

Supporting Information

Asymmetric Synthesis of *gem*-Difluoromethylenated Dihydroxypyrrolizidines and Indolizidines

Watcharaporn Thaharn,[†] Teerawut Bootwicha,[†] Darunee Soorukram,[†] Chutima Kuhakarn,[†]
Samran Prabpai,^{†,‡} Palangpon Kongsaree,^{†,‡} Patoomratana Tuchinda,[†] Vichai Reutrakul,[†] and
Manat Pohmakotr^{*,†}

[†] Center of Excellence for Innovation in Chemistry (PERCH-CIC) and Department of Chemistry,

[‡]Center for Excellence in Protein Structure and Function, Faculty of Science, Mahidol

University, Rama VI Road, Bangkok 10400, Thailand

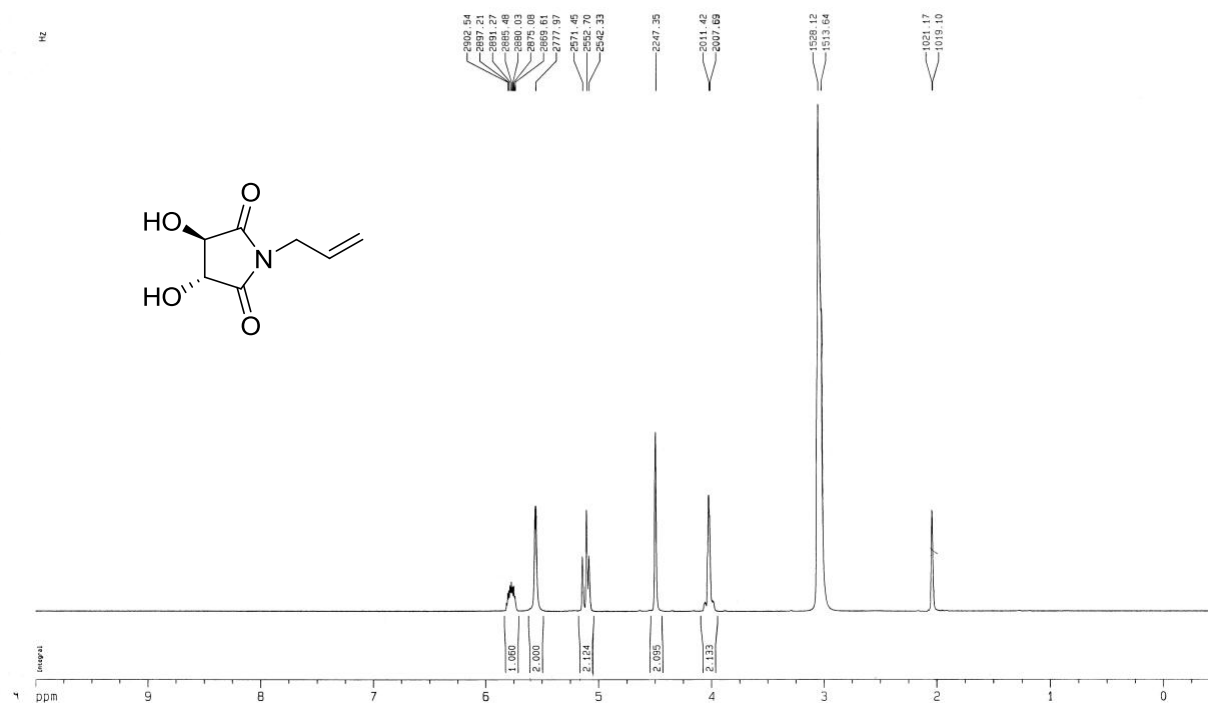
manat.poh@mahidol.ac.th

Content

	Page
Spectral data (¹ H, ¹⁹ F and ¹³ C spectra)	S2–S81
NOE spectra of compound 14	S39
NOE spectra of compound 16	S43
NOE spectra of compound 18	S46
NOE spectra of compounds 21a , 21b , 21c	S53–S58
NOE spectra of compound <i>trans</i> - 23	S64
NOE spectra of compound 24a	S66
X-ray crystal structures of <i>cis</i> - 10 , <i>trans</i> - 11 , <i>cis</i> - 13 , <i>cis</i> - 19 , 28b	S82–S86

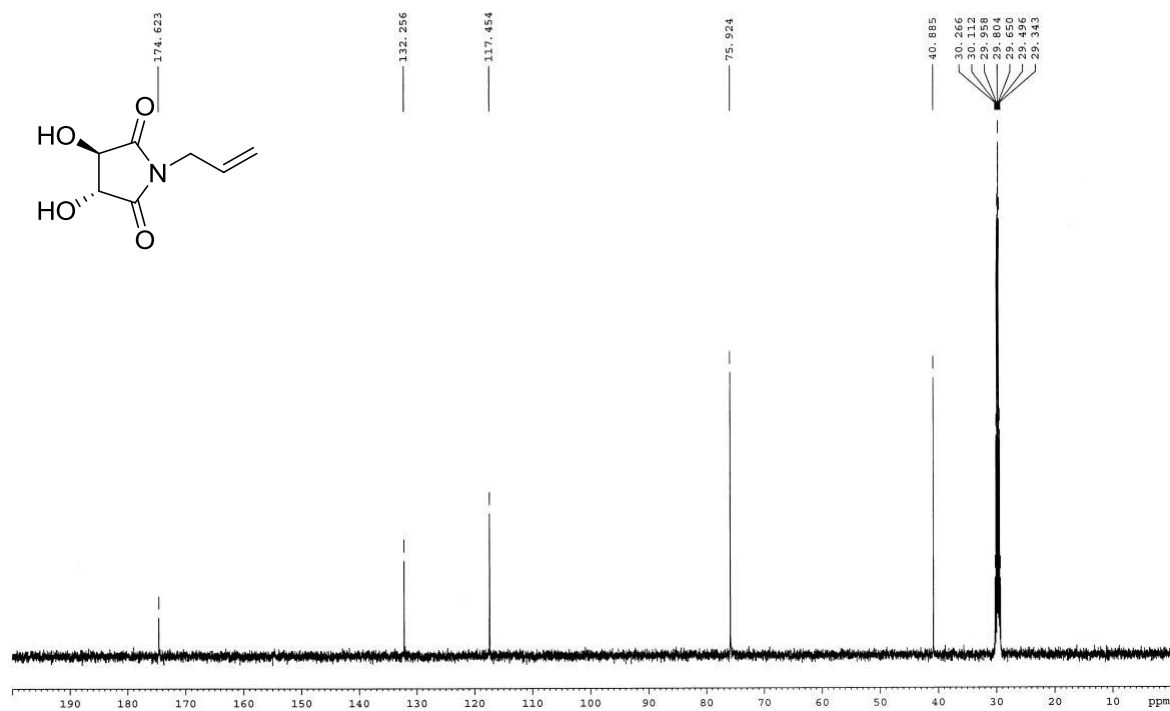
¹H NMR Spectrum of (3*R*,4*R*)-1-allyl-3,4-dihydroxypyrrolidine-2,5-dione

(500 MHz, acetone-d₆)

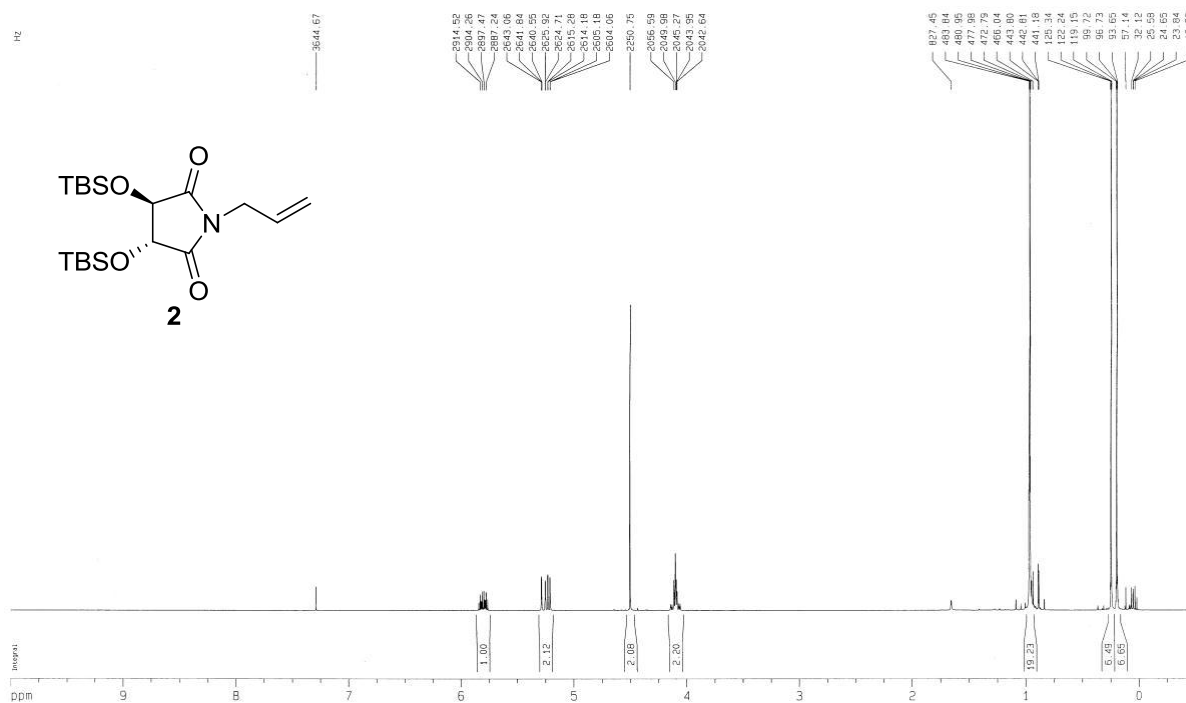


¹³C NMR Spectrum of (3*R*,4*R*)-1-allyl-3,4-dihydroxypyrrolidine-2,5-dione

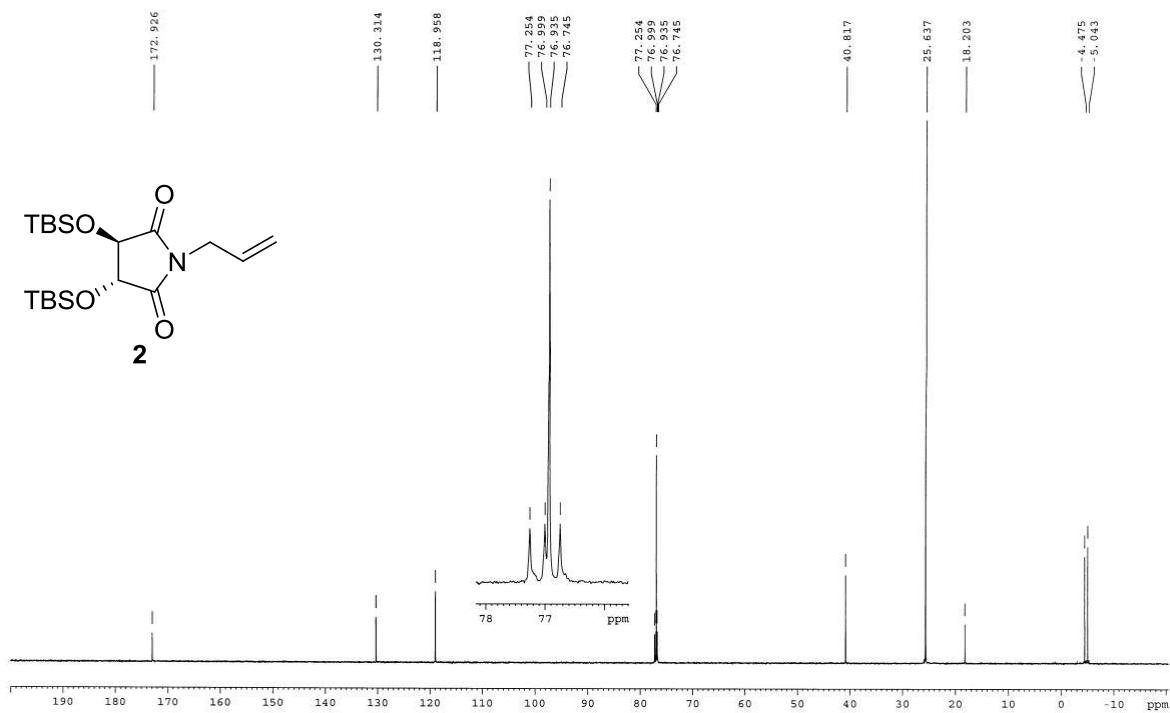
(125 MHz, acetone-d₆)



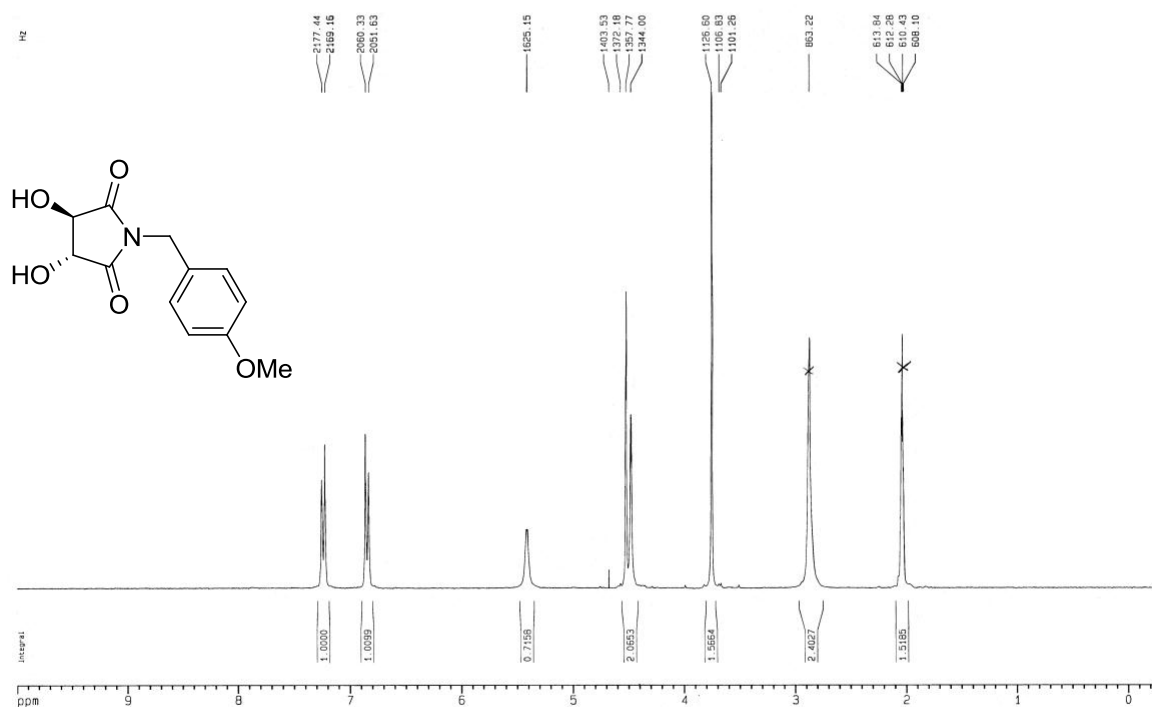
¹H NMR Spectrum of **2** (500 MHz, CDCl₃)



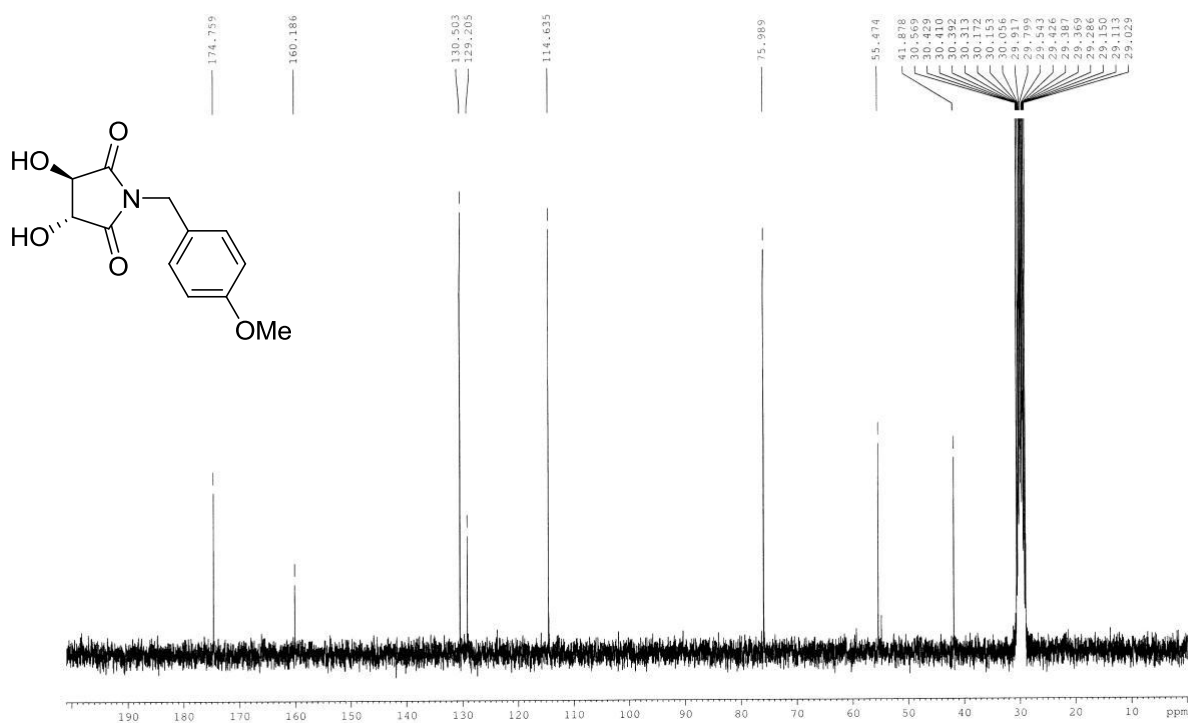
¹³C NMR Spectrum of **2** (125 MHz, CDCl₃)



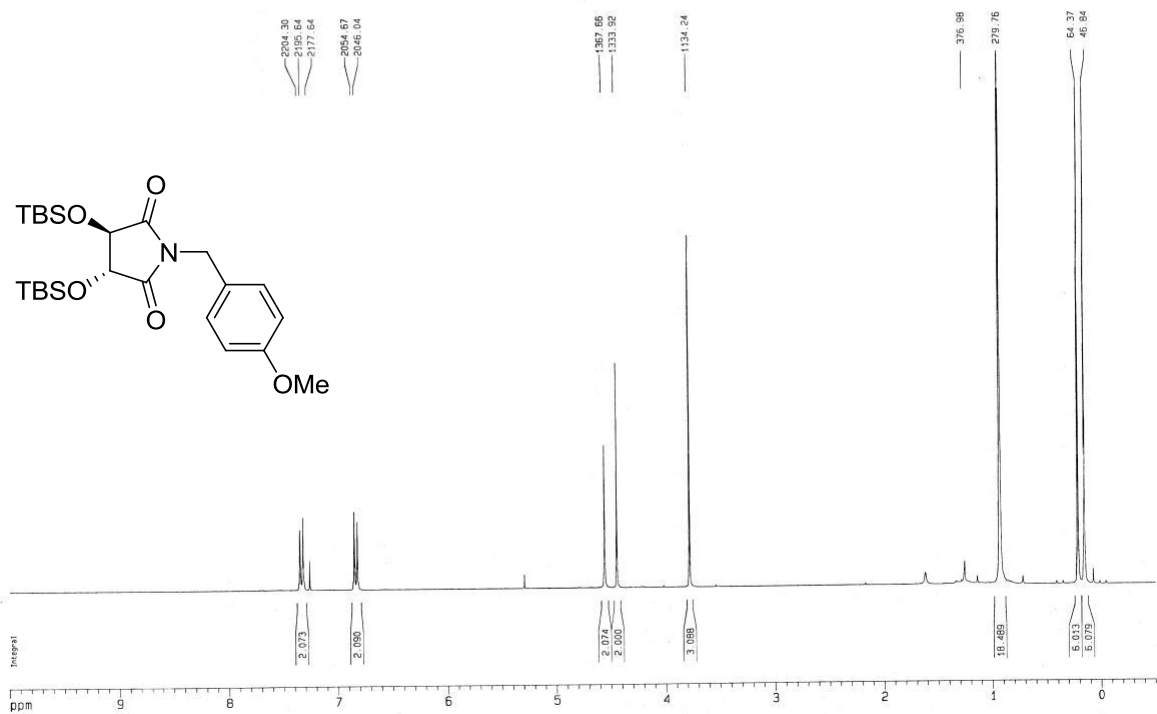
¹H NMR Spectrum of (3*R*,4*R*)-3,4-dihydroxy-1-(4-methoxybenzyl)pyrrolidine-2,5-dione
(300 MHz, acetone-d₆)



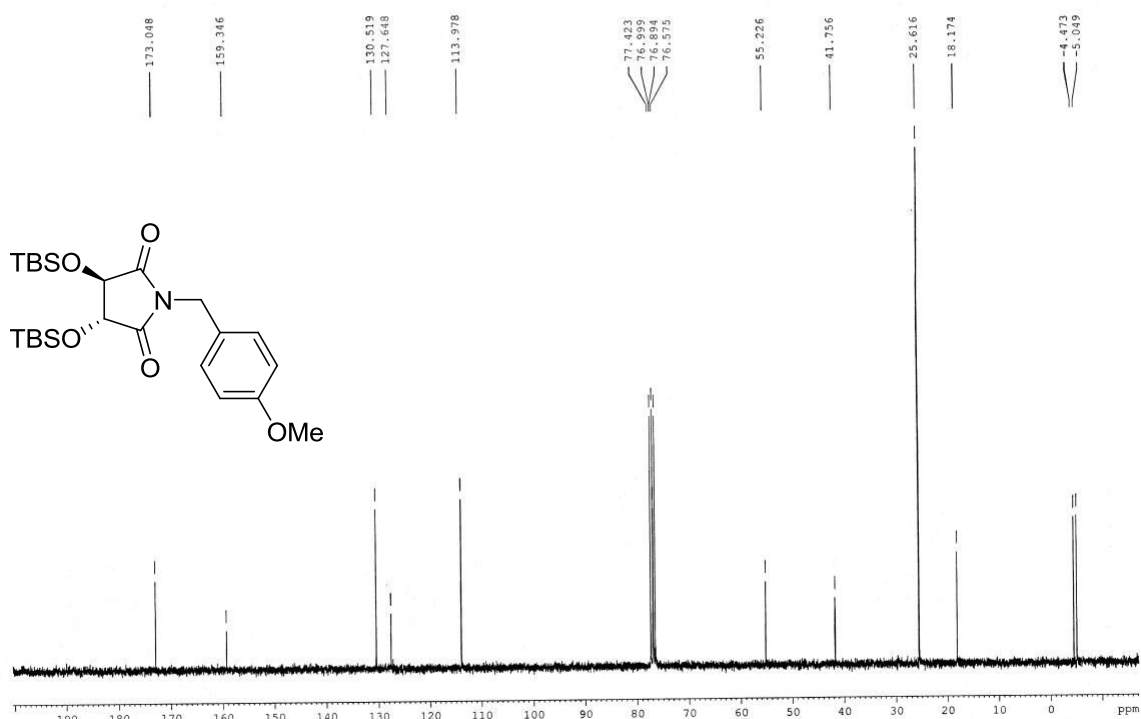
¹³C NMR Spectrum of (3*R*,4*R*)-3,4-dihydroxy-1-(4-methoxybenzyl)pyrrolidine-2,5-dione
(75 MHz, acetone-d₆)



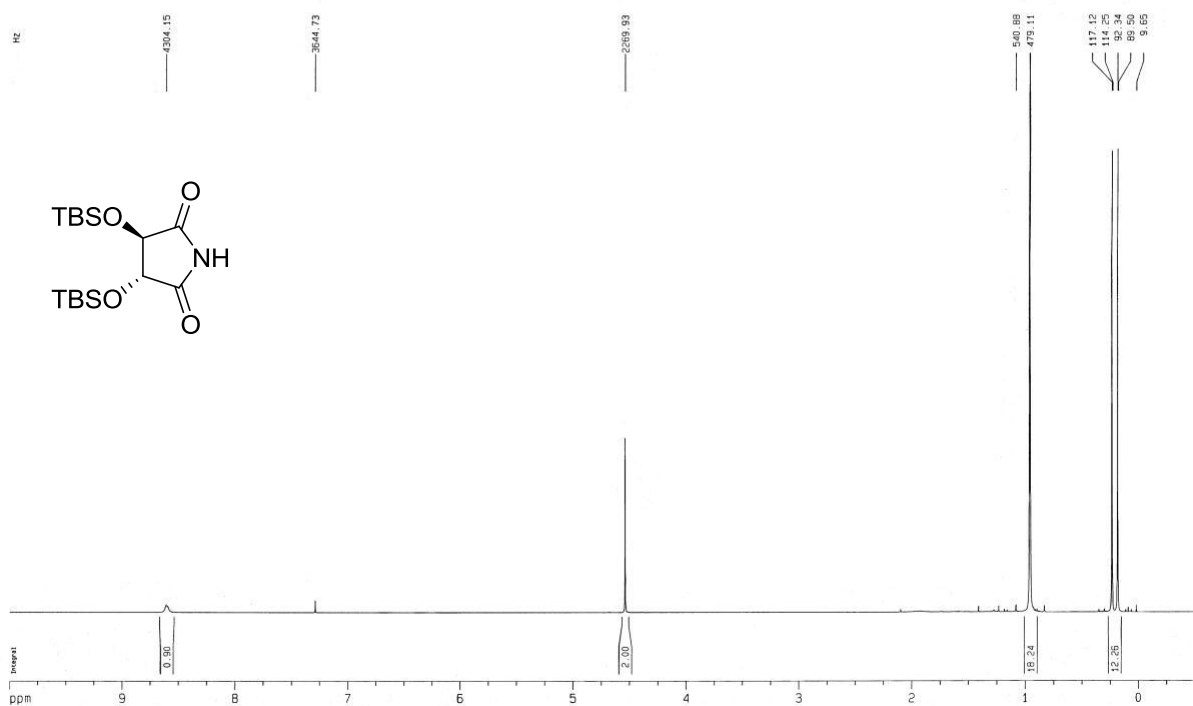
¹H NMR Spectrum of (3*R*,4*R*)-3,4-bis(*tert*-butyldimethylsilyloxy)-1-(4-methoxybenzyl)
pyrrolidine-2,5-dione (300 MHz, CDCl₃)



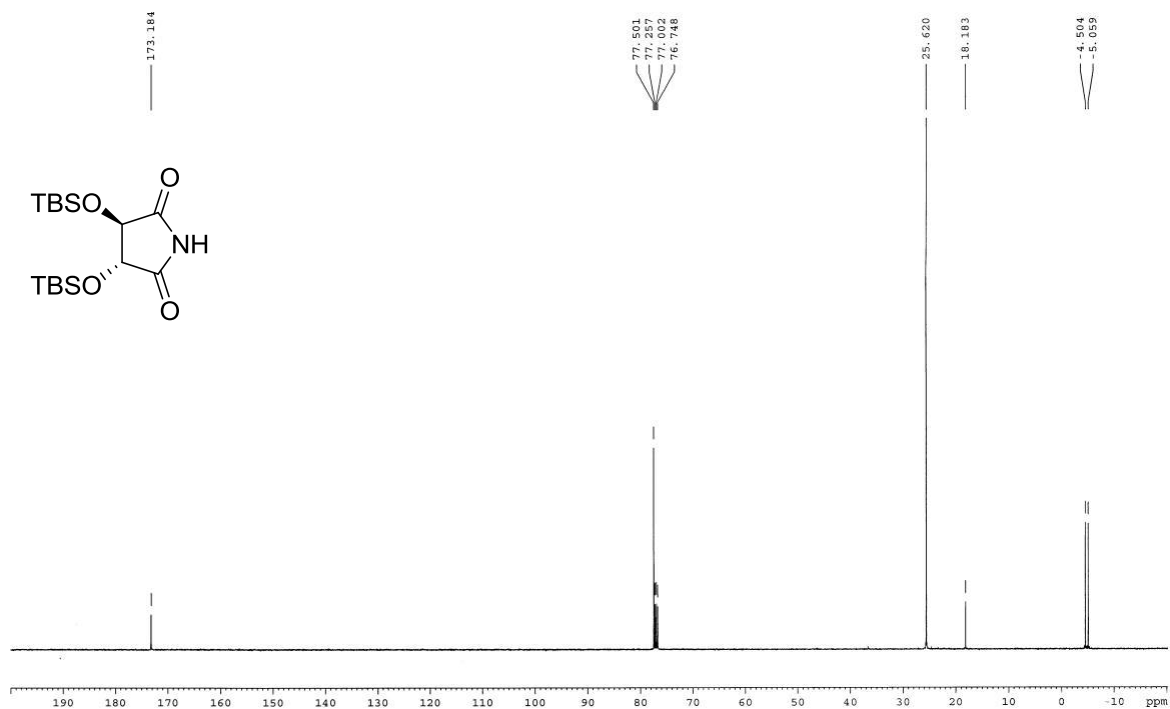
¹³C NMR Spectrum of (3*R*,4*R*)-3,4-bis(*tert*-butyldimethylsilyloxy)-1-(4-methoxybenzyl)
pyrrolidine-2,5-dione (75 MHz, CDCl₃)



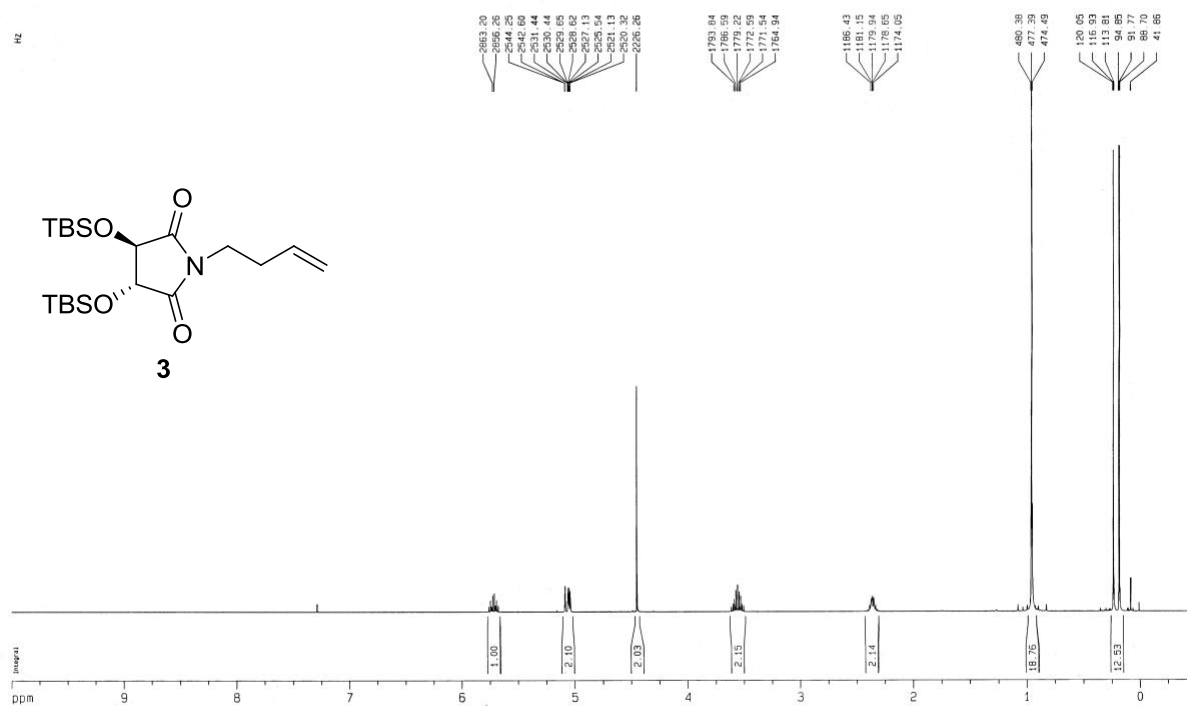
¹H NMR Spectrum of (3*R*,4*R*)-3,4-bis(*tert*-butyldimethylsilyloxy)pyrrolidine-2,5-dione
(500 MHz, CDCl₃)



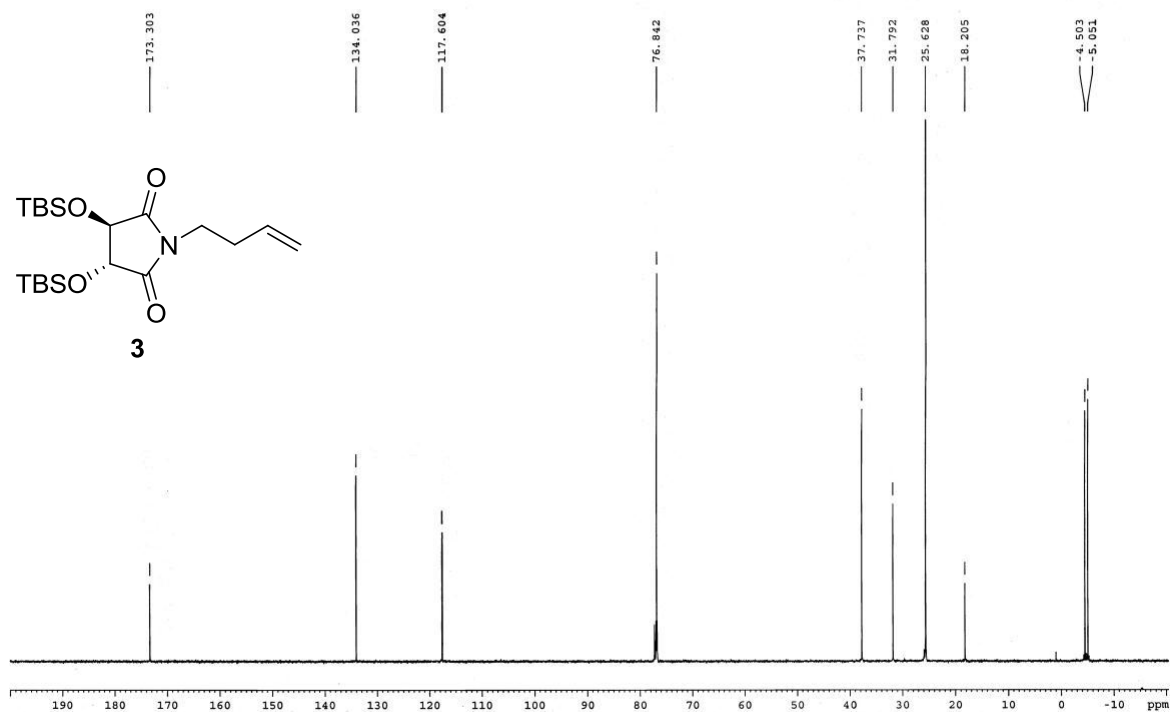
¹³C NMR Spectrum of (3*R*,4*R*)-3,4-bis(*tert*-butyldimethylsilyloxy)pyrrolidine-2,5-dione
(125 MHz, CDCl₃)



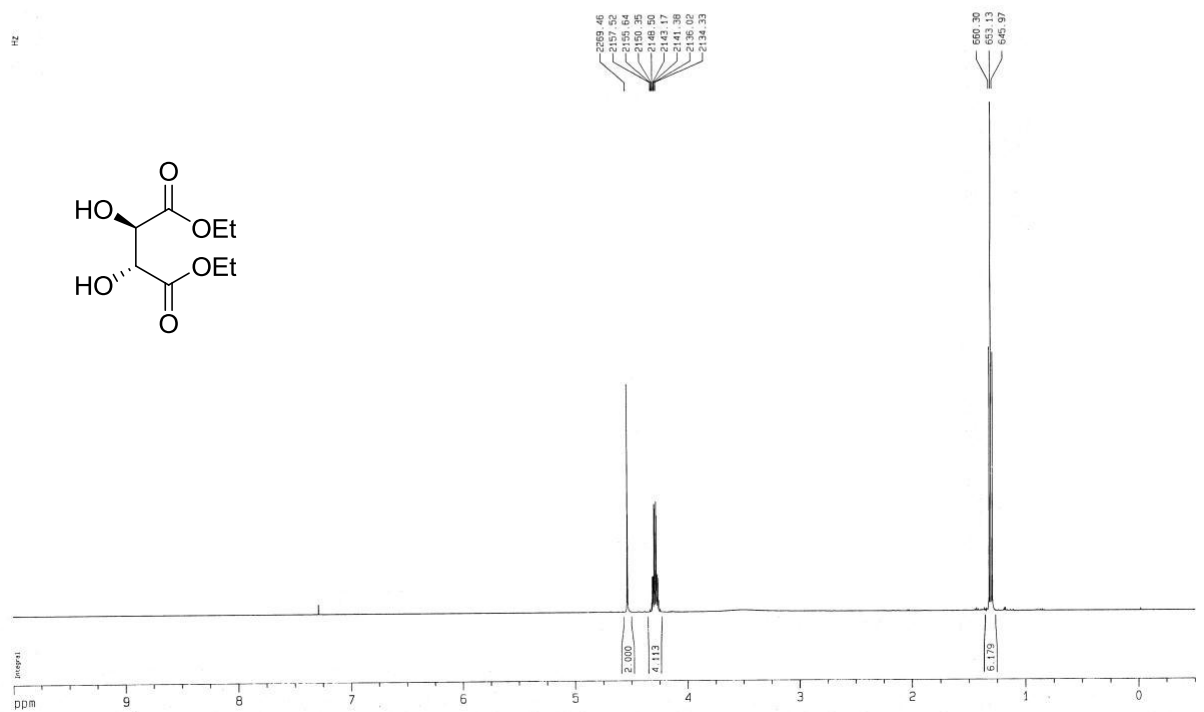
¹H NMR Spectrum of **3** (500 MHz, CDCl₃)



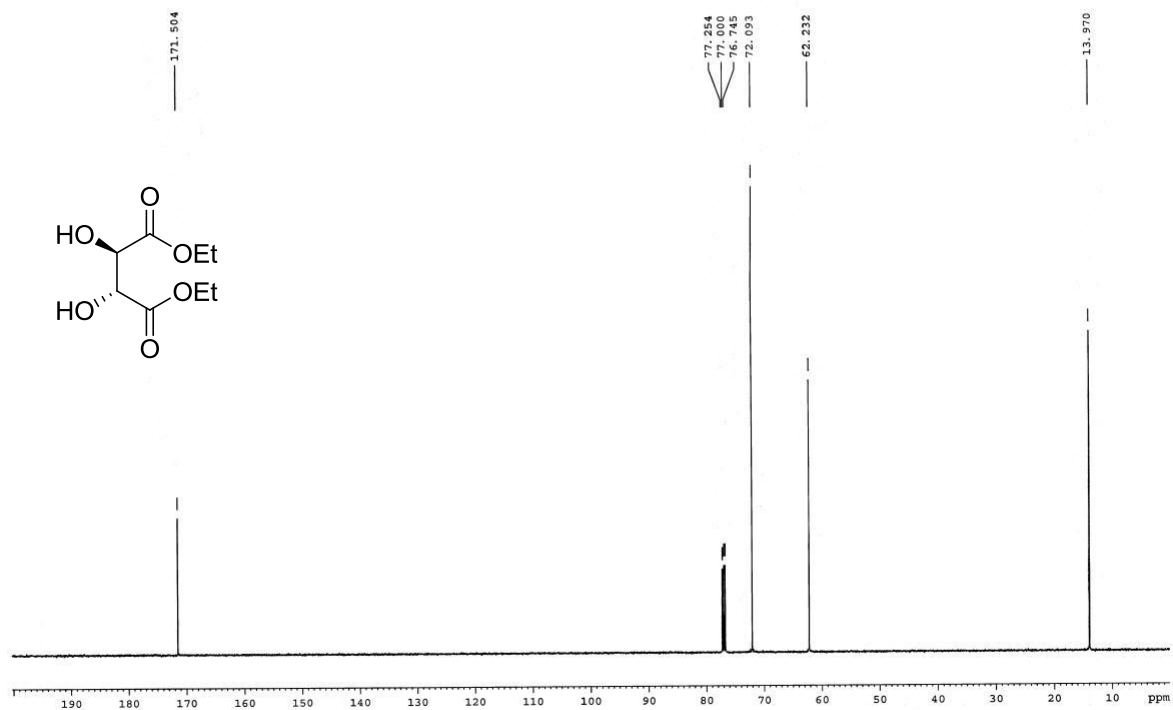
¹H NMR Spectrum of **3** (125 MHz, CDCl₃)



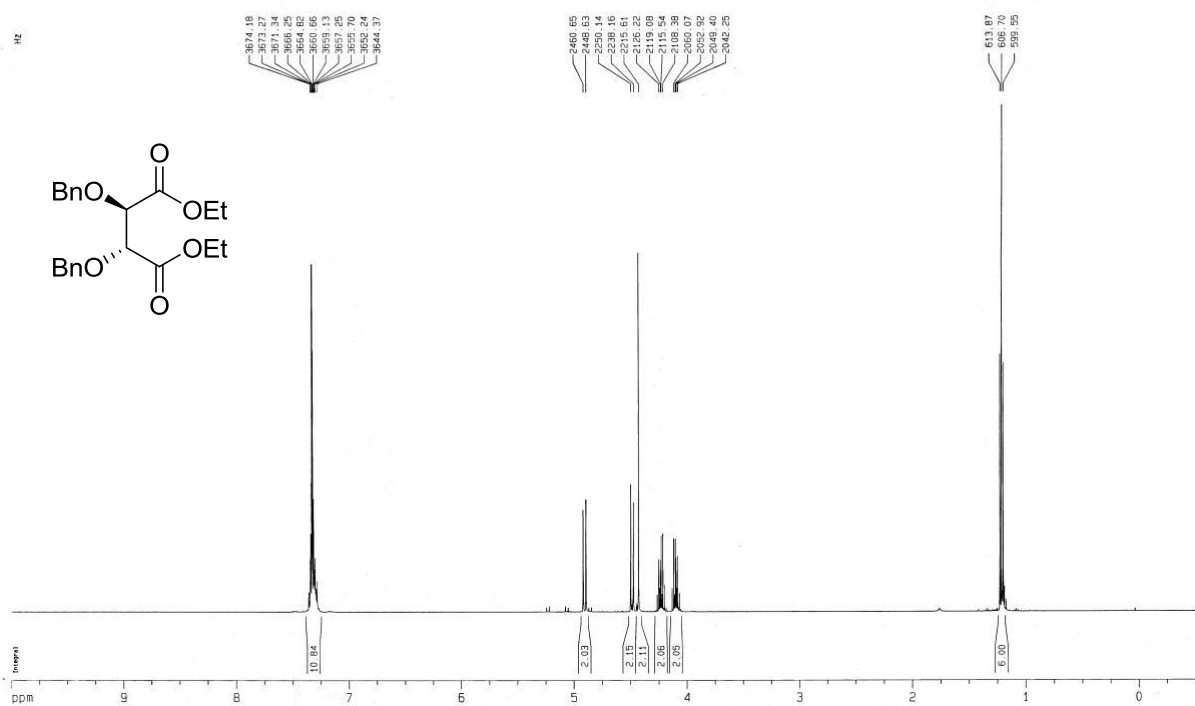
^1H NMR Spectrum of (2*R*,3*R*)-diethyl 2,3-dihydroxysuccinate (500 MHz, CDCl_3)



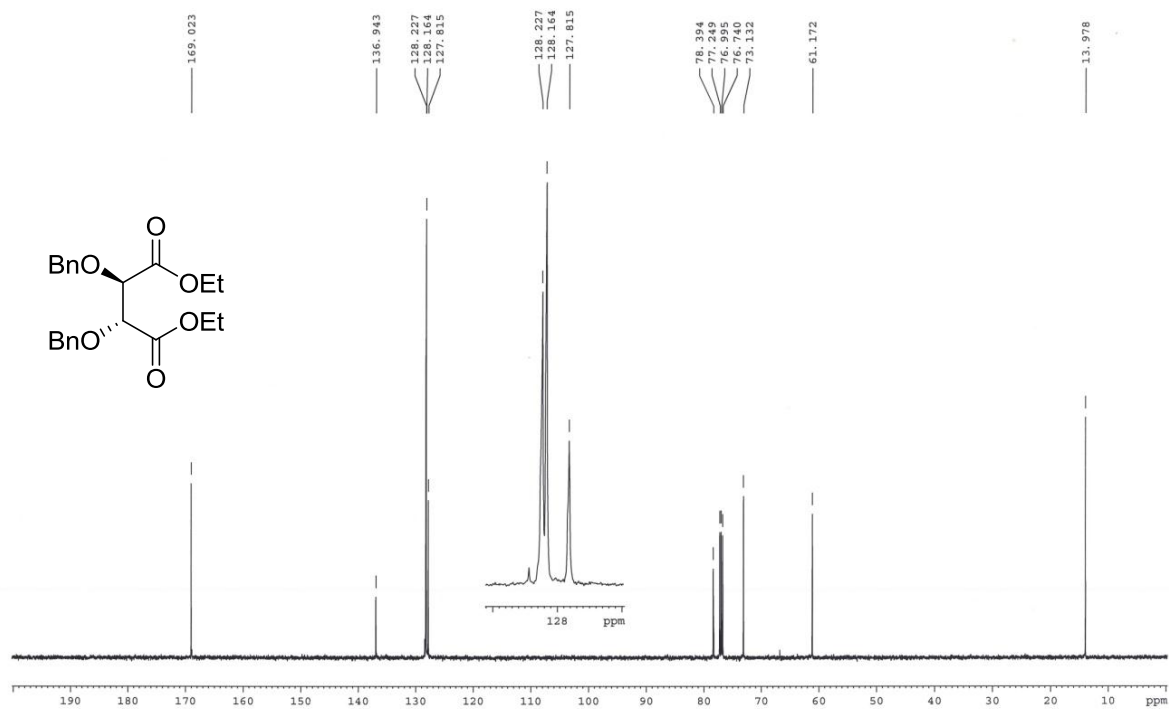
^{13}C NMR Spectrum of (2*R*,3*R*)-diethyl 2,3-dihydroxysuccinate (125 MHz, CDCl_3)



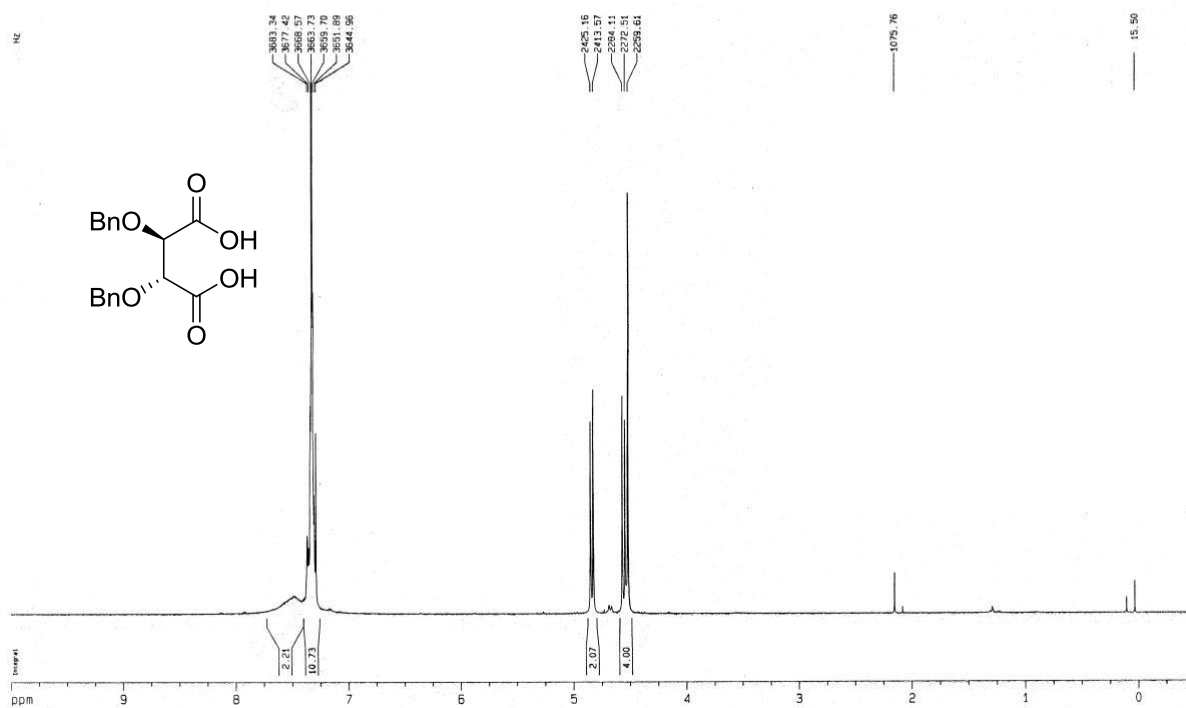
¹H NMR Spectrum of (2*R*,3*R*)-diethyl 2,3-bis(benzyloxy)succinate (500 MHz, CDCl₃)



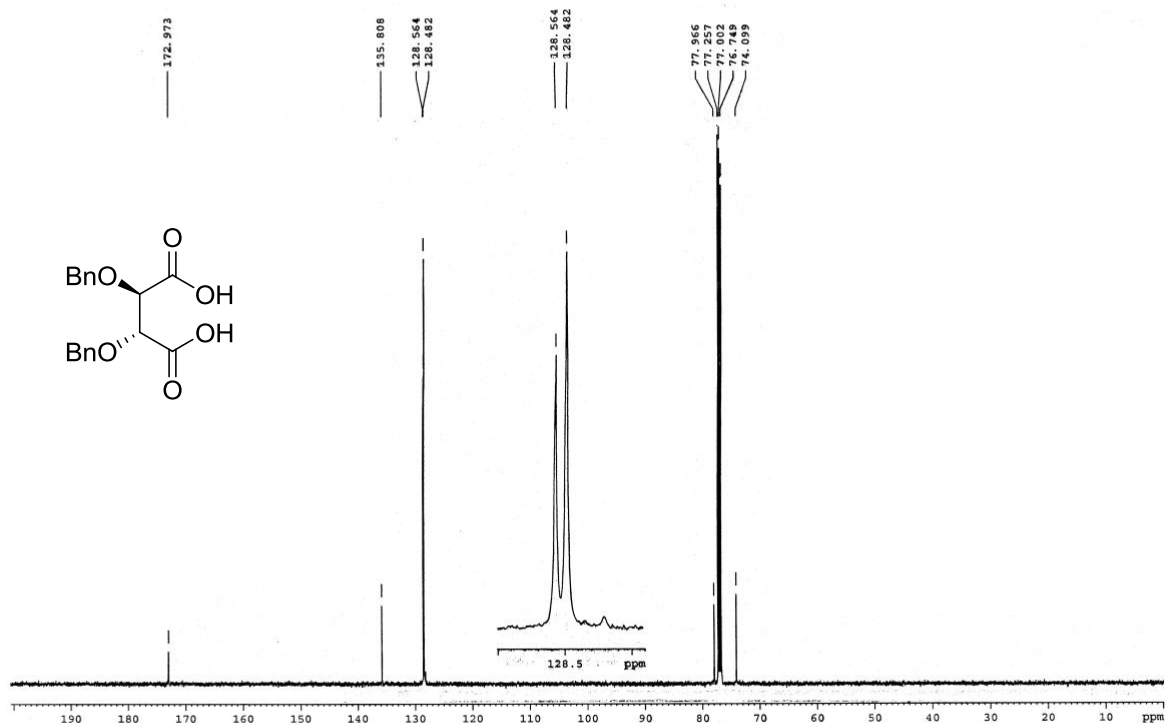
¹³C NMR Spectrum of (2*R*,3*R*)-diethyl 2,3-bis(benzyloxy)succinate (125 MHz, CDCl₃)



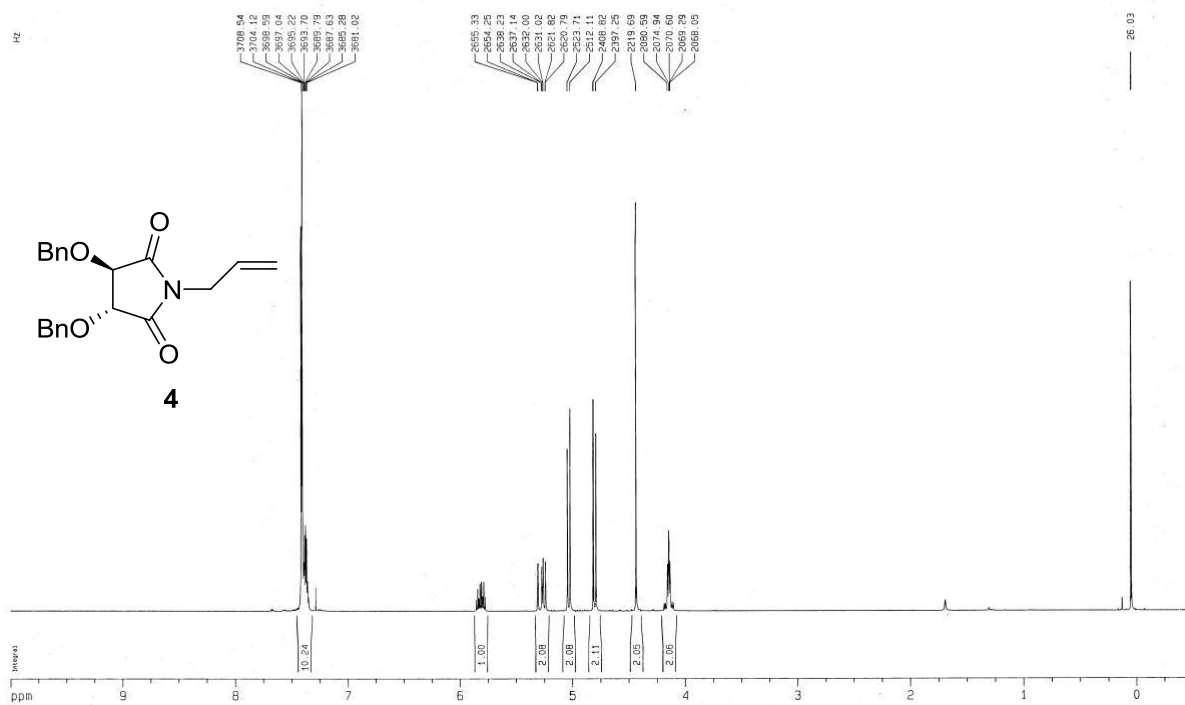
^1H NMR Spectrum of (2*R*,3*R*)-2,3-bis(benzyloxy)succinic acid (500 MHz, CDCl_3)



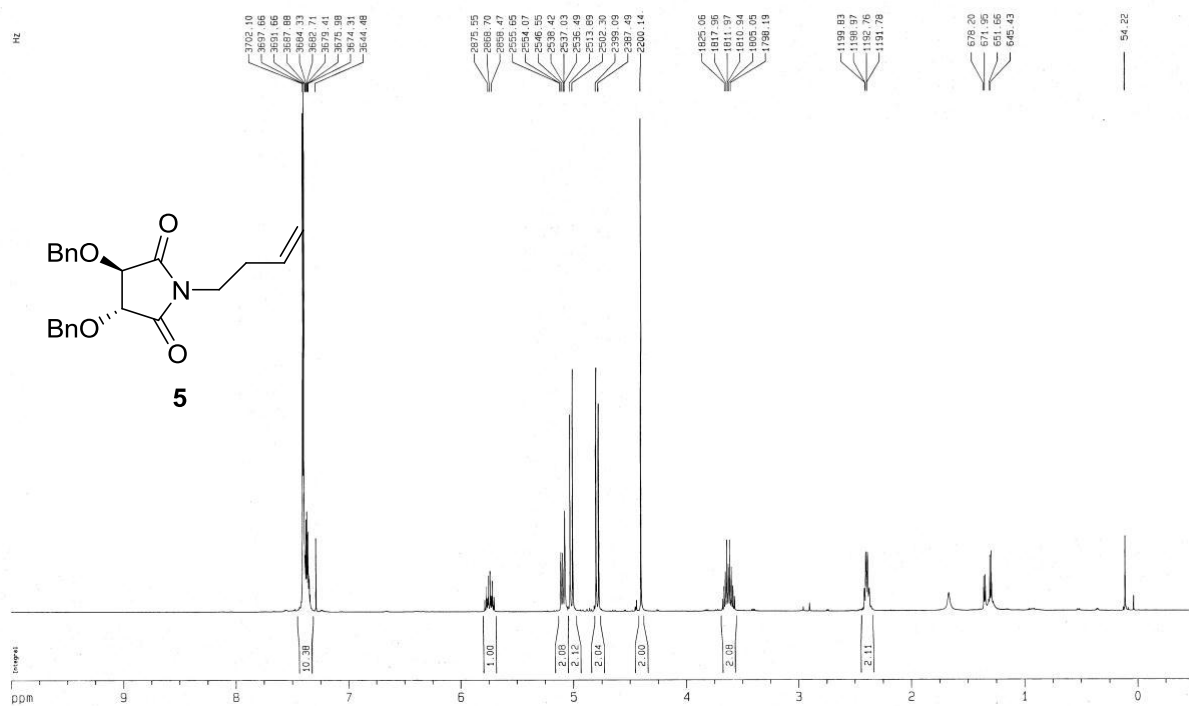
^{13}C NMR Spectrum of (2*R*,3*R*)-2,3-bis(benzyloxy)succinic acid (125 MHz, CDCl_3)



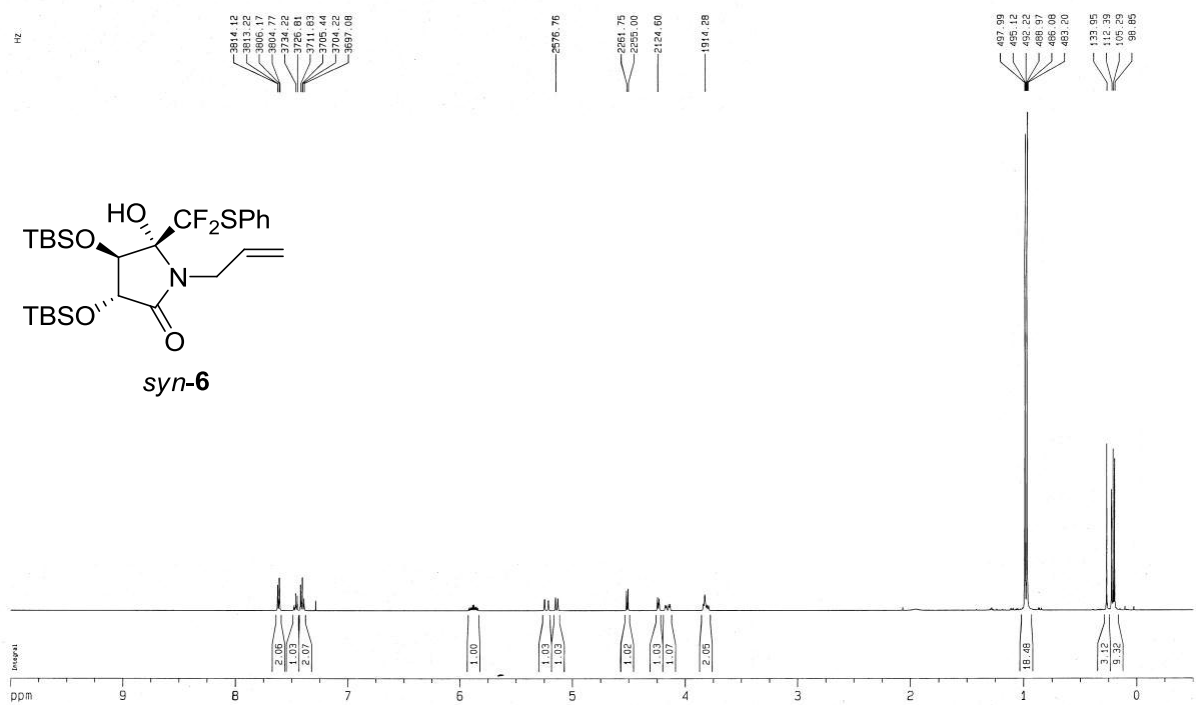
¹H NMR Spectrum of **4** (500 MHz, CDCl₃)



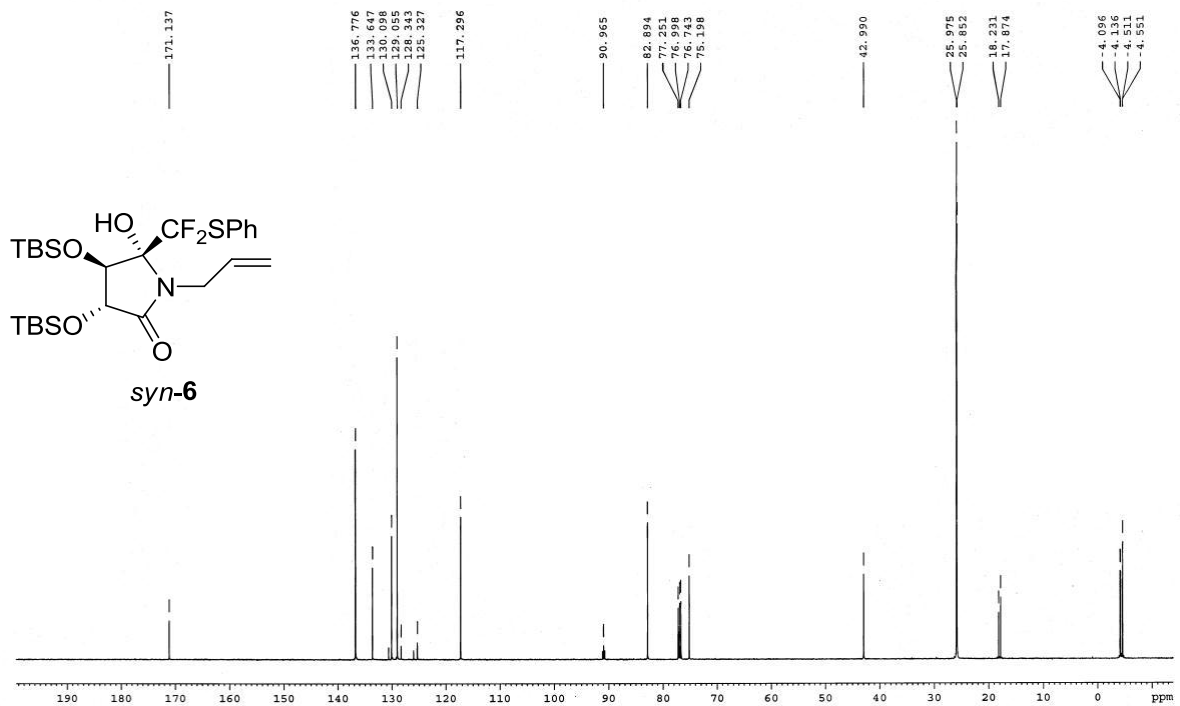
¹H NMR Spectrum of **5** (500 MHz, CDCl₃)



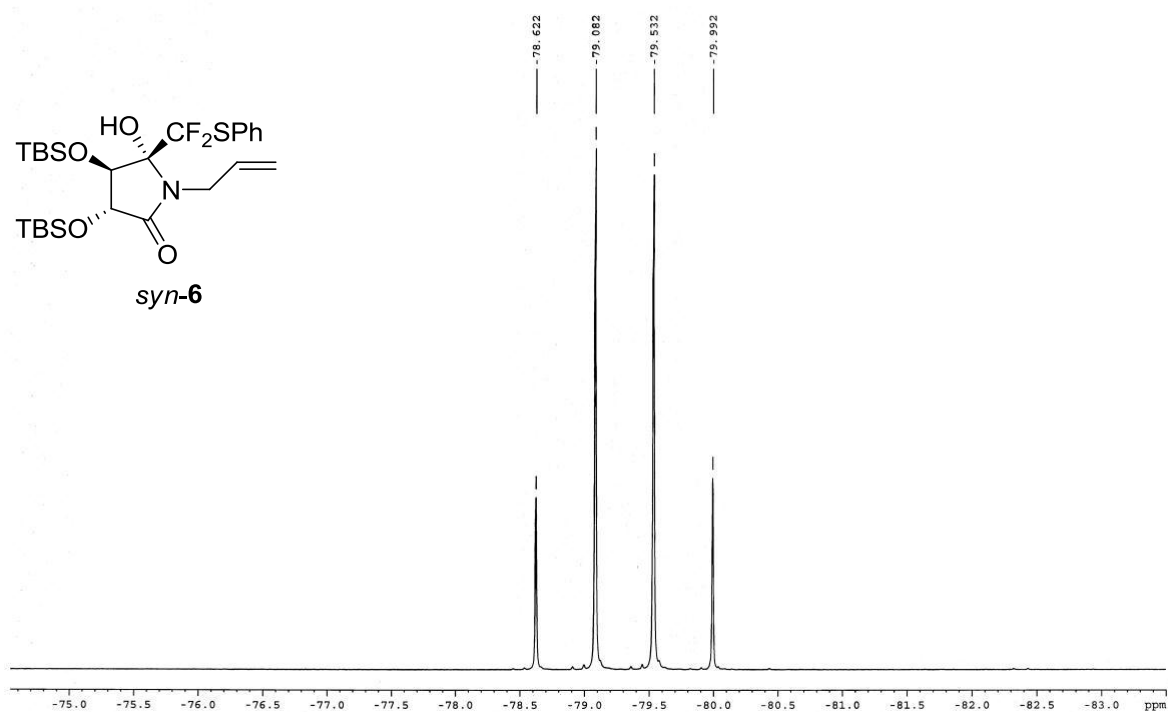
¹H NMR Spectrum of *syn*-**6** (500 MHz, CDCl₃)



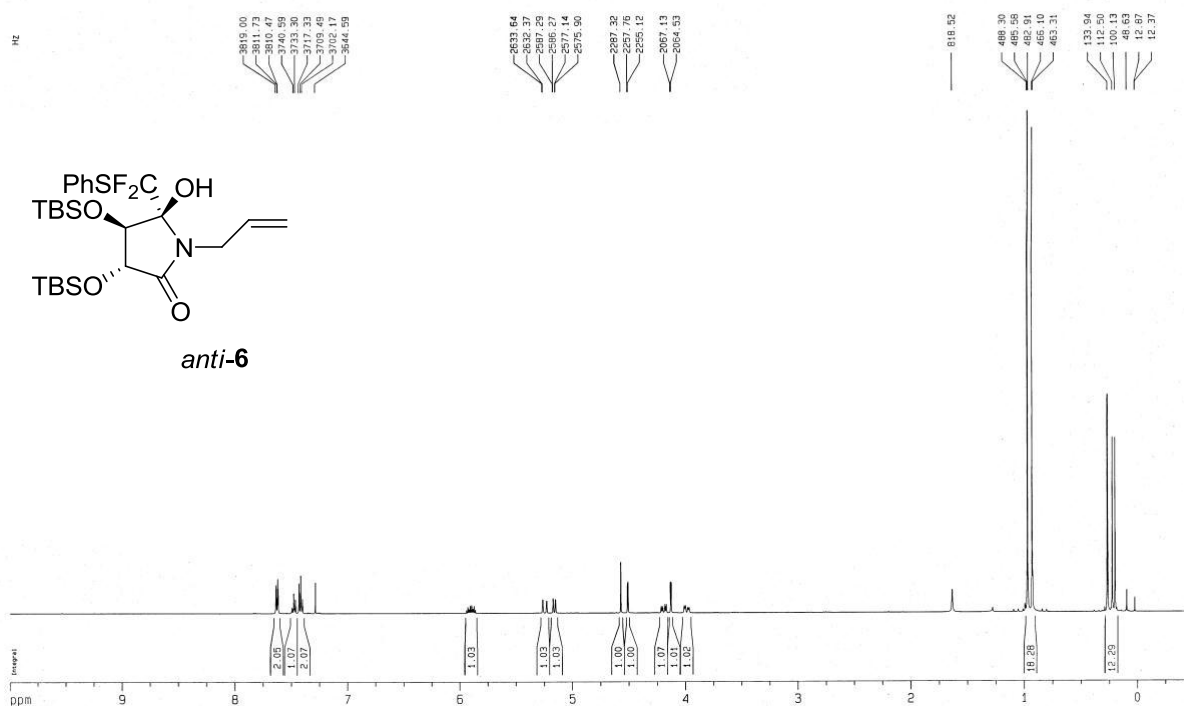
¹³C NMR Spectrum of *syn*-**6** (125 MHz, CDCl₃)



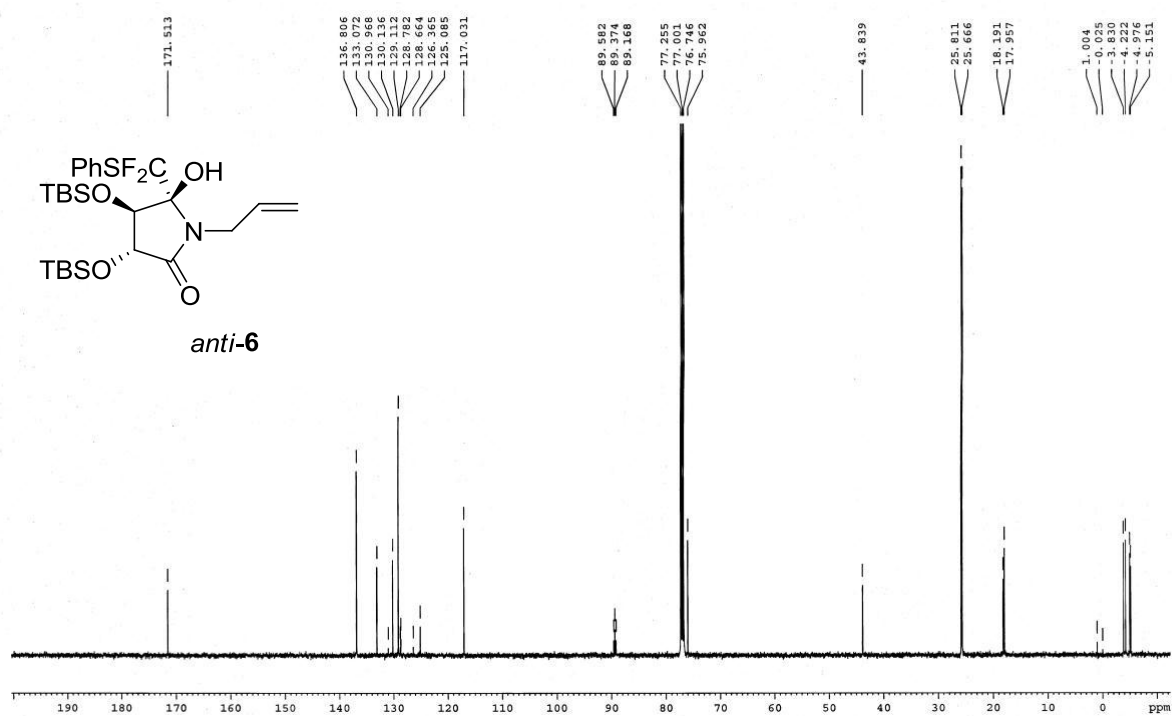
^{19}F NMR Spectrum of *syn*-**6** (470 MHz, CDCl_3)



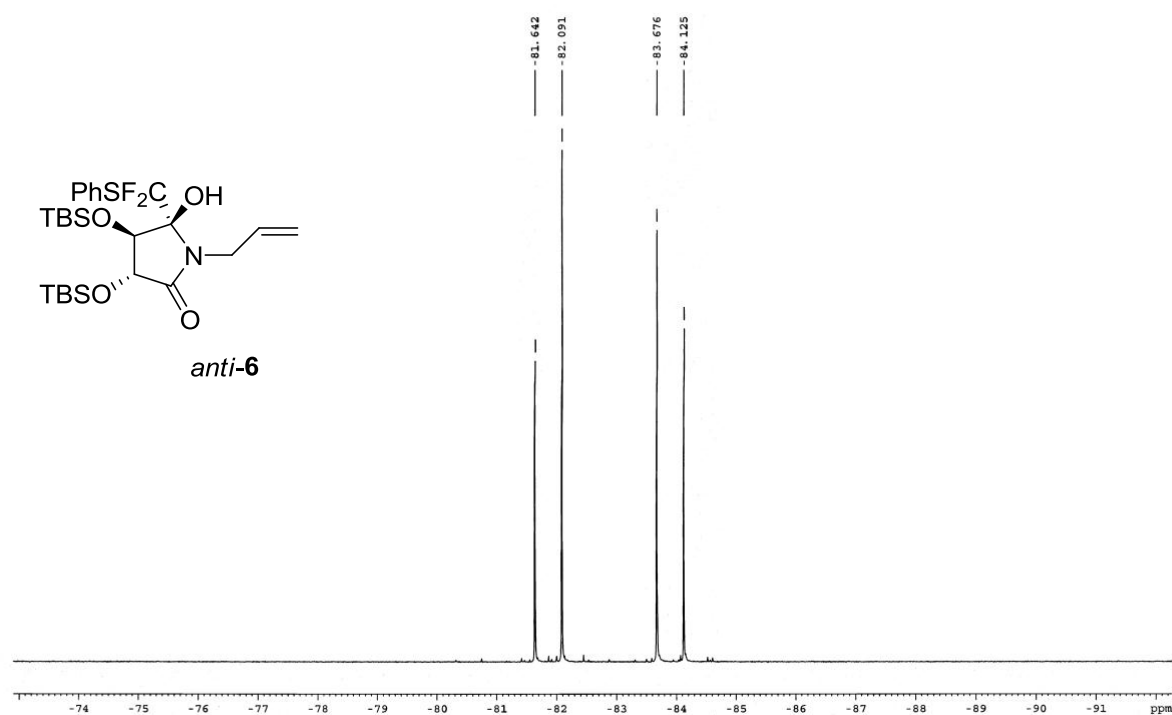
^1H NMR Spectrum of *anti*-**6** (500 MHz, CDCl_3)



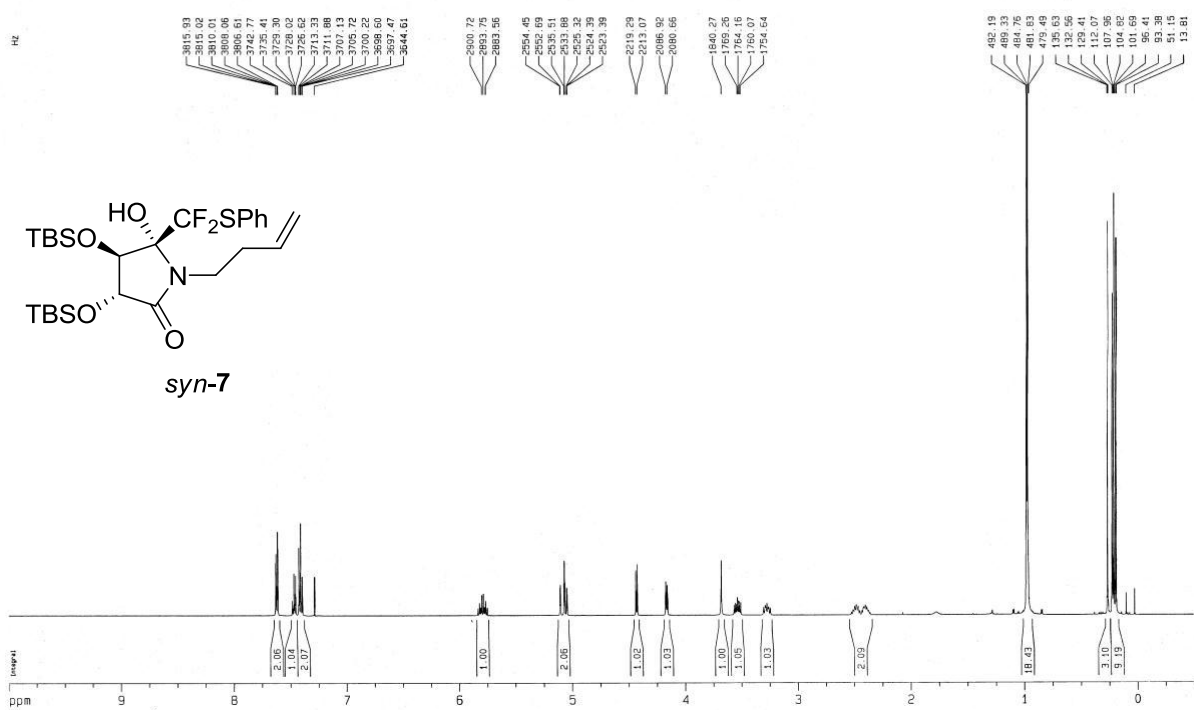
¹³C NMR Spectrum of *anti*-6 (125 MHz, CDCl₃)



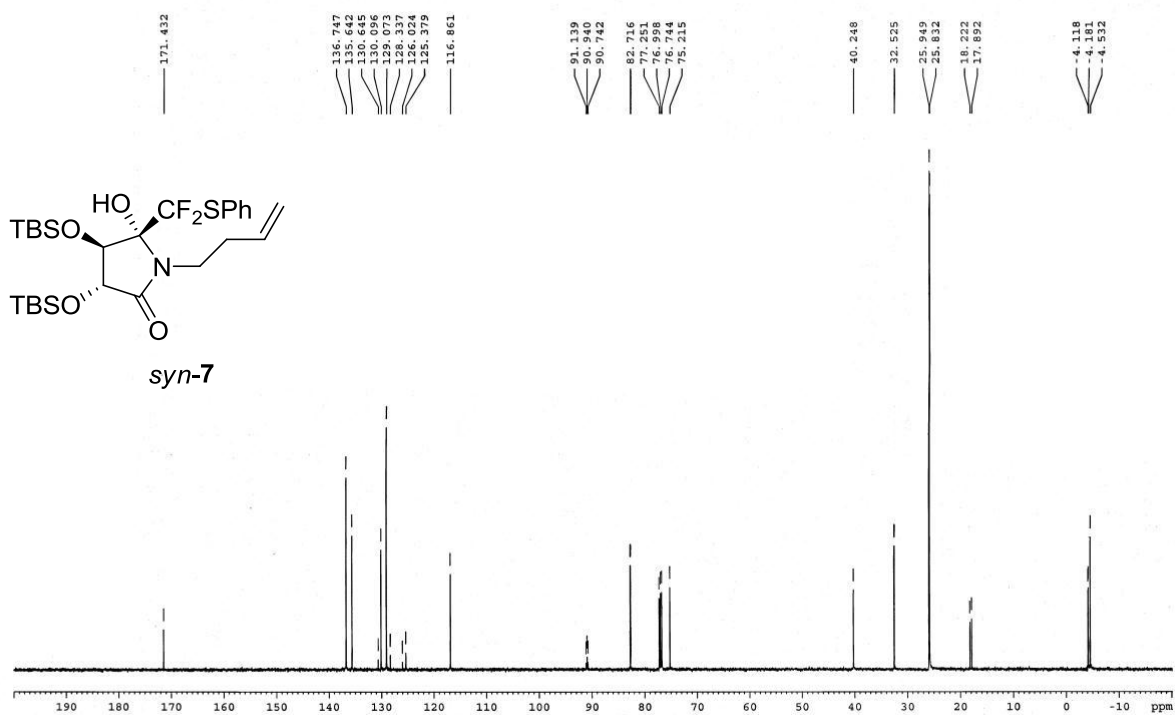
⁹F NMR Spectrum of *anti*-6 (470 MHz, CDCl₃)



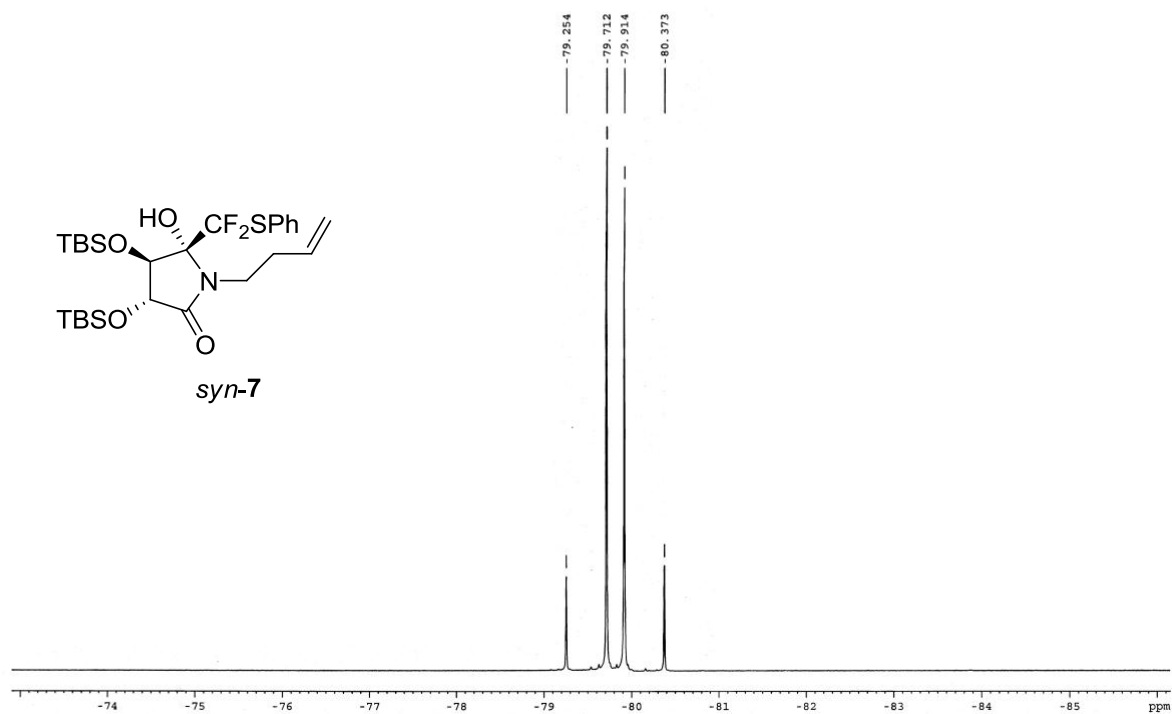
¹H NMR Spectrum of *syn-7* (500 MHz, CDCl₃)



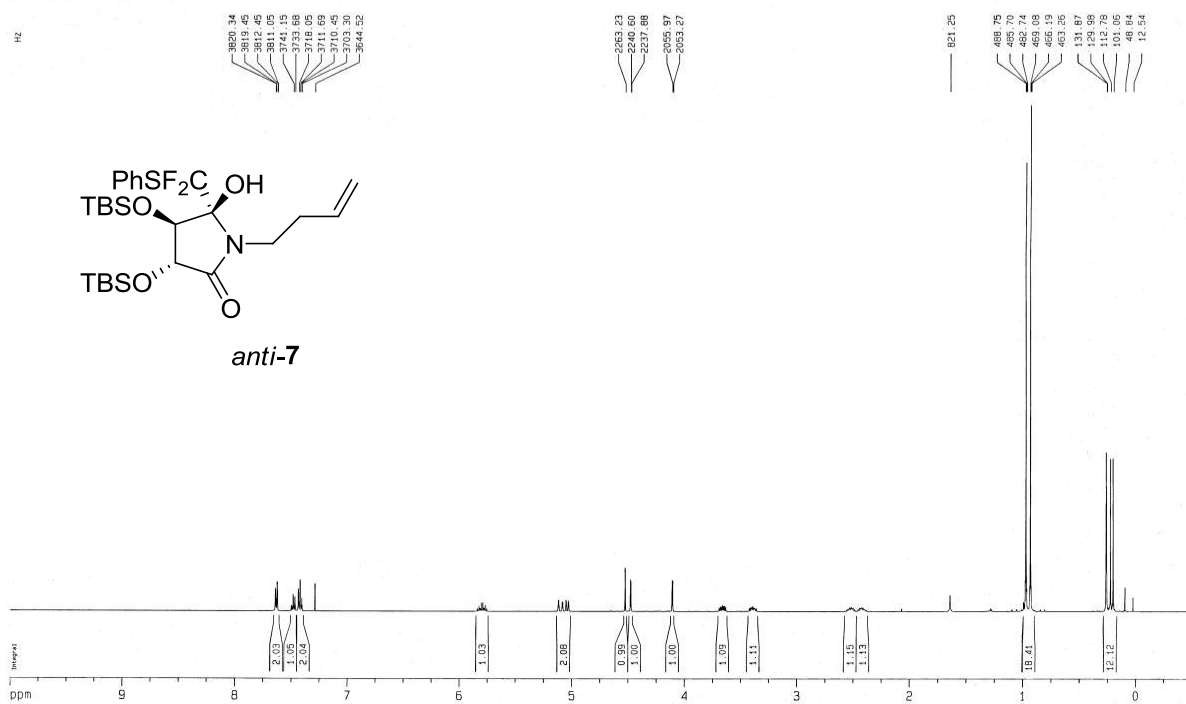
¹³C NMR Spectrum of *syn-7* (125 MHz, CDCl₃)



^{19}F NMR Spectrum of *syn*-7 (470 MHz, CDCl_3)



^1H NMR Spectrum of *anti*-7 (500 MHz, CDCl_3)

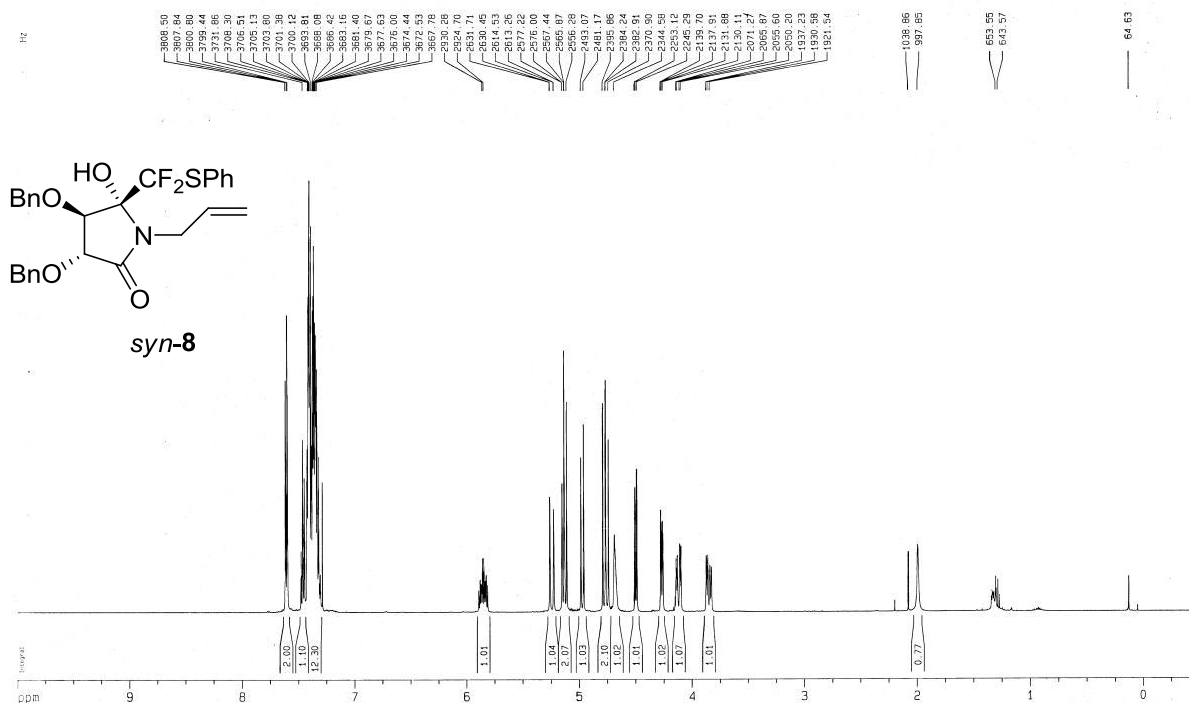


Chemical structure of *anti*-7 is shown above the ¹³C NMR spectrum. The structure is a cyclopentane ring with a ketone, a TBSO group, a PhSF₂C group, and a hydroxyl group, and a 3-butenyl group attached to the nitrogen. The spectrum displays peaks corresponding to the carbons in the molecule, with chemical shifts ranging from approximately -5 to 177 ppm. Key peaks are labeled with their chemical shifts: 177.614, 136.774, 135.385, 130.134, 129.120, 126.484, 125.095, 116.593, 89.646, 89.440, 89.233, 77.255, 77.000, 76.800, 76.713, 75.876, 40.953, 32.388, 25.820, 25.663, 18.203, 17.599, 0.999, 0.826, 4.223, 4.924, and -5.151.

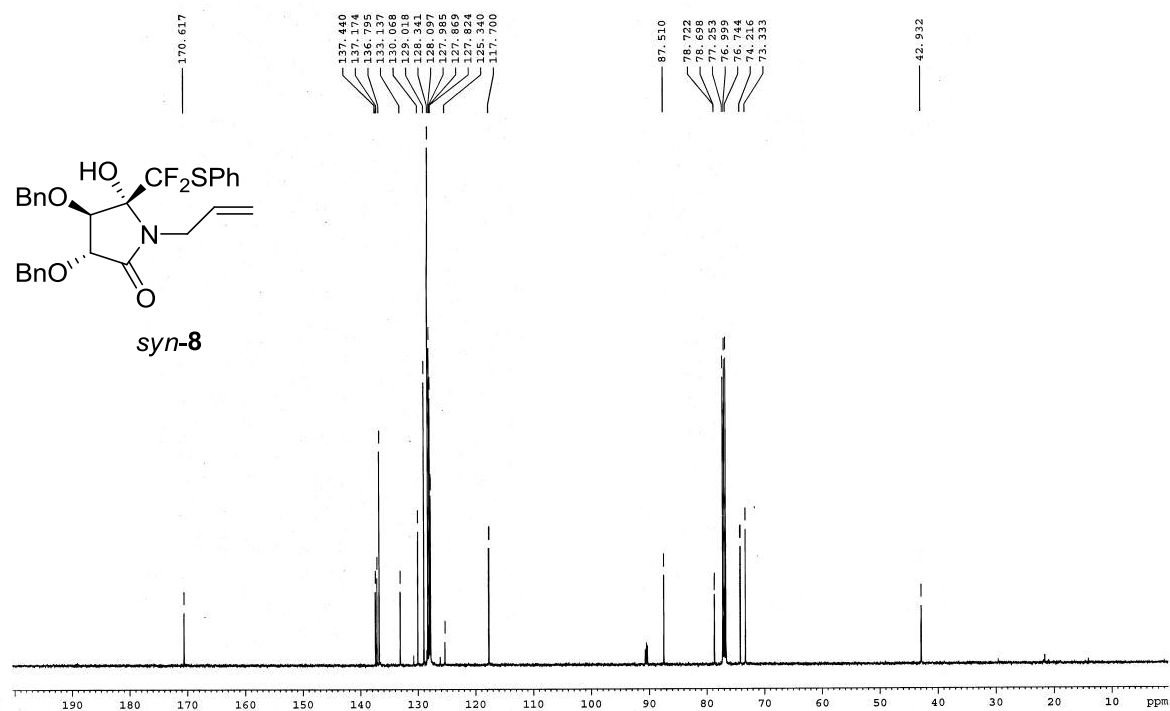
Chemical structure of *anti*-7 is shown, featuring a five-membered ring with a carbonyl group, a hydroxyl group, and two TBSO groups. The structure is labeled *anti*-7.

¹H NMR spectrum (CDCl₃) of *anti*-7. The spectrum shows four main peaks in the aliphatic region, corresponding to the protons of the five-membered ring. The peaks are labeled with their chemical shifts: 81.565, 82.114, 83.730, and 84.179 ppm.

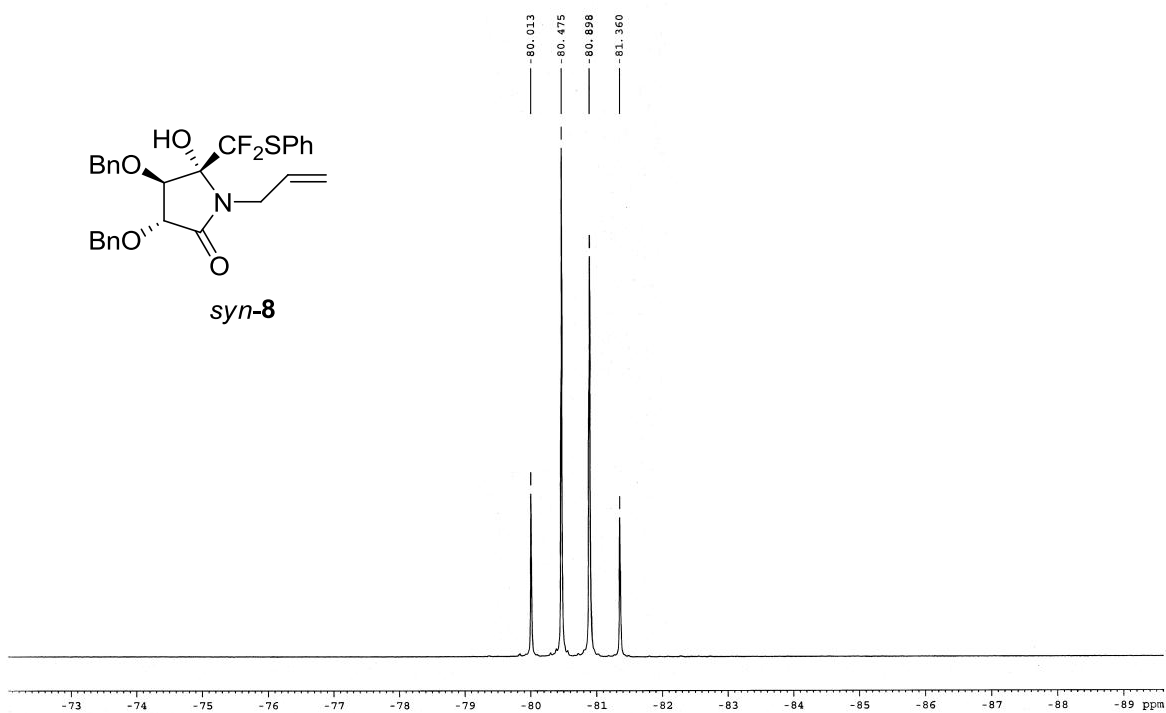
¹H NMR Spectrum of *syn*-**8** (500 MHz, CDCl₃)



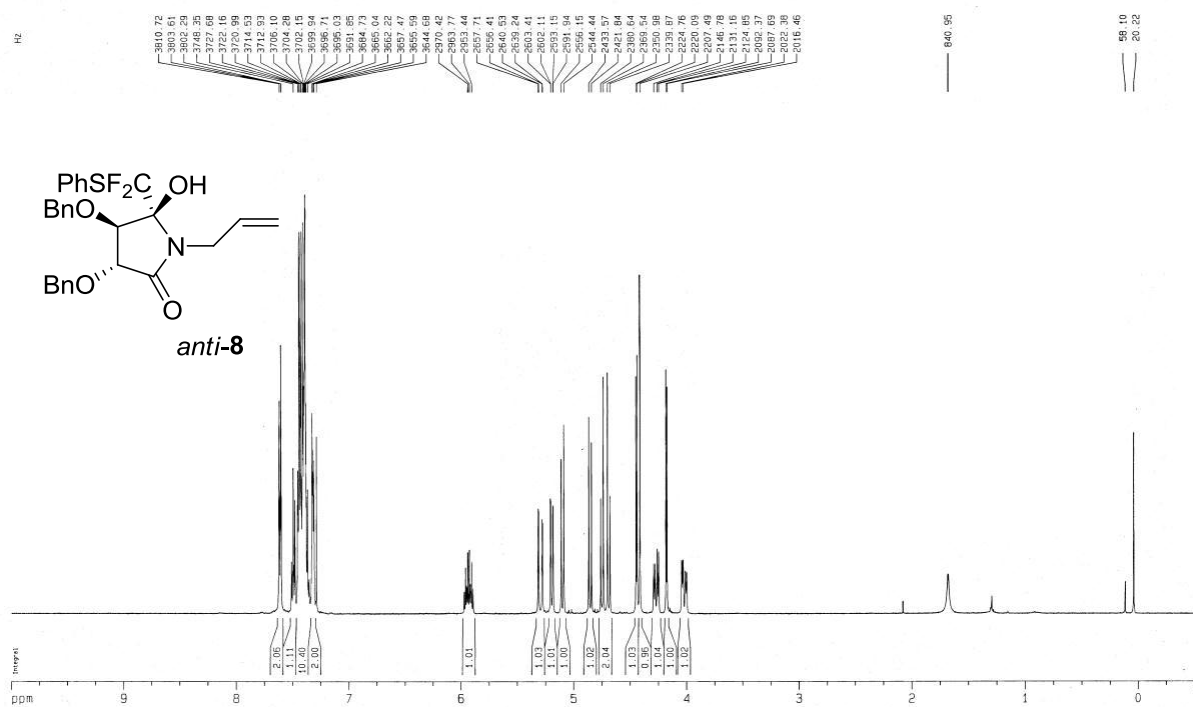
¹³C NMR Spectrum of *syn*-**8** (125 MHz, CDCl₃)



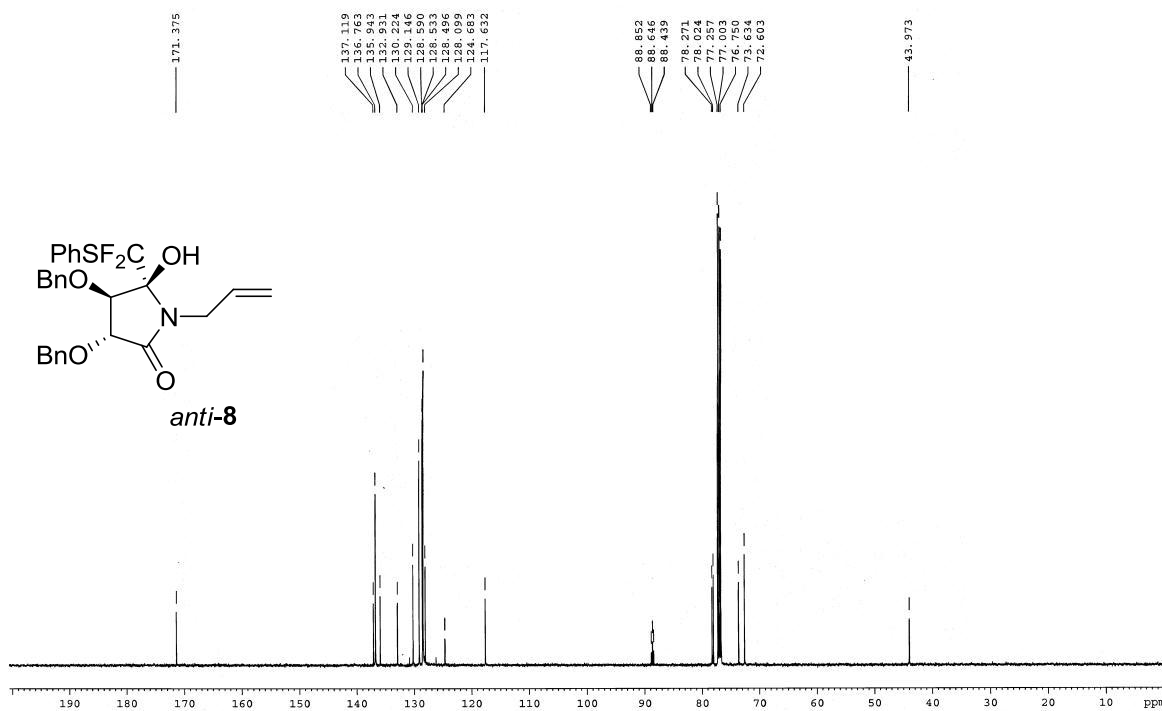
^{19}F NMR Spectrum of *syn*-**8** (470 MHz, CDCl_3)



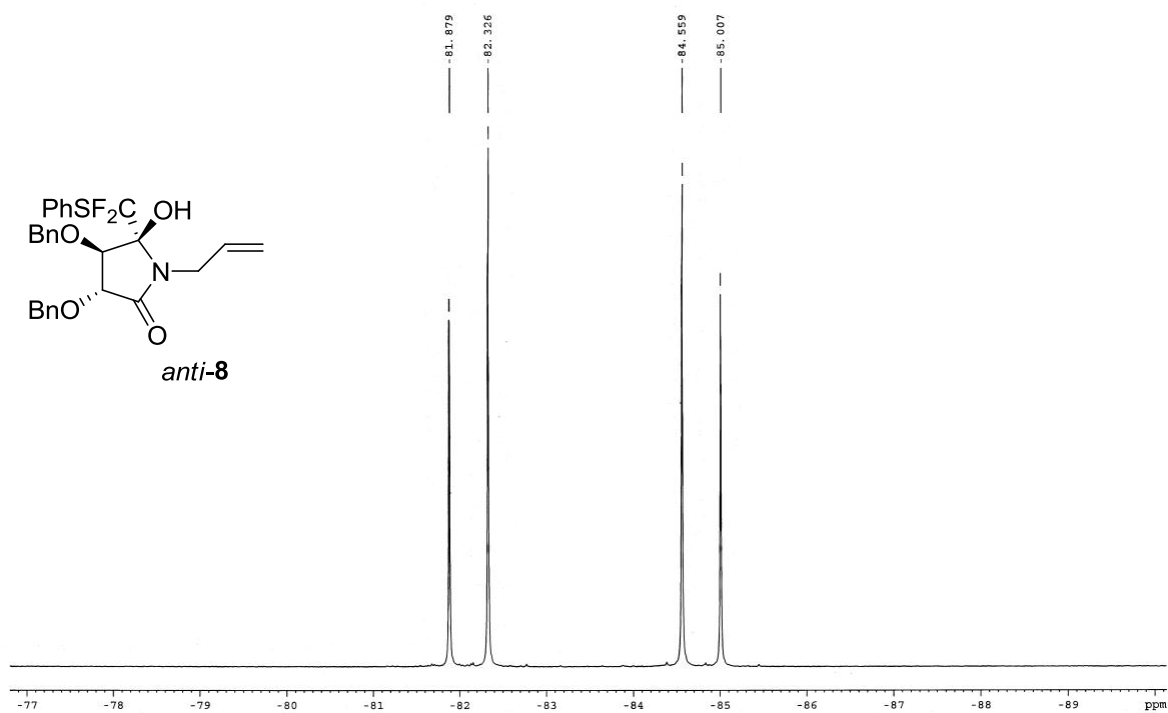
^1H NMR Spectrum of *anti*-**8** (500 MHz, CDCl_3)



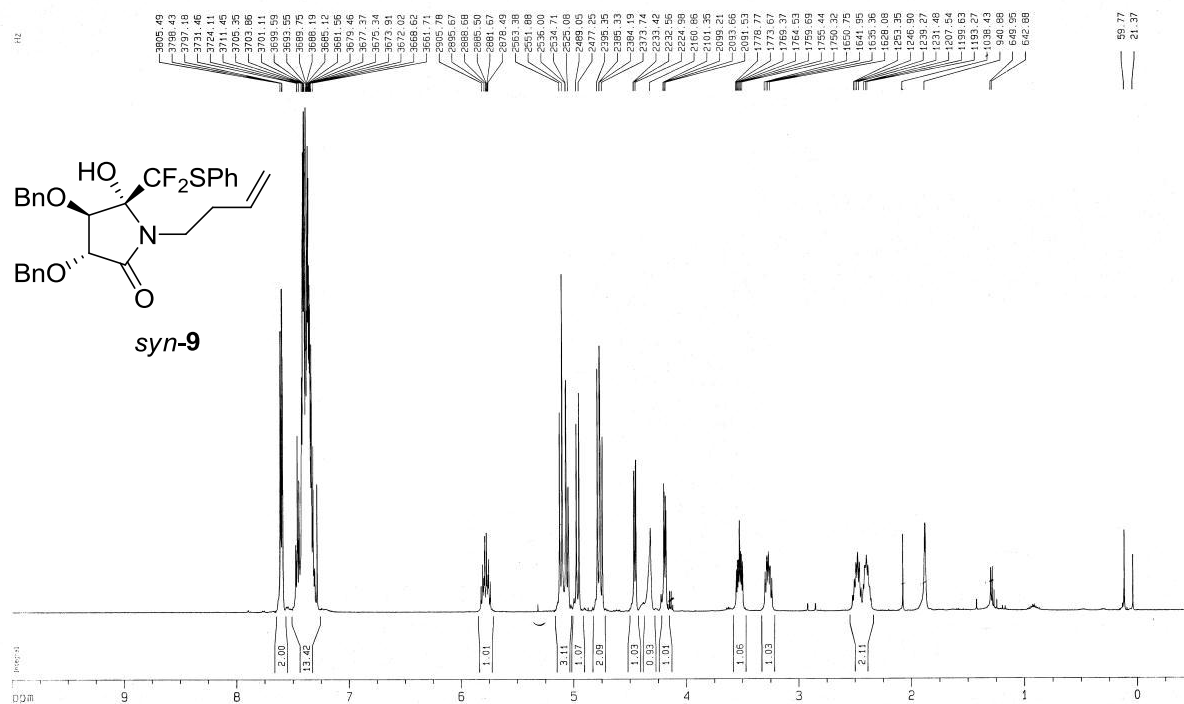
¹³C NMR Spectrum of *anti*-**8** (125 MHz, CDCl₃)



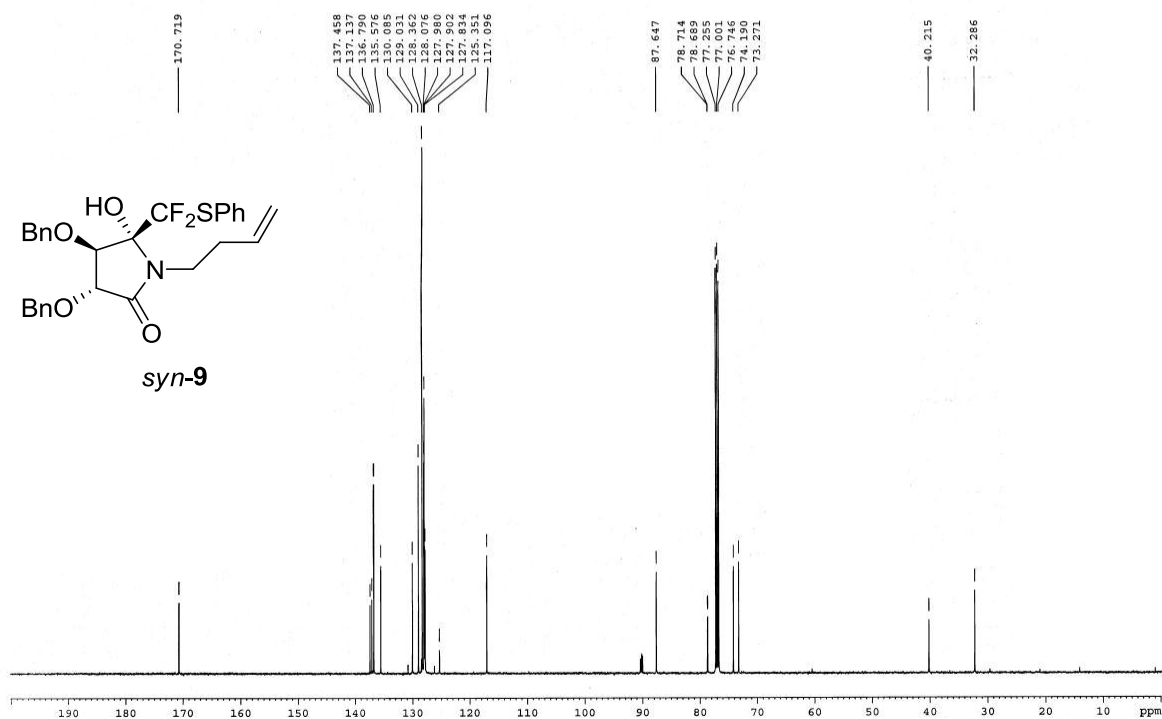
¹⁹F NMR Spectrum of *anti*-**8** (470 MHz, CDCl₃)



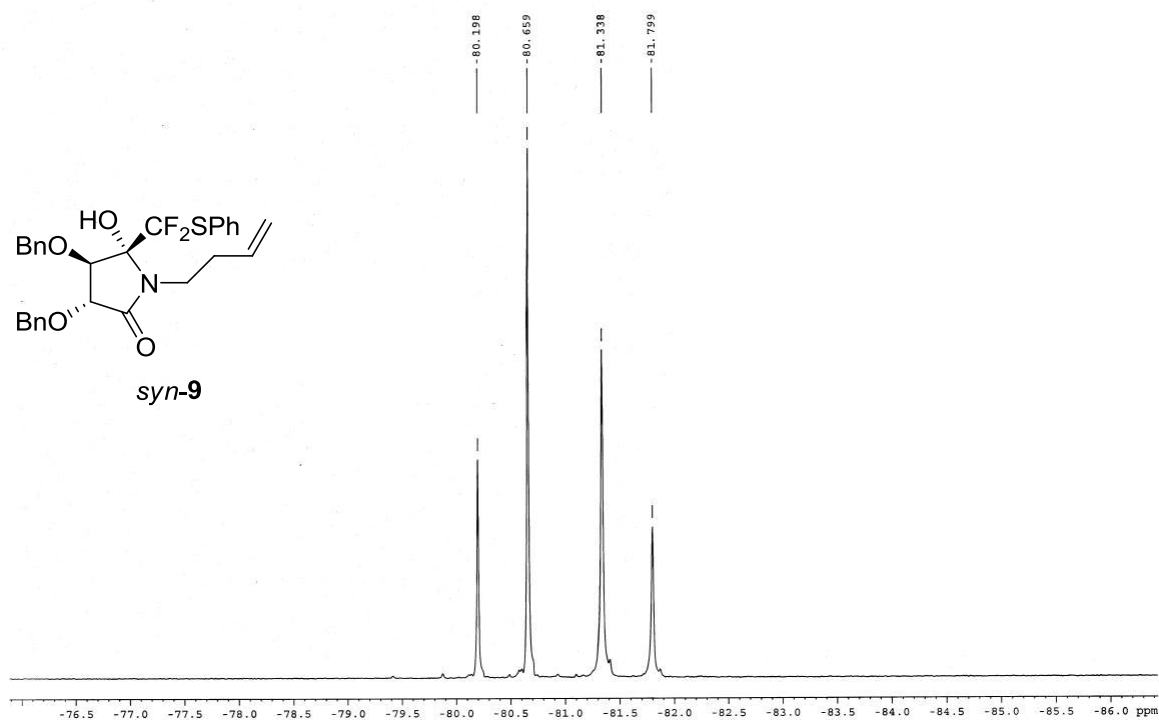
^1H NMR Spectrum of *syn-9* (500 MHz, CDCl_3)



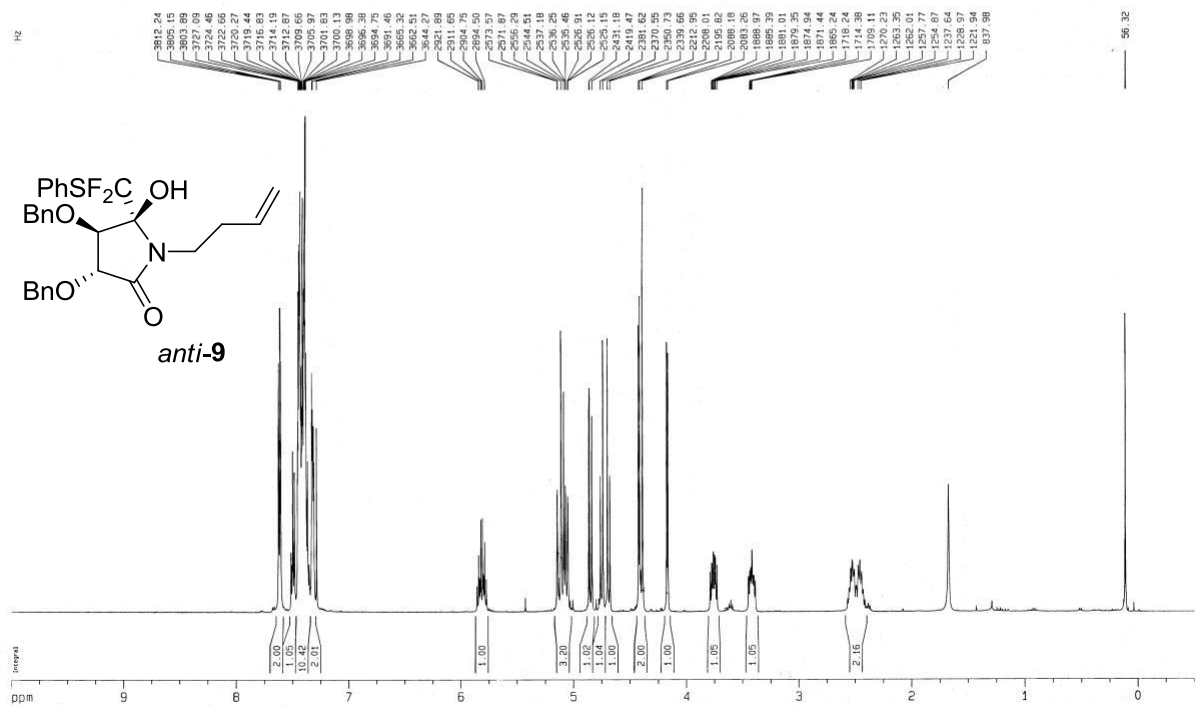
^{13}C NMR Spectrum of *syn-9* (125 MHz, CDCl_3)



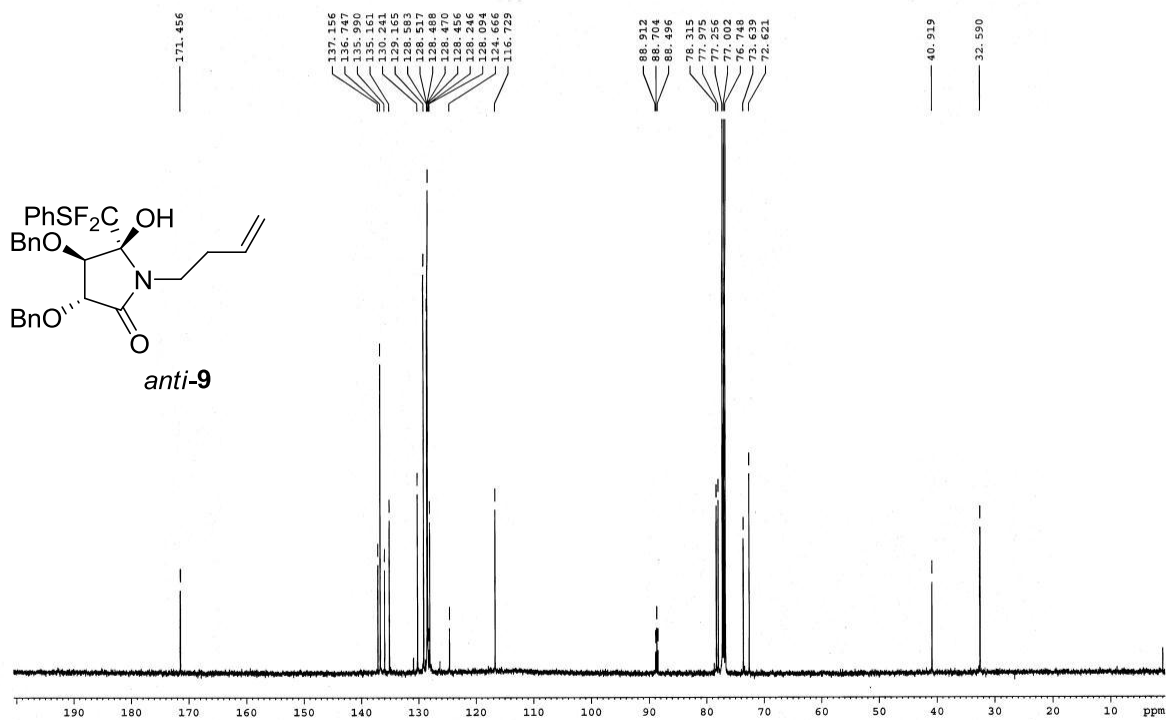
^{19}F NMR Spectrum of *syn*-**9** (470 MHz, CDCl_3)



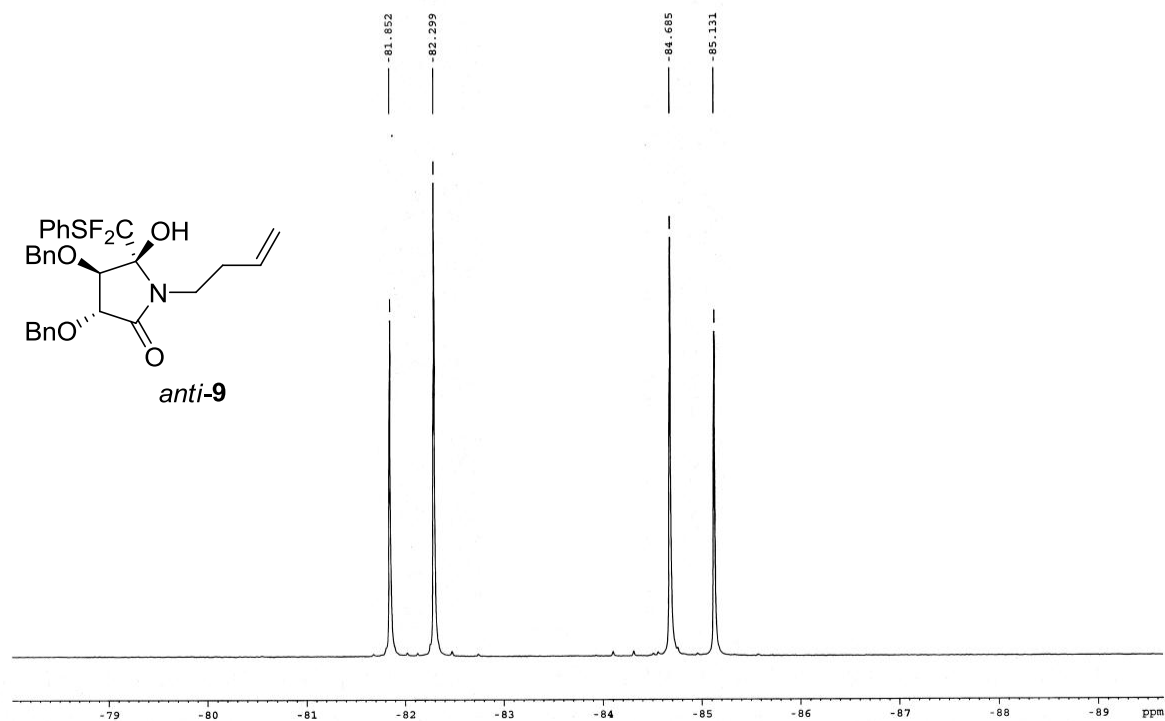
^1H NMR Spectrum of *anti*-**9** (500 MHz, CDCl_3)



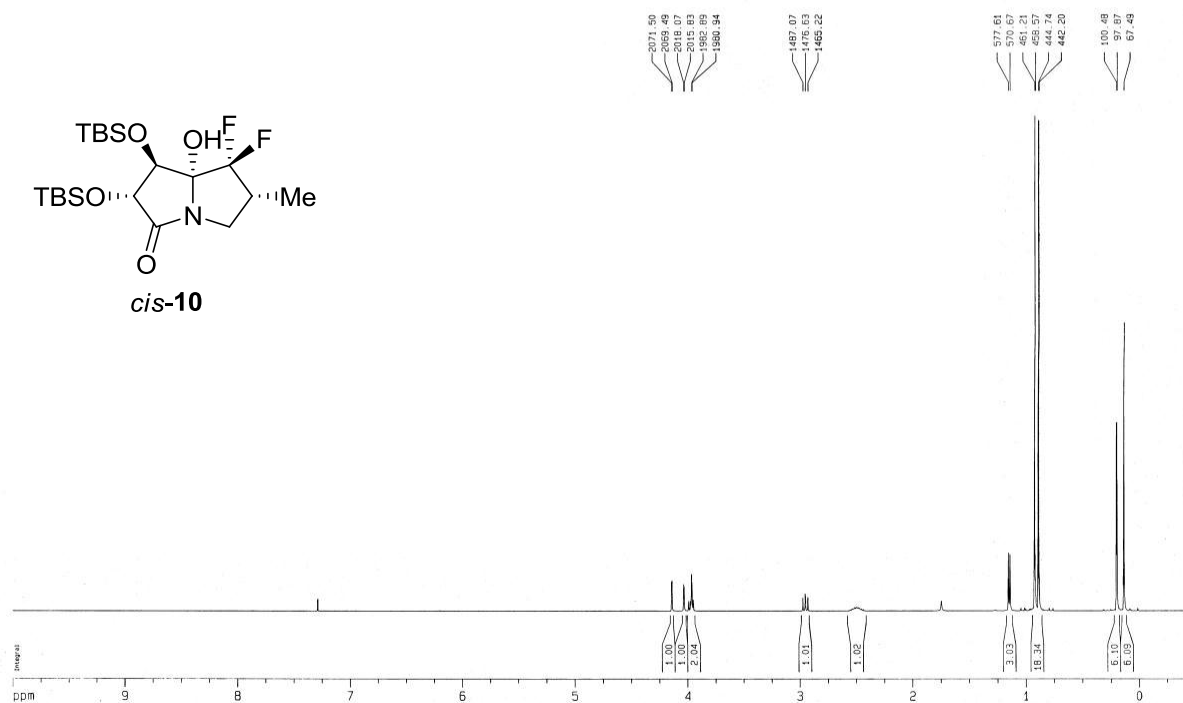
^{13}C NMR Spectrum of *anti*-**9** (125 MHz, CDCl_3)



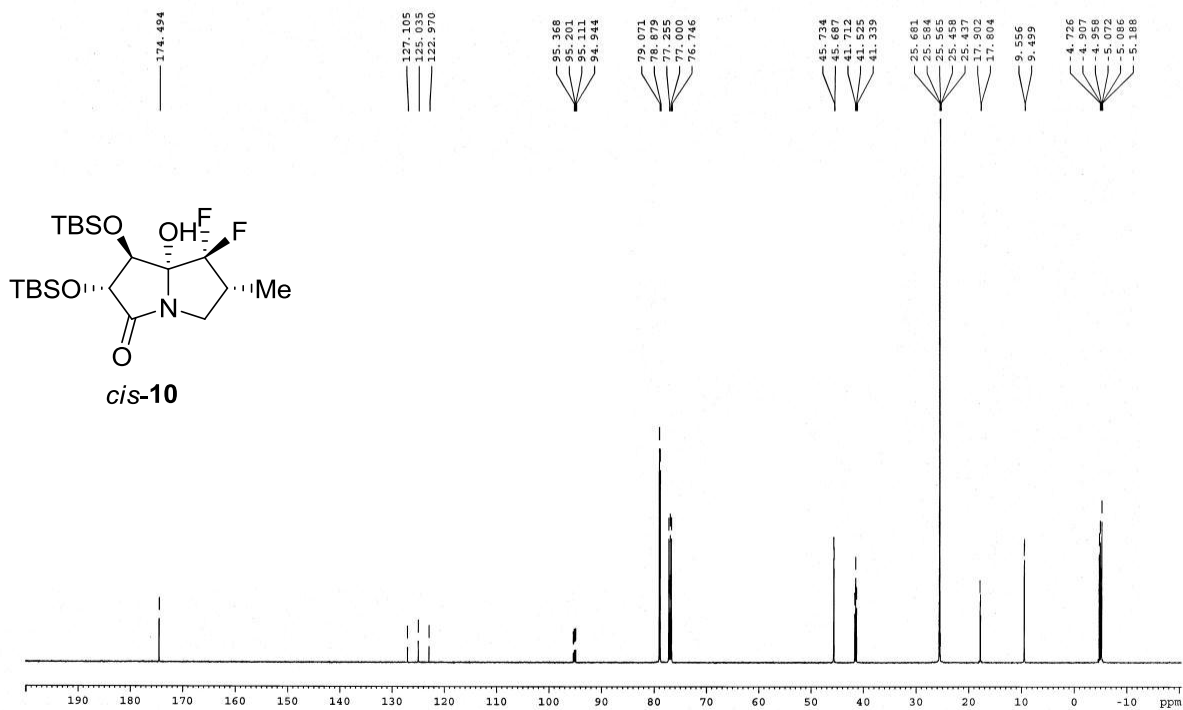
^{19}F NMR Spectrum of *anti*-**9** (470 MHz, CDCl_3)



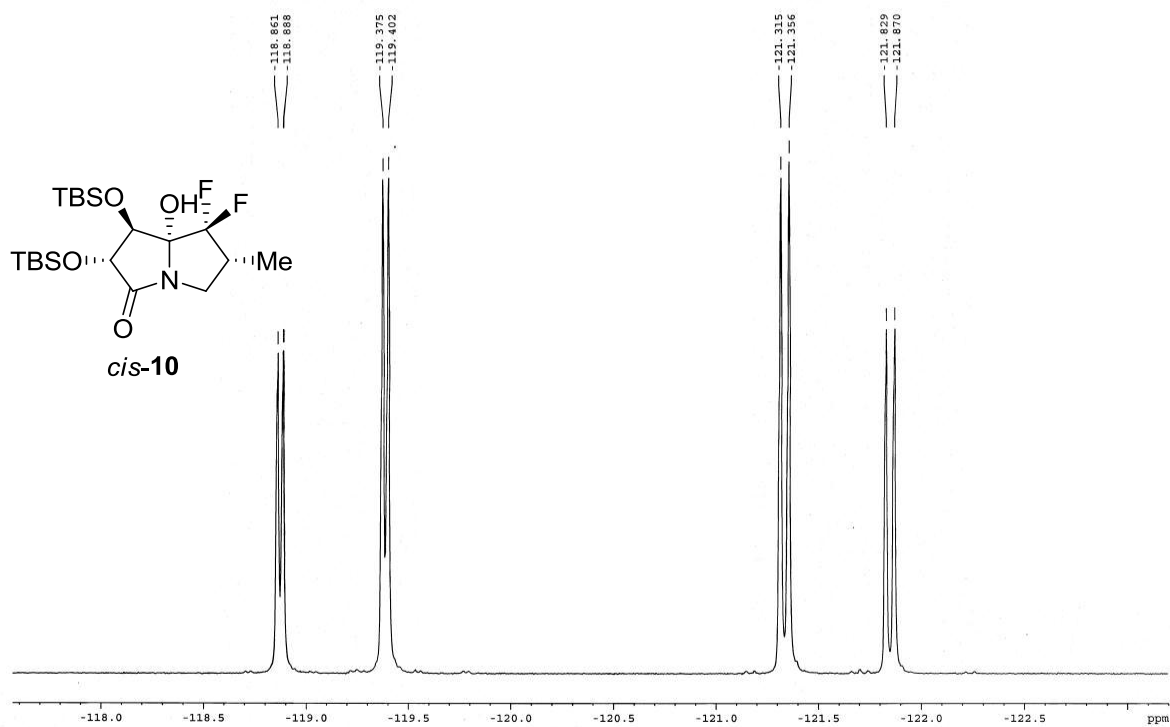
¹H NMR Spectrum of *cis*-**10** (500 MHz, CDCl₃)



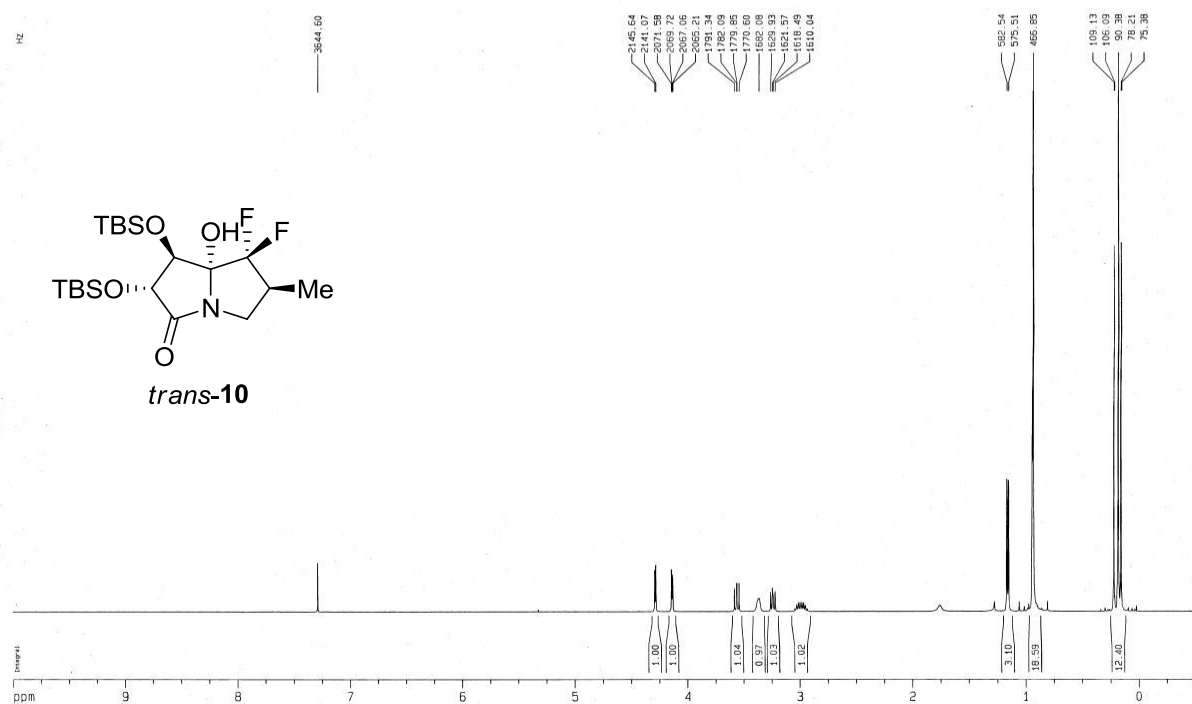
¹³C NMR Spectrum of *cis*-**10** (125 MHz, CDCl₃)



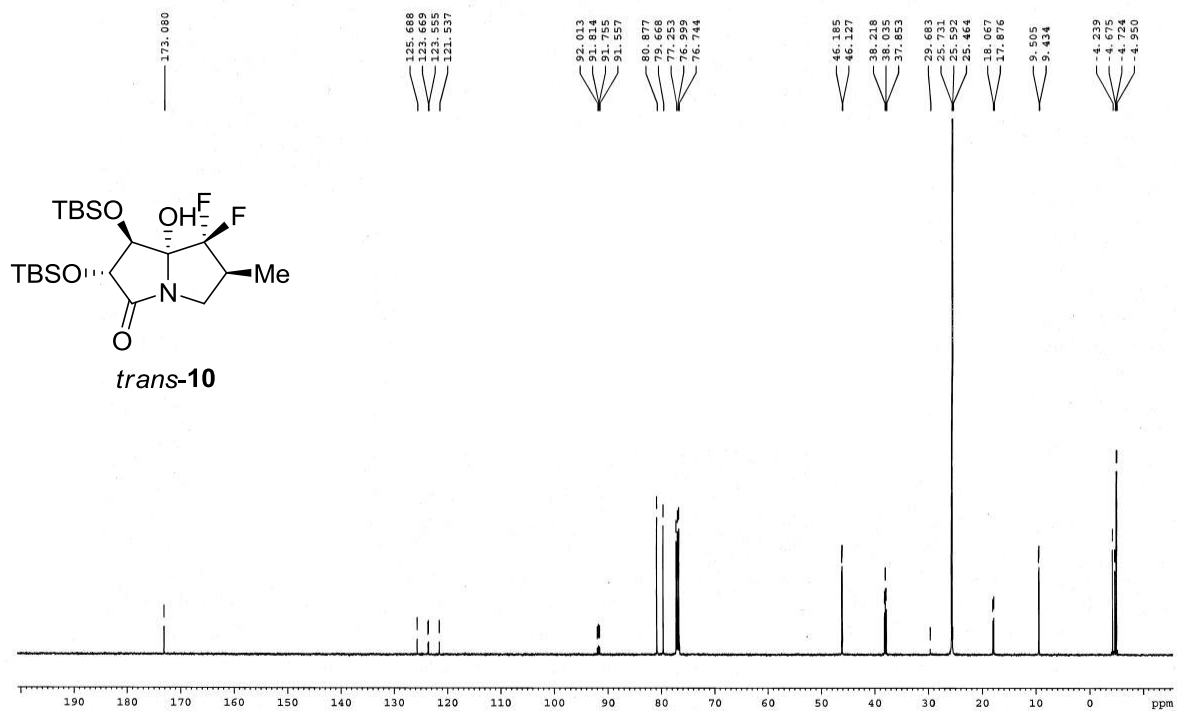
^{19}F NMR Spectrum of *cis*-**10** (470 MHz, CDCl_3)



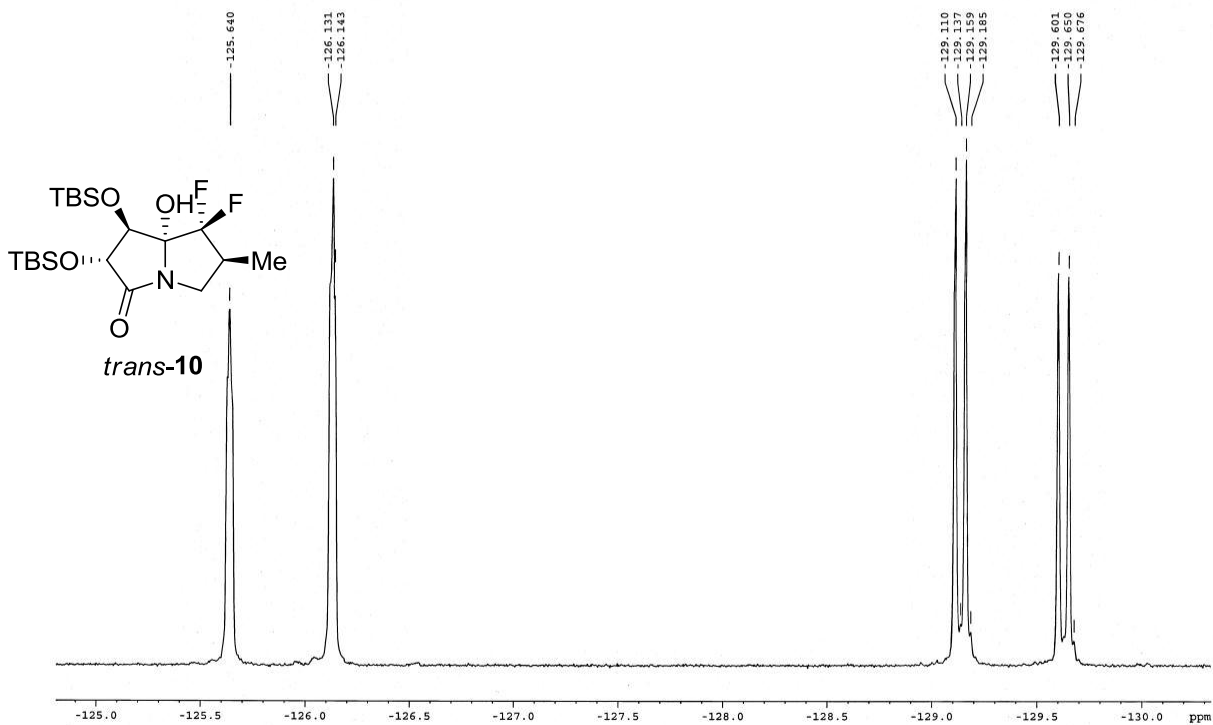
^1H NMR Spectrum of *trans*-**10** (500 MHz, CDCl_3)



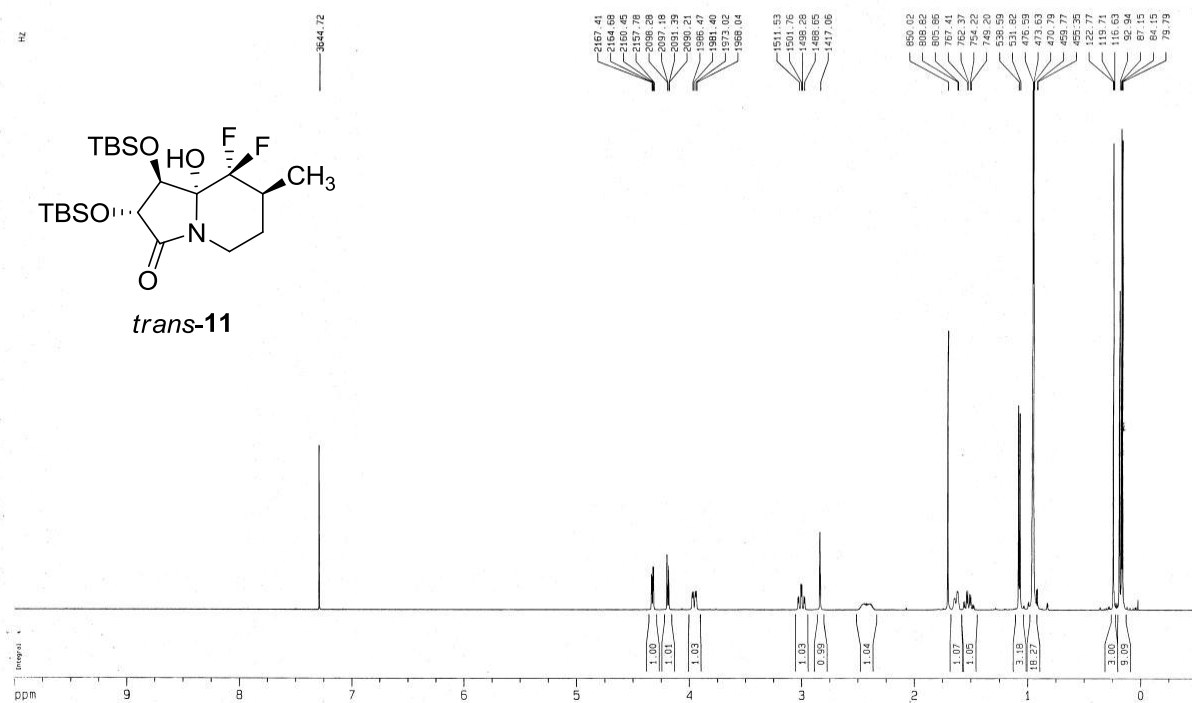
¹³C NMR Spectrum of *trans*-**10** (125 MHz, CDCl₃)



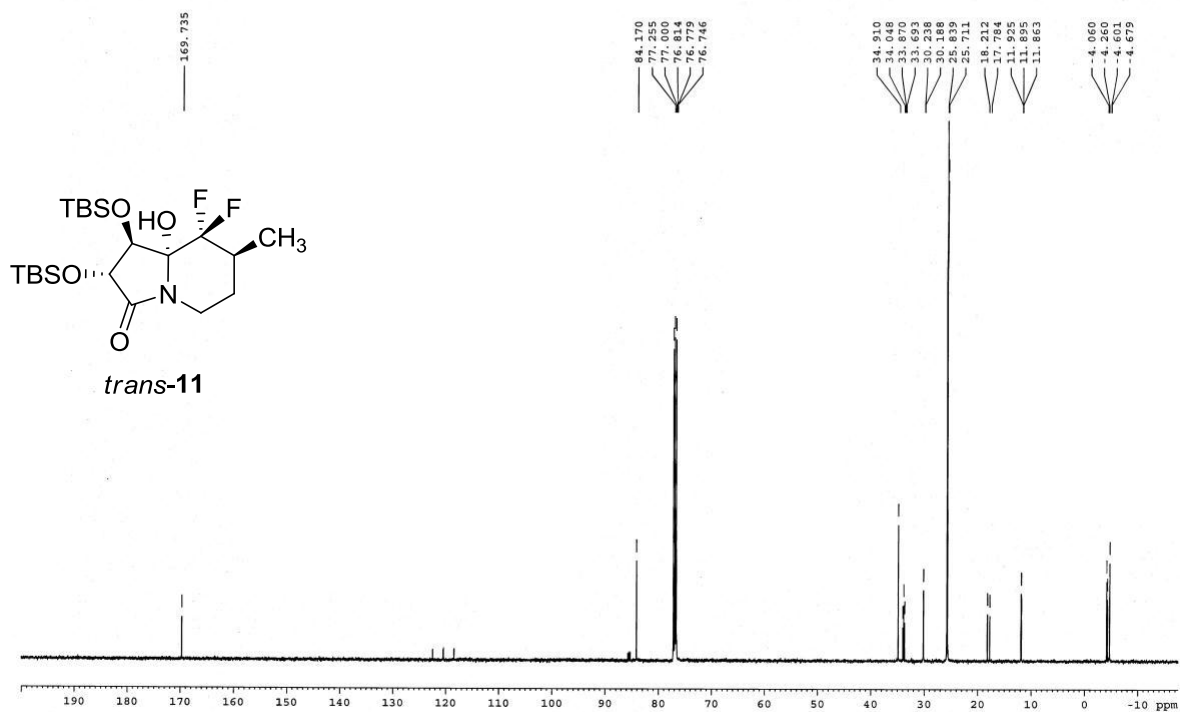
¹⁹F NMR Spectrum of *trans*-**10** (470 MHz, CDCl₃)



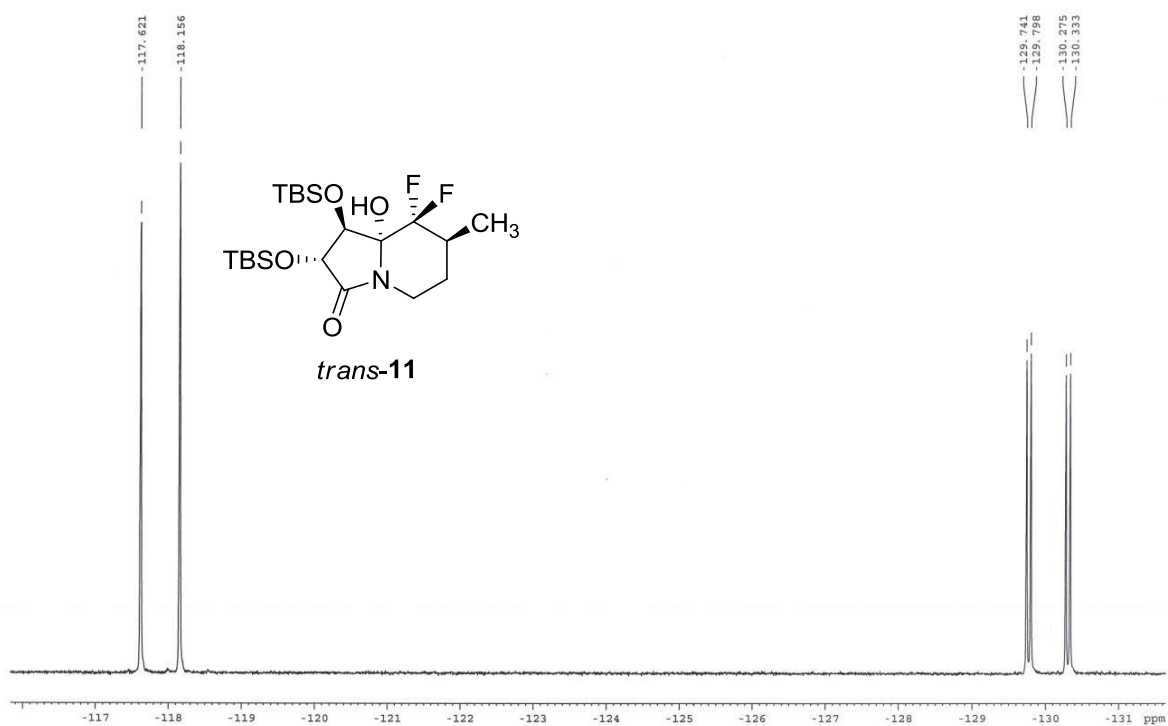
¹H NMR Spectrum of *trans*-11 (500 MHz, CDCl₃)



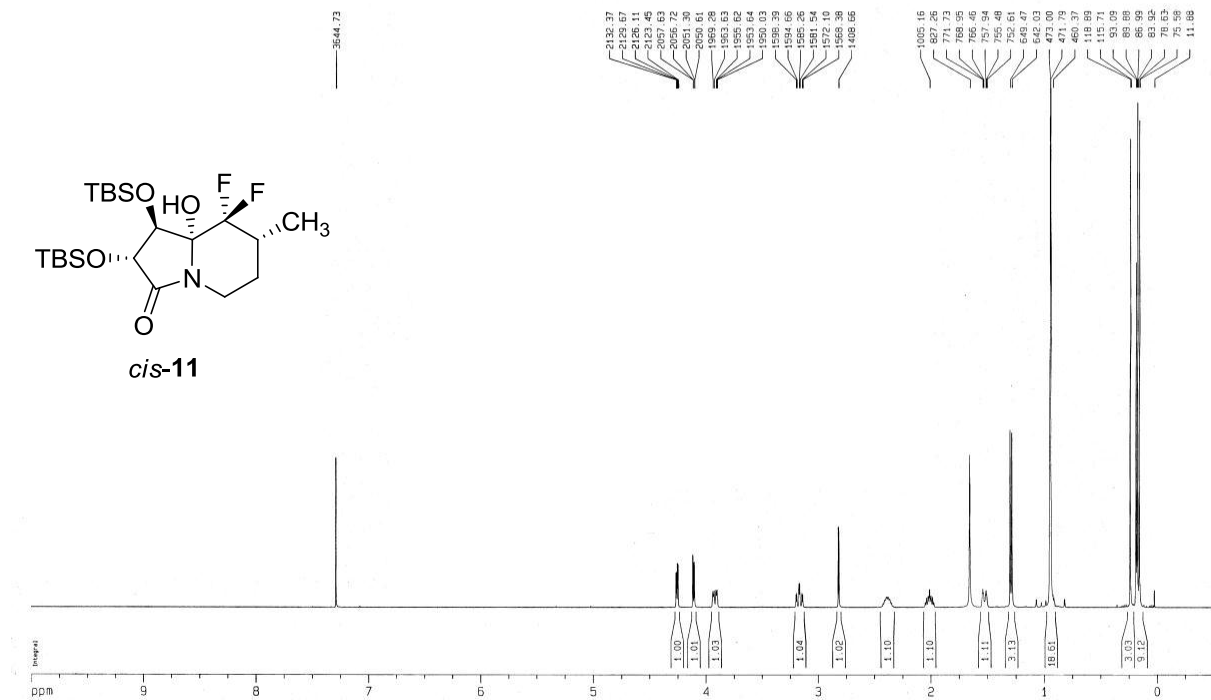
¹³C NMR Spectrum of *trans*-11 (125 MHz, CDCl₃)



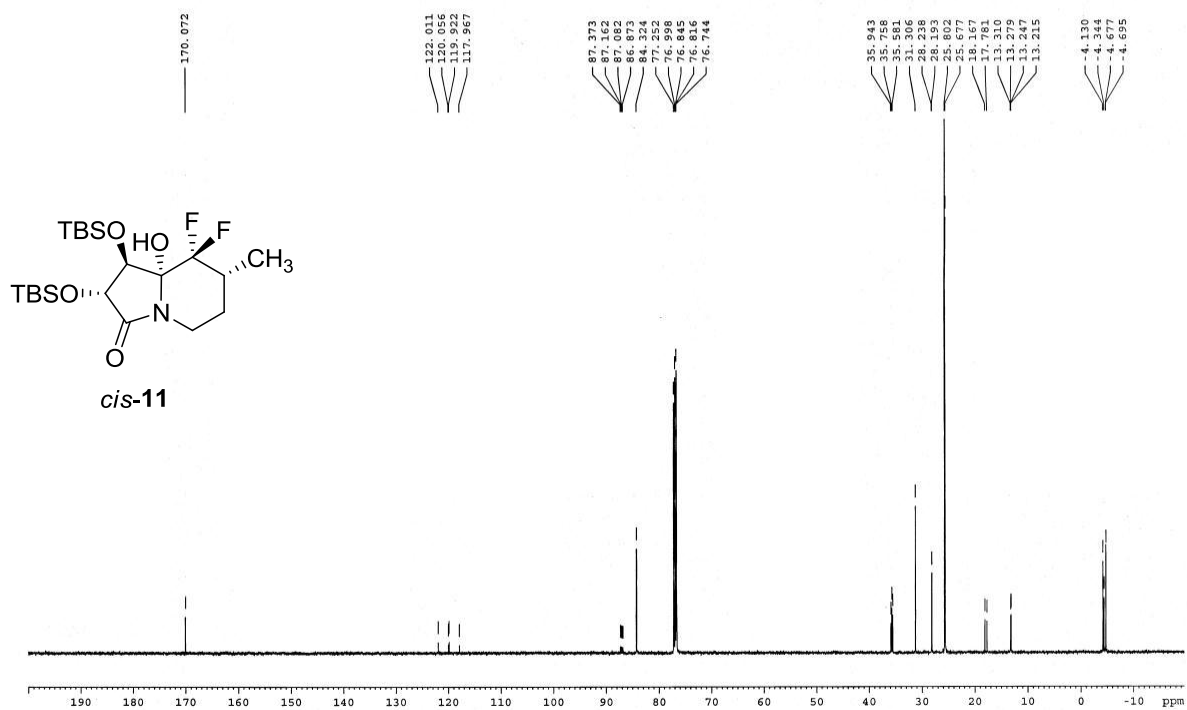
^{19}F NMR Spectrum of *trans*-**11** (470 MHz, CDCl_3)



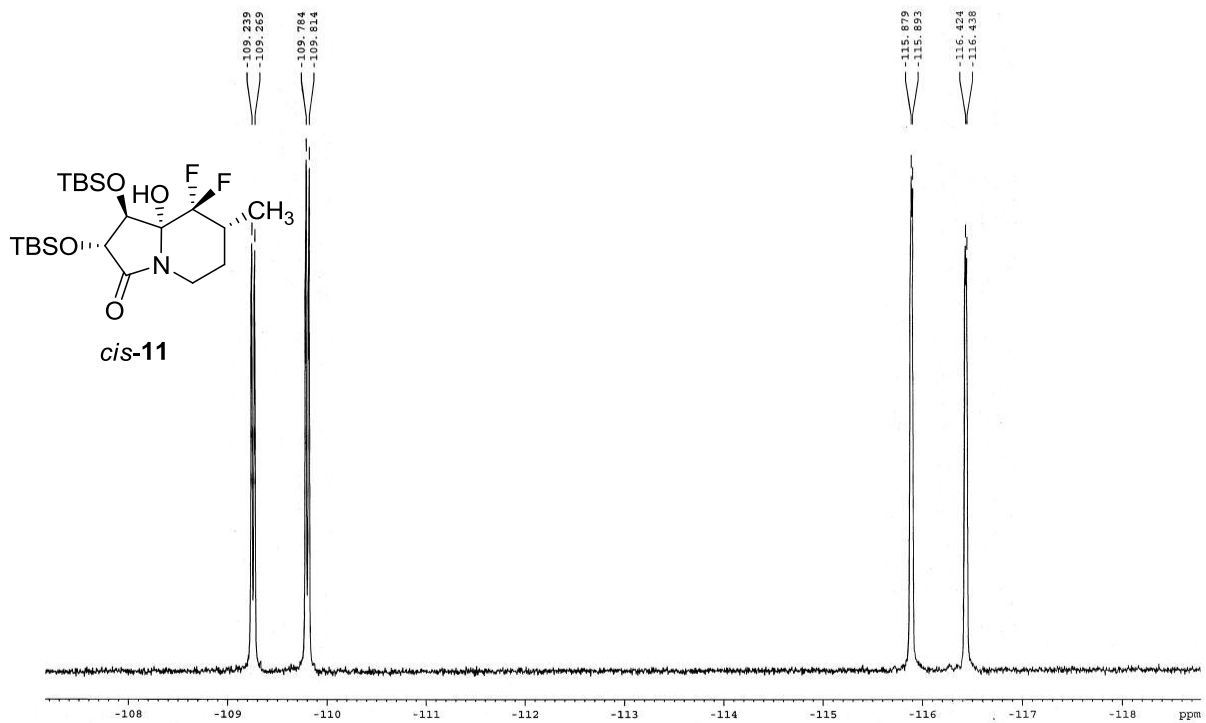
^1H NMR Spectrum of *cis*-**11** (500 MHz, CDCl_3)

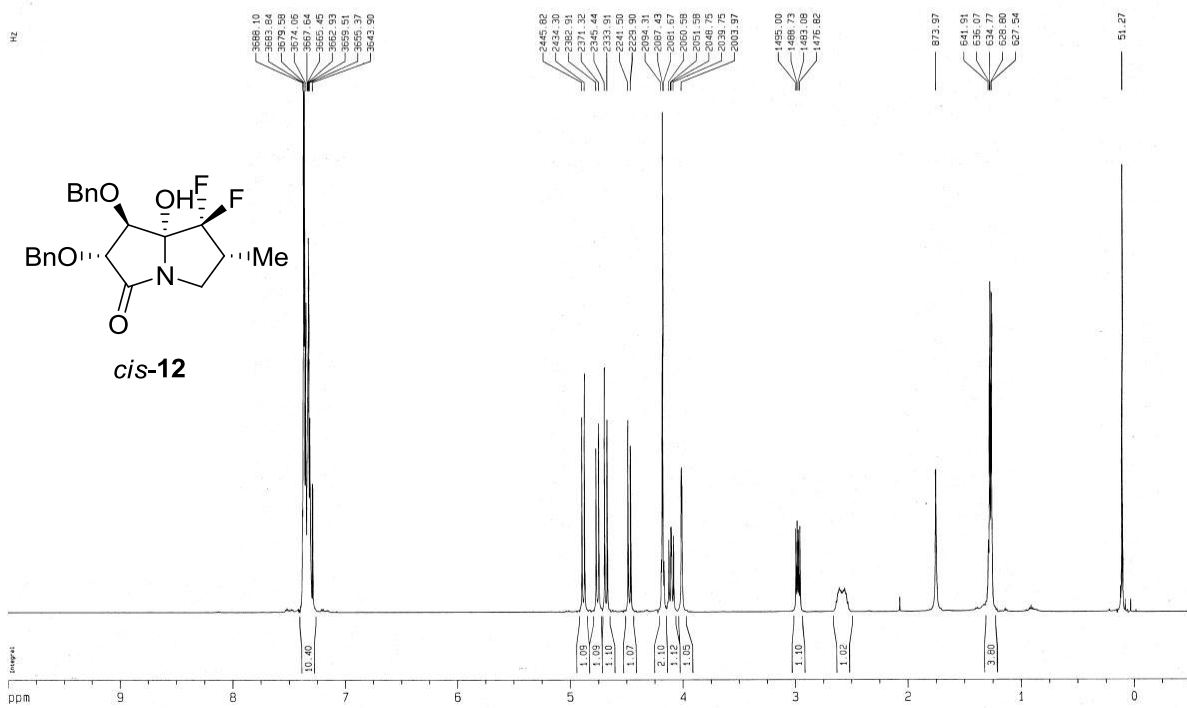


^{13}C NMR Spectrum of *cis*-**11** (125 MHz, CDCl_3)

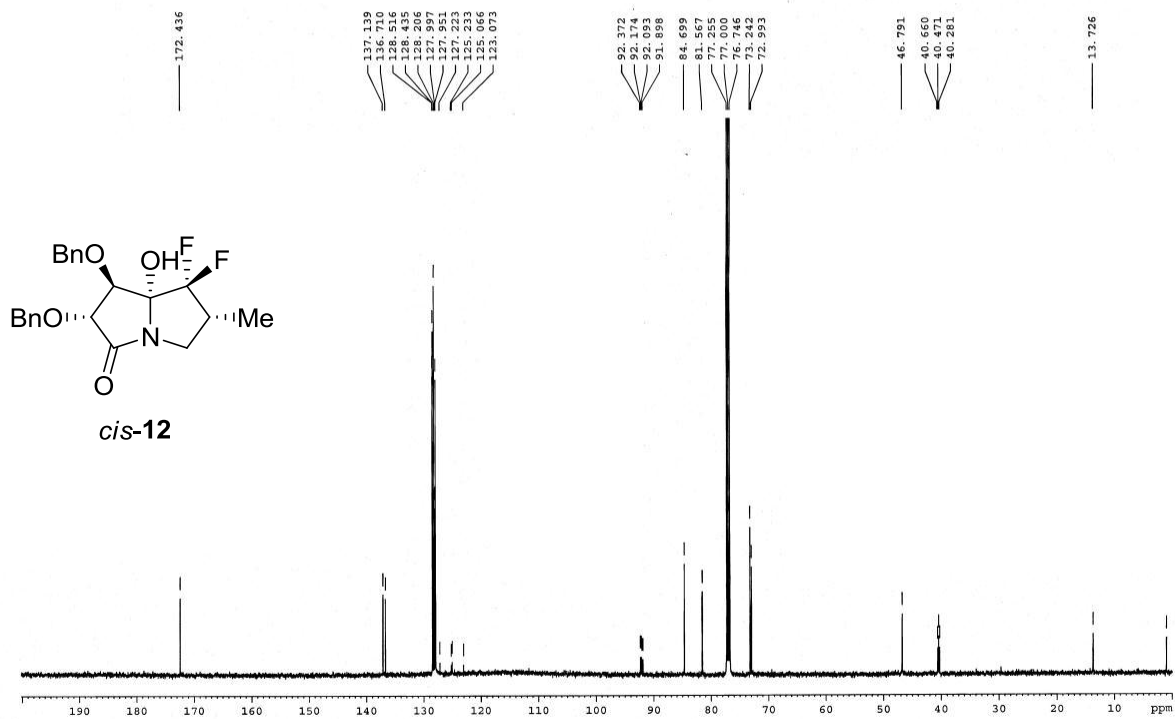


^{19}F NMR Spectrum of *cis*-**11** (470 MHz, CDCl_3)

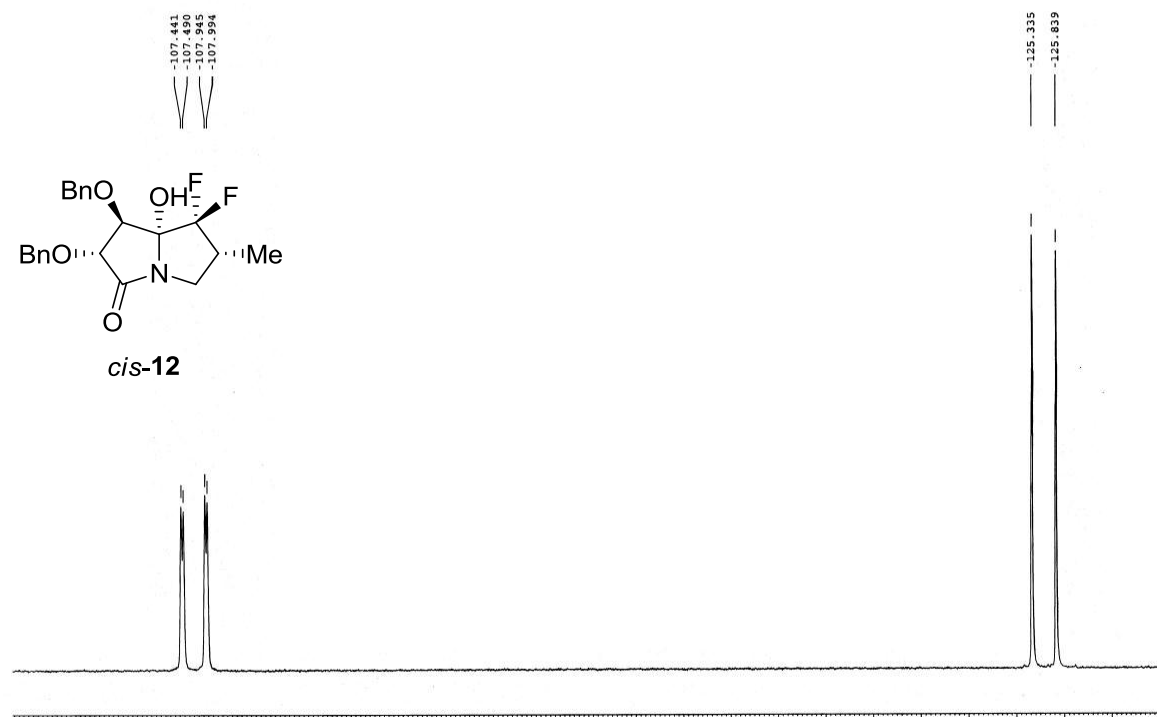


¹H NMR Spectrum of *cis*-**12** (500 MHz, CDCl₃)

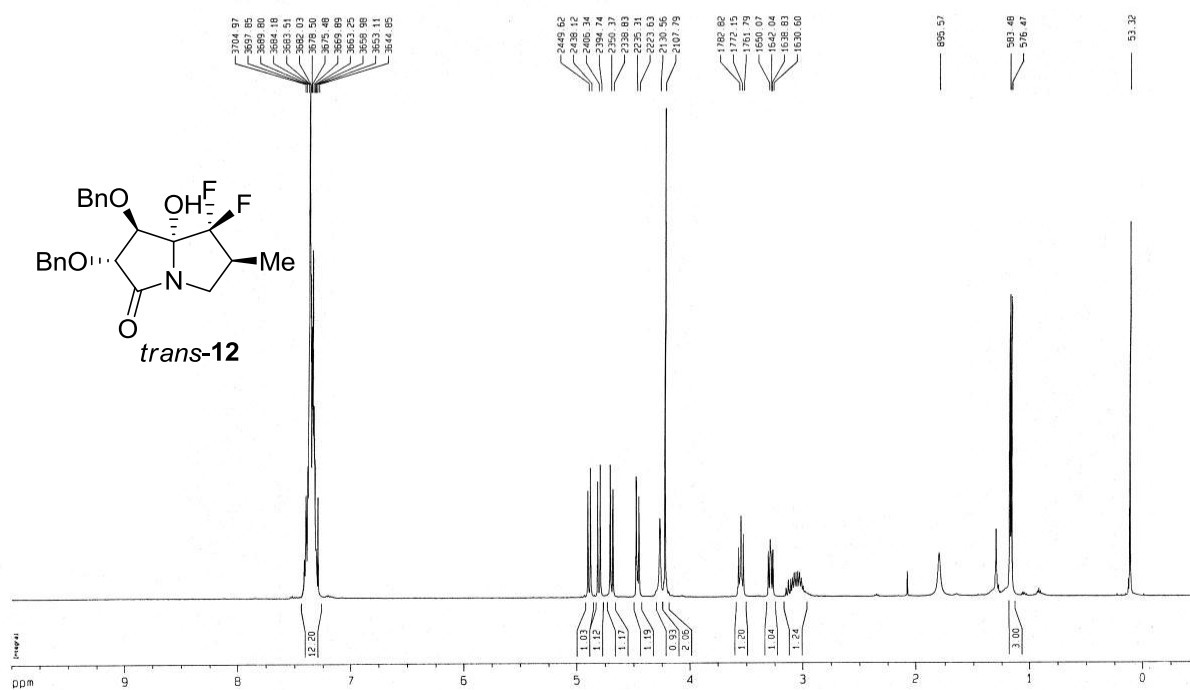
¹³C NMR Spectrum of *cis*-**12** (125 MHz, CDCl₃)



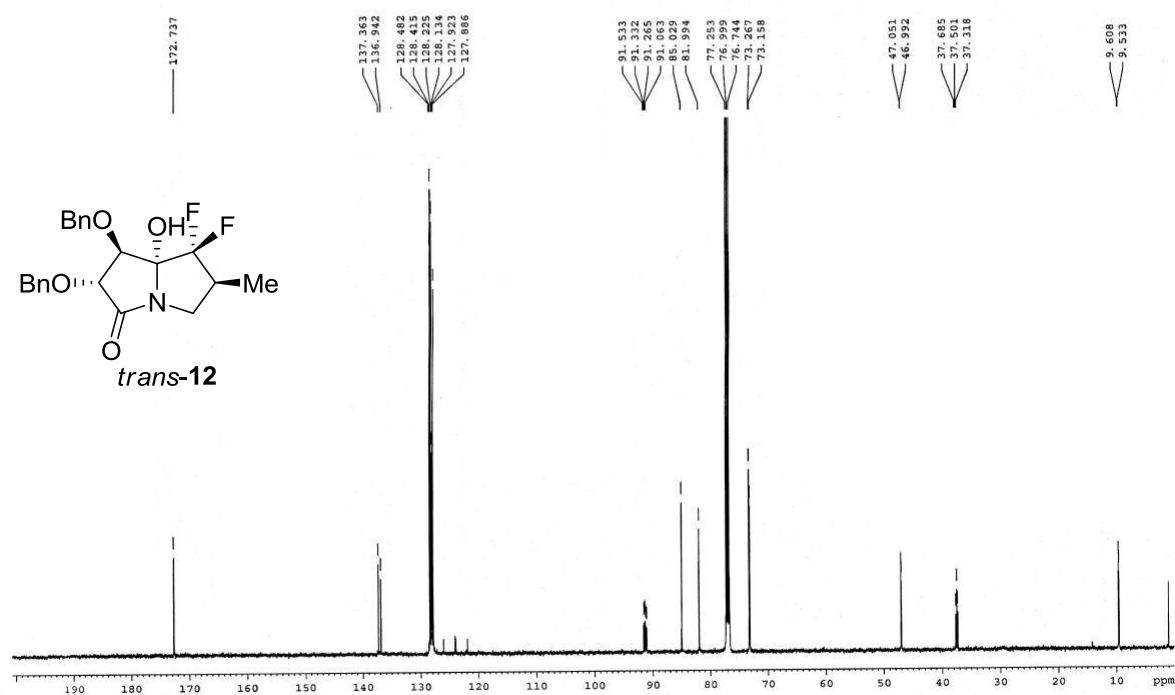
¹⁹F NMR Spectrum of *cis*-**12** (470 MHz, CDCl₃)



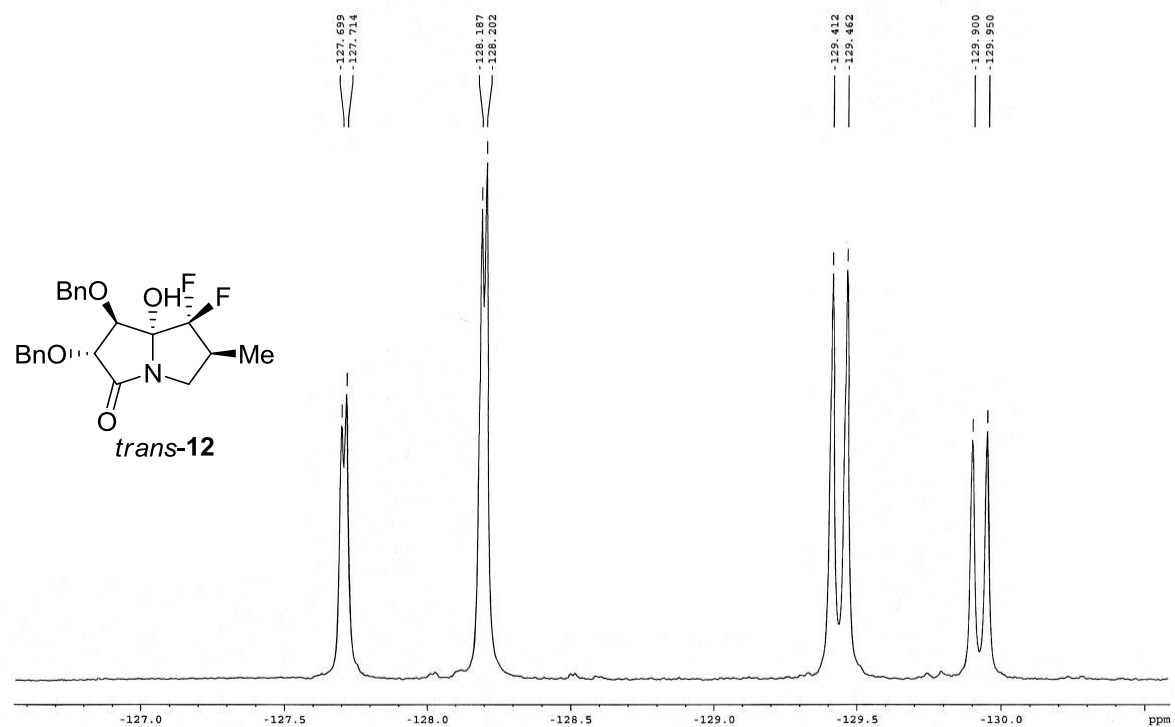
¹H NMR Spectrum of *trans*-**12** (500 MHz, CDCl₃)



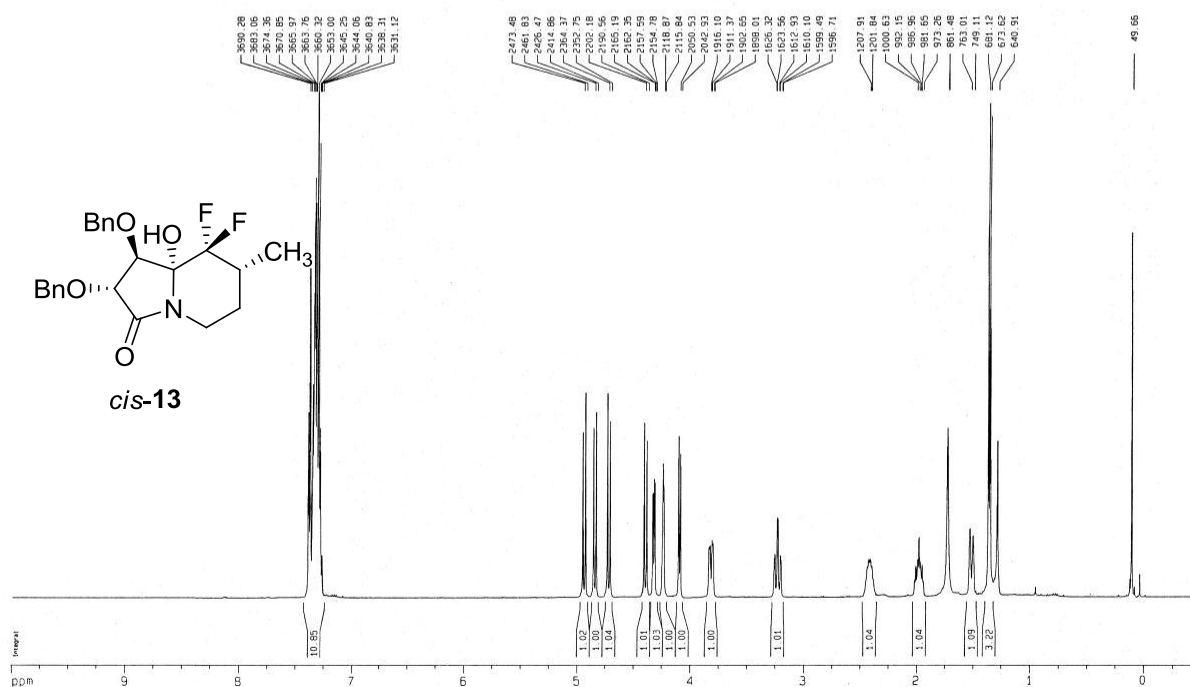
^{13}C NMR Spectrum of *trans*-**12** (125 MHz, CDCl_3)



^{19}F NMR Spectrum of *trans*-**12** (470 MHz, CDCl_3)



¹H NMR Spectrum of *cis*-**13** (500 MHz, CDCl₃)



***cis*-13**

The ¹³C NMR spectrum of *cis*-13 shows four main signals in the aromatic region: a doublet at -108.363 and -108.395 ppm, a doublet at -108.904 and -108.936 ppm, a singlet at -116.462 ppm, and a singlet at -117.003 ppm. The chemical structure of *cis*-13 is shown as an inset, featuring a bicyclic system with a benzyl ester, a hydroxyl group, and two fluorine atoms.

Chemical structure of *trans*-13:

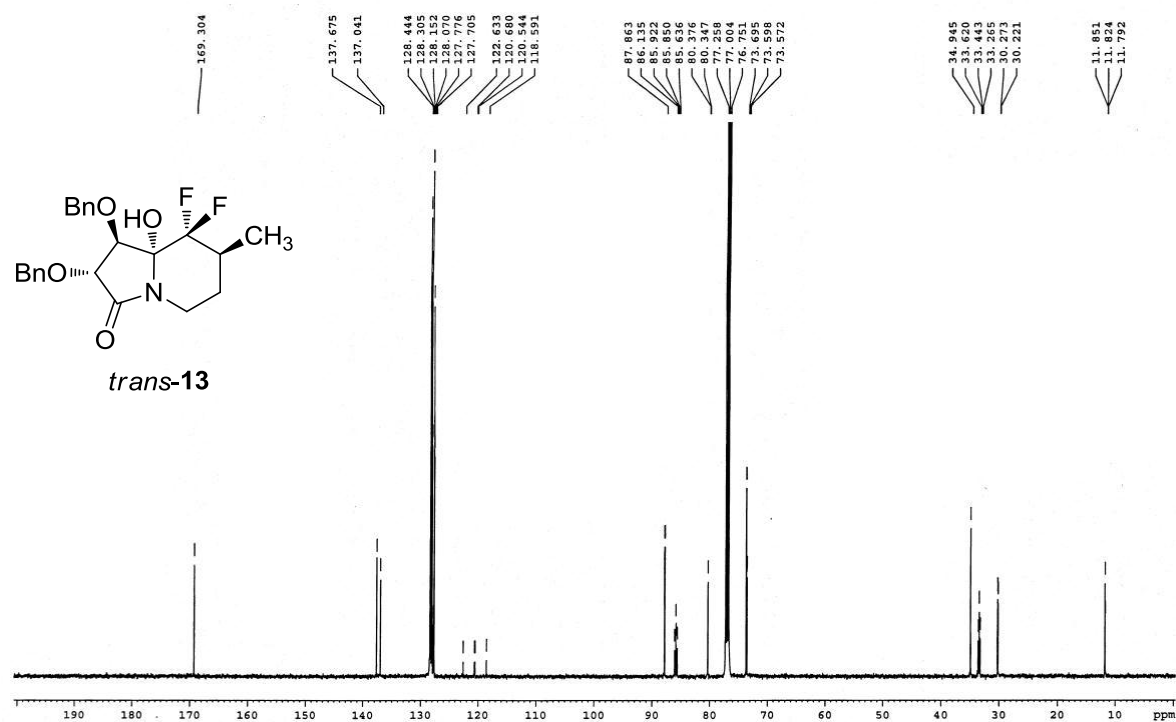
O=C1[C@@H](OC(=O)c2ccccc2)[C@H](O)[C@@H](F)[C@H](F)C1

***trans*-13**

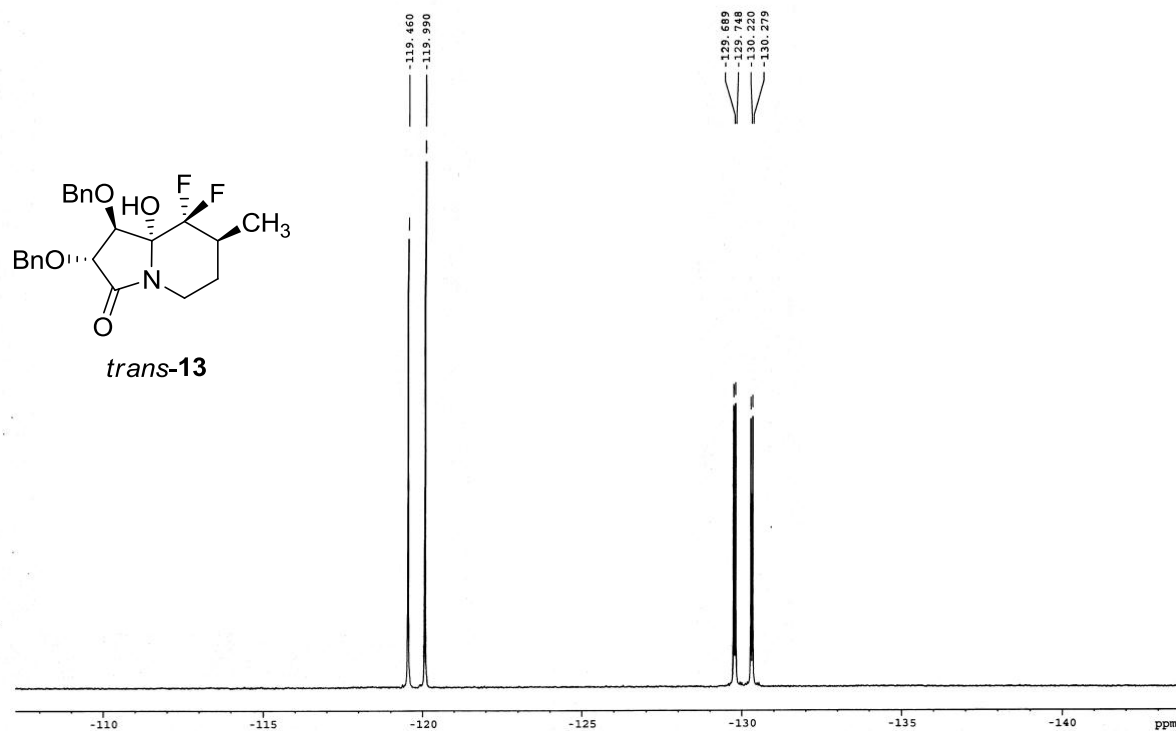
¹H NMR spectrum (CDCl₃):

Chemical Shift (ppm)	Integration
7.26 (triplet, solvent)	11.37
5.00 (multiplet)	1.13
4.80 (multiplet)	1.07
4.60 (multiplet)	1.17
4.40 (multiplet)	3.02
4.20 (multiplet)	1.17
4.00 (multiplet)	1.18
3.80 (multiplet)	1.10
3.60 (multiplet)	1.14
2.00 (multiplet)	1.30
1.80 (multiplet)	1.24
1.60 (multiplet)	3.00
0.00 (TMS)	-

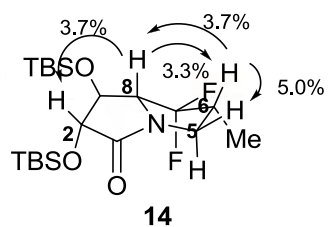
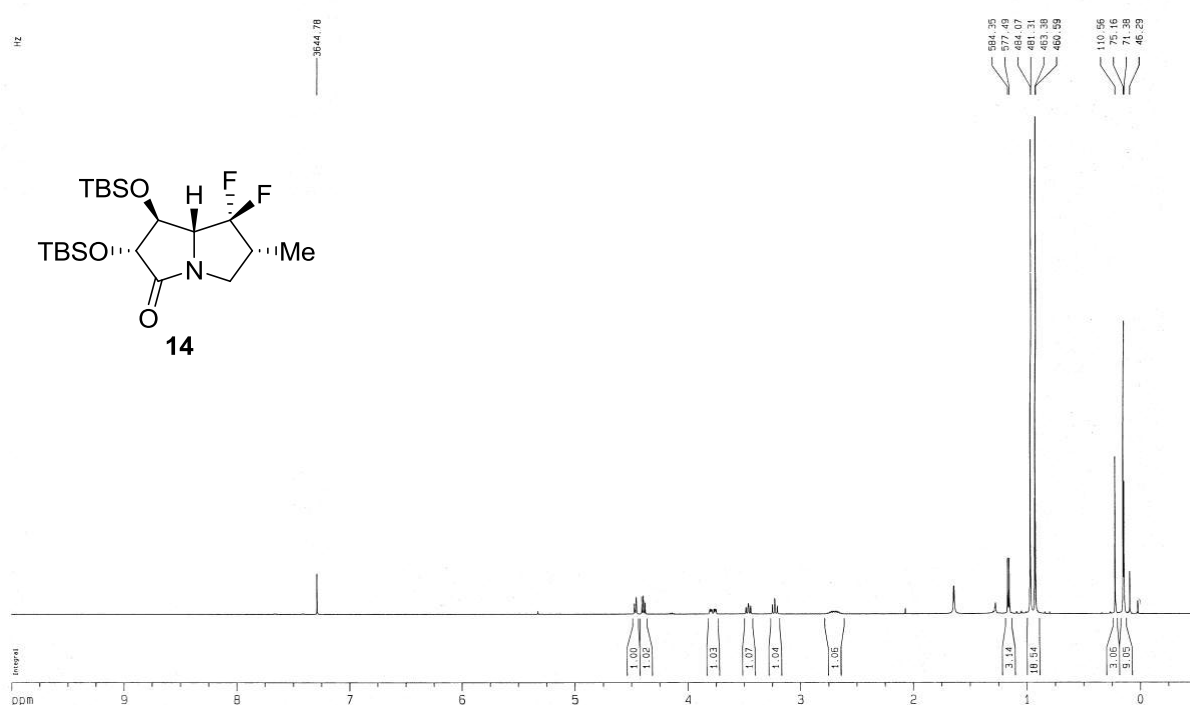
^{13}C NMR Spectrum of *trans*-**13** (125 MHz, CDCl_3)



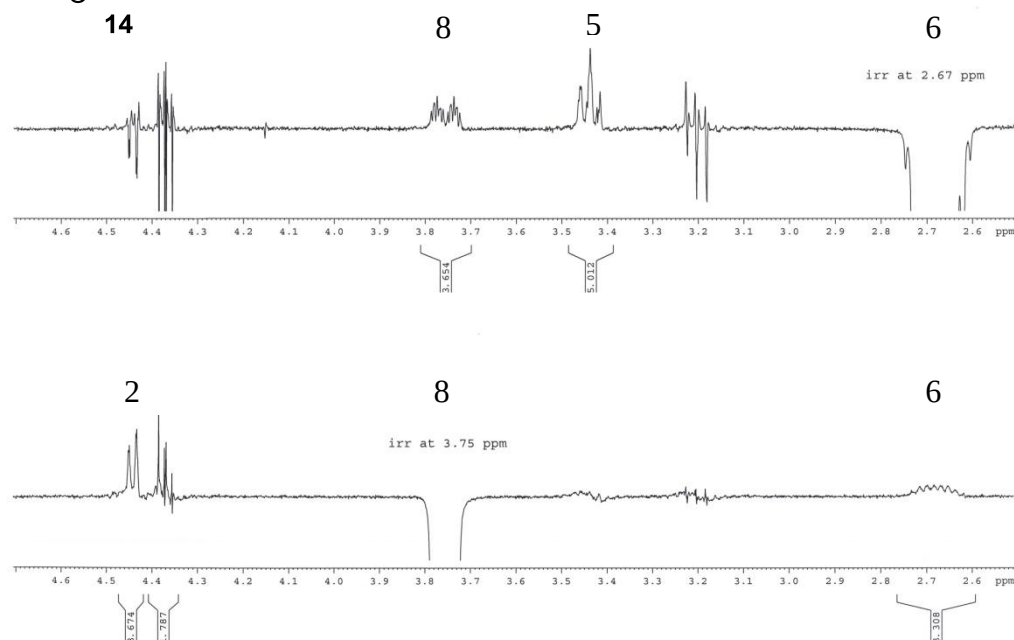
^{19}F NMR Spectrum of *trans*-**13** (470 MHz, CDCl_3)



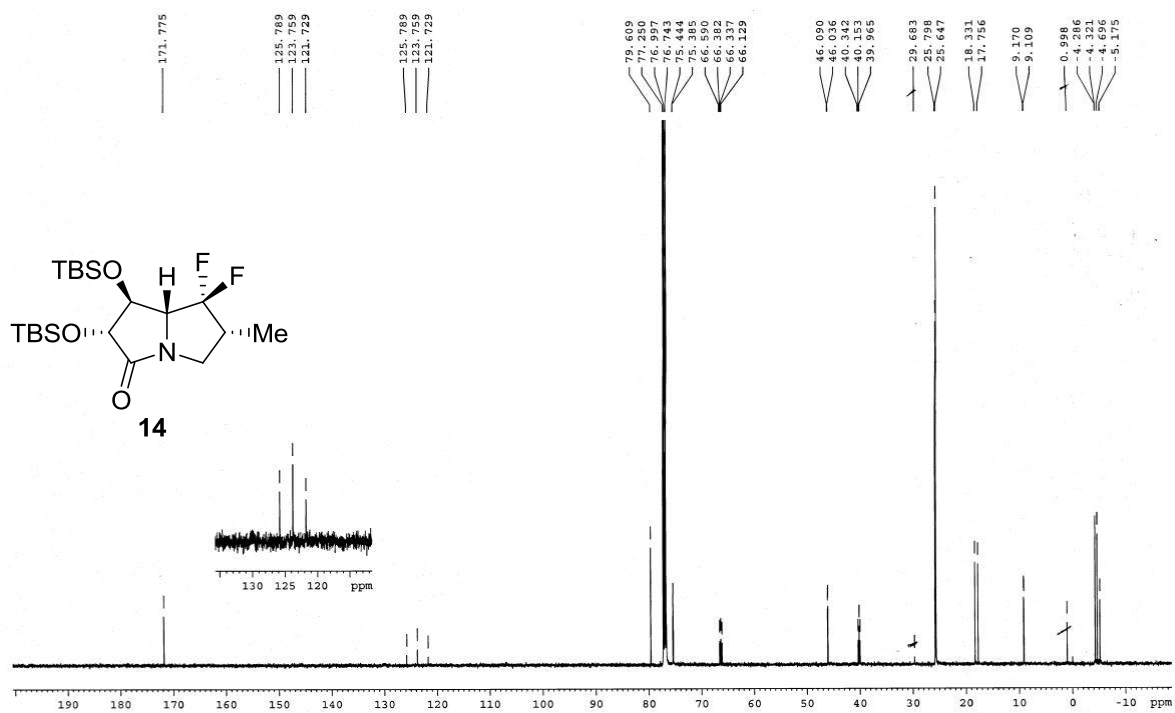
¹H NMR Spectrum of **14** (500 MHz, CDCl₃)



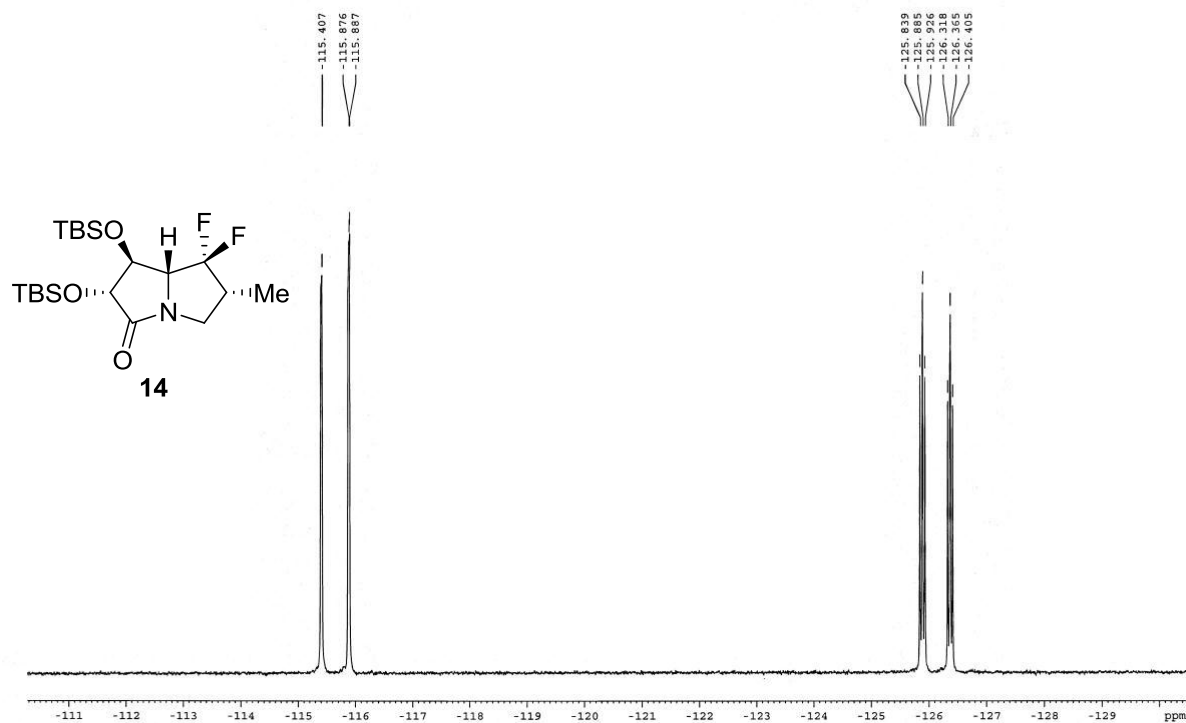
NOE Spectrum of **14**



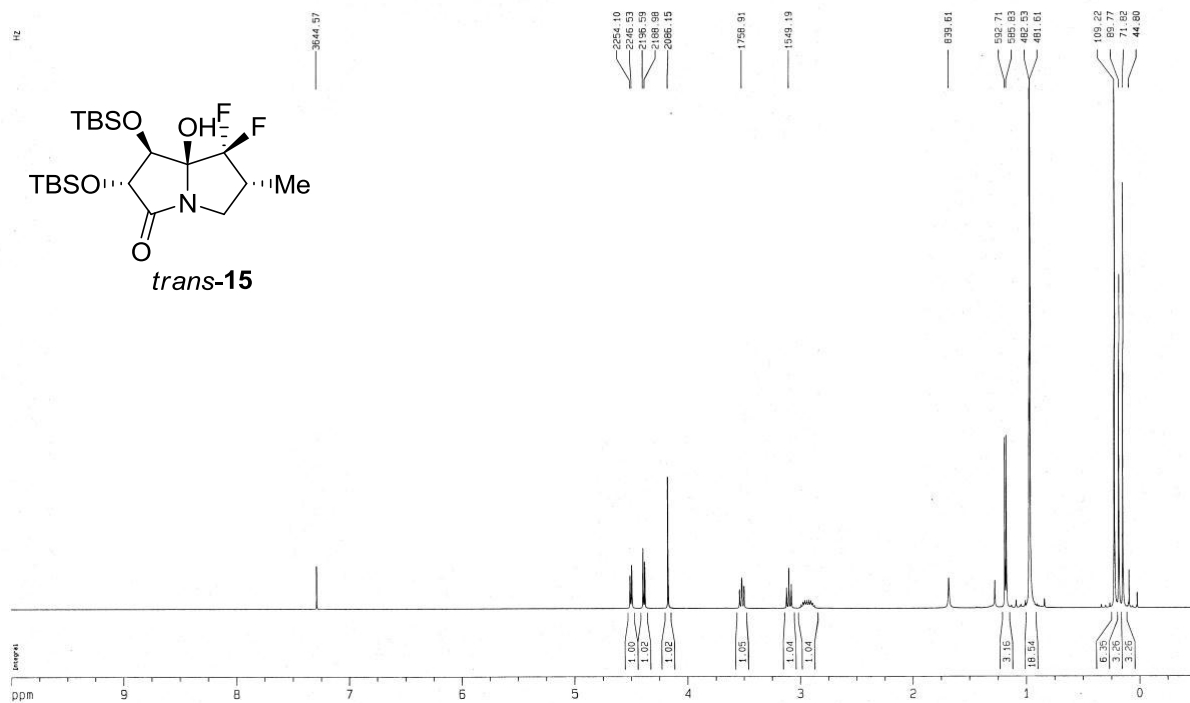
¹³C NMR Spectrum of **14** (125 MHz, CDCl₃)



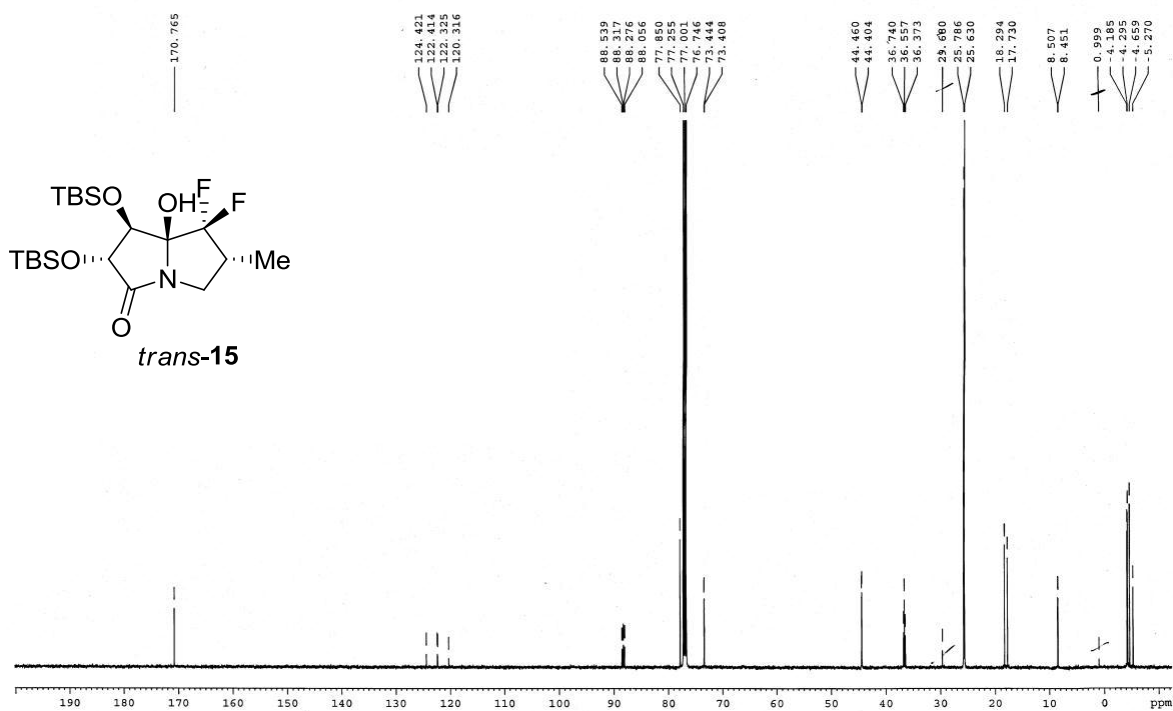
¹⁹F NMR Spectrum of **14** (470MHz, CDCl₃)



¹H NMR Spectrum of *trans*-**15** (500 MHz, CDCl₃)



¹³C NMR Spectrum of *trans*-**15** (125 MHz, CDCl₃)

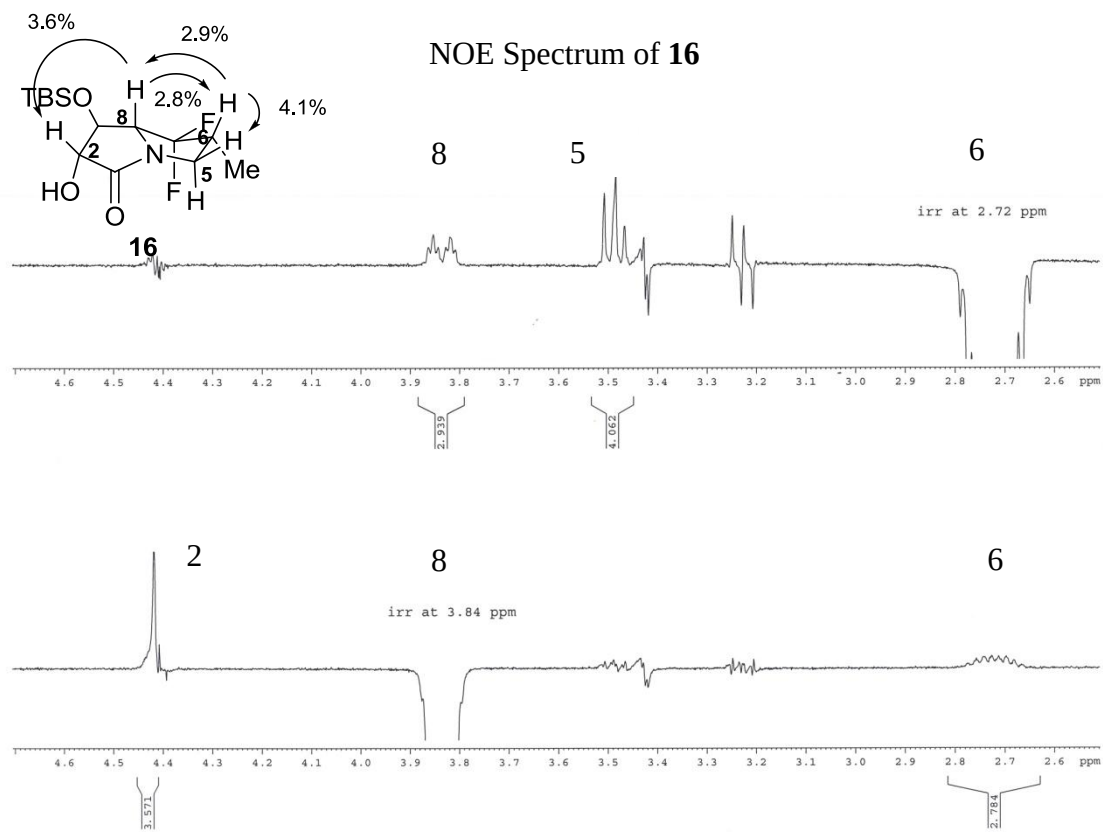


trans-15

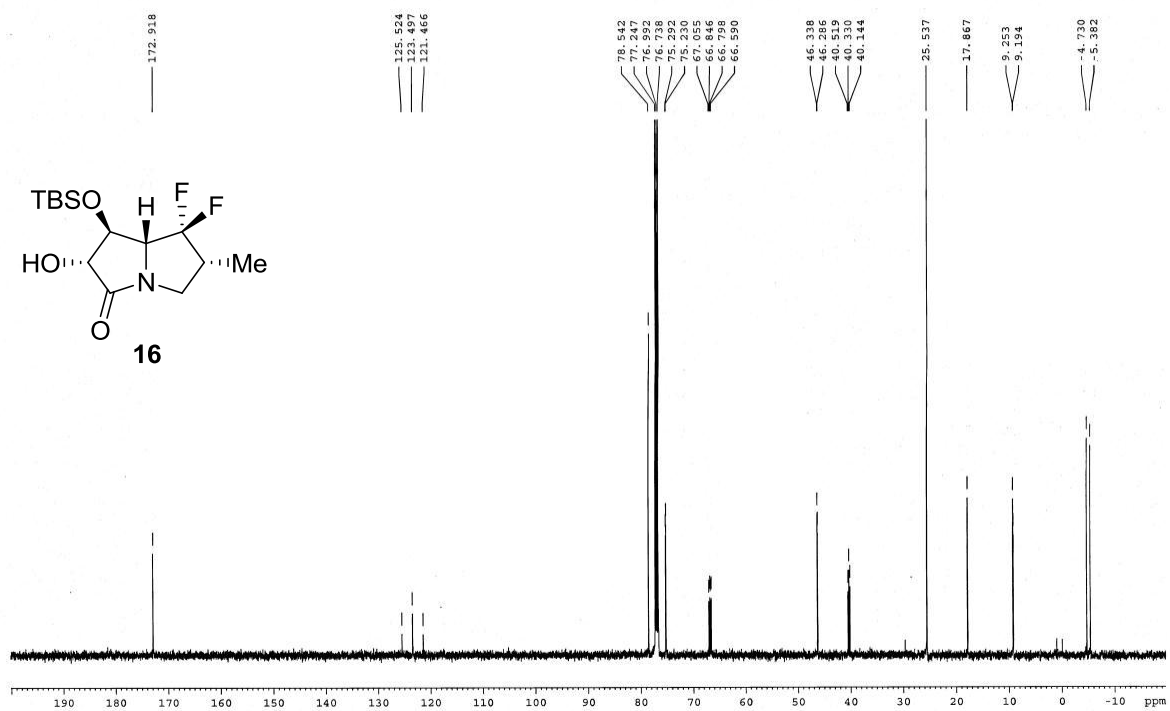
Chemical structure of **trans-15** is shown as an inset. The structure is a 5-membered ring containing a nitrogen atom, a carbonyl group, and a methyl group. The stereochemistry is trans, with the methyl group and the carbonyl group on opposite sides of the ring. The structure is labeled **trans-15**.

16

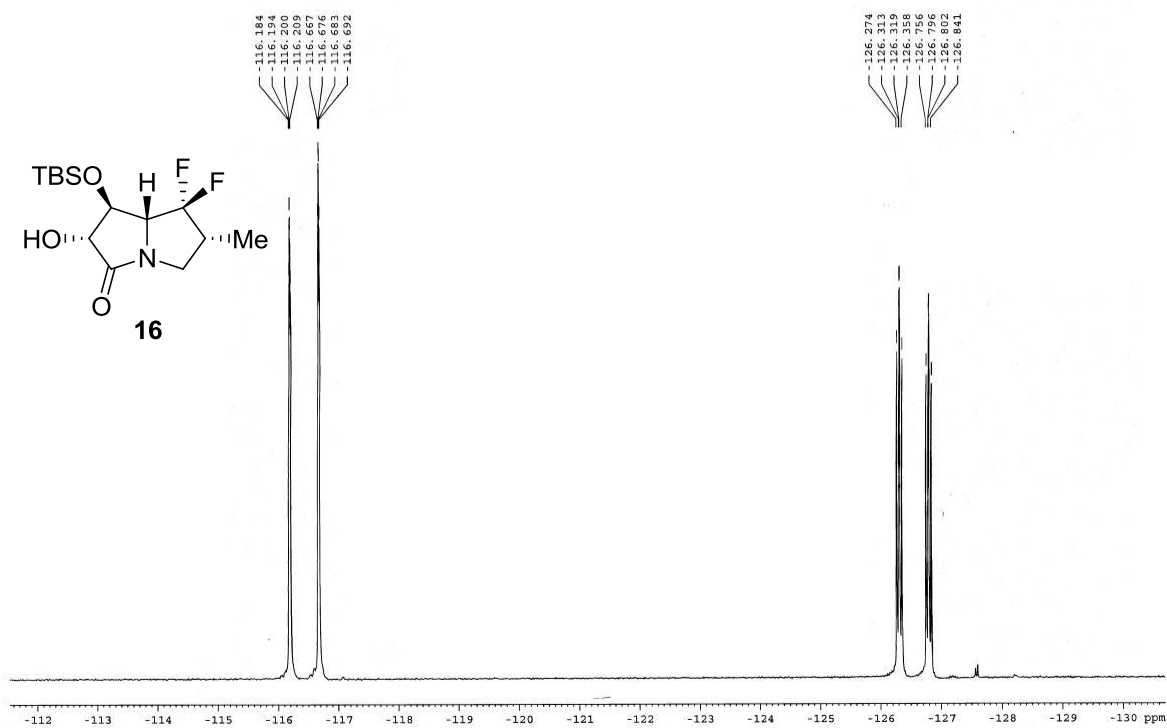
¹H NMR spectrum (CDCl₃) of compound **16**. The spectrum shows peaks at 7.26 (s, 1H, solvent), 4.52 (d, 1H, TBSO), 3.95 (s, 3H, Me), 3.12 (d, 1H, CH), 1.12 (d, 3H, CH₃), and 0.11 (s, 9H, TBSO). The integration values are 2.000, 1.008, 1.065, 1.005, 1.036, 1.038, 1.040, 3.112, 9.395, 6.562, and 9.116.



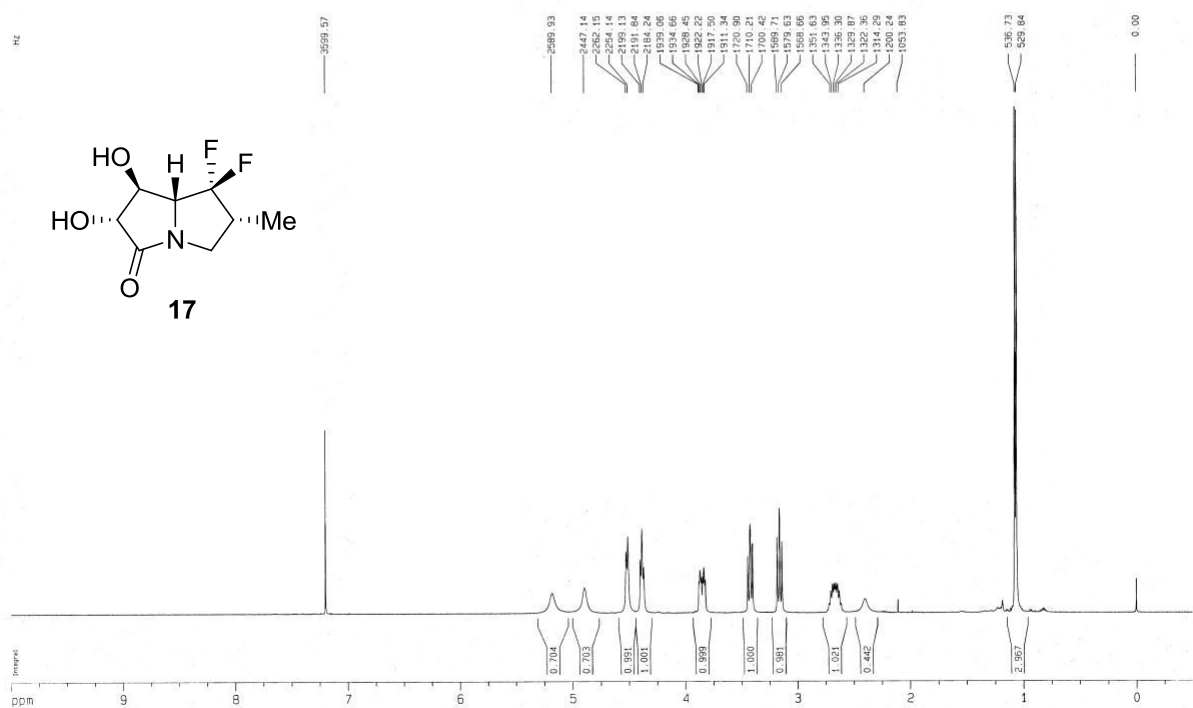
^{13}C NMR Spectrum of 16 (125 MHz, CDCl_3)



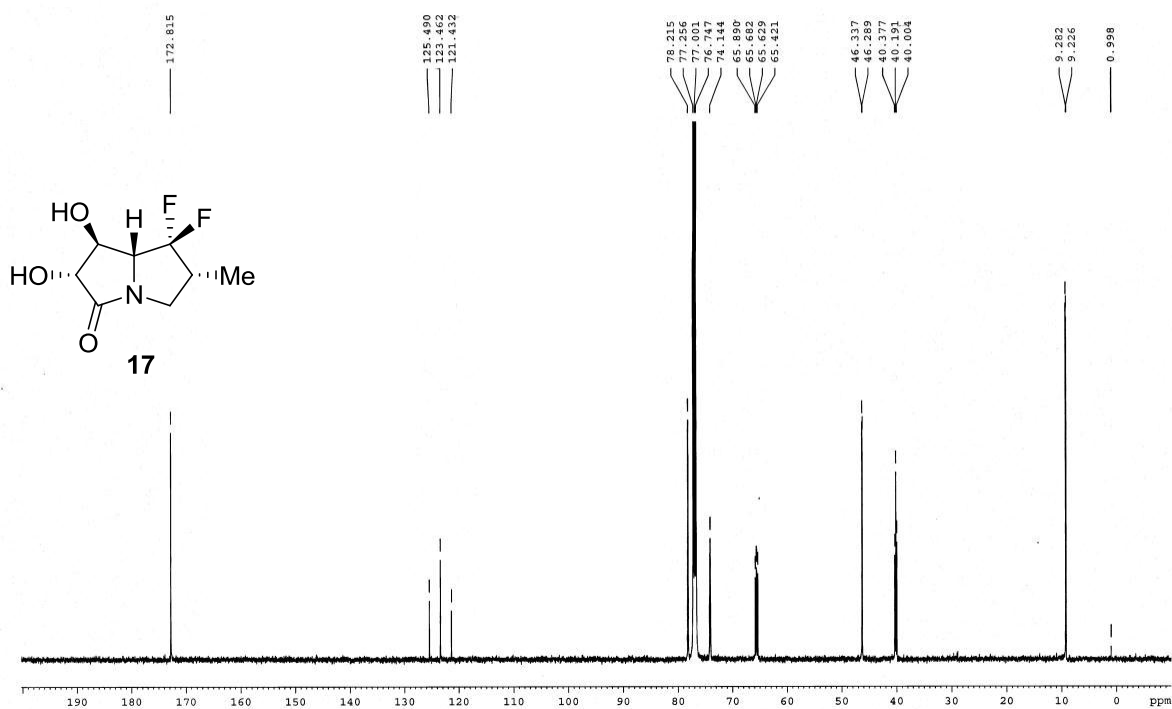
^{19}F NMR Spectrum of **16** (470 MHz, CDCl_3)



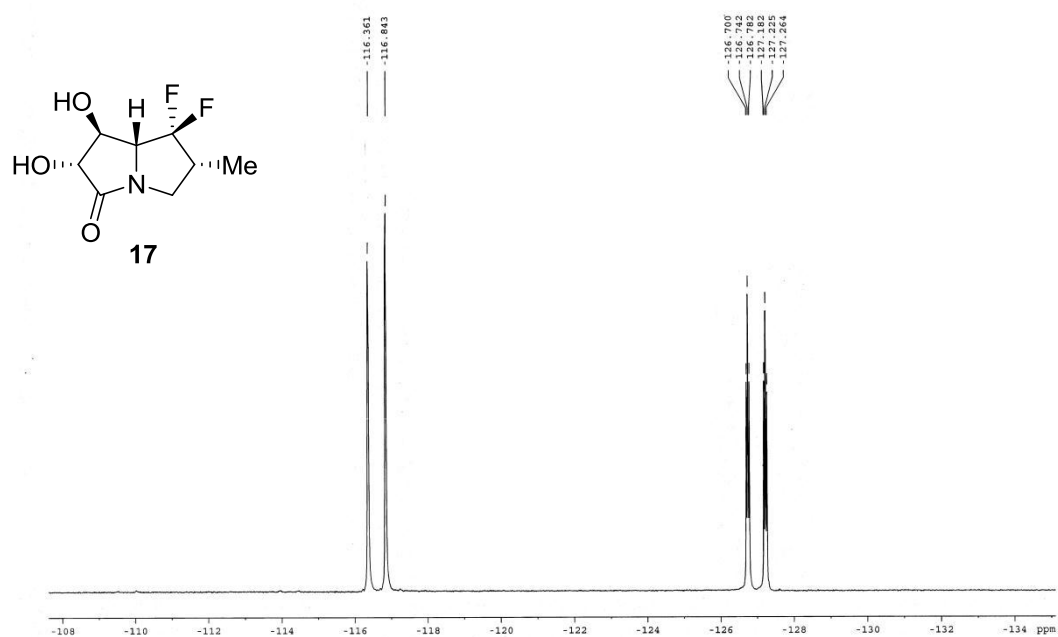
^1H NMR Spectrum of **17** (500 MHz, CD_3OD)

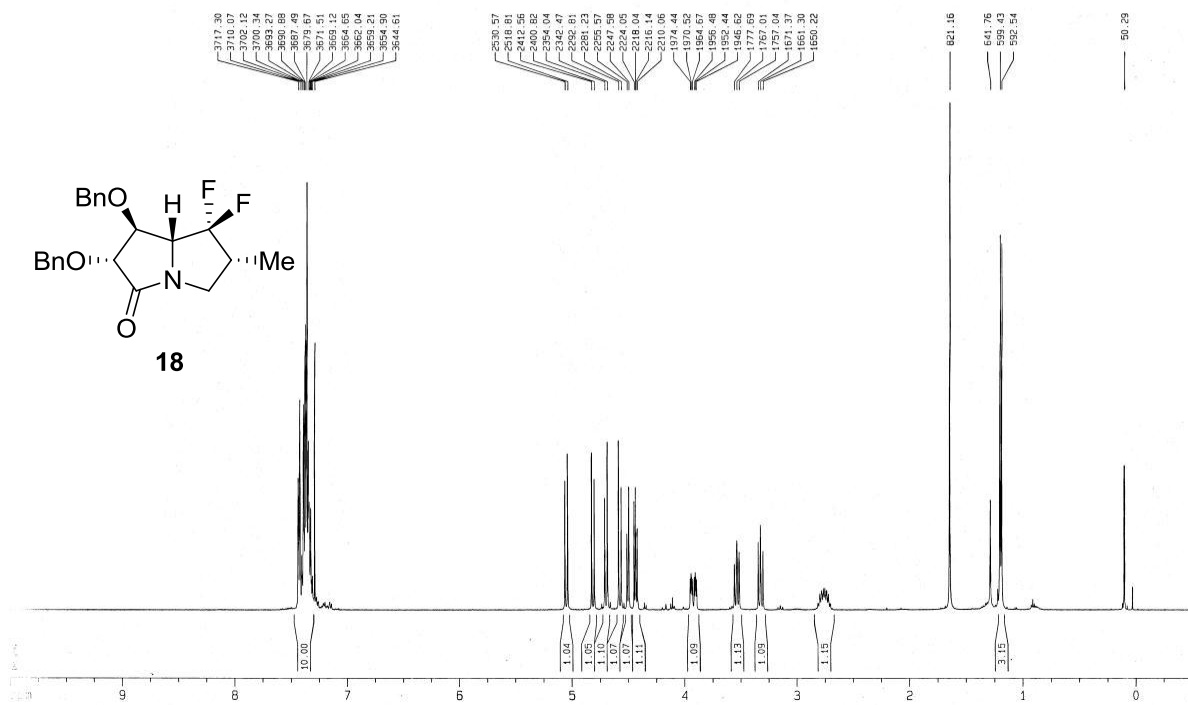
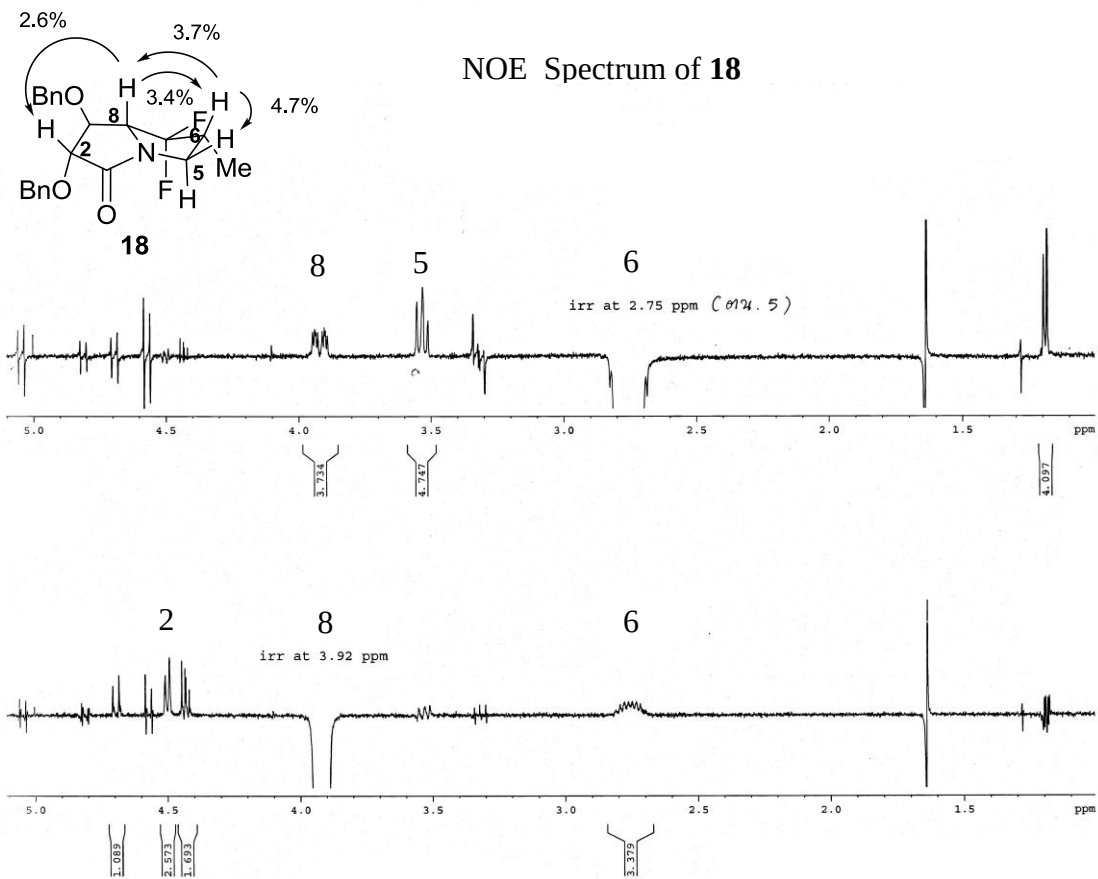


^{13}C NMR Spectrum of **17** (125 MHz, CD_3OD)

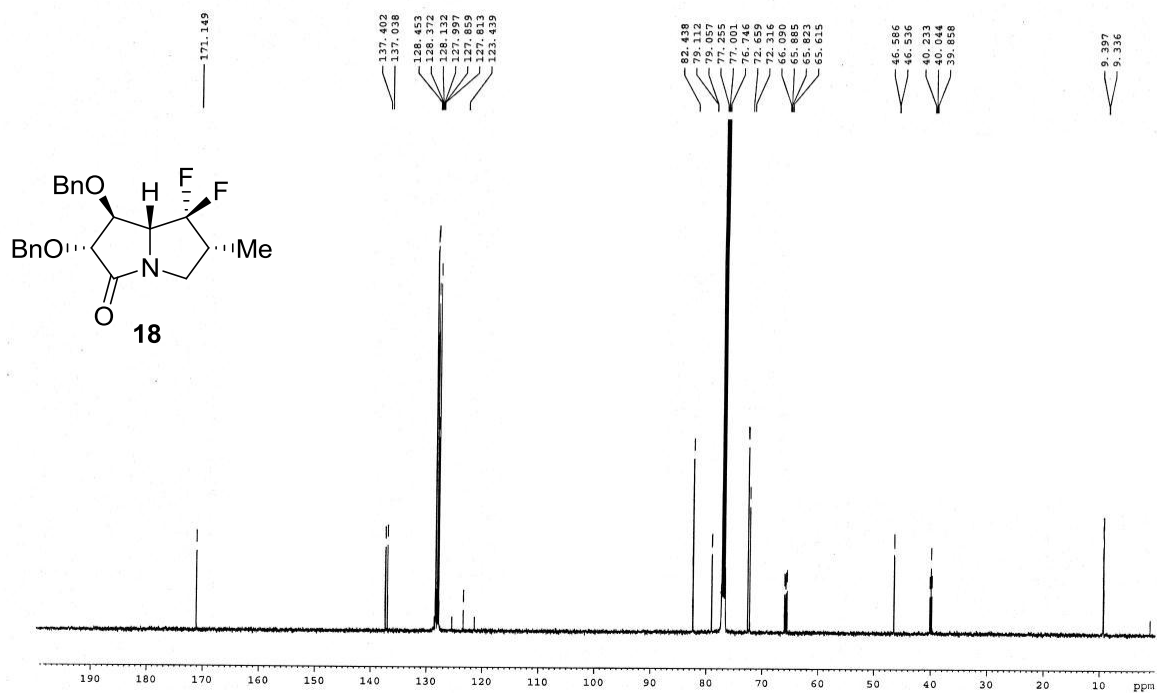


^{19}F NMR Spectrum of **17** (470 MHz CD_3OD)

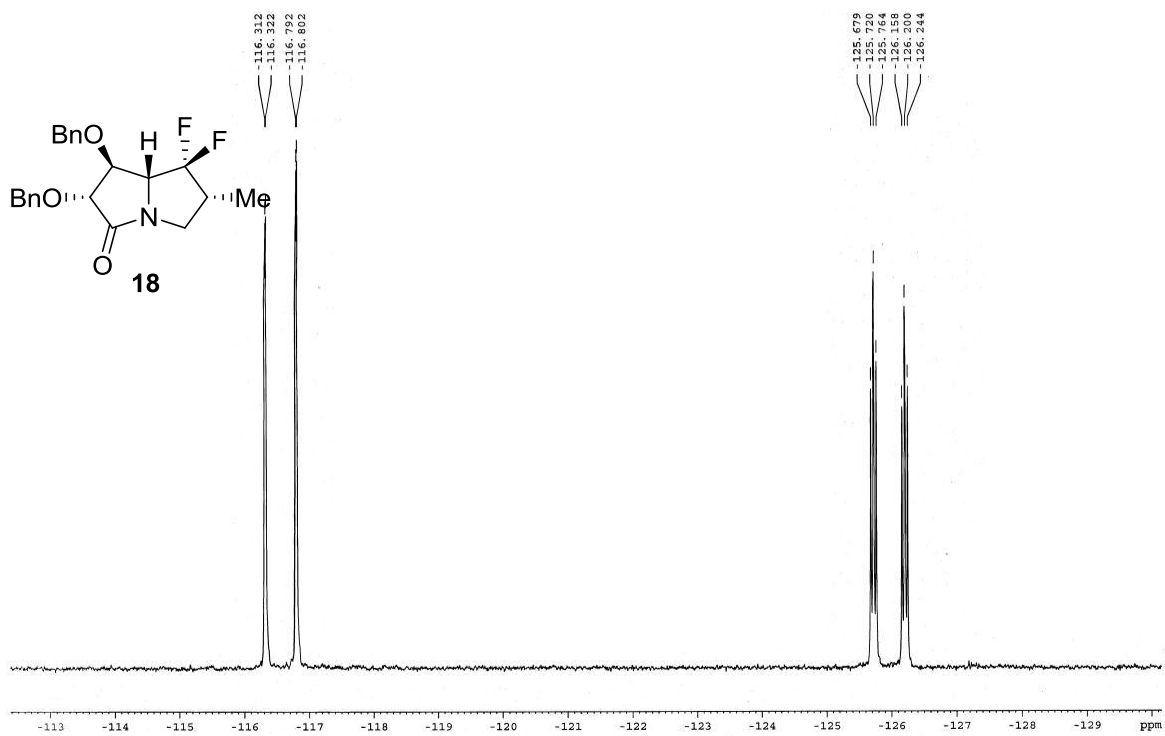


¹H NMR Spectrum of **18** (500 MHz, CDCl₃)NOE Spectrum of **18**

^{13}C NMR Spectrum of **18** (125 MHz, CDCl_3)



^{19}F NMR Spectrum of **18** (470 MHz, CDCl_3)



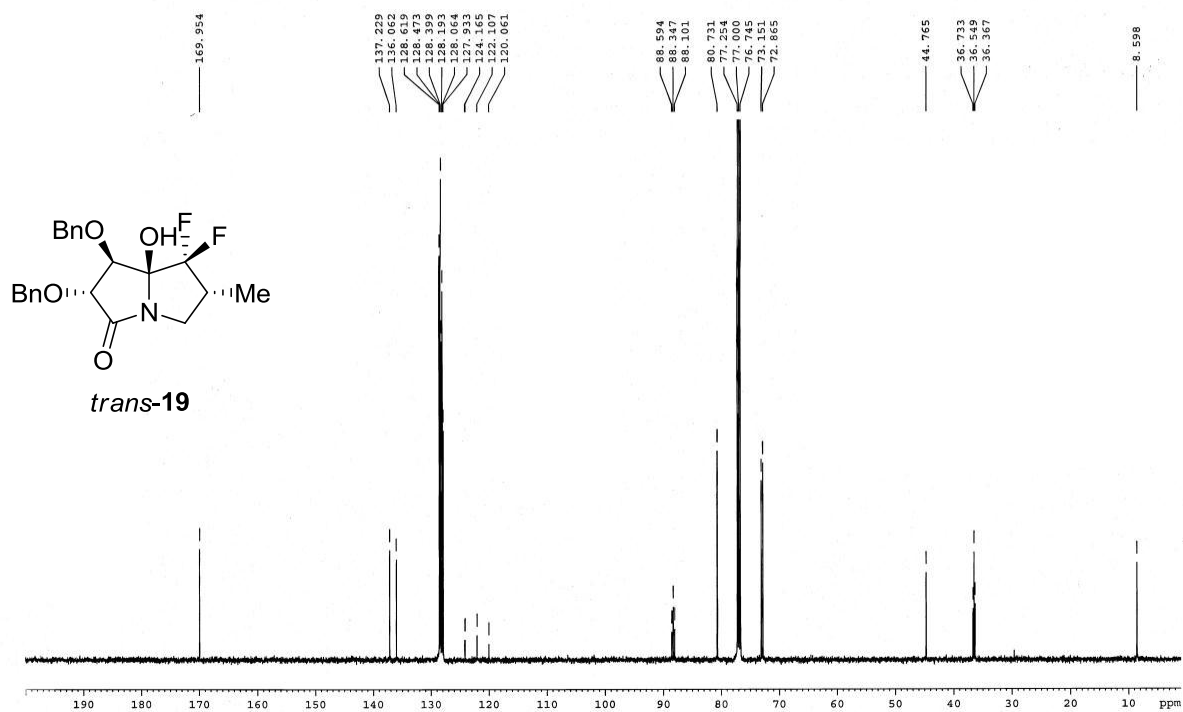
***cis*-19**

Chemical structure of ***cis*-19** is shown. The structure is a bicyclic compound with a benzodioxane core. It features a benzyl (Bn) group, a hydroxyl group (OH), a fluorine atom (F), and a methyl group (Me). The stereochemistry is *cis*.

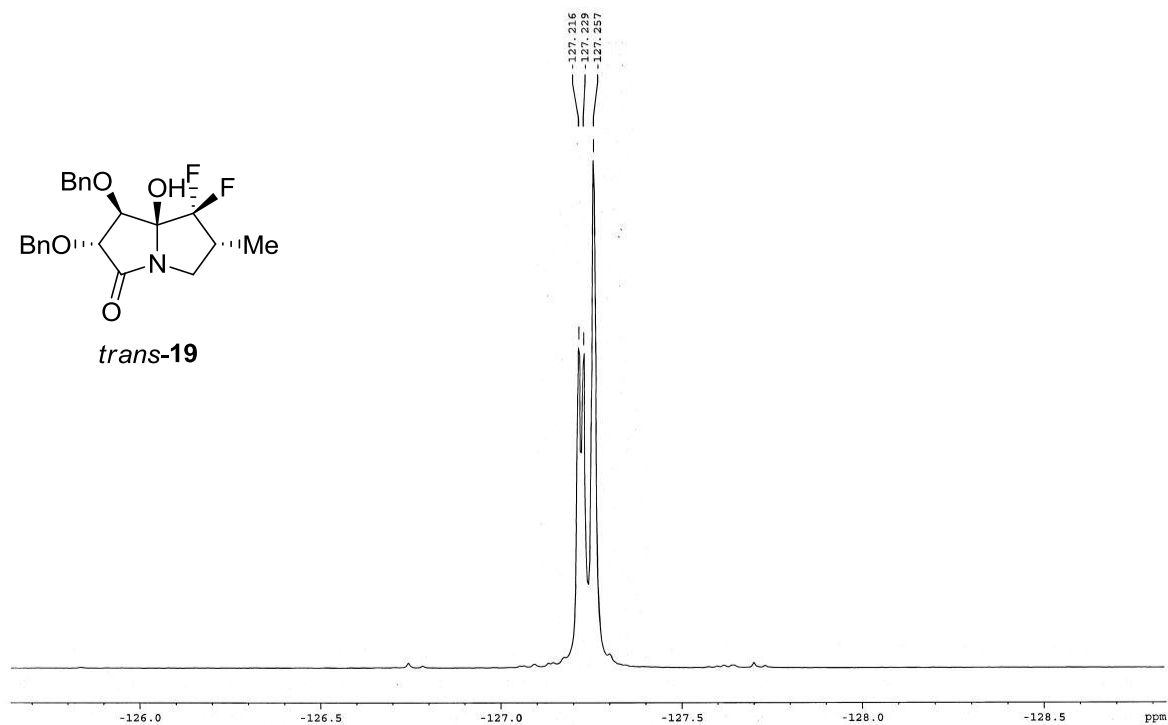
¹³C NMR spectrum (CDCl₃) of ***cis*-19** is shown. The spectrum displays two main regions of peaks. The aromatic region (115-117 ppm) contains two multiplets, each with three peaks. The aliphatic region (125-127 ppm) contains two multiplets, each with three peaks. The x-axis is labeled from -113 to -129 ppm.

[illegible]

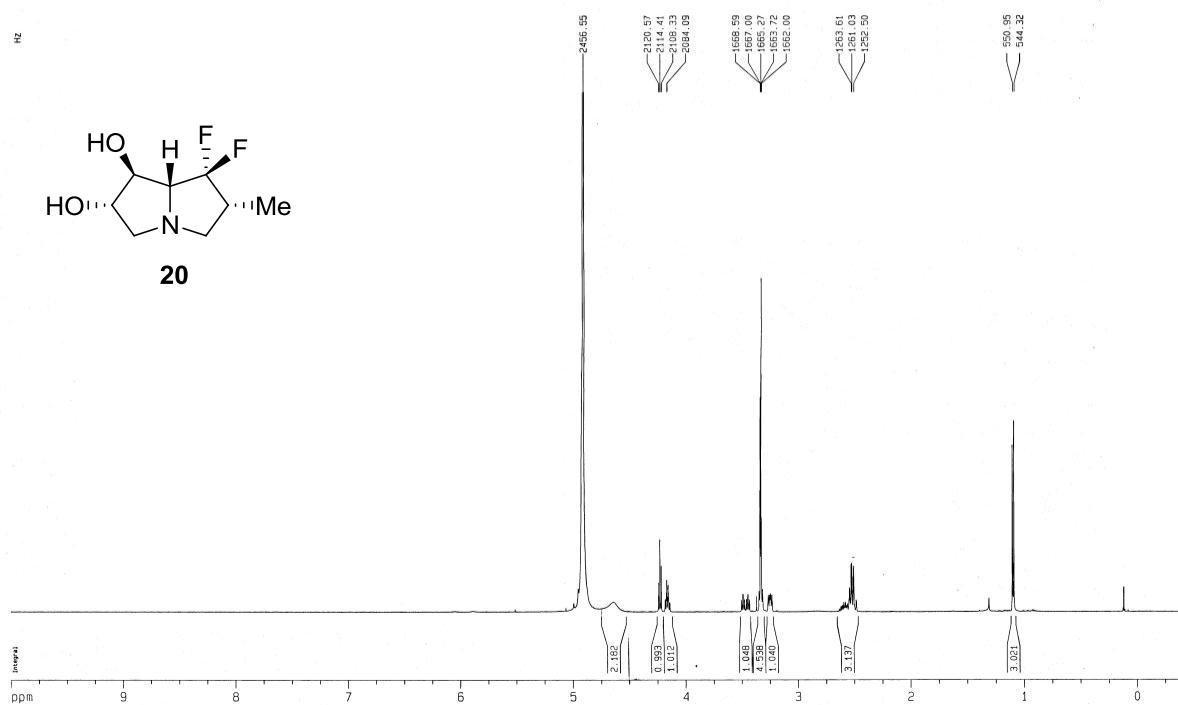
^{13}C NMR Spectrum of *trans*-**19** (125 MHz, CDCl_3)



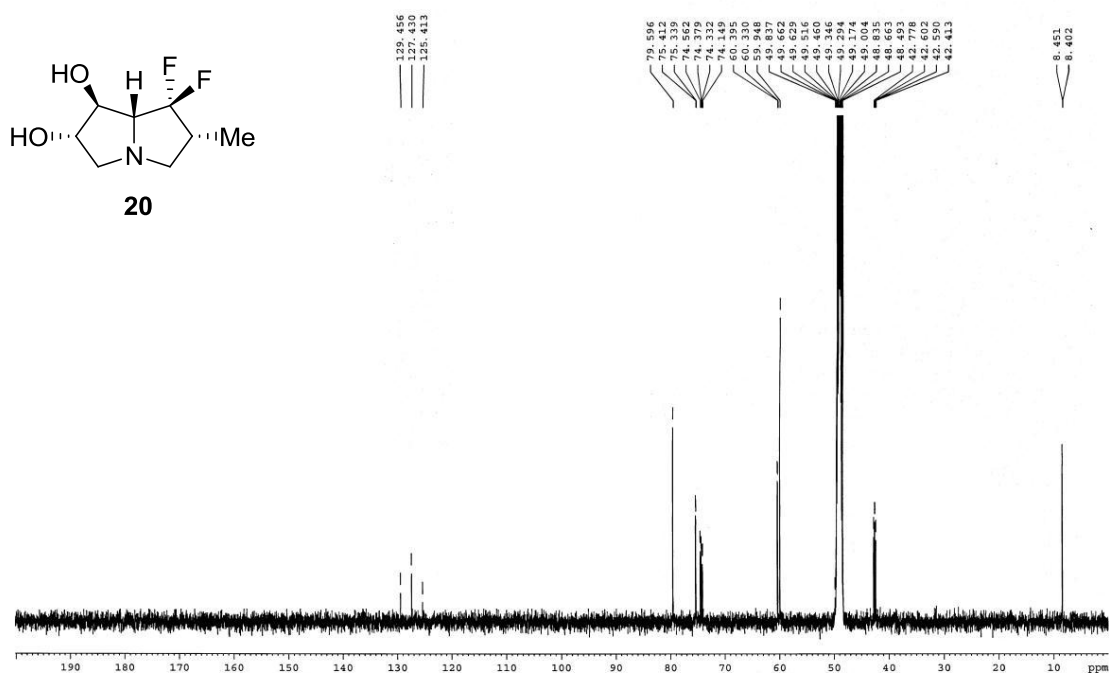
^{19}F NMR Spectrum of *trans*-**19** (470 MHz, CDCl_3)



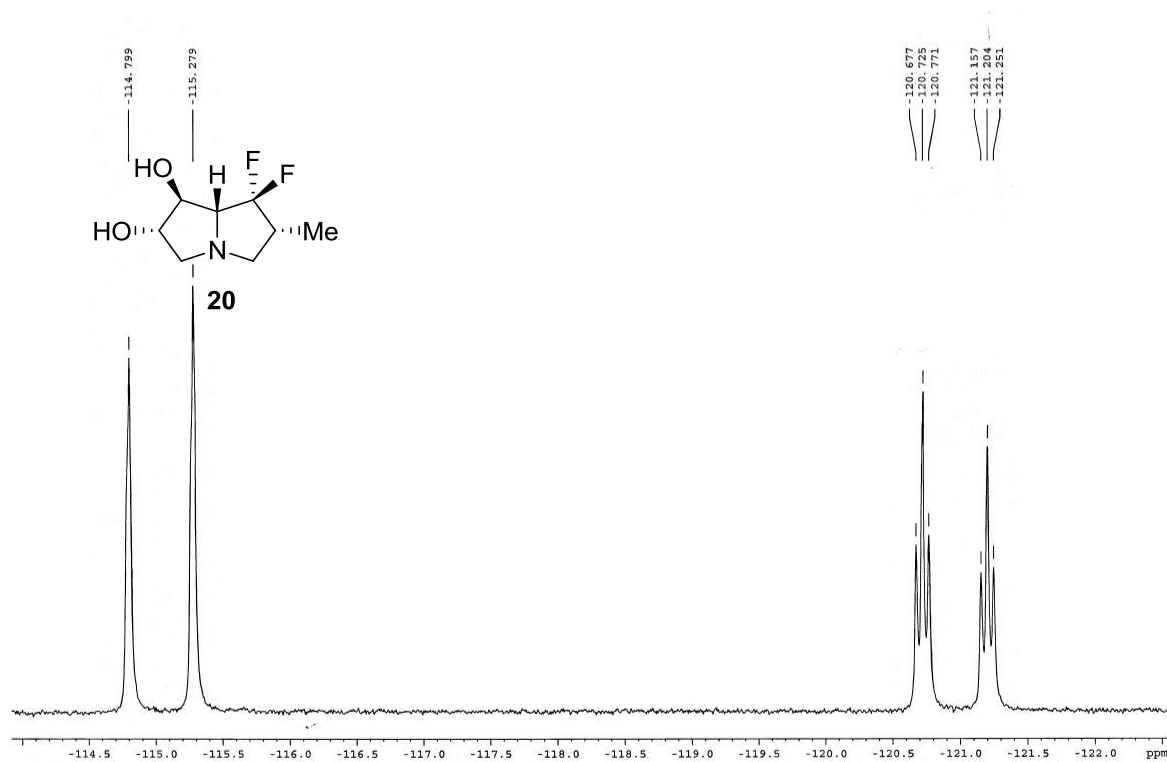
¹H NMR Spectrum of **20** (500 MHz, CD₃OD)



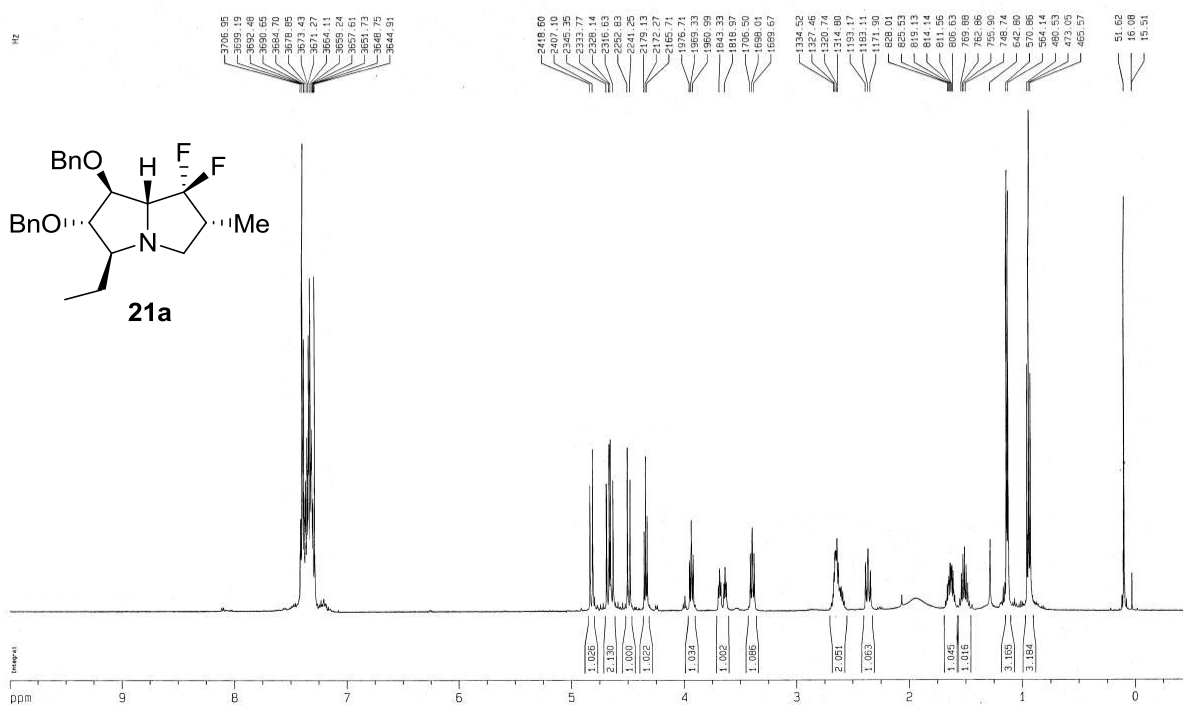
¹³C NMR Spectrum of **20** (125 MHz, CD₃OD)

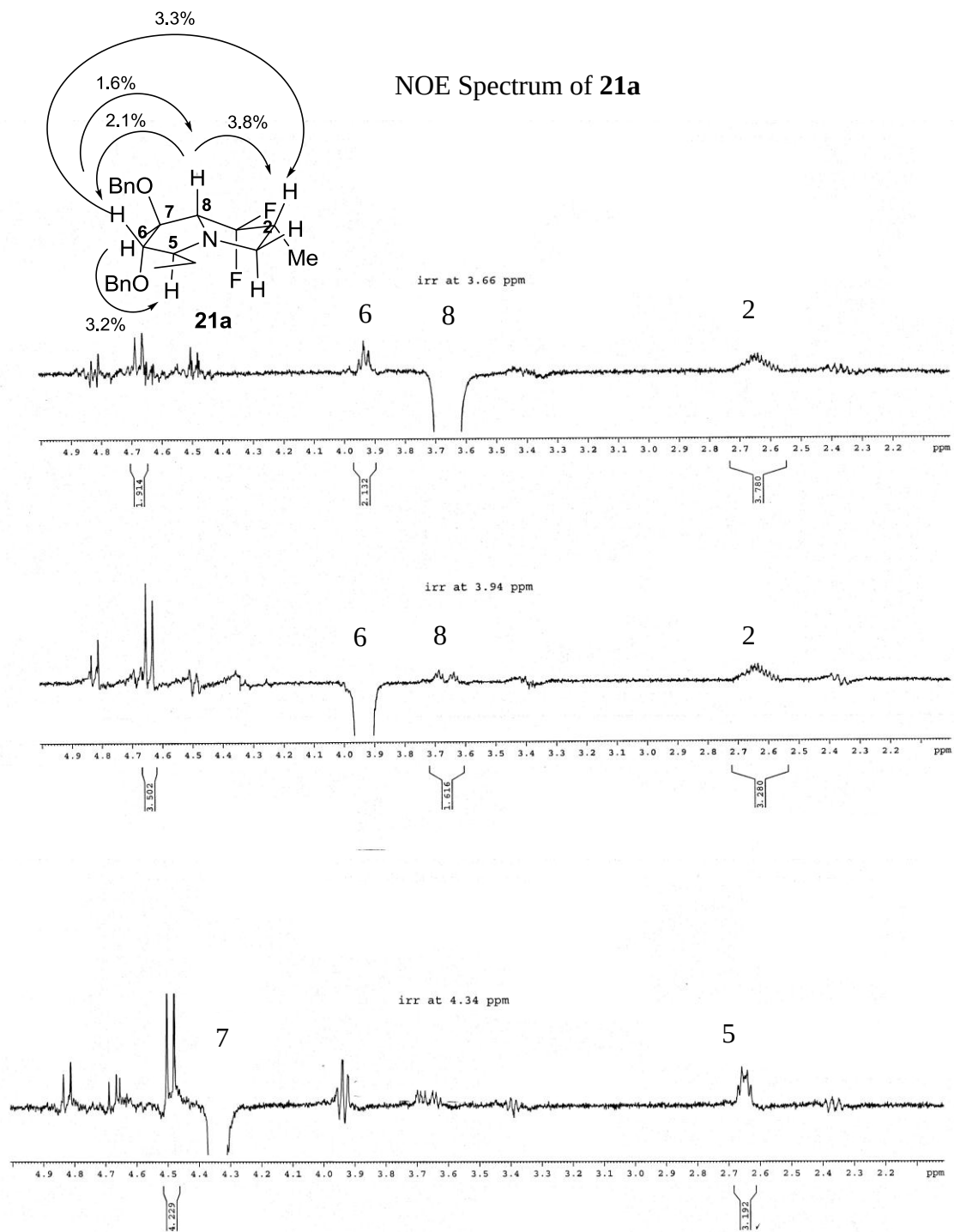


^{19}F NMR Spectrum of **20** (470 MHz, CD_3OD)

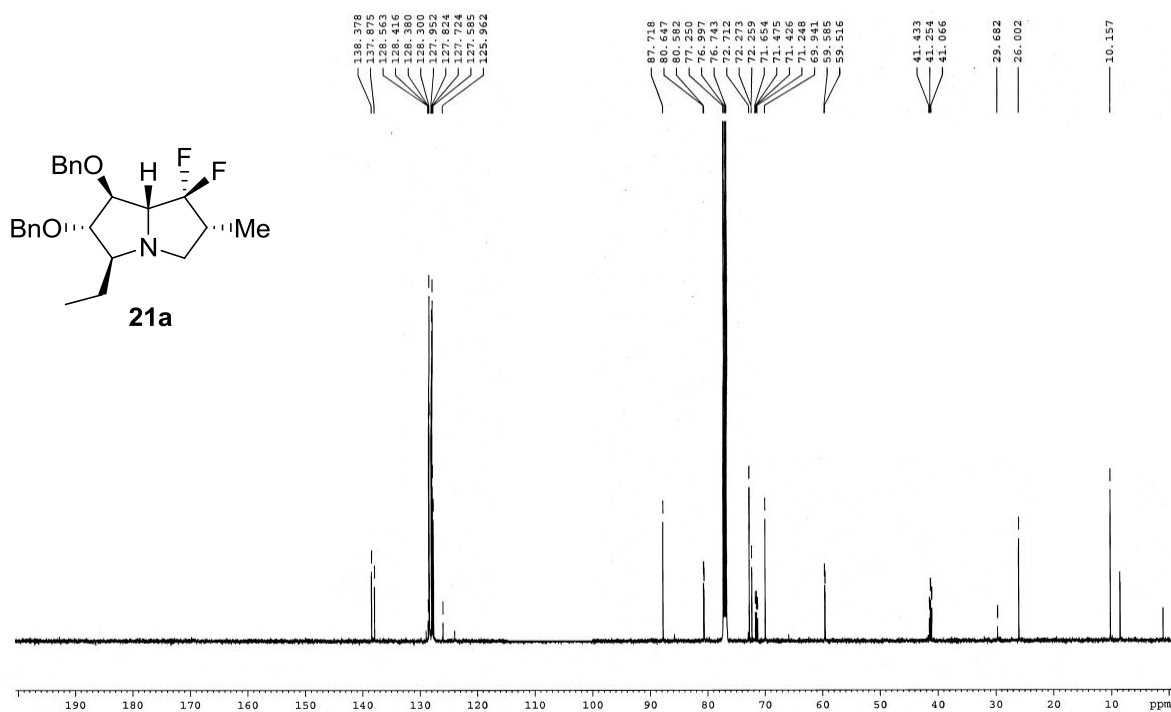


^1H NMR Spectrum of **21a** (500 MHz, CDCl_3)

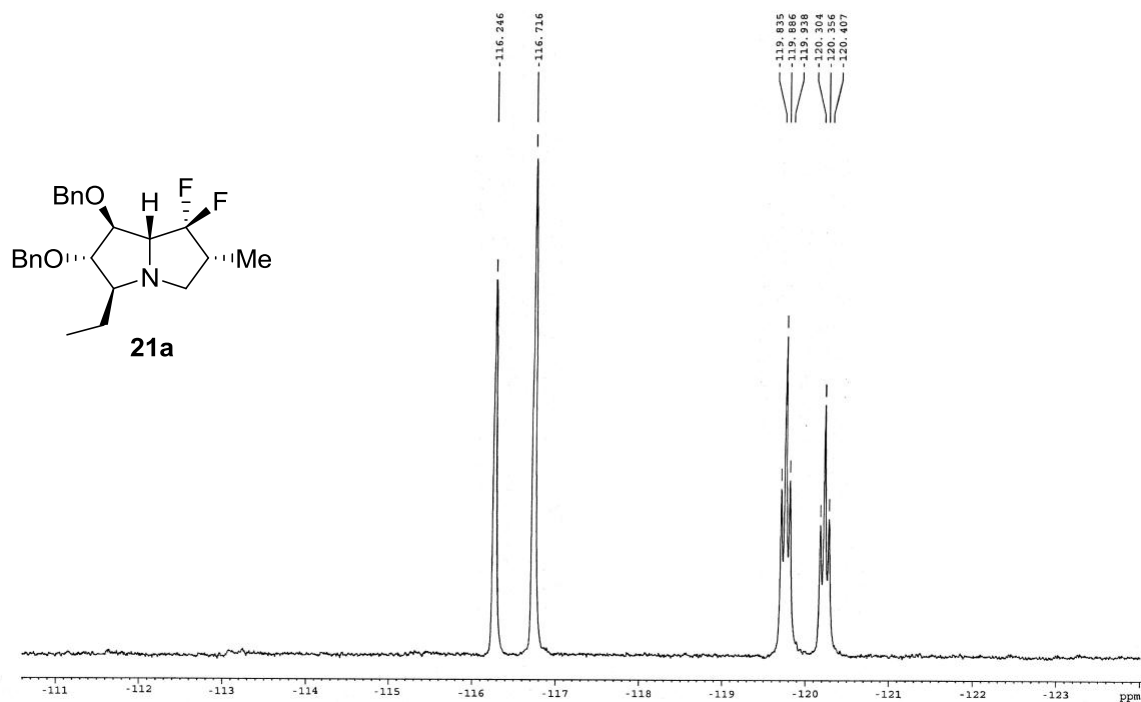




^{13}C NMR Spectrum of **21a** (125 MHz, CDCl_3)



^{19}F NMR Spectrum of **21a** (470 MHz, CDCl_3)



1H NMR spectrum (400 MHz, CDCl₃) of compound 21b.

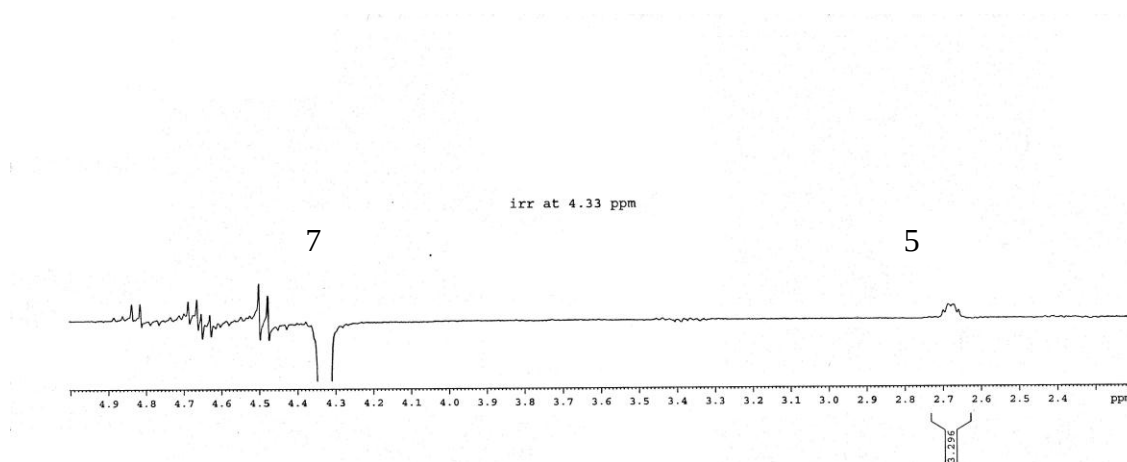
Chemical structure of 21b: CC[C@H]1[C@@H](OC(=O)c2ccccc2)[C@H](OC(=O)c3ccccc3)N1C(F)(F)F

1H NMR data (ppm):

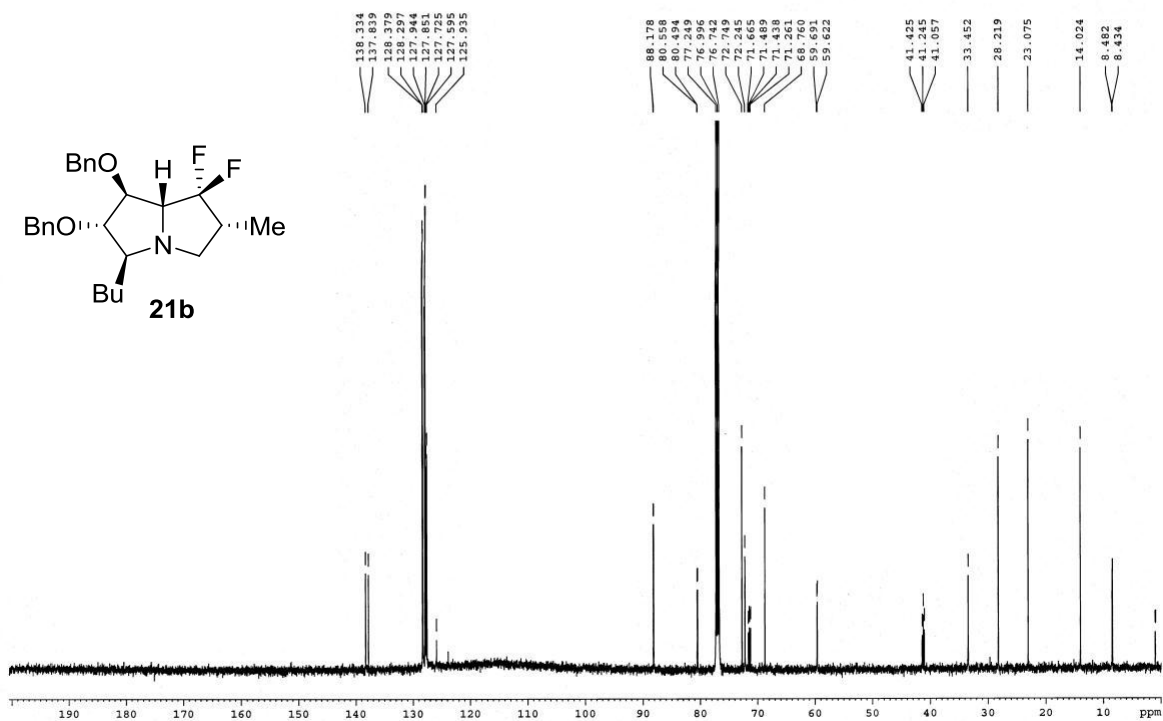
- 7.34 (d, 2H, aromatic)
- 7.27 (d, 2H, aromatic)
- 7.21 (d, 2H, aromatic)
- 7.17 (d, 2H, aromatic)
- 7.13 (d, 2H, aromatic)
- 7.09 (d, 2H, aromatic)
- 7.05 (d, 2H, aromatic)
- 7.01 (d, 2H, aromatic)
- 6.97 (d, 2H, aromatic)
- 6.93 (d, 2H, aromatic)
- 6.89 (d, 2H, aromatic)
- 6.85 (d, 2H, aromatic)
- 6.81 (d, 2H, aromatic)
- 6.77 (d, 2H, aromatic)
- 6.73 (d, 2H, aromatic)
- 6.69 (d, 2H, aromatic)
- 6.65 (d, 2H, aromatic)
- 6.61 (d, 2H, aromatic)
- 6.57 (d, 2H, aromatic)
- 6.53 (d, 2H, aromatic)
- 6.49 (d, 2H, aromatic)
- 6.45 (d, 2H, aromatic)
- 6.41 (d, 2H, aromatic)
- 6.37 (d, 2H, aromatic)
- 6.33 (d, 2H, aromatic)
- 6.29 (d, 2H, aromatic)
- 6.25 (d, 2H, aromatic)
- 6.21 (d, 2H, aromatic)
- 6.17 (d, 2H, aromatic)
- 6.13 (d, 2H, aromatic)
- 6.09 (d, 2H, aromatic)
- 6.05 (d, 2H, aromatic)
- 6.01 (d, 2H, aromatic)
- 5.97 (d, 2H, aromatic)
- 5.93 (d, 2H, aromatic)
- 5.89 (d, 2H, aromatic)
- 5.85 (d, 2H, aromatic)
- 5.81 (d, 2H, aromatic)
- 5.77 (d, 2H, aromatic)
- 5.73 (d, 2H, aromatic)
- 5.69 (d, 2H, aromatic)
- 5.65 (d, 2H, aromatic)
- 5.61 (d, 2H, aromatic)
- 5.57 (d, 2H, aromatic)
- 5.53 (d, 2H, aromatic)
- 5.49 (d, 2H, aromatic)
- 5.45 (d, 2H, aromatic)
- 5.41 (d, 2H, aromatic)
- 5.37 (d, 2H, aromatic)
- 5.33 (d, 2H, aromatic)
- 5.29 (d, 2H, aromatic)
- 5.25 (d, 2H, aromatic)
- 5.21 (d, 2H, aromatic)
- 5.17 (d, 2H, aromatic)
- 5.13 (d, 2H, aromatic)
- 5.09 (d, 2H, aromatic)
- 5.05 (d, 2H, aromatic)
- 5.01 (d, 2H, aromatic)
- 4.97 (d, 2H, aromatic)
- 4.93 (d, 2H, aromatic)
- 4.89 (d, 2H, aromatic)
- 4.85 (d, 2H, aromatic)
- 4.81 (d, 2H, aromatic)
- 4.77 (d, 2H, aromatic)
- 4.73 (d, 2H, aromatic)
- 4.69 (d, 2H, aromatic)
- 4.65 (d, 2H, aromatic)
- 4.61 (d, 2H, aromatic)
- 4.57 (d, 2H, aromatic)
- 4.53 (d, 2H, aromatic)
- 4.49 (d, 2H, aromatic)
- 4.45 (d, 2H, aromatic)
- 4.41 (d, 2H, aromatic)
- 4.37 (d, 2H, aromatic)
- 4.33 (d, 2H, aromatic)
- 4.29 (d, 2H, aromatic)
- 4.25 (d, 2H, aromatic)
- 4.21 (d, 2H, aromatic)
- 4.17 (d, 2H, aromatic)
- 4.13 (d, 2H, aromatic)
- 4.09 (d, 2H, aromatic)
- 4.05 (d, 2H, aromatic)
- 4.01 (d, 2H, aromatic)
- 3.97 (d, 2H, aromatic)
- 3.93 (d, 2H, aromatic)
- 3.89 (d, 2H, aromatic)
- 3.85 (d, 2H, aromatic)
- 3.81 (d, 2H, aromatic)
- 3.77 (d, 2H, aromatic)
- 3.73 (d, 2H, aromatic)
- 3.69 (d, 2H, aromatic)
- 3.65 (d, 2H, aromatic)
- 3.61 (d, 2H, aromatic)
- 3.57 (d, 2H, aromatic)
- 3.53 (d, 2H, aromatic)
- 3.49 (d, 2H, aromatic)
- 3.45 (d, 2H, aromatic)
- 3.41 (d, 2H, aromatic)
- 3.37 (d, 2H, aromatic)
- 3.33 (d, 2H, aromatic)
- 3.29 (d, 2H, aromatic)
- 3.25 (d, 2H, aromatic)
- 3.21 (d, 2H, aromatic)
- 3.17 (d, 2H, aromatic)
- 3.13 (d, 2H, aromatic)
- 3.09 (d, 2H, aromatic)
- 3.05 (d, 2H, aromatic)
- 3.01 (d, 2H, aromatic)
- 2.97 (d, 2H, aromatic)
- 2.93 (d, 2H, aromatic)
- 2.89 (d, 2H, aromatic)
- 2.85 (d, 2H, aromatic)
- 2.81 (d, 2H, aromatic)
- 2.77 (d, 2H, aromatic)
- 2.73 (d, 2H, aromatic)
- 2.69 (d, 2H, aromatic)
- 2.65 (d, 2H, aromatic)
- 2.61 (d, 2H, aromatic)
- 2.57 (d, 2H, aromatic)
- 2.53 (d, 2H, aromatic)
- 2.49 (d, 2H, aromatic)
- 2.45 (d, 2H, aromatic)
- 2.41 (d, 2H, aromatic)
- 2.37 (d, 2H, aromatic)
- 2.33 (d, 2H, aromatic)
- 2.29 (d, 2H, aromatic)
- 2.25 (d, 2H, aromatic)
- 2.21 (d, 2H, aromatic)
- 2.17 (d, 2H, aromatic)
- 2.13 (d, 2H, aromatic)
- 2.09 (d, 2H, aromatic)
- 2.05 (d, 2H, aromatic)
- 2.01 (d, 2H, aromatic)
- 1.97 (d, 2H, aromatic)
- 1.93 (d, 2H, aromatic)
- 1.89 (d, 2H, aromatic)
- 1.85 (d, 2H, aromatic)
- 1.81 (d, 2H, aromatic)
- 1.77 (d, 2H, aromatic)
- 1.73 (d, 2H, aromatic)
- 1.69 (d, 2H, aromatic)
- 1.65 (d, 2H, aromatic)
- 1.61 (d, 2H, aromatic)
- 1.57 (d, 2H, aromatic)
- 1.53 (d, 2H, aromatic)
- 1.49 (d, 2H, aromatic)
- 1.45 (d, 2H, aromatic)
- 1.41 (d, 2H, aromatic)
- 1.37 (d, 2H, aromatic)
- 1.33 (d, 2H, aromatic)
- 1.29 (d, 2H, aromatic)
- 1.25 (d, 2H, aromatic)
- 1.21 (d, 2H, aromatic)
- 1.17 (d, 2H, aromatic)
- 1.13 (d, 2H, aromatic)
- 1.09 (d, 2H, aromatic)
- 1.05 (d, 2H, aromatic)
- 1.01 (d, 2H, aromatic)
- 0.97 (d, 2H, aromatic)
- 0.93 (d, 2H, aromatic)
- 0.89 (d, 2H, aromatic)
- 0.85 (d, 2H, aromatic)
- 0.81 (d, 2H, aromatic)
- 0.77 (d, 2H, aromatic)
- 0.73 (d, 2H, aromatic)
- 0.69 (d, 2H, aromatic)
- 0.65 (d, 2H, aromatic)
- 0.61 (d, 2H, aromatic)
- 0.57 (d, 2H, aromatic)
- 0.53 (d, 2H, aromatic)
- 0.49 (d, 2H, aromatic)
- 0.45 (d, 2H, aromatic)
- 0.41 (d, 2H, aromatic)
- 0.37 (d, 2H, aromatic)
- 0.33 (d, 2H, aromatic)
- 0.29 (d, 2H, aromatic)
- 0.25 (d, 2H, aromatic)
- 0.21 (d, 2H, aromatic)
- 0.17 (d, 2H, aromatic)
- 0.13 (d, 2H, aromatic)
- 0.09 (d, 2H, aromatic)
- 0.05 (d, 2H, aromatic)
- 0.01 (d, 2H, aromatic)



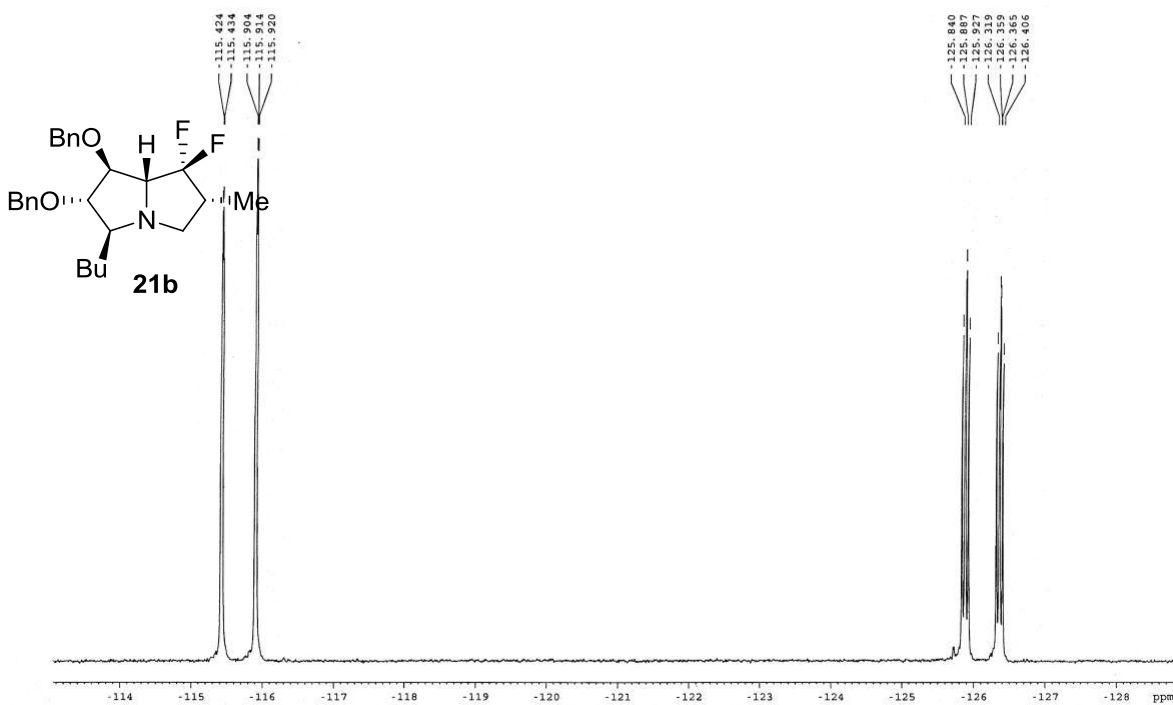
NOE Spectrum of **21b**



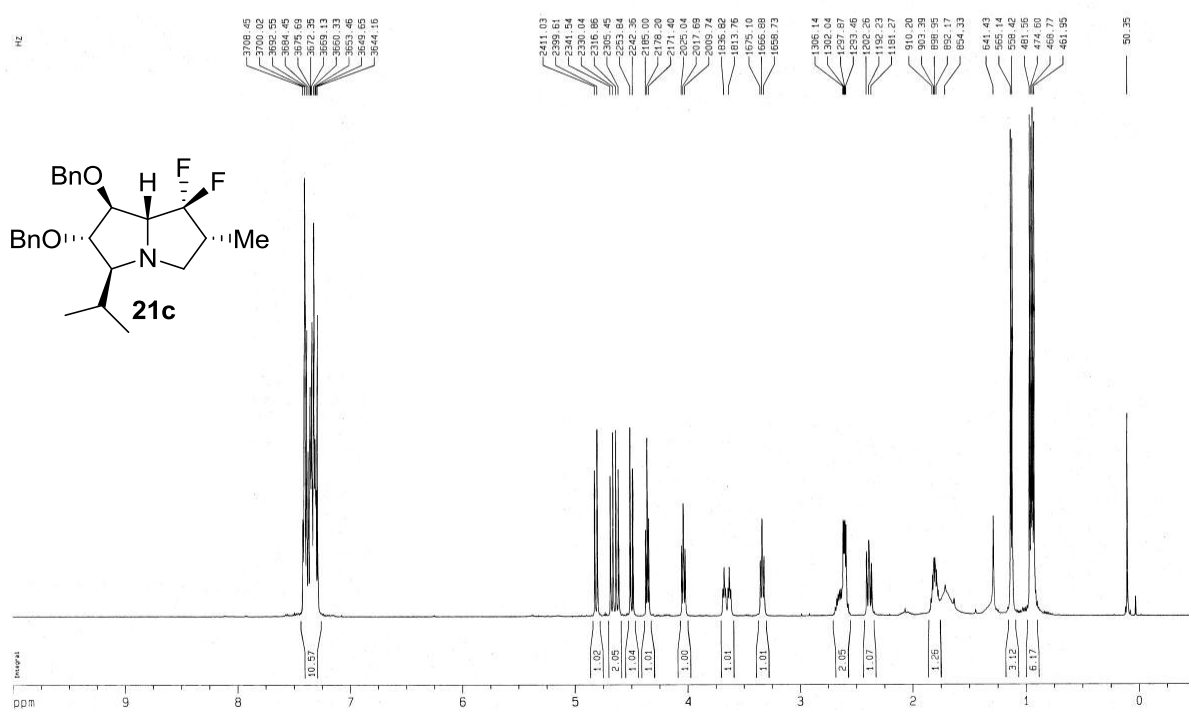
¹³C NMR Spectrum of **21b** (125 MHz, CDCl₃)

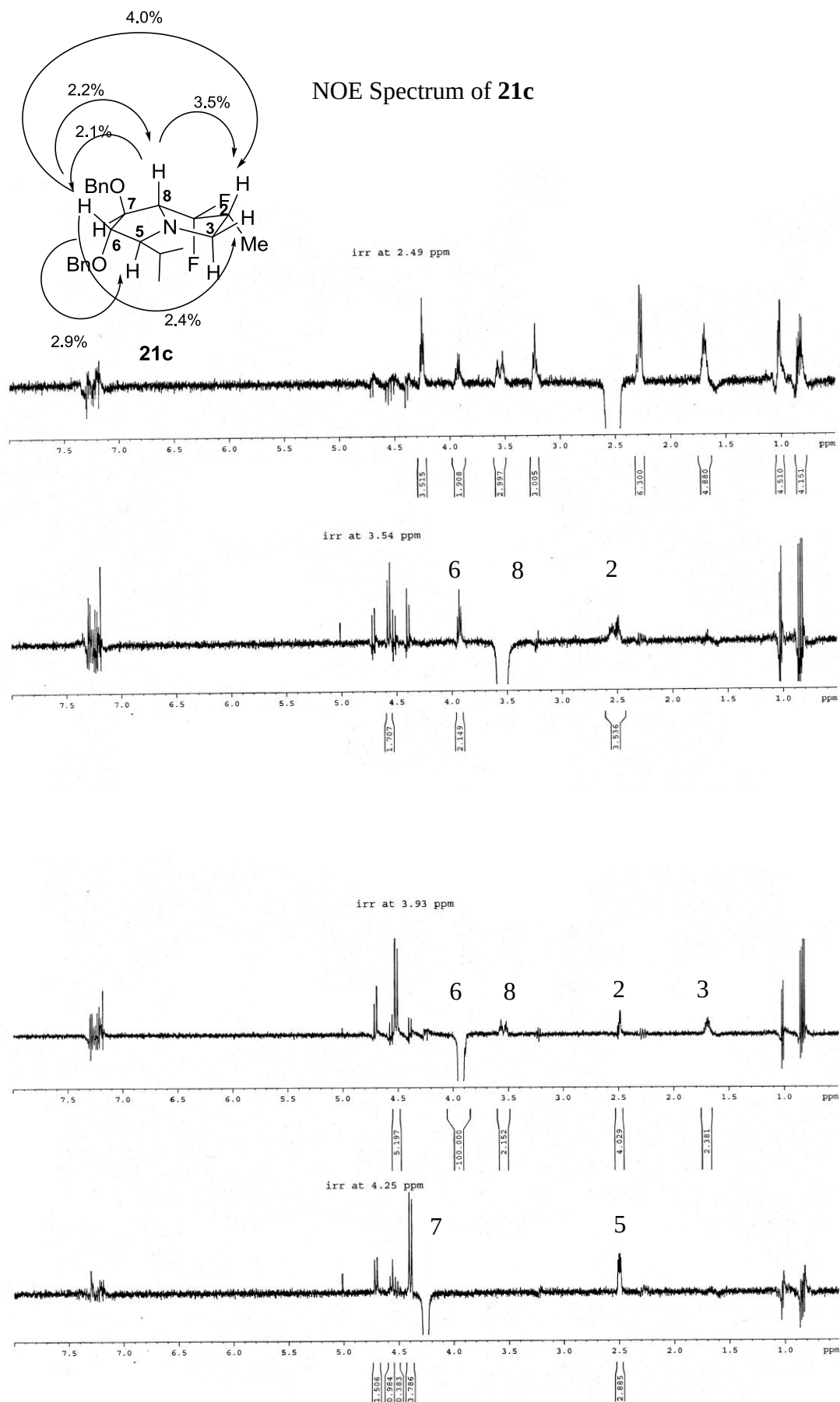


¹⁹F NMR Spectrum of **21b** (470 MHz, CDCl₃)

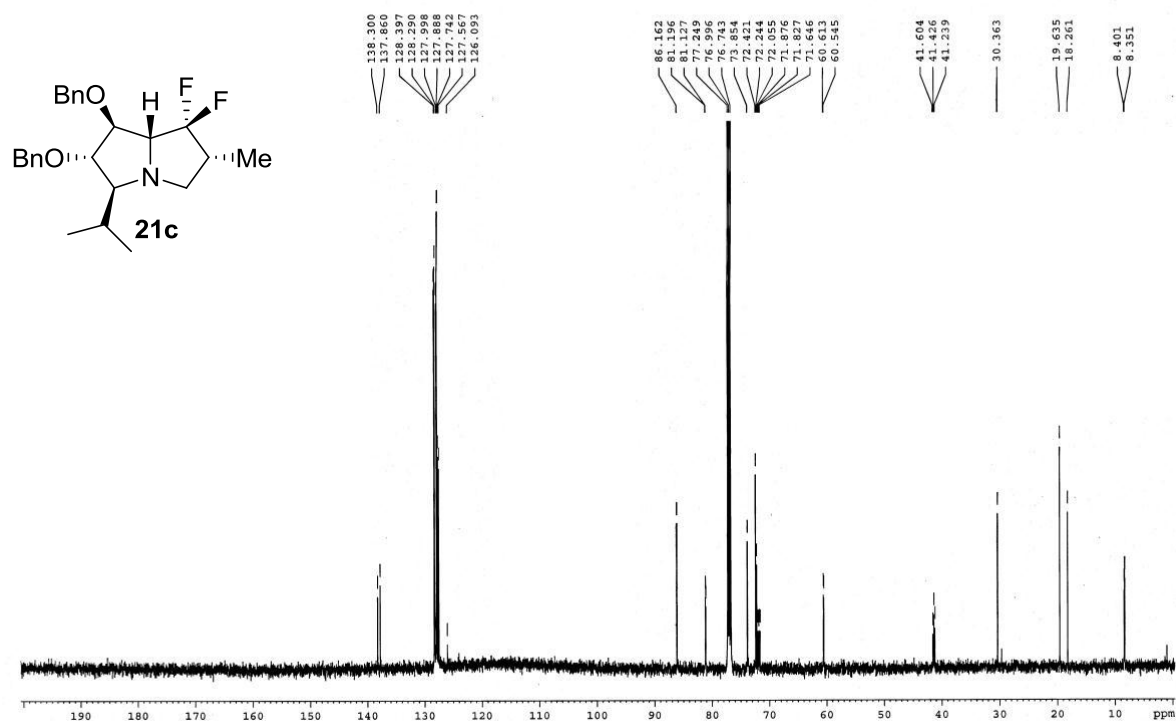


¹H NMR Spectrum of **21c** (500 MHz, CDCl₃)

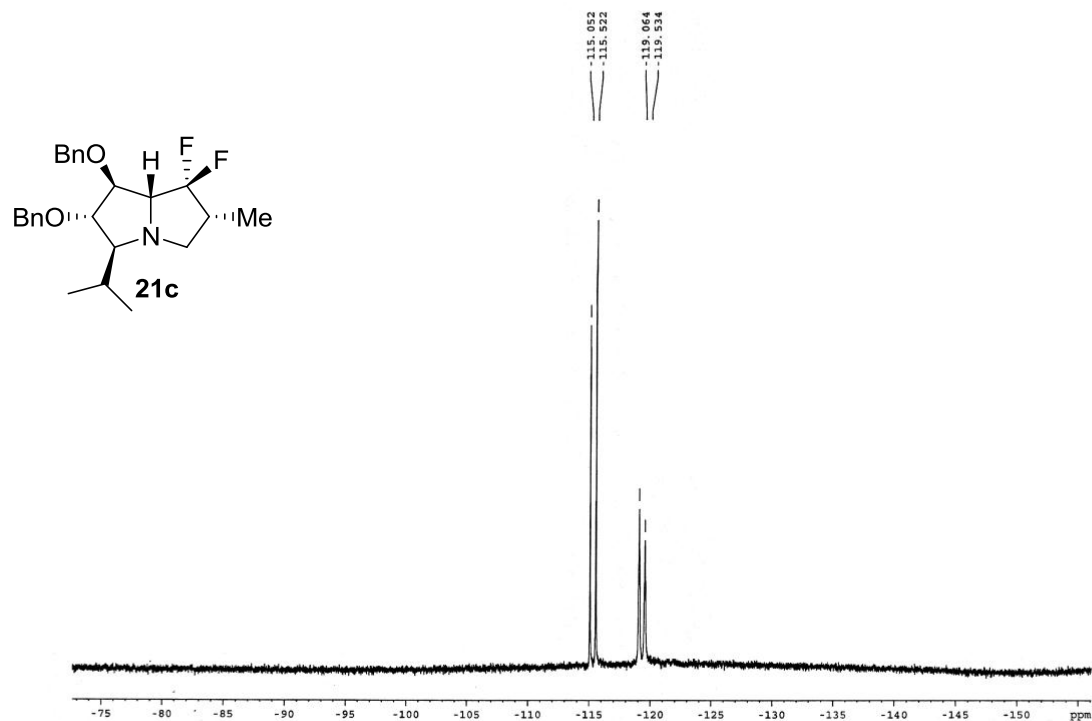




^{13}C NMR Spectrum of **21c** (125 MHz, CDCl_3)



^{19}F NMR Spectrum of **21c** (470 MHz, CDCl_3)



CCCC1=C(C)C(=O)N1C(=O)OC2=CC=CC=C2

22b

¹H NMR spectrum (CDCl₃) of compound **22b**. The spectrum displays peaks corresponding to the structure, with integrations and chemical shifts (ppm) indicated.

Chemical Shift (ppm)	Integration
7.714, 7.707, 7.703, 7.703, 7.696, 7.692, 7.686, 7.674, 7.671, 7.668, 7.661, 7.644	4.280, 1.097
6.399	0.959
5.002	2.002
4.063	1.063
3.680	1.080
3.045	1.045
2.115	2.115
1.983, 1.980, 1.976, 1.972, 1.968, 1.954, 1.950, 1.946, 1.939, 1.935, 1.929, 1.917, 1.913, 1.909	2.433, 5.220
1.639, 1.635, 1.631, 1.627, 1.623, 1.619, 1.615, 1.611, 1.607, 1.603, 1.599, 1.595, 1.591, 1.587, 1.583, 1.579, 1.575, 1.571, 1.567, 1.563, 1.559, 1.555, 1.551, 1.547, 1.543, 1.539, 1.535, 1.531, 1.527, 1.523, 1.519, 1.515, 1.511, 1.507, 1.503, 1.499, 1.495, 1.491, 1.487, 1.483, 1.479, 1.475, 1.471, 1.467, 1.463, 1.459, 1.455, 1.451, 1.447, 1.443, 1.439, 1.435, 1.431, 1.427, 1.423, 1.419, 1.415, 1.411, 1.407, 1.403, 1.399, 1.395, 1.391, 1.387, 1.383, 1.379, 1.375, 1.371, 1.367, 1.363, 1.359, 1.355, 1.351, 1.347, 1.343, 1.339, 1.335, 1.331, 1.327, 1.323, 1.319, 1.315, 1.311, 1.307, 1.303, 1.299, 1.295, 1.291, 1.287, 1.283, 1.279, 1.275, 1.271, 1.267, 1.263, 1.259, 1.255, 1.251, 1.247, 1.243, 1.239, 1.235, 1.231, 1.227, 1.223, 1.219, 1.215, 1.211, 1.207, 1.203, 1.199, 1.195, 1.191, 1.187, 1.183, 1.179, 1.175, 1.171, 1.167, 1.163, 1.159, 1.155, 1.151, 1.147, 1.143, 1.139, 1.135, 1.131, 1.127, 1.123, 1.119, 1.115, 1.111, 1.107, 1.103, 1.099, 1.095, 1.091, 1.087, 1.083, 1.079, 1.075, 1.071, 1.067, 1.063, 1.059, 1.055, 1.051, 1.047, 1.043, 1.039, 1.035, 1.031, 1.027, 1.023, 1.019, 1.015, 1.011, 1.007, 1.003, 0.999, 0.995, 0.991, 0.987, 0.983, 0.979, 0.975, 0.971, 0.967, 0.963, 0.959, 0.955, 0.951, 0.947, 0.943, 0.939, 0.935, 0.931, 0.927, 0.923, 0.919, 0.915, 0.911, 0.907, 0.903, 0.899, 0.895, 0.891, 0.887, 0.883, 0.879, 0.875, 0.871, 0.867, 0.863, 0.859, 0.855, 0.851, 0.847, 0.843, 0.839, 0.835, 0.831, 0.827, 0.823, 0.819, 0.815, 0.811, 0.807, 0.803, 0.799, 0.795, 0.791, 0.787, 0.783, 0.779, 0.775, 0.771, 0.767, 0.763, 0.759, 0.755, 0.751, 0.747, 0.743, 0.739, 0.735, 0.731, 0.727, 0.723, 0.719, 0.715, 0.711, 0.707, 0.703, 0.699, 0.695, 0.691, 0.687, 0.683, 0.679, 0.675, 0.671, 0.667, 0.663, 0.659, 0.655, 0.651, 0.647, 0.643, 0.639, 0.635, 0.631, 0.627, 0.623, 0.619, 0.615, 0.611, 0.607, 0.603, 0.599, 0.595, 0.591, 0.587, 0.583, 0.579, 0.575, 0.571, 0.567, 0.563, 0.559, 0.555, 0.551, 0.547, 0.543, 0.539, 0.535, 0.531, 0.527, 0.523, 0.519, 0.515, 0.511, 0.507, 0.503, 0.499, 0.495, 0.491, 0.487, 0.483, 0.479, 0.475, 0.471, 0.467, 0.463, 0.459, 0.455, 0.451, 0.447, 0.443, 0.439, 0.435, 0.431, 0.427, 0.423, 0.419, 0.415, 0.411, 0.407, 0.403, 0.399, 0.395, 0.391, 0.387, 0.383, 0.379, 0.375, 0.371, 0.367, 0.363, 0.359, 0.355, 0.351, 0.347, 0.343, 0.339, 0.335, 0.331, 0.327, 0.323, 0.319, 0.315, 0.311, 0.307, 0.303, 0.299, 0.295, 0.291, 0.287, 0.283, 0.279, 0.275, 0.271, 0.267, 0.263, 0.259, 0.255, 0.251, 0.247, 0.243, 0.239, 0.235, 0.231, 0.227, 0.223, 0.219, 0.215, 0.211, 0.207, 0.203, 0.199, 0.195, 0.191, 0.187, 0.183, 0.179, 0.175, 0.171, 0.167, 0.163, 0.159, 0.155, 0.151, 0.147, 0.143, 0.139, 0.135, 0.131, 0.127, 0.123, 0.119, 0.115, 0.111, 0.107, 0.103, 0.099, 0.095, 0.091, 0.087, 0.083, 0.079, 0.075, 0.071, 0.067, 0.063, 0.059, 0.055, 0.051, 0.047, 0.043, 0.039, 0.035, 0.031, 0.027, 0.023, 0.019, 0.015, 0.011, 0.007, 0.003, 0.000	3.145

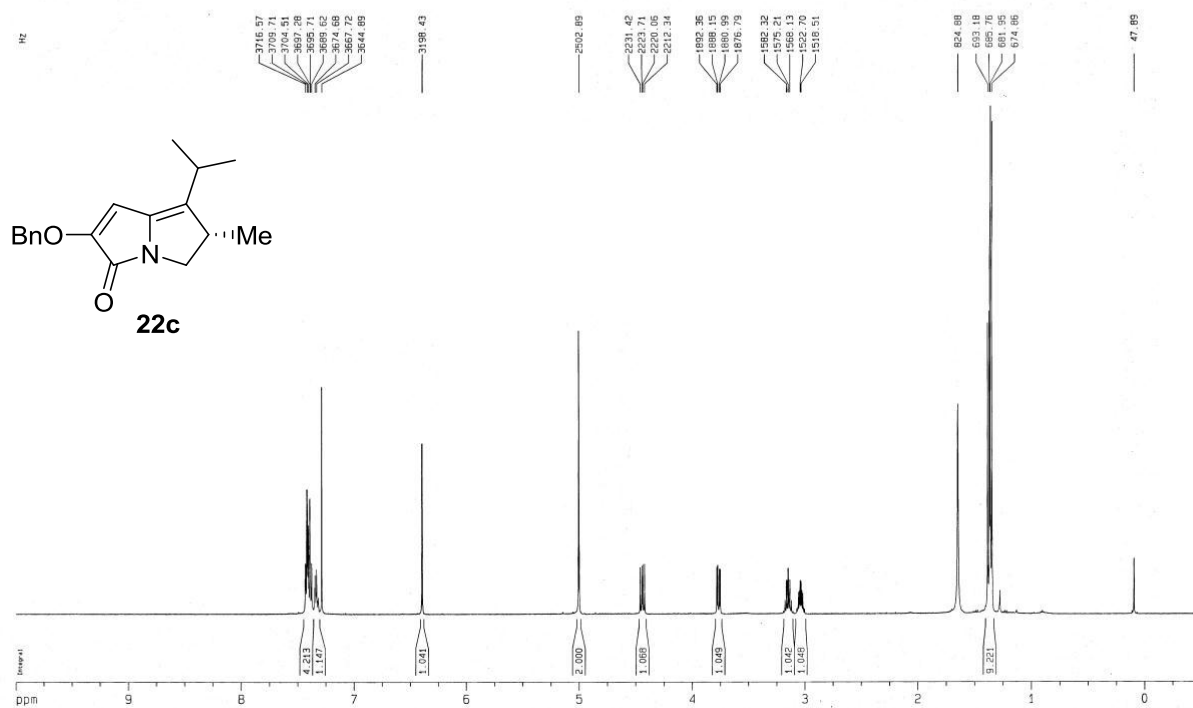
22b

CCCC1=C(C)C2C(=O)C(=C1)C(=O)C2C3CCCCC3

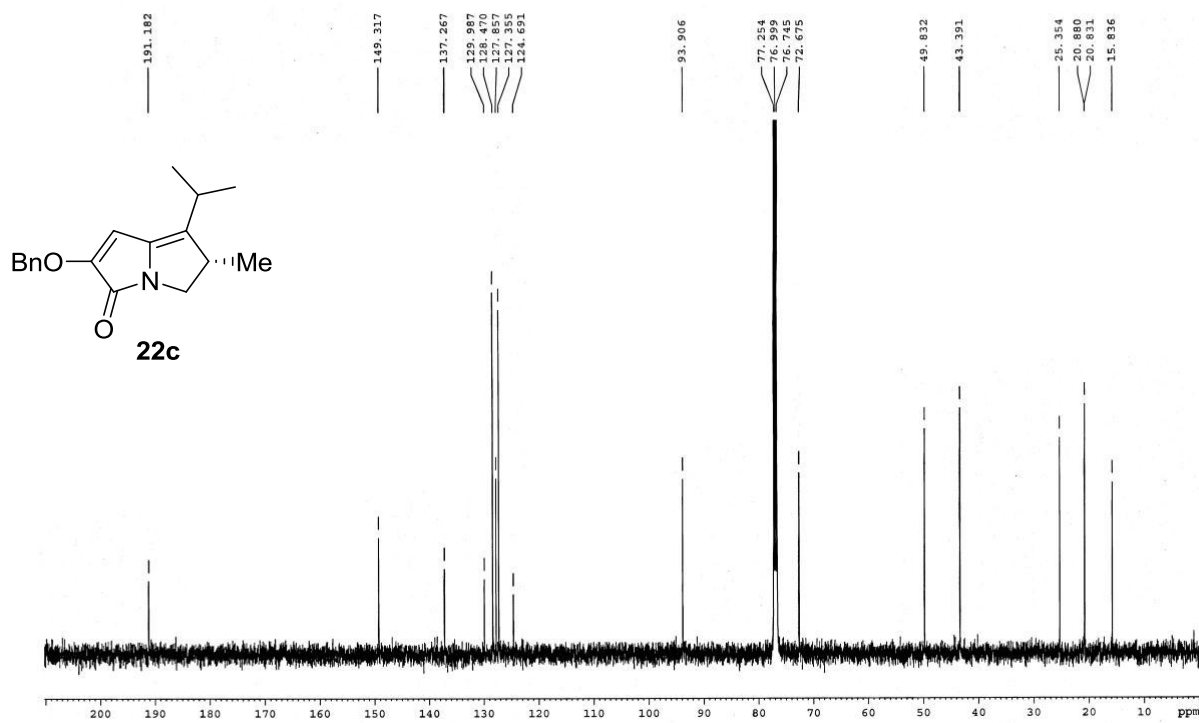
13C NMR (CDCl₃): 191.214, 149.893, 137.362, 128.466, 127.896, 127.841, 125.543, 124.885, 93.686, 77.251, 76.988, 76.741, 72.716, 49.039, 43.364, 30.466, 23.322, 22.436, 15.887, 13.778.

Chemical structure of **22b** is shown above the spectrum.

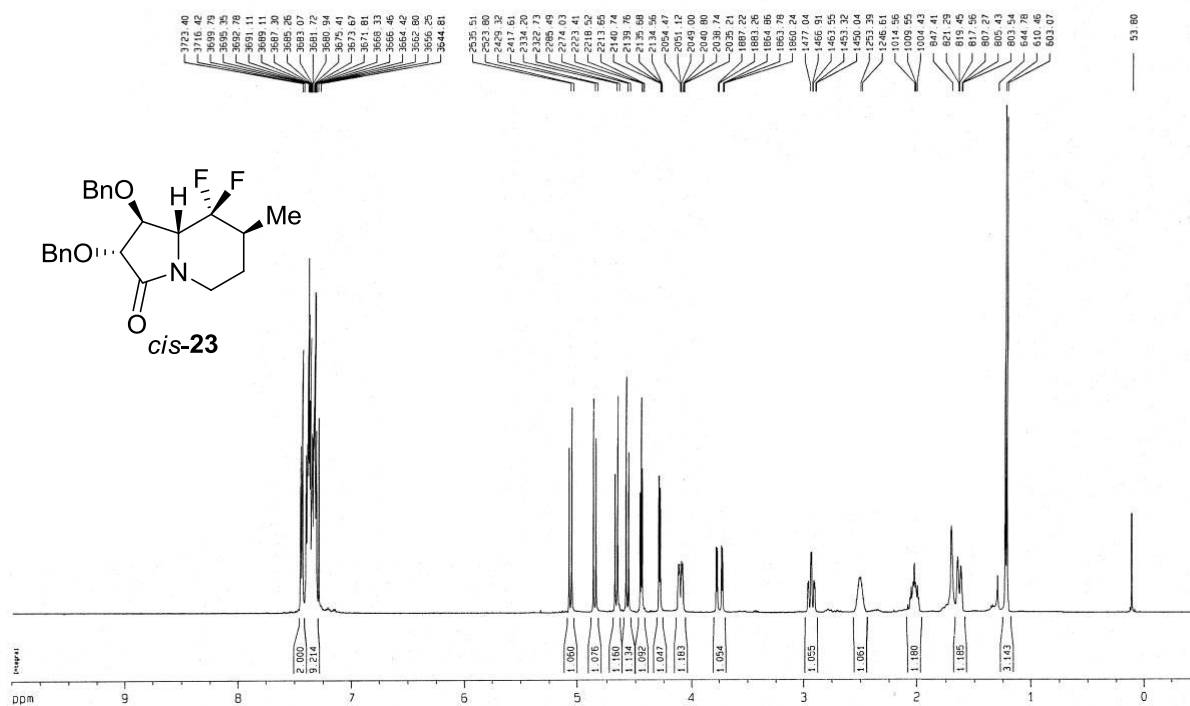
¹H NMR Spectrum of **22c** (500 MHz, CDCl₃)



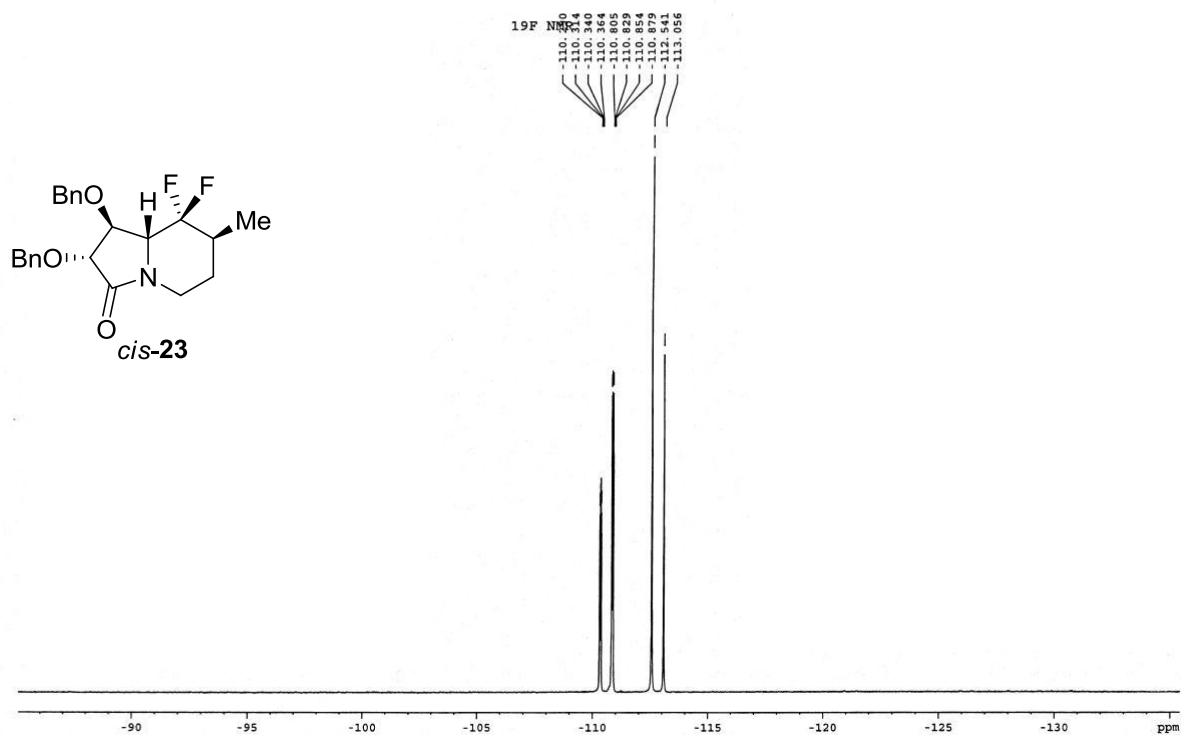
¹³C NMR Spectrum of **22c** (125 MHz, CDCl₃)



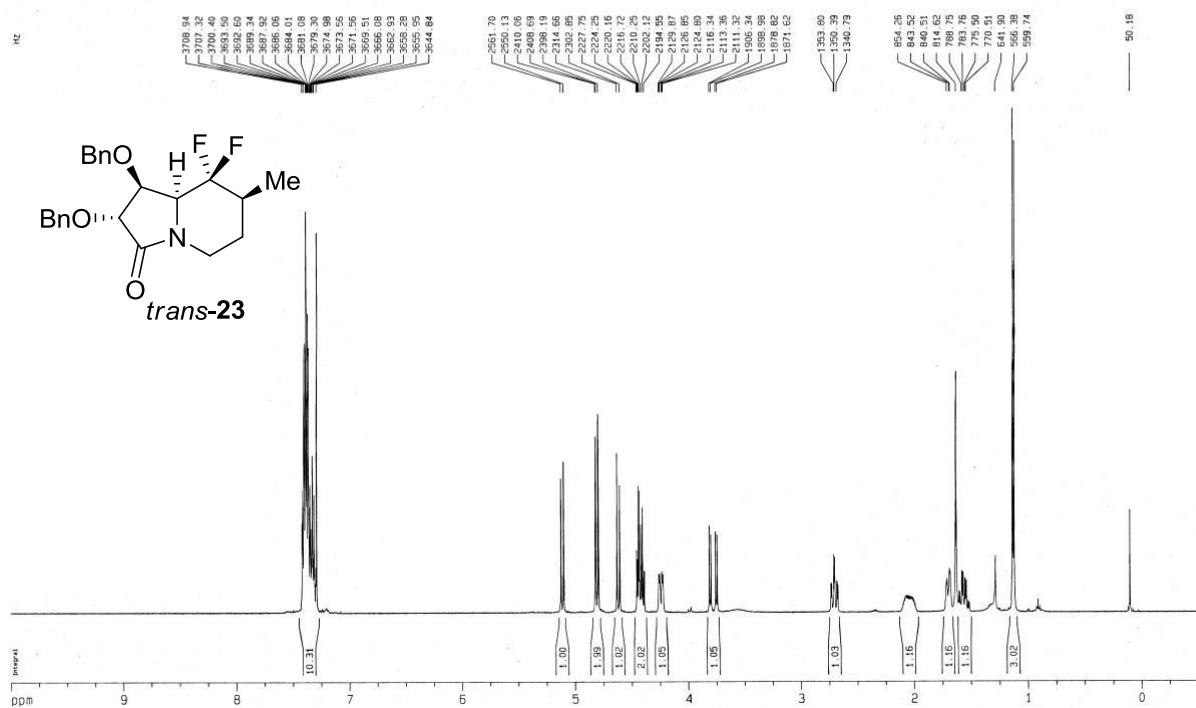
¹H NMR Spectrum of *cis*-23 (500 MHz, CDCl₃)

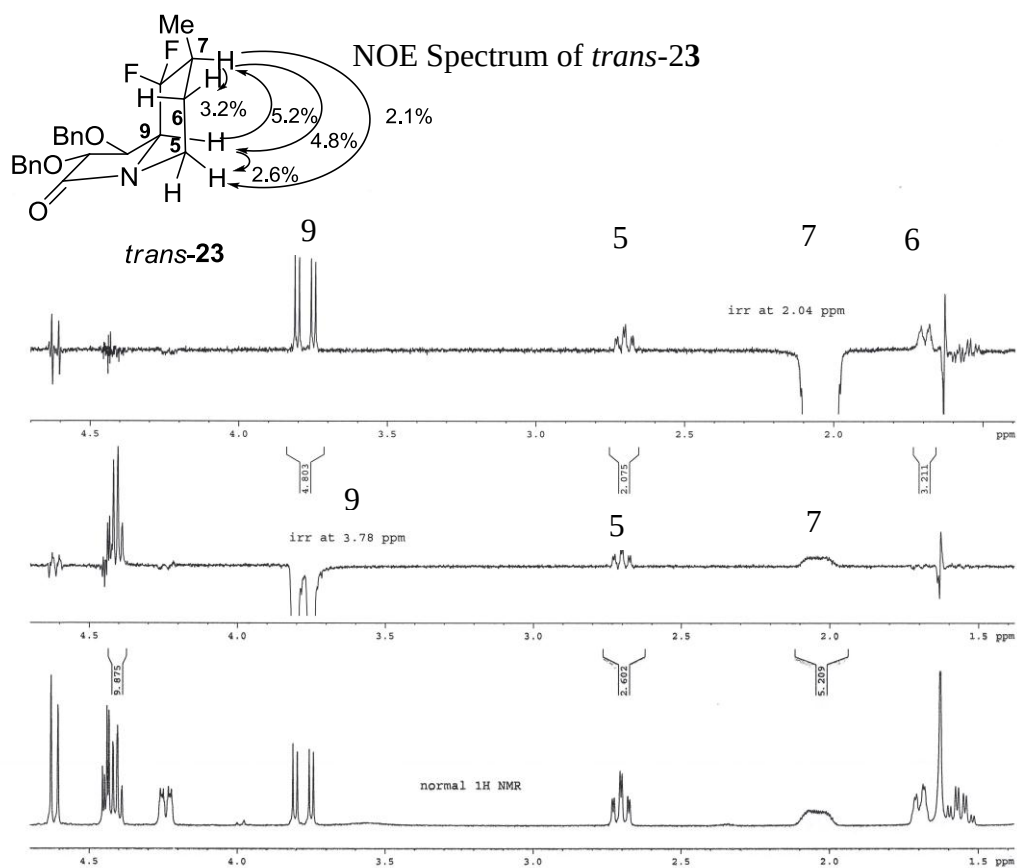


^{19}F NMR Spectrum of *cis*-23 (470 MHz, CDCl_3)

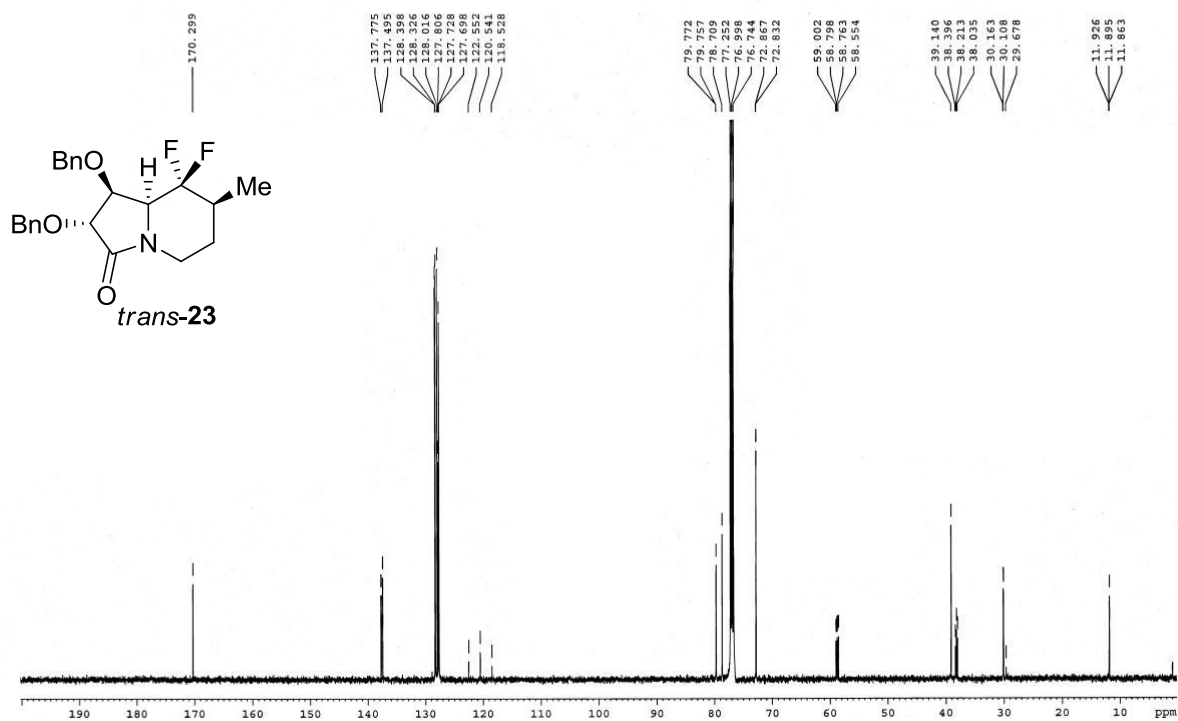


^1H NMR Spectrum of *trans*-23 (500 MHz, CDCl_3)

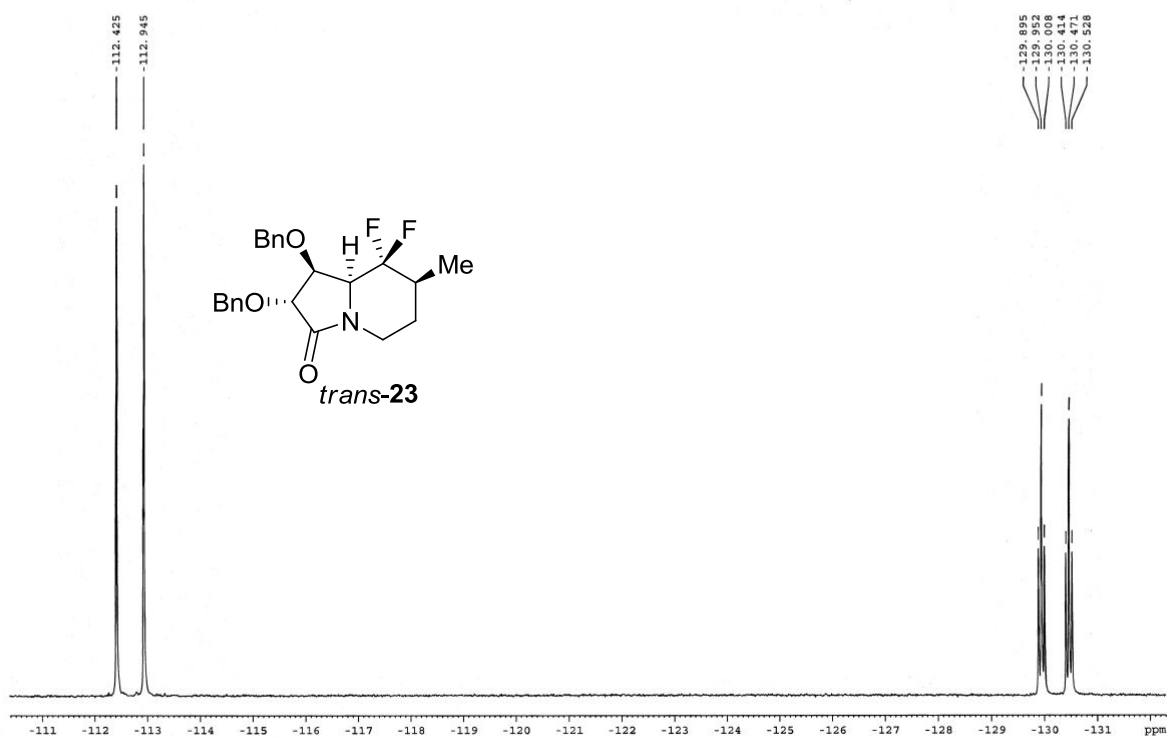




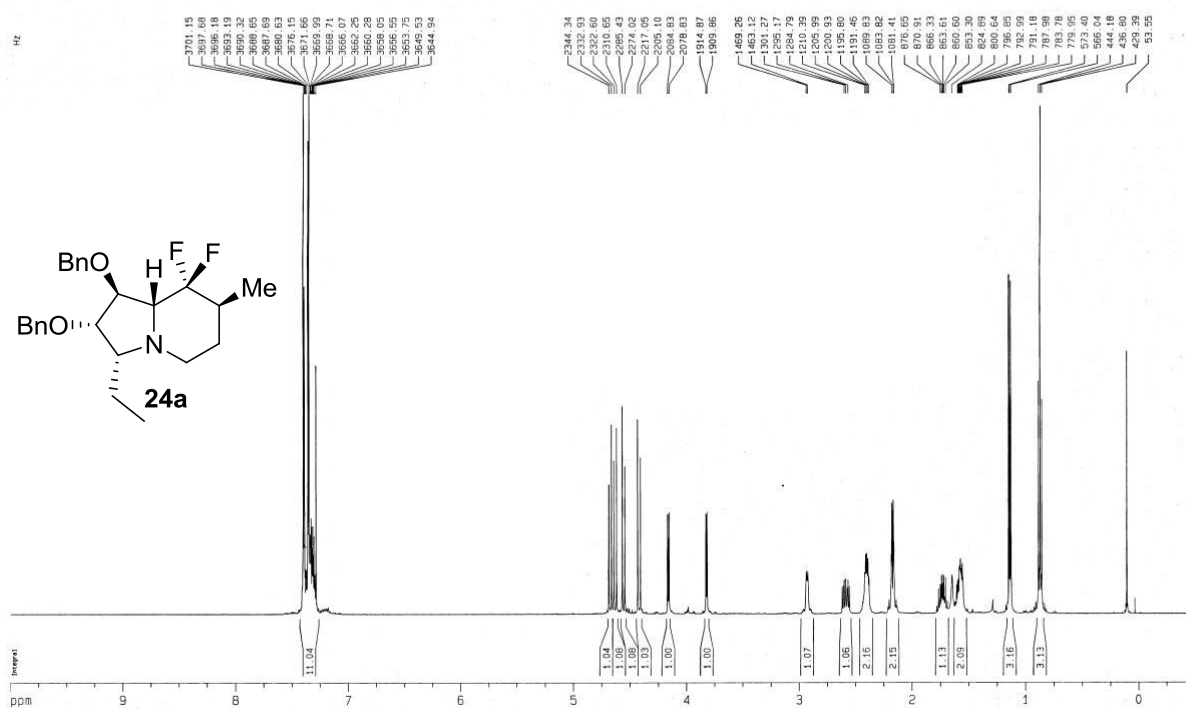
^{13}C NMR Spectrum of *trans*-23 (125 MHz, CDCl_3)



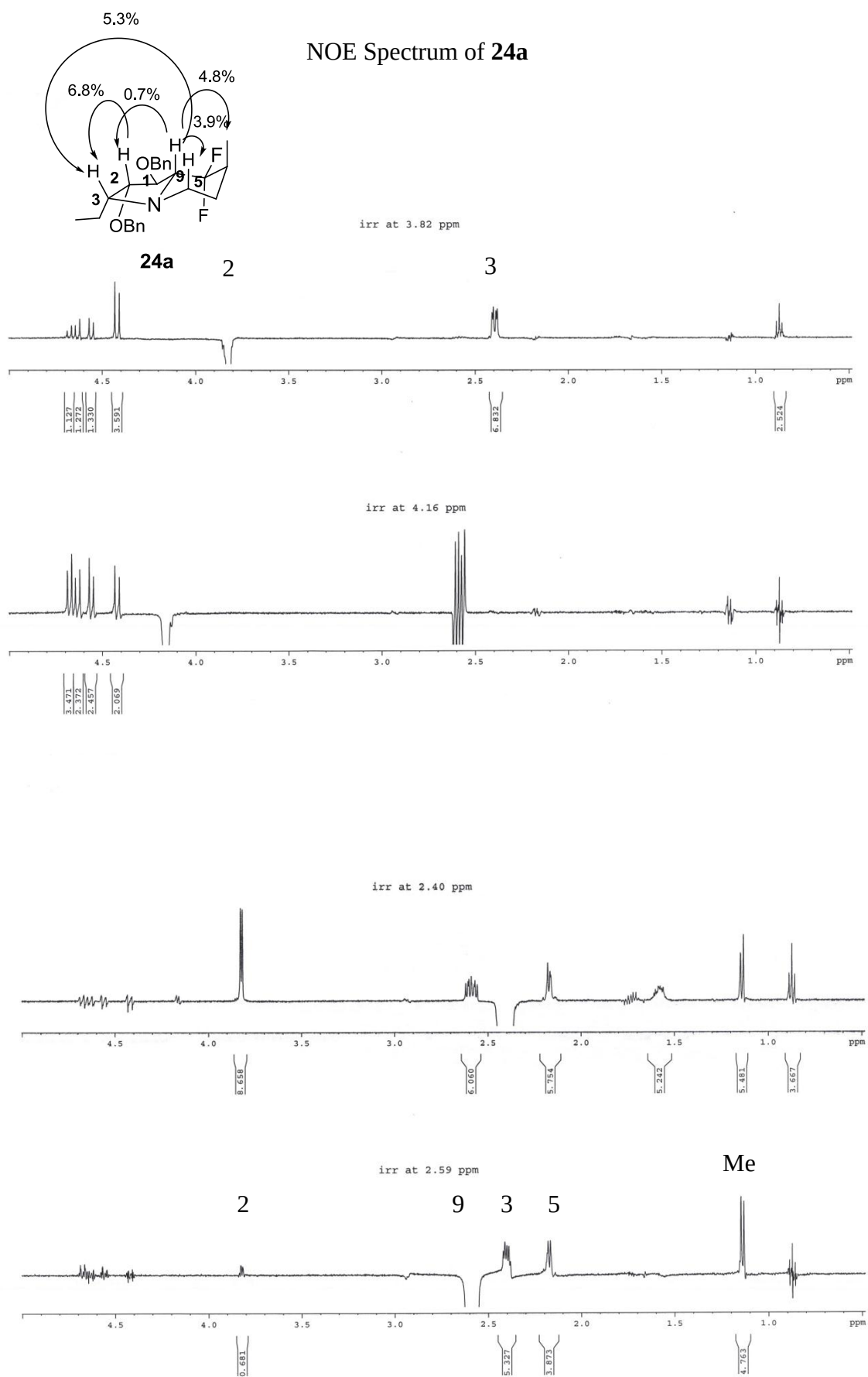
^{19}F NMR Spectrum of *trans*-23 (470 MHz, CDCl_3)



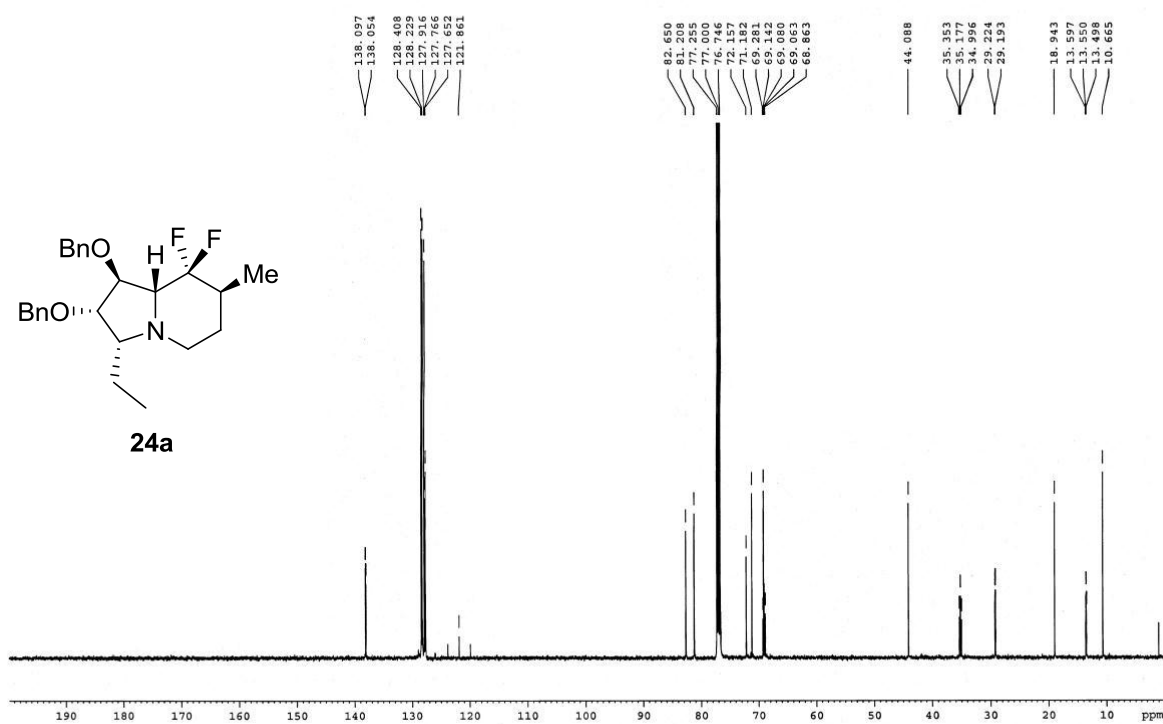
^1H NMR Spectrum of 24a (500 MHz, CDCl_3)



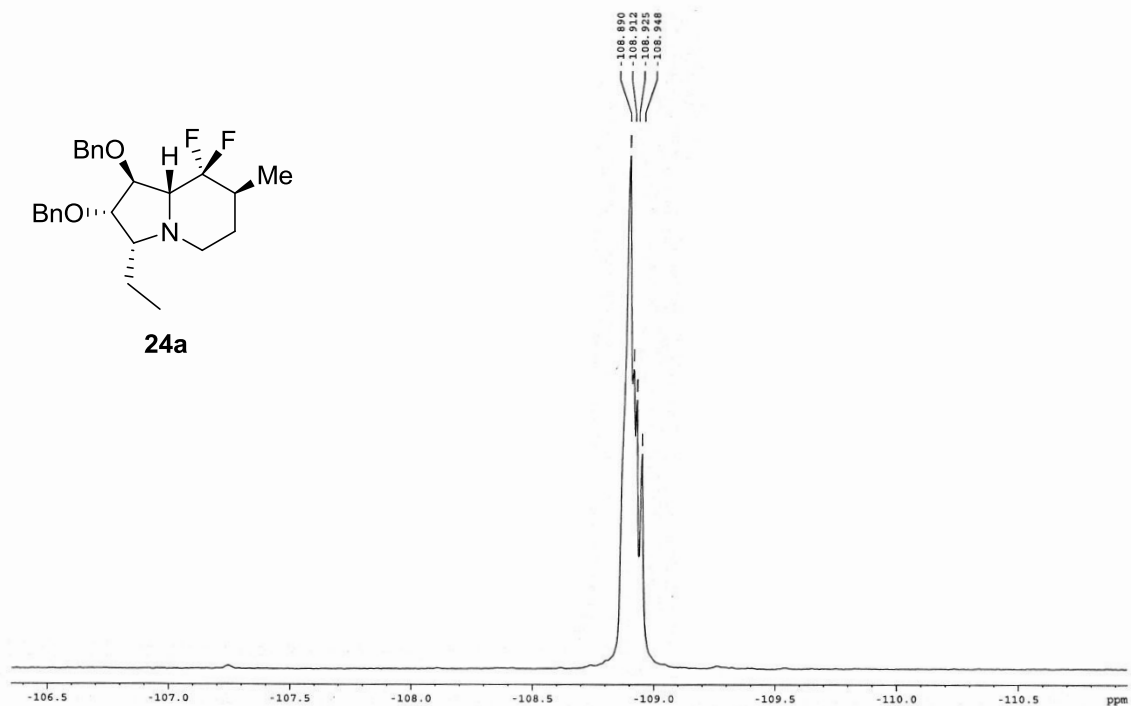
NOE Spectrum of 24a



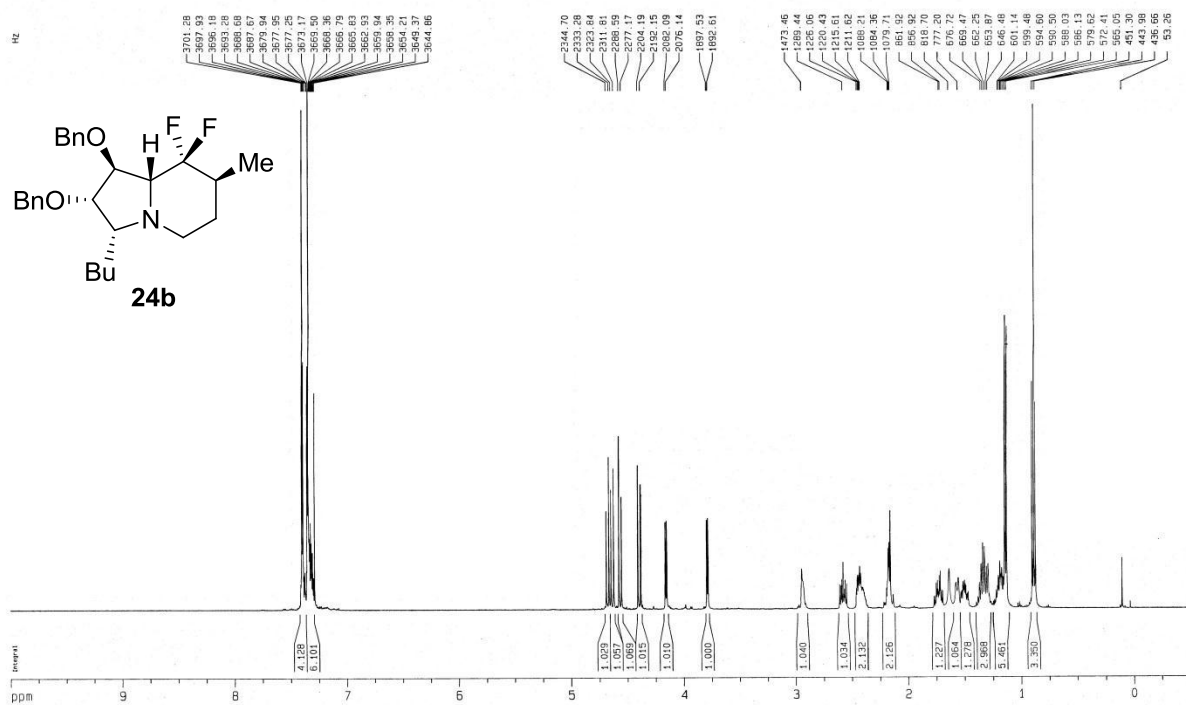
¹³C NMR Spectrum of **24a** (125 MHz, CDCl₃)



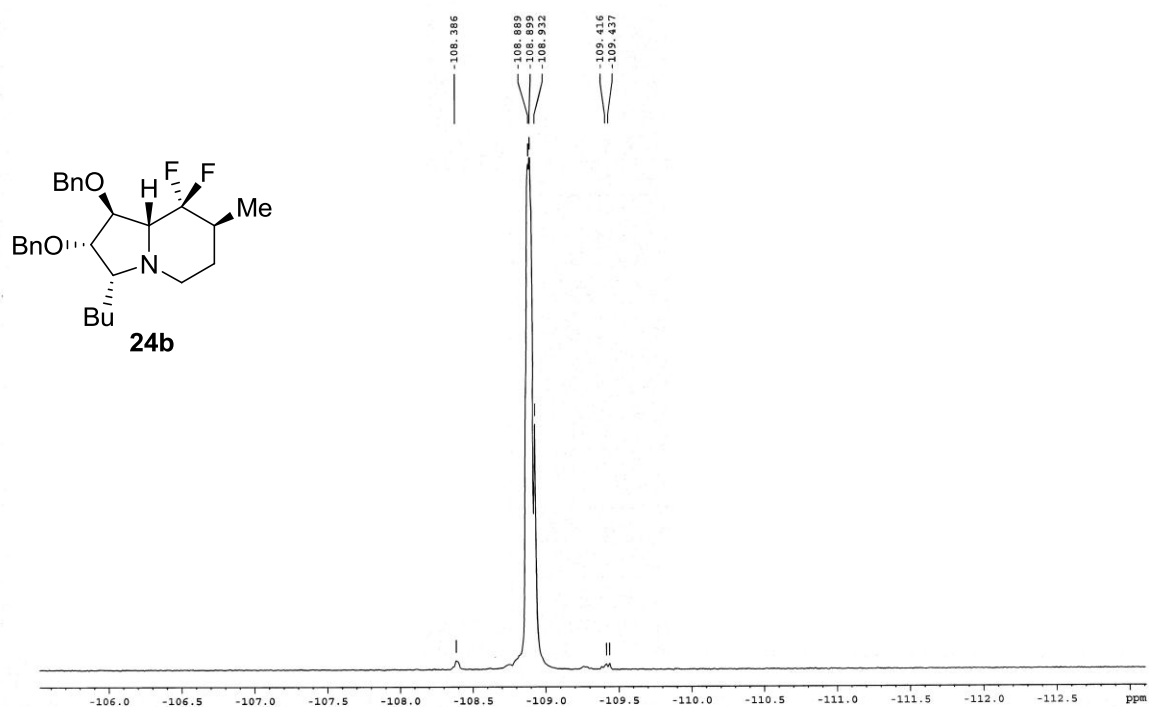
¹⁹F NMR Spectrum of **24a** (470 MHz, CDCl₃)



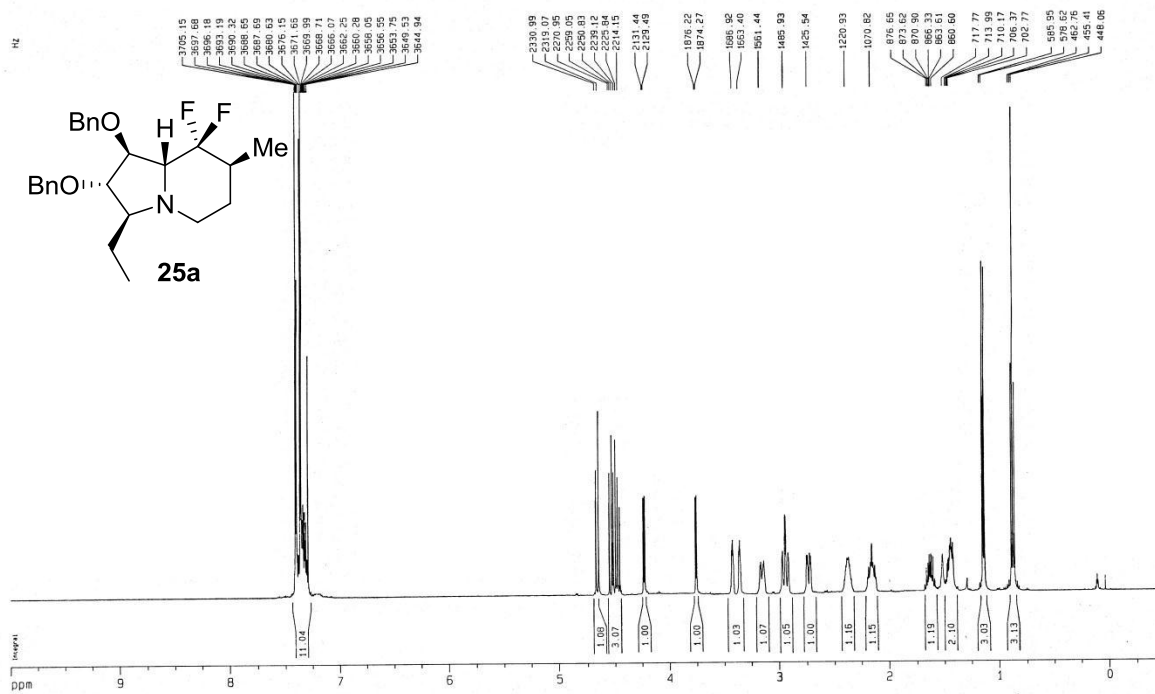
¹H NMR Spectrum of **24b** (500 MHz, CDCl₃)



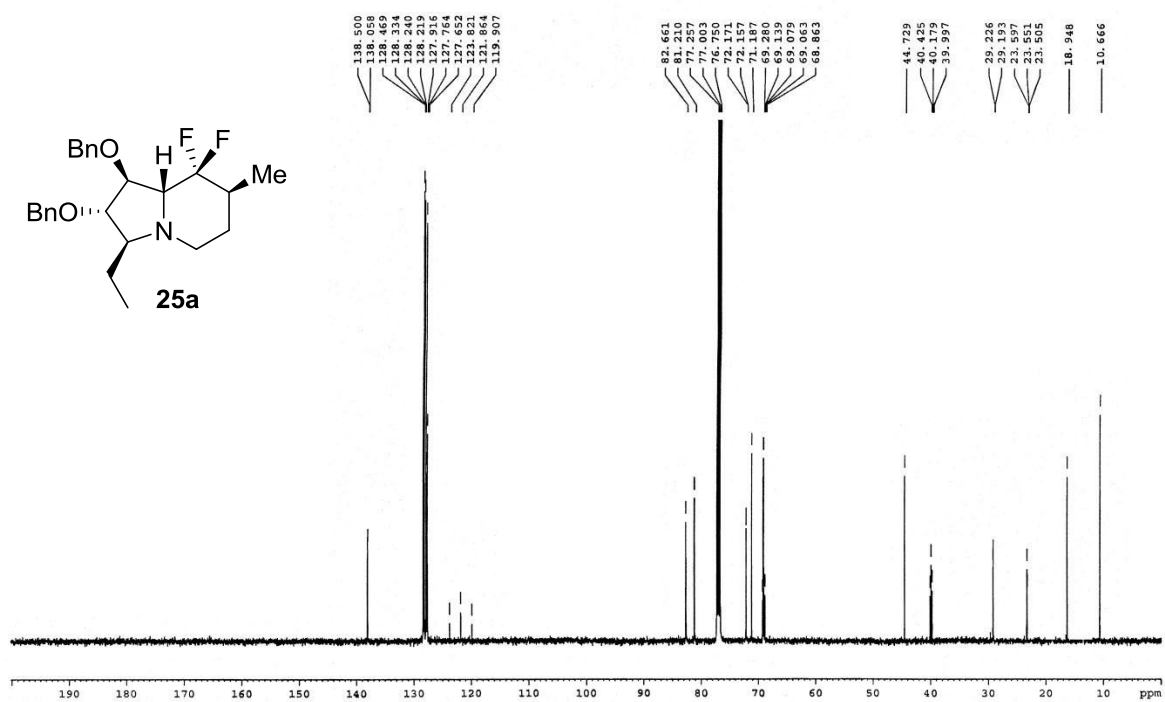
^{19}F NMR Spectrum of **24b** (470 MHz, CDCl_3)



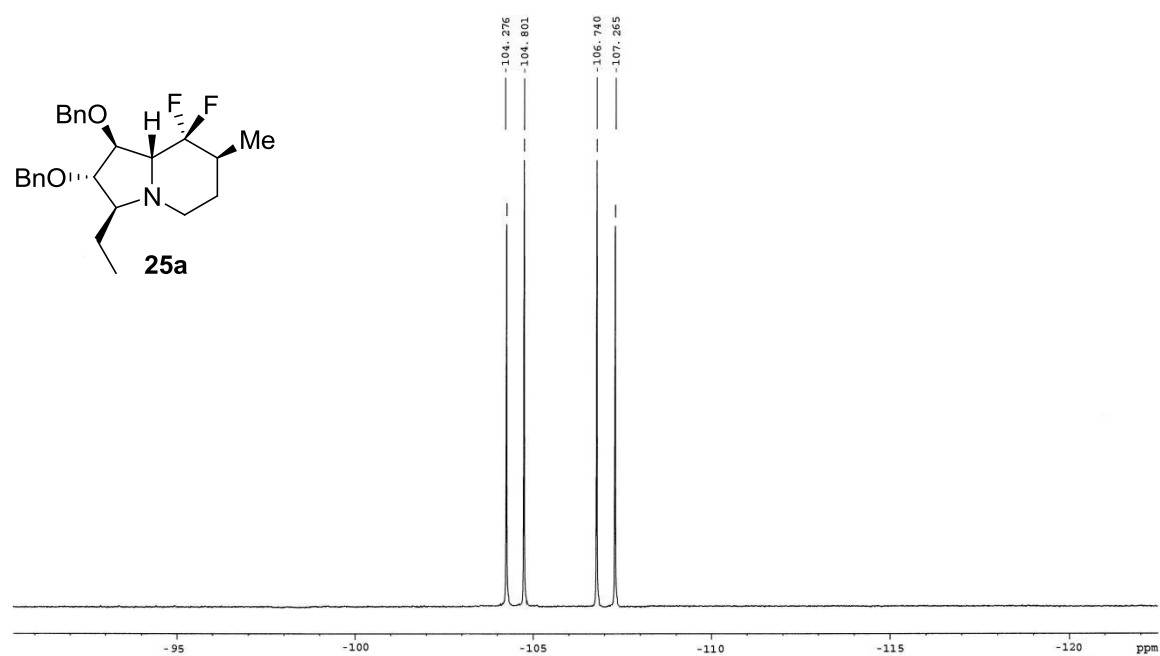
^1H NMR Spectrum of **25a** (500 MHz, CDCl_3)



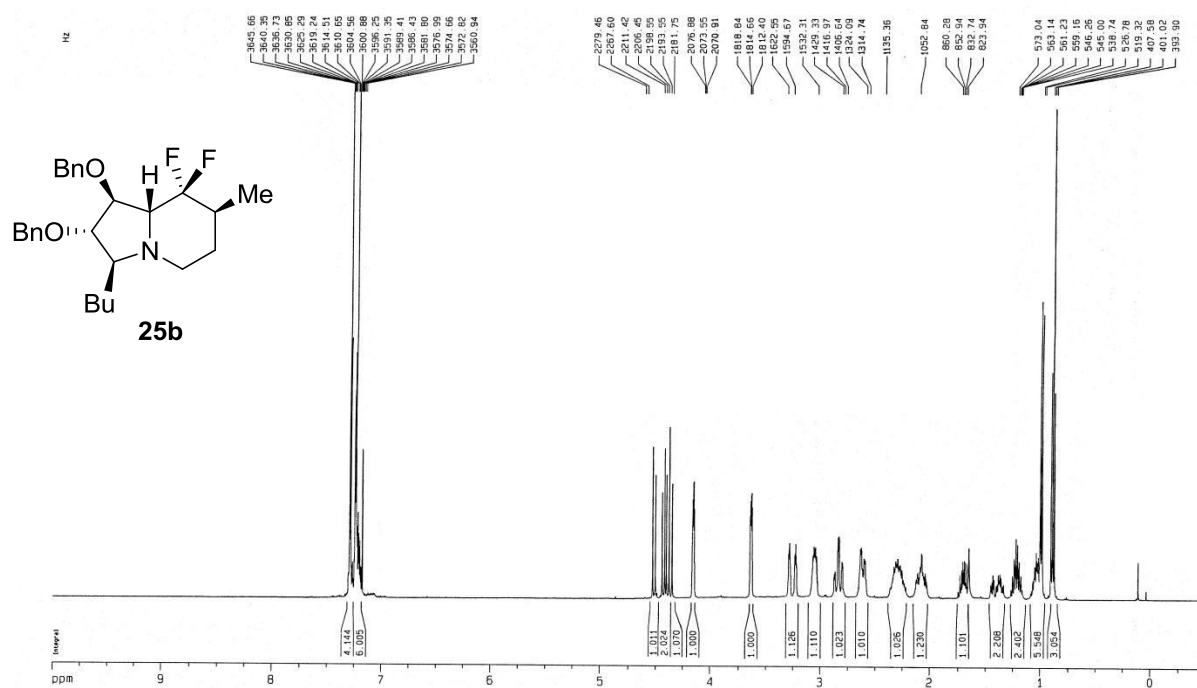
^{13}C NMR Spectrum of **25a** (125 MHz, CDCl_3)



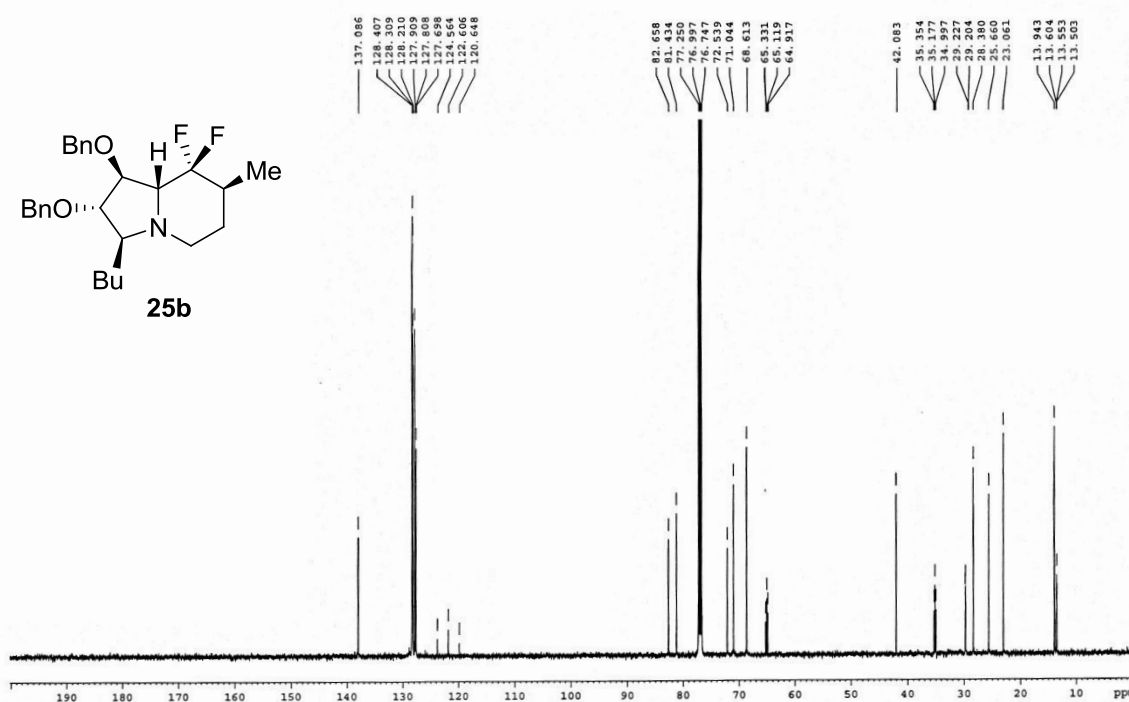
^{19}F NMR Spectrum of **25a** (470 MHz, CDCl_3)



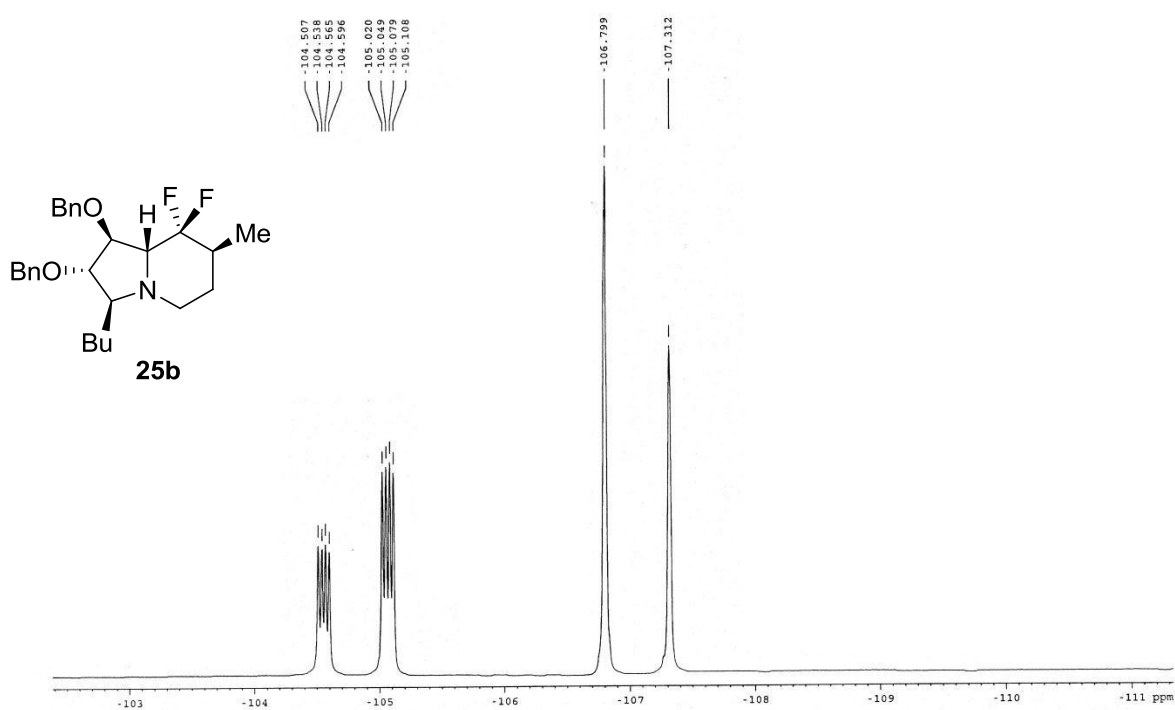
¹H NMR Spectrum of **25b** (500 MHz, CDCl₃)



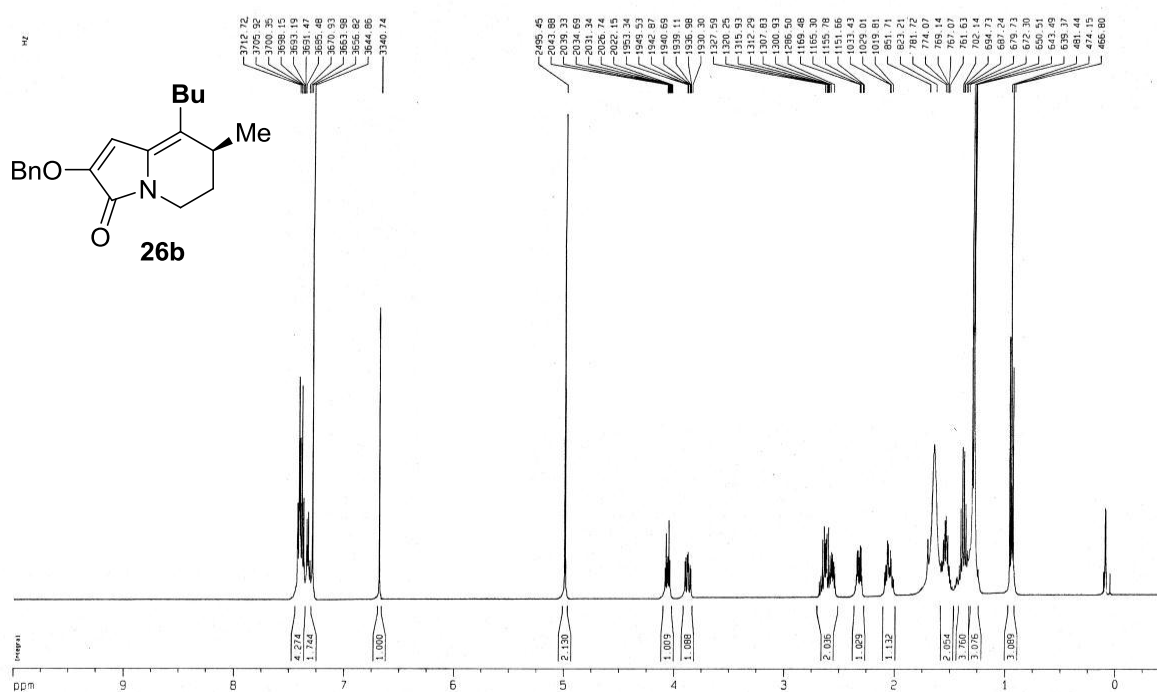
¹³C NMR Spectrum of **25b** (125 MHz, CDCl₃)



^{19}F NMR Spectrum of **25b** (470 MHz, CDCl_3)



^1H NMR Spectrum of **26b** (500 MHz, CDCl_3)



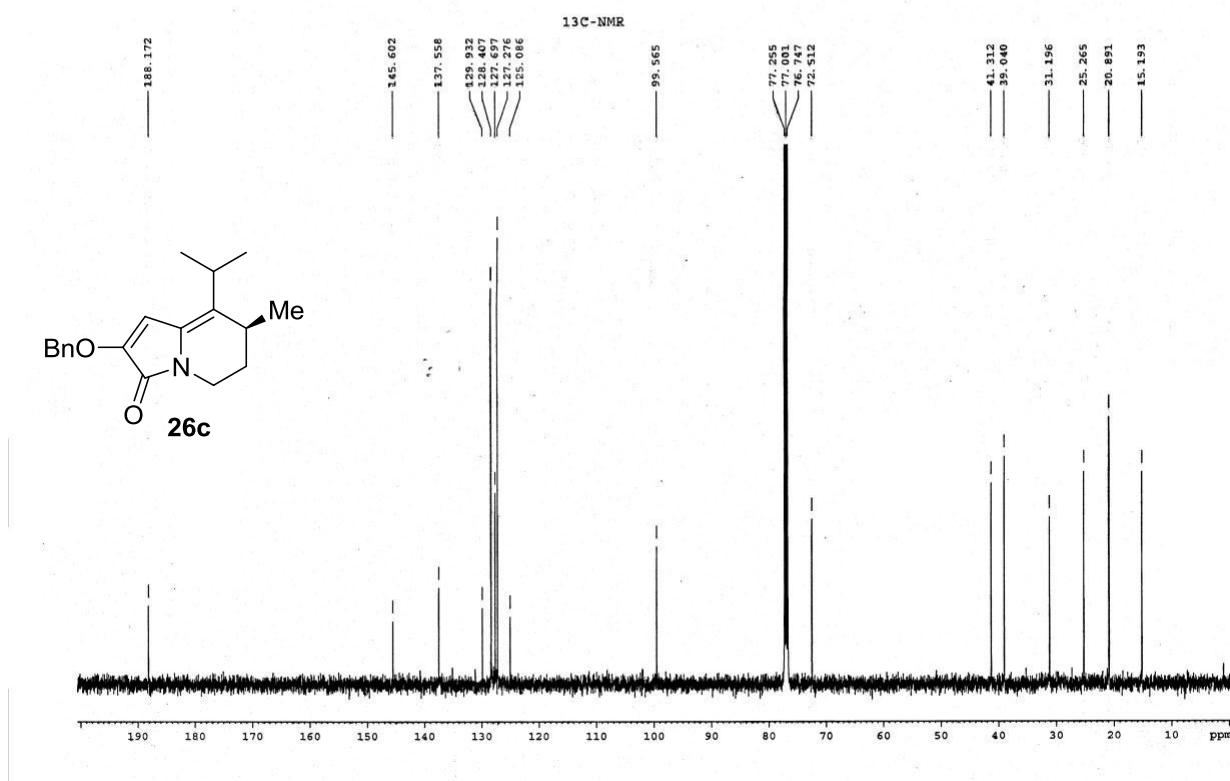
Chemical structure of **26b** is shown above the spectrum. The structure is a 6-membered ring with a nitrogen atom, a carbonyl group, a benzoyloxy group, a methyl group, and a butyl group.

13C NMR Spectrum (CDCl₃):

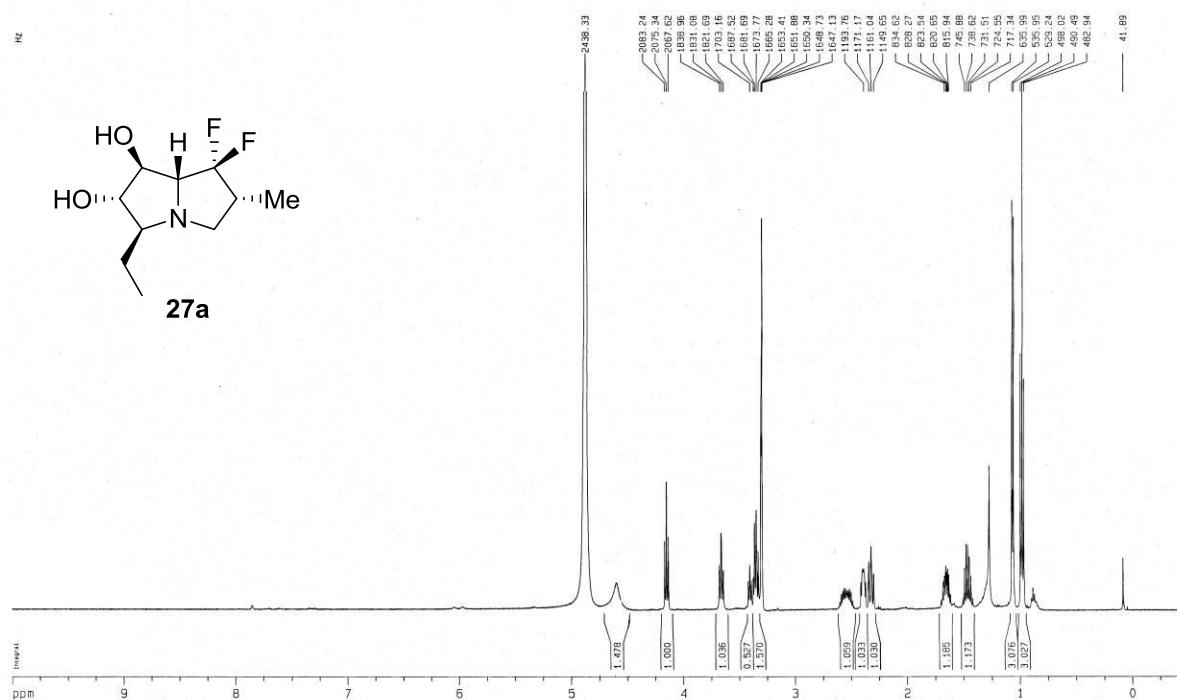
- 188.125
- 145.726
- 137.538
- 128.263
- 127.782
- 127.411
- 126.035
- 125.428
- 99.094
- 77.252
- 76.794
- 76.744
- 72.718
- 41.101
- 39.264
- 31.177
- 30.903
- 22.874
- 22.420
- 15.255
- 13.816

[illegible]

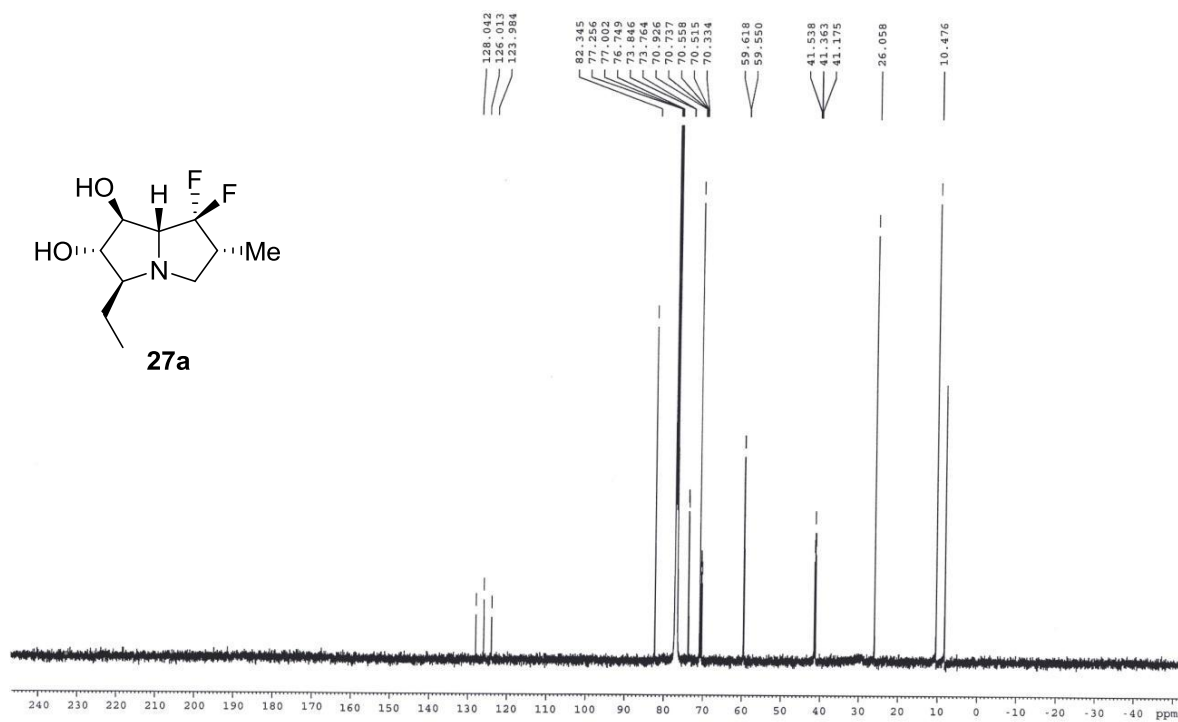
^{13}C NMR Spectrum of **26c** (125 MHz, CDCl_3)



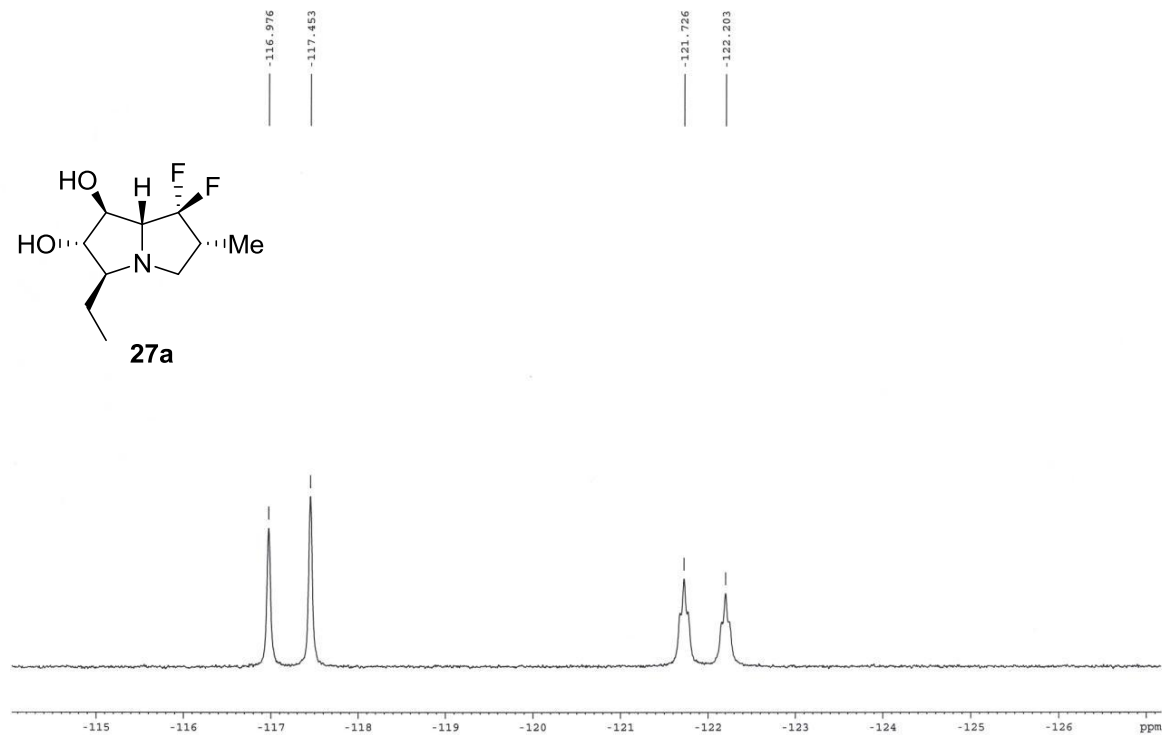
^1H NMR Spectrum of **27a** (500 MHz, CD_3OD)



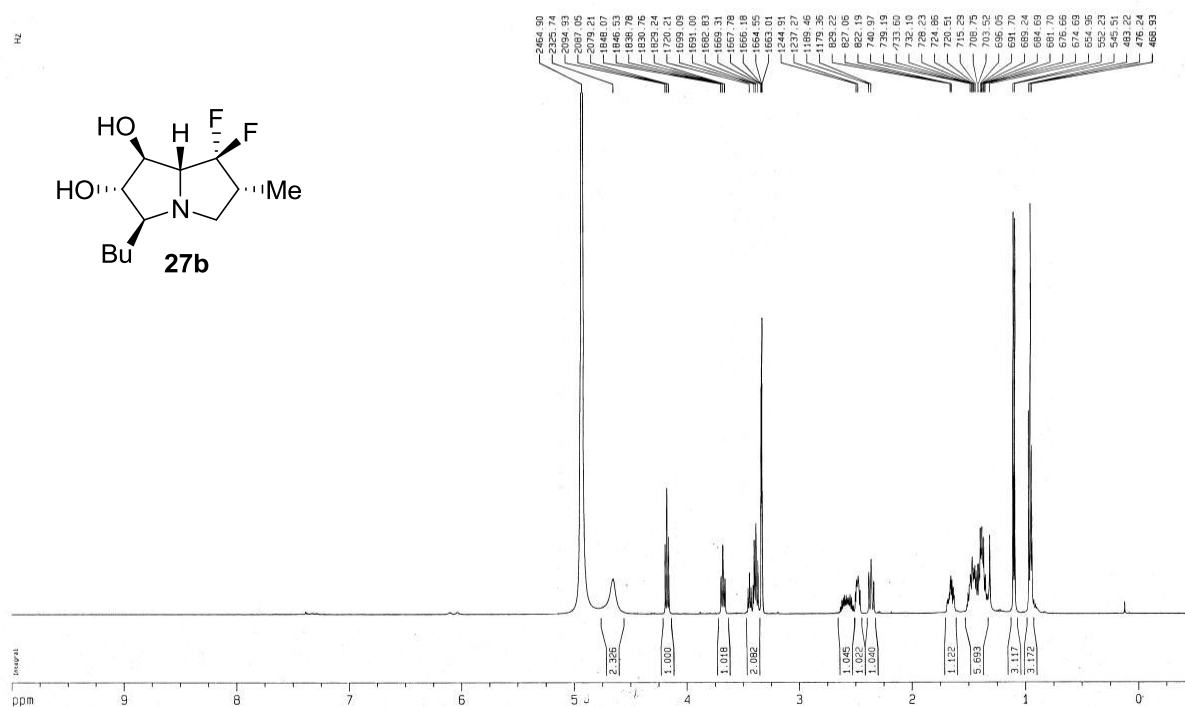
^{13}C NMR Spectrum of **27a** (125 MHz, CDCl_3)



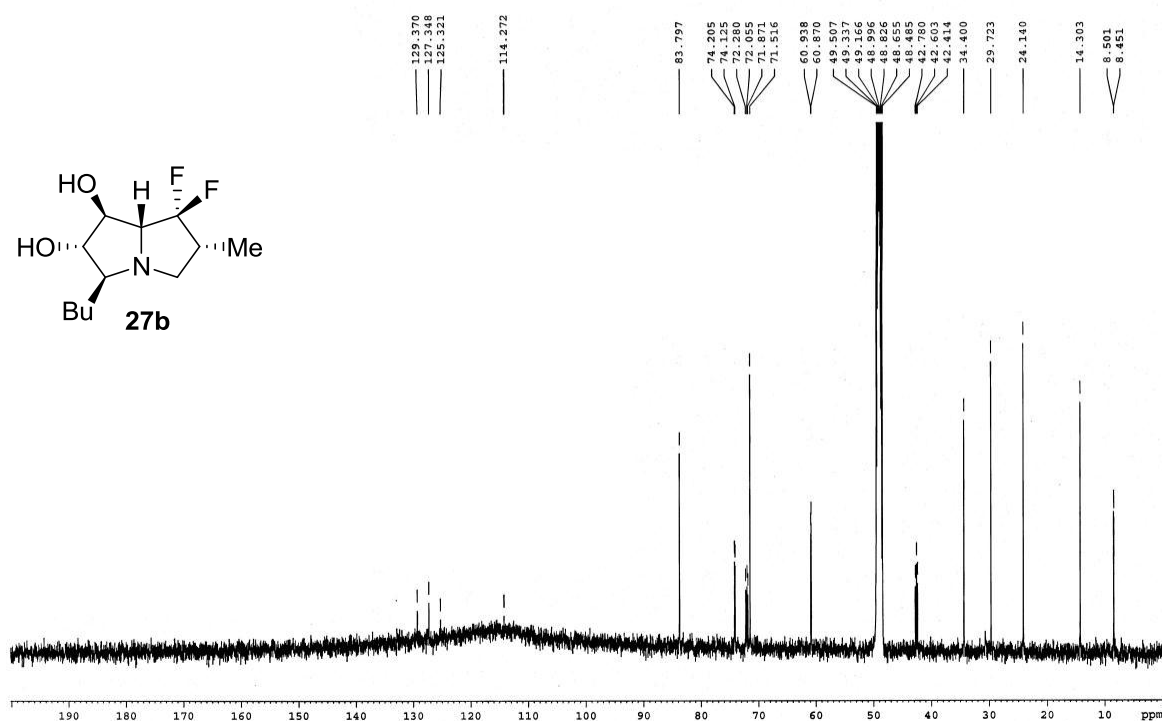
^{19}F NMR Spectrum of **27a** (470 MHz, CD_3OD)



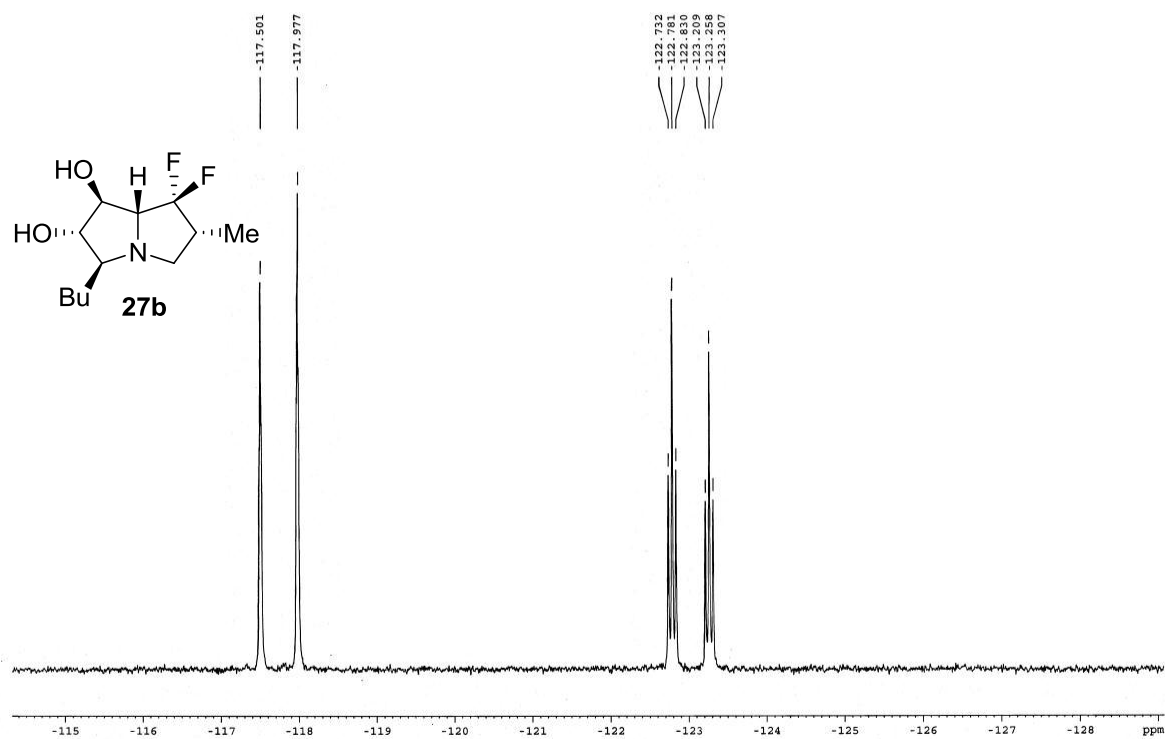
¹H NMR Spectrum of **27b** (500 MHz, CD₃OD)



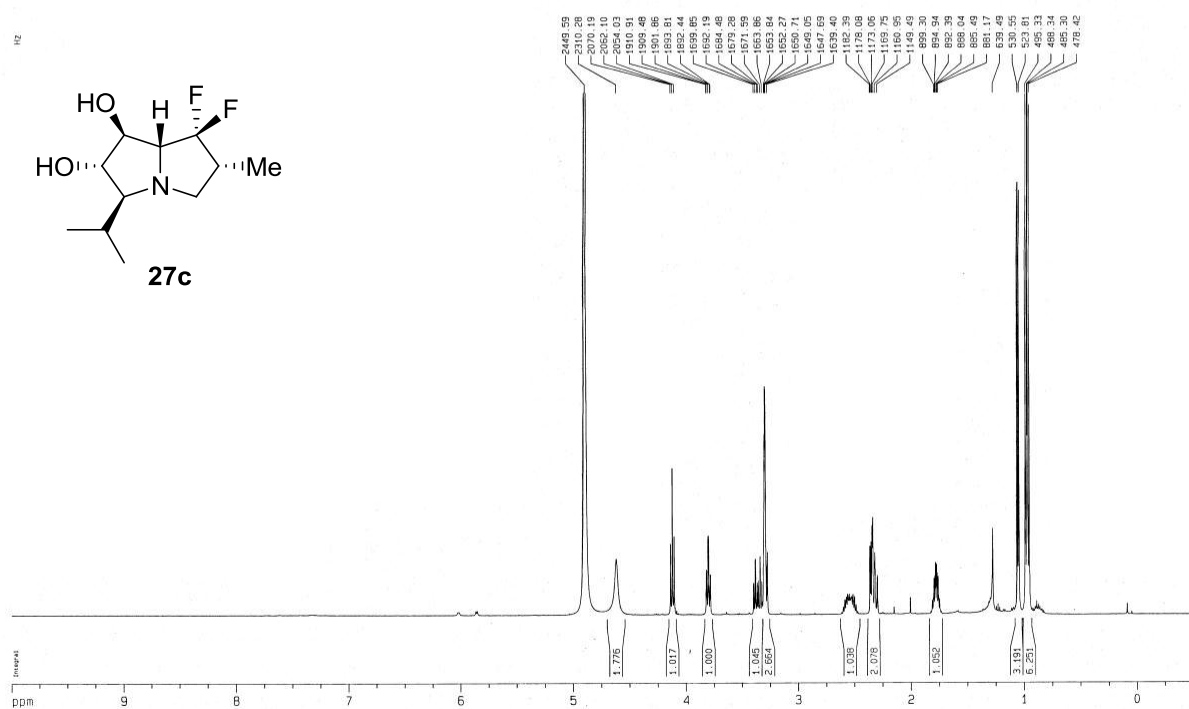
¹³C NMR Spectrum of **27b** (125 MHz, CD₃OD)



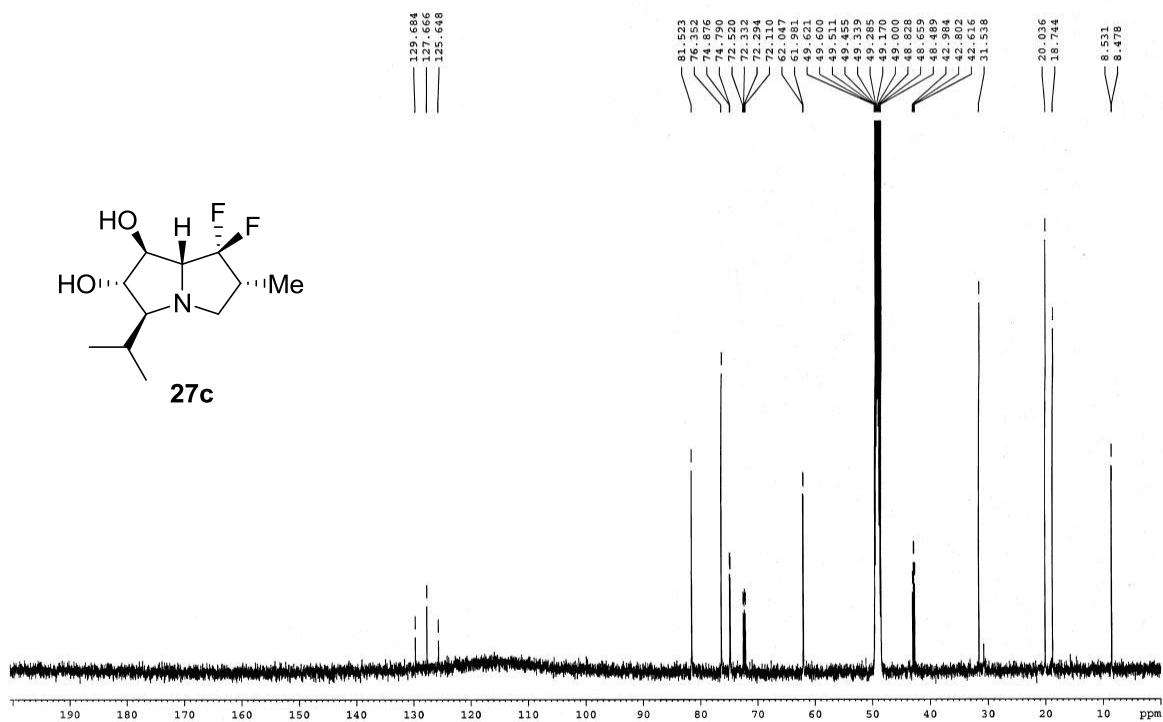
^{19}F NMR Spectrum of **27b** (470 MHz, CD_3OD)



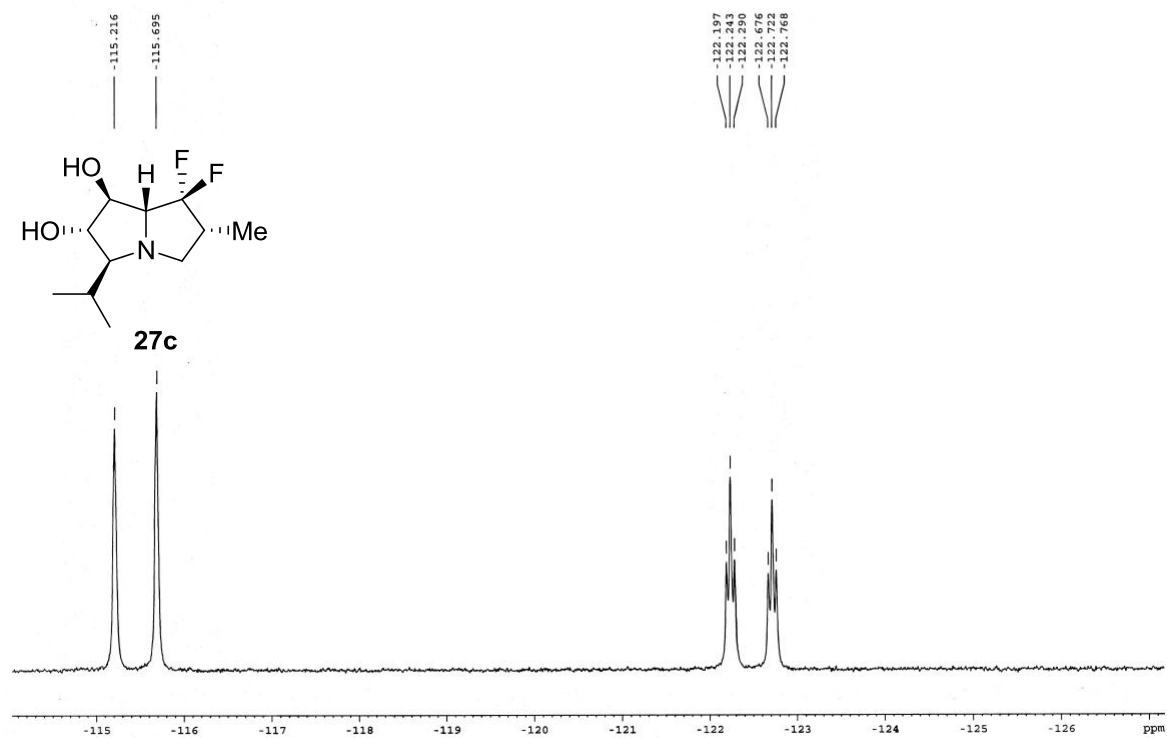
^1H NMR Spectrum of **27c** (500 MHz, CD_3OD)



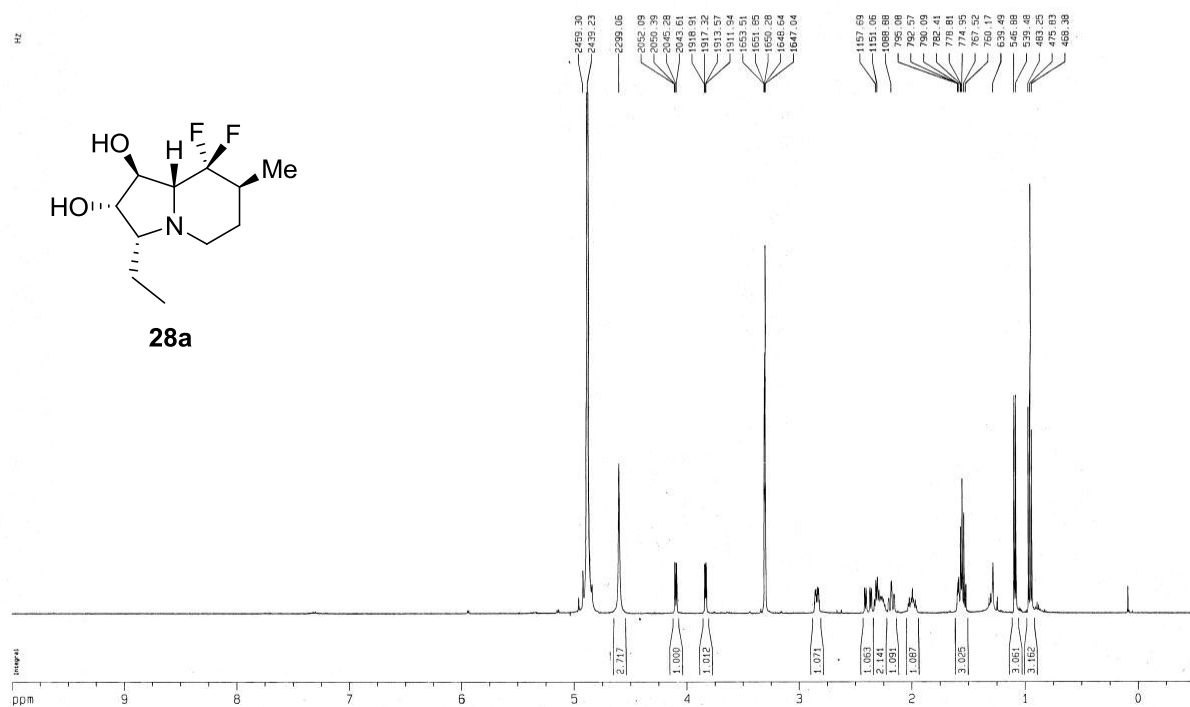
^{13}C NMR Spectrum of **27c** (125 MHz, CD_3OD)



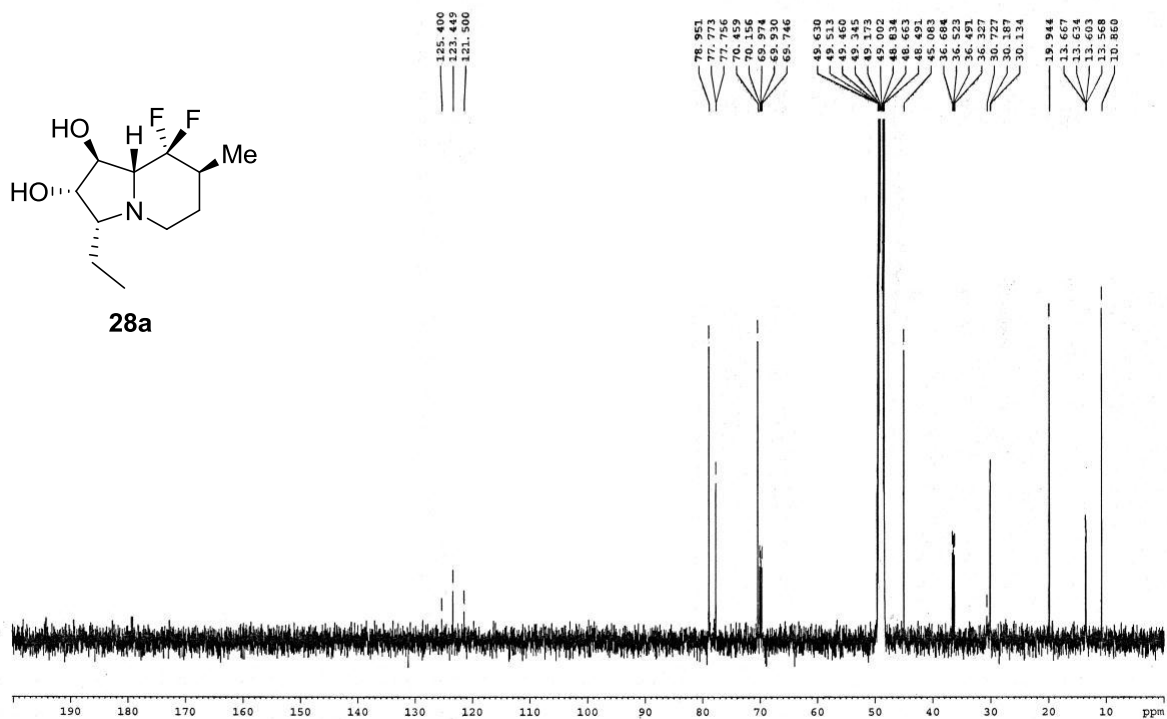
^{19}F NMR Spectrum of **27c** (470 MHz, CD_3OD)



^1H NMR Spectrum **28a** (500 MHz, CD_3OD)



^{13}C NMR Spectrum of **28a** (125 MHz, CD_3OD)



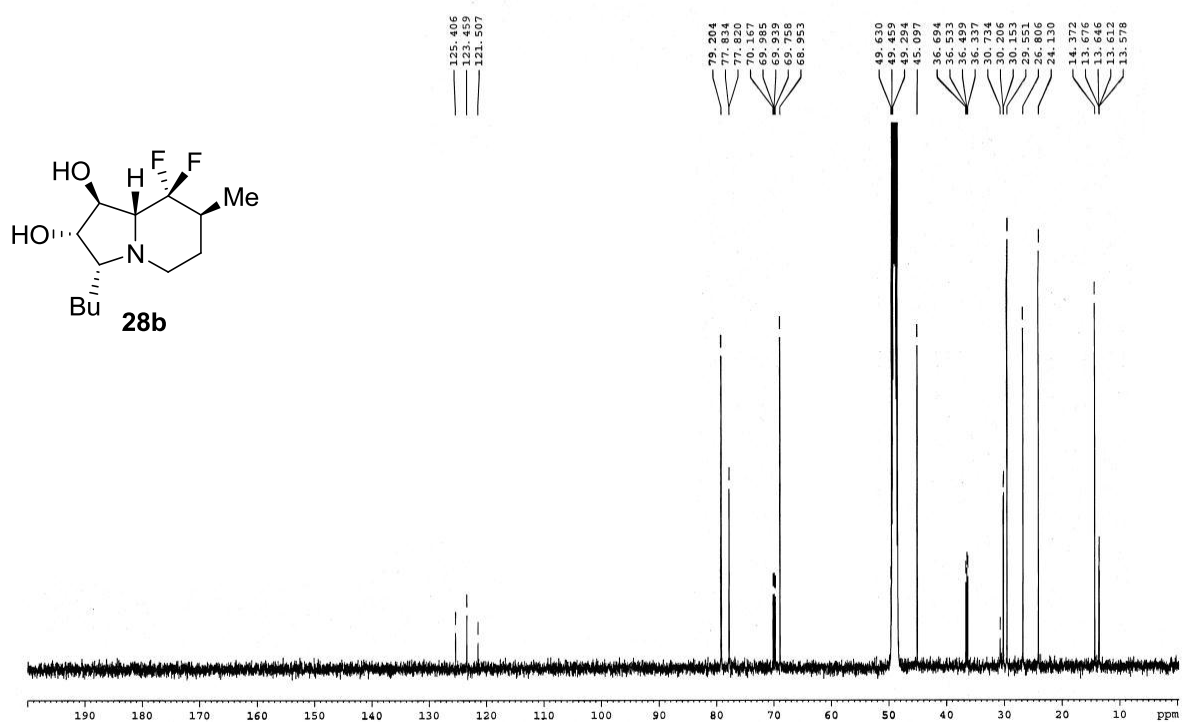
CC(C)C[C@H]1N[C@@H](C)[C@H](F)[C@H](F)[C@@H]1O

28b

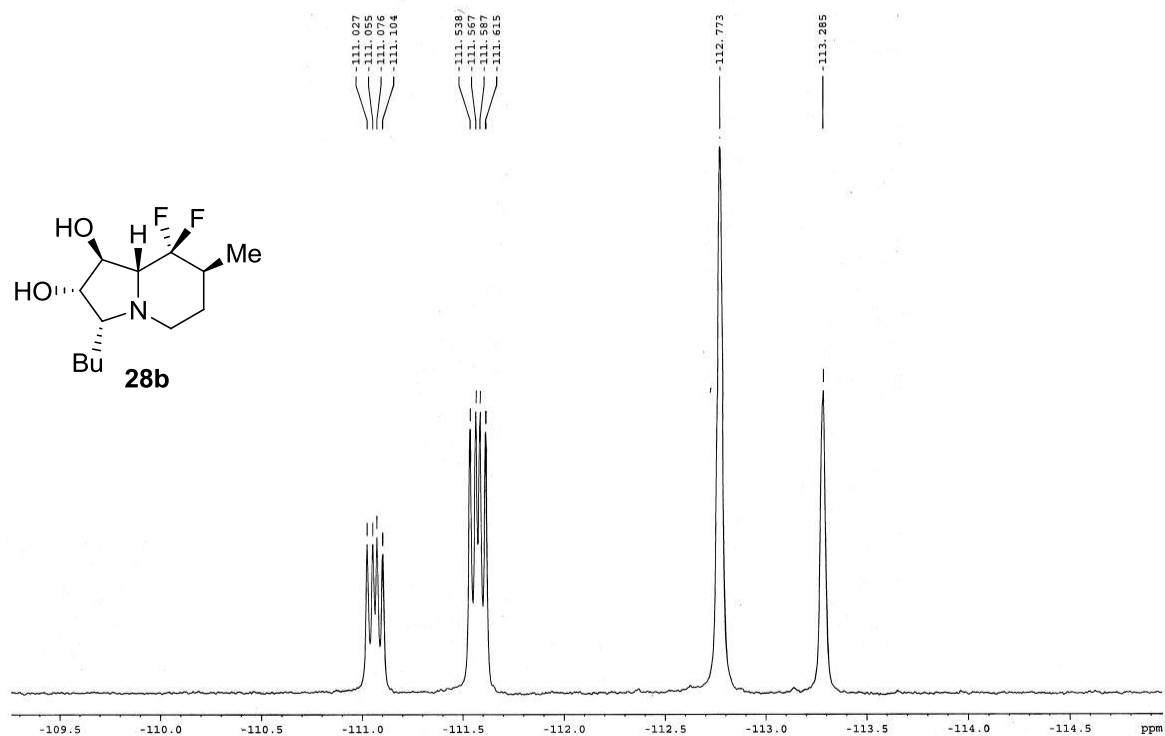
Integration values: 0.993, 1.000, 1.048, 1.071, 2.043, 1.050, 1.148, 1.140, 8.821, 3.055, 3.278.

Chemical shifts (ppm): 2042.88, 2003.89, 2048.36, 2041.60, 1902.43, 1897.31, 1650.46, 1485.85, 1446.81, 1199.41, 1192.29, 1176.09, 1147.45, 1120.96, 1083.51, 1071.43, 985.74, 968.19, 931.65, 917.65, 775.53, 769.33, 741.01, 739.59, 730.29, 724.36, 720.04, 694.99, 681.05, 676.25, 669.53, 639.33, 631.45, 621.06, 546.38, 539.04, 495.94, 495.19.

^{13}C NMR Spectrum of **28b** (125 MHz, CD_3OD)



^{19}F NMR Spectrum of **28b** (470 MHz, CD_3OD)



X-ray crystallographic analyses

X-ray diffraction data were measured on a Bruker-Nonius kappaCCD diffractometer with graphite monochromated MoK α radiation ($\lambda = 0.71073$ Å) at 298(2) K. The structures were solved by direct methods by SIR97,¹ and refined with full-matrix least-squares calculations on F^2 using SHELXL-97.² Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre under the reference numbers CCDC 887892 – 887896. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk).

X-ray data of cis-10

C₂₀H₃₉F₂NO₄Si₂, MW= 451.703, orthorhombic, dimensions: 0.25 × 0.20 × 0.10 mm³, $D = 1.141$ g/cm³, space group $P2_12_12_1$, $Z = 4$, $a = 8.6065(2)$, $b = 14.1372(6)$, $c = 21.6104(9)$ Å, $V = 2629.38(17)$ Å³, reflections collected/unique: 11,829/5160, number of observations [$>2 \sigma(I)$] 4436, final R indices [$I > 2 \sigma(I)$]: $R_1 = 0.0888$, $wR_2 = 0.2518$.

X-ray data of trans-11

C₂₁H₄₁F₂NO₄Si₂, MW= 451.703, orthorhombic, dimensions: 0.20 × 0.15 × 0.10 mm³, $D = 1.183$ g/cm³, space group $P2_12_12_1$, $Z = 4$, $a = 9.9430(2)$, $b = 12.3857(4)$, $c = 21.2265(7)$ Å, $V = 2614.06(13)$ Å³, reflections collected/unique: 17503/7443, number of observations [$>2 \sigma(I)$] 5888, final R indices [$I > 2 \sigma(I)$]: $R_1 = 0.0482$, $wR_2 = 0.1164$.

X-ray data of cis-13

C₂₃H₂₅F₂NO₄, MW= 417.452, monoclinic, dimensions: 0.30 × 0.15 × 0.10 mm³, $D = 1.267$ g/cm³, space group $P2_1$, $Z = 2$, $a = 11.8980(16)$, $b = 8.1310(6)$, $c = 12.4120(17)$ Å, $\beta = 114.293(4)^\circ$, $V =$

1410.14(7) Å³, reflections collected/unique: 4898/3388, number of observations [$>2 \sigma(I)$] 2255, final R indices [$I > 2 \sigma(I)$]: $R_1 = 0.0553$, $wR_2 = 0.1508$.

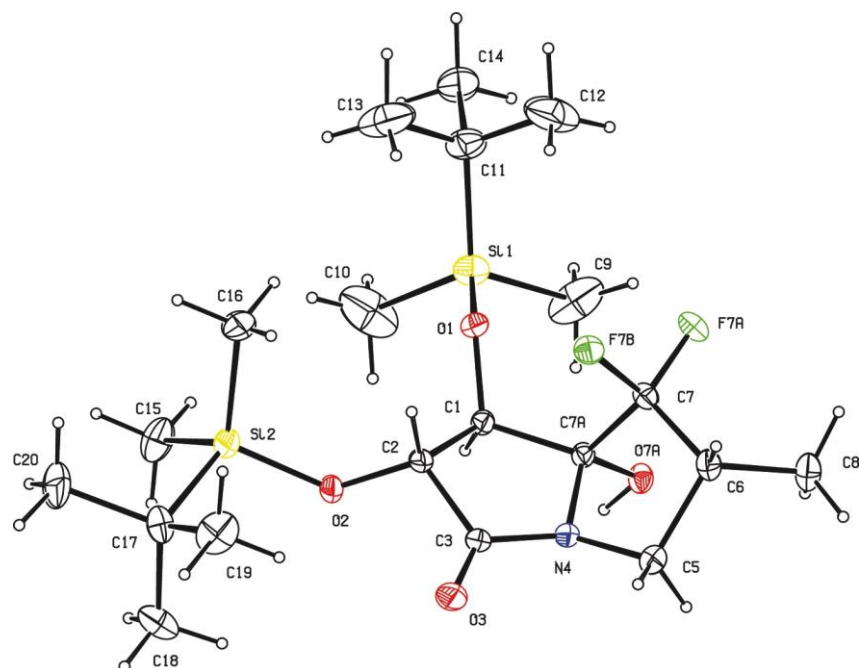
X-ray data of cis-19

C₂₂H₂₃F₂NO₄, MW= 403.425, orthorhombic, dimensions: 0.15 × 0.15 × 0.10 mm³, $D = 1.362$ g/cm³, space group $P2_12_12_1$, $Z = 4$, $a = 6.1397(1)$, $b = 10.0767(3)$, $c = 31.8096(1)$ Å, $V = 1967.99(10)$ Å³, reflections collected/unique: 8496/4359, number of observations [$>2 \sigma(I)$] 3626, final R indices [$I > 2 \sigma(I)$]: $R_1 = 0.0530$, $wR_2 = 0.1410$.

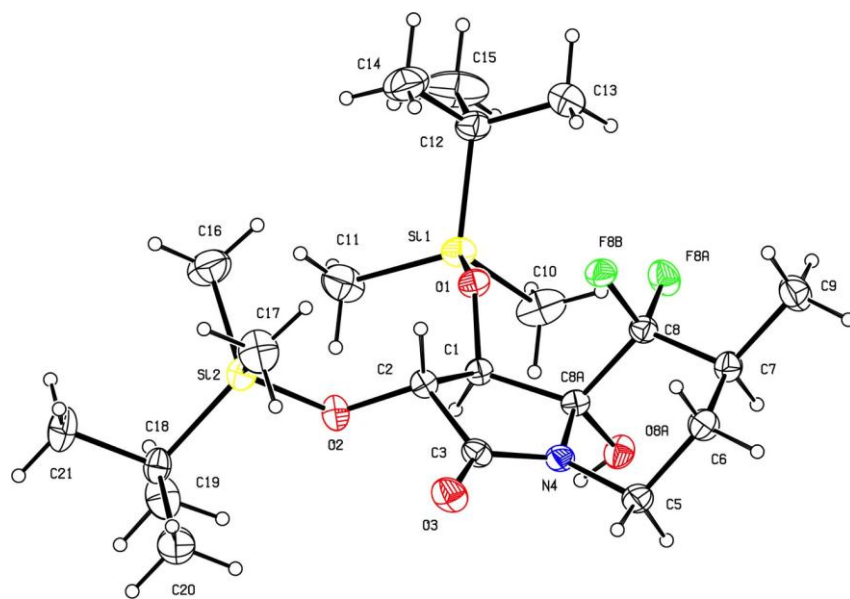
X-ray data of 28b

C₁₃H₂₃F₂NO₂, MW= 263.328, orthorhombic, dimensions: 0.20 × 0.10 × 0.10 mm³, $D = 1.240$ g/cm³, space group $P2_12_12_1$, $Z = 4$, $a = 6.4369(2)$, $b = 10.2183(2)$, $c = 21.4391(7)$ Å, $V = 1410.14(7)$ Å³, reflections collected/unique: 12913/2764, number of observations [$>2 \sigma(I)$] 2510, final R indices [$I > 2 \sigma(I)$]: $R_1 = 0.0449$, $wR_2 = 0.1292$.

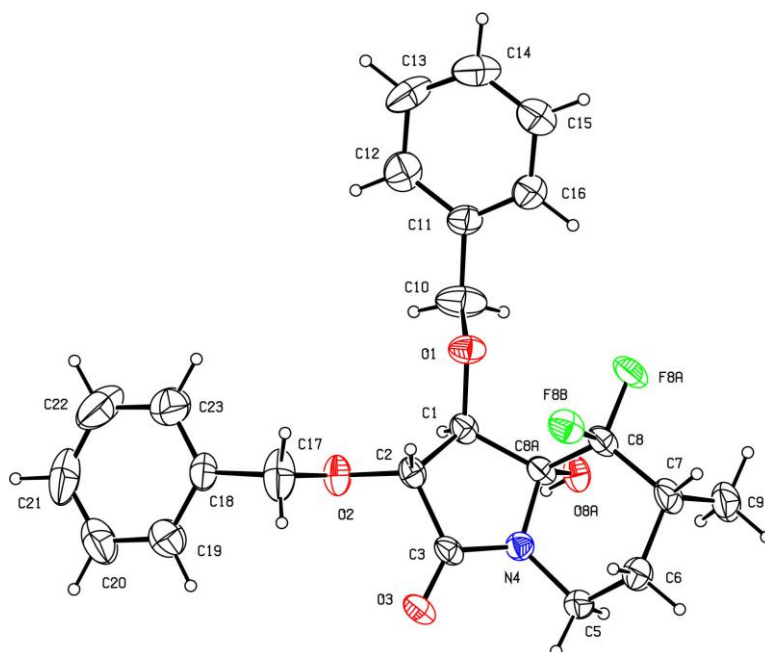
ORTEP plot of *cis*-**10**



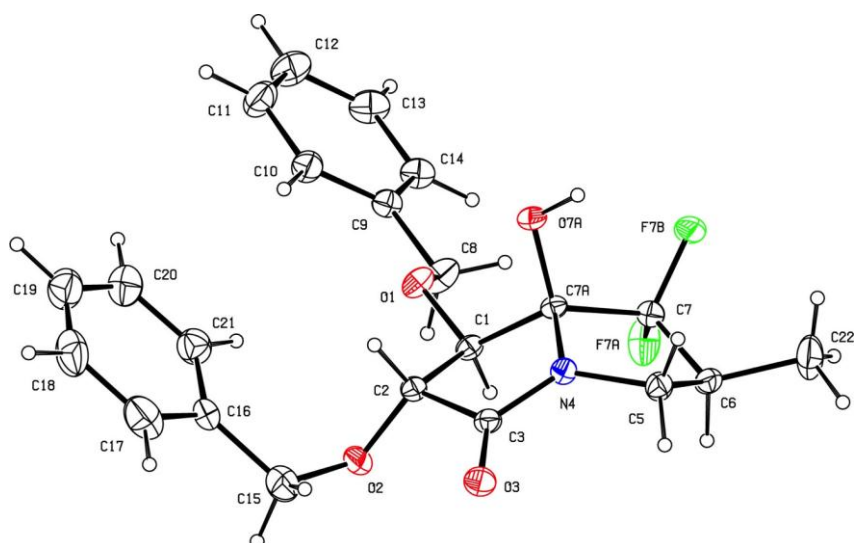
ORTEP plot of *trans*-**11**



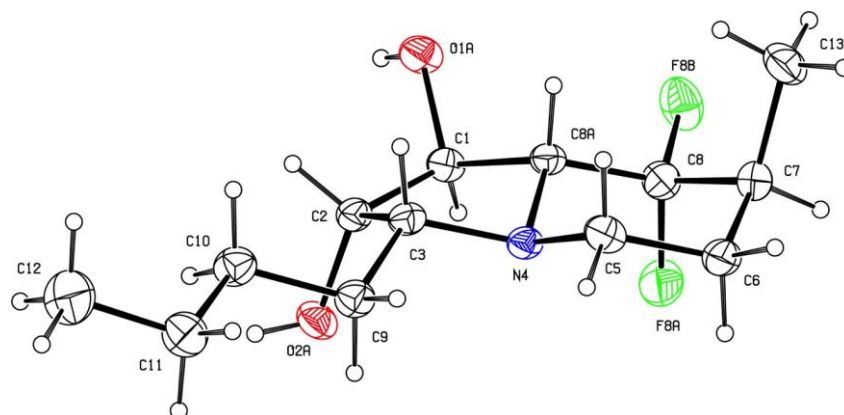
ORTEP plot of *cis*-**13**



ORTEP plot of *cis*-**19**



ORTEP plot of **28b**



References

1. Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A.G.G.; Polidori, G.; Spagna, R. *J. Appl. Cryst.* **1999**, 32, 115.
2. Sheldrick, G.M. *Acta Cryst.*, **2008**, A64, 112.