Supporting Information

Copper Catalyzed and Iodide Promoted Aerobic C-C Bond Cleavage/C-N Bond Formation toward the Synthesis of Amides

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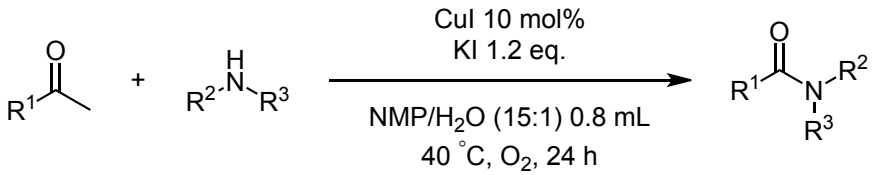
General information

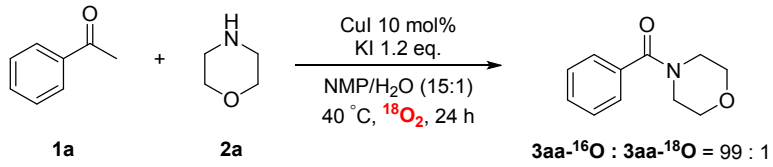
The reactions were conducted under oxygen atmosphere with a balloon fitted on a Schlenk tube. All glassware was oven dried at 110 °C for hours and cooled down under vacuum. NMP was purified by distillation with calcium hydride. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Imines were prepared following literature procedures. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 100-200 mesh silica gel in petroleum (bp. 60-90 °C). GC-MS spectra were recorded on a Varian GC-MS 3900-2100T. NMR spectra were recorded on a Bruker Advance III spectrometers at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR). Tetramethylsilane was used as an internal standard). All ^{1}H NMR spectra were reported in delta (δ) units, parts per million (ppm) downfield from the internal standard. Coupling constants (*J*) are reported in Hertz (Hz).

General procedure



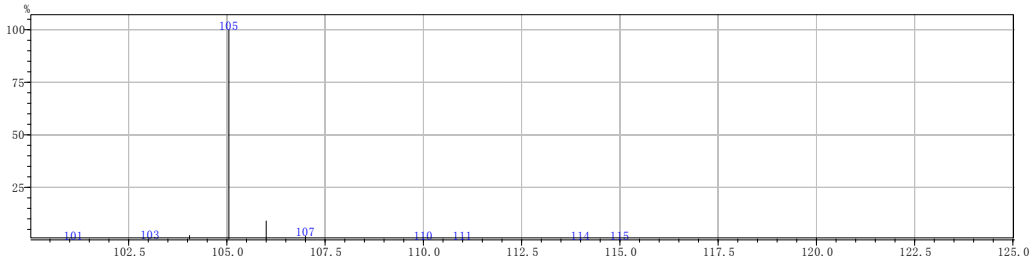
CuI (9.5 mg, 0.05 mmol), KI (99.6 mg, 0.60 mmol) was added in a Schlenk tube. The Schlenk tube was then sealed with septa and fitted with an oxygen balloon, filled with oxygen. NMP (0.75 mL), H_2O (0.05 mL), ketone (0.5 mmol) and amine (1.0 mmol) were injected in the tube via a syringe. The reaction was then heated up to 40 °C. After stirring for 24 hours, it was quenched by water and extracted with ethyl ether (3 * 10 mL). The organic layers were combined and pure product was obtained by flash column chromatography on silica gel (petroleum: ethyl acetate = 2:1).

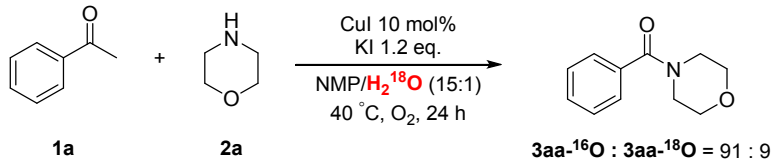
O^{18} Labeling experiments



1a **2a** **3aa-^{16}O : 3aa-^{18}O** = 99 : 1

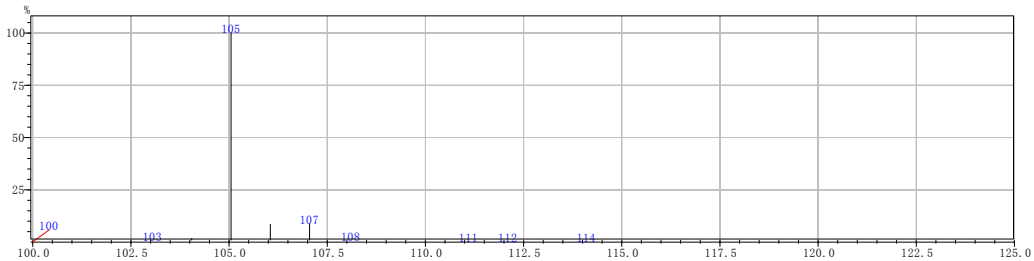
CuI (9.5 mg, 0.05 mmol), KI (99.6 mg, 0.60 mmol) was added in a Schlenk tube. The Schlenk tube was then sealed with septa and fitted with an $^{18}O_2$ balloon, filled with $^{18}O_2$. NMP (0.75 mL), H_2O (0.05 mL), **1a** (60 mg, 0.5 mmol) and **2aa** (87 mg, 1.0 mmol) were injected in the tube via a syringe. The reaction was then heated up to 40 °C. After stirring for 24 hours, it was quenched by water and extracted with ethyl ether, the organic layer was detected by GC-MS.

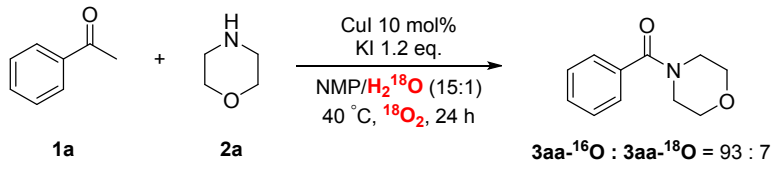




1a **2a** **3aa-^{16}O : 3aa-^{18}O** = 91 : 9

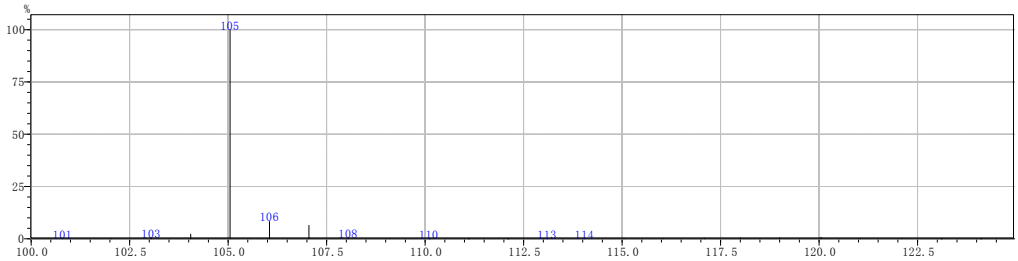
CuI (9.5 mg, 0.05 mmol), KI (99.6 mg, 0.60 mmol) was added in a Schlenk tube. The Schlenk tube was then sealed with septa and fitted with an O_2 balloon, filled with O_2. NMP (0.75 mL), $H_2{}^{18}O$ (0.05 mL), **1a** (60 mg, 0.5 mmol) and **2aa** (87 mg, 1.0 mmol) were injected in the tube via a syringe. The reaction was then heated up to 40 °C. After stirring for 24 hours, it was quenched by water and extracted with ethyl ether, the organic layer was detected by GC-MS.

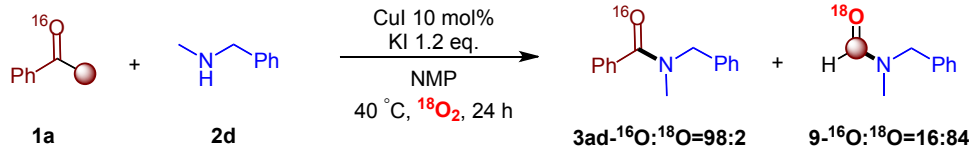




1a **2a** **3aa-^{16}O : 3aa-^{18}O** = 93 : 7

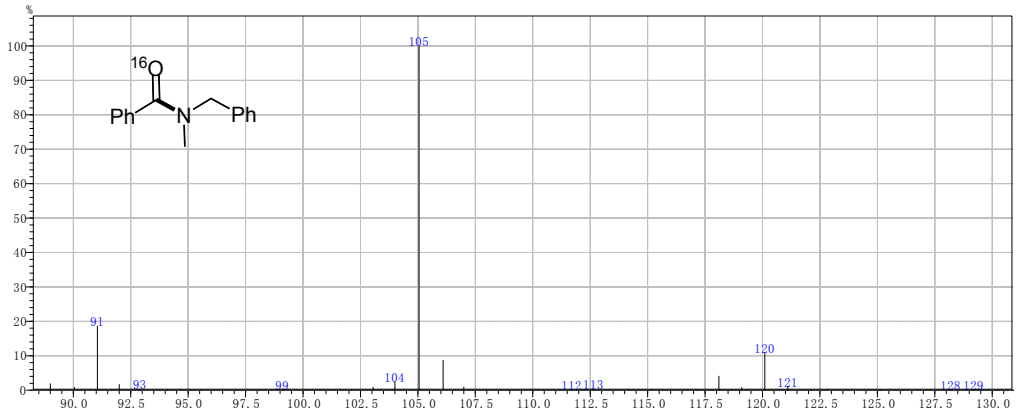
CuI (9.5 mg, 0.05 mmol), KI (99.6 mg, 0.60 mmol) was added in a Schlenk tube. The Schlenk tube was then sealed with septa and fitted with an $^{18}O_2$ balloon, filled with $^{18}O_2$. NMP (0.75 mL), $H_2{}^{18}O$ (0.05 mL), **1a** (60 mg, 0.5 mmol) and **2aa** (87 mg, 1.0 mmol) were injected in the tube via a syringe. The reaction was then heated up to 40 °C. After stirring for 24 hours, it was quenched by water and extracted with ethyl ether, the organic layer was detected by GC-MS.

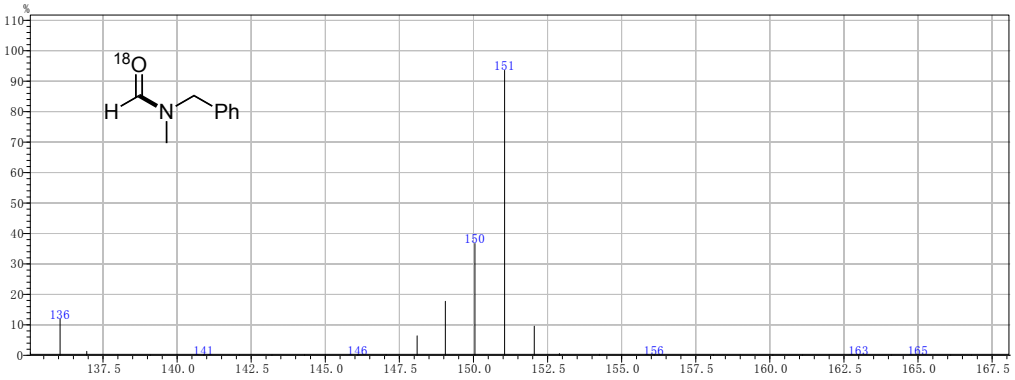




1a **2d** **3ad-^{16}O:^{18}O=98:2** **9-^{16}O:^{18}O=16:84**

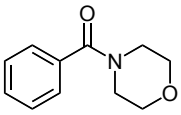
CuI (9.5 mg, 0.05 mmol), KI (99.6 mg, 0.60 mmol) was added in a Schlenk tube. The Schlenk tube was then sealed with septa and fitted with an $^{18}O_2$ balloon, filled with $^{18}O_2$. NMP (0.75 mL), **1a** (60 mg, 0.5 mmol) and **2d** (121 mg, 1.0 mmol) were injected in the tube via a syringe. The reaction was then heated up to 40 °C. After stirring for 24 hours, it was quenched by water and extracted with ethyl ether, the organic layer was detected by GC-MS.




%
110
100
90
80
70
60
50
40
30
20
10
0
18O
H
N
Ph
151
150
136
141
146
156
163
165
137.5
140.0
142.5
145.0
147.5
150.0
152.5
155.0
157.5
160.0
162.5
165.0
167.5

Detail descriptions for products

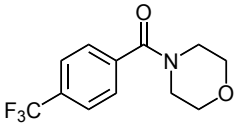
Morpholino(phenyl)methanone: 3aa[1]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.32 (m, 5H), 3.97 – 3.24 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 135.4, 130.1, 128.7, 127.2, 67.0, 48.4, 42.7.

Morpholino(4-(trifluoromethyl)phenyl)methanone: 3ba[1]

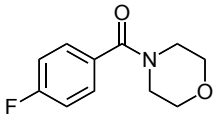


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 3.98 – 3.13 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 139.1, 132.0 (q, *J* = 32.8 Hz), 127.7, 125.9 (q, *J* = 3.7 Hz), 123.9 (q, *J* = 273.4 Hz), 67.0, 48.3, 42.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.92.

(4-Fluorophenyl)(morpholino)methanone: 3ca[1]

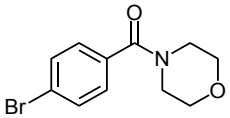


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.37 (m, 2H), 7.16 – 7.06 (m, 2H), 3.95 – 3.37 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 163.5 (d, *J* = 251.1 Hz), 131.3 (d, *J* = 3.5 Hz), 129.5 (d, *J* = 8.5 Hz), 115.7 (d, *J* = 21.8 Hz), 66.8, 48.3, 42.7.

^{19}F NMR (377 MHz, $CDCl_3$) δ -109.88.

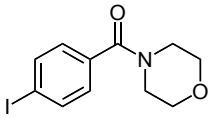
(4-Bromophenyl)(morpholino)methanone: 3da[1]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 4.04 – 3.21 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 134.3, 132.1, 129.1, 124.5, 67.1, 48.4, 42.8.

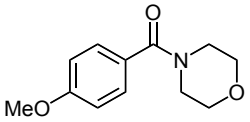
(4-Iodophenyl)(morpholino)methanone: 3ea[2]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.65 (m, 2H), 7.21 – 7.03 (m, 2H), 3.89 – 2.99 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 138.0, 134.8, 129.1, 96.4, 67.0, 48.5, 42.8.

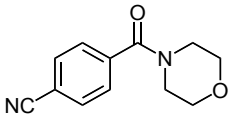
(4-Methoxyphenyl)(morpholino)methanone: 3fa[1]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H), 3.68 (s, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 161.0, 129.3, 127.4, 113.9, 67.0, 55.5.

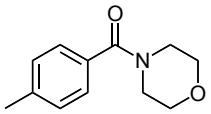
4-(Morpholine-4-carbonyl)benzonitrile: 3ga[3]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 3.94 – 3.06 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 139.8, 132.7, 128.0, 118.2, 113.8, 66.9, 48.2, 42.7.

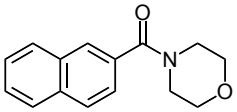
Morpholino(p-tolyl)methanone: 3ha[1]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 3.95 – 3.19 (m, 8H), 2.38 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 140.3, 132.5, 129.3, 127.4, 67.1, 21.6.

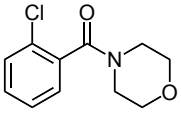
Morpholino(naphthalen-2-yl)methanone: 3ia[4]



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.73 (m, 4H), 7.60– 7.42 (m, 3H), 4.06 – 3.35 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 133.9, 132.8, 132.7, 128.6, 128.6, 128.0, 127.4, 127.2, 127.0, 124.4, 67.1, 48.5, 42.8.

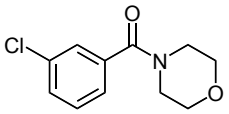
(2-Chlorophenyl)(morpholino)methanone: 3ja[5]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.26 (m, 4H), 3.94 – 3.83 (m, 1H), 3.80 – 3.65 (m, 4H), 3.62 – 3.55 (m, 1H), 3.32 – 3.15 (m, 2H).

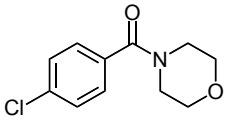
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 135.5, 130.6, 130.4, 129.8, 128.0, 127.5, 66.9, 66.8, 47.3, 42.2.

(3-Chlorophenyl)(morpholino)methanone: 3ka[6]



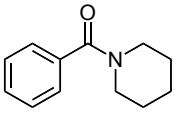
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.34 (m, 3H), 7.36 – 7.28 (m, 1H), 3.88 – 3.32 (m, 8H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 137.2, 134.8, 130.2, 130.1, 127.4, 125.3, 67.0, 48.3, 42.7.

(4-Chlorophenyl)(morpholino)methanone: 3la[1]



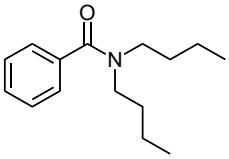
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.32 (m, 4H), 3.95 – 3.30 (m, 8H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 136.0, 133.6, 128.9, 128.7, 66.8, 48.2, 42.7.

Phenyl(piperidin-1-yl)methanone: 3ab[6]



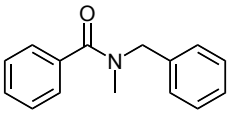
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 6.72 (m, 5H), 3.70 (s, 2H), 3.32 (s, 2H), 1.66 (s, 4H), 1.50 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 136.7, 129.5, 128.6, 126.9, 48.9, 43.3, 26.7, 25.8, 24.8.

N,N-dibutylbenzamide: 3ac[7]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.10 (m, 5H), 3.48 (d, J = 6.3 Hz, 2H), 3.18 (s, 2H), 1.64 (d, J = 5.9 Hz, 2H), 1.55 – 1.33 (m, 4H), 1.13 (d, J = 6.6 Hz, 2H), 0.98 (d, J = 6.2 Hz, 3H), 0.78 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 137.5, 129.1, 128.5, 126.6, 48.9, 44.6, 31.0, 29.8, 20.5, 19.9, 14.1, 13.8.

N-benzyl-N-methylbenzamide: 3ad[8]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.00 (m, 10H), 4.79 (s, 1H), 4.54 (s, 1H), 3.06 (s, 1.5H), 2.88 (s, 1.5H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 171.8, 137.2, 136.8, 136.5, 129.8, 129.0, 128.6, 128.4, 127.7, 127.1, 127.0, 55.3, 51.0, 37.7, 33.4.

References

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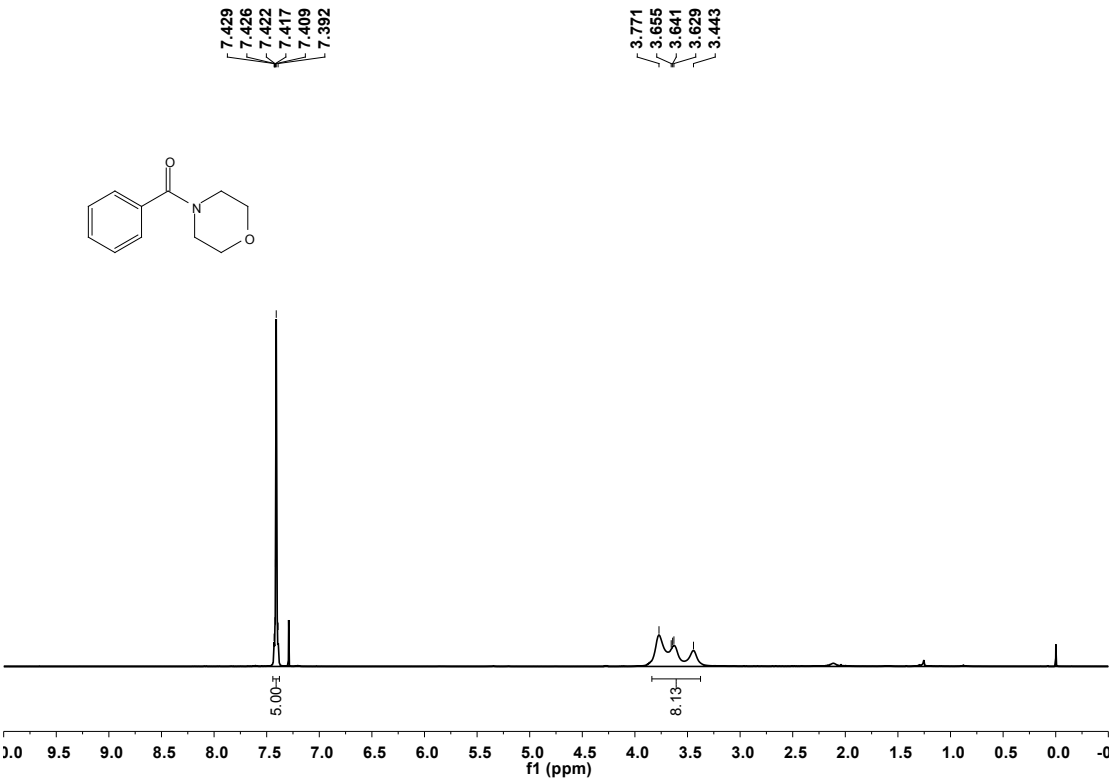
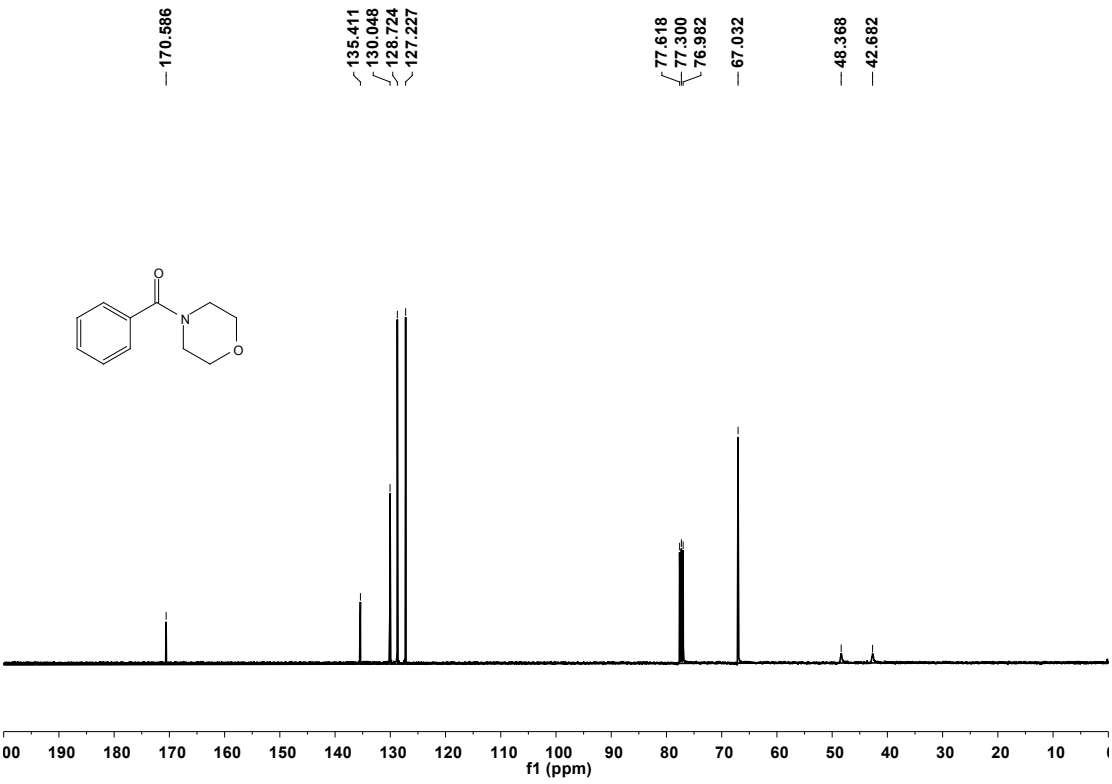
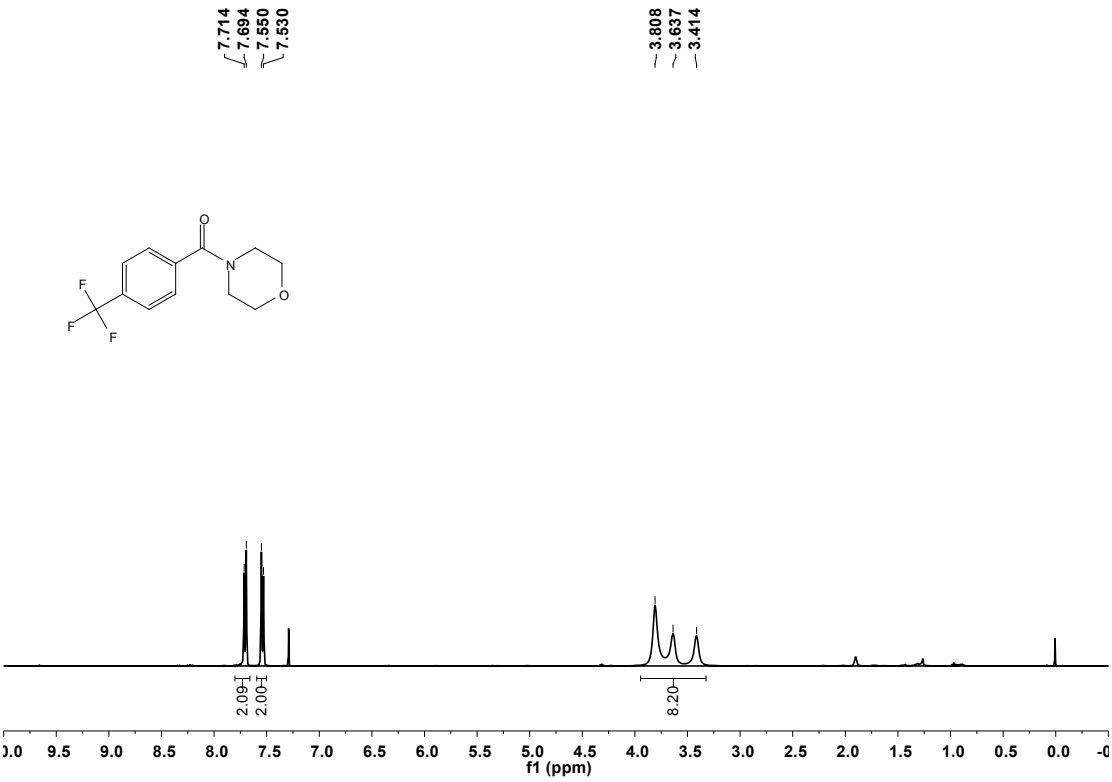


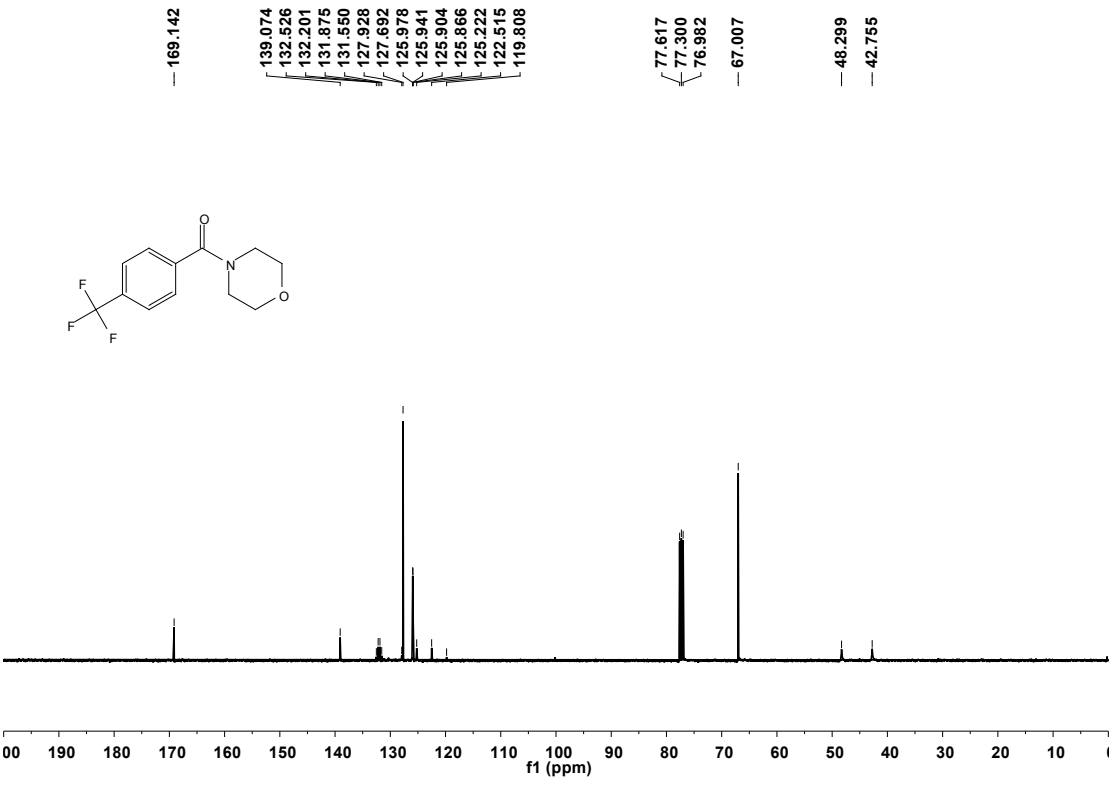
^{1}H NMR spectrum of morpholino(phenyl)methanone (3aa)



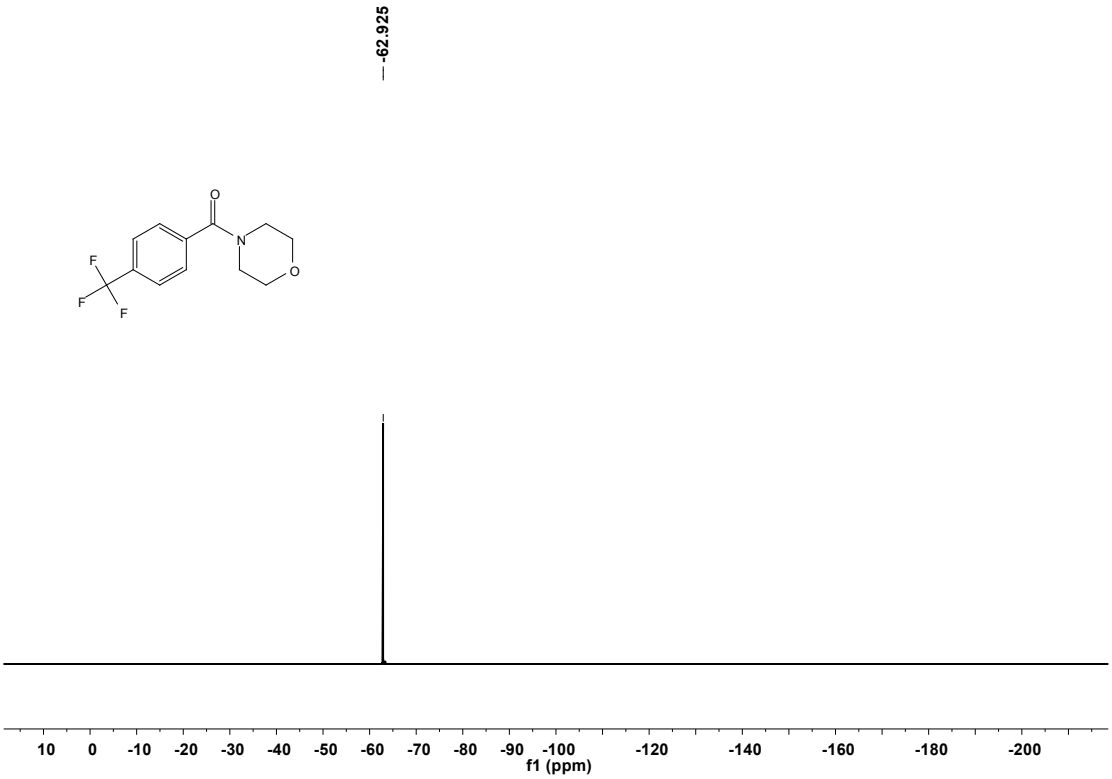
^{13}C NMR spectrum of morpholino(phenyl)methanone (3aa)



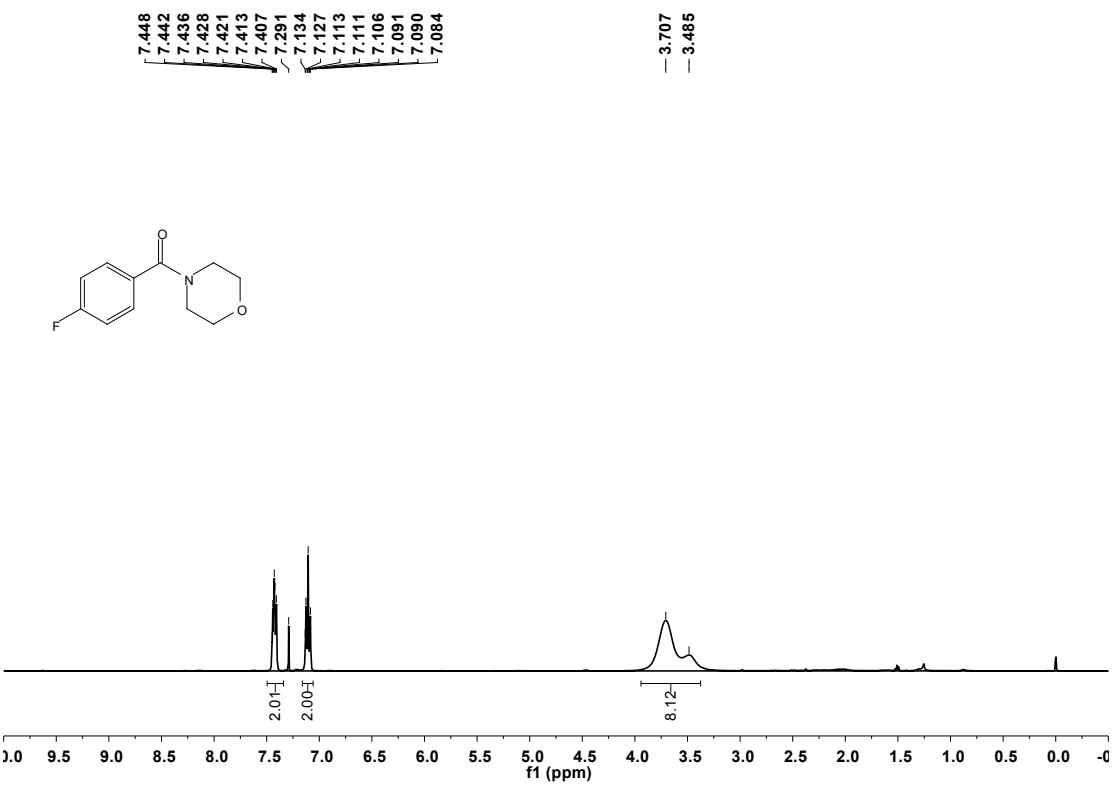
^{1}H NMR spectrum of morpholino(4-(trifluoromethyl)phenyl)methanone (3ba)



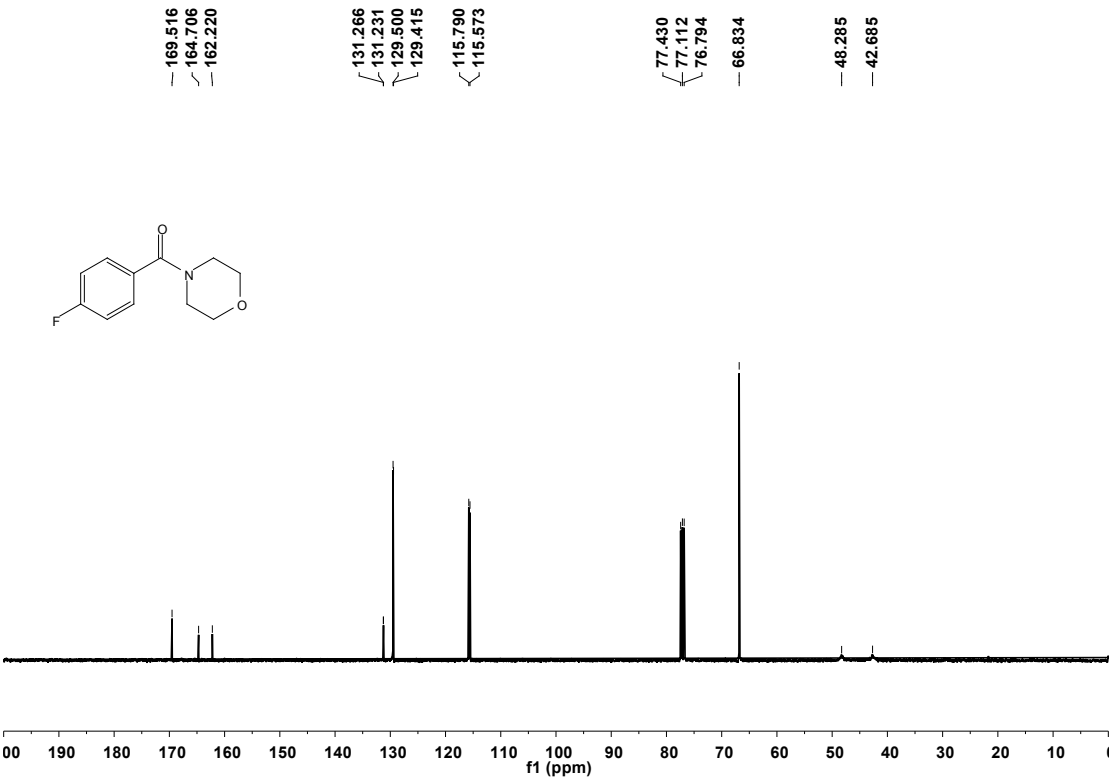
^{13}C NMR spectrum of morpholino(4-(trifluoromethyl)phenyl)methanone (3ba)



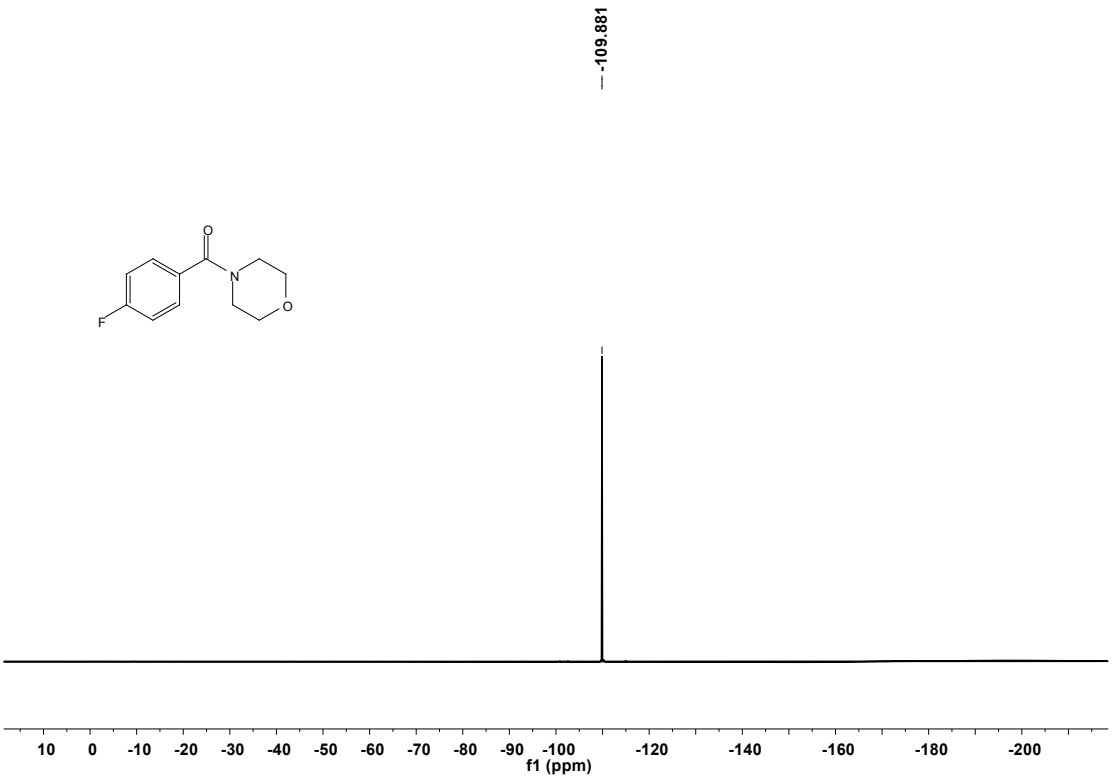
^{19}C NMR spectrum of morpholino(4-(trifluoromethyl)phenyl)methanone (3ba)



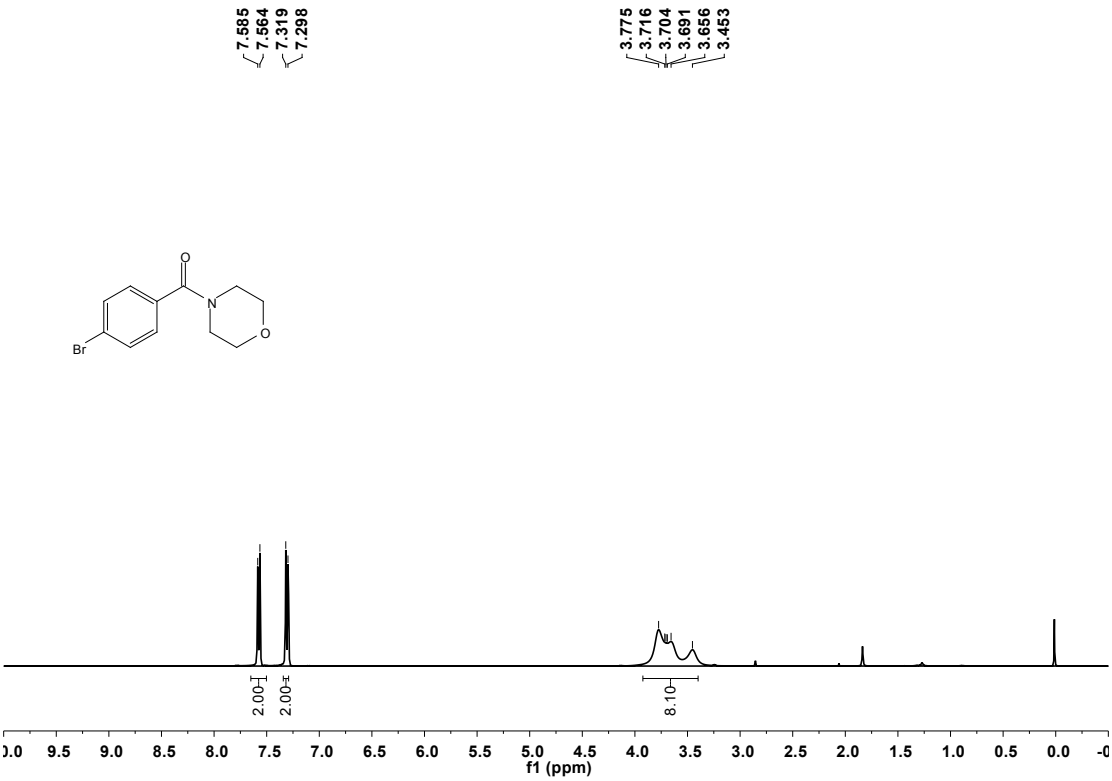
^{1}H NMR spectrum of (4-fluorophenyl)(morpholino)methanone (3ca)



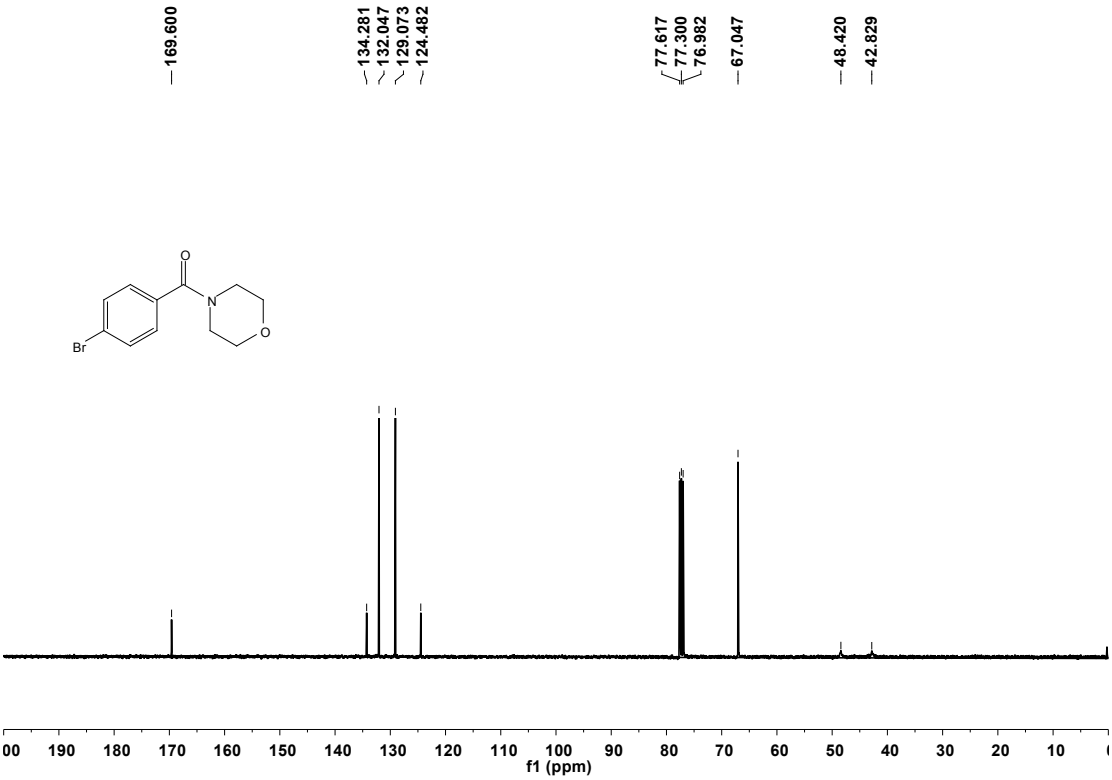
^{13}C NMR spectrum of (4-fluorophenyl)(morpholino)methanone (3ca)



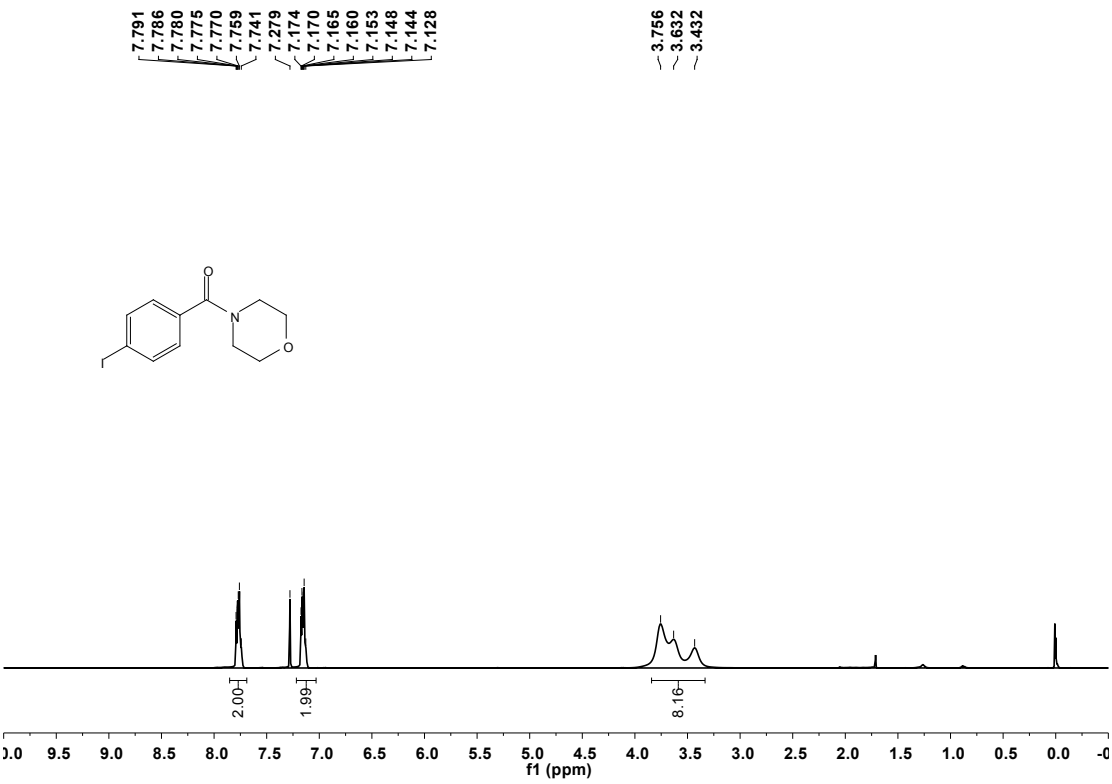
^{19}F NMR spectrum of (4-fluorophenyl)(morpholino)methanone (3ca)



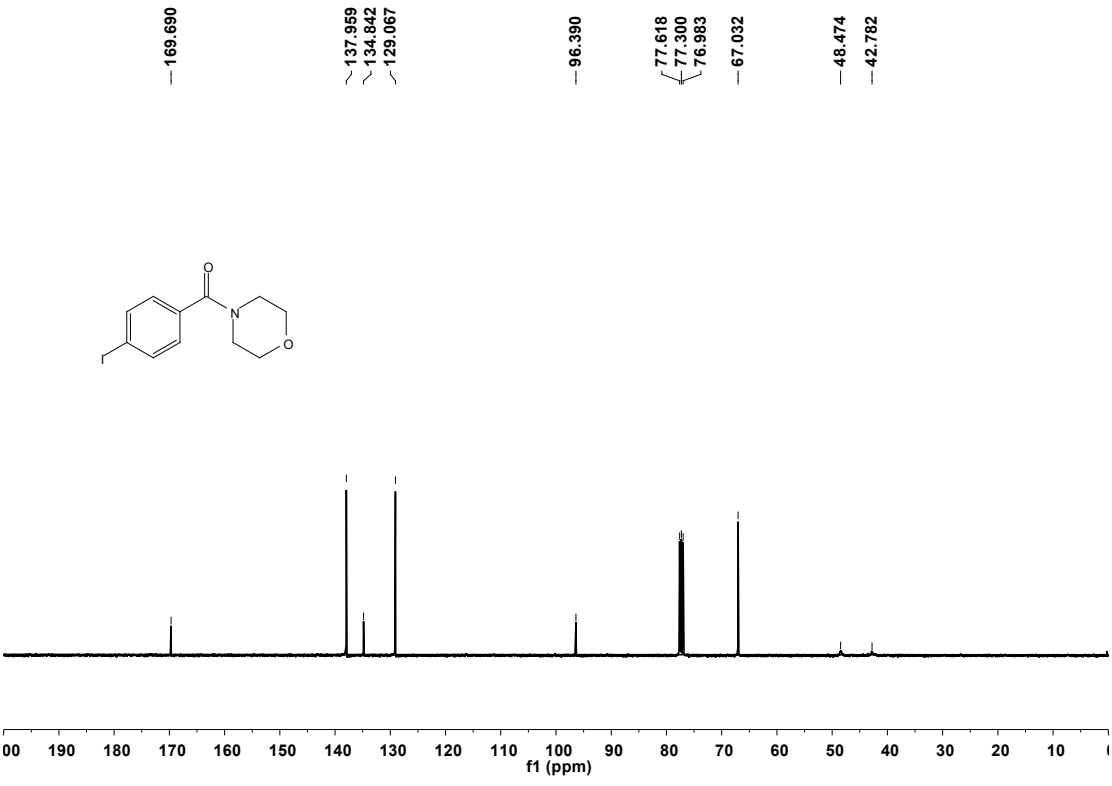
^{1}H NMR spectrum of (4-bromophenyl)(morpholino)methanone (3da)



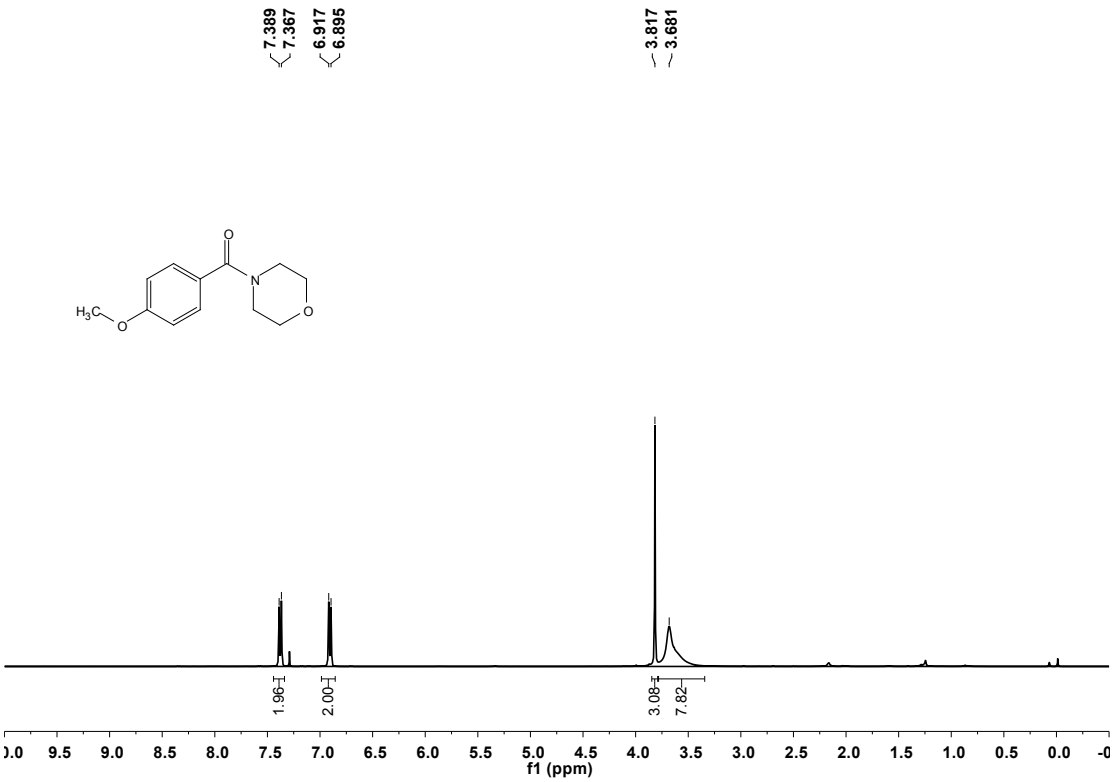
^{13}C NMR spectrum of (4-bromophenyl)(morpholino)methanone (3da)



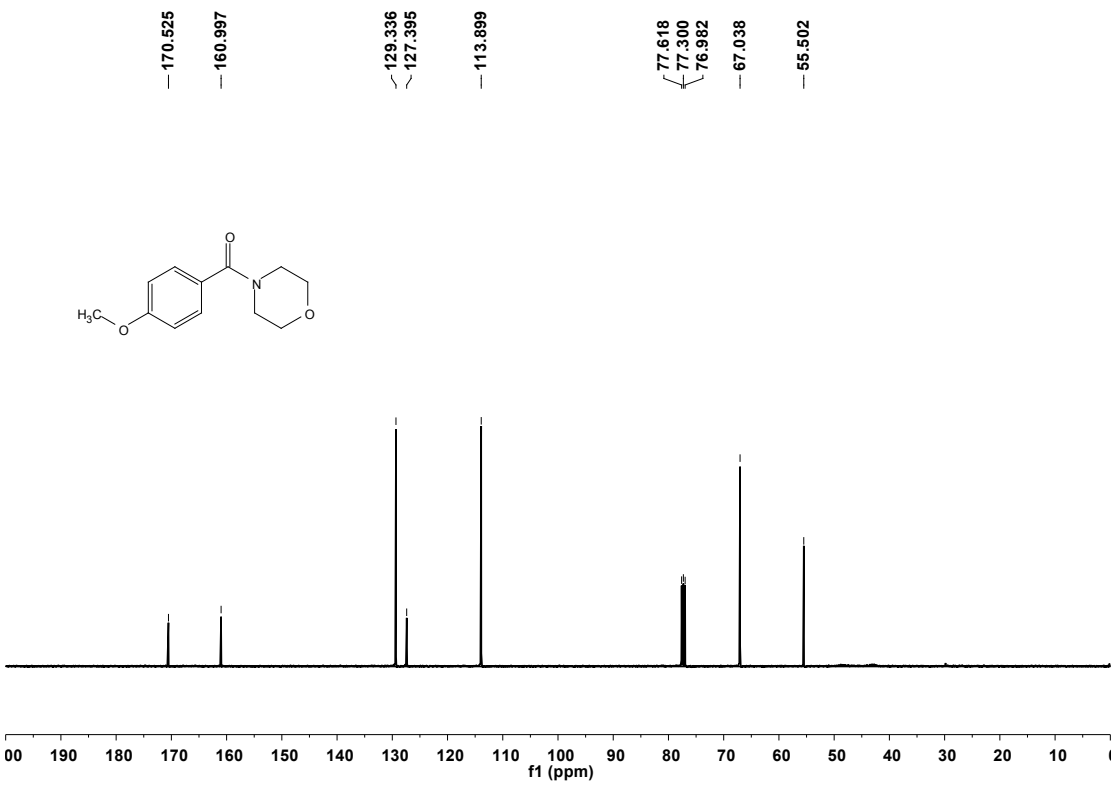
^{1}H NMR spectrum of (4-iodophenyl)(morpholino)methanone (3ea)



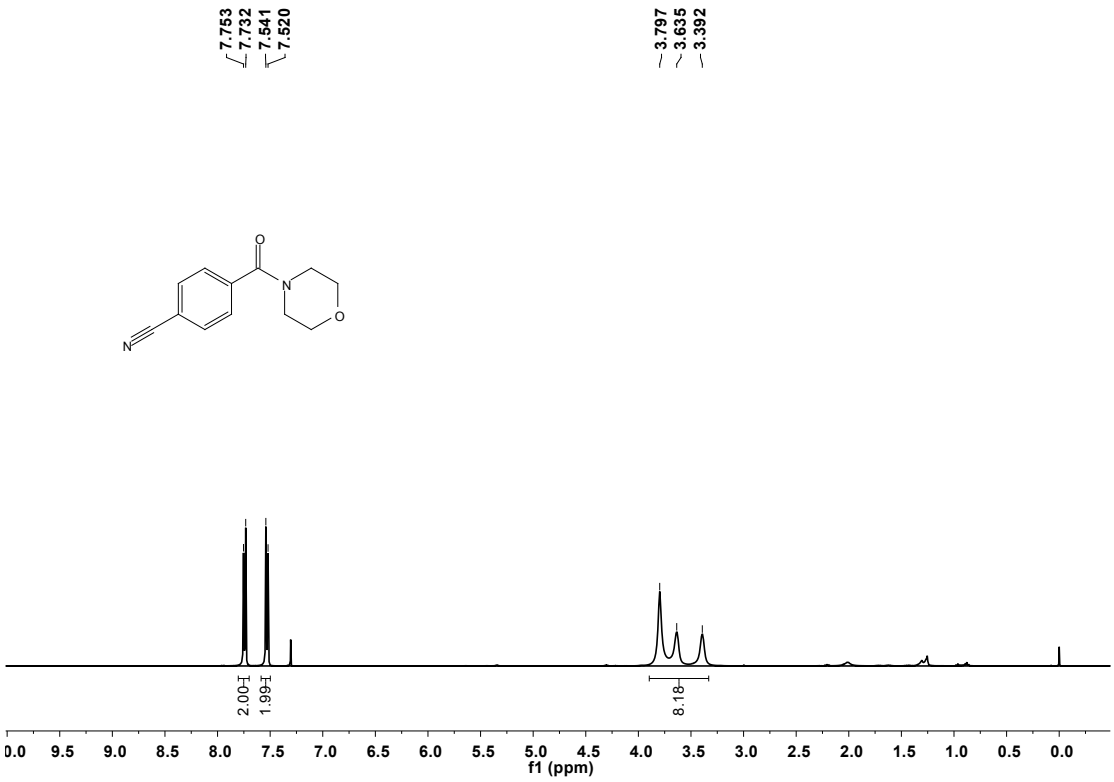
^{13}C NMR spectrum of (4-iodophenyl)(morpholino)methanone (3ea)



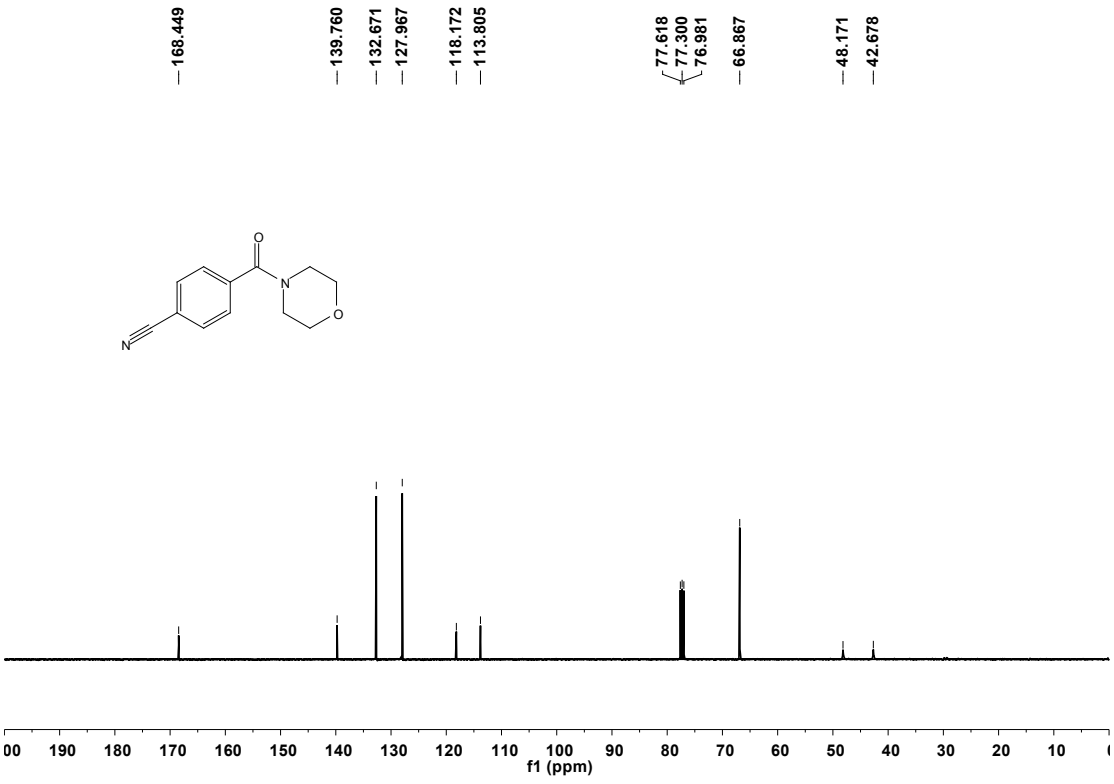
^{1}H NMR spectrum of (4-methoxyphenyl)(morpholino)methanone (3fa)



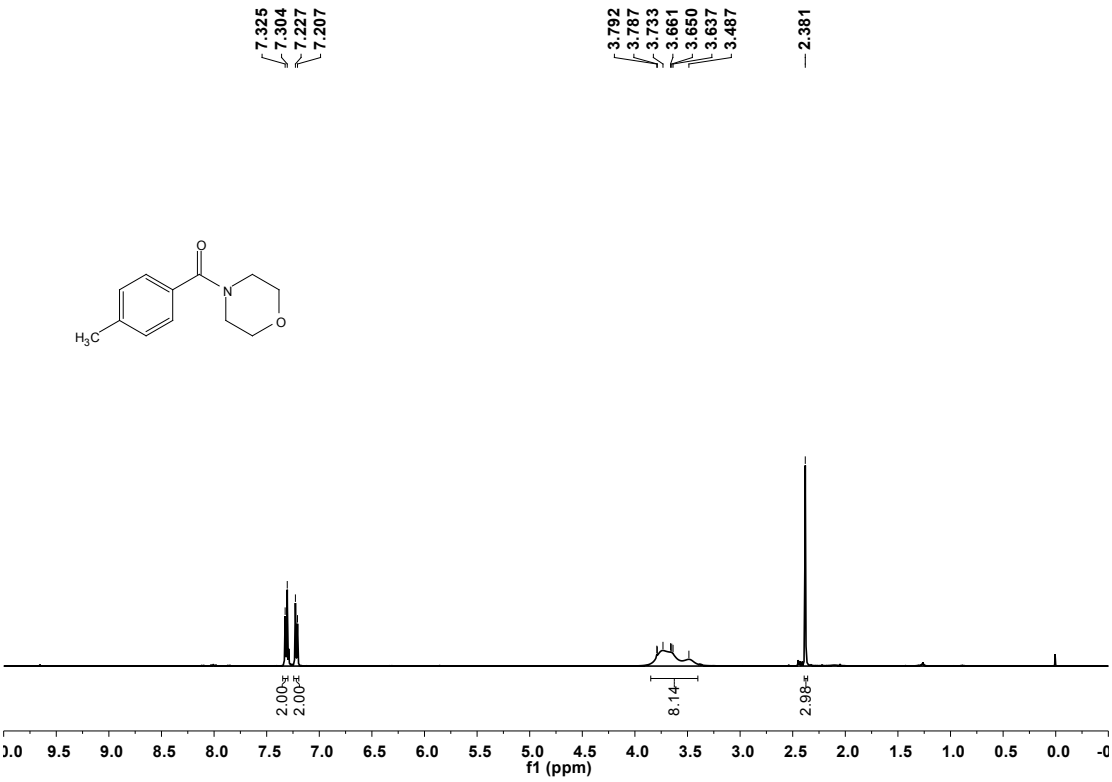
^{13}C NMR spectrum of (4-methoxyphenyl)(morpholino)methanone (3fa)



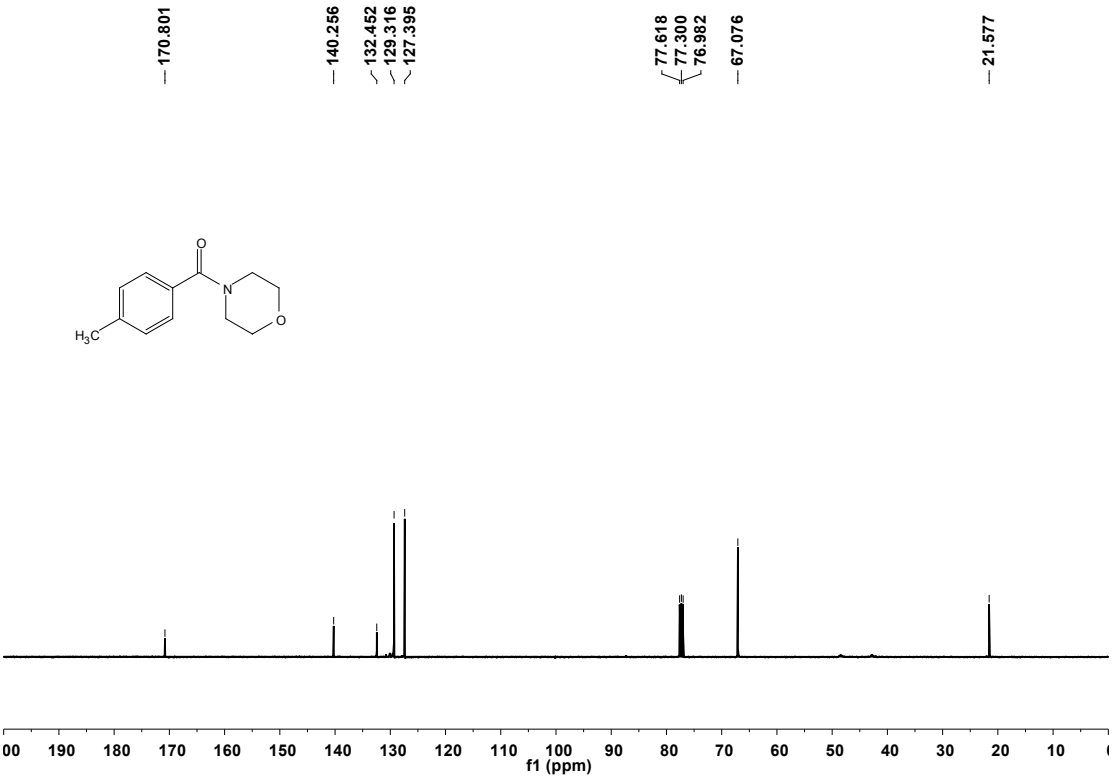
^{1}H NMR spectrum of 4-(morpholine-4-carbonyl)benzonitrile (3ga)



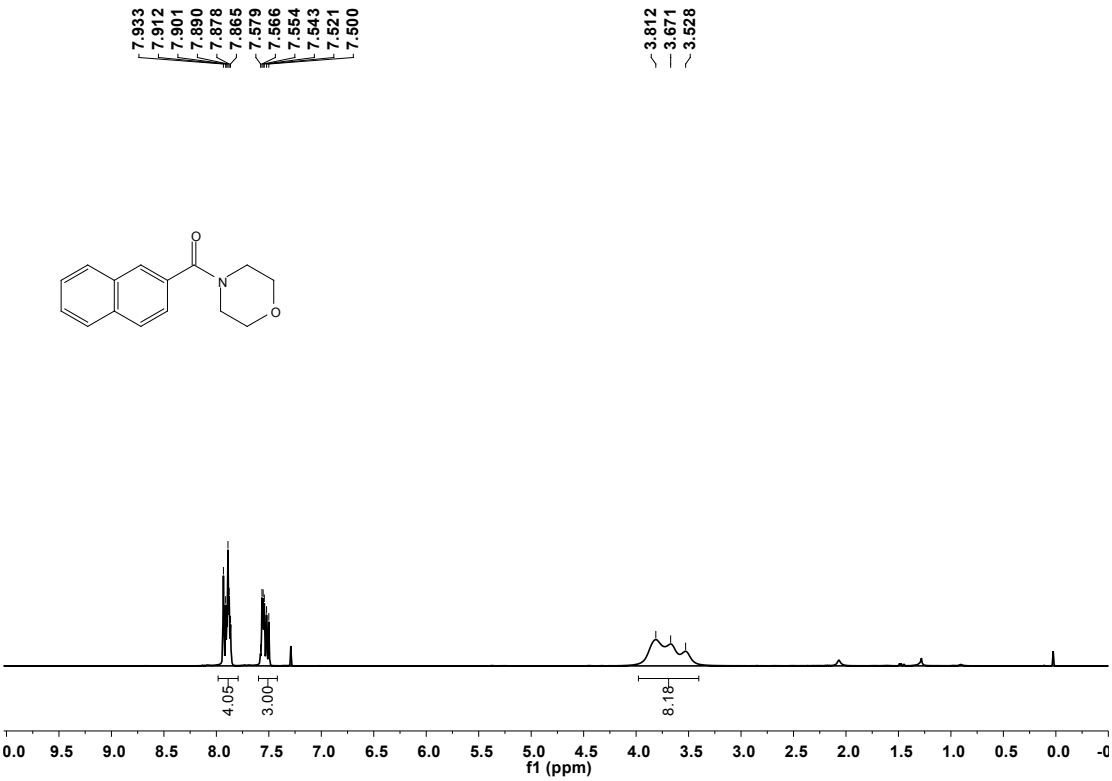
^{13}C NMR spectrum of 4-(morpholine-4-carbonyl)benzonitrile (3ga)



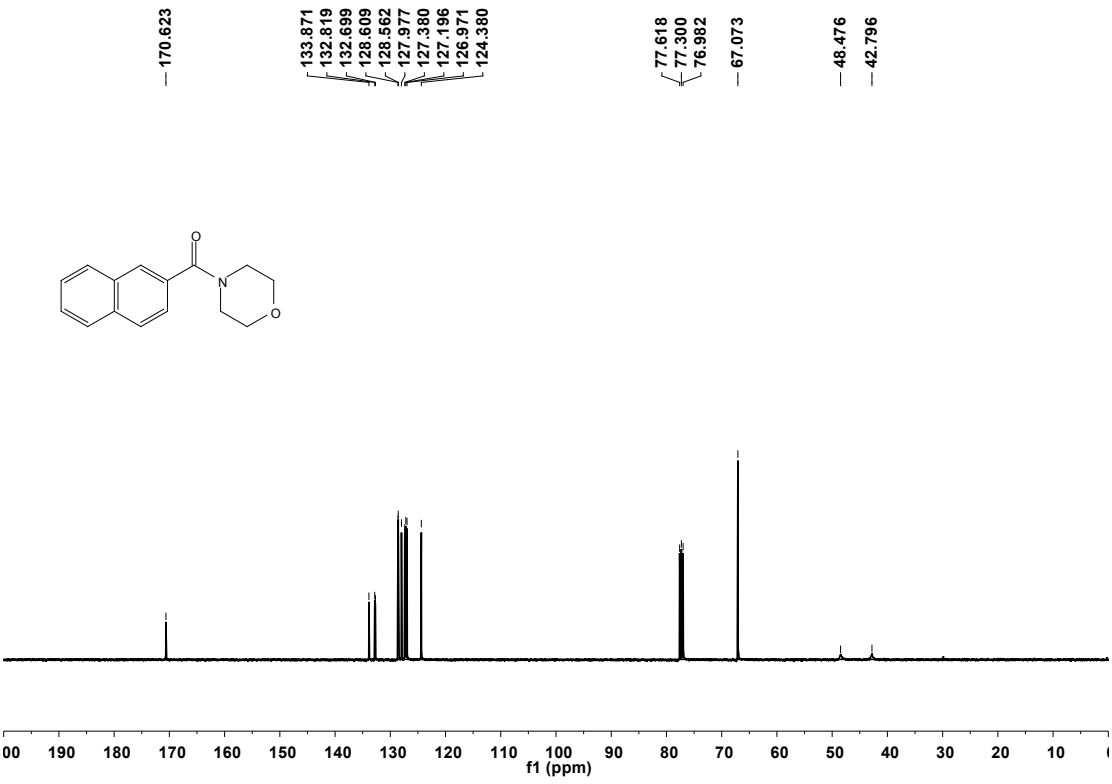
^{1}H NMR spectrum of morpholino(p-tolyl)methanone (3ha)



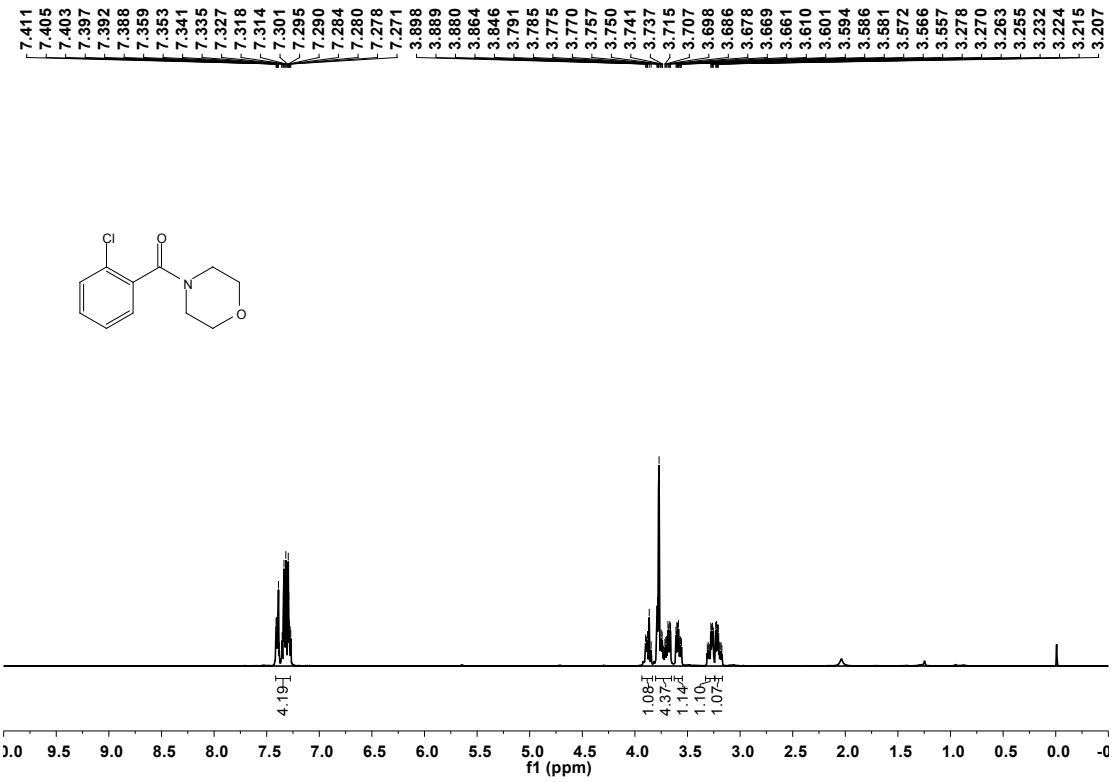
^{13}C NMR spectrum of morpholino(p-tolyl)methanone (3ha)



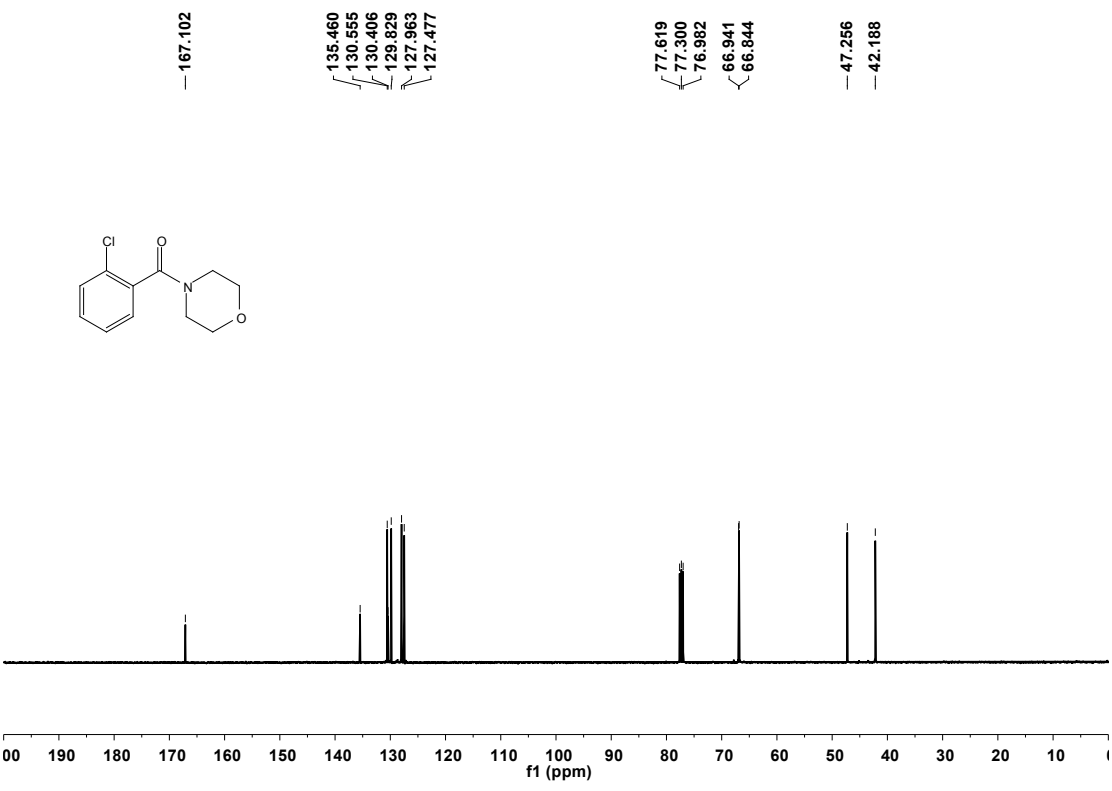
^{1}H NMR spectrum of morpholino(naphthalen-2-yl)methanone (3ia)



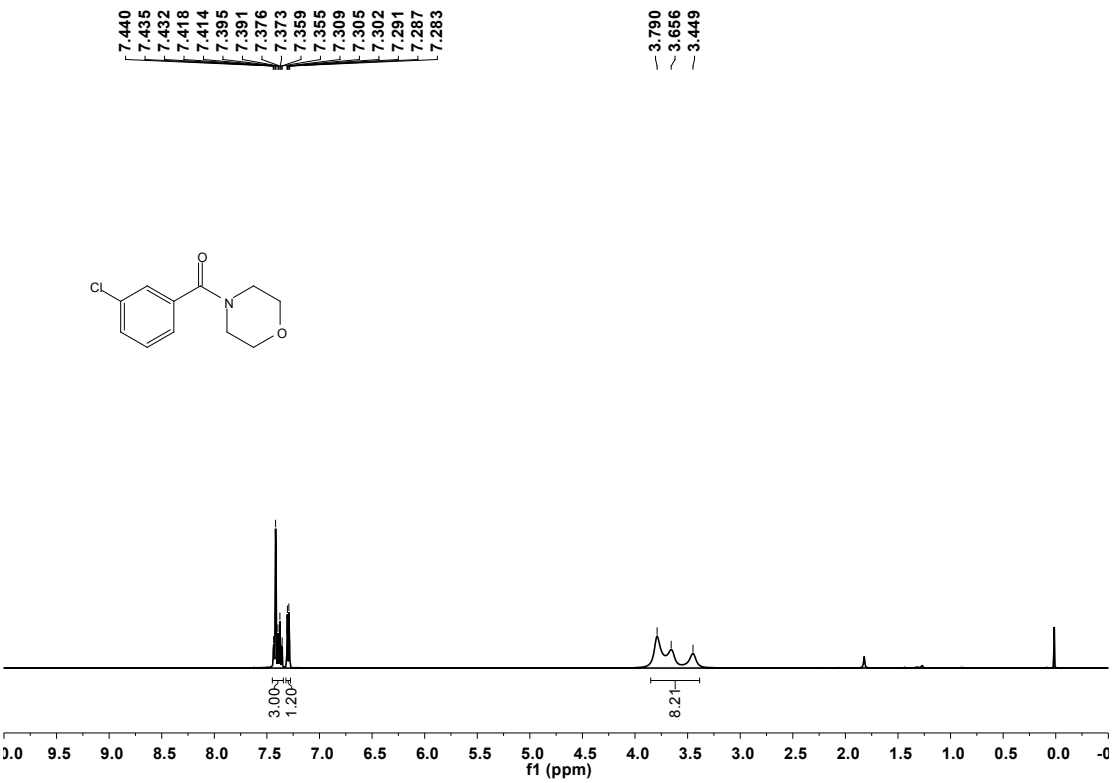
^{13}C NMR spectrum of morpholino(naphthalen-2-yl)methanone (3ia)



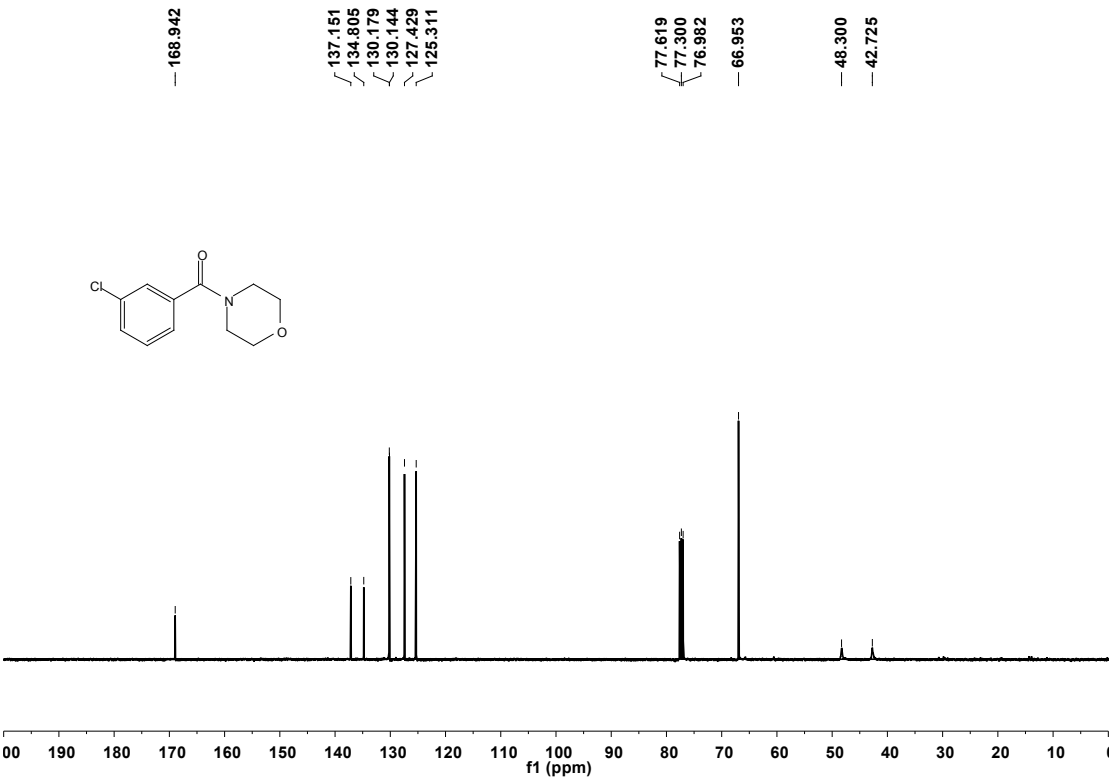
^{1}H NMR spectrum of (2-chlorophenyl)(morpholino)methanone (3ja)



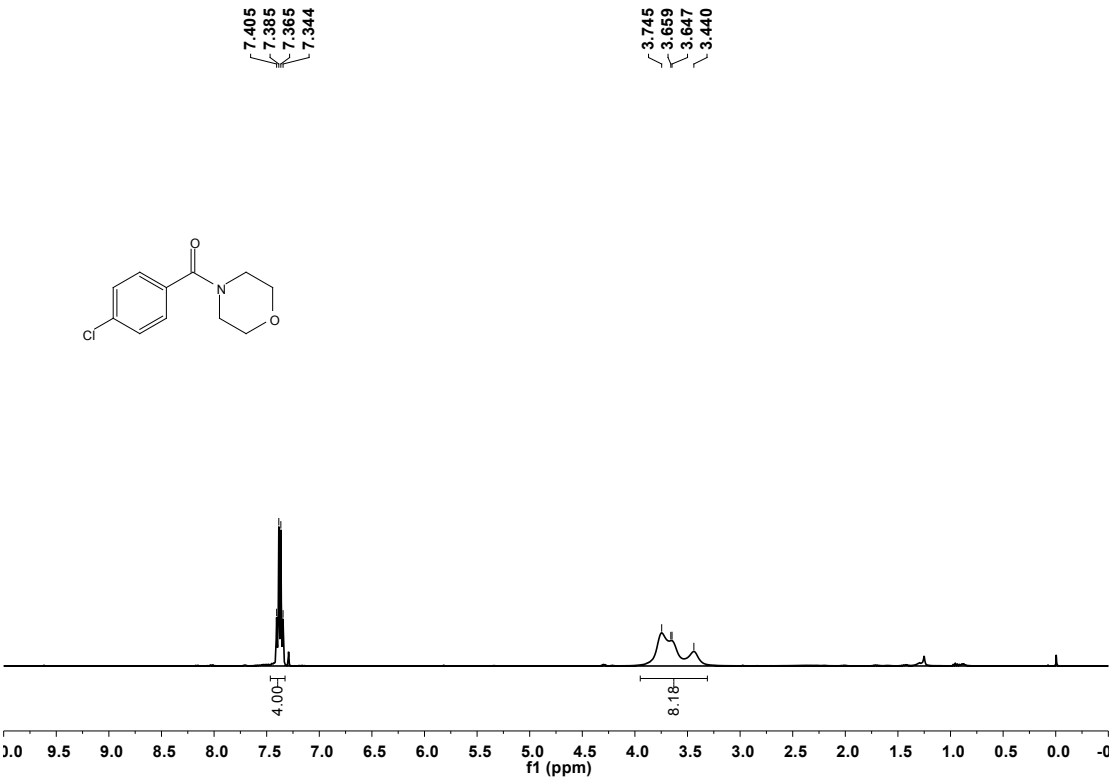
^{13}C NMR spectrum of (2-chlorophenyl)(morpholino)methanone (3ja)



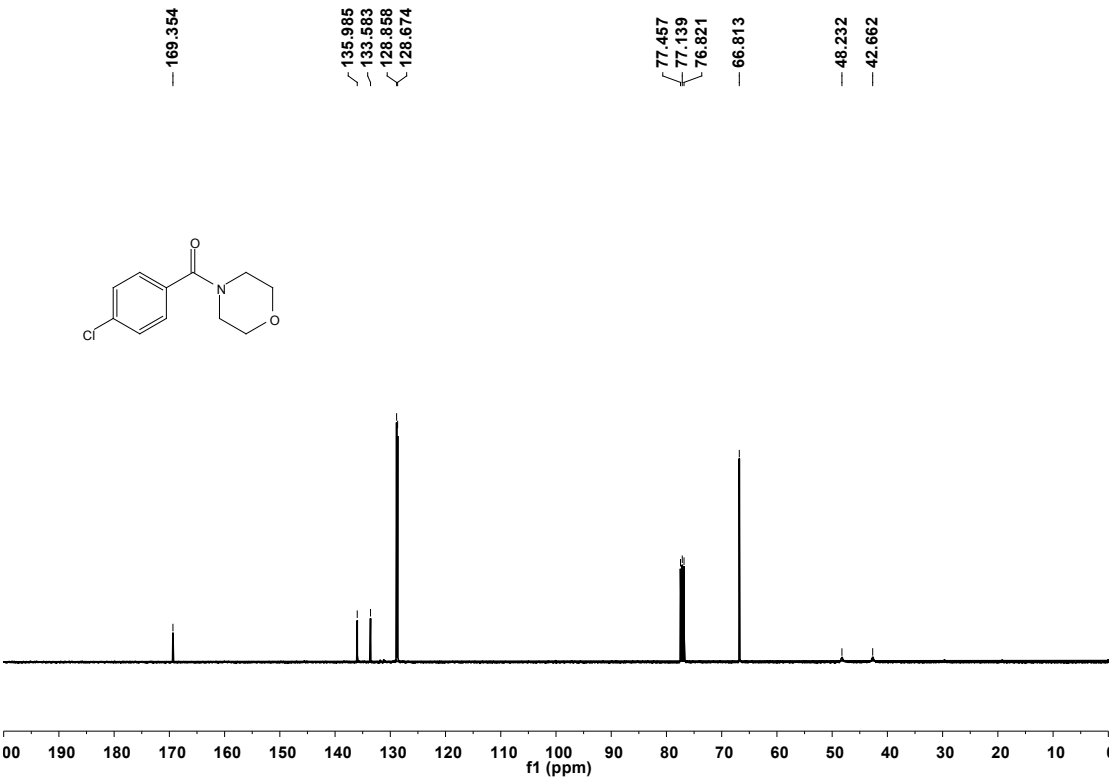
^{1}H NMR spectrum of (3-chlorophenyl)(morpholino)methanone (3ka)



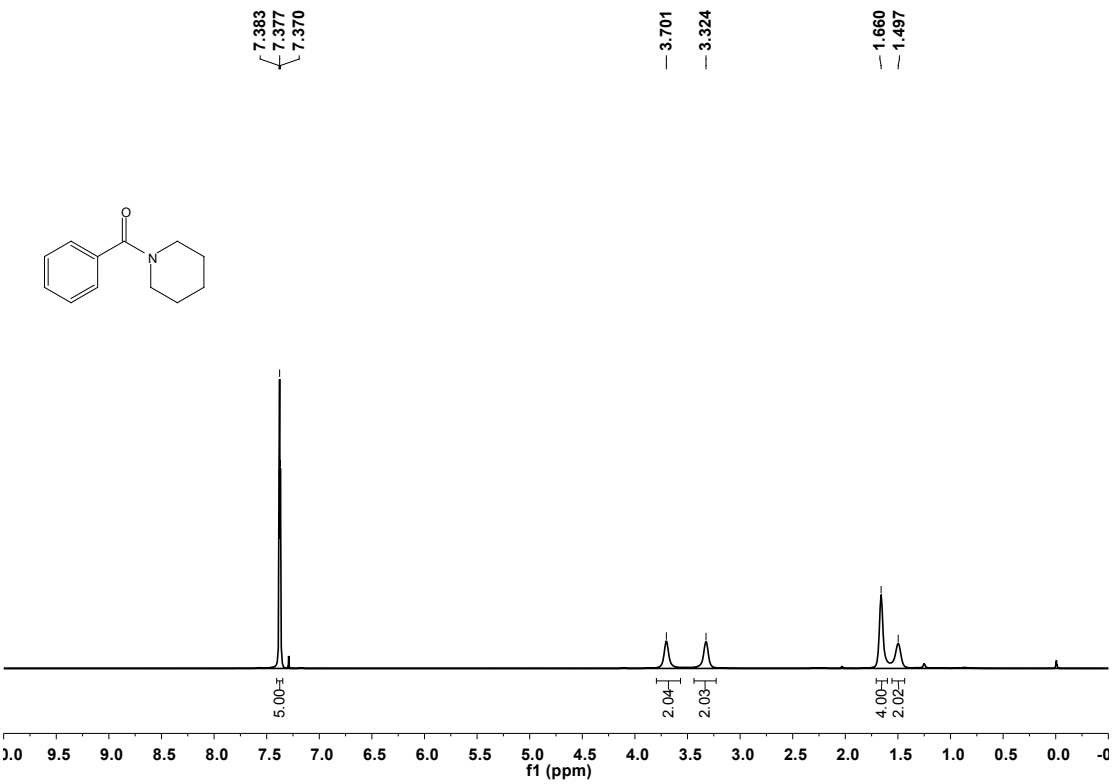
^{13}C NMR spectrum of (3-chlorophenyl)(morpholino)methanone (3ka)



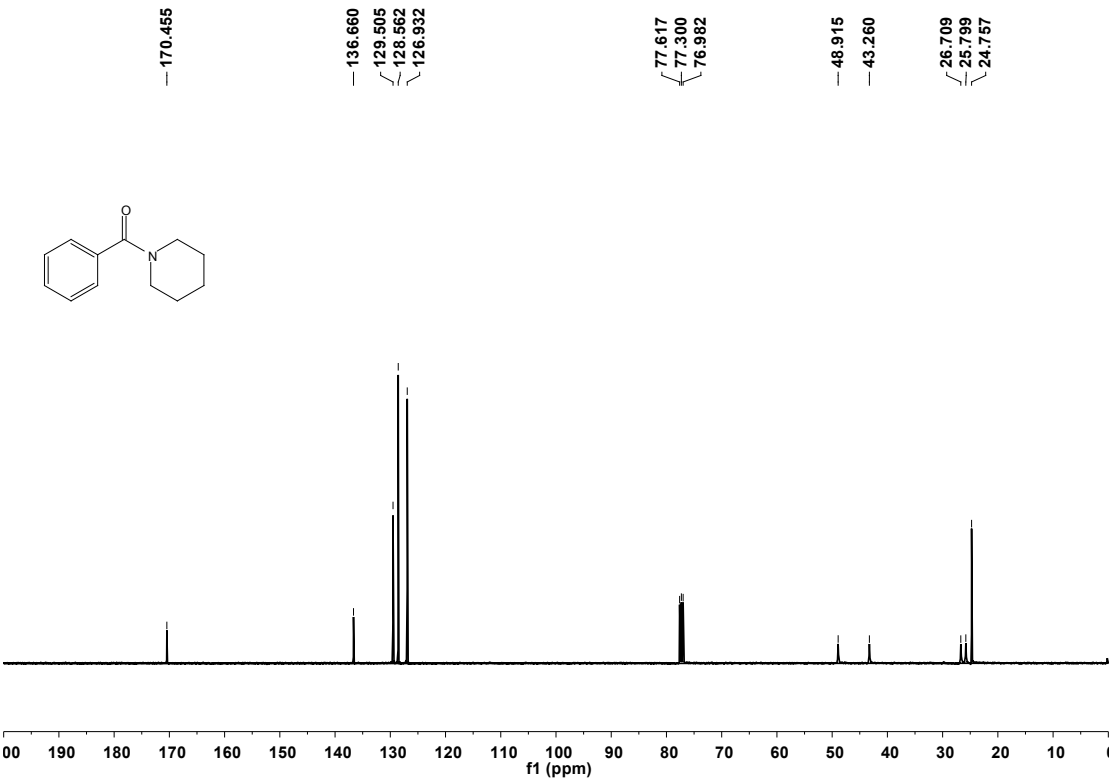
^{1}H NMR spectrum of (4-chlorophenyl)(morpholino)methanone (3la)



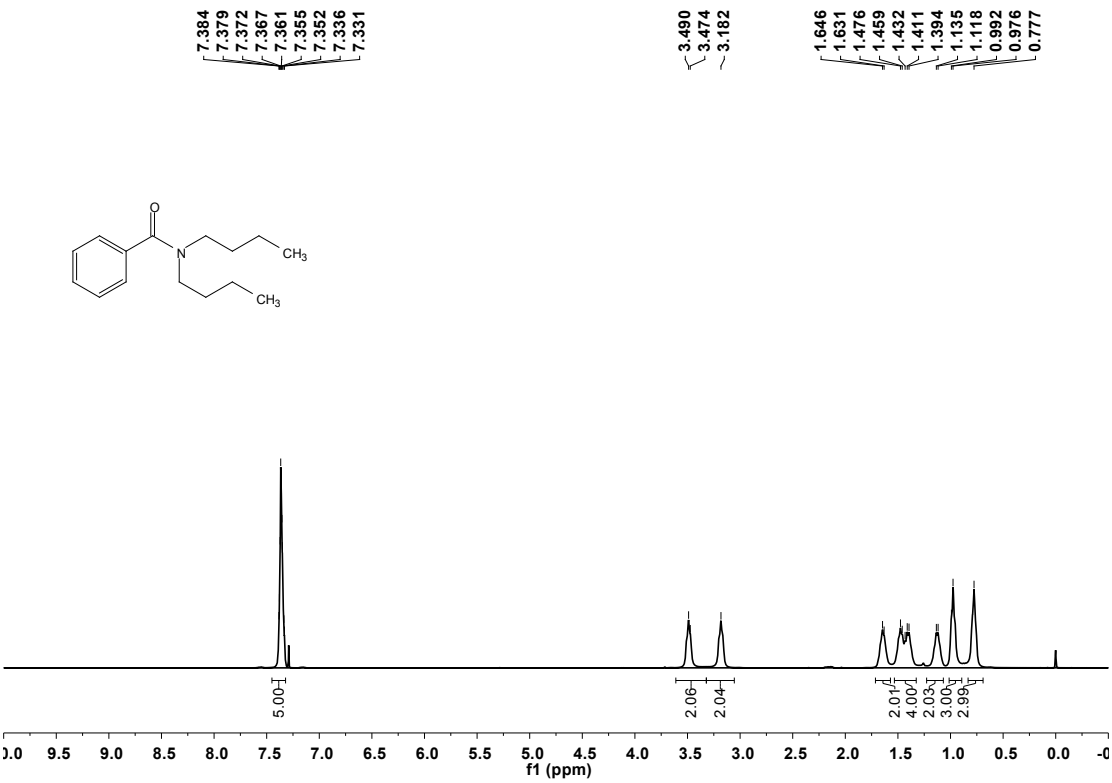
^{13}C NMR spectrum of (4-chlorophenyl)(morpholino)methanone (3la)



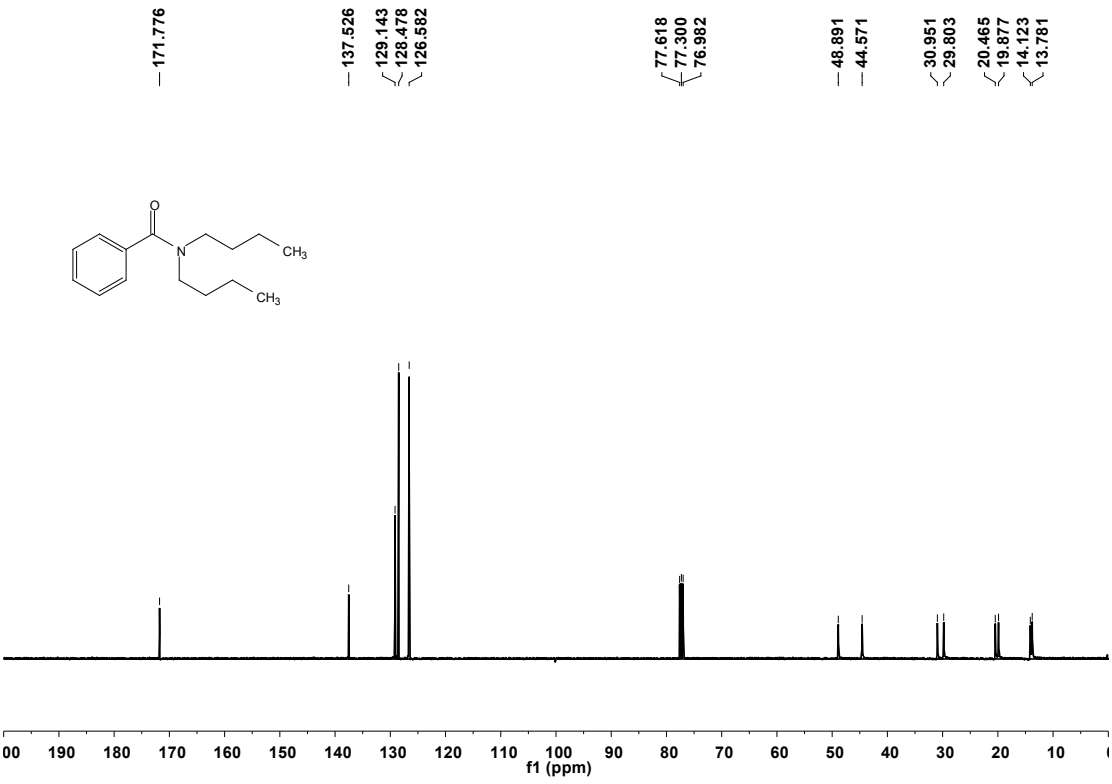
^{1}H NMR spectrum of phenyl(piperidin-1-yl)methanone (3ab)



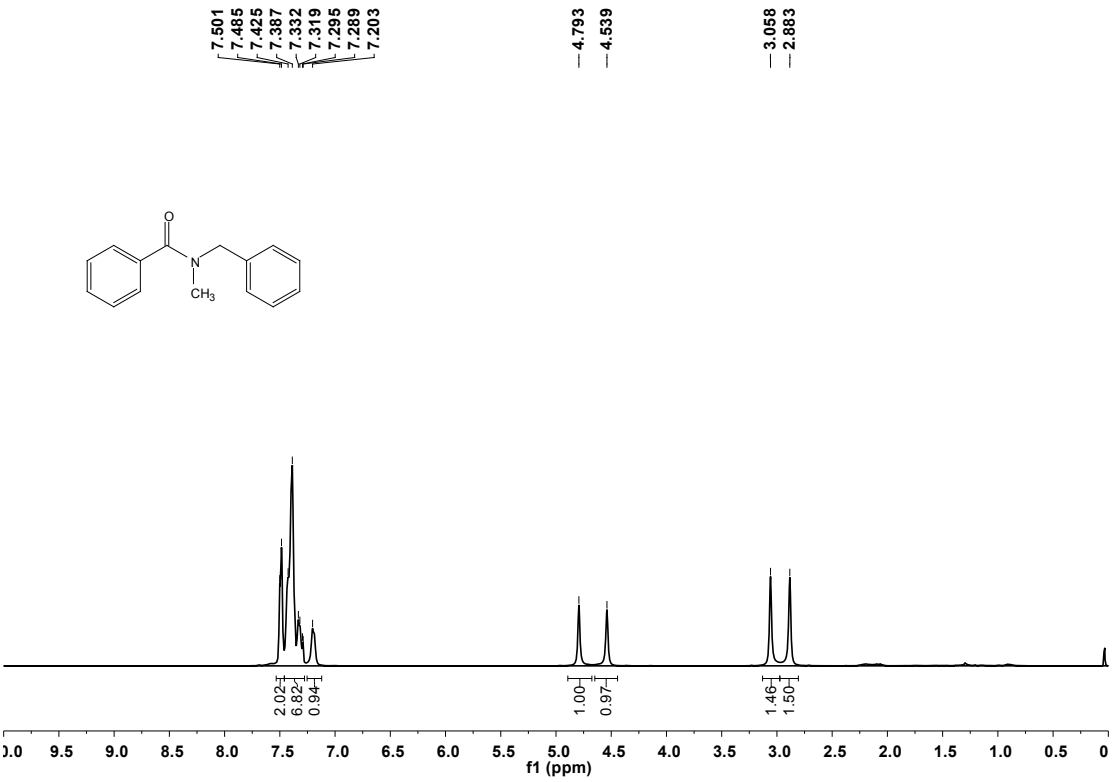
^{13}C NMR spectrum of phenyl(piperidin-1-yl)methanone (3ab)



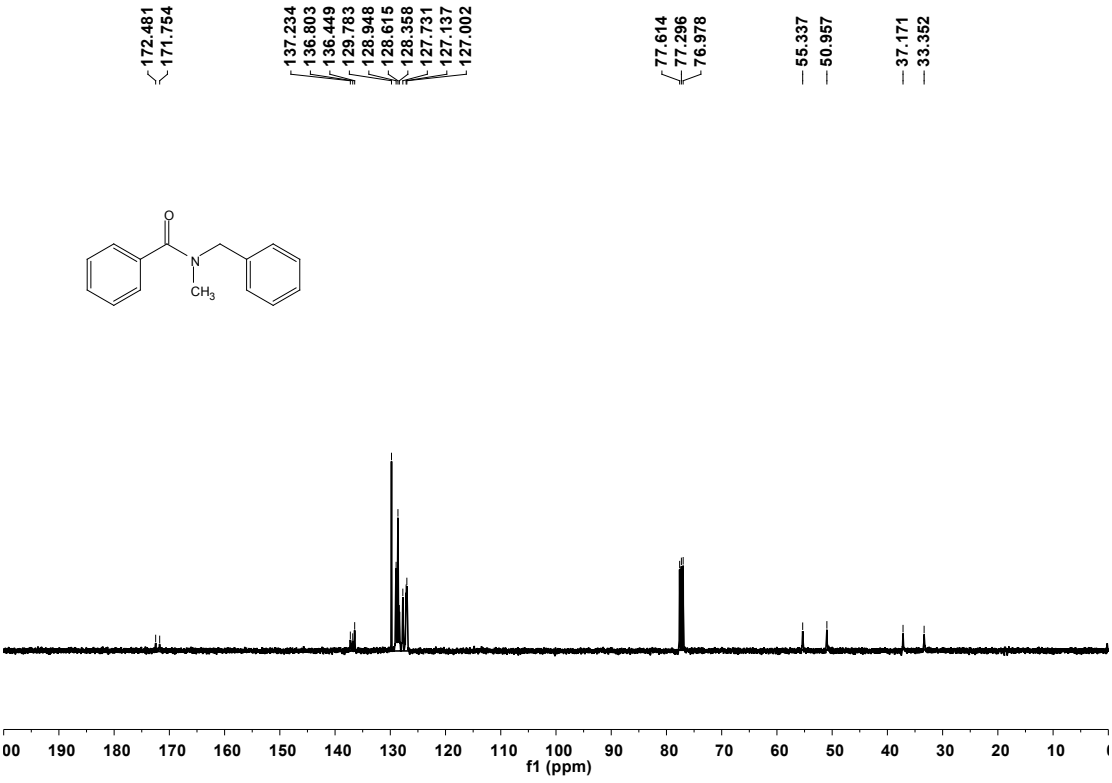
^{1}H NMR spectrum of N,N-dibutylbenzamide (3ac)



^{13}C NMR spectrum of N,N-dibutylbenzamide (3ac)



^{1}H NMR spectrum of N-benzyl-N-methylbenzamide (3ad)



^{13}C NMR spectrum of N-benzyl-N-methylbenzamide (3ad)