Palladium-catalyzed aminocarbonylation of halo-substituted 7-azaindoles and other heteroarenes using chloroform as a carbon monoxide source

Prakash Kannaboina,[a,b] Gaurav Raina,[a,b] K. Anil Kumar[a,b] and Parthasarathi Das[a, b]*

[a]Medicinal Chemistry Division, Indian Institute of Integrative Medicine (CSIR), Jammu 180001, India
[b]Academy of Scientific and Innovative Research (AcSIR), New Delhi 110025, India

E-mail: partha@iiim.ac.in

Table of contents

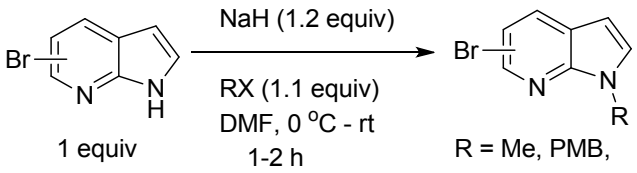
General experimental procedures	P2
Synthesis of iodides and bromides	P2-5
Table S1: Optimization studies for C-5 Aminocarbonylation of halo-substituted 7-azaindoles	P6
General Procedure for Aminocarbonylation of halo-substituted 7-azaindoles: (General Procedure A) and characterisation data	P6
General Procedure for Aminocarbonylation of halo-substituted 7-azaindoles: (General Procedure B) and characterisation data	P10
References	P15
The ^{1}H and ^{13}C NMR spectra of products	P15-54

General Experimental Methods

All of the reactions were carried out under an atmosphere of nitrogen oven/flame-dried glassware and standard syringe/septa techniques. Unless otherwise noted, all commercial reagents and solvents were obtained from the commercial provider and used without further purification. Thin layer chromatography (TLC) was performed using pre-coated silica gel 60 F254 MERCK. TLC plates were visualized by exposing UV light or by iodine vapors. Organic solutions were concentrated by rotary evaporation on BUCHI-Switzerland; R-120 rotary evaporator and vacuum pump V-710. Flash column chromatography was performed on Merck flash silica gel 100-200 size. Melting points of solid compounds were determined on BUCHI-B-545-Switzerland melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded with BRUKER 500 and 400 MHz NMR instruments. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of $CDCl_3$ as the internal standard (^{1}H NMR: TMS at 0.00 ppm, $CDCl_3$ at 7.26 ppm; ^{13}C NMR: $CDCl_3$ at 77.0 ppm). All the NMR spectra were processed in MestReNova. Mass spectra were recorded with VARIAN GC-MS-MS instrument. HRMS spectra were recorded with LCMS-QTOF Module No. G 654A (UHD).

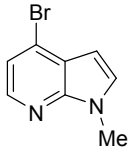
Synthesis of Starting materials (bromides and iodides):

(i) General Procedure for the synthesis of *N*-alkyl-7-Azaindole[1, 2, 3]:



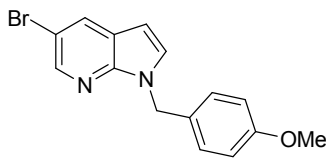
A dried round bottom flask equipped with a magnetic stirrer bar was charged 7-azaindole (1g, 8.47 mol) and DMF (5 mL) under nitrogen atmosphere. The reaction mixture was cool down to 0 °C and NaH (1.2 equiv) was added and stirred for 1 h. After 1 h stirring alkyl halide (iodide, bromide, chloride) (1.1 equiv) was added and continued the stirring for another 1 h. After completion of the reaction it was quenched with ice cold water (50 mL) and was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was dried over Na_2SO_4, the solvent was removed under reduced pressure to give *N*-alkyl-7-azaindoles in quantitative yield.

4-bromo-1-methyl-1*H*-pyrrolo[2,3-b]pyridine:



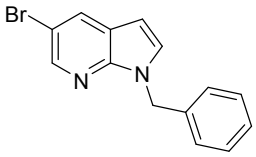
Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 5.1 Hz, 1H), 7.25 (d, J = 5.9 Hz, 1H), 7.22 (d, J = 3.5 Hz, 1H), 6.49 (d, J = 3.5 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 129.6, 125.3, 122.1, 118.8, 99.6, 31.7; HRMS (ESI): Calcd for $C_8H_8BrN_2$ $[M + H]^+$: 210.9866, found: 210.9868.

5-bromo-1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridine:



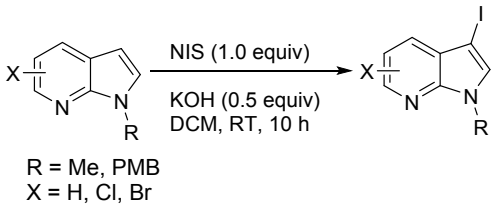
Brown liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 2.0 Hz, 1H), 8.02 (d, *J* = 2.0 Hz, 1H), 7.17 (d, *J* = 3.8 Hz, 1H), 7.16 (d, *J* = 4.2 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.40 (d, *J* = 3.5 Hz, 1H), 5.38 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 146.0, 143.4, 130.8, 130.2, 129.2, 129.0, 122.0, 114.1, 111.6, 99.5, 55.3, 47.5; HRMS (ESI): Calcd for $C_{15}H_{14}BrN_2O$ $[M + H]^+$: 317.0284, found: 317.0282.

1-benzyl-5-bromo-1*H*-pyrrolo[2,3-b]pyridine



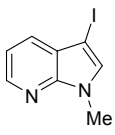
Brown semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 1.8 Hz, 1H), 8.03 (d, *J* = 2.0 Hz, 1H), 7.32 (d, *J* = 6.5 Hz, 1H), 7.29 (d, *J* = 2.6 Hz, 2H), 7.22 (d, *J* = 1.3 Hz, 1H), 7.21 – 7.17 (m, 2H), 6.42 (d, *J* = 3.5 Hz, 1H), 5.46 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.12, 143.57, 137.42, 130.83, 129.44, 128.83, 127.83, 127.53, 122.06, 111.83, 99.76, 48.10; HRMS (ESI): Calcd for $C_{14}H_{12}BrN_2$ $[M + H]^+$: 287.0179, found: 287.0180.

(ii) Synthesis of halo-substituted-7-Azaindole:



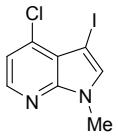
In a mixture of *N*-alkyl-1*H*-pyrrolo[2,3-b]pyridine (1.00 equiv) in CH_2Cl_2 was added KOH (0.50 equiv) at room temprature. After 30 min, N-iodosuccinimide (1.00 equiv) was added, and the mixture was stirred for 10 h, quenched with a saturated solution of $Na_2S_2O_3$, and extracted with CH_2Cl_2. The combined organic layers were dried and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc, 98:2) to give pure iodinated compound.

3-iodo-1-methyl-1*H*-pyrrolo[2,3-b]pyridine



Brown solid; m.p. 117-119 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 4.6 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.26 (s, 1H), 7.11 (dd, *J* = 7.3, 5.2 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.5, 143.9, 133.0, 129.1, 123.1, 116.4, 31.4; HRMS (ESI): Calcd for $C_8H_8IN_2$ $[M + H]^+$: 258.9727, found: 258.9720.

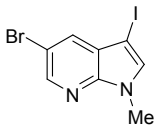
4-chloro-3-iodo-1-methyl-1*H*-pyrrolo[2,3-b]pyridine



Yellow solid; m.p. 129-131 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 5.1 Hz, 1H), 7.32 (s, 1H), 7.06 (d, *J* = 5.1 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 143.5,

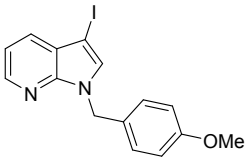
136.9, 135.2, 117.7, 117.4, 31.8; HRMS (ESI): Calcd for C_8H_7ClIN2 [M + H]$^+$: 292.9337, found: 292.9334.

5-bromo-3-iodo-1-methyl-1*H*-pyrrolo[2,3-b]pyridine



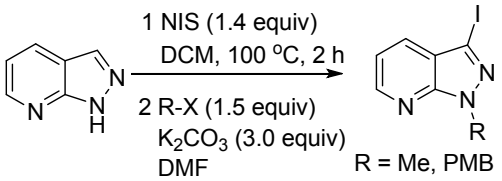
Brown solid; m.p. 118-120 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.79 (s, 1H), 7.24 (s, 1H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.9, 144.5, 134.4, 131.2, 124.6, 112.4, 31.6; HRMS (ESI): Calcd for C_8H_7BrIN2 [M + H]$^+$: 336.8832, found: 336.8826.

3-iodo-1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridine



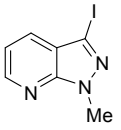
White solid; m.p. 97-99 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (dd, *J* = 4.7, 1.3 Hz, 1H), 7.71 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.24 (s, 1H), 7.20 (d, *J* = 8.6 Hz, 2H), 7.14 (dd, *J* = 7.9, 4.7 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.41 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 147.3, 144.1, 131.7, 129.3, 129.1, 123.1, 116.7, 114.2, 55.3, 47.6; HRMS (ESI): Calcd for $C_{15}H_{14}IN_2O$ [M + H]$^+$: 365.0146, found: 365.0140.

(iii) Synthesis of halo-substituted-Pyrazolopyridine:



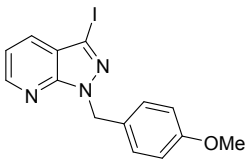
A solution of 1*H*-pyrazolo[3,4-b]pyridine (500 mg, 4.2 mmol) in dichloromethane(10 mL) was added to a solution of NIS (1.3 g, 5.9 mmol) in dichloromethane(20 mL). The reaction suspension was stirred at 100 ^{0}C for 2 h and the reaction mixture was washed with brine (100 mL). The solvent was removed under reduced pressure. To this add DMF (8 mL) and then K_2CO_3 (3.0 equiv) was added and the contents of the flask, sealed with a septum, were stirred for 60 min. Then CH_3I/PMB-Br (1.5 equiv) was added using a syringe and the reaction mixture was stirred for 20 h at room temperature. The crude product was purified by silica gel chromatography (gradient 10-85% EtOAc in hexanes) to give pure iodinated compound.

3-iodo-1-methyl-1*H*-pyrazolo[3,4-b]pyridine



White solid; m.p. 159-161 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 4.5, 1.4 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.13 (dd, *J* = 8.1, 4.5 Hz, 1H), 4.15 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.6, 149.9, 130.4, 120.4, 117.3, 89.0, 34.3; HRMS (ESI): Calcd for $C_7H_7IN_3$ [M + H]$^+$: 259.9679, found: 259.9683.

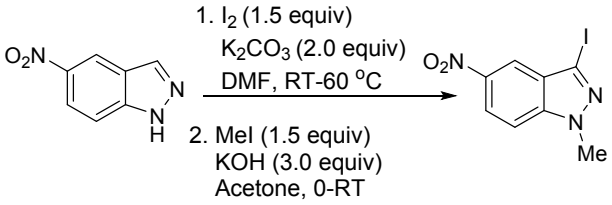
3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-b]pyridine



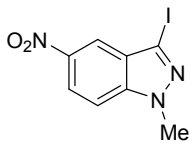
White solid; m.p. 127-129 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 4.5, 1.3 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.16 (dd, *J* = 8.1, 4.5 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 5.64 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 159.3, 150.0, 130.5, 129.6, 128.8, 128.6, 120.6, 117.5, 114.0, 89.8, 55.2, 50.7; HRMS (ESI): Calcd for $C_{14}H_{13}IN_3O$ $[M + H]^+$: 366.0098, found: 366.0098.

Synthesis of 3-iodo-1-methyl-5-nitro-1*H*-indazole:



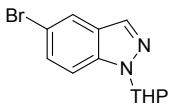
A dried round bottom flask equipped with a magnetic stirrer bar was charged with 5-nitro-1H-indazole (300 mg, 1.84 mmol) and K_2CO_3 (2.0 equiv) were added in DMF (3 mL) at room temperature. Iodine solution (1.5 equiv, dissolved in 2 mL of DMF) was added to reaction solution dropwise over 1-1.5 h, with the reaction temperature rising to 60 ^{0}C and the mixture was agitated for 6 h. The reaction was quenched with 10% sodium bisulfite aqueous solution and extracted with CH_2Cl_2. The combined organic layers were dried and evaporated under reduced pressure. To this added 5 mL of acetone at 0 °C, and then KOH (3.0 equiv) was added and the contents of the flask, sealed with a septum, were stirred for 60 min. Then CH_3I (1.5 equiv) was added using a syringe and the reaction mixture was warmed to room temperature and this temperature maintained for 18 h. The inorganic base was removed by filtration. The crude product was purified by silica gel chromatography (gradient 10-50% EtOAc in hexanes) to give pure iodinated compound.



Brown solid; m.p.177-179 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.32 (d, *J* = 8.9 Hz, 1H), 7.45 (d, *J* = 9.2 Hz, 1H), 4.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 142.5, 127.9, 122.5, 119.6, 109.7, 93.8, 36.5; HRMS (ESI): Calcd for $C_8H_7IN_3O_2$ $[M + H]^+$: 303.9578, found: 303.9581.

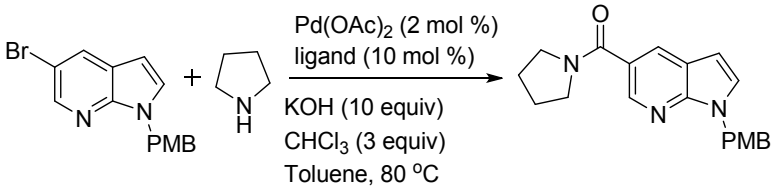
5-bromo-1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-indazole

Based on literature procedure[4] we performed THP protection by taking commercially available 5-Br-1*H*-indazole.



Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.85 (s, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 7.44 (dd, *J* = 8.9, 1.6 Hz, 1H), 5.69 (dd, *J* = 9.2, 2.7 Hz, 1H), 3.99 (dd, *J* = 12.7, 2.7 Hz, 1H), 3.79 – 3.65 (m, 1H), 2.60 – 2.45 (m, 1H), 2.18 – 2.09 (m, 1H), 2.10 – 2.00 (m, 1H), 1.79 – 1.71 (m, 2H), 1.71 – 1.60 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 133.04, 129.6, 126.23, 123.4, 114.3, 111.7, 85.56, 67.4, 29.4, 25.1, 22.4; HRMS (ESI): Calcd for $C_{12}H_{14}BrN_2O$ $[M + H]^+$: 281.0284, found: 281.0286.

Table S1: Optimization studies for C-5 Aminocarbonylation of halo-substituted 7-azaindoles:



entry	Pd-catalyst	L	yield[b] (%)
1	$Pd(OAc)_2$	PPh_3	33
2	$Pd(OAc)_2$	dppf	50
3	$Pd(OAc)_2$	XantPhos	60(35)
4	$Pd(OAc)_2$	dppp	20
5	$Pd(MeCN)_2Cl_2$	XantPhos	32
6	$Pd_2(dba)_3$	XantPhos	49

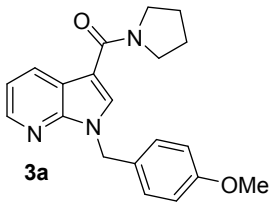
[a] Reaction conditions: *N*-PMB-7-azaindole (1.0 equiv), pyrrolidine (1.3 equiv), $Pd(OAc)_2$ (2 mol %), XantPhos (10 mol %), KOH (10 equiv), $CHCl_3$ (3.0 equiv) in toluene (1 mL), at 80 °C, 12 h. [b] Isolated yield, n.r. = no reaction, recovered starting material in the parentheses.

(I) General Procedure for Aminocarbonylation of Halo-substituted 7-Azaindoles: (General Procedure A)

Under nitrogen atmosphere $Pd(OAC)_2$ (1.54 mg, 2 mol %), dppf (15.23 mg, 10 mol %), KOH (154.14 mg, 10 equiv), toluene (1 mL), *N*-alkyl- halo 7-azaindole (100 mg, 0.27 mmol), amine (24.7 µL, 0.35 mmol), and chloroform (65.8 µL, 0.82 mmol) were added to a pressure tube sealed tightly and stirred vigorously at 80 °C for 12 h. After completion of the reaction, the combined organic layer was extracted with ethyl acetate, washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography through silicagel using MeOH-CH_2Cl_2 as eluent to provide the desired aminocarbonylated product.

By following general procedure **A** the following C-3 aminocarbonylated derivatives (**3a-l**, **4a-c**, **6a-c, and 7a**) have been synthesized.

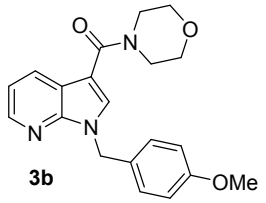
(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(pyrrolidin-1-yl)methanone (3a):



3a

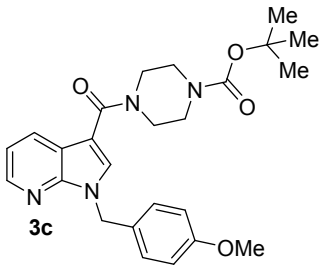
Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as yellow liquid; Yield: 75 mg (81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 7.9, 1.6 Hz, 1H), 8.41 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.49 (s, 1H), 7.21 (dd, *J* = 8.0, 4.6 Hz, 1H), 7.19 (d, *J* = 4.6 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 5.47 (s, 2H), 3.79 (s, 3H), 3.67 (br s, 4H), 1.95 (t, *J* = 6.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 159.4, 147.3, 144.1, 130.9, 129.2, 129.1, 128.9, 120.3, 117.5, 114.26, 110.2, 55.3, 47.9, 47.6, 25.5; HRMS (ESI): Calcd for $C_{20}H_{22}N_3O_2$ $[M + H]^+$: 336.1707, found: 336.1708.

(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(morpholino) methanone (3b):



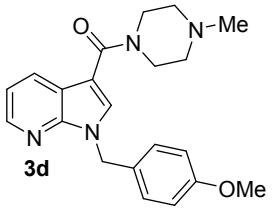
Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-1% MeOH in CH_2Cl_2 to obtain the product as yellow liquid; Yield: 55 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.05 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.49 (s, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.18 (dd, *J* = 7.9, 4.7 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 2H), 5.42 (s, 2H), 3.76 (s, 3H), 3.70 (br s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 159.5, 147.2, 144.1, 130.2, 129.4, 129.0, 128.6, 118.8, 117.4, 114.3, 108.7, 67.0, 55.3, 47.7; HRMS (ESI): Calcd for $C_{20}H_{22}N_3O_3$ $[M + H]^+$: 352.1656, found: 352.1651.

Tert-butyl 4-(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridine-3-carbonyl)piperazine-1-carboxylate



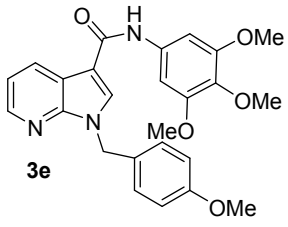
(3c): Prepared as shown in general procedure **A.** Crude reaction mixture was purified on a silicagel column using 0-1% MeOH in CH_2Cl_2 to obtain the product as brown semi solid; Yield: 60 mg (60%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.04 (dd, *J* = 9.6, 1.5 Hz, 1H), 7.47 (s, 1H), 7.21 (d, *J* = 8.7 Hz, 2H), 7.17 (dd, *J* = 7.9, 4.7 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.41 (s, 2H), 3.76 (s, 3H), 3.70 – 3.62 (m, 4H), 3.50 – 3.37 (m, 4H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 159.5, 154.6, 147.3, 144.1, 130.1, 129.4, 129.0, 118.8, 117.4, 114.3, 108.8, 80.3, 69.7, 55.3, 47.7, 45.4, 39.9, 28.4; HRMS (ESI): Calcd for $C_{25}H_{31}N_4O_4$ $[M + H]^+$: 451.2340, found: 451.2348.

(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(4-methylpiperazin-1-yl)methanone (3d):



Prepared as shown in general procedure **A.** Crude reaction mixture was purified on a silicagel column using 0-3% MeOH in CH_2Cl_2 to obtain the product as brown liquid; Yield: 48 mg (53%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.09 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.51 (s, 1H), 7.26 (d, *J* = 8.7 Hz, 2H), 7.22 (dd, *J* = 7.9, 4.7 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.46 (s, 2H), 3.81 (s, 3H), 3.76 (t, *J* = 4.9 Hz, 4H), 2.51 – 2.41 (m, 4H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.4, 147.2, 143.9, 130.1, 129.4, 129.1, 128.8, 118.9, 117.27, 114.3, 109.1, 55.3, 55.2, 47.7, 46.1; HRMS (ESI): Calcd for $C_{21}H_{25}N_4O_2$ $[M + H]^+$: 365.1972, found: 365.1975.

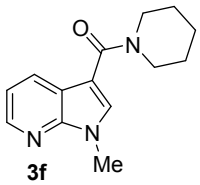
1-(4-methoxybenzyl)-N-(3, 4, 5-trimethoxyphenyl)-1*H*-pyrrolo[2,3-b]pyridine-3-carboxamide (3e):



Prepared as shown in general procedure **A.** Crude reaction mixture was purified on a silicagel column using 0-0.1% MeOH in CH_2Cl_2 to obtain the product as white solid; Yield: 46 mg (50%); m.p. 135-140 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 1.5 Hz, 1H), 8.46 (d, *J* = 1.5 Hz, 1H), 7.76 (s, 1H), 7.58 (s, 1H), 7.28 (dd, *J* = 7.7, 4.9 Hz, 1H), 7.23 (d, *J* = 8.6 Hz, 2H),

6.92 (s, 2H), 6.86 (d, J = 8.7 Hz, 2H), 5.45 (s, 2H), 3.85 (s, 6H), 3.83 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 159.5, 153.4, 147.9, 146.4, 144.4, 134.7, 134.3, 129.7, 129.5, 128.4, 118.6, 117.9, 114.3, 109.9, 98.0, 60.9, 56.1, 55.3, 47.8; HRMS (ESI): Calcd for $C_{25}H_{26}N_3O_5$ $[M + H]^+$: 448.1867, found: 448.1872.

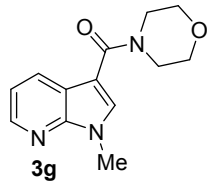
(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(piperidin-1-yl)methanone (3f):



3f

Prepared as shown in general procedure **A.** Crude reaction mixture was purified on a silicagel column using 0-1% MeOH in CH_2Cl_2 to obtain the product as white solid; Yield: 81 mg (71%); m.p. 110-114 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, J = 4.7, 1.5 Hz, 1H), 8.03 (dd, J = 7.9, 1.6 Hz, 1H), 7.50 (s, 1H), 7.14 (dd, J = 7.9, 4.7 Hz, 1H), 3.90 (s, 3H), 3.71 – 3.50 (m, 4H), 1.68 (dd, J = 11.0, 6.2 Hz, 2H), 1.61 (t, J = 7.5 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 147.4, 143.7, 130.9, 129.0, 118.9, 116.9, 109.3, 31.5, 26.3, 24.7; HRMS (ESI): Calcd for $C_{24}H_{18}N_3O$ $[M + H]^+$: 244.1445, found: 244.1435.

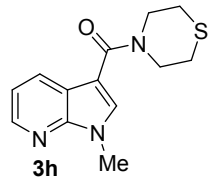
(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(morpholino)methanone (3g):



3g

Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-1% MeOH in CH_2Cl_2 to obtain the product as white solid; Yield: 59 mg (57%); m.p. 123-127 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (dd, J = 4.7, 1.5 Hz, 1H), 8.04 (dd, J = 7.9, 1.5 Hz, 1H), 7.55 (s, 1H), 7.17 (dd, J = 7.9, 4.7 Hz, 1H), 3.92 (s, 3H), 3.74 (br s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 147.4, 144.0, 131.5, 128.9, 118.7, 117.1, 108.3, 67.1, 31.6; HRMS (ESI): Calcd for $C_{13}H_{16}N_3O_2$ $[M + H]^+$: 246.1237, found: 246.1229.

(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(thiomorpholino)methanone (3h)

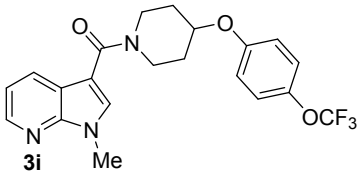


3h

Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-1% MeOH in CH_2Cl_2 to obtain the product as yellow liquid; Yield: 46 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (dd, J = 4.7, 1.5 Hz, 1H), 8.00 (dd, J = 7.9, 1.5 Hz, 1H), 7.51 (s, 1H), 7.16 (dd, J = 7.9, 4.7 Hz, 1H), 4.05 – 3.95 (m, 4H), 3.90 (s, 3H), 2.74 – 2.54 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 147.3, 144.0, 131.3, 128.9, 118.6, 117.1, 108.5, 31.6, 27.9; HRMS (ESI): Calcd for $C_{13}H_{16}N_3OS$ $[M + H]^+$: 262.1009, found: 262.1012.

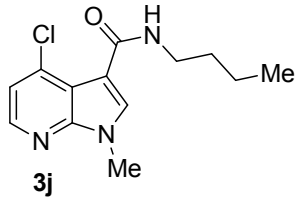
(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone (3i):

Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as brown semi solid; Yield: 175 mg (72%); ^{1}H



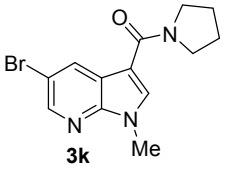
NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.08 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.58 (s, 1H), 7.20 (dd, *J* = 7.9, 4.6 Hz, 1H), 7.17 (d, *J* = 7.4 Hz, 2H), 6.94 (d, *J* = 9.1 Hz, 2H), 4.64 – 4.52 (m, 1H), 4.05 – 3.97 (m, 2H), 3.95 (s, 3H), 3.79 – 3.71 (m, 2H), 2.03 (ddd, *J* = 11.6, 8.3, 3.7 Hz, 2H), 1.90 (dtd, *J* = 10.6, 6.7, 3.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 155.6, 147.4, 143.9, 143.0, 131.3, 128.9, 122.6, 118.8, 117.0, 116.9, 108.8, 72.5, 41.8, 31.5, 30.9; HRMS (ESI): Calcd for $C_{21}H_{21}F_3N_3O_3$ $[M + H]^+$: 420.1530, found: 420.1535.

_N_-butyl-4-chloro-1-methyl-1_H_-pyrrolo[2,3-b]pyridine-3-carboxamide (3j):



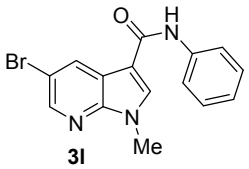
Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as yellow semi solid; Yield: 46 mg (50%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 5.1 Hz, 1H), 7.98 (s, 1H), 7.21 (d, *J* = 5.1 Hz, 1H), 6.76 (br s, 1H), 3.92 (s, 3H), 3.54 – 3.37 (m, 2H), 1.65 (dt, *J* = 14.8, 7.3 Hz, 2H), 1.46 (dq, *J* = 14.5, 7.3 Hz, 2H), 0.99 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 149.1, 143.5, 135.2, 134.9, 118.4, 115.0, 110.6, 39.8, 32.0, 31.6, 20.3, 13.8; HRMS (ESI): Calcd for $C_{13}H_{17}ClN_3O$ $[M + H]^+$: 266.1055, found: 266.1032.

(5-bromo-1-methyl-1_H_-pyrrolo[2,3-b]pyridin-3-yl)(pyrrolidin-1-yl)methanone (3k):



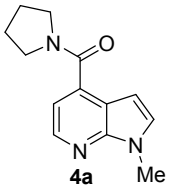
Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as white solid; Yield: 69 mg (76%); m.p. 125-129 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 2.2 Hz, 1H), 8.40 (d, *J* = 2.2 Hz, 1H), 7.52 (s, 1H), 3.90 (s, 3H), 3.71 (t, *J* = 6.7 Hz, 4H), 2.00 (br s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 145.8, 144.7, 133.0, 131.4, 121.8, 113.5, 109.2, 31.7; HRMS (ESI): Calcd for $C_{13}H_{15}BrN_3O$ $[M + H]^+$: 308.0393, found: 308.0393.

5-bromo-1-methyl-_N_-phenyl-1_H_-pyrrolo[2,3-b]pyridine-3-carboxamide (3l):



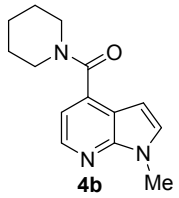
Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using CH_2Cl_2 to obtain the product as white solid; Yield: 20 mg (35%); m.p. 140-145 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 2.1 Hz, 1H), 8.41 (d, *J* = 2.1 Hz, 1H), 7.76 (s, 1H), 7.69 (s, 1H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.34 (t, *J* = 7.9 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 146.3, 144.9, 137.9, 131.8, 131.6, 129.1, 124.3, 120.3, 120.0, 113.9, 109.1, 31.9; HRMS (ESI): Calcd for $C_{15}H_{13}BrN_3O$ $[M + H]^+$: 330.0237, found: 330.0239.

(1-methyl-1_H_-pyrrolo[2,3-b]pyridin-4-yl)(pyrrolidin-1-yl)methanone (4a):



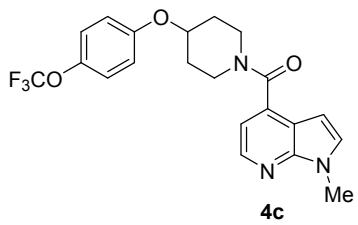
Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-1% MeOH in CH_2Cl_2 to obtain the product as yellow liquid; Yield: 88 mg (67%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 4.8 Hz, 1H), 7.23 (d, *J* = 3.5 Hz, 1H), 7.07 (d, *J* = 4.8 Hz, 1H), 6.46 (d, *J* = 3.5 Hz, 1H), 3.89 (s, 3H), 3.71 (t, *J* = 7.0 Hz, 2H), 3.28 (t, *J* = 6.7 Hz, 2H), 1.97 (dt, *J* = 13.7, 6.7 Hz, 2H), 1.91 – 1.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 148.4, 142.8, 137.1, 130.1, 117.1, 113.0, 98.8, 48.6, 45.9, 31.4, 26.1, 24.5; HRMS (ESI): Calcd for $C_{13}H_{16}N_3O$ $[M + H]^+$: 230.1288, found: 230.1282.

(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-4-yl)(piperidin-1-yl)methanone (4b):

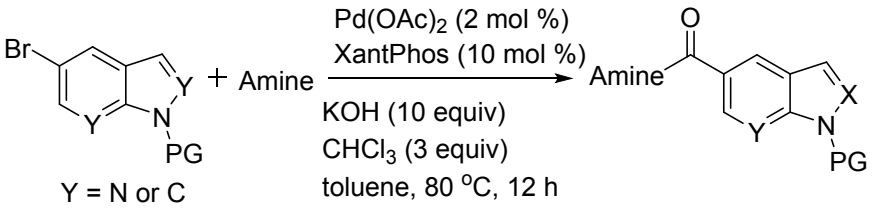


Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as yellow liquid; Yield: 71 mg (61%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 4.8 Hz, 1H), 7.22 (d, *J* = 3.5 Hz, 1H), 7.03 (d, *J* = 4.8 Hz, 1H), 6.44 (d, *J* = 3.5 Hz, 1H), 3.90 (s, 3H), 3.79 (br s, 2H), 3.23 (br s, 2H), 1.69 (br s, 4H), 1.46 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 148.2, 142.9, 136.5, 130.0, 117.3, 112.9, 98.4, 48.3, 42.9, 31.4, 26.8, 25.7, 24.5; HRMS (ESI): Calcd for $C_{14}H_{18}N_3O$ $[M + H]^+$: 244.1445, found: 244.1426.

(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-4-yl)(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone (4c):



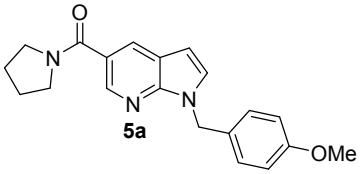
Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.8% MeOH in CH_2Cl_2 to obtain the product as brown liquid; Yield: 126 mg (70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 4.8 Hz, 1H), 7.23 (d, *J* = 3.5 Hz, 1H), 7.11 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 4.8 Hz, 1H), 6.87 (d, *J* = 6.9 Hz, 2H), 6.44 (d, *J* = 3.5 Hz, 1H), 4.56 – 4.42 (m, 1H), 3.98 – 3.90 (m, 2H), 3.89 (s, 3H), 3.54 (s, 1H), 3.25 (s, 1H), 2.06 – 1.92 (m, 2H), 1.81 – 1.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 155.5, 148.2, 143.0, 135.8, 130.3, 122.6, 117.2, 116.9, 113.0, 98.3, 72.1, 43.9, 38.5, 31.4, 30.2; HRMS (ESI): Calcd for $C_{21}H_{21}F_3N_3O_3$ $[M + H]^+$: 420.1530, found: 420.1532.



(II) General Procedure for Aminocarbonylation of Halo-substituted 7-Azaindoles: (General Procedure B)

Under nitrogen atmosphere $Pd(OAC)_2$ (1.77 mg 2 mol %), Xantphos (18.25 mg, 10 mol %), KOH (177.0 mg 10 equiv), toluene (1 mL), *N*-alkyl- halo 7-azaindole (100 mg, 0.31 mmol), amine (28.4 µL, 0.41 mmol), and chloroform (76.3 µL, 0.96 mmol) were added to a pressure tube sealed tightly and stirred vigorously at 80 °C for 12 h. After completion of the reaction, the combined organic layer was extracted with ethyl acetate, washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography through silicagel using MeOH-CH_2Cl_2 as eluent to provide the desired aminocarbonylated product.

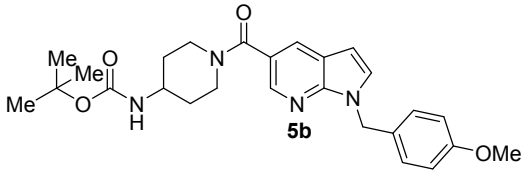
(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(pyrrolidin-1-yl)methanone (5a):



5a

Prepared as shown in general procedure **B**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as pale yellow liquid; Yield: 63 mg (60%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 1.9 Hz, 1H), 8.13 (d, *J* = 1.9 Hz, 1H), 7.21 (d, *J* = 3.5 Hz, 1H), 7.18 (d, *J* = 8.6 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.50 (d, *J* = 3.5 Hz, 1H), 5.44 (s, 2H), 3.78 (s, 3H), 3.71 (t, *J* = 6.6 Hz, 2H), 3.58 – 3.45 (m, 2H), 1.96 – 1.84 (m, 2H), 1.68 – 1.56 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.00, 159.21, 147.84, 142.34, 129.09, 129.00, 128.53, 125.27, 119.67, 114.13, 100.88, 55.26, 47.53, 46.51, 24.52, 22.72; HRMS (ESI): Calcd for $C_{20}H_{22}N_3O_2$ $[M + H]^+$: 336.1707, found: 336.1715.

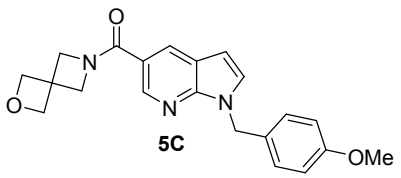
Tert-butyl(1-(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridine-5-carbonyl)piperidin-4-yl)carbamate



5b

(5b): Prepared as shown in general procedure **B**. Crude reaction mixture was purified on a silicagel column using 0-1% MeOH in CH_2Cl_2 to obtain the product as pale yellow liquid; Yield: 110 mg (58%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 1.9 Hz, 1H), 8.01 (d, *J* = 1.9 Hz, 1H), 7.25 (d, *J* = 3.5 Hz, 1H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.52 (d, *J* = 3.5 Hz, 1H), 5.46 (s, 2H), 4.66 – 4.39 (m, 1H), 3.80 (s, 3H), 3.78 – 3.61 (m, 2H), 3.20 – 3.05 (m, 2H), 2.09 – 1.85 (m, 4H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 159.2, 155.1, 147.9, 141.9, 129.2, 128.9, 128.3, 123.9, 119.8, 114.1, 100.7, 55.3, 47.5, 33.0, 32.0, 28.4; HRMS (ESI): Calcd for $C_{26}H_{33}N_4O_4$ $[M + H]^+$: 465.2497, found: 465.2499.

(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(2-oxa-6-azaspiro[3.3]heptan-6-yl)methanone

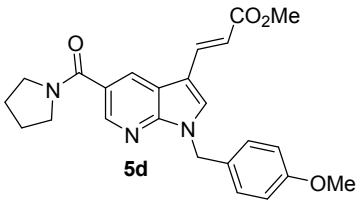


5C

(5c): Prepared as shown in general procedure **B**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as yellow liquid; Yield: 20 mg (36%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 2.0 Hz, 1H), 8.21 (d, *J* = 2.0 Hz, 1H), 7.22 (d, *J* = 3.6 Hz, 1H), 7.17 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.52 (d, *J* = 3.6 Hz, 1H), 5.43 (s, 2H), 4.82 (s, 4H), 4.45 (s, 4H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1,

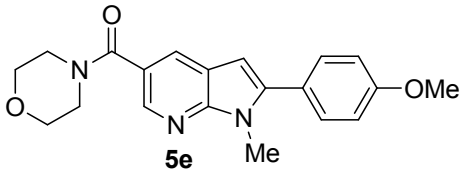
159.3, 148.5, 142.9, 129.4, 129.2, 129.0, 121.1, 119.9, 114.2, 101.2, 80.9, 55.3, 47.6, 38.5; HRMS (ESI): Calcd for $C_{21}H_{22}N_3O_3$ $[M + H]^+$: 364.1656, found: 364.1660.

Methyl(E)-3-(1-(4-methoxybenzyl)-5-(pyrrolidine-1-carbonyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)acrylate (5d): Prepared as shown in general procedure **B**. Crude reaction mixture was purified on a silicagel column using 0-0.1% MeOH in CH_2Cl_2 to obtain the product as brown liquid; Yield: 32 mg (52%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 5.7, 2.0 Hz, 1H), 8.38 (d, *J* = 1.9 Hz, 1H), 7.77 (d, *J* = 16.0 Hz, 1H), 7.47 (s, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.38 (d, *J* = 16.0 Hz, 1H), 5.43 (s, 2H), 3.79 (s, 6H), 3.54 (t, *J* = 8.1 Hz, 2H), 3.37 (t, *J* = 6.7 Hz, 2H), 1.97 – 1.89 (m, 2H), 1.86 – 1.72 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 168.1, 158.7, 145.0, 143.4, 137.1, 134.5, 132.6, 129.3, 129.1, 128.2, 120.2, 114.3, 114.2, 114.2, 111.5, 55.3, 47.9, 46.9, 45.1, 25.9, 25.6; HRMS (ESI): Calcd for $C_{24}H_{26}N_3O_4$ $[M + H]^+$: 420.1918, found: 420.1920.



5d

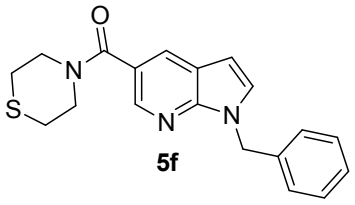
(2-(4-methoxyphenyl)-1-methyl-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(morpholino)methanone (5e):



5e

Prepared as shown in general procedure **B**. Crude reaction mixture was purified on a silicagel column using 0-2% MeOH in CH_2Cl_2 to obtain the product as brown liquid; Yield: 61 mg (50%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 1.9 Hz, 1H), 8.01 (d, *J* = 2.0 Hz, 1H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.26 (d, *J* = 4.3 Hz, 2H), 6.51 (d, *J* = 3.5 Hz, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.72 (br s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.86, 148.20, 142.01, 141.43, 130.53, 130.47, 128.51, 127.51, 123.02, 119.81, 114.26, 100.24, 99.42, 66.95, 55.42, 29.69; HRMS (ESI): Calcd for $C_{20}H_{22}N_3O_3$ $[M + H]^+$: 352.1656, found: 352.1666.

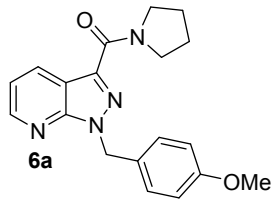
(1-benzyl-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(thiomorpholino)methanone (5f):



5f

Prepared as shown in general procedure **B**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as yellow liquid; Yield: 148 mg (63%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 1.9 Hz, 1H), 8.00 (d, *J* = 2.0 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.29 – 7.26 (m, 1H), 7.26 (d, *J* = 3.7 Hz, 1H), 7.22 – 7.16 (m, 2H), 6.54 (d, *J* = 3.5 Hz, 1H), 5.51 (s, 2H), 3.93 (br s, 4H), 2.69 (br s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 147.9, 141.8, 137.3, 129.5, 128.8, 128.3, 127.8, 127.5, 123.8, 119.8, 100.9, 48.0, 29.7, 27.9; HRMS (ESI): Calcd for $C_{19}H_{20}N_3OS$ $[M + H]^+$: 338.1322, found: 338.1330.

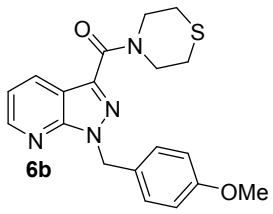
(1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-b]pyridin-3-yl)(pyrrolidin-1-yl)methanone (6a):



6a

Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as yellow liquid; Yield: 96 mg (70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (dd, *J* = 8.1, 1.5 Hz, 1H), 8.57 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.32 (d, *J* = 8.7 Hz, 2H), 7.22 (dd, *J* = 8.1, 4.5 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.67 (s, 2H), 4.06 (t, *J* = 6.7 Hz, 2H), 3.77 (s, 3H), 3.73 (t, *J* = 6.9 Hz, 2H), 2.05 – 1.97 (m, 2H), 1.97 – 1.89 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 159.3, 150.3, 149.2, 138.5, 132.7, 129.4, 128.8, 118.4, 116.6, 114.0, 55.2, 50.6, 48.8, 47.0, 26.7, 23.8; HRMS (ESI): Calcd for $C_{19}H_{21}N_4O_2$ $[M + H]^+$: 337.1659, found: 337.1667.

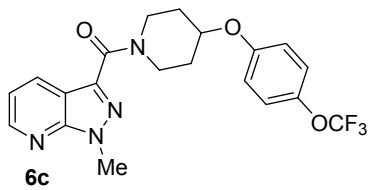
((1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-b]pyridin-3-yl)(thiomorpholino)methanone (6b):



6b

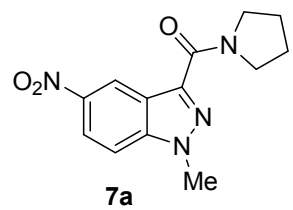
Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as brown liquid; Yield: 37 mg (62%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 4.5, 1.6 Hz, 1H), 8.48 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.32 (d, *J* = 8.7 Hz, 2H), 7.23 (dd, *J* = 8.1, 4.5 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.66 (s, 2H), 4.37 (br s, 2H), 4.10 (br s, 2H), 3.77 (s, 3H), 2.76 (br s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 159.4, 150.3, 149.5, 137.3, 132.0, 129.6, 128.5, 118.5, 116.7, 114.0, 55.3, 50.6, 49.8, 45.4, 29.7, 27.6; HRMS (ESI): Calcd for $C_{19}H_{21}N_4O_2S$ $[M + H]^+$: 369.1380, found: 369.1386.

(1-methyl-1*H*-pyrazolo[3,4-b]pyridin-3-yl)(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone (6c): Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as brown semi solid; Yield: 166 mg (57%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.5, 1.5 Hz, 1H), 8.51 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.23 (dd, *J* = 8.1, 4.5 Hz, 1H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.93 (d, *J* = 9.1 Hz, 2H), 4.65 – 4.47 (m, 1H), 4.38 – 4.22 (m, 2H), 4.19 (s, 3H), 4.04 – 3.82 (m, 2H), 2.10 – 1.99 (m, 2H), 1.96 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 159.3, 150.3, 149.2, 138.5, 132.7, 129.4, 128.80, 118.4, 116.6, 114.0, 55.2, 50.6, 48.8, 46.9, 26.7, 23.8; HRMS (ESI): Calcd for $C_{20}H_{20}F_3N_4O_3$ $[M + H]^+$:421.1482, found: 421.1485.



6c

(1-methyl-5-nitro-1*H*-indazol-3-yl)(pyrrolidin-1-yl)methanone (**7a**):

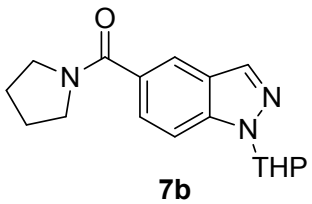


7a

Prepared as shown in general procedure **A**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as yellow semi solid; Yield: 39 mg (43%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35 (d, *J* = 1.9 Hz, 1H), 8.30 (dd, *J* = 9.2, 2.1 Hz, 1H), 7.45 (d, *J* = 9.2 Hz, 1H), 4.17 (s, 3H), 4.04 (t, *J* = 6.6 Hz, 2H), 3.77 (t, *J* = 6.7 Hz, 2H), 2.07 – 1.98 (m, 2H), 2.00 – 1.92 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 143.5, 142.0, 141.6,

123.81, 121.9, 121.4, 109.2, 48.9, 47.0, 36.5, 26.6, 23.9; HRMS (ESI): calcd for $C_{13}H_{15}N_4O_3$ $[M+H]^+$: 275.1139, found: 275.1144.

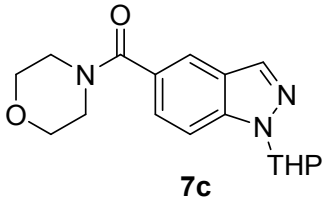
Pyrrolidin-1-yl(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-indazol-5-yl)methanone (7b):



7b

Prepared as shown in general procedure **B**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as yellow liquid: 21 mg (40%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.82 (s, 1H), 7.67 – 7.58 (m, 1H), 7.46 (dd, *J* = 8.6, 1.4 Hz, 1H), 5.80 – 5.50 (m, 1H), 4.10 – 3.94 (m, 2H), 3.76 (d, *J* = 10.4 Hz, 2H), 3.66 (d, *J* = 12.1 Hz, 2H), 2.59 – 2.47 (m, 2H), 2.16 (dd, *J* = 8.8, 5.2 Hz, 2H), 2.10 – 1.98 (m, 2H), 1.85 – 1.80 (m, 2H), 1.78 – 1.65 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 134.6, 134.4, 128.4, 125.8, 124.3, 120.8, 110.5, 85.6, 66.9, 47.9, 31.9, 31.6, 29.7, 25.1, 22.4; HRMS (ESI): Calcd for $C_{17}H_{22}N_3O_2$ $[M + H]^+$: 300.1707, found: 300.1709.

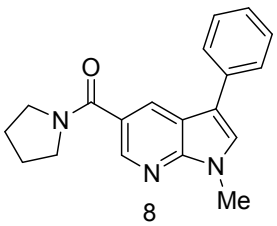
Morpholino(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-indazol-5-yl)methanone (7c):



7c

Prepared as shown in general procedure **B**. Crude reaction mixture was purified on a silicagel column using 0-0.5% MeOH in CH_2Cl_2 to obtain the product as brown liqiud; Yield: 24 mg (36%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.82 (s, 1H), 7.64 (d, *J* = 8.7 Hz, 1H), 7.46 (dd, *J* = 8.7, 1.4 Hz, 1H), 5.74 (dd, *J* = 9.3, 2.6 Hz, 1H), 4.10 – 3.95 (m, 2H), 3.70 (br s, 8H), 2.56 (dd, *J* = 22.4, 11.3 Hz, 2H), 2.19 – 1.98 (m, 2H), 1.85 – 1.61 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 139.8, 139.3, 134.5, 128.4, 125.8, 120.8, 110.5, 85.6, 67.5, 66.9, 29.7, 29.4, 25.1, 22.5; HRMS (ESI): Calcd for$C_{17}H_{22}N_3O_3$ $[M + H]^+$: 316.1656, found: 316.1660.

(1-methyl-3-phenyl-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(pyrrolidin-1-yl)methanone (8):



8

A solution of 5-bromo-3-iodo-1-methyl-1*H*-pyrrolo[2,3-b]pyridine (150 mg, 0.44 mmol), phenylboronic acid (65.3 mg, 0.53 mmol), $Pd(PPh_3)_4$ (12.9 mg, 0.01 mmol), and K_2CO_3 (123.3 mg, 0.9 mmol) in toluene:EtOH (1.5 mL, 3:1 mixture) was heated to 80 ^{o}C for 5 h under N_2 atmosphere. Then $Pd(OAC)_2$ (2 mol %), Xantphos (10 mol %), KOH (10 equiv), pyrrolidine (1.3 equiv) and chloroform (3.0 equiv) were added to a pressure tube sealed tightly and stirred vigorously at 80 °C for 12 h. After completion of the reaction, the combined organic layer was extracted with ethyl acetate, washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The crude reaction mixture was purified on a silicagel column using 0-1.5% MeOH in CH_2Cl_2 to obtain the product as colourless liquid: 78 mg (43%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 1.9 Hz, 1H), 8.43 (d, *J* = 1.9 Hz, 1H), 7.62 (d, *J* = 7.1 Hz, 2H), 7.48 – 7.40 (m, 3H), 7.31 (d, *J* = 7.4 Hz, 1H), 3.96 (s, 3H), 3.70 (t,

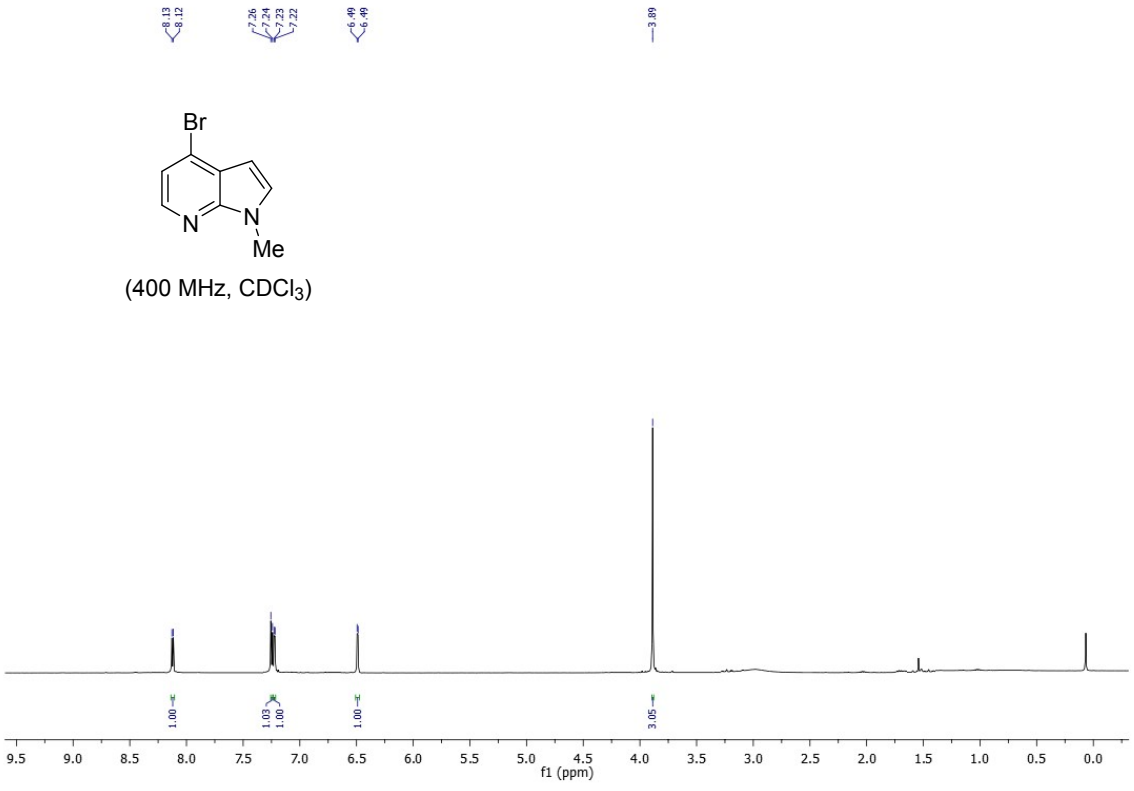
J = 6.7 Hz, 2H), 3.52 (t, *J* = 6.1 Hz, 2H), 2.07 – 1.94 (m, 2H), 1.97 – 1.82 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 148.6, 142.5, 134.3, 129.0, 127.8, 127.3, 127.0, 126.4, 125.6, 117.8, 115.9, 50.8, 46.5, 31.5, 26.5, 24.5; HRMS (ESI): Calcd for $C_{19}H_{20}N_3O$ $[M + H]^+$: 306.1601, found: 306.1607.

References;

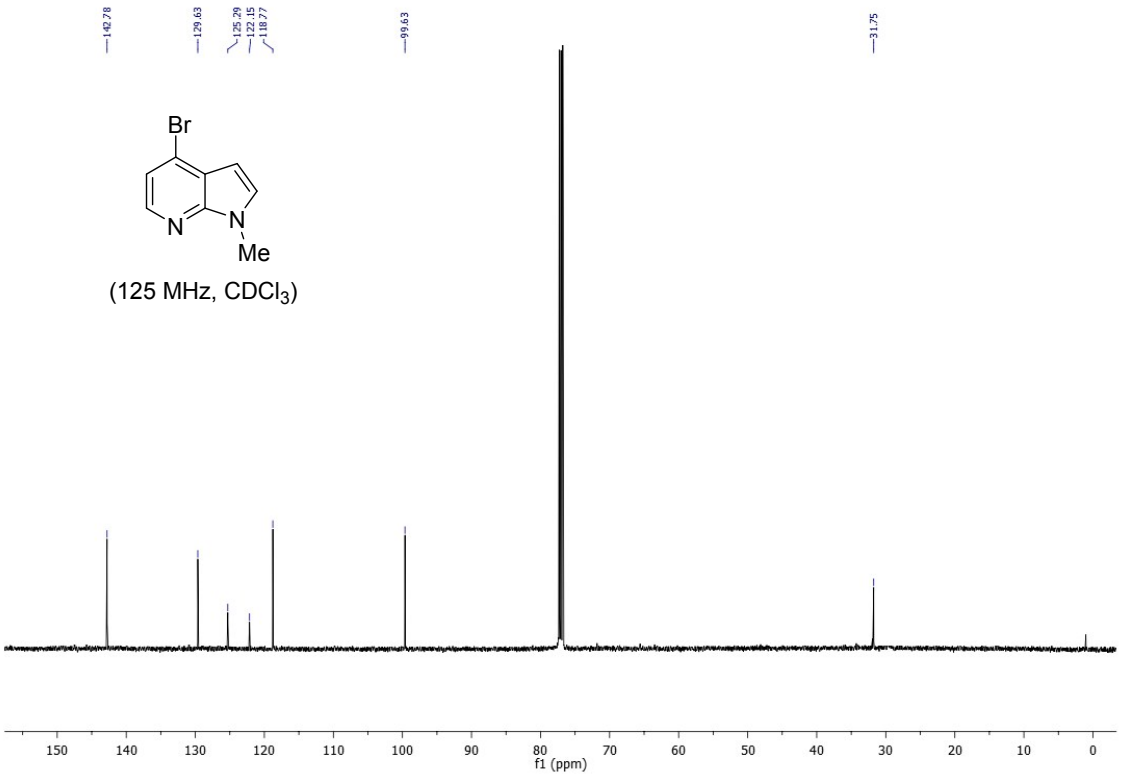
1. M. P. Huestis and K. Fagnou. *Org. Lett.,* 2009, **11***,* 1357.
2. P. Kannaboina, K. Anilkumar and P. Das, *Org. Lett.,* 2016*,* **18***,* 900.
3. H. Z. Li, H. G. Li, H. L. Yang, L. Yang and W. S. Wai. *Org. Process Res Dev*., 2015, **19**, 849.
4. D. J. Salde, N. F. Pelz, W. Bodnar, J. W. Lampe and P. S. Watson, *J. Org. Chem.,* 2009, 7**4**, 6331.

^{1}H NMR and ^{13}C NMR spectra of products

4-bromo-1-methyl-1*H*-pyrrolo[2,3-b]pyridine:

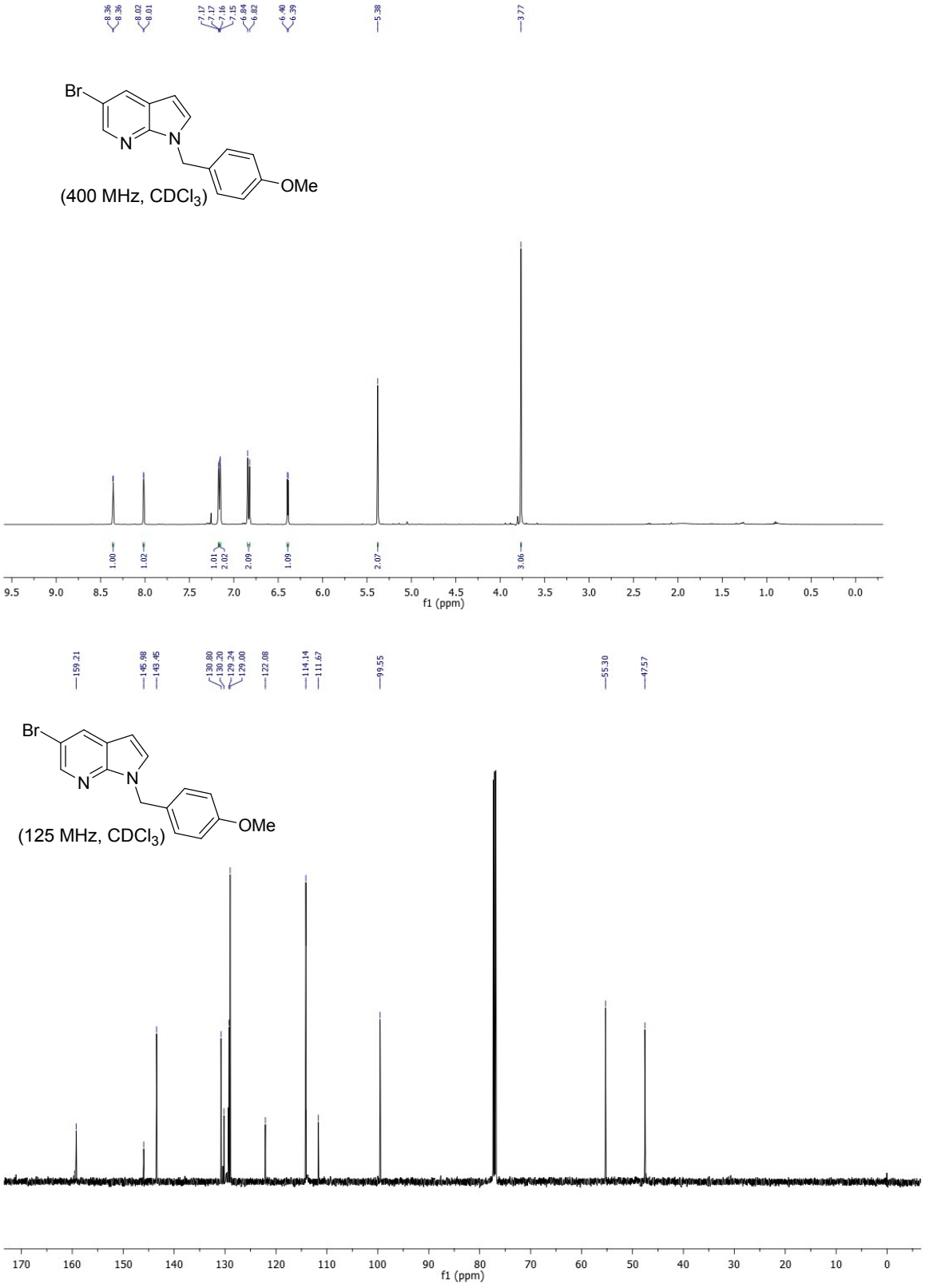


(400 MHz, $CDCl_3$)

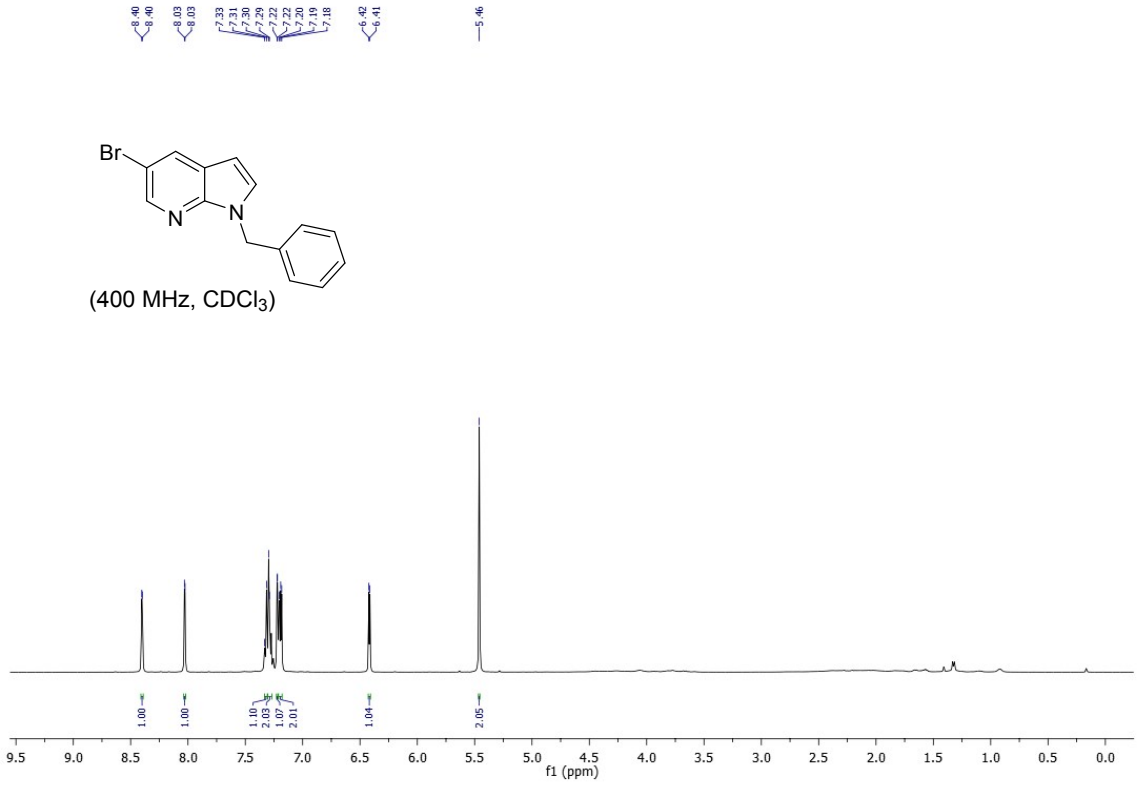


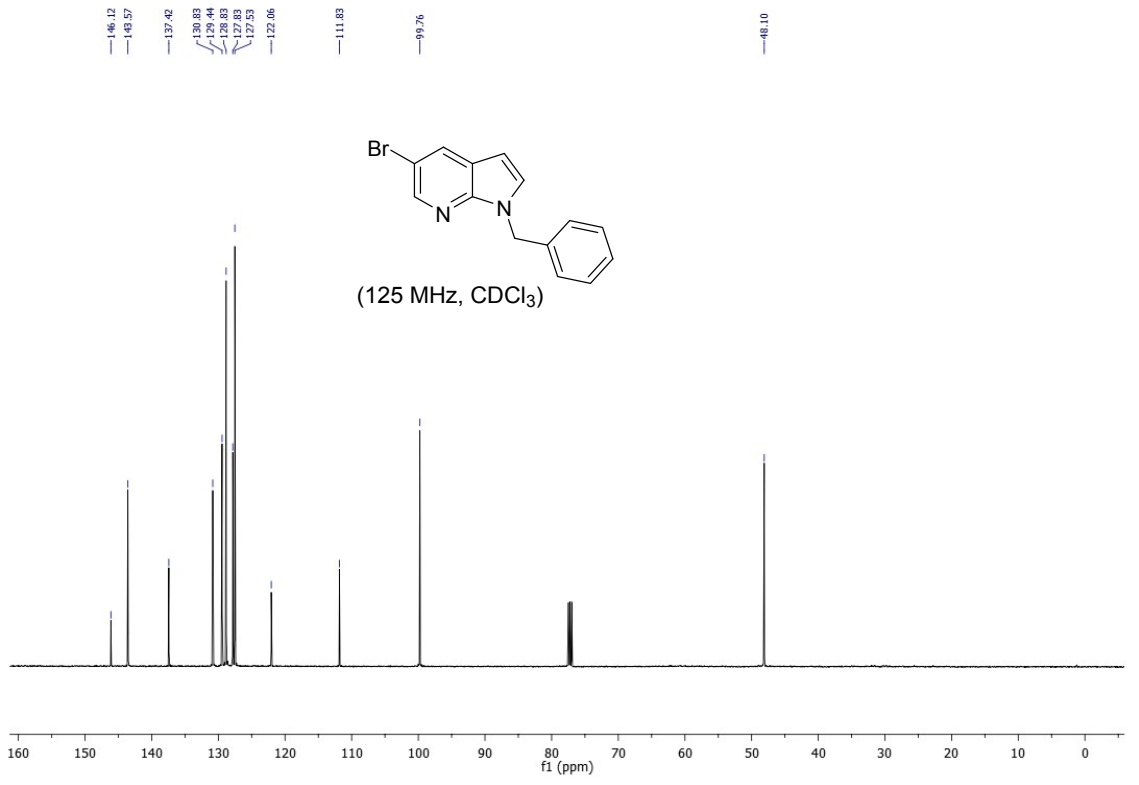
(125 MHz, $CDCl_3$)

5-Bromo-1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridine:

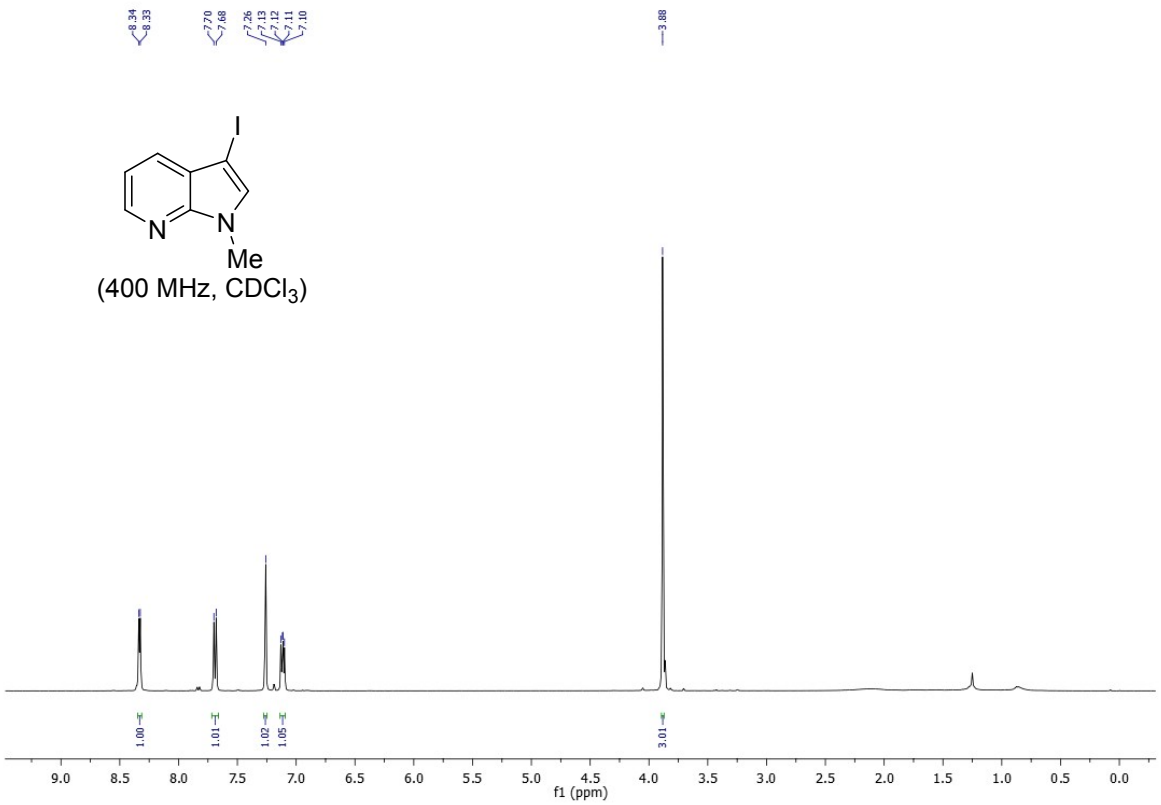


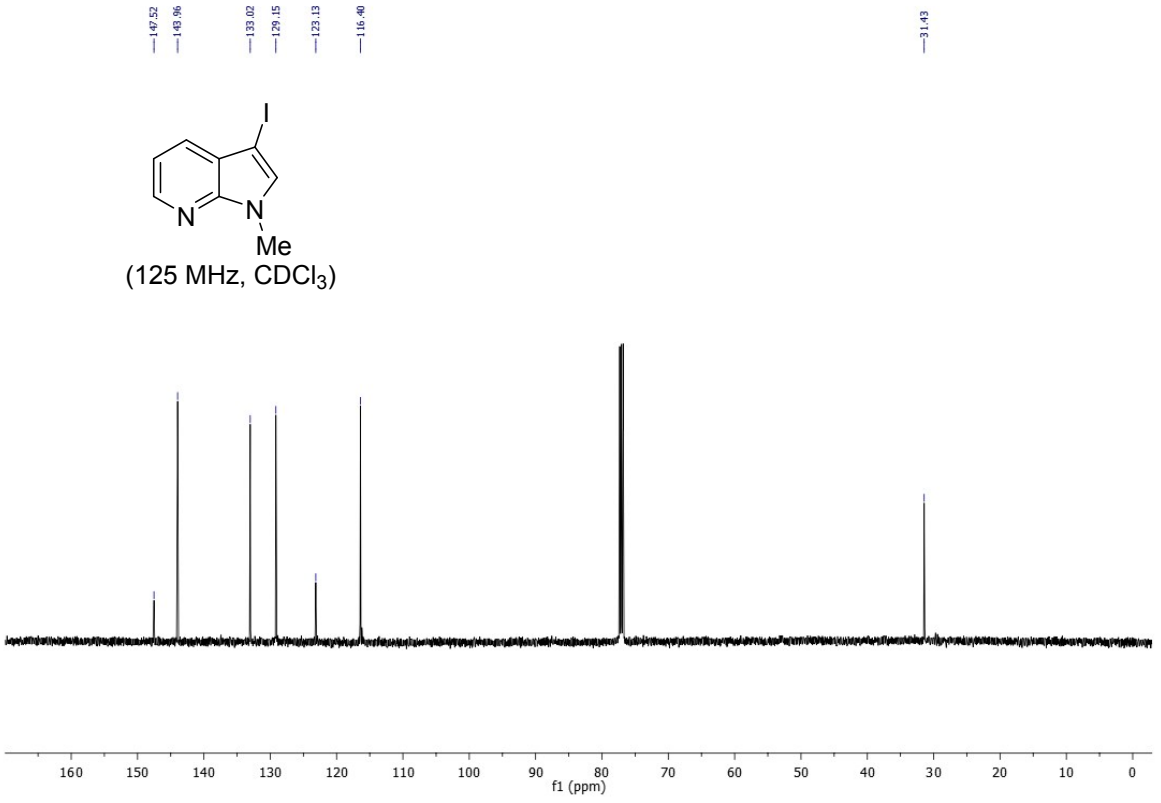
1-benzyl-5-bromo-1*H*-pyrrolo[2,3-b]pyridine:



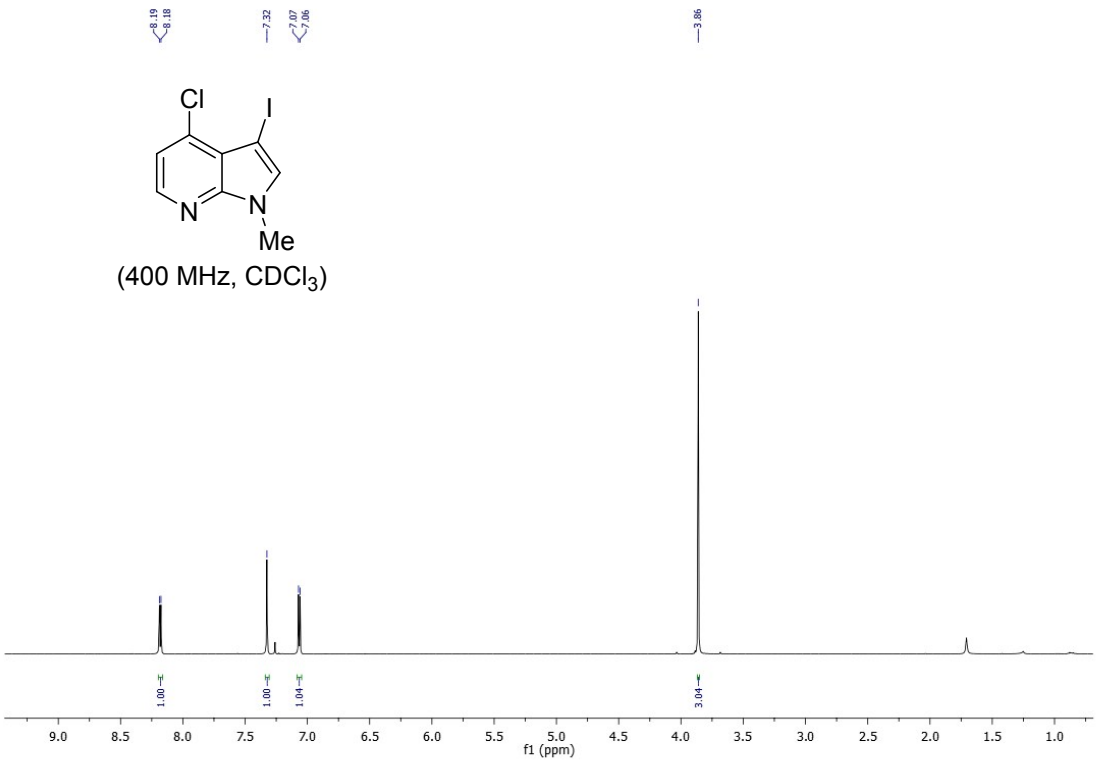


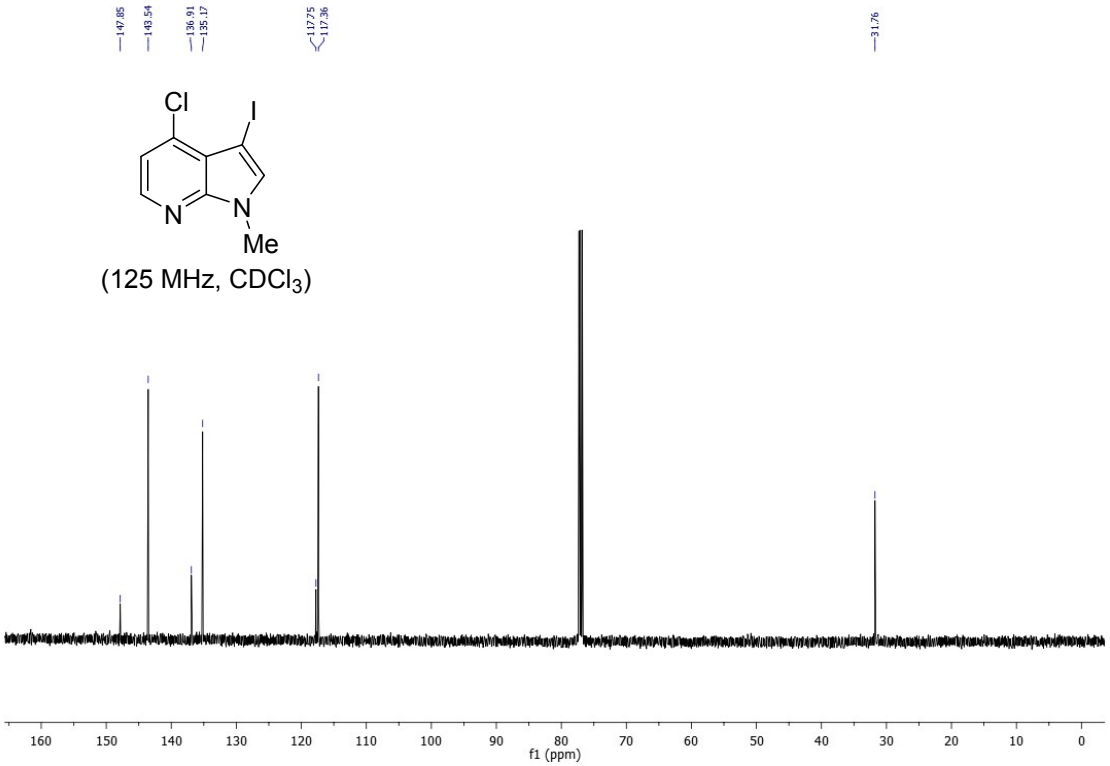
3-iodo-1-methyl-1*H*-pyrrolo[2,3-b]pyridine:



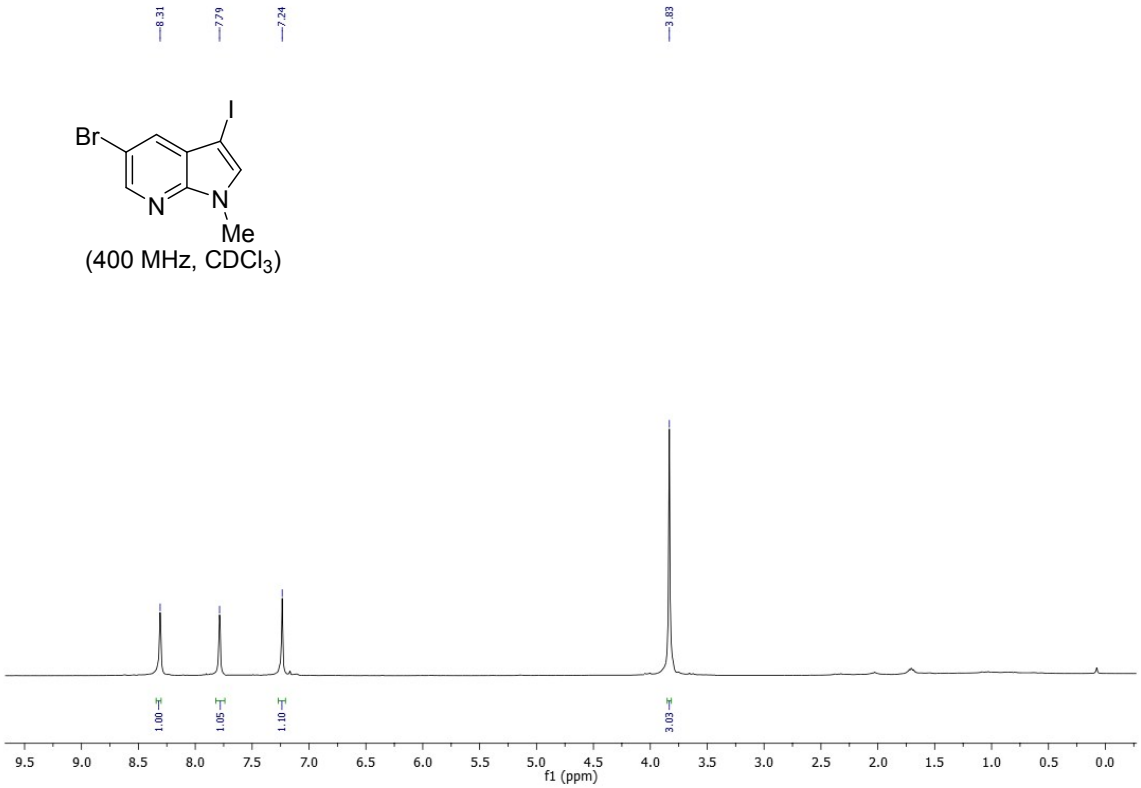


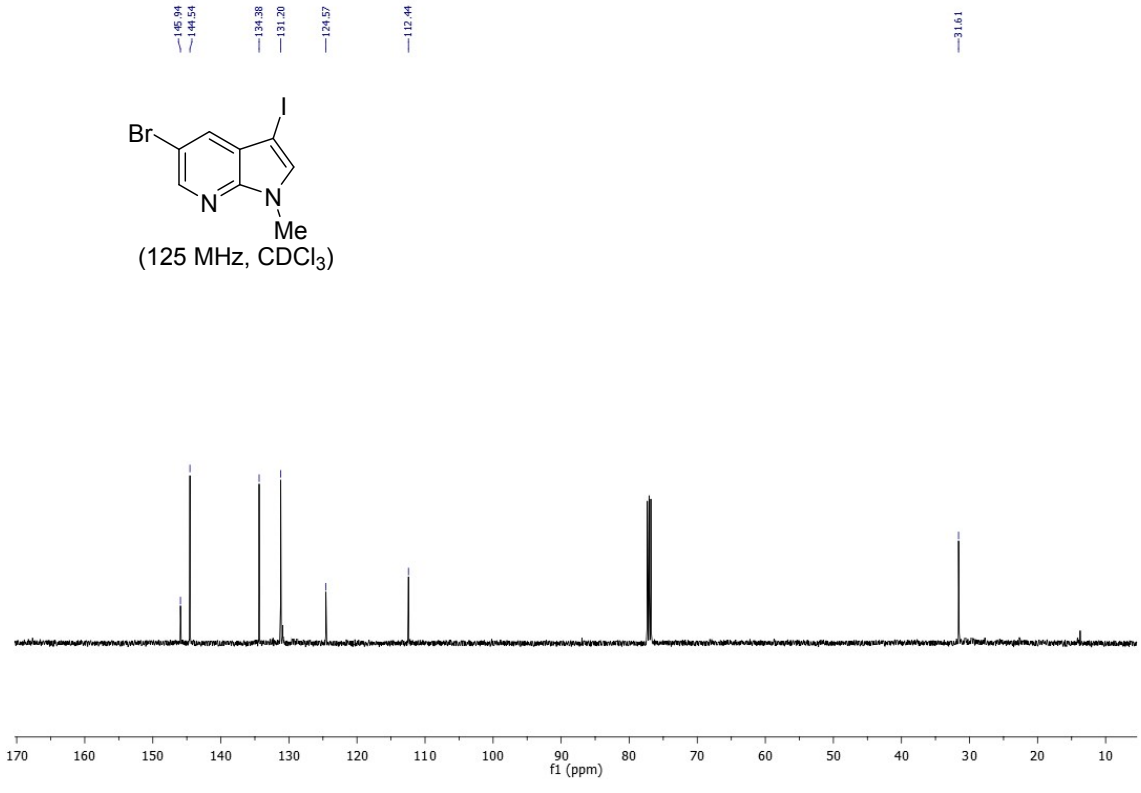
4-chloro-3-iodo-1-methyl-1*H*-pyrrolo[2,3-b]pyridine:



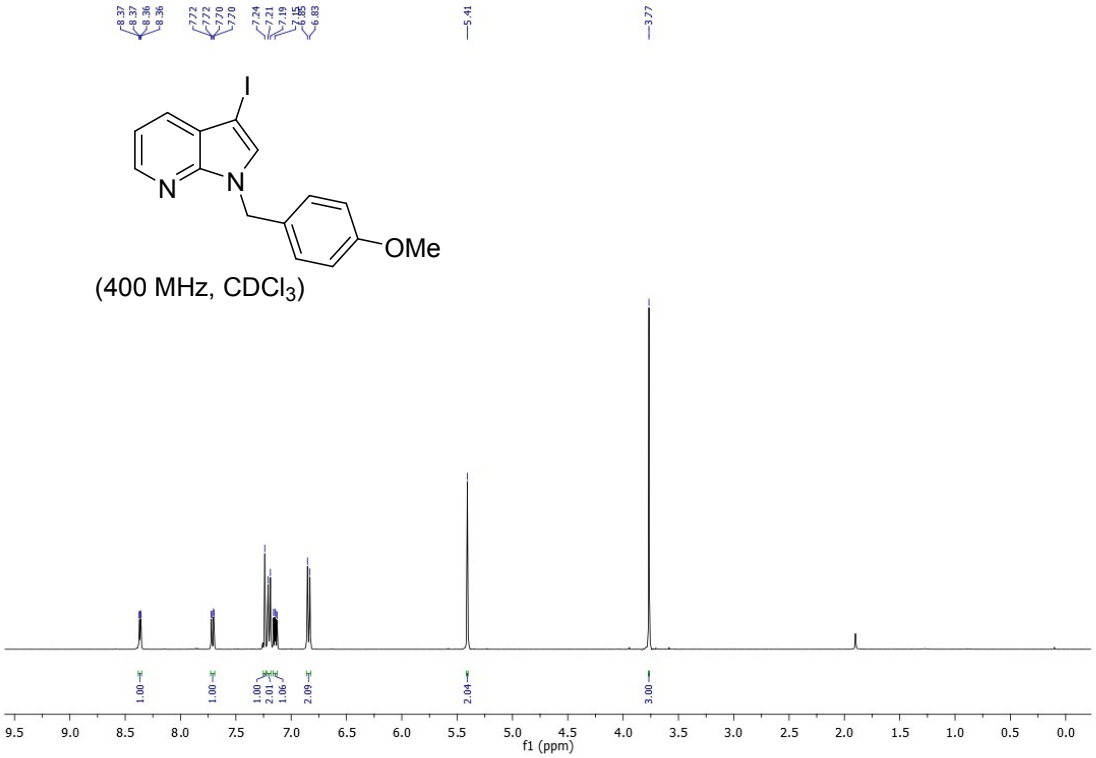


5-bromo-3-iodo-1-methyl-1*H*-pyrrolo[2,3-b]pyridine:

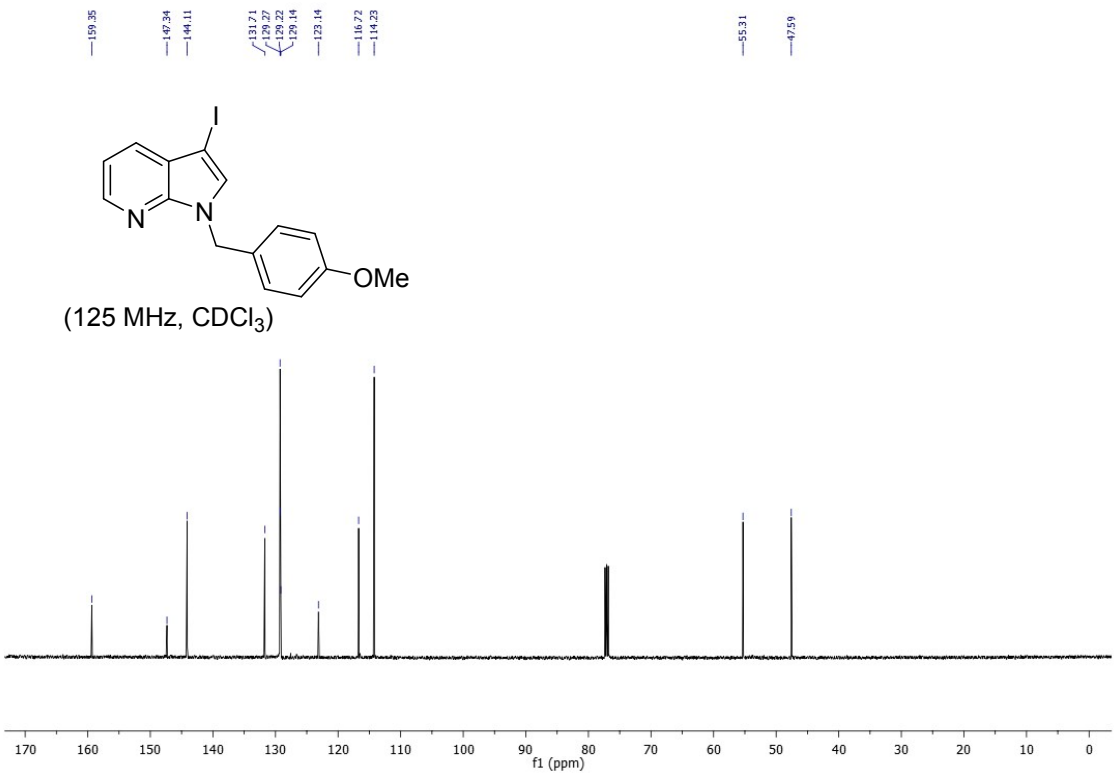




3-iodo-1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridine:

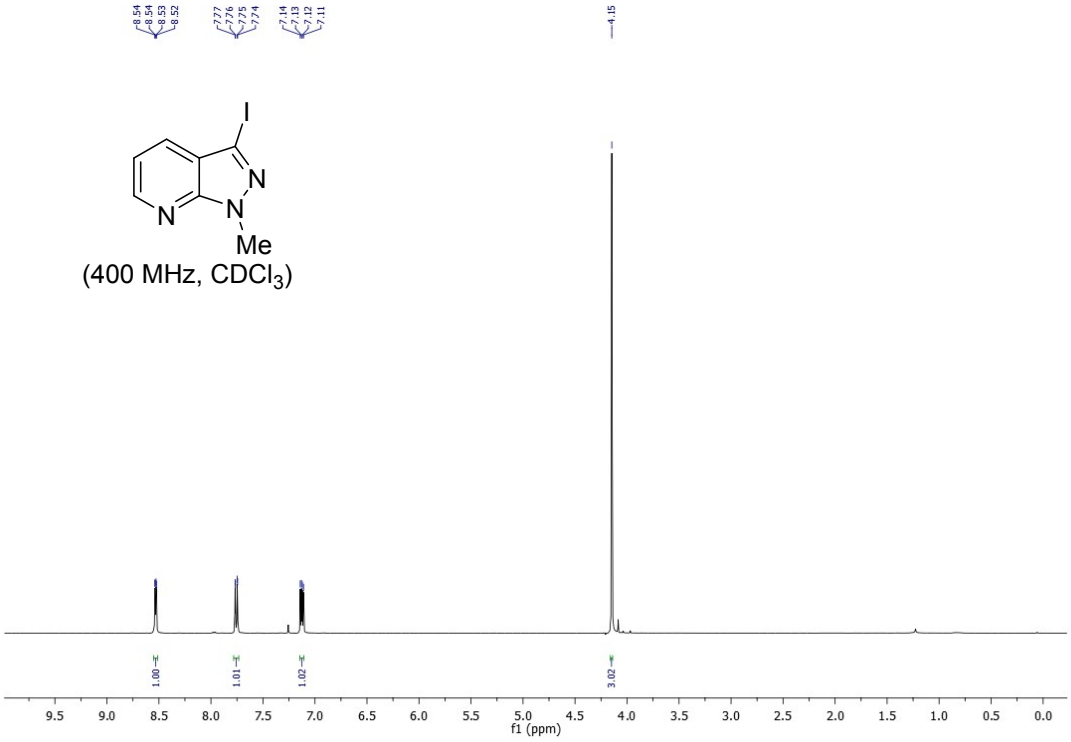


(400 MHz, $CDCl_3$)

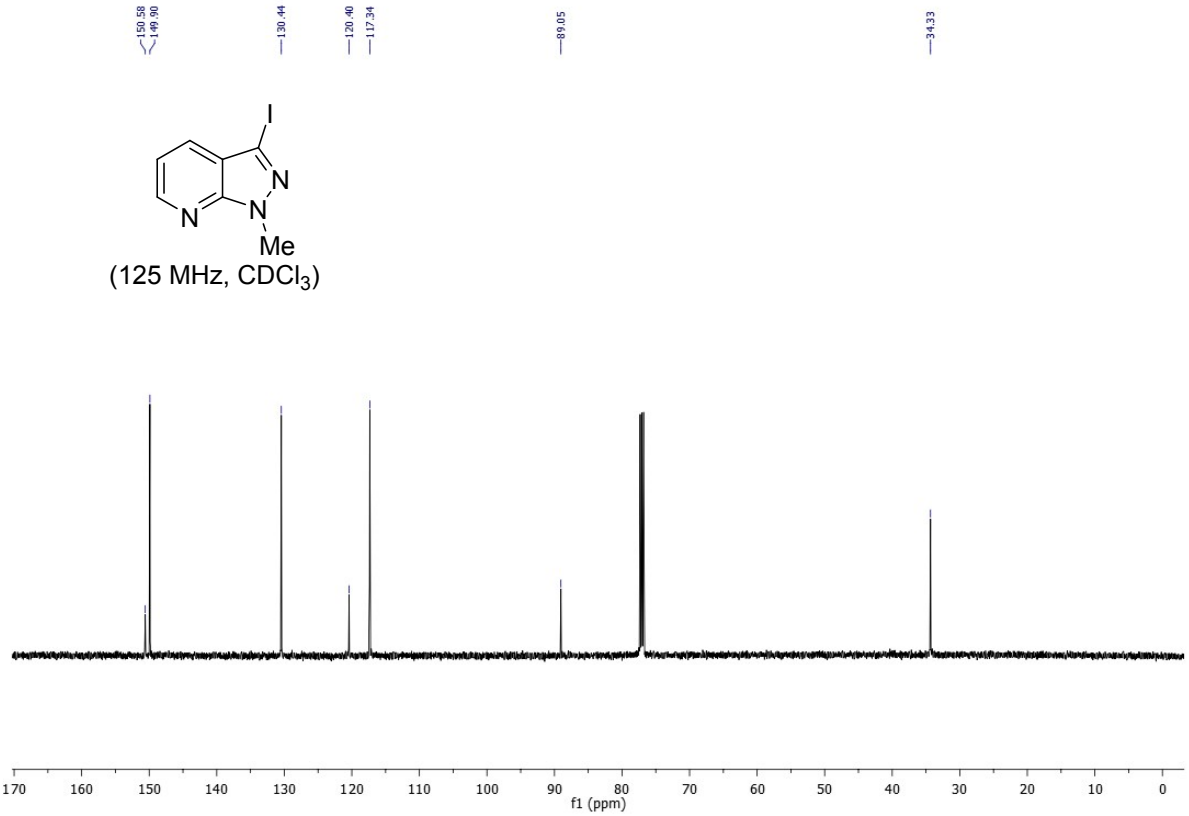


(125 MHz, $CDCl_3$)

3-iodo-1-methyl-1*H*-pyrazolo[3,4-b]pyridine:

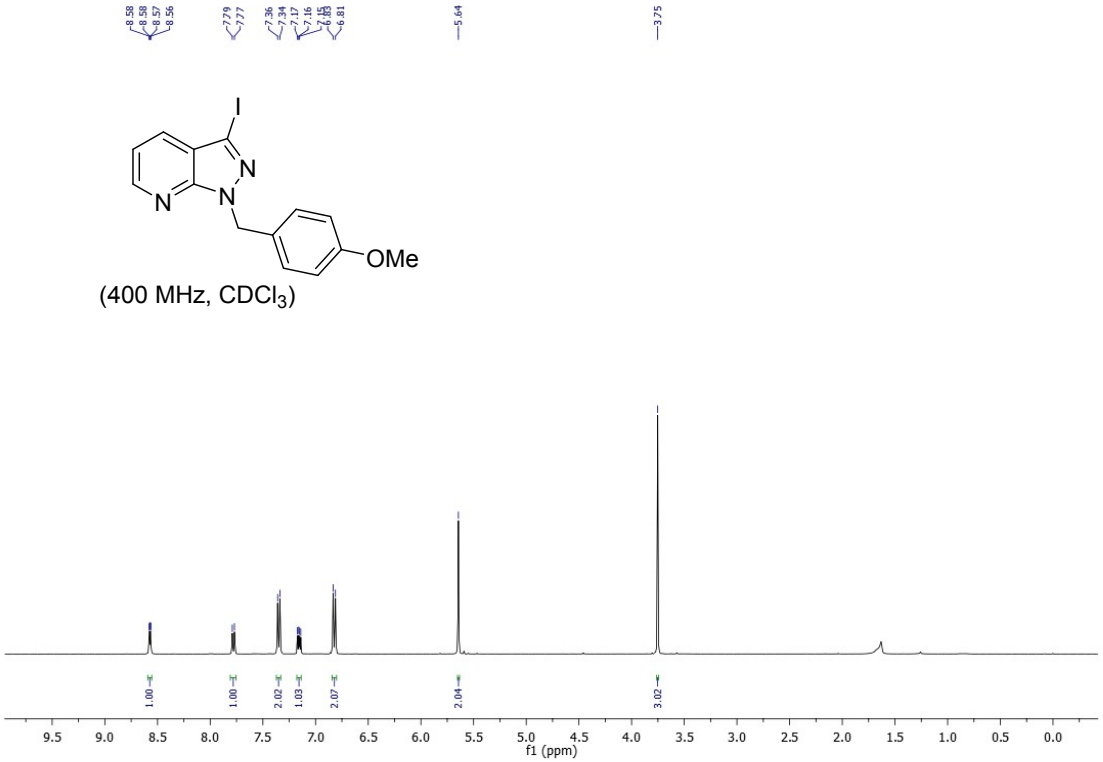


(400 MHz, $CDCl_3$)

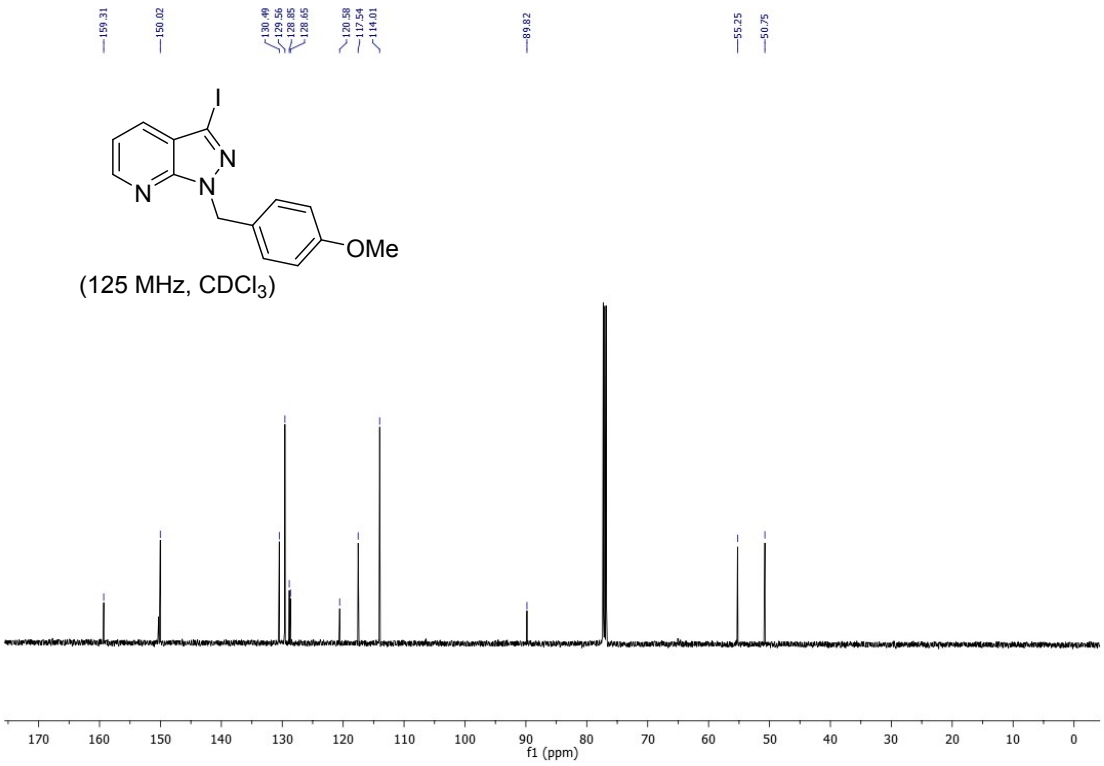


(125 MHz, $CDCl_3$)

3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-b]pyridine:



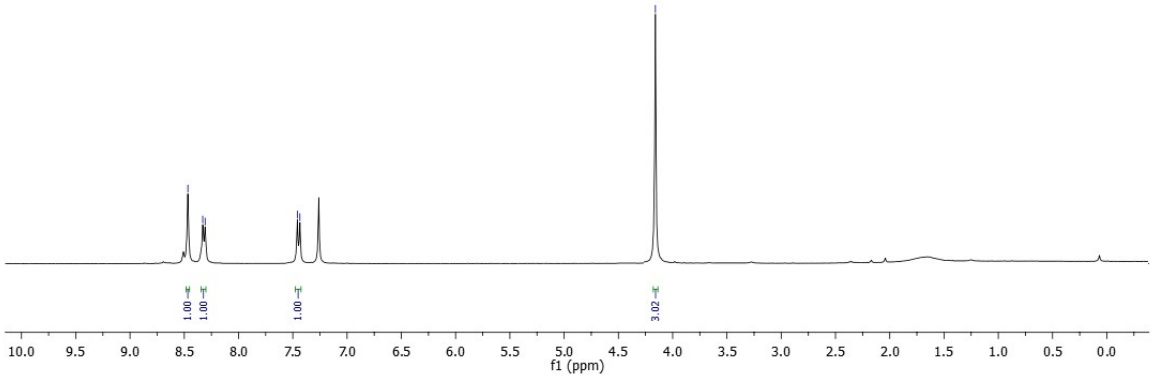
(400 MHz, $CDCl_3$)

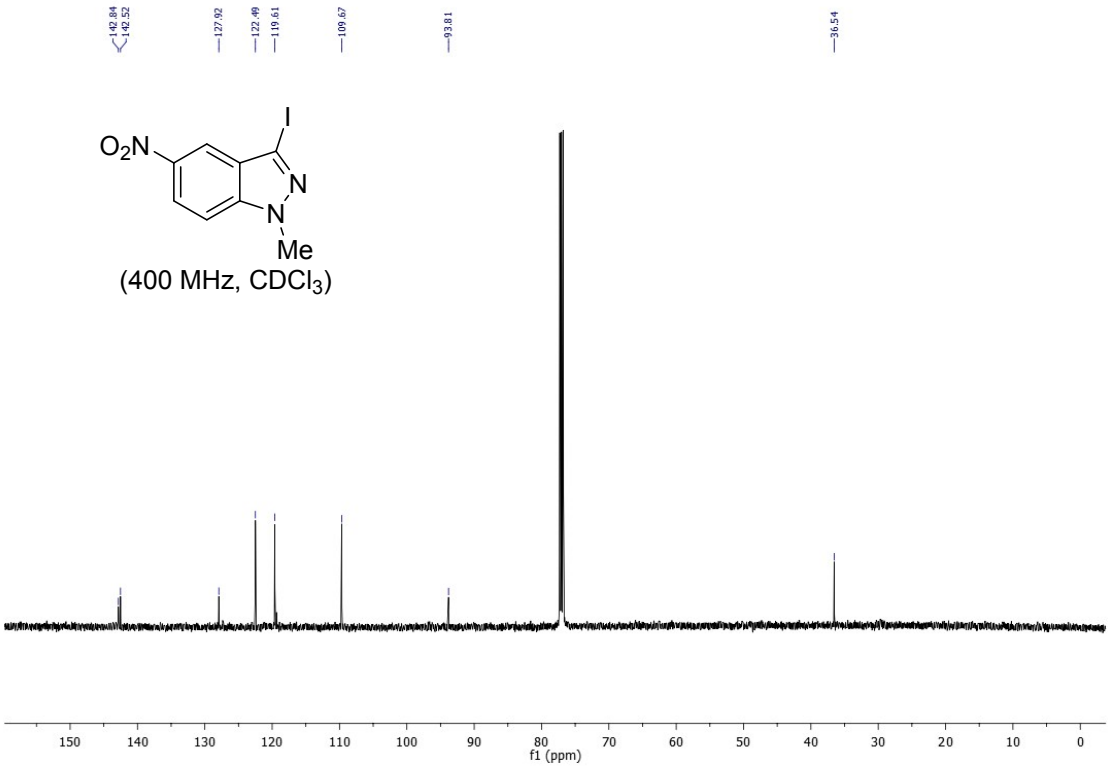


(125 MHz, $CDCl_3$)

3-iodo-1-methyl-5-nitro-1*H*-indazole:

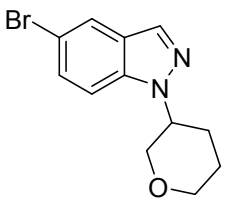
(400 MHz, $CDCl_3$)



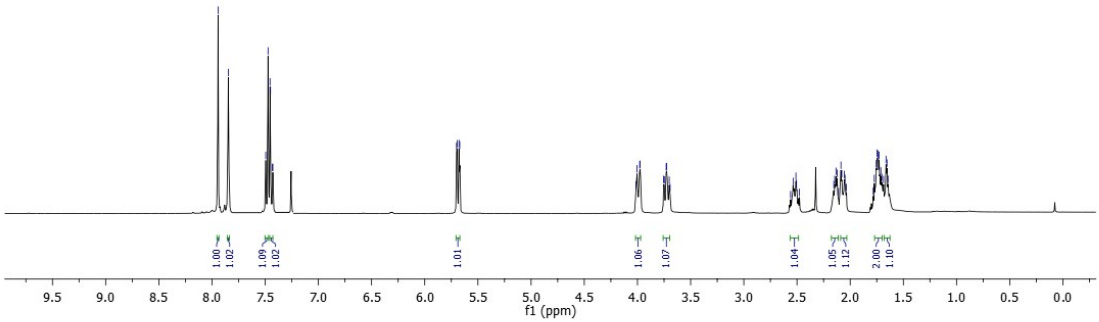


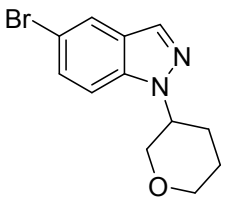
(400 MHz, $CDCl_3$)

5-bromo-1-(tetrahydro-2*H*-pyran-3-yl)-1*H*-indazole:

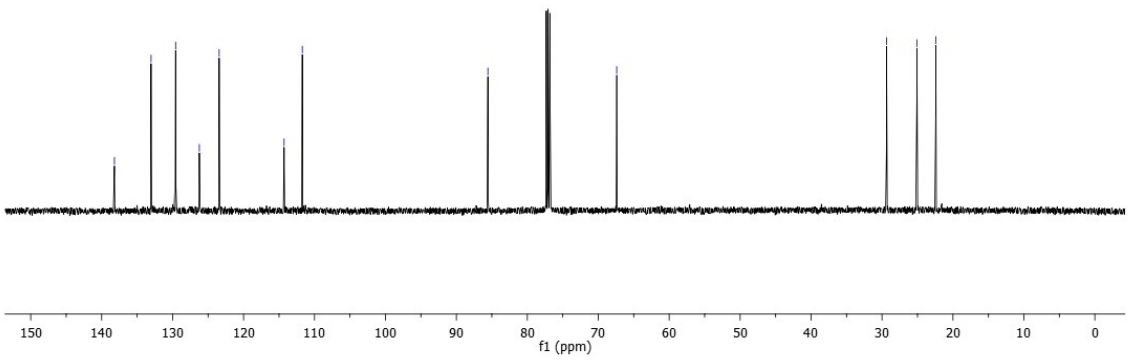


(400 MHz, $CDCl_3$)

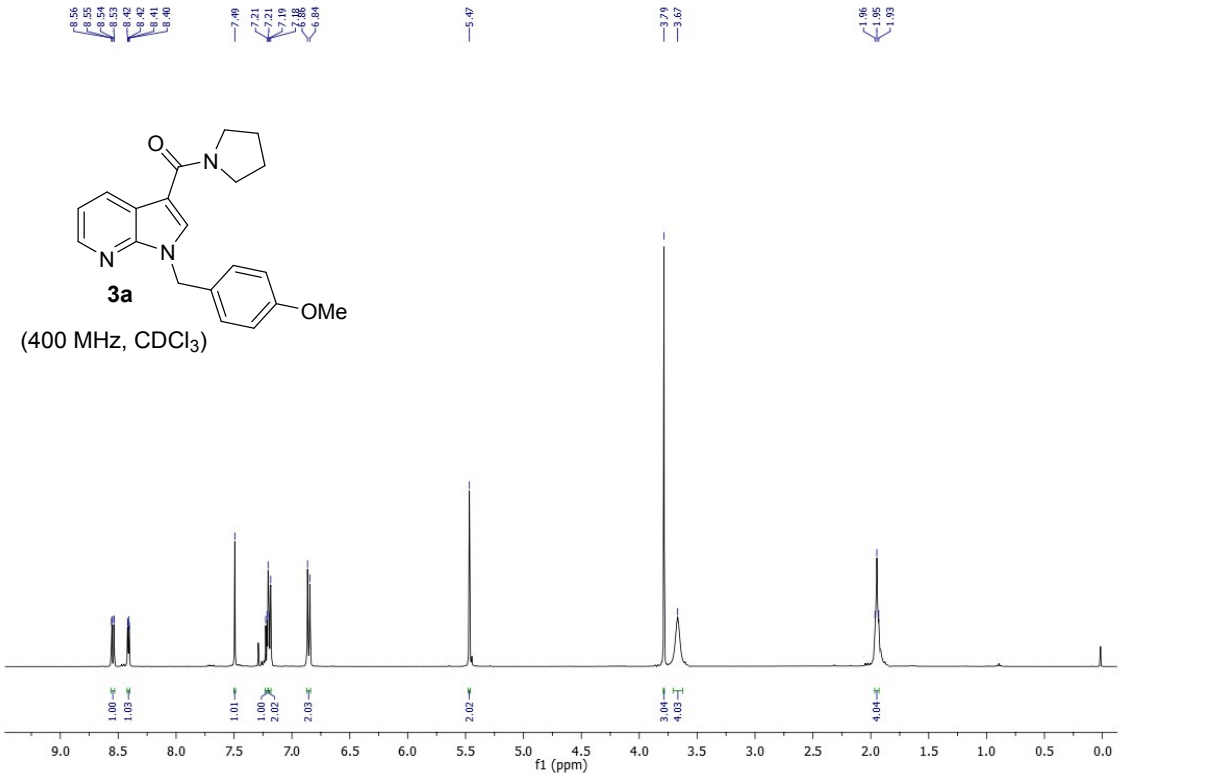


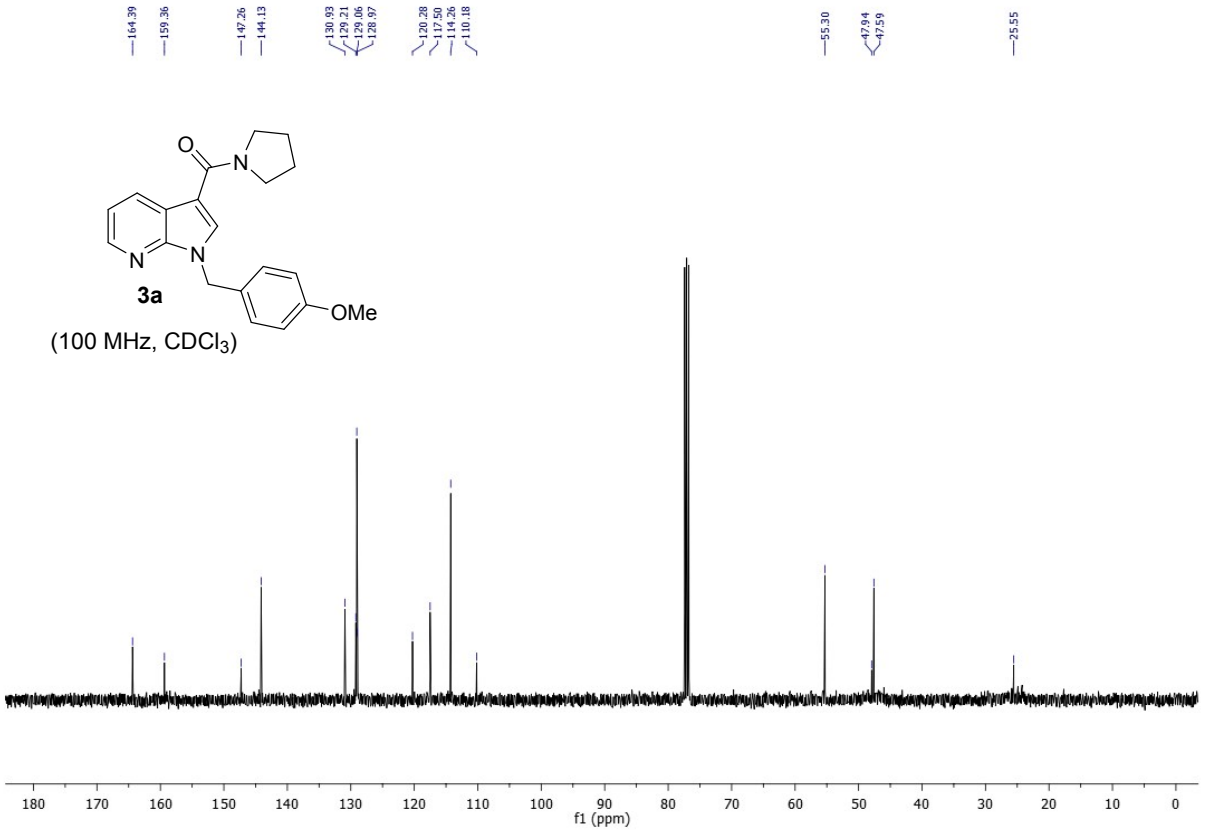


(125 MHz, $CDCl_3$)

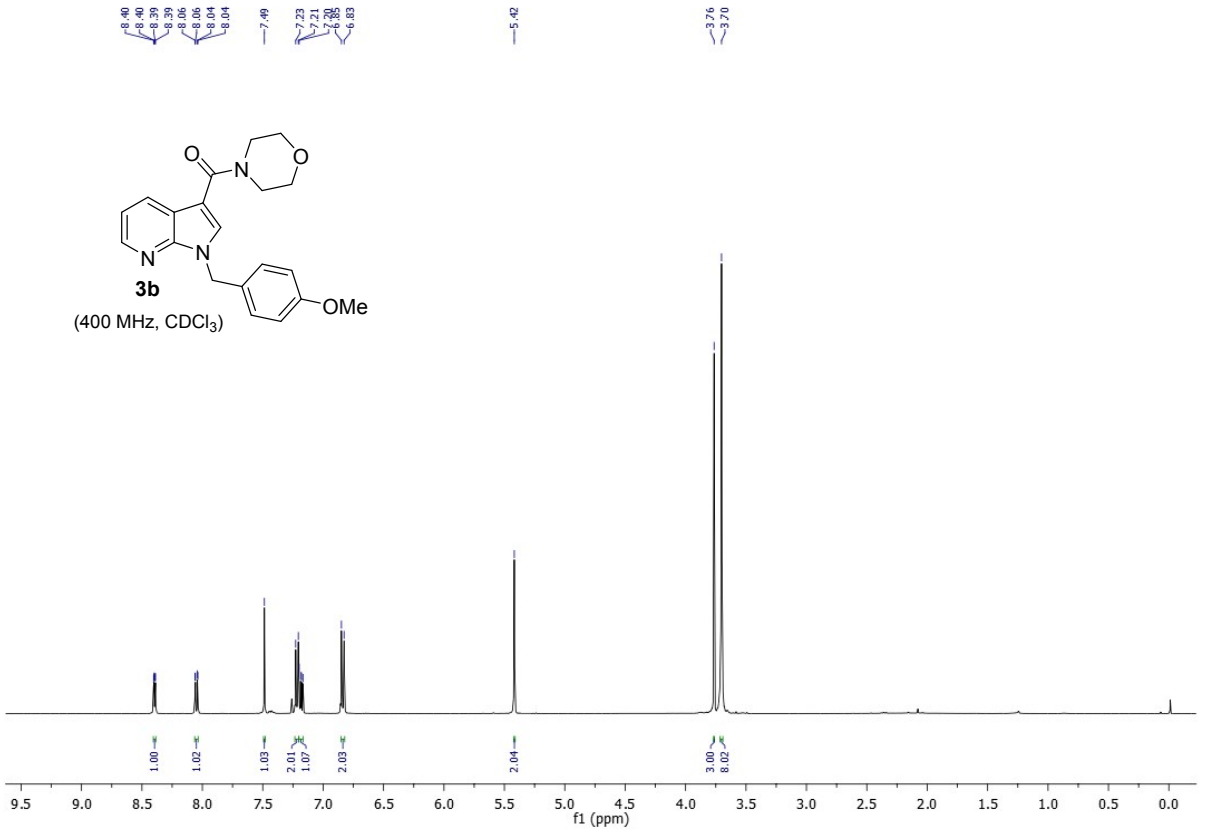


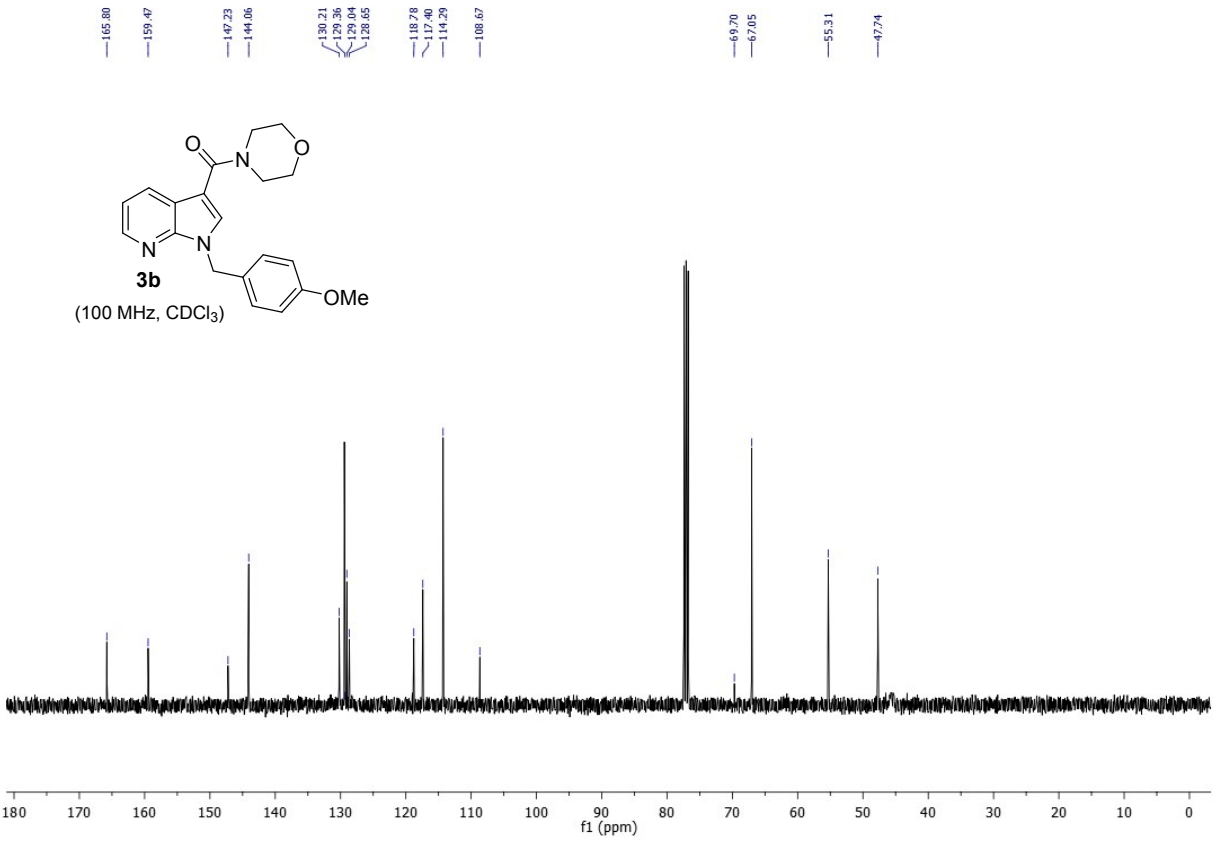
(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(pyrrolidin-1-yl)methanone



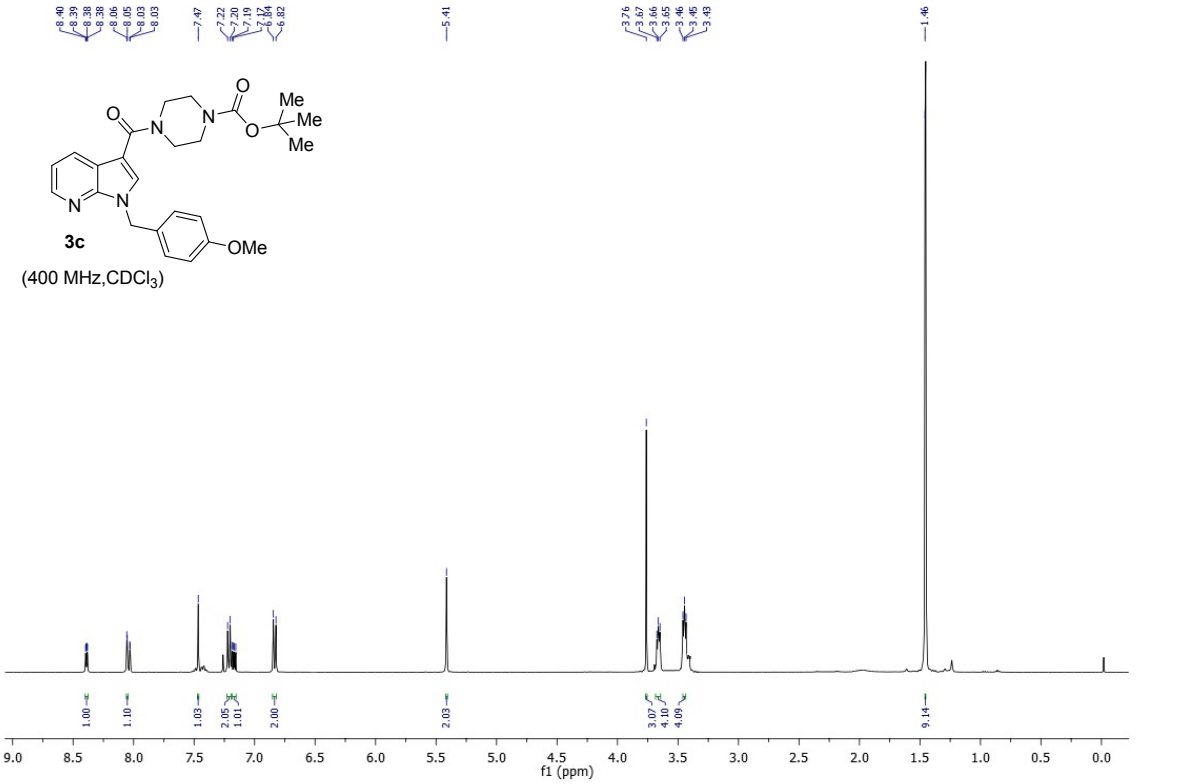


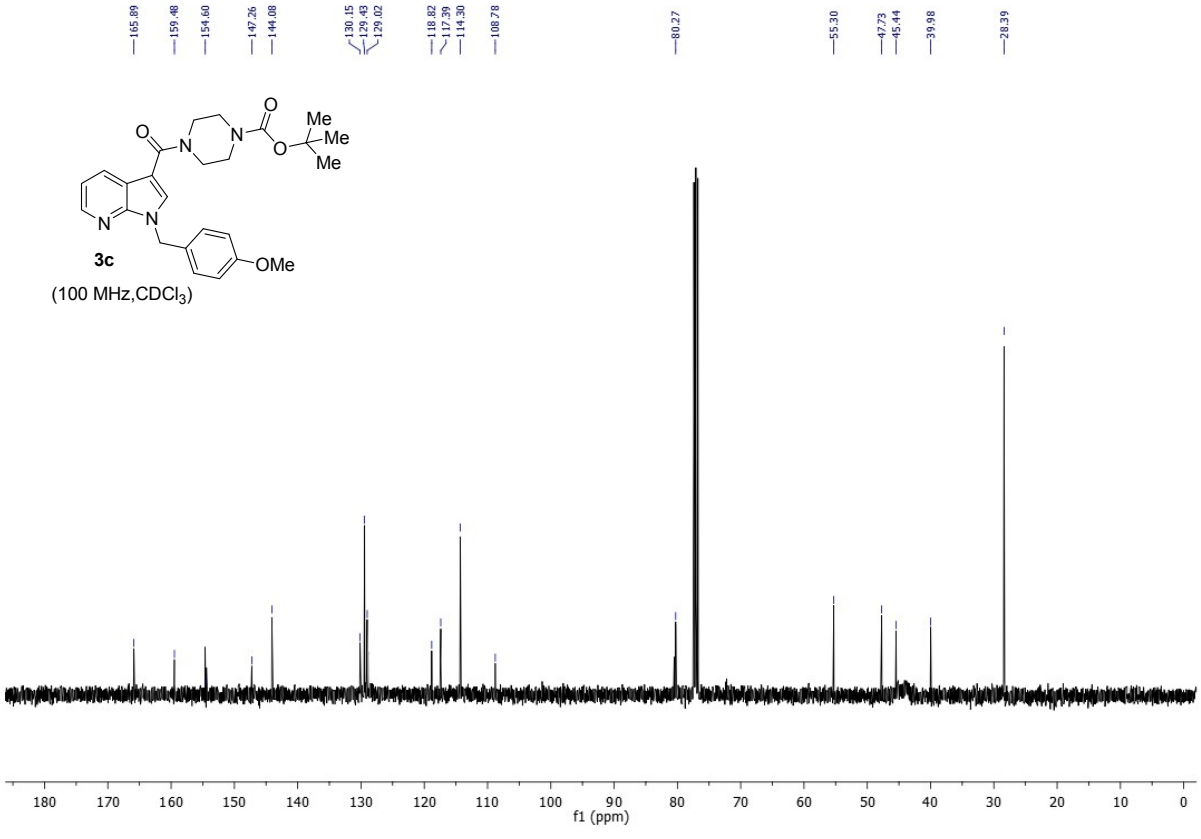
(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(morpholino)methanone



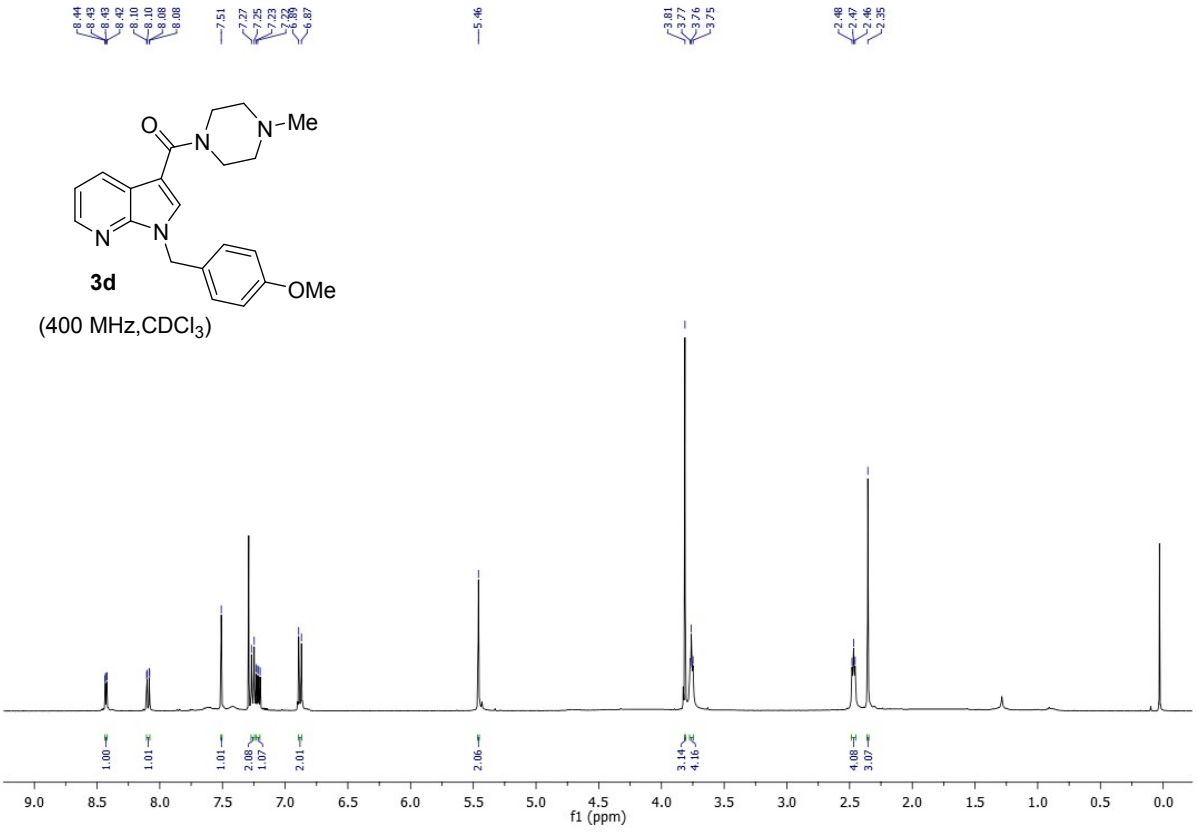


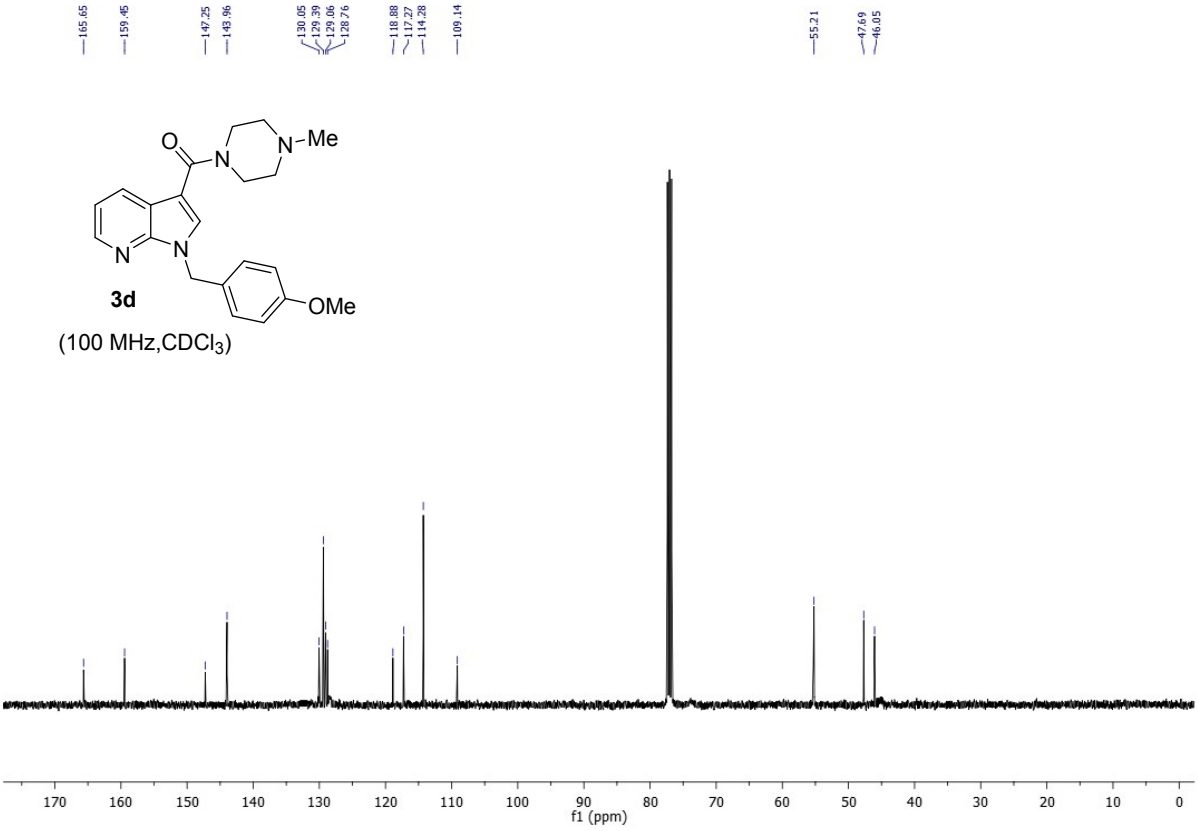
Tert-butyl 4-(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridine-3-carbonyl)piperazine-1-carboxylate



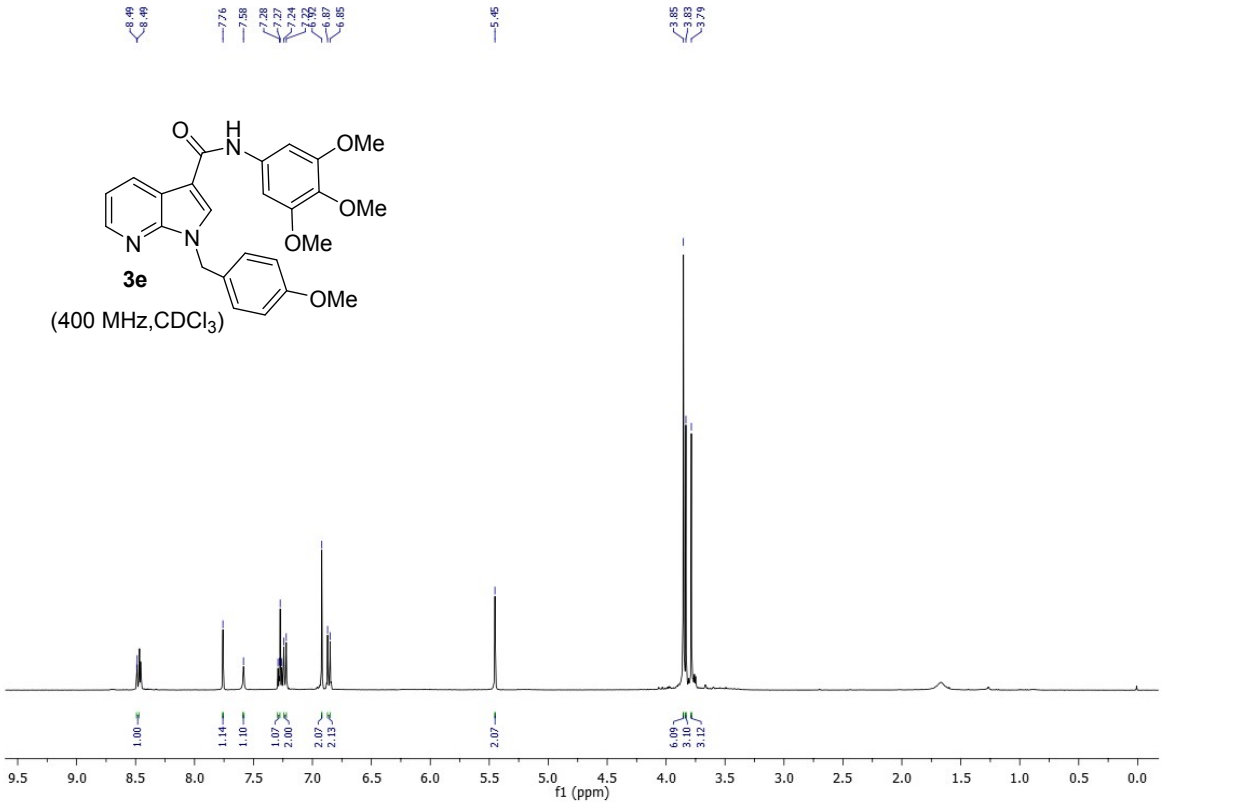


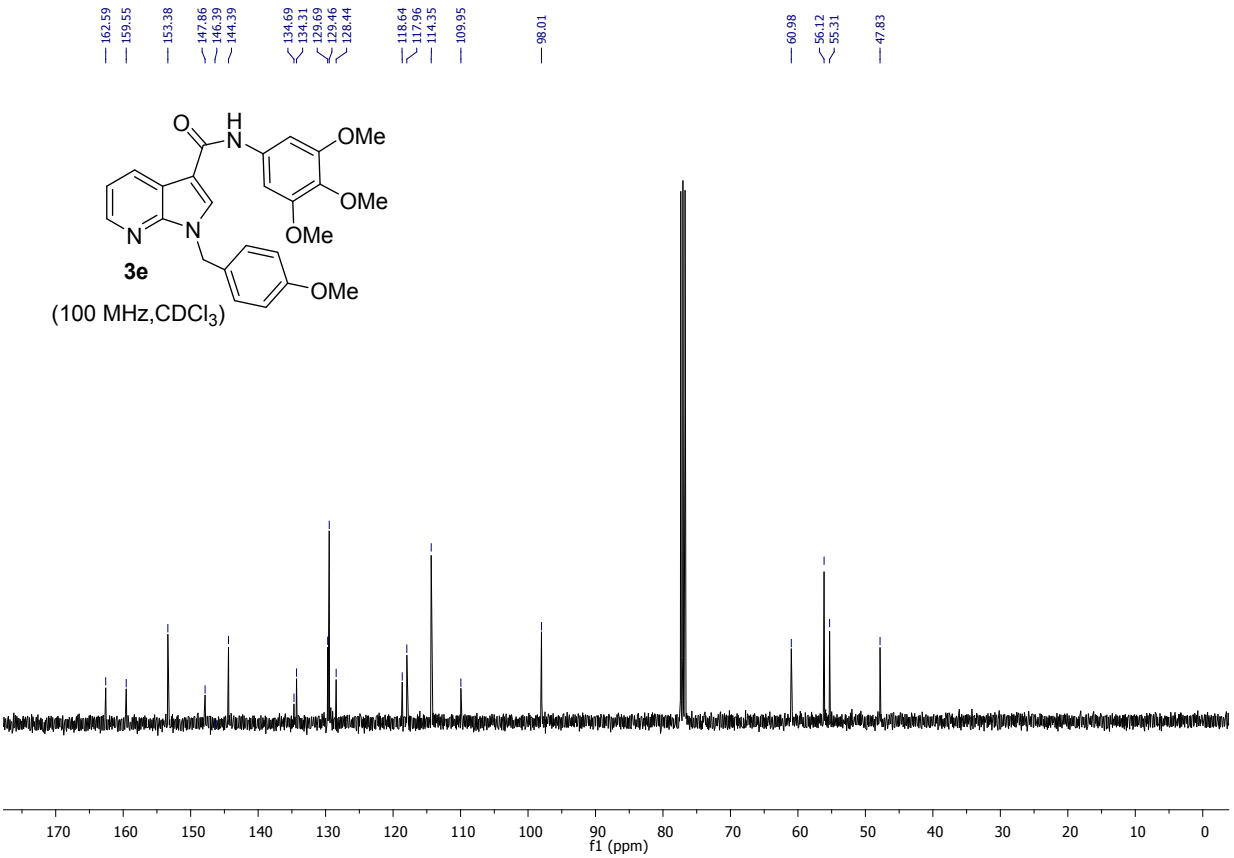
(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(4-methylpiperazin-1-yl)methanone



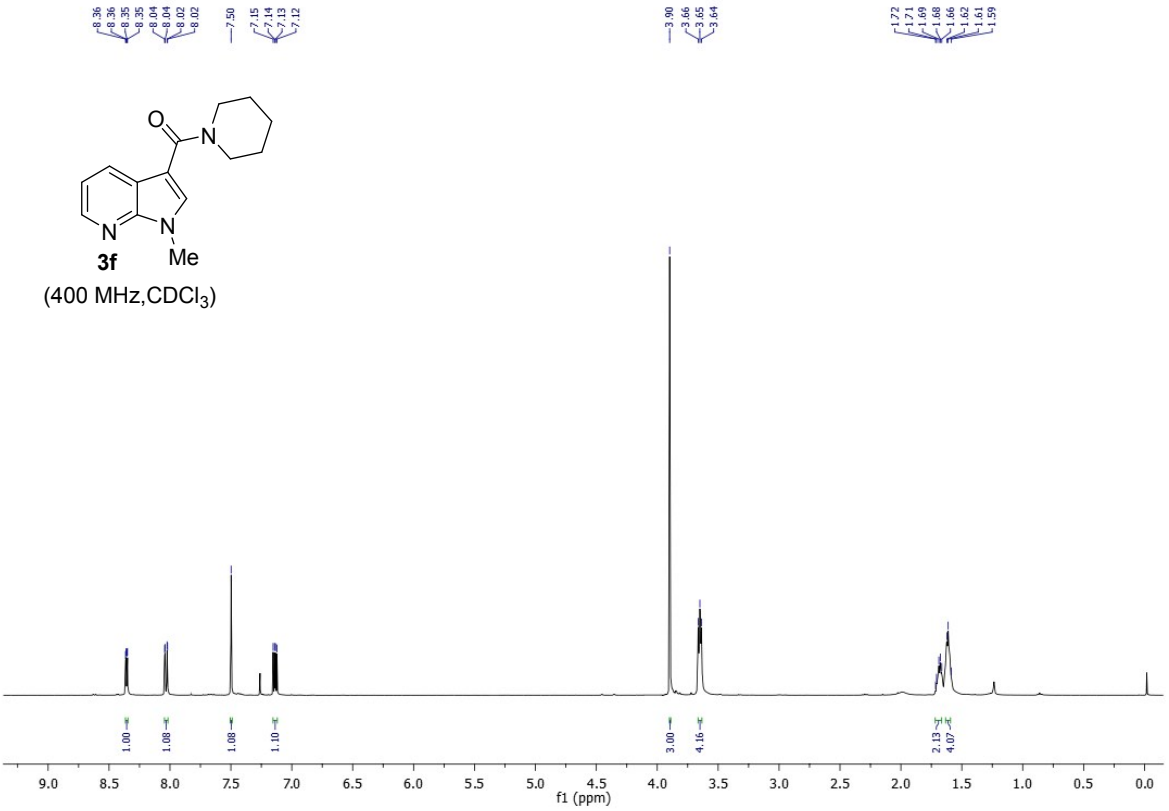


1-(4-methoxybenzyl)-*N*-(3,4,5-trimethoxyphenyl)-1*H*-pyrrolo[2,3-b]pyridine-3-carboxamide



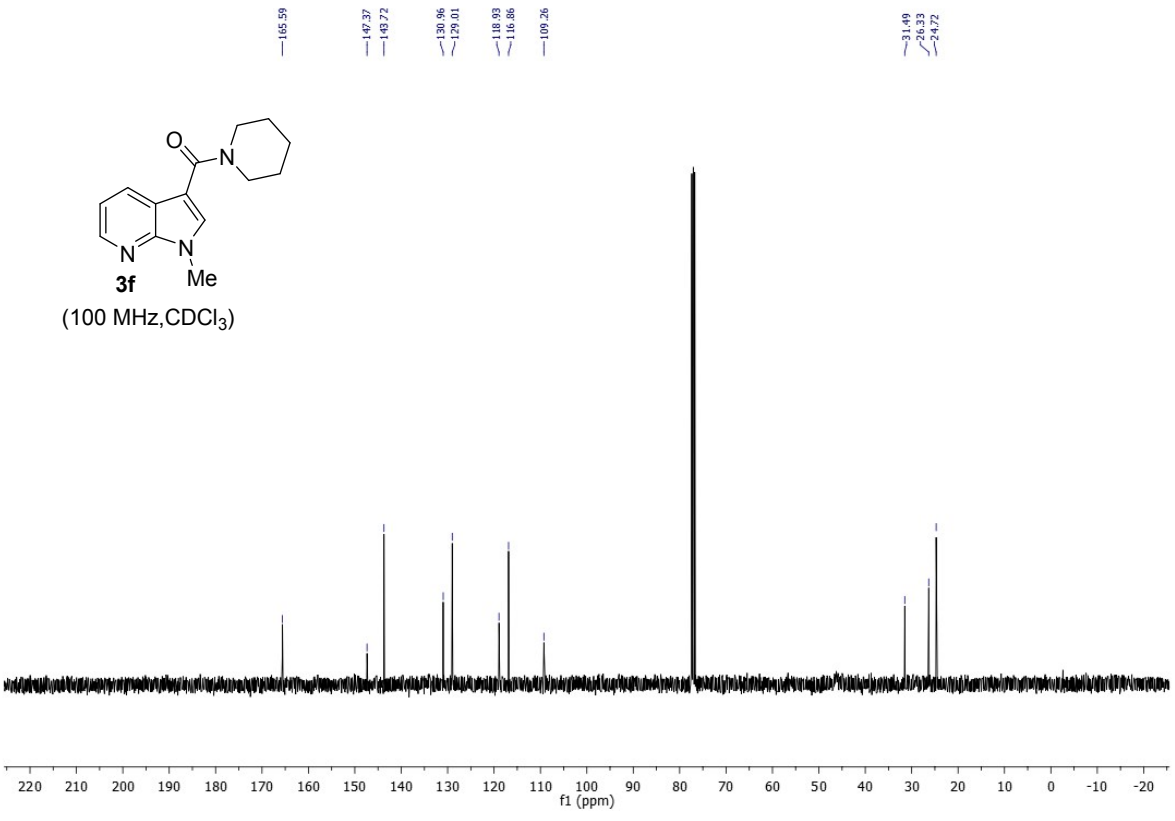


(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(piperidin-1-yl)methanone



3f

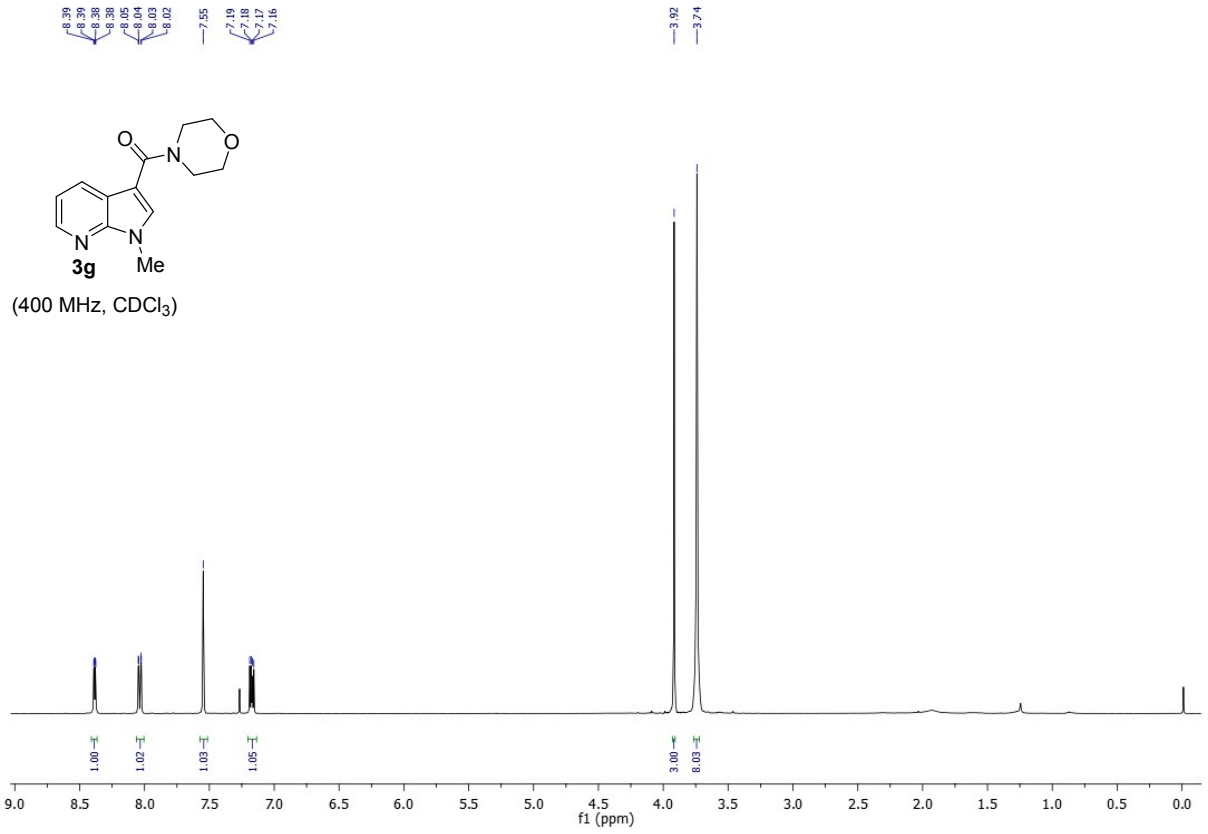
(400 MHz,$CDCl_3$)



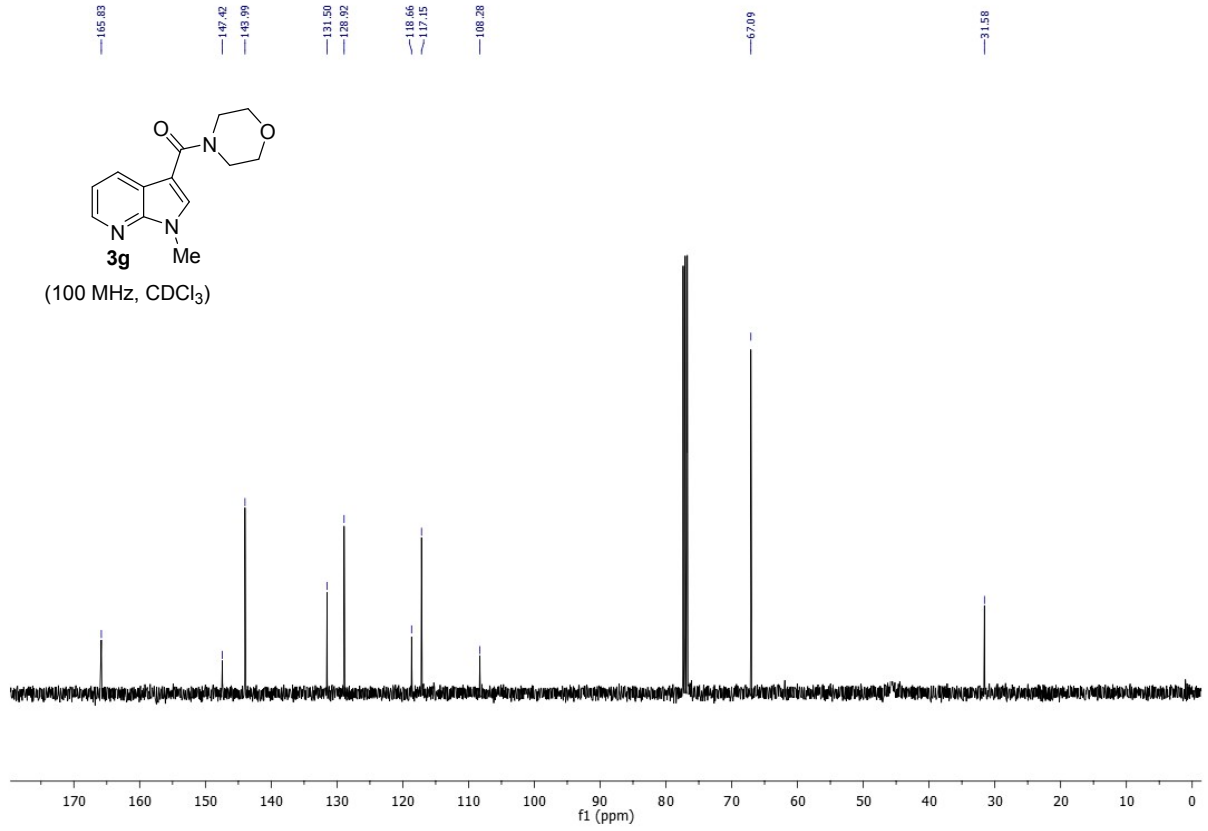
3f

(100 MHz,$CDCl_3$)

(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(morpholino)methanone

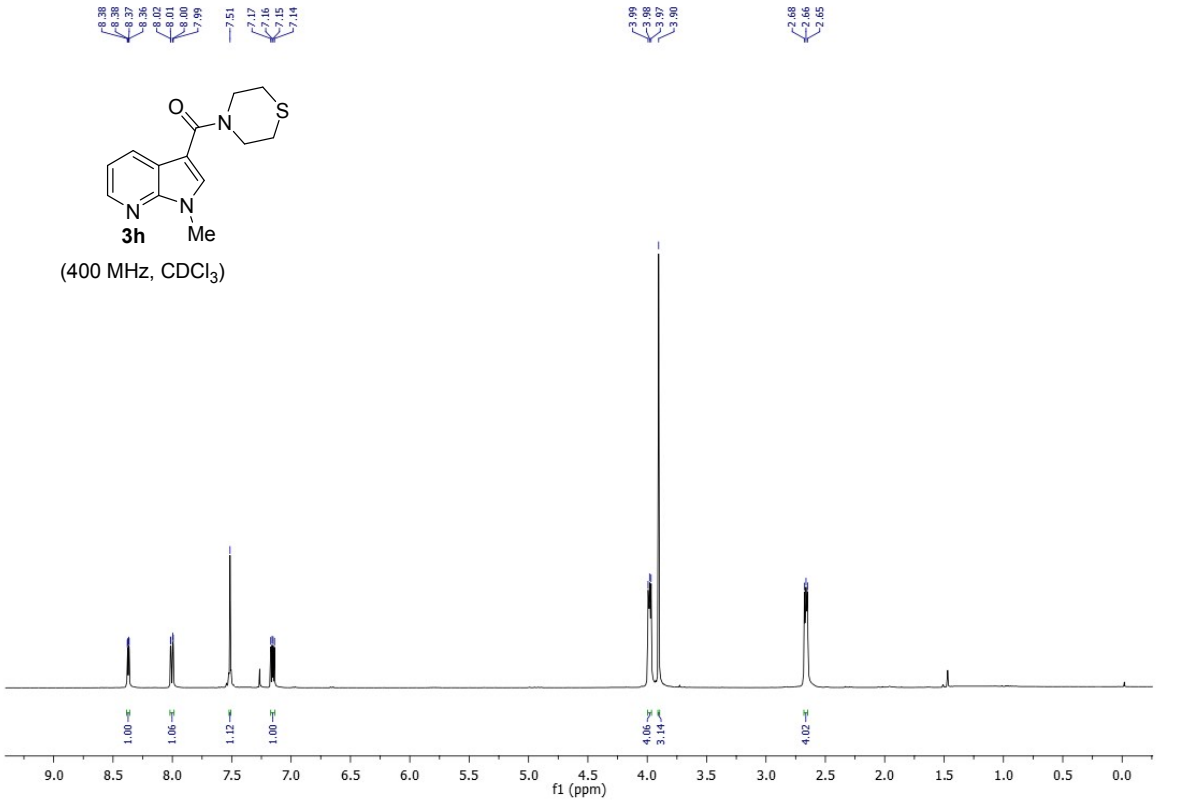


(400 MHz, $CDCl_3$)

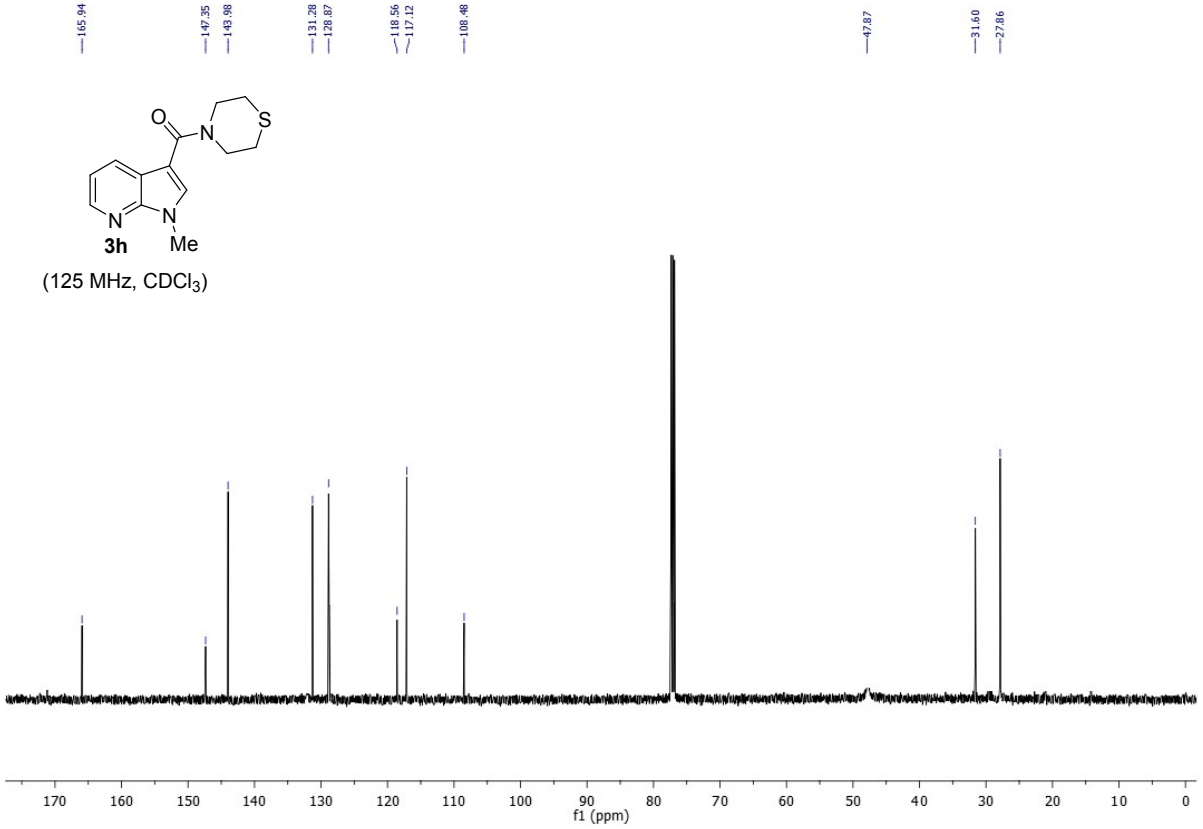


(100 MHz, $CDCl_3$)

(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(thiomorpholino)methanone

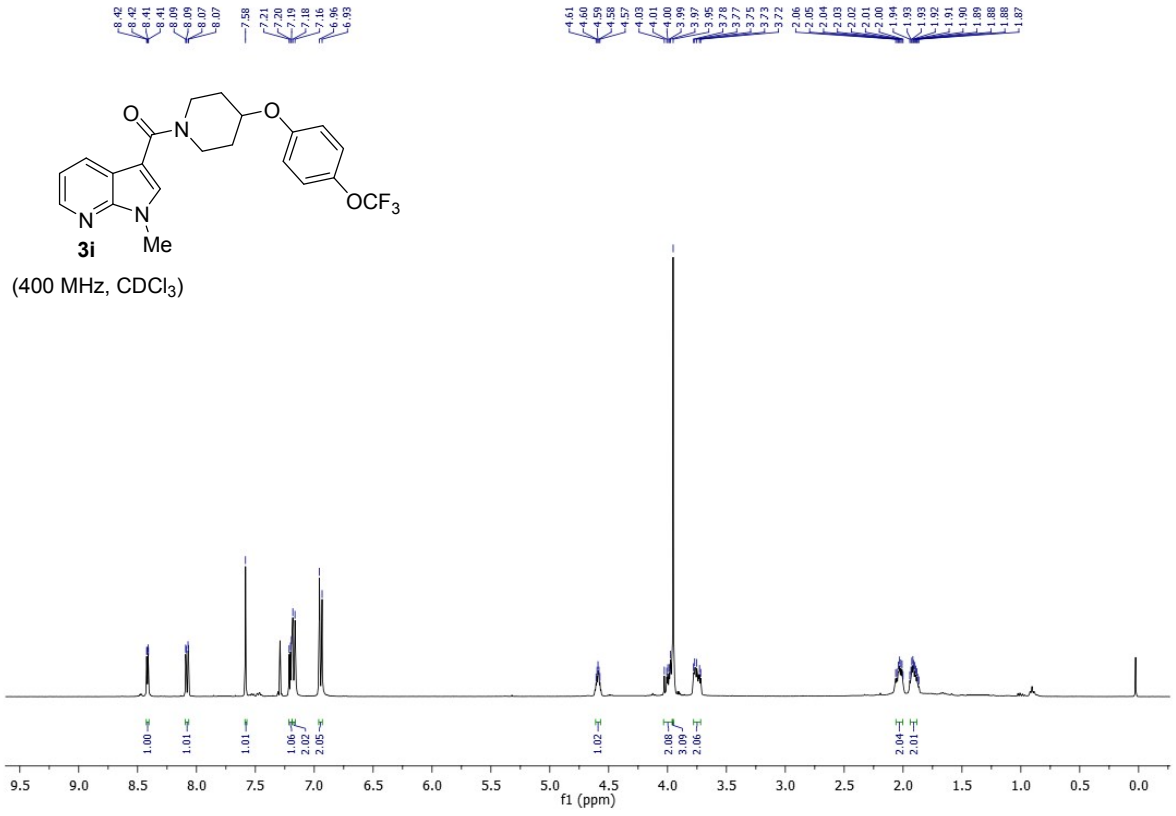


(400 MHz, $CDCl_3$)

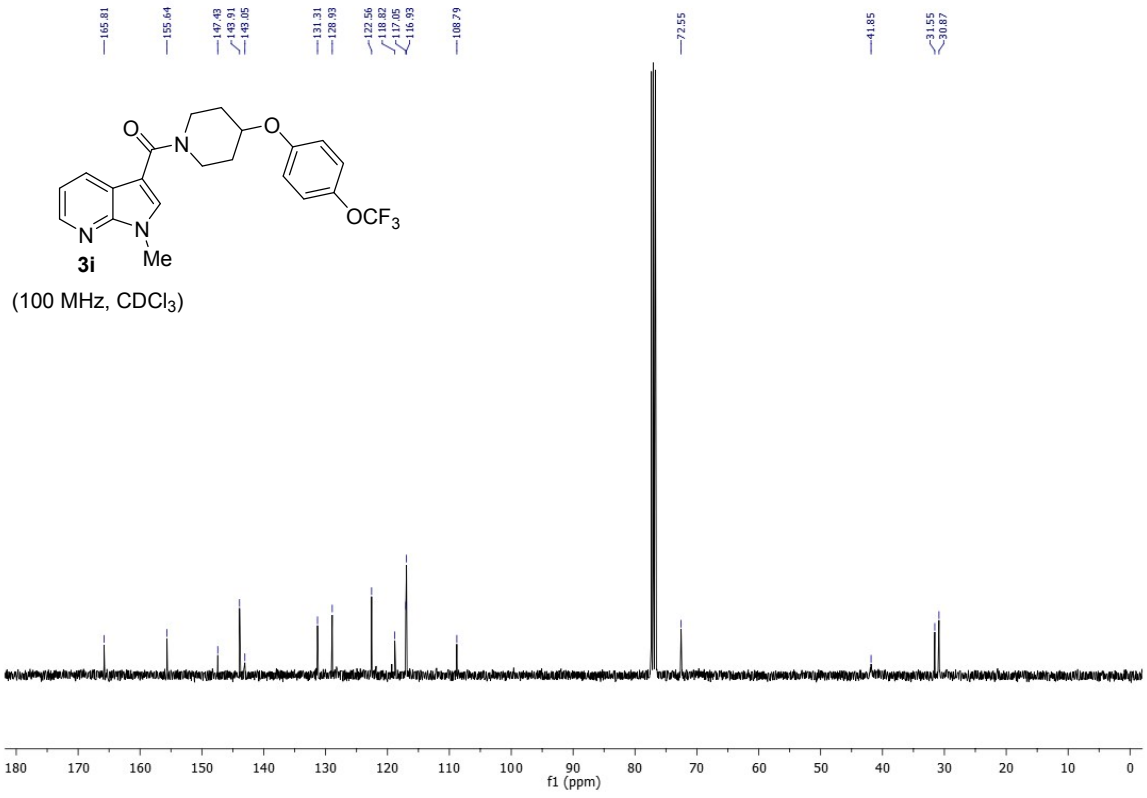


(125 MHz, $CDCl_3$)

(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone

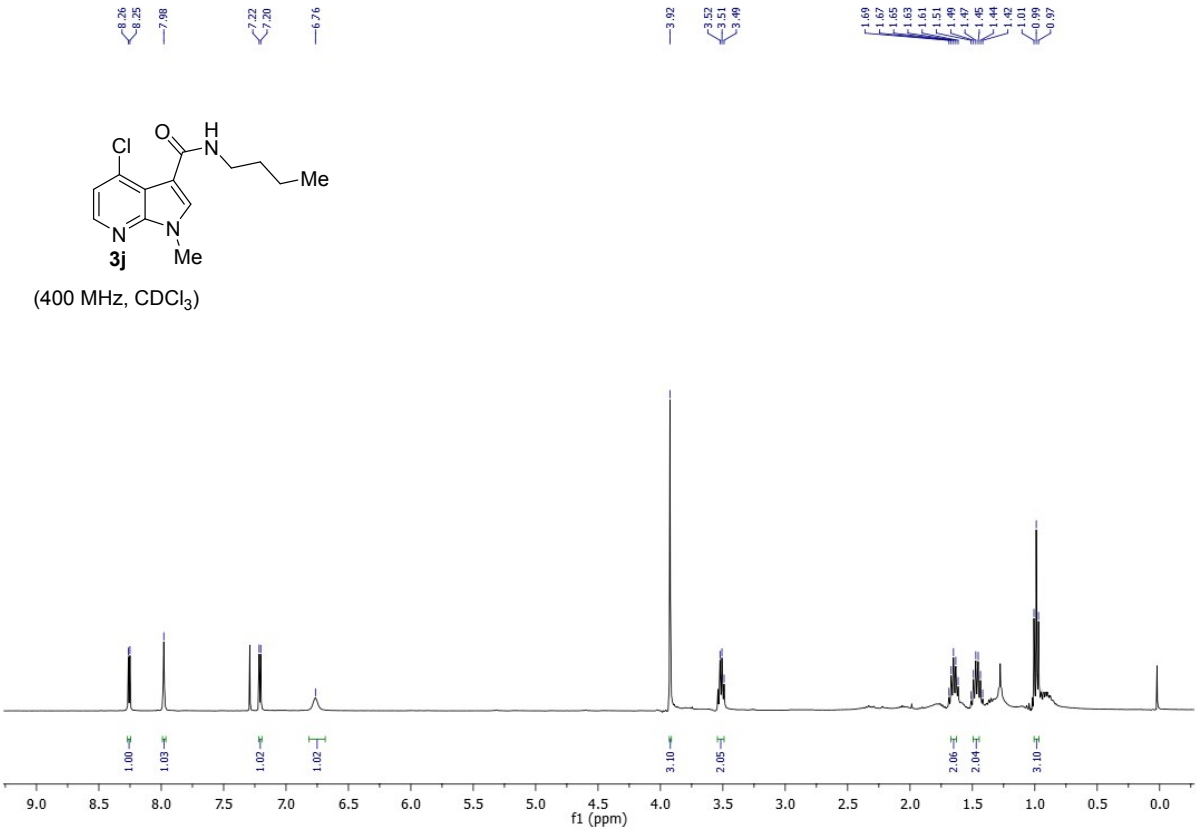


(400 MHz, $CDCl_3$)

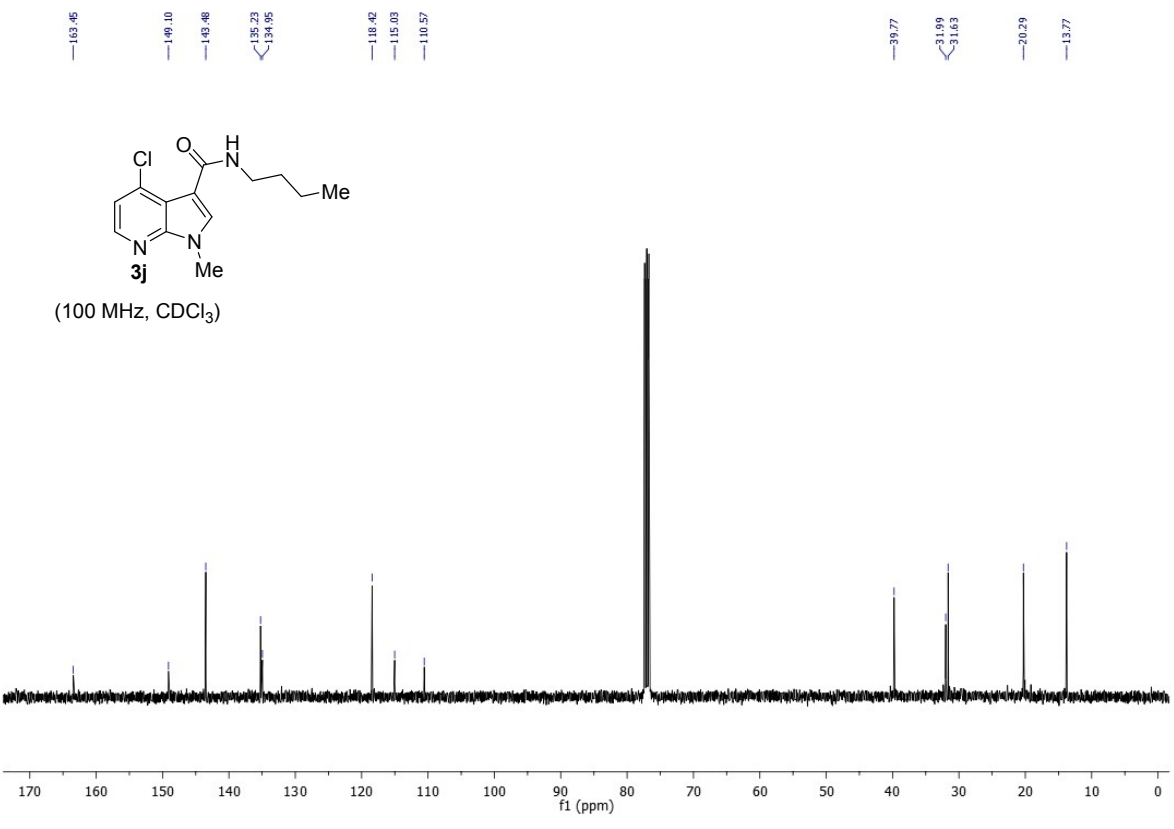


(100 MHz, $CDCl_3$)

***N*-butyl-4-chloro-1-methyl-1*H*-pyrrolo[2,3-b]pyridine-3-carboxamide**

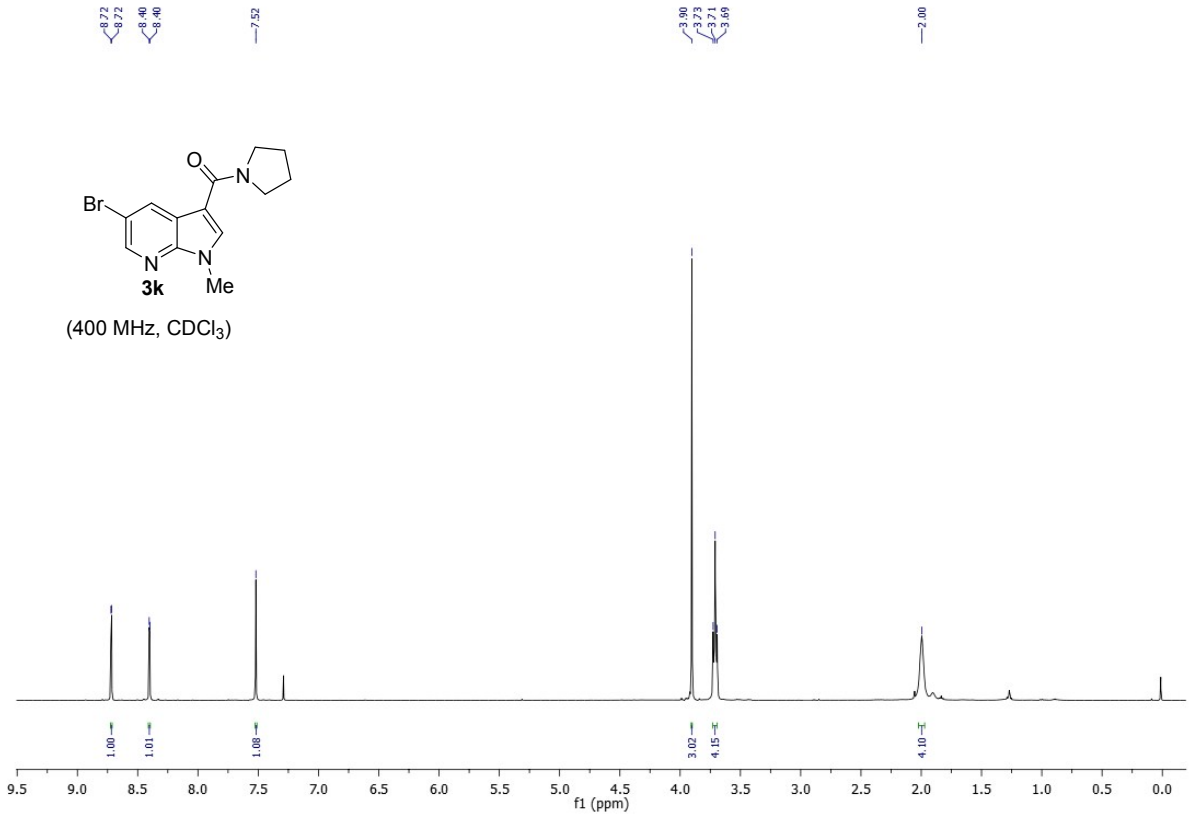


(400 MHz, $CDCl_3$)

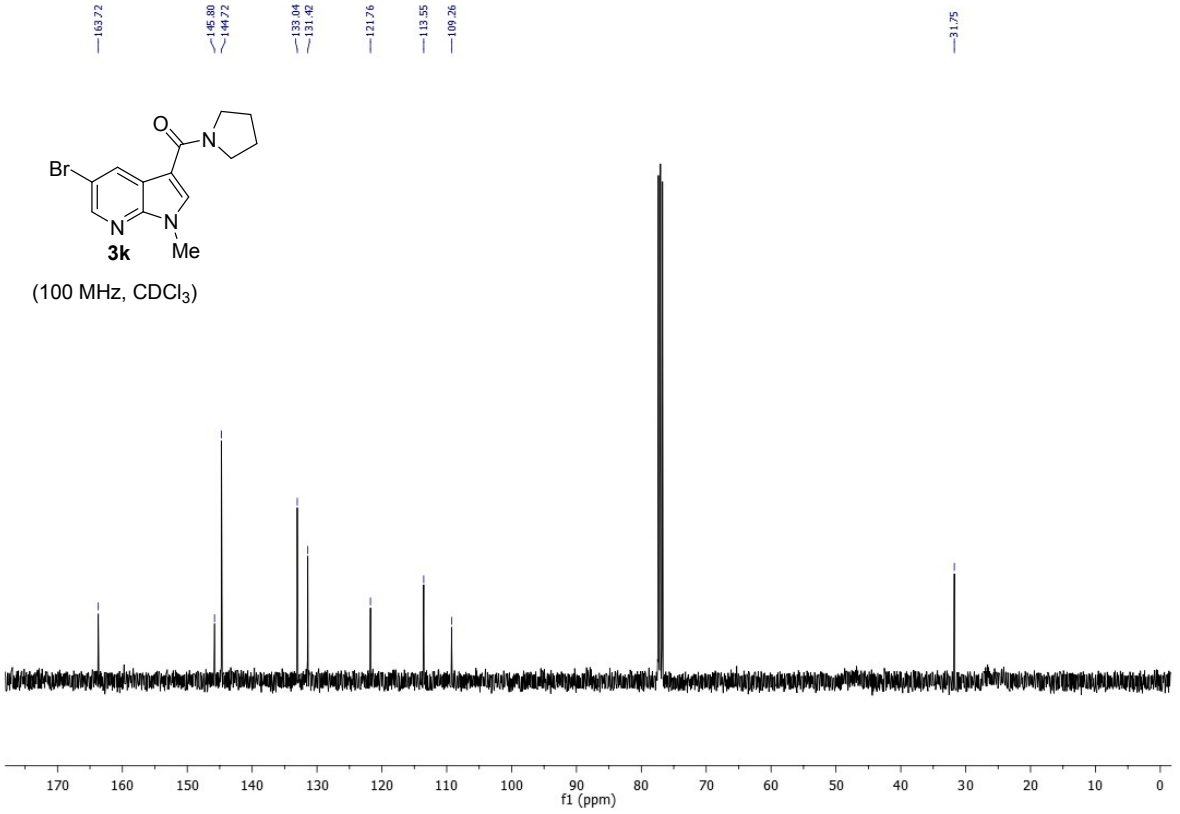


(100 MHz, $CDCl_3$)

(5-bromo-1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(pyrrolidin-1-yl)methanone

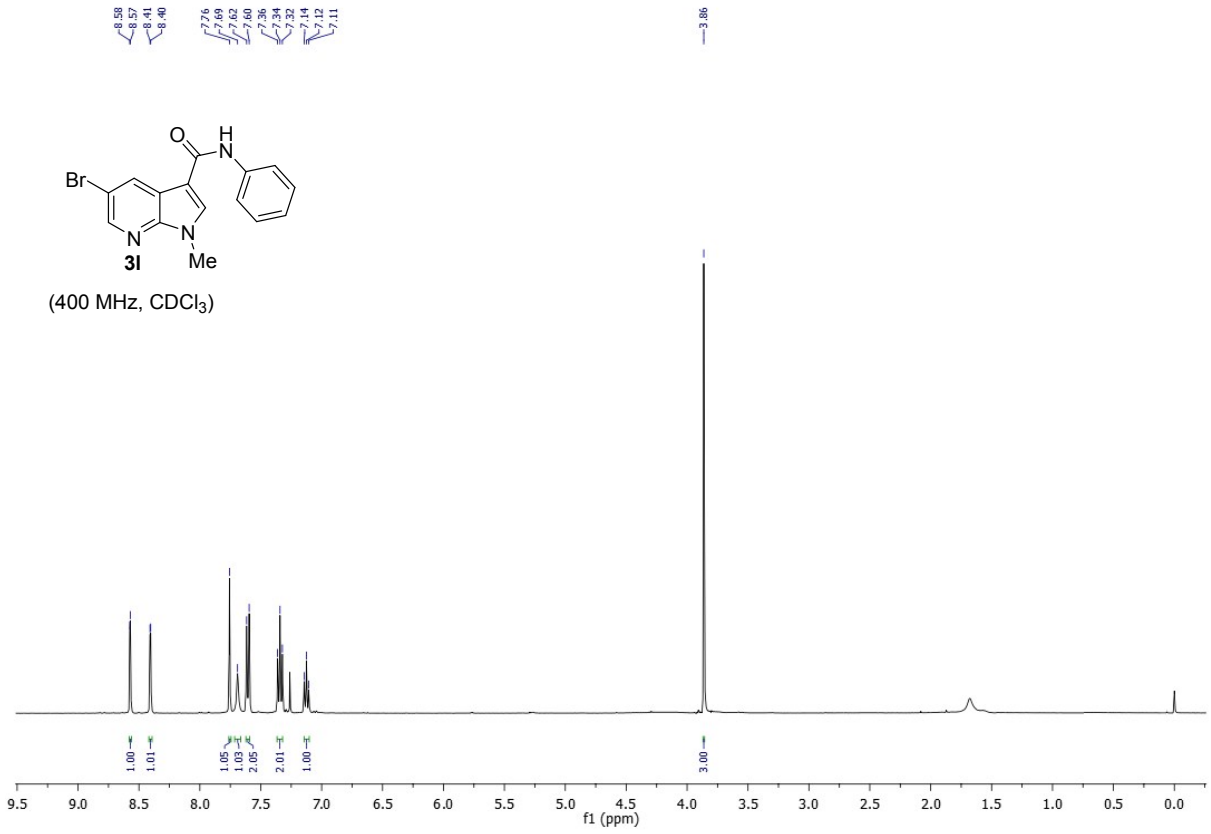


(400 MHz, $CDCl_3$)

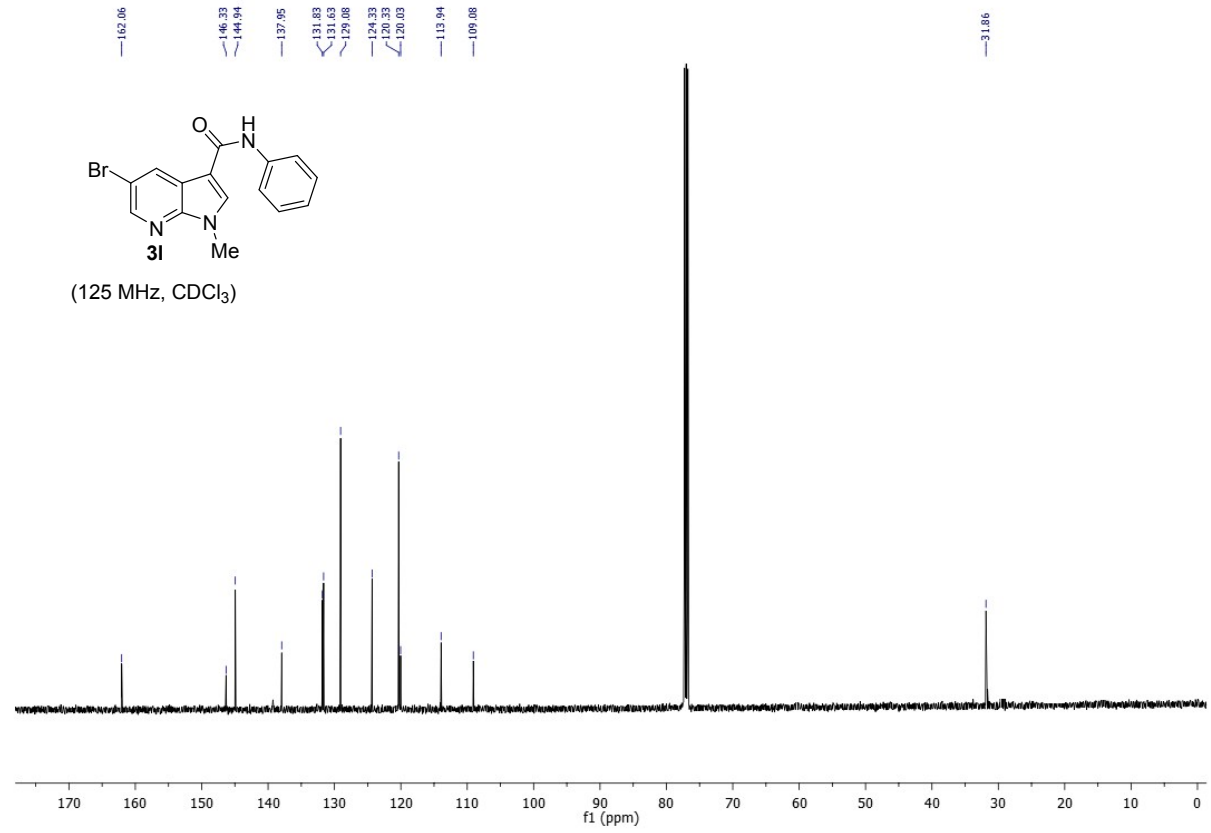


(100 MHz, $CDCl_3$)

5-bromo-1-methyl-*N*-phenyl-1*H*-pyrrolo[2,3-b]pyridine-3-carboxamide

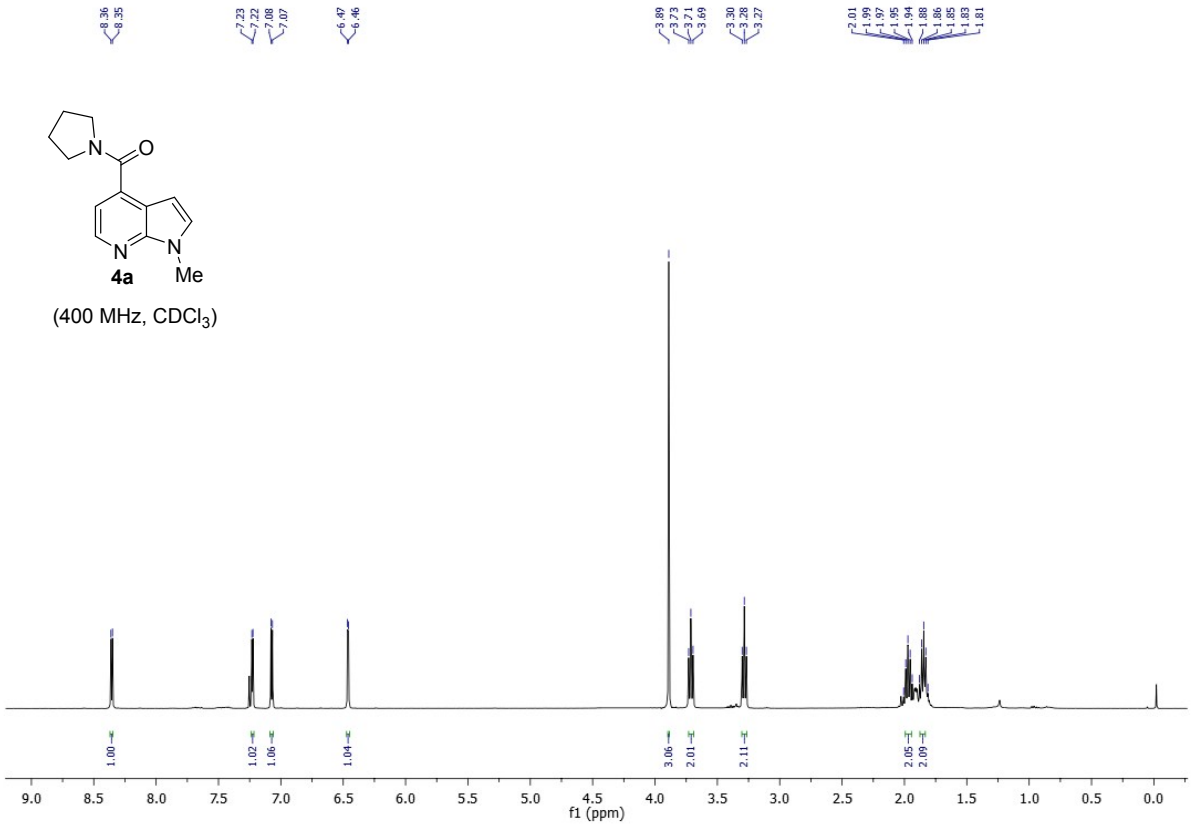


(400 MHz, $CDCl_3$)



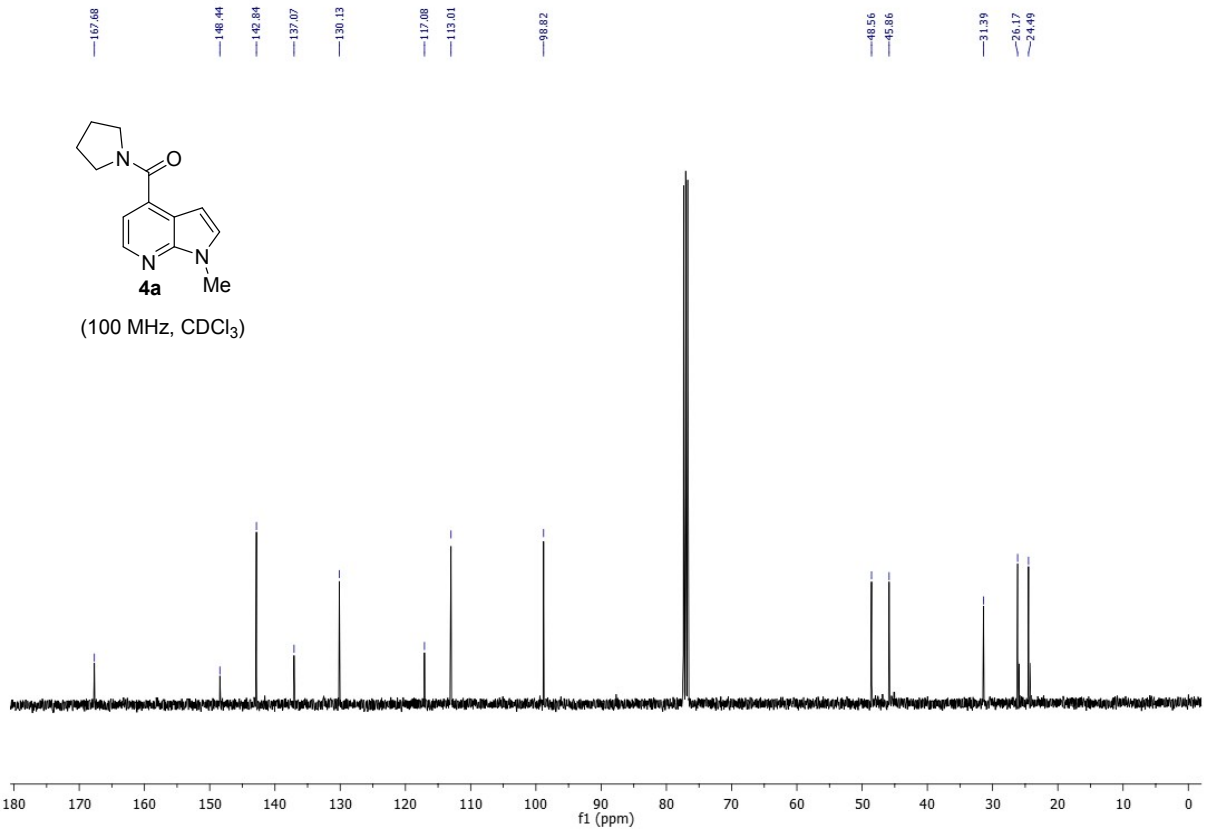
(125 MHz, $CDCl_3$)

(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-4-yl)(pyrrolidin-1-yl)methanone



4a

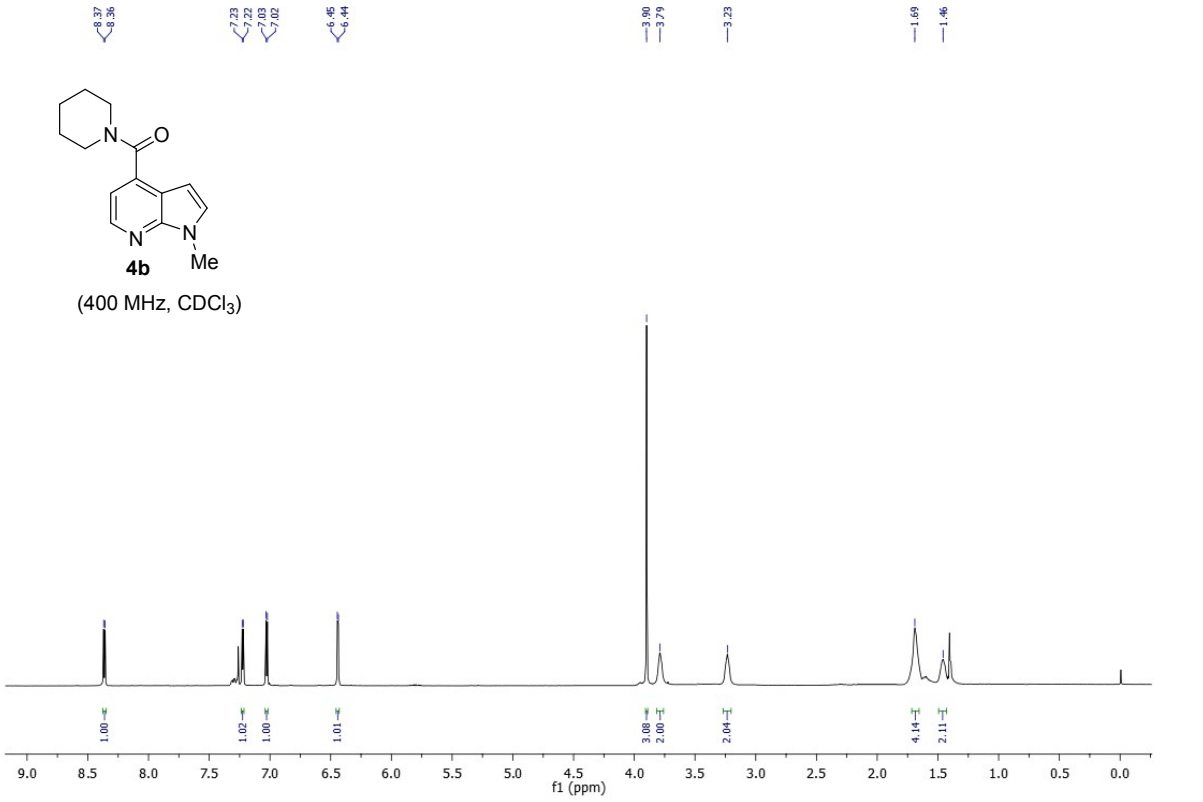
(400 MHz, $CDCl_3$)



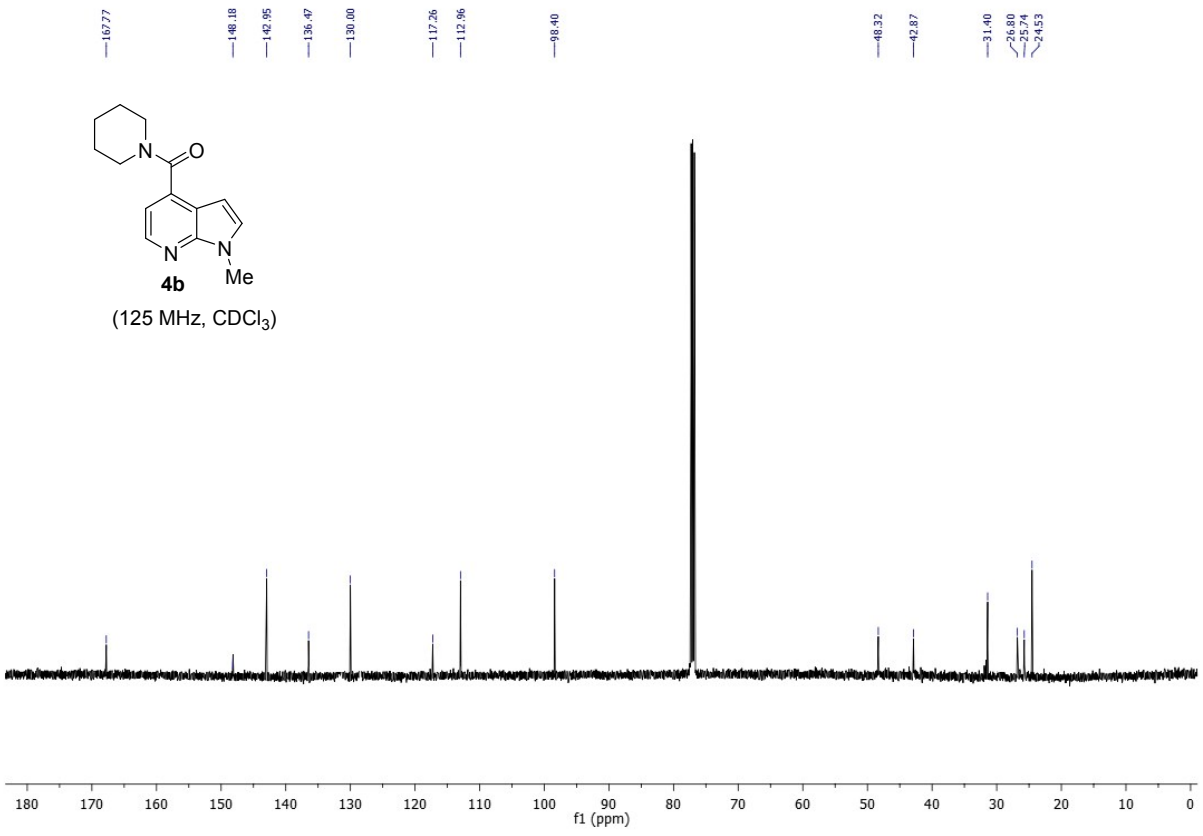
4a

(100 MHz, $CDCl_3$)

(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-4-yl)(piperidin-1-yl)methanone

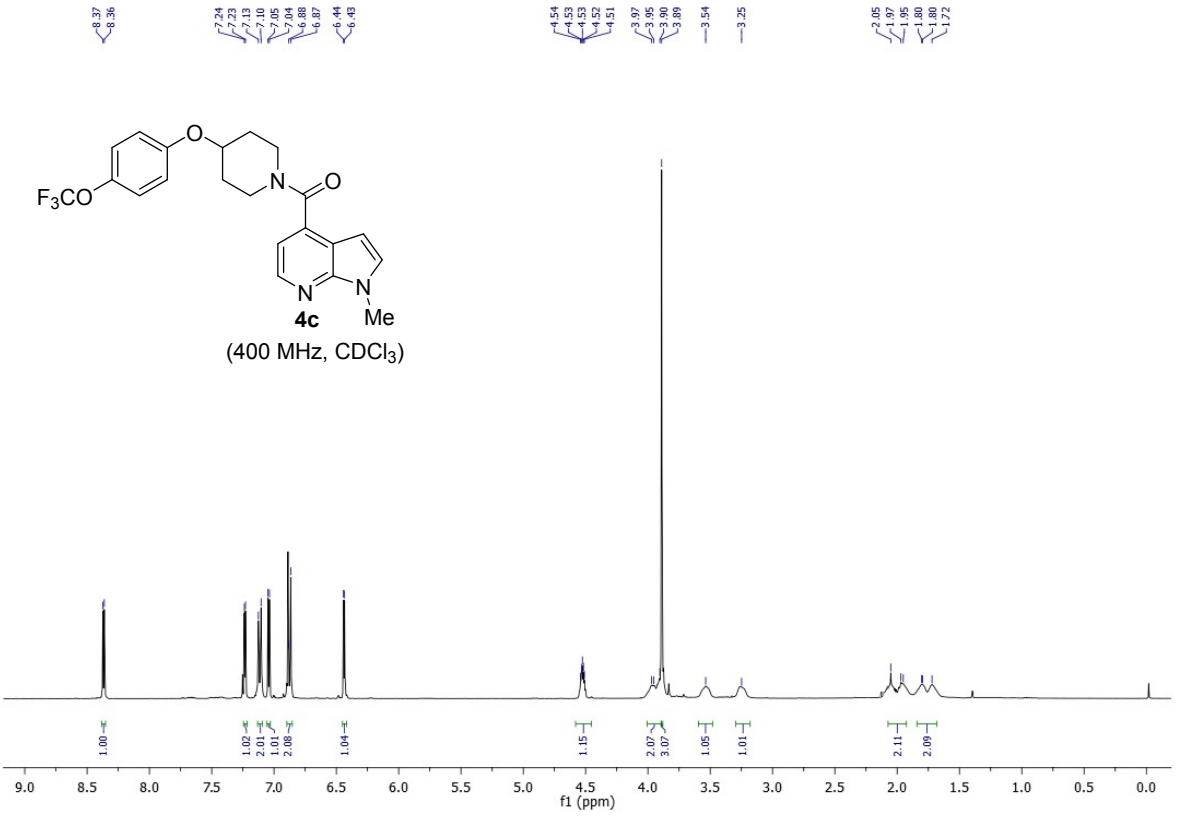


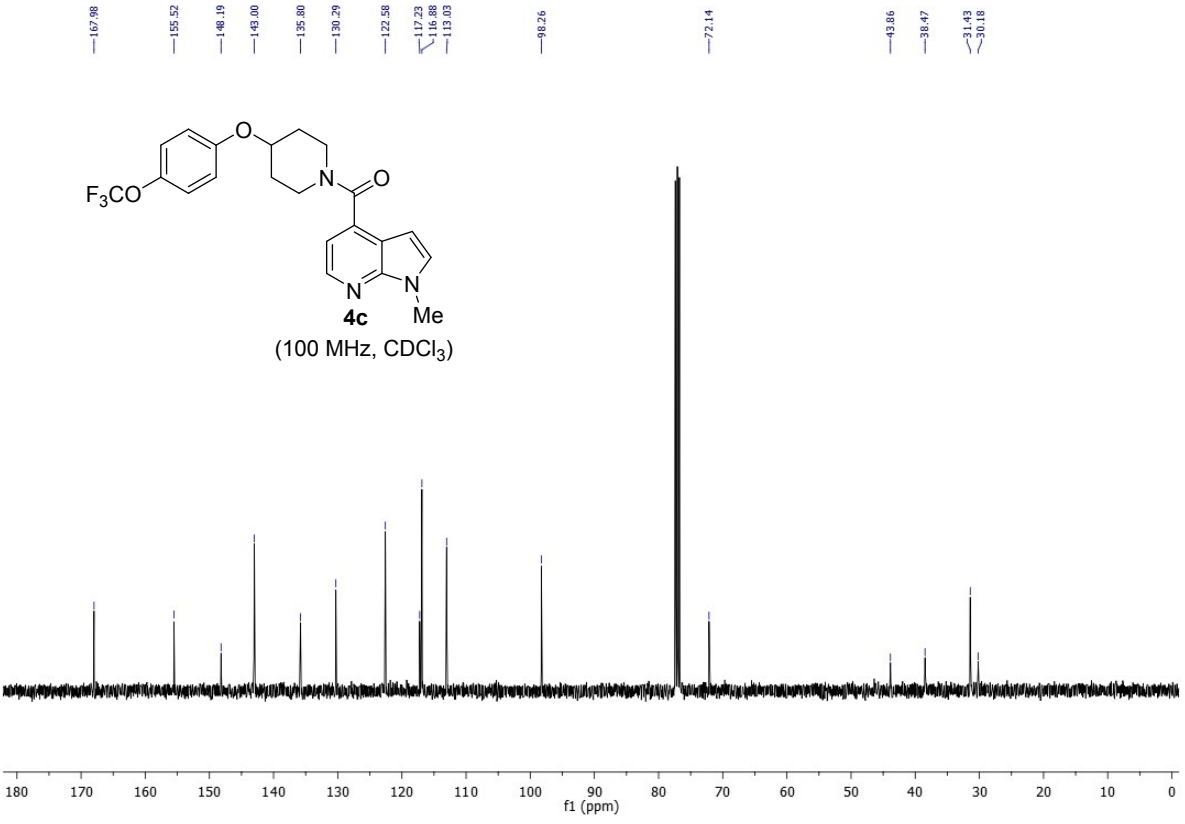
(400 MHz, $CDCl_3$)



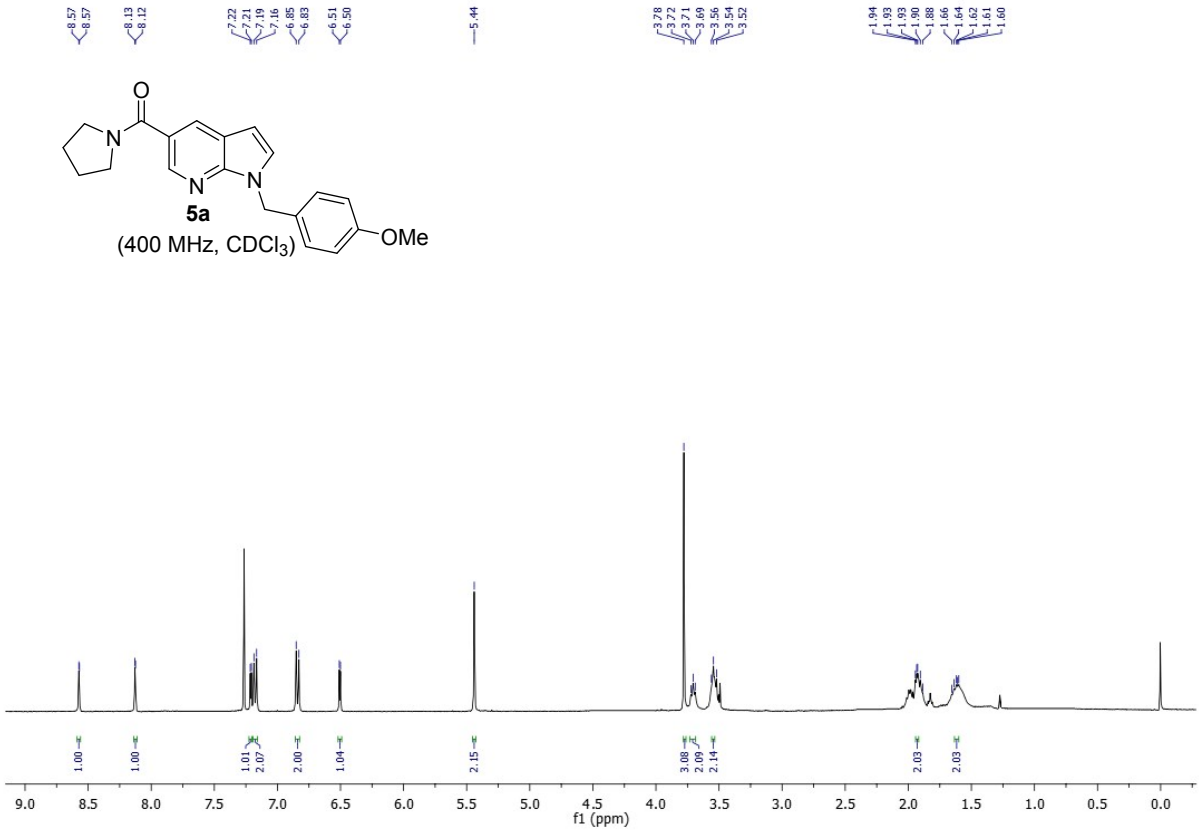
(125 MHz, $CDCl_3$)

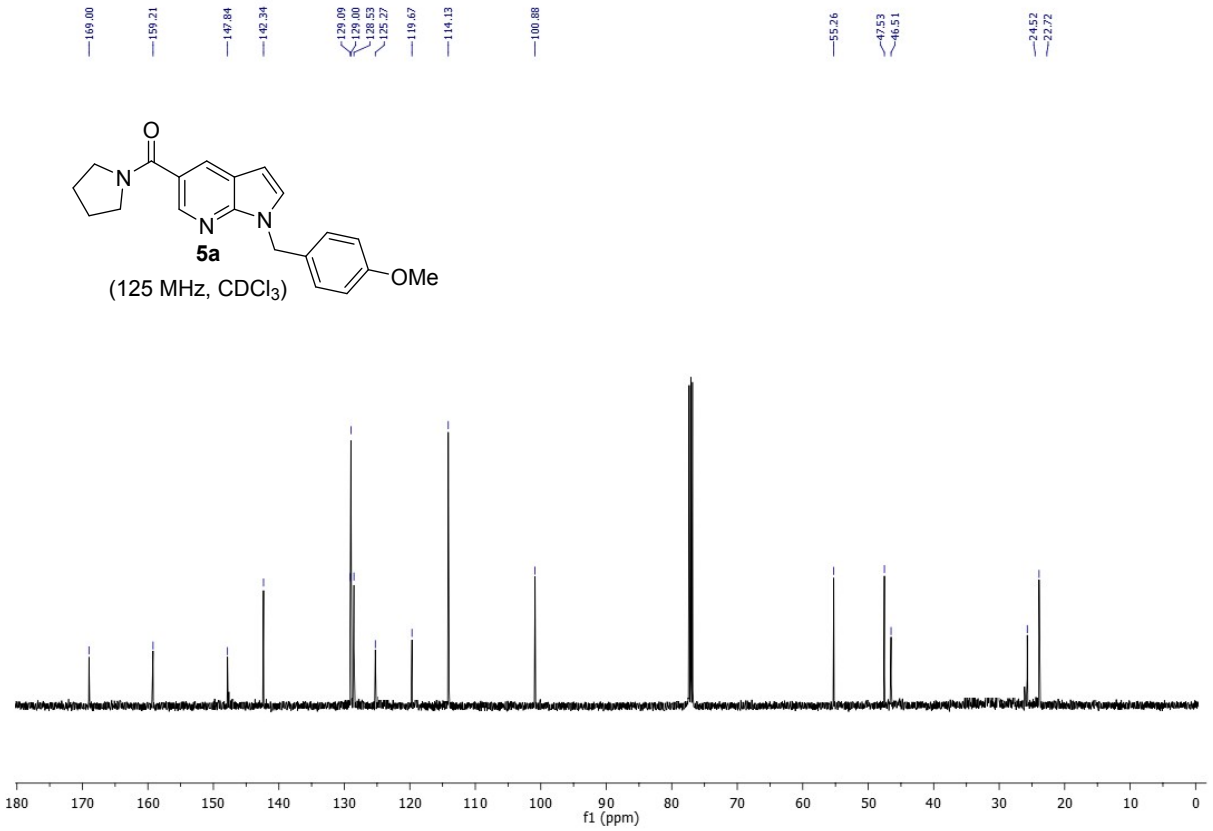
(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-4-yl)(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone



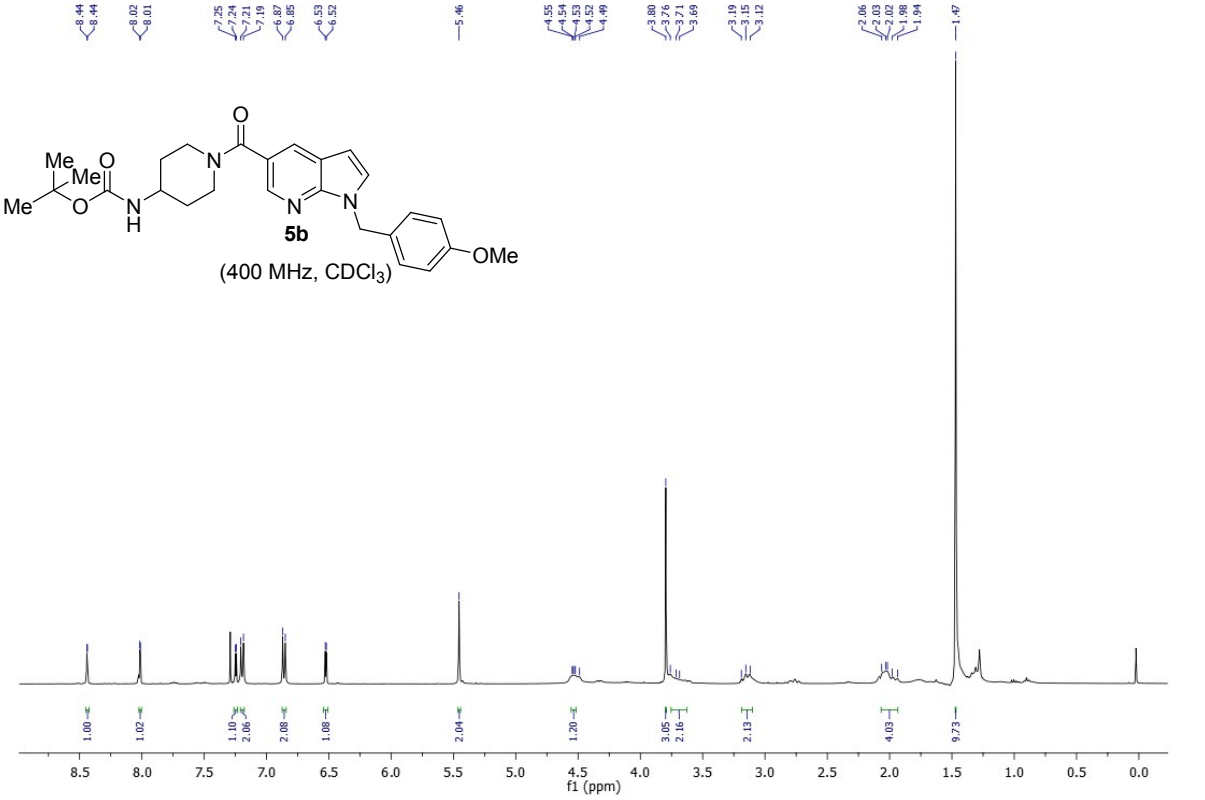


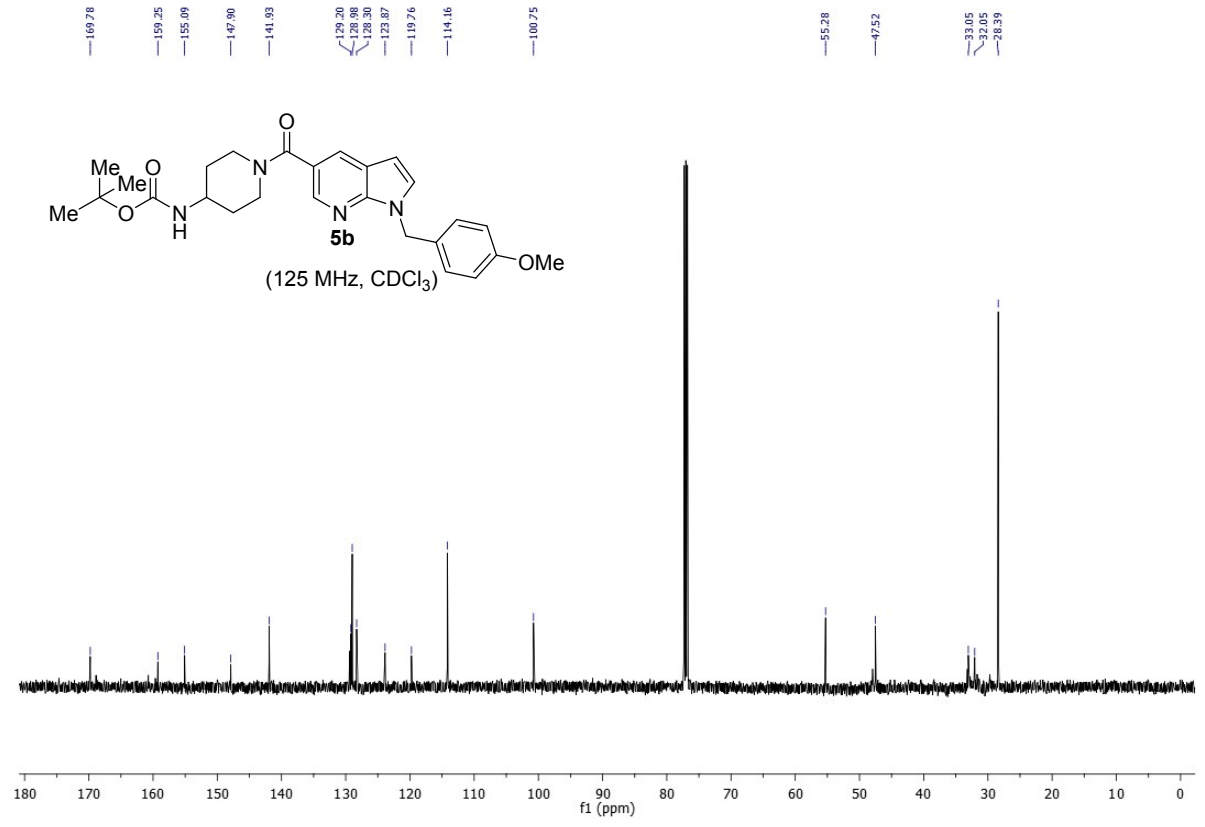
(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(pyrrolidin-1-yl)methanone



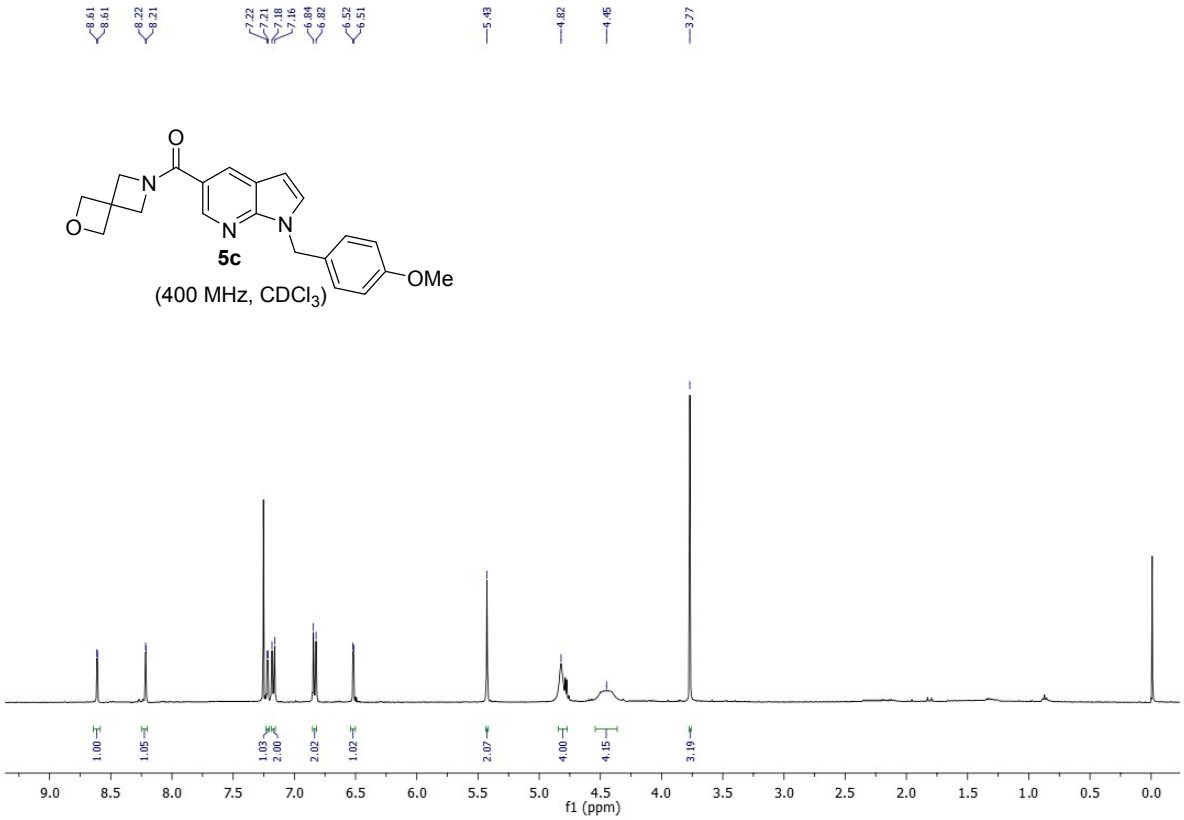


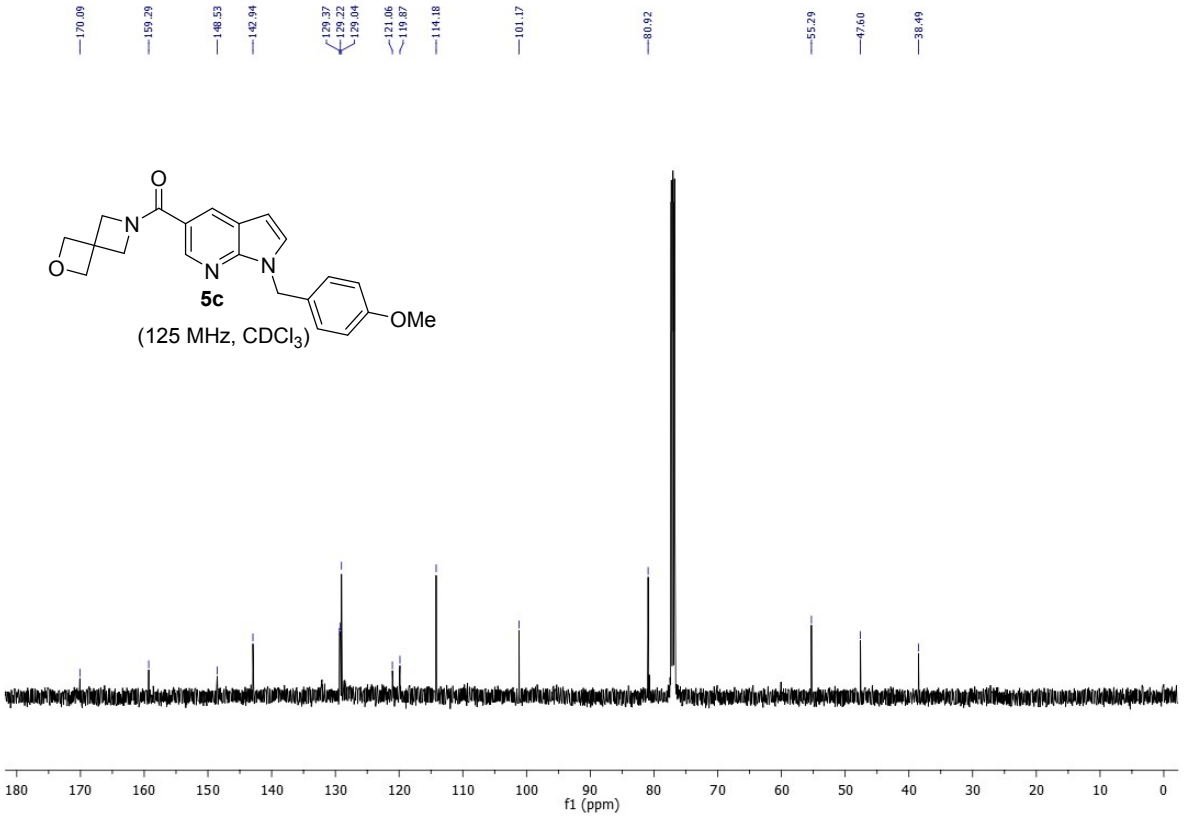
Tert-butyl (1-(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridine-5-carbonyl)piperidin-4-yl)carbamate



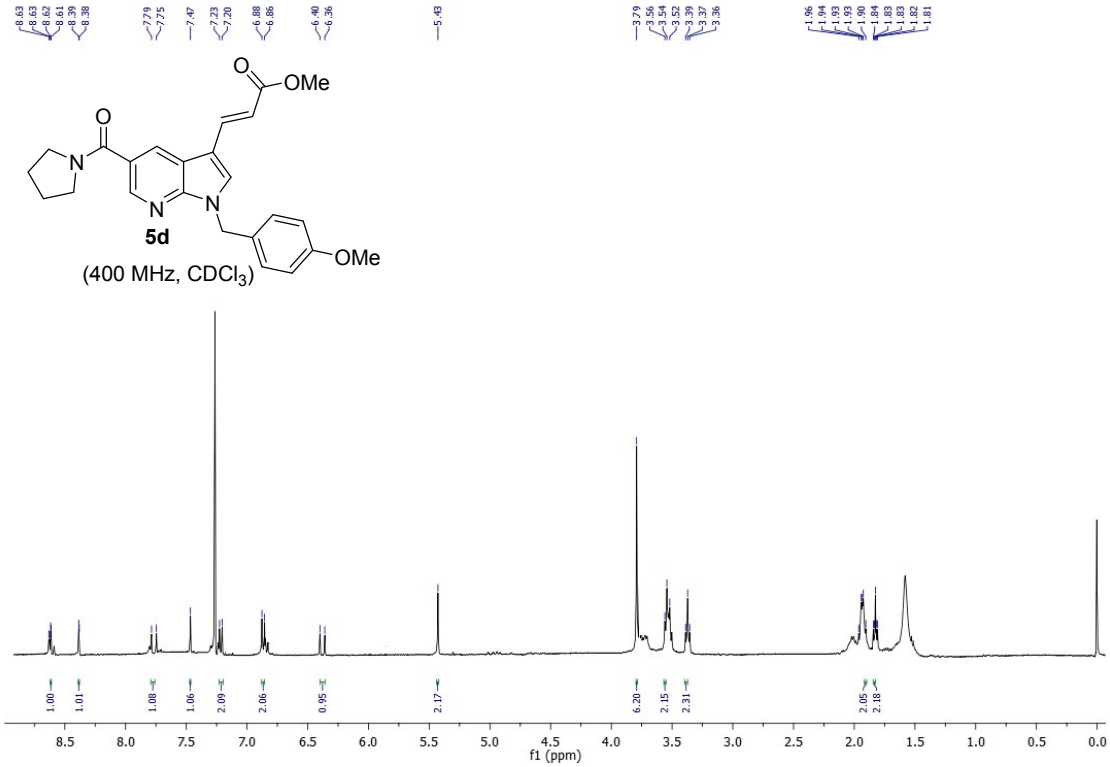


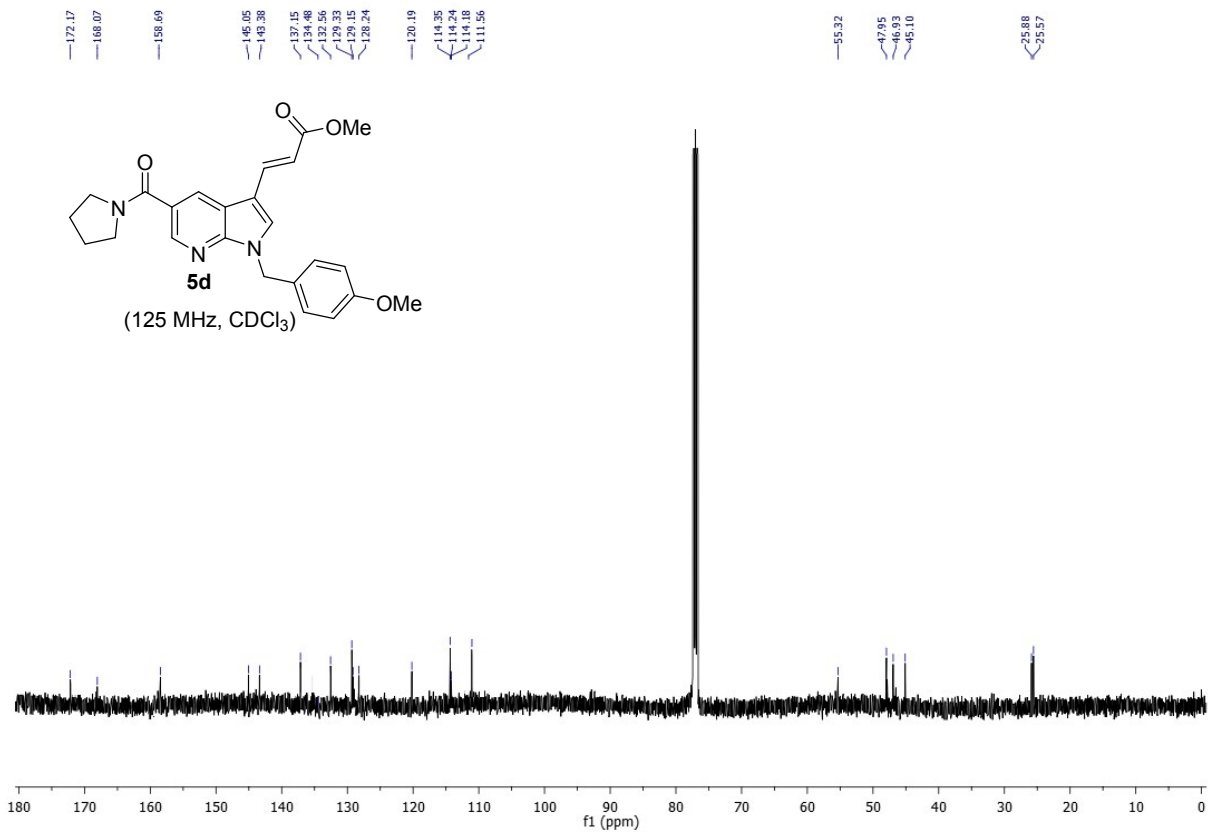
(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(2-oxa-6-azaspiro[3.3]heptan-6-yl)methanone



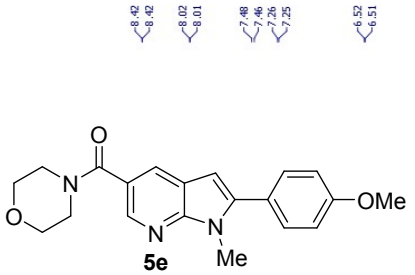


Methyl (E)-3-(1-(4-methoxybenzyl)-5-(pyrrolidine-1-carbonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)acrylate



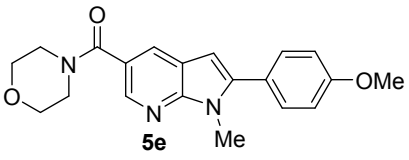


(2-(4-methoxyphenyl)-1-methyl-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(morpholino)methanone



5e

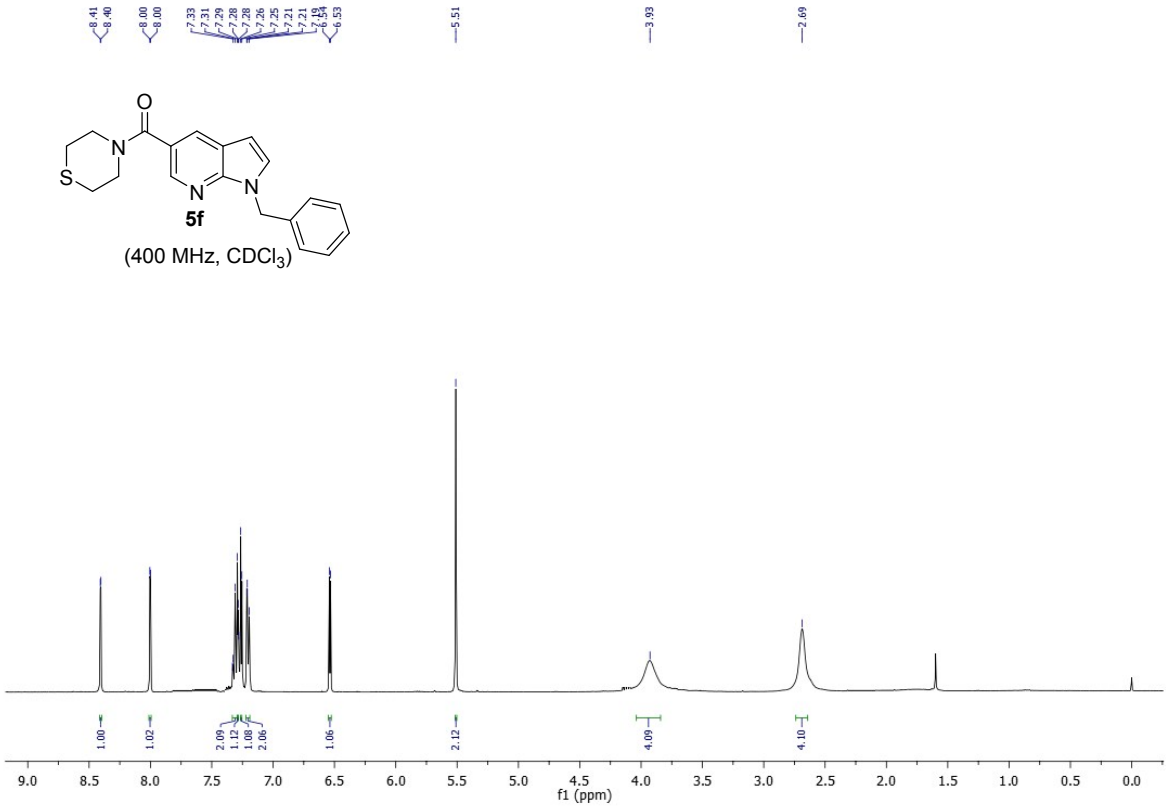
(400 MHz, $CDCl_3$)

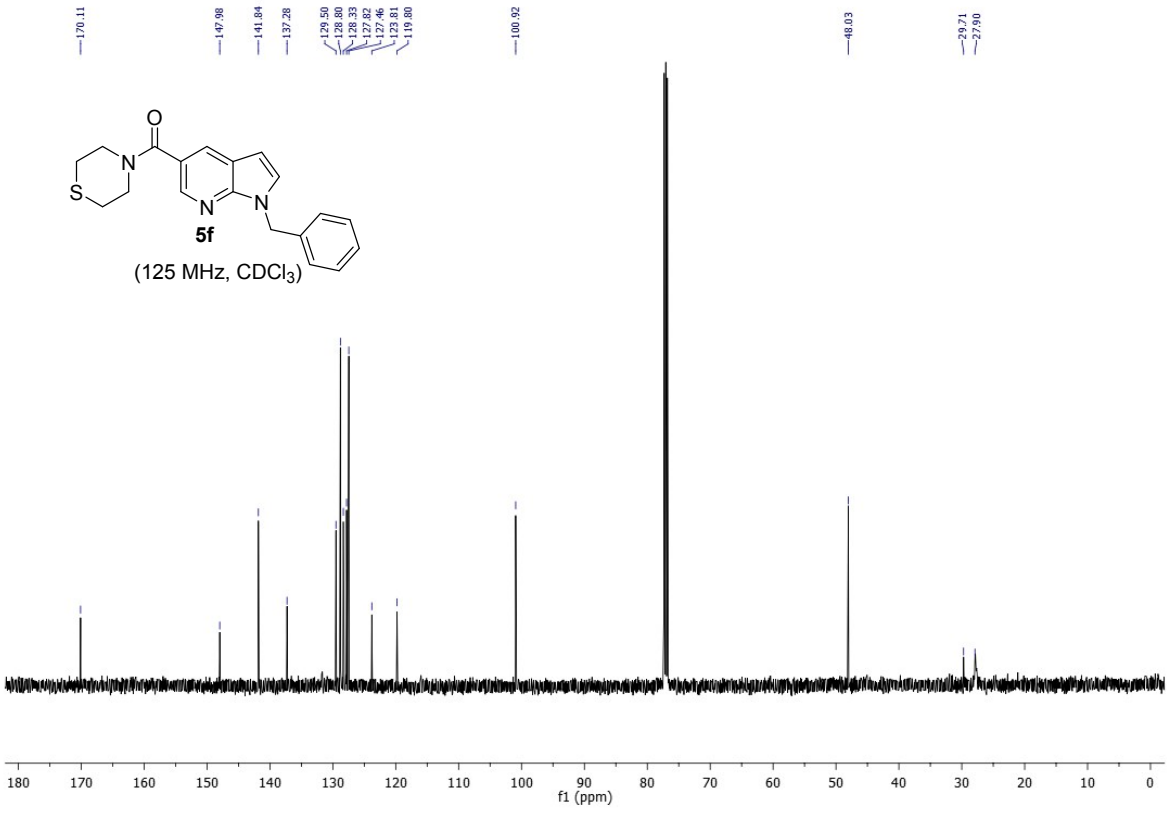


5e

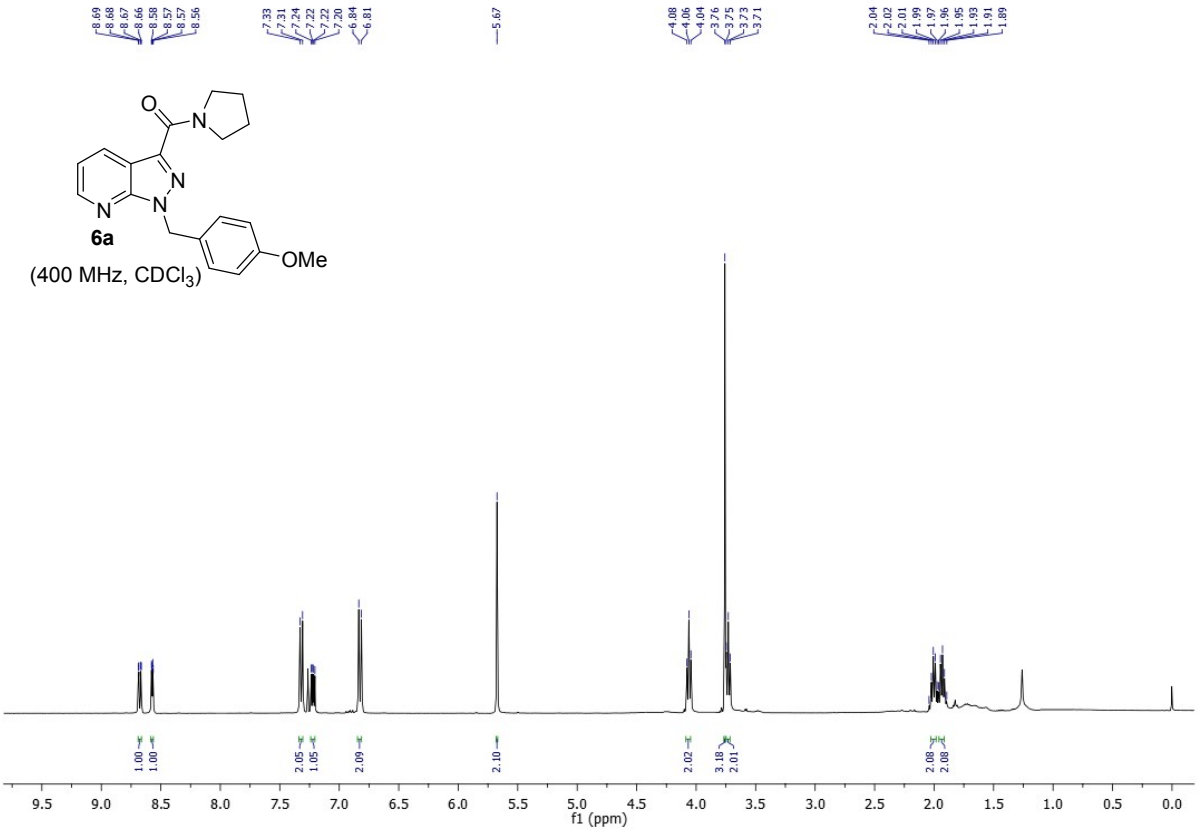
(100 MHz, $CDCl_3$)

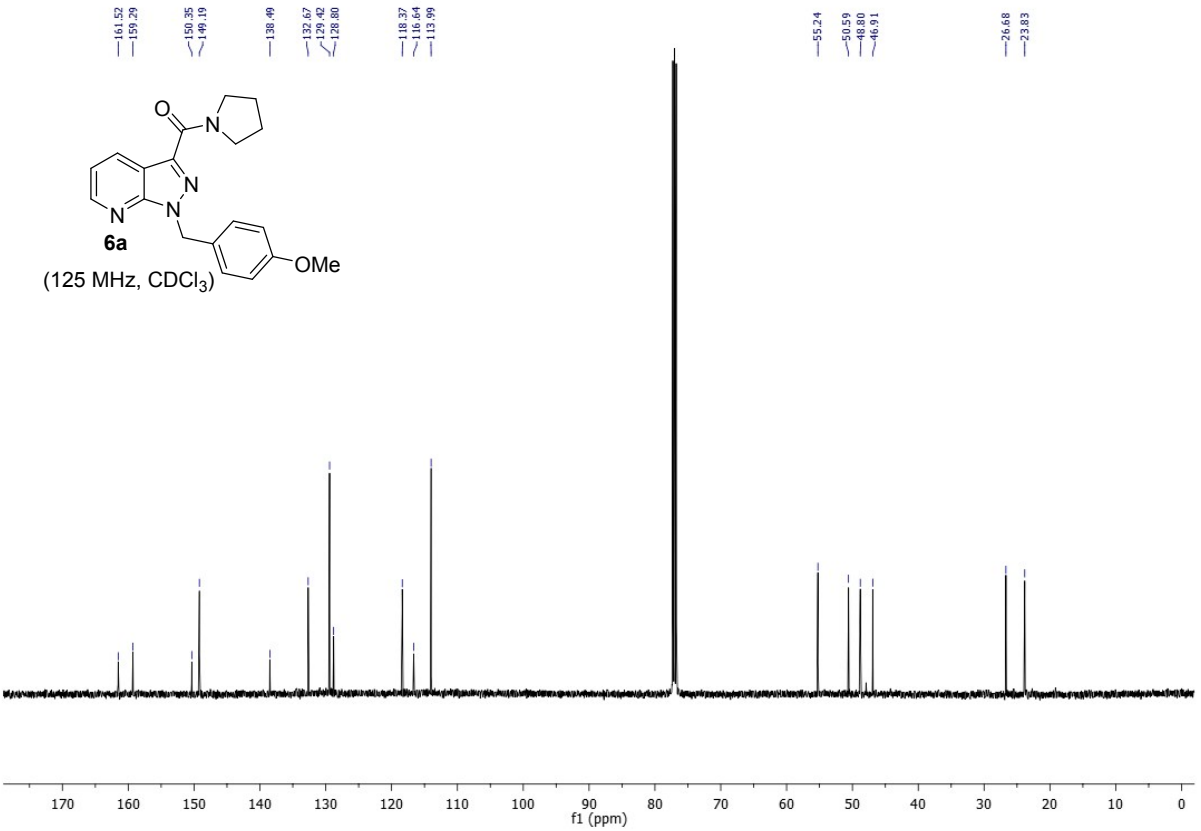
(1-benzyl-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(thiomorpholino)methanone



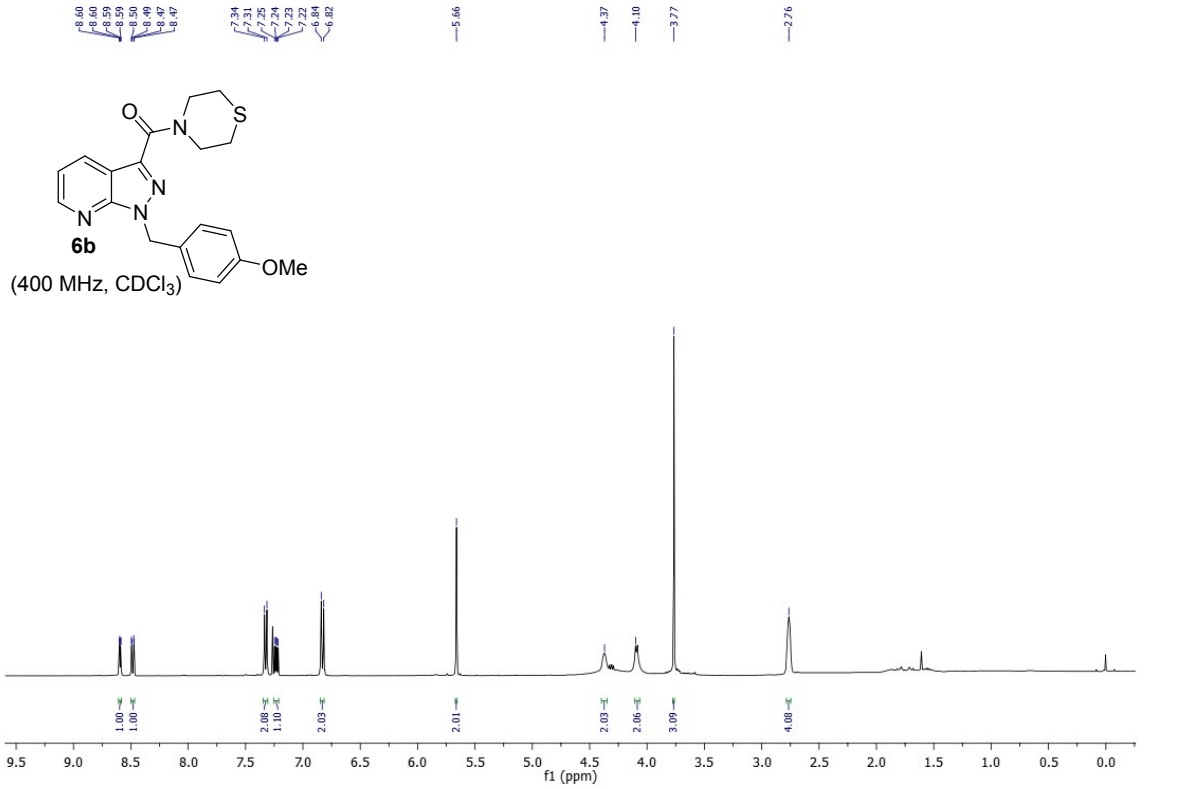


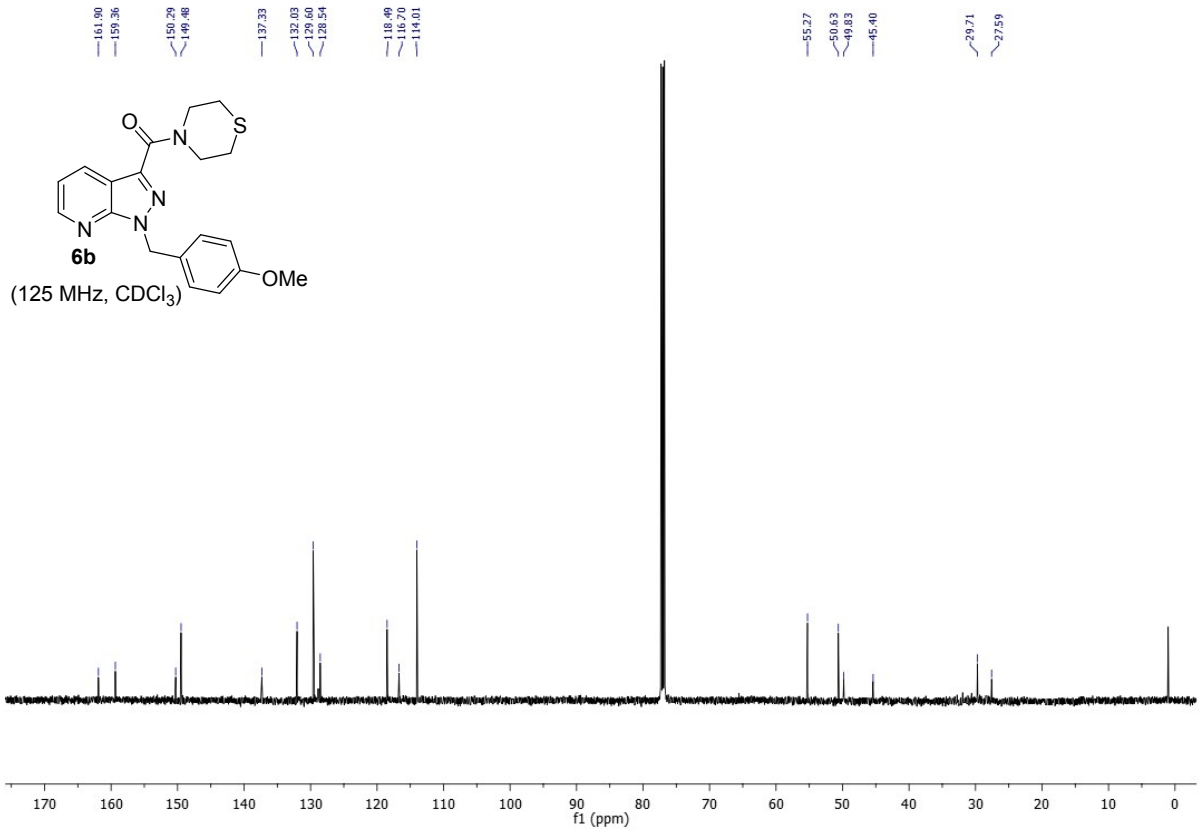
(1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)(pyrrolidin-1-yl)methanone



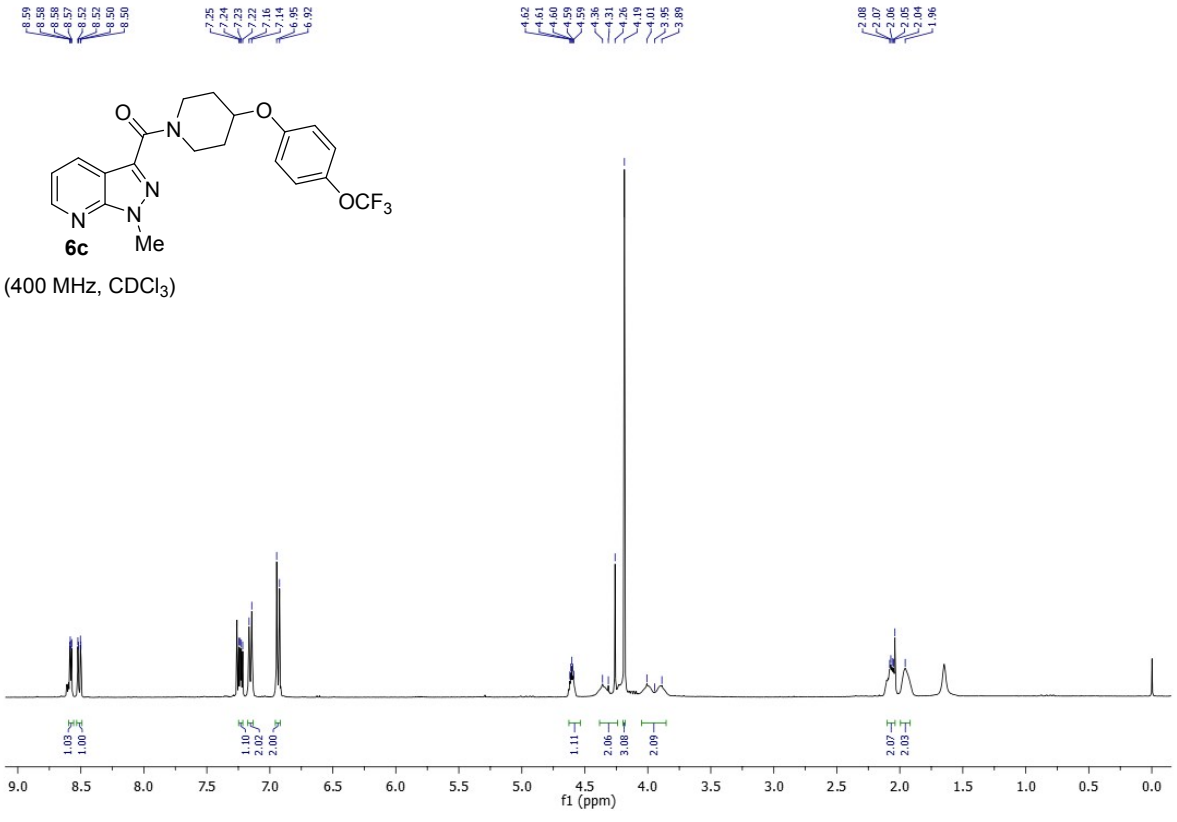


(1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-b]pyridin-3-yl)(thiomorpholino)methanone

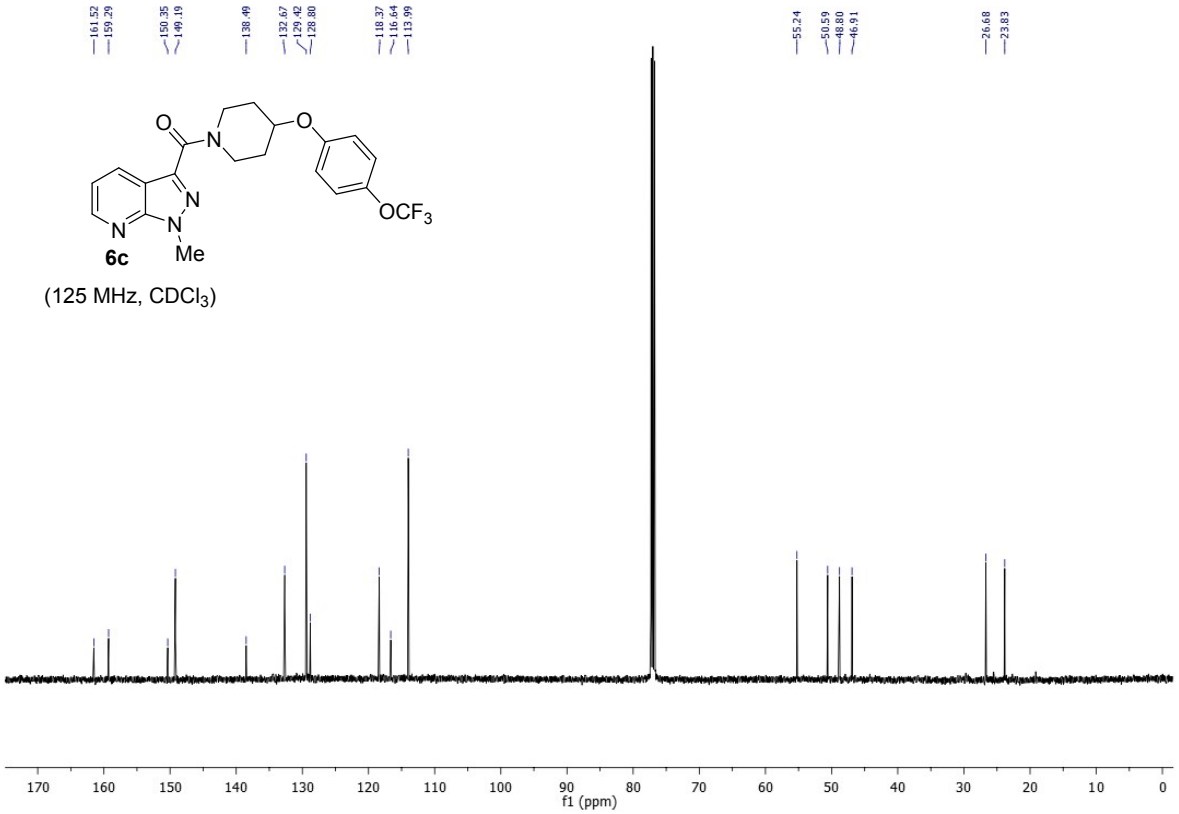




(1-methyl-1*H*-pyrazolo[3,4-b]pyridin-3-yl)(4-(4-(trifluoromethoxy)phenoxy)piperidin-1-yl)methanone

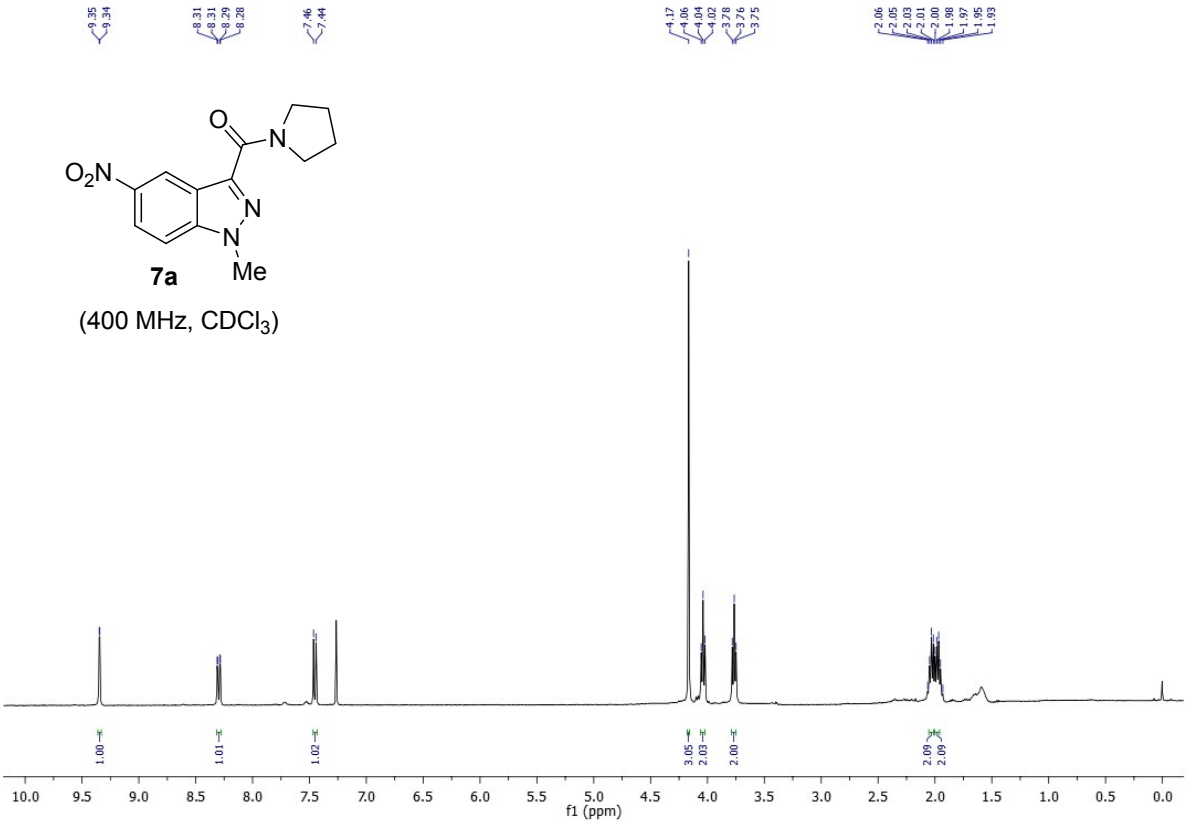


(400 MHz, $CDCl_3$)

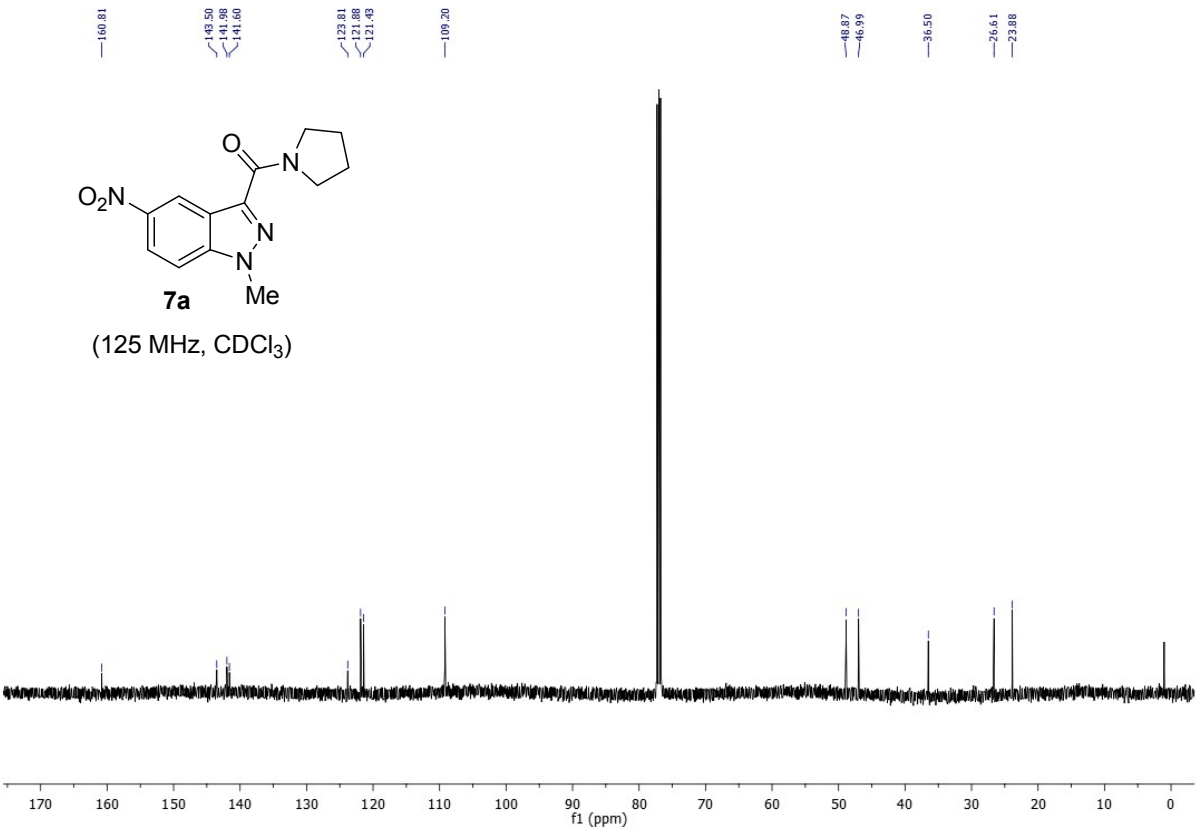


(125 MHz, $CDCl_3$)

(1-methyl-5-nitro-1*H*-indazol-3-yl)(pyrrolidin-1-yl)methanone



(400 MHz, $CDCl_3$)

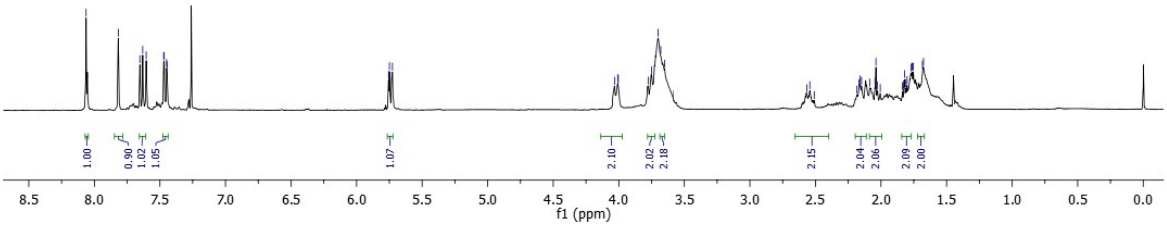


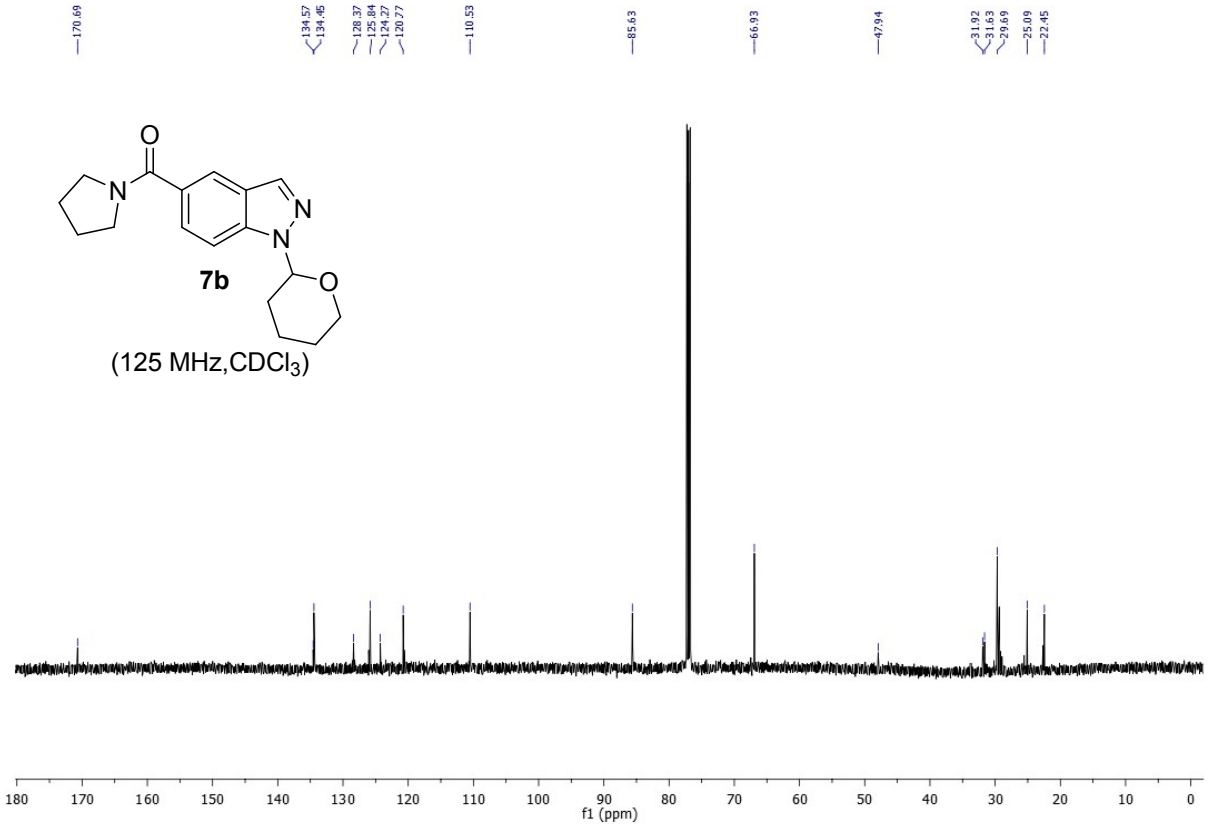
(125 MHz, $CDCl_3$)

Pyrrolidin-1-yl(1-(tetrahydro-2H-pyran-2-yl)-1*H*-indazol-5-yl)methanone

7b

(400 MHz,$CDCl_3$)





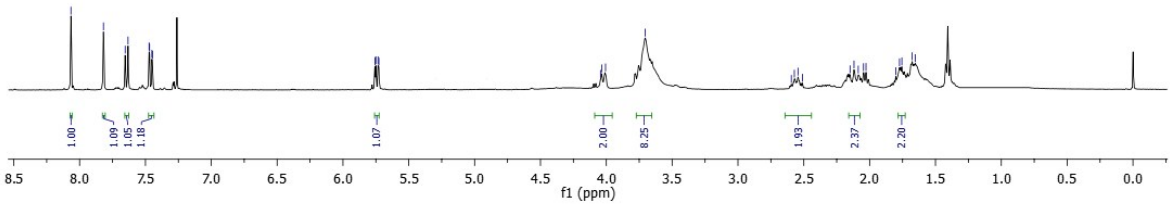
7b

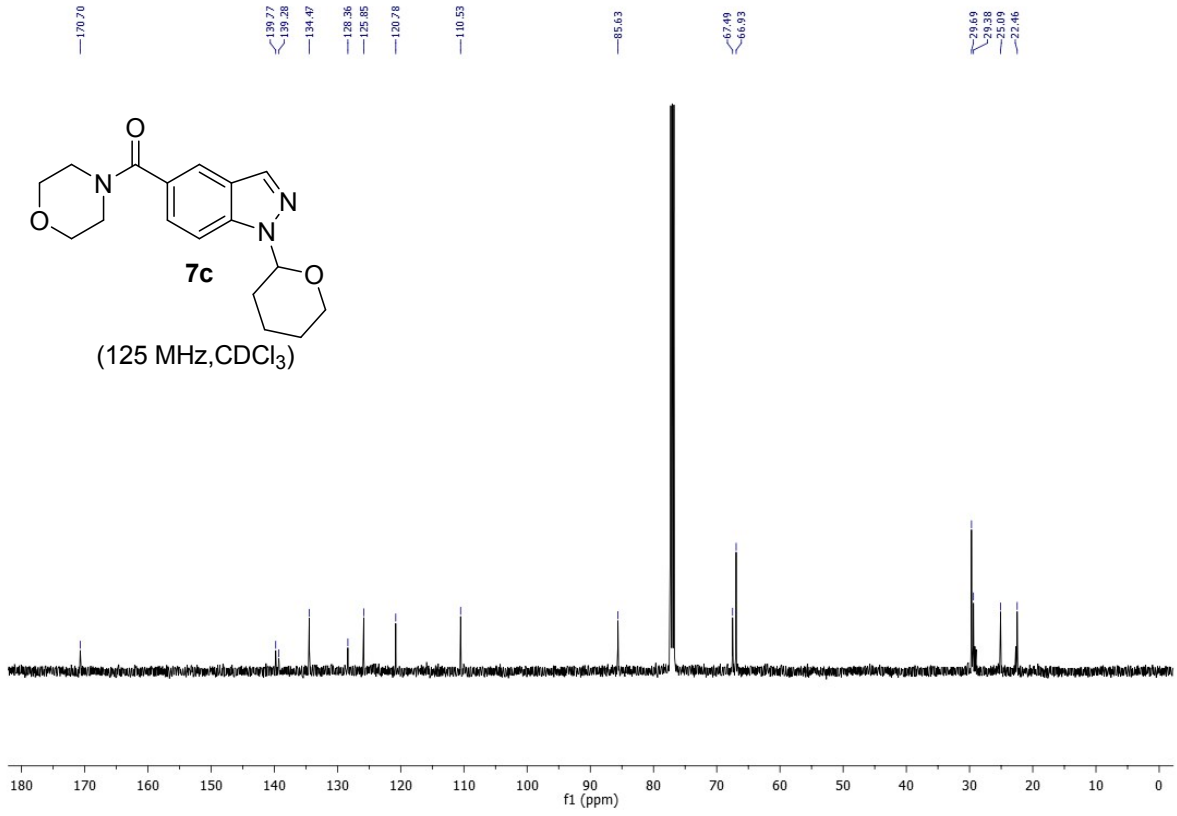
(125 MHz,$CDCl_3$)

Morpholino(1-(tetrahydro-2*H*-pyran-2-yl)-1H-indazol-5-yl)methanone

7c

(400 MHz,$CDCl_3$)





7c

(125 MHz,$CDCl_3$)

(1-methyl-3-phenyl-1*H*-pyrrolo[2,3-b]pyridin-5-yl)(pyrrolidin-1-yl)methanone