Chemodivergent alkylation of trifluoromethyl alkenes via photocatalytic coupling with alkanes

Pol Martínez-Balart, Álvaro Velasco-Rubio, Sergio Barbeira-Arán, Hugo Jiménez-Cristóbal and Martín Fañanás-Mastral*

Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CiQUS), Universidade de Santiago de Compostela, 15782 Santiago de Compostela, Spain

Supporting Information

Table of Contents

1. General Experimental Details

All reactions were performed under argon atmosphere using oven dried glassware and using standard Schlenk techniques. Solvents were dried using an MBraun SPS 800 system.
All chemicals purchased from. chemical companies and used without further purification, unless otherwise noted.

Analytical thin layer chromatography was carried out on silica-coated aluminium plates (silica gel 60 F254 Merck) and compounds were visualized using 254 nm UV light or by oxidation treatment (solution of 1.5 g of $KMnO_4$, 10 g of $KHCO_3$ and 1.25 mL of an aqueous solution of NaOH (10 (w/w)%) in 200 mL of H_2O) or (solution of 10g of phosphomolybdic acid in 100 mL of absolute ethanol) and heat. Compounds that were not visible using $KMnO_4$ were dazzled using phosphomolybdic acid solution (20 wt. %) in ethanol (PMA).

Flash column chromatography was performed on silica gel 60 (Merck, 230-400 mesh) without previous deactivation, unless otherwise stated.

Light-promoted reactions: The LED used are Kessil PR 160 370 nm (43 W) Gen 1 and Gen 2 (44 W) and 390 nm (52 W). The reaction vessel is an 8 mL vial of borosilicate glass.

Reactions performed from 2 to 8 bar were carried out in a tinyclave steel reactor from Büchiglasuster company equipped with steel screw cap with 2 openings 1/8" NPT for: Swagelok® fittings with bursting disc, manometer valve. Reaction vessel volume was 10 mL with protective mesh.

Reactions performed above 10 bar were carried out in a high-pressure photoreactor assembled from a standard pressure reactor (Parr Serie 4760, non-stirred), composed of a base of 6.3 cm total diameter and a head (height 6.5 cm, internal diameter 3.0 cm). The head contains a centered sapphire window (diameter 2.54 cm), two inlet/outlet valve for charging/discharging gases, and a safety release valve (safety pressure 10 MPa at 200 ºC). Reaction vessel was a 16 mL glass vial.

GC-MS analyses were performed in an Agilent instrument GC-8890 equipped with Chemical Ionization (CI) MS-5977B detector.

High Resolution Mass spectrometry was carried out on a Bruker microTOF spectrometer using APCI-FIA or APCI-FIA direct Sonda measurement.

^{1}H-,^{13}C- and ^{19}F-NMR experiments were carried out using a Bruker AVIII-500 MHz or a Varian Mercury 300 MHz or Agilent VNMRS-300 MHz NMR spectrometers. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: δ 7.26 for ^{1}H, δ 77.2 for ^{13}C). Coupling constants (*J*) are given in Hertz (Hz). Multiplicities are reported as follows: *bs* = broad singlet, *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *p* = pentet, *h* = sextet, *m* = multiplet or as a combination of them.

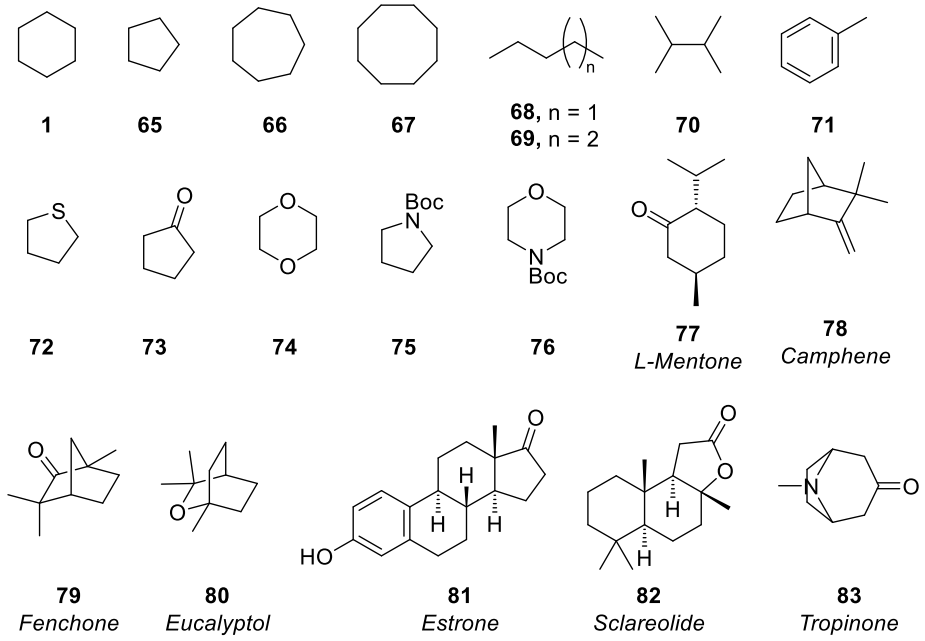
Tetrabutylammonium decatungstate (TBADT) was Synthesised according to a literature procedure[1].

[1] I. B. Perry, T. F. Brewer, P. J. Sarver, D. M. Schultz, D. A. DiRocco, D. W. C. MacMillan, *Nature*, **2018**, *560*, 70-75.

2. List of Starting Materials

2.1 Alkanes

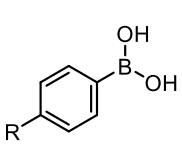
Alkanes **1**, **68**, **69** and **73** and **74** were purchased from Aldrich Chemical Co. Ltd., alkane **65** was purchased in Apollo Chemicals Ltd. Alkanes **66** and **67** were purchased in Alfa-Aesar, alkanes **70**, **75**, **78** to **80** were purchased in TCI Europe N. V. **71** was obtained from MBraun SPS 800 system. **76** was synthesized according to reported literature.[2] **77** was purchased from Thermo Scientific Chemicals. Alkane **72** was purchased from Fluorochem Ltd., alkanes **81 - 82** was purchased in Acros Organics B.V.B.A. Molecule **83** was purchased from BLD Pharmatech GmbH. Methane (99.5 % purity), ethane (99.5% purity) and propane (99.5% purity) were purchased from Nippon Gases company.



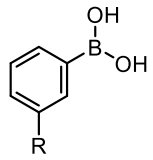
[2] Y. Basel and A. Hassner, *J. Org. Chem.*, **2000**, *65*, 20, 6368-6380.

2.2 Boronic acids

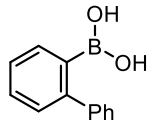
Boronic acids **84- 100** were purchased from BLD Pharmatech Ltd.



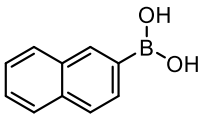
84, R = H
85, R = TMS
86, R = Cl
87, R = OMe
88, R = CN
89, R = CO_2Me
90, R = SMe



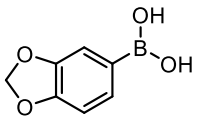
91, R = NO_2
92, R = F



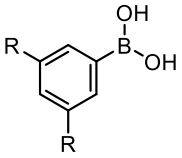
93



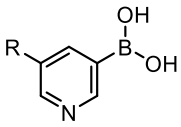
94



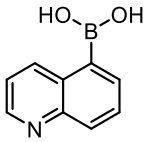
95



96, R = F
97, R = CF_3



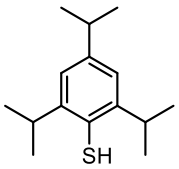
98, R = Cl
99, R = CN



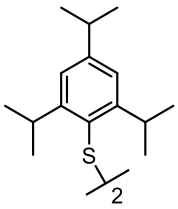
100

2.3 HAT co-catalysts (Thiols and disulfides)

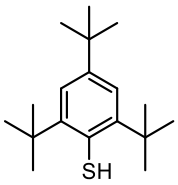
HAT co-catalysts **53,**[3] **101**[4] and (**102-103**)[5] were obtained as described in the reported literature. Molecule **54** was purchased from BLD Pharmatech Ltd. Co-catalysts **104** to **108** were bought in Aldrich Chemical Co. Ltd.



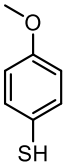
53



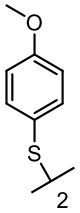
101



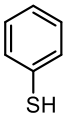
102



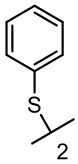
54



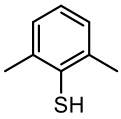
103



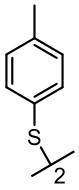
104



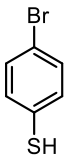
105



106



107

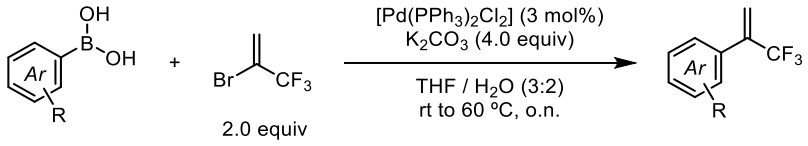


108

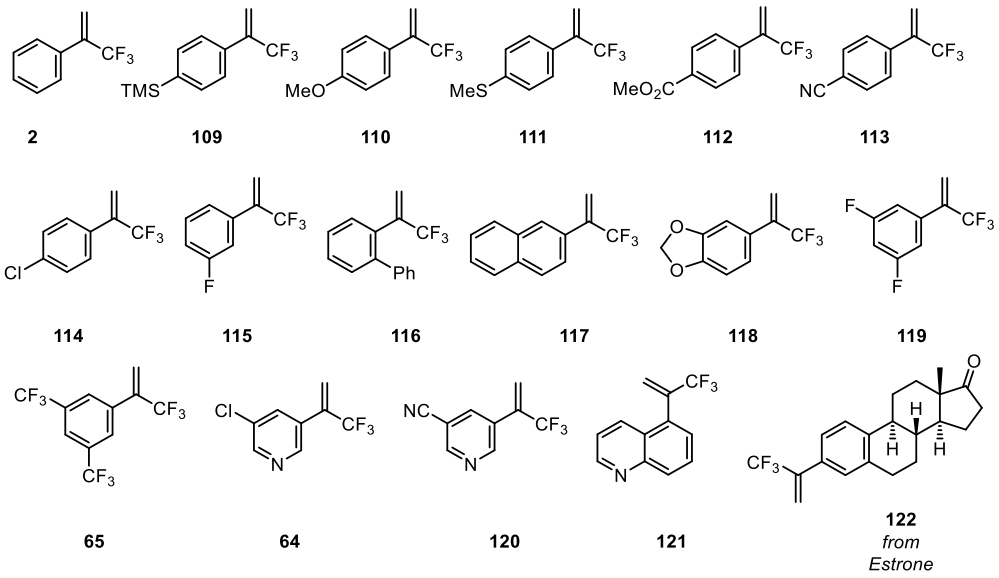
[3] A. J. Musacchio, B. R. Lainhart, X. Zhang, S. G. Naguib, T. C. Sherwood, and R. R. Knowles, *Science*, **2017**, *355*, 727–730.
[4] G. Occhialini, V. Palani, and A. E. Wendlandt, *J. Am. Chem. Soc*., **2022**, *144*, 1, 145–152
[5] M. Roger, N. Barros, T. Arliguie, P. Thuéry, L. Maron, M. Ephritikhine, *J. Am. Chem. Soc*., **2006**, *128* , 27, 8790–8802.

3. Synthesis of trifluoromethyl alkenes

α-Trifluoromethyl alkenes **2** and **103** to **116** were prepared following the next procedure described by R. Martin and coworkers.[6]



To a Schlenk tube equipped with a magnetic stirring bar, boronic acid (1.0 equiv), and $Pd(PPh_3)_2Cl_2$ (3 mol%) were added sequentially. The vessel was evacuated and filled with argon (three times), and then THF (15 mL, degassed) and aqueous K_2CO_3 (2.0 M, degassed) were added. After the addition of 2-bromo-3,3,3-trifluoropropene (2.0 equiv), the reaction mixture was stirred at 60 °C overnight under argon atmospheres. The resulting mixture was cooled to room temperature, quenched with saturated aqueous NH_4Cl, and extracted with Et_2O (three times). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (pentane or hexane/ethyl acetate) to give the desired trifluoromethylated alkene.

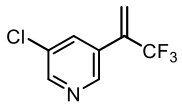


The spectral data of compounds **109-113**, [7] and **118**[7], **114**[8] and **117**[8], **115**,[9] **116**,[10] **119**,[11] **65**,[12,] **120**[13] and **122**[14] corresponded with the reported in the literature. Characterization of new substrates **64** and **121** is shown below.

---

[6] W.-J. Yue, C. S. Day, R. Martin, *J. Am. Chem. Soc*., **2021**, *143*, 6395−6400.
[7] Q.-P. Hu, J. Cheng, Y. Wang, J. Shi, B.-Q. Wang, P. Hu, K.-Q. Zhao, and F. Pan, *Org. Lett.*, **2021**, *11*, 23, 4457−4462.
[8] J. He, Z. Sun, Y. Deng, Y. Liu, P. Zheng, S. Cao, *Molecules*, **2023**, *28*, 3530.
[9] C. Yao, S. Wang, J. Norton, and M. Hammond, *J. Am. Chem. Soc*., **2020**, *142*, *10*, 4793-4799.
[10] C. Zhang, Z. Lin, Y. Zhu, and C. Wang, *J. Am. Chem. Soc*., **2021**, 143, 30, 11602-11610.
[11] M. Mishima, H. Inoue, S. Itai, M. Fujio, Y. Tsuno, *Bull. Chem. Soc. Jpn*, **1996**, *69*, 3273–3280.
[12] G. P. Lahm, D. Cordova, J. D. Barry, T. F. Pahutski, B. K. Smith, J. K. Long, E. A. Benner, C. W. Holyoke, K. Joraski, M. Xu, M. E. Schroeder, T. Wagerle, M. J. Mahaffey, R. M. Smith, M.-H. Tonget, *Bioorg. Med. Chem. Lett*, **2013**, *23*, 3001–3006
[13] B. M. Trost, L. Debien, *J. Am. Chem. Soc*., **2015**, *137*, 36, 11606–11609.
[14] Y. He, D. Anand, Z. Sun, and L. Zhou, *Org. Lett*., **2019**, *21*, 10, 3769-3773.

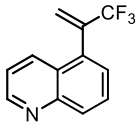
3-Chloro-5-(3,3,3-trifluoroprop-1-en-2-yl)pyridine (64)



Synthesised from the corresponding boronic acid **98** and following the above-mentioned general procedure.[5] Obtained as a colourless oil in 75% yield (780.0 mg) after flash column chromatography (Hexane/AcOEt 80:20).

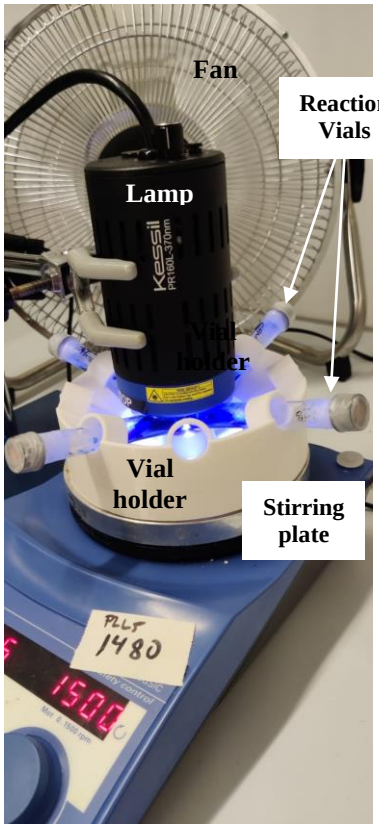
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, *J* = 9.8 Hz, 2H), 7.76 (s, 1 H), 6.12 (s, 1H), 5.89 (s, 1H). **^{13}C NMR (126 MHz,$CDCl_3$)** δ 148.1, 145.1, 134.0 (q, *J* = 31.7 Hz), 133.4, 130.9, 129.5, 122.1 (q, *J* = 5.6 Hz), 121.6 (q, *J* = 273.8 Hz). **^{19}F NMR (282 MHz, $CDCl_3$)** δ -65.2. **HRMS** (APCI, m/z): calculated for $C_8H_6ClF_3N$ [M+H$^+$]: 208.0135; found: 208.0131.

5-(3,3,3-Trifluoroprop-1-en-2-yl)quinoline (121)



Synthesised from the corresponding boronic acid **100** and following the above-mentioned general procedure.[5] Obtained as a yellow oil in 62% yield (694.0 mg) after flash column chromatography (Hexane/AcOEt 70:30). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 9.29 (s, 1H), 8.57 (d, *J* = 6.0 Hz, 2H), 8.12 – 7.95 (d, *J* = 7.9 Hz, 1H), 7.78 – 7.54 (m, 3H), 6.38 (s, 1H), 5.69 (s, 1H).**^{13}C NMR (126 MHz,$CDCl_3$)** δ 152.9, 144.0, 136.1 (q, *J* = 34.3 Hz), 134.9, 131.6, 130.7 (q, *J* = 135.7 Hz), 129.0, 126.5, 125.0 (q, *J* = 5.1 Hz), 124.8 (q, *J* = 274.7 Hz), 117.9. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -66.8 **HRMS** (APCI, m/z): calculated for $C_{12}H_9F_3N$ [M+H$^+$]: 224.0682; found: 224.0685.

4. Reaction Setup



Set-up for reactions at atmospheric pressure

A single LED lamp (Kessil PR 160 L 370 nm Gen 1) emitting light could illuminate four reaction vials positioned at a distance of 1 cm. The vial holder was fabricated using a 3D printer. A fan was utilized to keep the temperature constant (25 ºC). The stirring plate was set at 1500 rpm.

Set-up for reactions between 2 – 8 bar

A single LED lamp (Kessil PR 160 L 370 – Gen 2 or 390 nm) emitting light could illuminate one reaction positioned at a distance of 1 cm. A fan was utilized to keep the temperature constant (25 ºC). The stirring plate was set at 1500 rpm.

Set-up for reactions above 10 bar

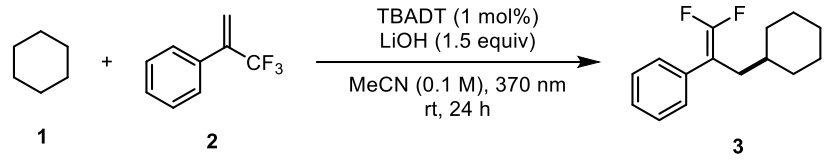
A single LED lamp (Kessil PR 160 L 390 nm*)* emitting light could illuminate one reaction positioned at 0.5 cm from the sapphire window. A plastic 3D printed piece was used to ensure the light distance constant and a fresh airflow to keep well-ventilated the head of the reactor. A fan was utilized to maintain the temperature constant (25 ºC). The stirring plate was set at 1500 rpm

Figure S1. Reaction Set-ups for different conditions

5. Optimization Studies

5.1. Optimization of *Method 1*

5.1.1. Optimization of reaction conditions (*Method 1)*

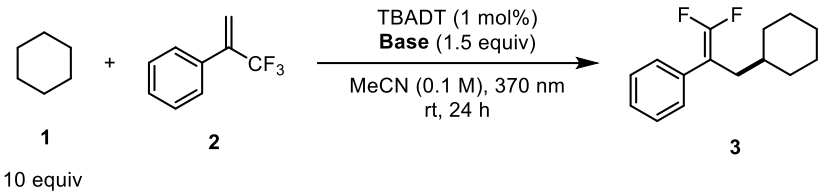


1 (10 equiv) + **2** → **3**

Entry[a]	Variation from standard conditions	3[b] (%)
1	none	32
2*	**3 mol% of TBADT**	**81 (81)[c]**
3	10 mol% $FeCl_3 \cdot 6H_2O$ instead of TBADT, no base	-
4[d]	5 mol% [Cu] as co-catalyst	11
5	K_3PO_4 instead of LiOH	17
6	$KHCO_3$ instead of LiOH	23
7	$KHCO_3$ instead of LiOH and 1.0 equiv of LiCl as additive	-
8	K_2CO_3 instead of LiOH	-
9	Li_2CO_3 instead of LiOH	20-75[e] **
10	collidine instead of LiOH	11
11	lutidine instead of LiOH	10
12	DMAP instead of LiOH	-
13	no base	-
14[e]	390 nm instead of 370 nm	63
15[e]	5 equiv of **1**	65
16	Absence of TBADT or light	-

Table S1. *a)* Reactions run on a 0.2 mmol scale. *b)* Yields were determined by ^{19}F-NMR analysis using α,α,α-trifluorotoluene as internal standard. *c*) Yield of isolated product. *d)* CuCl, 6 mol% of L = PPh_3 with collidine (1.1 equiv) instead of LiOH. *e)* 3 mol% TBADT. *These conditions correspond to *Method 1*. **Reproducibility issues due to stirring problems because of the amount of solid.

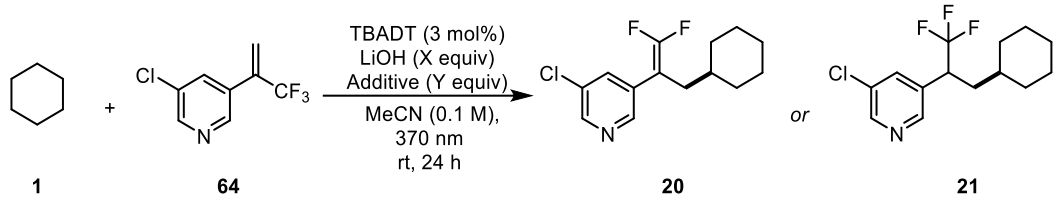
5.1.2. Optimization of Bases (*Method 1*)



Entry[a]	Base	3 (%)[b]
1	K_3PO_4	17
2	KOAc	<5
3	$KHCO_3$	23
4	KOMe	0
5	KO^{t}Bu	0
6	Pyridine	<5
7	DMAP	0
8	Lutidine	10
9	4-MePyr	6
10	Collidine	11
11	Li_2CO_3	38
12	LiOH	32

Table S2. *a)* Reactions run on a 0.2 mmol scale. *b*) Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. DMAP = 4-(Dimethylamino)pyridine. Lutidine = 2,6-Dimethylpyridine. 4-MePyr = 4-methylpyridine. Collidine = 2,4,6-Trimethylpyridine.

5.2. Optimization of *Method 2*



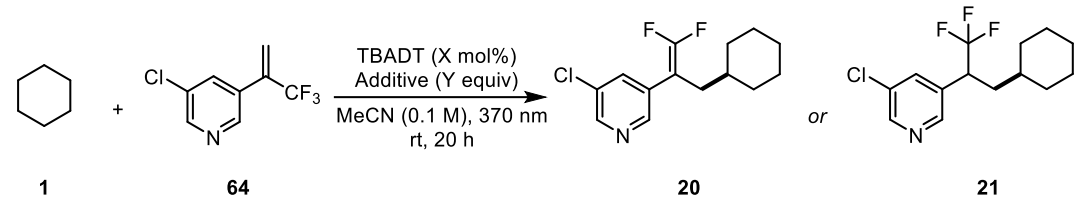
1 (10 equiv) + **64** → **20** or **21**

Entry[a]	LiOH X equiv	Additive Y equiv	20[b] (%)	21[b] (%)
1	1.5	-	10	70
2	3	-	24	36
3	6	-	21	41
4	1.5	1.5 collidine	24	24
5	1.5	3 collidine	36	11
6	3	1.5 collidine	40	12
7	3	1.5 lutidine	8	28
8	3	1.5 4-methylpyridine	11	10
9*	**3**	**1.5 K_3PO_4**	**50 (50)[c,d]**	**<5**
10	1.5	0.5 K_3PO_4	18	<5
11	-	1.5 K_3PO_4	11	<5
12	-	3 K_3PO_4	42	<5
13[d]	-	3 K_3PO_4	39	<5
14[e]	-	3 K_3PO_4	21	<5

Table S3. *a*) Reactions run on a 0.2 mmol scale. *b)* Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. *c)* Isolated yield in brackets. *d)* 5 mol% TBADT. *e)* 1 mol% TBADT. *These conditions correspond to *Method 2*.

5.3. Optimization of *Method 3*

5.3.1. Optimization of reaction conditions (*Method 3*)

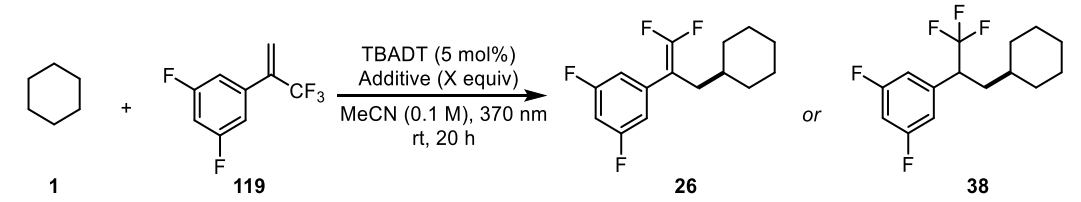


1 10 equiv + **64** → **20** or **21**

Entry[a]	Amount of TBADT (mol %)	Additive Y equiv	20[b] (%)	21[b] (%)
1	3	1.5 LiOH	10	70
2	1	-	-	30
3	3	-	-	40
4*	**5**	**-**	**-**	**75 (73)[c]**

Table S4. *a)* Reactions run on a 0.2 mmol scale. *b)* Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. *c)* Yield of isolated product.*These conditions correspond to *Method 3*.

5.3.2. Optimization of HFIP as additive

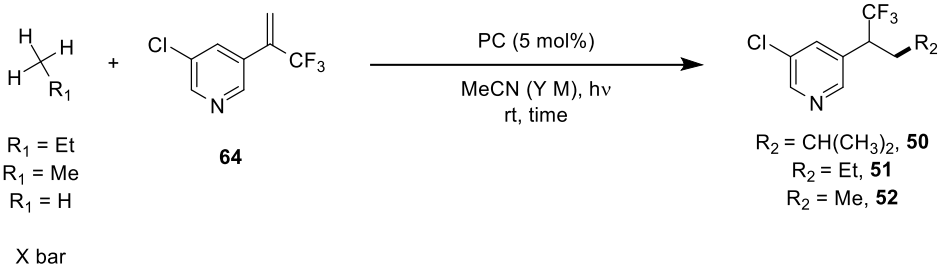


1 10 equiv + **119** → **26** or **38**

Entry[a]	Additive X equiv	26[b] (%)	38[b] (%)
1	-	9	47
2	MeCN:H_2O (20:1)	9	27
3	0.5 HFIP	-	30
4	**1.0 HFIP**	**-**	**51**
5	2.0 HFIP	-	53

Table S5. *a*) Reactions run on a 0.2 mmol scale. *b*) Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. HFIP = 1,1,1,3,3,3-hexafluoropropan-2-ol.

5.3.3. Optimization of the photocatalytic hydroalkylation of trifluoromethyl alkenes with gaseous alkanes

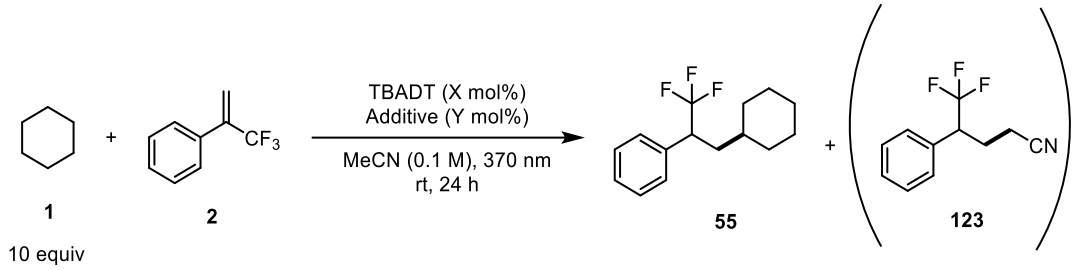


Entry[a]	R_1	PC	P (bar)	hν (nm)	[C] (M)	time (h)	Conv. (%)[b]	50-52 (%)[c]
1	Et	TBADT	1	370	0.05	14	95	22 (2:1)[d]
2*	**Et**	**TBADT**	**5**	**370**	**0.05**	**14**	**full**	**54 (5:1)[d]**
3[e]	Et	TBADT	5	370	0.05	14	full	52 (5:1)[d,e]
4	Me	TBADT	8	370	0.05	14	86	11[b]
5	Me	TBADT	30	370	0.0125	14	full	35
6*	**Me**	**$FeCl_3·6H_2O$**	**30**	**390**	**0.0125**	**14**	**full**	**83**
7	H	TBADT	50	370	0.0125[f]	24	50	0
8	H	$FeCl_3·6H_2O$	50	390	0.0125[f]	24	70	46[g]
9	H	$FeCl_3·6H_2O$	50	390	0.0125	24	85	41[b,h]
10*	**H**	**$FeCl_3·6H_2O$**	**50**	**390**	**0.0125[f]**	**48**	**full**	**74[i]**

Table S6. *a)* Reactions run on a 0.2 mmol scale. *b)* determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. *c)* Yield of Isolated Product. *d*) regioisomeric ratio (branched : linear). *e*) With 1.0 equiv of HFIP as an additive. *f*) Deuterated acetonitrile (MeCN-$_{d3}$). *g*) Isolated as inseparable mixture with starting material (**64**). *h*) 20% of side-product of activation of acetonitrile. *i)* Isolated with 10% of side-product of activation of non-deuterated acetonitrile. HFIP = 1,1,1,3,3,3-hexafluoropropan-2-ol. PC = photocatalyst. *Entries (2, 6 and 10) correspond to *General Procedures 1, 2, 3 (respectively).*

5.4 Optimization of *Method 4*

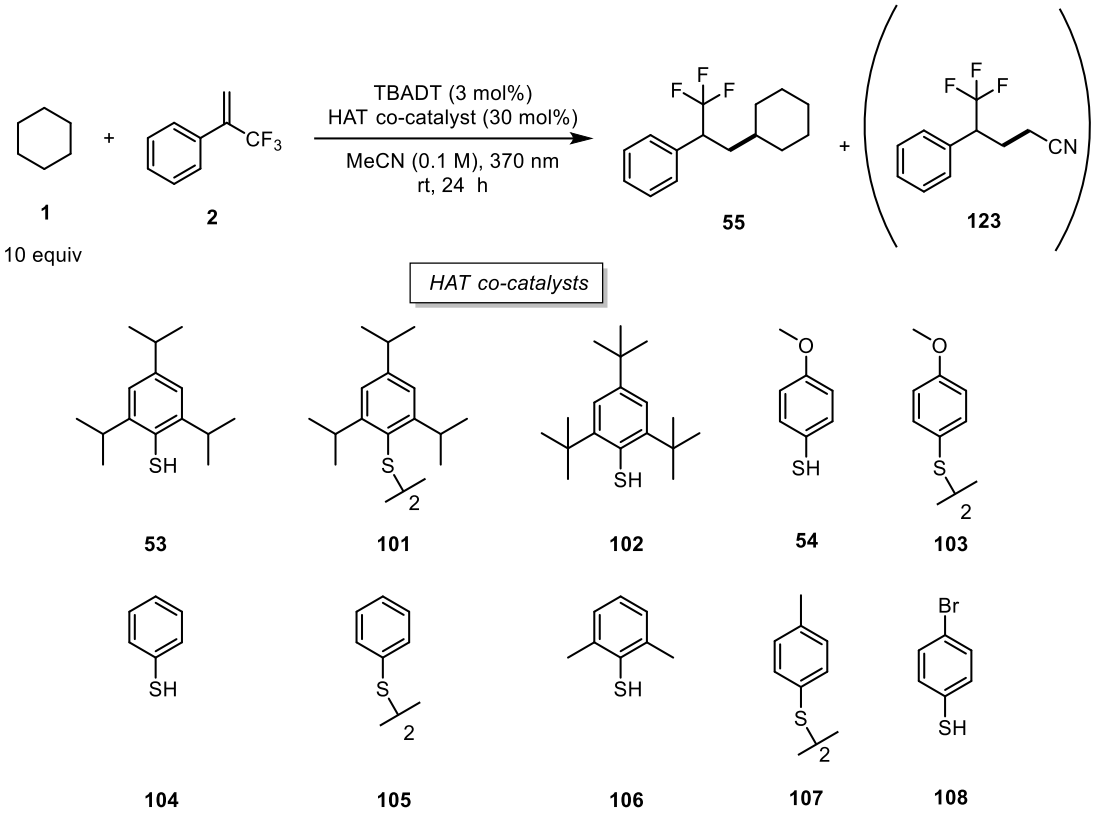
5.4.1. Screening of different additives for the TBADT-catalyzed hydroalkylation of 2



Entry[a]	TBADT (X mol%)	Additives (Y mol%)	55[b] (%)	123[b] (%)
1	5	-	-	-
2	5	1.0 equiv HFIP	11	-
3	3	1.5 equiv LiCl or Li(OTf) or LiBr	<5	-

Table S7. *a)* Reactions run on a 0.2 mmol scale. *b*) Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. HFIP = 1,1,1,3,3,3-hexafluoropropan-2-ol. LiOTf = lithium triflate.

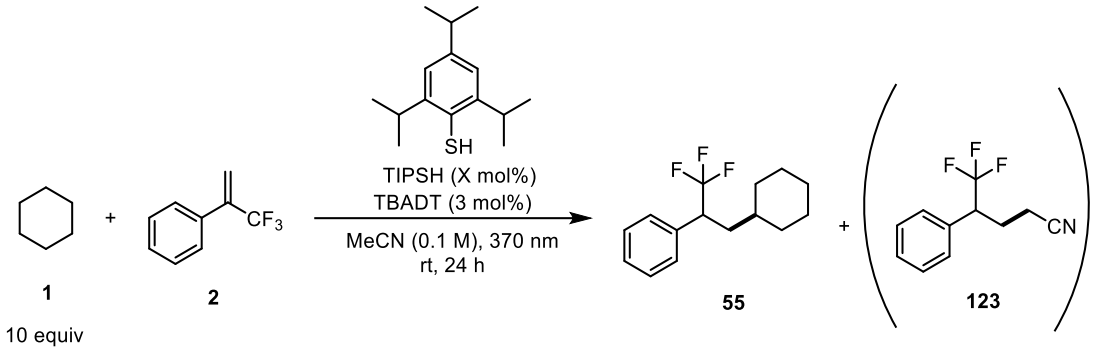
5.4.2. Optimization of the HAT co-catalyst for the dual TBADT/thiol catalysis (*Method 4*)



Entry[a]	HAT co-catalyst	55[b] (%)	123[b] (%)
1	**53**	19	<5
2	**101**	9	7
3	**102**	17	8
4	**54**	20	13
5	**103**	15	8
6	**104**	4	-
7	**105**	10	5
8	**106**	6	-
9	**107**	16	7
10	**108**	7	5

Table S8. *a*) Reactions run on a 0.2 mmol scale. *b*) Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard.

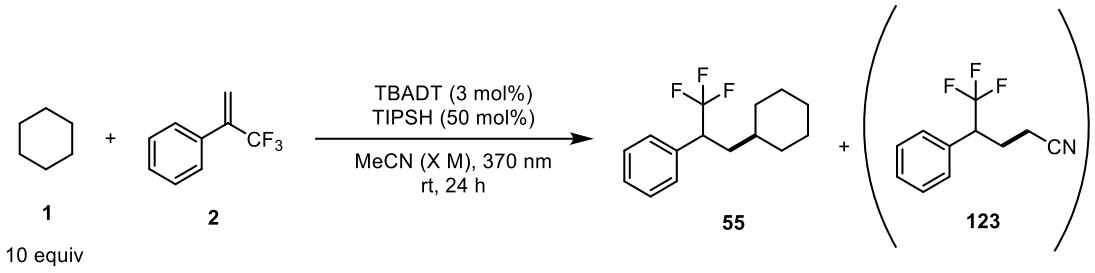
5.4.3. Optimization of the HAT co-catalyst stoichiometry (*Method 4*)



Entry[a]	TIPSH (mol%)	55[b] (%)	123[b] (%)
1	10	10	-
2	20	13	<5
3	30	19	<5
4	50	20	12
5	70	14	9
6	110	traces	traces
7	Absence of light or TBADT	-	-

Table S9. *a*) Reactions run on a 0.2 mmol scale. *b*) Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. TIPSH = 2,4,6-triisopropylbenzenethiol (**53**).

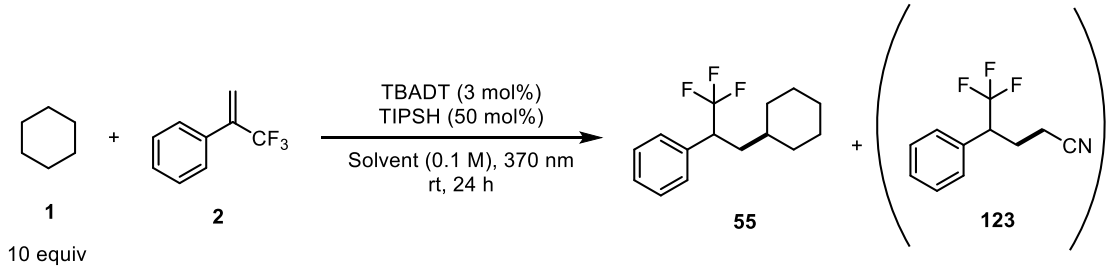
5.4.4. Optimization of the Concentration (*Method 4*)



Entry[a]	Concentration (M)	55[b] (%)	123[b] (%)
1	0.1	20	12
2	0.2	16	7
3	0.5	15	traces
4	0.05	9	traces

Table S10. *a*) Reactions run on a 0.2 mmol scale. *b*) Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. TIPSH = 2,4,6-triisopropylbenzenethiol (**53**).

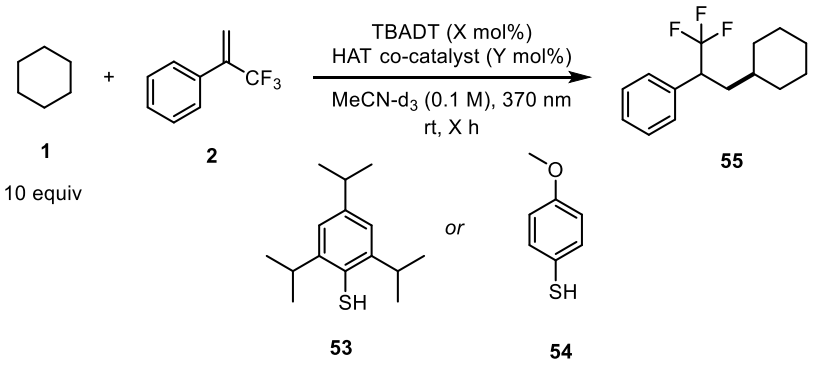
5.4.5. Optimization of Solvent (*Method 4*)



Entry[a]	Solvent	55[b] (%)	123[b] (%)
1	MeCN	20	12
2	benzonitrile	19	-
3	pivalonitrile	13	-
4*	*o*-tolunitrile	42	-
5	MeCN-d_3	36	-

Table S11. *a*) Reactions run on a 0.2 mmol scale. *b*) Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. TIPSH = 2,4,6-triisopropylbenzenethiol (**53**). *Solvent discarded due to problems in the purification.

5.4.6. Optimization in deuterated acetonitrile (*Method 4*)



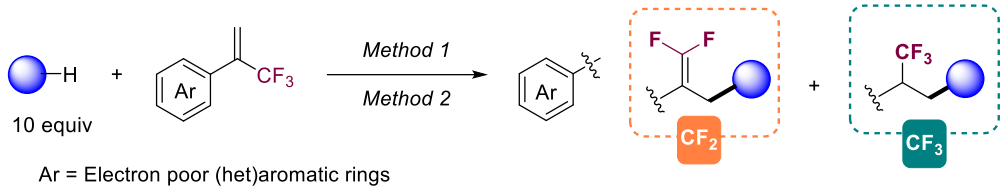
Entry[a]	Amount of TBADT (mol %)	HAT co-catalyst	Amount of co-catalyst (mol%)	time (h)	55[b] (%)
1	3	**53**	30	24	36
2	3	**53**	30	48	37
3	3	**53**	50	24	36
***4**	**3**	**53**	**50**	**48**	**50**
5	3	**53**	50	72	48
6	5	**53**	30	24	37
7	5	**53**	30	48	40
8	5	**53**	50	24	33
9	5	**53**	50	48	35
10	5	**53**	50	72	45
11	3	**54**	30	24	24
12	3	**54**	30	48	27
13	3	**54**	50	24	28
14	3	**54**	50	48	36 (30)[c]
15	3	**54**	50	72	37 (28)[c]
***16**	**5**	**54**	**30**	**24**	**51 (45)[c]**
17	5	**54**	30	48	45 (36)[c]
18	5	**54**	50	24	22
19	5	**54**	50	48	35
20	5	**54**	50	72	40 (32)[c]

Table S12. *a)* Reactions run on a 0.2 mmol scale. *b*) Yields were determined by ^{19}F-NMR analysis using α,α,α–trifluorotoluene as internal standard. 2,4,6-triisopropylbenzenethiol (**53**). 4-methoxybenzenethiol (**54**). c) yield of isolated product .*These conditions correspond to *Method 4*.

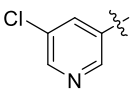
Observation: Thiol **53** was used in cases with polar C-H donors due to facilitate the separation of the desired products by column chromatography (same R_f with non-polar C-H donors). For nonpolar C-H donors thiol **54** was employed for the same reason.

6. Method Comparison Studies

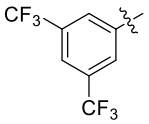
6.1 Comparison between *Method 1 vs Method 2* in the defluorinative alkylation of trifluoromethyl alkenes bearing electron-poor aryl rings



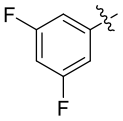
Ar = Electron poor (het)aromatic rings



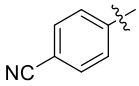
	CF_2 : CF_3
Method 1:	10 : 70
Method 2:	50 : 0



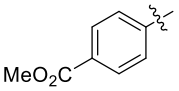
	CF_2 : CF_3
Method 1:	25 : 25
Method 2:	50 : 0



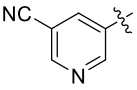
	CF_2 : CF_3
Method 1:	50 : 13
Method 2:	42 : 0



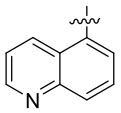
	CF_2 : CF_3
Method 1:	21 : 27
Method 2:	48 : <5



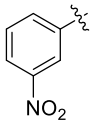
	CF_2 : CF_3
Method 1:	40 : 15
Method 2:	30 : 0



	CF_2 : CF_3
Method 1:	44 : 18
Method 2:	58 : <5



	CF_2 : CF_3
Method 1:	12 : <5
Method 2:	46 : 5

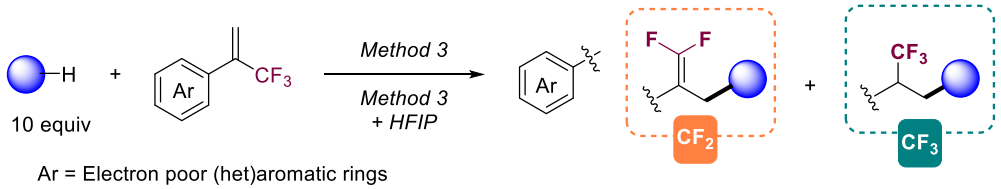


	CF_2 : CF_3
Method 1:	nd
Method 2:	6 : 0

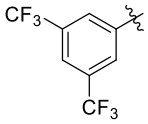
Method 1: (3 mol%) TBADT, (1.5 equiv) LiOH, MeCN (0.1 M), kessil LED 370 nm, RT, 24 h. VS
Method 2: (5 mol%) TBADT, (3.0 equiv) LiOH, (1.5 equiv) K_3PO_4, dry MeCN (0.1 M), kessil LED 370 nm, RT, 24 h.

The alkane employed for all the examples was cyclohexane. Yields determined by ^{19}F-NMR analysis with α,α,α–trifluorotoluene as internal standard in all the molecules.

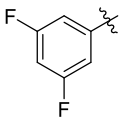
6.2 Comparison of Method 3 with and without HFIP



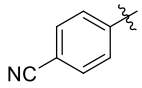
Ar = Electron poor (het)aromatic rings



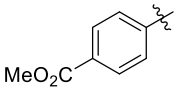
CF_2 : CF_3
Method 3: 9 : 63
Method 3 + HFIP: 0 : 62



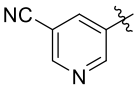
CF_2 : CF_3
Method 3: 9 : 47
Method 3 + HFIP: 0 : 43



CF_2 : CF_3
Method 3: 6 : 25
Method 3 + HFIP: 0 : 47



CF_2 : CF_3
Method 3: 27 : 58
Method 3 + HFIP: 0 : 58



CF_2 : CF_3
Method 3: 16 : 14
Method 3 + HFIP: 0 : 44
H = CyH

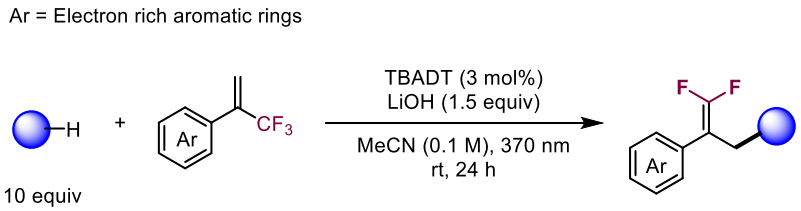
Method 3: 0 : 56
Method 3 + HFIP: 5 : 36
H = nHex

Method 3: (5 mol%) TBADT, MeCN (0.1 M), Kessil LED 370 nm, RT, 20 h. VS
Method 3 with 1.0 equiv of HFIP.

Yield determined by ^{19}F-NMR analysis with α,α,α–trifluorotoluene as internal standard in all the molecules.
HFIP = 1,1,1,3,3,3-hexafluoropropan-2-ol. CyH = cyclohexane. nHex = *n*-hexane.

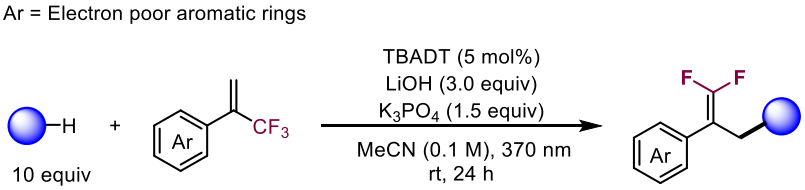
7. General Procedures for the Chemodivergent Alkylation of Trifluoromethyl Alkenes via Photocatalytic Coupling with Alkanes

7.1 General Procedure for the Defluorinative Alkylation of Trifluoromethyl Alkenes bearing Electron-Rich Aromatic Rings *(Method 1)*



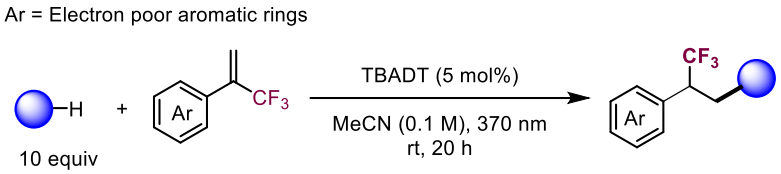
An oven-dried 8 mL vial equipped with stirring magnetic bar was charged with TBADT (0.03 equiv, 0.006 mmol), LiOH (1.5 equiv, 0.3 mmol), trifluoromethyl alkene (1 equiv, 0.2 mmol), alkane (10 equiv, 2 mmol) and 2 mL of dry MeCN. Then, the vial was capped.
The suspension of the vial was cooled-down at 0 ºC (ice-water bath) and bubbled with Ar for 10 min. Then the cap of the vial was sealed with parafilm, and the vial was placed to the direct flux of LED on the vial holder at 1 cm from the light source. In order to keep the temperature constant, a fan was placed in front of the vials (See Figure S1 Left). After 24 h, the solution was filtered through a silica plug and the residue was washed with Et_2O (20 mL). Then the crude was purified by flash column chromatography on silica gel.

7.2 General Procedure for the Defluorinative Alkylation of Trifluoromethyl Alkenes bearing Electron-Poor Aromatic Rings *(Method 2)*



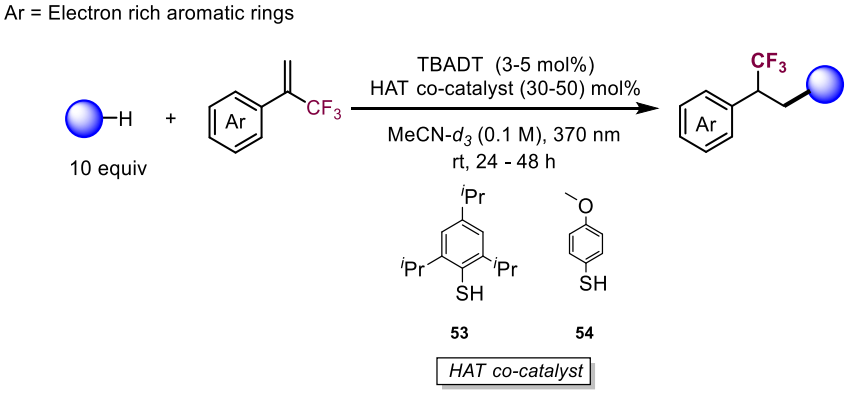
An oven-dried 8 mL vial equipped with stirring magnetic bar was charged with TBADT (0.05 equiv, 0.01 mmol), LiOH (3.0 equiv, 0.6 mmol), K_3PO_4 (1.5 equiv, 0.3 mmol), trifluoromethyl alkene (1 equiv, 0.2 mmol), alkane (10 equiv, 2 mmol) and 2 mL of dry MeCN. Then, the vial was capped. The suspension of the vial was cooled-down at 0 ºC (ice-water bath) and bubbled with Ar for 10 min. Then the cap of the vial was sealed with parafilm, and the vial was placed to the direct flux of LED on the vial holder at 1 cm from the light source. In order to keep the temperature constant, a fan was placed in front of the vials (See Figure S1 Left). After 24 h, the solution was filtered through a silica plug and the residue was washed with Et_2O (20 mL). Then the crude was purified by flash column chromatography on silica gel.

7.3 General Procedure for the Hydroalkylation of Trifluoromethyl Alkenes bearing Electron-Poor Aromatic Rings *(Method 3)*



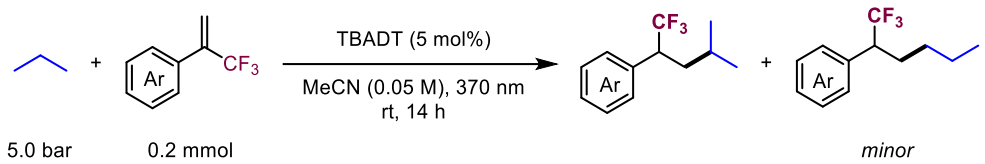
An oven-dried 8 mL vial equipped with stirring magnetic bar was charged with TBADT (0.05 equiv, 0.01 mmol), trifluoromethyl alkene (1 equiv, 0.2 mmol), alkane (10 equiv, 2 mmol) and 2 mL of dry MeCN. Then, the vial was capped. The solution of the vial was cooled-down at 0 ºC (ice-water bath) and bubbled with Ar for 10 min. Then the cap of the vial was sealed with parafilm, and the vial was placed to the direct flux of LED on the vial holder at 1 cm from the light source. In order to keep the temperature constant, a fan was placed in front of the vials (See Figure S1 Left). After 20 h, the solution was filtered through a silica plug and the residue was washed with Et_2O (20 mL). Then the crude was purified by flash column chromatography on silica gel.

7.4 General Procedure for the Hydroalkylation of Trifluoromethyl Alkenes bearing Electron-Rich Aromatic Rings *(Method 4)*



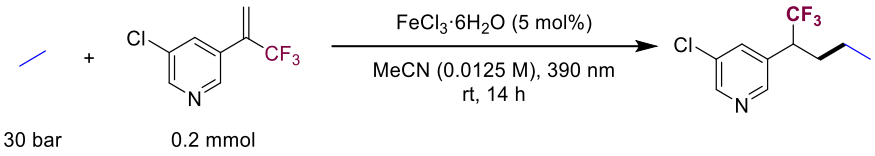
An oven-dried 8 mL vial equipped with stirring magnetic bar was charged with TBADT (0.03 - 0.05 equiv, 0.005 - 0.01 mmol), alkane (10 equiv, 2 mmol) and trifluoromethyl alkene (1.0 equiv, 0.2 mmol). In a second dry-oven 4 mL vial was charged with the HAT co-catalyst (0.3 – 0.5 equiv, 0.06 – 0.1 mmol). Then both vials were capped. MeCN-d_3 was added to the 4 mL vial x 4 times (0.5 mL each time) up to 2 mL. The solution of the vial was cooled-down at 0 ºC (ice-water bath) and bubbled with Ar for 10 min. Then the cap of the vial was sealed with parafilm, and the vial was placed to the direct flux of LED on the vial holder at 1 cm from the light source. In order to keep the temperature constant, a fan was placed in front of the vials (See Figure S1 Left). After 24 - 48 h, the solution was filtered through a silica plug and the residue was washed with Et_2O (20 mL). Then the crude was purified by flash column chromatography on silica gel.

7.5 General Procedure for the Hydroalkylation of Trifluoromethyl Alkenes with Propane (*GP1*)



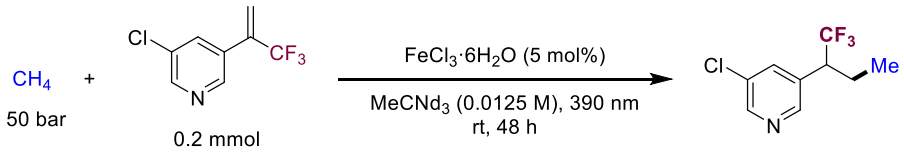
The glass vessel of the reactor was charged with TBADT (33 mg, 0.01 mmol, 0.05 equiv) trifluoromethyl alkene (0.2 mmol, 1.0 equiv), a magnetic stirring bar and dry MeCN (4 mL). The head was installed, and the headspace of the reactor was flushed 5 times with propane (5.0 bar). The reactor was then pressurized to 5.0 bar of propane and irradiated with a 370 nm kessil lamp. In order to keep the temperature constant, a fan was placed in front of the reactor (See Figure S1 Middle). The reaction was stirred for 14 h. After, the solution was filtered through a silica plug and the residue was washed with Et_2O (20 mL). Then the crude was purified by flash column chromatography on silica gel.

7.6 General Procedure for the Hydroalkylation of Trifluoromethyl Alkenes with Ethane (*GP2*)



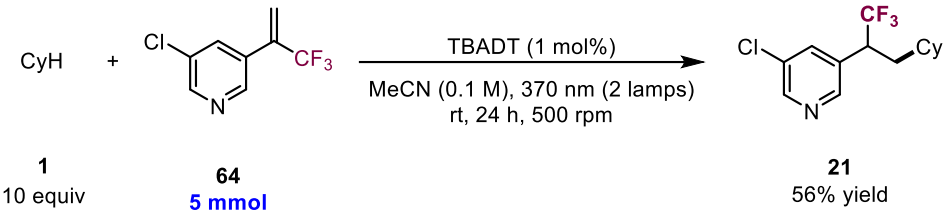
A glass vial was charged with $FeCl_3 \cdot 6H_2O$ (2.7 mg, 0.01 mmol, 0.05 equiv), trifluoromethyl alkene (0.2 mmol, 1.0 equiv), a magnetic stirring bar and dry MeCN (16 mL). The head was installed, and the headspace of the reactor was flushed 5 times with ethane (30.0 bar). The reactor was then pressurized to 30.0 bar of ethane, irradiated with a 390 nm kessil lamp. The reaction was stirred under lamp irradiation at ambient temperature for 14 h. In order to keep the temperature constant, a fan was placed in front of the reactor (See Figure S1 Right). After, the solution was filtered through a silica plug and the residue was washed with Et_2O (20 mL). Then the crude was purified by flash column chromatography on silica gel.

7.7 General Procedure for the Hydroalkylation of Trifluoromethyl Alkenes with Methane (*GP3*)



A glass vial was charged with $FeCl_3 \cdot 6H_2O$ (2.7 mg, 0.01 mmol, 0.05 equiv), trifluoromethyl alkene (0.2 mmol, 1.0 equiv), a magnetic stirring bar and MeCN-d_3 (16 mL). The vial was placed on the metal base and the head of the reactor was installed. The headspace of the reactor was flushed 5 times with methane (50.0 bar). The reactor was then pressurized to 50.0 bar of methane, irradiated with a 390 nm kessil lamp. The reaction was stirred under lamp irradiation at ambient temperature for 48 h. In order to keep the temperature constant, a fan was placed in front of the reactor (See Figure S1 Right). After, the solution was filtered through a silica plug and the residue was washed with Et_2O (20 mL). Then the crude was purified by flash column chromatography on silica gel.

7.8. Procedure for the hydroalkylation of trifluoromethyl alkenes in gram-scale



An oven-dried 250 mL Schlenk tube equipped with stirring magnetic bar and silicon cap was charged with TBADT (0.01 equiv, 0.05 mmol, 166 mg), substrate **64** (1 equiv, 5 mmol, 1.04 g), cyclohexane **1** (10 equiv, 50 mmol, 5.2 mL) and 50 mL of dry MeCN. Three cycles of freezing-pump were conducted to ensure the inert atmosphere. After, the tube was enclosed with parafilm and placed to the direct flux of two kessil 370 nm LED lamps. In order to keep the temperature constant a fan was placed in front of the schlenk tube (see full set-up in **Figure S2**-left). After 24 h, the blue solution was introduced to 100 mL round bottom flask and charged with SiO_2 to prepare directly the dry loading. The crude was purified by flash column chromatography on silica gel using a mixture of pentane and diethyl ether (95:5) to afford product **21** as yellow oil (817 mg, 56% yield) (**Figure S2**-right).

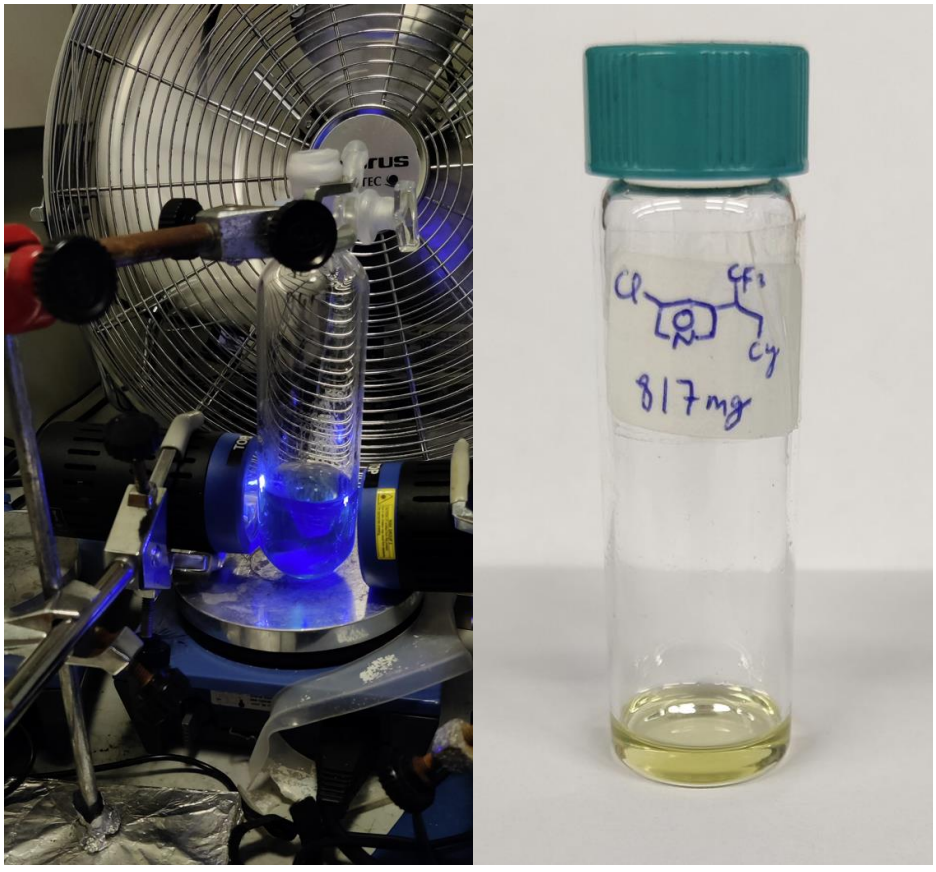
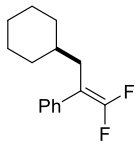


Figure S2. Left: Set-up for 5 mmol gram scale reaction. Right: Vial containing the product

8. Compound characterization

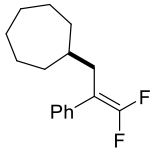
(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)benzene (3)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **2** following *Method 1*. Obtained as colourless oil in 81% yield (38.3 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 5H), 2.30 (t, *J* = 2.3, 1H), 2.28 (t, *J* = 2.3, 1H), 1.73 – 1.63 (m, 3H), 1.62-1.57 (m, 1H), 1.32 – 1.21 (m, 2H), 1.17 – 1.09 (m, 3H), 0.98-0.89 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.1 (dd, *J* = 290.0, 285.8 Hz), 134.3 (dd, *J* = 4.7, 3.0 Hz), 128.5, 128.4 (t, *J* = 3.2 Hz), 127.2, 91.2 (dd, *J* = 22.1, 12.6 Hz), 35.8 (t, *J* = 2.5 Hz), 35.4, 33.0, 26.6, 26.2. **^{19}F NMR (282 MHz, $CDCl_3$)** -91.5 (d, *J* = 44.3 Hz), -91.9 (d, *J* = 44.2 Hz). The spectroscopic data is in accordance with reported literature.[15]

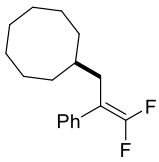
(3,3-Difluoro-2-phenylallyl)cycloheptane (4)



Synthesised from cycloheptane **66** and trifluoromethyl alkene **2** following *Method 1*. Obtained as colourless oil in 60% yield (30.4 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H), 7.31 – 7.25 (m, 2H), 2.31 (t, *J* = 2.8, 1H), 2.28 (t, *J* = 2.8, 1H),1.71 – 1.65 (m, 2H), 1.63 – 1.58 (m, 2H), 1.52 – 1.43 (m, 5H), 1.35 – 1.29 (m, 2H), 1.23 – 1.14 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.2 (dd, *J* = 289.7, 286.0 Hz), 134.2 (dd, *J* = 4.4, 2.7 Hz), 128.5 (t, *J* = 2.5 Hz), 127.3, 91.8 (dd, *J* = 21.5, 13.0 Hz), 37.2 (t, *J* = 2.3 Hz), 35.8, 34.2, 28.6, 26.2. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -91.8 (d, *J* = 44.6 Hz), -92.1 (d, *J* = 44.6 Hz). The spectroscopic data is in accordance with reported literature.[16]

(3,3-Difluoro-2-phenylallyl)cyclooctane (5)

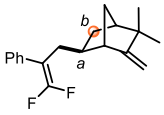


Synthesised from cyclooctane **67** and trifluoromethyl alkene **2** following *Method 1*. Colourless oil obtained 76% yield (40.3 mg) after flash column chromatography (Hexanes).

^{1}H NMR (**500 MHz, $CDCl_3$)** δ 7.37 – 7.32 (m, 2H), 7.31 – 7.24 (m, 3H), 2.22 (t, *J* = 2.4, 1H), 2.20 (t, *J* = 2.4, 1H), 1.62 – 1.57 (m, 3H), 1.53 – 1.43 (m, 6H), 1.39 – 1.24 (m, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.2 (dd, *J* = 289.5, 286.1 Hz), 134.2 (dd, *J* = 4.1, 2.3 Hz), 128.5 (t, *J* = 2.5 Hz), 127.3, 91.9 (dd, *J* = 20.9, 13.4 Hz), 35.7, 35.3 (t, *J* = 2.3 Hz), 31.6, 27.4, 26.2, 25.3. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -91.8 (d, *J* = 44.6 Hz), -92.0 (d, *J* = 44.5 Hz). The spectroscopic data is in accordance with reported literature.[17]

[15] H.-W. Du, Y. Chen, J. Sun, Q.-S. Gao, H. Wang, and M.-D. Zhou, *Org Lett.*, **2020**, *22*, 23, 9342-9345
[16] G.-D. Xia, Y.-Y. He, J. Zhang, Z.-K. Liu, Y. Gao, X.-Q. Hu, *Chem. Commun.*, **2022**,*58*, 6733-6736
[17] V. I. Supranovich, V. V. Levin, V. A. Kokorekin, A. D. Dilman, *Adv. Synth. Catal.*, **2021**, *363*, 2888-2892.

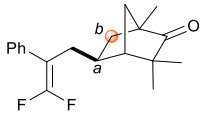
(1*R,4*R**,5*S**)-5-(3,3-Difluoro-2-phenylallyl)-2,2-dimethyl-3 methylenebicyclo[2.2.1]heptane (6)**



Synthesised from *Camphene* **78** and trifluoromethyl alkene **2** following *Method 1*. Colourless oil obtained 51% yield (29.5 mg) as a 2.85:1 mixture of regioisomers after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 2H **a** + 2H **b**), 7.31 – 7.25 (m, 3H **a** + 3H **b**), 4.70 (s, 1H **b**), 4.64 (s, 1H **a**), 4.47 (s, 1H **b**), 4.44 (s, 1H **a**), 2.68 – 2.63 (m, 1H **b**), 2.42 (d, *J* = 1.7 Hz, 1H **a**), 2.41 – 2.33 (m, 1H **a** + 1H **b**), 2.32 – 2.21 (m, 1H **a** + 1H **b**), 1.99 – 1.91 (m, 1H **a**), 1.88 (dd, *J* = 3.8, 1.8 Hz, 1H **b**), 1.81 (ddd, *J* = 12.8, 8.3, 2.8 Hz, 1H **a**), 1.66 – 1.60 (m, 2H **a** +1H **b**), 1.55 – 1.50 (m, 1H**a**), 1.44 – 1.44 - 1.34 (m, 2H **b**), 1.26 (s, 1H **b**), 1.21 (dt, *J* = 12.1, 4.4 Hz, 1H **b**), 1.01 (s, 3H **a** + 3H **b**), 0.99 – 0.95 (m, 1H **a**), 0.94 (s, 3H **a**), 0.82 (s, 3H **b**). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 165.5 165.4, 156.5 (dd, *J* = 289.5, 286.0 Hz), 154.2 (dd, *J* = 289.5, 286.0 Hz), 134.0 (dd, *J* = 4.2, 2.5 Hz), 133.9 (dd, *J* = 4.2, 2.5 Hz), 128.6 (t, *J* = 3.0 Hz), 128.5 (t, *J* = 3.0 Hz), 127.4, 99.9, 99.7, 92.0 (dd, *J* = 15.0, 7.1 Hz**)**, 91.8 (dd, *J* = 15.0, 7.1 Hz**)**, 52.2, 51.3, 48.7, 47.3, 42.3, 41.5, 39.2 (t, *J* = 2.5 Hz), 36.7, 34.4, 34.3, 34.2, 34.0, 33.1 (t, *J* = 2.6 Hz), 31.8, 29.8, 29.5, 25.7, 25.1. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -91.9 – -92.7 (m). **HRMS** (APCI, m/z): calculated for $C_{19}H_{23}F_2$ [M+H$^+$]: 289.1762; found: 288.1755.

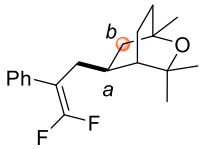
(1*R,4*R**,5*S**)-5-(3,3-Difluoro-2-phenylallyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-one (7)**



Synthesised from *Fenchone* **79** and trifluoromethyl alkene **2** following *Method 1*. Obtained as colourless oil in 61% yield (36.5 mg) as a 1.7:1 mixture of regioisomers after flash column chromatography (Hexane/AcOEt 97.5:2.5).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 2H **a** +2H **b**), 7.31 – 7.24 (m, 3H **a** + 3H **b**), 2.58 (ddq, *J* = 10.5, 5.6, 2.5 Hz, 1H **b**), 2.53 – 2.46 (m, 1H **a** + 1H **b**), 2.42 (ddt, *J* = 14.4, 6.9, 2.9 Hz, 1H **a**), 2.12 (dd, *J* = 4.2, 2.0 Hz, 1H **b**), 2.10 – 2.08 (m, 1H **a**), 2.04 (m, 1H **a**), 1.90 (s, 1H **b**), 1.89 – 1.78 (m, 2H **b**), 1.74 (d, *J* = 1.6 Hz, 2H **b**), 1.55 – 1.42 (m, 2H **a**), 1.32 – 1.24 (m, 2H **b**), 1.14 (dd, *J* = 13.5, 4.4 Hz, 2H **a**), 1.11 (s, 3H **a**), 1.02 (s, 3H **b**), 1.01 (s, 3H **a**), 0.98 (s, 3H **b**), 0.82 (s, 3H **b**), 0.79 (s, 3H **a**). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 223.0, 221.8, 154.8 (dd, *J* = 292.2, 288.0 Hz) 154.3 (dd, *J* = 292.2, 288.0 Hz), 135.0 (dd, *J* = 4.2, 2.4 Hz),133.5 (dd, *J* = 4.5, 2.4 Hz), 128.8 (t, *J* = 2.9 Hz), 128.6 (t, *J* = 2.7 Hz), 128.5 (t, *J* = 3.0 Hz), 127.7, 127.5, 91.6 (dd, *J* = 21.8, 13.9 Hz), 90.7 (dd, *J* = 21.1, 14.1 Hz), 60.3, 54.7, 49.2, 47.7, 47.2, 47.0, 40.1, 39.0, 38.3, 38.0, 34.3 (dd, *J* = 4.4, 1.7 Hz), 34.0, 25.0, 24.5, 23.9, 21.0, 20.9, 14.8. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -89.5 (d, *J* = 39.6 Hz), -91.3 (d, *J* = 39.6 Hz), -91.6 (d, *J* = 44.1 Hz), -92.0 (d, *J* = 44.1 Hz). **HRMS** (APCI, m/z): calculated for $C_{19}H_{23}F_2O$ [M+H$^+$]: 305.1711; found: 305.1714.

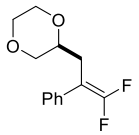
(1*R,4*S**,5*S**)-5-(3,3-Difluoro-2-phenylallyl)-1,3,3-trimethyl-2-oxabicyclo[2.2.2]octane (8)**



Synthesised from *Eucalyptol* **80** and trifluoromethyl alkene **2** following *Method 1*. Obtained as colourless oil in 49% yield (30.0 mg) as a 2.85:1 mixture of regioisomers after flash column chromatography (Hexane/AcOEt 97.5:2.5).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H **a** + 2H **b**), 7.31 – 7.26 (m, 3H **a** + 3H **b**), 2.52 – 2.43 (m, 2H **a**), 2.24 – 2.10 (m, 1H **a** + 1H **b**), 2.03 – 1.94 (m, 2H **a**), 1.85 (ttd, *J* = 12.0, 3.9, 1.8 Hz, 1H **a**), 1.79 – 1.56 (m, 3H **a** + 5H **b**), 1.48 – 1.37 (m, 1H **a** + 3H **b**), 1.25 (s, 3H **a**), 1.25 (s, 1H **b**) 1.21 (s, 3H **b**), 1.07 (m, 3H **b**), 1.04 (s, 3H **b**), 1.02 (s, 3H **a**), 0.97 (s, 3H **a**). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.17 (dd, *J* = 271.4, 269.2 Hz), 154.0 (dd, *J* = 285.0, 271.9 Hz), 133.6 (dd, *J* = 4.7, 2.6 Hz), 133.5 (d, *J* = 3.8 Hz),128.7, 128.6, 128.5 (t, *J* = 2.9 Hz), 128.4 (t, *J* = 3.0 Hz), 127.6, 127.5, 91.4 (dd, *J* = 21.7, 13.7 Hz), 91.1 (dd, *J* = 21.6, 13.8 Hz), 74.4, 73.4, 72.8, 70.7, 38.9, 38.6 (t, *J* = 2.2 Hz), 36.4, 33.7, 32.8 (d, *J* = 0.9 Hz), 31.8, 31.7 (d, *J* = 0.9 Hz), 29.7, 29.1, 28.8 (t, *J* = 2.5 Hz), 28.3, 27.5, 27.4, 25.6, 25.5, 22.9, 15.9. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -91.3 – -91.8 (m), -92.0 – 93.4 (m). **HRMS** (APCI, m/z): calculated for $C_{19}H_{23}F_2$ [M+H$^+$-H_2O]: 289.1762; found: 289.1768.

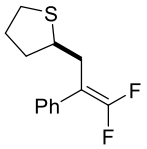
2-(3,3-Difluoro-2-phenylallyl)-1,4-dioxane (9)



Synthesised from dioxane **74** and trifluoromethyl alkene **2** following *Method 1*. Obtained as colourless oil in 75% yield (36.0 mg) after flash column chromatography (Hexane/AcOEt 90:10).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 3.80 – 3.47 (m, 6H), 3.28 (dd, *J* = 11.5, 9.8 Hz, 1H), 2.59 (ddt, *J* = 14.6, 6.9, 2.5 Hz, 1H), 2.42 (ddt, *J* = 14.6, 6.7, 2.4 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.3 (dd, *J* = 290.8, 287.9 Hz), 133.3 (t, *J* = 3.6 Hz), 128.7 ,128.4 (t, *J* = 3.2 Hz), 127.7, 88.8 (dd, *J* = 21.3, 15.8 Hz), 73.2 (t, *J* = 3.0 Hz), 70.9, 66.9, 66.5, 30.6 (d, *J* = 1.9 Hz). **^{19}F NMR (282 MHz, $CDCl_3$)** δ -89.7 (d, *J* = 40.2 Hz), -90.0 (d, *J* = 40.1 Hz). **HRMS** (APCI, m/z): calculated for $C_{13}H_{15}F_2O_2$ [M+H$^+$]: 241.1035; found:241.1031.

2-(3,3-Difluoro-2-phenylallyl)tetrahydrothiophene (10)

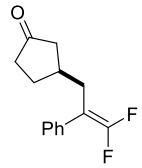


Synthesised from tetrahydrothiophene **72** and trifluoromethyl alkene **2** following *Method 1*. Obtained as colourless oil in 89% yield (43.0 mg) as a 10:1 mixture of regioisomers (91% selectivity) after flash column chromatography (Hexane/AcOEt 98:2). NMR data is only given of the major regioisomer.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 2H), 7.32-7.27 (m, 3H), 3.29 (p, *J* = 7.8 Hz, 1H), 2.95 – 2.89 (m, 1H), 2.83 – 2.77 (m, 1H), 2.70 – 2.65 (m, 2H), 2.10 – 2.03 (m, 1H), 2.02-1.93 (m, 1H), 1.92 – 1.82 (m, 1H), 1.64 – 1.57 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 153.6 (dd, *J* = 290.7, 290.1 Hz), 133.5 (dd, *J* = 2.9 Hz), 128.5, 128.4 (t, *J* = 3.1 Hz), 126.5, 92.0 (dd, *J* = 21.4, 14.4 Hz), 47.1 (t, *J* = 2.9 Hz), 36.8, 35.9 (d, *J* = 1.8 Hz), 32.8, 30.5. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -90.5 (d, *J* = 41.2 Hz), -91.3 (d, *J* = 41.0 Hz). **HRMS** (APCI, m/z): calculated for $C_{13}H_{15}F_2S$ [M+H$^+$]: 241.0857; found:241.0850.

3-(3,3-Difluoro-2-phenylallyl)cyclopentan-1-one (11)

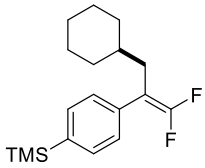
Synthesised from cyclopentanone **73** and trifluoromethyl alkene **2** following *Method 1*. Obtained as



colourless oil in 78% yield (37.1 mg) after flash column chromatography (Hexane/AcOEt 90:10).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.35 (m, 2H), 7.32 – 7.27 (m, 3H), 2.55 (t, *J* = 2.3, 1H), 2.54 (t, *J* = 2.3, 1H), 2.33 – 2.25 (m, 2H), 2.25 – 2.15 (m, 1H), 2.13 – 2.04 (m, 2H), 1.84 (ddd, *J* = 18.1, 9.8, 1.5 Hz, 1H), 1.62 – 1.52 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 218.7, 154.1 (dd, *J* = 290.0, 287.7 Hz), 133.3 (dd, *J* = 2.4, 1.0 Hz), 128.8, 128.4 (t, *J* = 3.1 Hz), 127.7, 91.2 (dd, *J* = 19.9, 15.6 Hz), 44.7, 38.4, 35.6 (t, *J* = 2.6 Hz), 33.4, 29.0. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -89.7 (d *J* = 45.9), -90.0 (d, *J* = 42.2 Hz). The spectroscopic data is in accordance with reported literature.[18]

(4-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)phenyl)trimethylsilane (12)

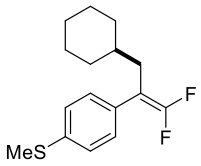


Synthesised from cyclohexane **1** and trifluoromethyl alkene **109** following *Method 1*. Obtained as colourless oil in 45% yield (28.0 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 – 7.47 (m, 2H), 7.33 – 7.26 (m, 2H), 2.28 (t, *J* = 2.5, 1H), 2.27 (t, *J* = 2.5, 1H), 1.73 – 1.57 (m, 5H), 1.33 – 1.24 (m, 1H), 1.18 – 1.06 (m, 3H), 0.99-0.88 (m, 2H), 0.28 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.2 (dd, *J* = 290.6, 286.1 Hz), 139.4, 134.7 (dd, *J* = 3.2, 1.0 Hz), 133.5, 127.6 (t, *J* = 3.2 Hz), 91.2 (dd, *J* = 21.9, 12.3 Hz), 35.8 (t, *J* = 2.5 Hz), 35.3, 33.0, 26.6, 26.2, -1.0. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -90.8 (d, *J* = 43.5 Hz), -91.4 (d, *J* = 43.1 Hz). **HRMS** (APCI, m/z): calculated for $C_{18}H_{26}F_2Si$ [M$^+$]: 308.1766; found: 308.1767.

[18] D. Anand, Z. Sun, and L. Zho, *Org. Lett.*, **2020**, *22*, 6, 2371-2375.

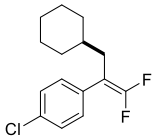
(4-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)phenyl)(methyl)sulfane (13)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **111** following *Method 1*. Obtained as colourless oil in 53% yield (30.2 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.23 (bs, 4H), 2.49 (s, 3H), 2.25 (t, *J* = 2.7 Hz, 1H), 2.24 (t, *J* = 2.7 Hz, 1H), 1.71 – 1.57 (m, 5H), 1.29 – 1.20 (m, 1H), 1.17–1.06 (m, 3H), 0.98 – 0.86 (m, 2H). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 154.1 (dd, *J* = 290.2, 286.2 Hz), 137.4, 130.9 (dd, *J* = 3.1, 1.2 Hz), 128.8 (t, *J* = 3.4 Hz), 126.6, 90.7 (dd, *J* = 22.5, 12.5 Hz), 35.8 (t, *J* = 2.3 Hz), 35.2, 33.0, 26.6, 26.2, 15.9. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -91.1 (d, *J* = 43.6 Hz), -91.6 (d, *J* = 43.9 Hz). The spectroscopic data is in accordance with reported literature.[19]

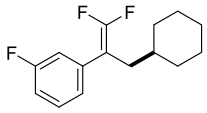
1-Chloro-4-(3-cyclohexyl-1,1-difluoroprop-1-en-2-yl)benzene (14)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **114** following *Method 1*. Obtained as colourless oil in 47% yield (26.5 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.30 – 7.24 (m, 2H), 7.22 – 7.16 (m, 2H), 2.20 (t, *J* = 2.5 Hz, 1H), 2.19 (t, *J* = 2.5 Hz), 1.62 – 1.53 (m, 5H), 1.20 – 1.12 (m, 1H), 1.09 – 1.0 (m, 3H), 0.92 – 0.77 (m, 2H). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 154.1 (dd, *J* = 290.7, 286.6 Hz), 133.1, 132.8 (dd, *J* = 4.9, 3.2 Hz), 129.7 (t, *J* = 3.2 Hz), 128.8, 90.5 (dd, *J* = 22.9, 12.4 Hz), 35.9 (t, *J* = 2.1 Hz), 35.2, 33.0, 26.5, 26.2. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -90.5 (d, *J* = 42.8 Hz) -91.1 (d, *J* = 42.8 Hz). The spectroscopic data is in accordance with reported literature.[20]

1-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)-3-fluorobenzene (15)



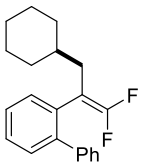
Synthesised from cyclohexane **1** and trifluoromethyl alkene **115** following *Method 1*. Obtained as colourless oil in 82% yield (41.2 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35-7.29 (m, 1H), 7.13 – 7.09 (m, 1H), 7.07 – 7.01 (m, 1H), 6.99 – 6.94 (m, 1H), 2.27 (t, *J* = 7.3 Hz, 1H),), 2.26 (t, *J* = 7.3 Hz, 1H) 1.70 – 1.66 (m, 5H), 1.28 – 1.25 (m, 1H), 1.15 – 1.10 (m, 3H), 0.98 – 0.90 (m, 2H). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 162.9 (d, *J* = 245.5 Hz), 154.3 (dd, *J* = 291.7, 286.6 Hz), 136.5 (ddd, *J* = 8.3, 5.1, 3.3 Hz), 129.9 (d, *J* = 8.7 Hz), 124.1 (q, *J* = 3.2 Hz), 115.4 (dt, *J* = 22.2, 3.5 Hz), 114.2 (d, *J* = 21.1 Hz), 90.7 (ddd, *J* = 22.8, 12.1, 2.3 Hz), 35.9 (t, *J* = 2.4 Hz), 35.2, 33.0, 26.5, 26.2. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -90.0 (d, *J* = 41.4 Hz), -90.4 (d, *J* = 41.5 Hz), -113.1 (t, *J* = 8.4 Hz). **HRMS** (APCI, m/z): calculated for $C_{15}H_{17}F_3$ [M^+]: 254.1277; found: 254.1285.

[19] H. Zhang, M. Liang, X. Zhang, M.-K. He, C. Yang, L. Guo and W. Xia, *Org. Chem. Front.*, **2022**, *9*, 95-101.

[20] H.-W. Du, Y. Chen, J. Sun, Q.-S. Gao, H. Wang, M.-D. Zhou, *Org. Lett.*, **2020**, *22*, 23, 9342−9345.

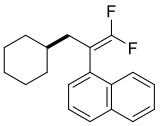
2-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)-1,1'-biphenyl (16)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **116** following *Method 1*. Obtained as colourless oil in 67% yield (42.0 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 9H), 1.68 – 1.53 (m, 5H), 1.46 (d, *J* = 10.7 Hz, 2H), 1.12 – 0.98 (m, 4H), 0.75 (qd, *J* = 11.8, 3.5 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.5 (dd, *J* = 289.2, 286.1 Hz), 141.8 (d, *J* = 3.1 Hz), 141.5, 132.7 (dd, *J* = 4.9, 1.5 Hz), 131.1 (t, *J* = 2.3 Hz), 130.5, 128.8, 128.3, 128.0, 127.3, 127.3, 91.4 (dd, *J* = 22.5, 15.6 Hz), 35.8, 35.4 (t, *J* = 2.5 Hz), 33.0, 26.5, 26.2. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -90.3 (d, *J* = 45.5 Hz), -93.9 (d, *J* = 45.5 Hz). The spectroscopic data is in accordance with reported literature.[21]

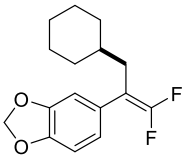
1-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)naphthalene (17)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **117** following *Method 1*. Obtained as colourless oil in 63% yield (36.1 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.87 (m, 2H), 7.84 (2 x bs, 1H), 7.59 – 7.43 (m, 3H), 7.36 (dd, *J* = 7.1, 1.2 Hz, 1H), 2.35 (s, 2H), 1.91 – 1.57 (m, 5H), 1.32 – 1.20 (m, 1H), 1.19 – 1.08 (m, 3H), 1.05 – 0.93 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.8 (dd, *J* = 290.6, 286.1 Hz), 134.0, 132.1 (dd, *J* = 3.7, 1.2 Hz), 131.8 (dd, *J* = 2.3, 0.9 Hz), 128.7, 128.3, 127.5 (dd, *J* = 3.2, 1.3 Hz), 126.4, 126.0, 125.4, 125.2, 89.2 (dd, *J* = 22.7, 16.7 Hz), 37.3, 35.9 (t, *J* = 2.6 Hz), 33.2, 26.6, 26.2. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -88.6 (d, *J* = 43.8 Hz), -93.0 (d, *J* = 43.8 Hz). The spectroscopic data is in accordance with reported literature.[22]

5-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)benzo[*d*][1,3]dioxole (18)

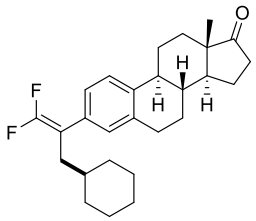


Synthesised from cyclohexane **1** and trifluoromethyl alkene **118** following *Method 1*. Obtained as colourless oil in 48% yield (26.9 mg) after flash column chromatography (Hexane/AcOEt 98:2).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 – 6.70 (m, 3H), 5.97 (s, 2H), 2.21 (t, *J* = 2.5 Hz, 1H), 2.20 (t, *J* = 2.5 Hz, 1H), 1.74 – 1.57 (m, 5H), 1.43 (s, 1H), 1.33 – 1.20 (m, 2H), 1.20 – 1.10 (m, 2H), 1.03 – 0.79 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.1 (dd, *J* = 288.0, 285.4 Hz), 147.8, 146.7, 127.9 (d, *J* = 1.8 Hz), 125.7, 122.0 (t, *J* = 3.3 Hz), 109.0 (t, *J* = 3.4 Hz), 108.4, 101.2, 91.0 (dd, *J* = 18.9, 16.5 Hz), 35.8 (t, *J* = 3.2 Hz), 35.7, 33.0, 26.6, 26.2. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -92.1. The spectroscopic data is in accordance with reported literature.[23]

[21] F. Yue, H. Ma, H. Song, Y. Liu, J. Dong, *Chem. Sci*., **2022**, *13*, 13466–13474.
[22] C. Zhu, Y.-F. Zhang, Z.-Y. Liu, L. Zhou, H. Liu, C. Feng, *Chem. Sci*., **2019**, *10*, 6721–6726.
[23] Y. Lan, F. Yang, and C. Wang, *ACS Catal*., **2018**, *8*, 10, 9245-9251.

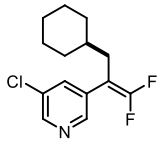
(8R,9S,13S,14S)-3-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (19)



Synthesised from cyclohexane **1** and modified trifluoromethyl alkene from *Estrone* **122** following *Method 1*. Obtained as colourless oil in 32% yield (26.2 mg) after flash column chromatography (Pentane/Et_2O 80:20).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.1 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 1H), 7.03 (s, 1H), 2.92 (dd, *J* = 8.8, 4.0 Hz, 2H), 2.55 – 2.48 (m, 1H), 2.46 – 2.40 (m, 1H), 2.31 (dt, *J* = 10.9, 5.2 Hz, 1H), 2.24 (dt, *J* = 7.2, 2.5 Hz, 2H), 2.19 – 1.95 (m, 4H), 1.69 – 1.47 (m, 11H), 1.31 – 1.26 (m, 1H), 1.16 – 1.10 (m, 3H), 0.96 – 0.89 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 220.8, 154.1 (dd, *J* = 290.0, 286.1 Hz), 138.7, 136.4, 131.6 (dd, *J* = 3.8, 2.6 Hz), 128.8 (t, *J* = 3.4 Hz), 125.6 (t, *J* = 3.0 Hz), 125.3, 90.8 (d, *J* = 22.0 Hz), 50.6, 48.0, 44.4, 38.1, 35.9, 35.6 (t, *J* = 2.8 Hz), 35.2, 32.9, 31.6, 29.4, 26.5, 26.1, 25.6, 21.6, 13.9. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -91.6 (d, *J* = 45.0 Hz), -91.9 (d, *J* = 45.0 Hz). The spectroscopic data is in accordance with reported literature.[24]

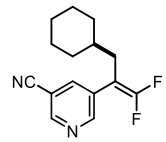
3-Chloro-5-(3-cyclohexyl-1,1-difluoroprop-1-en-2-yl)pyridine (20)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **64** following *Method 2*. Obtained as yellow oil in 50% yield (27.2 mg) after flash column chromatography (Hexane/AcOEt 95:5).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 – 8.40 (m, 2H), 7.61 (d, *J* = 2.4 Hz, 1H), 2.29 (t, *J* = 7.3 Hz, 2H), 2.27 (t, *J* = 7.3 Hz, 2H), 1.71 – 1.59 (m, 5H), 1.31 – 1.21 (m, 1H), 1.21 – 1.04 (m, 3H), 0.94 (t, *J* = 11.4 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 153.4 (dd, *J* = 293.0, 288.9 Hz), 146.2, 146.0 (t, *J* = 3.8 Hz), 134.1 (t, *J* = 3.8 Hz), 130.8, 130.3 (t, *J* = 4.4 Hz), 86.7 (dd, *J* = 24.7, 12.1 Hz), 34.7 (t, *J* = 2.4 Hz), 33.5, 31.7, 25.2, 24.9.**^{19}F NMR (282 MHz, $CDCl_3$)** δ -87.4 (d, *J* = 36.7 Hz), -88.6 (d, *J* = 37.2 Hz). **HRMS** (APCI, m/z): calculated for $C_{14}H_{17}ClF_2N$ [M+H$^+$]: 272.1012; found: 272.1004.

5-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)nicotinonitrile (22)

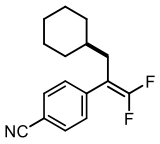


Synthesised from cyclohexane **1** and trifluoromethyl alkene **120** following *Method 2*. Obtained as colourless oil in 58% yield (30.4 mg) as a mixture of 19:1 of products (CF_2:CF_3) (95% selectivity) after flash column chromatography (Hexane/AcOEt 98:2). NMR data is only given for the major product.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 – 8.76 (m, 2H), 7.89 (td, *J* = 2.1, 0.7 Hz, 1H), 2.31 (t, *J* = 7.3, 1H),), 2.30 (t, *J* = 7.3, 1H)1.71 – 1.61 (m, 5H), 1.22 (m, 1H), 1.21 - 1.09 (m, 3H), 0.99 – 0.89 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 155.6 (dd, *J* = 293.9, 290.4 Hz), 152.6 (dd, *J* = 4.6, 3.3 Hz), 150.7, 138.4, 130.9 (dd, *J* = 4.6 Hz), 116.4, 110.1, 87.6 (dd, *J* = 25.4, 11.7 Hz), 36.0 (t, *J* = 2.3 Hz), 34.5, 32.9, 26.3, 26.0. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.7 (CF_3 – minor), -85.9 (d, *J* = 34.6 Hz), -87.8 (d, *J* = 34.6 Hz) (CF_2 – major). **HRMS** (APCI, m/z): calculated for $C_{15}H_{17}F_2N$ [M$^+$]: 263.1354; found: 263.1354.

[24] Y. Liu, X. Tao, Y. Mao, X. Yuan, J. Qiu, L. Kong, S. Ni, K.Guo, Y. Wang, Y. Pan, *Nat. Commun.*, **2021**, *12*, 6745.

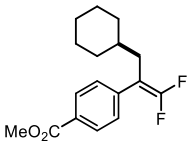
4-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)benzonitrile (23)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **113** following *Method 2*. Obtained as yellow oil in 48% yield (25.0 mg) as a mixture of 16:1 of products (CF_2:CF_3) (94% selectivity) after flash column chromatography (Hexane/AcOEt 98:2). NMR data is only given for the major product.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 – 7.62 (m, 2H), 7.45 – 7.41 (m, 2H), 2.30 (t, *J* = 7.3, 1H), 2.29 (t, *J* = 7.3, 1H), 1.70 – 1.60 (m, 5H), 1.24 – 1.19 (m, 1H), 1.14 – 1.09 (m, 3H), 0.94 – 0.89 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.5 (dd, *J* = 293.6, 292.7 Hz), 139.4 (dd, *J* = 4.0, 1.7 Hz), 132.4, 129.0 (t, *J* = 3.6 Hz), 118.8, 111.0, 90.8 (dd, *J* = 23.6, 11.4 Hz), 36.0 (t, *J* = 2.1 Hz), 34.8, 33.0, 26.4, 26.1. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.5 (CF_3 – minor), -87.6 (d, *J* = 36.4 Hz), -88.6 (d, *J* = 36.4 Hz). The spectroscopic signals are in accordance with reported literature.[25]

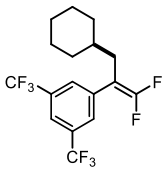
Methyl 4-(3-cyclohexyl-1,1-difluoroprop-1-en-2-yl)benzoate (24)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **112** following *Method 2*. Obtained as yellow oil in 30% yield (17.7 mg) after flash column chromatography (Hexane/AcOEt 98:2).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.4 Hz, 2H), 7.39 (dd, *J* = 8.4, 1.5 Hz, 2H), 3.92 (s, 3H), 2.30 (t, *J* = 7.3, 1H), 2.29 (t, *J* = 7.3, 1H), 1.69 – 1.62 (m, 5H), 1.24 – 1.19 (m, 1H), 1.13 – 1.09 (m, 3H), 0.95 – 0.89 (m, 2H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.9, 154.3 (dd, *J* = 293.2, 287.0 Hz), 139.2 (dd, *J* = 3.2, 1.2 Hz), 129.8, 129.0, 128.4 (t, *J* = 3.4 Hz), 91.0 (dd, *J* = 22.9, 11.8 Hz), 52.3, 36.0 (t, *J* = 2.6, 1.9 Hz), 35.0, 33.0, 26.5, 26.2. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -89.0 (d, *J* = 39.1 Hz), -89.6 (d, *J* = 39.7 Hz). The spectroscopic signals are in accordance with reported literature.[26]

1-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)-3,5-bis(trifluoromethyl)benzene (25)

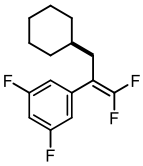


Synthesised from cyclohexane **1** and trifluoromethyl alkene **65** following *Method 2*. Obtained as yellow oil in 50% yield (37.2 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.75 (s, 2H), 2.33 (dt, *J* = 7.3, 2.5 Hz, 2H), 1.72 – 1.61 (m, 5H), 1.27 – 1.21 (m, 1H), 1.16 – 1.12 (m, 3H), 0.97 – 0.91 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 155.9 (q, *J* = 290.0, 289.2 Hz), 136.8 (dd, *J* = 5.4, 3.3 Hz), 132.1 (q, *J* = 33.3 Hz), 128.4 (d, *J* = 4.2 Hz), 124.4 (q, *J* = 271.7, 269.3 Hz), 121.2 (p, *J* = 3.6, 3.6, 3.1 Hz), 90.1 (dd, *J* = 24.4, 11.5 Hz), 36.0 (t, *J* = 2.8, 2.1 Hz), 35.0, 33.0, 26.4, 26.1. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.9, -87.4 (d, *J* = 36.5 Hz), -88.8 (d, *J* = 36.6 Hz). **HRMS** (APCI, m/z): calculated for $C_{17}H_{16}F_8$ [M^+]: 373.1119; found: 373.1123.

[25] X. Lu, X.-X. Wang, T.-J. Gong, J.-J. Pi, S.-J. He, Y. Fu, *Chem. Sci*., **2019**,*10*, 809-814.
[26] F. Yue, J. Dong, Y. Liu, and Q. Wang, *Org. Lett*., **2021**, *23*, 18, 7306-7310.

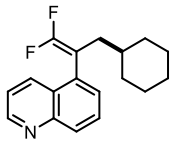
1-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)-3,5-difluorobenzene (26)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **119** following *Method 2*. Obtained as colourless oil in 42% yield (22.8 mg) after flash column chromatography (Hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 – 6.82 (m, 1H), 6.72 (tt, *J* = 8.8, 2.3 Hz, 1H), 2.24 (t, *J* = 7.3 Hz, 1H), 2.23 (t, *J* = 7.3 Hz, 1H), 1.69 – 1.64 (m, 5H), 1.27 – 1.23 (m, 1H), 1.15 – 1.11 (m, 3H), 0.98 – 0.89 (m, 2H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 163.1 (dd, *J* = 247.7, 13.2 Hz) 154.4 (dd, *J* = 289.3, 288.4 Hz), 137.6 (dd, *J* = 6.6, 3.8 Hz), 111.4 (q, *J* = 3.8, 3.2 Hz), 111.2 (q, *J* = 3.5, 2.8 Hz), 102.8 (t, *J* = 25.4 Hz), 90.3 (dd, *J* = 12.6, 2.6 Hz), 35.9 (t, *J* = 2.4 Hz), 35.0, 33.0, 26.5, 26.2. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -88.4 (d, *J* = 38.0 Hz), -88.8 (d, *J* = 38.3 Hz), -109.9 (t, *J* = 8.1 Hz). **HRMS** (APCI, m/z): calculated for $C_{15}H_{17}F_4$ [M+H$^+$]: 273.1261; found: 273.1250.

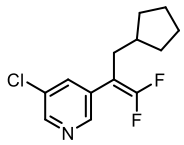
5-(3-Cyclohexyl-1,1-difluoroprop-1-en-2-yl)quinoline (27)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **121** following *Method 2*. Obtained as yellow oil in 46% yield (26.5 mg) after flash column chromatography (Hexane/AcOEt 98:2).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.57 (d, *J* = 6.0 Hz, 1H), 7.96 (dt, *J* = 7.9, 1.2 Hz, 1H), 7.66 (dd, *J* = 6.3, 1.2 Hz, 1H), 7.62 – 7.52 (m, 2H), 2.34 (t, *J* = 7.0 Hz, 1H), 2.33 (t, *J* = 7.0Hz, 1H), 1.73 – 1.59 (m, 5H), 1.31 – 1.04 (m, 4H), 1.03 – 0.87 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 153.7, 150.5 (dd, *J* = 291.8, 288.4 Hz), 144.1, 132.0 (dd, *J* = 4.3, 2.7 Hz), 129.6, 128.3, 127.3, 118.3, 88.74 (dd, J = 23.8, 12.6 Hz), 37.6, 36.4 (t, *J* = 2.6, 1.9 Hz), 33.6, 26.9, 26.6. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -87.5 (dq, *J* = 41.6, 2.1 Hz), -91.6 (dt, *J* = 41.8, 2.7 Hz). **HRMS** (APCI, m/z): calculated for $C_{18}H_{20}F_2N$ [M+H$^+$]: 288.1554; found: 288.1551.

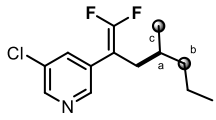
3-Chloro-5-(3-cyclopentyl-1,1-difluoroprop-1-en-2-yl)pyridine (28)



Synthesised from cyclopropane **65** and trifluoromethyl alkene **64** following *Method 2*. Obtained as colourless oil in 25% yield (13.4 mg) after flash column chromatography (Pentane/Et_2Ot 95:5).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (d, *J* = 2.3 Hz, 1H), 8.45 (t, *J* = 1.6 Hz, 1H), 7.61 (t, *J* = 2.1 Hz, 1H), 2.40 (t, *J* = 2.4 Hz, 2H), 2.39 (t, *J* = 2.4 Hz, 2H), 1.70 – 1.58 (m, 5H), 1.52 – 1.45 (m, 2H), 1.18 – 1.07 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.5 (dd, *J* = 292.4, 288.9 Hz), 147.4, 147.3 (t, *J* = 3.6 Hz), 135.4 (t, *J* = 3.4 Hz), 132.0, 131.4 (dd, *J* = 4.8, 3.8 Hz), 89.2 (dd, *J* = 24.5, 12.3 Hz), 38.4 (t, *J* = 2.5 Hz), 33.1, 32.3, 25.1. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -88.3 (d, *J* = 38.2 Hz), -89.3 (d, *J* = 37.7 Hz). **HRMS** (APCI, m/z): calculated for $C_{13}H_{15}ClF_2N$ [M+H$^+$]:258.0856; found: 258.0858.

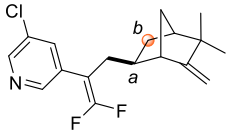
3-Chloro-5-(1,1-difluoro-4-methylhept-1-en-2-yl)pyridine (29-a) and 3-chloro-5-(4-ethyl-1,1-difluorohex-1-en-2-yl)pyridine (29-b) and 3-chloro-5-(1,1-difluorooct-1-en-2-yl)pyridine (29-c)



Synthesised from n-pentane **68** and trifluoromethyl alkene **64** following *Method 2*. Obtained as colourless oil in 37% yield (18.2 mg) as a 6.0:1.6:1.0 mixture of regioisomers (**29-a**) and (**29-b**) and (**29-c**) – (70% selectivity) after flash column chromatography (Pentane/Et_2Ot 95:5).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (bs, 1H**a**, 1H**b**,1H**c**), 8.45 (bs, 1H**a**, 1H**b**,1H**c**), 7.61 (bs, 1H**a**, 1H**b**,1 H**c**), 2.40 (dt, *J* = 6.1, 2.9 Hz, 1H**a**), 2.37 (dt, *J* = 6.1, 2.9 Hz, 1H**a**), 2.34 (t, *J* = 2.4 Hz, 1H**b**), 2.33 (t, *J* = 2.3 Hz, 1H**b**),), 2.22 (ddd, *J* = 8.5, 2.6, 1.0 Hz, 1H**a**), 2.19 (ddd, J = 8.5, 2.5, 1.0 Hz, 1H**b**), 1.42 – 1.39 (m, 2H**c**), 1.33 – 1.21 (m, 4H**a**, 4H**b**, 6H**c**), 1.15 – 1.11 (m, 2H**c**), 0.87 – 0.79 (m, 6H**a**, 6H**b**, 3H**c**).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.7 (dd, *J* = 292.8, 289.0 Hz), 147.4, 147.2 (t, *J* = 3.4 Hz), 135.3 (t, *J* = 3.0 Hz), 132.1 (dd, *J* = 4.5, 2.0 Hz), 131.5 (dd, *J* = 4.4, 3.5 Hz), 88.5 (dd, *J* = 12.7, 2.5 Hz), 88.3 (dd, *J* = 12.6, 2.3 Hz), 38.8, 38.5 (t, *J* = 2.2 Hz), 34.5, 32.1, 31.5, 31.1 (t, *J* = 2.2 Hz), 30.9, 30.5, 29.9, 29.8, 29.5, 28.7, 27.8 (t, *J* = 2.3 Hz), 27.2, 24.9, 22.8, 22.7, 20.1, 19.2, 14.4, 14.3, 14.1, 10.5. **^{19}F NMR (282 MHz, $CDCl_3$)**. δ -87.7 (dt, *J* = 37.1, 2.5 Hz), -87.9 (dt, *J* = 38.5, 2.6 Hz), -88.1 (dt, *J* = 37.5, 2.4 Hz), -88.5 (d, *J* = 37.1 Hz), -88.7 (dt, *J* = 38.5, 2.6 Hz), -88.8 (d, *J* = 37.5 Hz). **HRMS** (APCI, m/z): calculated for $C_{13}H_{16}ClF_2N$ [M$^+$]: 259.0888 found: 259.0890.

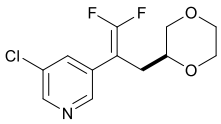
3-Chloro-5-(3-((1R,2S,4R)-5,5-dimethyl-6-methylenebicyclo[2.2.1]heptan-2-yl)-1,1-difluoroprop-1-en-2-yl)pyridine (30)



Synthesised from Camphene **78** and trifluoromethyl alkene **64** following *Method 2*. Obtained as colourless oil in 23% yield (15.3 mg) as a mixture of 1.4:1 of regioisomers (60% selectivity) after flash column chromatography (Hexane/AcOEt 95:5).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 – 8.41 (m, 2H **a** + 2H **b**), 7.62 – 7.59 (m, 1H **a** + 1H **b**), 4.71 (s, 1H **b**), 4.69 – 4.60 (m, 1H **a**), 4.49 (s, 1H **b**), 4.46 (s, 1H **a**), 2.67 (dd, *J* = 4.6, 1.3 Hz, 1H **b**), 2.44 – 2.40 (m, 1H **a**), 2.39 – 2.35 (m, 1H **a** + 1H **b**), 2.31 – 2.24 (m, 1H **a** + 1H **b**), 1.93 – 1.89 (m, 1H **a**), 1.85 – 1.80 (m, 1H **b**), 1.67 (dt, *J* = 3.9, 1.7 Hz, 2H **a** + 1H **b**), 1.64 (ddd, *J* = 8.8, 2.8, 1.4 Hz, 1H **a**), 1.50 – 1.46 (m, 1H **a**), 1.40 (dt, *J* = 10.5, 1.6 Hz, 2H **b**), 1.25 (s, 1H **b**), 1.20 (dt, *J* = 12.1, 4.4 Hz, 2H **a**), 1.01 (s, 3H **a**), 1.01 (s, 3H **b**), 0.94 (s, 3H **a**), 0.92 – 0.90 (m, 1H **b**), 0.85 (s, 3H **b**). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 165.0, 164.8, 154.7 (dd, *J* = 293.0, 289.3 Hz), 147.6, 147.5, 147.3 (dd, *J* = 3.6, 3.2 Hz), 135.6 (dd, *J* = 3.4, 3 Hz), 132.1 (dd, *J* = 3.8, 3.1 Hz), 131.2 (dd, *J* = 4.6, 4.2 Hz), 100.4, 100.2, 88.7 (dd, *J* = 14.9, 12.8 Hz), 88.6 (dd, *J* = 24.4, 9.5 Hz), 52.2, 51.2, 48.7, 47.2, 42.3, 41.5, 39.2 (t, *J* = 2.5 Hz), 36.6, 34.3, 34.0, 33.7, 33.5, 33.1 (t, *J* = 2.3 Hz), 31.8, 29.7, 29.4, 25.7, 25.2. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -88.3 (d, *J* = 7.5 Hz), -88.4 (d, *J* = 7.5 Hz), -88.8 (d, *J* = 2.0 Hz), -88.9 (d, *J*= 2.0 Hz). **HRMS** (APCI, m/z): calculated for $C_{18}H_{21}ClF_2N$ [M+H$^+$]: 324.1325; found: 324.1327.

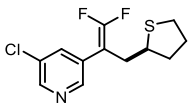
3-(3-(1,4-Dioxan-2-yl)-1,1-difluoroprop-1-en-2-yl)-5-chloropyridine (31)



Synthesised from dioxane **74** and trifluoromethyl alkene **64** following *Method 2*. Obtained as colourless oil in 24% yield (13.2 mg) after flash column chromatography (Hexane/AcOEt 90:10).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 – 8.47 (m, 2H), 7.68 (td, *J* = 2.2, 0.7 Hz, 1H), 3.79 – 3.68 (m, 3H), 3.65 – 3.53 (m, 3H), 3.30 (dd, *J* = 11.4, 9.8 Hz, 1H), 2.50 (ddt, *J* = 14.9, 8.0, 2.2 Hz, 1H), 2.42 (dddd, *J* = 14.9, 5.3, 3.0, 2.3 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.8 (dd, *J* = 292.9, 290.6 Hz), 147.6, 147.2 (t, *J* = 3.6 Hz), 135.7 (t, *J* = 3.4 Hz), 132.1, 131.0 (t, *J* = 4.3 Hz), 85.9 (dd, *J* = 23.8, 15.2 Hz), 73.2 (t, *J* = 3.2, 2.4 Hz), 70.8, 66.9, 66.5, 30.0 (d, *J* = 1.3 Hz), 29.8. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -86.0 (d, *J* = 33.5 Hz), -86.5 (d, *J* = 33.6 Hz). **HRMS** (APCI, m/z): calculated for $C_{12}H_{13}ClF_2NO_2$ [M+H$^+$]: 276.0597; found 276.0597

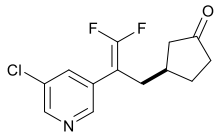
3-Chloro-5-(1,1-difluoro-3-(tetrahydrothiophen-2-yl)prop-1-en-2-yl)pyridine (32)



Synthesised from tetrahydrothiophene **72** and trifluoromethyl alkene **64** following *Method 2*. Obtained as yellow oil in 66% yield (36.4 mg) after flash column chromatography (Hexane/AcOEt 90:10).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.3 Hz, 1H), 8.45 (t, *J* = 1.6 Hz, 1H), 7.63 (td, *J* = 2.1, 0.8 Hz, 1H), 3.31 – 3.26 (m, 1H), 2.92 (ddd, *J* = 10.3, 7.5, 6.2 Hz, 1H), 2.83 (ddd, *J* = 10.4, 5.3, 1.1 Hz, 1H), 2.75 – 2.69 (m, 1H), 2.61 (ddt, *J* = 14.6, 8.0, 2.2 Hz, 2H), 2.12 – 2.05 (m, 1H), 2.03 – 1.98 (m, 1H), 1.94 – 1.85 (m, 2H), 1.63 – 1.57 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.9 (dd, *J* = 290.8, 289.9 Hz), 147.7, 147.3 (t, *J* = 3.6 Hz), 135.6 (t, *J* = 3.4 Hz), 132.1, 130.7 (dd, *J* = 3.7, 1.6 Hz), 88.5 (dd, *J* = 23.7, 14.0 Hz). 46.7 (t, *J* = 2.8 Hz), 36.8, 35.1, 32.6, 30.2. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -86.4 (d, *J* = 33.6 Hz), -88.0 (d, *J* = 33.5 Hz). **HRMS** (APCI, m/z): calculated for $C_{12}H_{13}ClF_2NS$ [M+H$^+$]: 276.0420; found: 276.0416.

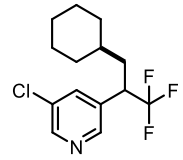
3-(2-(5-Chloropyridin-3-yl)-3,3-difluoroallyl)cyclopentan-1-one (33)



Synthesised from cyclopentanone **73** and trifluoromethyl alkene **64** following *Method 2*. Obtained as yellow oil in 30% yield (16.3 mg) after flash column chromatography (Hexane/AcOEt 90:10).

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.51 (d, *J* = 2.2 Hz, 1H), 8.47 (t, *J* = 1.6 Hz, 1H), 7.63 (td, *J* = 2.1, 0.8 Hz, 1H), 2.58 – 2.54 (m, 2H), 2.37 – 2.28 (m, 2H), 2.16 – 2.08 (m, 2H), 1.85 (ddd, *J* = 18.0, 9.8, 1.5 Hz, 2H), 1.62 – 1.55 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 217.8, 155.5 (dd, *J* = 290.9, 286.9 Hz), 147.8, 147.0 (t, *J* = 3.6 Hz), 135.4 (t, *J* = 3.5 Hz), 132.3, 130.7 (t, *J* = 5.3, 4.0 Hz), 87.9 (dd, *J* = 24.1, 13.6 Hz), 44.6, 38.3, 35.5 (t, *J* = 2.7 Hz), 32.9, 29.0. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -86.9 (d, *J* = 35.5 Hz), -87.7 (d, *J* = 35.5 Hz). **HRMS** (APCI, m/z): calculated for $C_{13}H_{13}ClF_2NO$ [M+H$^+$]: 272.0637; found: 272.0642.

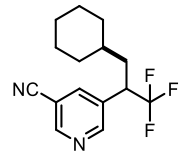
3-Chloro-5-(3-cyclohexyl-1,1,1-trifluoropropan-2-yl)pyridine (21)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **64** following *Method 3*. Obtained as colourless oil in 73% yield (43.7 mg) after flash column chromatography (Hexane/AcOEt 90:10). Gram-scale: Obtained as yellow oil in 56% yield (817 mg) after flash column chromatography (Pentane/Et$_2$O 95:5) *see section 7.8* for further details.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.56 (s, 1H), 8.40 (s, 1H), 7.63 (s, 1H), 3.40 (h, *J* = 8.9 Hz, 1H), 1.82 (d, *J* = 6.9 Hz, 1H), 1.79 (d, *J* = 7.2 Hz, 1H), 1.71 – 1.53 (m, 5H), 1.20 – 0.81 (m, 6H). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 148.8, 148.5, 135.9, 132.4, 128.5 (q, *J* = 281.4, 279.8 Hz), 44.8 (q, *J* = 27.2 Hz), 35.8, 34.1, 31.9, 26.4, 26.1, 25.9. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -69.8 (d, *J* = 9.1 Hz). **HRMS** (APCI, m/z): calculated for $C_{14}H_{18}ClF_3N$ [M+H$^+$]: 292.1074found: 292.1081.

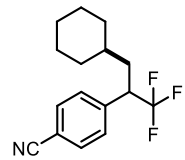
5-(3-Cyclohexyl-1,1,1-trifluoropropan-2-yl)nicotinonitrile (34)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **120** following *Method 3* with HFIP (21.0 µl, 0.2 mmol, 1.0 equiv) as additive. Obtained as colourless oil in 44% yield (25.6 mg) after flash column chromatography (Hexane/AcOEt 98:2).

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.87 (d, *J* = 1.9 Hz, 1H), 8.72 (d, *J* = 2.3 Hz, 1H), 7.91 (t, *J* = 2.3 Hz, 1H), 3.50 (dqd, *J* = 10.9, 8.9, 4.9 Hz, 1H), 1.91 – 1.82 (m, 2H), 1.71 – 1.61 (m, 5H), 1.16 – 1.06 (m, 3H), 1.01 – 0.86 (m, 3H).**^{13}C NMR (126 MHz, CDCl$_3$)** δ 154.2, 152.4, 139.6, 132.0 (q, *J* = 1.8 Hz), 126.6 (q, *J* = 279.7 Hz), 116.5, 110.8, 45.1 (q, *J* = 27.5 Hz), 35.8, 34.5, 32.0, 26.5, 26.3, 26.1. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -69.8 (d, *J* = 8.9 Hz). **HRMS** (APCI, m/z): calculated for $C_{15}H_{18}F_3N_2$ [M+H$^+$]: 283.1417; found: 283.1417.

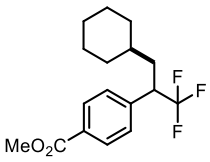
4-(3-Cyclohexyl-1,1,1-trifluoropropan-2-yl)benzonitrile (35)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **113** following *Method 3* with HFIP (21.0 µl, 0.2 mmol, 1.0 equiv) as additive. Obtained as colourless oil in 47% yield (24.6 mg) after flash column chromatography (Hexane/AcOEt 95:5).

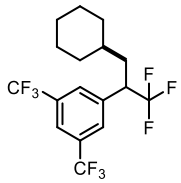
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 3.44 (pd, *J* = 9.1, 5.6 Hz, 1H), 1.88 – 1.79 (m, 2H), 1.75 – 1.59 (m, 5H), 1.15 – 1.07 (m, 3H), 0.99 – 0.84 (m, 3H). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 140.6 (q, *J* = 1.9 Hz), 132.6, 130.1, 128.6 (q, *J* = 279.1 Hz), 118.6, 112.4, 47.5 (q, *J* = 26.7 Hz), 36.0, 34.2, 31.9, 26.39, 26.1, 25.9. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -69.6 (d, *J* = 9.1 Hz). The spectroscopic signals are in accordance with reported literature.[26]

Methyl 4-(3-cyclohexyl-1,1,1-trifluoropropan-2-yl)benzoate (36)



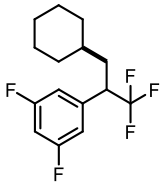
Synthesised from cyclohexane **1** and trifluoromethyl alkene **112** following *Method 3* with HFIP (21.0 μl, 0.2 mmol, 1.0 equiv) as additive. Obtained as colourless oil in 58% yield (34.1 mg) after flash column chromatography (Hexane/AcOEt 95:5). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.03 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 3.92 (s, 3H), 3.43 (dqd, *J* = 10.9, 9.2, 4.2 Hz, 1H), 1.99 – 1.76 (m, 2H), 1.75 – 1.62 (m, 3H), 1.59 – 1.51 (m, 2H), 1.14 – 0.82 (m, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.9, 140.4 (q, *J* = 2.0 Hz), 130.2, 130.0, 129.3, 127.9 (q, *J* = 279.1 Hz), 52.3, 47.4 (q, *J* = 26.5 Hz), 36.1, 34.2, 31.9, 26.4, 26.0 (d, *J* = 27.4 Hz). **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.6 (d, *J* = 9.1 Hz). The spectroscopic signals are in accordance with reported literature.[27]

1-(3-Cyclohexyl-1,1,1-trifluoropropan-2-yl)-3,5-bis(trifluoromethyl)benzene (37)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **65** following *Method 3* with HFIP (21.0 μl, 0.2 mmol, 1.0 equiv) as additive. Obtained as yellow oil in 62% yield (48.8 mg) after flash column chromatography (Hexanes). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.88 (s, 1H), 7.73 (s, 2H), 3.53 (dqd, *J* = 10.2, 8.6, 5.2 Hz, 1H), 1.92 – 1.83 (m, 2H), 1.76 – 1.59 (m, 5H), 1.17 – 1.09 (m, 4H), 1.01 – 0.91 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 138.0 (q, *J* = 2.3 Hz), 132.3 (q, *J* = 33.6 Hz), 129.3, 126.5 (q, *J* = 279.9 Hz), 122.5 (q, *J* = 4.9, Hz), 122.2 (q, *J* = 274.4 Hz), 47.3 (q, *J* = 27.0 Hz), 34.2, 32.1, 26.4, 26.0, 25.9. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.9 (s), -69.9 (d, *J* = 8.6 Hz). **HRMS** (APCI, m/z): calculated for $C_{17}H_{17}F_9$ [M^+]: 392.1181; found: 392.1191.

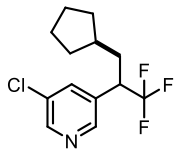
1-(3-Cyclohexyl-1,1,1-trifluoropropan-2-yl)-3,5-difluorobenzene (38)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **119** following *Method 3* with HFIP (21.0 μl, 0.2 mmol, 1.0 equiv) as additive. Obtained as yellow oil in 43% yield (25.1 mg) after flash column chromatography (Pentane). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 6.87 – 6.76 (m, 3H), 3.35 (h, *J* = 8.7 Hz, 1H), 1.81 – 1.75 (m, 2H), 1.74 – 1.58 (m, 5H), 1.28 – 1.20 (m, 3H), 1.00 – 0.93 (m, 1H), 0.88 (dtd, *J* = 12.2, 6.0, 3.8 Hz, 2H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 163.2 (dd, *J* = 249.0, 12.9 Hz), 139.0 (td, *J* = 9.1, 1.9 Hz), 126.7 (q, *J* = 279.9 Hz), 112.2 (dd, *J* = 20.1, 6.1 Hz), 103.9 (t, *J* = 25.2 Hz), 47.2 (qt, *J* = 26.4, 1.9 Hz), 36.1 (q, *J* = 2.2 Hz), 34.2, 31.9, 26.4, 26.1, 25.9. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.9 (d, *J* = 9.1 Hz), -109.3 (t, *J* = 7.9 Hz). **HRMS** (APCI, m/z): calculated for $C_{15}H_{17}F_5$ [$M+H^+$]: 292.1245; found: 292.1246.

[27] Z. Cai, R. Gu, W. Si, Y. Xiang, J. Sun, Y. Jiao, X. Zhang, *Green Chem.*, **2022**, *24*, 6830-6835.

3-Chloro-5-(3-cyclopentyl-1,1,1-trifluoropropan-2-yl)pyridine (39)

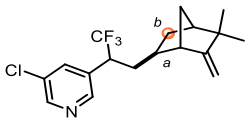


Synthesised from cyclopentane **65** and trifluoromethyl alkene **64** following *Method 3*. Obtained as yellow oil in 39% yield (21.4 mg) after flash column chromatography (Pentane/Et_2O 95:5).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 2.3 Hz, 1H), 8.40 (d, *J* = 2.0 Hz, 1H), 7.64 (s, 1H), 3.31 (dqd, *J* = 11.3, 9.1, 4.0 Hz, 1H), 2.00 (ddd, *J* = 13.7, 11.3, 5.0 Hz, 1H), 1.90 (ddd, *J* = 13.8, 10.0, 4.0 Hz, 1H), 1.74 – 1.56 (m, 5H), 1.54 – 1.44 (m, 2H), 1.14 – 1.03 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 148.8, 148.5, 135.9, 132.4, 132.4 (q, *J* = 2.0, 1.1 Hz), 126.5 (q, *J* = 279.9 Hz), 47.0 (q, *J* = 27.2 Hz), 36.8, 34.7 (q, *J* = 1.9 Hz), 33.3, 31.6, 25.2, 25.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -69.8 (d, *J* = 9.0 Hz). **HRMS** (APCI, m/z): calculated for $C_{13}H_{16}ClF_3N$ [M+H$^+$]: 278.0918 found: 278.0922.

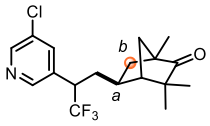
3-Chloro-5-(3-((1R,2S,4R)-5,5-dimethyl-6-methylenebicyclo[2.2.1]heptan-2-yl)-1,1,1-trifluoropropan-2-yl)pyridine (40)



Synthesised from Camphene **78** and trifluoromethyl alkene **64** following *Method 3*. Obtained as colourless oil in 73% yield (50.0 mg) as a 1:1 mixture of two regioisomers (50% selectivity) and for each regioisomer 2 major diastereomers **a** (1.4:1:0:0) + **b** (1.8:1:0:0), after flash column chromatography (Hexanes/AcOEt 95:5).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 – 8.48 (m, 1H **a** + 1H **b**), 8.39 (d, *J* = 9.5 Hz, 1H **a** + 1H **b**), 7.65 – 7.62 (m, 1H **a** + 1H **b**), 4.67 (dd, *J* = 10.7, 7.4 Hz, 2H **b**), 4.46 (dd, *J* = 14.0, 4.0 Hz, 2H **a**), 3.41 – 3.30 (m, 1H **b**), 3.29 – 3.19 (m, 1H **a**), 2.46 (bs, 1H **b**), 2.69 (d, *J* = 3.6 Hz, 1H **b**), 2.63 (d, *J* = 3.6 Hz, 1 H **b**) 2.33 – 2.24 (m, 1H **a**), 2.22 – 2.13 (m, 1H **a**), 2.00 – 1.91 (m, 2H **b**), 1.90 – 1.85 (m, 2H **a**), 1.85 – 1.80 (m, 1H **b**), 1.76 – 1.72 (m, 1H **b**), 1.70 – 1.56 (m, 1H **a**), 1.65 – 1.60 (m, 1H **b**), 1.45 – 1.39 (m, 1H **a**), 1.46 – 1.38 (m, 1H **b**), 1.00 (d, *J* = 12.1 Hz, 3H **b**), 1.00 (bs, 3H **a**), 0.97 (d, *J* = 10.0 Hz, 3H **b**), 0.92 (d, *J* = 6.1 Hz, 3H **a**), 0.91 – 0.85 (m, 1H **a**), 0.85 – 0.77 (bs, 2H **b**), 0.80 (bs, 2H **a**). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 2x[164.6], 164.3, 164.2, 2x[148.9], 148.8, 148.5, 2x[148.4], 2x[135.8], 135.7, 2x[132.4 (q, *J* = 2.6, 1.3 Hz)], 132.3 (q, *J* = 3.2, 1.5 Hz), 132.2 (q, *J* = 3.2, 1.5 Hz), 2x[131.0 (q, *J* = 258.7 Hz)], 2x[127.6 (q, *J* = 280.2, 278.0 Hz)], 2x[127.5 (q, *J* = 280.2, 279.5 Hz)], 2x[123.2 (q, *J* = 287.5, 272.9 Hz)], 2x[100.6], 100.4, 100.3, signals from 53.7 to 11.1 ppm were unable to assign due to overlapping and the high complexity of the spectra. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.2 (bs), -69.1 (bs), -69.3 (d, *J* = 3.5 Hz). **HRMS** (APCI, m/z): calculated for $C_{18}H_{22}ClF_3N$ [M+H$^+$]: 344.1387; found: 344.1393.

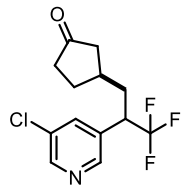
(1R,4R,5R)-5-(2-(5-Chloropyridin-3-yl)-3,3,3-trifluoropropyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-one (41)



Synthesised from Fenchone **79** and trifluoromethyl alkene **64** following *Method 3*. Obtained as colourless oil in 58% yield (42.2 mg) as a 1.4:1 mixture of two regioisomers and for each regioisomer 2 major diastereomer **a** (1.2:1:0:0) + **b** (1.4:1:0:0), and traces of other regioisomer, after flash column chromatography (Hexane/AcOEt 90:10).

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.57 (s, 1H **a**), 8.55 (d, *J* = 2.3 Hz, 1H **b**), 8.45 (s, 1H **b**), 8.41 – 8.37 (m, 1H **a** + 1H **b**), 7.70 – 7.66 (m, 1H **b**), 7.66 – 7.61 (m, 1H **a**), 3.39 – 3.31 (m, 1H **a**), 3.30 – 3.21 (m, 1H **b**), 2.25 – 2.17 (m, 1H **b**), 2.12 (dd, *J* = 5.0, 1.8 Hz, 1H **a**), 2.06 – 1.97 (m, 1H **a**), 1.92 – 1.81 (m, 2H **a**), 1.81 – 1.74 (m, 2H **a**), 1.67 (ddt, *J* = 11.2, 9.3, 2.3 Hz, 2H **b**), 1.61 – 1.51 (m, 2H **a**), 1.50 – 1.35 (m, 2H **b**), 1.35 – 1.23 (m, 2H **b**), 1.11 (d, *J* = 8.4 Hz, 1H **b**), 1.07 (d, *J* = 11.6 Hz, 3H **a**), 1.02 (d, *J* = 7.4 Hz, 3H **a**), 0.99 (d, *J* = 7.2 Hz, 3H **a**), 0.83 (t, *J* = 5.1 Hz, 6H **b**), 0.77 (s, 3H **b**). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 2x[223.5], 221.9, 221.8, 221.4, 221.1, 220.8, 207.0, 149.3, 149.1, 149.0, 148.9, 148.8, 148.5, 148.4, 148.3, 148.2, 136.2, 136.1, 2x[135.9], 135.8, 135.7, 133.9 (q, *J* = 2.5, 1.9 Hz), 133.5 (q, *J* = 2.5, 1.9 Hz), 132.5 q, *J* = 12.2, 9.7 Hz), 131.9 (q, *J* = 12.1, 9.7 Hz), 2x[127.4 (q, *J* = 286.5, 276.0 Hz)], 2x[125.2 (q, *J* = 281.7, 275.4 Hz)] signals from 60.3 to 11.9 ppm were unable to assign due to overlapping and the high complexity of the spectra. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -68.3 (d, *J* = 8.2 Hz), -68.9 (d, *J* = 8.2 Hz), -69.2 (d, *J* = 9.0 Hz), -69.3 (d, *J* = 8.9 Hz), -69.6 (d, *J* = 12.8 Hz), -69.7 (d, *J* = 8.7 Hz), -70.1 (d, *J* = 9.3 Hz), -70.2 (d, *J* = 9.5 Hz), -70.3 (d, *J* = 9.5 Hz), -70.4 (d, *J* = 9.4 Hz). **HRMS** (APCI, m/z): calculated for [M+H$^+$]: 360.1337; found: 360.1341.

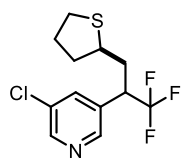
3-(2-(5-Chloropyridin-3-yl)-3,3,3-trifluoropropyl)cyclopentan-1-one (42)



Synthesised from cyclopentanone **73** and trifluoromethyl alkene **64** following *Method 3* with HFIP (21.0 µl, 0.2 mmol, 1.0 equiv) as additive. Obtained as colourless oil in 44% yield (25.8 mg) as a 1:1 mixture of diastereoisomers after flash column chromatography (Hexane/AcOEt 90:10).

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.64 – 8.57 (m, 1H), 8.47 – 8.37 (m, 1H), 7.75 – 7.60 (m, 1H), 3.40 (dqd, *J* = 10.9, 8.4, 4.6 Hz, 1H), 3.30 (dqd, *J* = 11.0, 8.7, 4.6 Hz, 1H), 2.36 – 2.26 (m, 2H), 2.16 – 2.07 (m, 4H), 2.00 – 1.91 (m, 1H), 1.84 – 1.75 (m, 1H), 1.59 – 1.50 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 217.2, 217.1, 149.3 (q, *J* = 3.2 Hz), 148.3, 148.2, 135.8, 135.7, 132.7, 131.6, 129.5 (q, *J* = 291.0, 283.4 Hz), 126.2 (q, *J* = 290.6, 287.3 Hz), 46.6 (q, *J* = 27.6, 26.1 Hz), 45.9 (q, *J* = 28.1, 25.6 Hz), 45.2, 44.0, 38.5, 38.2, 34.6 (q, *J* = 2.3 Hz), 34.4 (q, *J* = 1.8 Hz), 34.2, 34.0, 30.0, 28.8. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -69.8 (dd, *J* = 26.1, 8.7 Hz). **HRMS** (APCI, m/z): calculated for $C_{13}H_{14}ClF_3NO$ [M+H$^+$]: 292.0711; found: 292.0699.

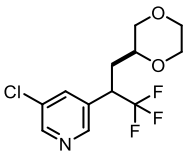
3-Chloro-5-(1,1,1-trifluoro-3-(tetrahydrothiophen-2-yl)propan-2-yl)pyridine (43)



Synthesised from tetrahydrothiophene **72** and trifluoromethyl alkene **64** following *Method 3* with HFIP (21.0 µl, 0.2 mmol, 1.0 equiv) as additive. Obtained as yellow oil in 50% yield (29.7 mg) as a 1:1 mixture of diastereoisomers (both overlap perfectly in NMR data) after flash column chromatography (Hexane/AcOEt 90:10).

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.57 (d, *J* = 2.2 Hz, 1H), 8.44 (d, *J* = 2.1 Hz, 1H), 7.64 (t, *J* = 2.3 Hz, 1H), 3.50 (dqd, *J* = 12.5, 9.1, 3.6 Hz, 1H), 2.94 – 2.87 (m, 2H), 2.83 – 2.78 (m, 1H), 2.26 (ddd, *J* = 13.8, 11.9, 3.7 Hz, 2H), 2.11 – 2.00 (m, 3H), 1.95 – 1.87 (m, 1H). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 149.1, 148.6, 136.1, 132.4, 131.2 (q, *J* = 1.8 Hz), 126.3 (q, *J* = 280.0 Hz), 47.4 (q, *J* = 27.7 Hz), 45.4, 37.7, 36.5 (q, *J* = 2.3 Hz), 32.4, 30.2. **^{19}F NMR (282 MHz, CDCl$_3$)** δ -69.5 (d, *J* = 8.7 Hz). **HRMS** (APCI, m/z): calculated for $C_{12}H_{14}ClF_3NS$ [M+H$^+$]: 296.0482; found: 296.0481.

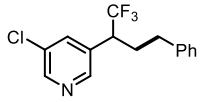
3-(3-(1,4-Dioxan-2-yl)-1,1,1-trifluoropropan-2-yl)-5-chloropyridine (44)



Synthesised from dioxane **74** and trifluoromethyl alkene **64** following *Method 3* with HFIP (21.0 μl, 0.2 mmol, 1.0 equiv) as additive. Obtained as yellow oil in 45% yield (26.6 mg) as a 1:1 mixture of diastereoisomers after flash column chromatography (Hexane/AcOEt 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.43 (s, 1H), 7.65 (s, 1H), 3.79 – 3.41 (m, 6H), 3.31 (ddd, *J* = 11.6, 9.6, 2.0 Hz, 1H), 3.07 (td, *J* = 10.4, 9.5, 2.5 Hz, 1H), 2.06 (ddt, *J* = 13.6, 11.2, 2.7 Hz, 1H), 1.78 (ddt, *J* = 14.5, 12.3, 2.4 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 149.1, 148.6, 135.8, 132.5, 131.3 (q, *J* = 1.6 Hz), 126.7 (q, *J* = 280.1, 279.3 Hz), 71.1, 70.7, 66.7, 66.5, 42.9 (q, *J* = 28.1 Hz), 30.5 (q, *J* = 2.1 Hz). **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.2 (d, *J* = 9.0 Hz), -69.6 (d, *J* = 9.4 Hz). **HRMS** (APCI, m/z): calculated for $C_{12}H_{14}ClF_3NO_2$ [M+H$^+$]: 296.0660; found: 296.0642.

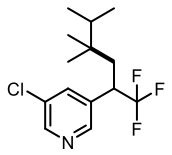
3-Chloro-5-(1,1,1-trifluoro-4-phenylbutan-2-yl)pyridine (45)



Synthesised from *Toluene* **71** and trifluoromethyl alkene **64** following *Method 3*. Obtained as colourless oil in 53% yield (32 mg) after flash column chromatography (Pentane/Et_2O 95:5).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, *J* = 2.3 Hz, 1H), 8.24 (d, *J* = 2.0 Hz, 1H), 7.50 (bs, 1H), 7.19 – 7.05 (m, 3H), 6.95 – 6.91 (m, 2H), 3.11 (dqd, *J* = 12.1, 9.0, 4.4 Hz, 1H), 2.54 – 2.46 (m, 1H), 2.35 – 2.23 (m, 2H), 2.11 – 2.01 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 149.0, 148.7, 139.6, 135.9, 132.5, 131.8 (q, *J* = 2.3 Hz), 128.9, 128.4, 126.8, 126.2 (q, *J* = 279.9, 279.1 Hz), 46.6 (q, *J* = 27.4 Hz), 32.4, 29.8 (q, *J* = 2.2 Hz). **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.6 (d, *J* = 8.9 Hz). **HRMS** (APCI, m/z): calculated for $C_{15}H_{14}ClF_3N$ [M+H$^+$]: 300.0761; found: 300.0760.

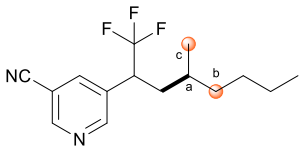
3-Chloro-5-(1,1,1-trifluoro-4,4,5-trimethylhexan-2-yl)pyridine (46)



Synthesised from 2,3-dimethylbutane **70** and trifluoromethyl alkene **64** following *Method 3*. Obtained as colourless oil in 23% yield (13.6 mg) after flash column chromatography (Hexane/AcOEt 98:2).

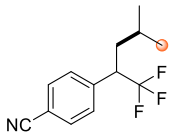
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 2.3 Hz, 1H), 8.45 (d, *J* = 2.1 Hz, 1H), 7.67 (t, *J* = 2.4 Hz, 1H), 3.37 (pd, *J* = 9.6, 1.9 Hz, 1H), 2.02 (dd, *J* = 14.5, 1.9 Hz, 1H), 1.85 (dd, *J* = 14.4, 9.8 Hz, 1H), 1.47 – 1.39 (m, 1H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.75 (d, *J* = 7.0 Hz, 3H), 0.74 (s, 3H), 0.64 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 148.8 (q, *J* = 4.1 Hz), 148.6, 136.2, 134.3 (q, *J* = 2.3 Hz), 132.3, 126.8 (q, *J* = 280.2 Hz), 43.9 (q, *J* = 27.2 Hz), 38.3, 36.0, 35.8, 24.8, 24.6, 17.4, 17.3. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -70.0 (d, *J* = 9.8 Hz). **HRMS** (APCI, m/z): calculated for $C_{14}H_{20}ClF_3N$ [M+H$^+$]: 294.1231; found: 294.1236.

5-(1,1,1-Trifluoro-4-methyloctan-2-yl)nicotinonitrile (47-a) and 5-(4-Ethyl-1,1,1-trifluoroheptan-2-yl)nicotinonitrile (47-b) and 5-(1,1,1-trifluorononan-2-yl)nicotinonitrile (47-c)



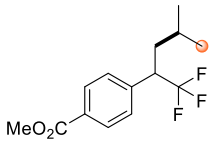
Synthesised from n-hexane **69** and trifluoromethyl alkene **120** following *Method 3*. Obtained as colourless oil in 56% yield (33.7 mg) as a 6:3:1 mixture of regioisomers (**47-a**) and (**47-b**) with d.r. = 1:1 for each isomer (60% selectivity) after flash column chromatography (Hexanes).
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (s, 1H **a**), 8.87 (s, 1H **b**), 8.78 – 8.75 (m, 1H **c**), 8.73 (s, 1H **a**), 8.73 (s, 1H **b**), 7.94 (s, 1H **c**), 7.91 (s, 1H **a**), 7.91 (s, 1H **b**), 3.77 – 3.70 (m, 1H **c**), 3.54 – 3.33 (m, 1H **a**), 3.54 – 3.33 (m, 1H **b**), 2.09 – 1.68 (m, 3H **a**), 2.09 – 1.68 (m, 3H **b**), 2.09 – 1.68 (m, 2H **c**), 1.38 – 1.08 (m, 6H **a**), 1.38 – 1.08 (m, 6H **b**), 1.38 – 1.08 (m, 10H **c**), 0.92 – 0.74 (m, 3H **a**), 0.92 – 0.74 (m, 6H **b**), 0.92 – 0.72 (m, 3H **c**). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 153.9, 3x[152.2], 4x[139.3], 2x[132.0 (q, *J* = 14.1, 9.7 Hz)], 2x[128.2 (q, *J* = 282.7 Hz)], 2x[124.5 (d, *J* = 281.9 Hz), 116.2, 110.5, 45.7 (q, *J* = 27.9, 3.7 Hz), 45.3 (q, *J* = 27.9, 3,7 Hz), 37.3, 35.9, 2x[35.8], 35.5, 35.0, 34.9, 34.3, 32.1 (q, *J* = 4.7, 1.5 Hz), 31.8 (q, *J* = 4.7, 1.5 Hz), 29.8, 29.5, 29.1, 29.0, 28.9, 28.5, 28.4, 26.8, 26.3, 24.4, 2x[22.9], 22.7, 20.3, 19.8, 19.1, 18.5, 14.5, 14.3, 14.1, 10.8, 9.7. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.5 (d, *J* = 8.9 Hz), -69.6 (d, *J* = 8.8 Hz), -69.6 (d, *J* = 8.8 Hz), -69.7 (d, *J* = 8.8 Hz), -69.8 (d, *J* = 8.7 Hz). **HRMS** (APCI, m/z): calculated for $C_{15}H_{20}F_3N_2$ [M+H$^+$]: 285.1573; found: 285.1570.

4-(1,1,1-Trifluoro-4-methylpentan-2-yl)benzonitrile (48)



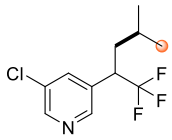
Synthesised from propane and trifluoromethyl alkene **113** with HFIP (21.0 µl, 0.2 mmol, 1.0 equiv) following *GP1*. Obtained as a yellow oil in 46% yield (22.4 mg) as a mixture regioisomers branched / linear (5.5 : 1) after flash column chromatography (Pentane/Et_2O 99.5:0.5). NMR data is only given for the major regioisomer.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 3.39 (dqd, *J* = 11.9, 9.1, 4.5 Hz, 1H), 1.89 (ddd, *J* = 13.8, 11.4, 4.7 Hz, 1H), 1.75 (ddd, *J* = 13.9, 9.8, 4.1 Hz, 1H), 1.37 – 1.27 (m, 1H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 7.0 Hz, 3H) . **^{13}C NMR (126 MHz, $CDCl_3$)** δ 140.5 (q, *J* = 1.9 Hz), 132.6, 130.1, 126.5 (q, *J* = 279.6 Hz), 118.5, 112.5, 48.3 (q, *J* = 26.8 Hz), 37.8 (q, *J* = 2.0 Hz), 24.9, 23.5, 21.0. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.5 (d, *J* = 10.1 Hz), -69.6 (d, *J* = 9.0 Hz). **HRMS** (APCI, m/z): calculated for $C_{13}H_{15}F_3N$ [M+H$^+$]: 242.1151, found 242.1156.

Methyl 4-(1,1,1-trifluoro-4-methylpentan-2-yl)benzoate (49)



Synthesised from propane and trifluoromethyl alkene **112** with HFIP (21.0 µl, 0.2 mmol, 1.0 equiv) following *GP1*. Obtained as a yellow oil in 74% yield (40.6 mg) as a mixture of 10:1 of products (CF_3 : CF_2) (90% selectivity), and for the major product as a mixture of regioisomers branched / linear (5.6 : 1) after flash column chromatography (Pentane/Et_2O 90:10). NMR data is only given for the major regioisomer.
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 2H), 3.92 (s, 3H), 3.39 (dqd, *J* = 11.4, 9.3, 4.2 Hz, 1H), 1.92 (ddd, *J* = 13.5, 11.4, 4.4 Hz, 1H), 1.74 (ddd, *J* = 13.8, 9.9, 4.1 Hz, 1H), 1.40 – 1.28 (m, 1H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.8, 140.2 (q, *J* = 2.2 Hz), 130.2, 130.0, 129.3, 127.0 (q, *J* = 280.2 Hz), 52.3, 48.2 (q, *J* = 26.7 Hz), 37.5 (q, *J* = 2.0 Hz), 24.9, 23.6, 21.0. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.5 (d, *J* = 9.2 Hz), -69.6 (d, *J* = 9.1 Hz). HRMS (APCI, m/z): calculated for $C_{14}H_{18}F_3O_2$ [M+H$^+$]: 275.1253, found 275.1257.

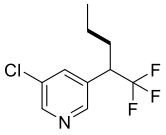
3-Chloro-5-(1,1,1-trifluoro-4-methyl pentane-2-yl)pyridine (50)



Synthesised from propane and trifluoromethyl alkene **64** following *GP1*. Obtained as a yellow oil in 54% yield (27.4 mg) as a mixture regioisomers branched / linear (4.9 : 1) after flash column chromatography (Hexane/AcOEt 90:10). NMR data is only given for the major regioisomer.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, *J* = 2.3 Hz, 1H), 8.41 (d, *J* = 2.0 Hz, 1H), 7.63 (s, 1H), 3.36 (dqd, *J* = 10.6, 8.9, 4.5 Hz, 1H), 1.94 – 1.70 (m, 2H), 1.41 – 1.23 (m, 2H), 0.90 (d, *J* = 9.9 Hz, 3H), 0.88 (d, *J* = 9.9 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 148.7, 148.4, 136.0, 132.5, 132.3 (q, *J* = 2.3 Hz), 126.5 (q, *J* = 279.8 Hz), 45.6 (q, *J* = 27.3 Hz), 37.2 (q, *J* = 1.8 Hz), 24.8, 23.5, 20.9. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.7 (d, *J* = 9.3 Hz), -69.8 (d, *J* = 9.0 Hz). **HRMS** (APCI, m/z): calculated for $C_{11}H_{14}ClF_3N$ [[M+H$^+$]: 252.0761, found 252.0759.

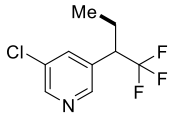
3-Chloro-5-(1,1,1-trifluoropentan-2-yl)pyridine (51)



Synthesised from ethane and trifluoromethyl alkene **64** following *GP2*. Obtained as yellow oil in 83% yield (39.2 mg) after flash column chromatography (Pentane/Et_2O 98:2).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 2.1 Hz, 1H), 8.40 (s, 1H), 7.63 (s, 1H), 3.29 (dqd, *J* = 11.1, 9.0, 4.5 Hz, 1H), 2.0 (ddd, *J* = 8.5, 4.3, 3.7 Hz, 1H), 1.93 – 1.73 (m, 1H), 1.32 – 1.15 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 148.8, 148.5, 135.9, 132.4, 132.3 (q, *J* = 2.3 Hz), 126.4 (q, *J* = 279.9 Hz), 47.4 (q, *J* = 27.4 Hz), 30.5 (q, *J* = 2.2 Hz), 20.0, 13.7. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.7 (d, *J* = 8.8 Hz). **HRMS** (APCI, m/z): calculated for $C_{10}H_{12}ClF_3N$ [M+H$^+$]: 238.0605; found: 238.0608

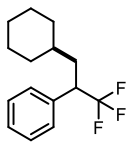
3-Chloro-5-(1,1,1-trifluorobutan-2-yl)pyridine (52)



Synthesised from methane and trifluoromethyl alkene **64** following *GP3*. Obtained as a yellow oil in 74% yield (33.0 mg) as a mixture (9 : 1) of desired product and acetonitrile activation coming from the residues of deuterated bottle, after flash column chromatography (Pentane/Et_2O 90:10). NMR data is only given of the major product.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.40 (d, *J* = 1.9 Hz, 1H), 7.63 (s, 1H), 3.18 (pd, *J* = 9.2, 4.3 Hz, 1H), 2.13 (dqd, *J* = 14.9, 7.4, 4.2 Hz, 1H), 1.85 (dqd, *J* = 14.9, 7.4, 4.2 Hz, 1H), 0.86 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 148.8, 148.6, 135.8, 132.4, 132.0 (q, *J* = 2.0 Hz), 127.5 (q, *J* = 279.9, 279.0 Hz), 49.2 (q, *J* = 27.2 Hz), 21.9 (q, *J* = 2.2 Hz), 11.5. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.6 (d, *J* = 9.2 Hz). **HRMS** (APCI, m/z): calculated for $C_9H_{10}ClF_3N$ [M+H$^+$]: 224.0448; found: 224.0455.

4-(3-Cyclohexyl-1,1,1-trifluoropropan-2-yl)benzonitrile (55)

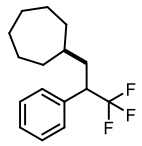


Synthesised from cyclohexane **1** and trifluoromethyl alkene **2** following *Method 4* with thiol **50**. Obtained as colourless oil in 45% yield (23.1 mg) after flash column chromatography (Pentane). Only visible by PMA stain.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.04 (m, 5H), 3.28 (pd, *J* = 9.6, 4.3 Hz, 1H), 1.81 – 1.62 (m, 2H), 1.62 – 1.48 (m, 5H), 1.09 – 0.72 (m, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 129.2, 128.7, 128.1, 47.4 (q, *J* = 27.4, 26.1 Hz), 36.2, 34.3, 34.1, 32.0, 29.9, 26.6, 26.2, 26.0. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.9 (d, *J* = 9.6 Hz). The spectroscopic data is in accordance with reported literature.[28]

[28] M. Ueda and H. Ito, *J. Polym. Sci. A Polym. Chem.* **1988**, *26*, 89-98.

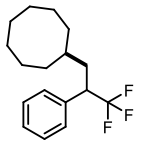
(3,3,3-Trifluoro-2-phenylpropyl)cycloheptane (56)



Synthesised from cycloheptane **66** and trifluoromethyl alkene **2** following *Method 4* with thiol **54**. Obtained as colourless oil in 40% yield (21.6 mg) after flash column chromatography (Pentane). Only visible by PMA stain.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.06 (m, 5H), 3.55 – 3.18 (h, *J* = 9.0, 7.9 Hz, 1H), 1.83 (t, *J* = 8.3, 5.6 Hz, 2H), 1.75 – 1.52 (m, 4H), 1.46 (m, 3H), 1.37 – 1.25 (m, 3H), 1.26 – 1.10 (m, 2H), 0.92 – 0.80 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 128.9, 128.3, 127.7, 47.5 (q, *J* = 26.4, 25.9 Hz), 36.2, 35.4, 35.1, 33.9, 32.3, 28.4, 28.2, 25.9, 25.6, 22.1, 13.8. **^{19}F NMR (282 MHz, $CDCl_3$)** δ. -69.8 (d, *J* = 9.3 Hz). **HRMS** (APCI, m/z): calculated for $C_{16}H_{21}F_3$ [M^+]: 270.1590; found: 270.1586.

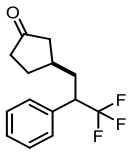
3,3,3-Trifluoro-2-phenylpropyl)cyclooctane (57)



Synthesised from cyclooctane **67** and trifluoromethyl alkene **2** following *Method 4* with thiol **54**. Obtained as colourless oil in 35% yield (19.9 mg) after flash column chromatography (Pentane). Only visible by PMA stain.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.20 (m, 5H), 3.32 (pd, *J* = 9.4, 5.6 Hz, 1H), 1.83 (t, *J* = 6.1 Hz, 2H), 1.67 – 1.26 (m, 15H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 129.3, 128.7, 128.2, 47.9 (q, *J* = 26.0 Hz), 36.4, 33.7, 33.5, 30.0, 27.6, 27.2, 26.3, 25.3, 25.1. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.7 (d, *J* = 9.6 Hz). **HRMS** (APCI, m/z): calculated for $C_{17}H_{23}F_3$ [M^+]: 284.1746; found: 284.1742.

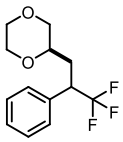
3-(3,3,3-Trifluoro-2-phenylpropyl)cyclopentan-1-one (58)



Synthesised from cyclopentanone **73** and trifluoromethyl alkene **2** following *Method 4* with thiol **53**, in 48 h. Obtained as colourless oil in 53% yield (27.5 mg) as a 1:1 mixture of diastereoisomers after flash column chromatography (Pentane/Et_2O 90:10).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 – 6.95 (m, 5H), 3.49 – 3.19 (m, 1H), 2.33 – 1.92 (m, 7H), 1.86 – 1.43 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 218.2, 218.0, 129.0, 128.6, 128.5, 49.8 (q, *J* = 39.4 Hz), 49.4 (q, *J* = 39.4 Hz), 45.4, 44.2, 38.6, 38.5, 38.3, 34.9, 34.7, 34.3, 30.0, 29.8, 28.9, 23.4. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.9 (d, *J* = 9.1 Hz), -70.0 (d, *J* = 9.3 Hz). **HRMS** (APCI, m/z): calculated for $C_{14}H_{16}F_3O$ [$M+H^+$]: 257.1148; found: 257.1143.

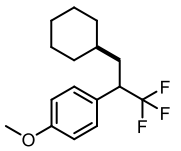
2-(3,3,3-Trifluoro-2-phenylpropyl)-1,4-dioxane (59)



Synthesised from dioxane **74** and trifluoromethyl alkene **2** following *Method 4* with thiol **53**, in 48 h. Obtained as colourless oil in 42% yield (22.6 mg) as a 1:1 mixture of diastereoisomers after flash column chromatography (Pentane/Et_2O 50:50). Only visible by PMA stain.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.15 (m, 5H), 3.94 – 3.38 (m, 6H), 3.22 (m, 1H), 2.21 – 1.70 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 129.2, 129.0, 128.9, 128.4, 128.4, 72.7, 71.4, 71.3, 70.9, 66.9, 66.7, 66.6, 45.5 (q, *J* = 21.1, 18.1 Hz), 32.0, 30.9. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.5 (d, *J* = 9.6 Hz), -69.7 (d, *J* = 9.7 Hz). **HRMS** (APCI, m/z): calculated for $C_{13}H_{16}F_3O_2$ [$M+H^+$]: 261.1097; found: 261.1095.

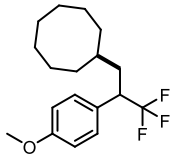
1-(3-Cyclohexyl-1,1,1-trifluoropropan-2-yl)-4-methoxybenzene (60)



Synthesised from cyclohexane **1** and trifluoromethyl alkene **110** following *Method 4* with thiol **53** in 48 h. Obtained as colourless oil in 30% isolated yield, 40% yield (*based on recovered starting material*) (17.2 mg) after flash column chromatography (Pentane/Et_2O 95:5). Only visible by PMA stain.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.2 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 3.82 (s, 3H), 3.31 (pd, *J* = 10.0, 4.1 Hz, 1H), 1.89 – 1.58 (m, 8H), 1.20 – 0.79 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 159.4, 130.2, 127.1 (q, *J* = 160.2, 152.0 Hz) 114.1, 55.4, 46.5 (q, *J* = 26.3, 25.8 Hz), 36.1, 34.3, 34.0, 31.9, 31.1, 29.9, 26.6, 26.2, 26.0.**^{19}F NMR (282 MHz, $CDCl_3$)** δ -70.3 (d, *J* = 9.6 Hz). **HRMS** (APCI, m/z): calculated for $C_{16}H_{22}F_3O$ [M^+]: 287.1617; found: 287.1614.

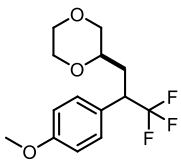
(3,3,3-Trifluoro-2-(4-methoxyphenyl)propyl)cyclooctane (61)



Synthesised from cyclooctane **67** and trifluoromethyl alkene **110** following *Method 4* with thiol **53** in 48 h. Obtained as colourless oil in 35% isolated yield, 53% yield (*based on recovered starting material*) (22.8 mg) after flash column chromatography (Pentane/Et_2O 95:5). Only visible by PMA stain.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 3.81 (s, 3H), 3.27 (pd, *J* = 9.8, 5.0 Hz, 1H), 1.84 – 1.73 (m, 2H), 1.66 – 1.27 (m, 15H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 159.5, 130.3, 114.2, 55.4, 47.2 (q, *J* = 26.0 Hz), 36.3, 33.8, 33.5, 29.9, 27.6, 27.2, 26.3, 25.4, 25.1. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -70.1 (d, *J* = 9.5 Hz). **HRMS** (APCI, m/z): calculated for $C_{18}H_{26}F_3O$ [$M+H^+$]: 315.1930; found: 315.1928.

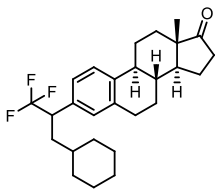
2-(3,3,3-Trifluoro-2-(4-methoxyphenyl)propyl)-1,4-dioxane (62)



Synthesised from dioxane **74** and trifluoromethyl alkene **110** following *Method 4* with thiol **53** in 48 h. Obtained as colourless oil in 54% isolated yield, 61% yield (*based on recovered starting material*) (32.8 mg) as a 1:1 mixture of diastereoisomers after flash column chromatography (Pentane/Et_2O 20:80). Only visible by PMA stain.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.3 Hz, 2H), 6.89 (dd, *J* = 8.6, 6.9 Hz, 2H), 3.81 (s, 3H), 3.74 – 3.39 (m, 7H), 3.25 (pd, *J* = 11.4, 9.9 Hz, 1H), 2.14 – 1.89 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 159.7, 159.6, 130.3, 130.0, 127.2 (q, *J* = 159.4, 152.1Hz), 126.1 (q, *J* = 159.4, 152.1Hz), 114.3, 114.3, 72.8, 71.5, 71.3, 70.9, 66.9, 66.7, 66.6, 55.4, 44.9 (q, *J* = 23.5 Hz), 44.7 (q, *J* = 30.5, 26.8, Hz), 32.0, 31.9, 31.0, 30.9. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.7 (d, *J* = 9.5 Hz), -70.1 (d, *J* = 9.8 Hz). **HRMS** (APCI, m/z): calculated for $C_{14}H_{17}F_3O_3$ [M^+]: 290.1124; found: 290.1116.

(8R,9S,13S,14S)-3-(3-Cyclohexyl-1,1,1-trifluoropropan-2-yl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (63)



Synthesised from cyclohexane **1** and modified trifluoromethyl alkene from *Estrone* **122** following *Method 4* with thiol **53**, in 48 h. Obtained as colourless oil in 31% isolated yield (26.8 mg) as a 1:1 mixture of diastereoisomers after flash column chromatography (Pentane/Et_2O 80:20).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 2.7 Hz, 1H), 6.98 (s, 1H), 3.28 (pd, *J* = 9.7, 4.2 Hz, 1H), 2.92 (dd, *J* = 9.1, 4.3 Hz, 2H), 2.51 (dd, *J* = 18.7, 8.7 Hz, 2H), 2.45 – 2.28 (m, 2H), 2.19 – 1.95 (m, 4H), 1.83 – 1.72 (m, 2H), 1.68 – 1.45 (m, 10H), 1.39 – 1.21 (m, 4H), 1.16 – 1.06 (m, 2H), 0.92 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 221.0, 139.6, 2x[136.8], 132.7 (q, *J* = 2.8, 0.3 Hz)], 132.6 (q, *J* = 2.8, 0.3 Hz)], 129.9, 129.6, 129.2, 128.6, 126.6, 126.3, 126.0 (q, *J* = 160.3, 158.1 Hz), 2x[125.6], 125.5, 2x[124.4], 117.3, 50.7, 48.2, 46.9 (q, *J* = 26.6 Hz), 44.5, 38.2, 38.1, 36.3, 36.2, 35.9, 34.3, 34.0, 32.0, 31.8, 29.8, 29.6, 29.5, 3x[26.6], 26.2, 25.9, 25.7, 21.7, 14.0. **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.7 (d, *J* = 5.4 Hz), -69.7 (d, *J* = 5.5 Hz). **HRMS** (APCI, m/z): calculated for $C_{27}H_{36}F_3O$ [M+H$^+$]: 433.2713; found: 433.2716.

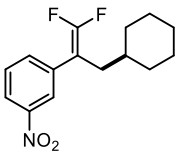
5,5,5-Trifluoro-4-phenylpentanenitrile (123)

Obtained as a Side-Product when non-deuterated acetonitrile was used with trifluoromethyl alkene **2** following *Method 4* with thiol **53**. Colourless oil obtained after flash column chromatography (Pentane/Et_2O 90:10). Only visible by PMA stain. Product was obtained with *grease* impurities shown in ^{1}H NMR.

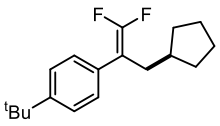
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.374 (m, 3H), 7.22 – 7.08 (m, 1H), 3.42 (m, 1H), 2.50 – 2.30 (m, 2H), 2.23 – 2.11 (m, 2H). **^{19}F NMR (282 MHz, $CDCl_3$)** δ -69.7 (d, *J* = 8.9 Hz).The spectroscopic data is in accordance with reported literature.[29]

[29] Z. Liu, H. Shen, H. Xiao, Z. Wang, L. Zhu, and C. Li, *Org. Lett.*, **2019**, *21*, 13, 5201-5205.

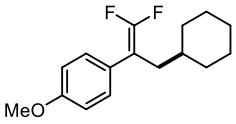
9. Unsuccessful Results



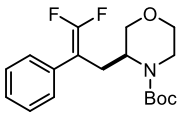
124
-%



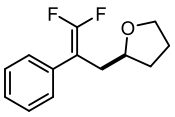
125
traces



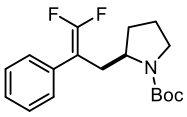
126, 10 % isolated yield
mixture 2:1 with SM



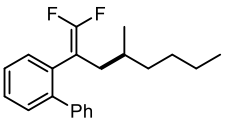
127
-%



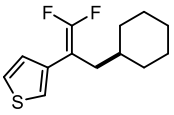
128
-%



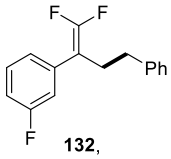
129
-%



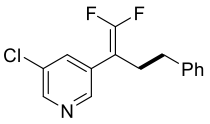
130
-%



131
15 %

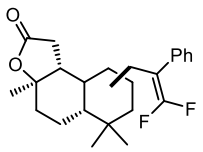


132,
30 % mixture of products
(20% + 8% hydroalkylation + undefined)

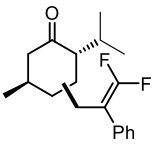


133,
12 % isolated yield

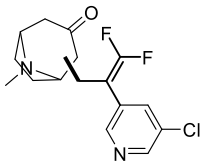
Selectivity Issues



From Scareolide
134, 20 %, complex mixture of isomers



From L-Mentone
135, 37 %, complex mixture of isomers



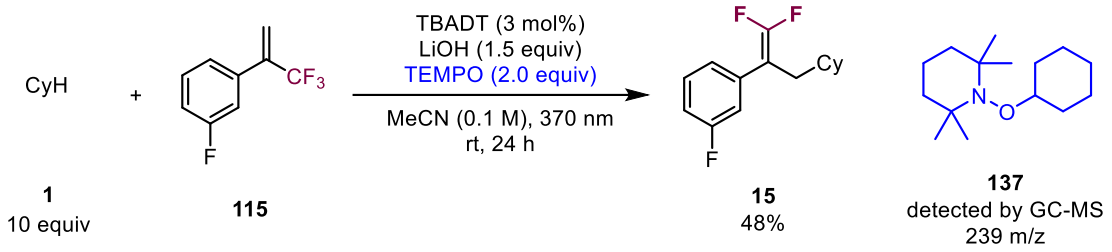
From Tropinone
136, 9 %, complex mixture of isomers

Otherwise noted, yields were determined by ^{19}F-NMR analysis with α,α,α–trifluorotoluene as internal standard. *Method 1* was employed for all molecules, except molecules **133** and **136** where *Method 2* was used.

10. Mechanistic studies

10.1 Radical trapping experiment

The radical trapping experiment was performed using TEMPO as radical scavenger. The experiment was performed following Method *1*, adding 2 equiv of TEMPO.



1
10 equiv

115

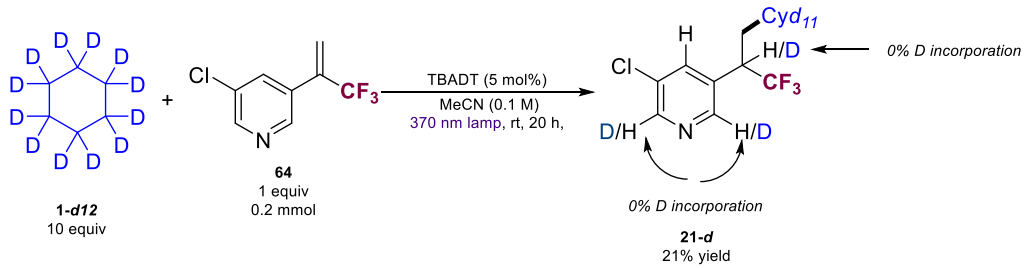
15
48%

137
detected by GC-MS
239 m/z

Observation: GC-MS analysis of the reaction crude revealed the formation of the TEMPO-cyclohexyl adduct **137** was obtained (rt: 8.59 min, 239 m/z). Product **15** was formed in a reduced 48% yield (determined by ^{19}F-NMR analysis using α,α,α−trifluorotoluene as internal standard) thus showing partial inhibition due to the presence of the radical scavenger.

10.2 Deuterium Labelling Experiments

The reaction was carried out following *Method 3* using deuterated cyclohexane (99.95% *d*) without drying MeCN prior to the reaction.

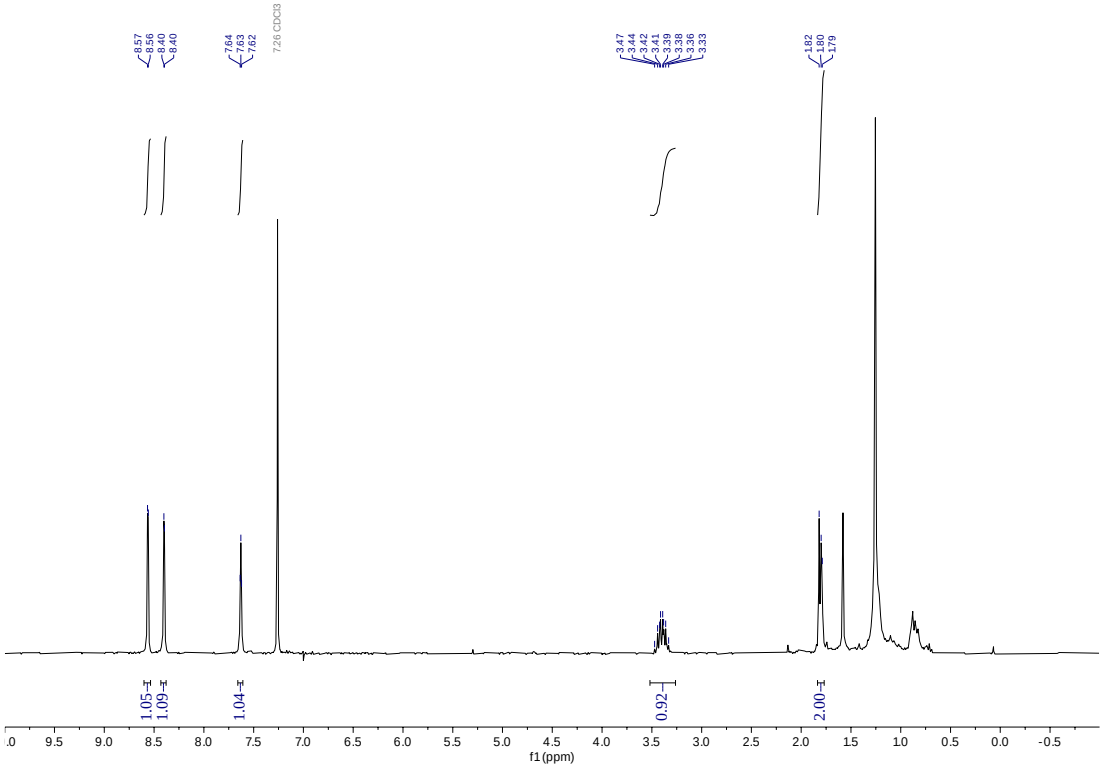


1-*d12*
10 equiv

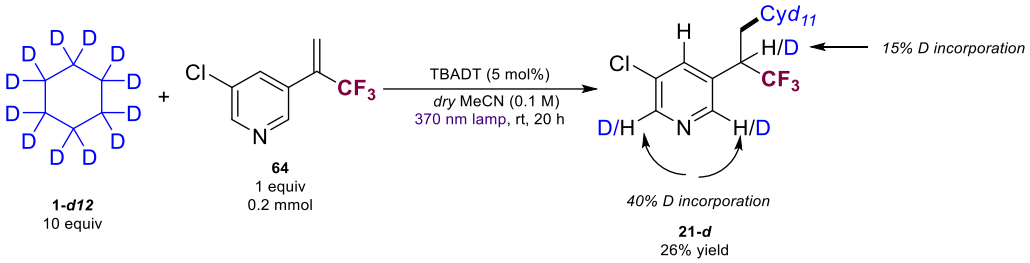
64
1 equiv
0.2 mmol

21-*d*
21% yield

^{1}H NMR (300 MHz, $CDCl_3$)



The reaction was carried out following *Method 3* using deuterated cyclohexane (99.95% *d*) and *dry* MeCN

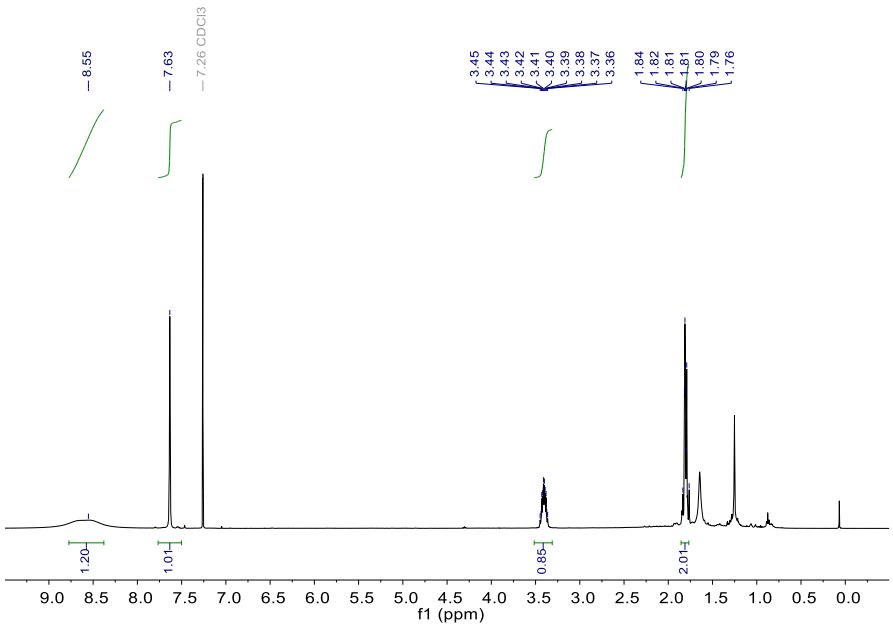


1-*d12*
10 equiv

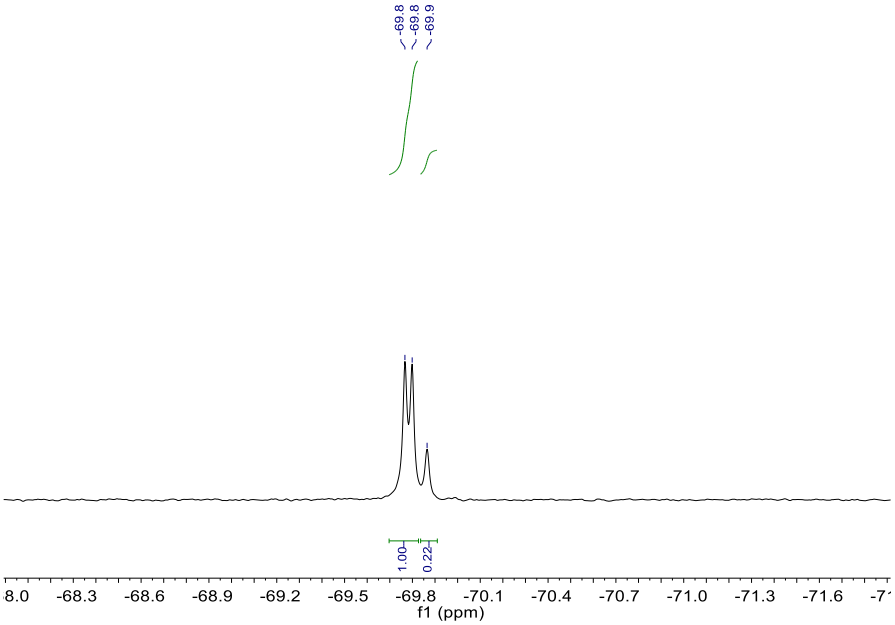
64
1 equiv
0.2 mmol

21-*d*
26% yield

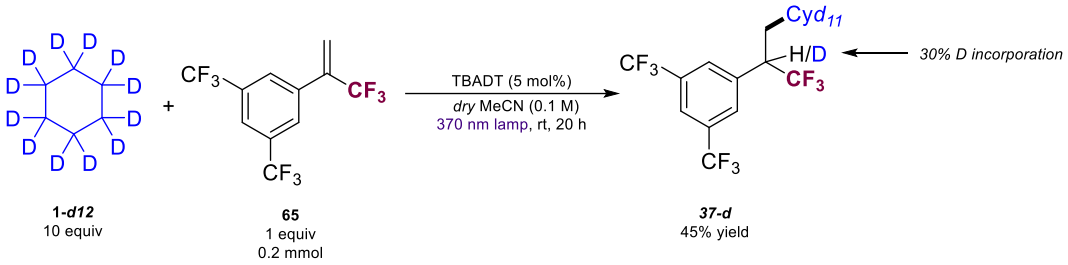
^{1}H NMR (300 MHz, $CDCl_3$)



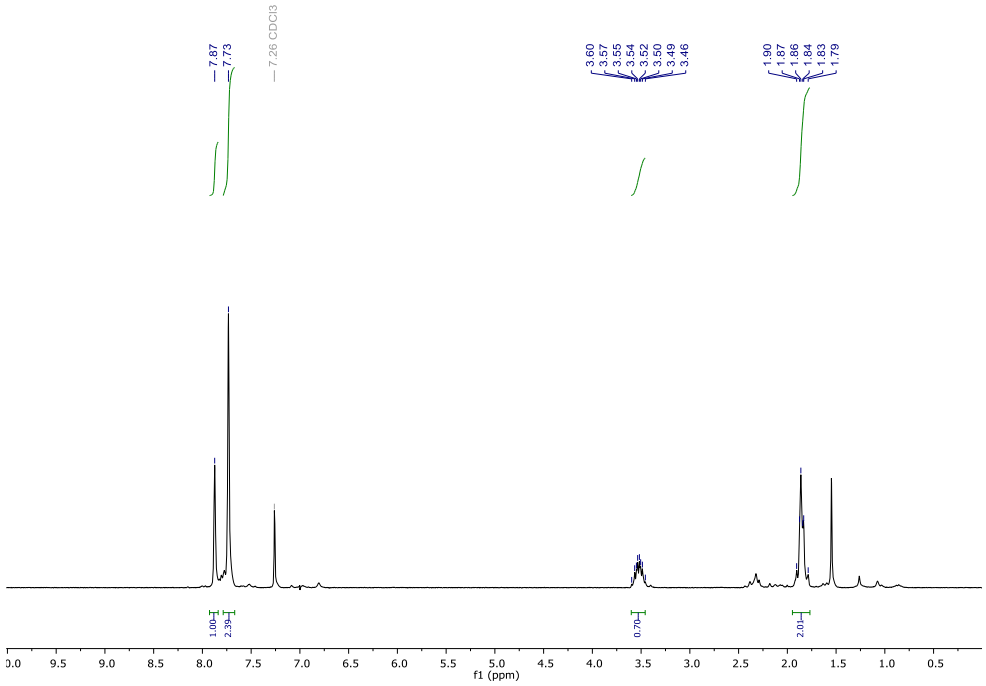
^{19}F-NMR (282 MHz, $CDCl_3$)



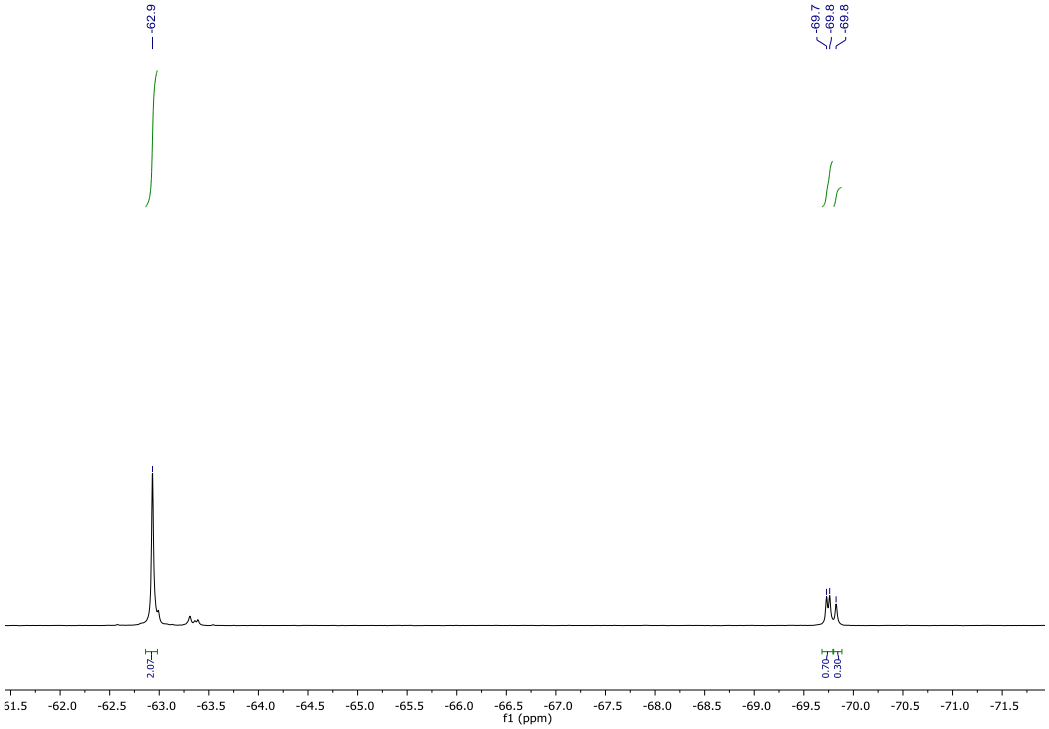
The reaction was carried out following *Method 3* using deuterated cyclohexane (99.95% *d*) and *dry* MeCN



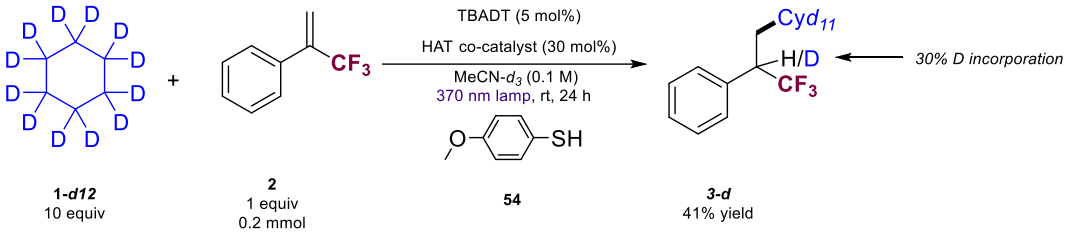
^{1}H NMR (300 MHz, $CDCl_3$)



^{19}F-NMR (282 MHz, $CDCl_3$)



The reaction was carried out following *Method 4* using deuterated cyclohexane (99.95% *d*).



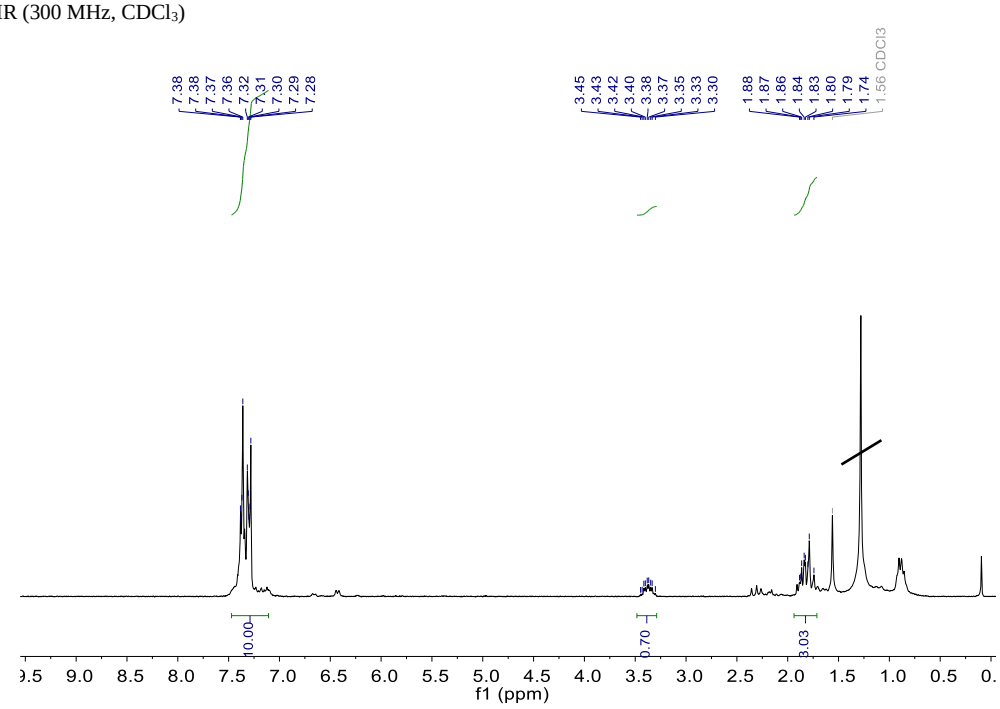
1-*d12*
10 equiv

2
1 equiv
0.2 mmol

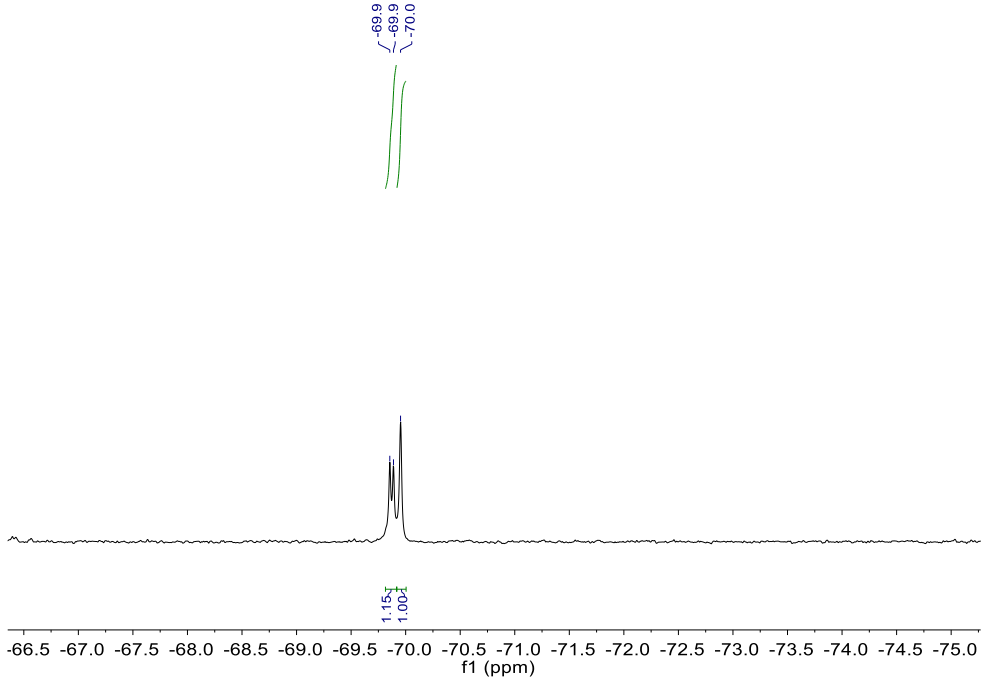
54

3-d
41% yield

^{1}H NMR (300 MHz, $CDCl_3$)

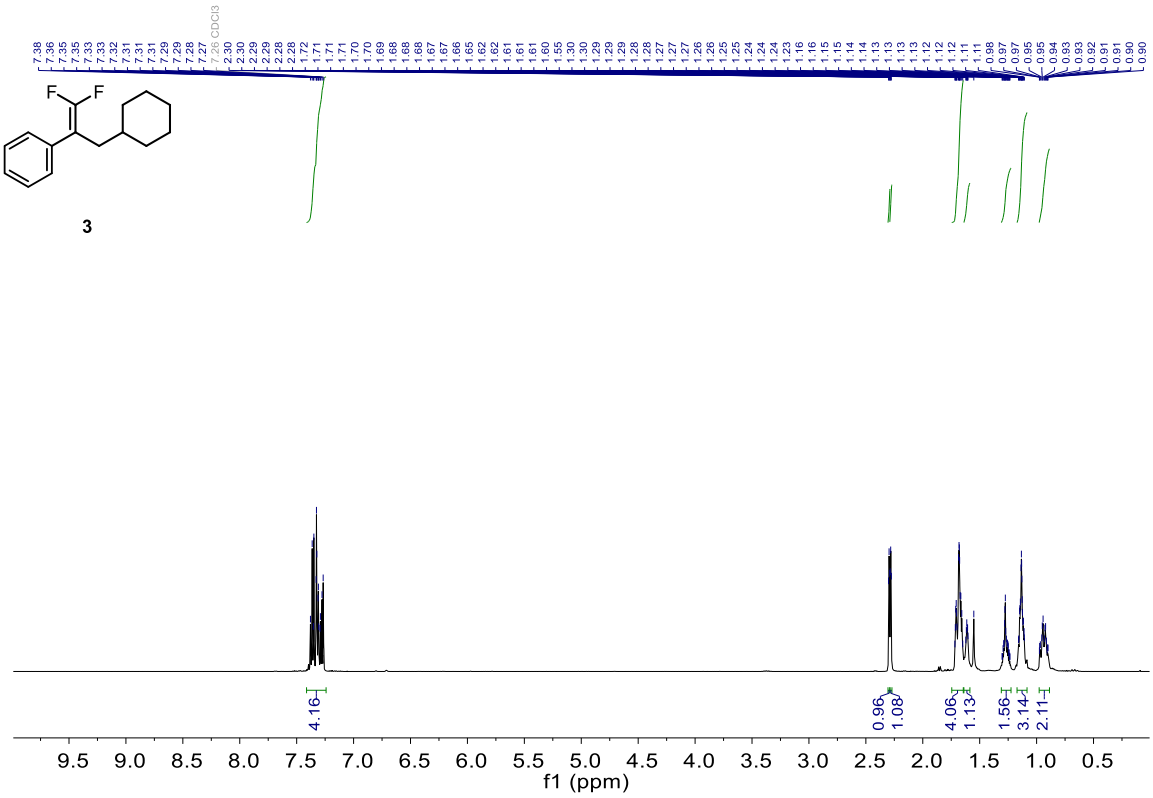


^{19}F-NMR (282 MHz, $CDCl_3$)

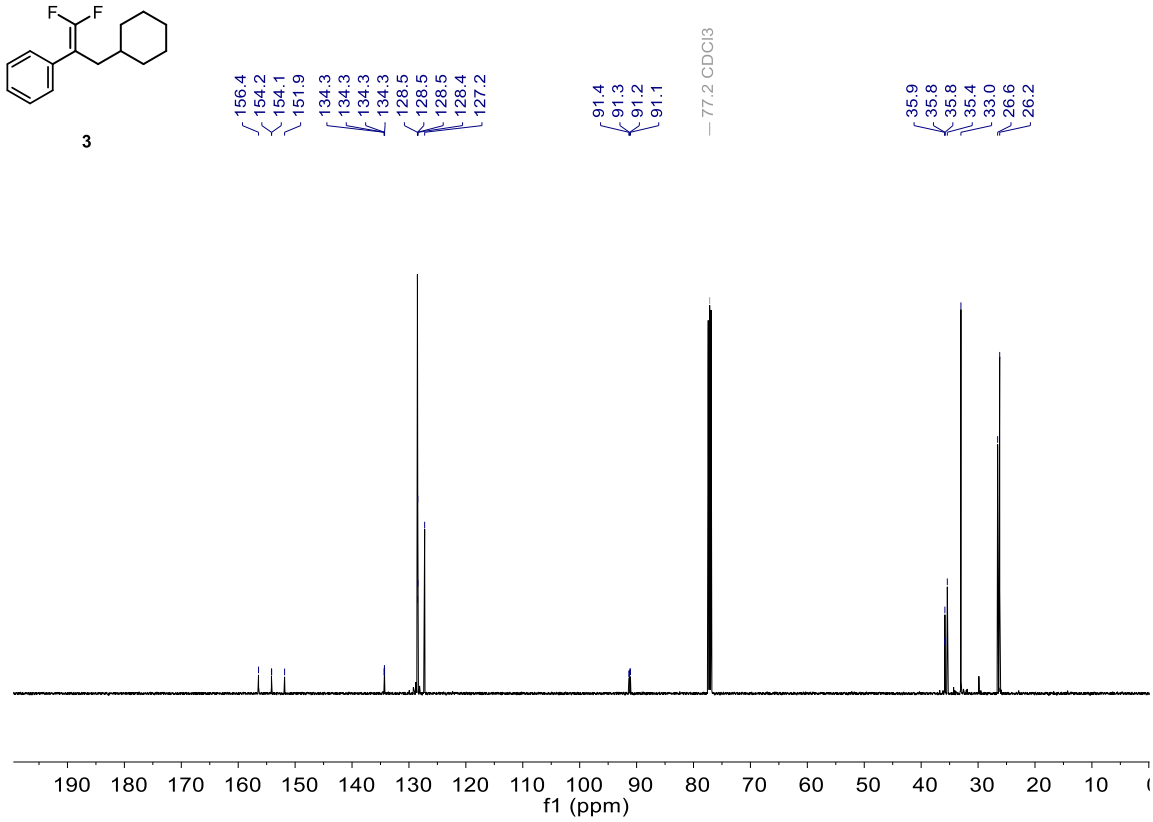


11. NMR spectra

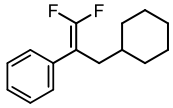
^{1}H NMR (500 MHz, $CDCl_3$)



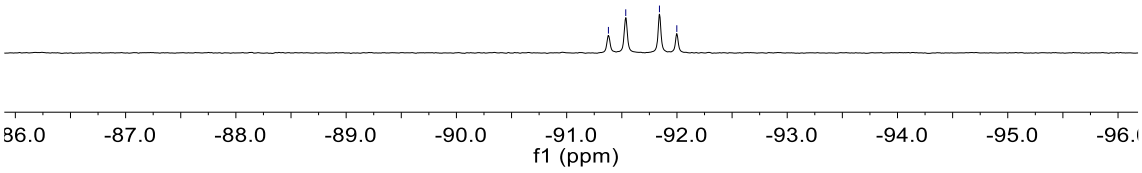
^{13}C NMR (126 MHz, $CDCl_3$)



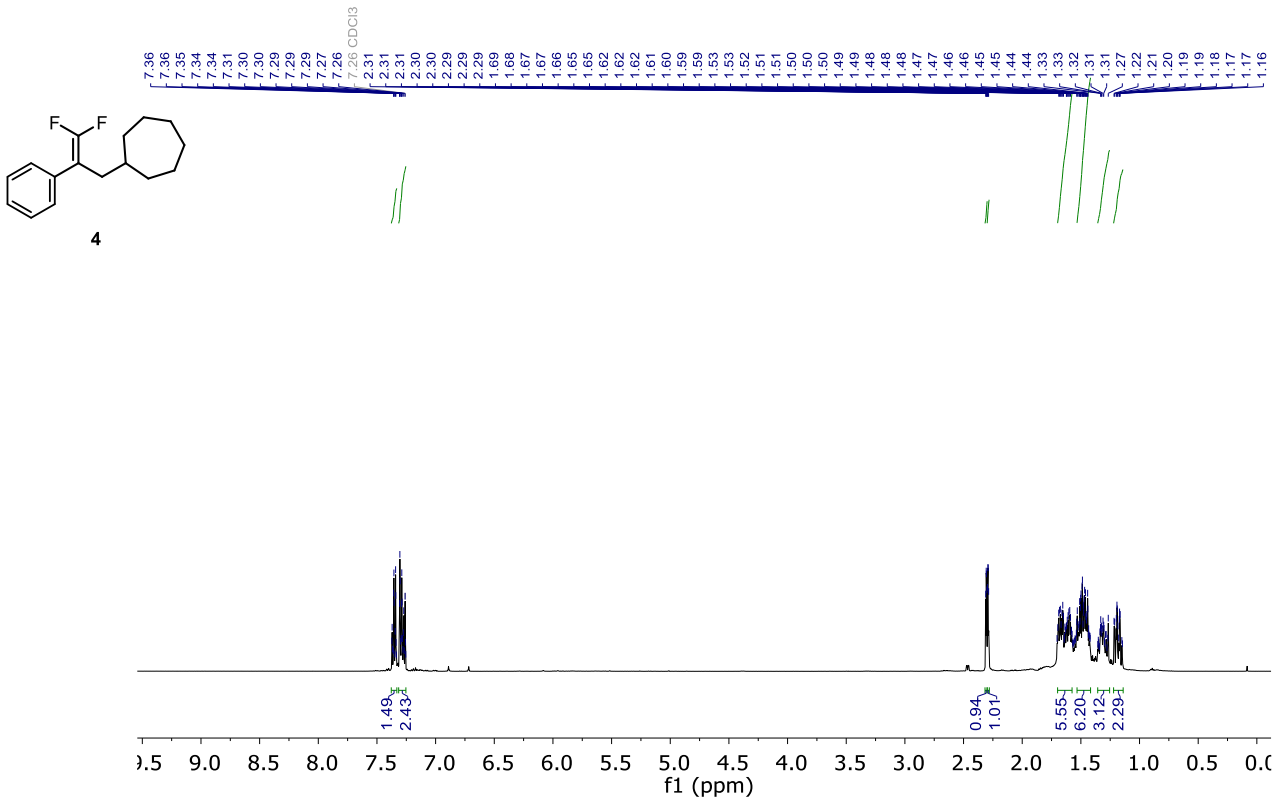
^{19}F NMR (282 MHz, $CDCl_3$)



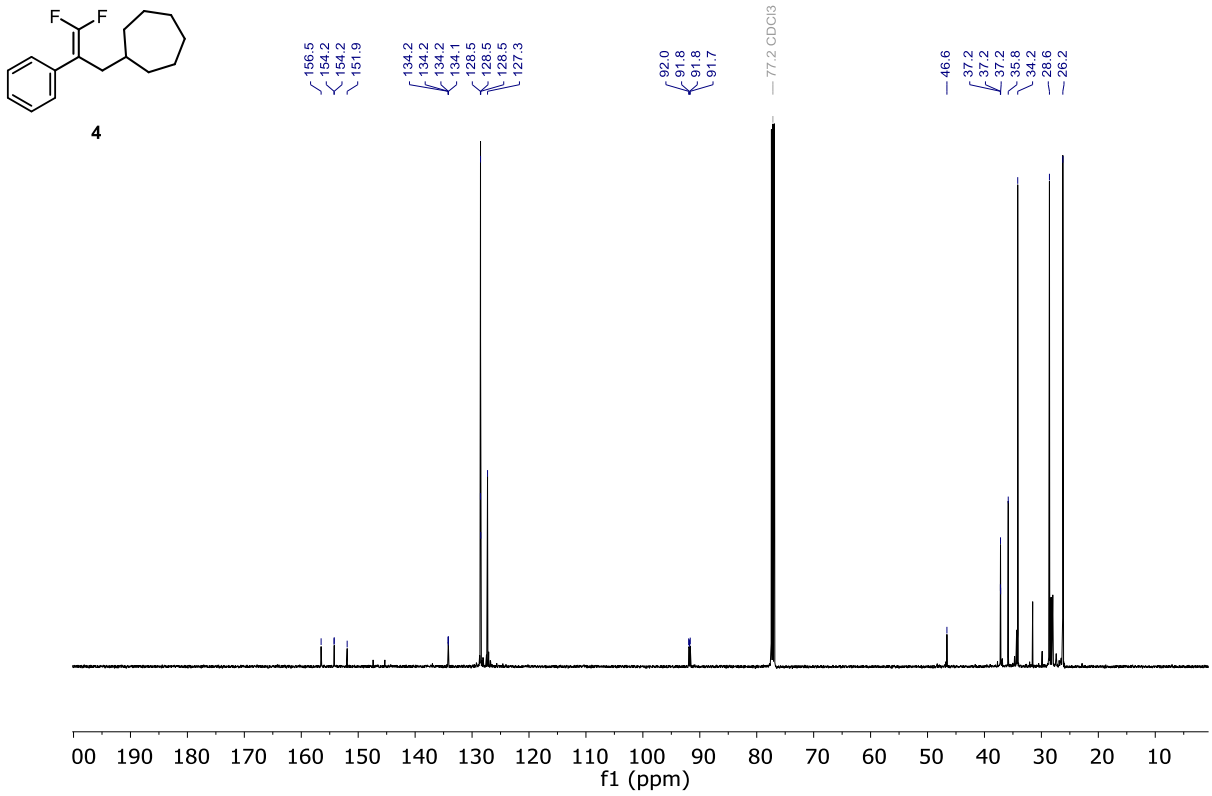
3



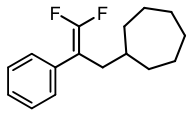
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

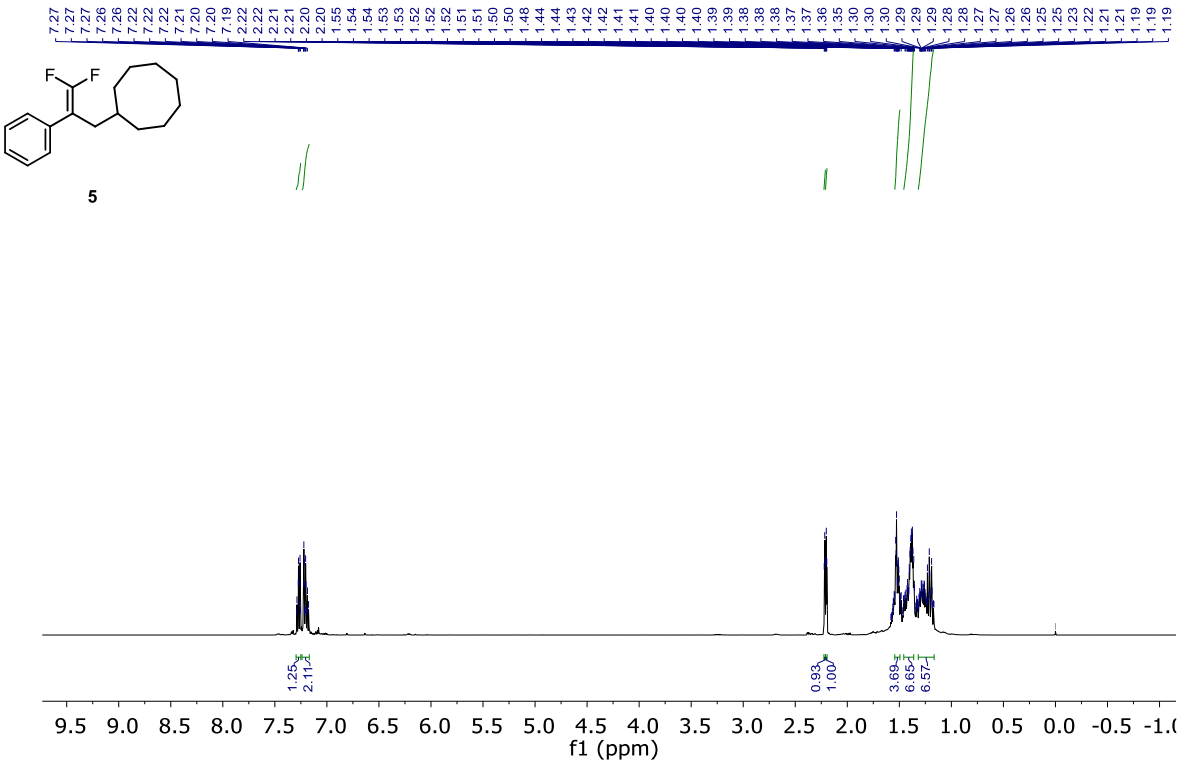


^{19}F NMR (282 MHz, $CDCl_3$)

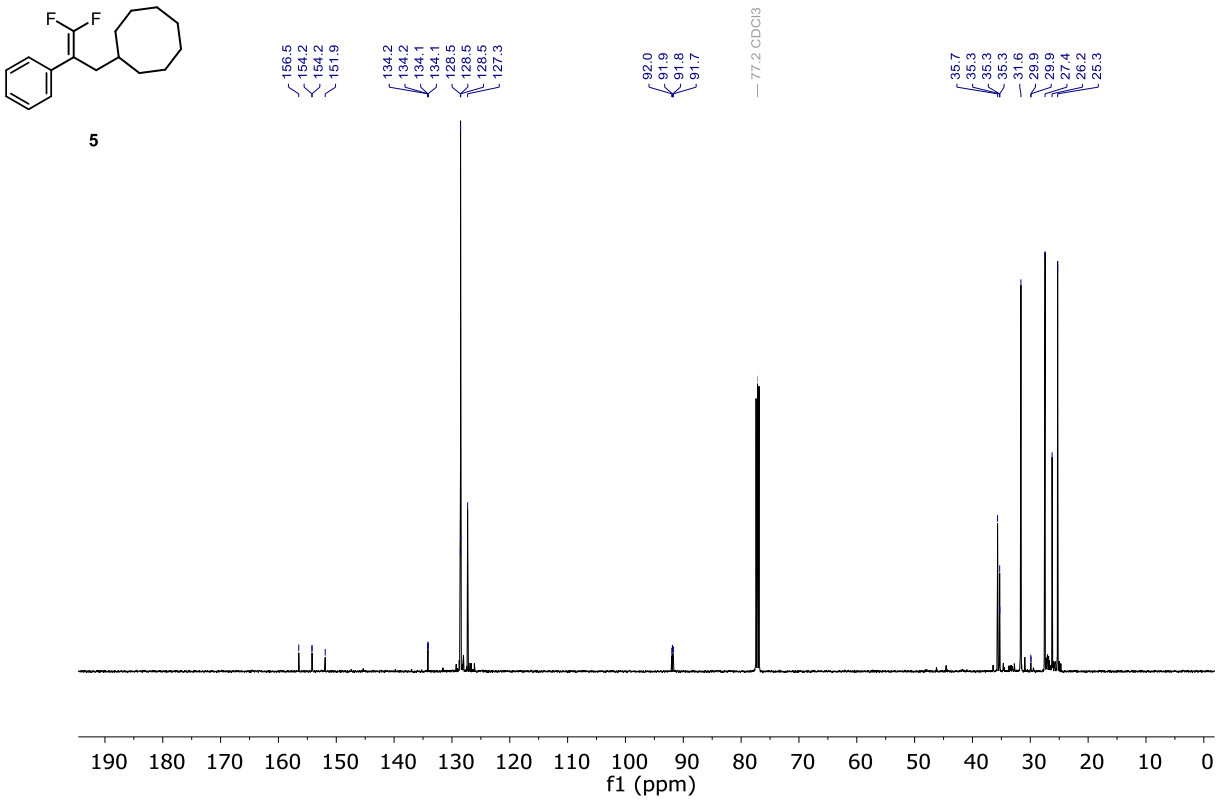


4

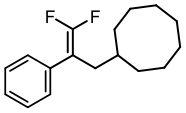
^{1}H NMR (500 MHz, $CDCl_3$)



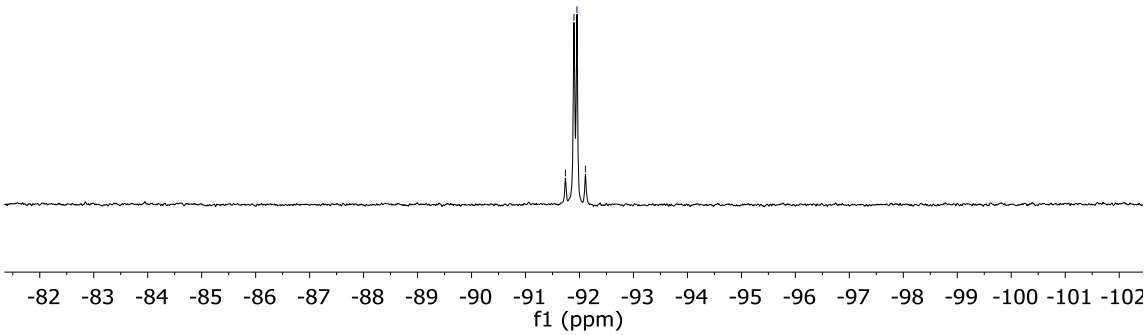
^{13}C NMR (126 MHz, $CDCl_3$)



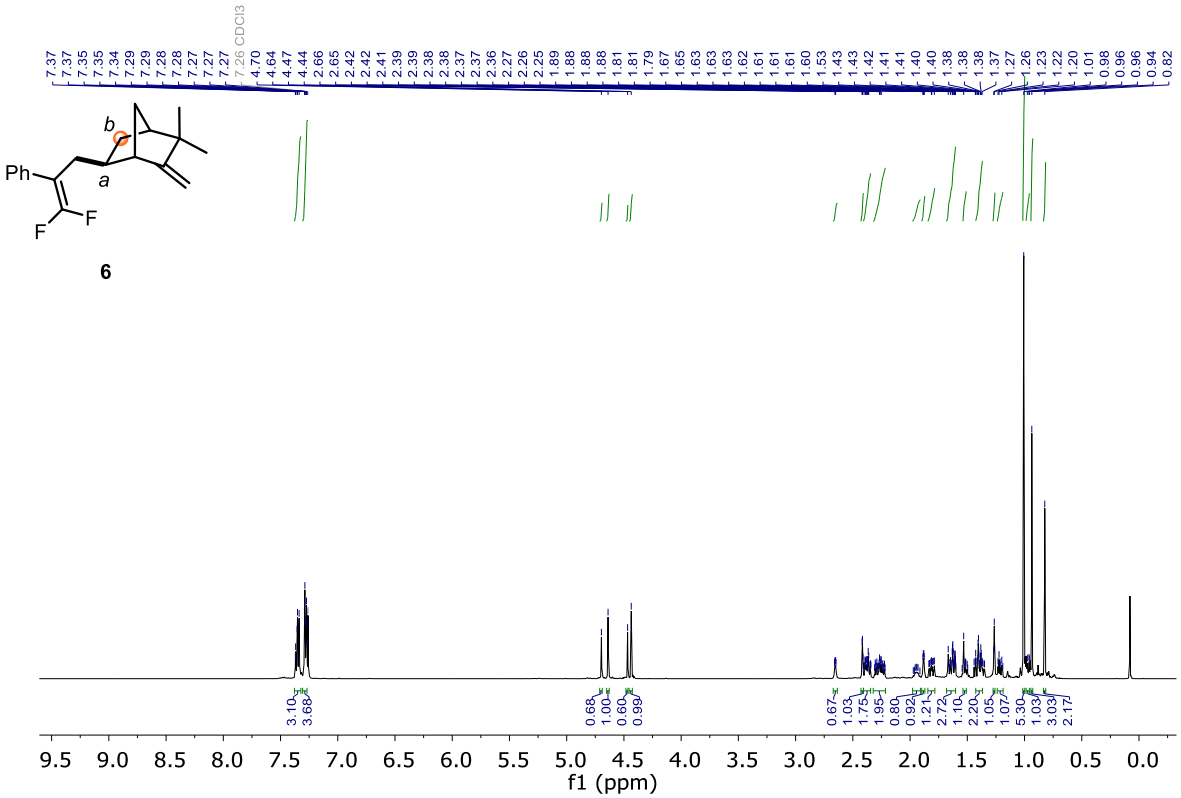
^{19}F NMR (282 MHz, $CDCl_3$)



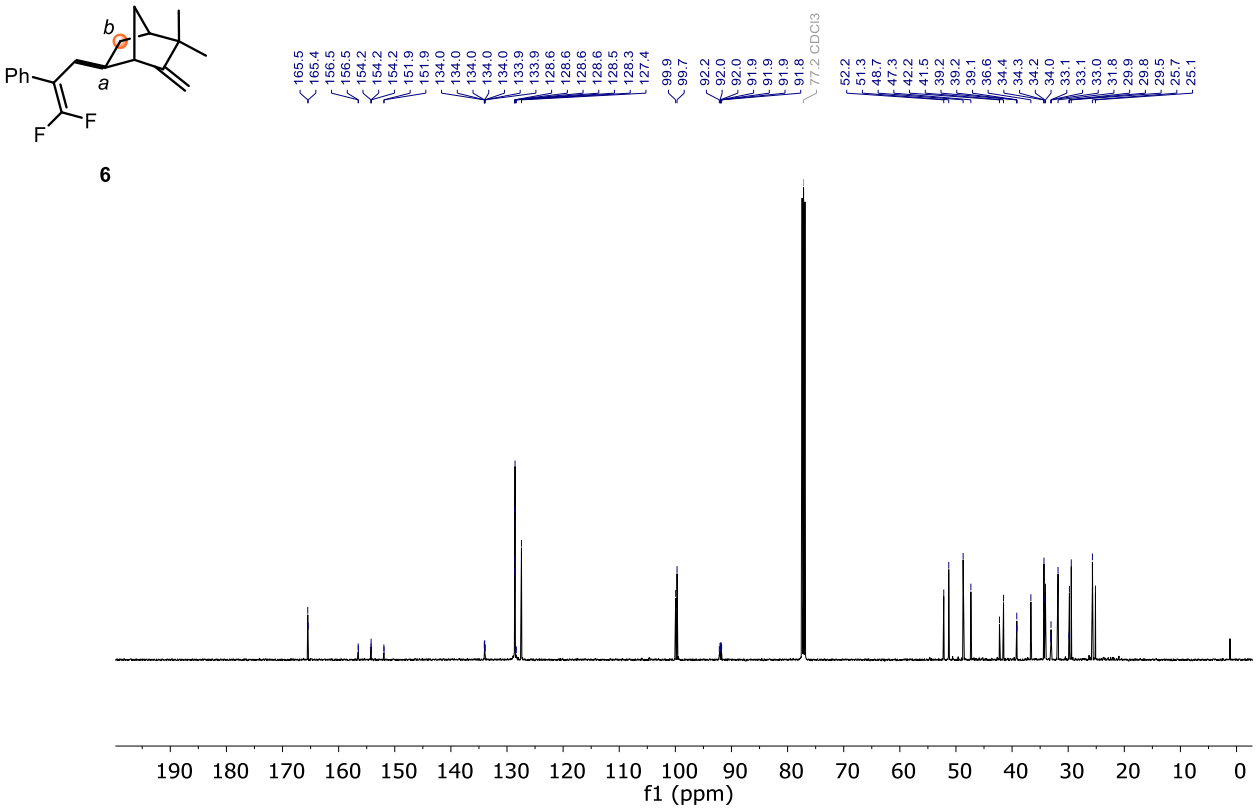
5



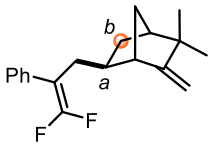
^{1}H NMR (500 MHz, $CDCl_3$)



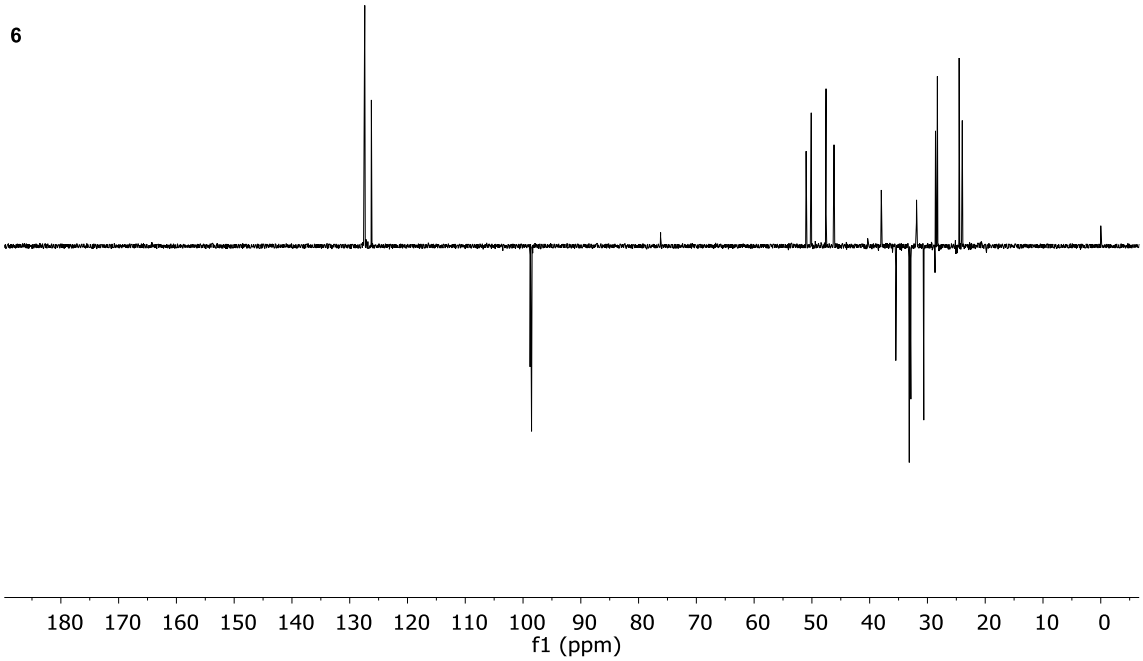
^{13}C NMR (126 MHz, $CDCl_3$)



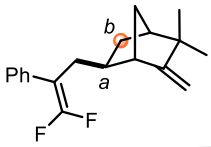
DEPT-135 (126 MHz, $CDCl_3$)



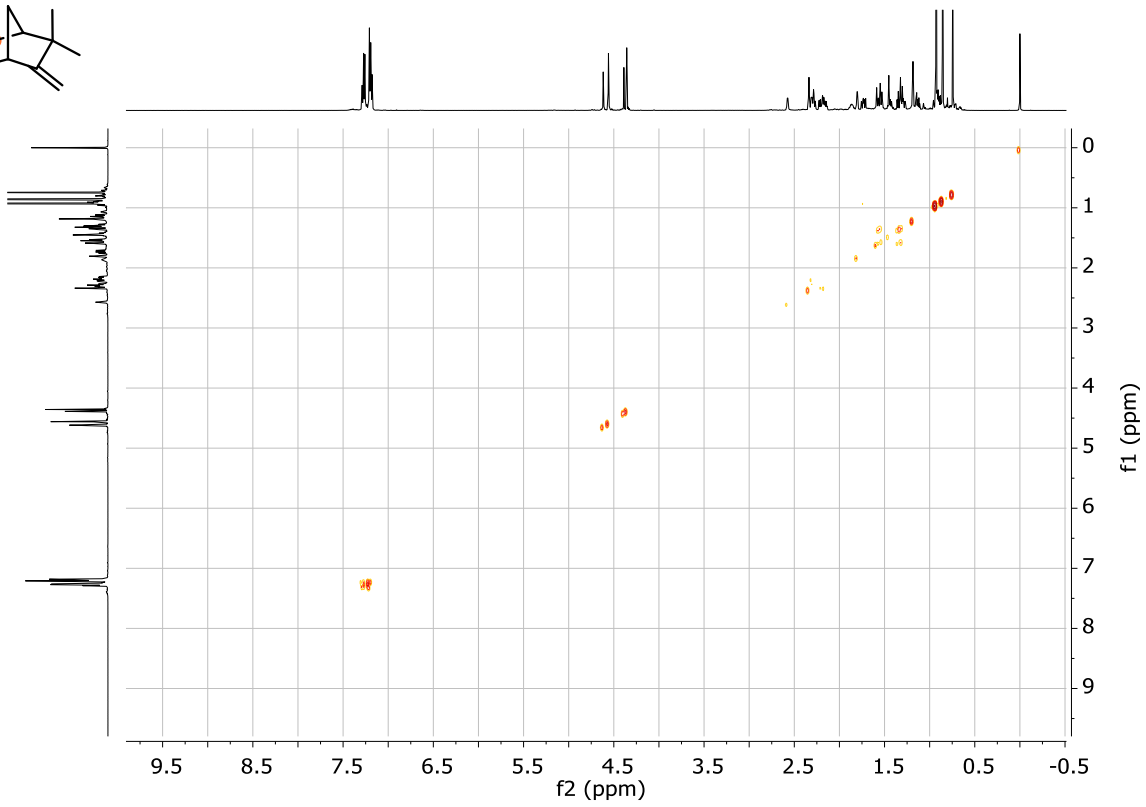
6



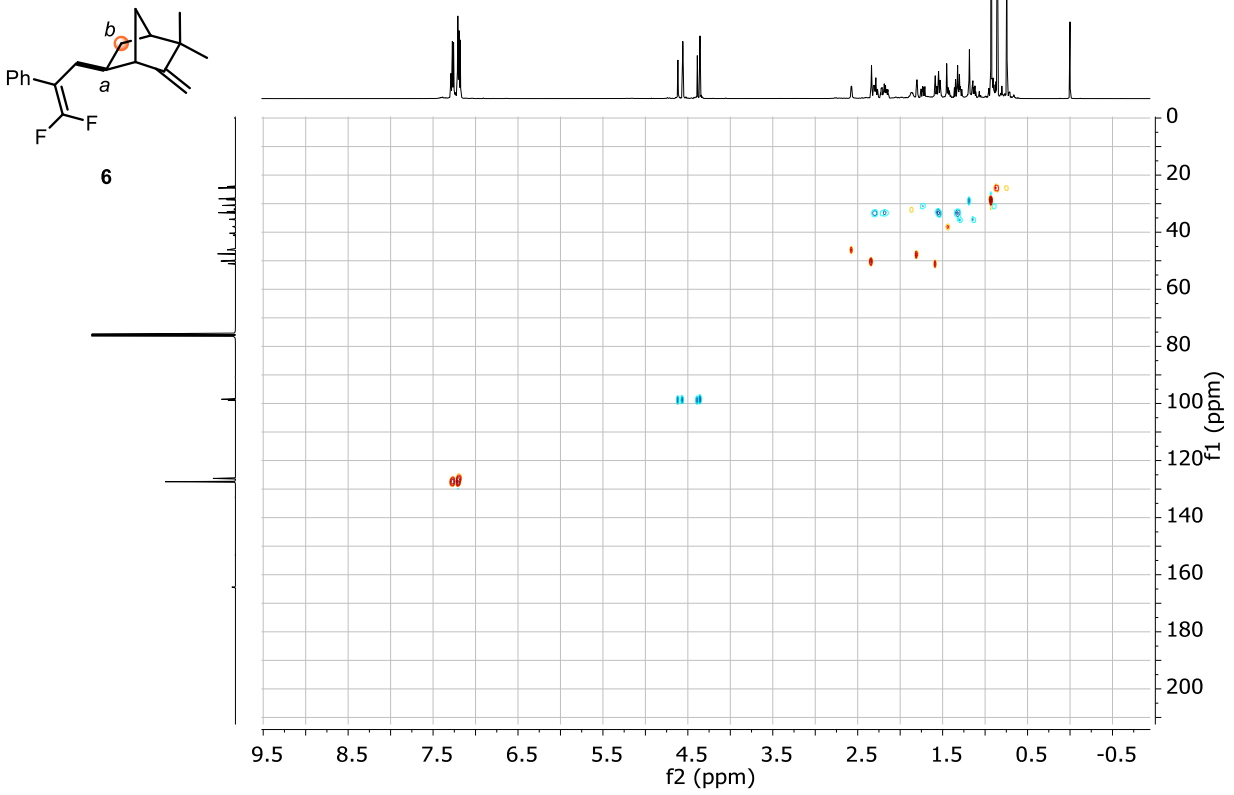
COSY (500 MHz, $CDCl_3$)



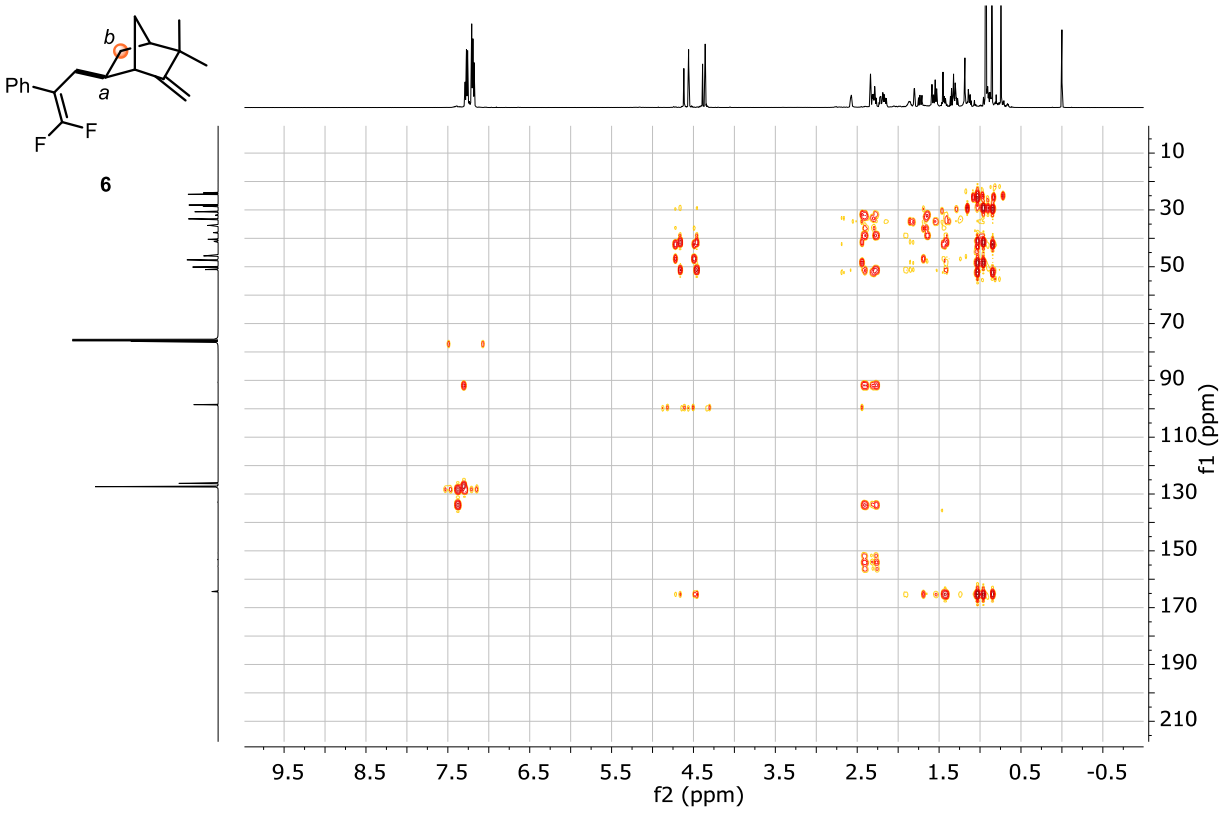
6



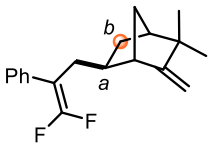
HSQC (500, 126, MHz, $CDCl_3$)



HMBC (500, 126, MHz, $CDCl_3$)

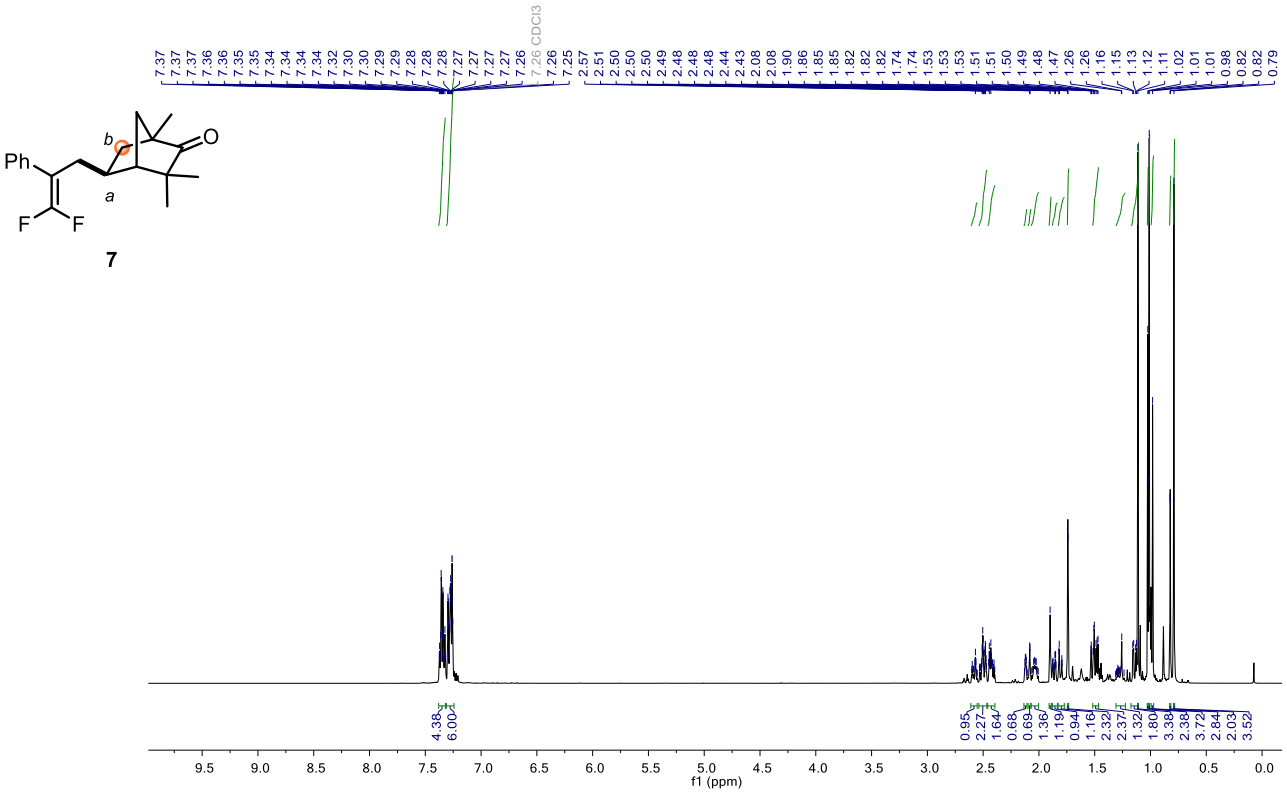


^{19}F NMR (282 MHz, $CDCl_3$)

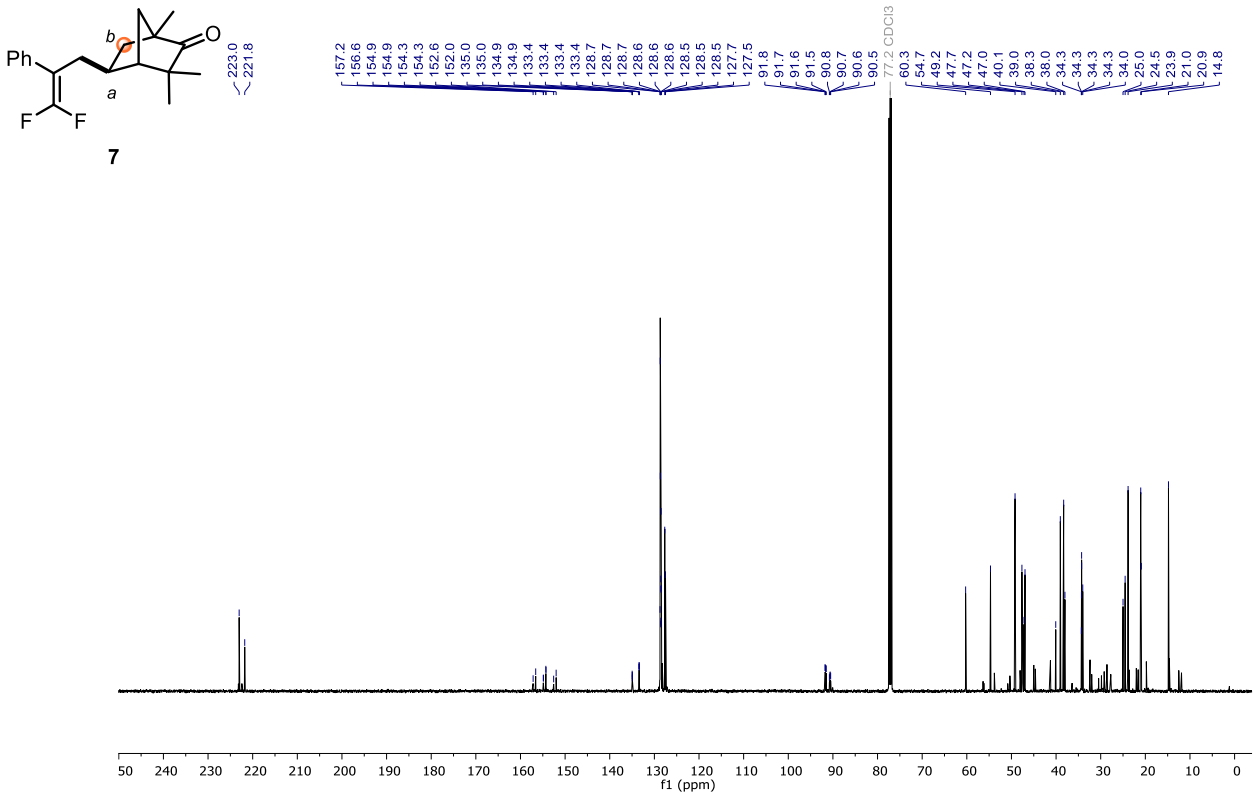


6

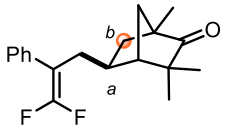
^{1}H NMR (500 MHz, $CDCl_3$)



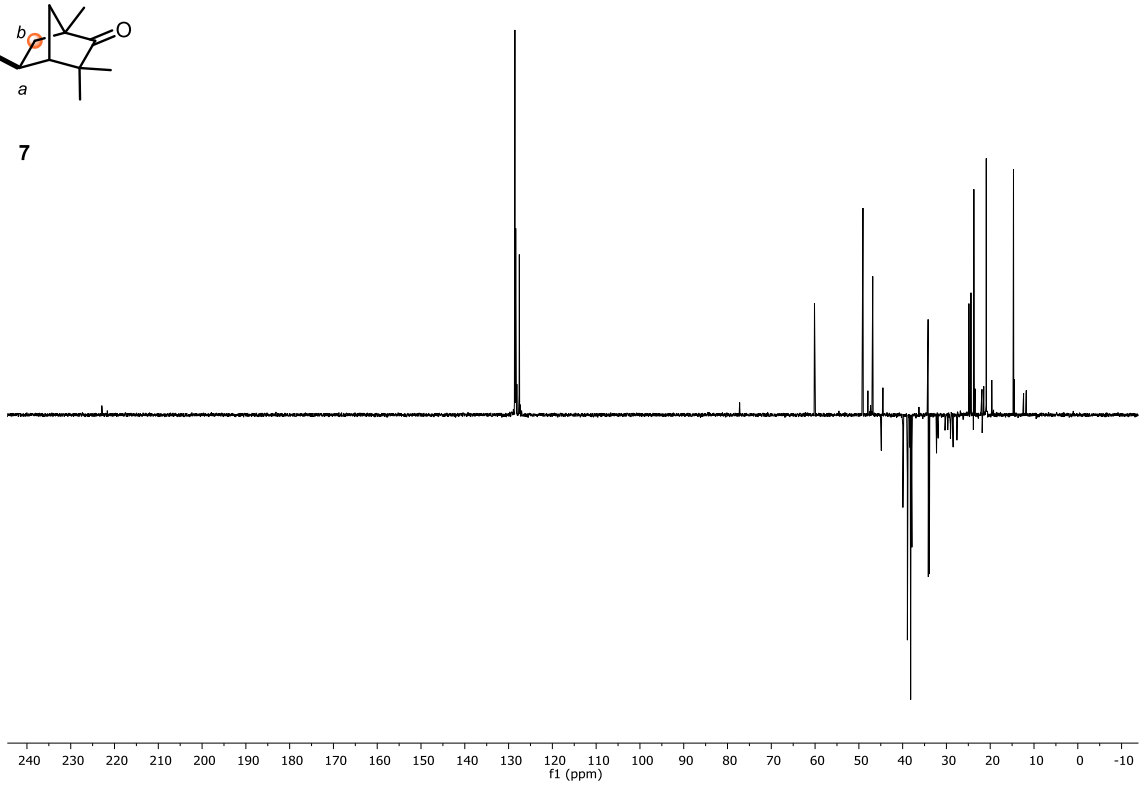
^{13}C NMR (126 MHz, $CDCl_3$)



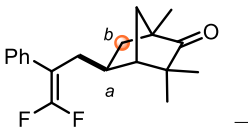
DEPT-135 (126 MHz, $CDCl_3$)



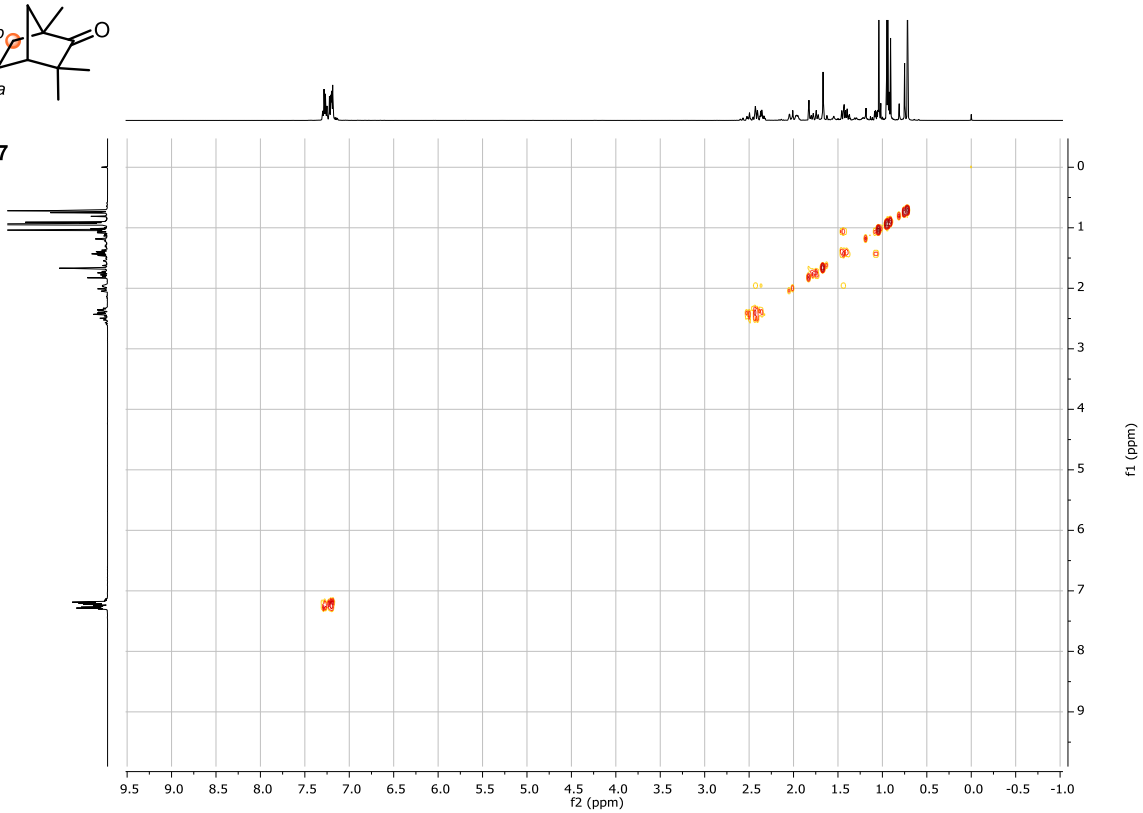
7



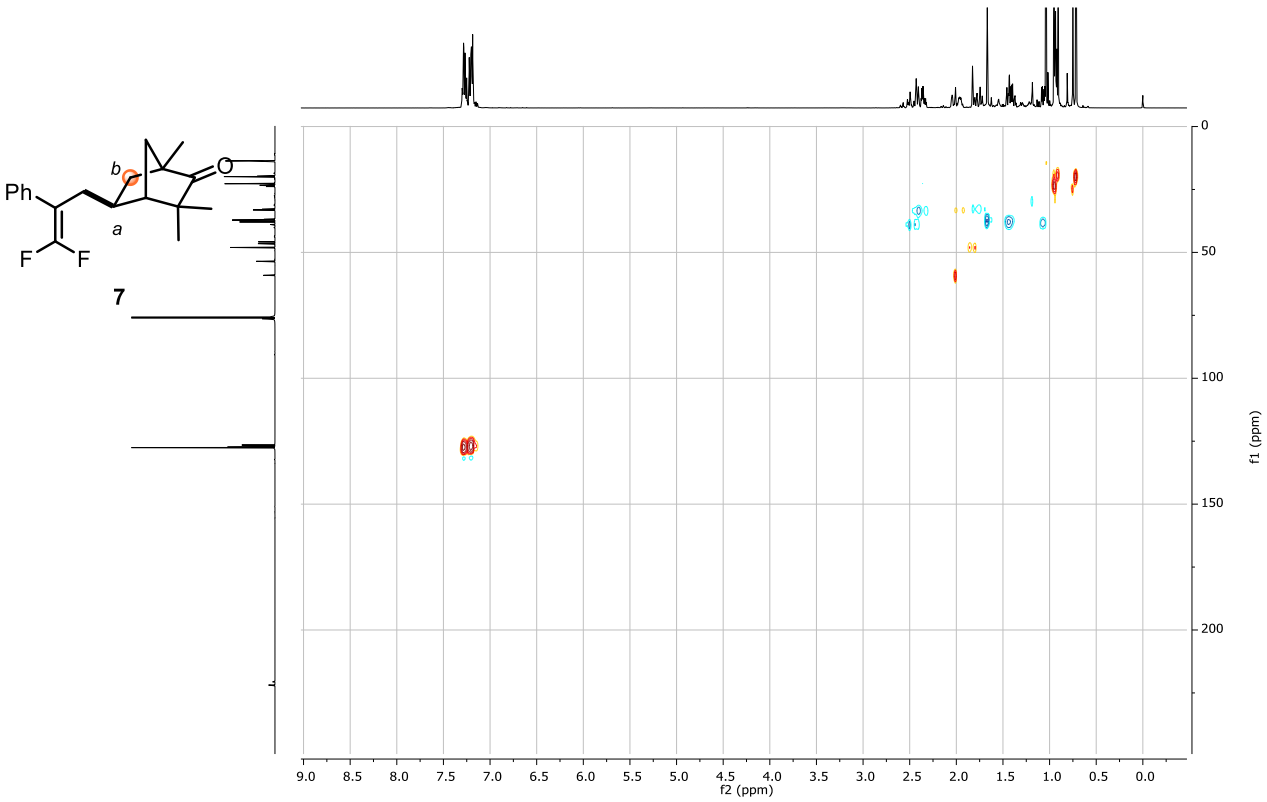
COSY (500 MHz, $CDCl_3$)



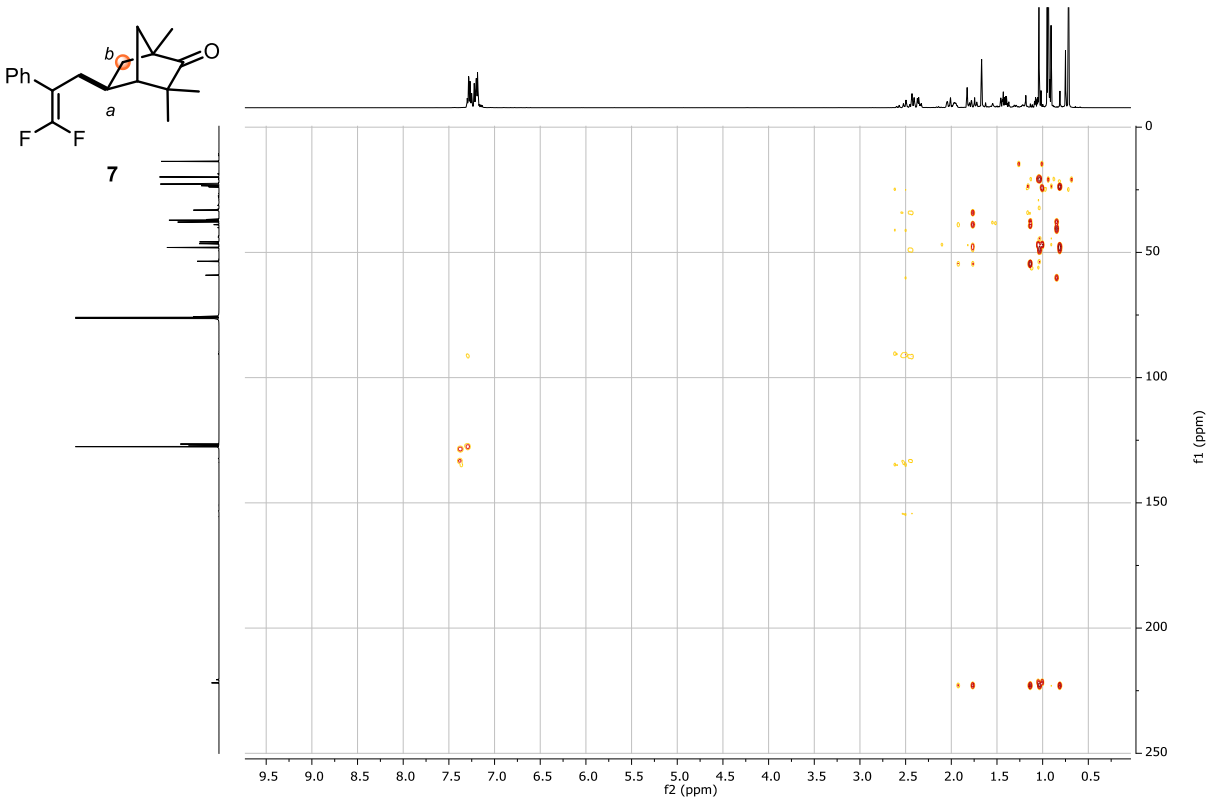
7



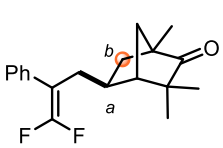
HSQC (500, 126, MHz, $CDCl_3$)



HMBC (500, 126, MHz, $CDCl_3$)

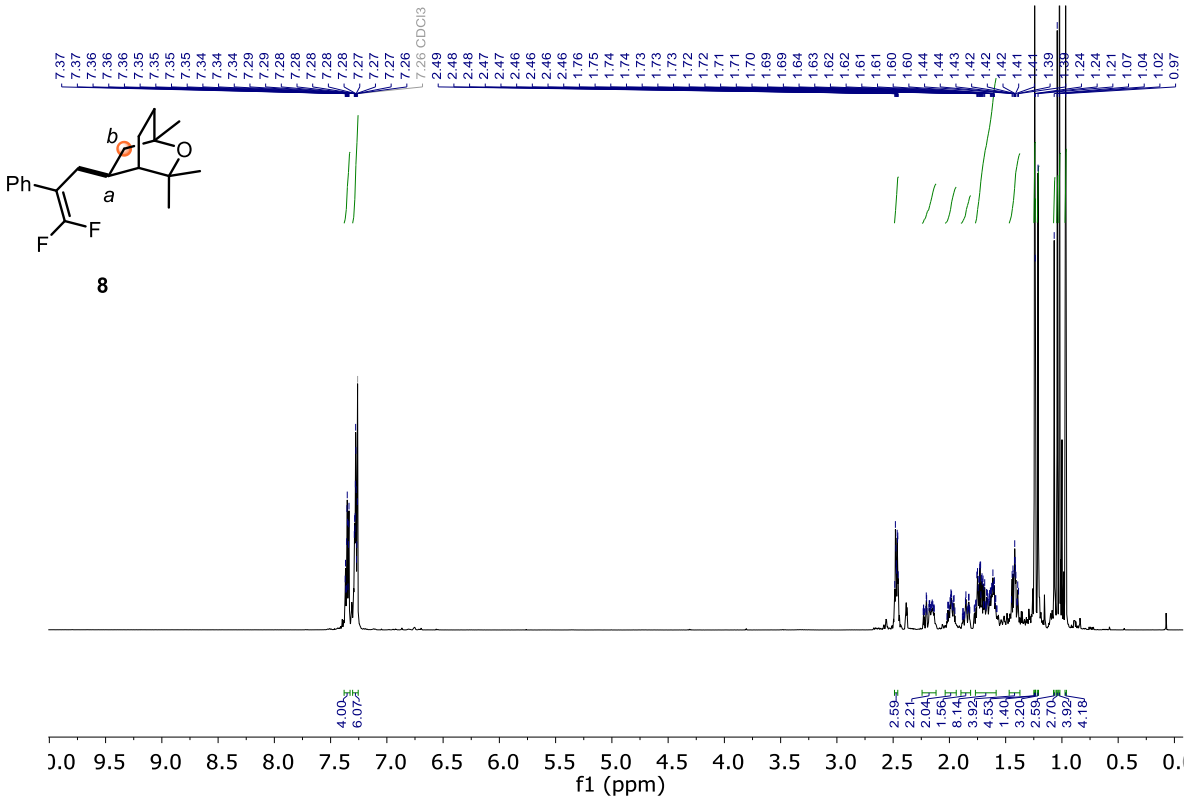


^{19}F NMR (282 MHz, $CDCl_3$)

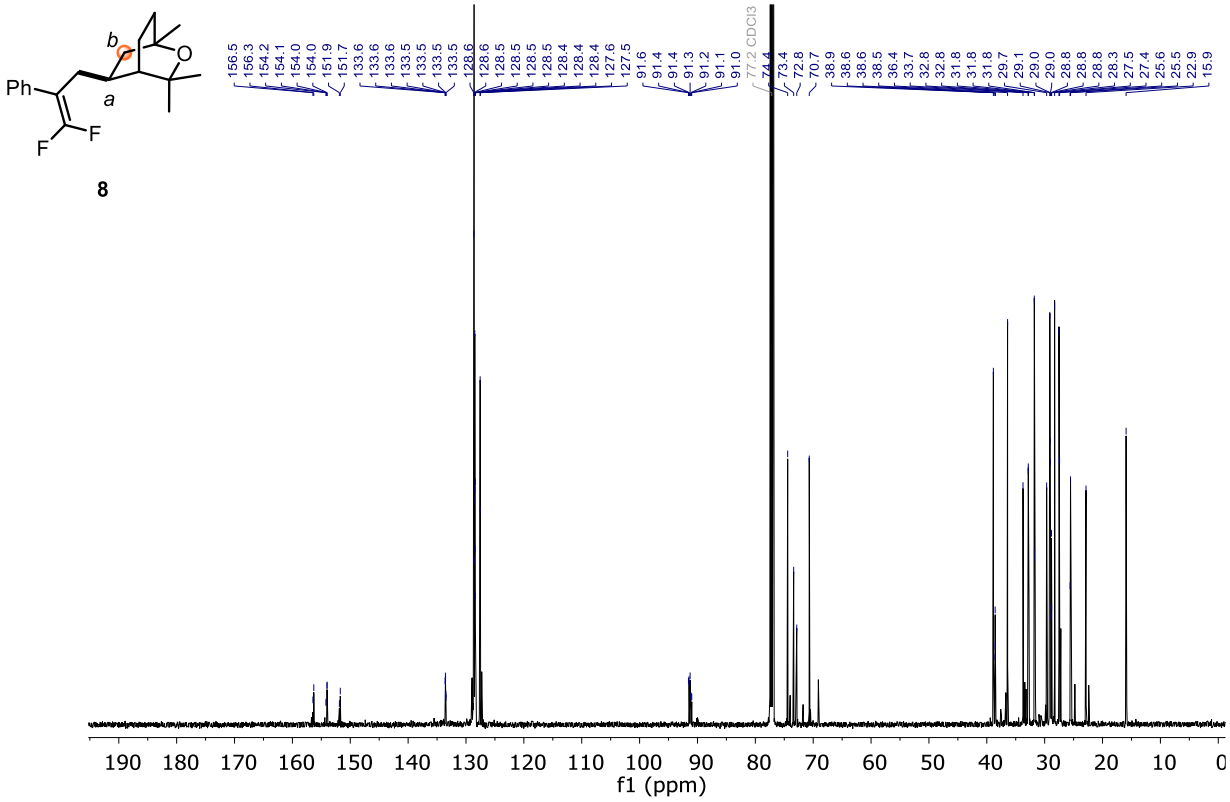


7

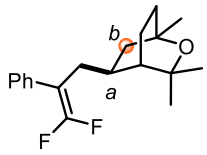
^{1}H NMR (500 MHz, $CDCl_3$)



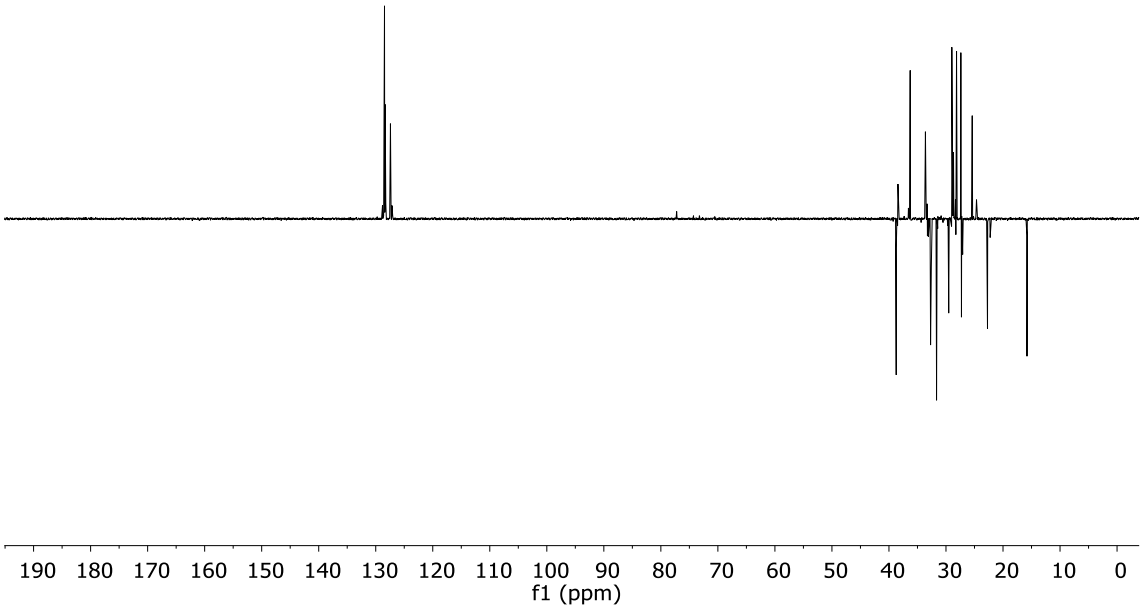
^{13}C NMR (126 MHz, $CDCl_3$)



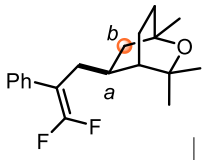
DEPT-135 (126 MHz, $CDCl_3$)



8

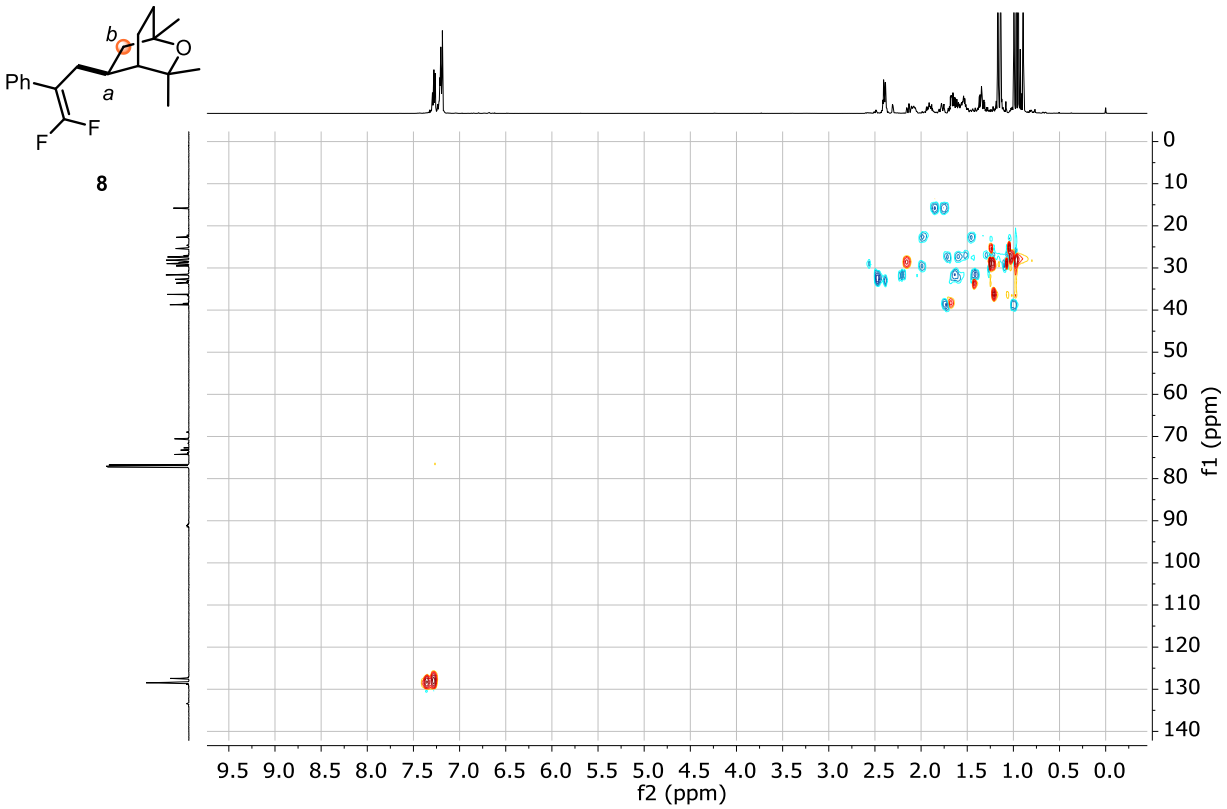


COSY (500 MHz, $CDCl_3$)

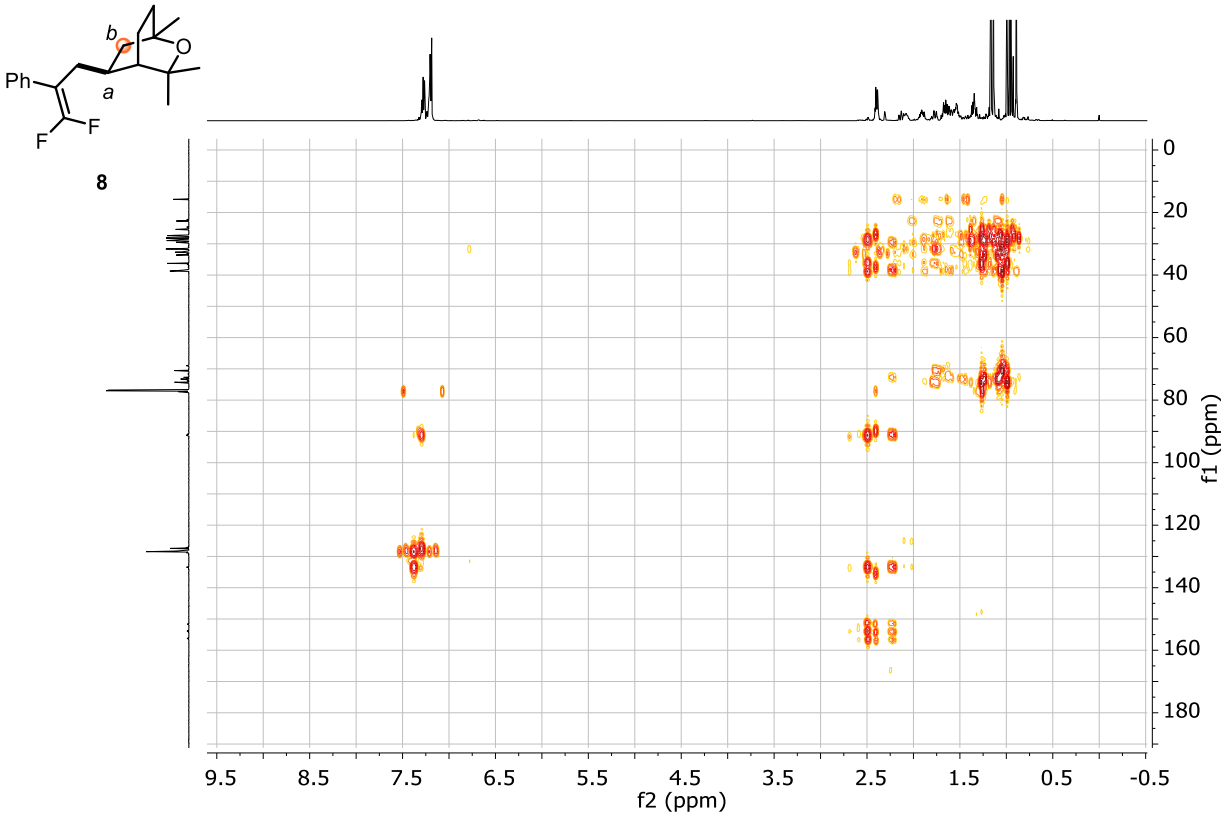


8

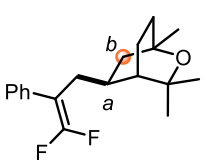
HSQC (500, 126, MHz, $CDCl_3$)



HMBC (500, 126, MHz, $CDCl_3$)

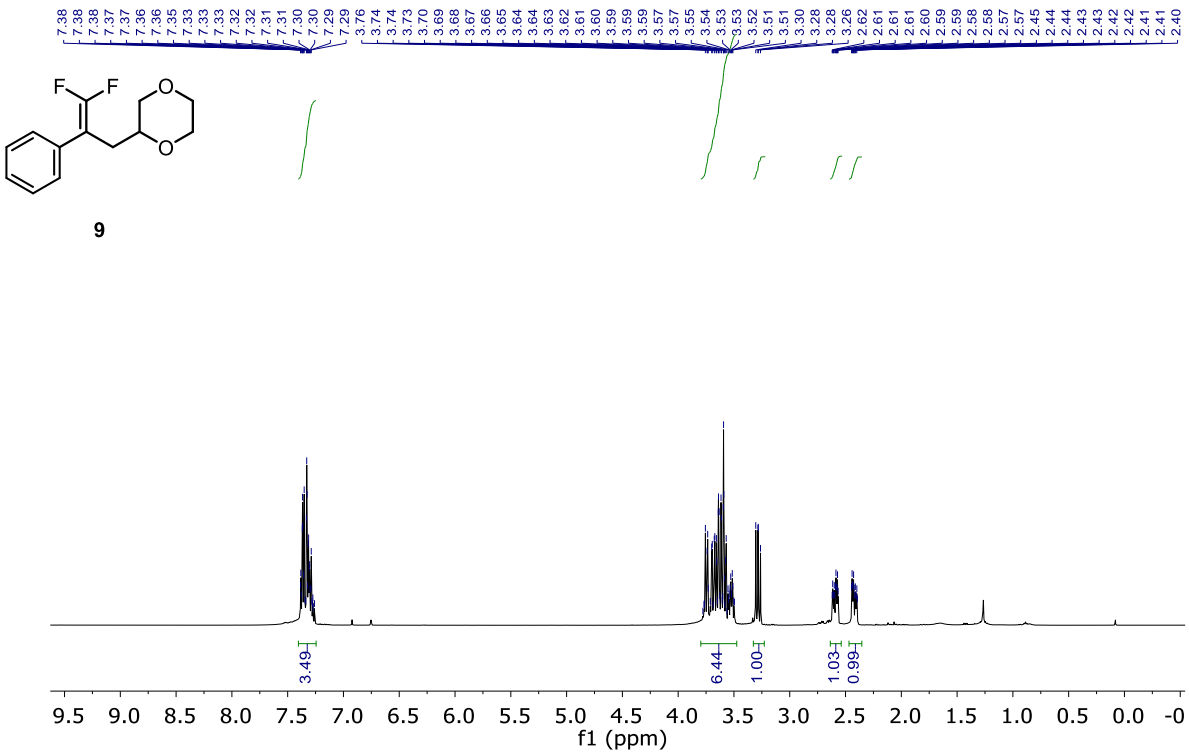


^{19}F NMR (282 MHz, $CDCl_3$)

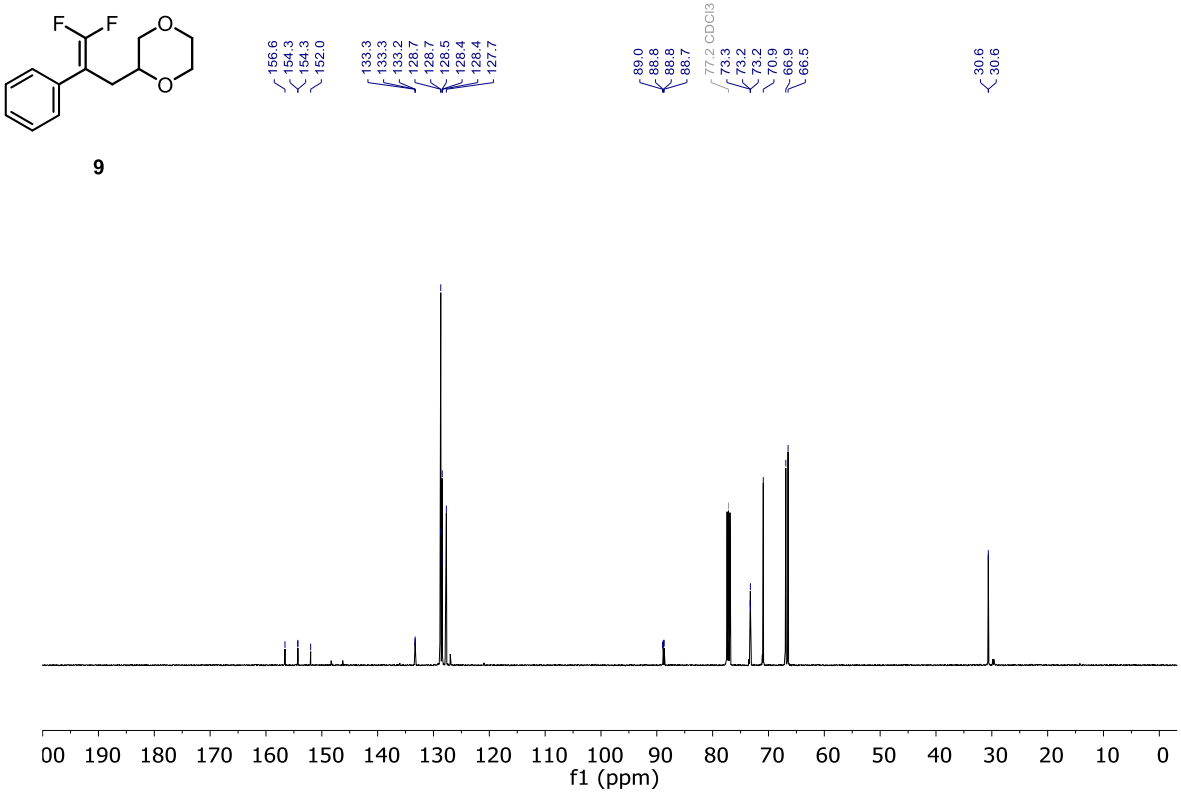


8

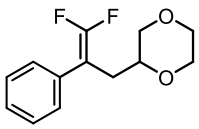
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

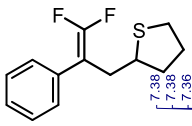


^{19}F NMR (282 MHz, $CDCl_3$)

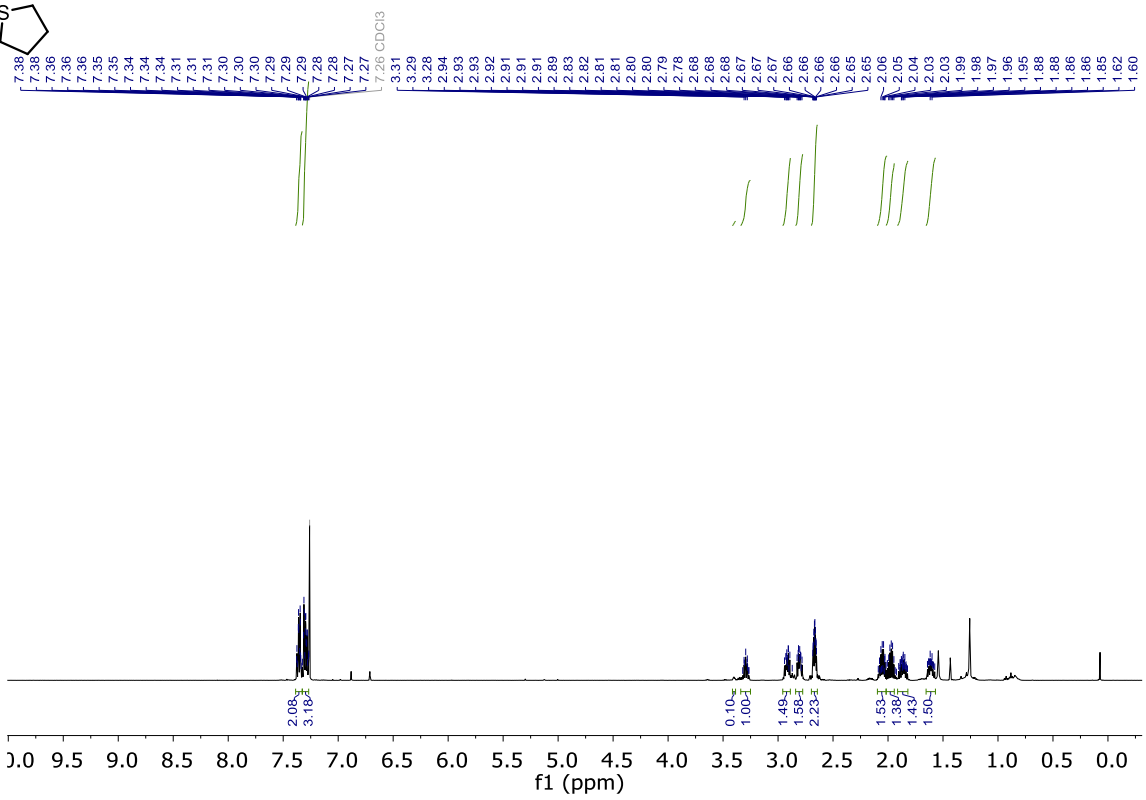


9

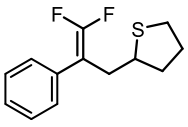
^{1}H NMR (500 MHz, $CDCl_3$)



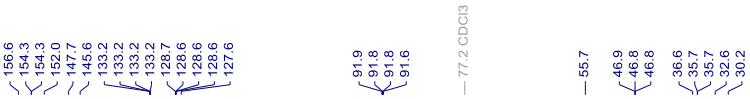
10

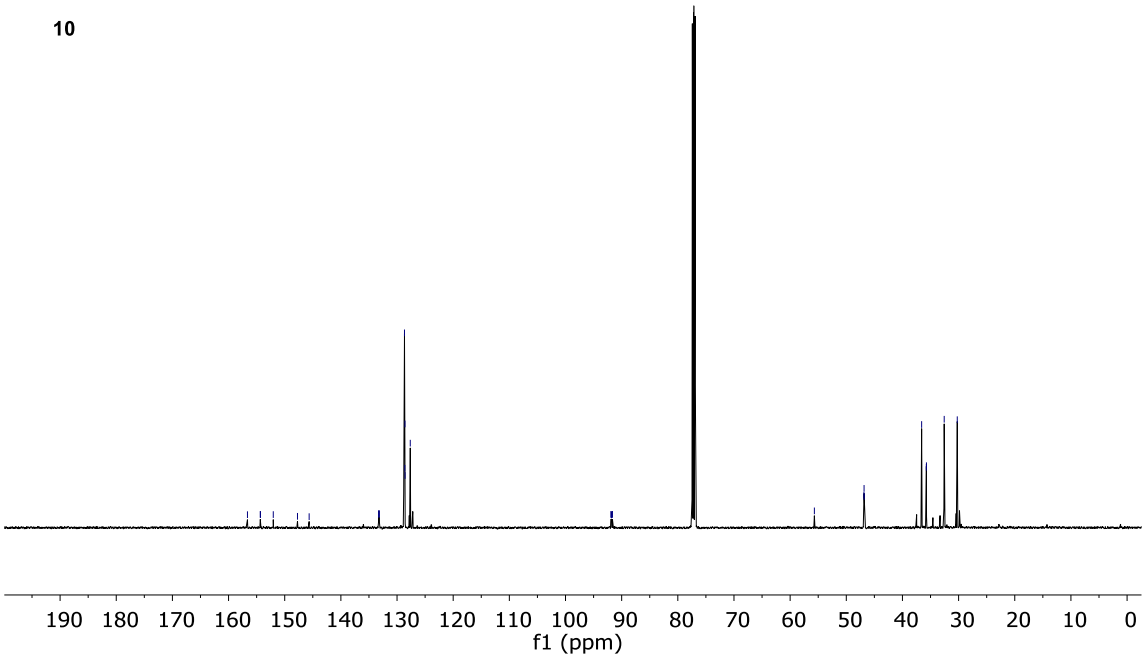


^{13}C NMR (126 MHz, $CDCl_3$)

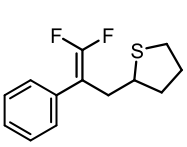


10



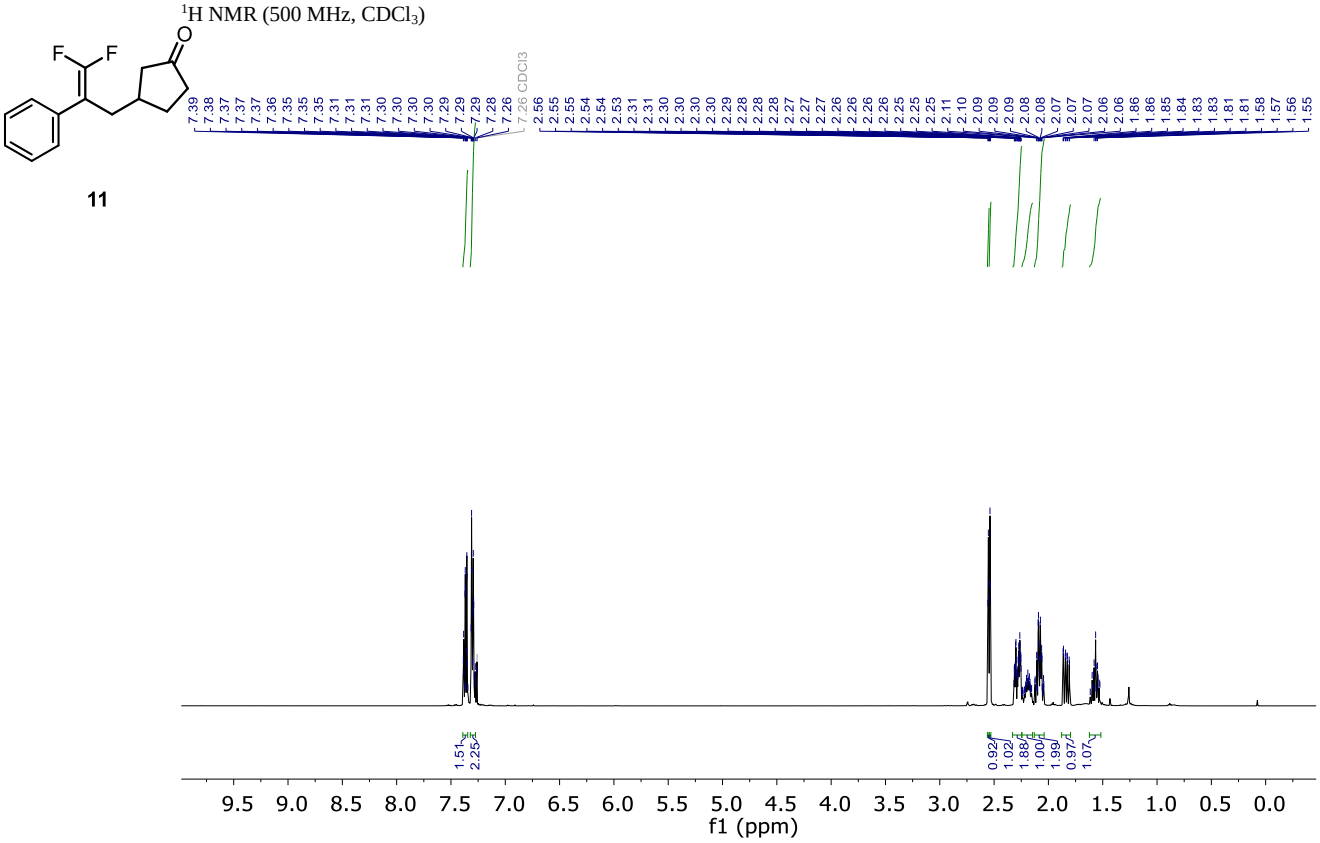


^{19}F NMR (282 MHz, $CDCl_3$)

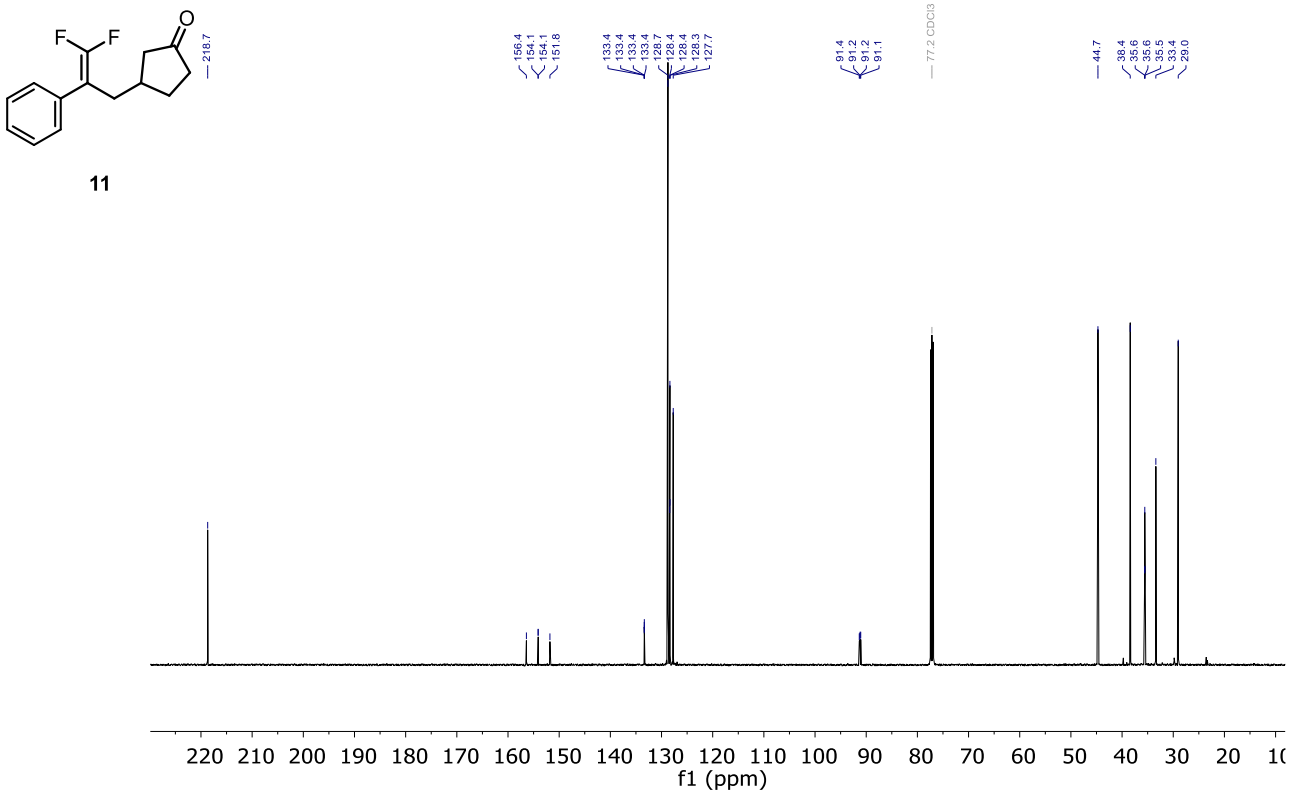


10

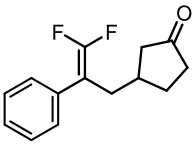
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

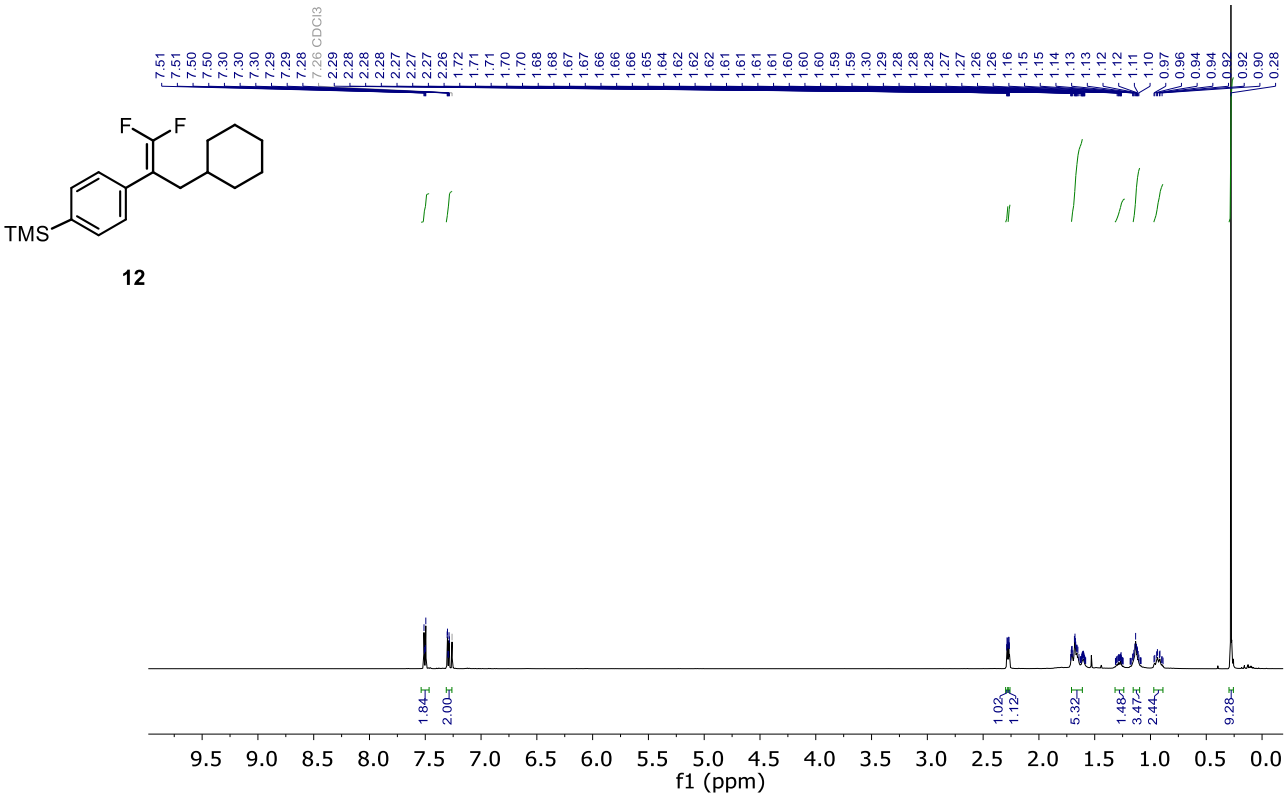


^{19}F NMR (282 MHz, $CDCl_3$)

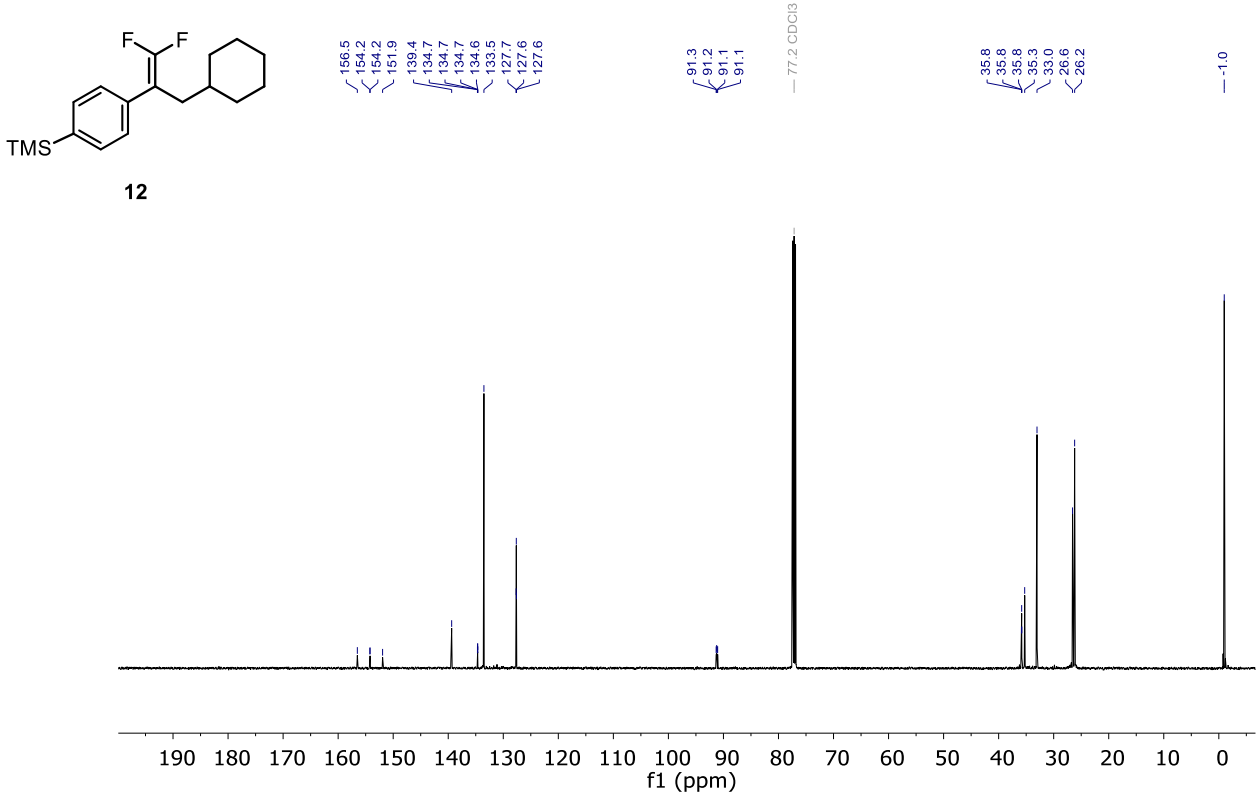


11

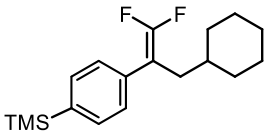
^{1}H NMR (500 MHz, $CDCl_3$)



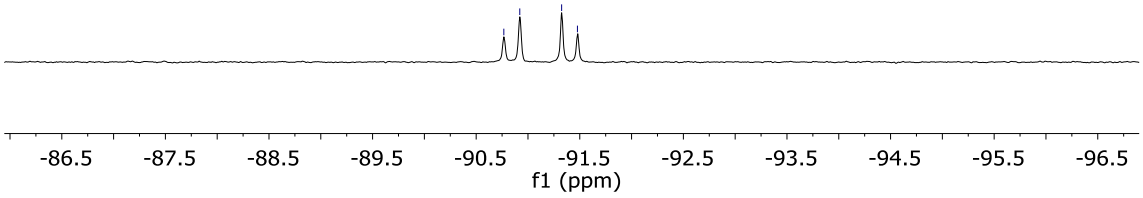
^{13}C NMR (126 MHz, $CDCl_3$)



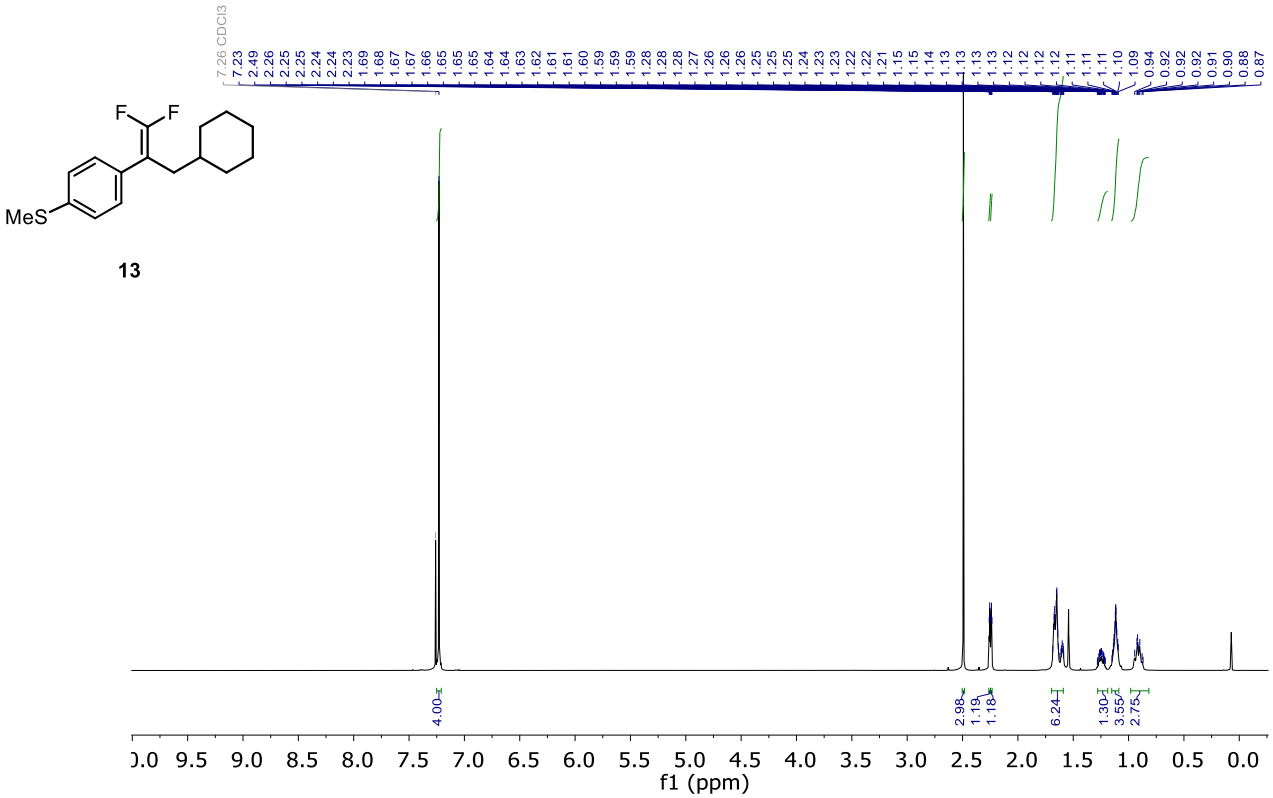
^{19}F NMR (282 MHz, $CDCl_3$)



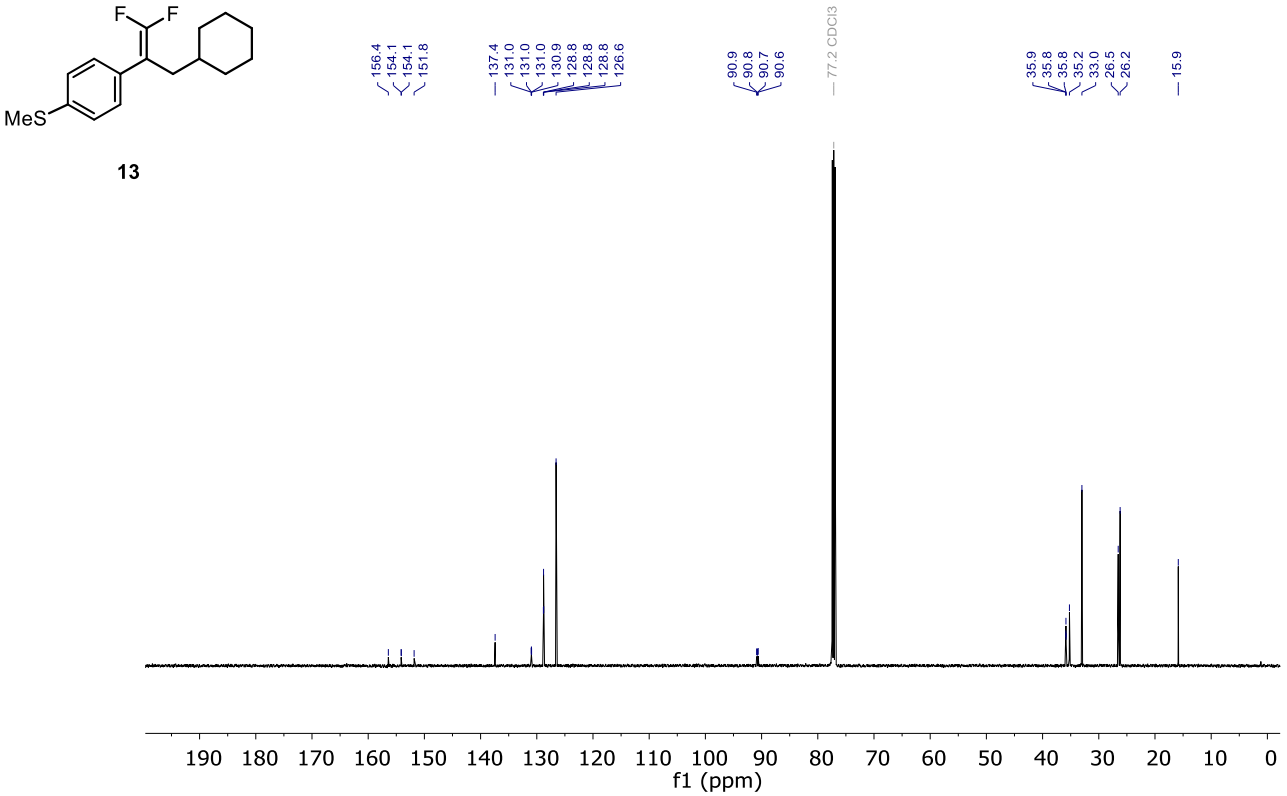
12



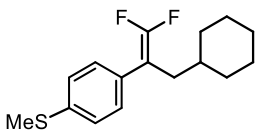
^{1}H NMR (500 MHz, $CDCl_3$)



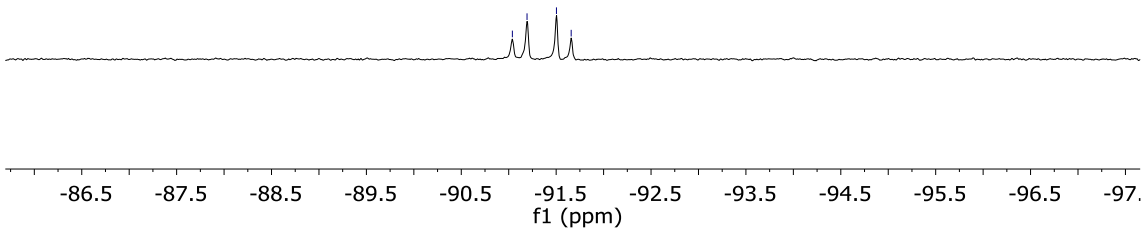
^{13}C NMR (126 MHz, $CDCl_3$)



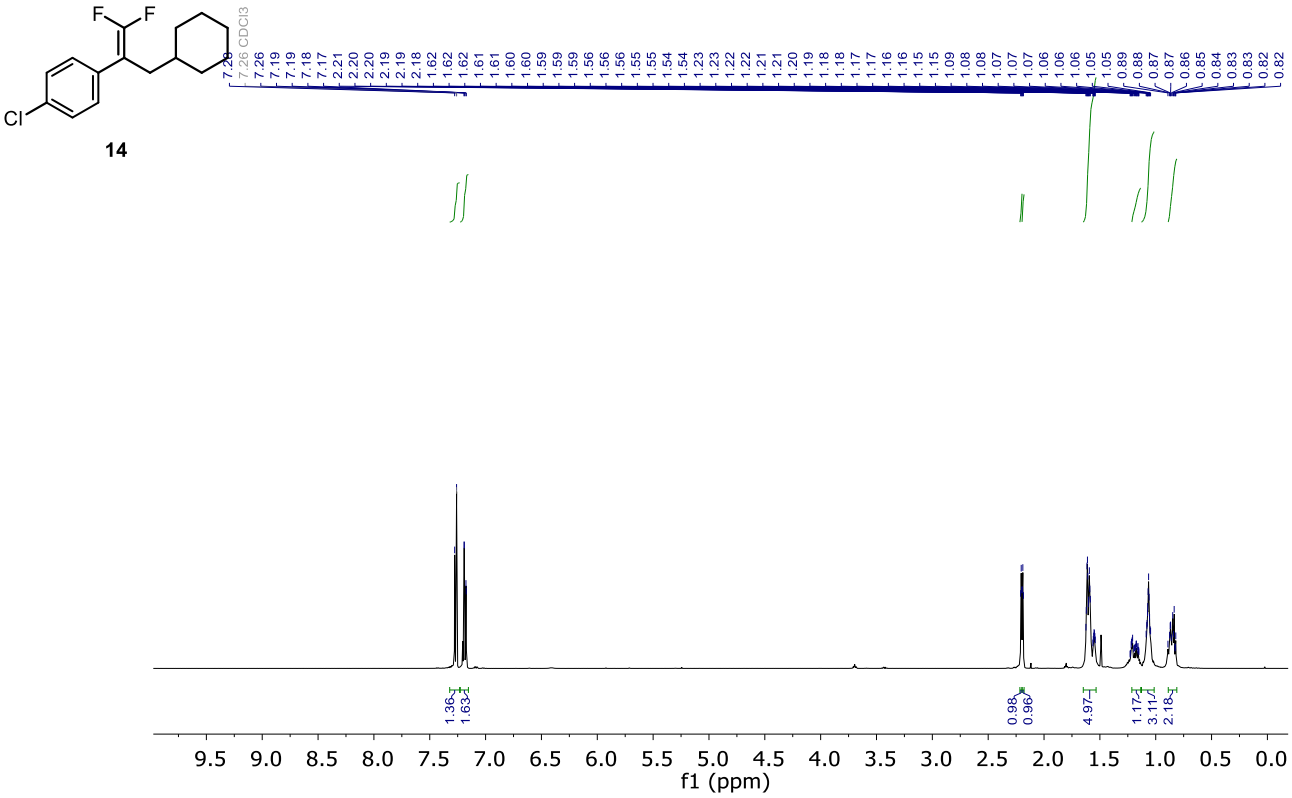
^{19}F NMR (282 MHz, $CDCl_3$)



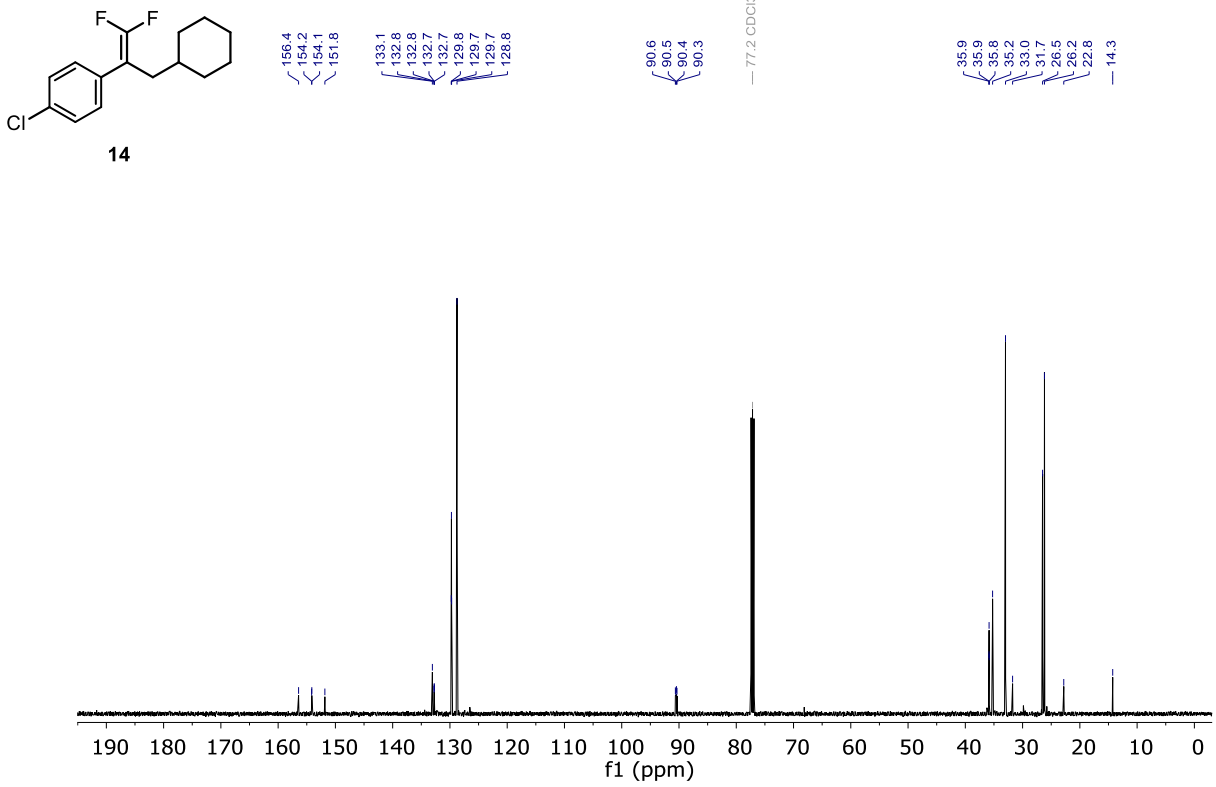
13



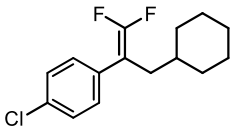
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

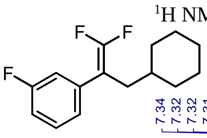


^{19}F NMR (282 MHz, $CDCl_3$)

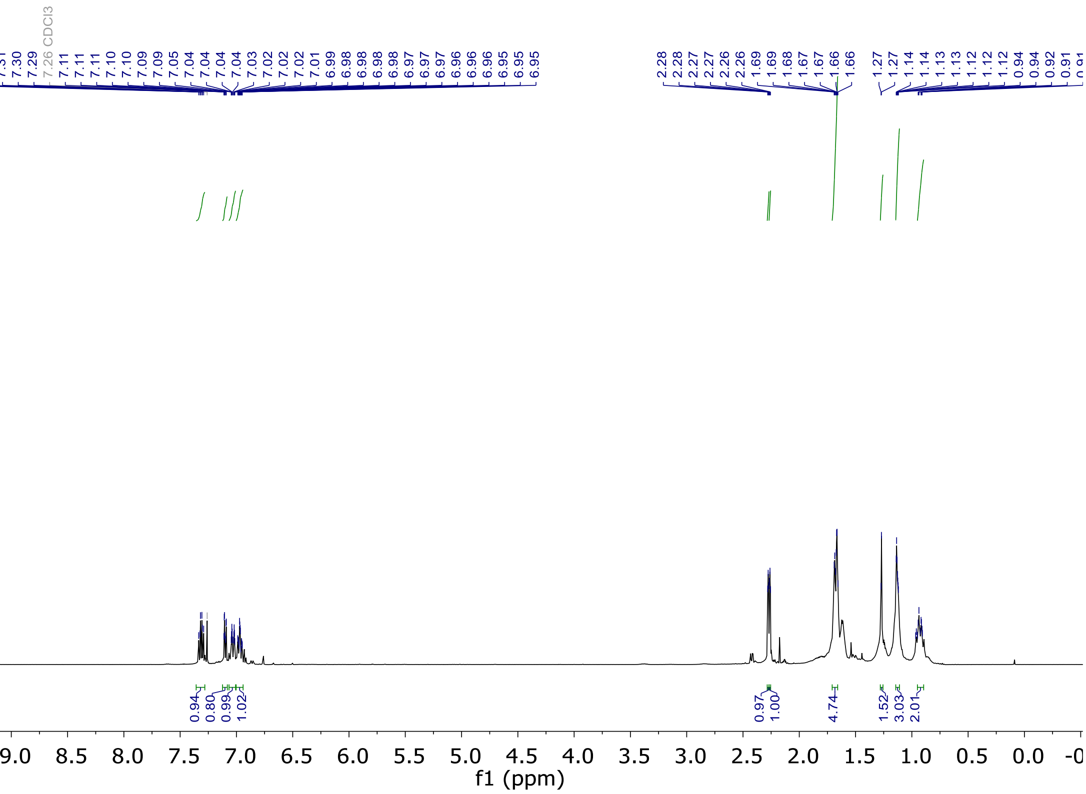


14

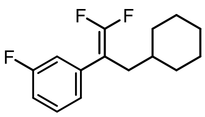
^{1}H NMR (500 MHz, $CDCl_3$)



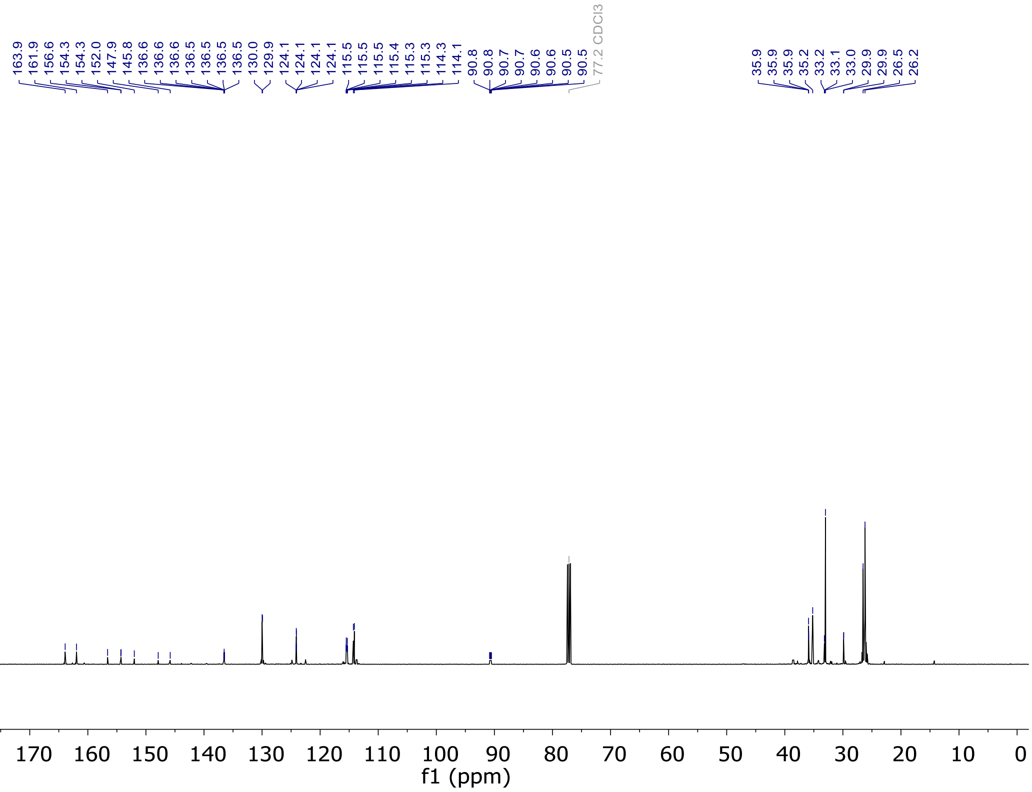
15



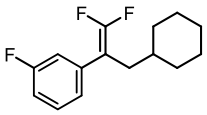
^{13}C NMR (126 MHz, $CDCl_3$)



15

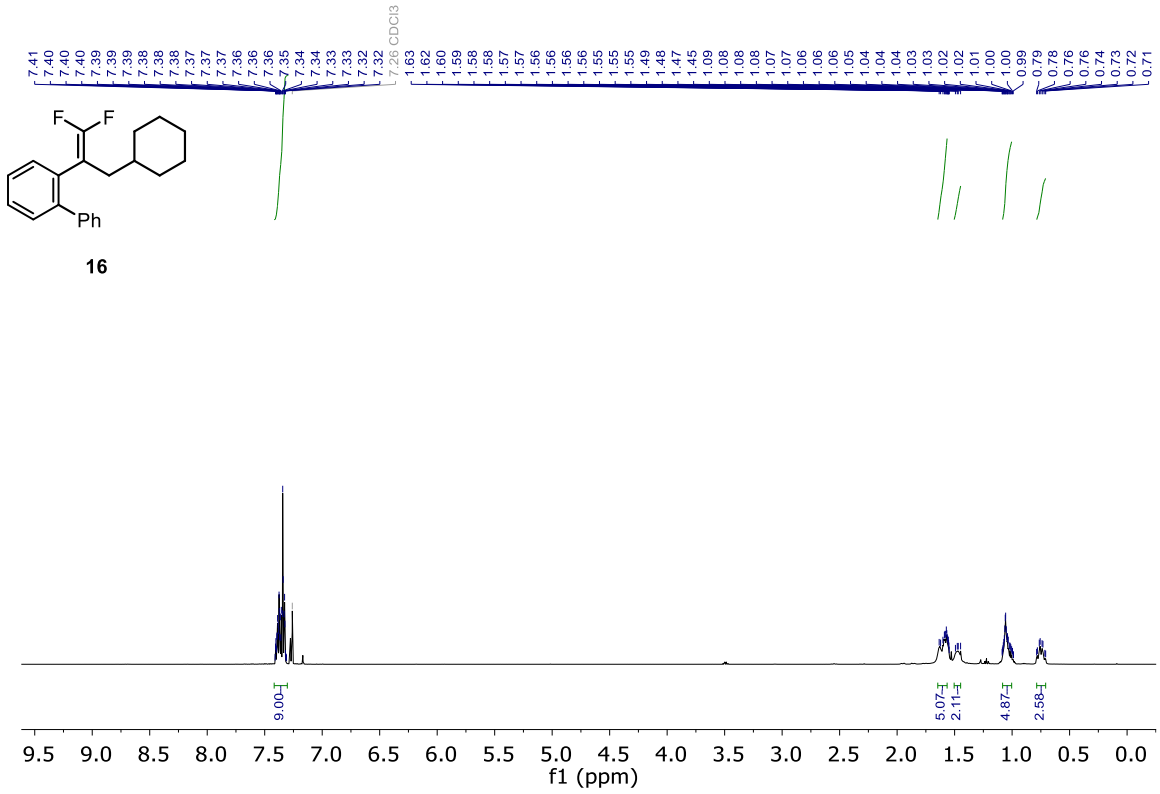


^{19}F NMR (282 MHz, $CDCl_3$)



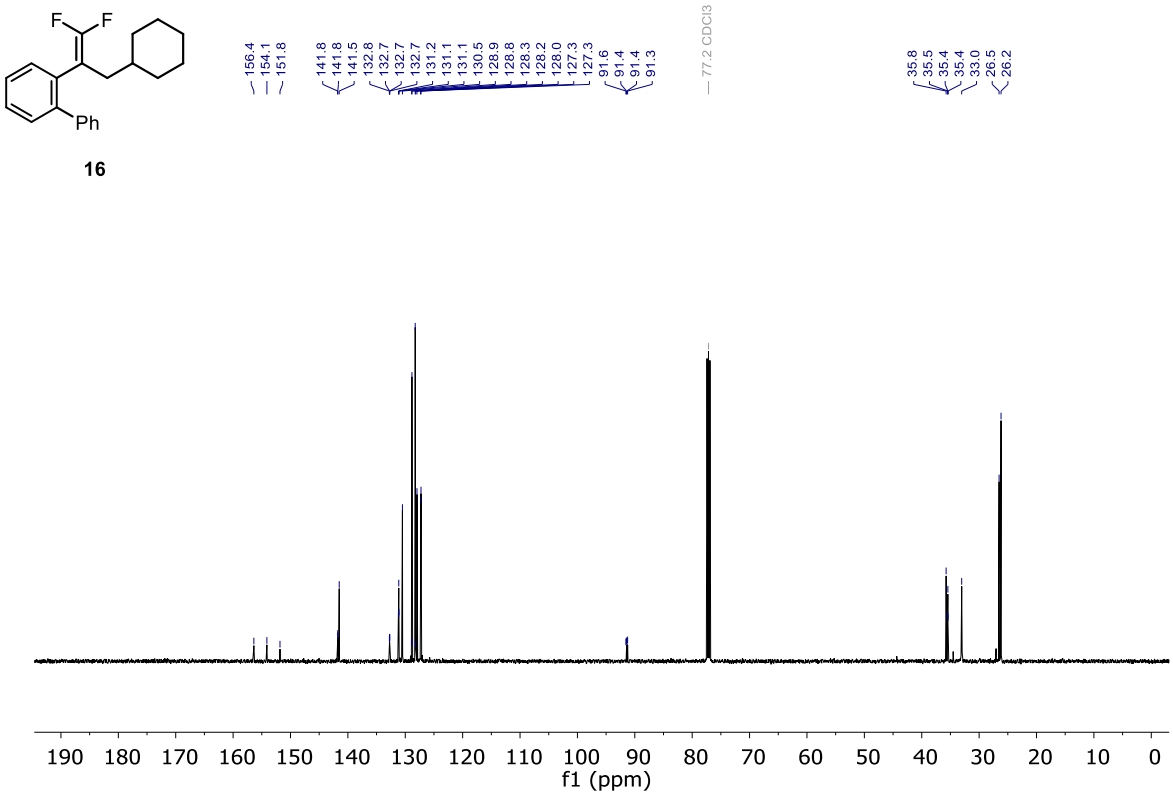
15

^{1}H NMR (500 MHz, $CDCl_3$)



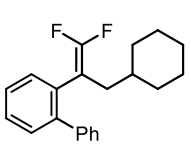
16

^{13}C NMR (126 MHz, $CDCl_3$)



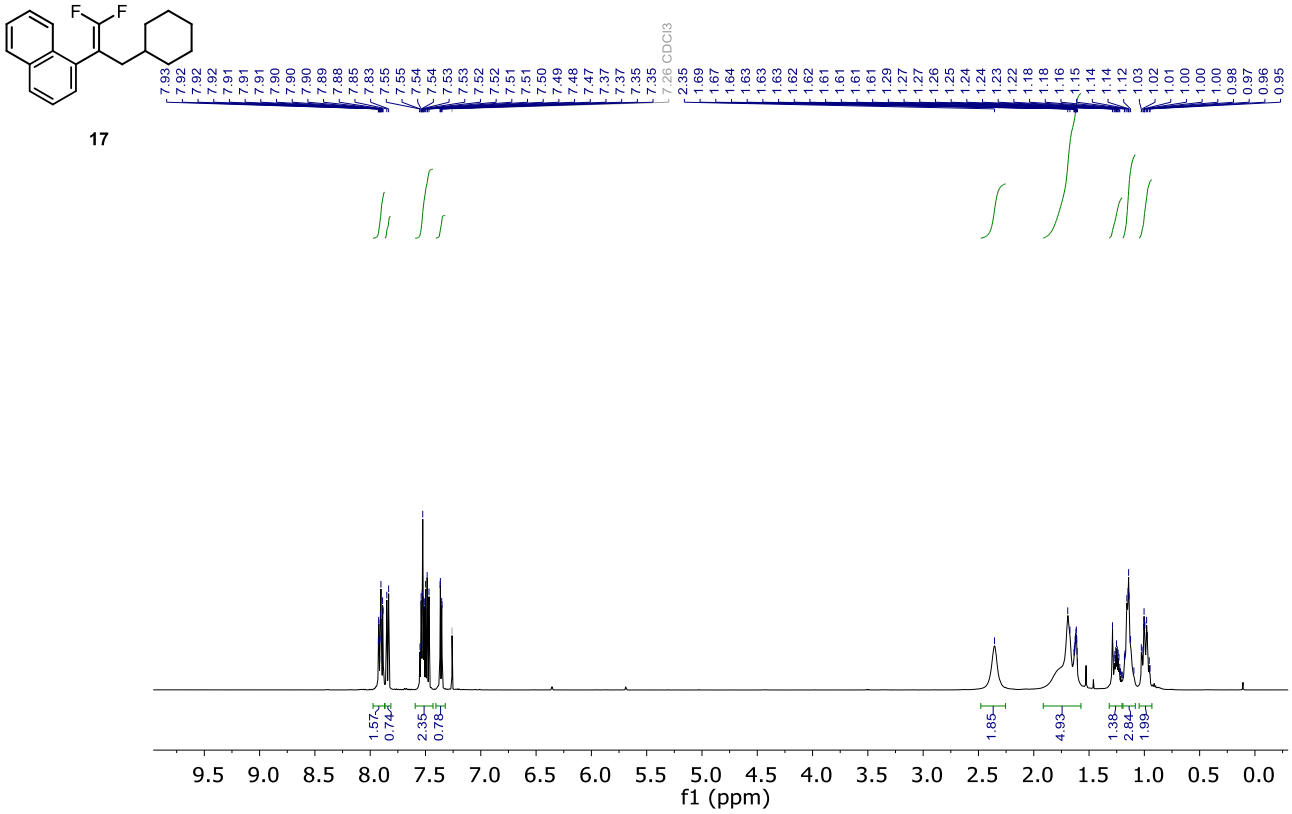
16

^{19}F NMR (282 MHz, $CDCl_3$)

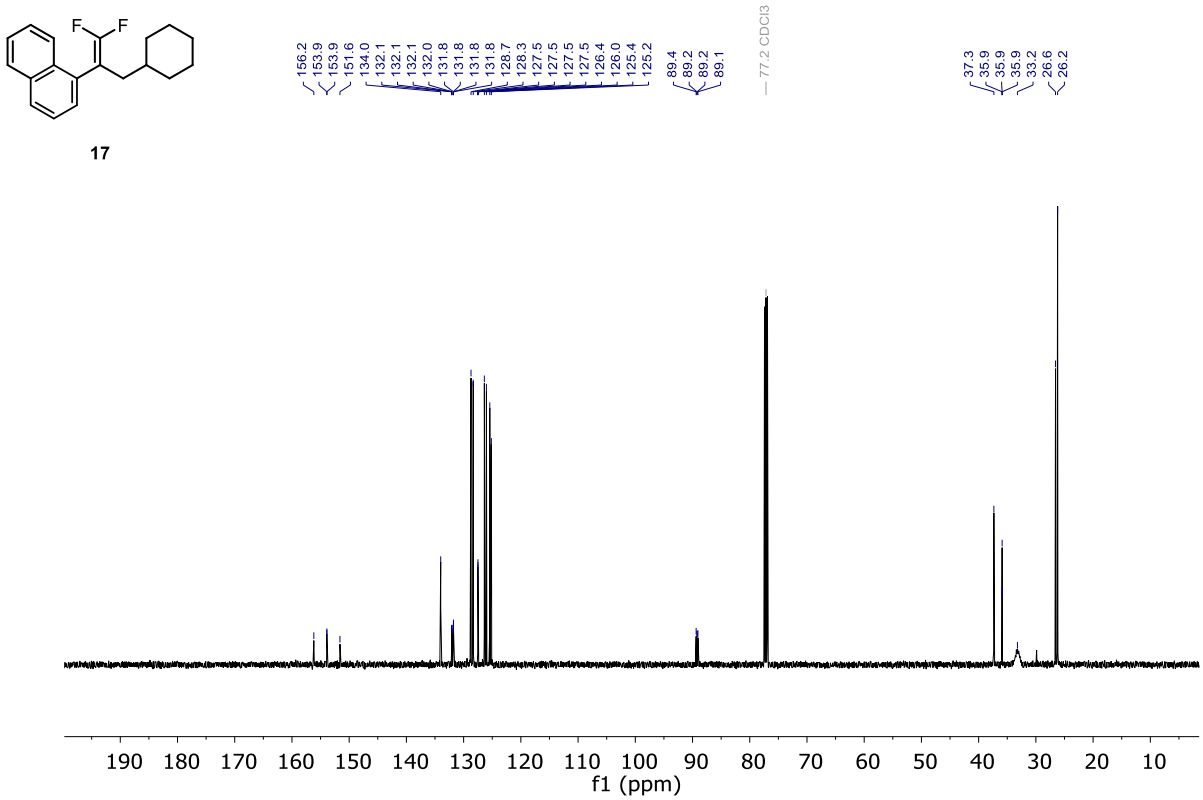


16

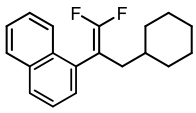
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

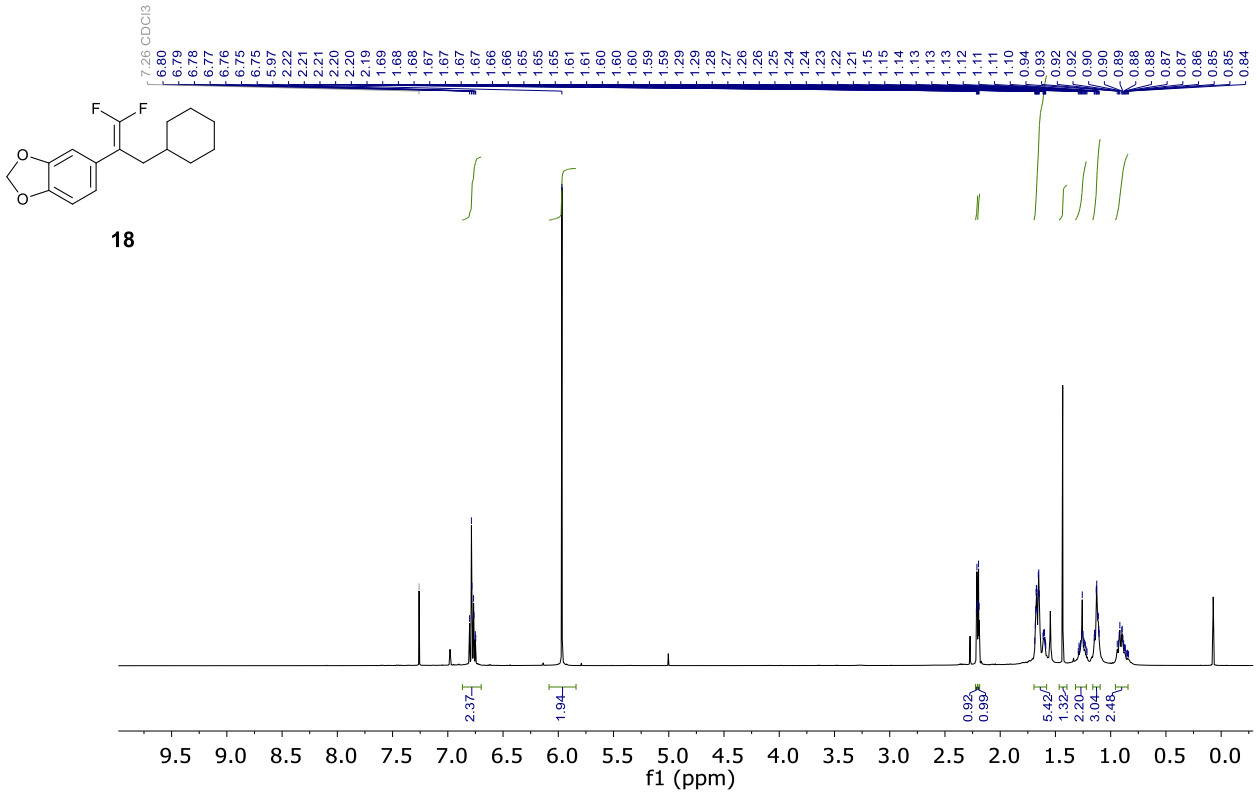


^{19}F NMR (282 MHz, $CDCl_3$)

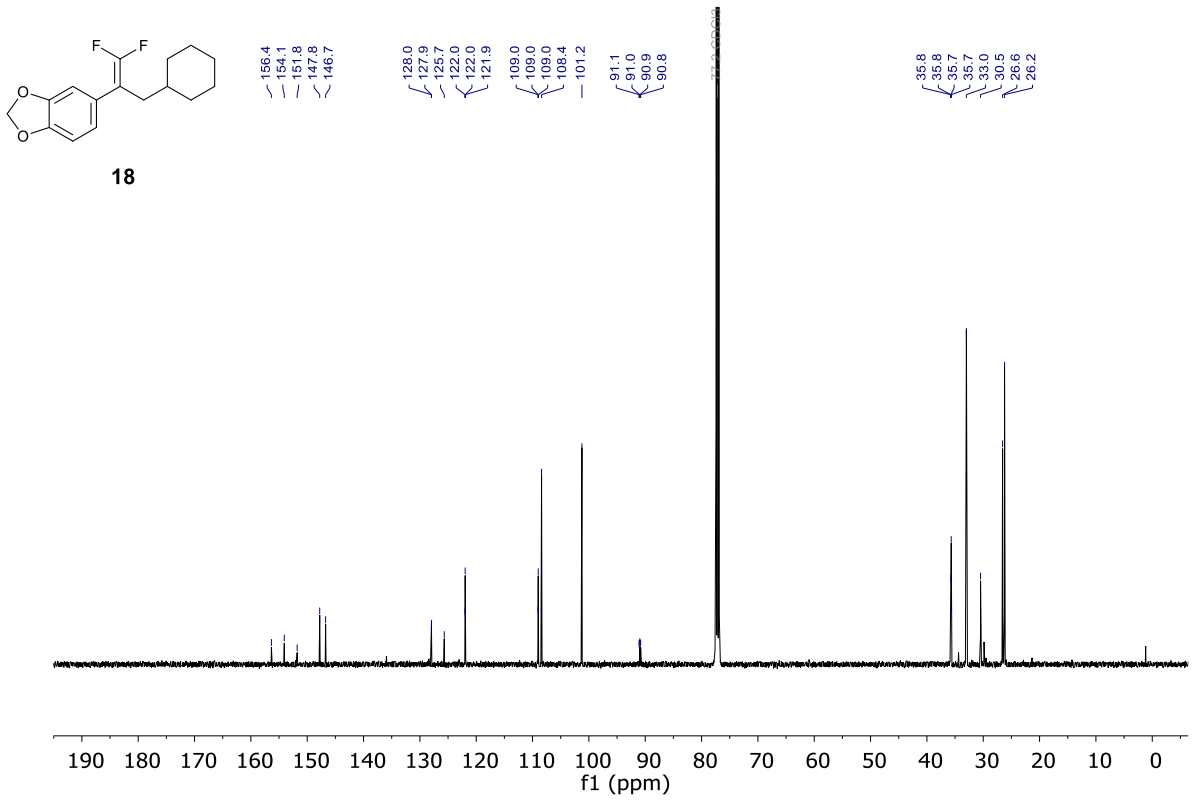


17

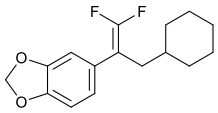
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

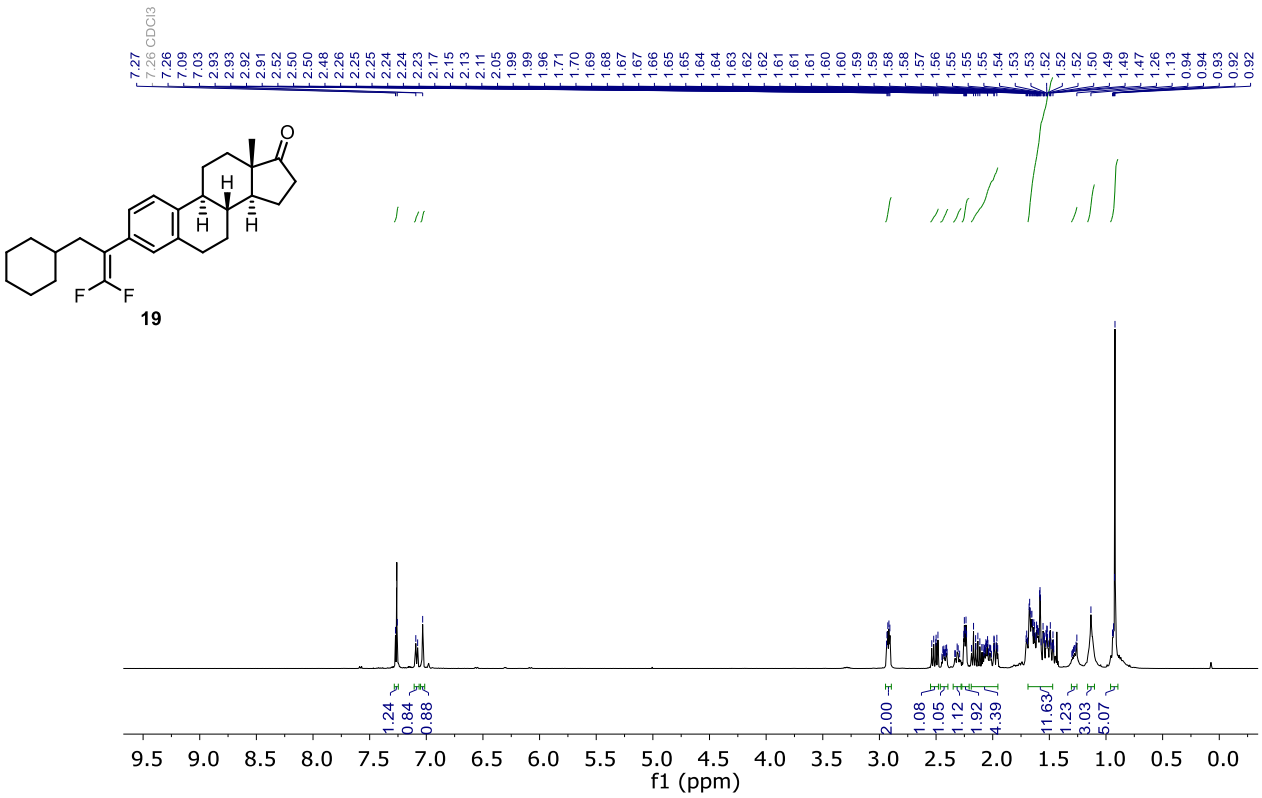


^{19}F NMR (282 MHz, $CDCl_3$)

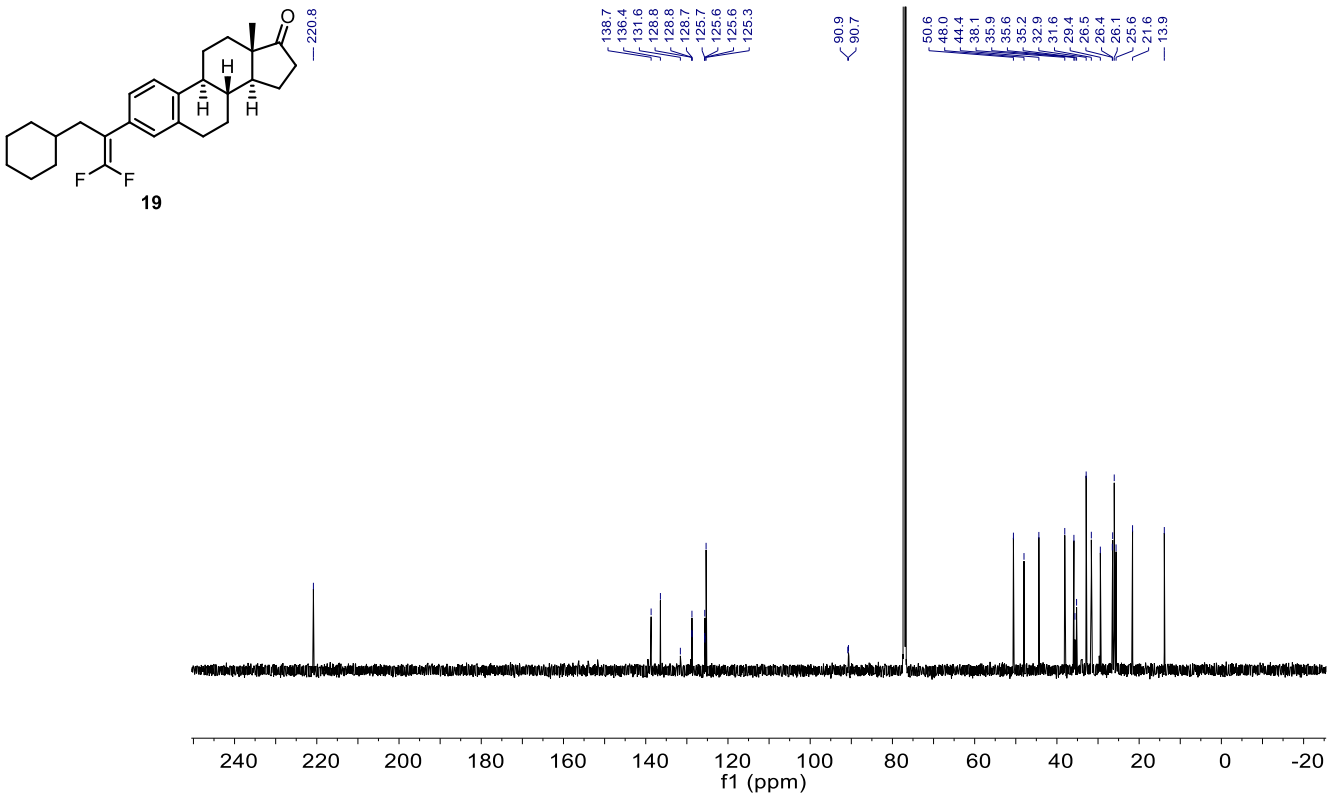


18

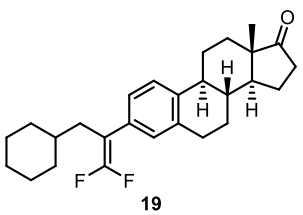
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

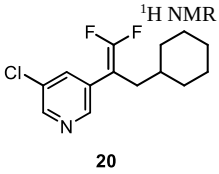


^{19}F NMR (282 MHz, $CDCl_3$)

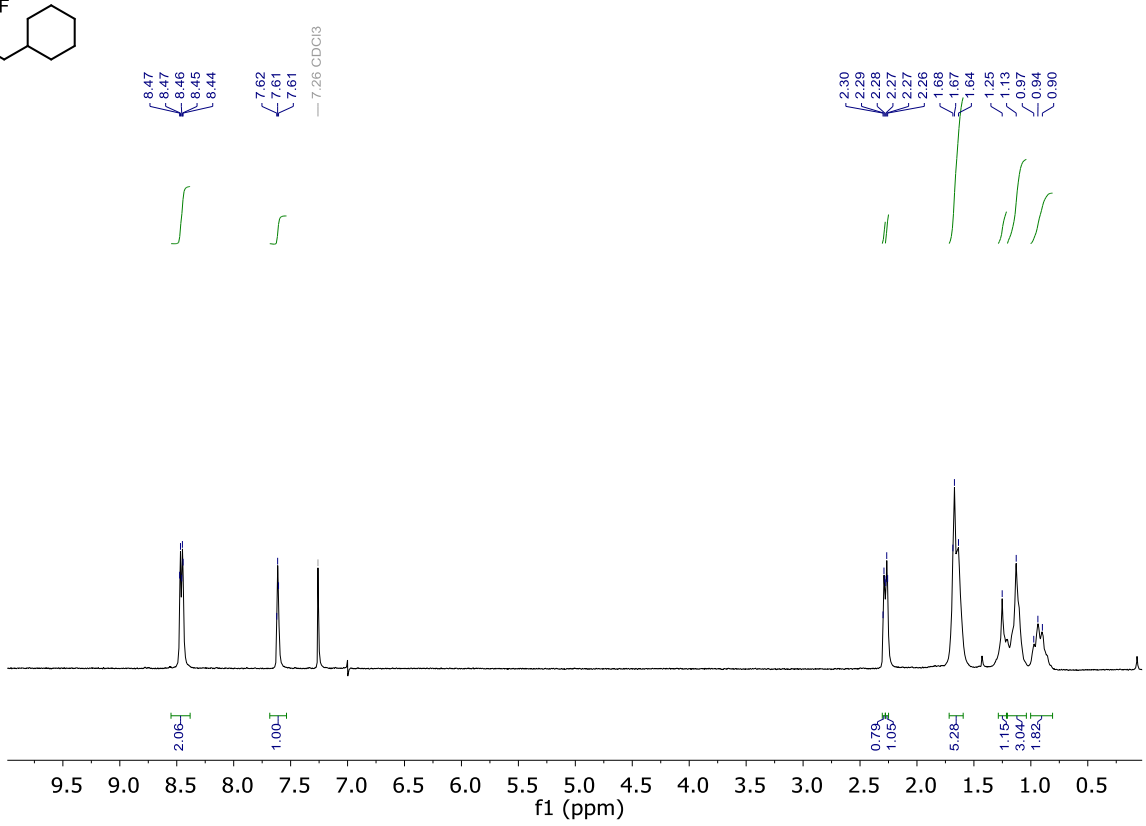


19

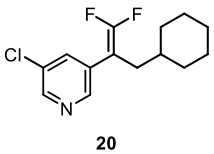
^{1}H NMR (500 MHz, $CDCl_3$)



20

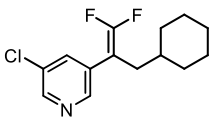


^{13}C NMR (126 MHz, $CDCl_3$)



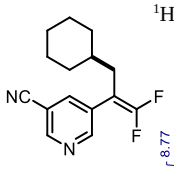
20

^{19}F NMR (282 MHz, $CDCl_3$)

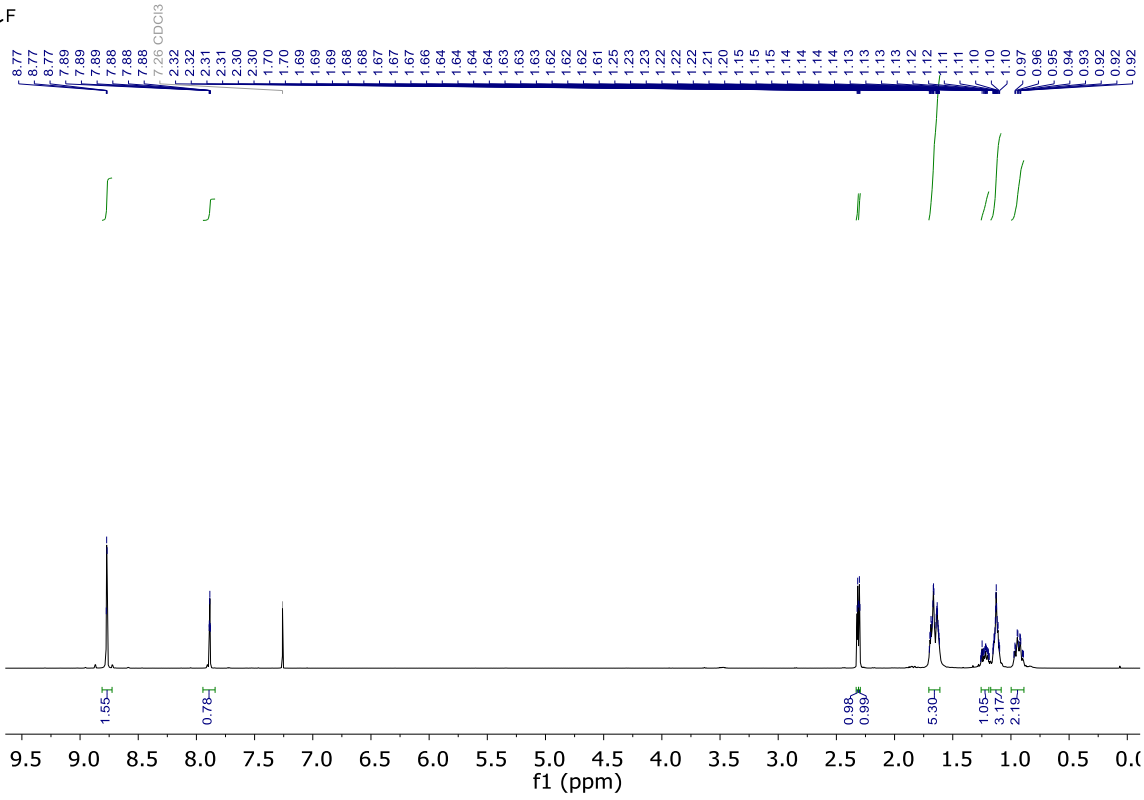


20

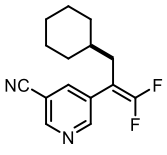
^{1}H NMR (500 MHz, $CDCl_3$)



22

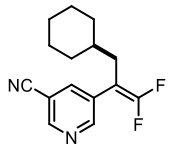


^{13}C NMR (126 MHz, $CDCl_3$)



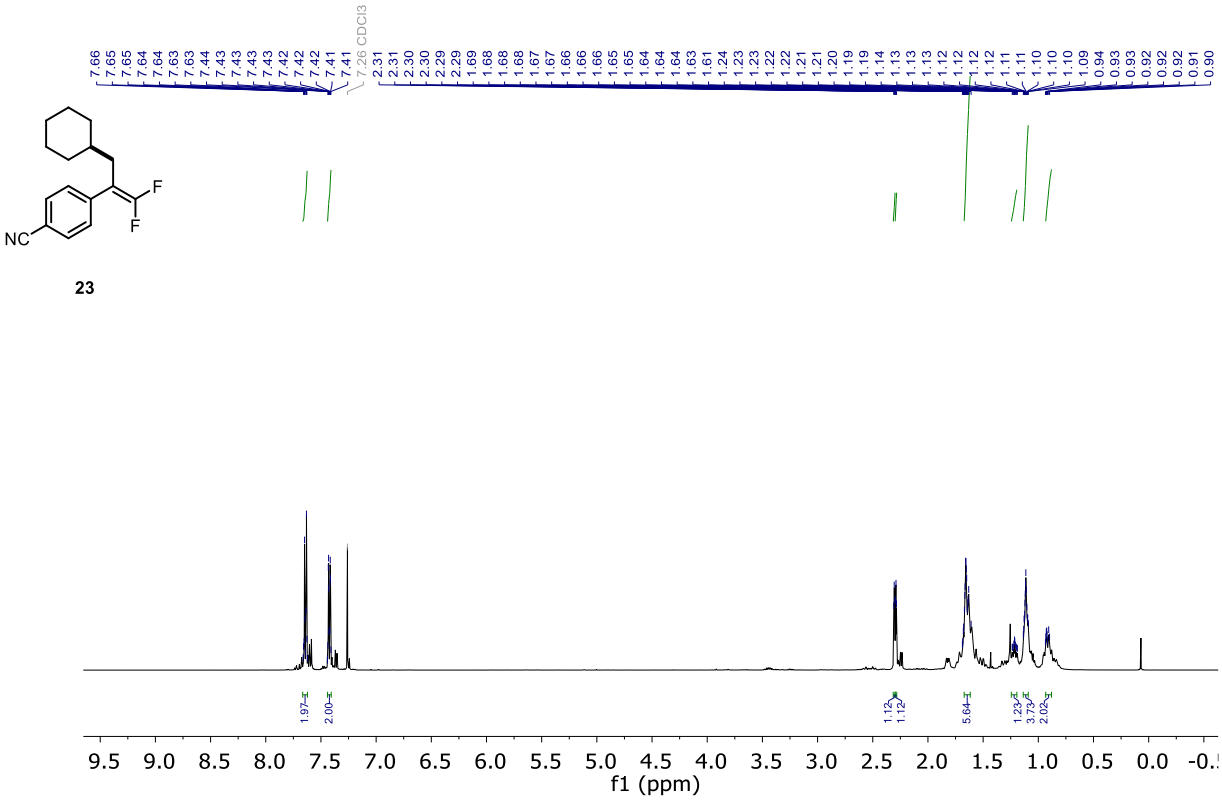
22

^{19}F NMR (282 MHz, $CDCl_3$)

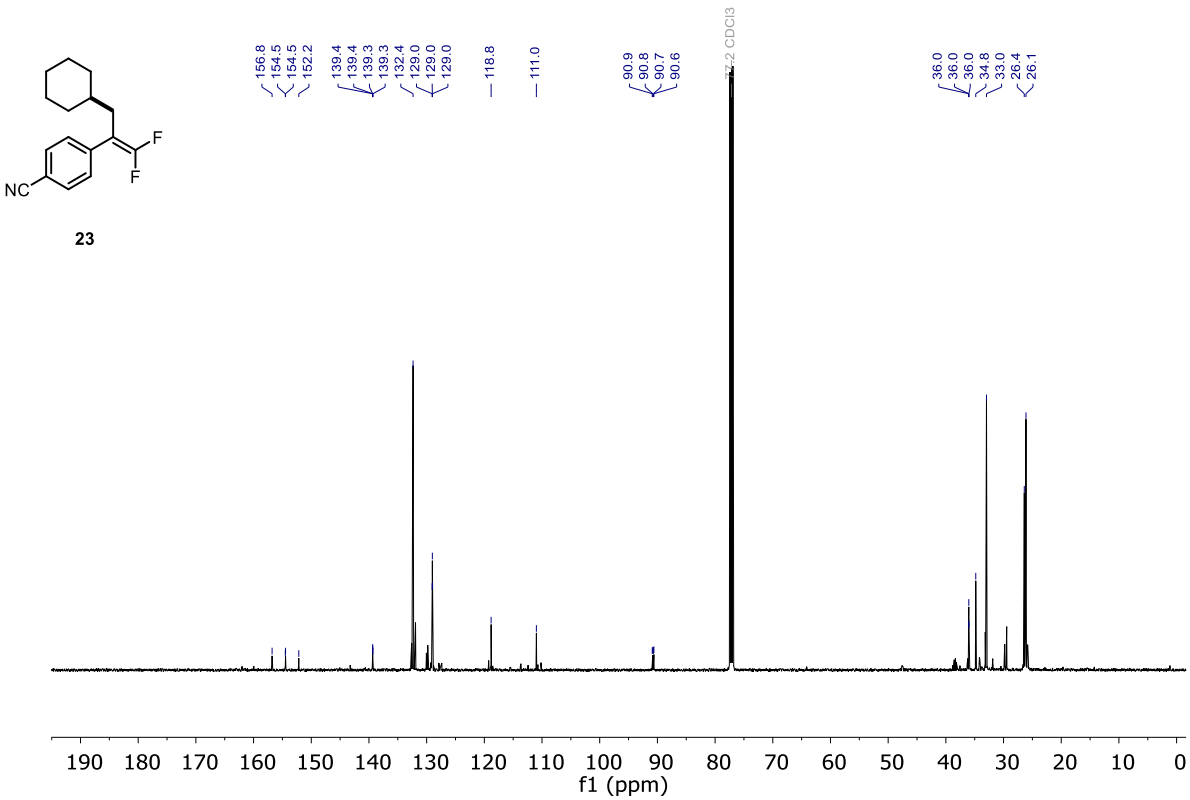


22

^{1}H NMR (500 MHz, $CDCl_3$)

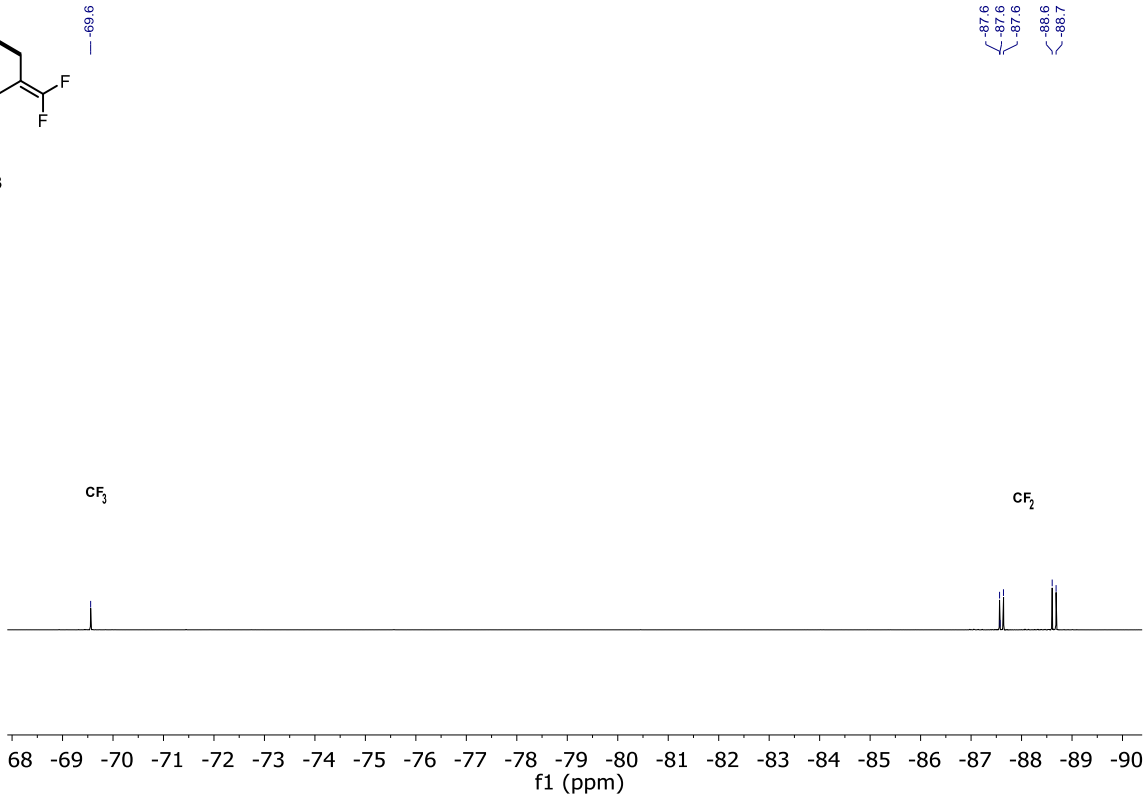


^{13}C NMR (126 MHz, $CDCl_3$)

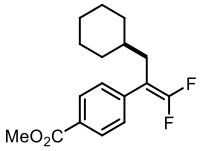


^{19}F NMR (282 MHz, $CDCl_3$)

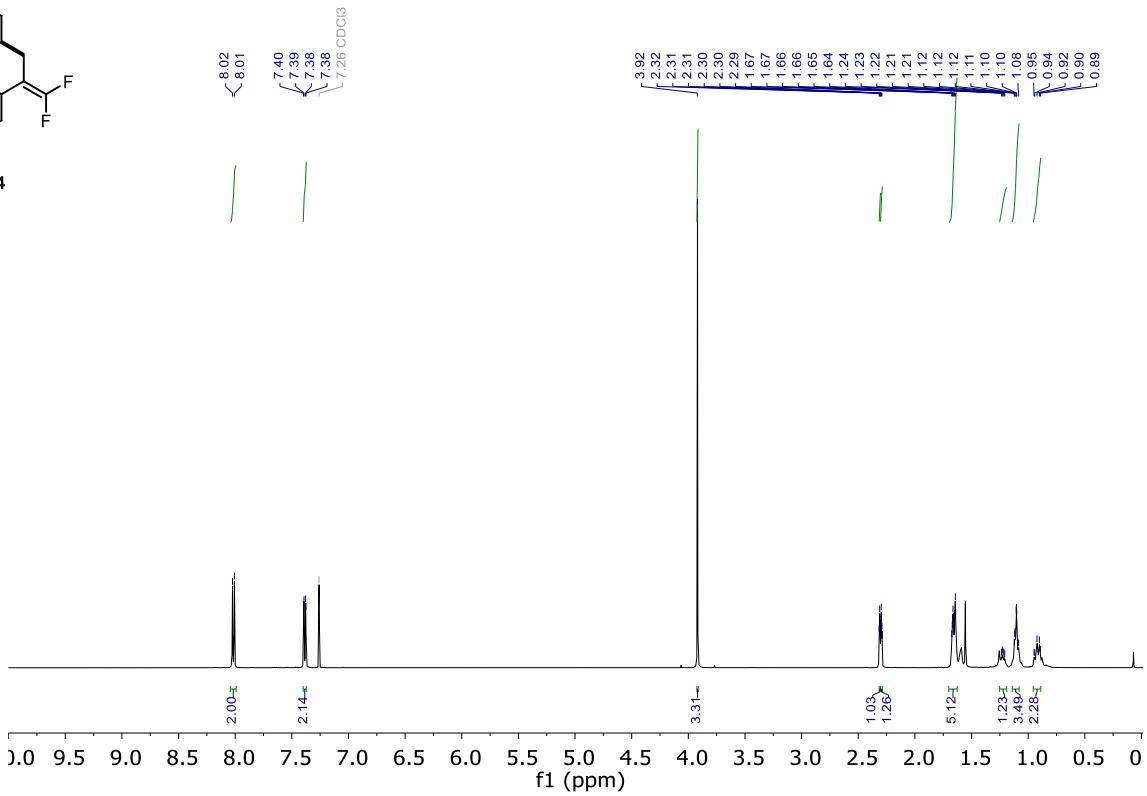
23



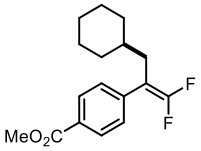
^{1}H NMR (500 MHz, $CDCl_3$)



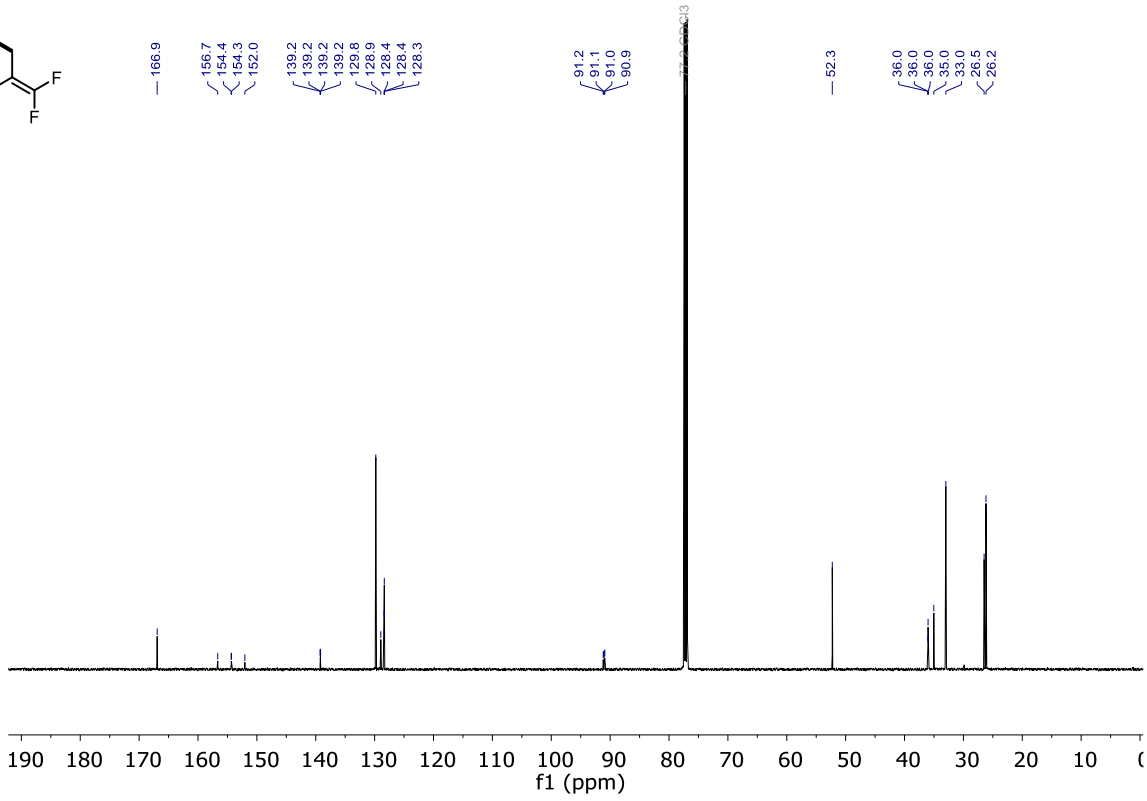
24



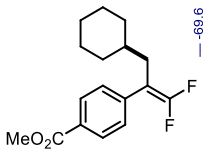
^{13}C NMR (126 MHz, $CDCl_3$)



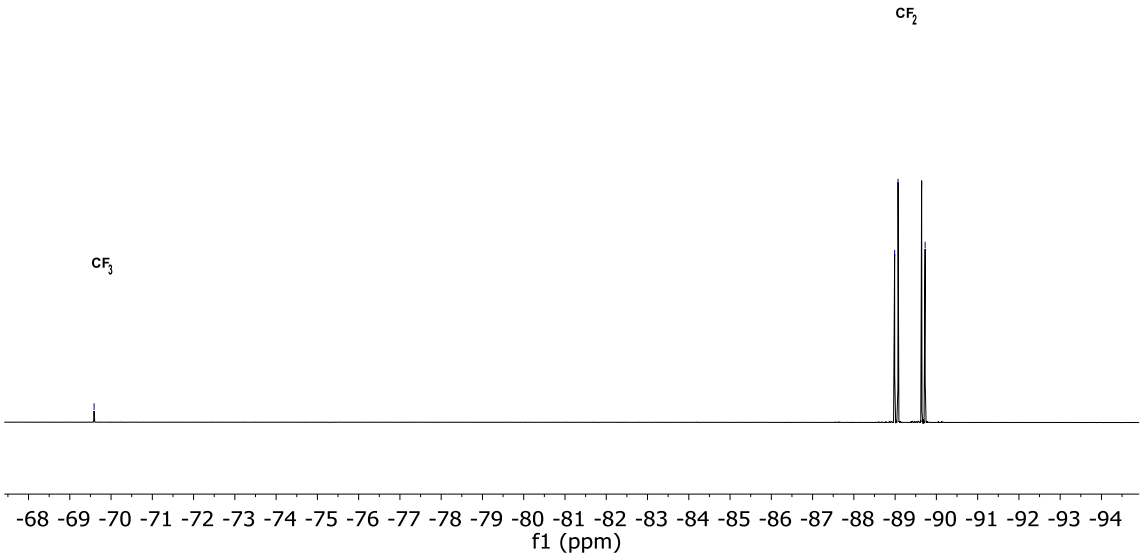
24



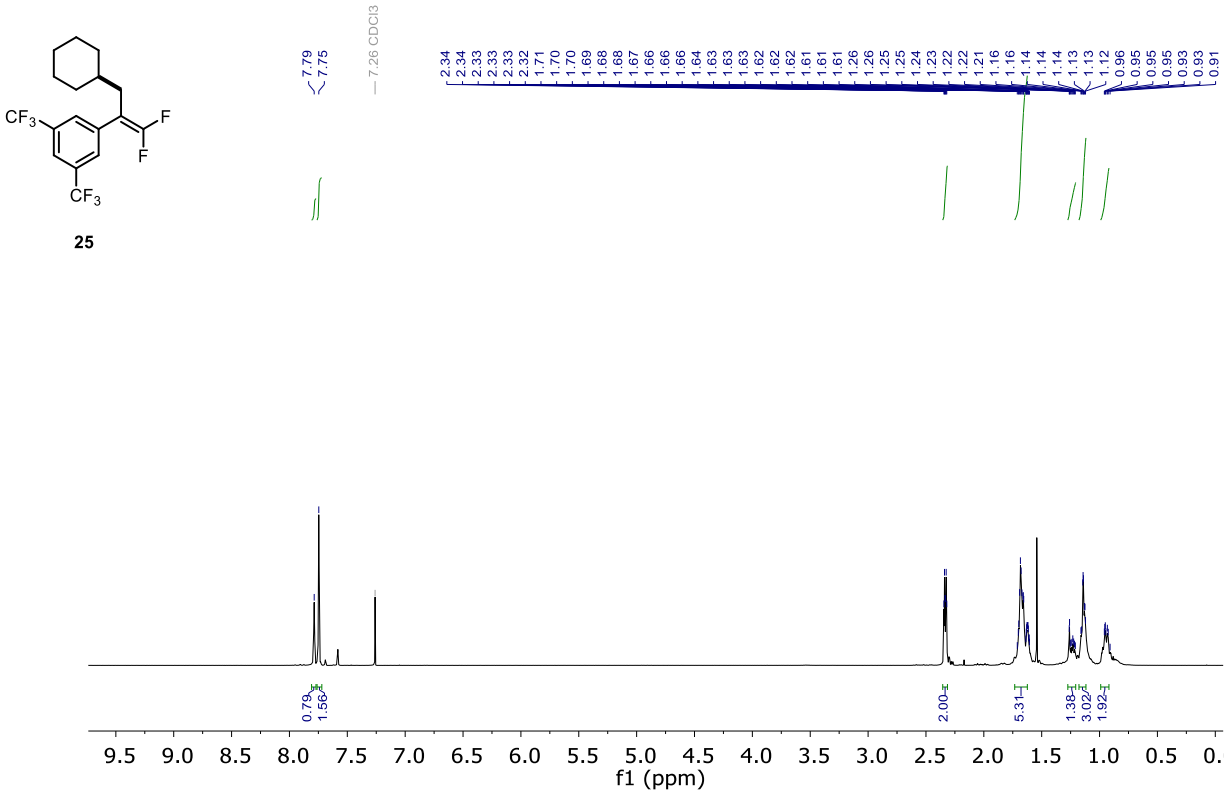
^{19}F NMR (282 MHz, $CDCl_3$)



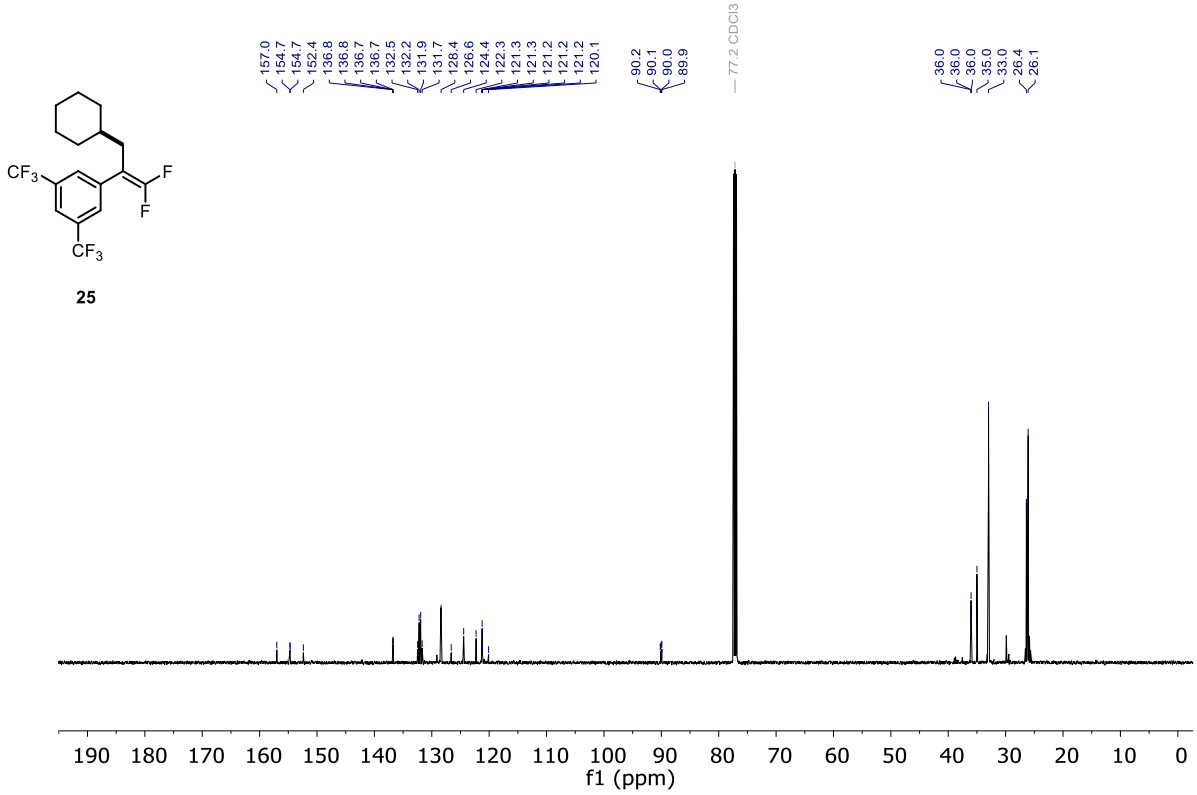
24



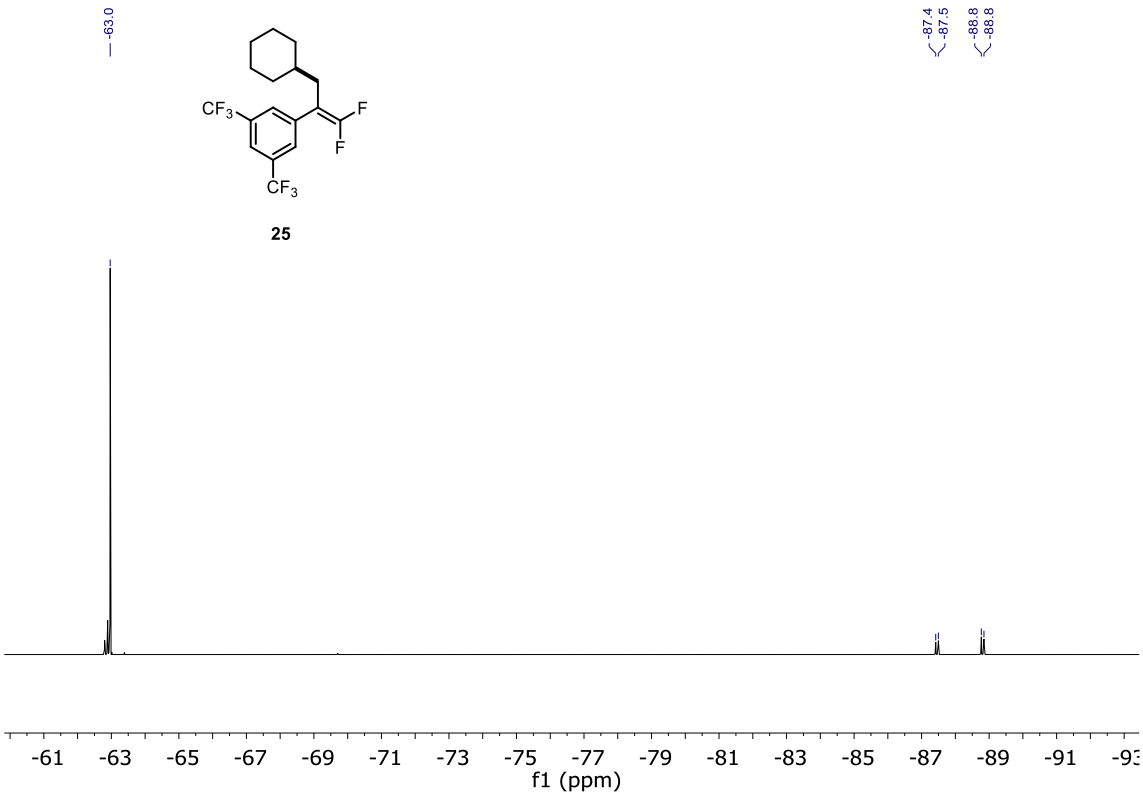
^{1}H NMR (500 MHz, $CDCl_3$)



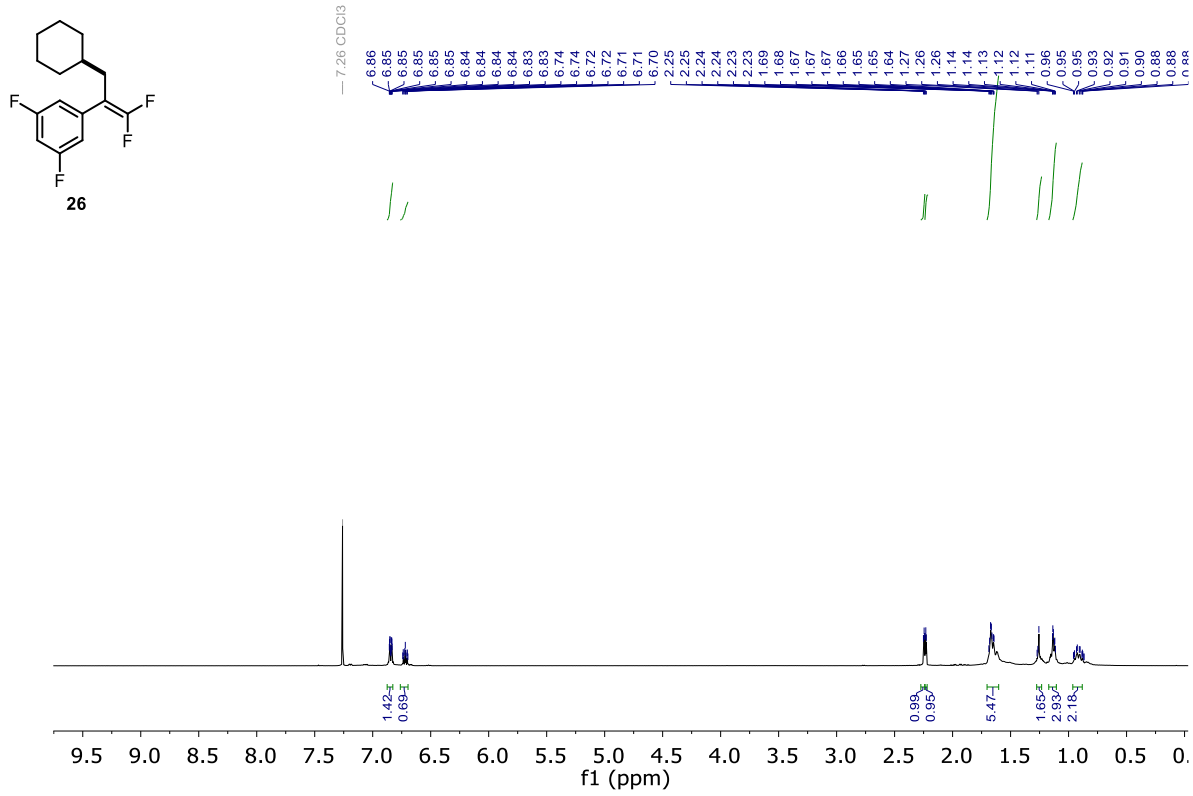
^{13}C NMR (126 MHz, $CDCl_3$)



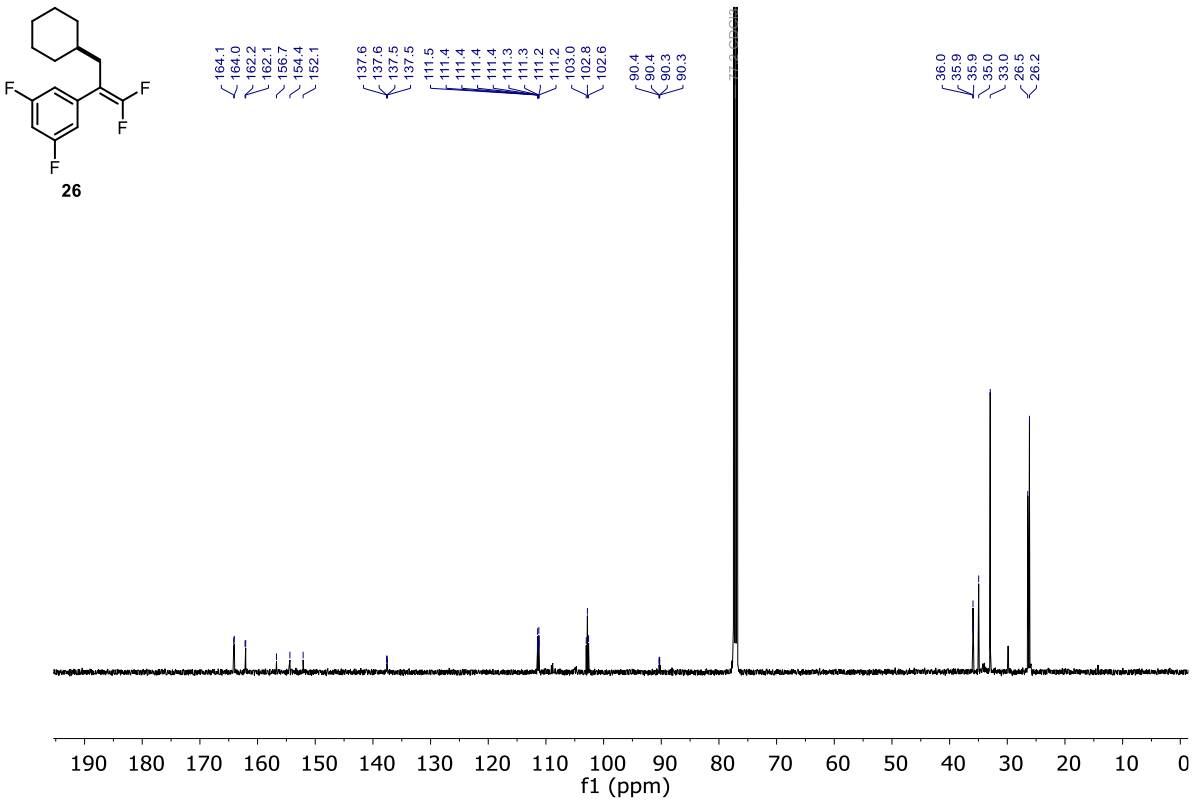
^{19}F NMR (282 MHz, $CDCl_3$)



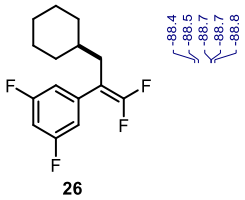
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

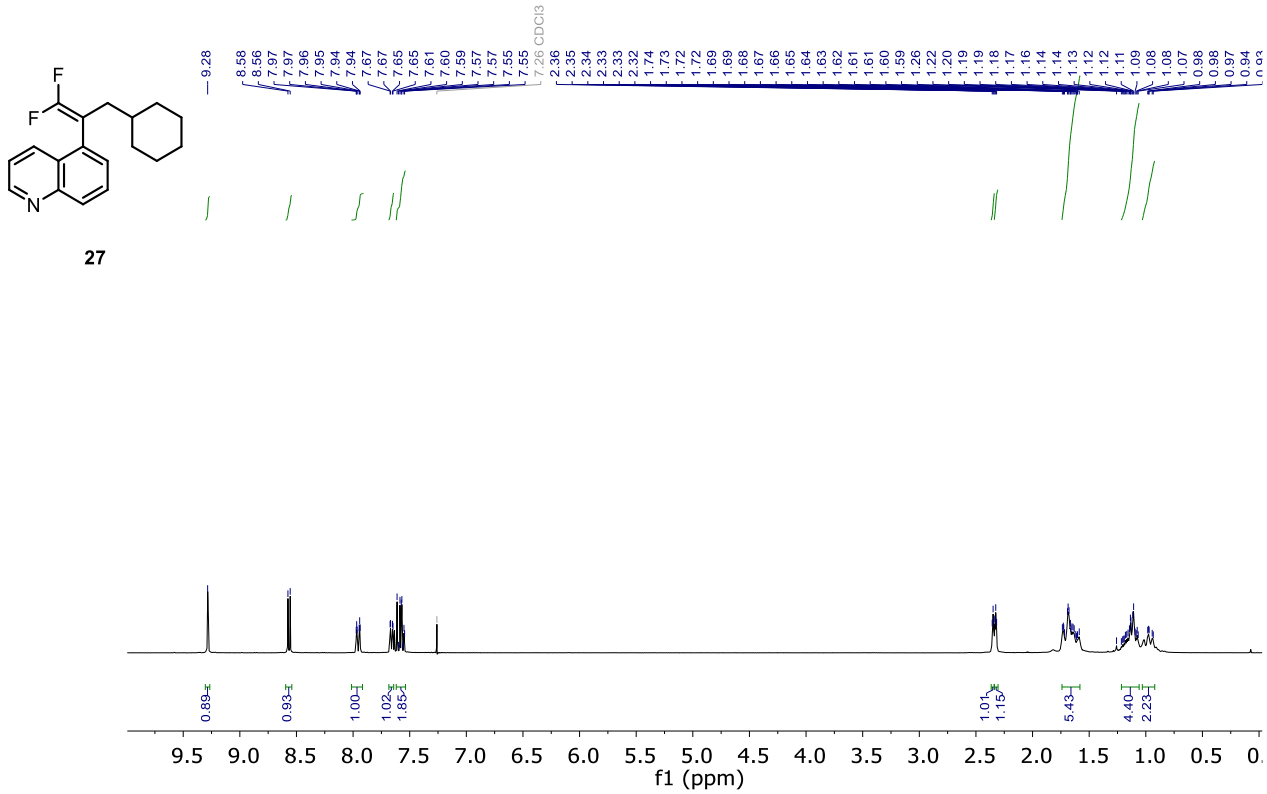


^{19}F NMR (282 MHz, $CDCl_3$)



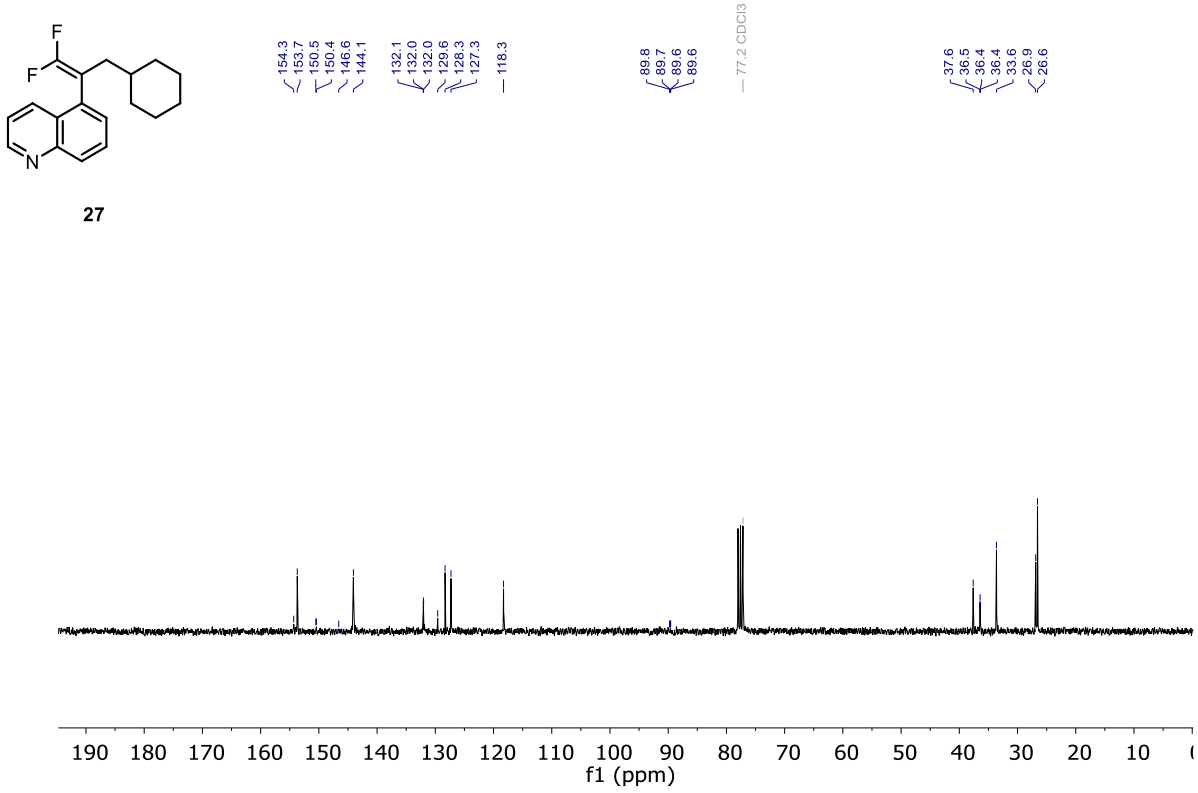
26

^{1}H NMR (500 MHz, $CDCl_3$)



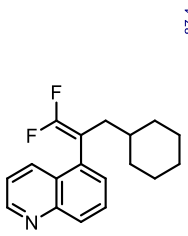
27

^{13}C NMR (126 MHz, $CDCl_3$)



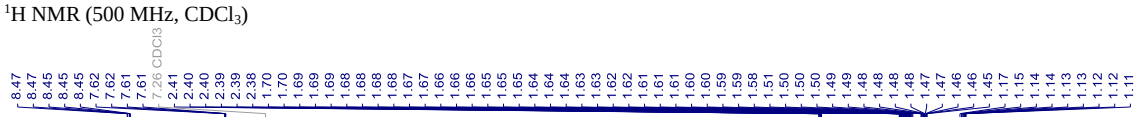
27

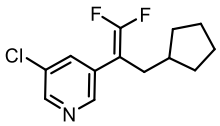
^{19}F NMR (282 MHz, $CDCl_3$)



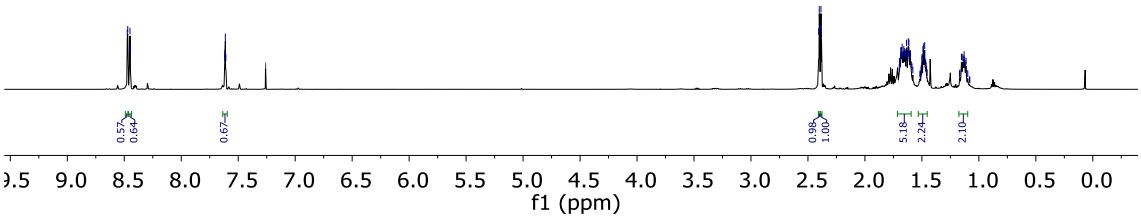
27

^{1}H NMR (500 MHz, $CDCl_3$)

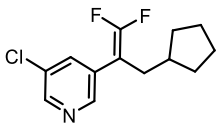




28

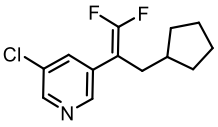


^{13}C NMR (126 MHz, $CDCl_3$)



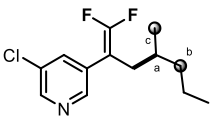
28

^{19}F NMR (282 MHz, $CDCl_3$)

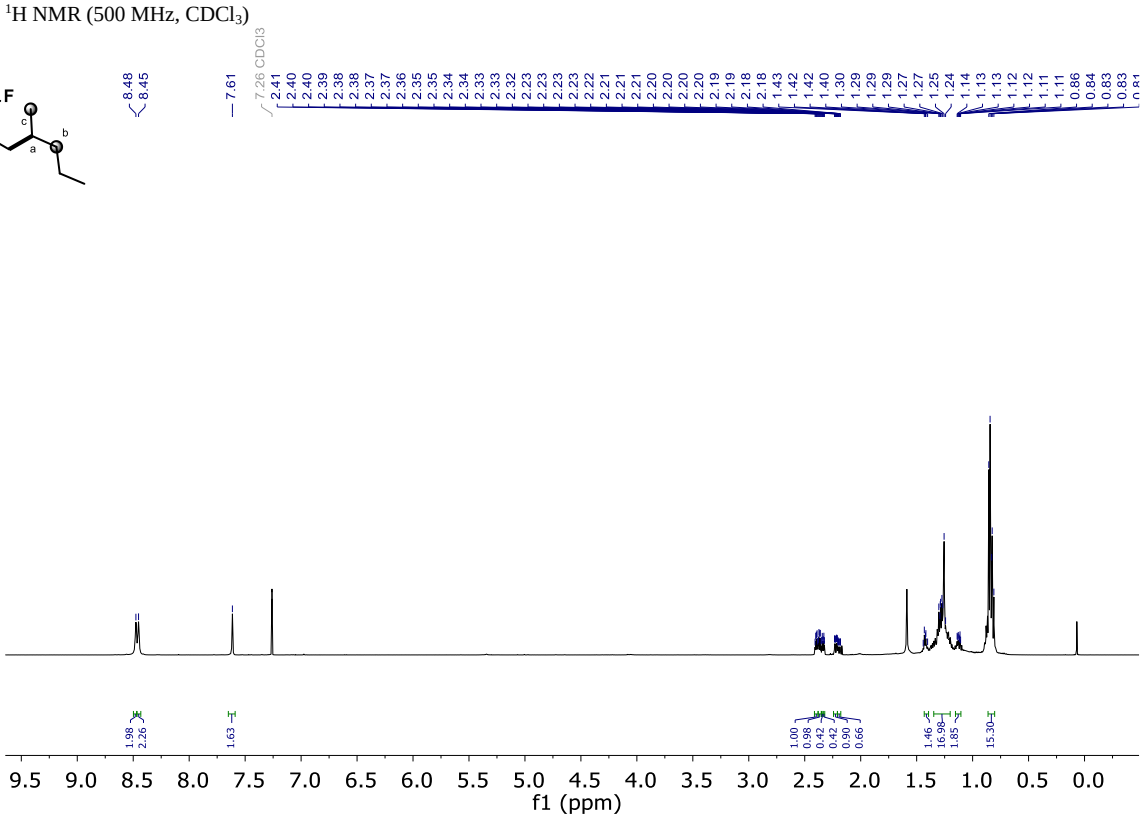


28

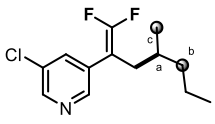
^{1}H NMR (500 MHz, $CDCl_3$)



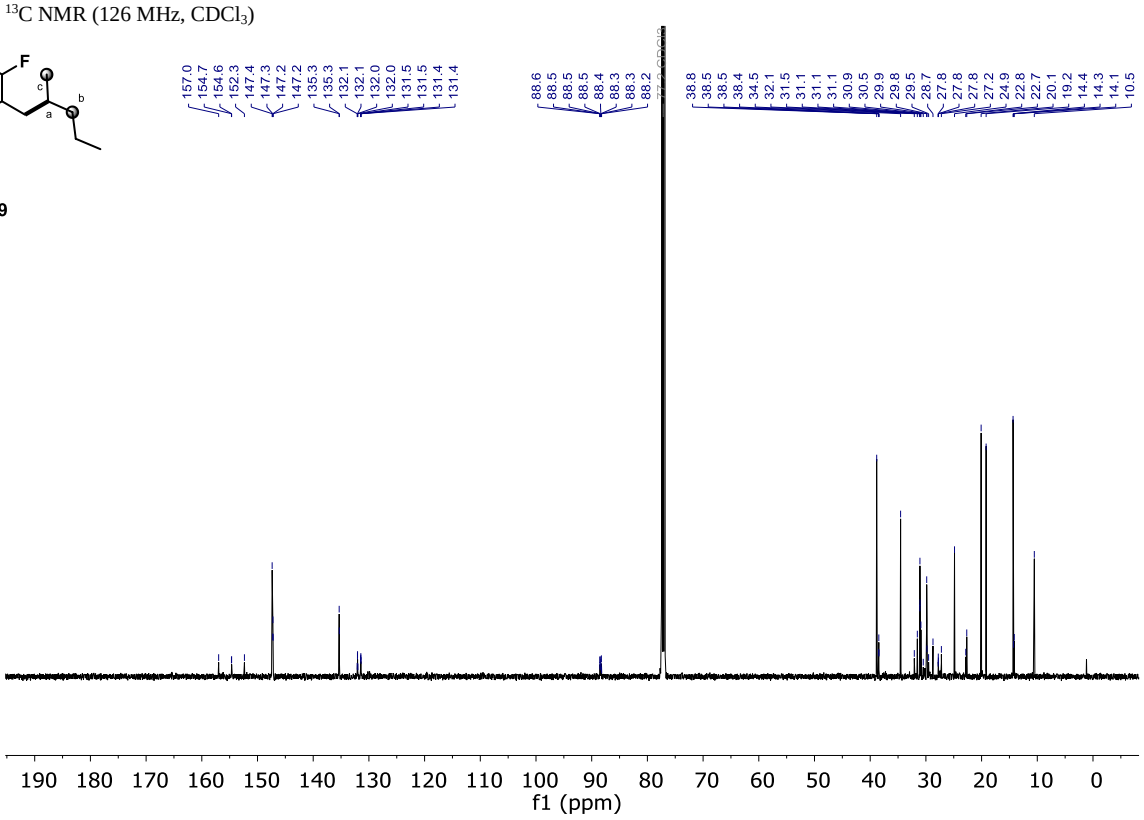
29



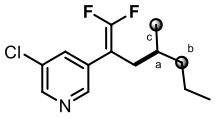
^{13}C NMR (126 MHz, $CDCl_3$)



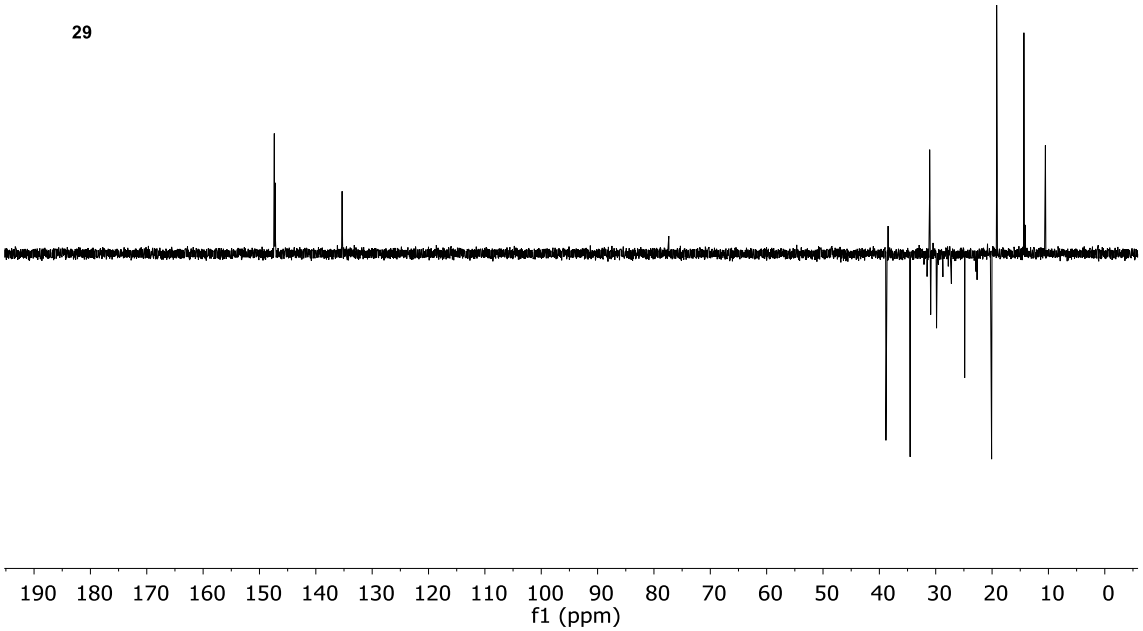
29



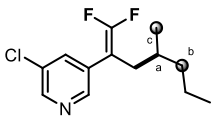
DEPT-135 (126 MHz, $CDCl_3$)



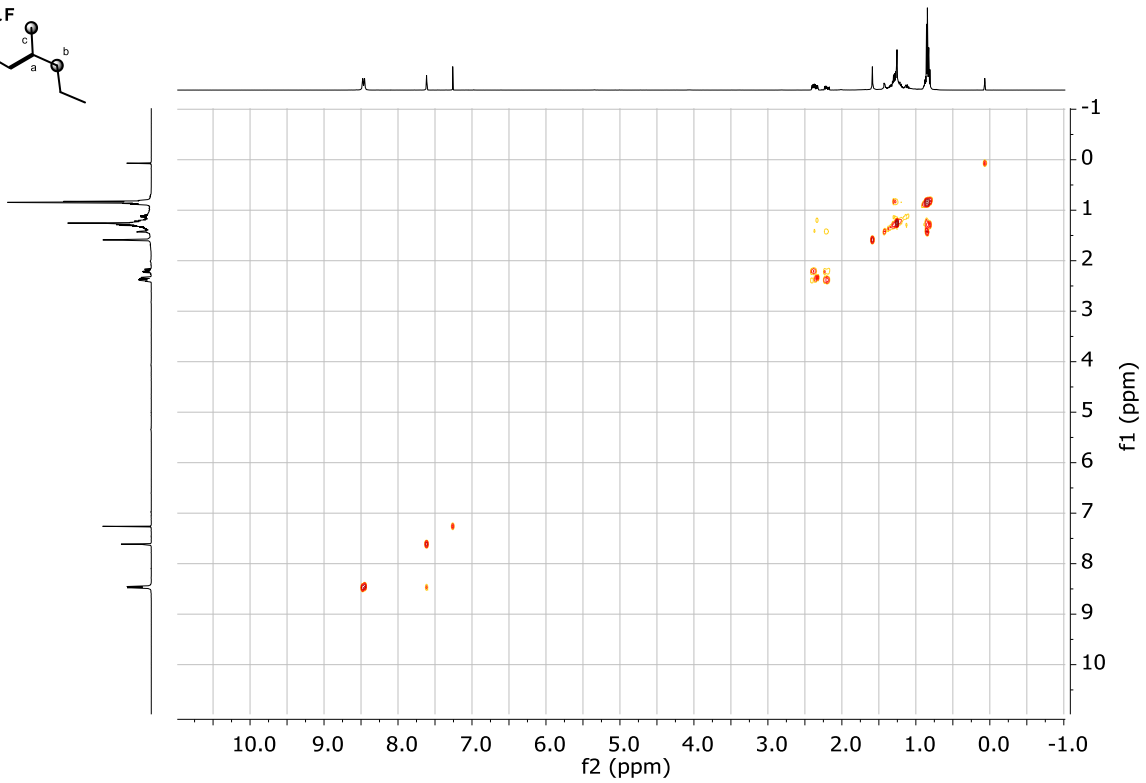
29



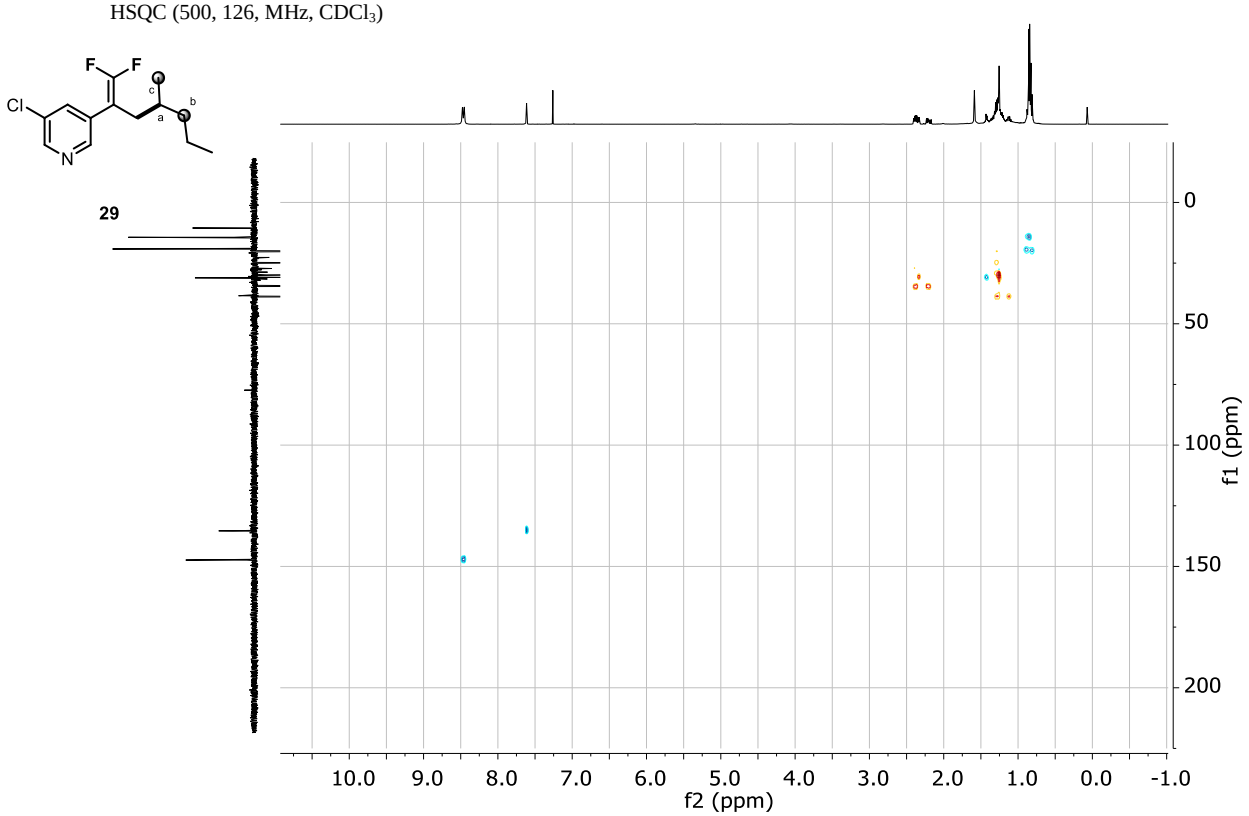
COSY (500 MHz, $CDCl_3$)



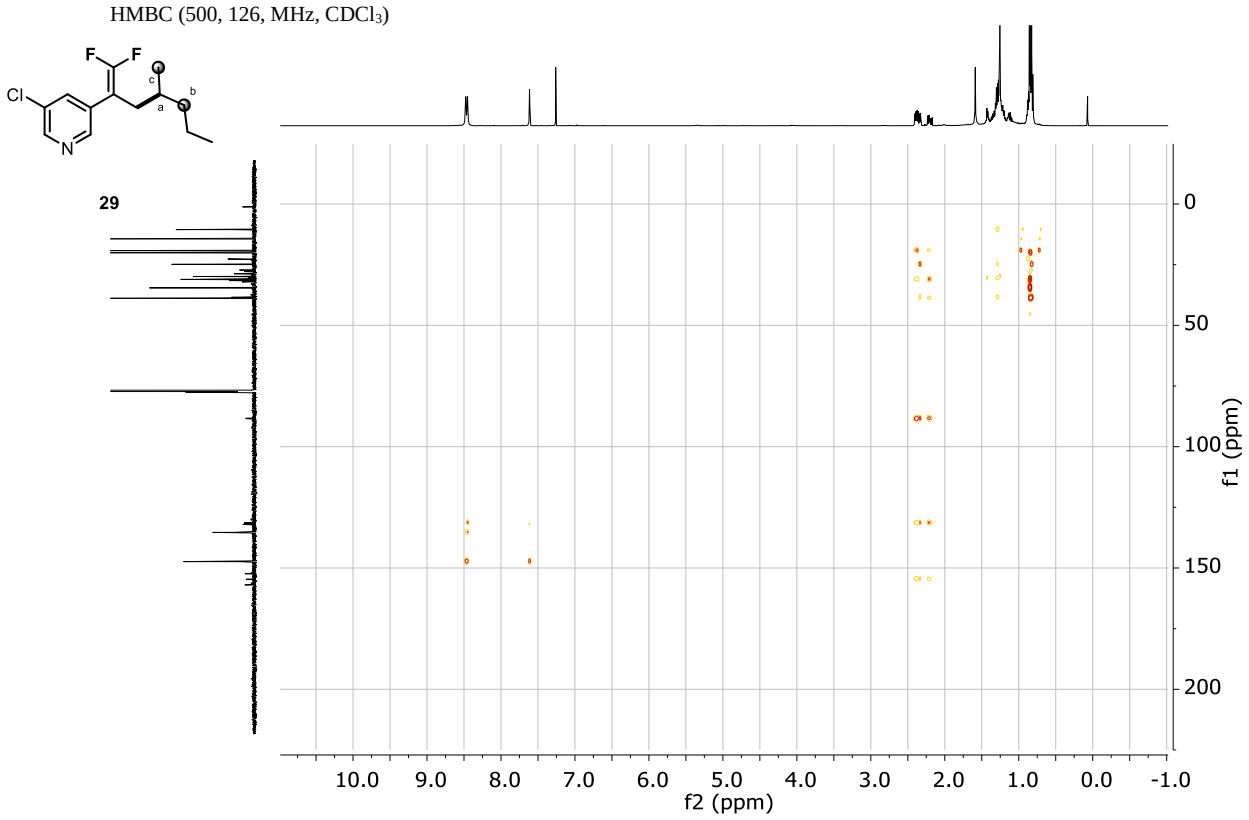
29



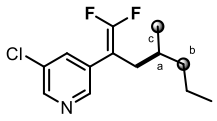
HSQC (500, 126, MHz, $CDCl_3$)



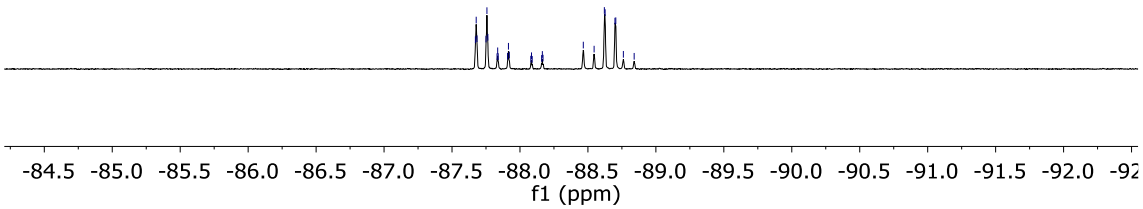
HMBC (500, 126, MHz, $CDCl_3$)



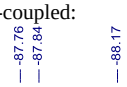
^{19}F NMR (282 MHz, $CDCl_3$) proton coupled:

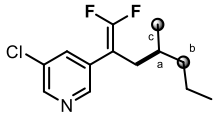


29

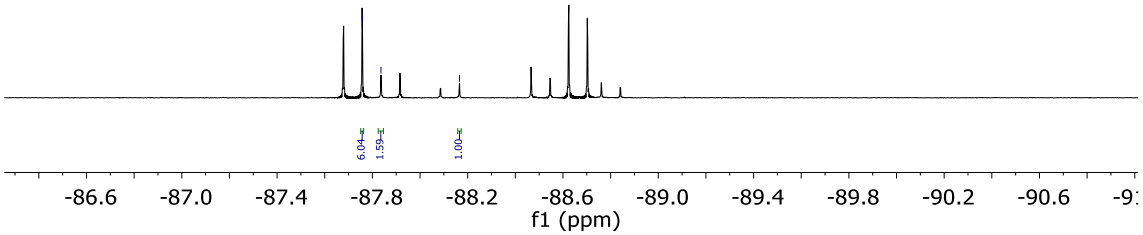


^{19}F NMR (282 MHz, $CDCl_3$) proton de-coupled:

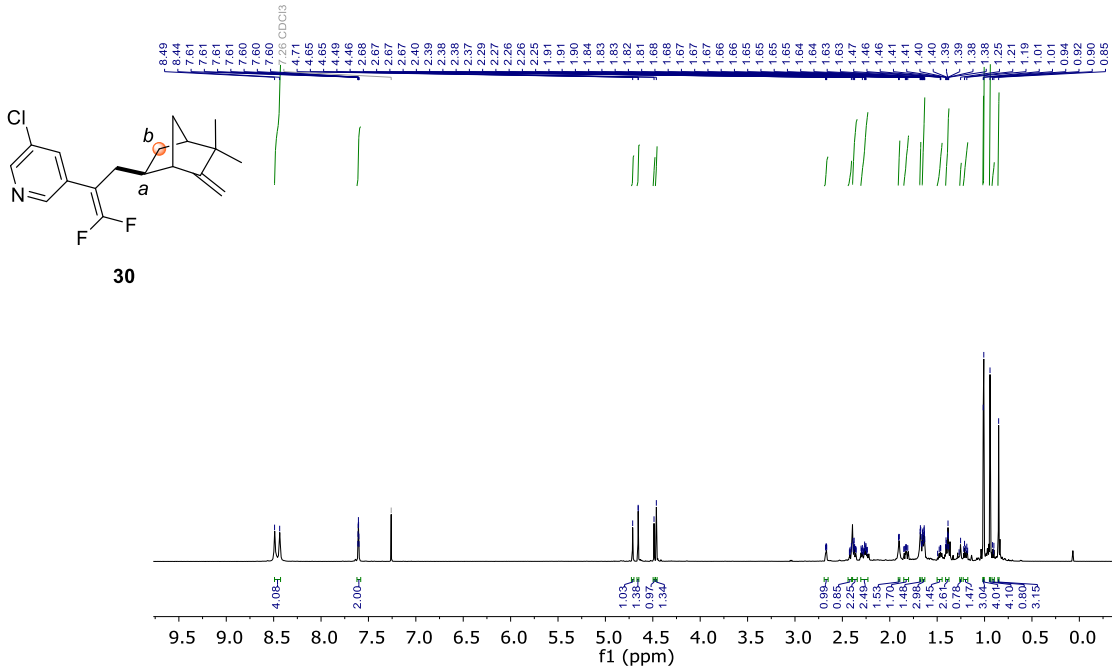




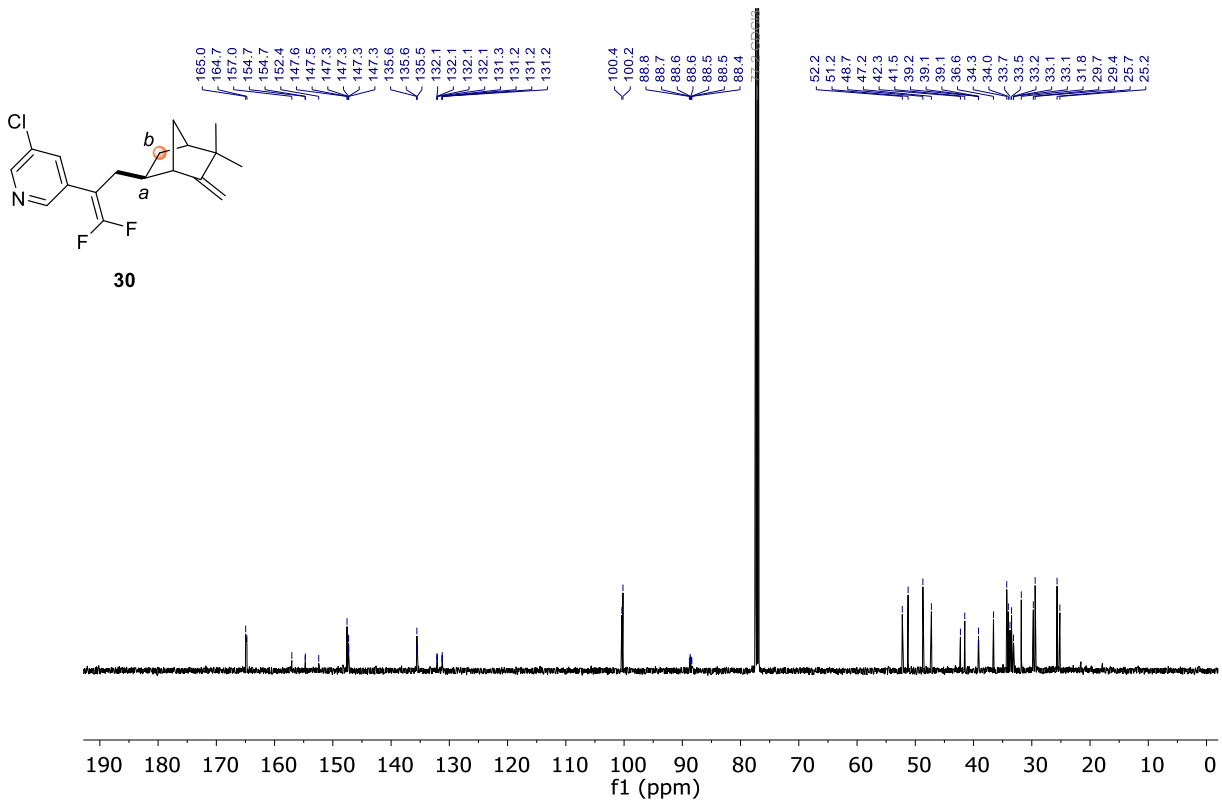
29



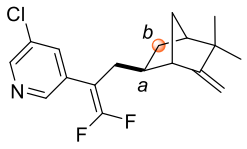
^{1}H NMR (500 MHz, $CDCl_3$)



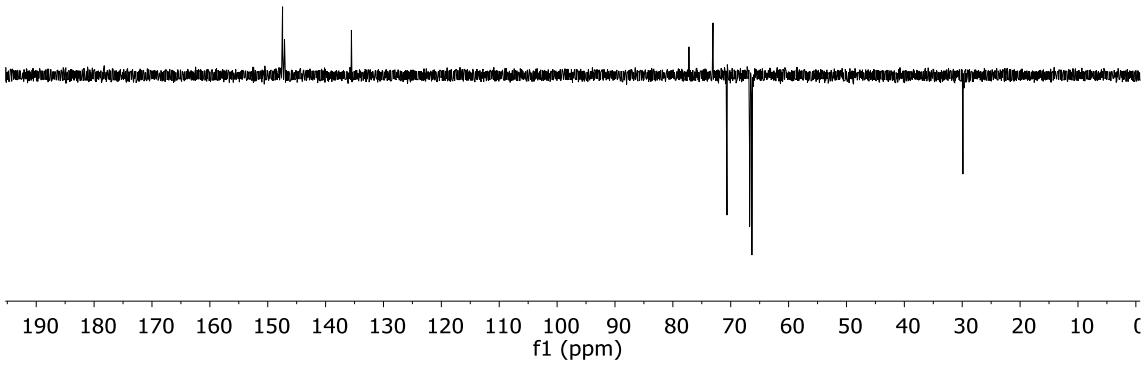
^{13}C NMR (126 MHz, $CDCl_3$)



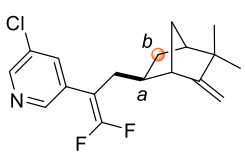
DEPT-135 (126 MHz, $CDCl_3$)



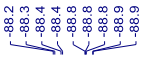
30

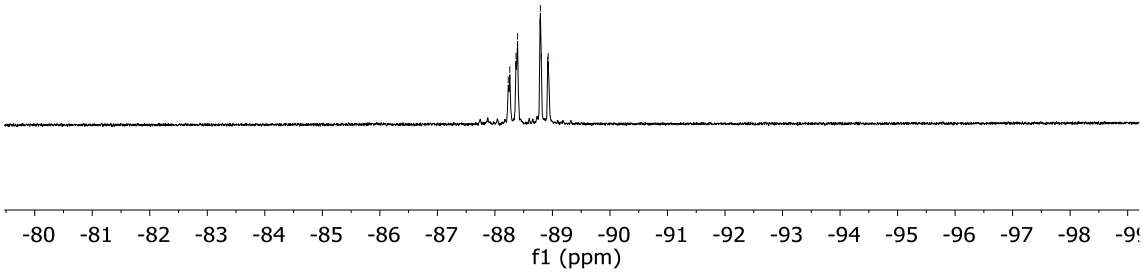


^{19}F NMR (282 MHz, $CDCl_3$)

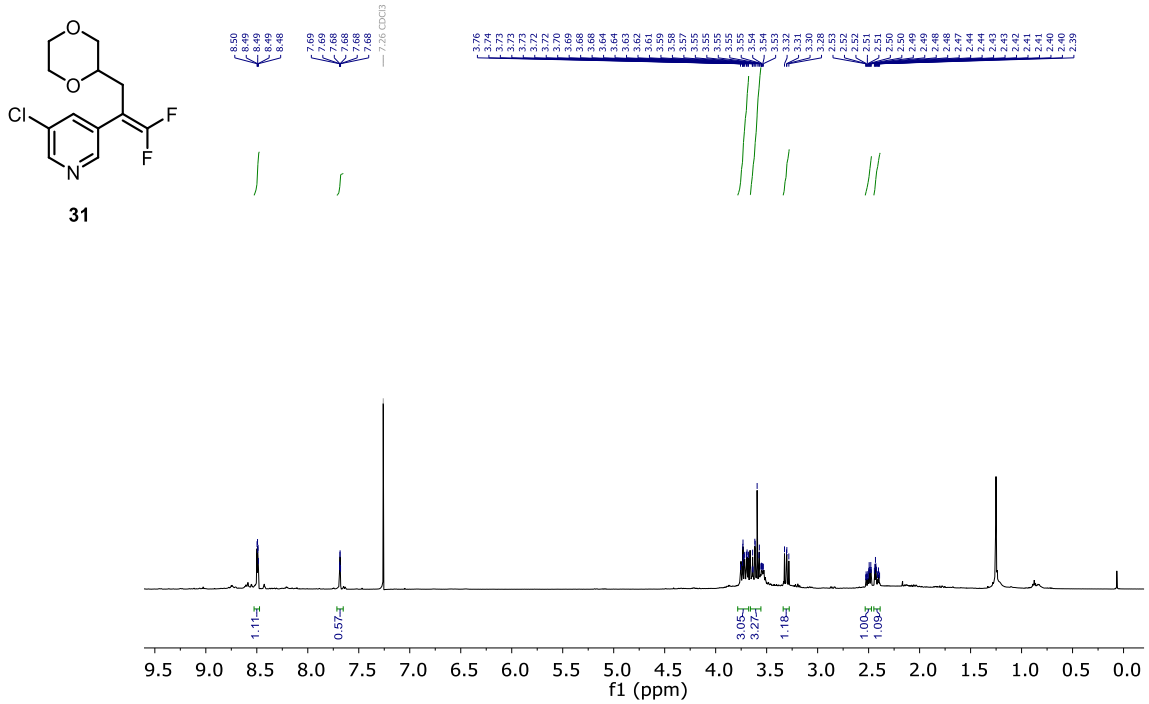


30

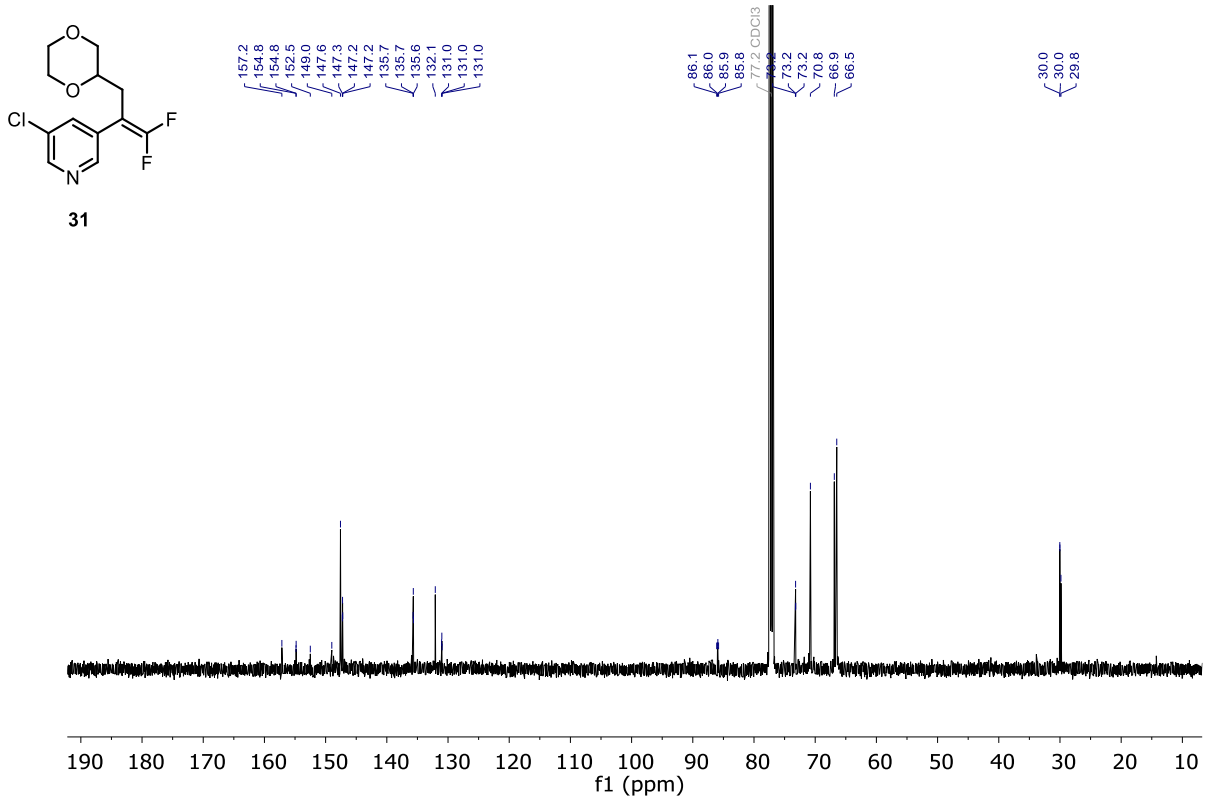




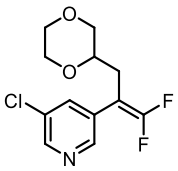
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

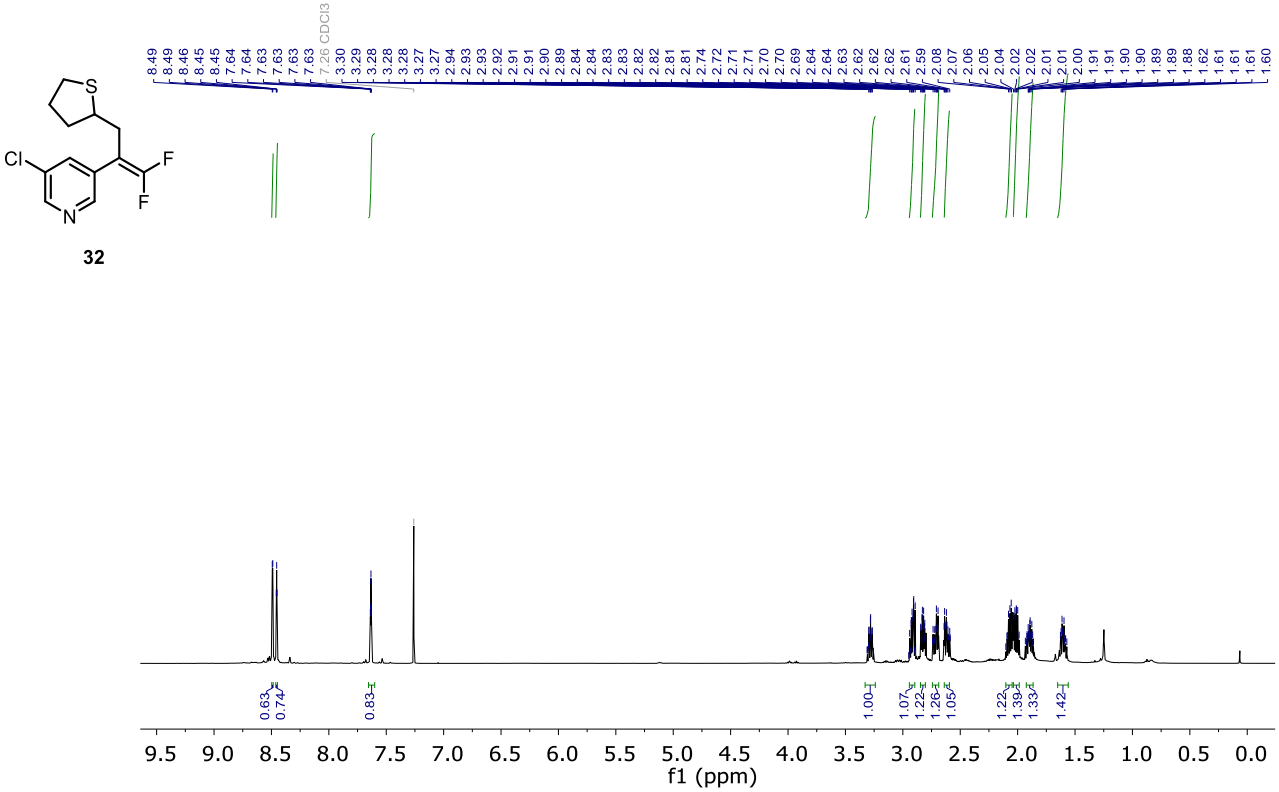


^{19}F NMR (282 MHz, $CDCl_3$)

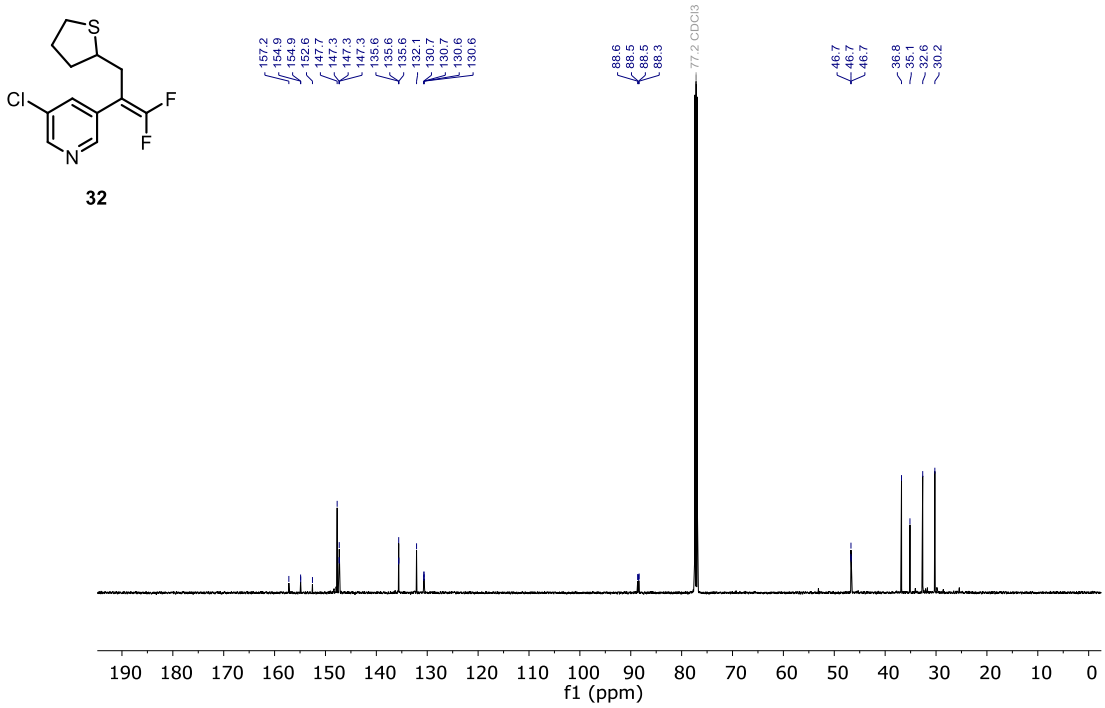


31

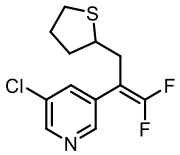
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

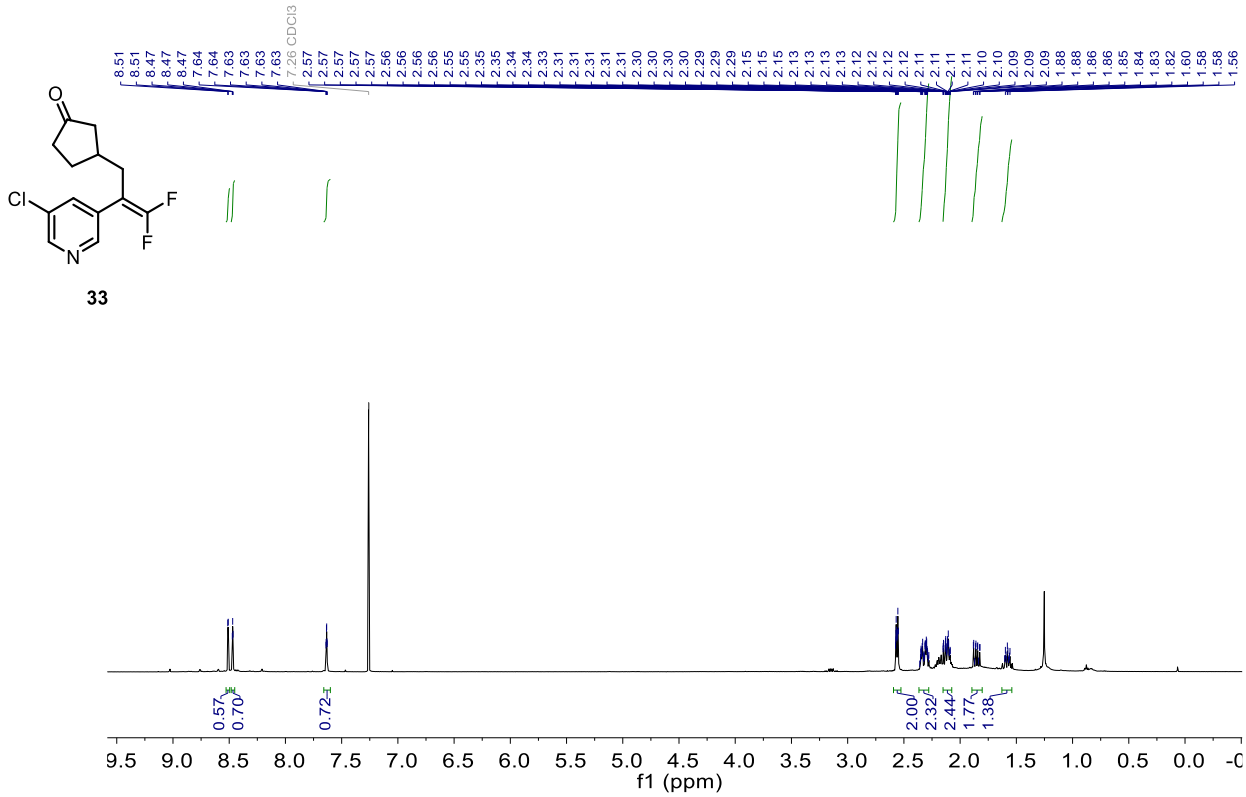


^{19}F NMR (282 MHz, $CDCl_3$)

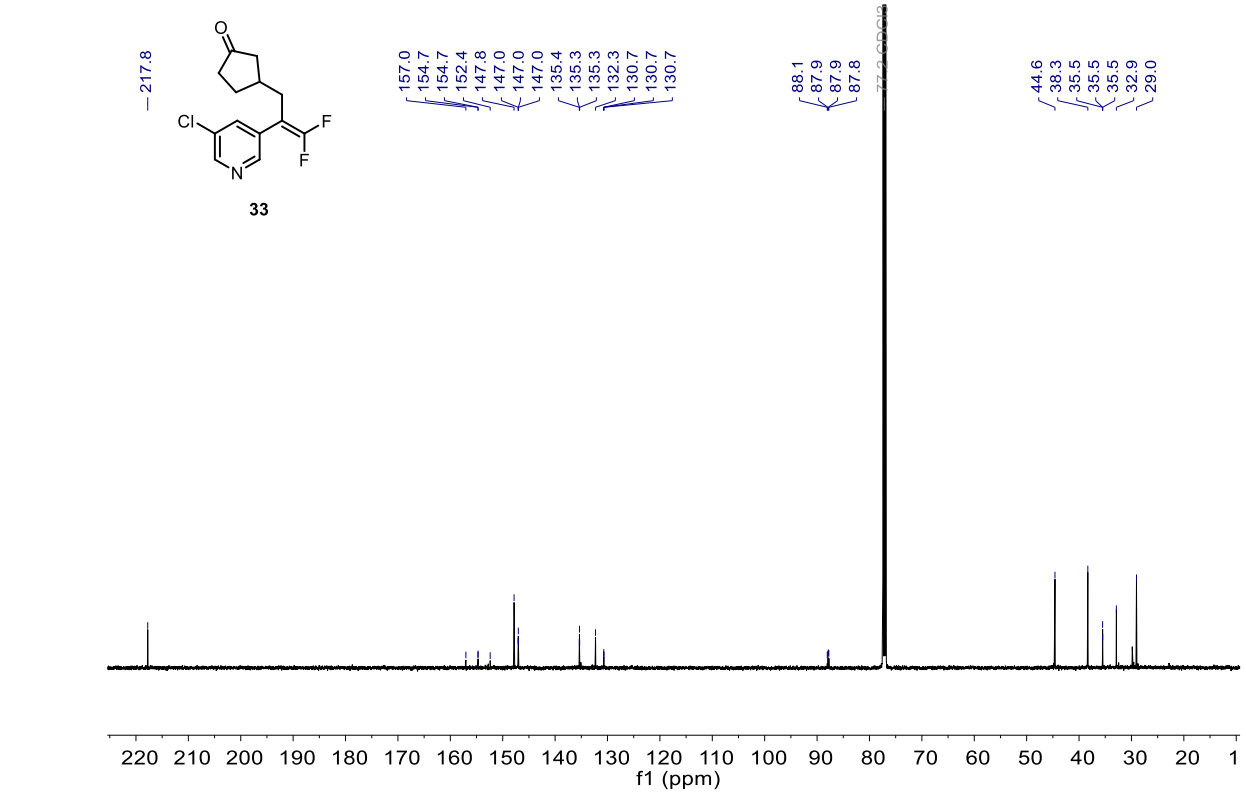


32

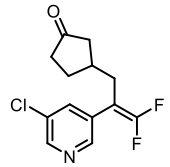
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

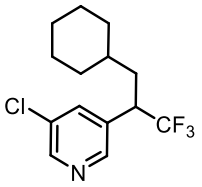


^{19}F NMR (282 MHz, $CDCl_3$)

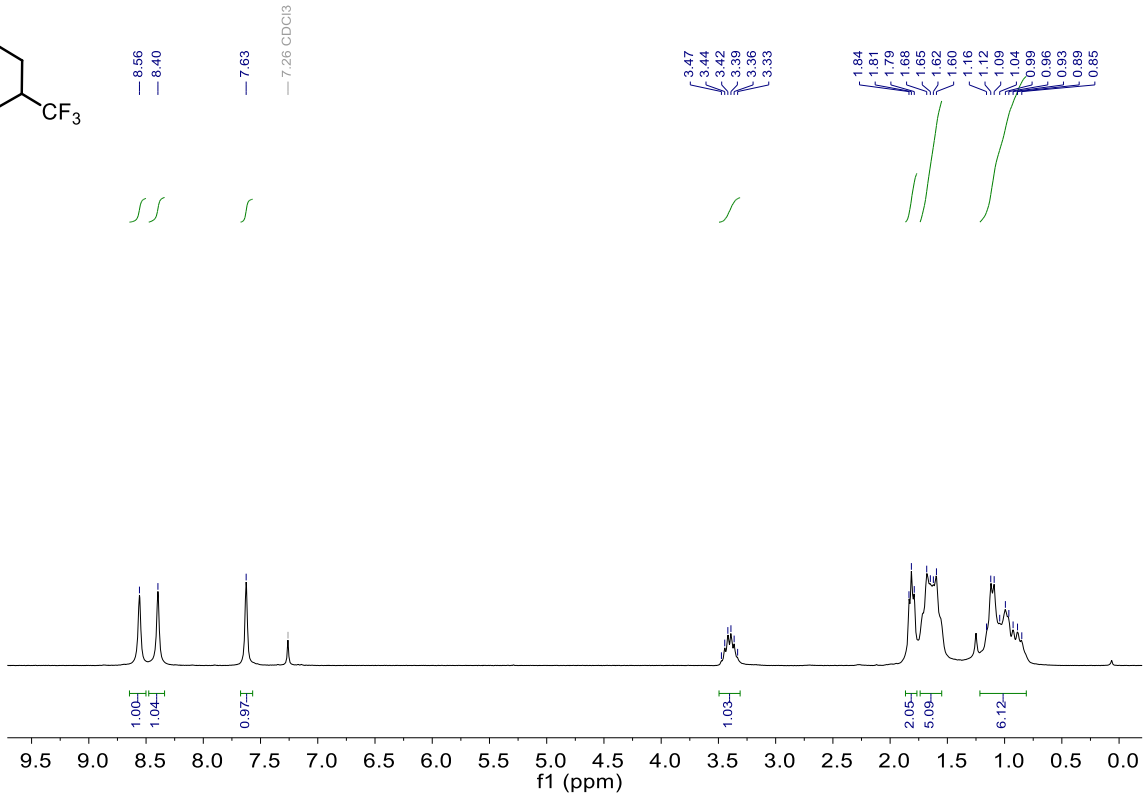


33

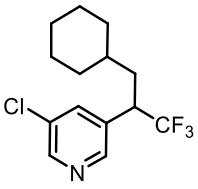
^{1}H NMR (500 MHz, $CDCl_3$)



21

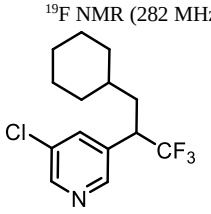


^{13}C NMR (126 MHz, $CDCl_3$)



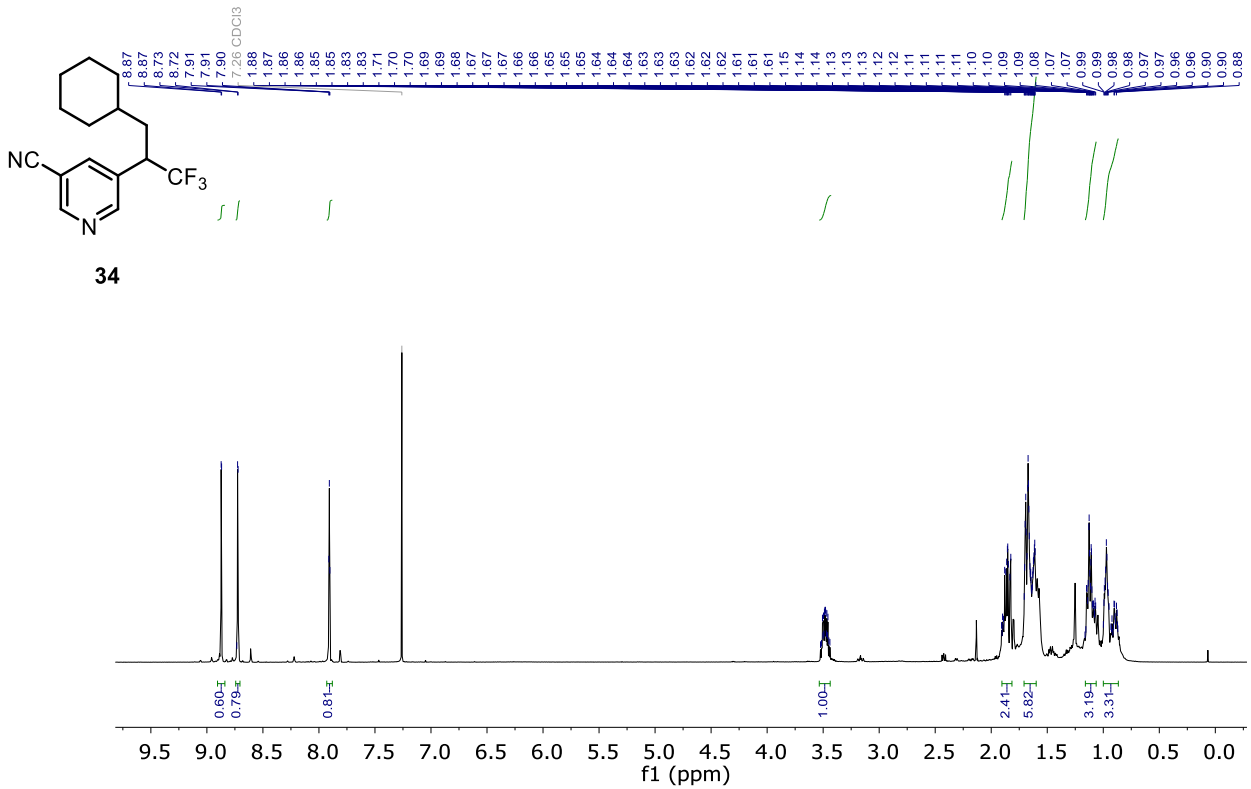
21

^{19}F NMR (282 MHz, $CDCl_3$)

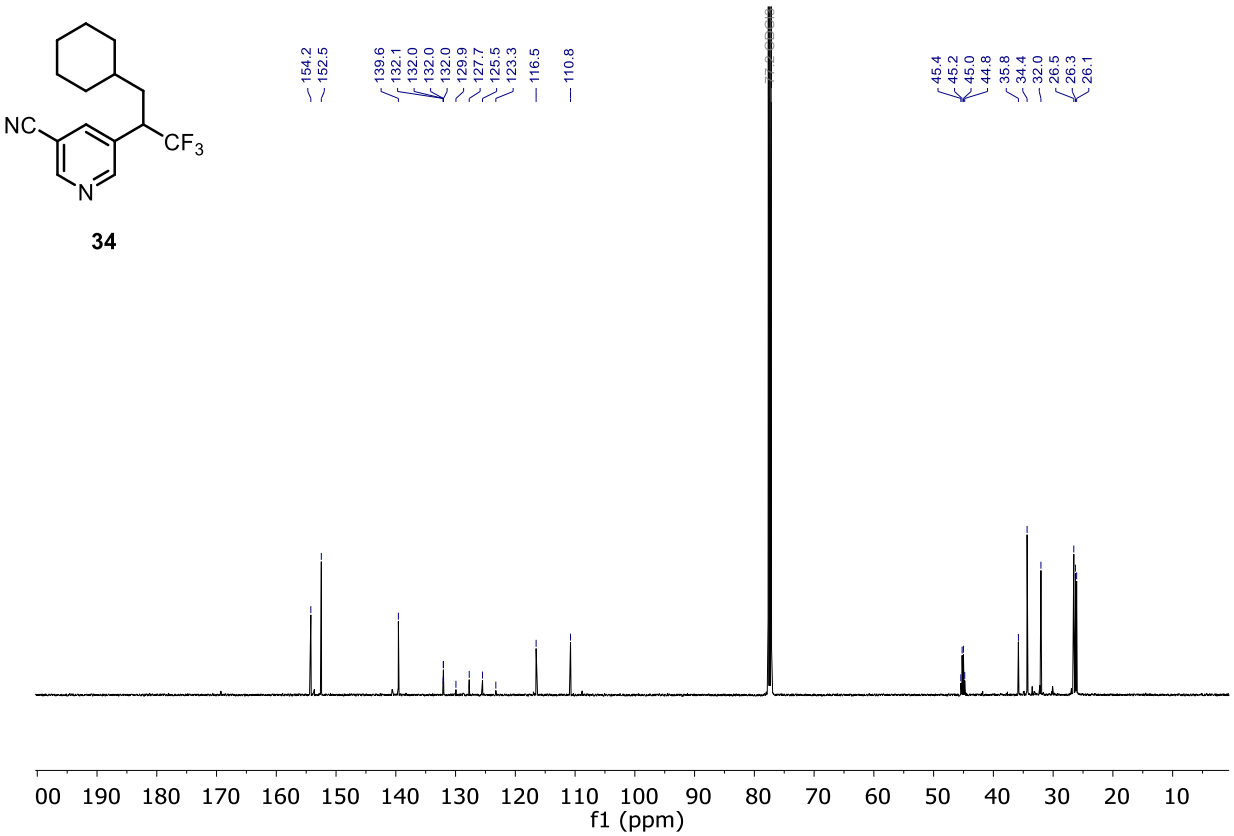


21

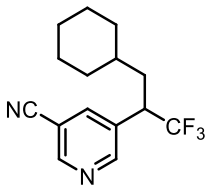
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

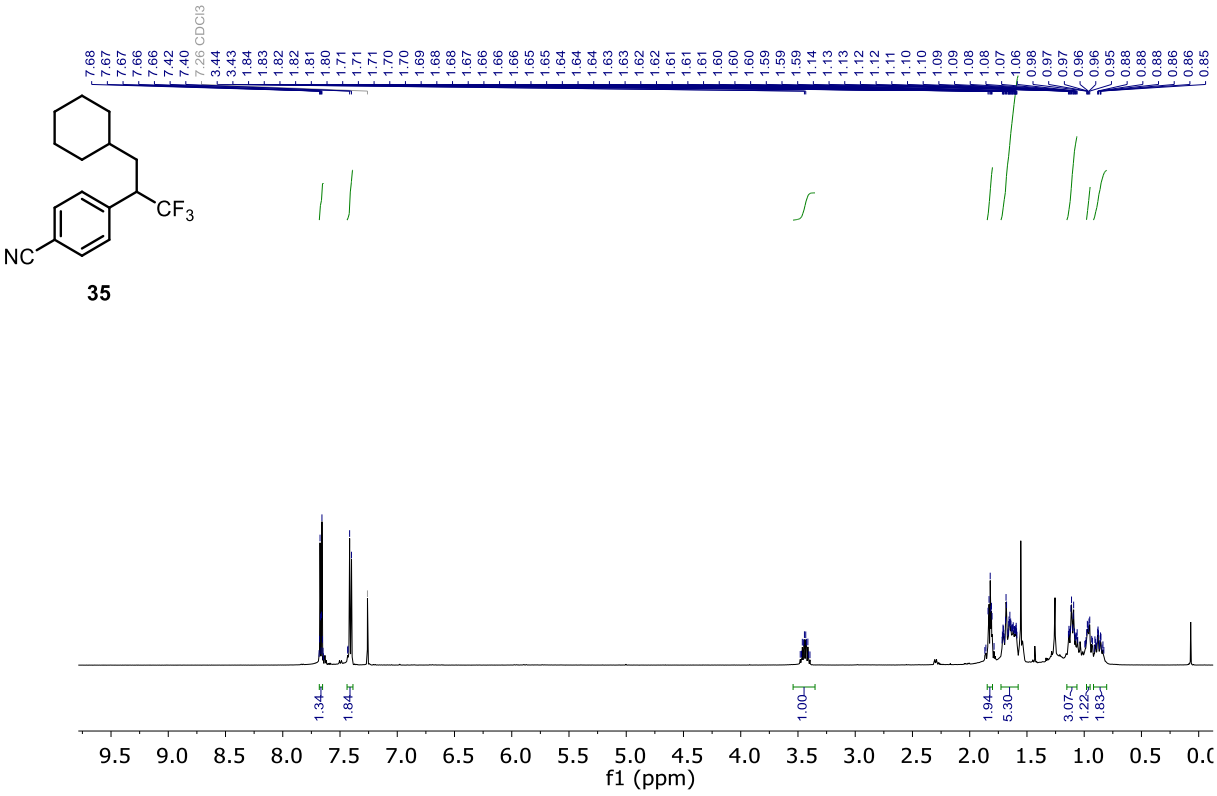


^{19}F NMR (282 MHz, $CDCl_3$)

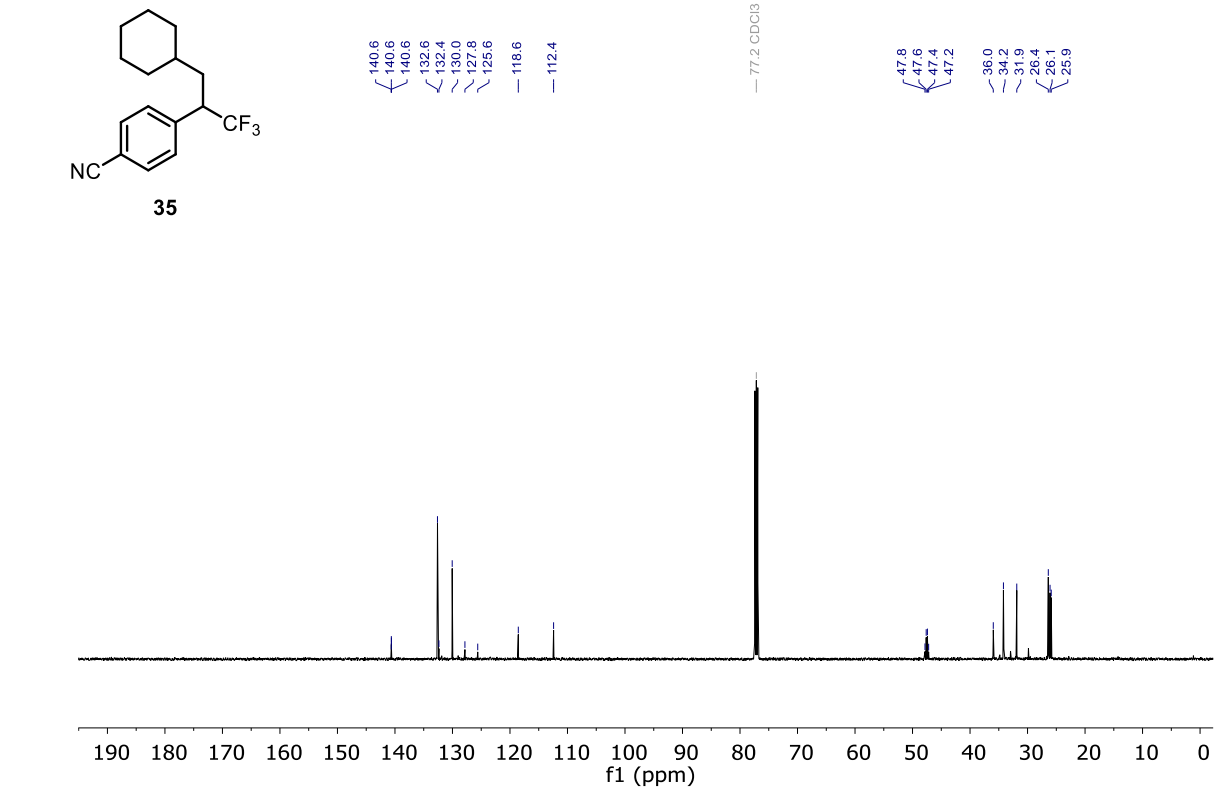


34

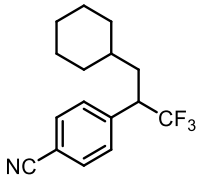
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

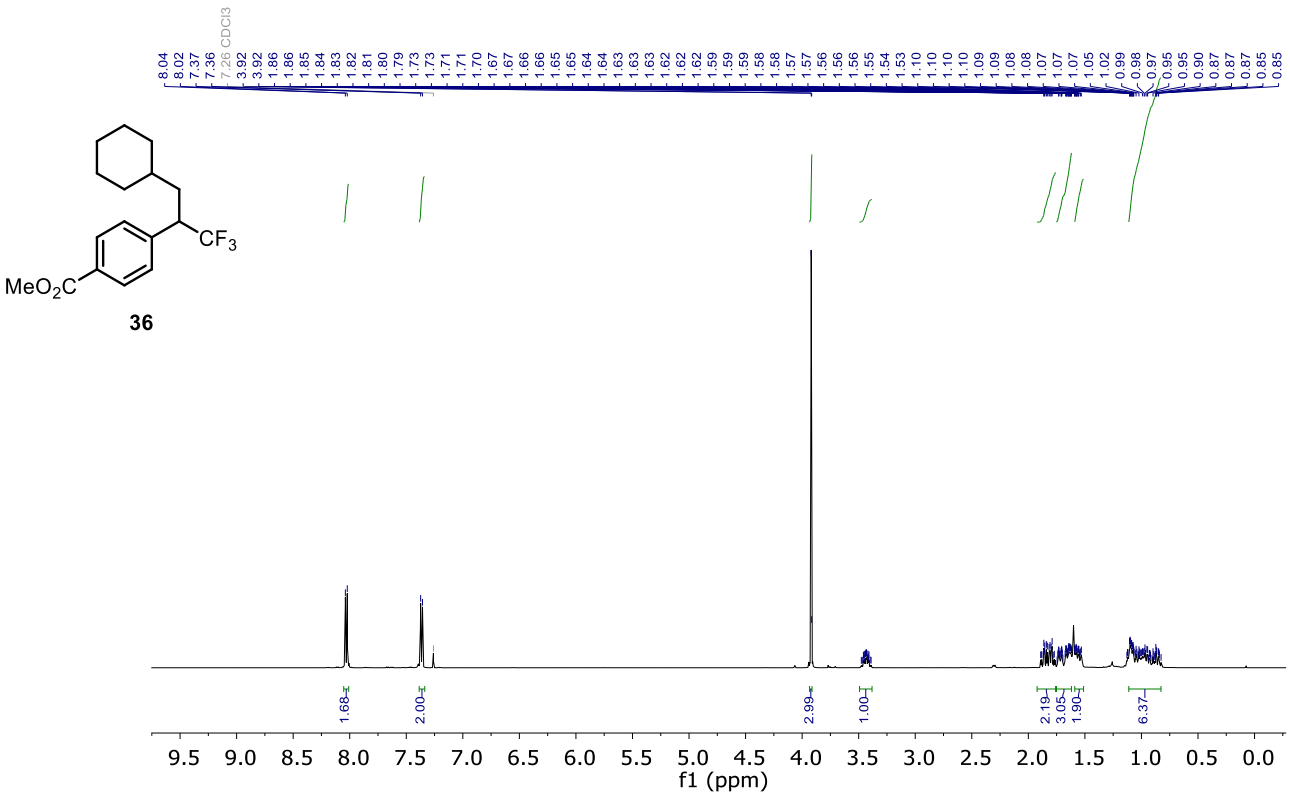


^{19}F NMR (282 MHz, $CDCl_3$)

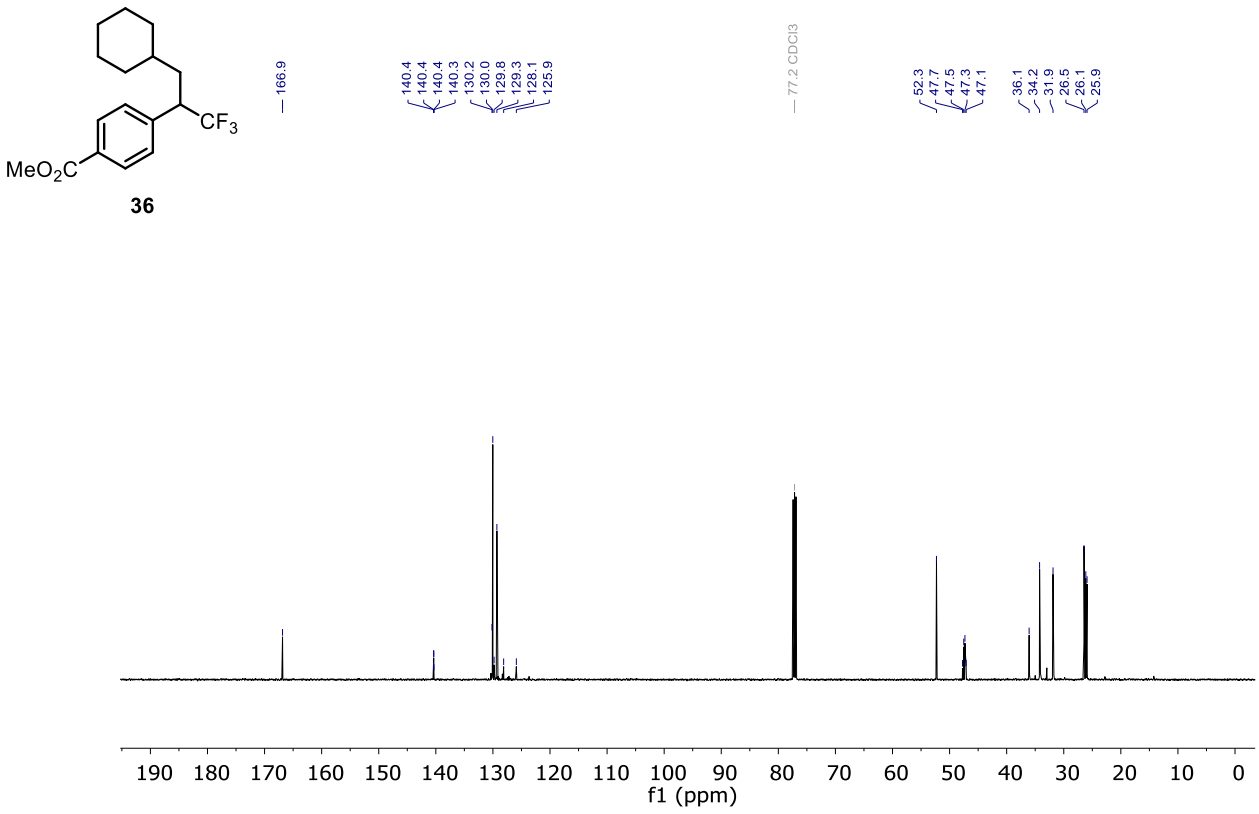


35

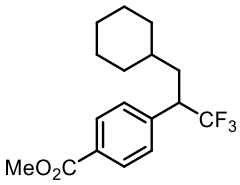
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

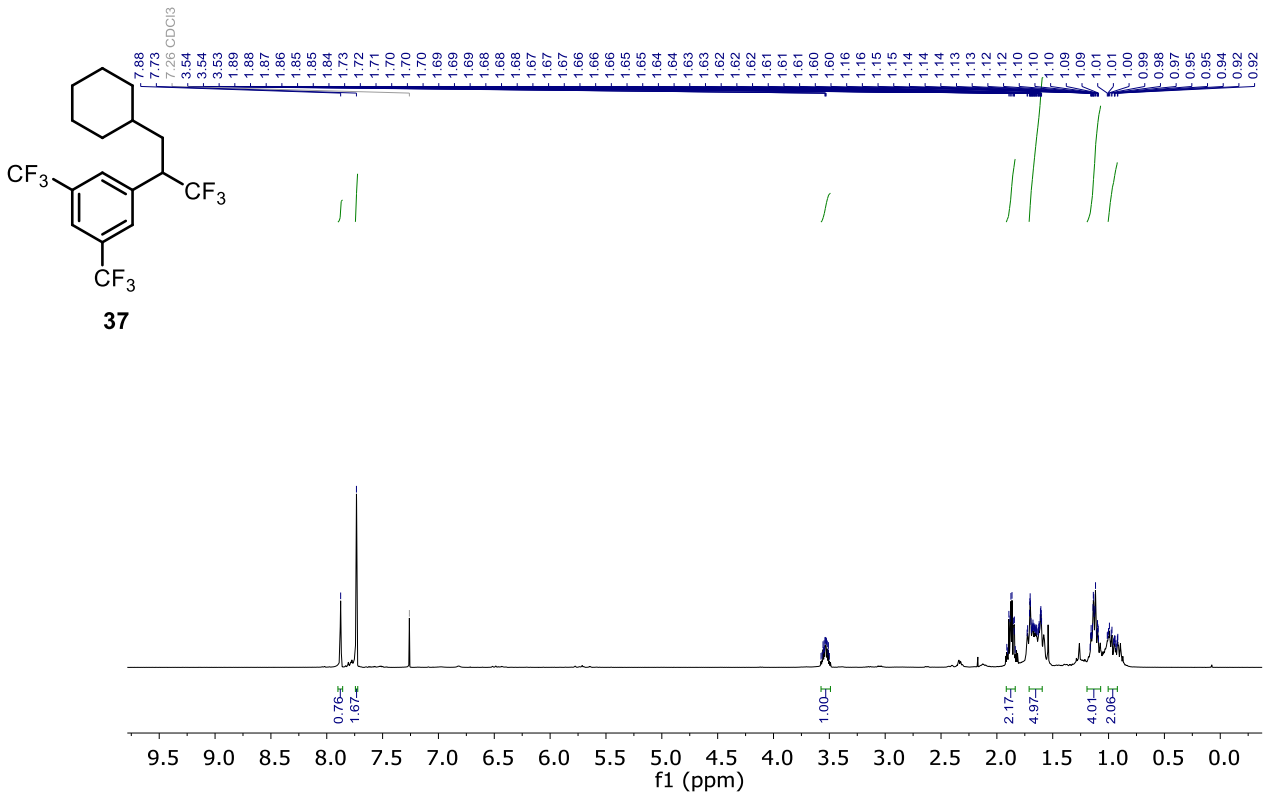


^{19}F NMR (282 MHz, $CDCl_3$)

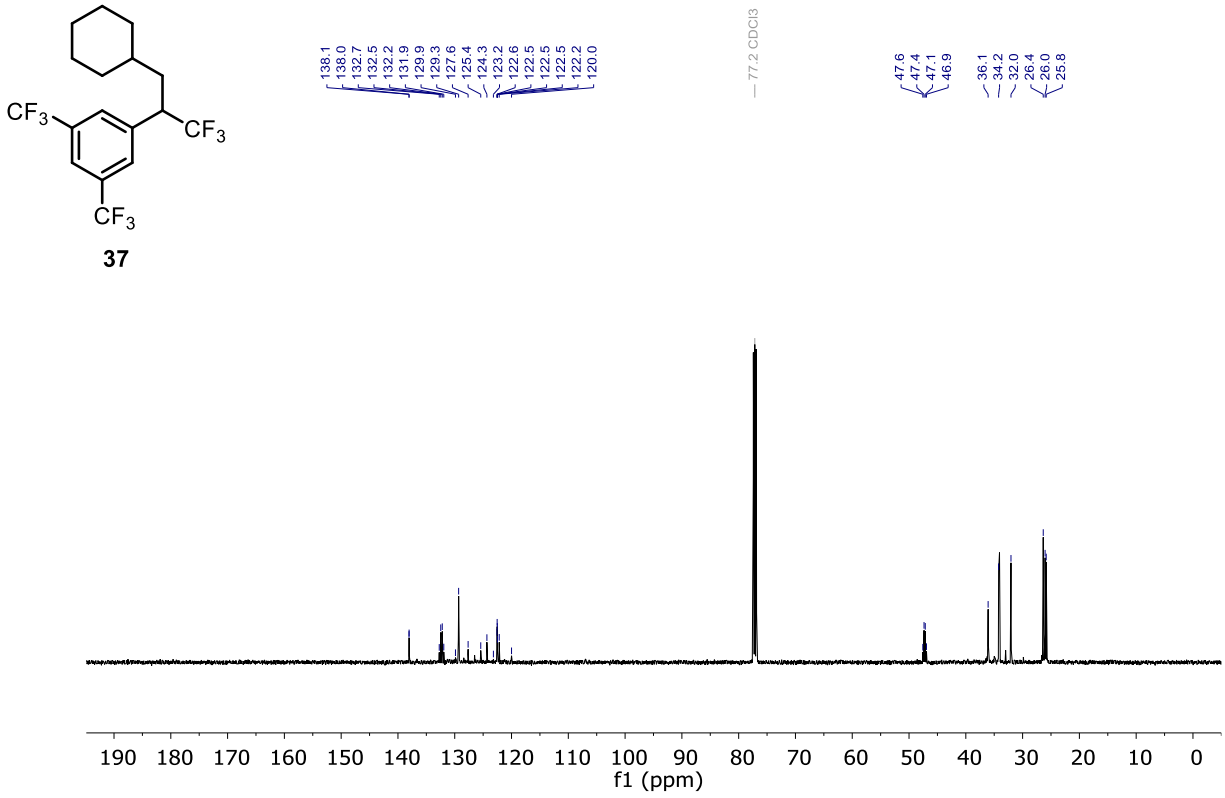


36

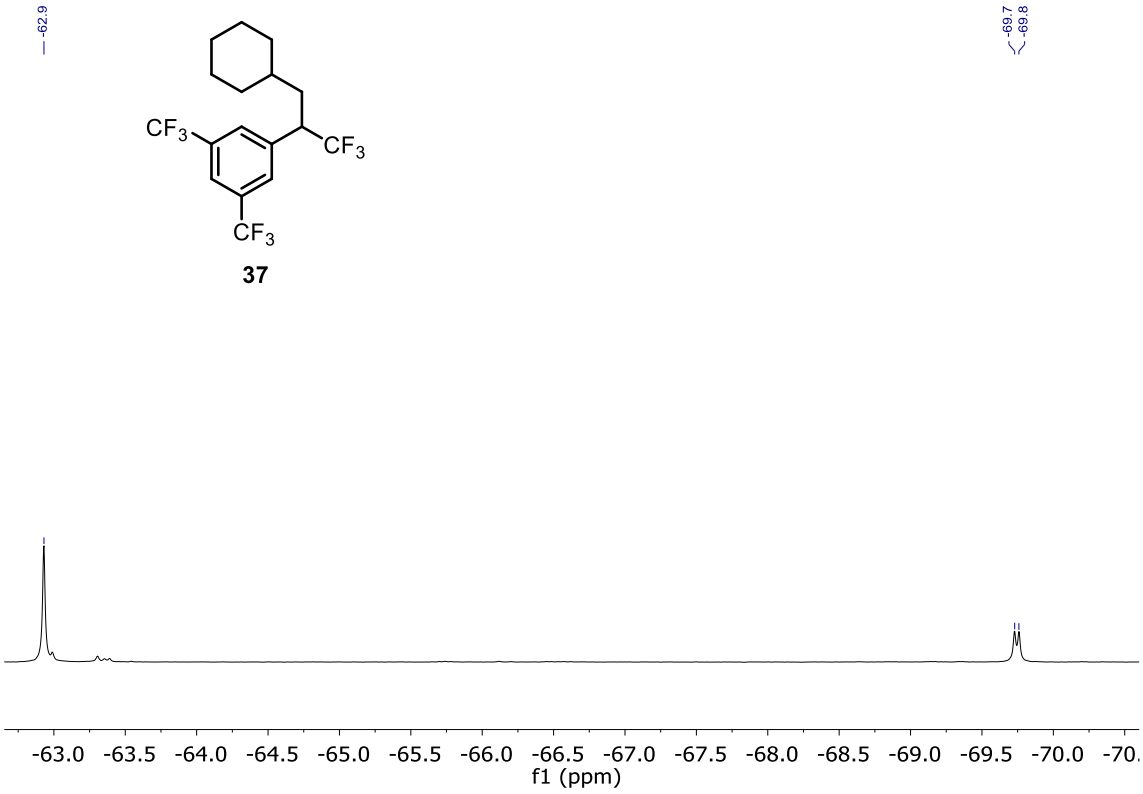
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

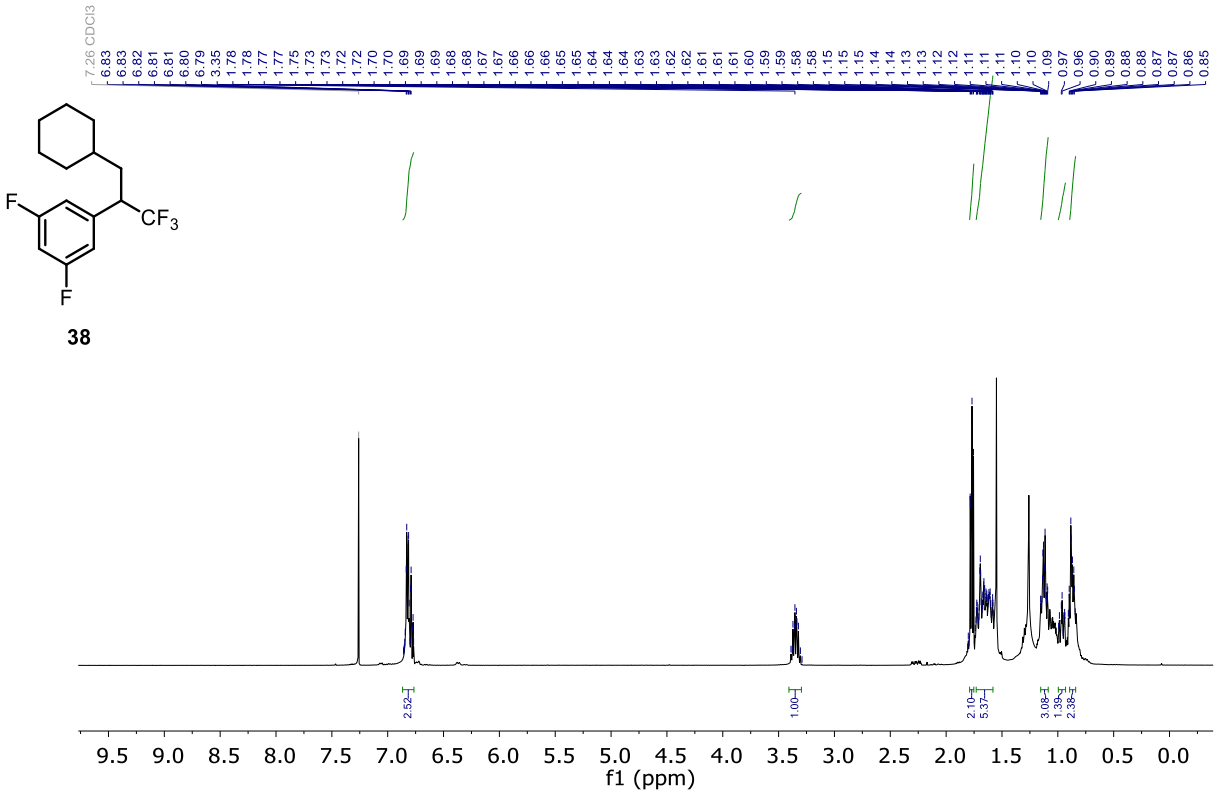


^{19}F NMR (282 MHz, $CDCl_3$)

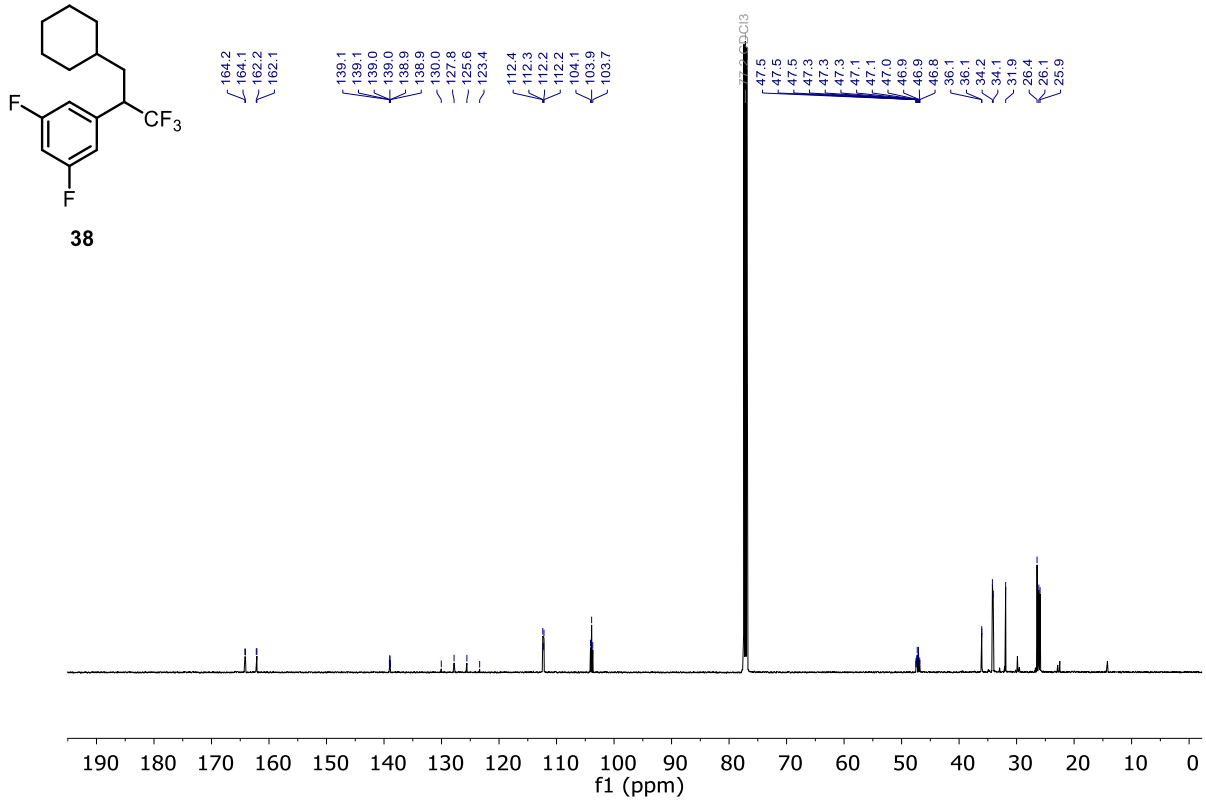


37

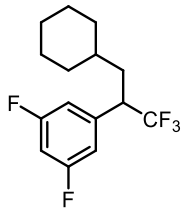
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)



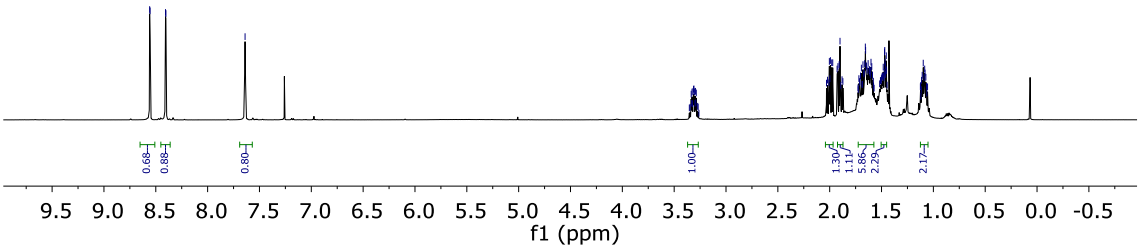
^{19}F NMR (282 MHz, $CDCl_3$)



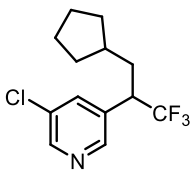
38

^{1}H NMR (500 MHz, $CDCl_3$)

39



^{13}C NMR (126 MHz, $CDCl_3$)

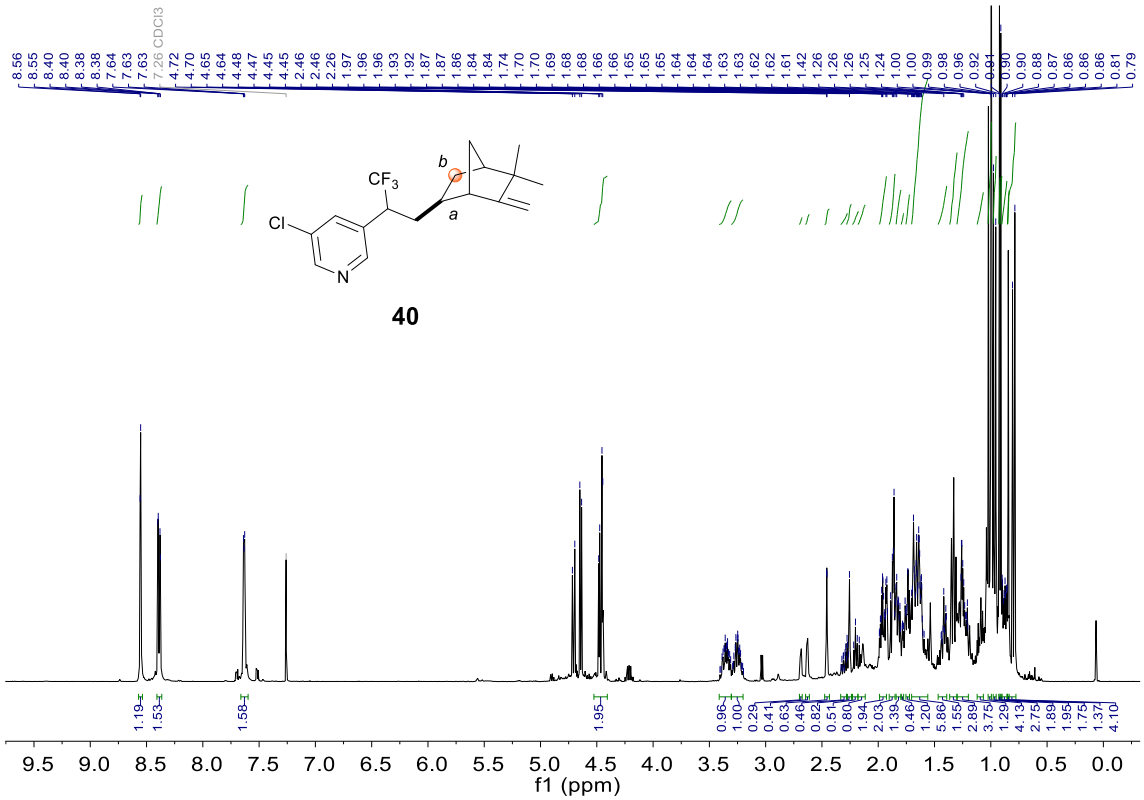


39

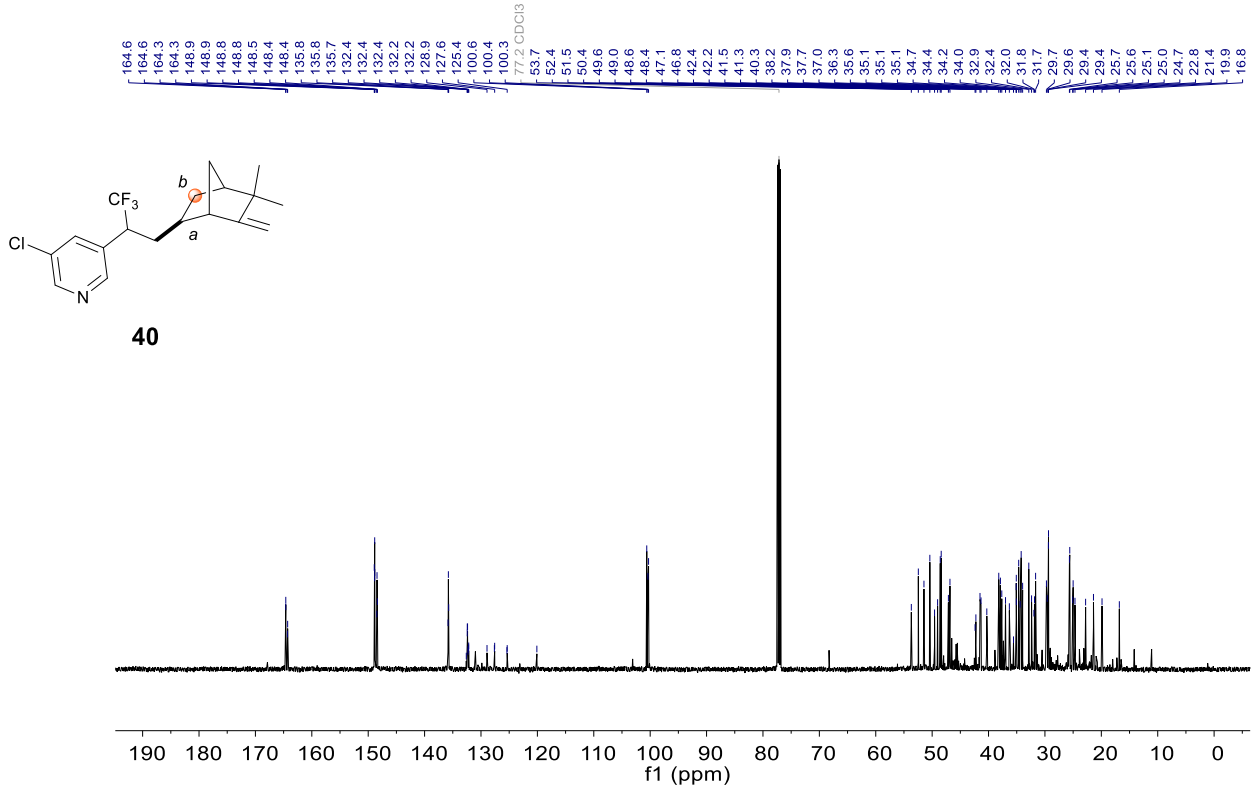
^{19}F NMR (282 MHz, $CDCl_3$)

39

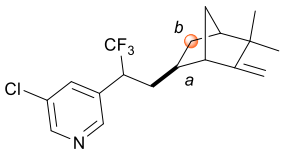
^{1}H NMR (500 MHz, $CDCl_3$)



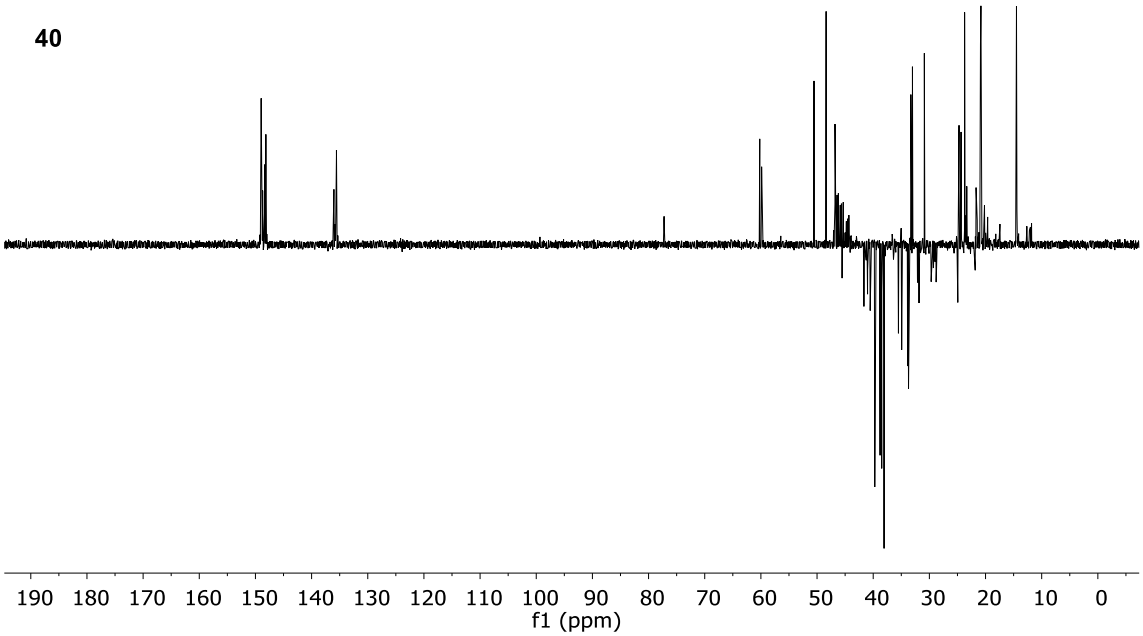
^{13}C NMR (126 MHz, $CDCl_3$)



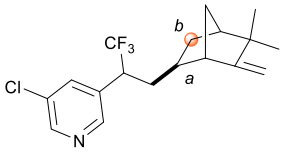
DEPT-135 (126 MHz, $CDCl_3$)



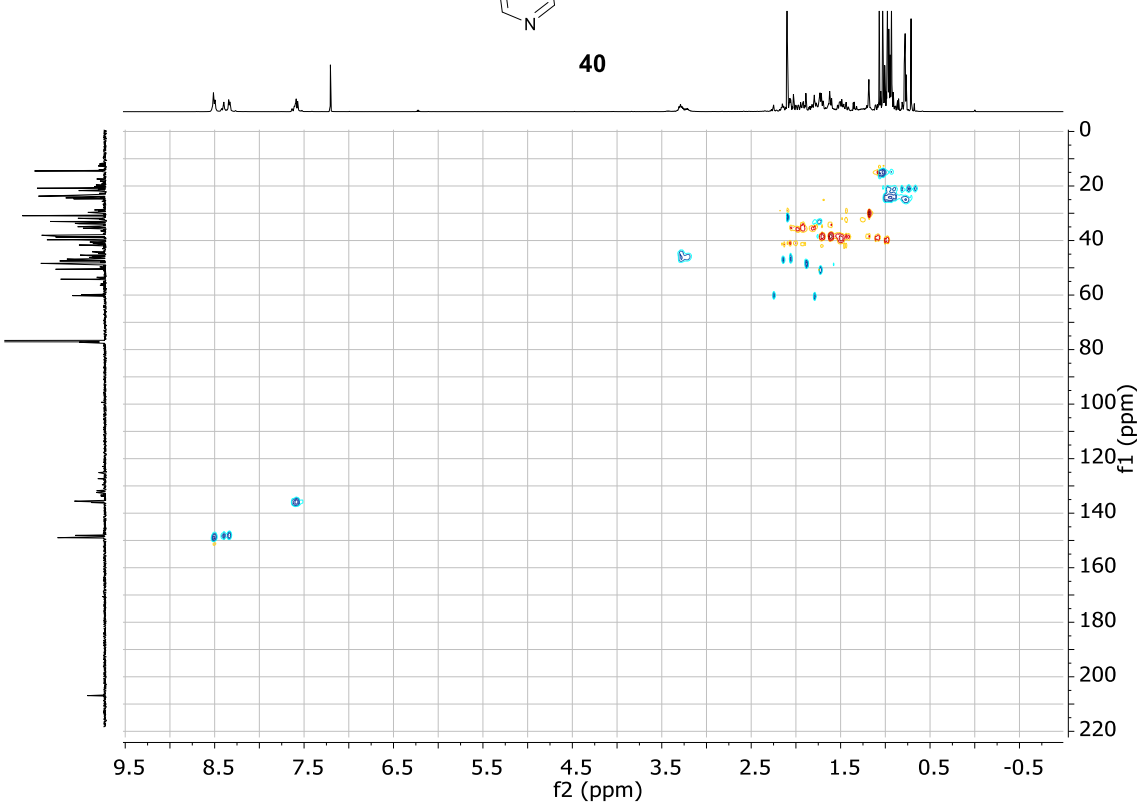
40



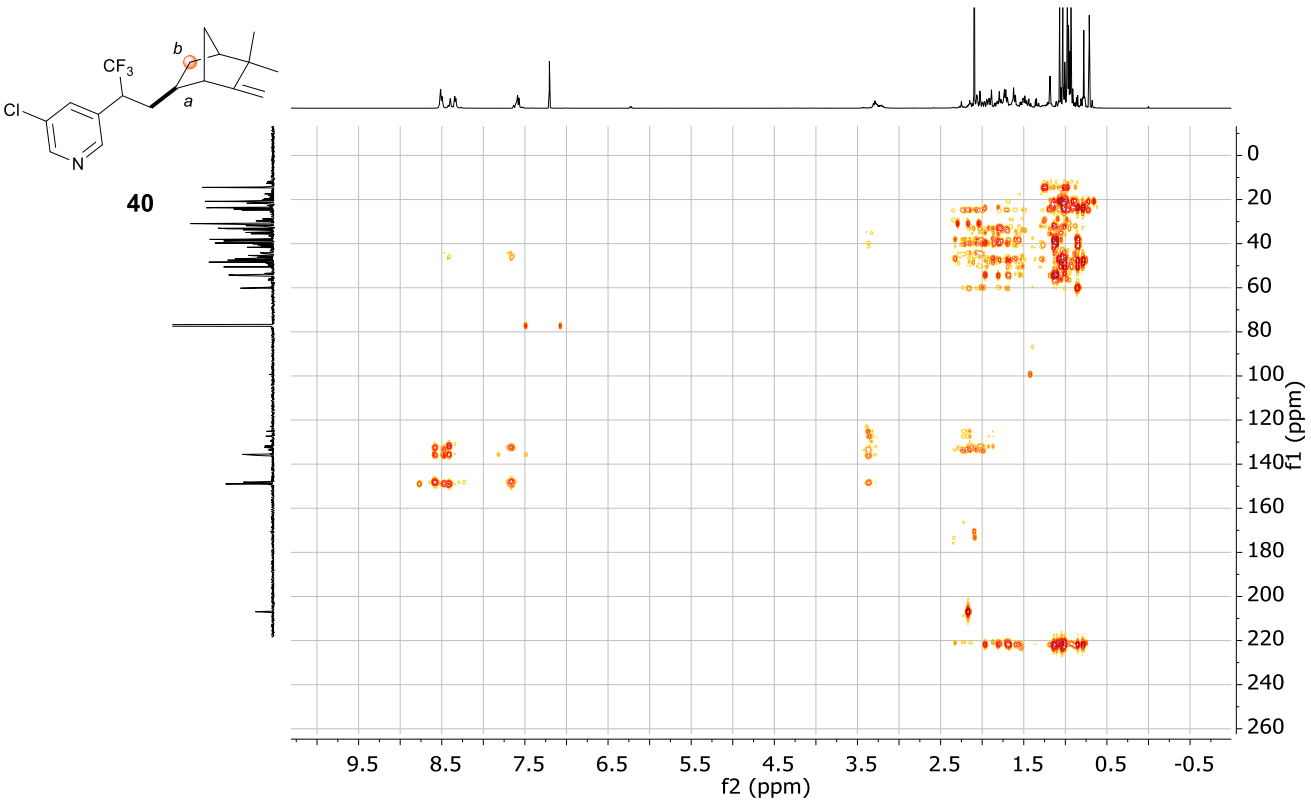
HSQC (500, 126, MHz, $CDCl_3$)



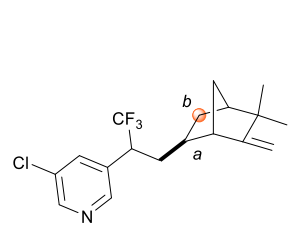
40



HMBC (500, 126, MHz, $CDCl_3$)

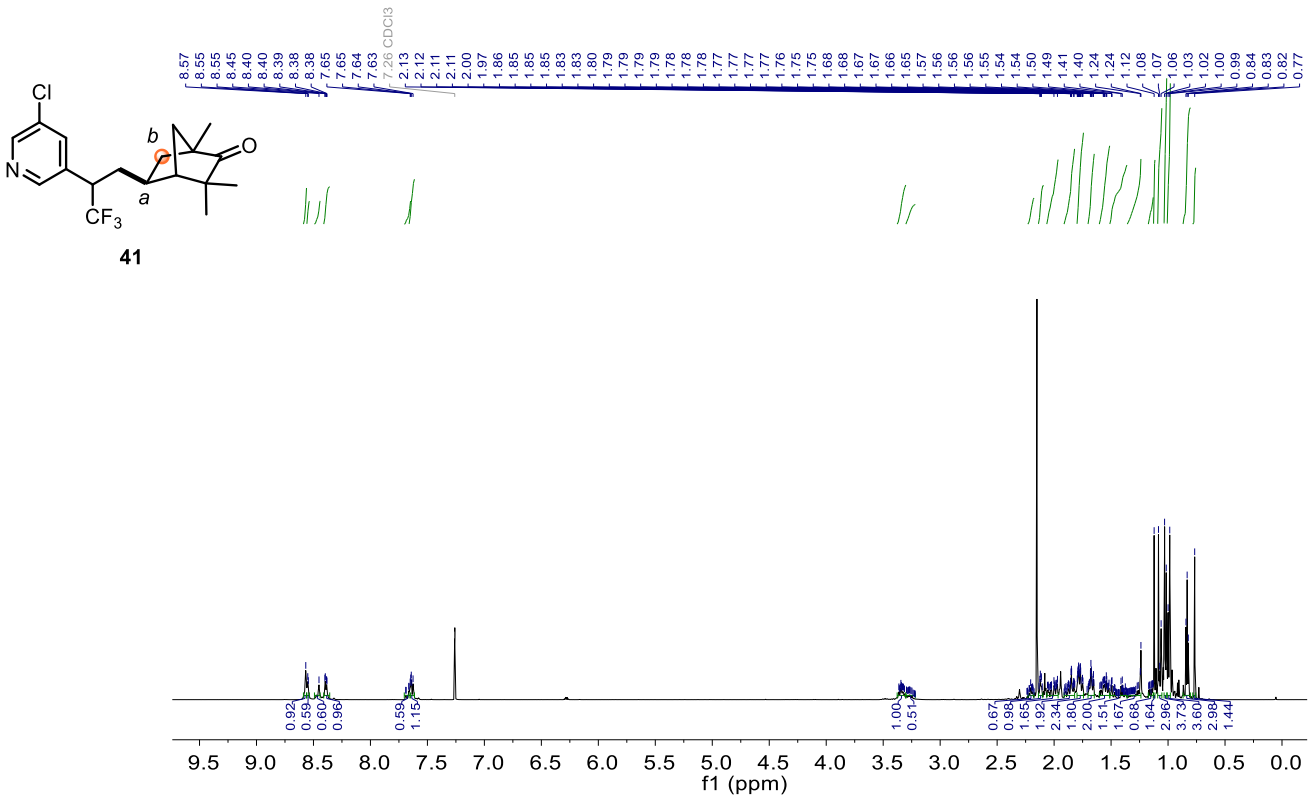


^{19}F NMR (282 MHz, $CDCl_3$)

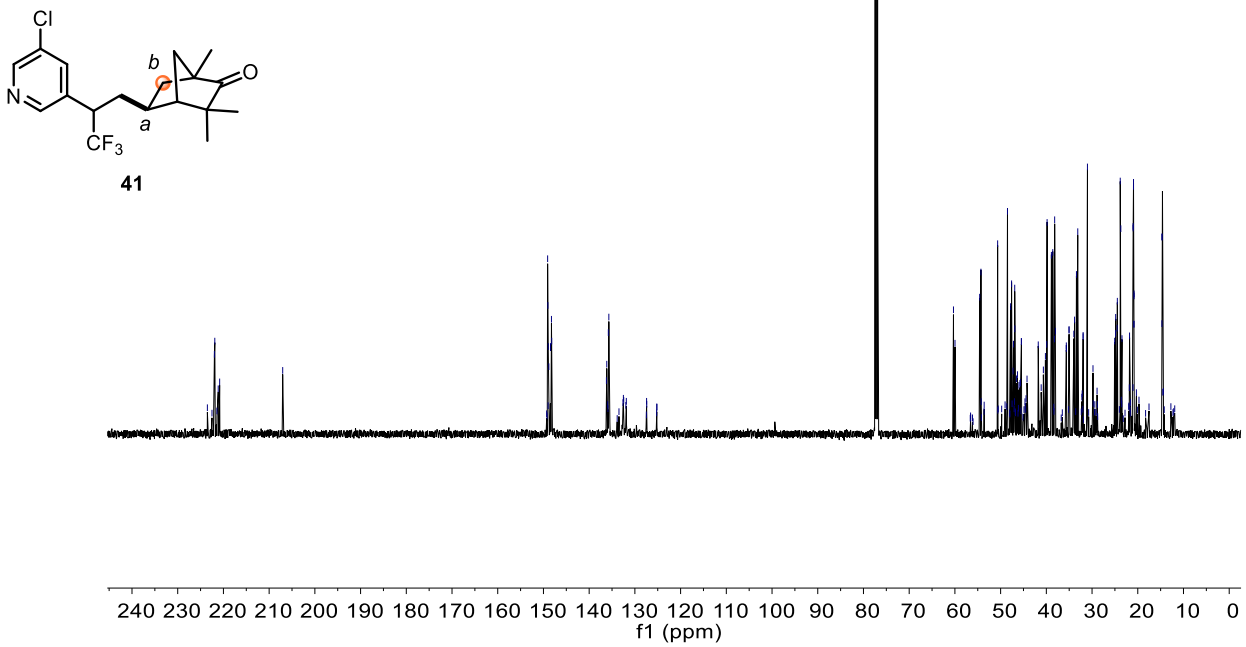


40

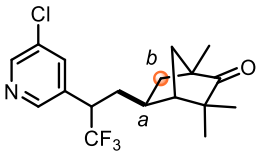
^{1}H NMR (500 MHz, $CDCl_3$)



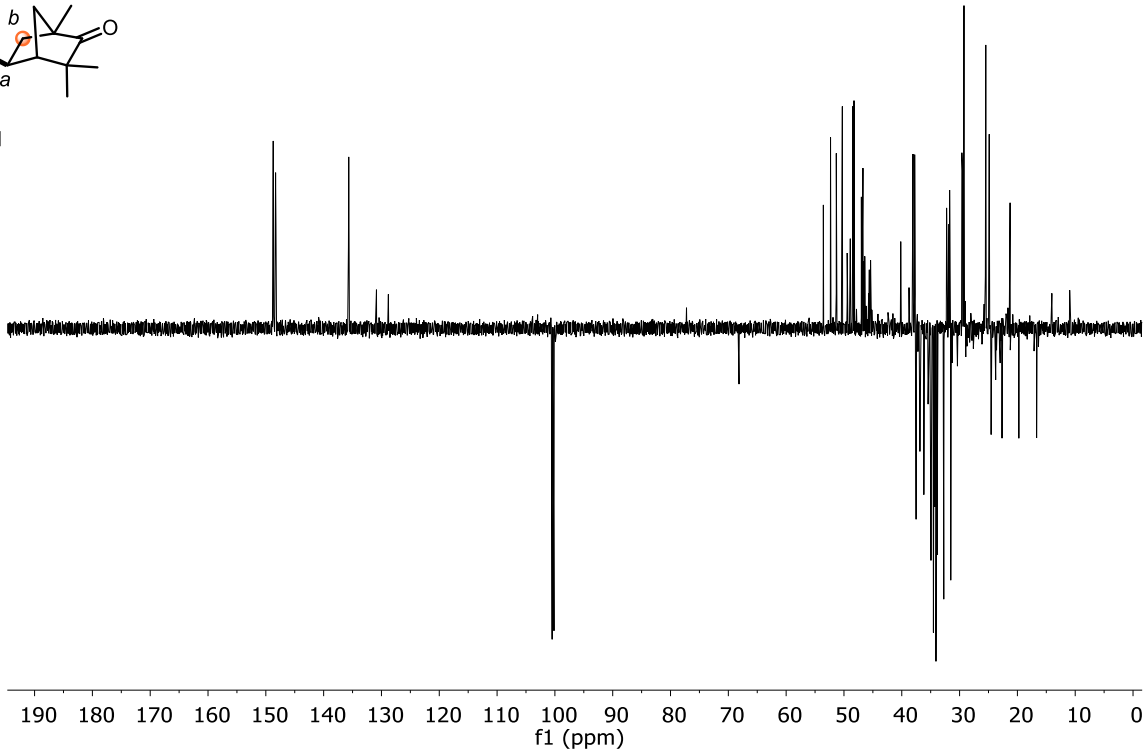
^{13}C NMR (126 MHz, $CDCl_3$)



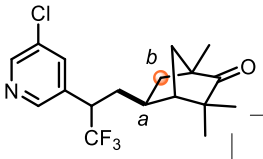
DEPT-135 (126 MHz, $CDCl_3$)



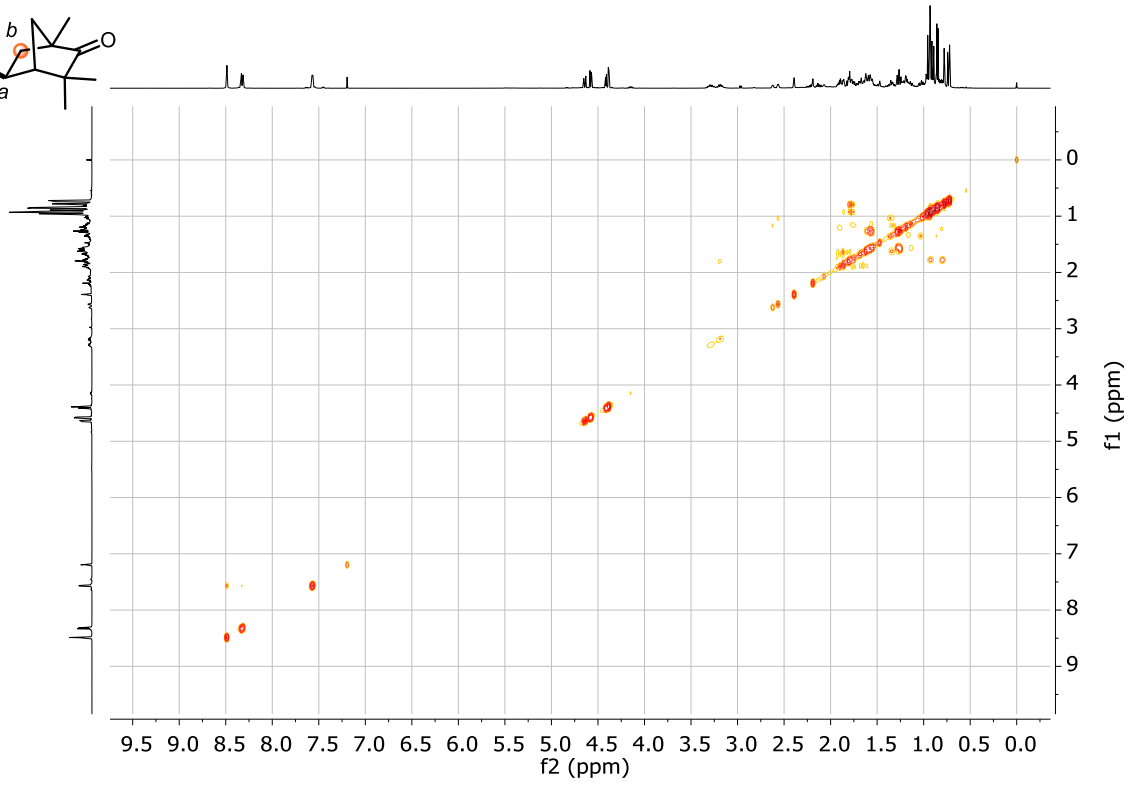
41



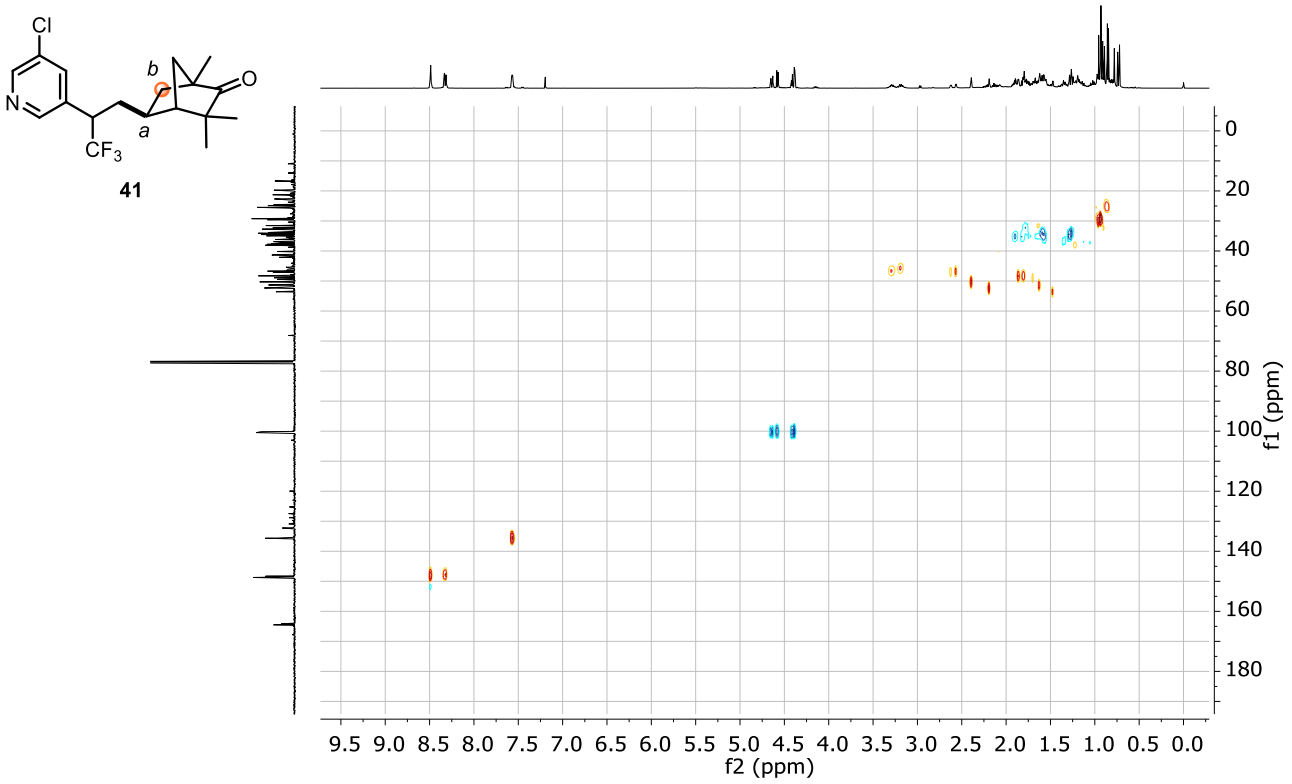
COSY (500 MHz, $CDCl_3$)



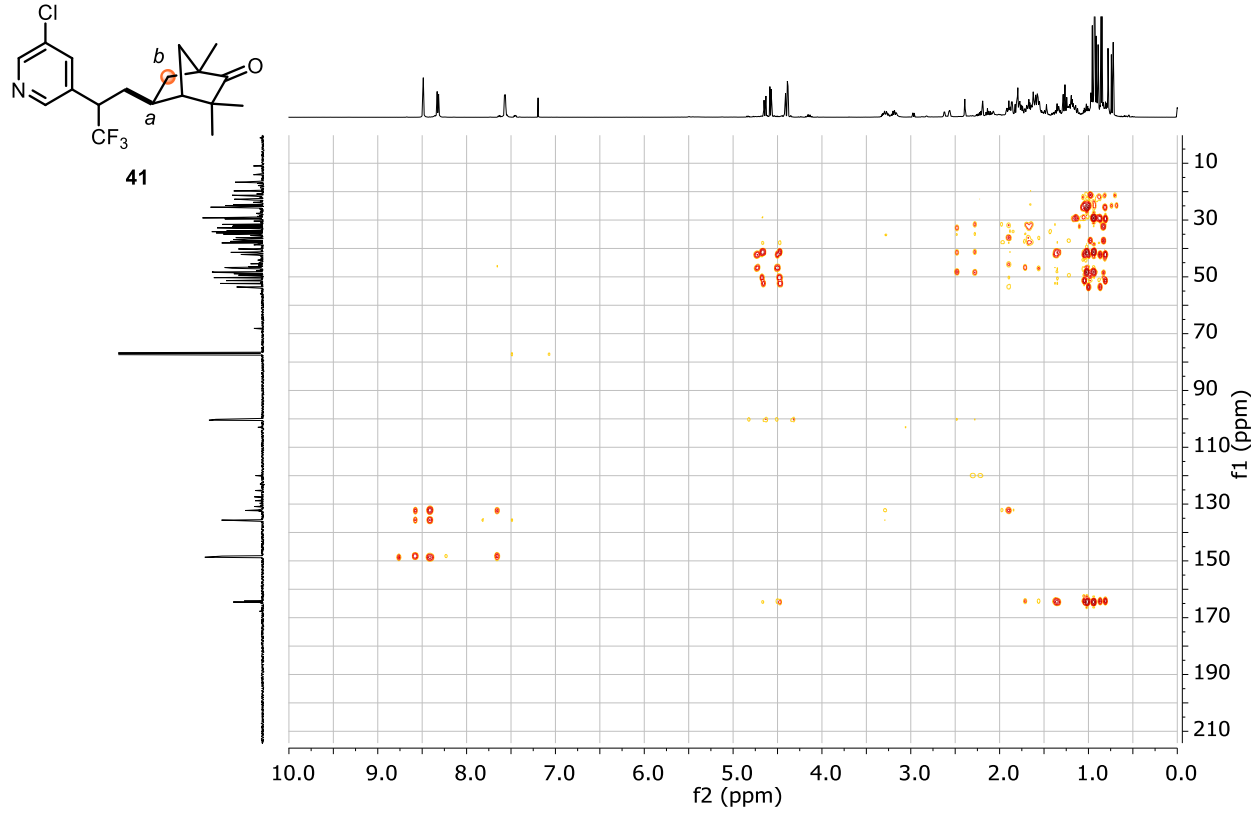
41



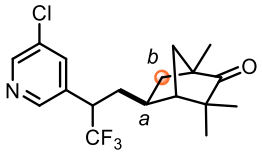
HSQC (500, 126, MHz, $CDCl_3$)



HMBC (500, 126, MHz, $CDCl_3$)

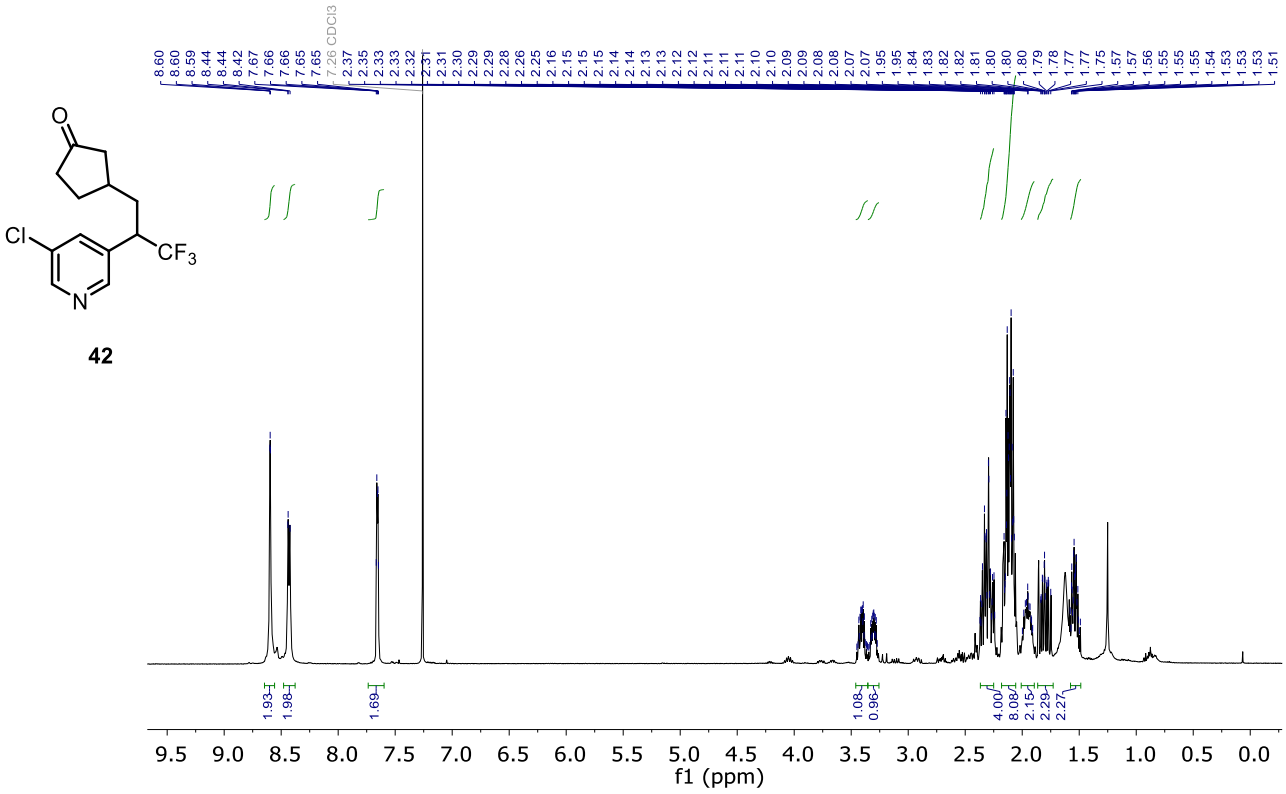


^{19}F NMR (282 MHz, $CDCl_3$)

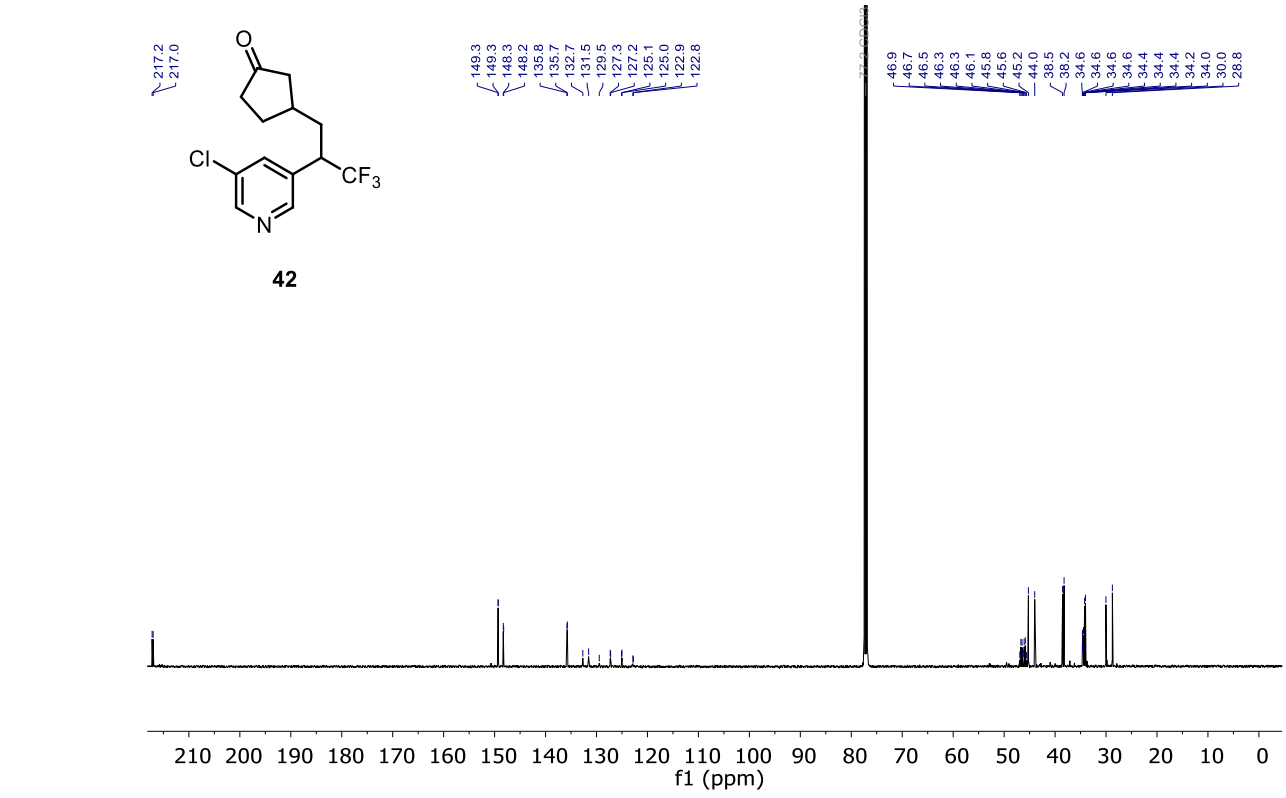


41

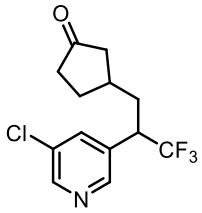
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

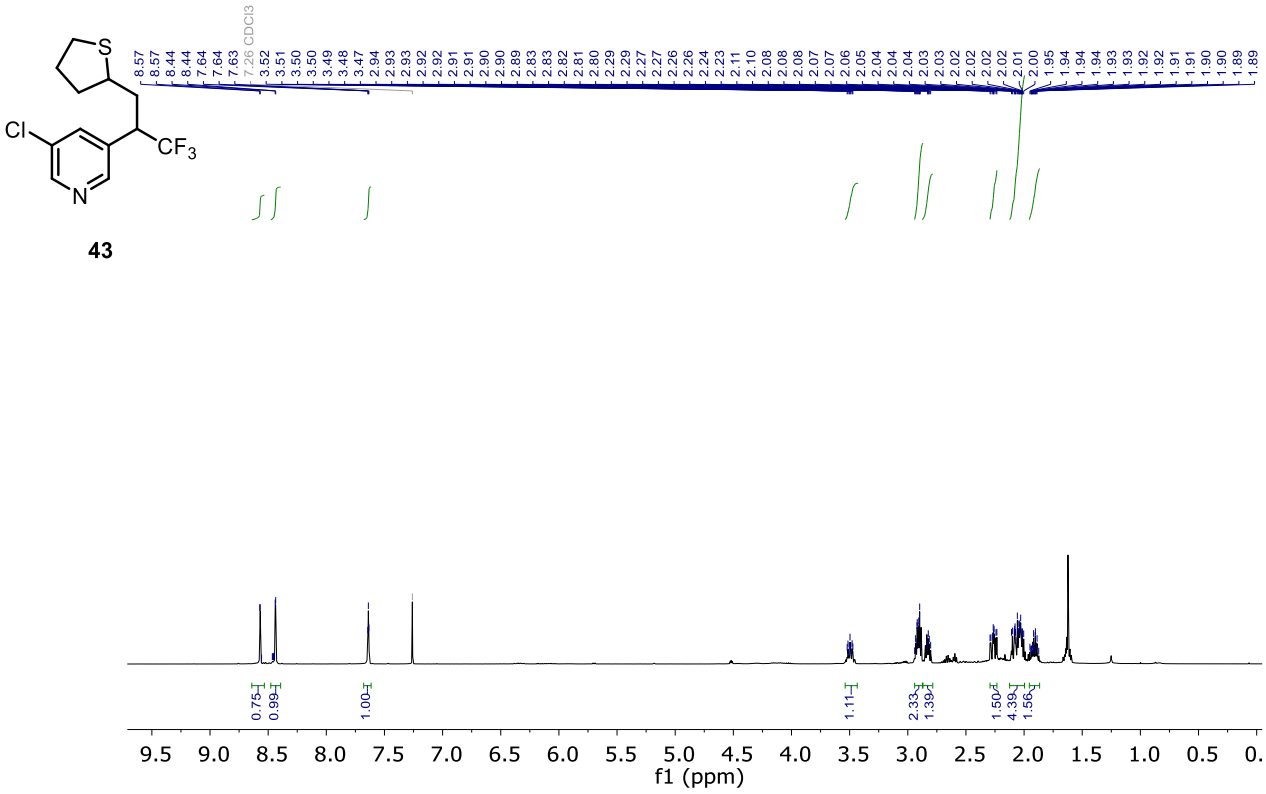


^{19}F NMR (282 MHz, $CDCl_3$)

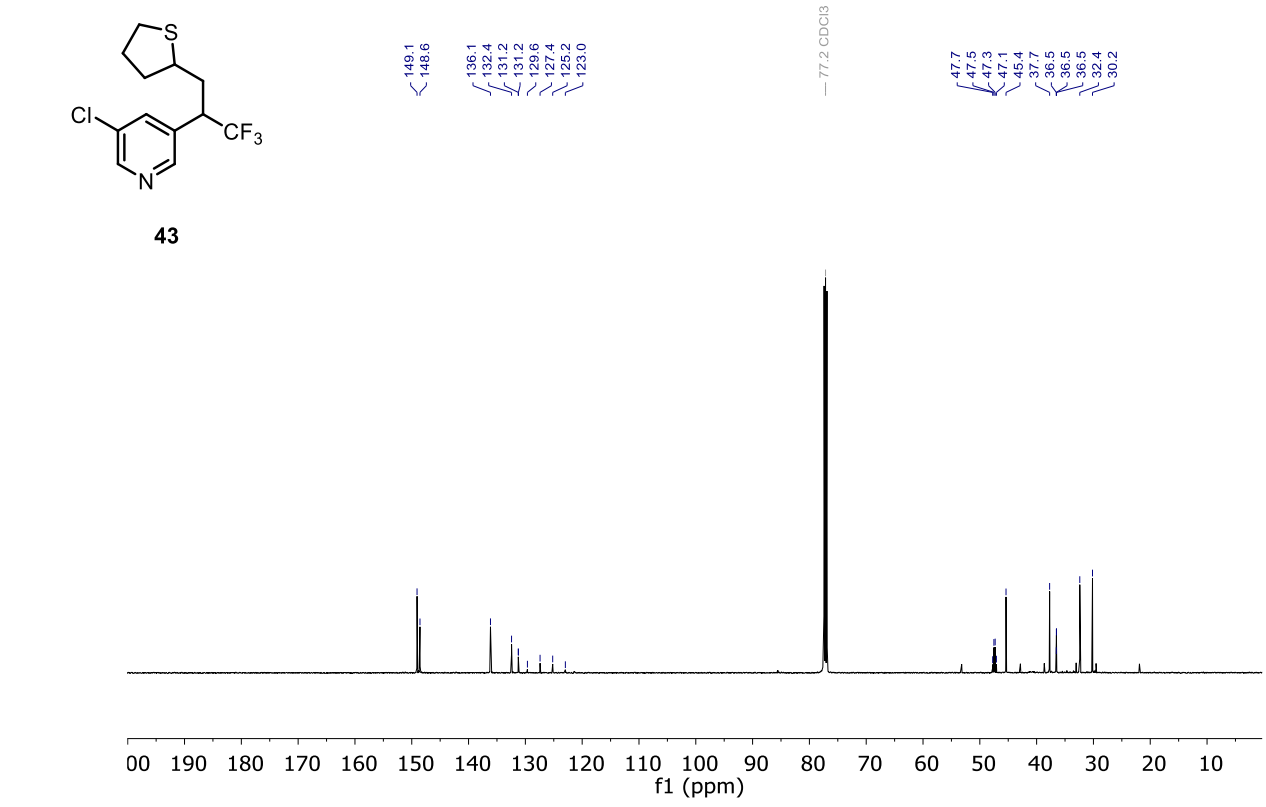


42

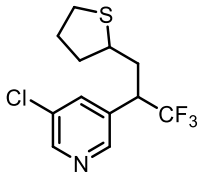
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

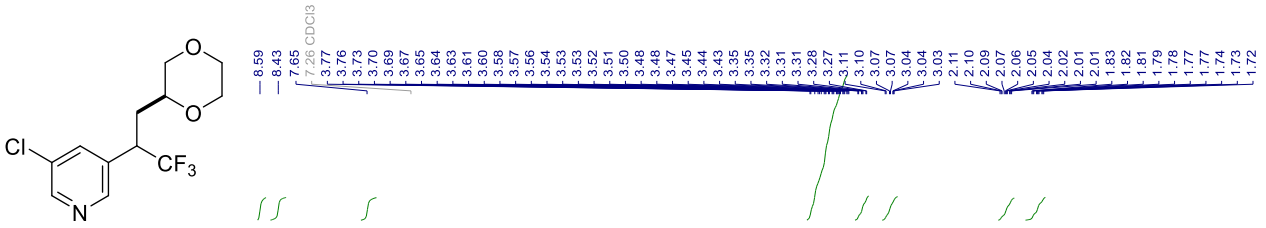


^{19}F NMR (282 MHz, $CDCl_3$)

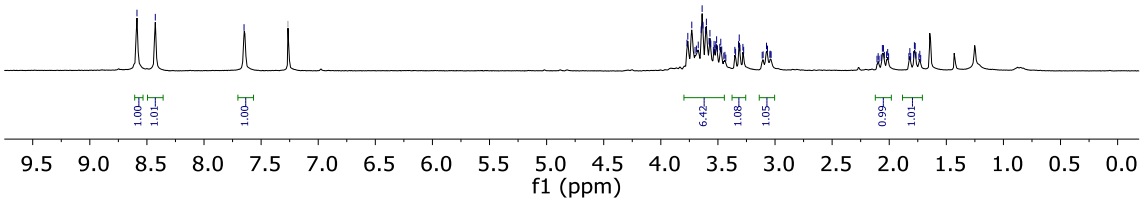


43

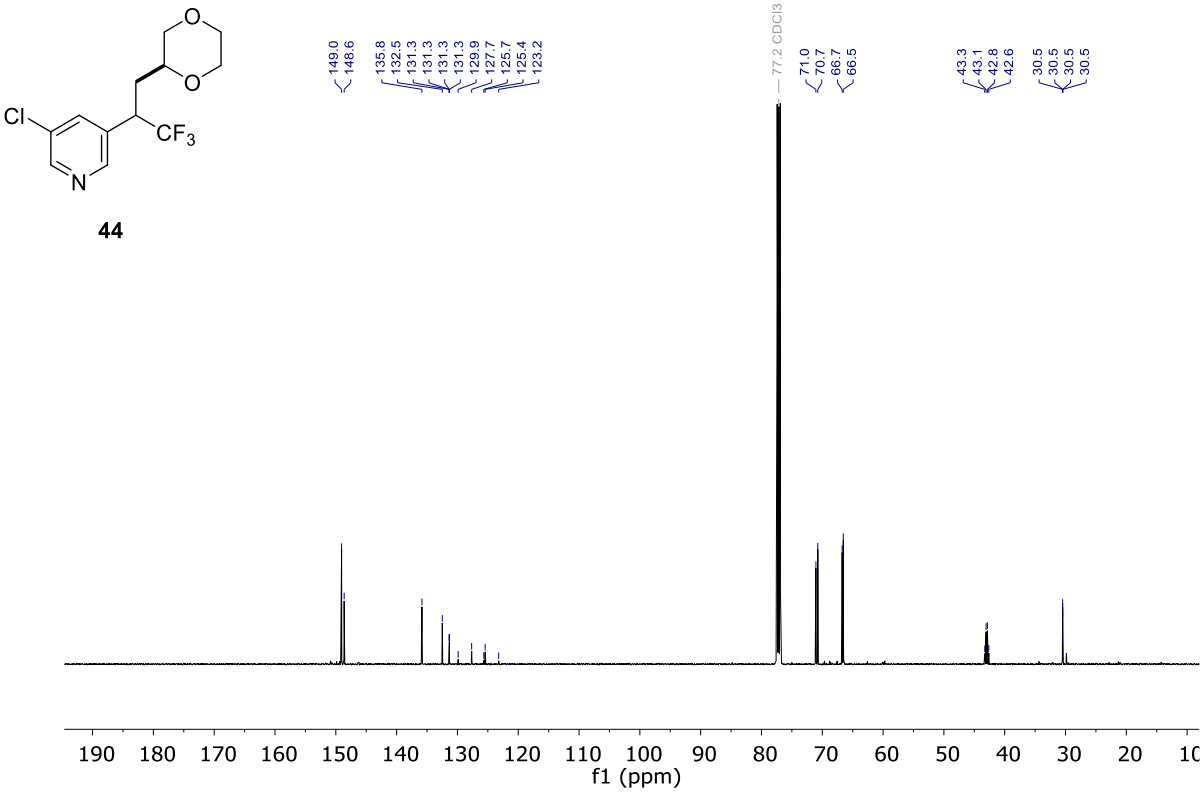
^{1}H NMR (500 MHz, $CDCl_3$)



44

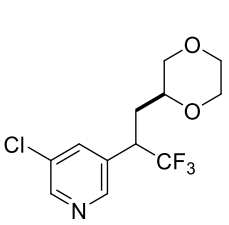


^{13}C NMR (126 MHz, $CDCl_3$)



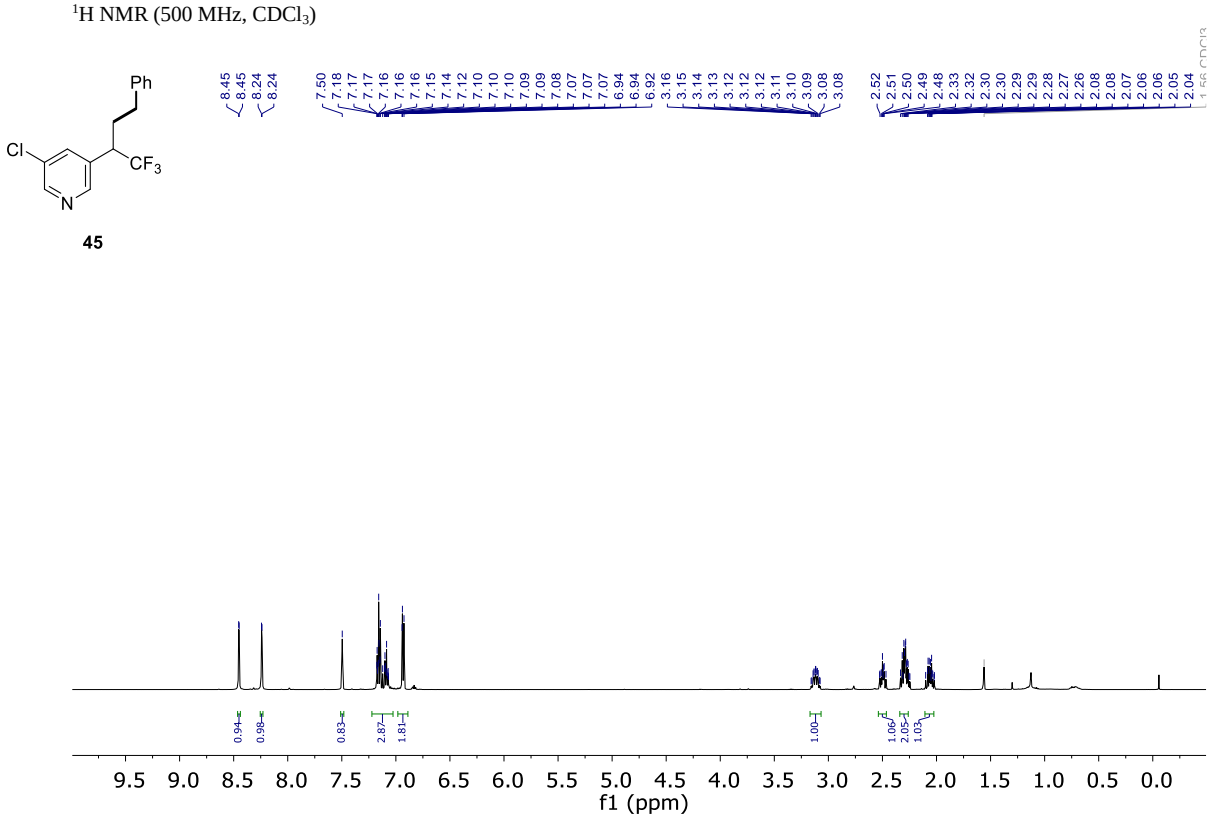
44

^{19}F NMR (282 MHz, $CDCl_3$)

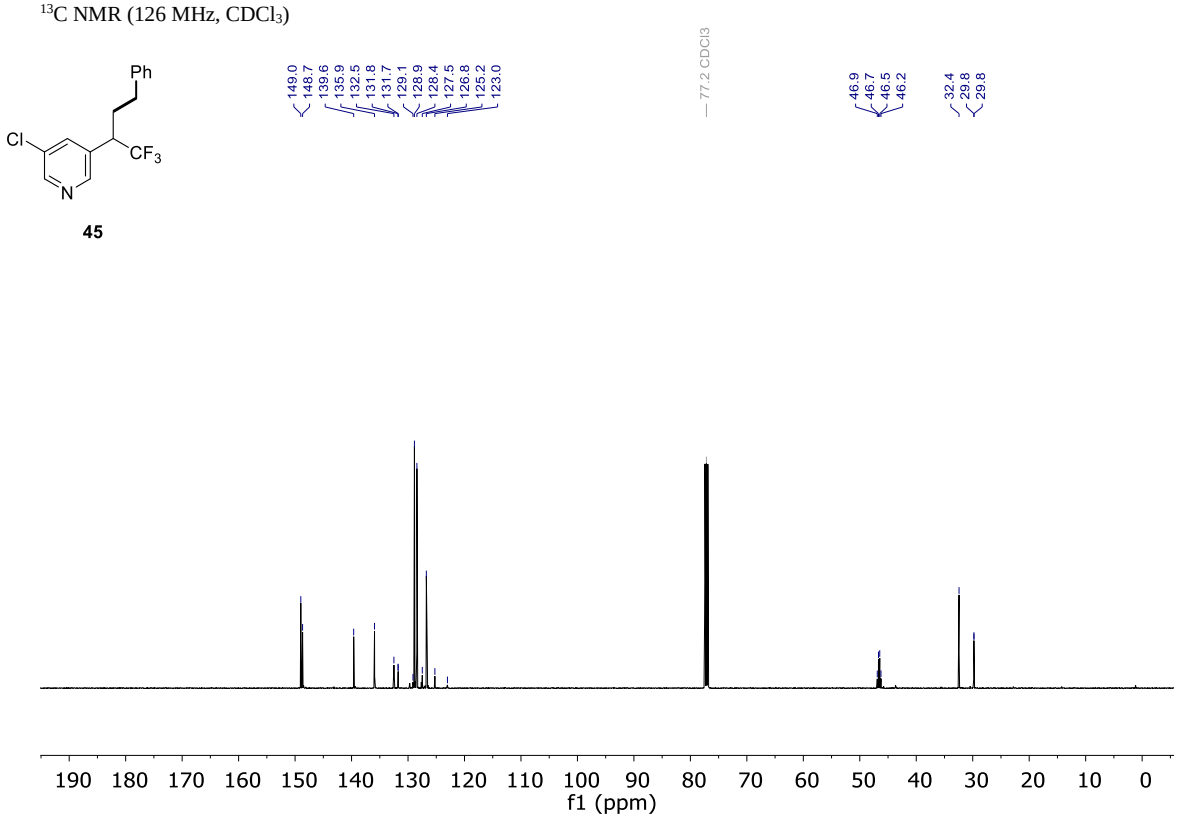


44

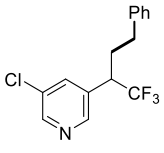
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

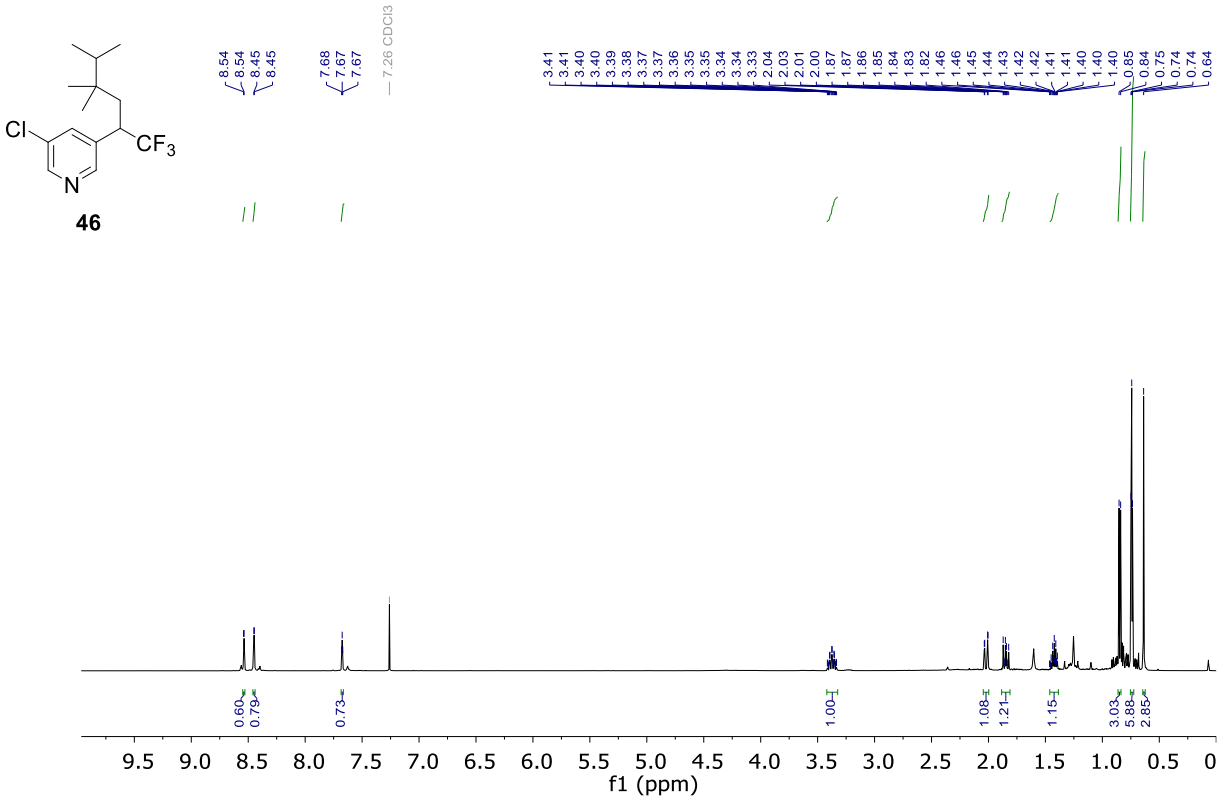


^{19}F NMR (282 MHz, $CDCl_3$)

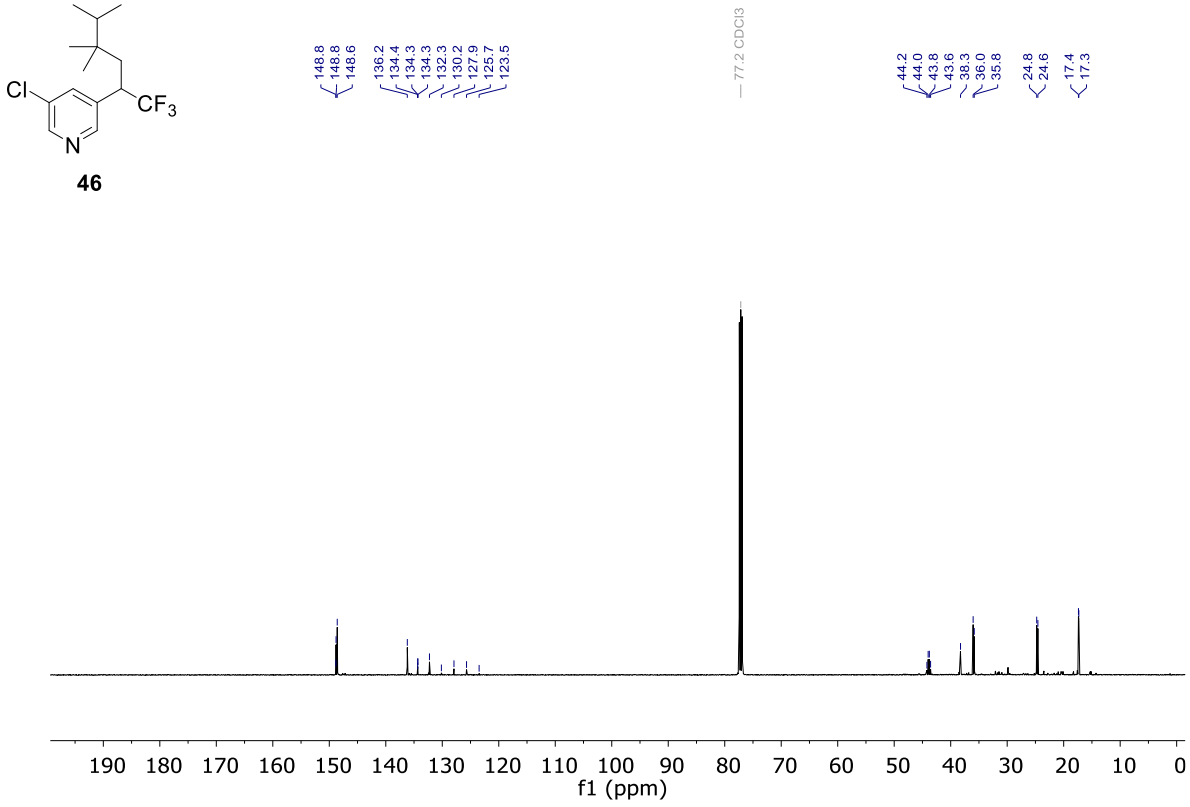


45

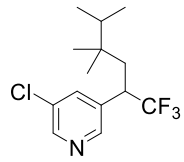
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

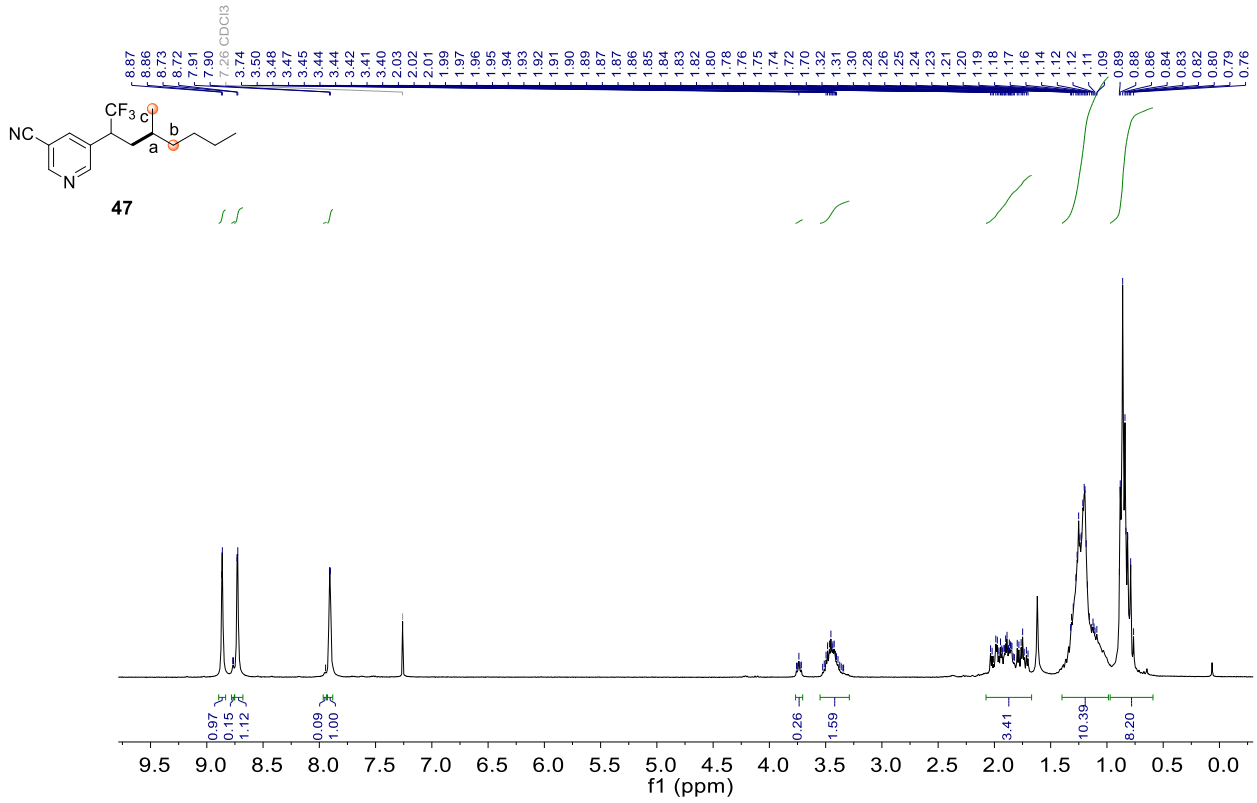


^{19}F NMR (282 MHz, $CDCl_3$)

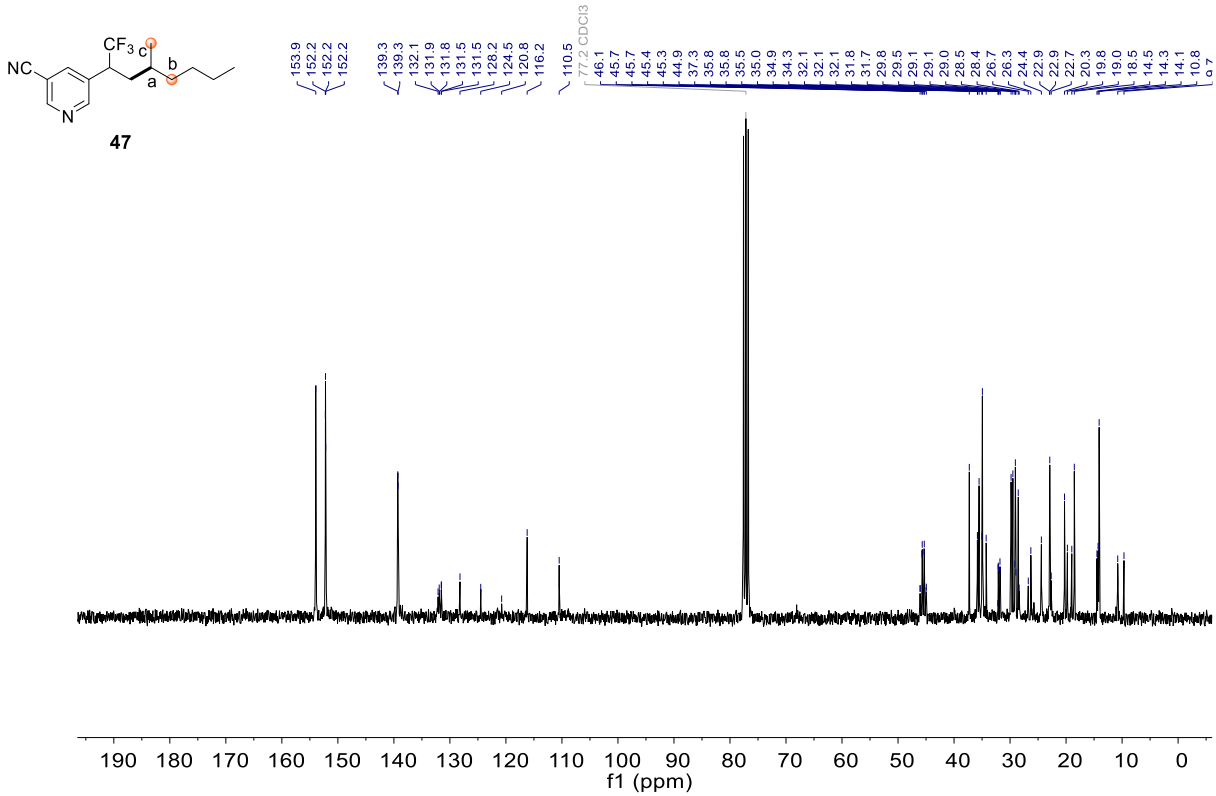


46

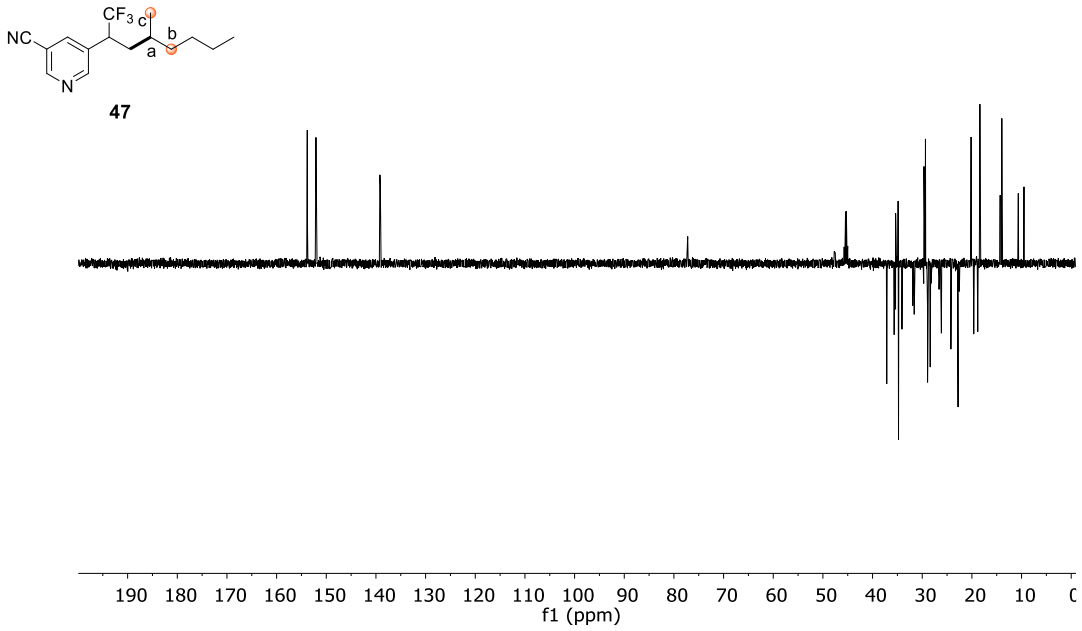
^{1}H NMR (500 MHz, $CDCl_3$)



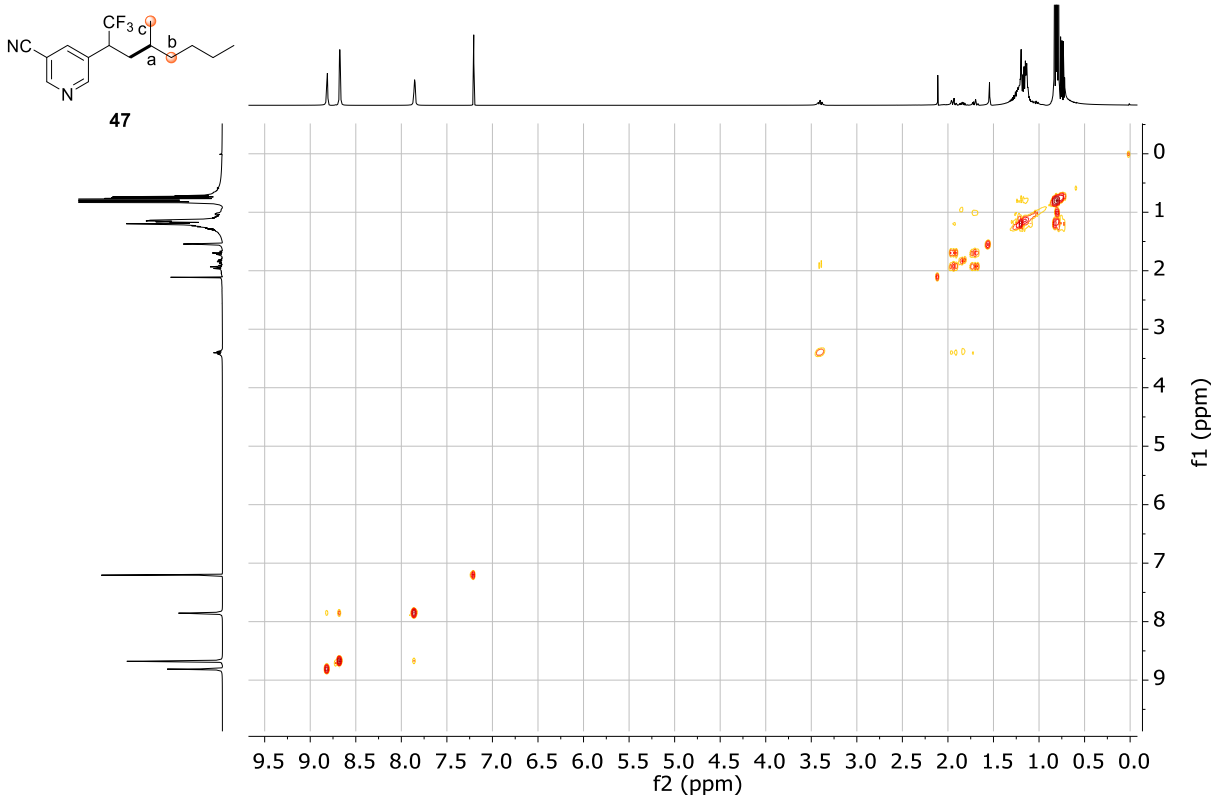
^{13}C NMR (126 MHz, $CDCl_3$)



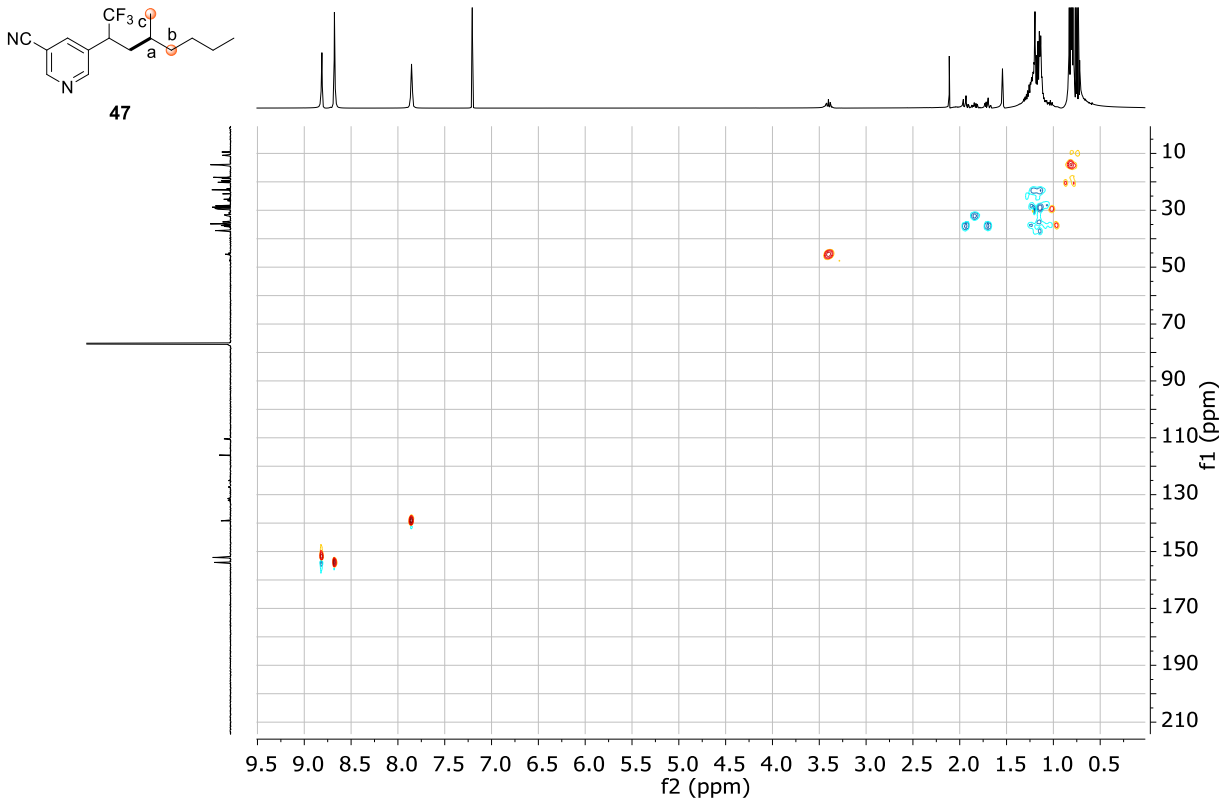
DEPT-135 (126 MHz, $CDCl_3$)



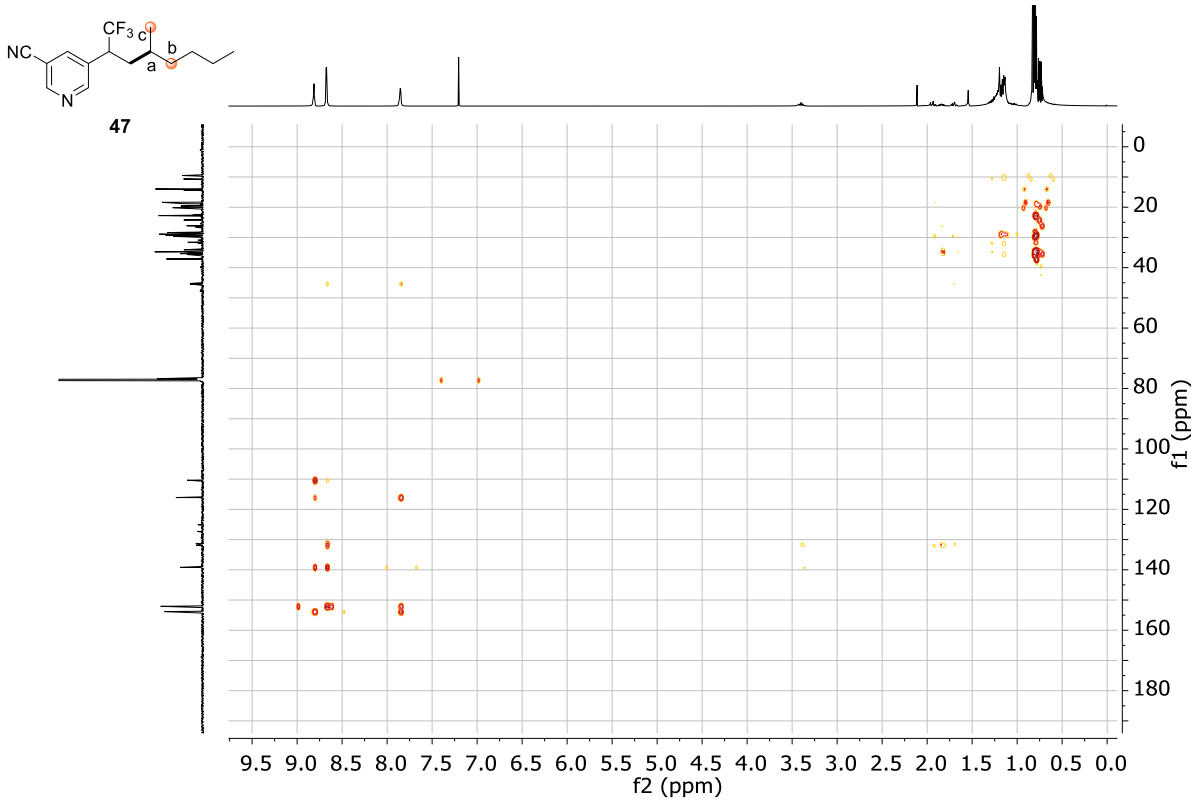
COSY (500 MHz, $CDCl_3$)



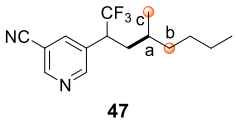
HSQC (500, 126, MHz, $CDCl_3$)



HMBC (500, 126, MHz, $CDCl_3$)

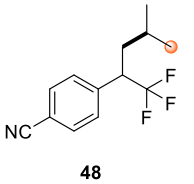


^{19}F NMR (282 MHz, $CDCl_3$)

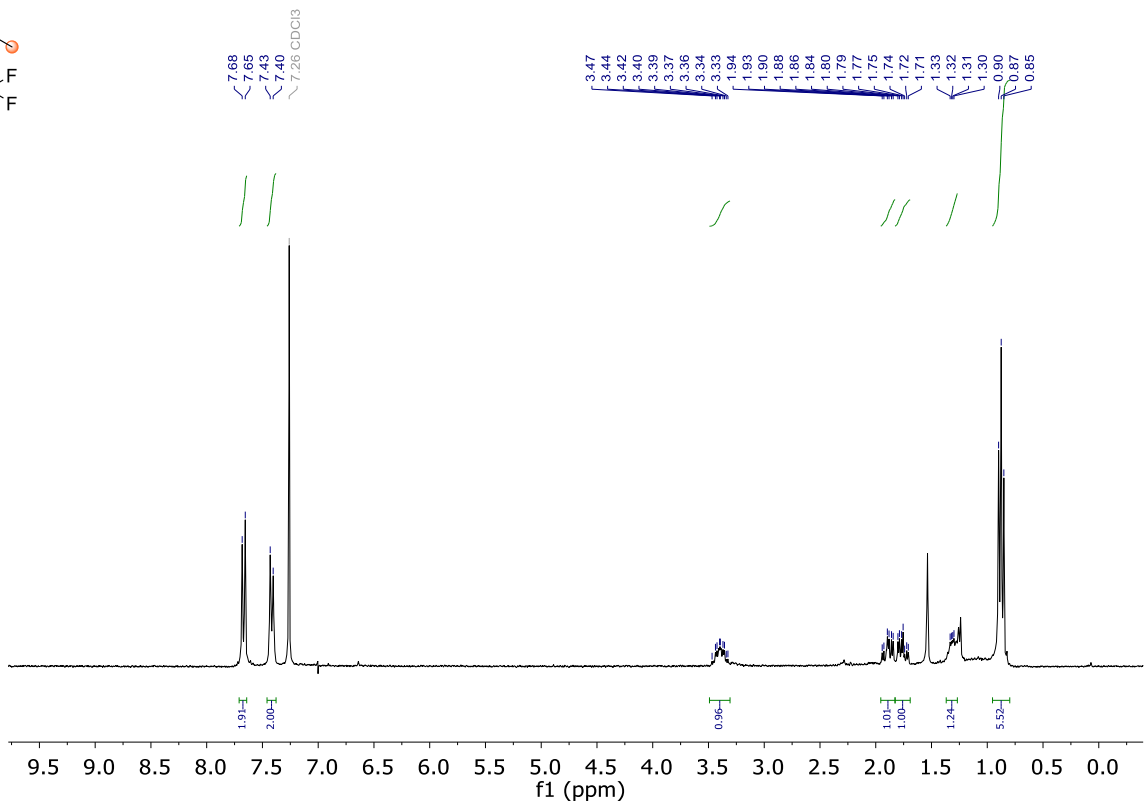


47

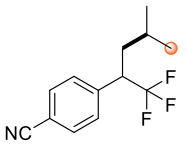
^{1}H NMR (500 MHz, $CDCl_3$)



48

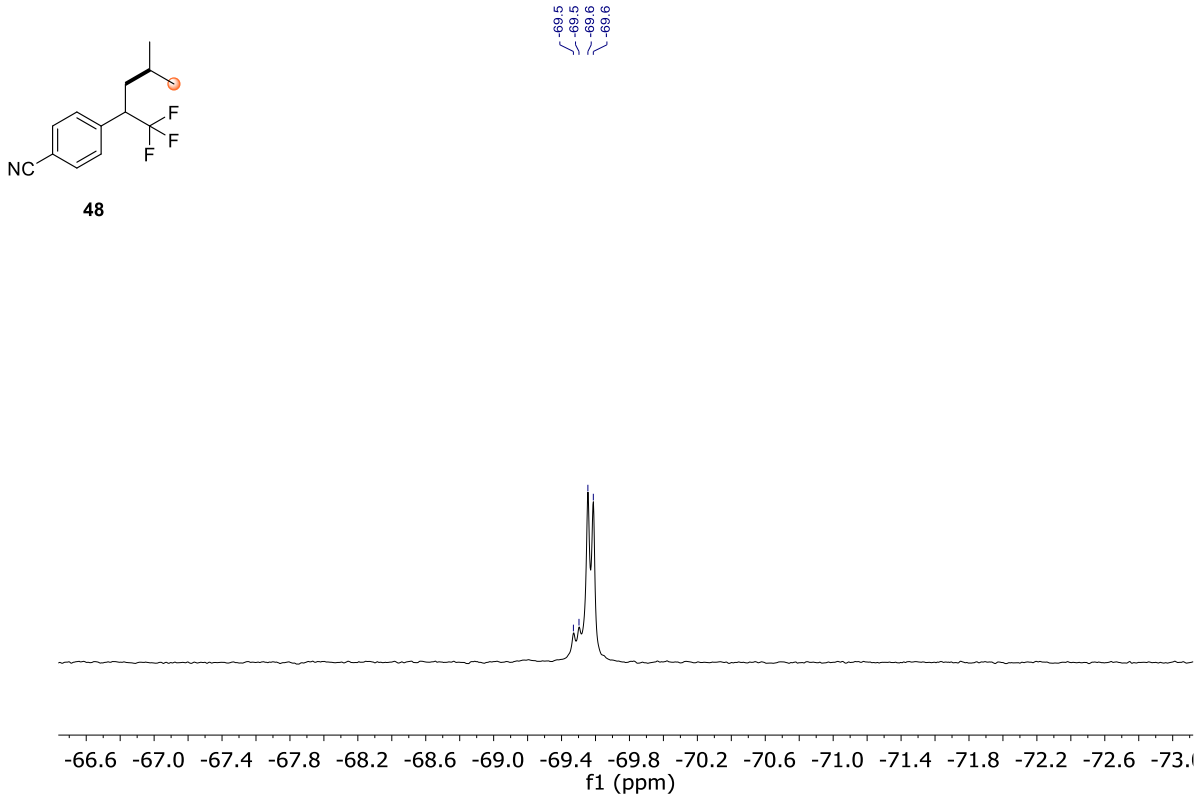


^{13}C NMR (126 MHz, $CDCl_3$)



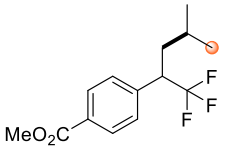
48

^{19}F NMR (282 MHz, $CDCl_3$)

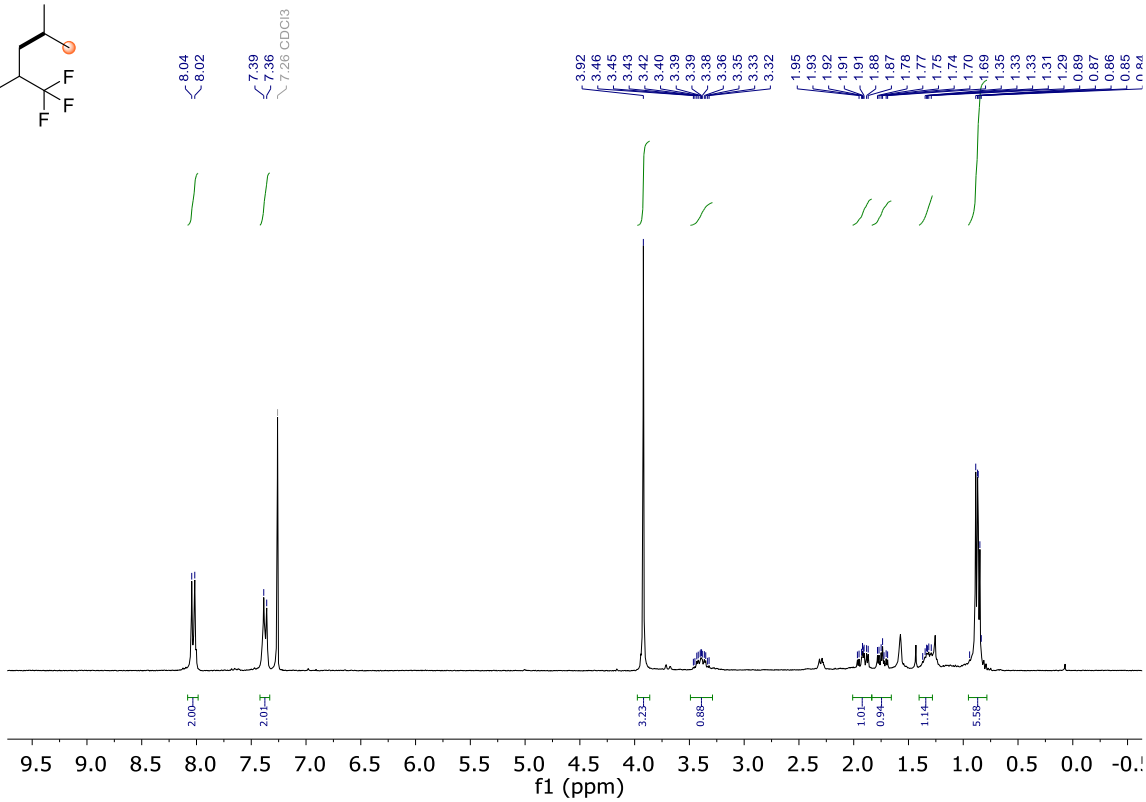


48

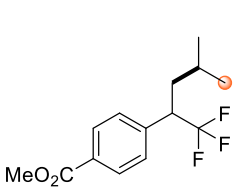
^{1}H NMR (500 MHz, $CDCl_3$)



49

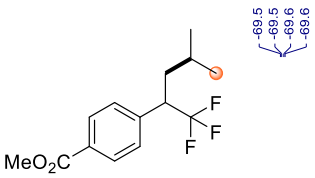


^{13}C NMR (126 MHz, $CDCl_3$)

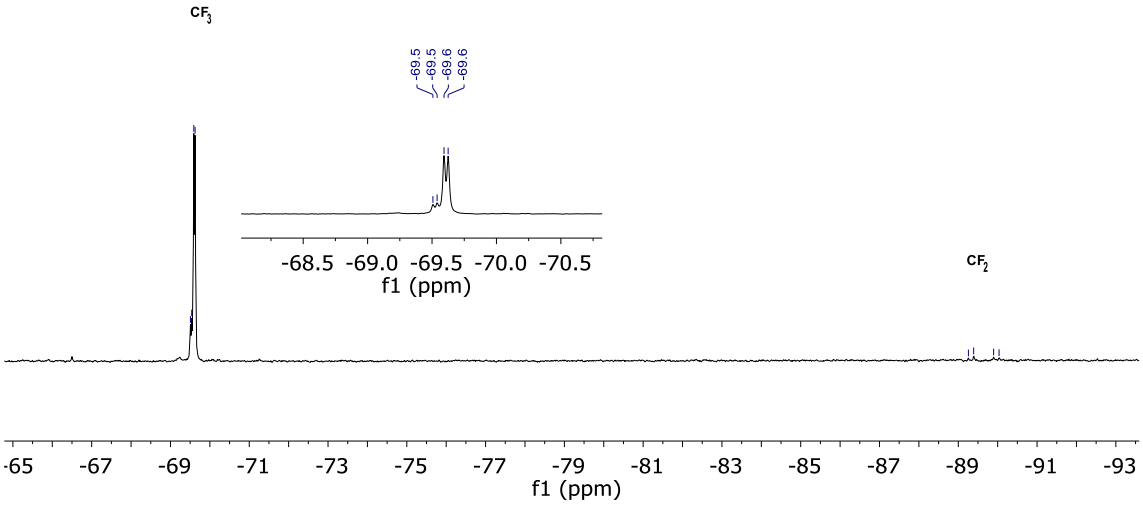


49

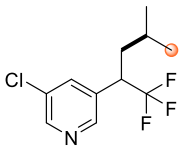
^{19}F NMR (282 MHz, $CDCl_3$)



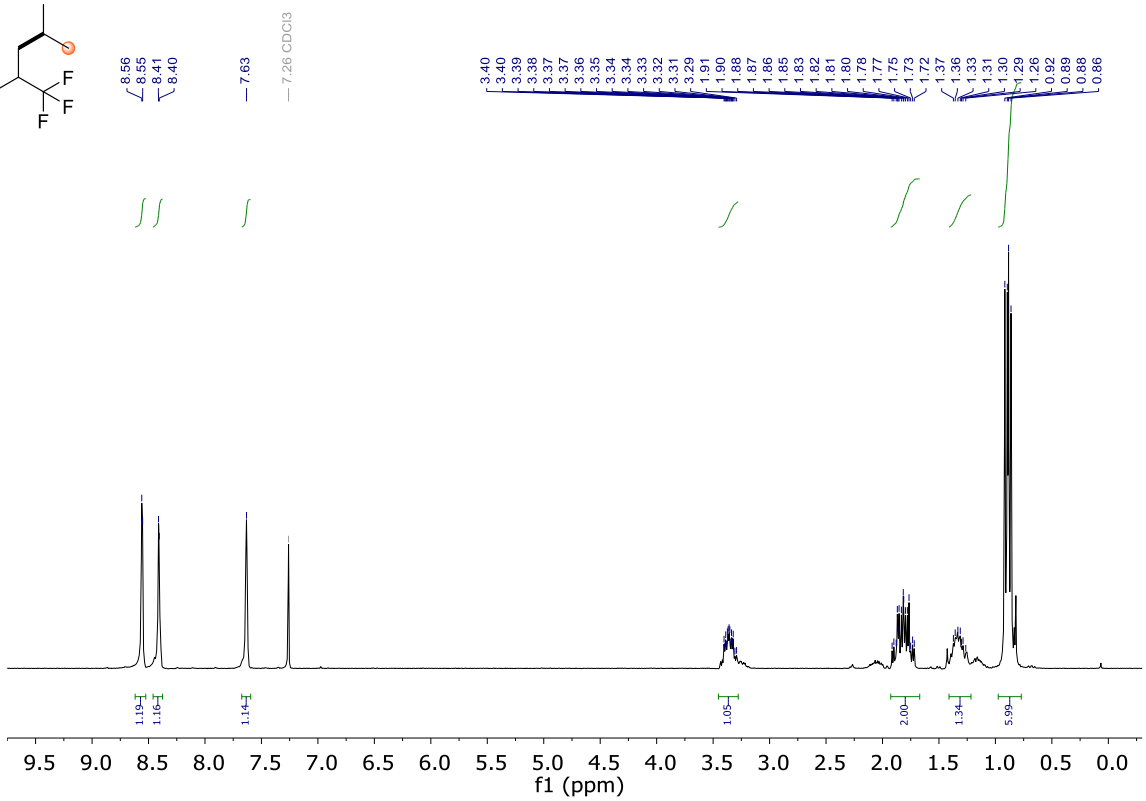
49



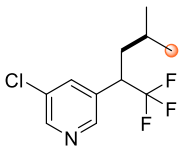
^{1}H NMR (500 MHz, $CDCl_3$)



50

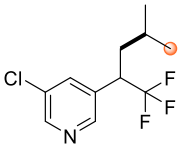


^{13}C NMR (126 MHz, $CDCl_3$)



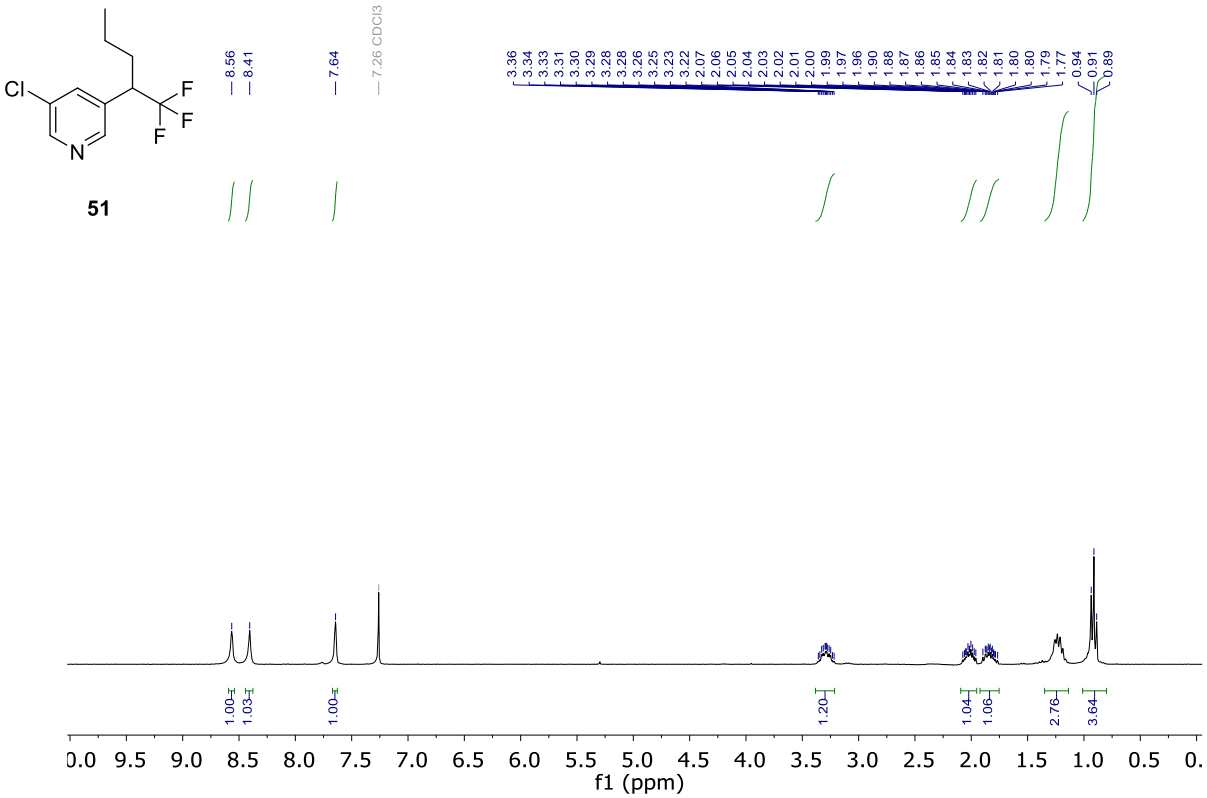
50

^{19}F NMR (282 MHz, $CDCl_3$)

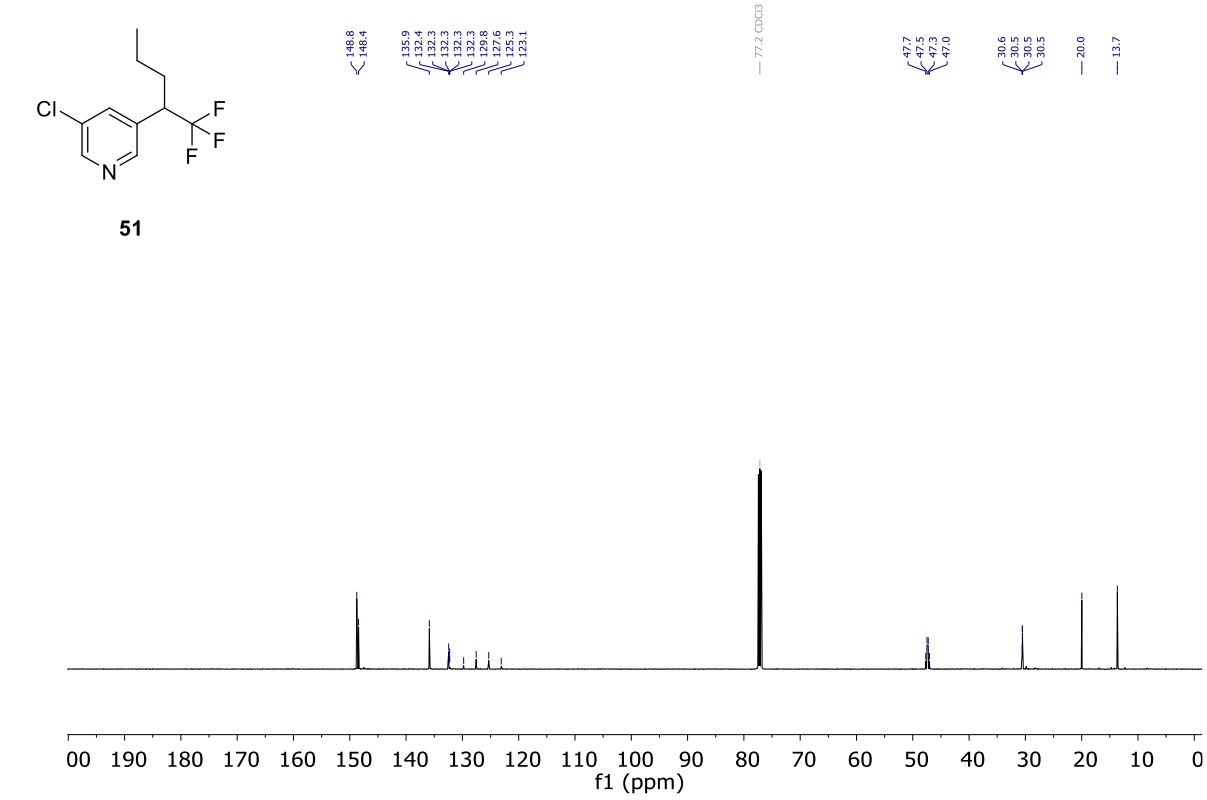


50

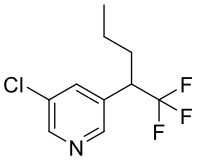
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

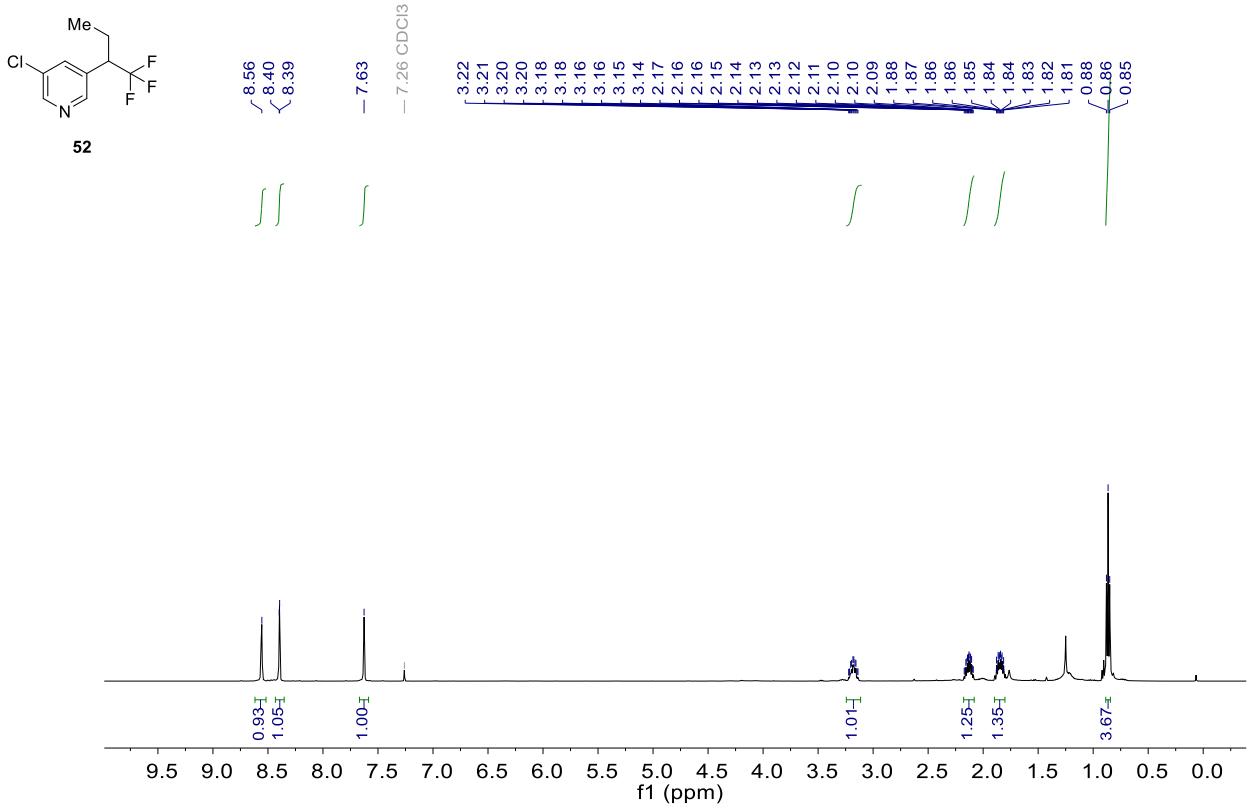


^{19}F NMR (282 MHz, $CDCl_3$)

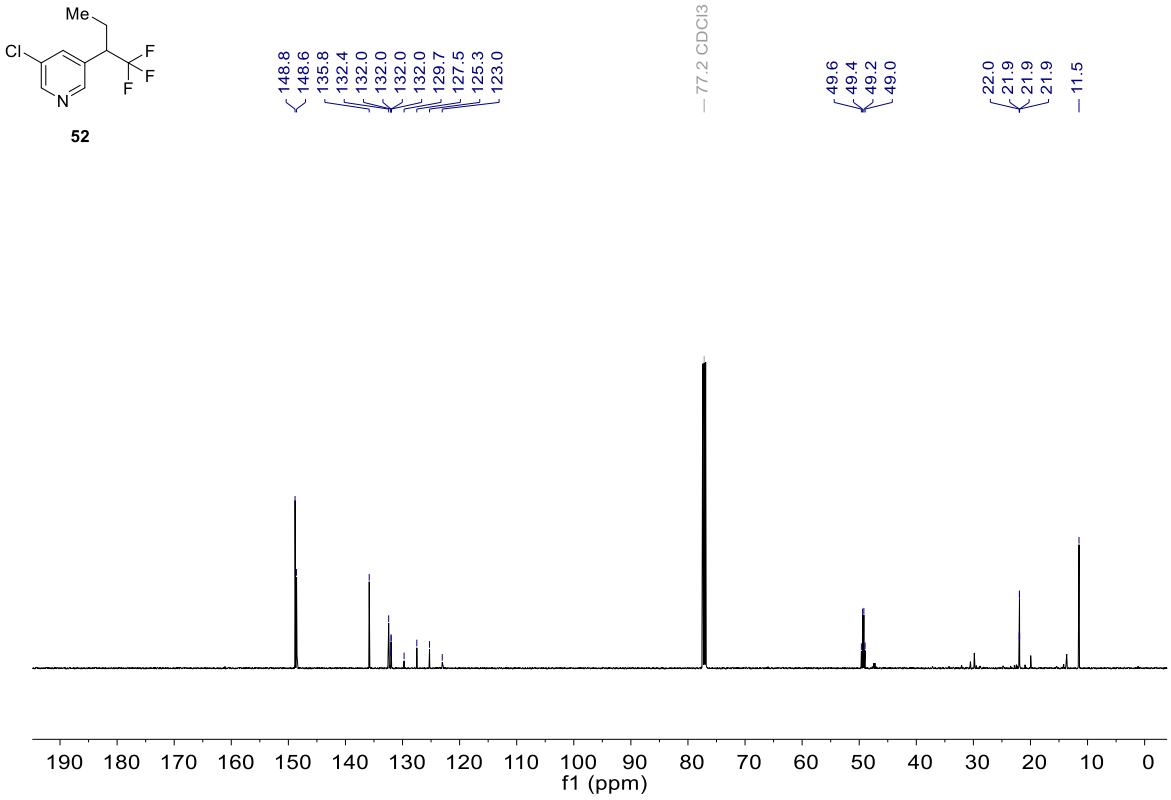


51

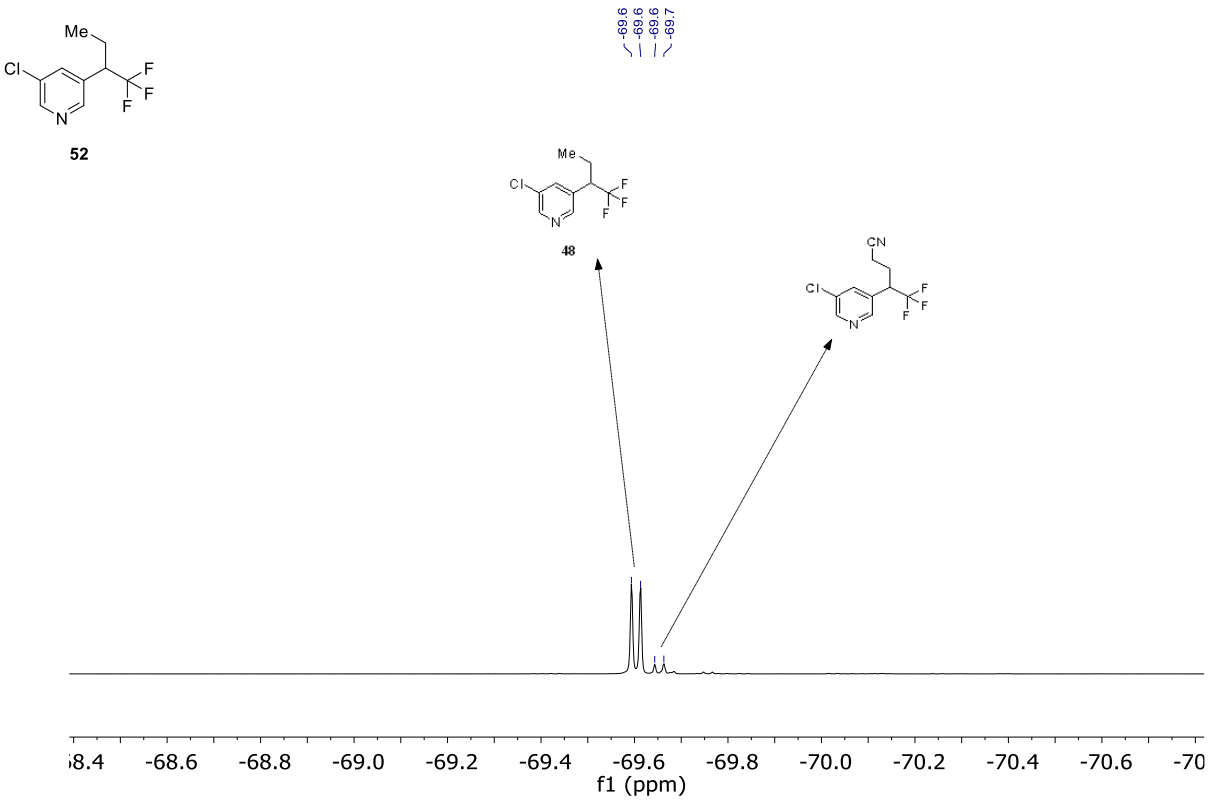
^{1}H NMR (500 MHz, $CDCl_3$)



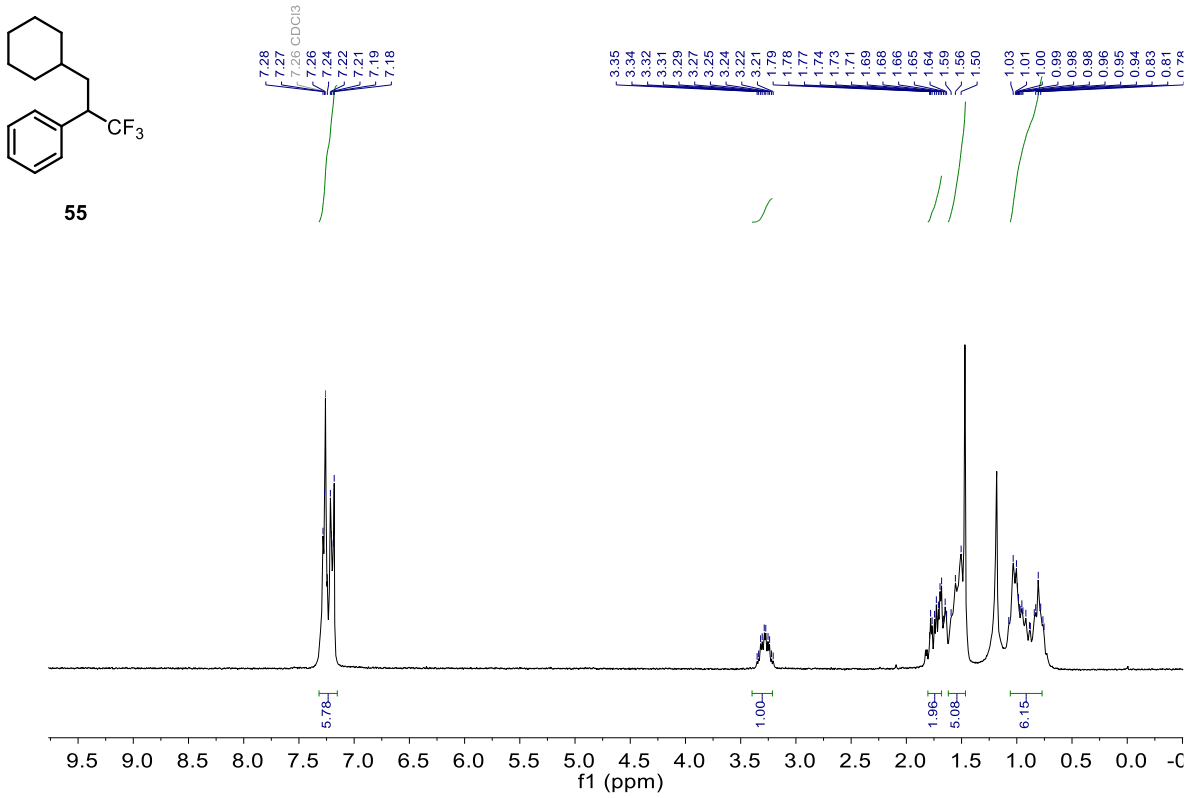
^{13}C NMR (126 MHz, $CDCl_3$)



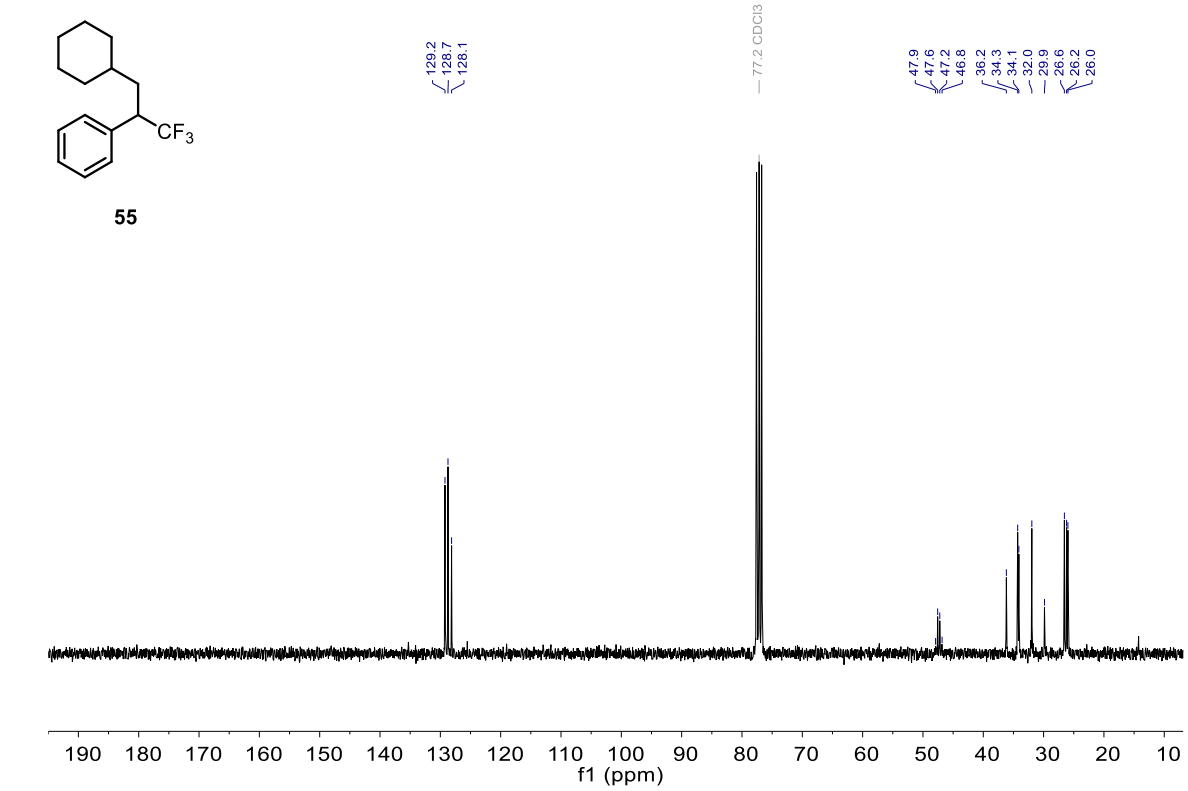
^{19}F NMR (282 MHz, $CDCl_3$)



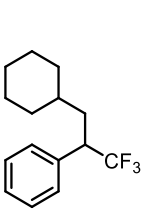
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

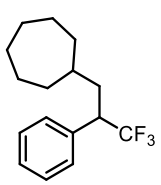


^{19}F NMR (282 MHz, $CDCl_3$)



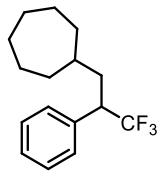
55

^{1}H NMR (500 MHz, $CDCl_3$)



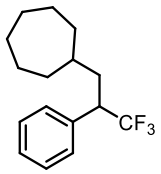
56

^{13}C NMR (126 MHz, $CDCl_3$)



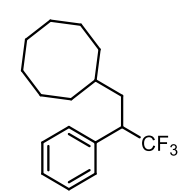
56

^{19}F NMR (282 MHz, $CDCl_3$)



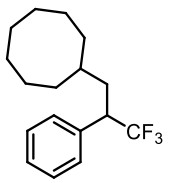
56

^{1}H NMR (500 MHz, $CDCl_3$)



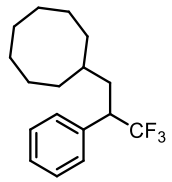
57

^{13}C NMR (126 MHz, $CDCl_3$)



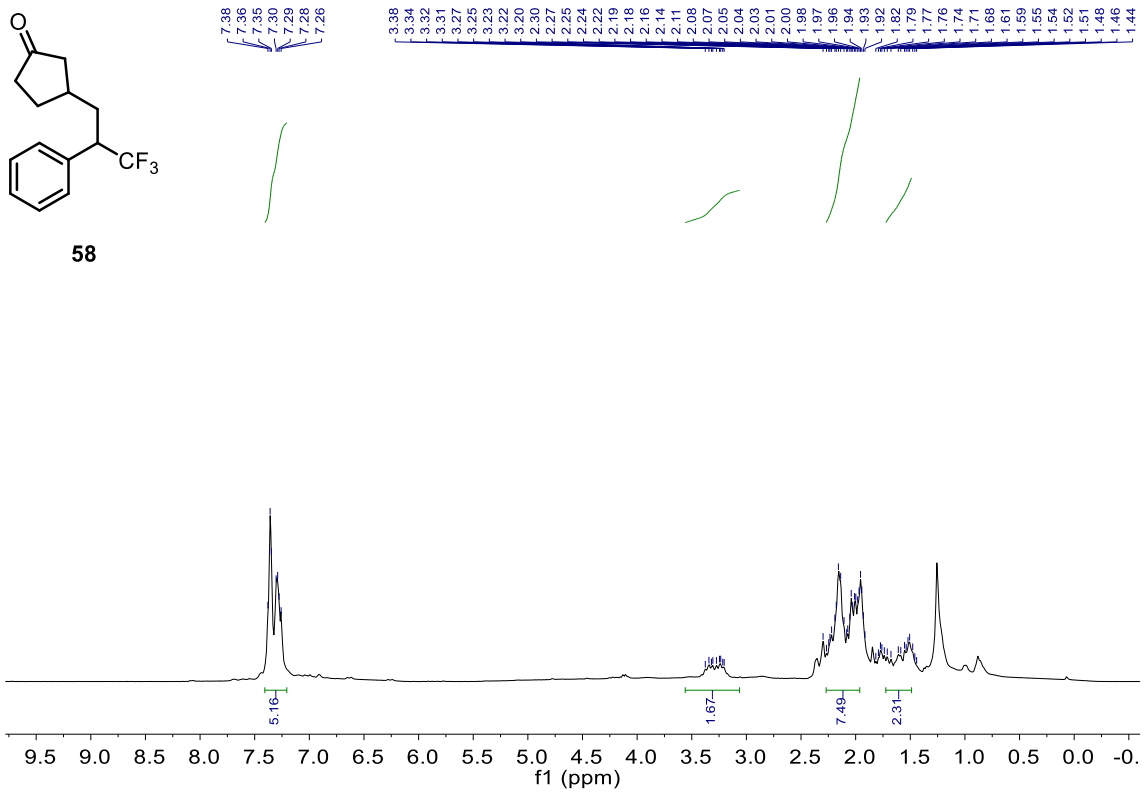
57

^{19}F NMR (282 MHz, $CDCl_3$)

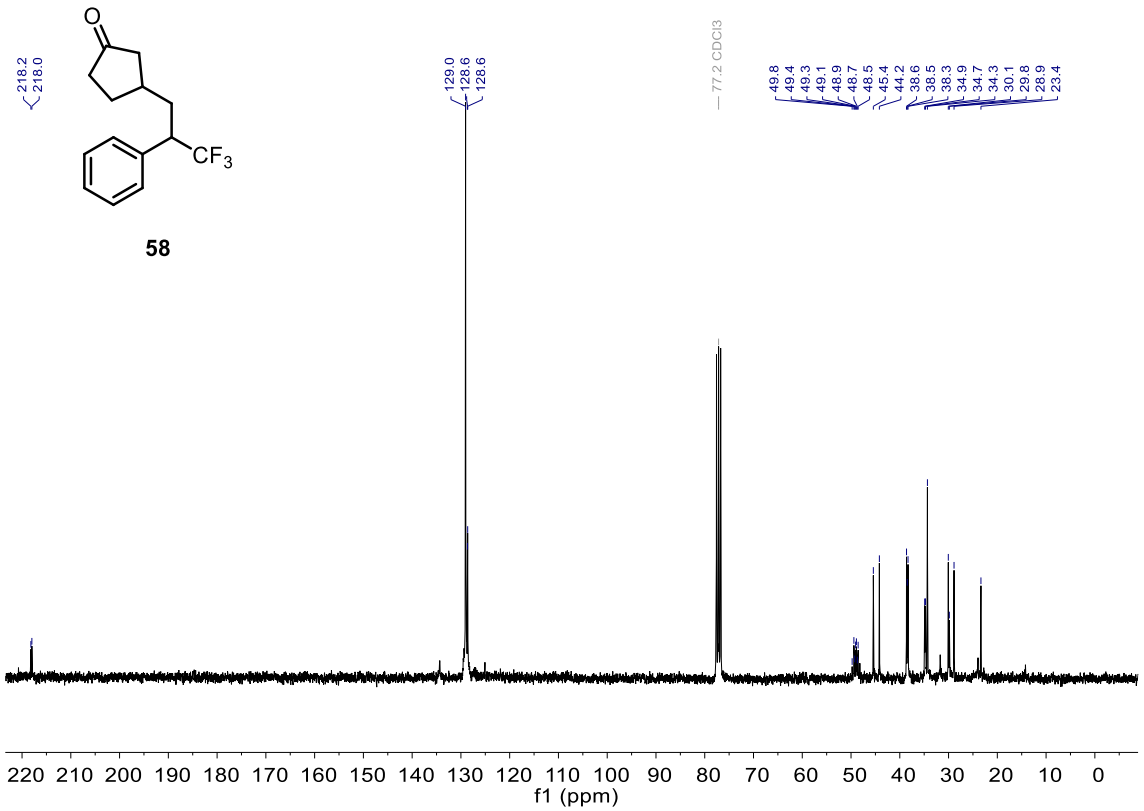


57

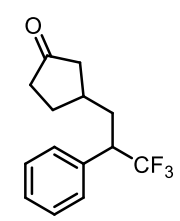
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

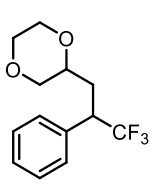


^{19}F NMR (282 MHz, $CDCl_3$)



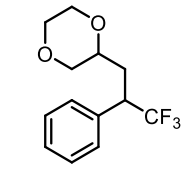
58

^{1}H NMR (500 MHz, $CDCl_3$)



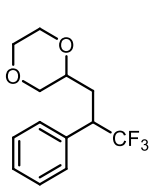
59

^{13}C NMR (126 MHz, $CDCl_3$)



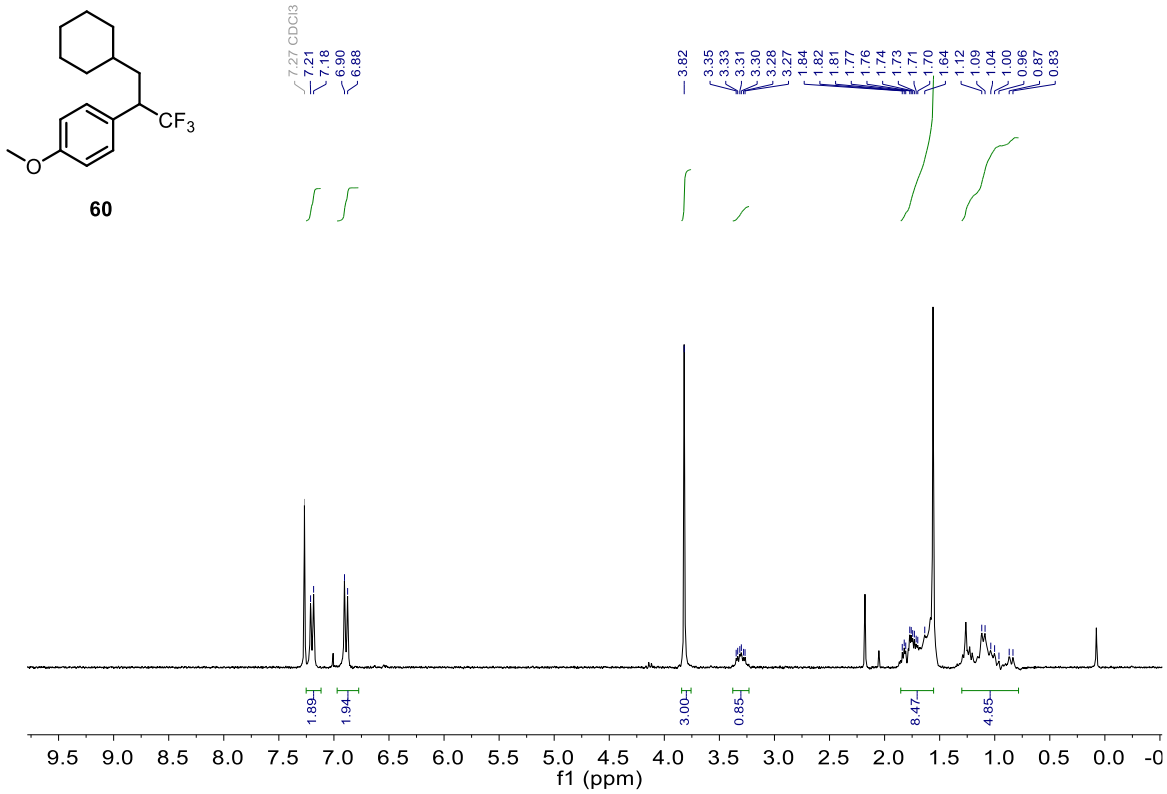
59

^{19}F NMR (282 MHz, $CDCl_3$)

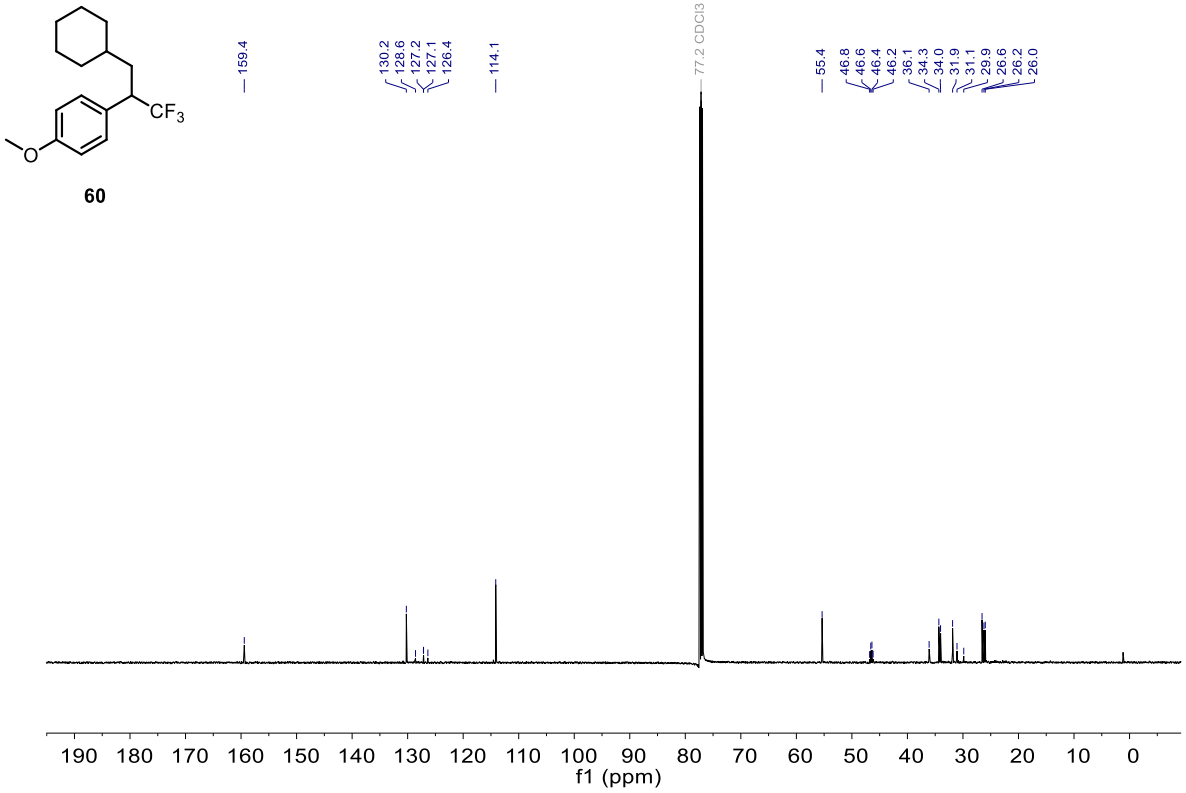


59

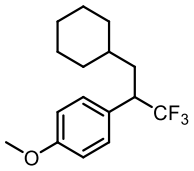
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

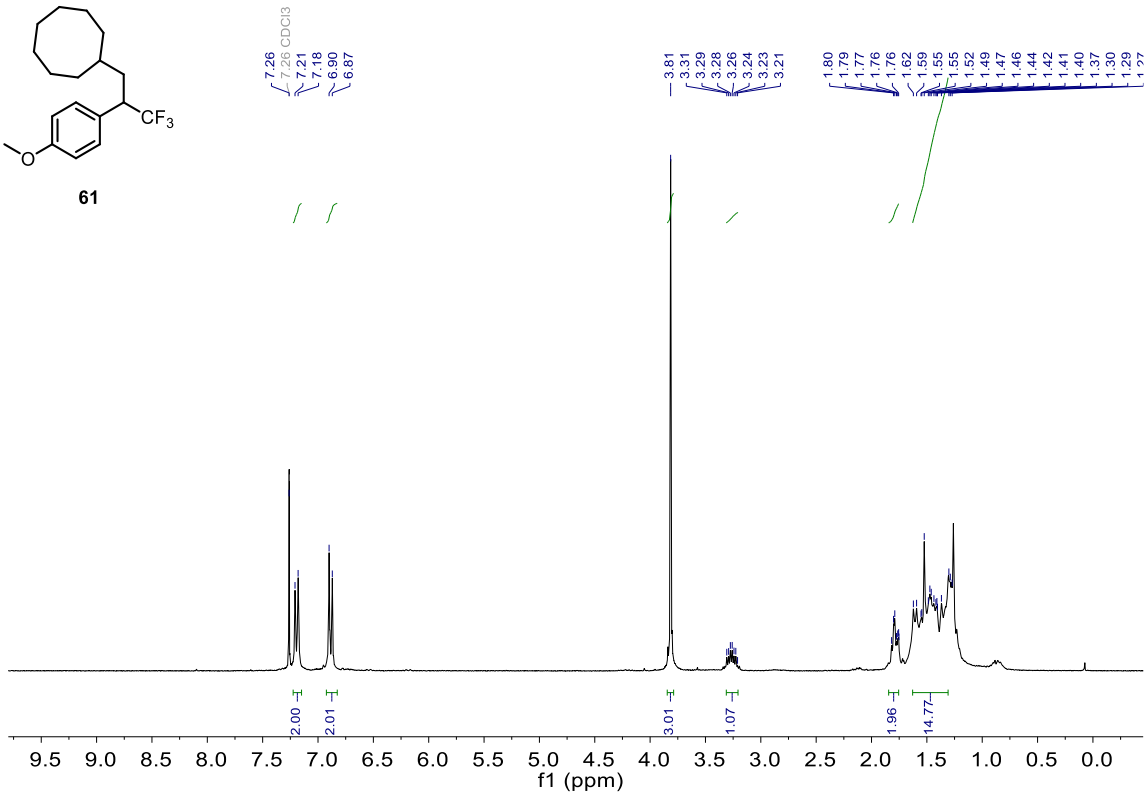


^{19}F NMR (282 MHz, $CDCl_3$)

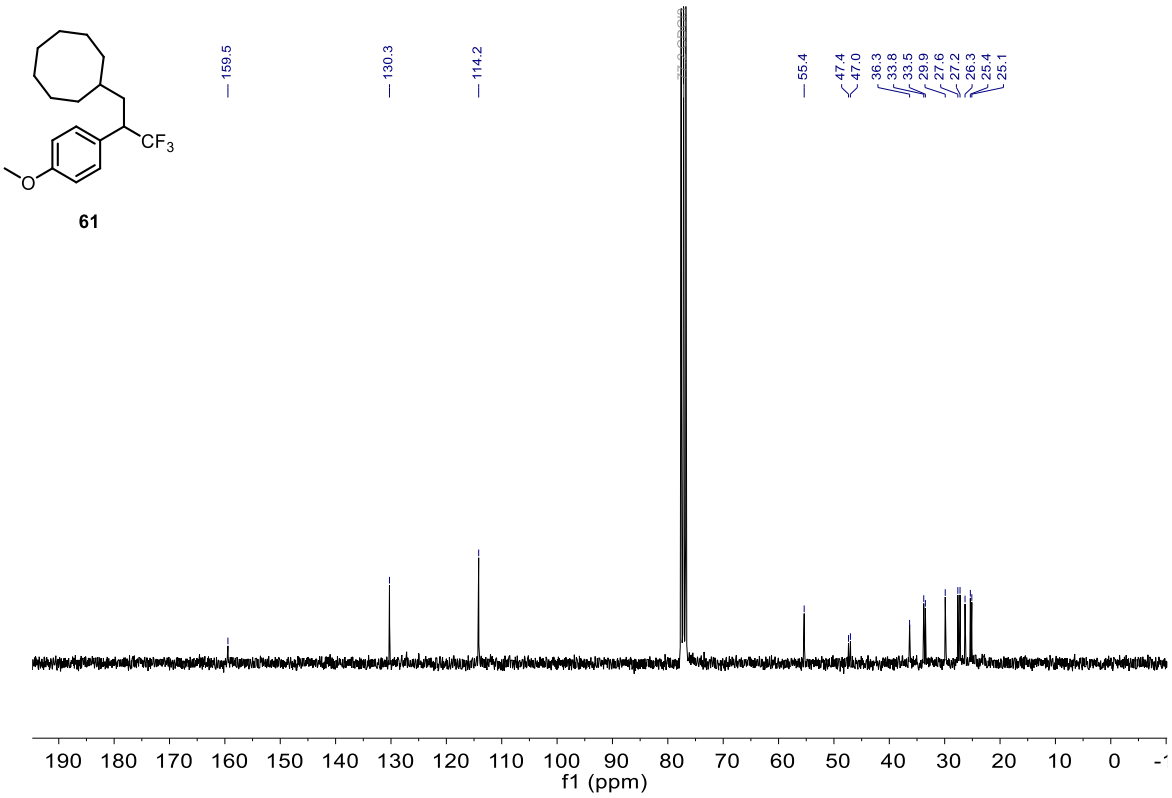


60

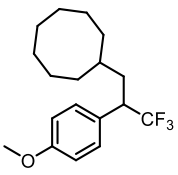
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

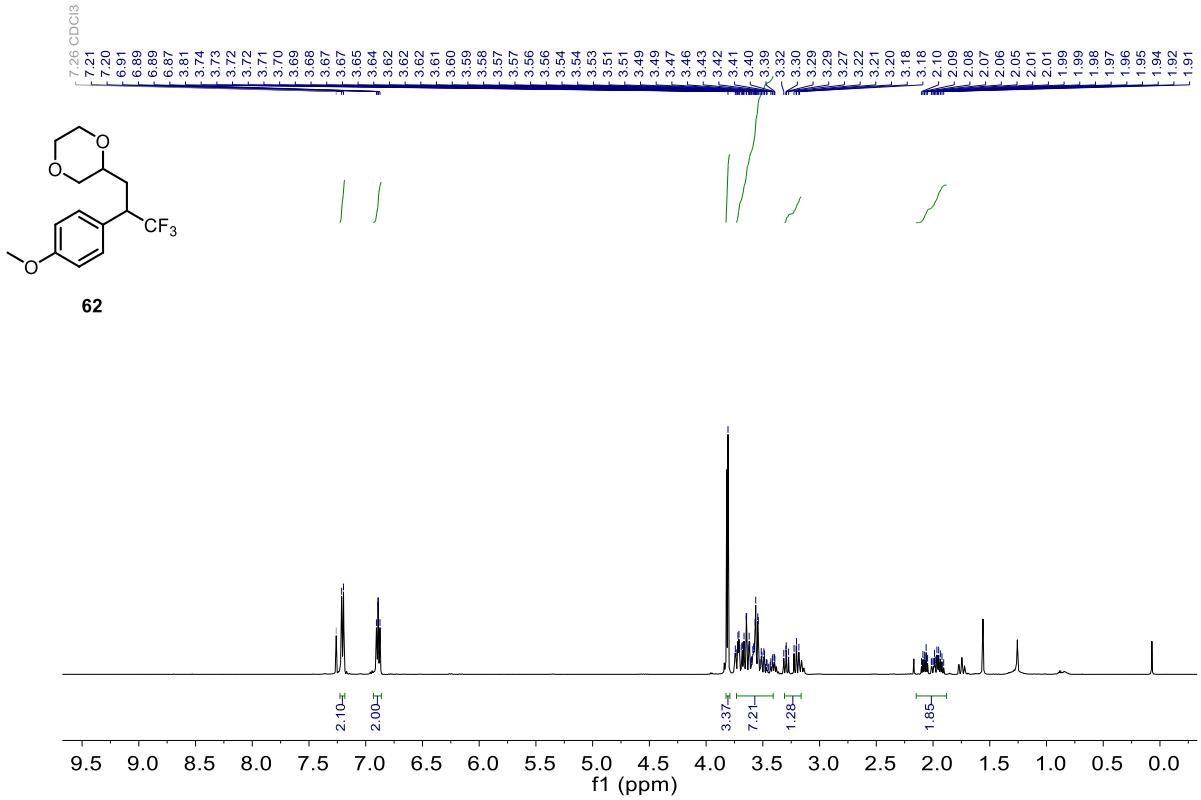


^{19}F NMR (282 MHz, $CDCl_3$)

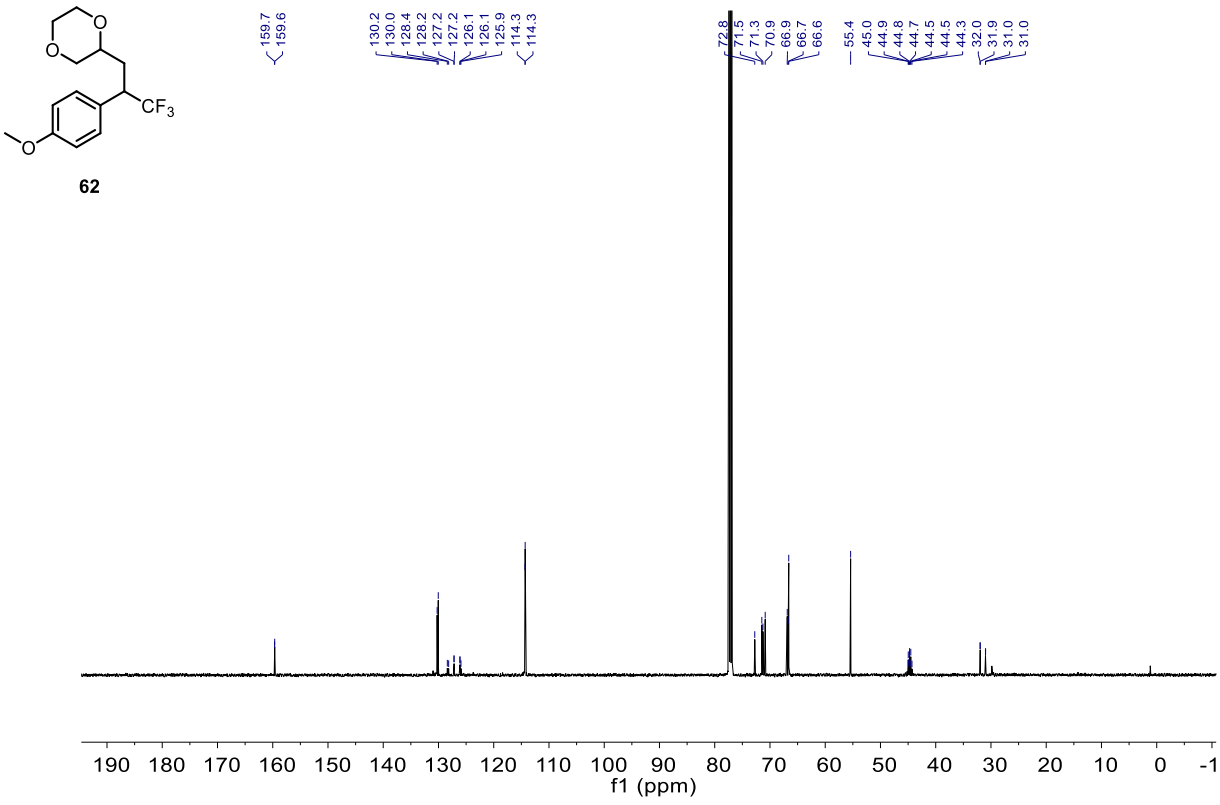


61

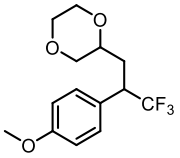
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

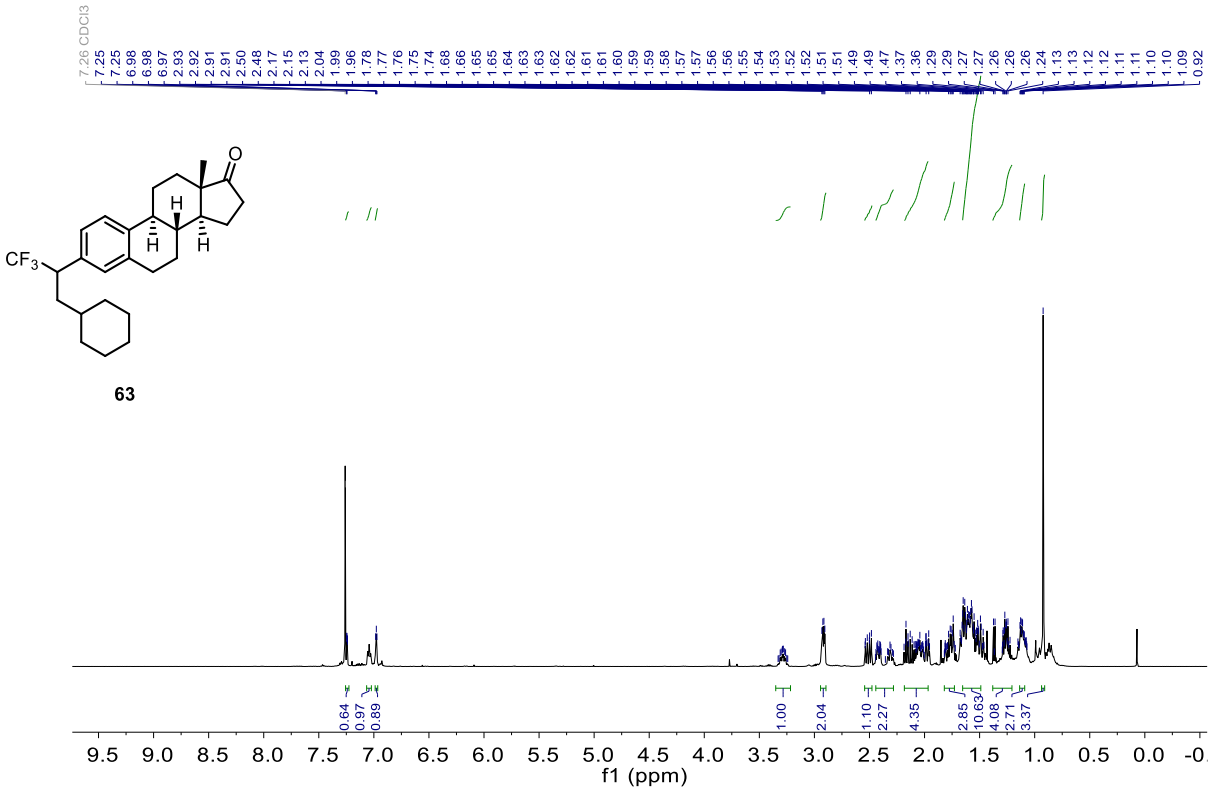


^{19}F NMR (282 MHz, $CDCl_3$)

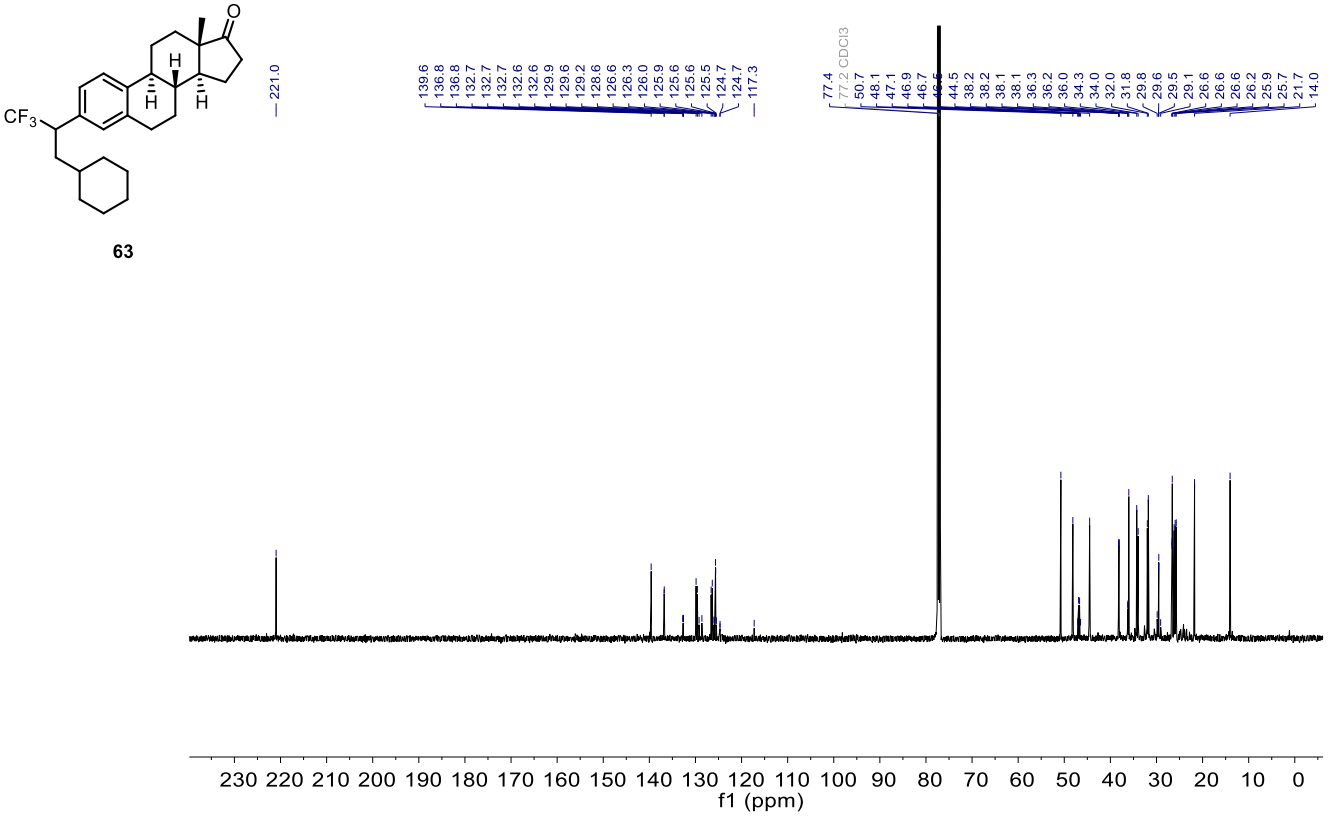


62

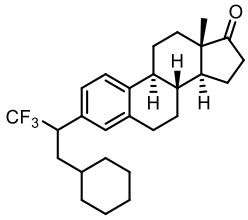
^{1}H NMR (500 MHz, $CDCl_3$)



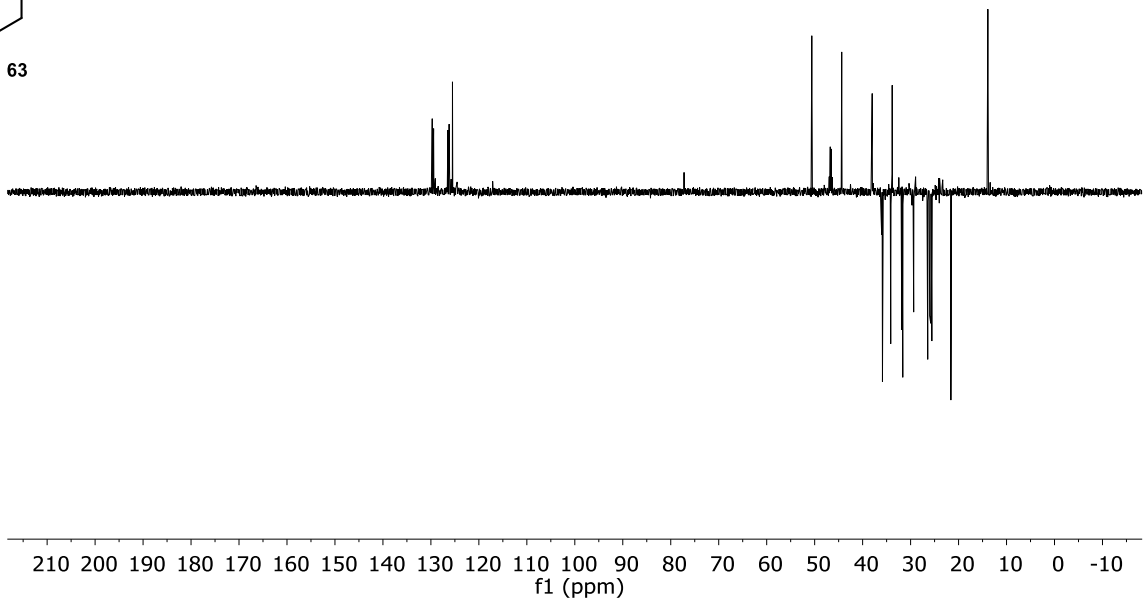
^{13}C NMR (126 MHz, $CDCl_3$)



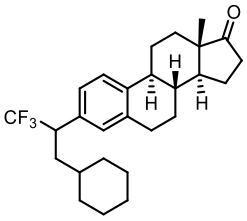
DEPT-135 (126 MHz, $CDCl_3$)



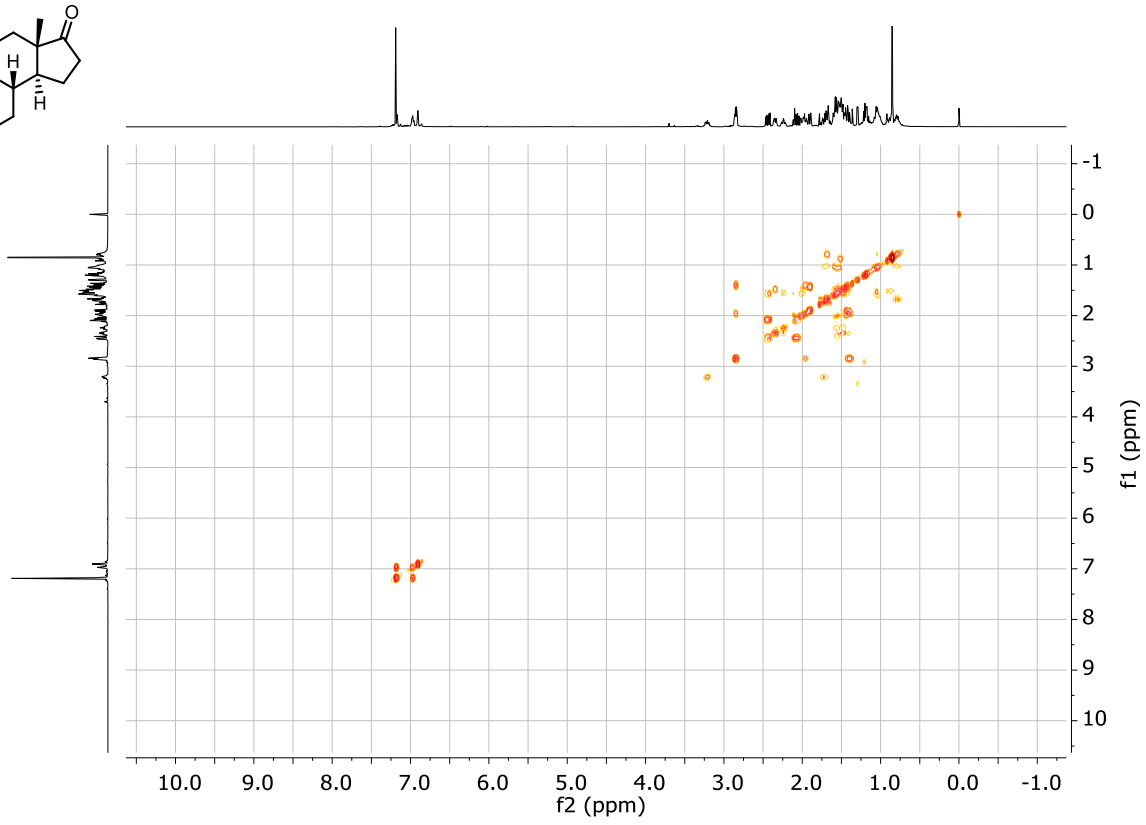
63



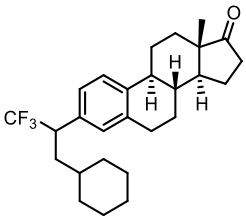
COSY (500 MHz, $CDCl_3$)



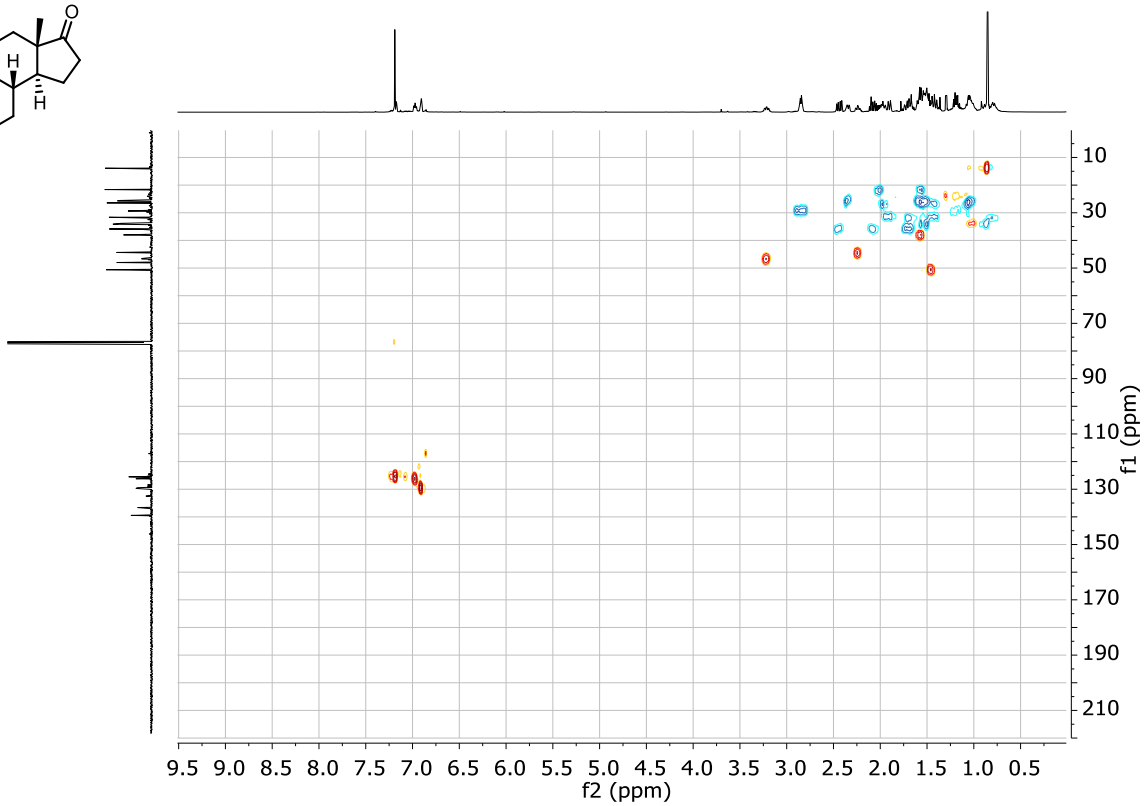
63



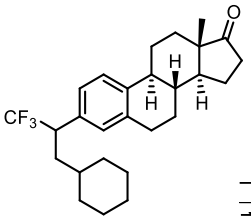
HSQC (500, 126, MHz, $CDCl_3$)



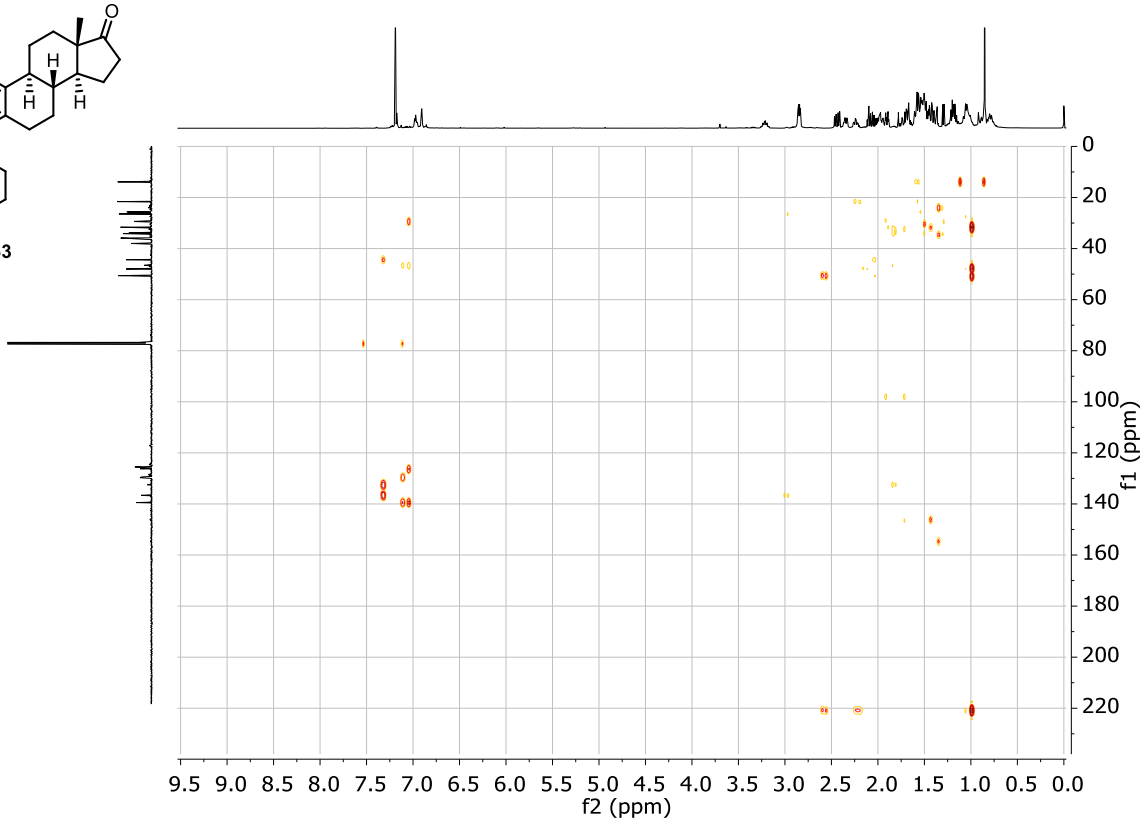
63



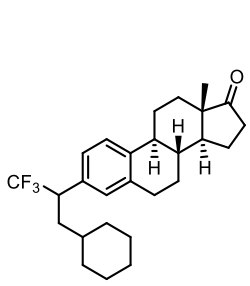
HMBC (500, 126, MHz, $CDCl_3$)



63

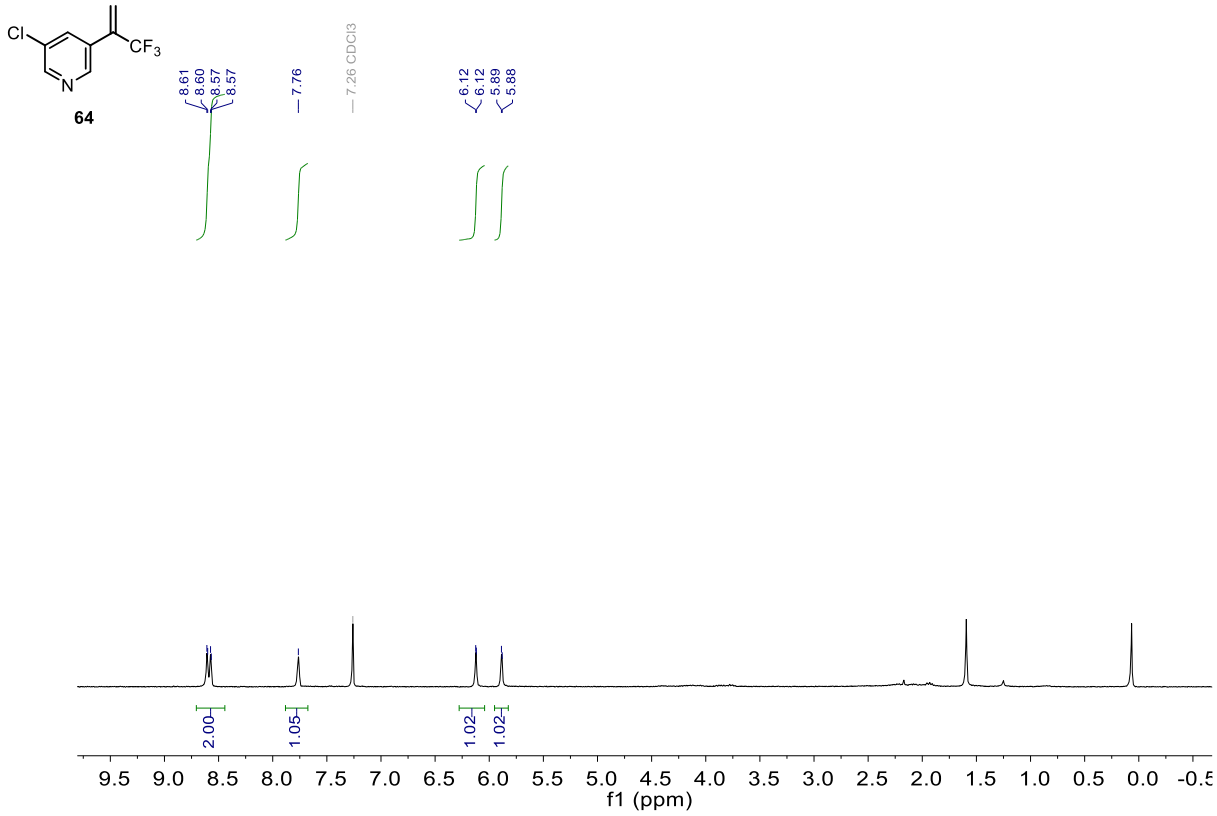


^{19}F NMR (282 MHz, $CDCl_3$)

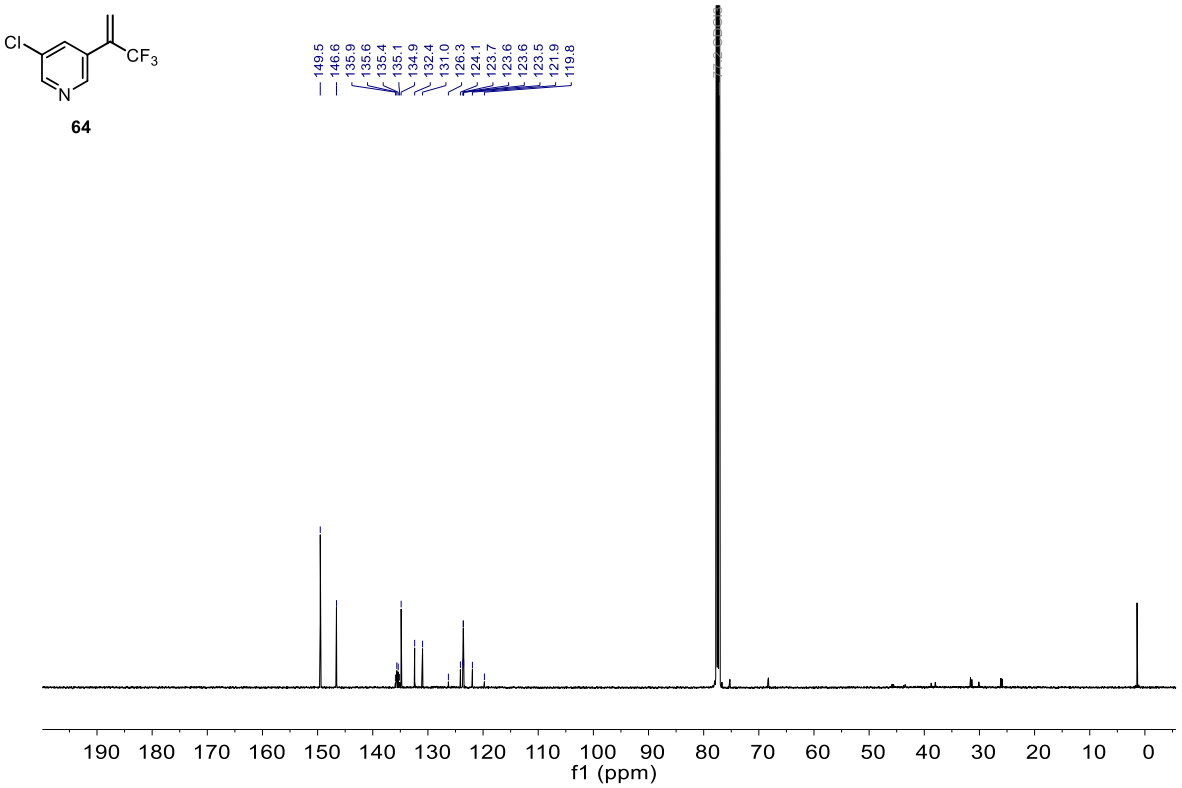


63

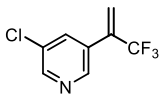
^{1}H NMR (300 MHz, $CDCl_3$)



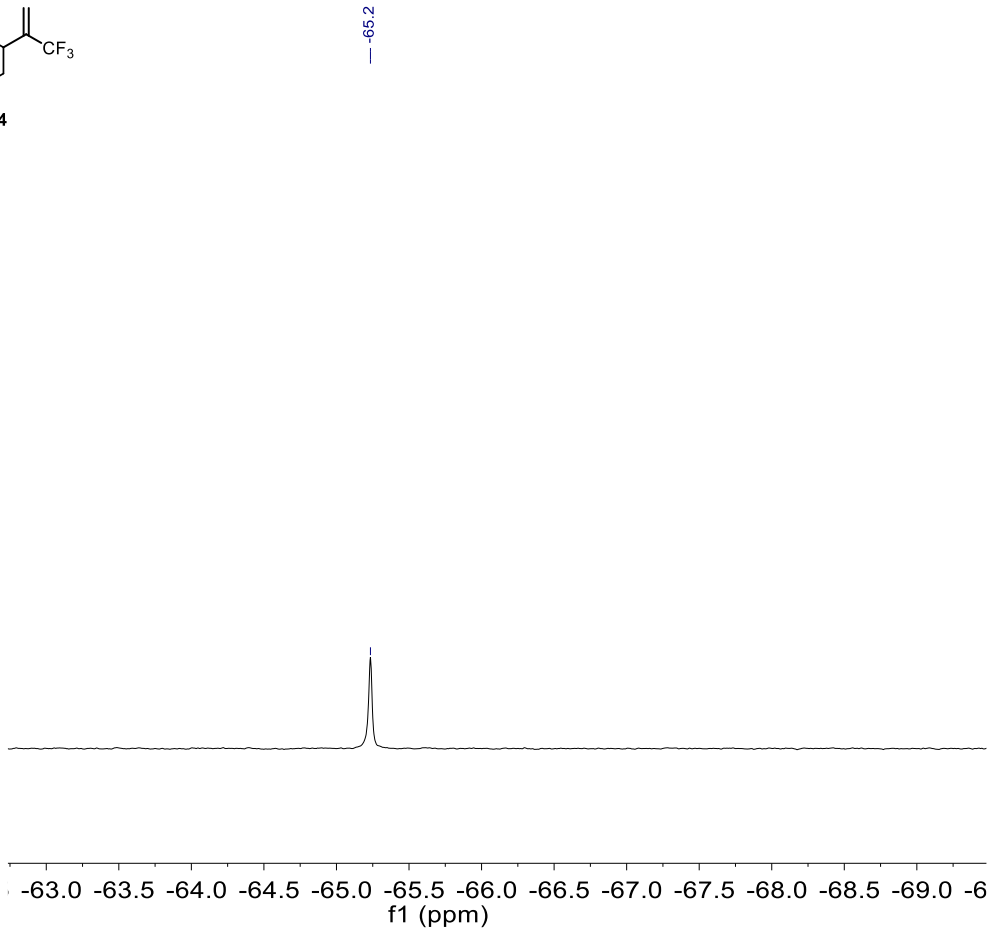
^{13}C NMR (126 MHz, $CDCl_3$)



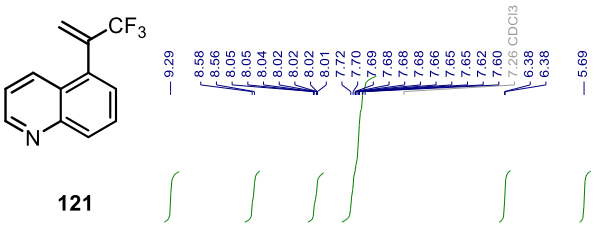
^{19}F NMR (282 MHz, $CDCl_3$)



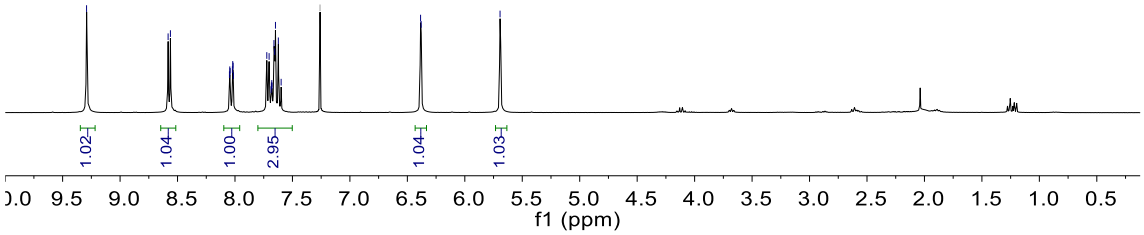
64



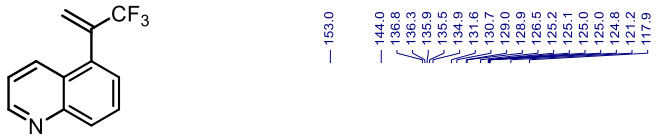
^{1}H NMR (500 MHz, $CDCl_3$)



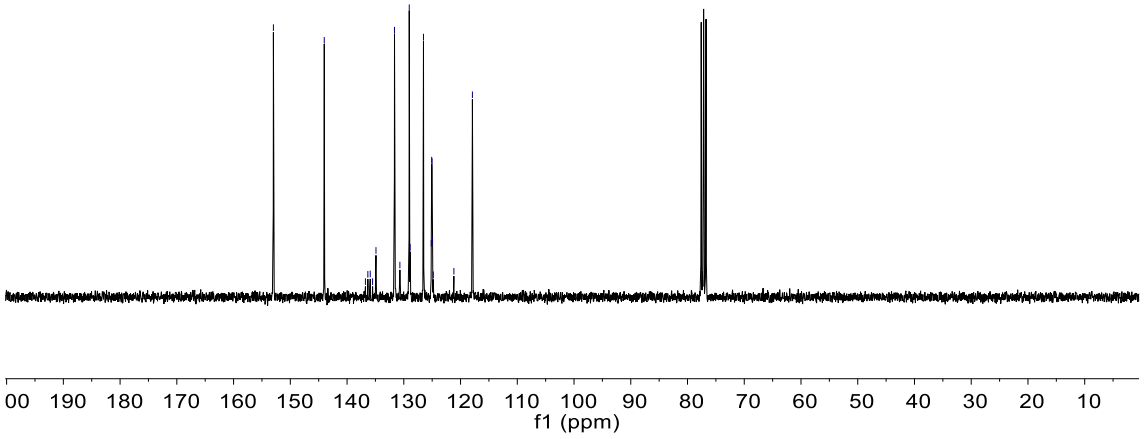
121



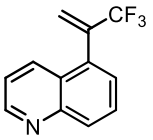
^{13}C NMR (126 MHz, $CDCl_3$)



121

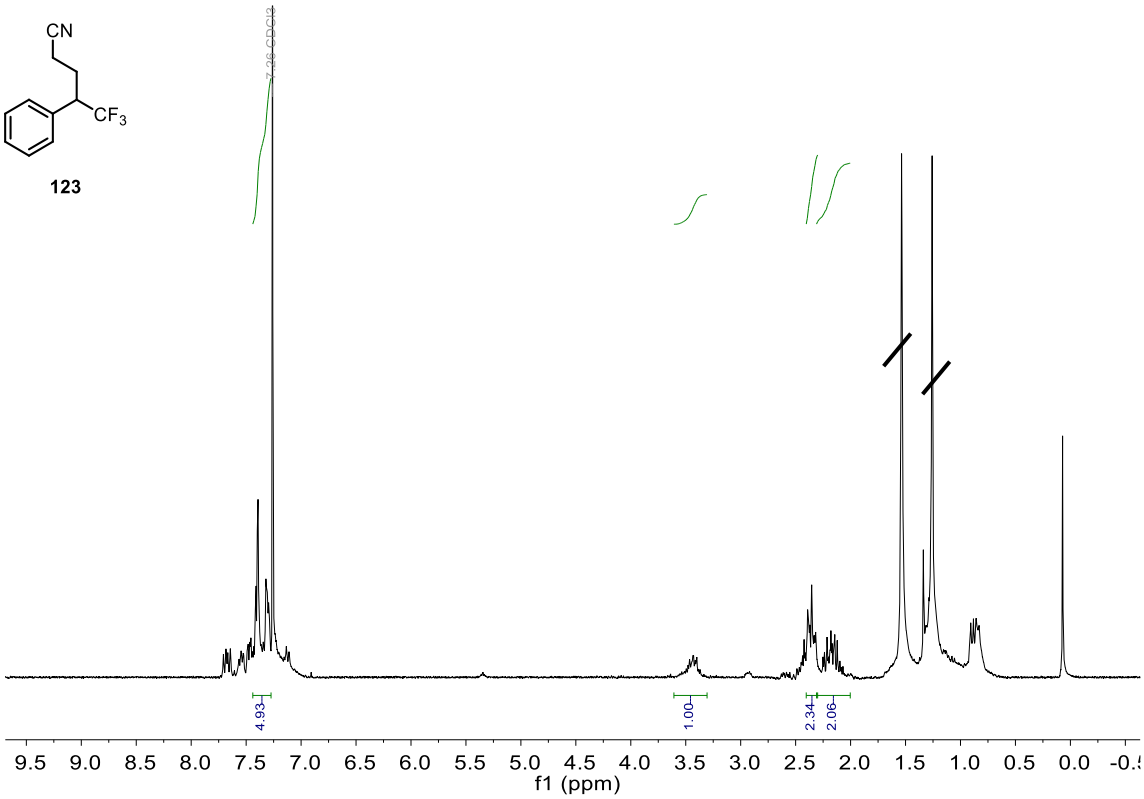


^{19}F NMR (282 MHz, $CDCl_3$)



121

^{1}H NMR (500 MHz, $CDCl_3$)



^{19}F NMR (282 MHz, $CDCl_3$)