Supporting Information

Cobalt-Catalyzed α-Arylation of Substituted α-Halogeno-β-Lactams

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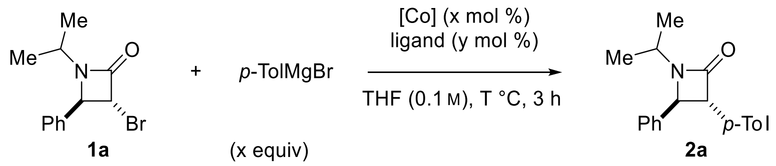
General remarks

NMR spectra were recorded on a Bruker Avance 400 as solutions at room temperature. Chemical shifts δ are expressed in parts per million (ppm) downfield from tetramethylsilane (TMS). References for ^{1}H NMR and ^{13}C NMR were the residual solvent peaks of chloroform (^{1}H: δ = 7.26 ppm)/ acetone (^{1}H: δ = 2.84 ppm) and d1-chloroform (^{13}C: δ = 77.16 ppm)/ d6-acetone (^{13}C: δ = 206.26 ppm). All coupling constants (*J*) are absolute values and are expressed in Hertz (Hz). The description of signals includes: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, hept = septet, m = multiplet, dd = doublet of doublets and ddd = double doublet of doublets and so forth. The spectra were analyzed according to first order. IR spectra were recorded on a FT-IR Bruker IFS 88 spectrometer. The compounds were measured as pure substances by ATR technique (ATR = attenuated total reflection). The position of the absorption band is given in wave numbers $\tilde{\nu}$ in cm^{-1}. Mass spectra were measured by EI-MS (electron impact mass spectrometry) and were recorded on a Finnigan MAT 95. The peaks are given as mass-to-charge-ratio (m/z). The molecule peak is given as $[M]^{+}$ and characteristic fragment peaks are given as $[M - \text{fragment}]^{+}$ or $[\text{fragment}]^{+}$. The signal intensities are given in percent, relatively to the intensity of the base signal (100%). For the high resolution mass, the following abbreviations were used: calc. = calculated data, found = measured data. Analytical thin layer chromatography (TLC) was carried out on Merck silica gel coated aluminum plates (silica gel 60, F254), detected under UV-light at λ = 254 nm or stained with "Seebach staining solution" (mixture of molybdato phosphoric acid, cerium(IV)-sulfate tetrahydrate, sulfuric acid and water) or basic potassium permanganate solution. Solvent mixtures are understood as volume/volume. Solvents, reagents and chemicals were purchased from Sigma-Aldrich, TCI and Alfa Aesar. All solvents, reagents and chemicals were used as purchased unless stated otherwise. THF, Et_2O, CH_2Cl_2 and PhMe were dried using a Mbraun SPS800 purification system. Air- or moisture-sensitive reactions were carried out under argon atmosphere in oven-dried and previously evacuated glassware. Liquids were transferred with plastic syringes and steel cannula. If not stated otherwise, crude products were purified by flash chromatography by the procedure of Still.[1] Silica gel 60 (Merck, 230-400) was used as stationary phase and as mobile phase.

Optimization Studies

Table S1. Optimization of the cobalt-catalyzed arylation of β-lactam **1a**.[a]

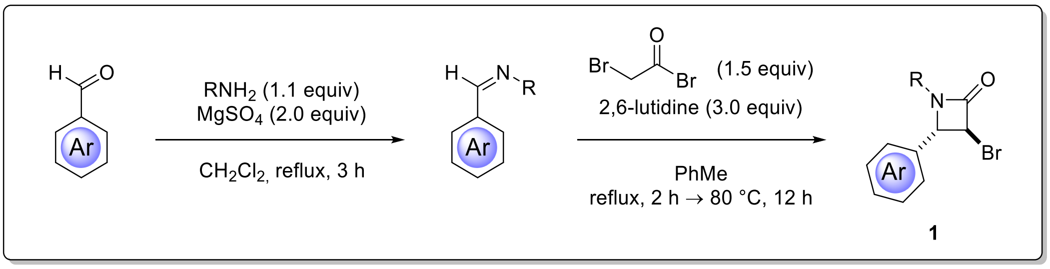


entry	[Co] (x mol %)	ligand (y mol %)	x equiv	T (°C)	yield (%)	Note
1[b]	$CoCl_2$ (10)	XantPhos (10)	2.0	0	34	
2[b]	$CoCl_2$ (10)	dppbz (10)	2.0	0	10	
3[b]	$CoCl_2$ (10)	dppe (10)	2.0	0	16	
4[b]	$CoCl_2$ (10)	PPh_3 (20)	2.0	0	13	
5[b]	$CoCl_2$ (10)	TMEDA (10)	2.0	0	68	
6[b]	$CoCl_2$ (10)	TMEDA (1.9 equiv)	2.0	0	72	
7[b]	CoF_2 (10)	TMEDA (10)	2.0	0	0	
8[b]	$CoBr_2$ (10)	TMEDA (10)	2.0	0	47	
9[b]	CoI_2 (10)	TMEDA (10)	2.0	0	45	
10[b]	$Co(acac)_2$ (10)	TMEDA (10)	2.0	0	41	
11[b]	$Co(OAc)_2$ (10)	TMEDA (10)	2.0	0	31	
12[b]	$CoCl_2$ (10)	TMCD (10)	2.0	0	66	
13[b]	$CoCl_2$ (10)	PyBox (10)	2.0	0	26	
14[b]	$CoCl_2$ (10)	bipy (10)	2.0	0	0	
15[b]	$CoCl_2$ (10)	--	2.0	0	20	
16[b]	$CoCl_2$ (10)	TMEDA (10)	2.0	25	69	Formation of dehalogenated byproducts observed
17[c]	$CoCl_2$ (10)	TMEDA (10)	1.5	0	32	+ LiCl (1.5 equiv)
18[c]	$CoCl_2$ (10)	TMEDA (10)	1.5	25	35	In 1,4-dioxane
19[c]	$CoCl_2$ (10)	TMEDA (10)	1.5	0	36	In PhMe
20[c]	$CoCl_2$ (10)	TMEDA (10)	1.5	0	56	In Et_2O
21[c]	$CoCl_2$ (10)	TMEDA (10)	1.5	- 20	67	
22[c]	$CoCl_2$ (10)	TMEDA (10)	1.5	- 50	48	

23[b]	--	--	2.0	0	0	
24[c]	--	TMEDA (10)	1.5	0	0	
25[c]	$CoCl_2$ (10)	TMEDA (10)	1.5	0	36	Using *p*-TolMgBr•LiCl
26[c, d]	$CoCl_2$ (10)	TMEDA (10)	1.5	0	76	
27[c, d]	$CoCl_2$ (5)	TMEDA (5)	1.5	0	82	
28[c, d]	**$CoCl_2$ (2)**	**TMEDA (2)**	**1.5**	**0**	**79**	
29[c, e]	$CoCl_2$ (2)	TMEDA (2)	1.5	0	73	
30[c, d, f]	$CoCl_2$ (2)	TMEDA (2)	1.5	0	52	

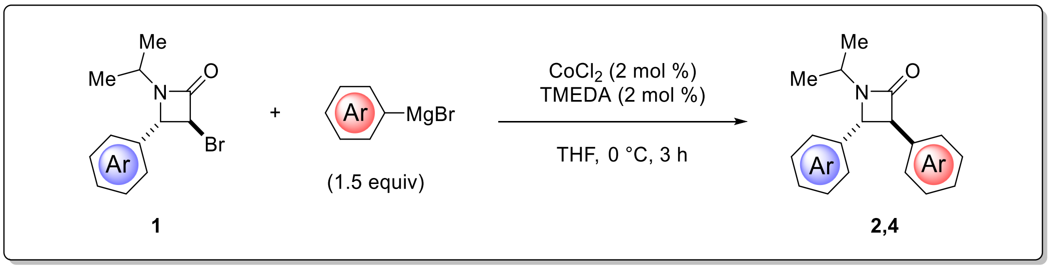
[a] Reaction conditions: **1a** (0.225 mmol), 3 h; yields of isolated products. [b] Manual addition of *p*-TolMgBr over 5 min. [c] Syringe pump addition of *p*-TolMgBr (2.4 mL/h). [d] **1a** (0.750 mmol), *p*-TolMgBr (1.50 equiv). [e] **1a** (2.00 mmol), *p*-TolMgBr (1.50 equiv). [f] Using (3,4-*trans*)-3-Chloro 1-*iso*propyl-4-phenylazetidin-2-one **1a'**.

General Procedure A: synthesis of (3,4-*trans)*-3-bromo-4-aryl-β-lactams 1.



Based on a reported procedure,[2] the arylaldehyde (10.0 mmol, 1.00 equiv), the alkylamine (11.0 mmol, 1.10 equiv) and $MgSO_4$ (2.40 g, 20.0 mmol, 2.00 equiv) were suspended in CH_2Cl_2 (20 mL) and refluxed for 3 hours. After cooling to room temperature, the mixture was filtered over Celite® (CH_2Cl_2) and the solvent was removed *in vacuo.* The imine was obtained in high quality according to the ^{1}H NMR spectrum and was used without further purification. The corresponding imine (10.0 mmol) was dissolved in PhMe (60 mL) and 2,6-lutidine (3.5 mL, 3.21 g, 30.0 mmol, 3.00 equiv) was added. The reaction mixture was heated to 120 °C and bromoacetyl bromide (1.2 mL, 1.69 g, 15.0 mmol, 1.50 equiv) was added dropwise. The reaction mixture was refluxed for 2 hours and then stirred at 80 °C overnight. The reaction was cooled to room temperature and then filtered over Celite® (CH_2Cl_2). The filtrate was washed with aqueous 1M HCl solution (220 mL) and brine (30 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*. The bromo β-lactam **1** was purified by flash column chromatography on silica gel (PE/EtOAc) followed by recrystallization (PE/CH_2Cl_2) or a second flash column chromatography on silica gel (PE/EtOAc).

General Procedure B: cobalt-catalyzed arylation of β-lactam 1.

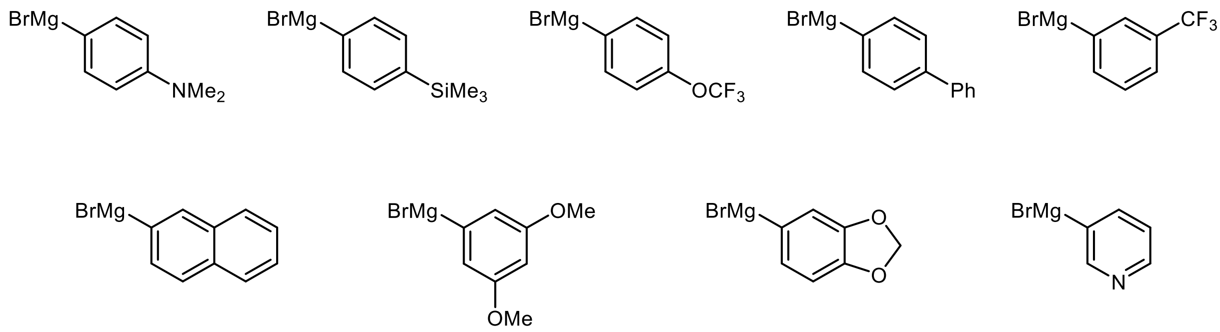


In a 25 mL round bottom flask, bromo β-lactam **1** (0.75 mmol, 1.00 equiv) was dissolved in THF (in total 0.1 M) under argon atmosphere and cooled to 0 °C. $CoCl_2$ (0.015 mmol, 0.30 mL of 0.05 M solution in THF, 2.0 mol %) and TMEDA (0.015 mmol, 0.30 mL of 0.05 M solution in THF, 2.0 mol %) were added. The Grignard reagent in THF (if not stated otherwise: 1.14 mmol, 1.50 equiv) was then added dropwise with a syringe pump (rates of addition were given). After stirring for 3 hours at 0 °C, the reaction was quenched with a saturated aqueous solution of NH_4Cl (0.30 mL) and extracted with CH_2Cl_2 (1×30 mL) and EtOAc (2×20 mL). The combined organic phases were washed with brine (20 mL) and dried over Na_2SO_4. After filtration the solvent was removed *in vacuo* and the crude product was purified *via* flash column chromatography on silica gel (*n*-pentane/EtOAc).

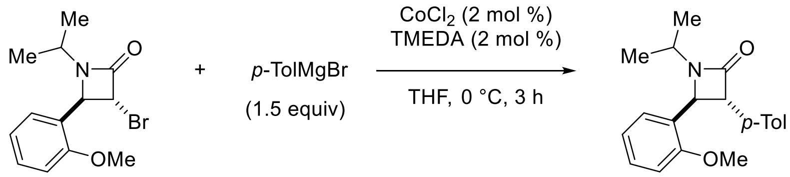
General Procedure for the synthesis of Grignard reagents

The commercially available Grignard reagents were purchased from Sigma Aldrich whereby the concentrations were determined by using Knochel's titration method[3] for organometallic magnesium reagents: *p*-tolylmagnesium bromide solution in THF, *p*-methoxyphenylmagnesium bromide solution in THF, *p*-fluorophenylmagnesium bromide solution in THF and *m*-methoxyphenylmagnesium bromide solution in THF.

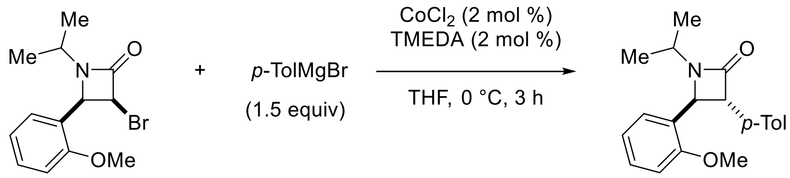
When not commercially available, the Grignard reagents were synthesized as follows:
A two-necked round bottom flask equipped with a reflux condenser was charged with magnesium (379 mg, 15.6 mmol, 1.30 equiv) under argon atmosphere. THF (2.0–4.0 mL) and 1,2-dibromoethane (0.10 mL, 225 mg, 1.2 mmol, 0.10 equiv) were added and the reaction mixture was heated to 60 °C for a couple of minutes in order to activate the magnesium. The aryl bromide (12.0 mmol, 1.00 equiv) dissolved in THF (10.0 mL) was added dropwise and the mixture was heated to 60 °C for 2–4 h. The concentration of the Grignard reagent in THF was determined by Knochel's titration method.[3]



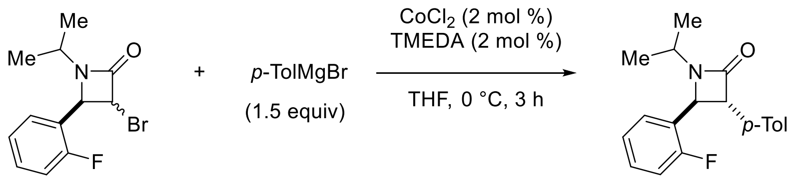
Reactions with (3,4-*cis)*-3-bromo-4-aryl-β-lactams 1



3,4-*trans*-**1j** **2j** (86%)

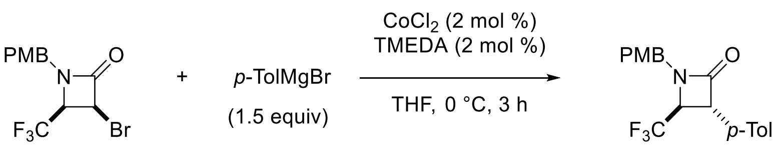


3,4-*cis*-**1j** **2j** (79%)



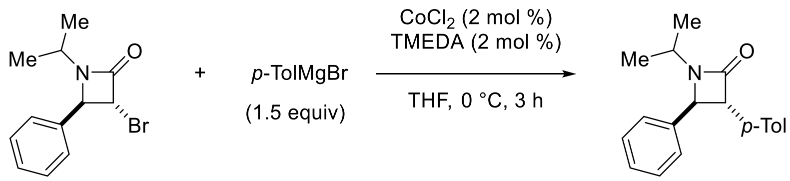
3,4-*cis/trans*-**1k**
(*cis*/*trans* = 1/4)

2k (82%)



3,4-*cis*-**7** **10** (70%)

Reaction on 2 mmol scale

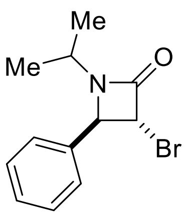


1a (2 mmol) **2a** (73%)

In a 50 mL round bottom flask, bromo β-lactam **1** (2.00 mmol, 1.00 equiv) was dissolved in THF (in total 0.1 M) under argon atmosphere and cooled to 0 °C. $CoCl_2$ (0.04 mmol, 0.80 mL of 0.05 M solution in THF, 2.0 mol %) and TMEDA (0.04 mmol, 0.80 mL of 0.05 M solution in THF, 2.0 mol %) were added. *p*-tolylmagnesium bromide (0.70 M in THF, 4.35 mL, 3.04 mmol, 1.52 equiv) was then added dropwise with a syringe pump (4.35 mL/h). After stirring for 3 hours at 0 °C, the reaction was quenched with a saturated aqueous solution of NH_4Cl (1.0 mL) and extracted with CH_2Cl_2 (1×50 mL) and EtOAc (2×40 mL). The combined organic phases were washed with brine (40 mL) and dried over Na_2SO_4. After filtration the solvent was removed *in vacuo*. After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2a** (407 mg, 1.45 mmol, 73%) was obtained as a colorless oil.

Synthesis and Characterization Data of Substrates 1

(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-phenylazetidin-2-one (1a):



Chemical Formula: $C_{12}H_{14}BrNO$
Molecular Weight: 268,15 g.mol^{-1}

Prepared according to the general procedure **A** using benzaldehyde (3.0 mL, 3.18 g, 30.0 mmol) and *iso*propylamine (2.8 mL, 1.95 g, 33.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) and recrystallisation (PE/CH_2Cl_2) yielded **1a** (6.99 g, 26.1 mmol, 87%) as a white solid.

m.p. (uncorrected) = 46 – 47 °C.

IR (ATR): $\tilde{\nu}$ = 2968, 2912, 1759, 1497, 1459, 1380, 1363, 1339, 1313, 1285, 1247, 1204, 1012, 928 cm^{-1}.

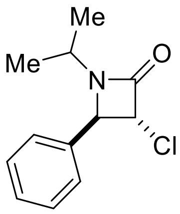
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 – 7.33 (m, 5H), 4.61 (d, J = 1.7 Hz, 1H), 4.49 (d, J = 1.7 Hz, 1H), 3.76 (hept, J = 6.8 Hz, 1H), 1.30 (d, J = 6.8 Hz, 3H), 1.06 (d, J = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.5, 136.9, 129.5, 129.3 (2C), 126.7 (2C), 65.2, 49.9, 46.2, 21.1, 20.1.

MS (+ESI) m/z (%) = 270 (^{81}Br)/ 268 (^{79}Br) (96:100) $[M+H]^+$.

HRMS (+ESI) m/z calcd for $C_{12}H_{15}BrNO$ (^{81}Br) $[M+H]^+$: 270.0311; found: 270.0311; calcd for $C_{12}H_{15}BrNO$ (^{79}Br) $[M+H]^+$: 268.0332; found: 268.0332.

(3,4-*trans*)-3-Chloro-1-isopropyl-4-phenylazetidin-2-one (1a'):



Chemical Formula: $C_{12}H_{14}ClNO$
Molecular Weight: 223,70 g.mol^{-1}

Prepared according to the general procedure **A** using benzaldehyde (1.0 mL, 10.0 mmol), *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol) and chloroacetyl chloride. Purification by flash column chromatography on silica gel (PE/EtOAc, 10:1) and recrystallisation (PE/CH_2Cl_2) yielded **1a'** (1.52 g, 6.80 mmol, 68%) as a white solid.

m.p. (uncorrected) = 39 °C.

IR (ATR): $\tilde{\nu}$ = 2969, 2912, 1762, 1498, 1459, 1384, 1363, 1263, 1252 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.36 (m, 3H), 7.39 – 7.32 (m, 2H), 4.51 (d, J = 1.8 Hz, 1H), 4.46 (d, J = 1.7 Hz, 1H), 3.74 (hept, J = 6.7 Hz, 1H), 1.31 (d, J = 6.8 Hz, 3H), 1.06 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.7, 136.7, 129.5, 129.3 (2C), 126.8 (2C), 65.2, 62.7, 46.0, 21.2, 20.2.

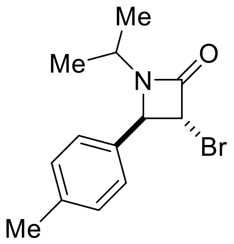
MS (+ESI) *m/z* (%) = 224 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{12}H_{15}ClNO$ $[M+H]^+$: 224.0837; found: 224.0387.

The analytical data match with those reported in the literature.[4]

However, contrary to the description in the literature, the β-lactam **1a'** was obtained as a solid and not as a yellow oil as reported.

(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-(*p*-tolyl)-azetidin-2-one (1b):

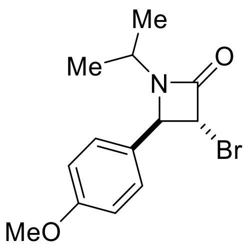


Chemical Formula: $C_{13}H_{16}BrNO$
Molecular Weight: 282,18 g.mol^{-1}

Prepared according to the general procedure **A** using *p*-tolylaldehyde (1.2 mL, 1.20 g, 10.0 mmol) and *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) yielded **1b** (1.77 g, 6.27 mmol, 63%) as a light yellow oil.

IR (ATR): $\tilde{\nu}$ = 2972, 2931, 1757, 1514, 1367, 1330, 1182 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 – 7.12 (m, 4H), 4.50 (d, J = 1.7 Hz, 1H), 4.39 (d, J = 1.7 Hz, 1H), 3.67 (hept, J = 6.7 Hz, 1H), 2.30 (s, 3H), 1.22 (d, J = 6.8 Hz, 3H), 0.98 (d, J = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.6, 139.5, 133.9, 129.9 (2C), 126.7 (2C), 65.0, 50.0, 46.1, 21.3, 21.1, 20.1.
MS (+ESI) *m/z* (%) = 567 (^{81,81}Br)/ 565(^{81,79}Br)/ 563 (^{79,79}Br) (30:100:34) [2M+H]$^+$.
HRMS (+ESI) *m/z* calcd for $C_{13}H_{17}BrNO$ (^{81}Br) [M+H]$^+$: 284.0468, found: 284.0467.; calcd for $C_{13}H_{17}BrNO$ (^{79}Br) [M+H]$^+$: 282.0488; found: 282.0488.

(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-(*p*-methoxyphenyl)azetidin-2-one (1c):



Chemical Formula: $C_{13}H_{16}BrNO_2$
Molecular Weight: 298,18 g.mol^{-1}

Prepared according to the general procedure **A** using *p*-methoxybenzaldehyde (1.36 g, 10.0 mmol) and *iso*propylamine (0.95 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 9:1) yielded **1c** (1.56 g, 5.23 mmol, 52%) as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2972, 1753, 1610, 1585, 1512, 1366, 1289, 1248, 1174, 1029 cm^{-1}.

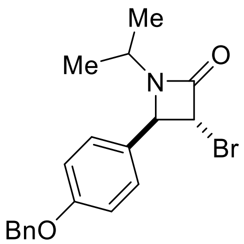
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (d, J = 8.6 Hz, 2H), 6.92 (d, J = 8.6 Hz, 2H), 4.55 (d, J = 1.8 Hz, 1H), 4.45 (d, J = 1.8 Hz, 1H), 3.82 (s, 3H), 3.73 (hept, J = 6.7 Hz, 1H), 1.27 (d, J = 6.7 Hz, 3H), 1.04 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.6, 160.5, 128.7, 128.0 (2C), 114.6 (2C), 64.8, 55.5, 50.0, 46.0, 21.2, 20.1.

MS (ESI) m/z (%) = 300 (^{81}Br)/ 298 (^{79}Br) (95:100) $[M+H]^+$.

HR-MS (ESI) m/z calcd for $C_{13}H_{17}BrNO_2$ (^{81}Br) $[M+H]^+$: 300.0417, found: 300.0412; calcd for $C_{13}H_{17}BrNO_2$ (^{79}Br) $[M+H]^+$: 298.0437, found: 298.0433.

(3,4-*trans*)-3-Bromo-4-(*p*-(benzyloxy)phenyl)-1-*iso*propylazetidin-2-one (1d):



Chemical Formula: $C_{19}H_{20}BrNO_2$
Molecular Weight: 374,28 $g.mol^{-1}$

Prepared according to the general procedure **A** using *p*-(benzyloxy)benzaldehyde (2.12 g, 10.0 mmol) and *iso*propylamine (0.95 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 9:1) and recrystallisation (PE/CH_2Cl_2) yielded **1d** (970 mg, 2.59 mmol, 26%) as a white solid.

m.p. (uncorrected): 100 – 101 °C.

IR (ATR): $\tilde{\nu}$ = 2978, 2930, 2900, 1759, 1610, 1583, 1511, 1467, 1454, 1394, 1373 1331, 1305, 1231, 1205, 1175, 1138, 1116, 1003, 937 cm^{-1}.

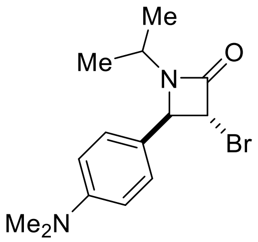
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 – 7.34 (m, 5H), 7.29 (d, J = 8.7 Hz, 2H), 7.00 (d, J = 8.7 Hz, 2H), 5.08 (s, 2H), 4.56 (d, J = 1.7 Hz, 1H), 4.45 (d, J = 1.7 Hz, 1H), 3.74 (hept, J = 6.7 Hz, 1H), 1.28 (d, J = 6.7 Hz, 3H), 1.05 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.6, 159.7, 136.7, 129.1, 128.8 (2C), 128.3, 128.1 (2C), 127.6 (2C), 115.6 (2C), 70.3, 64.8, 50.1, 46.1, 21.2, 20.2.

MS (ESI) m/z (%) = 751 (^{81,81}Br)/ 749 (^{81,79}Br)/ 747 (^{79,79}Br) (20:52:20) $[2M+H]^+$, 376 (^{81}Br)/ 374 (^{79}Br) (98:100) $[M+H]^+$.

HR-MS (ESI) m/z calcd for $C_{19}H_{21}BrNO_2$ (^{81}Br) $[M+H]^+$: 376.0730, found: 376.0728; calcd for $C_{19}H_{21}BrNO_2$ (^{79}Br) $[M+H]^+$: 374.0750, found: 374.0749.

(3,4-*trans*)-3-Bromo-4-[*p*-(N,N-dimethylamino)phenyl]-1-*iso*propylazetidin-2-one (1e):

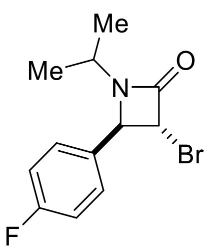


Chemical Formula: $C_{14}H_{19}BrN_2O$
Molecular Weight: 311,22 g.mol^{-1}

Prepared according to the general procedure **A** using *p*-(N,N-dimethylamino)benzaldehyde (1.22 mL, 1.49 g, 10.0 mmol) and *iso*propylamine (0.95 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 9:1) and recrystallisation (PE/CH_2Cl_2) yielded **1e** (1.44 g, 4.62 mmol, 46%) as a pale yellow solid.

m.p. (uncorrected): 84 – 85 °C.
IR (ATR): $\tilde{\nu}$ = 2997, 2800, 1747, 1612, 1524, 1448, 1390, 1355, 1289, 1243, 1229, 1195, 1124, 1060, 945 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18 (d, J = 8.8 Hz, 2H), 6.70 (d, J = 8.8 Hz, 2H), 4.52. (d, J = 1.8 Hz, 1H), 4.45 (d, J = 1.8 Hz, 1H), 3.71 (hept, J = 6.8 Hz, 1H), 2.96 (s, 6H), 1.27 (d, J = 6.8 Hz, 3H), 1.04 (d, J = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.6, 151.1, 127.7 (2C), 123.4, 112.4 (2C), 65.1, 50.1, 45.8, 40.4 (2C), 21.1, 20.0.
MS (+ESI) m/z (%) = 313 (^{81}Br)/ 311 (^{79}Br) (98:100) [M+H]$^+$.
HRMS (+ESI) m/z calcd for $C_{14}H_{20}BrN_2O$ (^{81}Br) [M+H]$^+$: 313.0733; found: 313.0733; calcd for $C_{14}H_{20}BrN_2O$ (^{79}Br) [M+H]$^+$: 311.0754; found: 311.0754.

(3,4-*trans*)-3-Bromo-4-(*p*-fluorophenyl)-1-*iso*propylazetidin-2-one (1f):



Chemical Formula: $C_{12}H_{13}BrFNO$
Molecular Weight: 286,14 g.mol^{-1}

Prepared according to the general procedure **A** using *p*-fluorobenzaldehyde (1.1 mL, 1.24 g, 10.0 mmol) and *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) and crystallization (PE/CH_2Cl_2) yielded **1f** (1.90 g, 6.63 mmol, 66%) as a white solid.

m.p. (uncorrected) = 50 – 51 °C.

IR (ATR): $\tilde{\nu}$ = 2973, 2932, 1758, 1601, 1513, 1422, 1377, 1366, 1248, 1221, 1147 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 – 7.29 (m, 2H), 7.10 (br t_{app}, J = 8.6 Hz, 2H), 4.59 (d, J = 1.9 Hz, 1H), 4.44 (d, J = 1.8 Hz, 1H), 3.74 (hept, J = 6.7 Hz, 1H), 1.28 (d, J = 6.8 Hz, 3H), 1.04 (d, J = 6.8 Hz, 3H).

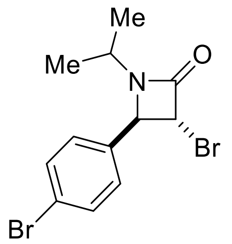
^{19}F NMR (376 MHz, $CDCl_3$): δ = -111.7.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.4, 163.3 (d, J = 249.2 Hz), 132.8 (d, J = 3.4 Hz), 128.5 (d, J = 8.4 Hz, 2C), 116.4 (d, J = 21.9 Hz, 2C), 64.4, 49.9, 46.2, 21.1, 20.2.

MS (+ESI) *m/z* (%) = 288 (^{81}Br)/ 286 (^{79}Br) (97:100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{12}H_{14}BrFNO$ (^{81}Br) $[M+H]^+$: 288.0217; found: 288.0219; calcd for $C_{12}H_{15}BrNO$ (^{79}Br) $[M+H]^+$: 286.0237; found: 286.0240.

(3,4-*trans*)-3-Bromo-4-(*p*-bromophenyl)-1-*iso*propylazetidin-2-one (1g):



Chemical Formula: $C_{12}H_{13}Br_2NO$
Molecular Weight: 347,05 g.mol^{-1}

Prepared according to the general procedure **A** using *p*-bromobenzaldehyde (1.85 g, 10.0 mmol) and *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) and crystallization (PE/CH_2Cl_2) yielded **1g** (2.00 g, 5.75 mmol, 58%) as a white solid.

m.p. (uncorrected) = 61 – 62 °C.

IR (ATR): $\tilde{\nu}$ = 3010, 1751, 1606, 1596, 1411, 1331, 1293, 1194, 1163, 1086, 1040 cm^{-1}.

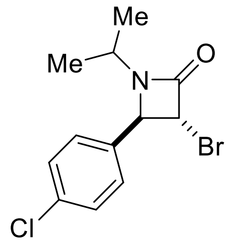
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.5 Hz, 2H), 4.58 (d, J = 1.7 Hz, 1H), 4.45 (d, J = 1.6 Hz, 1H), 3.77 (hept, J = 6.7 Hz, 1H), 1.30 (d, J = 6.7 Hz, 3H), 1.07 (d, J = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.4, 136.1, 132.5 (2C), 128.3 (2C), 123.5, 64.5, 49.7, 46.3, 21.2, 20.2.

MS (+ESI) *m/z* (%) = 349 (^{81,81}Br)/ 347 (^{79,81}Br)/ 345 (^{79,79}Br) (42:100:31) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{12}H_{14}Br_2NO$ (^{81,81}Br) $[M+H]^+$: 349.9396; found: 349.9396, calcd for $C_{12}H_{14}Br_2NO$ (^{79,81}Br) $[M+H]^+$: 347.9415; found: 347.9416, calcd for $C_{12}H_{14}Br_2NO$ (^{79,79}Br) $[M+H]^+$: 345.9437; found: 345.9438.

(3,4-*trans*)-3-Bromo-4-(*p*-chlorophenyl)-1-*iso*propylazetidin-2-one (1h):

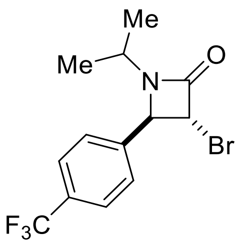


Chemical Formula: $C_{12}H_{13}BrClNO$
Molecular Weight: 302,60 g.mol^{-1}

Prepared according to the general procedure **A** using p-chlorobenzaldehyde (1.41 g, 10.0 mmol) and *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) and crystallization (PE/CH_2Cl_2) yielded **1h** (2.10 g, 6.96 mmol, 70%) as a slightly yellow oil.

IR (ATR): $\tilde{\nu}$ = 2973, 1757, 1491, 1414, 1320, 1088, 1011, 856, 833, 758 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 4.58 (d, *J* = 1.7 Hz, 1H), 4.43 (d, *J* = 1.6 Hz, 1H), 3.75 (hept, *J* = 6.8 Hz, 1H), 1.28 (d, *J* = 6.8 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.4, 135.6, 135.4, 129.6 (2C), 128.0 (2C), 64.5, 49.7, 46.3, 21.1, 20.2.
MS (+ESI) *m/z* (%) = 303 (^{81}Br)/ 301 (^{79}Br) (100:74) [M+H]$^+$.
HRMS (+ESI) *m/z* calcd for $C_{12}H_{14}BrClNO$ (^{81}Br) [M+H]$^+$: 303.9921; found: 303.9917; calcd for $C_{12}H_{14}BrClNO$ (^{79}Br) [M+H]$^+$: 301.9942; found: 301.9941.

(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-[*p*-(trifluoromethyl)phenyl]azetidin-2-one (1i):



Chemical Formula: $C_{13}H_{13}BrF_3NO$
Molecular Weight: 336,15 g.mol^{-1}

Prepared according to the general procedure **A** using *p*-(trifluoromethyl)benzaldehyde (1.4 mL, 1.74 g, 10.0 mmol) and *iso*propylamine (0.90 mL, 650 mg 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) and crystallization (PE/CH_2Cl_2) yielded **1i** (2.21 g, 6.57 mmol, 66%) as a white solid.

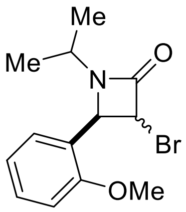
m.p. (uncorrected) = 63 – 65 °C.
IR (ATR): $\tilde{\nu}$ = 2973, 2929, 1766, 1741, 1621, 1425, 1321, 1158, 1110, 1066, 1015 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.1 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 4.66 (d, *J* = 1.8 Hz, 1H), 4.45 (d, *J* = 1.8 Hz, 1H), 3.77 (hept, *J* = 6.7 Hz, 1H), 1.29 (d, *J* = 6.8 Hz, 3H), 1.06 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.3, 141.1, 131.7 (q, J = 32.8 Hz), 127.1 (2C), 126.3 (q, J = 3.8 Hz, 2C), 123.8 (q, J = 272.3 Hz), 64.4, 49.6, 46.5, 21.1, 20.2.

MS (+ESI) *m/z* (%) = 338 (^{81}Br)/ 336 (^{79}Br) (96:100) $[M+H]^+$.

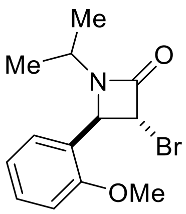
HRMS (+ESI) *m/z* calcd for $C_{13}H_{14}BrF_3NO$ (^{81}Br) $[M+H]^+$: 338.0185; found: 338.0185; calcd for $C_{13}H_{14}BrF_3NO$ (^{79}Br) $[M+H]^+$: 336.0205; found: 336.0206.

(3,4-*trans*)- and (3,4-*cis*)-3-Bromo-1-*iso*propyl-4-(*o*-methoxyphenyl)azetidin-2-one (1j):



Prepared according to the general procedure **A** using *o*-methoxybenzaldehyde (1.21 mL, 1.36 g, 10.0 mmol) and *iso*propylamine (0.95 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 9:1) and recrystallisation (PE/CH_2Cl_2) yielded *trans*-**1j** (1.25 g, 4.20 mmol, 42%) as a white solid and *cis*-**1j** (686 mg, 2.30 mmol, 23%) as a white solid.

- **(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-(*o*-methoxyphenyl)azetidin-2-one (*trans*-1j):**



Chemical Formula: $C_{13}H_{16}BrNO_2$
Molecular Weight: 298,18 g.mol^{-1}

m.p. (uncorrected) = 77 – 78 °C.

IR (ATR): $\tilde{\nu}$ = 2970, 1754, 1600, 1587, 1494, 1464, 1437, 1381, 1366, 1289, 1249, 1195, 1165, 1153, 1049, 1024 cm^{-1}.

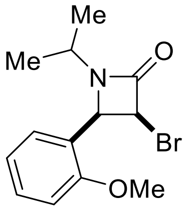
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (ddd, J = 8.3, 7.4, 1.7 Hz, 1H), 7.28 (dd, J = 7.4, 1.7 Hz, 1H), 6.98 (t_{app}, J = 7.5, 1.1 Hz, 1H), 6.92 (dd, J = 8.3, 1.1 Hz, 1H), 4.92 (d, J = 1.7 Hz, 1H), 4.72 (d, J = 1.7 Hz, 1H), 3.87 (s, 3H), 3.73 (hept, J = 6.7 Hz, 1H), 1.29 (d, J = 6.7 Hz, 3H), 1.03 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.9, 158.0, 130.5, 128.5, 124.5, 120.9, 111.2, 61.1, 55.6, 48.8, 46.0, 20.7, 20.0.

MS (ESI) m/z (%) = 599 (^{81,81}Br)/ 597 (^{81,79}Br)/ 595 (^{79,79}Br) (10/20:10) $[2M+H]^+$, 300 (^{81}Br)/ 298 (^{79}Br) (98:100) $[M+H]^{+.}$

HR-MS (ESI) m/z calcd for $C_{13}H_{17}BrNO_2$ (^{81}Br) $[M+H]^+$: 300.0417, found: 300.0413; calcd for $C_{13}H_{17}BrNO_2$ (^{79}Br) $[M+H]^+$: 298.0437, found: 298.0435.

- **(3,4-*cis*)-3-Bromo-1-*iso*propyl-4-(*o*-methoxyphenyl)azetidin-2-one (*cis*-1j):**



Chemical Formula: $C_{13}H_{16}BrNO_2$
Molecular Weight: 298,18 g.mol^{-1}

m.p. (uncorrected) = 98 – 99 °C.

IR (ATR): $\tilde{\nu}$ = 2980, 1746, 1602, 1590, 1491, 1466, 1443, 1404, 1382, 1367, 1327, 1300, 1242, 1200, 1185, 1110, 1047, 1021, 949 cm^{-1}.

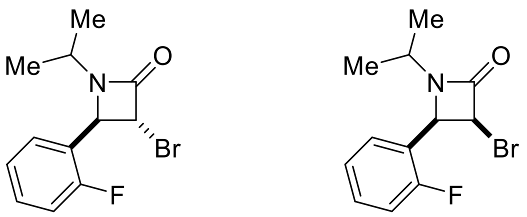
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (ddd, J = 8.3, 7.4, 1.7 Hz, 1H), 7.28 (dd, J = 7.4, 1.7 Hz, 1H), 6.98 (t_{app}, J = 7.5, 1.1 Hz, 1H), 6.92 (dd, J = 8.3, 1.1 Hz, 1H), 5.37 (d, J = 4.9 Hz, 1H), 5.14 (d, J = 4.9 Hz, 1H), 3.87 (s, 3H), 3.73 (hept, J = 6.7 Hz, 1H), 1.41 (d, J = 6.7 Hz, 3H), 1.21 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.7, 157.5, 129.8, 127.8, 124.0, 120.1, 110.5, 55.6, 53.6, 50.2, 46.7, 21.1, 20.4.

MS (ESI) m/z (%) = 599 (^{81,81}Br)/ 597 (^{81,79}Br)/ 595 (^{79,79}Br) (20:50:20) $[2M+H]^+$, 300 (^{81}Br)/ 298 (^{79}Br) (98:100) $[M+H]^{+.}$

HR-MS (ESI) m/z calcd for $C_{13}H_{17}BrNO_2$ (^{81}Br) $[M+H]^+$: 300.0417, found: 300.0412; calcd for $C_{13}H_{17}BrNO_2$ (^{79}Br) $[M+H]^+$: 298.0437, found: 298.0434.

(3,4-*trans*)- and (3,4-*cis*)-3-Bromo-4-(*o*-fluorophenyl)-1-*iso*propyl-azetidin-2-one (1k):



Chemical Formula: $C_{12}H_{13}BrFNO$
Molecular Weight: 286,14 g.mol^{-1}

Prepared according to the general procedure **A** using *o*-fluorobenzaldehyde (1.1 mL, 1.24 g, 10.0 mmol, 1.00 equiv) and *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) yielded ***trans*-1k** and ***cis*-1k** (1.23 g, 7.45 mmol, 75%) as inseparable mixture (*cis*/*trans* = 1:4) as a light yellow oil.

IR (ATR): $\tilde{\nu}$ = 2973, 2932, 1759, 1490, 1457, 1368, 1318, 1238, 1221 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$, [*cis*,*trans*]): δ = 7.41 – 7.32 (m, 2H), 7.25 – 7.18 (m, 1H), 7.14 – 7.06 (m, 1H), 5.32 [(d, *J* = 5.1 Hz, 0.2H), 4.89 (d, *J* = 1.8 Hz, 0.8H)], 5.17 [(d, *J* = 5.1 Hz, 1H), 4.65 (d, *J* = 1.7 Hz, 1H)], 3.77 (hept, *J* = 6.6 Hz, 1H), [1.38 (d, *J* = 6.8 Hz, 0.6H), 1.29 (d, *J* = 6.8 Hz, 2.4H)], [1.17 (d, *J* = 6.7 Hz, 0.6H), 1.05 (d, *J* = 6.7 Hz, 2.4H)].

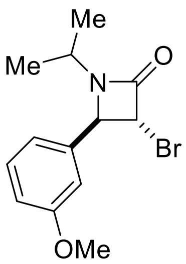
^{19}F NMR (376 MHz, $CDCl_3$): δ = -118.4.

^{13}C NMR (101 MHz, $CDCl_3$, [*cis*,*trans*]): δ = [163.9, 163.2], [161.0 (d, *J* = 247.8 Hz), 160.9 (d, *J* = 249.2 Hz)], [131.0 (d, *J* = 8.4 Hz), 130.5 (d, *J* = 8.5 Hz)], [128.9 (d, *J* = 3.1 Hz), 128.2 (d, *J* = 3.7 Hz)], [123.8 (d, *J* = 3.5 Hz), 124.8 (d, *J* = 3.8 Hz)], [123.9, 123.8], [115.6 (d, *J* = 21.2 Hz), 116.3 (d, *J* = 21.3 Hz)], [52.3 (d, *J* = 5.2 Hz), 58.9 (d, *J* = 3.4 Hz)], [49.4, 48.6 (d, *J* = 2.3 Hz)], [46.5, 46.0], [20.9, 20.7], [20.2, 20.0].

MS (+ESI) *m/z* (%) = 288 (^{81}Br)/ 286 (^{79}Br) (96:100) [M+H]$^+$.

HRMS (+ESI) *m/z* calcd for $C_{12}H_{14}BrFNO$ (^{81}Br) [M+H]$^+$: 288.0215; found:288.0217; calcd for $C_{12}H_{14}BrFNO$ (^{79}Br) [M+H]$^+$: 286.0236; found:286.0236.

(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-(*m*-methoxypheny)-azetidin-2-one (1l):



Chemical Formula: $C_{13}H_{16}BrNO_2$
Molecular Weight: 298,18 g.mol^{-1}

Prepared according to the general procedure **A** using *m*-methoxybenzaldehyde (1.1 mL, 1.23 g, 10.0 mmol) and *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) and crystallization (PE/CH_2Cl_2) yielded **1l** (1.89 g, 6.36 mmol, 64%) as a slightly yellow solid.

m.p. (uncorrected) = 51 – 52 °C.

IR (ATR): $\tilde{\nu}$ = 1750, 1602, 1491, 1466, 1329, 1291, 1260, 1161, 1038 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (t_{app}, *J* = 7.9 Hz, 1H,), 6.96 – 6.89 (m, 2H), 6.87 (m, 1H), 4.56 (d, *J* = 1.7 Hz, 1H), 4.47 (d, *J* = 1.7 Hz, 1H), 3.81 (s, 3H), 3.74 (hept, *J* = 6.8 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 6.7 Hz, 3H).

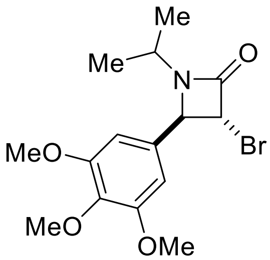
^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.5, 160.3, 138.6, 130.4, 118.9, 114.8, 112.2, 65.1, 55.5, 49.8, 46.3, 21.1, 20.1.

MS (+ESI) *m/z* (%) = 300 (^{81}Br)/ 298 (^{79}Br) (98:100) [M+H]$^+$.

HRMS (+ESI) *m/z* calcd for $C_{13}H_{17}BrNO_2$ (^{81}Br) [M+H]$^+$: 300.0417; found: 300.0416; calcd for $C_{13}H_{17}BrNO_2$

(^{79}Br) [M+H]$^+$: 298.0437; found: 298.0437.

(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-(3ˈ,4ˈ,5ˈ–trimethoxyphenyl)azetidin-2-one (1m):

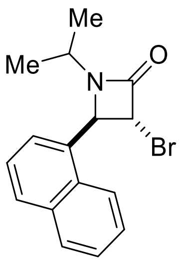


Chemical Formula: $C_{15}H_{20}BrNO_4$
Molecular Weight: 358,23 g.mol^{-1}

Prepared according to the general procedure **A** using 3ˈ,4ˈ,5ˈ–trimethoxybenzaldehyde (1.96 g, 10.0 mmol) and *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) and crystallization (PE/CH_2Cl_2) yielded **1m** (1.94 g, 5.42 mmol, 54%) as a white solid.

m.p. (uncorrected) = 124 – 125 °C.
IR (ATR): $\tilde{\nu}$ = 2974, 2936, 1752, 1591, 1506, 1459 1420, 1349, 1320, 1234 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.55 (s, 2H), 4.53 (d, *J* = 1.7 Hz, 1H), 4.46 (d, *J* = 1.6 Hz, 1H), 3.87 (s, 6H), 3.85 (s, 3H), 3.77 (hept, *J* = 6.8 Hz, 1H), 1.32 (d, *J* = 6.8 Hz, 3H), 1.12 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.7, 154.0 (2C), 132.5, 103.3 (2C), 65.5, 61.0, 56.4 (3C), 49.9, 46.3, 21.2, 20.2.
MS (+ESI) *m/z* (%) = 719 (^{81,81}Br)/ 717 (^{81,79}Br)/ 715 (^{79,79}Br) (22:66:24) [2M+H], 360 (^{81}Br)/ 358 (^{79}Br) (96:100) [M+H], 278 (68).
HRMS (+ESI) *m/z* calcd for $C_{15}H_{21}BrNO_4$ [M+H]$^+$: 358.0648/360.0628; found: 358.0645/360.0623.

(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-(naphth-1ˈ-yl)-azetidin-2-one (1n):



Chemical Formula: $C_{16}H_{16}BrNO$
Molecular Weight: 318,21 g.mol^{-1}

Prepared according to the general procedure **A** using 1-naphthaldehyde (1.36 mL, 1.56 g, 10.0 mmol.) and *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol). Purification by multiple flash column chromatography on silica gel (PE/EtOAc = 20:1 → 10:1) yielded **1n** (1.93 g, 6.09 mmol, 61%) as a light yellow oil.

IR (ATR): $\tilde{\nu}$ = 2971, 1756, 1510, 1456, 1384, 1330, 1310, 1217 1185 cm^{-1}.

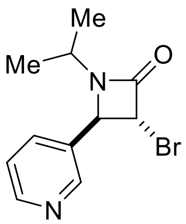
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (br d, J = 8.2 Hz, 1H), 7.93 (br td, J = 8.4 Hz, 1H), 7.87 (d, J = 7.9 Hz, 1H), 7.68 – 7.47 (m, 4H), 5.44 (d, J = 1.7 Hz, 1H), 4.47 (d, J = 1.9 Hz, 1H), 3.79 (hept, J = 6.7 Hz, 1H), 1.48 (d, J = 6.8 Hz, 3H), 1.22 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.1, 133.9, 132.9, 130.7, 129.4, 129.2, 127.2, 126.4, 125.4, 123.1, 122.7, 61.7, 49.8, 47.1, 20.8, 20.3.

MS (+ESI) *m/z* (%) = 320 (^{81}Br)/ 318 (^{79}Br) (56:60) [M+H]$^+$.

HRMS (+ESI) *m/z* calcd for $C_{16}H_{17}BrNO$ (^{81}Br) [M+H]$^+$: 320.0468; found: 320.0468; calcd for $C_{16}H_{17}BrNO$ (^{79}Br) [M+H]$^+$: 318.0488; found: 318.0489.

(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-(pyridin-3'-yl)azetidin-2-one (1o):



Chemical Formula: $C_{11}H_{13}BrN_2O$
Molecular Weight: 269,14 g.mol^{-1}

Prepared according to the general procedure **A** using 3-pyridinecarboxaldehyde (0.94 mL, 1.07 g, 10.0 mmol) and *iso*propylamine (0.95 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc/CH_2Cl_2 = 4:1:0 → 4:4:1) and recrystallisation (PE/CH_2Cl_2) yielded **1o** (431 mg, 1.60 mmol, 16%) as a pale yellow solid.

m.p. (uncorrected) = 112 – 113 °C.

IR (ATR): $\tilde{\nu}$ = 2976, 1746, 1598, 1577, 1482, 1435, 1380, 1369, 1330, 1256, 1224, 1183, 1028 cm^{-1}.

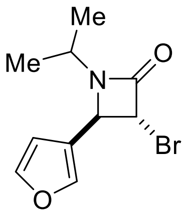
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.66 – 8.62 (m, 2H), 7.69 (dt, J = 7.9, 2.0 Hz, 1H), 7.36 (dd$_{app}$, J = 7.9, 4.8 Hz, 1H), 4.63 (d, J = 1.8 Hz, 1H), 4.49 (d, J = 1.8 Hz, 1H), 3.76 (hept, J = 6.7 Hz, 1H), 1.28 (d, J = 6.7 Hz, 3H), 1.05 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.1, 151.0, 148.6, 133.9, 132.7, 124.1, 62.7, 49.5, 46.4, 21.2, 20.2.

MS (ESI) m/z (%) = 271 (^{81}Br)/ 269 (^{79}Br) (100/96) [M+H]$^+$.

HR-MS (ESI) m/z calcd for $C_{11}H_{14}BrN_2O$ (^{81}Br) [M+H]$^+$: 271.0264, found: 271.0262; calcd for $C_{11}H_{14}BrN_2O$ (^{79}Br) [M+H]$^+$: 269.0284, found: 269.0283.

(3,4-*trans*)-3-Bromo-4-(furan-3ˈ-yl)-1-*iso*propylazetidin-2-one (1p):

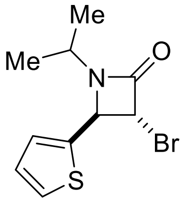


Chemical Formula: $C_{10}H_{12}BrNO_2$
Molecular Weight: 258,12 g.mol^{-1}

Prepared according to the general procedure **A** using 3-furaldehyde (0.86 mL, 961 mg, 10.0 mmol) and *iso*propylamine (0.90 mL, 650 mg, 11.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 9:1) and recrystallisation (PE/CH_2Cl_2) yielded **1p** (1.50 g, 5.81 mmol, 58%) as a white solid.

m.p. (uncorrected) = 68 – 69 °C.
IR (ATR): $\tilde{\nu}$ = 3115, 3071, 2982, 2972, 1746, 1593, 1504, 1464, 1390, 1350, 1335, 1225, 1185, 1159, 1150, 1048, 1026, 978 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (br t$_{app}$, J = 1.2 Hz, 1H), 7.47 (br t$_{app}$, J = 1.7 Hz, 1H), 6.40 (br dd, J = 2.1, 0.9 Hz, 1H), 4.61. (d, J = 1.8 Hz, 1H), 4.51 (d, J = 1.8 Hz, 1H), 3.76 (hept, J = 6.7 Hz, 1H), 1.28 (d, J = 6.7 Hz, 3H), 1.11 (d, J = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): = δ 163.0, 144.8, 141.2, 122.4, 107.9, 56.9, 48.9, 45.9, 21.2, 20.1.
MS (+ESI) m/z (%) = 260 (^{81}Br)/ 258 (^{79}Br) (98:100) [M+H]$^+$.
HRMS (+ESI) m/z calcd for $C_{10}H_{13}BrNO_2$ (^{81}Br) [M+H]$^+$: 260.0104; found: 260.0104; calcd for $C_{10}H_{13}BrNO_2$ (^{79}Br) [M+H]$^+$: 258.0124; found: 258.0125.

(3,4-*trans*)-3-Bromo-1-*iso*propyl-4-(thiophen-2ˈ-yl)azetidin-2-one (1q):



Chemical Formula: $C_{10}H_{12}BrNOS$
Molecular Weight: 274,18 g.mol^{-1}

Prepared according to the general procedure **A** using 2-thiophenecarboxaldehyde (0.93 mL, 1.12 g, 10.0 mmol) and *iso*propylamine (2.6 mL, 1.88 g, 30.0 mmol, 3.00 equiv) and refluxing overnight. Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) and crystallization (PE/CH_2Cl_2) yielded **1q** (2.06 g, 7.50 mmol, 75%) as a white solid.

m.p. (uncorrected) = 33 – 35 °C.
IR (ATR): $\tilde{\nu}$ = 3010, 1759, 1375, 1365, 1341, 1309, 1247, 1198, 1180, 1125 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.37 (m, 1H), 7.14 (br dd, J = 3.5, 1.3 Hz, 1H), 7.02 (dd, J = 5.1, 3.5 Hz, 1H), 4.88 (d, J = 1.7 Hz, 1H), 4.58 (d, J = 1.7 Hz, 1H), 3.74 (hept, J = 6.7 Hz, 1H), 1.32 (d, J = 6.8 Hz, 3H), 1.12 (d, J = 6.7 Hz, 3H).

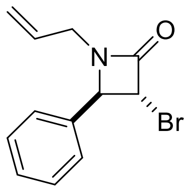
^{13}C NMR (101 MHz, CDCl$_3$): δ = 162.9, 140.6, 127.5, 127.0, 126.7, 60.5, 50.4, 46.3, 20.9, 20.0.

MS (+ESI) *m/z* (%) = 276 (^{81}Br)/ 274 (^{79}Br) (98:100) [M+H]$^+$.

HRMS (+ESI) *m/z* calcd for (^{81}Br) $C_{10}H_{13}BrNOS$ [M+H]$^+$: 275.9875; found: 275.9879; calcd for (^{79}Br) $C_{10}H_{13}BrNOS$ [M+H]$^+$: 273.9896; found: 273.9897.

Synthesis and Characterization Data of Substrates 5, 6 and 7

(3,4-*trans*)-1-Allyl-3-bromo-4-phenylazetidin-2-one (5):



Chemical Formula: $C_{12}H_{12}BrNO$
Molecular Weight: 266,14 g.mol^{-1}

Prepared according to the general procedure **A** using benzaldehyde (3.0 mL, 3.18 g, 30.0 mmol), MgSO$_4$ (7.22 g, 60.0 mmol) and allylamine (2.5 mL, 1.88 g, 33.0 mmol). Purification by two flash column chromatography on silica gel (PE/EtOAc = 20:1 → 10:1) yielded **5** (5.22 g, 19.7 mmol, 66%) as a light yellow oil.

IR (ATR): $\tilde{\nu}$ = 2984, 2914, 1762, 1456, 1387, 1203 cm^{-1}.

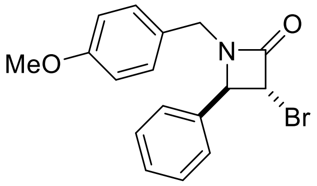
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.38 – 7.28 (m, 3H), 7.25 – 7.20 (m, 2H), 5.72 – 5.59 (m, 1H), 5.11 (dq$_{app}$, J = 10.2, 1.2 Hz, 1H), 5.04 (dq$_{app}$, J = 17.0, 1.3 Hz, 1H), 4.58 (d, J = 1.8 Hz, 1H), 4.46 (dd, J = 1.8, 0.7 Hz, 1H), 4.12 (ddt$_{app}$, J_{AB} = 15.6, 5.1, 1.6 Hz, 1H), 3.31 (ddq$_{app}$, J_{AB} = 15.6, 7.2, 1.0 Hz, 1H).

^{13}C NMR (101 MHz, CDCl$_3$): δ = 163.5, 135.2, 130.3, 129.5, 129.3 (2C), 126.5 (2C), 119.4, 65.6, 50.1, 43.6.

MS (+ESI) *m/z* (%) = 268 (^{81}Br)/ 266 (^{79}Br) (98:100) [M+H]$^+$.

HRMS (+ESI) *m/z* calcd for $C_{12}H_{13}BrNO$ (^{81}Br) [M+H]$^+$: 268.0155; found: 268.0154; calcd for $C_{12}H_{13}BrNO$ (^{79}Br) [M+H]$^+$: 266.0175; found: 266.0155.

(3,4-*trans*)-3-Bromo-1-(*p*-methoxybenzyl)-4-phenylazetidin-2-one (6):

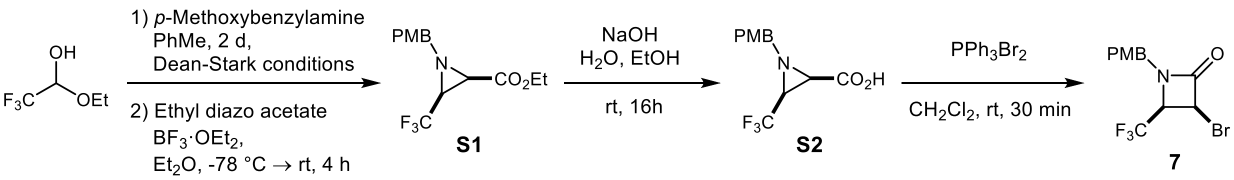


Chemical Formula: $C_{17}H_{16}BrNO_2$
Molecular Weight: 346,22 g.mol^{-1}

Prepared according to the general procedure **A** using benzaldehyde (4.0 mL, 4.24 g, 40.0 mmol) and *p*-methoxybenzylamine (5.75 mL, 6.04 g, 44.0 mmol). Purification by flash column chromatography on silica gel (PE/EtOAc = 10:1) yielded **6** (8.04 g, 23.2 mmol, 58%) as a slightly yellow oil.

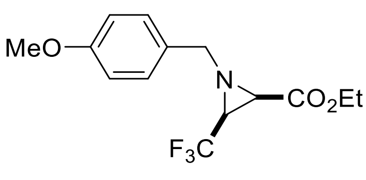
IR (ATR): $\tilde{\nu}$ = 2911, 2834, 1755, 1609, 1584, 1510, 1456, 1388, 1355, 1243, 1174, 1101, 1028, 911 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 – 7.39 (m, 3H), 7.25 – 7.23 (m, 2H), 7.04 (d, J = 8.6 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 4.80 (d, J_{AB} = 14.9 Hz, 1H), 4.55 (br dd, J = 1.8, 0.9 Hz, 1H), 4.43 (d, J = 1.8 Hz, 1H), 3.79 (s, 3H), 3.76 (d, J_{AB} = 14.9 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.6, 159.4, 135.2, 129.9 (2C), 129.5, 129.3 (2C), 126.7 (2C), 126.3, 114.3 (2C), 65.1, 55.4, 50.3, 44.7.
MS (+ESI) m/z (%) = 370 (^{81}Br)/ 368 (^{79}Br) (98:100) [M+Na]$^+$.
HRMS (+ESI) m/z calcd for $C_{17}H_{16}BrNO_2Na$ (^{81}Br) [M+H]$^+$: 370.0236; found: 370.0236; calcd for $C_{17}H_{16}BrNO_2Na$ (^{79}Br) [M+H]$^+$: 368.0257; found: 368.0257.

Synthesis of Substrate 7



Scheme S1: Synthesis of (3,4-*cis*)-3-bromo-1-(*p*-methoxybenzyl)-4-(trifluoromethyl)azetidin-2-one **7**.[5]

***cis*-1-(*p*-Methoxybenzyl)-3-trifluoromethyl-aziridine-2-ethyl ester (S1):**



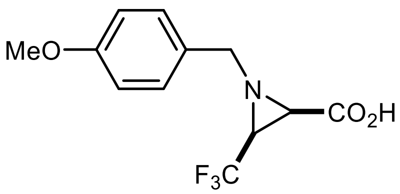
Chemical Formula: $C_{14}H_{16}F_3NO_3$
Molecular Weight: 303,28 g.mol^{-1}

According to a known procedure,[6] 1-ethoxy-2,2,2-trifluoroethanol (1.6 mL, 1.95 g, 13.6 mmol, 1.26 equiv) and *p*-methoxybenzylamine (1.4 mL, 1.49 g, 10.8 mmol, 1.00 equiv) were dissolved in PhMe (36 mL) and refluxed for 2 d under Dean-Stark conditions. After evaporation of the solvent, the corresponding imine was obtained in high purity (>95% based on ^{1}H NMR spectrum). Following the literature[5], the aldimine was dissolved in Et_2O (45 mL) and cooled to -78 °C. Boron trifluoride diethyl etherate (133 µL, 153 mg, 1.08 mmol, 0.1 equiv) was added followed by dropwise addition of ethyl diazoacetate (1.4 mL, 1.48 g, 13.0 mmol, 1.20 equiv). The reaction was stirred for 4 h at rt and was then quenched with an aqueous saturated $NaHCO_3$ solution and extracted with CH_2Cl_2 (3x 50 mL). The combined organic layers were washed with H_2O and brine. After phase separation, the organic phase was dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Purification by column chromatography on silica gel (PE/EtOAc = 10/1 → 3/1) yielded **S1** as a white solid (2.64 g, 8.70 mmol, 81%).

m.p. (uncorrected) = 74 – 75 °C.
IR (ATR): $\tilde{\nu}$ = 3675, 2988, 2971, 1745, 1613, 1512, 1400, 1303, 1289, 1218, 1141, 1096, 1033 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, J = 8.6 Hz, 2H), 6.91 – 6.84 (m, 2H), 4.36 – 4.15 (m, 2H), 3.80 (s, 3H), 3.76 (d, J_{AB} = 13.4 Hz, 1H), 3.69 (d, J_{AB} = 13.4 Hz, 1H), 2.53 (d, J = 6.6 Hz, 1H), 2.46 – 2.35 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H).
^{19}F NMR (376 MHz, $CDCl_3$): δ = -67.0.
^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.2, 159.3, 129.8 (2C), 127.3, 123.3 (q, J = 274.6 Hz), 114.0 (2C), 61.7, 61.3, 55.3, 42.0 (q, J = 40.6 Hz), 40.8, 13.9.

Analytical data match with those reported in the literature.[5]

***cis*-1-(*p*-Methoxybenzyl)-3-trifluoromethyl-aziridine-2-carboxylic acid (S2)**:



Chemical Formula: $C_{12}H_{12}F_3NO_3$
Molecular Weight: 275,23 $g.mol^{-1}$

According to a known procedure,[5] aziridine **S1** (2.64 g, 8.70 mmol, 1.00 equiv) was dissolved in EtOH (57 mL) and a 2 M aqueous solution of NaOH (43 mL, 87.0 mmol, 10.0 equiv) was added. The resulting solution was stirred overnight at rt before the solvent was removed *in vacuo*. Then, a 1 M aqueous solution of HCl was added until pH = 1 – 2. The white precipitate was dissolved in EtOAc (50 mL) and washed with H_2O and brine. The organic phase was dried over Na_2SO_4, filtered and the solvent was evaporated. The title compound **S2** was obtained without further purification as a white solid (2.21 g, 8.04 mmol, 92%).

m.p. (uncorrected) = 116 °C.

IR (ATR): $\tilde{\nu}$ = 3674, 2960, 2900, 1744, 1514, 1373, 1258, 1177, 1115, 1104, 1090 cm^{-1}.

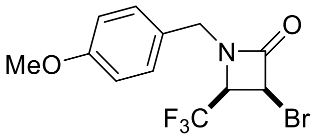
^{1}H NMR (400 MHz, acetone-d_6): δ = 11.0 (br m, 1H), 7.27 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 3.69 (s, 3H), 3.68 (d, J_{AB} = 13.2 Hz, 1H), 3.54 (d, J_{AB} = 13.2 Hz, 1H), 2.85 – 2.78 (m, 2H).

^{19}F NMR (376 MHz, acetone-d_6): δ = -67.9.

^{13}C NMR (101 MHz, acetone-d_6): δ = 167.4, 160.1, 130.4 (2C), 130.1, 124.9 (q, J = 272.3 Hz), 114.5 (2C), 61.9, 55.5, 43.1 (q, J = 39.8 Hz), 42.1.

Analytical data match with those reported in the literature.[5]

(3,4-*cis*)-3-Bromo-1-(*p*-methoxybenzyl)-4-(trifluoromethyl)azetidin-2-one (7):



Chemical Formula: $C_{12}H_{11}BrF_3NO_2$
Molecular Weight: 338,12 $g.mol^{-1}$

According to a known procedure,[5] the aziridine carboxylic acid **S2** (2.10 g, 7.63 mmol, 1.00 equiv) was suspended in CH_2Cl_2 (40 mL) and triphenylphosphine dibromide (3.22 g, 7.63 mmol, 1.00 equiv) in CH_2Cl_2 (25 mL) was added to the suspension. The reaction was stirred at rt. After 30 min, the reaction was quenched with an aqueous solution of $Na_2S_2O_4$ and the product was extracted with CH_2Cl_2 (2×15 mL). The combined organic layers were washed with H_2O and brine. After separation of the phases, the organic phase was dried over Na_2SO_4, filtered and the solvent was removed. Purification by column chromatography on silica gel (PE/EtOAc = 4:1) yielded **7** as white solid (2.00 g, 5.92 mmol, 78%).

m.p. (uncorrected) = 92 – 93 °C.

IR (ATR): $\tilde{\nu}$ = 3012, 2941, 2844, 1758, 1725, 1514, 1443, 1403, 1376, 1352, 1281, 1209, 1180, 1127, 1112, 1029, 948 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 4.94 (d, J = 5.1 Hz, 1H), 4.83 (d, J_{AB} = 14.9 Hz, 1H), 4.05 (p_{app}, J = 6.0 Hz, 1H), 3.95 (d, J_{AB} = 4.9 Hz, 1H), 3.80 (s, 3H).

^{19}F NMR (376 MHz, $CDCl_3$): δ = -69.1.

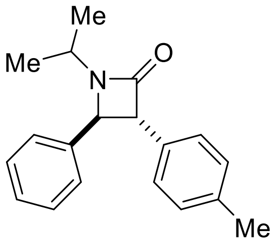
^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.4, 159.9, 130.1 (2C), 125.6, 123.2 (q, J = 280.5 Hz), 114.6 (2C), 55.4, 54.7 (q, J = 33.6 Hz), 45.9, 41.0.

HRMS (+ESI) *m/z* calcd for $C_{12}H_{12}BrF_3NO_2$ (^{81}Br) $[M+H]^+$: 339.9978; found: 339.9977; calcd for $C_{12}H_{12}BrF_3NO_2$ (^{79}Br) $[M+H]^+$: 337.9998; found: 337.9997.

Analytical and spectroscopical data match with those reported in the literature.[5]

Characterization Data of Products 2 and 4

(3,4-*trans*)-1-*iso*Propyl-4-phenyl-3-(*p*-tolyl)azetidin-2-one (2a):

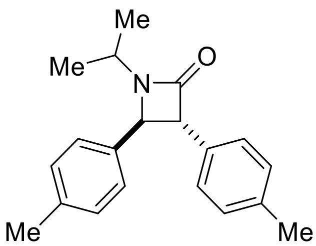


Chemical Formula: $C_{19}H_{21}NO$
Molecular Weight: 279,38 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2a** (166 mg, 0.593 mmol, 79%) was obtained as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2971, 1744, 1514, 1454, 1381, 1364, 1225, 1021, 910 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.34 (m, 5H), 7.17 (s, 4H), 4.47 (d, J = 2.3 Hz, 1H), 4.08 (d, J = 2.3 Hz, 1H), 3.88 (hept, J = 6.8 Hz, 1H), 2.35 (s, 3H), 1.36 (d, J = 6.8 Hz, 3H), 1.10 (d, J = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.5, 139.2, 137.2, 132.4, 129.6 (2C), 129.0 (2C), 128.5, 127.2 (2C), 126.6 (2C), 64.0, 63.0, 45.2, 21.3, 21.1, 20.7.
MS (+ESI) m/z (%) = 581 (48) $[2M+Na]^+$, 559 (100) $[2M+H]^+$.
HRMS (+ESI) m/z calcd for $C_{19}H_{22}NO$ $[M+H]^+$: 280.1696, found: 280.1686.

(3,4-*trans*)-1-*iso*Propyl-3,4-di-(*p*-tolyl)azetidin-2-one (2b):



Chemical Formula: $C_{20}H_{23}NO$
Molecular Weight: 293,41 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1b** (212 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2b** (162 mg, 0.551 mmol, 73%) was obtained as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2970, 2920, 1742, 1514, 1380, 1365, 1321, 1043, 1016, 822, 787 cm^{-1}.

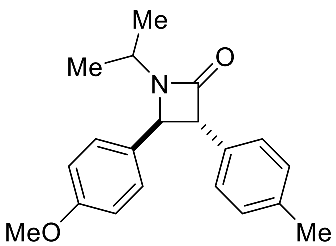
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 – 7.28 (m, 2H), 7.25 (d, J = 7.7 Hz, 2H), 7.24 – 7.15 (m, 4H), 4.46 (d, J = 2.3 Hz, 1H), 4.08 (d, J = 2.3 Hz, 1H), 3.90 (hept, J = 6.7 Hz, 1H), 2.42 (s, 3H), 2.38 (s, 3H), 1.39 (d, J = 6.8 Hz, 3H), 1.12 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.7, 138.5, 137.3, 136.3, 132.6, 129.7 (2C), 129.7 (2C), 127.4 (2C), 126.7 (2C), 64.0, 63.0, 45.2, 21.5, 21.3, 21.3, 20.8.

MS (+ESI) *m/z* (%) = 587 (24) [2M+H], 294 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{20}H_{24}NO$ $[M+H]^+$: 294.1852; found: 294.1852.

(3,4-*trans*)-1-*iso*Propyl-4-(*p*-methoxyphenyl)-3-(*p*-tolyl)azetidin-2-one (2c):



Chemical Formula: $C_{20}H_{23}NO_2$
Molecular Weight: 309,41 $g.mol^{-1}$

According to the general procedure **B**, bromo lactam **1c** (224 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1 → 6:1), **2c** (186 mg, 0.601 mmol, 80%) was obtained as a white solid.

m.p. (uncorrected) = 45 – 46 °C.

IR (ATR): $\tilde{\nu}$ = 2968, 2928, 1723, 1612, 1586, 1512, 1460, 1438, 1397, 1366, 1307, 1239, 1197, 1037, 1008, 968 cm^{-1}.

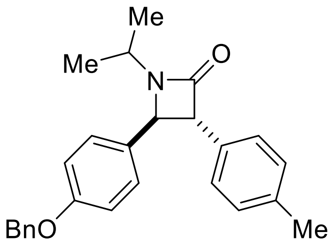
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (br d, J = 8.7 Hz, 2H), 7.15 (s, 4H), 6.92 (br d, J = 8.7 Hz, 2H), 4.40 (d, J = 2.2 Hz, 1H), 4.03 (d, J = 2.2 Hz, 1H), 3.89 (hept, J = 6.7 Hz, 1H), 3.85 (s, 3H), 2.33 (s, 3H), 1.33 (d, J = 6.7 Hz, 3H), 1.07 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 159.9, 137.3, 132.6, 131.2, 129.7 (2C), 127.9 (2C), 127.4 (2C), 114.4 (2C), 64.0, 62.8, 55.5, 45.1, 21.5, 21.3, 20.8.

MS (+ESI) m/z (%) = 619 (15) $[2M+H]^+$, 310 (100) $[M+H]^+$.

HRMS (+ESI) m/z calcd for $C_{20}H_{24}NO_2$ $[M+H]^+$: 310.1802; found: 310.1801.

(3,4-*trans*)-4-[*p*-(Benzyloxy)phenyl]-1-*iso*propyl-3-(*p*-tolyl)azetidin-2-one (2d):

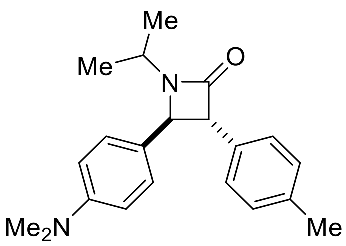


Chemical Formula: $C_{26}H_{27}NO_2$
Molecular Weight: 385,51 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1d** (281 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1 → 6:1), **2d** (210 mg, 0.551 mmol, 73%) was obtained as a white solid.

m.p. (uncorrected): 103 – 104 °C.
IR (ATR): $\tilde{\nu}$ = 2965, 2917, 1737, 1610, 1582, 1510, 1454, 1379, 1360, 1233, 1173, 1142, 1110 1004 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.35 (m, 5H), 7.33 (br d, J = 8.7 Hz, 2H), 7.15 (s, 4H), 7.01 (d, J = 8.7 Hz, 2H), 5.09 (s, 2H), 4.41 (d, J = 2.2 Hz, 1H), 4.04 (d, J = 2.2 Hz, 1H), 3.85 (hept, J = 6.8 Hz, 1H), 2.34 (s, 3H), 1.34 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 159.1, 137.3, 136.9, 132.6, 131.5, 129.7 (2C), 128.8 (2C), 128.2, 128.0 (2C), 127.6 (2C), 127.4 (2C), 115.3 (2C), 70.2, 64.0, 62.8, 45.1, 21.5, 21.3, 20.8.
MS (+ESI) m/z (%) = 386 (100) [M+H]$^+$.
HRMS (+ESI) m/z calcd for $C_{26}H_{28}NO_2$ [M+H]$^+$: 386.2115; found: 386.2116.

(3,4-*trans*)-4-(*p*-(Dimethylamino)phenyl)-1-*iso*propyl-3-(*p*-tolyl)azetidin-2-one (2e):



Chemical Formula: $C_{21}H_{26}N_2O$
Molecular Weight: 322,45 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1e** (233 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1 → 5:1), **2e** (150 mg, 0.470 mmol, 62%) was obtained as a pale yellow solid.

m.p. (uncorrected): 77 – 78 °C.

IR (ATR): $\tilde{\nu}$ = 2973, 2898, 1735, 1611, 1527, 1394, 1360, 1228, 1201, 1187, 1166, 1140, 1043, 1020, 946 cm^{-1}.

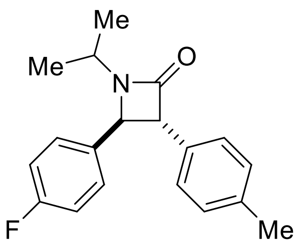
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (d, J = 8.7 Hz, 2H), 7.15 (s, 4H), 6.73 (d, J = 8.7 Hz, 2H), 4.36 (d, J = 2.2 Hz, 1H), 4.05 (d, J = 2.2 Hz, 1H), 3.83 (hept, J = 6.8 Hz, 1H), 2.98 (s, 6H), 2.34 (s, 3H), 1.34 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.8, 150.8, 137.1, 132.9, 129.6 (2C), 127.8 (2C), 127.4 (2C), 126.3, 112.6 (2C), 63.9, 63.1, 45.0, 40.6 (2C), 21.5, 21.3, 20.8.

MS (+ESI) m/z (%) = 323 (100) [M+H]$^+$.

HRMS (+ESI) m/z calcd for $C_{21}H_{27}NO_2$ [M+H]$^+$: 323.2118; found: 323.2117.

(3,4-*trans*)-4-(*p*-Fluorophenyl)-1-*iso*propyl-3-(*p*-tolyl)azetidin-2-one (2f):



Chemical Formula: $C_{19}H_{20}FNO$
Molecular Weight: 297,37 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1f** (214 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2f** (143 mg, 0.480 mmol, 64%) was obtained as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2971, 2923, 1742, 1602, 1508, 1381, 1366, 1321, 1227, 1155 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 – 7.35 (m, 2H), 7.18 – 7.06 (m, 6H), 4.44 (d, J = 2.2 Hz, 1H), 4.02 (d, J = 2.2 Hz, 1H), 3.86 (hept, J = 6.8 Hz, 1H), 2.34 (s, 3H), 1.34 (d, J = 6.8 Hz, 3H), 1.07 (d, J = 6.8 Hz, 3H).

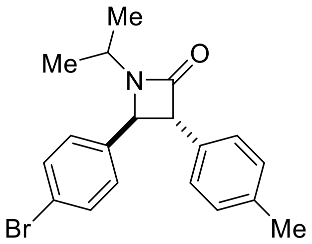
^{19}F NMR (376 MHz, $CDCl_3$): δ = -113.2.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.5, 162.9 (d, J = 247.4 Hz), 137.5, 135.2 (d, J = 3.1 Hz), 132.2, 129.7 (2C), 128.3 (d, J = 8.3 Hz, 2C), 127.3 (2C), 116.1 (d, J = 21.9 Hz, 2C), 64.3, 62.4, 45.3, 21.5, 21.3, 20.8.

MS (+ESI) *m/z* (%) = 595 (8) [2M+H], 298 (100) [M+H]$^+$.

HRMS (+ESI) *m/z* calcd for $C_{19}H_{21}FNO$ [M+H]$^+$: 298.1602; found: 298.1601.

(3,4-*trans*)-4-(*p*-Bromophenyl)-1-*iso*propyl-3-(*p*-tolyl)azetidin-2-one (2g):



Chemical Formula: $C_{19}H_{20}BrNO$
Molecular Weight: 358,28 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1g** (260 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2g** was obtained in an inseparable mixture with **2g'** and **2a** as colorless oil (201 mg).

The yields of the products **2g**, **2g'** and **2a** were determined by ^{1}H NMR spectroscopy:

Yield: 65% (calcd)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 4.52 (d, *J* = 2.3 Hz, 1H), 4.11 (d, *J* = 2.2 Hz, 1H), 3.97 (hept, *J* = 6.8 Hz, 1H), 2.44 (s, 3H), 1.44 (d, *J* = 6.8 Hz, 3H), 1.19 (d, *J* = 6.7 Hz, 3H).

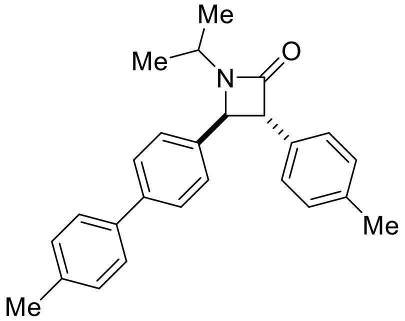
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.3, 138.4, 137.5, 132.2 (2C), 132.0, 129.7 (2C), 128.2 (2C), 127.2 (2C), 122.4, 64.1, 62.4, 45.3, 21.4, 21.1, 20.7.

MS (LC-MS, +ESI) *m/z* (%) = 719 (^{81,81}Br)/ 717 (^{81,79}Br)/ 715 (^{79,79}Br) (53:100:53) [2M+H], 399/401 (88:88), 360 (^{81}Br)/ 358 (^{79}Br) (92:92) $[M+H]^+$.

HRMS (LC-MS, +ESI) *m/z* calcd for $C_{19}H_{21}BrNO$ $[M+H]^+$: 360.0781; found: 360.0791.

Minor products 2g' and 2a:

(3,4-*trans*)-1-*iso*Propyl-4-[*p*-methyl-(1,1ˈ-biphenyl)-4-yl]-3-(*p*-tolyl)azetidin-2-one 2g':



Chemical Formula: $C_{26}H_{27}NO$
Molecular Weight: 369,51 g.mol^{-1}

Yield: 10% (calcd)

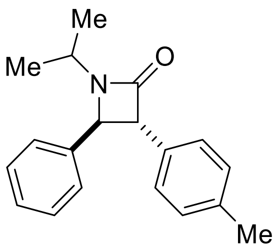
Only the aliphatic signals of the side product **2g'** in the ^{1}H NMR spectrum were given.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.56 (d, J = 2.2 Hz, 1H), 4.17 (d, J = 2.3 Hz, 1H), 3.97 (hept, J = 6.8 Hz, 1H), 2.44 (s, 3H), 1.45 (d, J = 6.7 Hz, 3H), (d, J = 6.7 Hz, 3H).

MS (LC-MS, +ESI) *m/z* (%) = 761 (35), 535 (36), 433 (100), 370 (55) $[M+H]^+$.

HRMS (LC-MS, +ESI) *m/z* calcd for $C_{26}H_{28}NO$ $[M+H]^+$: 370.2165; found: 370.2166.

(3,4-*trans*)-1-*iso*Propyl-4-phenyl-3-(*p*-tolyl)azetidin-2-one (2a):



Chemical Formula: $C_{19}H_{21}NO$
Molecular Weight: 279,38 g.mol^{-1}

Yield: 3.9% (calcd)

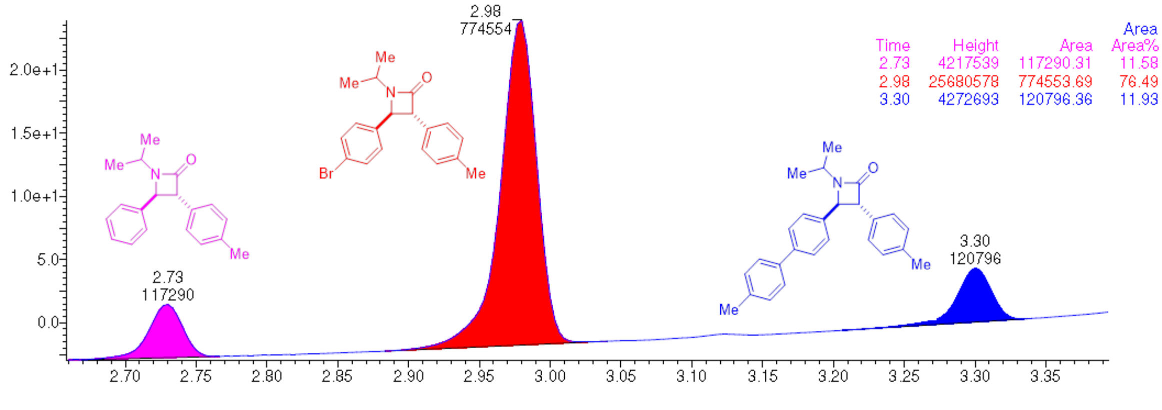
Only the aliphatic signals of the side product **2a** in the ^{1}H NMR spectrum were given.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.60 (d, J = 2.2 Hz, 1H), 4.20 (d, J = 2.2 Hz, 1H), 3.97 (hept, J = 6.8 Hz, 1H), 2.50 (s, 3H), 1.48 (d, J = 6.8 Hz, 3H), 1.23 (d, J = 6.7 Hz, 3H).

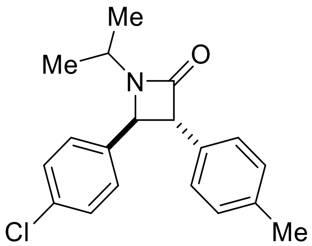
MS (LC-MS, +ESI) *m/z* (%) = 581 [2M+Na]559 [2M+H]343 (82), 280 (100) $[M+H]^+$.

HRMS (LC-MS, +ESI) *m/z* calcd for $C_{19}H_{22}NO$ $[M+H]^+$: 280.1696; found: 280.1705.

Chromatogram of the LC-MS analysis:



(3,4-*trans*)-4-(*p*-Chlorophenyl)-1-*iso*propyl-3-(*p*-tolyl)azetidin-2-one (2h):

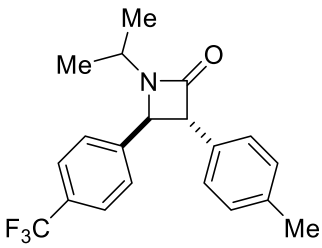


Chemical Formula: $C_{19}H_{20}ClNO$
Molecular Weight: 313,83 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1h** (227 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2h** (186 mg, 0.592 mmol, 79%) was obtained as a white oil.

IR (ATR): $\tilde{\nu}$ = 2971, 2921, 1743, 1541, 1490, 1380, 1330, 1088, 1011 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 4.42 (d, *J* = 2.2 Hz, 1H), 4.01 (d, *J* = 2.2 Hz, 1H), 3.87 (hept, *J* = 6.7 Hz, 1H), 2.34 (s, 3H), 1.34 (d, *J* = 6.7 Hz, 3H), 1.08 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.4, 138.0, 137.6, 134.4, 132.1, 129.7 (2C), 129.3 (2C), 128.0 (2C), 127.3 (2C), 64.2, 62.4, 45.3, 21.4, 21.2, 20.8.
MS (+ESI) *m/z* (%) = 627 (6) [2M+H]370 (12), 314 (100) $[M+H]^+$.
HRMS (+ESI) *m/z* calcd for $C_{19}H_{21}ClNO$ $[M+H]^+$: 314.1306; found: 314.1307.

(3,4-*trans*)-1-*iso*Propyl-3-(*p*-tolyl)-4-[*p*-(trifluoromethyl)phenyl]azetidin-2-one (2i):



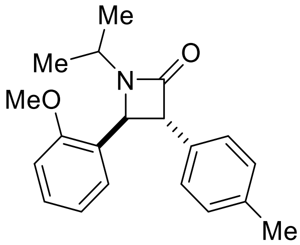
Chemical Formula: $C_{20}H_{20}F_3NO$
Molecular Weight: 347,38 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1i** (252 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.3 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.7 mL, 1.28 mmol, 1.71 equiv) was added with a syringe pump (2.7 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2i** (170 mg, 0.488 mmol, 65%) was obtained as a white oil.

IR (ATR): $\tilde{\nu}$ = 2973, 2929, 1745, 1618, 1515, 1423, 1321, 1162, 1121, 1109, 1066, 1015 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 4.51 (d, *J* = 2.2 Hz, 1H), 4.03 (d, *J* = 2.2 Hz, 1H), 3.89 (hept, *J* = 6.7 Hz, 1H), 2.35 (s, 3H), 1.36 (d, *J* = 6.7 Hz, 3H), 1.10 (d, *J* = 6.7 Hz, 3H).
^{19}F NMR (376 MHz, $CDCl_3$): δ = -62.6.
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.4, 143.7, 137.7, 131.9, 130.9 (q, *J* = 32.5 Hz), 129.8 (2C), 127.3 (2C), 126.9 (2C), 126.15 (q, *J* = 3.8 Hz, 2C), 125.4 (q, *J* = 272.3 Hz), 64.4, 62.5, 45.5, 21.5, 21.3, 20.9.
MS (+ESI) *m/z* (%) = 695 (2) [2M+H], 348 (100) $[M+H]^+$.
HRMS (+ESI) *m/z* calcd for $C_{20}H_{21}F_3NO$ $[M+H]^+$: 348.1570; found: 348.1570.

(3,4-*trans*)-1-*iso*Propyl-4-(*o*-methoxyphenyl)-3-(*p*-tolyl)azetidin-2-one (2j):



Chemical Formula: $C_{20}H_{23}NO_2$
Molecular Weight: 309,41 g.mol^{-1}

- From *trans*-**1j**

According to the general procedure **B**, bromo lactam *trans*-**1j** (224 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1 ⟶ 6:1), **2j** (199 mg, 0.643 mmol, 86%) was obtained as a pale yellow solid.

- From *cis*-**1j**

According to the general procedure **B**, bromo lactam *cis*-**1j** (224 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1 → 6:1), **2j** (184 mg, 0.594 mmol, 79%) was obtained as a pale yellow solid.

m.p. (uncorrected): 101 – 102 °C.
IR (ATR): $\tilde{\nu}$ = 2970, 1740, 1600, 1587, 1514, 1491, 1463, 1438, 1381, 1364, 1320, 1286, 1243, 1173, 1160, 1110, 1048, 1024 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.31 (ddd, *J* = 8.2, 7.5, 1.8 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.00 (ddd, *J* = 8.3, 7.5, 1.1 Hz, 1H), 6.91 (dd, *J* = 8.3, 1.1 Hz, 1H),

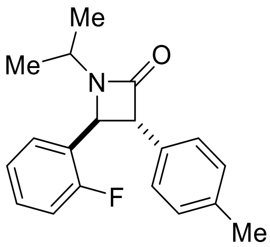
4.90 (d, J = 2.2 Hz, 1H), 4.16 (d, J = 2.2 Hz, 1H), 3.89 (hept, J = 6.7 Hz, 1H), 3.79 (s, 3H), 2.34 (s, 3H), 1.35 (d, J = 6.7 Hz, 3H), 1.07 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.9, 157.7, 136.9, 133.1, 129.5 (2C), 129.4, 127.7, 127.5 (2C), 127.2, 120.9, 110.9, 62.2, 57.2, 55.5, 45.3, 21.3, 21.1, 20.7.

MS (+ESI) m/z (%) = 619 (100) $[2M+H]^+$, 310 (40) $[M+H]^+$.

HRMS (+ESI) m/z calcd for $C_{20}H_{24}NO_2$ $[M+H]^+$: 310.1802; found: 310.1801.

(3,4-*trans*)-4-(*o*-Fluorophenyl)-1-*iso*propyl-3-(*p*-tolyl)azetidin-2-one (2k):



Chemical Formula: $C_{19}H_{20}FNO$
Molecular Weight: 297,37 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1k** (214 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2k** (183 mg, 0.615 mmol, 82%) was obtained as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2970, 2922, 1745, 1588, 1514, 1489, 1456, 1382, 1366, 1320 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (td$_{app}$, J = 7.5, 1.8 Hz, 1H), 7.39 – 7.28 (m, 1H), 7.24 – 7.13 (m, 5H), 7.09 (ddd, J = 10.5, 8.2, 1.2 Hz, 1H), 4.83 (d, J = 2.3 Hz, 1H), 4.18 (d, J = 2.3 Hz, 1H), 3.86 (hept, J = 6.7 Hz, 1H), 2.34 (s, 3H), 1.35 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 6.8 Hz, 3H).

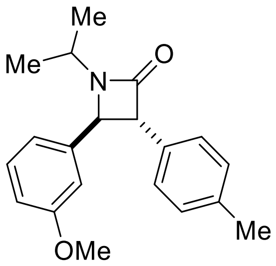
^{19}F NMR (376 MHz, $CDCl_3$): δ = -119.1.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.4, 160.9 (d, J = 247.9 Hz), 137.4, 132.2, 130.1 (d, J = 8.3 Hz), 129.7 (2C), 128.1 (d, J = 3.8 Hz), 127.3 (2C), 126.3 (d, J = 12.2 Hz), 124.8 (d, J = 3.6 Hz), 116.1 (d, J = 21.4 Hz), 62.8 (d, J = 3.3 Hz), 55.8 (d, J = 3.3 Hz), 45.3, 21.3, 21.2, 20.7.

MS (+ESI) *m/z* (%) = 595 (15) [2M+H], 298 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{19}H_{21}FNO$ $[M+H]^+$: 298.1602; found: 298.1602.

(3,4-*trans*)-1-*iso*Propyl-4-(*m*-methoxyphenyl)-3-(*p*-tolyl)azetidin-2-one (2l):

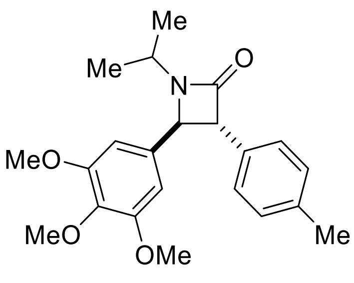


Chemical Formula: $C_{20}H_{23}NO_2$
Molecular Weight: 309,41 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1l** (223 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2l** (196 mg, 0.632 mmol, 84%) was obtained as a white solid.

m.p. (uncorrected) = 122 – 123 °C.
IR (ATR): $\tilde{\nu}$ = 2966, 2929, 1721, 1597, 1514, 1489, 1466, 1436, 1399, 1259, 1215, 1163, 1036 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (t_{app}, J = 7.9 Hz, 1H), 7.15 – 7.13 (m, 4H), 7.01 – 6.85 (m, 3H), 4.41 (d, J = 2.2 Hz, 1H), 4.05 (d, J = 2.2 Hz, 1H), 3.91 – 3.84 (m, 1H), 3.82 (s, 3H), 2.34 (s, 3H), 1.35 (d, J = 6.8 Hz, 3H), 1.10 (d, J = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.5, 160.1, 141.0, 137.3, 132.4, 130.0, 129.6 (2C), 127.3 (2C), 118.9, 113.9, 111.9, 63.9, 63.0, 55.3, 45.3, 21.3, 21.2, 20.7.
MS (+ESI) *m/z* (%) = 619 (11) [2M+H], 310 (100) [M+H]$^+$.
HRMS (+ESI) *m/z* calcd for $C_{20}H_{24}NO_2$ [M+H]$^+$: 310.1802; found: 310.1801.

(3,4-*trans*)-1-*iso*Propyl-3-(*p*-tolyl)-4-(3',4',5'–trimethoxyphenyl)azetidin-2-one (2m):



Chemical Formula: $C_{22}H_{27}NO_4$
Molecular Weight: 369,46 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1m** (269 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2m** (187 mg, 0.507 mmol, 68%) was obtained as a white solid.

m.p. (uncorrected) = 134 – 135 °C.

IR (ATR): $\tilde{\nu}$ = 2968, 1747, 1593, 1508, 1462, 1428, 1352, 1328, 1239, 1158, 1121, 1004 cm^{-1}.

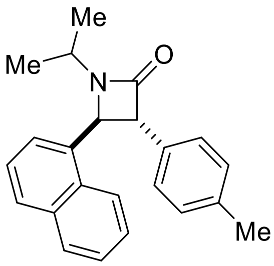
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 – 7.10 (m, 4H), 6.59 (s, 2H), 4.36 (d, *J* = 2.2 Hz, 1H), 4.03 (d, *J* = 2.1 Hz, 1H), 3.90 – 3.83 (m, 1H), 3.85 (s, 9H), 2.33 (s, 3H), 1.36 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.7, 153.7 (2C), 138.0, 137.4, 134.9, 132.3, 129.6 (2C), 127.3 (2C), 103.1 (2C), 64.1, 63.5, 60.9 (2C), 56.2, 45.3, 21.4, 21.2, 20.7.

MS (+ESI) *m/z* (%) = 739 (36) [2M+H], 370 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{22}H_{28}NO_4$ $[M+H]^+$: 370.2013; found: 370.2012.

(3,4-*trans*)-1-*iso*Propyl-3-(*p*-tolyl)-4-(naphth-1'-yl)azetidin-2-one (2n):



Chemical Formula: $C_{23}H_{23}NO$
Molecular Weight: 329,44 $g.mol^{-1}$

According to the general procedure **B**, bromo lactam **1n** (238 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2n** (185 mg, 0.562 mmol, 75%) was obtained as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2970, 2928, 1753, 1513, 1455, 1383, 1366, 1310 cm^{-1}.

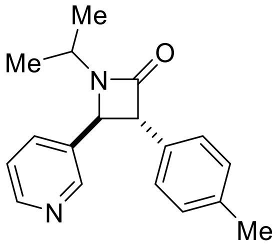
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 7.0 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.37 – 7.31 (m, 1H), 7.15 – 7.05 (m, 4H), 5.17 (d, *J* = 2.3 Hz, 1H), 3.99 (d, *J* = 2.3 Hz, 1H), 3.80 (hept, *J* = 6.8 Hz, 1H), 2.29 (s, 3H), 1.45 (d, *J* = 6.7 Hz, 3H), 1.16 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.3, 137.5, 135.2, 134.0, 132.8, 131.0, 129.8 (2C), 129.1, 128.7, 127.7 (2C), 126.6, 126.1, 125.6, 123.0, 122.9, 64.3, 60.3, 46.3, 21.3, 21.3, 21.0.

MS (+ESI) *m/z* (%) = 659 (21) [2M+H], 330 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{23}H_{24}NO$ $[M+H]^+$: 330.1852; found: 330.1852.

(3,4-*trans*)-1-*iso*Propyl-4-(pyridin-3-yl)-3-(*p*-tolyl)azetidin-2-one (2o):

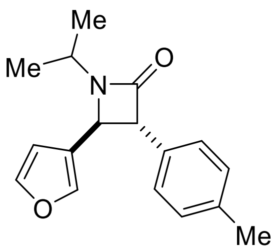


Chemical Formula: $C_{18}H_{20}N_2O$
Molecular Weight: 280,37 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1o** (202 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc/CH_2Cl_2 = 4:1:0 → 4:4:1), **2o** (101 mg, 0.360 mmol, 48%) was obtained as a pale yellow solid.

m.p. (uncorrected): 99 – 100 °C.
IR (ATR): $\tilde{\nu}$ = 2968, 2922, 1733, 1665, 1597, 1514, 1457, 1434, 1388, 1366, 1311, 1209, 1190, 1148, 1124, 1041, 1014 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 – 8.62 (m, 2H), 7.77 (dt$_{app}$, J = 7.9, 2.0 Hz, 1H), 7.37 (dd, J = 7.9, 4.7 Hz, 1H), 7.21 – 7.10 (m, 4H), 4.48 (d, J = 2.3 Hz, 1H), 4.07 (d, J = 2.3 Hz, 1H), 3.89 (hept, J = 6.8 Hz, 1H), 2.34 (s, 3H), 1.34 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.3, 150.3, 148.7, 137.8, 135.0, 133.9, 131.8, 129.8 (2C), 127.3 (2C), 124.1, 64.2, 60.7, 45.4, 21.6, 21.3, 20.9.
MS (+ESI) m/z (%) = 281 (100) $[M+H]^+$.
HRMS (+ESI) m/z calcd for $C_{18}H_{21}N_2O$ $[M+H]^+$: 281.1648, found: 281.1649.

(3,4-*trans*)-4-(Furan-3-yl)-1-*iso*propyl-3-(*p*-tolyl)azetidin-2-one (2p):

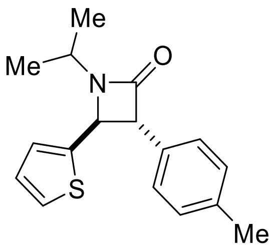


Chemical Formula: $C_{17}H_{19}NO_2$
Molecular Weight: 269,34 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1p** (194 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2p** (142 mg, 0.530 mmol, 70%) was obtained as a white solid.

m.p. (uncorrected): 91 – 92 °C.
IR (ATR): $\tilde{\nu}$ = 3132, 2978, 1723, 1609, 1592, 1506, 1452, 1409, 1392, 1332, 1232, 1207, 1180, 1158, 1045, 1026, 975 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (m, 1H), 7.44 (m, 1H), 7.15 (s, 4H), 6.52 (m, 1H), 4.45 (d, J = 2.2 Hz, 1H), 4.08 (d, J = 2.2 Hz, 1H), 3.87 (hept, J = 6.8 Hz, 1H), 2.33 (s, 3H), 1.32 (d, J = 6.8 Hz, 3H), 1.13 (d, J = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.9, 144.4, 140.6, 137.4, 132.3, 129.7 (2C), 127.3 (2C), 124.4, 108.3, 62.4, 54.6, 44.9, 21.4, 21.2, 20.6.
MS (+ESI) m/z (%) = 270 (100) $[M+H]^+$.
HRMS (+ESI) m/z calcd for $C_{17}H_{20}NO_2$ $[M+H]^+$: 270.1489; found: 270.1489.

(3,4-*trans*)-1-*iso*Propyl-3-(*p*-tolyl)-4-(thiophen-2ˈ-yl)azetidin-2-one (2q):



Chemical Formula: $C_{17}H_{19}NOS$
Molecular Weight: 285,41 $g.mol^{-1}$

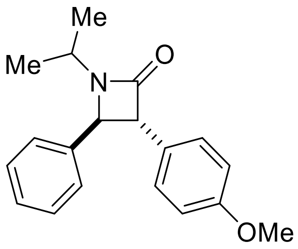
According to the general procedure **B**, bromo lactam **1q** (206 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.52 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **2q** (140 mg, 0.490 mmol, 65%) was obtained as a white solid.

m.p. (uncorrected) = 75 – 77 °C.
IR (ATR): $\tilde{\nu}$ = 2965, 1728, 1513, 1438, 1380, 1367, 1339, 1315, 1218, 1186, 1038 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, J = 4.9 Hz, 1H), 7.16 (m, 4H), 7.09 (dd, J = 3.5, 1.2 Hz, 1H), 7.00 (dd, J = 5.0, 3.5 Hz, 1H), 4.74 (d, J = 2.2 Hz, 1H), 4.21 (d, J = 2.2 Hz, 1H), 3.84 (hept, J = 6.8 Hz, 1H), 2.34 (s, 3H), 1.38 (d, J = 6.7 Hz, 3H), 1.15 (d, J = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.9, 143.4, 137.5, 132.0, 129.6 (2C), 127.2 (2C), 127.1, 126.0, 125.8, 64.8, 58.5, 45.4, 21.2, 21.2, 20.6.

MS (+ESI) *m/z* (%) = 308 (100) [M+Na]$^+$, 324 (46).

HRMS (+ESI) m/z calcd for $C_{17}H_{19}NO_2SNa$ [M+Na]$^+$: 308.1080; found: 308.1082.

(3,4-*trans*)-1-*iso*Propyl-3-(*p*-methoxyphenyl)-4-phenylazetidin-2-one (4a):



Chemical Formula: $C_{19}H_{21}NO_2$
Molecular Weight: 295,38 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (4.0 mL) and *p*-methoxyphenylmagnesium bromide (0.38 M in THF, 3.0 mL, 1.14 mmol) was added with a syringe pump (4.7 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1 → 5:1), **4a** (162 mg, 0.547 mmol, 73%) was obtained as a white solid.

m.p. (uncorrected) = 73 – 75 °C.

IR (ATR): $\tilde{\nu}$ = 2967, 2929, 1721, 1597, 1489, 1466, 1436, 1399, 1364, 1259, 1162, 1036 cm^{-1}.

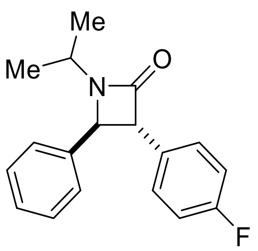
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 – 7.36 (m, 4H), 7.38 – 7.31 (m, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.42 (d, *J* = 2.2 Hz, 1H), 4.04 (d, *J* = 2.2 Hz, 1H), 3.87 (hept, *J* = 6.8 Hz, 1H), 3.79 (s, 3H), 1.35 (d, *J* = 6.7 Hz, 3H), 1.08 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.8, 159.1, 139.3, 129.1 (2C), 128.6, 128.6 (2C), 127.6 (2C), 126.7, 114.4 (2C), 63.7, 63.3, 55.4, 45.3, 21.4, 20.8.

MS (+ESI) *m/z* (%) = 591 (31) [2M+H], 296 (100) [M+H]$^+$.

HRMS (+ESI) *m/z* calcd for $C_{19}H_{22}NO_2$ [M+H]$^+$: 296.1645; found: 296.1644.

(3,4-*trans*)-3-(*p*-Fluorophenyl)-1-*iso*propyl-4-phenylazetidin-2-one (4b):



Chemical Formula: $C_{18}H_{18}FNO$
Molecular Weight: 283,35 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.6 mL) and *p*-fluorophenylmagnesium bromide (0.80 M in THF, 1.4 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.3 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **4b** (142 mg, 0.501 mmol, 67%) was obtained as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2971, 2931, 1740, 1603, 1509, 1455, 1382, 1366, 1334, 1221, 1157 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.34 (m, 5H), 7.29 – 7.21 (m, 2H), 7.11 – 7.00 (m, 2H), 4.45 (d, J = 2.3 Hz, 1H), 4.10 (d, J = 2.2 Hz, 1H), 3.88 (hept, J = 6.7 Hz, 1H), 1.37 (d, J = 6.8 Hz, 3H), 1.11 (d, J = 6.7 Hz, 3H).

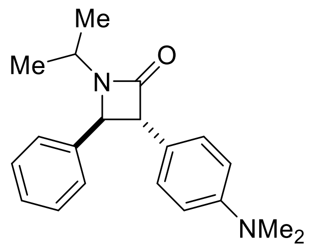
^{19}F NMR (376 Hz, $CDCl_3$): δ = -114.6.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.2, 162.3 (d, J = 246.2 Hz), 139.0, 131.3 (d, J = 3.1 Hz), 129.2 (2C), [129.13, 128.94 (d, J = 31.2 Hz, 2C)] or [129.05, 128.98 (d, J = 23.2 Hz, 2C)], 126.7 (2C), 115.9 (d, J = 21.7 Hz, 2C), 63.5, 63.2, 45.4, 21.4, 20.8 .

MS (+ESI) *m/z* (%) = 284 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{18}H_{19}FNO$ $[M+H]^+$: 284.1445; found: 284.1445.

(3,4-*trans*)-3-[*p*-(*N,N*-Dimethylamino)phenyl]-1-*iso*propyl-4-phenylazetidin-2-one (4c):



Chemical Formula: $C_{20}H_{24}N_2O$
Molecular Weight: 308,43 $g.mol^{-1}$

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.6 mL) and *p*-(N,N-dimethylamino)phenylmagnesium bromide (0.80 M in THF, 1.4 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.3 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1 → 4:1), **4c** (147 mg, 0.477 mmol, 64%) was obtained as a yellow oil.

IR (ATR): $\tilde{\nu}$ = 2969, 2926, 1741, 1614, 1521, 1454, 1380, 1336, 1165, 1125 cm^{-1}.

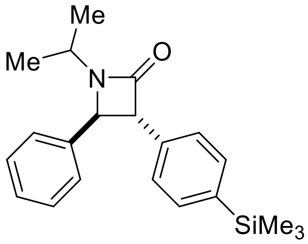
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.38 (m, 4H), 7.38 – 7.31 (m, 1H), 7.12 (d, J = 8.7 Hz, 2H), 6.71 (d, J = 8.7 Hz, 2H), 4.42 (d, J = 2.2 Hz, 1H), 4.00 (d, J = 2.2 Hz, 1H), 3.87 (hept, J = 6.7 Hz, 1H), 2.94 (s, 6H), 1.35 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.3, 150.2, 139.6, 129.9 (2C), 128.5, 128.3 (2C), 126.7 (2C), 123.2, 113.0 (2C), 64.0, 63.5, 45.2, 40.7 (2C), 21.5, 20.8.

MS (+ESI) *m/z* (%) = 617 (19) [2M+H], 309 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{20}H_{25}N_2O$ $[M+H]^+$: 309.1961; found: 309.1962.

(3,4-*trans*)-1-*iso*Propyl-4-phenyl-3-[*p*-(trimethylsilyl)phenyl]azetidin-2-one (4d):

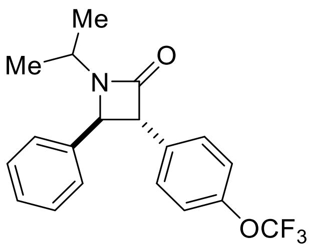


Chemical Formula: $C_{21}H_{27}NOSi$
Molecular Weight: 337,54 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.7 mL) and *p*-trimethylsilylphenylmagnesium bromide (0.87 M in THF, 1.33 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.1 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **4d** (137 mg, 0.405 mmol, 54%) was obtained as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2955, 1748, 1601, 1455, 1389, 1365, 1248, 1108 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (br d, J = 8.1 Hz, 2H), 7.28 – 7.20 (m, 5H), 7.11 (br d, J = 8.1 Hz, 2H), 4.36 (d, J = 2.2 Hz, 1H), 3.94 (d, J = 2.2 Hz, 1H), 3.72 (hept, J = 6.8 Hz, 1H), 1.21 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 0.12 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.3, 139.9, 139.3, 135.9, 134.0 (2C), 129.1 (2C), 128.7, 126.8 (2C), 126.7 (2C), 64.3, 62.8, 45.4, 21.4, 20.8, 1.0 (3C).
MS (+ESI) m/z (%) = 338 (100) $[M+H]^+$.
HRMS (+ESI) m/z calcd for $C_{21}H_{28}NOSi$ $[M+H]^+$: 338.1935; found: 338.1935.

(3,4-*trans*)-1-*iso*Propyl-4-phenyl-3-[*p*-(trifluoromethoxy)phenyl]azetidin-2-one (4e):



Chemical Formula: $C_{19}H_{18}F_3NO_2$
Molecular Weight: 349,35 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.750 mmol, 1.00 mmol) was dissolved in THF (5.6 mL) and *p*-[(trifluoromethoxy)phenyl]magnesium bromide (0.82 M in THF, 1.4 mL, 1.14 mmol, 1.51 mmol) was added (an addition with a syringe pump with the corresponding rate of 2.2 mL/h was not possible, thus manually added over 5 min). After flash column chromatography on silica gel (n-pentane/EtOAc = 10:1), **4e** (107 mg, 0.305 mmol, 41%) was obtained as a white oil.

IR (ATR): $\tilde{\nu}$ = 2973, 1745, 1508, 1382, 1367, 1253, 1219, 1160 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.44 – 7.41 (m, 4H), 7.40 – 7.35 (m, 1H), 7.30 (d, J = 8.6 Hz, 2H), 7.20 (d, J = 7.8, 1.1 Hz, 2H), 4.46 (d, J = 2.2 Hz, 1H), 4.10 (d, J = 2.3 Hz, 1H), 3.85 (hept, J = 6.8 Hz, 1H), 1.35 (d, J = 6.8 Hz, 3H), 1.09 (d, J = 6.7 Hz, 3H).

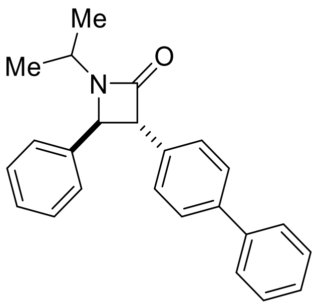
^{13}C NMR (101 MHz, CDCl$_3$): δ = 167.7, 148.6, 138.7, 134.1, 129.1 (2C), 128.8 (2C), 126.5 (2C), 121.5 (2C), 120.45 (q, J = 257.3 Hz), 63.3, 62.8, 45.4, 21.3, 20.6.

One quaternary carbon is not visible.

MS (+ESI) m/z (%) = 372 (100) [M+Na]$^+$.

HRMS (+ESI) m/z calcd for $C_{19}H_{18}F_3NO_2Na$ [M+Na]$^+$: 372.1182; found: 372.1183.

(3,4-*trans*)-3-[(1,1ˈ-Biphenyl)-4-yl]-1-*iso*propyl-4-phenylazetidin-2-one (4f):



Chemical Formula: $C_{24}H_{23}NO$

Molecular Weight: 341,45 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.3 mL) and 4-[(1,1ˈ-biphenyl)-4-yl]magnesium bromide (0.68 M in THF, 1.7 mL, 1.14 mmol) was added (an addition with a syringe pump with the corresponding rate of 2.7 mL/h was not possible, manually added over 5 min). After flash column chromatography on silica gel (n-pentane/EtOAc = 10:1), **4e** (132 mg, 0.444 mmol, 59%) was obtained as a white solid.

m.p. (uncorrected) = 73 – 75 °C.

IR (ATR): $\tilde{\nu}$ = 2970, 1741, 1487, 1455, 1381, 1365, 1321, 1224, 1172, 1007 cm^{-1}.

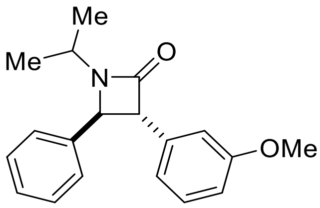
^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.65 – 7.56 (m, 4H), 7.48 – 7.42 (m, 6H), 7.44 – 7.31 (m, 4H), 4.55 (d, J = 2.2 Hz, 1H), 4.16 (d, J = 2.3 Hz, 1H), 3.90 (hept, J = 6.8 Hz, 1H), 1.39 (d, J = 6.8 Hz, 3H), 1.12 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, CDCl$_3$): δ = 168.3, 140.8, 140.7, 139.2, 134.5, 129.1 (2C), 128.9 (2C), 128.7, 127.9 (2C), 127.7 (2C), 127.5, 127.2 (2C), 126.7 (2C), 64.0, 63.0, 45.4, 21.4, 20.8.

MS (+ESI) m/z (%) = 364 (100) [M+Na]$^+$, 380 (50), 540 (38).

HRMS (+ESI) m/z calcd for $C_{24}H_{23}NONa$ [M+Na]$^+$: 364.1672; found: 364.1372.

(3,4-*trans*)-3-(*m*-Methoxyphenyl)-1-*iso*propyl-4-phenylazetidin-2-one (4g):

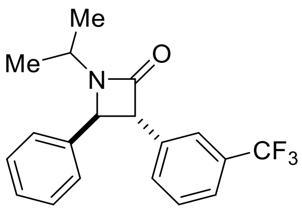


Chemical Formula: $C_{19}H_{21}NO_2$
Molecular Weight: 295,38 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.7 mL) and *m*-methoxyphenylmagnesium bromide (0.80 M in THF, 1.4 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.0 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **4g** (185 mg, 0.627 mmol, 84%) was obtained as a white oil.

IR (ATR): $\tilde{\nu}$ = 2969, 2932, 1741, 1599, 1582, 1490, 1454, 1382. 1321, 1156, 1047 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 – 7.41 (m, 4H), 7.41 – 7.36 (m, 1H), 7.32 – 7.26 (m, 1H), 6.90 – 6.83 (m, 3H), 4.51 (d, *J* = 2.2 Hz, 1H), 4.09 (d, *J* = 2.2 Hz, 1H), 3.89 (hept, *J* = 6.8 Hz, 1H), 3.81 (s, 3H), 1.37 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.2, 160.0, 139.2, 136.9, 130.0, 129.1 (2C), 128.7, 126.7 (2C), 119.7, 113.2, 113.1, 64.2, 62.8, 55.3, 45.3, 21.4, 20.8.
MS (+ESI) *m/z* (%) = 591 (5) [2M+H], 296 (100) $[M+H]^+$.
HRMS (+ESI) *m/z* calcd for $C_{19}H_{22}NO_2$ $[M+H]^+$: 296.1645; found: 296.1645.

(3,4-*trans*)-1-*iso*Propyl-4-phenyl-3-(*m*-trifluorotolyl)azetidin-2-one (4h):



Chemical Formula: $C_{19}H_{18}F_3NO$
Molecular Weight: 333,35 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.6 mL) and *m*-(trifluorotolyl)magnesium bromide (0.60 M in THF, 2.1 mL, 1.28 mmol, 1.70 equiv) was added with a syringe pump (3.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **4h** (195 mg, 0.584 mmol, 78%) was obtained as a white oil.

IR (ATR): $\tilde{\nu}$ = 2974, 1742, 1456, 1384, 1367, 1352, 1163, 1119, 1073 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 – 7.53 (m, 1H), 7.51 – 7.46 (m, 4H), 7.42 – 7.32 (m, 4H), 7.30 (m, 1H), 4.49 (d, J = 2.2 Hz, 1H), 4.16 (d, J = 2.2 Hz, 1H), 3.86 (hept, J = 6.7 Hz, 1H), 1.36 (d, J = 6.8 Hz, 3H), 1.10 (d, J = 6.7 Hz, 3H).

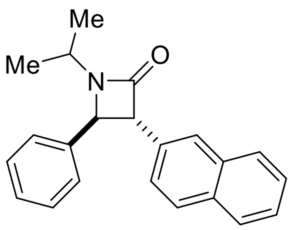
^{19}F NMR (376 MHz, $CDCl_3$): δ = -62.7.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.3, 138.6, 136.3, 131.3 (q, J = 32.2 Hz), 130.7, 123.9 (q, J = 272.4 Hz), 129.5, 129.2 (2C), 128.9, 126.6 (2C), 124.5 (q, J = 3.8 Hz), 124.3 (q, J = 3.8 Hz), 63.6, 62.7, 45.5, 21.3, 20.6.

MS (+ESI) *m/z* (%) = 667 (4) [2M+H], 334 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{19}H_{19}F_3NO$ $[M+H]^+$: 334.1413; found: 334.1413.

(3,4-*trans*)-1-*iso*Propyl-3-(naphth-2'-yl)-4-phenylazetidin-2-one (4i):



Chemical Formula: $C_{22}H_{21}NO$
Molecular Weight: 315,42 $g.mol^{-1}$

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.1 mL) and 2-naphthalenylmagnesium bromide (0.60 M in THF, 1.9 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (3.0 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **4i** (189 mg, 0.600 mmol, 80%) was obtained as a white solid.

m.p. (uncorrected) = 89 – 90 °C.

IR (ATR): $\tilde{\nu}$ = 2976, 1740, 1455, 1380, 1328, 1124, 1014 cm^{-1}.

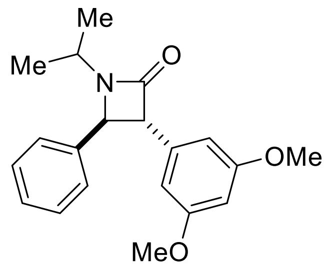
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 – 7.77 (m, 4H), 7.51 – 7.43 (m, 6H), 7.42 – 7.33 (m, 2H), 4.56 (d, J = 2.2 Hz, 1H), 4.29 (d, J = 2.2 Hz, 1H), 3.92 (hept, J = 6.7 Hz, 1H), 1.39 (d, J = 6.7 Hz, 3H), 1.13 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.3, 139.2, 133.6, 132.9, 132.8, 129.2 (2C), 128.9, 128.8, 128.0, 127.8, 126.7 (2C), 126.5, 126.5, 126.1, 125.1, 64.4, 63.0, 45.4, 21.5, 20.8.

MS (+ESI) *m/z* (%) = 631 (13) [2M+H], 316 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{22}H_{22}NO$ $[M+H]^+$: 316.1696; found: 316.1696.

(3,4-*trans*)-3-(3',5'–Dimethoxyphenyl)-1-*iso*propyl-4-phenylazetidin-2-one (4j):

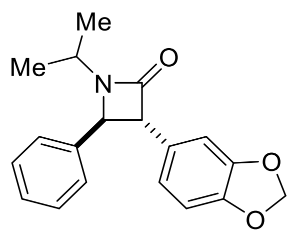


Chemical Formula: $C_{20}H_{23}NO_3$
Molecular Weight: 325,41 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.2 mL) and 3',5'–dimethoxyphenylmagnesium bromide (0.62 M in THF, 1.9 mL, 1.14 mmol, 1.51 equiv) was added (an addition with a syringe pump with the corresponding rate of 2.9 mL/h was not possible, thus manually added over 5 min). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **4j** (155 mg, 0.475 mmol, 63%) was obtained as a white solid.

m.p. (uncorrected) = 69 – 70 °C.
IR (ATR): $\tilde{\nu}$ = 2966, 1735, 1596, 1454, 1222, 1364, 1184, 1092, 1039, 989, 963, 920 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.39 (m, 4H), 7.41 – 7.30 (m, 1H), 6.43 (d, *J* = 2.2 Hz, 2H), 6.38 (t, *J* = 2.3 Hz, 1H), 4.49 (d, *J* = 2.3 Hz, 1H), 4.02 (d, *J* = 2.2 Hz, 1H), 3.86 (hept, *J* = 6.7 Hz, 1H), 3.77 (s, 6H), 1.35 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.1, 161.2 (2C), 139.2, 137.6, 129.1 (2C), 128.7, 126.7 (2C), 105.5 (2C), 99.5, 64.3, 62.7, 55.4 (2C), 45.3, 21.4, 20.8.
MS (+ESI) *m/z* (%) = 651 (12) [2M+H], 326 (100) [M+H]$^+$.
HRMS (+ESI) *m/z* calcd for $C_{20}H_{24}NO_3$ [M+H]$^+$: 326.1751; found: 326.1751.

(3,4-*trans*)-3-(Benzo[1,3]dioxol-5’-yl)-1-*iso*propyl-4-phenylazetidin-2-one (4k):



Chemical Formula: $C_{19}H_{19}NO_3$
Molecular Weight: 309,37 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.6 mL) and 1,3-benzodioxol-5-ylmagnesium bromide (0.80 M in THF, 1.4 mL, 1.14 mmol, 1.51 equiv) was added with a syringe pump (2.3 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **4k** (152 mg, 0.490 mmol, 65%) was obtained as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2970, 2900, 1740, 1501, 1489, 1455, 1441, 1382, 1244, 1035, 928 cm^{-1}.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ = 7.47 – 7.38 (m, 4H), 7.38 – 7.32 (m, 1H), 6.87 – 6.68 (m, 3H), 5.95 (d, J_{AB} = 1.4 Hz, 1H), 5.94 (d, J_{AB} = 1.4 Hz, 1H), 4.41 (d, J = 2.2 Hz, 1H), 4.00 (d, J = 2.2 Hz, 1H), 3.85 (hept, J = 6.7 Hz, 1H), 1.34 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 6.7 Hz, 3H).

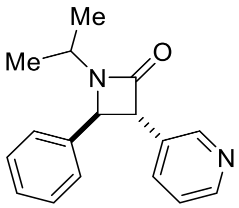
^{13}**C NMR** (101 MHz, $CDCl_3$): δ = 168.5, 148.2, 147.2, 139.1, 129.1 (2C), 128.7, 126.6 (2C), 121.0, 108.7, 107.7, 101.2, 64.1, 63.3, 45.3, 21.4, 20.8.

One quaternary carbon is not visible.

MS (+ESI) *m/z* (%) = 619 (12) [2M+H], 310 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{19}H_{20}NO_3$ $[M+H]^+$: 310.1438; found: 310.1438.

(3,4-*trans*)-1-*iso*Propyl-4-phenyl-3-(pyrid-3ʹ-yl)azetidin-2-one (4l):



Chemical Formula: $C_{17}H_{18}N_2O$
Molecular Weight: 266,34 g.mol^{-1}

According to the general procedure **B**, bromo lactam **1a** (201 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.2 mL) and 3-pyridylmagnesium bromide solution in THF (0.59 M in THF, 1.9 mL, 1.14 mmol, 1.51 equiv) was added (an addition with a syringe pump with the corresponding rate of 2.9 mL/h was not possible, thus manually added over 5 min). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1 → 5:1), **4l** (55 mg, 0.206 mmol, 28%) was obtained as a colorless oil.

IR (ATR): $\tilde{\nu}$ = 2971, 2930, 1741, 1455, 1382, 1366, 1332, 1025 cm^{-1}.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ = 8.54 – 8.50 (d, J = 3.2 Hz, 1H), 7.63 (dt$_{app}$, J = 7.9, 2.0 Hz, 1H), 7.48 – 7.36 (m, 5H), 7.29 (dd, J = 7.8, 4.8 Hz, 1H), 4.48 (d, J = 2.3 Hz, 1H), 4.11 (d, J = 2.2 Hz, 1H), 3.84 (hept, J = 6.7 Hz, 1H), 1.35 (d, J = 6.8 Hz, 3H), 1.09 (d, J = 6.7 Hz, 3H).

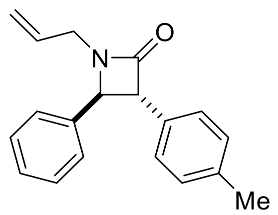
^{13}**C NMR** (101 MHz, $CDCl_3$): δ = 167.2, 149.1, 149.1, 138.5, 134.8, 131.3, 129.3 (2C), 129.0, 126.6 (2C), 123.9, 62.6, 61.7, 45.6, 21.4, 20.7.

MS (+ESI) *m/z* (%) = 267 (100) $[M+H]^+$.

HRMS (+ESI) *m/z* calcd for $C_{17}H_{19}N_2O$ $[M+H]^+$: 267.1492; found: 267.1492.

Characterization Data of Products 8, 9 and 10

(3,4-*trans*)-1-Allyl-3-(*p*-tolyl)-4-phenylazetidin-2-one (8):

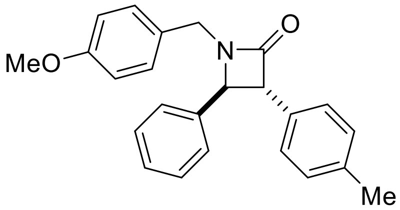


Chemical Formula: $C_{19}H_{19}NO$
Molecular Weight: 277,37 g.mol^{-1}

According to the general procedure **B**, bromo lactam **5** (200 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.5 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **8** (162 mg, 0.584 mmol, 78%) was obtained as a white solid.

m.p. (uncorrected) = 91 °C.
IR (ATR): $\tilde{\nu}$ = 2919, 1741, 1512, 1494, 1440, 1393, 1359, 1153, 1039, 994, 946 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 – 7.31 (m, 5H), 7.21 – 7.15 (m, 4H), 5.79 (m, 1H), 5.20 – 5.08 (m, 2H), 4.50 (d, J = 2.2 Hz, 1H), 4.31 (dddd, J_{AB} = 15.6, 5.2, 1.5 Hz, 1H), 4.15 (d, J_{AB} = 2.2 Hz, 1H), 3.41 (dddd, J_{AB} = 15.6, 7.2, 1.1 Hz, 1H), 2.35 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 137.7, 137.5, 132.2, 131.7, 129.7 (2C), 129.2 (2C), 128.7, 127.4 (2C), 126.6 (2C), 118.9, 65.0, 63.7, 43.2, 21.3.
MS (+ESI) *m/z* (%) = 555 (78) [2M+H], 296 (100), 278 (16) $[M+H]^+$.
HRMS (+ESI) *m/z* calcd for $C_{19}H_{20}NO$ $[M+H]^+$: 278.1539; found: 278.1523.

(3,4-*trans*)-1-(*p*-Methoxybenzyl)-4-phenyl-3-(*p*-tolyl)azetidin-2-one (9):



Chemical Formula: $C_{24}H_{23}NO_2$
Molecular Weight: 357,45 g.mol^{-1}

According to the general procedure **B**, bromo lactam **6** (260 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.80 M in THF, 1.59 mL, 1.27 mmol, 1.70 equiv) was added with a syringe pump (2.5 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **9** (204 mg, 0.570 mmol, 76%) was obtained as a white solid.

m.p. (uncorrected): 93 – 94 °C.

IR (ATR): $\tilde{\nu}$ = 3003, 2933, 2834, 1760, 1734, 1613, 1586, 1511, 1496, 1456, 1447, 1426, 1398, 1351, 1304, 1242, 1171, 1124, 1030, 934, 918 cm^{-1}.

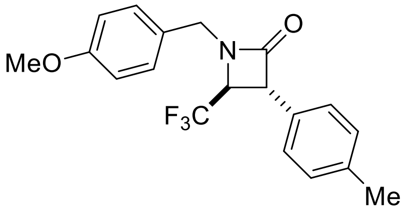
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.37 (m, 3H), 7.29 – 7.26 (m, 2H), 7.15 – 7.06 (m, 6H), 6.83 (br d, J = 8.6 Hz, 2H), 4.91 (d, J_{AB} = 14.8 Hz, 1H), 4.29 (d, J = 2.2 Hz, 1H), 4.14 (d, J = 2.2 Hz, 1H), 3.79 (s, 3H), 3.77 (d, J_{AB} = 14.8 Hz, 1H), 2.32 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 159.3, 137.6, 137.4, 132.2, 130.0 (2C), 129.7 (2C), 129.2 (2C), 128.7, 127.9, 127.4 (2C), 126.7 (2C), 114.3 (2C), 64.9, 63.2, 55.4, 44.1, 21.3.

MS (+ESI) m/z (%) = 358 (100) $[M+H]^+$.

HRMS (+ESI) m/z calcd for $C_{24}H_{24}NO_2$ $[M+H]^+$: 358.1802; found: 358.1802.

(3,4-*trans*)-1-(*p*-Methoxybenzyl)-3-(*p*-tolyl)-4-(trifluoromethyl)azetidin-2-one (10):



Chemical Formula: $C_{19}H_{18}F_3NO_2$
Molecular Weight: 349,35 g.mol^{-1}

According to the general procedure **B**, bromo lactam **7** (254 mg, 0.75 mmol, 1.00 equiv) was dissolved in THF (5.5 mL) and *p*-tolylmagnesium bromide (0.76 M in THF, 1.5 mL, 1.14 mmol, 1.52 equiv) was added with a syringe pump (2.4 mL/h). After flash column chromatography on silica gel (*n*-pentane/EtOAc = 10:1), **10** (183 mg, 0.524 mmol, 70%) was obtained as a slightly yellow solid.

m.p. (uncorrected) = 50 – 51 °C.

IR (ATR): $\tilde{\nu}$ = 2926, 2913, 1745, 1614, 1515, 1387, 1249, 1217, 1166, 1126, 1031, 1107 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (d, J = 8.7 Hz, 2H), 7.14 (d, J = 8.2 Hz, 2H), 7.08 (d, J = 8.1 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 4.92 (d, J_{AB} = 15.0 Hz, 1H), 4.40 (d, J = 2.4 Hz, 1H), 3.97 (d, J_{AB} = 14.9 Hz, 1H), 3.81 (s, 3H), 3.75 (qd, J = 6.0, 2.4 Hz, 1H), 2.33 (s, 3H).

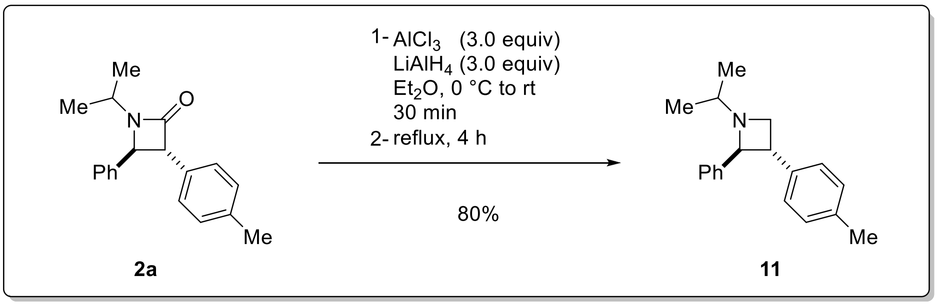
^{19}F NMR (376 MHz, $CDCl_3$): δ = -73.7.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.8, 159.5, 138.1, 129.9 (2C), 129.8 (2C), 129.7, 127.1 (2C), 126.7, 124.4 (q, J = 280.0 Hz), 114.4 (2C), 57.8 (q, J = 33.8 Hz), 55.8 (d, J = 1.7 Hz), 55.3, 45.1, 21.1.

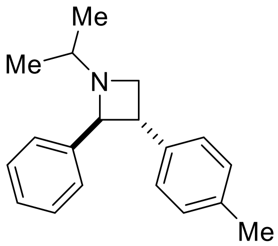
MS (+ESI) *m/z* (%) = 372 (90) $[M+Na]^+$, 388 (48), 740 (90).

HRMS (+ESI) m/z calcd for $C_{19}H_{18}F_3NO_2Na$ $[M+Na]^+$: 372.1182; found: 372.1181.

Synthetic transformations of α-arylated β-lactams



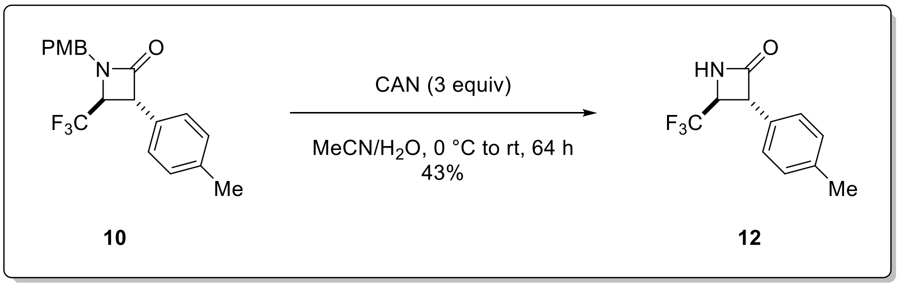
(3,4-*trans*)-1-*iso*Propyl-3-(*p*-tolyl)-2-phenylazetidine (11):



Chemical Formula: $C_{19}H_{23}N$
Molecular Weight: 265,40 g.mol^{-1}

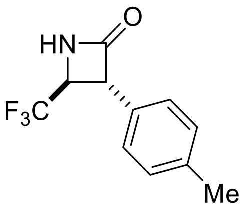
$AlCl_3$ (226 mg, 1.70 mmol, 3.00 equiv) was dissolved in Et_2O (3.8 mL) and at 0 °C, $LiAlH_4$ (64 mg, 1.70 mmol, 3.00 equiv) was slowly added. The reaction was stirred for 10 min at 0 °C and then refluxed for 30 min. After cooling to rt, the azetidin-2-one **2a** (158 mg, 0.566 mmol, 1.00 equiv) dissolved in Et_2O (3.8 mL) was added dropwise. The reaction was refluxed for 4 h and quenched with an aqueous 1 M NaOH solution (2 mL). After addition of H_2O and extraction with CH_2Cl_2 (3×25 mL), the combined organic phases were washed brine, dried over Na_2SO_4 and filtered. The solvent was removed *in vacuo* to obtain **11** as a white oil (120 mg, 0.451 mmol, 80%).

IR (ATR): $\tilde{\nu}$ = 3023, 2963, 2925, 2818, 1515, 1451, 1364, 1329, 1065, 1020 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 – 7.32 (m, 2H), 7.25 – 7.12 (m, 2H), 7.19 (m, 1H), 7.05 – 6.98 (m, 4H), 3.89 (d, J = 8.2 Hz, 1H), 3.74 (br t_{app}, J = 7.5 Hz, 1H), 3.29 (q_{app}, J = 8.1 Hz, 1H), 2.93 (dd, J = 9.2, 6.6 Hz, 1H), 2.46 (hept, J = 6.3 Hz, 1H), 2.24 (s, 3H), 0.95 (d, J = 6.2 Hz, 3H), 0.68 (d, J = 6.3 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.1, 138.2, 136.2, 129.1 (2C), 128.3 (2C), 127.4 (2C), 127.2, 126.9 (2C), 76.7, 59.4, 56.4, 45.3, 21.2, 21.1, 20.3.
MS (+ESI) *m/z* (%) = 266 (100) [M+H]$^+$.
HRMS (+ESI) *m/z* calcd for $C_{19}H_{24}N$ [M+H]$^+$: 266.1903; found: 266.1903.



Lactam **10** (342 mg, 0.979 mmol, 1.00 equiv) was dissolved in 9:1 mixture of CH_3CN/H_2O (20 mL) under air. At 0 °C, ceric ammonium nitrate (1.61 g, 2.94 mmol, 3.00 equiv) was added in one portion. The mixture was stirred for 64 h at rt and was then quenched with a saturated aqueous $NaHCO_3$ solution (20 mL) followed by extraction with EtOAc (3×40 mL). The combined organic phases were washed with an aqueous 10% Na_2SO_3 solution and brine and dried over Na_2SO_4. After filtration, the solvent was removed *in vacuo*. Flash column chromatography on silica gel (PE/EtOAc = 10:1) yielded **12** (95 mg, 0.416 mmol, 43%) as a white solid.

(3,4-*trans*)-3-(*p*-Tolyl)-4-(trifluoromethyl)azetidin-2-one (12):



Chemical Formula: $C_{11}H_{10}F_3NO$
Molecular Weight: 229,20 g.mol^{-1}

m.p. (uncorrected) = 98 – 99 °C.

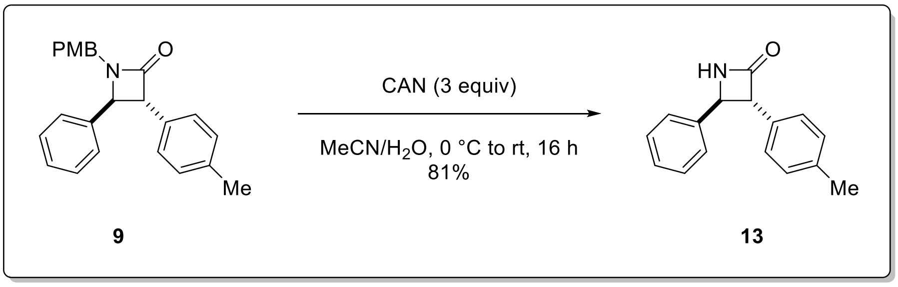
IR (ATR): $\tilde{\nu}$ = 3186, 3118, 2985, 1734, 1516, 1389, 1283, 1167, 1148, 1130, 1043, 1020 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 – 7.10 (m, 4H), 6.52 (br s, 1H), 4.49 (d, J = 2.5 Hz, 1H), 4.02 (qd, J = 5.9, 2.5 Hz, 1H), 2.35 (s, 3H).

^{19}F NMR (376 MHz, $CDCl_3$): δ = -76.5.

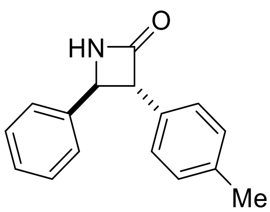
^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.2, 138.4, 130.0 (2C), 129.4, 127.2 (2C), 124.3 (q, J = 278.7 Hz), 57.7 (d, J = 1.5 Hz), 55.9 (q, J = 35.0 Hz), 21.3.

HRMS (+ESI) *m/z* calcd for $C_{11}H_{11}F_3NO$ $[M+H]^+$: 230.0787; found: 230.0786.



Lactam **9** (185 mg, 0.518 mmol, 1.00 equiv) was dissolved in 9:1 mixture of CH_3CN/H_2O (12 mL) under air. At 0 °C, ceric ammonium nitrate (855 mg, 1.56 mmol, 3.00 equiv) was added in one portion. The mixture was stirred for 16 h at rt and was then quenched with a saturated aqueous $NaHCO_3$ solution (15 mL) followed by extraction with EtOAc (3×30 mL). The combined organic phases were washed with an aqueous 10% Na_2SO_3 solution and brine and dried over Na_2SO_4. After filtration, the solvent was removed *in vacuo*. Flash column chromatography on silica gel (PE/EtOAc = 8:1 → 3:1) yielded **13** (100 mg, 0.421 mmol, 81%) as a white solid.

(3,4-*trans*)-4-Phenyl-3-(*p*-tolyl)azetidin-2-one (13):



Chemical Formula: $C_{16}H_{15}NO$
Molecular Weight: 237,30 g.mol^{-1}

m.p. (uncorrected): 125 – 126 °C.

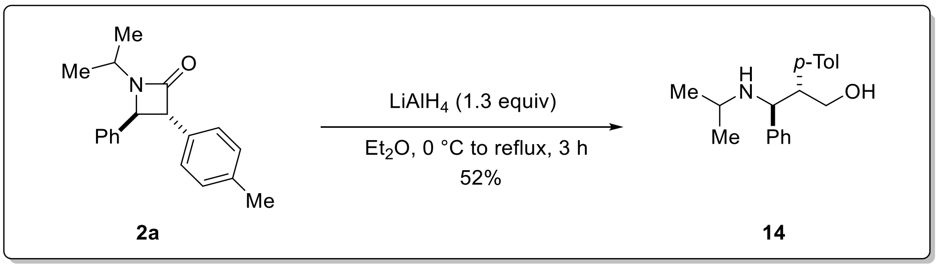
IR (ATR): $\tilde{\nu}$ = 3292, 2913, 1745, 1514, 1494, 1450, 1426, 1401, 1348, 1298, 1152, 1108, 1139, 1025, 975 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.32 (m, 5H), 7.22 (br d, J = 8.3 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 6.38 (br s, 1H), 4.65 (d, J = 2.5 Hz, 1H), 4.18 (d, J = 2.5 Hz, 1H), 2.36 (s, 3H).

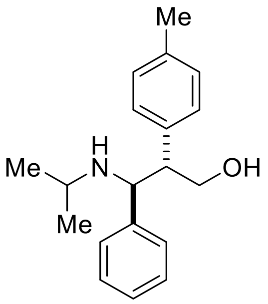
^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.3, 139.7, 137.7, 131.8, 129.8 (2C), 129.1 (2C), 128.5, 127.4 (2C), 125.7 (2C), 66.3, 60.5, 21.3.

MS (+ESI) m/z (%) = 238 (100) $[M+H]^+$.

HRMS (+ESI) m/z calcd for $C_{16}H_{16}NO$ $[M+H]^+$: 238.1226; found: 238.1227.



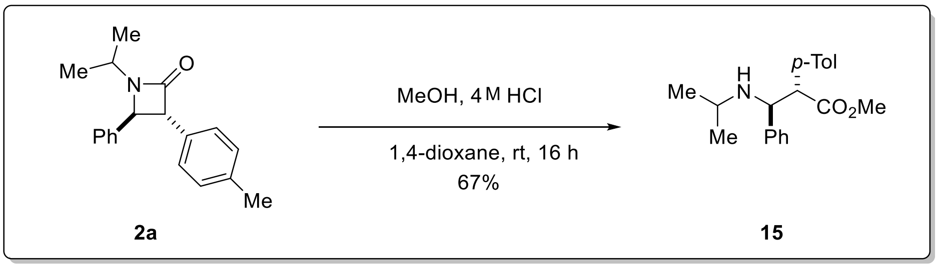
(2,3-*anti*)-3-*iso*Propylamino-2-(*p*-tolyl)-3-phenylpropan-1-ol (14):



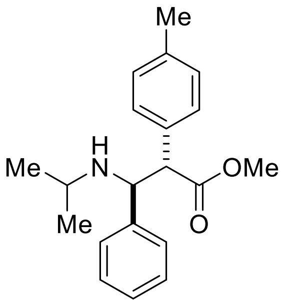
Chemical Formula: $C_{19}H_{25}NO$
Molecular Weight: 283,42 g.mol^{-1}

The azetidin-2-one **2a** (84 mg, 0.301 mmol, 1.00 equiv) was dissolved in Et_2O (4.0 mL) and at 0 °C, $LiAlH_4$ (15 mg, 0.375 mmol, 1.25 equiv) was slowly added. The reaction was warmed to rt and refluxed for 3 h. After cooling to rt, the reaction was quenched with an aqueous 1 M NaOH solution (2 mL). After addition of H_2O and extraction with Et_2O (3×25 mL), the combined organic phases were washed with brine, dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure and after flash column chromatography on silica gel (PE/EtOAc = 10:1), **14** (45 mg, 0.158 mmol, 52%) was obtained as a white solid.

m.p. (uncorrected) = 110 – 112 °C.
IR (ATR): $\tilde{\nu}$ = 3280, 2992, 2969, 1470, 1407, 1163, 1062, 1034, 957, 926 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19 – 7.12 (m, 2H), 7.11 – 6.98 (m, 3H), 6.89 (d, J = 8.5 Hz, 2H), 6.84 (d, J = 8.1 Hz, 2H), 4.12 (dd, J_{AB} = 11.0, 9.8 Hz, 1H), 4.04 (d, J = 10.6 Hz, 1H), 3.80 (dd, J_{AB} = 11.0, 3.4 Hz, 1H), 3.11 (td, J = 10.1, 3.3 Hz, 1H), 2.62 (hept, J = 6.2 Hz, 1H), 2.18 (s, 3H), 1.16 (d, J = 6.1 Hz, 3H), 0.97 (d, J = 6.3 Hz, 3H).
O*H* and N*H* are not visible.
^{13}C NMR (101 MHz, $CDCl_3$): δ = 142.3, 137.1, 135.9, 129.0 (2C), 128.4 (2C), 128.0 (2C), 127.1 (2C), 127.0, 69.7, 67.0, 52.8, 45.5, 24.5, 21.6, 21.1.
MS (+ESI) *m/z* (%) = 284 (100) [M+H]$^+$.
HRMS (+ESI) *m/z* calcd for $C_{19}H_{26}NO$ [M+H]$^+$: 284.2009; found: 284.2008.



(2,3-*anti*)-3-*iso*Propylamino-2-(*p*-tolyl)-3-phenylpropanoic methyl ester (15):



Chemical Formula: $C_{20}H_{25}NO_2$
Molecular Weight: 311,43 g.mol^{-1}

Azetidin-2-one **2a** (150 mg, 0.537 mmol, 1.00 equiv) was dissolved in MeOH (1.3 mL) under air and HCl (4 M in 1,4-dioxane,1.3 mL, 5.37 mmol, 10.0 equiv) was added. The mixture was heated to 60 °C for 20 h. The reaction was cooled to rt and a saturated aqueous $NaHCO_3$ solution (5 mL) was added carefully. After addition of water and extraction with CH_2Cl_2 (3×20 mL), the combined organic phases were washed with brine, dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure. Flash column chromatography on silica gel (PE/EtOAc = 10:1) yielded **15** (112 mg, 0.358 mmol, 67%) as a white solid.

m.p. (uncorrected) = 108 – 109 °C.
IR (ATR): $\tilde{\nu}$ = 2950, 2919, 1727, 1431, 1277, 1262, 1176, 1159, 1147, 1130 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 – 7.08 (m, 3H), 7.05 – 7.02 (m, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 4.29 (d, *J* = 10.5 Hz, 1H), 3.73 (d, 1H), 3.70 (s, 3H), 2.55 (hept, *J* = 6.3 Hz, 1H), 2.21 (s, 3H), 1.48 (br s, 1H), 1.03 (d, *J* = 6.1 Hz, 3H), 0.94 (d, *J* = 6.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.9, 141.3, 136.8, 133.2, 129.0 (2C), 128.7 (2C), 128.1 (2C), 127.8 (2C), 127.0, 63.5, 59.8, 52.0, 45.7, 24.6, 21.8, 21.1.
MS (+ESI) *m/z* (%) = 312 (100) $[M+H]^+$.
HRMS (+ESI) *m/z* calcd for $C_{20}H_{26}NO_2$ $[M+H]^+$: 312.1958; found: 312.1958.

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2. D'Hooghe, M.; Mollet, K.; Dekeukeleire, S.; De Kimpe, N., *Org. Biomol. Chem.* **2010,** *8*, 607-615.
3. Krasovskiy, A.; Knochel, P., *Synthesis* **2006,** *2006*, 0890-0891.
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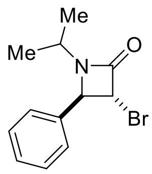
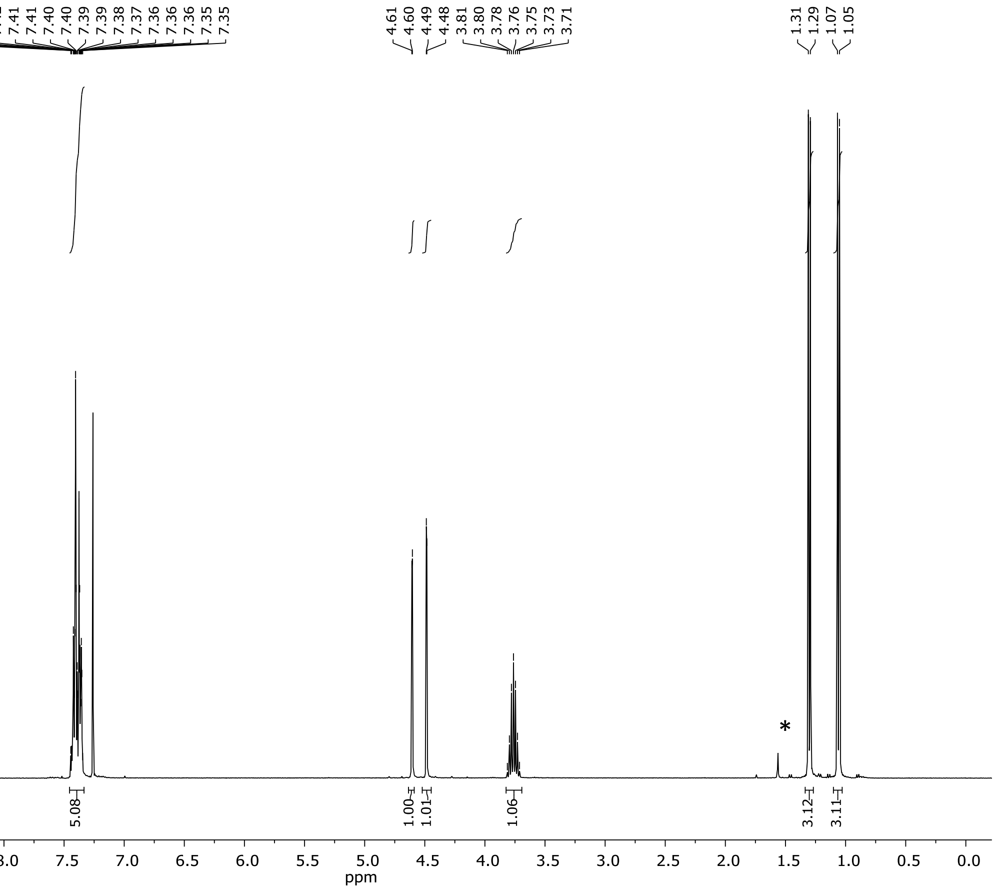
^{1}H, ^{13}C and ^{19}F-NMR Spectra

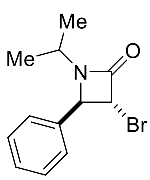
** = impurity (solvent, water, unknown)*



1a

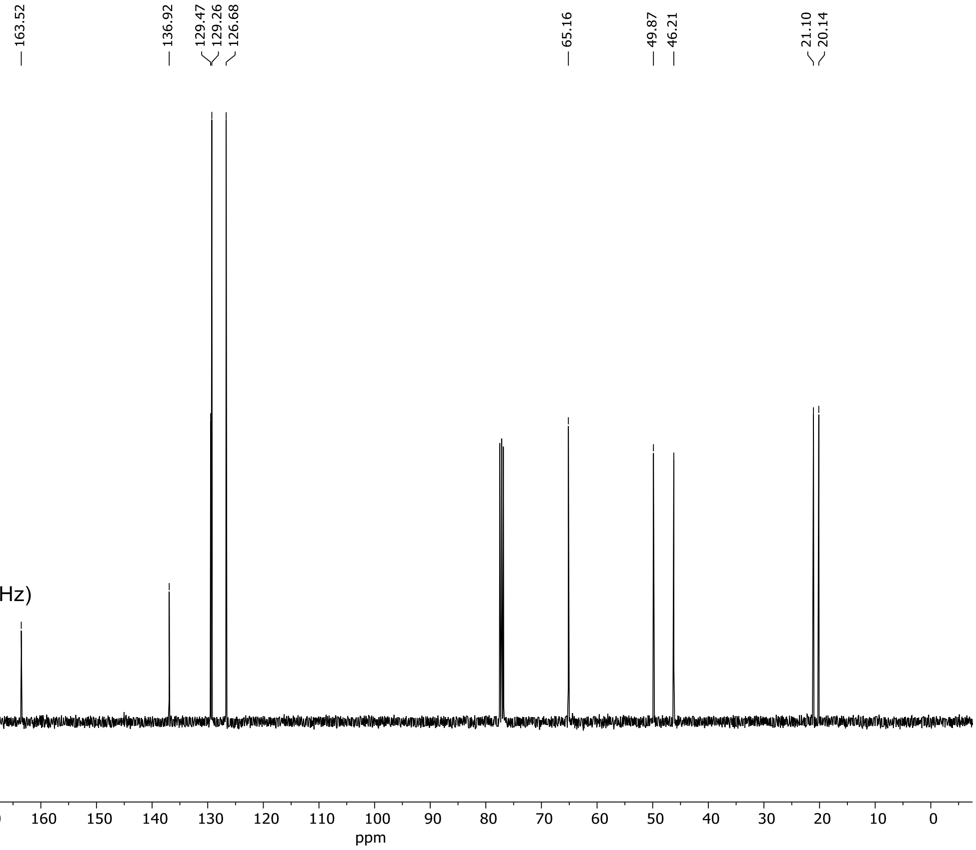
^{1}H NMR ($CDCl_3$, 400 MHz)





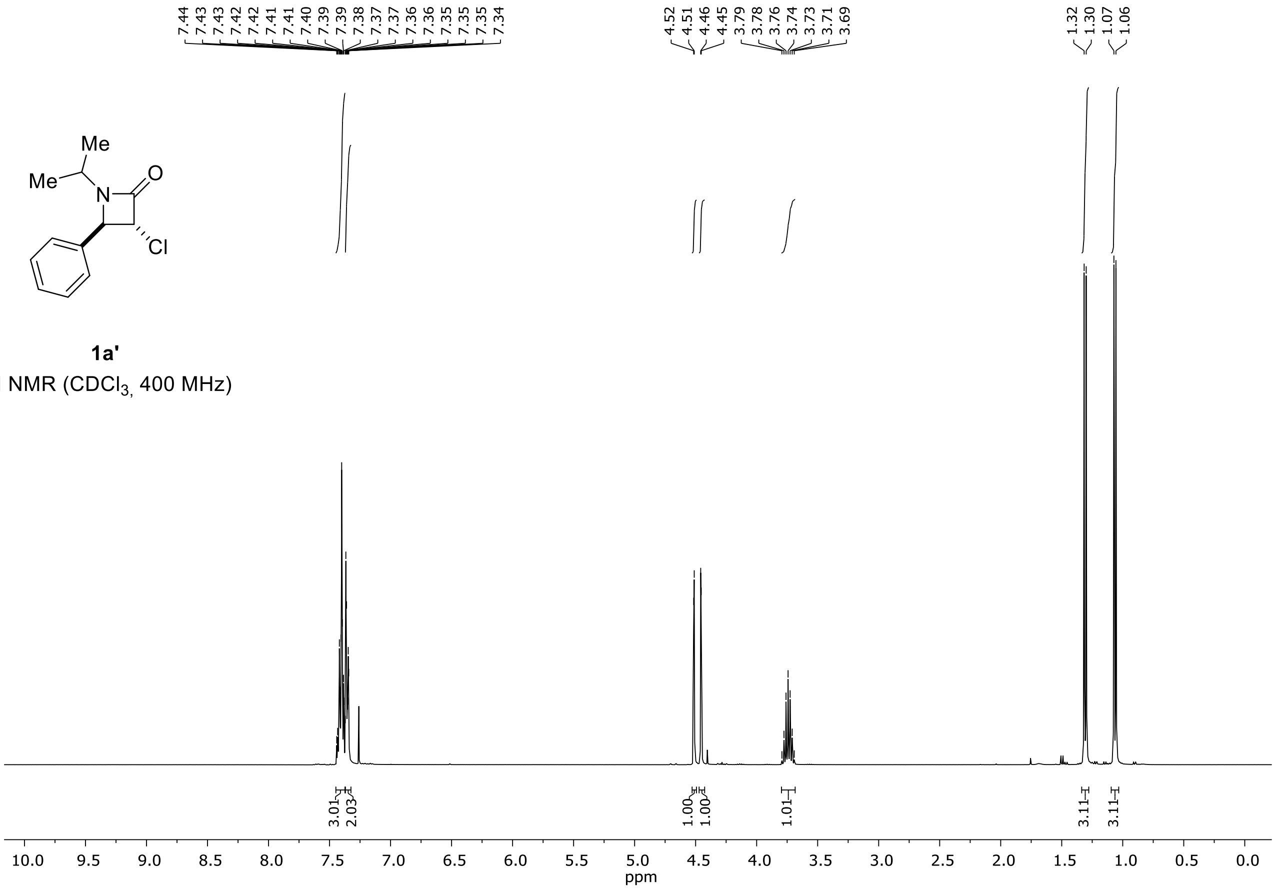
1a

^{13}C NMR ($CDCl_3$, 101 MHz)



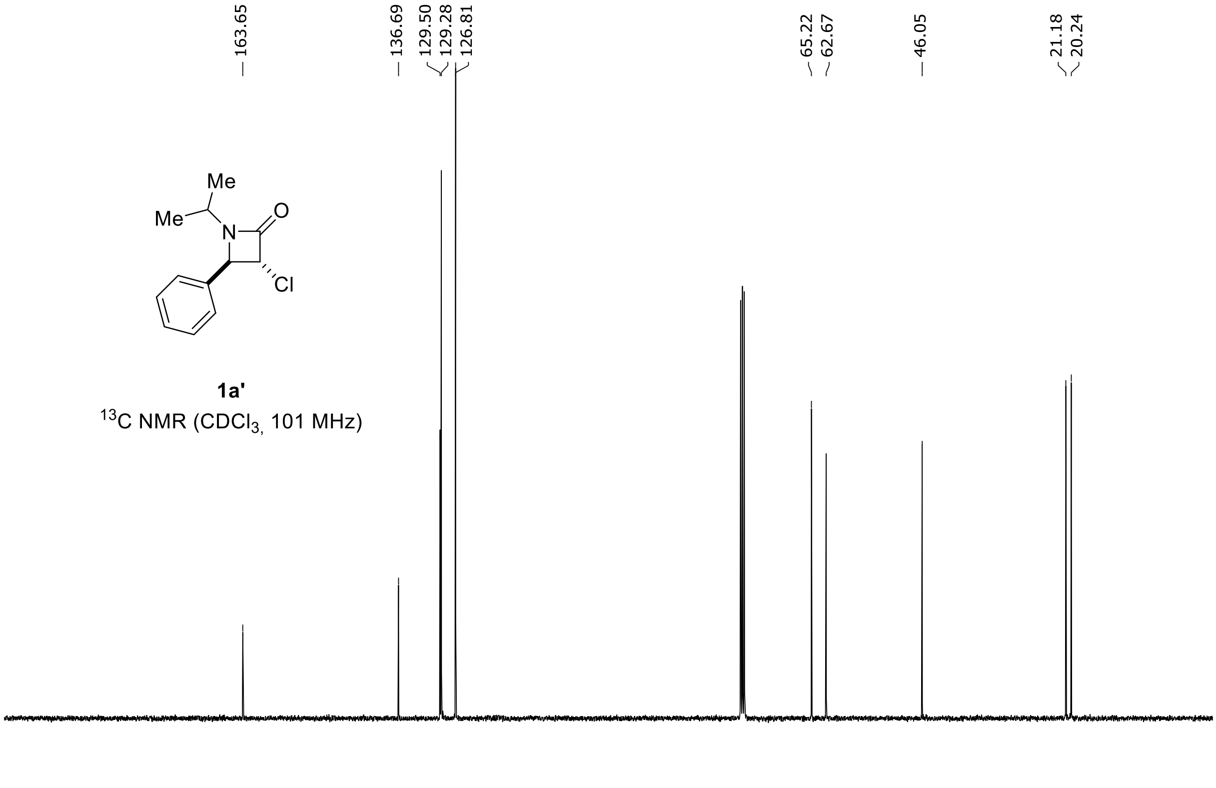
1a'

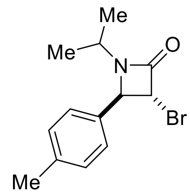
^{1}H NMR ($CDCl_3$, 400 MHz)

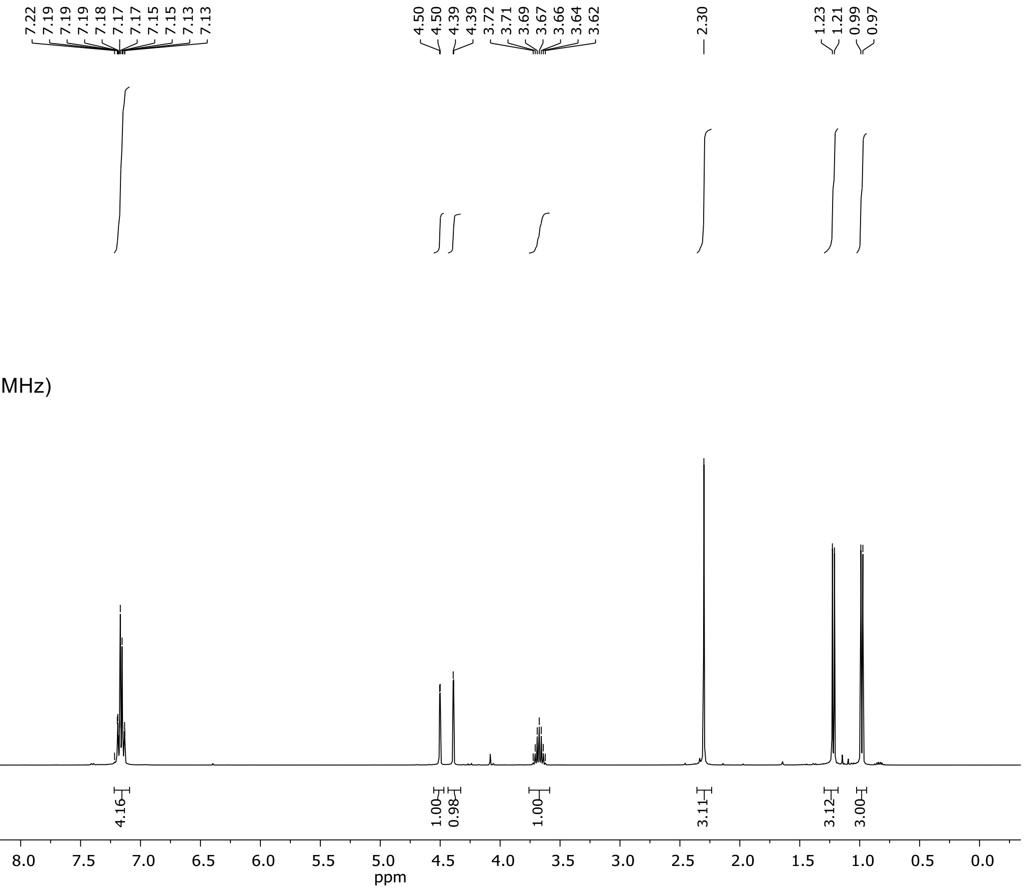


1a'

^{13}C NMR ($CDCl_3$, 101 MHz)

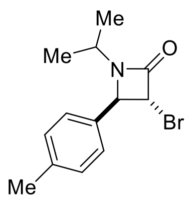


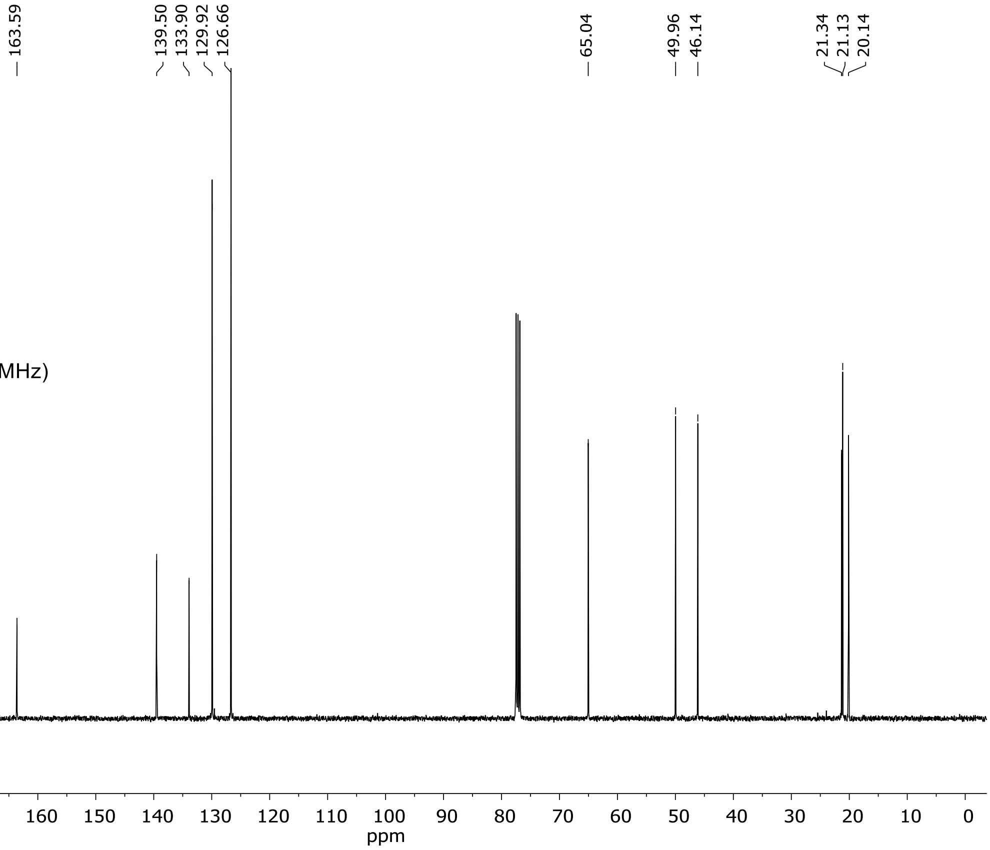




1b

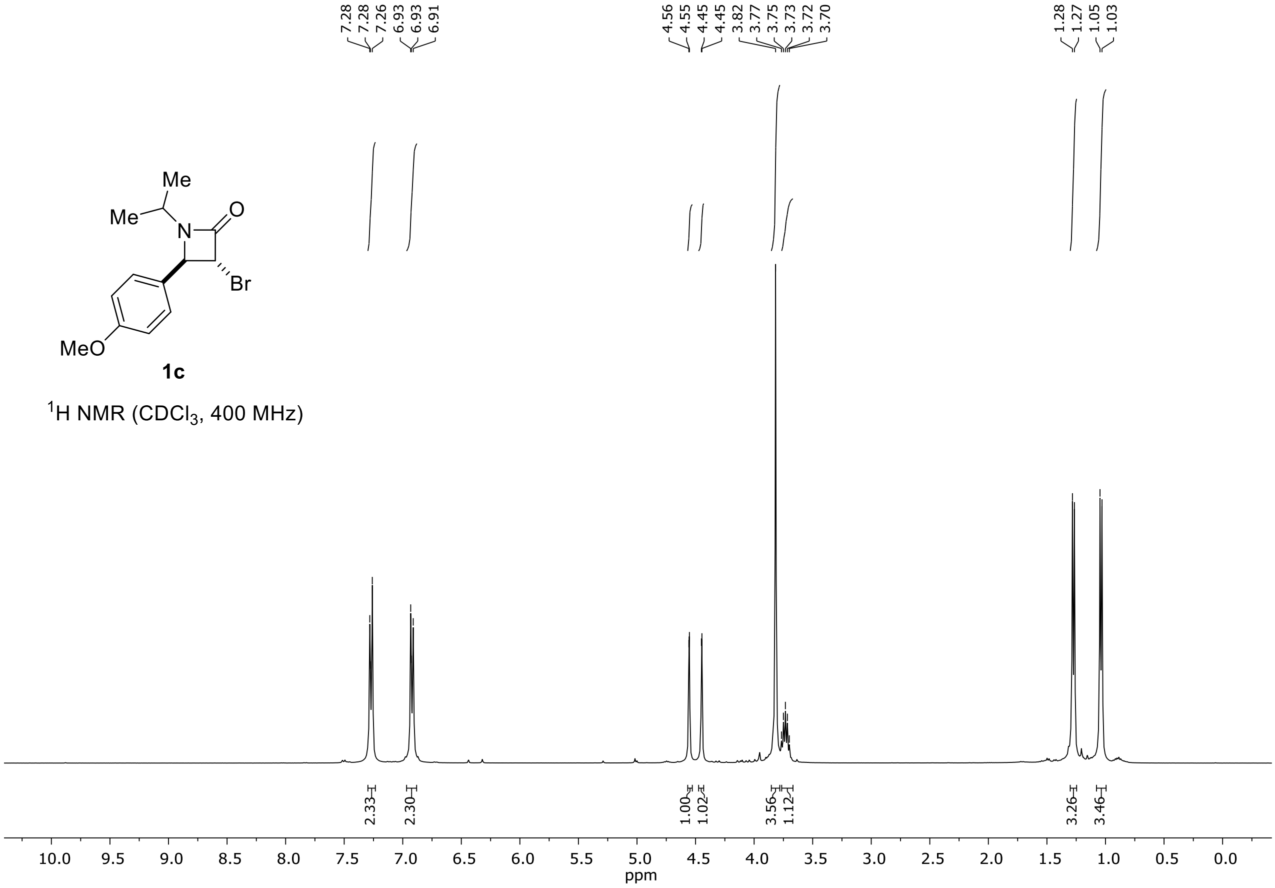
^{1}H NMR ($CDCl_3$, 400 MHz)





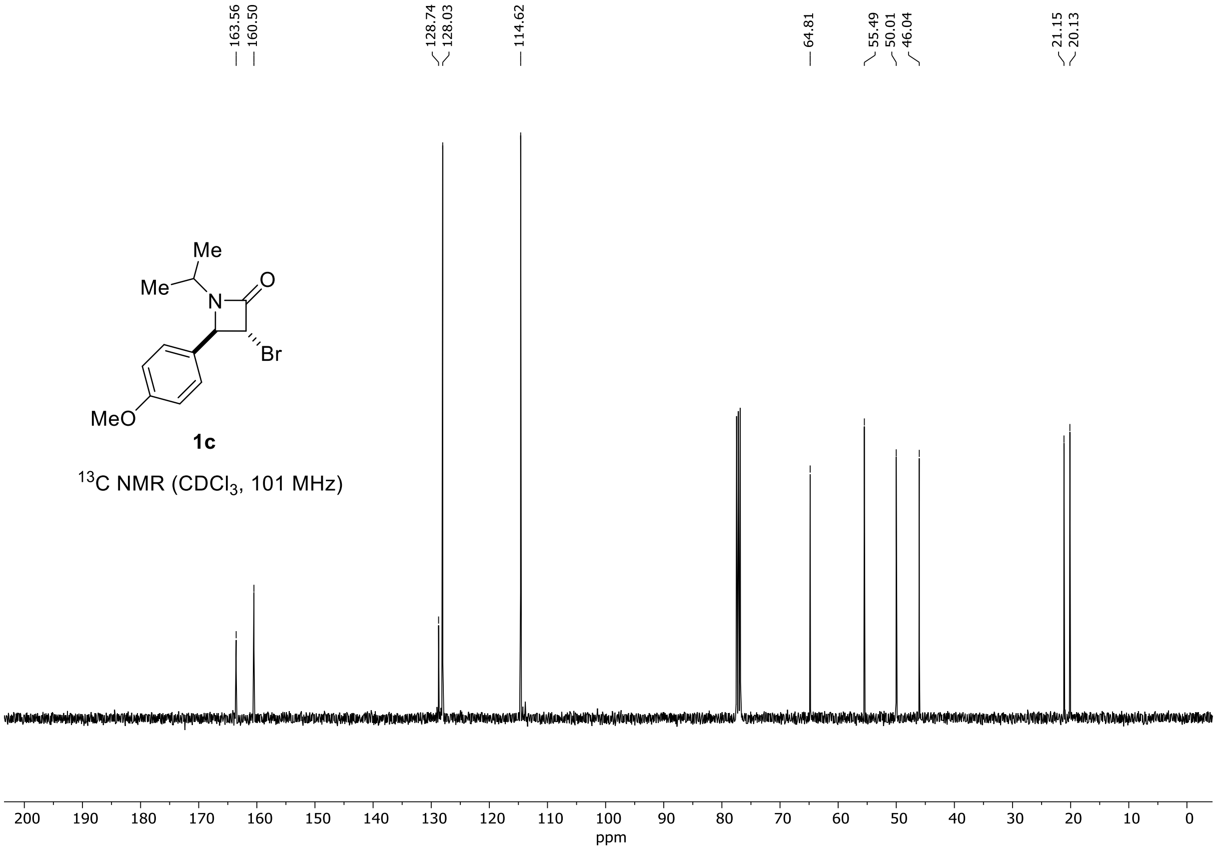
1b

^{13}C NMR ($CDCl_3$, 101 MHz)



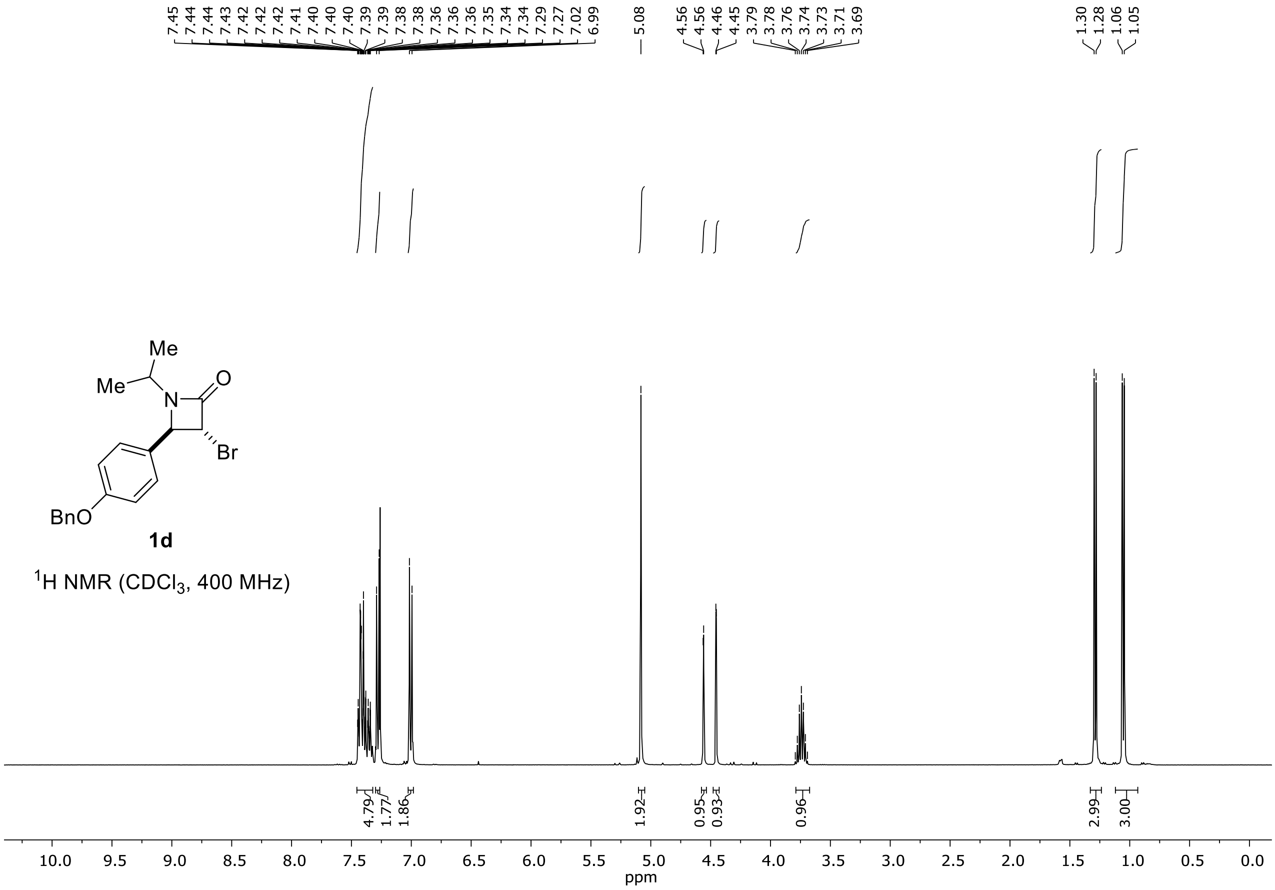
1c

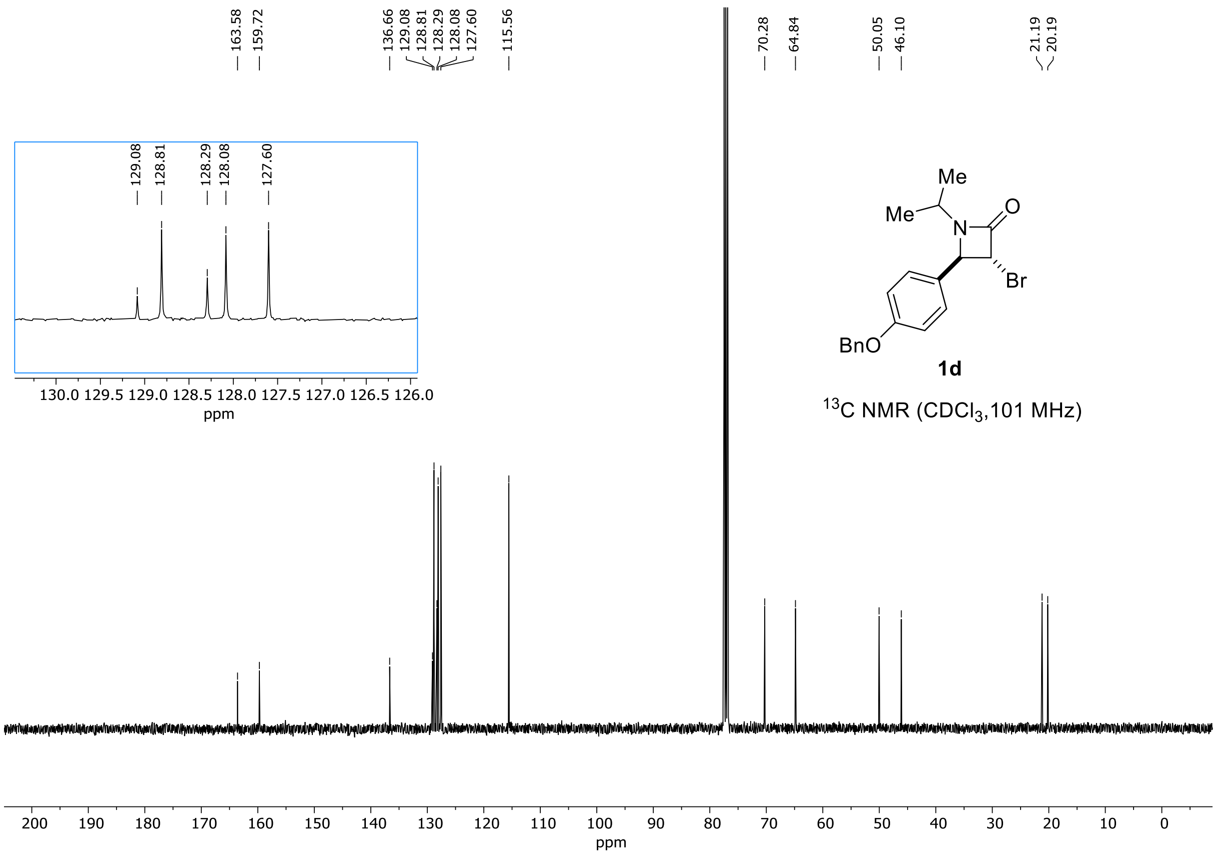
^{1}H NMR ($CDCl_3$, 400 MHz)

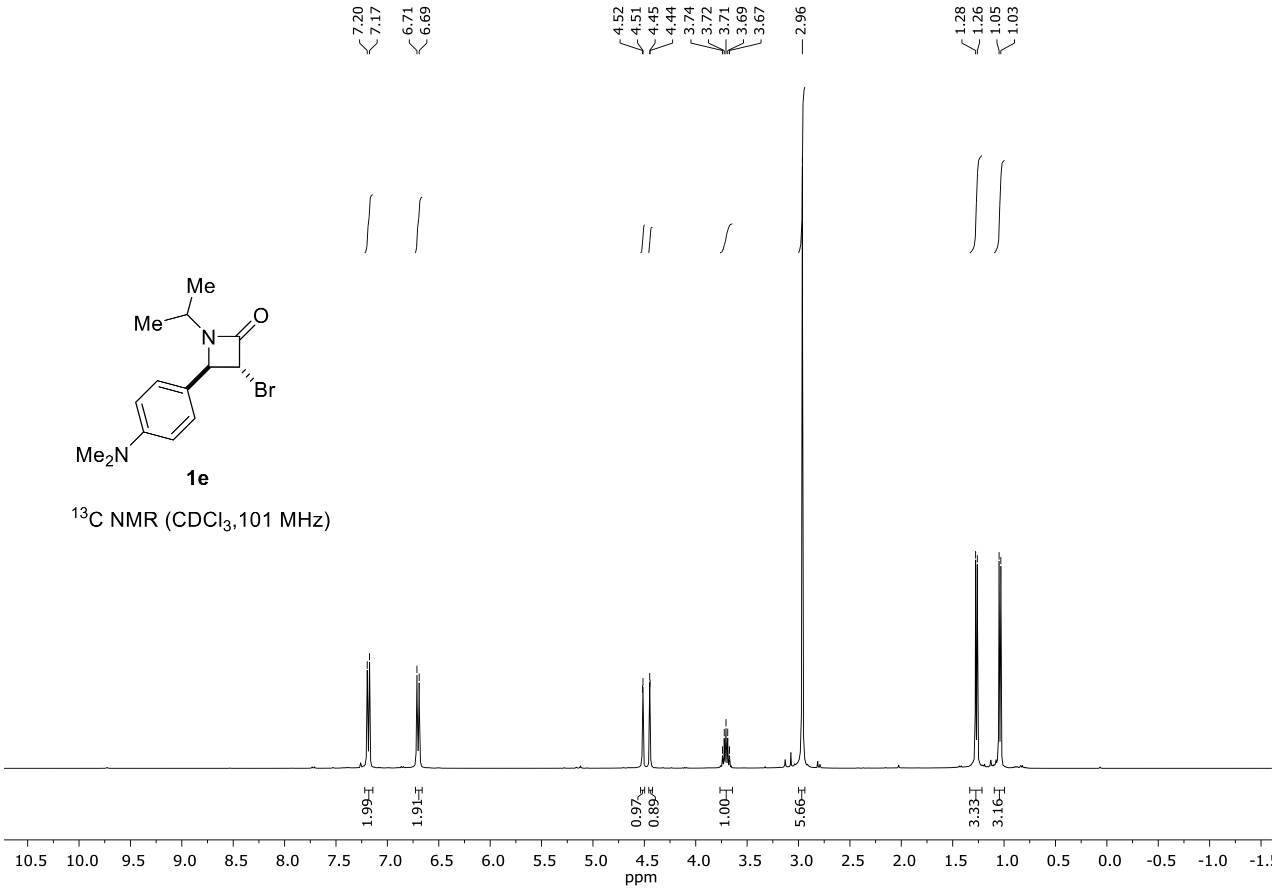


1c

^{13}C NMR ($CDCl_3$, 101 MHz)

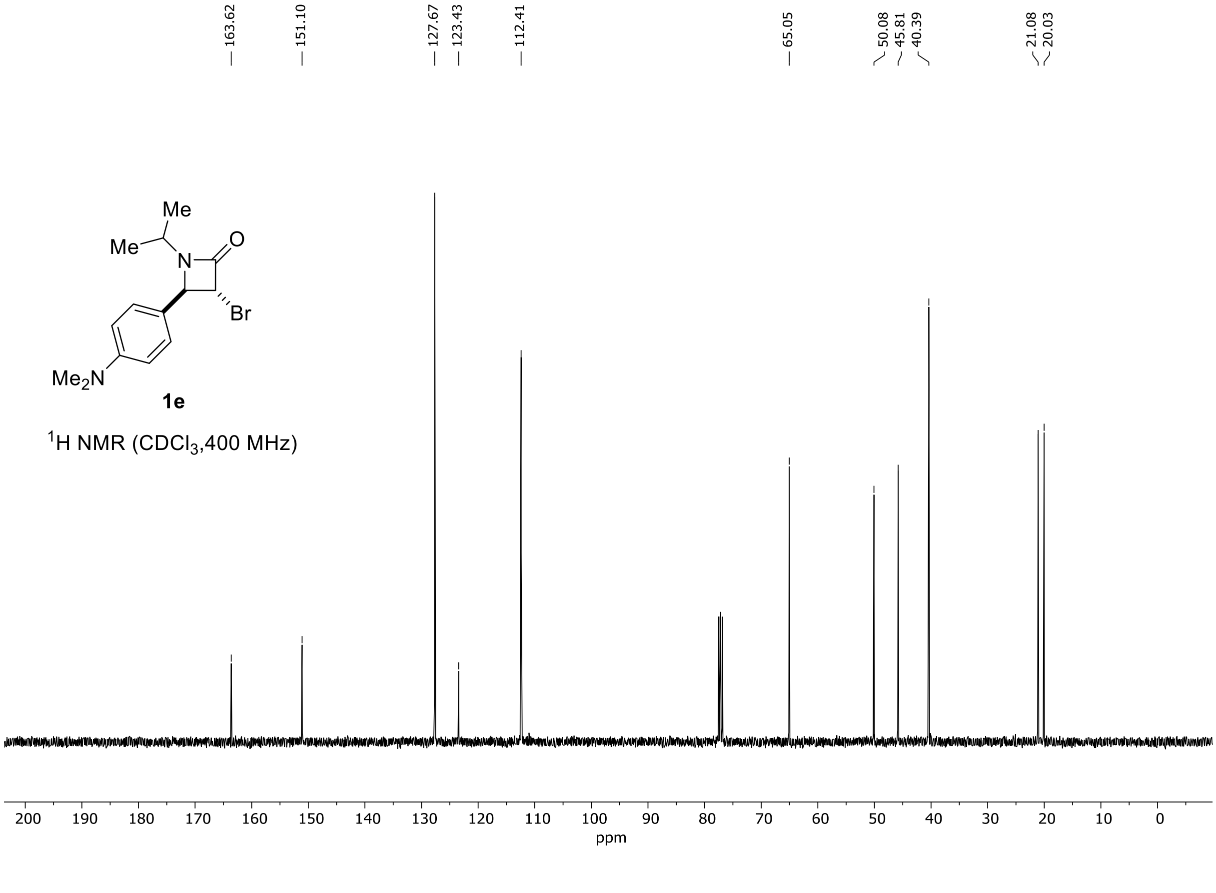






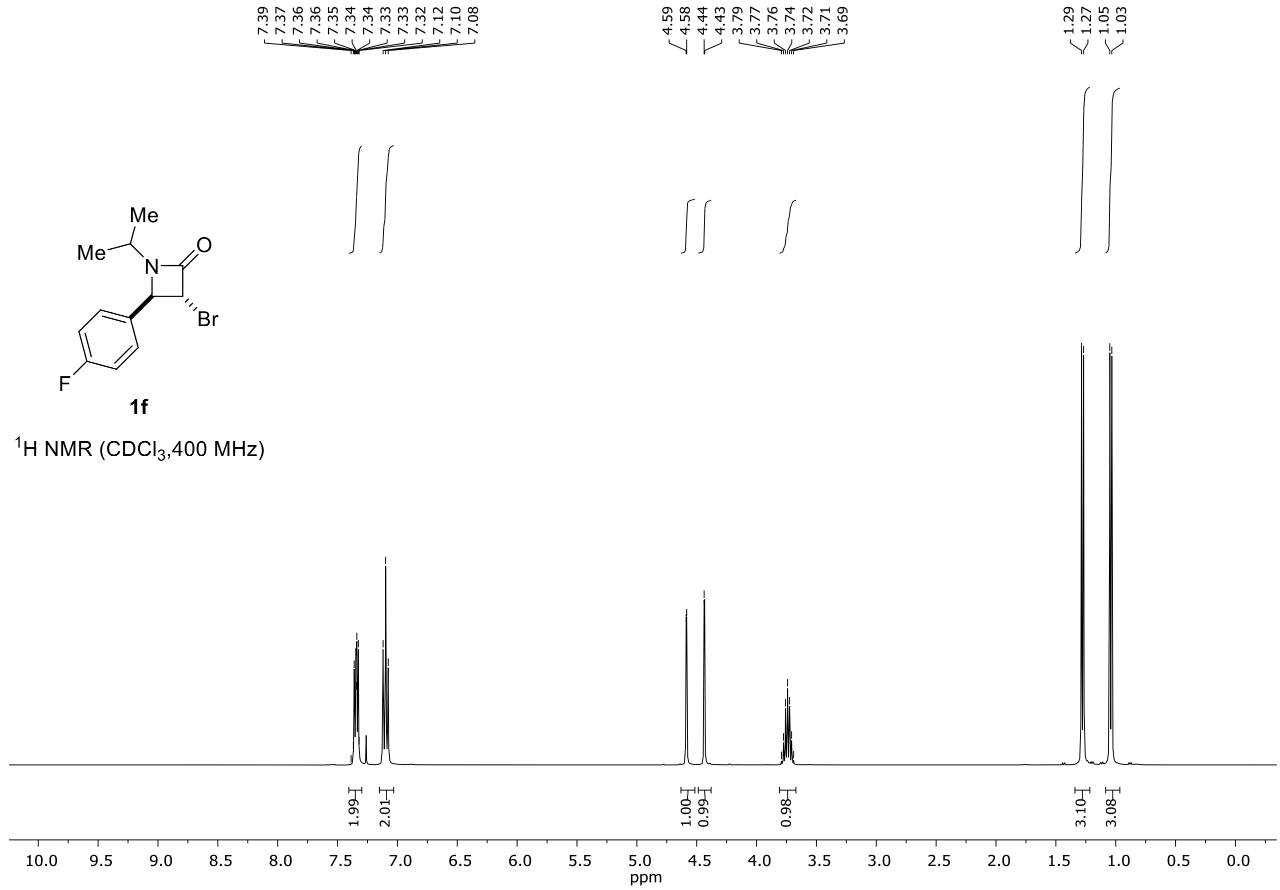
1e

^{13}C NMR (CDCl$_3$,101 MHz)



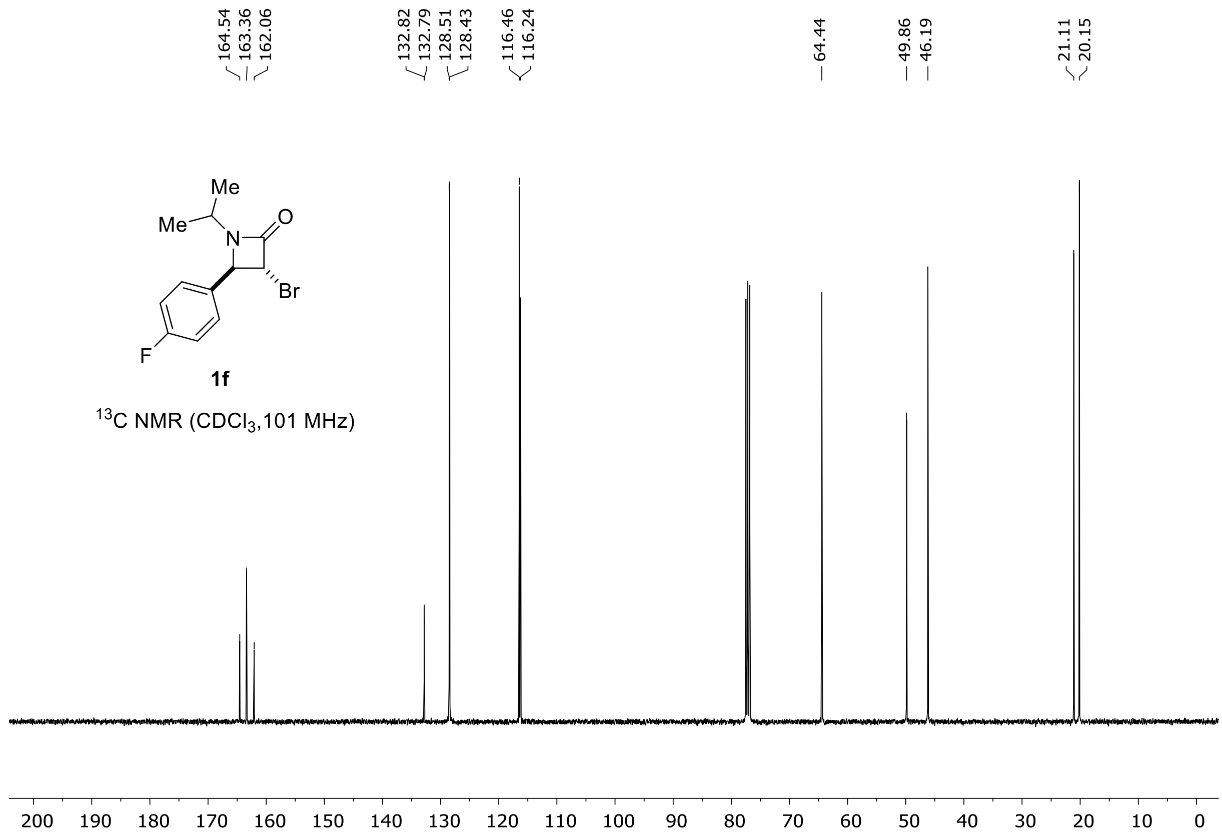
1e

^{1}H NMR (CDCl$_3$,400 MHz)



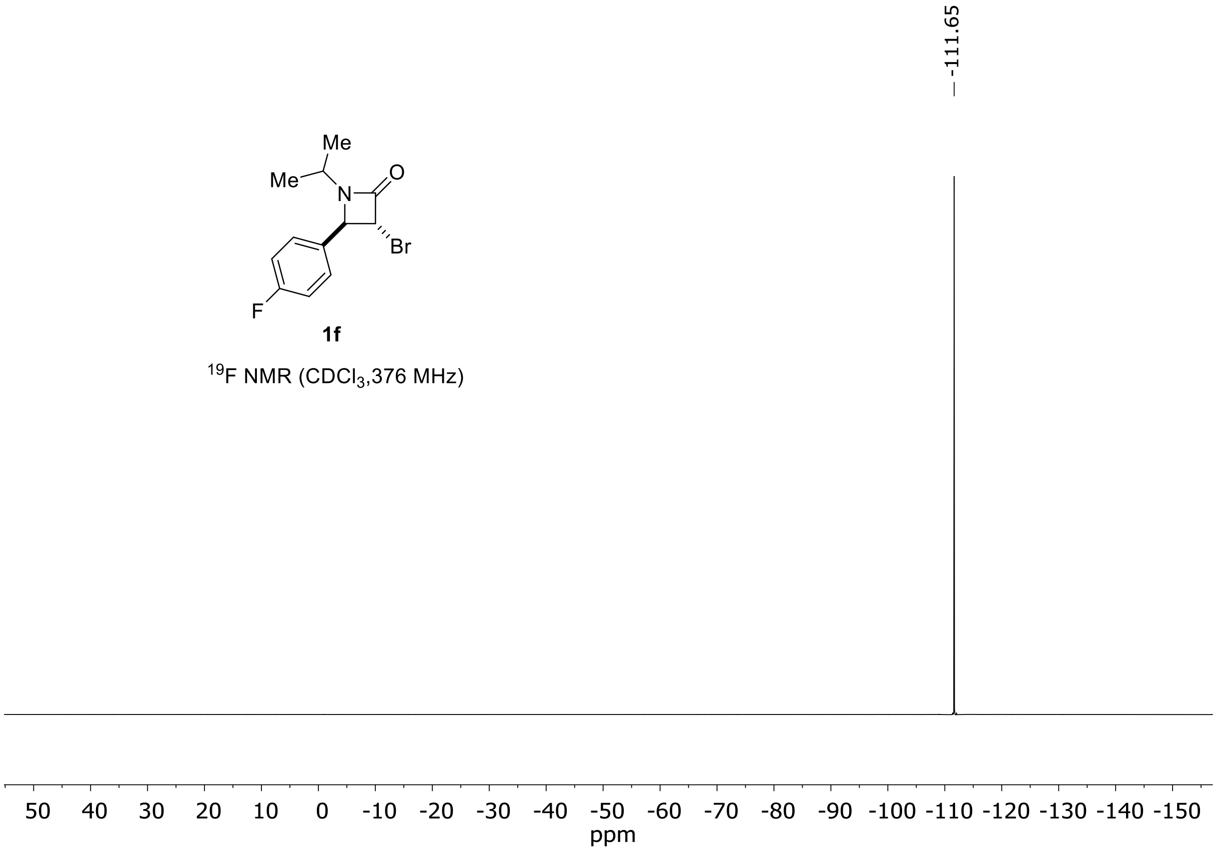
1f

^{1}H NMR ($CDCl_3$,400 MHz)



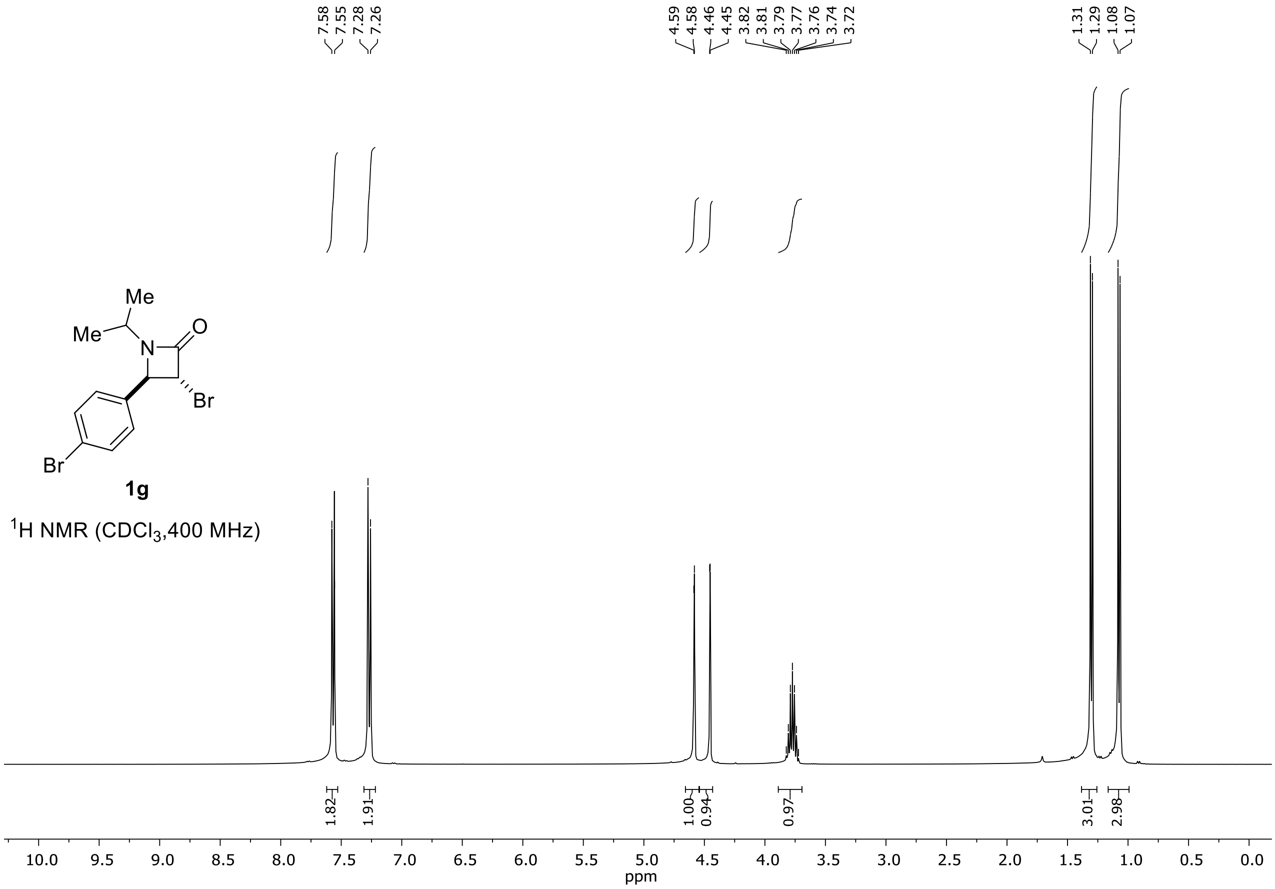
1f

^{13}C NMR ($CDCl_3$,101 MHz)



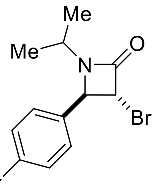
1f

^{19}F NMR ($CDCl_3$,376 MHz)



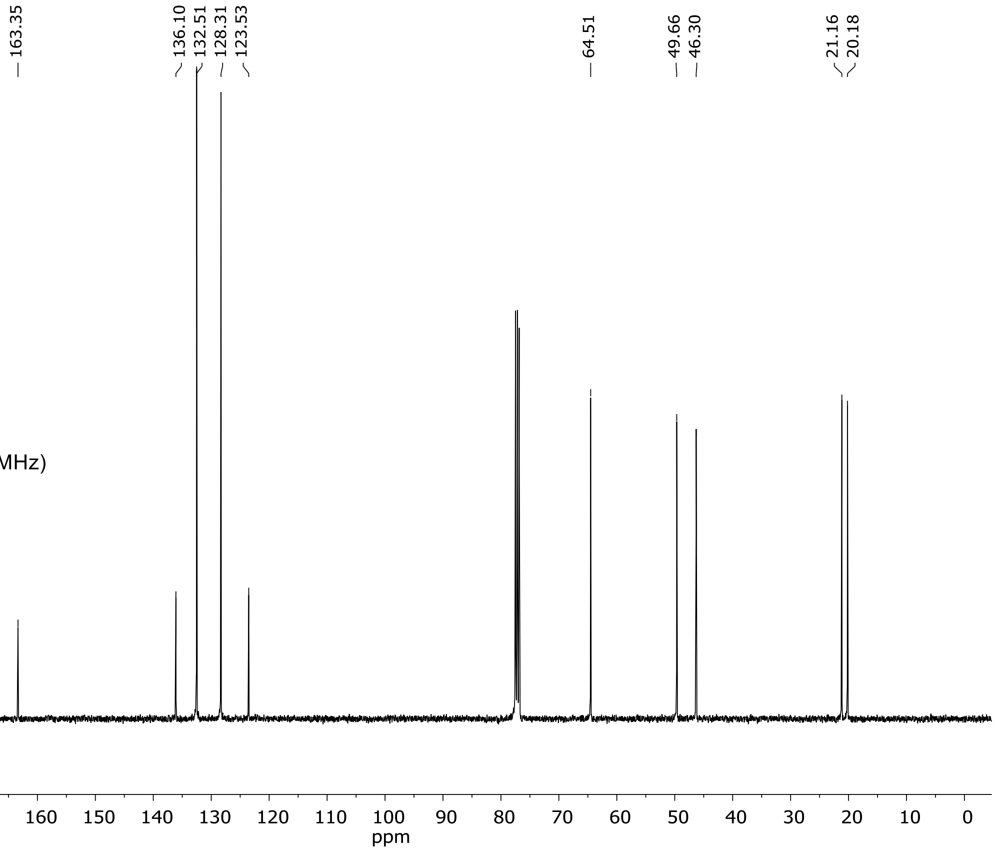
1g

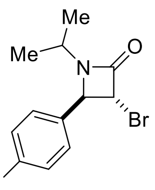
^{1}H NMR ($CDCl_3$,400 MHz)



1g

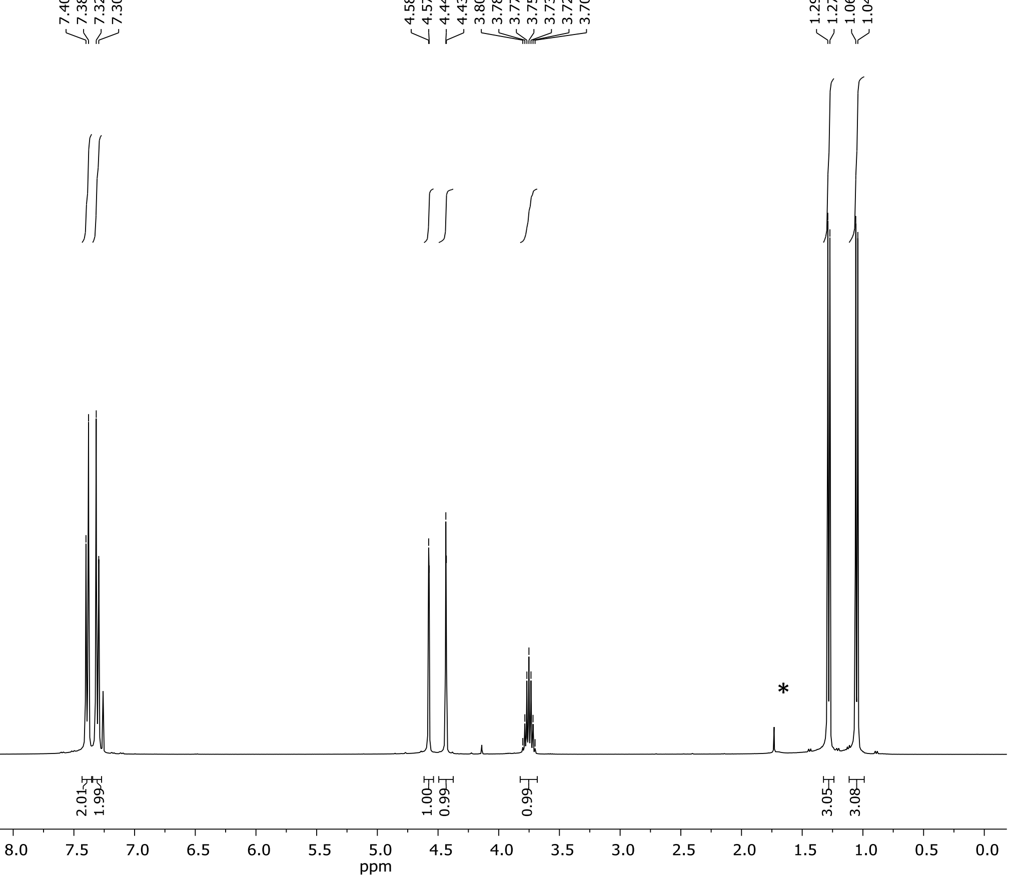
^{13}C NMR ($CDCl_3$,101 MHz)

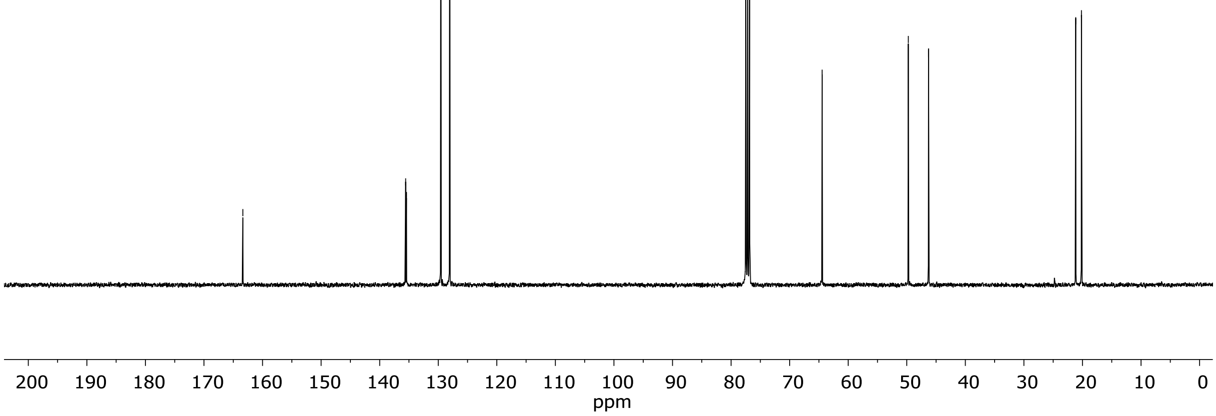


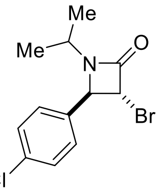


1h

^{1}H NMR ($CDCl_3$, 400 MHz)

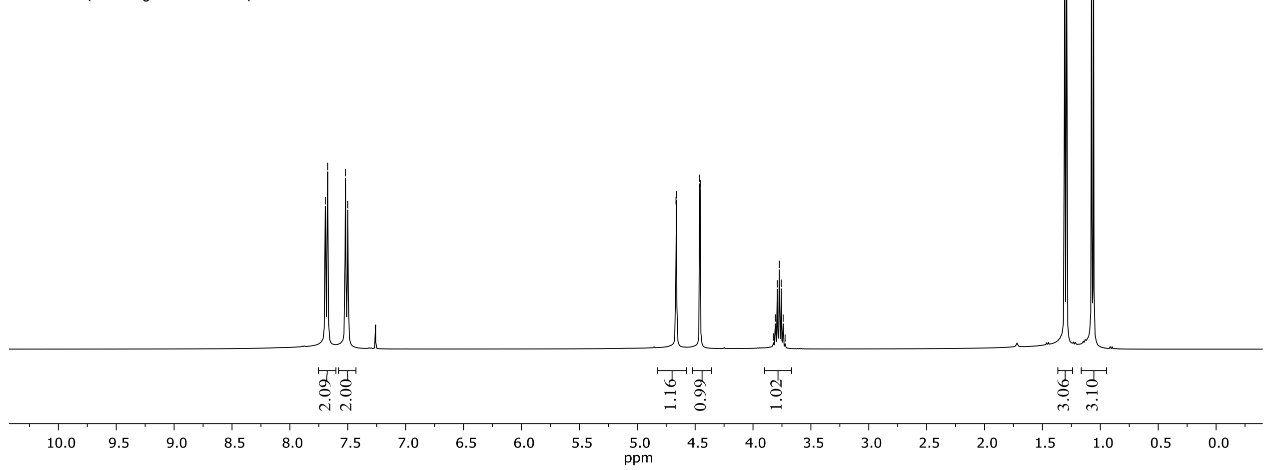


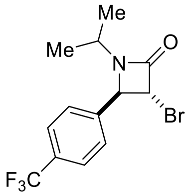




1h

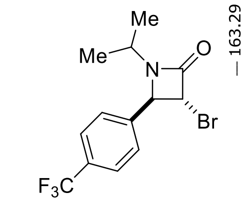
^{13}C NMR (CDCl$_3$, 101 MHz)





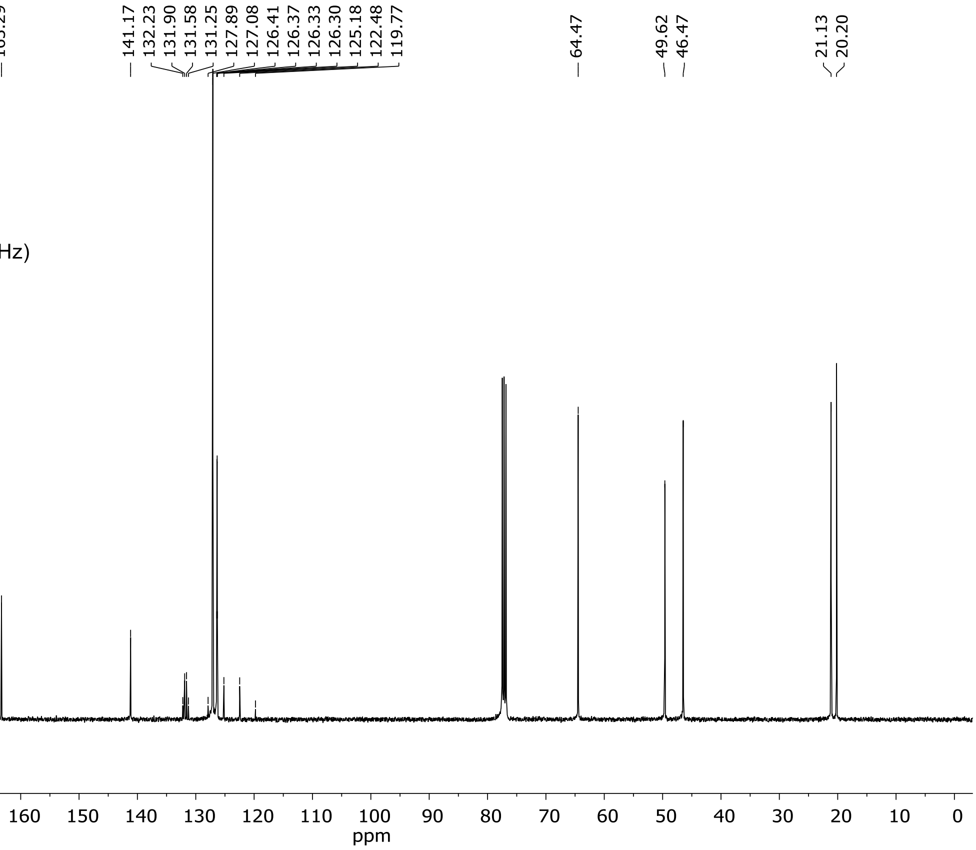
1i

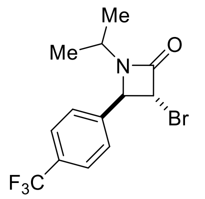
^{1}H NMR (CDCl$_3$, 400 MHz)



1i

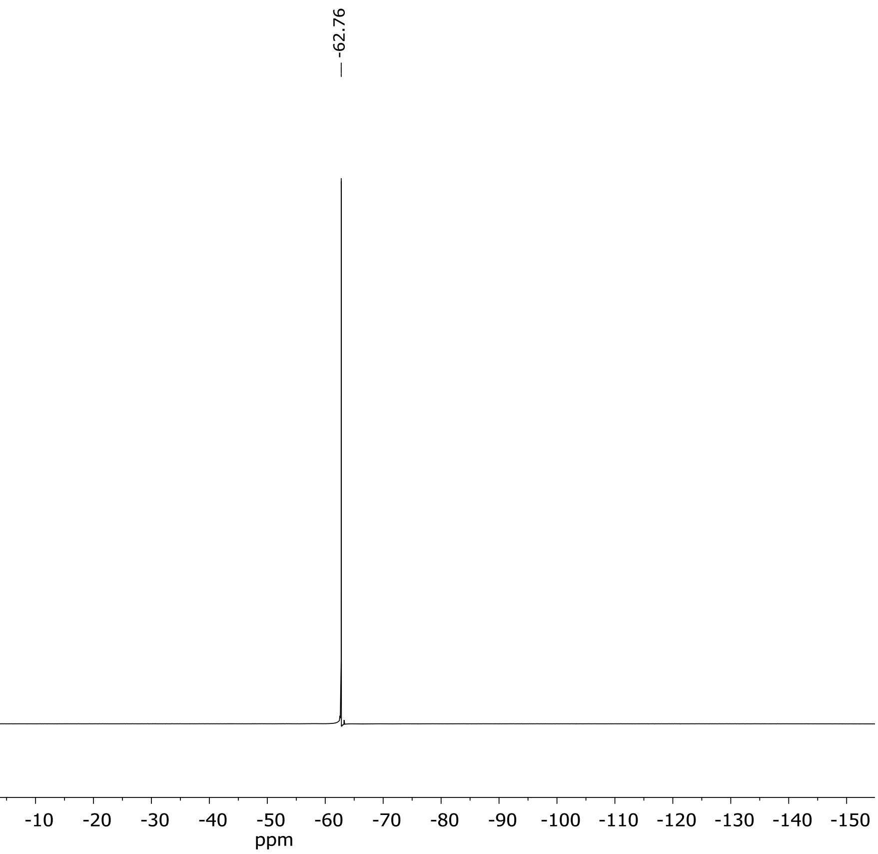
^{13}C NMR ($CDCl_3$, 101 MHz)

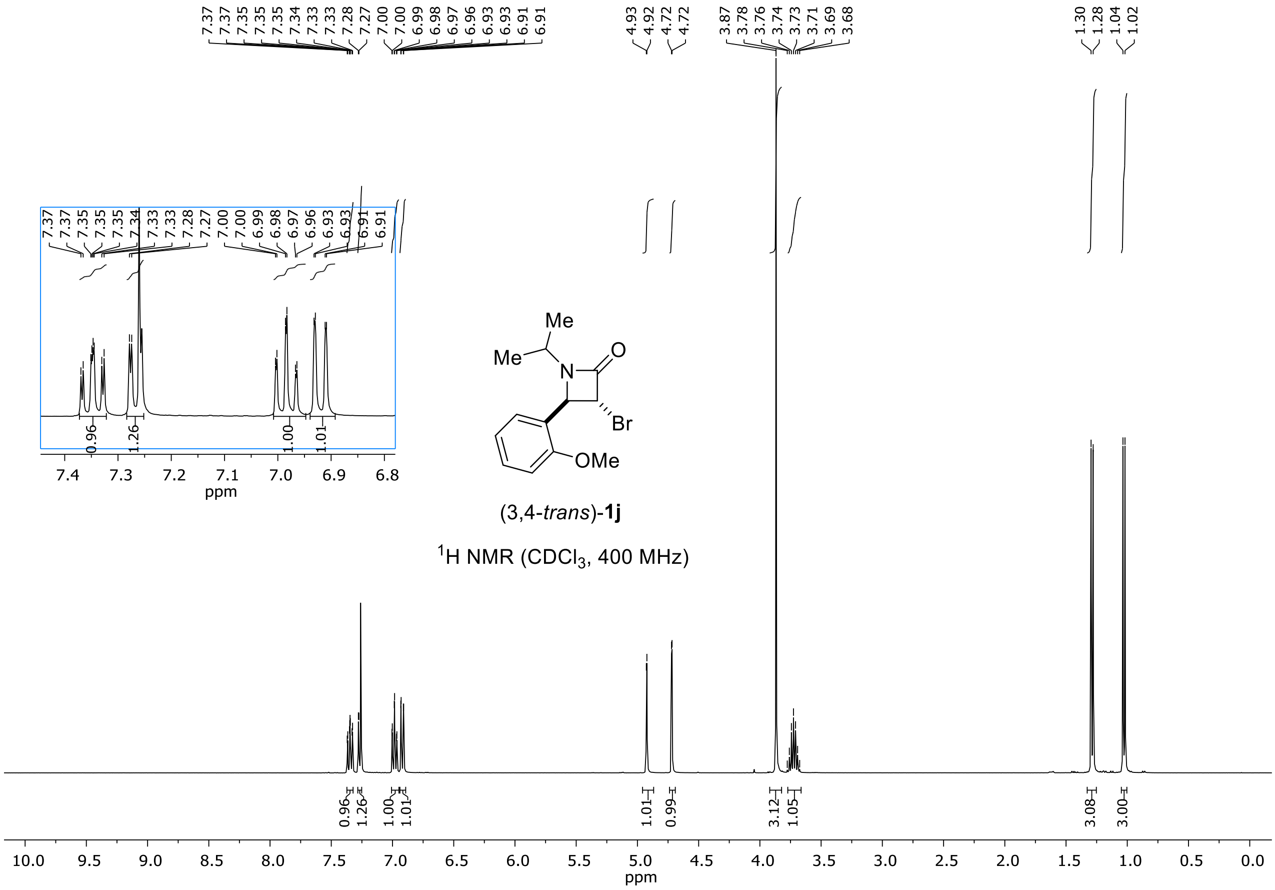




1i

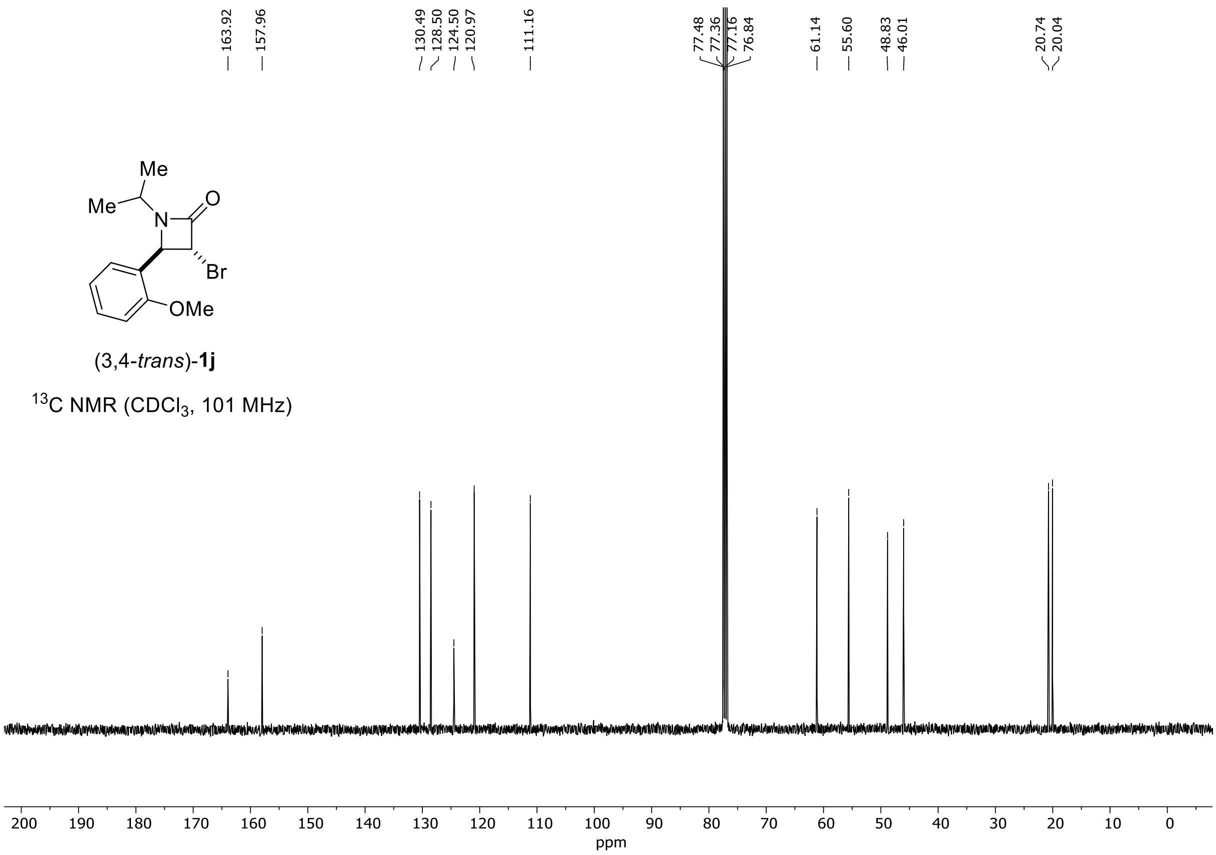
^{19}F NMR ($CDCl_3$, 376 MHz)





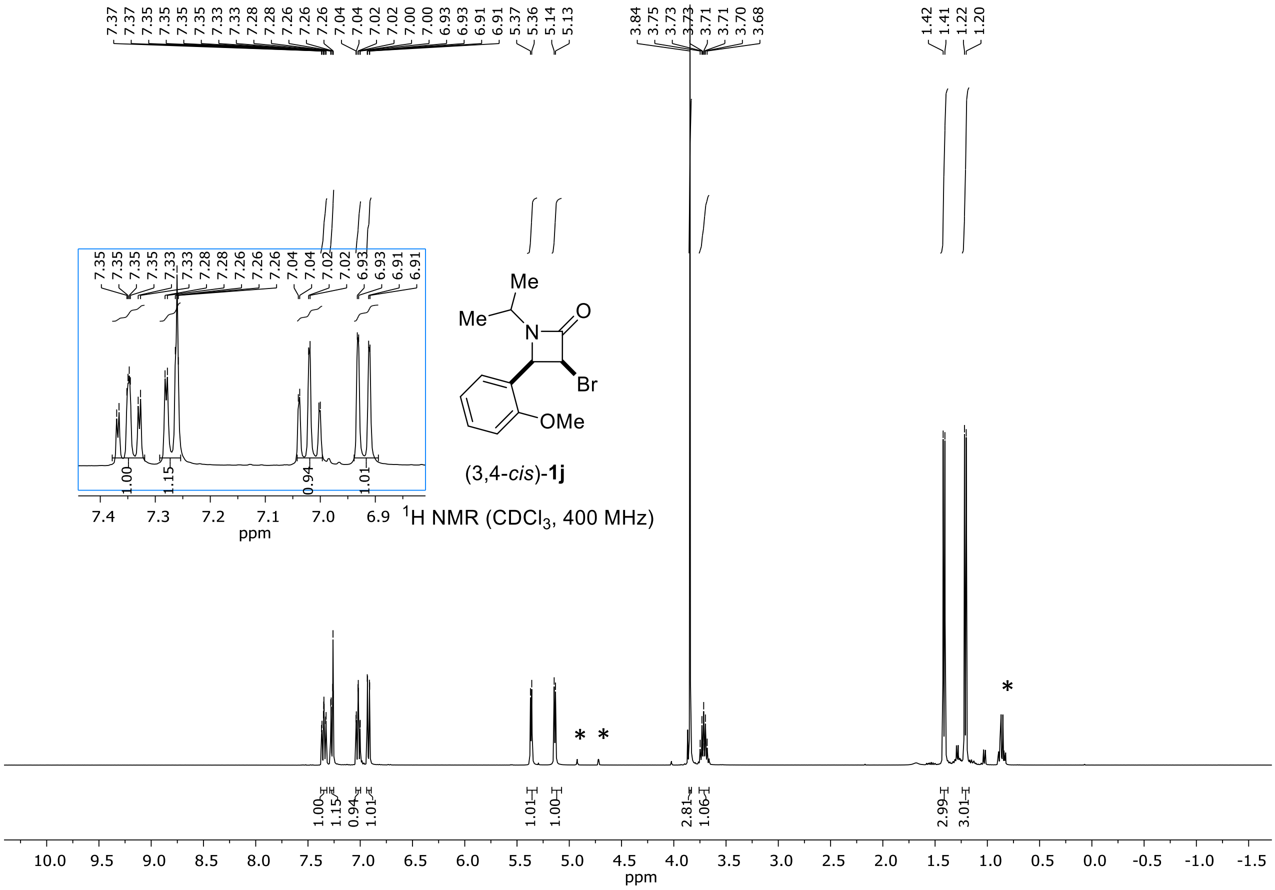
(3,4-*trans*)-**1j**

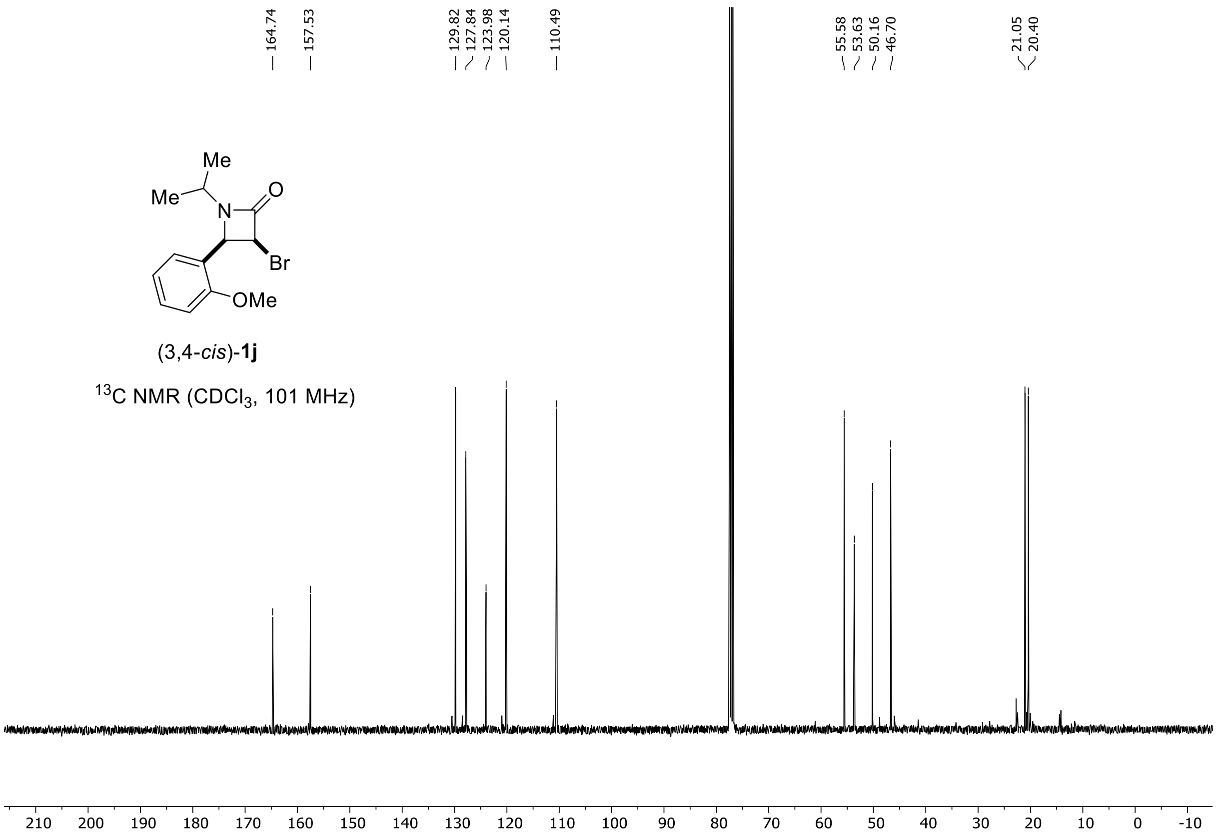
^{1}H NMR ($CDCl_3$, 400 MHz)

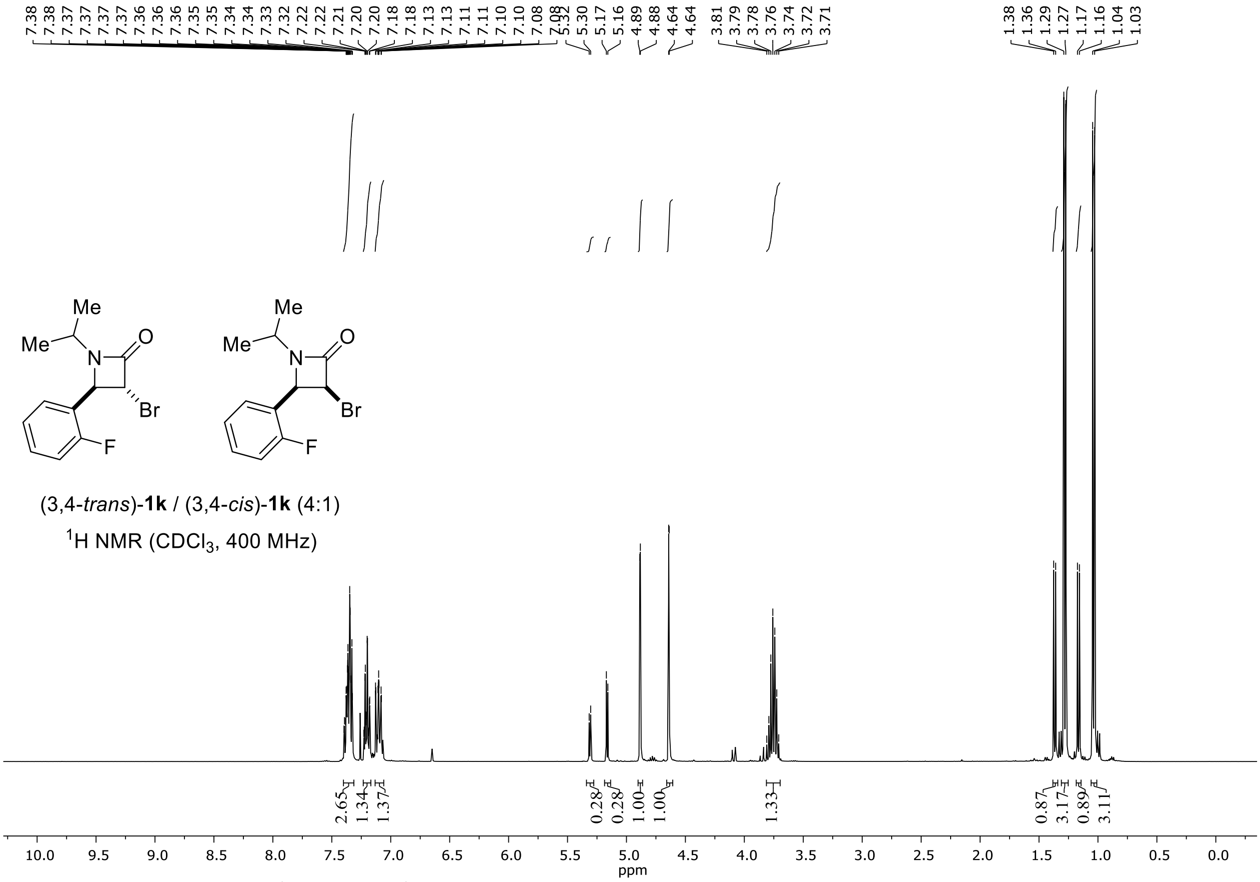


(3,4-*trans*)-**1j**

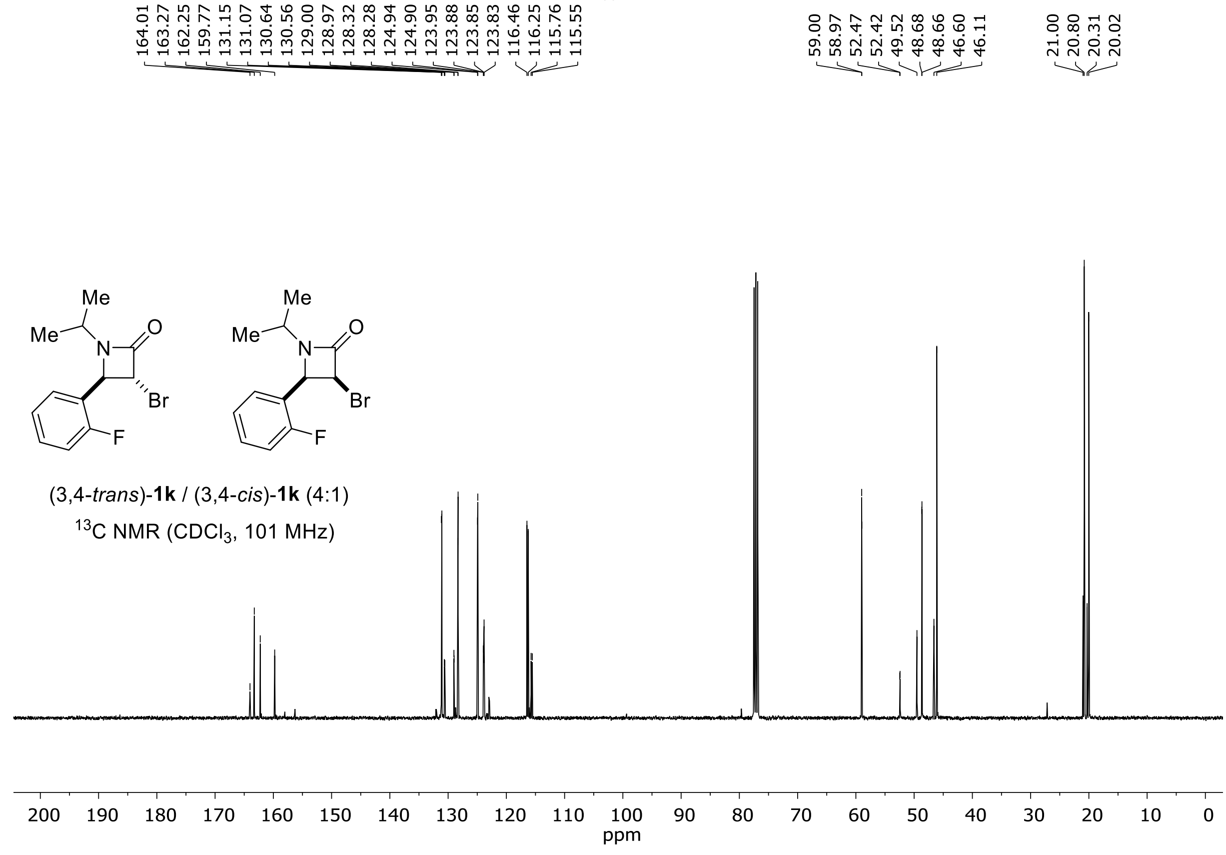
^{13}C NMR ($CDCl_3$, 101 MHz)


7.37 7.37 7.35 7.35 7.35 7.35 7.33 7.33 7.28 7.28 7.26 7.26 7.26 7.04 7.04 7.02 7.02 7.00 7.00 6.93 6.93 6.91 6.91 5.37 5.36 5.14 5.13
3.84 3.75 3.73 3.73 3.71 3.71 3.70 3.68
1.42 1.41 1.22 1.20
Me
Me
N
O
Br
OMe
(3,4-*cis*)-**1j**
^{1}H NMR (CDCl$_3$, 400 MHz)
1.00 1.15 0.94 1.01 1.01 1.00 2.81 1.06 2.99 3.01
ppm

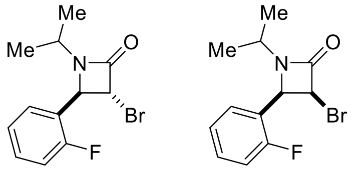

164.74 157.53 129.82 127.84 123.98 120.14 110.49 55.58 53.63 50.16 46.70 21.05 20.40
Me
Me
N
O
Br
OMe
(3,4-*cis*)-**1j**
^{13}C NMR (CDCl$_3$, 101 MHz)
ppm



7.38
7.38
7.37
7.37
7.37
7.37
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.32
7.22
7.22
7.21
7.20
7.20
7.18
7.18
7.13
7.13
7.11
7.11
7.10
7.10
7.08
7.08
5.32
5.30
5.17
5.16
4.89
4.88
4.64
4.64
3.81
3.79
3.78
3.76
3.74
3.72
3.71
1.38
1.36
1.29
1.27
1.17
1.16
1.04
1.03
Me
Me
N
O
Br
F
(3,4-*trans*)-**1k** / (3,4-*cis*)-**1k** (4:1)
^{1}H NMR ($CDCl_3$, 400 MHz)
2.65
1.34
1.37
0.28
0.28
1.00
1.00
1.33
0.87
3.17
0.89
3.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

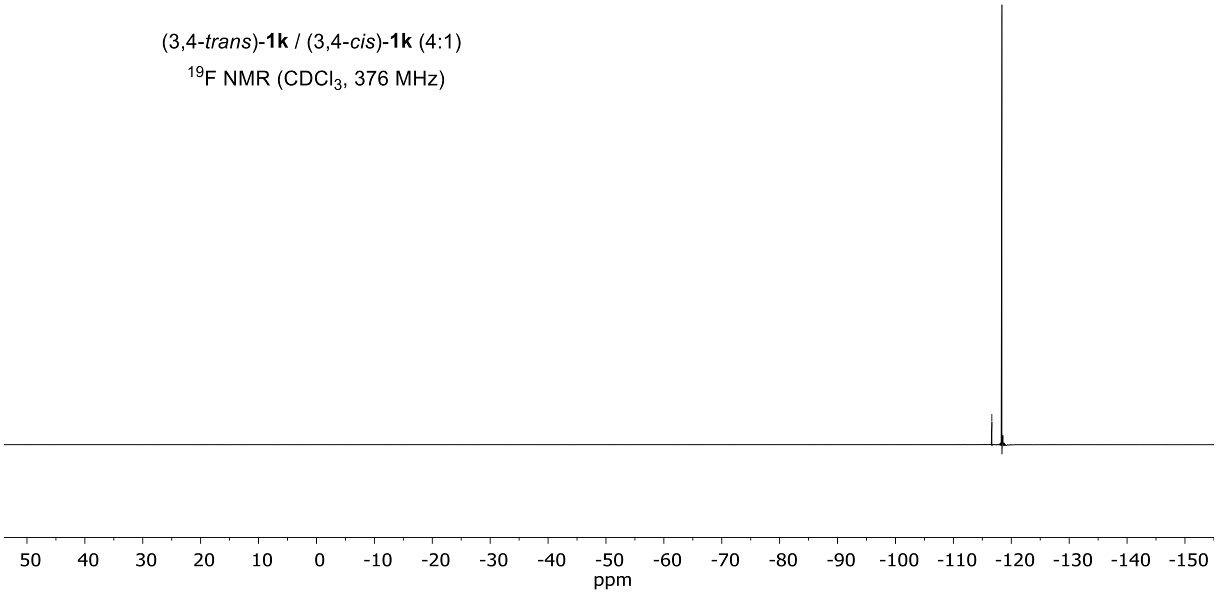


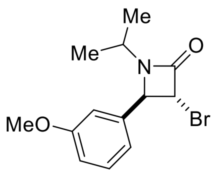
164.01
163.27
162.25
159.77
131.15
131.07
130.64
130.56
129.00
128.97
128.32
128.28
124.94
124.90
123.95
123.88
123.85
123.83
116.46
116.25
115.76
115.55
59.00
58.97
52.47
52.42
49.52
48.68
48.66
46.60
46.11
21.00
20.80
20.31
20.02
Me
Me
N
O
Br
F
(3,4-*trans*)-**1k** / (3,4-*cis*)-**1k** (4:1)
^{13}C NMR ($CDCl_3$, 101 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm



(3,4-*trans*)-**1k** / (3,4-*cis*)-**1k** (4:1)

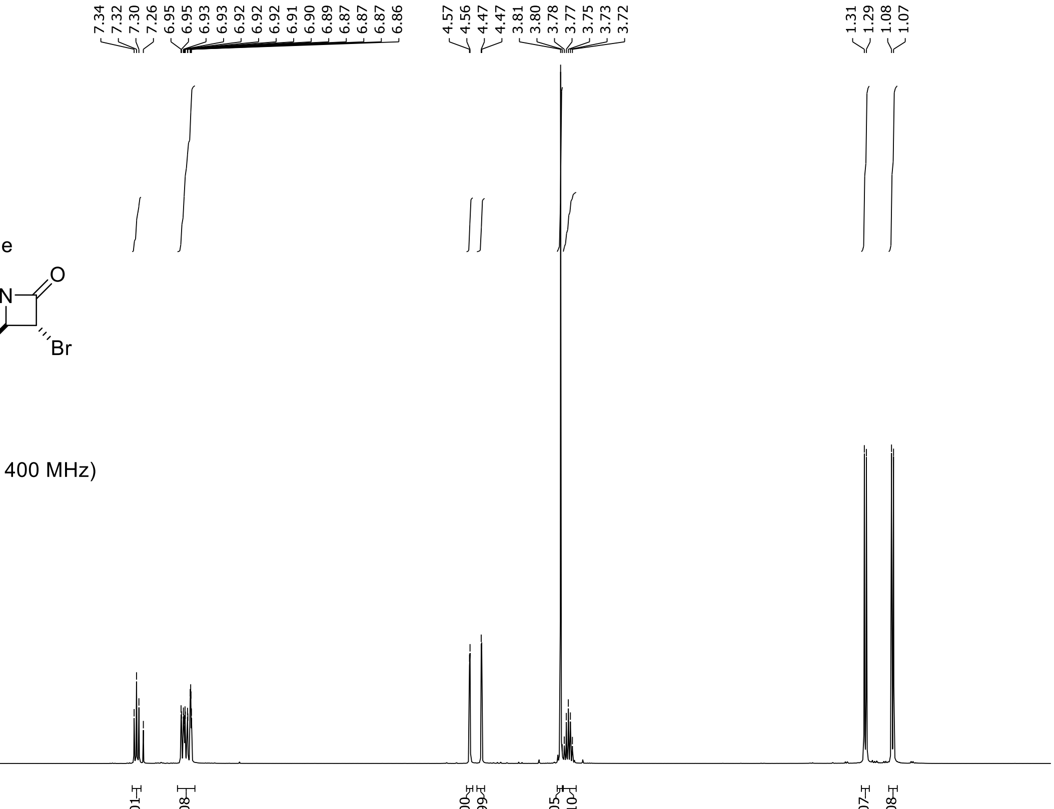
^{19}F NMR ($CDCl_3$, 376 MHz)

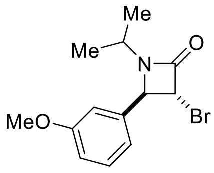




1l

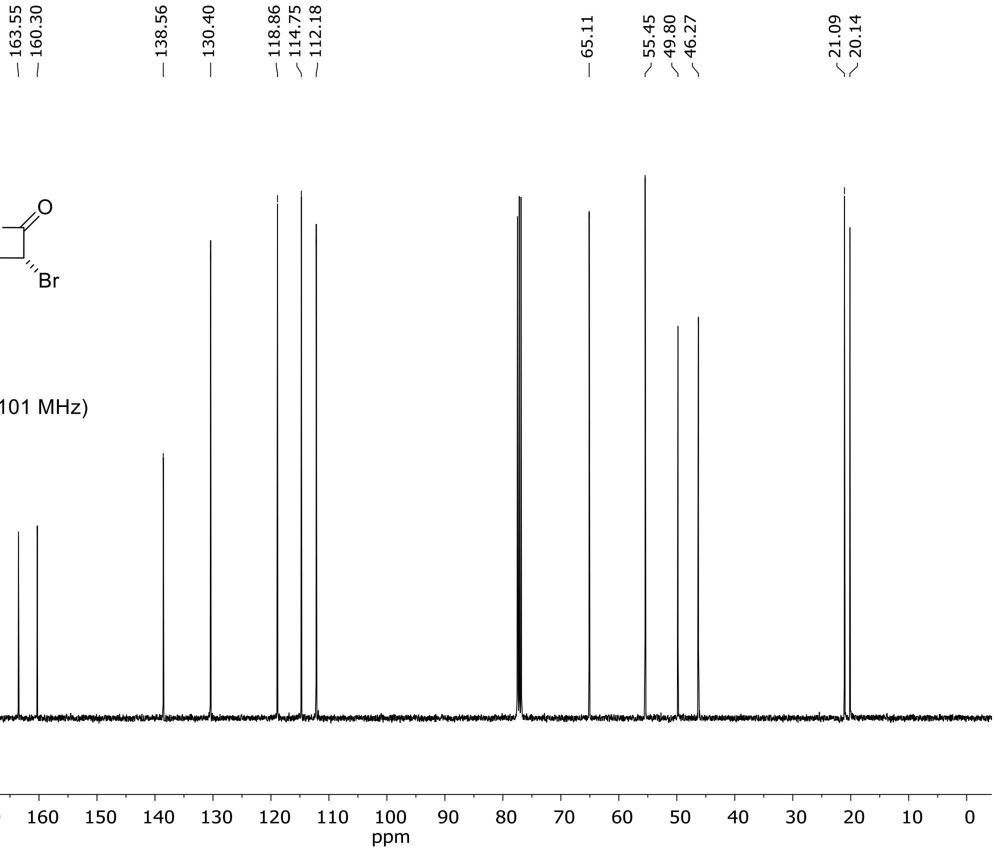
^{1}H NMR ($CDCl_3$, 400 MHz)

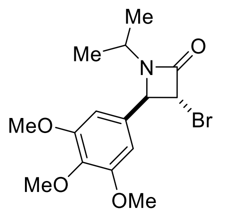




1l

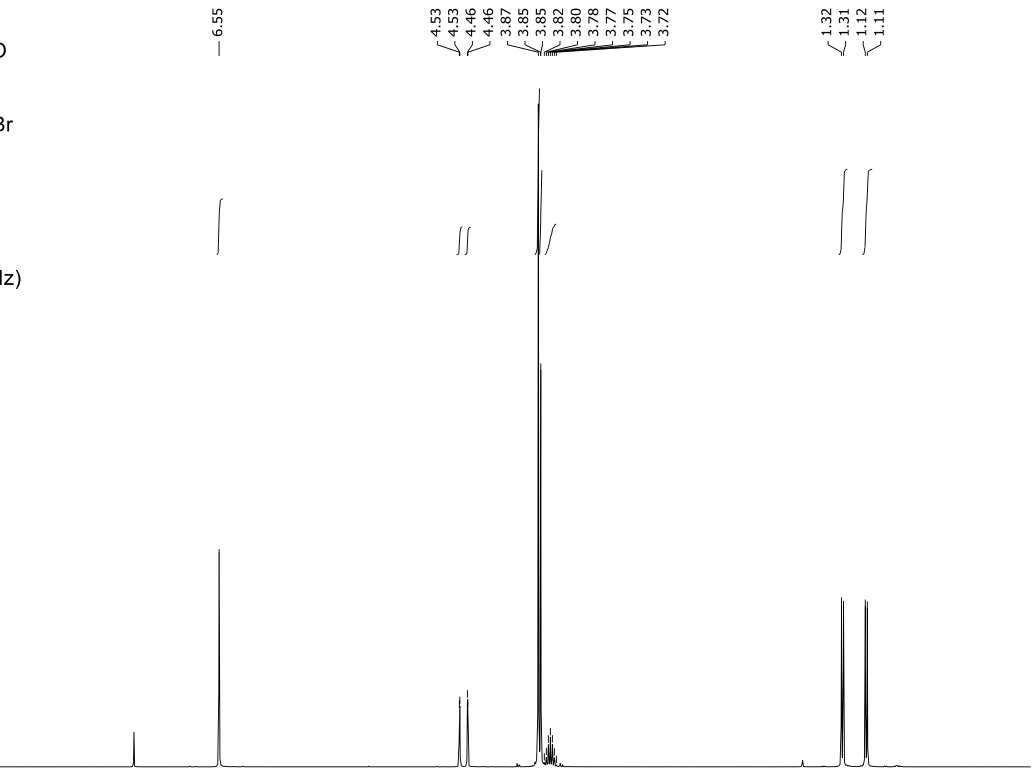
^{13}C NMR (CDCl$_3$, 101 MHz)

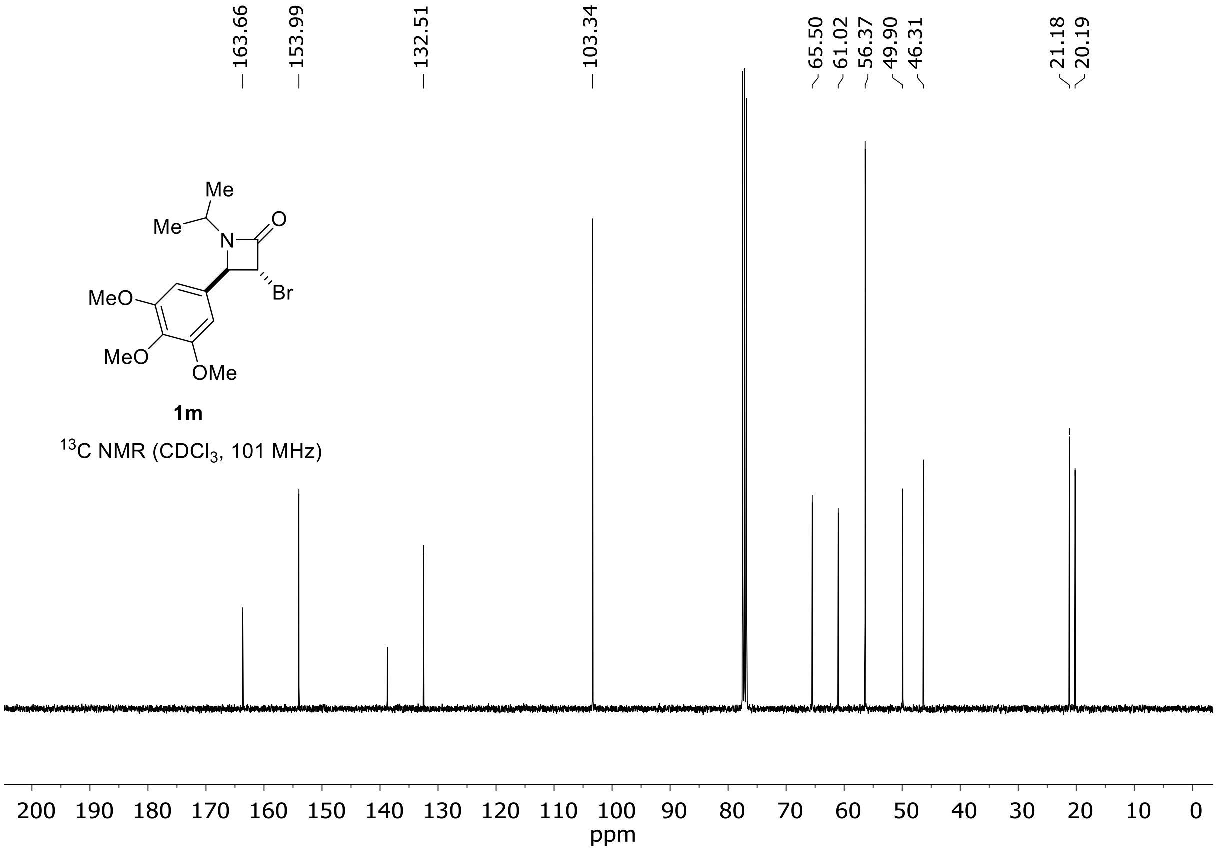




1m

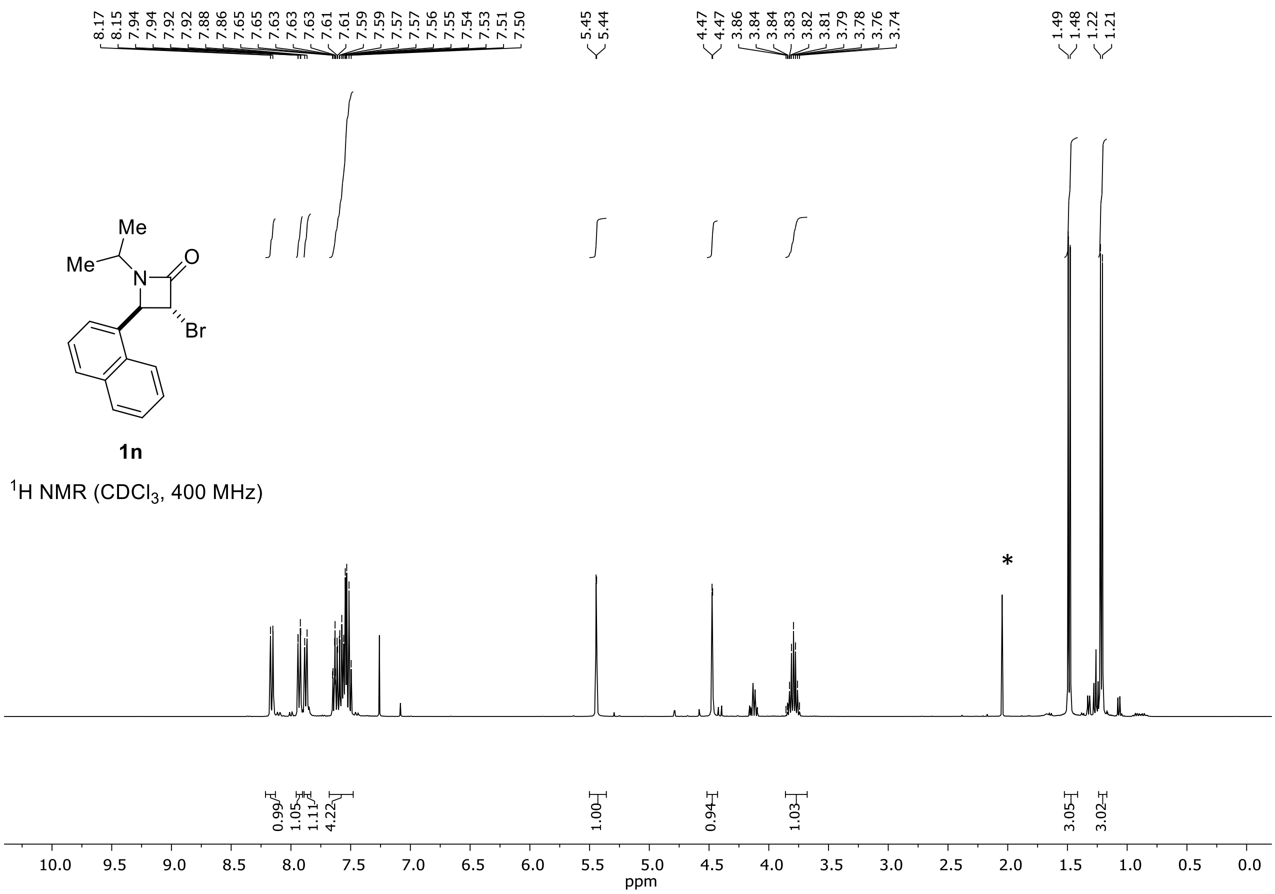
^{1}H NMR (CDCl$_3$, 400 MHz)





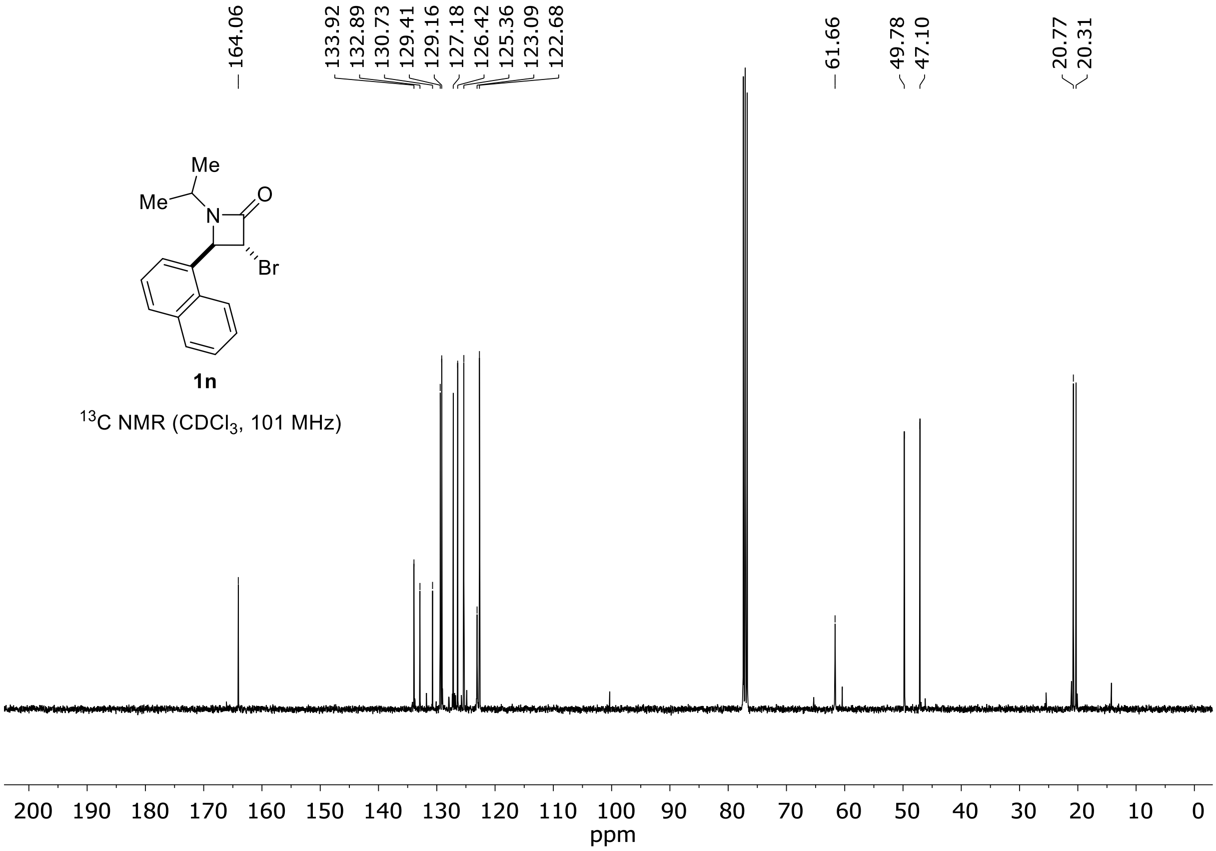
1m

^{13}C NMR ($CDCl_3$, 101 MHz)



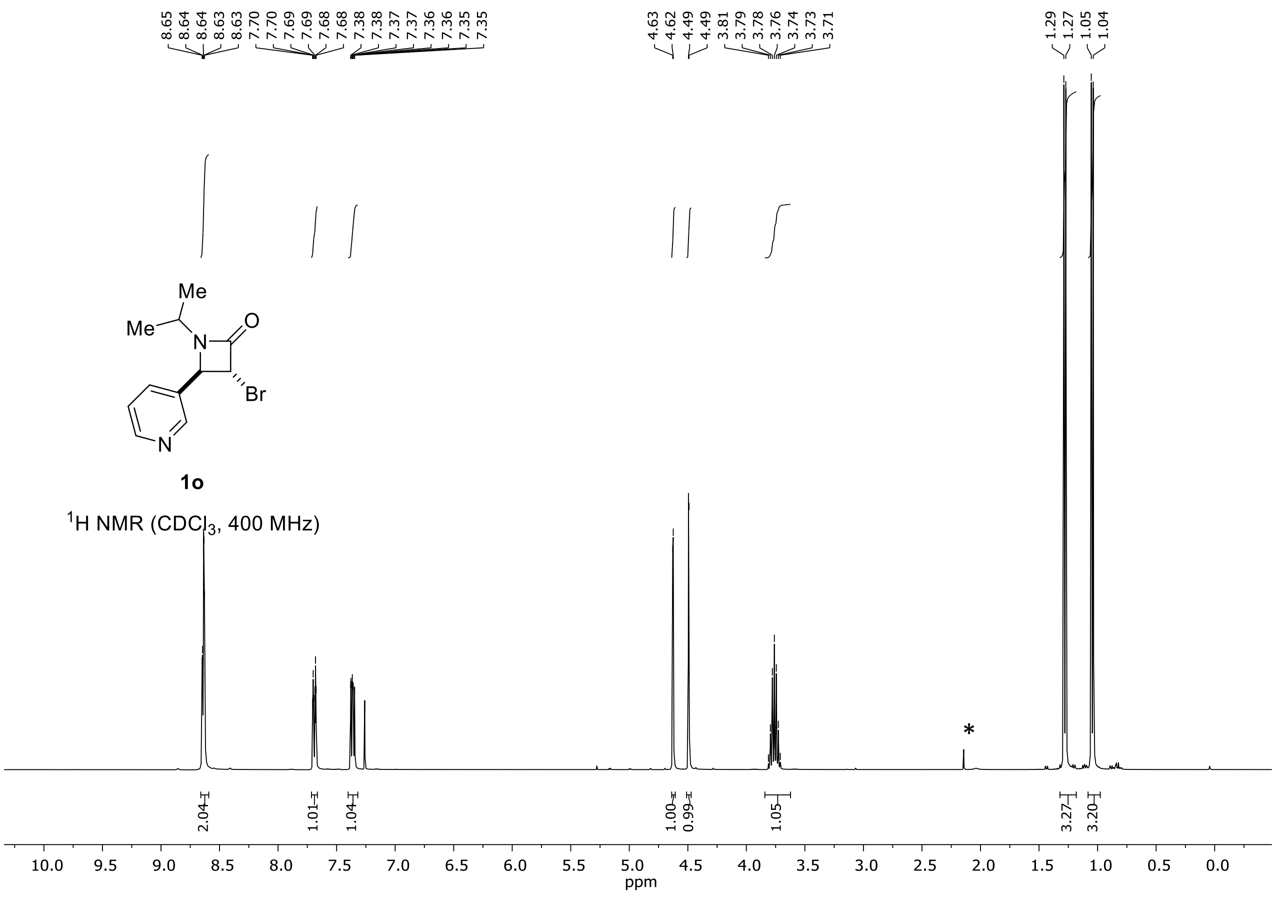
1n

^{1}H NMR ($CDCl_3$, 400 MHz)



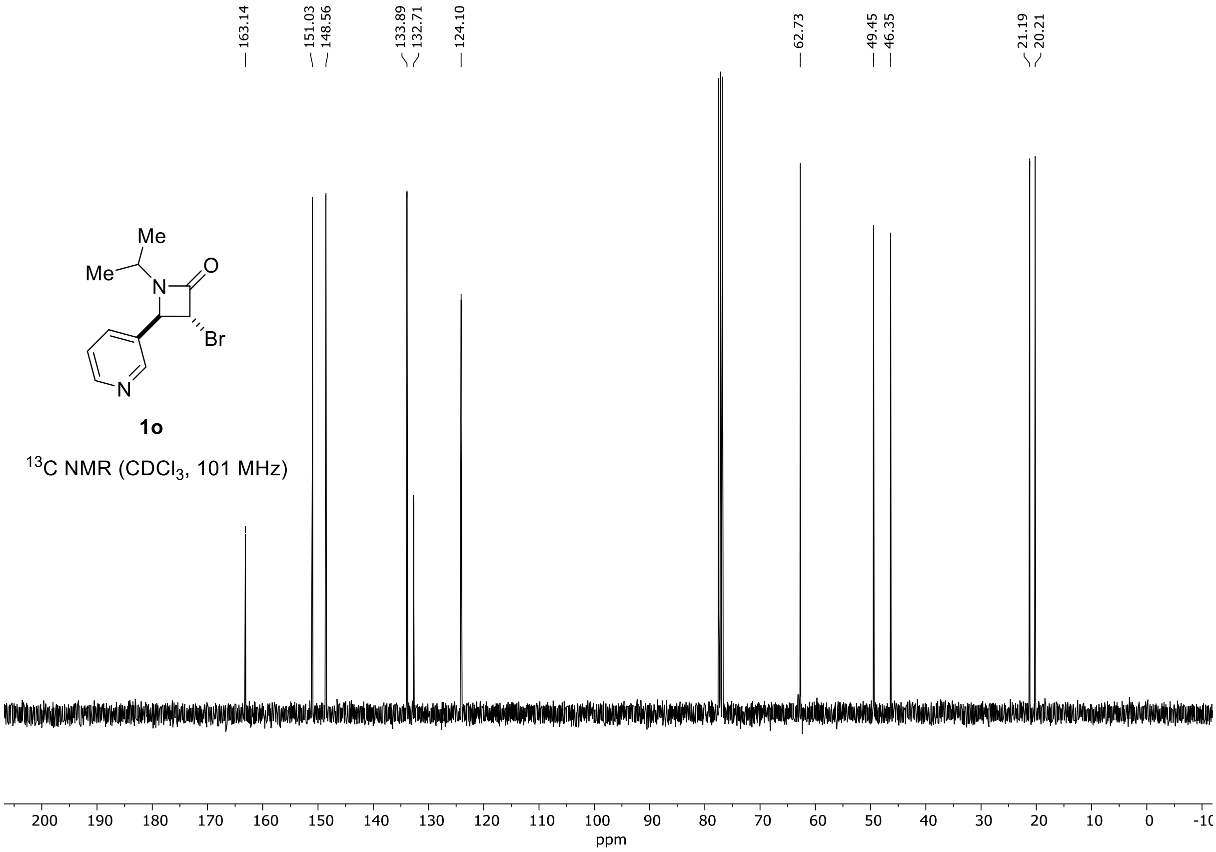
1n

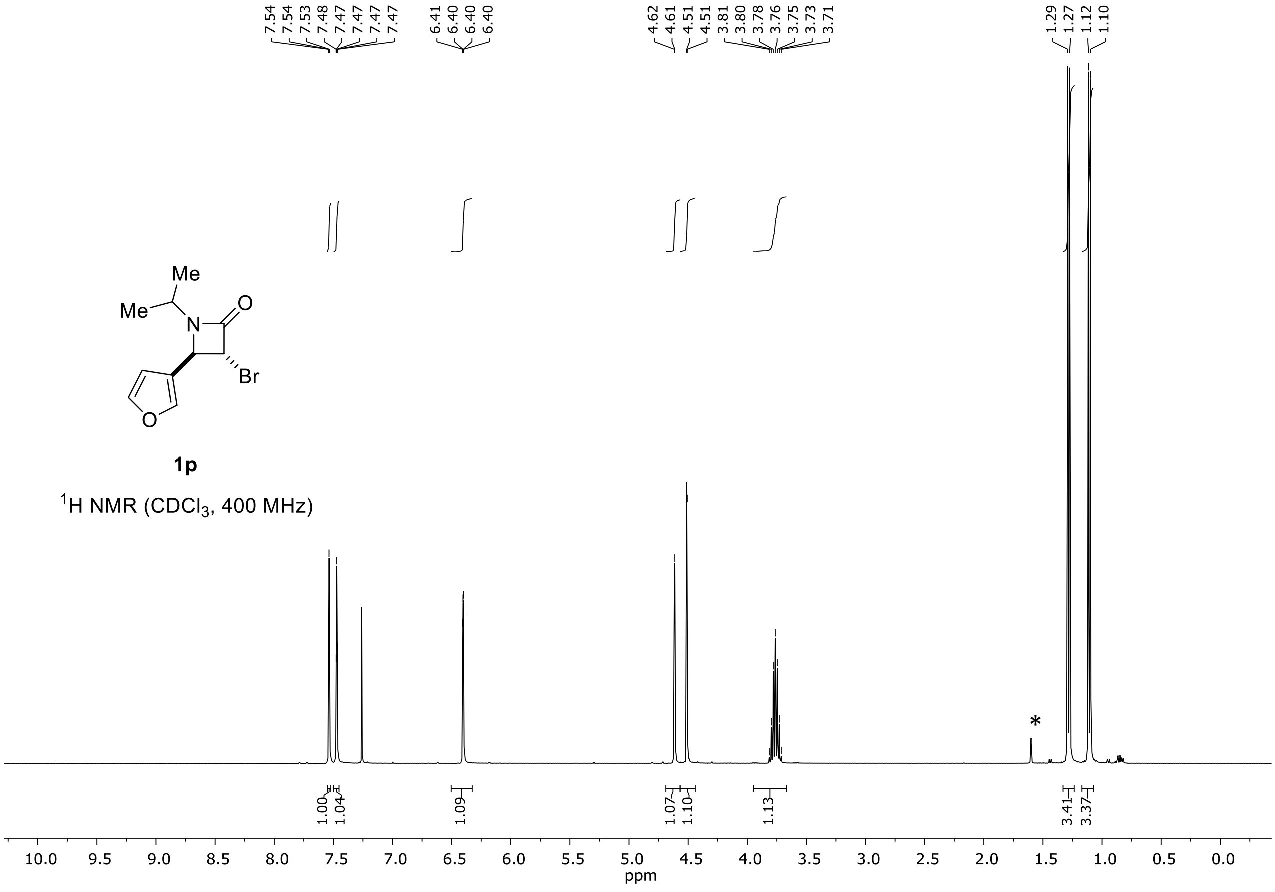
^{13}C NMR (CDCl$_3$, 101 MHz)

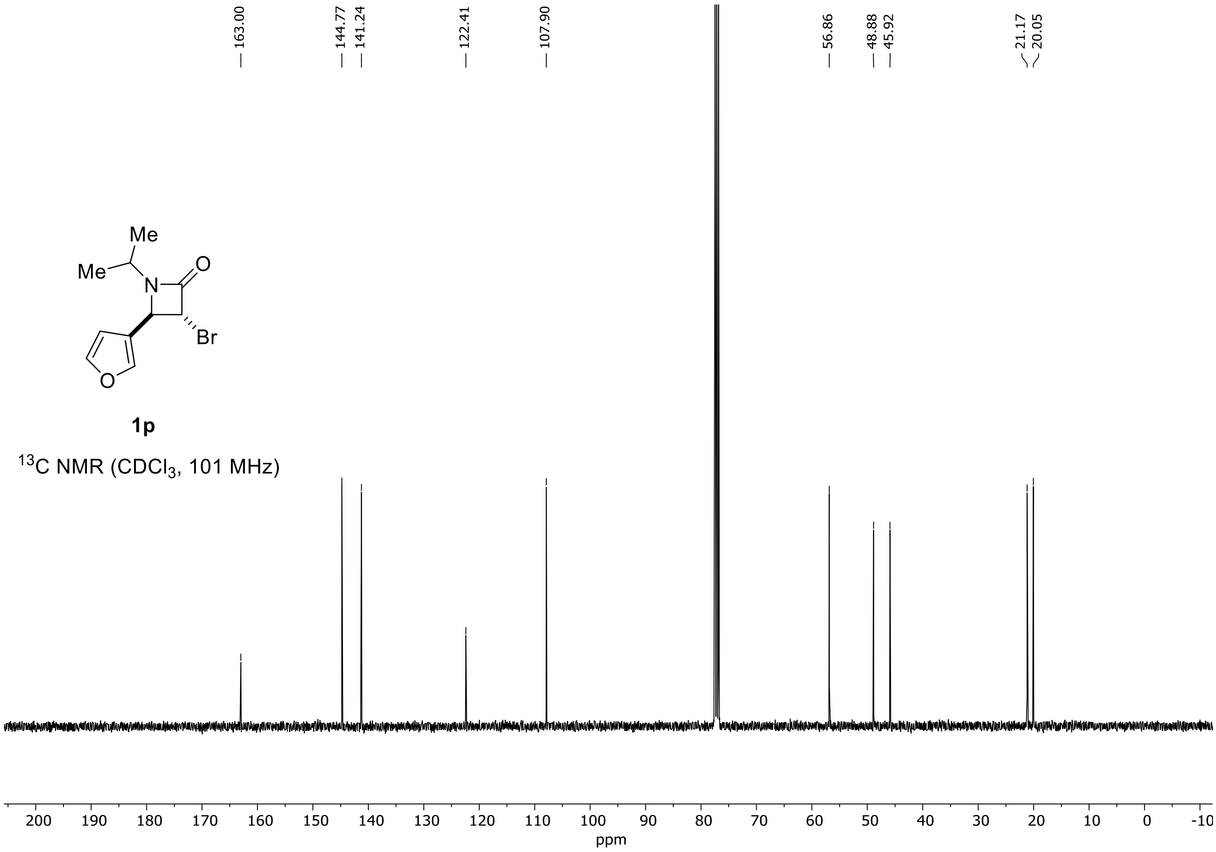


1o

^{1}H NMR (CDCl$_3$, 400 MHz)

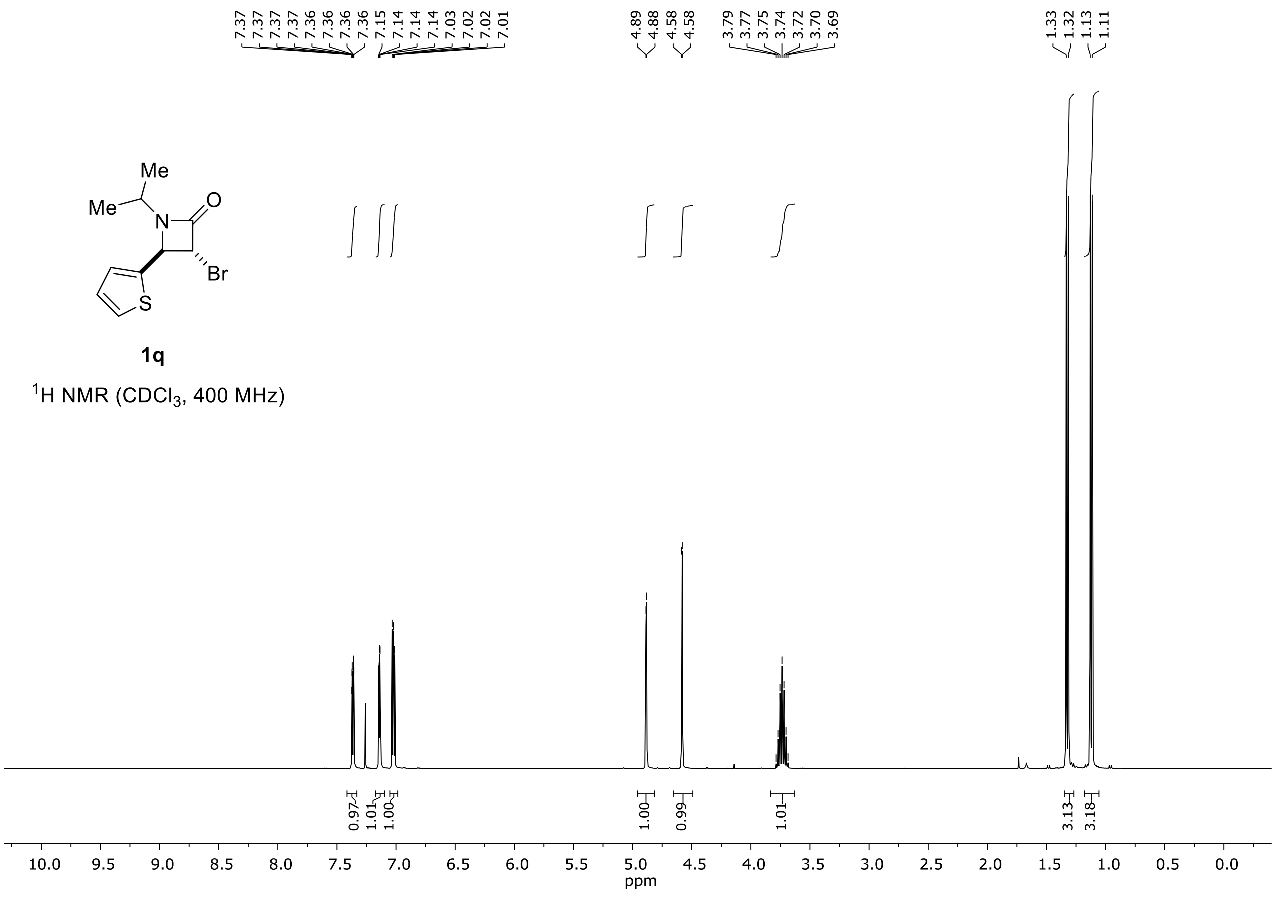

163.14
151.03
148.56
133.89
132.71
124.10
62.73
49.45
46.35
21.19
20.21
Me
Me
N
O
Br
N
1o
13C NMR (CDCl3, 101 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm


7.54
7.54
7.53
7.48
7.47
7.47
7.47
7.47
6.41
6.40
6.40
6.40
4.62
4.61
4.51
4.51
3.81
3.80
3.78
3.76
3.75
3.73
3.71
1.29
1.27
1.12
1.10
Me
Me
N
O
Br
O
1p
1H NMR (CDCl3, 400 MHz)
*
1.00
1.04
1.09
1.07
1.10
1.13
3.41
3.37
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm



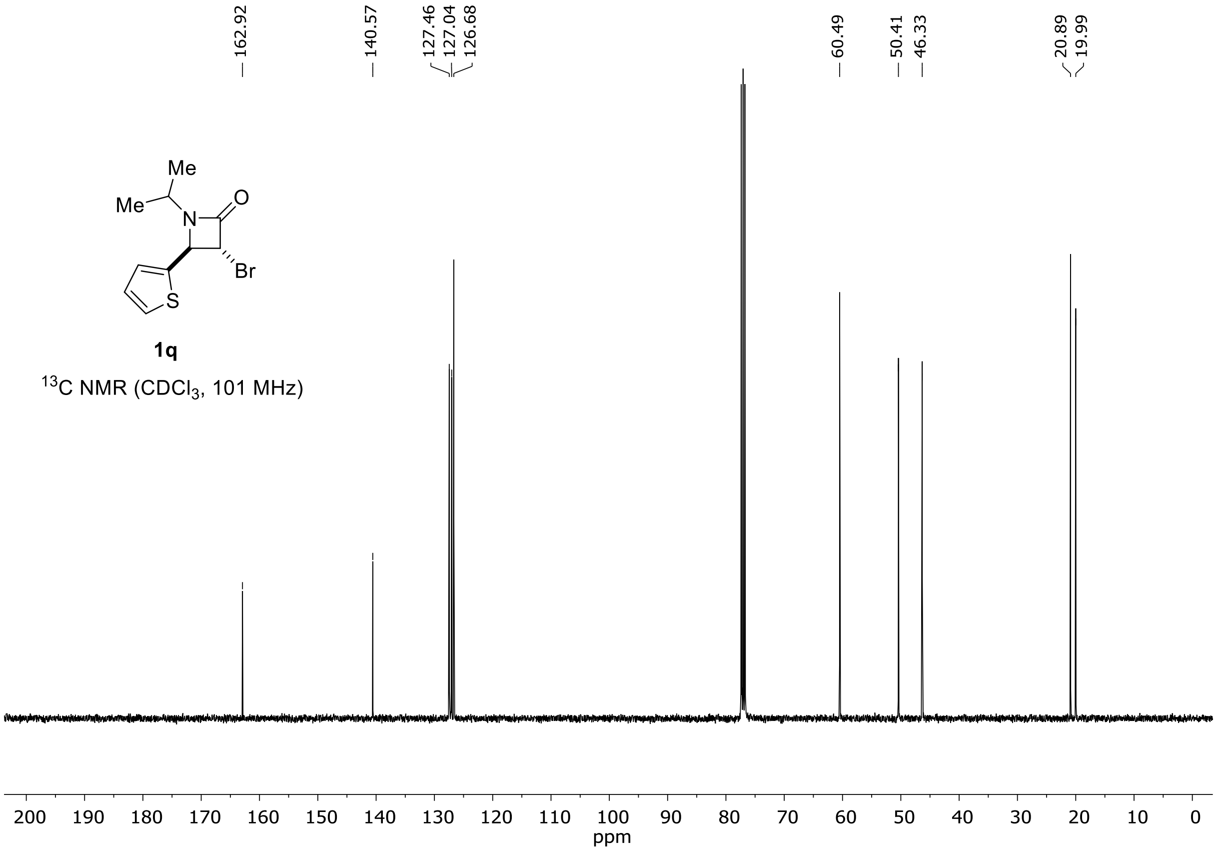
1p

^{13}C NMR (CDCl$_3$, 101 MHz)



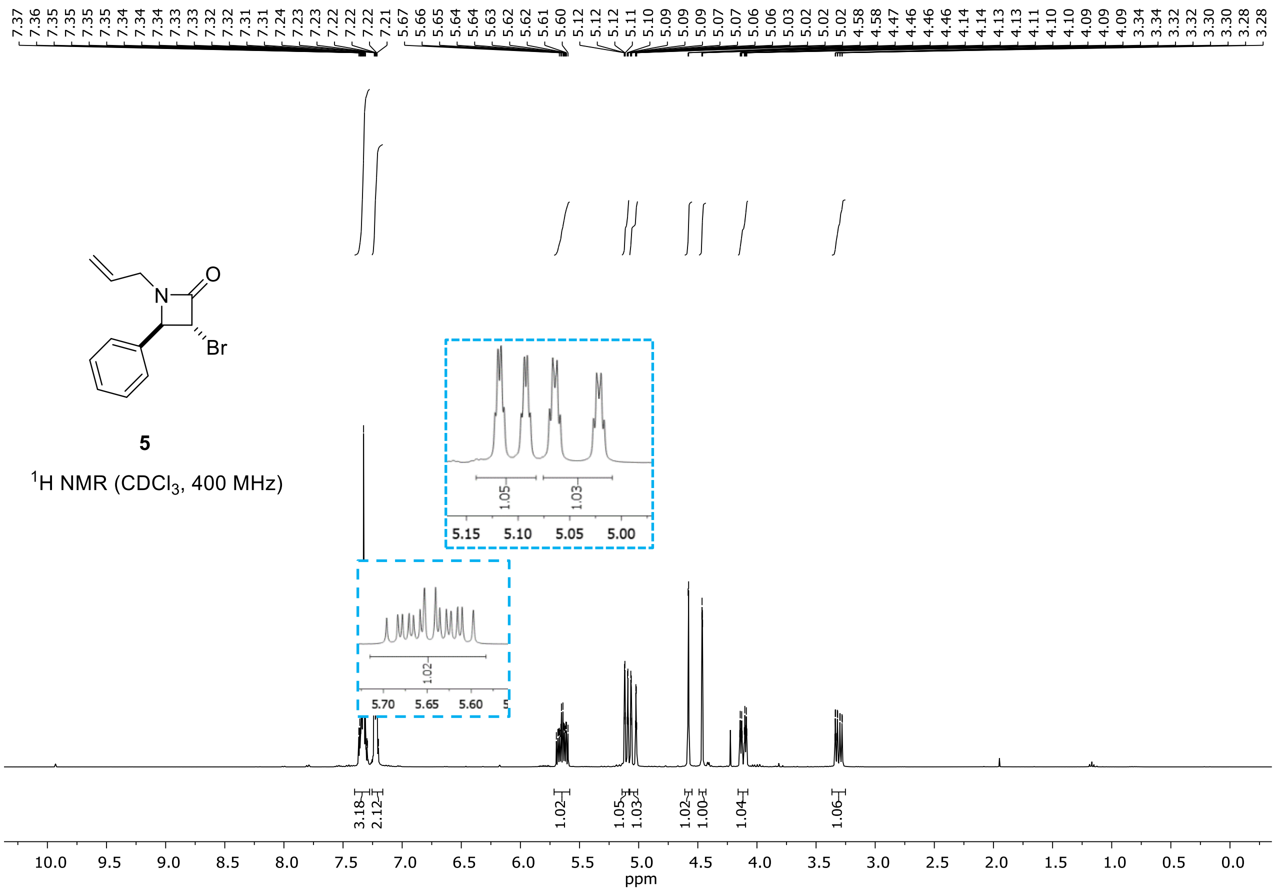
1q

^{1}H NMR (CDCl$_3$, 400 MHz)



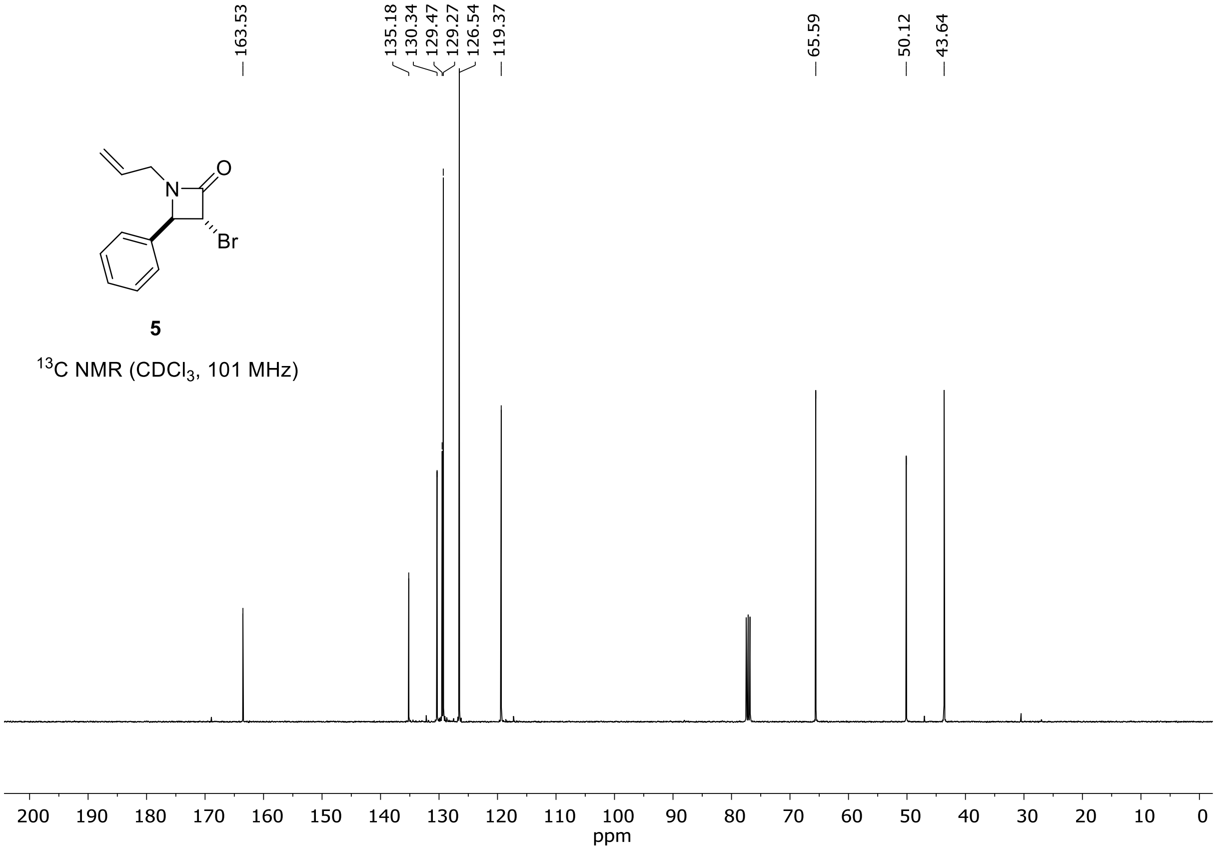
1q

^{13}C NMR ($CDCl_3$, 101 MHz)



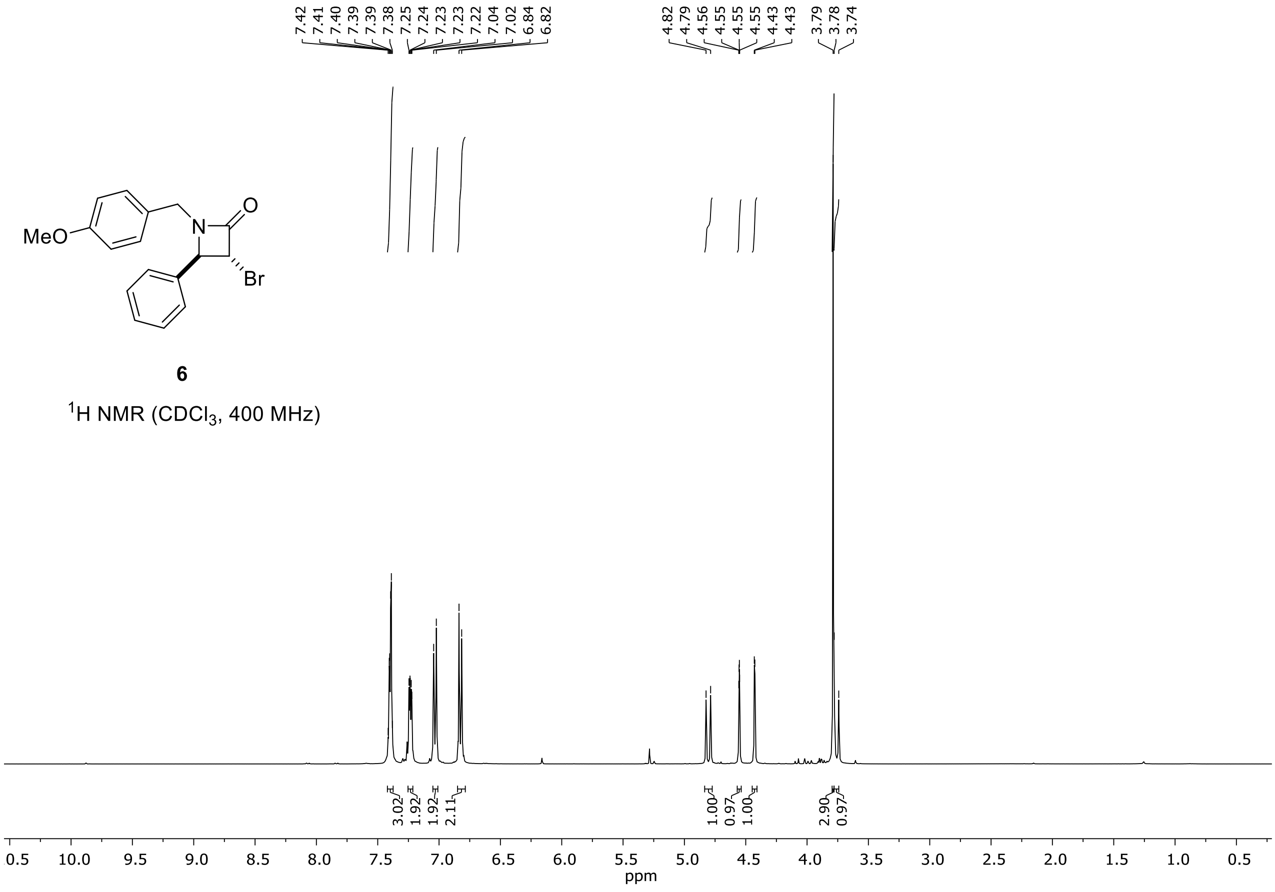
5

^{1}H NMR ($CDCl_3$, 400 MHz)



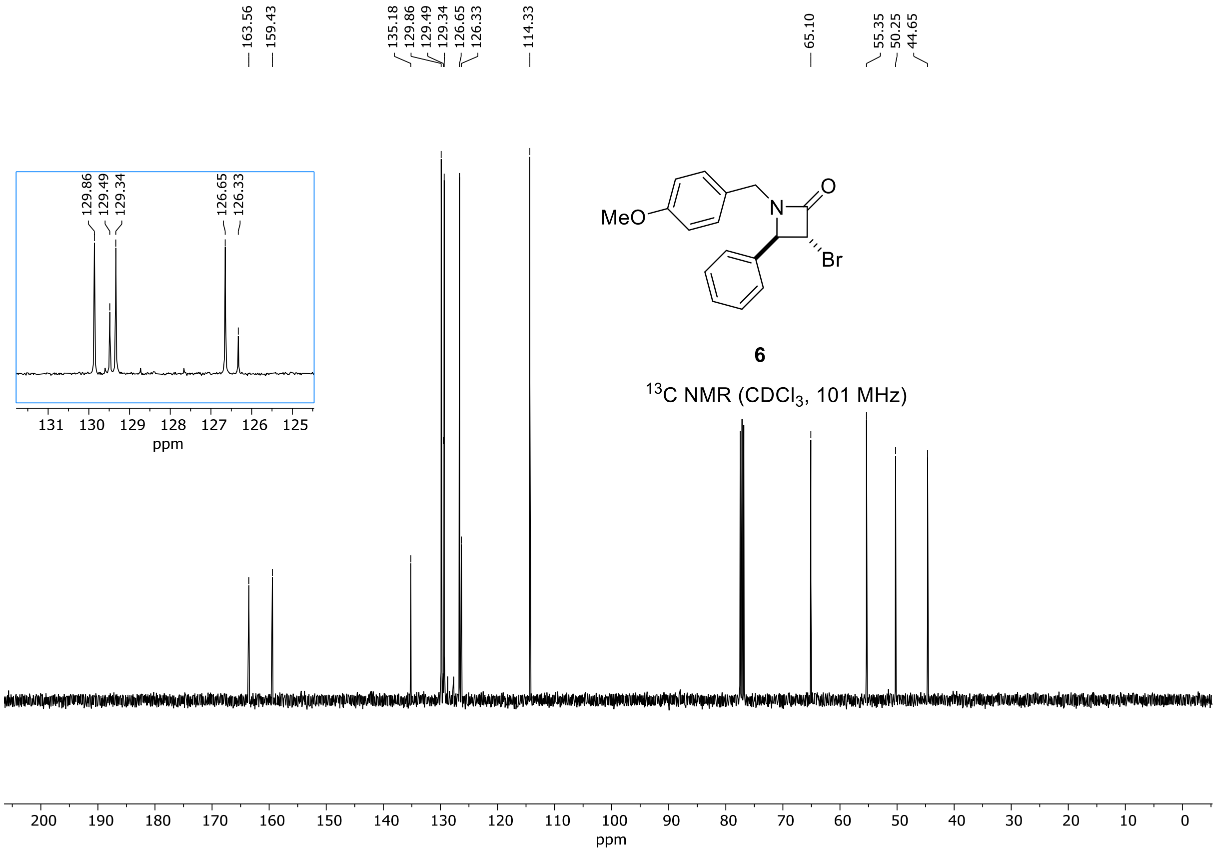
5

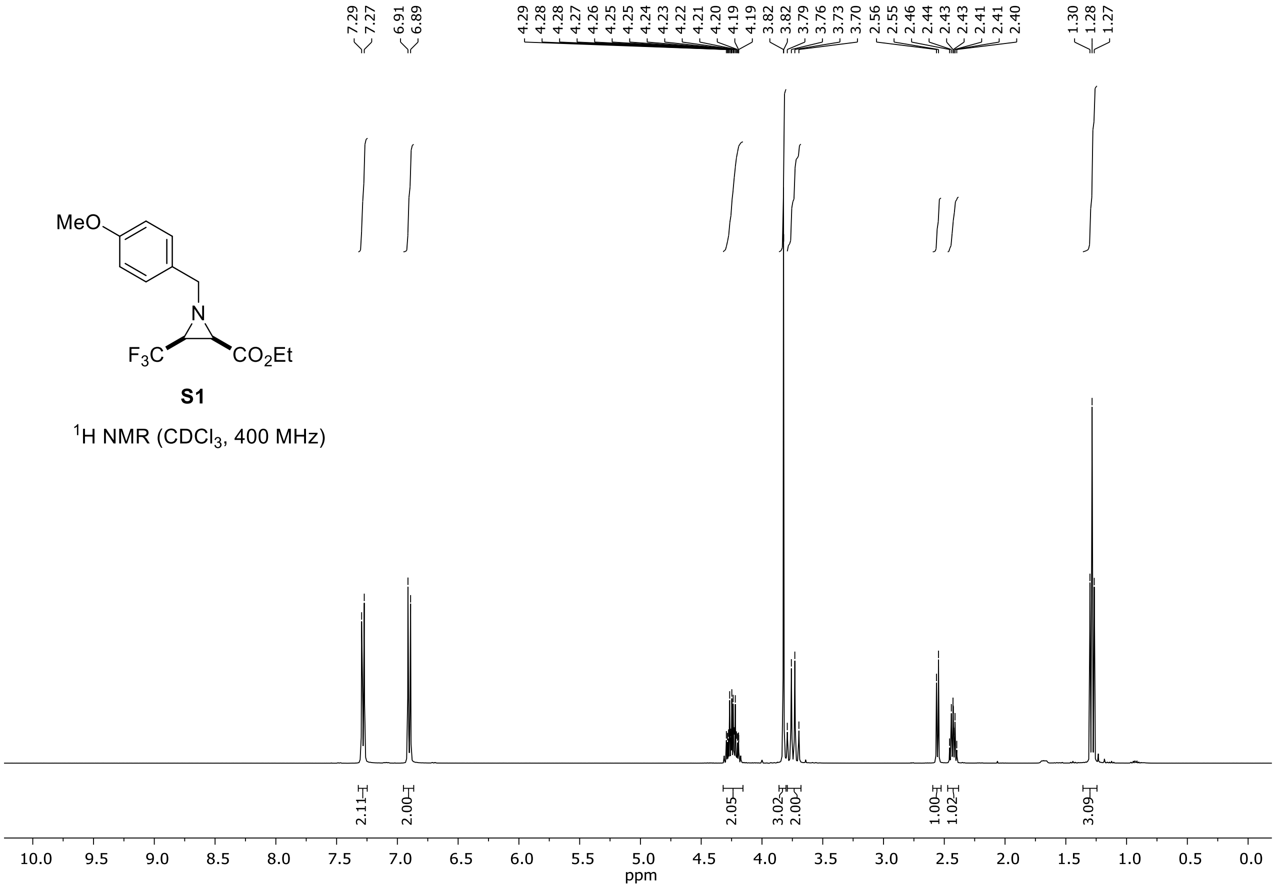
^{13}C NMR ($CDCl_3$, 101 MHz)

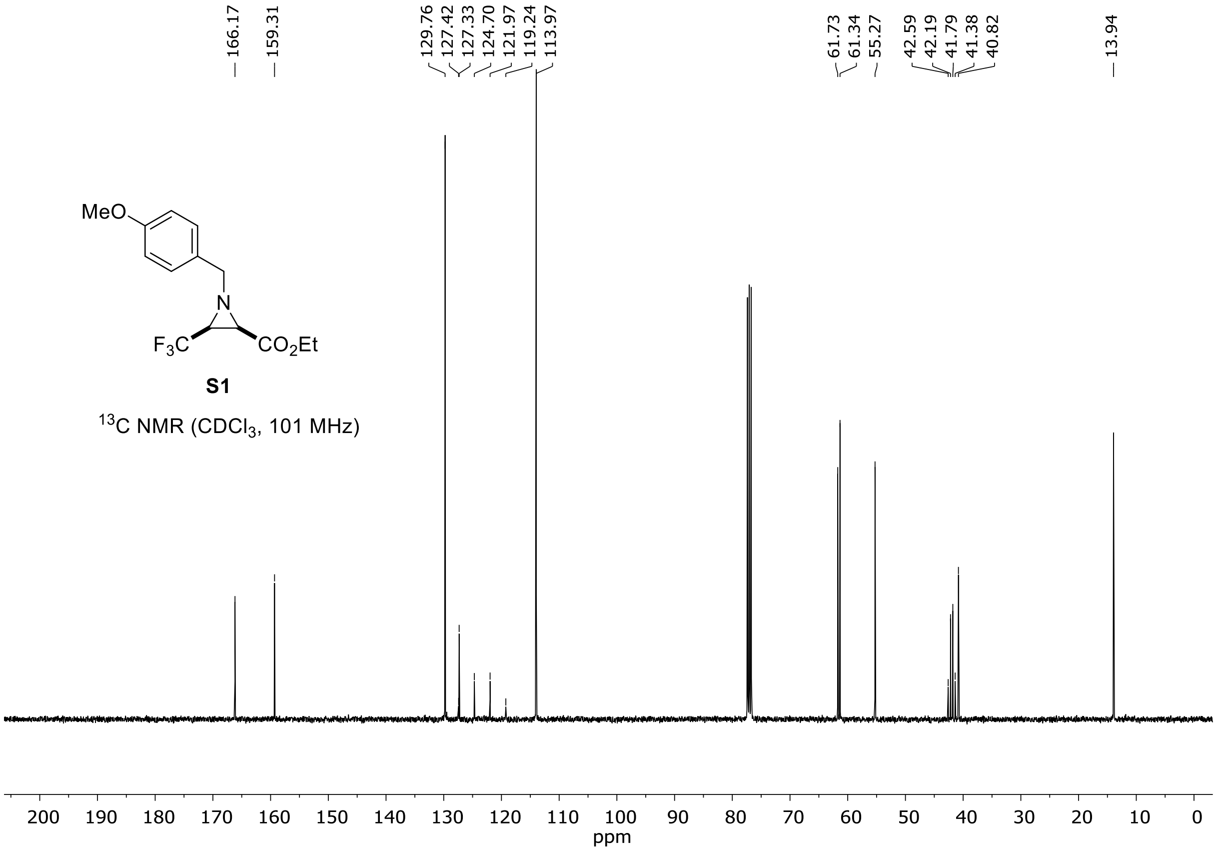


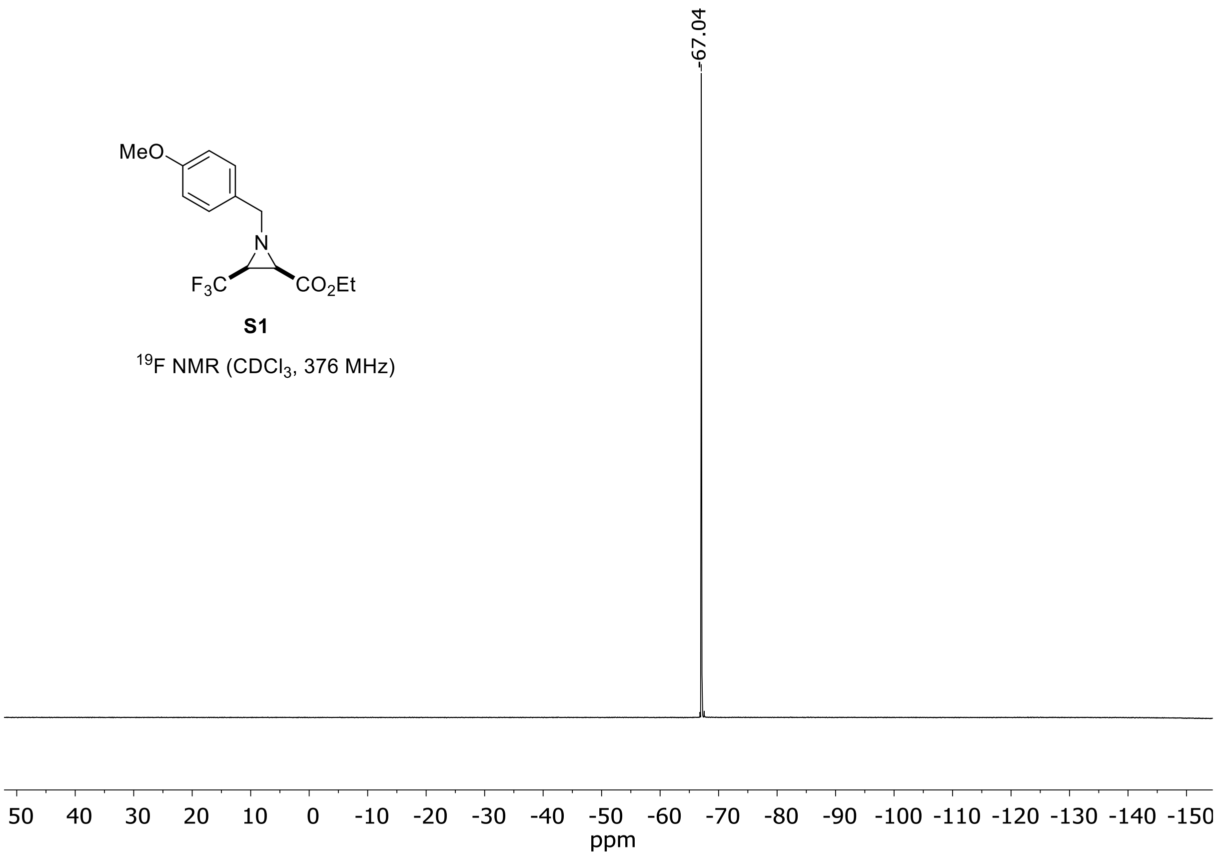
6

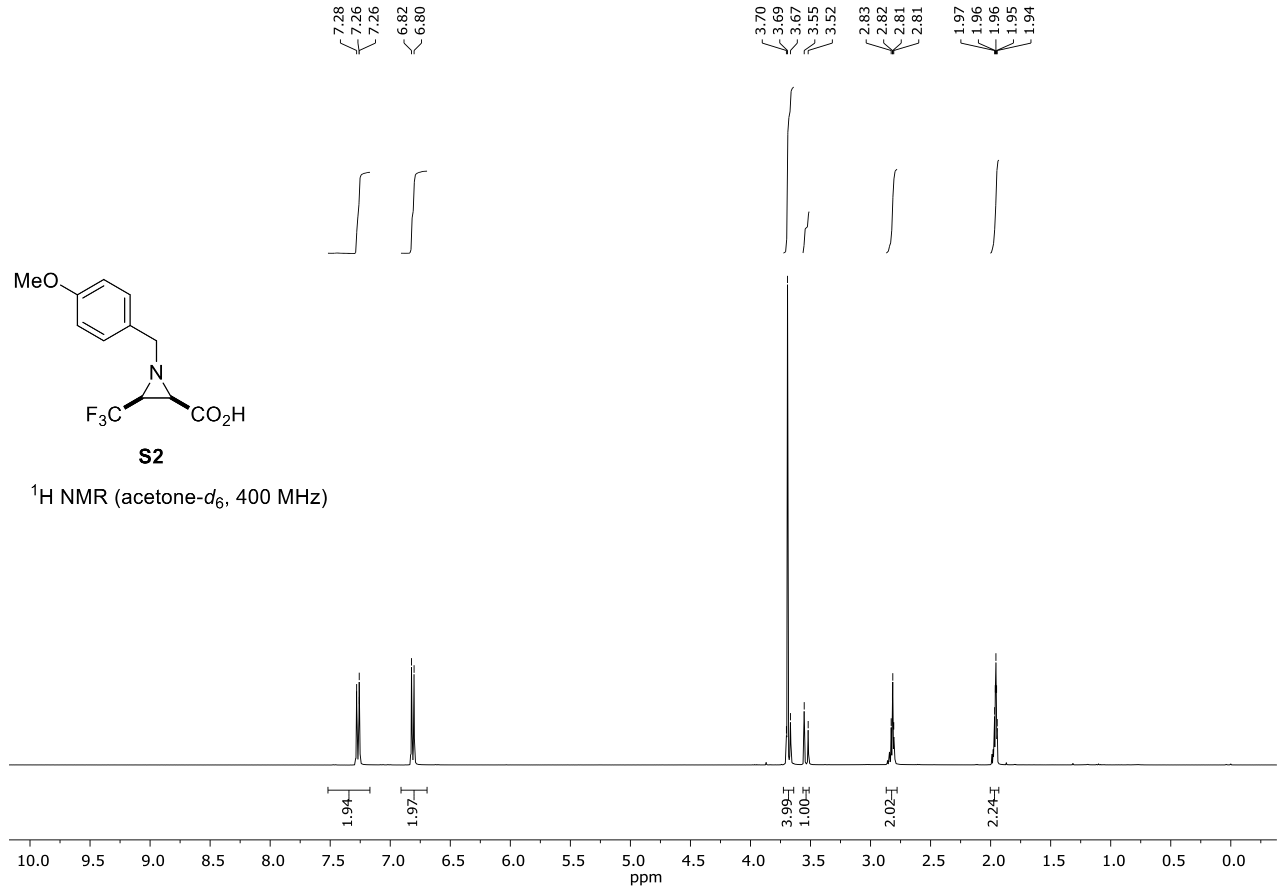
^{1}H NMR ($CDCl_3$, 400 MHz)

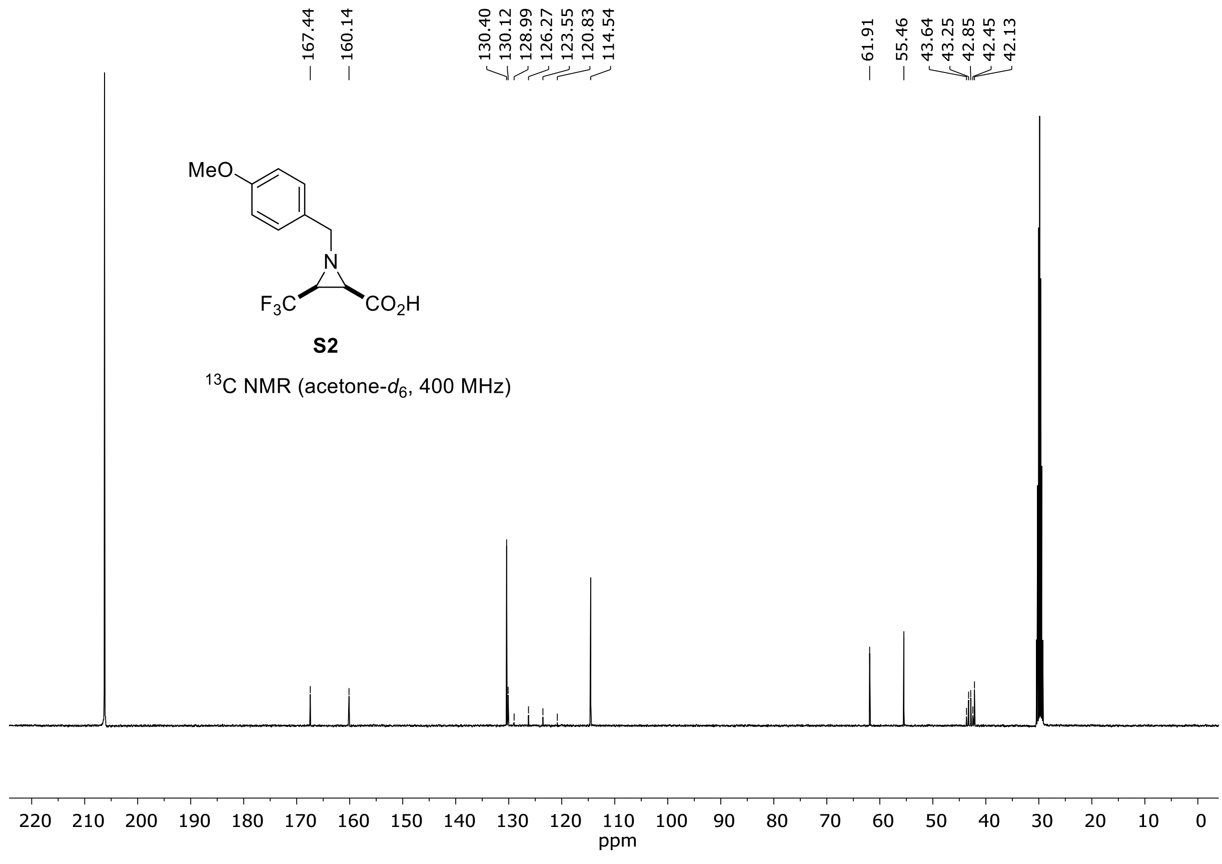

163.56
159.43
135.18
129.86
129.49
129.34
126.65
126.33
114.33
65.10
55.35
50.25
44.65
MeO
N
O
Br
6
^{13}C NMR ($CDCl_3$, 101 MHz)
ppm

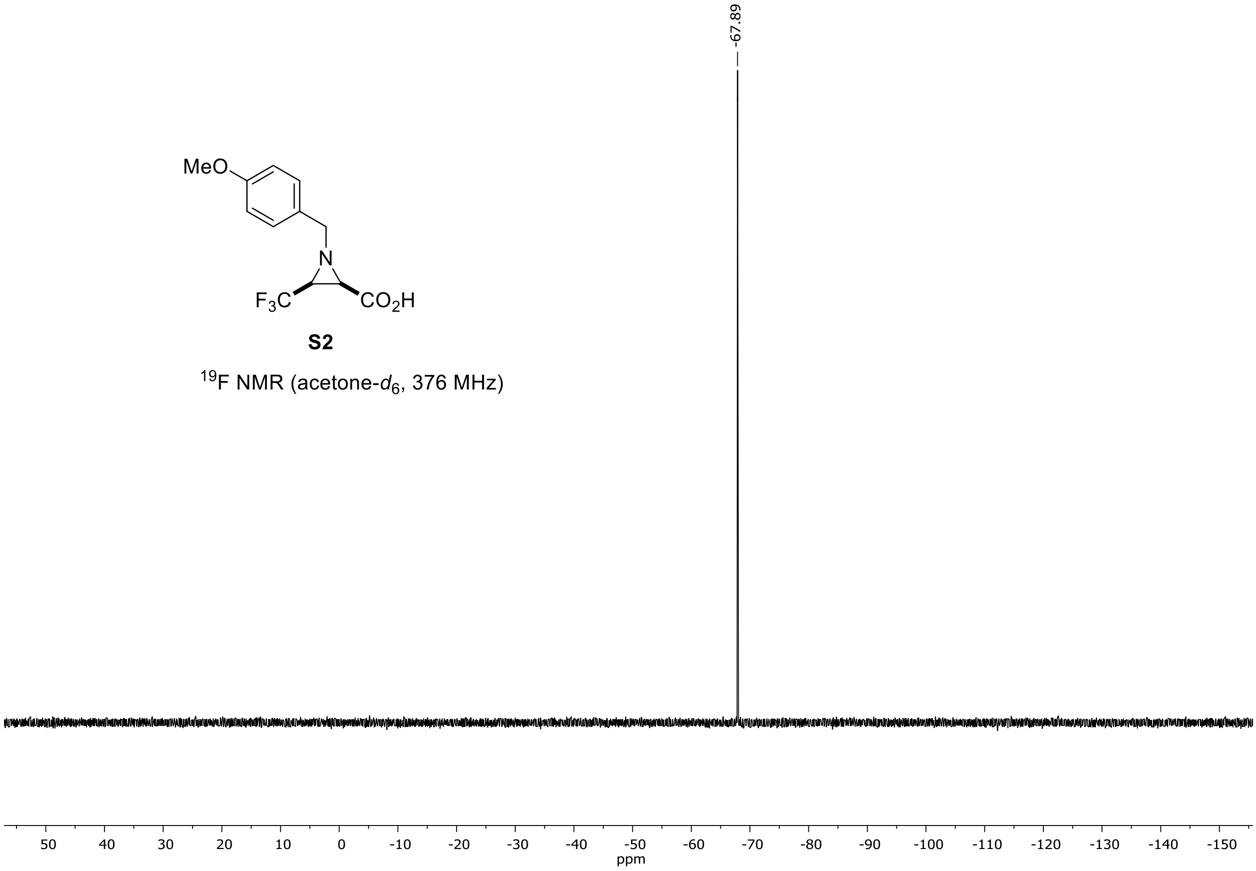

7.29
7.27
6.91
6.89
4.29
4.28
4.28
4.27
4.26
4.25
4.25
4.24
4.23
4.22
4.21
4.20
4.19
4.19
3.82
3.82
3.79
3.76
3.73
3.70
2.56
2.55
2.46
2.44
2.43
2.43
2.41
2.41
2.40
1.30
1.28
1.27
MeO
N
F_3C
CO_2Et
S1
^{1}H NMR ($CDCl_3$, 400 MHz)
2.11
2.00
2.05
3.02
2.00
1.00
1.02
3.09
ppm

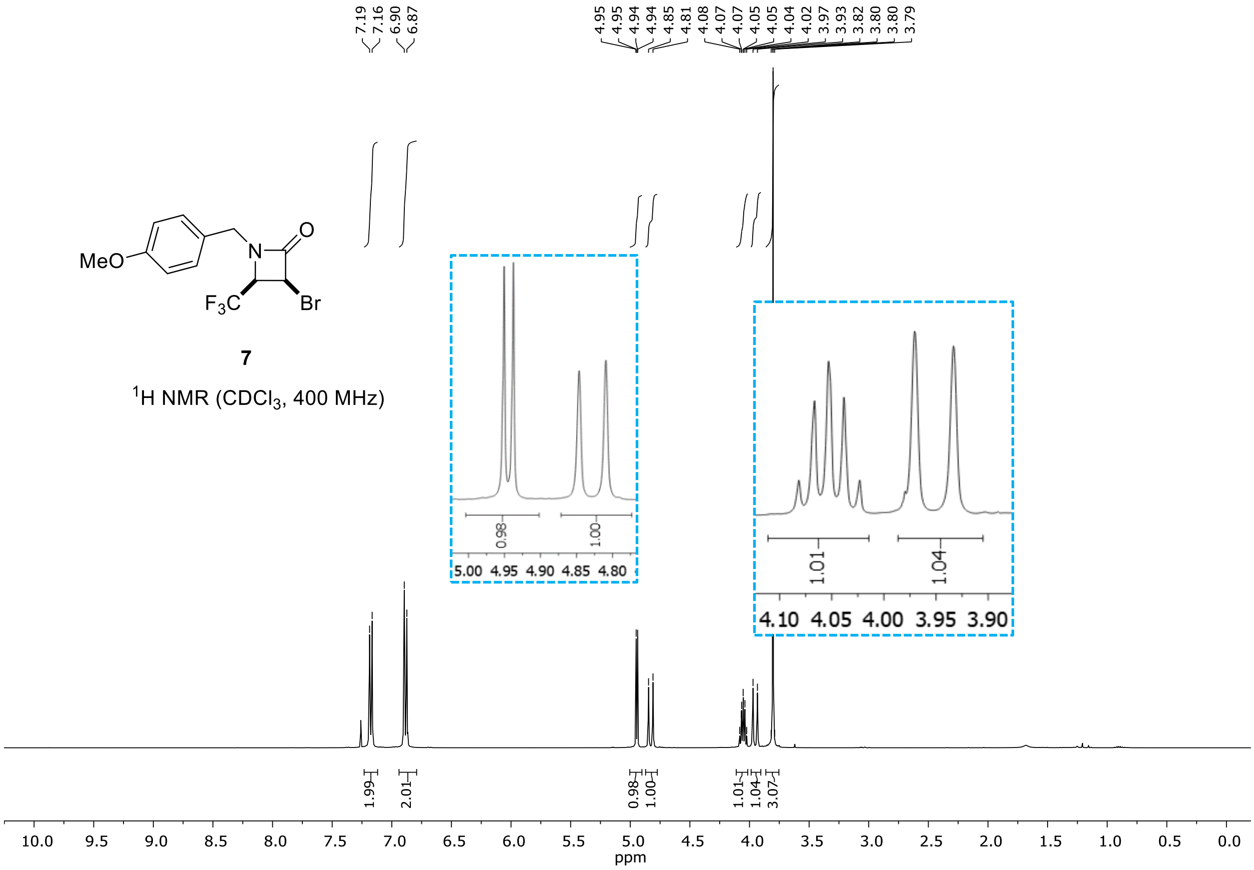

166.17
159.31
129.76
127.42
127.33
124.70
121.97
119.24
113.97
61.73
61.34
55.27
42.59
42.19
41.79
41.38
40.82
13.94
MeO
N
F_3C
CO_2Et
S1
^{13}C NMR ($CDCl_3$, 101 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

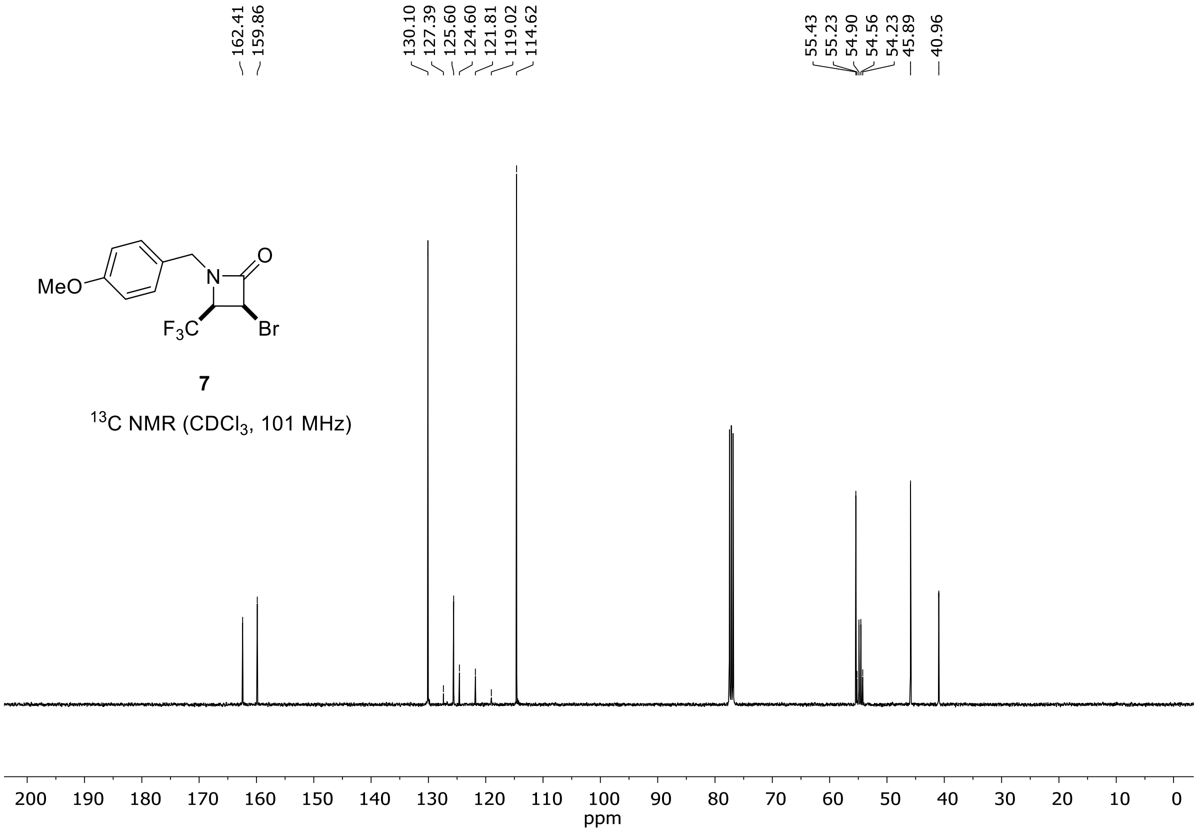

-67.04
MeO
N
F_3C
CO_2Et
S1
^{19}F NMR ($CDCl_3$, 376 MHz)
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150
ppm


MeO
N
F_3C
CO_2H
S2
^{1}H NMR (acetone-d_6, 400 MHz)
7.28 7.26 7.26 6.82 6.80
3.70 3.69 3.67 3.55 3.52 2.83 2.82 2.81 2.81 1.97 1.96 1.96 1.95 1.94
1.94 1.97 3.99 1.00 2.02 2.24
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


167.44 160.14
130.40 130.12 128.99 126.27 123.55 120.83 114.54
61.91 55.46 43.64 43.25 42.85 42.45 42.13
MeO
N
F_3C
CO_2H
S2
^{13}C NMR (acetone-d_6, 400 MHz)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

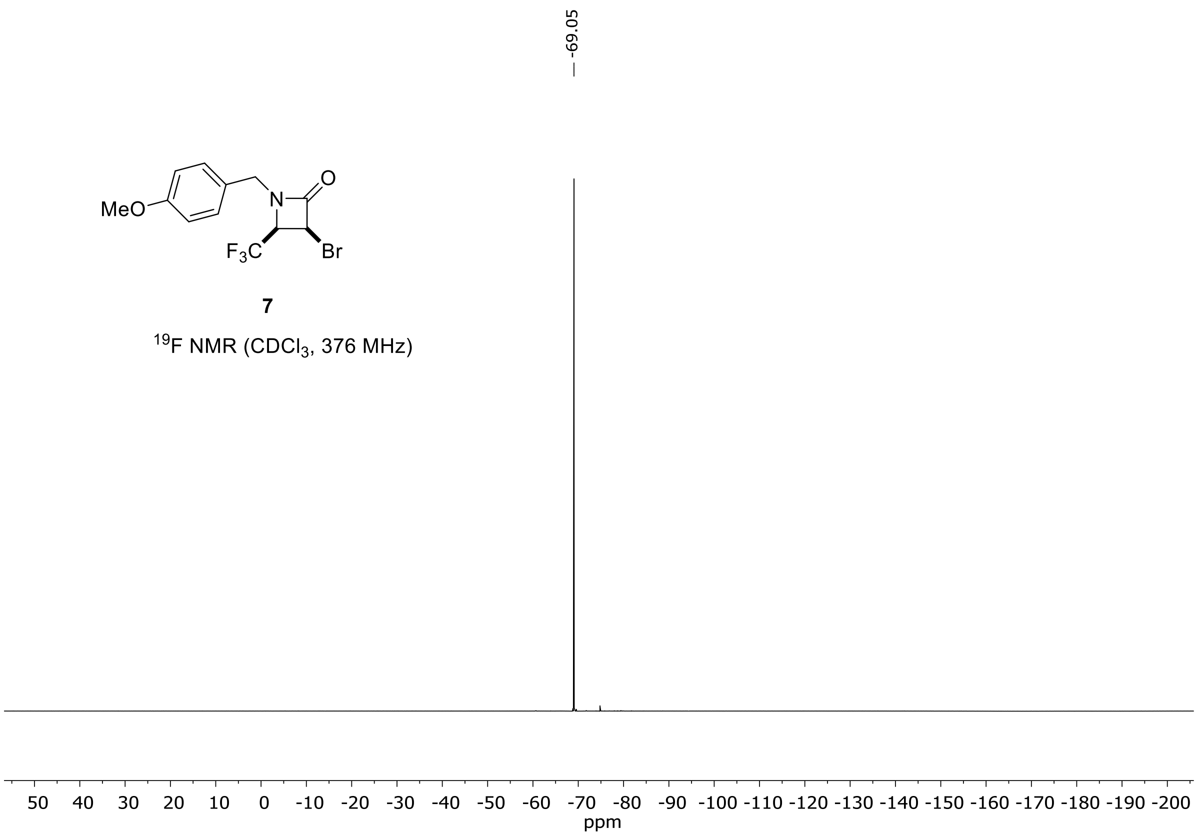

MeO
N
F_3C
CO_2H
S2
^{19}F NMR (acetone-d_6, 376 MHz)
-67.89
ppm


MeO
N
O
F_3C
Br
7
^{1}H NMR ($CDCl_3$, 400 MHz)
7.19 7.16 6.90 6.87
4.95 4.95 4.94 4.94 4.85 4.81 4.08 4.07 4.07 4.05 4.05 4.04 4.02 3.97 3.93 3.82 3.80 3.79
0.98 1.00
1.01 1.04
1.99 2.01 0.98 1.00 1.01 1.04 3.07
ppm



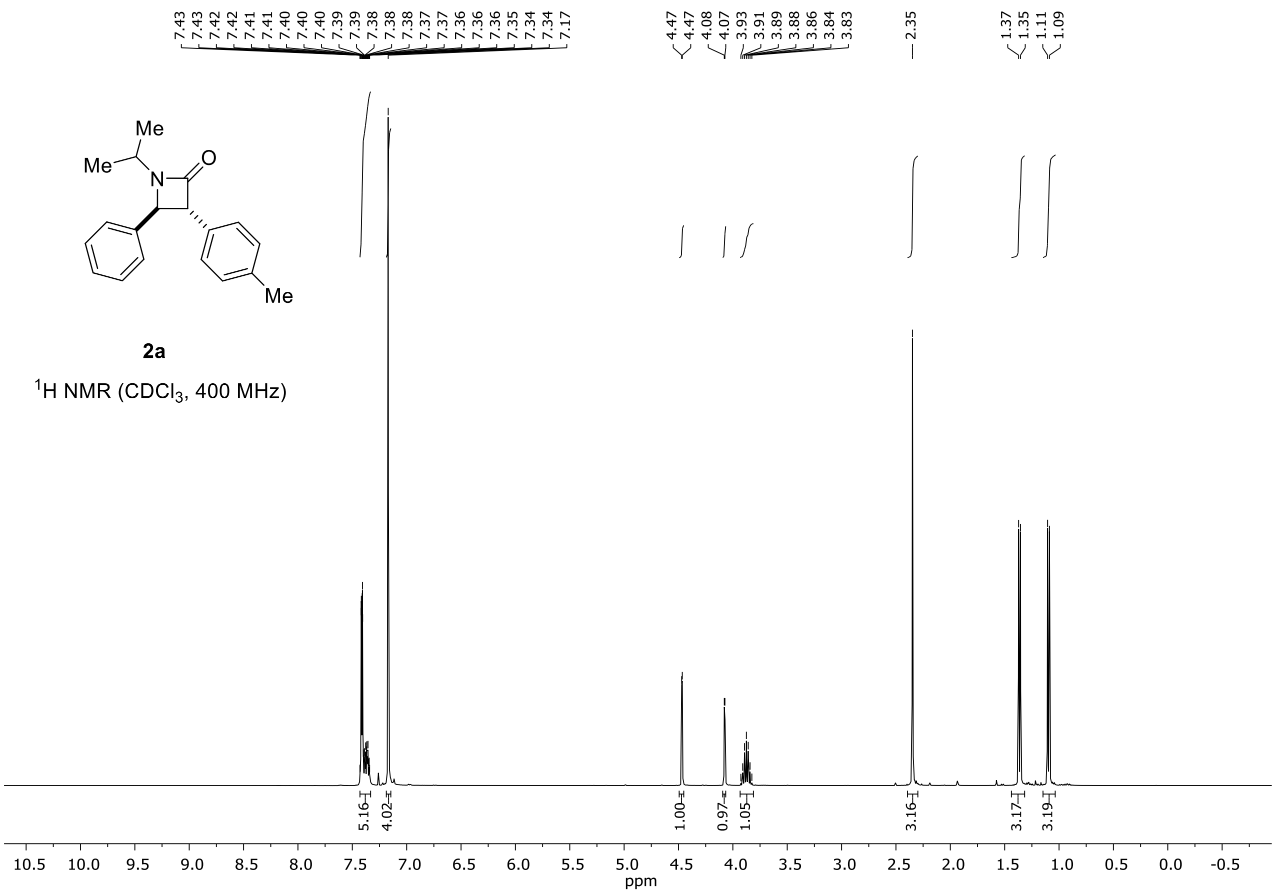
7

^{13}C NMR ($CDCl_3$, 101 MHz)



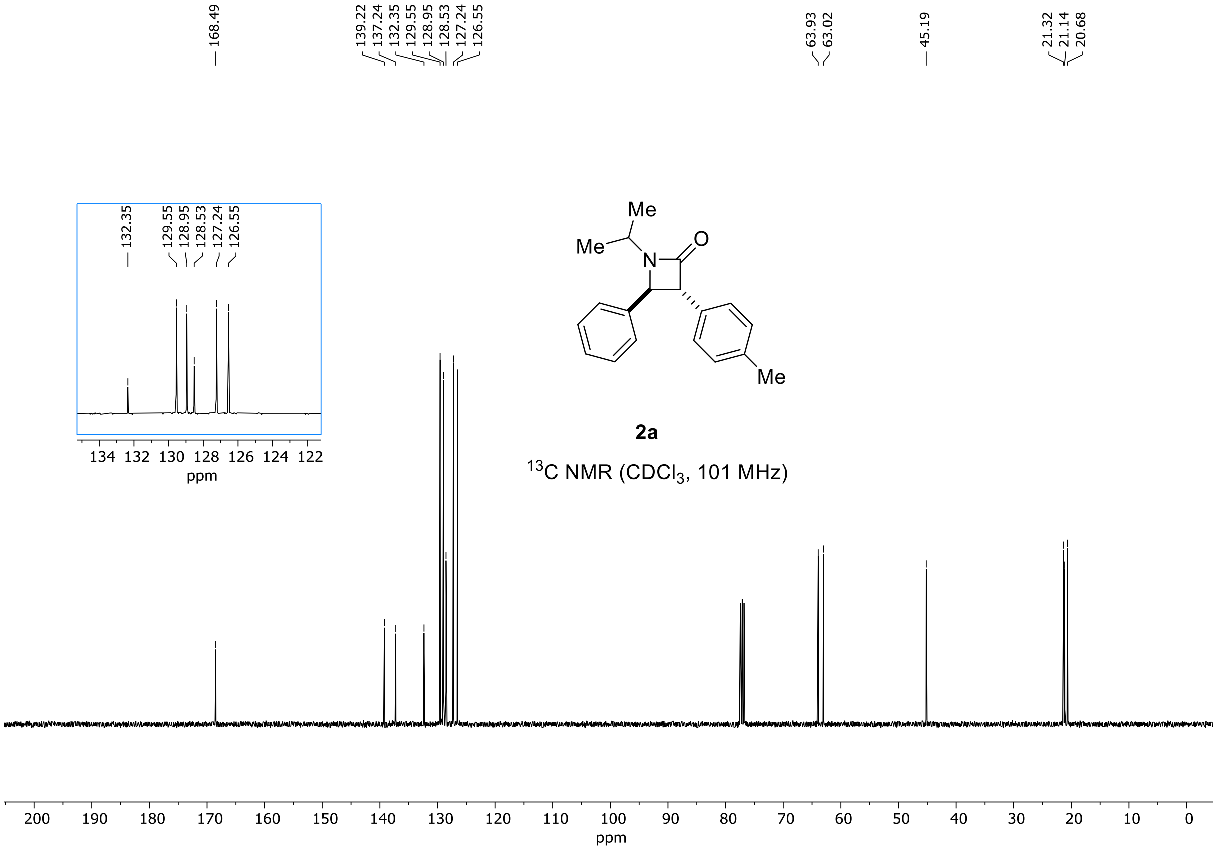
7

^{19}F NMR ($CDCl_3$, 376 MHz)



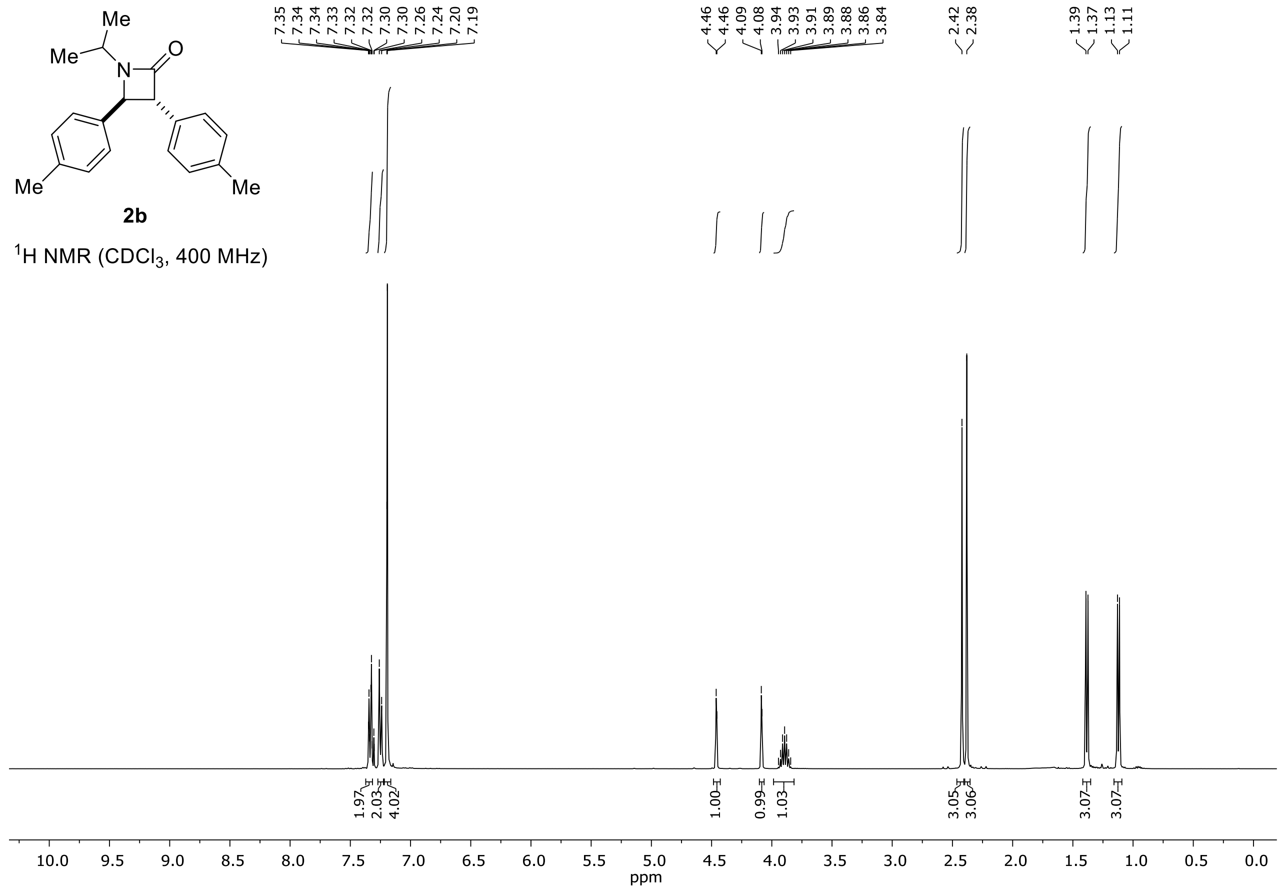
2a

^{1}H NMR ($CDCl_3$, 400 MHz)

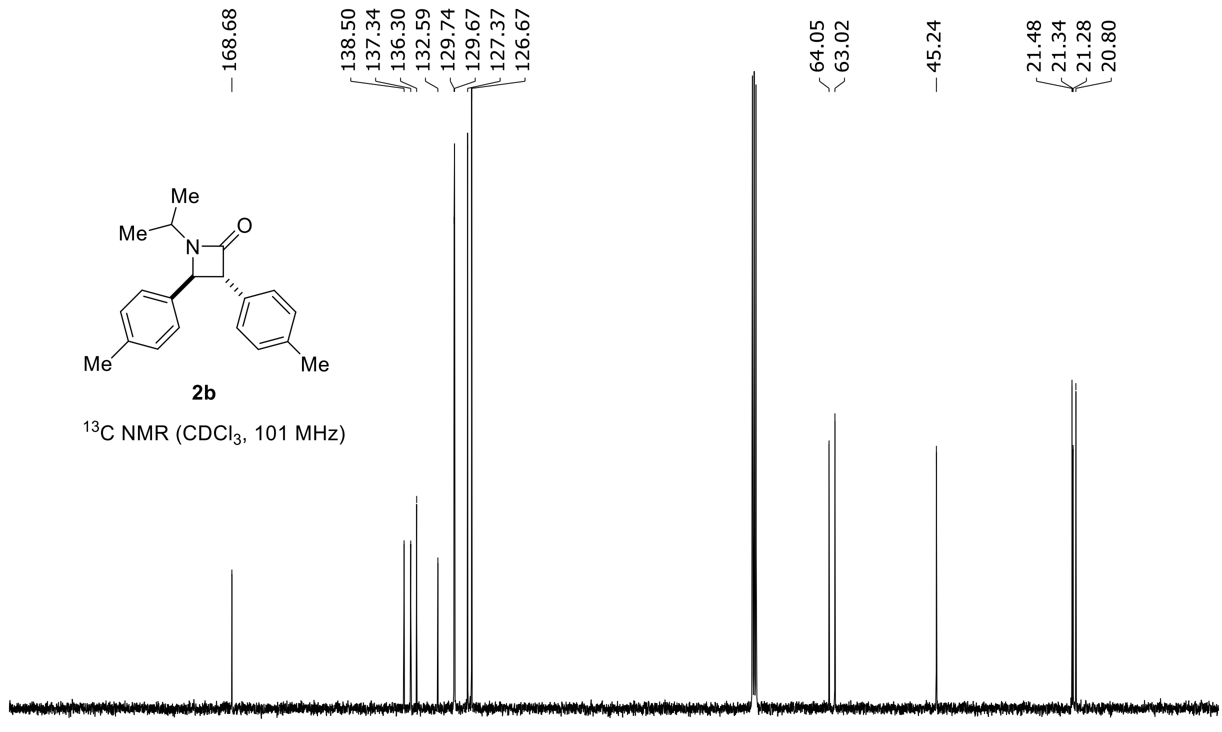


2a

^{13}C NMR ($CDCl_3$, 101 MHz)



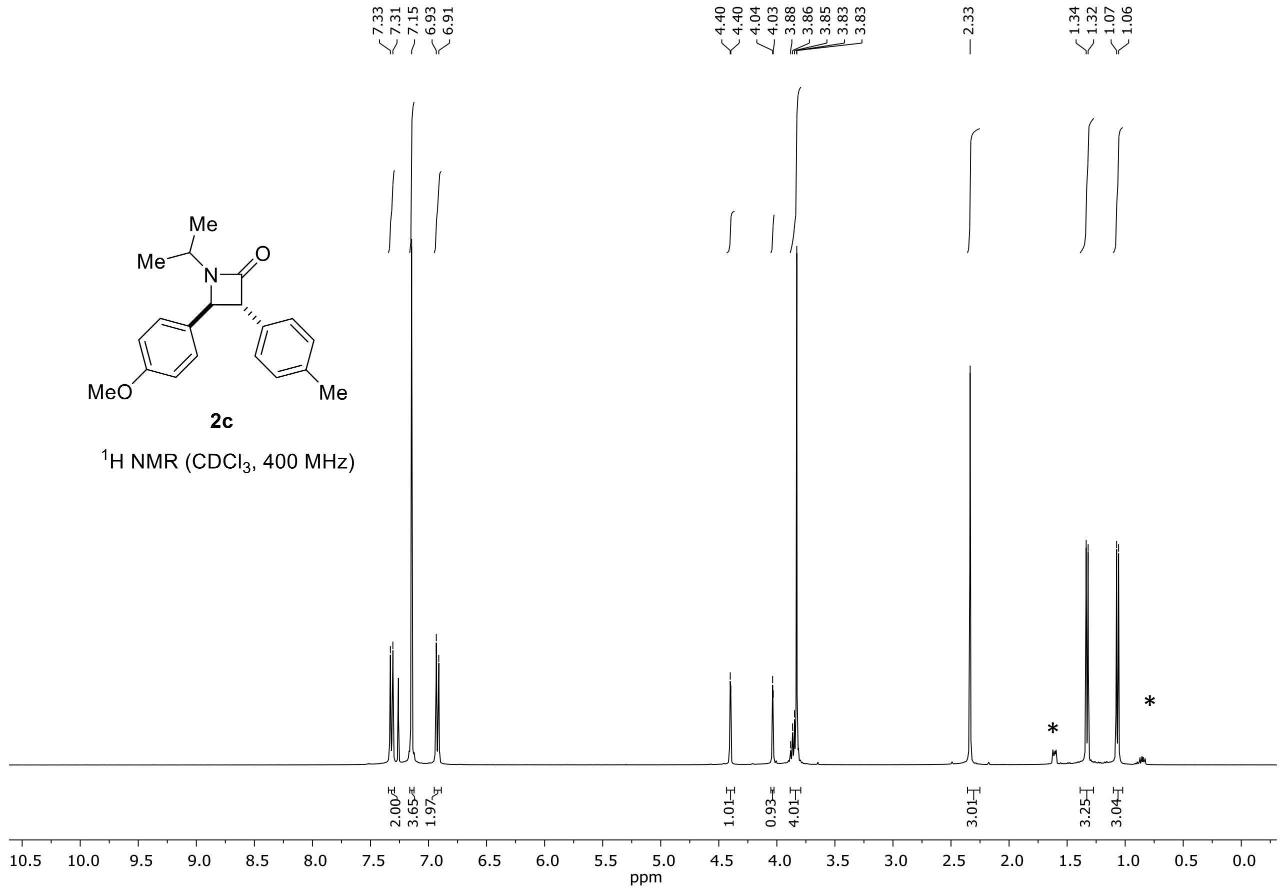
Me
Me
N
O
Me
Me
2b
^{1}H NMR ($CDCl_3$, 400 MHz)
7.35 7.34 7.34 7.33 7.32 7.32 7.30 7.30 7.26 7.24 7.20 7.19
4.46 4.46 4.09 4.08 3.94 3.93 3.91 3.89 3.88 3.86 3.84
2.42 2.38
1.39 1.37 1.13 1.11
1.97 2.03 4.02 1.00 0.99 1.03 3.05 3.06 3.07 3.07
ppm



168.68
138.50 137.34 136.30 132.59 129.74 129.67 127.37 126.67
64.05 63.02
45.24
21.48 21.34 21.28 20.80
Me
Me
N
O
Me
Me
2b
^{13}C NMR ($CDCl_3$, 101 MHz)
ppm

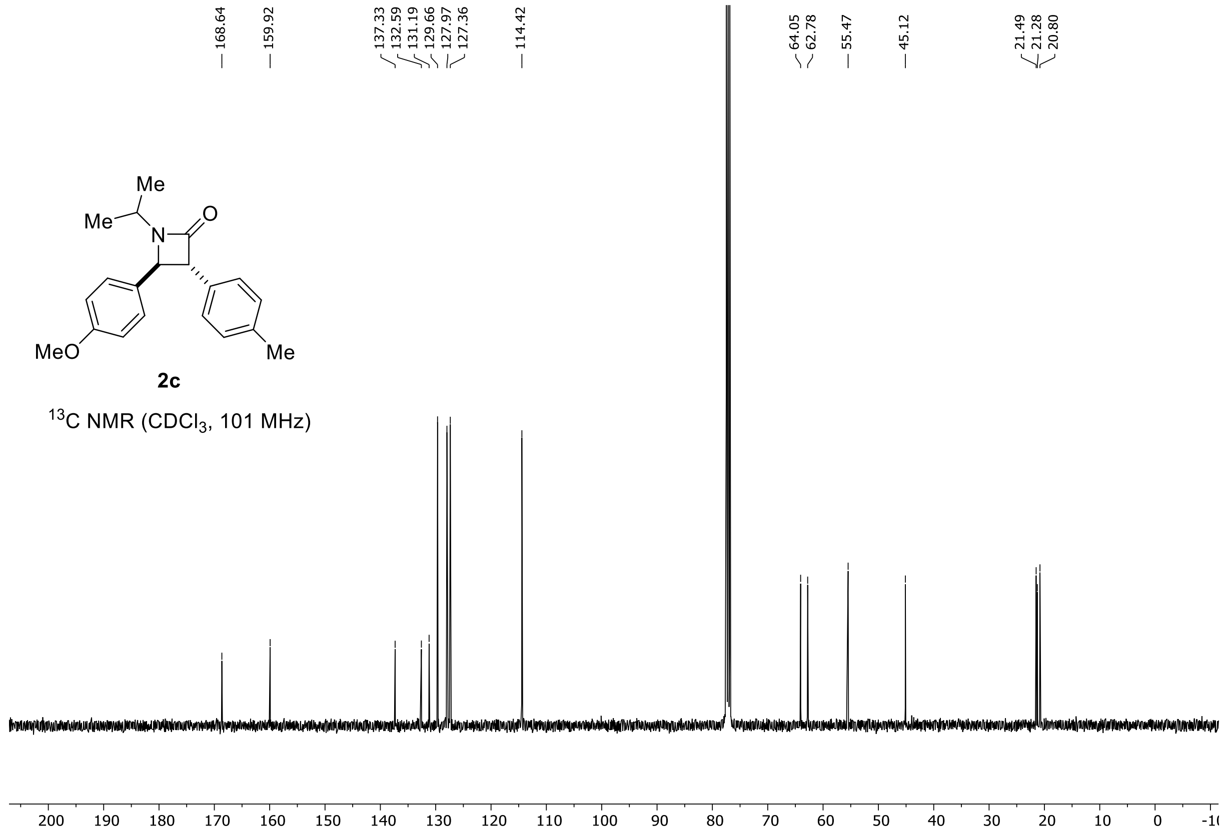
2c

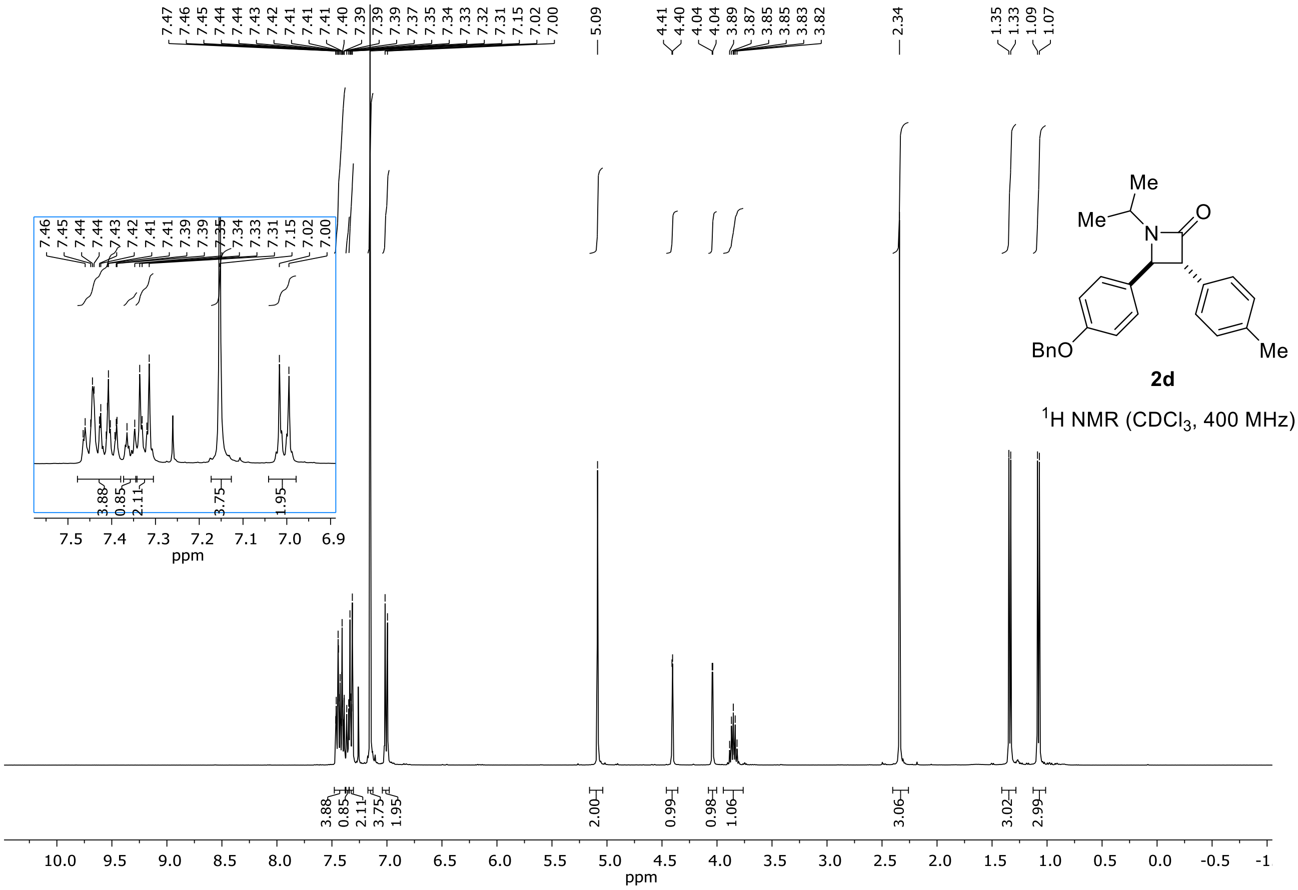
^{1}H NMR ($CDCl_3$, 400 MHz)



2c

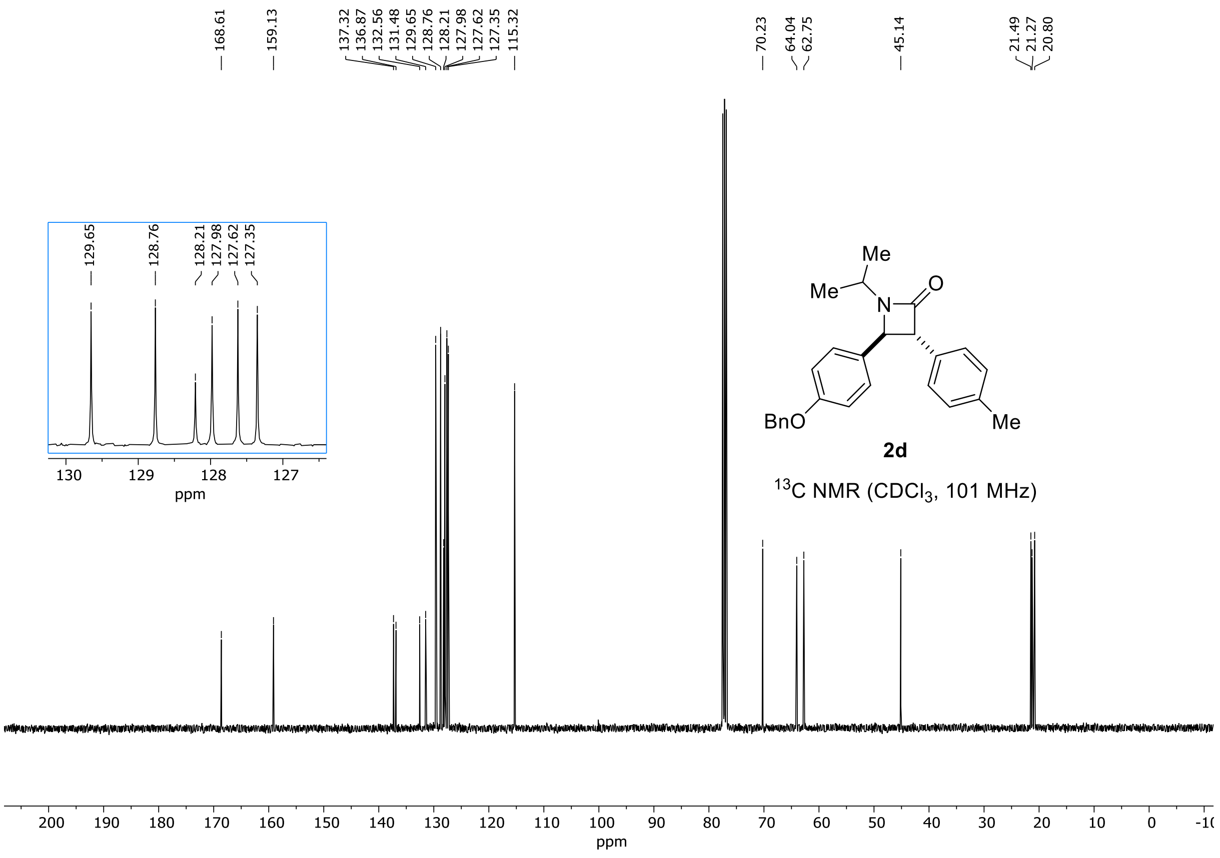
^{13}C NMR ($CDCl_3$, 101 MHz)





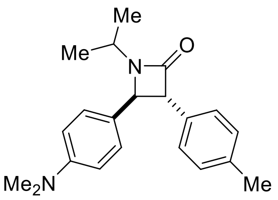
2d

^{1}H NMR ($CDCl_3$, 400 MHz)



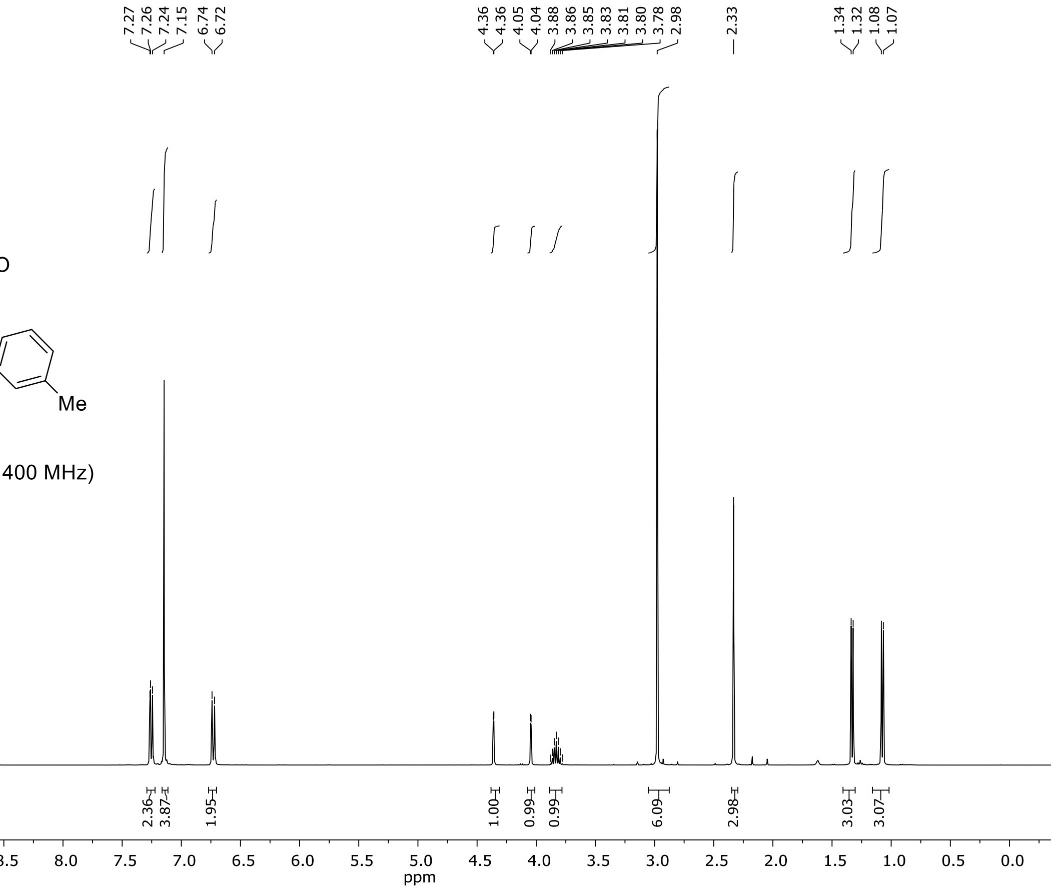
2d

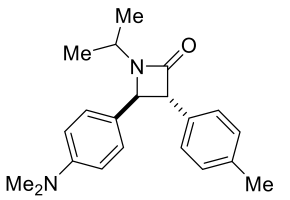
^{13}C NMR ($CDCl_3$, 101 MHz)



2e

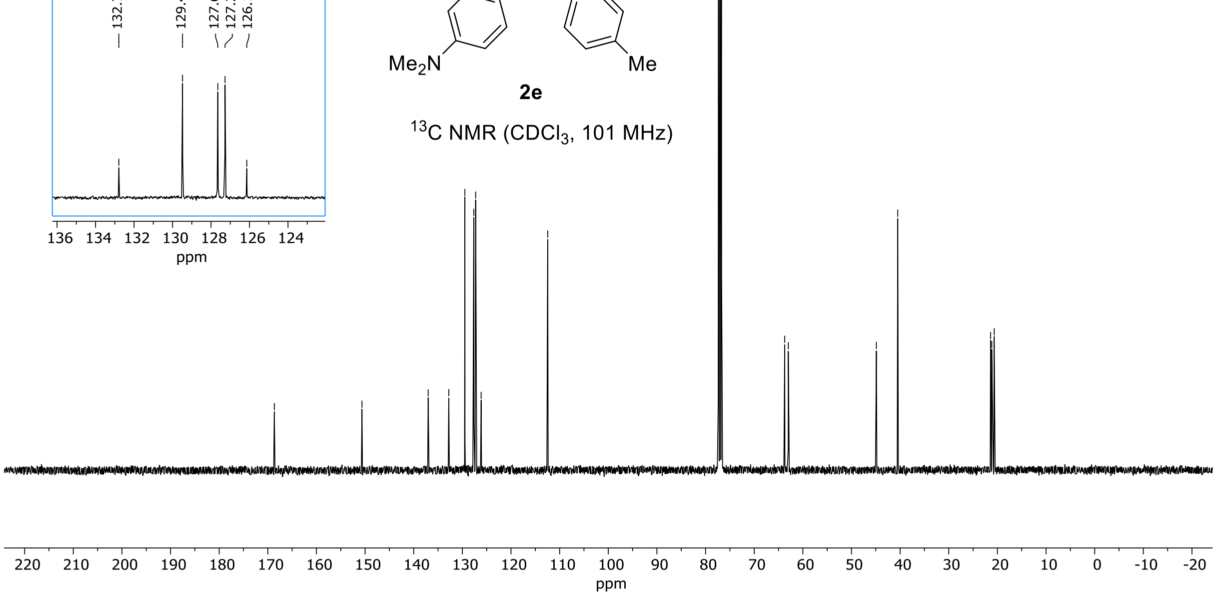
^{1}H NMR ($CDCl_3$, 400 MHz)

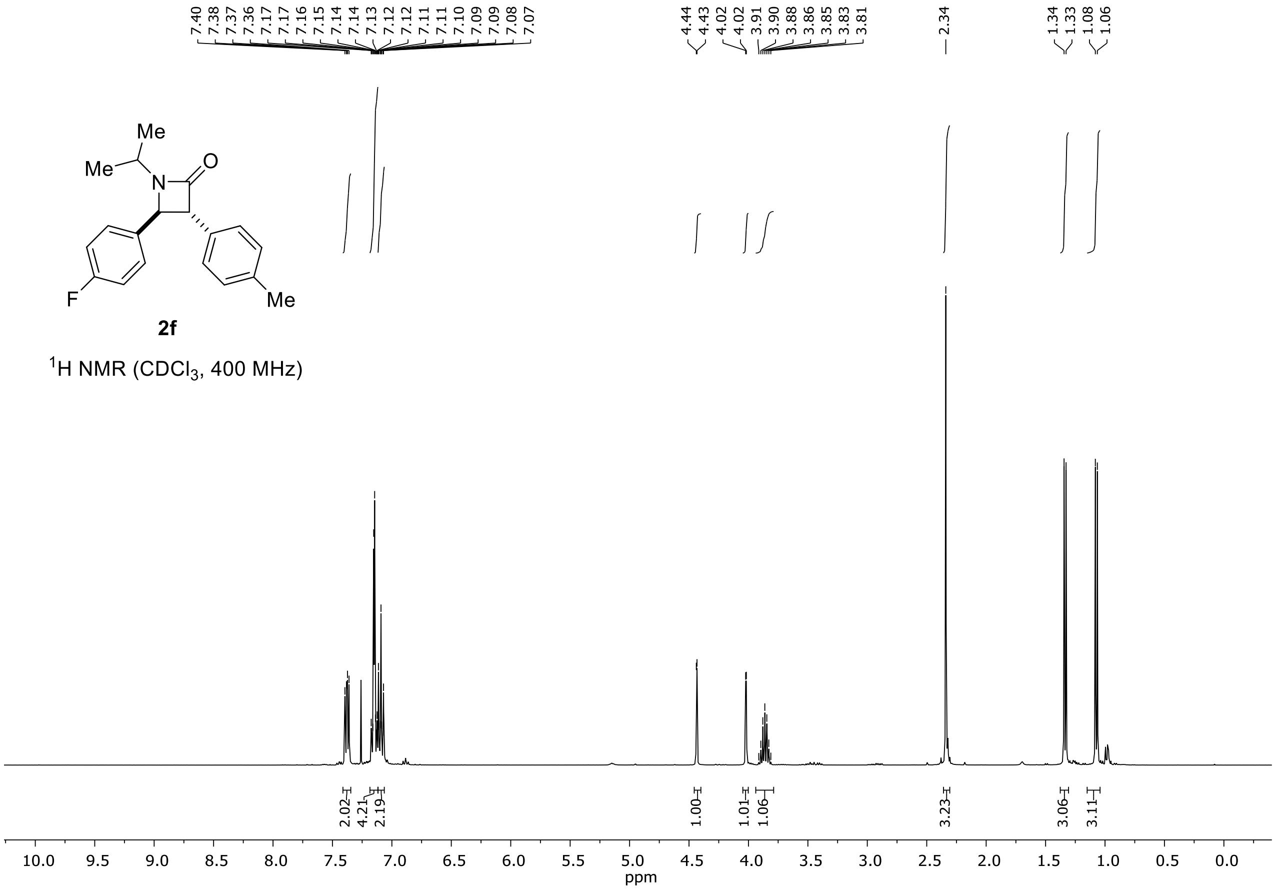




2e

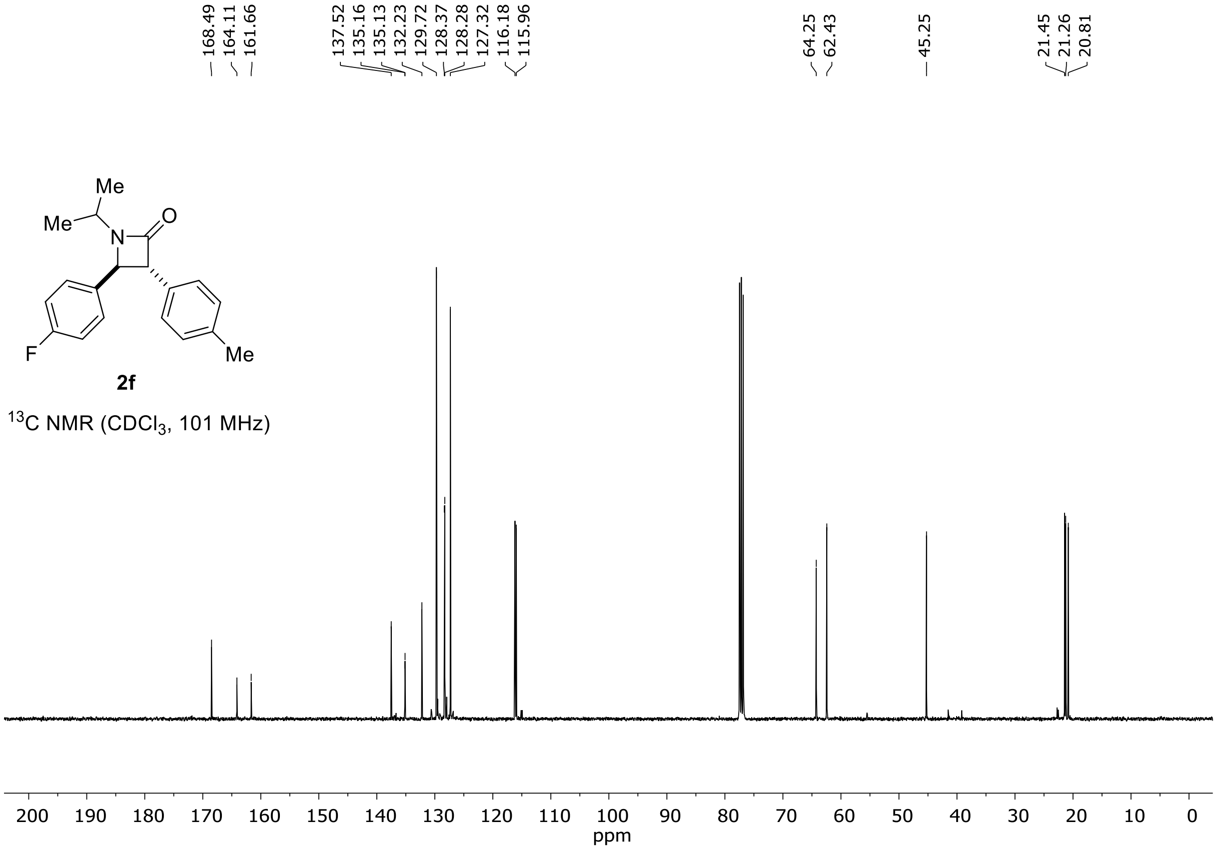
^{13}C NMR ($CDCl_3$, 101 MHz)





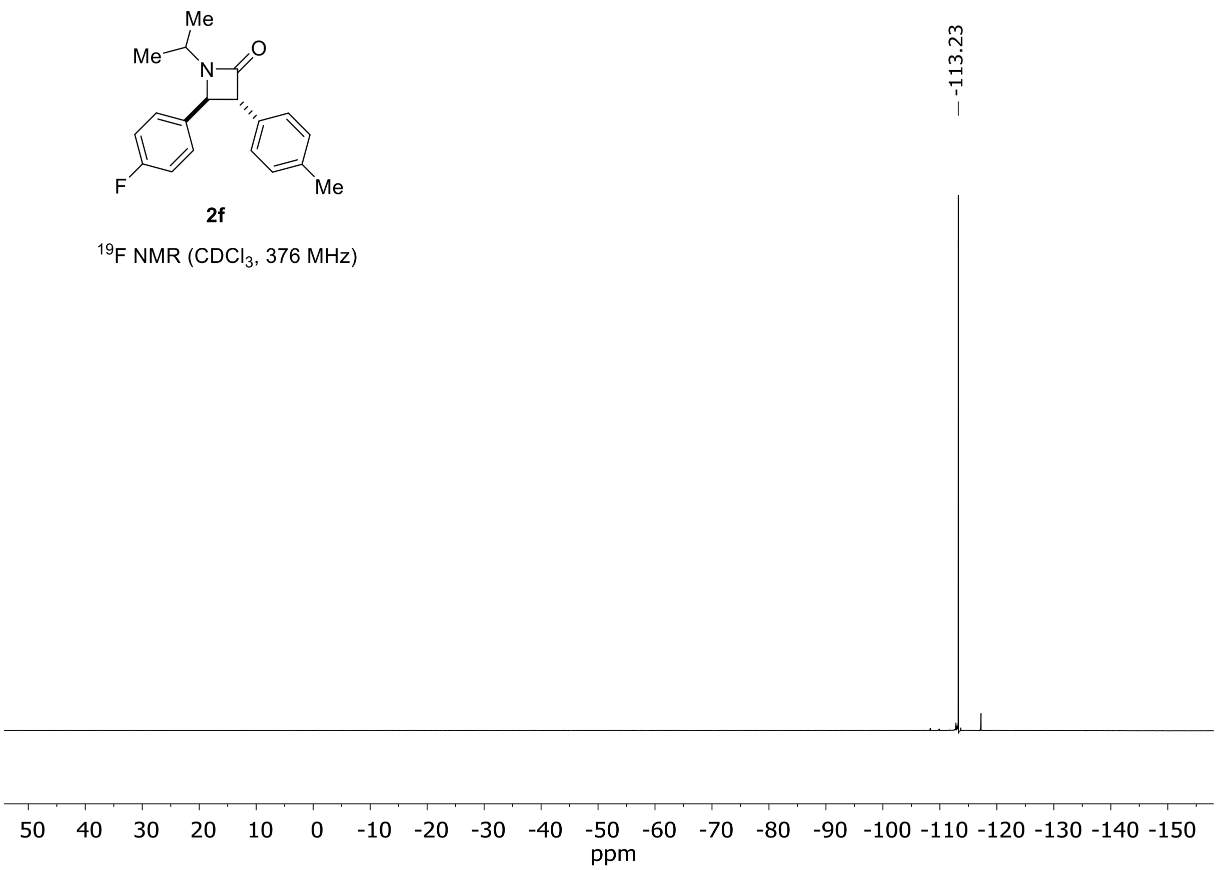
2f

^{1}H NMR ($CDCl_3$, 400 MHz)

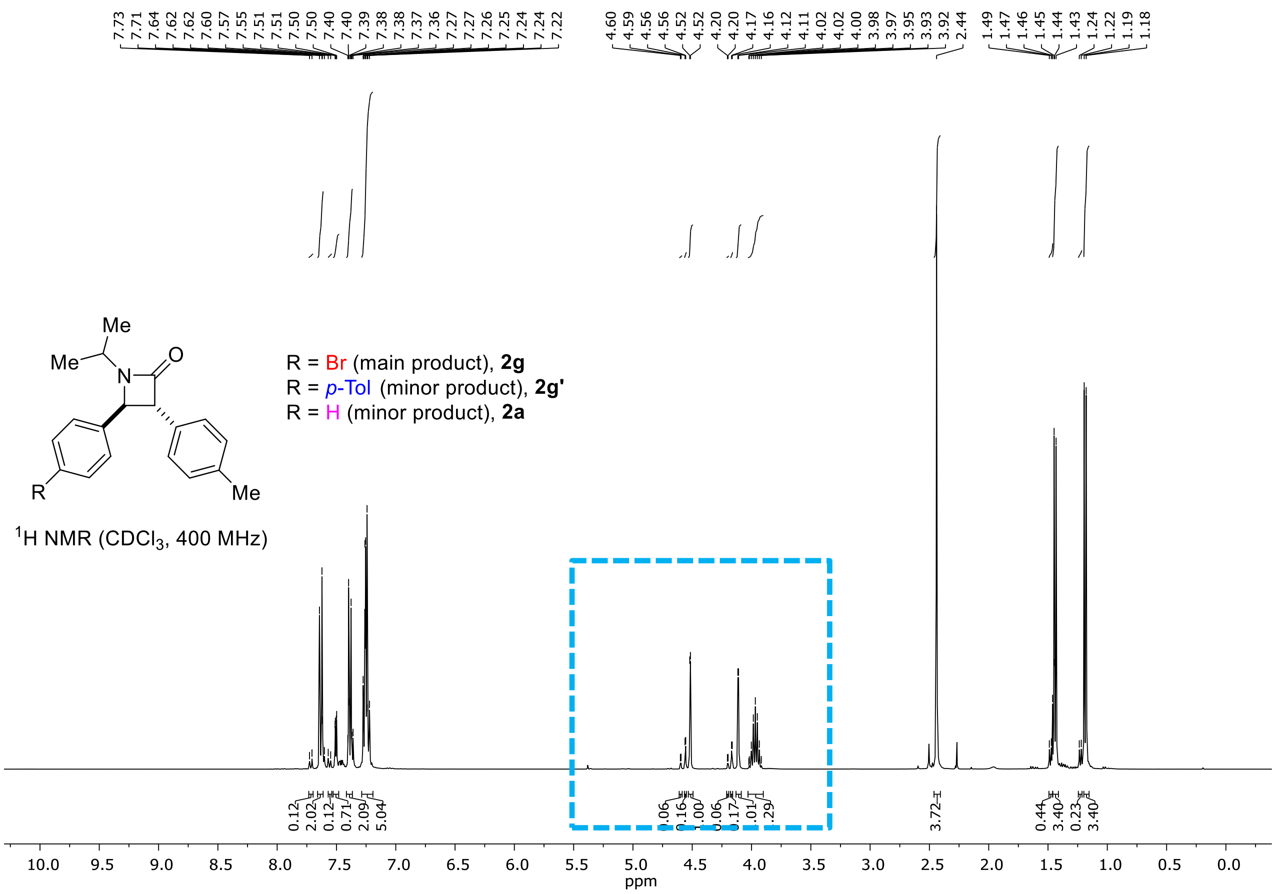


2f

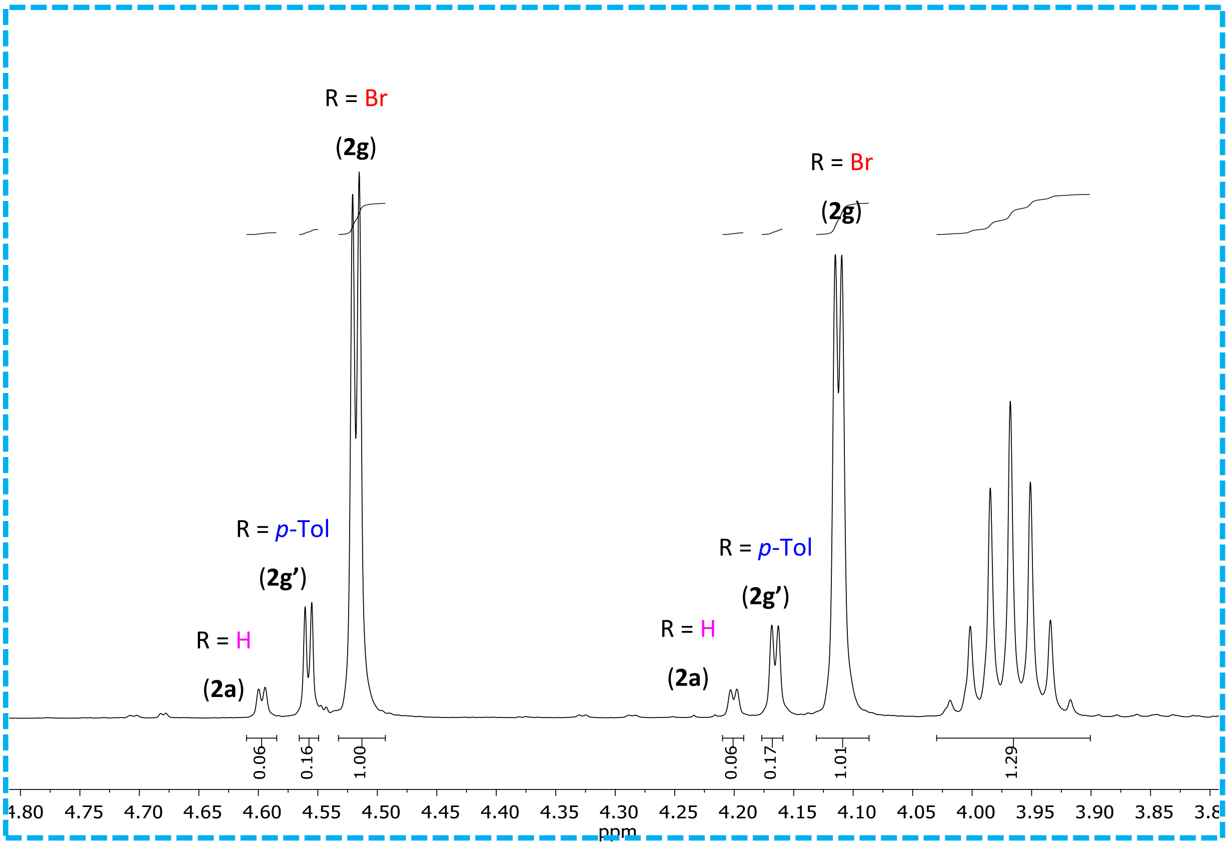
^{13}C NMR ($CDCl_3$, 101 MHz)

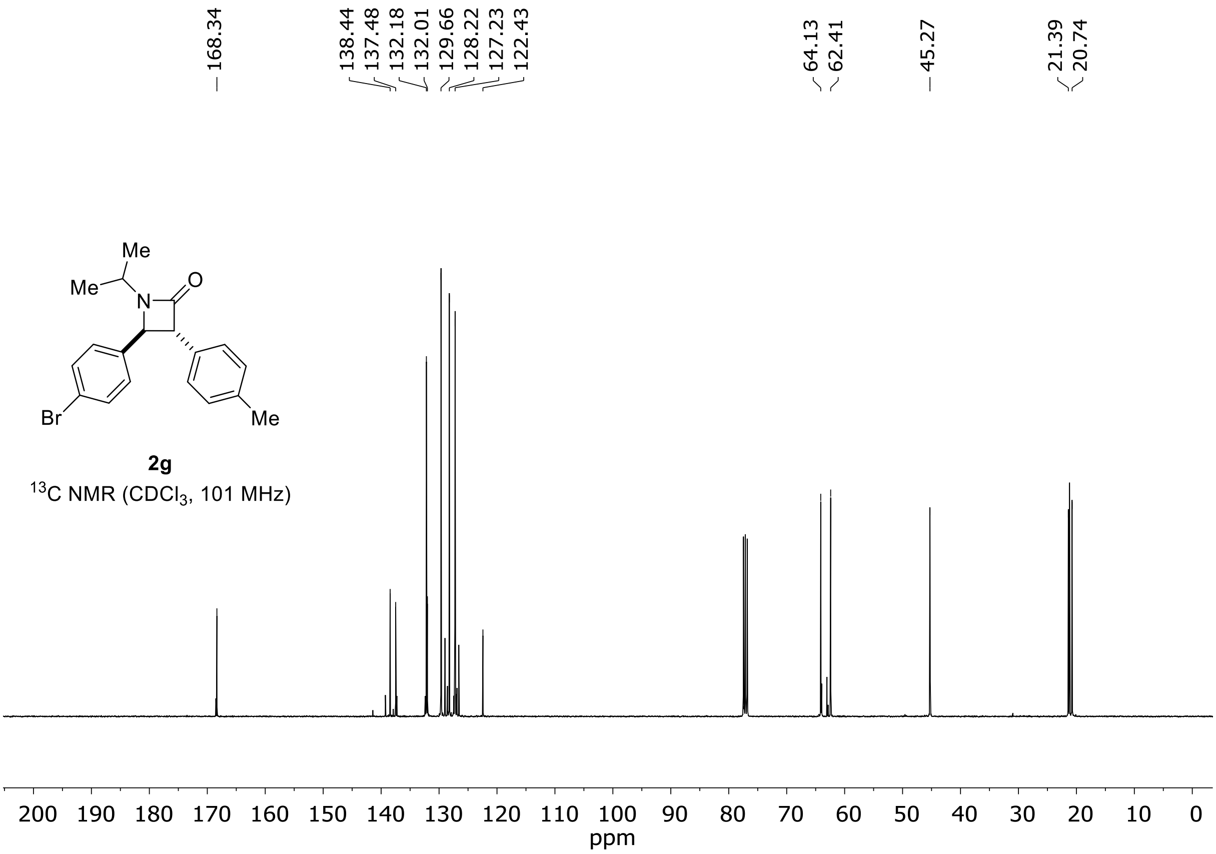


Me
Me
N
O
F
Me
2f
19F NMR (CDCl3, 376 MHz)
-113.23
ppm

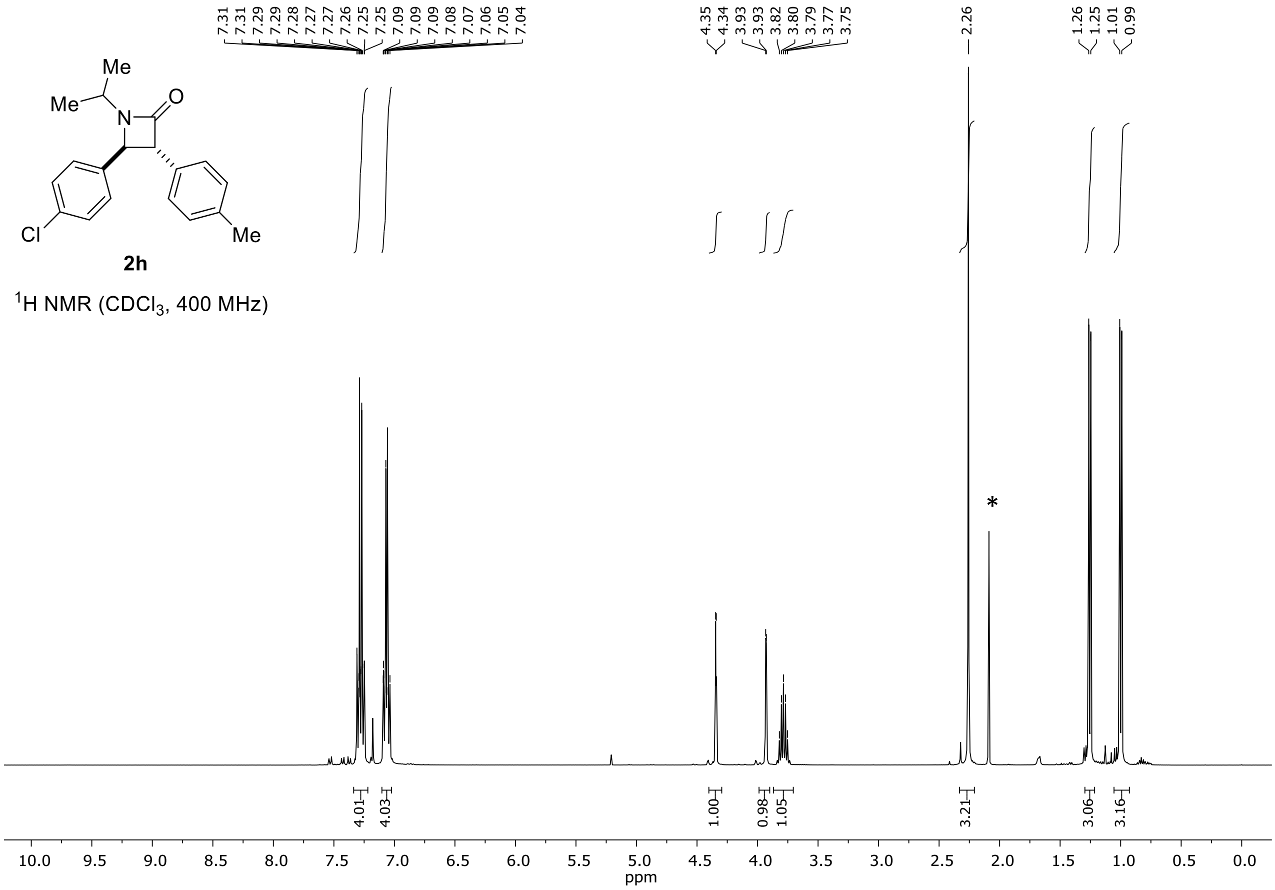


Me
Me
N
O
R
Me
R = Br (main product), 2g
R = p-Tol (minor product), 2g'
R = H (minor product), 2a
1H NMR (CDCl3, 400 MHz)
ppm

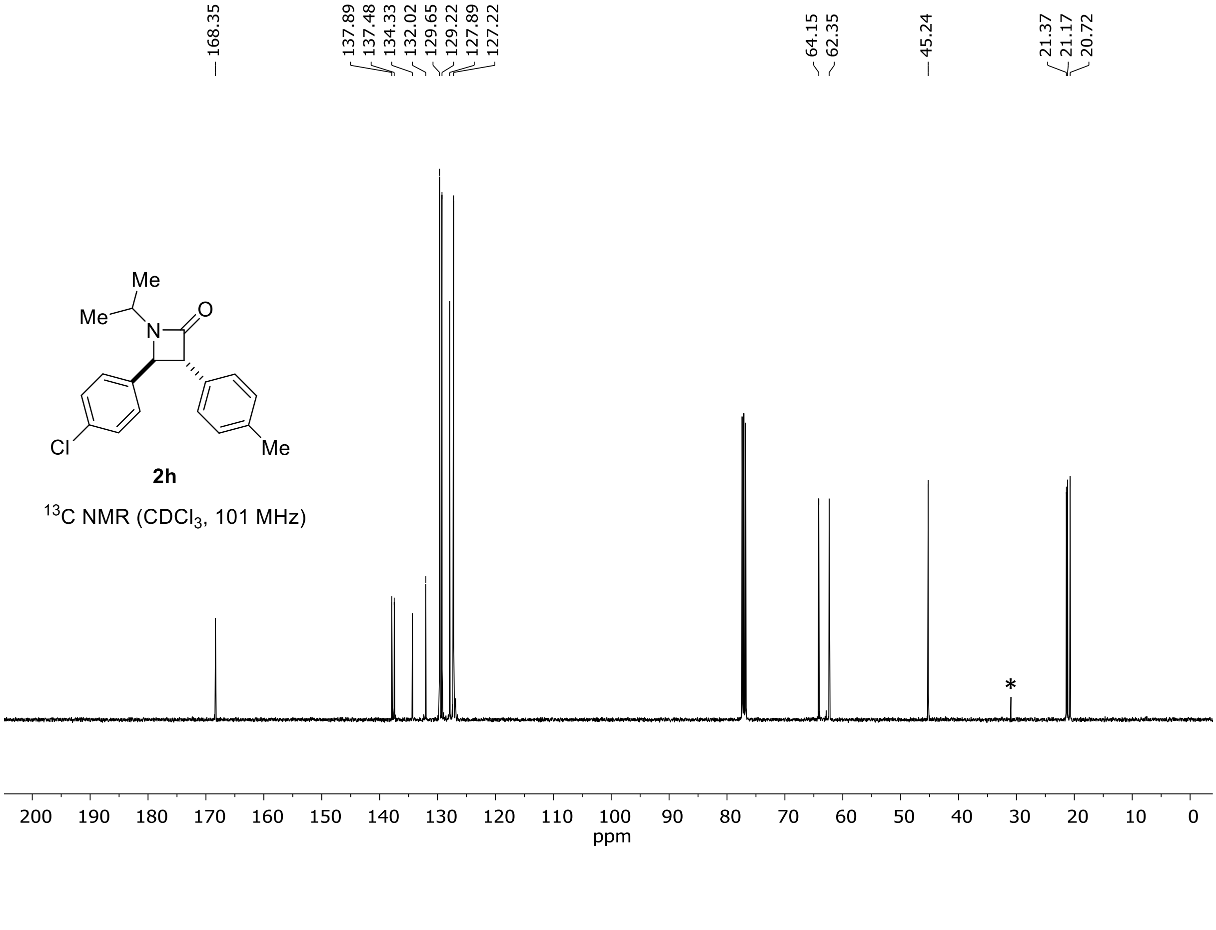




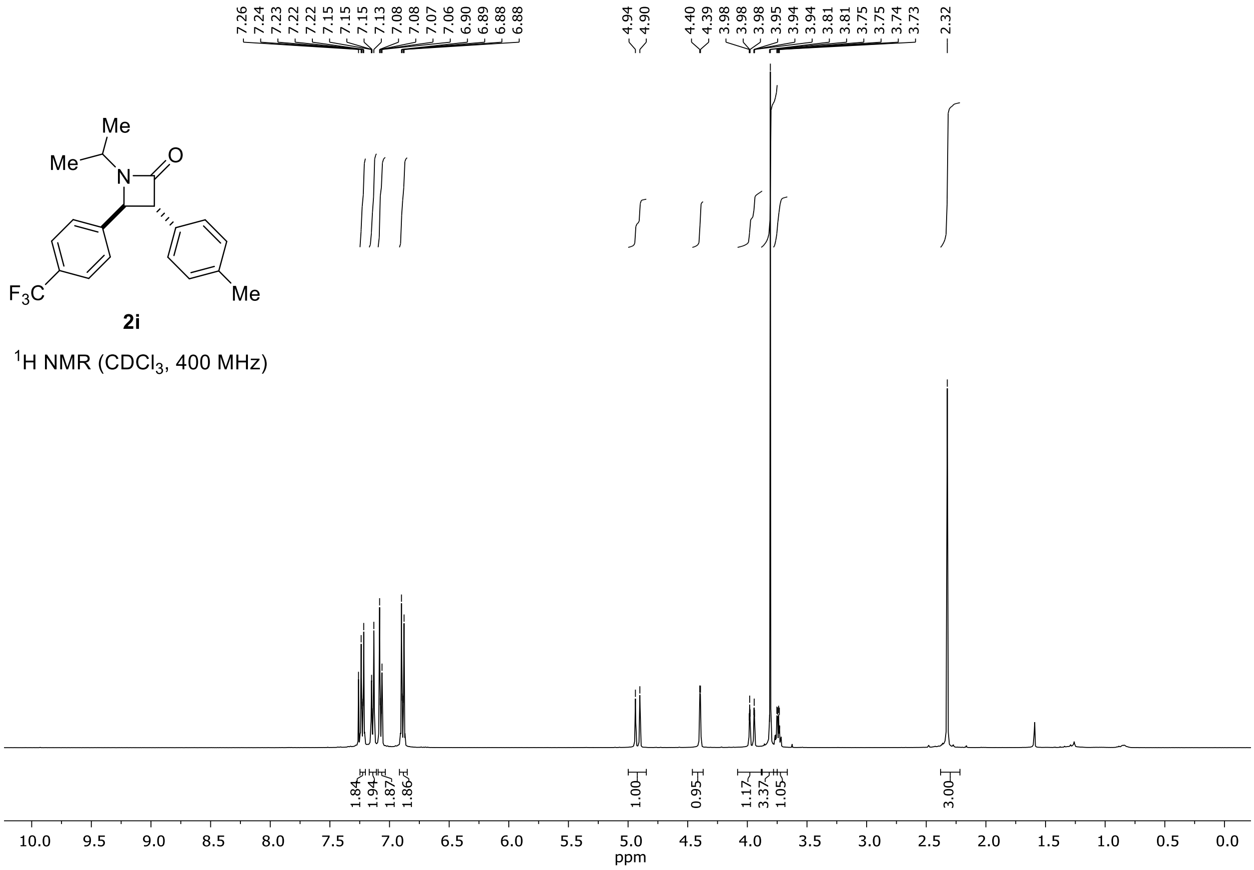
2g
^{13}C NMR ($CDCl_3$, 101 MHz)

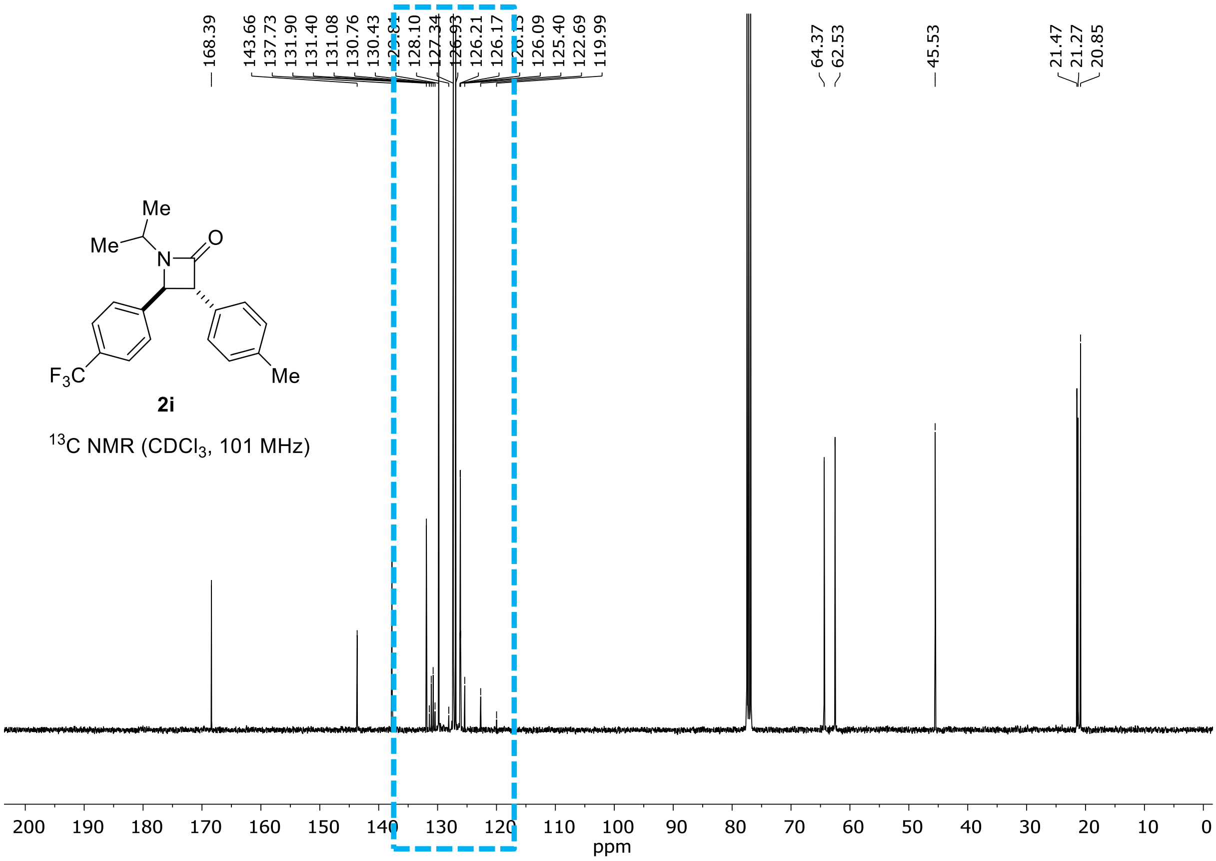


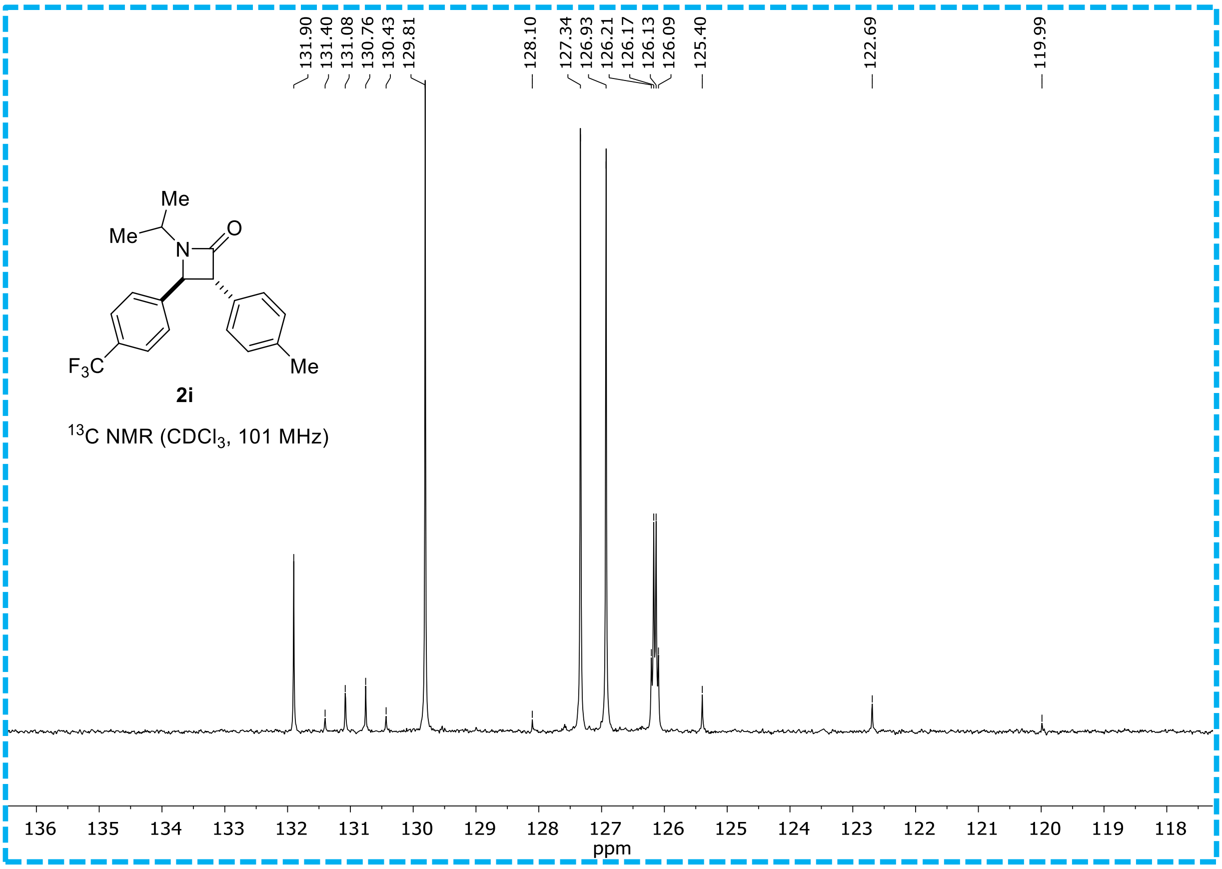
7.31
7.31
7.29
7.29
7.28
7.27
7.27
7.26
7.25
7.25
7.09
7.09
7.09
7.08
7.07
7.06
7.05
7.04
4.35
4.34
3.93
3.93
3.82
3.80
3.79
3.77
3.75
2.26
1.26
1.25
1.01
0.99
Me
Me
N
O
Cl
Me
2h
^{1}H NMR (CDCl$_3$, 400 MHz)
*
4.01
4.03
1.00
0.98
1.05
3.21
3.06
3.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

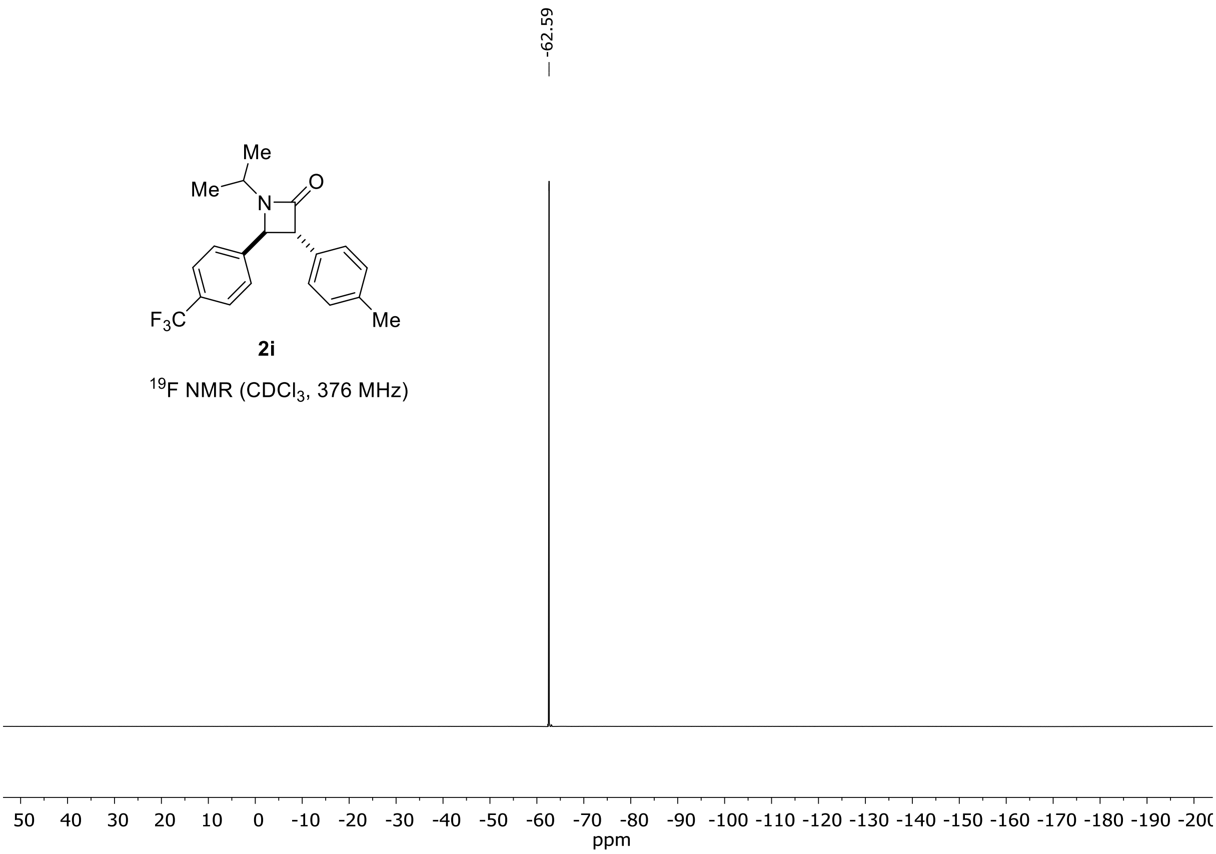


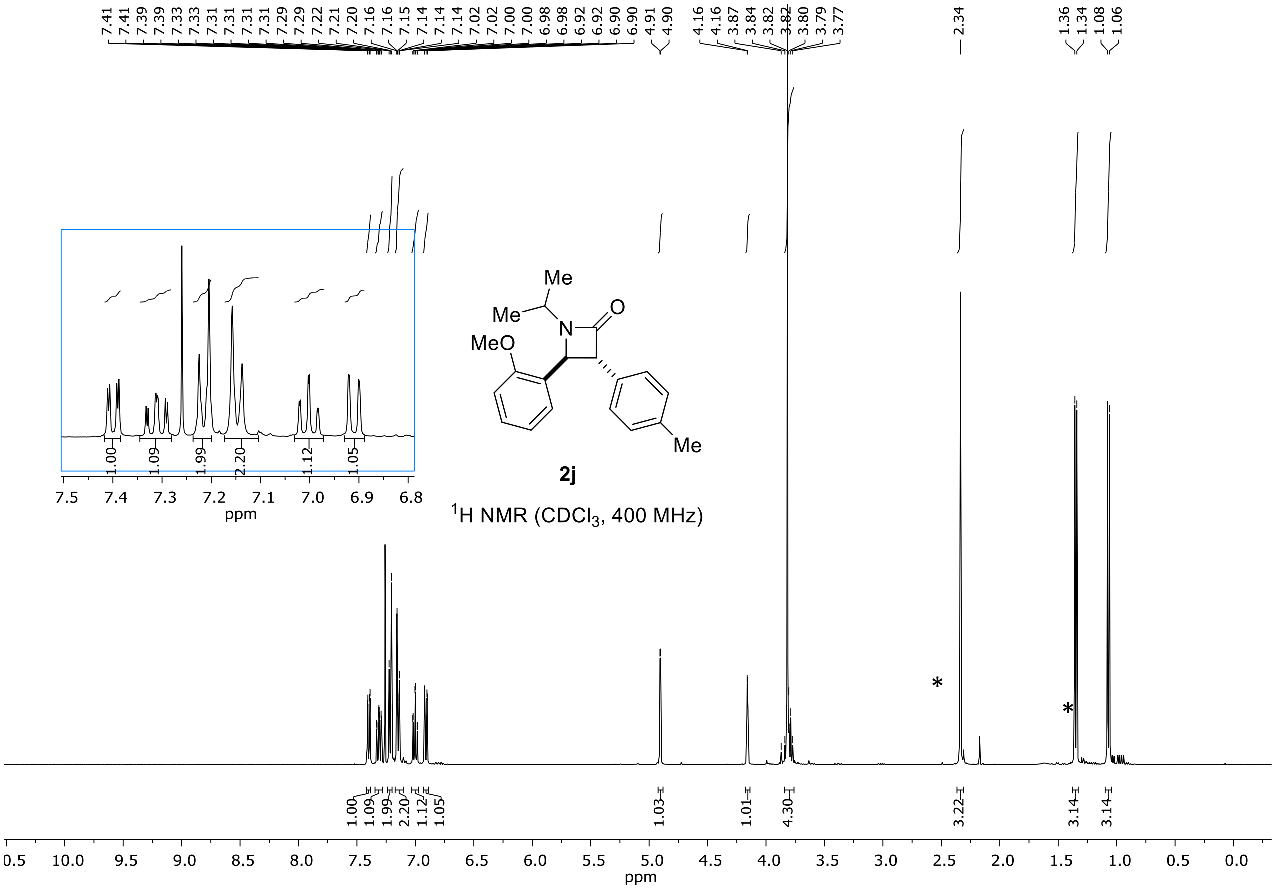
168.35
137.89
137.48
134.33
132.02
129.65
129.22
127.89
127.22
64.15
62.35
45.24
21.37
21.17
20.72
Me
Me
N
O
Cl
Me
2h
^{13}C NMR (CDCl$_3$, 101 MHz)
*
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

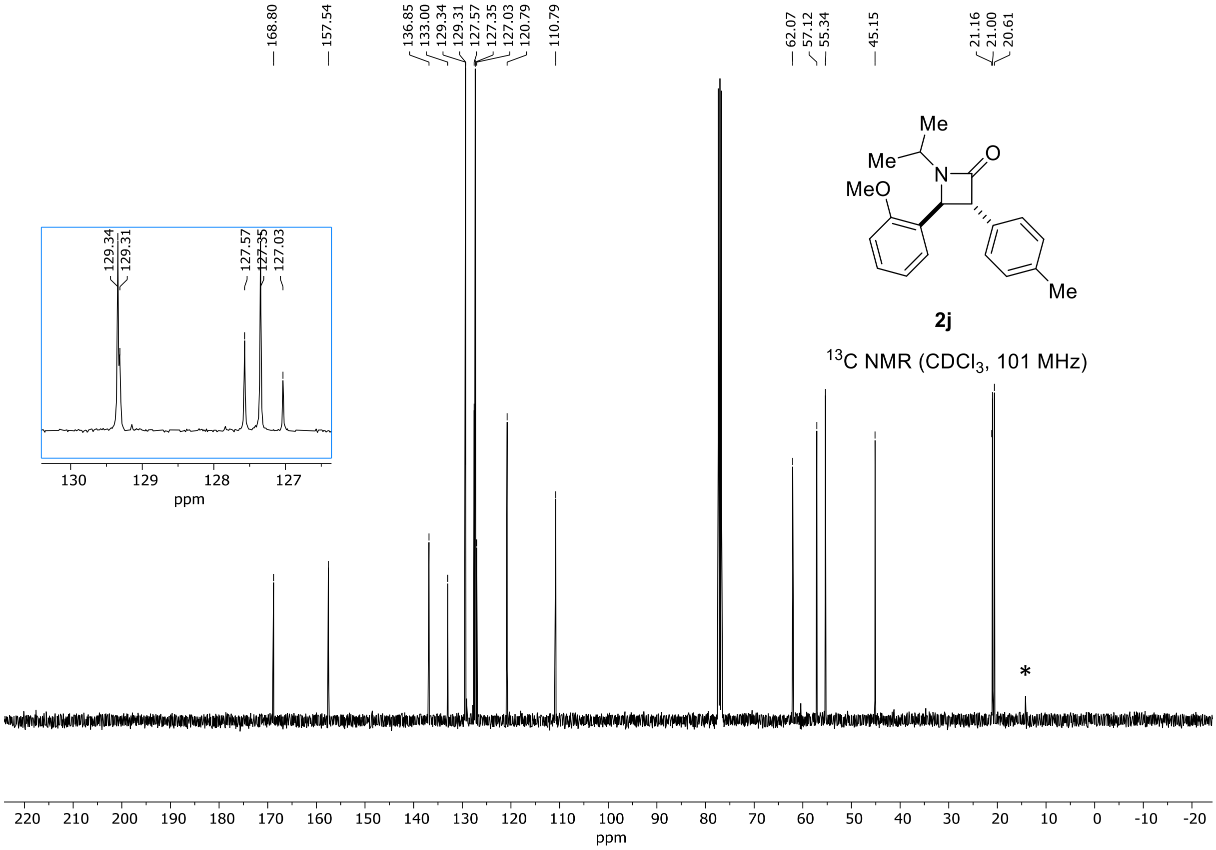

7.26
7.24
7.23
7.22
7.22
7.15
7.15
7.13
7.08
7.08
7.07
7.06
6.90
6.89
6.88
6.88
4.94
4.90
4.40
4.39
3.98
3.98
3.98
3.95
3.94
3.94
3.81
3.81
3.75
3.75
3.74
3.73
2.32
Me
Me
N
O
F3C
Me
2i
1H NMR (CDCl3, 400 MHz)
1.84
1.94
1.87
1.86
1.00
0.95
1.17
3.37
1.05
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

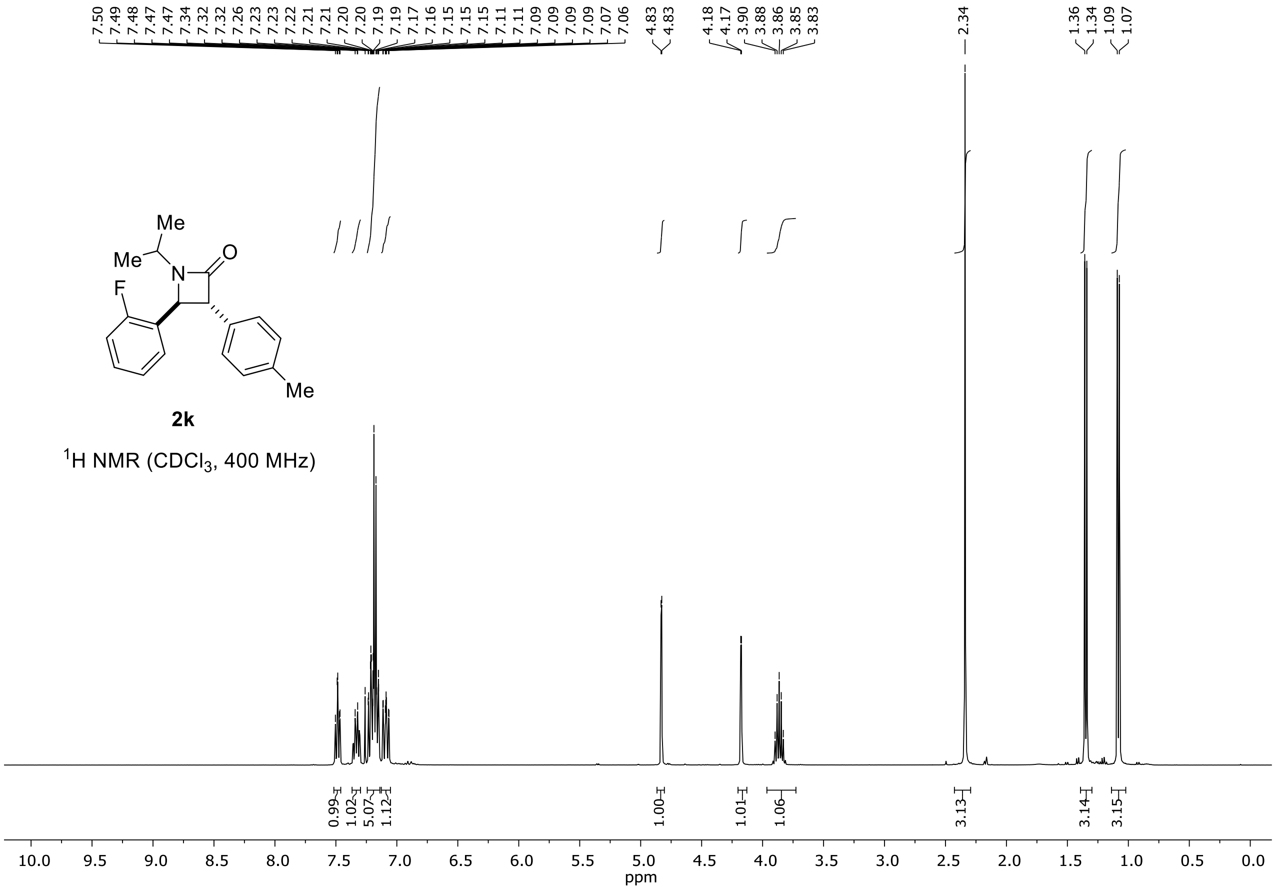

168.39
143.66
137.73
131.90
131.40
131.08
130.76
130.43
128.10
127.34
126.93
126.21
126.17
126.09
125.40
122.69
119.99
64.37
62.53
45.53
21.47
21.27
20.85
Me
Me
N
O
F3C
Me
2i
13C NMR (CDCl3, 101 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

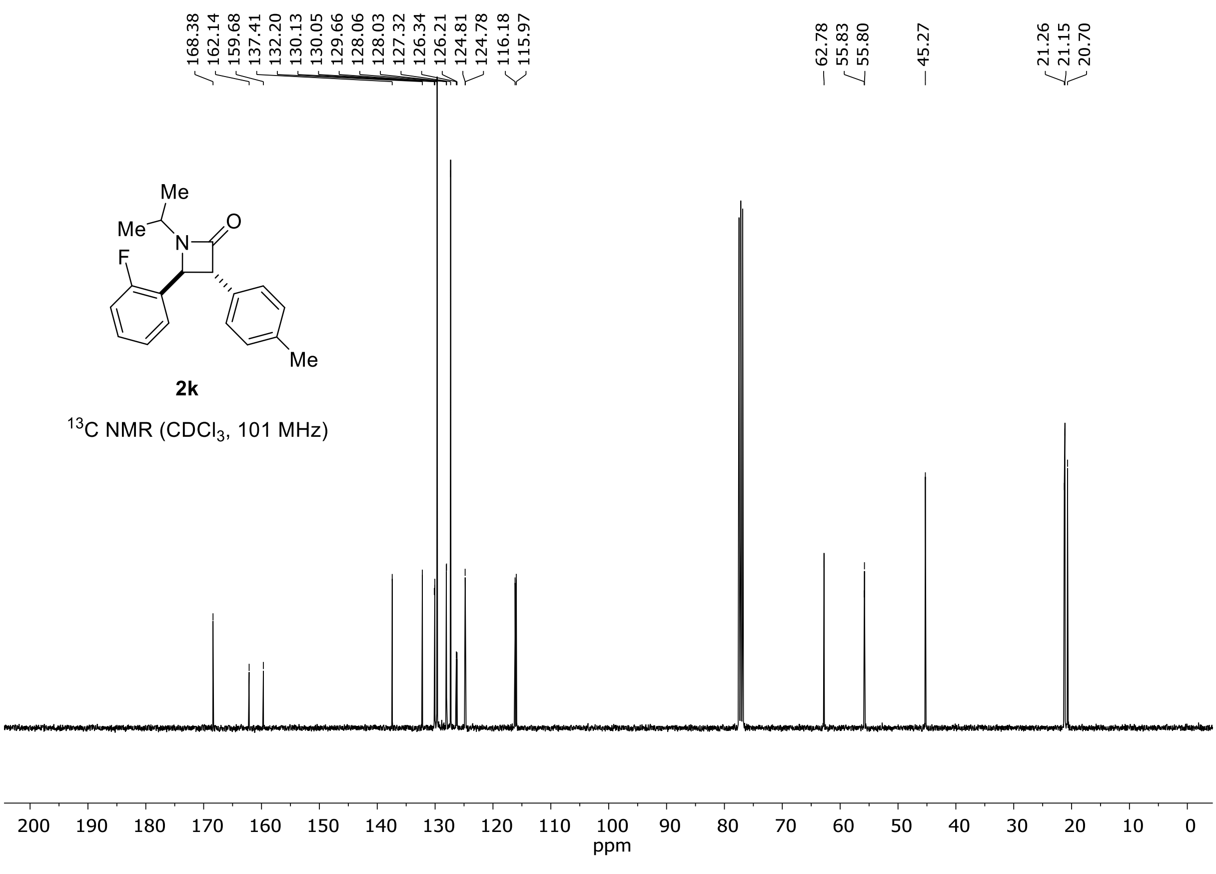

131.90
131.40
131.08
130.76
130.43
129.81
128.10
127.34
126.93
126.21
126.17
126.13
126.09
125.40
122.69
119.99
Me
Me
N
O
F3C
Me
2i
13C NMR (CDCl3, 101 MHz)
ppm

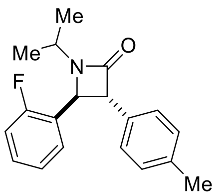

-62.59
Me
Me
N
O
F3C
Me
2i
19F NMR (CDCl3, 376 MHz)
ppm


2j
^{1}H NMR ($CDCl_3$, 400 MHz)


2j
^{13}C NMR ($CDCl_3$, 101 MHz)

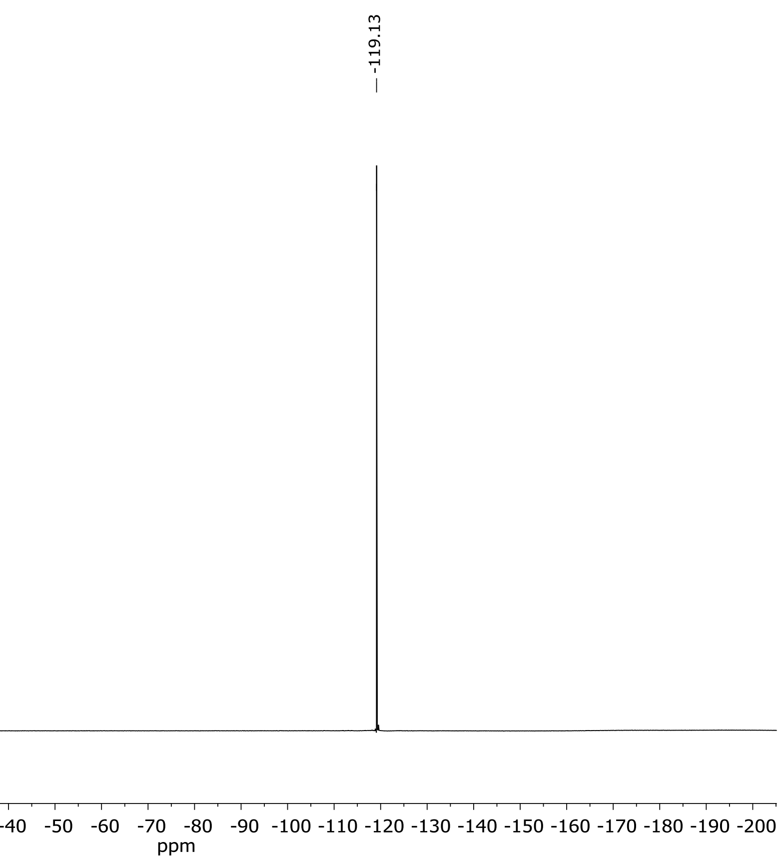

7.50 7.49 7.48 7.47 7.47 7.34 7.32 7.32 7.26 7.23 7.23 7.22 7.21 7.21 7.20 7.20 7.19 7.19 7.17 7.16 7.15 7.15 7.15 7.11 7.11 7.09 7.09 7.09 7.07 7.06
4.83 4.83
4.18 4.17 3.90 3.88 3.86 3.85 3.83
2.34
1.36 1.34 1.09 1.07
Me
Me
N
O
F
Me
2k
^{1}H NMR ($CDCl_3$, 400 MHz)
0.99 1.02 5.07 1.12 1.00 1.01 1.06 3.13 3.14 3.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

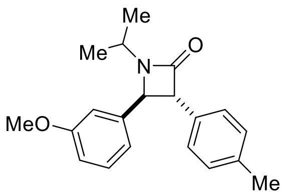

168.38 162.14 159.68 137.41 132.20 130.13 130.05 129.66 128.06 128.03 127.32 126.34 126.21 124.81 124.78 116.18 115.97
62.78 55.83 55.80
45.27
21.26 21.15 20.70
Me
Me
N
O
F
Me
2k
^{13}C NMR ($CDCl_3$, 101 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm



2k

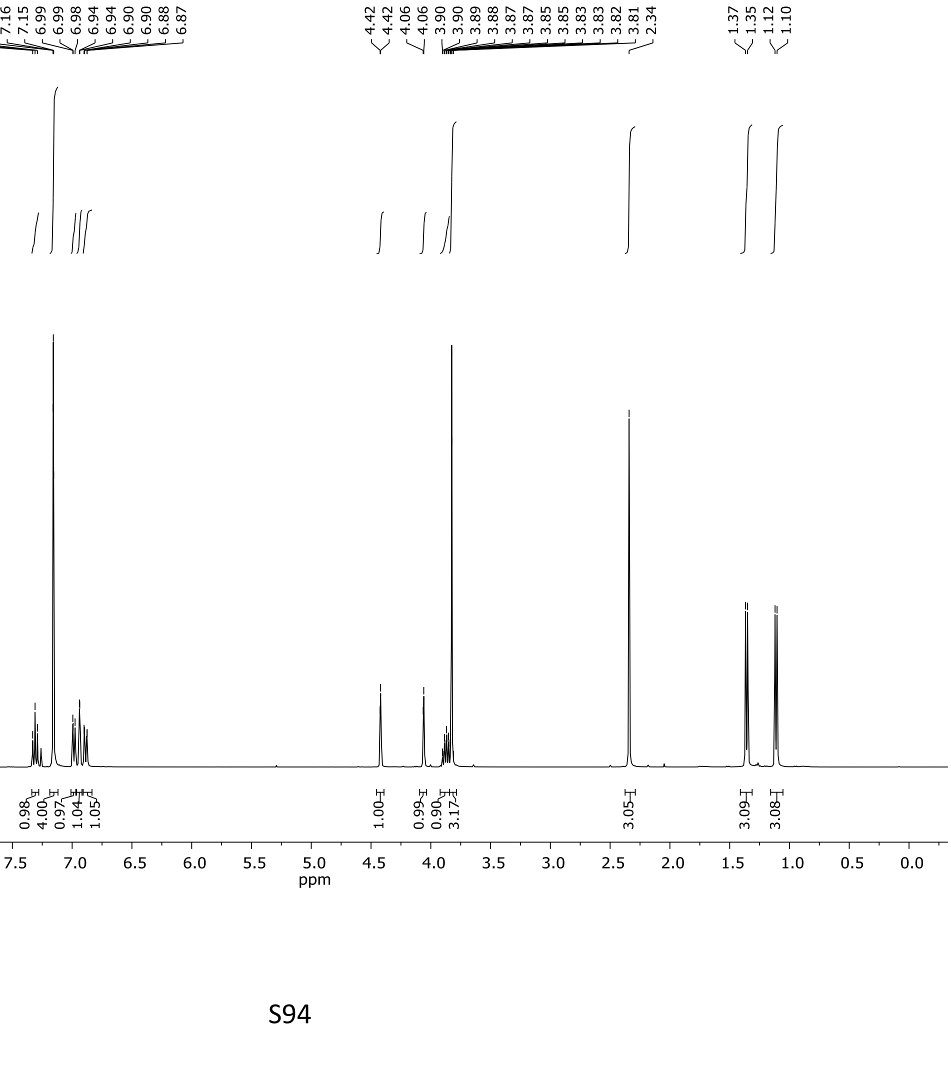
^{19}F NMR ($CDCl_3$, 376 MHz)

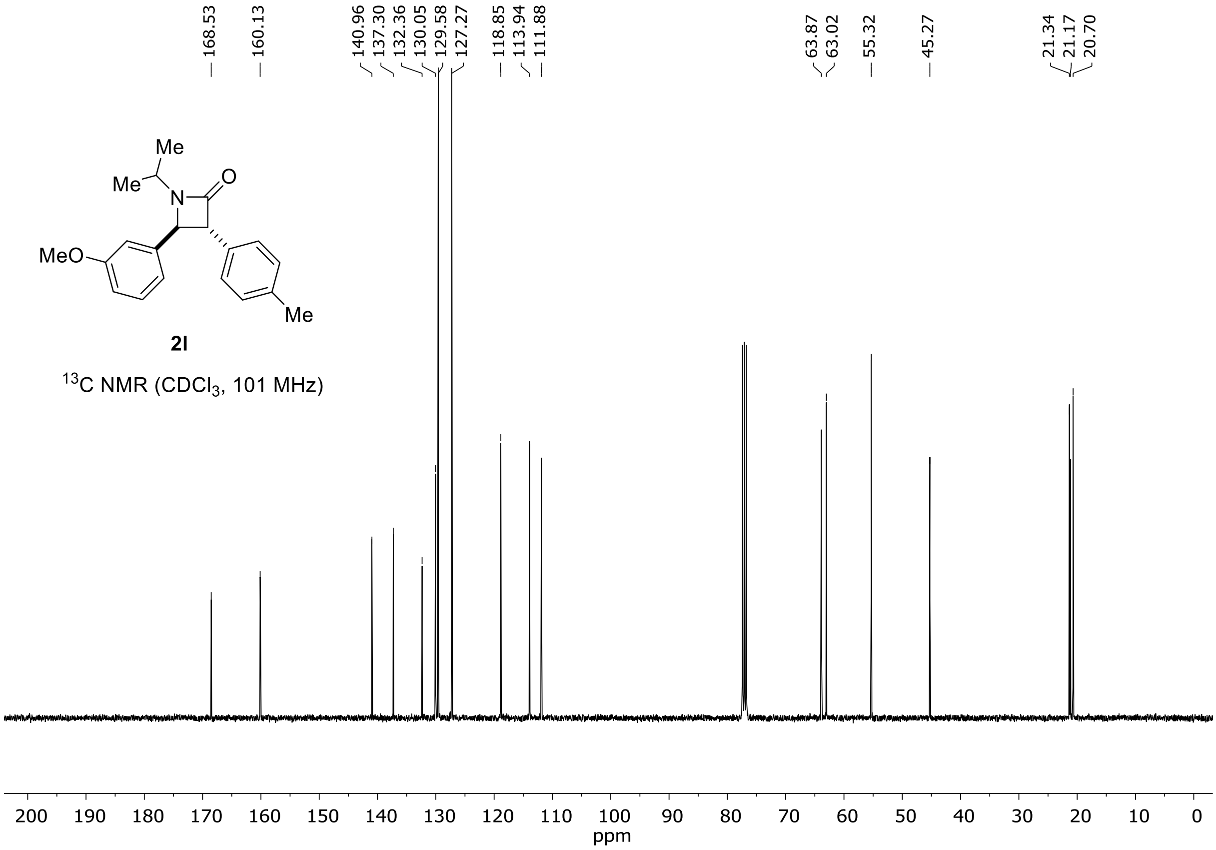


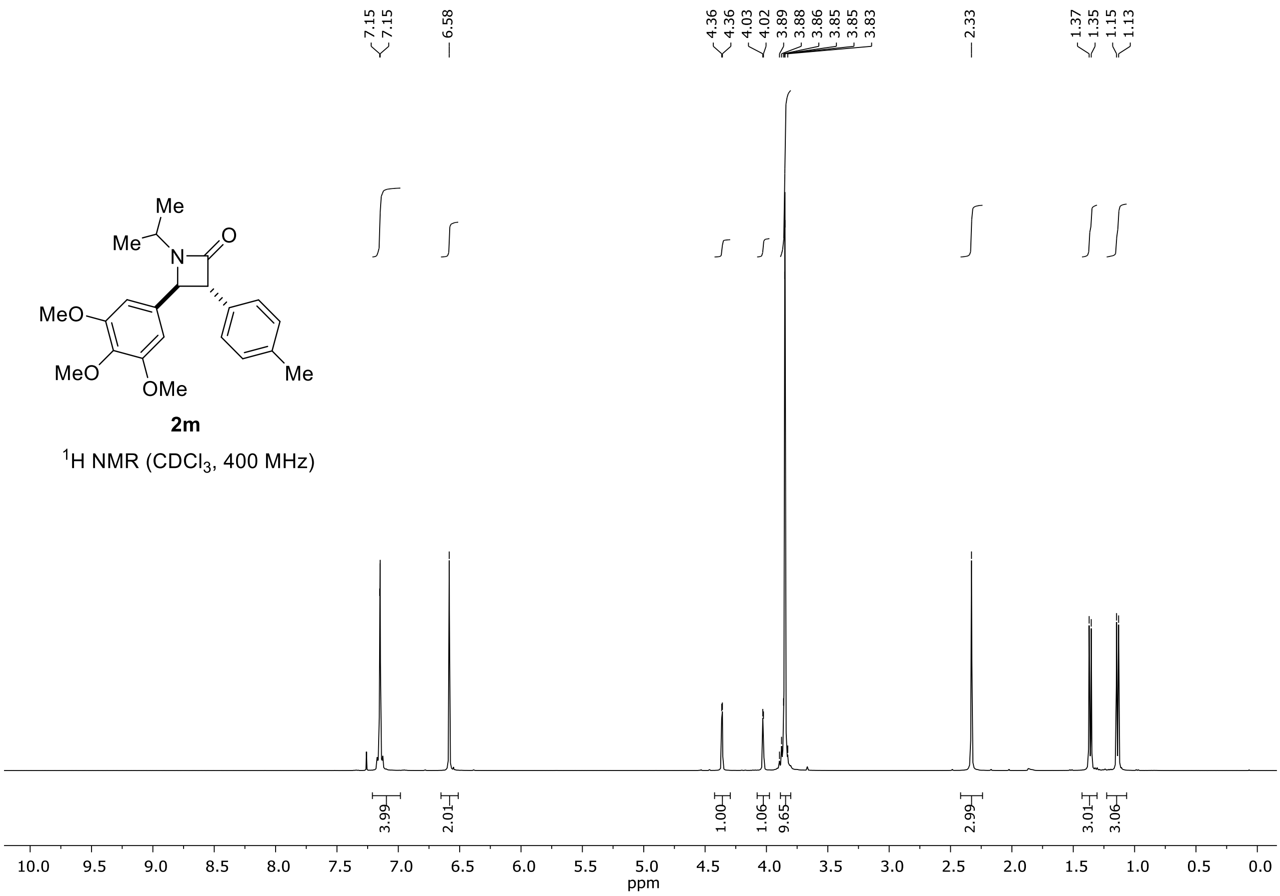


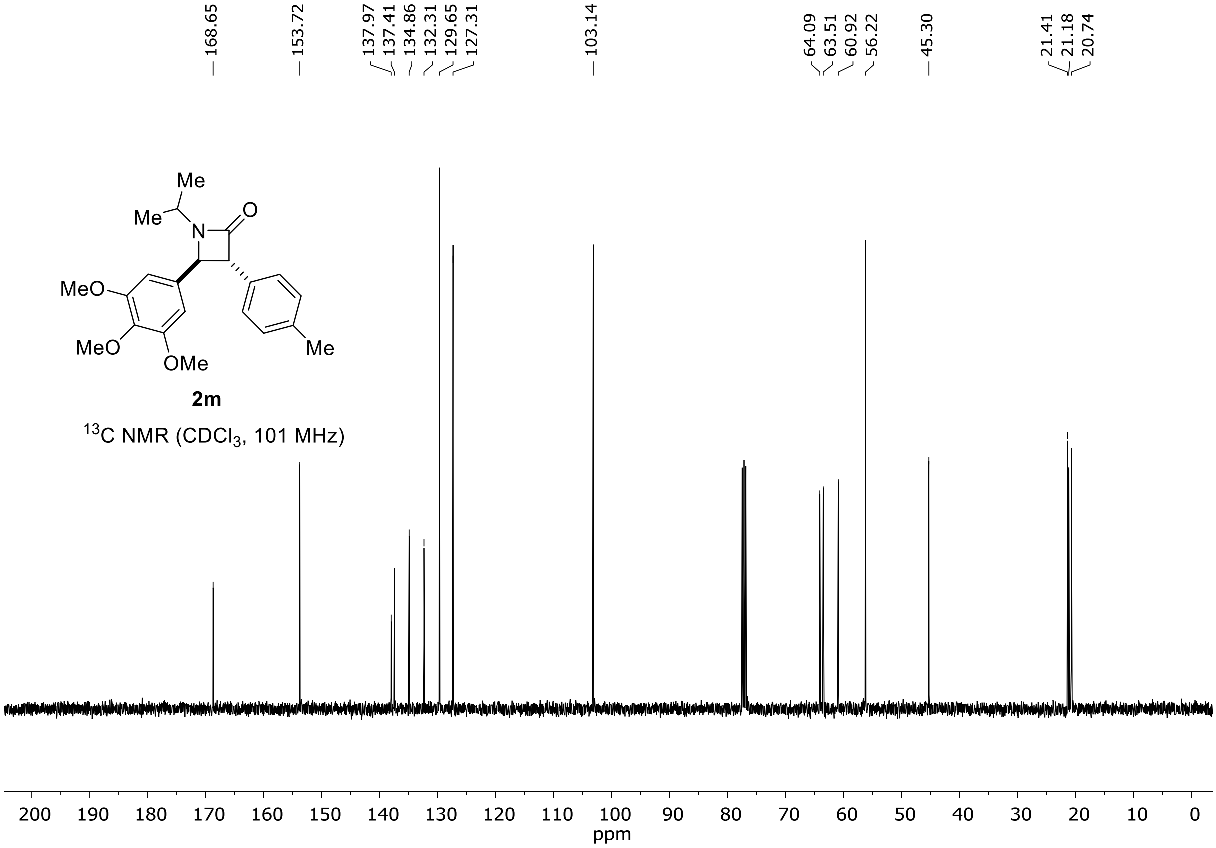
2l

^{1}H NMR ($CDCl_3$, 400 MHz)



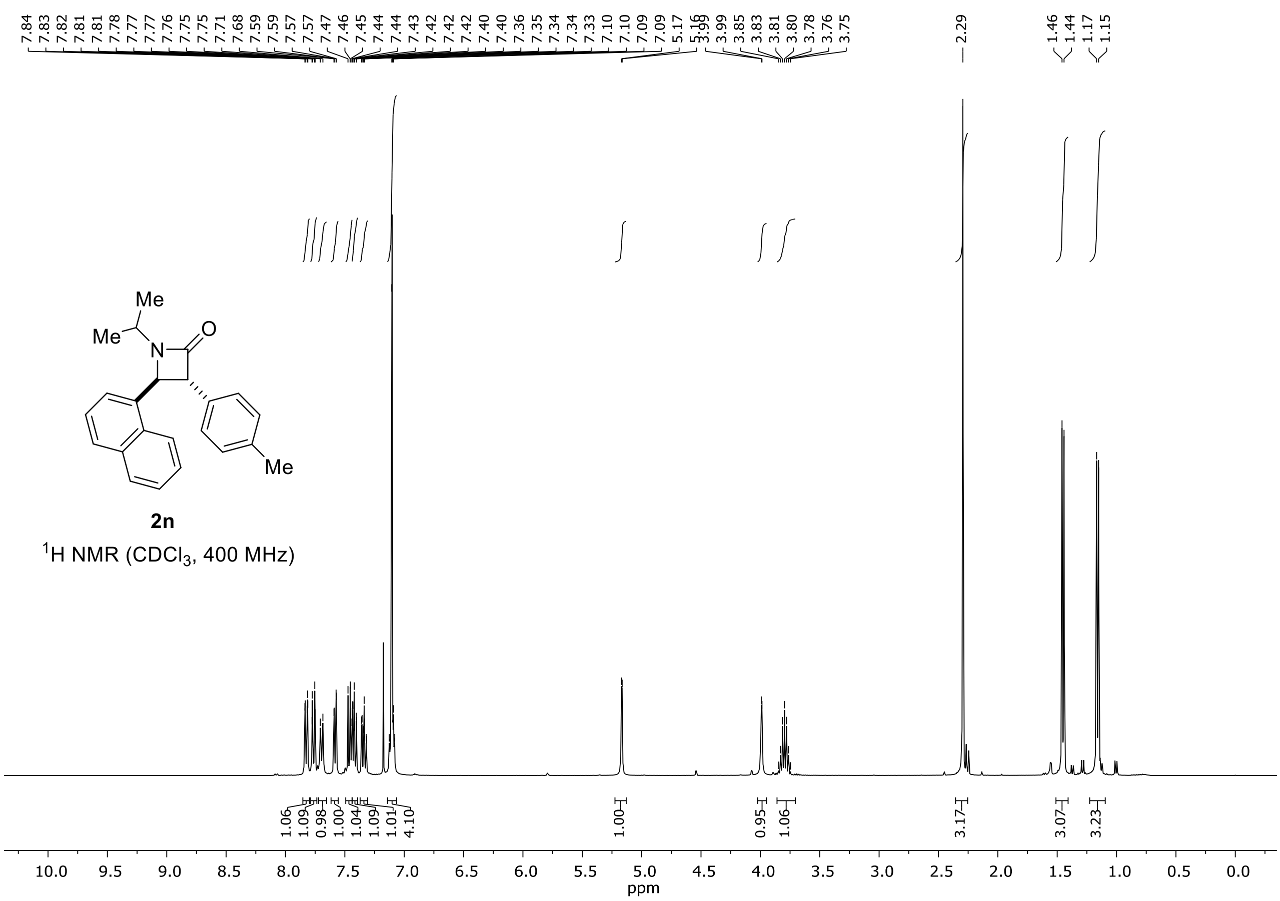

168.53
160.13
140.96
137.30
132.36
130.05
129.58
127.27
118.85
113.94
111.88
63.87
63.02
55.32
45.27
21.34
21.17
20.70
Me
Me
N
O
MeO
Me
2l
^{13}C NMR (CDCl$_3$, 101 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


7.15
7.15
6.58
4.36
4.36
4.03
4.02
3.89
3.88
3.86
3.85
3.85
3.83
2.33
1.37
1.35
1.15
1.13
Me
Me
N
O
MeO
MeO
OMe
Me
2m
^{1}H NMR (CDCl$_3$, 400 MHz)
3.99
2.01
1.00
1.06
9.65
2.99
3.01
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm



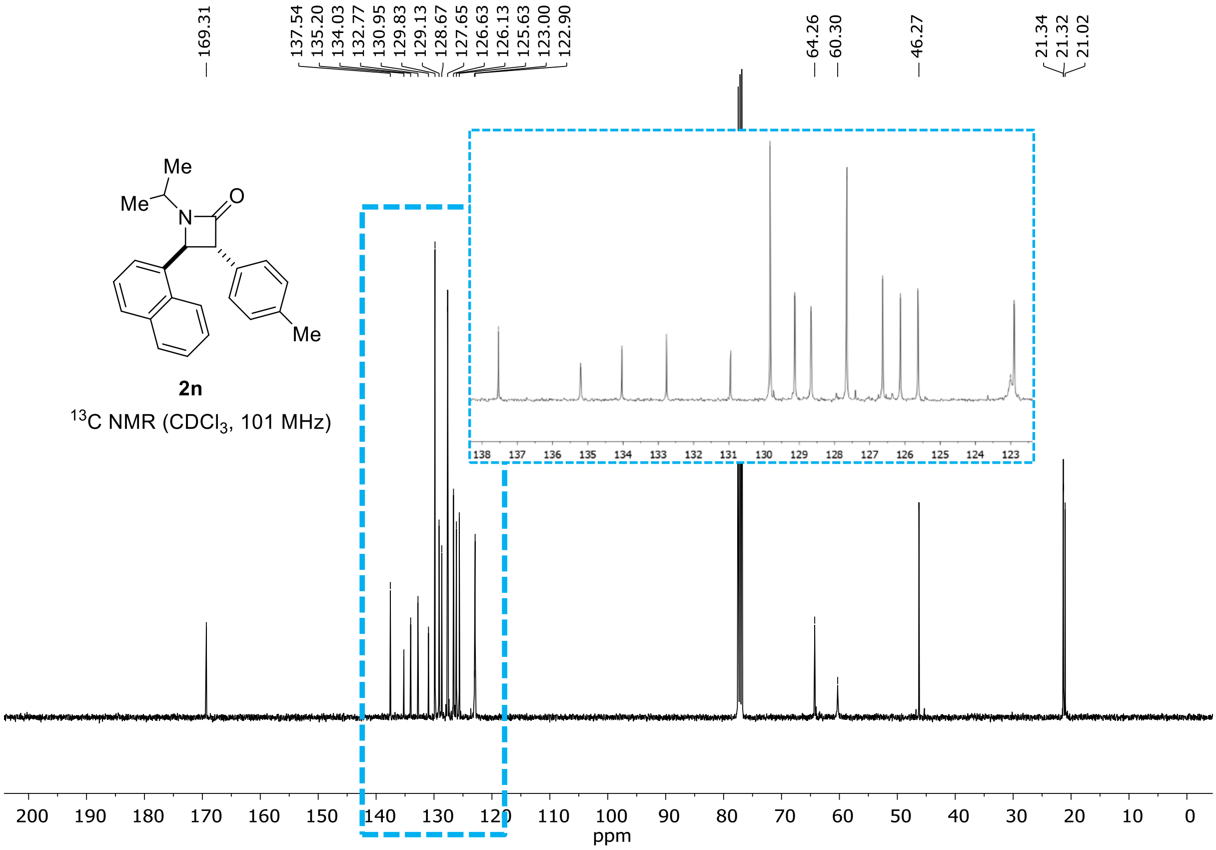
2m

^{13}C NMR (CDCl$_3$, 101 MHz)



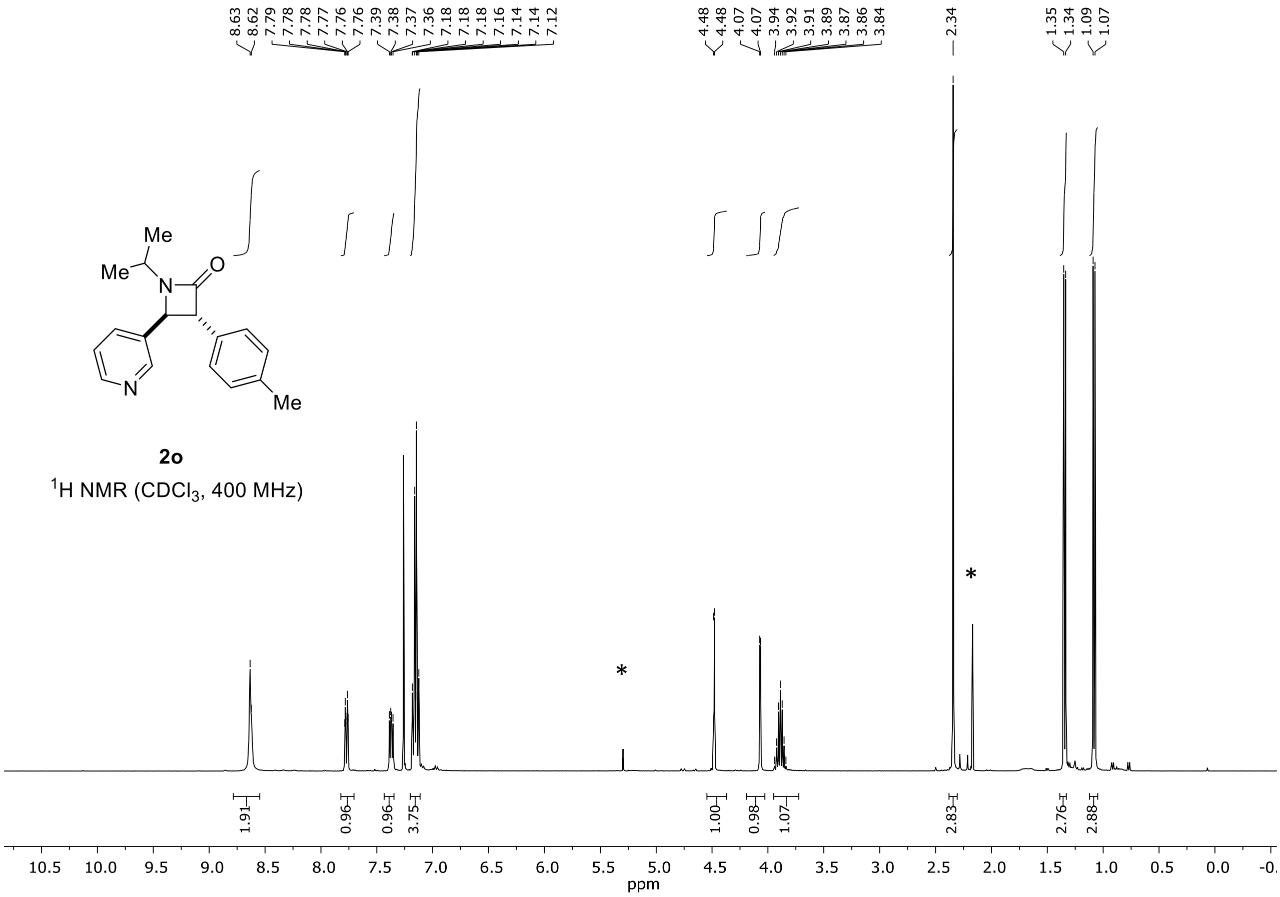
2n

^{1}H NMR (CDCl$_3$, 400 MHz)



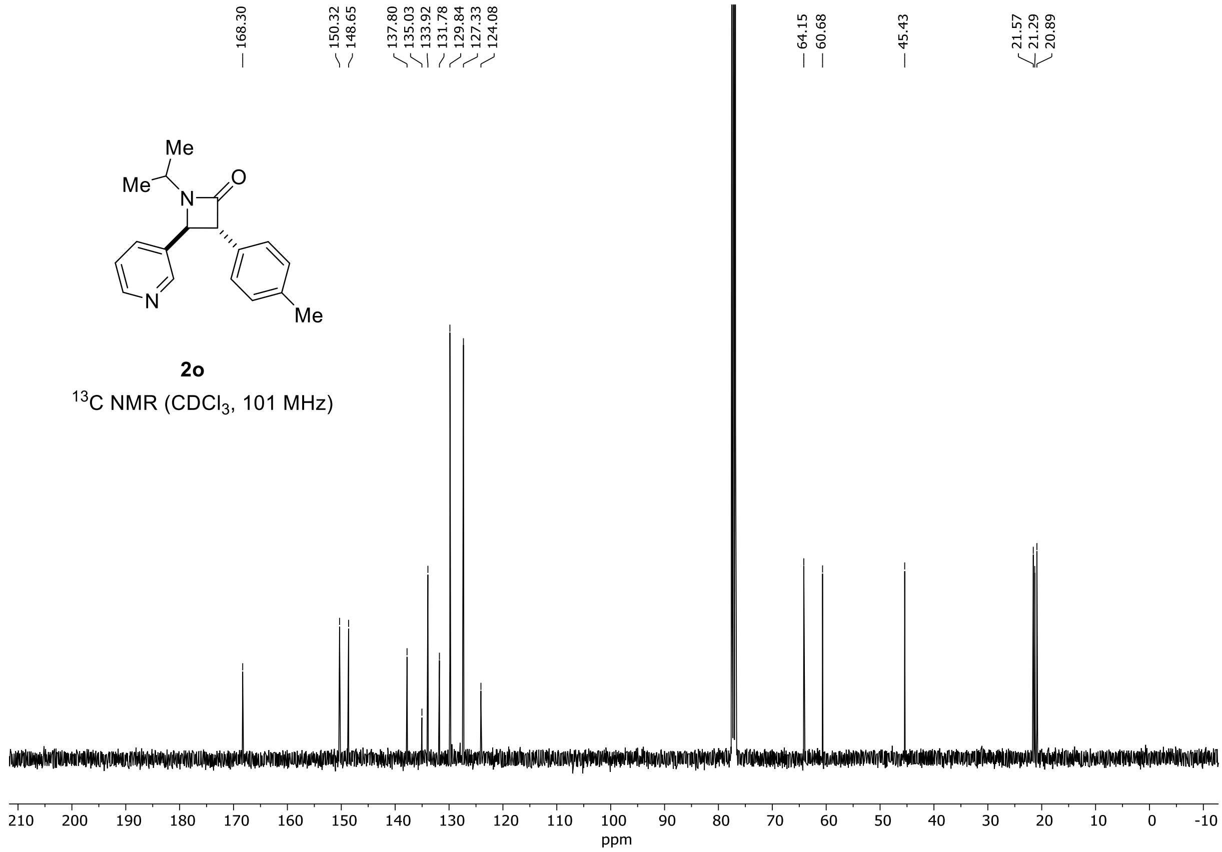
2n

^{13}C NMR ($CDCl_3$, 101 MHz)



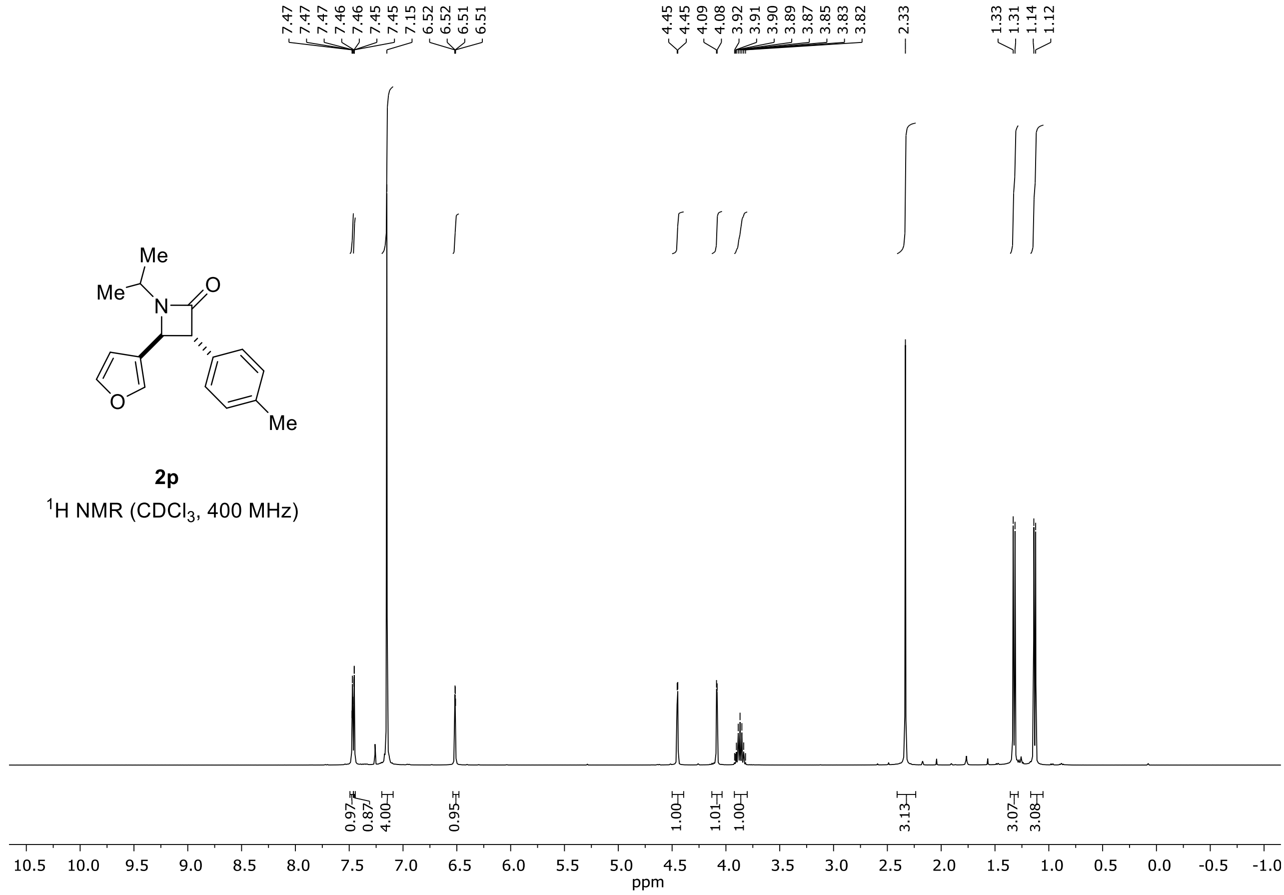
2o

^{1}H NMR ($CDCl_3$, 400 MHz)



2o

^{13}C NMR ($CDCl_3$, 101 MHz)

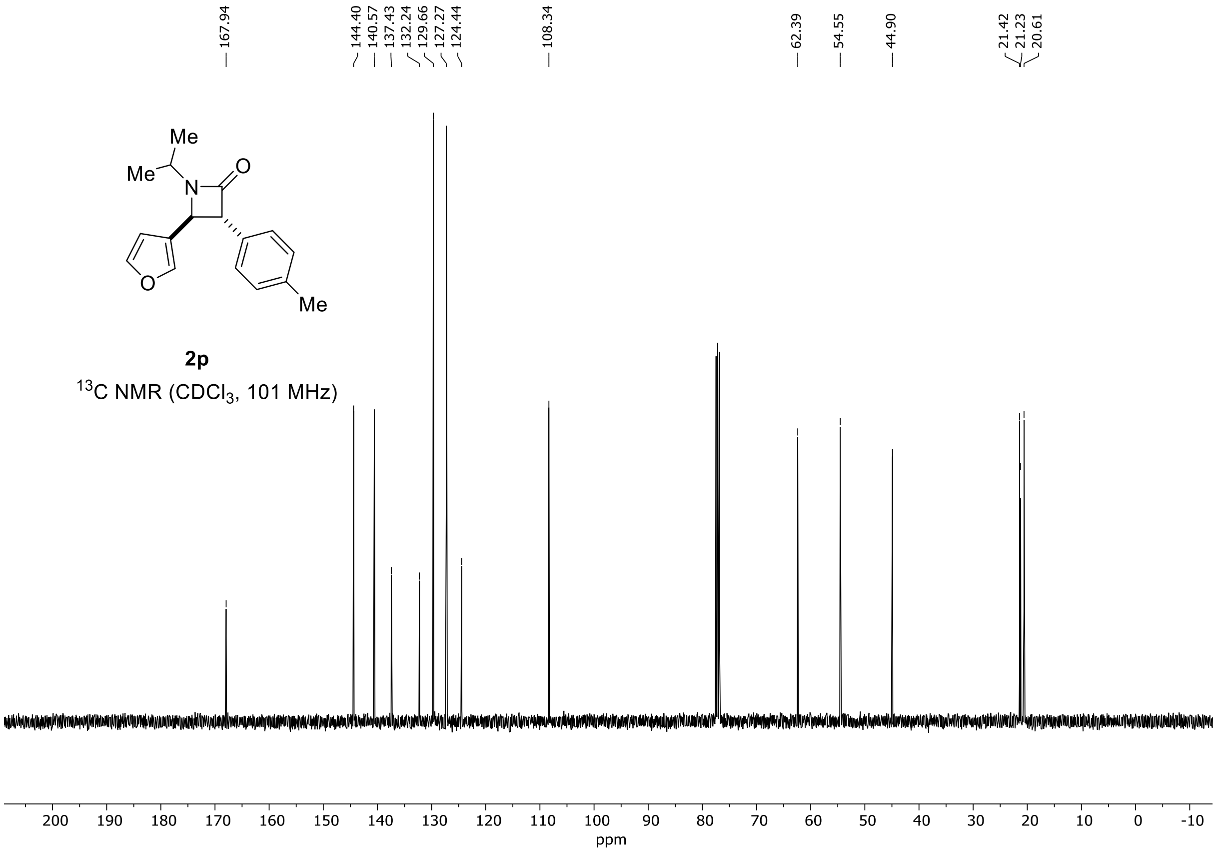


2p

^{1}H NMR ($CDCl_3$, 400 MHz)

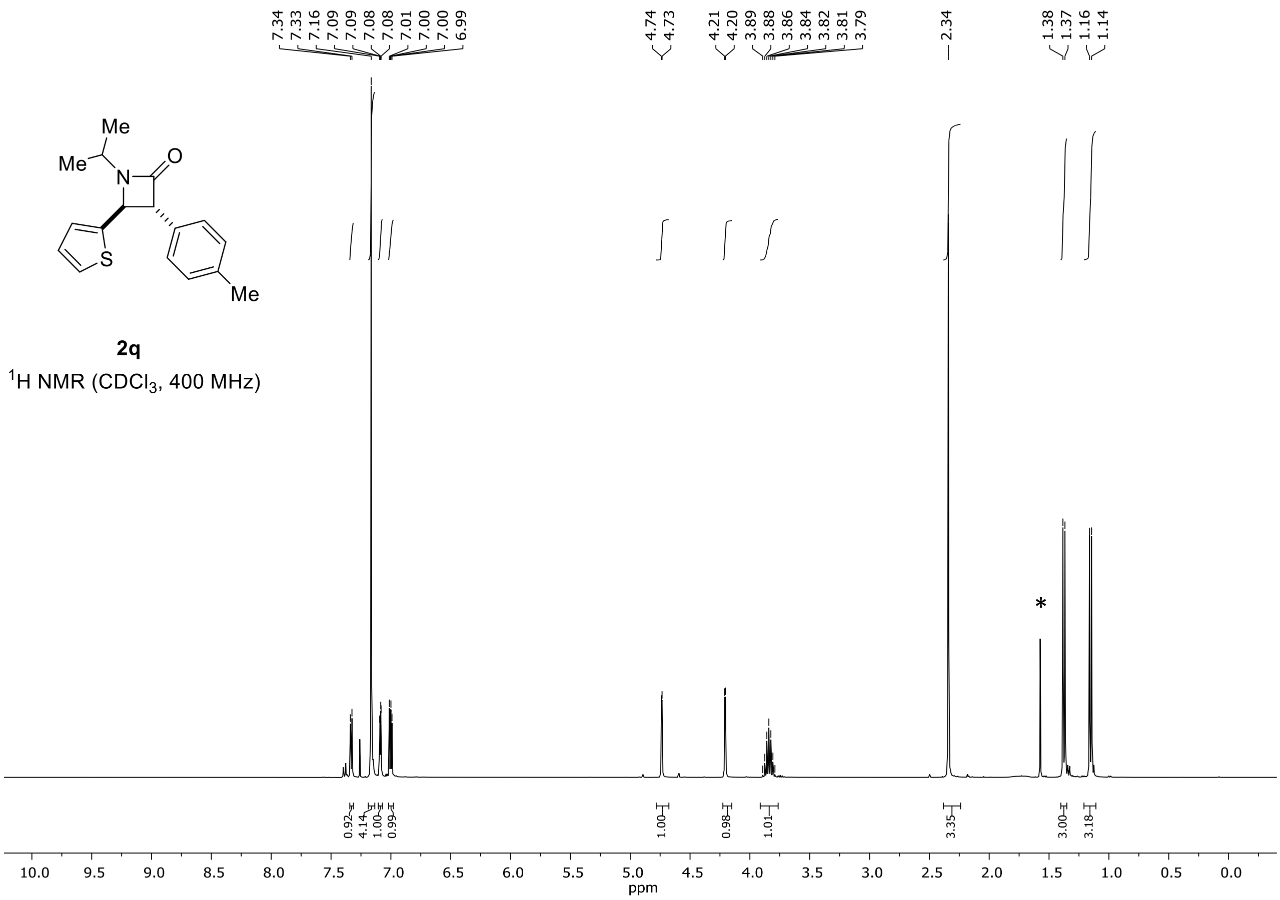
2p

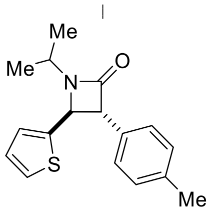
^{13}C NMR ($CDCl_3$, 101 MHz)



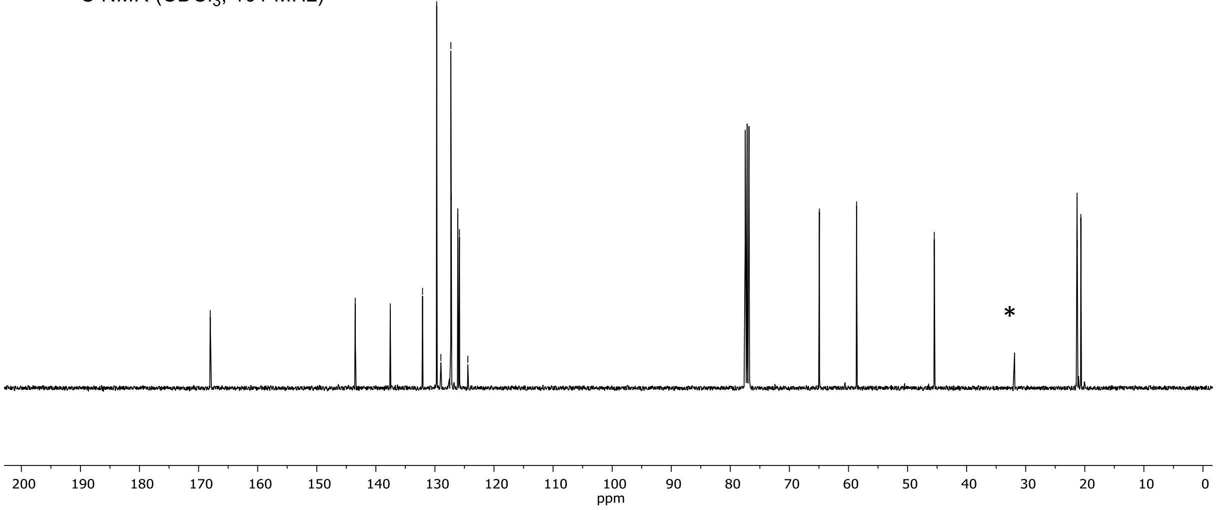
2q

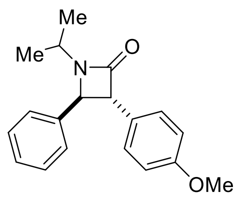
^{1}H NMR ($CDCl_3$, 400 MHz)



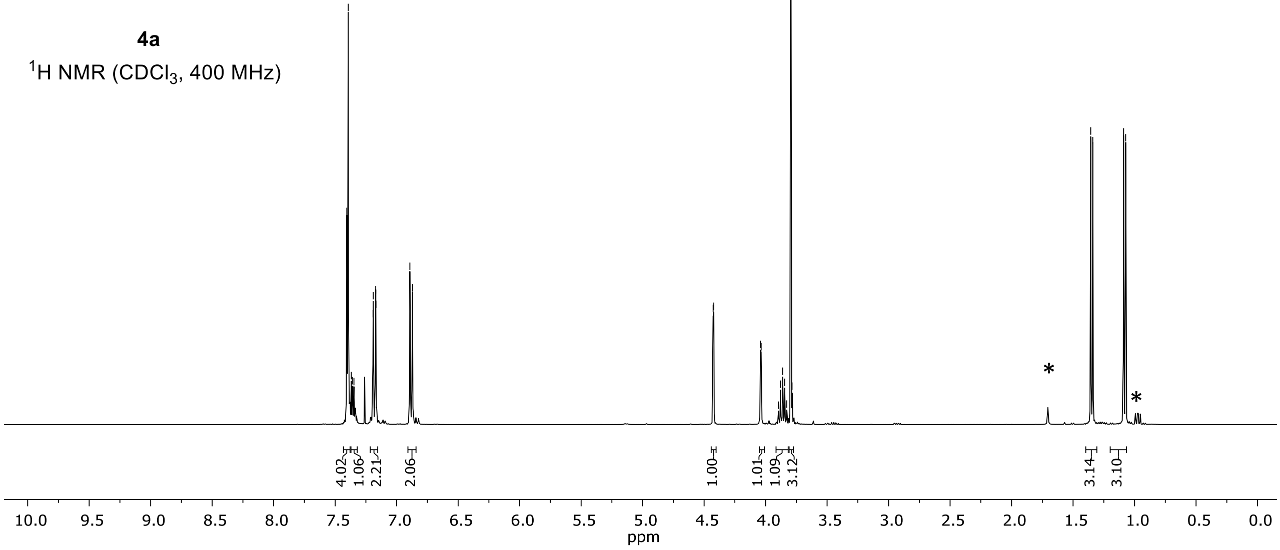


2q
^{13}C NMR ($CDCl_3$, 101 MHz)



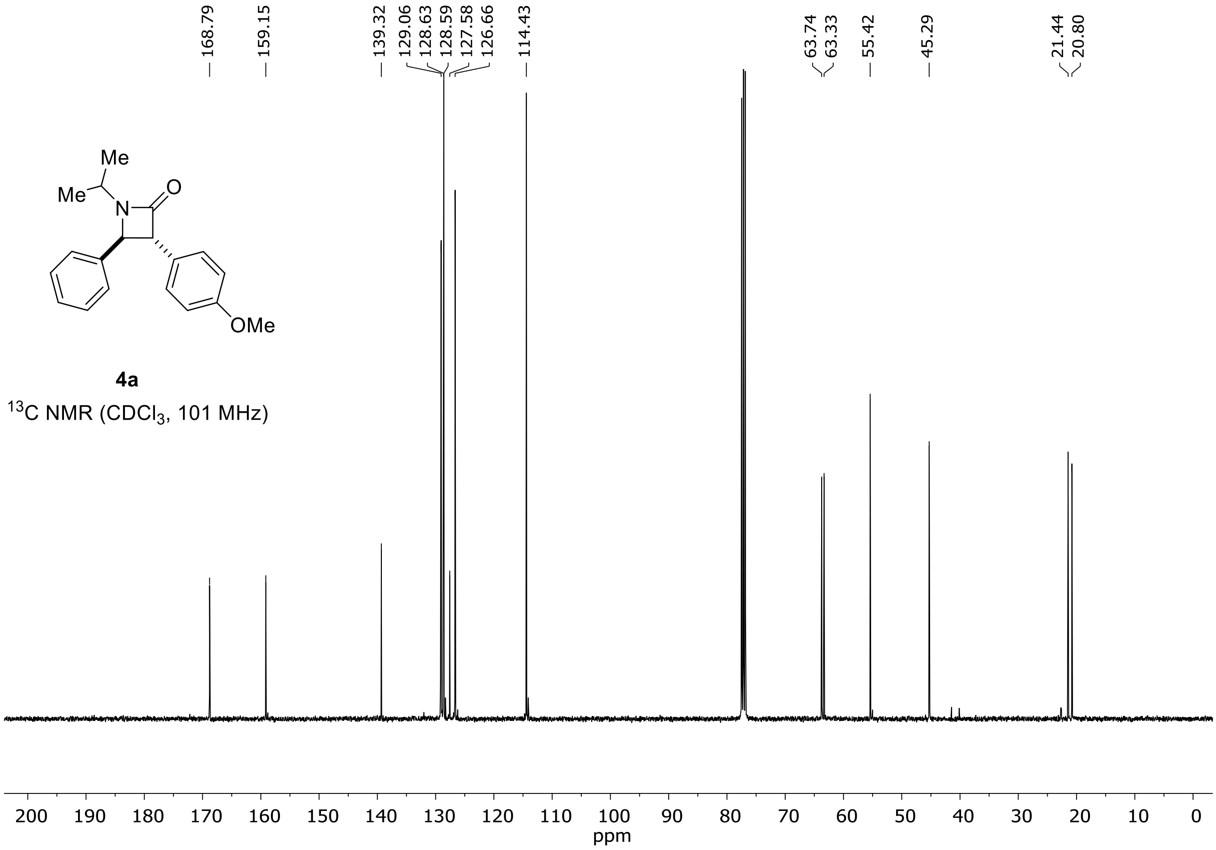


4a
^{1}H NMR ($CDCl_3$, 400 MHz)



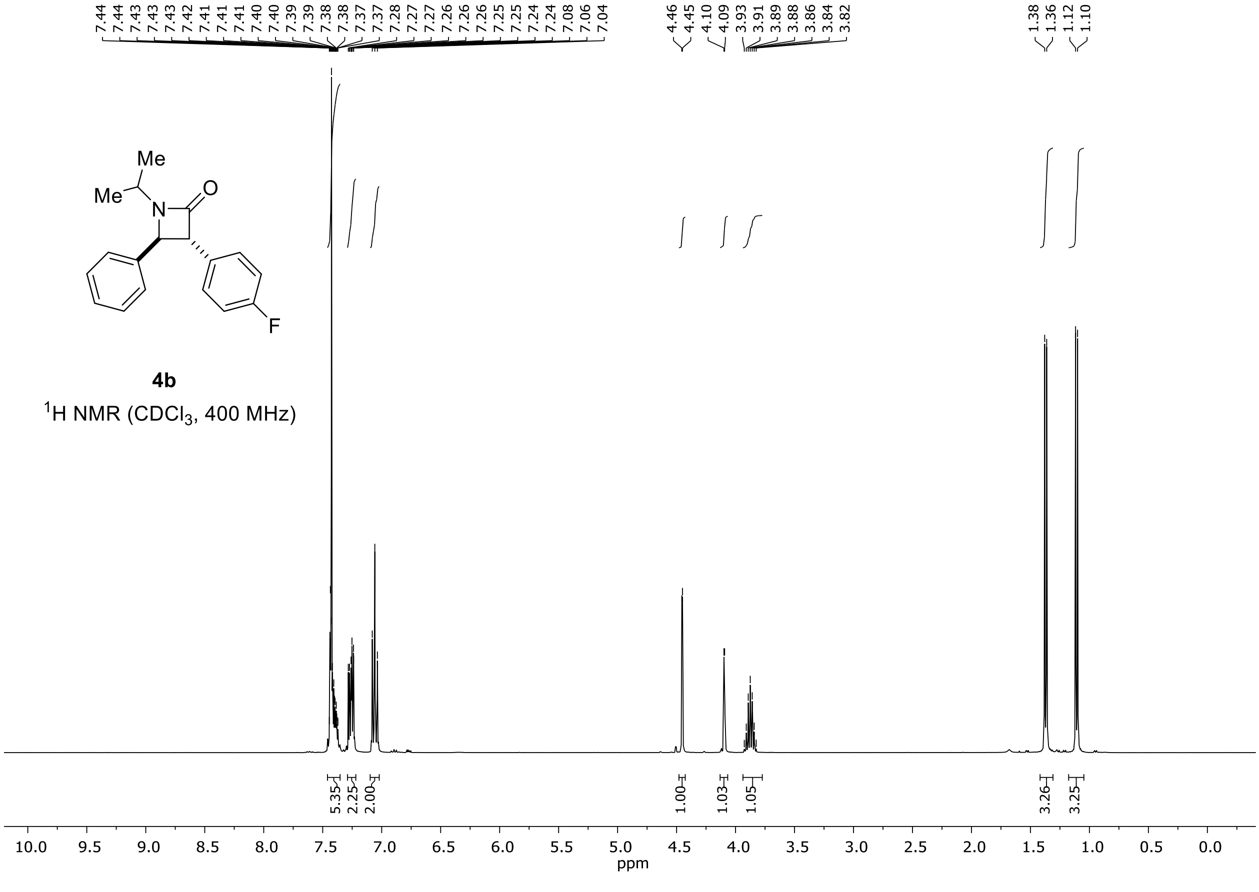
4a

^{13}C NMR (CDCl$_3$, 101 MHz)



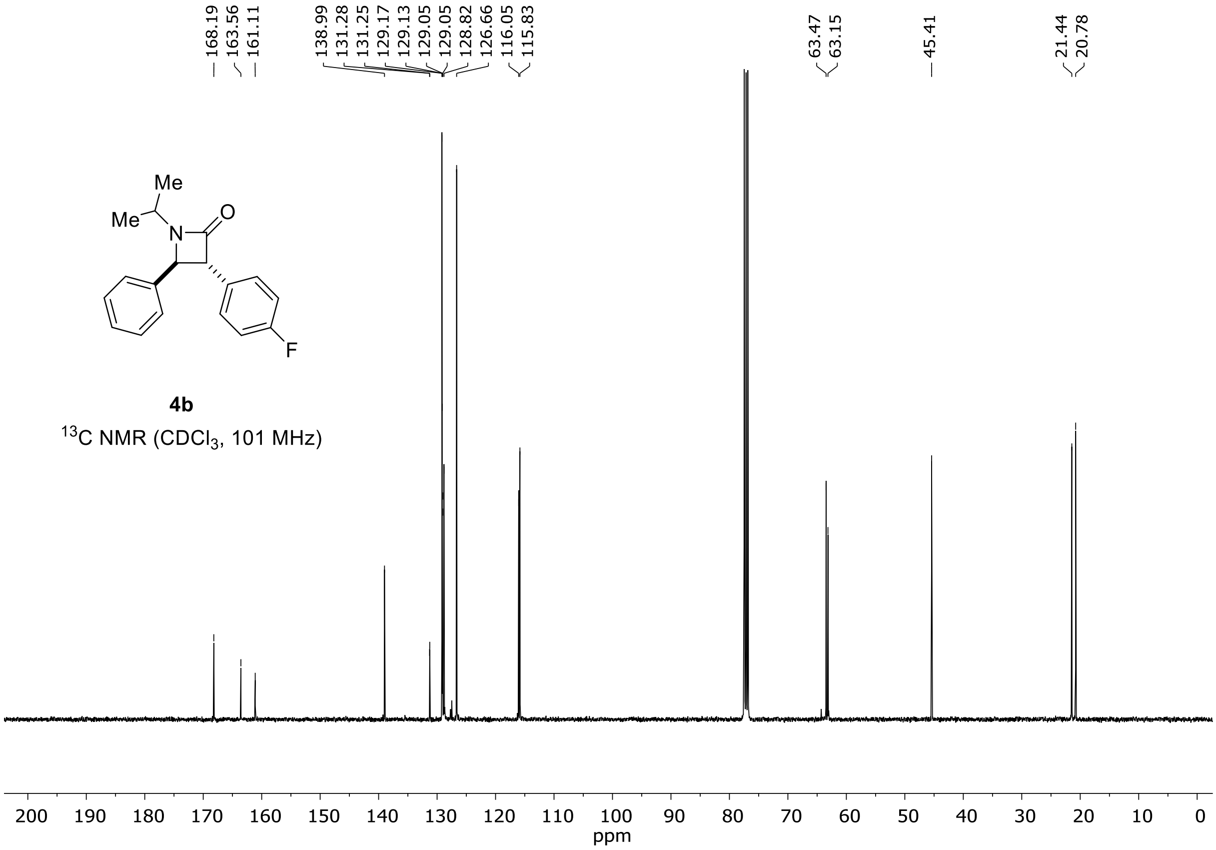
4b

^{1}H NMR (CDCl$_3$, 400 MHz)



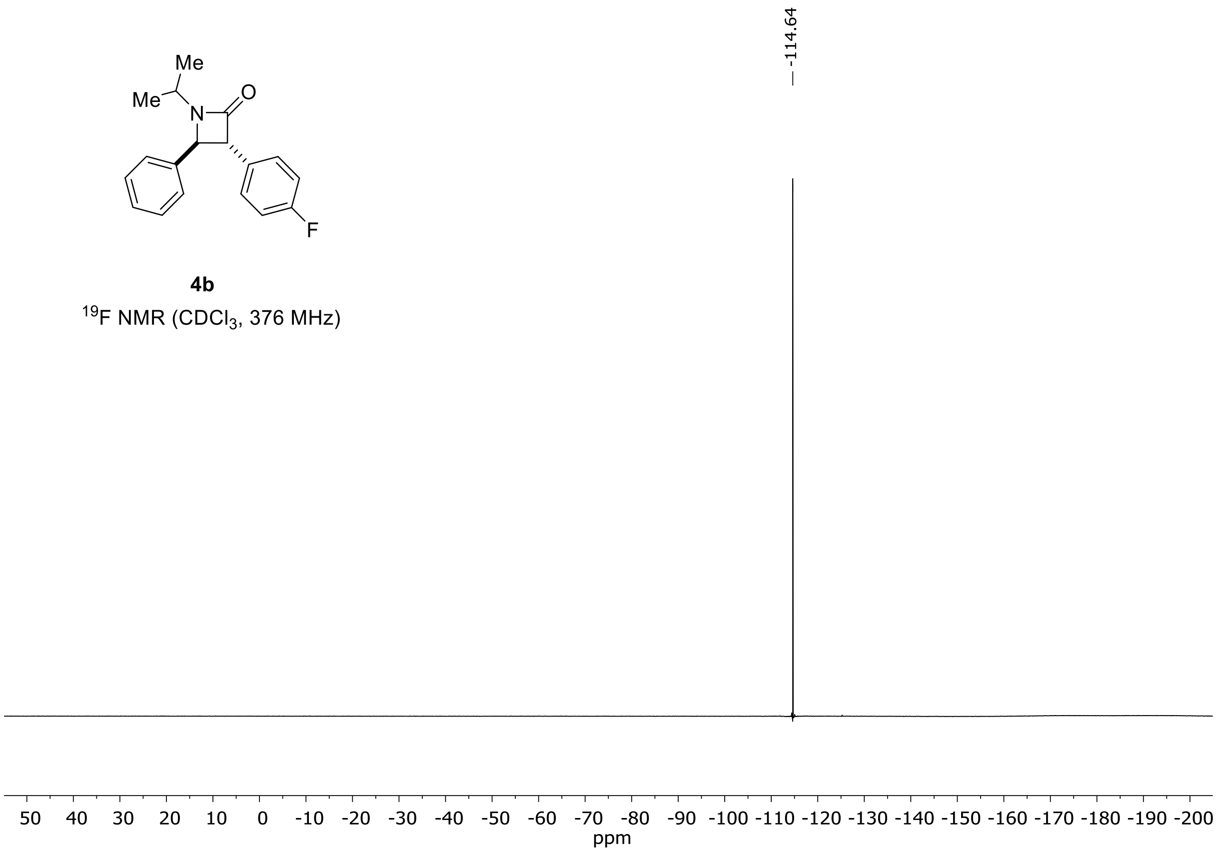
4b

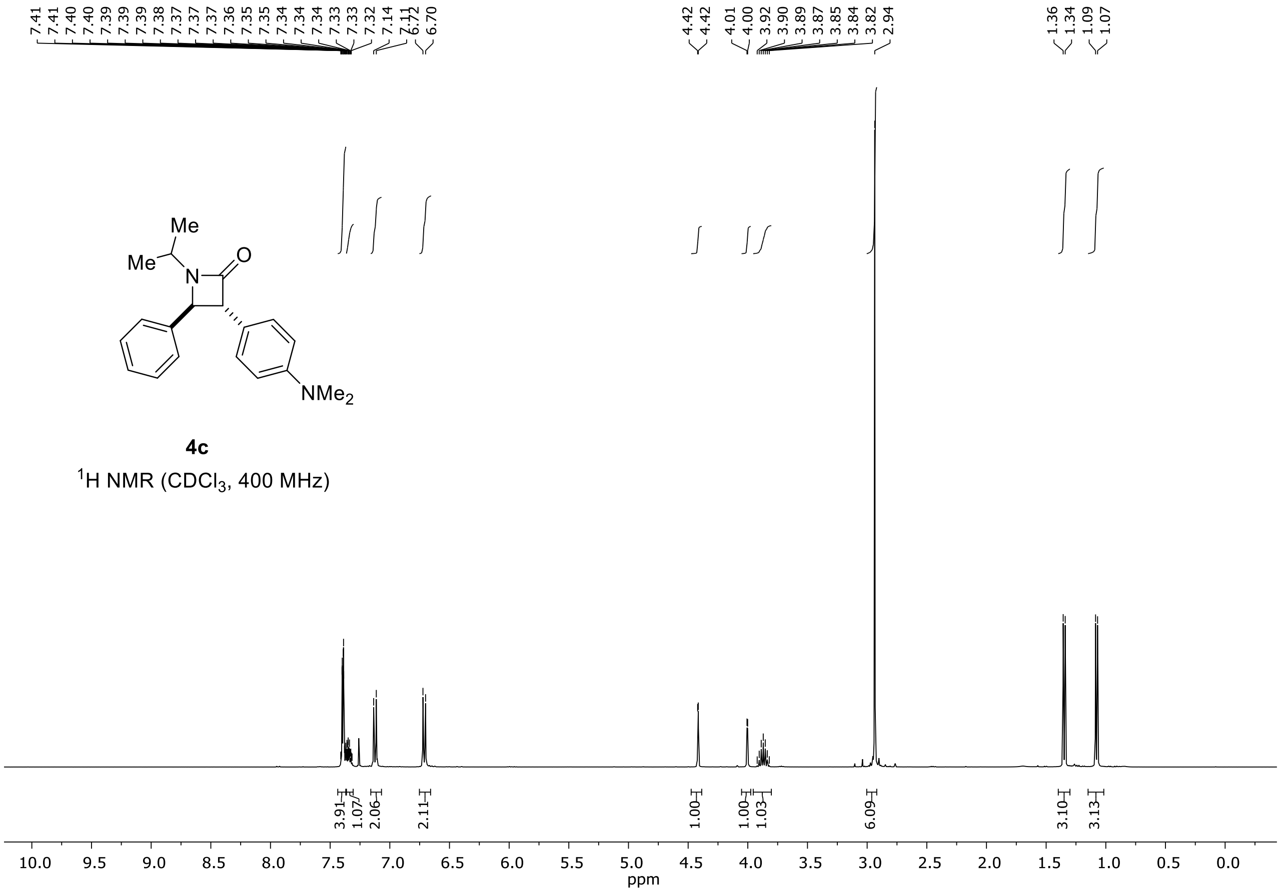
^{13}C NMR ($CDCl_3$, 101 MHz)



4b

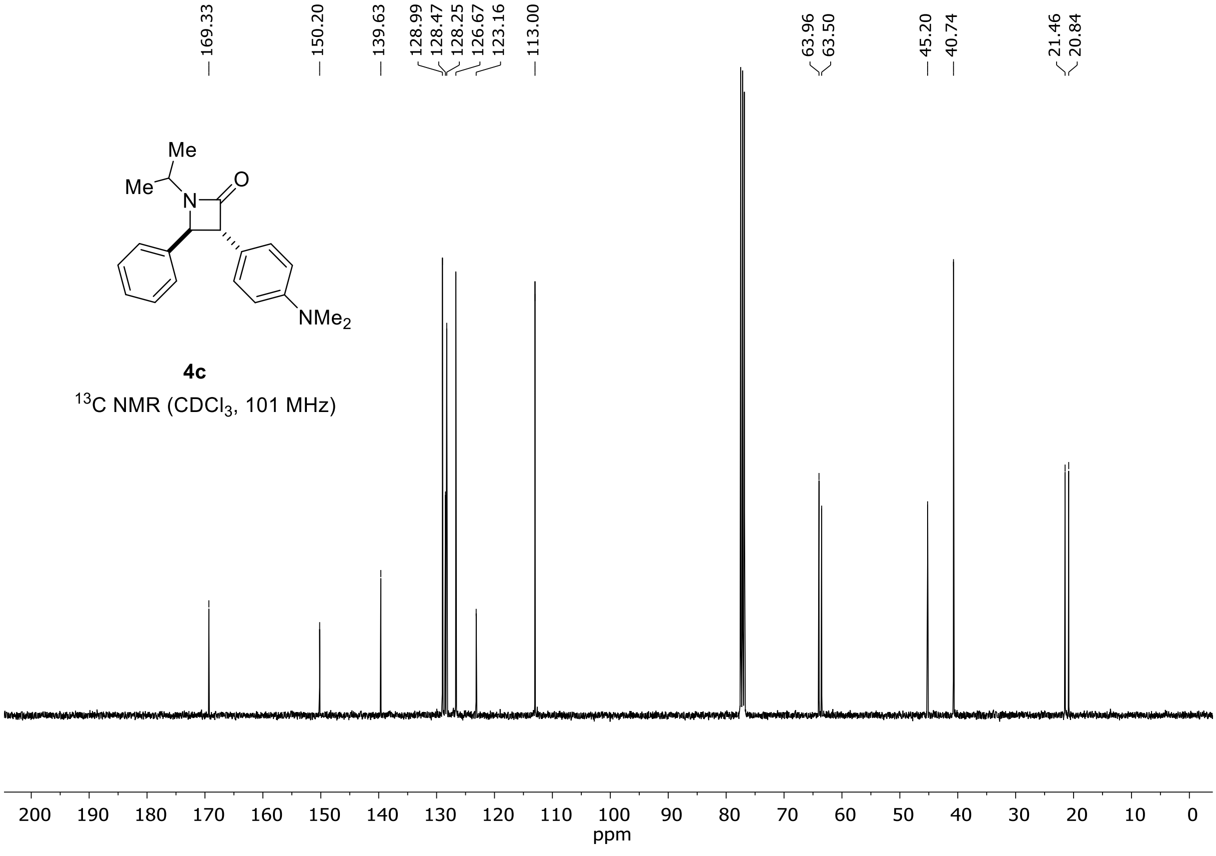
^{19}F NMR ($CDCl_3$, 376 MHz)





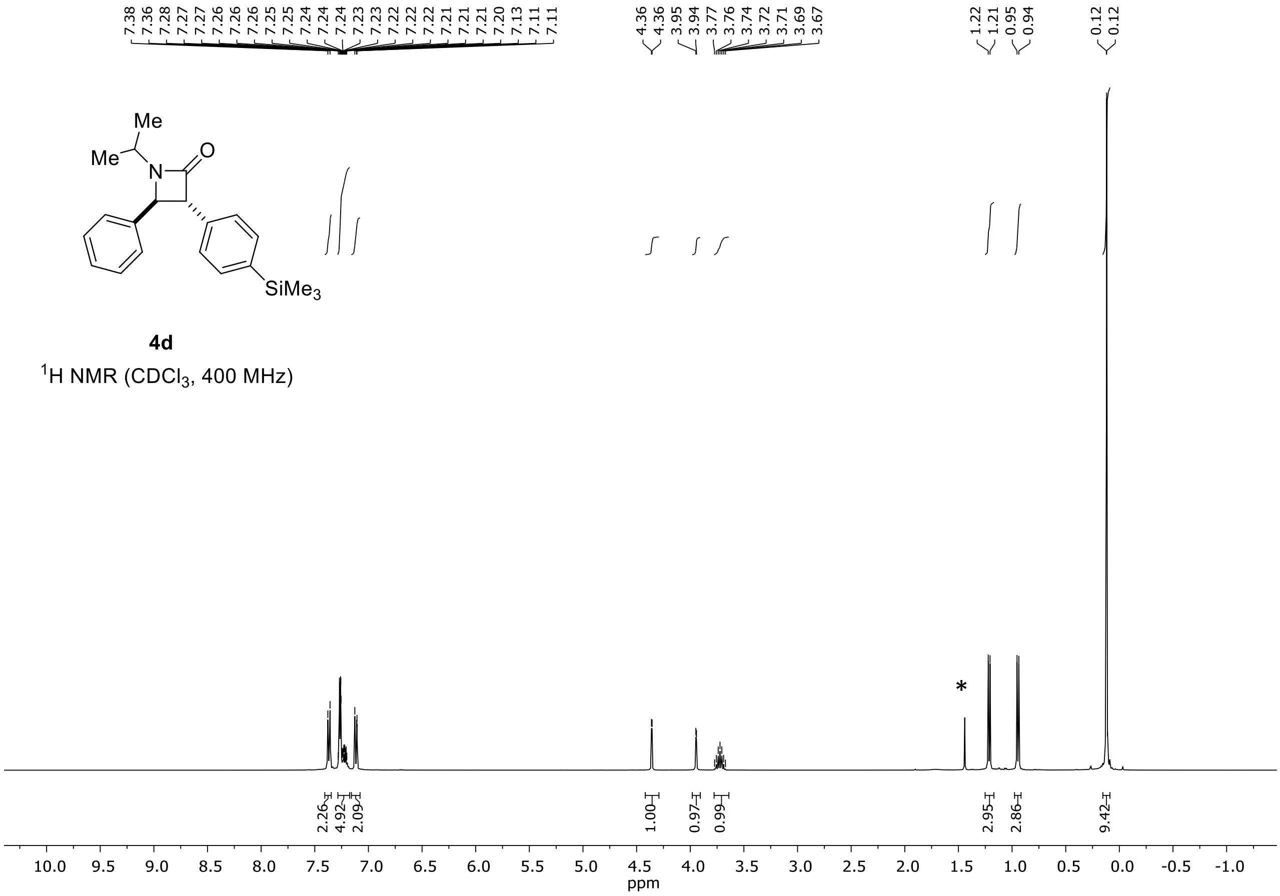
4c

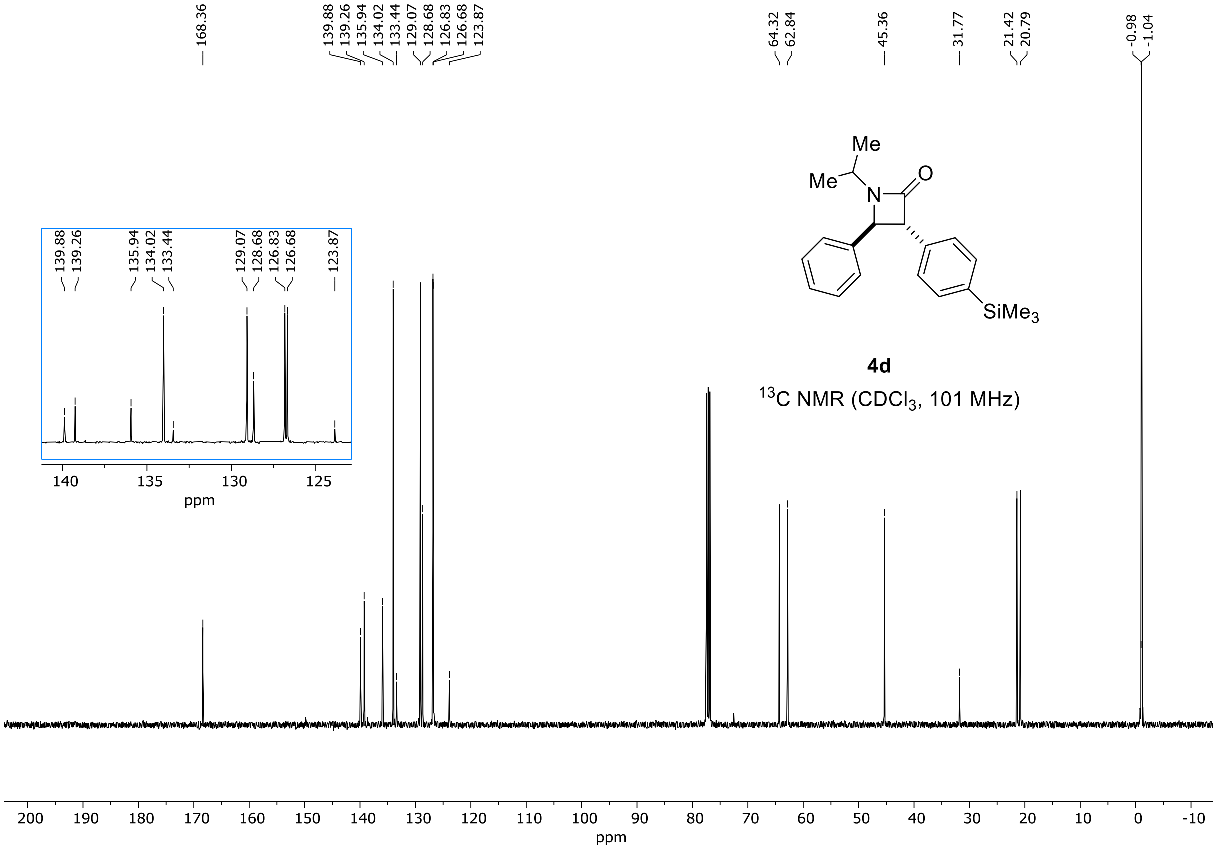
^{1}H NMR ($CDCl_3$, 400 MHz)

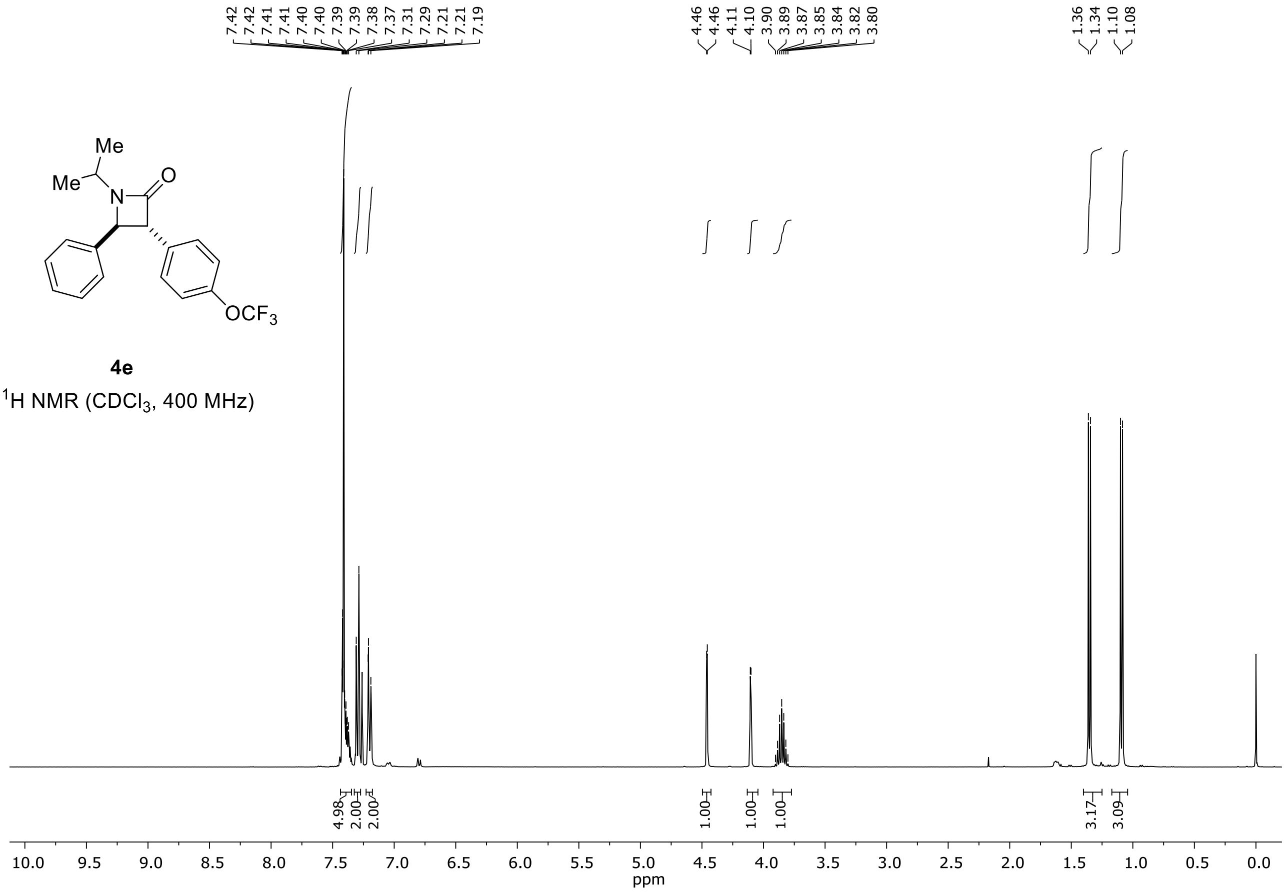


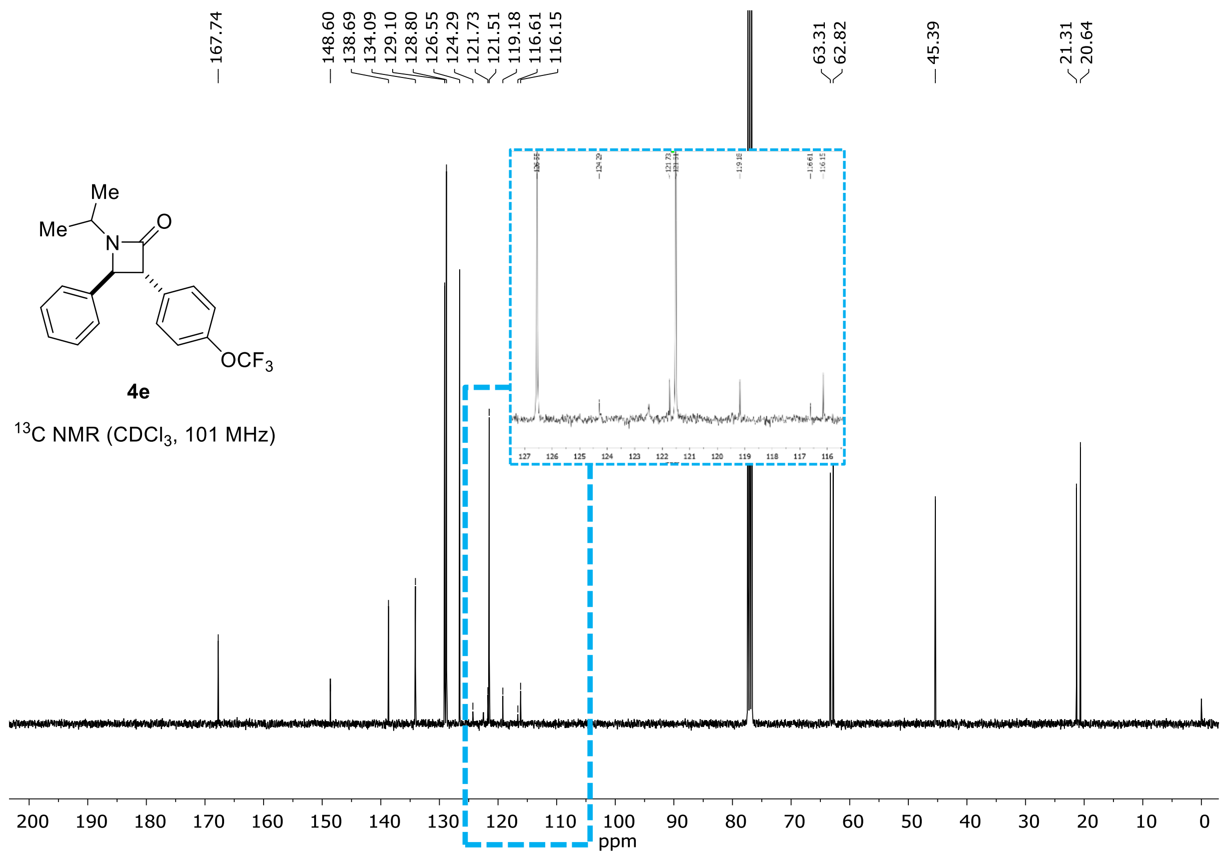
4c

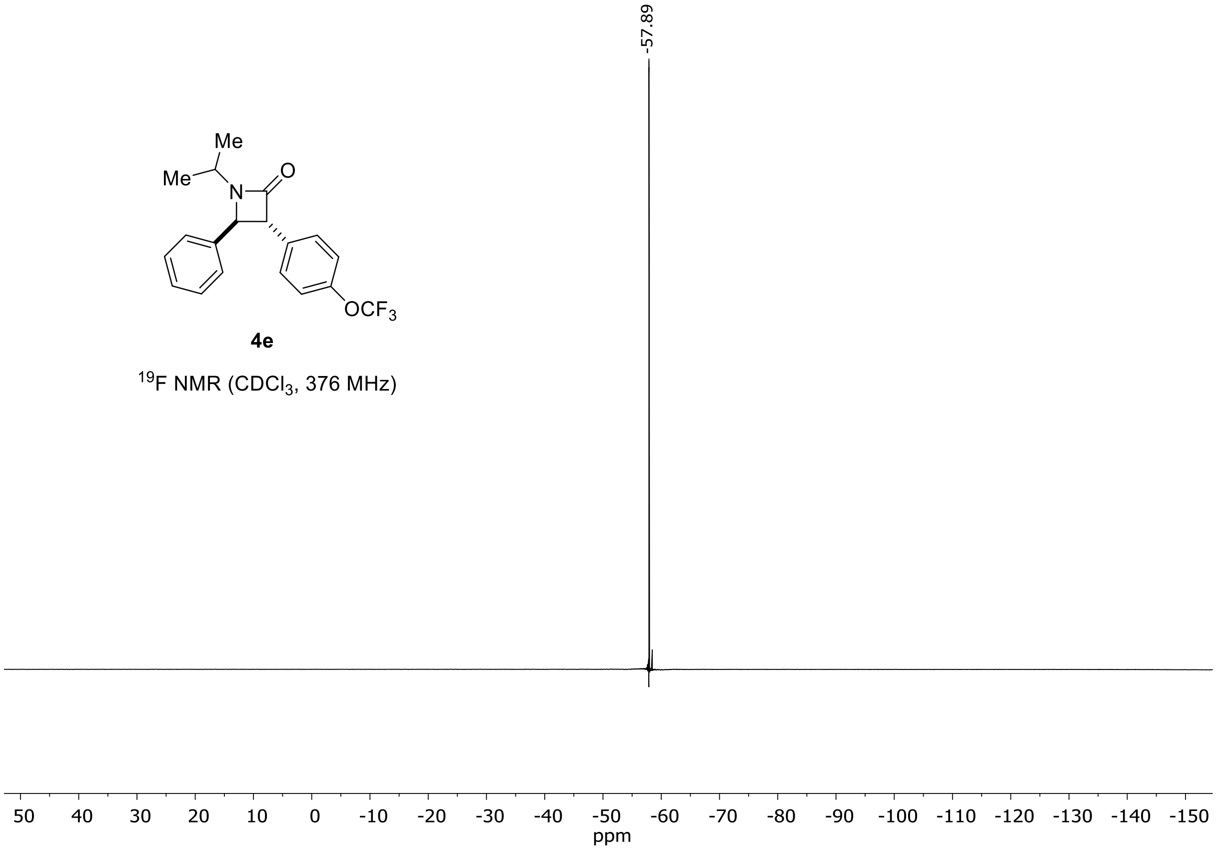
^{13}C NMR ($CDCl_3$, 101 MHz)

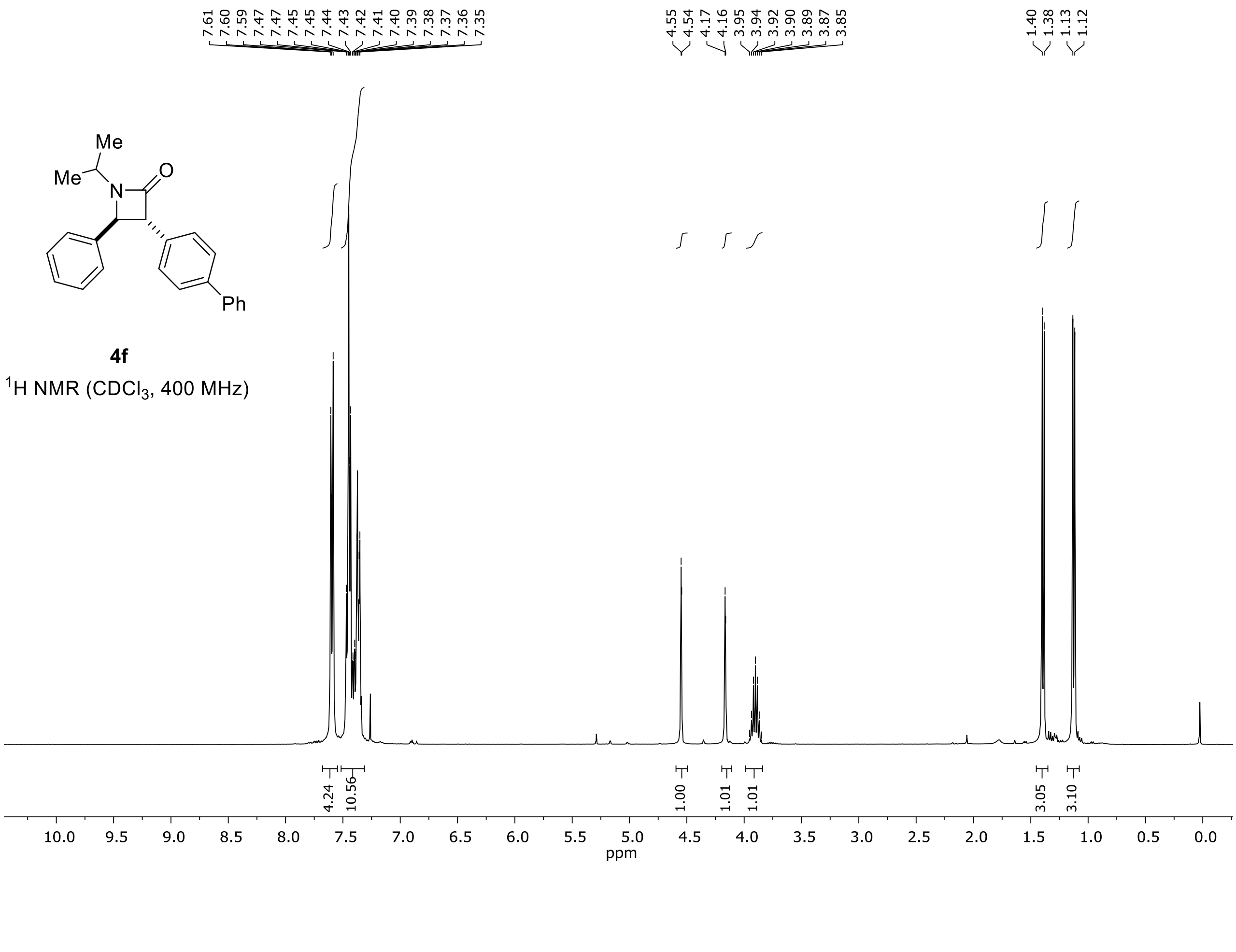

7.38 7.36 7.28 7.27 7.27 7.26 7.26 7.26 7.25 7.25 7.24 7.24 7.24 7.23 7.23 7.22 7.22 7.22 7.21 7.21 7.21 7.21 7.20 7.13 7.11 7.11
4.36 4.36 3.95 3.94 3.77 3.76 3.74 3.72 3.71 3.69 3.67
1.22 1.21 0.95 0.94
0.12 0.12
Me
Me
N
O
SiMe3
4d
1H NMR (CDCl3, 400 MHz)
*
2.26 4.92 2.09 1.00 0.97 0.99 2.95 2.86 9.42
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
ppm

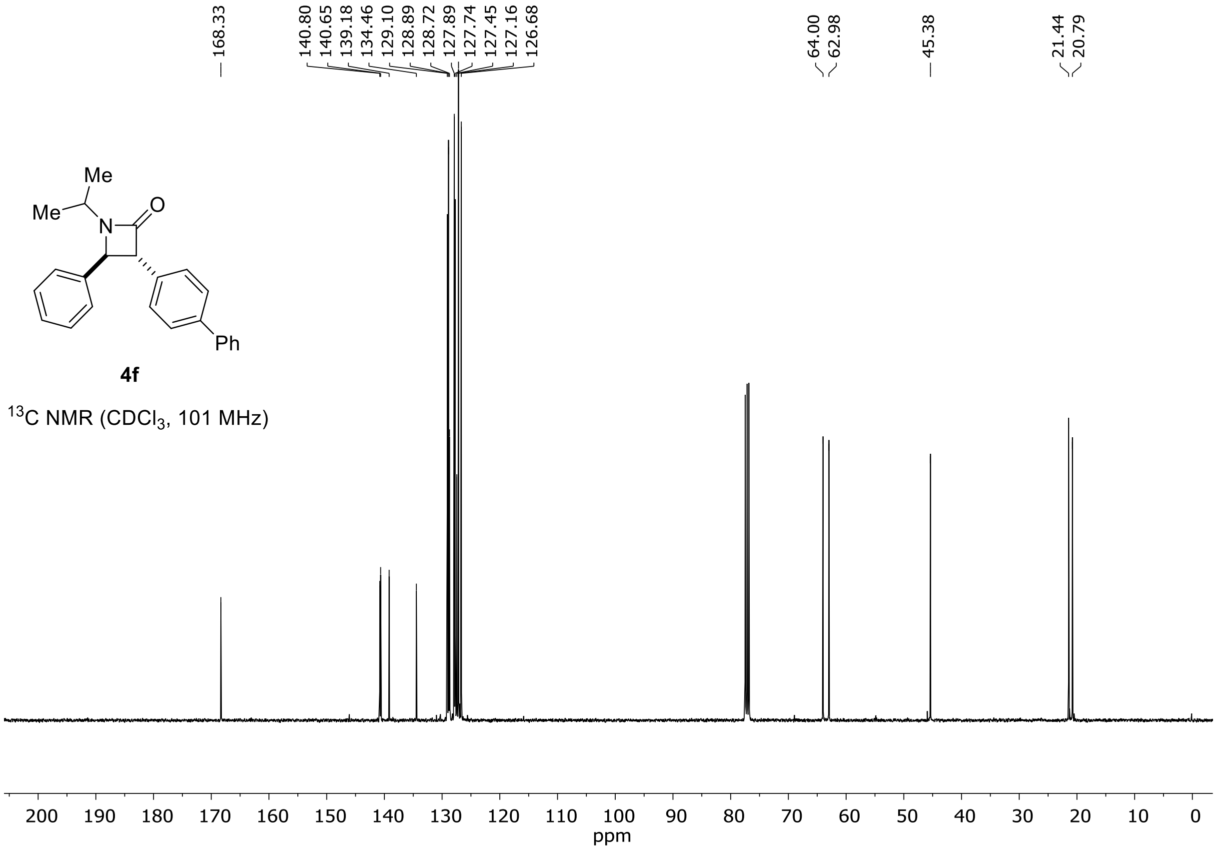

168.36
139.88 139.26 135.94 134.02 133.44 129.07 128.68 126.83 126.68 123.87
64.32 62.84
45.36
31.77
21.42 20.79
-0.98 -1.04
Me
Me
N
O
SiMe3
4d
13C NMR (CDCl3, 101 MHz)
140 135 130 125
ppm
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm


7.42 7.42 7.41 7.41 7.40 7.40 7.39 7.39 7.38 7.37 7.31 7.29 7.21 7.21 7.19
4.46 4.46 4.11 4.10 3.90 3.89 3.87 3.85 3.84 3.82 3.80
1.36 1.34 1.10 1.08
Me
Me
N
O
OCF3
4e
1H NMR (CDCl3, 400 MHz)
4.98 2.00 2.00 1.00 1.00 1.00 3.17 3.09
ppm


167.74
148.60 138.69 134.09 129.10 128.80 126.55 124.29 121.73 121.51 119.18 116.61 116.15
63.31 62.82
45.39
21.31 20.64
Me
Me
N
O
OCF3
4e
13C NMR (CDCl3, 101 MHz)
ppm

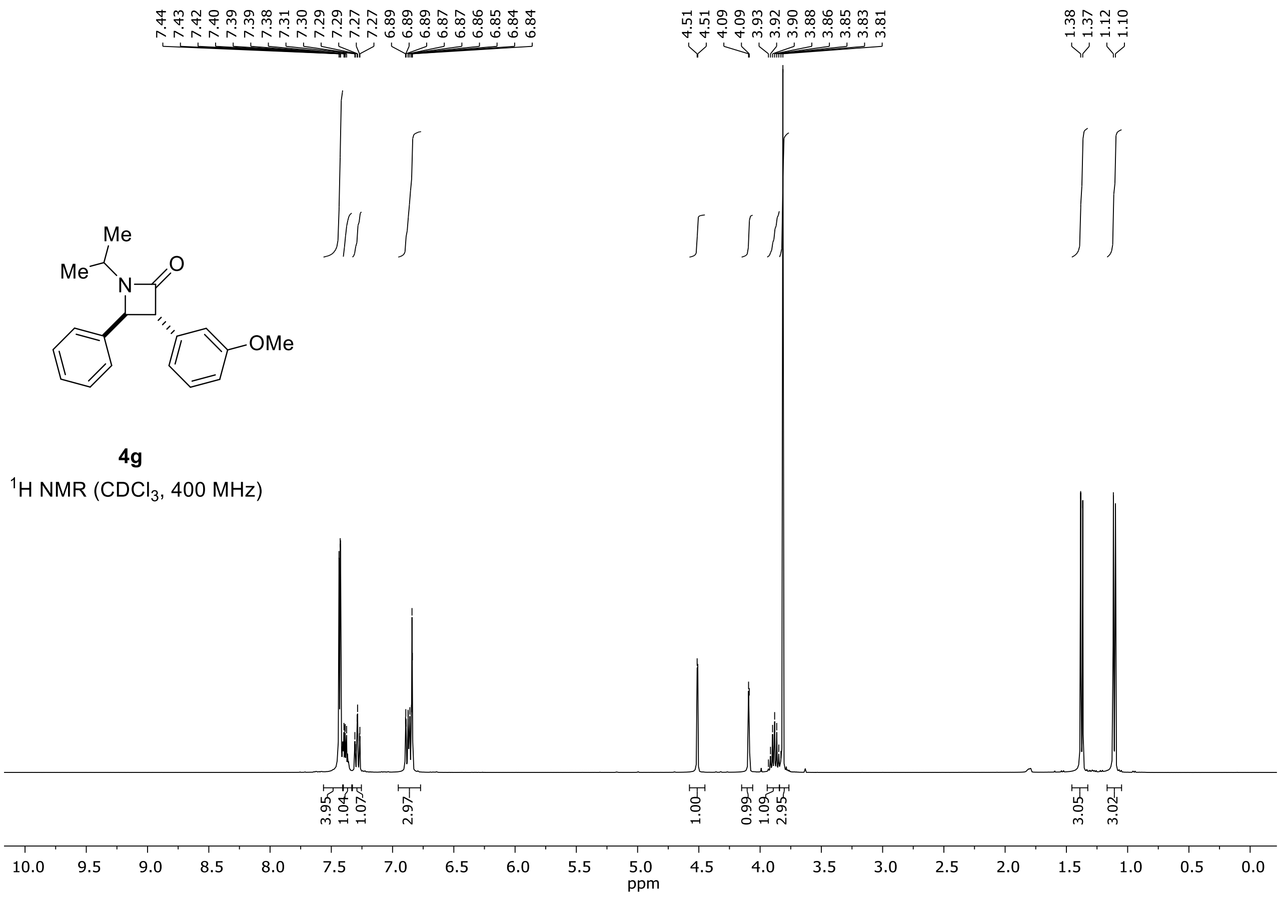

-57.89
Me
Me
N
O
OCF$_3$
4e
^{19}F NMR (CDCl$_3$, 376 MHz)
ppm


7.61 7.60 7.59 7.47 7.47 7.45 7.45 7.44 7.43 7.42 7.41 7.40 7.39 7.38 7.37 7.36 7.35
4.55 4.54 4.17 4.16 3.95 3.94 3.92 3.90 3.89 3.87 3.85
1.40 1.38 1.13 1.12
Me
Me
N
O
Ph
4f
^{1}H NMR (CDCl$_3$, 400 MHz)
4.24 10.56 1.00 1.01 1.01 3.05 3.10
ppm



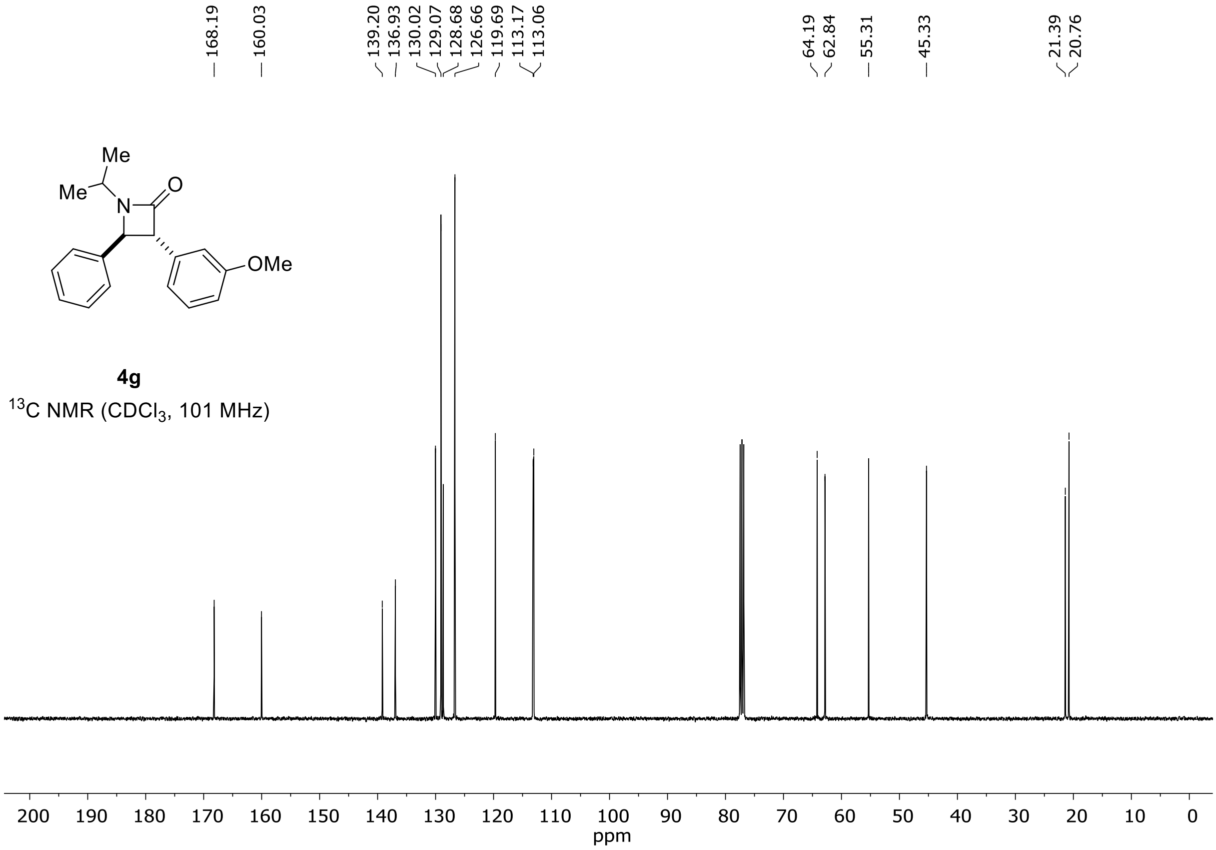
4f

^{13}C NMR ($CDCl_3$, 101 MHz)



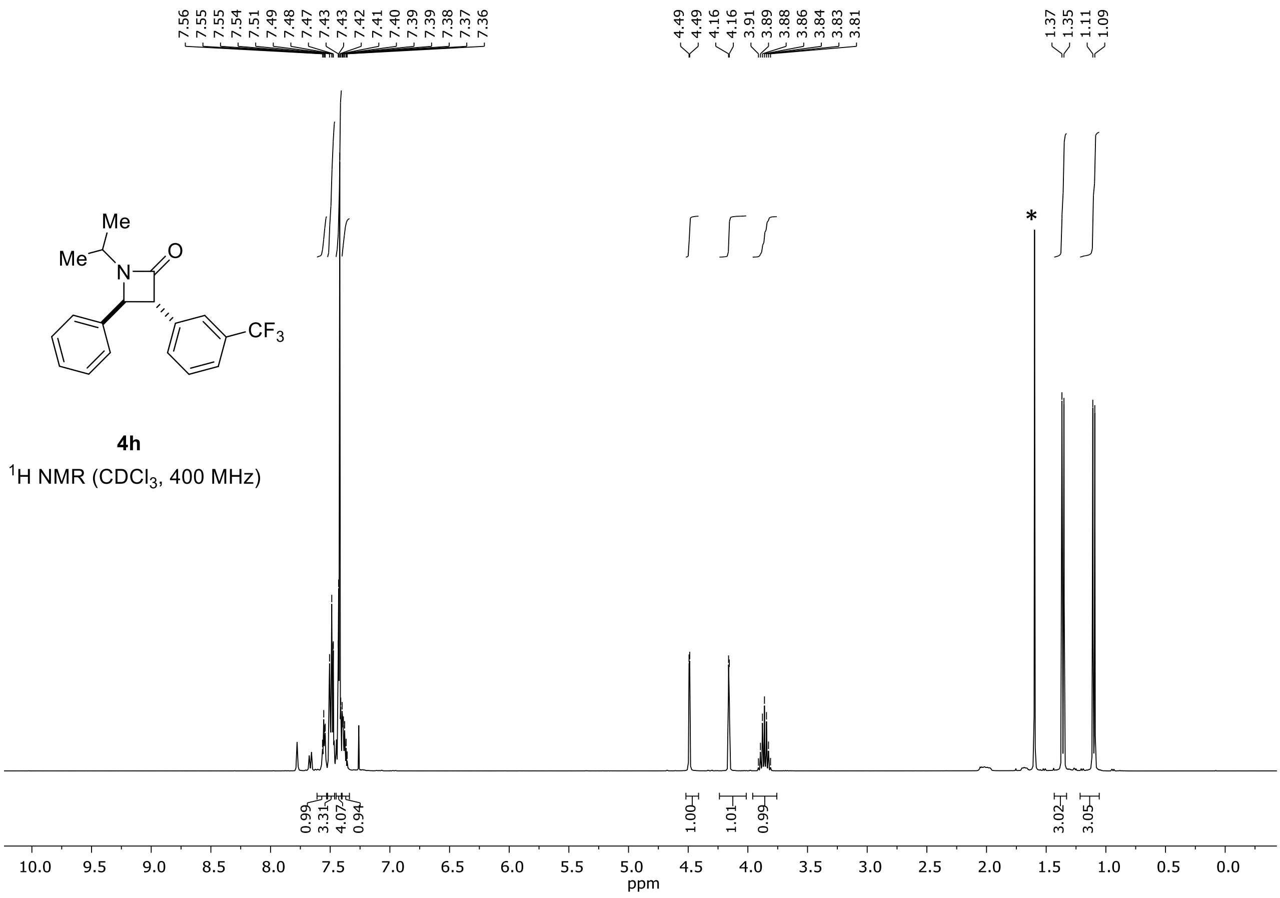
4g

^{1}H NMR ($CDCl_3$, 400 MHz)



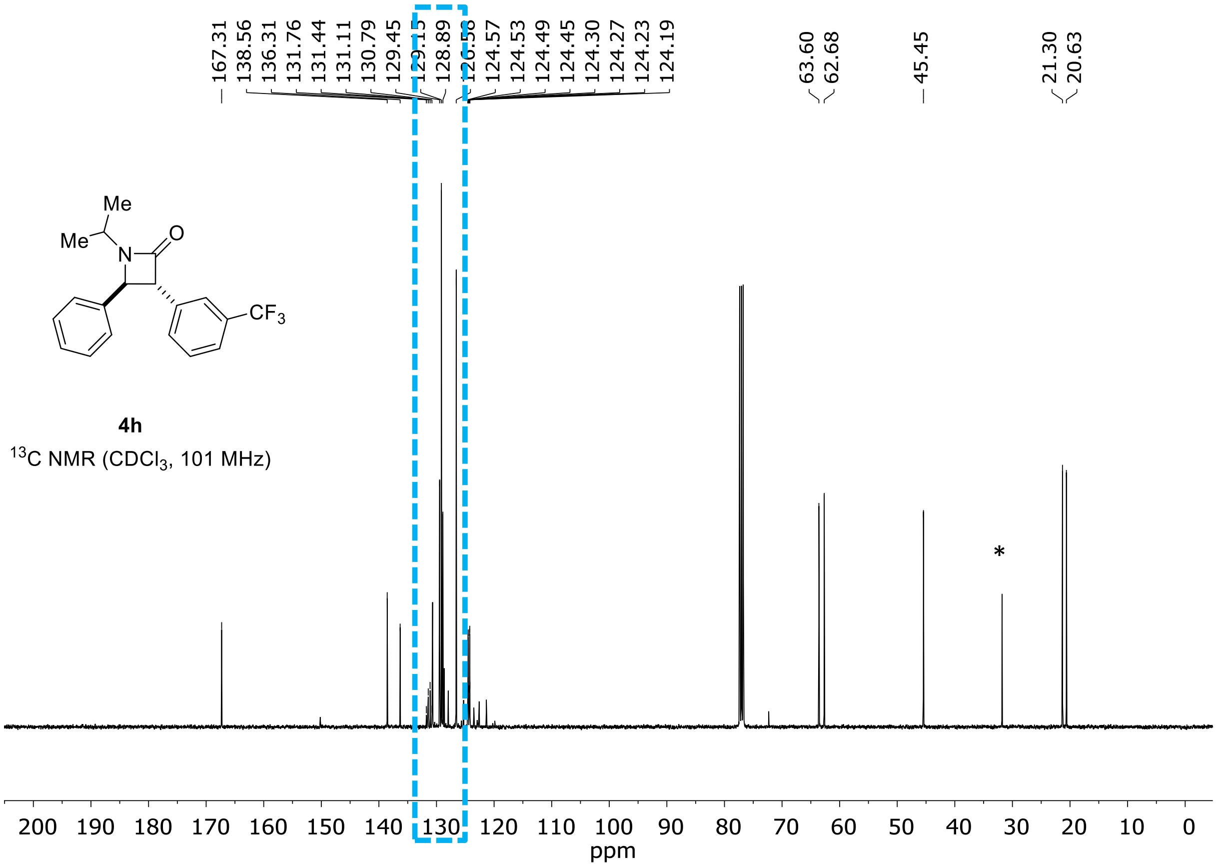
4g

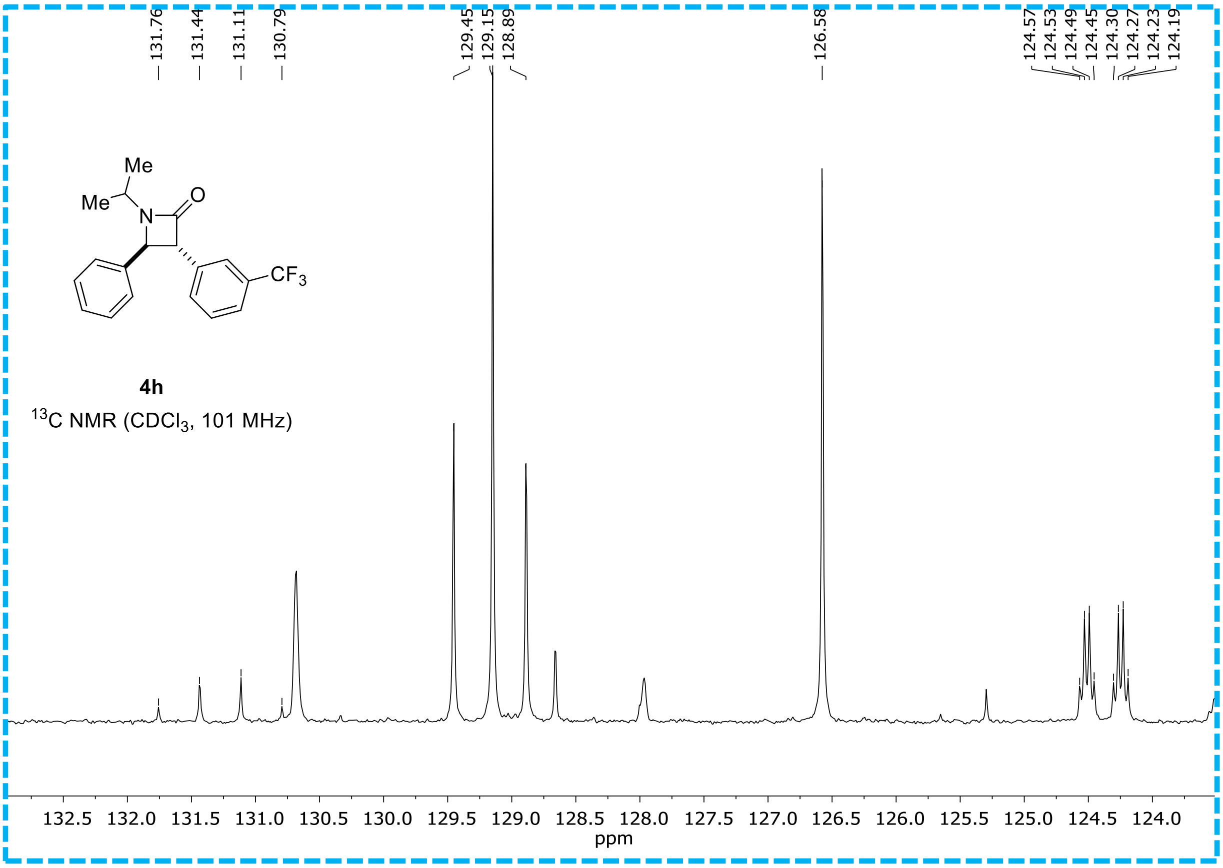
^{13}C NMR ($CDCl_3$, 101 MHz)

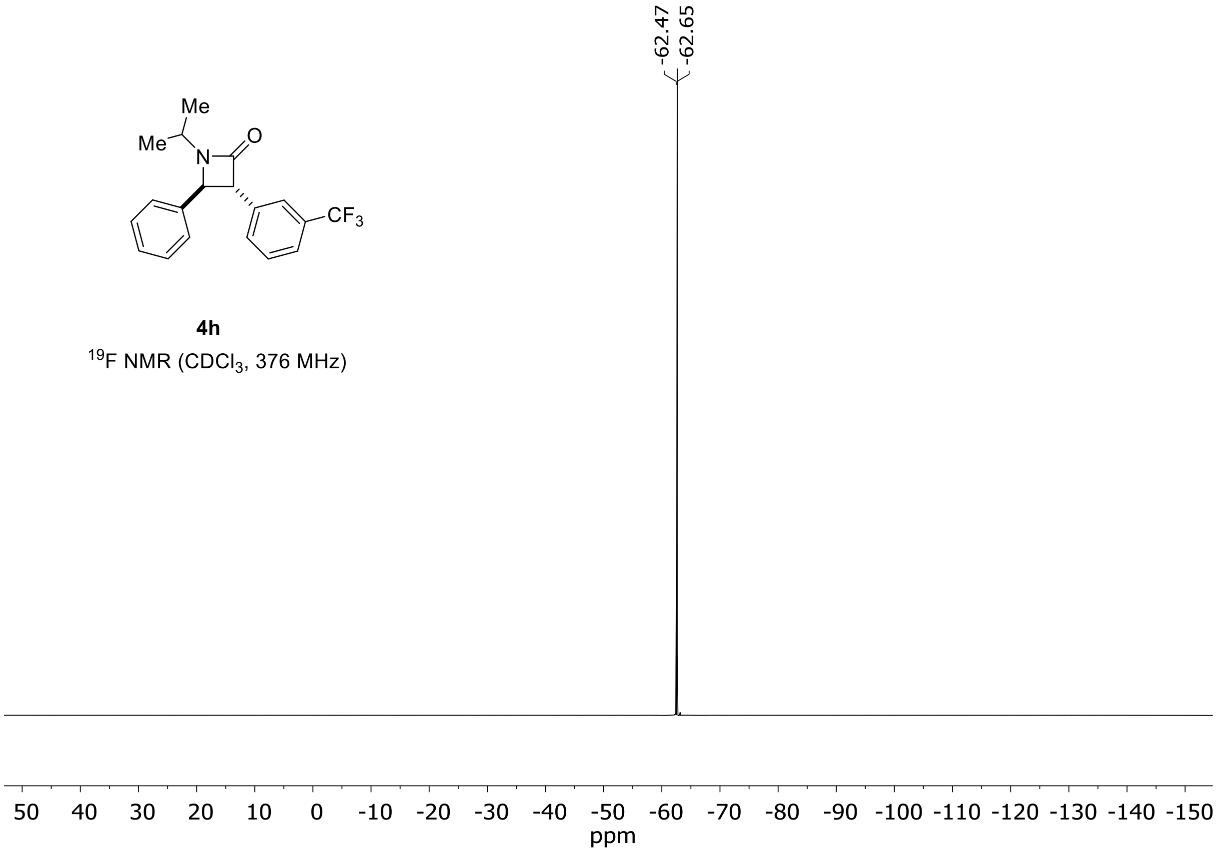


4h

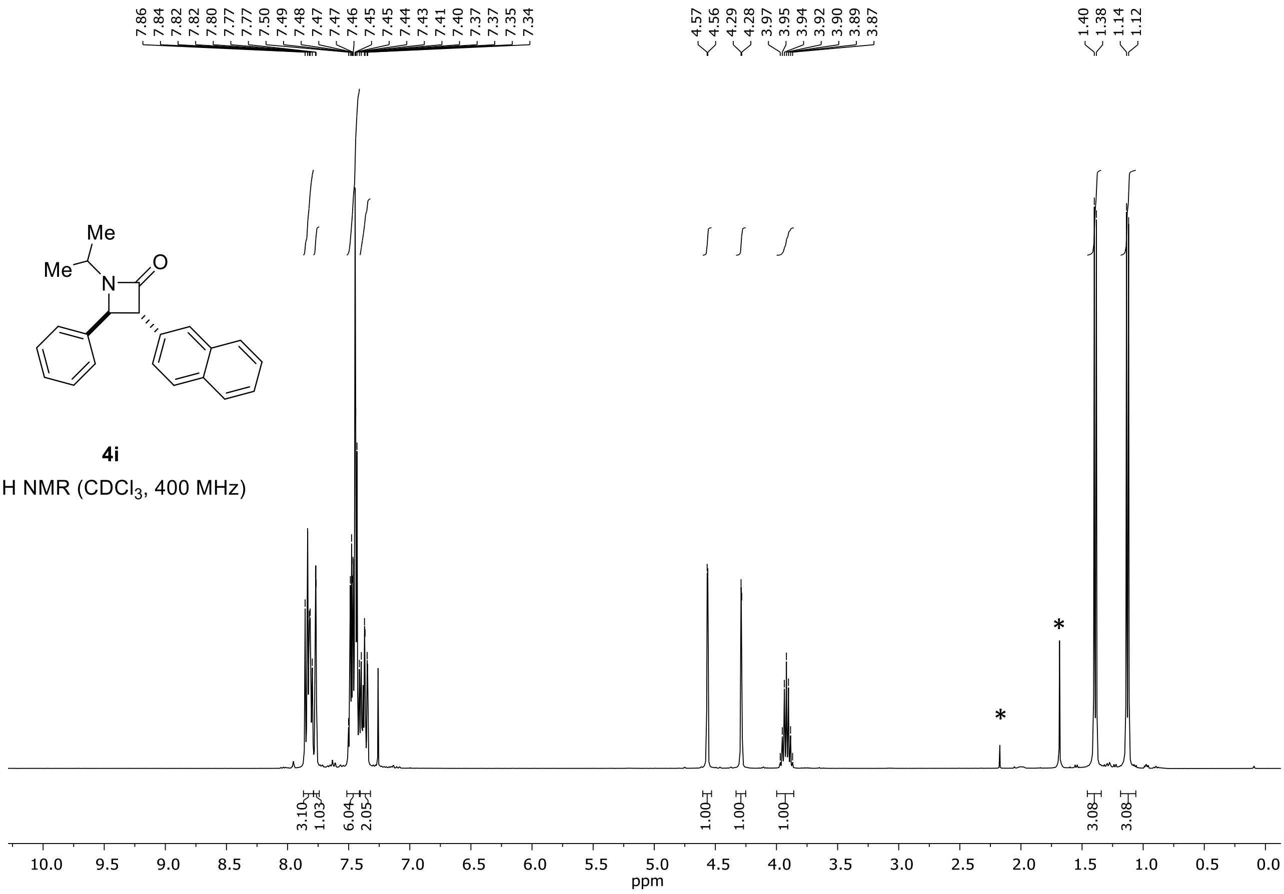
^{1}H NMR ($CDCl_3$, 400 MHz)


167.31
138.56
136.31
131.76
131.44
131.11
130.79
129.45
129.15
128.89
126.58
124.57
124.53
124.49
124.45
124.30
124.27
124.23
124.19
63.60
62.68
45.45
21.30
20.63
Me
Me
N
O
CF3
4h
13C NMR (CDCl3, 101 MHz)
*
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

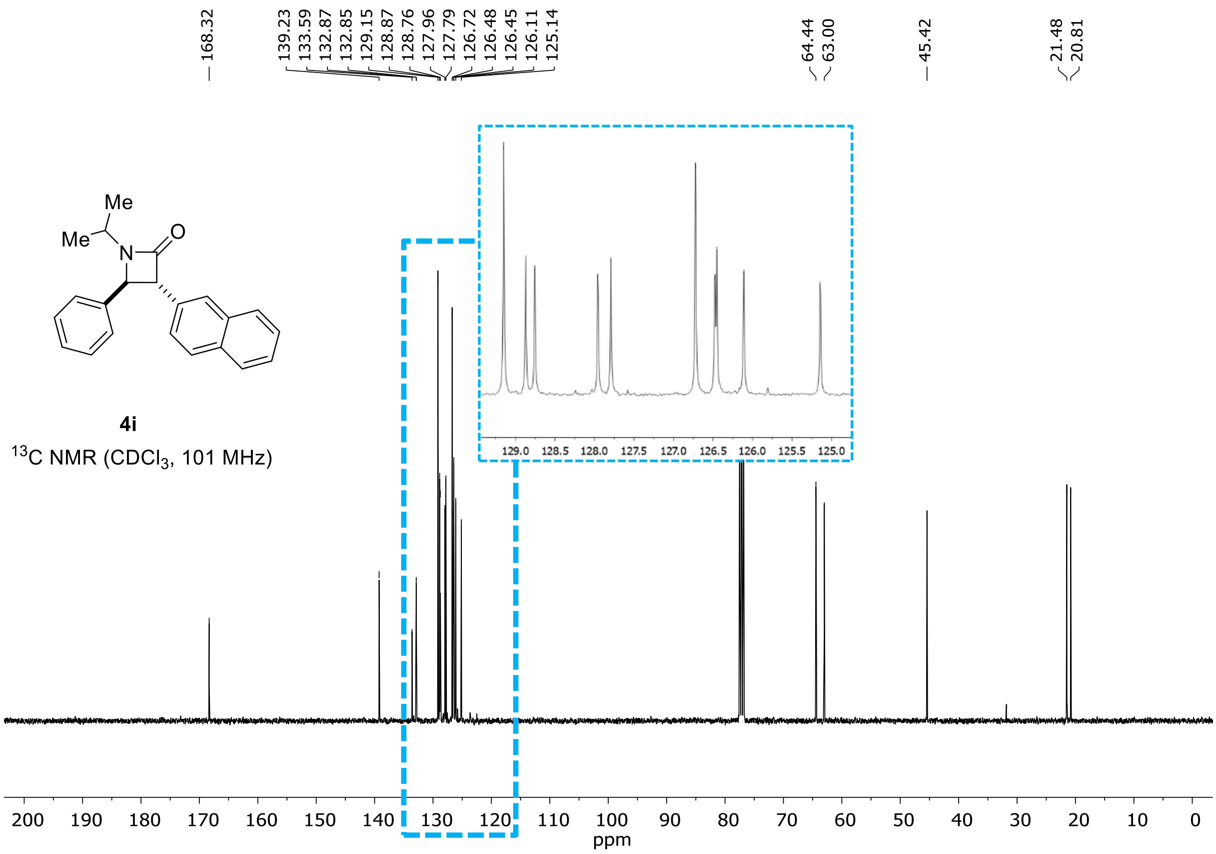

131.76
131.44
131.11
130.79
129.45
129.15
128.89
126.58
124.57
124.53
124.49
124.45
124.30
124.27
124.23
124.19
Me
Me
N
O
CF3
4h
13C NMR (CDCl3, 101 MHz)
132.5 132.0 131.5 131.0 130.5 130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5 126.0 125.5 125.0 124.5 124.0
ppm



4h
^{19}F NMR (CDCl$_3$, 376 MHz)

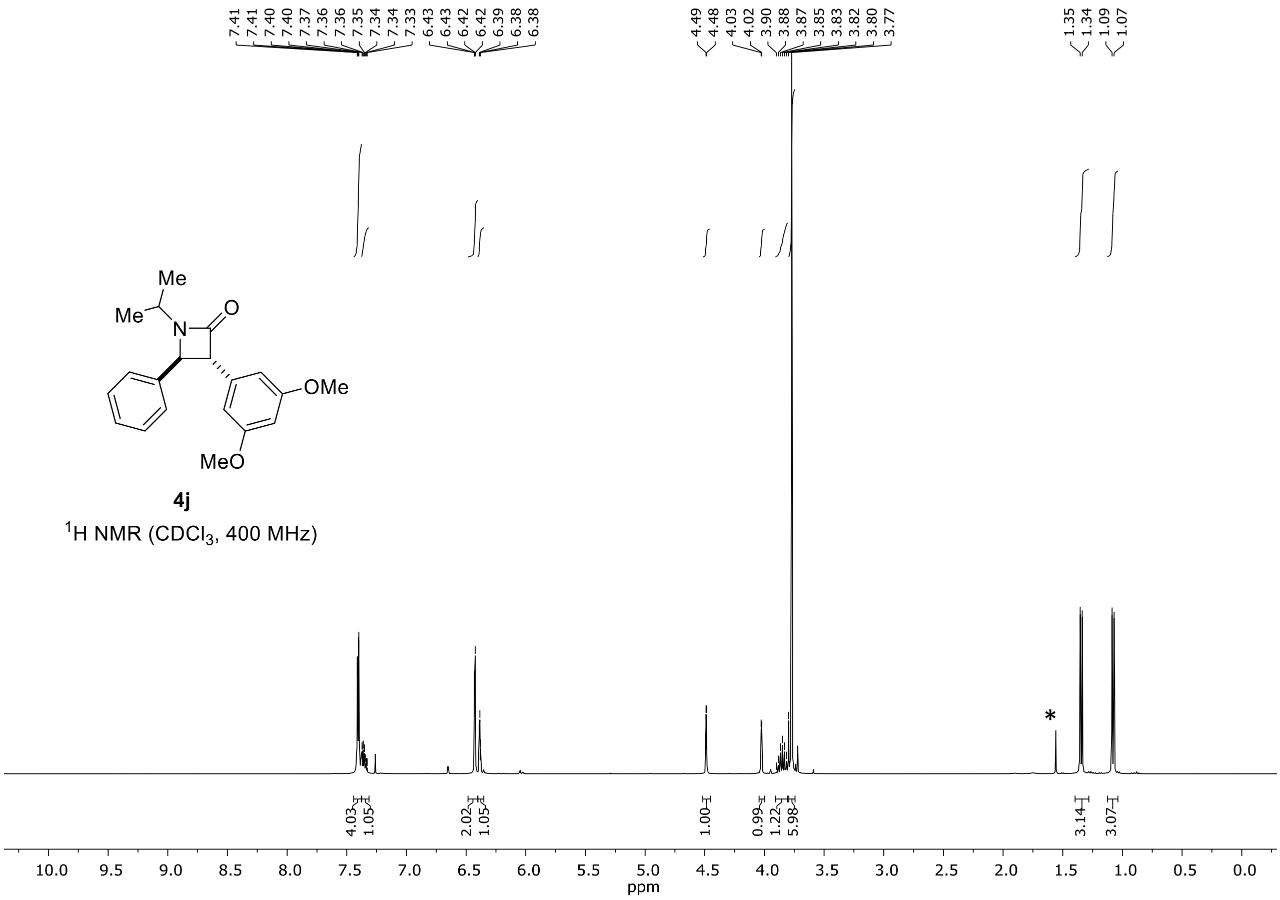


4i
^{1}H NMR (CDCl$_3$, 400 MHz)



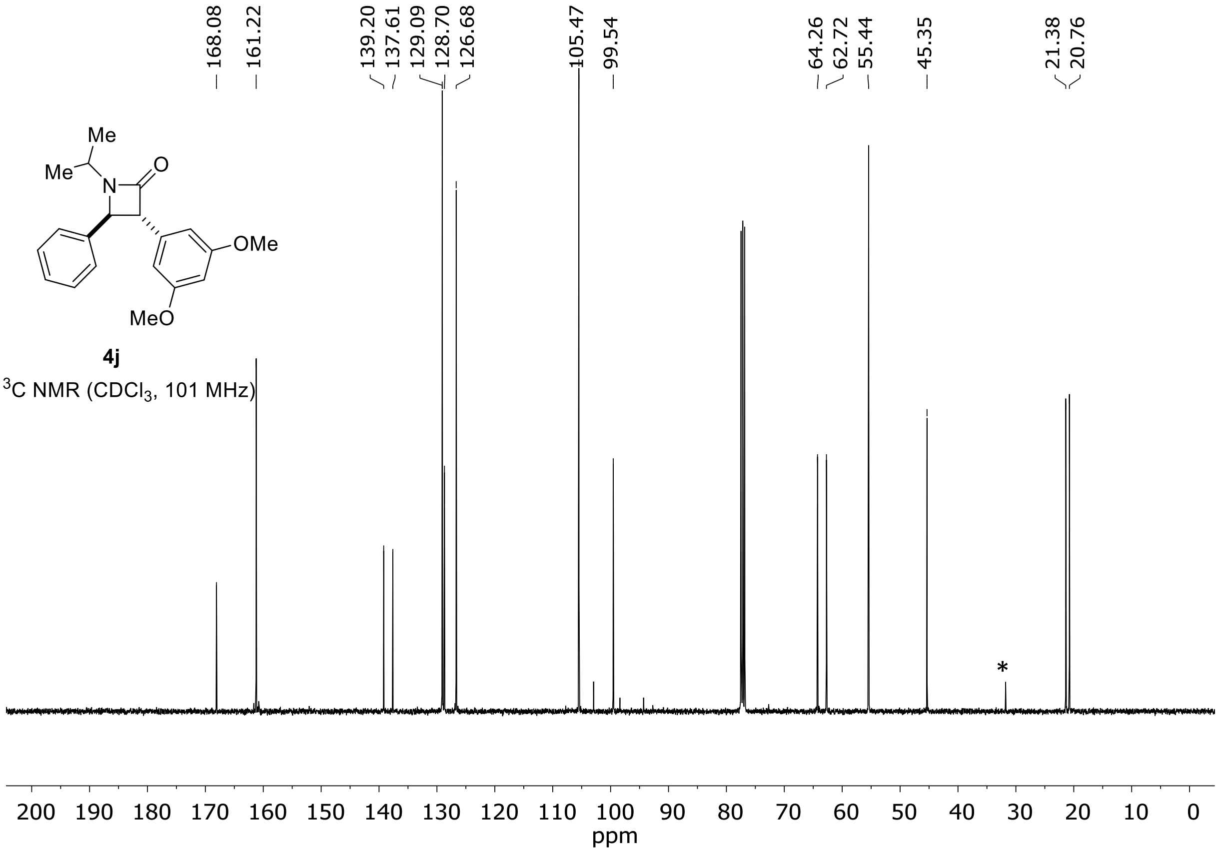
4i

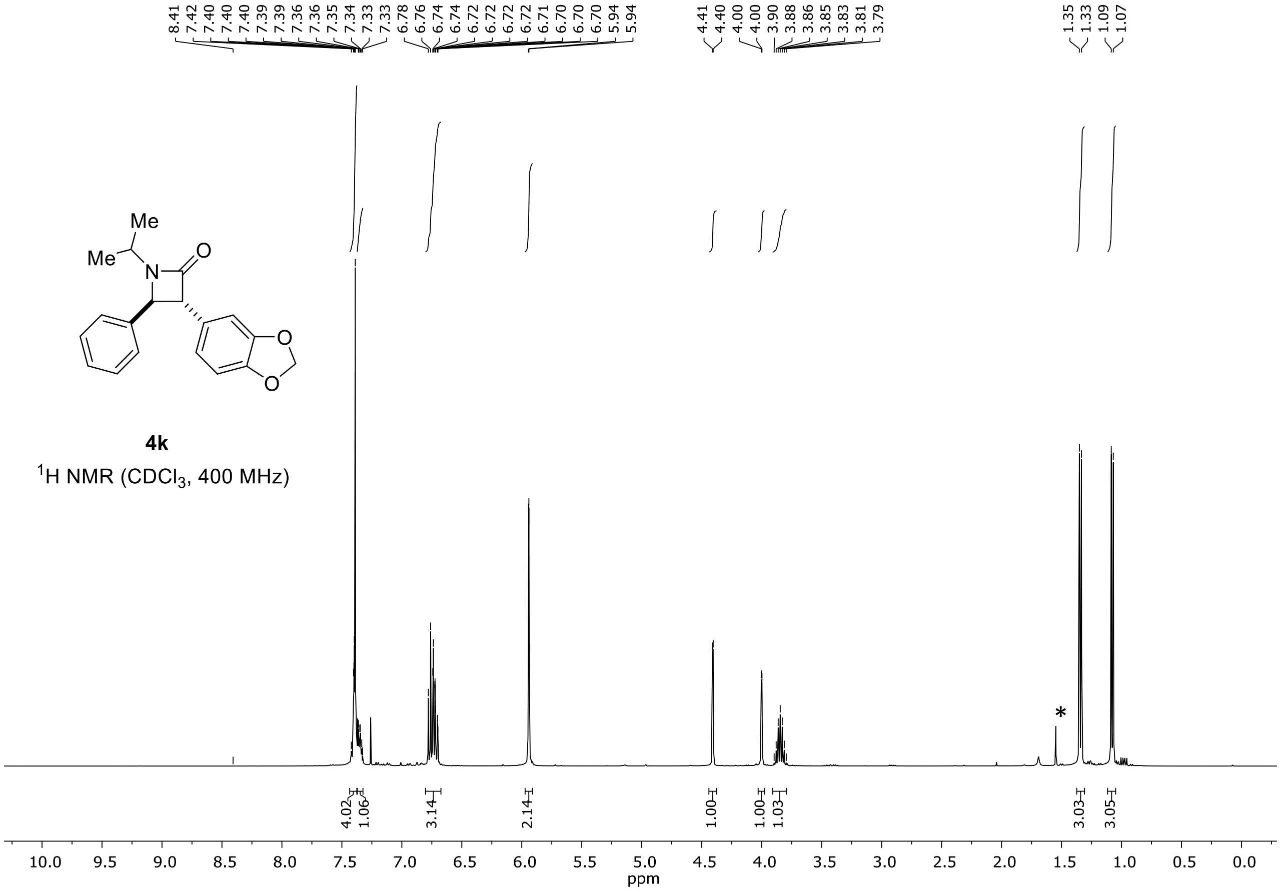
^{13}C NMR ($CDCl_3$, 101 MHz)

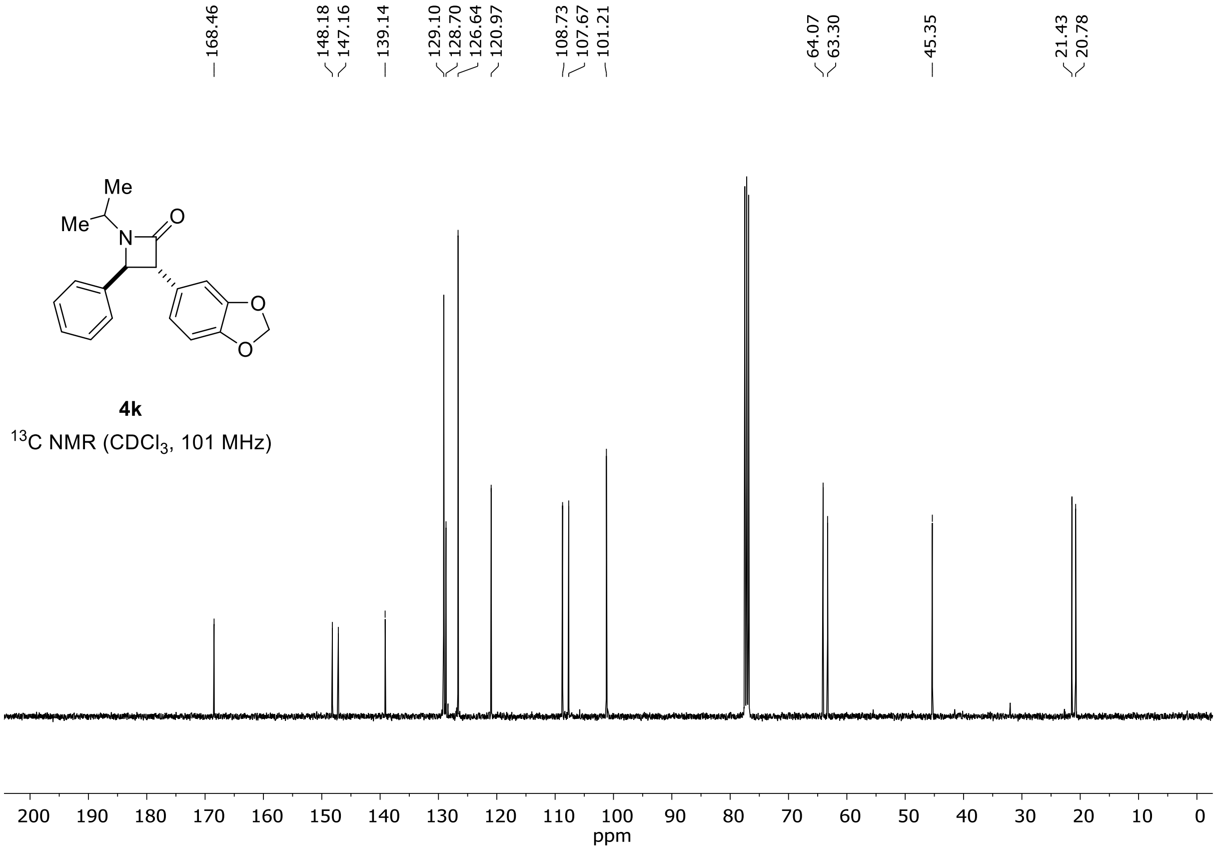


4j

^{1}H NMR ($CDCl_3$, 400 MHz)

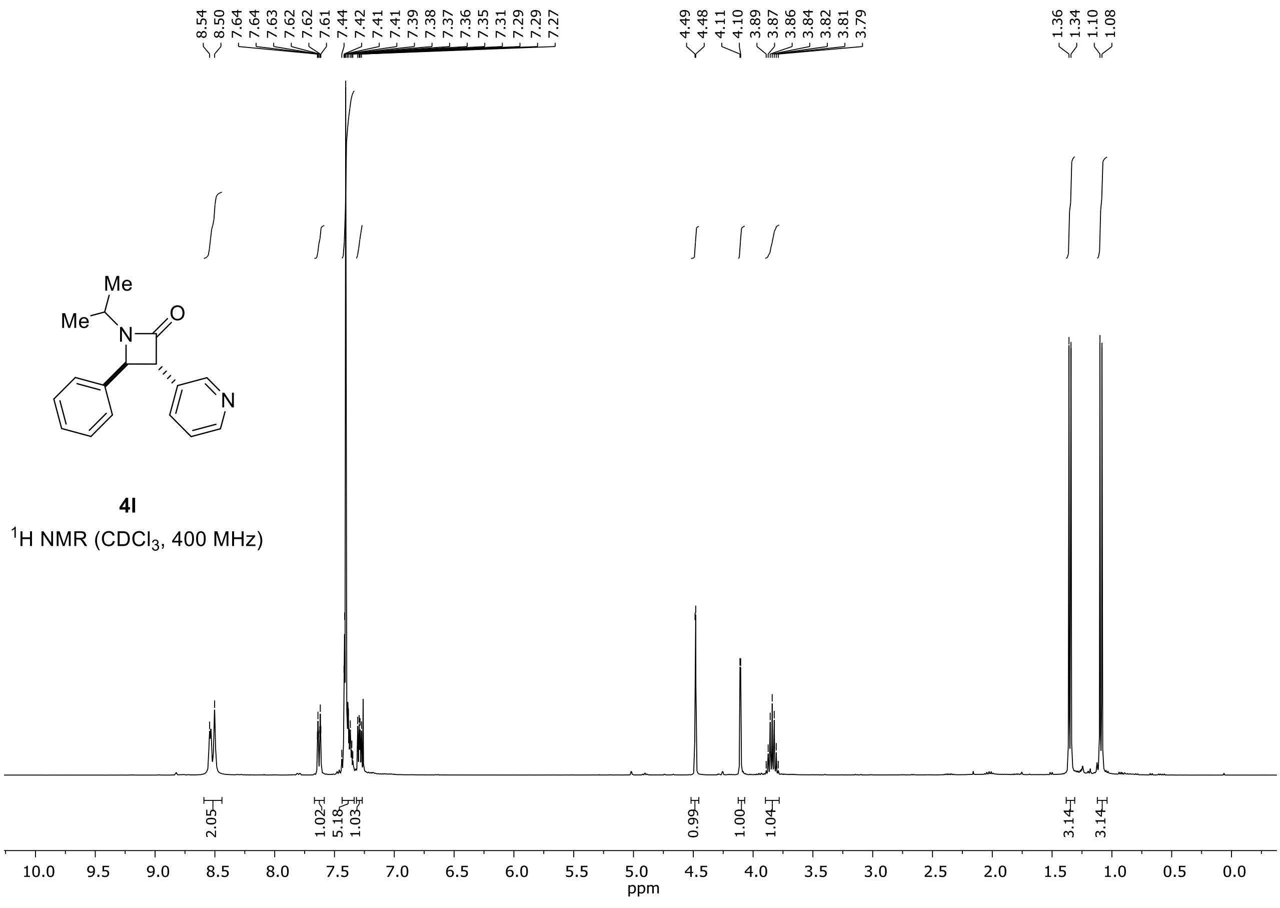

168.08
161.22
139.20
137.61
129.09
128.70
126.68
105.47
99.54
64.26
62.72
55.44
45.35
21.38
20.76
Me
Me
N
O
OMe
MeO
*
ppm
4j
^{13}C NMR ($CDCl_3$, 101 MHz)


8.41
7.42
7.40
7.40
7.40
7.39
7.39
7.36
7.36
7.35
7.34
7.33
7.33
6.78
6.76
6.74
6.74
6.72
6.72
6.72
6.72
6.71
6.70
6.70
6.70
5.94
5.94
4.41
4.40
4.00
4.00
3.90
3.88
3.86
3.85
3.83
3.81
3.79
1.35
1.33
1.09
1.07
Me
Me
N
O
O
O
*
4.02
1.06
3.14
2.14
1.00
1.00
1.03
3.03
3.05
ppm
4k
^{1}H NMR ($CDCl_3$, 400 MHz)



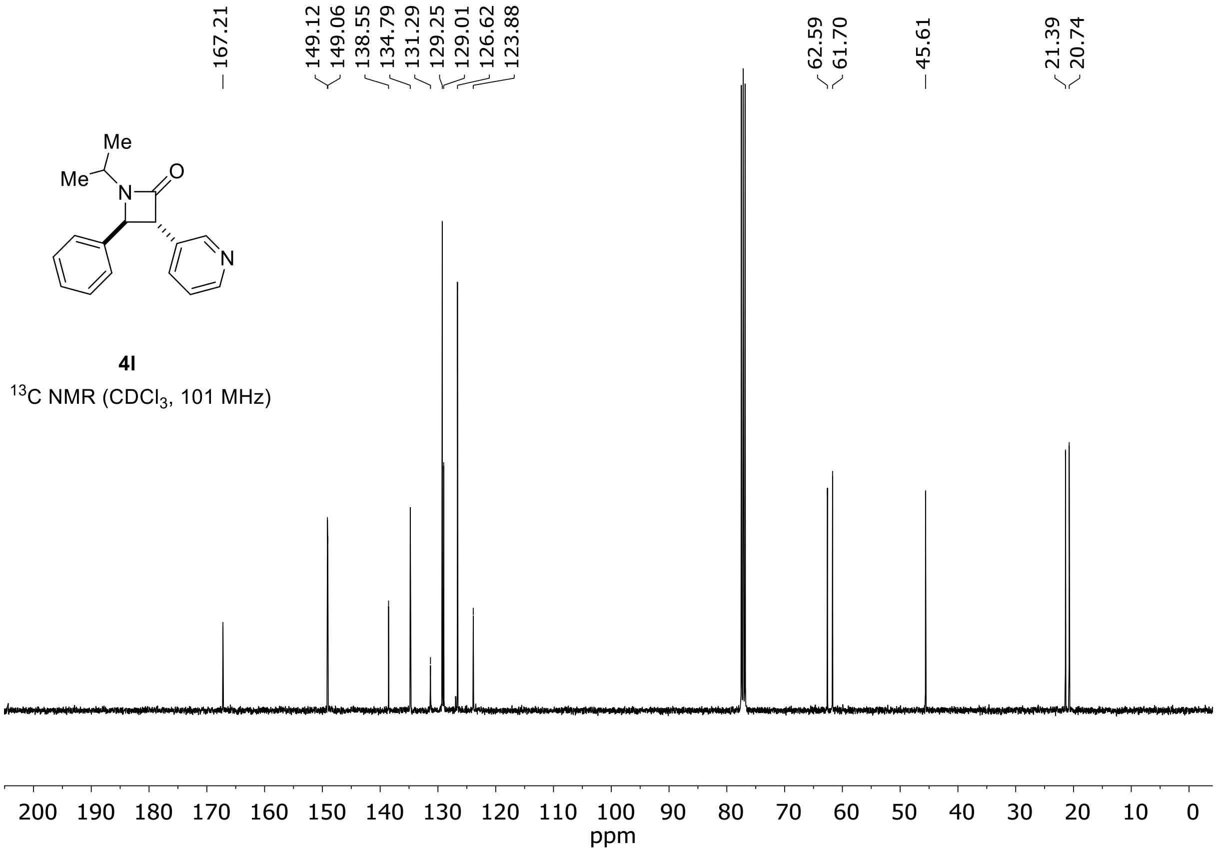
4k

^{13}C NMR ($CDCl_3$, 101 MHz)



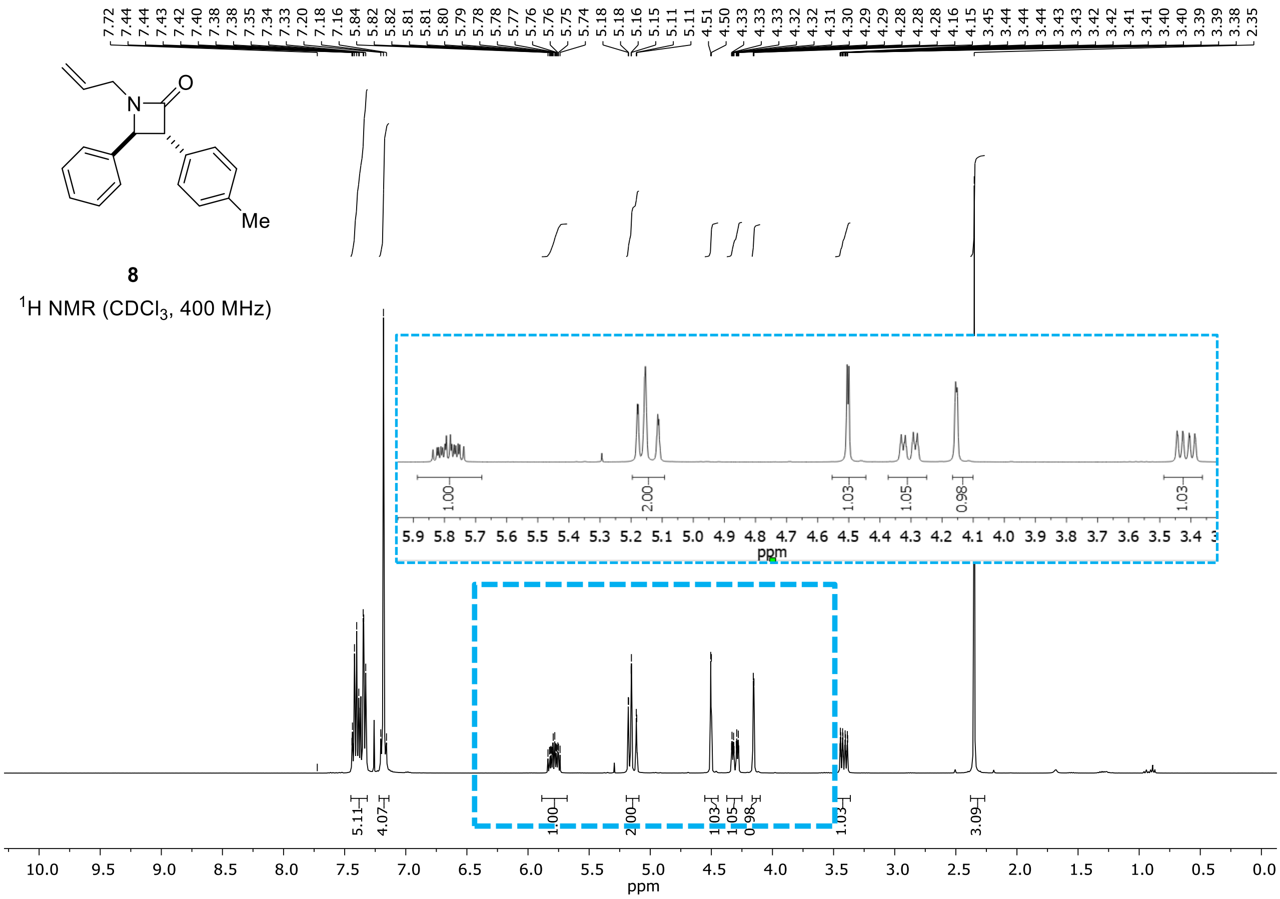
4l

^{1}H NMR ($CDCl_3$, 400 MHz)



4l

^{13}C NMR (CDCl$_3$, 101 MHz)

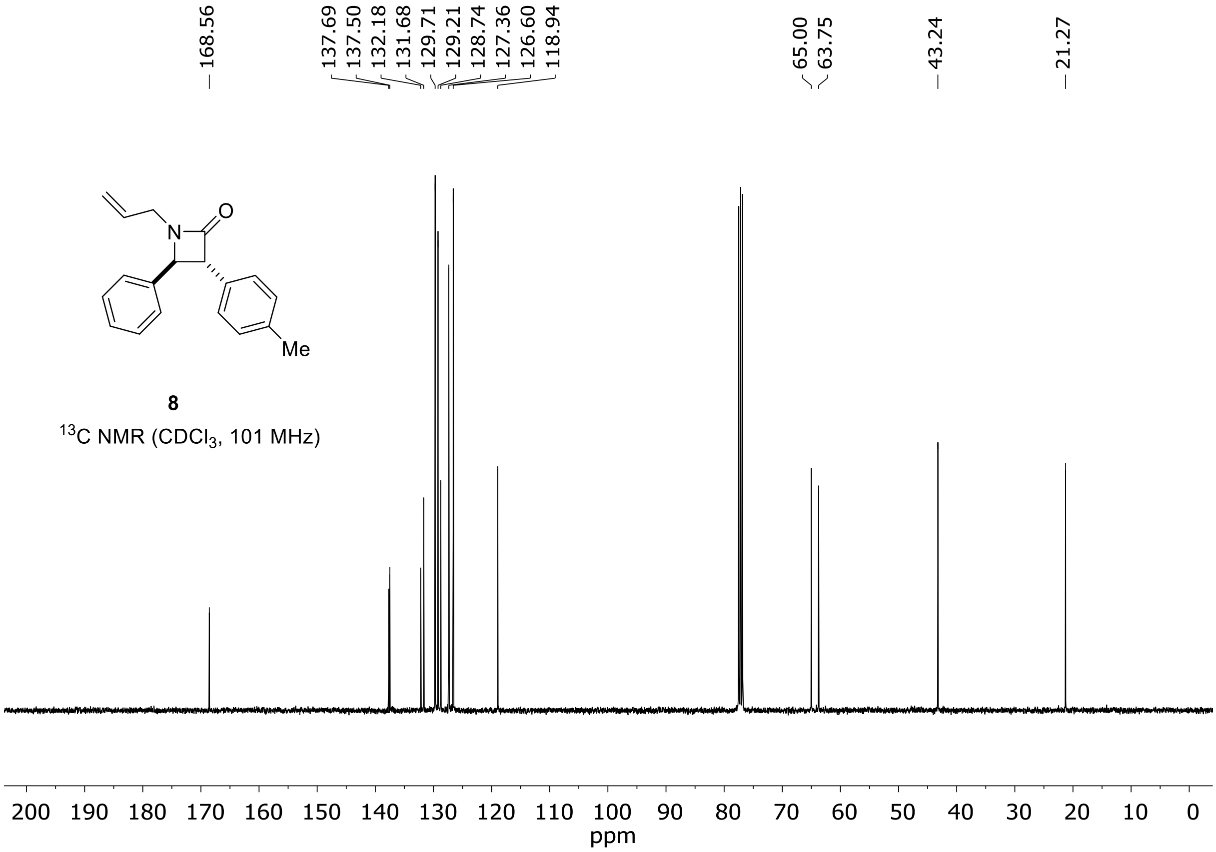


8

^{1}H NMR (CDCl$_3$, 400 MHz)

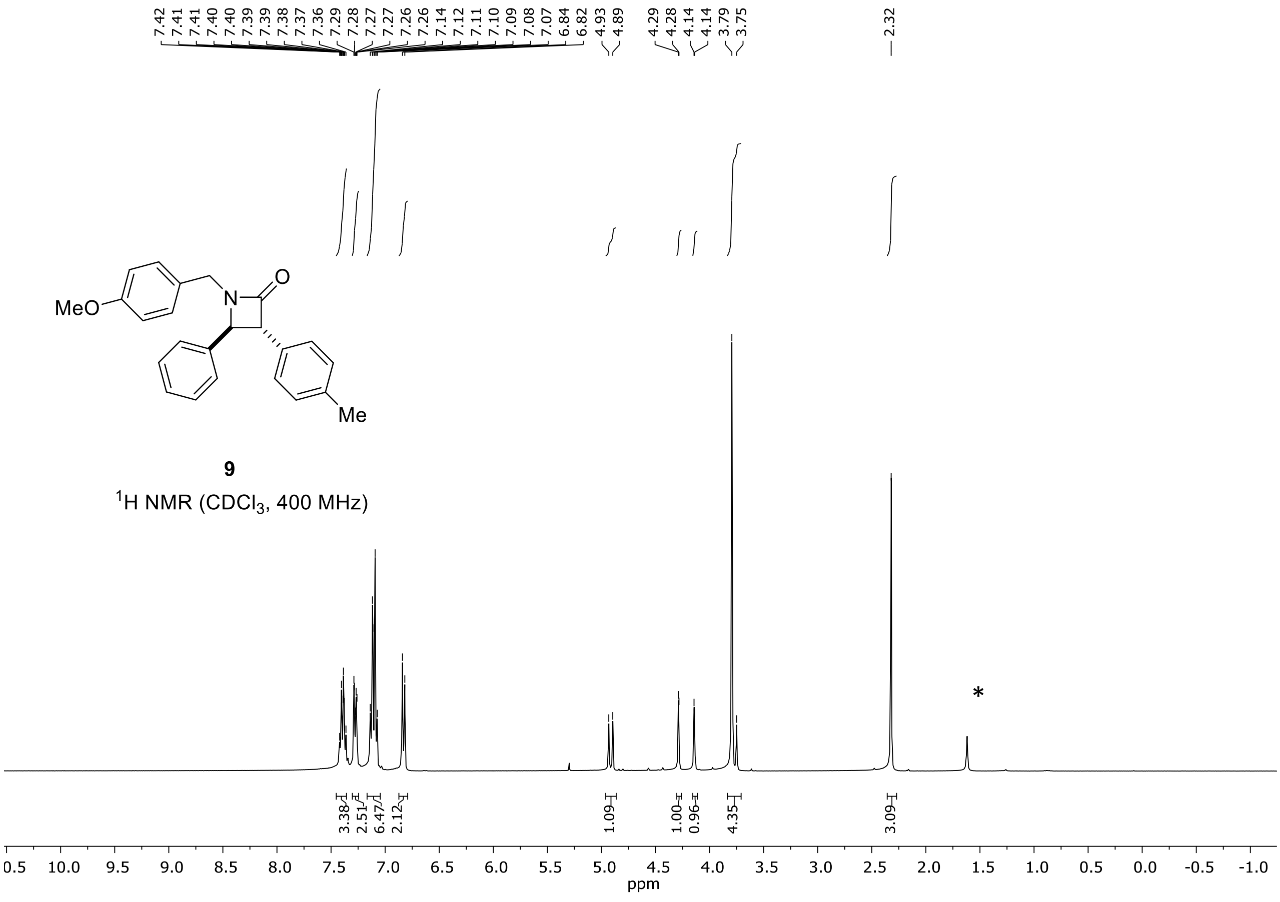
8

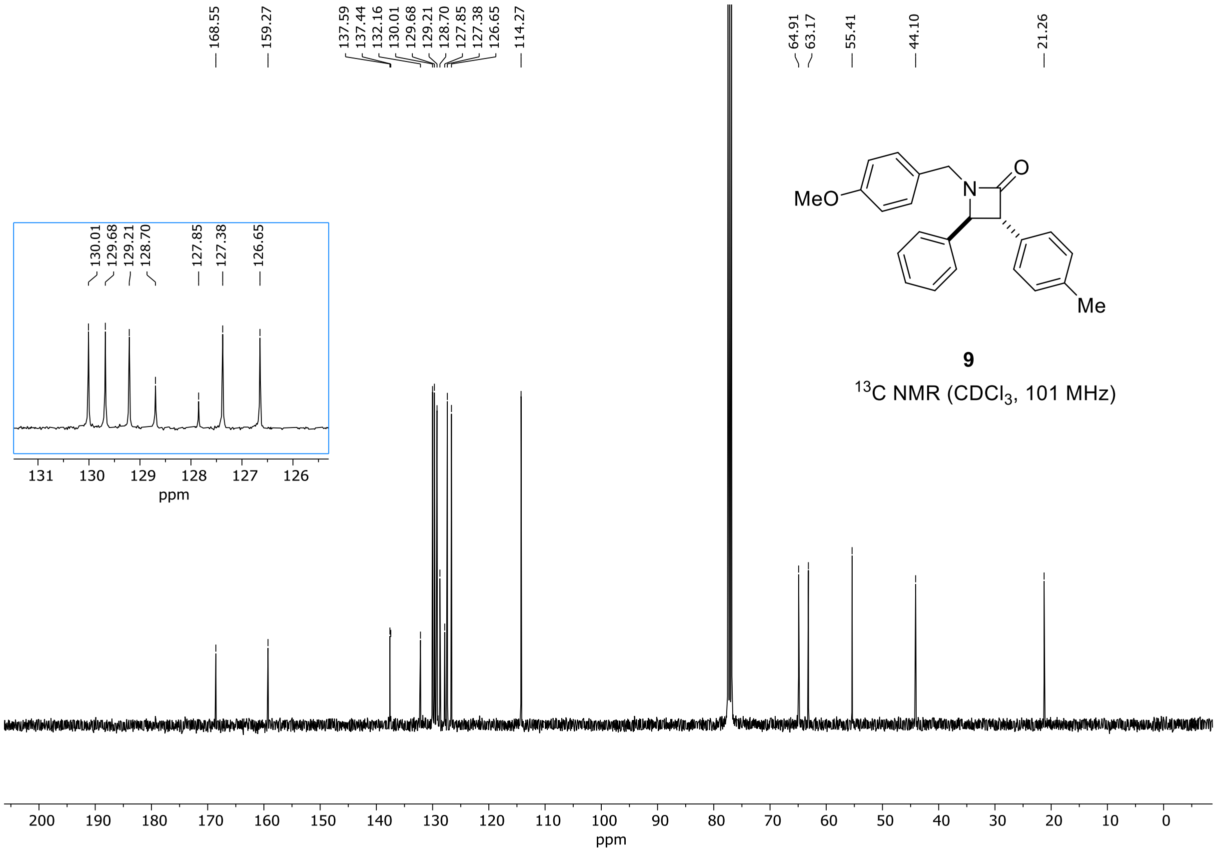
^{13}C NMR (CDCl$_3$, 101 MHz)



9

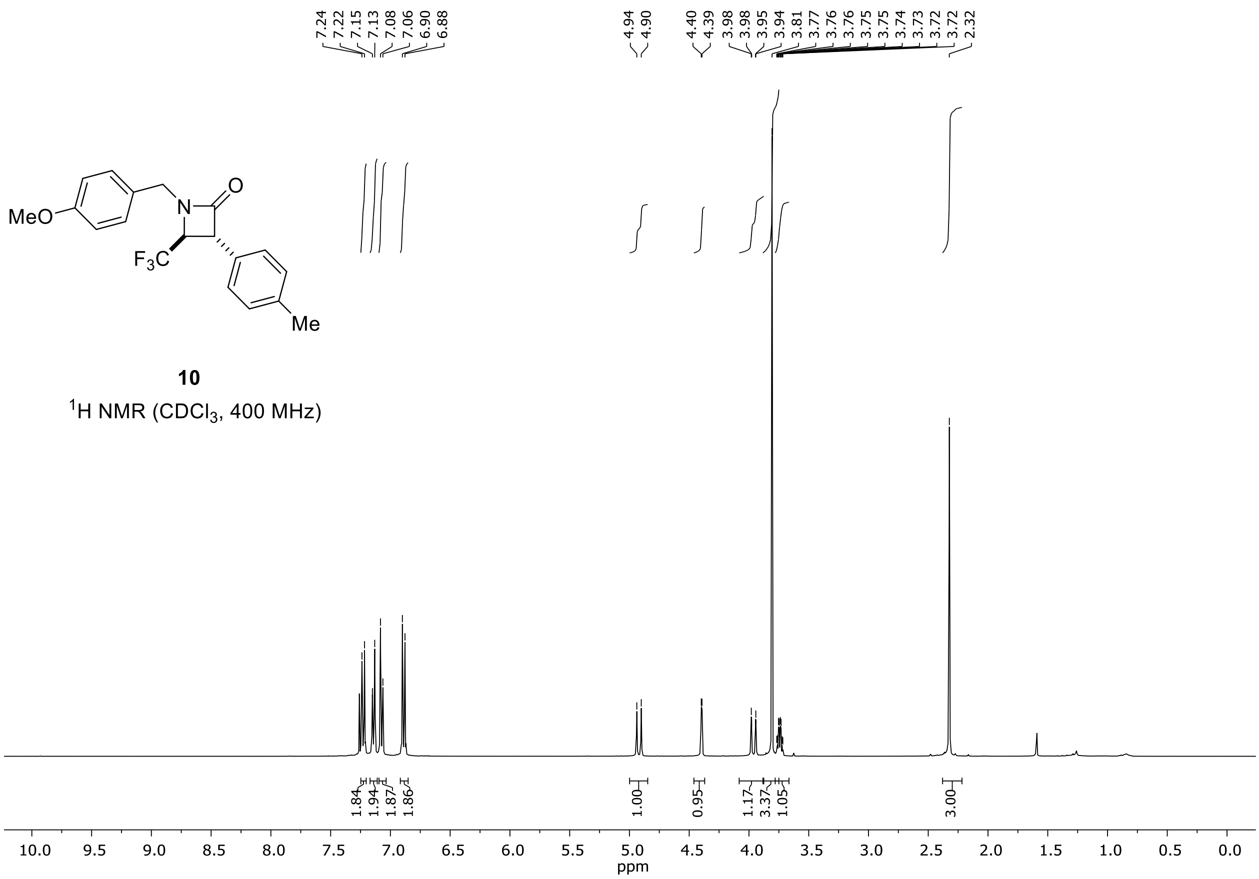
^{1}H NMR (CDCl$_3$, 400 MHz)





9

^{13}C NMR ($CDCl_3$, 101 MHz)

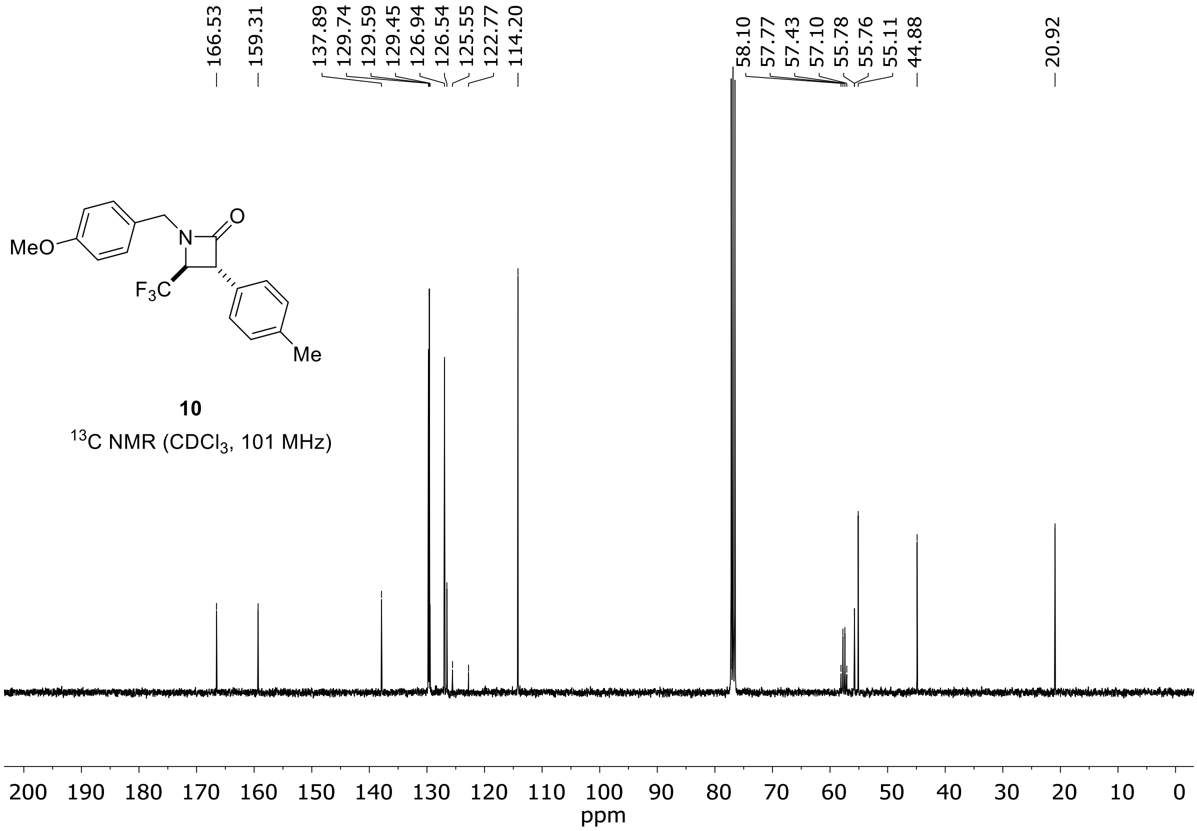


10

^{1}H NMR ($CDCl_3$, 400 MHz)

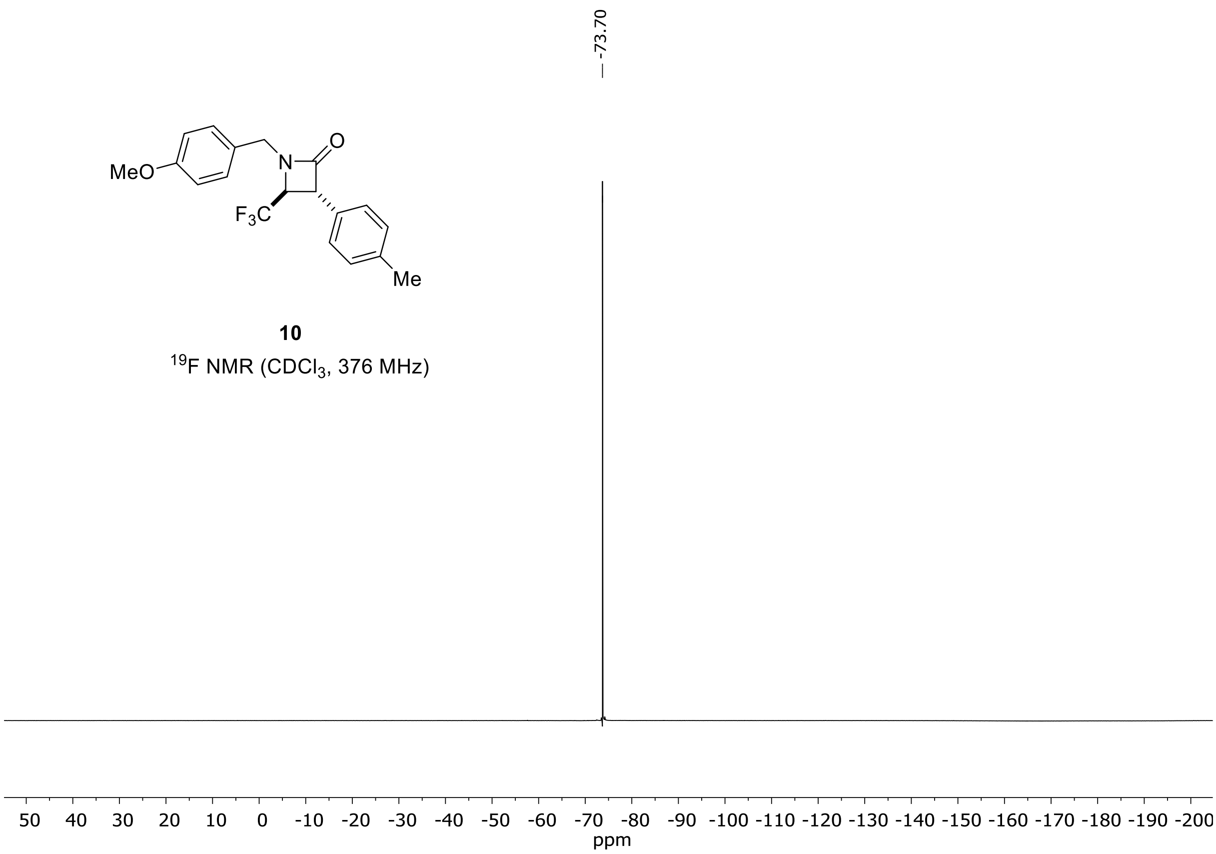
10

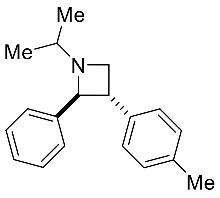
^{13}C NMR ($CDCl_3$, 101 MHz)



10

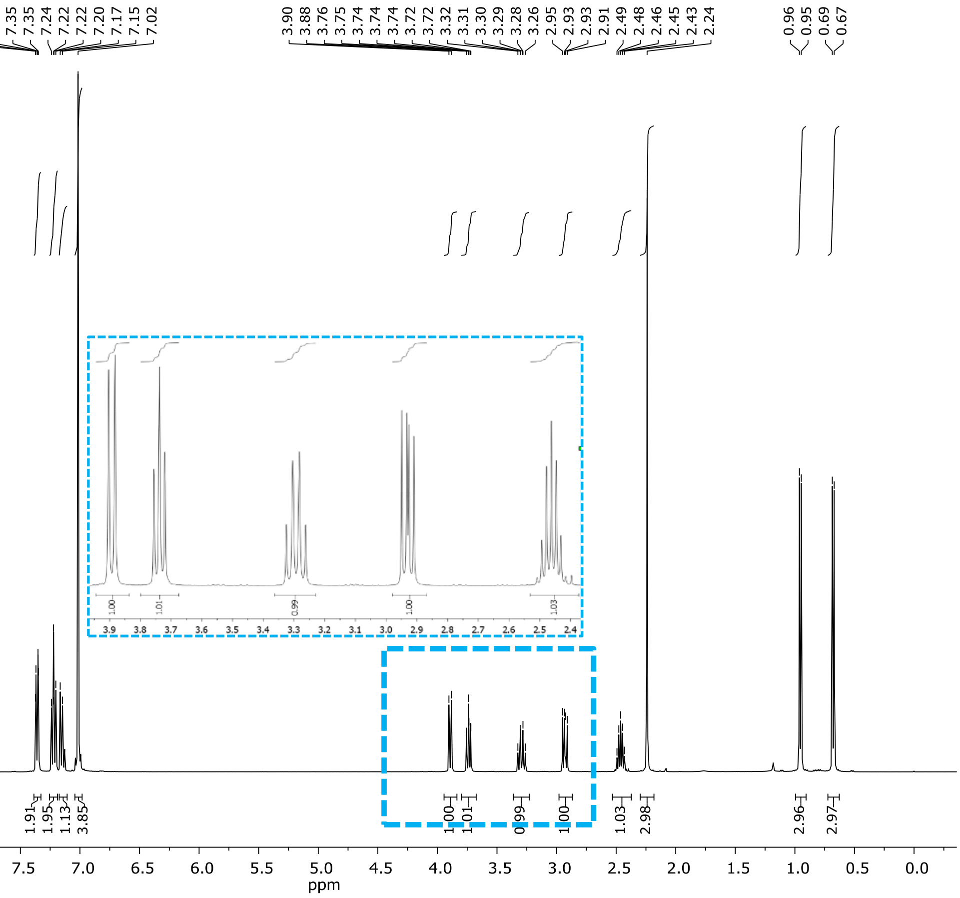
^{19}F NMR ($CDCl_3$, 376 MHz)

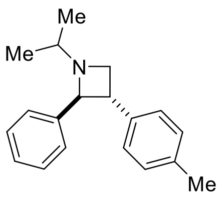




11

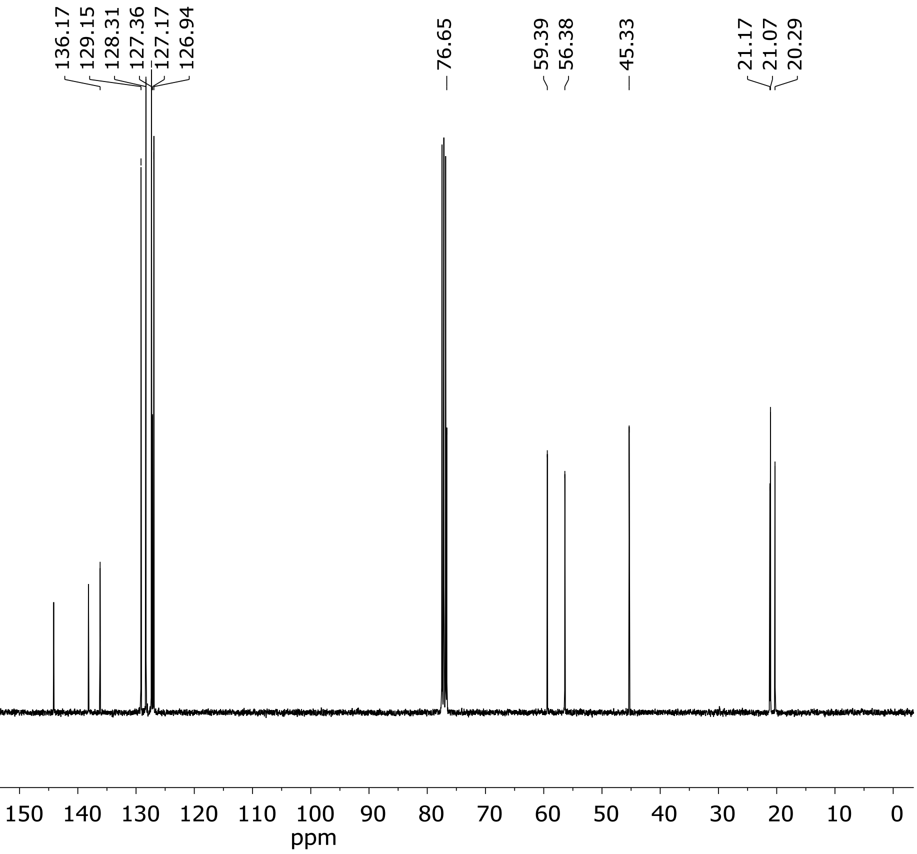
^{1}H NMR ($CDCl_3$, 400 MHz)

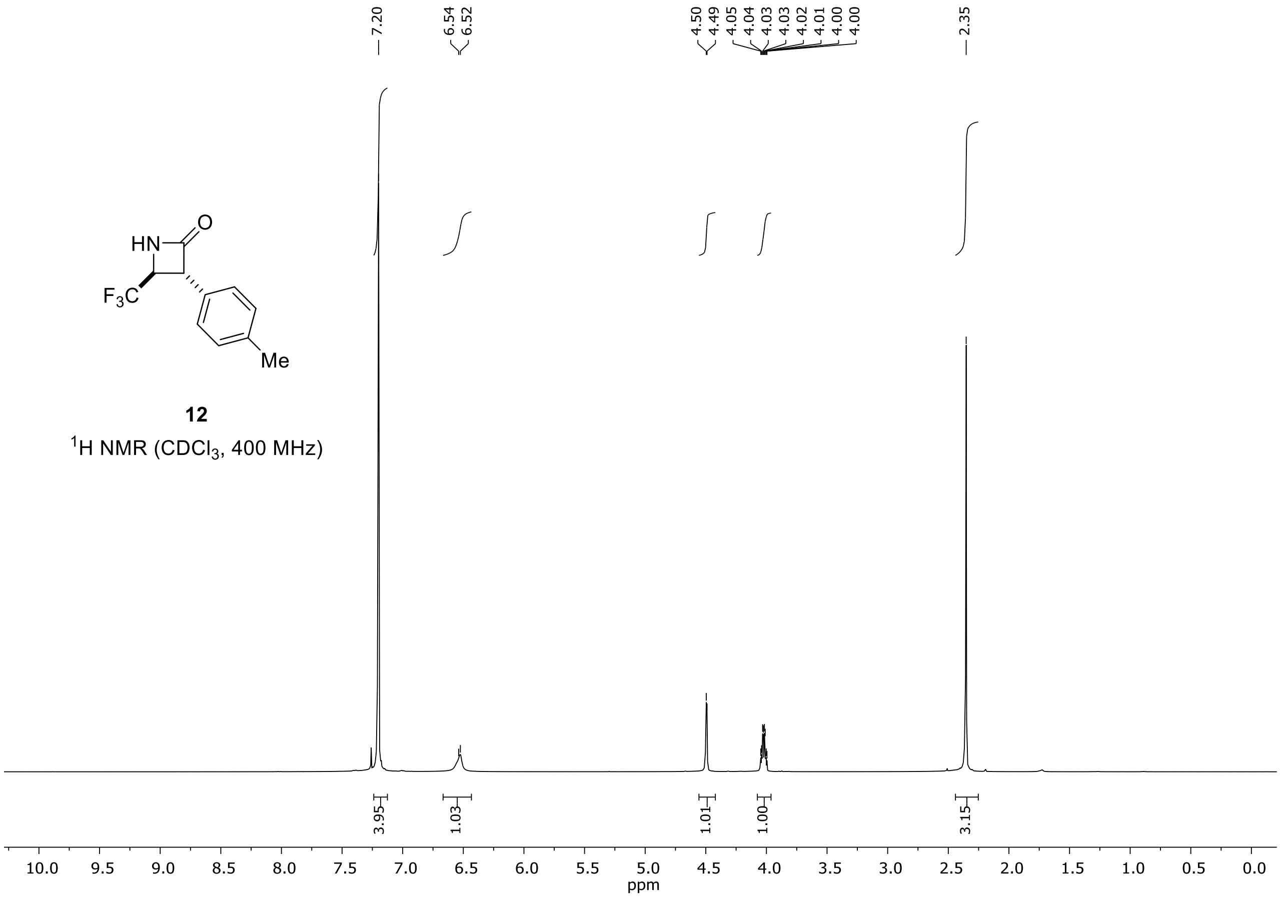




11

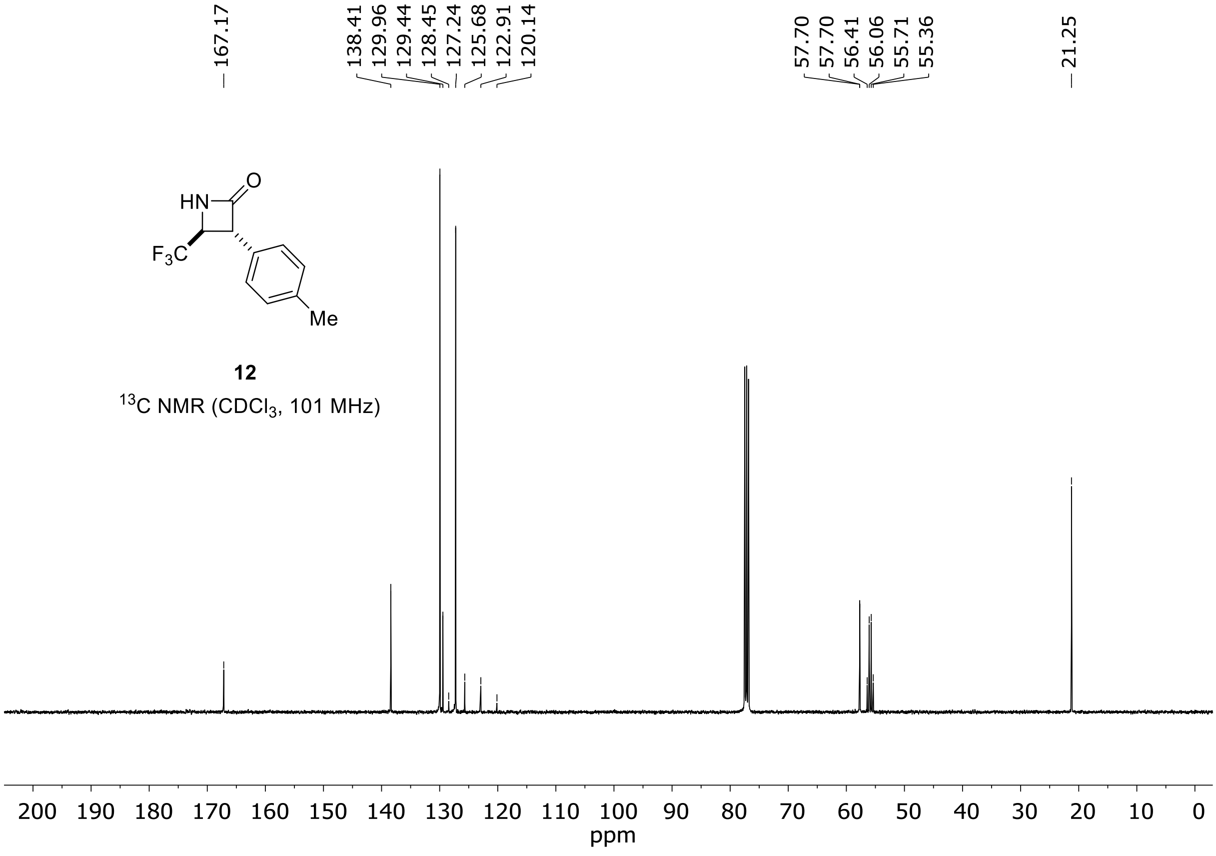
^{13}C NMR ($CDCl_3$, 101 MHz)





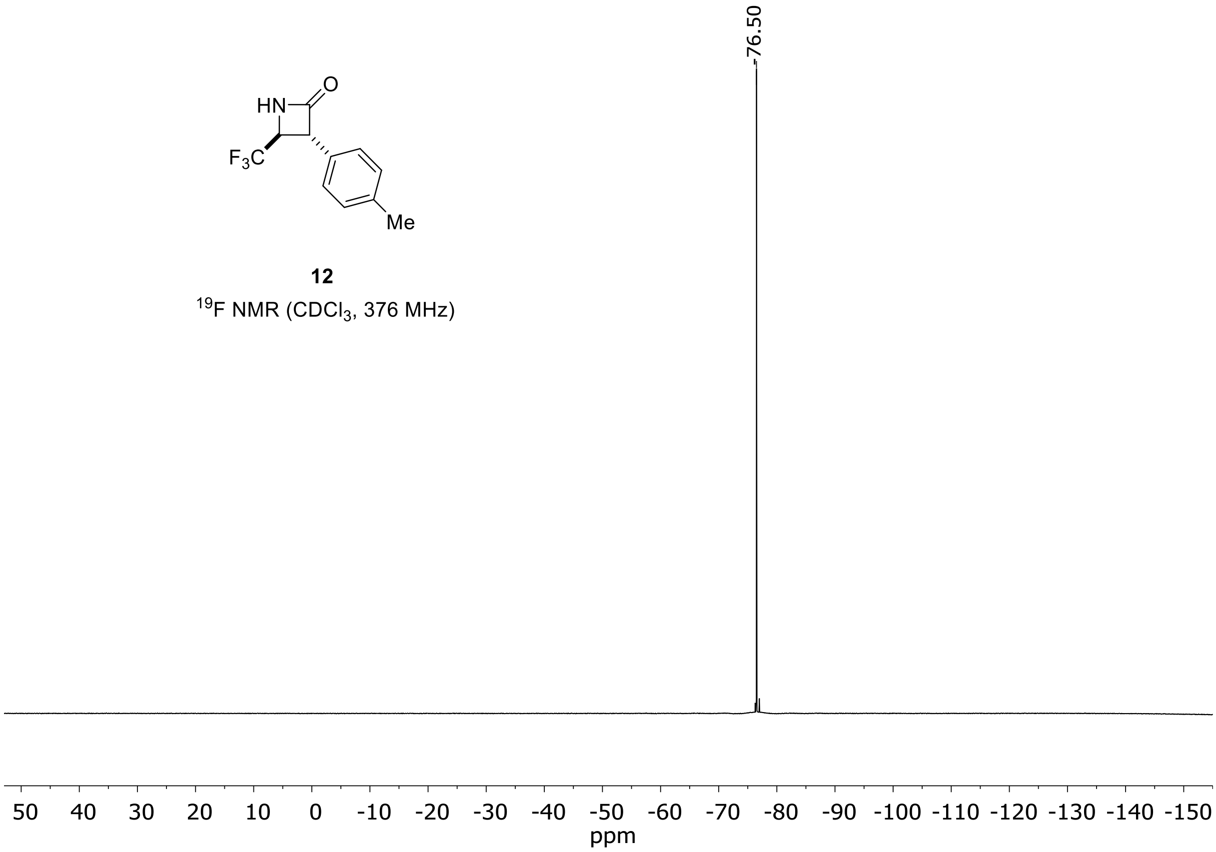
12

^1H NMR ($CDCl_3$, 400 MHz)



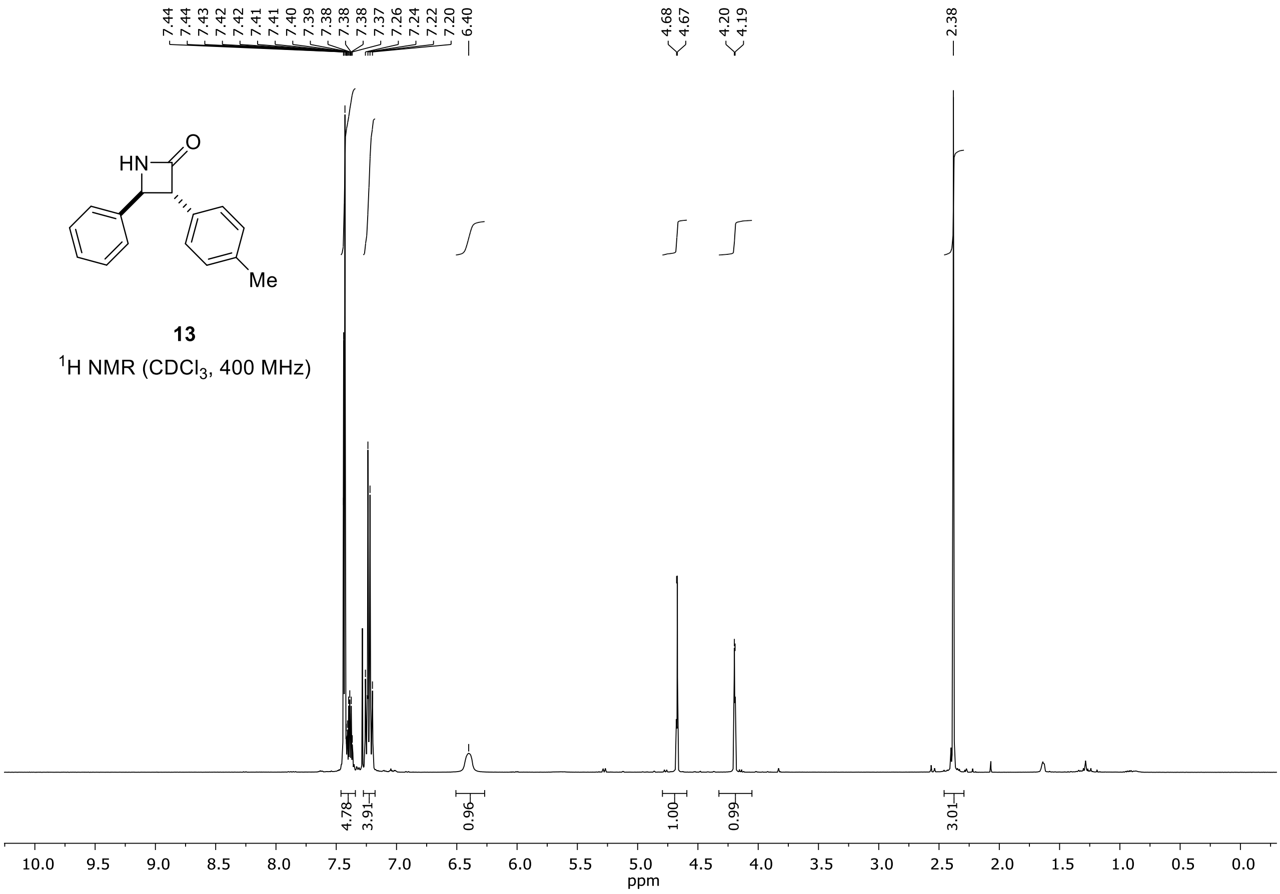
12

^{13}C NMR ($CDCl_3$, 101 MHz)



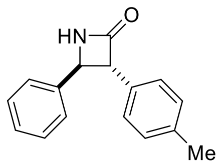
12

^{19}F NMR ($CDCl_3$, 376 MHz)



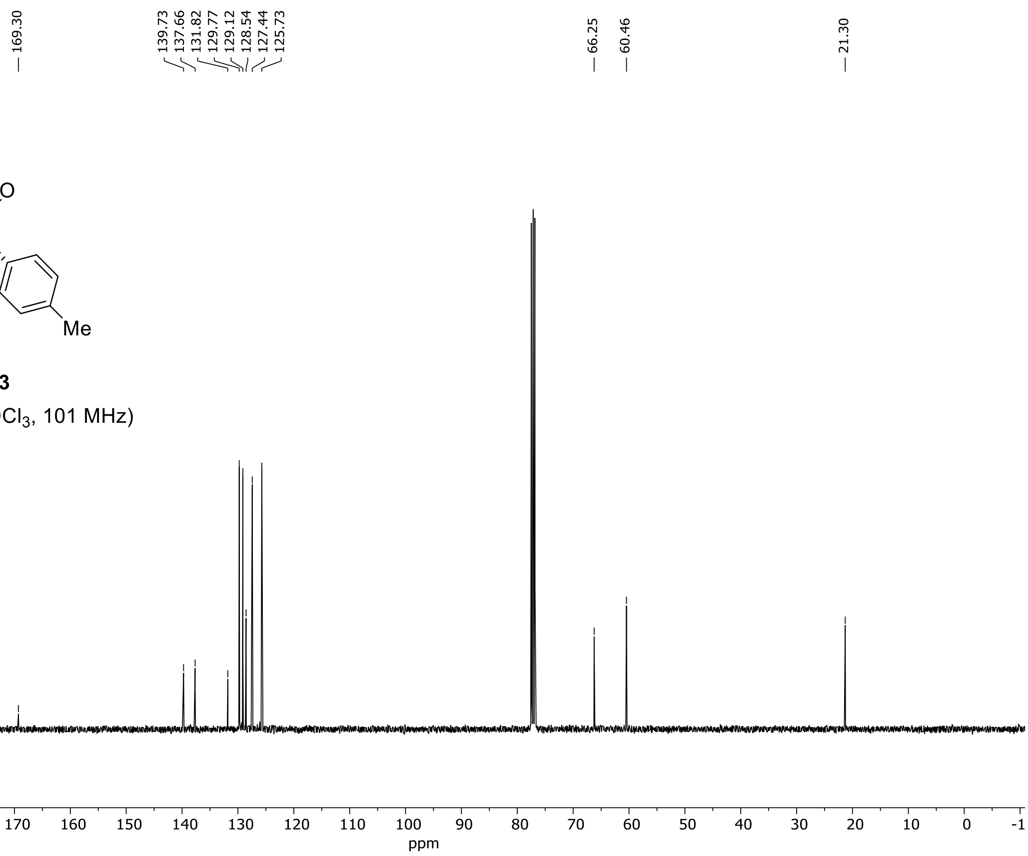
13

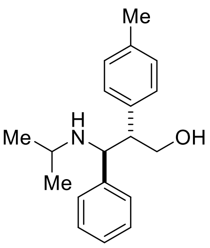
^{1}H NMR ($CDCl_3$, 400 MHz)



13

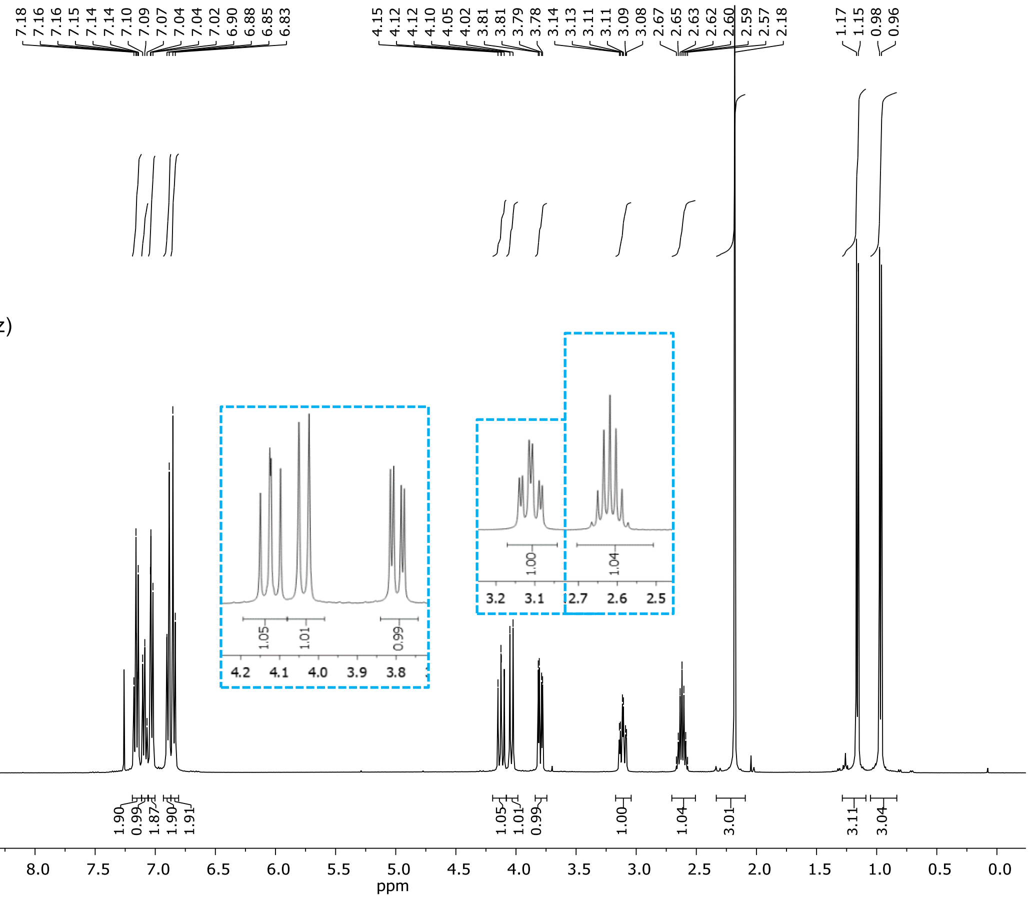
^{13}C NMR ($CDCl_3$, 101 MHz)

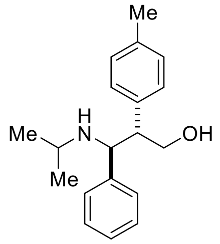




14

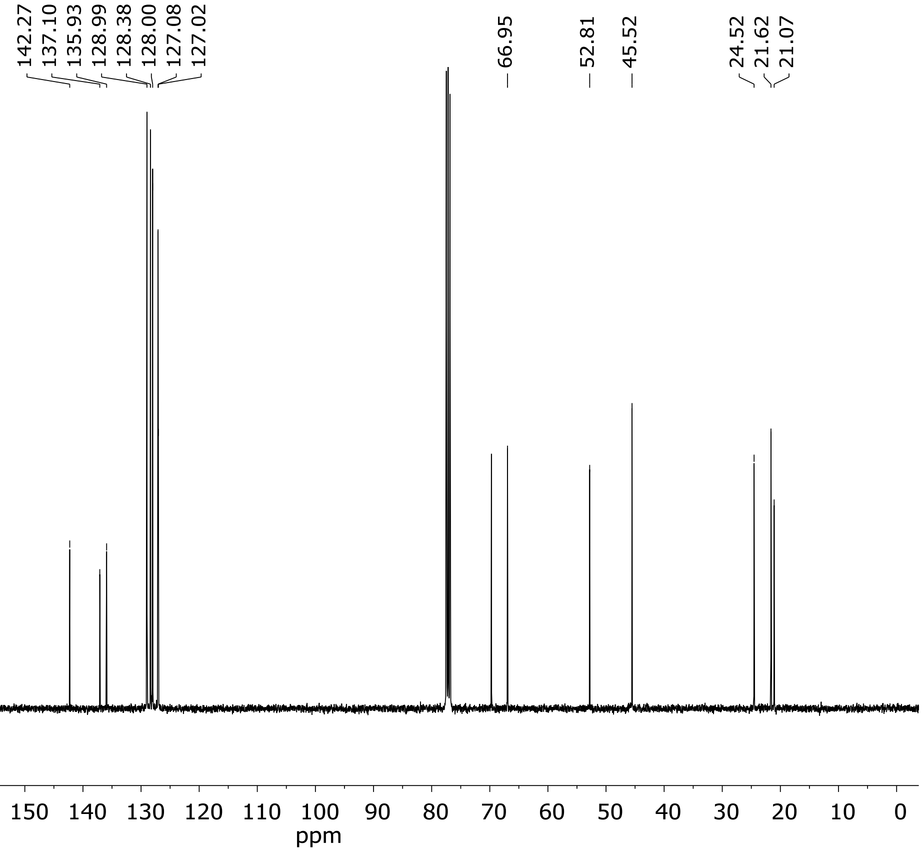
^{1}H NMR ($CDCl_3$, 400 MHz)

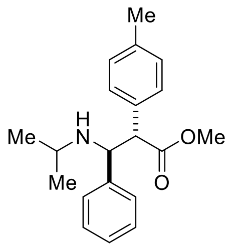




14

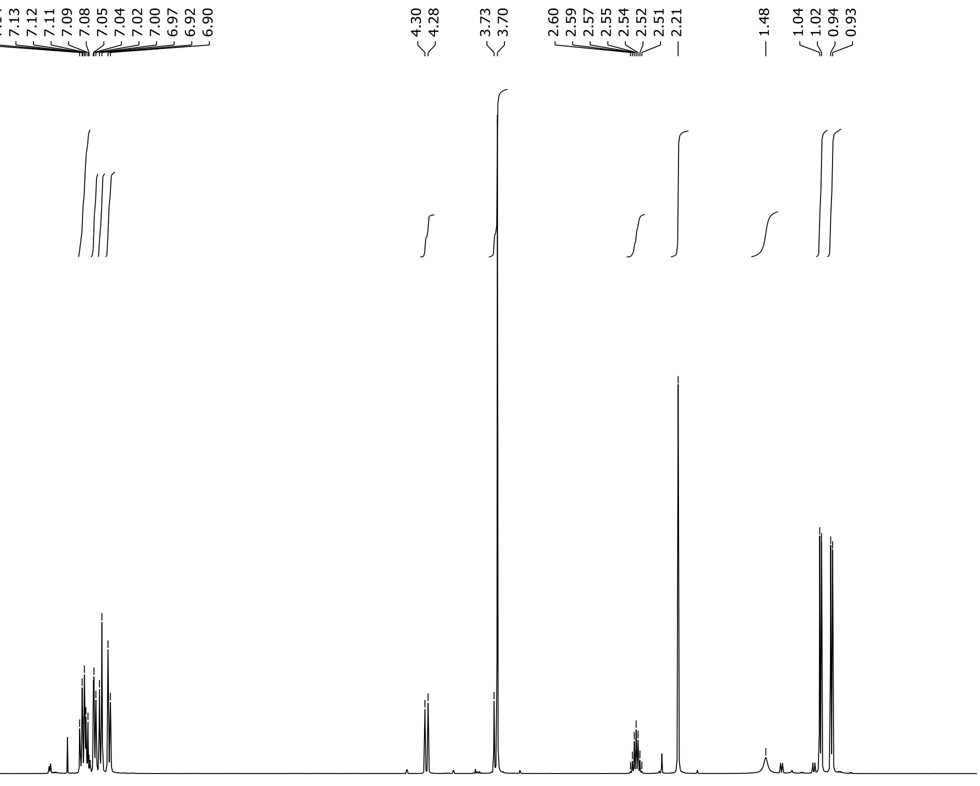
^{13}C NMR ($CDCl_3$, 101 MHz)

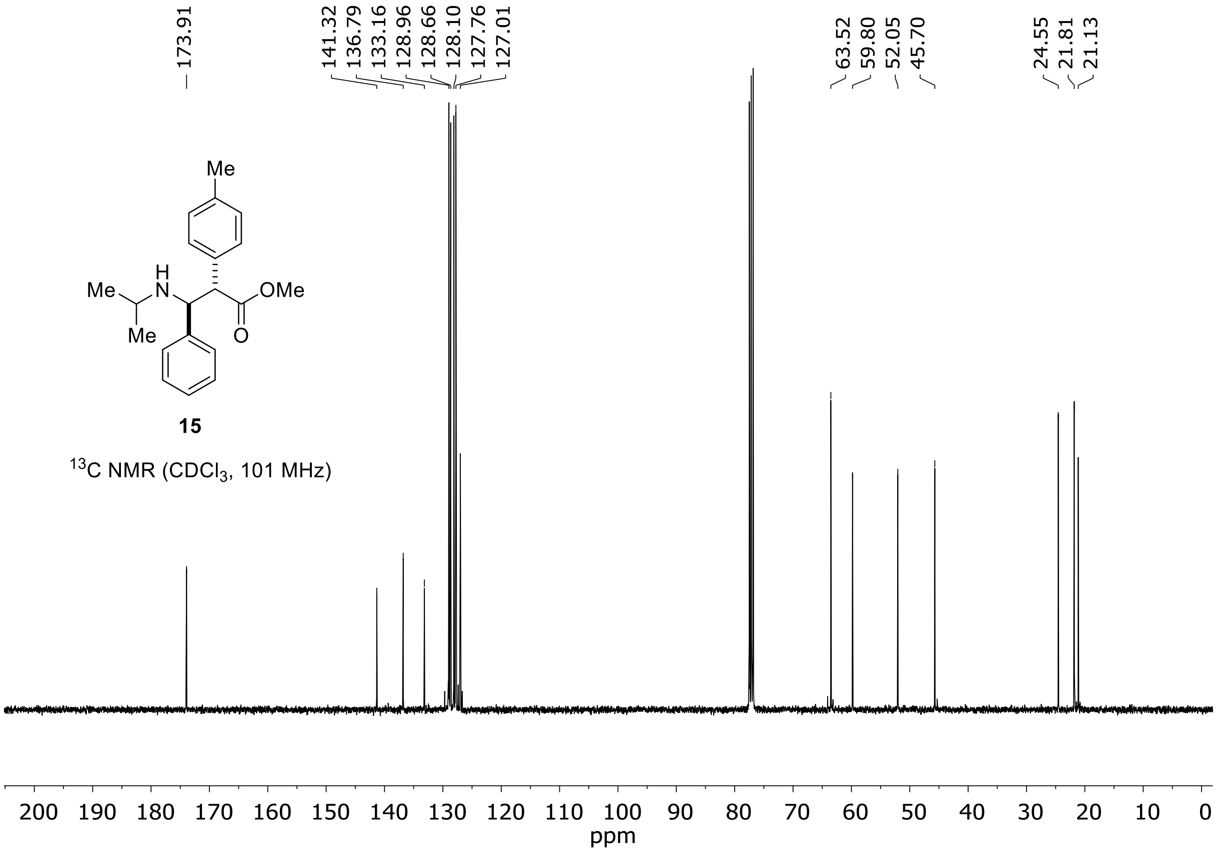




15

^{1}H NMR ($CDCl_3$, 400 MHz)





173.91
141.32
136.79
133.16
128.96
128.66
128.10
127.76
127.01
63.52
59.80
52.05
45.70
24.55
21.81
21.13
Me
H
N
Me
Me
OMe
O
15
^{13}C NMR ($CDCl_3$, 101 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm