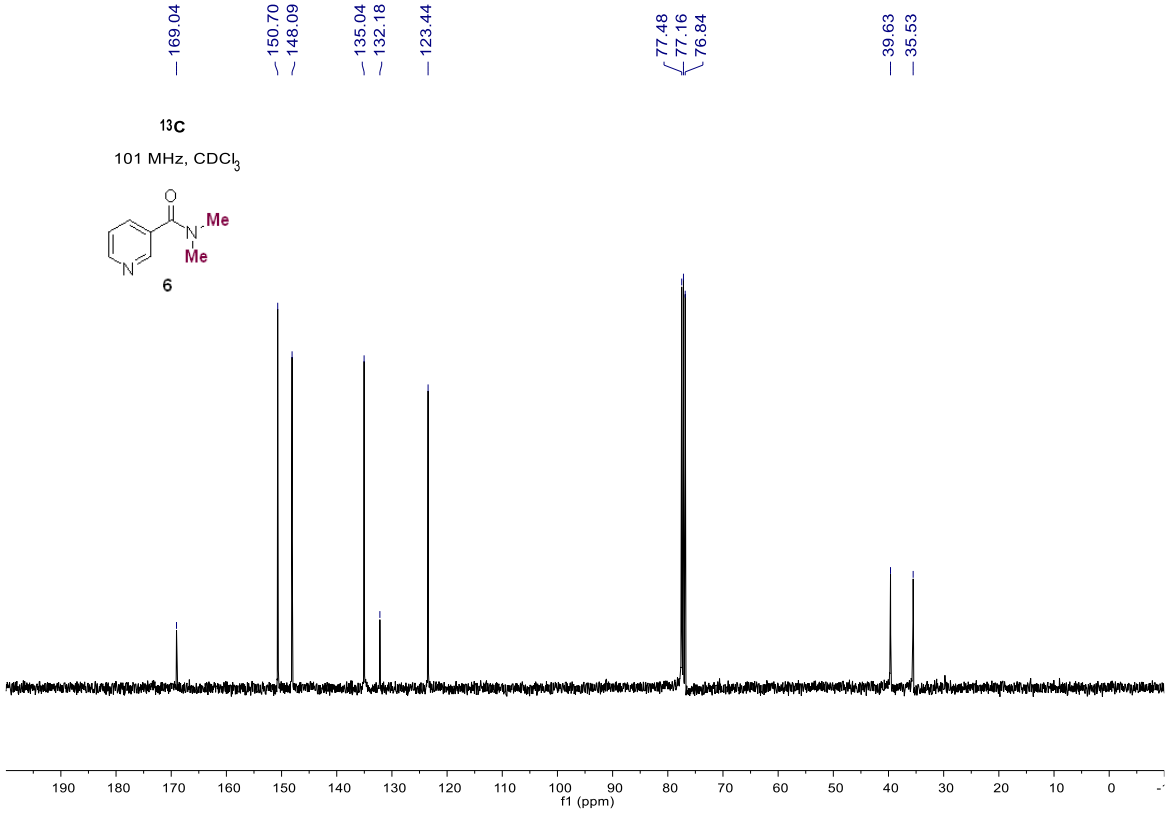
N-methyl-*N*-(pyridin-4-yl)acetamide (5)



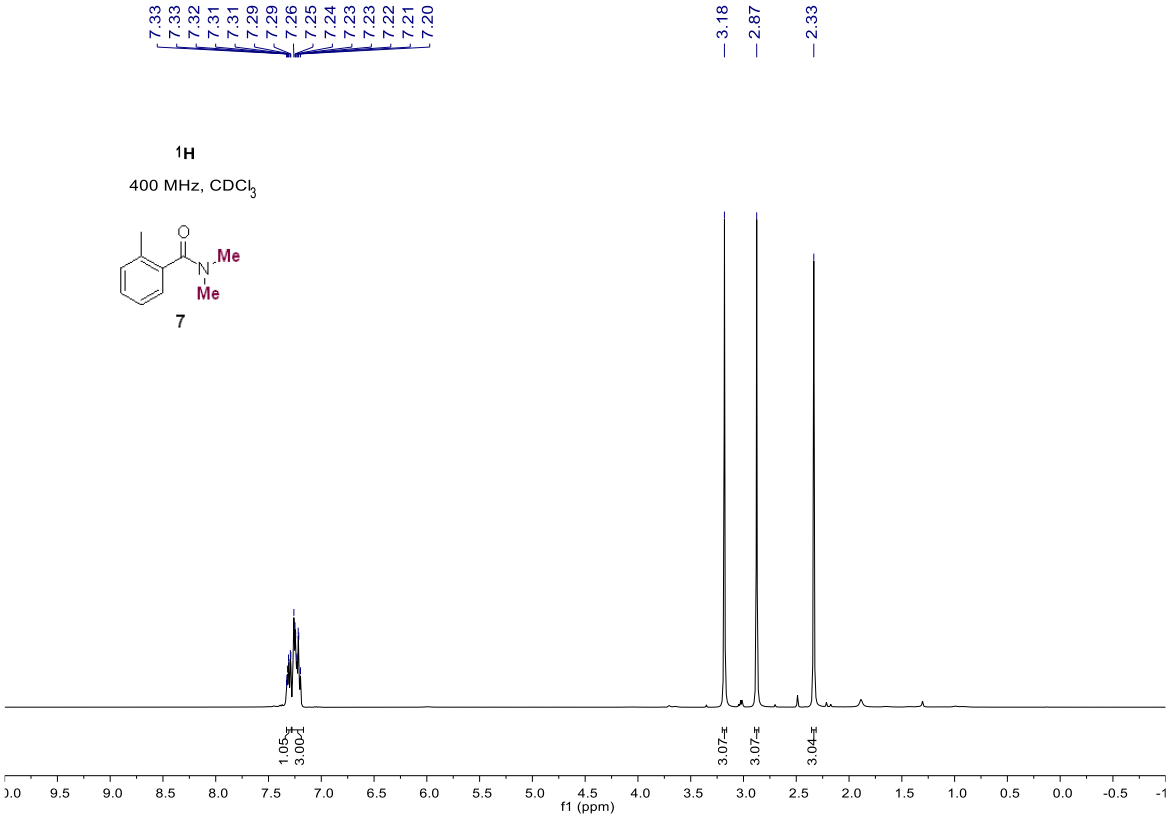


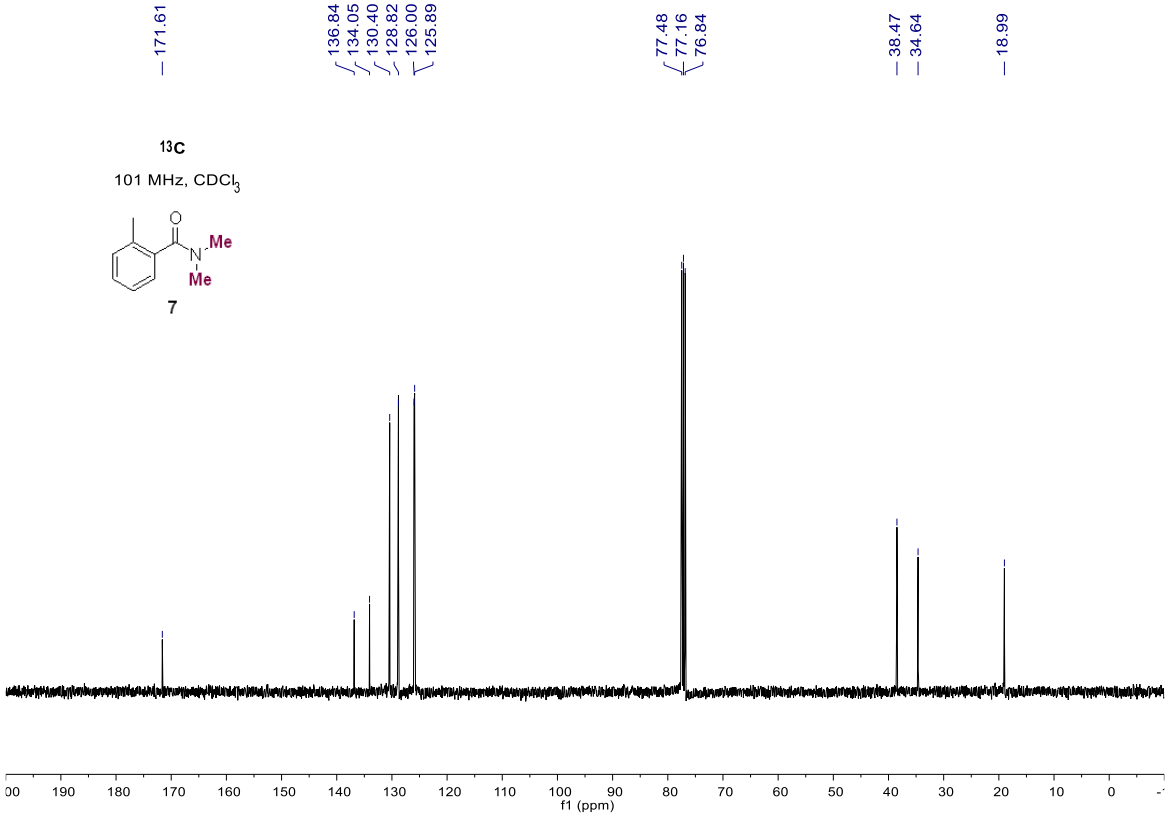
N,N-dimethylnicotinamide (6)



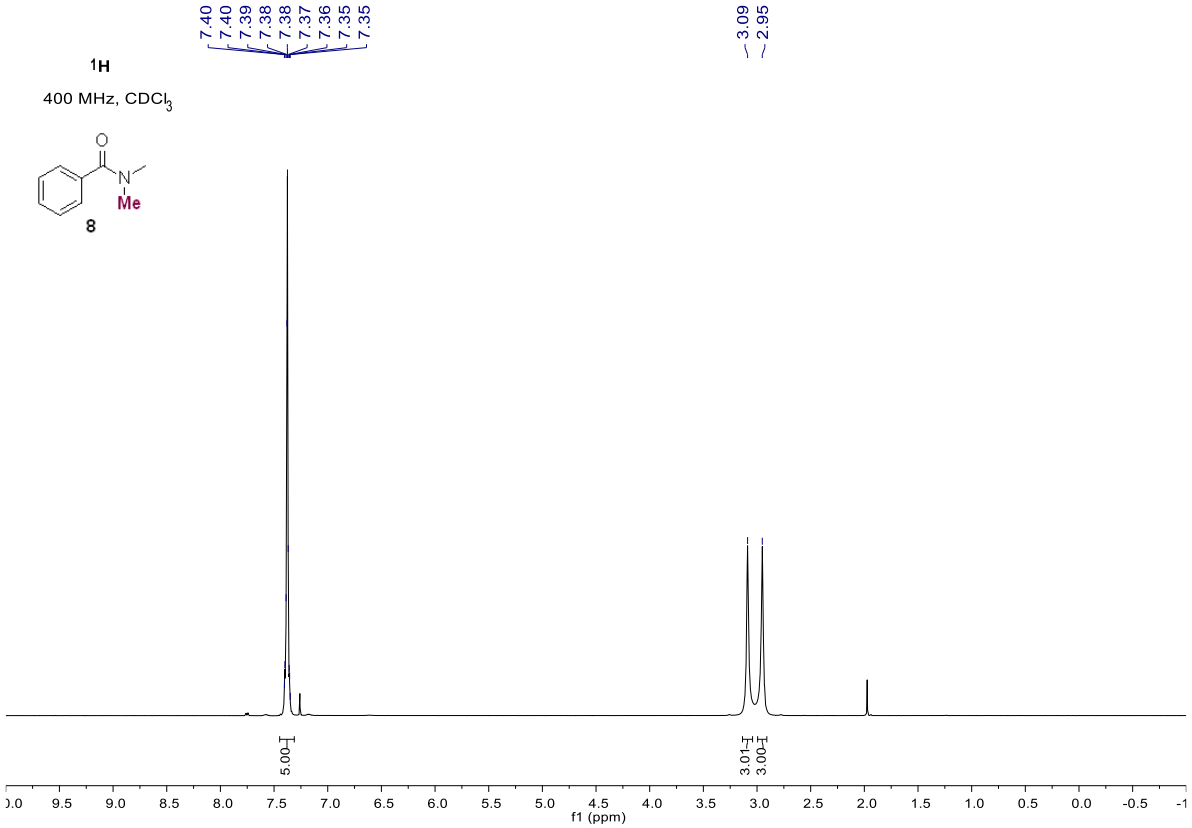


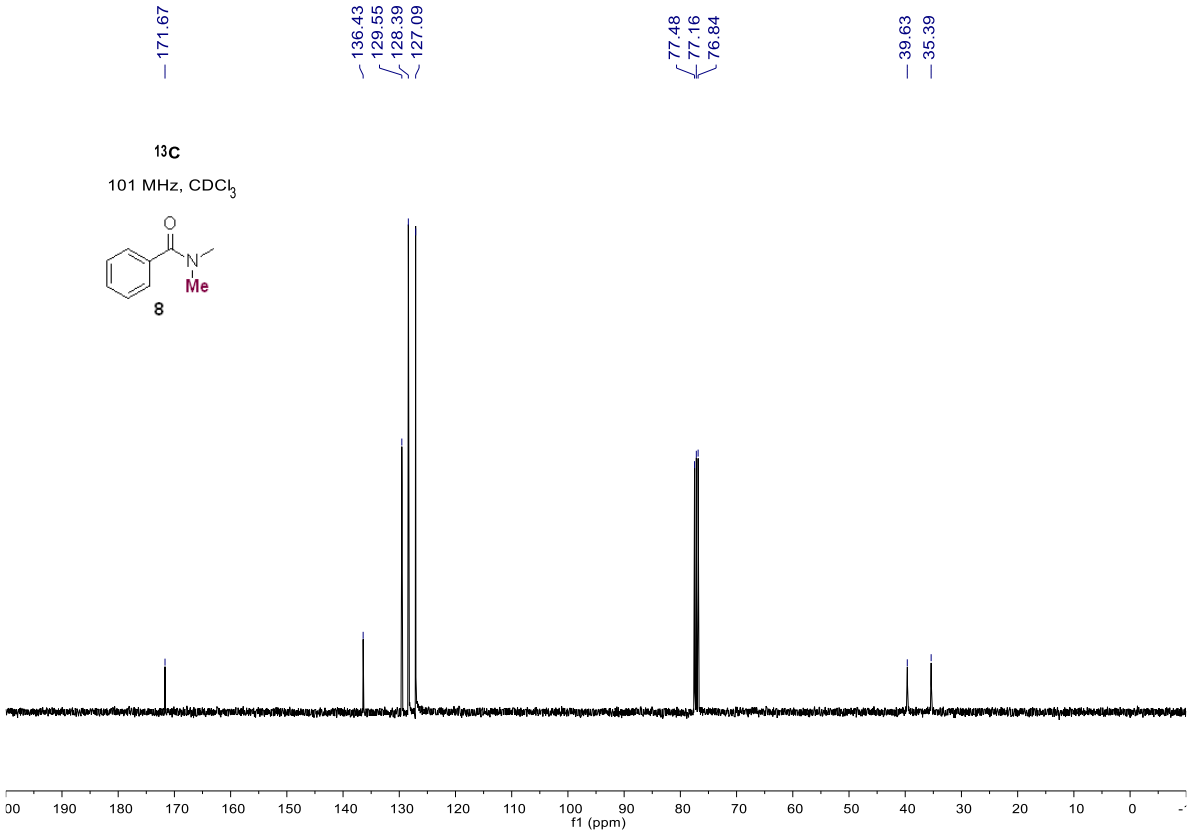
N,*N*,2-trimethylbenzamide (7)



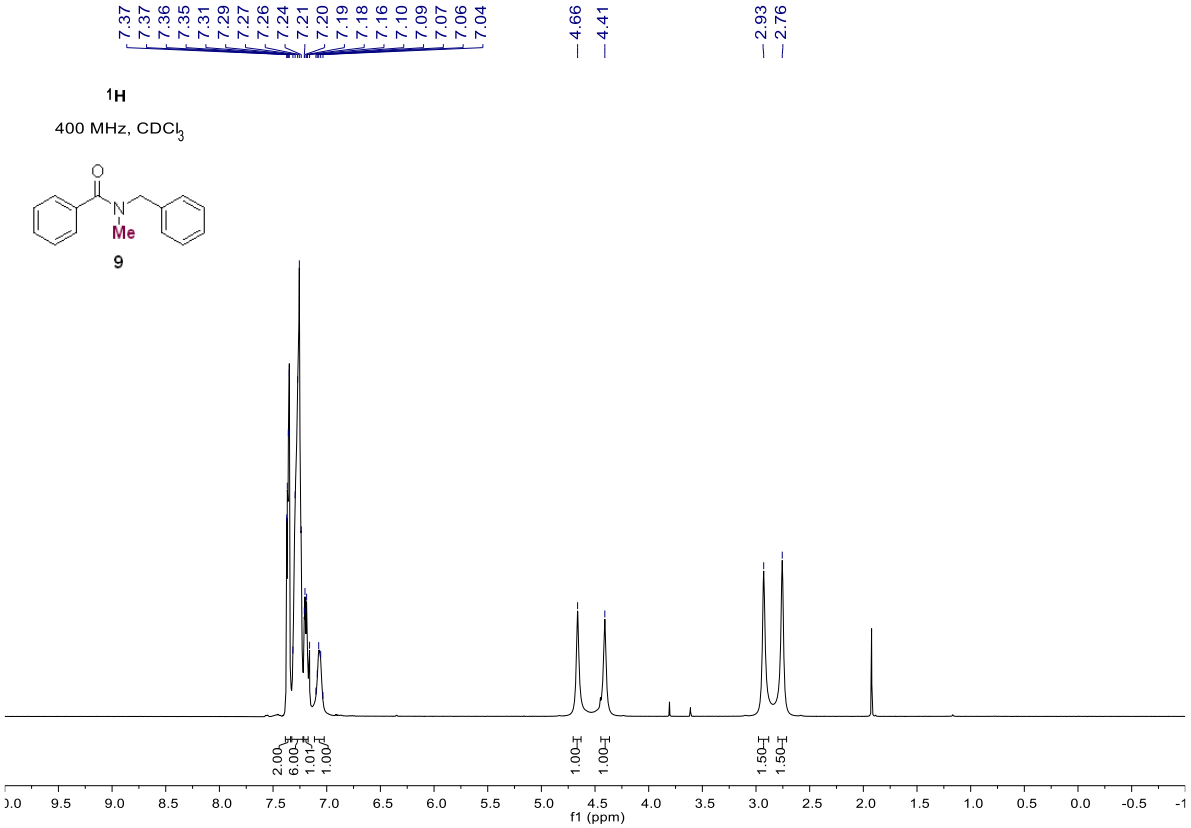


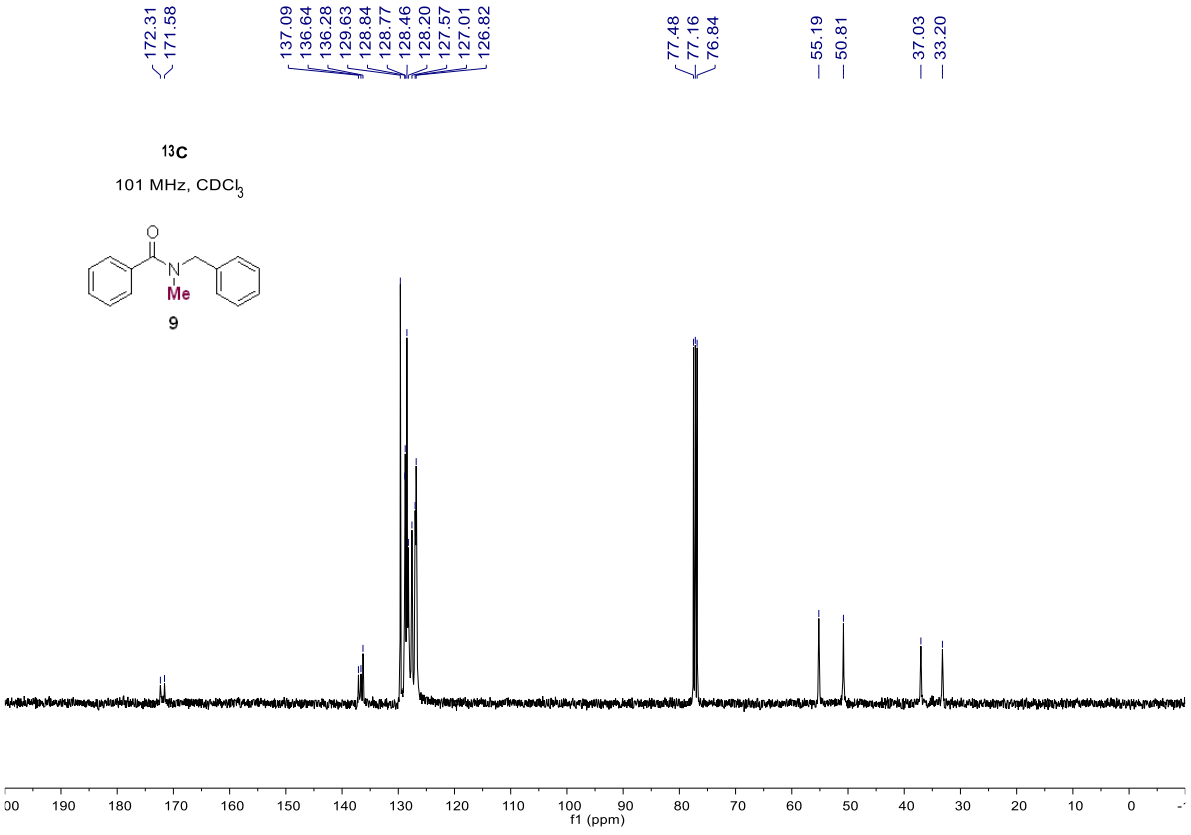
N,N-dimethylbenzamide (**8**)



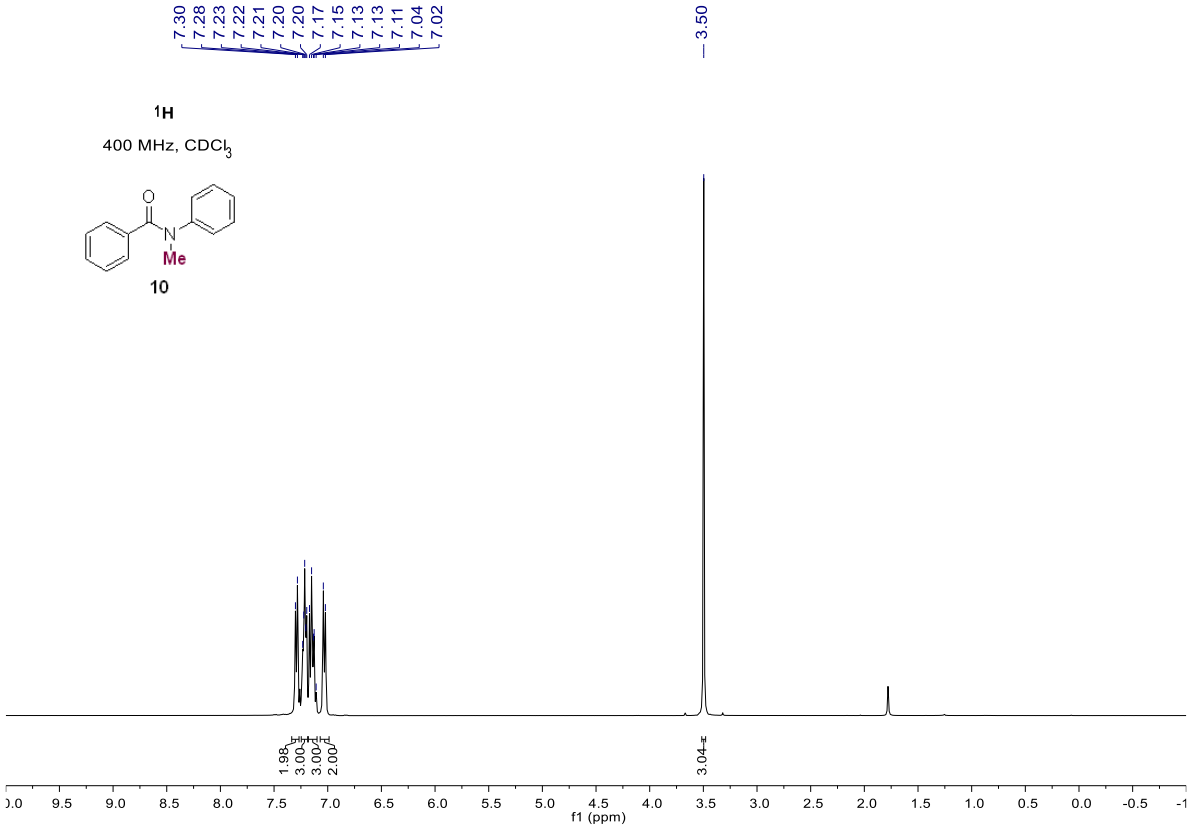


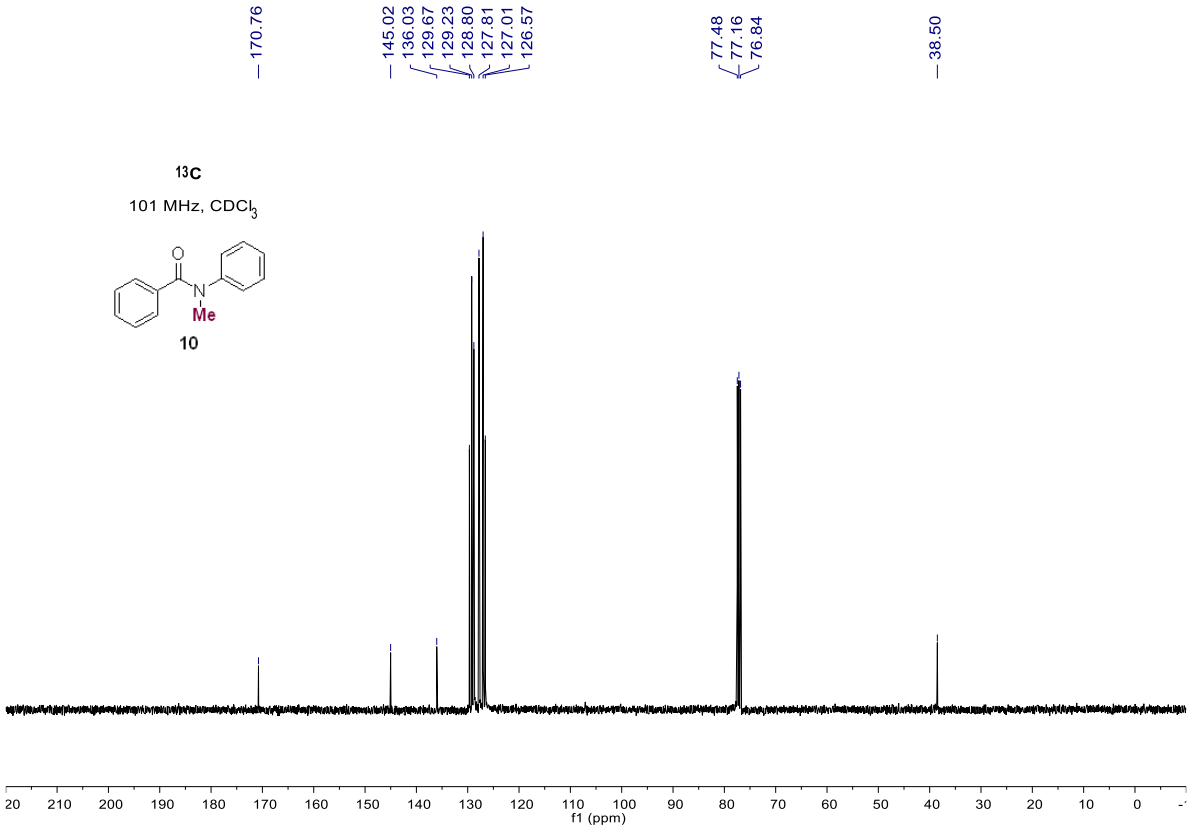
N-benzyl-*N*-methylbenzamide (9)



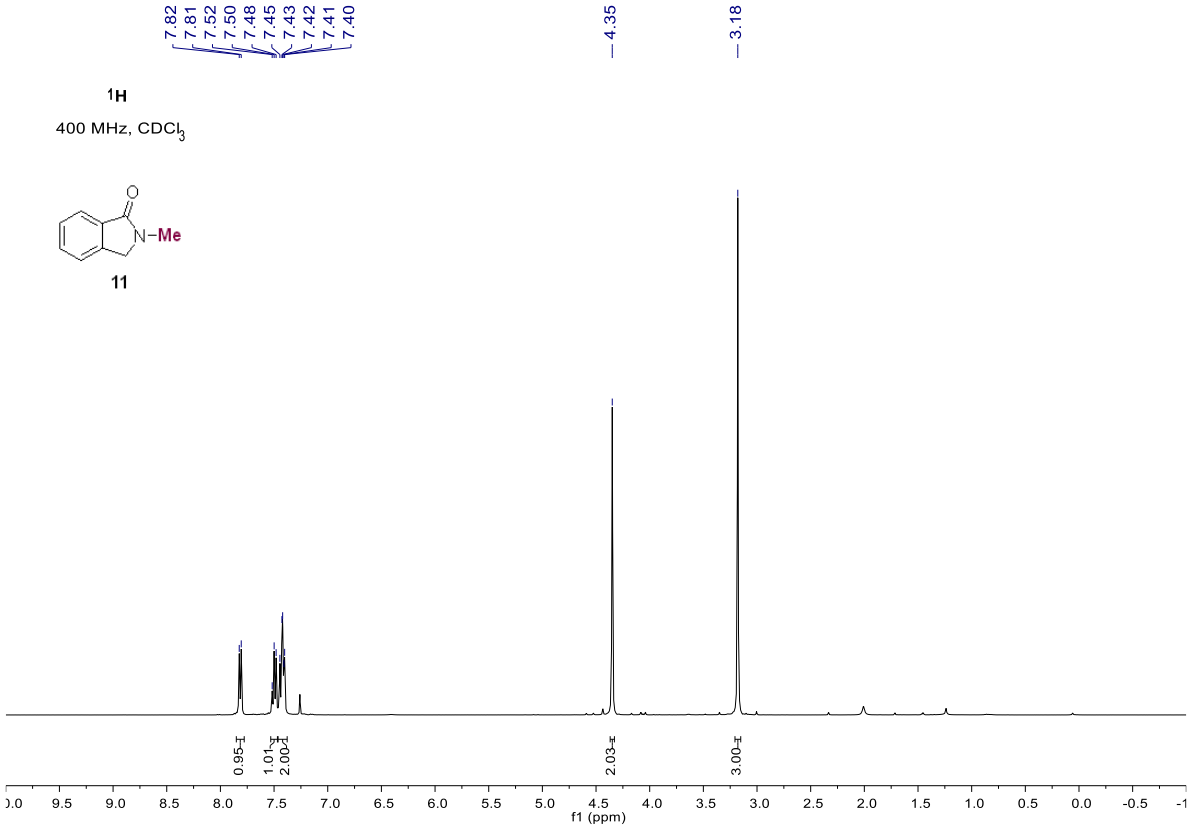


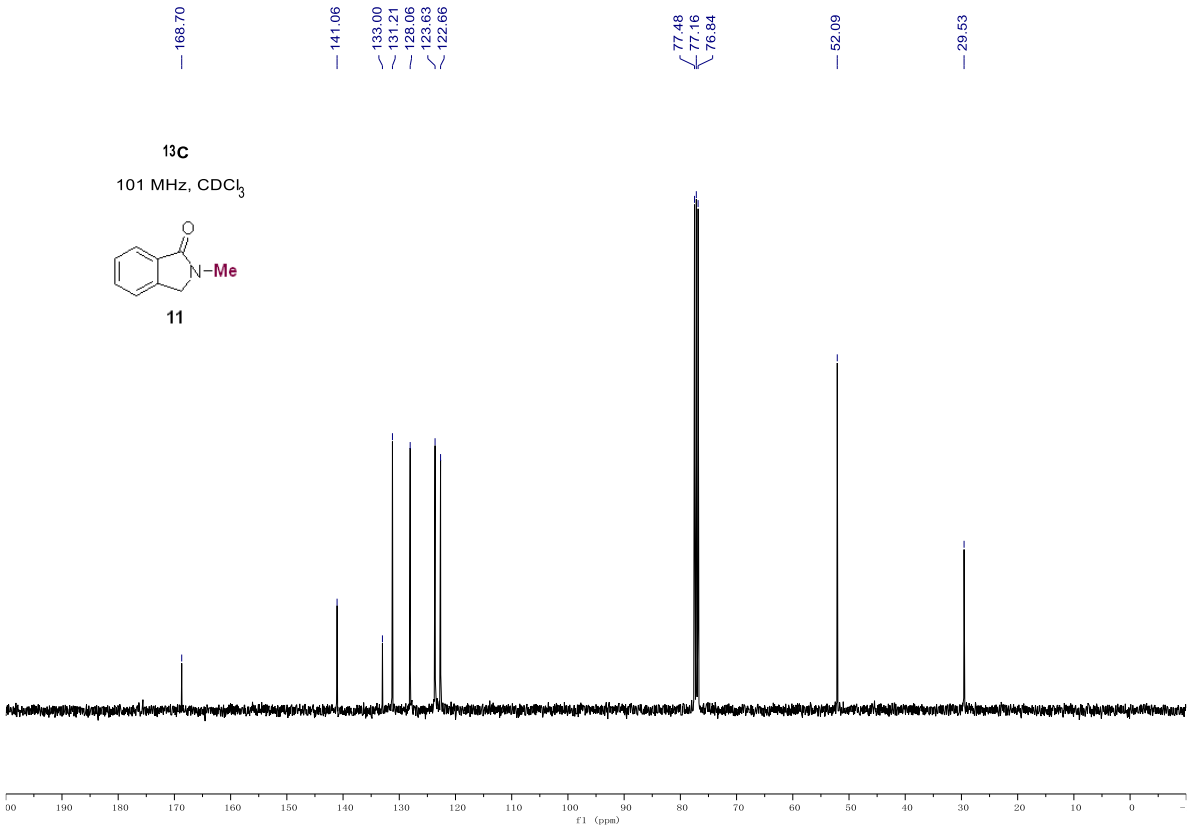
N-methyl-*N*-phenylbenzamide (10)



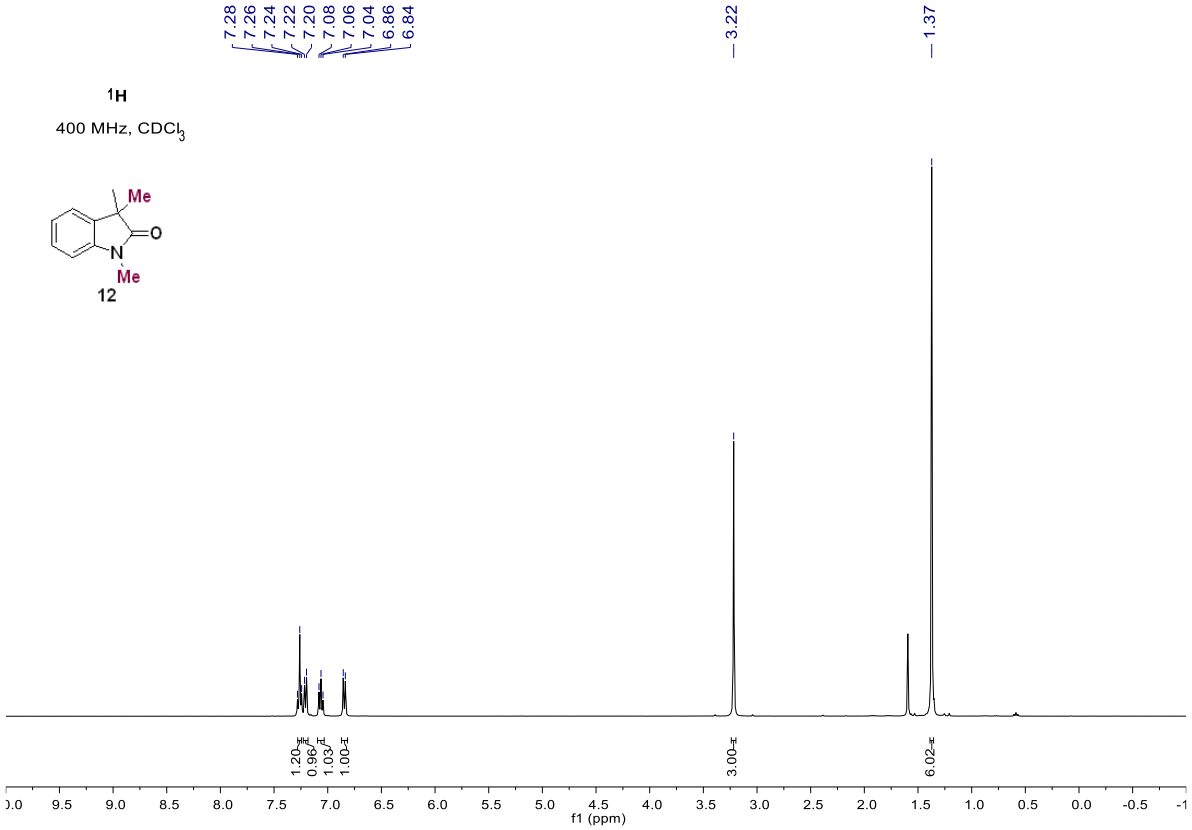


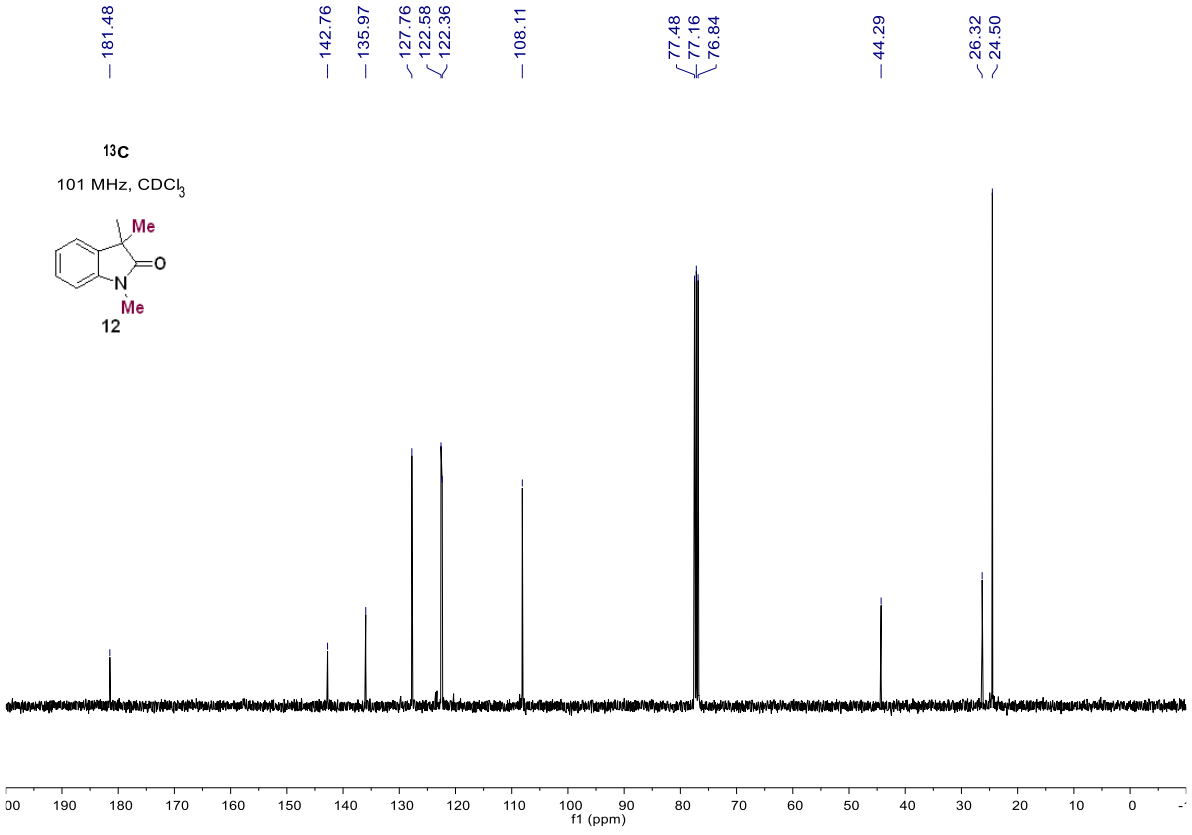
2-methylisoindolin-1-one (11)



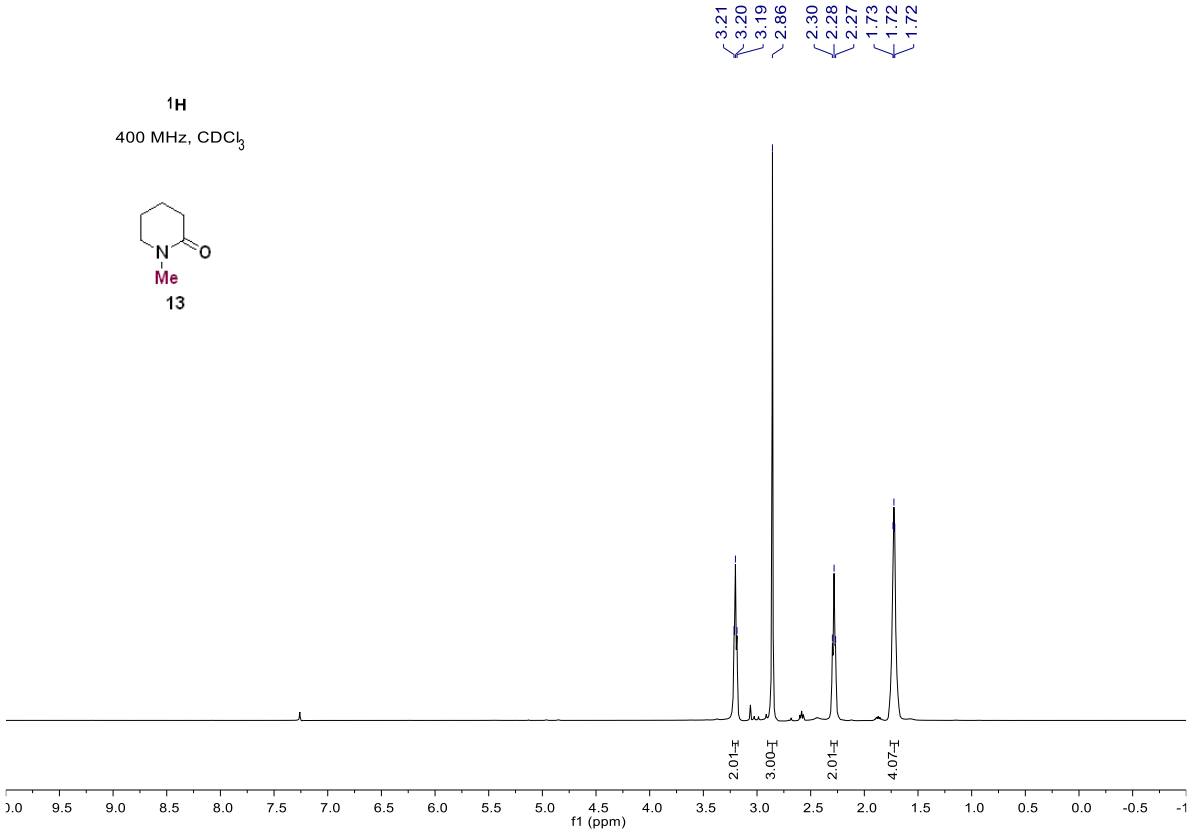


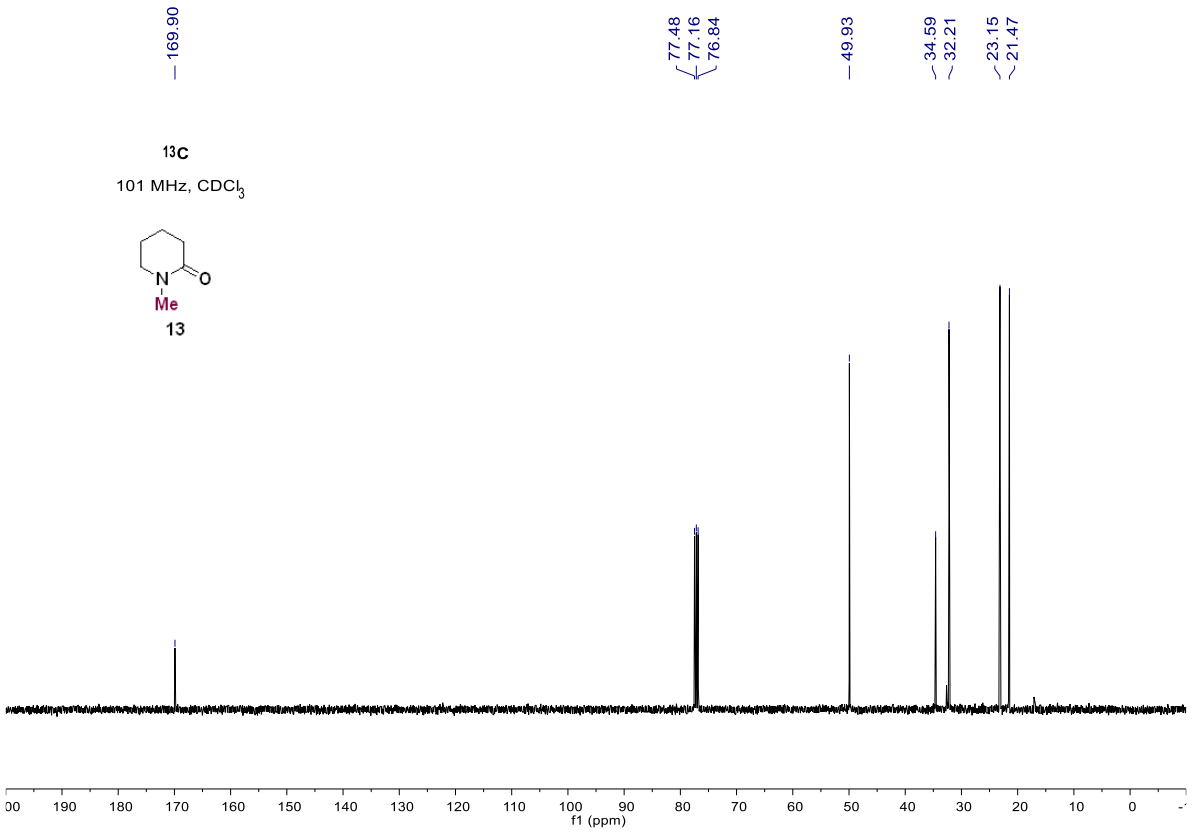
1,3,3-trimethylindolin-2-one (12)



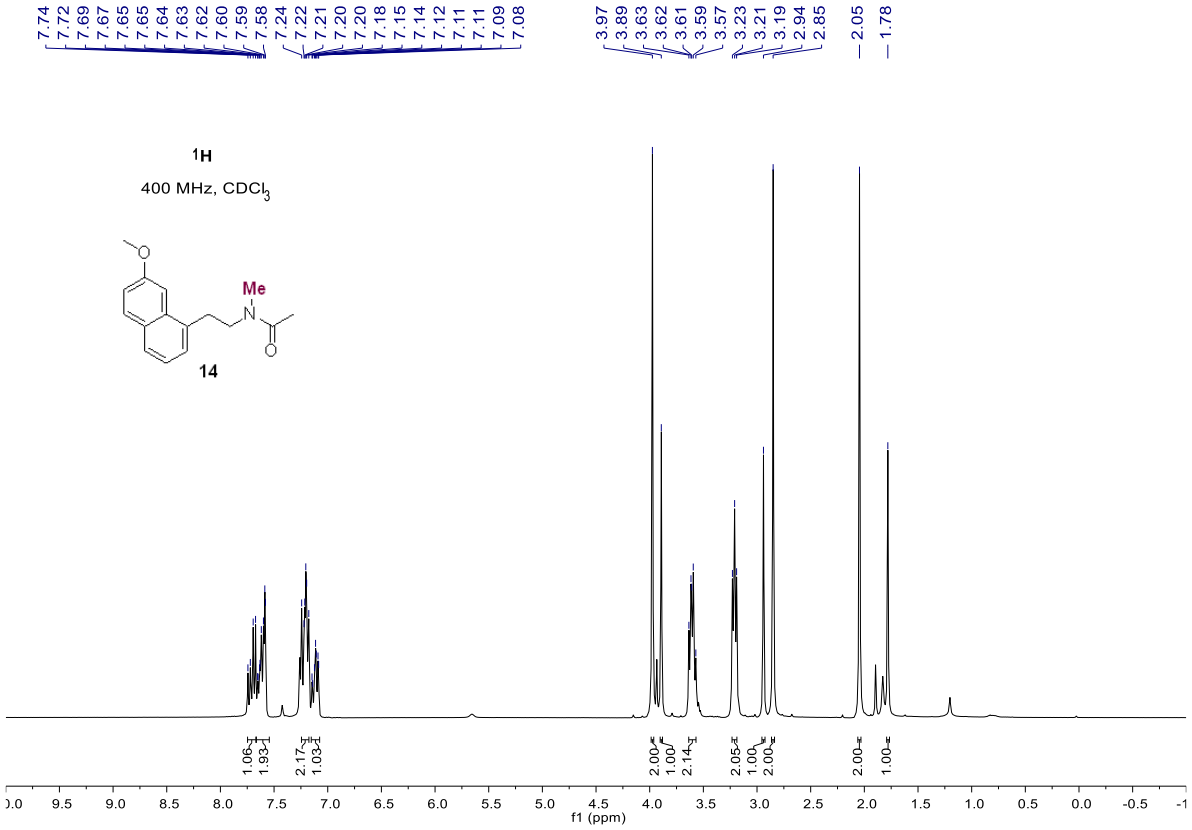


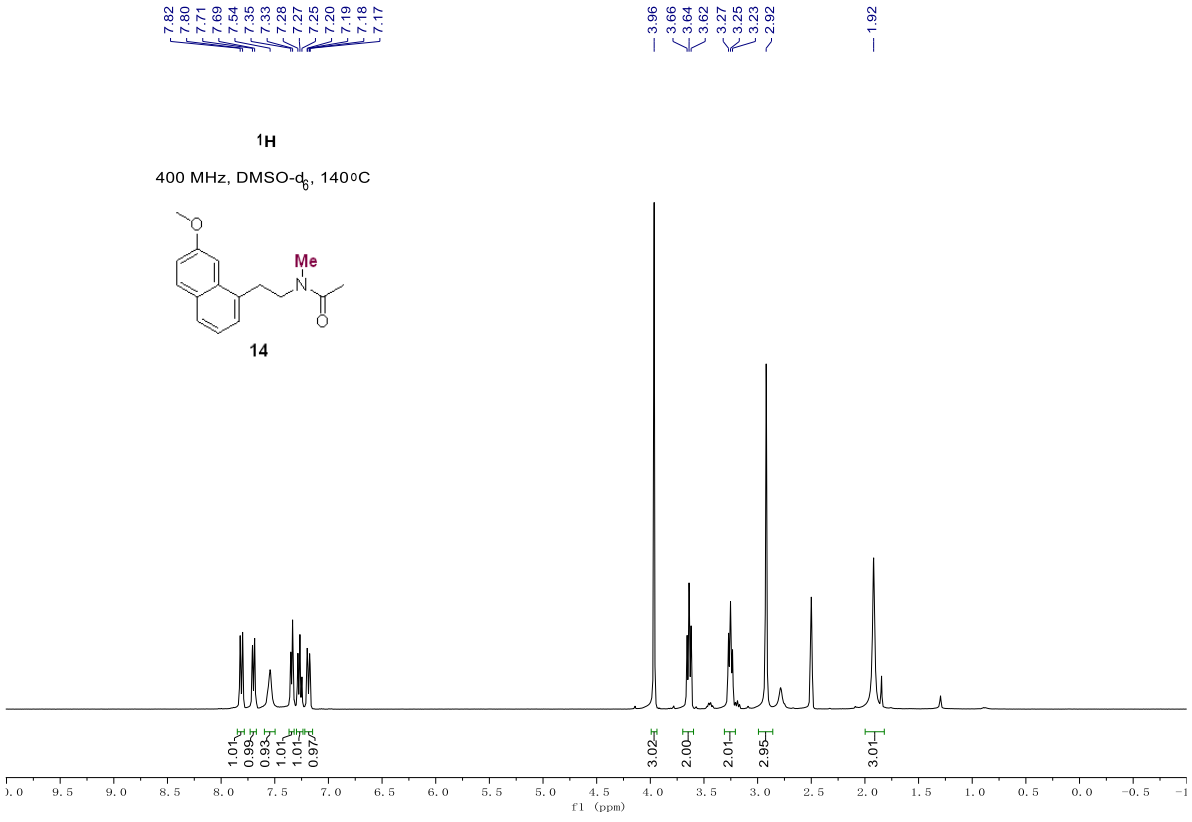
1-methylpiperidin-2-one (13)

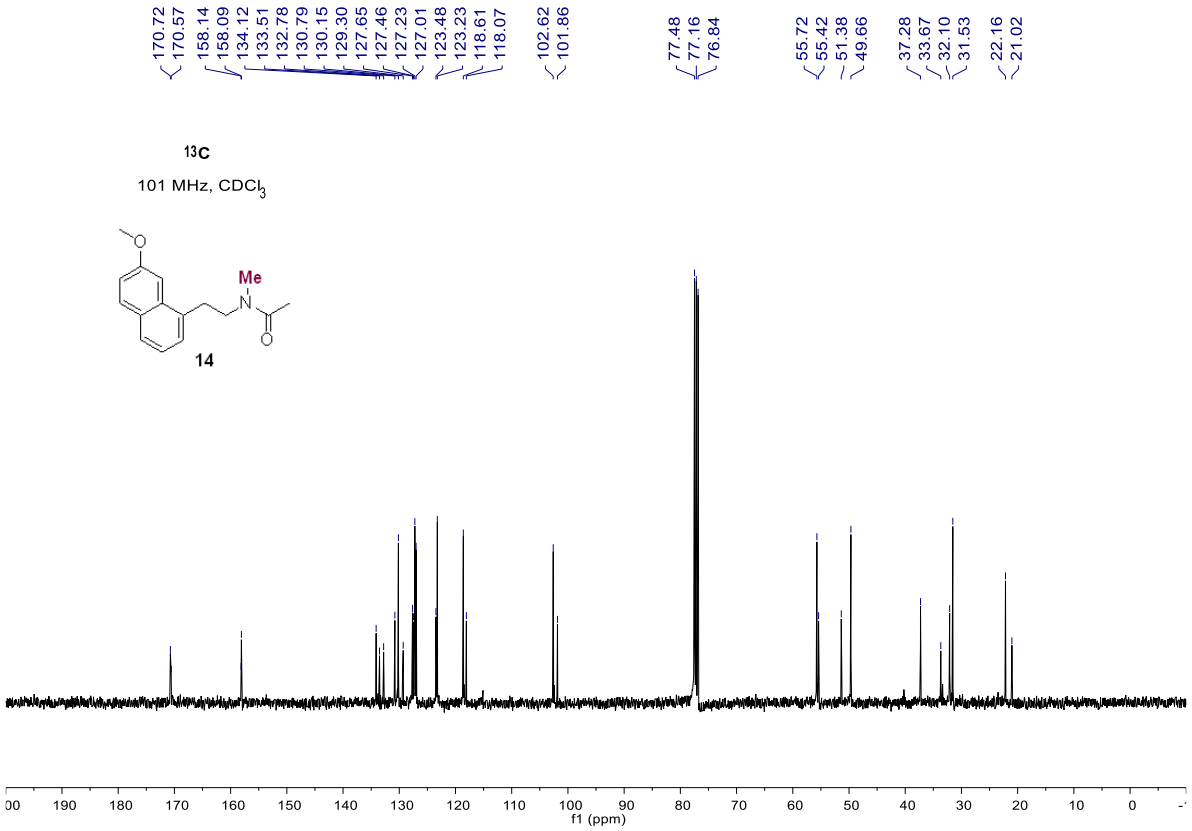




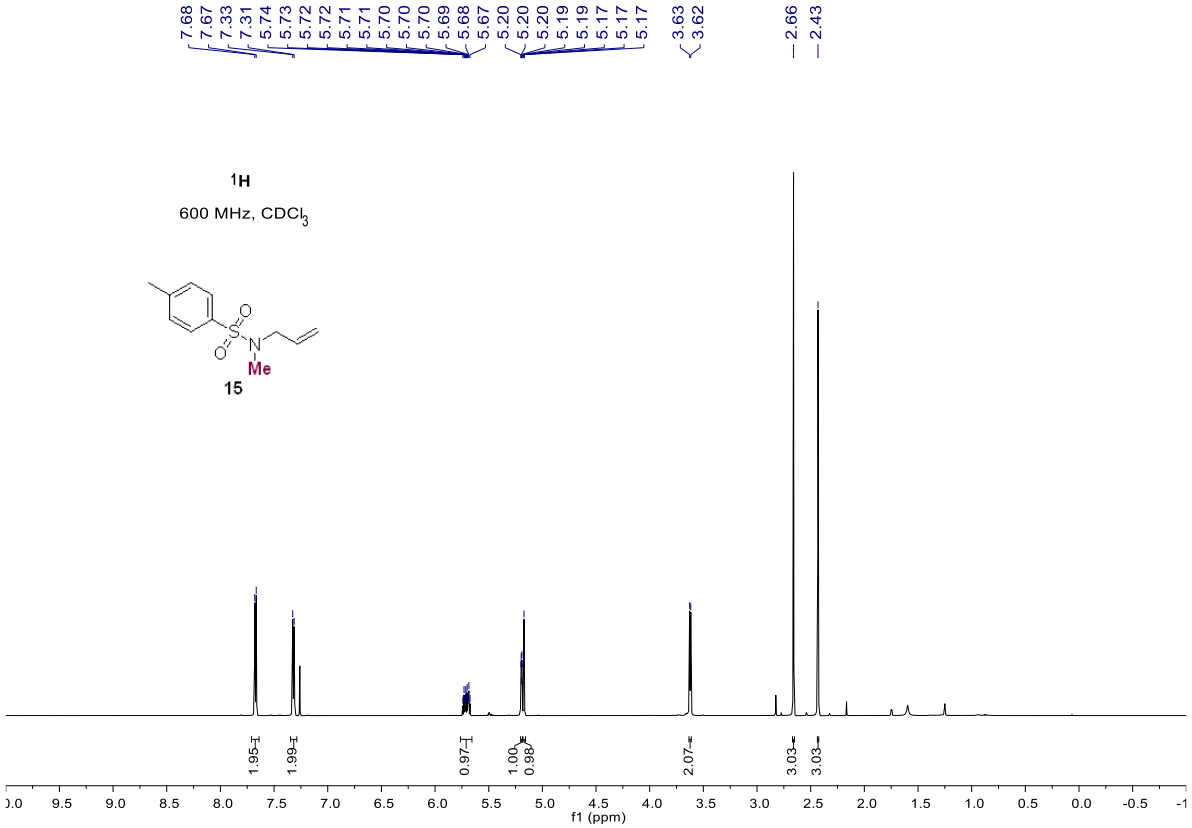
***N*-(2-(7-methoxynaphthalen-1-yl)ethyl)-*N*-methylacetamide (14)**:

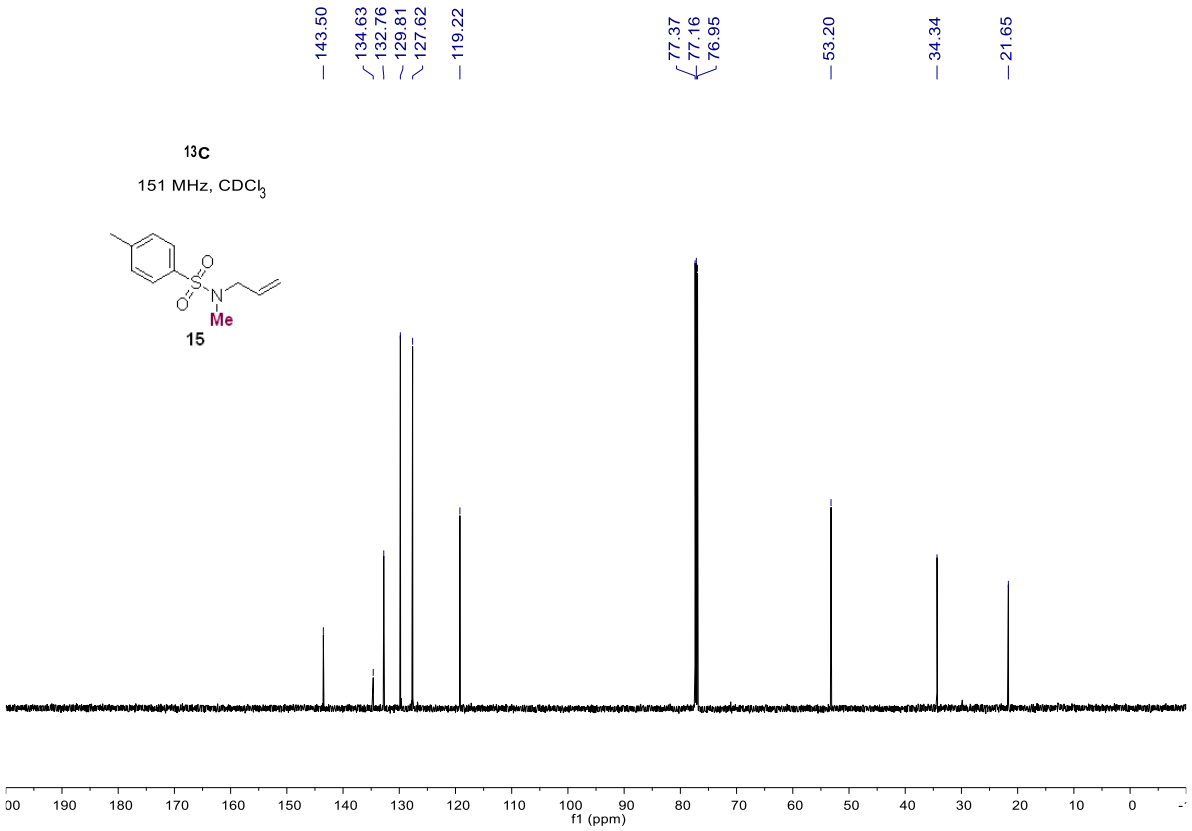




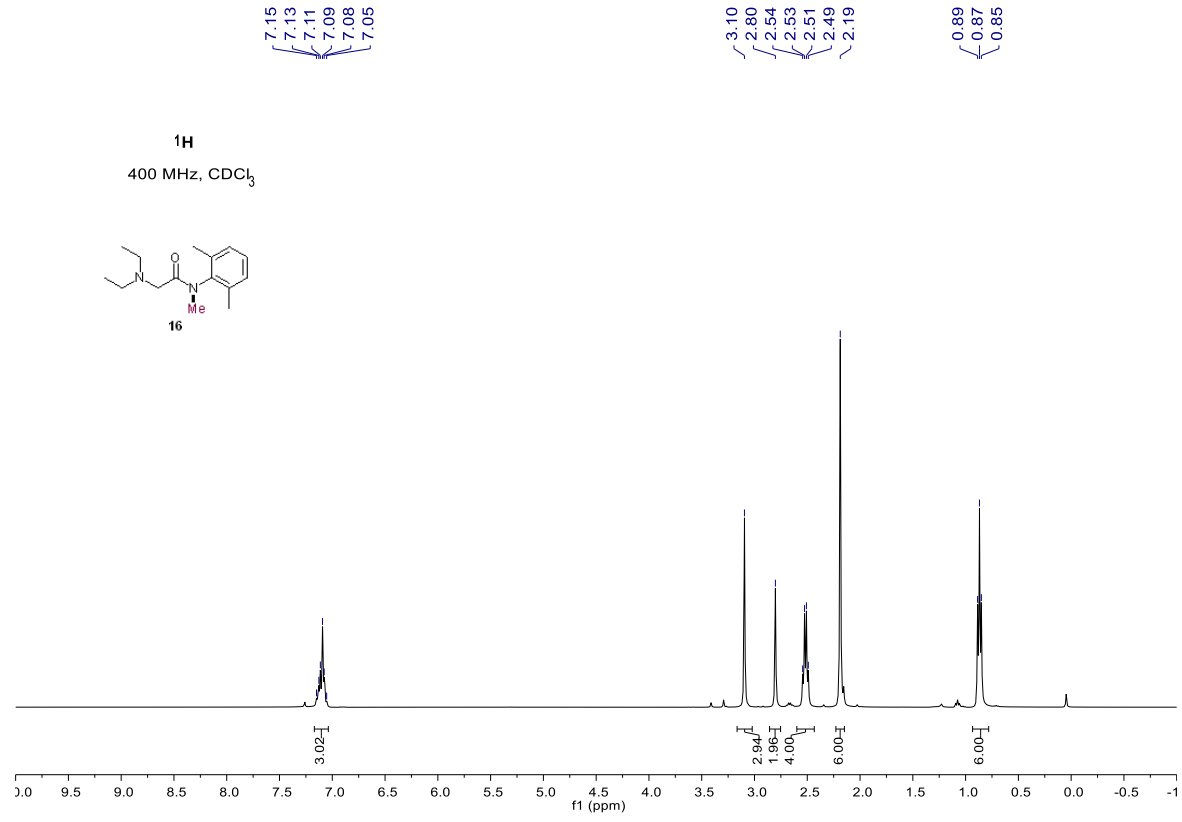


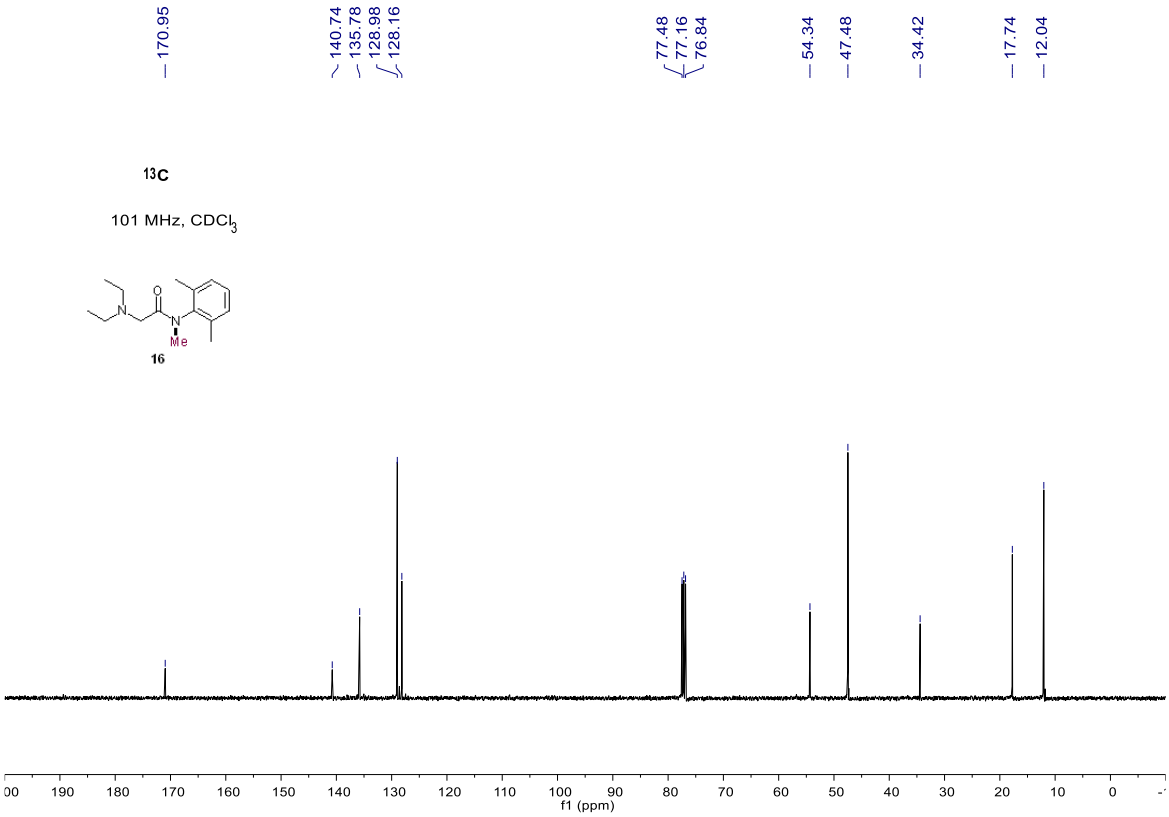
N-allyl-*N*,4-dimethylbenzenesulfonamide (15)



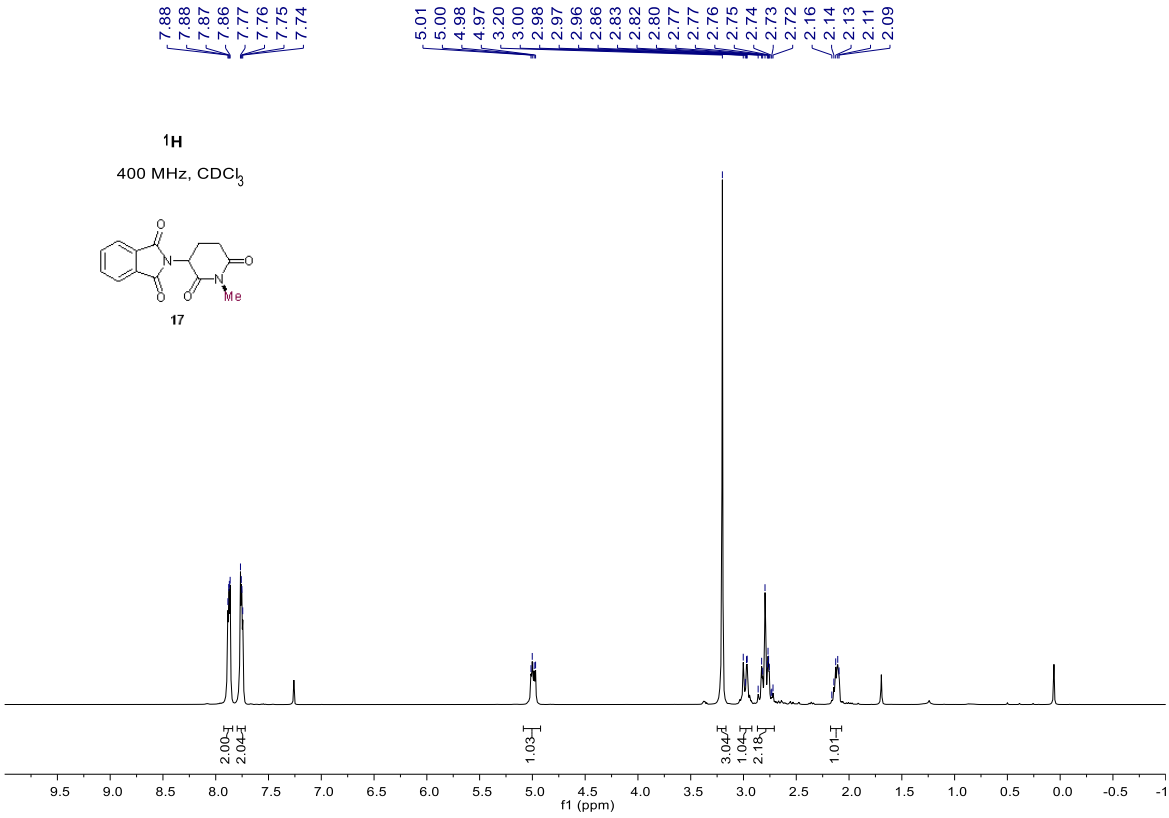


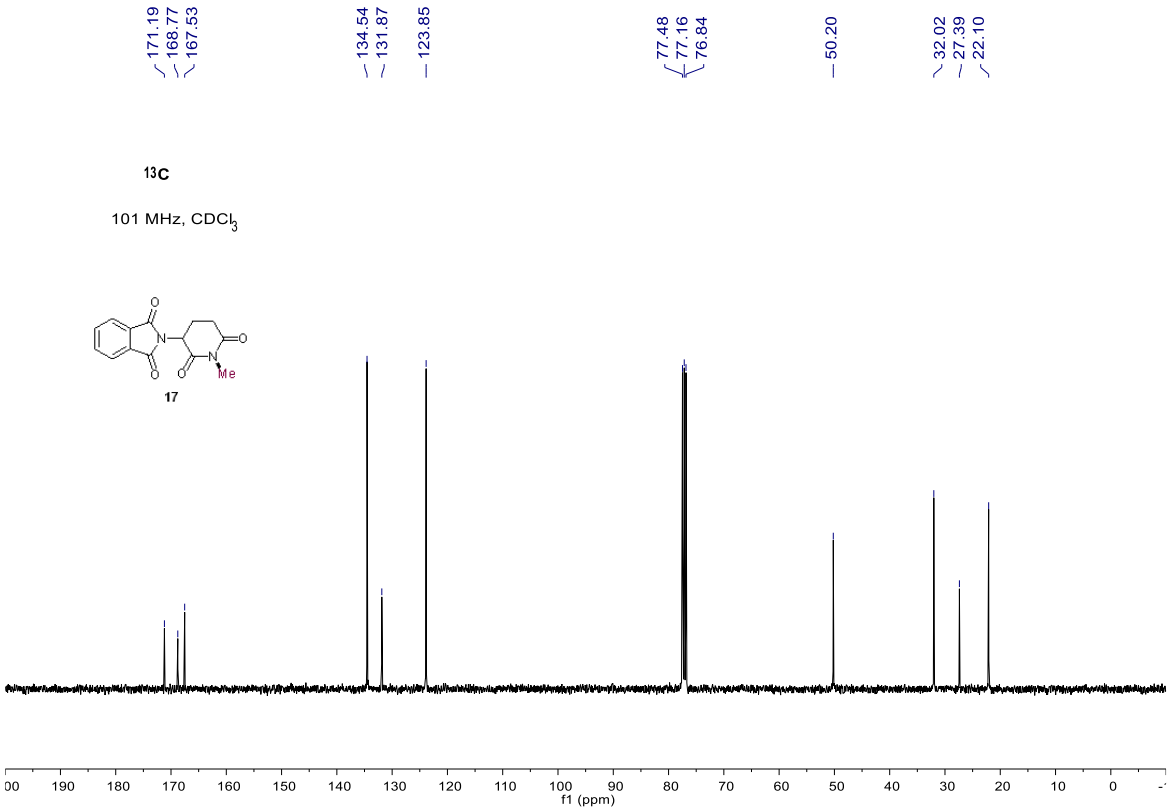
2-(diethylamino)-*N*-(2,6-dimethylphenyl)-*N*-methylacetamide (16)



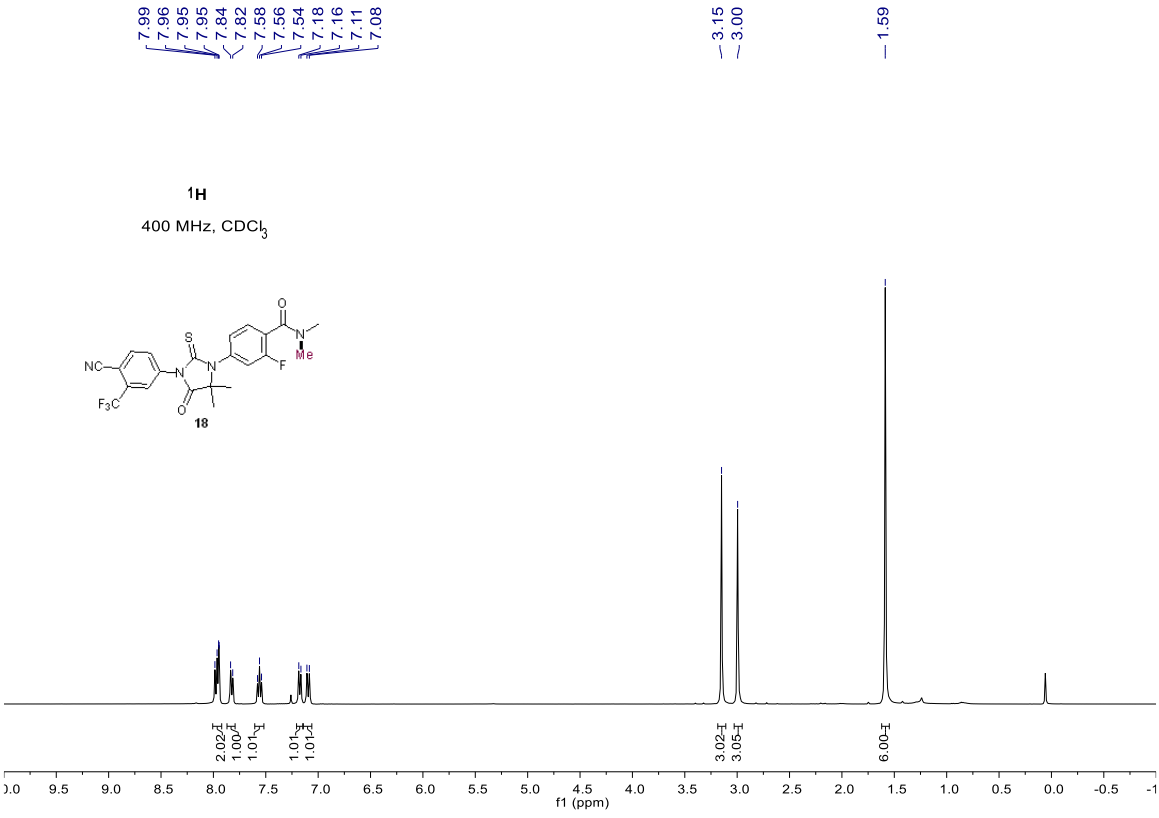


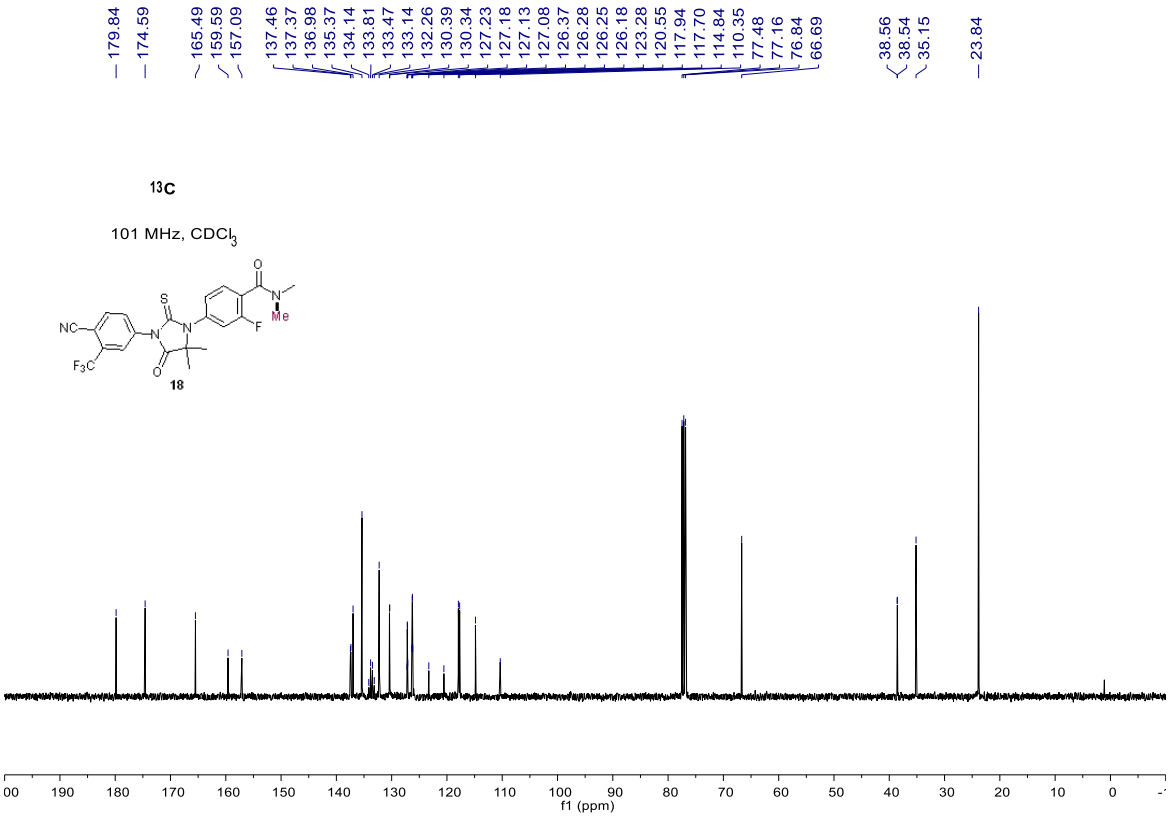
2-(1-methyl-2,6-dioxopiperidin-3-yl)isoindoline-1,3-dione (17)

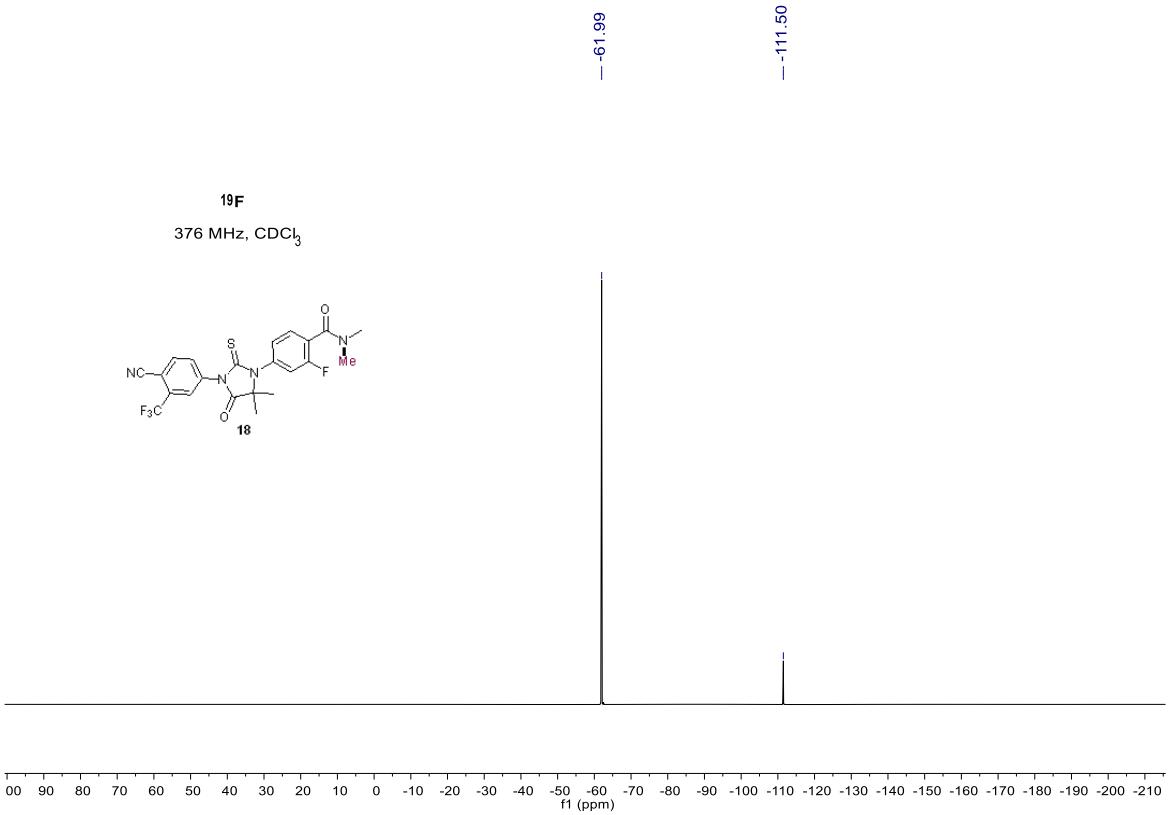




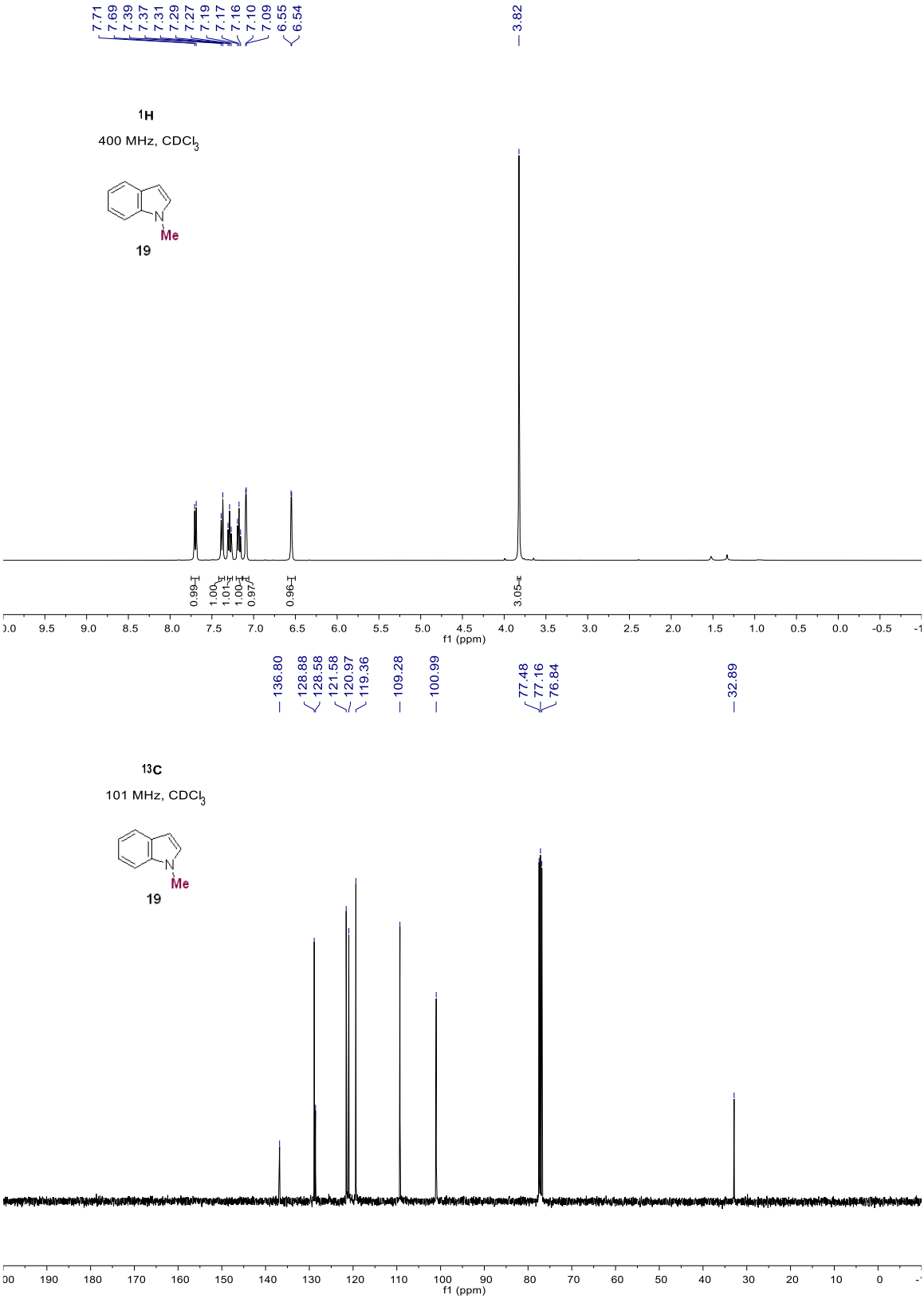
4-(3-(4-cyano-3-(trifluoromethyl)phenyl)-5,5-dimethyl-4-oxo-2-thioxoimidazolidin-1-yl)-2-fluoro-*N*,*N*-dimethylbenzamide (18)



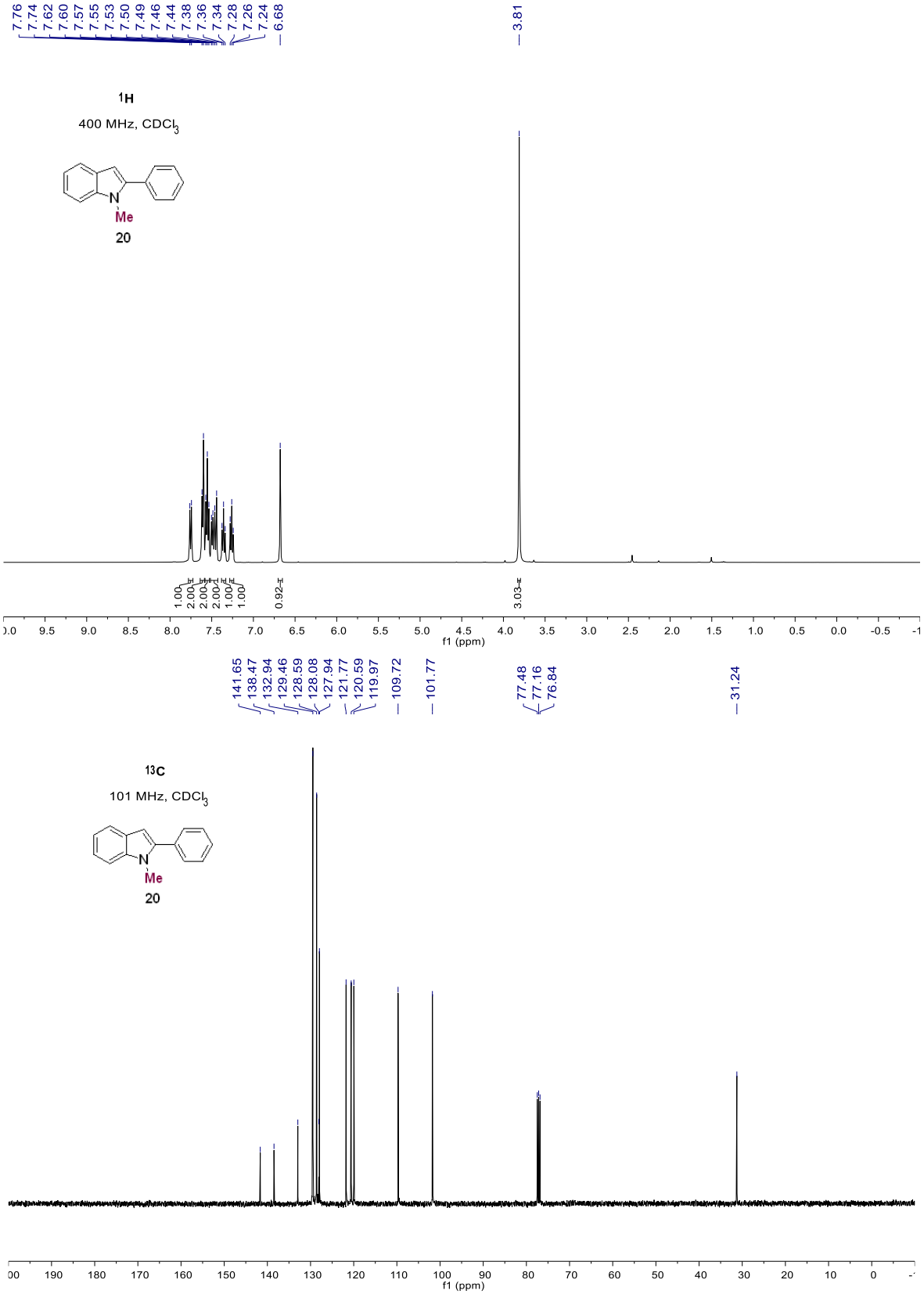

179.84
174.59
165.49
159.59
157.09
137.46
137.37
136.98
135.37
134.14
133.81
133.47
133.14
132.26
130.39
130.34
127.23
127.18
127.13
127.08
126.37
126.28
126.25
126.18
123.28
120.55
117.94
117.70
114.84
110.35
77.48
77.16
76.84
66.69
38.56
38.54
35.15
23.84
13C
101 MHz, CDCl3
18
f1 (ppm)


-61.99
-111.50
19F
376 MHz, CDCl3
18
f1 (ppm)

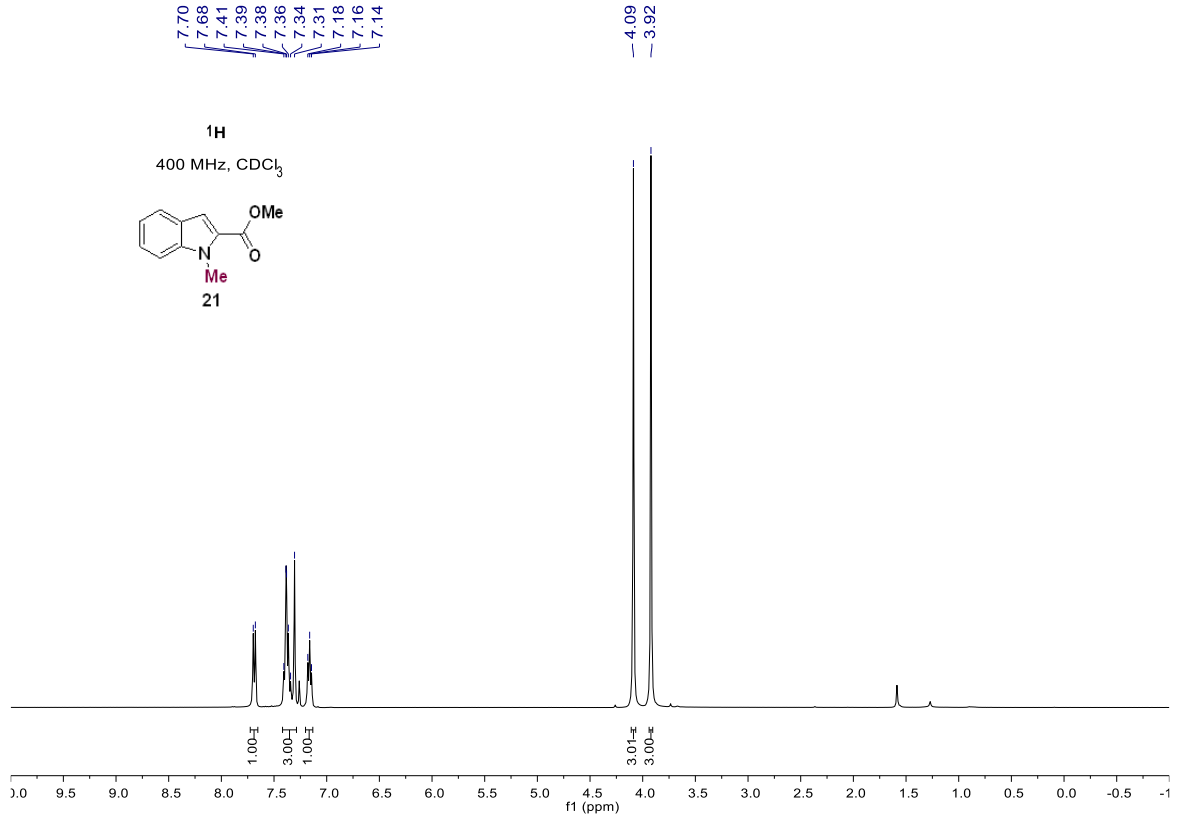
1-methyl-1*H*-indole (19)

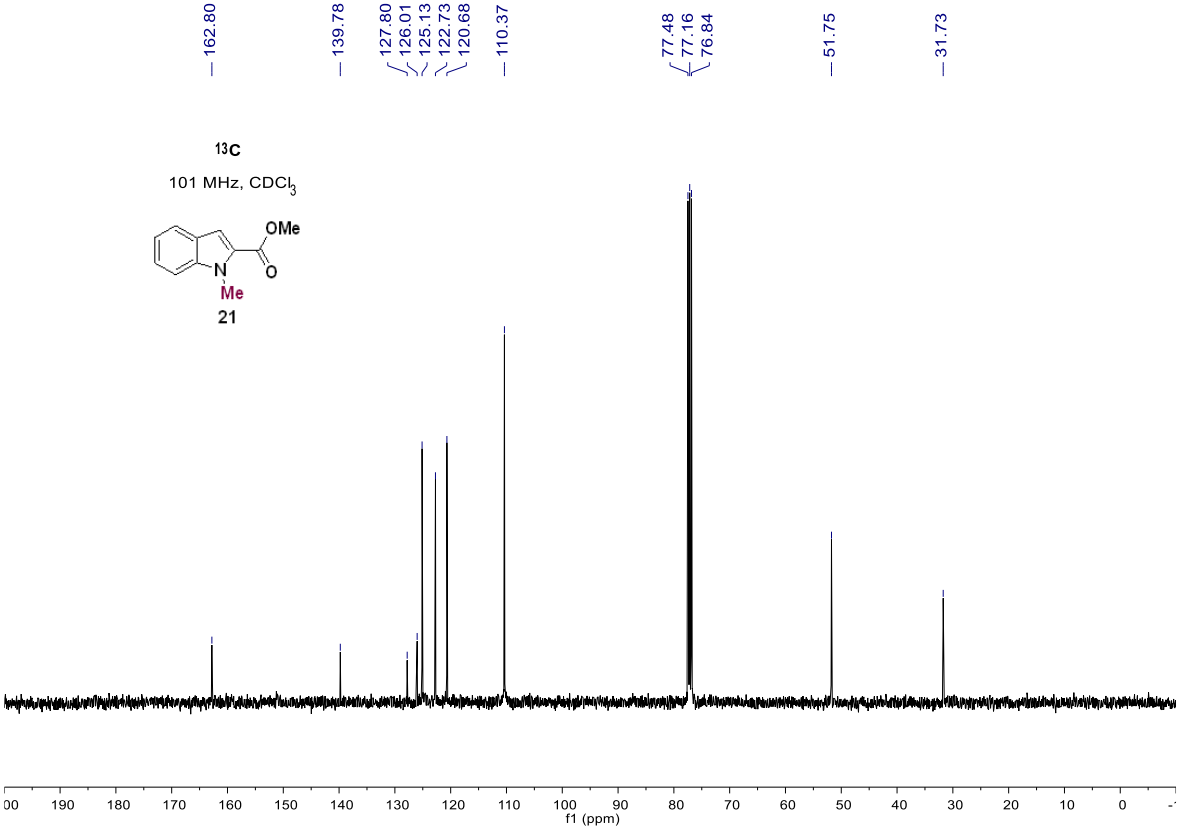


1-methyl-2-phenyl-1*H*-indole (20)

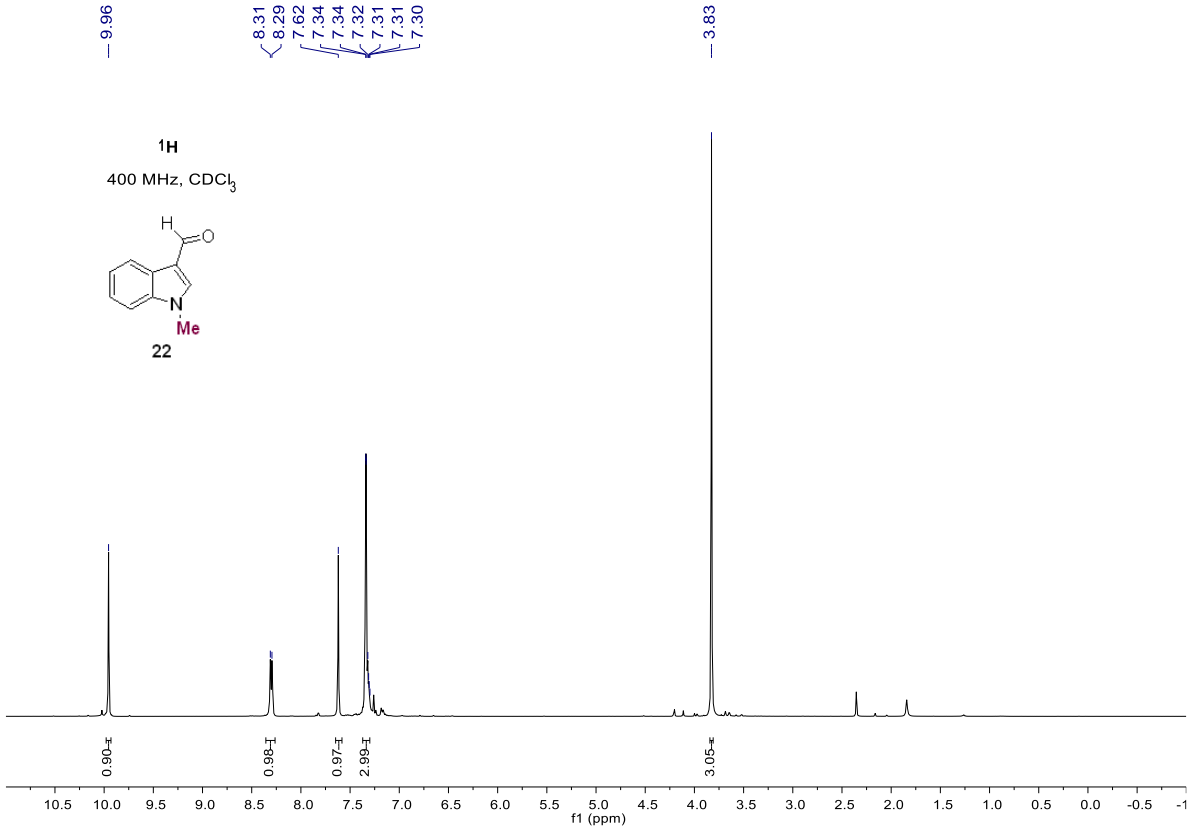


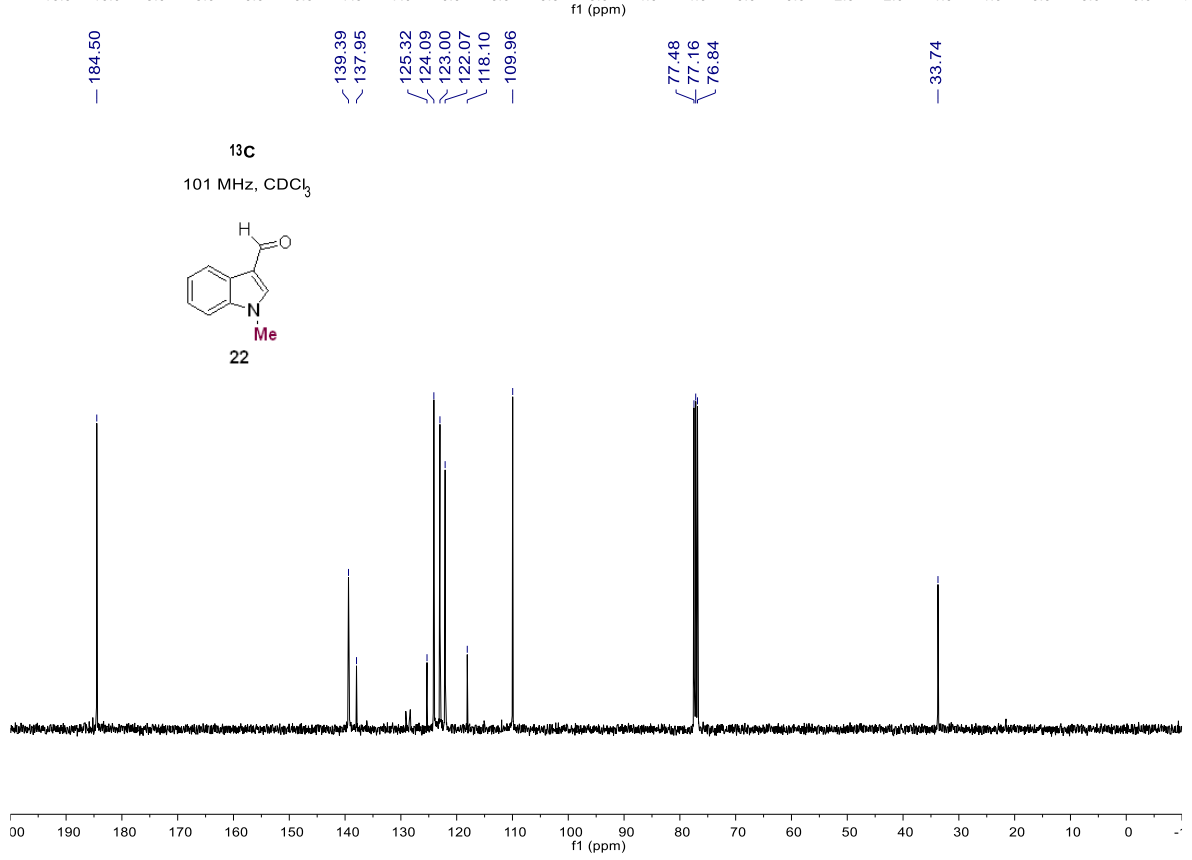
methyl 1-methyl-1*H*-indole-2-carboxylate (**21**)



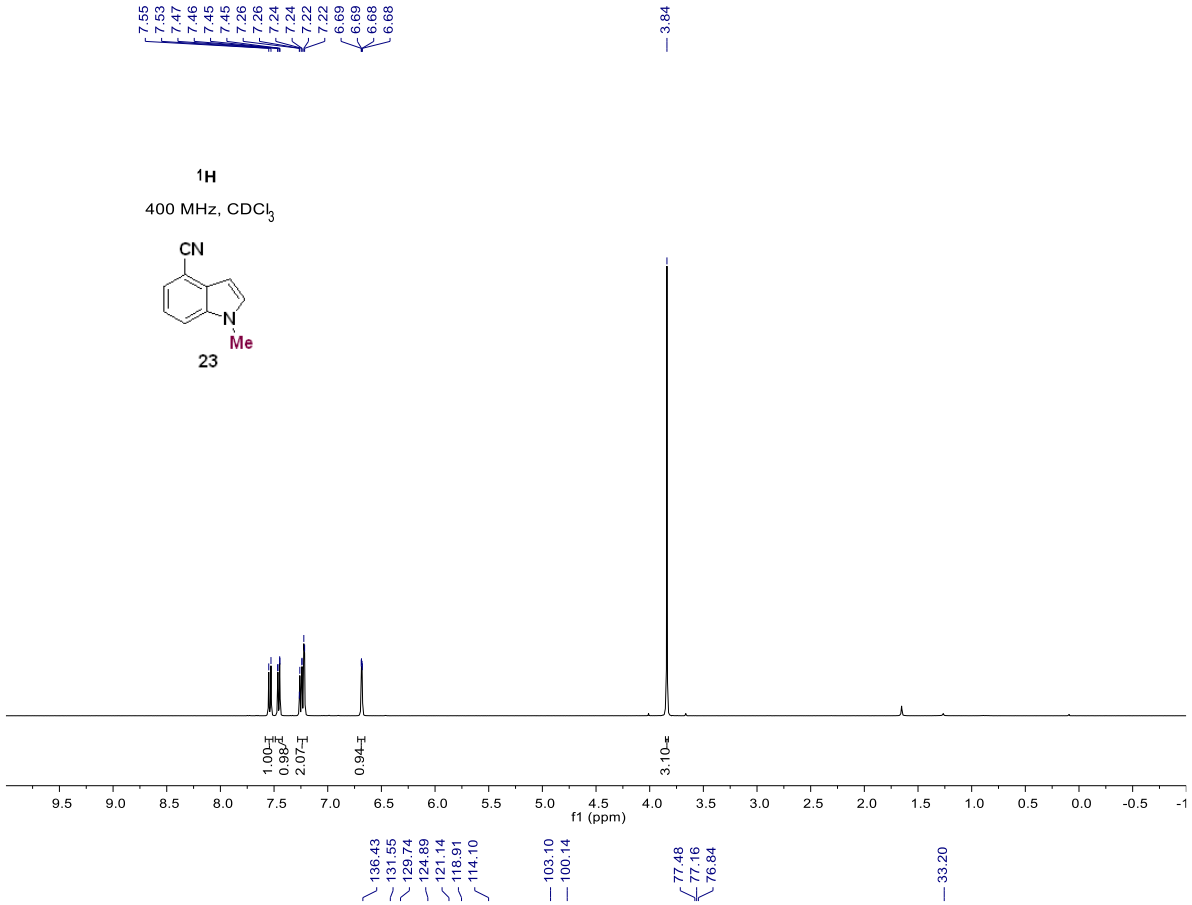


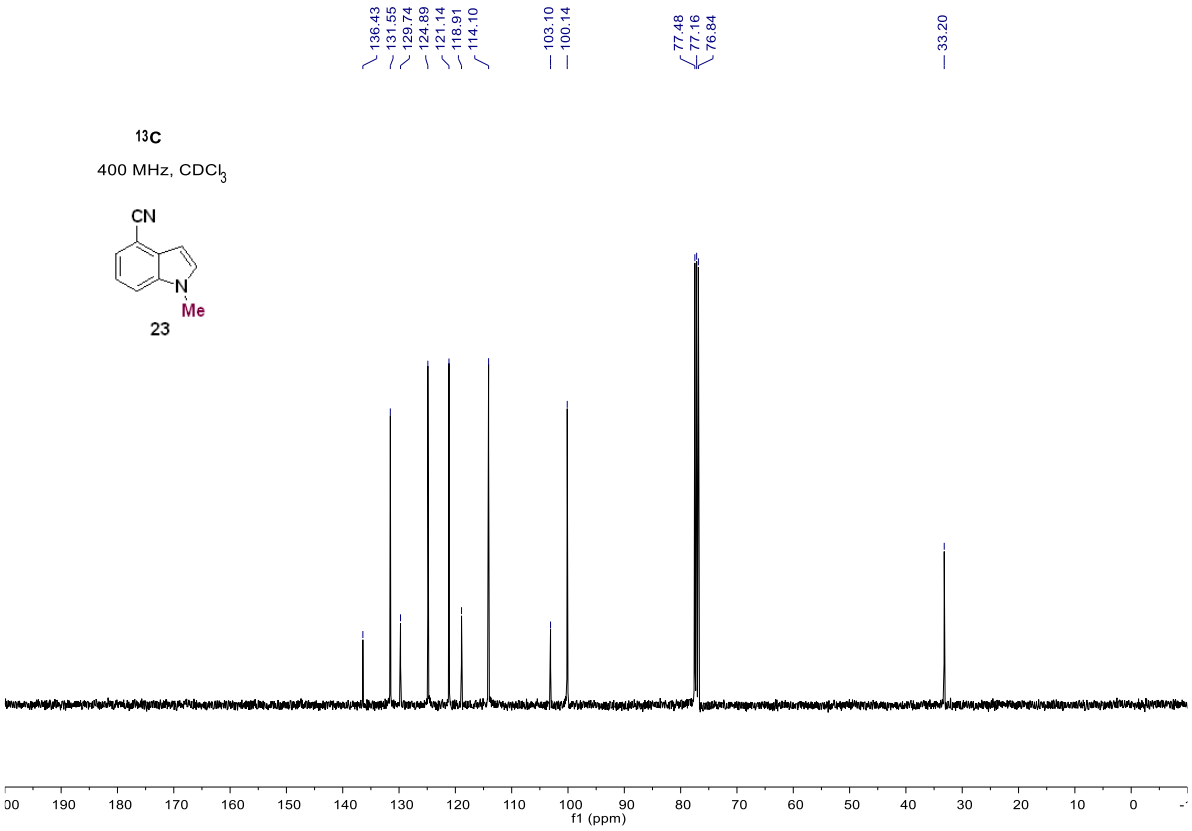
1-methyl-1*H*-indole-3-carbaldehyde (22)



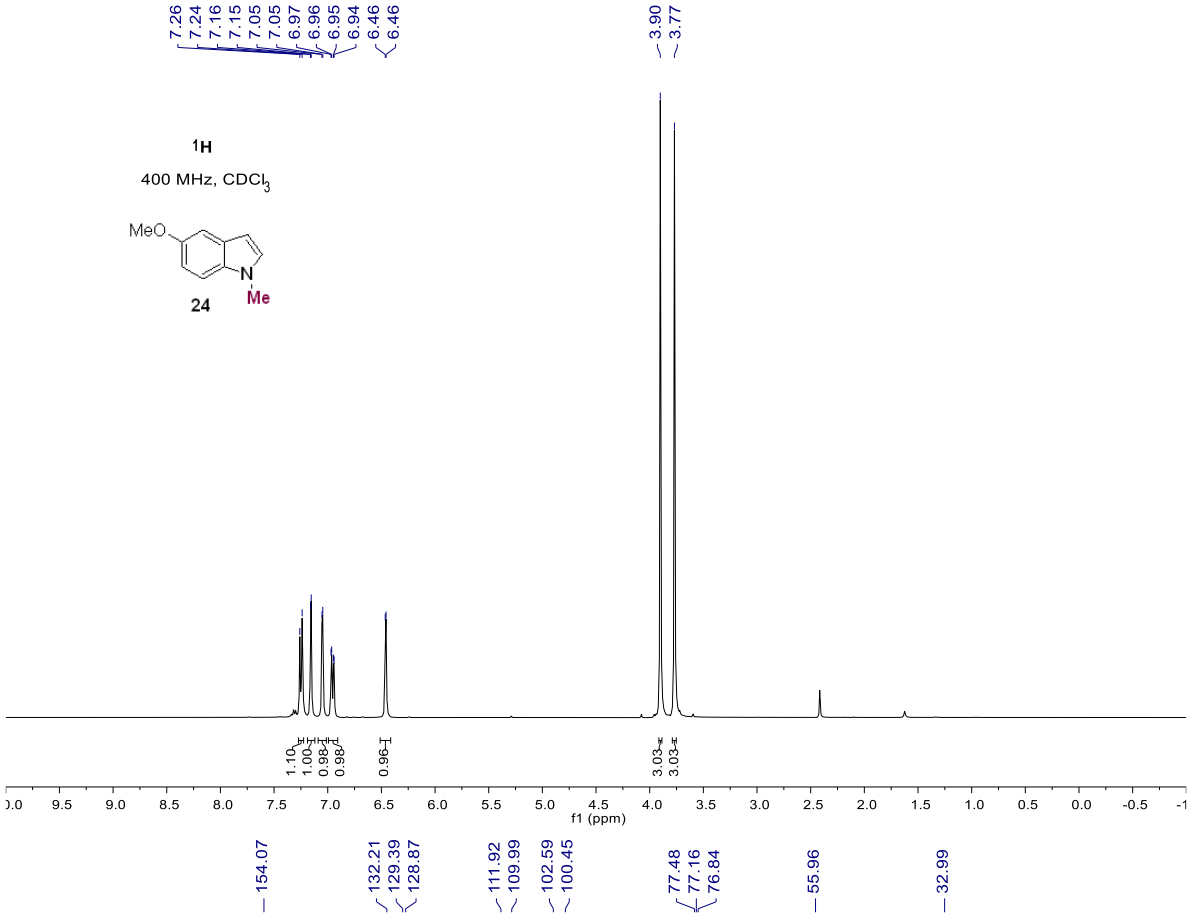


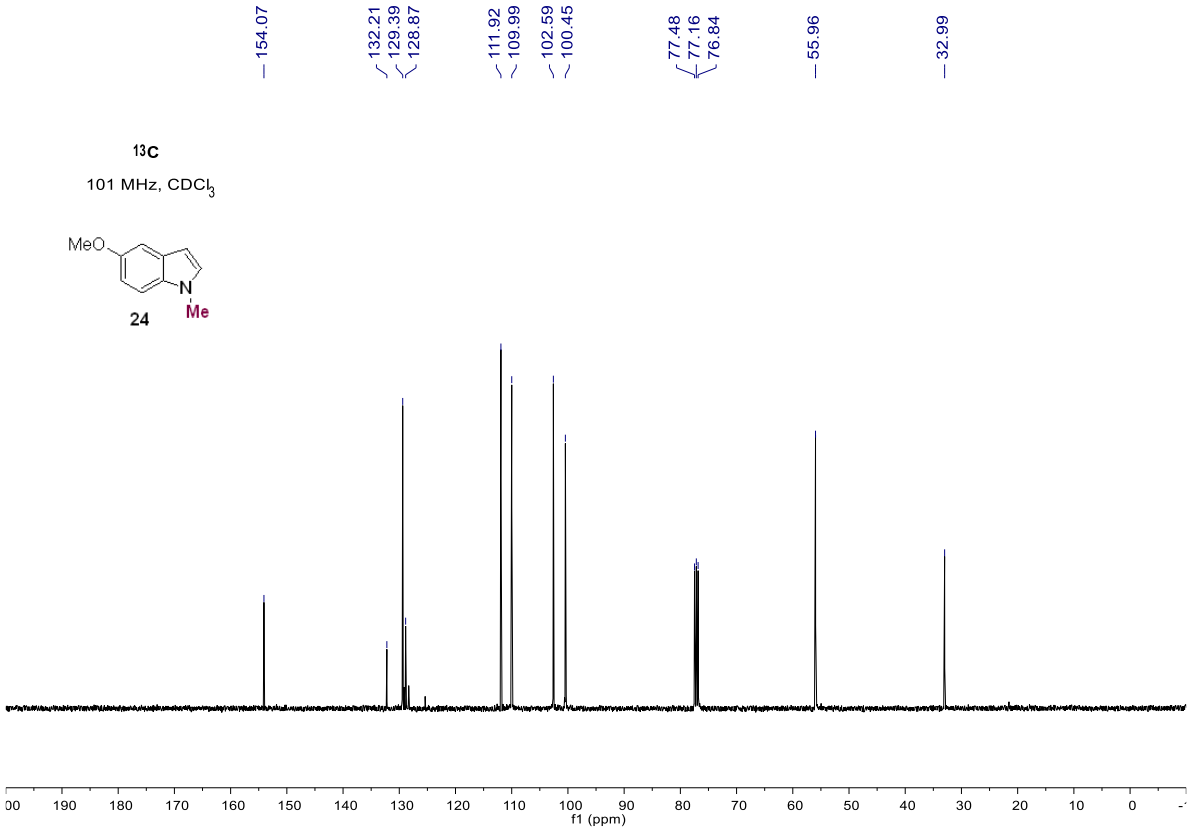
1-methyl-1*H*-indole-4-carbonitrile (23)



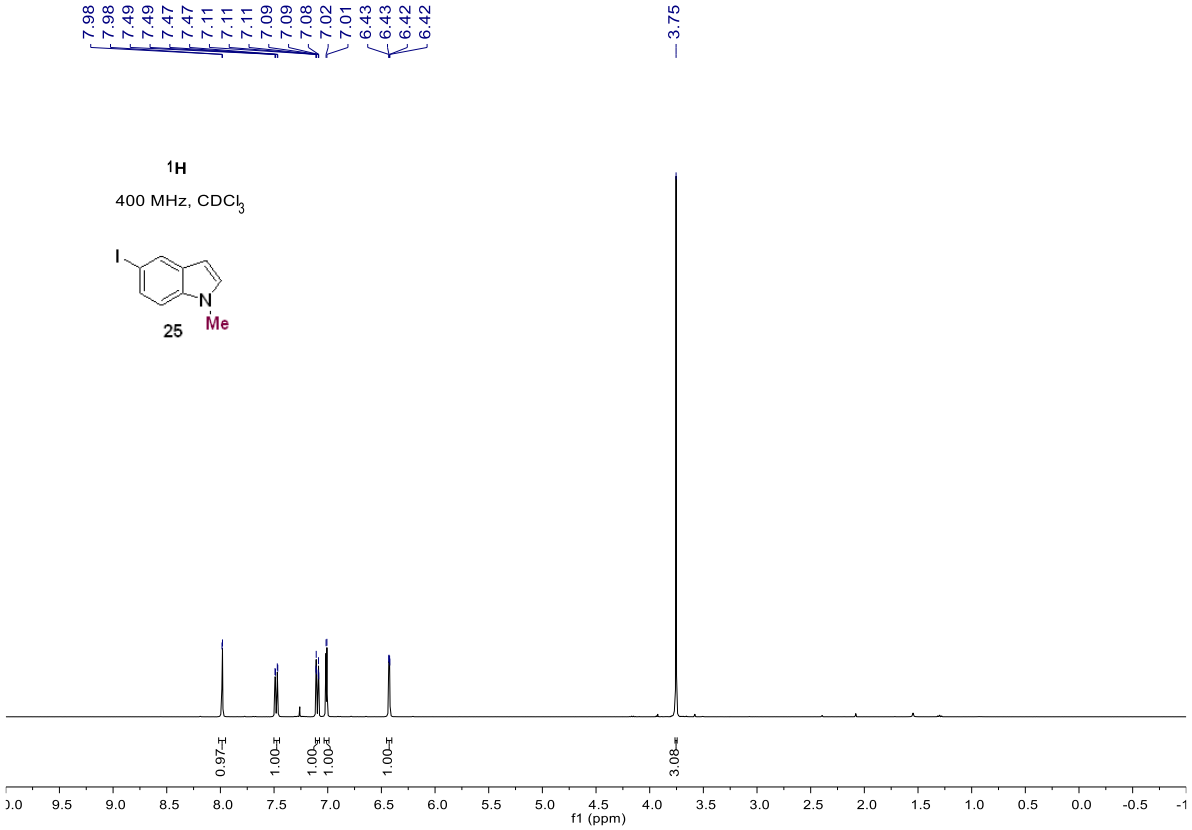


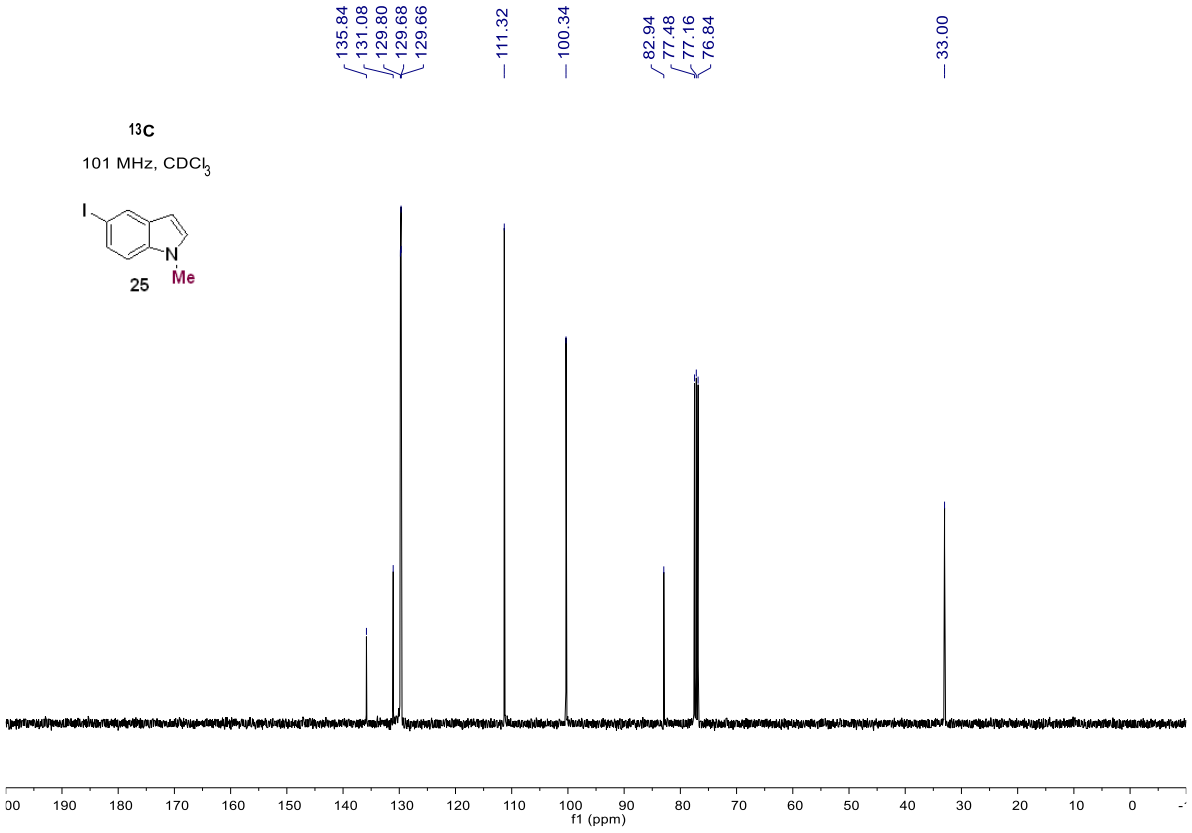
5-methoxy-1-methyl-1*H*-indole (24)



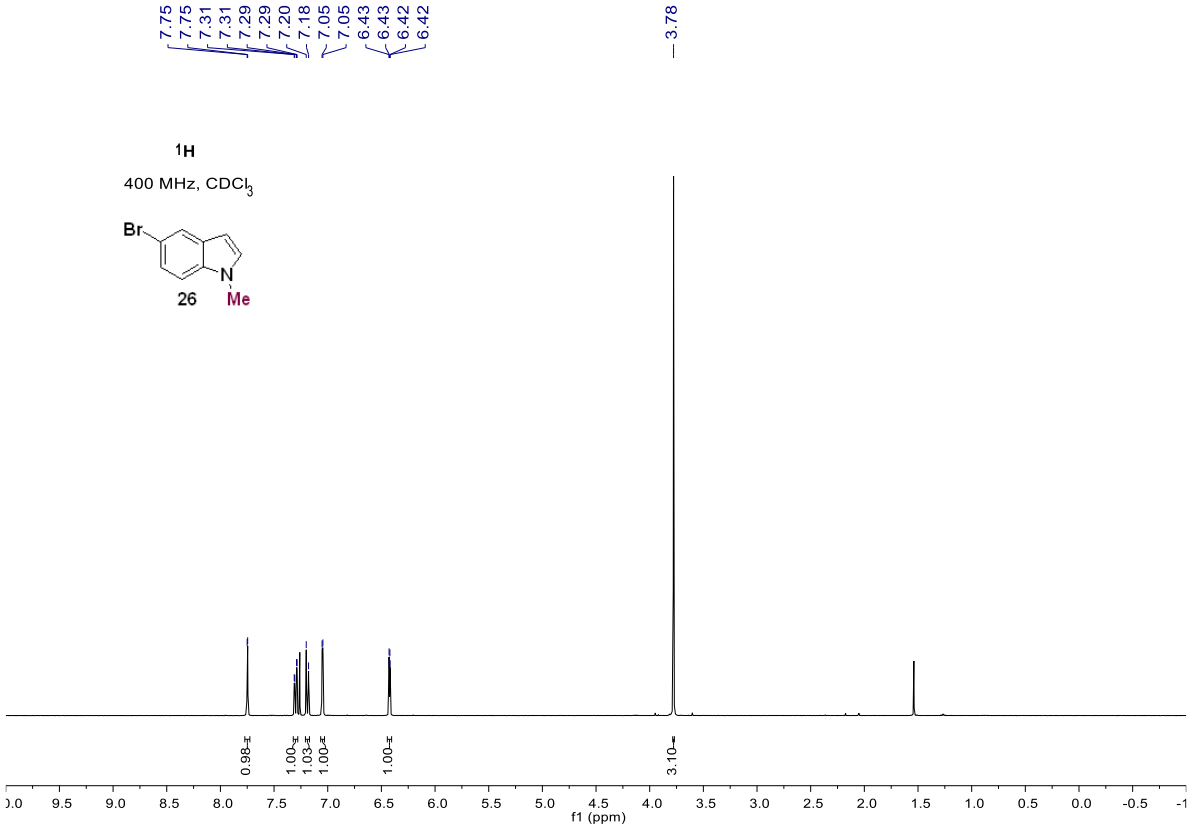


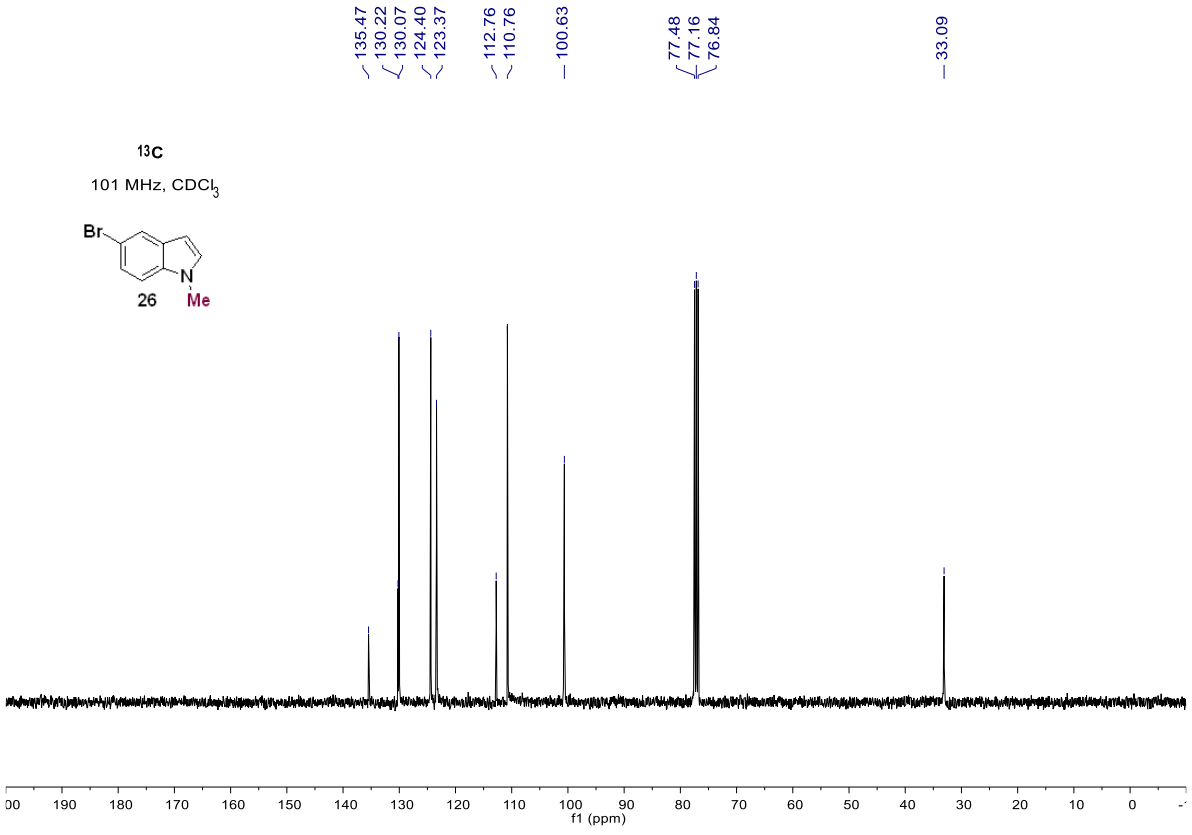
5-iodo-1-methyl-1*H*-indole (25)



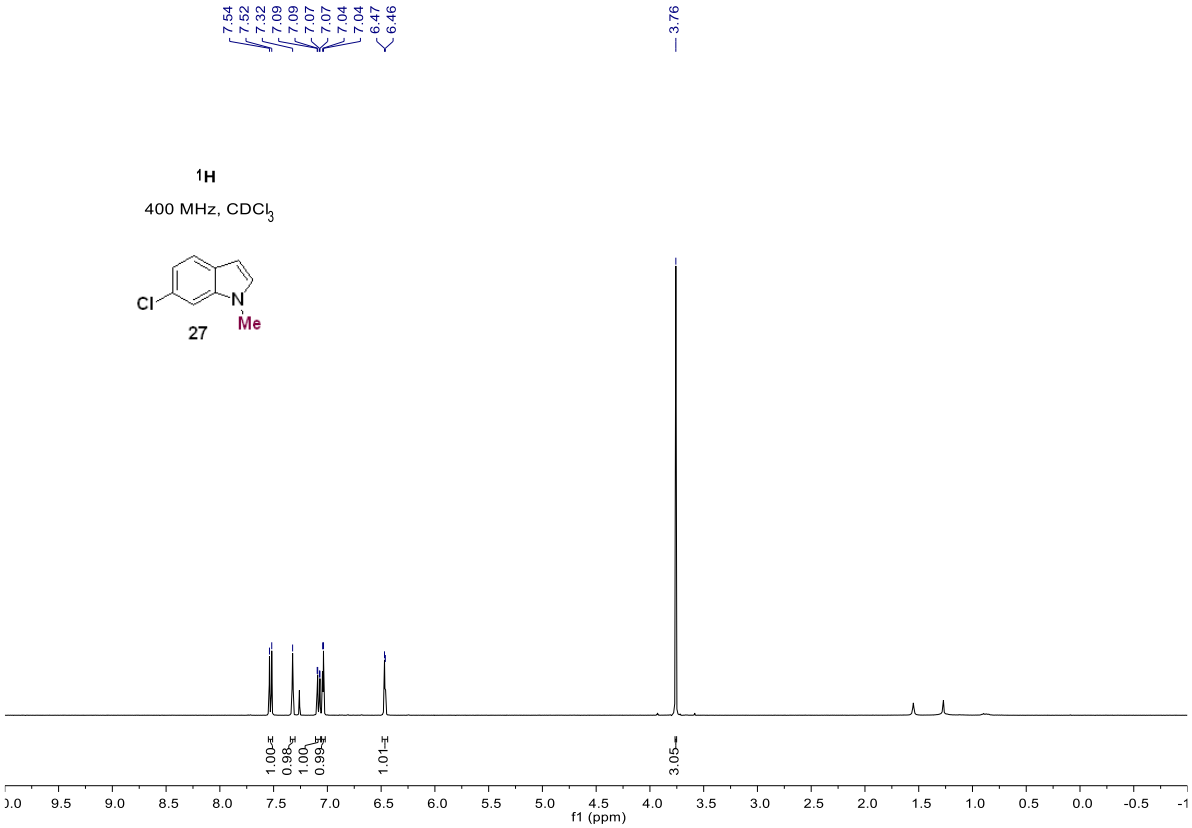


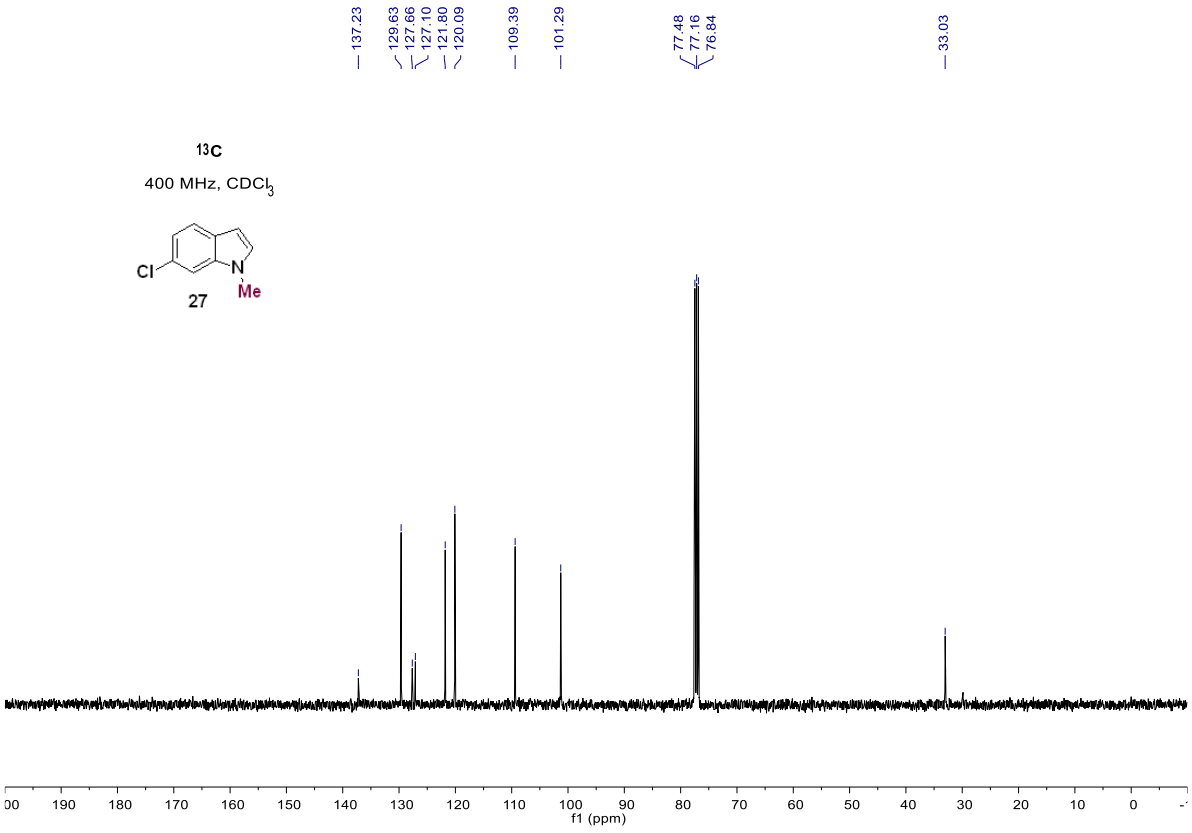
5-bromo-1-methyl-1*H*-indole (26)



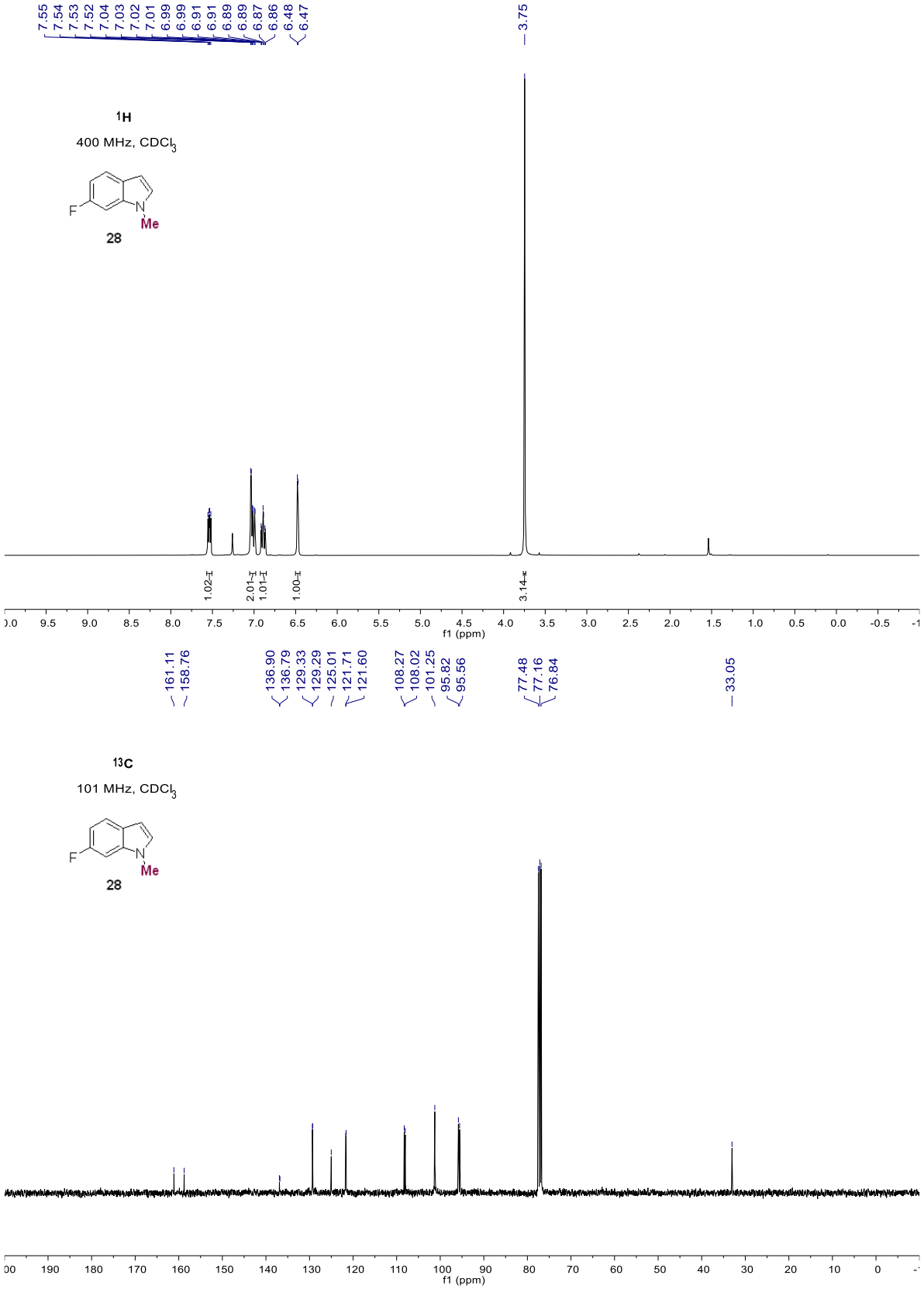


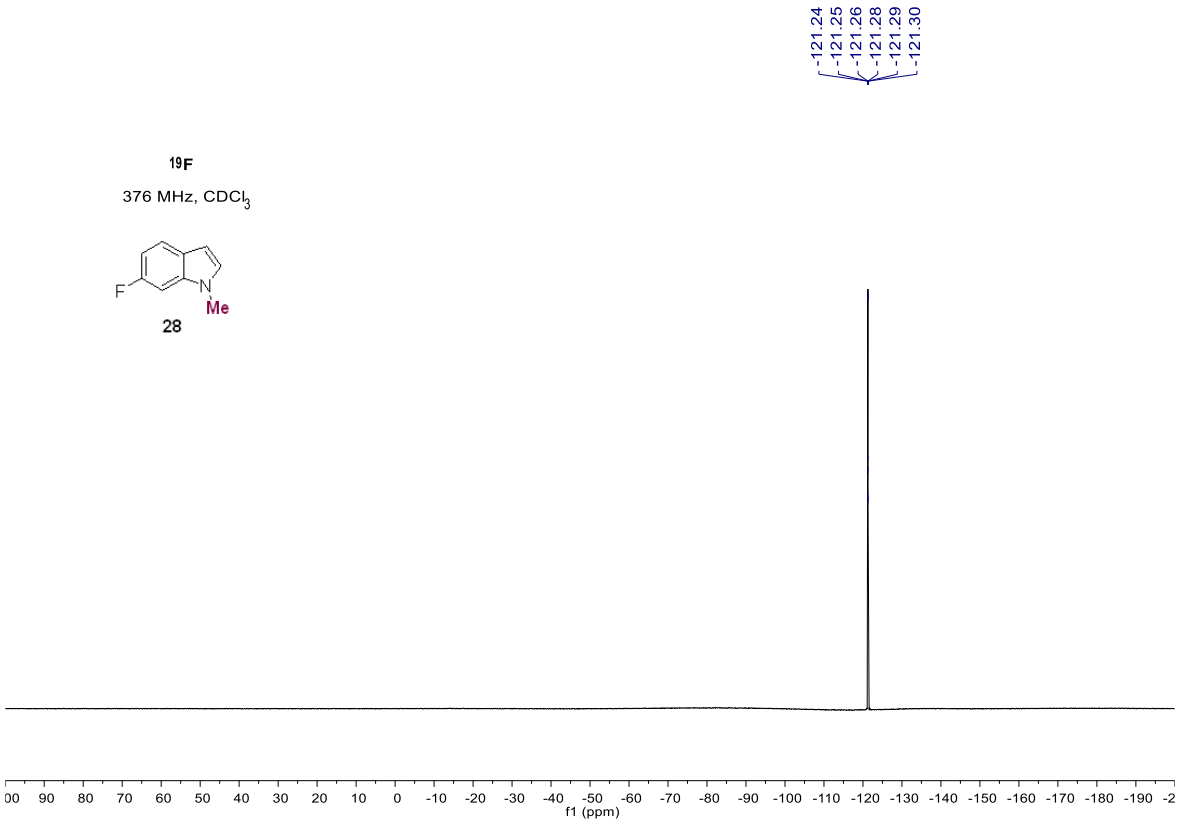
6-chloro-1-methyl-1*H*-indole (27)



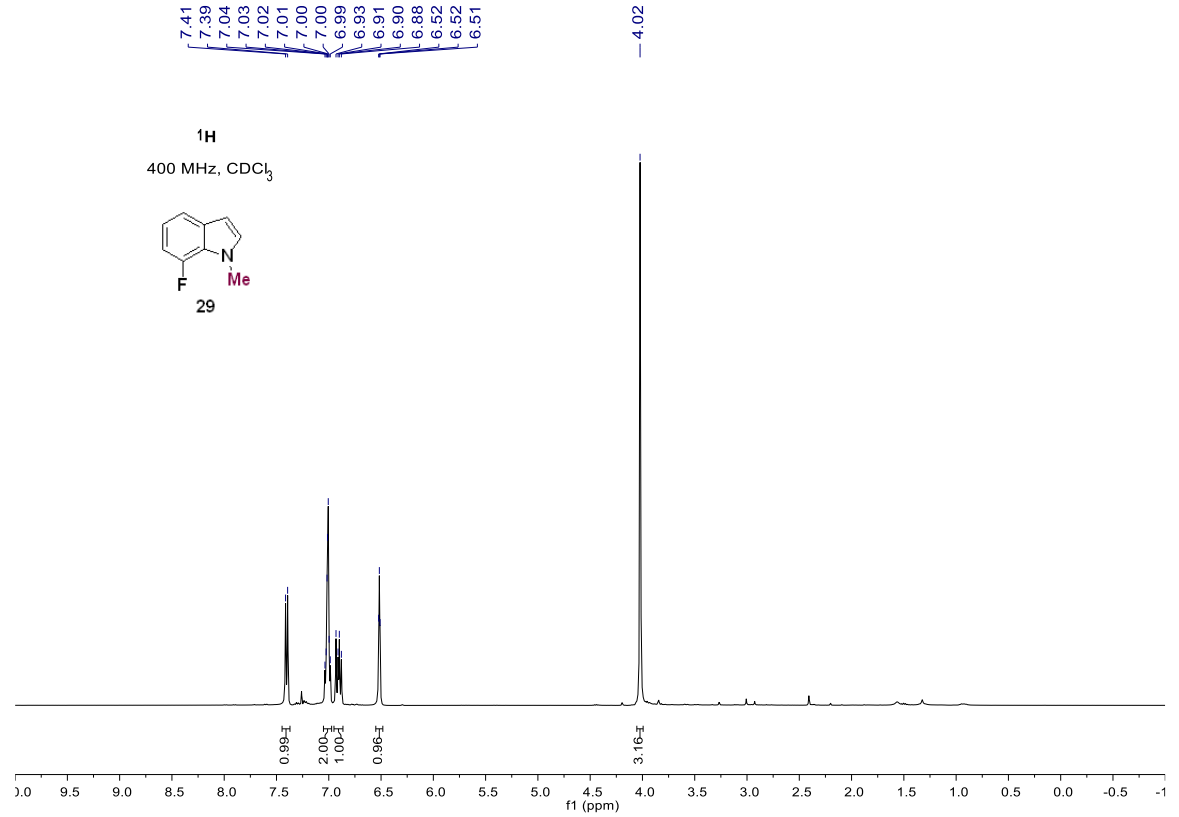


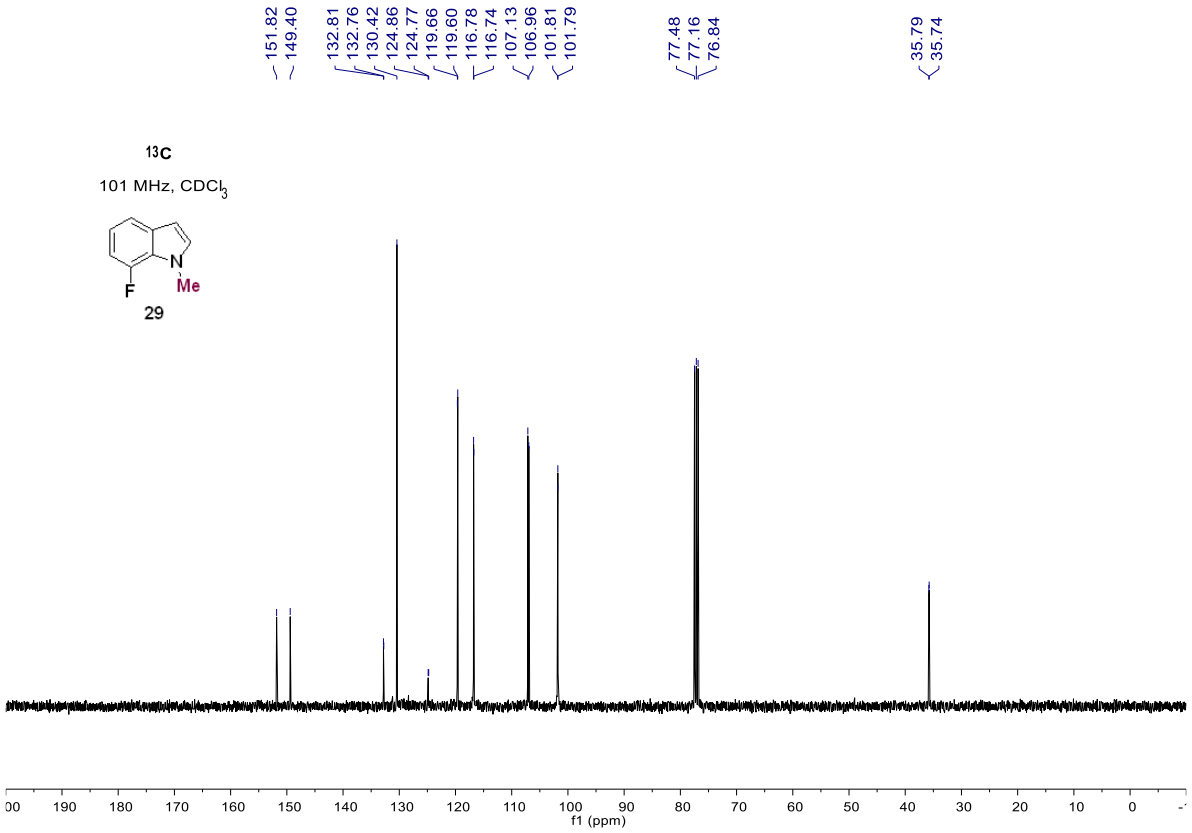
6-fluoro-1-methyl-1*H*-indole (28)

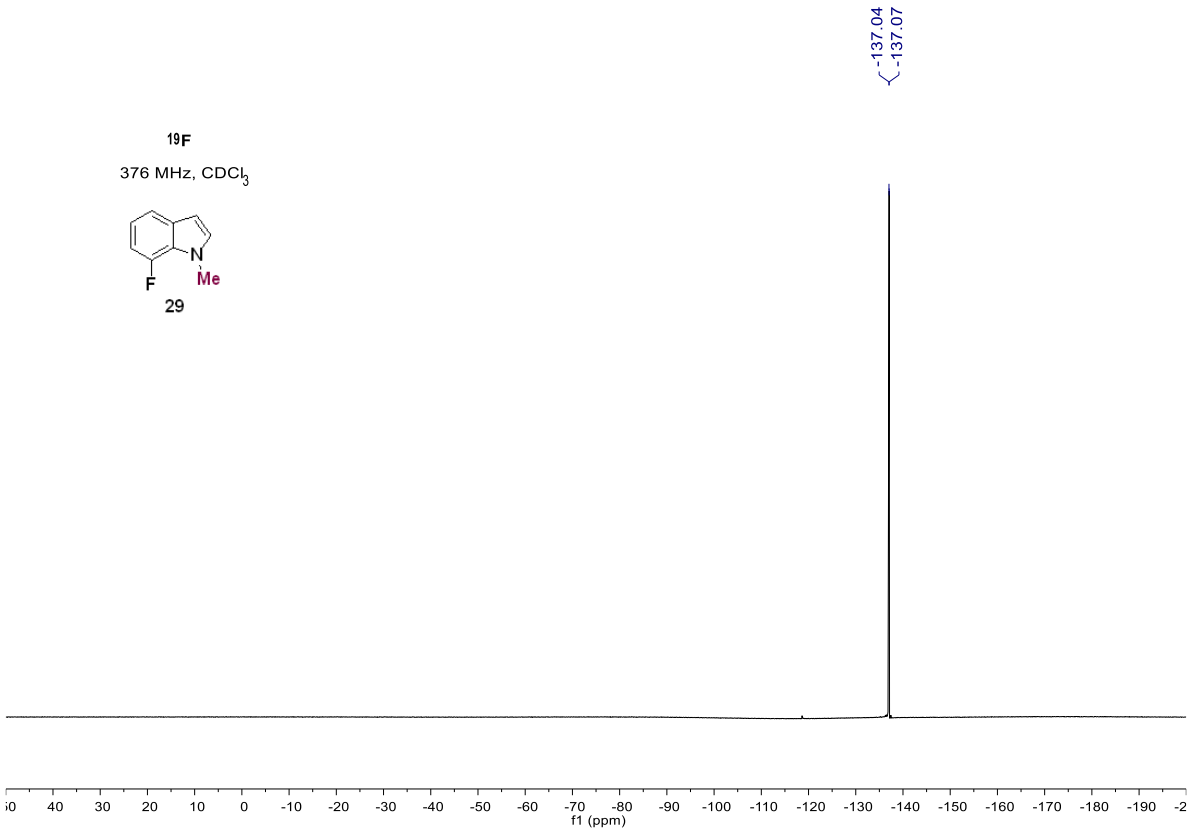




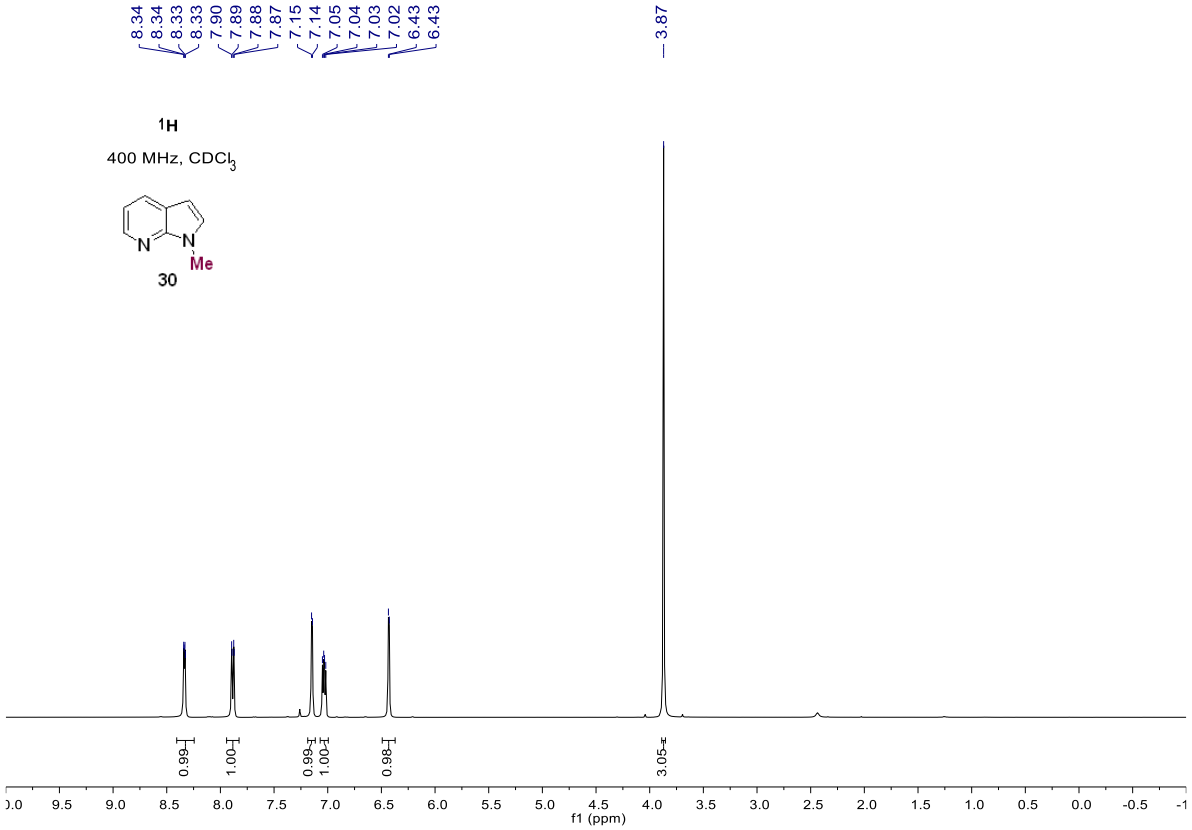
7-fluoro-1-methyl-1*H*-indole (29)

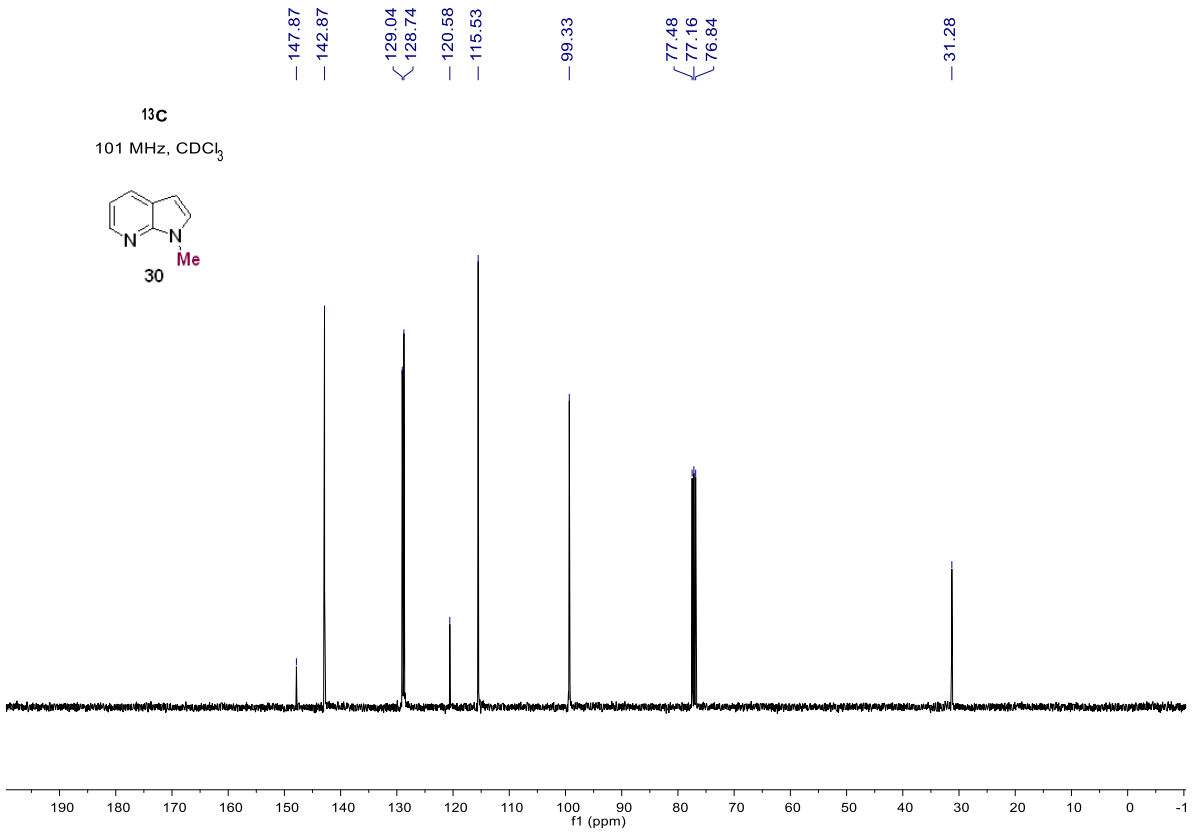



151.82
149.40
132.81
132.76
130.42
124.86
124.77
119.66
119.60
116.78
116.74
107.13
106.96
101.81
101.79
77.48
77.16
76.84
35.79
35.74
13C
101 MHz, CDCl3
N
Me
F
29
f1 (ppm)

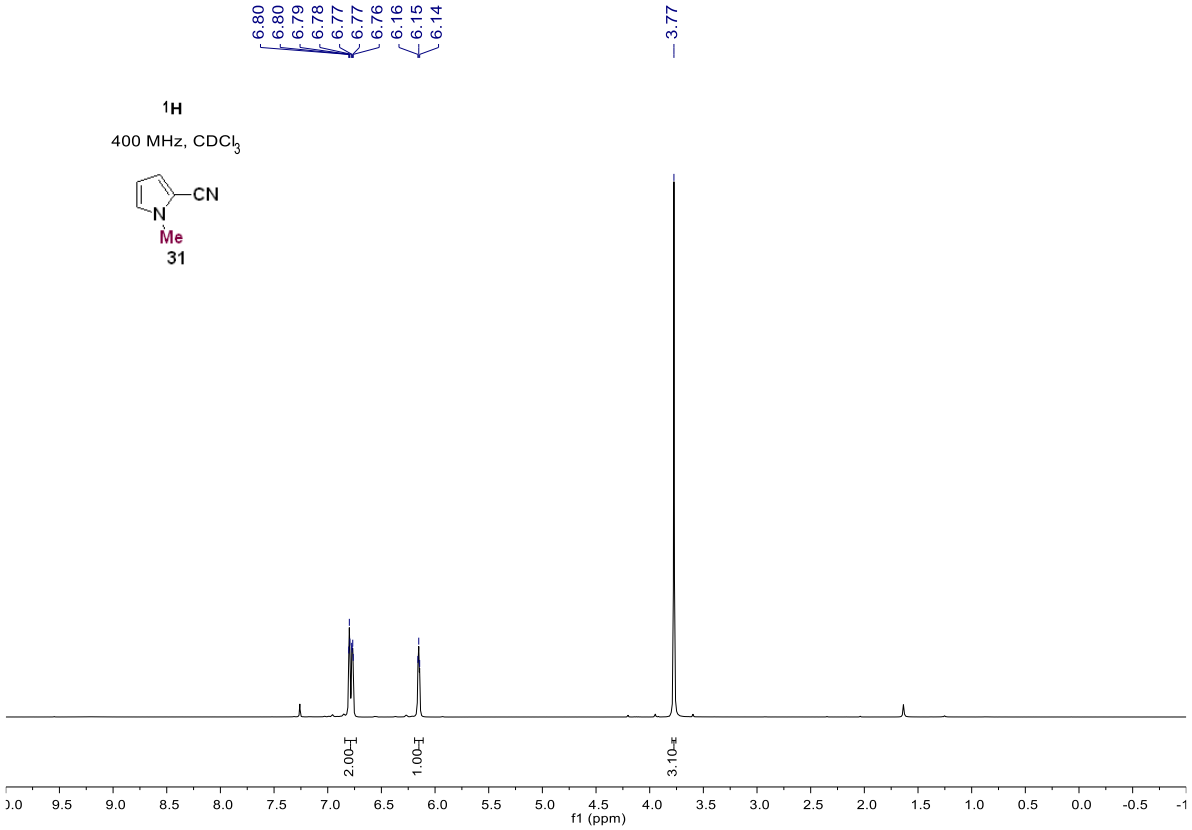

-137.04
-137.07
19F
376 MHz, CDCl3
N
Me
F
29
f1 (ppm)

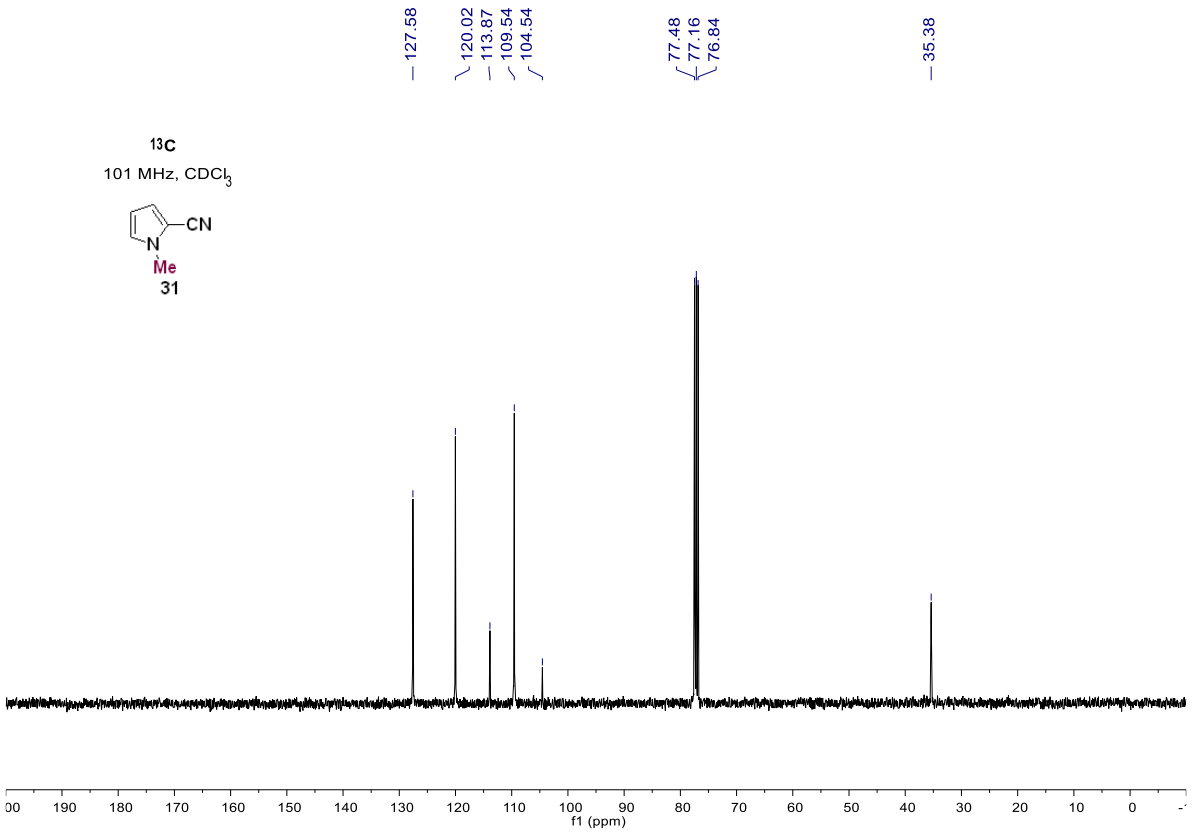
1-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (30)



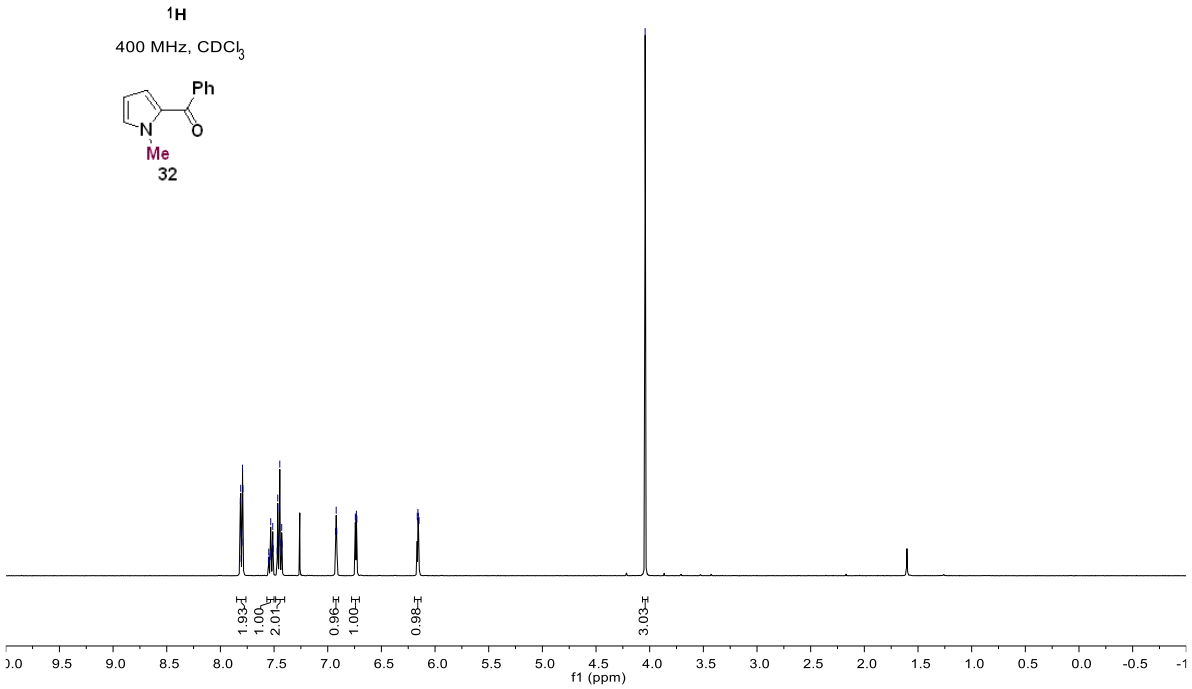


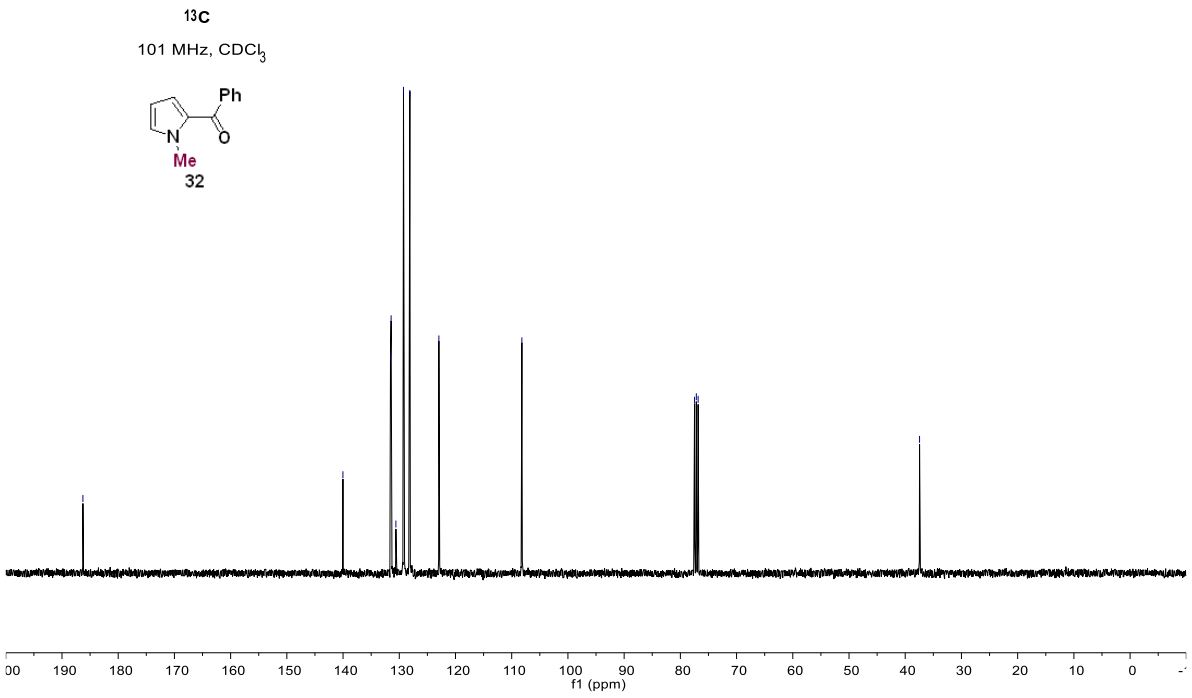
1-methyl-1*H*-pyrrole-2-carbonitrile (31)



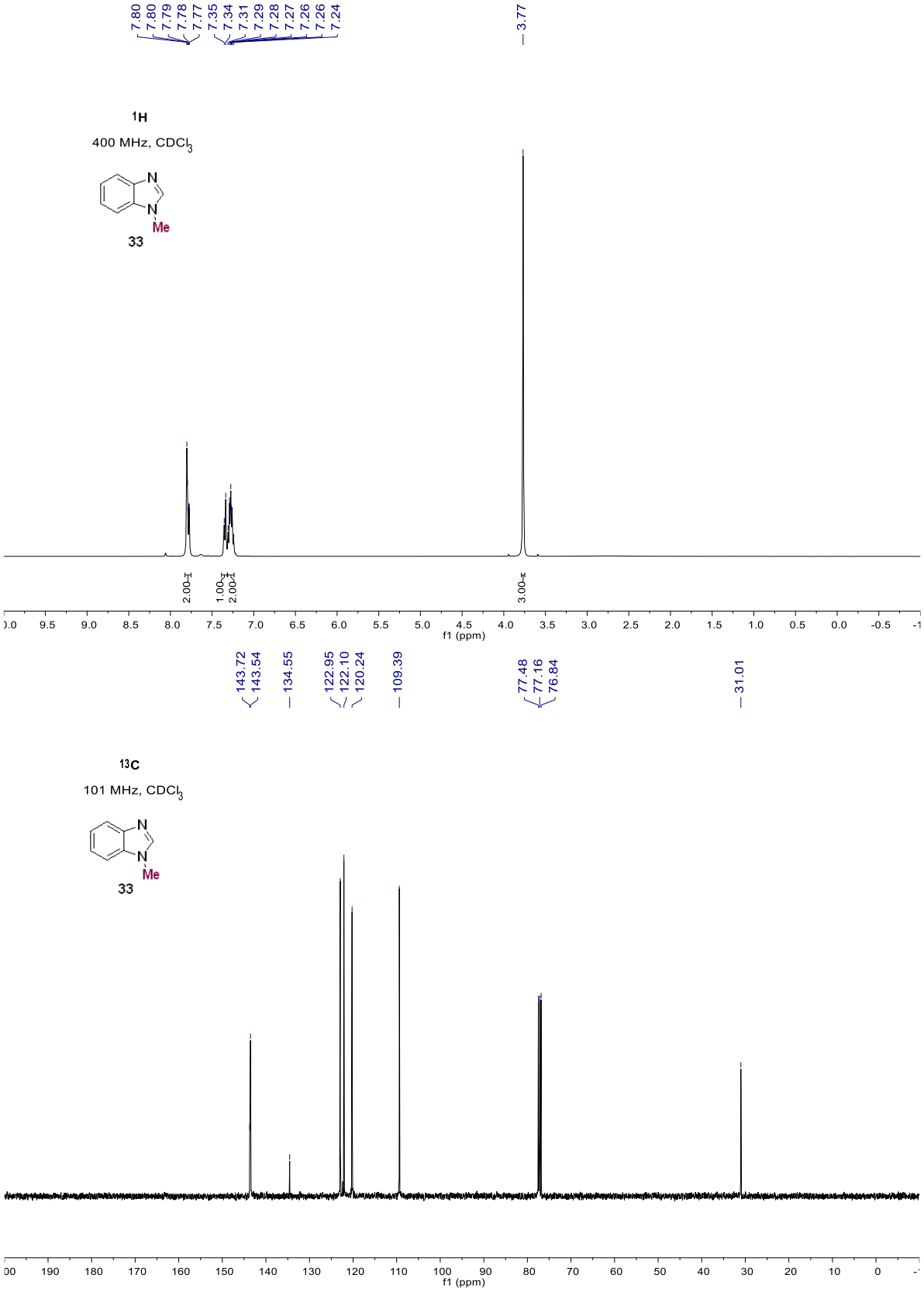


(1-methyl-1*H*-pyrrol-2-yl)(phenyl)methanone (32)

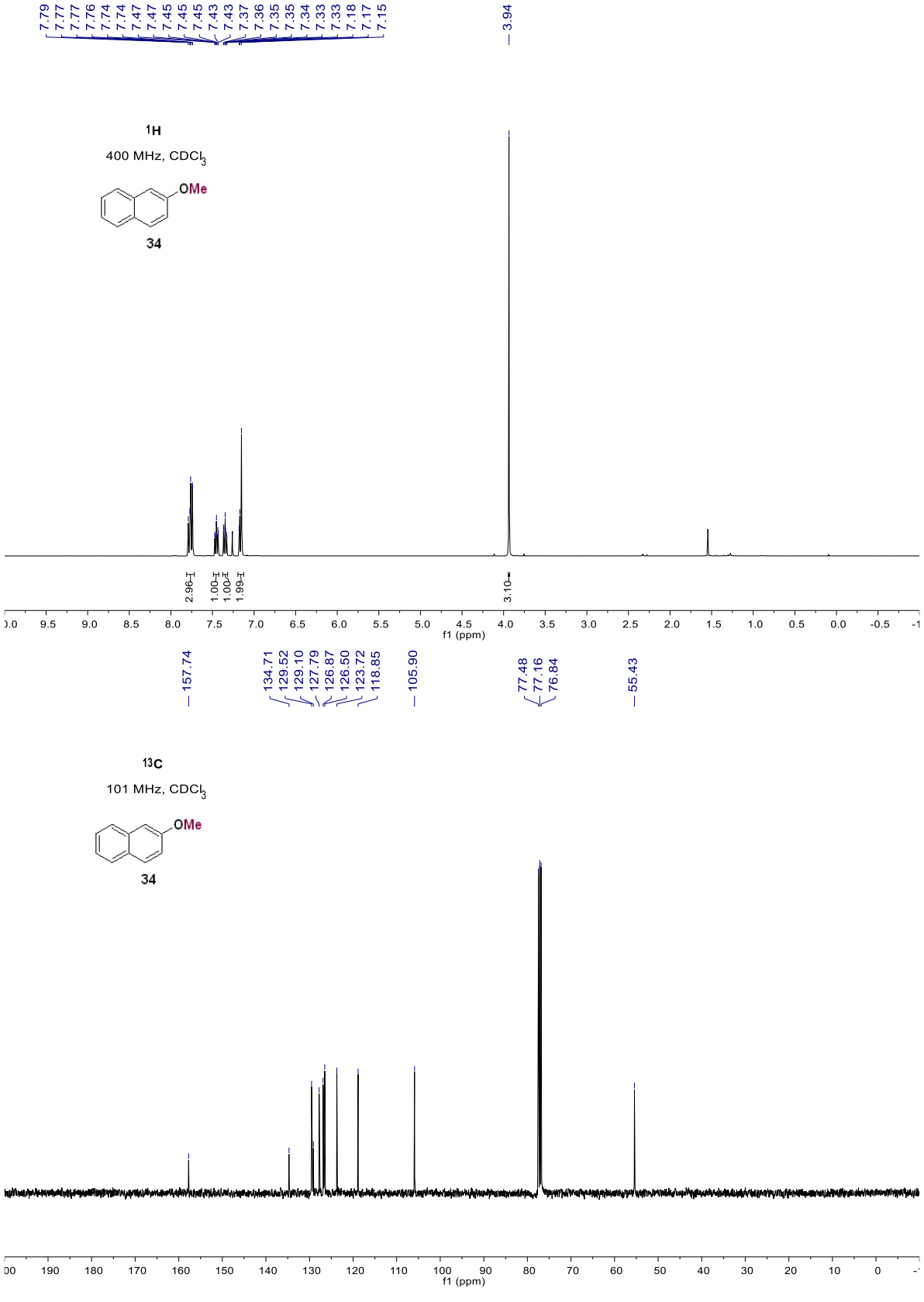




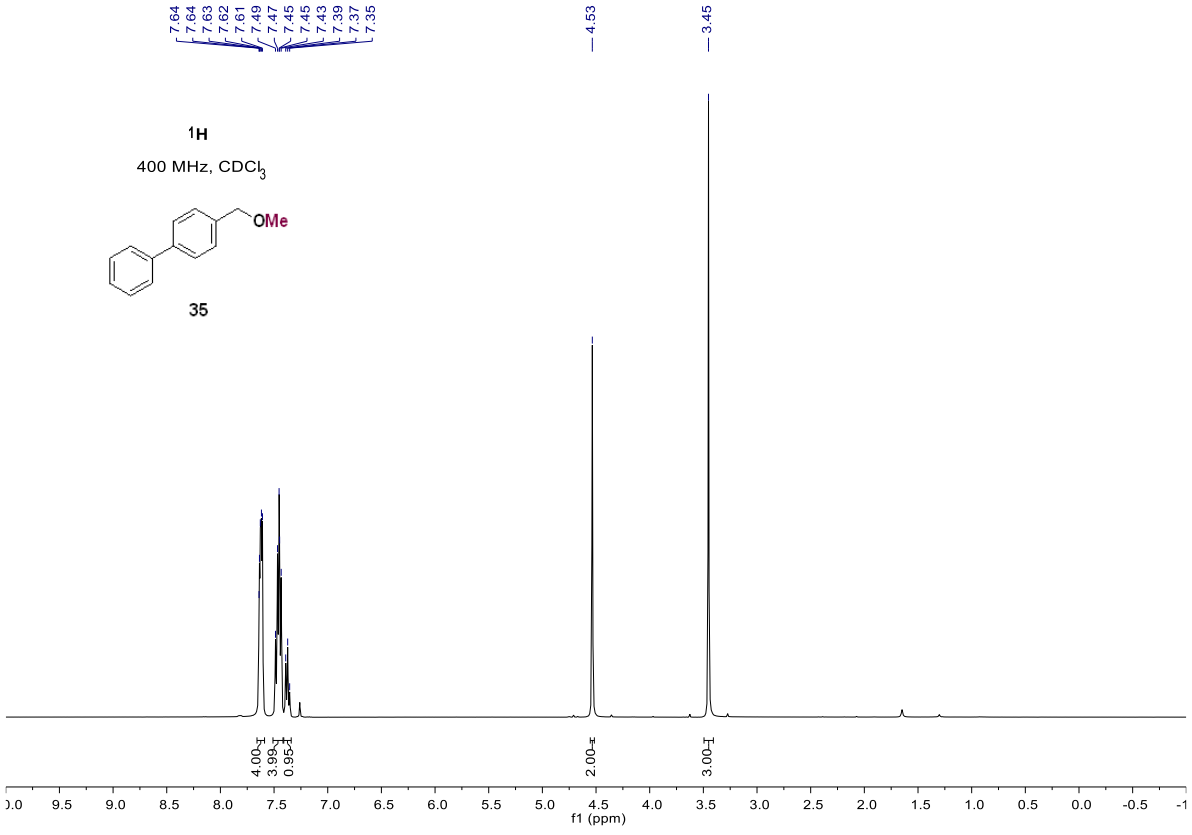
1-methyl-1*H*-benzo[*d*]imidazole (33)

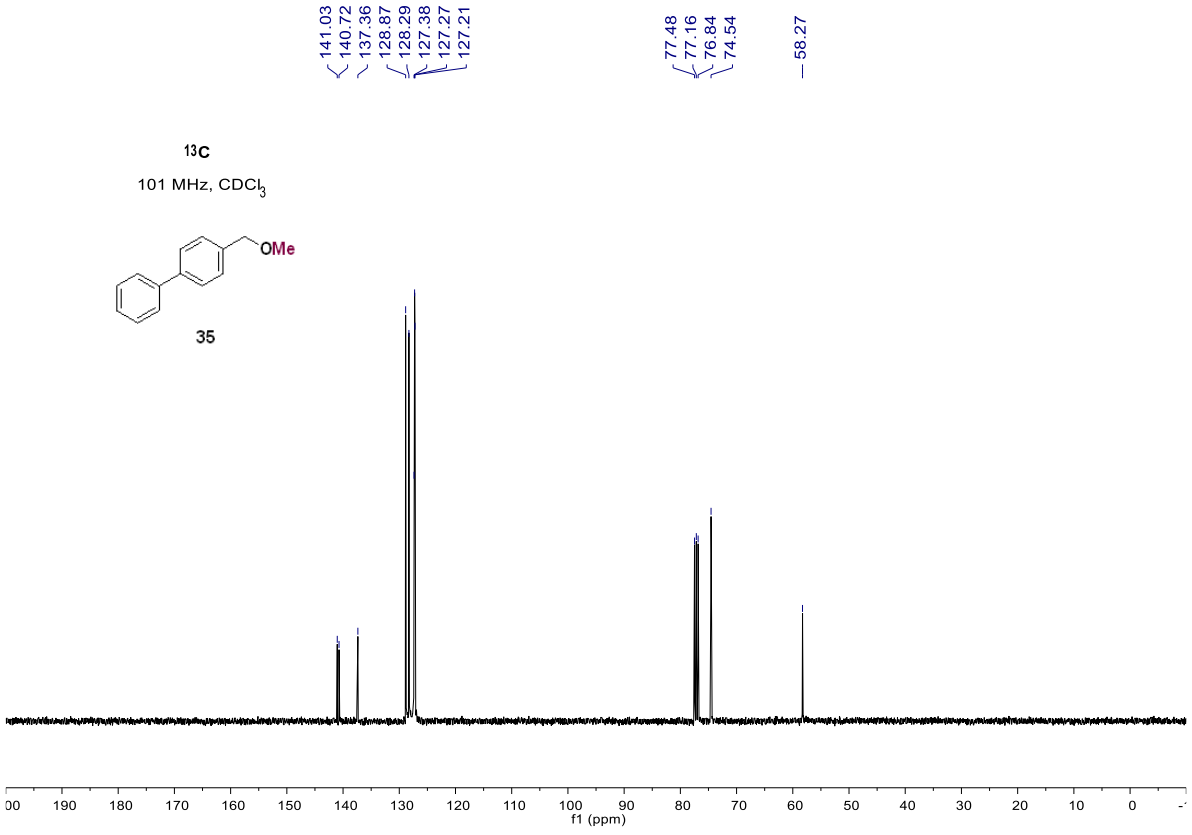


2-methoxynaphthalene (34)

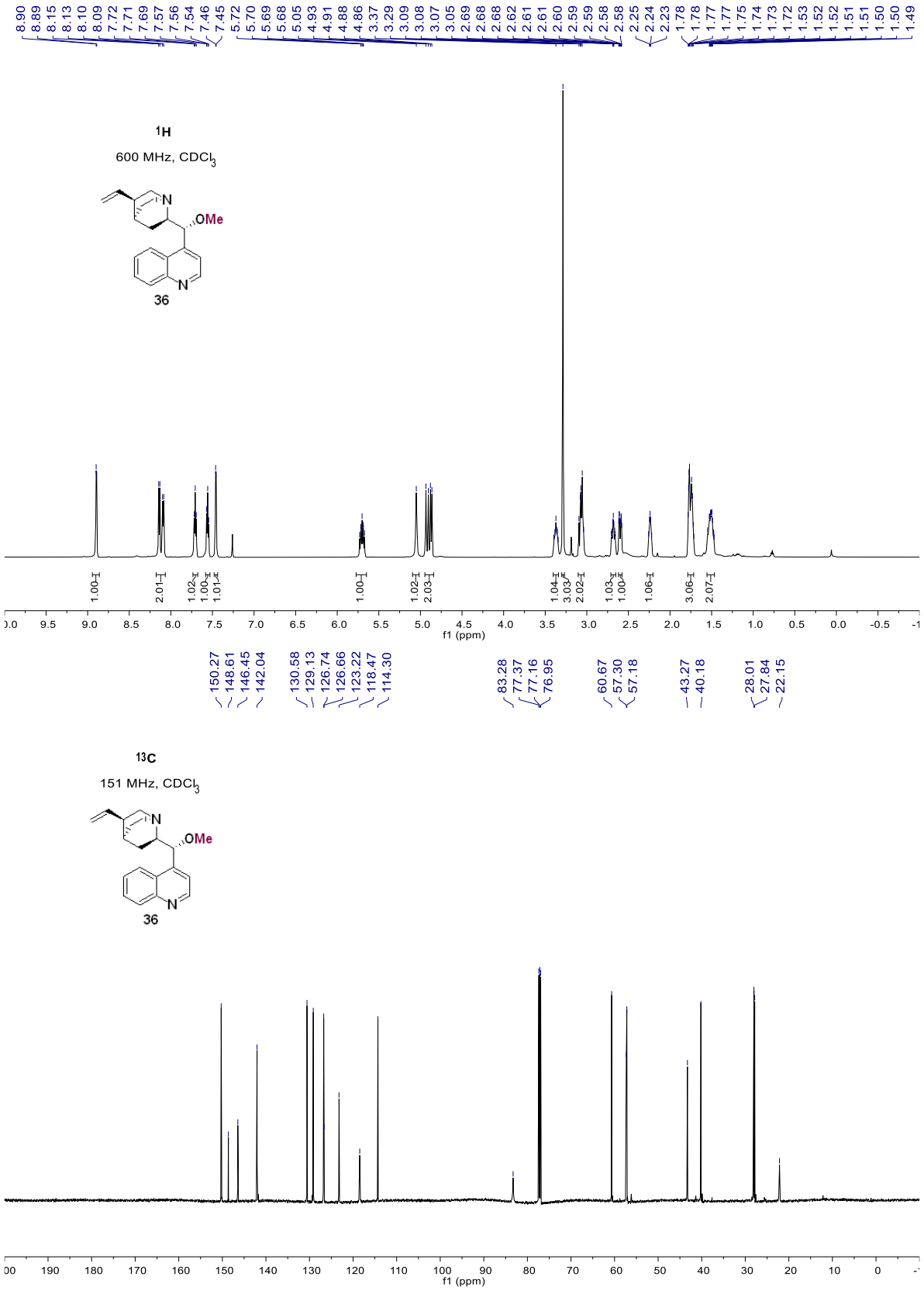


4-(methoxymethyl)-1,1'-biphenyl (35)

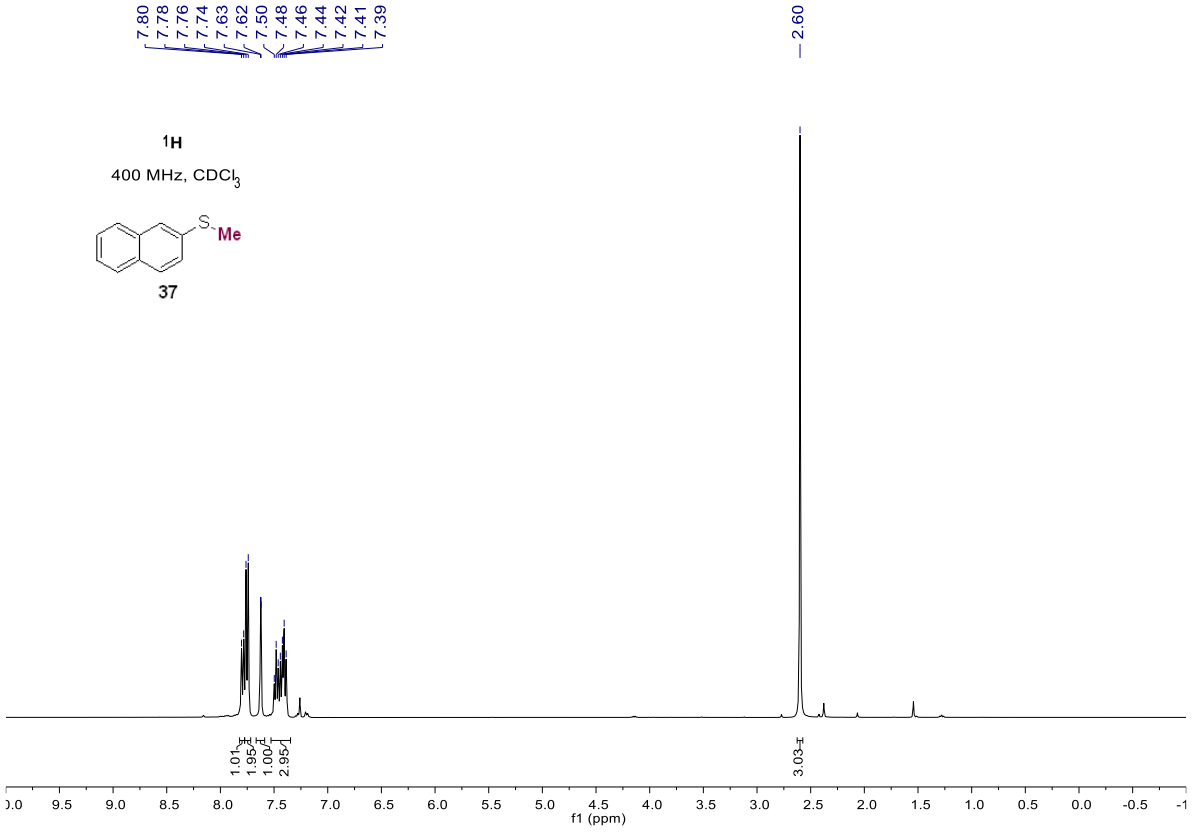


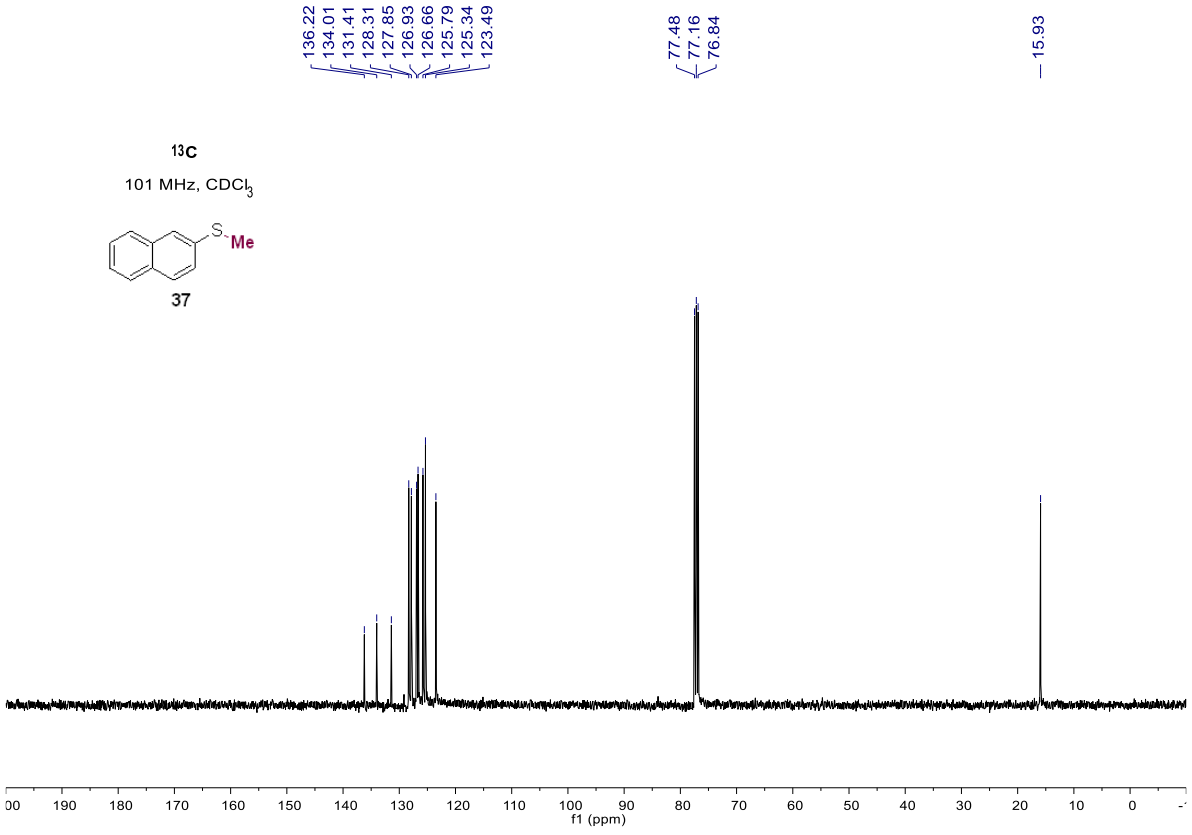


(1*S*,2*R*,4*S*,5*R*)-2-((*R*)-methoxy(quinolin-4-yl)methyl)-5-vinylquinuclidine (36)

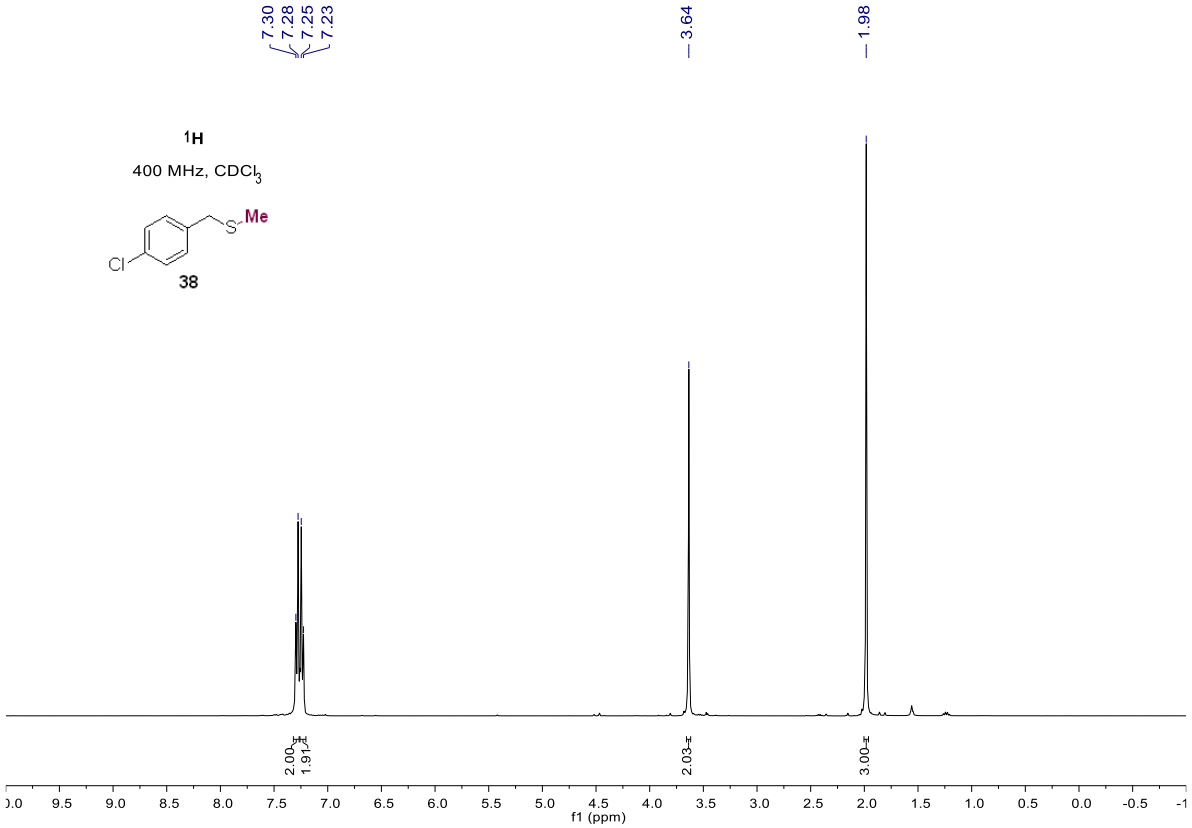


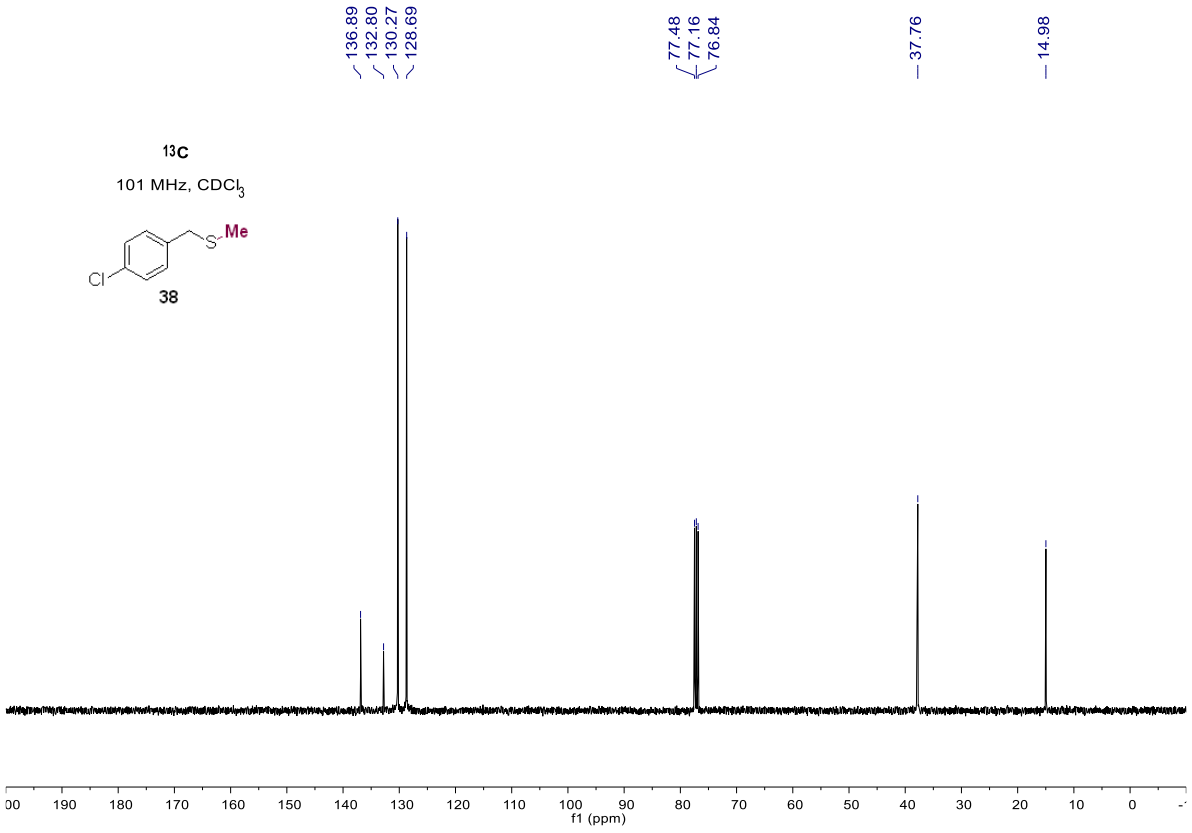
methyl(naphthalen-2-yl)sulfane (37)



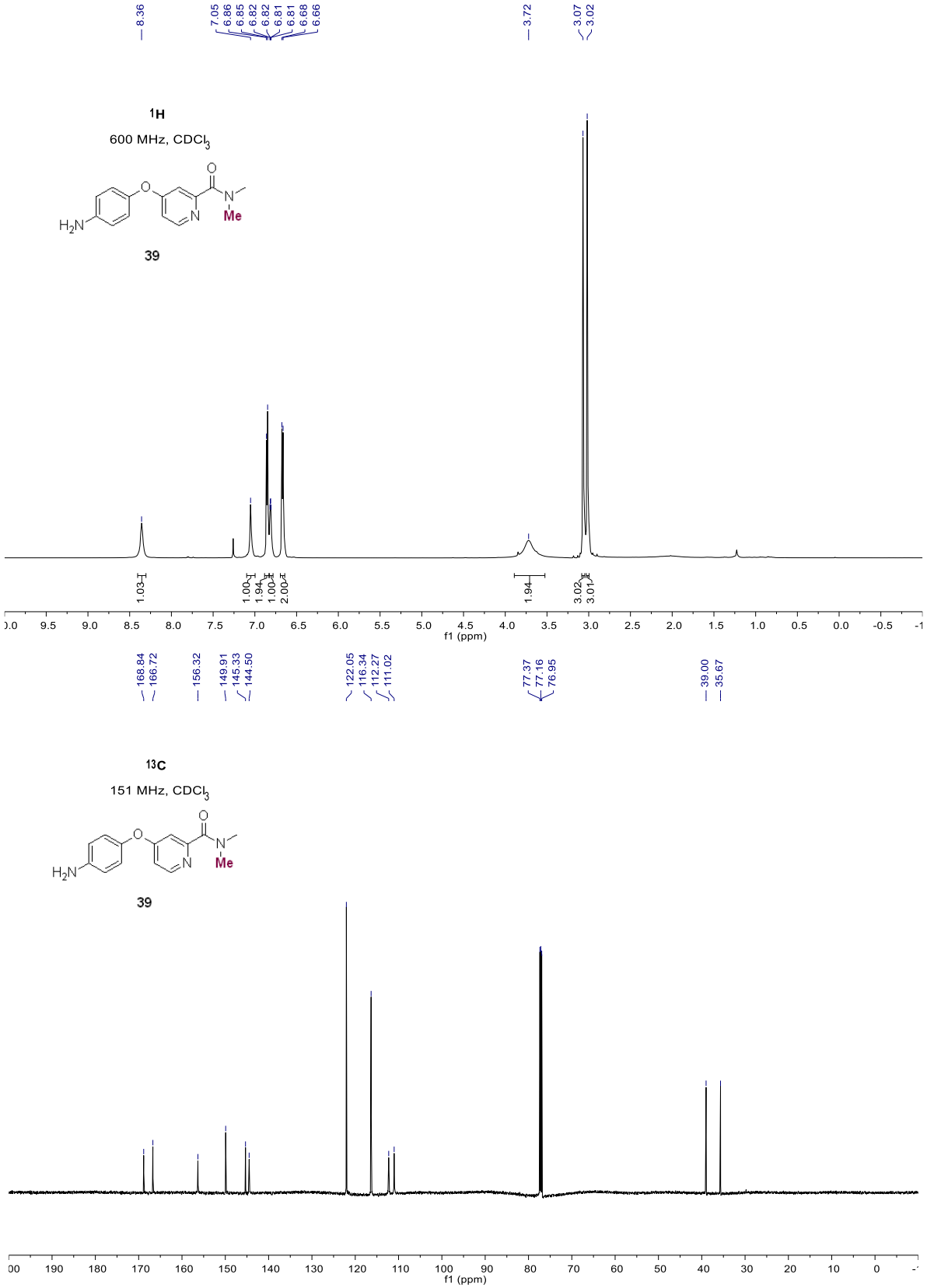


(4-chlorobenzyl)(methyl)sulfane (38)

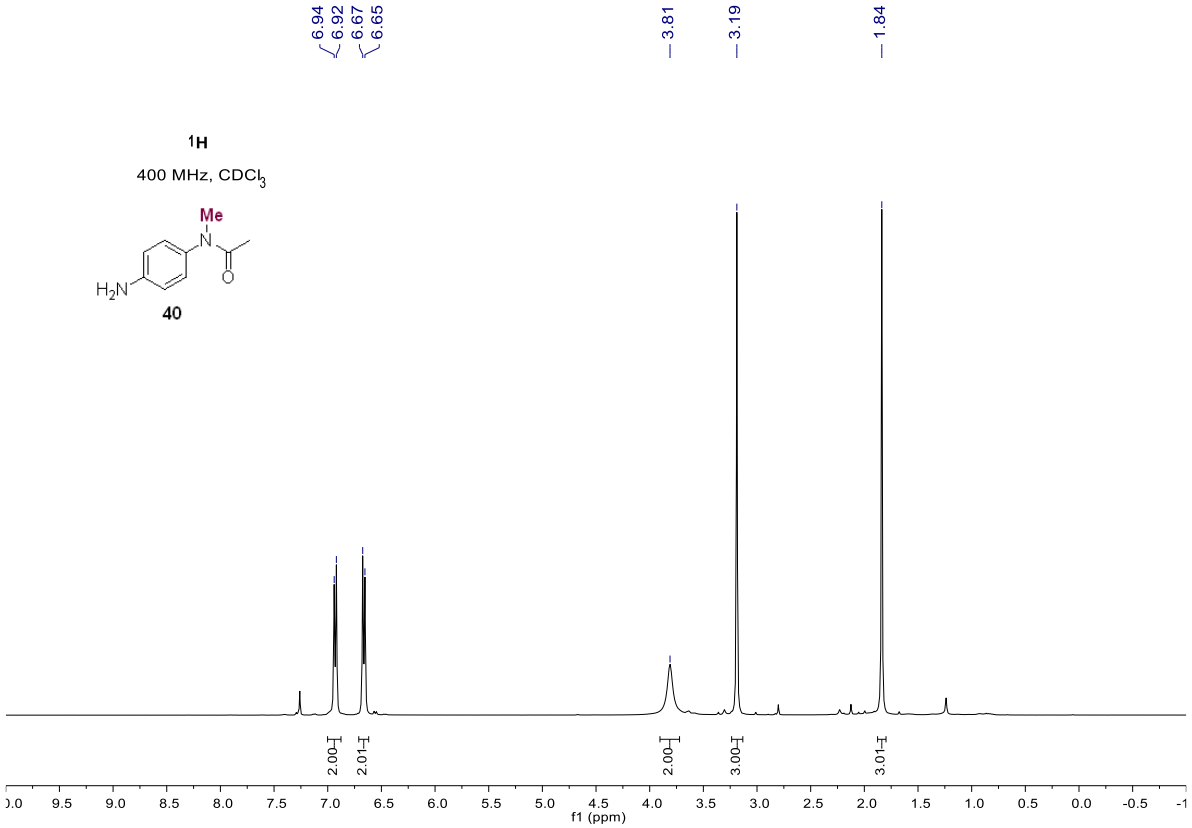


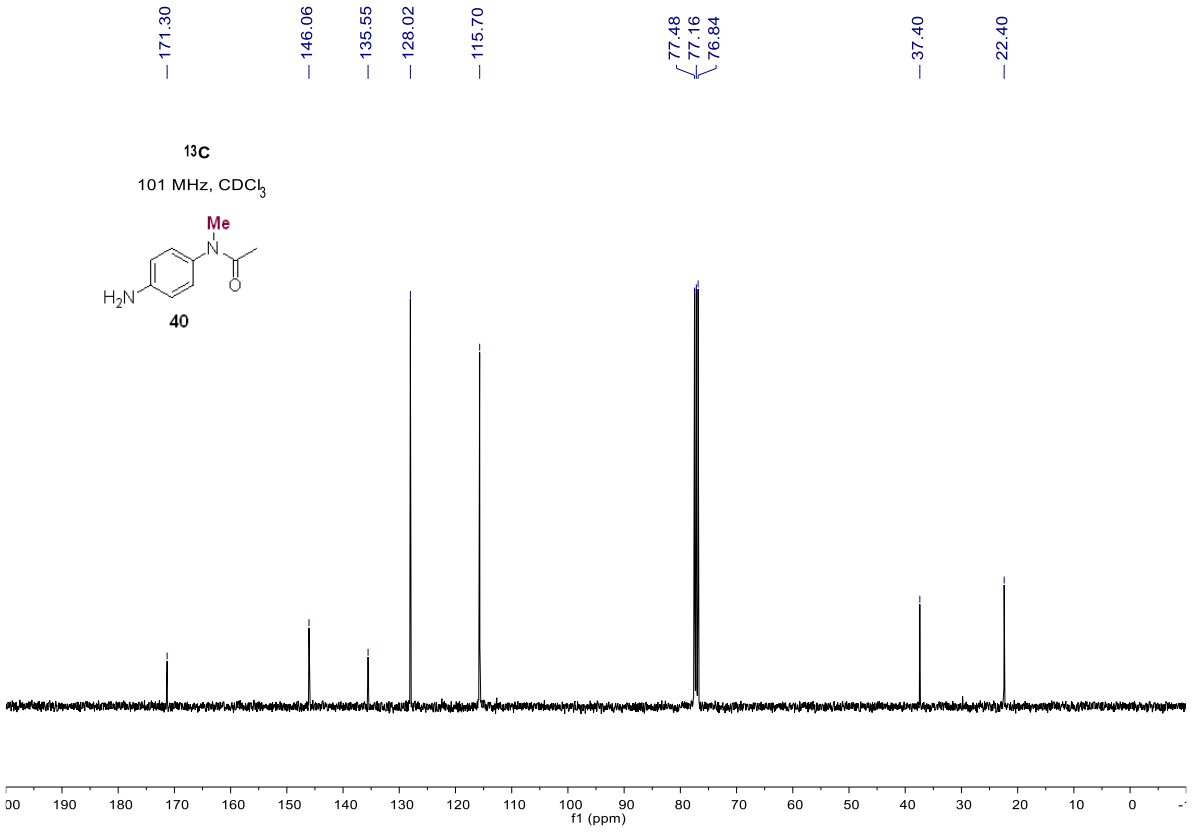


4-(4-aminophenoxy)-*N*,*N*-dimethylpicolinamide (39)

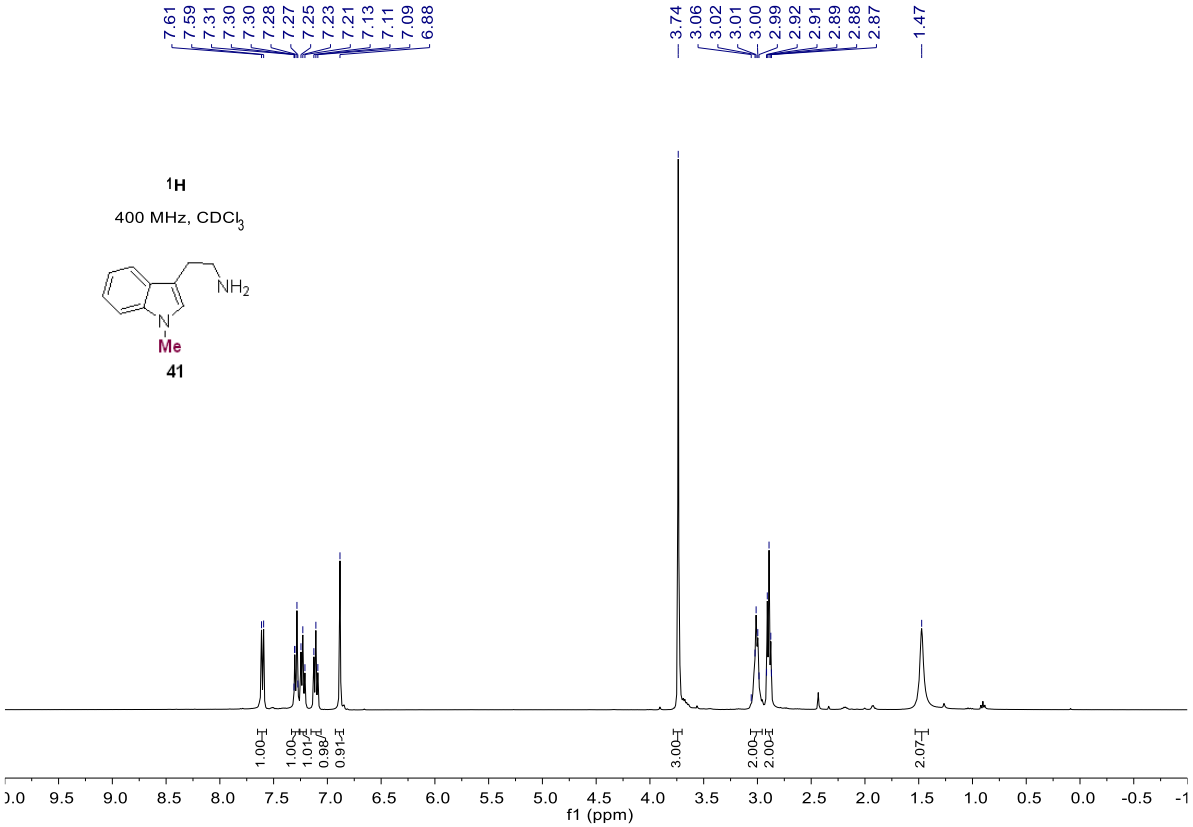


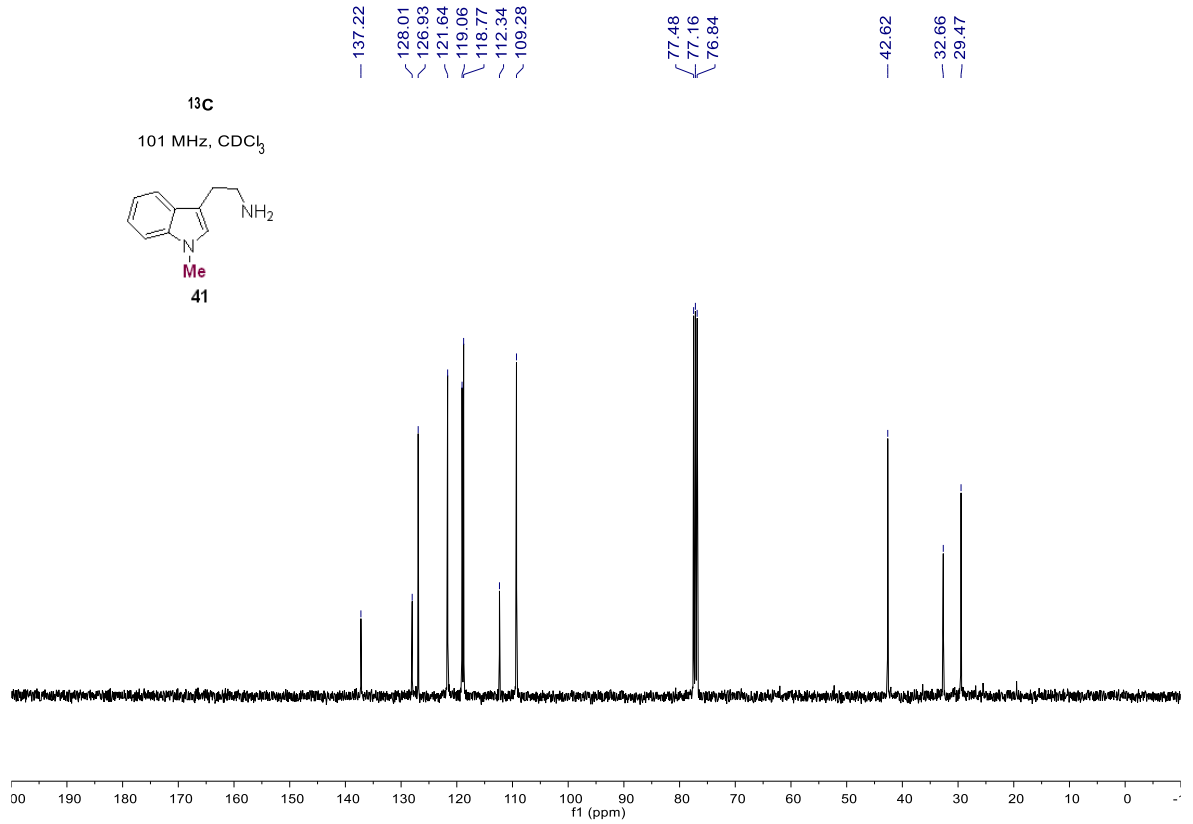
N-(4-aminophenyl)-*N*-methylacetamide (40)



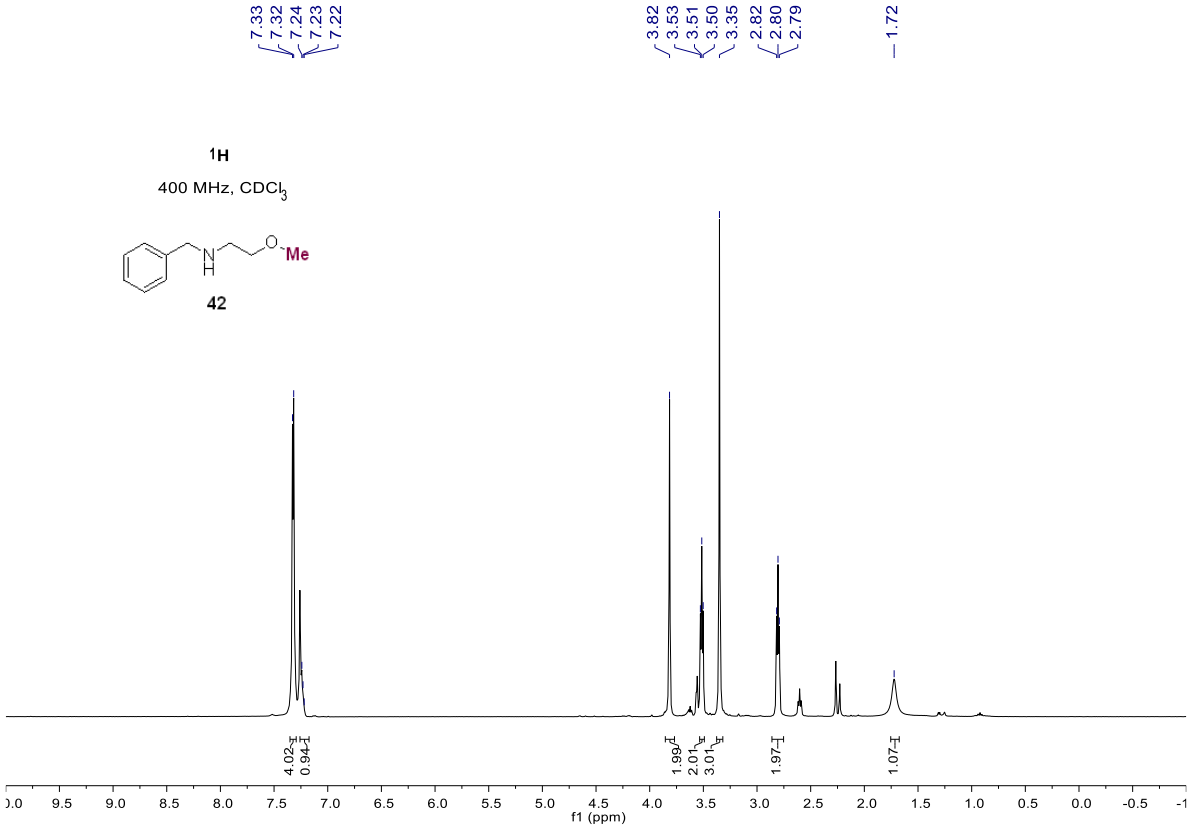


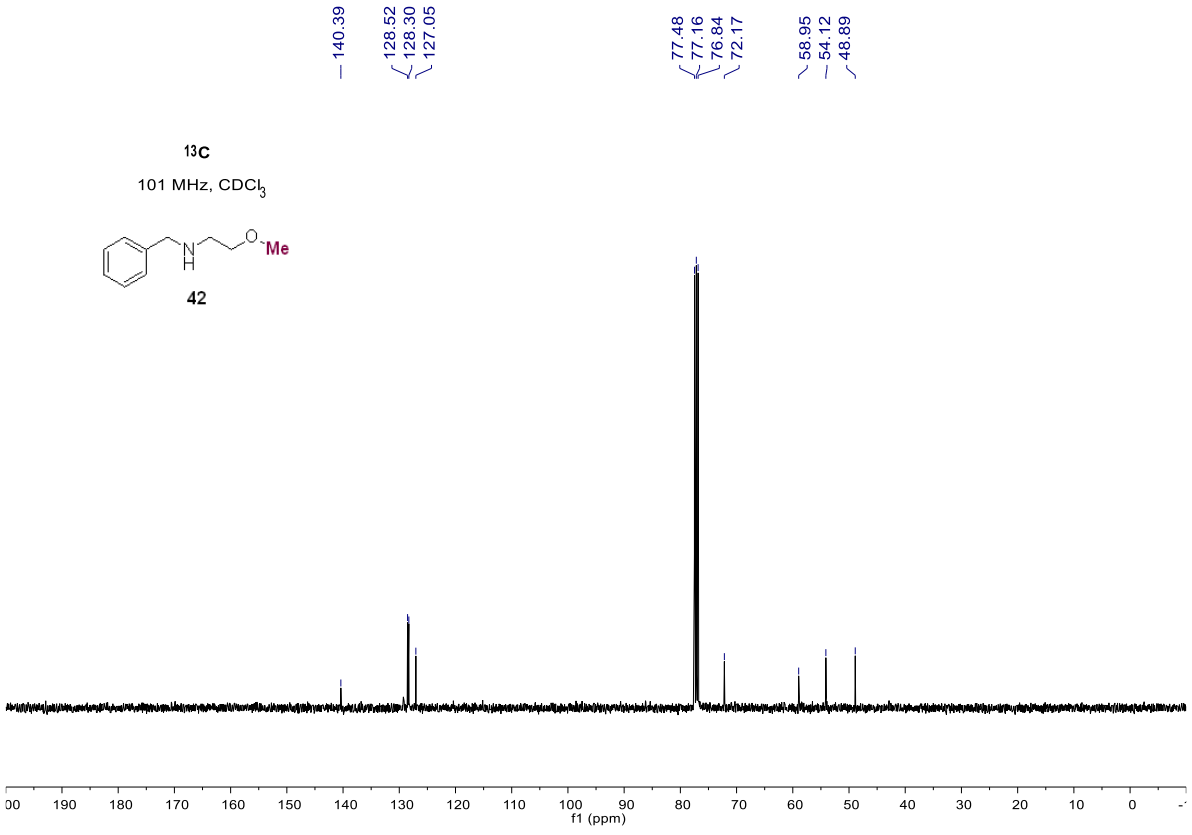
2-(1-methyl-1*H*-indol-3-yl)ethan-1-amine (41)



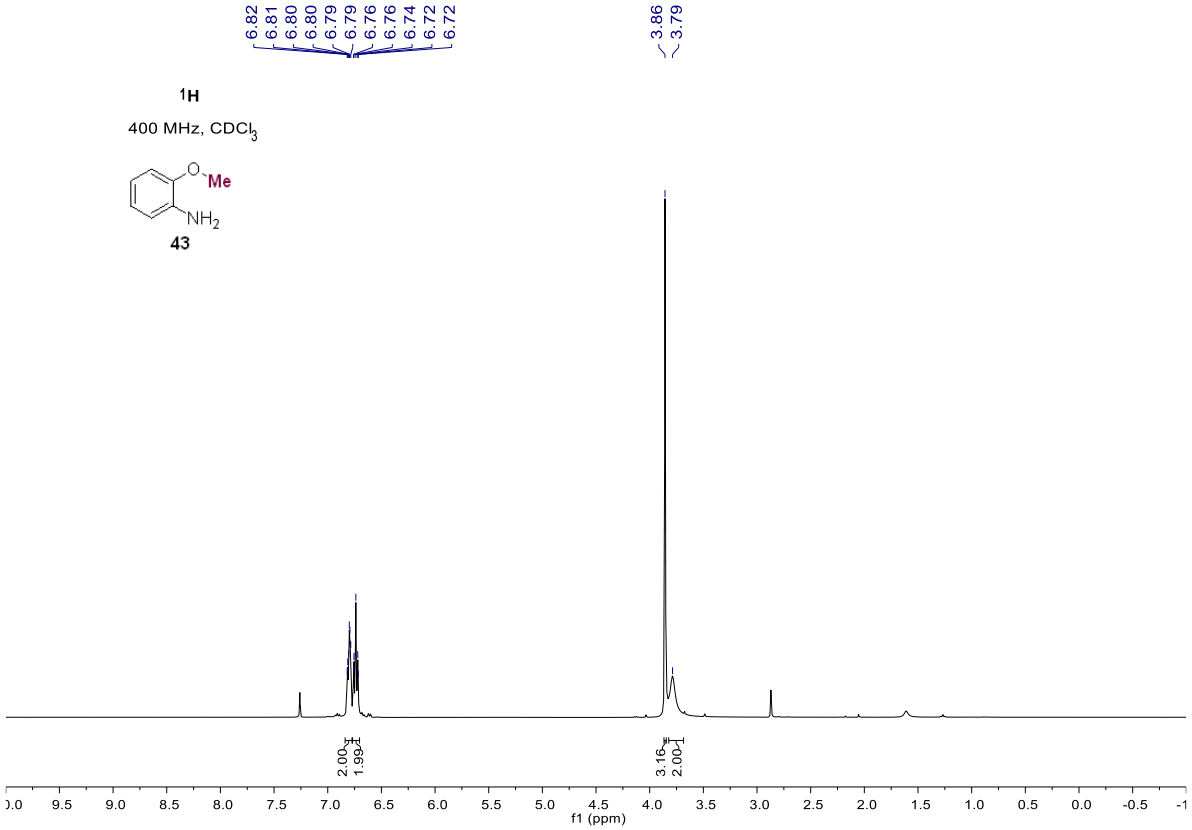


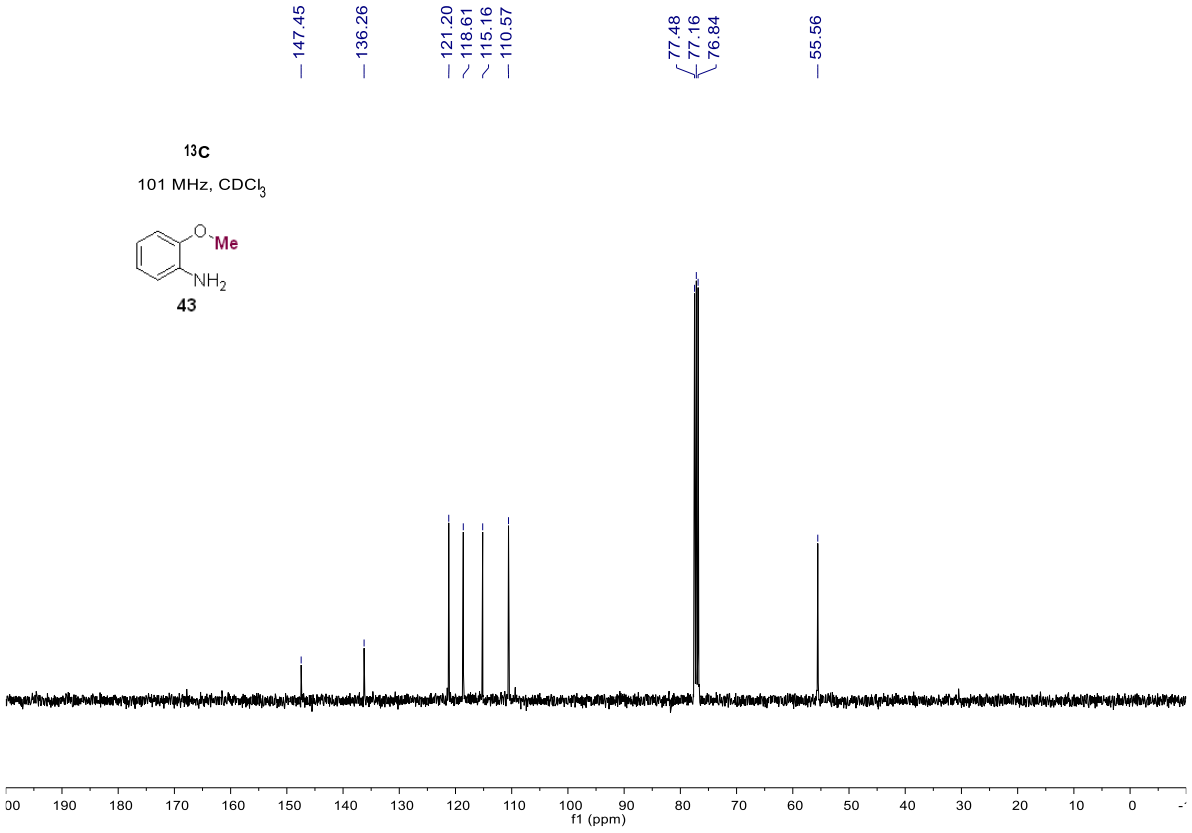
N-benzyl-2-methoxyethan-1-amine (42)



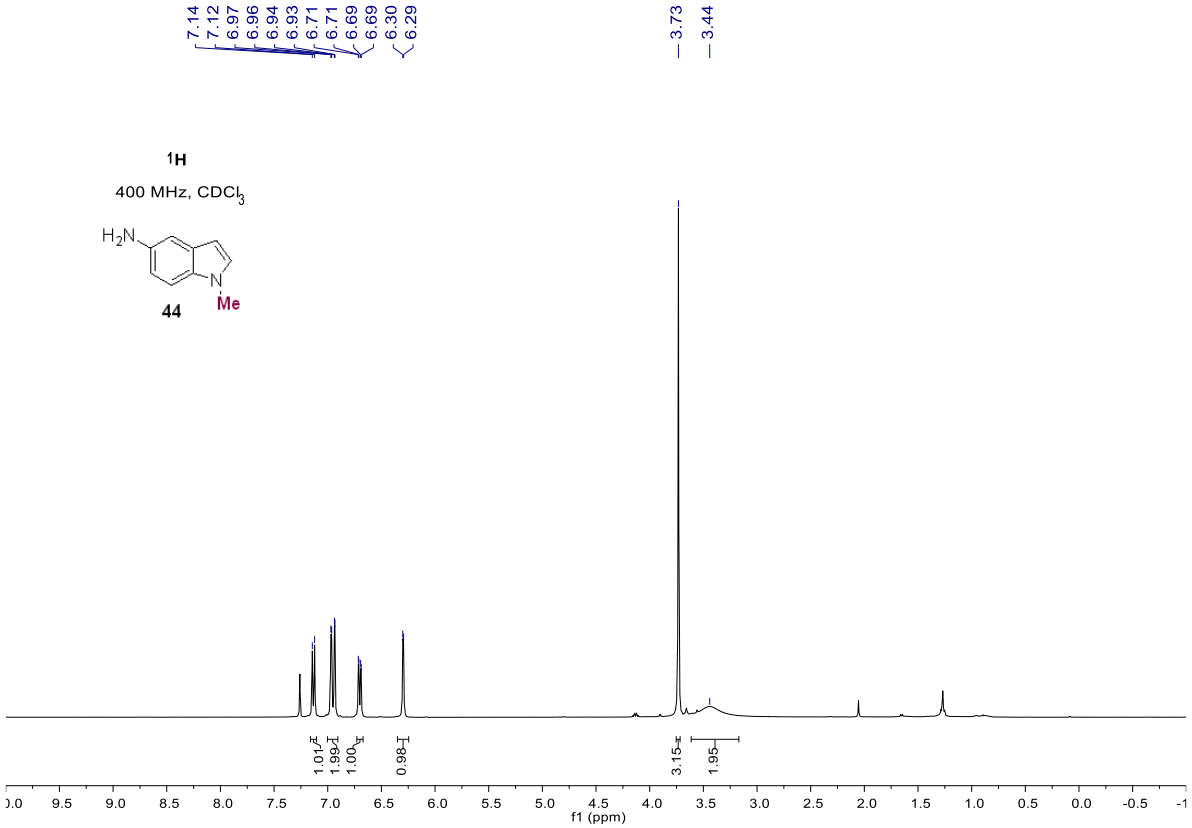


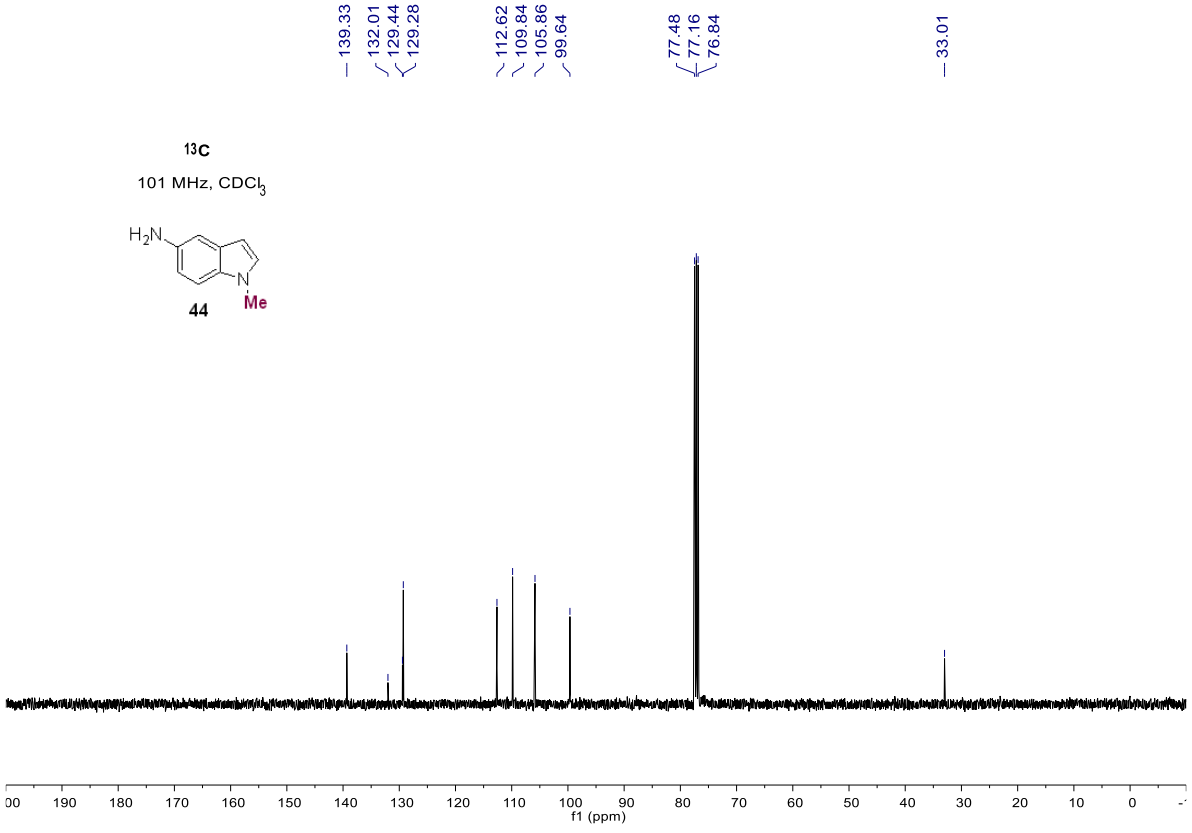
2-methoxyaniline (43)





1-methyl-1*H*-indol-5-amine (44)





7. References

(1) Drillaud, N.; Banaszak-Leonard, E.; Pezron, I.; Len, C. *J. Org. Chem.* **2012**, *77*, 9553.

(2) Cheng, H. C.; Hou, W. J.; Li, Z. W.; Liu, M. Y.; Guan, B. T. *Chem. Commun.* **2015**, *51*, 17596.

(3) Xia, Q.; Liu, X.; Zhang, Y.; Chen, C.; Chen, W. *Org. Lett.* **2013**, *15*, 3326.

(4) Iranpoor, N.; Panahi, F.; Roozbin, F.; Erfan, S.; Rahimi, S. *Eur. J. Org. Chem.* **2016**, *2016*, 1781.

(5) Xu, K.; Hu, Y.; Zhang, S.; Zha, Z.; Wang, Z. *Chem. Eur. J.* **2012**, *18*, 9793.

(6) Ren, W.; Yamane, M. *J. Org. Chem.* **2010**, *75*, 8410.

(7) Racine, E.; Monnier, F.; Vors, J. P.; Taillefer, M. *Org. Lett.* **2011**, *13*, 2818.

(8) Adachi, S.; Onozuka, M.; Yoshida, Y.; Ide, M.; Saikawa, Y.; Nakata, M. *Org. Lett.* **2014**, *16*, 358.

(9) Yang, S.; Li, P.; Wang, Z.; Wang, L. *Org. Lett.* **2017**, *19*, 3386.

(10) Abraham, R. J.; Griffiths, L.; Perez, M. *Magn. Reson. Chem.* **2013**, *51*, 143.

(11) Sweeney, J. B.; Ball, A. K.; Lawrence, P. A.; Sinclair, M. C.; Smith, L. J. *Angew. Chem. Int. Ed.* **2018**, *57*, 10202.

(12) C. Goosen; T. J. Laing; J. d. Plessis; T. C. Goosen; Flynn, G. L. *Pharm. Res.* **2002**, *19*, 13.

(13) Su, Y. M.; Hou, Y.; Yin, F.; Xu, Y. M.; Li, Y.; Zheng, X.; Wang, X. S. *Org. Lett.* **2014**, *16*, 2958.

(14) Pena-Lopez, M.; Neumann, H.; Beller, M. *Chem. Eur. J.* **2014**, *20*, 1818.

(15) Murar, C. E.; Thuaud, F.; Bode, J. W. *J. Am. Chem. Soc.* **2014**, *136*, 18140.

(16) Rajagopal, B.; Chou, C. H.; Chung, C. C.; Lin, P. C. *Org. Lett.* **2014**, *16*, 3752.

(17) Li, B.; Wendlandt, A. E.; Stahl, S. S. *Org. Lett.* **2019**, *21*, 1176.

(18) Caramenti, P.; Nandi, R. K.; Waser, J. *Chem. Eur. J.* **2018**, *24*, 10049.

(19) Hong, X.; Tan, Q.; Liu, B.; Xu, B. *Angew. Chem. Int. Ed.* **2017**, *56*, 3961.

(20) Al-Huniti, M. H.; Rivera-Chavez, J.; Colon, K. L.; Stanley, J. L.; Burdette, J. E.; Pearce, C. J.; Oberlies, N. H.; Croatt, M. P. *Org. Lett.* **2018**, *20*, 6046.

(21) Wakeham, R. J.; Taylor, J. E.; Bull, S. D.; Morris, J. A.; Williams, J. M. *Org. Lett.* **2013**, *15*, 702.

(22) Zhang, Z.; Sun, Q.; Xia, C.; Sun, W. *Org. Lett.* **2016**, *18*, 6316.

(23) Dash, P.; Janni, M.; Peruncheralathan, S. *Eur. J. Org. Chem.* **2012**, *2012*, 4914.

(24) Guan, B. T.; Xiang, S. K.; Wang, B. Q.; Sun, Z. P.; Wang, Y.; Zhao, K. Q.; Shi, Z. J. *J. Am. Chem. Soc.* **2008**, *130*, 3268.

(25) Busygin, I.; Nieminen, V.; Taskinen, A.; Sinkkonen, J.; Toukoniitty, E.; Sillanpaa, R.; Murzin, D. Y.; Leino, R. *J. Org. Chem.* **2008**, *73*, 6559.

(26) Uetake, Y.; Niwa, T.; Hosoya, T. *Org. Lett.* **2016**, *18*, 2758.

(27) Olah, G. A.; Wang, Q.; Neyer, G. *Synthesis* **1994**, 276.

(28) Stockwell, B. R.; Dixon, S. J.; Skouta, R. **2015**, WO201551149A1. ^{1}H spectrum only.

(29) Wang, X.; Xu, Y.; Mo, F.; Ji, G.; Qiu, D.; Feng, J.; Ye, Y.; Zhang, S.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2013**, *135*, 10330.

(30) Wesche, F.; Adihou, H.; Kaiser, A.; Wurglics, M.; Schubert-Zsilavecz, M.; Kaiser, M.; Bode, H. B. *J. Med. Chem.* **2018**, *61*, 3930.

(31) Cheng, C.; Brookhart, M. *J. Am. Chem. Soc.* **2012**, *134*, 11304.

(32) MacNair, A. J.; Tran, M. M.; Nelson, J. E.; Sloan, G. U.; Ironmonger, A.; Thomas, S. P. *Org. Biomol. Chem.* **2014**, *12*, 5082.

(33) Laufer, S.; Lehmann, F. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 1461.

(34) Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H.

Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G.A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2013.

(35) CYLview, 1.0b; C. Y. Legault, Université de Sherbrooke, 2009 (http://www.cylview.org).