Electronic Supplementary Material (ESI) for ChemComm.

Strain-Release Arylations for the Bis-Functionalizytion of Azetidines

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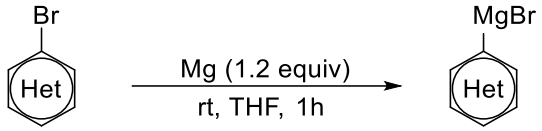
Supporting Information

1. General Considerations

All reactions were carried out under N_2 atmosphere in flame-dried glassware unless otherwise stated. Syringes, which were used to transfer anhydrous solvents or reagents, were purged with nitrogen three times prior to use. THF was purchased in 99.5 % purity from Acros Organics. Toluene was purchased in 99.85 % purity from Acros Organics. *t*BuOH was purchased 99.5 % purity from Acros Organics. Chromatography purifications were performed using silica gel (SiO_2, 0.040-0.063 mm, 230- 400 mesh ASTM) from Merck. The spots were visualized under UV (254 nm) or by staining the TLC plate with either $KMnO_4$ solution (K_2CO_3, 10 g – $KMnO_4$, 1.5 g – H_2O, 150 ml – NaOH 10% in H_2O, 1.25 ml) or *p*-anisaldehyde solution (conc. H_2SO_4, 10 ml – EtOH, 200 ml – AcOH, 3 ml – *p*-anisaldehyde, 4 ml). Yields refer to isolated yields of compounds estimated to be >95% pure as determined by ^{1}H NMR and GC-analysis. The ^{13}C and ^{1}H NMR spectra were recorded on VARIAN Mercury 200, BRUKER ARX 300, VARIAN VXR 400 S and BRUKER AMX 600 instruments. Chemical shifts are reported as δ values in ppm relative to the residual solvent peak (^{1}H-NMR, ^{13}C-NMR) in deuterated chloroform ($CDCl_3$: δ 7.26 ppm for ^{1}H-NMR and δ 77.16 ppm for ^{13}C-NMR). Abbreviations for signal coupling are as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet) and br (broad). Reaction endpoints were determined by GC monitoring of the reactions with *n*-undecane as an internal standard. Gas chromatography was performed with machines of Agilent Technologies 7890, using a column of type HP 5 (Agilent 5% phenylmethylpolysiloxane; length: 15 m; diameter: 0.25 mm; film thickness: 0.25 µm) or Hewlett-Packard 6890 or 5890 series II, using a column of type HP 5 (Hewlett-Packard, 5% phenylmethylpolysiloxane; length: 15 m; diameter: 0.25 mm; film thickness: 0.25 µm). High resolution mass spectra (HRMS) and low-resolution mass spectra (LRMS) were recorded on Finnigan MAT 95Q, Finnigan MAT 90 instrument or JEOL JMS-700. Infrared spectra were recorded on a Perkin 281 IR spectrometer and samples were measured neat (ATR, Smiths Detection DuraSample IR II Diamond ATR). The absorption bands were reported in wave numbers (cm^{-1}) and abbreviations for intensity are as follows: vs (very strong; maximum intensity), s (strong; above 75% of max. intensity), m (medium; from 50% to 75% of max. intensity), w (weak; below 50% of max. intensity) and br (broad). Melting points were determined on a Büchi B-540 apparatus and are uncorrected. *n*BuLi solution in hexane was purchased from Rockwood Lithium and the concentration was determined by titration using 1,10-phenanthroline in THF with iPrOH. Phenylmagnesiumchloride solution in THF was purchased from Rockwood Lithium and the concentration was determined by titration using iodine in THF. Aryl Grignard reagents were titrated using iodine in THF at 0 °C.

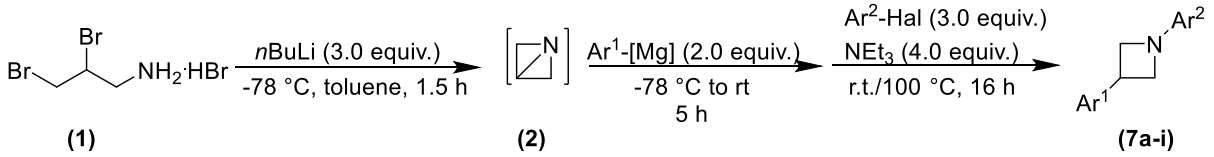
2. General Procedures

General Procedure I: Synthesis of Aryl Grignard Reagents



A Schlenk flask was charged with magnesium turnings (583 mg, 24 mmol, 1.2 equiv.) and dried *in vacuo* using a heat gun (600 °C, 2 x 5 min). After addition of THF (2.0 mL) and iodine (1 pellet), the mixture was heated to reflux with a heat gun to activate the magnesium. The corresponding aryl bromide (20 mmol, 1.0 equiv.) was dissolved in THF (18.0 mL for approximately 1 M solution or 38 ml for 0.5 M solution) and added to the activated magnesium suspension dropwise, while keeping the THF refluxing. After completion of the addition, the mixture was stirred for 0.5 h at room temperature to yield a THF-solution of the arylmagnesium reagents. The concentration was determined by titrating set aliquots against iodine.

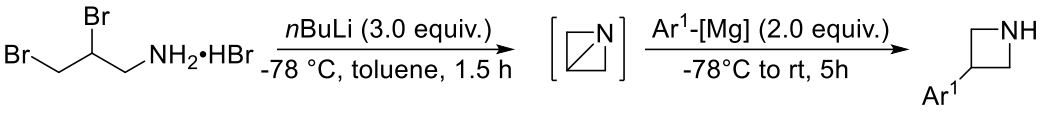
General Procedure J: One-Pot Synthesis of Fuctionalized Azetidines via 1-Azabiclo[1.1.0]butane and Nucleophilic Aromatic Substitution



(1) **(2)** **(7a-i)**

A flame-dried flask was charged with 2,3-dibromopropan-1-amine hydrobromide **(1)** (60 mg, 0.2 mmol, 1.0 equiv.) and suspended in toluene (2 mL). The suspension was cooled to -78 °C using a dry ice acetone bath, and *n*BuLi (0.6 mmol, 3.0 equiv.) was added. Following the addition, the mixture was stirred for 1.5 h. Then, the desired organomagnesium compound (0.4 mmol, 2.0 equiv.) was added. After 1 h the dry ice acetone bath was removed, and the reaction was stirred for an additional 4 h. In a separate flask, the desired arylchloride or arylfluoride (0.6 mmol, 3.0 equiv.) was dissolved in toluene (2 mL) and NEt_3 (0.11 mL, 0.8 mmol, 4.0 equiv.) was added. This mixture was then added to the previously prepared reaction. The mixture was then stirred overnight at 100 °C or room temperature. After completion, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. The combined organic phases were dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography over silica gel to give pure 1,3-disubstituted azetidines **(7a-7i)**.

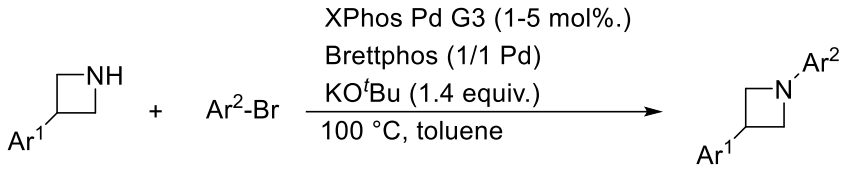
General Procedure K: Synthesis of 3-substituted Azetidines as Intermediates for *Buchwald-Hartwig* Cross-Coupling.



(1) **(2)** **(9a-9g)**

A flame-dried flask equipped with a magnetic stirring bar was charged with starting salt 2,3-dibromopropan-1-amine hydrobromide **(1)** (2.24 g, 8.00 mmol, 1.00 equiv.) and suspended in toluene (40 mL). The suspension was cooled to -78 °C using a dry ice acetone bath, and *n*BuLi (24 mmol, 3.0 equiv.) was added. Following the addition, the mixture was stirred for 1.5 h. Then, the respective organomagnesium compound (16 mmol, 2.0 equiv.) was added. After 1 h the dry ice acetone bath was removed, and the reaction was stirred for an additional 4 h. The reaction was quenched with saturated aqueous NH_4Cl and acidified to pH 1 with 2 M HCl (typically 10 mL). The mixture was thoroughly shaken, and the organic layer was separated and discarded. Then, the aqueous layer was basified to pH 9 with 2 M NaOH and extracted with dichloromethane (5 × 30 mL). In case of no phase separation centrifugation was used. The combined organic phases were dried over $MgSO_4$ and the solvents were removed *in vacuo* to afford pure 1-substituted azetidines **(9a-9g)**. 3-Substituted azetidines except **9b** and **9d** were directly engaged without any further purification.

General Procedure L: Synthesis of 1,3-disubstituted Azetidines via *Buchwald-Hartwig* Cross-Coupling of 3-substituted Azetidines.



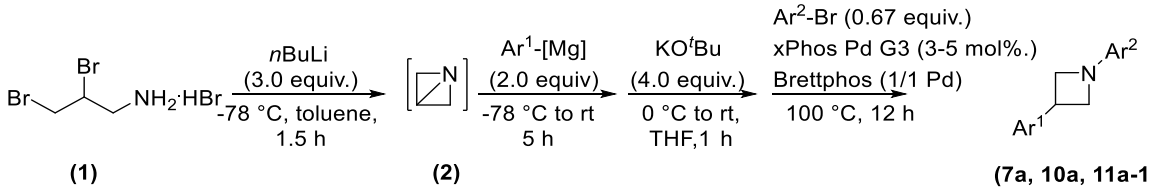
1.4 equiv. 1.0 equiv.

(9a-9g) **(10a-10t)**

In a flame-dried pressure tube equipped with magnetic stirring bar was added in the following order solvent (2 mL), 3-substituted azetidine (0.28 mmol, 1.4 equiv.), aryl halogenide (0.2 mmol, 1.0 equiv.), xPhos Pd G3 (1-5 mol%), Brettphos (1/1 Pd), and base (1.4 equiv.) under nitrogen atmosphere. The septum was changed to a screw-cap and the pressure tube was heated to 100 °C for the respective amount of time. The reaction was monitored by TLC and GC-analysis. Once no further reaction progress or full consumption of the aryl halide was observed the brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude

mixture was purified by flash column chromatography over silica gel to yield pure 1,3-disubstituted azetidines **(10a-10t)**.

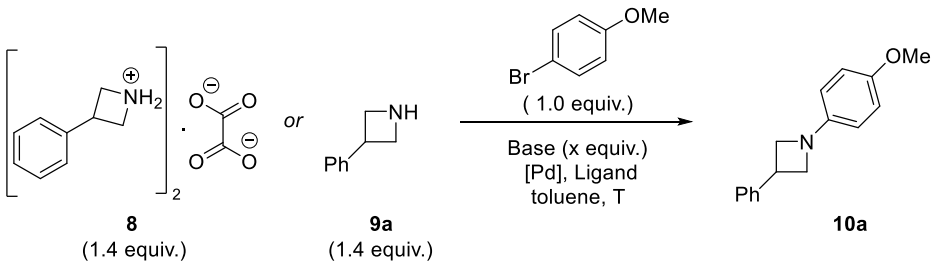
General Procedure M: One-Pot Synthesis of Functionalized Azetidines via 1-Azabiclo[1.1.0]butane and following *Buchwald-Hartwig* Amination



A flame-dried flask was charged with 2,3-dibromopropan-1-amine hydrobromide **(1)** (89 mg, 0.3 mmol, 1.0 equiv.) and suspended in toluene (2 mL). The suspension was cooled to -78 °C using a dry ice acetone bath, and *n*BuLi (0.9 mmol, 3.0 equiv.) was added. Following the addition, the mixture was stirred for 1.5 h. Then, the desired organomagnesium compound (0.6 mmol, 2.0 equiv.) was added. After 1 h the dry ice acetone bath was removed, and the reaction was stirred for an additional 4 h. After this, KO^{t}Bu (134 mg, 4.0 equiv.) was suspended in THF (1 mL) and added dropwise to the mixture at 0 °C. After 0.5 h at 0 °C and 0.5 h warming to rt., the suspension was cannulated to a flame-dried pressure tube containing: aryl-bromide (0.2 mmol, 0.67 equiv.), xPhos Pd G3 (3-5 mol%), Brettphos (1/1 Pd). The reaction was then stirred overnight (12 h) at 100 °C. After set time, the reaction was either checked by GC-analysis or it was extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography over silica gel to give pure 1,3-disubstituted azetidines **(7a, 10a, 11a-11f)**.

3. Optimizations on Buchwald-Hartwig coupling

General Procedure for Screening of Catalyst-Ligand Combinations for Buchwald-Hartwig Coupling of Azetidines



8 (1.4 equiv.) **9a** (1.4 equiv.) **10a**

Entry	Substrate	Catalyst	Ligand	Base	T (°C)	Yield (%)
1	8	$Pd_2(dba)_3$	*rac*-BINAP	KO^{t}Bu	100	17[a]
2	8	$Pd_2(dba)_3$	*rac*-BINAP	NaO^{t}Bu	100	16[a]
3	8	$Pd(OAc)_2$	Xantphos	KO^{t}Bu	100	4[a]
4	8	$Pd(OAc)_2$	Xantphos	NaO^{t}Bu	100	4[a]
5	8	xPhos Pd G3	Brettphos	KO^{t}Bu	100	24[b,c]
6	8	Ruphos Pd G3	RuPhos	KO^{t}Bu	100	22[b,c]
7	9a	xPhos Pd G3	Brettphos	KO^{t}Bu	100	82[b,c]
8	9a	xPhos Pd G3	Brettphos	KO^{t}Bu	80	73[b,c]
9	9a	Ruphos Pd G3	Ruphos	KO^{t}Bu	100	71[b,c]
10	9a	RuPhos Pd G3	Ruphos	KO^{t}Bu	80	68[b,c]

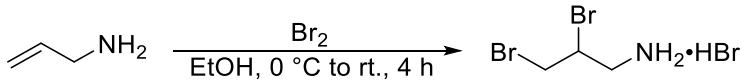
[a] Reactions performed with 3 mol% [Pd], [Pd]/ligand = 1.5:1 and 3 equiv. of Base, [b] Reactions performed with 1 mol% [Pd], [Pd]/ligand = 1:1 and 1.4 equiv. of Base,[c] Yields refer to isolated compounds.

In a flame-dried pressure tube equipped with magnetic stirring bar was added in the following order: toluene (2 mL), 3-phenylazetidin-1-ium oxalate (100 mg, 0.28 mmol, 1.4 equiv.) or 3-phenylazetidine (37 mg, 0.28 mmol, 1.4 equiv.), 4-bromoanisole (25 µL, 0.2 mmol, 1.0 equiv.), catalyst (3 mol% for reactions involving substrate **8,** 1 mol% for reactions involving substrate

9a), ligand ([Pd]/ligand = 1.5:1 for reactions involving substrate **8**, [Pd]/ligand = 1:1 for reactions involving substrate **9a**) , and base (3 mol% for reactions involving substrate **8**, 1.4 mol% for reactions involving substrate **9a**) under nitrogen atmosphere. The septum was changed to a screw-cap and the pressure tube was stirred overnight (14 h) at the indicated temperature. After set time, the reaction was either checked by GC-analysis or it was filtered through a plug of Celite 545. The filtrate was concentrated *in vacuo* and the crude mixture was purified by flash column chromatography over silica gel (*i*-hexane/EtOAc; 98:2) to give pure 1-(4-methoxyphenyl)-3-phenylazetidine **10a**.

4. Experimental Section

2,3-Dibromopropan-1-amine hydrobromide (1)



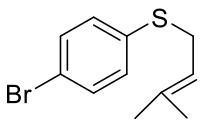
(1)

The compound was prepared according to a modified literature procedure.[1] Bromine (10.75 mL, 210 mmol, 2.10 equiv.) was added dropwise to 40 mL EtOH in a round necked flask at 0 °C. Allylamine (7.48 mL, 100 mmol, 1.00 eq.) was added dropwise to the dark solution. The icebath was removed and the solution was allowed to warm to room temperature. After 4 h the precipitate was filtered off and the crude product was washed with cold Et_2O (3 × 15 mL). The colorless solid was recrystallized two times from methanol (30 mL) to obtain colorless crystals of the title compound (17.6 g, 58.9 mmol, 58.9 % overall yield).

^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 4.49 (dddd, J = 9.4, 8.0, 4.6, 3.2 Hz, 1H), 4.00 (dd, J = 11.0, 4.6 Hz, 1H), 3.85 (dd, J = 11, 8.7 Hz, 1H), 3.69 (dd, J = 14.0, 3.2 Hz, 1H), 3.39 – 3.31 (m, 1H).
^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 47.95, 45.54, 33.90.

[1] J. L. Tyler, A. Noble, V. K. Aggarwal, *Angew. Chem., Int. Ed.* **2021**, *60*, 11824-11829.

(4-Bromophenyl)(3-methylbut-2-en-1-yl)sulfane

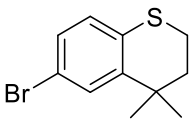


The compound was prepared according to a modified literature procedure.[2] 4-bromobenzenethiol (3.03 g, 16.0 mmol, 1.00 equiv.) was charged in a flame dried flask under nitrogen atmosphere and dissolved in dry acetone (120 mL). 1-Bromo-3-methylbut-2-ene (3.7 mL, 32 mmol, 2.0 equiv.) was added to the solution under continuous stirring. Then NEt_3 (3.05 mL, 21.8 mmol, 1.36 equiv.) was added dropwise at 0 °C upon which immediately a colorless precipitate was formed. The mixture was then allowed to warm to rt and was stirred overnight at this temperature. After 24 h the precipitate was filtered off and washed thoroughly with acetone (around 50 mL). Then the filtrate was diluted with water (40 mL) and extracted with EtOAc (3 × 40 mL). Combined organic layers were washed with brine (40 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane) to afford the title compound as a yellowish oil (3.1 g, 12 mmol, 75 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.49 – 7.28 (m, 4H), 7.22 – 7.15 (m, 2H), 5.27 (tt, J = 7.7, 1.3 Hz, 1H), 3.51 (d, J = 7.7 Hz, 2H), 1.71 (s, 3H), 1.59 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 136.95, 136.16, 132.35, 131.84, 131.34, 129.50, 119.95, 119.06, 32.38, 25.80, 17.87.

[2] J. S. Meisner, D. F. Sedbrook, M. Krikorian, J. Chen, A. Sattler, M. E. Carnes, C. B. Murray, M. Steigerwald, C. Nuckolls, *Chem. Sci.* **2012,** *3*, 1007-1014.

6-Bromo-4,4-dimethylthiochromane

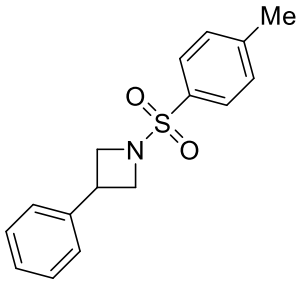


The compound was prepared according to a modified literature procedure.[3] Polyphosphoric acid (2.7 g, 27 mmol, 3.5 eq.) was charged into a pressure tube and flushed with nitrogen. (4-Bromophenyl)(3-methylbut-2-en-1-yl)sulfane (2.0 g, 7.7 mmol, 1.0 equiv.) was dissolved in toluene (5 mL) and added. The brownish mixture was heated to 100 °C for 48 h and the mixture including the solid residues were transferred to a separatory funnel by washing with EtOAc (3 × 10 mL) and water (2 × 10 mL). The aqueous layer was extracted with EtOAc (3 × 25 mL), the combined organic phases were washed with saturated aq. $NaHCO_3$ (20 mL), water (30 mL), brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane), and recrystallized from *i*hexane to obtain the title compound as colorless needles (1.7 g, 6.6 mmol, 86 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.45 (d, J = 2.2 Hz, 1H), 7.13 (dd, J = 8.4, 2.2 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.04 – 2.99 (m, 2H), 1.95 – 1.91 (m, 2H), 1.31 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 144.07, 131.05, 129.43, 128.99, 128.03, 117.31, 77.35, 77.03, 76.72, 37.10, 33.24, 30.02, 23.00.

[3] I. S. Makarov, C. E. Brocklehurst, K. Karaghiosoff, G. Koch, P. Knochel, *Angew. Chem., Int. Ed.* **2017**, *56*, 12774-12777.

3-Phenyl-1-tosylazetidine (3a)

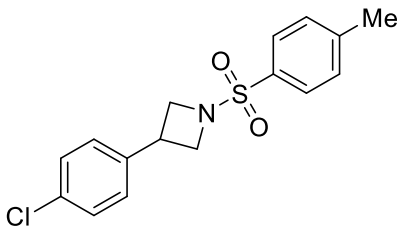


Cyclization was carried out using phenylmagnesium chloride (0.4 mmol, 2.0 equiv.) according to general procedure J, deviating from this, tosylchloride (76 mg, 0.4 mmol, 2.0 equiv.) in THF (1 mL) was added at 0 °C as the electrophile. After warming to room temperature the reaction was stirred for 3 h. After completion, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. The combined organic phases were dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography over silica gel to give pure 3-phenyl-1-tosylazetidine (42 mg, 0.15 mmol, 73 %) as a colorless solid (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.83 – 7.76 (m, 2H), 7.46 – 7.38 (m, 2H), 7.28 – 7.16 (m, 3H), 7.03 – 6.94 (m, 2H), 4.16 (t, J = 8.5 Hz, 2H), 3.81 (dd, J = 8.1, 7.0 Hz, 2H), 3.68 – 3.56 (m, 1H), 2.50 ppm (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 144.3, 140.7, 131.6, 130.0, 128.9, 128.7, 127.5, 127.0, 58.0, 33.4, 21.8 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 155 (24), 103 (100), 92 (20), 78 (58).
HRMS (ESI) m/z: $[M]^+$ calcd for $C_{16}H_{17}NO_2S^+$: 287.0980; found: 288.0987.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2971 (w), 1595 (m), 1494 (m), 1492 (m), 1454 (m), 1338 (s), 1325 (m), 1308 (m), 1292 (m), 1161 (s), 1152 (s), 1121 (m), 1105 (m), 1087 (m), 1072 (m), 1056 (s), 1019 (m), 999 (m), 960 (m), 956 (m), 872 (m), 870 (m), 816 (s), 800 (m), 766 (s), 763 (s), 723 (s), 708 (s), 705 (s), 671 (vs), 667 (vs), 664 (s), 660 (s), 658 (s), 655 (s), 652 cm^{-1} (m).
Melting point: mp = 134 °C.

3-(4-Chlorophenyl)-1-tosylazetidine (3b)

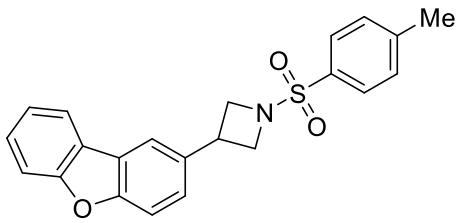


Cyclization was carried out using (4-chlorophenyl)magnesium bromide (0.4 mmol, 2.0 equiv.) according to general procedure J, deviating from this, tosylchloride (76 mg, 0.4 mmol, 2.0 equiv.) in THF (1 mL) was added at 0 °C as the electrophile. After warming to room temperature the reaction was stirred for 3 h. After completion, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. The combined organic phases were dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography over silica gel to give pure 3-(4-chlorophenyl)-1-tosylazetidine (42 mg, 0.13 mmol, 65 %) as a colorless solid (hexane/EtOAc 8.5:1.5).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.78 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 8.4 Hz, 2H), 4.14 (t, J = 8.4 Hz, 2H), 3.79 – 3.71 (m, 2H), 3.63 – 3.52 (m, 1H), 2.50 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 144.35, 139.12, 133.15, 131.23, 129.90, 128.88, 128.58, 128.23, 77.36, 77.05, 76.73, 57.76, 32.63, 21.67.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 140 (33), 138 (100), 103 (25).
HRMS (ESI) m/z: $[M]^+$ calcd for: $C_9H_9ClN^+$:166.0424 found: 166.0416.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2966 (w), 2950 (w), 2921 (w), 2884 (w), 1729 (vw), 1598 (w), 1493 (m), 1475 (w), 1453 (w), 1414 (w), 1401 (w), 1377 (vw), 1339 (vs), 1306 (m), 1297 (m), 1240 (w), 1225 (vw), 1208 (vw), 1174 (m), 1151 (vs), 1114 (m), 1093 (s), 1056 (m), 1038 (w), 1023 (m), 1013 (s), 980 (w), 960 (m), 864 (m), 836 (w), 814 (s), 766 (w), 711 (m).
Melting point: mp = 123 °C.

3-(Dibenzo[b,d]furan-2-yl)-1-tosylazetidine (3c)

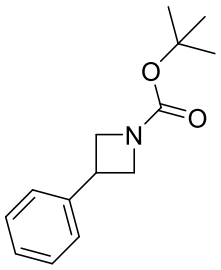


Cyclization was carried out using dibenzo[b,d]furan-2-ylmagnesium bromide lithium chloride (0.4 mmol, 2.0 equiv.) according to general procedure J, deviating from this, tosylchloride (76 mg, 0.4 mmol, 2.0 equiv.) in THF (1 mL) was added at 0 °C as the electrophile. After warming to room temperature the reaction was stirred for 3 h. After completion, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. The combined organic phases were dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography over silica gel to give pure 3-(dibenzo[b,d]furan-2-yl)-1-tosylazetidine (39 mg, 0.10 mmol, 51 %) as a yellow solid (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.84 (dd, J = 7.6, 3.4 Hz, 3H), 7.55 (d, J = 8.7 Hz, 2H), 7.46 (dd, J = 7.6, 5.4 Hz, 3H), 7.41 (d, J = 8.7 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.07 (dd, J = 8.7, 1.8 Hz, 1H), 4.25 (t, J = 8.3 Hz, 2H), 3.93 – 3.87 (m, 1H), 3.79 (p, J = 8.3 Hz, 1H), 2.54 (s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 156.58, 155.34, 144.26, 135.23, 131.39, 129.95, 128.73, 127.51, 126.16, 124.62, 123.75, 122.82, 120.54, 118.66, 111.82, 111.72, 77.35, 77.03, 76.71, 58.54, 33.29, 21.72.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 195 (15), 194 (100), 165 (18).
HRMS (ESI) m/z: $[M]^+$ calcd for $C_{15}H_{12}NO^+$: 222.0919; found: 222.0914.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2950 (w), 2919 (w), 2888 (w), 2359 (vw), 1931 (vw), 1898 (vw), 1731 (vw), 1651 (vw), 1594 (w), 1480 (m), 1447 (m), 1430 (w), 1397 (w), 1382 (w), 1371 (w), 1343 (s), 1319 (m), 1305 (m), 1292 (w), 1260 (w), 1244 (w), 1230 (w), 1200 (m), 1186 (w), 1174 (m), 1156 (vs), 1143 (s), 1123 (m), 1111 (w), 1102 (m), 1088 (s), 1073 (s), 1058 (m), 1020 (m), 1007 (w), 989 (w), 957 (m), 941 (w), 887 (w), 875 (w), 851 (w), 841 (m), 823 (s), 802 (m), 782 (w), 770 (m), 758 (s), 733 (w), 713 (s).
Melting point: mp = 144 °C

***tert*-Butyl 3-phenylazetidine-1-carboxylate (3d)**

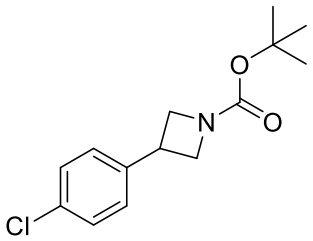


Cyclization was carried out using phenylmagnesium chloride (0.4 mmol, 2.0 equiv.) according to general procedure J, deviating from this, Boc_2O (87 mg, 0.4 mmol, 2.0 equiv.) in THF (1 mL) was added at 0 °C as the electrophile. After warming to room temperature the reaction was stirred for 3 h. After completion, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. The combined organic phases were dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography over silica gel to give pure tert-butyl 3-phenylazetidine-1-carboxylate (32 mg, 0.14 mmol, 69 %) as a colorless oil (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.38 – 7.30 (m, 4H), 7.29 – 7.27 (m, 1H), 4.33 (t, J = 8.7 Hz, 2H), 3.98 (t, J = 8.7 Hz, 2H), 3.73 (tt, J = 8.7, 6.1 Hz, 1H), 1.47 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 156.55, 142.41, 128.86, 127.10, 126.91, 79.65, 77.48, 77.16, 76.84, 33.63, 28.57.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 104 (100), 103 (22), 91 (17), 78 (29).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_{10}NO_2^+$: 176.0712; found: 176.0705.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2884 (w), 1699 (vs), 1605 (vw), 1495 (w), 1480 (w), 1455 (w), 1391 (s), 1365 (s), 1354 (m), 1296 (w), 1283 (vw), 1254 (w), 1161 (m), 1127 (s), 1085 (w), 1031 (vw), 965 (w), 908 (w), 860 (w), 774 (w), 756 (m).

***tert*-Butyl 3-(4-chlorophenyl)azetidine-1-carboxylate (3e)**

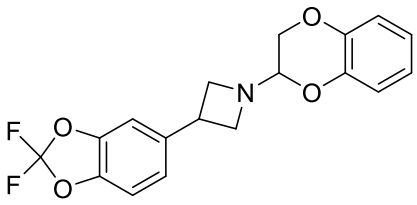


Cyclization was carried out using (4-chlorophenyl)magnesium bromide (0.4 mmol, 2.0 equiv.) according to general procedure J, deviating from this, Boc_2O (87 mg, 0.4 mmol, 2.0 equiv.) in THF (1 mL) was added at 0 °C as the electrophile. After warming to room temperature the reaction was stirred for 3 h. After completion, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. The combined organic phases were dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography over silica gel to give pure *tert*-butyl 3-phenylazetidine-1-carboxylate (37 mg, 0.14 mmol, 69 %) as a colorless oil (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.32 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 8.3 Hz, 2H), 4.32 (t, J = 8.7 Hz, 1H), 3.92 (dd, J = 8.7, 6.0 Hz, 2H), 3.69 (tt, J = 8.7, 6.0 Hz, 1H), 1.46 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 156.36, 140.78, 132.74, 128.86, 128.18, 79.69, 77.35, 77.04, 76.72, 32.98, 28.42.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 140 (17), 138 (61), 125 (17), 57 (100), 41 (14).
HRMS (ESI) m/z: $[M]^+$ calcd for $C_{14}H_{18}ClNO_2$: 267.1026; found: 267.1036.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2885 (w), 2362 (vw), 1699 (vs), 1598 (vw), 1494 (m), 1478 (w), 1457 (w), 1417 (m), 1391 (s), 1366 (m), 1338 (w), 1297 (w), 1254 (w), 1160 (m), 1132 (s), 1094 (m), 1014 (w), 967 (w), 908 (w), 859 (w), 822 (m), 774 (w), 762 (w), 715 (vw).

3-(2,2-Difluorobenzo[d][1,3]dioxol-5-yl)-1-(2,3-dihydrobenzo[b][1,4]dioxin-2-yl)azetidine (3f)



Cyclization was carried out using (2,2-difluorobenzo[d][1,3]dioxol-5-yl)magnesium bromide (0.4 mmol, 2.0 equiv.) according to general procedure J, deviating from this, 2-bromo-2,3-dihydrobenzo[b][1,4]dioxine (86 mg, 0.4 mmol, 2.0 equiv.) in THF (1 mL) was added at 0 °C as the electrophile. After warming to room temperature the reaction was stirred for 3 h. After completion, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. The combined organic phases were dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography over silica gel (hexane/EtOAc 8:2) to obtain the title compound as a colorless oil (43 mg, 0.12 mmol, 61 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.16 (d, *J* = 1.6 Hz, 1H), 7.06 – 6.97 (m, 2H), 6.79 – 6.75 (m, 1H), 6.08 – 6.01 (m, 2H), 4.29 – 4.18 (m, 6H), 3.87 – 3.79 (m, 1H), 3.74 (t, *J* = 6.2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 147.12, 144.14, 143.96, 142.52, 139.14, 136.21, 122.17, 117.57, 109.22, 108.29, 105.25, 100.82, 77.35, 77.03, 76.71, 64.78, 64.22, 60.03, 35.03.

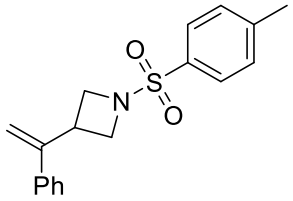
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -50.07.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 347 (21), 163 (100), 107 (19), 79 (10), 43 (10).

HRMS (EI): for: $C_{18}H_{15}F_2NO_4$ calc. [M^+]: 347.0969; found: 347.0967.

IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2850 (w), 1622 (w), 1587 (w), 1503 (s), 1481 (m), 1460 (w), 1384 (vw), 1344 (vw), 1306 (m), 1277 (m), 1235 (s), 1217 (vs), 1184 (m), 1146 (s), 1125 (s), 1067 (s), 1035 (m), 971 (w), 925 (m), 904 (w), 888 (m), 864 (w), 830 (m), 795 (m), 746 (m), 719 (w), 702 (m).

3-(1-Phenylvinyl)-1-tosylazetidine (3i)

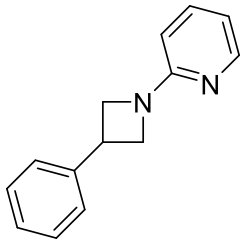


Cyclization was carried out using (1-phenylvinyl) magnesium bromide (0.4 mmol, 2.0 equiv.) according to general procedure J, deviating from this tosylchloride (76 mg, 0.4 mmol, 2.0 equiv.) in THF (1 mL) was added at 0 °C as the electrophile. After warming to room temperature the reaction was stirred for 3 h. After completion, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. The combined organic phases were dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography over silica gel (hexane/EtOAc 9:1) to obtain the title compound as a yellow oil (27 mg, 0.09 mmol, 43 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.72 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.31 – 7.27 (m, 3H), 7.16 (dd, J = 7.6, 1.9 Hz, 2H), 5.36 (s, 1H), 4.89 (s, 1H), 4.10 – 3.95 (m, 2H), 3.73 – 3.64 (m, 3H), 2.46 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 146.71, 144.21, 139.24, 131.61, 129.87, 128.69, 128.57, 128.14, 125.86, 112.44, 77.48, 77.16, 76.84, 55.69, 32.25, 21.78.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 313 (11), 206 (34), 104 (19), 103 (100).
HRMS (EI): for: $C_{18}H_{19}NO_2S$ calc. [M^+]: 313.1136; found: 313.1131.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2958 (vw), 2924 (vw), 2875 (vw), 1629 (vw), 1597 (w), 1574 (vw), 1495 (w), 1474 (vw), 1446 (w), 1400 (vw), 1342 (s), 1304 (m), 1291 (w), 1262 (vw), 1185 (w), 1156 (vs), 1119 (m), 1092 (s), 1064 (m), 1029 (m), 1019 (w), 905 (m), 816 (m), 777 (m), 722 (m), 707 (m), 673 (s).

2-(3-Phenylazetidin-1-yl)pyridine (7a)

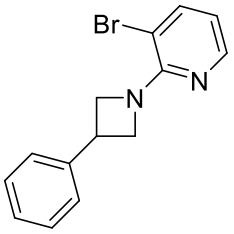


Using phenylmagnesium chloride (0.4 mmol, 2.0 equiv.) and 2-fluoropyridine (58 mg, 0.6 mmol, 3.0 equiv.) according to general procedure J, yielded **7a** (34 mg, 0.16 mmol, 80 %) as colorless oil (hexane/EtOAc 9:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) = 8.19 (ddd, J = 5.1, 2.0, 0.9 Hz, 1H), 7.47 (ddd, J = 8.7, 7.2, 1.9 Hz, 1H), 7.41 – 7.32 (m, 4H), 7.29 – 7.23 (m, 1H), 6.63 (ddd, J = 7.2, 5.1, 1.1 Hz, 1H), 6.35 (dd, J = 8.4, 1.1 Hz, 1H), 4.45 (t, J = 8.1 Hz, 2H), 4.07 (dd, J = 7.8, 6.0 Hz, 2H), 3.95 ppm (ddd, J = 14.4, 8.4, 6.0 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 160.9, 148.3, 142.8, 137.2, 128.8, 127.1, 127.0, 113.1, 106.1, 58.1, 35.0 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 210.1 (37), 181.1 (14), 104.1 (100), 79.0 (65)
HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{14}N_2$: 210.1157; found: 210.1148.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3061 (w), 3026 (w), 3008 (w), 2951 (w), 2862 (w), 1756 (w), 1589 (s), 1557 (m), 1490 (s), 1472 (vs), 1454 (m), 1436 (vs), 1374 (m), 1351 (m), 1301 (m), 1294 (m), 1273 (m), 1147 (s), 1081 (m), 1062 (w), 1025 (m), 977 (m), 947 (w), 907 (w), 880 (w), 846 (w), 772 (s), 756 (s), 735 (s), 723 (m), 715 (m), 697 (vs), 675 (m), 673 (m), 669 (m), 667 (m), 661 (m), 657 (m), 655 cm^{-1} (w).

3-Bromo-2-(3-phenylazetidin-1-yl)pyridine (7b)

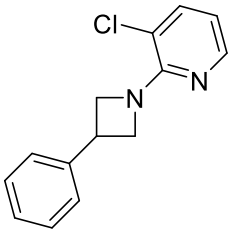


Using phenylmagnesium chloride (0.4 mmol, 2.0 equiv.) and 3-bromo-2-fluoropyridine (106 mg, 0.6 mmol, 3.0 equiv.) according to general procedure J, yielded **7b** (43 mg, 0.15 mmol, 75 %) as yellow solid (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.15 (dd, J = 4.8, 1.6 Hz, 1H), 7.65 (dd, J = 7.7, 1.5 Hz, 1H), 7.42 – 7.32 (m, 4H), 7.30 – 7.21 (m, 1H), 6.58 (dd, J = 7.6, 4.8 Hz, 1H), 4.69 (t, J = 8.5 Hz, 2H), 4.30 (dd, J = 8.4, 6.4 Hz, 2H), 3.87 ppm (tt, J = 8.6, 6.4 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 157.45, 146.5, 142.7, 141.8, 128.8, 127.1, 126.9, 115.4, 104.7, 60.1, 34.6 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 288.0 (9), 156.9 (25), 104.1 (100).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{13}BrN_2$: 288.0262; found: 288.0259.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3058 (w), 3026 (w), 2955 (w), 2928 (w), 2870 (w), 1580 (s), 1540 (w), 1455 (s), 1443 (vs), 1434 (s), 1337 (m), 1290 (m), 1247 (m), 1153 (w), 1077 (m), 1024 (m), 1007 (m), 957 (m), 777 (m), 747 (s), 698 cm^{-1} (s).

3-Chloro-2-(3-phenylazetidin-1-yl)pyridine (7c)

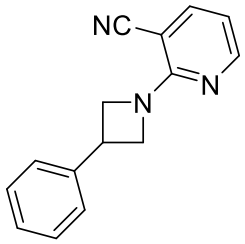


Using phenylmagnesium chloride (0.4 mmol, 2.0 equiv.) and 3-chloro-2-fluoropyridine (79 mg, 0.6 mmol, 3.0 equiv.) according to general procedure J, yielded **7c** (31 mg, 0.13 mmol, 65 %) as yellow solid (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.43 – 7.31 (m, 5H), 7.31 – 7.22 (m, 1H), 6.62 (d, J = 7.5 Hz, 1H), 6.19 (d, J = 8.1 Hz, 1H), 4.46 (t, J = 8.3 Hz, 2H), 4.08 (dd, J = 8.1, 6.0 Hz, 2H), 3.94 ppm (tt, J = 8.5, 5.9 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 160.7, 150.2, 142.5, 139.4, 128.9, 127.1, 127.0, 112.1, 103.9, 58.2, 34.8 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 244.0 (7), 104.1 (100).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{13}ClN_2$: 244.0767; found: 244.0760.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3080 (vw), 3056 (w), 3022 (w), 2957 (w), 2924 (w), 2871 (w), 2852 (m), 1584 (s), 1544 (m), 1484 (s), 1463 (vs), 1449 (vs), 1436 (s), 1413 (s), 1409 (s), 1400 (s), 1375 (s), 1352 (m), 1293 (s), 1282 (m), 1277 (m), 1254 (m), 1177 (m), 1148 (s), 1112 (s), 1091 (m), 1072 (m), 1062 (m), 1043 (m), 1030 (m), 973 (s), 949 (m), 912 (m), 894 (w), 771 (vs), 762 (vs), 725 (s), 704 (vs), 652 cm^{-1} (m).
Melting point: mp = 66 °C.

2-(3-Phenylazetidin-1-yl)nicotinonitrile (7d)

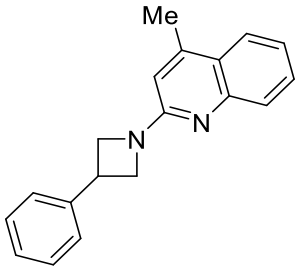


Using phenylmagnesium chloride (0.4 mmol, 2.0 equiv.) and 2-fluoronicotinonitrile (73 mg, 0.6 mmol, 3.0 equiv.) according to general procedure J, yielded **7d** (35 mg, 0.16 mmol, 75 %) as yellow solid (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.30 (dd, J = 4.9, 1.9 Hz, 1H), 7.68 (dd, J = 7.7, 1.9 Hz, 1H), 7.37 (d, J = 5.0 Hz, 4H), 7.33 – 7.24 (m, 1H), 6.64 (dd, J = 7.7, 4.9 Hz, 1H), 4.76 (t, J = 8.8 Hz, 2H), 4.38 (dd, J = 8.9, 6.2 Hz, 2H), 3.98 ppm (tt, J = 8.8, 6.2 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 159.7, 152.7, 143.1, 142.0, 128.9, 127.2, 126.9, 117.9, 112.5, 90.2, 59.2, 34.7 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 235.1 (5), 104.1 (100), 78.0 (27).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{15}H_{13}N_3$: 235.1109; found: 235.1100.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3061 (vw), 3028 (w), 2956 (w), 2876 (w), 2213 (m), 1582 (vs), 1553 (vs), 1489 (s), 1462 (vs), 1445 (vs), 1354 (w), 1294 (m), 1278 (w), 1256 (m), 1243 (s), 1184 (w), 1155 (w), 1087 (w), 1048 (w), 1025 (w), 953 (w), 907 (w), 788 (m), 756 (vs), 698 (s), 652 cm^{-1} (w).
Melting point: mp = 126 °C.

4-Methyl-2-(3-phenylazetidin-1-yl)quinoline (7e)

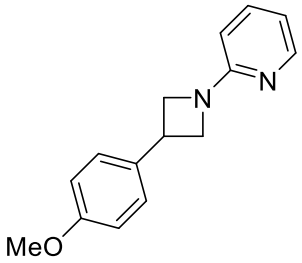


Phenylmagnesium chloride (0.4 mmol, 2.0 equiv.) and 2-chloro-4-methylquinoline (106 mg, 0.6 mmol, 3.0 equiv.) were used according to general procedure J. After addition of the electrophile this reaction was stirred overnight at 100 °C, yielded **7e** (38 mg, 0.14 mmol, 70 %) as yellow solid (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.82 – 7.74 (m, 2H), 7.58 – 7.52 (m, 1H), 7.42 – 7.38 (m, 2H), 7.38 – 7.33 (m, 2H), 7.29 – 7.23 (m, 2H), 6.49 (d, J = 1.3 Hz, 1H), 4.60 (t, J = 8.3 Hz, 2H), 4.23 (t, J = 8.0, 6.0 Hz, 2H), 3.98 (ddd, J = 14.5, 8.5, 6.0 Hz, 1H), 2.61 ppm (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 158.8, 148.1, 145.2, 142.8, 129.6, 129.5, 128.8, 127.1, 127.0, 123.8, 123.7, 122.2, 109.1, 58.0, 34.8, 19.1 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 274.1 (25), 170.1 (25), 143.1 (100), 115.1 (12).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{18}N_2$: 274.1470; found: 274.1477.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3050 (w), 2957 (w), 2924 (m), 2859 (m), 1612 (s), 1552 (s), 1503 (s), 1493 (s), 1479 (s), 1468 (s), 1447 (m), 1424 (s), 1412 (s), 1378 (m), 1356 (m), 1341 (m), 1299 (m), 1278 (m), 1260 (m), 1225 (m), 1182 (m), 1154 (m), 1091 (m), 1075 (m), 1030 (m), 1025 (m), 946 (w), 918 (w), 849 (s), 761 (s), 751 (vs), 708 (m), 702 (vs), 690 cm^{-1} (s).
Melting point: mp = 126 °C.

2-(3-(4-Methoxyphenyl)azetidin-1-yl)pyridine (7f)

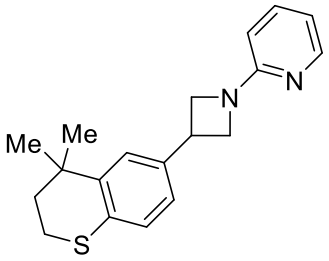


Using (4-methoxyphenyl)magnesium bromide (0.4 mmol, 2.0 equiv.) and 2-fluoropyridine (58 mg, 0.6 mmol, 3.0 equiv.) according to general procedure J, yielded **7f** (25 mg, 0.10 mmol, 50 %) as light yellow solid (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.18 (ddd, J = 5.1, 1.9, 0.9 Hz, 1H), 7.47 (ddd, J = 8.7, 7.1, 1.9 Hz, 1H), 7.34 – 7.24 (m, 2H), 6.93 – 6.85 (m, 2H), 6.62 (ddd, J = 7.2, 5.0, 1.0 Hz, 1H), 6.34 (dd, J = 8.3, 1.1 Hz, 1H), 4.43 (t, J = 8.1 Hz, 2H), 4.02 (dd, J = 7.7, 6.0 Hz, 2H), 3.90 (tt, J = 8.4, 5.9 Hz, 1H), 3.80 ppm (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 160.8, 158.6, 148.2, 137.3, 134.9, 128.1, 114.2, 113.0, 106.2, 58.4, 55.5, 34.3 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 240.1 (5), 134.1 (100), 119.0 (20).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{14}N_2O$: 240.1263; found: 240.1251.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3032 (vw), 3003 (w), 2951 (w), 2862 (w), 2833 (w), 1590 (s), 1557 (m), 1513 (s), 1490 (s), 1471 (vs), 1435 (vs), 1372 (m), 1301 (m), 1295 (m), 1273 (m), 1244 (vs), 1177 (s), 1147 (s), 1114 (m), 1081 (m), 1034 (s), 1028 (s), 1011 (m), 977 (m), 953 (w), 885 (w), 826 (s), 804 (m), 802 (m), 772 (s), 736 (s), 722 (m), 720 (m), 719 (m), 712 cm^{-1} (m).
Melting point: mp = 57 °C.

2-(3-(4,4-Dimethylthiochroman-6-yl)azetidin-1-yl)pyridine (7g)

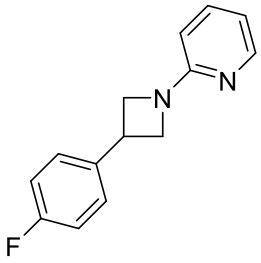


Using (4,4-dimethylthiochroman-6-yl)magnesium bromide (0.4 mmol, 2.0 equiv.) and 2-fluoropyridine (58 mg, 0.6 mmol, 3.0 equiv.) according to general procedure J, yielded **7g** (25 mg, 0.08 mmol, 40 %) as colorless solid (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.18 (ddd, J = 5.0, 2.0, 0.9 Hz, 1H), 7.47 (ddd, J = 8.8, 7.1, 1.9 Hz, 1H), 7.30 (d, J = 1.8 Hz, 1H), 7.12 – 7.05 (m, 2H), 6.63 (ddd, J = 7.2, 5.1, 1.0 Hz, 1H), 6.34 (d, J = 8.4 Hz, 1H), 4.42 (t, J = 8.1 Hz, 2H), 4.02 (dd, J = 7.8, 6.1 Hz, 2H), 3.87 (tt, J = 8.5, 6.1 Hz, 1H), 3.07 – 2.96 (m, 2H), 2.01 – 1.92 (m, 2H), 1.33 ppm (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 160.8, 148.2, 142.2, 138.4, 137.3, 130.3, 127.1, 125.5, 124.6, 113.0, 106.2, 58.2, 37.9, 34.9, 33.2, 30.4, 23.2 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 310.1 (1), 204.1 (100), 189.1 (39), 156.1 (15).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{22}N_2S$: 310.1504; found: 310.1501.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2957 (m), 2931 (m), 2856 (w), 1592 (s), 1558 (m), 1490 (s), 1471 (vs), 1435 (vs), 1362 (m), 1301 (m), 1287 (m), 1272 (m), 1251 (m), 1213 (m), 1146 (s), 1115 (m), 1057 (s), 980 (m), 884 (m), 815 (m), 772 (s), 734 (s), 710 (m).

2-(3-(4-Fluorophenyl)azetidin-1-yl)pyridine (7h)

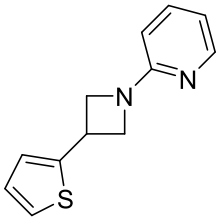


Using (4-fluorophenyl)magnesium bromide (0.4 mmol, 2.0 equiv.) and 2-fluoropyridine (58 mg, 0.6 mmol, 3.0 equiv.) according to general procedure J, yielded **7h** (33 mg, 0.14 mmol, 72 %) as light yellow oil (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.18 (ddd, J = 5.1, 1.9, 0.9 Hz, 1H), 7.47 (ddd, J = 8.4, 7.2, 1.9 Hz, 1H), 7.39 – 7.29 (m, 2H), 7.08 – 6.98 (m, 2H), 6.63 (ddd, J = 7.2, 5.1, 1.0 Hz, 1H), 6.34 (dt, J = 8.3, 1.0 Hz, 1H), 4.44 (t, J = 8.1 Hz, 2H), 4.01 (dd, J = 7.6, 5.9 Hz, 2H), 3.91 ppm (tt, J = 8.4, 6.0 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 161.9 (d, J = 245.1 Hz), 160.9, 148.4, 138.6 (d, J = 3.2 Hz), 137.2, 128.6 (d, J = 8.0 Hz), 115.6 (d, J = 21.4 Hz), 113.2, 106.1, 58.3 (d, J = 1.0 Hz), 34.4 ppm.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -115.99 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 228.1 (18), 122.0 (100), 79.0 (40).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{13}FN_2$: 228.1063; found: 228.1053.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3069 (vw), 3046 (vw), 3011 (vw), 2956 (w), 2863 (w), 1756 (w), 1599 (s), 1592 (s), 1558 (m), 1511 (s), 1491 (s), 1473 (vs), 1437 (vs), 1371 (m), 1299 (m), 1273 (w), 1222 (s), 1159 (m), 1148 (m), 1103 (w), 1082 (w), 1053 (w), 1030 (w), 978 (w), 955 (w), 831 (s), 817 (m), 774 (s), 737 (m), 718 cm^{-1} (w).

2-(3-(Thiophen-2-yl)azetidin-1-yl)pyridine (7i)

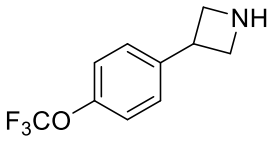


Using thiophen-2-ylmagnesium bromide (0.4 mmol, 2.0 equiv.) and 2-Fluoropyridine (58 mg, 0.6 mmol, 3.0 equiv.) according to general procedure J, yielded **7i** (28 mg, 0.13 mmol, 65 %) as light yellow solid (hexane/EtOAc 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.18 (ddd, J = 5.1, 2.0, 1.0 Hz, 1H), 7.48 (ddd, J = 8.3, 7.1, 1.9 Hz, 1H), 7.23 – 7.20 (m, 1H), 6.97 (d, J = 3.4 Hz, 2H), 6.64 (ddd, J = 7.1, 5.1, 1.0 Hz, 1H), 6.34 (d, J = 8.3 Hz, 1H), 4.47 (t, J = 7.9 Hz, 2H), 4.22 (tt, J = 8.1, 6.2 Hz, 1H), 4.07 ppm (dd, J = 7.6, 6.2 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 160.8, 148.2, 146.2, 137.3, 127.2, 124.4, 124.2, 113.3, 106.3, 59.3, 30.8 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 216.0 (12), 110.0 (100).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{12}H_{12}N_2S$: 216.0721; found: 216.0714.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2955 (w), 2923 (w), 2855 (w), 1598 (s), 1589 (s), 1559 (m), 1489 (s), 1471 (vs), 1435 (vs), 1377 (m), 1360 (m), 1301 (m), 1147 (s), 1079 (m), 1049 (m), 1024 (m), 976 (m), 843 (m), 823 (m), 772 (vs), 735 (s), 696 (s), 694 cm^{-1} (s).

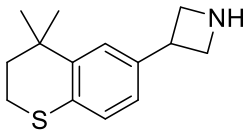
3-(4-(Trifluoromethoxy)phenyl)azetidine (9b/3h)



According to general procedure K, 2,3-dibromopropan-1-amine hydrobromide **1** (2.24 g, 8.00 mmol, 1.00 equiv.) was suspended in toluene (40 mL). *n*BuLi (24 mmol, 3.0 equiv.) was added dropwise at -78 °C and the mixture was stirred for 1.5 h. Then (4-(trifluoromethoxy)phenyl)magnesium bromide (16 mmol, 2.0 equiv.) was added. After 1 h the dry ice acetone bath was removed, and the reaction was stirred for an additional 4 h. Extraction and evaporation of the solvent *in vacuo* afforded the title compound as a brown oil (1.34 g, 4.9 mmol, 62 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.41 – 7.37 (m, 2H), 7.23 – 7.18 (m, 2H), 4.14 (t, J = 7.1 Hz, 2H), 3.99 (t, J = 7.1 Hz, 2H), 3.73 (tt, J = 7.1, 3.9 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 148.28, 139.57, 128.33, 121.35, 53.70, 37.73.

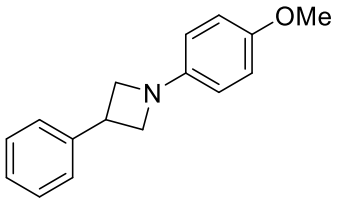
3-(4,4-Dimethylthiochroman-6-yl)azetidine (9d/3g)



According to general procedure K, 2,3-dibromopropan-1-amine hydrobromide **1** (0.48 g, 1.6 mmol, 1.00 equiv.) was suspended in toluene (40 mL). *n*BuLi (4.8 mmol, 3.0 equiv.) was added dropwise at -78 °C and the mixture was stirred for 1.5 h. Then (4,4-dimethylthiochroman-6-yl)magnesium bromide (3.2 mmol, 2.0 equiv.) was added. After 1 h the dry ice acetone bath was removed, and the reaction was stirred for an additional 4 h. Extraction and evaporation of the solvent *in vacuo* afforded the title compound as a brown oil (0.23 g, 1.0 mmol, 62 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.24 (d, J = 1.5 Hz, 1H), 7.06 – 7.04 (m, 2H), 3.93 (t, J = 5.9 Hz, 2H), 3.83 (t, J = 5.9 Hz, 2H), 3.74 (ddd, J = 6.6, 4.2, 2.5 Hz, 1H), 3.04 – 2.99 (m, 2H), 1.95 (ddd, J = 6.1, 4.0, 2.9 Hz, 2H), 1.33 (s, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 142.13, 129.17, 128.36, 126.88, 125.26, 124.56, 77.48, 77.16, 76.84, 68.12, 54.76, 39.66, 37.89, 33.20, 30.38, 25.75, 23.19.

1-(4-Methoxyphenyl)-3-phenylazetidine (10a)

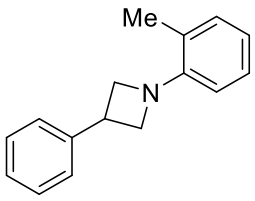


According to general procedure L, 3-phenylazetidine **9a** (37 mg, 0.28 mmol, 1.4 equiv.), 4-bromoanisole (25 µL, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (1.7 mg, 1 mol%), Brettphos (1.1 mg, 1 mol%), and KO^{t}Bu (31 mg, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 18 h. The now brownish mixture was cooled to rt and filtered over celite 545. After the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo.* The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) to obtain the title compound as a colorless solid (39 mg, 0.16 mmol, 82 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40 – 7.31 (m, 4H), 7.25 – 7.22 (m, 1H), 6.88 – 6.81 (m, 2H), 6.53 – 6.46 (m, 2H), 4.26 (t, J = 6.5 Hz, 2H), 3.97 – 3.88 (m, 1H), 3.83 (t, J = 6.5 Hz, 2H), 3.77 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 152.47, 146.87, 142.76, 128.72, 127.21, 126.85, 114.82, 113.00, 77.48, 77.16, 76.84, 60.17, 55.96, 35.41.

LRMS (DEP/EI-Orbitrap): m/z (%): 135 (96), 120 (100), 92 (10).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{16}H_{17}NO$: 239.1310; found: 239.1302.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2921 (vs), 2852 (s), 2721 (vw), 2675 (vw), 2353 (vw), 1730 (w), 1698 (vw), 1692 (vw), 1681 (vw), 1619 (vw), 1604 (vw), 1579 (vw), 1511 (m), 1492 (w), 1478 (w), 1461 (m), 1454 (m), 1441 (w), 1377 (w), 1366 (w), 1333 (w), 1288 (w), 1258 (m), 1237 (m), 1210 (w), 1181 (w), 1175 (w), 1163 (w), 1119 (m), 1087 (m), 1073 (m), 1051 (m), 1035 (m), 1029 (m), 1004 (w), 950 (w), 919 (w), 873 (vw), 822 (m), 799 (w), 789 (w), 762 (m), 749 (w), 741 (w), 722 (w), 709 (m).
Melting point: mp = 87 °C.

3-Phenyl-1-(*o*-tolyl)azetidine (10b)

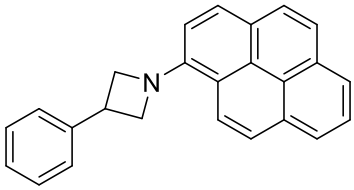


According to general procedure L, 3-phenylazetidine **9a** (37 mg, 0.28 mmol, 1.4 equiv.), 2-bromotoluene (24 µL, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (3.4 mg, 2 mol%), Brettphos (2.1 mg, 2 mol%), and KO^{t}Bu (31 mg, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 0.5 h. The now brownish mixture was cooled to rt and filtered over celite 545. After the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo* the crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) to obtain the title compound as a colorless oil (44 mg, 0.198 mmol, 99 %). Gram-scale synthesis was performed with 3-phenylazetidine **9a** (0.93 g, 7 mmol, 1.4 equiv.), 2-bromotoluene (0.86 g, 5 mmol, 1.0 equiv.), xPhos Pd G3 (85 mg, 2 mol%), Brettphos (54 mg, 2 mol%) and KO^{t}Bu (0.79 g, 7 mmol, 1.4 equiv.), to afford the title compound as a colorless oil (1.06 g, 4.8 mmol, 95 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.42 – 7.31 (m, 4H), 7.28 – 7.22 (m, 1H), 7.13 (td, 7.4, 1.0 Hz, 1H), 7.06 (d, J = 7.4 Hz, 1H), 6.80 (td, J = 7.4, 1.0 Hz, 1H), 6.57 (m, 1H), 4.36 (t, J = 7.2 Hz, 2H), 3.97 – 3.84 (m, 3H), 2.26 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 163.94, 160.22, 142.96, 139.78, 128.79, 127.11, 126.93, 97.46, 97.29, 77.48, 77.16, 76.84, 58.21, 53.32, 35.03.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 120 (23), 119 (100), 78 (11).
HRMS (EI): for $C_{16}H_{17}N$: calc. [M^+]: 223.1361; found: 223.1351.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 3062 (w), 3028 (w), 2954 (m), 2923 (m), 2852 (m), 2726 (vw), 2606 (vw), 2358 (vw), 2340 (vw), 2331 (vw), 2199 (vw), 1940 (vw), 1764 (vw), 1725 (s), 1693 (vw), 1681 (vw), 1673 (vw), 1600 (m), 1579 (w), 1510 (w), 1493 (s), 1477 (m), 1463 (m), 1454 (m), 1438 (m), 1413 (vw), 1401 (vw), 1378 (w), 1366 (w), 1310 (m), 1286 (s), 1272 (s), 1261 (s), 1208 (w), 1133 (m), 1121 (m), 1072 (s), 1051 (m), 1032 (m), 1018 (m), 987 (m), 955 (w), 947 (w), 923 (w), 907 (w), 889 (w), 884 (w), 878 (w), 872 (w), 796 (m), 749 (vs), 715 (m), 698 (s).

3-Phenyl-1-(pyren-1-yl)azetidine (10c)

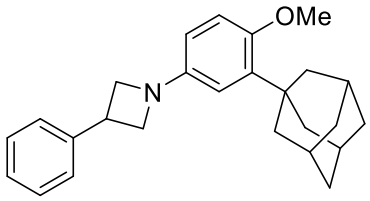


According to general procedure L, 3-phenylazetidine **9a** (37 mg, 0.28 mmol, 1.4 equiv.), 1-bromopyrene (56 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%), and KO^{t}Bu (31 mg, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 1.5 h. The now brownish mixture was cooled to rt and filtered over celite 545. After the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo* the crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) to obtain the title compound as a colorless solid (65 mg, 0.195 mmol, 97 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.19 (d, J = 9.3 Hz, 1H), 8.06 (d, J = 8.4 Hz, 1H), 8.03 (dd, J = 7.4, 4.6 Hz, 2H), 7.96 – 7.88 (m, 3H), 7.83 (d, J = 8.4 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.38 (t, J = 7.4 Hz, 2H), 7.29 (t, J = 7.4 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 4.82 (t, J = 7.8 Hz, 2H), 4.39 (t, J = 7.8 Hz, 2H), 4.14 – 4.05 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 128.90, 127.67, 127.20, 127.12, 126.12, 125.81, 123.55, 122.96, 77.48, 77.16, 76.84, 62.90, 35.70.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 333 (27), 230 (15), 229 (82), 228 (100), 201 (42), 200 (28).
HRMS (EI): for $C_{25}H_{19}N$: calc. [M^+]: 333.1517; found: 333.1510.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 3023 (w), 2952 (w), 2921 (w), 2865 (w), 2848 (m), 1887 (w), 1872 (w), 1726 (w), 1620 (w), 1600 (s), 1540 (w), 1511 (s), 1494 (m), 1478 (s), 1464 (m), 1452 (m), 1436 (s), 1410 (m), 1380 (s), 1359 (m), 1354 (m), 1348 (m), 1302 (s), 1294 (s), 1267 (m), 1238 (m), 1209 (m), 1195 (m), 1176 (m), 1147 (m), 1134 (s), 1086 (m), 1065 (m), 1052 (w), 1032 (w), 1016 (w), 998 (w), 976 (w), 957 (w), 943 (w), 936 (w), 906 (w), 882 (w), 837 (m), 824 (vs), 786 (m), 756 (s), 749 (vs), 710 (s), 696 (vs).
Melting point: mp = 133 °C.

1-(3-(Adamantan-1-yl)-4-methoxyphenyl)-3-phenylazetidine (10d)

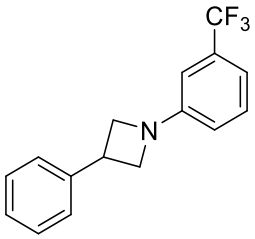


According to general procedure L, 3-phenylazetidine **9a** (37 mg, 0.28 mmol, 1.4 equiv.), 1-(5-bromo-2-methoxyphenyl)adamantane (64 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%), and KO^{t}Bu (31 mg, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 1 h. The now brownish mixture was cooled to rt and filtered over celite 545. After the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo* the crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) to obtain the title compound as a colorless solid (71 mg, 0.19 mmol, 95 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40 – 7.31 (m, 4H), 7.26 – 7.21 (m, 1H), 6.81 (d, J = 8.6 Hz, 1H), 6.45 (d, J = 2.8 Hz, 1H), 6.36 (dd, J = 8.6, 2.8 Hz, 1H), 4.26 (t, J = 7.1 Hz, 2H), 3.96 – 3.87 (m, 1H), 3.84 (t, J = 7.1 Hz, 2H), 3.78 (s, 3H), 2.09 (d, J = 2.6 Hz, 6H), 2.05 (s, 3H), 1.76 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 151.88, 146.47, 142.91, 139.67, 128.68, 127.23, 126.77, 113.31, 111.11, 109.50, 77.48, 77.16, 76.84, 60.06, 55.95, 40.72, 37.27, 37.20, 35.38, 29.26, 1.17.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 373 (10), 270 (20), 269 (100), 184 (19), 175 (13).
HRMS (EI): for $C_{26}H_{31}NO$: calc. [M^+]: 373.2406; found: 373.2398.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2914 (m), 2900 (m), 2885 (m), 2849 (s), 2829 (w), 1728 (w), 1610 (w), 1605 (w), 1575 (m), 1491 (s), 1477 (m), 1460 (m), 1453 (m), 1446 (m), 1439 (m), 1414 (m), 1384 (w), 1377 (w), 1366 (w), 1357 (w), 1334 (m), 1316 (w), 1296 (m), 1287 (m), 1255 (m), 1225 (vs), 1210 (m), 1187 (m), 1179 (w), 1174 (w), 1150 (m), 1129 (m), 1099 (m), 1087 (w), 1061 (m), 1038 (m), 1034 (m), 1024 (m), 1000 (w), 979 (w), 976 (w), 964 (w), 907 (w), 856 (m), 816 (m), 801 (s), 792 (m), 769 (w), 763 (w), 755 (vs), 730 (w).
Melting point: mp = 131 °C.

3-Phenyl-1-(3-(trifluoromethyl)phenyl)azetidine (10e):

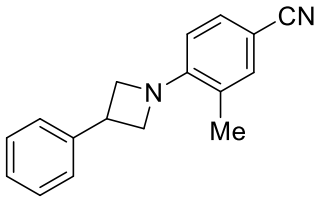


According to general procedure L, 3-phenylazetidine **9a** (37 mg, 0.28 mmol, 1.4 equiv.), 1-bromo-3-(trifluoromethyl)benzene (28 µL, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (1.7 mg, 1 mol%), Brettphos (1.1 mg, 1 mol%), and KO^{t}Bu (31 mg, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 13 h. The now brownish mixture was cooled to rt and filtered over celite 545. After the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo.* The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) to obtain the title compound as a colorless oil (51 mg, 0.18 mmol, 92 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.46 (d, J = 8.4 Hz, 2H), 7.39 – 7.33 (m, 4H), 7.30 – 7.24 (m, 1H), 6.50 (d, J = 8.4 Hz, 2H), 4.43 – 4.26 (m, 2H), 4.05 – 3.90 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 128.90, 127.17, 127.06, 126.47, 126.43, 110.77, 77.48, 77.16, 76.84, 59.30, 35.06.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -60.94.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 173 (100), 172 (69), 145 (29), 104 (26), 78 (12).
HRMS (EI): for $C_{16}H_{14}F_3N$: calc. [M^+]: 277.1078; found: 277.1070.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 3030 (vw), 2923 (w), 2918 (w), 2863 (w), 2847 (w), 2639 (vw), 2357 (vw), 1893 (vw), 1726 (w), 1638 (vw), 1609 (s), 1602 (m), 1581 (w), 1569 (w), 1528 (m), 1493 (w), 1477 (m), 1461 (w), 1454 (w), 1430 (vw), 1381 (m), 1353 (w), 1313 (vs), 1295 (s), 1260 (m), 1216 (w), 1179 (m), 1164 (s), 1150 (m), 1124 (s), 1105 (vs), 1062 (vs), 1047 (s), 1016 (m), 1003 (m), 998 (m), 977 (w), 955 (w), 949 (w), 939 (w), 916 (w), 880 (vw), 872 (vw), 855 (w), 824 (s), 811 (m), 772 (vw), 764 (s), 730 (w), 705 (s), 690 (m).

3-Methyl-4-(3-phenylazetidin-1-yl)benzonitrile (10f)

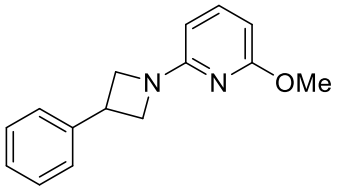


According to general procedure L, 3-phenylazetidine **9a** (37 mg, 0.28 mmol, 1.4 equiv.), 4-bromo-3-methylbenzonitrile (39 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (3.4 mg, 2 mol%), Brettphos (2.1 mg, 2 mol%), and KO^{t}Bu (31 mg, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 1 h. The now brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo.* The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 95:5) to obtain the title compound as a colorless solid (42 mg, 0.17 mmol, 85 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.41 – 7.34 (m, 5H), 7.33 – 7.26 (m, 2H), 6.43 (d, J = 8.4 Hz, 1H), 4.49 (t, J = 8.0 Hz, 2H), 4.08 (t, J = 8.0 Hz, 2H), 3.91 (tt, J = 8.0, 6.0 Hz, 1H), 2.27 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 153.24, 142.06, 135.09, 131.29, 128.92, 127.25, 126.98, 124.53, 120.48, 112.53, 100.72, 77.48, 77.16, 76.84, 60.98, 34.93, 19.63.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 144 (37), 143 (100), 116 (17), 104 (22).
HRMS (EI): for $C_{17}H_{16}N_2$: calc. [M^+]: 248.1313; found: 248.1305.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2957 (w), 2923 (w), 2866 (w), 2852 (w), 2616 (vw), 2215 (s), 2165 (vw), 2161 (vw), 1736 (vw), 1723 (vw), 1599 (vs), 1561 (w), 1530 (vw), 1502 (vs), 1473 (s), 1453 (m), 1412 (m), 1374 (m), 1342 (s), 1334 (s), 1300 (m), 1289 (m), 1264 (w), 1223 (s), 1163 (m), 1156 (m), 1140 (m), 1116 (w), 1093 (m), 1082 (m), 1057 (m), 1033 (w), 1017 (m), 998 (m), 954 (w), 944 (w), 918 (w), 888 (w), 881 (m), 859 (vw), 817 (s), 757 (s), 724 (w), 698 (s).
Melting point: mp = 79 °C.

2-Methoxy-6-(3-phenylazetidin-1-yl)pyridine (10g):

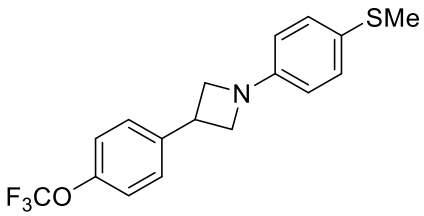


According to general procedure L, 3-phenylazetidine **9a** (37 mg, 0.28 mmol, 1.4 equiv.), 2-bromo-6-methoxypyridine (25 µL, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%), and KO*t*Bu (31 mg, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 0.5 h. The now brownish mixture was cooled to rt and filtered over celite 545. After the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo* the crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) to obtain the title compound as a colorless solid (47 mg, 0.197 mmol, 99 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.43 – 7.32 (m, 5H), 7.29 – 7.21 (m, 1H), 6.07 (d, *J* = 7.9 Hz, 1H), 5.90 (d, *J* = 7.9 Hz, 1H), 4.41 (t, *J* = 8.2 Hz, 2H), 4.03 (t, *J* = 8.2 Hz, 2H), 3.96 – 3.89 (m, 1H), 3.87 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 163.93, 160.22, 142.96, 139.78, 128.78, 127.10, 126.93, 97.46, 97.29, 77.48, 77.16, 76.84, 58.21, 53.31, 35.03.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 240 (13), 136 (62), 135 (26), 109 (100), 80 (11).
HRMS (EI): for $C_{15}H_{16}N_2O$: calc. [M^+]: 240.1263; found: 240.1255.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 3010 (vw), 2963 (w), 2928 (w), 2859 (w), 1727 (w), 1643 (vw), 1589 (s), 1574 (s), 1512 (w), 1486 (m), 1472 (s), 1455 (s), 1449 (s), 1411 (s), 1379 (m), 1350 (w), 1292 (m), 1281 (w), 1261 (s), 1250 (s), 1218 (m), 1204 (w), 1178 (w), 1138 (s), 1090 (w), 1080 (m), 1070 (w), 1021 (s), 978 (w), 960 (w), 916 (w), 839 (vw), 829 (vw), 782 (vs), 758 (s), 734 (m), 702 (vs), 679 (w).
Melting point: mp = 99 °C.

1-(4-(Methylthio)phenyl)-3-(4-(trifluoromethoxy)phenyl)azetidine (10h)

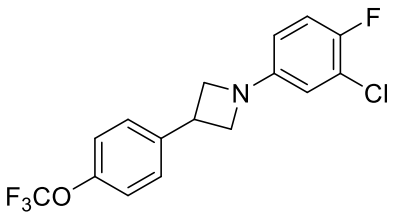


According to general procedure L, 3-(4-(trifluoromethoxy)phenyl)azetidine **9b** (61 mg, 0.28 mmol, 1.4 equiv.), (4-bromophenyl)(methyl)sulfane (41 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (51 mg, 3 mol%), Brettphos (32 mg, 3 mol%), and KO^{t}Bu (31 mg, 0.28 mmol, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 2 h. The now brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 97:3) to obtain the title compound as a colorless solid (58 mg, 0.17 mmol, 86 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 7.20 (d, J = 8.3 Hz, 2H), 6.58 (s, 2H), 4.35 (t, J = 6.7 Hz, 2H), 4.02 – 3.95 (m, 1H), 3.92 (t, J = 6.7 Hz, 2H), 2.44 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 148.26, 130.76, 128.51, 121.44, 60.00, 34.52, 18.75.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -57.92.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 339 (31), 151 (100), 136 (35).
HRMS (EI): for: $C_{17}H_{16}F_3NOS$ calc. [M^+]: 339.0905; found: 339.0901.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2921 (w), 2853 (w), 1597 (w), 1508 (w), 1495 (m), 1479 (m), 1436 (w), 1345 (w), 1330 (m), 1322 (m), 1257 (vs), 1218 (s), 1188 (s), 1153 (s), 1129 (s), 1106 (s), 1095 (s), 1082 (s), 1062 (s), 1012 (s), 968 (w), 953 (w), 919 (w), 848 (m), 806 (vs), 739 (w), 712 (w), 703 (w).
Melting point: mp = 109 °C.

1-(3-Chloro-4-fluorophenyl)-3-(4-(trifluoromethoxy)phenyl)azetidine (10i)

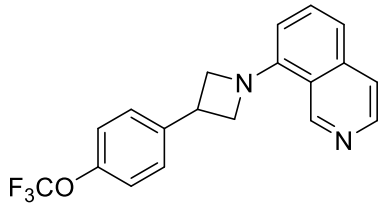


According to general procedure L, 3-(4-(trifluoromethoxy)phenyl)azetidine **9b** (61 mg, 0.28 mmol, 1.4 equiv.), 4-bromo-2-chloro-1-fluorobenzene (24 µL, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%), and KO^{t}Bu (31 mg, 0.28 mmol, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 3 h. The now brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) to obtain the title compound as a colorless solid (53 mg, 0.15 mmol, 77 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.39 (d, J = 8.6 Hz, 2H), 7.20 (d, J = 8.6 Hz, 2H), 7.01 (t, J = 8.9 Hz, 1H), 6.50 (dd, J = 6.1, 2.8 Hz, 1H), 6.33 (dt, J = 8.9, 2.8 Hz, 1H), 4.28 (t, J = 7.4 Hz, 2H), 3.92 (dt, J = 13.7, 7.4 Hz, 1H), 3.84 (t, J = 7.4 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 152.81, 150.44, 148.65, 148.26, 141.09, 128.47, 121.88, 121.42, 121.19, 119.33, 117.00, 116.78, 113.37, 111.16, 111.09, 59.93, 34.46.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -57.92, -130.54.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 345 (12), 188 (68), 159 (28), 158 (15), 157 (100), 156 (25), 128 (11), 119 (10), 91 (11).
HRMS (EI): for: $C_{16}H_{12}ClF_4NO$ calc. [M^+]: 345.0544; found: 345.0536.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2853 (w), 1607 (w), 1582 (w), 1501 (vs), 1479 (s), 1339 (w), 1253 (vs), 1221 (vs), 1199 (vs), 1154 (vs), 1109 (s), 1070 (m), 1052 (m), 1018 (m), 958 (w), 921 (w), 899 (vw), 835 (m), 803 (s), 713 (m), 686 (w).
Melting point: mp = 92 °C.

8-(3-(4-(Trifluoromethoxy)phenyl)azetidin-1-yl)isoquinoline (10j)

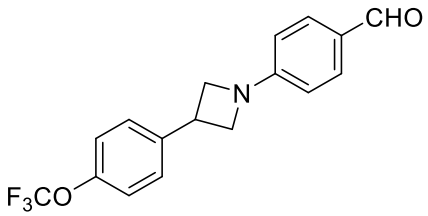


According to general procedure L, 3-(4-(trifluoromethoxy)phenyl)azetidine **9b** (61 mg, 0.28 mmol, 1.4 equiv.), 8-bromoisoquinoline (42 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (68 mg, 4 mol%), Brettphos (42 mg, 4 mol%), and KO^{t}Bu (31 mg, 0.28 mmol, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 6 h. The now brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 7:3) to obtain the title compound as a colorless solid (50 mg, 0.15 mmol, 73 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.41 (s, 1H), 8.40 (d, J = 5.7 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.45 (d, J = 8.7 Hz, 2H), 7.28 (d, J = 7.9 Hz, 1H), 7.23 (d, J = 8.7 Hz, 2H), 6.61 (d, J = 7.9 Hz, 1H), 4.74 (t, J = 8.0 Hz, 2H), 4.29 (t, J = 8.0 Hz, 2H), 4.12 – 4.03 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 149.28, 148.37, 147.25, 140.79, 139.89, 138.03, 132.44, 128.45, 121.88, 121.55, 116.87, 109.28, 62.62, 35.08.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -57.92.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 344 (30), 207 (17), 188 (18), 157 (12), 156 (100), 155 (78), 129 (71), 128 (28), 101 (14), 91 (12), 61 (14), 45 (12), 44 (24), 43 (84).
HRMS (EI): for: $C_{19}H_{15}F_3N_2O$ calc. [M^+]: 344.1136; found: 344.1131.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2929 (vw), 2855 (w), 1613 (m), 1594 (vw), 1562 (s), 1509 (m), 1482 (w), 1445 (s), 1407 (s), 1369 (w), 1332 (m), 1311 (m), 1251 (s), 1219 (s), 1199 (s), 1150 (vs), 1108 (s), 1066 (m), 1052 (m), 1018 (m), 995 (w), 965 (w), 945 (w), 920 (w), 888 (vw), 847 (m), 824 (s), 806 (m), 795 (m), 739 (m), 671 (w).
Melting point: mp = 107 °C.

4-(3-(4-(Trifluoromethoxy)phenyl)azetidin-1-yl)benzaldehyde (10k)

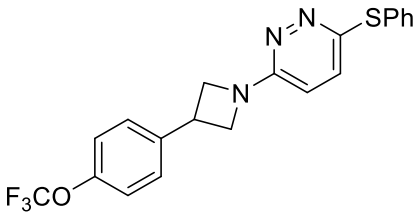


According to general procedure L, 3-(4-(trifluoromethoxy)phenyl)azetidine **9b** (61 mg, 0.28 mmol, 1.4 equiv.), 4-bromobenzaldehyde (37 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (51 mg, 3 mol%), Brettphos (32 mg, 3 mol%), and K_2CO_3 (39 mg, 0.28 mmol, 1.4 equiv.) in *t*BuOH (2 mL) were heated to 100 °C for 14 h. The now brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 8:2) to obtain the title compound as a colorless solid (38 mg, 0.12 mmol, 59 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.77 (s, 1H), 7.75 (d, J = 8.7 Hz, 2H), 7.40 (d, J = 8.7 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 6.49 (d, J = 7.9 Hz, 2H), 4.45 (t, J = 7.7 Hz, 2H), 4.05 – 3.95 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 190.63, 154.91, 140.92, 132.10, 128.41, 126.60, 121.55, 110.44, 58.87, 34.25.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -57.93.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 321 (19), 189 (10), 188 (97), 134 (10), 133 (100), 132 (67), 119 (13), 91 (16), 77 (18).
HRMS (EI): for: $C_{17}H_{14}F_3NO_2$ calc. [M^+]: 321.0977; found: 321.0971.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2928 (w), 2862 (w), 2734 (w), 2646 (w), 1679 (m), 1592 (s), 1554 (m), 1527 (m), 1509 (m), 1474 (m), 1437 (w), 1392 (m), 1343 (w), 1326 (w), 1250 (s), 1217 (s), 1198 (s), 1145 (vs), 1108 (s), 1017 (m), 997 (m), 948 (w), 921 (w), 846 (m), 816 (s), 701 (w), 683 (m), 671 (m).
Melting point: mp = 112 °C.

3-(Phenylthio)-6-(3-(4-(trifluoromethoxy)phenyl)azetidin-1-yl)pyridazine (10l)

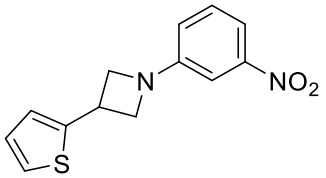


According to general procedure L, 3-(4-(trifluoromethoxy)phenyl)azetidine **9b** (61 mg, 0.28 mmol, 1.4 equiv.), 3-bromo-6-(phenylthio)pyridazine (61 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (68 mg, 4 mol%), Brettphos (42 mg, 4 mol%), and KO^{t}Bu (31 mg, 0.28 mmol, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 5 h. The now brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 7:3) to obtain the title compound as a colorless solid (35 mg, 0.11 mmol, 53 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.53 – 7.50 (m, 2H), 7.42 – 7.31 (m, 5H), 7.21 (d, J = 7.9 Hz, 2H), 7.08 (d, J = 9.2 Hz, 1H), 6.49 (d, J = 9.2 Hz, 1H), 4.54 (t, J = 8.4 Hz, 2H), 4.13 (t, J = 8.4 Hz, 2H), 4.05 – 3.96 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 159.02, 153.25, 148.21, 140.83, 133.11, 132.58, 129.42, 129.04, 128.29, 128.26, 121.39, 112.52, 77.35, 77.03, 76.71, 58.17, 34.74.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -57.91.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 403 (21), 402 (19), 215 (19), 214 (100), 188 (15).
HRMS (EI): for: $C_{20}H_{16}F_3N_3OS$ calc. [M$^+$]: 403.0966; found: 403.0958.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2920 (w), 2875 (w), 1585 (m), 1527 (w), 1508 (m), 1468 (s), 1440 (m), 1273 (s), 1234 (s), 1201 (s), 1154 (vs), 1104 (m), 1079 (m), 1069 (m), 1018 (m), 997 (w), 967 (w), 945 (w), 921 (w), 888 (w), 872 (w), 849 (s), 806 (m), 756 (w), 735 (s), 688 (m).
Melting point: mp = 128 °C.

1-(3-Nitrophenyl)-3-(thiophen-2-yl)azetidine (10m)

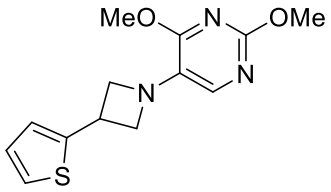


According to general procedure L, 3-(thiophen-2-yl)azetidine **9c** (39 mg, 0.28 mmol, 1.4 equiv.), 1-bromo-3-nitrobenzene (40 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (8.5 mg, 5 mol%), Brettphos (5.4 mg, 5 mol%), and $CsCO_3$ (91 mg, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 5 h. The now brownish mixture was cooled to rt and filtered over celite 545. After the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 97:3) to obtain the title compound as a yellow crystalline solid (32 mg, 0.12 mmol, 62 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.59 (ddd, J = 8.1, 2.2, 0.7 Hz, 1H), 7.35 (t, J = 8.1 Hz, 1H), 7.28 (t, J = 2.2 Hz, 1H), 7.23 (dd, J = 4.6, 1.7 Hz, 1H), 7.00 – 6.95 (m, 2H), 6.75 (ddd, J = 8.1, 2.2, 0.7 Hz, 1H), 4.45 – 4.37 (m, 2H), 4.32 – 4.20 (m, 1H), 3.97 (t, J = 7.2 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 152.08, 149.33, 145.52, 129.78, 127.24, 124.55, 124.43, 117.44, 112.48, 106.03, 77.48, 77.16, 76.84, 60.67, 30.96.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 110 (100).
HRMS (EI): for $C_{13}H_{12}N_2O_2S$: calc. [M^+]: 260.0619; found: 260.0615.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 3079 (vw), 3069 (vw), 2949 (w), 2922 (w), 2854 (w), 1737 (w), 1613 (m), 1572 (w), 1518 (vs), 1486 (m), 1474 (m), 1461 (m), 1442 (w), 1433 (w), 1396 (vw), 1380 (w), 1342 (s), 1325 (m), 1295 (m), 1287 (m), 1277 (m), 1260 (m), 1243 (m), 1223 (m), 1205 (w), 1160 (m), 1130 (m), 1117 (m), 1092 (w), 1078 (m), 1071 (m), 1039 (m), 1028 (m), 989 (m), 968 (w), 946 (w), 910 (vw), 883 (vw), 877 (w), 861 (m), 853 (m), 845 (m), 828 (m), 786 (m), 746 (w), 741 (vw), 730 (s), 720 (vs), 715 (vs), 671 (s).
Melting point: mp = 97 °C.

2,4-Dimethoxy-5-(3-(thiophen-2-yl)azetidin-1-yl)pyrimidine (10n)

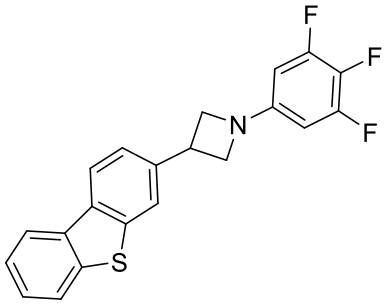


According to general procedure L, 3-(thiophen-2-yl)azetidine **9c** (39 mg, 0.28 mmol, 1.4 equiv.), 5-bromo-2,4-dimethoxypyrimidine (44 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%), and KO^{t}Bu (31 mg, 0.28 mmol, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 6 h. The now brownish mixture was cooled to rt and filtered over celite 545. After the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 97:3) to obtain the title compound as a colorless solid (26 mg, 0.09 mmol, 46 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.45 (s, 1H), 7.20 (dd, J = 5.0, 1.2 Hz, 1H), 7.00 – 6.90 (m, 2H), 4.31 (t, J = 7.7 Hz, 2H), 4.22 – 4.11 (m, 1H), 3.99 (s, 3H), 3.94 (s, 3H), 3.82 (t, J = 7.7 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 162.41, 159.33, 145.63, 139.44, 129.12, 127.15, 124.38, 124.17, 77.48, 77.16, 76.84, 62.09, 54.72, 54.01, 32.39.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 167 (100), 166 (68), 152 (16), 138 (52), 137 (19), 110 (22).
HRMS (EI): for $C_{13}H_{15}N_3O_2S$: calc. [M^+]: 277.0885; found: 277.0881.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2853 (w), 1736 (vw), 1725 (vw), 1597 (w), 1564 (s), 1479 (m), 1463 (s), 1455 (s), 1407 (s), 1374 (vs), 1297 (s), 1259 (m), 1239 (s), 1187 (m), 1130 (w), 1075 (s), 1014 (s), 1002 (m), 961 (w), 938 (w), 919 (w), 901 (w), 845 (w), 823 (w), 802 (w), 781 (m), 759 (w).
Melting point: mp = 92 °C.

3-(Dibenzo[b,d]thiophen-3-yl)-1-(3,4,5-trifluorophenyl)azetidine (10o)

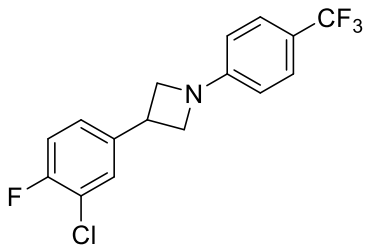


According to general procedure L, 3-(dibenzo[b,d]thiophen-3-yl)azetidine **9e** (67 mg, 0.28 mmol, 1.4 equiv.), 5-bromo-1,2,3-trifluorobenzene (24 µL, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (51 mg, 3 mol%), Brettphos (32 mg, 3 mol%), and KO^{t}Bu (31 mg, 0.28 mmol, 1.4 equiv.) in toluene (2 mL) were heated to 100 °C for 4 h. The now brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 97:3) to obtain the title compound as a colorless solid (44 mg, 0.12 mmol, 60 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.22 – 8.14 (m, 1H), 8.12 (d, J = 1.7 Hz, 1H), 7.91 – 7.81 (m, 2H), 7.54 – 7.42 (m, 3H), 6.08 (dd, J = 9.8, 5.6 Hz, 2H), 4.34 (t, J = 7.5 Hz, 2H), 4.10 (ddd, J = 14.0, 7.5, 5.9 Hz, 1H), 3.95 (t, J = 7.5 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 139.93, 138.43, 138.17, 135.94, 135.19, 126.95, 125.71, 124.44, 123.16, 122.95, 121.62, 119.81, 95.53, 95.28, 77.34, 77.03, 76.71, 59.86, 34.72.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -122.48, -122.50, -134.52, -134.54, -134.57, -134.60, -175.71, -175.72, -175.74, -175.77, -175.78, -175.80, -175.82, -175.84, -175.85.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 211 (13), 210 (100).
HRMS (EI): for: $C_{21}H_{14}F_3NS$ calc. [M^+]: 369.0799; found: 369.0806.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2919 (w), 2851 (m), 1641 (m), 1628 (m), 1592 (m), 1574 (m), 1526 (s), 1509 (s), 1471 (s), 1444 (m), 1431 (m), 1392 (w), 1368 (m), 1298 (m), 1259 (m), 1239 (vs), 1209 (s), 1188 (w), 1156 (m), 1136 (m), 1106 (m), 1083 (w), 1069 (w), 1024 (s), 924 (w), 879 (m), 823 (s), 808 (s), 776 (w), 762 (s), 732 (s), 718 (w).
Melting point: mp = 113 °C.

3-(3-Chloro-4-fluorophenyl)-1-(4-(trifluoromethyl)phenyl)azetidine (10p)

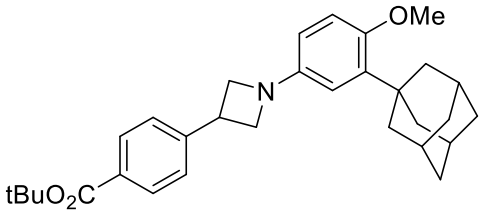


According to general procedure L, 3-(3-chloro-4-fluorophenyl)azetidine **9f** (0.40 g, 1.4 mmol, 1.4 equiv.), 1-bromo-4-(trifluoromethyl)benzene (0.14 mL, 1.0 mmol, 1.0 equiv.), xPhos Pd G3 (25 mg, 3 mol%), Brettphos (16 mg, 3 mol%), and KO^{t}Bu (0.16 g, 0.28 mmol, 1.4 equiv.) in toluene (10 mL) were heated to 100 °C for 7 h. The now brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) to obtain the title compound as a colorless solid (0.29 g, 0.88 mmol, 88 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.47 (d, J = 8.4 Hz, 2H), 7.43 (dd, J = 6.9, 2.2 Hz, 1H), 7.24 (ddd, J = 8.6, 4.6, 2.2 Hz, 1H), 7.12 (t, J = 8.6 Hz, 1H), 6.50 (d, J = 8.4 Hz, 2H), 4.38 – 4.31 (m, 2H), 3.94 – 3.84 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 158.51, 156.04, 153.39, 139.58, 139.54, 129.25, 126.82, 126.75, 126.55, 126.51, 126.47, 126.44, 123.75, 121.45, 121.27, 119.66, 119.34, 119.01, 117.04, 116.84, 110.92, 77.48, 77.16, 76.84, 59.23, 34.28.
^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = -61.02, -117.80, -117.81, -117.82, -117.82, -117.83, -117.84, -117.84, -117.86.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 329 (11), 174 (10), 173 (100), 172 (36), 158 (17), 156 (53), 145 (29), 121 (10), 42 (31).
HRMS (EI): for: $C_{16}H_{12}ClF_4N$ calc. [M^+]: 329.0594; found: 329.0590.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2858 (w), 2359 (w), 1611 (m), 1573 (w), 1526 (w), 1500 (s), 1482 (m), 1417 (w), 1365 (m), 1326 (m), 1315 (m), 1298 (m), 1265 (w), 1249 (m), 1207 (m), 1181 (w), 1151 (m), 1124 (m), 1100 (vs), 1062 (s), 1002 (w), 961 (w), 940 (w), 875 (w), 854 (w), 821 (s), 727 (w), 708 (w).
Melting point: mp = 92 °C.

***tert*-Butyl 4-(1-(3-(adamantan-1-yl)-4-methoxyphenyl)azetidin-3-yl)benzoate (10q)**

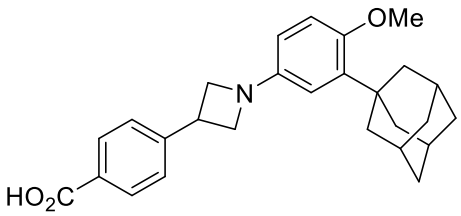


According to general procedure L, *tert*-butyl 4-(azetidin-3-yl)benzoate **9g** (65 mg, 0.28 mmol, 1.4 equiv.), 1-(5-bromo-2-methoxyphenyl)adamantane (64 mg, 0.2 mmol, 1.0 equiv.), xPhos Pd G3 (8.5 mg, 5 mol%), Brettphos (5.4 mg, 5 mol%), and K_2CO_3 (39 mg, 0.28 mmol, 1.4 equiv.) in DME (2 mL) were heated to 100 °C for 48 h. The now brownish mixture was cooled to rt and filtered over celite 545. The filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 95:5) to obtain the title compound as a brown solid (65 mg, 0.14 mmol, 68 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.95 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 6.82 (d, J = 8.6 Hz, 1H), 6.45 (d, J = 2.8 Hz, 1H), 6.36 (dd, J = 8.6, 2.8 Hz, 1H), 4.27 (t, J = 7.3 Hz, 2H), 3.93 (dt, J = 13.8, 7.3 Hz, 1H), 3.84 (t, J = 7.3 Hz, 2H), 3.78 (s, 3H), 2.07 (d, J = 13.1 Hz, 9H), 1.76 (s, 6H), 1.59 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 165.68, 151.87, 147.59, 146.09, 139.60, 130.44, 129.74, 126.92, 113.17, 110.96, 109.38, 80.95, 77.35, 77.03, 76.71, 59.64, 55.81, 40.57, 37.13, 37.08, 35.17, 29.12, 28.23.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 473 (32), 270 (20), 269 (100), 197 (12), 131 (10).
HRMS (EI): for: $C_{31}H_{39}NO_3$ calc. [M^+]: 473.2930; found: 473.2926.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2823 (m), 2290 (m), 1645 (s), 1587 (m), 1571 (m), 1481 (s), 1466 (s), 1423 (m), 1412 (s), 1330 (w), 1319 (m), 1286 (vs), 1229 (s), 1199 (w), 1179 (m), 1055 (m), 1019 (w), 860 (m), 803 (m), 791 (m).
Melting point: mp = 143 °C.

4-(1-(3-(Adamantan-1-yl)-4-methoxyphenyl)azetidin-3-yl)benzoic acid (10r)

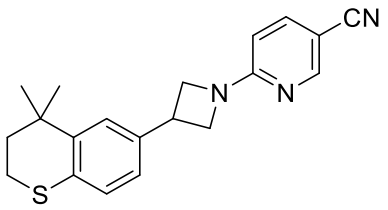


tert-Butyl 4-(1-(3-(adamantan-1-yl)-4-methoxyphenyl)azetidin-3-yl)benzoate **10q** (47 mg, 0.1 mmol, 1.0 equiv.) was suspended in DCM (1 mL) and treated with $ZnBr_2$ (0.11 g, 0.5 mmol, 5.0 equiv.). After stirring for 14 h, the solvent was removed *in vacuo,* and the crude mixture was purified by flash column chromatography (silica gel, DCM/MeOH = 9.5:0.5) to obtain the title compound as a brown solid (36 mg, 0.09 mmol, 87 %).

^{1}H NMR (400 MHz, DMSO-D$_6$): δ (ppm) = 12.89 (s, 1H), 7.93 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 6.89 – 6.79 (m, 1H), 6.37 – 6.28 (m, 2H), 4.19 (t, J = 7.4 Hz, 2H), 4.02 – 3.92 (m, 1H), 3.72 (d, J = 6.6 Hz, 5H), 2.02 (s, 9H), 1.72 (s, 6H).
^{13}C NMR (100 MHz, DMSO-D$_6$): δ (ppm) = 167.22, 151.23, 147.93, 146.15, 138.31, 129.62, 129.09, 127.17, 113.43, 110.23, 109.50, 59.10, 55.77, 40.20, 40.15, 39.94, 39.73, 39.52, 39.31, 39.10, 38.89, 36.58, 36.43, 34.23, 28.41.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 417 (32), 270 (20), 269 (100), 184 (26), 184 (13), 148 (14), 134 (11), 131 (10).
HRMS (ESI): for: $C_{27}H_{30}NO_3$ calc. [M^+]: 417.2304; found: 417.2309.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2850 (m), 2363 (m), 1675 (vs), 1608 (s), 1574 (m), 1496 (s), 1478 (m), 1448 (m), 1432 (s), 1418 (s), 1332 (m), 1319 (m), 1294 (s), 1229 (vs), 1193 (m), 1179 (m), 1037 (m), 1019 (m), 860 (m), 803 (m), 791 (m).
Melting point: mp = 130 °C.

6-(3-(4,4-Dimethylthiochroman-6-yl)azetidin-1-yl)nicotinonitrile (10s)

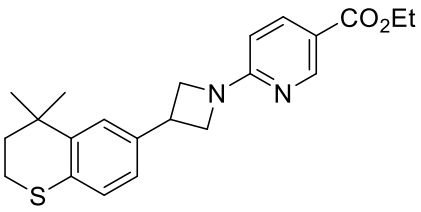


According to general procedure L, 3-(4,4-dimethylthiochroman-6-yl)azetidine **9d** (54 mg, 0.28 mmol, 1.4 equiv.), 2-bromo-5-cyanopyridine (37 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (8.5 mg, 5 mol%), Brettphos (5.4 mg, 5 mol%), and KO^{t}Bu (31 mg, 0.28 mmol, 1.4 equiv.) in *t*BuOH (2 mL) were heated to 100 °C for 1 h. The now brownish mixture was cooled to rt and filtered over celite 545. After that, the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 4:1) to obtain the title compound as a colorless solid (56 mg, 0.17 mmol, 83 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.42 (dd, J = 2.2, 0.8 Hz, 1H), 7.60 (dd, J = 8.8, 2.2 Hz, 1H), 7.27 (d, J = 1.9 Hz, 1H), 7.12 – 7.04 (m, 2H), 6.27 (dd, J = 8.7, 0.9 Hz, 1H), 4.50 (t, J = 8.7 Hz, 2H), 4.11 (dd, J = 8.7, 6.0 Hz, 2H), 3.92 (tt, J = 8.6, 6.0 Hz, 1H), 3.06 – 2.98 (m, 2H), 2.00 – 1.92 (m, 2H), 1.33 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 153.37, 142.44, 139.37, 137.44, 127.29, 125.37, 124.33, 105.10, 77.48, 77.16, 76.84, 57.76, 37.72, 34.49, 33.23, 30.34, 23.19, 1.17.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 205 (15), 204 (100), 189 (36), 156 (18).
HRMS (EI): for $C_{20}H_{21}N_3S$: calc. [M^+]: 335.1456; found: 335.1450.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2935 (w), 2880 (w), 2217 (m), 1598 (vs), 1543 (m), 1502 (s), 1469 (s), 1418 (s), 1401 (s), 1364 (m), 1347 (w), 1302 (m), 1279 (m), 1249 (m), 1207 (m), 1188 (w), 1173 (w), 1159 (w), 1141 (m), 1108 (m), 1072 (w), 1056 (m), 1022 (w), 1007 (m), 989 (w), 967 (w), 942 (w), 891 (w), 826 (m), 814 (s), 782 (w), 750 (w).
Melting point: mp = 131 °C.

Ethyl 6-(3-(4,4-dimethylthiochroman-6-yl)azetidin-1-yl)nicotinate (10t)

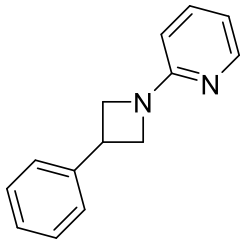


According to general procedure L, 3-(4,4-dimethylthiochroman-6-yl)azetidine **9d** (54 mg, 0.28 mmol, 1.4 equiv.), ethyl 6-bromonicotinate (46 mg, 0.20 mmol, 1.0 equiv.), xPhos Pd G3 (8.5 mg, 5 mol%), Brettphos (5.4 mg, 5 mol%), and K_2CO_3 (39 mg, 0.28 mmol, 1.4 equiv.) in *t*BuOH (2 mL) were heated to 100 °C for 3 days. The now brownish mixture was cooled to rt and filtered over celite 545. After that, the filter cake was washed with ethyl acetate (3 × 10 mL) and the filtrate was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) to obtain the title compound as a light brown solid (68 mg, 0.18 mmol, 89 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.82 – 8.81 (m, 1H), 8.02 (dd, J = 8.8, 2.2 Hz, 1H), 7.28 (s, 1H), 7.08 (d, J = 1.5 Hz, 2H), 6.26 (d, J = 9.3 Hz, 1H), 4.50 (t, J = 8.6 Hz, 2H), 4.33 (q, J = 7.1 Hz, 2H), 4.11 (dd, J = 8.4, 6.1 Hz, 2H), 3.90 (ddd, J = 14.5, 8.7, 6.0 Hz, 1H), 3.05 – 3.00 (m, 2H), 1.99 – 1.91 (m, 2H), 1.37 (t, J = 7.1 Hz, 3H), 1.33 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 166.31, 166.21, 161.54, 151.64, 151.59, 142.34, 138.25, 138.10, 137.87, 130.70, 127.20, 125.39, 124.46, 115.15, 104.54, 104.44, 77.48, 77.16, 76.84, 60.67, 60.59, 57.89, 37.76, 34.75, 34.59, 34.55, 33.22, 30.35, 29.85, 23.18, 14.54.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 205 (17), 204 (100), 189 (34), 156 (13), 97 (11), 83 (11), 71 (12), 69 (14), 57 (15), 55 (17), 43 (12), 42 (12), 39 (12).
HRMS (EI):): for $C_{22}H_{26}N_2O_2S$: calc. [M^+]: 382.1715; found: 382.1704.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2920 (m), 2872 (w), 2854 (m), 2710 (vw), 2550 (vw), 2360 (vw), 1701 (s), 1599 (s), 1555 (m), 1523 (s), 1473 (m), 1461 (m), 1436 (s), 1411 (m), 1386 (w), 1365 (m), 1297 (m), 1267 (vs), 1172 (m), 1153 (m), 1107 (vs), 1054 (m), 1038 (m), 1017 (m), 1003 (m), 961 (w), 922 (w), 886 (w), 868 (w), 832 (m), 816 (w), 779 (s), 733 (w), 721 (w).
Melting point: mp = 126 °C.

2-(3-Phenylazetidin-1-yl)pyridine (7a)

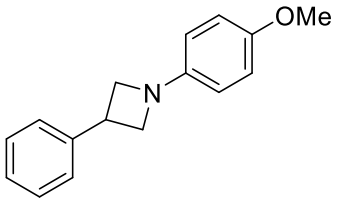


Following general procedure K, with phenylmagnesiumchloride (0.6 mmol, 2.0 equiv.). After quenching with KO^{t}Bu (134 mg, 4.0 equiv.) the mixture was transferred to a pressure tube containing 2-bromopyridine (24 µL, 0.20 mmol, 0.67 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%). After heating to 100 °C for 14 h, the grey suspension was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) over silica gel to give 1-(4-methoxyphenyl)-3-phenylazetidine as a colorless oil (29 mg, 0.14 mmol, 68 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.19 (ddd, J = 5.1, 2.0, 0.9 Hz, 1H), 7.47 (ddd, J = 8.7, 7.2, 1.9 Hz, 1H), 7.41 – 7.32 (m, 4H), 7.29 – 7.23 (m, 1H), 6.63 (ddd, J = 7.2, 5.1, 1.1 Hz, 1H), 6.35 (dd, J = 8.4, 1.1 Hz, 1H), 4.45 (t, J = 8.1 Hz, 2H), 4.07 (dd, J = 7.8, 6.0 Hz, 2H), 3.95 ppm (ddd, J = 14.4, 8.4, 6.0 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 160.9, 148.3, 142.8, 137.2, 128.8, 127.1, 127.0, 113.1, 106.1, 58.1, 35.0 ppm.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 210.1 (37), 181.1 (14), 104.1 (100), 79.0 (65)
HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{14}N_2$: 210.1157; found: 210.1148.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3061 (w), 3026 (w), 3008 (w), 2951 (w), 2862 (w), 1756 (w), 1589 (s), 1557 (m), 1490 (s), 1472 (vs), 1454 (m), 1436 (vs), 1374 (m), 1351 (m), 1301 (m), 1294 (m), 1273 (m), 1147 (s), 1081 (m), 1062 (w), 1025 (m), 977 (m), 947 (w), 907 (w), 880 (w), 846 (w), 772 (s), 756 (s), 735 (s), 723 (m), 715 (m), 697 (vs), 675 (m), 673 (m), 669 (m), 667 (m), 661 (m), 657 (m), 655 cm^{-1} (w).

1-(4-Methoxyphenyl)-3-phenylazetidine (10a)

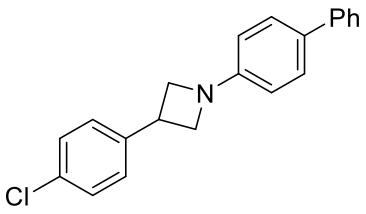


Following general procedure K, with phenylmagnesiumchloride (0.6 mmol, 2.0 equiv.). After quenching with KO^{t}Bu (134 mg, 4.0 equiv.) the mixture was transferred to a pressure tube containing 4-bromoanisole (25 µL, 0.20 mmol, 0.67 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%). After heating to 100 °C for 14 h, the grey suspension was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) over silica gel to give 1-(4-methoxyphenyl)-3-phenylazetidine as a colorless solid (35 mg, 0.14 mmol, 72 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40 – 7.31 (m, 4H), 7.25 – 7.22 (m, 1H), 6.88 – 6.81 (m, 2H), 6.53 – 6.46 (m, 2H), 4.26 (t, *J* = 6.5 Hz, 2H), 3.97 – 3.88 (m, 1H), 3.83 (t, *J* = 6.5 Hz, 2H), 3.77 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 152.47, 146.87, 142.76, 128.72, 127.21, 126.85, 114.82, 113.00, 77.48, 77.16, 76.84, 60.17, 55.96, 35.41.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 135 (96), 120 (100), 92 (10).
HRMS (EI): for $C_{16}H_{17}NO$: calc. [M^+]: 239.1310; found: 239.1302.
IR (Diamond-ATR, neat): $\tilde{\nu}$/ cm^{-1} = 2921 (vs), 2852 (s), 2721 (vw), 2675 (vw), 2353 (vw), 1730 (w), 1698 (vw), 1692 (vw), 1681 (vw), 1619 (vw), 1604 (vw), 1579 (vw), 1511 (m), 1492 (w), 1478 (w), 1461 (m), 1454 (m), 1441 (w), 1377 (w), 1366 (w), 1333 (w), 1288 (w), 1258 (m), 1237 (m), 1210 (w), 1181 (w), 1175 (w), 1163 (w), 1119 (m), 1087 (m), 1073 (m), 1051 (m), 1035 (m), 1029 (m), 1004 (w), 950 (w), 919 (w), 873 (vw), 822 (m), 799 (w), 789 (w), 762 (m), 749 (w), 741 (w), 722 (w), 709 (m).
Melting point: mp = 87 °C.

1-([1,1'-Biphenyl]-4-yl)-3-(4-chlorophenyl)azetidine (11a)

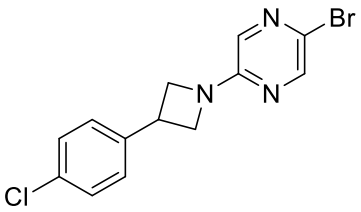


Following general procedure K, with (4-chlorophenyl)magnesium bromide (0.6 mmol, 2.0 equiv.). After quenching with KO^{t}Bu (134 mg, 4.0 equiv.) the mixture was transferred to a pressure tube containing 4-bromobiphenyl (47 mg, 0.20 mmol, 0.67 equiv.), xPhos Pd G3 (6.8 mg, 4 mol%), Brettphos (4.3 mg, 4 mol%). After heating to 100 °C for 14 h, the grey suspension was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 99:1) to give 1-([1,1'-biphenyl]-4-yl)-3-(4-chlorophenyl)azetidine as a colorless solid (33 mg, 0.10 mmol, 51 %).

^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 7.60 – 7.56 (m, 2H), 7.52 (d, J = 8.6 Hz, 2H), 7.44 – 7.35 (m, 6H), 7.27 (t, J = 7.5 Hz, 1H), 6.60 (d, J = 8.6 Hz, 2H), 4.30 (t, J = 7.5 Hz, 1H), 3.99 – 3.91 (m, 1H), 3.86 (t, J = 7.5 Hz, 2H).
^{13}C NMR (100 MHz, CD_3CN): δ (ppm) = 152.53, 142.99, 142.00, 132.77, 130.85, 129.76, 129.72, 129.50, 128.37, 127.17, 127.01, 112.94, 60.02, 35.25.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 319 (14), 182 (12), 181 (100), 153 (14), 152 (14).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{21}H_{18}ClN$: 319.1128; found: 319.1127.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3032 (w), 2924 (w), 2860 (w), 2842 (w), 1607 (m), 1596 (m), 1526 (m), 1488 (s), 1416 (w), 1398 (w), 1363 (m), 1331 (m), 1279 (w), 1254 (w), 1219 (w), 1205 (m), 1181 (w), 1158 (w), 1138 (m), 1123 (w), 1107 (w), 1090 (m), 1078 (m), 1042 (w), 1013 (m), 991 (w), 942 (w), 889 (w), 835 (w), 817 (vs), 759 (vs), 735 (w), 714 (m).
Melting point: mp = 145 °C.

2-Bromo-5-(3-(4-chlorophenyl)azetidin-1-yl)pyrazine (11b)

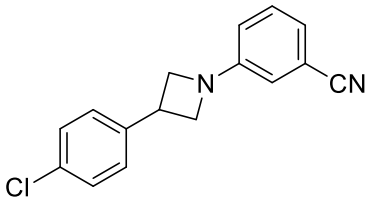


Following general procedure K, with (4-chlorophenyl)magnesium bromide (0.6 mmol, 2.0 equiv.). After quenching with KO^{t}Bu (134 mg, 4.0 equiv.) the mixture was transferred to a pressure tube containing 2,5-dibromopyrazine (48 mg, 0.20 mmol, 0.67 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%). After heating to 100 °C for 14 h, the grey suspension was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 9:1) to give 2-bromo-5-(3-(4-chlorophenyl)azetidin-1-yl)pyrazine as a yellow solid (31 mg, 0.09 mmol, 47 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.13 (d, J = 1.3 Hz, 1H), 7.60 (d, J = 1.3 Hz, 1H), 7.40 – 7.28 (m, 4H), 4.50 (t, J = 8.4 Hz, 2H), 4.11 – 4.06 (m, 2H), 4.05 – 3.94 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 154.15, 143.51, 140.10, 133.11, 129.93, 129.03, 128.20, 126.34, 77.35, 77.03, 76.72, 58.24, 34.73.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 140 (33), 138 (100), 103 (29).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{13}H_{11}BrClN_3$: 322.9825; found: 322.9817.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2869 (w), 1564 (s), 1512 (m), 1493 (m), 1472 (vs), 1394 (w), 1292 (w), 1192 (w), 1167 (w), 1114 (m), 1094 (m), 1014 (w), 1002 (w), 822 (m).
Melting point: mp = 138 °C.

3-(3-(4-Chlorophenyl)azetidin-1-yl)benzonitrile (11c)

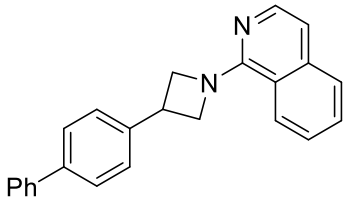


Following general procedure K, with (4-chlorophenyl)magnesium bromide (0.6 mmol, 2.0 equiv.). After quenching with KO^{t}Bu (134 mg, 4.0 equiv.) the mixture was transferred to a pressure tube containing 3-bromobenzonitrile (36 mg, 0.20 mmol, 0.67 equiv.), xPhos Pd G3 (6.8 mg, 4 mol%), Brettphos (4.3 mg, 4 mol%). After heating to 100 °C for 14 h, the grey suspension was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 98:2) to give 3-(3-(4-chlorophenyl)azetidin-1-yl)benzonitrile as a colorless oil (25 mg, 0.09 mmol, 47 %).

^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 7.41 – 7.30 (m, 5H), 7.03 (dt, J = 7.6, 1.2 Hz, 1H), 6.81 – 6.73 (m, 2H), 4.29 (t, J = 7.8 Hz, 2H), 4.00 – 3.91 (m, 1H), 3.85 (t, J = 7.8 Hz, 2H).
^{13}C NMR (100 MHz, CD_3CN): δ (ppm) = 152.89, 142.62, 132.89, 130.80, 129.66, 129.53, 121.46, 120.21, 116.87, 115.22, 113.24, 59.82, 35.07.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 140 (27), 138 (100), 130 (12), 103 (16), 102 (11).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{16}H_{13}ClN_2$: 268.0767; found: 268.0766.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2925 (m), 2855 (m), 2225 (m), 1735 (w), 1598 (vs), 1573 (s), 1526 (w), 1491 (s), 1474 (s), 1438 (s), 1416 (m), 1365 (s), 1341 (m), 1323 (m), 1292 (m), 1259 (m), 1206 (m), 1173 (m), 1149 (m), 1123 (m), 1107 (m), 1091 (m), 1043 (w), 1013 (m), 985 (w), 962 (w), 883 (w), 860 (m), 844 (w), 820 (vs), 778 (s), 761 (m), 715 (w), 681 (s).

1-(3-([1,1'-Biphenyl]-4-yl)azetidin-1-yl)isoquinoline (11d)

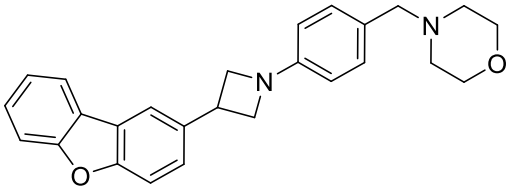


Following general procedure K, with [1,1'-biphenyl]-4-ylmagnesium bromide (0.6 mmol, 2.0 equiv.). After quenching with KO^{t}Bu (134 mg, 4.0 equiv.) the mixture was transferred to a pressure tube containing 1-bromoisoquinoline (42 mg, 0.20 mmol, 0.67 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%). After heating to 100 °C for 14 h, the grey suspension was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 8:2) to give 1-(3-([1,1'-biphenyl]-4-yl)azetidin-1-yl)isoquinoline as a yellow solid (48 mg, 0.14 mmol, 71 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.09 (d, J = 5.8 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.63 – 7.56 (m, 5H), 7.51 (d, J = 8.4 Hz, 2H), 7.47 – 7.40 (m, 3H), 7.35 (t, J = 7.3 Hz, 1H), 7.05 (d, J = 5.8 Hz, 1H), 4.88 (t, J = 8.5 Hz, 2H), 4.55 – 4.49 (m, 2H), 4.06 (ddd, J = 14.7, 8.5, 6.2 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 158.83, 141.82, 141.24, 140.79, 139.90, 138.00, 129.64, 128.81, 127.46, 127.44, 127.29, 127.07, 126.99, 125.30, 124.77, 119.22, 112.33, 77.35, 77.03, 76.72, 60.99, 35.20.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 181 (14), 180 (100), 129 (15).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{24}H_{20}N_2$: 336.1626; found: 336.1622.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3030 (w), 2922 (m), 2857 (m), 1614 (w), 1583 (m), 1549 (s), 1504 (s), 1485 (m), 1453 (s), 1435 (vs), 1422 (vs), 1357 (s), 1314 (w), 1291 (s), 1268 (m), 1254 (m), 1218 (m), 1174 (w), 1157 (m), 1134 (m), 1120 (m), 1076 (w), 1052 (w), 1040 (w), 1021 (w), 1006 (m), 950 (w), 890 (w), 874 (m), 827 (m), 805 (s), 794 (m), 761 (vs), 750 (s), 722 (s), 690 (s).
Melting point: mp = 106 °C.

4-(4-(3-(Dibenzo[b,d]furan-2-yl)azetidin-1-yl)benzyl)morpholine (11e)

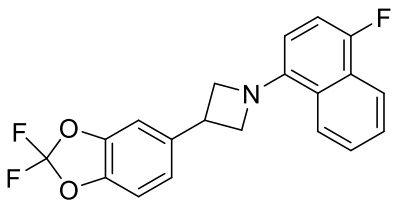


Following general procedure K, with dibenzo[b,d]furan-2-ylmagnesium bromide (0.6 mmol, 2.0 equiv.). After quenching with KO^{t}Bu (134 mg, 4.0 equiv.) the mixture was transferred to a pressure tube containing 4-(4-bromobenzyl)morpholine (59 mg, 0.20 mmol, 0.67 equiv.), xPhos Pd G3 (8.5 mg, 5 mol%), Brettphos (5.4 mg, 5 mol%). After heating to 100 °C for 14 h, the grey suspension was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 1:1) to give 4-(4-(3-(dibenzo[b,d]furan-2-yl)azetidin-1-yl)benzyl)morpholine as a colorless solid (44 mg, 0.11 mmol, 56 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.99 (d, J = 1.6 Hz, 1H), 7.95 (d, J = 7.6 Hz, 1H), 7.55 (dd, J = 14.6, 8.3 Hz, 2H), 7.46 (ddd, J = 8.3, 6.1, 1.6 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.21 (d, J = 8.3 Hz, 2H), 6.53 (d, J = 8.3 Hz, 2H), 4.38 (t, J = 7.3 Hz, 2H), 4.08 (dt, J = 13.9, 7.3 Hz, 1H), 3.97 (t, J = 7.3 Hz, 2H), 3.71 (t, J = 4.6 Hz, 4H), 3.44 (s, 2H), 2.44 (s, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 156.59, 155.20, 151.12, 137.39, 130.21, 127.26, 126.35, 124.54, 124.07, 122.75, 120.69, 118.86, 111.74, 111.61, 111.45, 77.35, 77.03, 76.71, 67.06, 63.16, 60.13, 53.53, 35.31.

LRMS (DEP/EI-Orbitrap): *m/z* (%): 398 (29), 313 (26), 312 (100), 204 (33), 195 (10), 194 (63), 181 (20), 165 (16), 119 (16), 118 (100), 86 (12).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{26}H_{26}N_2O_2$: 398.1994; found: 398.1991.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2959 (w), 2948 (w), 2919 (w), 2894 (w), 2853 (m), 2801 (w), 2760 (w), 2688 (vw), 2359 (vw), 1746 (vw), 1609 (m), 1571 (vw), 1517 (s), 1477 (m), 1449 (m), 1432 (w), 1391 (w), 1369 (m), 1343 (s), 1331 (m), 1318 (m), 1297 (w), 1285 (w), 1262 (m), 1198 (s), 1172 (w), 1148 (m), 1113 (vs), 1072 (m), 1034 (w), 1023 (w), 1005 (m), 952 (w), 930 (w), 911 (w), 862 (s), 831 (m), 818 (s), 793 (m), 765 (w), 743 (vs), 728 (m).
Melting point: mp = 126 °C.

3-(2,2-Difluorobenzo[d][1,3]dioxol-5-yl)-1-(4-fluoronaphthalen-1-yl)azetidine (11f)



Following general procedure K, with (2,2-difluorobenzo[d][1,3]dioxol-5-yl)magnesium bromide (0.6 mmol, 2.0 equiv.). After quenching with KO^{t}Bu (134 mg, 4.0 equiv.) the mixture was transferred to a pressure tube containing 1-bromo-4-fluoronaphthalene (45 mg, 0.20 mmol, 0.67 equiv.), xPhos Pd G3 (5.1 mg, 3 mol%), Brettphos (3.2 mg, 3 mol%). After heating to 100 °C for 14 h, the grey suspension was quenched with saturated aqueous NH_4Cl and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and the solvents were removed *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, *i*hexane/EtOAc = 95:5) to give 3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-1-(4-fluoronaphthalen-1-yl)azetidine as a colorless oil (46 mg, 0.13 mmol, 64 %).

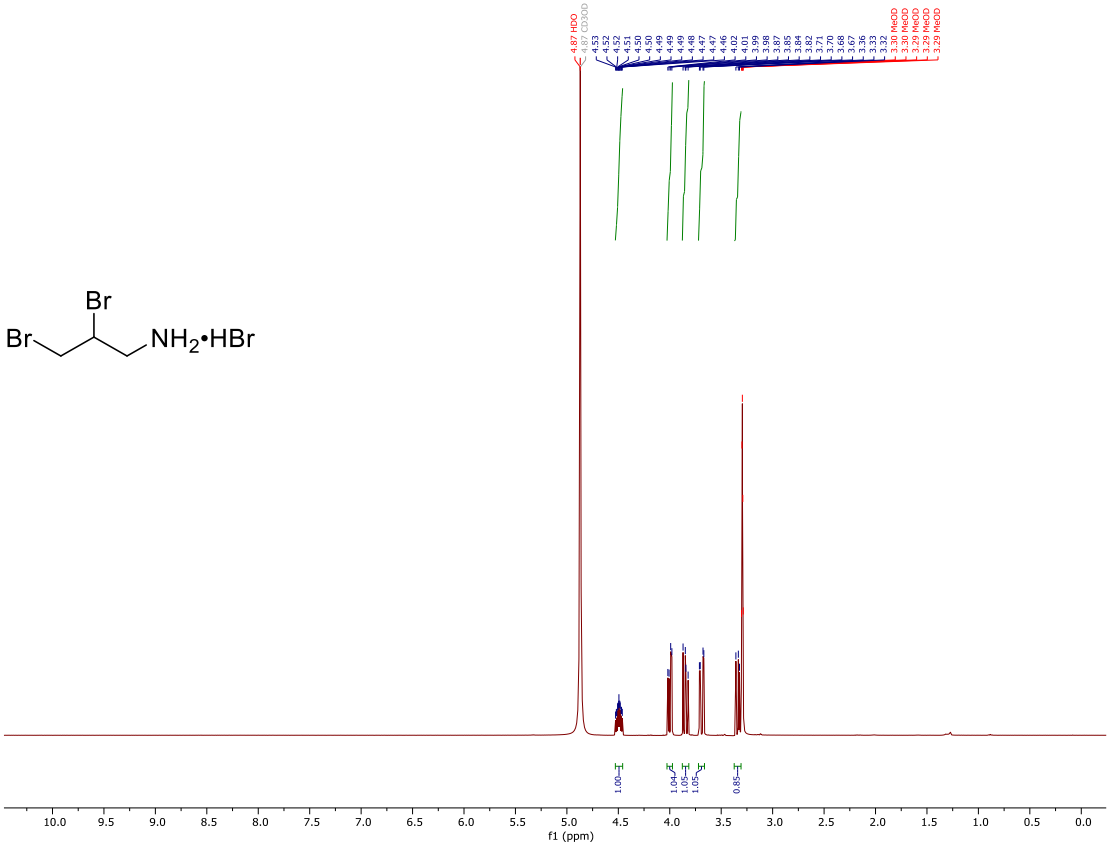
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.09 (d, J = 8.1 Hz, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.57 – 7.45 (m, 2H), 7.26 (s, 1H), 7.14 – 7.01 (m, 3H), 6.53 (dd, J = 8.1, 4.4 Hz, 1H), 4.51 (t, J = 7.6 Hz, 2H), 4.03 (t, J = 7.6 Hz, 2H), 3.97 – 3.87 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 154.77, 152.35, 144.53, 144.50, 144.19, 142.62, 139.00, 134.22, 131.69, 129.15, 126.17, 126.13, 126.11, 125.51, 124.65, 124.47, 123.61, 123.58, 122.22, 121.11, 121.06, 109.33, 109.08, 108.87, 108.31, 107.53, 107.45, 77.36, 77.04, 76.72, 61.99, 35.56.

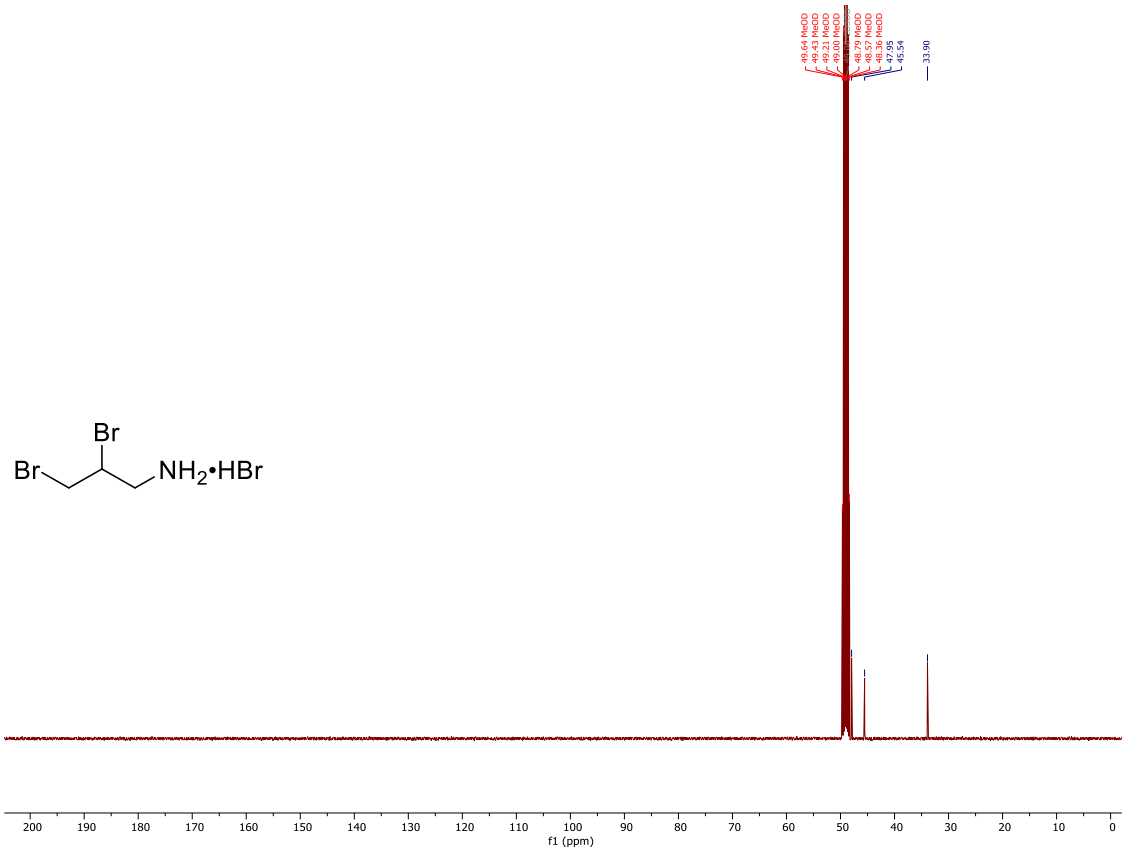
LRMS (DEP/EI-Orbitrap): *m/z* (%): 357 (33), 174 (12), 173 (100), 172 (72), 146 (11), 145 (20), 83 (11).
HRMS (EI) m/z: $[M]^+$ calcd for $C_{20}H_{14}F_3NO_2$: 357.0977; found: 357.0970.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2854 (vw), 1632 (vw), 1600 (w), 1582 (w), 1503 (m), 1463 (m), 1449 (w), 1430 (w), 1400 (m), 1341 (vw), 1292 (w), 1233 (vs), 1148 (s), 1102 (w), 1037 (m), 949 (w), 937 (vw), 900 (vw), 863 (vw), 810 (m), 789 (vw), 774 (w), 759 (m).

5. NMR Spectra

2,3-Dibromopropan-1-amine hydrobromide (1)

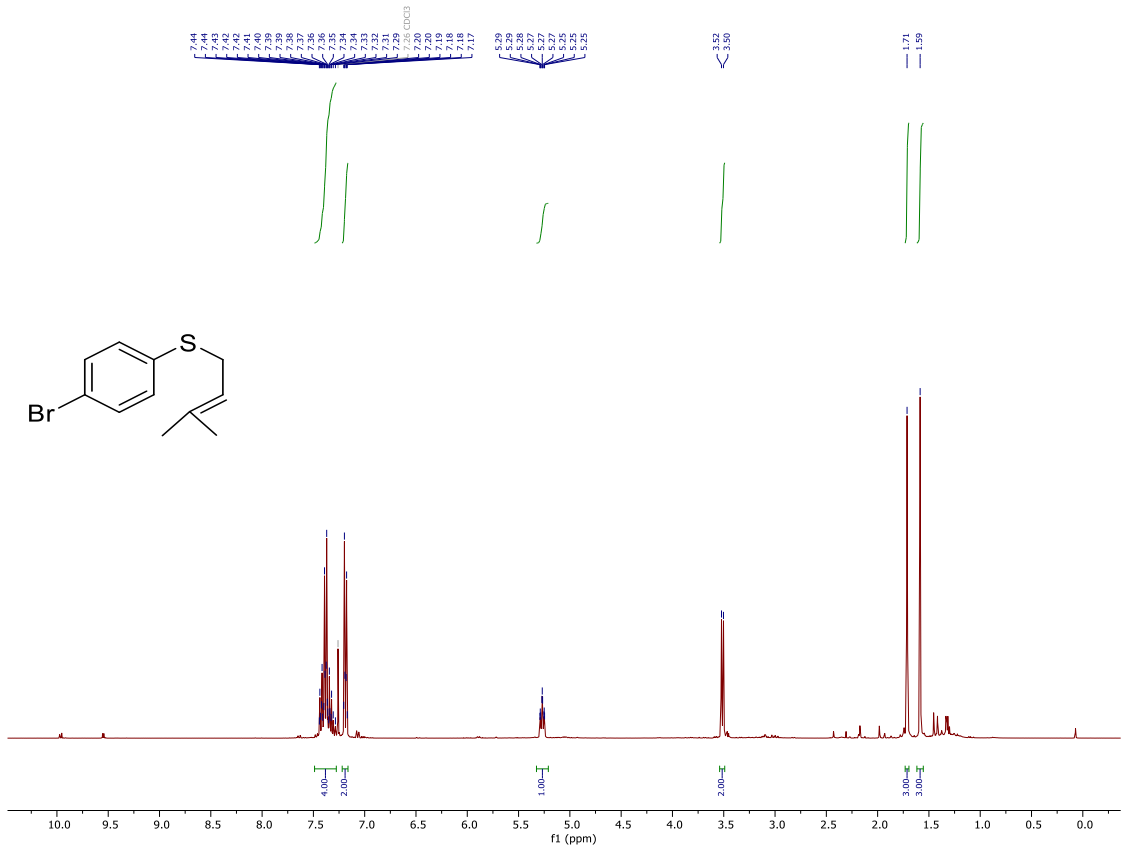
^{1}H NMR (400 MHz, CD_3OD) and **^{13}C NMR** (100 MHz, CD_3OD)

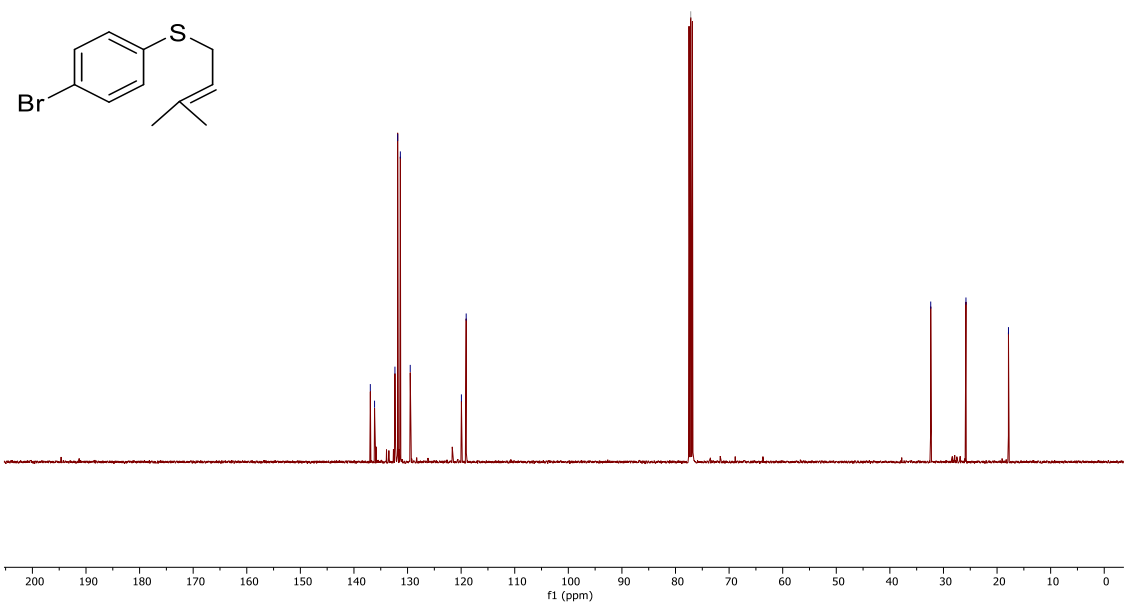




(4-Bromophenyl)(3-methylbut-2-en-1-yl)sulfane

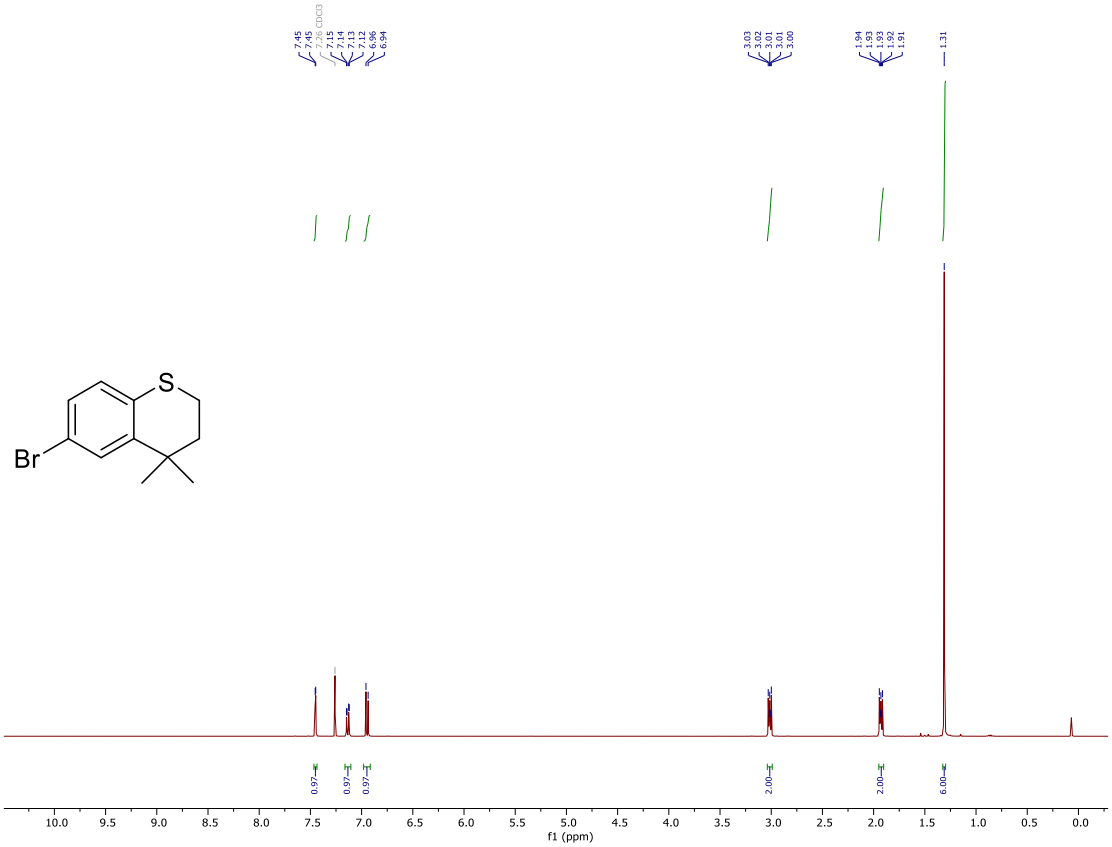
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

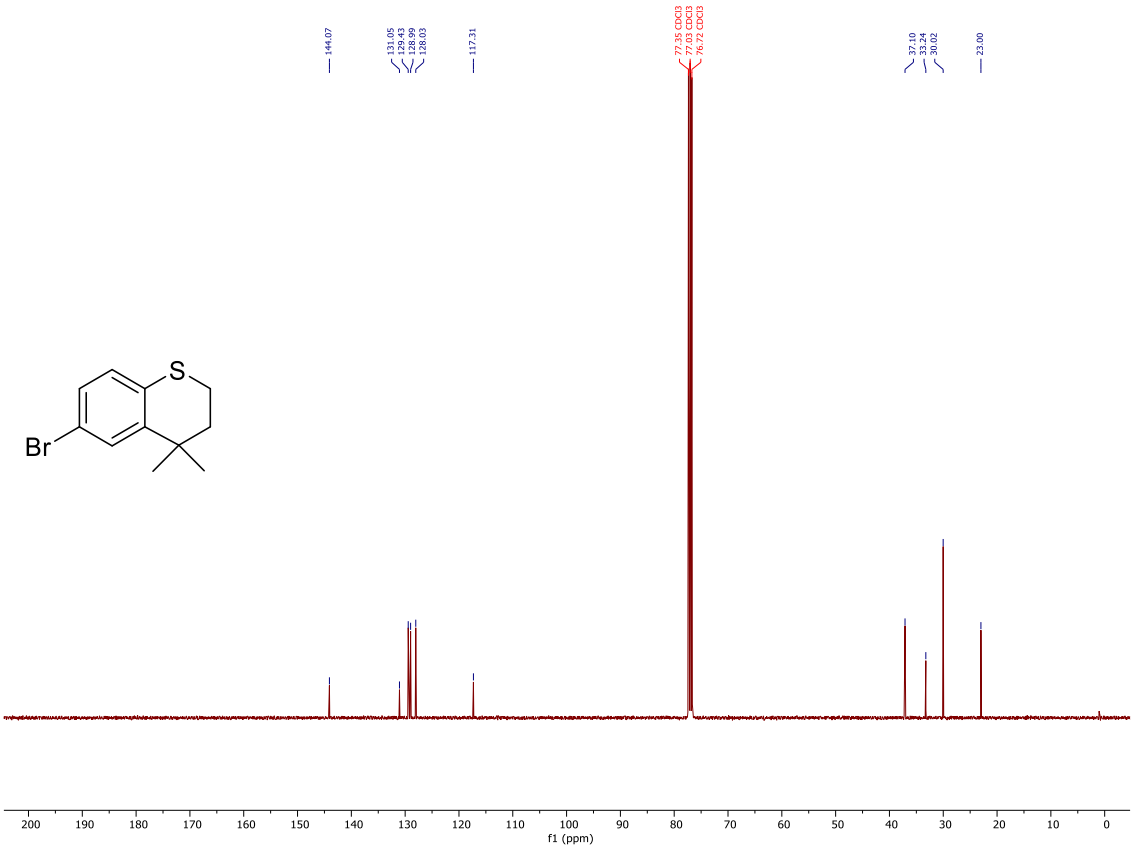




6-Bromo-4,4-dimethylthiochromane

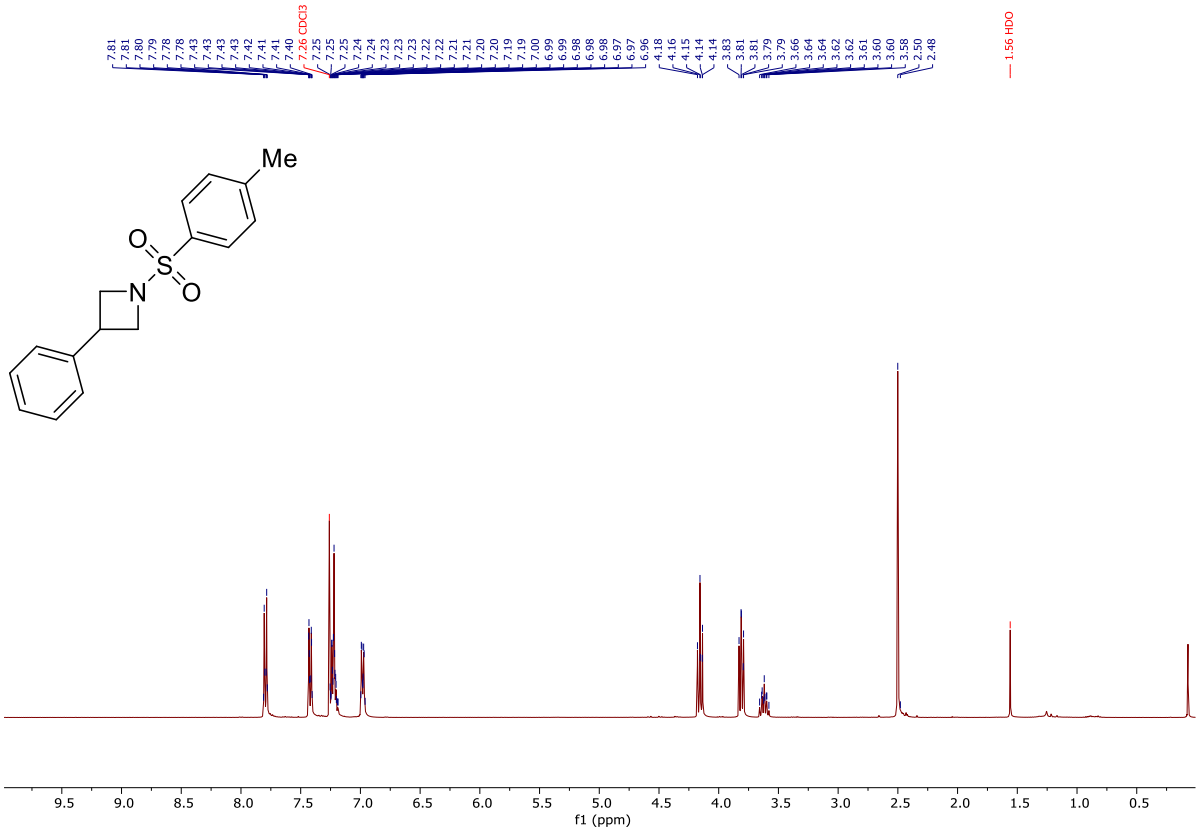
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

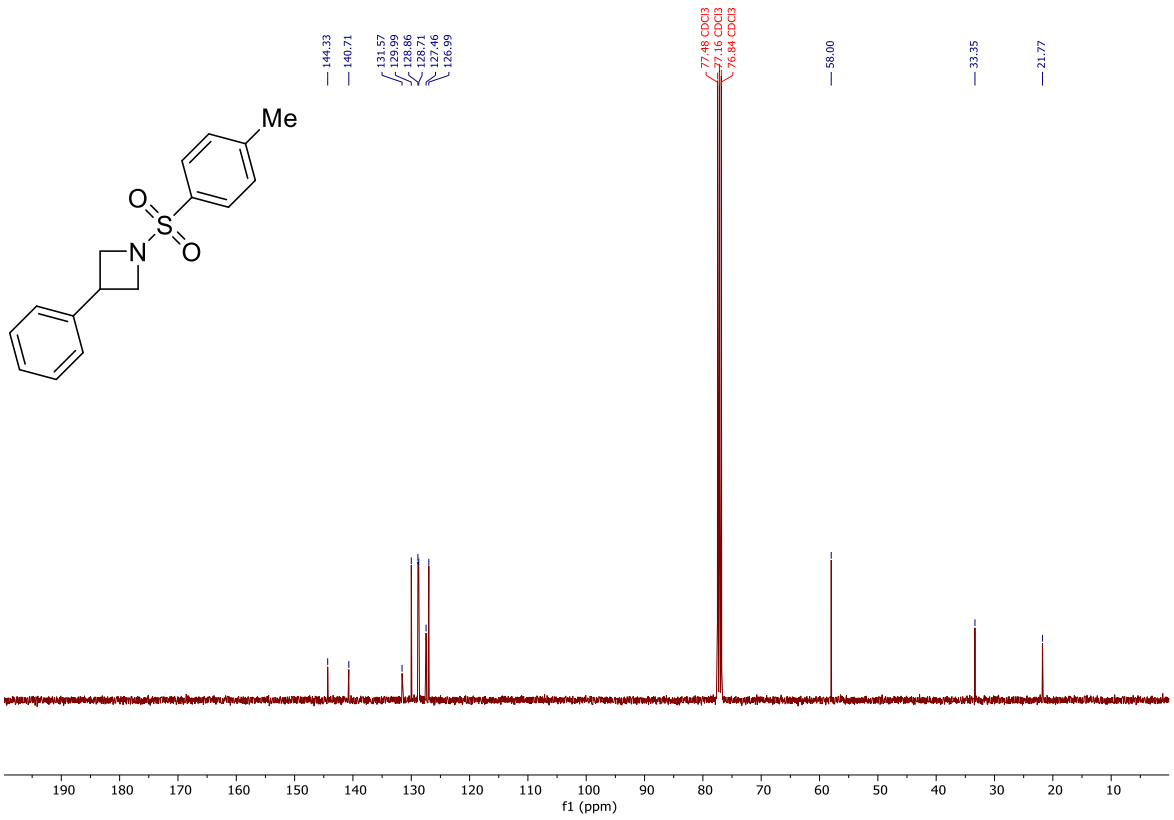




3-Phenyl-1-tosylazetidine (3a)

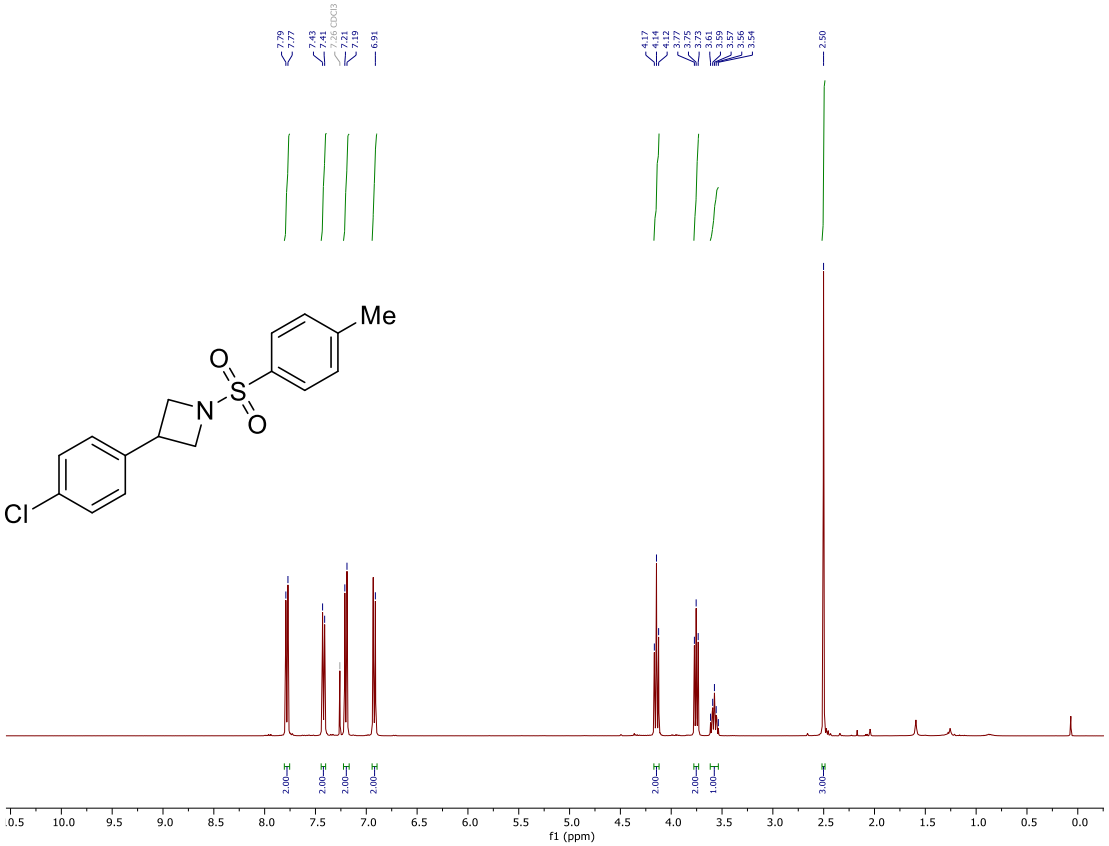
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

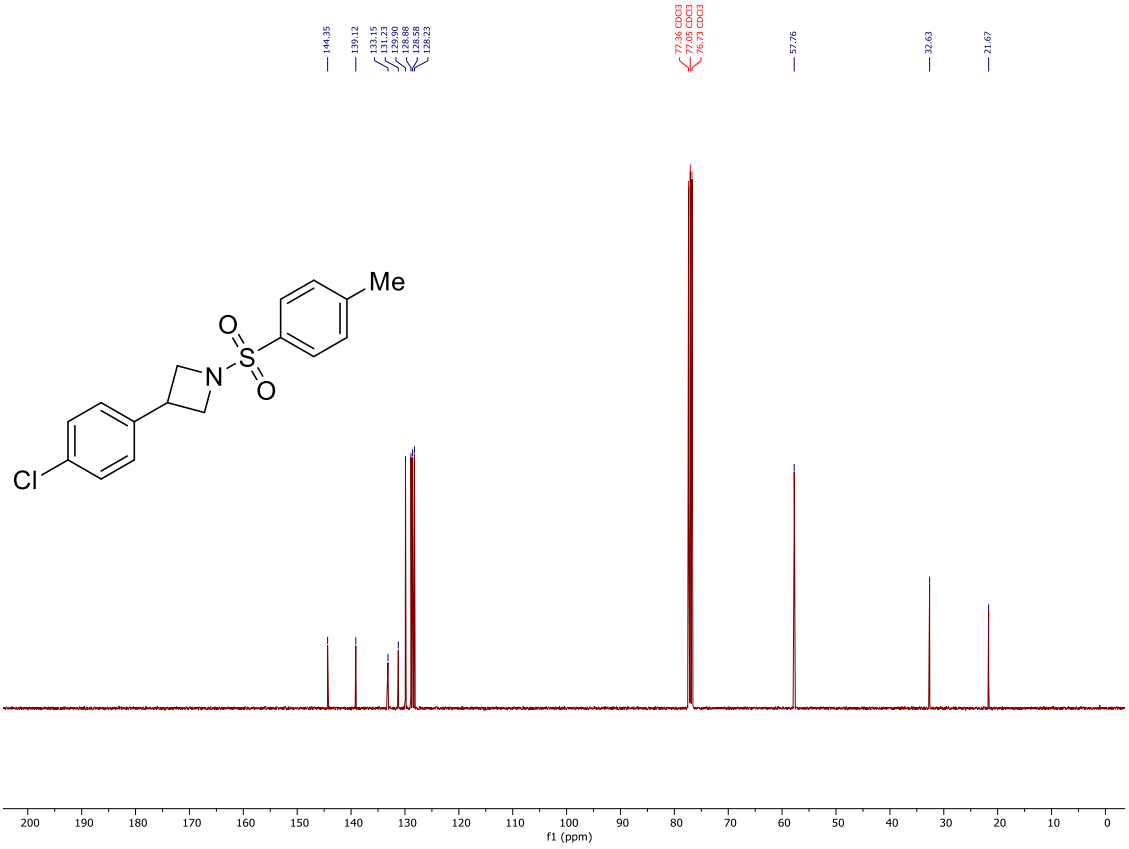




3-(4-Chlorophenyl)-1-tosylazetidine (3b)

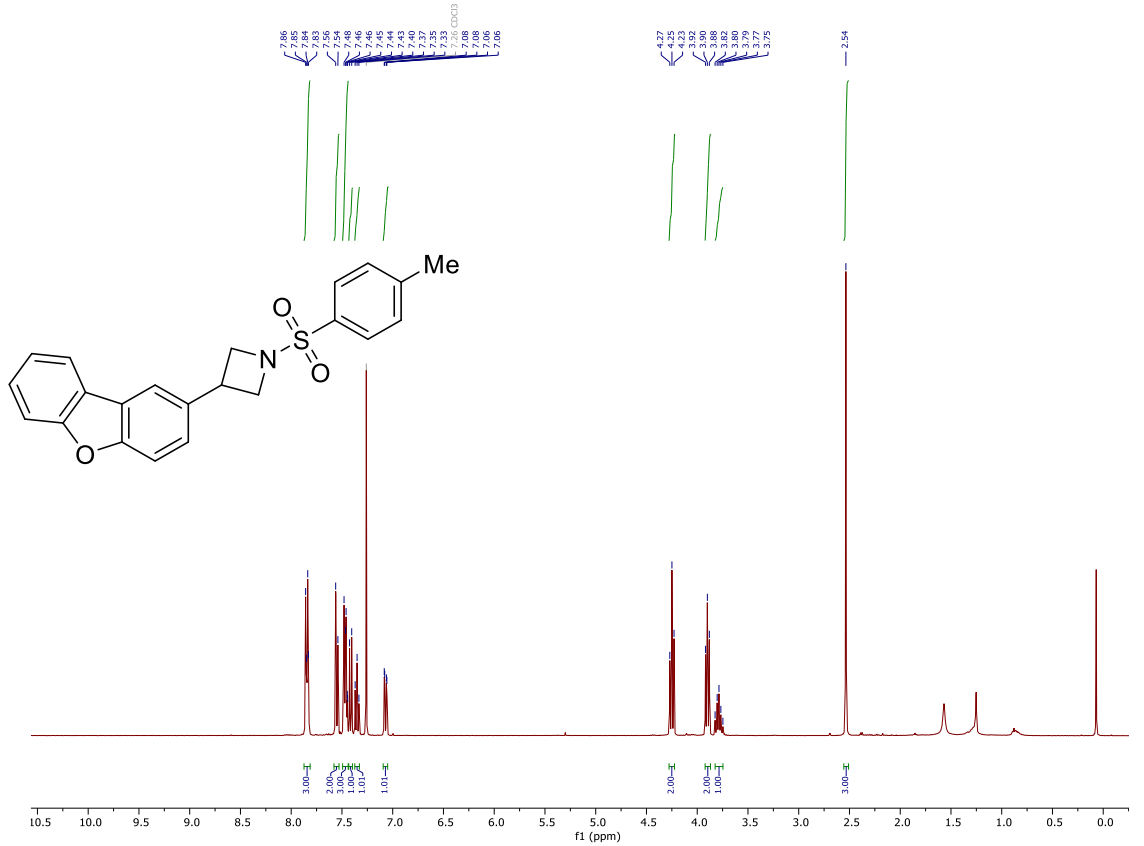
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

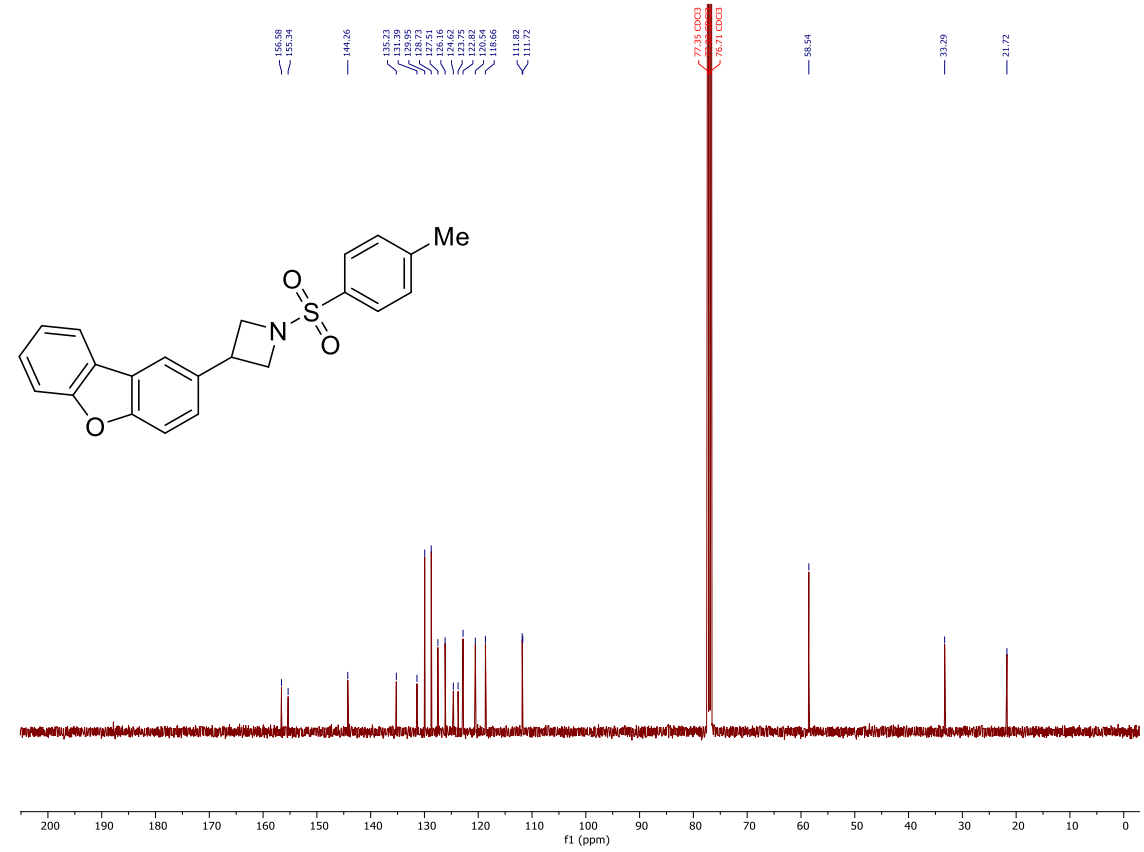




3-(Dibenzo[b,d]furan-2-yl)-1-tosylazetidine (3c)

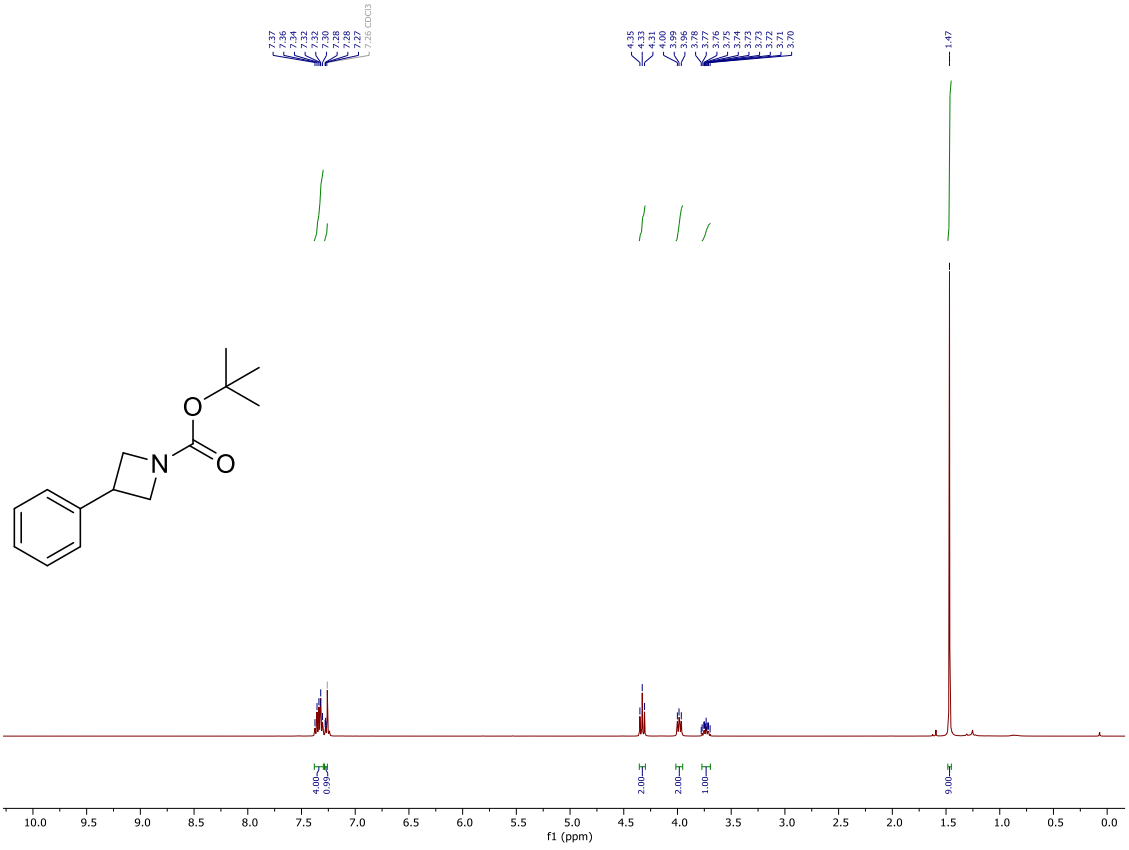
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

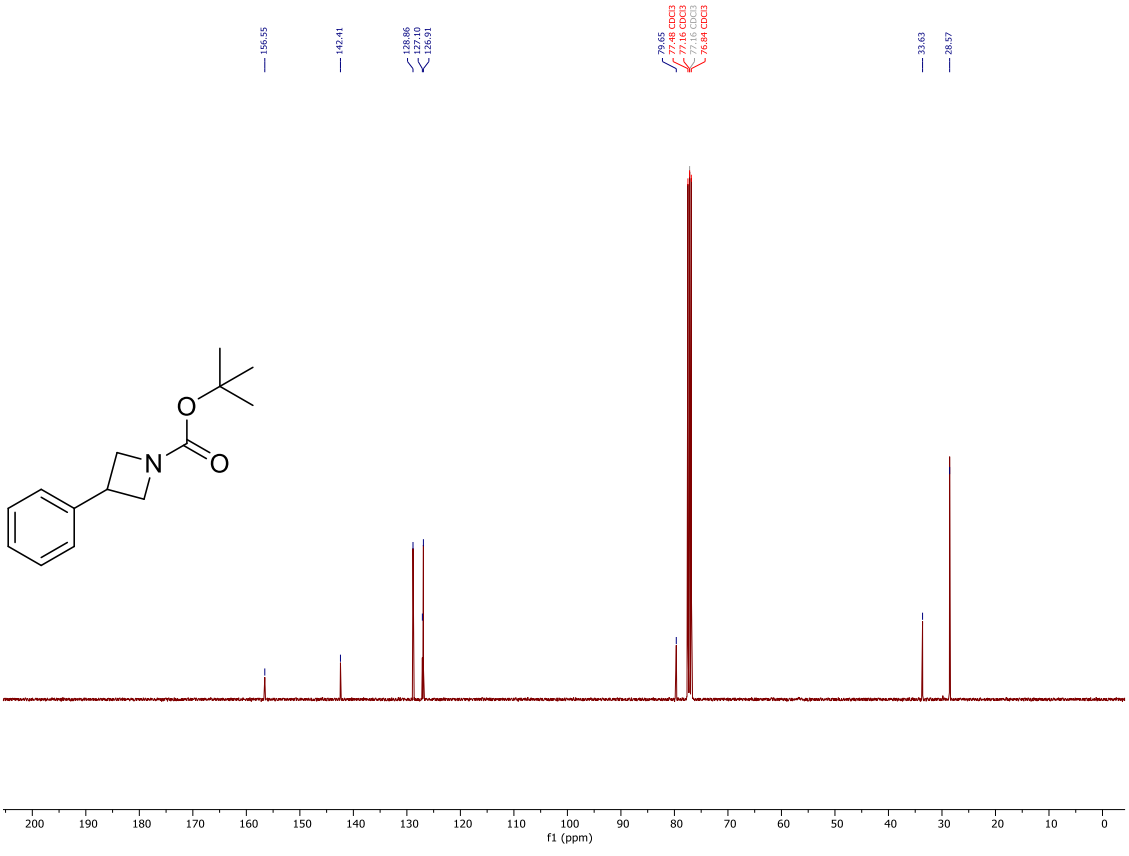




***tert*-Butyl 3-phenylazetidine-1-carboxylate (3d)**

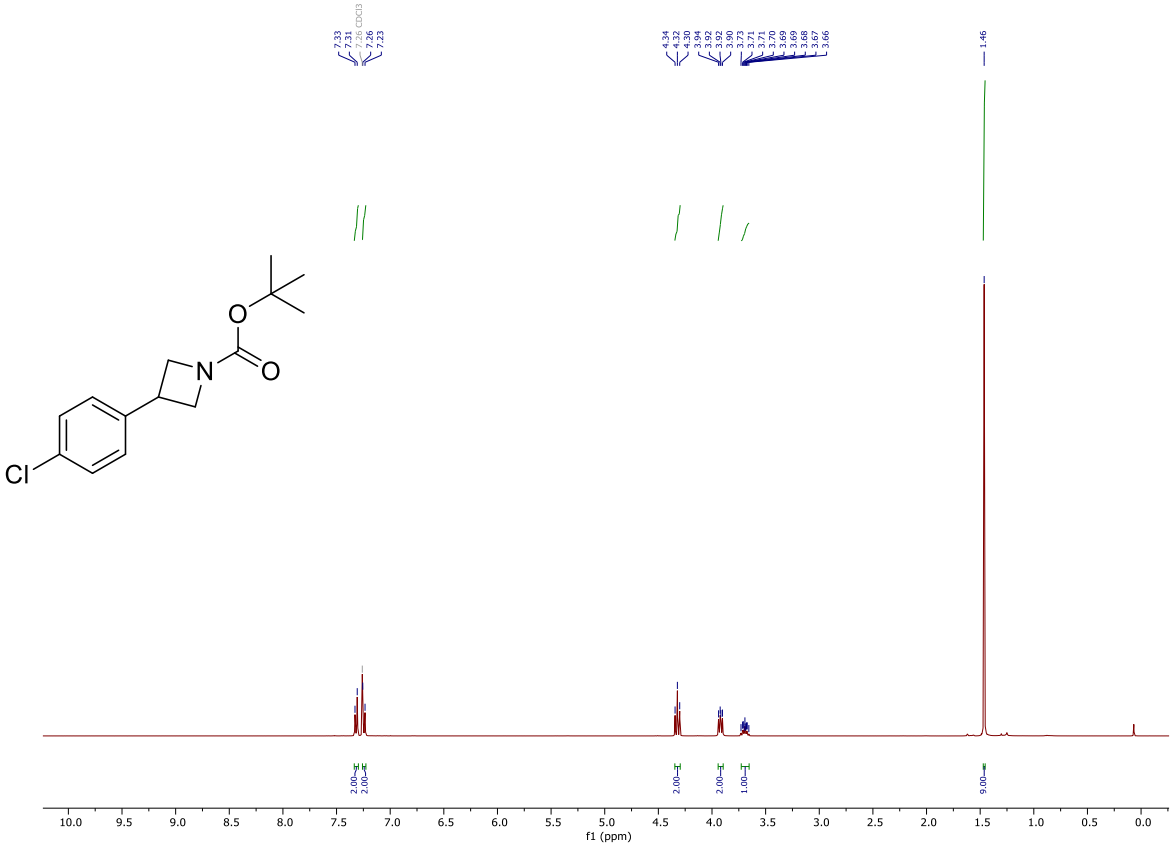
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

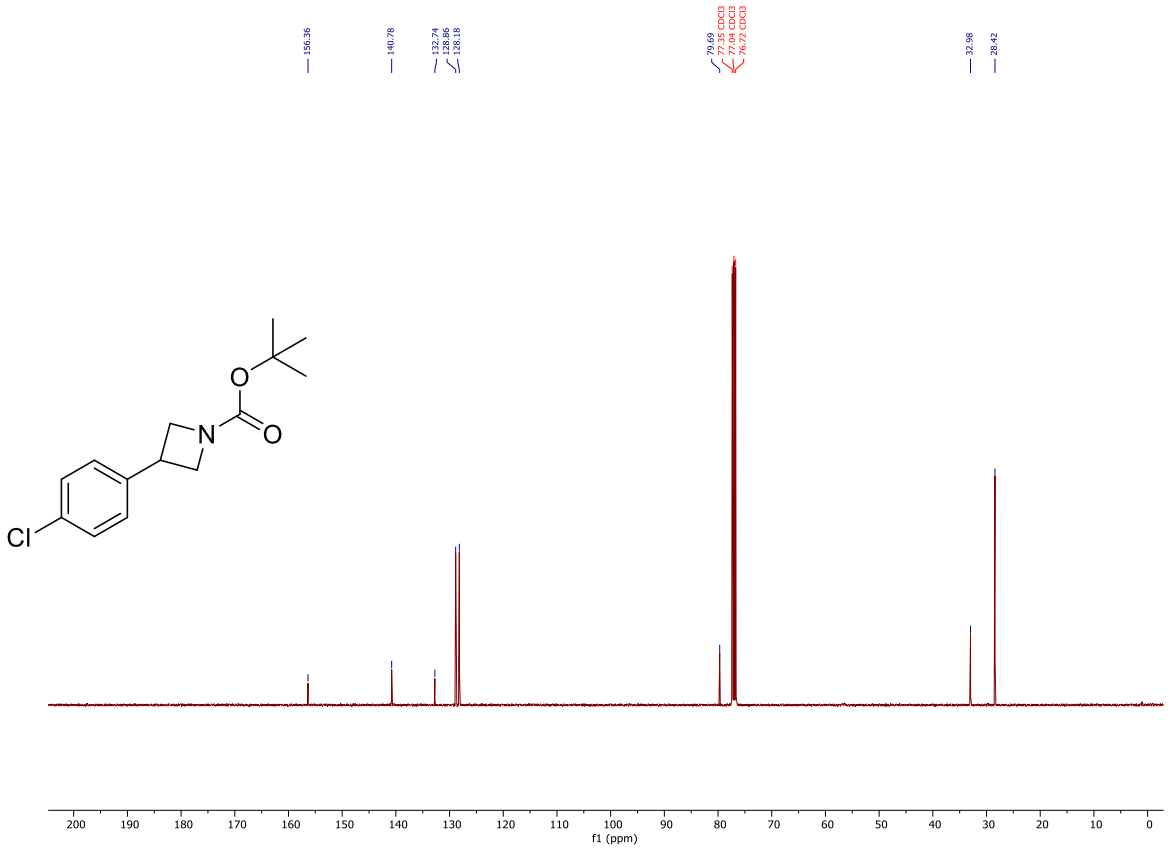




***tert*-Butyl 3-(4-chlorophenyl)azetidine-1-carboxylate (3e)**

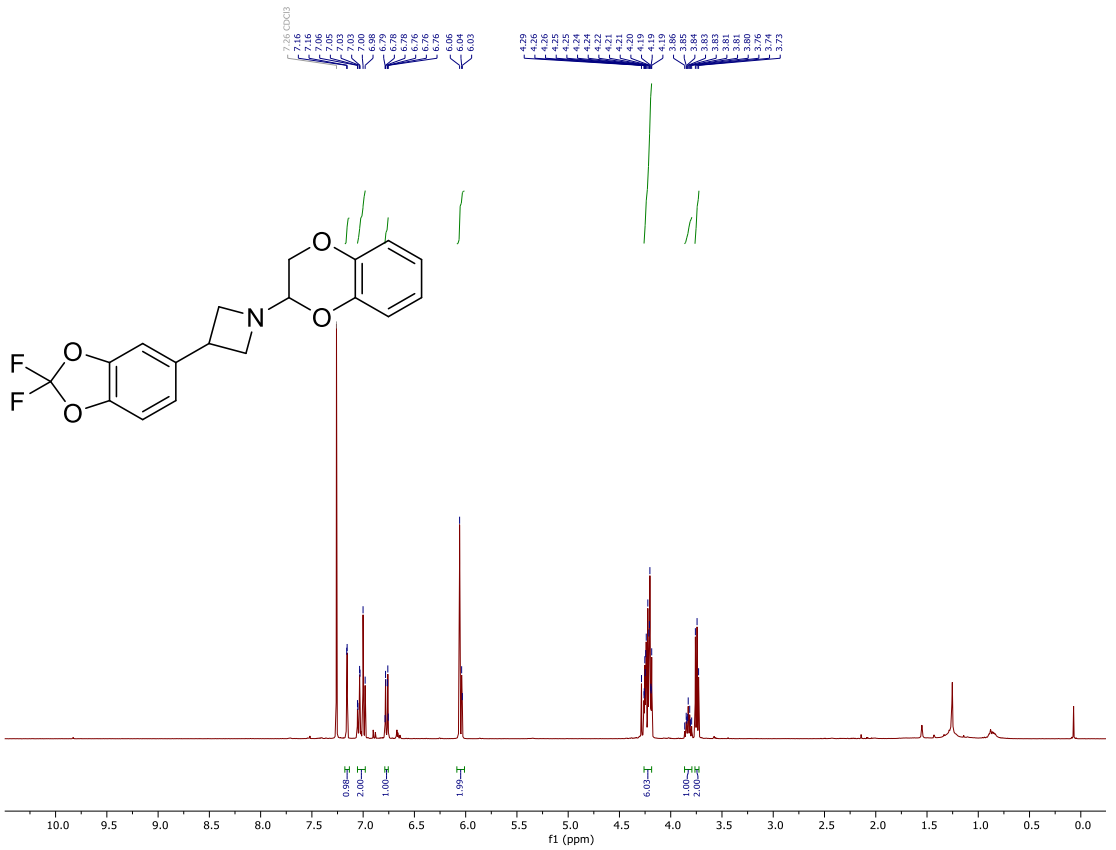
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

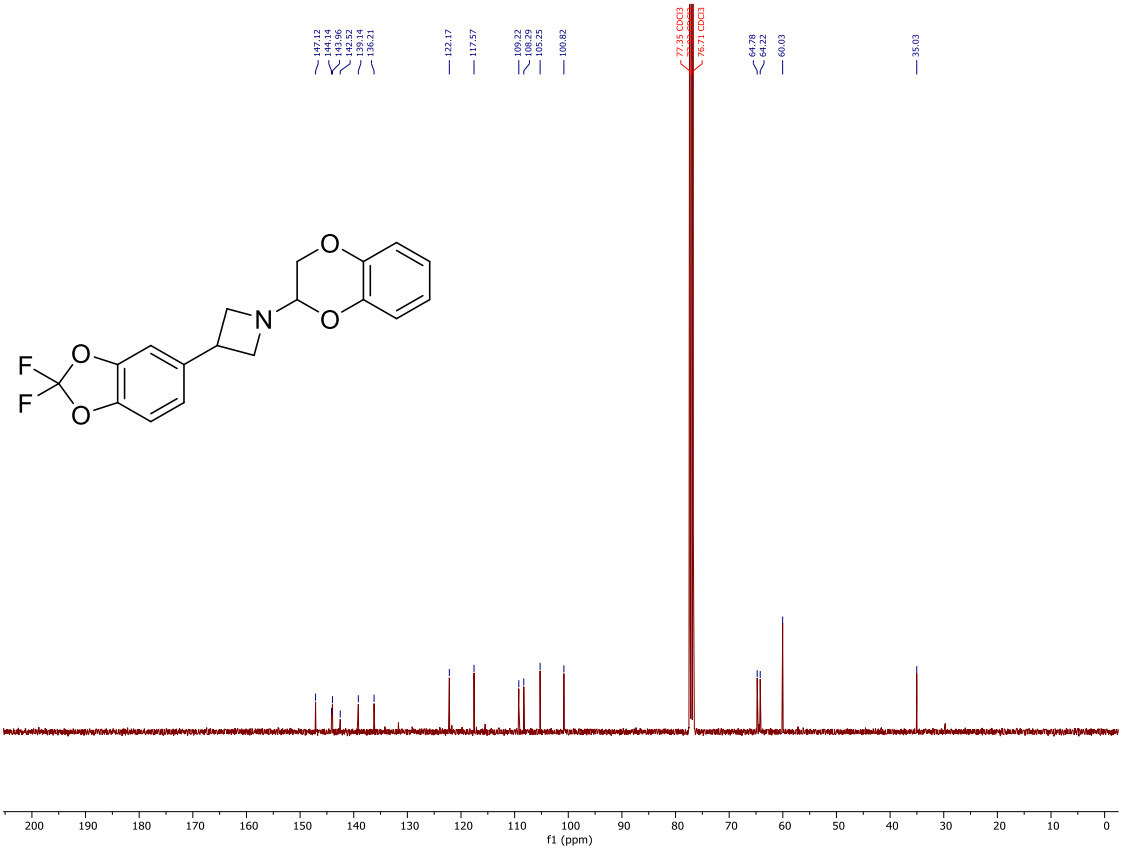


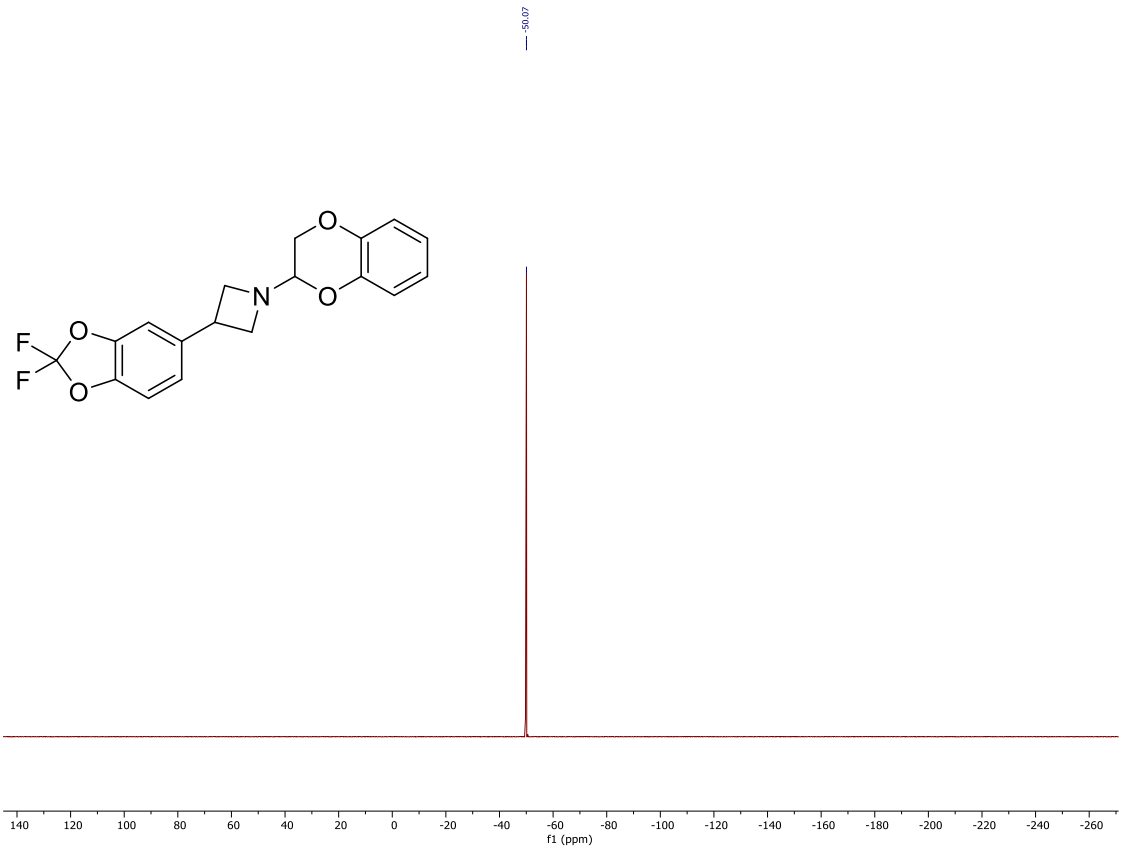


3-(2,2-Difluorobenzo[*d*][1,3]dioxol-5-yl)-1-(2,3-dihydrobenzo[*b*][1,4]dioxin-2-yl)azetidine (3f)

^{1}H NMR (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)



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20
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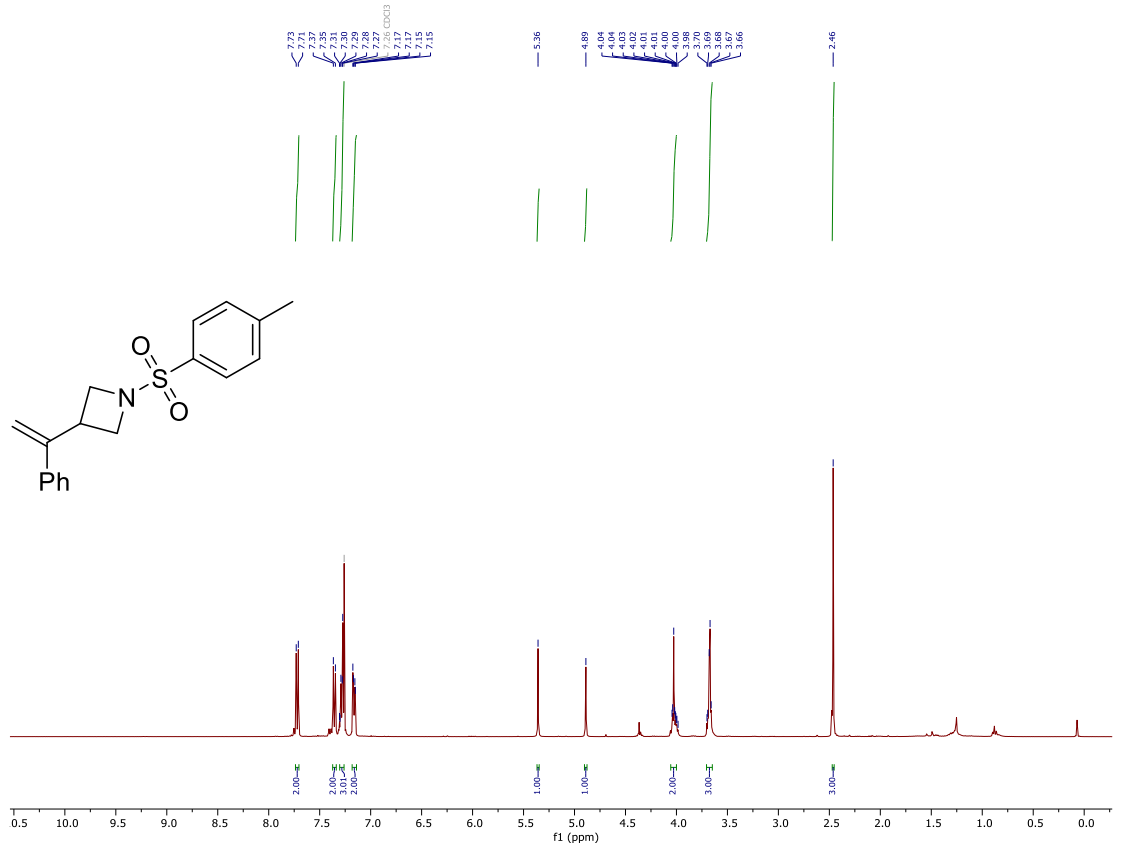
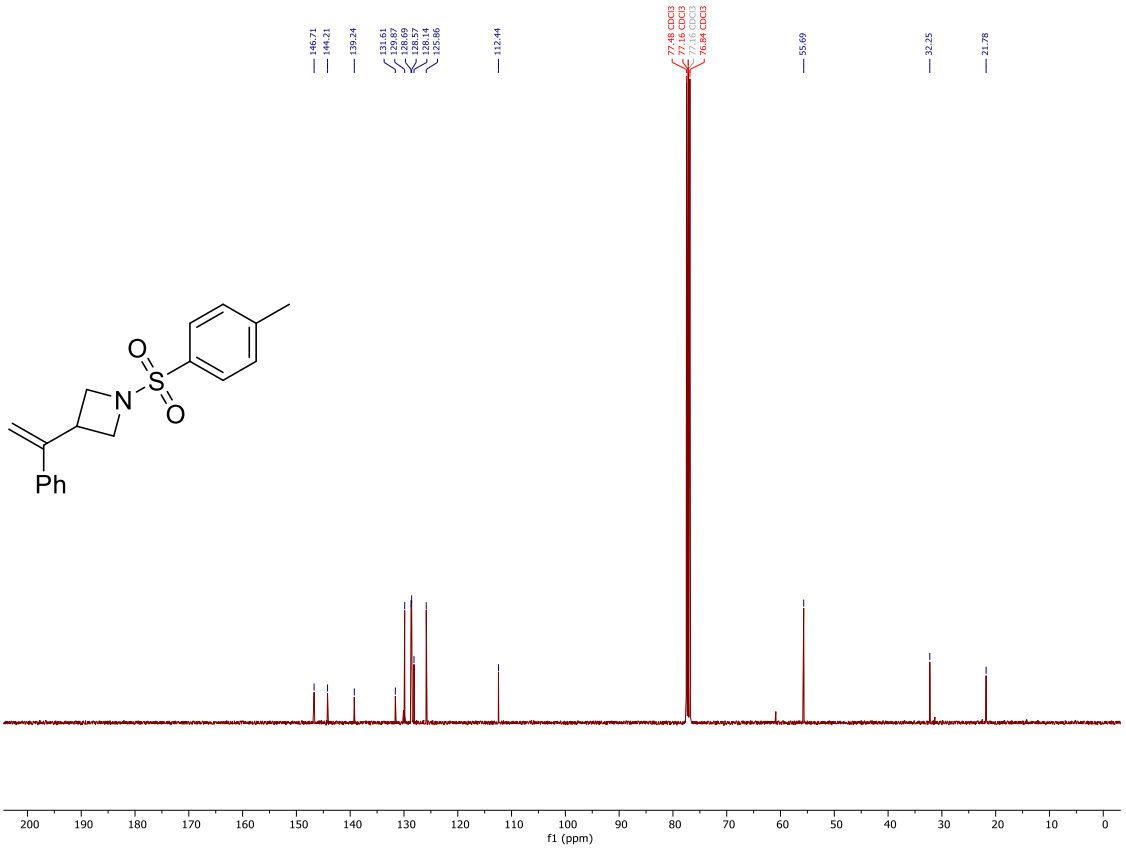
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
f1 (ppm)

3-(1-Phenylvinyl)-1-tosylazetidine (3i)

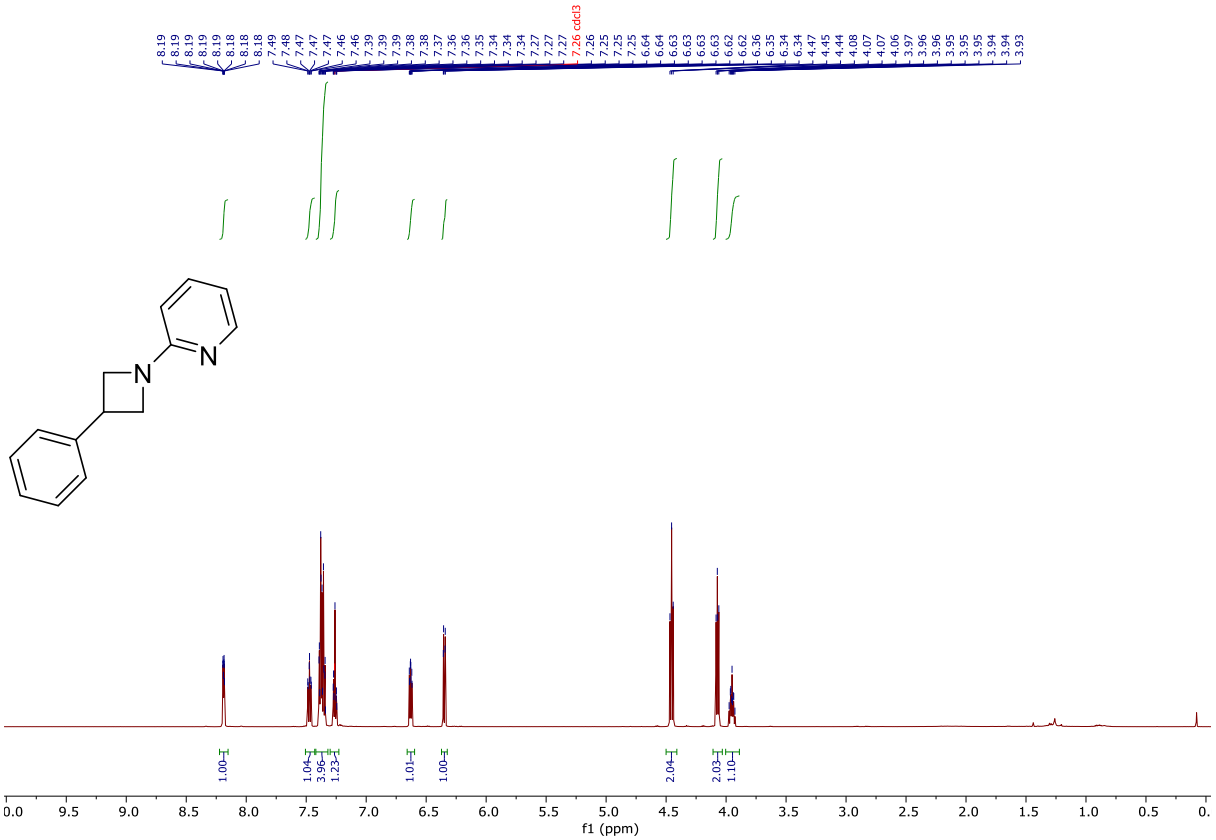
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

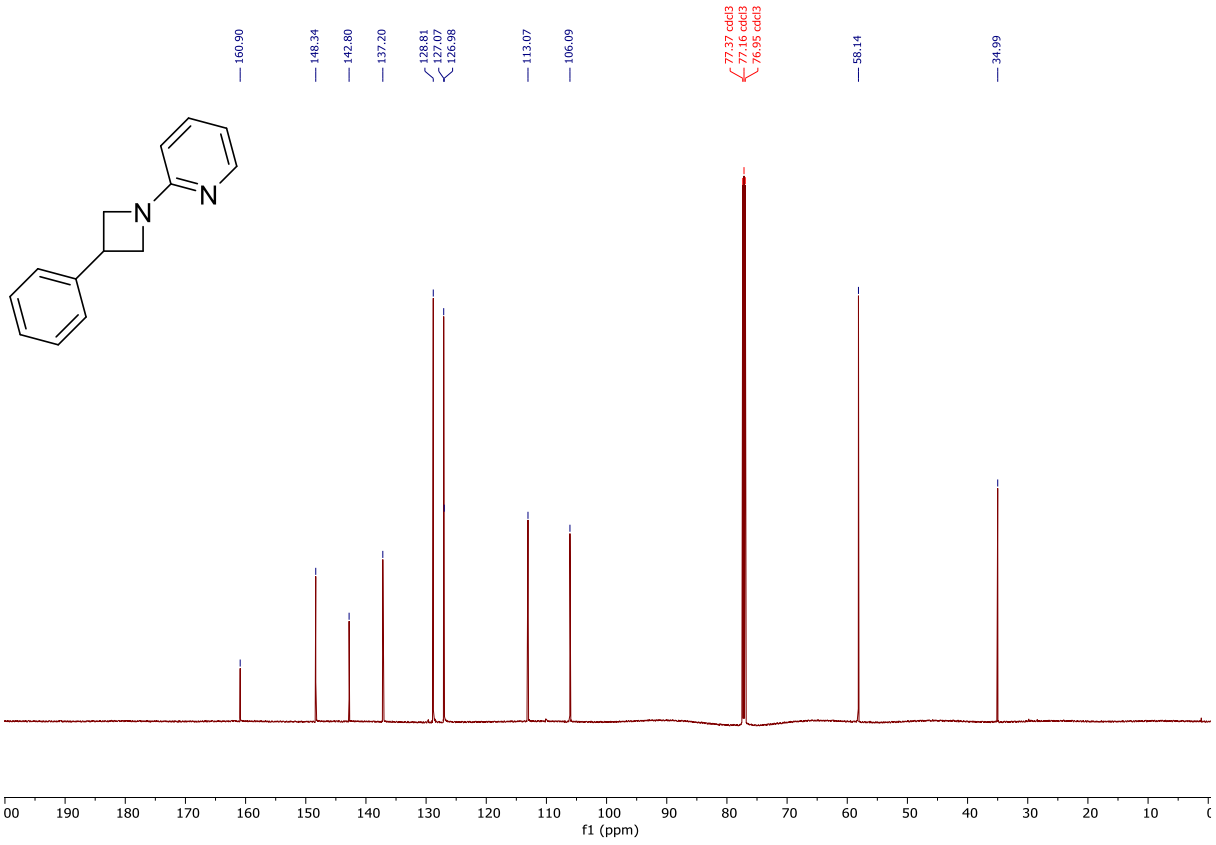




2-(3-Phenylazetidin-1-yl)pyridine (7a)

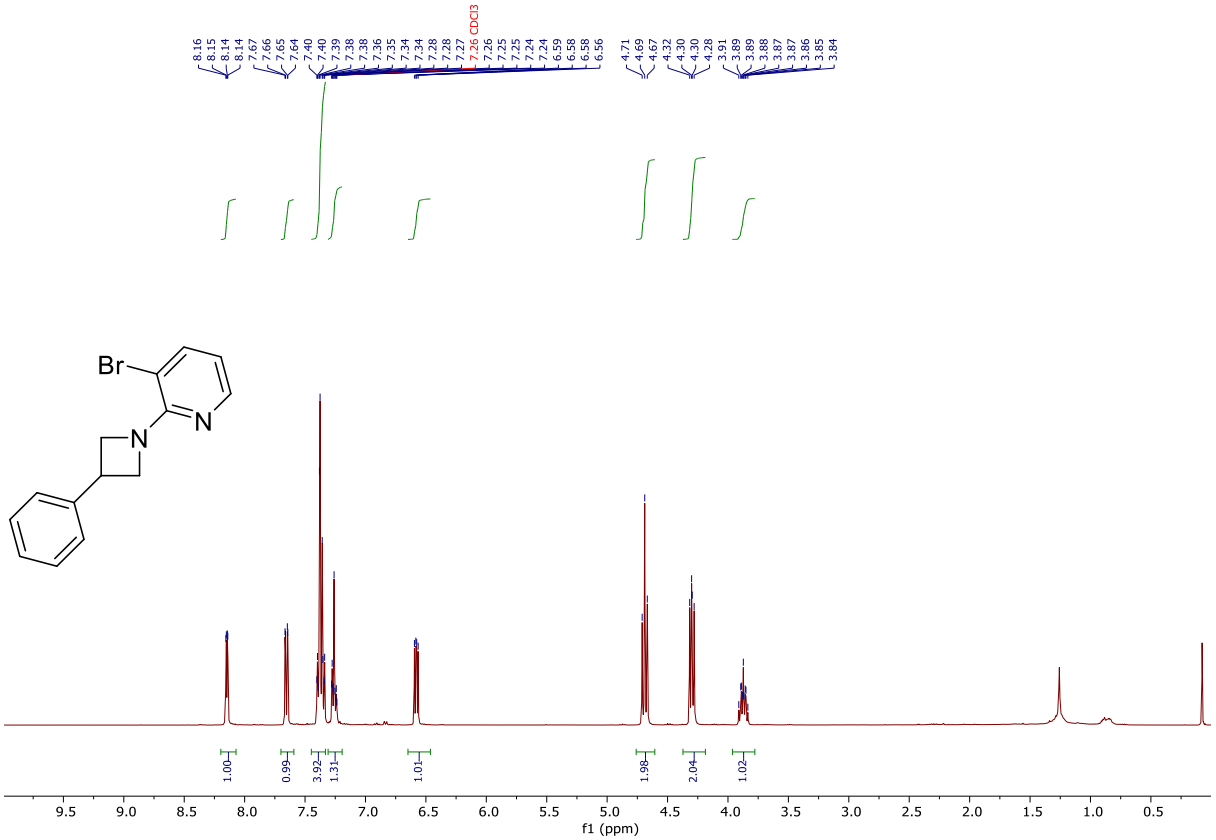
^{1}H NMR (600 MHz, $CDCl_3$) and **^{13}C NMR** (150 MHz, $CDCl_3$)

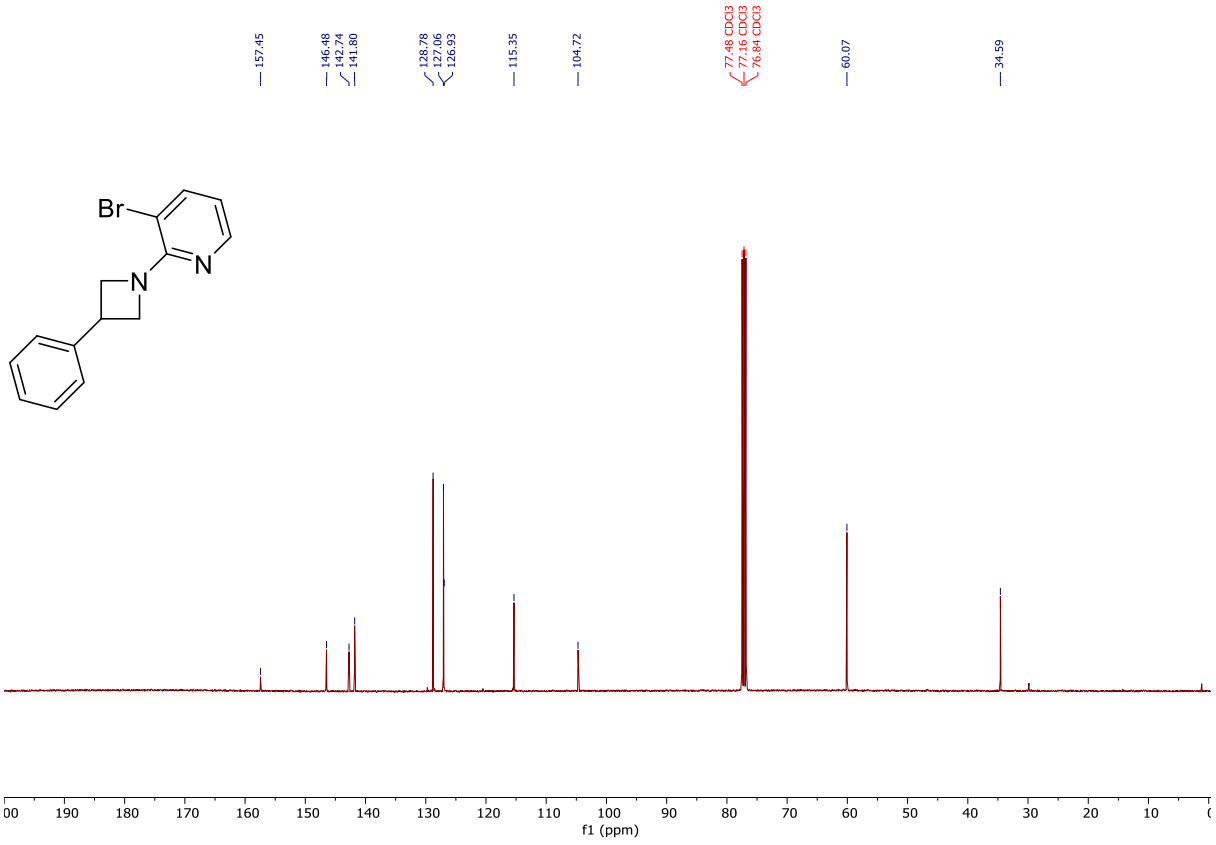




3-Bromo-2-(3-phenylazetidin-1-yl)pyridine (7b)

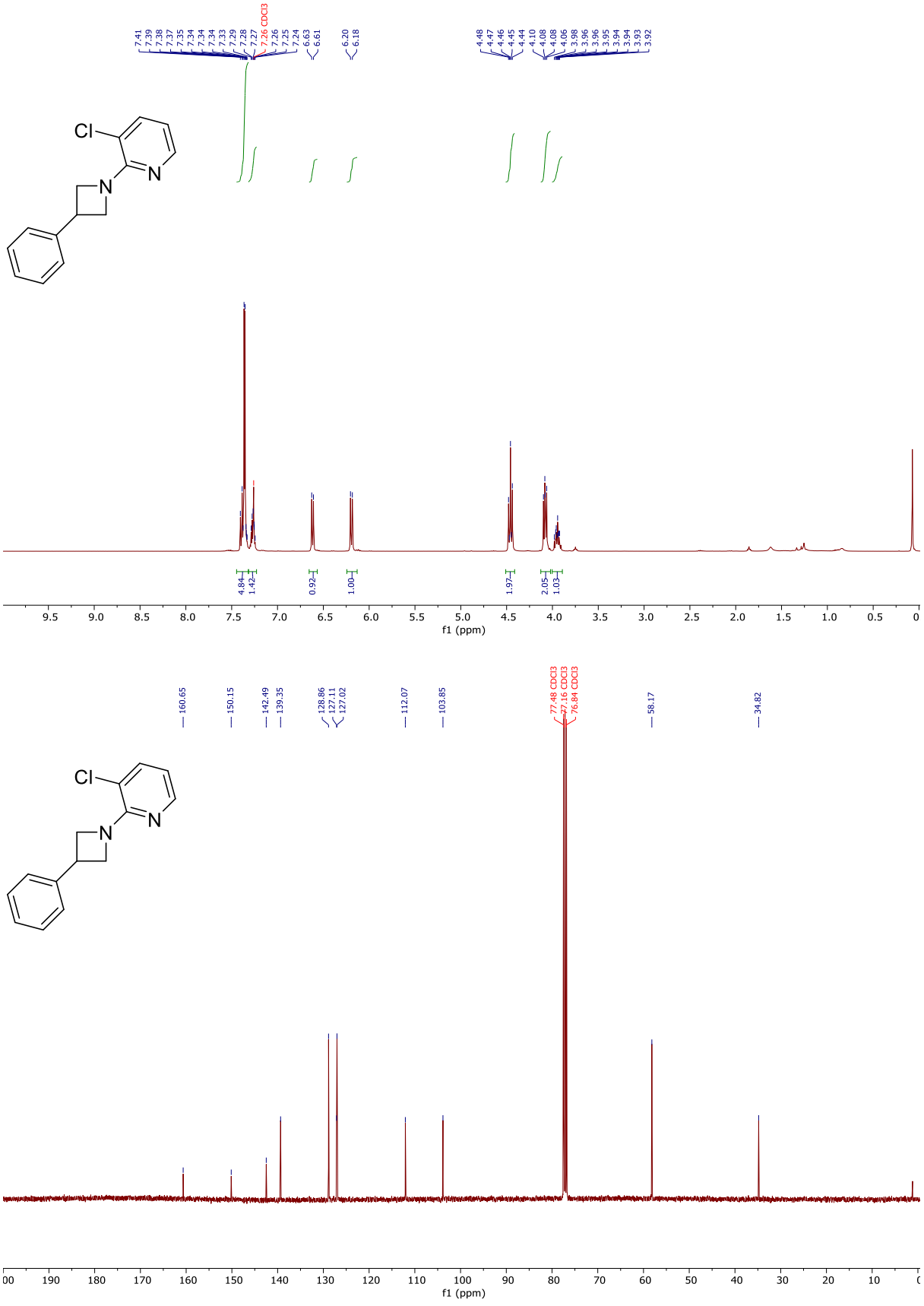
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)





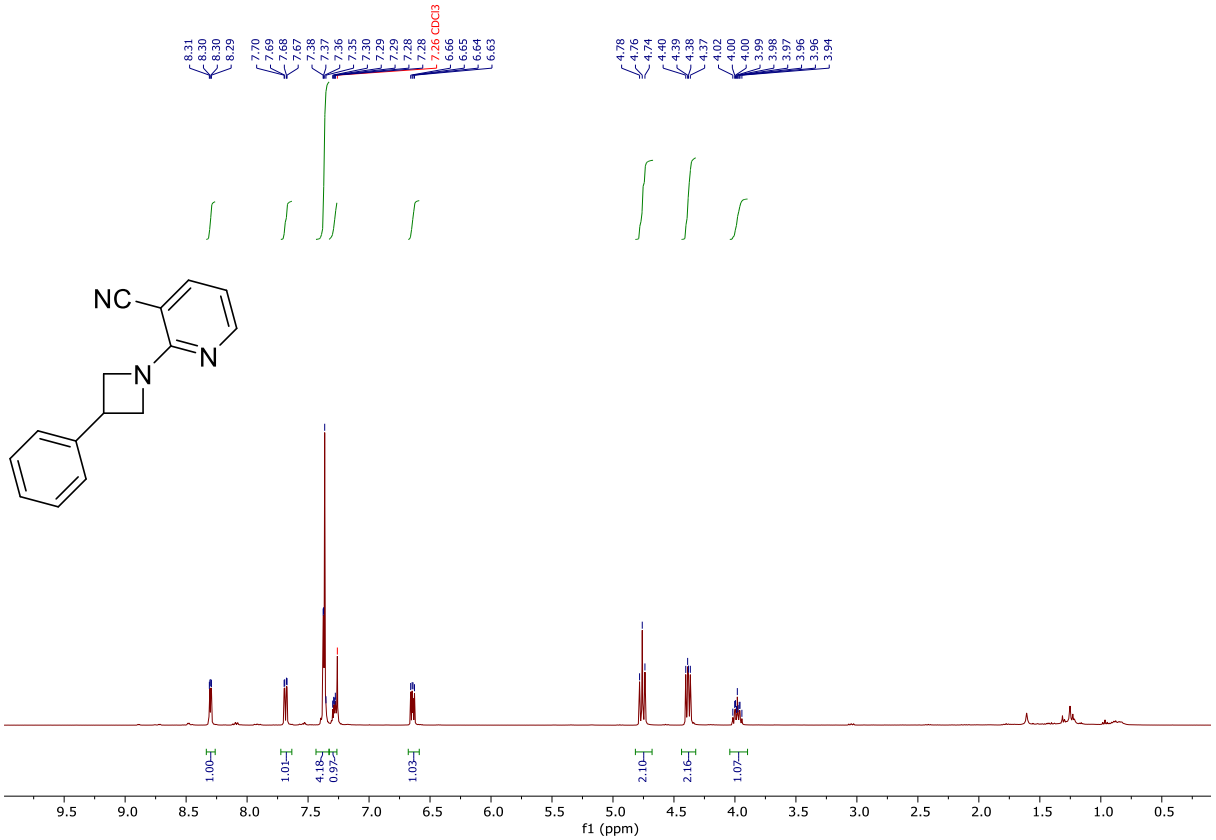
3-chloro-2-(3-phenylazetidin-1-yl)pyridine (7c)

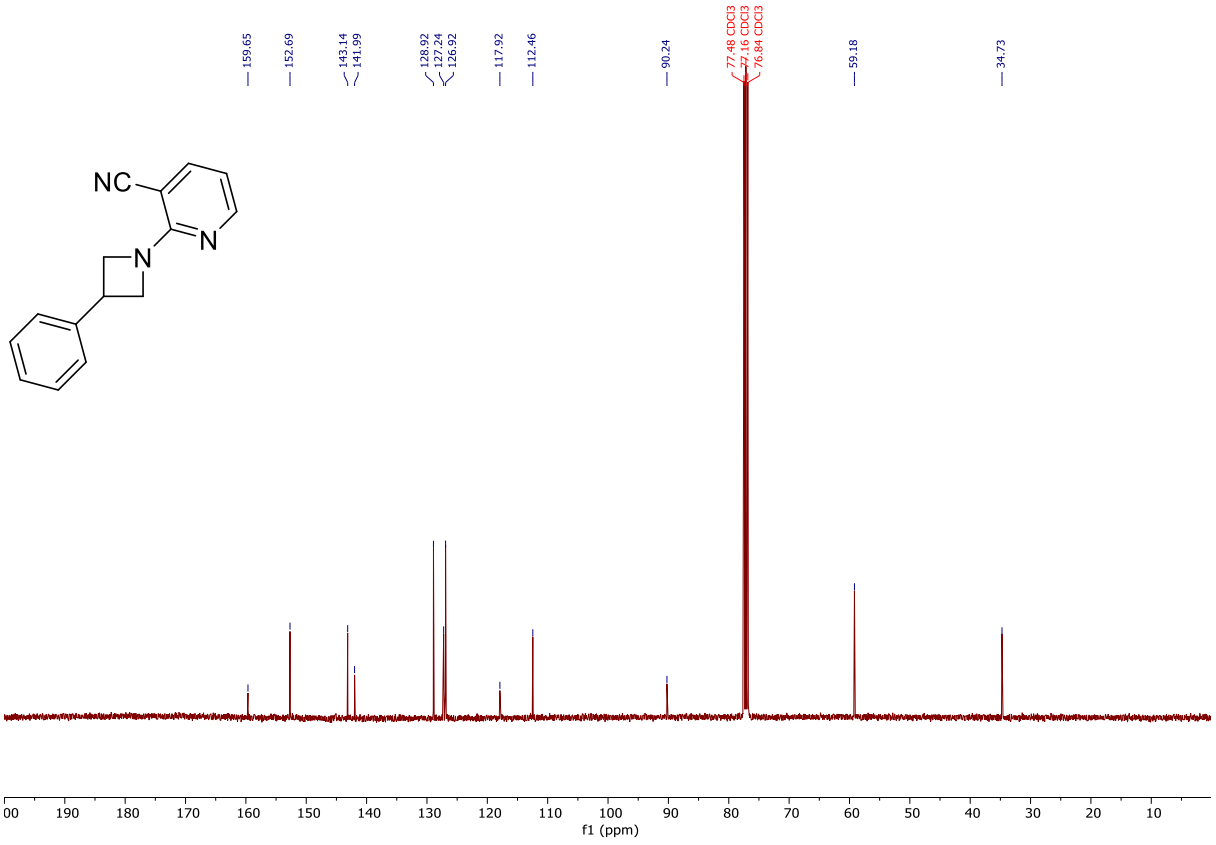
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)



2-(3-Phenylazetidin-1-yl)nicotinonitrile (7d)

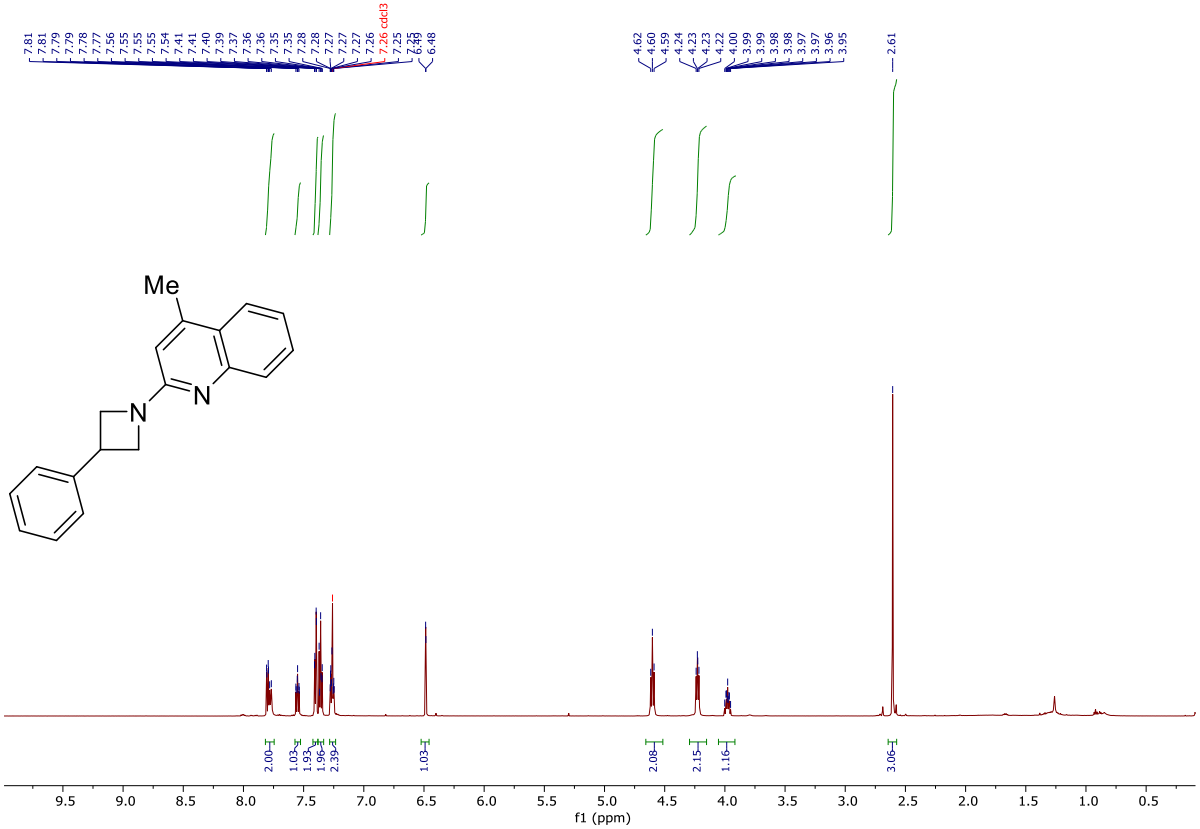
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

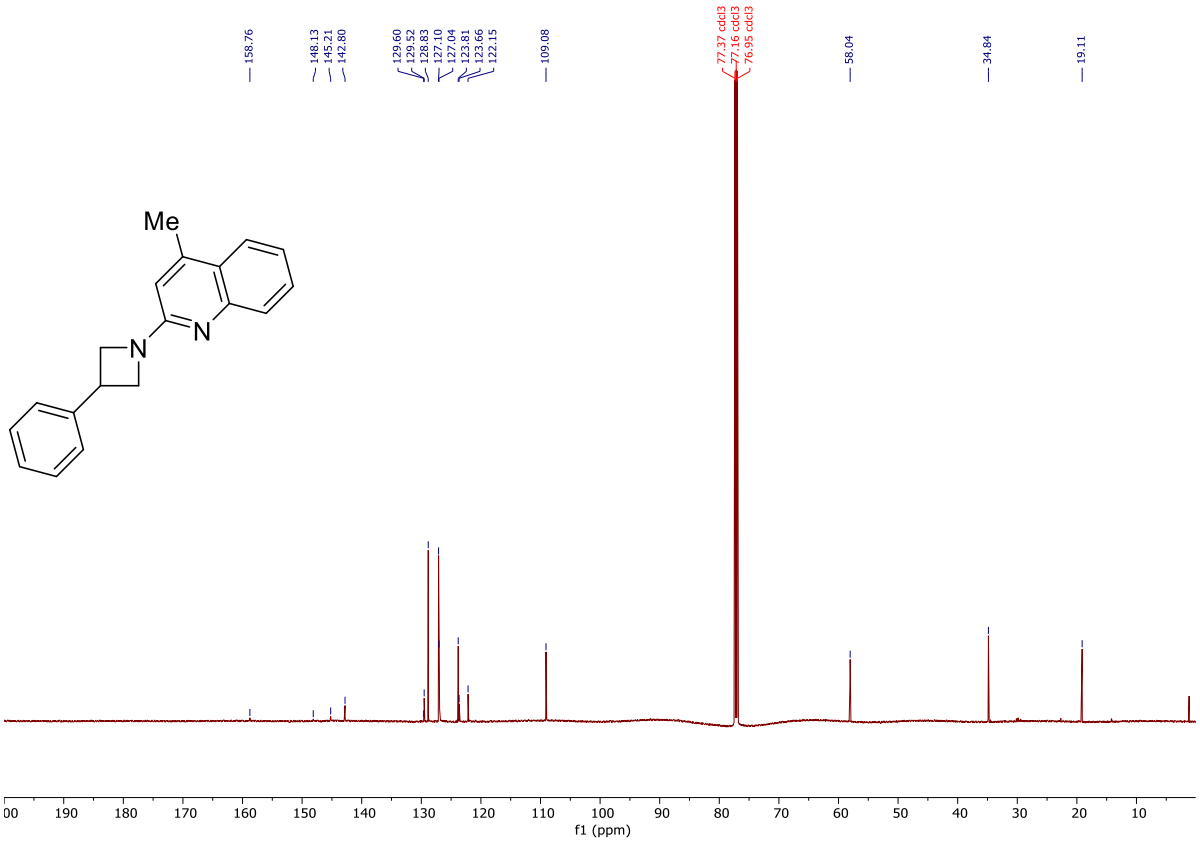




4-Methyl-2-(3-phenylazetidin-1-yl)quinoline (7e)

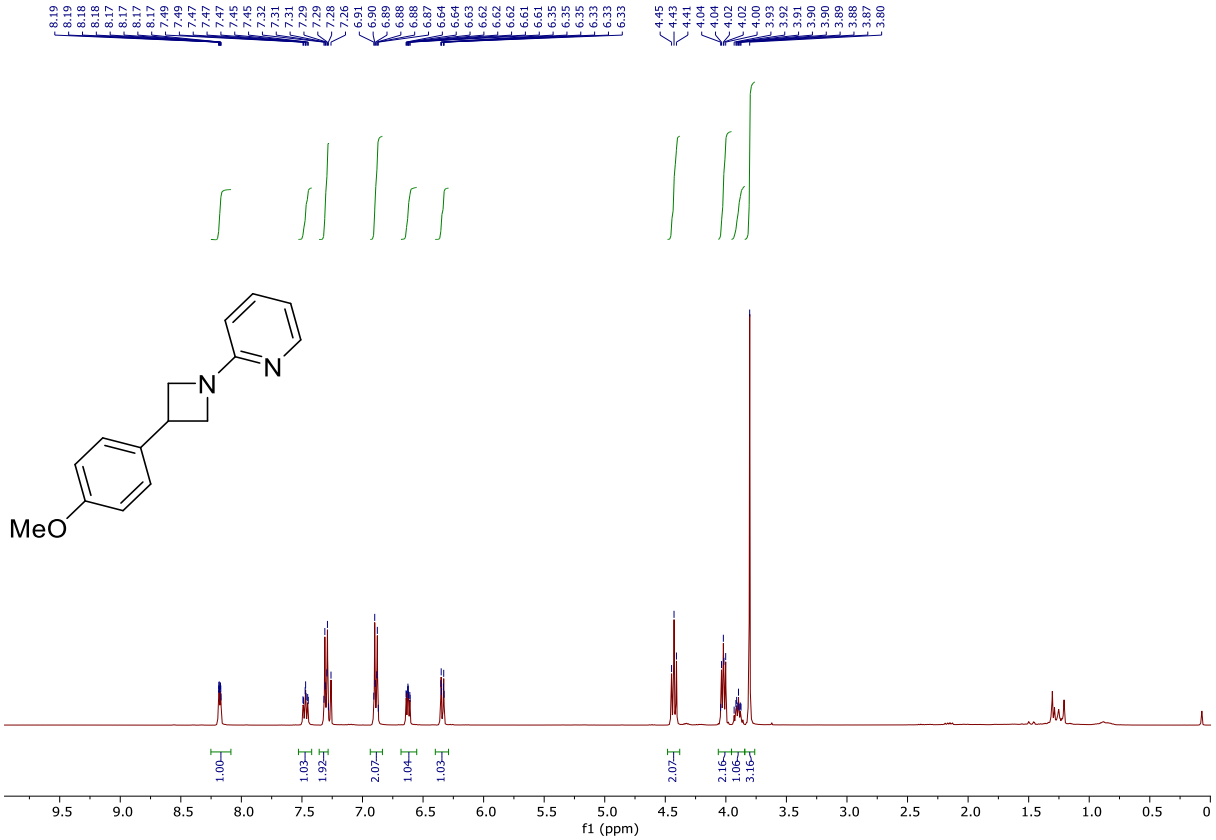
^{1}H NMR (600 MHz, $CDCl_3$) and **^{13}C NMR** (150 MHz, $CDCl_3$)

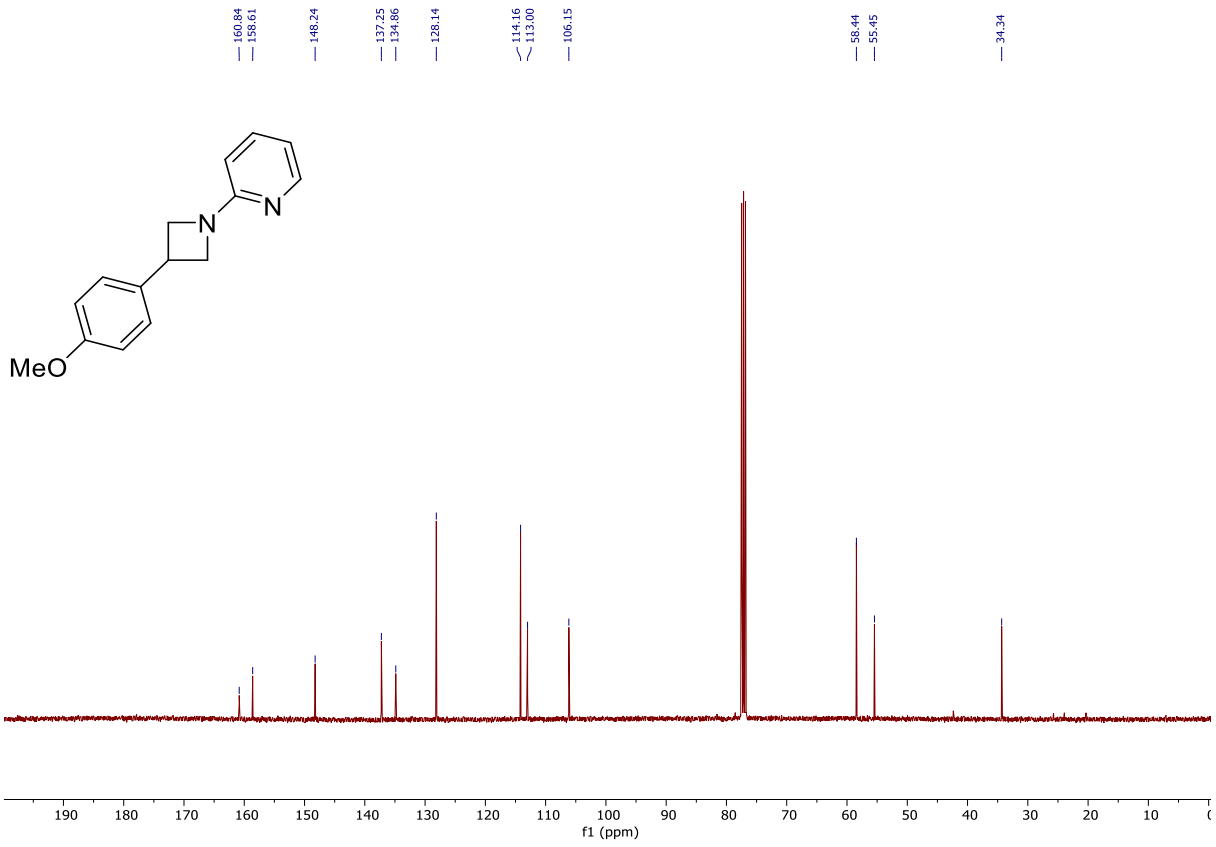




2-(3-(4-Methoxyphenyl)azetidin-1-yl)pyridine (7f)

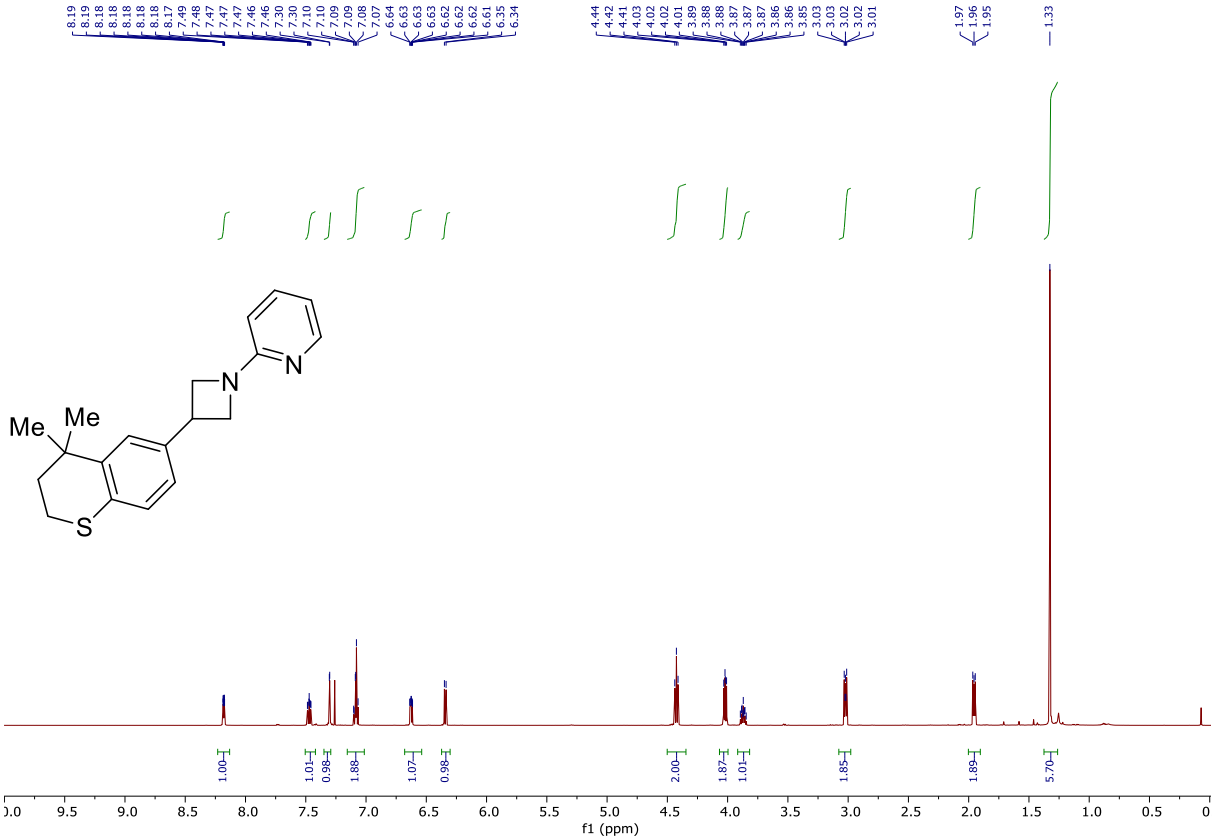
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

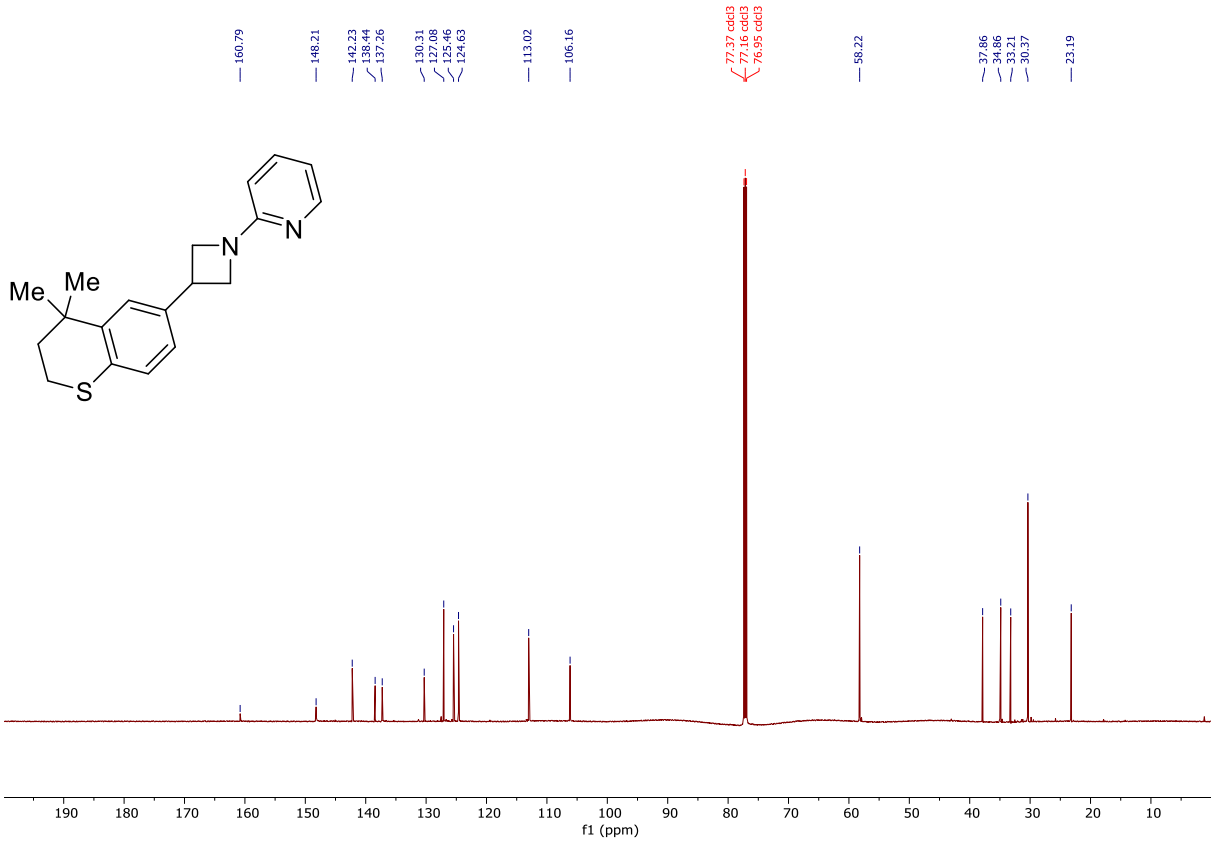




2-(3-(4,4-Dimethylthiochroman-6-yl)azetidin-1-yl)pyridine (7g)

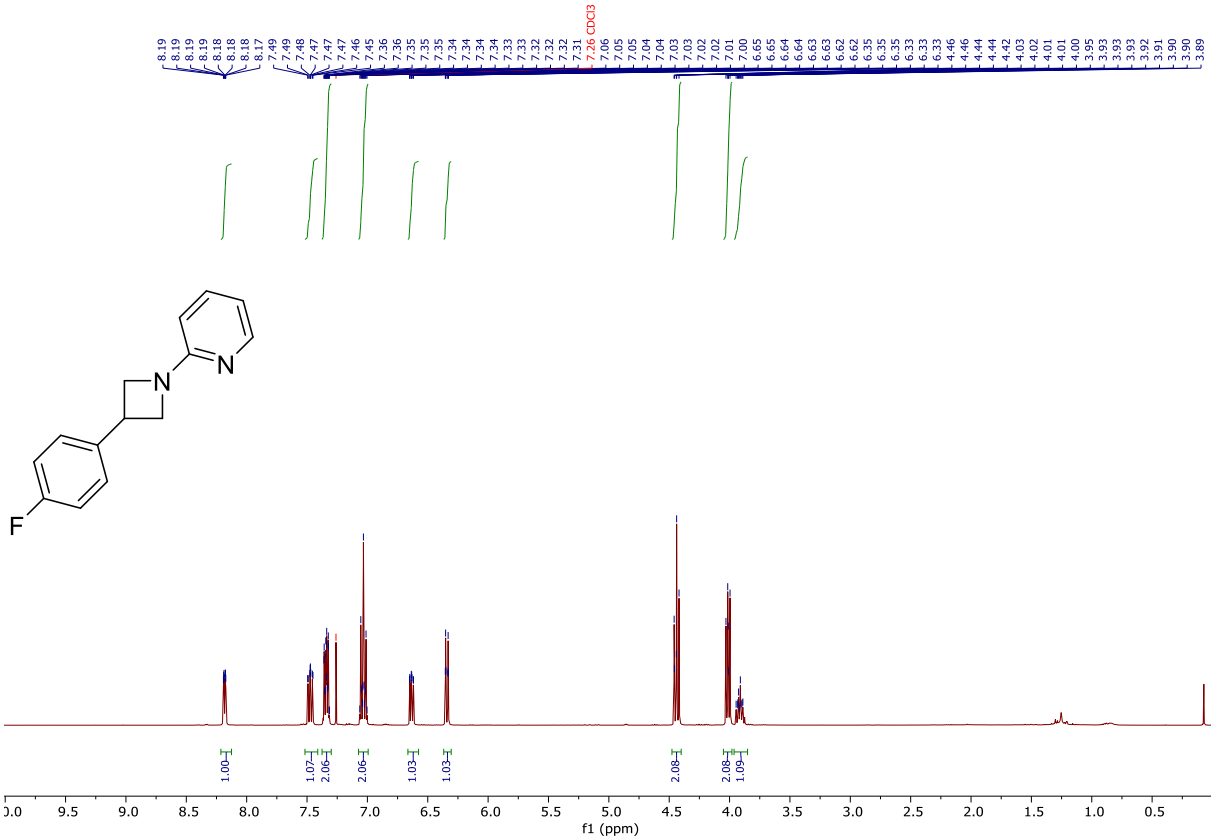
^{1}H NMR (600 MHz, $CDCl_3$) and **^{13}C NMR** (150 MHz, $CDCl_3$)

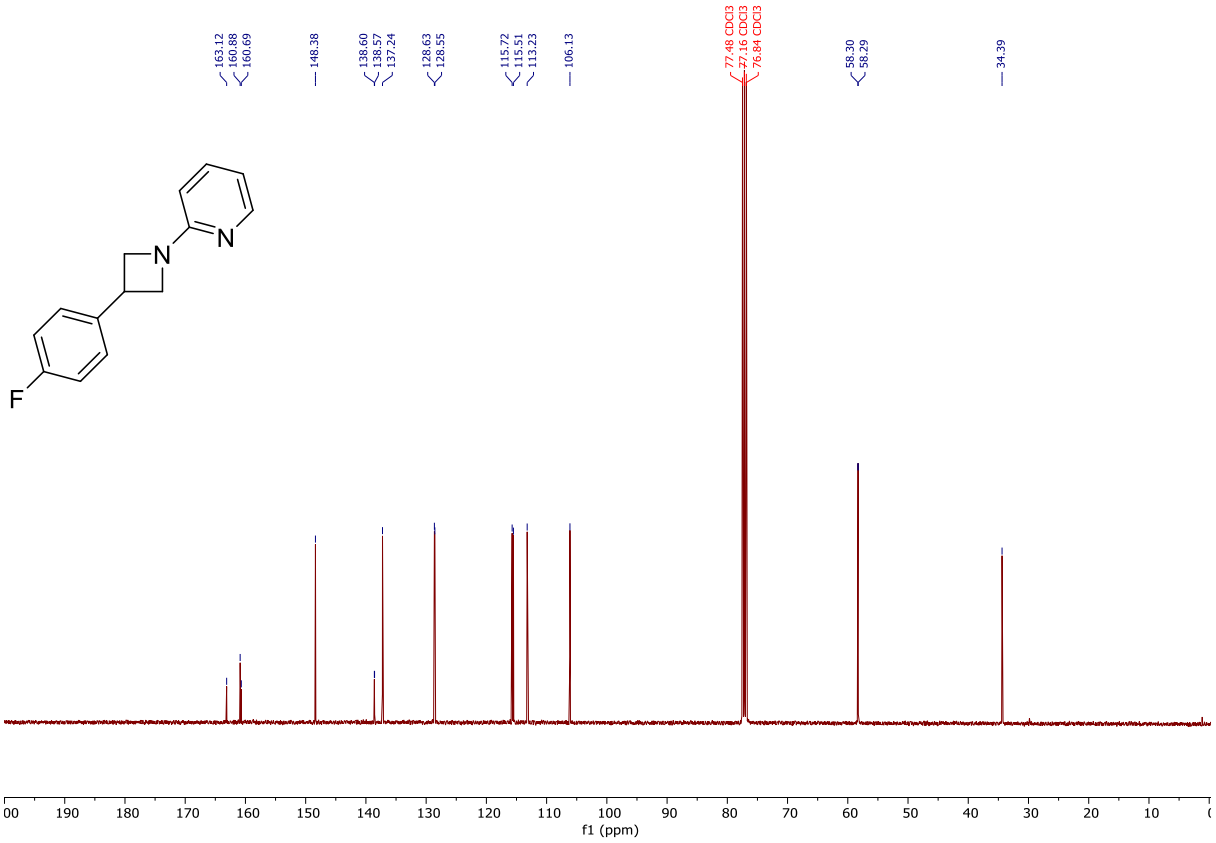


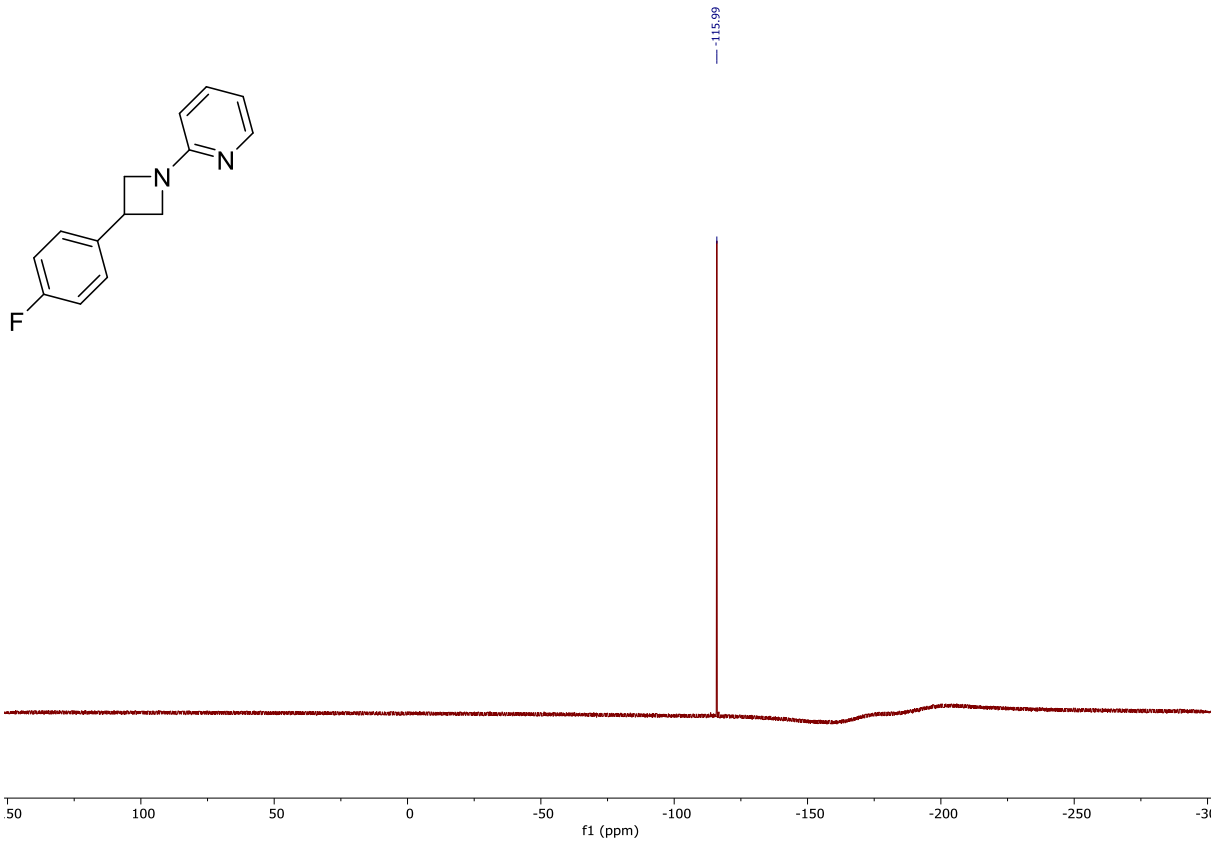


2-(3-(4-Fluorophenyl)azetidin-1-yl)pyridine (7h)

^{1}H NMR (400 MHz, $CDCl_3$),**^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)






-115.99
N
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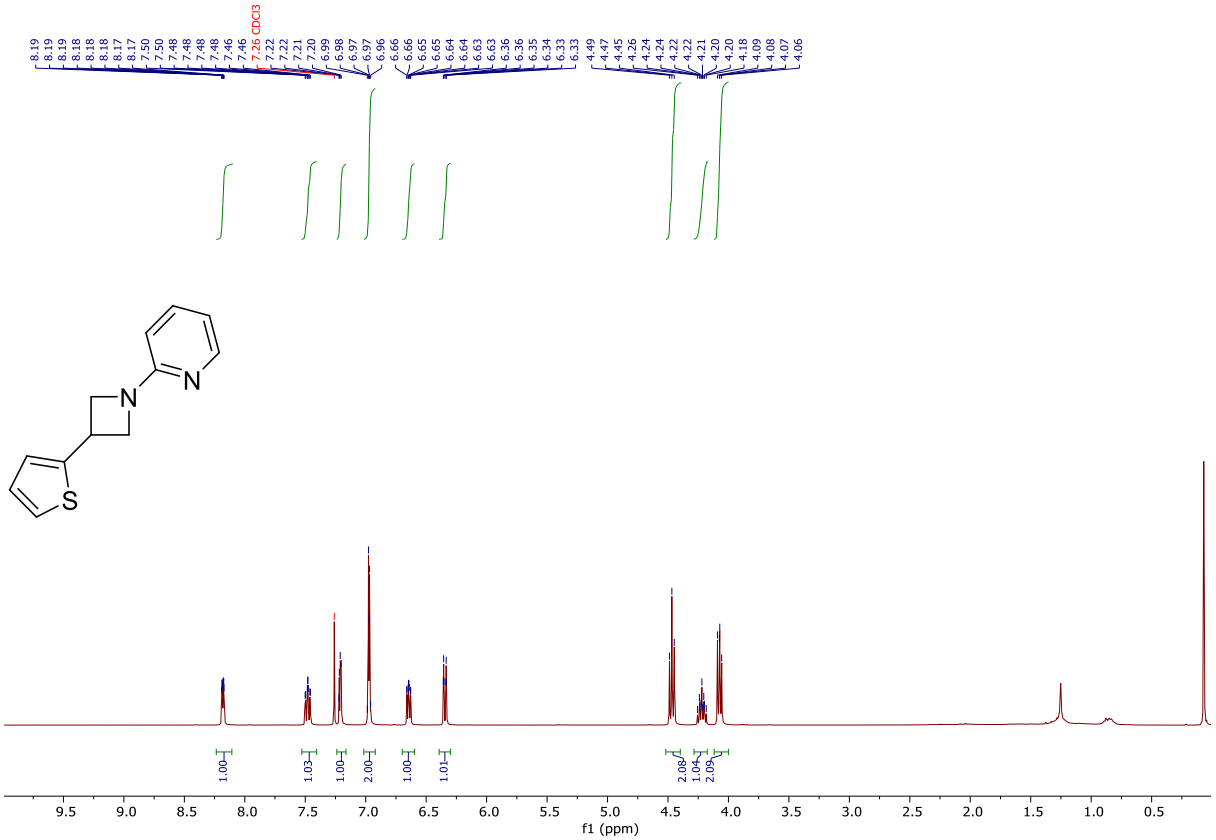
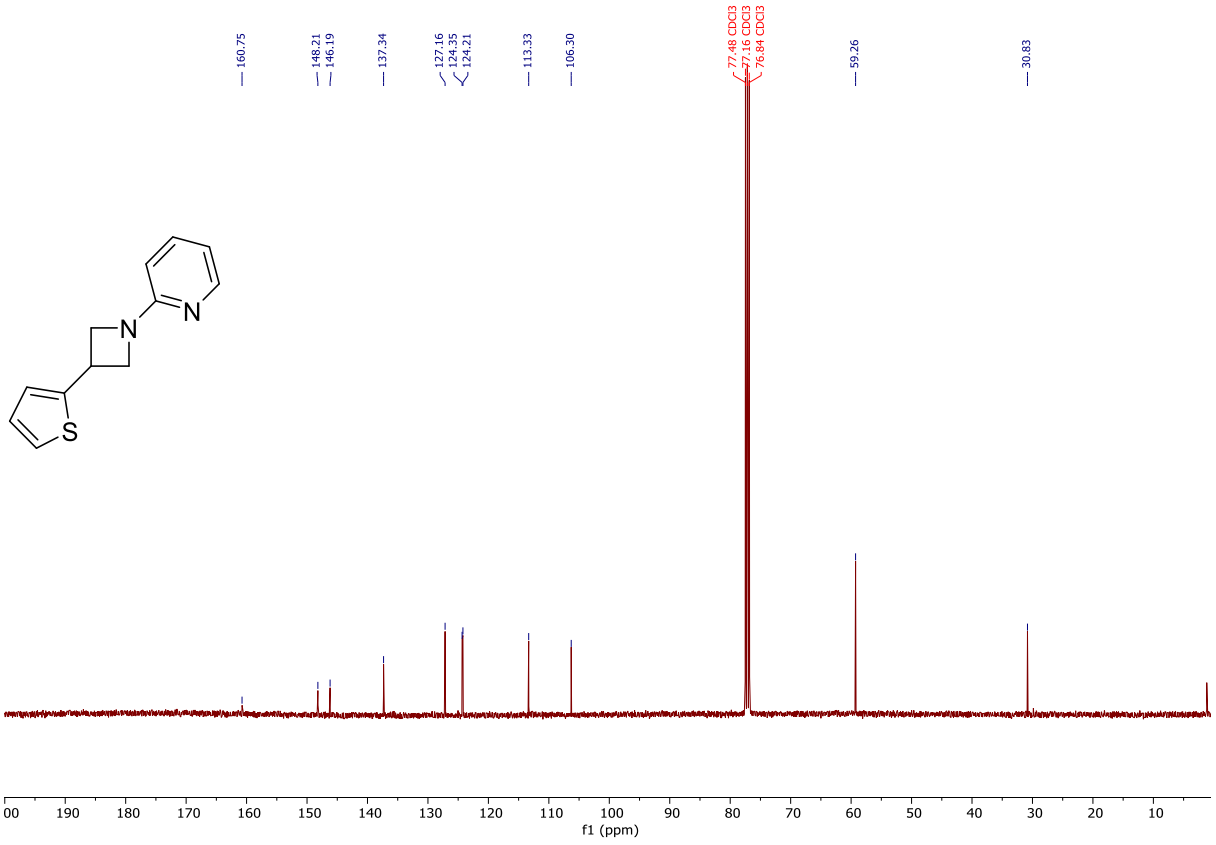
-100
-150
-200
-250
f1 (ppm)

2-(3-(Thiophen-2-yl)azetidin-1-yl)pyridine (7i)

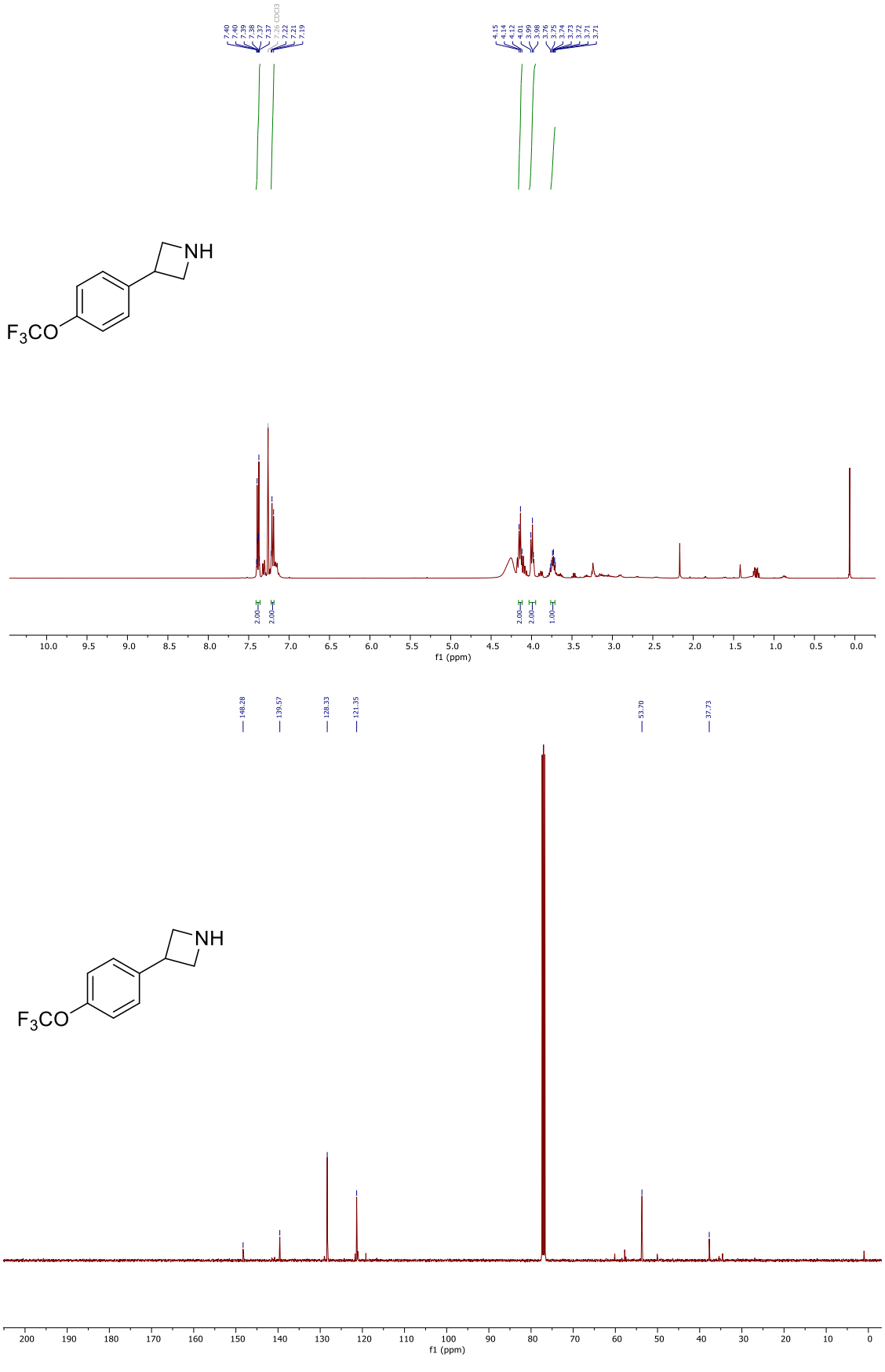
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)





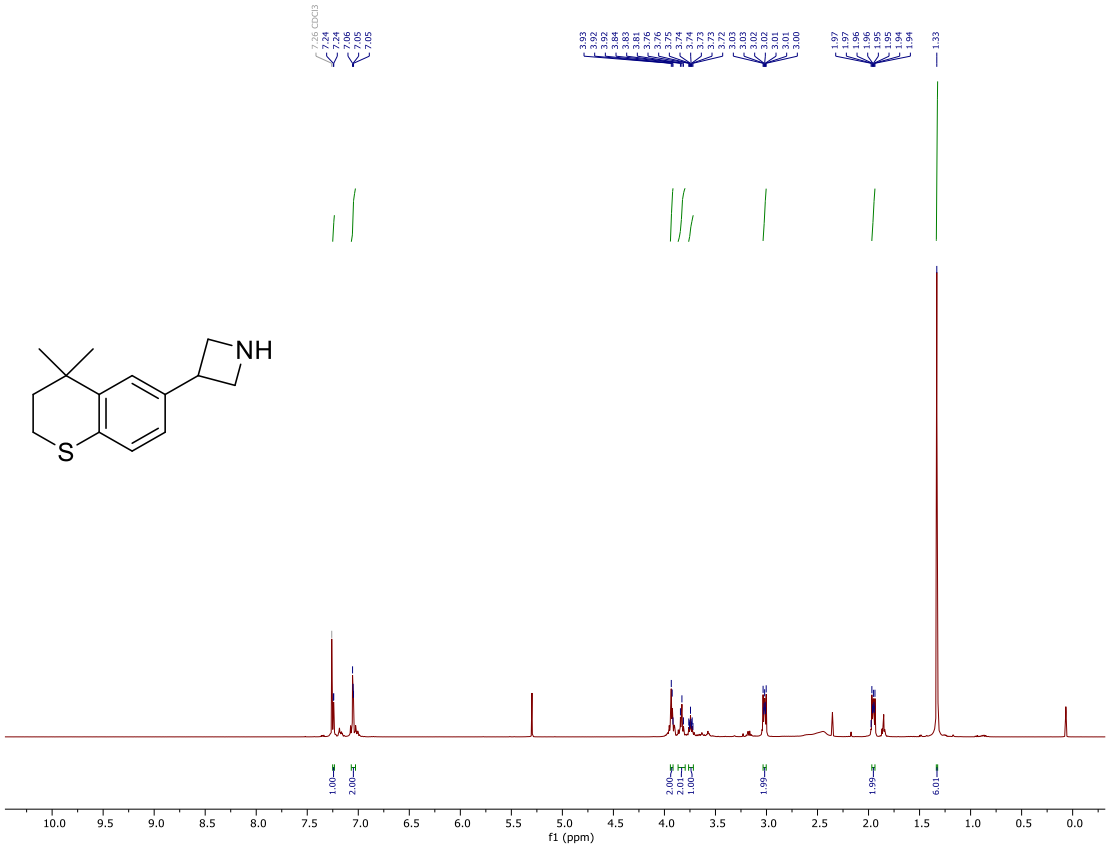
3-(4-(Trifluoromethoxy)phenyl)azetidine (9b/3h)

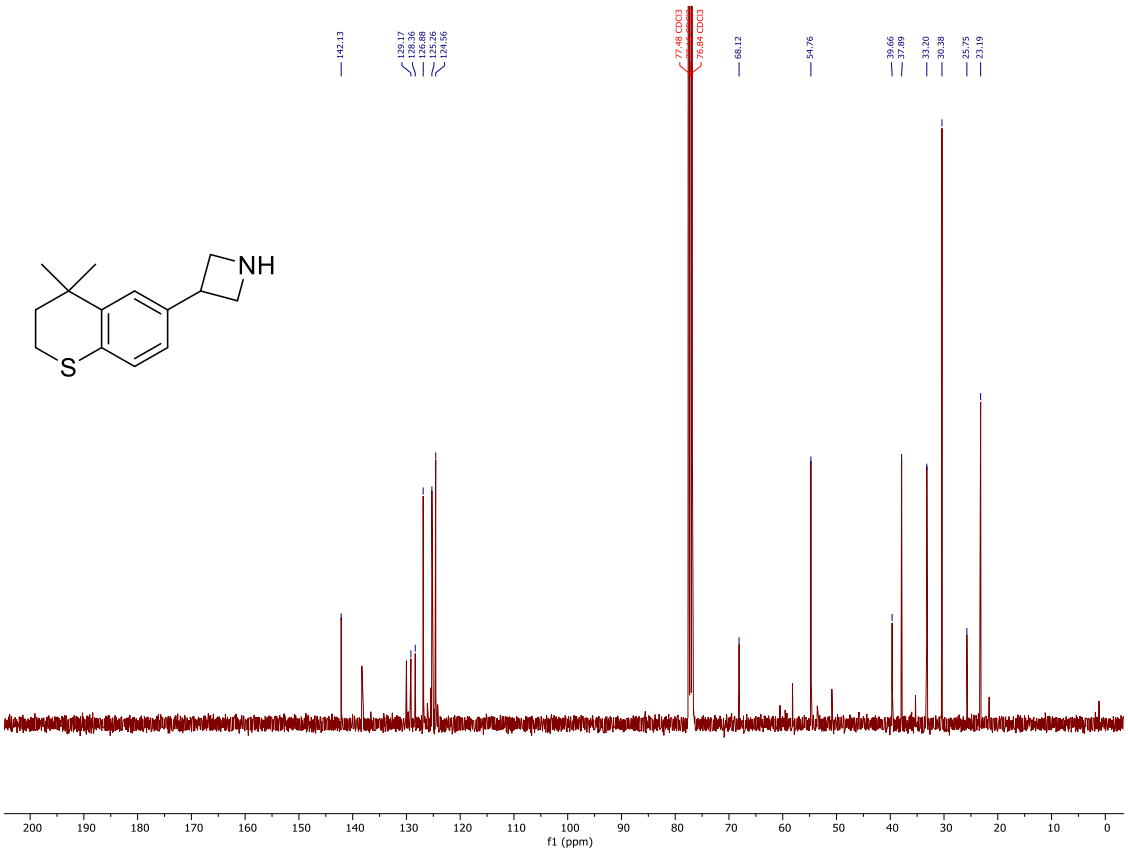
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)



3-(4,4-Dimethylthiochroman-6-yl)azetidine (9d/3g)

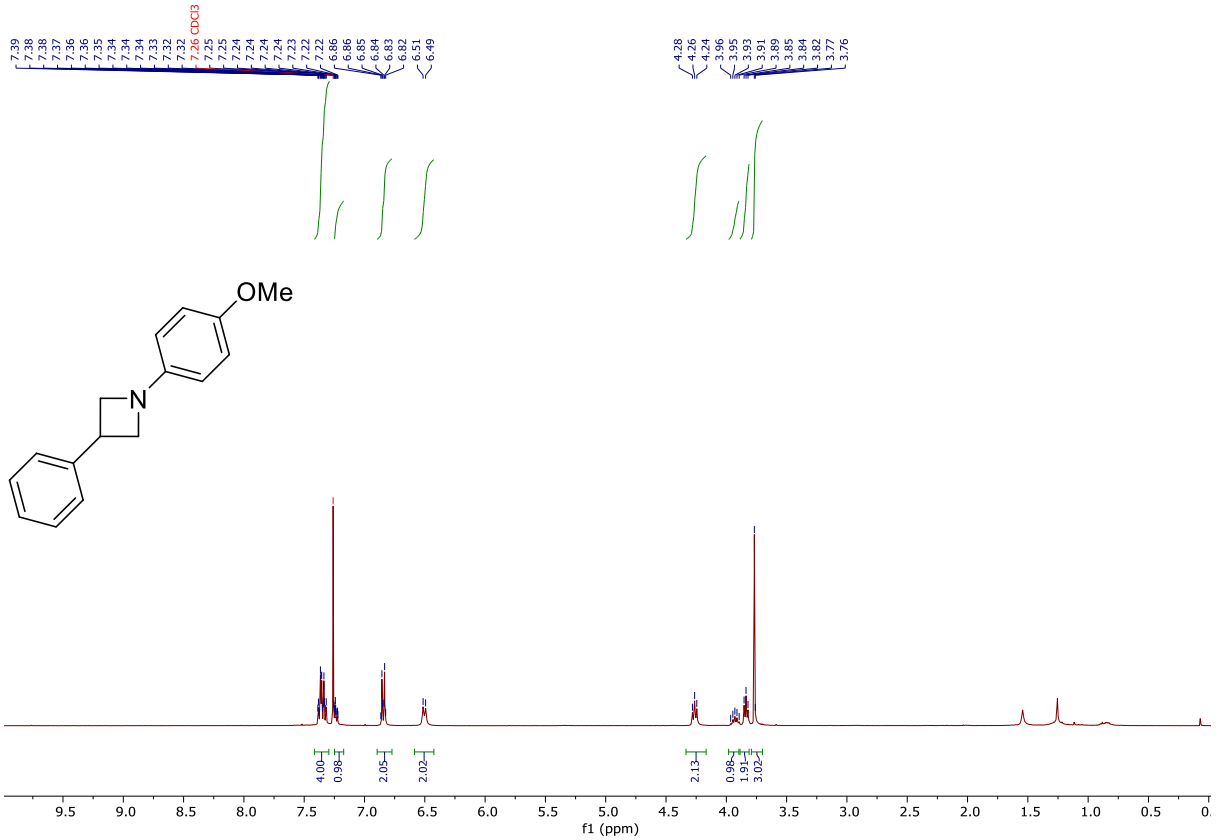
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

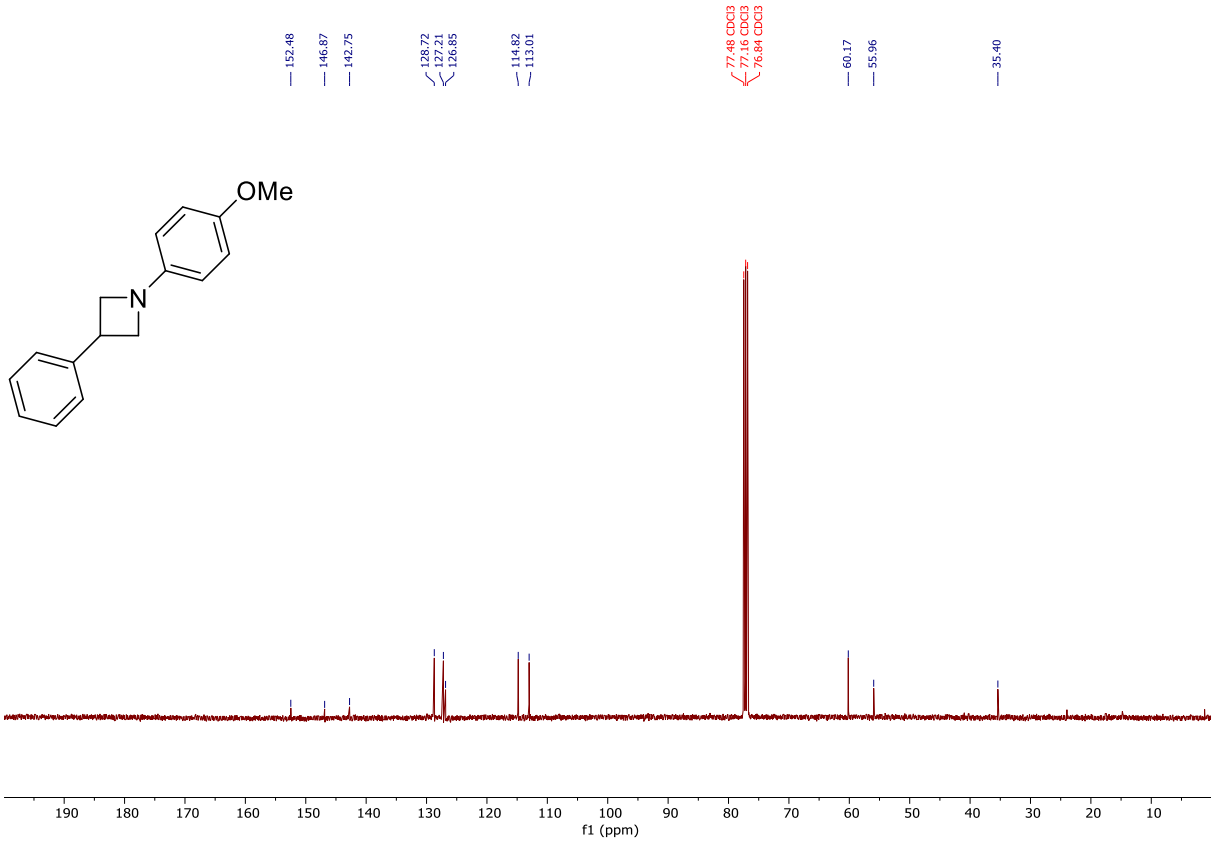




1-(4-Methoxyphenyl)-3-phenylazetidine (10a)

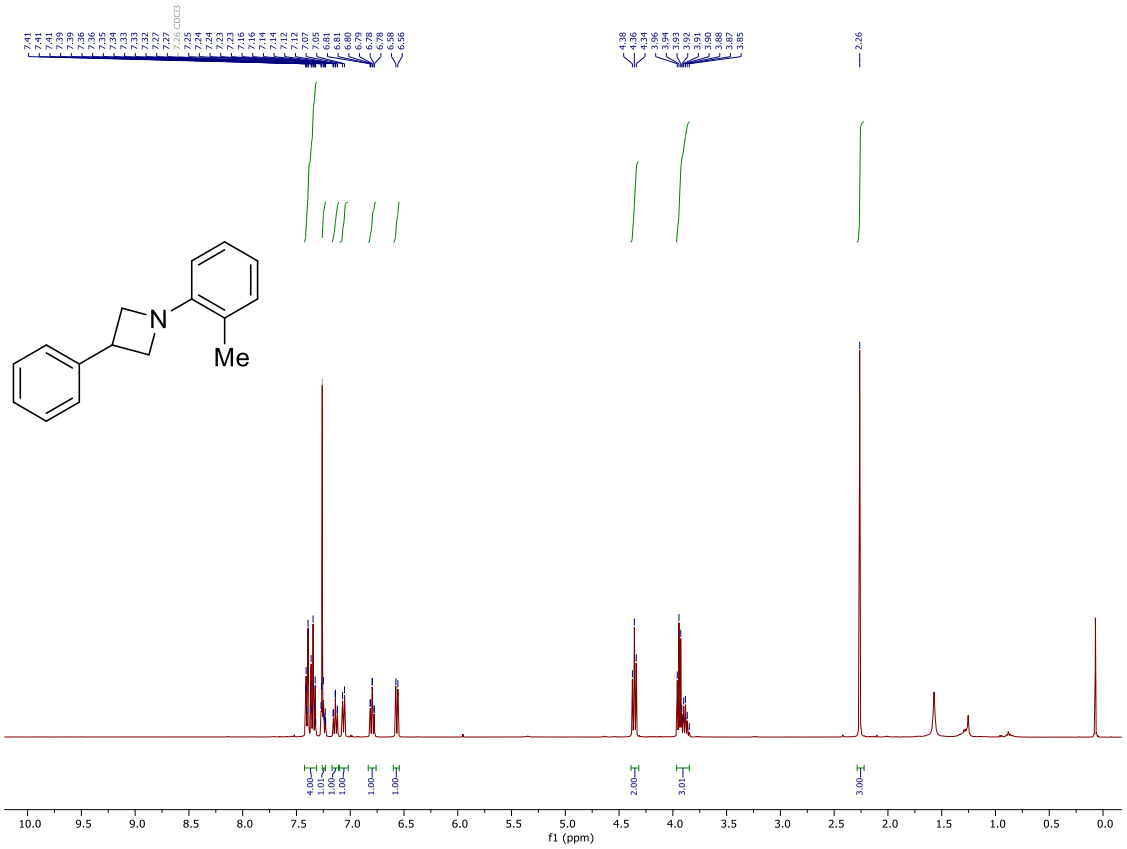
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

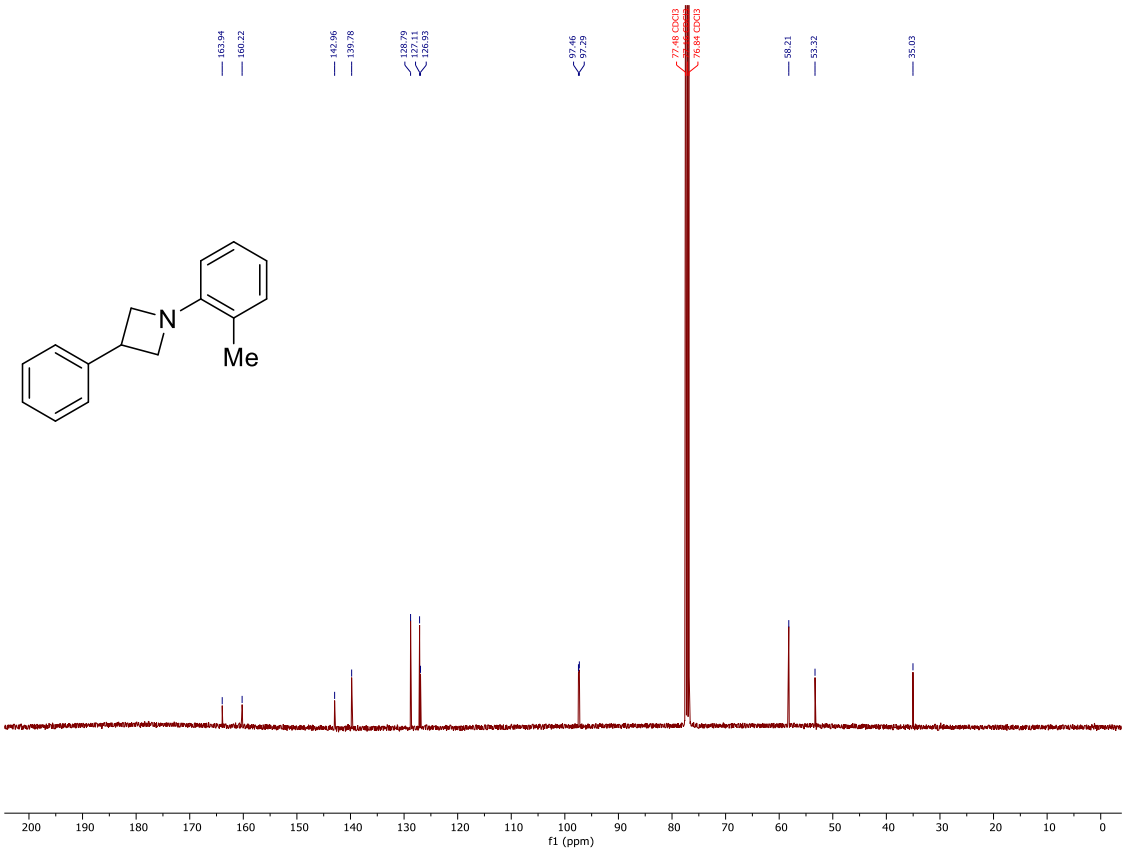




3-Phenyl-1-(*o*-tolyl)azetidine (10b)

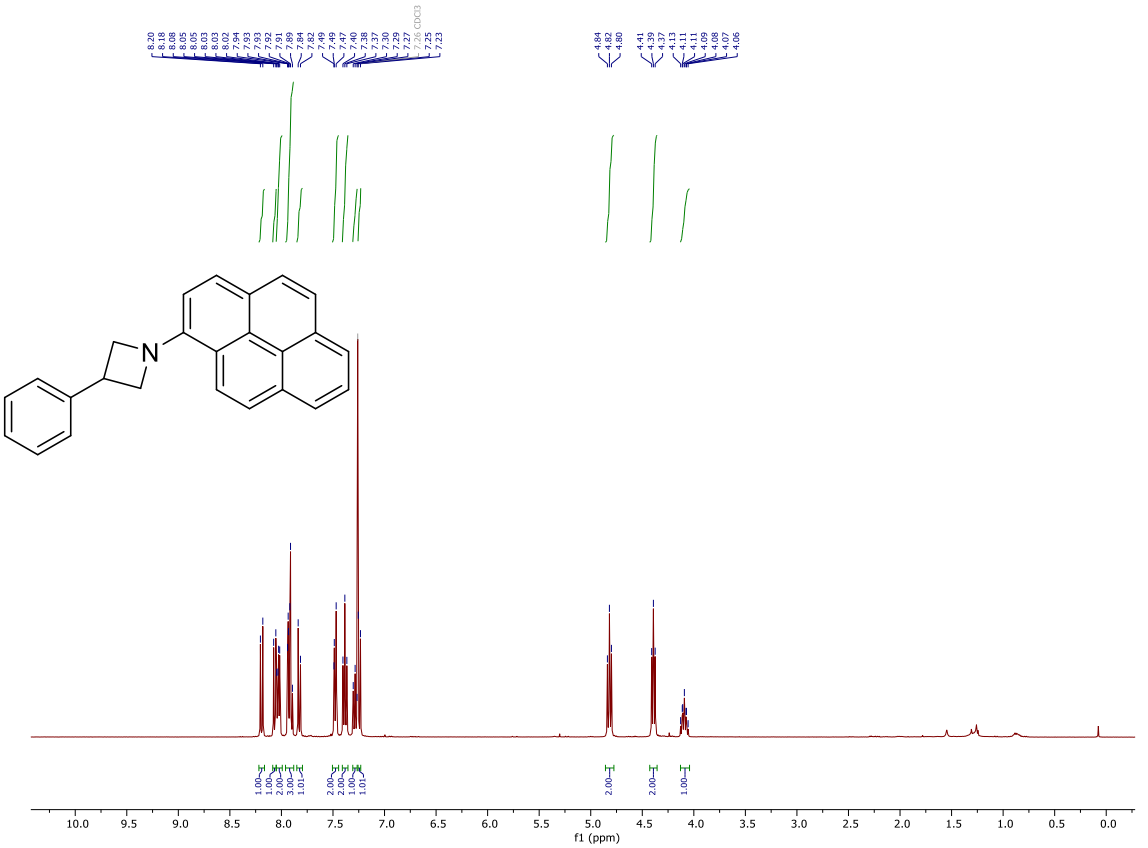
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

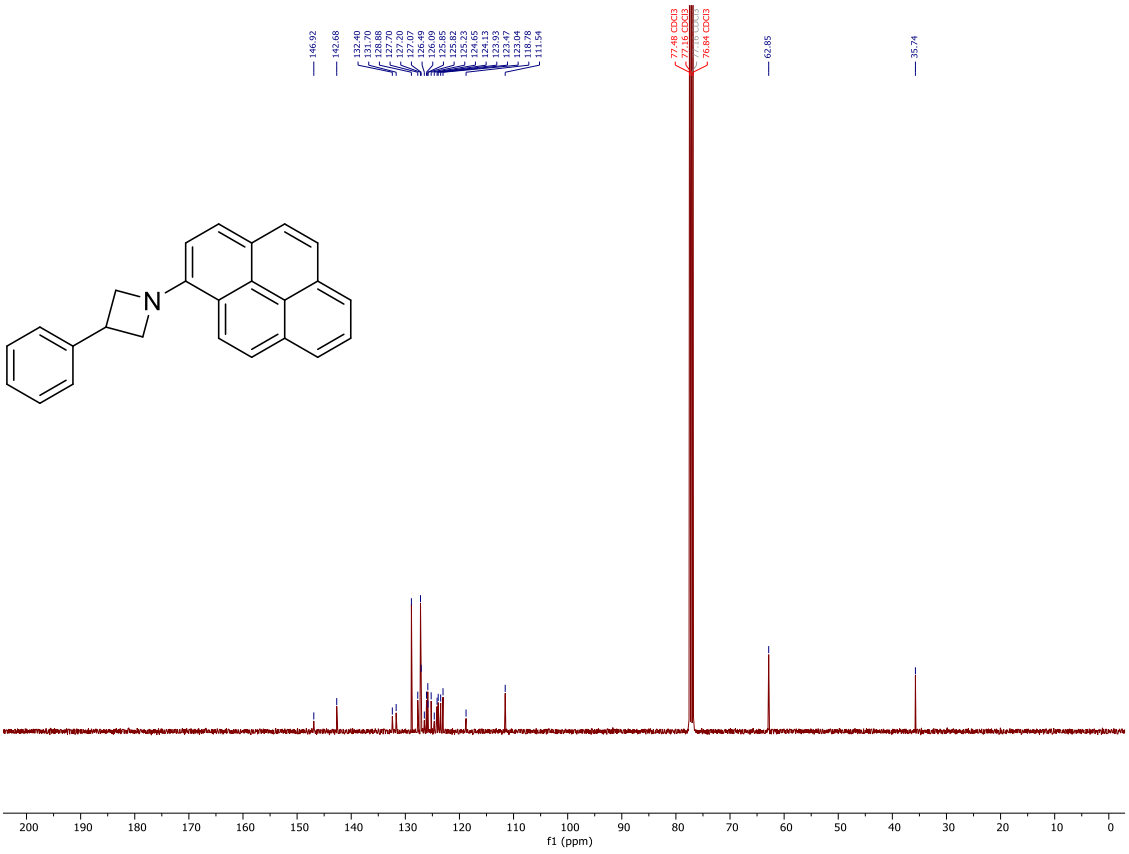




3-Phenyl-1-(pyren-1-yl)azetidine (10c)

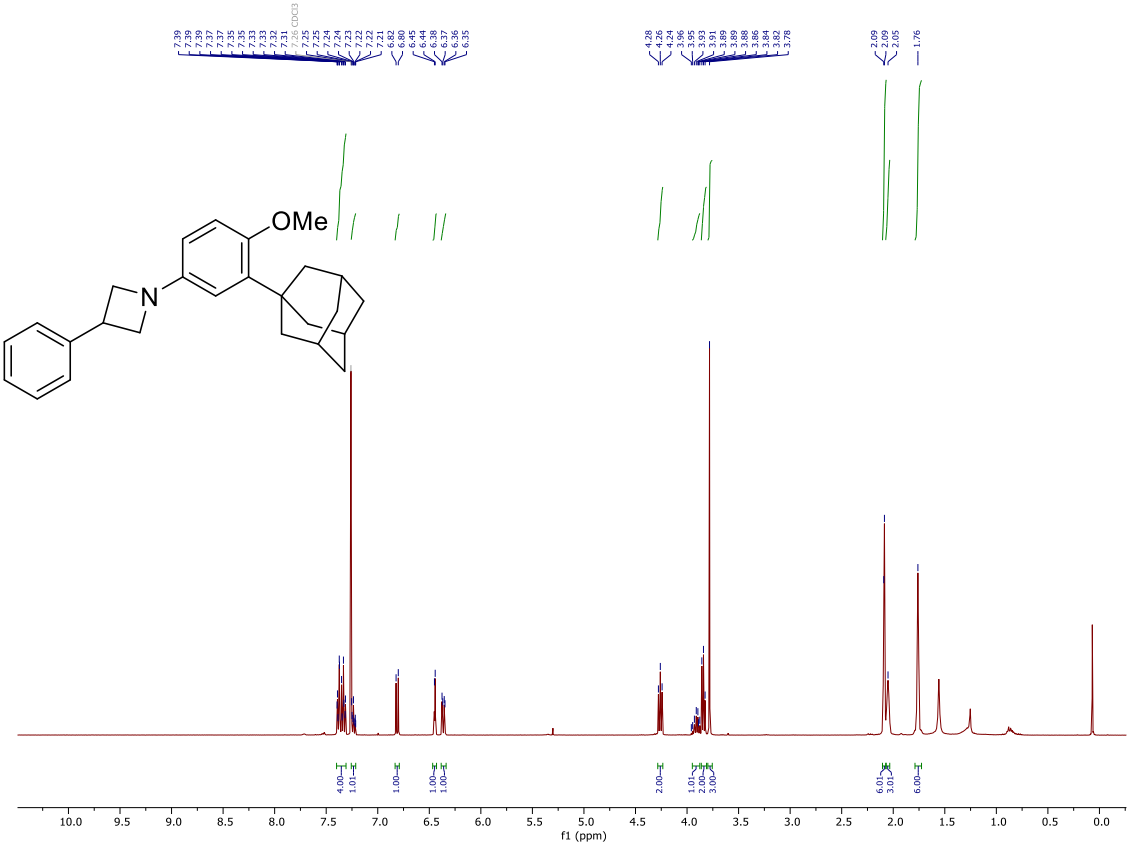
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

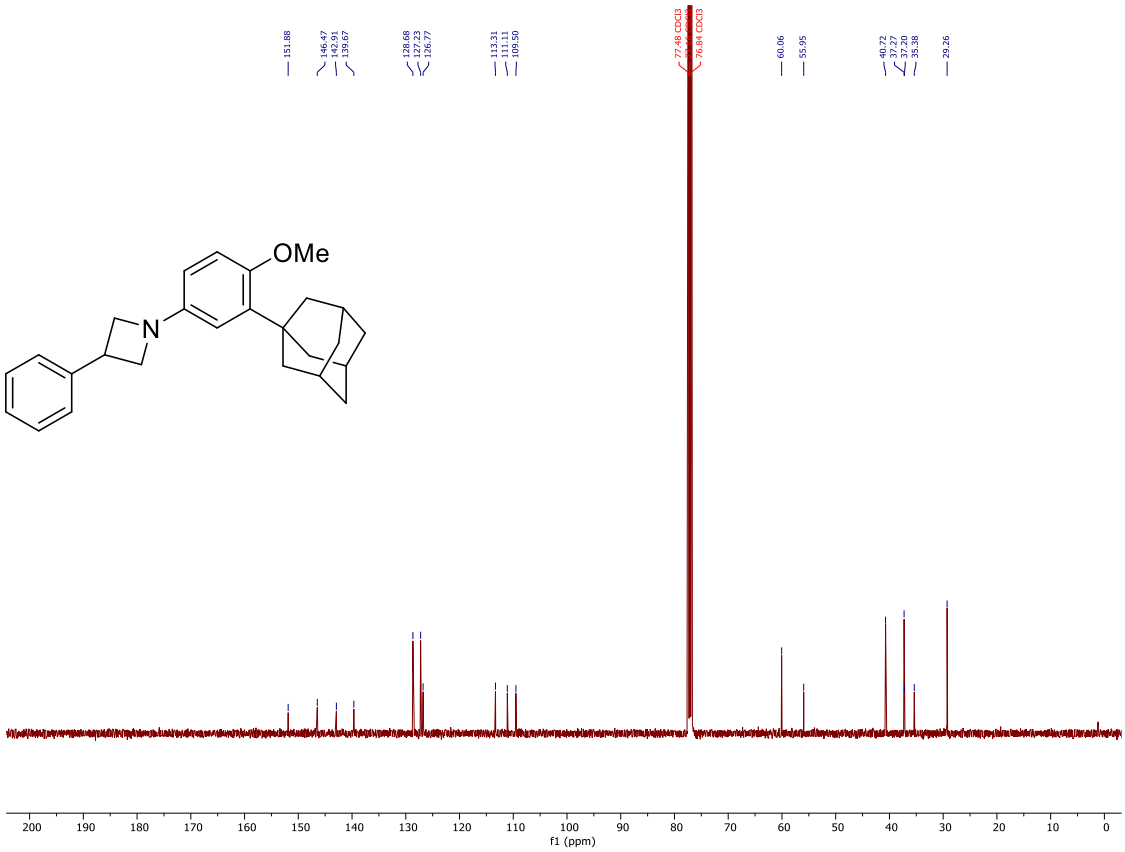




1-(3-(Adamantan-1-yl)-4-methoxyphenyl)-3-phenylazetidine (10d)

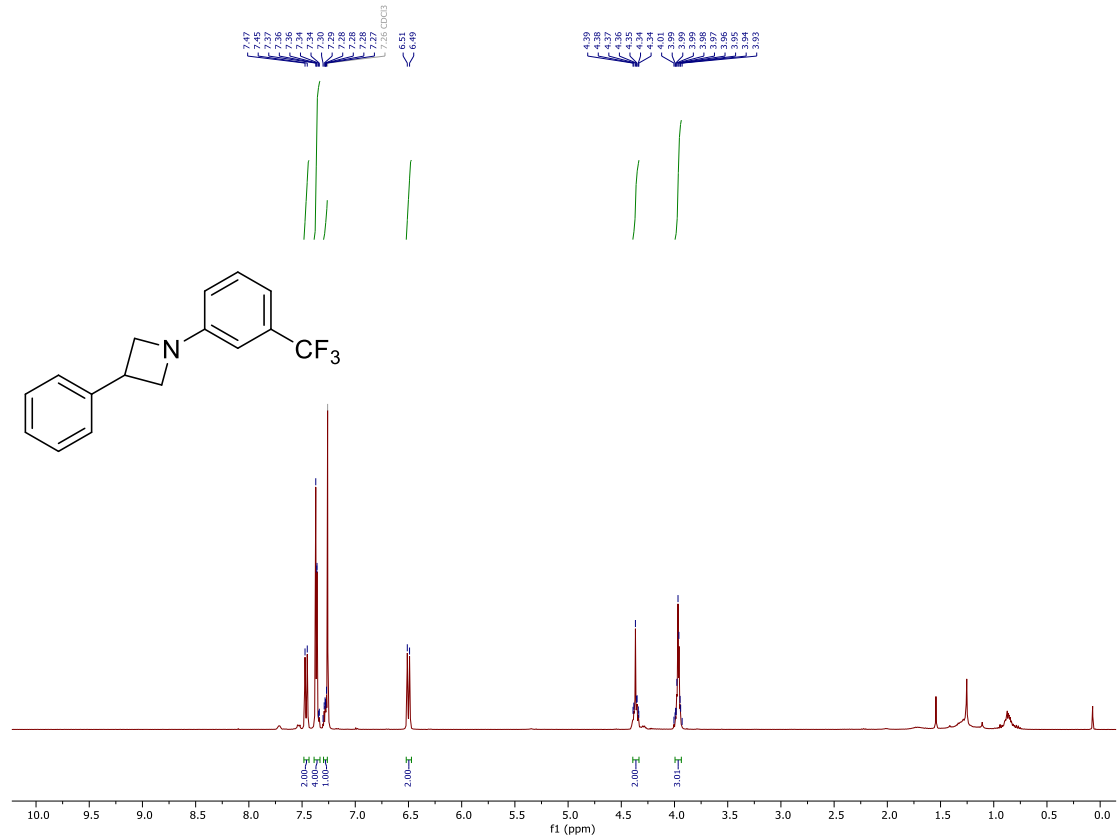
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

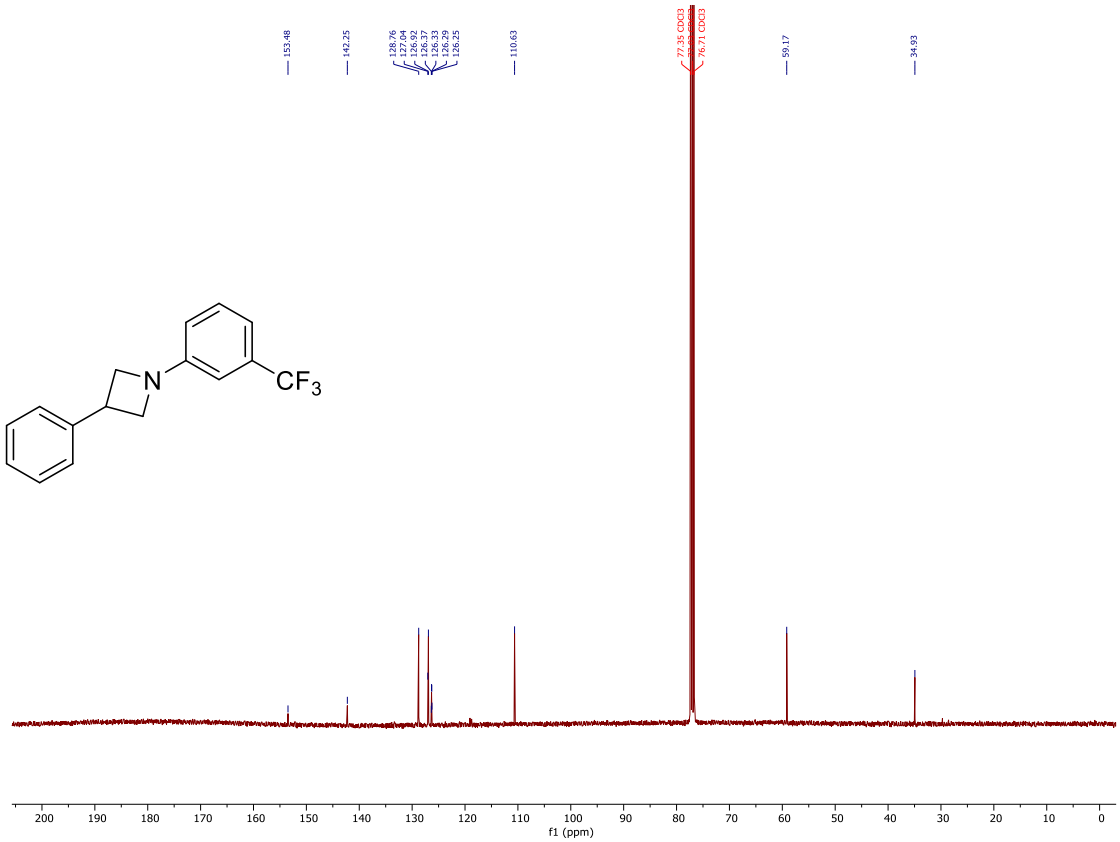


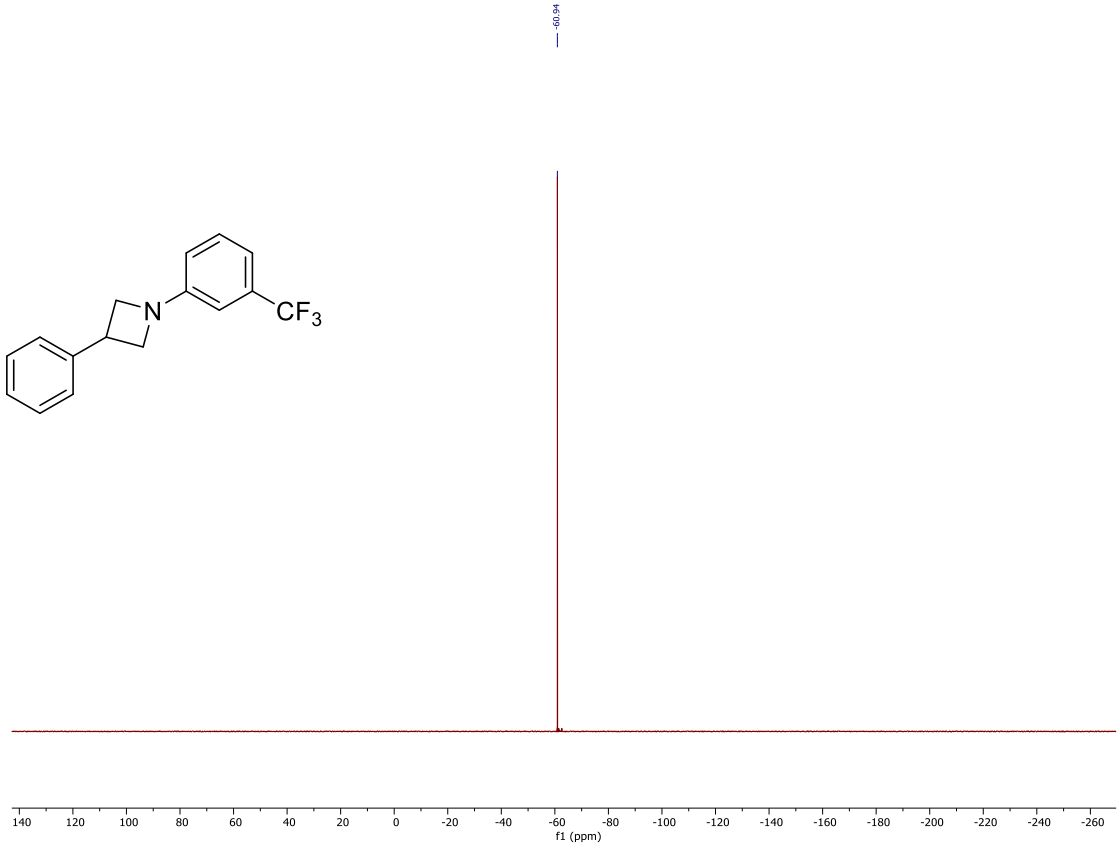


3-Phenyl-1-(3-(trifluoromethyl)phenyl)azetidine (10e)

^{1}H NMR (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)

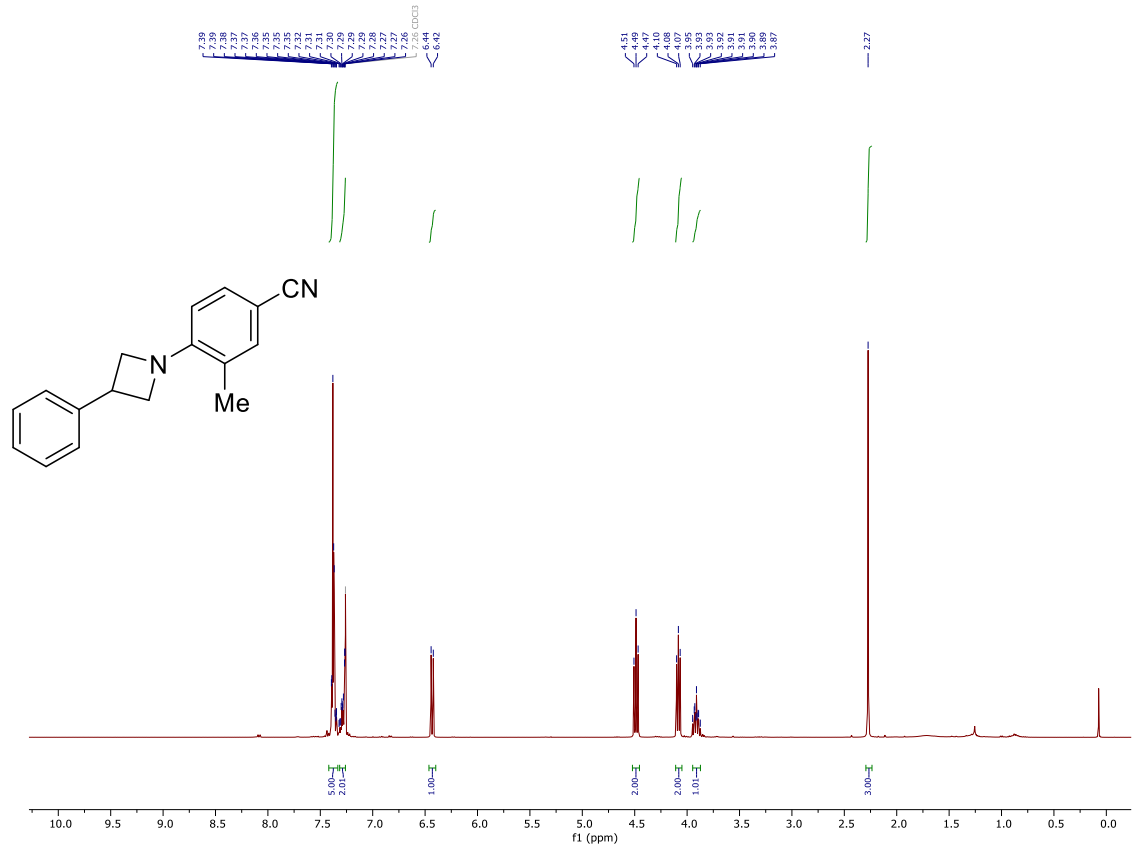


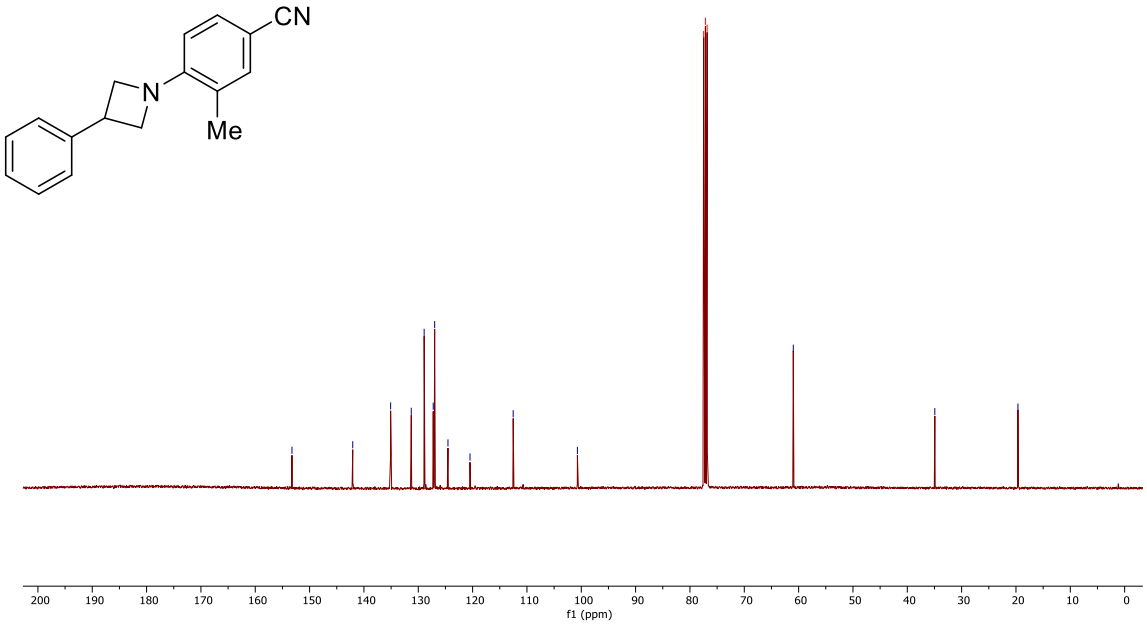



-60.94
N
CF3
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
f1 (ppm)

3-Methyl-4-(3-phenylazetidin-1-yl)benzonitrile (10f)

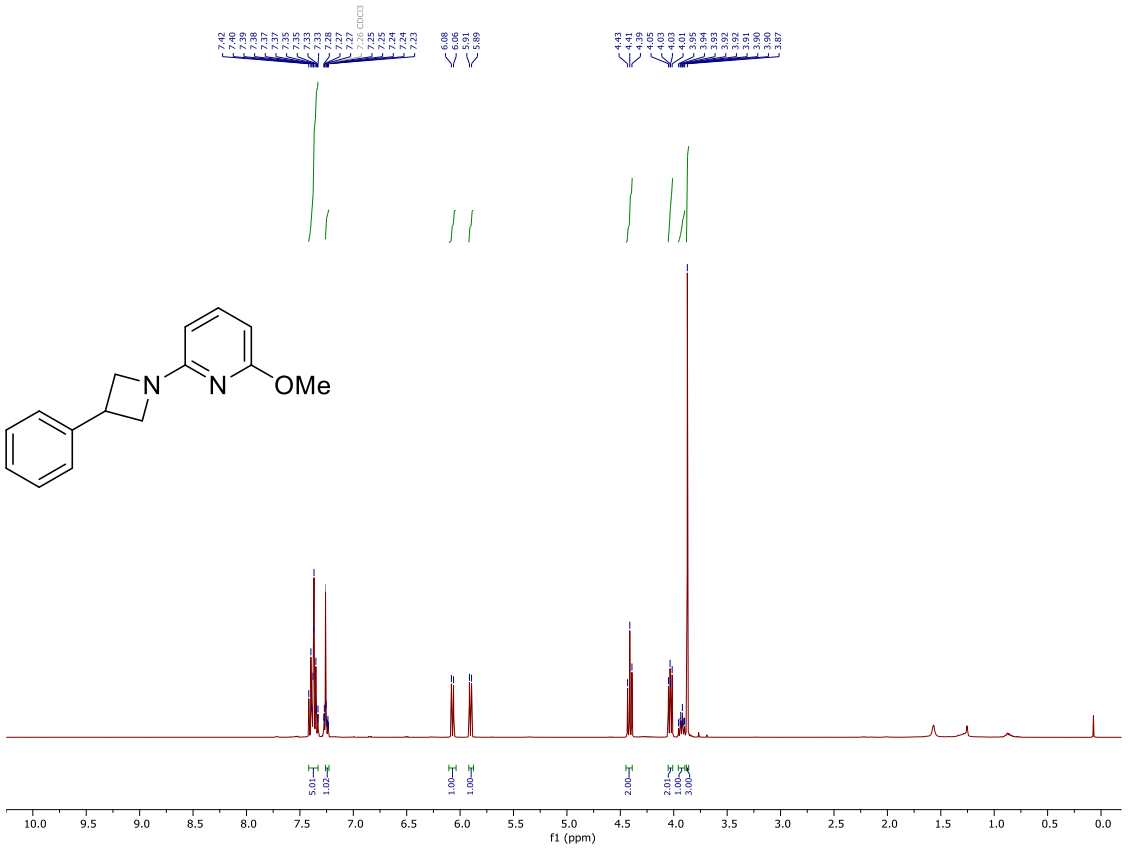
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

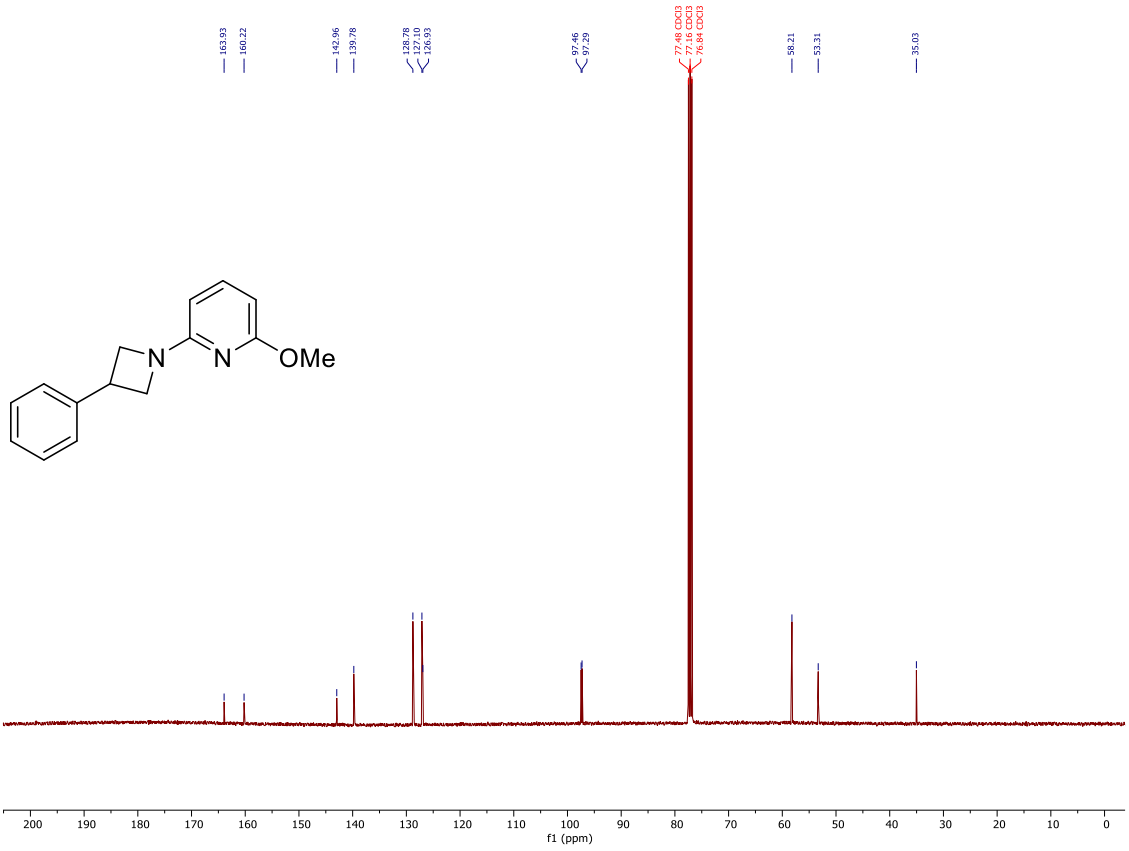




2-Methoxy-6-(3-phenylazetidin-1-yl)pyridine (10g)

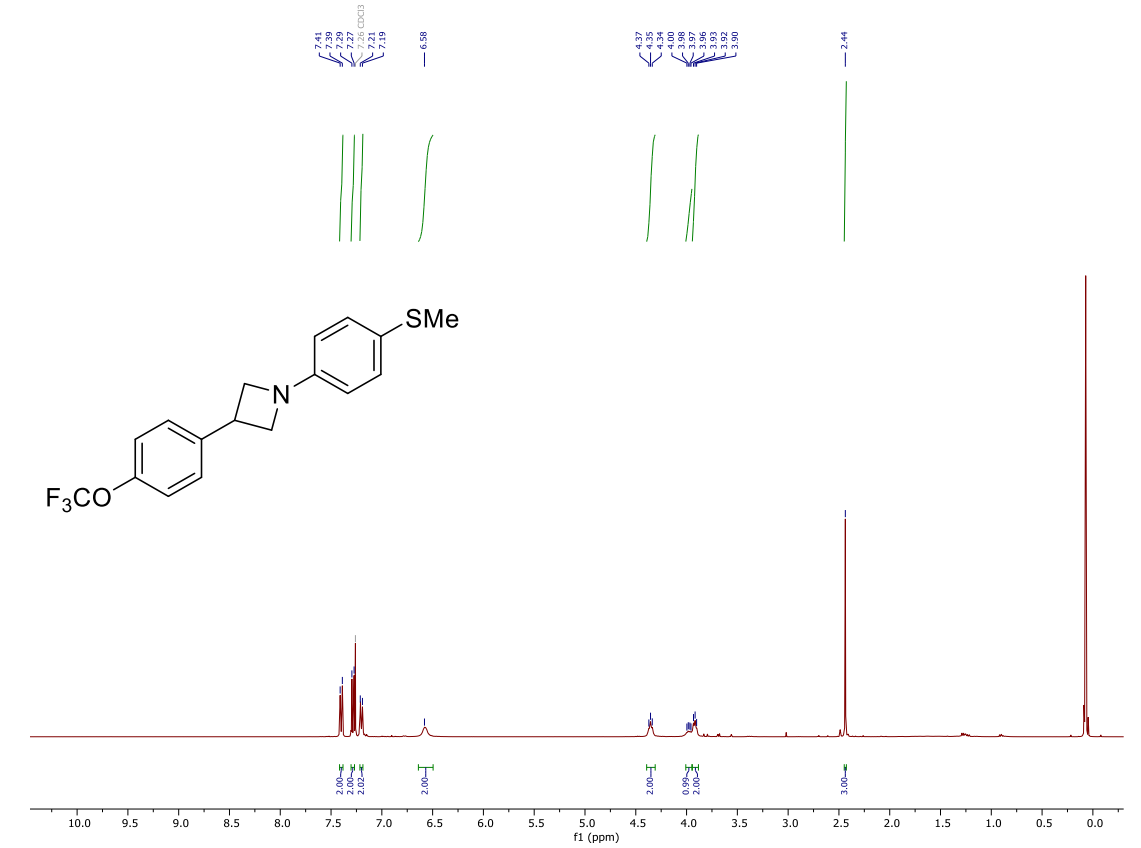
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

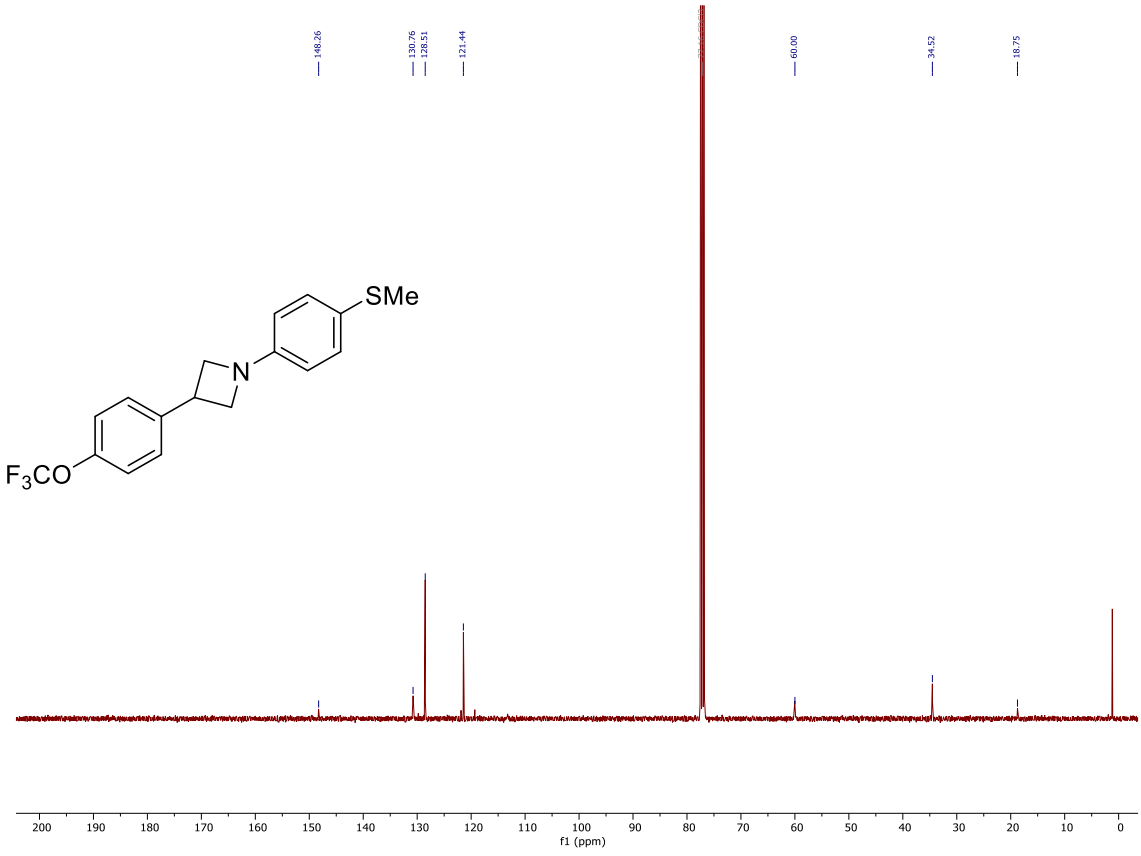


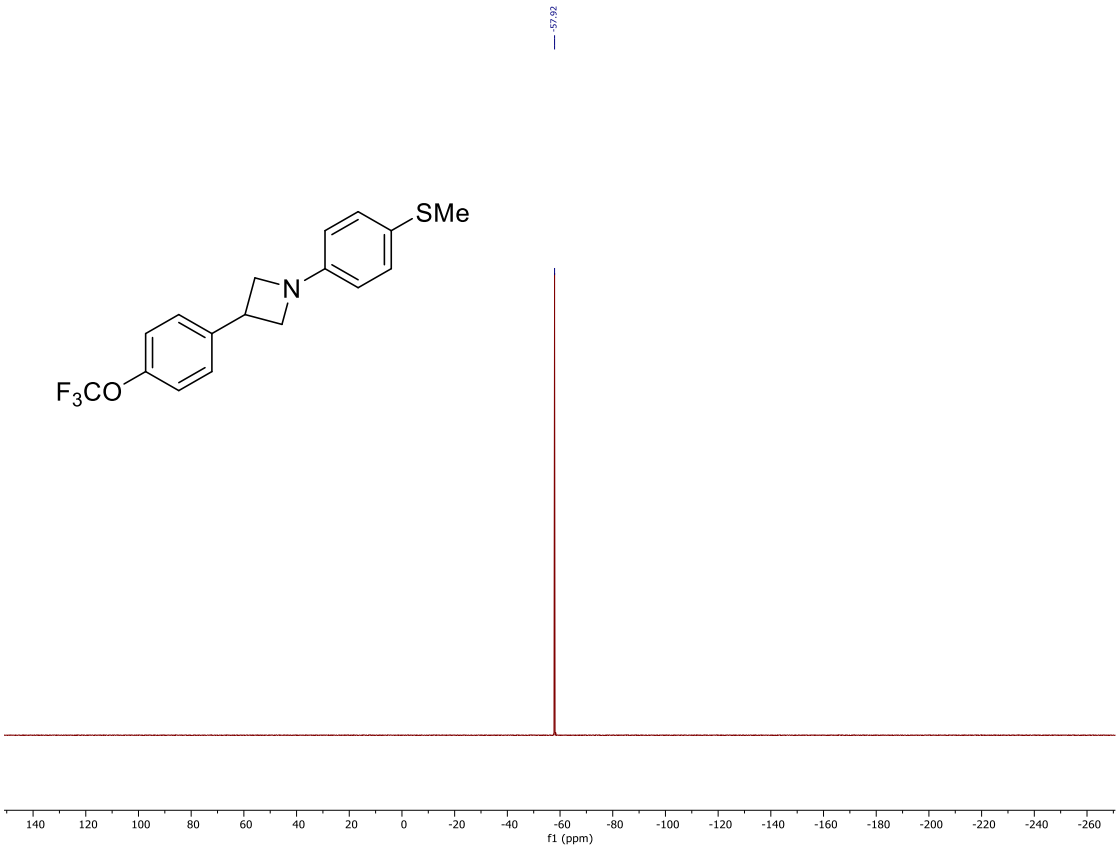


1-(4-(Methylthio)phenyl)-3-(4-(trifluoromethoxy)phenyl)azetidine (10h)

^{1}H NMR (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)

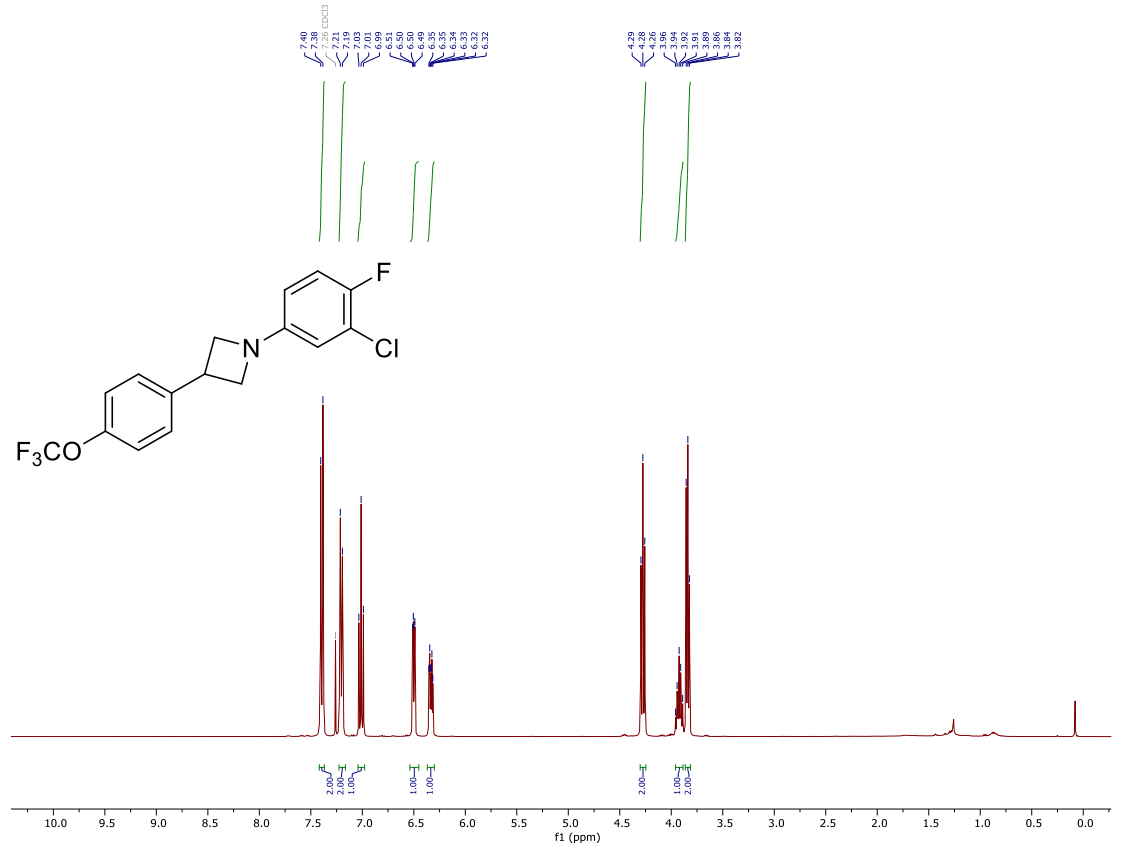


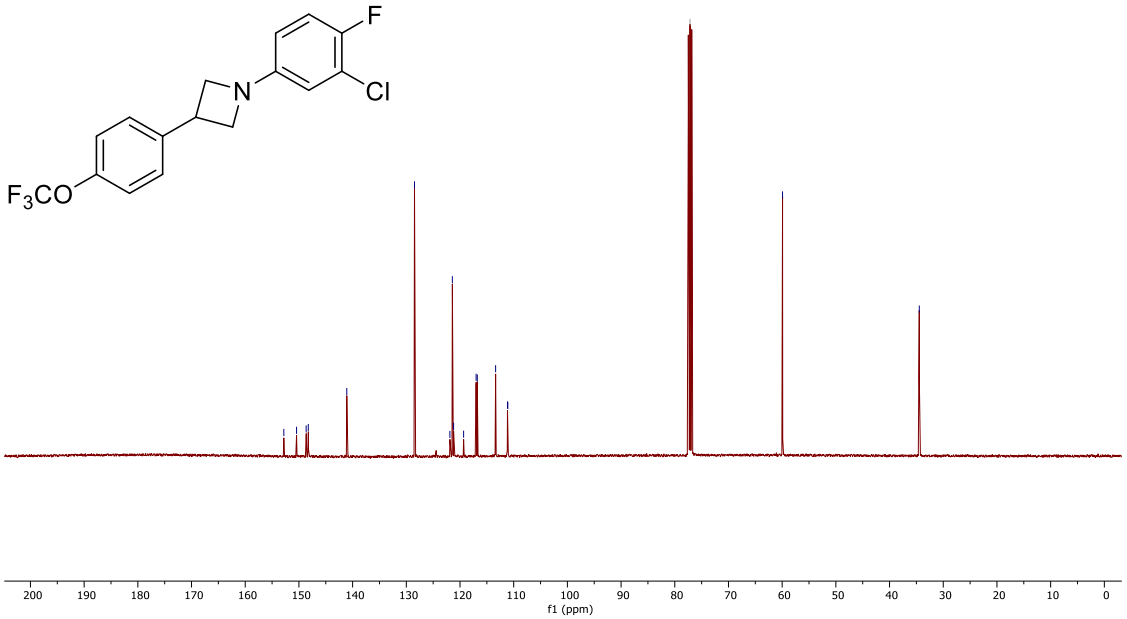


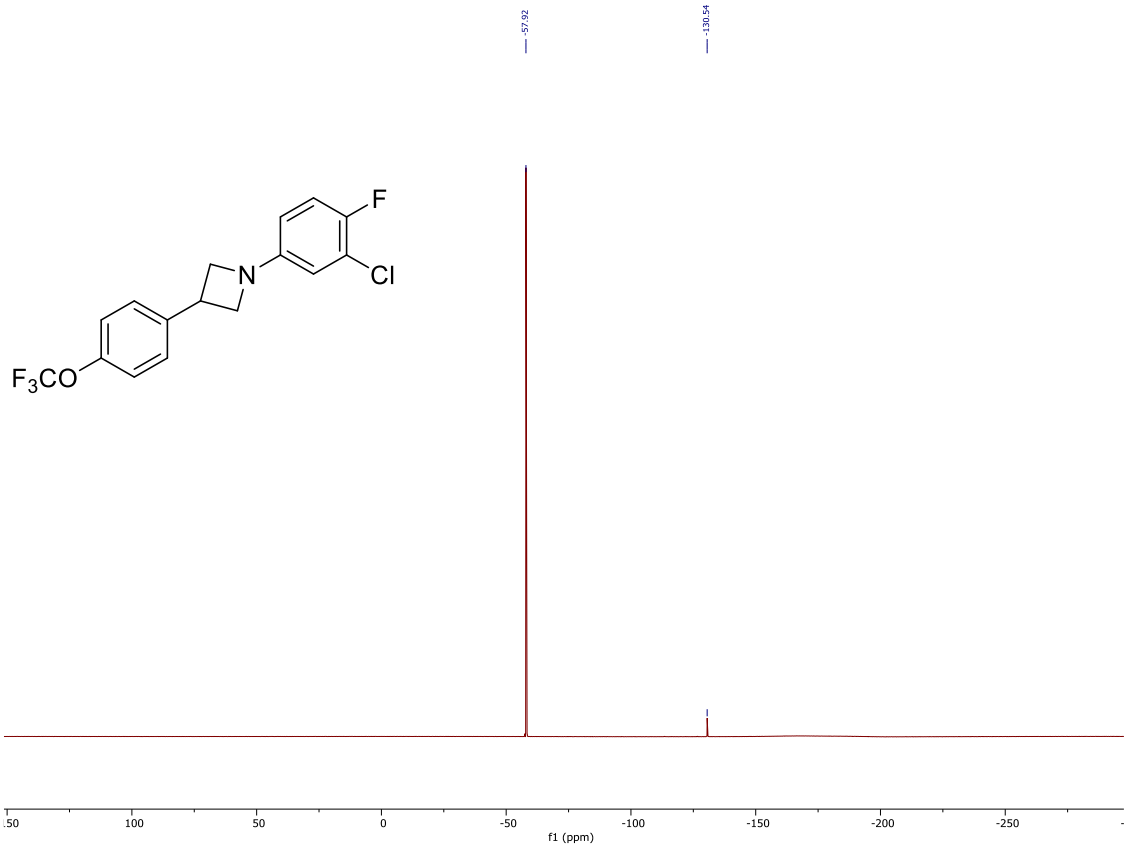

-57.92
SMe
N
F3CO
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
f1 (ppm)

1-(3-Chloro-4-fluorophenyl)-3-(4-(trifluoromethoxy)phenyl)azetidine (10i)

^{1}H NMR (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)

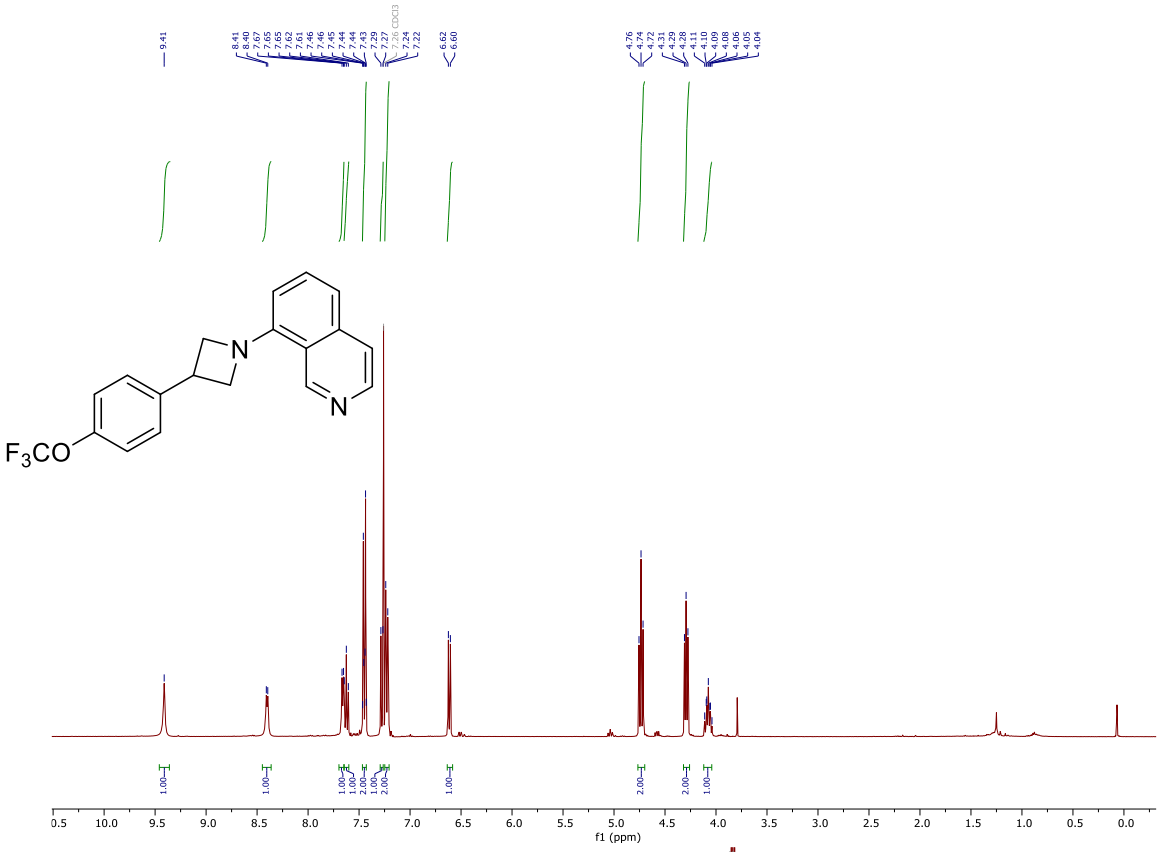


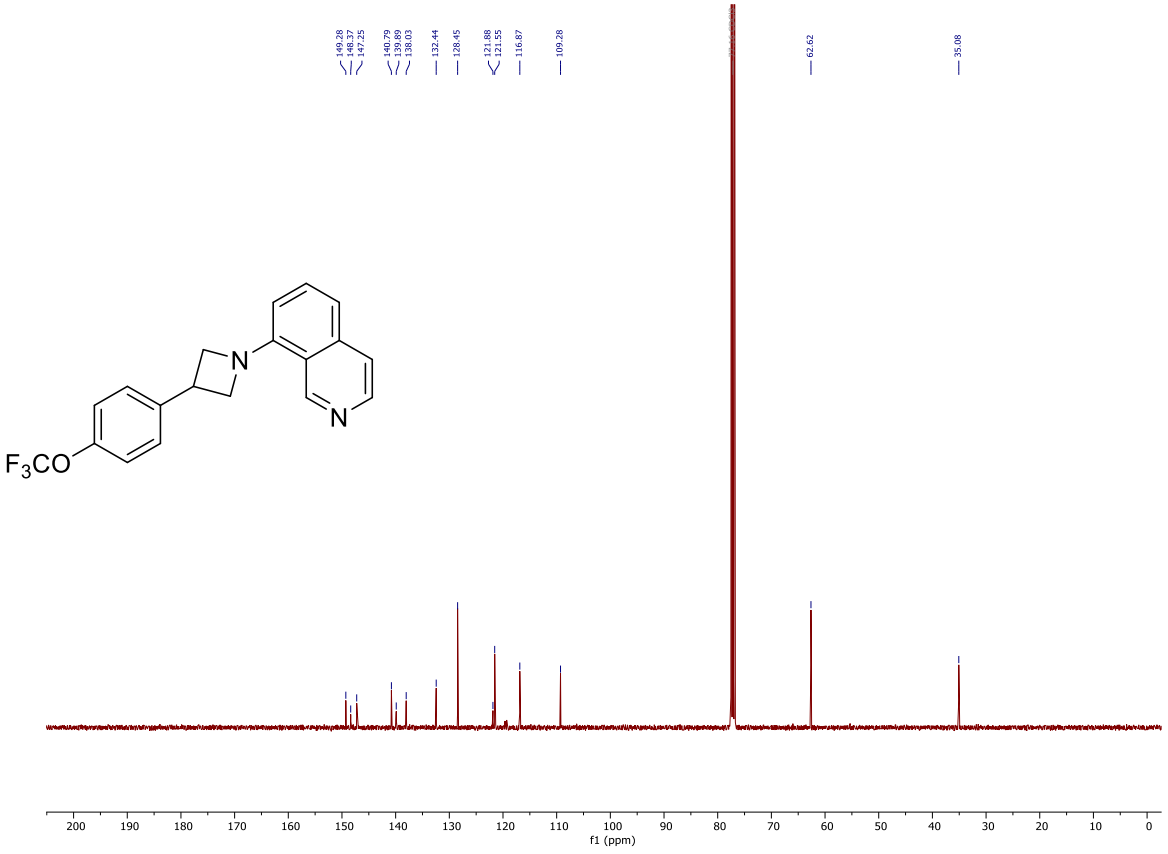


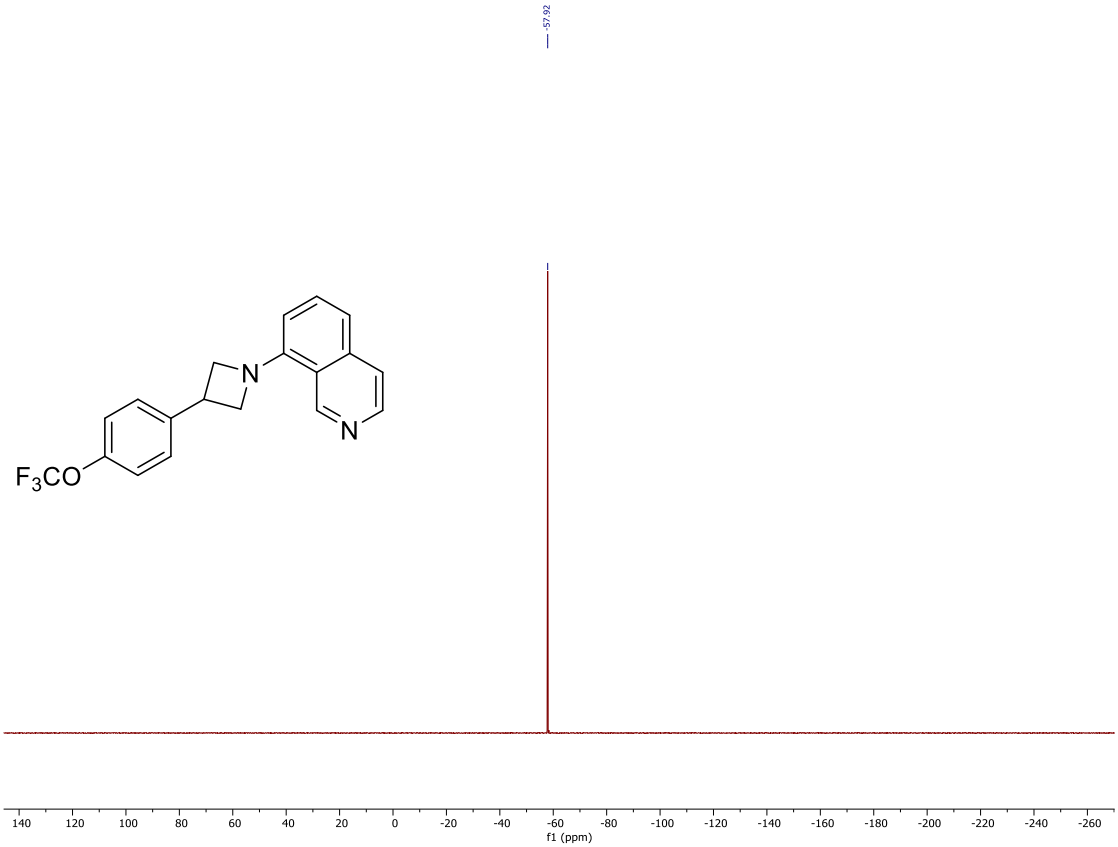

-57.92
-130.54
F
Cl
N
F3CO
100
50
0
-50
-100
-150
-200
-250
f1 (ppm)

8-(3-(4-(Trifluoromethoxy)phenyl)azetidin-1-yl)isoquinoline (10j)

^{1}H NMR (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)

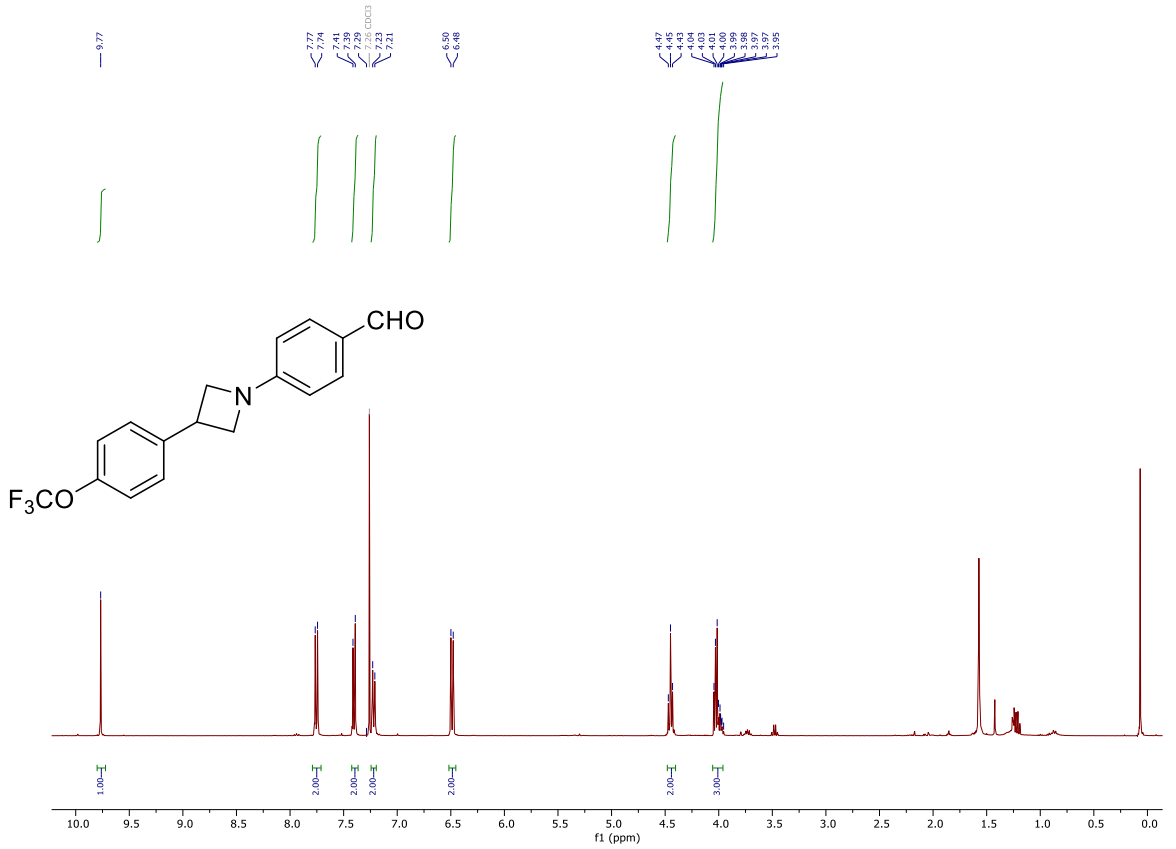


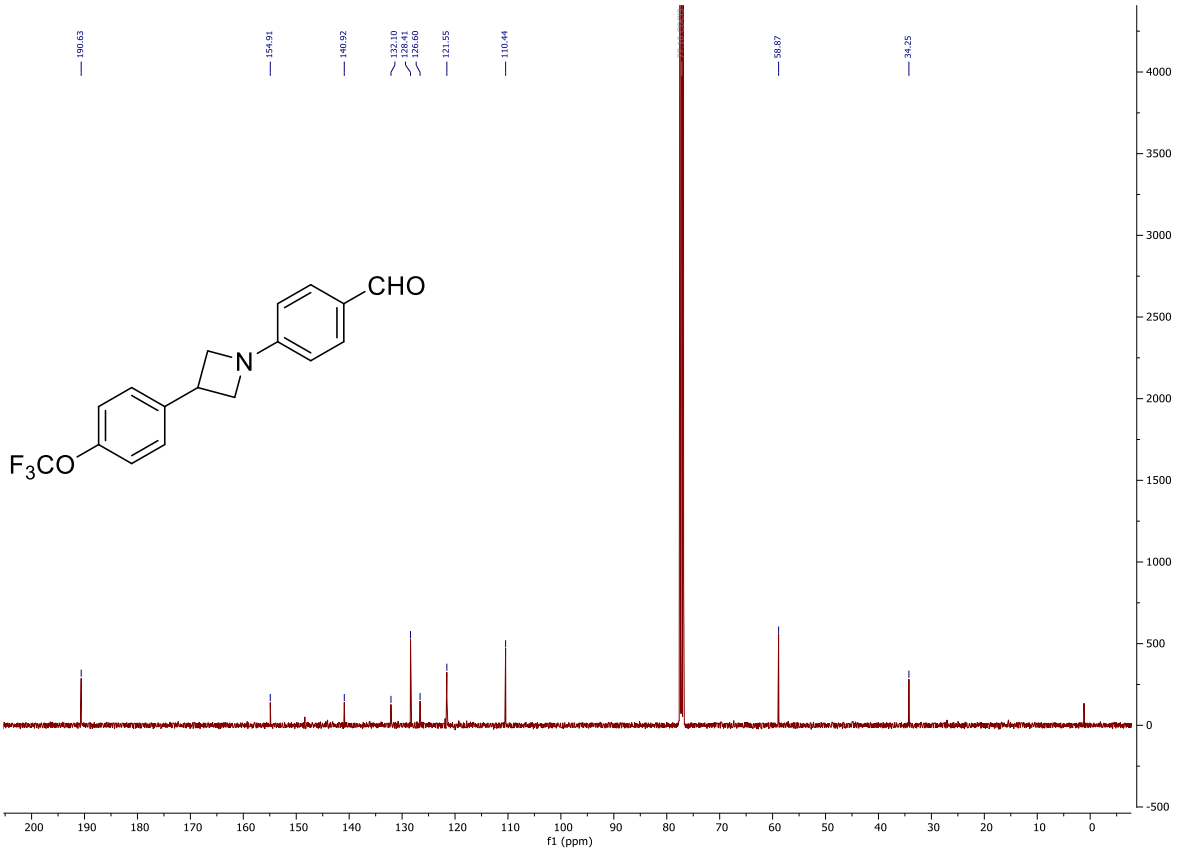


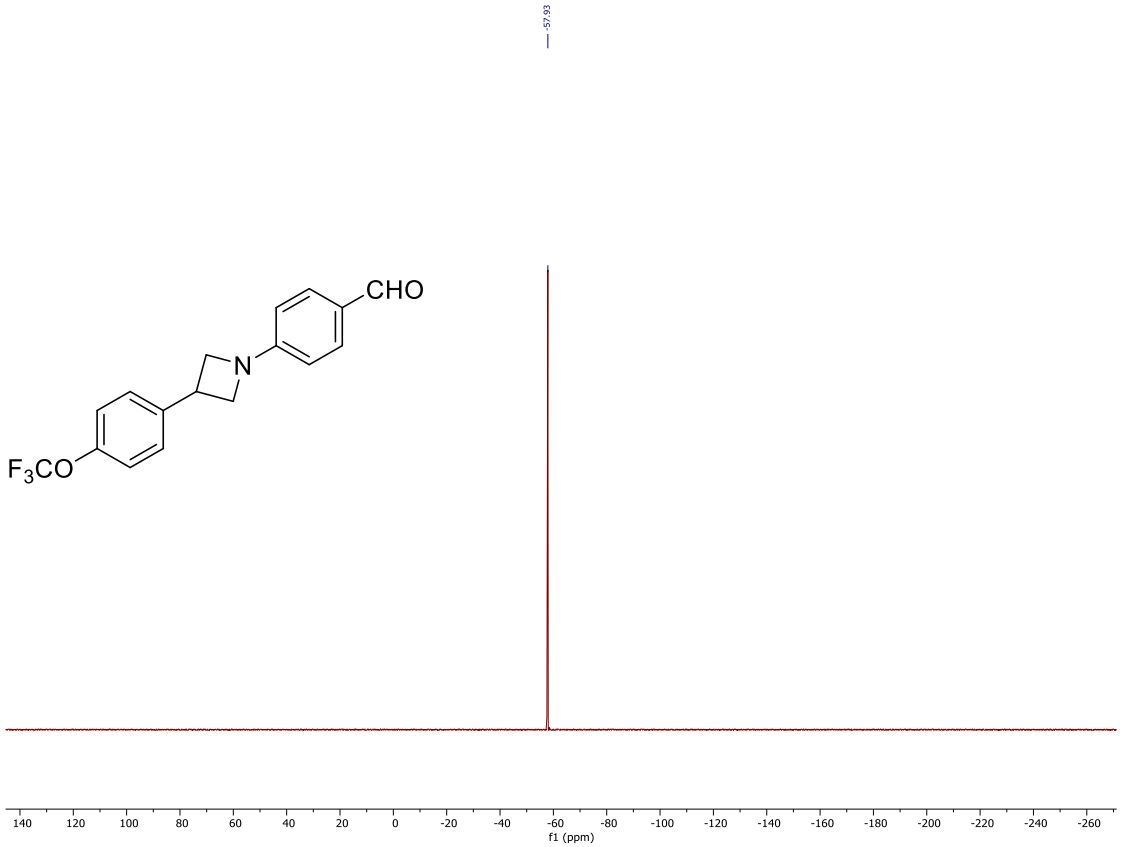

-57.92
N
N
F3CO
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
f1 (ppm)

4-(3-(4-(Trifluoromethoxy)phenyl)azetidin-1-yl)benzaldehyde (10k)

^{1}H NMR (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)

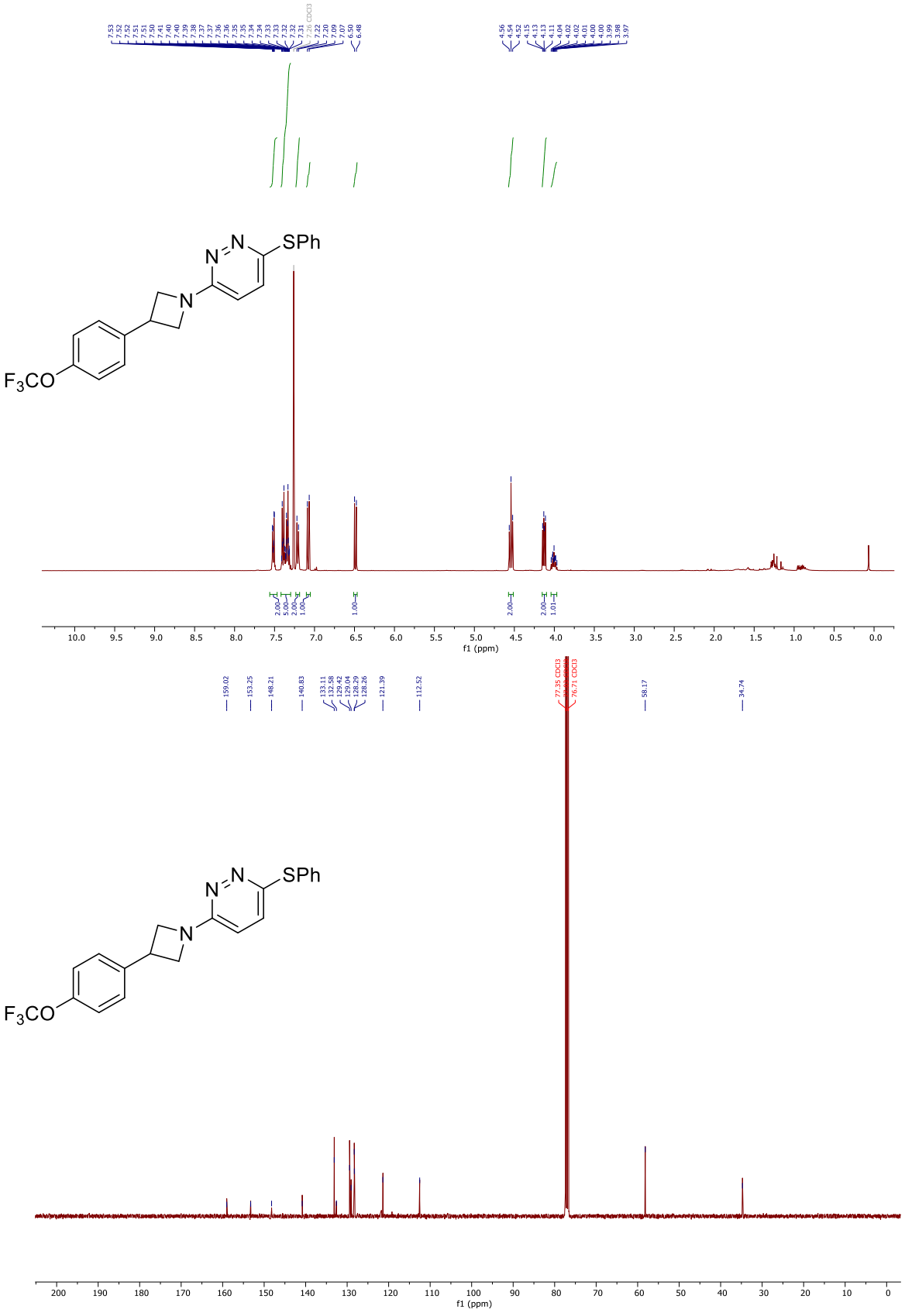


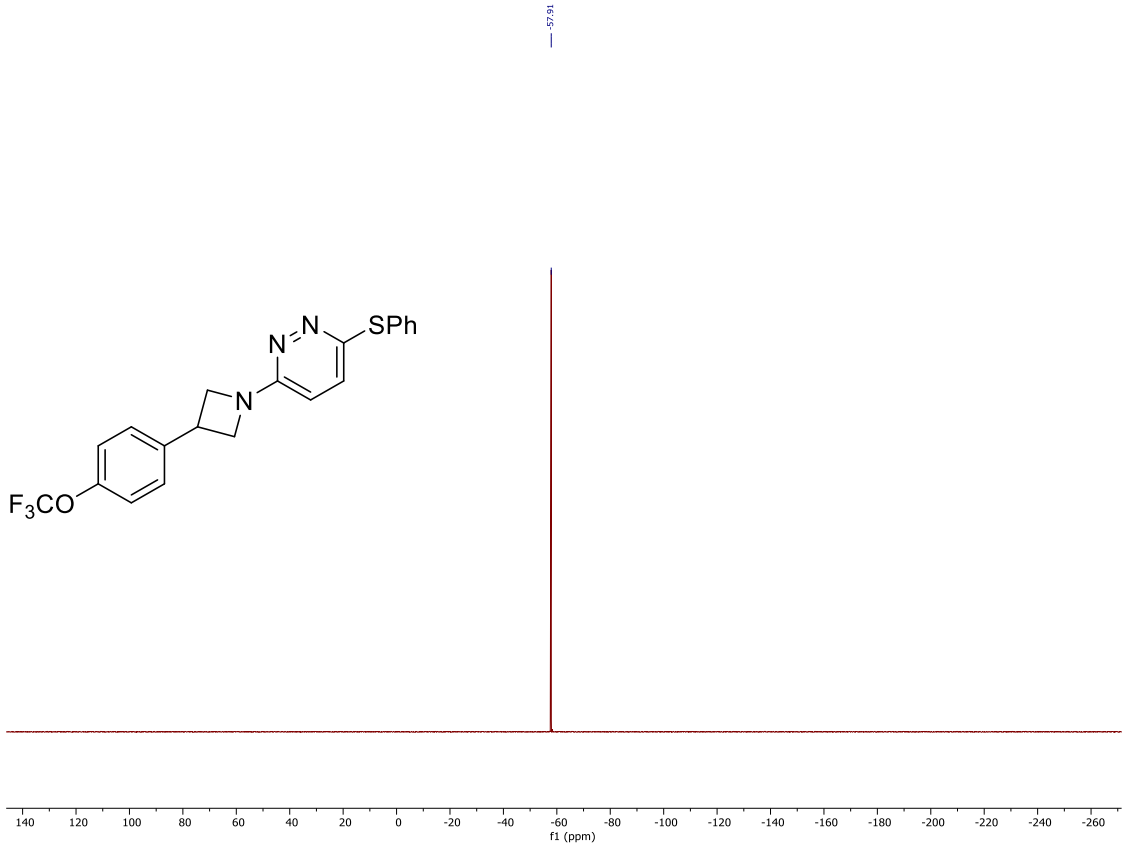



-57.93
CHO
N
F3CO
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
f1 (ppm)

3-(Phenylthio)-6-(3-(4-(trifluoromethoxy)phenyl)azetidin-1-yl)pyridazine (10l)

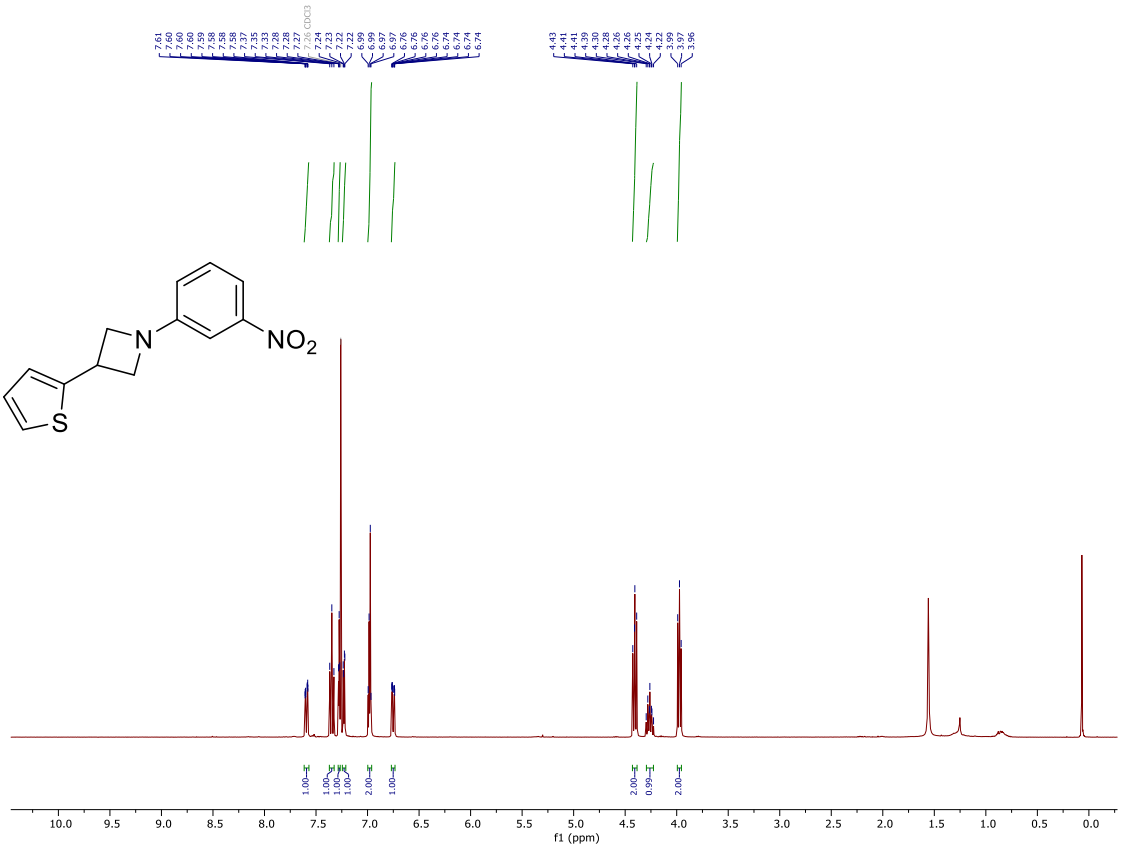
^{1}H NMR (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)

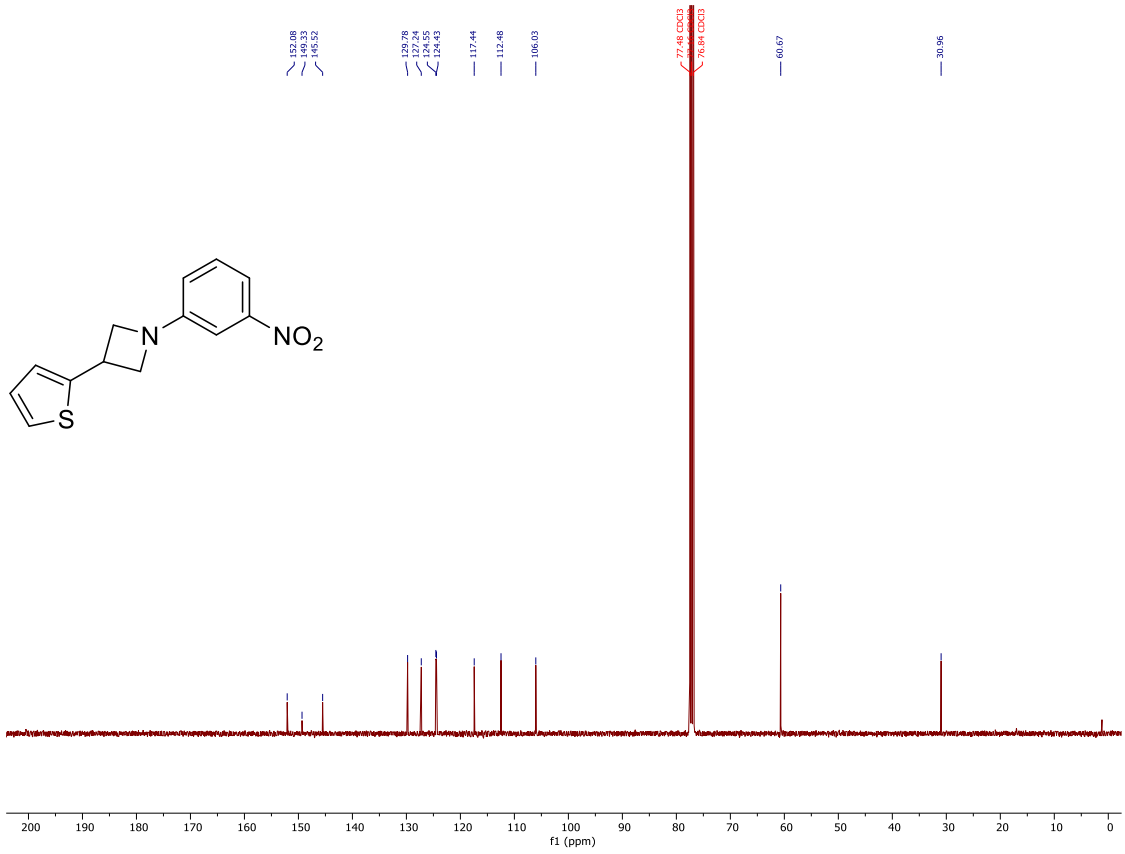



-57.91
N
N
SPh
N
F3CO
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
f1 (ppm)

1-(3-Nitrophenyl)-3-(thiophen-2-yl)azetidine (10m)

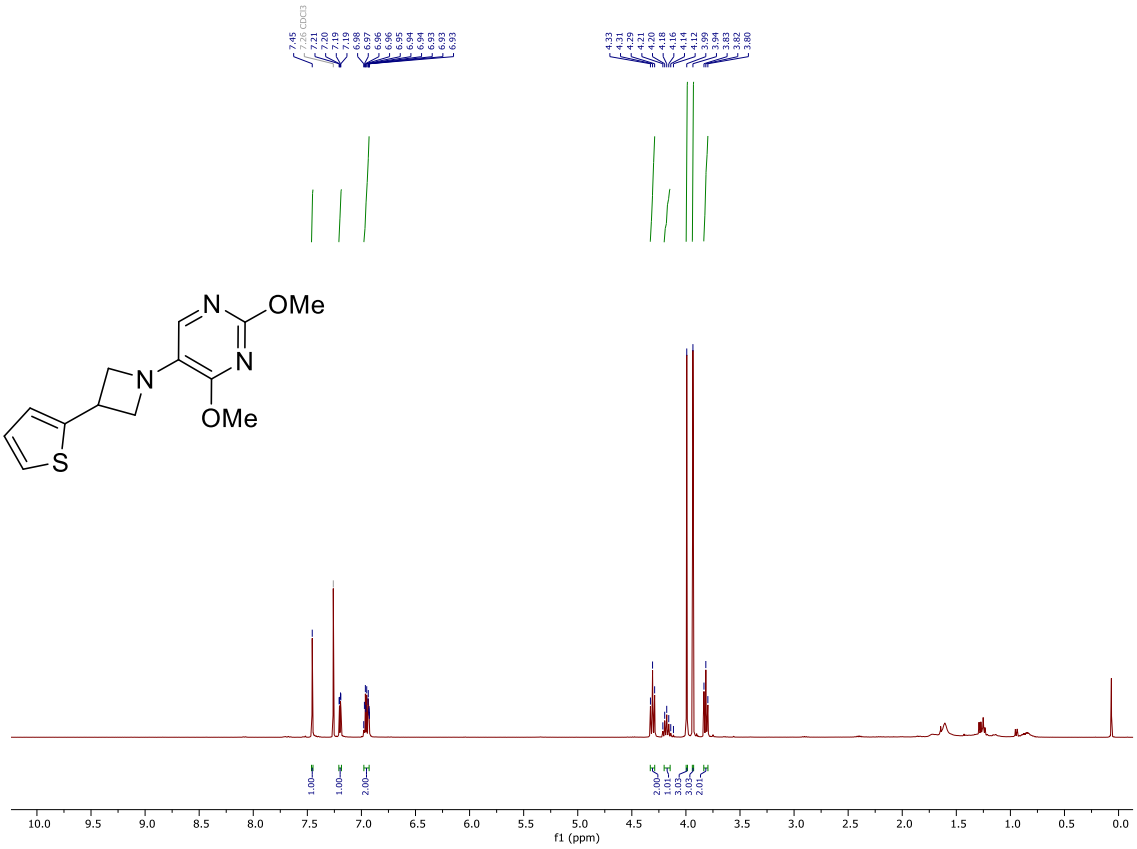
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

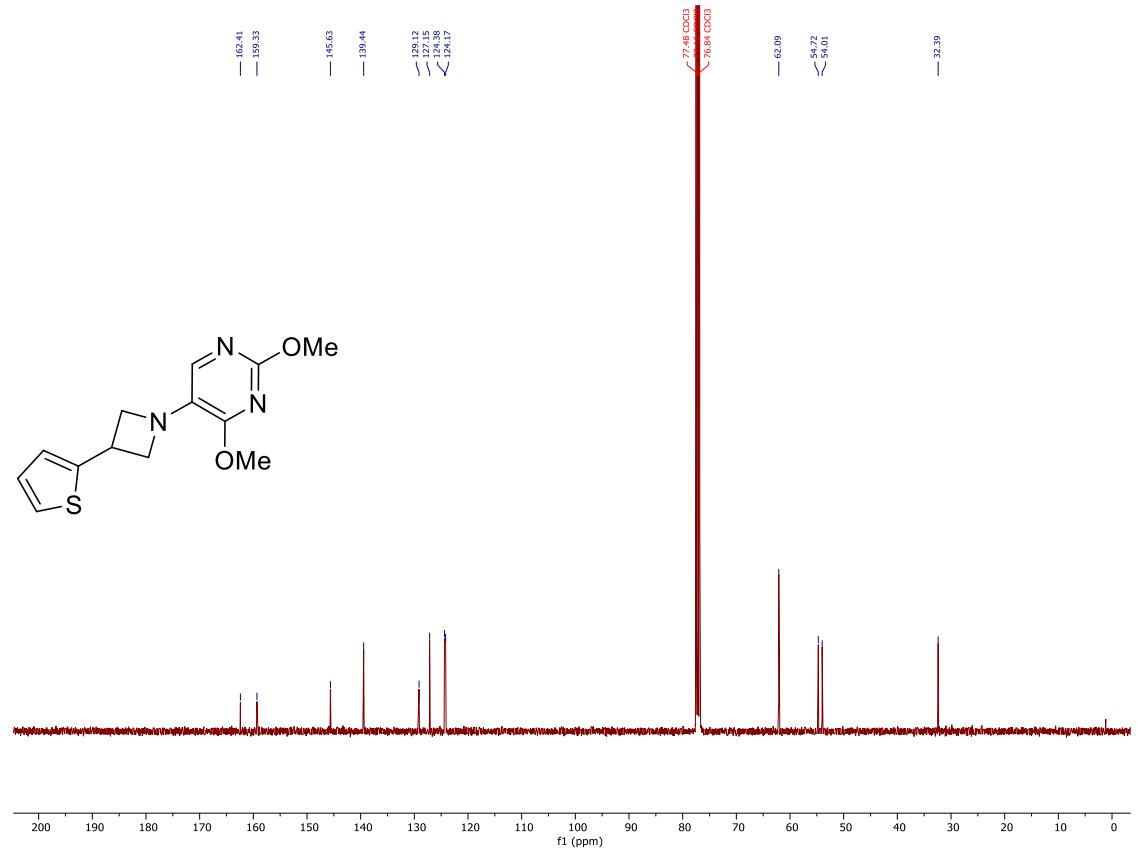




2,4-Dimethoxy-5-(3-(thiophen-2-yl)azetidin-1-yl)pyrimidine (10n)

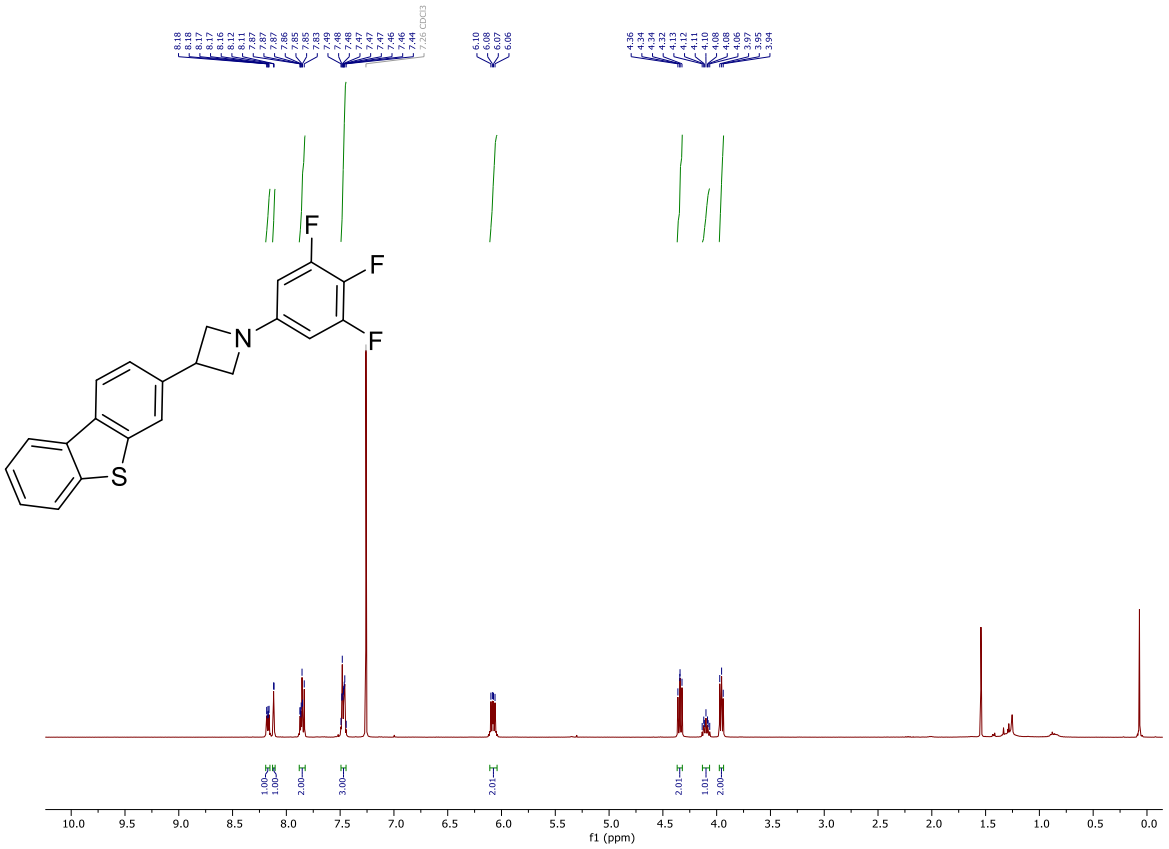
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

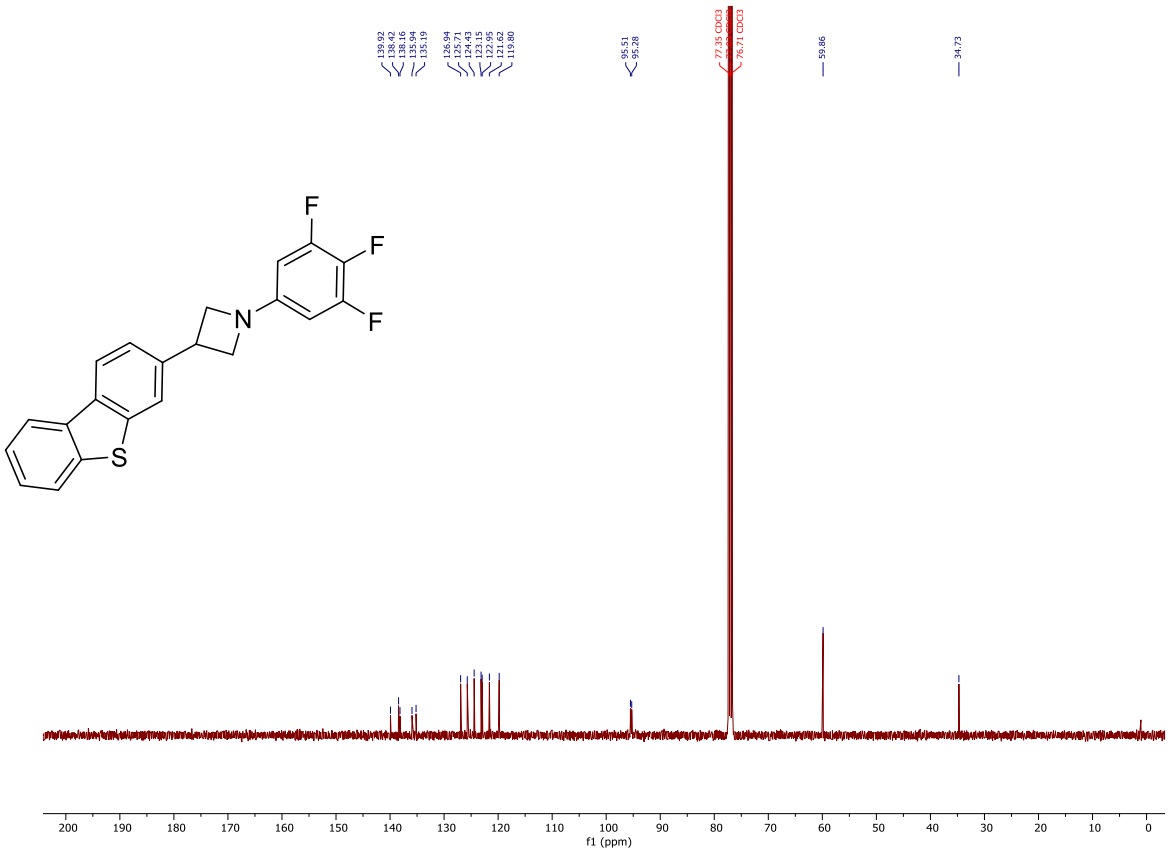


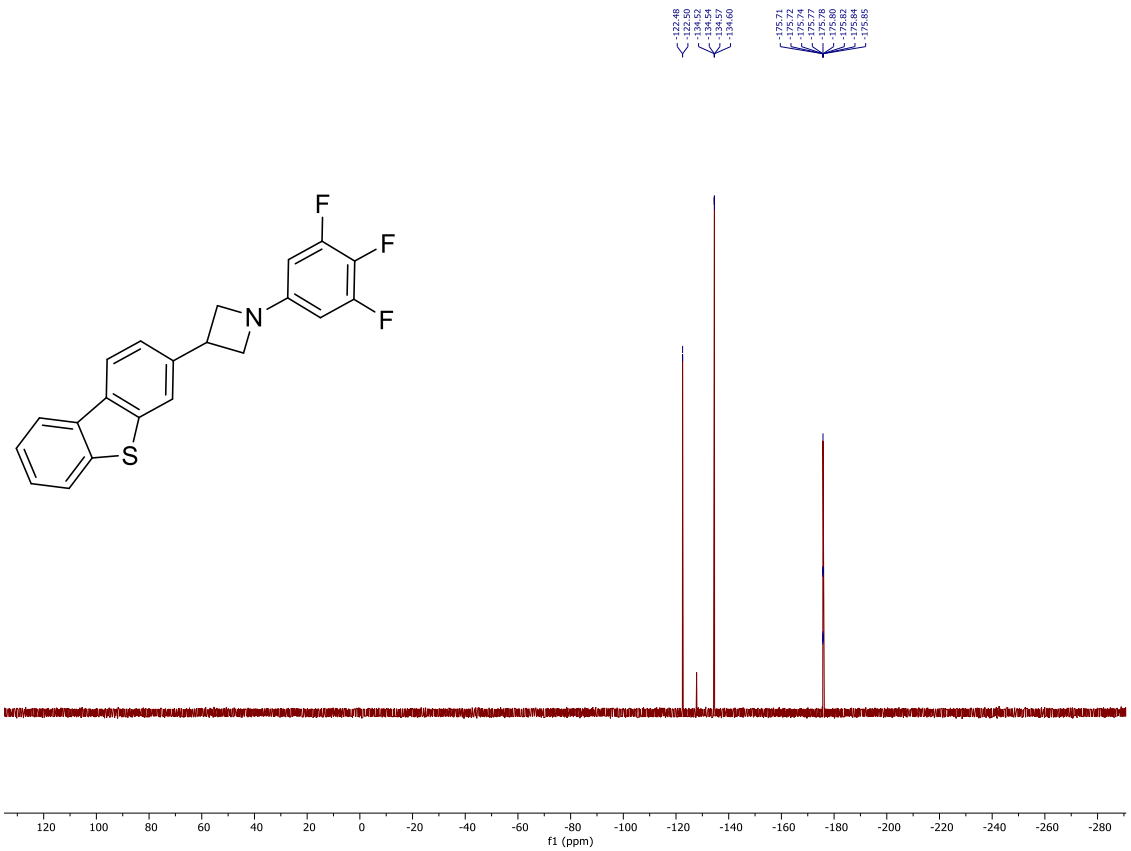


3-(Dibenzo[*b*,*d*]thiophen-3-yl)-1-(3,4,5-trifluorophenyl)azetidine (10o)

^{1}H NMR (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)

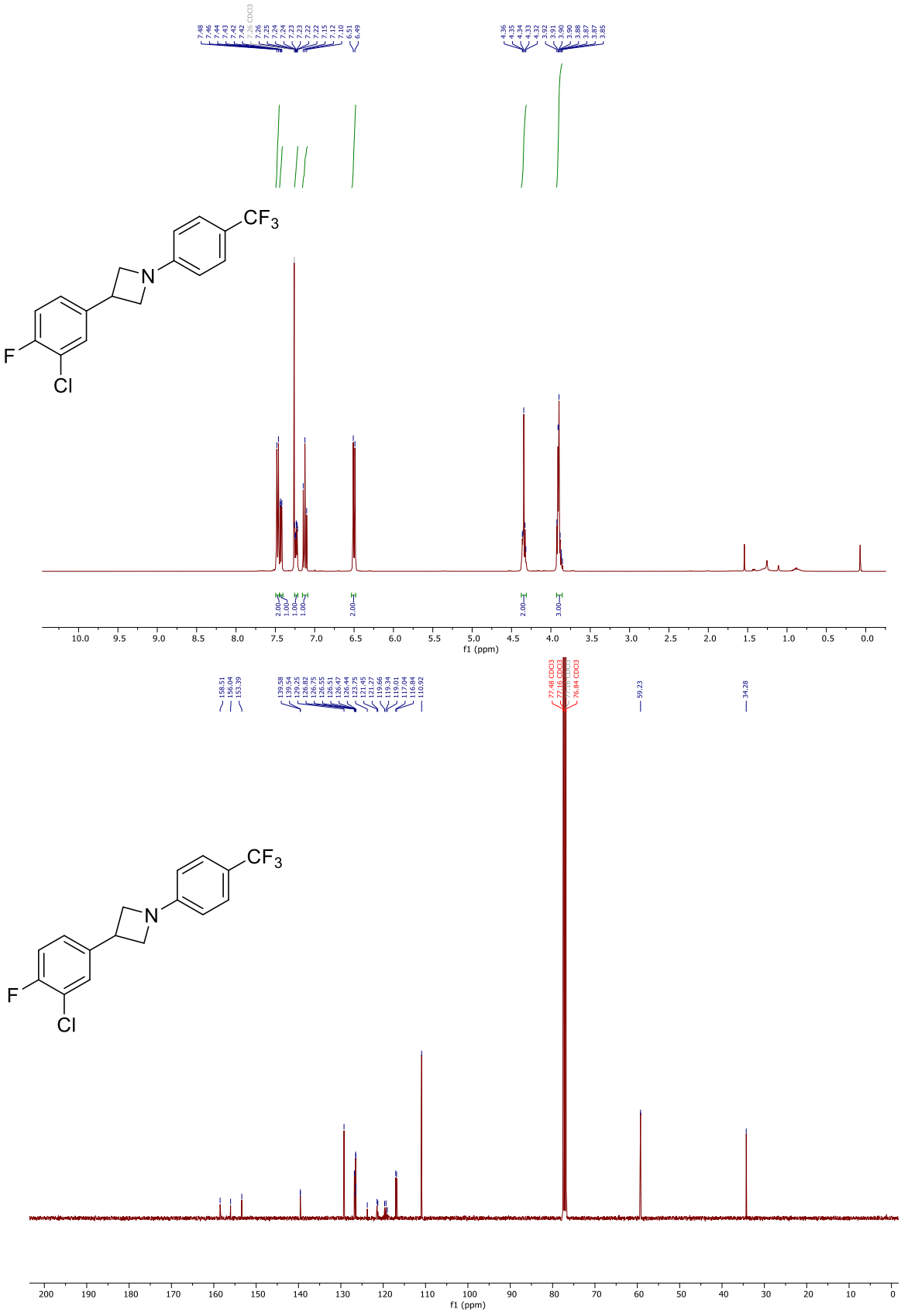


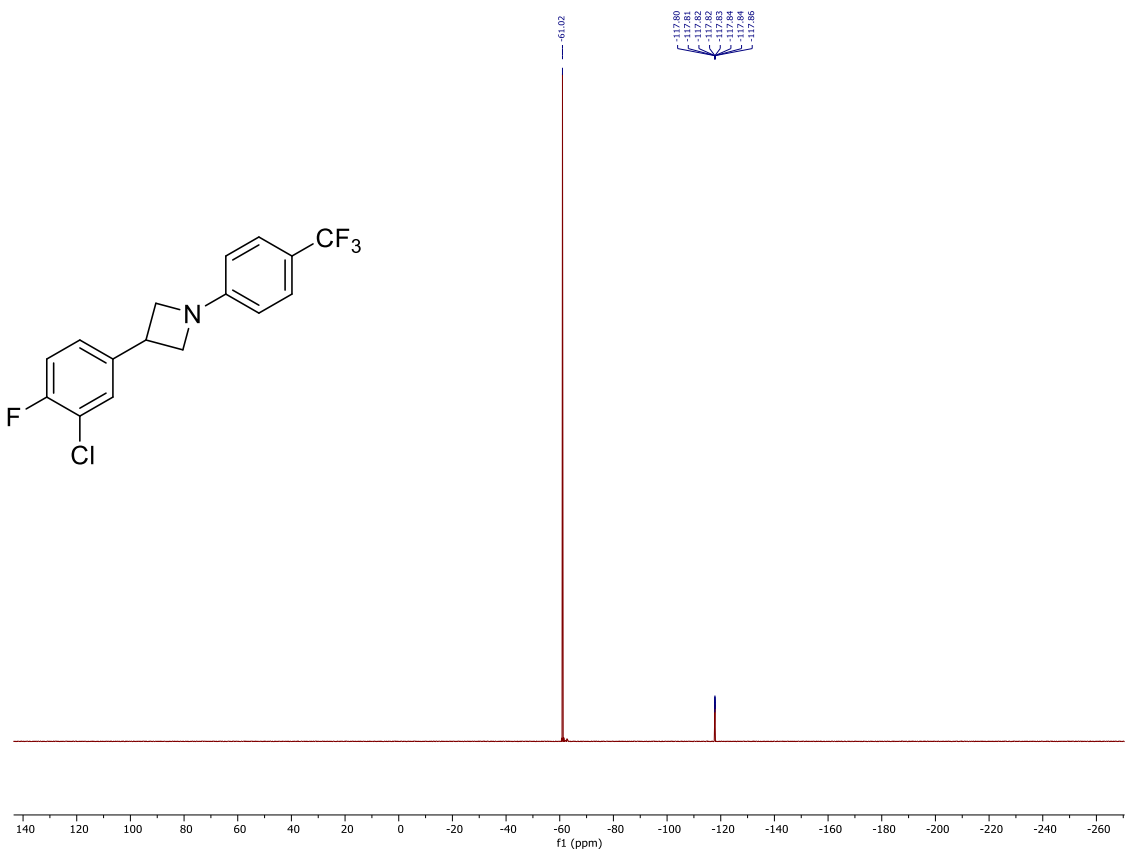



-122.48
-122.50
-134.52
-134.54
-134.57
-134.60
-175.71
-175.72
-175.74
-175.77
-175.78
-175.80
-175.82
-175.84
-175.85
F
F
F
N
S
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
-280
f1 (ppm)

3-(3-Chloro-4-fluorophenyl)-1-(4-(trifluoromethyl)phenyl)azetidine (10p)

^{1}H NMR (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$) and **^{19}F NMR** (377 MHz, $CDCl_3$)




CF3
N
F
Cl
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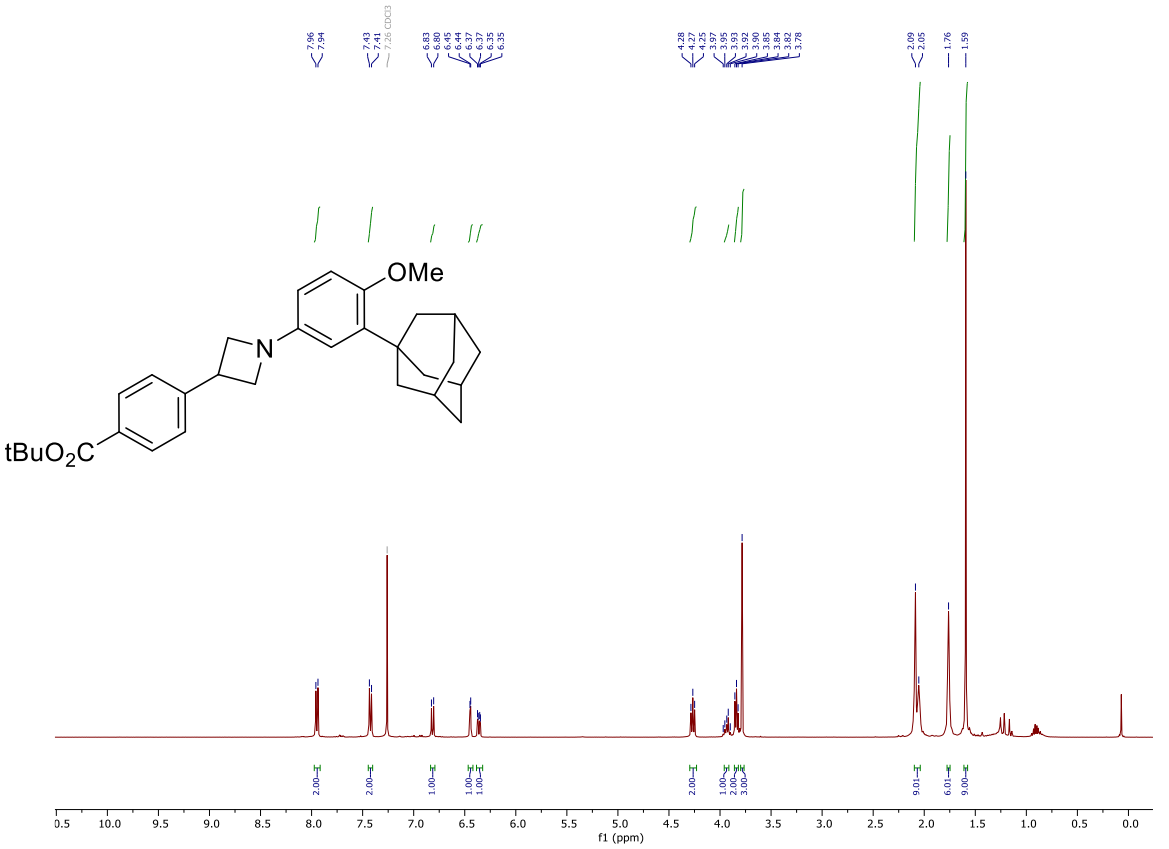
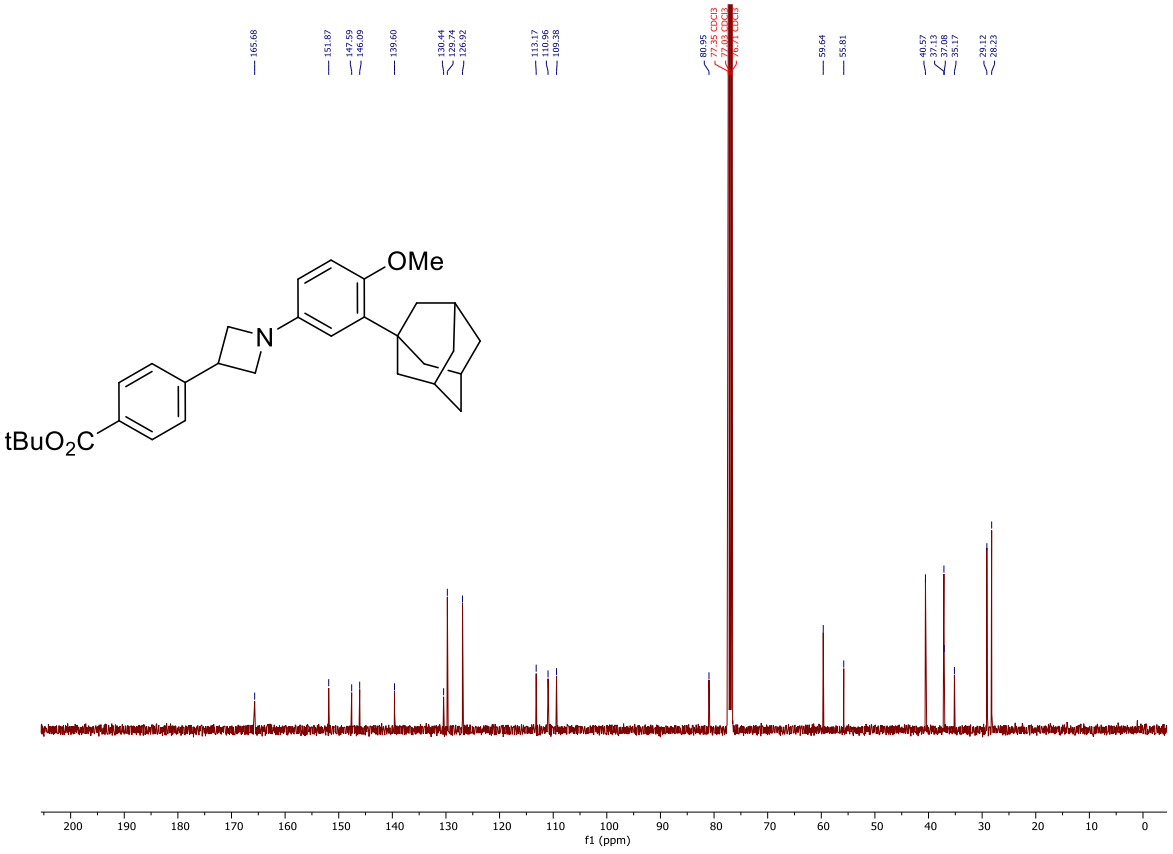
-117.80
-117.81
-117.82
-117.82
-117.83
-117.84
-117.84
-117.86
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
f1 (ppm)

***tert*-Butyl 4-(1-(3-(adamantan-1-yl)-4-methoxyphenyl)azetidin-3-yl)benzoate (10q)**

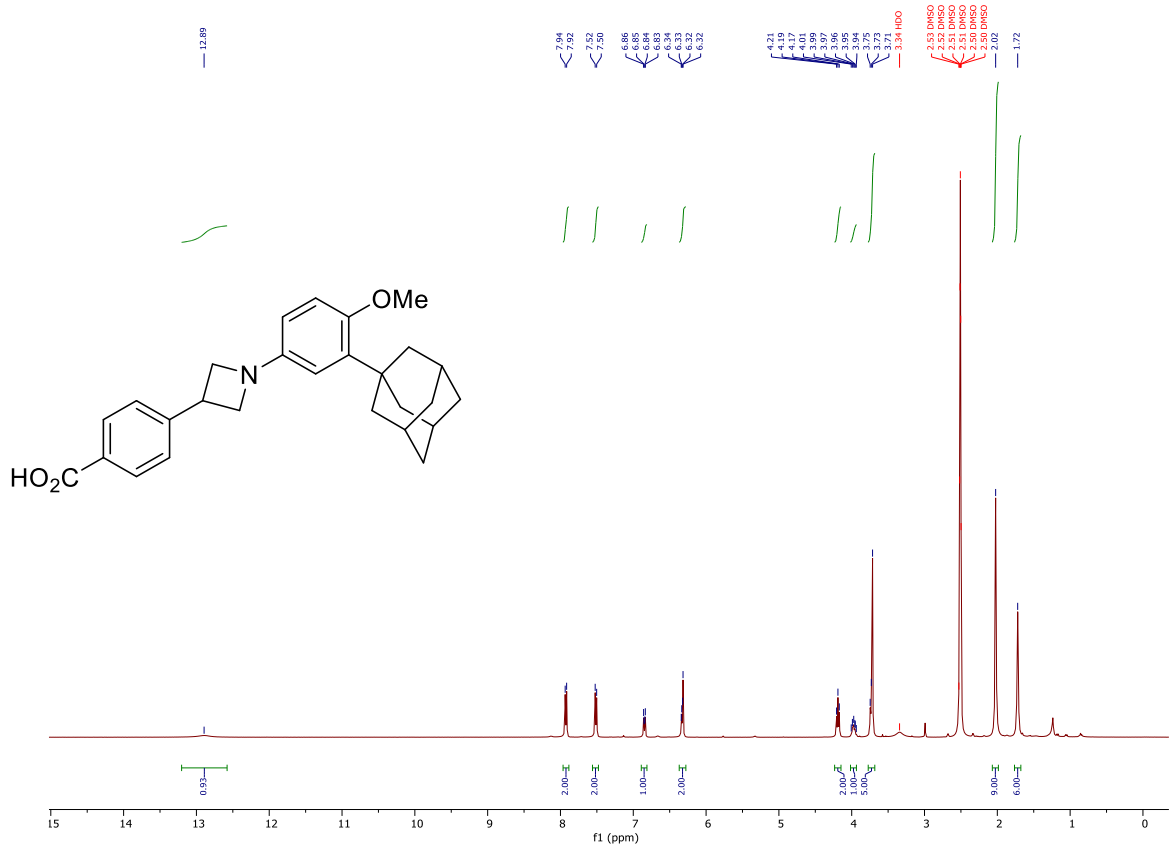
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

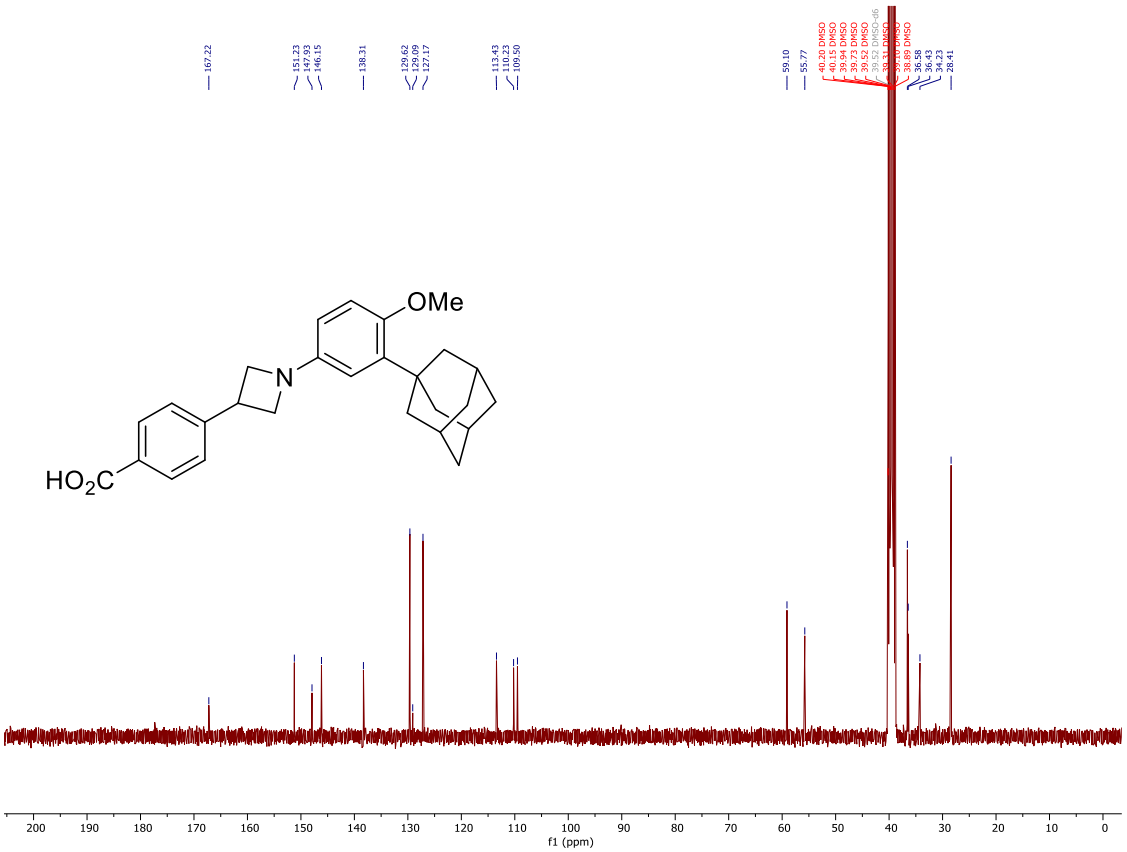




4-(1-(3-((Adamantan-1-yl)-4-methoxyphenyl)azetidin-3-yl)benzoic acid (10r)

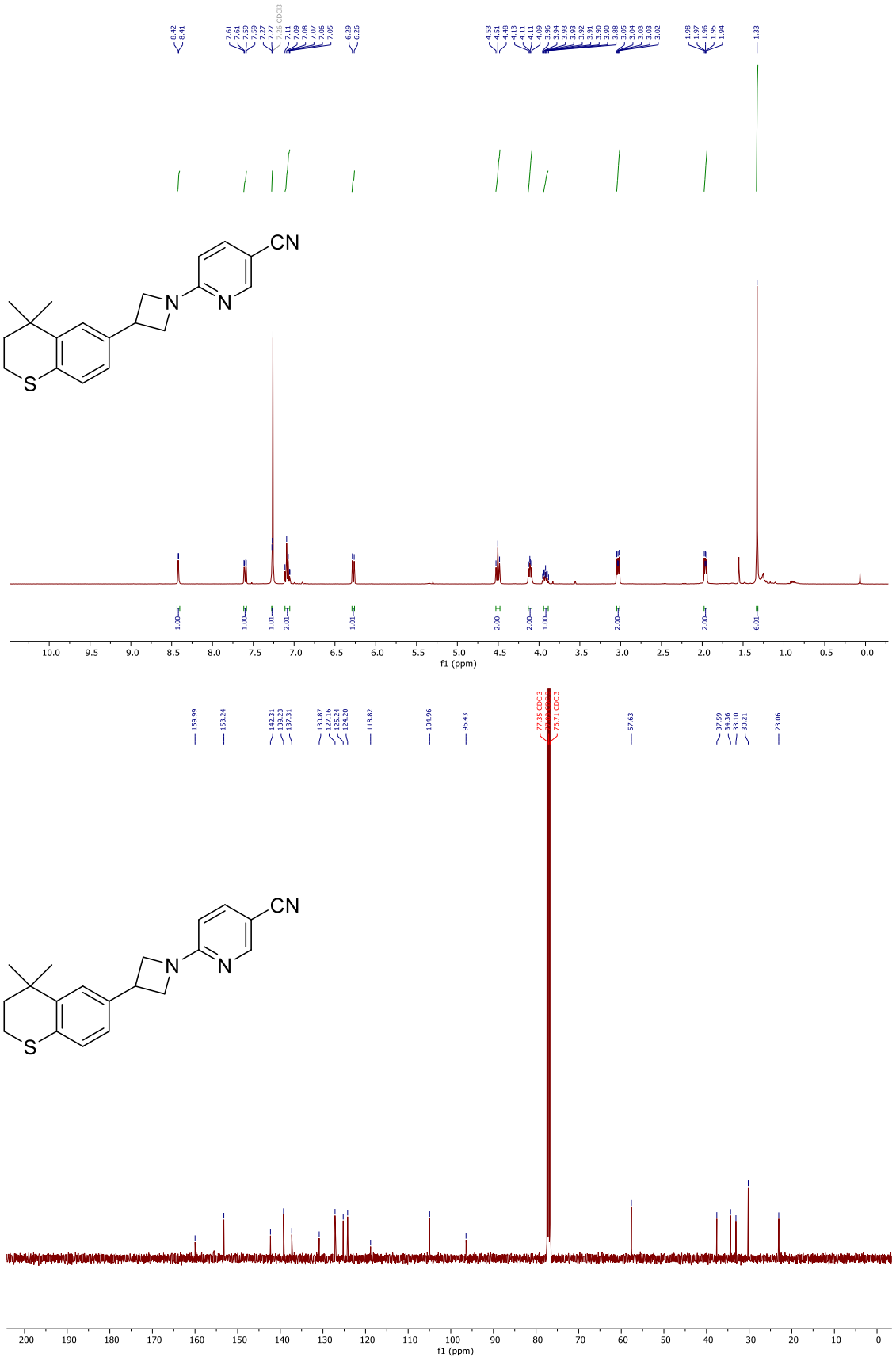
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, DMSO-D_6)





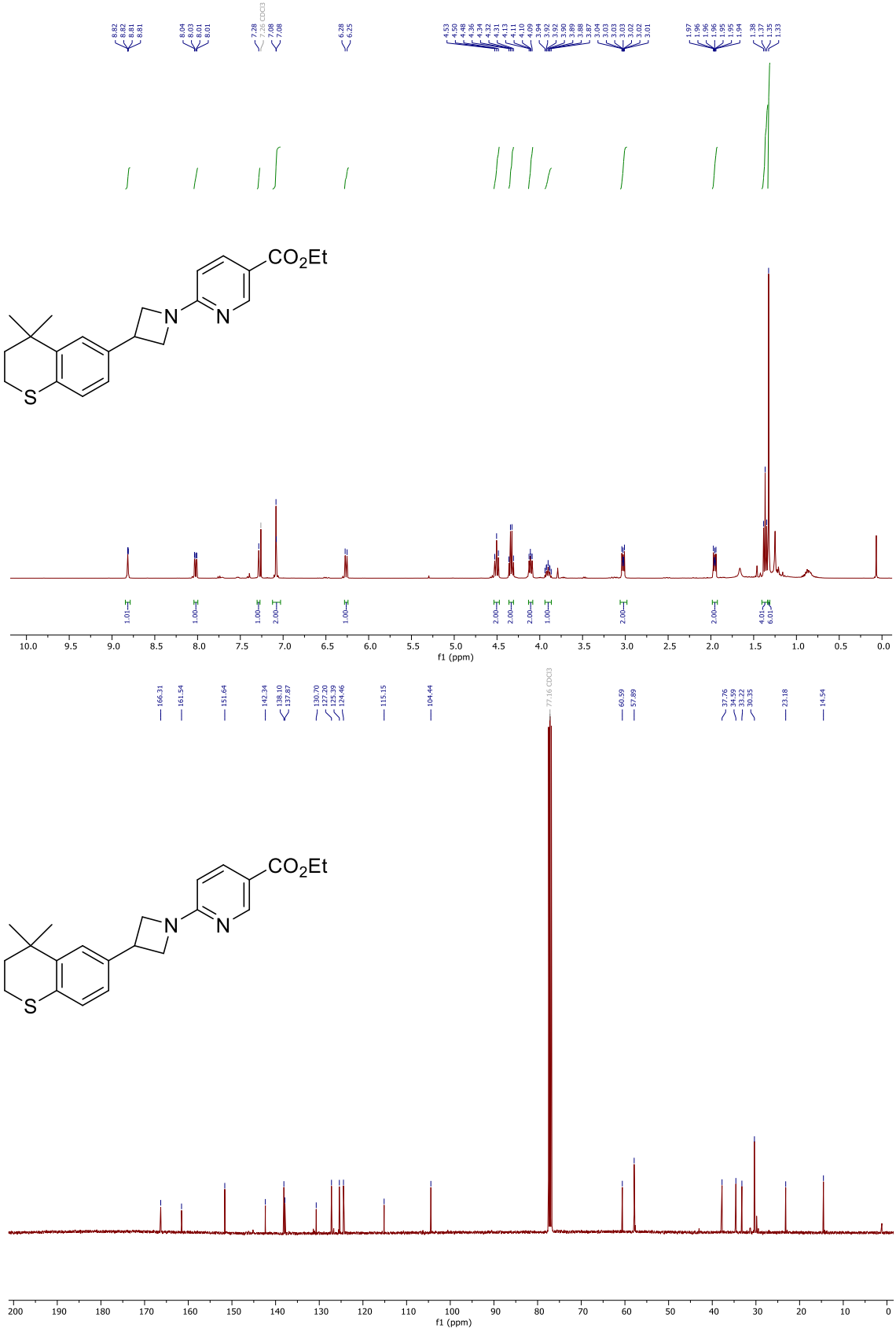
6-(3-(4,4-Dimethylthiochroman-6-yl)azetidin-1-yl)nicotinonitrile (10s)

^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)



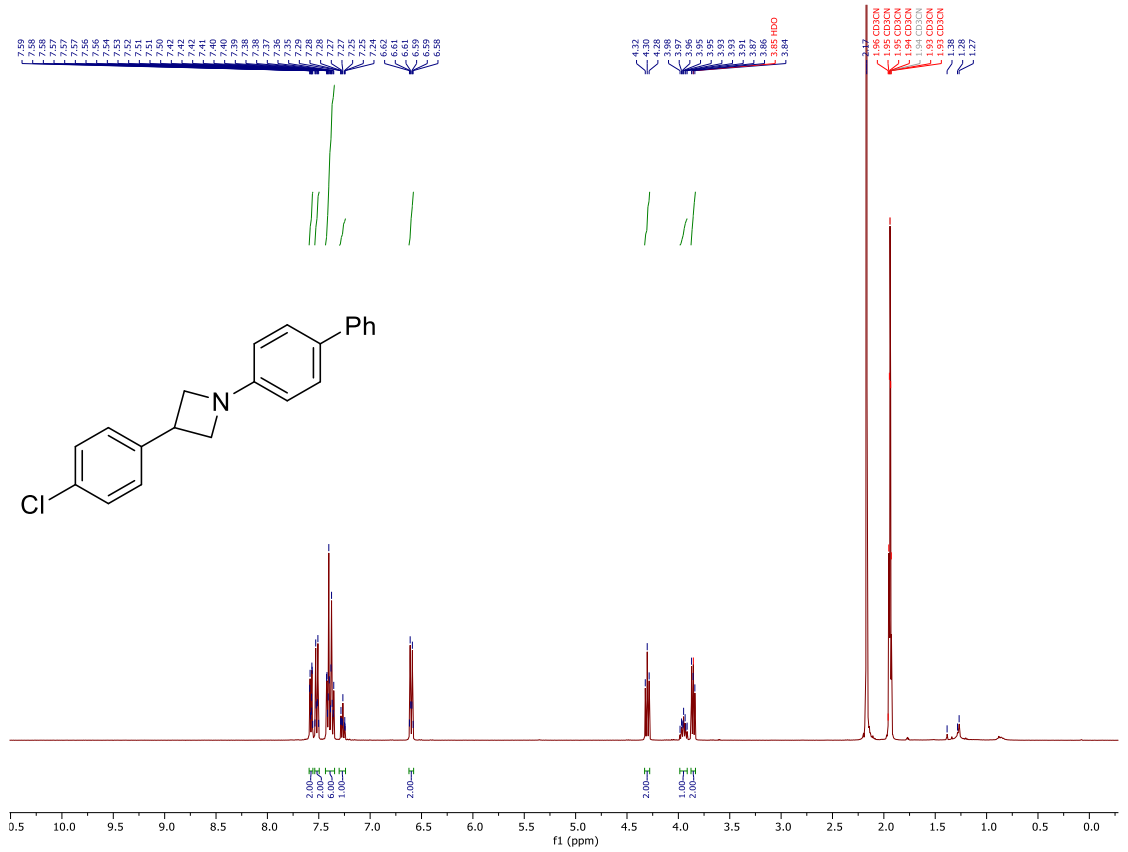
Ethyl 6-(3-(4,4-dimethylthiochroman-6-yl)azetidin-1-yl)nicotinate (10t)

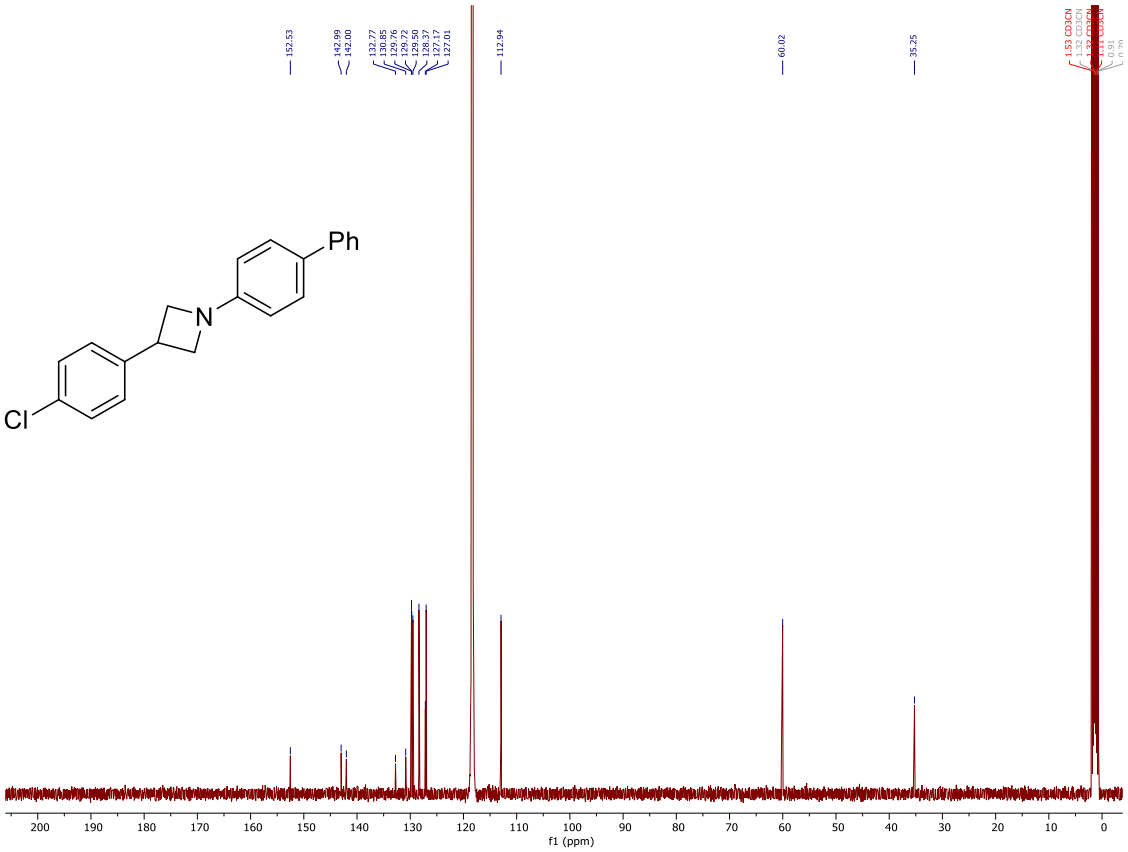
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)



1-([1,1'-Biphenyl]-4-yl)-3-(4-chlorophenyl)azetidine (11a)

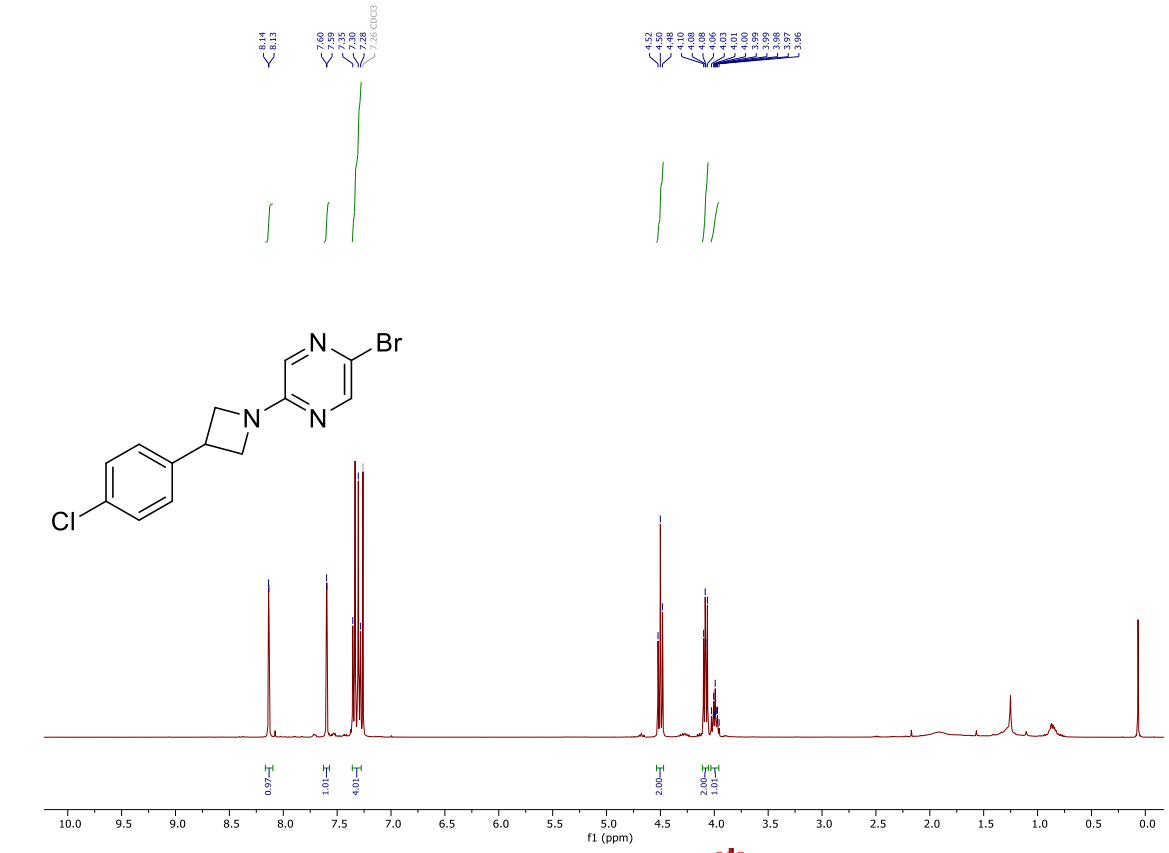
^{1}H NMR (400 MHz, CD_3CN) and **^{13}C NMR** (100 MHz, CD_3CN)

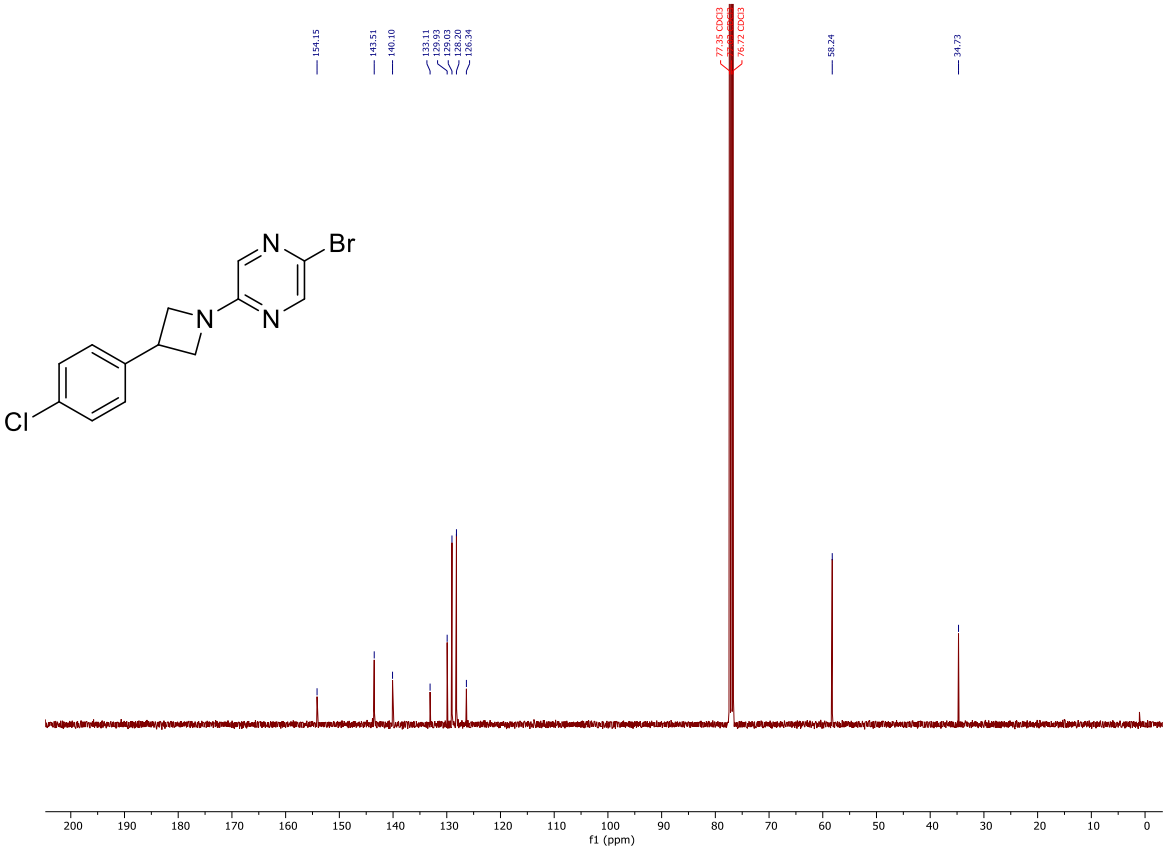




2-Bromo-5-(3-(4-chlorophenyl)azetidin-1-yl)pyrazine (11b)

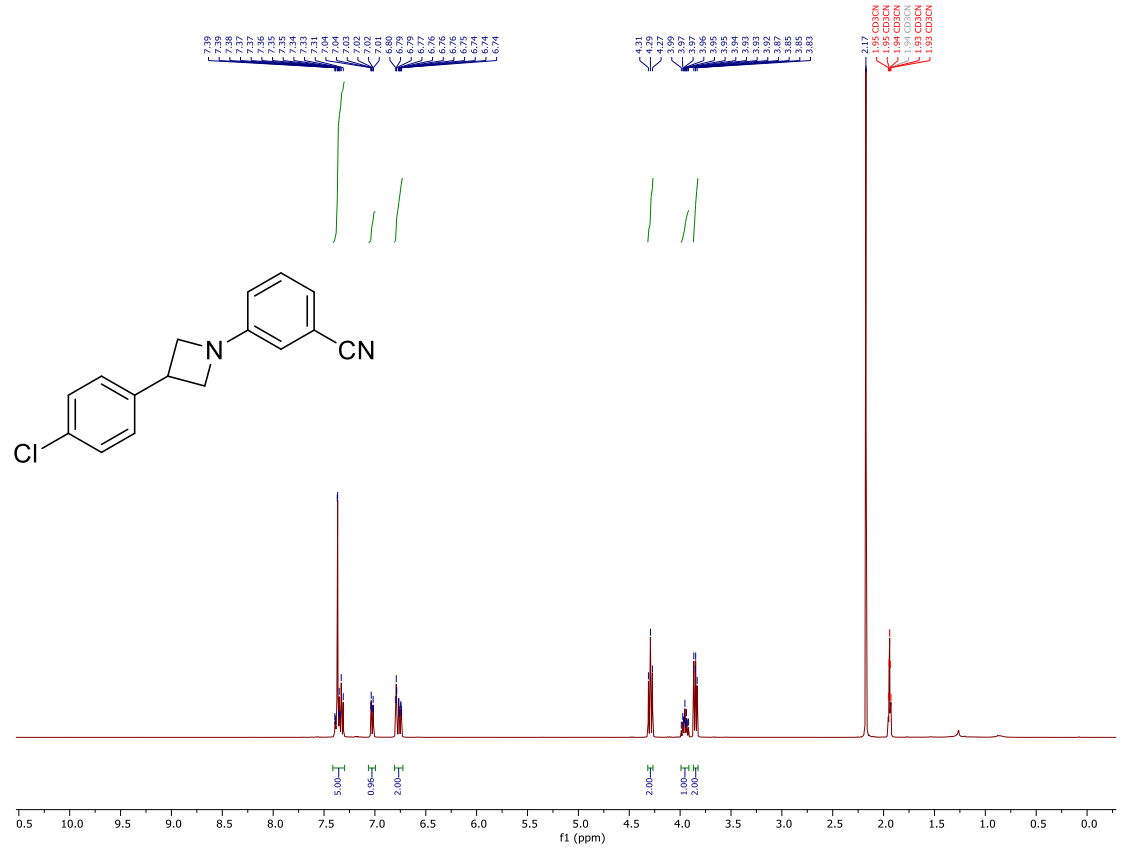
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

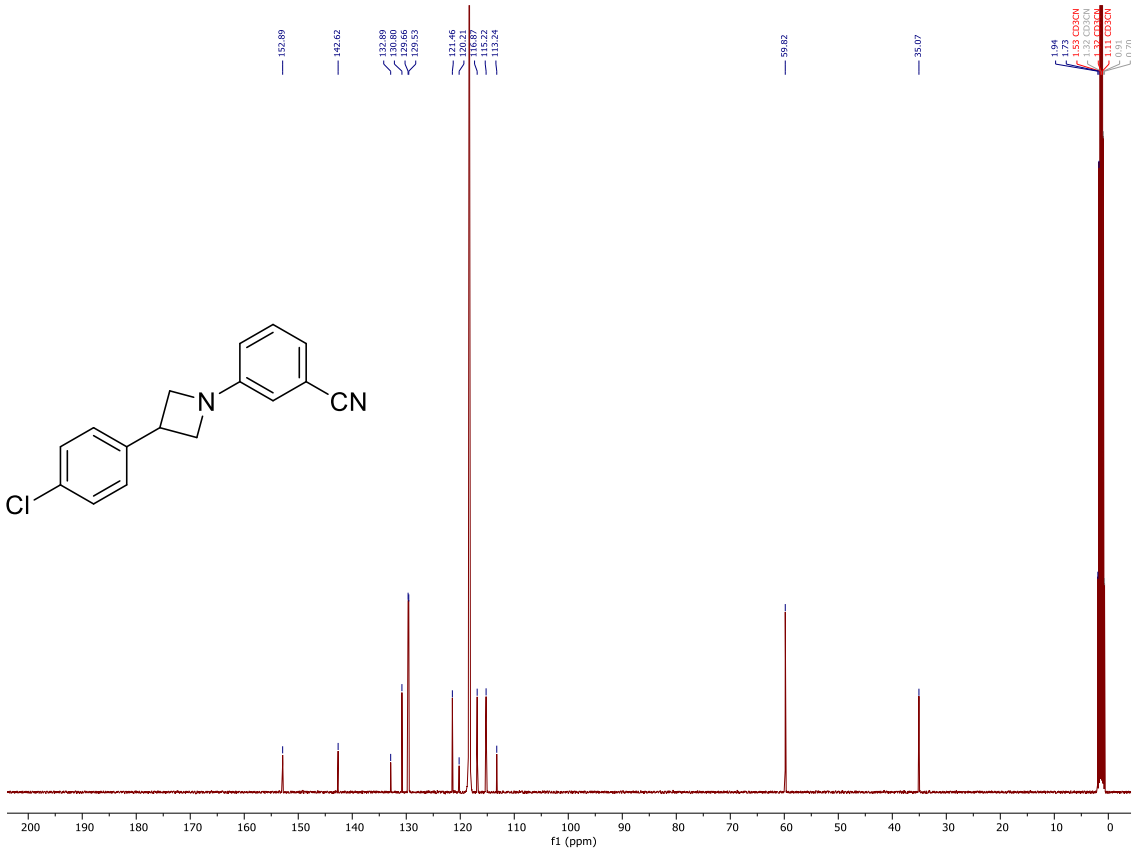




3-(3-(4-Chlorophenyl)azetidin-1-yl)benzonitrile (11c)

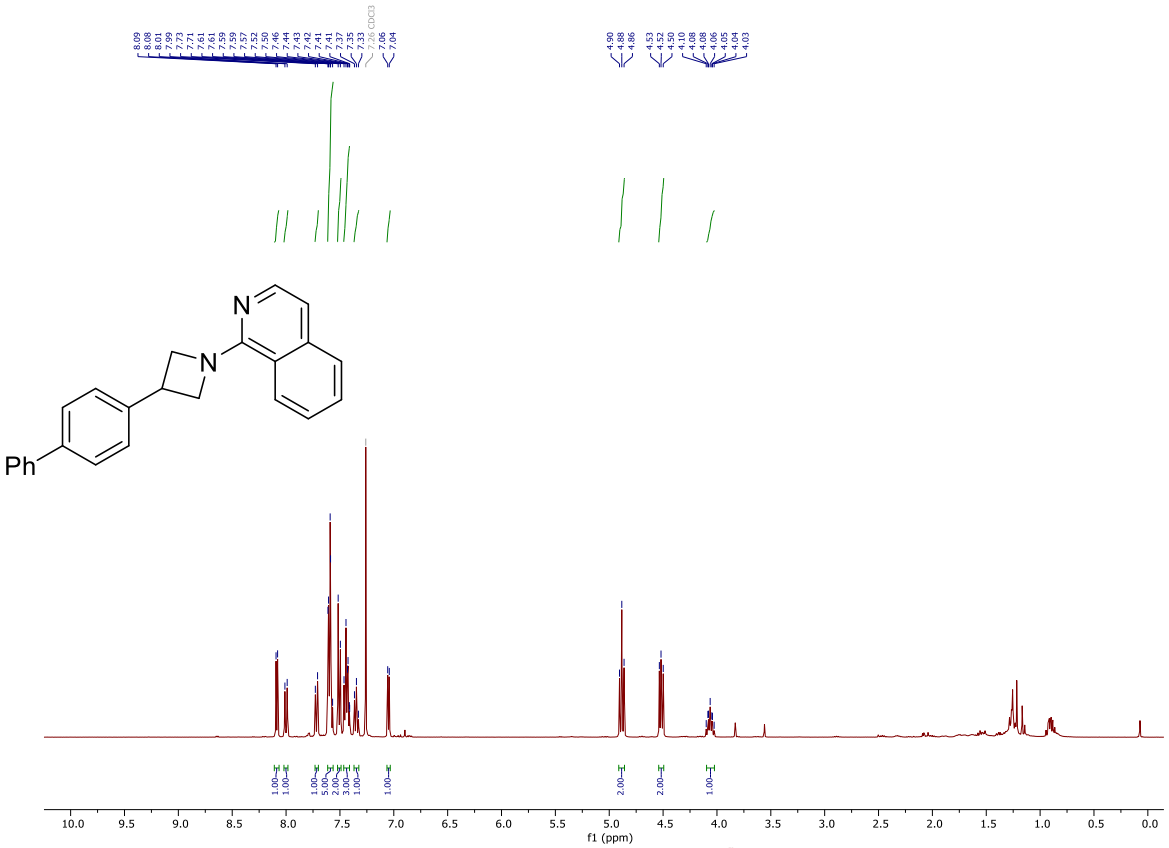
^{1}H NMR (400 MHz, CD_3CN) and **^{13}C NMR** (100 MHz, CD_3CN)

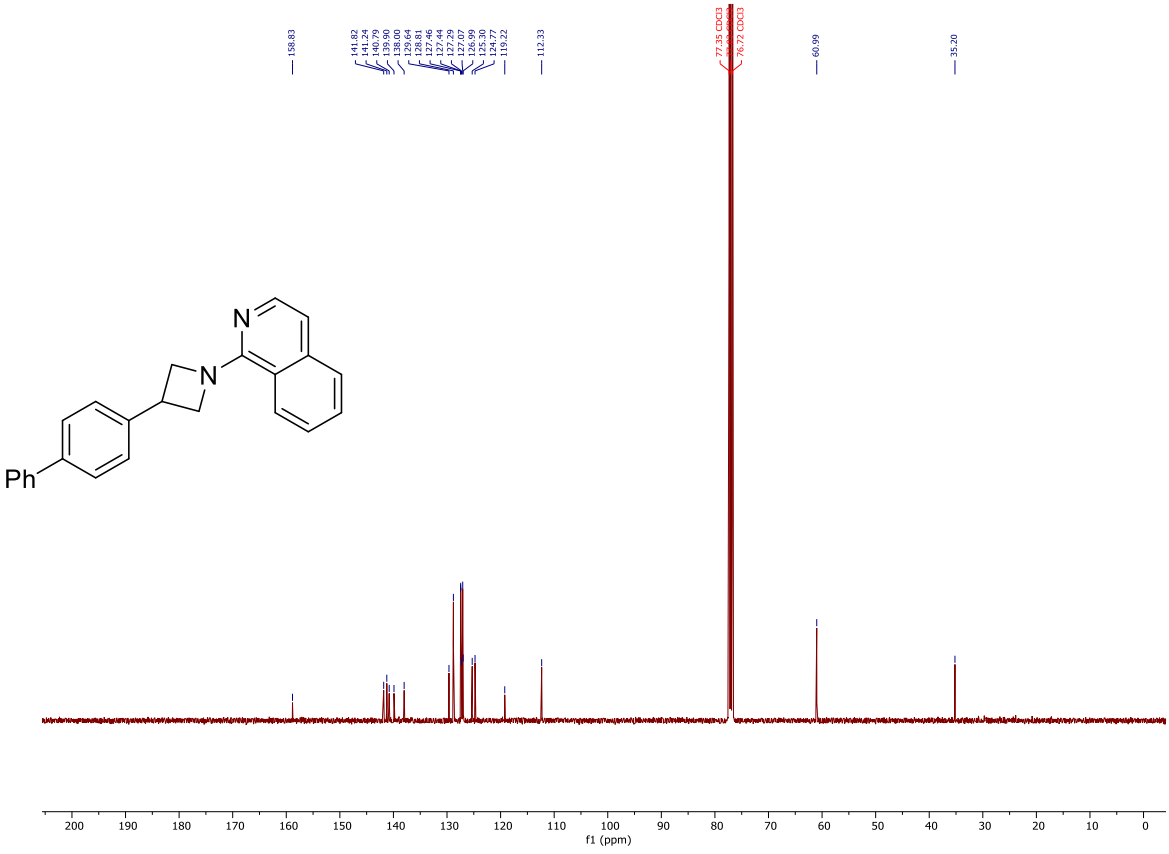




1-(3-([1,1'-Biphenyl]-4-yl)azetidin-1-yl)isoquinoline (11d)

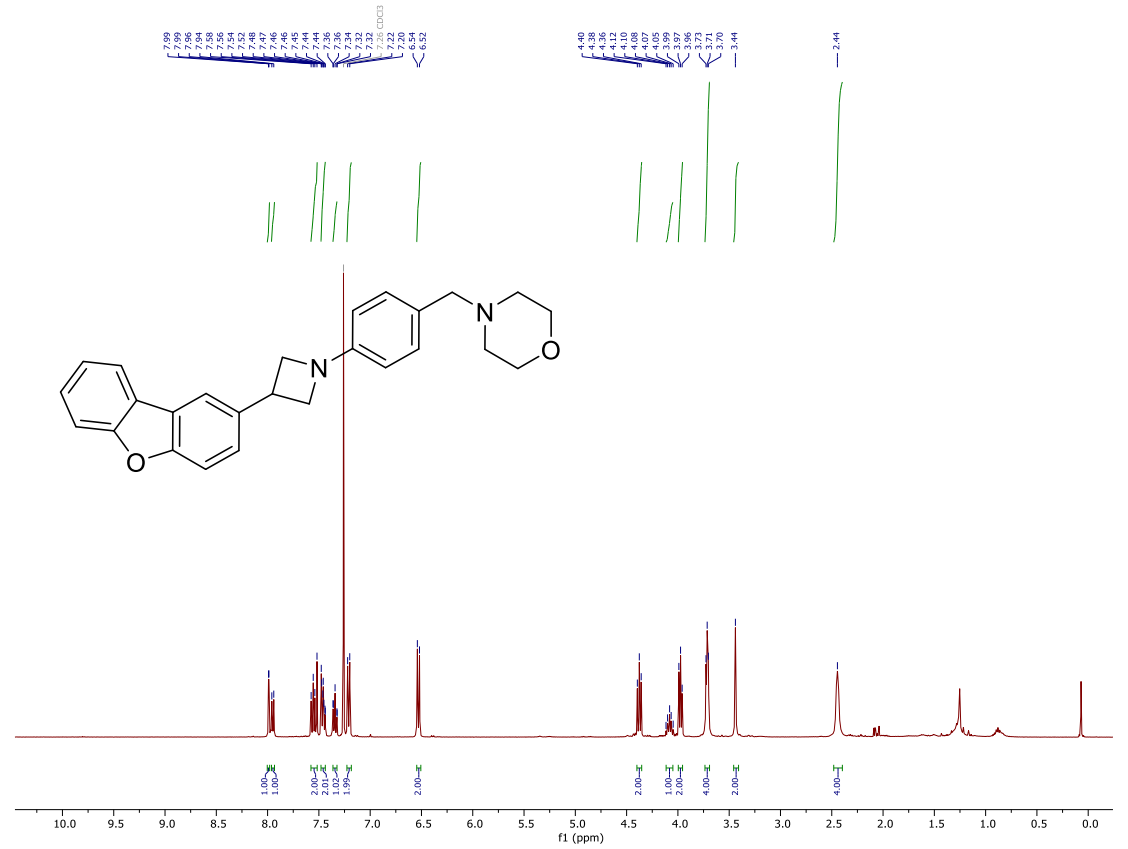
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

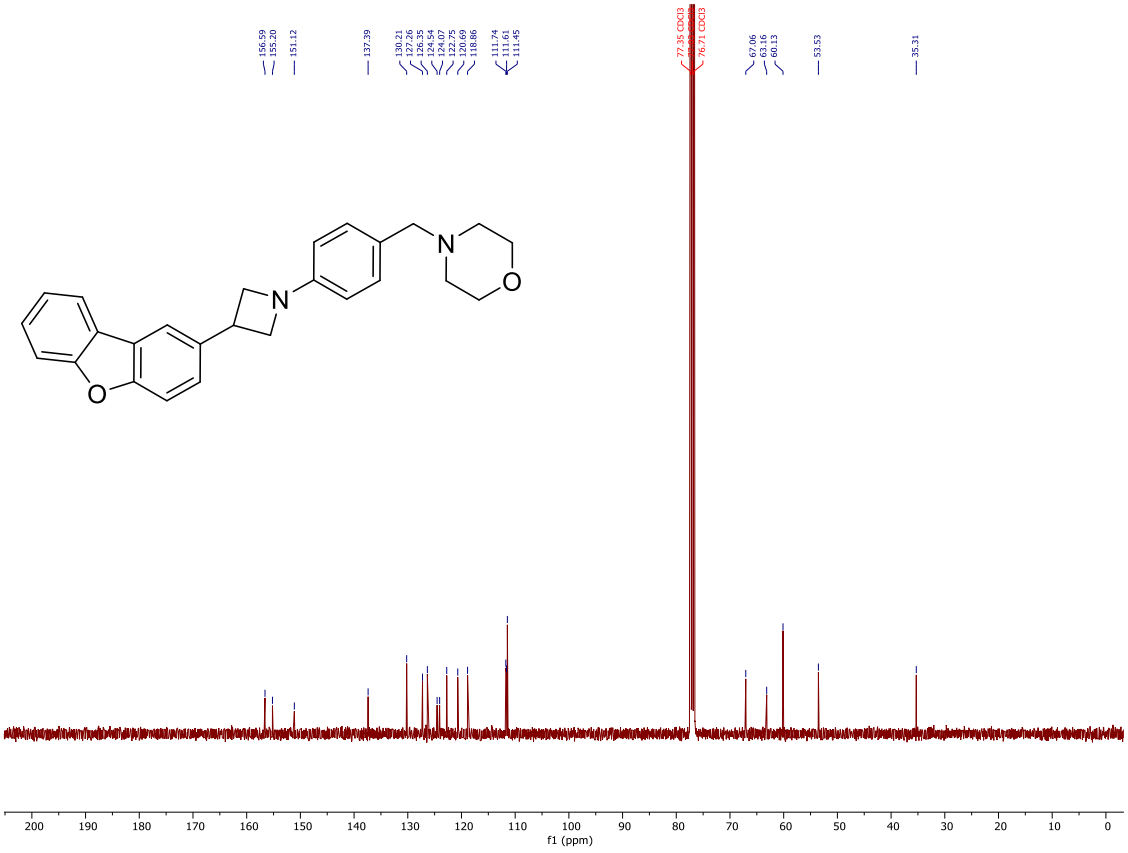




4-(4-(3-(Dibenzo[*b*,*d*]furan-2-yl)azetidin-1-yl)benzyl)morpholine (11e)

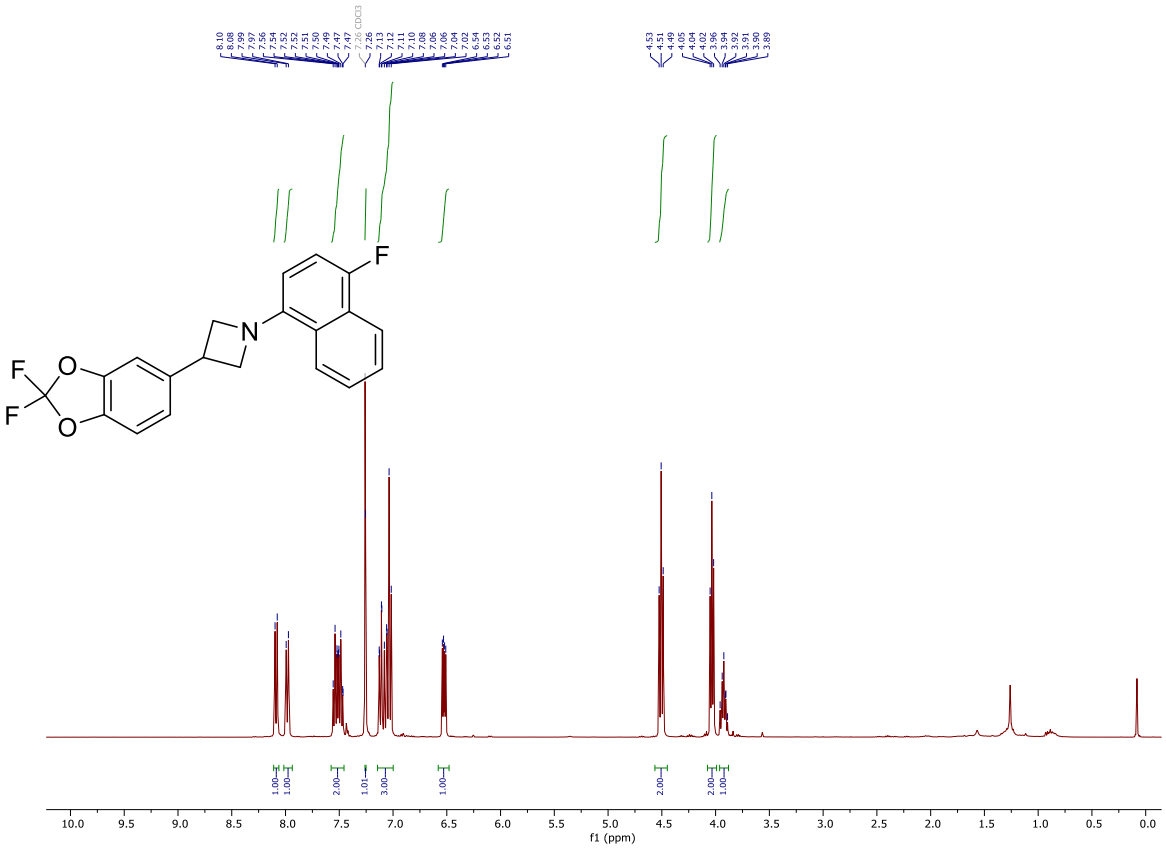
^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)

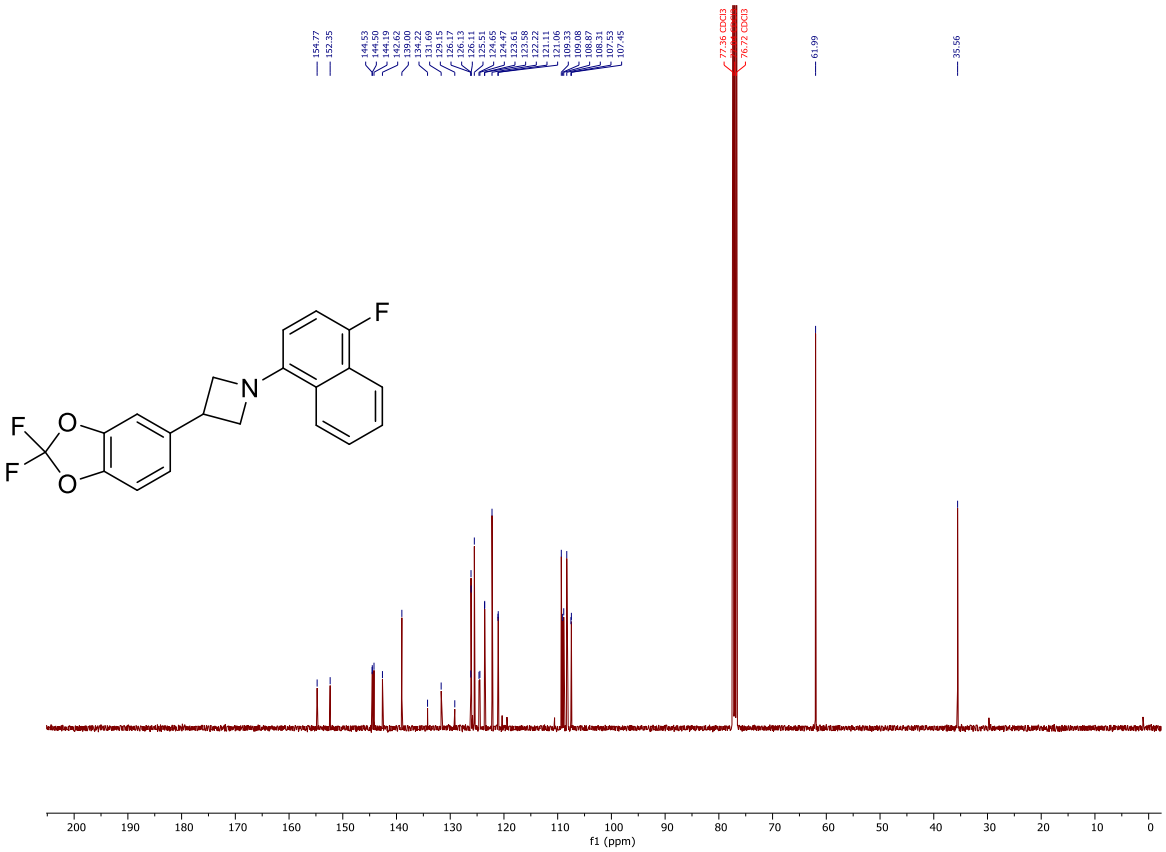




3-(2,2-Difluorobenzo[*d*][1,3]dioxol-5-yl)-1-(4-fluoronaphthalen-1-yl)azetidine (11f)

^{1}H NMR (400 MHz, $CDCl_3$) and **^{13}C NMR** (100 MHz, $CDCl_3$)





6. Single Crystal X-Ray Diffraction Studies

Single crystals of compound **3a**, suitable for X-ray diffraction, were obtained by slow evaporation of a CH_2Cl_2/ MeOH mixture in a NMR Tube. The X-ray intensity data of **3a** were measured on a Bruker D8 Venture TXS system equipped with a multilayer mirror monochromator and a Mo Kα rotating anode X-ray tube (λ = 0.71073 Å). The frames were integrated with the Bruker SAINT software package.[4] Data were corrected for absorption effects using the Multi-Scan method (SADABS).[5] The structure was solved and refined using the Bruker SHELXTL Software Package.[6] All hydrogen atoms have been calculated in ideal geometry riding on their parent atoms. The figures have been drawn at the 25% ellipsoid probability level.[7]

[4] Bruker (2012). SAINT. Bruker AXS Inc., Madison, Wisconsin, USA.

[5] G. M. Sheldrick, *SADABS*. **1996**, University of Göttingen, Germany.

[6] G. M. Sheldrick, *Acta Cryst.* **2015,** *71*, 3-8.

[7] L. J. Farrugia, *J. Appl. Cryst.* **2012,** *45*, 849-854.

Table 1: Details for X-ray data collection and structure refinement for compound **3a**.

	3a
Net formula	$C_{16}H_{17}NO_2S$
M_r/g mol^{-1}	287.36
Crystal size/mm	0.120 × 0.090 × 0.030
T/K	173.(2)
Radiation	MoKα
Diffractometer	'Bruker D8 Venture TXS
Crystal system	monoclinic
Space group	'P 1 21/c 1'
a/Å	15.2425(6)
b/Å	8.2235(3)
c/Å	11.6263(5)
α/°	90
β/°	100.9660(10)
γ/°	90
V/Å^3	1430.71(10)
Z	4
Calc. density/g cm^{-3}	1.334
μ/mm^{-1}	0.227
Absorption correction	Multi-Scan
Transmission factor range	0.95–0.99
Refls. measured	24576
R_{int}	0.0373
Mean $\sigma(I)/I$	0.0222
θ range	3.053–27.485
Observed refls.	2849
x, *y* (weighting scheme)	0.0484, 0.7417
Hydrogen refinement	constr
Flack parameter	?
Refls in refinement	3266
Parameters	182
Restraints	0
$R(F_{obs})$	0.0403
$R_w(F^2)$	0.1083
S	1.063
Shift/error$_{max}$	0.001
Max electron density/e Å^{-3}	0.257
Min electron density/e Å^{-3}	−0.455

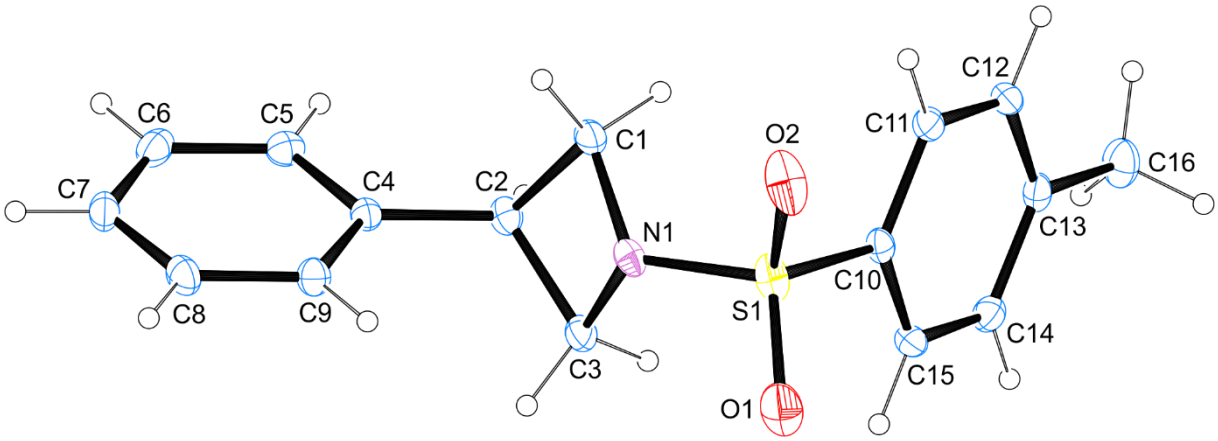


Figure 1: Molecular Structure of compound **3a** in the crystal. DIAMOND[8] representation; thermal ellipsoids are drawn at 25 % probability level.

Table 2: Selected bond lengths (Å) of compound **3a**.

S1-O1	1.4298(15)	C13-C14	1.394(2)
S1-O2	1.4332(14)	C13-C16	1.505(2)
S1-N1	1.6330(15)	C14-C15	1.380(2)
S1-C10	1.7582(15)	C1-H1AB	0.9900
N1-C1	1.488(2)	C1-H1A	0.9900
N1-C3	1.488(2)	C2-H2	1.0000
C1-C2	1.547(2)	C3-H3AB	0.9900
C2-C3	1.543(2)	C3-H3A	0.9900
C2-C4	1.506(2)	C5-H5	0.9500
C4-C5	1.389(2)	C6-H6	0.9500
C4-C9	1.392(2)	C7-H7	0.9500
C5-C6	1.391(2)	C8-H8	0.9500
C6-C7	1.377(2)	C9-H9	0.9500
C7-C8	1.383(3)	C11-H11	0.9500
C8-C9	1.392(2)	C12-H12	0.9500
C10-C11	1.390(2)	C14-H14	0.9500
C10-C15	1.391(2)	C15-H15	0.9500
C11-C12	1.382(2)	C16-H16A	0.9800
C12-C13	1.389(2)	C16-H16B	0.9800

[8] DIAMOND, Crystal Impact GbR., Version 3.2i

Table 3: Selected bond angles (°) of compound **3a**.

O1-S1-O2	120.65(10)	C12-C13-C16	120.95(14)
O1 -S1-N1	106.02(8)	C14-C13-C16	120.52(15)
O1 -S1-C10	107.92(8)	C13-C14-C15	120.84(15)
O2 -S1-N1	105.58(8)	C10-C15-C14	119.63(14)
O2-S1-C10	108.56(8)	N1-C1-H1AB	114.00
N1-S1-C10	107.45(7)	N1-C1-H1A	114.00
S1 -N1-C1	122.13(11)	C2-C1-H1AB	114.00
S1-N1-C3	122.26(11)	C2-C1-H1A	114.00
C1-N1-C3	91.33(12)	H1AB-C1-H1A	111.00
N1-C1-C2	88.65(12)	C1-C2-H2	112.00
C1-C2-C3	87.06(12)	C3-C2-H2	112.00
C1-C2-C4	115.91(12)	C4-C2-H2	112.00
C3-C2-C4	116.90(13)	N1-C3-H3AB	114.00
N1-C3-C2	88.77(12)	N1-C3-H3A	114.00
C2-C4-C5	119.34(14)	C2-C3-H3AB	114.00
C2-C4-C9	122.44(14)	C2-C3-H3A	114.00
C5-C4-C9	118.22(14)	H3AB-C3-H3A	111.00
C4-C5-C6	121.12(15)	C4-C5-H5	119.00
C5-C6-C7	120.04(16)	C6-C5-H5	119.00
C6-C7-C8	119.75(16)	C5-C6-H6	120.00
C7-C8-C9	120.18(16)	C7-C6-H6	120.00
C4-C9-C8	120.68(15)	C6-C7-H7	120.00
S1-C10-C11	120.07(12)	C8-C7-H7	120.00
S1-C10-C15	119.38(11)	C7-C8-H8	120.00
C11-C10-C15	120.43(14)	C9-C8-H8	120.00
C10-C11-C12	119.07(14)	C4-C9-H9	120.00
C11-C12-C13	121.49(14)	C8-C9-H9	120.00
C12-C13-C14	118.54(15)	C10-C11-H11	120.00

Table 4: Selected torsion angles (°) of compound **3a**.

O1-S1-N1-C1	-170.10(12)	C3-C2-C4-C9	28.8(2)
O1-S1-N1-C3	-54.71(14)	C1-C2-C4-C9	-71.67(19)
O2-S1-N1-C1	60.81(14)	C1-C2-C3-N1	15.12(11)
O2-S1-N1-C3	176.20(13)	C2-C4-C5-C6	178.17(15)
C10-S1-N1-C1	-54.91(13)	C9-C4-C5-C6	-1.6(2)
C10-S1-N1-C3	60.49(14)	C2-C4-C9-C8	-178.75(15)
O1-S1-C10-C11	-154.46(13)	C5-C4-C9-C8	1.0(2)
O1-S1-C10-C15	29.50(15)	C4-C5-C6-C7	0.9(3)
O2-S1-C10-C11	-22.11(15)	C5-C6-C7-C8	0.4(3)
O2-S1-C10-C15	161.85(13)	C6-C7-C8-C9	-1.0(3)
N1-S1-C10-C11	91.62(13)	C7-C8-C9-C4	0.3(2)
N1-S1-C10-C15	-84.43(13)	S1-C10-C11-C12	-175.64(12)
S1-N1-C1-C2	145.86(11)	C15-C10-C11-C12	0.4(2)
C3-N1-C1-C2	15.69(11)	S1-C10-C15-C14	175.20(12)
S1-N1-C3-C2	-145.81(11)	C11-C10-C15-C14	-0.8(2)
C1-N1-C3-C2	-15.73(11)	C10-C11-C12-C13	0.6(2)
N1-C1-C2-C3	-15.13(11)	C11-C12-C13-C14	-1.1(2)
N1-C1-C2-C4	103.46(14)	C11-C12-C13-C16	178.74(15)
C4-C2-C3-N1	-102.55(14)	C12-C13-C14-C15	0.6(2)
C1-C2-C4-C5	108.60(16)	C16-C13-C14-C15	-179.21(15)
C3-C2-C4-C5	-150.90(14)	C13-C14-C15-C10	0.4(2)