Supporting Information

cis-Diphosphine Ethene Ligands Enable Ni-Catalyzed Amination of Aryl Chlorides

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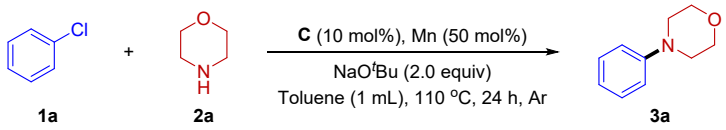
1. General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods.[1,2] All reactions dealing with air- or moisture-sensitive compound were performed by standard Schlenk techniques in oven-dried reaction vessels under nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. The products were purified by column chromatography by 200-300 mesh silica. The elution solvent used for column chromatography was PE (petroleum ether, boiling point range 60-90 °C), EA (ethyl acetate) and DCM (dichloromethane). ^{1}H, ^{13}C, and ^{19}F nuclear magnetic resonance (NMR) spectra were recorded on Bruker AVANCE NEO 400M NMR spectrometers at the College of Chemistry of Zhengzhou University. ^{1}H and ^{13}C NMR spectra were reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and $CDCl_3$ (77.0 ppm), respectively. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. High-resolution mass spectra (HRMS) were obtained with a Q-Tof Premier LC HR mass spectrometer.

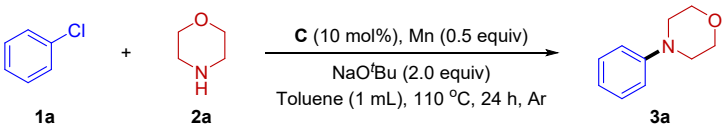
2. Optimization studies



1a **2a** **3a**

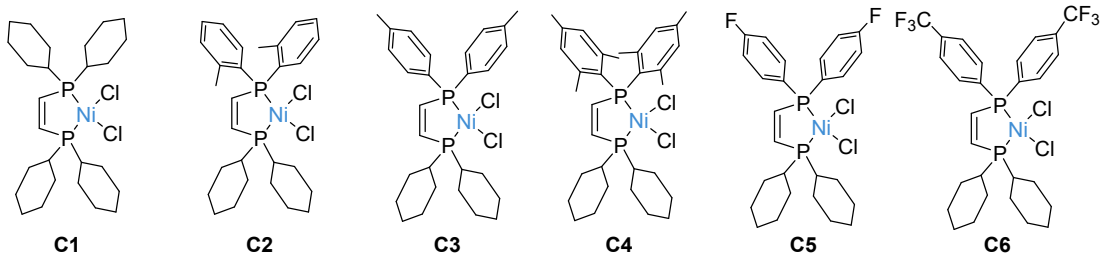
General produces: A 10 mL schlenk tube with screw-cap was charged with pre-catalyst **C** (10 mol%), Mn (5.5 mg, 0.5 equiv), NaO^{t}Bu (38.4 mg, 0.4 mmol, 2.0 equiv) and an oven-dried stirring bar. The tubes were evacuated and back purged with nitrogen and repeated three times, dry toluene (1.0 mL), chlorobenzene **1a** (21.0 μL, 0.2 mmol), morpholine **2a** (39.0 μL, 0.4 mmol) and additives were injected by syringe. The resulting mixture was stirred at 110 °C for 24 h. After the reaction, the tubes were cooled to room temperature. Then naphthalene (12.8 mg, 0.1 mmol) was added as an internal standard, the organic phase was filtered through a cartridge and detected by GC to give the GC yields of **3a**.

Table S1. The effect of catalyst.[a]



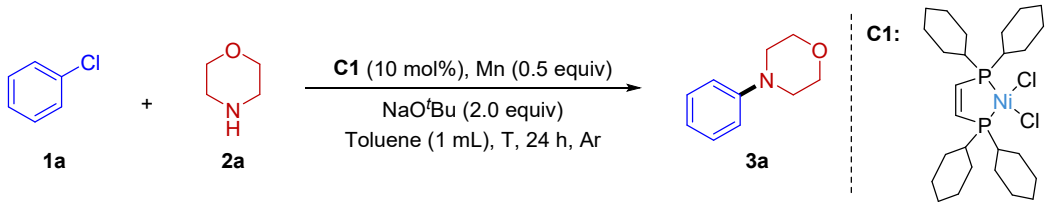
1a **2a** **3a**

Entry	Pre-Catalyst **C**	Yield (%)[b]
1	**C1**	16
2	**C2**	15
3	**C3**	n.d.
4	**C4**	10
5	**C5**	5
6	**C6**	n.d.



[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2 equiv), **C** (10 mol%), Mn (0.5 equiv), NaO^{t}Bu (2.0 equiv), Toluene (1.0 mL), Ar, 110 °C, 24 h. [b] Detected by GC using naphthalene as an internal standard.

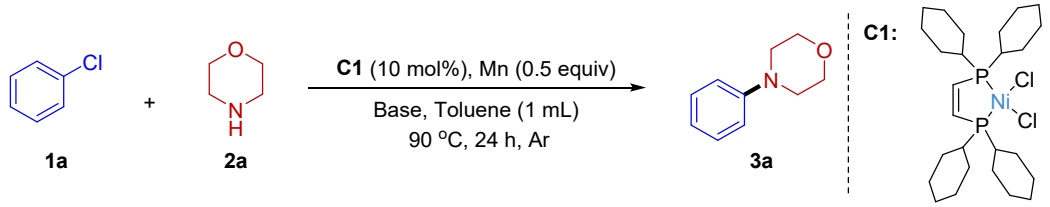
Table S2. The effect of temperature.[a]



Entry	T (°C)	Yield (%)[b]
1	110	16
2	100	19
3	90	22
4	80	18

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2 equiv), **C1** (10 mol%), Mn (0.5 equiv), NaO^{t}Bu (2.0 equiv), Toluene (1.0 mL), Ar, T, 24 h. [b] Detected by GC using naphthalene as an internal standard.

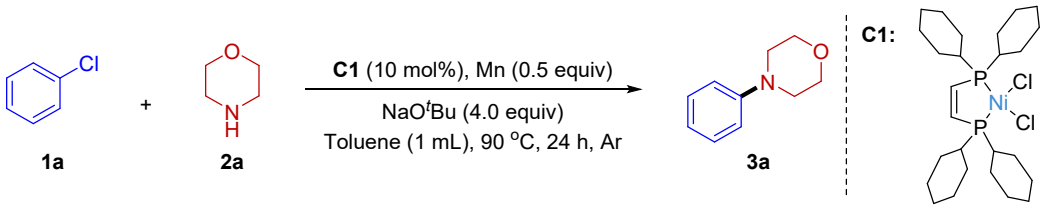
Table S3. The effect of equivalent of base.[a]



Entry	Base	Yield (%)[b]
1	NaO^{t}Bu (2 equiv)	22
2	NaO^{t}Bu (3 equiv)	34
3	NaO^{t}Bu (4 equiv)	42
4	NaO^{t}Bu (5 equiv)	40
5	Cs_2CO_3 (4 equiv)	8
6	KO^{t}Bu (4 equiv)	n.d.

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2 equiv), **C1** (10 mol%), Mn (0.5 equiv), Base, Toluene (1.0 mL), Ar, 90 °C, 24 h. [b] Detected by GC using naphthalene as an internal standard.

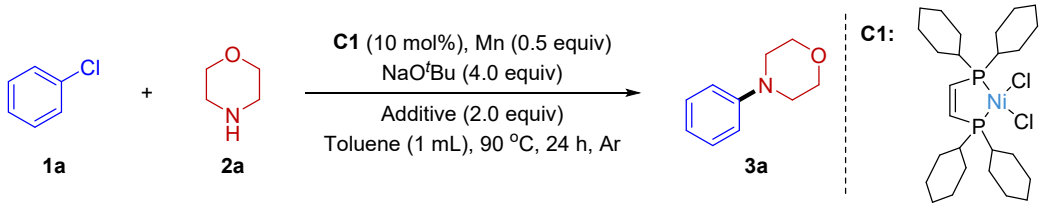
Table S4. The effect of reactant ratio.[a]



Entry	**2a** (equiv)	Yield (%)[b]
1	1.5	25
2	2.0	42
3	2.5	40
4	3	37

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a**, **C1** (10 mol%), Mn (0.5 equiv), NaO^{t}Bu (4.0 equiv), Toluene (1.0 mL), Ar, 90 °C, 24 h. [b] Detected by GC using naphthalene as an internal standard.

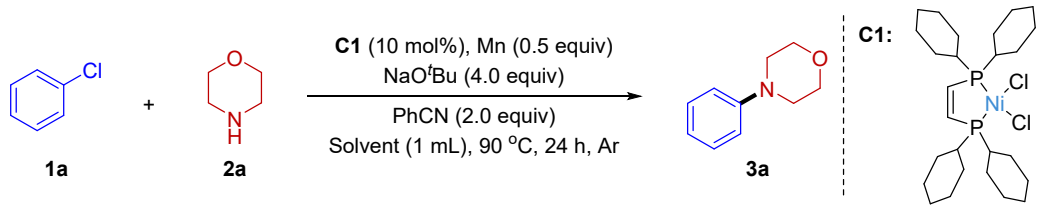
Table S5. The effect of additive.[a]



Entry	Additive	Yield (%)[b]
1	/	42
2	MeCN	51
3	PhCN	95
4	DMAP	65
5[c]	PhCN	4

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2.0 equiv), **C1** (10 mol%), Mn (0.5 equiv), NaO^{t}Bu (4.0 equiv), Additive (2.0 equiv), Toluene (1.0 mL), Ar, 90 °C, 24 h. [b] Detected by GC using naphthalene as an internal standard. [c] Without **1a**.

Table S6. The effect of solvents.[a]

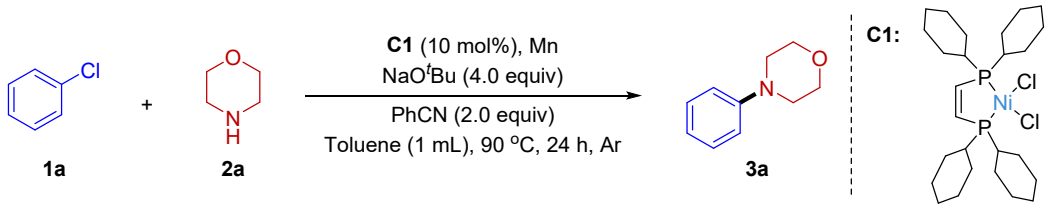


Entry	Solvent	Yield (%)[b]
1	Toluene	95
2	MeCN	62
3	THF	16

4	2-MeTHF	65

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2.0 equiv), **C1** (10 mol%), Mn (0.5 equiv), NaO^{t}Bu (4.0 equiv), PhCN (2.0 equiv), Solvent (1.0 mL), Ar, 90 °C, 24 h. [b] Detected by GC using naphthalene as an internal standard.

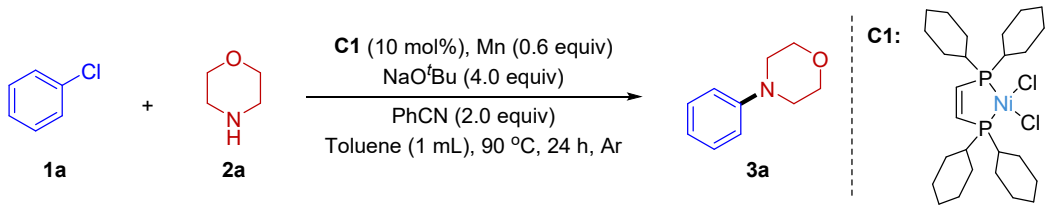
Table S7. The amount of Mn.[a]



Entry	Mn (equiv)	Yield (%)[b]
1	0.4	86
2	0.5	95
3	0.6	99
4	0.7	99

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2.0 equiv), **C1** (10 mol%), Mn, NaO^{t}Bu (2.0 equiv), PhCN (2.0 equiv), Toluene (1.0 mL), Ar, 90 °C, 24 h. [b] Detected by GC using naphthalene as an internal standard.

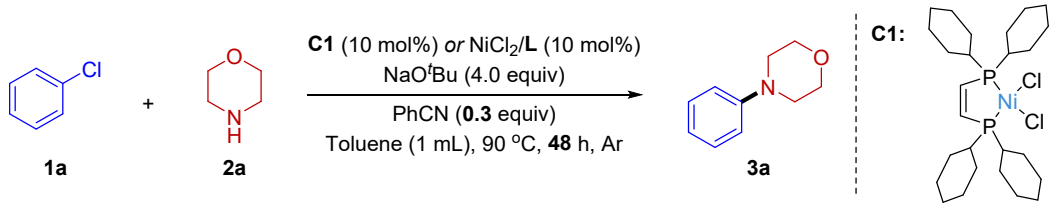
Table S8. The effect of Mn and PhCN in the reaction.[a]

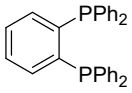
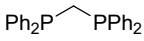
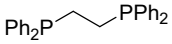
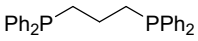
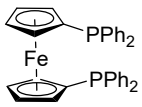
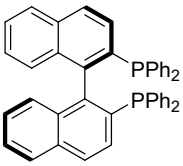


Entry	Base	Mn (mol%)	PhCN (equiv)	Yield of **3a** (%)[b]
1	NaO^{t}Bu (4.0)	60	2.0	99
2	Cs_2CO_3 (4.0)	60	2.0	50
3	NaO^{t}Bu (4.0)	60	/	40
4	NaO^{t}Bu (4.0)	/	2.0	93
5	NaO^{t}Bu (4.0)	/	0.3	82
6[c]	NaO^{t}Bu (4.0)	/	0.3	99
7	NaO^{t}Bu (4.0)	/	/	36

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2.0 equiv), **C1** (10 mol%), Mn (0.6 equiv), NaO^{t}Bu (4.0 equiv), PhCN (2.0 equiv), Toluene (1.0 mL), Ar, 90 °C, 24 h. [b] Detected by GC using naphthalene as an internal standard. [c] 48 h.

Table S9. The comparison with commercially available ligands.[a]



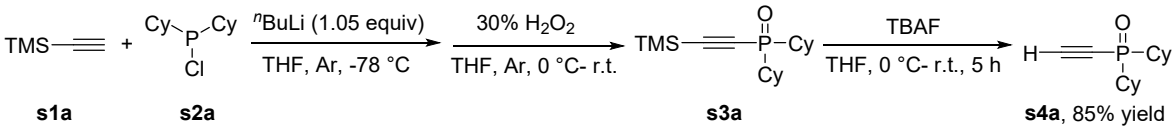
No.	C1 or L	Yield of 3a (%)
1	C1	99
2		69
3		n.d.
4		n.d.
5		n.d.
6		n.d.
7		n.d.
8		11
9		n.d.

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2.0 equiv), **C1** (10 mol%) or $NiCl_2$ (10 mol%) and **L** (10 mol%), NaO^{t}Bu (4.0 equiv), PhCN (0.3 equiv), Toluene (1.0 mL), Ar, 90 °C, 48 h. [b] Detected by GC using naphthalene as an internal standard.

3. General procedure for the synthesis of ligands and Ni-complexes

The precatalysts used in the paper were synthesized according to the literature.[3]

Step 1:

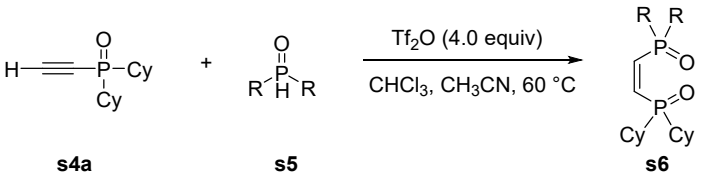


s1a **s2a** **s3a** **s4a**, 85% yield

General procedure for synthesis of alkynyl phosphine oxides (**Step1**): To an oven-dried flask was added THF (200.0 mL) and alkyne **s1a** (21 mmol, 1.05 equiv), the mixture was cooled to -78 °C, followed by the dropwise addition of ^{n}BuLi (21 mmol, 1.05 equiv.) for 0.5-1 h under argon. The mixture was transferred to room temperature and stirred for 20-30 minutes, then the resulting mixture was again cooled to -78 °C and the dicyclohexylchlorophosphine **s2a** (20 mmol, 1.0 equiv) was added dropwise over 10-20 minutes. The resulting mixture was stirred at room temperature for 2 hours, then cooled to 0 °C and H_2O_2 (30%, 5 mL) was added slowly. The reaction mixture was warmed to room temperature and stirred for 15 minutes. The reaction was quenched with water (20 mL), and the aqueous phase was extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with brine, dried over $MgSO_4$, and the solvent removed under reduced pressure, the crude product was directly subjected to desilication reaction without purification

The crude product was added THF (40.0 mL), and then TBAF (1.0 M in THF, 0.18 equiv relative to phosphorus chloride) was added at 0 °C. The mixture was stirred under air at room temperature for 5 h. Afterwards, water was added and extracted with EtOAc (3 x 30 mL), The combined organic layer was washed with brine, dried over $MgSO_4$, and the solvent removed under reduced pressure, the target product was finally separated and purified by silica gel column chromatography to give **s4a** as white solid (85% yield). The spectral data are agreement with those reported previously.[4]

Step 2:

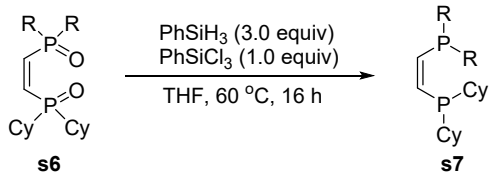


s4a **s5** **s6**

General procedure for the synthesis of *cis*-vinyl bisphosphine oxide (**Step 2**): A 50 mL oven-dried sealed tube equipped with a magnetic stir bar was charged with secondary phosphine oxide **s5** (4 mmol, 2.0 equiv), alkynylphosphine oxide **s4a** (2 mmol, 1.0 equiv). The tube was evacuated and backfilled with Ar (three times) and then $CHCl_3$ (20.0 mL) and CH_3CN (2 mL) was added sequentially via a syringe. The resulting mixture was stirred until it became a homogeneous solution. Tf_2O (8 mmol, 4.0 equiv) was then added by a syringe. The resulting mixture was stirred for 3 h at 60 °C. After cooled to ambient temperature, sat. $NaHCO_3$ aq. was added until no gas was released, and the resulting mixture was extracted with DCM (3 x 20.0 mL). The organic layer was washed with brine, and dried over $MgSO_4$ and volatiles were removed under reduced pressure. The residue was purified by flash column

chromatography on silica gel to give the desired products *cis*-vinyl bisphosphine oxide **s6** as white solid (50%-80% yield). The spectral data are consistent with previously reported data.[3]

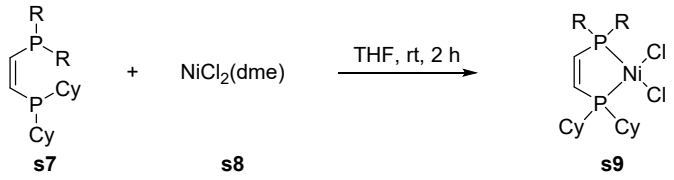
Step 3:



s6 **s7**

General procedure for reduction of *cis*-vinyl bisphosphine oxide (Step 3): A 50 mL oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl bisphosphine oxids **s6** (2 mmol, 1.0 equiv). The tube was evacuated and backfilled with Ar (three times) and then THF (20 mL), $PhSiH_3$ (6 mmol, 3.0 equiv) and $PhSiCl_3$ (2 mmol, 1.0 equiv) was added sequentially via a syringe. The resulting mixture was stirred for 16 h at 60 °C. After that, the reaction was cooled to room temperature and the reaction was quenched with water (5.0 mL) and the resulting mixture was extracted with EtOAc (3 x 20.0 mL). The organic layer was washed with brine, and dried over $MgSO_4$ and volatiles were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel to give the desired product **s7** (50%-75% yield).

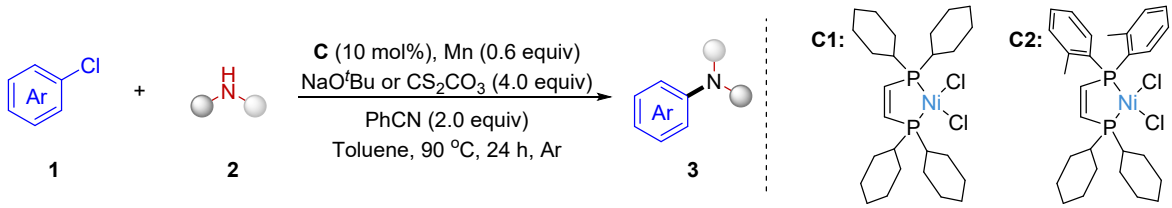
Step 4:



s7 **s8** **s9**

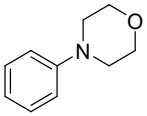
General steps for the synthesis of *cis*-diphosphine ethene ligand-Ni complexes (Step 4)[8]: A 50 mL oven-dried sealed tube equipped with a magnetic stir bar was charged with *cis*-diphosphine ethene ligand **s7** (1.05 mmol, 1.05 equiv), $NiCl_2$(dme) (1.0 mmol, 1.0 equiv). The tube was evacuated and backfilled with Ar (three times) and then THF (15 mL) was added sequentially via a syringe. The resulting mixture was stirred at room temperature for 2 h. When yellow flocculent precipitate appeared in the system, *n*-hexane (5 mL) was added to promote the precipitation of the product. The suspension was filtered, and washed with *n*-pentane for 3 times, and the obtained solid was dried to obtain the target product (60%-80% yield). The structures of the complexes were characterized by single crystals.

4. General procedure for the C-N coupling reaction of aryl chlorides

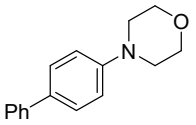


General procedure A: A 10 mL schlenk tube with screw-cap was charged with pre-catalyst **C** (10 mol%, **C1**: 5.5 mg, **C2**: 5.7 mg), Mn (6.6 mg, 0.6 equiv), amines (if solid, 0.4 mmol, 2.0 equiv), NaO^{t}Bu (76.9 mg, 0.8 mmol, 4.0 equiv) or Cs_2CO_3 (260 mg, 0.8 mmol, 4.0 equiv), PhCN (41.0 μL, 0.4 mmol, 2.0 equiv) and an oven-dried stirring bar. The tube was evacuated and back purged with nitrogen and repeated three times, dry toluene (1.0 mL), alkyl clorides (0.2 mmol, 1.0 equiv) and amines (if liquid, 0.4 mmol, 2.0 equiv) were injected by syringe. The resulting mixture was stirred at 90 °C for 24 h. After the reaction, the tube was cooled to room temperature. The mixture was concentrated under reduced pressure and the crude mixture was purified by column chromatography on silica gel (PE/EA) to afford the corresponding products **3**.

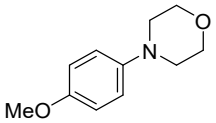
5. Characterization and procedure of the products



4-Phenylmorpholine (3a):[5] The title compound was prepared according to the general procedure A from chlorobenzene (21.0 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a white solid (32.2 mg, 99%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.9 Hz, 2H), 6.94 (d, *J* = 8.2 Hz, 2H), 6.90 (d, *J* = 7.3 Hz, 1H), 3.98 – 3.79 (m, 4H), 3.26 – 3.09 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.2, 129.1, 120.0, 115.6, 66.9, 49.3.

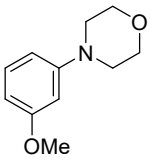


4-([1,1'-Biphenyl]-4-yl)morpholine (3b):[6] The title compound was prepared according to the general procedure A from 4-chloro-1,1'-biphenyl (37.7 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a white solid (40.1 mg, 84%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.52 (m, 4H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.01 (d, *J* = 8.6 Hz, 2H), 4.03 – 3.81 (m, 4H), 3.36 – 3.13 (m, 4H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.5, 140.7, 132.6, 128.7, 127.7, 126.5, 126.5, 115.7, 66.8, 49.1.

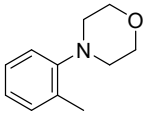


4-(4-Methoxyphenyl)morpholine (3c):[5] The title compound was prepared according to the general procedure A from 1-chloro-4-methoxybenzene (24.5 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified

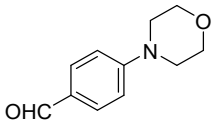
by flash chromatography (PE/EA = 8:1) to give the product as a white solid (26.7 mg, 69%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.97 – 6.78 (m, 4H), 3.92 – 3.81 (m, 4H), 3.77 (s, 1H), 3.14 – 2.99 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.0, 145.7, 117.8, 114.5, 67.0, 55.6, 50.9.



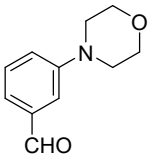
4-(3-Methoxyphenyl)morpholine (3d):[7] The title compound was prepared according to the general procedure A from 1-chloro-3-methoxybenzene (24.5 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 8:1) to give the product as a yellow oil (35.7 mg, 92%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 8.0 Hz, 1H), 6.54 (d, *J* = 7.3 Hz, 1H), 6.45 (d, *J* = 7.8 Hz, 2H), 3.95 – 3.82 (m, 4H), 3.80 (s, 3H), 3.25 – 3.08 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.6, 152.6, 129.8, 108.4, 104.6, 102.2, 66.8, 55.1, 49.2.



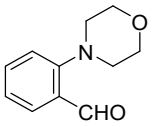
4-(*o*-Tolyl)morpholine (3e):[8] The title compound was prepared according to the general procedure A from 1-chloro-2-methylbenzene (23.5 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 5:1) to give the product as a white solid (12.9 mg, 36%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.2 Hz, 2H), 7.08 – 6.95 (m, 2H), 4.20 – 3.40 (m, 4H), 2.92 (dd, *J* = 5.5, 3.6 Hz, 4H), 2.33 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.2, 132.6, 131.1, 126.6, 123.4, 118.9, 67.4, 52.2, 17.8.



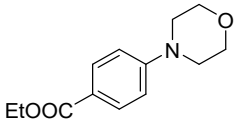
4-Morpholinobenzaldehyde (3f):[9] The title compound was prepared according to the general procedure A from 4-chlorobenzaldehyde (28.1 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 6:1) to give the product as a yellow solid (31.1 mg, 81%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.76 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 3.98 – 3.74 (m, 4H), 3.45 – 3.21 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.5, 155.1, 131.8, 127.6, 113.4, 66.4, 47.2.



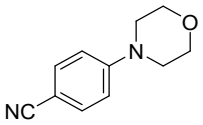
3-Morpholinobenzaldehyde (3g):[6] The title compound was prepared according to the general procedure A from 3-chlorobenzaldehyde (23.5 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 6:1) to give the product as a yellow oil (19.1 mg, 50%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.50 – 7.32 (m, 3H), 7.17 (dd, *J* = 8.1, 2.4 Hz, 1H), 3.96 – 3.78 (m, 4H), 3.30 – 3.14 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.6, 151.7, 137.3, 129.8, 122.2, 121.5, 114.6, 66.7, 48.8.



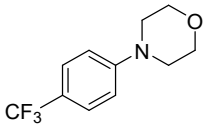
2-Morpholinobenzaldehyde (3h):[10] The title compound was prepared according to the general procedure A from 2-chlorobenzaldehyde (23.4 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 6:1) to give the product as a yellow oil (15.3 mg, 40%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.34 (s, 1H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.20 – 7.00 (m, 2H), 4.18 – 3.58 (m, 4H), 3.08 (t, *J* = 4.5 Hz, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.1, 155.3, 135.1, 130.3, 128.7, 122.9, 118.8, 66.9, 54.1.



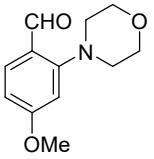
Ethyl 4-morpholinobenzoate (3i):[11] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (31 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 8:1) to give the product as a white solid (36.7 mg, 78%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.9 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.95 – 3.71 (m, 4H), 3.38 – 3.12 (m, 4H), 1.36 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.5, 154.1, 131.1, 120.6, 113.4, 66.5, 60.3, 47.7, 14.3.



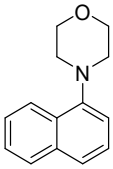
4-Morpholinobenzonitrile (3j):[7] The title compound was prepared according to the general procedure A from 4-chlorobenzonitrile (27.5 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 5:1) to give the product as a white solid (36.6 mg, 97%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.82 (s, 4H), 3.25 (s, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.3, 133.3, 119.8, 113.9, 100.6, 66.2, 47.1.



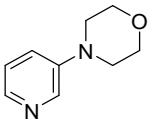
4-(4-(Trifluoromethyl)phenyl)morpholine (3k):[8] The title compound was prepared according to the general procedure A from 1-chloro-4-(trifluoromethyl)-benzene (28.0 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a colorless solid (32.2 mg, 70%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.6 Hz, 2H), 3.98 – 3.79 (m, 4H), 3.36 – 3.17 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.5, 126.4 (q, *J* = 3.6 Hz), 124.7 (q, *J* = 270.6 Hz), 121.0 (q, *J* = 32.6 Hz), 114.3, 66.6, 48.2. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -61.4.



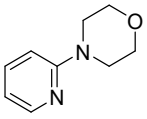
4-Methoxy-2-morpholinobenzaldehyde (3l):[10] The title compound was prepared according to the general procedure A from 2-chloro-4-methoxybenzaldehyde (34.1 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 8:1) to give the product as a white solid (39.3 mg, 89%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.12 (s, 1H), 7.77 (d, *J* = 8.6 Hz, 1H), 6.63 (d, *J* = 10.3 Hz, 1H), 6.53 (s, 1H), 3.87 (d, *J* = 4.4 Hz, 7H), 3.14 – 2.97 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.4, 165.2, 157.2, 133.4, 122.2, 107.8, 104.5, 66.8, 55.4, 53.9.



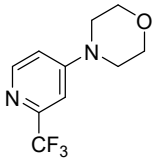
4-(Naphthalen-1-yl)morpholine (3m):[6] The title compound was prepared according to the general procedure A from 1-chloronaphthalene (27.5 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a white solid (26.7 mg, 63%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 9.0 Hz, 1H), 7.85 (d, *J* = 9.2 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 7.4 Hz, 1H), 4.06 – 3.92 (m, 4H), 3.23 – 3.00 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.4, 134.8, 128.8, 128.4, 125.9, 125.8, 125.4, 123.8, 123.4, 114.7, 67.5, 53.5.



4-(Pyridin-3-yl)morpholine (3n):[8] The title compound was prepared according to the general procedure A from 3-chloropyridine (19 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 2:1) to give the product as a white solid (27.5mg, 84%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.10 (s, 1H), 7.15 (s, 2H), 3.93 – 3.73 (m, 4H), 3.25 – 3.08 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.8, 141.0, 138.2, 123.4, 122.0, 66.6, 48.5.

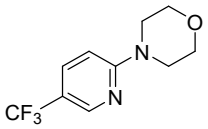


4-(Pyridin-2-yl)morpholine (3o):[8] The title compound was prepared according to the general procedure A from 2-chloropyridine (19.0 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 2:1) to give the product as a colorless oil (23.8 mg, 73%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 3.8 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 6.72 – 6.55 (m, 2H), 3.89 – 3.73 (m, 4H), 3.57 – 3.38 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.5, 147.9, 137.4, 113.7, 106.8, 66.7, 45.5.

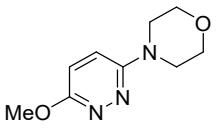


4-(2-(Trifluoromethyl)pyridin-4-yl)morpholine (3p): The title compound was prepared according to the general procedure A from 4-chloro-2-(trifluoromethyl)- pyridine (26.0 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol).

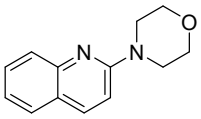
The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a yellow solid (38.6 mg, 83%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.00 (s, 1H), 6.74 (s, 1H), 3.94 – 3.73 (m, 4H), 3.45 – 3.23 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.7, 150.4, 149.0 (q, *J* = 33.4 Hz), 121.7 (q, *J* = 274.5 Hz), 109.6, 104.6, 66.1, 45.9. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -68.4. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{12}F_3N_2O$ 233.0896; Found 233.0900.



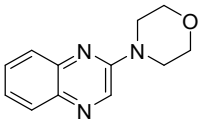
4-(5-(Trifluoromethyl)pyridin-2-yl)morpholine (3q):[12] The title compound was prepared according to the general procedure A from 2-chloro-5-(trifluoromethyl)- pyridine (36.3 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 6:1) to give the product as a yellow solid (31.6 mg, 68%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.65 (d, *J* = 8.9 Hz, 1H), 6.62 (d, *J* = 9.0 Hz, 1H), 3.89 – 3.75 (m, 4H), 3.69 – 3.54 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.6, 145.8, 134.5, 124.5 (q, *J* = 270.4 Hz), 115.7 (q, *J* = 33.0 Hz), 105.5, 66.6, 45.0. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -61.2.



4-(6-Methoxypyridazin-3-yl)morpholine (3r): The title compound was prepared according to the general procedure A from 3-chloro-6-methoxypyridazine (28.9 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a white solid (20.7 mg, 53%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.98 (d, *J* = 9.6 Hz, 1H), 6.85 (d, *J* = 9.6 Hz, 1H), 4.01 (s, 3H), 3.91 – 3.76 (m, 4H), 3.53 – 3.41 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.4, 157.7, 119.4, 118.5, 66.5, 54.3, 46.5. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_9H_{14}N_3O_2$ 196.1084; Found 196.1085.

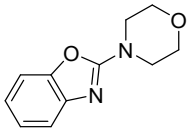


4-(Quinolin-2-yl)morpholine (3s):[13] The title compound was prepared according to the general procedure A from 2-chloroquinoline (32.7 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 5:1) to give the product as a yellow solid (37.3 mg, 87%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 9.1 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.4 Hz, 1H), 6.91 (d, *J* = 9.1 Hz, 1H), 3.90 – 3.78 (m, 4H), 3.74 – 3.63 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.4, 147.7, 137.5, 129.5, 127.2, 126.7, 123.2, 122.6, 109.2, 66.8, 45.5.

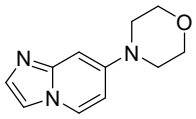


4-(Quinoxalin-2-yl)morpholine (3t):[13] The title compound was prepared according to the general procedure A from 2-chloroquinoxaline (32.9 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a tan solid (40.3 mg, 94%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 3.90

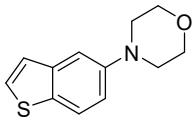
– 3.80 (m, 4H), 3.78 – 3.69 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.2, 141.4, 137.1, 135.3, 130.1, 128.6, 126.5, 125.0, 66.5, 45.0.



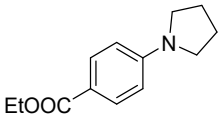
2-Morpholinobenzo[d]oxazole (3u):[14] The title compound was prepared according to the general procedure A from 2-chlorobenzo[*d*]oxazole (24.9 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a yellow solid (24.9 mg, 61%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 7.7 Hz, 1H), 7.04 (t, *J* = 8.1 Hz, 1H), 3.87 – 3.76 (m, 4H), 3.74 – 3.63 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.1, 148.7, 142.8, 124.1, 120.9, 116.4, 108.8, 66.2, 45.7.



4-(Imidazo[1,2-*a*]pyridin-7-yl)morpholine (3v): The title compound was prepared according to the general procedure A from 7-chloroimidazo[1,2-*a*]pyridine (22.0 μL, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (EA/MeOH = 20:1) to give the product as a yellow solid (35.4 mg, 86%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.5 Hz, 1H), 7.45 (s, 1H), 7.34 (s, 1H), 6.80 (s, 1H), 6.56 (dd, *J* = 7.5, 2.2 Hz, 1H), 3.92 – 3.81 (m, 4H), 3.25 – 3.13 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.5, 147.1, 133.0, 125.7, 110.6, 106.2, 97.9, 66.5, 48.7. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}N_3O$ 204.1131; Found 204.1136.

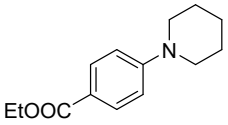


4-(Benzo[b]thiophen-5-yl)morpholine (3w):[8] The title compound was prepared according to the general procedure A from 5-chlorobenzo[*b*]thiophene (33.7 mg, 0.2 mmol) and morpholine (39.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a white solid (37.7 mg, 86%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.8 Hz, 1H), 7.39 (d, *J* = 5.4 Hz, 1H), 7.27 (s, 1H), 7.22 (d, *J* = 5.5 Hz, 1H), 7.04 (dd, *J* = 8.8, 2.2 Hz, 1H), 3.95 – 3.78 (m, 4H), 3.23 – 3.05 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.1, 140.7, 132.0, 127.1, 123.6, 122.8, 116.1, 109.4, 66.9, 50.5.

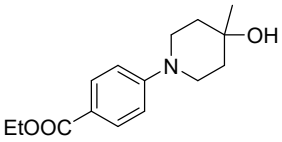


Ethyl 4-(pyrrolidin-1-yl)benzoate (3x):[15] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and pyrrolidine (36.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a white solid (38.5 mg, 88%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 – 7.86 (m, 2H), 6.48 (d, *J* = 8.9 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.32 (t, *J* = 6.6 Hz, 4H), 2.08 – 1.95

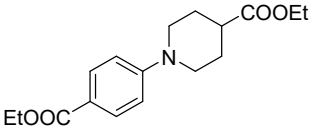
(m, 4H), 1.36 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.1, 150.7, 131.2, 116.5, 110.5, 59.9, 47.4, 25.3, 14.4.



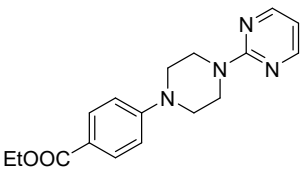
Ethyl 4-(piperidin-1-yl)benzoate (3y):[16] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and piperidine (39.5 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 8:1) to give the product as a white solid (24.5 mg, 53%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 4.32 (q, J = 7.1 Hz, 2H), 3.32 (s, 4H), 1.73 – 1.58 (m, 6H), 1.36 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 154.4, 131.1, 119.0, 113.6, 60.2, 48.8, 25.3, 24.3, 14.4.



Ethyl 4-(4-hydroxy-4-methylpiperidin-1-yl)benzoate (3z): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and 4-methylpiperidin-4-ol (46.1 mg, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 3:1) to give the product as a white solid (46.3 mg, 88%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.89 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 4.30 (q, J = 7.1 Hz, 2H), 3.51 (d, J = 13.0 Hz, 2H), 3.38 – 3.26 (m, 2H), 1.81 (s, 1H), 1.73 – 1.62 (m, 4H), 1.35 (t, J = 7.1 Hz, 3H), 1.27 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.7, 153.8, 131.2, 119.1, 113.5, 67.8, 60.2, 44.2, 37.8, 29.9, 14.4. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{22}NO_3$ 264.1594; Found 264.1598.

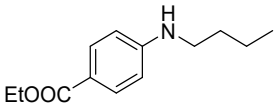


Ethyl 1-(4-(ethoxycarbonyl)phenyl)piperidine-4-carboxylate (3aa): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and ethyl piperidine-4-carboxylate (63.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a white solid (39.5 mg, 65%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 4.31 (q, J = 7.1 Hz, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.79 (d, J = 12.9 Hz, 2H), 2.92 (t, J = 12.0 Hz, 2H), 2.55 – 2.43 (m, 1H), 2.00 (d, J = 13.3 Hz, 2H), 1.89 – 1.74 (m, 2H), 1.35 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.4, 166.6, 153.9, 131.1, 119.7, 113.8, 60.5, 60.2, 47.4, 40.9, 27.5, 14.4, 14.2. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{24}NO_4$ 306.1700; Found 306.1705.

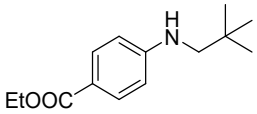


Ethyl 4-(4-(pyrimidin-2-yl)piperazin-1-yl)benzoate (3ab):[17] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and 2-(piperazin-1-yl)pyrimidine (65.7 mg, 0.4

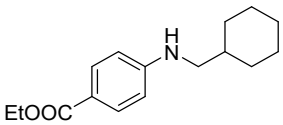
mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a white solid (46.2 mg, 74%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.32 (d, *J* = 4.7 Hz, 2H), 7.94 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.51 (t, *J* = 4.7 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.04 – 3.91 (m, 4H), 3.46 – 3.31 (m, 4H), 1.35 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.5, 161.5, 157.7, 153.9, 131.1, 120.3, 113.7, 110.2, 60.3, 47.3, 43.2, 14.4.



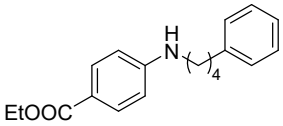
Ethyl 4-(butylamino)benzoate (3ac):[18] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and butan-1-amine (39.6 mg, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a white solid (39.6 mg, 89%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.8 Hz, 2H), 6.53 (d, *J* = 8.8 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.14 (s, 1H), 3.15 (t, *J* = 7.1 Hz, 2H), 1.64 – 1.56 (m, 2H), 1.46 – 1.38 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.95 (t, *J* =7.4 Hz, 3H). **^{13}C NMR** (151 MHz, CDCl3) δ 166.9, 152.1, 131.4, 118.2, 111.2, 60.1, 43.0, 31.3, 20.1, 14.4, 13.8.



Ethyl 4-(neopentylamino)benzoate (3ad): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and 2,2-dimethylpropan-1-amine (47.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a white solid (44.0 mg, 99%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.7 Hz, 2H), 6.56 (d, *J* = 8.7 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.18 (s, 1H), 2.95 (s, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.99 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 152.6, 131.4, 118.1, 111.2, 60.0, 54.9, 32.0, 27.5, 14.4. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{22}NO_2$ 236.1645; Found 236.1648.

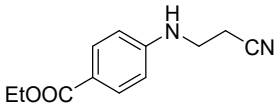


Ethyl 4-((cyclohexylmethyl)amino)benzoate (3ae):[19] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and cyclohexylmethanamine (52.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a white solid (47.3 mg, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.8 Hz, 2H), 6.53 (d, *J* = 8.8 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.24 (s, 1H), 2.99 (d, *J* = 6.4 Hz, 2H), 1.85 – 1.65 (m, 5H), 1.63 – 1.50 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.31 – 1.13 (m, 3H), 1.05 – 0.90 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 152.2, 131.4, 118.0, 111.2, 60.0, 49.8, 37.5, 31.1, 26.4, 25.8, 14.4.

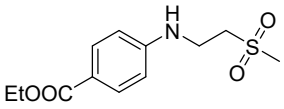


Ethyl 4-((4-phenylbutyl)amino)benzoate (3af):[20] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and 4-phenylbutan-1-amine (66.5 μL, 0.4 mmol). The

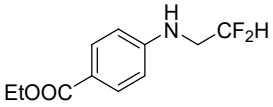
crude residue was purified by flash chromatography (PE/EA = 8:1) to give the product as a white solid (54.9 mg, 92%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.25 – 7.17 (m, 3H), 6.54 (d, *J* = 8.8 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.15 (s, 1H), 3.18 (t, *J* = 7.0 Hz, 2H), 2.68 (t, *J* = 7.5 Hz, 2H), 1.81 – 1.71 (m, 2H), 1.71 – 1.61 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.8, 151.9, 141.9, 131.4, 128.3, 125.8, 118.3, 111.2, 60.0, 43.1, 35.5, 28.7, 14.4.



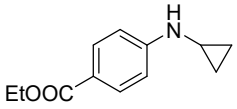
Ethyl 4-((2-cyanoethyl)amino)benzoate (3ag): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and 3-aminopropanenitrile (31.5 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a white solid (23.3 mg, 53%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.5 Hz, 2H), 6.58 (d, *J* = 8.5 Hz, 2H), 4.51 (s, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.57 (q, *J* = 6.3 Hz, 2H), 2.66 (t, *J* = 6.5 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.5, 150.0, 131.6, 120.1, 117.9, 111.7, 60.4, 39.2, 18.1, 14.4. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{15}N_2O_2$ 219.1128; Found 219.1133.



Ethyl 4-((2-(methylsulfonyl)ethyl)amino)benzoate (3ah): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and 2-(methylsulfonyl)ethan-1-amine (41.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a white solid (43.8 mg, 80%). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.73 (d, *J* = 8.6 Hz, 2H), 6.66 (t, *J* = 7.1 Hz, 3H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.56 (q, *J* = 6.4 Hz, 2H), 3.36 (t, *J* = 6.6 Hz, 2H), 3.03 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 165.8, 151.8, 131.0, 117.0, 111.2, 59.6, 52.6, 41.1, 36.2, 14.3. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{18}NO_4S$ 272.0951; Found 272.0956.

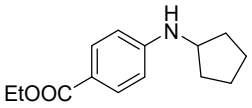


Ethyl 4-((2,2-Difluoroethyl)amino)benzoate (3ai):[21] The title compound was prepared according to the general procedure A from 4-chlorobenzoate (31.1 μL, 0.2 mmol) and 2,2-difluoroethanamine (21.1 μL, 0.3 mmol). The crude residue was purified by flash chromatography (PE/EA = 5:1) to give the product as a white solid (34.4 mg, 75%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.5 Hz, 2H), 6.64 (s, 2H), 5.92 (tt, *J* = 55.8, 4.2 Hz, 1H), 4.36 – 4.28 (m, 3H, overlapping Hs), 3.60 (td, J = 14.5, 4.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.6, 150.6, 131.6, 120.4, 114.1 (t, *J* = 242.3 Hz), 111.8, 60.4, 45.8 (t, *J* = 26.1 Hz), 14.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -122.6.

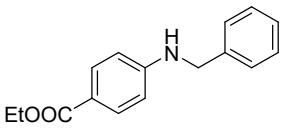


Ethyl 4-(cyclopropylamino)benzoate (3aj):[15] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and cyclopropanamine (25.5 μL, 0.4 mmol). The crude residue

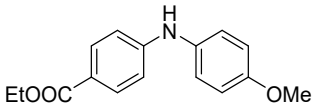
was purified by flash chromatography (PE/EA = 8:1) to give the product as a white solid (31.9 mg, 78%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.6 Hz, 2H), 6.73 (d, *J* = 8.7 Hz, 2H), 4.59 (s, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.46 (s, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 0.78 (d, *J* = 5.3 Hz, 2H), 0.53 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.9, 152.4, 131.3, 119.1, 111.9, 60.1, 24.7, 14.4, 7.5.



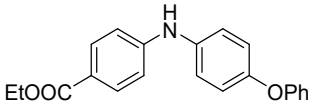
Ethyl 4-(cyclopentylamino)benzoate (3ak):[22] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and cyclopentanamine (39.5 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 10:1) to give the product as a white solid (44.9 mg, 96%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.9 Hz, 2H), 6.53 (d, *J* = 7.9 Hz, 2H), 4.31 (q, *J* = 6.5 Hz, 2H), 4.21 (s, 1H), 3.82 (s, 1H), 2.13 – 1.92 (m, 2H), 1.72 (s, 2H), 1.62 (s, 2H), 1.51 – 1.42 (m, 2H), 1.35 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.8, 151.6, 131.3, 118.0, 111.6, 60.0, 54.1, 33.3, 23.9, 14.4.



Ethyl 4-(benzylamino)benzoate (3al):[23] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and phenylmethanamine (44.0 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 8:1) to give the product as a white solid (52.0 mg, 96%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.8 Hz, 2H), 7.41 – 7.33 (m, 4H), 7.33 – 7.27 (m, 1H), 6.59 (d, *J* = 8.8 Hz, 2H), 4.60 (s, 1H), 4.38 (s, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.8, 151.7, 138.4, 131.4, 128.7, 127.4, 127.3, 118.9, 111.6, 60.1, 47.6, 14.4.

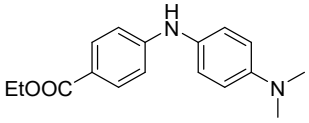


Ethyl 4-((4-methoxyphenyl)amino)benzoate (3am):[24] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and 4-methoxyaniline (49.3 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 8:1) to give the product as a white solid (52.0 mg, 96%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 6.01 (d, *J* = 6.3 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.6, 156.3, 149.7, 133.5, 131.4, 124.2, 120.2, 114.7, 113.2, 60.3, 55.4, 14.4.

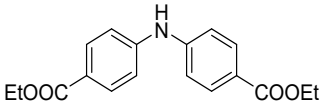


Ethyl 4-((4-phenoxyphenyl)amino)benzoate (3an): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and 4-phenoxyaniline (73.3 mg, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 8:1) to give the product as a yellow solid (62.8 mg, 94%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.5 Hz, 2H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H), 7.11 (t, *J* = 7.4

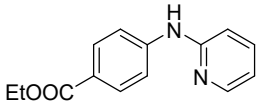
Hz, 1H), 7.03 (t, *J* = 8.5 Hz, 4H), 6.93 (d, *J* = 8.6 Hz, 2H), 6.17 (s, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.5, 157.5, 152.8, 148.7, 136.2, 131.4, 129.7, 123.0, 122.8, 120.8, 120.1, 118.3, 113.8, 60.4, 14.3. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{20}NO_3$ 334.1438; Found 334.1442.



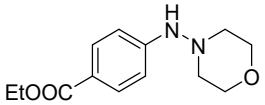
Ethyl 4-((4-(dimethylamino)phenyl)amino)benzoate (3ao):[25] The title compound was prepared according to the general procedure A from A ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and N^1,N^1-dimethylbenzene-1,4-diamine (54.4 mg, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 6:1) to give the product as a yellow solid (53.0 mg, 93%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.7 Hz, 2H), 7.10 (d, *J* = 8.7 Hz, 2H), 6.81 – 6.71 (m, 4H) 5.94 (s, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.95 (s, 6H), 1.37 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.7, 150.5, 148.0, 131.3, 129.8, 124.8, 119.5, 113.4, 112.7, 60.1, 40.8, 14.4.



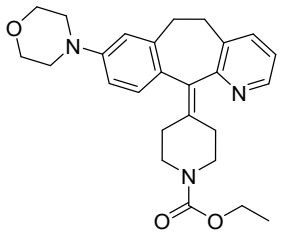
Diethyl 4,4'-azanediyldibenzoate (3ap):[26] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and ethyl 4-aminobenzoate (66.1 mg, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a white solid (59.3 mg, 95%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.6 Hz, 4H), 7.13 (d, *J* = 8.5 Hz, 4H), 4.34 (q, *J* = 7.1 Hz, 4H), 1.36 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.3, 145.9, 131.2, 123.0, 116.7, 60.6, 14.3.



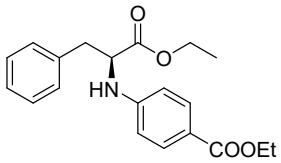
Ethyl 4-(pyridin-2-ylamino)benzoate (3aq):[27] The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and pyridin-2-amine (37.6 mg, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a white solid (42.2 mg, 87%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.27 (d, *J* = 4.6 Hz, 1H), 7.98 (d, *J* = 8.7 Hz, 2H), 7.59 (s, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.3 Hz, 1H), 6.86 – 6.77 (m, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.4, 154.7, 148.2, 145.2, 137.8, 131.0, 123.1, 117.3, 116.1, 110.1, 60.5, 14.3.



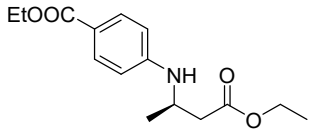
Ethyl 4-(morpholinoamino)benzoate (3ar): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and morpholin-4-amine (37.5 μL, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a white solid (31.9 mg, 64%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.89 (s, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.80 (t, *J* = 4.5 Hz, 4H), 2.74 (s, 4H), 1.35 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.6, 151.0, 131.3, 120.9, 111.9, 66.8, 60.2, 56.2, 14.4. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{19}N_2O_3$ 251.1390; Found 251.1395.



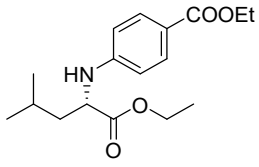
Ethyl 4-(8-morpholino-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (3as): The title compound was prepared according to the general procedure A from Loratadine (76.6 mg, 0.2 mmol) and morpholine (39 μL, 0.4 mmol). The crude residue was purified by flash chromatography (EA) to give the product as a white solid (46.2 mg, 53%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 4.4 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.13 – 6.98 (m, 2H), 6.77 – 6.63 (m, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.95 – 3.70 (m, 6H), 3.45 – 3.26 (m, 2H), 3.24 – 3.01 (m, 6H), 2.79 (tt, *J* = 15.3, 5.5 Hz, 2H), 2.52 – 2.21 (m, 4H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.3, 155.4, 150.3, 146.3, 138.2, 136.9, 136.0, 134.8, 133.6, 130.4, 130.3, 121.8, 115.8, 113.1, 66.8, 61.1, 49.0, 44.7, 32.4, 31.5, 30.6, 30.4, 14.6. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{32}N_3O_3$ 434.2438; Found 434.2428.



Ethyl (*S*)-4-((1-ethoxy-1-oxo-3-phenylpropan-2-yl)amino)benzoate (3at): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and ethyl *L*-phenylalaninate (77.3 mg, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 3:1) to give the product as a colourless oil (51.0 mg, 75%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.7 Hz, 2H), 7.32 – 7.18 (m, 3H), 7.12 (d, *J* = 6.6 Hz, 2H), 6.54 (d, *J* = 8.7 Hz, 2H), 4.66 (d, *J* = 8.3 Hz, 1H), 4.44 – 4.36 (m, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.18 – 4.06 (m, 2H), 3.20 – 3.06 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.2, 166.6, 150.0, 135.8, 131.4, 129.2, 128.5, 127.0, 119.7, 112.1, 61.3, 60.2, 56.8, 38.2, 14.3, 14.0. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{24}NO_4$ 342.1700; Found 342.1705.



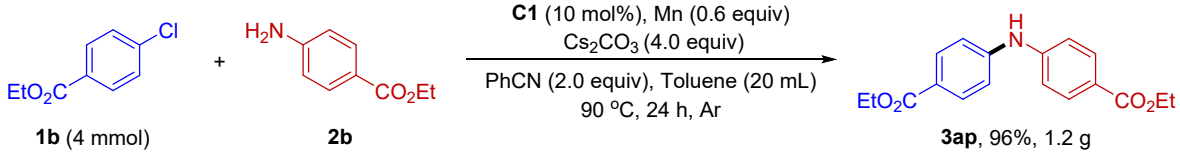
Ethyl (*R*)-4-((4-ethoxy-4-oxobutan-2-yl)amino)benzoate (3au): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and ethyl (*R*)-3-aminobutanoate (52.5 mg, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 4:1) to give the product as a colourless oil (47.8 mg, 86%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.7 Hz, 2H), 6.55 (d, *J* = 8.8 Hz, 2H), 4.40 (d, *J* = 7.7 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 4.04 – 3.91 (m, 1H), 2.65 – 2.54 (m, 1H), 2.50 – 2.40 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.27 (d, *J* = 6.5 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 166.7, 150.5, 131.5, 118.7, 111.8, 60.5, 60.1, 45.4, 40.7, 20.3, 14.3, 14.1. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{22}NO_4$ 280.1543; Found 280.1551.



Ethyl (*S*)-4-((1-ethoxy-4-methyl-1-oxopentan-2-yl)amino)benzoate (3av): The title compound was prepared according to the general procedure A from ethyl 4-chlorobenzoate (30.0 μL, 0.2 mmol) and ethyl *L*-leucinate (63.7 mg, 0.4 mmol). The crude residue was purified by flash chromatography (PE/EA = 3:1) to give the product as a colourless oil (44.2 mg, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.6 Hz, 2H), 6.56 (d, *J* = 8.7 Hz, 2H), 4.52 (d, *J* = 8.7 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 1.86 – 1.57 (m, 4H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.06 – 0.85 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.8, 166.6, 150.7, 131.4, 119.6, 111.9, 61.1, 60.2, 54.5, 41.9, 24.8, 22.6, 22.1, 14.3, 14.1. **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{26}NO_4$ 308.1856; Found 308.1859.

6. Synthetic applications of Ni complex-catalyzed C-N coupling reactions

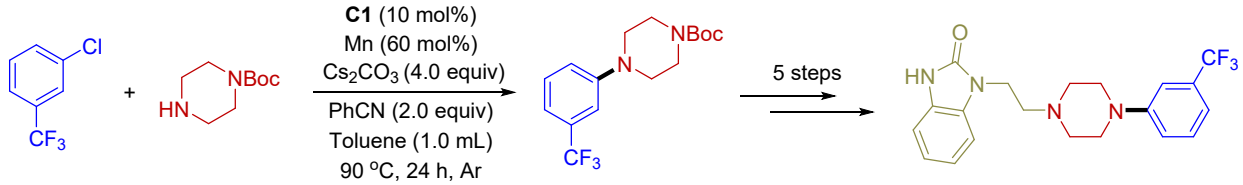
6.1 The gram-scale reaction



1b (4 mmol) **2b** **3ap**, 96%, 1.2 g

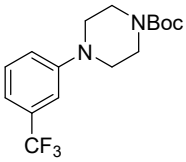
A 50 mL schlenk tube with screw-cap was charged with **C1** (110 mg, 5 mol%), Mn (132 mg, 60 mol%), and Cs_2CO_3 (5.2 g, 8 mmol, 4.0 equiv), and an oven-dried stirring bar. The tubes were evacuated and back purged with nitrogen and repeated three times, dry toluene (20 mL), ethyl 4-chlorobenzoate **1b** (600.0 μL, 4 mmol), ethyl 4-aminobenzoate **2b** (1.3 g, 8.0 mmol) and PhCN (820.0 μL, 8.0 mmol, 2.0 equiv) were injected by syringe. The resulting mixture was stirred at 90 °C for 24 h. After the reaction, the tubes were cooled to room temperature. The mixture was concentrated under reduced pressure and the crude mixture was purified by column chromatography on silica gel (PE/EA) to afford the corresponding products **3ap** as a white solid (1.2 g, 96%).

6.2 The synthesis of *Flibanserin* intermediates



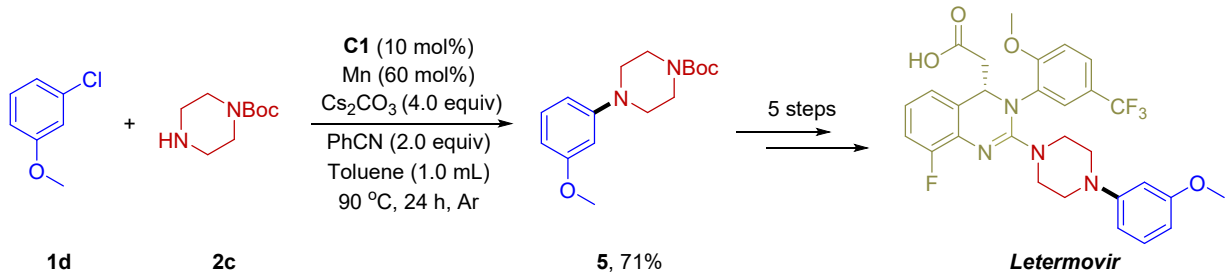
1c **2c** **4**, 82% ***Flibanserin***

A 10 mL schlenk tube with screw-cap was charged with **C1** (5.5 mg, 5 mol%), Mn (6.6 mg, 60 mol%), **2c** (74.5 mg, 0.4 mmol, 2.0 equiv), Cs_2CO_3 (260.6 mg, 0.8 mmol, 4.0 equiv), PhCN (41.0 μL, 0.4 mmol, 2.0 equiv) and an oven-dried stirring bar. The tubes were evacuated and back purged with nitrogen and repeated three times, dry toluene (1.0 mL), **1c** (27 μL, 0.2 mmol, 1.0 equiv) and PhCN (41.0 μL, 0.4 mmol, 2.0 equiv) were injected by syringe. The resulting mixture was stirred at 90 °C for 24 h. After the reaction, the tubes were cooled to room temperature. The mixture was concentrated under reduced pressure and the crude mixture was purified by column chromatography on silica gel (PE/EA) to afford the corresponding products **4** as a white solid (54.4 mg, 82%). ***Flubanserin*** can be synthesized based on the remaining steps reported in the literature.[28]



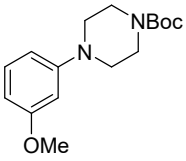
***tert*-Butyl 4-(3-(trifluoromethyl)phenyl)piperazine-1-carboxylate (4):**[28] white solid (54.4 mg, 82%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 (t, *J* = 8.1 Hz, 1H), 7.14 – 7.02 (m, 3H), 3.64 – 3.52 (m, 4H), 3.23 – 3.10 (m, 4H), 1.48 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.6, 151.3, 131.4 (q, *J* = 31.8 Hz), 129.6, 124.2 (q, *J* = 272.4 Hz), 119.3, 116.3 (q, *J* = 3.9 Hz), 112.6 (q, *J* = 3.9 Hz), 80.0, 48.8 (2C), 28.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.7.

6.3 The synthesis of *Letermovir* intermediates



1d **2c** **5**, 71% ***Letermovir***

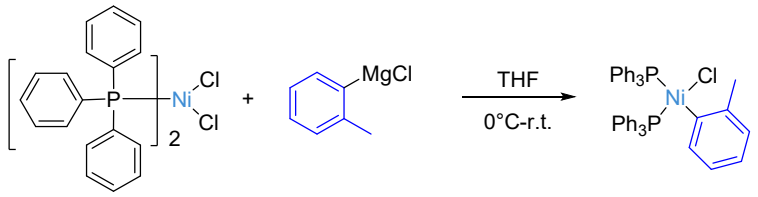
A 10 mL schlenk tube with screw-cap was charged with **C1** (5.5 mg, 5 mol%), Mn (6.6 mg, 60 mol%), **2c** (74.5 mg, 0.4 mmol, 2.0 equiv), Cs_2CO_3 (260.6 mg, 0.8 mmol, 4.0 equiv), PhCN (41.0 μL, 0.4 mmol, 2.0 equiv) and an oven-dried stirring bar. The tubes were evacuated and back purged with nitrogen and repeated three times, dry toluene (1.0 mL), **1d** (24.5 μL, 0.2 mmol, 1.0 equiv) and PhCN (41.0 μL, 0.4 mmol, 2.0 equiv) were injected by syringe. The resulting mixture was stirred at 90 °C for 24 h. After the reaction, the tubes were cooled to room temperature. The mixture was concentrated under reduced pressure and the crude mixture was purified by column chromatography on silica gel (PE/EA) to afford the corresponding products **5** as a colorless oil (41.3 mg, 71%). ***Letermovir*** can be synthesized based on the remaining steps reported in the literature.[29]



***tert*-Butyl 4-(3-methoxyphenyl)piperazine-1-carboxylate (5):**[30] colorless oil (41.3 mg, 71%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.18 (t, *J* = 8.1 Hz, 1H), 6.58 – 6.50 (m, 1H), 6.49 – 6.40 (m, 2H), 3.79 (s, 3H), 3.63 – 3.50 (m, 4H), 3.22 – 3.04 (m, 4H), 1.48 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.5, 154.7, 152.6, 129.8, 109.2, 104.9, 102.9, 79.8, 55.1, 49.3, 28.4.

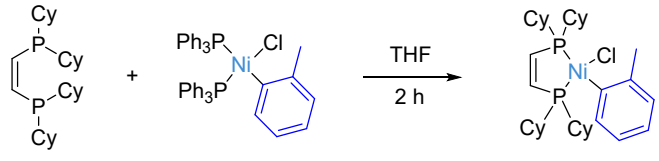
7. Mechanistic experiments

7.1 The synthesis of C3



s10 **s11**

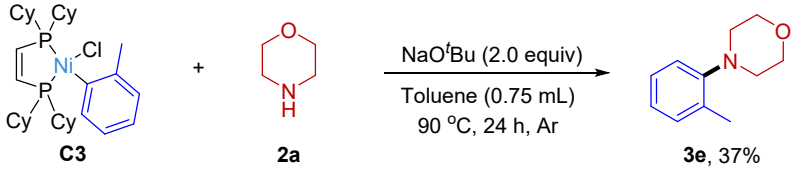
s11 was synthesized based on literature reports:[31] Bis(triphenylphosphine)nickel(II) dichloride **s10** (11.4 g, 17.4 mmol) was added to an oven-dried 500 mL round bottom flask equipped with a magnetic stir-bar and purged with nitrogen. THF (240 mL) was added via syringe and the reaction mixture was cooled to 0 ˚C in an ice bath. *o*-tolylmagnesium chloride (22.8 mL, 0.8 M in THF, 18.3 mmol) was then added dropwise via syringe. The reaction mixture was stirred for 15 min at 0˚C and an additional 1 h at room temperature and then was quenched with methanol (15 mL). The mixture was concentrated with the aid of a rotary evaporator and the resulting residue was triturated with the aid of sonication in methanol (450 mL) to produce a yellow suspension. The yellow suspension was filtered and the yellow solid was washed with methanol. The solid was then dissolved in CH_2Cl_2 (80 mL) and carefully filtered through a Whatman GF/D glass fiber filter to afford a homogenous orange solution that was concentrated with the aid of a rotary evaporator. The resulting orange solid was collected and triturated with pentane to afford the desired product as a yellow solid **s11** (7.4 g, 60%).



s7a **s11** **C3**

A 10 mL oven-dried sealed tube equipped with a magnetic stir bar was charged with *cis*-diphosphine ethene ligand **s9** (0.2 mmol, 1.0 equiv), bistriphenylphosphine-*o*-methylphenyl nickel chloride **s11** (0.2 mmol, 1.0 equiv). The tube was evacuated and backfilled with Ar (three times) and then THF (4.0 mL) was added sequentially via a syringe. The resulting mixture was stirred for 1 h. After the reaction, *n*-pentane was added to the system to obtain a suspension, the suspension was filtered, and washed with *n*-pentane for 3 times, and the obtained solid was dried to obtain the target product **C3** (74% yield). The structures of the complexes were characterized by single crystals.

7.2 The C-N coupling reactions of complex C3 with 2a



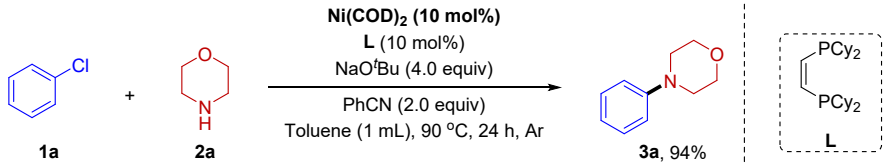
C3 **2a** **3e**, 37%

A 10 mL schlenk tube with screw-cap was charged with **C3** (60.6 mg, 0.1 mmol), NaO^{t}Bu (38.4 mg, 0.4 mmol, 2.0 equiv) and an oven-dried stirring bar. The tube was evacuated and back purged with nitrogen and repeated three times,

dry toluene (0.75 mL) and morpholine **2a** (18.5 μL, 0.2 mmol) were injected by syringe. The resulting mixture was stirred at 90 °C for 24 h. After the reaction, the tube was cooled to room temperature. The mixture was concentrated under reduced pressure and the crude mixture was purified by column chromatography on silica gel (PE/EA) to afford **3e** (6.6 mg, 37%).

This result suggests that this complex may be an intermediate product of the reaction, which undergoes amine binding and reductive elimination reactions to produce the C-N coupling product.

7.3 The reactivity of nickel in other valence states in the reaction



In a nitrogen-filled glovebox, $Ni(COD)_2$ (5.6 mg, 0.02 mmol, 10 mol%), **L** (8.4 mg, 0.02 mmol, 10 mol%) and NaO^tBu (76.9 mg, 0.8 mmol, 4.0 equiv) were added to a 10 mL Schlenk tube fitted with a magnetic stirring bar, followed by addition of dry toluene (1.0 mL), chlorobenzene (21.0 μL, 0.2 mmol), morpholine (39.0 μL, 0.4 mmol) and PhCN (41.0 μL, 0.4 mmol, 2.0 equiv) to the Schlenk tube. Subsequently, the tube was sealed and removed to the outside of the glove box. The reaction was carried out at 90 °C for 24 h. When the reaction mixture was cooled to room temperature, then naphthalene (12.8 mg) was added as an internal standard, and the organic phase was filtered through a cartridge and detected by GC to obtain **3a** in 94% yield.

These results suggested that the reaction may involve a cycle between Ni(0)/Ni(II).

8. X-Ray diffraction data of pre-catalyst

8.1 X-Ray diffraction data of C1

Single crystals of **C1** ($C_{26}H_{46}Cl_2NiP_2$) was obtained from $CHCl_3$. A suitable crystal was selected and the crystal data of compound **C1** was collected on a 'Bruker APEX-II CCD' diffractometer using graphite-monochromatic Mo Kα radiation (λ = 0.71073 Å). The crystal was kept at 292.0 K during data collection. Using Olex2,[32] the structure was solved with the ShelXS[33] structure solution program using Direct Methods and refined with the ShelXL[34] refinement package using Least Squares minimisation. Crystallographic data for the structure has been deposited to the Cambridge Crystallographic Data Center (CCDC 2272277).

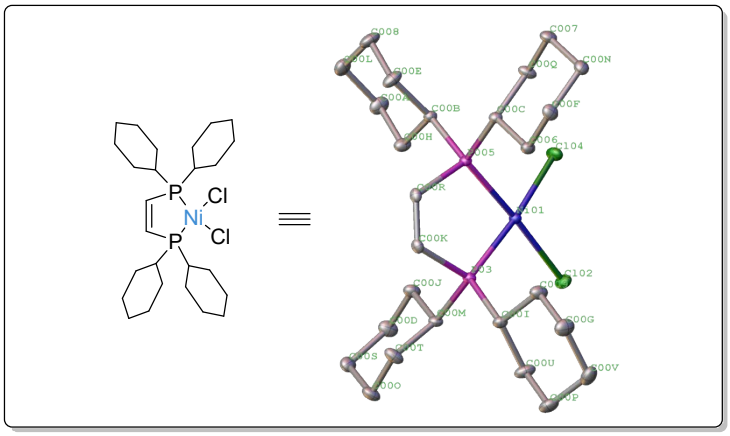


Figure S1. ORTEP drawing of **C1** at 50% probability

Table S10. Crystal data and structure refinement for **C1**

CCDC number	**2272277**
Empirical formula	$C_{26}H_{46}Cl_2NiP_2$
Formula weight	550.18
Temperature/K	298
Crystal system	triclinic
Space group	P1
a/Å	7.324(3)
b/Å	9.448(4)
c/Å	10.757(4)
α/°	92.196(18)
β/°	105.699(15)
γ/°	101.677(17)
Volume/Å^3	698.3(5)
Z	1
ρ_{calc}g/cm^3	1.308
μ/mm^{-1}	1.013
F(000)	294
Crystal size/mm^3	0.19 × 0.15 × 0.05
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.634 to 54.976
Index ranges	-9 ≤ h ≤ 9, -12 ≤ k ≤ 12, -13 ≤ l ≤ 13
Reflections collected	18349
Independent reflections	6169 [Rint = 0.0392, Rsigma = 0.0422]
Data/restraints/parameters	6169/3/281
Goodness-of-fit on F^2	1.023
Final R indexes [I>=2σ (I)]	R^1 = 0.0272, wR^2 = 0.0648
Final R indexes [all data]	R^1 = 0.0304, wR^2 = 0.0663
Largest diff. peak/hole / e Å^{-3}	0.42/-0.26

8.2 X-Ray diffraction data of C2

Single crystals of **C2** ($C_{28}H_{38}Cl_2NiP_2$) was obtained from $CHCl_3$. A suitable crystal was selected and the crystal data of compound **C2** was collected on a 'Bruker APEX-II CCD' diffractometer using graphite-monochromatic Mo Kα radiation (λ = 0.71073 Å). The crystal was kept at 292.0 K during data collection. Using Olex2,[32] the structure was solved with the ShelXS[33] structure solution program using Direct Methods and refined with the ShelXL[34] refinement package using Least Squares minimisation. Crystallographic data for the structure has been deposited to the Cambridge Crystallographic Data Center (CCDC 2440088).

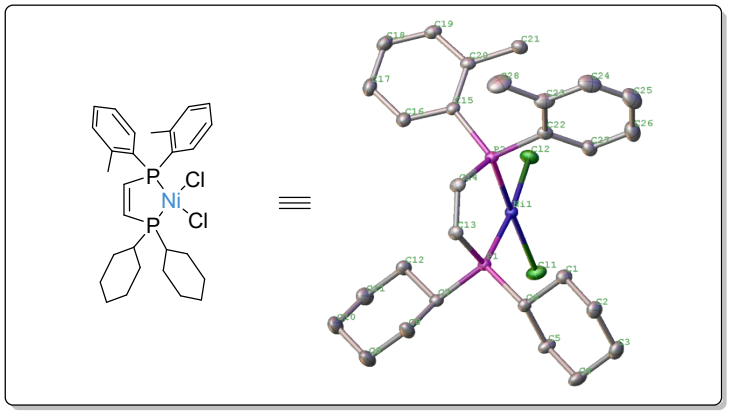


Figure S2. ORTEP drawing of **C2** at 50% probability

Table S11. Crystal data and structure refinement for **C2**

CCDC number	**2440088**
Empirical formula	$C_{28}H_{38}Cl_2NiP_2$
Formula weight	566.13
Temperature/K	294.15
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	13.378(5)
b/Å	14.413(7)
c/Å	17.056(8)
α/°	90
β/°	94.257(19)
γ/°	90
Volume/Å^3	3280(3)
Z	4
ρ_{calc}g/cm^3	1.147
μ/mm^{-1}	0.865
F(000)	1192.0
Crystal size/mm^3	0.45 × 0.35 × 0.25
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.912 to 50.68
Index ranges	-16 ≤ h ≤ 16, -17 ≤ k ≤ 17, -20 ≤ l ≤ 20
Reflections collected	81415
Independent reflections	5959 [R_{int} = 0.0754, R_{sigma} = 0.0273]
Data/restraints/parameters	5959/0/300

Goodness-of-fit on F^2	1.052
Final R indexes [I>=2σ (I)]	R_1 = 0.0415, wR_2 = 0.0984
Final R indexes [all data]	R_1 = 0.0514, wR_2 = 0.1035
Largest diff. peak/hole / e Å^{-3}	0.26/-0.30

8.3 X-Ray diffraction data of C3

Single crystals of **C3** ($C_{66}H_{106}Cl_2Ni_2P_4$) was obtained from $CHCl_3$. A suitable crystal was selected and the crystal data of compound **C3** was collected on a 'Bruker APEX-II CCD' diffractometer using graphite-monochromatic Mo Kα radiation (λ = 0.71073 Å). The crystal was kept at 292.0 K during data collection. Using Olex2,[32] the structure was solved with the ShelXS[33] structure solution program using Direct Methods and refined with the ShelXL[34] refinement package using Least Squares minimisation. Crystallographic data for the structure has been deposited to the Cambridge Crystallographic Data Center (CCDC 2340247).

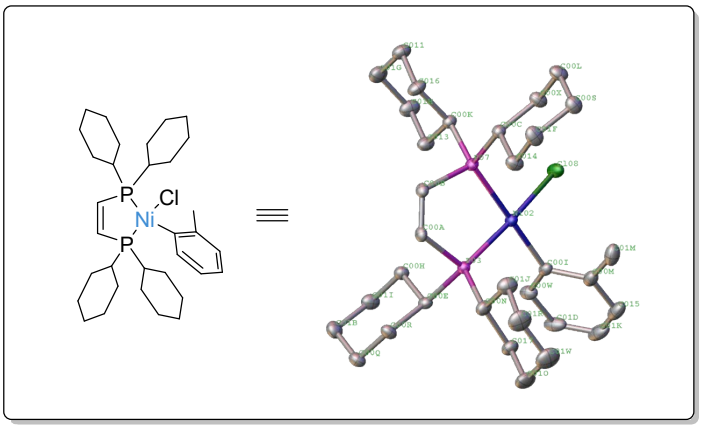


Figure S3. ORTEP drawing of **C3** at 50% probability

Table S12. Crystal data and structure refinement for **C3**

CCDC number	2340247
Empirical formula	$C_{66}H_{106}Cl_2Ni_2P_4$
Formula weight	1211.70
Temperature [K]	293.15
Crystal system	triclinic
Space group (number)	$P\bar{1}$ (2)
a [Å]	12.351(15)
b [Å]	13.866(19)
c [Å]	20.364(15)
α [°]	99.57(6)
β [°]	93.62(5)
γ [°]	105.92(7)
Volume [Å^3]	3285(7)
Z	2
ρ_{calc} [gcm^{-3}]	1.225
μ [mm^{-1}]	0.789
F(000)	1304
Crystal size [mm^3]	0.16×0.14×0.13
Crystal shape	block

Radiation	MoK_α (λ=0.71073 Å)
2θ range [°]	3.92 to 59.49 (0.72 Å)
Index ranges	$-16 \le h \le 16$, $-18 \le k \le 18$, $-27 \le l \le 27$
Reflections collected	118123
Independent reflections	15940, R_{int} = 0.1486, R_{sigma} = 0.0823
Completeness to θ = 25.242°	99.7 %
Data / Restraints / Parameters	15940/106/724
Absorption correction	0.4891/0.7456
Goodness-of-fit on F^2	1.023
Final R indexes [$I \ge 2\sigma(I)$]	R_1 = 0.0764, wR_2 = 0.1967
Final R indexes [all data]	R_1 = 0.1262, wR_2 = 0.2273
Largest peak/hole [eÅ^{-3}]	1.26/−0.60

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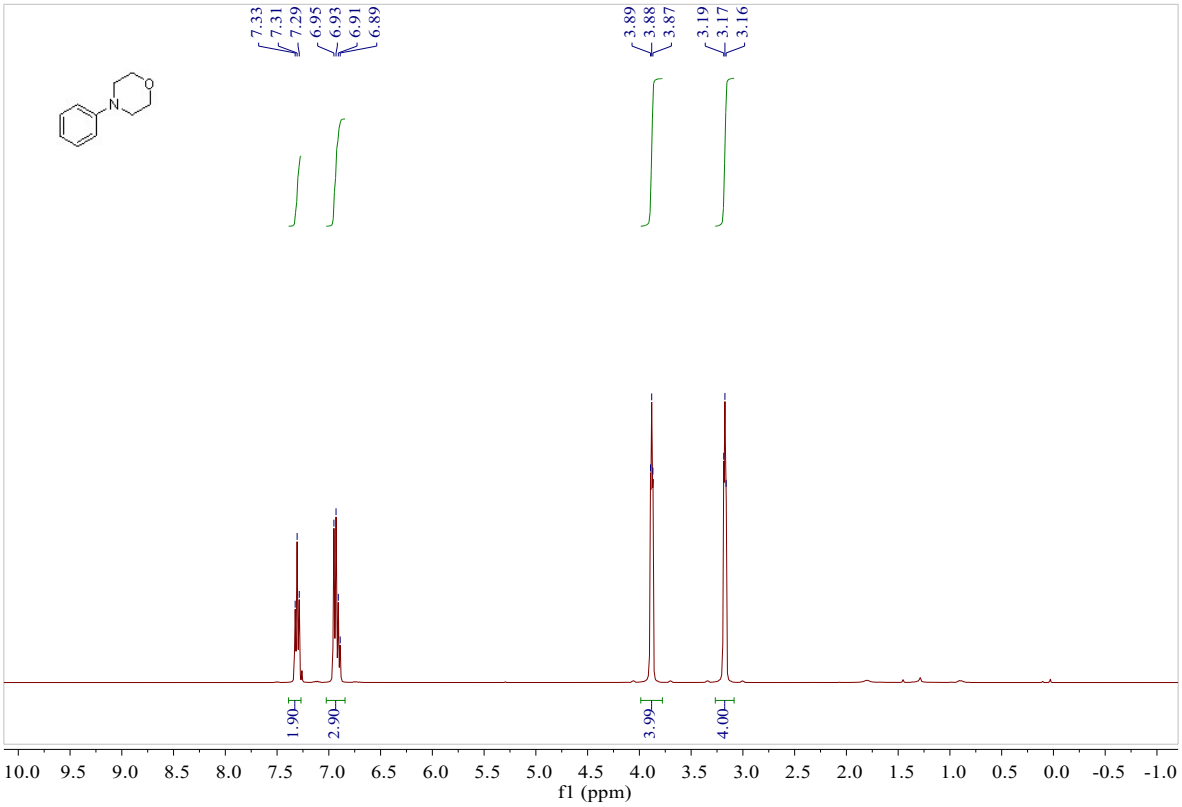
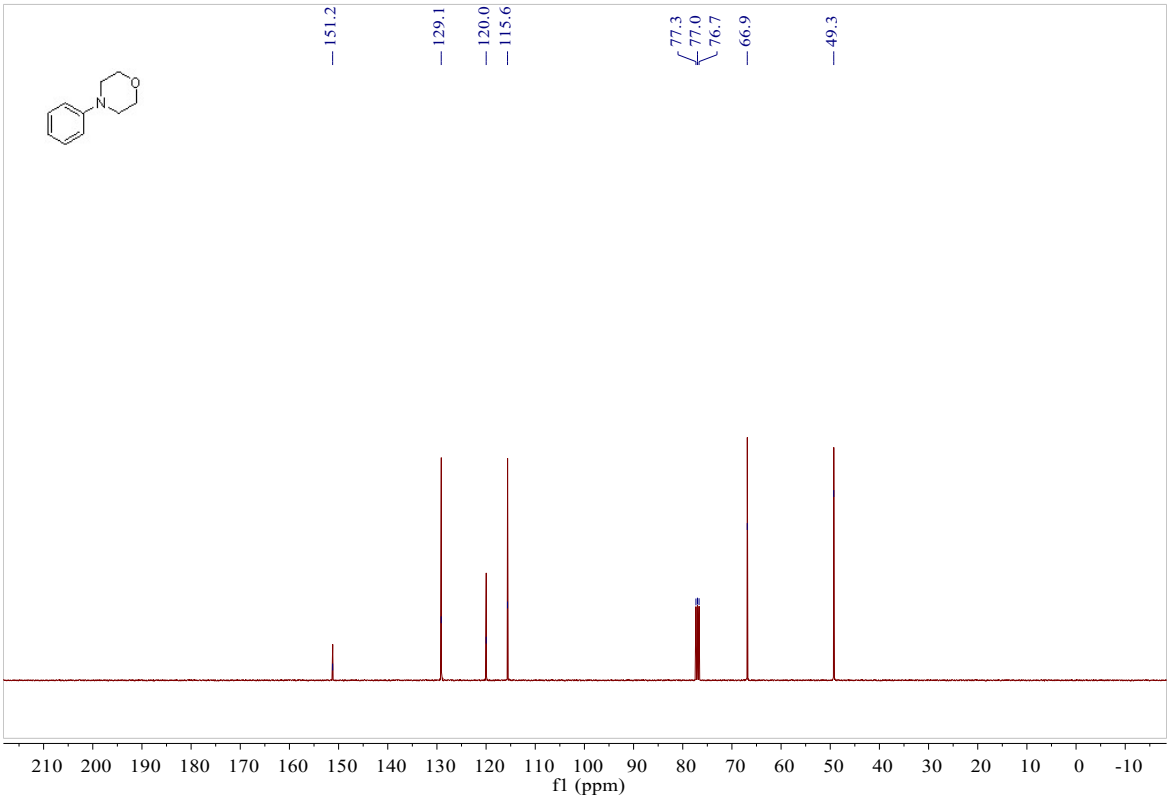
10. NMR Spectra of products: ^{1}H, ^{13}C and ^{19}F NMR

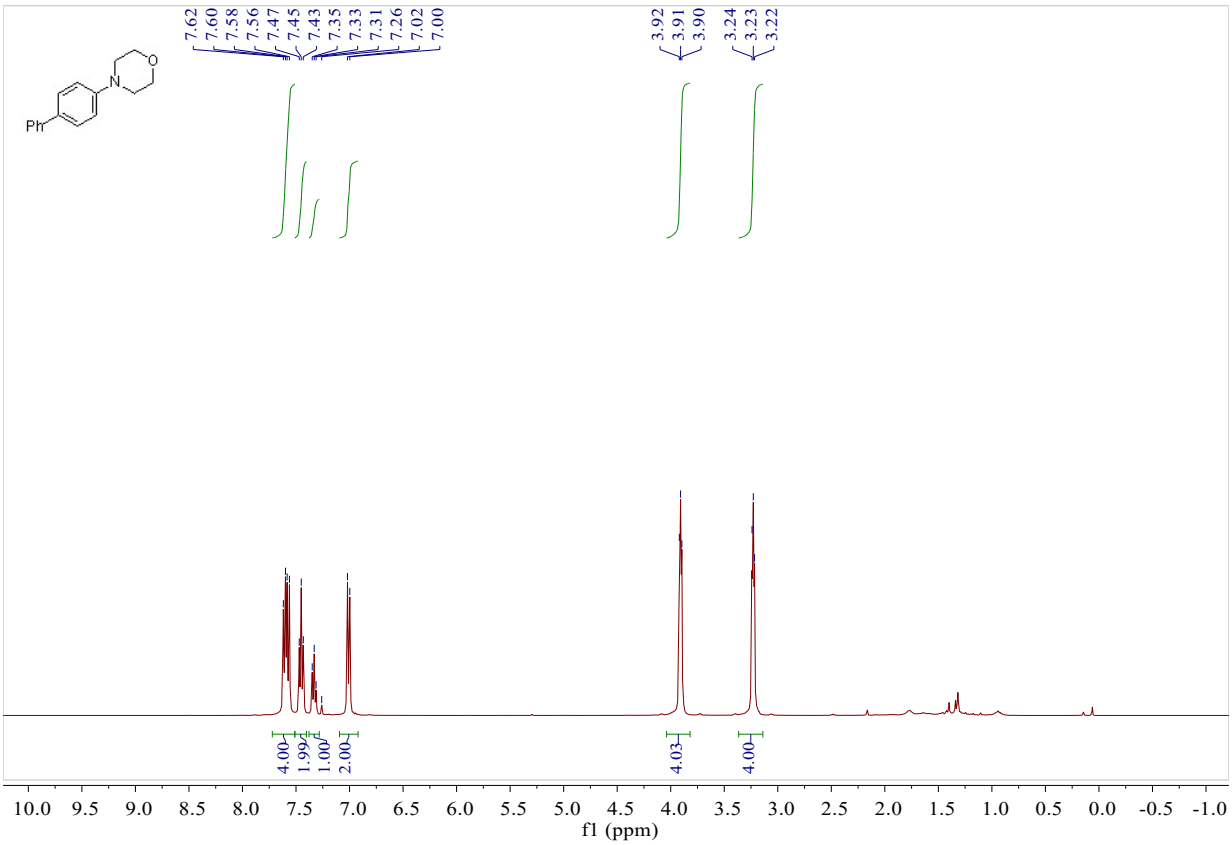
4-Phenylmorpholine (3a): ^{1}H NMR (400 MHz, $CDCl_3$)



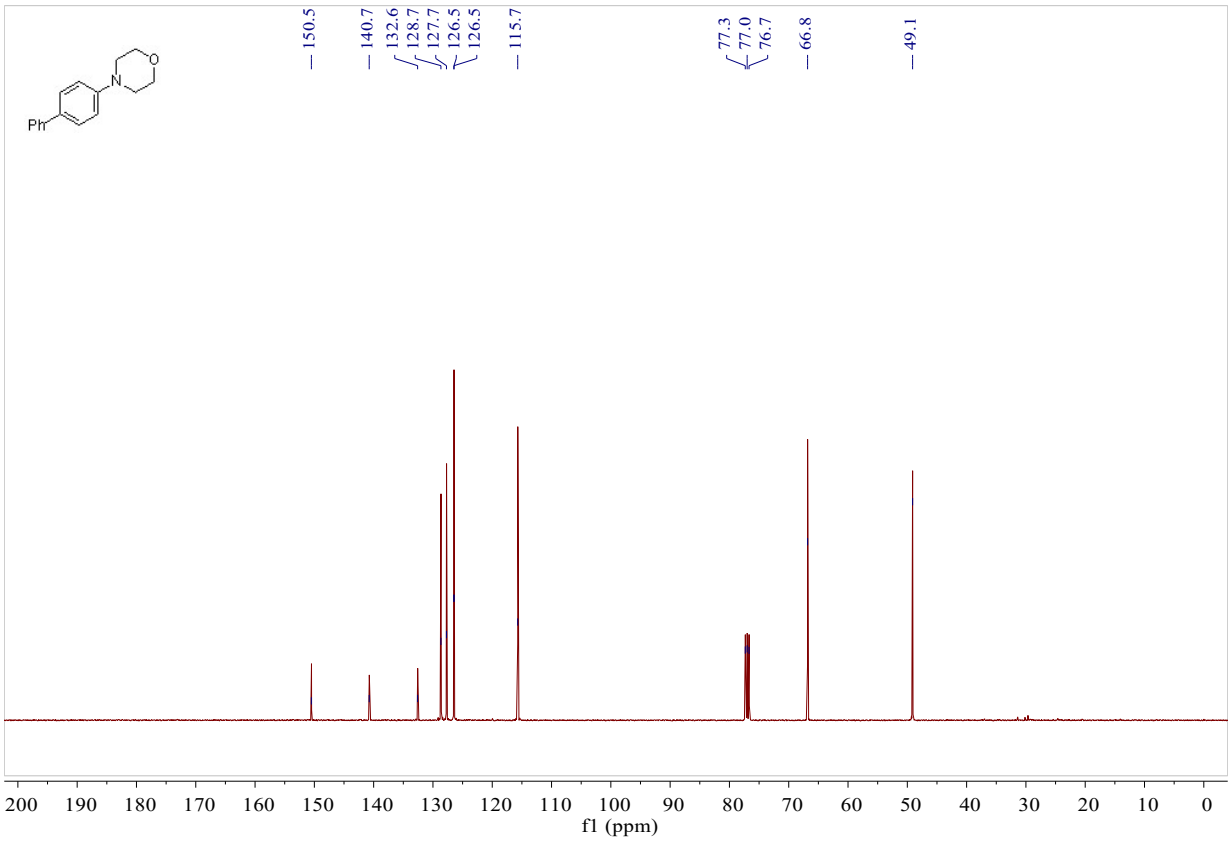
4-Phenylmorpholine (3a): ^{13}C NMR (101 MHz, $CDCl_3$)



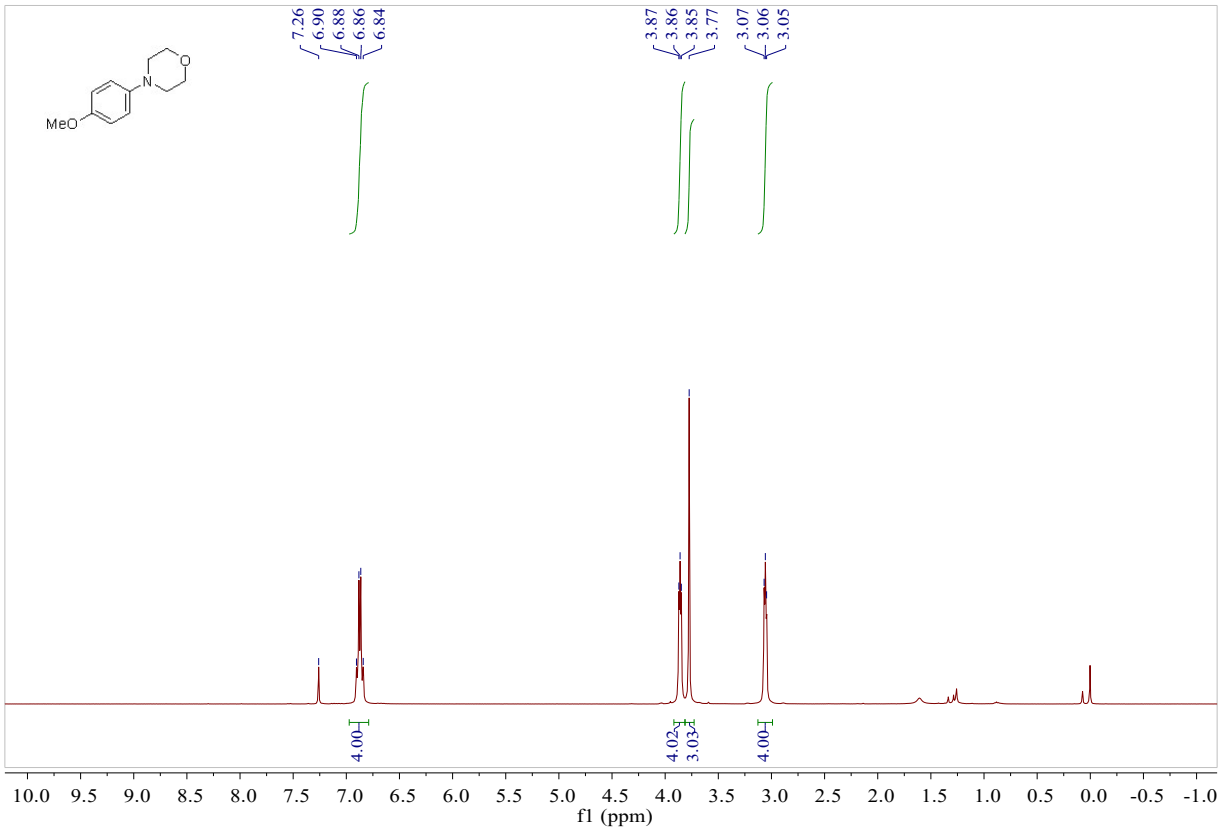
4-([1,1'-Biphenyl]-4-yl)morpholine (3b): ^{1}H NMR (400 MHz, $CDCl_3$)



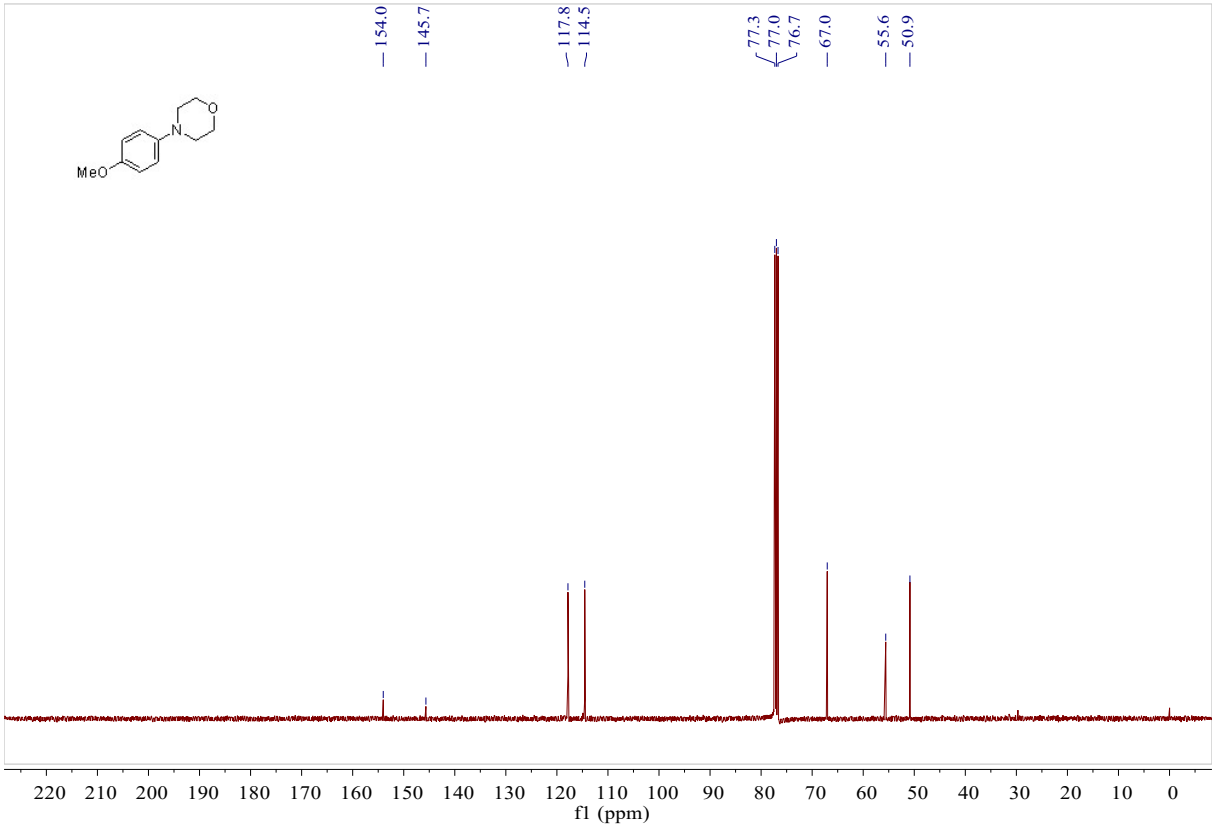
4-([1,1'-biphenyl]-4-yl)morpholine (3b): ^{13}C NMR (100 MHz, $CDCl_3$)



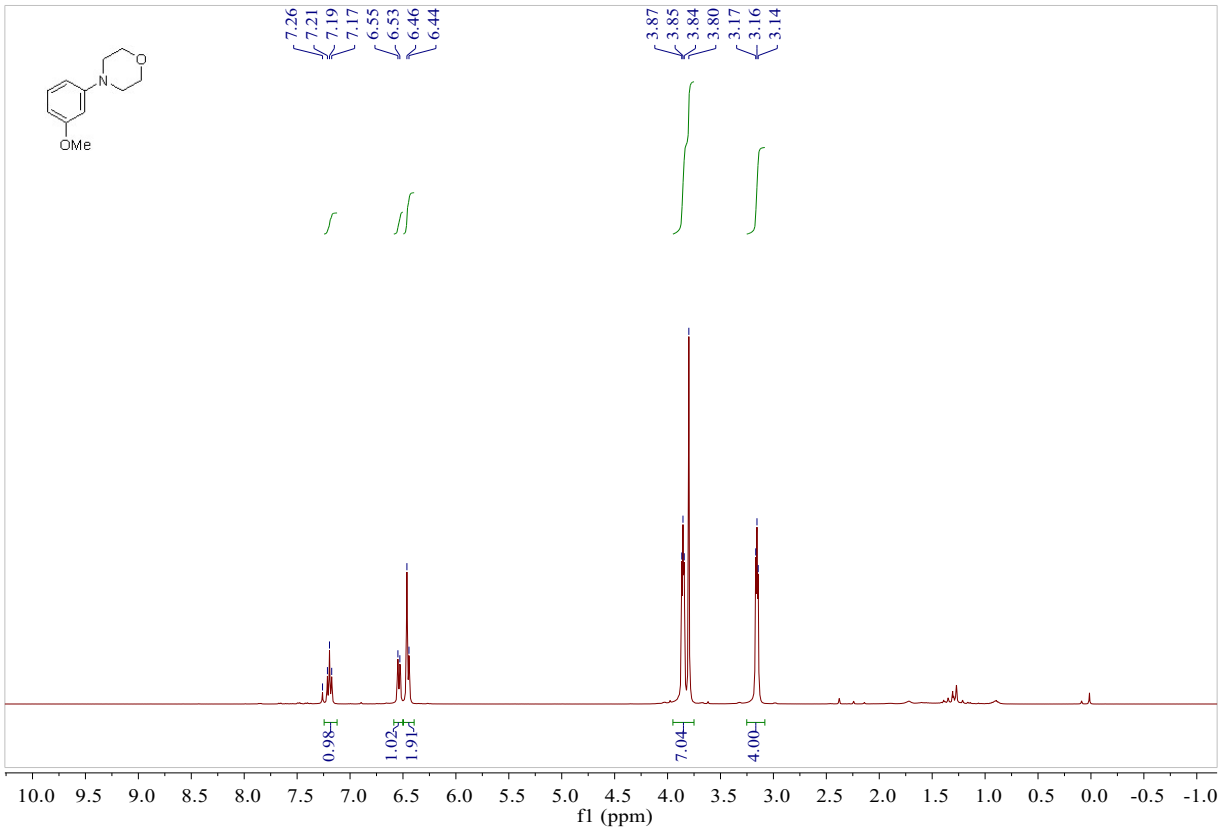
4-(4-Methoxyphenyl)morpholine (3c): ^{1}H NMR (400 MHz, $CDCl_3$)



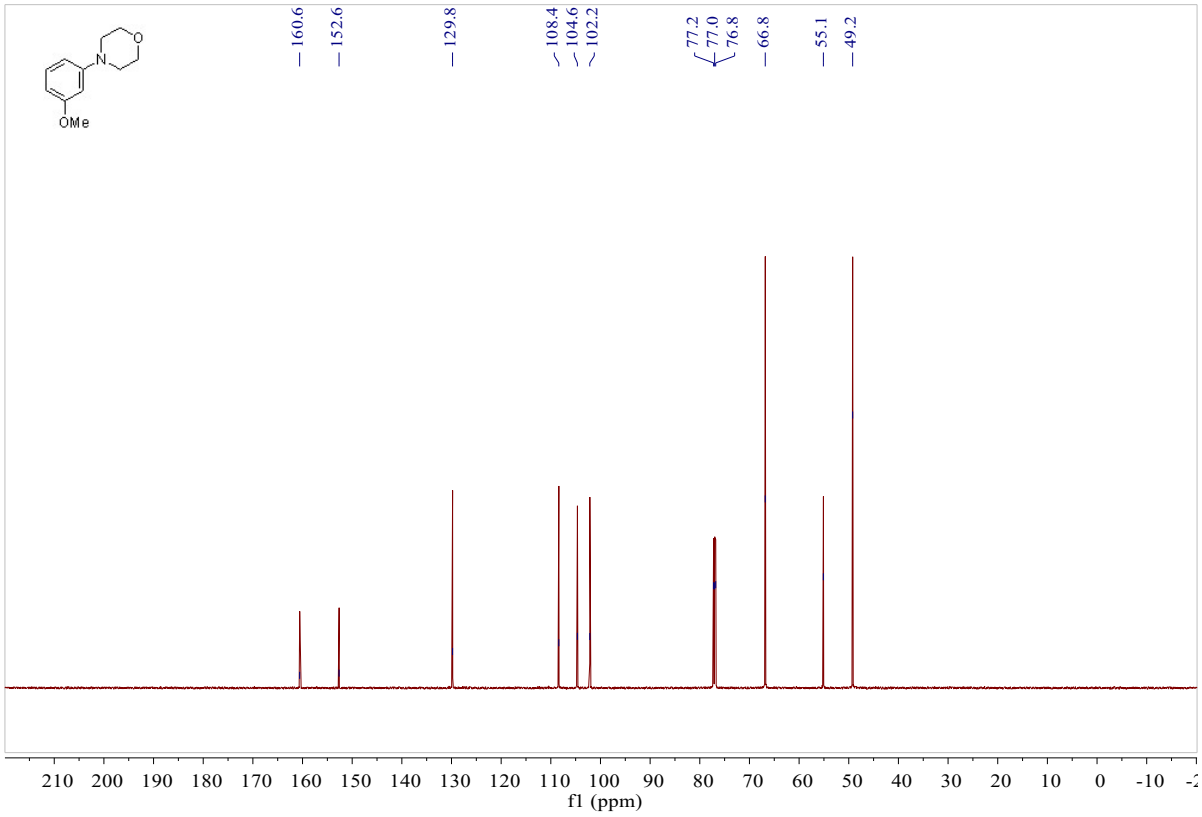
4-(4-Methoxyphenyl)morpholine (3c): ^{13}C NMR (101 MHz, $CDCl_3$)



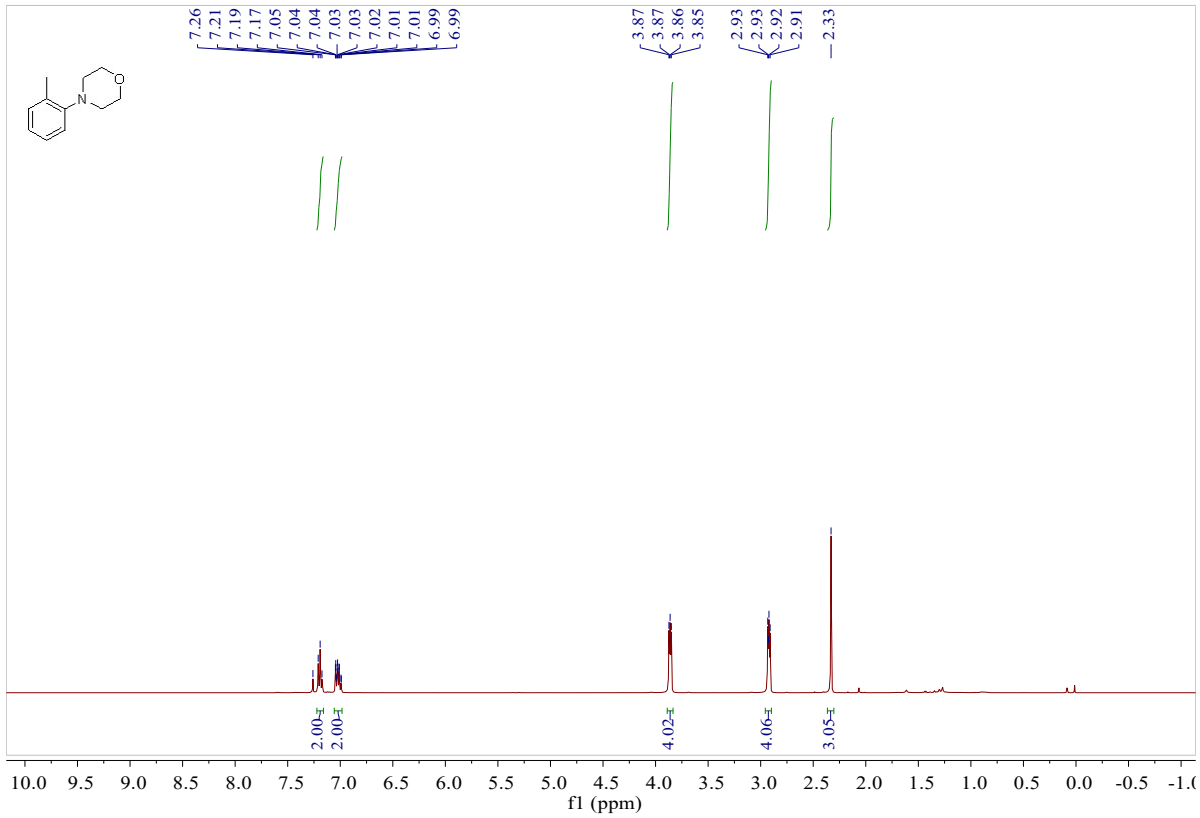
4-(3-Methoxyphenyl)morpholine (3d): ^{1}H NMR (400 MHz, $CDCl_3$)



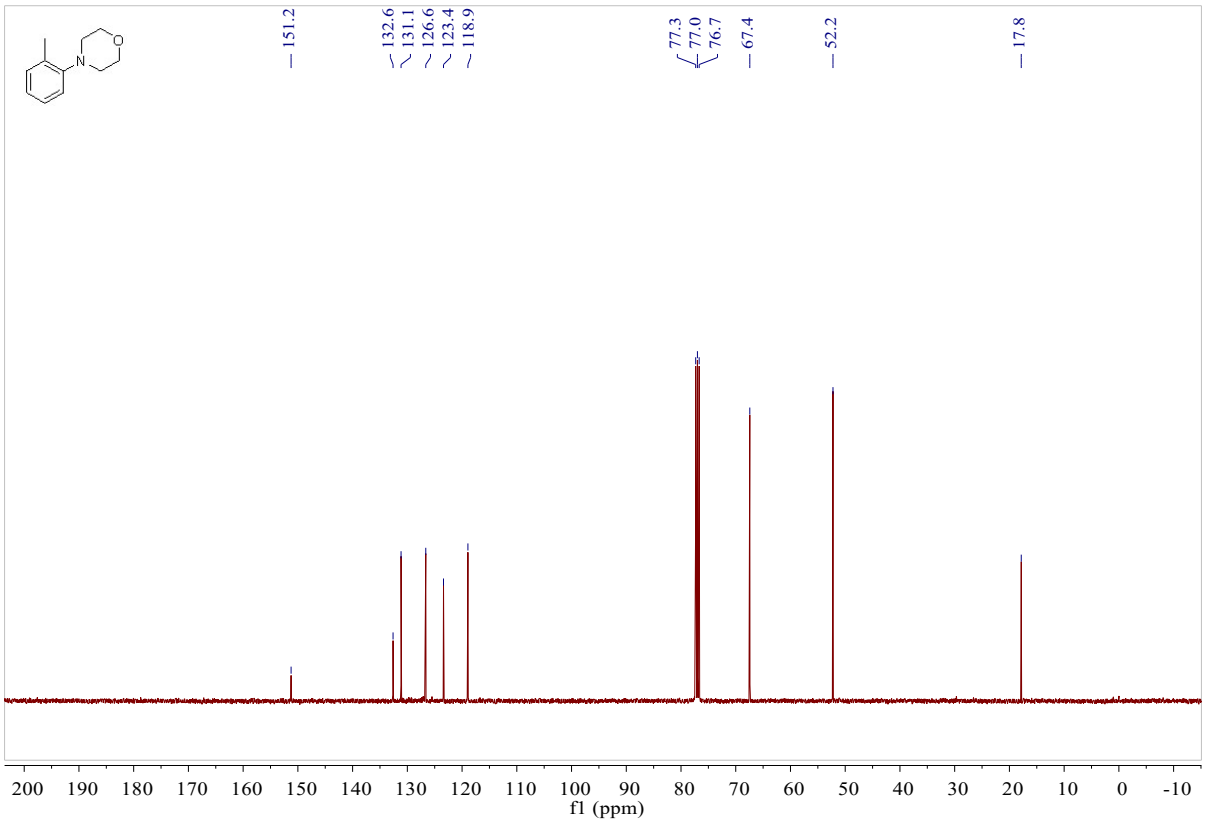
4-(3-Methoxyphenyl)morpholine (3d): ^{13}C NMR (151 MHz, $CDCl_3$)



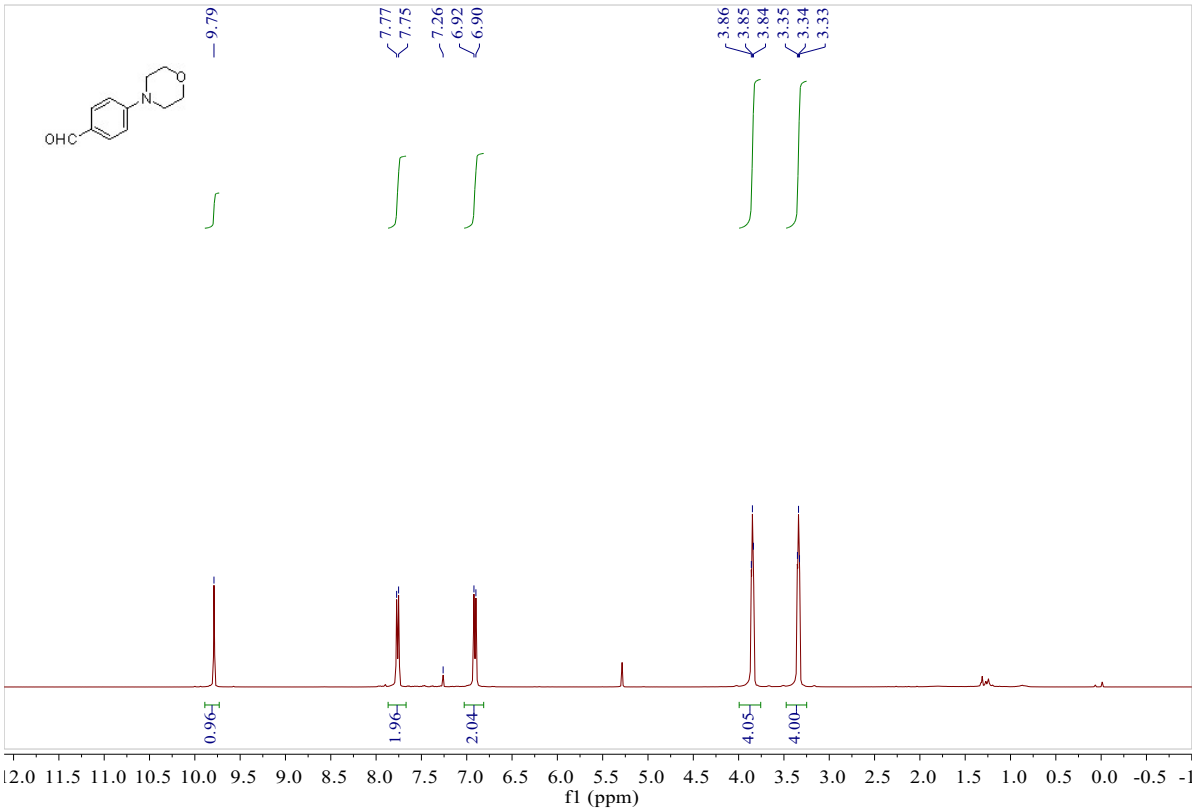
4-(*o*-tolyl)Morpholine (3e): ^{1}H NMR (400 MHz, $CDCl_3$)



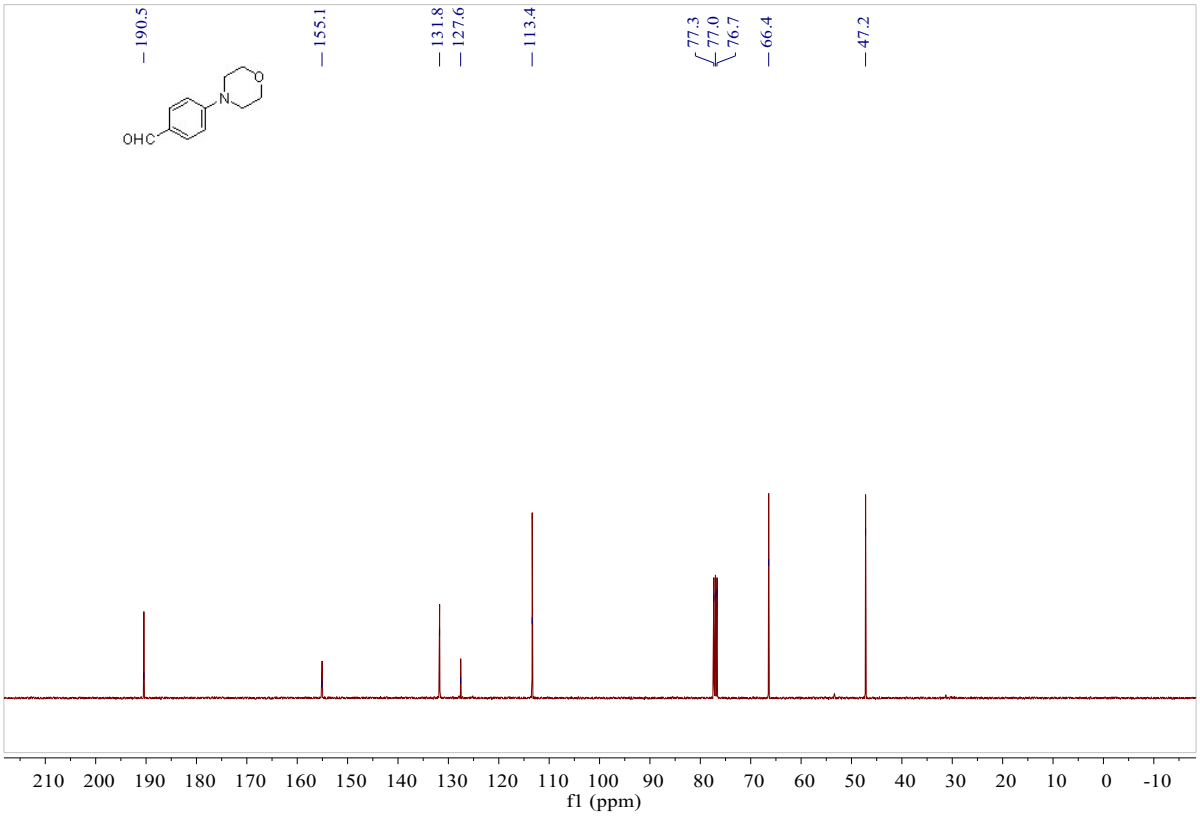
4-(*o*-tolyl)Morpholine (3e): ^{13}C NMR (101 MHz, $CDCl_3$)



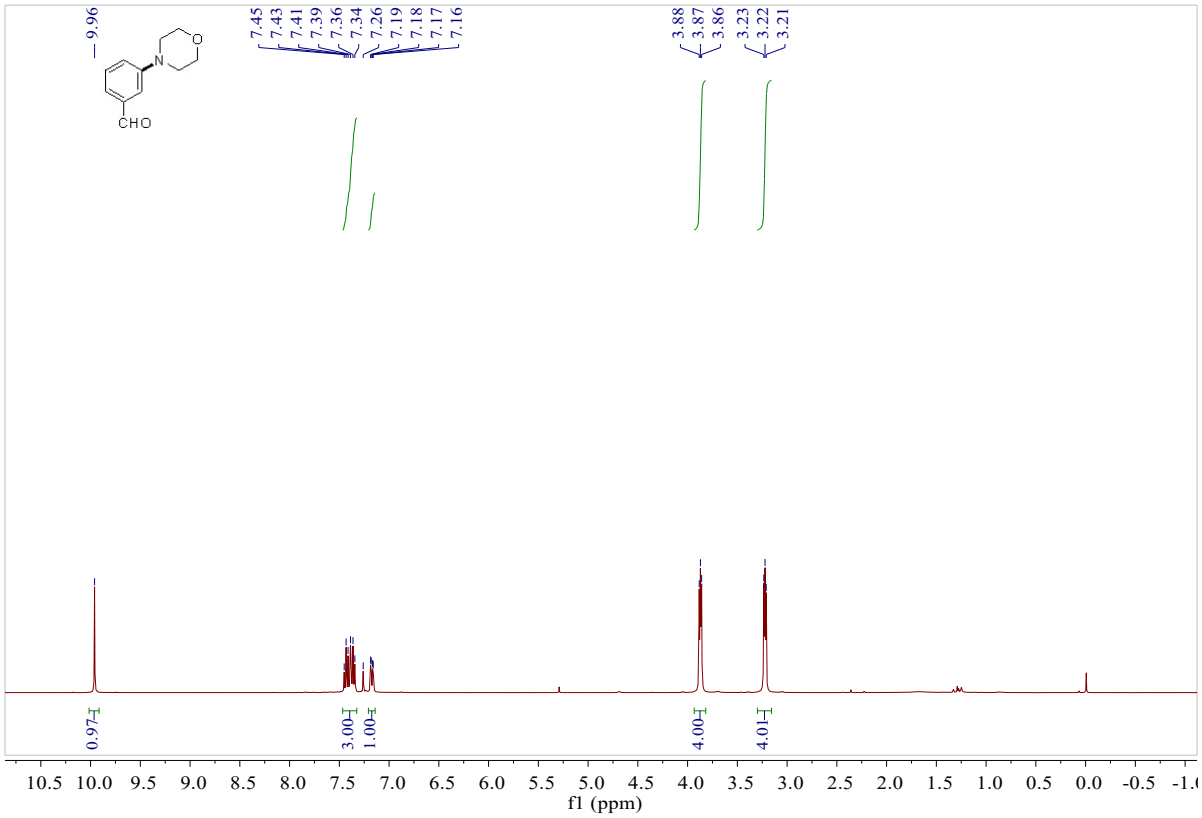
4-Morpholinobenzaldehyde (3f): ^{1}H NMR (400 MHz, $CDCl_3$)



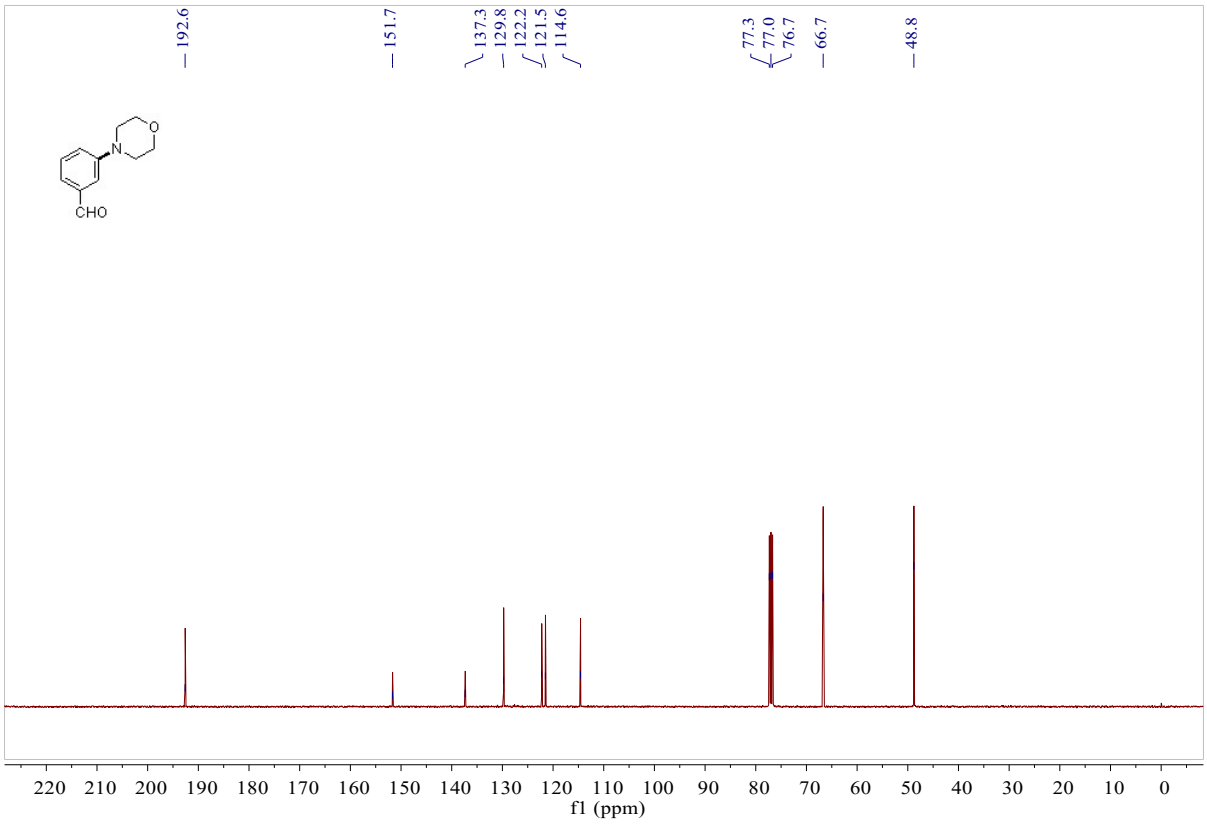
4-Morpholinobenzaldehyde (3f): ^{13}C NMR (101 MHz, $CDCl_3$)



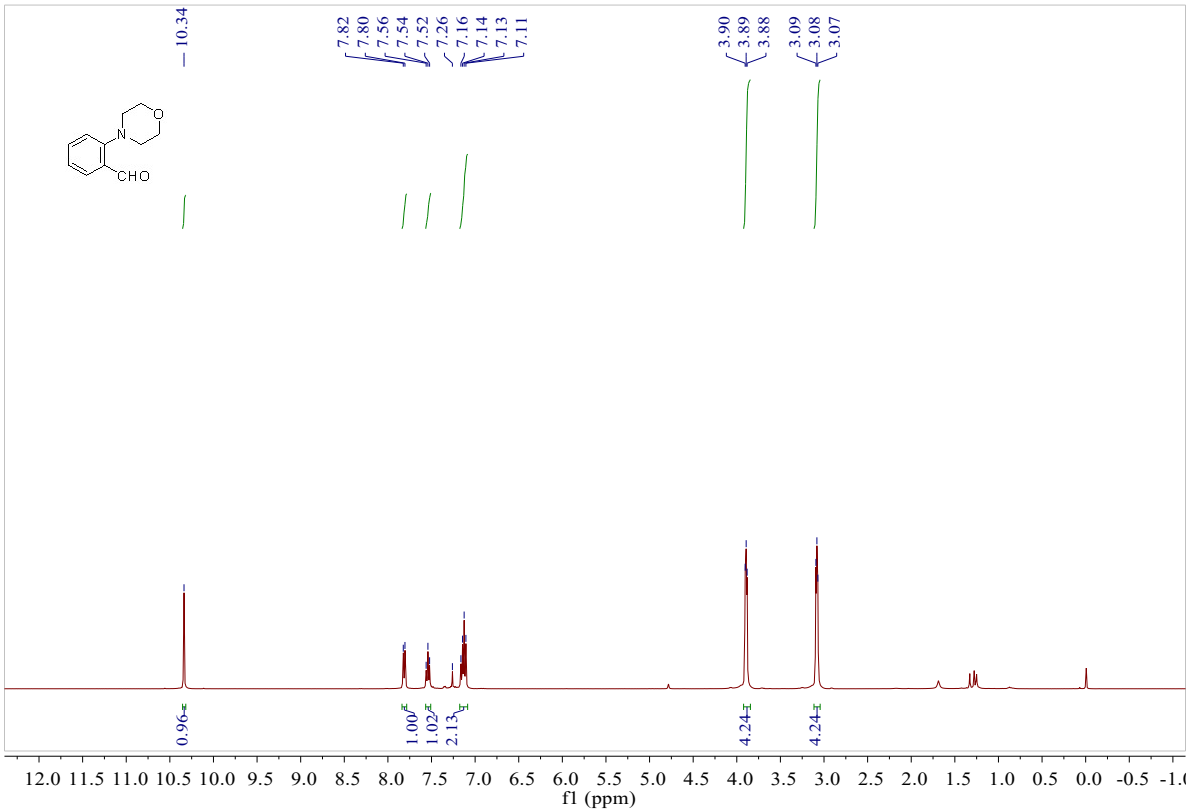
3-Morpholinobenzaldehyde (3g): ^{1}H NMR (400 MHz, $CDCl_3$)



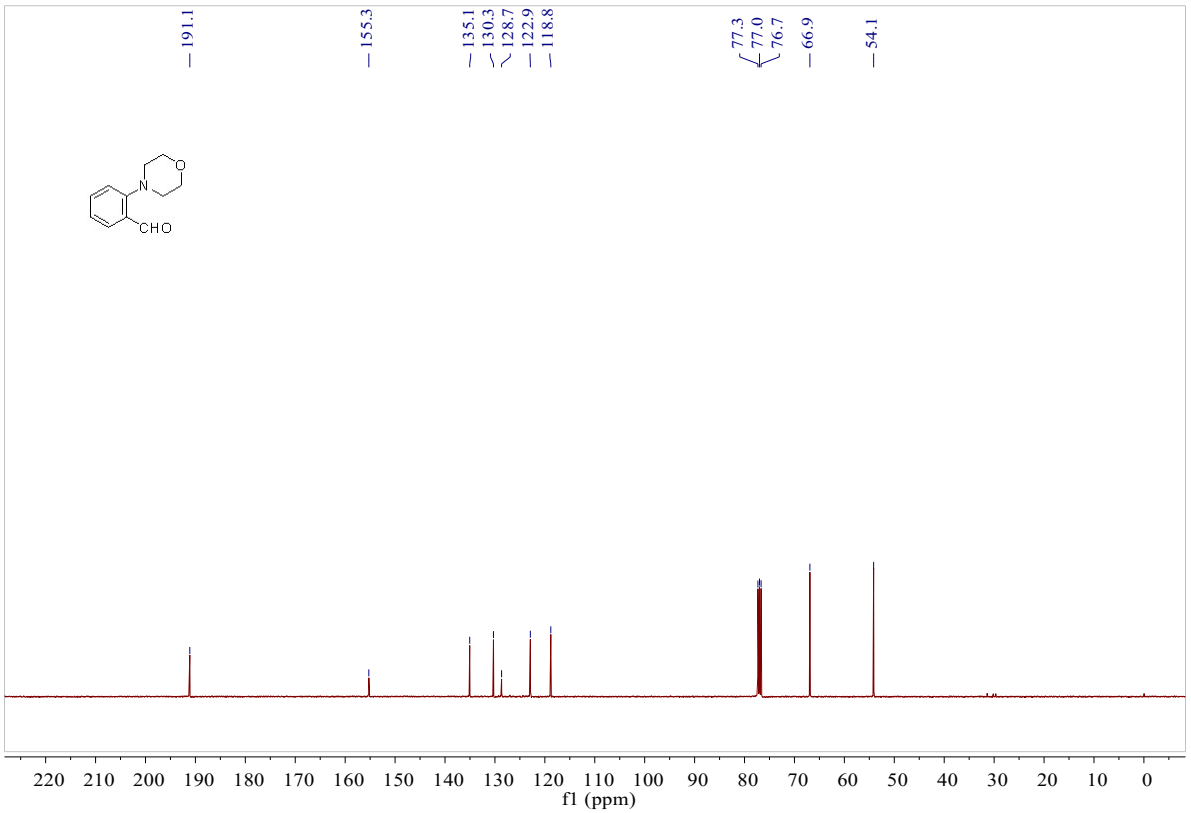
3-Morpholinobenzaldehyde (3g): ^{13}C NMR (101 MHz, $CDCl_3$)



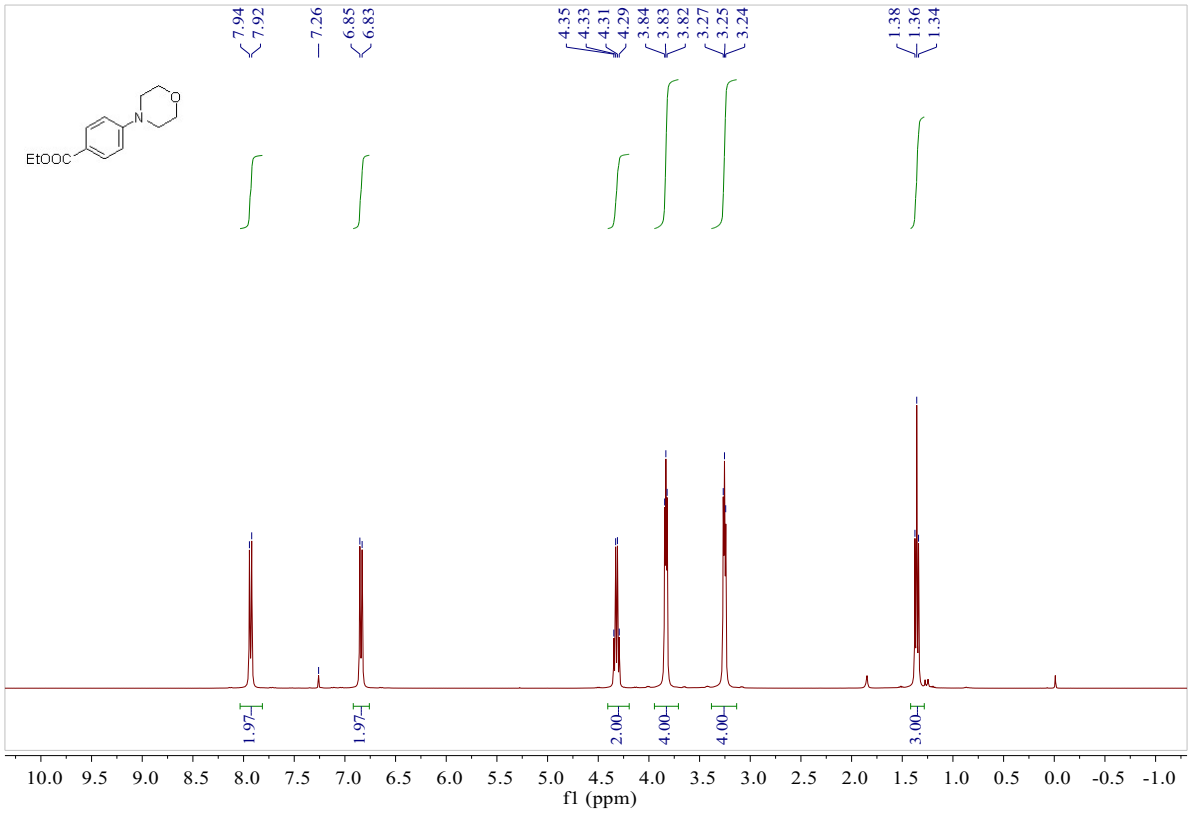
2-Morpholinobenzaldehyde (3h): ^{1}H NMR (400 MHz, $CDCl_3$)



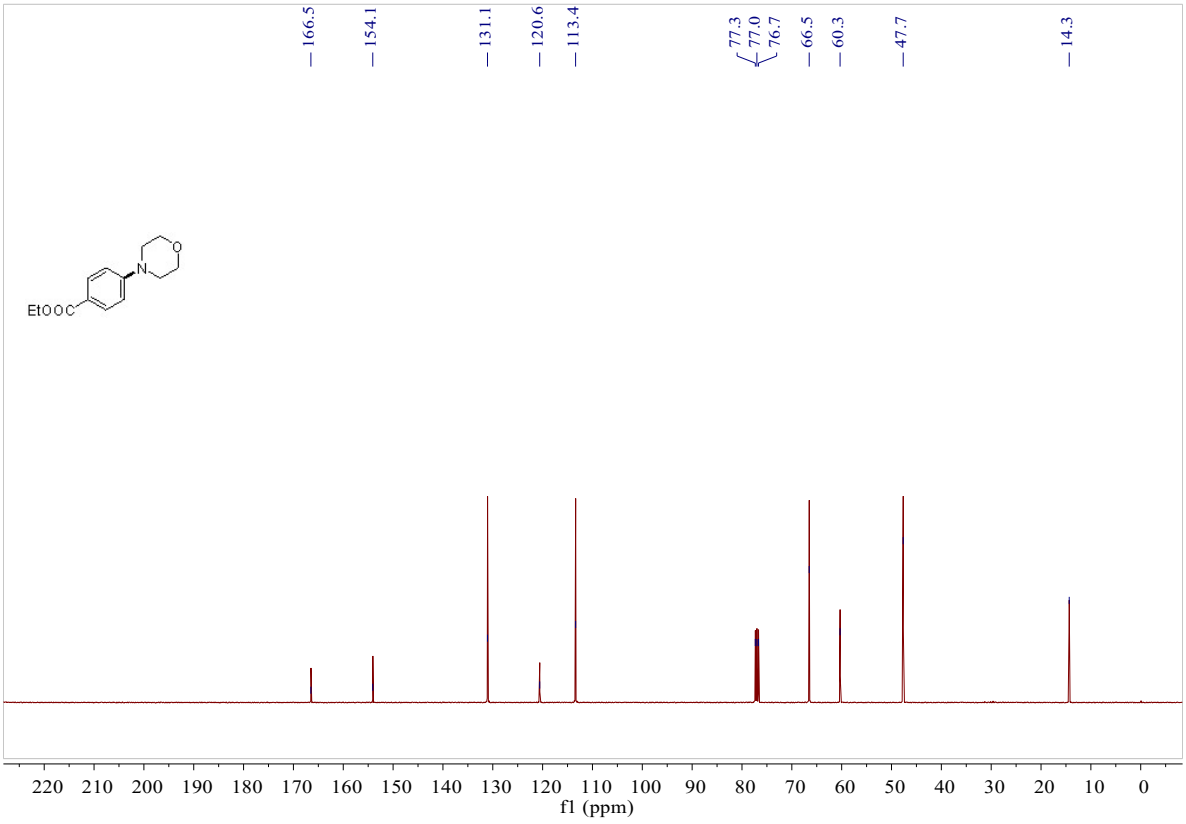
2-Morpholinobenzaldehyde (3h): ^{13}C NMR (101 MHz, $CDCl_3$)



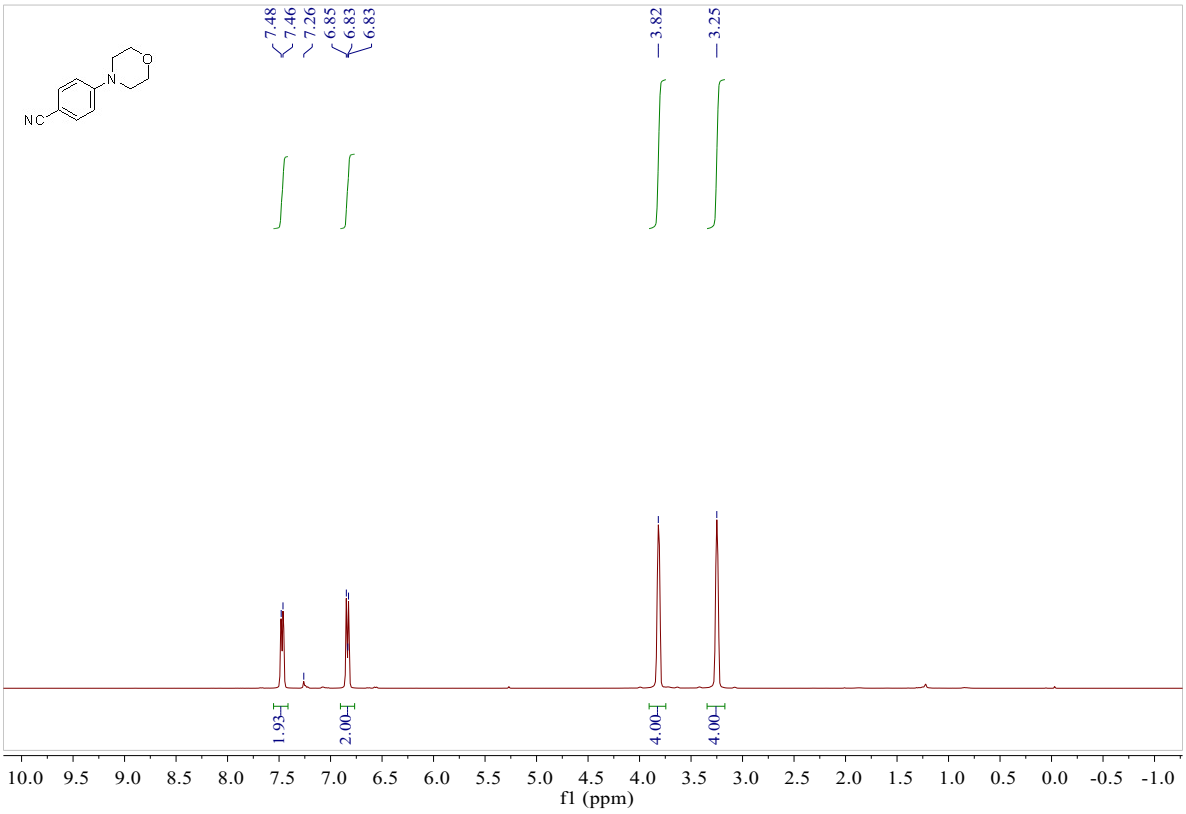
Ethyl 4-morpholinobenzoate (3i): ^{1}H NMR (400 MHz, $CDCl_3$)



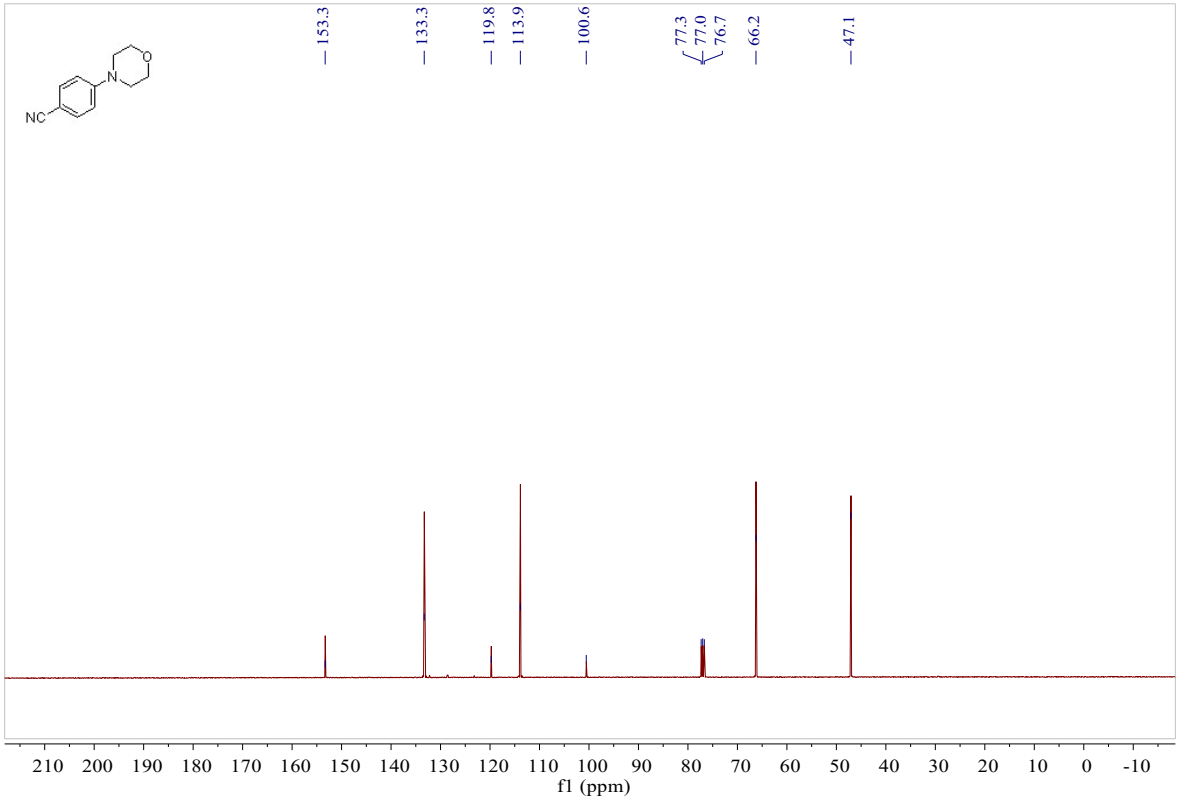
Ethyl 4-morpholinobenzoate (3i): ^{13}C NMR (101 MHz, $CDCl_3$)



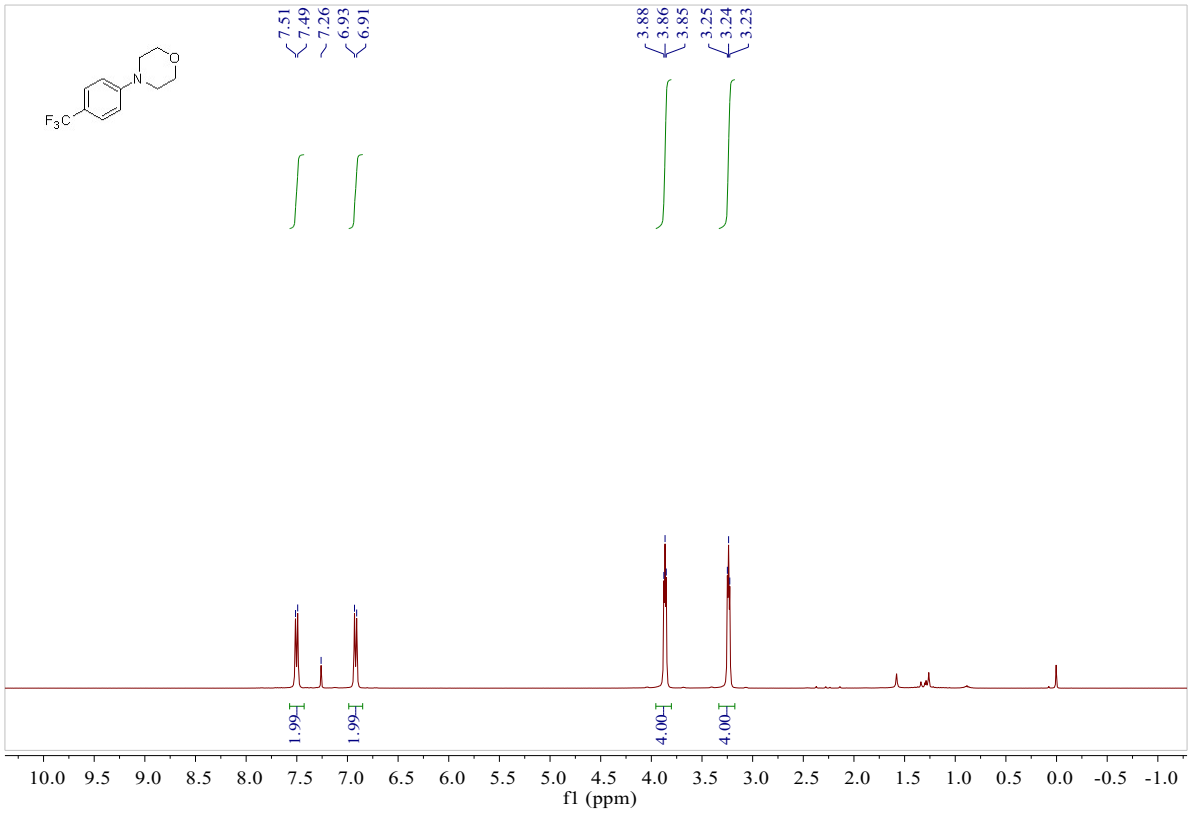
4-Morpholinobenzonitrile (3j): ^{1}H NMR (400 MHz, $CDCl_3$)



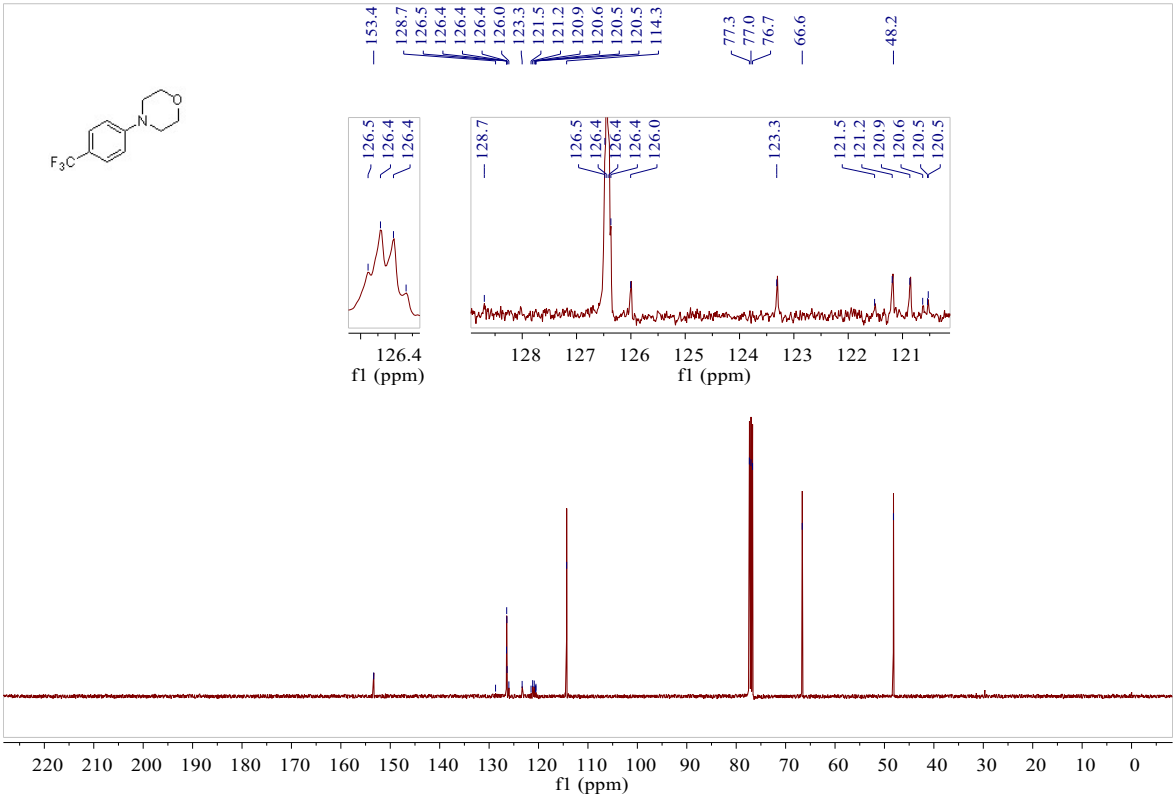
4-Morpholinobenzonitrile (3j): ^{13}C NMR (101 MHz, $CDCl_3$)



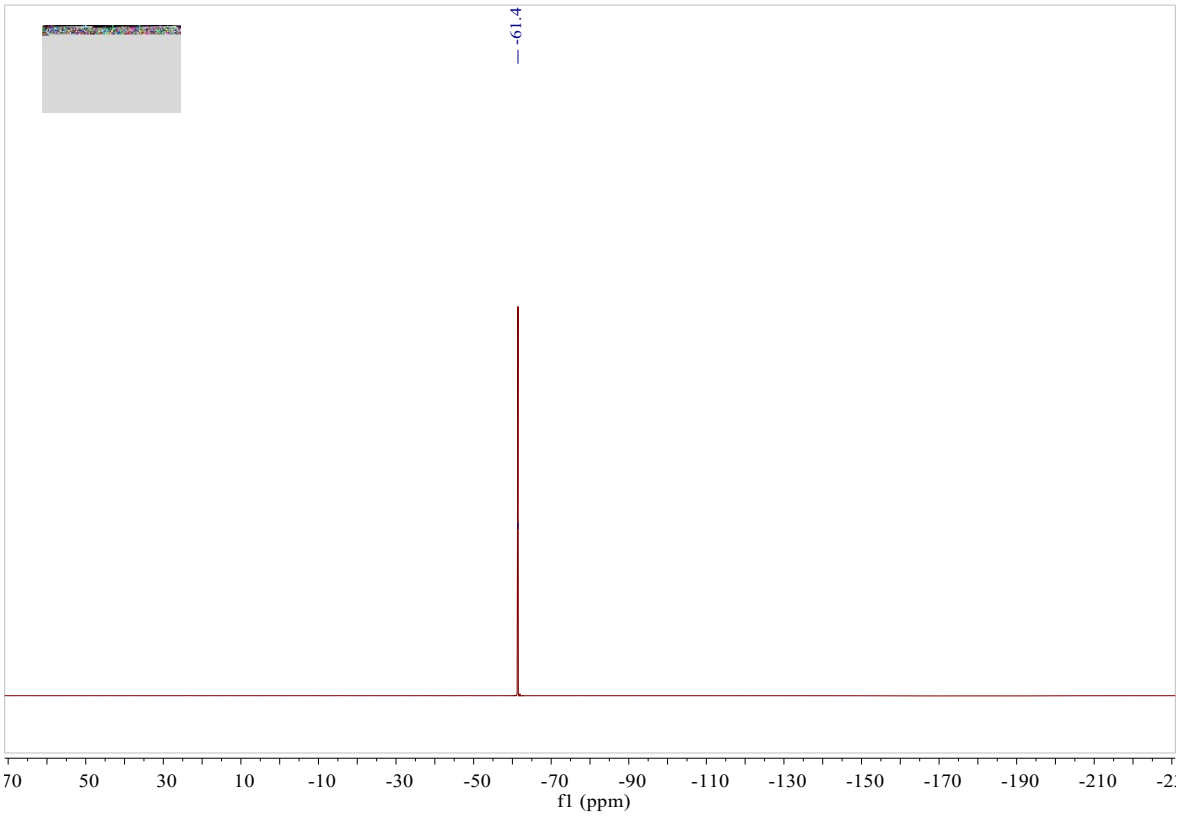
4-(4-(Trifluoromethyl)phenyl)morpholine (3k): ^{1}H NMR (400 MHz, $CDCl_3$)



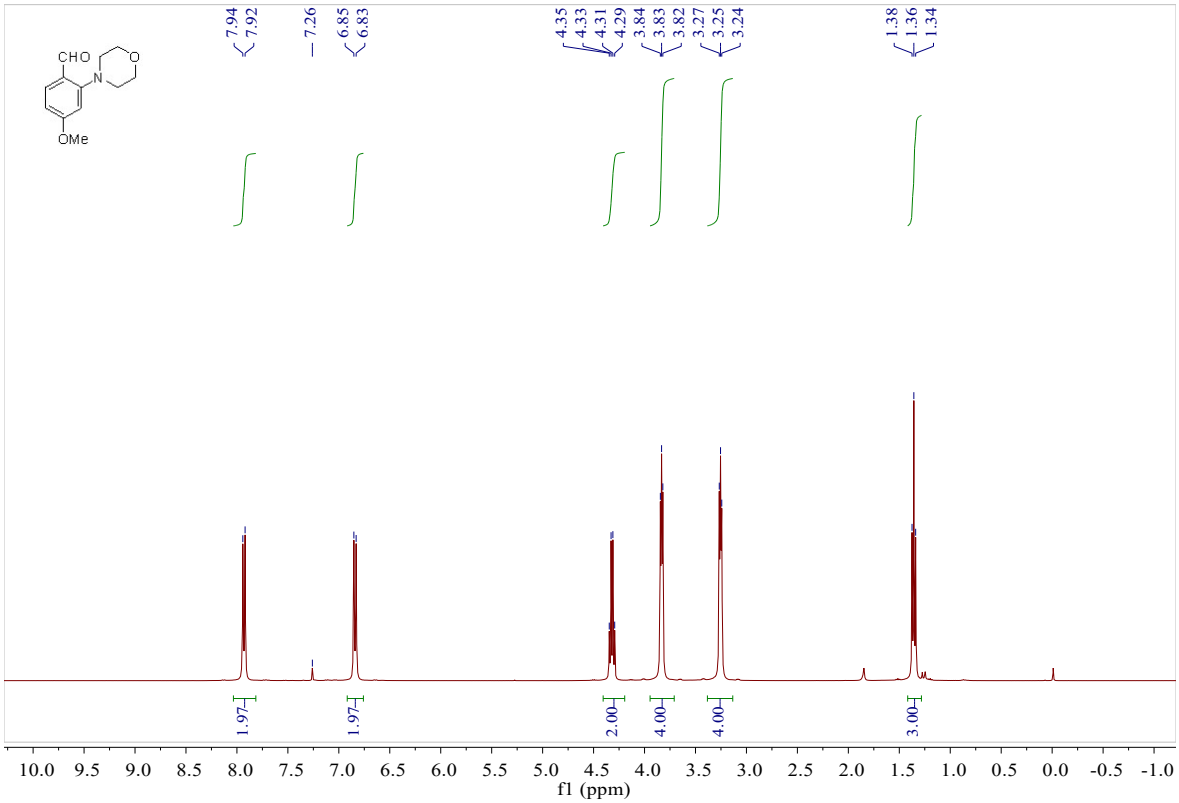
4-(4-(Trifluoromethyl)phenyl)morpholine (3k): ^{13}C NMR (101 MHz, $CDCl_3$)



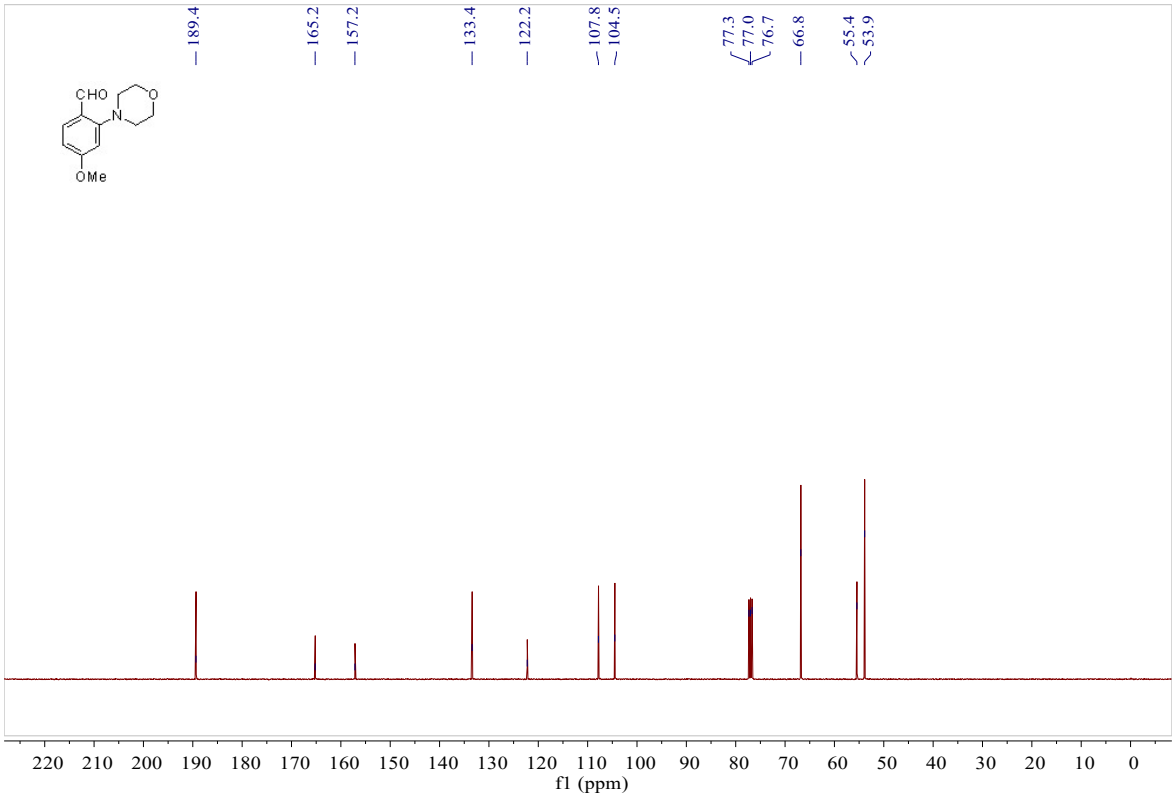
4-(4-(Trifluoromethyl)phenyl)morpholine (3k): ^{19}F NMR (377 MHz, $CDCl_3$)



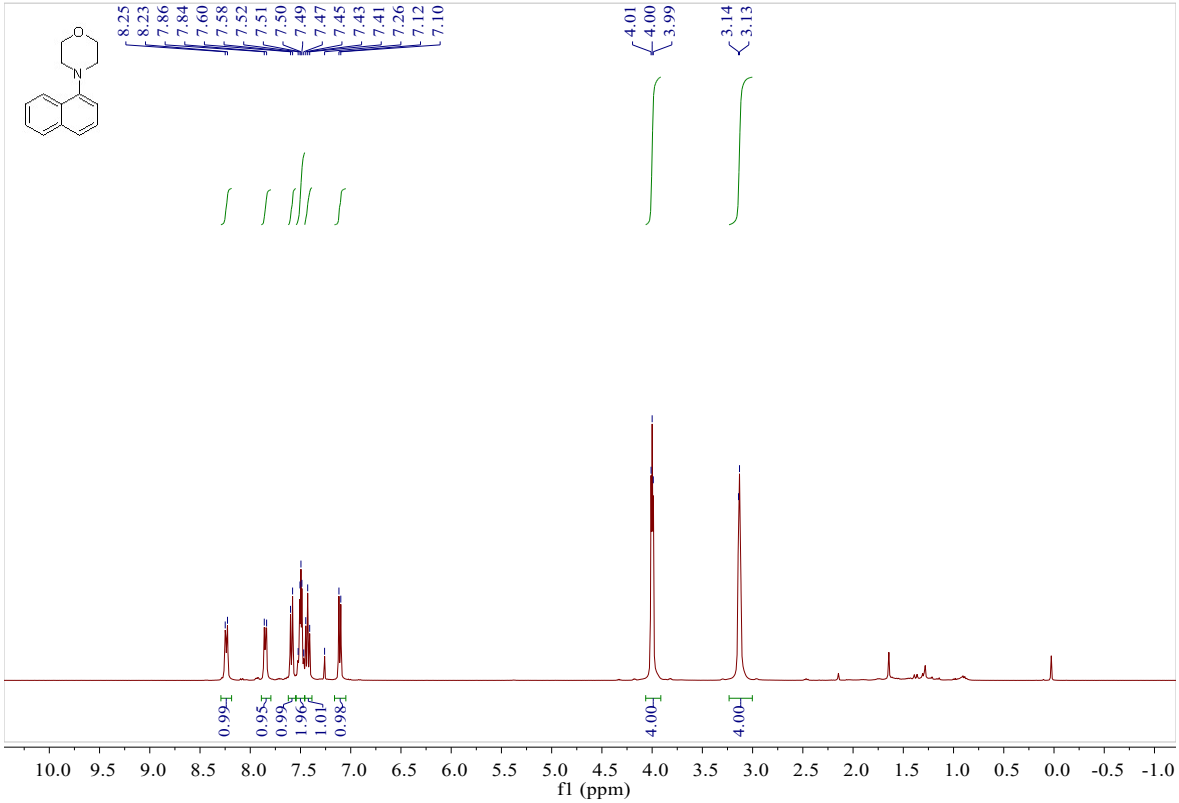
4-Methoxy-2-morpholinobenzaldehyde (3l): ^{1}H NMR (400 MHz, $CDCl_3$)



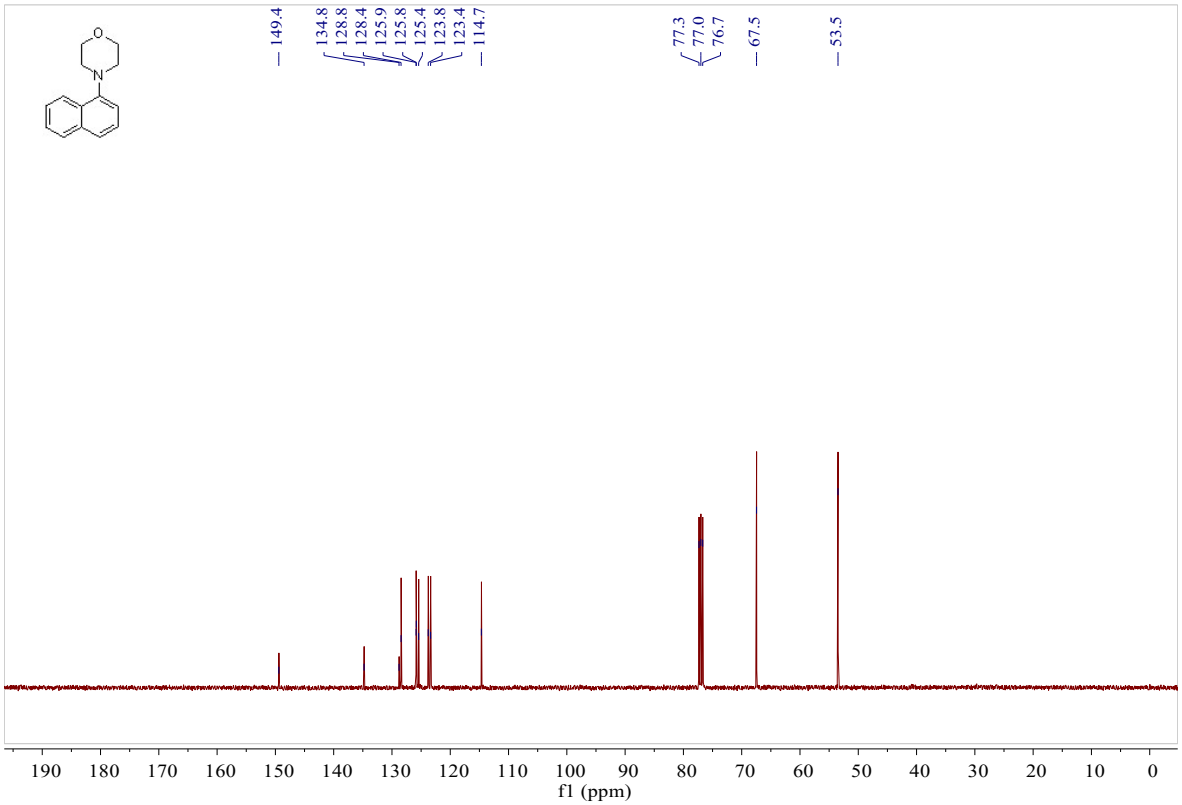
4-Methoxy-2-morpholinobenzaldehyde (3l): ^{13}C NMR (101 MHz, $CDCl_3$)



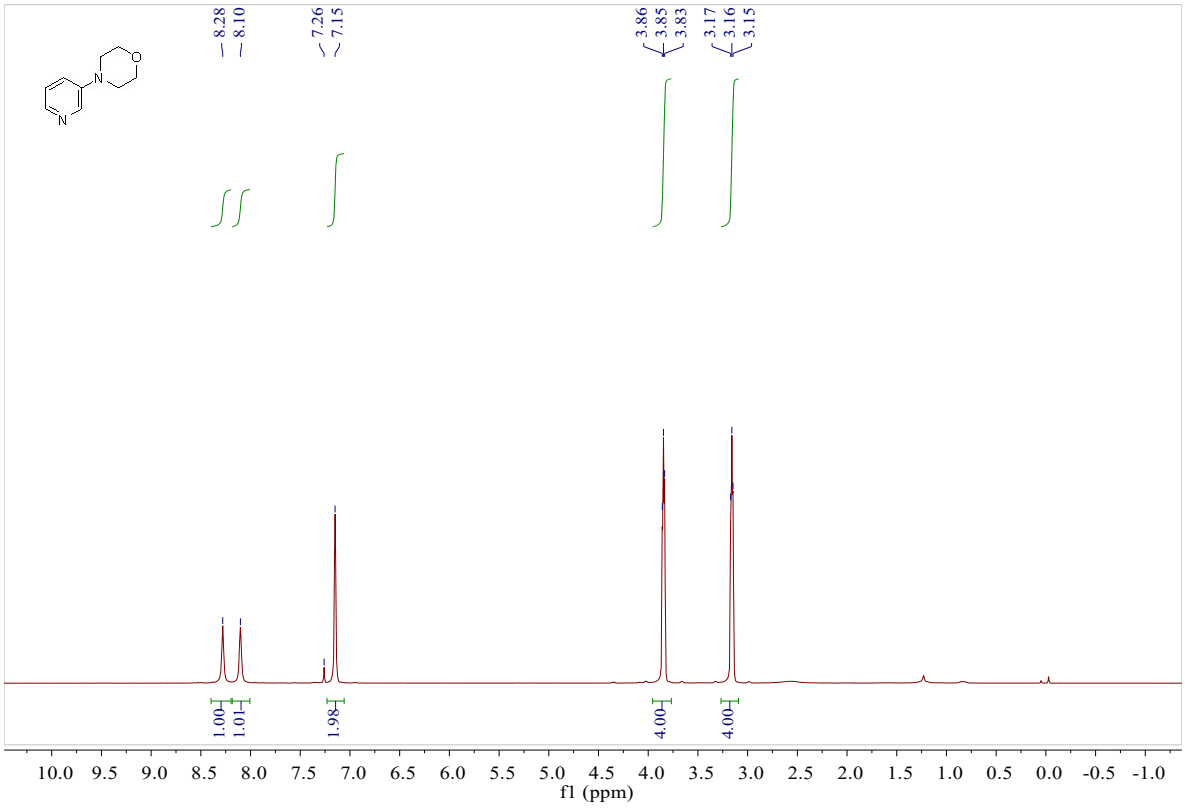
4-(Naphthalen-1-yl)morpholine (3m): ^{1}H NMR (400 MHz, $CDCl_3$)



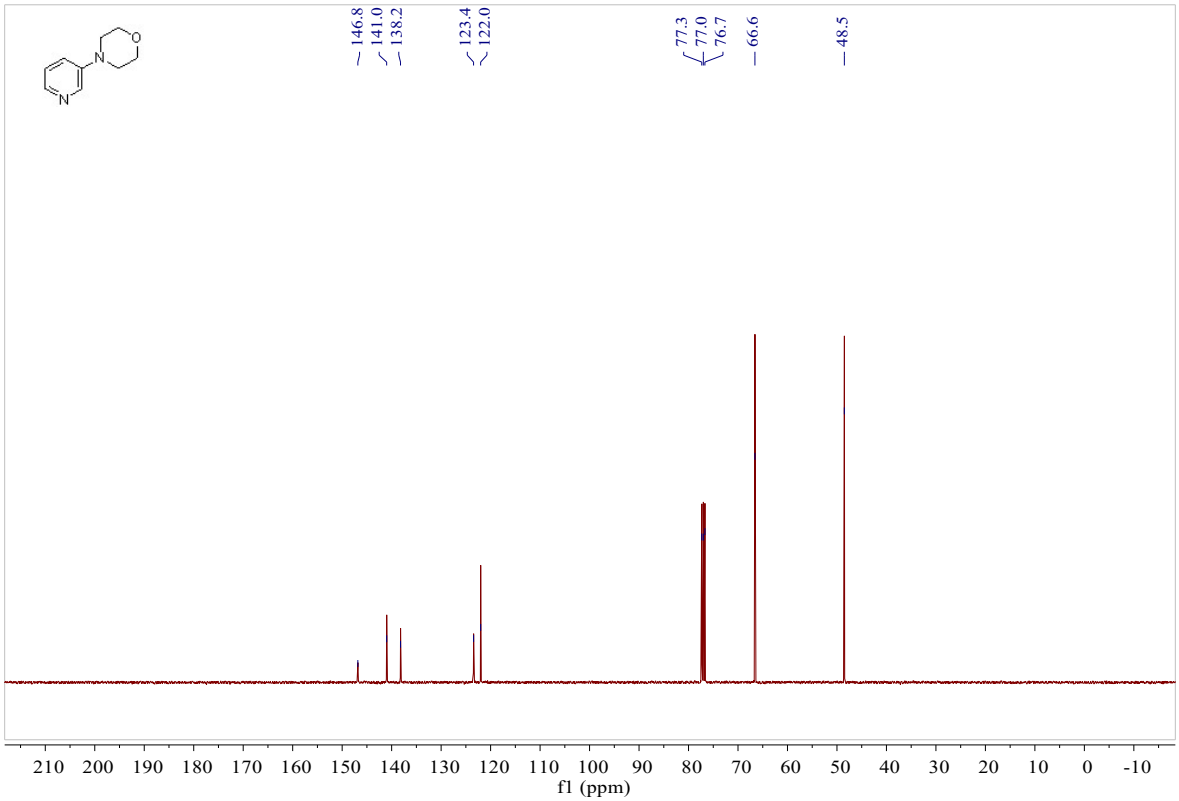
4-(Naphthalen-1-yl)morpholine (3m): ^{13}C NMR (101 MHz, $CDCl_3$)



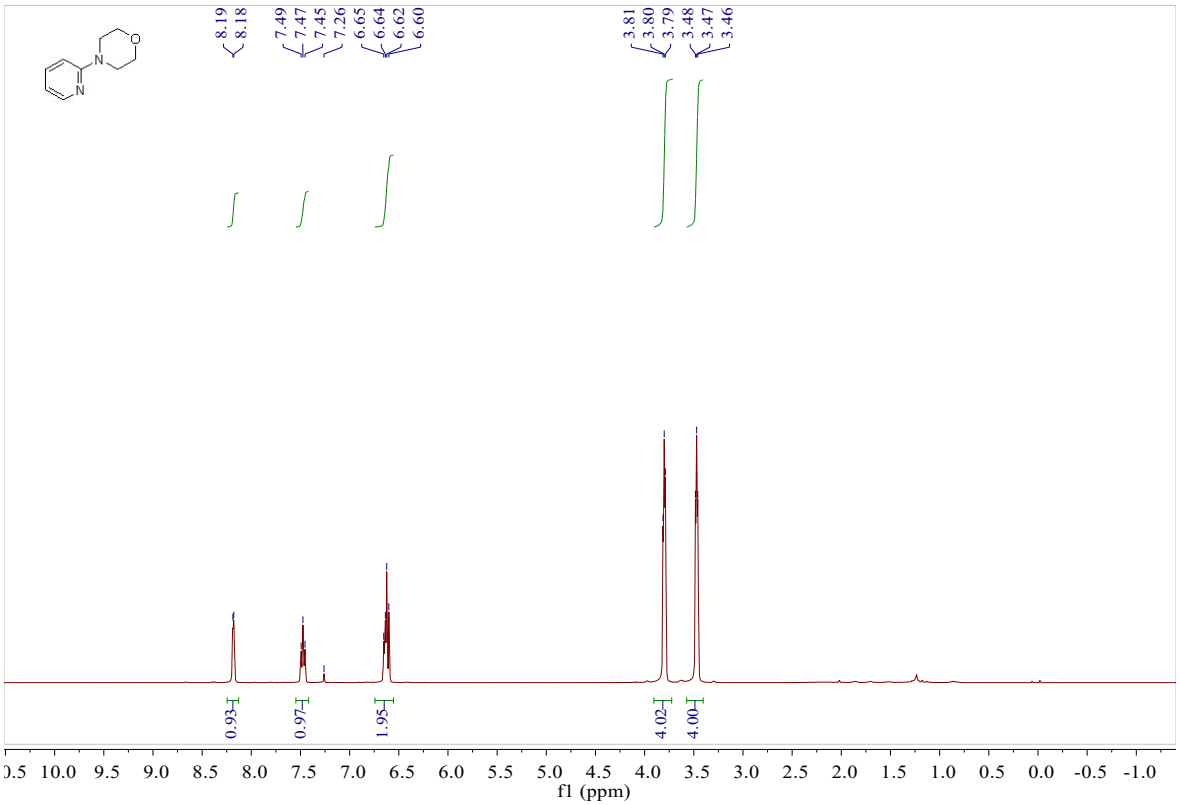
4-(Pyridin-3-yl)morpholine (3n): ^{1}H NMR (400 MHz, $CDCl_3$)



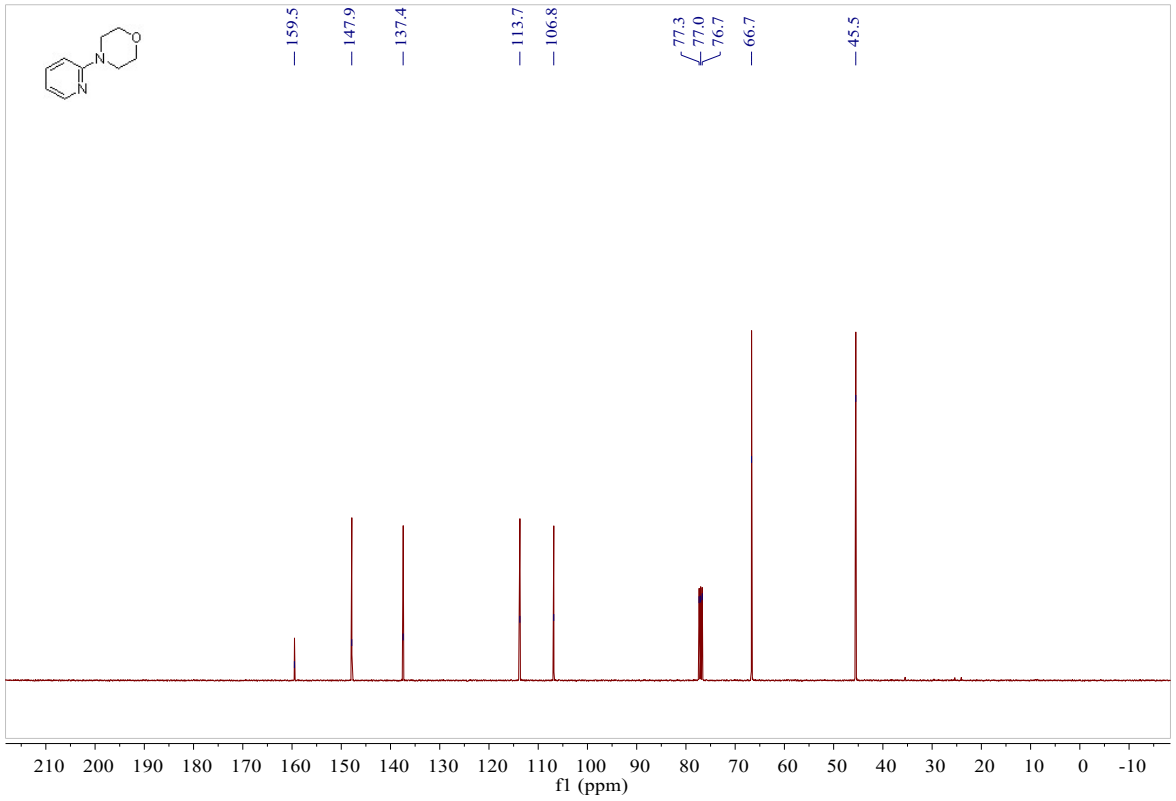
4-(Pyridin-3-yl)morpholine (3n): ^{13}C NMR (101 MHz, $CDCl_3$)



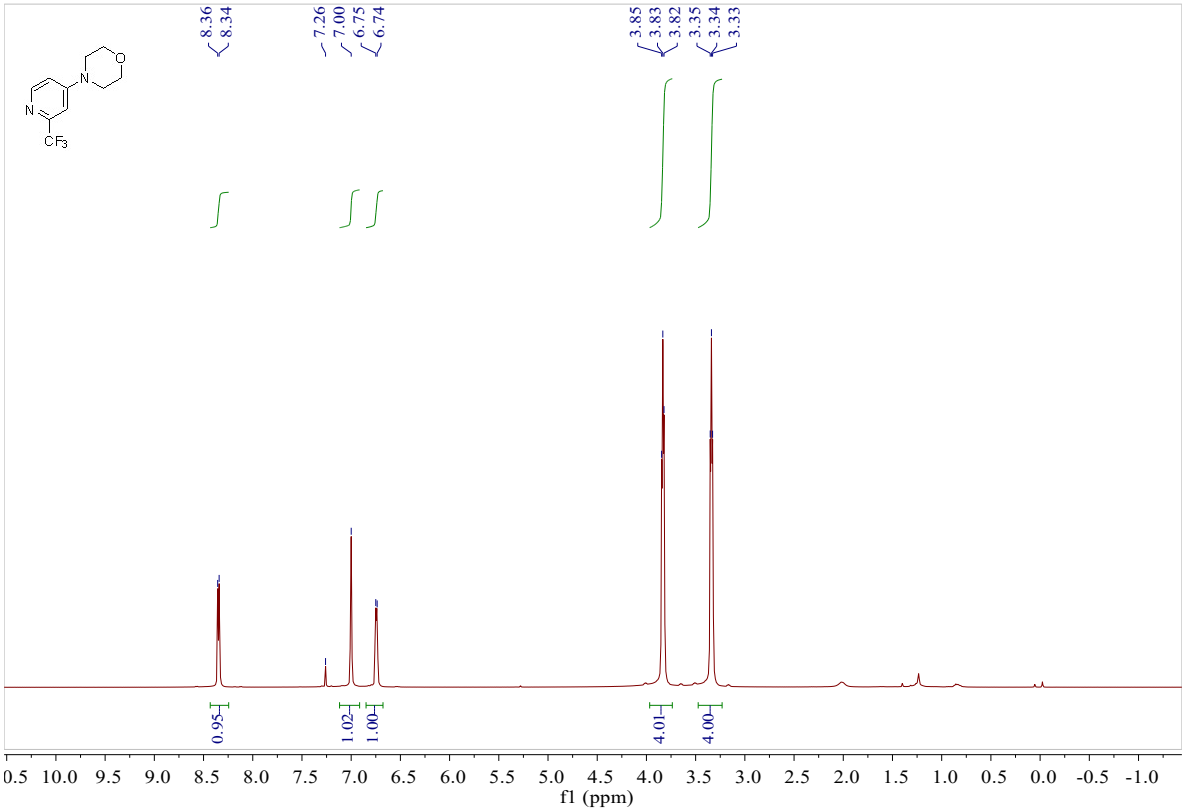
4-(Pyridin-2-yl)morpholine (3o): ^{1}H NMR (400 MHz, $CDCl_3$)



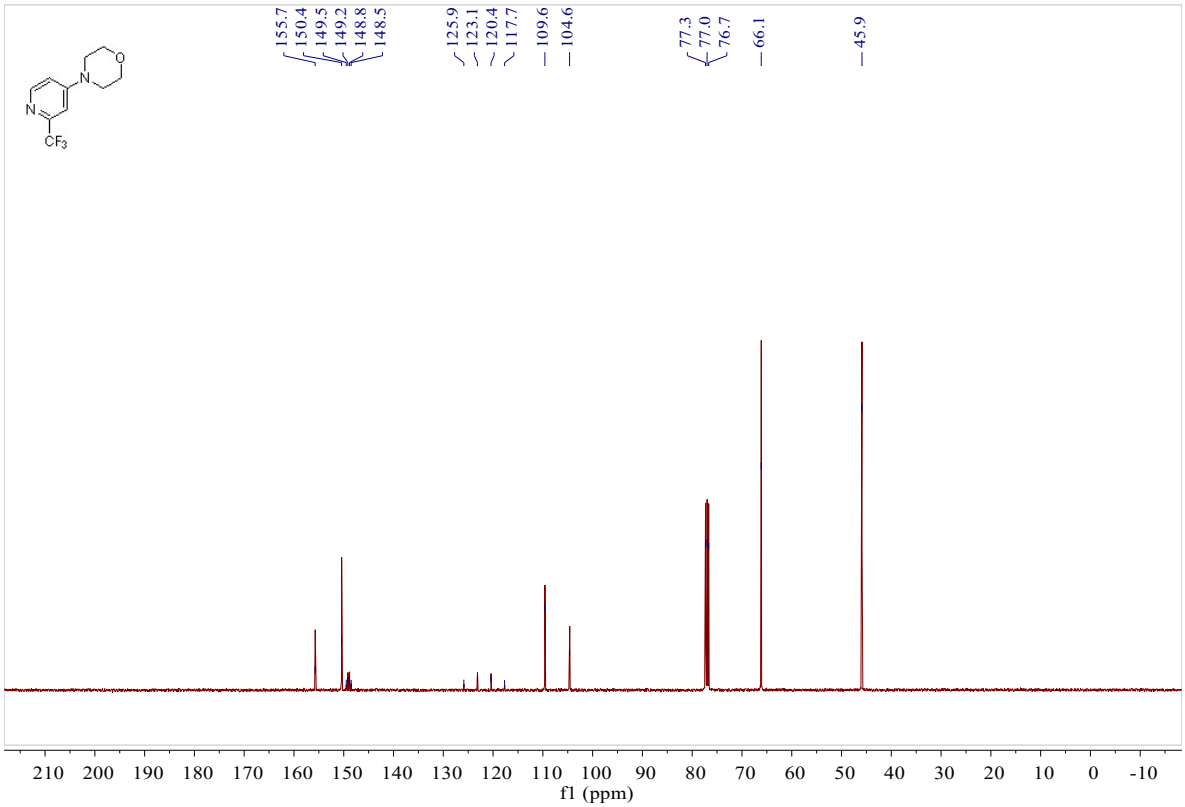
4-(Pyridin-2-yl)morpholine (3o): ^{13}C NMR (101 MHz, $CDCl_3$)



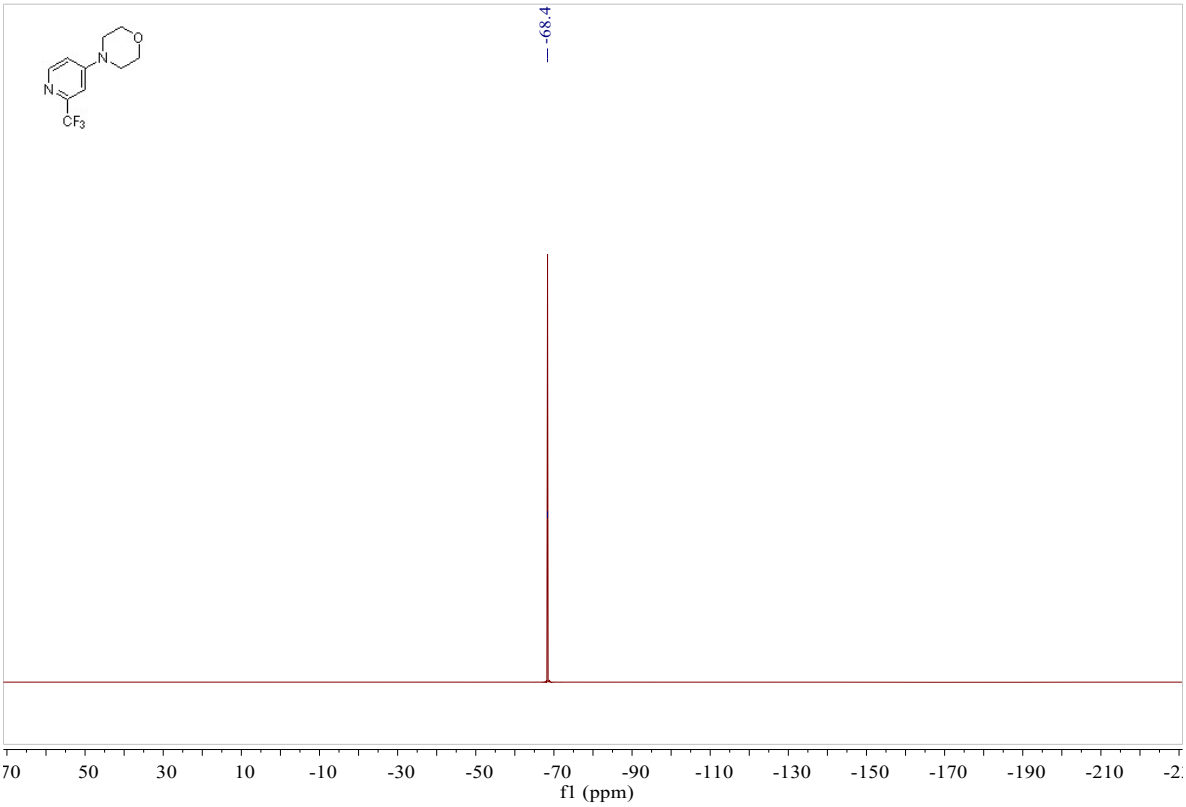
4-(2-(Trifluoromethyl)pyridin-4-yl)morpholine (3p): ^{1}H NMR (400 MHz, $CDCl_3$)



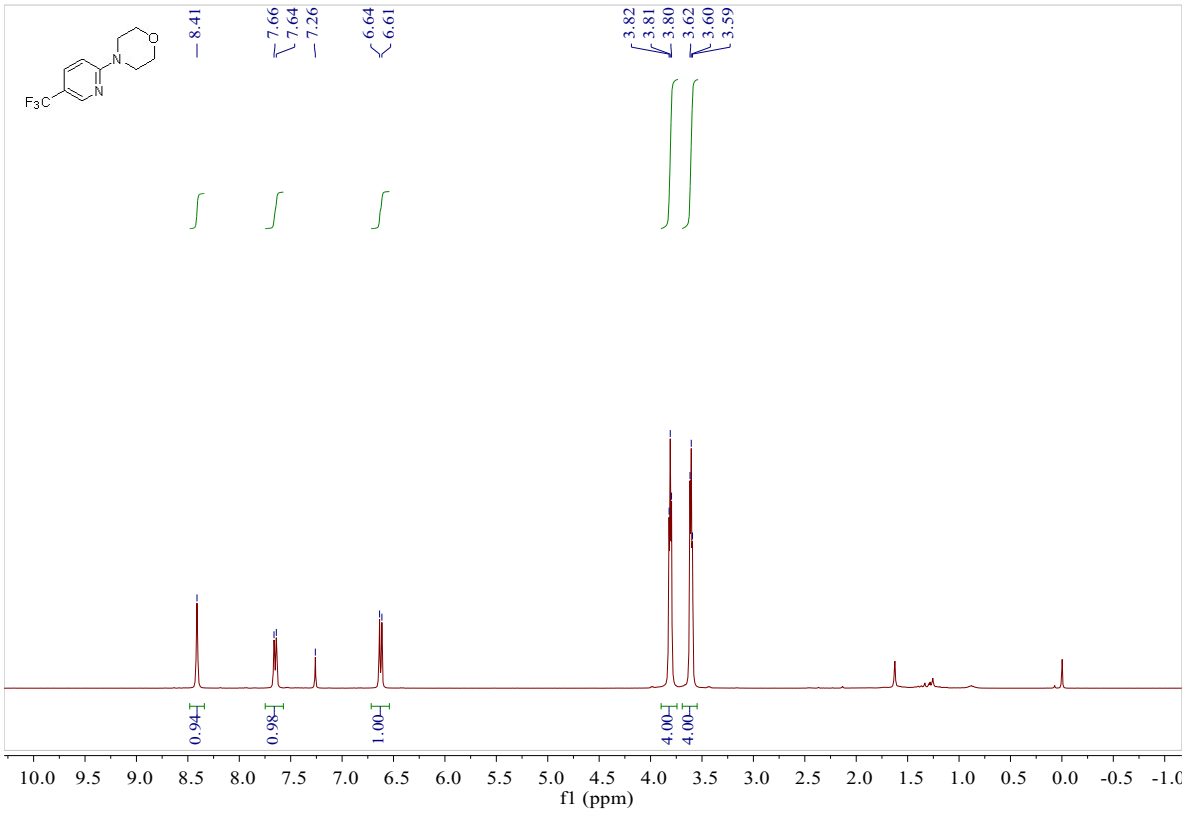
4-(2-(Trifluoromethyl)pyridin-4-yl)morpholine (3p): ^{13}C NMR (101 MHz, $CDCl_3$)



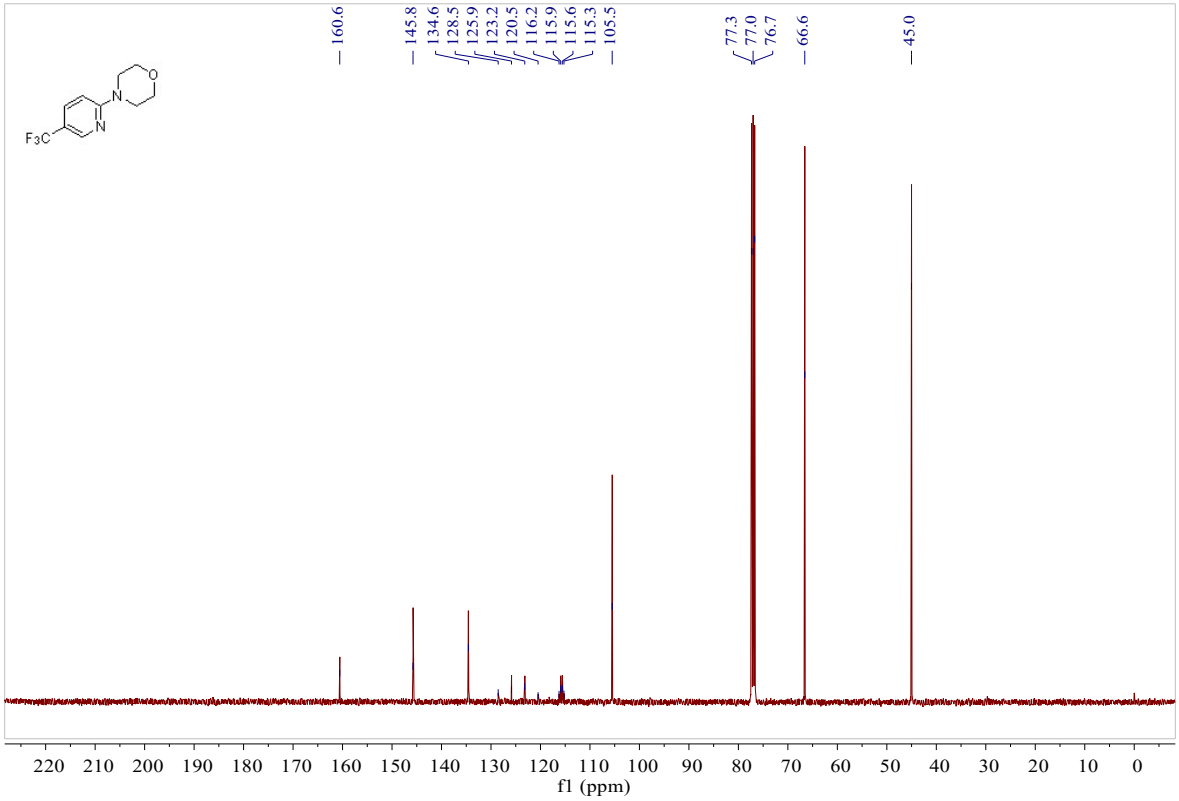
4-(2-(Trifluoromethyl)pyridin-4-yl)morpholine (3p): ^{19}F NMR (377 MHz, $CDCl_3$)



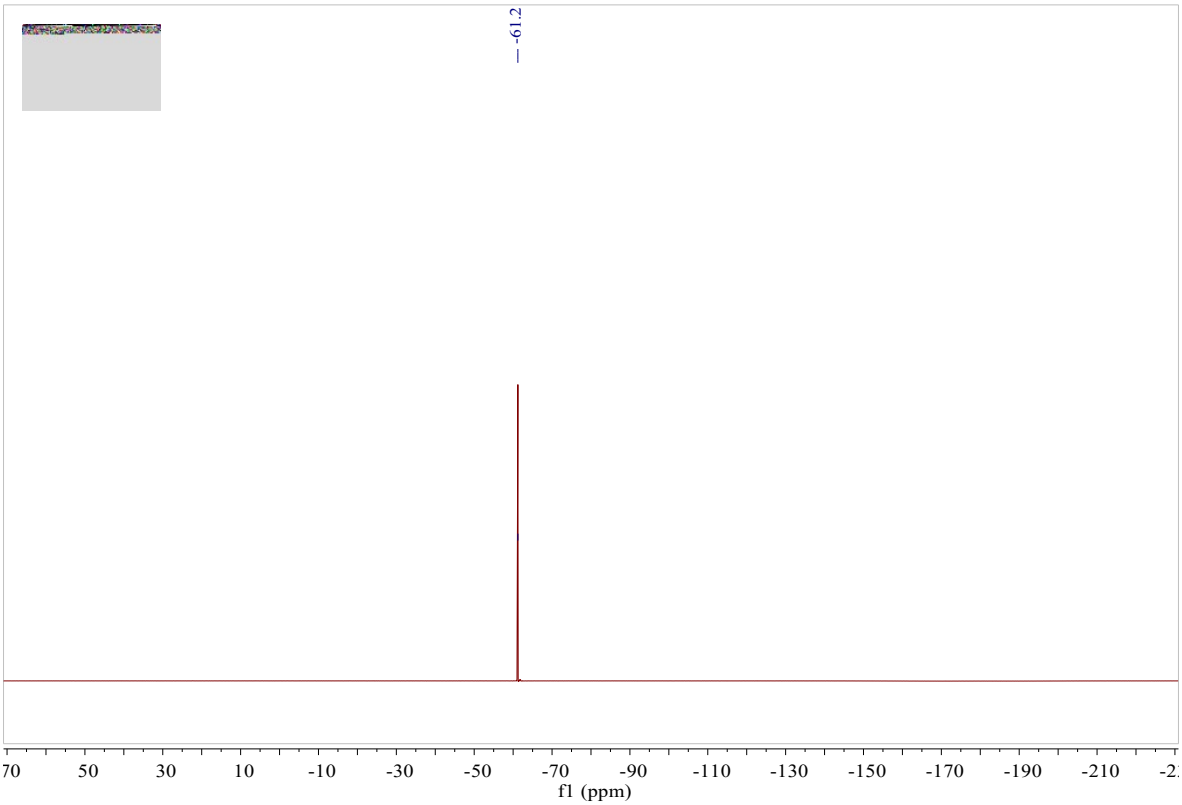
4-(5-(Trifluoromethyl)pyridin-2-yl)morpholine (3q): ^{1}H NMR (400 MHz, $CDCl_3$)



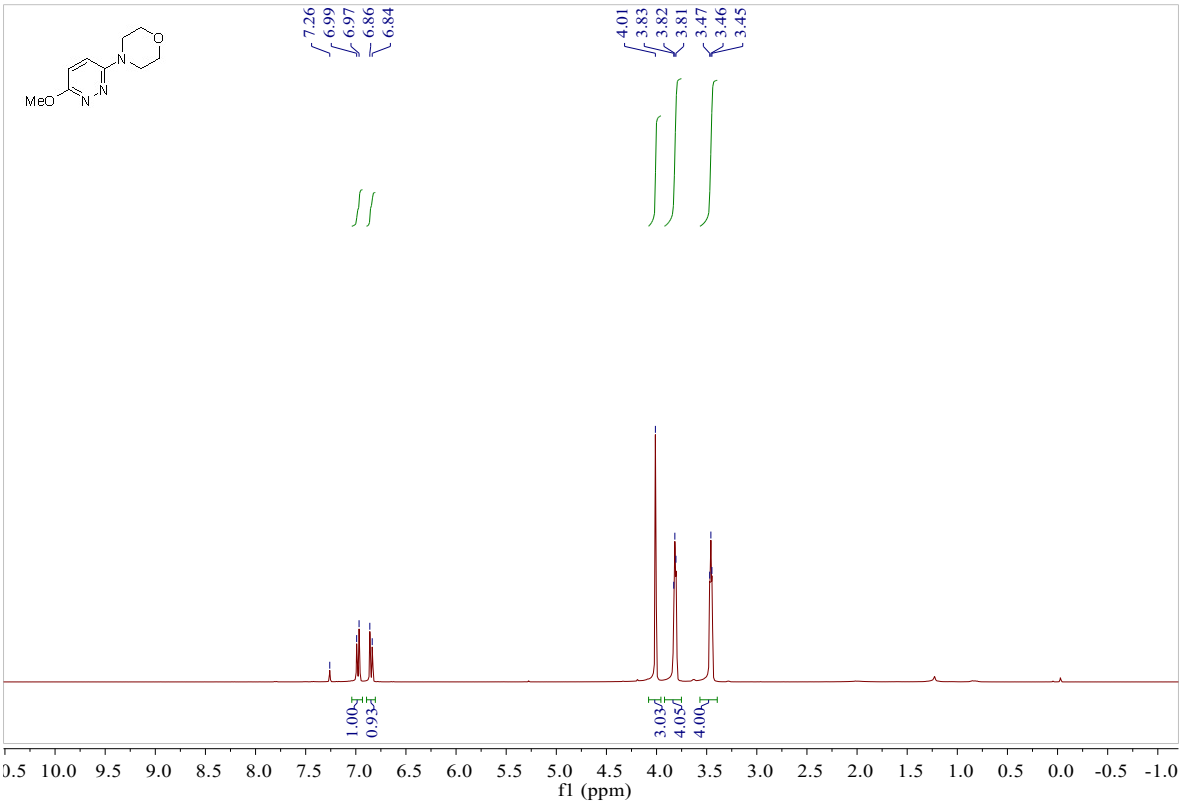
4-(5-(Trifluoromethyl)pyridin-2-yl)morpholine (3q): ^{13}C NMR (101 MHz, $CDCl_3$)



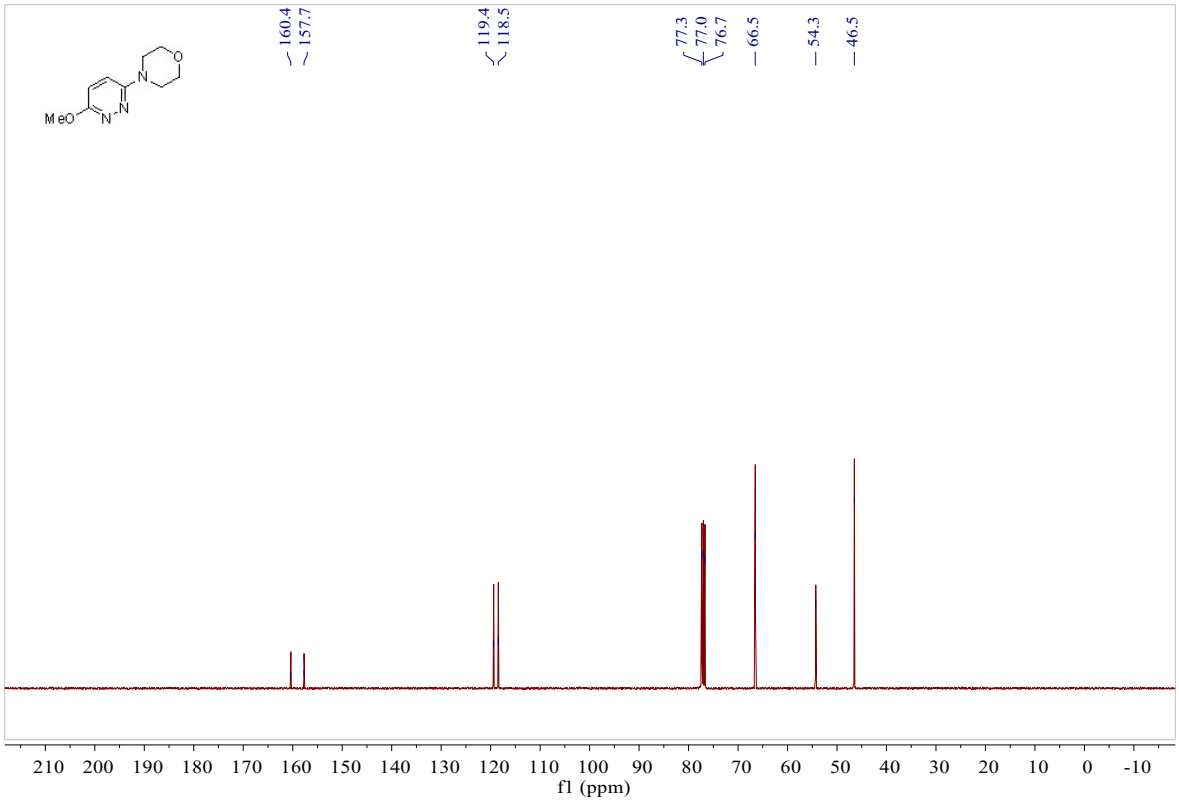
4-(5-(Trifluoromethyl)pyridin-2-yl)morpholine (3q): ^{19}F NMR (377 MHz, $CDCl_3$)



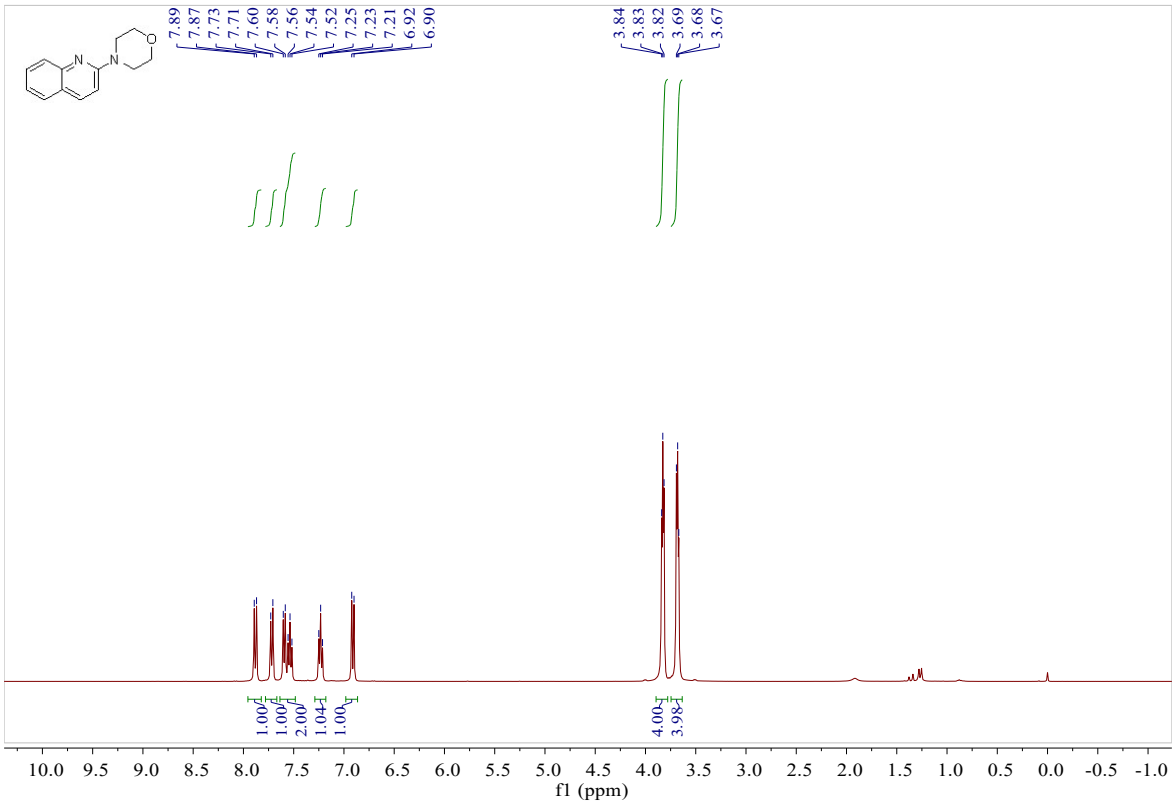
4-(6-Methoxypyridazin-3-yl)morpholine (3r): ^{1}H NMR (400 MHz, $CDCl_3$)



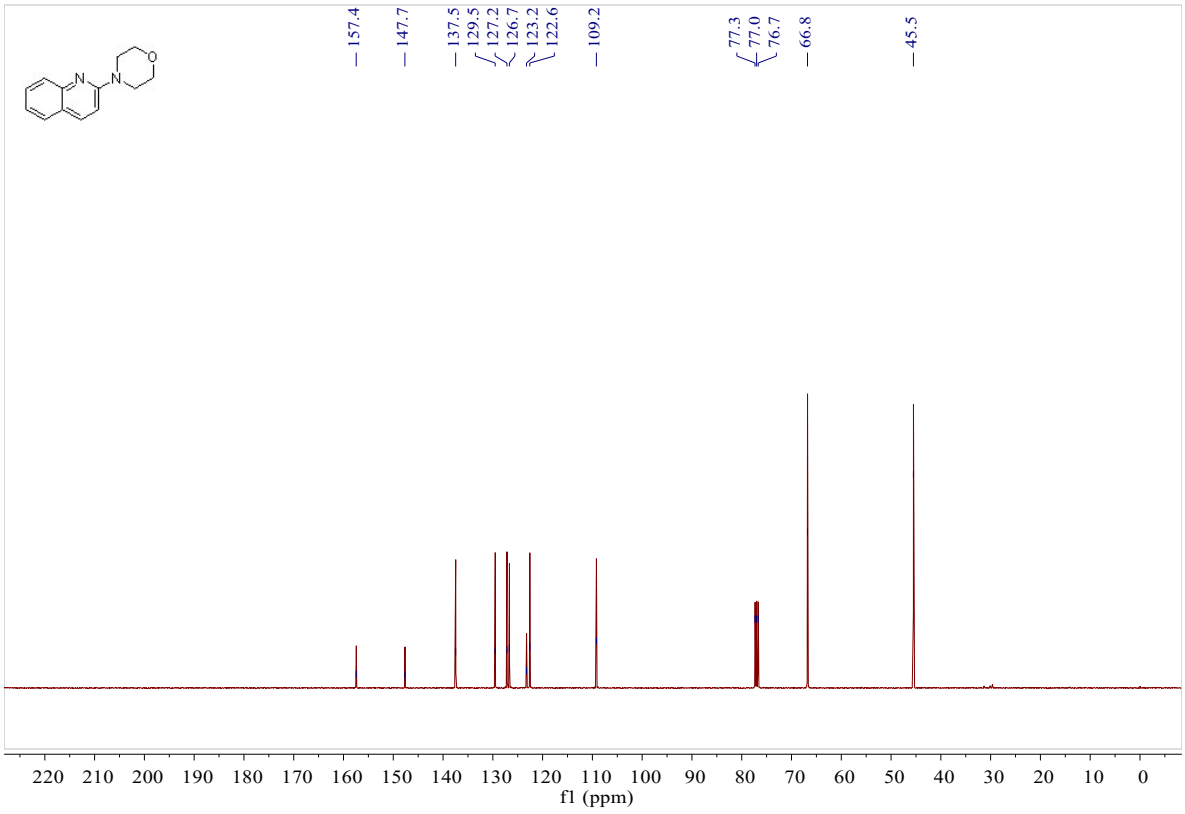
4-(6-Methoxypyridazin-3-yl)morpholine (3r): ^{13}C NMR (101 MHz, $CDCl_3$)



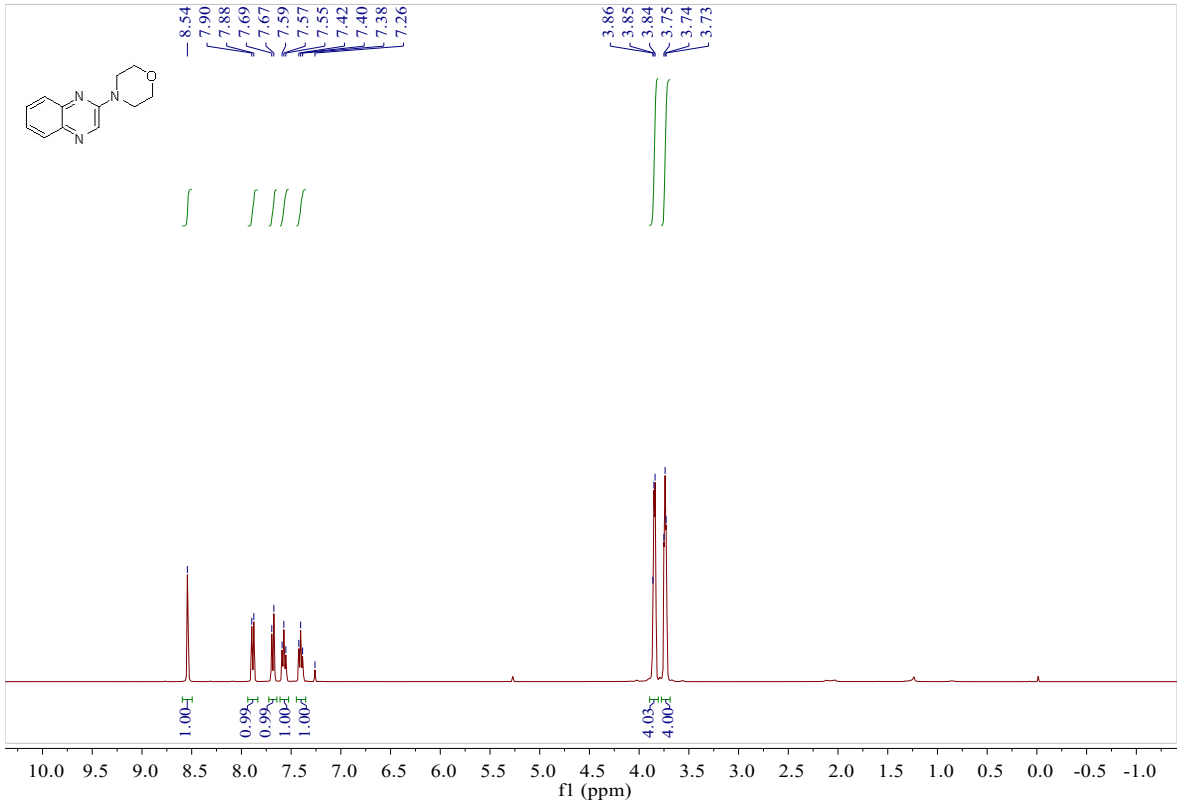
4-(Quinolin-2-yl)morpholine (3s): ^{1}H NMR (400 MHz, $CDCl_3$)



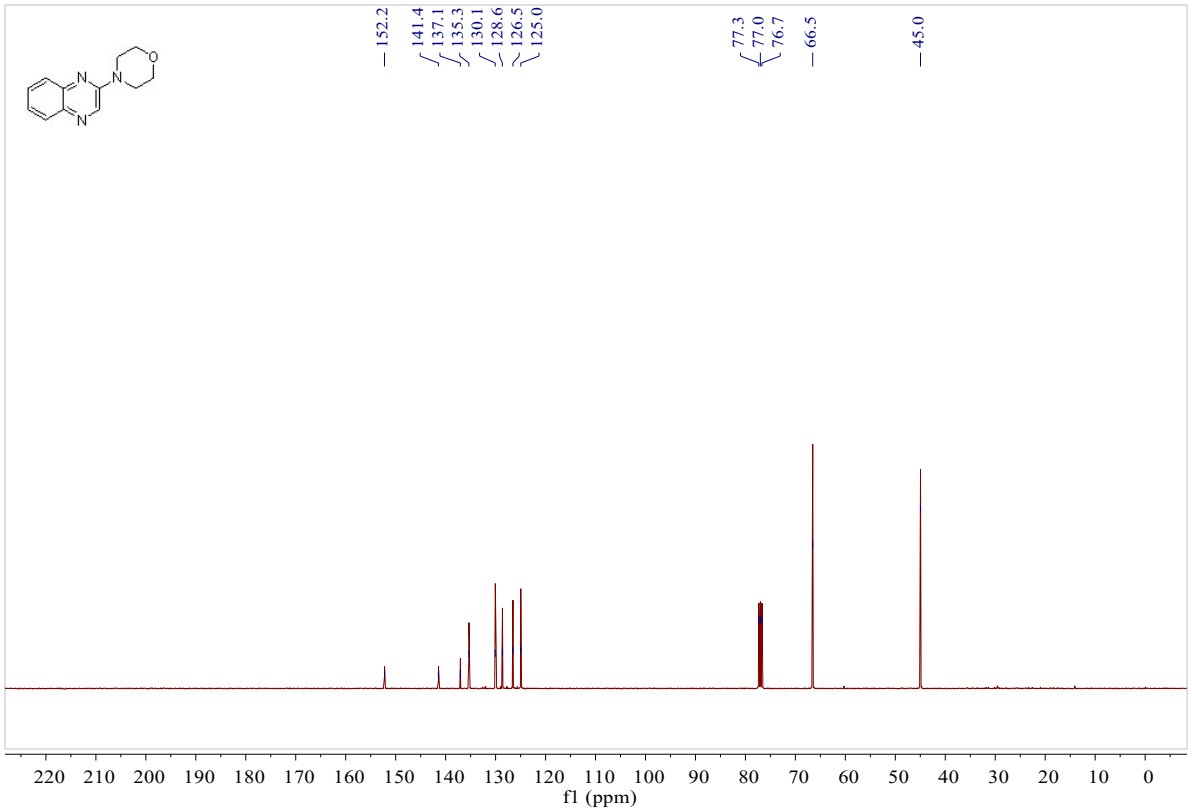
4-(Quinolin-2-yl)morpholine (3s): ^{13}C NMR (101 MHz, $CDCl_3$)



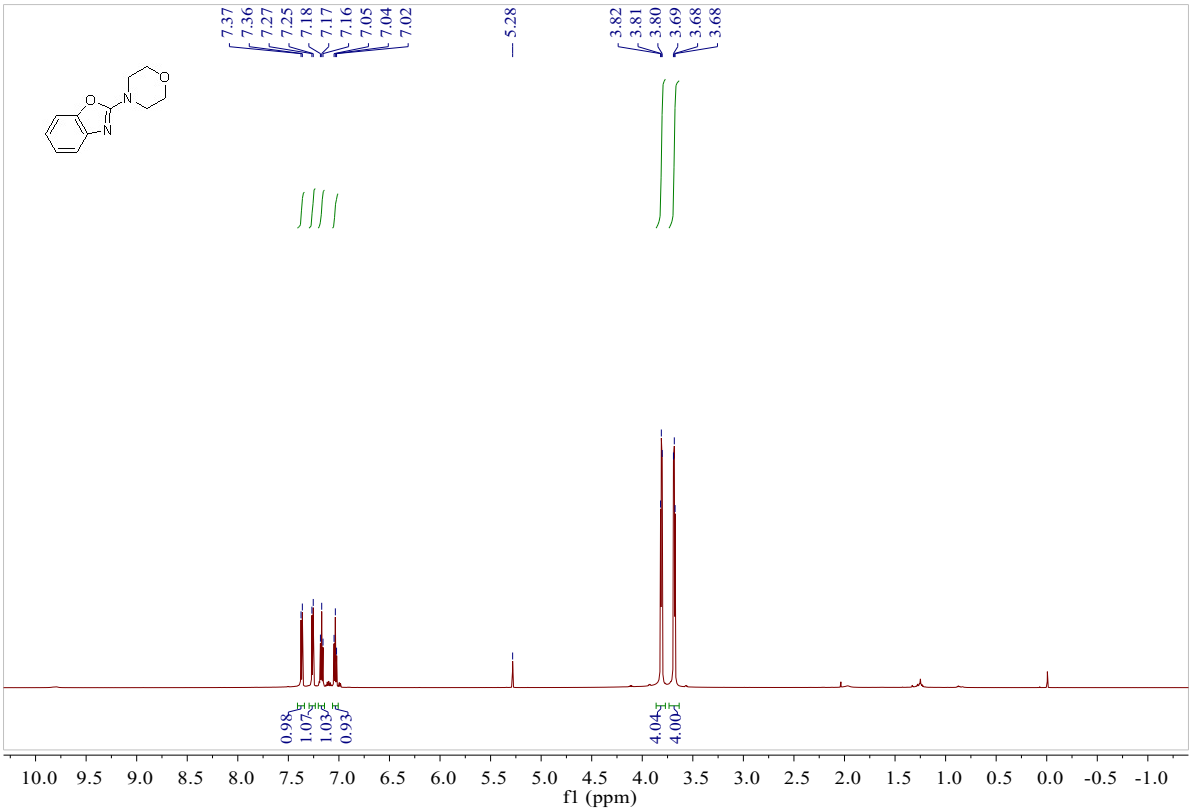
4-(Quinoxalin-2-yl)morpholine (3t): ^{1}H NMR (400 MHz, $CDCl_3$)



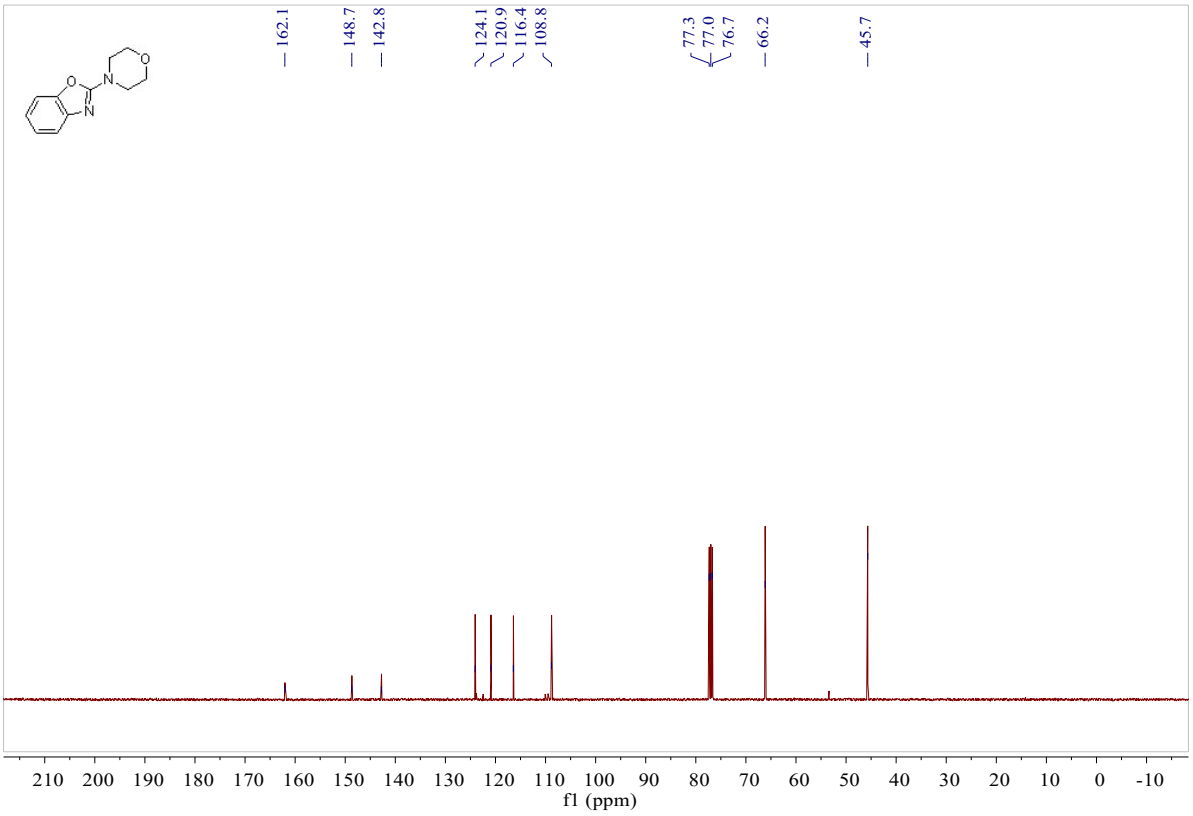
4-(Quinoxaline-2-yl)morpholine (3t): ^{13}C NMR (101 MHz, $CDCl_3$)



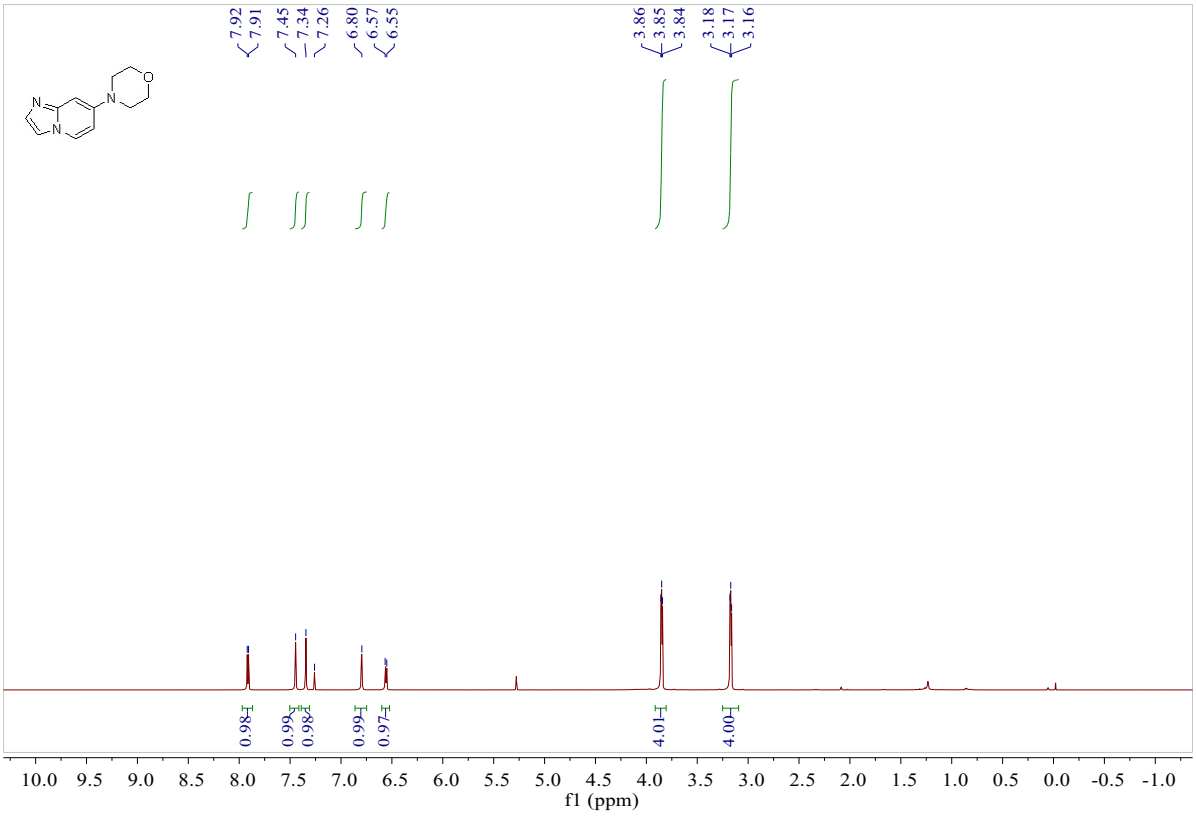
2-Morpholinobenzo[d]oxazole (3u): ^{1}H NMR (400 MHz, $CDCl_3$)



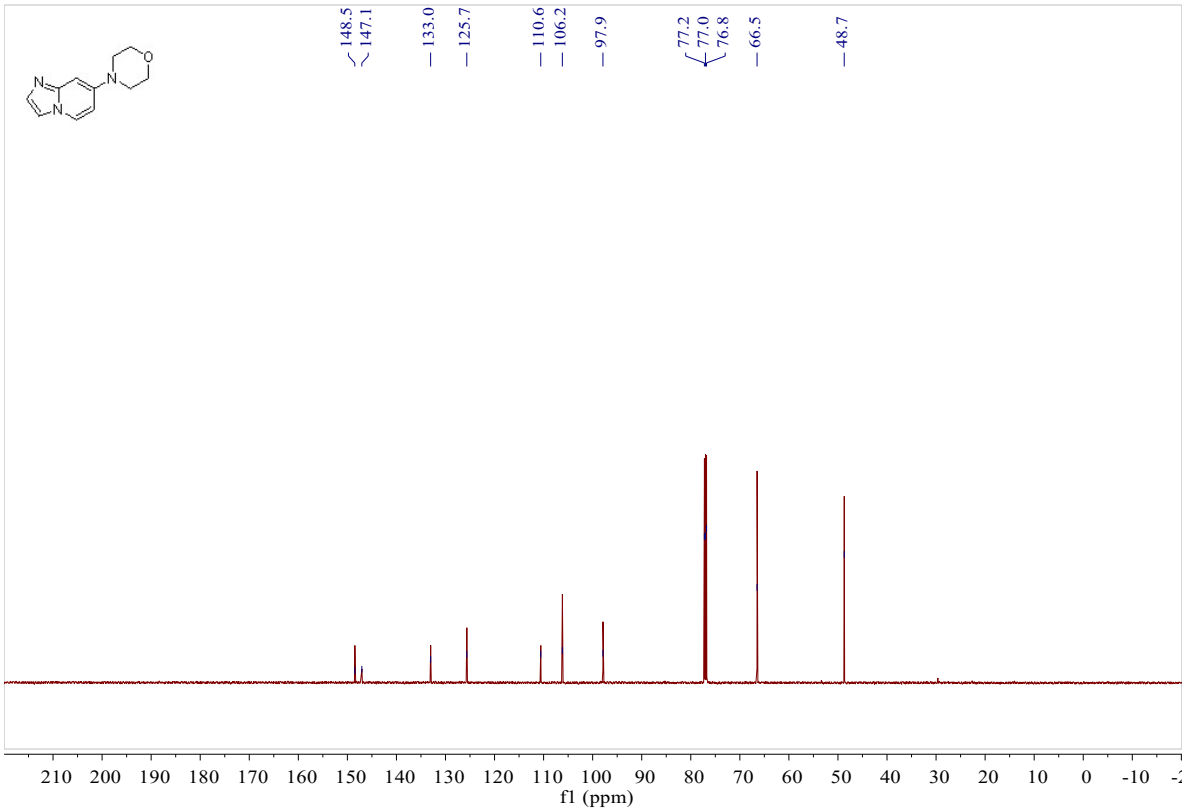
2-Morpholinobenzo[d]oxazole (3u): ^{13}C NMR (101 MHz, $CDCl_3$)



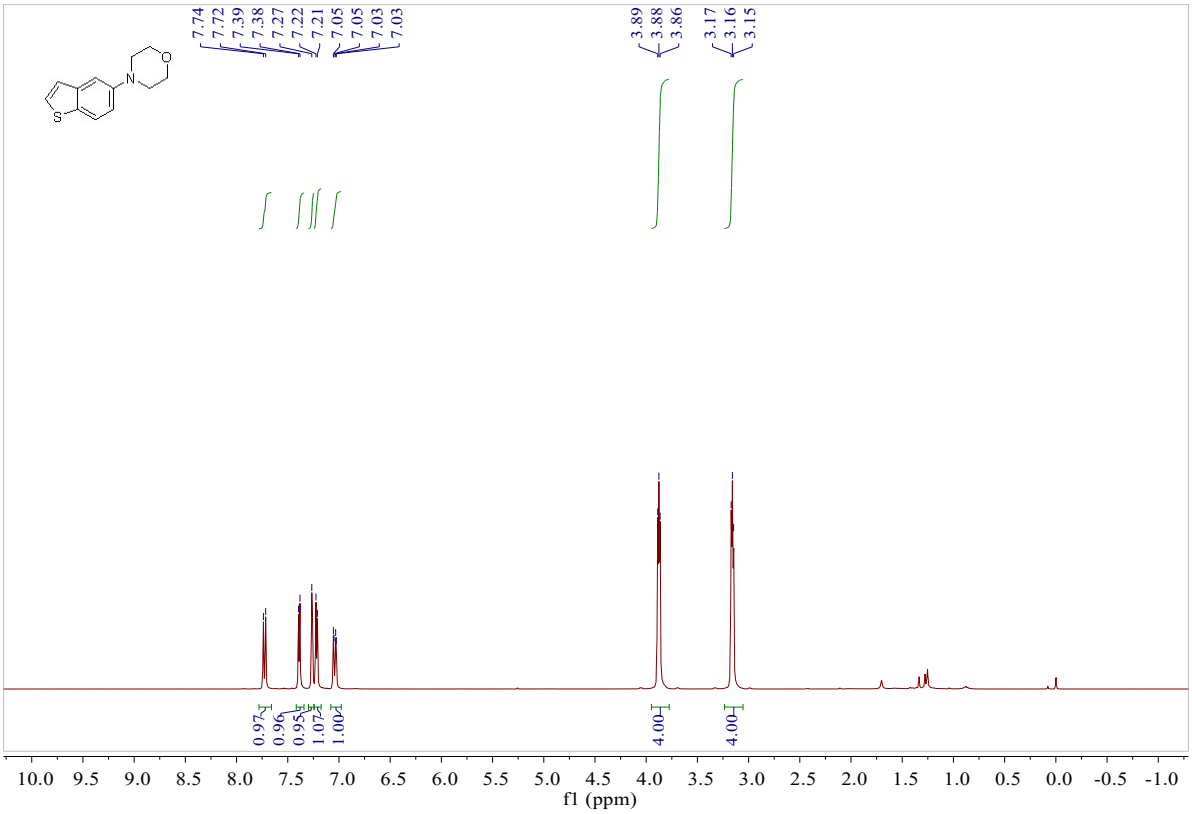
4-(Imidazo[1,2-*a*]pyridin-7-yl)morpholine (3v): ^{1}H NMR (600 MHz, $CDCl_3$)



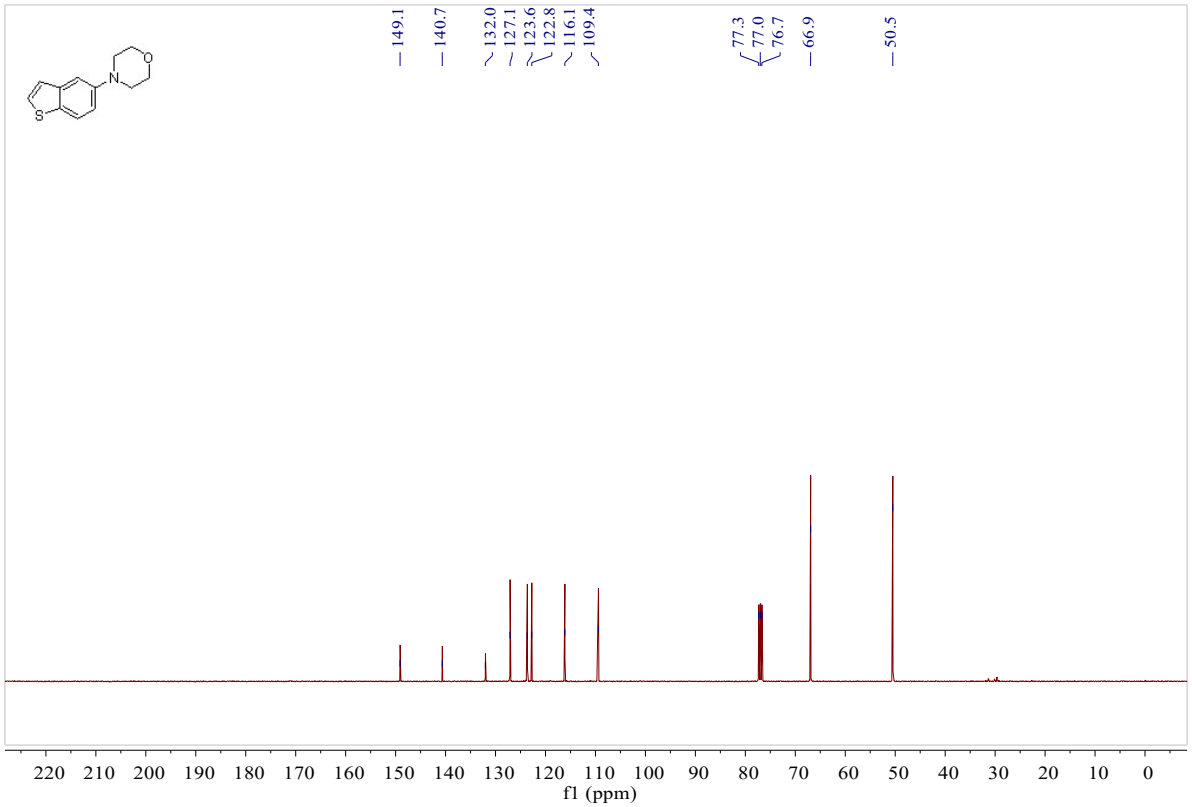
4-(Imidazo[1,2-*a*]pyridin-7-yl)morpholine (3v): ^{13}C NMR (151 MHz, $CDCl_3$)



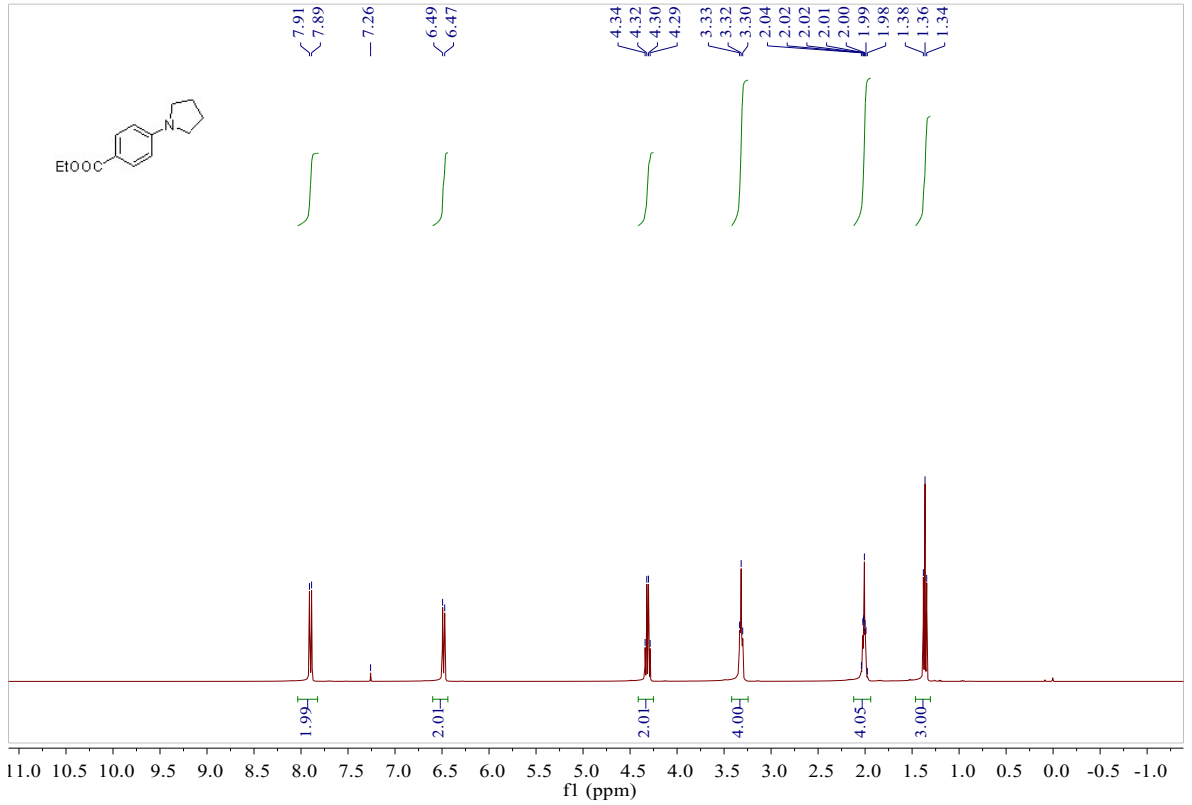
4-(Benzo[*b*]thiophen-5-yl)morpholine (3w): ^{1}H NMR (400 MHz, $CDCl_3$)



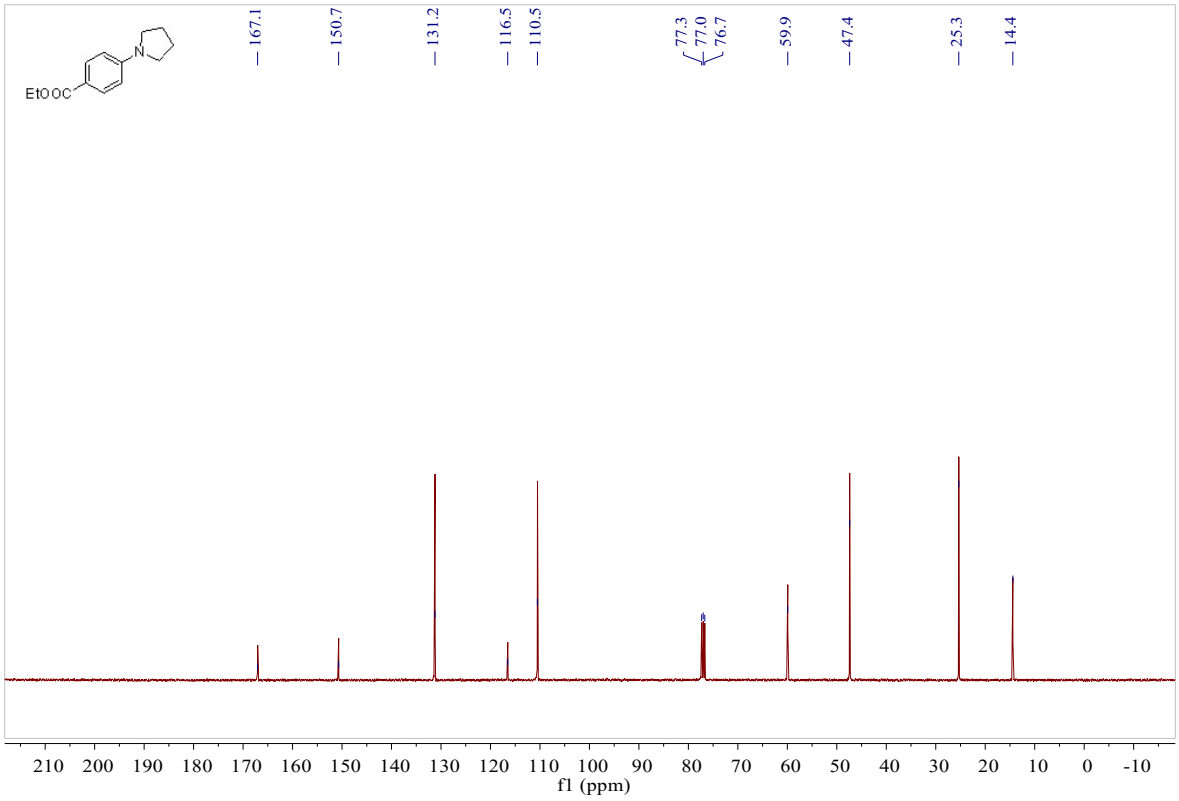
4-(Benzo[*b*]thiophen-5-yl)morpholine (3w): ^{13}C NMR (101 MHz, $CDCl_3$)



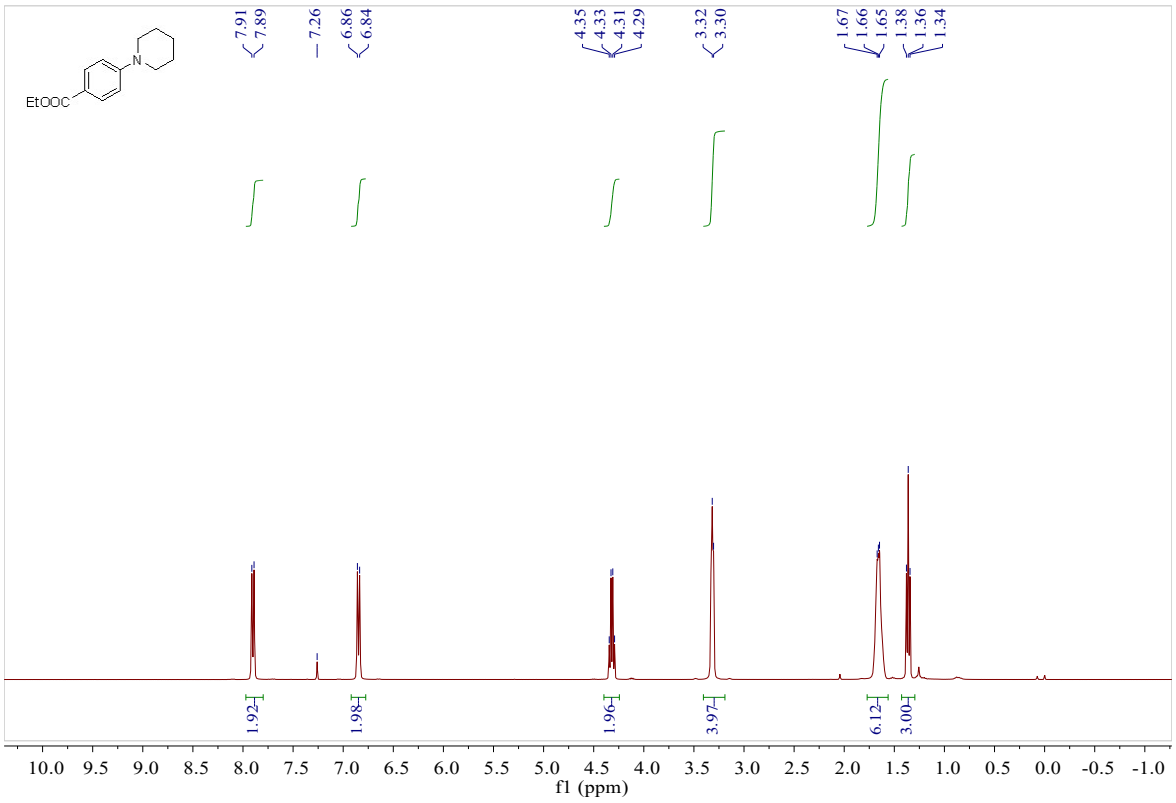
Ethyl 4-(pyrrolidin-1-yl)benzoate (3x): ^{1}H NMR (400 MHz, $CDCl_3$)



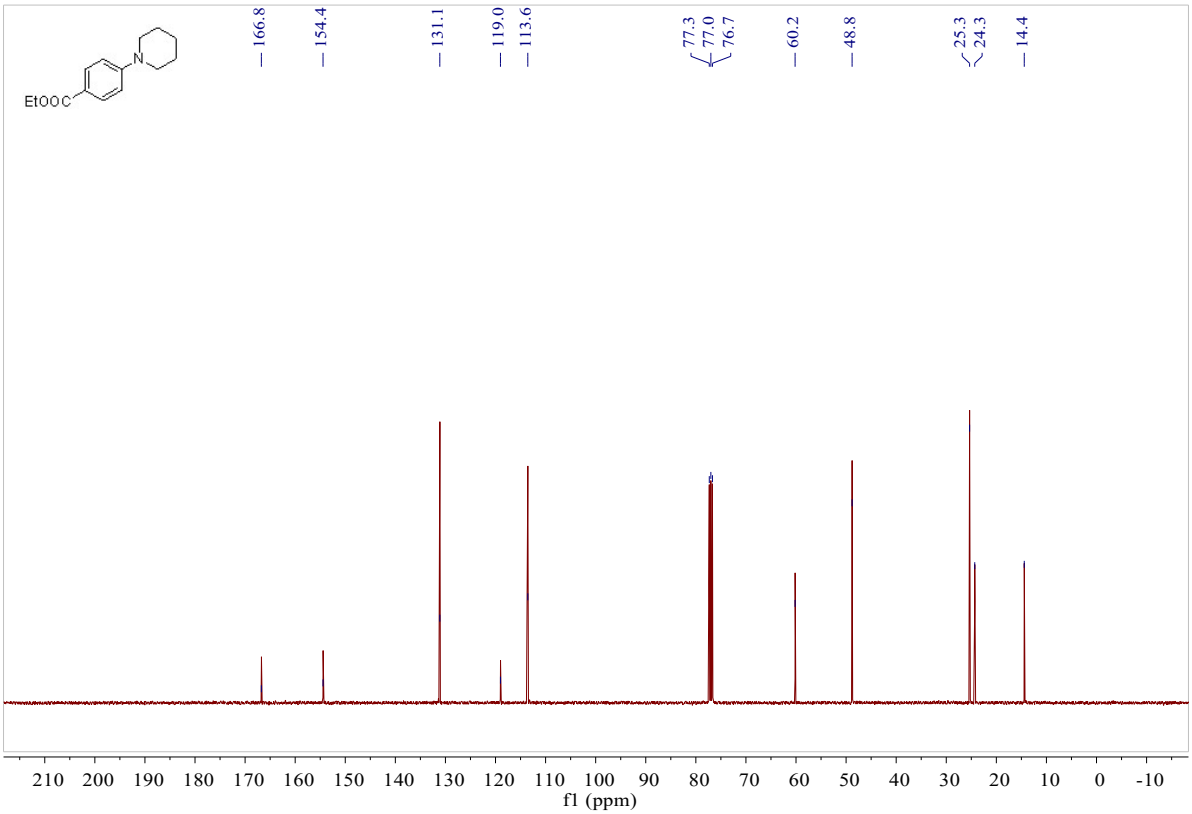
Ethyl 4-(pyrrolidin-1-yl)benzoate (3x): ^{13}C NMR (100 MHz, $CDCl_3$)



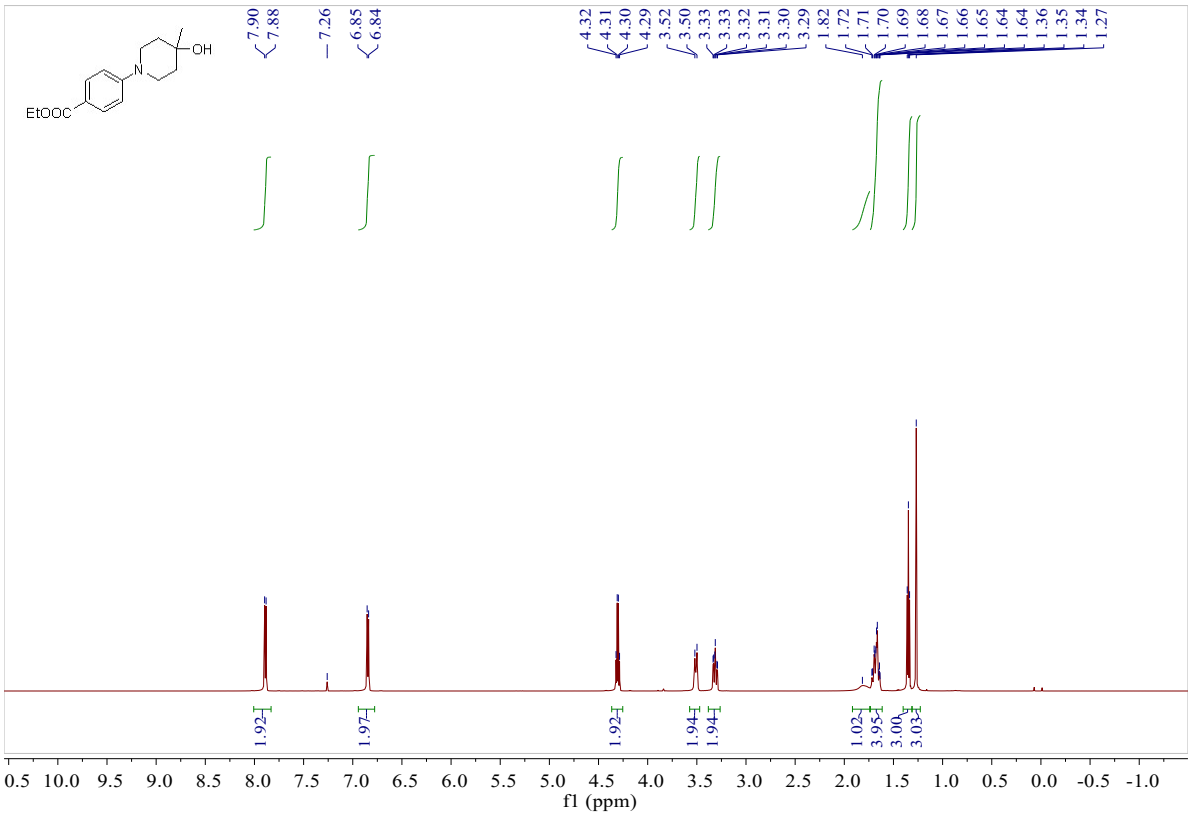
Ethyl 4-(piperidin-1-yl)benzoate (3y): ^{1}H NMR (400 MHz, $CDCl_3$)



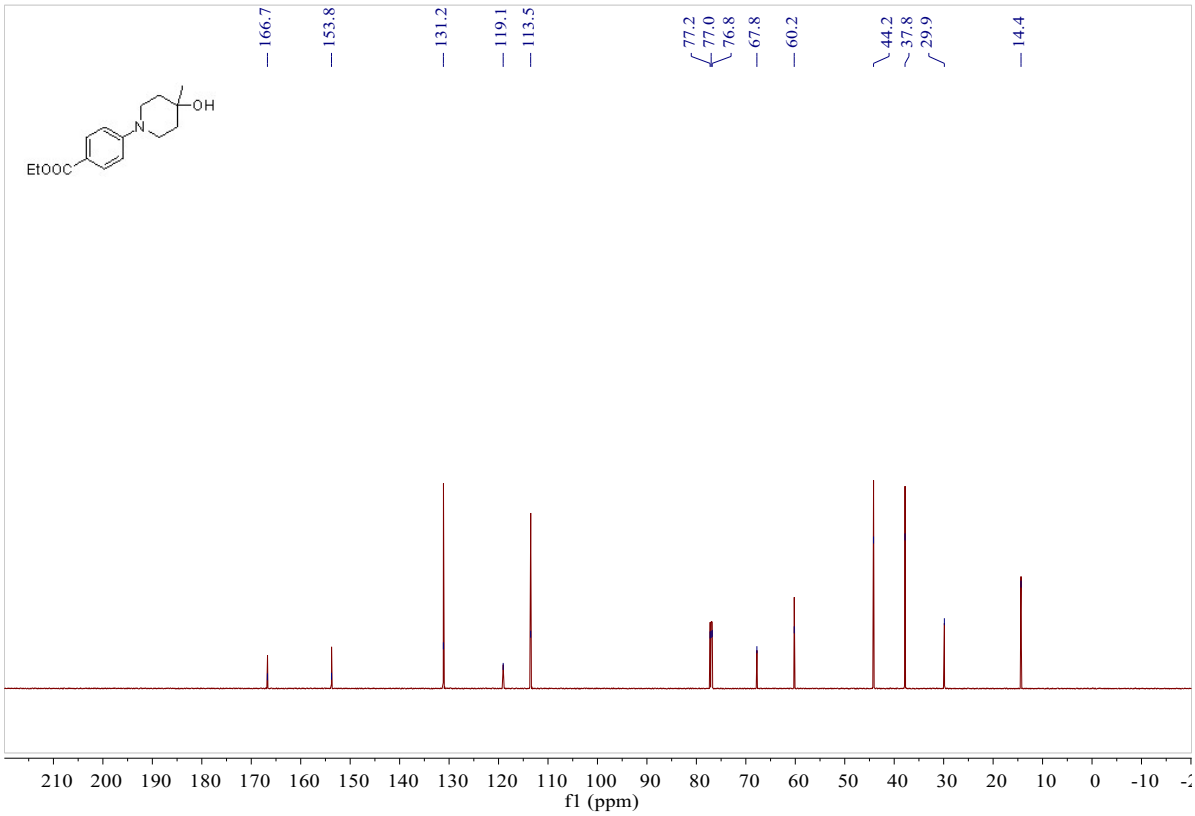
Ethyl 4-(piperidin-1-yl)benzoate (3y): ^{13}C NMR (100 MHz, $CDCl_3$)



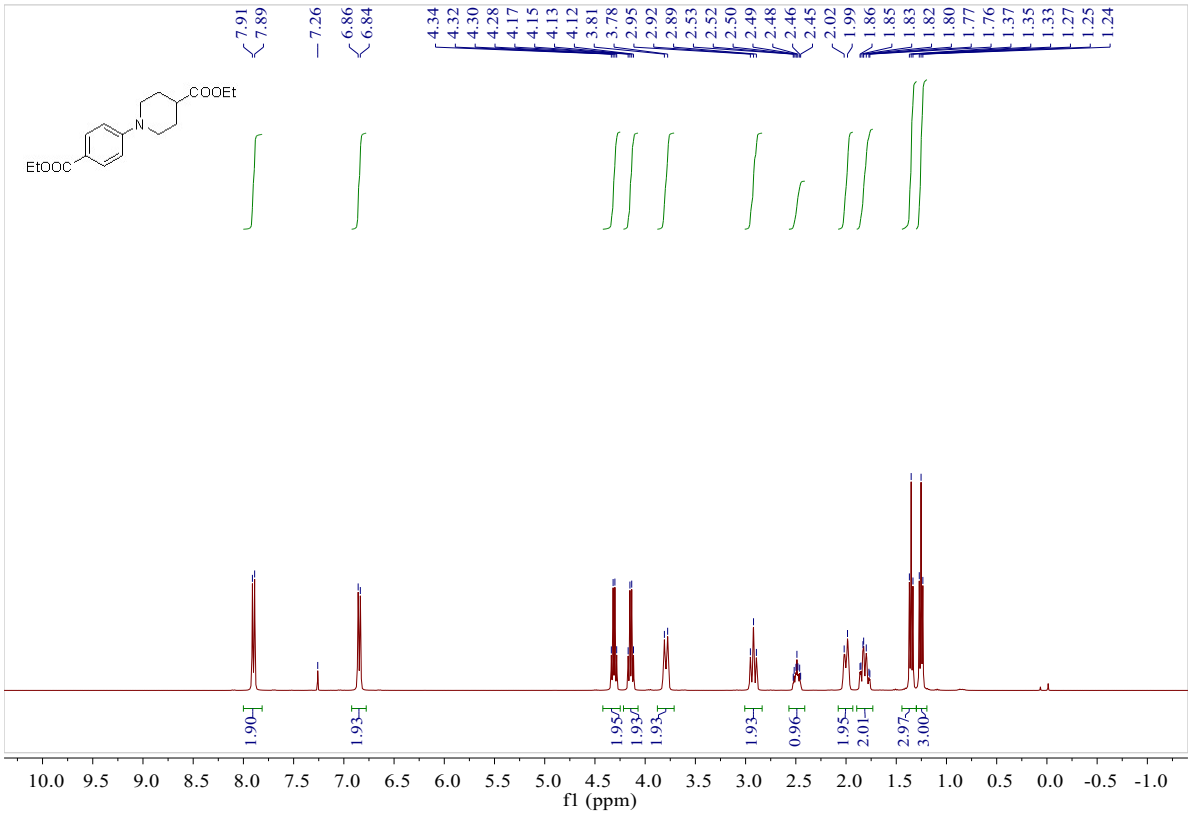
Ethyl 4-(4-hydroxy-4-methylpiperidin-1-yl)benzoate (3z): ^{1}H NMR (400 MHz, $CDCl_3$)



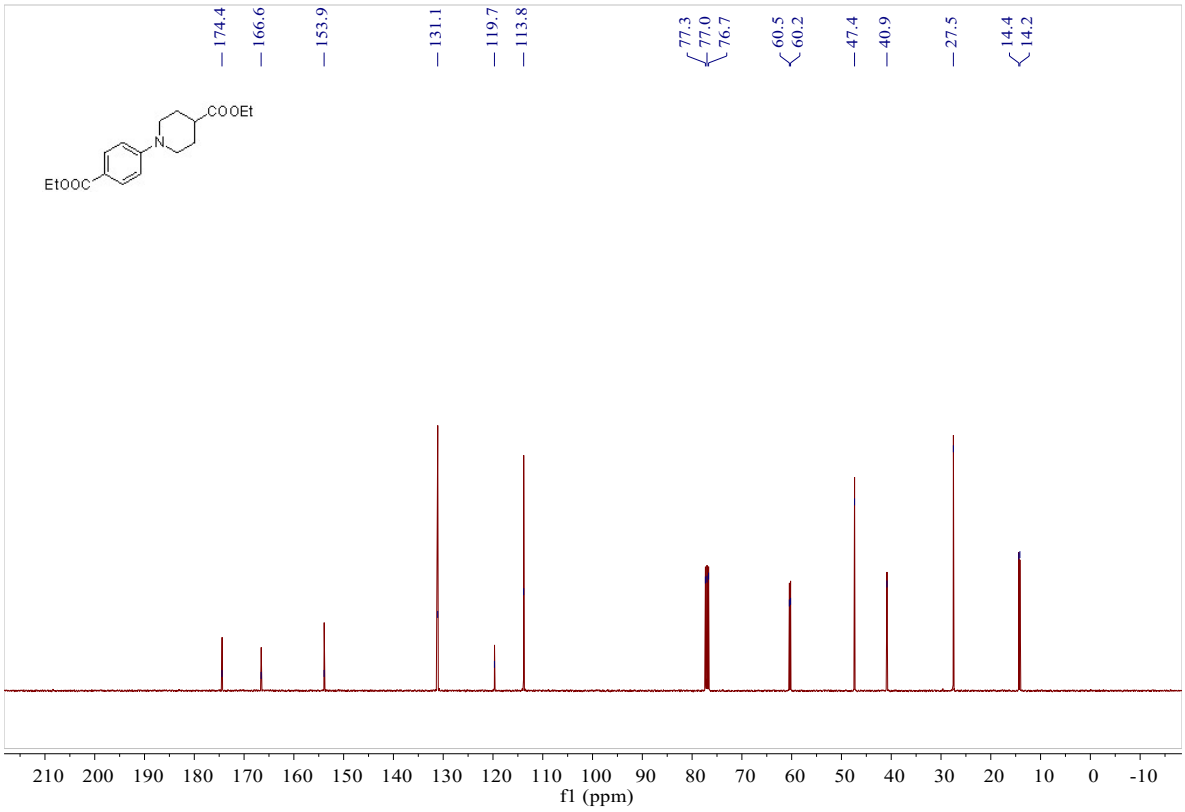
Ethyl 4-(4-hydroxy-4-methylpiperidin-1-yl)benzoate (3z): ^{13}C NMR (100 MHz, $CDCl_3$)



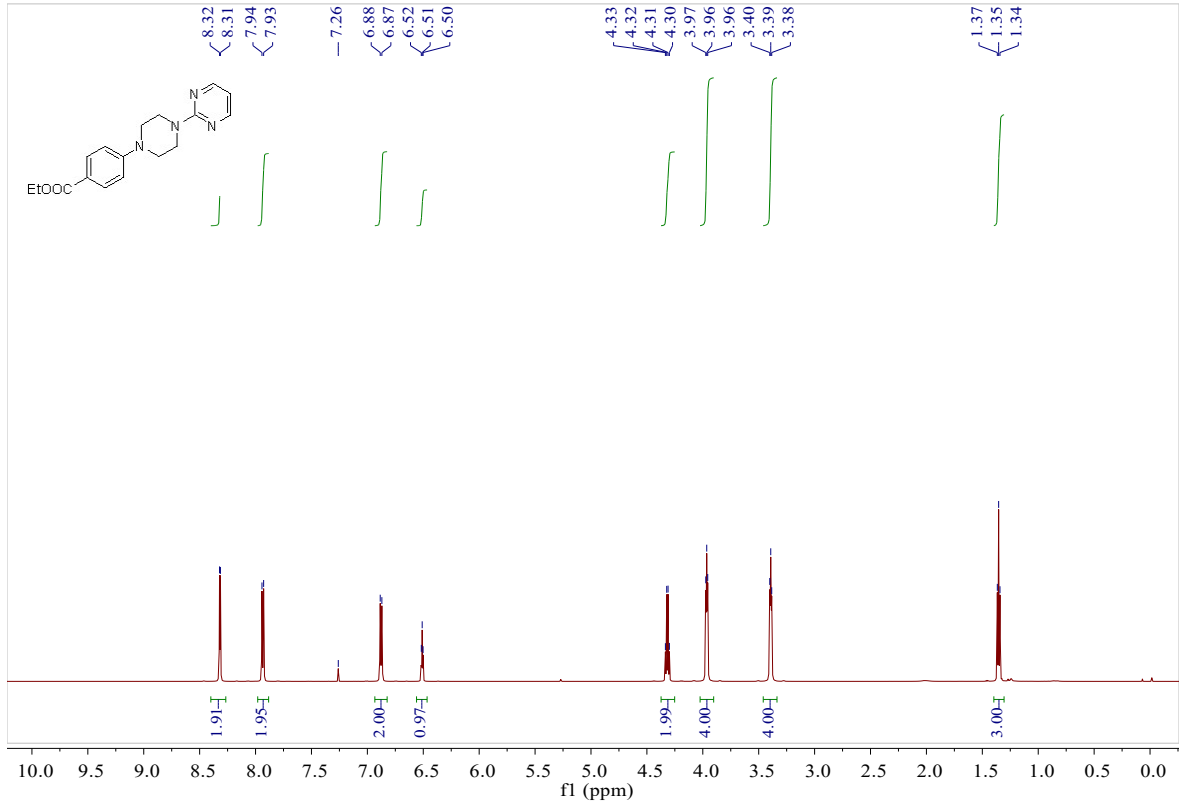
Ethyl 1-(4-(ethoxycarbonyl)phenyl)piperidine-4-carboxylate (3aa): ^{1}H NMR (400 MHz, $CDCl_3$)



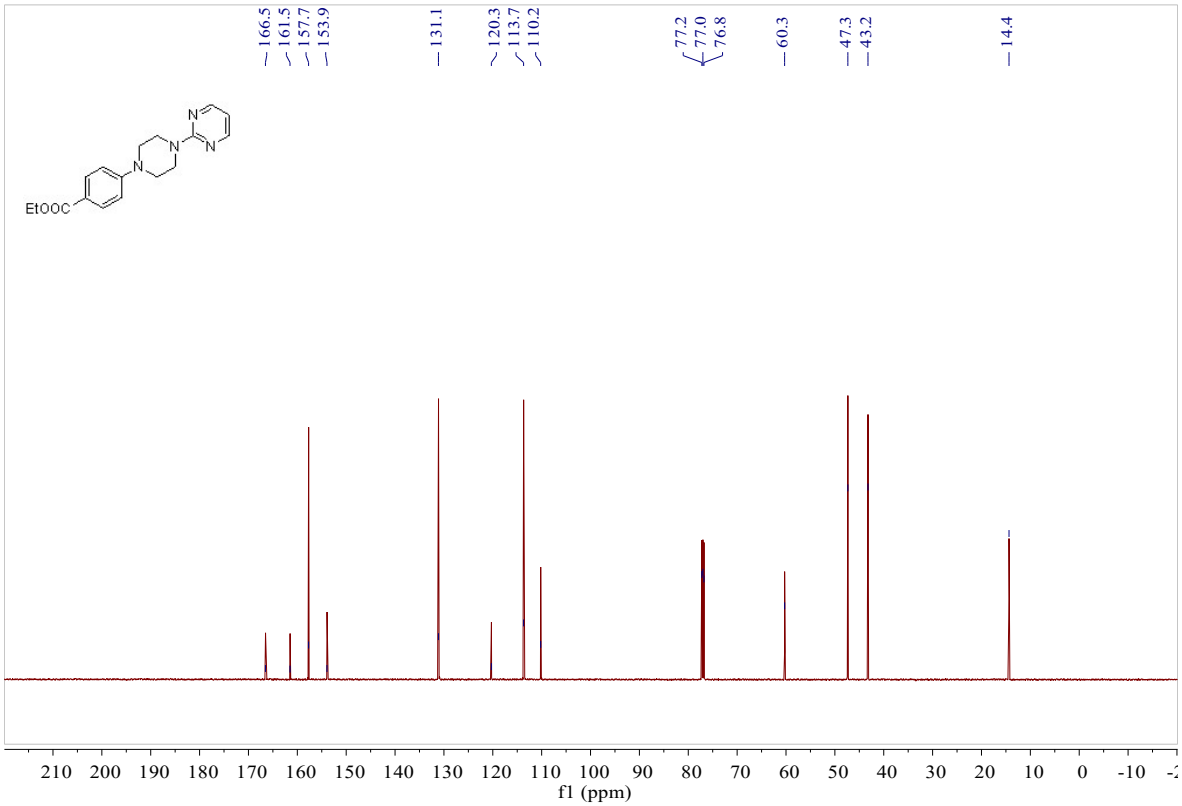
Ethyl 1-(4-(ethoxycarbonyl)phenyl)piperidine-4-carboxylate (3aa): ^{13}C NMR (100 MHz, $CDCl_3$)



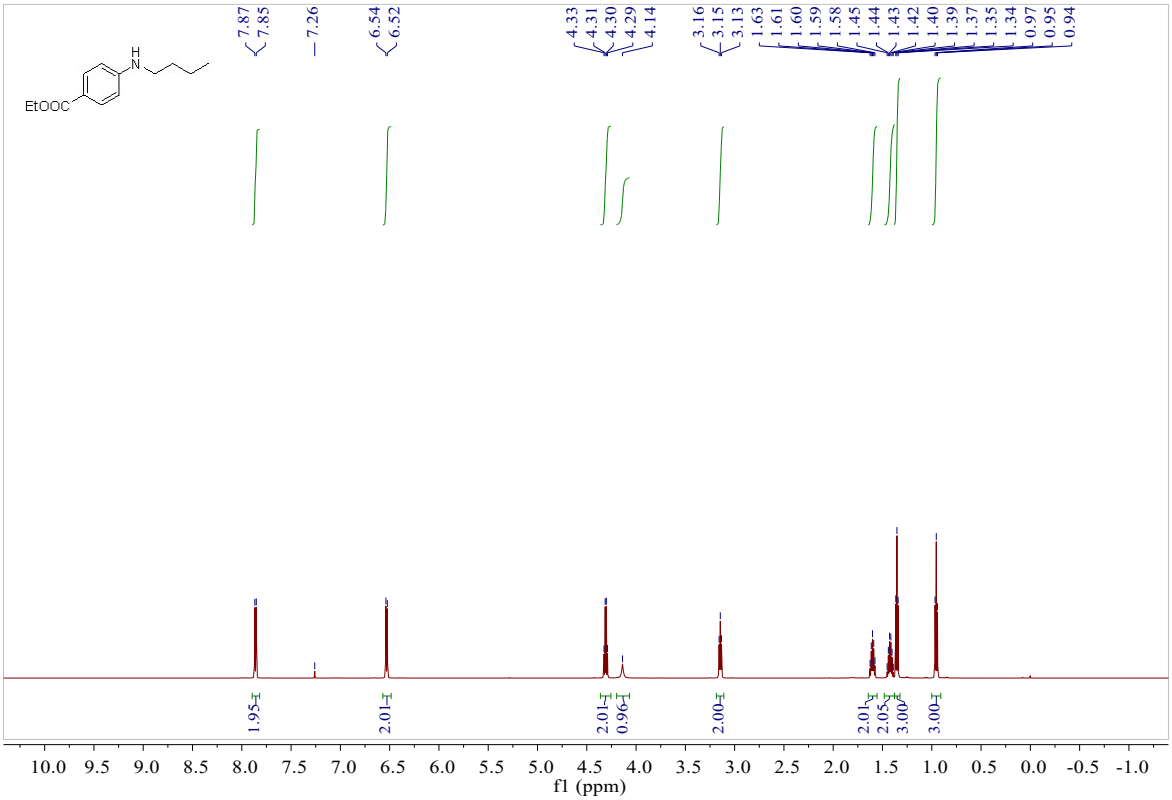
Ethyl 4-(4-(pyrimidin-2-yl)piperazin-1-yl)benzoate (3ab): ^{1}H NMR (400 MHz, $CDCl_3$)



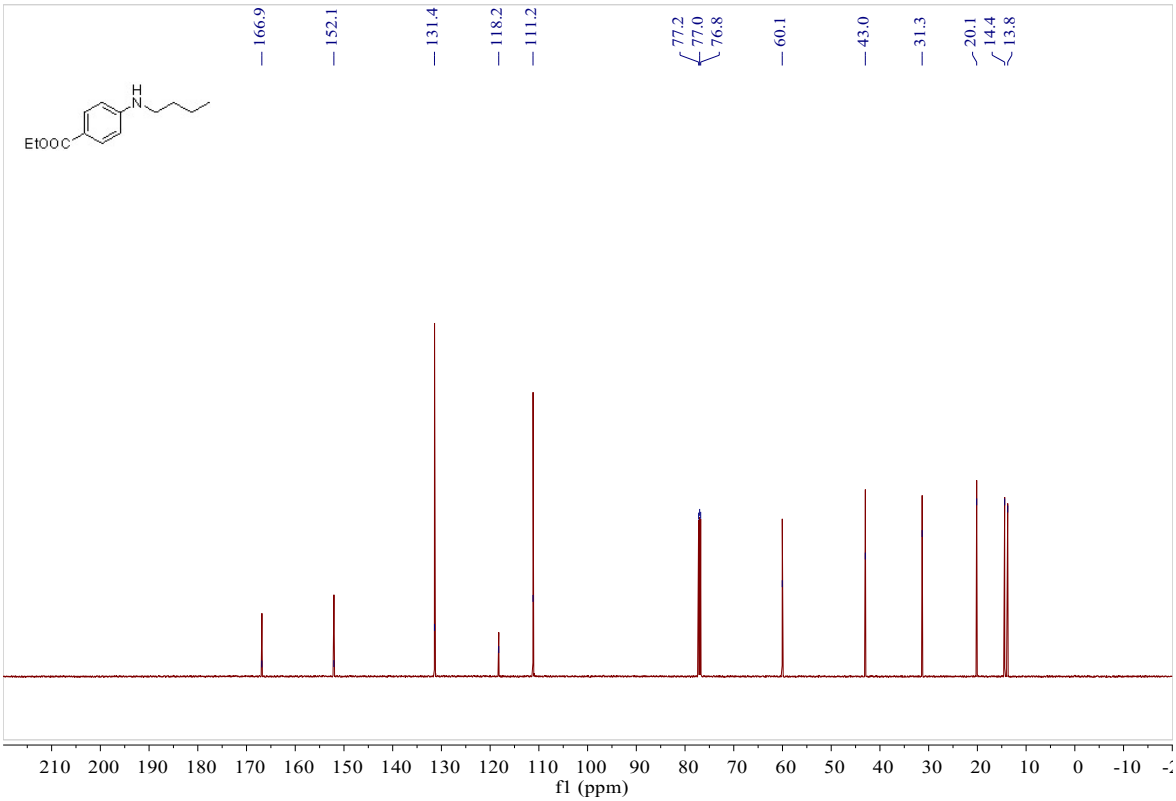
Ethyl 4-(4-(pyrimidin-2-yl)piperazin-1-yl)benzoate (3ab): ^{13}C NMR (100 MHz, $CDCl_3$)



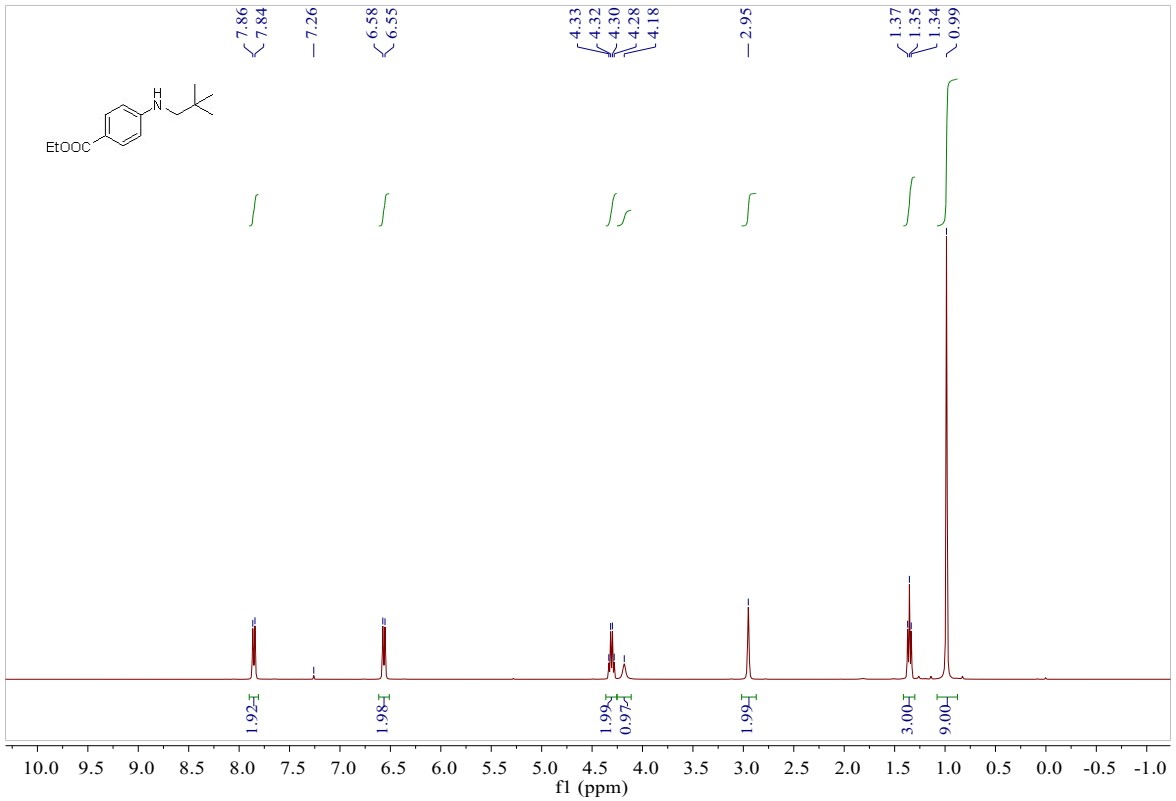
Ethyl 4-(butylamino)benzoate (3ac): ^{1}H NMR (600 MHz, $CDCl_3$)



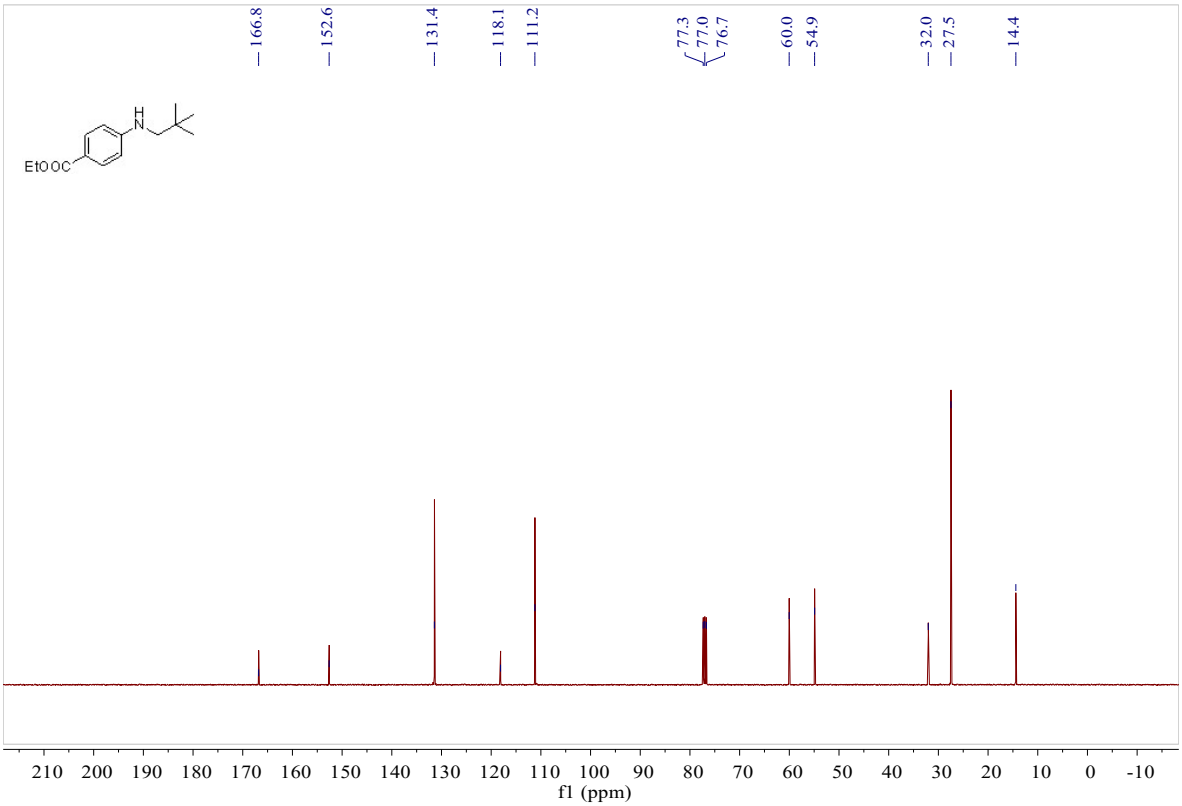
Ethyl 4-(butylamino)benzoate (3ac): ^{13}C NMR (151 MHz, $CDCl_3$)



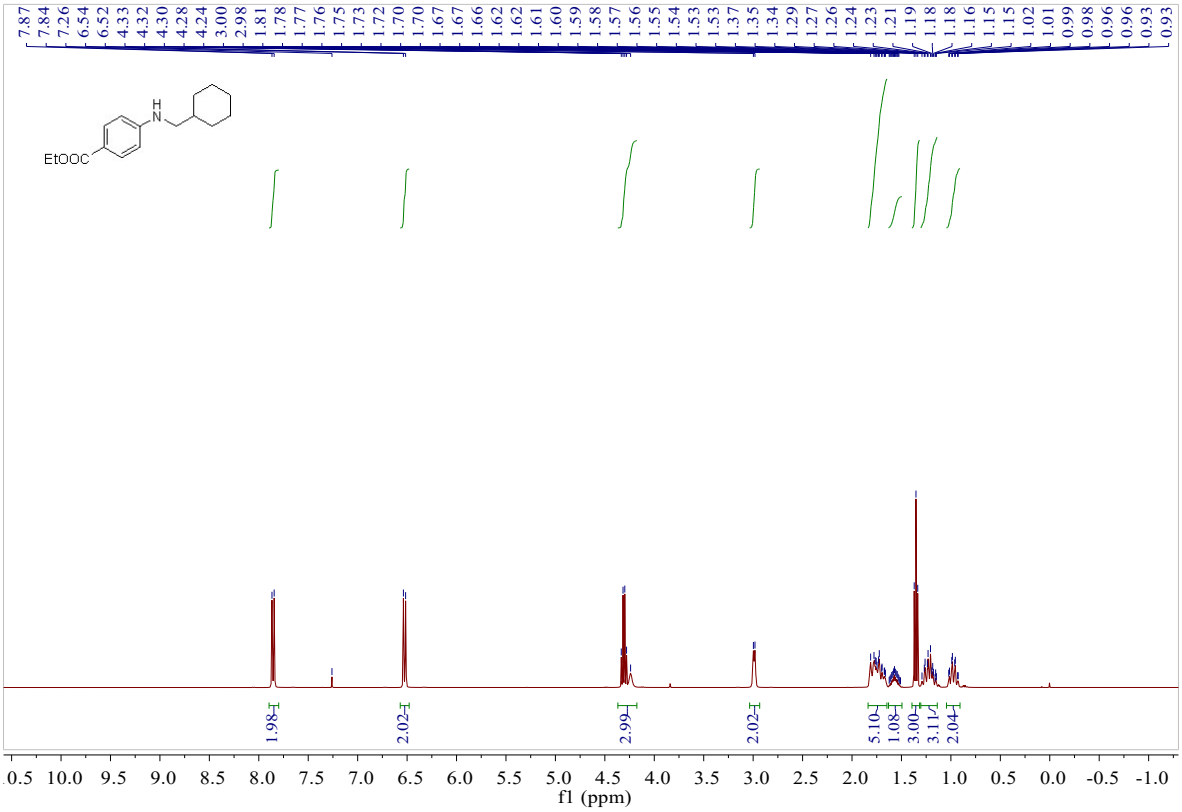
Ethyl 4-(neopentylamino)benzoate (3ad): ^{1}H NMR (400 MHz, $CDCl_3$)



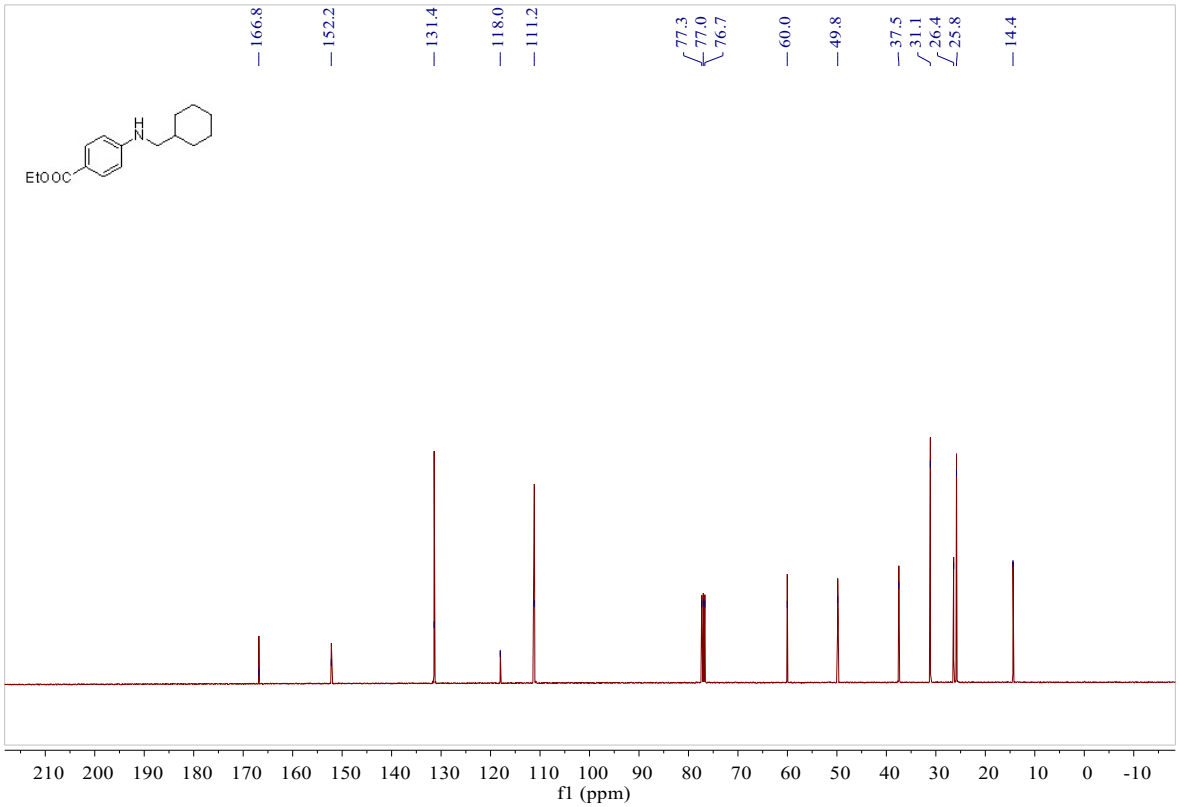
Ethyl 4-(neopentylamino)benzoate (3ad): ^{13}C NMR (101 MHz, $CDCl_3$)



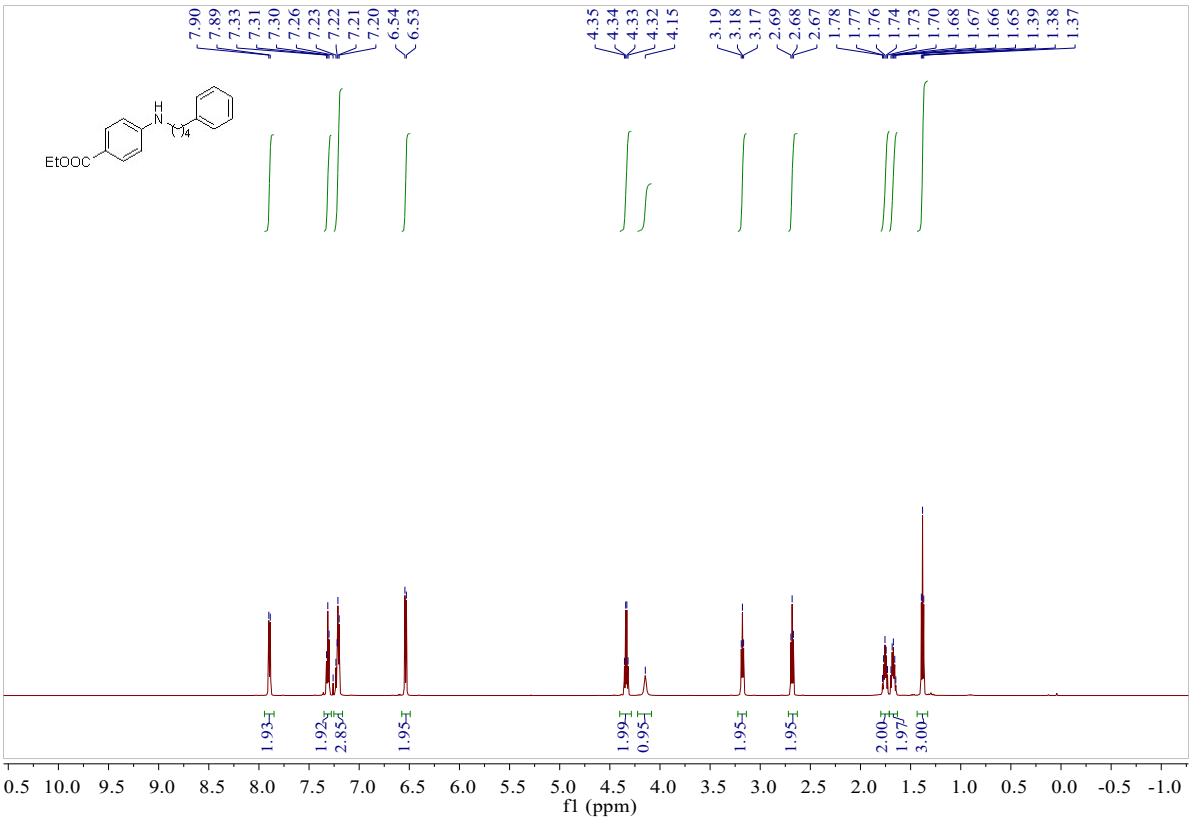
Ethyl 4-((cyclohexylmethyl)amino)benzoate (3ae): ^{1}H NMR (400 MHz, $CDCl_3$)



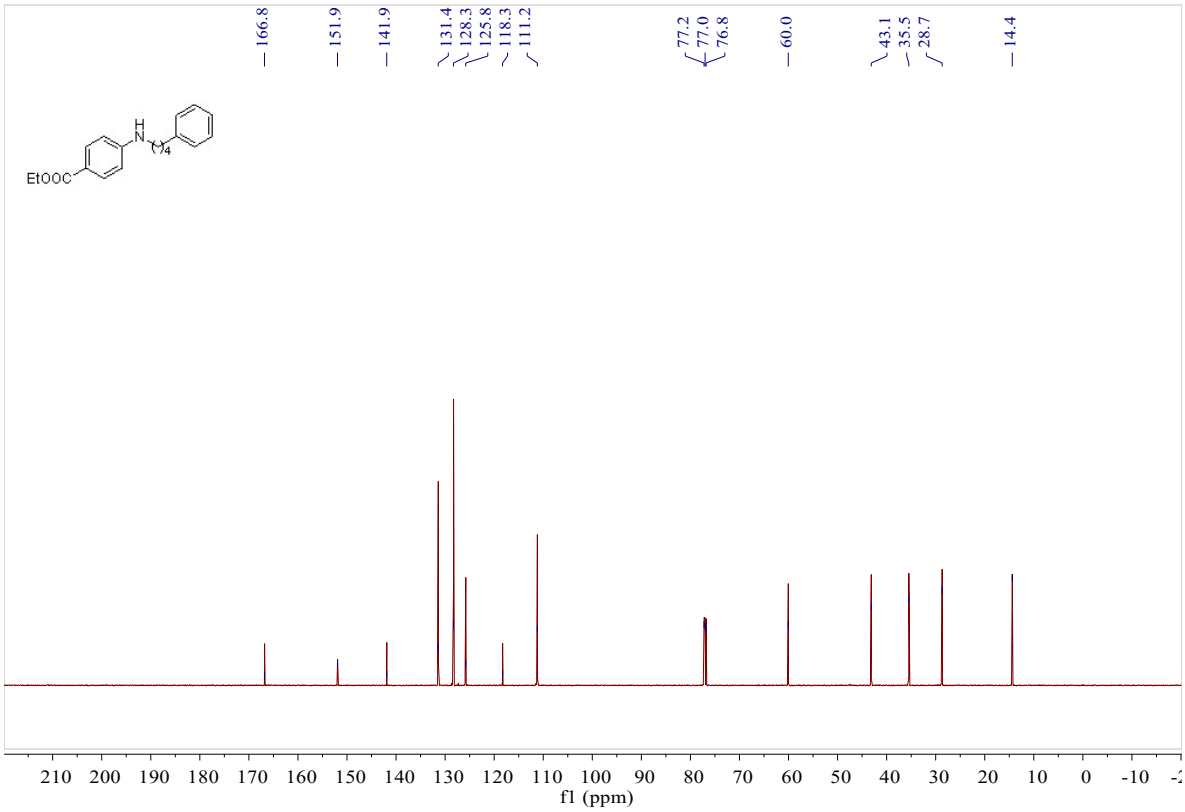
Ethyl 4-((cyclohexylmethyl)amino)benzoate (3ae): ^{13}C NMR (101 MHz, $CDCl_3$)



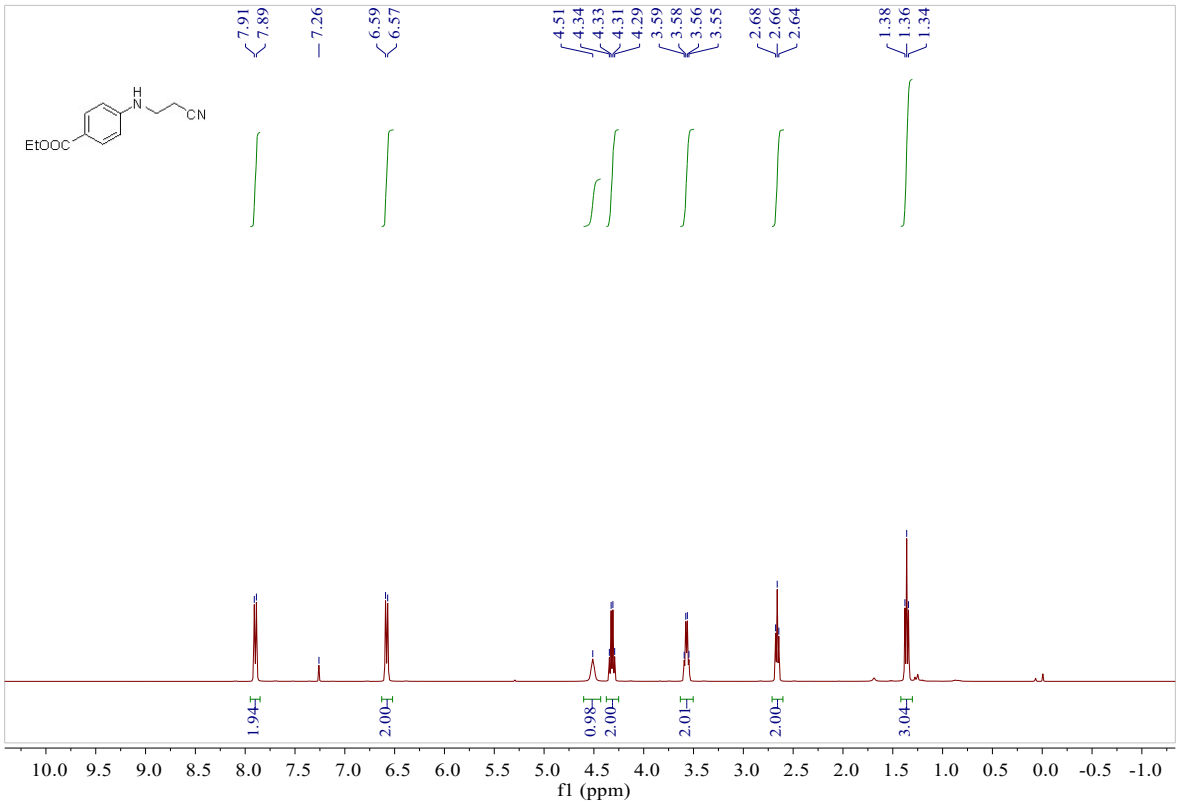
Ethyl 4-((4-phenylbutyl)amino)benzoate (3af): ^{1}H NMR (600 MHz, $CDCl_3$)



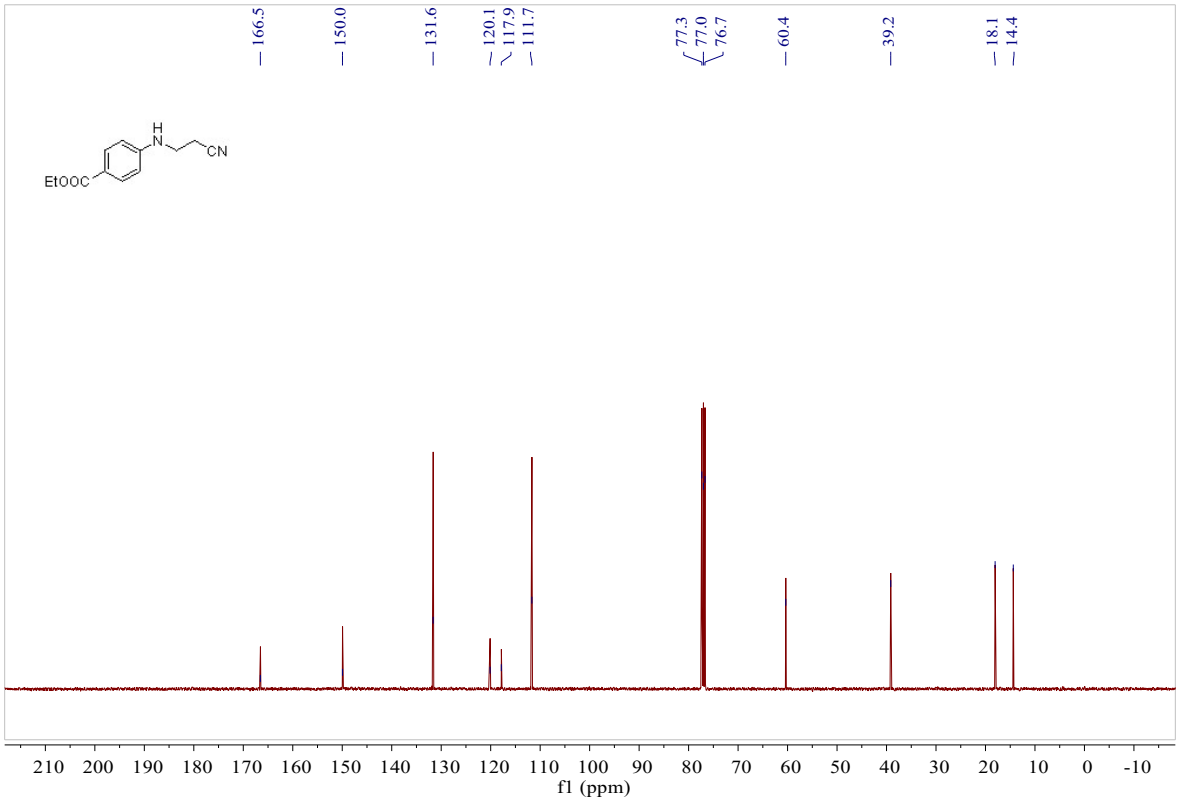
Ethyl 4-((4-phenylbutyl)amino)benzoate (3af): ^{13}C NMR (151 MHz, $CDCl_3$)



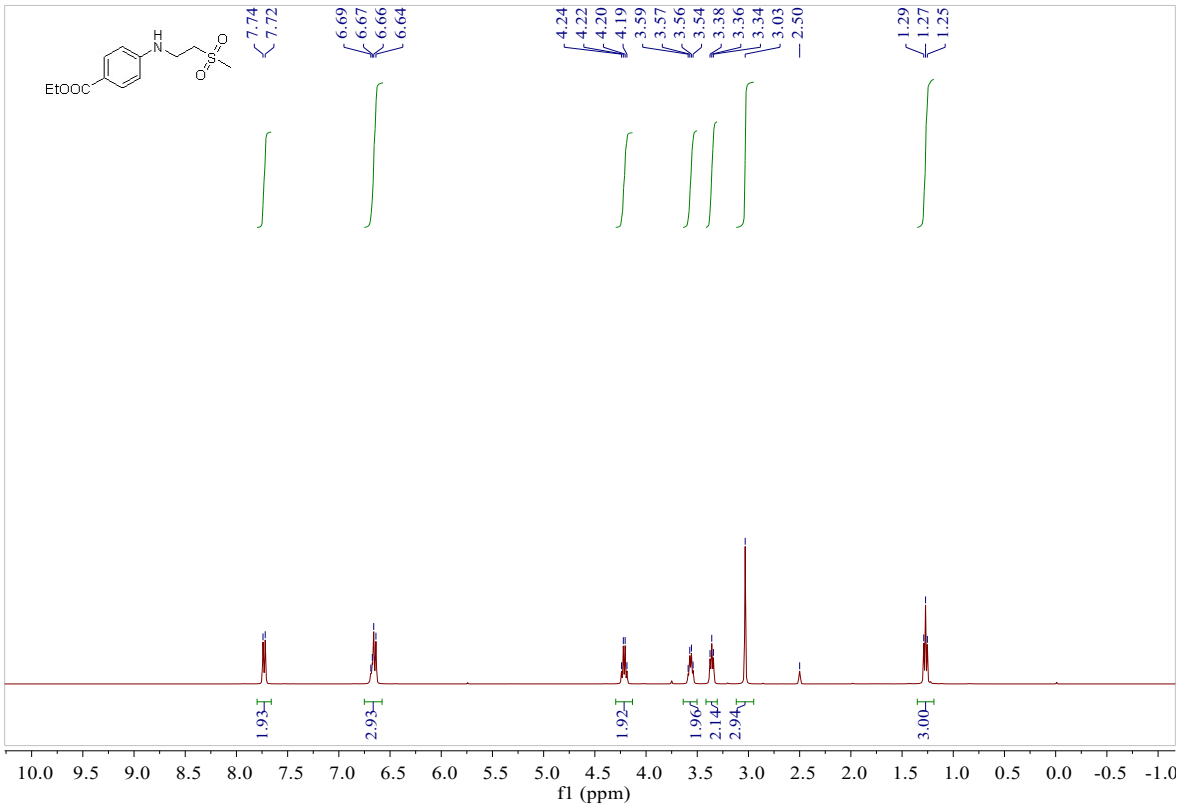
Ethyl 4-((2-cyanoethyl)amino)benzoate (3ag): ^{1}H NMR (400 MHz, $CDCl_3$)



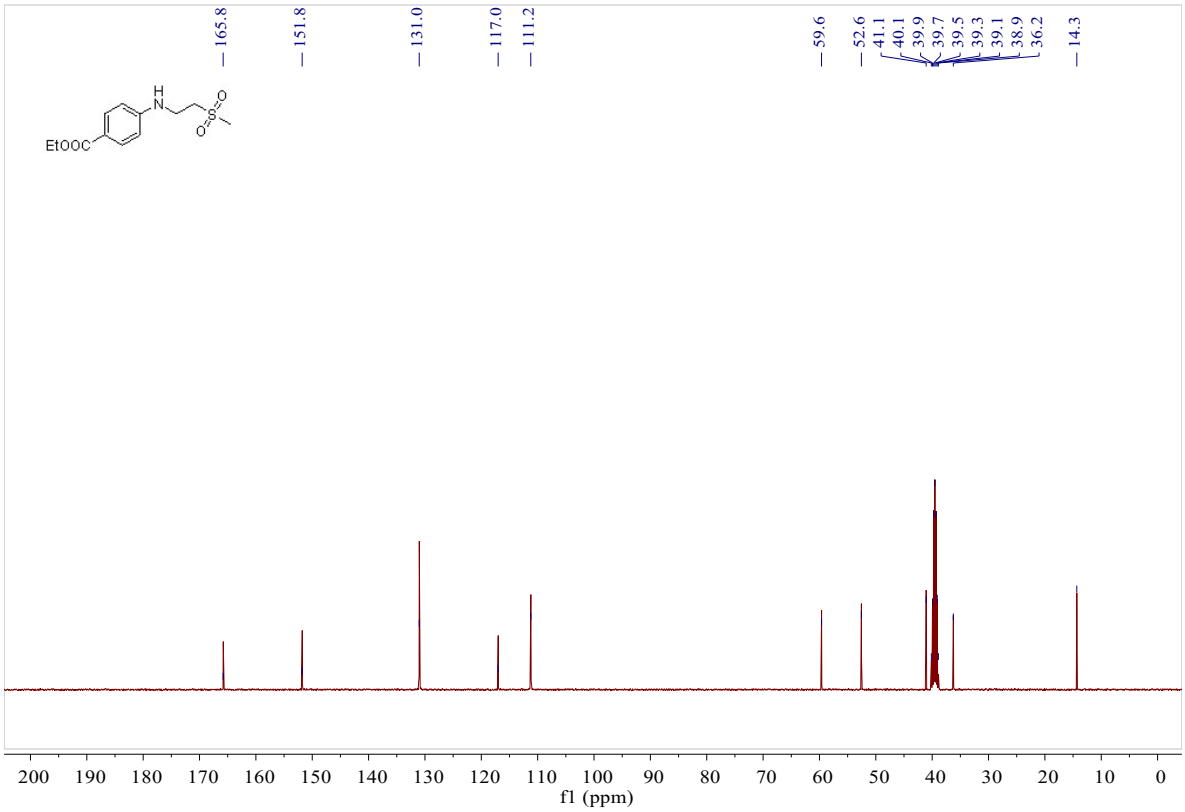
Ethyl 4-((2-cyanoethyl)amino)benzoate (3ag): ^{13}C NMR (101 MHz, $CDCl_3$)



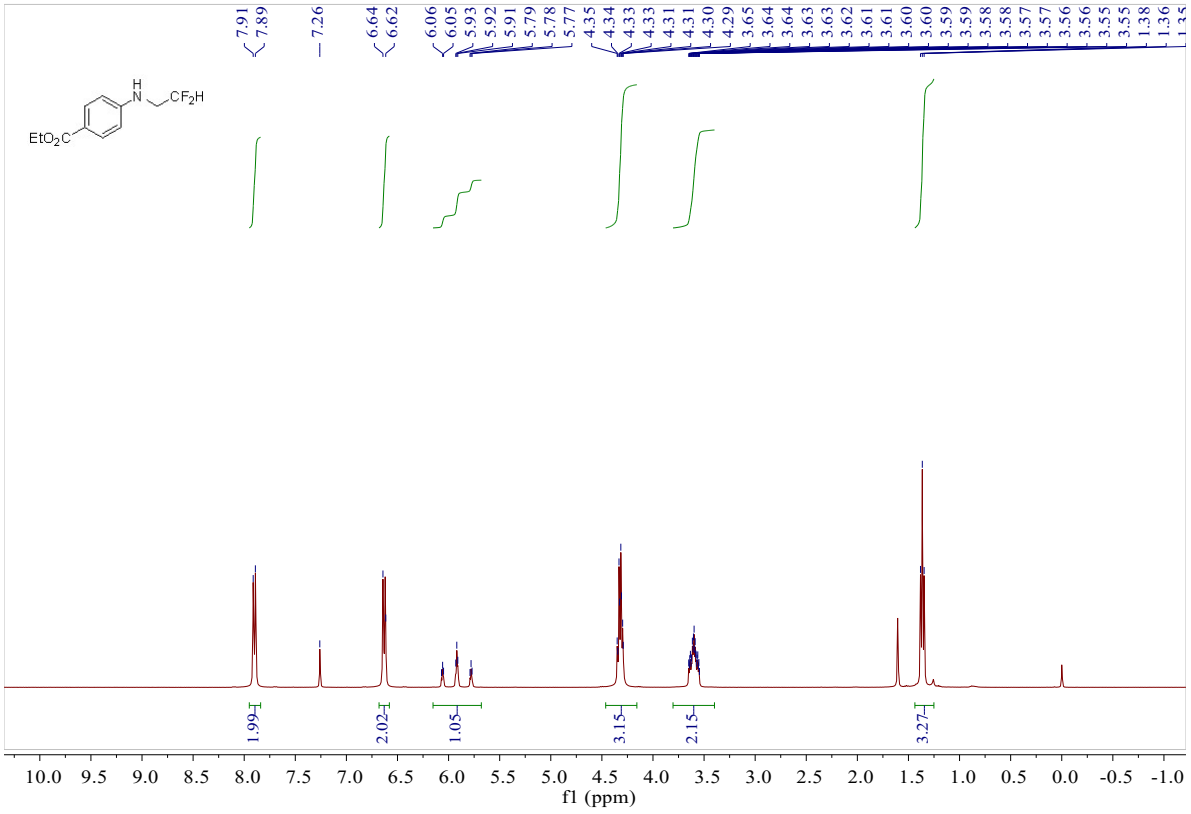
Ethyl 4-((2-(methylsulfonyl)ethyl)amino)benzoate (3ah): ^{1}H NMR (400 MHz, DMSO-d_6)



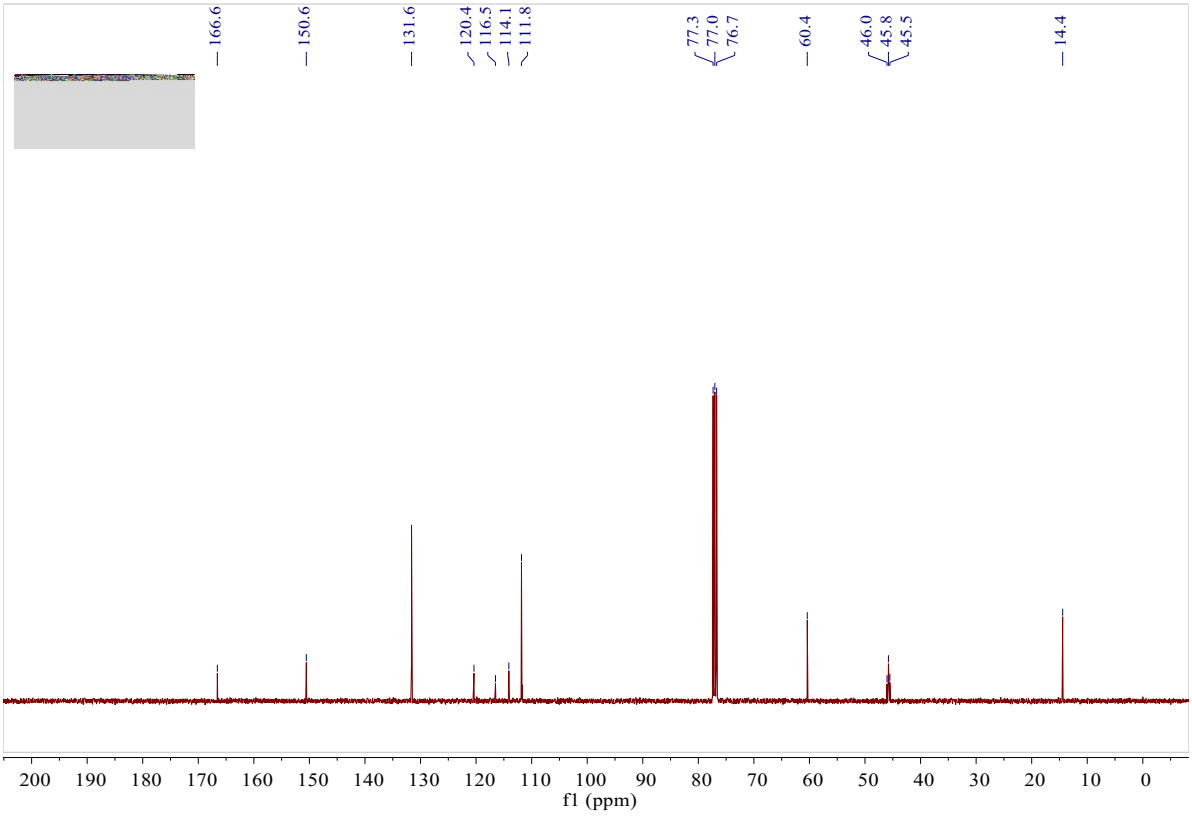
Ethyl 4-((2-(methylsulfonyl)ethyl)amino)benzoate (3ah): ^{13}C NMR (101 MHz, DMSO-d_6)



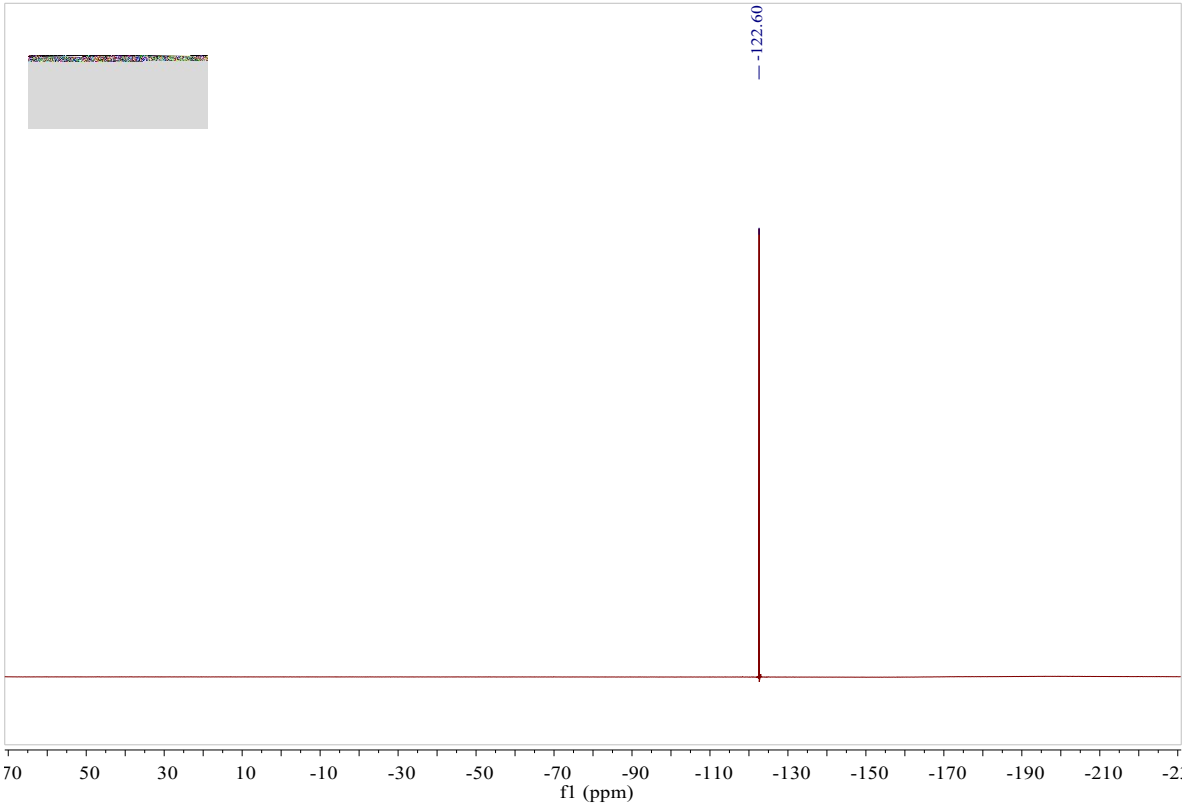
Ethyl 4-((2,2-difluoroethyl)amino)benzoate (3ai): **^{1}H NMR** (400 MHz, $CDCl_3$)



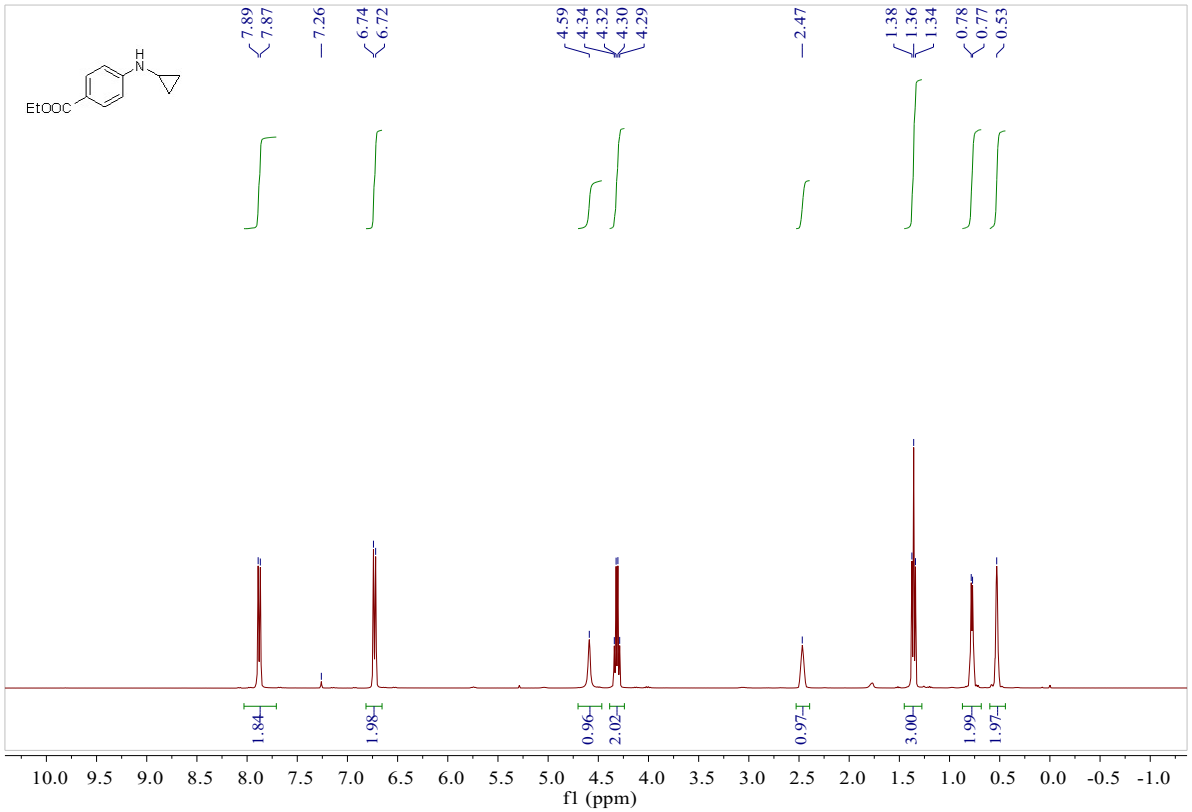
Ethyl 4-((2,2-difluoroethyl)amino)benzoate (3ai): ^{13}C NMR (101 MHz, $CDCl_3$)



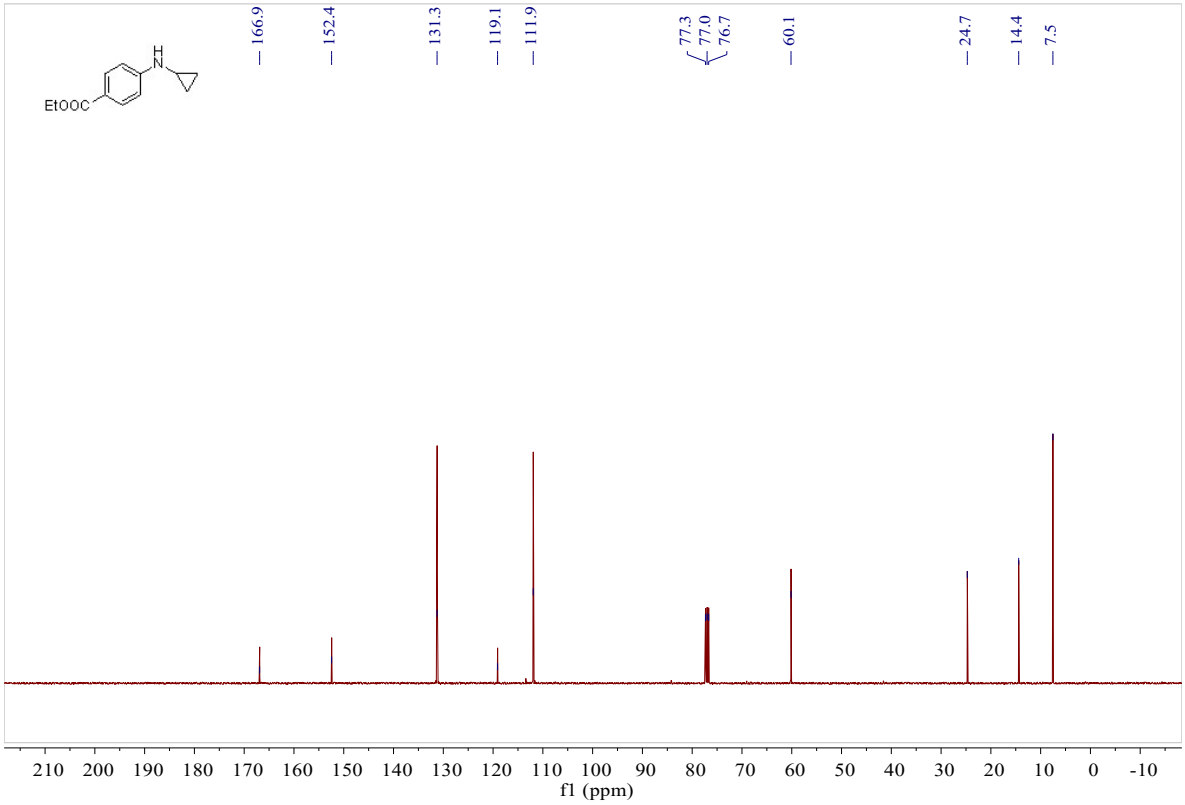
Ethyl 4-((2,2-difluoroethyl)amino)benzoate (3ai): ^{19}F NMR (376 MHz, $CDCl_3$)



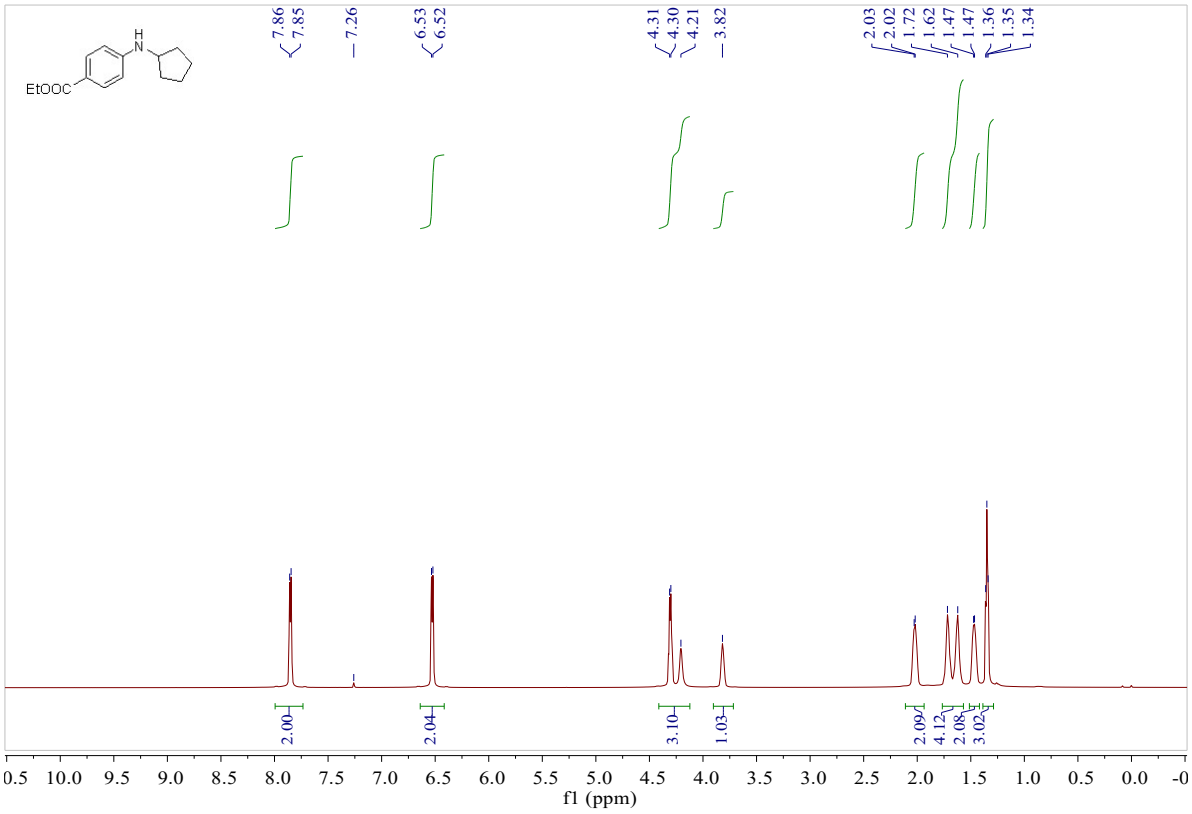
Ethyl 4-(cyclopropylamino)benzoate (3aj): ^{1}H NMR (400 MHz, $CDCl_3$)



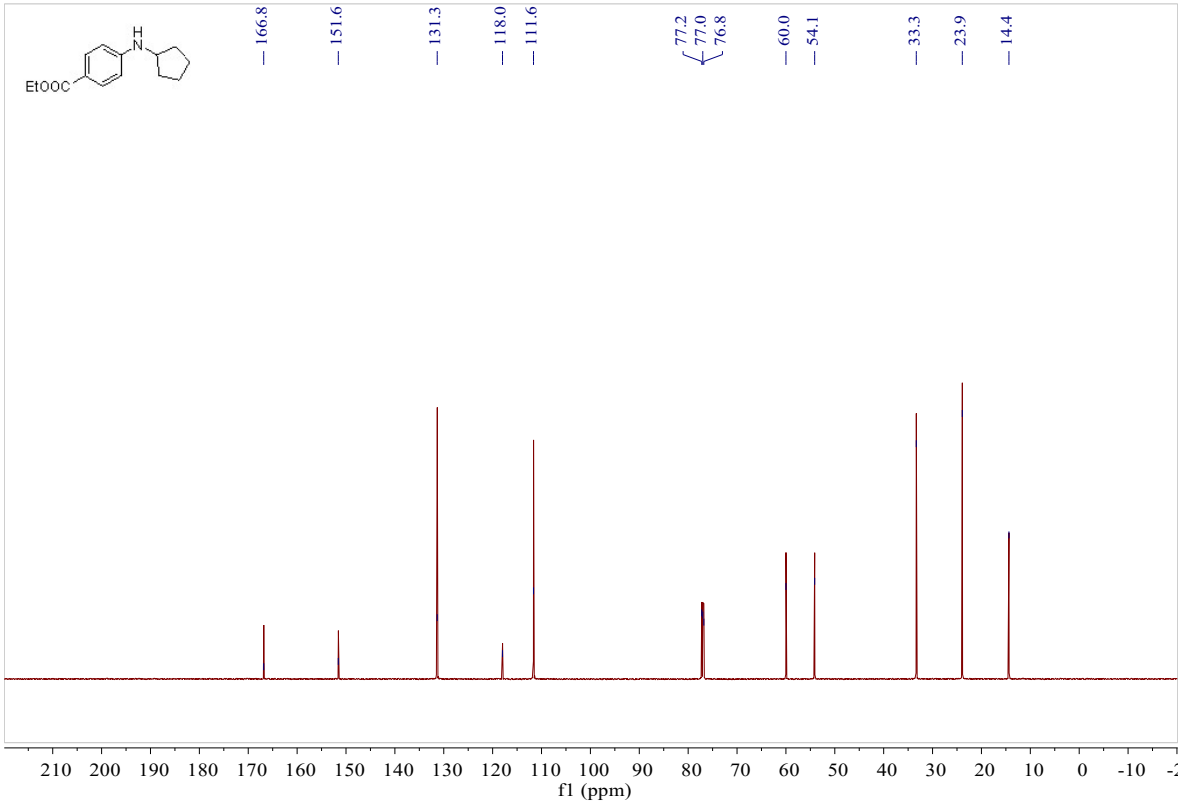
Ethyl 4-(cyclopropylamino)benzoate (3aj): ^{13}C NMR (101 MHz, $CDCl_3$)



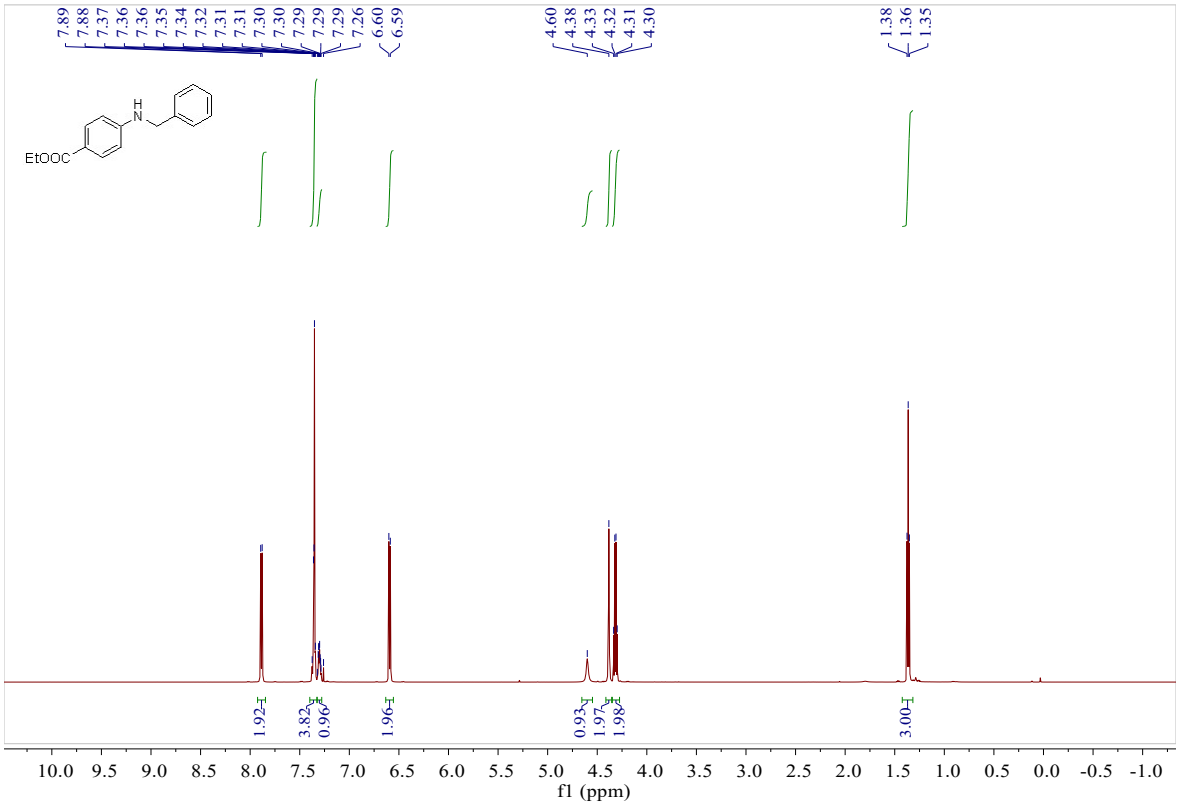
Ethyl 4-(cyclopentylamino)benzoate (3ak): ^{1}H NMR (600 MHz, $CDCl_3$)



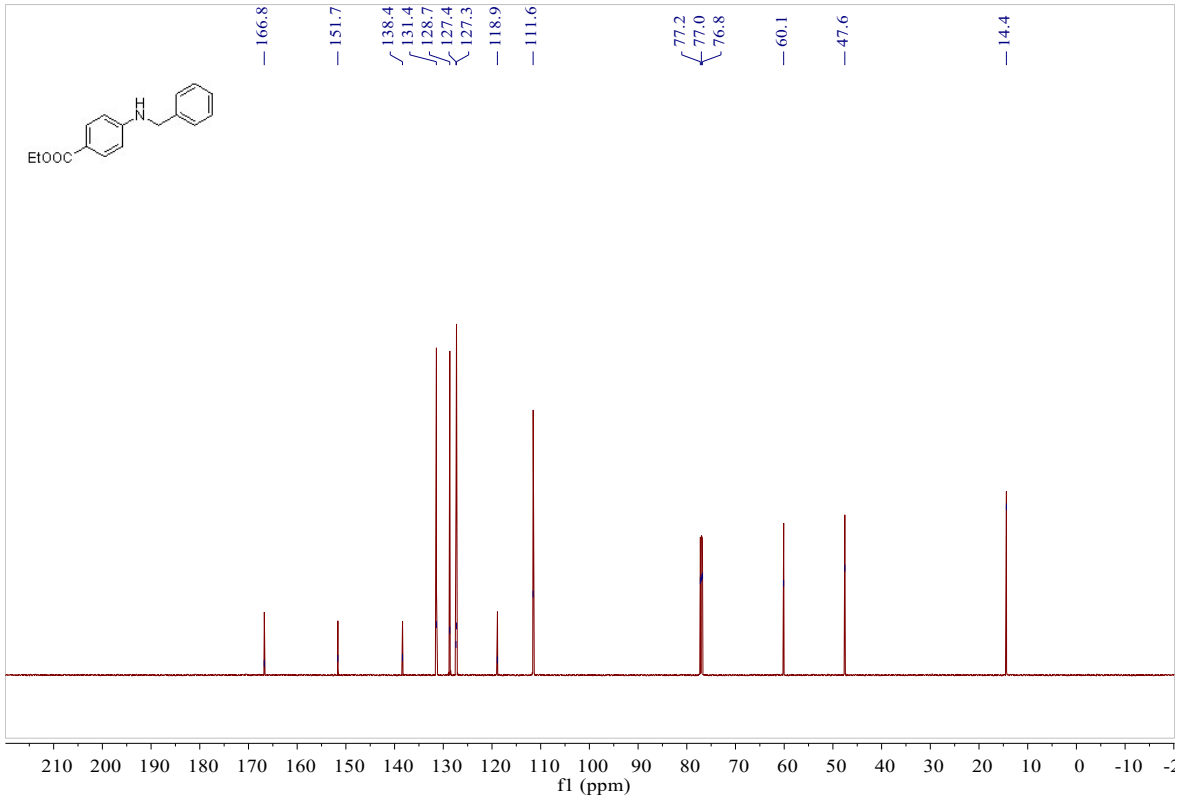
Ethyl 4-(cyclopentylamino)benzoate (3ak): ^{13}C NMR (151 MHz, $CDCl_3$)



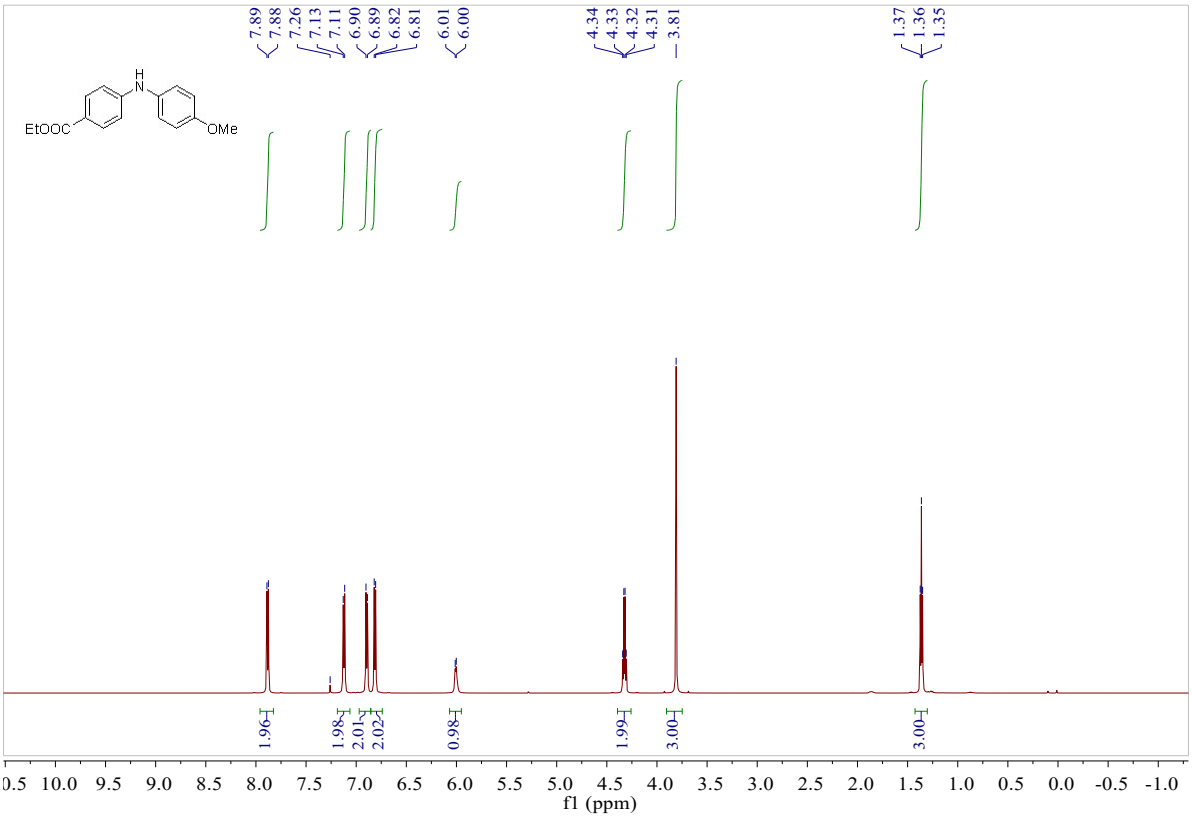
Ethyl 4-(benzylamino)benzoate (3al): ^{1}H NMR (600 MHz, $CDCl_3$)



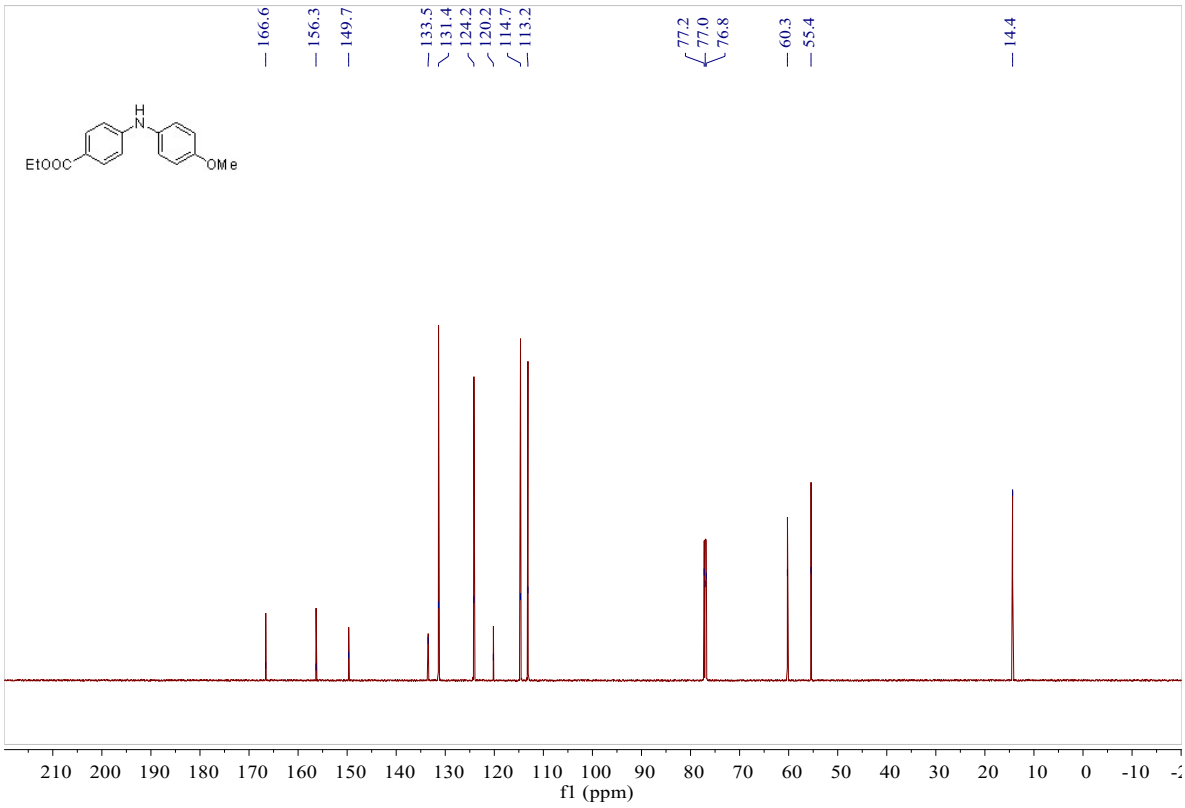
Ethyl 4-(benzylamino)benzoate (3al): ^{13}C NMR (151 MHz, $CDCl_3$)



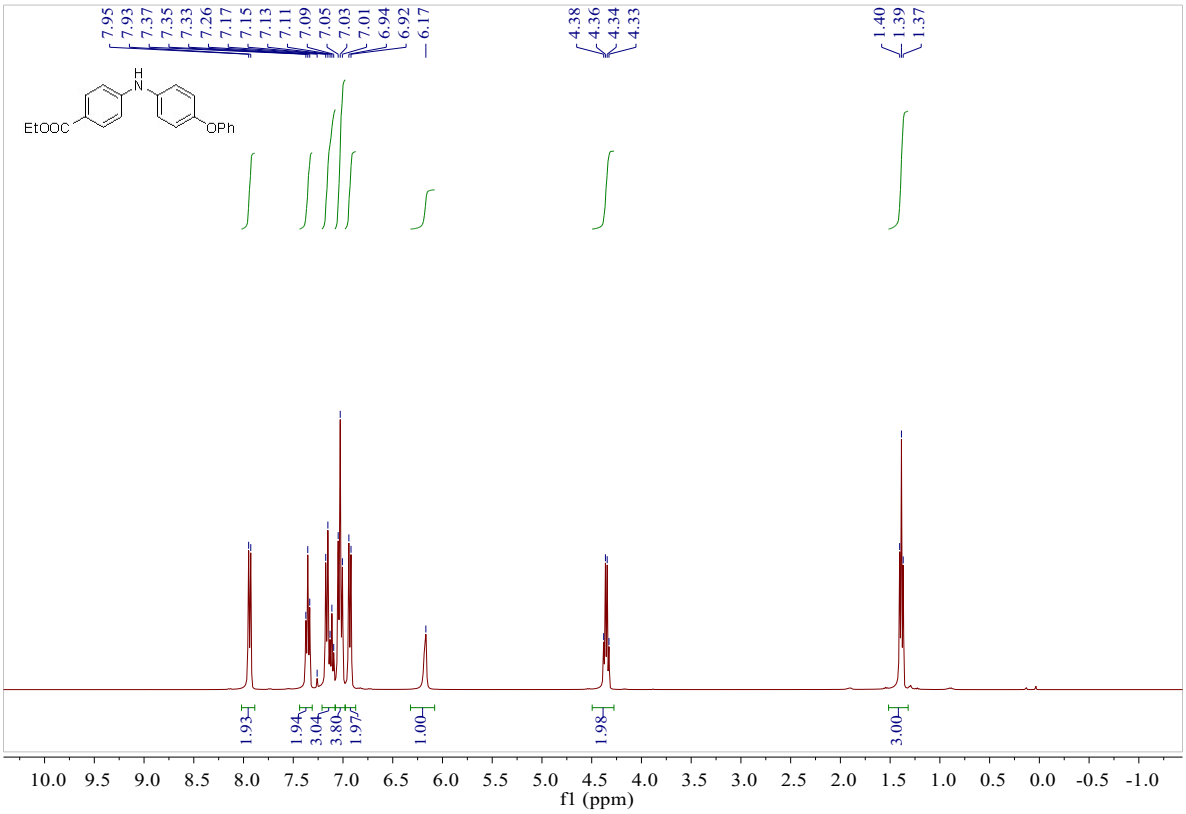
Ethyl 4-((4-methoxyphenyl)amino)benzoate (3am): ^{1}H NMR (600 MHz, $CDCl_3$)



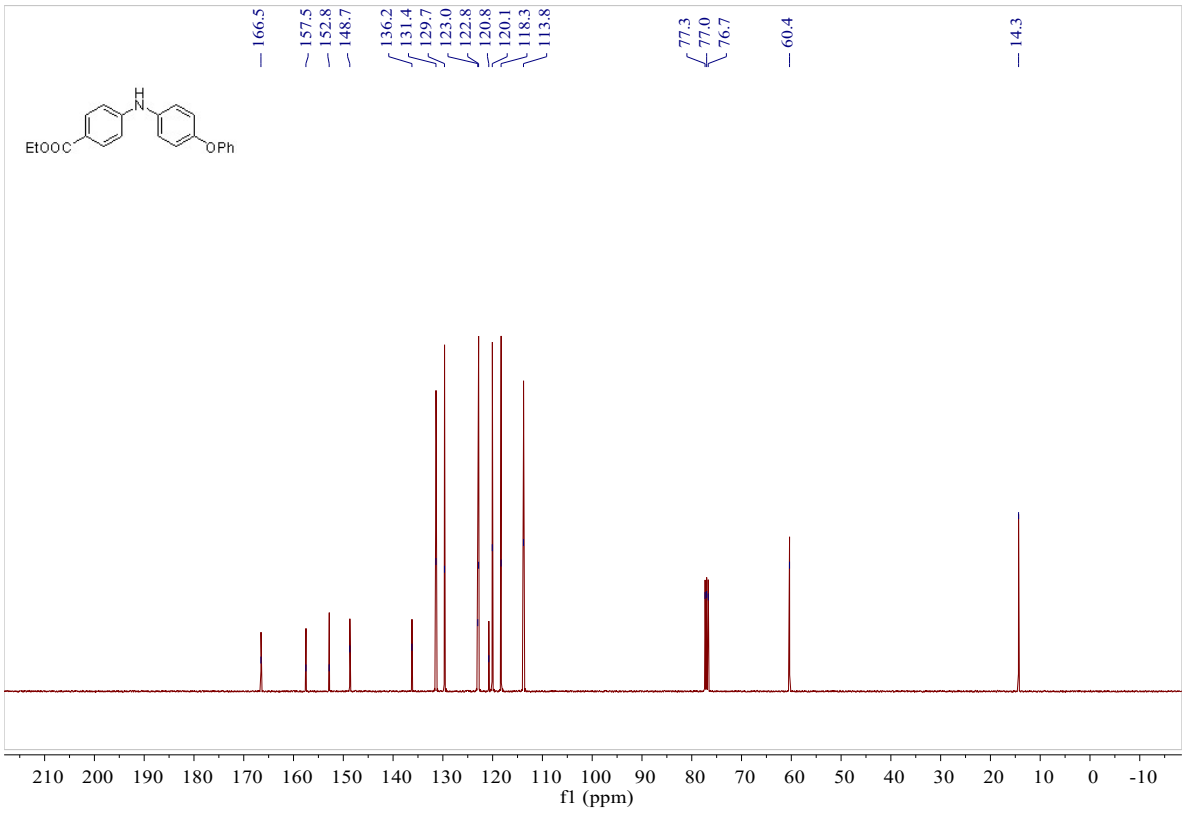
Ethyl 4-((4-methoxyphenyl)amino)benzoate (3am): ^{13}C NMR (151 MHz, $CDCl_3$)



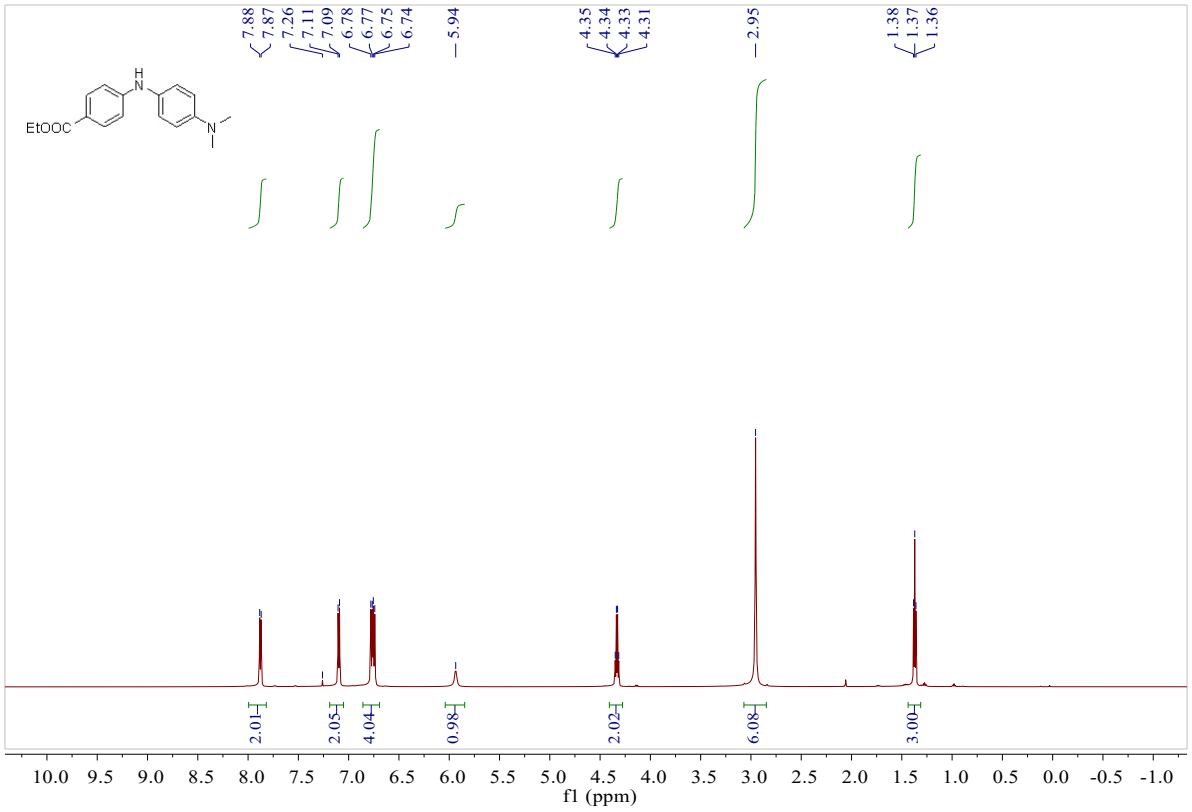
Ethyl 4-((4-phenoxyphenyl)amino)benzoate (3an): ^{1}H NMR (400 MHz, $CDCl_3$)



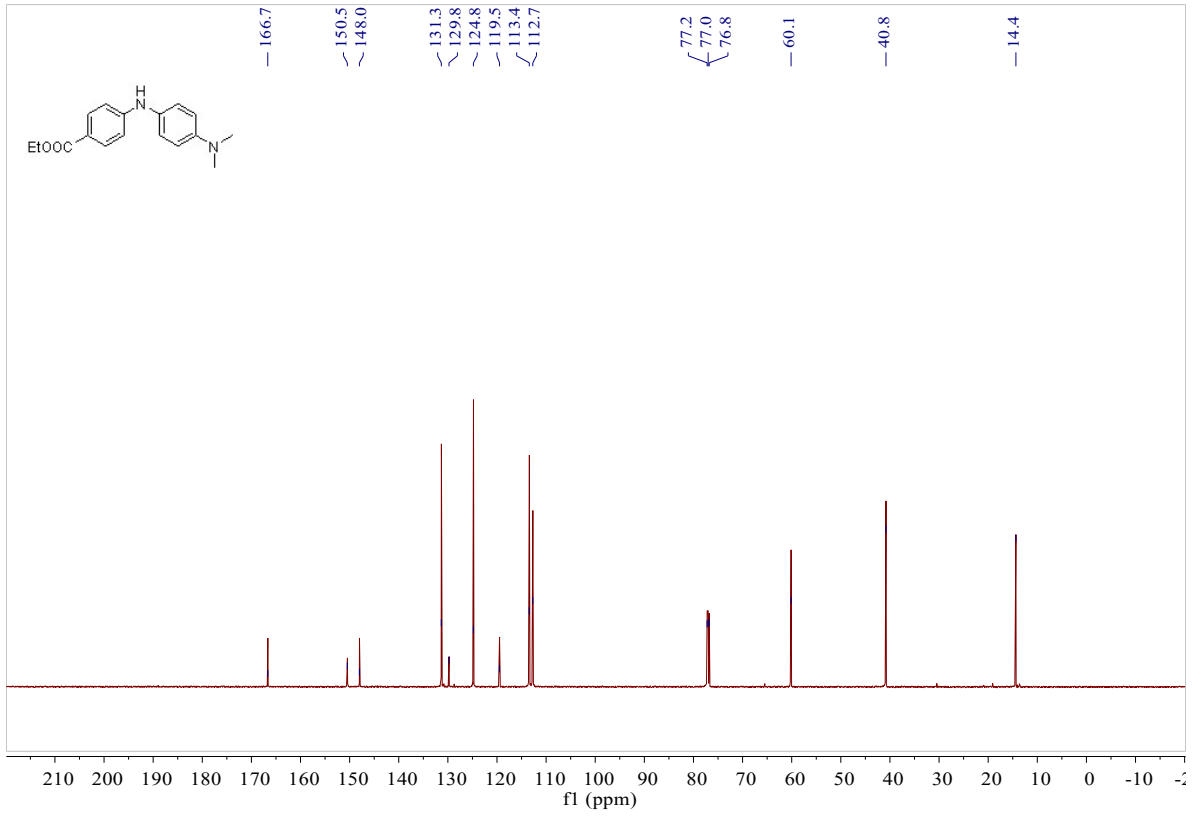
Ethyl 4-((4-phenoxyphenyl)amino)benzoate (3an): ^{13}C NMR (101 MHz, $CDCl_3$)



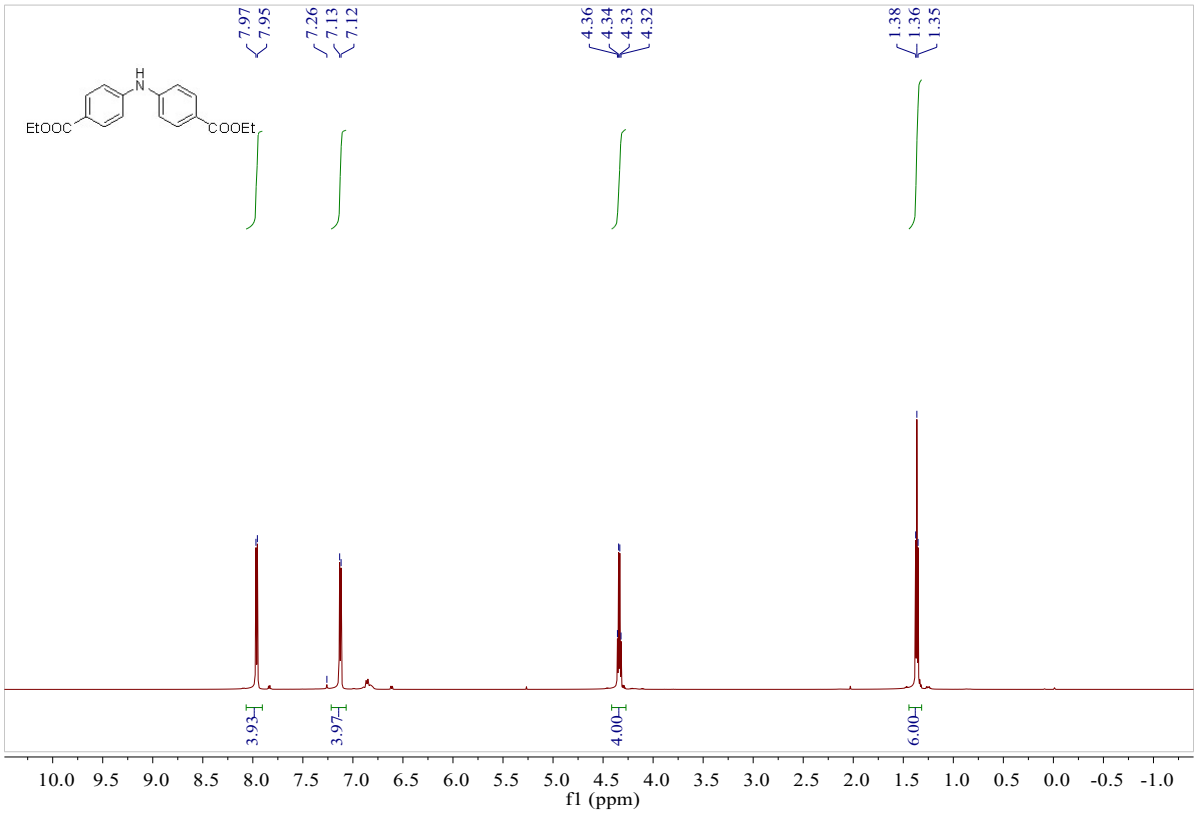
Ethyl 4-((4-(dimethylamino)phenyl)amino)benzoate (3ao): ^{1}H NMR (600 MHz, $CDCl_3$)



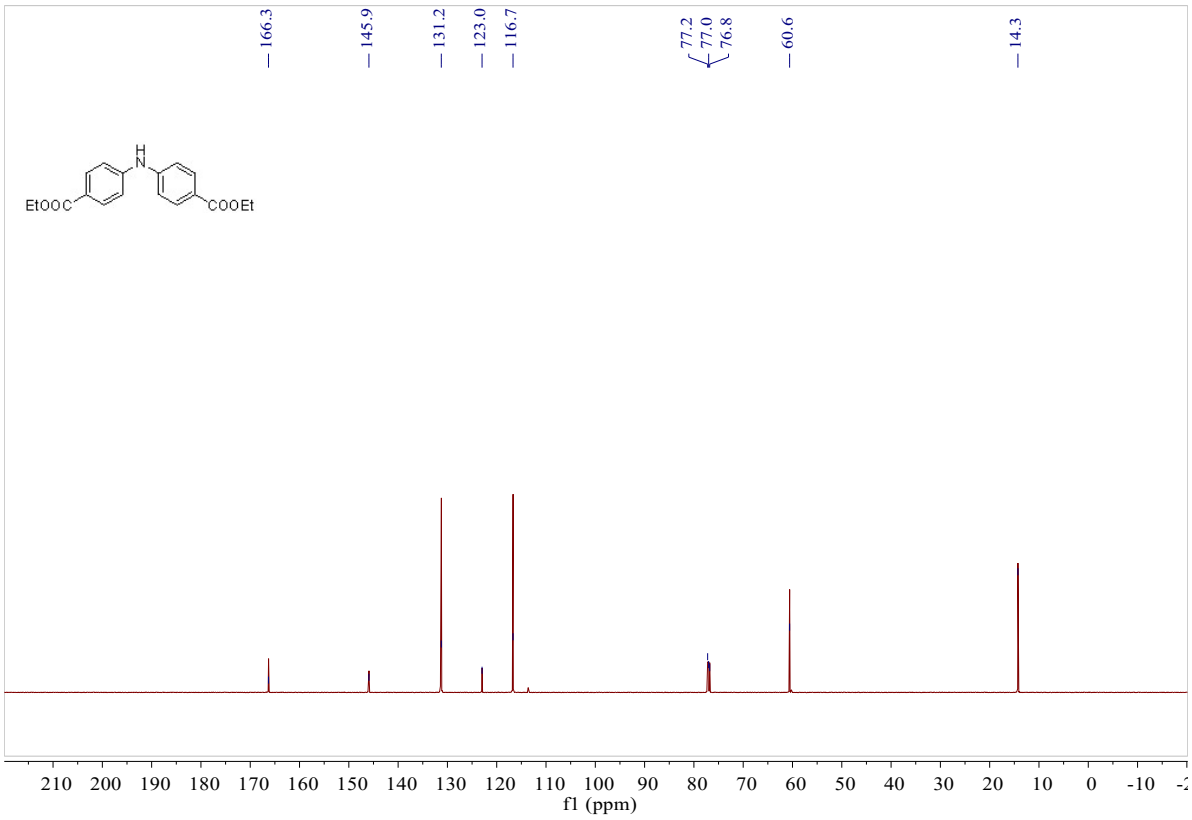
Ethyl 4-((4-(dimethylamino)phenyl)amino)benzoate (3ao): ^{13}C NMR (151 MHz, $CDCl_3$)



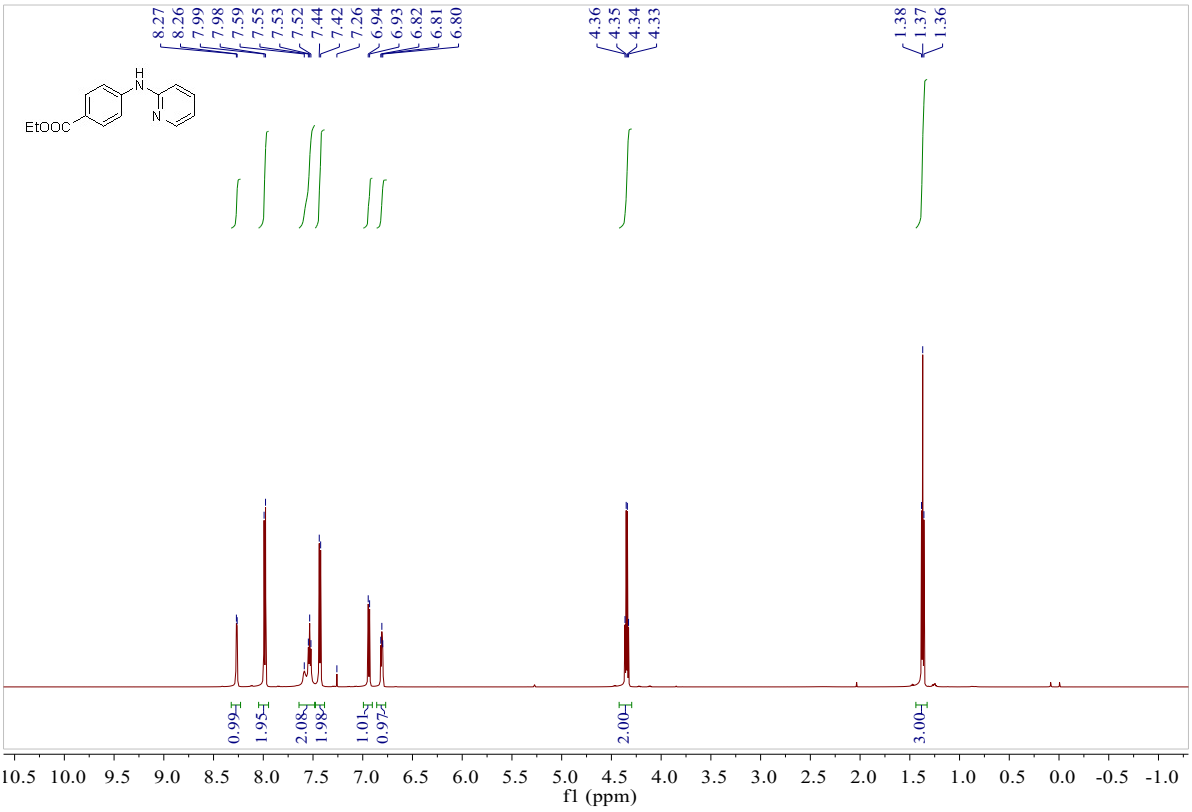
Diethyl 4,4'-azanediyldibenzoate (3ap): ^{1}H NMR (600 MHz, $CDCl_3$)



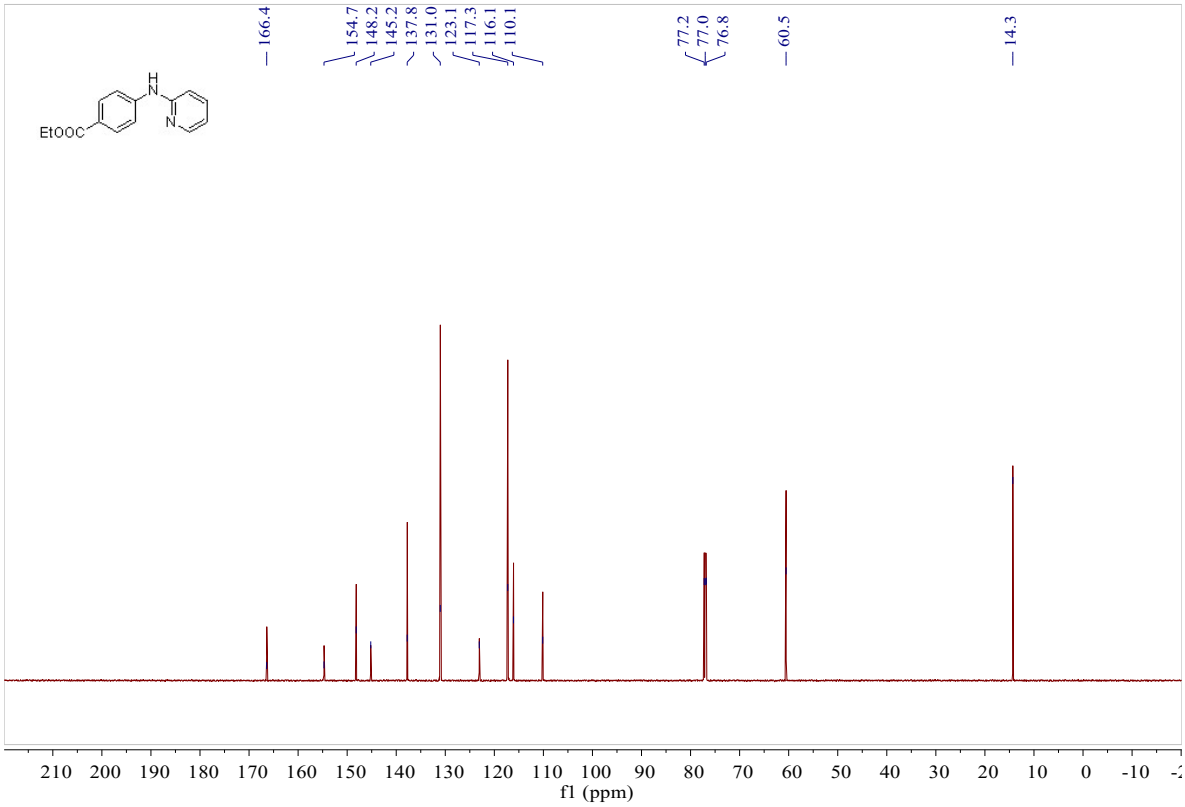
Diethyl 4,4'-azanediyldibenzoate (3ap): ^{13}C NMR (151 MHz, $CDCl_3$)



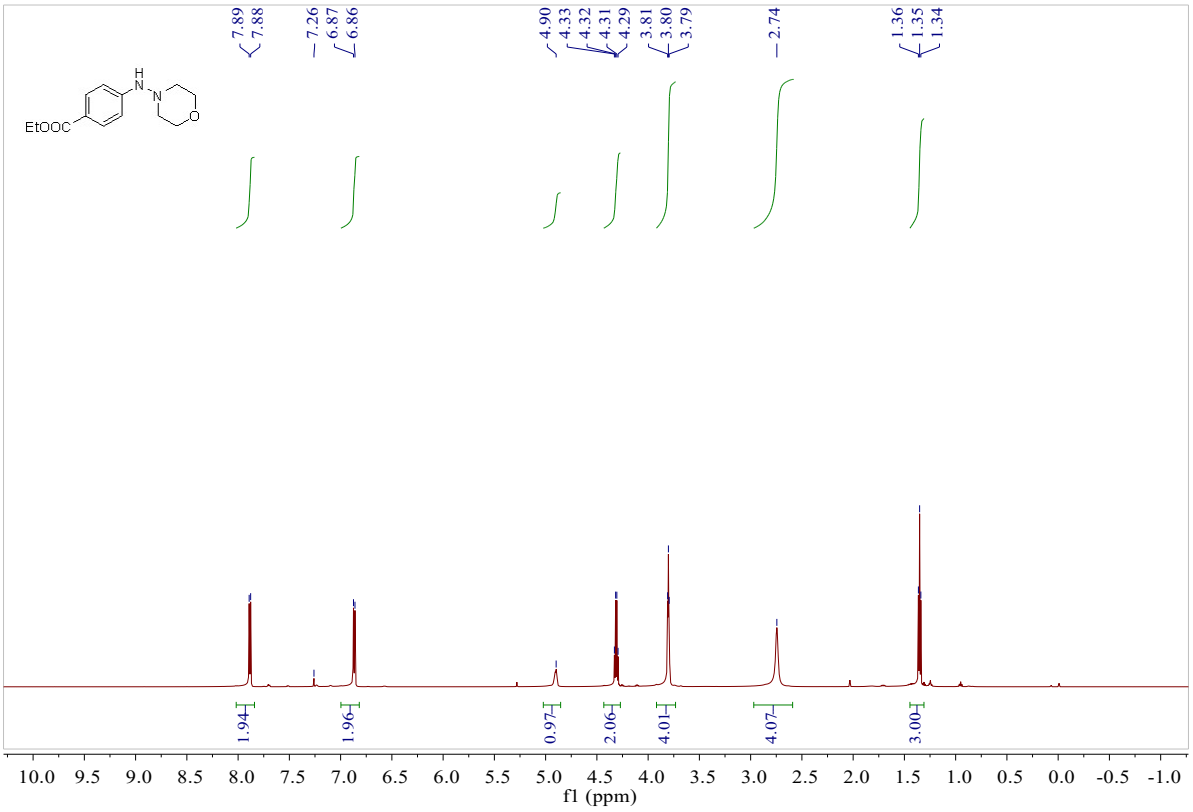
Ethyl 4-(pyridin-2-ylamino)benzoate (3aq): ^{1}H NMR (600 MHz, $CDCl_3$)



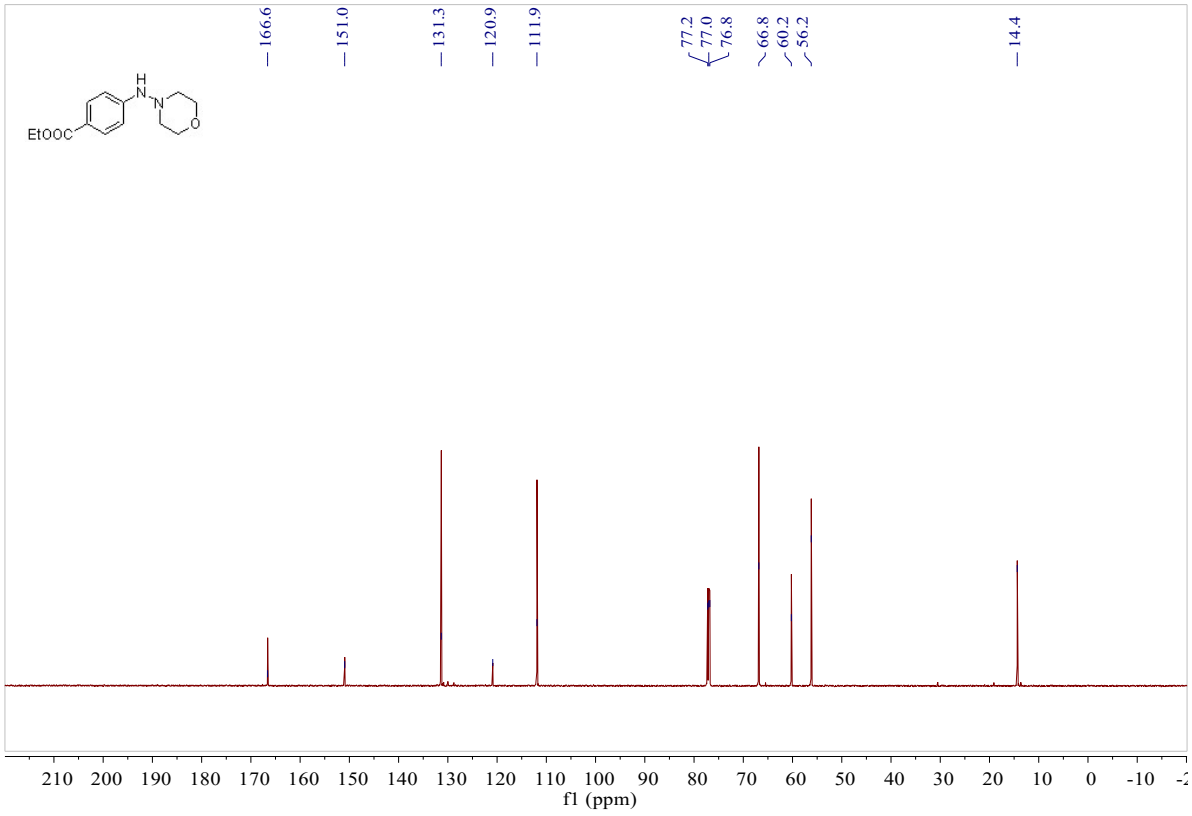
Ethyl 4-(pyridin-2-ylamino)benzoate (3aq): ^{13}C NMR (151 MHz, $CDCl_3$)



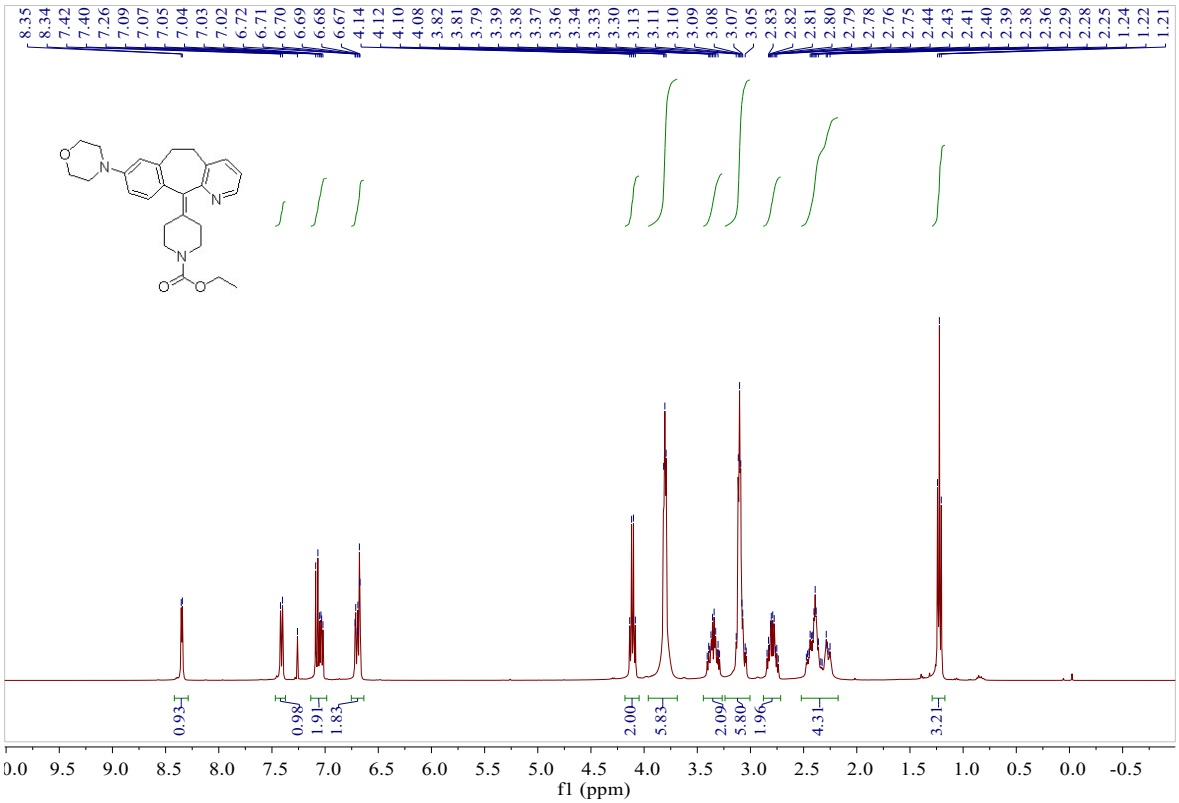
Ethyl 4-(morpholinoamino)benzoate (3ar): ^{1}H NMR (600 MHz, $CDCl_3$)



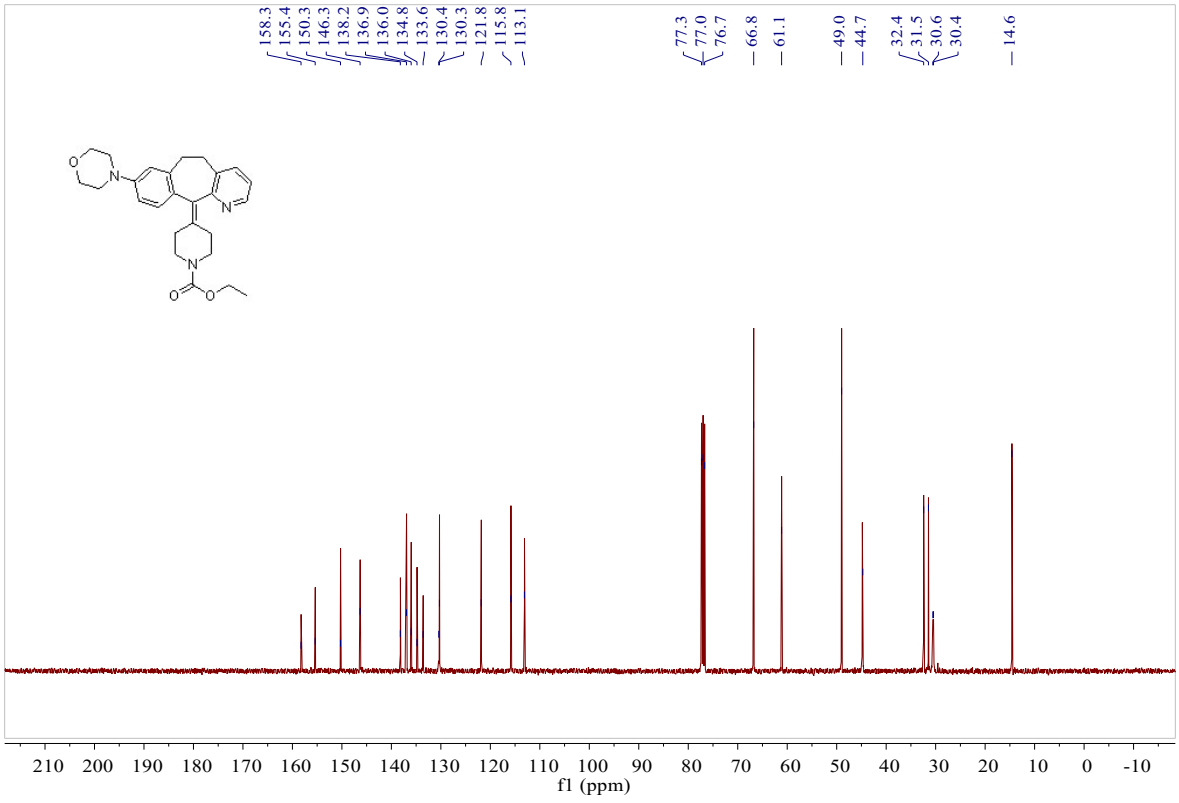
Ethyl 4-(morpholinoamino)benzoate (3ar): ^{13}C NMR (151 MHz, $CDCl_3$)



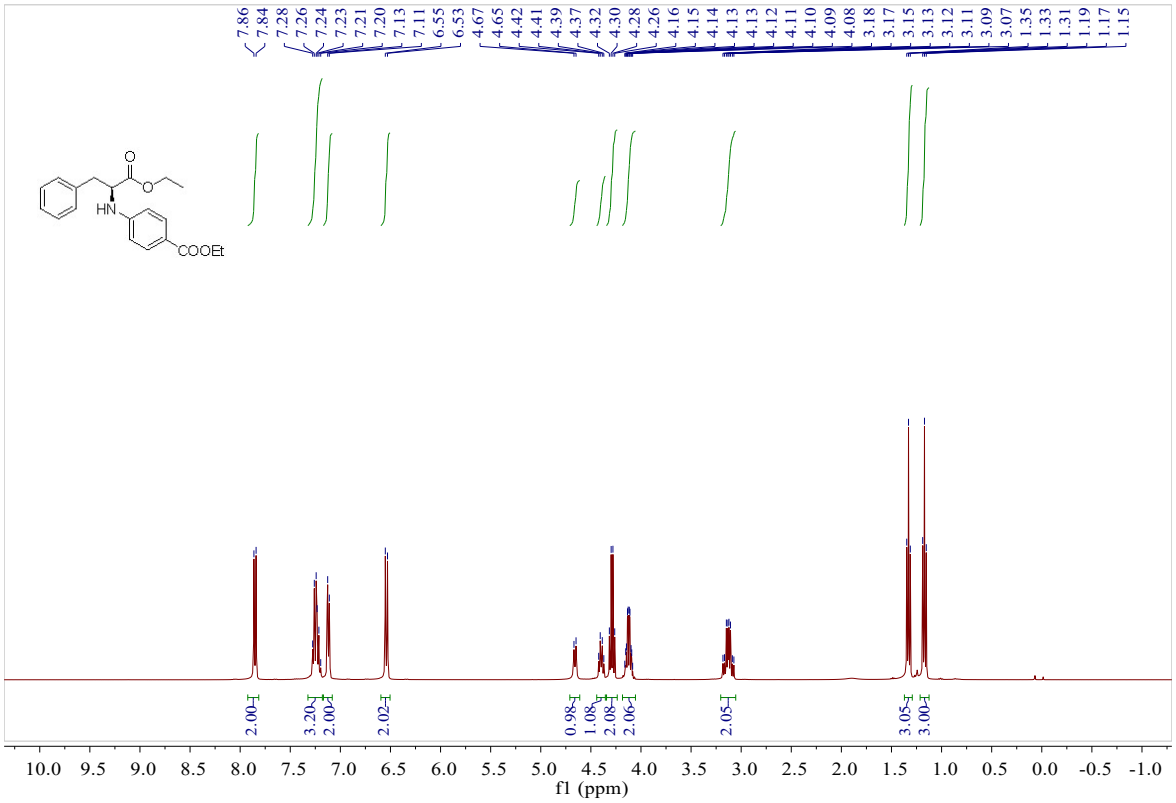
Ethyl 4-(8-morpholino-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-y lidene) piperidine-1-carboxylate (3as): ^{1}H NMR (400 MHz, $CDCl_3$)



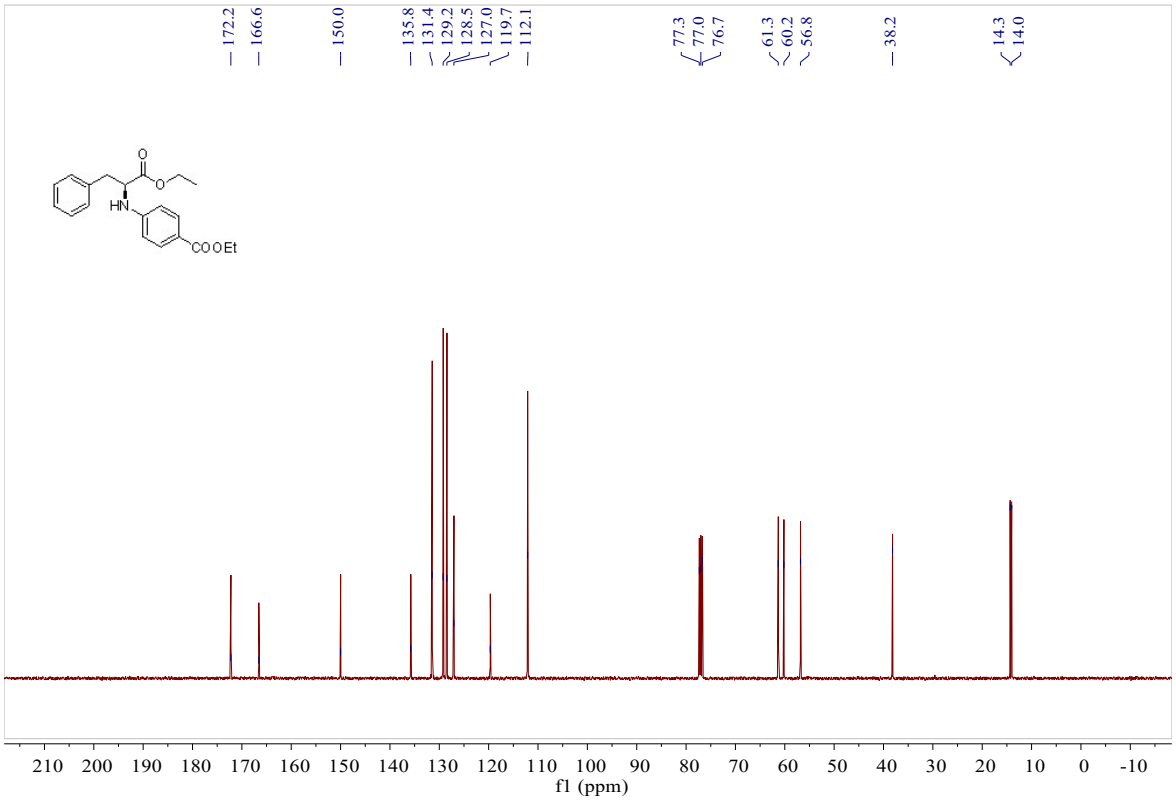
Ethyl 4-(8-morpholino-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-y lidene) piperidine-1-carboxylate (3as): ^{13}C NMR (101 MHz, $CDCl_3$)



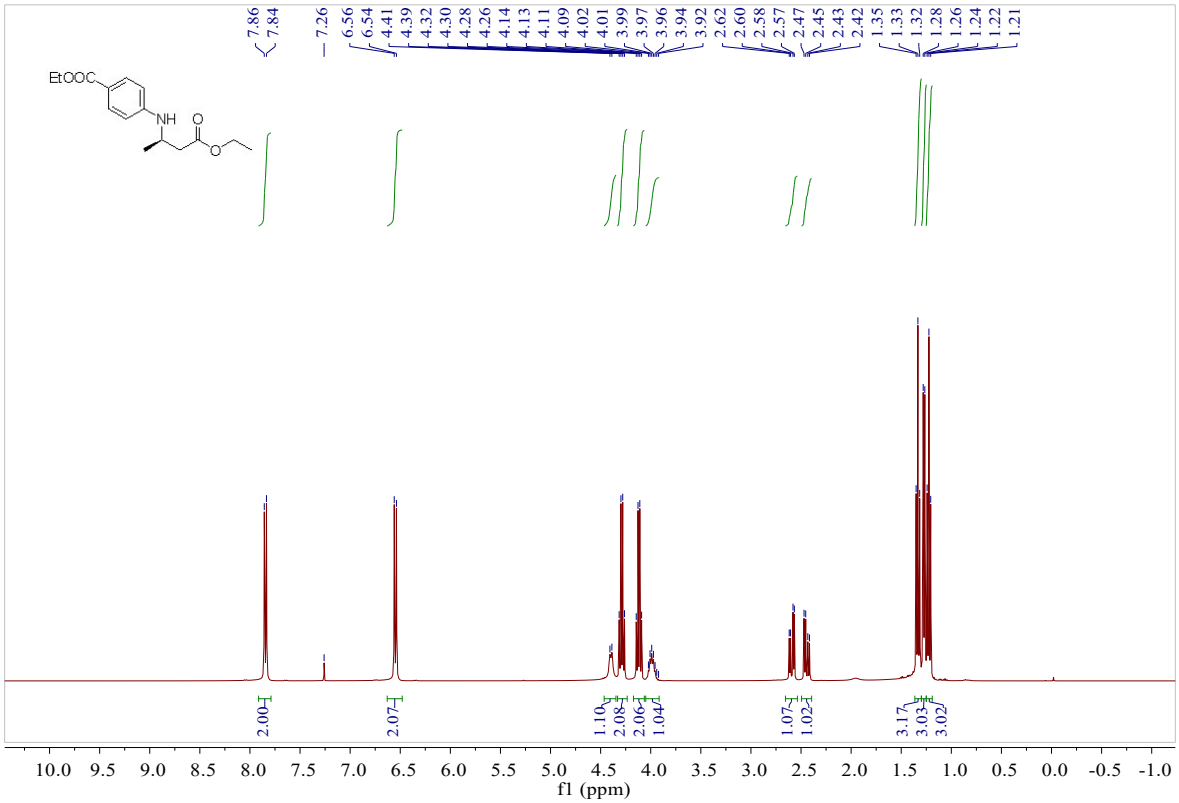
Ethyl (*S*)-4-((1-ethoxy-1-oxo-3-phenylpropan-2-yl)amino)benzoate (3at): ^{1}H NMR (400 MHz, $CDCl_3$)



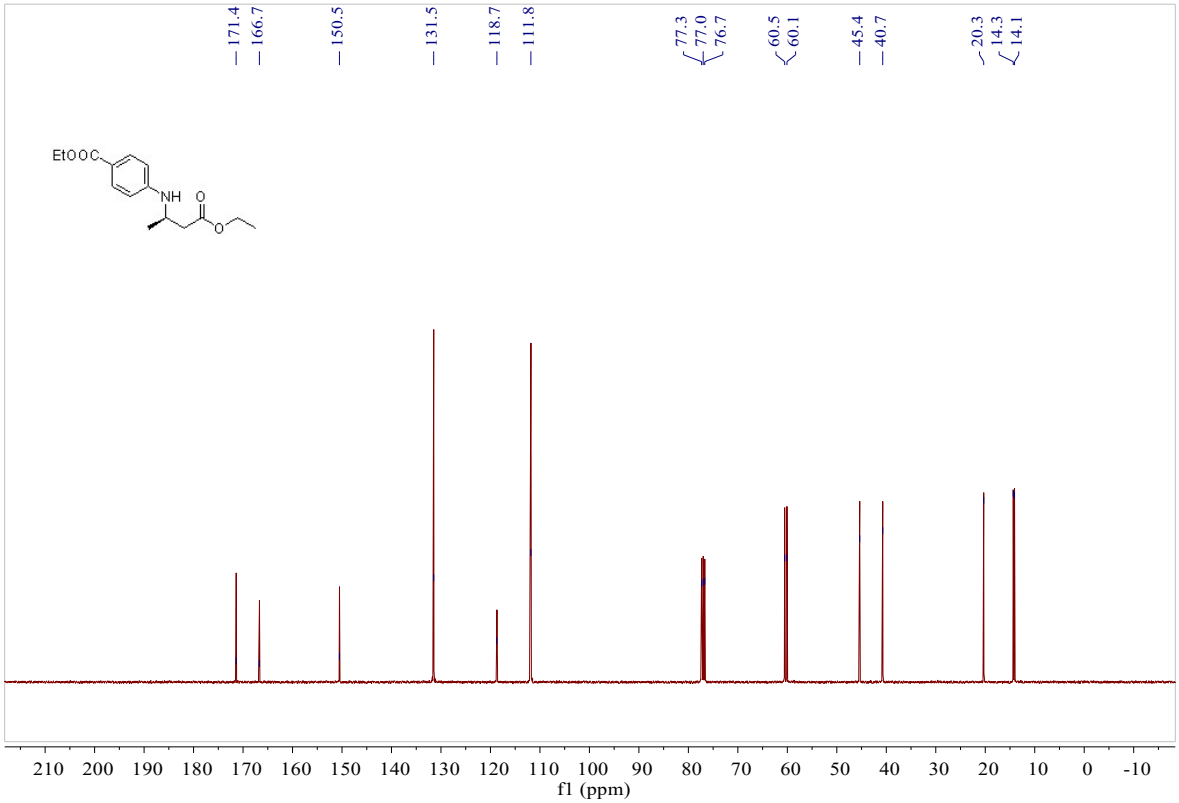
Ethyl (*S*)-4-((1-ethoxy-1-oxo-3-phenylpropan-2-yl)amino)benzoate (3at): ^{13}C NMR (101 MHz, $CDCl_3$)



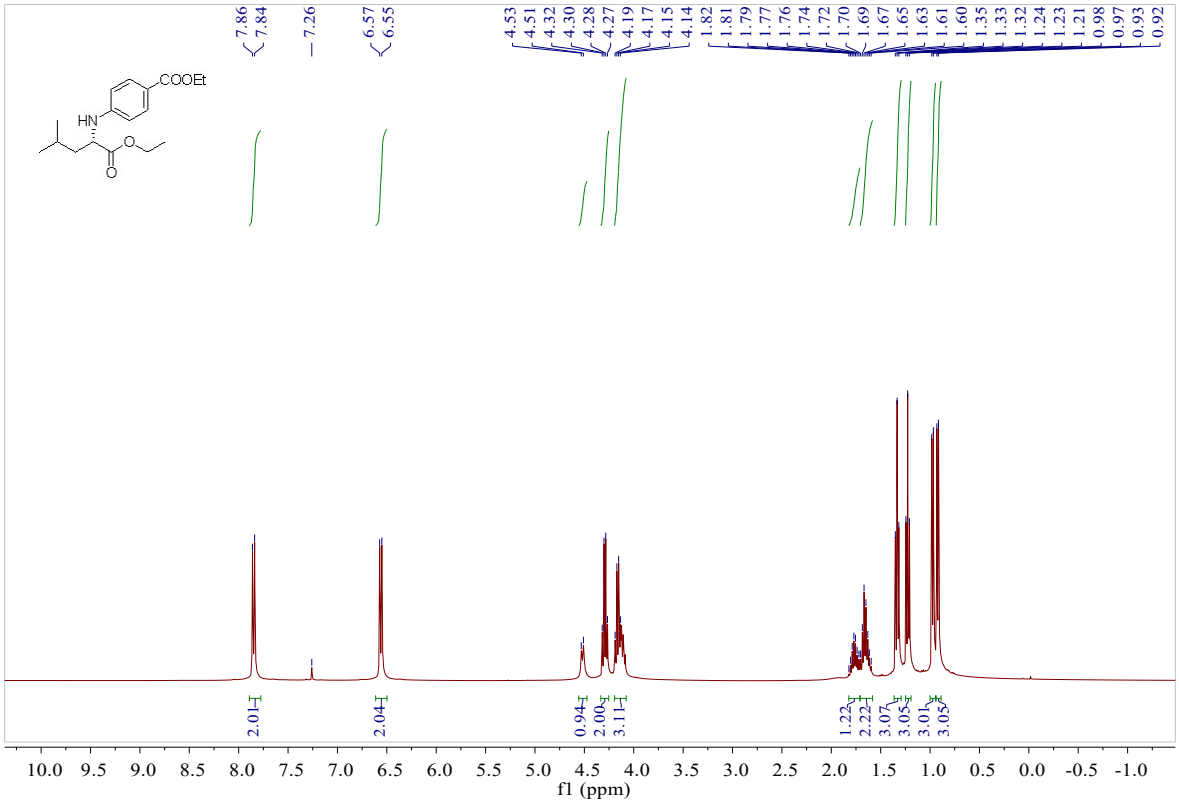
Ethyl (*R*)-4-((4-ethoxy-4-oxobutan-2-yl)amino)benzoate (3au): ^{1}H NMR (400 MHz, $CDCl_3$)



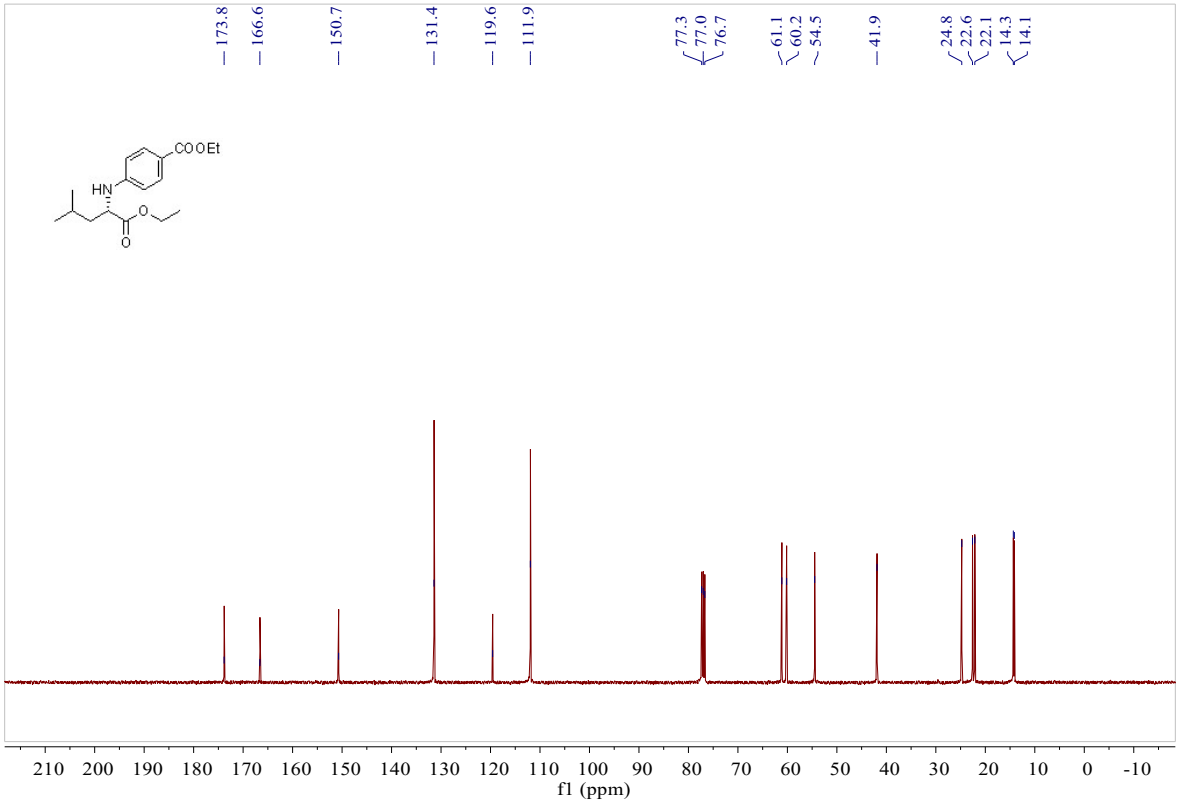
Ethyl (*R*)-4-((4-ethoxy-4-oxobutan-2-yl)amino)benzoate (3au): ^{13}C NMR (101 MHz, $CDCl_3$)



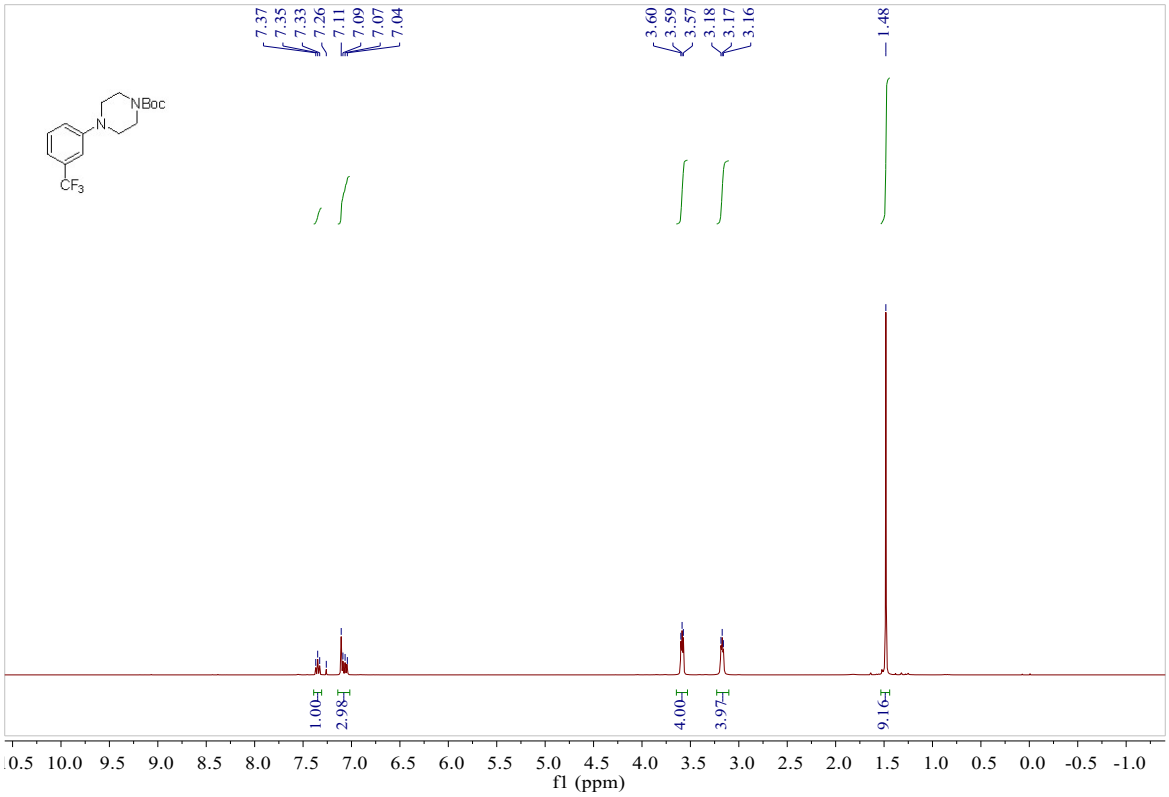
Ethyl (*S*)-4-((1-ethoxy-4-methyl-1-oxopentan-2-yl)amino)benzoate (3av): ^{1}H NMR (400 MHz, $CDCl_3$)



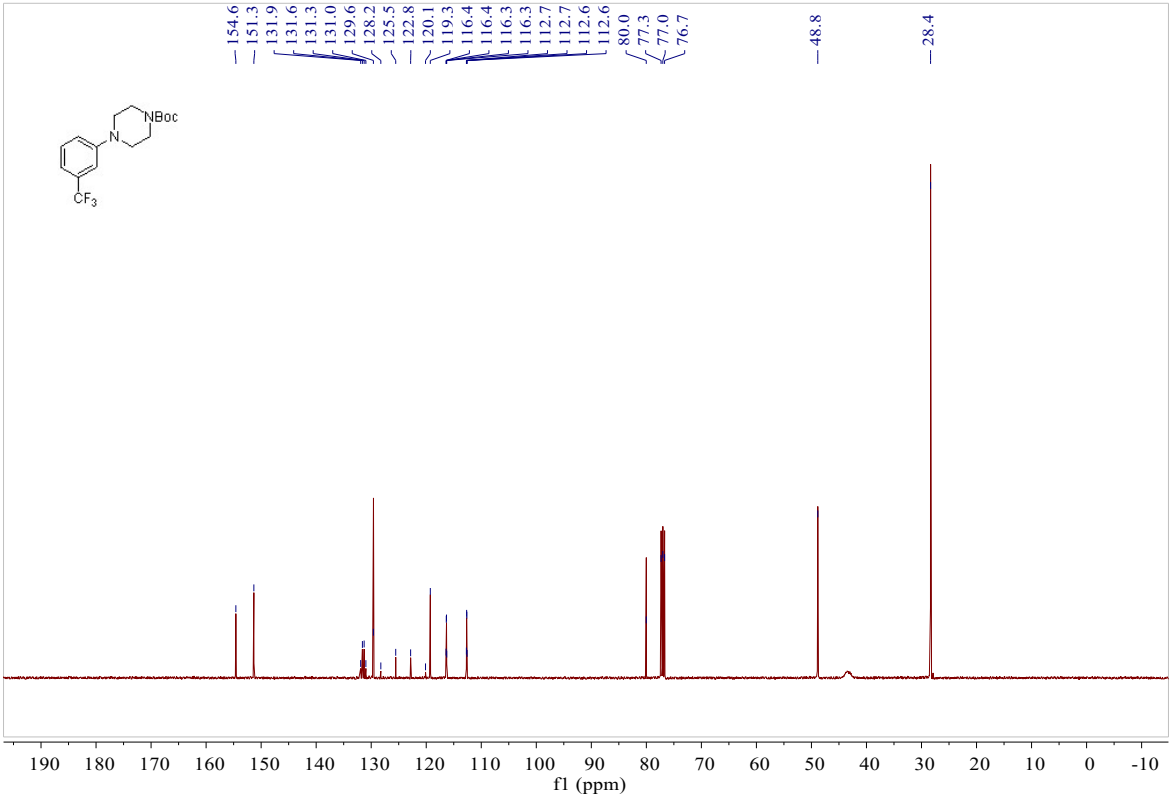
Ethyl (*S*)-4-((1-ethoxy-4-methyl-1-oxopentan-2-yl)amino)benzoate (3av): ^{13}C NMR (101 MHz, $CDCl_3$)



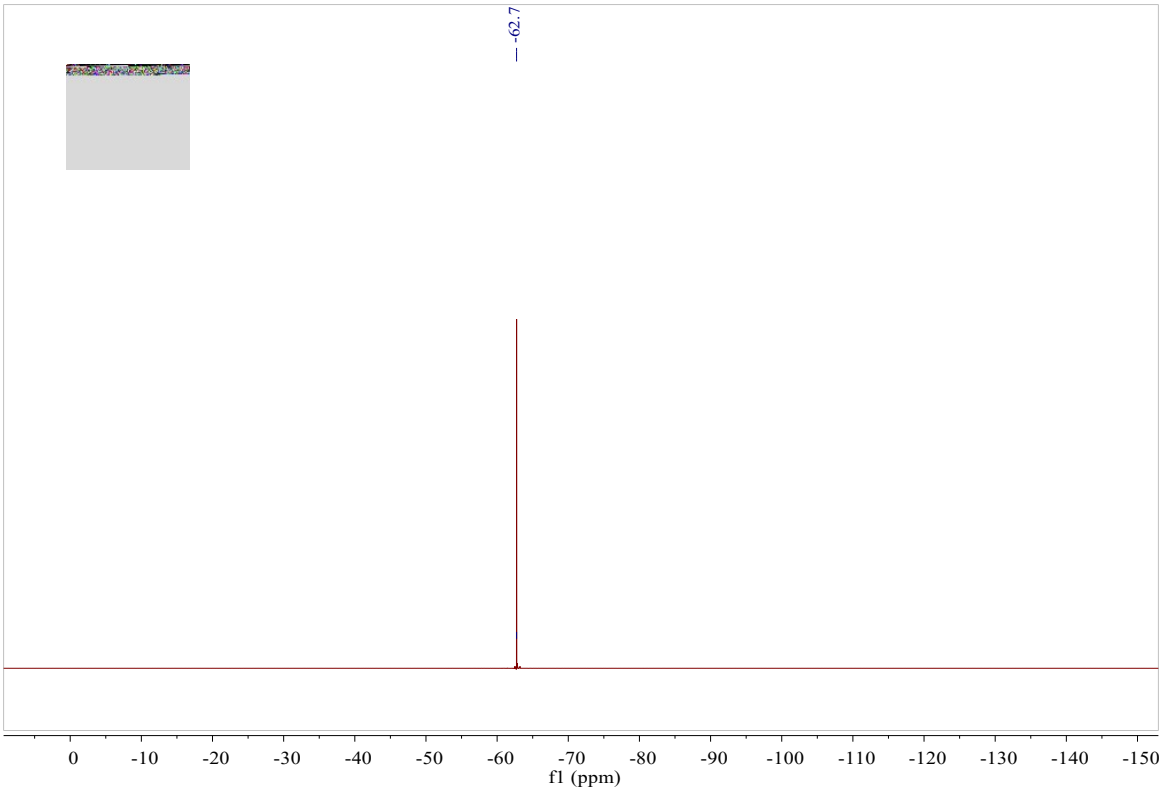
***tert*-Butyl 4-(3-(trifluoromethyl)phenyl)piperazine-1-carboxylate (4): ^{1}H NMR** (400 MHz, $CDCl_3$)



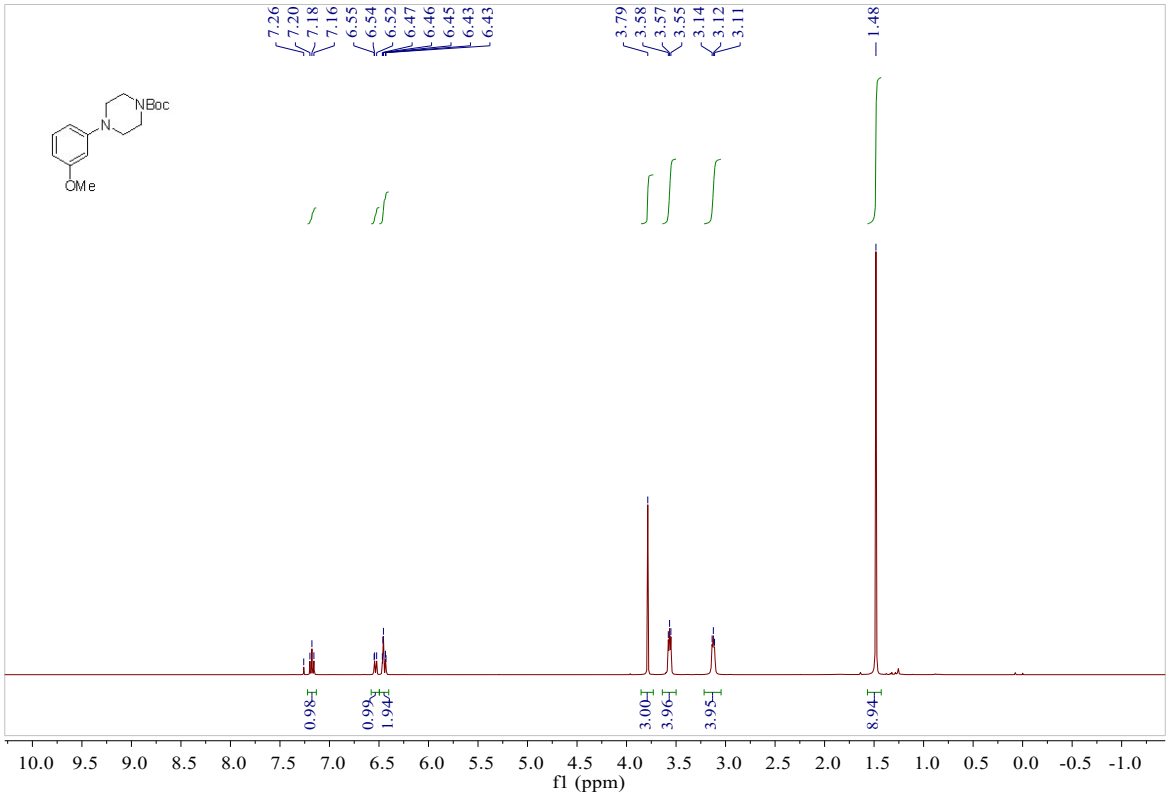
***tert*-Butyl 4-(3-(trifluoromethyl)phenyl)piperazine-1-carboxylate (4): ^{13}C NMR** (101 MHz, $CDCl_3$)



***tert*-Butyl 4-(3-(trifluoromethyl)phenyl)piperazine-1-carboxylate (4): ^{19}F NMR** (367 MHz, $CDCl_3$)



***tert*-Butyl 4-(3-methoxyphenyl)piperazine-1-carboxylate (5): ^{1}H NMR** (400 MHz, $CDCl_3$)



***tert*-Butyl 4-(3-methoxyphenyl)piperazine-1-carboxylate (5): ^{13}C NMR** (101 MHz, $CDCl_3$)