Synthesis of optically active α-trifluoromethylamines by rearrangement of β-amino-α-trifluoromethyl alcohols

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Supporting Information

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General information

All reactions were carried out under an argon atmosphere unless otherwise specified. Flasks were oven-dried at 120 °C and cooled under argon prior to use. CH_2Cl_2 was distilled over calcium hydride, THF and Et_2O were distilled over sodium/benzophenone prior to use. All other commercially available chemicals were used directly without purification.

^1H NMR spectra were recorded on a Bruker Avance 400 at 400 MHz. The chemical shifts δ are reported in ppm relative to tetramethylsilane (TMS) or residual protonated solvents (TMS: δ_H = 0.00 ppm, $CHCl_3$: δ_H = 7.26 ppm). The multiplicity is designated by the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, pent = quintet, hex = hextuplet, hept = heptuplet, m = multiplet, br = broad, app = apparent. Coupling constants *J* are reported in Hertz (Hz).

^{19}F spectra were recorded on a Bruker Avance 400 at 376 MHz. The chemical shifts δ are reported in ppm. Coupling constants *J* are reported in Hertz (Hz).

^{13}C NMR spectra were recorded on a Bruker Avance 400 at 100 MHz. The chemical shifts δ are reported in ppm relative to the solvent as an internal indicator ($CDCl_3$ δ 77.16 ppm). Coupling constants *J* are reported in Hertz (Hz).

TLCs were performed on Merck $60F_{254}$ silica gel plates and visualized with UV lamp (254 nm), and by treatment with a solution of $KMnO_4/K_2CO_3/AcOH/H_2O$ or with a solution of phosphomolybdic acid in ethanol followed by heating.

Flash column chromatography was performed with Merck Geduran Si 60 silica gel (40-63 µm).

Infrared (IR) spectra were recorded on a Bruker TENSOR^{TM} 27 (IRTF). The samples were prepared as neat films or as fine powders and the wave numbers are reported in cm^{-1}.

Mass spectra with electronic impact (MS-EI) were recorded from a Shimadzu GCMS-QP 2010S (70 eV). High resolution mass spectra (HRMS) were performed by the Centre Regional de Microanalyse (Sorbonne University, Campus Pierre et Marie Curie, Paris, France).

Melting points were determined on a Büchi Melting Point M-560 apparatus with open capillaries.

Optical rotations were measured with an Anton Paar Polarimeter MCP 100 in a 10 cm cell. The concentrations indicated are in g/100mL.

The enantiomeric ratios were determined by supercritical fluid chromatography (SFC) on a chiral stationary phase using a Minigram Berger SFC-Mettler Toledo apparatus, MeOH was used as polar eluent.

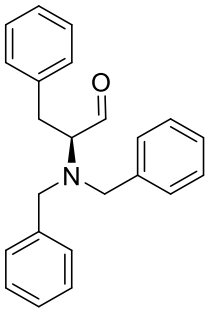
1. Preparation of the starting materials

a. Swern oxidation

General procedure[1]

To a stirred solution of oxalyl chloride (1.24 equiv) in CH_2Cl_2 (*c* = 0.49 M) at – 78 °C was added DMSO (2.58 equiv). After 15 min, a solution of the commercially available *N*,*N*-dibenzyl aminoalcohols **1** (1.0 equiv) in CH_2Cl_2 (*c* = 0.4 M) was added. After 30 min, Et_3N (2.63 equiv) was added and the resulting mixture was then partitioned between CH_2Cl_2 and saturated aqueous solution of $NaHCO_3$. The organic phase was separated and was dried over Na_2SO_4 and then concentrated under reduced pressure to yield aldehydes **2** that were used without further purification in the next step to avoir epimerization. The spectral data of aldehydes **2** are in agreement with those reported in the literature.

(*S*)-2-(Dibenzylamino)-3-phenylpropanal (2a)[1]



Formula: $C_{23}H_{23}NO$ **MW**= 329.44 g.mol^{-1}

Compound **2a** was synthesized from commercially available *N,N*-dibenzyl-L-phenylalaninol (1.3 g, 4.0 mmol) as a colorless oil (1.2 g, 3.75 mmol, 94%).

IR (neat): ν_{max} 3062, 3028, 2923, 2849, 2806, 1722, 1673, 1637, 1600, 1495, 1453, 1367, 1269, 1177, 1119, 1074, 1028, 979 cm^{-1}.

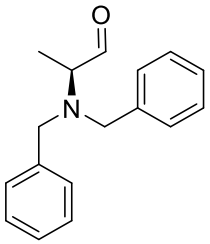
^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.72 (s, 1H), 7.32–7.18 (m, 13H), 7.16–7.14 (m, 2H), 3.82 (d, J_{AB} = 13.7 Hz, 2H), 3.67 (d, J_{AB} = 13.7 Hz, 2H), 3.56 (dd, *J* = 7.1, 6.4 Hz, 1H), 3.14 (dd, J_{AB} = 13.9, 7.3 Hz, 1H), 2.94 (dd, J_{AB} = 13.9, 6.1 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.4, 139.3, 139.0 (2C), 129.6 (2C), 128.9 (4C), 128.6 (2C), 128.5 (4C), 127.5 (2C), 126.4, 68.6, 54.9 (2C), 30.2.

MS (EI, 70 eV): *m/z* (relative intensity) = 329 ($M^{+\bullet}$, 0.1), 301 (11), 300 (45), 210 (10), 91 (100), 65 (11).

[1] Andrés, J. M.; Barrio, R.; Martínez, M. A.; Pedrosa, R.; Pérez-Encabo, A. *J. Org. Chem.* **1996**, *61*, 4210–4213.

(*S*)-2-(Dibenzylamino)propanal (2b)[1]



Formula: $C_{17}H_{19}NO$ **MW**= 253.35 g.mol^{-1}

Compound **2b** was synthesized from commercially available (*S*)-(+)-2-(dibenzylamino)-1-propanol (900 mg, 3.49 mmol) as a colorless oil (835.8 mg, 3.30 mmol, 95%).

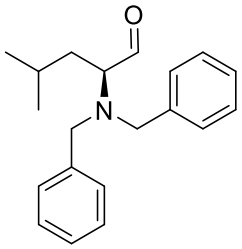
IR (neat): ν_{max} 3062, 3028, 2977, 2807, 1726, 1602, 1494, 1453, 1378, 1325, 1247, 1153, 1075, 1028, 975, 909 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.73 (s, 1H), 7.41 (d, J = 7.2 Hz, 4H), 7.34–7.30 (m, 4H), 7.27–7.23 (m, 2H), 3.73 (d, J_{AB} = 13.7 Hz, 2H), 3.57 (d, J_{AB} = 13.7 Hz, 2H), 3.33 (q, J = 6.8 Hz, 1H), 1.18 (d, J = 6.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 204.6, 139.1 (2C), 128.9 (4C), 128.6 (4C), 127.5 (2C), 63.0, 55.1 (2C), 6.9.

MS (EI, 70 eV): *m/z* (relative intensity) = 253 ($M^{+\bullet}$, 0.03), 225 ([$M^{+\bullet}$+1–$^\bullet$CHO]), 224 ([$M^{+\bullet}$–$^\bullet$CHO], 54), 181 (13), 132 (5), 91 (100), 65 (17).

(*S*)-2-(Dibenzylamino)-4-methylpentanal (2c)[1]



Formula: $C_{20}H_{25}NO$ **MW**= 295.43 g.mol^{-1}

Compound **2c** was synthesized from commercially available *N,N*-dibenzyl-L-leucinol (693 mg, 2.33 mmol) as a cloudy colorless oil (578.2 mg, 1.96 mmol, 84%).

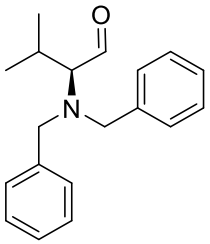
IR (neat): ν_{max} 3063, 3028, 2955, 2928, 2868, 2805, 1726, 1678, 1603, 1494, 1454, 1366, 1206, 1145, 1075, 1028, 975 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.75 (s, 1H), 7.39–7.36 (m, 4H), 7.34–7.30 (m, 4H), 7.27–7.22 (m, 2H), 3.78 (d, J_{AB} = 13.7 Hz, 2H), 3.70 (d, J_{AB} = 13.7 Hz, 2H), 3.22 (t, J = 6.6 Hz Hz, 1H), 1.71 (dt_{app}, J = 13.2, 6.6 Hz, 1H), 1.61 (dt_{app}, J = 13.9, 7.0 Hz, 1H), 1.49 (m, 1H), 0.82 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.5 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 204.2, 139.5 (2C), 129.0 (4C), 128.5 (4C), 127.4 (2C), 65.0, 54.9 (2C), 33.2, 25.4, 22.8, 22.6.

MS (EI, 70 eV): *m/z* (relative intensity) = 295 ($M^{+\bullet}$, 0.01), 266 ([$M^{+\bullet}$–$^\bullet$CHO], 56), 181 (9), 91 (100), 65 (9).

(*S*)-2-(Dibenzylamino)-3-methylbutanal (2d)[1]



Formula: $C_{19}H_{23}NO$ **MW**= 281.18 g.mol^{-1}

Compound **2d** was synthesized from commercially available (*S*)-2-(*N*,*N*-dibenzylamino)-3-methylbutanol (1.3 g, 4.14 mmol) as a brown oil (1.1 g, 3.96 mmol, 96%).

IR (neat): ν_{max} 3062, 3029, 2960, 2929, 2871, 2804, 2722, 1715, 1676, 1602, 1495, 1454, 1367, 1245, 1204, 1142, 1106, 1074, 1028, 975 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.82 (d, J = 3.4 Hz, 1H), 7.38–7.30 (m, 8H), 7.26–7.23 (m, 2H), 4.02 (d, J_{AB} = 13.8 Hz, 2H), 3.71 (d, J_{AB} = 13.8 Hz, 2H), 2.72 (dd, J = 10.0, 3.5 Hz, 1H), 2.28 (m, 1H), 1.08 (d, J = 6.7 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.3, 139.4 (2C), 128.9 (4C), 128.5 (4C), 127.3 (2C), 71.7, 54.7 (2C), 26.2, 20.3, 20.0.

MS (EI, 70 eV): *m/z* (relative intensity) = 281 ($M^{+\bullet}$, 0.03), 252 ([$M^{+\bullet}$–$^{\bullet}$CHO], 53), 210 (6), 181 (11), 91 (100), 65 (11).

b. Trifluoromethylation reaction

General procedure[2]

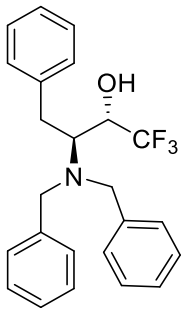
To a stirred solution of the *N*,*N*-dibenzylaminoaldehydes **2** (1.0 equiv) in THF (*c* = 0.2 M) at 0 °C was added $TMSCF_3$ (2.0 equiv). A solution of TBAF (1 M in THF, 2.0 equiv) was added dropwise and the resulting mixture was stirred at rt. After 19 h, the solution was quenched with a saturated aqueous solution of NH_4Cl (20 mL) and stirred for another 30 min. The solution was concentrated under reduced pressure and diluted in CH_2Cl_2. Both layers were separated and the aqueous phase was extracted once with CH_2Cl_2. The organic layer was washed twice with H_2O, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography (PE/EtOAc) to afford both diastereoisomers of products **3**-**6**. The *anti*/*syn* ratio was determined by analysis of ^{19}F NMR spectra of the crude. The spectral data of compounds **3**-**6** are in agreement with those reported in the literature. However, for some compounds, the signal of the "CF_3" group is not visible in the ^{13}C NMR spectra.

[2] Ryu, J. H.; Kim, S. A.; Ryu, R. H.; Kim, J. S.; Kim, N. H.; Han, H. Y.; Kim, Y. H.; Youn, W.-N.; Lee, Y.-J.; Son, H. J.; Lee, B.-Y.; Park, S. H.; Lee, J.-Y.; Lee, H. J.; Jung, H. C.; Shin, Y. A.; Lee, J. A.; Lee, B. R.; Sa, J. H. (2011). *PICOLINAMIDE AND PYRIMIDINE-4-CARBOXAMIDE COMPOUNDS, PROCESS FOR PREPARING AND PHAMACEUTICAL COMPOSITION COMPRISING THE SAME*. WO/2011/139107.

(3*S*)-3-(Dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (3)

Compound **3** was synthesized from (*S*)-2-(dibenzylamino)-3-phenylpropanal **2a** (655 mg, 1.99 mmol) as a mixture of two diastereoisomers in a ratio *anti*/*syn* = 79:21 determined from the ^{19}F NMR spectrum of the crude. Purification by flash column chromatography (PE/EtOAc = 98:2 then 95:5) afforded (+)-*anti*-**3** (416.6 mg, 1.04 mmol, 52%) as a white solid (from hexane/EtOAc) and (+)-*syn*-**3** (155.7 mg, 0.39 mmol, 20%) as a beige solid (from hexane).
For the crude:
^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 75.57 (3 x F, CF_3, *syn*), – 75.94 (3 x F, CF_3, *anti*) .

(+)-**(2*S*,3*S*)-3-(Dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol [**(+)-*anti*-**3]**[3]



Formula: $C_{24}H_{24}F_3NO$ **MW**= 399.46 g.mol^{-1}

mp = 106–108 °C.

$[\alpha]_D^{25}$ + 8.7 (*c* 0.31, $CHCl_3$); litterature: **$[\alpha]_D^{20}$** – 11.9 (*c* 1.0, $CHCl_3$).

IR (neat): ν_{max} 3550, 3065, 3030, 2935, 2803, 1605, 1497, 1456, 1349, 1273, 1167, 1142, 1112, 1031, 979, 905 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27–7.09 (m, 15 H), 4.21 (m, 1H), 3.80 (d, J_{AB} = 13.9 Hz, 2H), 3.55 (d, J_{AB} = 13.9 Hz, 2H), 3.35 (m, 1H), 3.09 (dd, J_{AB} = 14.3, 9.4 Hz, 1H), 2.90 (dd, J_{AB} = 14.3, 5.3 Hz, 1H), 2.67 (d, J = 5.6 Hz, 1H, OH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.2, 138.9 (2C), 129.6 (2C), 128.9 (4C), 128.5 (6C), 127.3 (2C), 126.4, 125.4 (d_{app}, J = 283.3 Hz)*, 68.4 (q, J = 29.7 Hz), 59.1, 54.6 (2C), 31.8.

(*) only the two main intense signals of the quadruplet are visible.

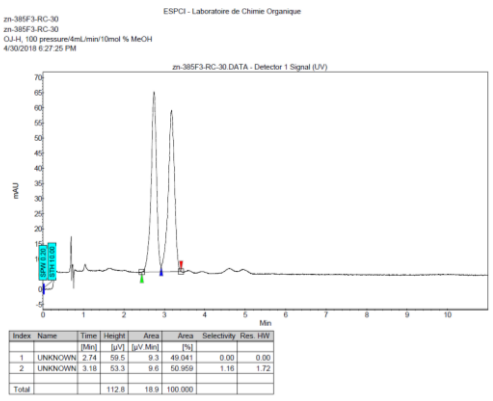
^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 75.64 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 308 ([$M^{+\bullet}$–$^{\bullet}CH_2Ph$], 26), 300 (12), 181 (4), 91 (100), 65 (6).

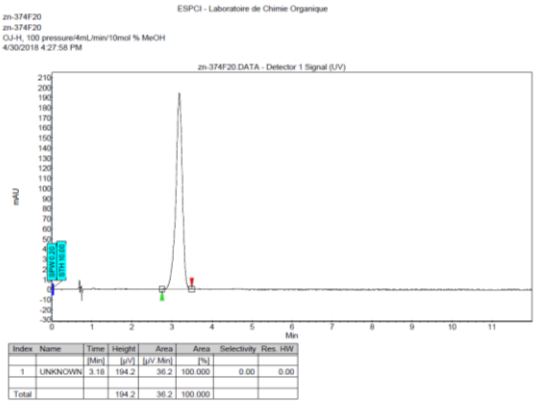
The enantiomeric excess of (+)-*anti*-**3** (ee > 99%) was determined by super-critical fluid chromatography (SFC) using a chiral stationary phase (OJ-H column, P = 100 bars, flow rate = 4 mL/min, eluent = sc CO_2/MeOH = 90:10, detection at 210 nm).

(±)-*anti*-**3** :[4] (+)-*anti*-**3** :

[3] Andrés, J. M.; Pedrosa, R.; Pérez-Encabo, A. *Eur. J. Org. Chem*. **2004**, 1558–1566.
[4] Compounds (±)-*anti*-**3** and (±)-*syn*-**3** were synthesized from (±)-**2a** according to the general procedure of the trifluoromethylation (described above).

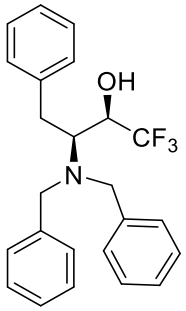


Index	Name	Time [Mn]	Height [µV]	Area [µV.Mn]	Area [%]	Selectivity	Res. HW
1	UNKNOWN	2.74	59.5	9.3	49.041	0.00	0.00
2	UNKNOWN	3.18	53.3	9.6	50.959	1.16	1.72
Total			112.8	18.9	100.000		



Index	Name	Time [Mn]	Height [µV]	Area [µV.Mn]	Area [%]	Selectivity	Res. HW
1	UNKNOWN	3.18	194.2	36.2	100.000	0.00	0.00
Total			194.2	36.2	100.000		

(+)-**(2*R*,3*S*)-3-(Dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol [**(+)-*syn*-**3**]^{3}



Formula: $C_{24}H_{24}F_3NO$ **MW**= 399.46 g.mol^{-1}

mp = 81–83 °C.

[α]$_D^{25}$ + 28.1 (*c* 0.19, $CHCl_3$); litterature: **[α]$_D^{20}$** + 30.5 (*c* 1.0, $CHCl_3$).

IR (neat): ν_{max} 3063, 3029, 2929, 2856, 1603, 1496, 1454, 1366, 1271, 1200, 1162, 1135, 1098, 1029, 964, 904 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42–7.09 (m, 15 H), 5.16 (br s, 1H, OH), 3.84–3.79 (m, 3H), 3.38–3.36 (m, 3H), 3.12 (dd, J_{AB} = 14.6, 9.7 Hz, 1H), 2.97 (dd, J_{AB} = 14.6, 3.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.1, 137.7 (2C), 129.5 (2C), 129.3 (4C), 129.0 (2C), 128.7 (4C), 127.7 (2C), 127.0, 69.4 (q, *J* = 29.6 Hz), 58.0, 54.2 (2C), 34.5.

CF_3 is not visible.

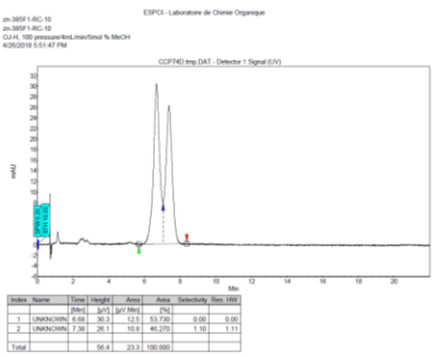
^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 75.69 (3 x F, CF_3).

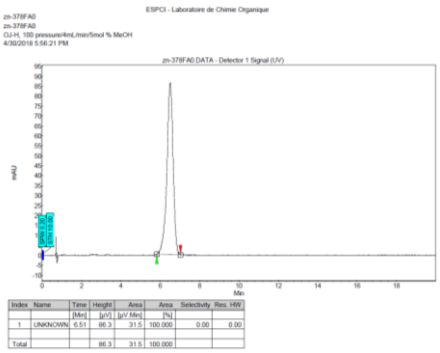
MS (EI, 70 eV): *m/z* (relative intensity) = 308 ([$M^{+\bullet}$–$^{\bullet}CH_2Ph$], 30), 300 (12), 181 (4), 91 (100), 65 (7).

The enantiomeric excess of (+)-*syn*-**3** (ee > 99%) was determined by super-critical fluid chromatography (SFC) using a chiral stationary phase (OJ-H column, P = 100 bars, flow rate = 4 mL/min, eluent = sc CO_2/MeOH = 95:5, detection at 210 nm).

(±)-*syn*-**3** :^{4}

(+)-*syn*-**3** :





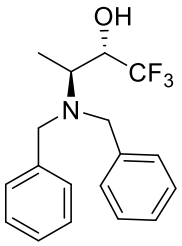
(3*S*)-3-(Dibenzylamino)-1,1,1-trifluorobutan-2-ol (4)

Compound **4** was synthesized from (*S*)-2-(dibenzylamino)propanal **2b** (413 mg, 1.63 mmol) as a mixture of two diastereoisomers in a ratio *anti*/*syn* = 79:21 determined from the ^{19}F NMR spectrum of the crude. Purification by flash column chromatography (PE/EtOAc = 98:2 and 95:5) afforded (+)-*anti*-**4** (350.6 mg, 1.08 mmol, 67%) as a colorless oil and (+)-*syn*-**4** (92.1 mg, 0.28 mmol, 18%) as a colorless oil.

For the crude:

^{19}F NMR (CDCl$_3$, 376 MHz): δ –75.96 (3 x F, CF_3, *syn*), –76.02 (3 x F, CF_3, *anti*).

(+)-**(2*S*,3*S*)-3-(Dibenzylamino)-1,1,1-trifluorobutan-2-ol [**(+)-*anti*-**4**]^3



Formula: $C_{18}H_{20}F_3NO$ **MW**= 323.36 g.mol^{-1}

[α]$_D^{25}$ + 24.2 (*c* 0.19, $CHCl_3$); litterature: **[α]$_D^{20}$** + 27.7 (*c* 1.0, $CHCl_3$).

IR (neat): ν_{max} 3416, 3064, 3029, 2991, 2942, 2806, 1602, 1494, 1453, 1367, 1326, 1273, 1152, 1125, 1072, 1028, 905, 845, 745, 697 cm^{-1}.

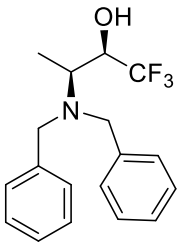
^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.35–7.29 (m, 8 H), 7.26–7.21 (m, 2 H), 4.10 (m, 1H), 3.74 (d, J_{AB} = 13.9 Hz, 2H), 3.58 (d, J_{AB} = 13.9 Hz, 2H), 3.19 (qd, *J* = 7.0, 3.7 Hz ,1H), 2.71 (br s, 1H, OH), 1.21 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (CDCl$_3$, 100 MHz): δ 139.5 (2C), 128.8 (4C), 128.5 (4C), 127.3 (2C), 125.2 (q, *J* = 283.2 Hz), 71.5 (q, *J* = 29.3 Hz), 54.7 (2C), 52.7, 9.0.

^{19}F NMR (CDCl$_3$, 376 MHz) : δ –76.08 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 323 ($M^{+\bullet}$, 0.1), 224 (57), 181 (8), 132 (4), 91 (100), 65 (10).

(+)-**(2*R*,3*S*)-3-(Dibenzylamino)-1,1,1-trifluorobutan-2-ol [**(+)-*syn*-**4**]^3



Formula: $C_{18}H_{20}F_3NO$ **MW**= 323.36 g.mol^{-1}

$[\alpha]_D^{25}$ + 60.7 (*c* 0.14, $CHCl_3$); litterature: **$[\alpha]_D^{20}$** + 74.4 (*c* 1.0, $CHCl_3$).

IR (neat): ν_{max} 3256, 3065, 3030, 2976, 2943, 2848, 1603, 1496, 1453, 1365, 1326, 1272, 1154, 1115, 1063, 1029, 905 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.24 (m, 10 H), 5.09 (br s, 1H, OH), 3.79 (d, J_{AB} = 13.9 Hz, 2H), 3.74 (m, 1H), 3.38 (d, J_{AB} = 13.9 Hz, 2H), 3.00 (dq, *J* = 9.5, 6.7 Hz ,1H), 1.20 (dd, *J* = 6.7, 1.0 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.8 (2C), 129.2 (4C), 128.9 (4C), 127.9 (2C), 125.3 (d_{app}, *J* = 281.0 Hz)*, 70.4 (q, *J* = 30.0 Hz), 53.3 (2C), 52.9, 9.5.

(*) only the two main intense signals of the quadruplet are visible.

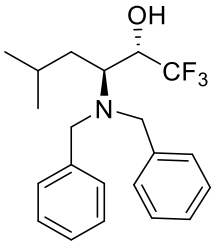
^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 76.00 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 323 ($M^{+\bullet}$, 0.02), 224 (55), 181 (8), 132 (4), 91 (100), 65 (10).

(3*S*)-3-(Dibenzylamino)-1,1,1-trifluoro-5-methylhexan-2-ol (5)

Compound **5** was synthesized from (*S*)-2-(dibenzylamino)-4-methylpentanal **2c** (583 mg, 1.93 mmol) as a mixture of two diastereoisomers in a ratio *anti*/*syn* = 72:28 determined from the ^{19}F NMR spectrum of the crude. Purification by flash column chromatography (PE/EtOAc = 98:2 to 95:5) afforded (–)-*anti*-**5** (362.3 mg, 0.99 mmol, 51%) as a colorless oil and (+)-*syn*-**5** (168.3 mg, 0.46 mmol, 24%) as a colorless oil.
For the crude:
^{19}F NMR (**$CDCl_3$, 376 MHz):** δ – 75.72 (3 x F, CF_3, *syn*), – 76.10 (3 x F, CF_3, *anti*) .

(–)-**(2*S*,3*S*)-3-(Dibenzylamino)-1,1,1-trifluoro-5-methylhexan-2-ol [**(–)-*anti*-**5**]**[3]**



Formula: $C_{21}H_{26}F_3NO$ **MW**= 365.44 g.mol^{-1}

$[\alpha]_D^{25}$ – 11.5 (*c* 0.48, $CHCl_3$); litterature: **$[\alpha]_D^{20}$** – 12.3 (*c* 1.0, $CHCl_3$).

IR (neat): ν_{max} 3426, 3064, 3030, 2956, 2869, 2801, 1602, 1495, 1454, 1367, 1270, 1167, 1144, 1131, 1088, 1028, 968 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34–7.22 (m, 10H), 4.27 (m, 1H), 3.83 (d, J_{AB} = 13.6 Hz, 2H), 3.44 (d, J_{AB} = 13.6 Hz, 2H), 3.05 (ddd, *J* = 9.4, 4.5, 1.9 Hz ,1H), 2.60 (d, *J* = 6.6 Hz, 1H, OH), 1.85 (m, 1H), 1.69 (ddd, *J*

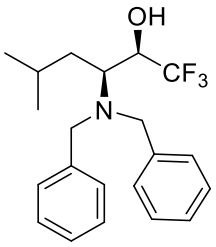
= 14.0, 9.5, 4.5 Hz, 1H), 1.21 (ddd, *J* = 14.0, 9.3, 4.9 Hz, 1H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.51 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (CDCl$_3$, 100 MHz): δ 139.5 (2C), 129.3 (4C), 128.5 (4C), 127.4 (2C), 125.5 (q, *J* = 283.7 Hz), 68.0 (q, *J* = 29.6 Hz), 54.6 (2C), 54.4, 34.7, 24.2, 23.8, 21.5.

^{19}F NMR (**CDCl$_3$, 376 MHz) :** δ – 76.09 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 365 ($M^{+\bullet}$, 0.02), 266 (68), 181 (8), 132 (2), 91 (100), 65 (7).

(+)-**(2*R*,3*S*)-3-(Dibenzylamino)-1,1,1-trifluoro-5-methylhexan-2-ol [**(+)-*syn*-**5**]^3



Formula: $C_{21}H_{26}F_3NO$ **MW**= 365.44 g.mol^{-1}

[α]$_D^{25}$ + 23.5 (*c* 0.39, $CHCl_3$); litterature: **[α]$_D^{20}$** + 33.4 (*c* 1.0, $CHCl_3$).

IR (neat): ν_{max} 3500, 3064, 3030, 2959, 2869, 1603, 1496, 1454, 1369, 1266, 1150, 1111, 1075, 1029, 952 cm^{-1}.

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.34–7.24 (m, 10H), 5.26 (br s, 1H, OH), 3.86 (d, J_{AB} = 13.2 Hz, 2H), 3.64 (m, 1H), 3.56 (d, J_{AB} = 13.3 Hz, 2H), 3.04 (m, 1H), 1.83 (m, 2H), 1.34 (m, 1H), 0.98 (d, *J* = 6.4 Hz, 3H), 0.96 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (CDCl$_3$, 100 MHz): δ 138.0 (2C), 129.2 (4C), 128.8 (4C), 127.8 (2C), 125.4 (q, *J* = 281.5 Hz), 70.3 (q, *J* = 29.5 Hz), 55.1, 54.4 (2C), 38.0, 25.8, 23.5, 22.4.

^{19}F NMR (**CDCl$_3$, 376 MHz) :** δ – 75.81 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 365 ($M^{+\bullet}$, 0.01), 266 (60), 181 (7), 132 (2), 91 (100), 65 (7).

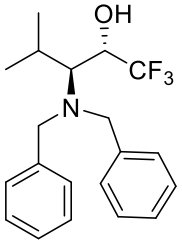
(3*S*)-3-(Dibenzylamino)-1,1,1-trifluoro-4-methylpentan-2-ol (6)

Compound **6** was synthesized from (*S*)-2-(dibenzylamino)-3-methylbutanal **2d** (557 mg, 1.98 mmol) as a mixture of two diastereoisomers in a ratio *anti*/*syn* = 84:16 determined from the ^{19}F NMR spectrum of the crude. Purification by flash column chromatography (PE/EtOAc =98:2 to 95:5) afforded (+)-*anti*-**6** (392 mg, 1.12 mmol, 56%) as a viscous yellow oil and (+)-*syn*-**6** (70.1 mg, 0.20 mmol, 10%) as a yellow oil.

For the crude:

^{19}F NMR (**CDCl$_3$, 376 MHz) :** δ – 73.45 (3 x F, CF_3, *anti*), – 76.17 (3 x F, CF_3, *syn*).

(+)-**(2*S*,3*S*)-3-(Dibenzylamino)-1,1,1-trifluoro-4-methylpentan-2-ol [**(+)-*anti*-**6]** ^{3}



Formula: $C_{20}H_{24}F_3NO$ **MW**= 351.41 g.mol^{-1}

[α]$_D^{25}$ + 4.6 (*c* 0.32, $CHCl_3$); litterature: **[α]$_D^{20}$** + 3.8 (*c* 0.9, $CHCl_3$).

IR (neat): ν_{max} 3431, 3064, 3029, 2961, 2874, 2804, 1694, 1602, 1495, 1453, 1345, 1270, 1149, 1126, 1069, 1028, 971, 910 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.24 (m, 10H), 4.06 (m, 1H), 3.78 (d, J_{AB} = 13.4 Hz, 2H), 3.73 (d, J_{AB} = 13.4 Hz, 2H), 3.15 (d, *J* = 8.4 Hz, 1H, OH), 2.75 (dd, *J* = 9.6, 4.0 Hz ,1H), 2.34 (dq, *J* = 13.2, 6.5 Hz, 1H), 1.24 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.5 Hz, 3H).

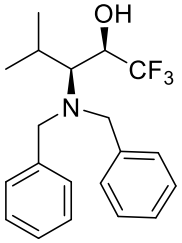
^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.2 (2C), 129.4 (4C), 128.7 (4C), 127.6 (2C), 125.7 (d_{app}, *J* = 283.6 Hz)*, 68.2 (q, *J* = 29.4 Hz), 64.6, 55.5 (2C), 27.9, 23.1, 21.3.

(*) only the two main intense signals of the quadruplet are visible.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 73.07 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 351 ($M^{+\bullet}$, 0.04), 308 (17), 252 (37), 181 (7), 91 (100), 65 (9).

(+)-**(2*R*,3*S*)-3-(Dibenzylamino)-1,1,1-trifluoro-4-methylpentan-2-ol [**(+)-*syn*-**6**]^3



Formula: $C_{20}H_{24}F_3NO$ **MW**= 351.41 g.mol^{-1}

[α]$_D^{25}$ + 13.7 (*c* 0.17, $CHCl_3$); litterature: **[α]$_D^{20}$** + 18.2 (*c* 1.0, $CHCl_3$).

IR (neat): ν_{max} 3490, 3064, 3029, 2964, 2876, 1603, 1495, 1454, 1393, 1271, 1151, 1073, 1029, 981, 913 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34–7.23 (m, 10H), 5.35 (br s, 1H), 4.02 (pent, *J* = 6.7 Hz, 1H), 3.91 (d, J_{AB} = 13.1 Hz, 2H), 3.60 (d, J_{AB} = 13.1 Hz, 2H), 2.86 (dd, *J* = 7.6, 4.2 Hz, 1H), 2.29 (m, 1H), 1.10 (d, *J* = 3.2 Hz, 3H), 1.09 (d, *J* = 3.3 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.8 (2C), 129.5 (4C), 128.8 (4C), 127.9 (2C), 125.3 (d_{app}, *J* = 281.4 Hz)*, 66.4 (q, *J* = 30.7 Hz), 61.1, 54.6 (2C), 27.1, 22.5, 19.8.

(*) only the two main intense signals of the quadruplet are visible.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 76.32 (3 x F, CF_3).

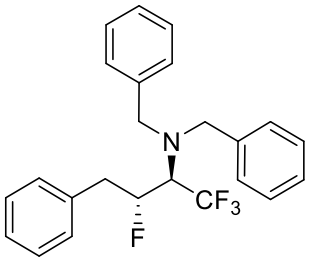
MS (EI, 70 eV): *m/z* (relative intensity) = 351 ($M^{+\bullet}$, 0.06), 308 (12), 252 (31), 181 (5), 91 (100), 65 (7).

2. Treatment with DAST

General procedure

To a stirred solution of *anti*-β-amino-α-trifluoromethyl alcohols **4**-**6** (1 equiv) in THF (*c* = 0.095 M) at 0 °C, was added DAST (1.4 equiv) and the resulting mixture was stirred for 1 h at 0 °C. After 2 h at rt, the reaction mixture was quenched with a saturated aqueous solution of Na_2CO_3 (5 mL), extracted with EtOAc (2 x 10 mL) and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography to afford the desired compounds.

(−)-(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1,3-tetrafluoro-4-phenylbutan-2-amine [(−)-*anti*-7]



Formula: $C_{24}H_{23}F_4N$ **MW**= 401.45 g.mol^{-1}

Compound (−)-*anti*-**7** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (75.9 mg, 0.19 mmol). Purification by flash column chromatography (pentane/EtOAc = 98:2) afforded (−)-*anti*-**7** (66 mg, 0.16 mmol, 87%) as a viscous colorless oil.

$[\alpha]_D^{25}$ − 39.2 (*c* 0.36, $CHCl_3$).

IR (neat): ν_{max} 3088, 3064, 3030, 2927, 2858, 1603, 1496, 1365, 1247, 1140, 1118, 1073, 1029, 971 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34−7.19 (m, 13H), 7.08 (br d, *J* = 6.5 Hz, 2H), 4.89 (dddd, *J* = 47.4, 9.3, 7.2, 3.6 Hz, 1H), 3.92 (d, J_{AB} = 13.6 Hz, 2H), 3.81 (d, J_{AB} = 13.6 Hz, 2H), 3.34 (m, 1H), 3.21 (ddd, J_{AB} = 35.0, 14.7, 3.6 Hz, 1H), 2.65 (ddd, J_{AB} = 17.1, 14.8, 9.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.3 (2C), 136.8 (d, *J* = 2.7 Hz), 129.4 (2C), 129.3 (4C), 128.76 (2C), 128.75 (4C), 127.8 (2C), 127.0, 91.3 (d, *J* = 181.1 Hz), 61.0 (qd, *J* = 24.9, 22.4 Hz), 55.3 (2C), 39.4 (d, *J* = 20.9 Hz).

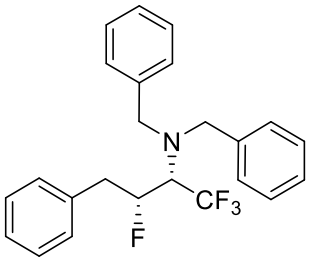
CF_3 is not visible.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 63.27 (d, *J* = 15.2 Hz, 3 x F, CF_3), − 191.69 (q, *J* = 15.0 Hz, F).

MS (EI, 70 eV): *m/z* (relative intensity) = 401 ($M^{+\bullet}$, 0.87), 312 (24), 278 (15), 122 (3), 91 (100), 65 (12).

HRMS: calcd for $C_{24}H_{24}F_4N$ $(M+H)^+$: 402.1839, found : 402.1834.

(+)-**(2*S*,3*R*)-*N*,*N*-Dibenzyl-1,1,1,3-tetrafluoro-4-phenylbutan-2-amine [**(+)-*syn*-**7]**



Formula: $C_{24}H_{23}F_4N$ **MW**= 401.45 g.mol^{-1}

Compound (+)-*syn*-**7** was synthesized from (2*R*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*syn*-**3** (79.9 mg, 0.2 mmol). Purification by flash column chromatography (PE/EtOAc = 98:2) afforded (+)-*syn*-**7** (73.3 mg, 0.18 mmol, 91%) as a colorless oil.

$[\alpha]_D^{25}$ + 62.7 (*c* 0.78, $CHCl_3$).

IR (neat): ν_{max} 3087, 3065, 3031, 2926, 2856, 1604, 1496, 1366, 1254, 1152, 1131, 1075, 1029, 985 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.21 (m, 13H), 7.01 (br d, *J* = 6.3 Hz, 2H), 4.97 (ddt, *J* = 47.7, 8.7, 3.5 Hz, 1H), 4.19 (d, J_{AB} = 13.5 Hz, 2H), 3.79 (d, J_{AB} = 13.4 Hz, 2H), 3.30–3.16 (m, 2H), 2.56 (ddd, *J* = 33.6, 14.7, 3.6 Hz, 1H).

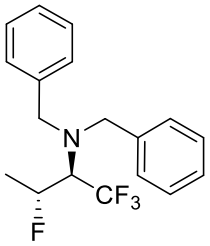
^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.0 (2C), 136.7 (d, *J* = 2.8 Hz), 129.43 (4C), 129.40 (2C), 128.7 (6C), 127.6 (2C), 126.9, 126.8 (q, *J* = 291.6 Hz), 92.6 (d, *J* = 181.1 Hz), 60.1 (qd, *J* = 24.7, 17.9 Hz), 56.00, 55.97, 39.1 (d, *J* = 21.5 Hz).

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 64.86 (d, *J* = 6.8 Hz, 3 x F, CF_3), – 191.75 (q, *J* = 6.7 Hz, F).

MS (EI, 70 eV): *m/z* (relative intensity) = 401 ($M^{+\bullet}$, 0.44), 312 (28), 278 (17), 181 (4), 91 (100), 65 (10).

HRMS: calcd for $C_{24}H_{24}F_4N$ $(M+H)^+$: 402.1839, found : 402.1853.

(+)-**(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1,3-tetrafluorobutan-2-amine [**(+)-**8]**



Formula: $C_{18}H_{19}F_4N$ **MW**= 325.35 g.mol^{-1}

Compound (+)-**8** was synthesized from (2*R*,3*R*)-*N*,*N*-dibenzyl-1,1,1,3-tetrafluorobutan-2-amine (+)-*anti*-**4** (168 mg, 0.52 mmol). Purification by flash column chromatography (PE/EtOAc = 98:2) afforded (+)-**8** (130.5 mg, 0.40 mmol, 77%) as a colorless oil.

$[\alpha]_D^{25}$ + 34.8 (*c* 0.90, $CHCl_3$)

IR (neat): ν_{max} 3071, 3031, 2942, 2859, 1603, 1495, 1454, 1382, 1364, 1247, 1174, 1134, 1101, 1063, 1028, 977, 945 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.24 (m, 10H), 4.91 (ddq, J = 47.3, 7.8, 6.3 Hz, 1H), 3.94 (d, J_{AB} = 13.6 Hz, 2H), 3.75 (dd, J_{AB} = 13.6, 1.3 Hz, 2H), 3.19 (hex_{app}, J = 8.5 Hz, 1H), 1.36 (dd, J = 24.7, 6.3 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.3 (2C), 129.2 (4C), 128.7 (4C), 127.7 (2C), 127.1 (d_{app}, J = 292.5 Hz)*, 87.4 (d, J = 172.6 Hz), 62.4 (qd, J = 23.5, 1.2 Hz), 55.1 (2C), 19.6 (d, J = 22.2 Hz).

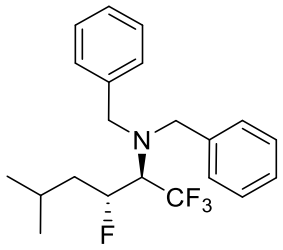
(*) only the two main intense signals of the quadruplet are visible.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 63.48 (d, J = 15.1 Hz, 3 x F, CF_3), – 185.23 (q, J = 14.0 Hz, F).

MS (EI, 70 eV): *m/z* (relative intensity) = 325 ($M^{+\bullet}$, 3), 278 (27), 234 (4), 181 (4), 91 (100), 65 (12).

HRMS: calcd for $C_{18}H_{20}F_4N$ $(M+H)^+$: 326.1526, found : 326.1528.

(+)-(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1,3-tetrafluoro-5-methylhexan-2-amine [(+)-9]



Formula: $C_{21}H_{25}F_4N$ **MW**= 367.43 g.mol^{-1}

Compound (+)-**9** was synthesized from (2S,3S)-3-(dibenzylamino)-1,1,1-trifluoro-5-methylhexan-2-ol (–)-*anti*-**5** (73.1 mg, 0.2 mmol). Purification by flash column chromatography (PE/EtOAc = 98:2) afforded (+)-**9** (70.1 mg, 0.19 mmol, 95%) as a colorless oil.

$[\alpha]_D^{25}$ + 12.6 (*c* 0.53, $CHCl_3$).

IR (neat): ν_{max} 3066, 3031, 2959, 2870, 1603, 1496, 1455, 1366, 1247, 1172, 1138, 1116, 1100, 1071, 1029, 970 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.25 (m, 10H), 4.79 (ddt, J = 48.7, 8.0, 2.6 Hz, 1H), 3.94 (d, J_{AB} = 13.5 Hz, 2H), 3.75 (d, J_{AB} = 13.5 Hz, 2H), 3.21 (hex_{app}, J = 8.5 Hz, 1H), 1.75–1.53 (m, 2H), 1.34 (m, 1H), 0.91 (t_{app}, J = 6.7 Hz, 6H).

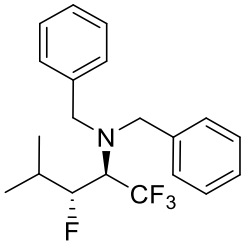
^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.4 (2C), 129.3 (4C), 128.7 (4C), 127.7 (2C), 127.1 (q, J = 292.1 Hz), 89.5 (d, J = 176.7 Hz), 61.6 (qd, J = 24.4, 2.4 Hz), 55.2 (2C), 41.9 (d, J = 20.2 Hz), 24.5 (d, J = 2.3 Hz), 23.4, 21.8.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 63.20 (d, J = 15.2 Hz, 3 x F, CF_3), – 193.27 (q, J = 15.2 Hz, F).

MS (EI, 70 eV): *m/z* (relative intensity) = 367 ($M^{+\bullet}$, 1), 298 (3), 278 (43), 181 (6), 91 (100), 65 (11).

HRMS: calcd for $C_{21}H_{26}F_4N$ $(M+H)^+$: 368.1996, found : 368.1992.

(+)-**(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1,3-tetrafluoro-4-methylpentan-2-amine [(+)-10]**



Formula: $C_{20}H_{23}F_4N$ **MW**= 353.40 g.mol^{-1}

Compound (+)-**10** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-5-methylhexan-2-ol (+)-*anti*-**6** (56.2 mg, 0.16 mmol). Purification by flash column chromatography (PE 100%) afforded (+)-**10** (36.8 mg, 0.10 mmol, 66%) as a colorless oil.

$[\alpha]_D^{25}$ + 7.9 (*c* 0.21, $CHCl_3$).

IR (neat): ν_{max} 3065, 3031, 2967, 2935, 2859, 1603, 1495, 1455, 1366, 1248, 1140, 1116, 1093, 1072, 1029, 994, 940 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.24 (m, 10H), 4.48 (ddd, *J* = 47.2, 7.9, 3.3 Hz, 1H), 3.93 (d, *J* = 13.5 Hz, 2H), 3.75 (d, J_{AB} = 13.5 Hz, 2H), 3.38 (hex$_{app}$, *J* = 8.4 Hz, 1H), 2.10 (m, 1H), 0.91 (d, *J* = 7.1 Hz, 3H), 0.41 (dd, J_{AB} = 6.7, 1.0 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.5 (2C), 129.4 (4C), 128.7 (4C), 127.7 (2C), 94.4 (d, *J* = 182.1 Hz), 58.5 (qd, J = 23.7 , 2.2 Hz), 55.1 (2C), 28.8 (d, *J* = 20.1 Hz), 19.7 (d, *J* = 3.3 Hz), 14.4 (d, *J* = 6.8 Hz).

CF_3 is not visible.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 63.11 (d, *J* = 15.6 Hz, 3 x F, CF_3), – 207.9 (q, *J* = 16.3 Hz, F).

MS (EI, 70 eV): *m/z* (relative intensity) = 353 ($M^{+\bullet}$, 1), 278 (25), 262 (10), 181 (4), 91 (100), 65 (9).

HRMS: calcd for $C_{20}H_{24}F_4N$ $(M+H)^+$: 354.1839, found : 354.1857.

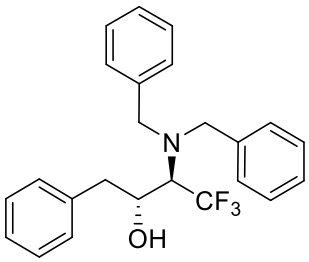
3. Rearrangement of β-amino-α-trifluoromethyl alcohols

General procedure

To a stirred solution of β-amino-α-trifluoromethyl alcohols **3**-**6** (1.0 equiv) and proton sponge (2.1 equiv) in CH_2Cl_2 (concentration of the substrate *c* = 0.10 M) at –15 °C was added Tf_2O (1.5 equiv). After 2 h to 2.5 h of stirring, the nucleophile (Nu) was added at – 15 °C and the resulting mixture was warmed to rt and stirred for 2.5 h to 4 h. The reaction mixture was diluted with H_2O (15 mL), extracted with CH_2Cl_2 (2 x 15 mL) and the combined extracts were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography to afford the desired compounds **11**-**14**.

a. Synthesis of β-trifluoromethyl-β-aminoalcohols

(–)-(2*R*,3*R*)-3-(Dibenzylamino)-4,4,4-trifluoro-1-phenylbutan-2-ol [(–)-*anti*-11]



Formula: $C_{24}H_{24}F_3NO$ **MW**= 399.46 g.mol^{-1}

Compound (–)-*anti*-**11** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (79.9 mg, 0.20 mmol) using H_2O as the nucleophile (20 µL, 1.12 mmol, 5.6 equiv). Purification by flash column chromatography (pentane/EtOAc = 95:5) afforded (–)-*anti*-**11** (64.5 mg, 0.16 mmol, 81%) as a sticky colorless oil.

$[\alpha]_D^{25}$ – 44.0 (*c* 0.40, $CHCl_3$).

IR (neat): ν_{max} 3567, 3457, 3087, 3063, 3029, 2929, 2856, 1603, 1495, 1454, 1367, 1244, 1138, 1071, 1029, 970, 883 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.35 (m, 7H), 7.31–7.23 (m, 6H), 7.09–7.07 (m, 2H), 4.10 (m, 1H), 4.01 (d, J_{AB} = 13.6 Hz, 2H), 3.81 (dd, J_{AB} = 13.6, 1.3 Hz, 2H), 3.35 (dd, J_{AB} = 13.6, 2.9 Hz, 1H), 3.24 (pent$_{app}$, J = 8.6 Hz, 1H), 2.28 (dd, J_{AB} = 13.8, 10.0 Hz, 1H), 1.66 (d, J = 5.0 Hz, 1H, OH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.6 (2C), 138.0, 129.6 (2C), 129.4 (4C), 128.9 (2C), 128.7 (4C), 127.7 (2C), 126.9, 70.6, 62.8 (q, J = 23.0 Hz), 55.4 (2C), 41.7.

CF_3 is not visible.

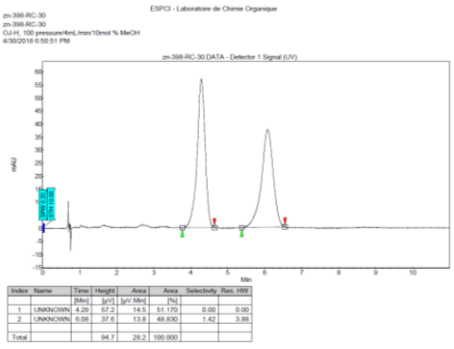
^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 62.04 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 399 ($M^{+\bullet}$, 1), 278 (25), 91 (100), 65 (5).

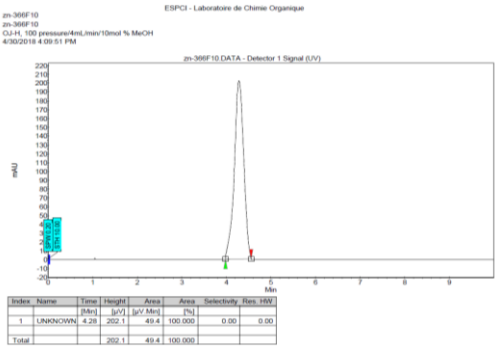
HRMS: calcd for $C_{24}H_{25}F_3NO$ $(M+H)^+$: 400.1883, found : 400.1879.

The enantiomeric excess of (–)-*anti*-**11** (ee > 99%) was determined by super-critical fluid chromatography (SFC) using a chiral stationary phase (OJ-H column, P = 100 bars, flow rate = 4 mL/min, eluent = sc CO_2/MeOH = 90:10, detection at 210 nm).

(±)-*anti*-**11** :[5]

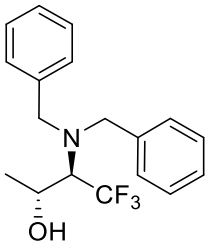


(–)-*anti*-**11** :



[5] Compound (±)-*anti*-**11** was synthesized from (±)-*anti*-**3** according to the general procedure of the rearrangement (described above).

(+)-**(2*R*,3*R*)-3-(Dibenzylamino)-4,4,4-trifluorobutan-2-ol [**(+)-*anti*-**12]**



Formula: $C_{18}H_{20}F_3NO$ **MW**= 323.36 g.mol^{-1}

Compound (+)-*anti*-**12** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluorobutan-2-ol (+)-*anti*-**4** (100 mg, 0.31 mmol) using H_2O as the nucleophile (32 µL, 1.75 mmol, 5.6 equiv). Purification by flash column chromatography (PE/EtOAc = 95:5 to 90:10) afforded (+)-*anti*-**12** (89.9 mg, 0.28 mmol, 89%) as a yellow solid.

mp = 77–79 °C.

$[\alpha]_D^{25}$ + 42.4 (*c* 0.20, $CHCl_3$).

IR (neat): ν_{max} 3370, 3086, 3064, 3029, 2974, 2935, 2858, 1603, 1495, 1455, 1366, 1247, 1139, 1071, 1029, 978, 916 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.26 (m, 10H), 4.12 (hex_{app}, J = 7.4 Hz, 1H), 3.98 (d, J_{AB} = 13.5 Hz, 2H), 3.72 (dd, J_{AB} = 13.5, 1.4 Hz, 2H), 3.08 ($pent_{app}$, J = 8.8 Hz, 1H), 1.66 (d, J = 6.6 Hz, 1H, OH), 1.28 (d, J = 6.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.6 (2C), 129.3 (4C), 128.7 (4C), 127.7 (2C), 65.9, 63.9 (q, J = 22.6 Hz), 55.3 (2C), 21.9.

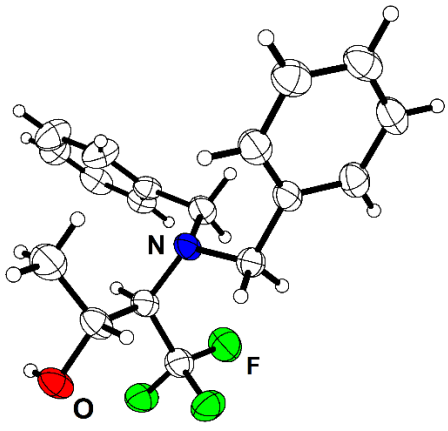
CF_3 is not visible.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 62.27 (3 x F, CF_3).

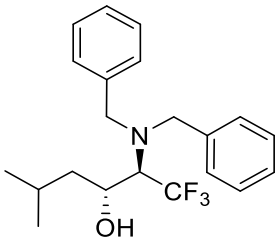
MS (EI, 70 eV): *m/z* (relative intensity) = 323 ($M^{+\bullet}$, 1), 278 (20), 91 (100), 65 (7).

HRMS: calcd for $C_{18}H_{21}F_3NO$ $(M+H)^+$: 324.1570, found : 324.1566.

Crystals suitable for X-ray diffraction analysis were obtained by slow evaporation of a solution of (+)-*anti*-**12** in PE 100% at rt. In the Supplementary Information, CCDC 1848221 corresponds to crystallographic data. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif.



(+)-**(2*R*,3*R*)-2-(Dibenzylamino)-1,1,1-trifluoro-5-methylhexan-3-ol [**(+)-*anti*-**13]**



Formula: $C_{21}H_{26}F_3NO$ **MW**= 365.44 g.mol^{-1}

Compound (+)-*anti*-**13** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-5-methyl-hexan-2-ol (−)-*anti*-**5** (73.1 mg, 0.2 mmol) using H_2O as the nucleophile (20 µL, 1.12 mmol, 5.6 equiv). Purification by flash column chromatography (PE/EtOAc = 95:5) afforded (+)-*anti*-**13** (59.7 mg, 0.163 mmol, 82%) as a white solid.

mp = 57−59 °C.

$[\alpha]_D^{25}$ + 18.4 (*c* 0.49, $CHCl_3$).

IR (neat): ν_{max} 3431, 3064, 3031, 2956, 1603, 1495, 1455, 1367, 1245, 1167, 1136, 1096, 1072, 1029, 971, 915 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36−7.24 (m, 10H), 3.97 (d, J_{AB} = 13.4 Hz, 2H), 3.95 (m, 1H), 3.73 (dd, J_{AB} = 13.5, 1.3 Hz, 2H), 3.09 (qd, *J* = 8.9, 1.2 Hz, 1H), 1.75 (m, 1H), 1.64 (m, 1H), 1.55 (d, *J* = 6.9 Hz, 1H, OH), 1.13 (ddd, *J* = 14.2, 10.6, 3.9 Hz, 1H), 0.90 (d, *J* = 5.4 Hz, 3H), 0.89 (d, *J* = 5.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.7 (2C), 129.3 (4C), 128.6 (4C), 127.6 (2C), 68.0, 63.2 (q, *J* = 22.4 Hz), 55.4 (2C), 44.2, 24.5, 24.0, 21.5.

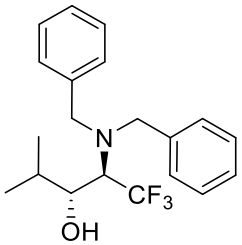
CF_3 is not visible.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ − 61.93 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 365 ($M^{+\bullet}$, 0.7), 278 (38), 181 (5), 91 (100), 65 (7).

HRMS: calcd for $C_{21}H_{27}F_3NO$ $(M+H)^+$: 366.2039, found : 366.2048.

(+)-**((2*R*,3*R*)-2-(Dibenzylamino)-1,1,1-trifluoro-4-methylpentan-3-ol [**(+)-*anti*-**14]**



Formula: $C_{20}H_{24}F_3NO$ **MW**= 351,41 g.mol^{-1}

Compound (+)-*anti*-**14** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-methyl-pentan-2-ol (+)-*anti*-**6** (91.3 mg, 0.26 mmol) using H_2O as the nucleophile (27 µL, 1.47 mmol, 5.6 equiv). Purification by flash column chromatography (PE/EtOAc = 98:2) afforded (+)-*anti*-**14** (48 mg, 0.136 mmol, 52%) as a colorless oil.

$[\alpha]_D^{25}$ + 15.9 (*c* 0.54, $CHCl_3$).

IR (neat): ν_{max} 3498, 3087, 3065, 3030, 2962, 2933, 2870, 1603, 1495, 1455, 1368, 1245, 1166, 1136, 1029, 969, 918 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.25 (m, 10H), 3.94 (d, J_{AB} = 13.4 Hz, 2H), 3.74 (m, 1H), 3.72 (dd, J_{AB} = 13.4, 1.2 Hz, 2H), 3.18 ($pent_{app}$, *J* = 8.8 Hz, 1H), 2.16 (m, 1H), 1.35 (d, *J* = 7.3 Hz, 1H, OH), 0.92 (d, *J* = 7.1 Hz, 3H), 0.27 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.7 (2C), 129.5 (4C), 128.6 (4C), 127.6 (2C), 73.8, 60.3 (q, *J* = 22.2 Hz), 55.1 (2C), 28.9, 20.4, 13.7.

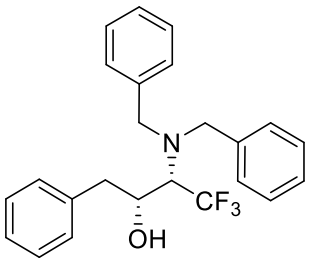
CF_3 is not visible.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 61.55 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 351 ($M^{+\bullet}$, 0.9), 278 (34), 181 (4), 91 (100), 65 (8).

HRMS: calcd for $C_{20}H_{25}F_3NO$ $(M+H)^+$: 352.1883, found : 352.1882.

(+)-(2*R*,3*S*)-3-(Dibenzylamino)-4,4,4-trifluoro-1-phenylbutan-2-ol [(+)-*syn*-11]



Formula: $C_{24}H_{24}F_3NO$ **MW**= 399.46 $g.mol^{-1}$

Compound (+)-*syn*-**11** was synthesized from (2*R*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*syn*-**3** (107.9 mg, 0.27 mmol) using H_2O as the nucleophile (30 µL, 1.5 mmol, 5.6 equiv). Purification by flash column chromatography (PE/EtOAc = 95:5) afforded (+)-*syn*-**11** (96.9 mg, 0.24 mmol, 91%) as a sticky yellow oil.

$[\alpha]_D^{25}$ + 38.4 (*c* 0.39, $CHCl_3$).

IR (neat): ν_{max} 3569, 3453, 3088, 3063, 3030, 2864, 1603, 1496, 1454, 1368, 1250, 1130, 1075, 1029, 1003, 989, 968, 878 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32–7.14 (m, 15H), 4.12 (m, 1H), 4.10 (d, J_{AB} = 13.3 Hz, 2H), 3.69 (dd, J_{AB} = 13.2, 1.2 Hz, 2H), 3.50 (s, 1H, OH), 3.12 ($pent_{app}$, *J* = 8.5 Hz, 1H), 2.90 (d, J_{AB} = 14.0 Hz, 1H), 2.54 (dd, J_{AB} = 14.1, 8.7 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.93, 137.86 (2C), 129.6 (2C), 129.4 (4C), 128.9 (4C), 128.4 (2C), 127.9 (2C), 127.2 (d_{app}, *J* = 291.6 Hz)*, 126.5, 67.1, 62.8 (q, *J* = 24.4 Hz), 54.7 (2C), 39.7.

(*) only the two main intense signals of the quadruplet are visible.

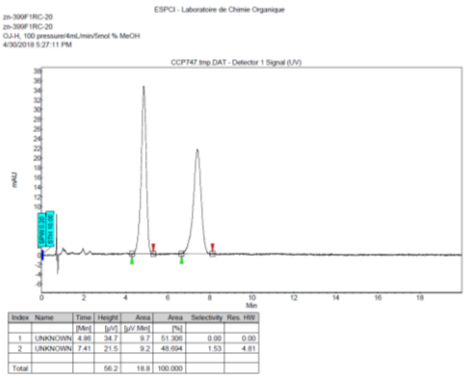
^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 62.13 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 399 ($M^{+\bullet}$, 2), 278 (26), 91 (100), 65 (6).

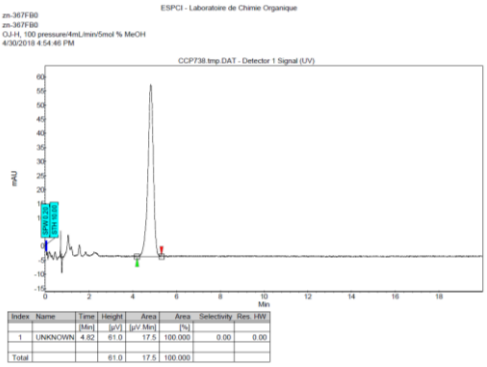
HRMS: calcd for $C_{24}H_{25}F_3NO$ $(M+H)^+$: 400.1883, found : 400.1872.

The enantiomeric excess of (–)-*syn*-**11** (ee > 99%) was determined by super-critical fluid chromatography (SFC) using a chiral stationary phase (OJ-H column, P = 100 bars, flow rate = 4 mL/min, eluent = sc CO_2/MeOH = 95:5, detection at 210 nm).

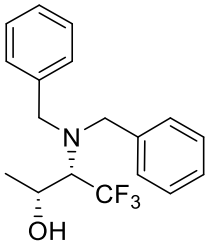
(±)-*syn*-**11** :[6]



(+)-*syn*-**11** :



(–)-(2*R*,3*S*)-3-(Dibenzylamino)-4,4,4-trifluorobutan-2-ol [(–)-*syn*-12]



Formula: $C_{18}H_{20}F_3NO$ **MW**= 323.36 g.mol^{-1}

Compound (–)-*syn*-**12** was synthesized from (2*R*,3*S*)-3-(dibenzylamino)-1,1,1-trifluorobutan-2-ol (+)-*syn*-**4** (74.3 mg, 0.23 mmol) using H_2O as the nucleophile (23 µL, 1.27 mmol, 5.6 equiv). Purification by flash column chromatography (PE/EtOAc = 95:5) afforded (–)-*syn*-**12** (59.3 mg, 0.18 mmol, 81%) as a yellow oil.

$[\alpha]_D^{25}$ – 59.4 (*c* 0.16, $CHCl_3$).

IR (neat): ν_{max} 3450, 3065, 3030, 2974, 2935, 2865, 1603, 1496, 1455, 1369, 1250, 1169, 1130, 1093, 1075, 1028, 978, 913 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.23 (m, 10H), 4.07 (d, J_{AB} = 13.2 Hz ,2H), 3.96 (dq, *J* = 8.9, 6.1 Hz, 1H), 3.68 (dd, J_{AB} = 13.2, 1.4 Hz, 2H), 3.47 (s, 1H, OH), 2.91 ($pent_{app}$, *J* = 8.8 Hz, 1H), 1.17 (dd, *J* = 6.0, 1.5 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.0 (2C), 129.4 (4C), 128.9 (4C), 127.9 (2C), 127.0 (q, *J* = 291.3 Hz), 65.3 (q, *J* = 24.1 Hz), 62.4, 54.5 (2C), 19.1.

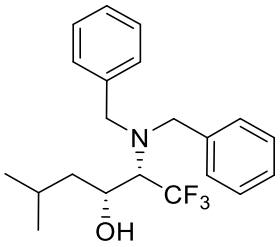
^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 62.36 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 323 ($M^{+\bullet}$, 2), 278 (36), 181 (4), 91 (100), 65 (18).

HRMS: calcd for $C_{18}H_{21}F_3NO$ $(M+H)^+$: 324.1570, found : 324.1568.

[6] Compound (±)-*syn*-**11** was synthesized from (±)-*syn*-**3** according to the general procedure of the rearrangement (described above).

(–)-**(2*S*,3*R*)-2-(Dibenzylamino)-1,1,1-trifluoro-5-methylhexan-3-ol [**(–)-*syn*-**13]**



Formula: $C_{21}H_{26}F_3NO$ **MW**= 365.44 g.mol^{-1}

Compound (–)-*syn*-**13** was synthesized from (2*R*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-5-methylhexan-2-ol (+)-*syn*-**5** (84 mg, 0.23 mmol) using H_2O as the nucleophile (23 µL, 1.29 mmol, 5.6 equiv). Purification by flash column chromatography (PE/EtOAc = 98:2) afforded (–)-*syn*-**13** (53.3 mg, 0.146 mmol, 63%) as a colorless oil.

$[\alpha]_D^{25}$ – 12.5 (*c* 0.36, $CHCl_3$).

IR (neat): ν_{max} 3451, 3067, 3032, 2958, 2871, 1605, 1498, 1457, 1369, 1280, 1167, 1132, 1105, 1073, 1031, 975, 917 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.23 (m, 10H), 4.09 (d, J_{AB} = 13.2 Hz, 2H), 3.89 (m, 1H), 3.68 (dd, J_{AB} = 13.2, 1.3 Hz, 2H), 3.48 (s, 1H, OH), 2.96 (pent$_{app}$, J = 8.7 Hz, 1H), 1.81 (hept$_{app}$, J = 8.0 Hz, 1H), 1.25 (d, J_{AB} = 7.1 Hz, Hz, 1H), 1.21 (d, J_{AB} = 7.3 Hz, 1H), 0.867 (d, J = 6.5 Hz, 3H), 0.872 (d, J = 6.7 Hz, 3H).

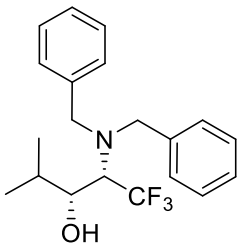
^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.0 (2C), 129.4 (4C), 128.9 (4C), 127.9 (2C), 127.1 (q, J = 291.4 Hz), 64.3 (q, J = 24.0 Hz), 64.2, 54.7 (2C), 42.3, 24.5, 24.1, 21.2.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 61.90 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 365 ($M^{+\bullet}$, 1), 278 (43), 181 (6), 91 (100), 65 (8).

HRMS: calcd for $C_{21}H_{27}F_3NO$ $(M+H)^+$: 366.2039, found : 366.2054.

(–)-**(2*S*,3*R*)-2-(Dibenzylamino)-1,1,1-trifluoro-4-methylpentan-3-ol [**(–)-*syn*-**14]**



Formula: $C_{20}H_{24}F_3NO$ **MW**= 351,41 g.mol^{-1}

Compound (–)-*syn*-**14** was synthesized from (2*R*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-methyl-pentan-2-ol (+)-*syn*-**6** (56.2 mg, 0.16 mmol) using H_2O as the nucleophile (18 µL, 0.98 mmol, 5.6 equiv). Purification by flash column chromatography (PE/EtOAc =98:2) afforded (–)-*syn*-**14** (18 mg, 0.05 mmol, 31%) as a colorless oil.

$[\alpha]_D^{25}$ – 13. 2 (*c* 0.75, $CHCl_3$).

IR (neat): ν_{max} 3429, 3091, 3066, 3033, 2965, 2935, 2874, 1605, 1498, 1457, 1369, 1251, 1164, 1131, 1076, 1031, 967, 919 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.25 (m, 10H), 4.08 (d, J = 12.9 Hz, 2H), 3.74 (dd, J_{AB} = 9.1, 1.6 Hz, 1H), 3.66 (dd, J_{AB} = 13.0, 1.4 Hz, 2H), 3.61 (s, 1H, OH), 3.19 ($pent_{app}$, J = 8.6 Hz, 1H), 1.74 ($pent_{app}$, J = 6.7 Hz, 1H), 0.98 (d, J = 6.9 Hz, 3H), 0.47 (d, J = 6.7 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.8 (2C), 129.5 (4C), 128.9 (4C), 127.9 (2C), 69.2, 60.3 (q, J = 24.4 Hz), 54.5 (2C), 29.1, 21.0, 13.5.

CF_3 is not visible.

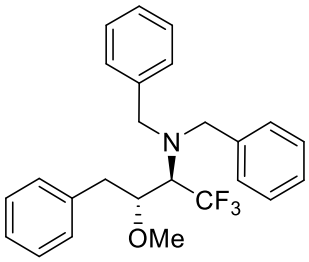
^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 62.74 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 351 ($M^{+\bullet}$, 0.5), 278 (22), 91 (100), 65 (5).

HRMS: calcd for $C_{20}H_{25}F_3NO$ $(M+H)^+$: 352.1883, found : 352.1876.

b. Synthesis of α-trifluoromethylamines

(–)-(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1-trifluoro-3-methoxy-4-phenylbutan-2-amine [(–)-15a]



Formula: $C_{25}H_{26}F_3NO$ **MW**= 413.48 $g.mol^{-1}$

Compound (–)-**15a** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (79.9 mg, 0.20 mmol) using anhydrous MeOH as the nucleophile (41 µL, 1.0 mmol, 5 equiv). Purification by flash column chromatography (PE 100% to PE/EtOAc = 95:5) afforded (–)-**15a** (69.5 mg, 0.17 mmol, 84%) as a vicsous yellow oil.

$[\alpha]_D^{25}$ – 39.4 (*c* 0.34, $CHCl_3$).

IR (neat): ν_{max} 3087, 3063, 3029, 2935, 2835, 1603, 1495, 1454, 1364, 1247, 1138, 1100, 1075, 1024, 984, 968 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33–7.21 (m, 13H), 7.13–7.11 (m, 2H), 3.87 (d, J_{AB} = 13.6 Hz, 2H), 3.82 (d, J_{AB} = 13.7 Hz, 2H), 3.65 (m, 1H), 3.24 (dd, J_{AB} = 13.6, 4.6 Hz, 1H), 3.19 (dd, J = 8.5, 7.3 Hz, 1H), 3.04 (s, 3H), 2.48 (dd, J_{AB} = 13.8, 8.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.69, 138.66 (2C), 129.6 (2C), 129.3 (4C), 128.7 (2C), 128.6 (4C), 127.5 (2C), 126.5, 81.2, 61.5 (q, J = 23.5 Hz), 59.2, 55.3 (2C), 39.6.

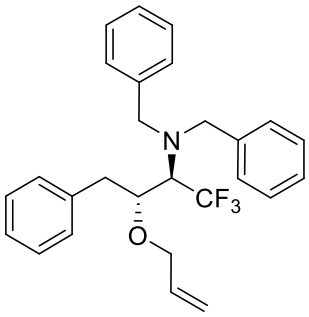
CF_3 is not visible.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 62.73 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 413 ($M^{+\bullet}$, 1.5), 278 (36), 135 (15), 103 (7), 91 (100), 65 (7).

HRMS: calcd for $C_{25}H_{26}F_3NONa$ $(M+Na)^+$: 436.1859, found : 436.1840.

(–)-(2*R*,3*R*)-3-(Allyloxy)-*N*,*N*-dibenzyl-1,1,1-trifluoro-4-phenylbutan-2-amine [(–)-15b]



Formula: $C_{27}H_{28}F_3NO$ **MW**= 439,52 g.mol^{-1}

Compound (–)-**15b** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (79.9 mg, 0.20 mmol) using allylic alcohol as the nucleophile (70 µL, 1.0 mmol, 5 equiv). Purification by flash column chromatography (PE/EtOAc = 95:5) afforded (–)-**15b** (61.5 mg, 0.14 mmol, 70%) as a colorless oil.

$[\alpha]_D^{25}$ – 32.3 (*c* 0.19, $CHCl_3$).

IR (neat): ν_{max} 3086, 3063, 3029, 2925, 2856, 1603, 1544, 1495, 1328, 1188, 1137, 1074, 1027, 989, 970, 921 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34–7.19 (m, 13H), 7.13–7.11 (m, 2H), 5.62 (m, 1H), 5.04–4.99 (m, 2H), 3.91 (d, J_{AB} = 13.5 Hz, 2H), 3.81 (d, J_{AB} = 13.1 Hz, 2H), 3.80 (m, 1H), 3.71 (dd, J_{AB} = 11.5, 5.8 Hz, 1H), 3.41 (dd, J_{AB} = 11.5, 6.0 Hz, 1H), 3.32 (dd, J_{AB} = 13.9, 3.9 Hz, 1H), 3.24 ($pent_{app}$, J = 8.2 Hz, 1H), 2.44 (dd, J_{AB} = 13.8, 9.1 Hz, 1H).

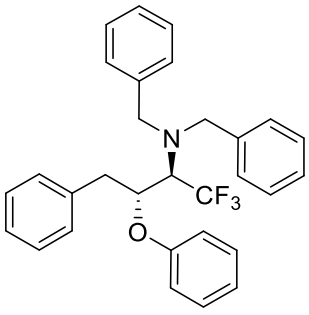
^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.8, 138.6 (2C), 134.1, 129.7 (2C), 129.3 (4C), 128.6 (6C), 127.7 (q, J = 292.7 Hz), 127.6 (2C), 126.6, 117.4, 79.2, 72.9, 61.8 (q, J = 23.2 Hz), 55.3 (2C), 40.1.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 62.23 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 439 ($M^{+\bullet}$, 0.35), 278 (32), 197 (10), 143 (13), 91 (100), 65 (7).

HRMS: calcd for $C_{27}H_{29}F_3NO$ $(M+H)^+$: 440.2196, found : 440.2193.

(–)-(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1-trifluoro-3-phenoxy-4-phenylbutan-2-amine [(–)-15c]



Formula: $C_{30}H_{28}F_3NO$ **MW**= 475.56 g.mol^{-1}

Compound (–)-**15c** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (59.9 mg, 0.15 mmol) using dry NaOPh as the nucleophile (44 mg, 0.38 mmol, 2.5 equiv). Purification by flash column chromatography (PE/EtOAc = 98:2) afforded (–)-**15c** (53.7 mg, 0.11 mmol, 75%) as a sticky colorless oil.

$[\alpha]_D^{25}$ – 22.4 (*c* 0.25, $CHCl_3$).

IR (neat): ν_{max} 3089, 3065, 3031, 2930, 2857, 2812, 1600, 1590, 1496, 1456, 1366, 1239, 1142, 1112, 1076, 1004, 973, 922 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30–7.14 (m, 15H), 7.07–7.05 (m, 2H), 6.87 (t_{app}, J = 7.3 Hz, 1H), 6.69 (d, J = 7.9 Hz, 2H), 4.77 (q_{app}, J = 5.9 Hz, 1H), 3.87 (d, J_{AB} = 13.6 Hz, 2H), 3.71 (d, J_{AB} = 13.6 Hz, 2H), 3.43 (m, 1H), 3.25 (dd, J_{AB} = 14.0, 6.5 Hz, 1H), 2.88 (dd, J_{AB} = 14.0, 7.0 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.6, 138.6 (2C), 137.3, 129.8 (2C), 129.5 (2C), 129.2 (4C), 128.8 (2C), 128.6 (4C), 127.5 (2C), 126.9, 121.3, 115.6 (2C), 76.8, 60.7 (q, J = 24.4 Hz), 55.4 (2C), 38.8.

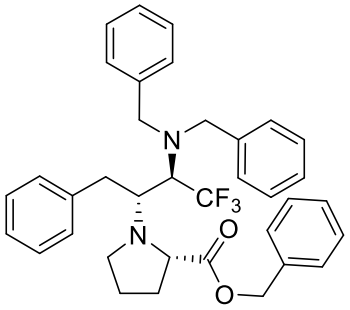
CF_3 is not visible.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 63.10 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 475 ($M^{+\bullet}$, 0.01), 382 ([$M^{+\bullet}$–$^{\bullet}$OPh], 20), 278 (26), 119 (4), 91 (100), 65 (5).

HRMS: calcd for $C_{30}H_{29}F_3NO$ $(M+H)^+$: 476.2196, found : 476.2186.

(–)-Benzyl-*N*-[(2*R*,3*R*)-3-(dibenzylamino)-4,4,4-trifluoro-1-phenylbutan-2-yl]-L-prolinate [(–)-15d]



Formula: $C_{36}H_{37}F_3N_2O_2$ **MW**= 586.70 $g.mol^{-1}$

Compound (–)-**15d** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenyl-butan-2-ol (+)-*anti*-**3** (79.9 mg, 0.20 mmol) using L-proline benzyl ester as the nucleophile (103 mg, 0.5 mmol, 2.5 equiv). Purification by flash column chromatography (PE/EtOAc = 98:2 to 95:5) afforded (–)-**15d** (80 mg, 0.13 mmol, 68%) as a colorless sticky oil.

$[\alpha]_D^{25}$ – 28.9 (*c* 0.38, $CHCl_3$).

IR (neat): ν_{max} 3063, 3029, 2947, 2864, 1742, 1602, 1495, 1454, 1367, 1241, 1157, 1132, 1105, 1075, 1029, 996, 970, 908 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33–7.14 (m, 20H), 5.01 (d, J_{AB} = 12.4 Hz, 1H), 4.96 (d, J_{AB} = 12.4 Hz, 1H), 4.00–3.89 (m, 3H), 3.69 (d, J_{AB} = 13.4 Hz, 2H), 3.47 (dd, J_{AB} = 14.4, 2.9 Hz, 1H), 3.16 (dq, J = 16.3, 8.1 Hz, 1H), 2.80 (dd, J = 8.9, 3.1 Hz, 1H), 2.72 (m, 1H), 2.60 (td, J = 7.3, 2.0 Hz, 1H), 2.39 (dd, J_{AB} = 14.4, 10.9 Hz, 1H), 1.79 (m, 1H), 1.71–157 (m, 2H), 1.23 (m, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.6, 140.5, 138.8 (2C), 136.3, 129.54 (4C), 129.49 (2C), 128.63 (2C), 128.58 (4C), 125.51 (2C), 128.2 (2C), 128.1, 127.5 (2C), 126.4, 66.2, 63.9, 61.8 (q, J = 21.6 Hz), 58.4, 54.9 (2C), 44.5, 34.3, 28.6, 25.0.

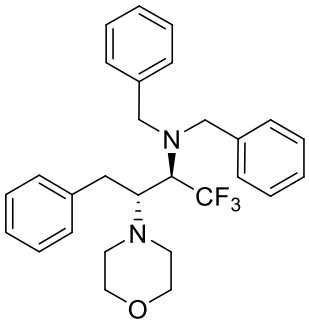
CF_3 is not visible.

^{19}F NMR (CDCl$_3$, 376 MHz) : δ – 62.86 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 451 ([$M^{+\bullet}$ – $^{\bullet}CO_2Bn$], 1), 308 (100), 217 (7), 172 (9), 104 (8), 91 (67).

HRMS: calcd for $C_{36}H_{37}F_3N_2O_2Na$ $(M+Na)^+$: 609.2699, found : 609.2696.

(–)-(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1-trifluoro-3-morpholino-4-phenylbutan-2-amine [(–)-15e]



Formula: $C_{28}H_{31}F_3N_2O$ **MW**= 468.56 g.mol^{-1}

Compound (–)-**15e** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenyl-butan-2-ol (+)-*anti*-**3** (59.9 mg, 0.15 mmol) using morpholine as the nucleophile (38 µL, 0.42 mmol, 2.8 equiv). Purification by flash column chromatography (PE 100% and PE/EtOAc = 95:5) afforded (–)-**15e** (57 mg, 0.12 mmol, 80%) as a pale pink solid.

mp = 101–103 °C.

$[\alpha]_D^{25}$ – 12.4 (*c* 0.48, $CHCl_3$).

IR (neat): ν_{max} 3086, 3062, 3028, 2951, 2856, 1683, 1602, 1495, 1265, 1156, 1132, 1115, 1075, 997, 970, 912 cm^{-1}.

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.33–7.16 (m, 15H), 4.05 (br d, J_{AB} = 11.5 Hz, 2H), 3.79 (d, J_{AB} = 13.4 Hz, 2H), 3.48–3.43 (m, 3H), 3.40–3.28 (m, 3H), 3.18 (pent$_{app}$, *J* = 8.5 Hz, 1H), 2.43–2.33 (m, 3H), 2.19–2.14 (m, 2H).

^{13}C NMR (CDCl$_3$, 100 MHz): δ 141.0 (2C), 138.7, 129.4 (2C), 129.3 (4C), 128.8 (2C), 128.7 (4C), 128.3 (d$_{app}$, *J* = 293.3 Hz)*, 127.6 (2C), 126.3, 67.5 (2C), 64.8, 61.0 (q, *J* = 20.9 Hz), 55.1 (2C), 50.0 (2C), 34.4.

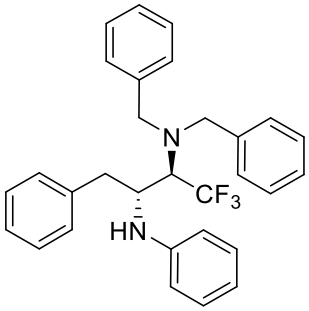
(*) only the two main intense signals of the quadruplet are visible.

^{19}F NMR (CDCl$_3$, 376 MHz) : δ – 61.57 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 377 ([$M^{+\bullet}$ – $^{\bullet}Bn$], 0.1), 190 (100), 91 (24).

HRMS: calcd for $C_{28}H_{32}F_3N_2O$ $(M+H)^+$: 469.2461, found : 469.2443.

(+)-**(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1-trifluoro-*N*',4-diphenylbutane-2,3-diamine [**(+)-**15f]**



Formula: $C_{30}H_{29}F_3N_2$ **MW**= 474,57 g.mol^{-1}

Compound (+)-**15f** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (79.9 mg, 0.20 mmol) using $PhNH_2$ as the nucleophile (50 µL, 0.55 mmol, 2.7 equiv). Purification by flash column chromatography (PE/EtOAc = 95:5) afforded (+)-**15f** (90 mg, 0.19 mmol, 95%) as a sticky yellow oil.

$[\alpha]_D^{25}$ + 3.1 (*c* 0.65, $CHCl_3$).

IR (neat): ν_{max} 3405, 3087, 3062, 3028, 2927, 2855, 1601, 1496, 1454, 1366, 1323, 1244, 1133, 1097, 1074, 1028, 970, 919 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31–7.17 (m, 13H), 7.07–7.05 (m, 2H), 6.94 (dd, *J* = 6.5, 2.9 Hz, 2H), 6.64 (t_{app}, *J* = 7.3 Hz, 1H), 6.40 (d, *J* = 7.8 Hz, 2H), 4.02 (m, 1H), 3.88 (d, J_{AB} = 13.7 Hz, 2H), 3.83 (d, J_{AB} = 13.7 Hz, 2H), 3.57 (d, *J* = 10.9 Hz, 1H, NH), 3.34 (m, 1H), 3.07 (dd, J_{AB} = 13.6, 6.7 Hz, 1H), 2.80 (dd, J_{AB} = 13.6, 6.9 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.6, 138.8 (2C), 138.0, 129.6 (2C), 129.4 (2C), 129.3 (4C), 128.7 (2C), 128.6 (4C), 127.5 (2C), 126.7, 117.8, 113.5 (2C), 60.5 (q, *J* = 23.3 Hz), 55.5 (2C), 54.0, 39.3.

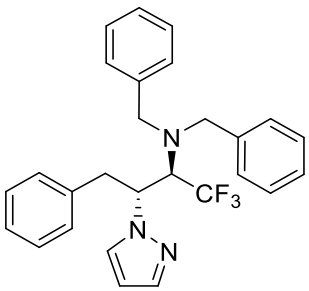
CF_3 is not visible.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 62.77 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 474 ($M^{+\bullet}$, 0.16), 259 (11), 196 (100), 118 (12), 104 (8), 91 (38).

HRMS: calcd for $C_{30}H_{30}F_3N_2$ $(M+H)^+$: 475.2356, found : 475.2353.

(+)-**(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1-trifluoro-4-phenyl-3-(1H-pyrazol-1-yl)butan-2-amine [**(+)-**15g]**



Formula: $C_{27}H_{26}F_3N_3$ **MW**= 449.52 g.mol^{-1}

Compound (+)-**15g** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (59.9 mg, 0.15 mmol) using sodium 1*H*-pyrazolide as the nucleophile (0.5 M in THF) (0.9 mL,

0.45 mmol, 3 equiv). Purification by flash column chromatography (EP/EtOAc 98:2) afforded (+)-**15g** (64 mg, 0.14 mmol, 95%) as a sticky colorless oil.

$[\alpha]_D^{25}$ + 50.9 (*c* 0.22, $CHCl_3$).

IR (neat): ν_{max} 3064, 3030, 2946, 2860, 1603, 1495, 1455, 1367, 1239, 1140, 1108, 1076, 1028, 969, 917 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.47–7.30 (m, 11H), 7.09–7.07 (m, 3H), 6.89 (d, J = 2.1 Hz, 1H), 6.68 (dd, J = 6.5, 2.8 Hz, 2H), 5.96 (t_{app}, J = 2.0 Hz, 1H), 4.47 (td, J = 9.8, 2.6 Hz, 1H), 4.13 (d, J_{AB} = 13.4 Hz, 2H), 4.01 (m, 1H), 3.84 (d, J_{AB} = 13.6 Hz, 2H), 3.73 (dd, J_{AB} = 13.8, 2.5 Hz, 1H), 3.02 (dd, J_{AB} = 13.6, 11.9 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.0, 138.2, 138.0 (2C), 131.1, 129.4 (4C), 128.9 (6C), 128.4 (2C), 127.9 (2C), 126.6, 125.7 (d_{app}, J = 294.5 Hz)*, 104.6, 62.8 (q, J = 23.5 Hz), 62.6, 55.3 (2C), 38.6.

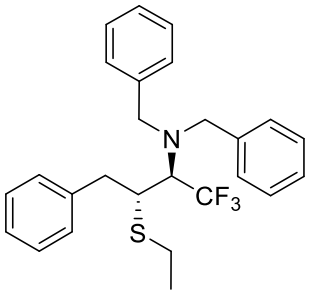
(*) only the two main intense signals of the quadruplet are visible.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 64.21 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 449 ($M^{+\bullet}$, 0.01), 358 ([$M^{+\bullet}$ – $^\bullet$Bn], 40), 290 (13), 278 (10), 91 (100), 65 (6).

HRMS: calcd for $C_{27}H_{27}F_3N_3$ $(M+H)^+$: 450.2152, found : 450.2164.

(–)-(2*S*,3*R*)-*N*,*N*-Dibenzyl-3-(ethylthio)-1,1,1-trifluoro-4-phenylbutan-2-amine [(–)-15h]



Formula: $C_{26}H_{28}F_3NS$ **MW**= 443.57 $g.mol^{-1}$

Compound (–)-**15h** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenyl-butan-2-ol (+)-*anti*-**3** (59.9 mg, 0.15 mmol) using EtSH as the nucleophile (28 µL, 0.37 mmol, 2.5 equiv). Purification by flash column chromatography (PE/EtOAc = 98:2 then 95:5) afforded (–)-**15h** (50 mg, 0.11 mmol, 75%) as a colorless oil.

$[\alpha]_D^{25}$ – 28.7 (*c* 1.78, $CHCl_3$).

IR (neat): ν_{max} 3087, 3063, 3029, 2969, 2929, 2857, 1603, 1495, 1454, 1367, 1245, 1130, 1101, 1074, 1029, 969, 919 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31–7.21 (m, 13H), 7.12–7.10 (m, 2H), 3.97 (d, J_{AB} = 13.7 Hz, 2H), 3.88 (d, J_{AB} = 13.5 Hz, 2H), 3.46 (dd, J_{AB} = 13.9, 5.1 Hz, 1H), 3.38 (dd, J = 8.8, 6.2 Hz, 1H), 3.02 ($pent_{app}$, J = 5.1 Hz, 1H), 2.52 (dd, J_{AB} = 13.9, 10.0 Hz, 1H), 2.21–2.05 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.5, 138.7 (2C), 129.5 (2C), 129.3 (4C), 128.5 (6C), 127.5 (2C), 126.6, 61.6 (q, J = 23.6 Hz), 55.5 (2C), 46.7, 40.3, 26.0, 14.2.

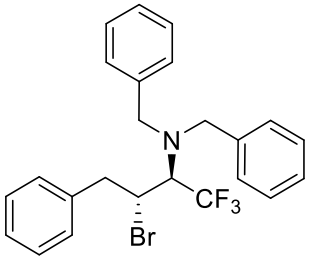
CF_3 is not visible.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 62.22 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 382 ([$M^{+\bullet}$ – $^{\bullet}$SEt], 13), 278 (33), 181 (4), 91 (100), 65 (6).

HRMS: calcd for $C_{26}H_{28}F_3NSNa$ $(M+Na)^+$: 466.1787, found : 466.1766.

(–)-(2*S*,3*R*)-*N*,*N*-Dibenzyl-3-bromo-1,1,1-trifluoro-4-phenylbutan-2-amine [(–)-15i]



Formula: $C_{24}H_{23}BrF_3N$ **MW**= 462.35 g.mol^{-1}

Compound (–)-**15i** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (79.9 mg, 0.20 mmol) using dry *n*-Bu_4NBr as the nucleophile (195.4, 0.6 mmol, 3 equiv). Purification by flash column chromatography (PE 100% and PE/EtOAc = 95:5) afforded (–)-**15i** (74 mg, 0.16 mmol, 80%) as a pale green oil.

$[\alpha]_D^{25}$ – 32.9 (*c* 2.47, $CHCl_3$).

IR (neat): ν_{max} 3089, 3066, 3032, 2926, 2859, 1605, 1498, 1456, 1369, 1252, 1127, 1103, 1076, 1031, 969 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34–7.25 (m, 13H), 7.07 (dd_{app}, *J* = 7.4, 1.9 Hz, 2H), 4.25 (ddd, *J* = 10.5, 6.6, 4.7 Hz, 1H), 3.96 (d, J_{AB} = 13.6 Hz, 2H), 3.88 (d, J_{AB} = 13.6 Hz, 2H), 3.72 (dd, J_{AB} = 14.6, 4.6 Hz, 1H), 3.55 (m, 1H), 2.72 (dd, J_{AB} = 14.6, 10.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.24, 138.2 (2C), 129.3 (6C), 128.8 (2C), 128.7 (4C), 127.8 (2C), 127.1, 126.7 (d_{app}, *J* = 291.2 Hz)*, 63.0 (q, *J* = 24.7 Hz), 55.3 (2C), 49.4, 43.3.

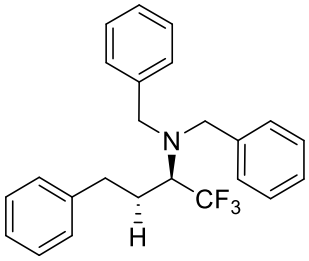
(*) only the two main intense signals of the quadruplet are visible.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 62.02 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 462 ($M^{+\bullet}$, 0.02), 382 ([$M^{+\bullet}$ – $^{\bullet}$Br], 27), 278 (4), 196 (8), 185 (13), 91 (100).

HRMS: calcd for $C_{24}H_{24}{}^{19}BrF_3N$ $(M+H)^+$: 462.1039, found : 462.1029 and calcd for $C_{24}H_{24}{}^{18}BrF_3N$ $(M+H)^+$: 464.1018, found : 464.1007.

(−)-(*R*)-*N*,*N*-Dibenzyl-1,1,1-trifluoro-4-phenylbutan-2-amine [(−)-15j]



Formula: $C_{24}H_{24}F_3N$ **MW**= 383.46 g.mol^{-1}

Compound (−)-**15j** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (79.9 mg, 0.20 mmol) using *n*-Bu_4NBH_4 as the nucleophile (131.3 mg, 0.5 mmol, 2.5 equiv). Purification by flash column chromatography (EP/EtOAc 98:2) afforded (−)-**15j** (69 mg, 0.18 mmol, 90%) as a brown oil.

$[\alpha]_D^{25}$ − 30.9 (*c* 0.48, $CHCl_3$).

IR (neat): ν_{max} 3064, 3029, 2956, 2858, 1603, 1495, 1454, 1371, 1250, 1140, 1102, 1073, 1029, 969 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35−7.14 (m, 13H), 7.01 (br d, J = 7.0 Hz, 2H), 3.96 (d, J_{AB} = 13.6 Hz, 2H), 3.71 (dd, J_{AB} = 13.6, 1.3 Hz, 2H), 3.16 (m, 1H), 2.91 (ddd, J_{AB} = 14.6, 10.4, 5.6 Hz, 1H), 2.41 (ddd, J_{AB} = 13.9, 10.1, 6.4 Hz, 1H), 2.00 (m, 1H), 1.87 (m, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.4, 139.2 (2C), 129.2 (4C), 128.61 (2C), 128.58 (4C), 128.5 (2C), 128.1 (d_{app}, J = 291.5 Hz)*, 127.4 (2C), 126.2, 58.1 (q, J = 24.8 Hz), 54.3 (2C), 32.7, 28.6.

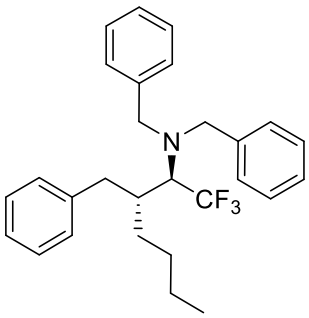
(*) only the two main intense signals of the quadruplet are visible.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 67.72 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 383 ($M^{+\bullet}$,7), 314 (21), 292 (27), 188 (6), 91 (100), 65 (10).

HRMS: calcd for $C_{24}H_{25}F_3N$ $(M+H)^+$: 384.1934, found : 384.1934.

(−)-(2*R*,3*R*)-*N*,*N*,3-Tribenzyl-1,1,1-trifluoroheptan-2-amine [(−)-15k]



Formula: $C_{28}H_{32}F_3N$ **MW**= 439.57 g.mol^{-1}

Compound (−)-**15k** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (79.9 mg, 0.20 mmol) using *n*BuCu(CN)Li as the nucleophile (0.15 M/Et_2O) (5 mL, 0.74 mmol, 3.7 equiv). Purification by flash column chromatography (PE 100%) afforded (−)-**15k** (52.9 mg, 0.12 mmol, 60%) as a cloudy colorless oil.

$[\alpha]_D^{25}$ – 6.9 (*c* 0.47, $CHCl_3$).

IR (neat): ν_{max} 3062, 3028, 2957, 2861, 1603, 1496, 1454, 1367, 1242, 1134, 1091, 1073, 1029, 968, 913 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.24–7.07 (m, 13H), 6.98 (d_{app}, J = 7.0 Hz, 2H), 3.87 (d, J_{AB} = 13.5 Hz, 2H), 3.68 (dd, J_{AB} = 13.5, 0.7 Hz, 2H), 3.19–3.11 (m, 2H), 2.21 (dd, J = 13.5, 10.5 Hz, 1H), 2.01 (m, 1H), 1.26 (m, 1H), 1.12 (m, 1H), 1.01–0.85 (m, 2H), 0.74–0.68 (m, 2H), 0.60 (t, J = 7.3 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.0, 139.1 (2C), 129.4 (4C), 129.3 (2C), 128.5 (6C), 127.4 (2C), 126.1, 59.6 (q, J = 23.3 Hz), 55.5 (2C), 39.3, 37.0, 28.3, 27.7, 22.8, 13.9.

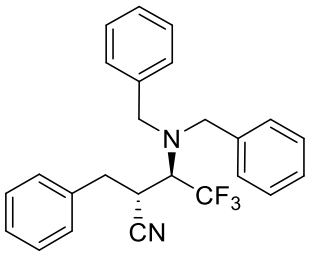
CF_3 is not visible.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 63.15 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 439 ($M^{+\bullet}$, 5), 348 (13), 278 (29), 188 (4), 91 (100), 65 (6).

HRMS: calcd for $C_{28}H_{33}F_3N$ $(M+H)^+$: 440.2560, found : 440.2559.

(–)-(2*R*,3*R*)-2-Benzyl-3-(dibenzylamino)-4,4,4-trifluorobutanenitrile [(–)-15l]



Formula: $C_{25}H_{23}F_3N_2$ **MW**= 408.47 $g.mol^{-1}$

Compound (–)-**15l** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-4-phenylbutan-2-ol (+)-*anti*-**3** (59.9 mg, 0.15 mmol) using dry *n*-Bu_4NCN as the nucleophile (120 mg, 0.42 mmol, 2.9 equiv). Purification by flash column chromatography (EP/EtOAc 95:5) afforded (–)-**15l** (36.6 mg, 0.089 mmol, 60%) as a yellow oil.

$[\alpha]_D^{25}$ – 41.0 (*c* 0.61, $CHCl_3$).

IR (neat): ν_{max} 3064, 3031, 2933, 2861, 1603, 1496, 1455, 1369, 1247, 1143, 1128, 1103, 1075, 1028, 970 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37–7.25 (m, 13H), 7.10–7.07 (m, 2H), 3.92 (d, J_{AB} = 13.5 Hz, 2H), 3.83 (d, J_{AB} = 13.5 Hz, 2H), 3.42 ($pent_{app}$, J = 8.1 Hz, 1H), 3.27 (dd, J_{AB} = 13.7, 5.3 Hz, 1H), 3.05 (ddd, J = 10.1, 7.7, 5.3 Hz, 1H), 2.58 (dd, J_{AB} = 13.7, 10.2 Hz, 1H).

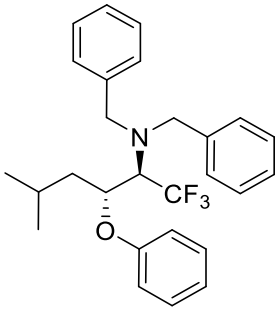
^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.6 (2C), 136.3, 129.20 (4C), 129.15 (2C), 129.1 (2C), 128.9 (4C), 128.0 (2C), 127.7, 126.4 (q, J = 291.5 Hz), 118.5, 60.2 (q, J = 26.0 Hz), 54.8 (2C), 36.6, 32.8.

^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ – 64.05 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 408 ($M^{+\bullet}$, 0.6), 278 (18), 91 (100), 65 (6).

HRMS: calcd for $C_{25}H_{23}F_3N_2Na$ $(M+Na)^+$: 431.1706, found : 431.1704.

(−)-**(2*R*,3*R*)-*N*,*N*-Dibenzyl-1,1,1-trifluoro-5-methyl-3-phenoxyhexan-2-amine [**(−)-**16]**



Formula: $C_{27}H_{30}F_3NO$ **MW**= 441.54 g.mol^{-1}

Compound (−)-**16** was synthesized from (2*S*,3*S*)-3-(dibenzylamino)-1,1,1-trifluoro-5-methylhexan-2-ol (−)-*anti*-**5** (174 mg, 0.476 mmol) using dry NaOPh as the nucleophile (139.4 mg, 1.19 mmol, 2.5 equiv). Purification by flash column chromatography (PE/EtOAc = 99:1) afforded (−)-**16** (148.9 mg, 0.34 mmol, 71%) as a colorless oil.

$[\alpha]_D^{25}$ − 31.0 (*c* 0.39, $CHCl_3$).

IR (neat): ν_{max} 3064, 3030, 2957, 2869, 1598, 1493, 1455, 1368, 1238, 1135, 1097, 1074, 1028, 971 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32−7.20 (m, 12H), 6.90 (tt_{app}, *J* = 1.0 , 0.8 Hz, 1H), 6.84−6.82 (m, 2H), 4.69 (dt_{app}, *J* = 7.5, 5.5 Hz, 1H), 3.95 (d, J_{AB} = 13.6 Hz, 2H), 3.81 (dd, J_{AB} = 13.6, 1.0 Hz, 2H), 3.42 (m, 1H), 1.76 (m, 1H), 1.57−1.40 (m, 2H), 0.82 (d, *J* = 6.5 Hz, 3H), 0.81 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.1, 138.7 (2C), 129.6 (2C), 129.3 (4C), 128.6 (4C), 127.6 (2C), 127.4 (q, *J* = 292.1 Hz), 121.0, 115.3 (2C), 74.2, 61.2 (q, *J* = 23.7 Hz), 55.5 (2C), 41.8, 24.3, 23.4, 22.6.

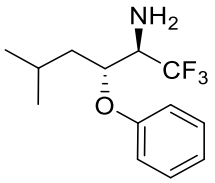
^{19}F NMR (**$CDCl_3$, 376 MHz) :** δ − 62.44 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 441 ($M^{+\bullet}$, 0.4), 278 (64), 107 (8), 91 (100), 69 (9), 65 (8).

HRMS: calcd for $C_{27}H_{31}F_3NO$ $(M+H)^+$: 442.2352, found : 442.2350.

4. Application of α-trifluoromethylamines

(+)-(2*R*,3*R*)-1,1,1-Trifluoro-5-methyl-3-phenoxyhexan-2-amine [(+)-17]



Formula: $C_{13}H_{18}F_3NO$ **MW**= 261.29 g.mol^{-1}

To a stirred solution of (2*R*,3*R*)-*N*,*N*-dibenzyl-1,1,1-trifluoro-5-methyl-3-phenoxyhexan-2-amine (–)-**16** (99.2 mg, 0.22 mmol, 1.0 equiv) in anhydrous methanol, 10% Pd/C (20 mol %) was added. The mixture was stirred under hydrogen pressure (1 atm) at rt for 4 days. The mixture was then filtered over a Celite pad, washed with methanol and CH_2Cl_2 and concentrated under reduced pressure. Purification by flash column chromatography (PE/EtOAc = 99:1 then 95:5) afforded (+)-**17** (35.6 mg, 0.14 mmol, 61%) as a colorless oil.

$[\alpha]_D^{25}$ + 38.7 (*c* 0.47, $CHCl_3$).

IR (neat): ν_{max} 3350, 2959, 1597, 1493, 1268, 1228, 1165, 1133, 1115, 992, 958 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33–7.25 (m, 2H), 7.00–6.93 (m, 3H), 4.64 (dt, *J* = 9.9, 2.6 Hz, 1H), 3.62 (qd, *J* = 8.3, 2.8 Hz, 1H), 1.90–1.82 (m, 2H), 1.52 (br s, 2H, NH_2), 1.39 (m, 1H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H).

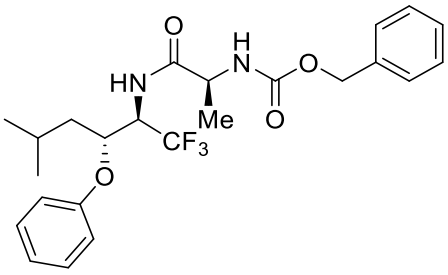
^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.5, 131.0 (q, *J* = 261.7 Hz), 130.0 (2C), 121.8, 116.0 (2C), 73.9, 55.1 (q, *J* = 27.3 Hz), 37.8, 24.5, 23.7, 21.8.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 73.61 (3 x F, CF_3).

MS (EI, 70 eV): *m/z* (relative intensity) = 261 ($M^{+\bullet}$, 14), 163 (100), 121 (33), 107 (78), 98 (54), 69 (97).

HRMS: calcd for $C_{13}H_{19}F_3NO$ $(M+H)^+$: 262.1413, found : 262.1414.

(–)-Benzyl-((*S*)-1-oxo-1-{[(2*R*,3*R*)-1,1,1-trifluoro-5-methyl-3-phenoxyhexan-2-yl]amino}-propan-2-yl)carbamate [(–)-18]



Formula: $C_{24}H_{29}F_3N_2O_4$ **MW**= 466.50 g.mol^{-1}

Compound (–)-**18** was prepared according to a described procedure.[7] To a stirred solution of *N*-CBz-L-Alanine (28.3 mg, 0.124 mmol, 1.0 equiv) in anhydrous ethyl acetate (1.25 mL) at –15 °C, were added *N*-methylmorpholine (15.3 µL, 0.137 mmol, 1.1 equiv) and isobutyl chloroformate (18.2 µL, 0.137 mmol, 1.1 equiv). After 30 min, a solution of (2*R*,3*R*)-1,1,1-trifluoro-5-methyl-3-phenoxy-hexan-2-amine (+)-**17** (32.8 mg, 0.124 mmol, 1.0 equiv) in anhydrous EtOAc (0.7 mL) was added, the resulting mixture was stirred at – 15 °C for 1 h and then warmed to rt before stirring for 14 h. The reaction mixture was extracted with the following order: H_2O (x 2), a 10 % aqueous solution of citric acid (x 2), H_2O (x 2), a saturated aqueous solution of $NaHCO_3$ (x 2) and H_2O (x 2). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (PE/EtOAc = 95:5 to 80:20) afforded (–)-**18** (33.6 mg, 0.072 mmol, 58%) as a colorless oil.

$[\alpha]_D^{25}$ – 19.2 (*c* 0.10, $CHCl_3$).

IR (neat): ν_{max} 3292, 3067, 3036, 2958, 2873, 1672, 1597, 1588, 1533, 1493, 1330, 1224, 1180, 1150, 1112, 1073, 1028, 996, 952 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37–7.25 (m, 7H), 6.99 (t_{app}, *J* = 7.4 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 2H), 6.88 (m, 1H), 5.28 (d, *J* = 5.2 Hz, 1H), 5.08–5.01 (m, 2H), 4.94 (m, 1H), 4.60 (m, 1H), 4.30 (m, 1H), 1.87–1.74 (m, 2H), 1.49 (m, 1H), 1.36 (d, *J* = 7.1 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.5, 157.6, 156.4, 136.0, 130.0 (2C), 128.7 (2C), 128.4, 128.2 (2C), 124.4 (q, *J* = 282.9 Hz), 122.3, 116.5 (2C), 74.5, 67.4, 52.5 (q, *J* = 28.9 Hz), 50.6, 39.2, 24.5, 23.4, 22.1, 17.9.

^{19}F NMR ($CDCl_3$, 376 MHz) : δ – 70.49 (3 x F, CF_3).

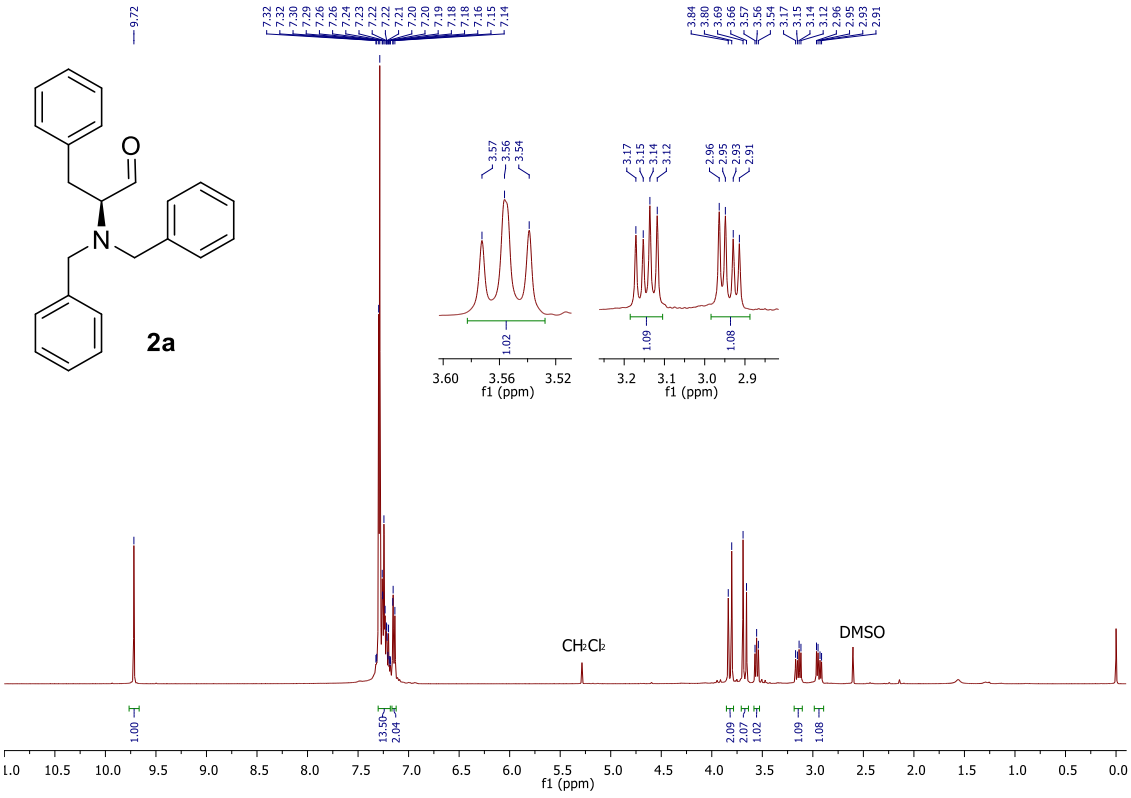
MS (EI, 70 eV): *m/z* (relative intensity) = 466 ($M^{+\bullet}$, 0.2), 373 (25), 163 (19), 107 (16), 91 (100), 69 (18).

HRMS: calcd for $C_{24}H_{29}F_3N_2O_4$ $(M+Na)^+$: 489.1972, found : 489.1970.

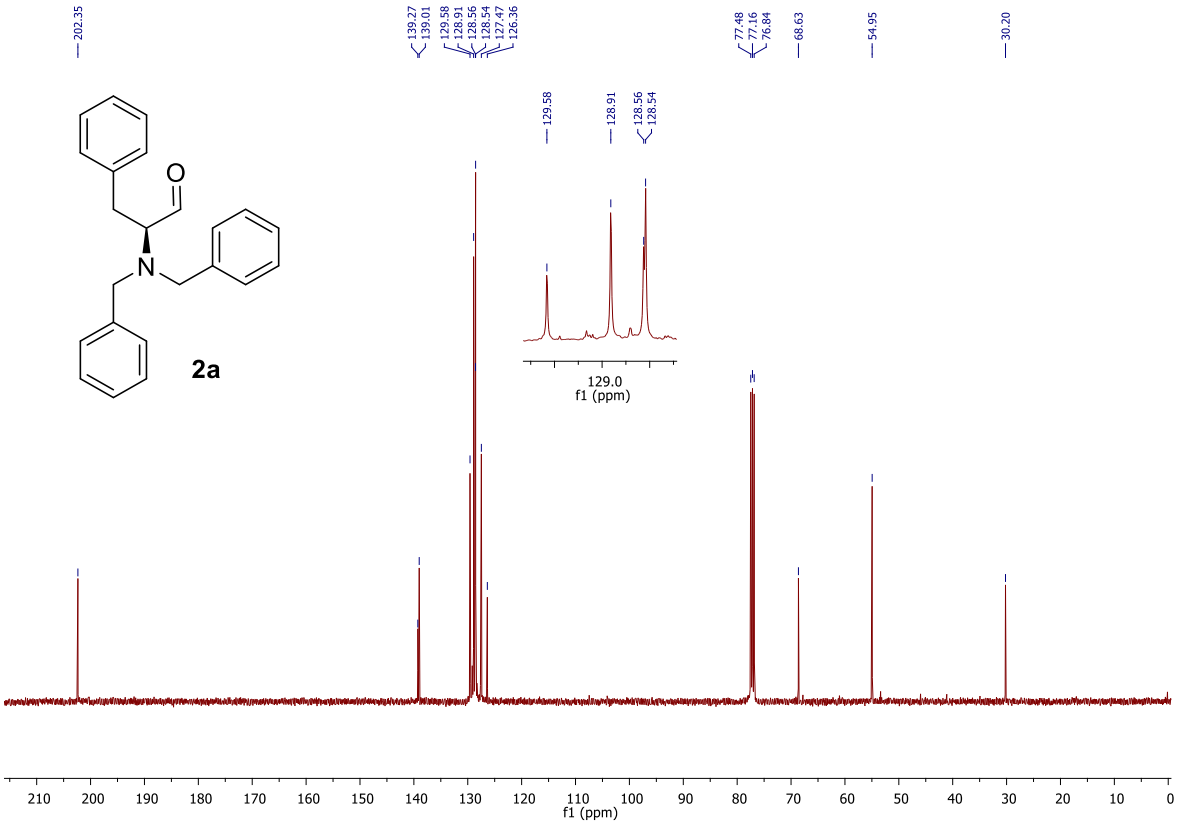
[7] Koksch, B.; Sewald, N.; Hofmann, H.-J.; Burger, K.; Jakubke, H.-D. *J. Pept. Sci.* **1997**, *3*, 157–167.

ALDEHYDES

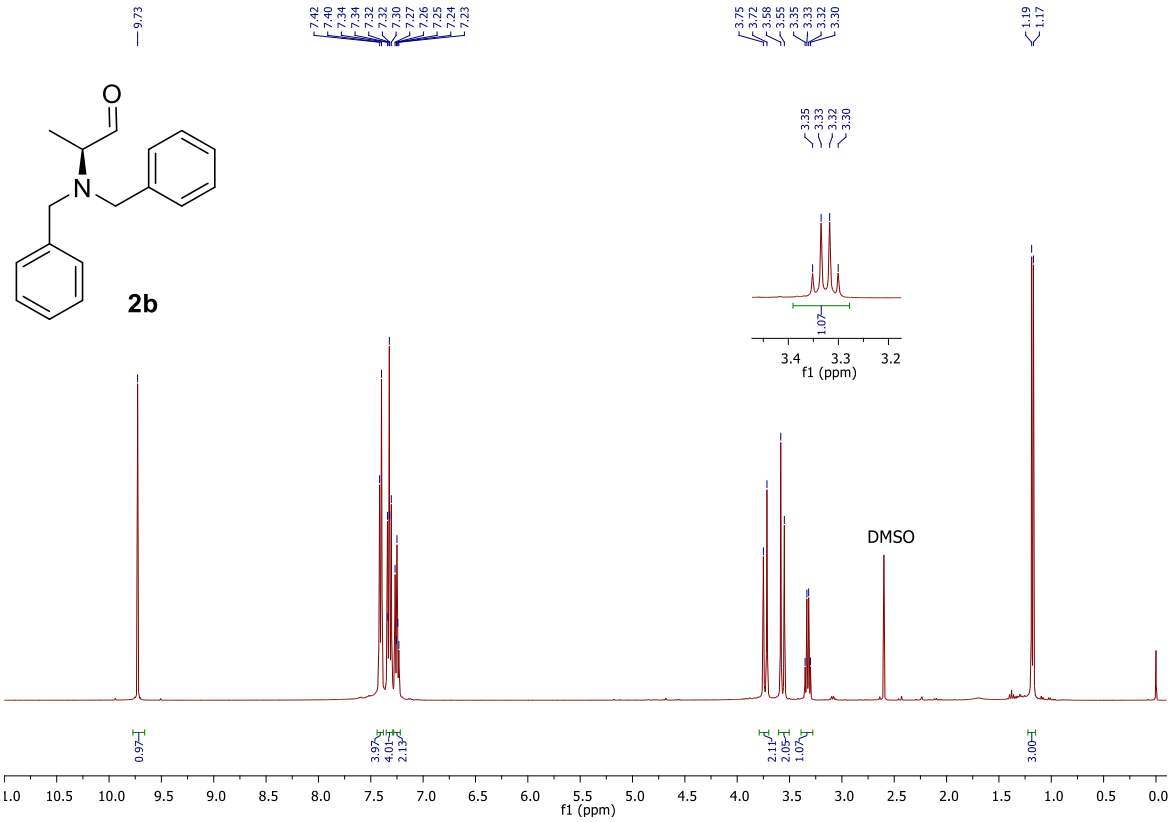
^{1}H NMR, 400 MHz, $CDCl_3$



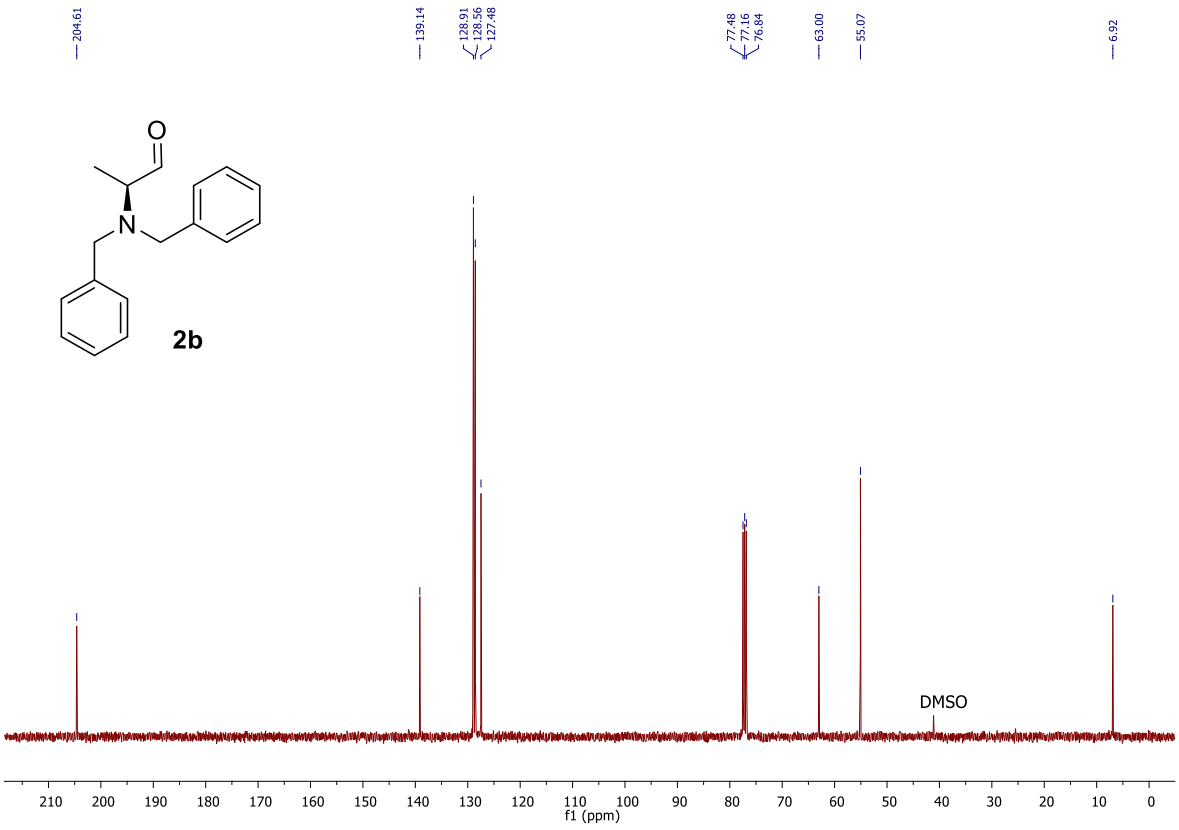
^{13}C NMR, 100 MHz, $CDCl_3$



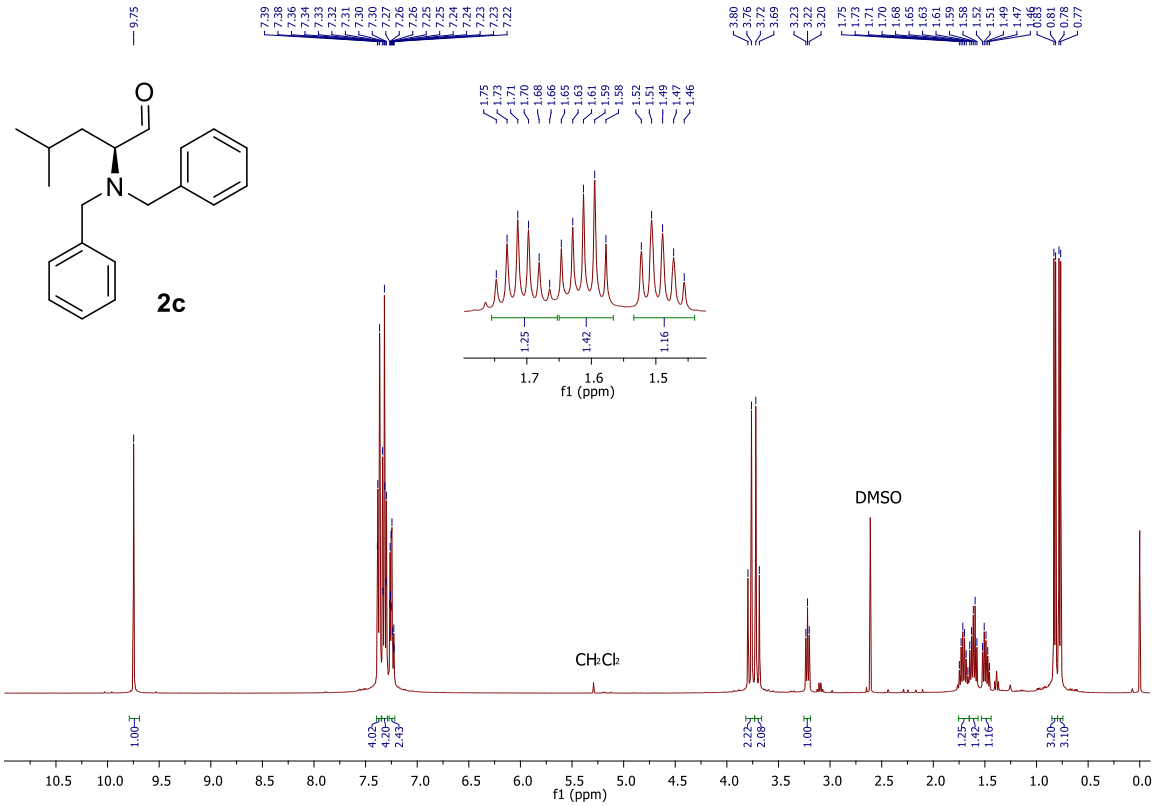
^{1}H NMR, 400 MHz, $CDCl_3$



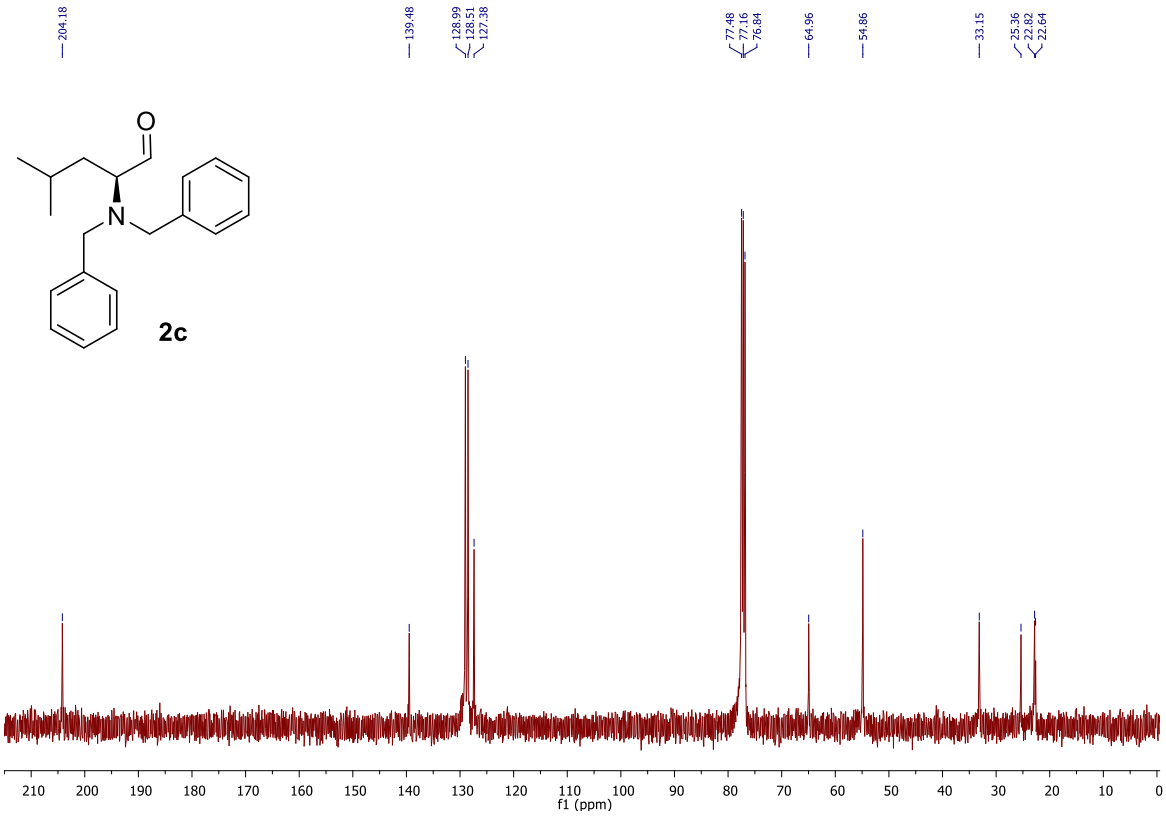
^{13}C NMR, 100 MHz, $CDCl_3$



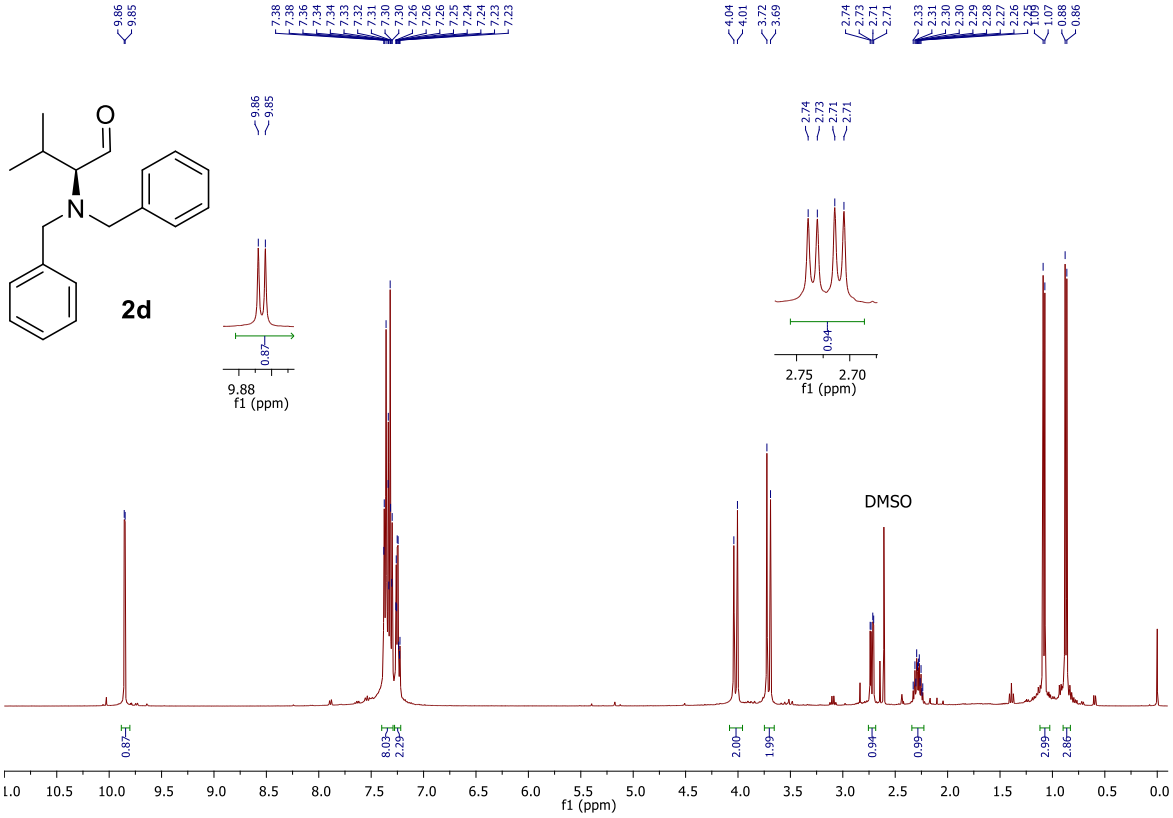
^{1}H NMR, 400 MHz, $CDCl_3$



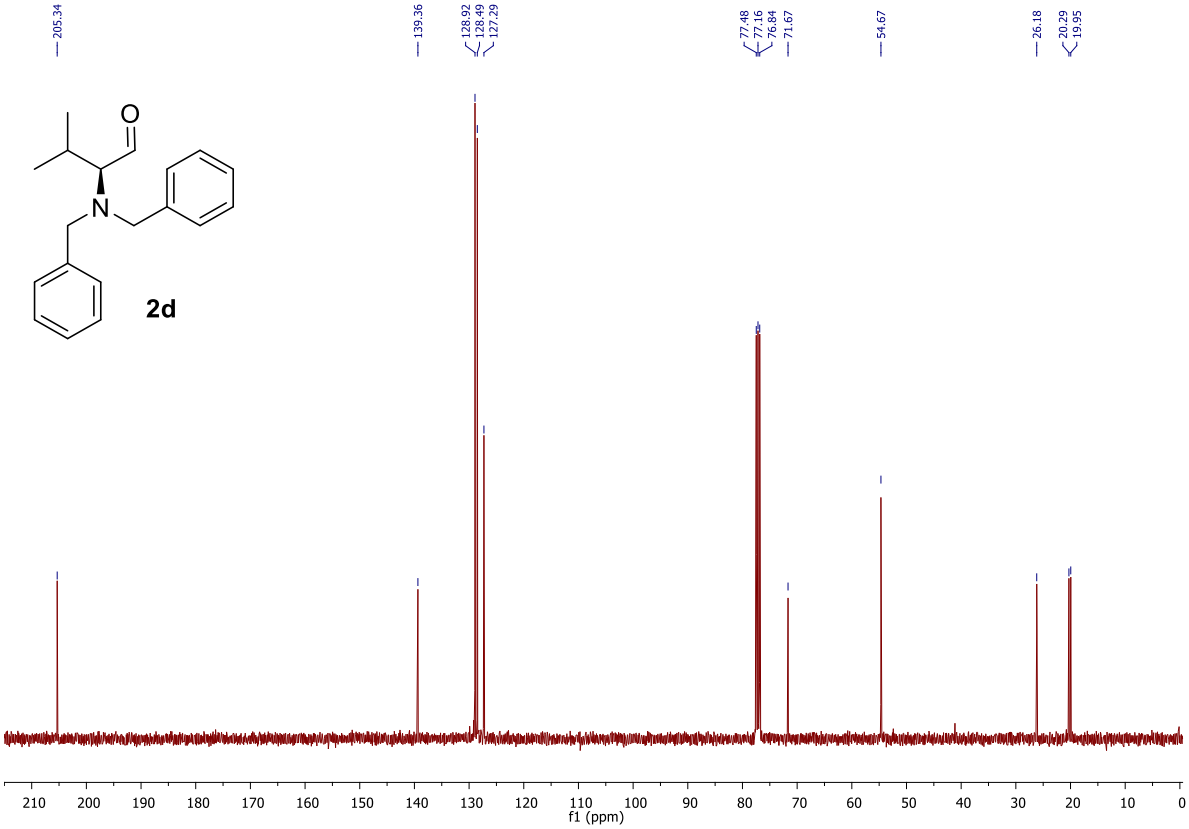
^{13}C NMR, 100 MHz, $CDCl_3$



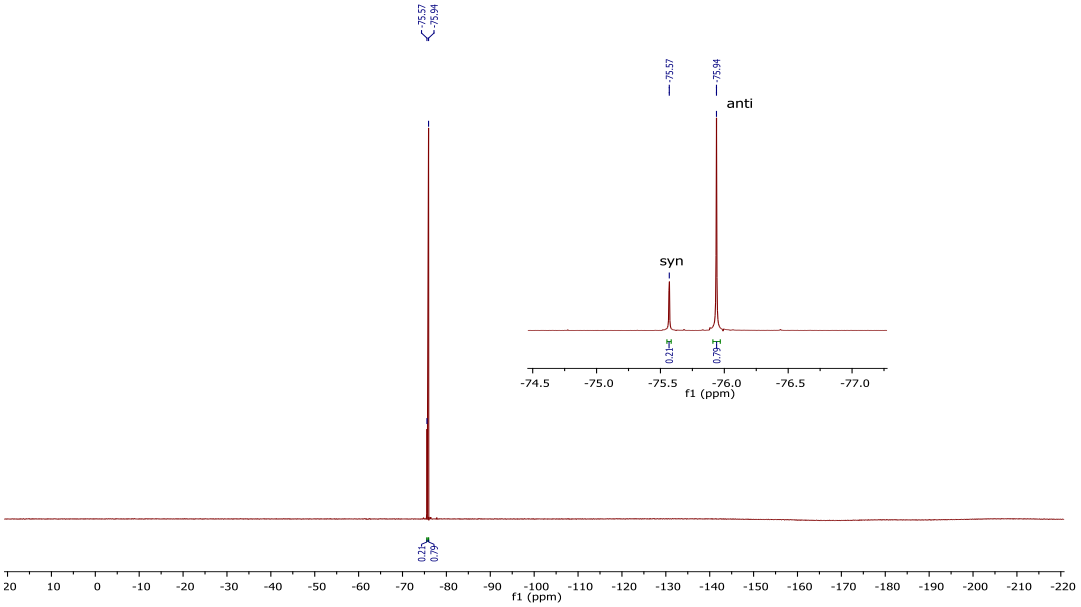
^{1}H NMR, 400 MHz, $CDCl_3$



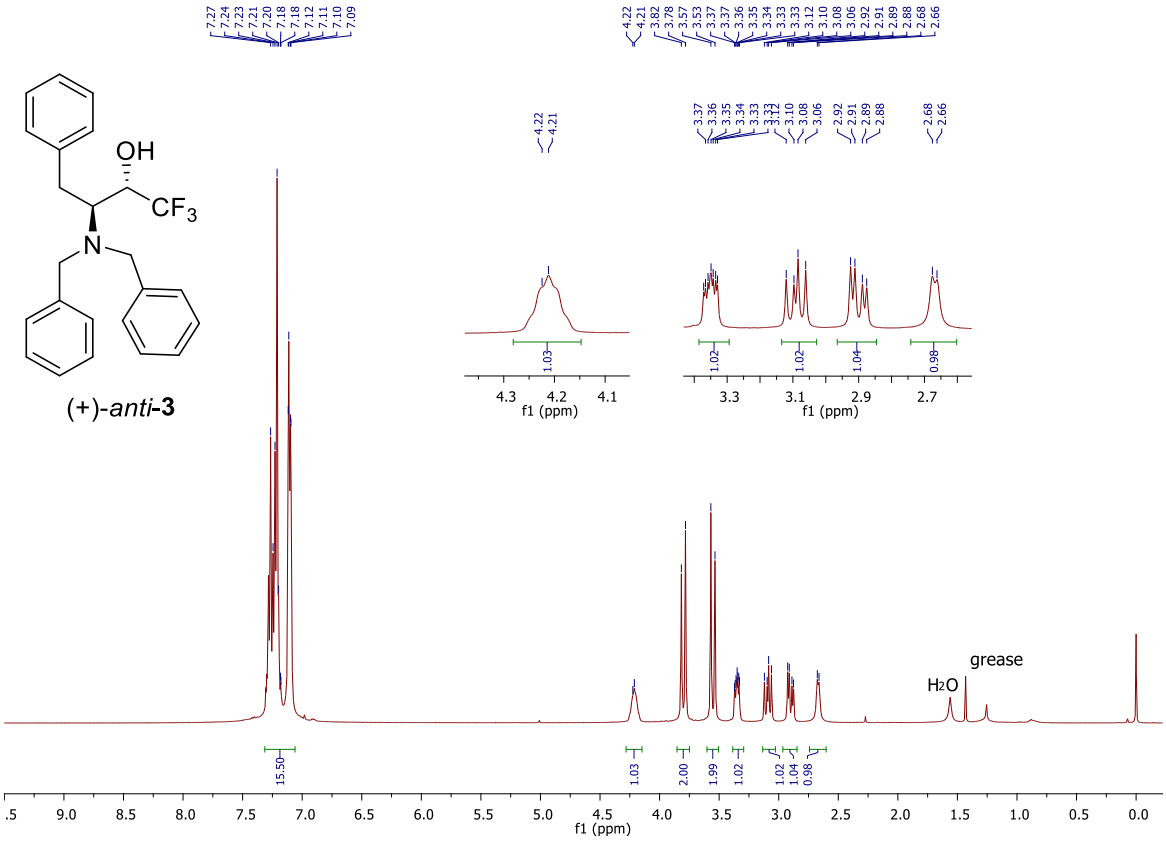
^{13}C NMR, 100 MHz, $CDCl_3$



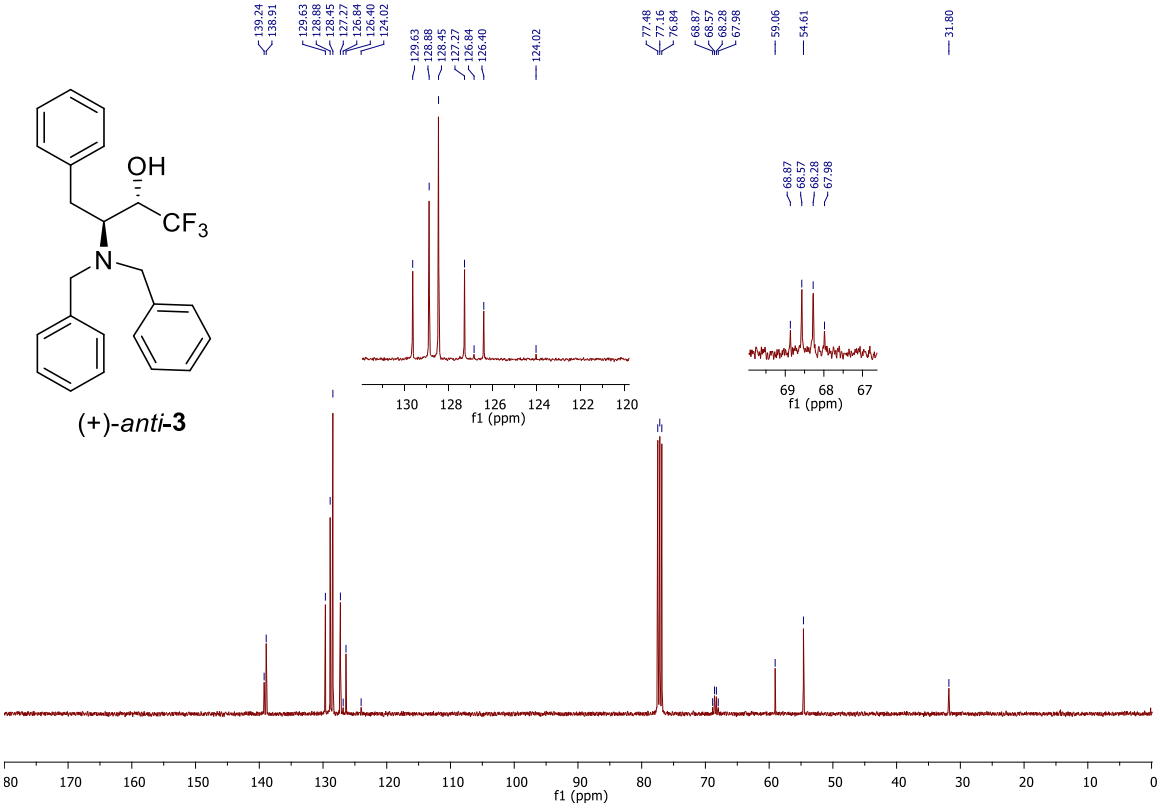
Crude of 3: ^{19}F NMR, 376 MHz, $CDCl_3$



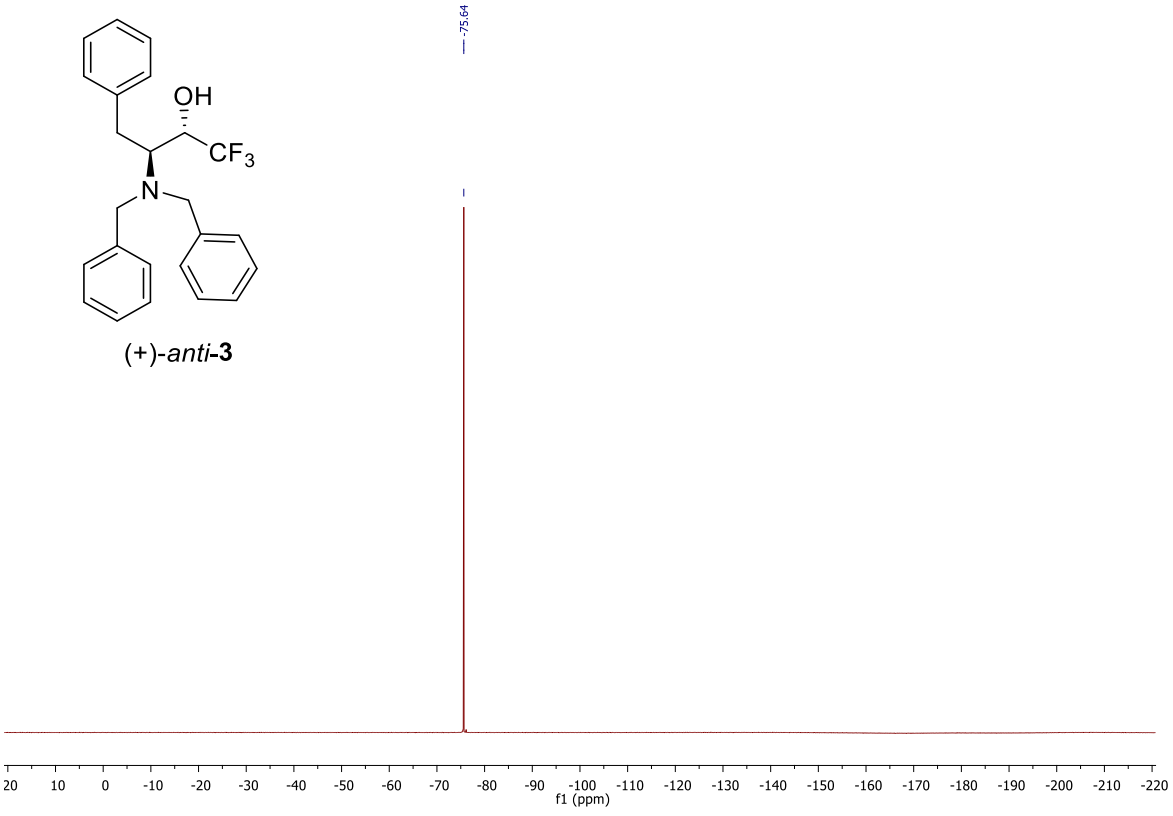
^{1}H NMR, 400 MHz, $CDCl_3$



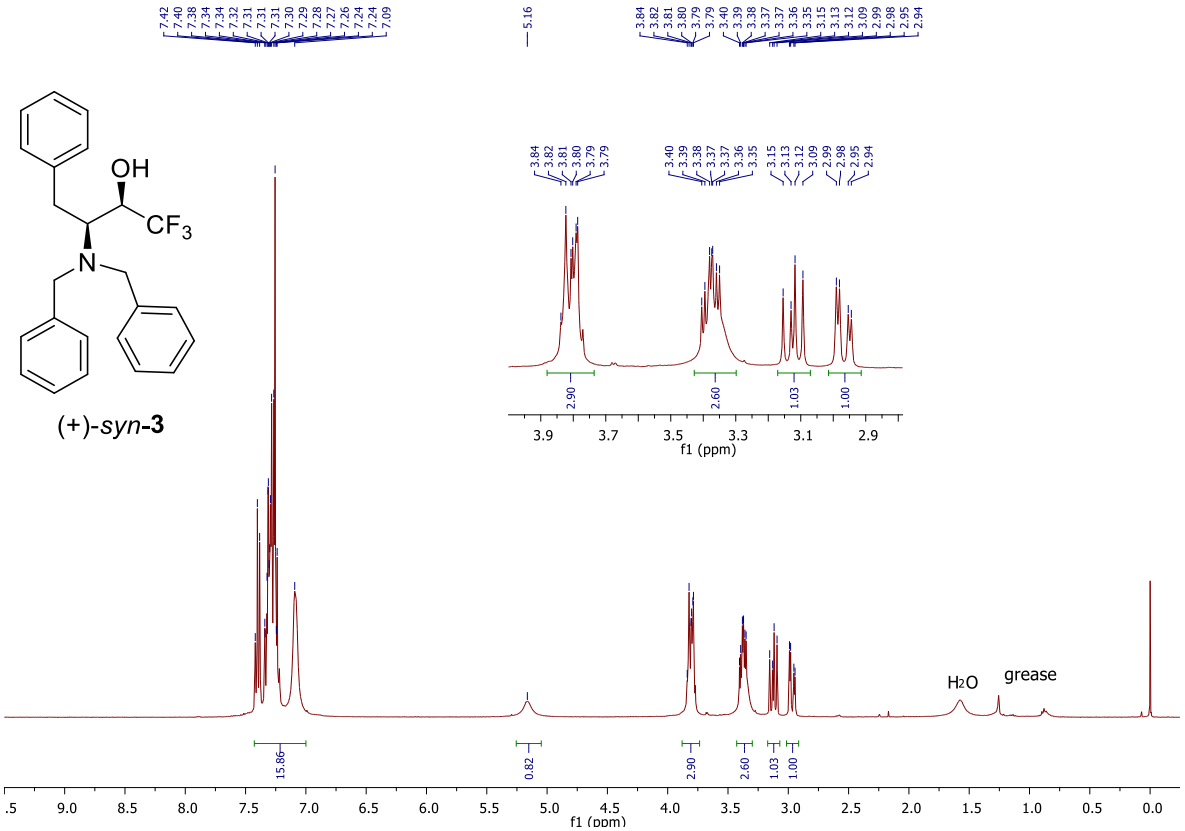
^{13}C NMR, 100 MHz, $CDCl_3$



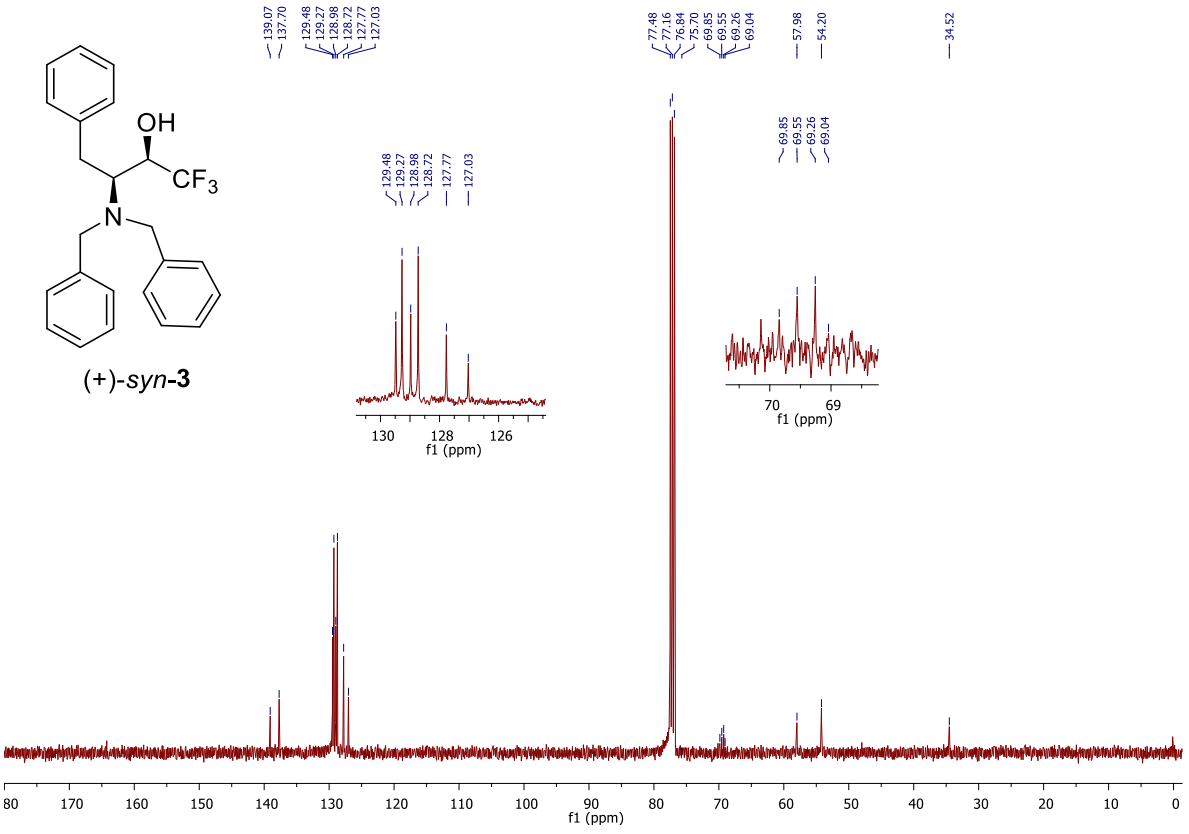
^{19}F NMR, 376 MHz, $CDCl_3$



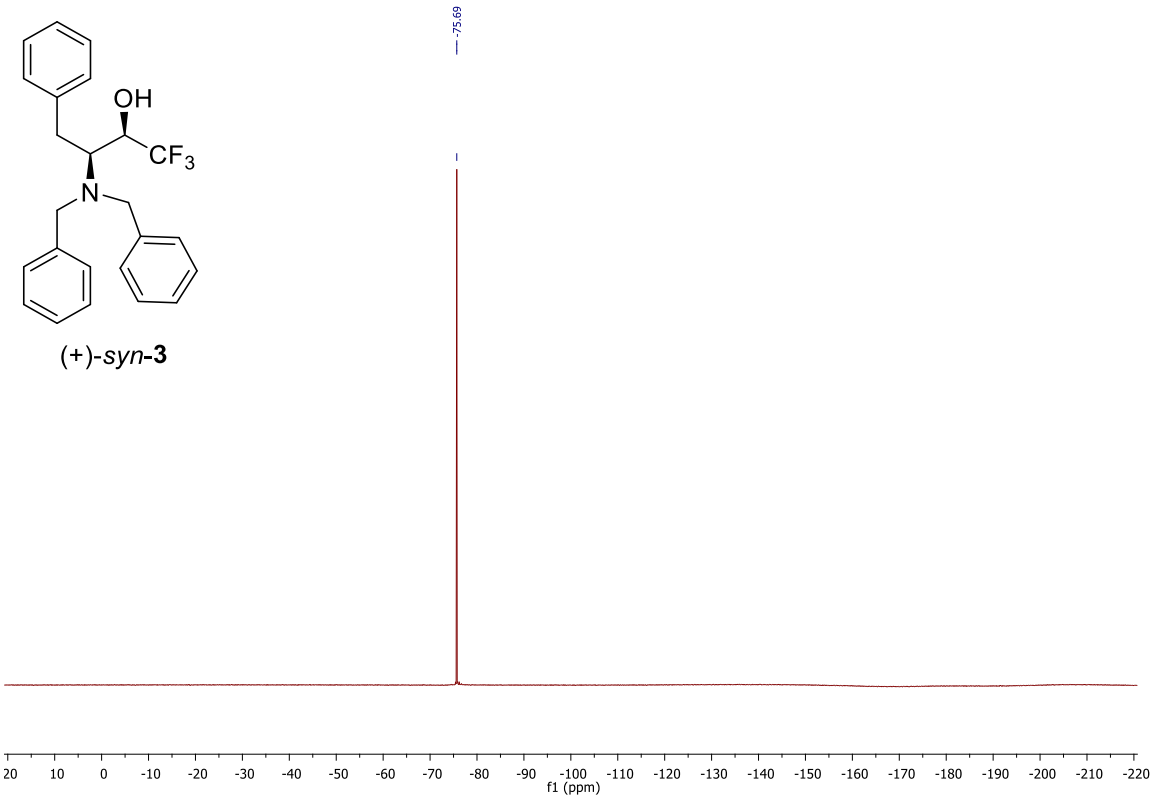
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

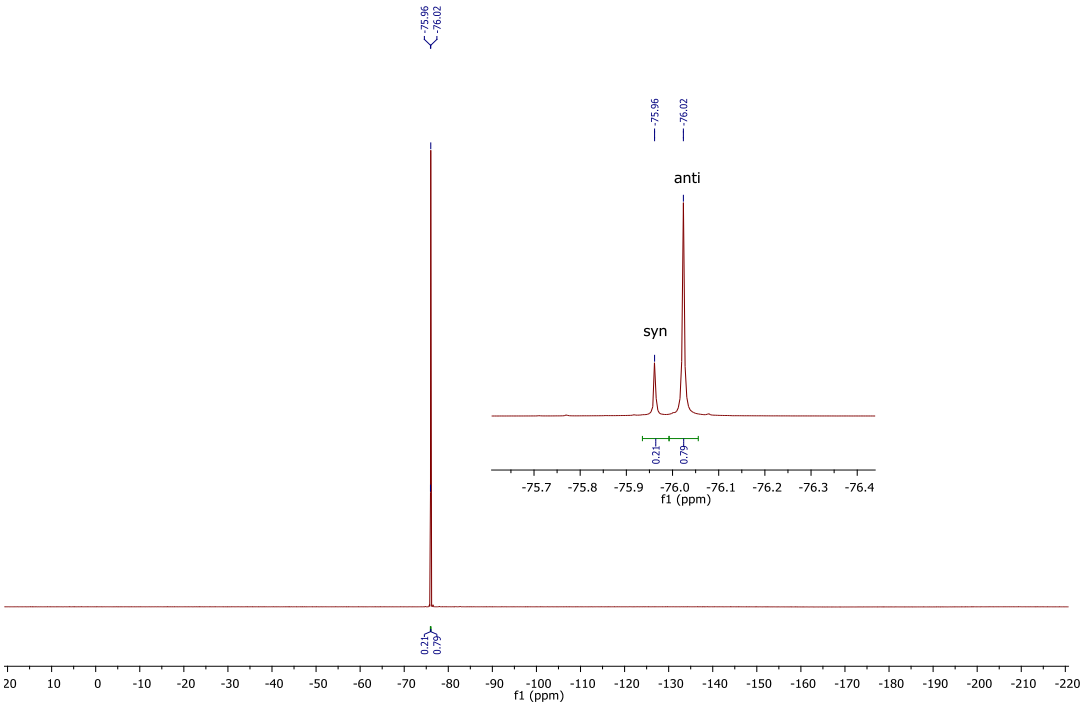


^{19}F NMR, 376 MHz, $CDCl_3$

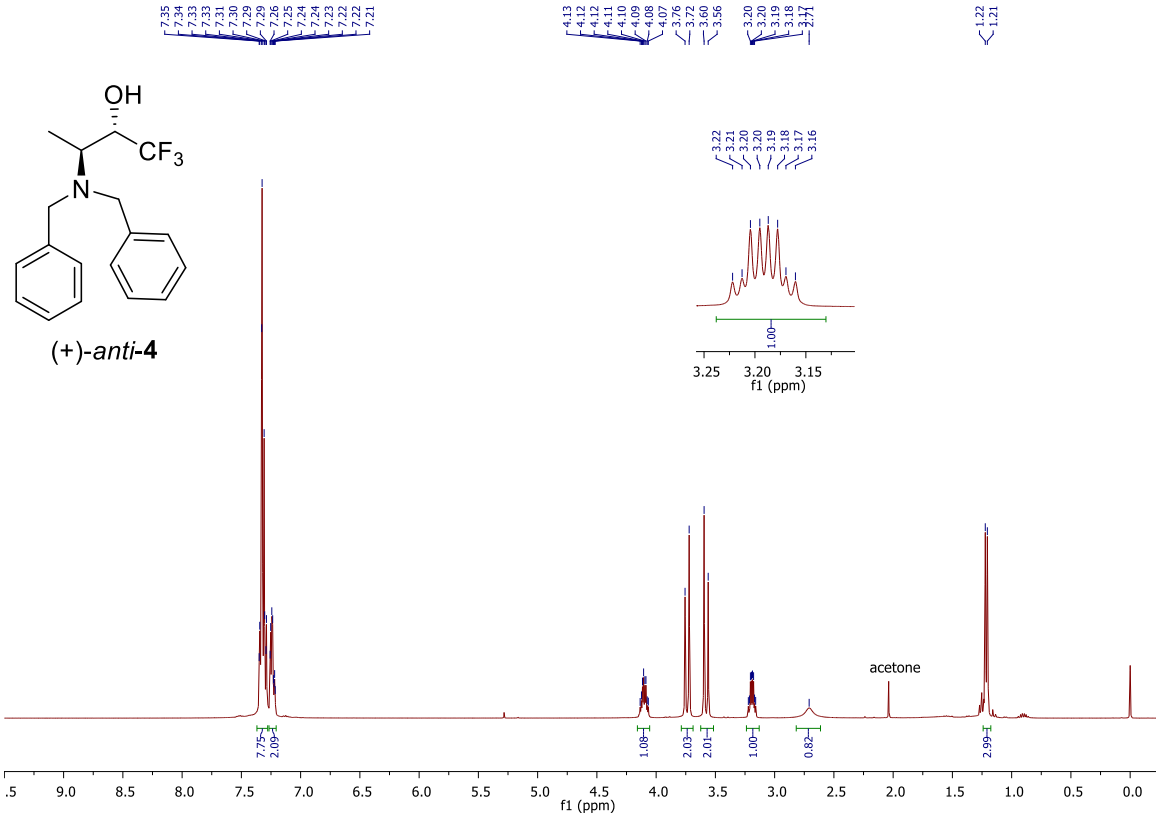


(+)-*syn*-**3**

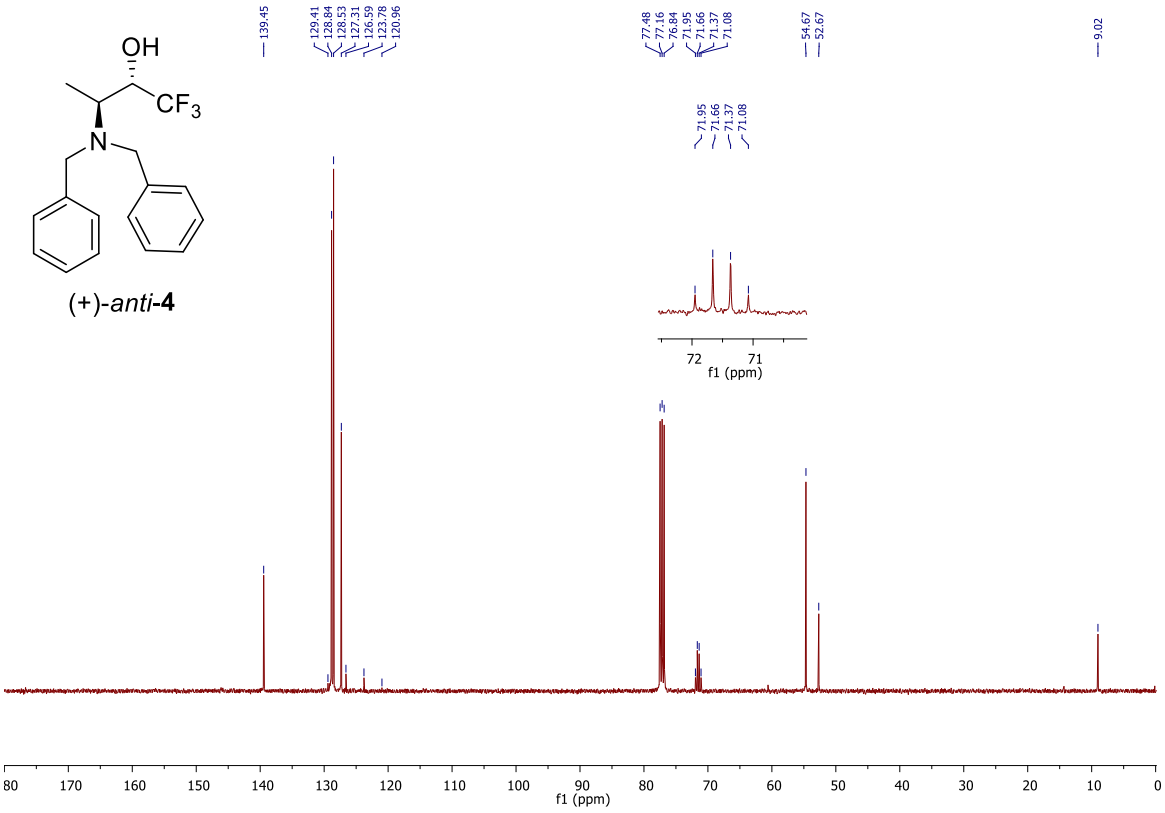
Crude of 4: ^{19}F NMR, 376 MHz, $CDCl_3$



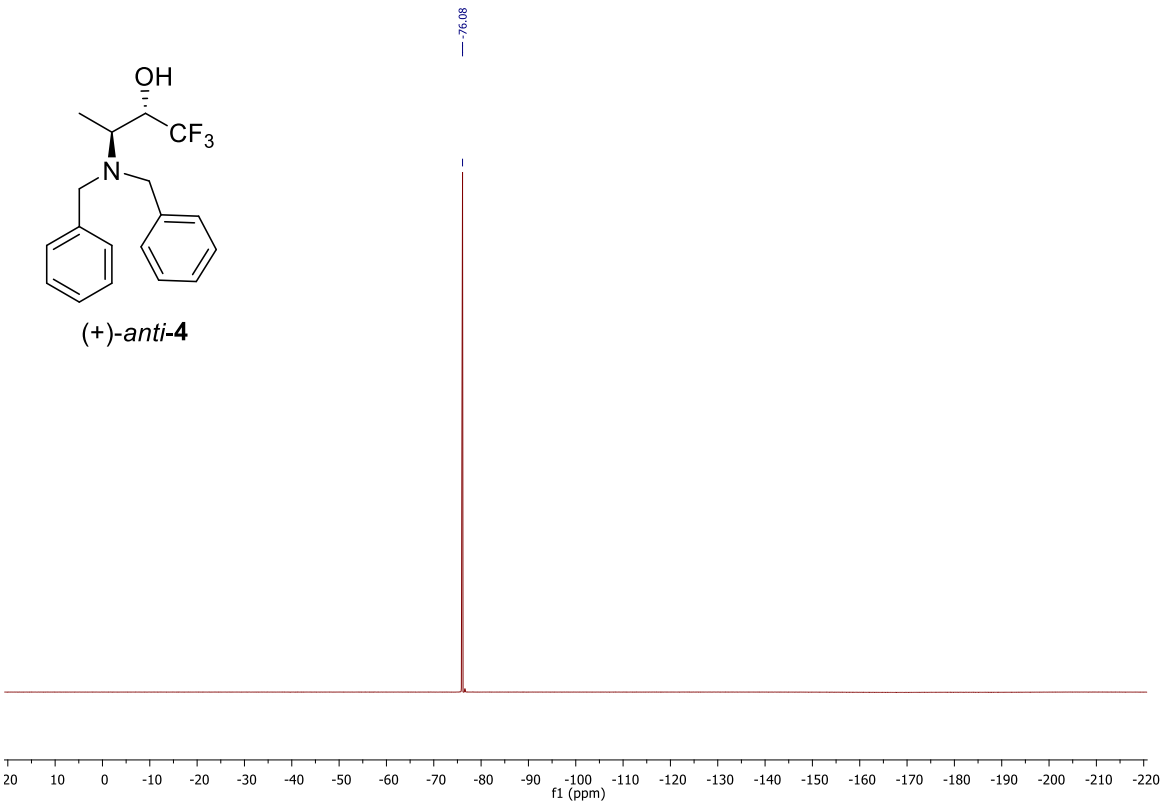
^{1}H NMR, 400 MHz, $CDCl_3$



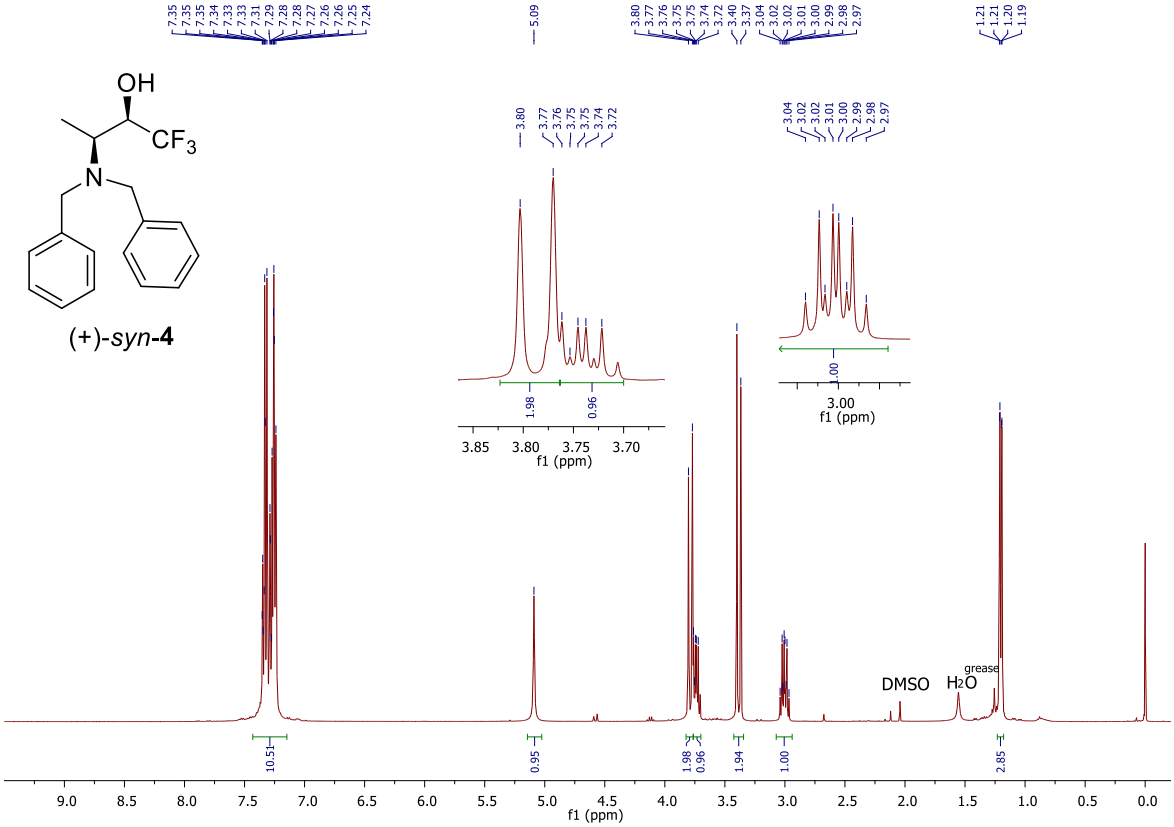
^{13}C NMR, 100 MHz, $CDCl_3$



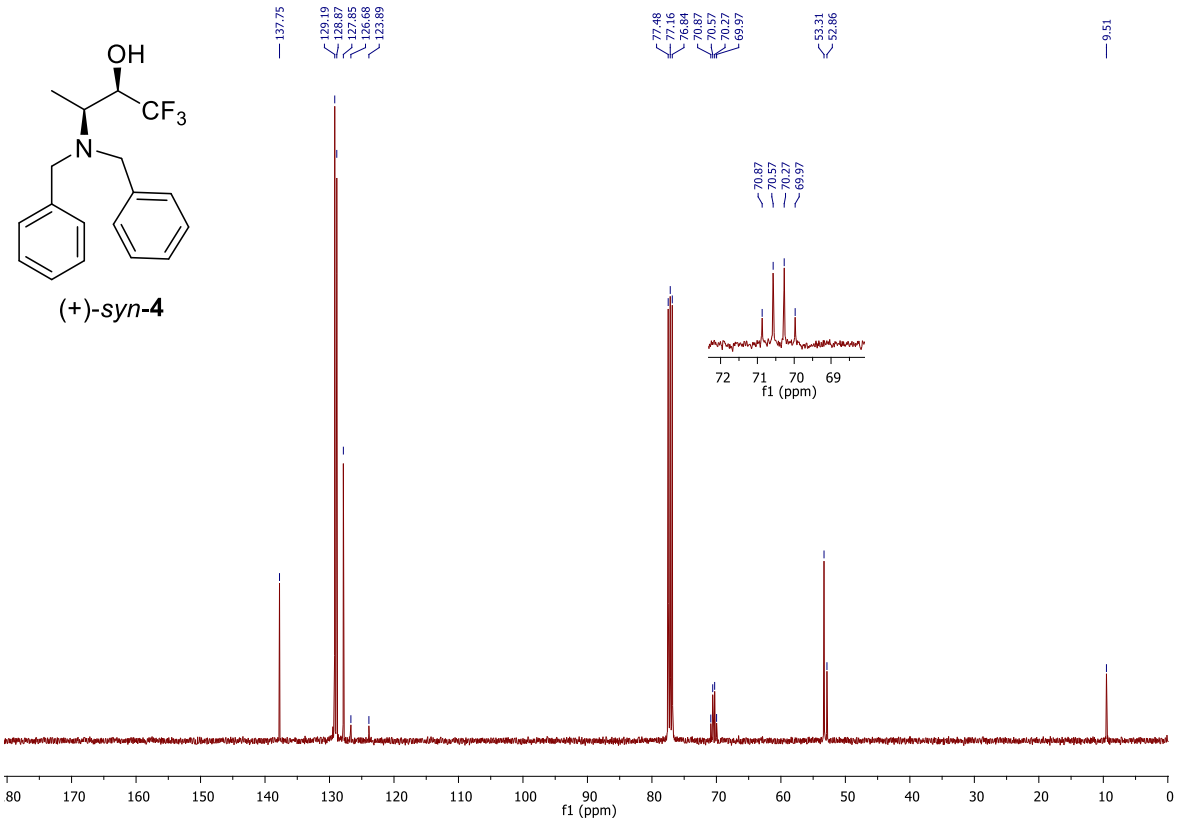
^{19}F NMR, 376 MHz, $CDCl_3$



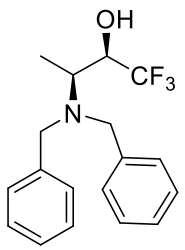
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

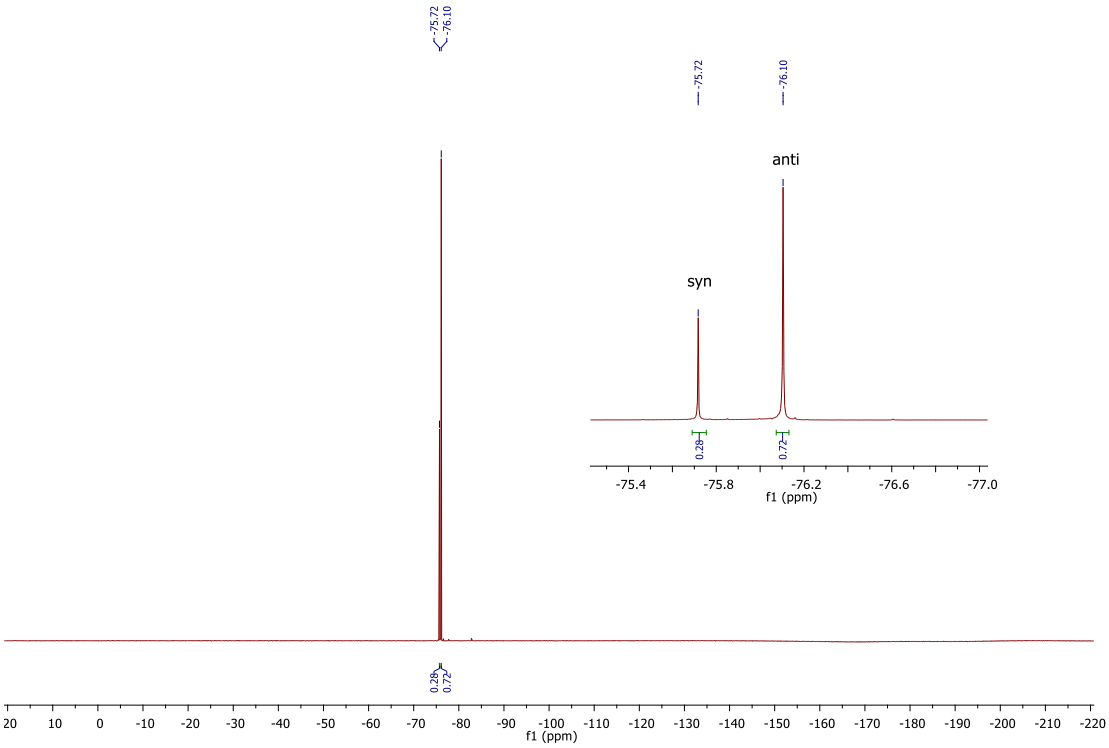


^{19}F NMR, 376 MHz, $CDCl_3$

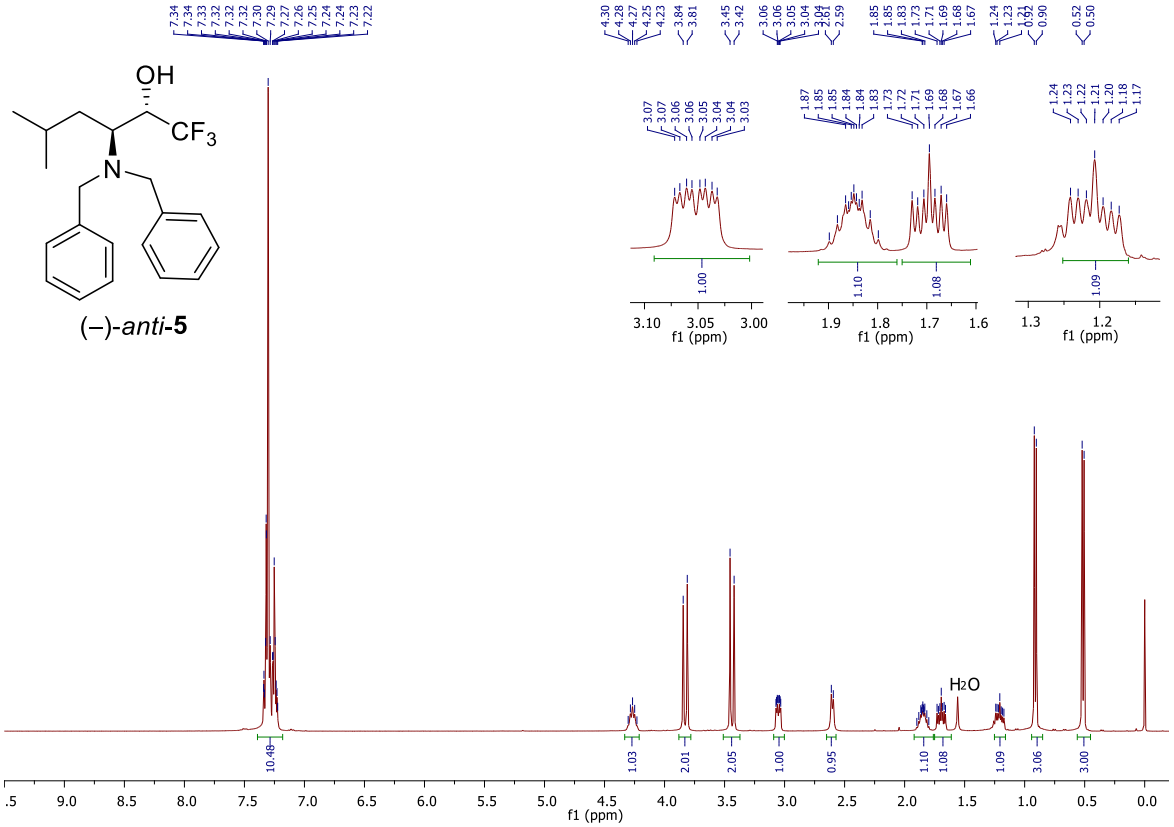


(+)-*syn*-**4**

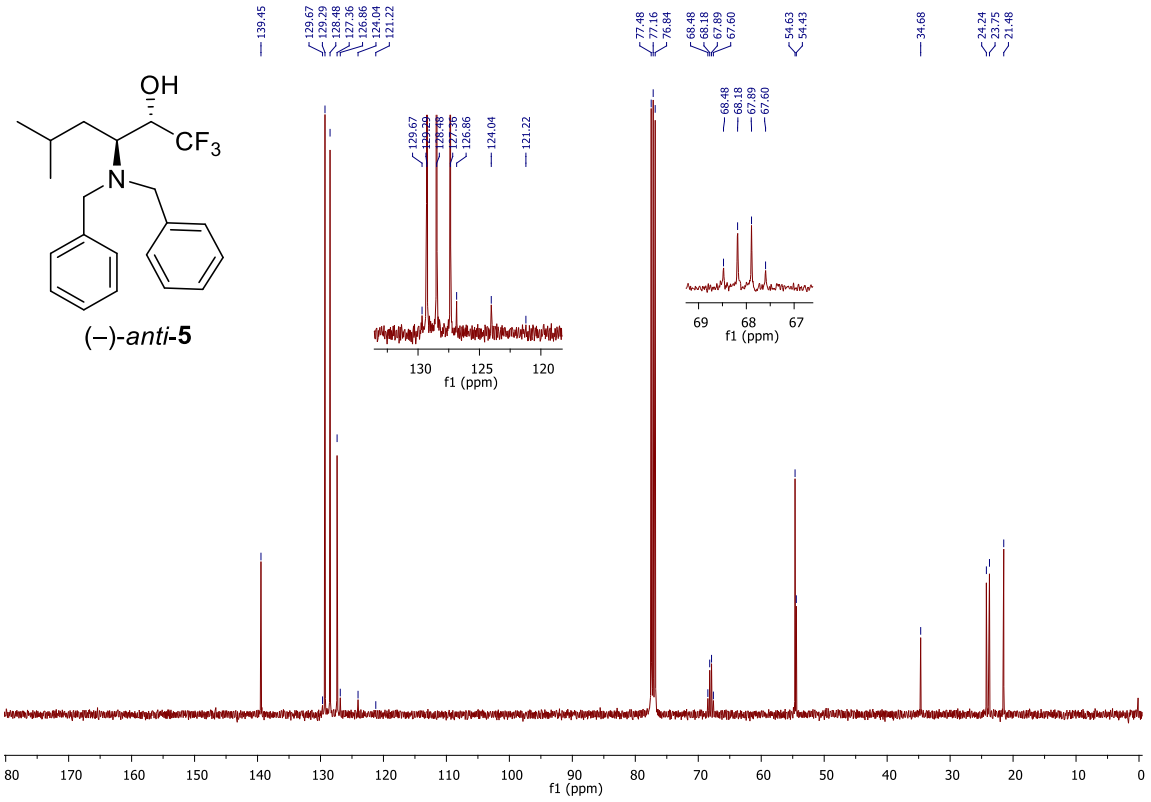
Crude of 5: ^{19}F NMR, 376 MHz, $CDCl_3$



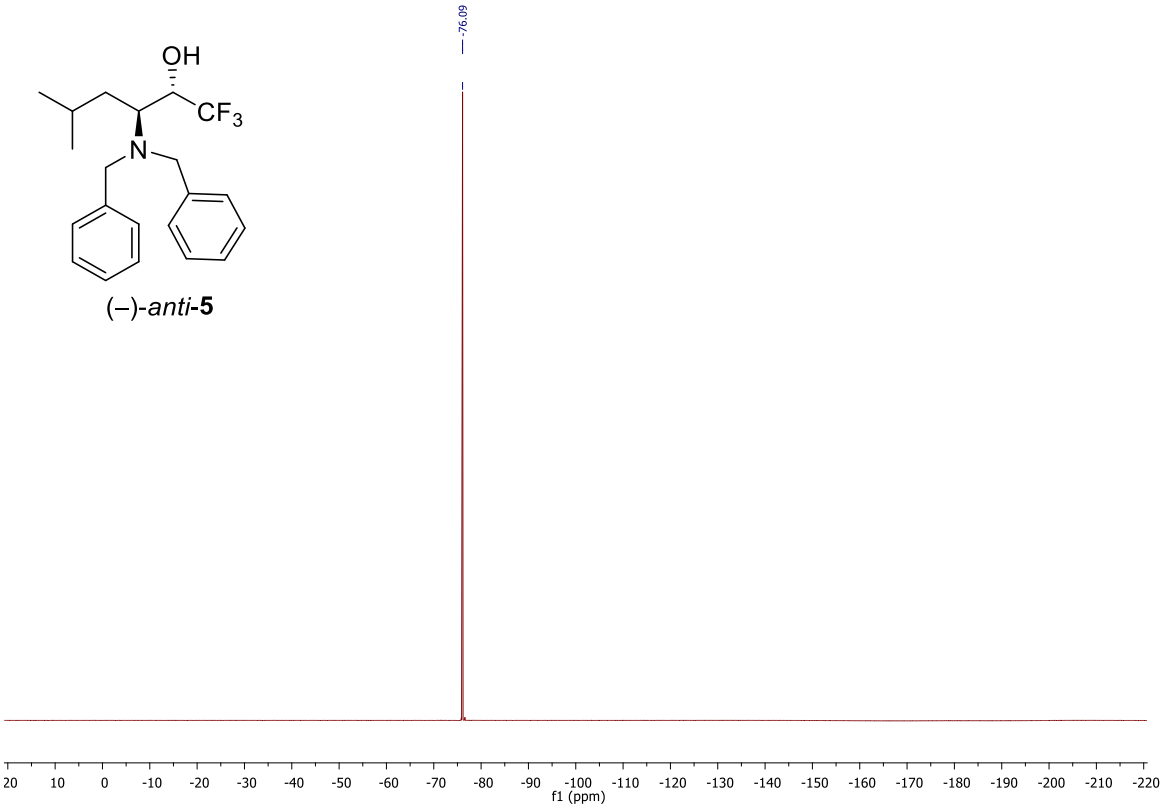
^{1}H NMR, 400 MHz, $CDCl_3$



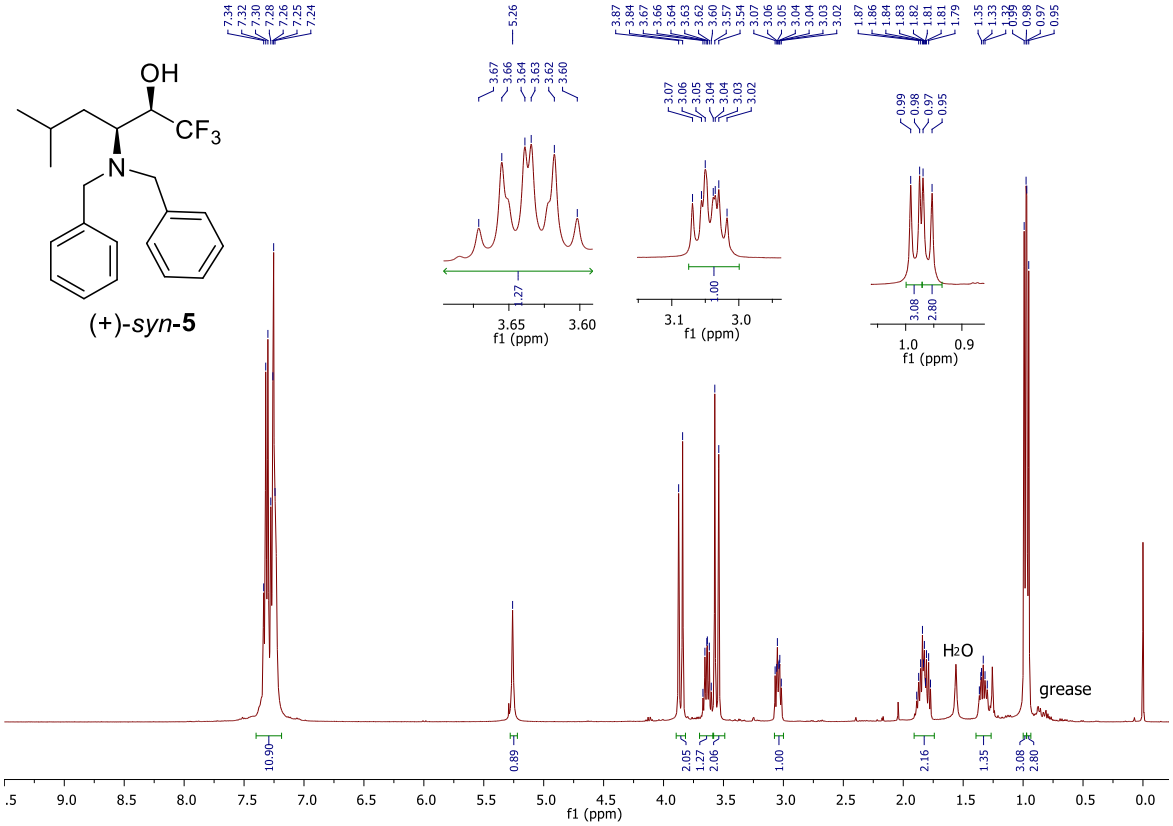
^{13}C NMR, 100 MHz, $CDCl_3$



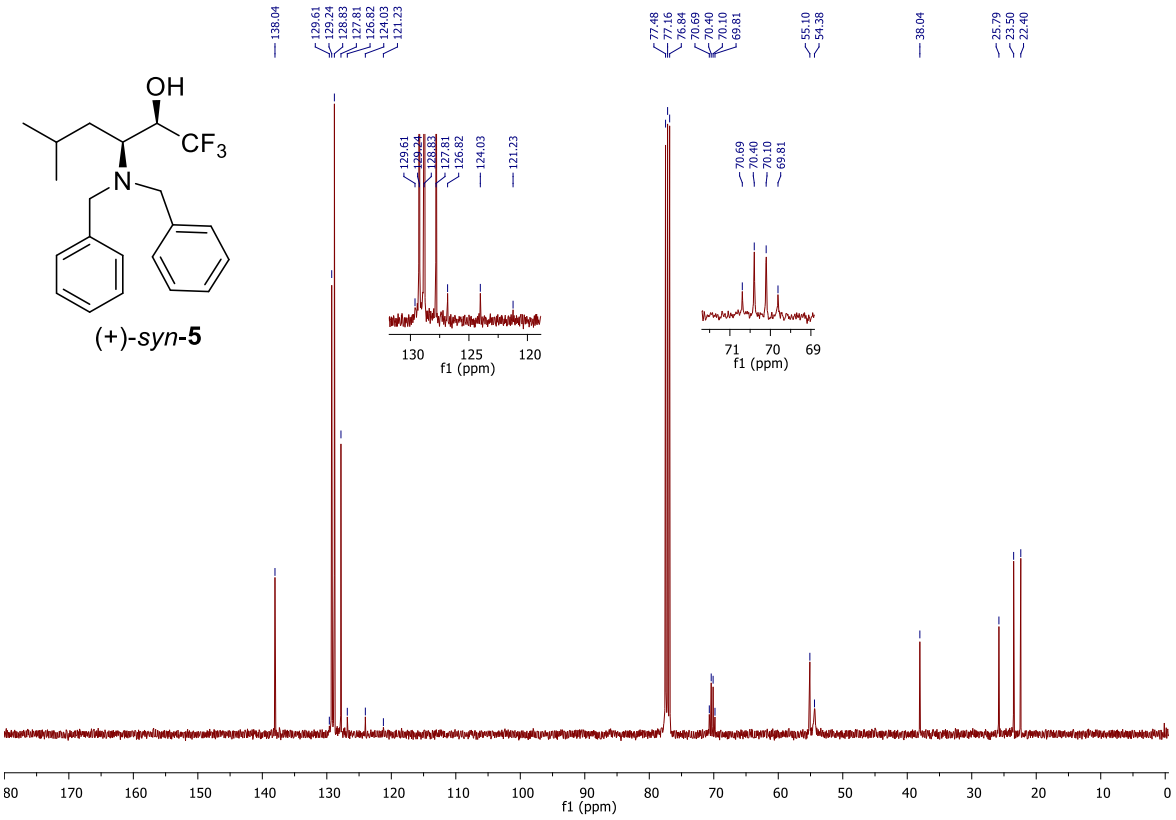
^{19}F NMR, 376 MHz, $CDCl_3$



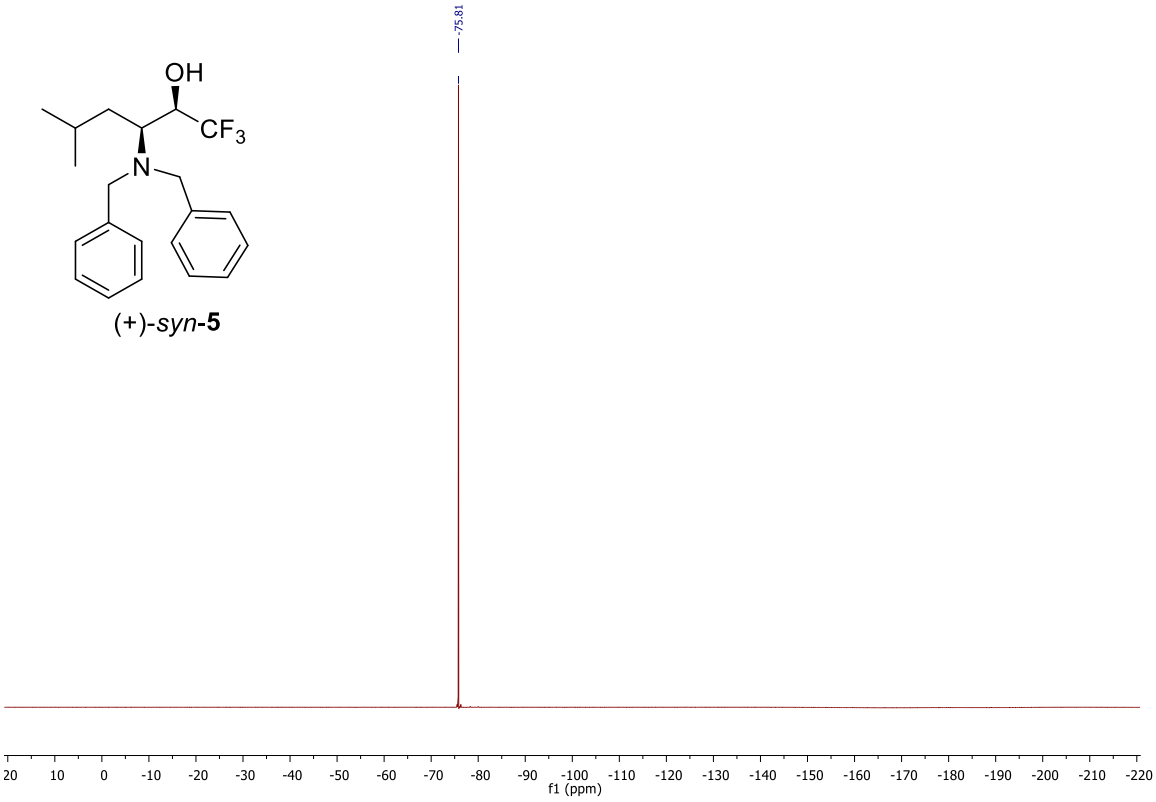
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

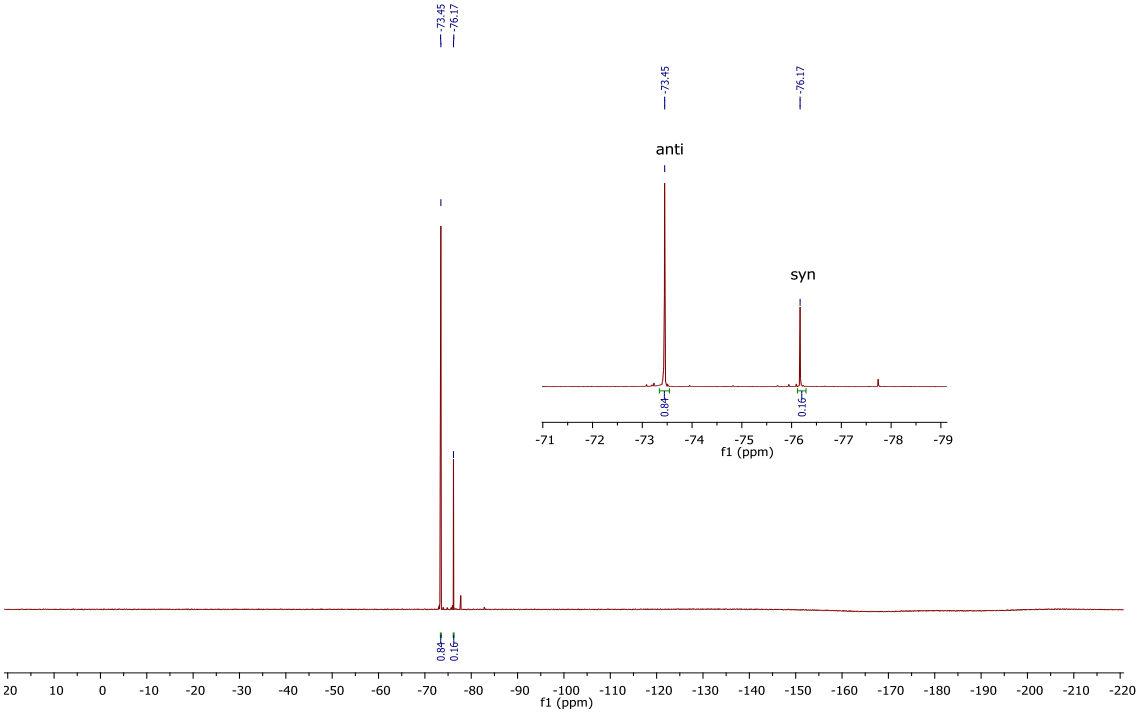


^{19}F NMR, 376 MHz, $CDCl_3$

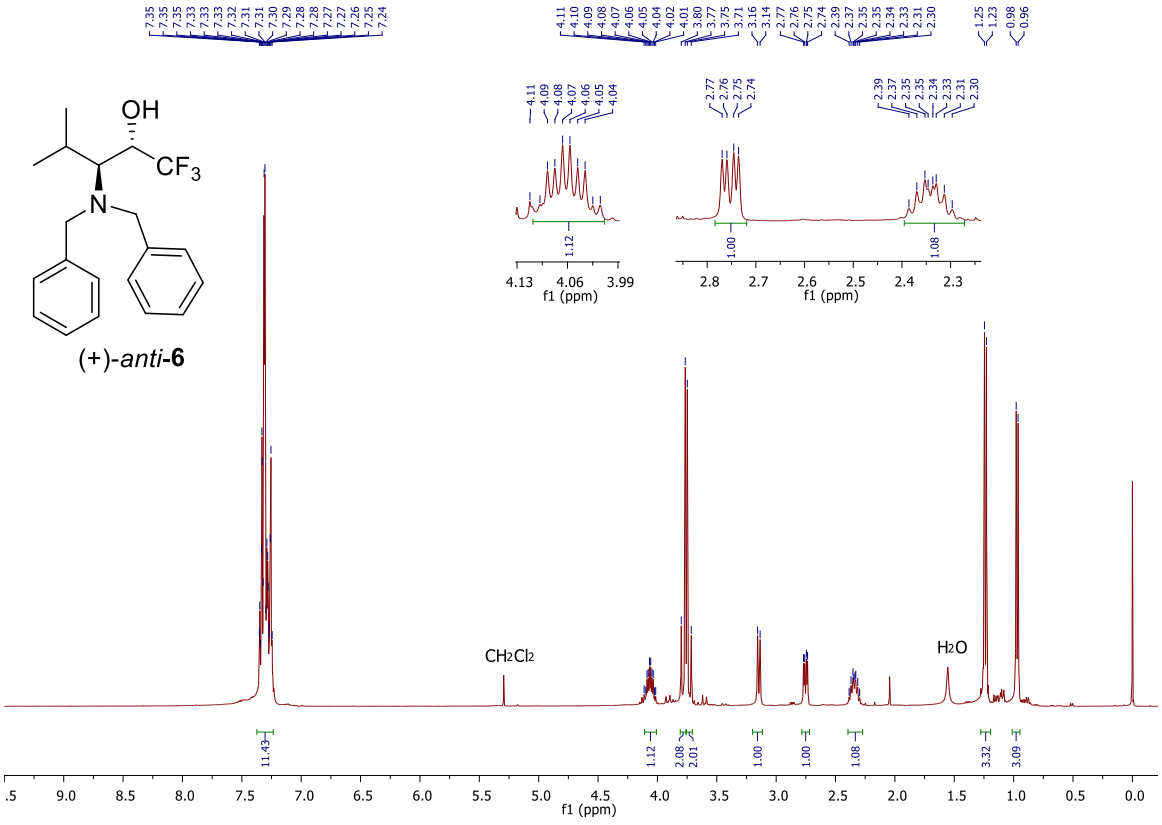


(+)-*syn*-**5**

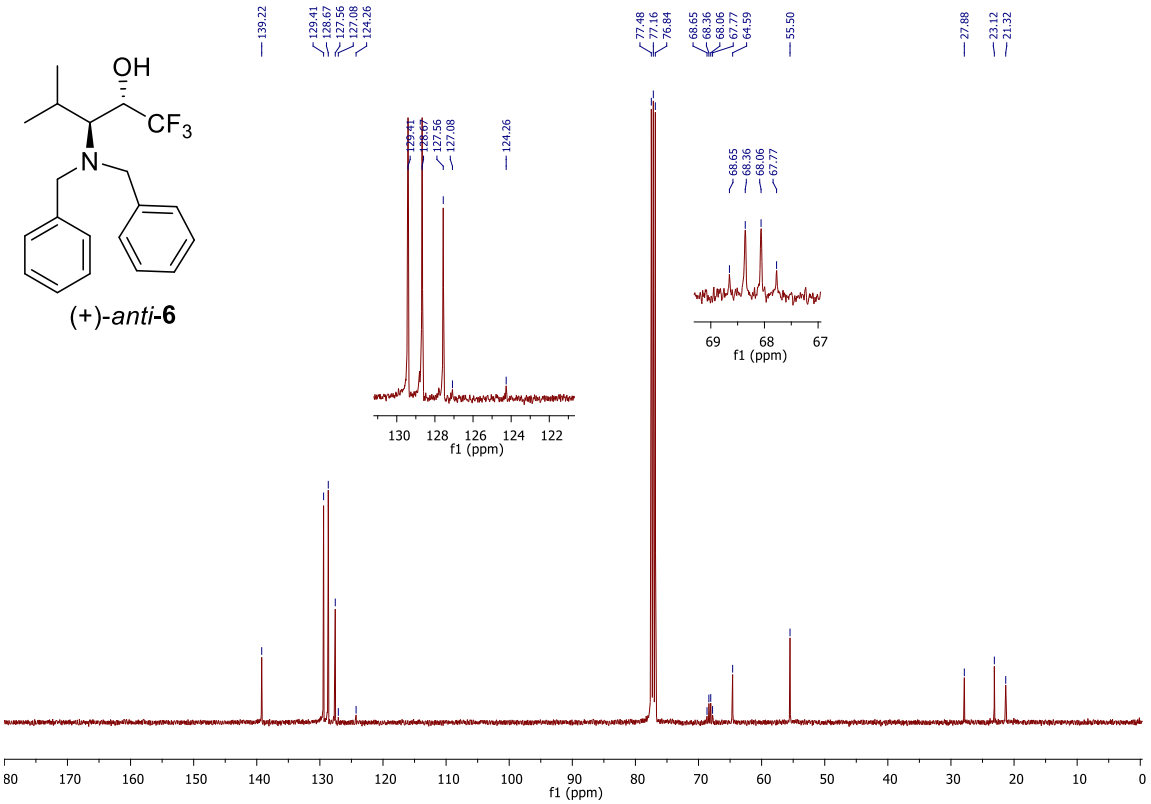
Crude of 6: ^{19}F NMR, 376 MHz, $CDCl_3$



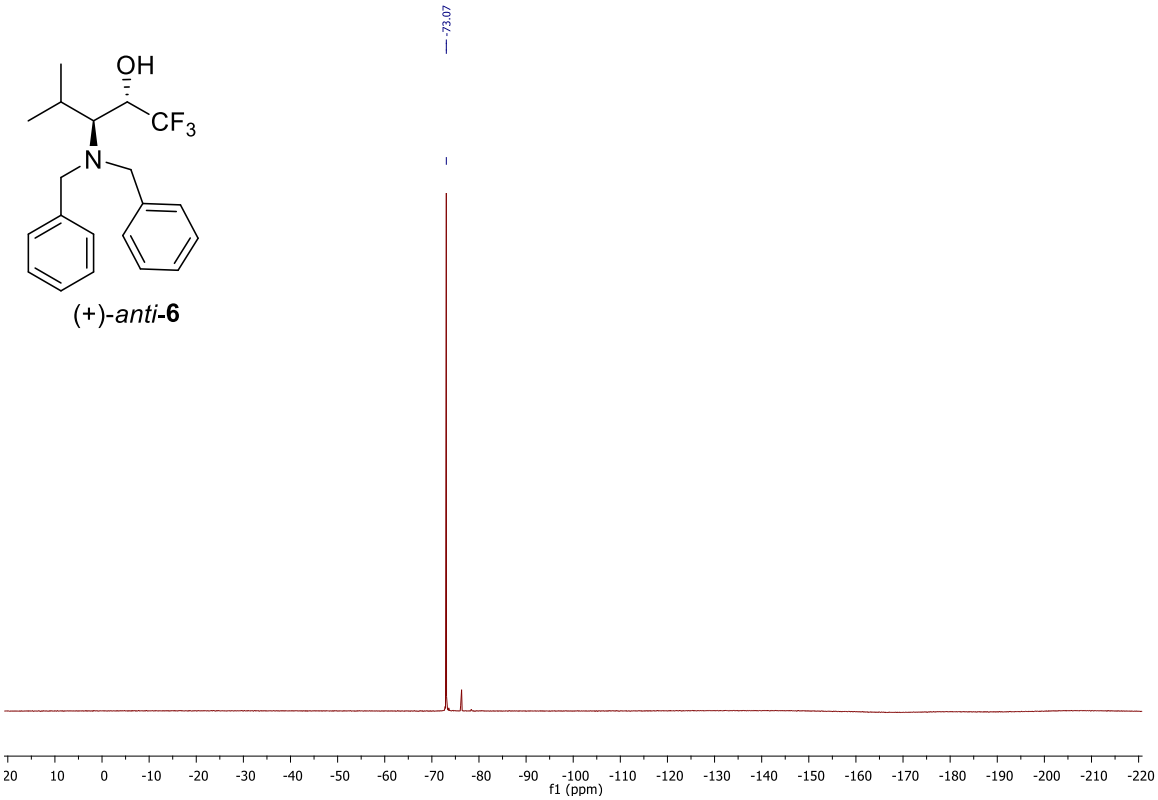
^{1}H NMR, 400 MHz, $CDCl_3$ [contains a trace of (+)-*syn*-6]



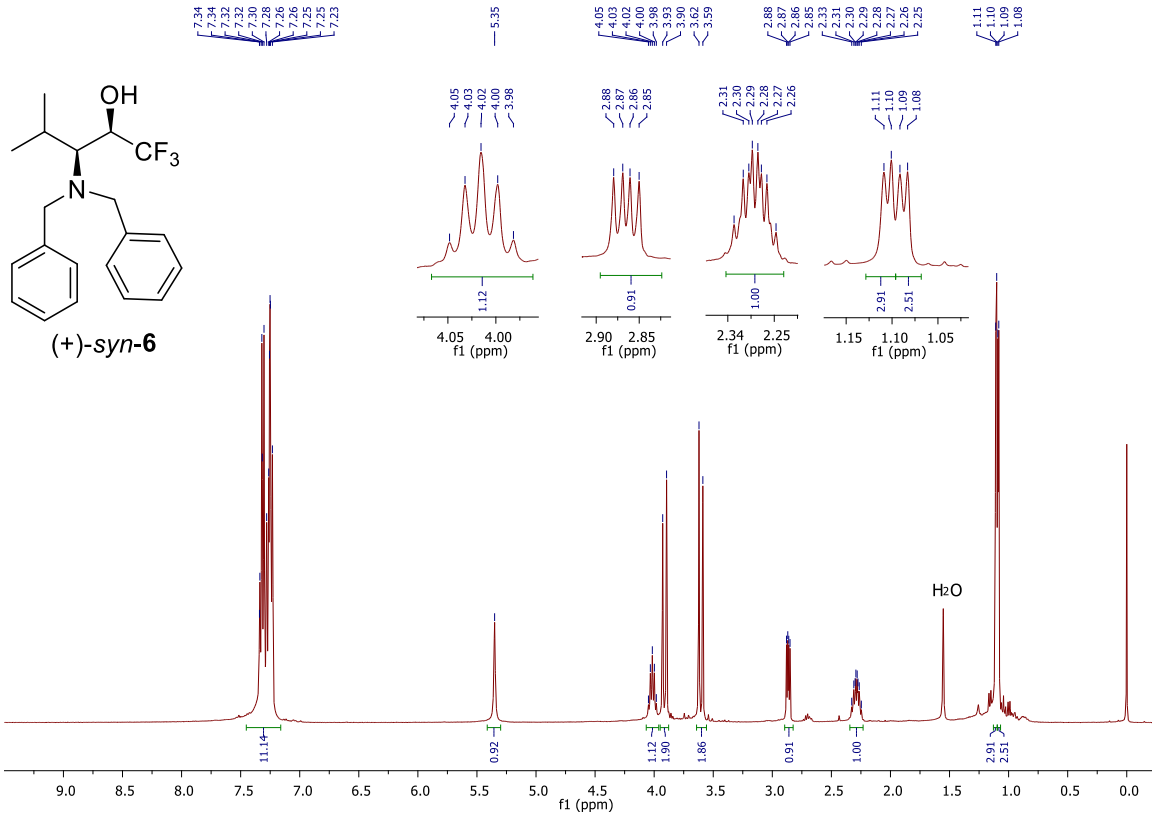
^{13}C NMR, 100 MHz, $CDCl_3$



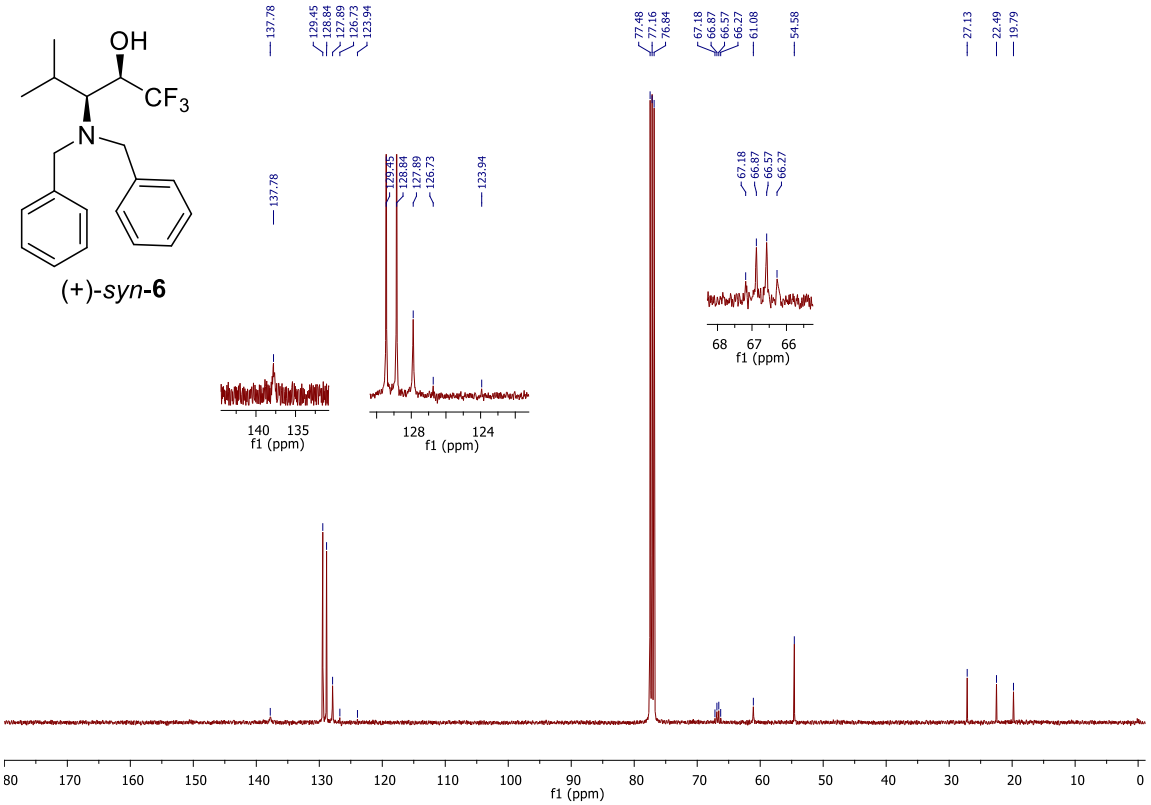
^{19}F NMR, 376 MHz, $CDCl_3$ [contains a trace of (+)-*syn*-6]



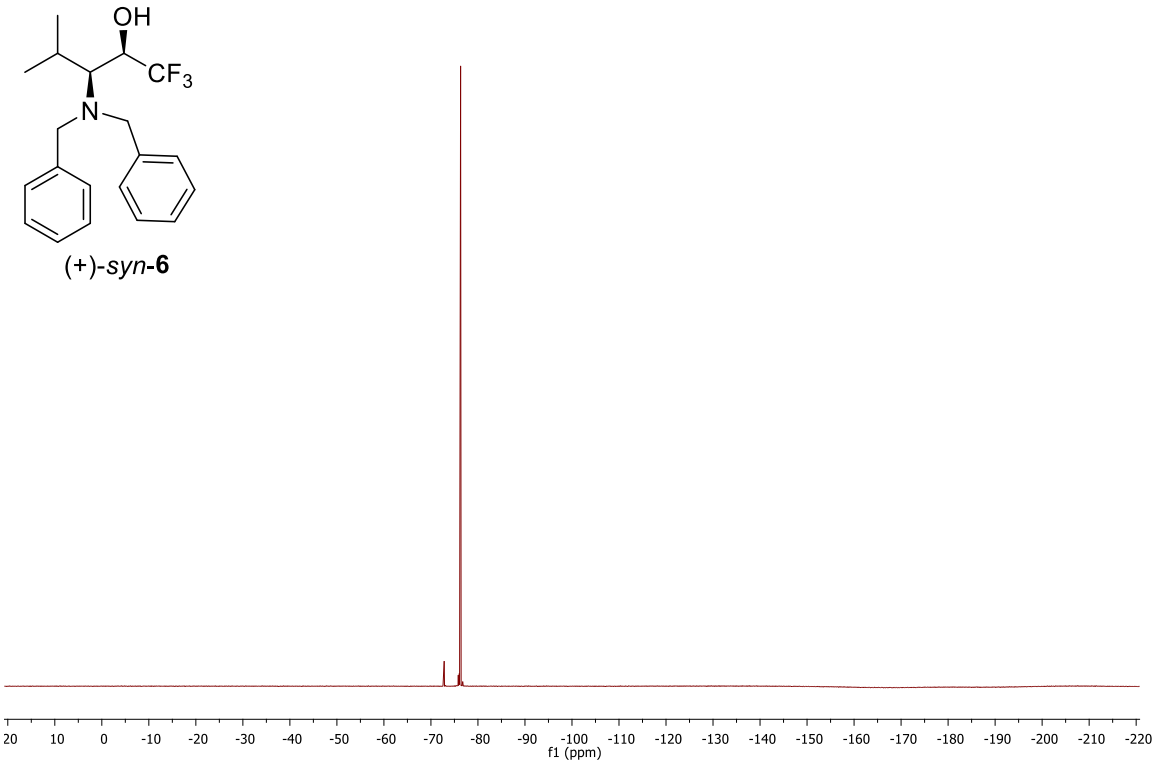
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

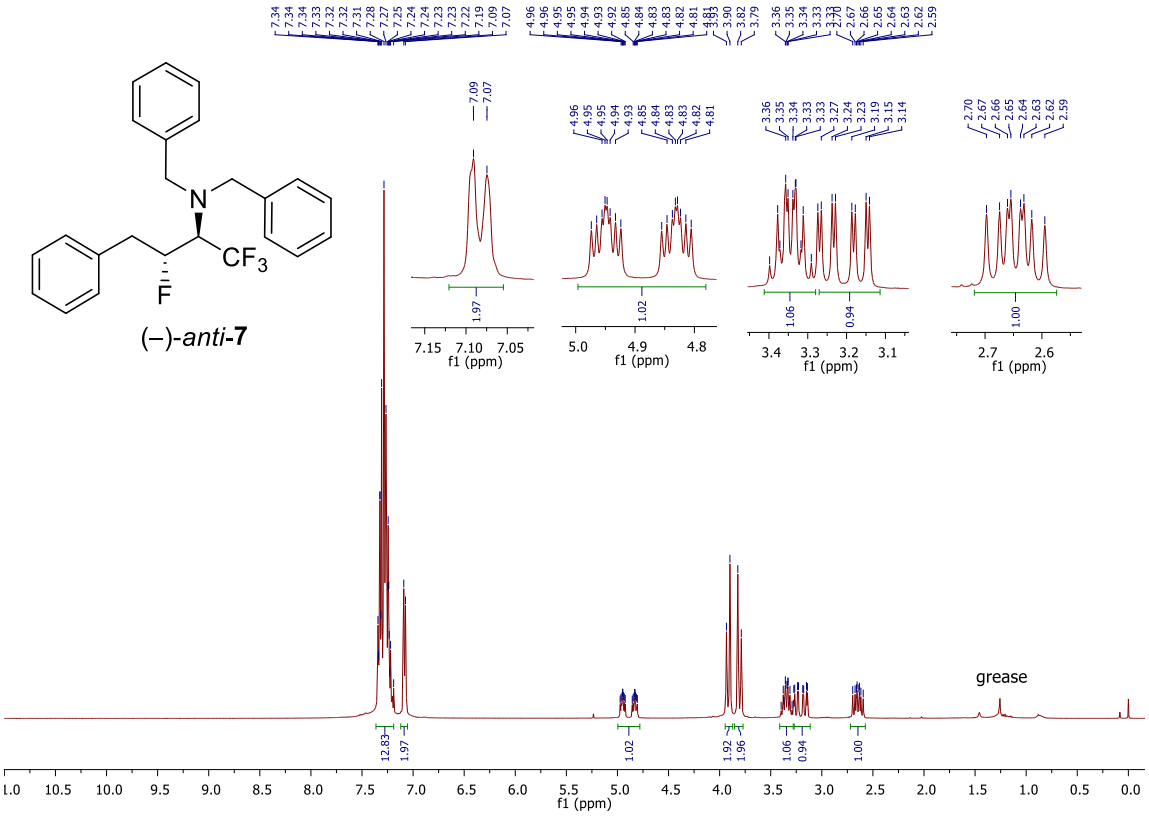


^{19}F NMR, 376 MHz, $CDCl_3$ [contains a trace of (+)-*anti*-6]

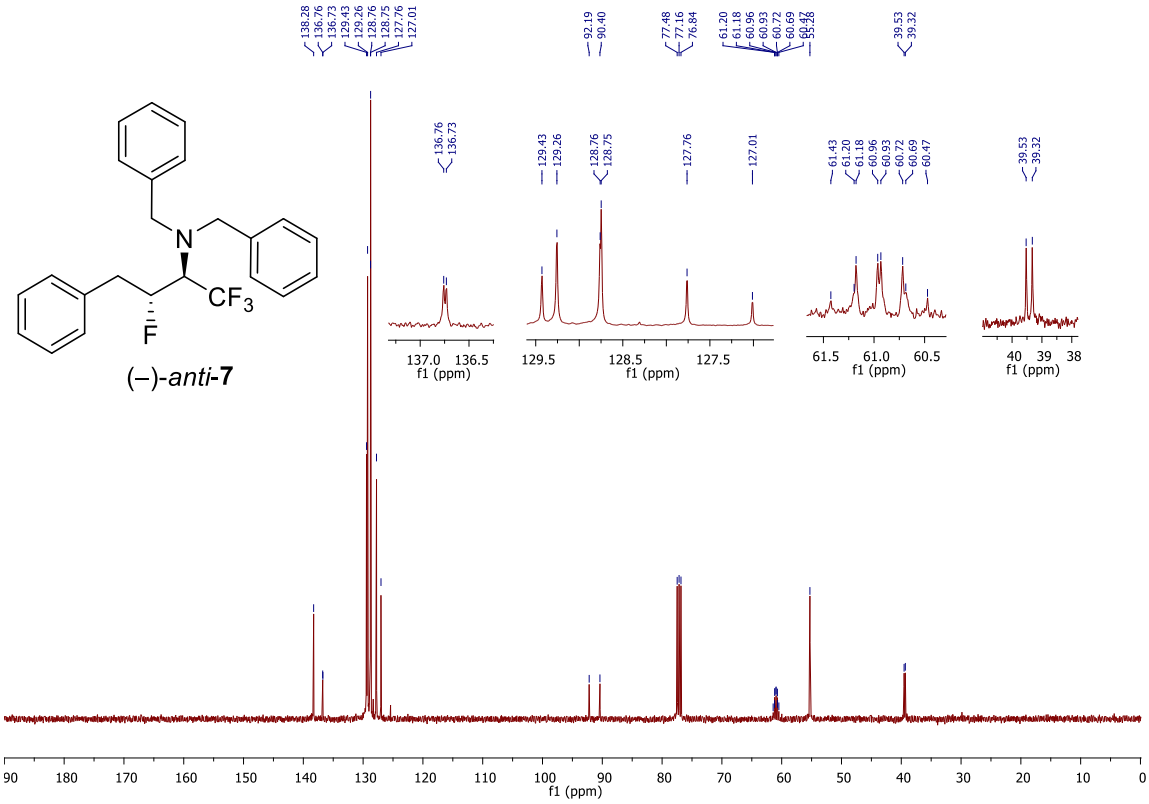


β-FLUORO-α-TRIFLUOROMETHYLAMINE DERIVATIVES

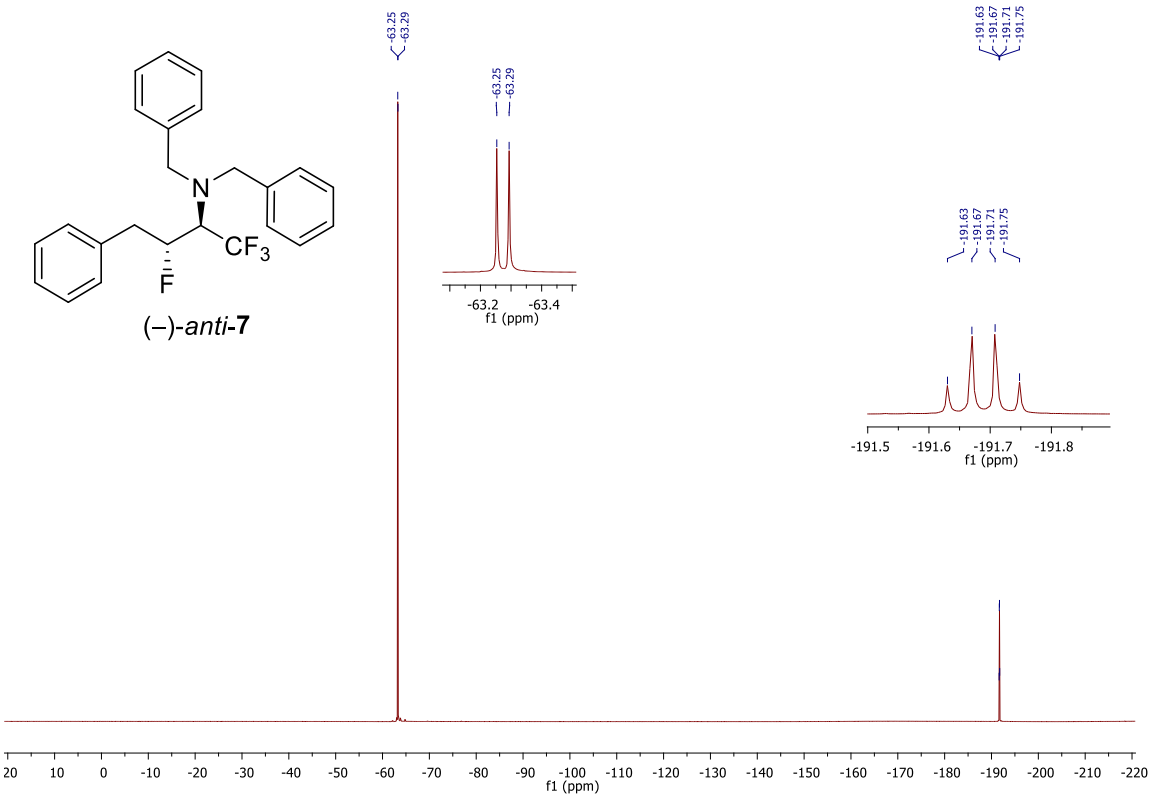
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

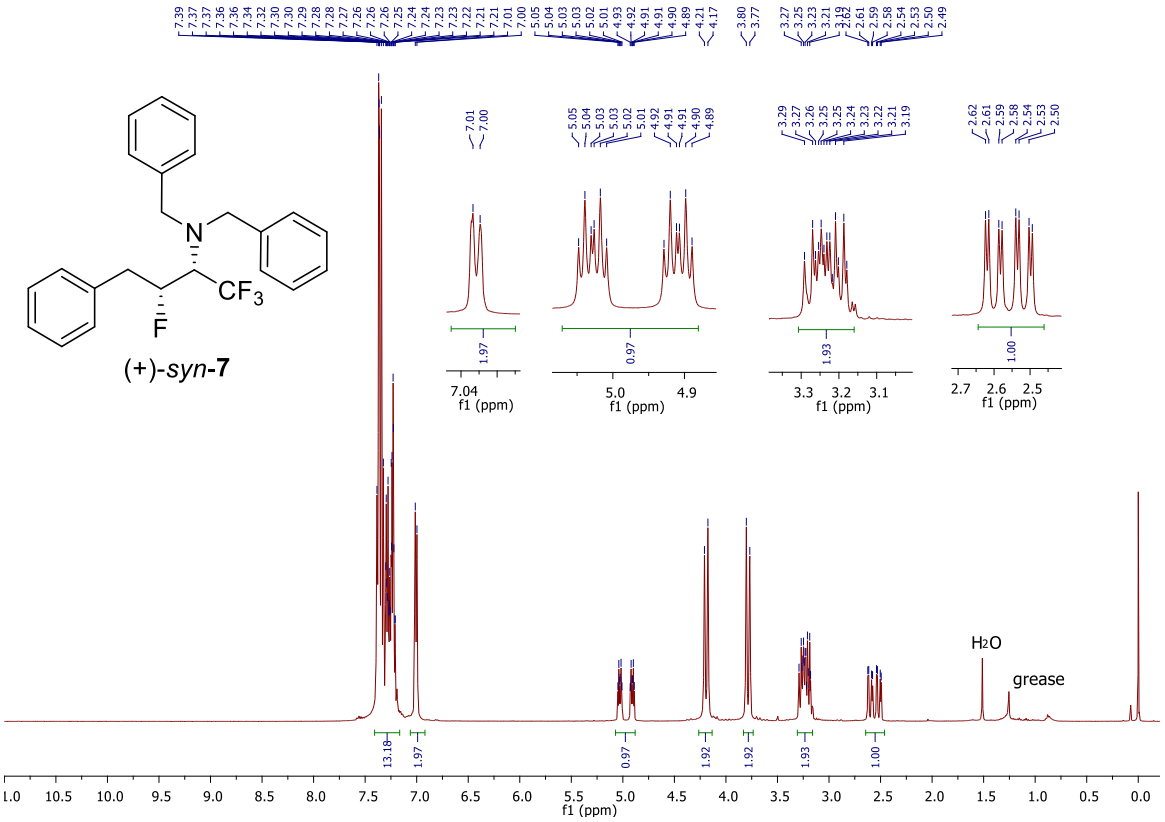


^{19}F NMR, 376 MHz, $CDCl_3$

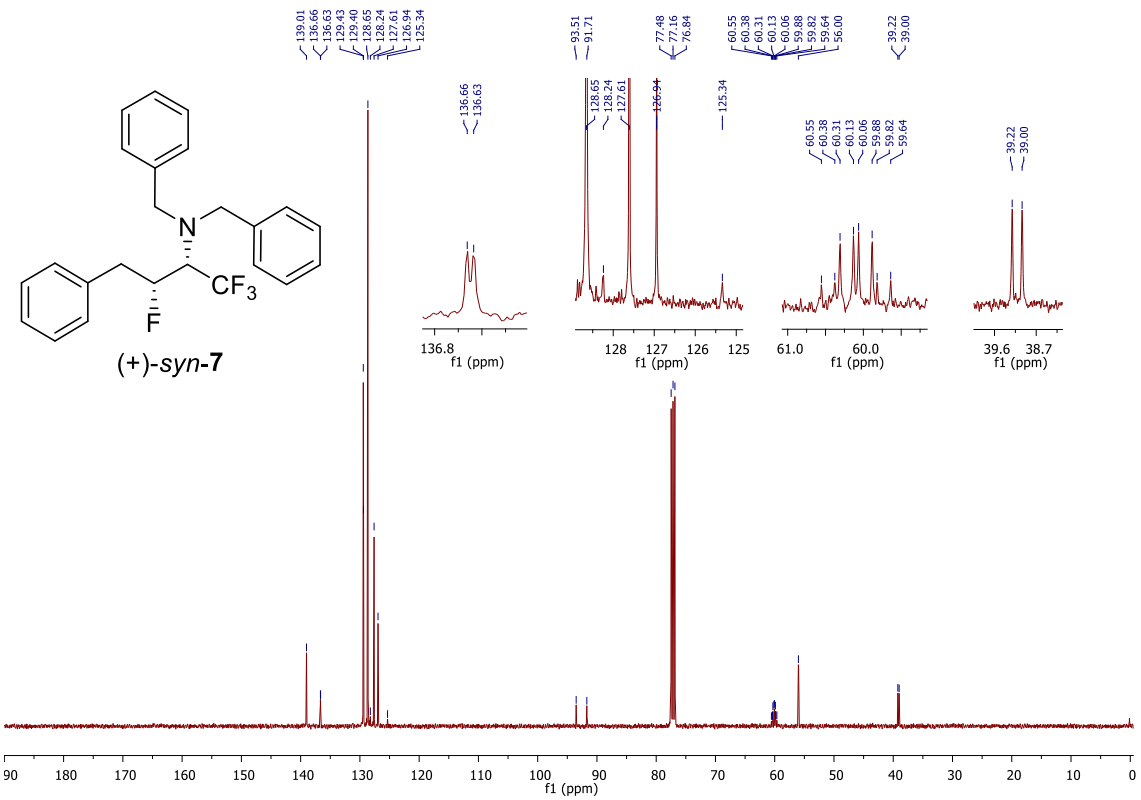


(–)-*anti*-**7**

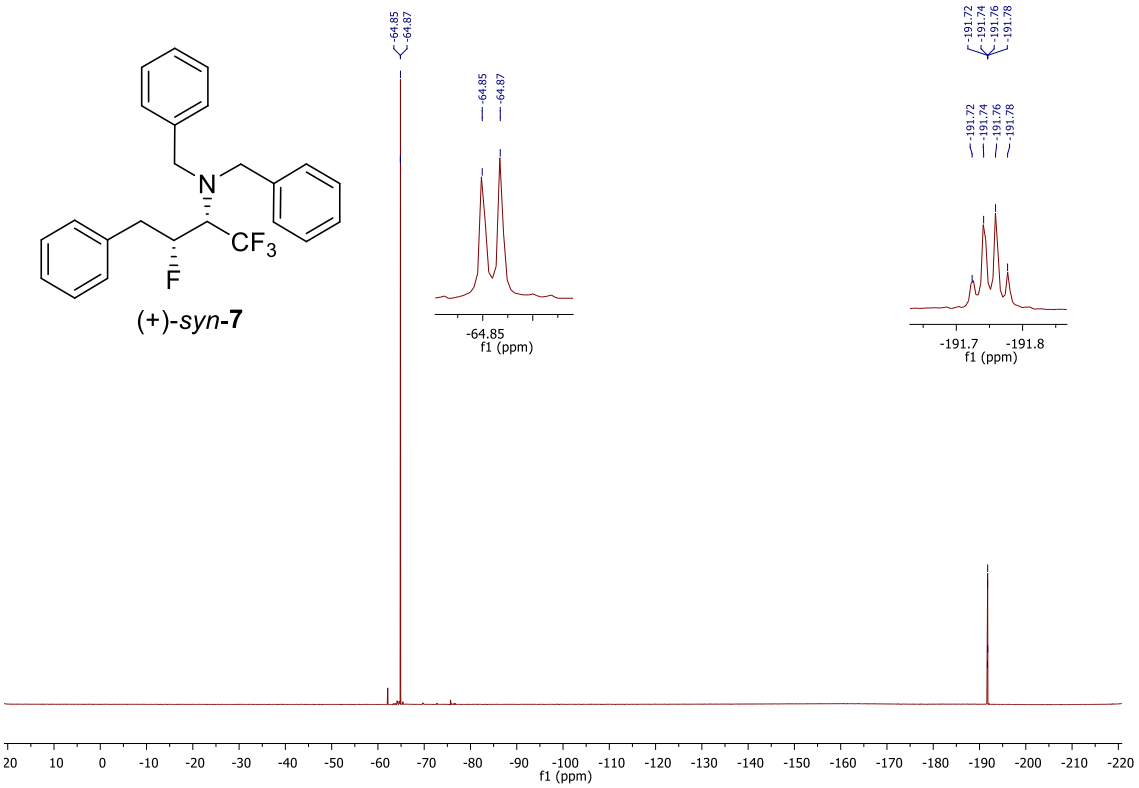
^{1}H NMR, 400 MHz, $CDCl_3$



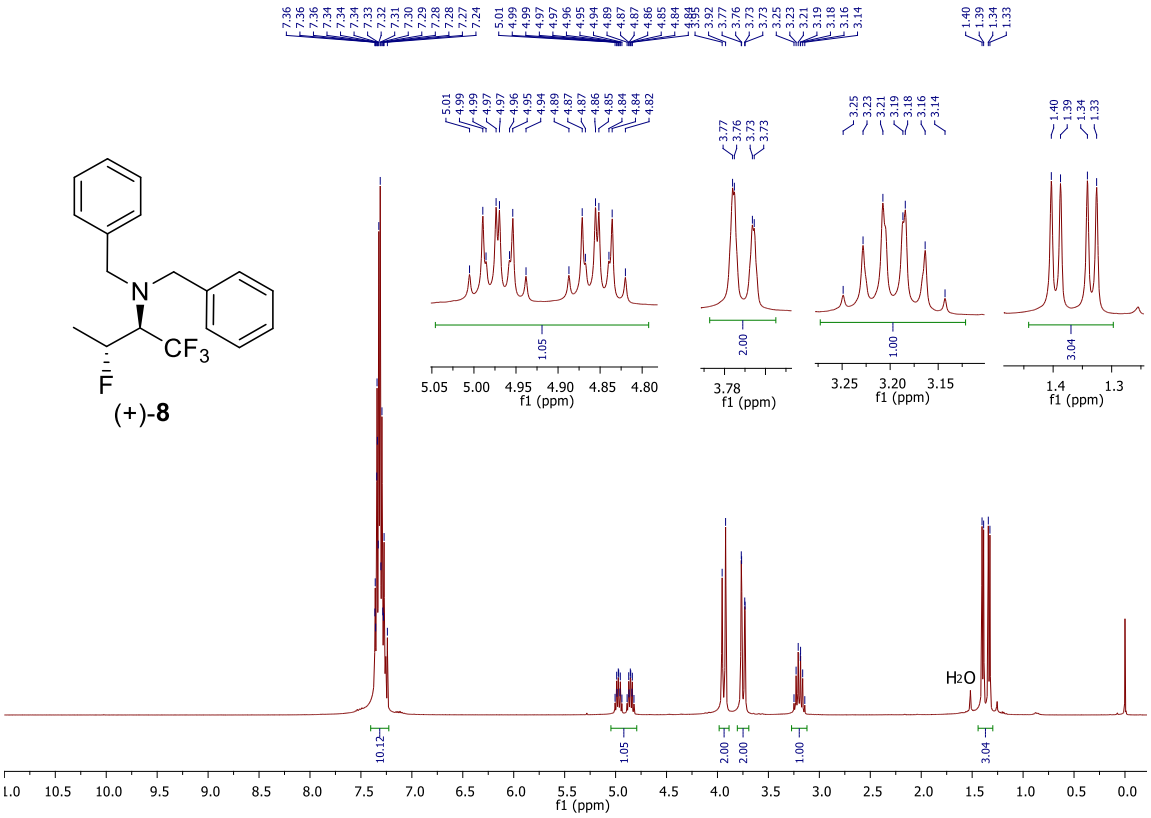
^{13}C NMR, 100 MHz, $CDCl_3$



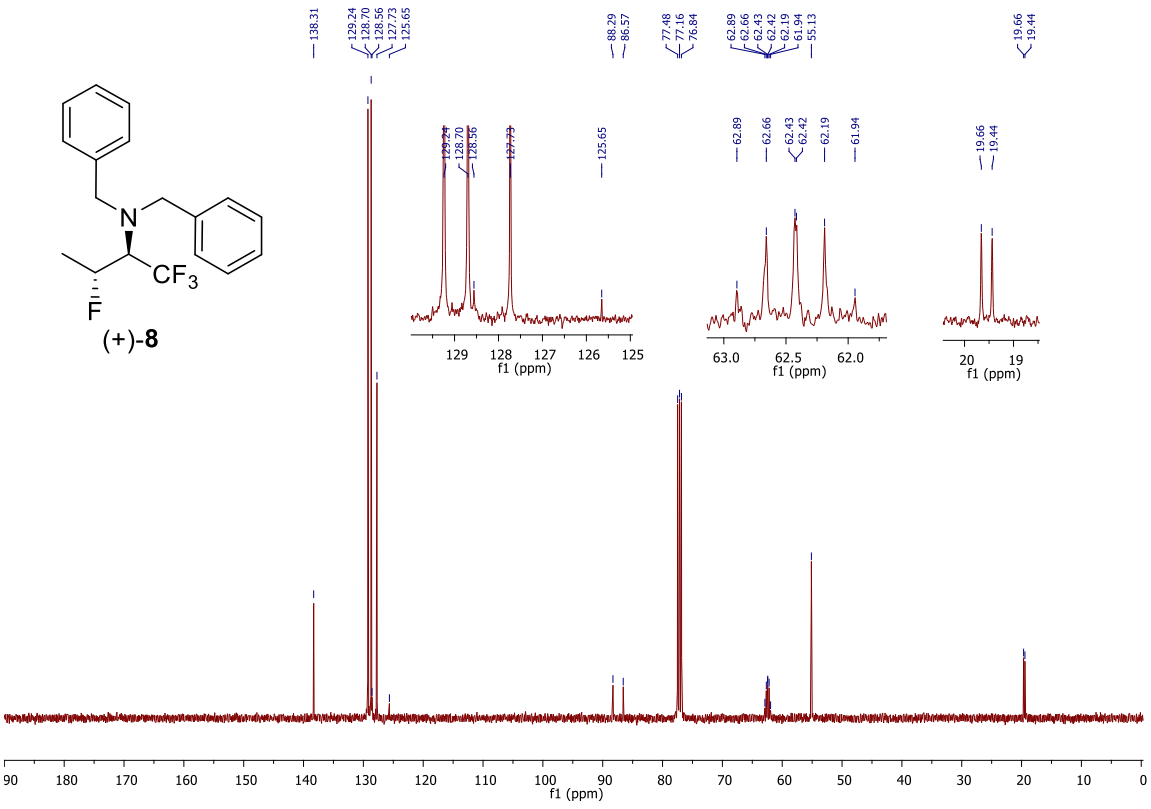
^{19}F NMR, 376 MHz, $CDCl_3$



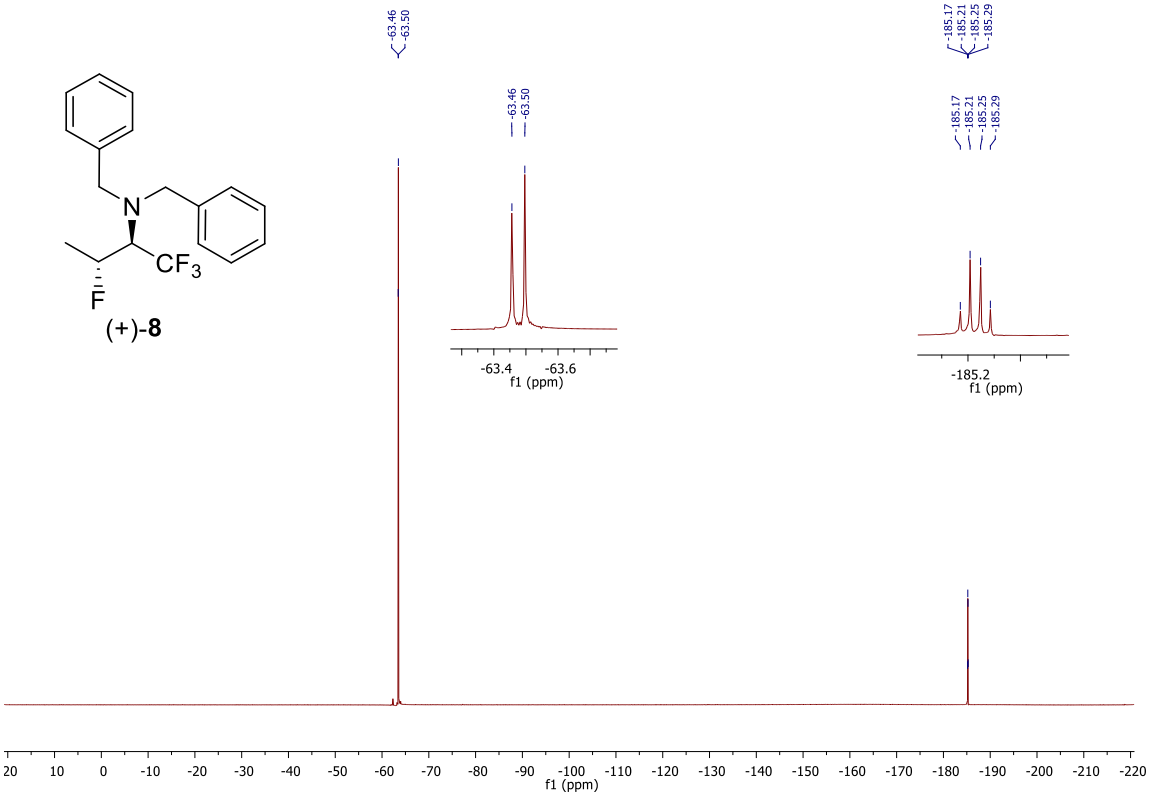
^{1}H NMR, 400 MHz, $CDCl_3$



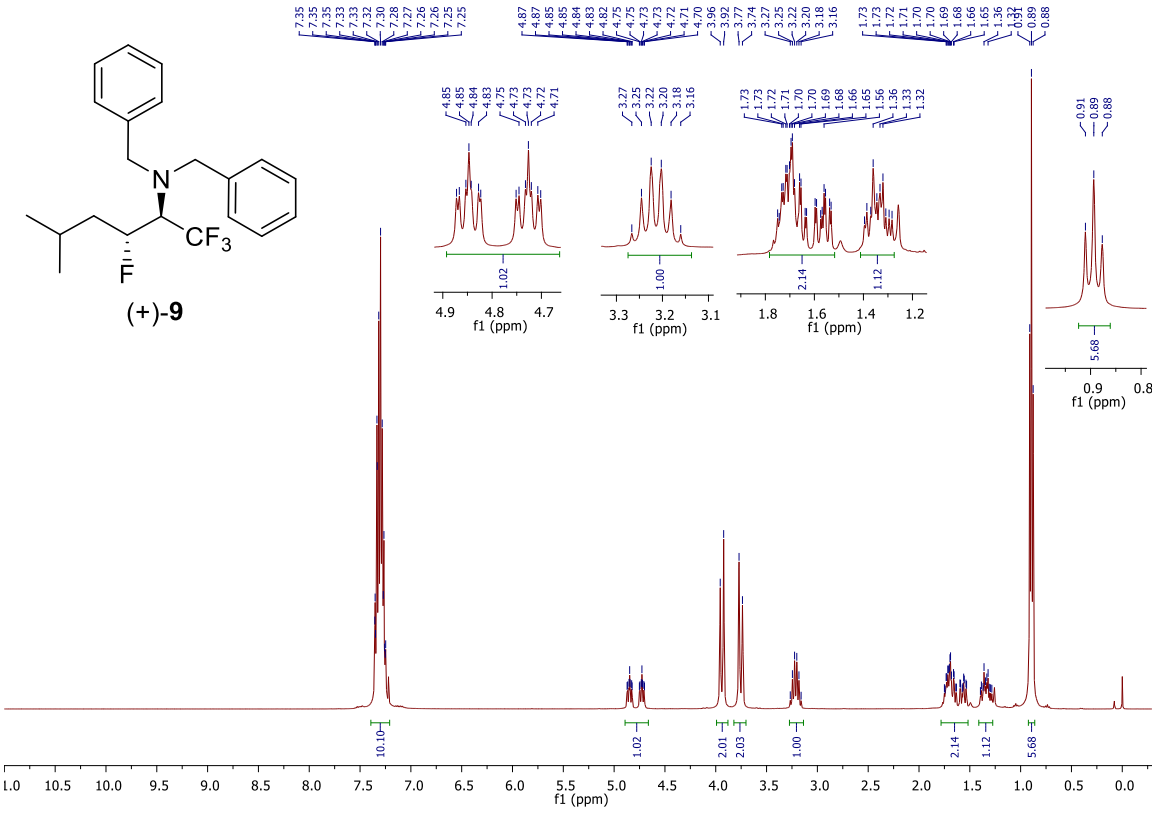
^{13}C NMR, 100 MHz, $CDCl_3$



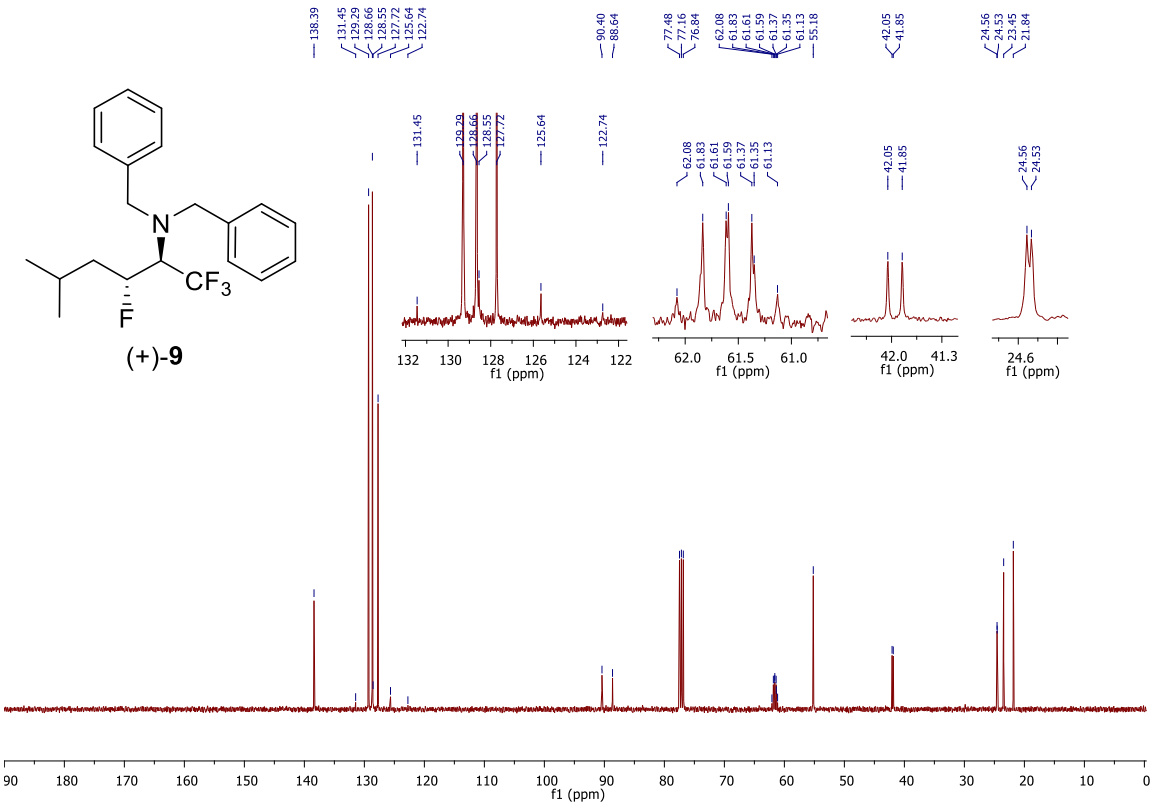
^{19}F NMR, 376 MHz, $CDCl_3$



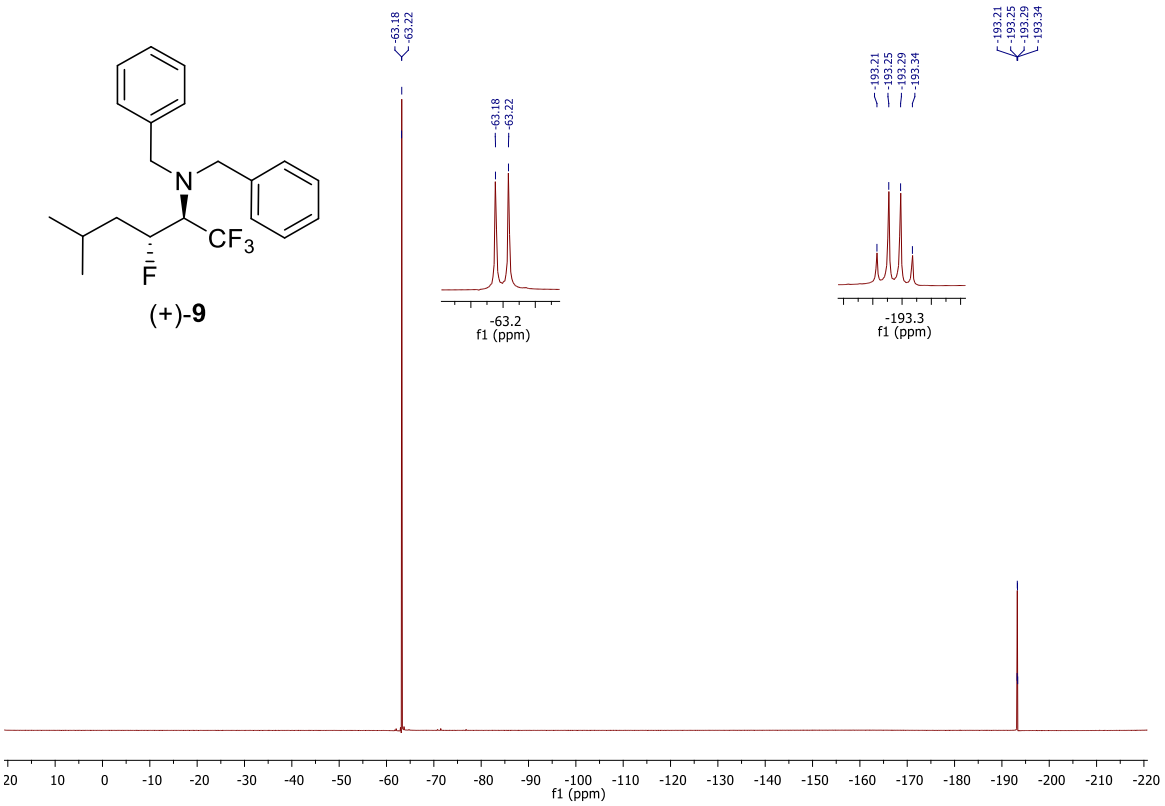
^{1}H NMR, 400 MHz, $CDCl_3$



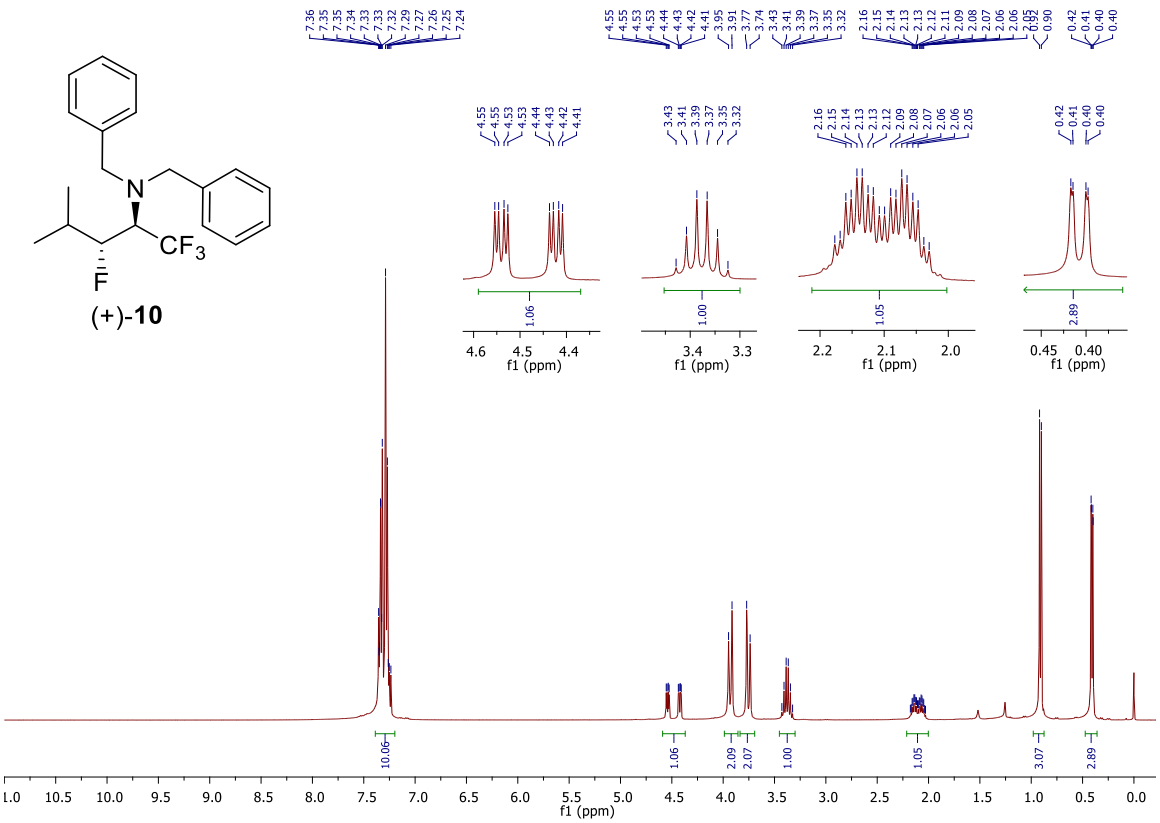
^{13}C NMR, 100 MHz, $CDCl_3$



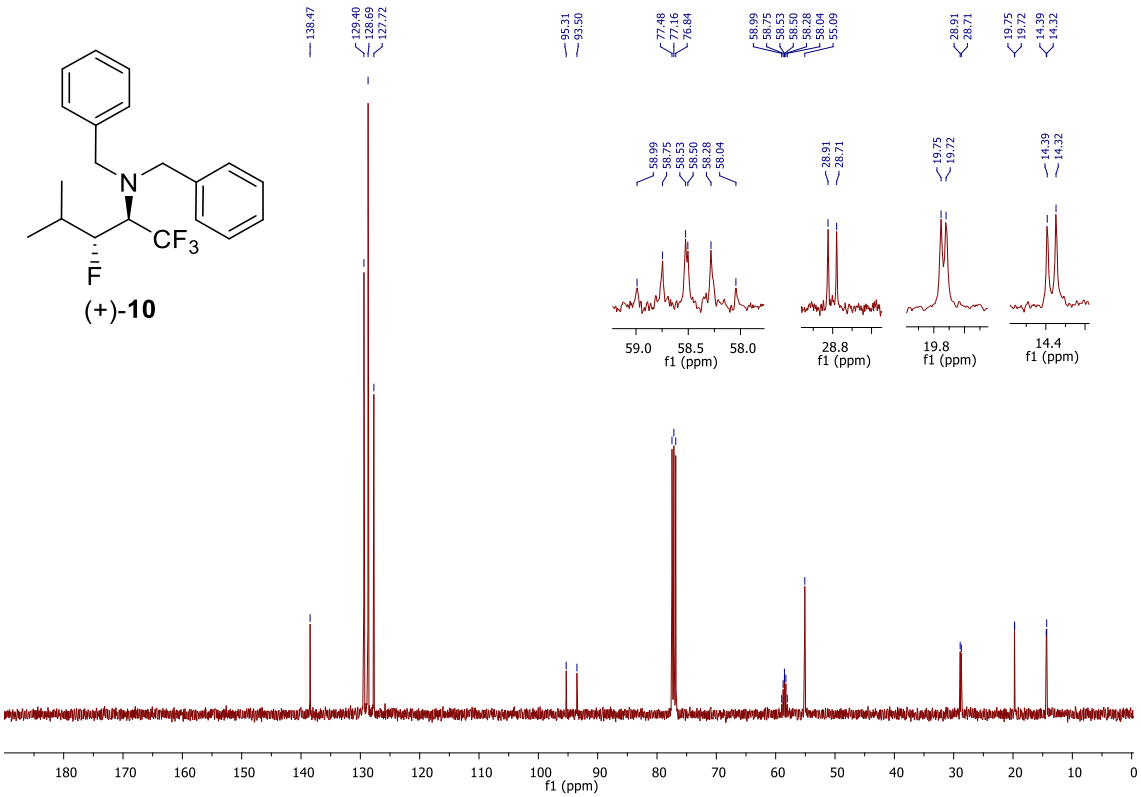
^{19}F NMR, 376 MHz, $CDCl_3$



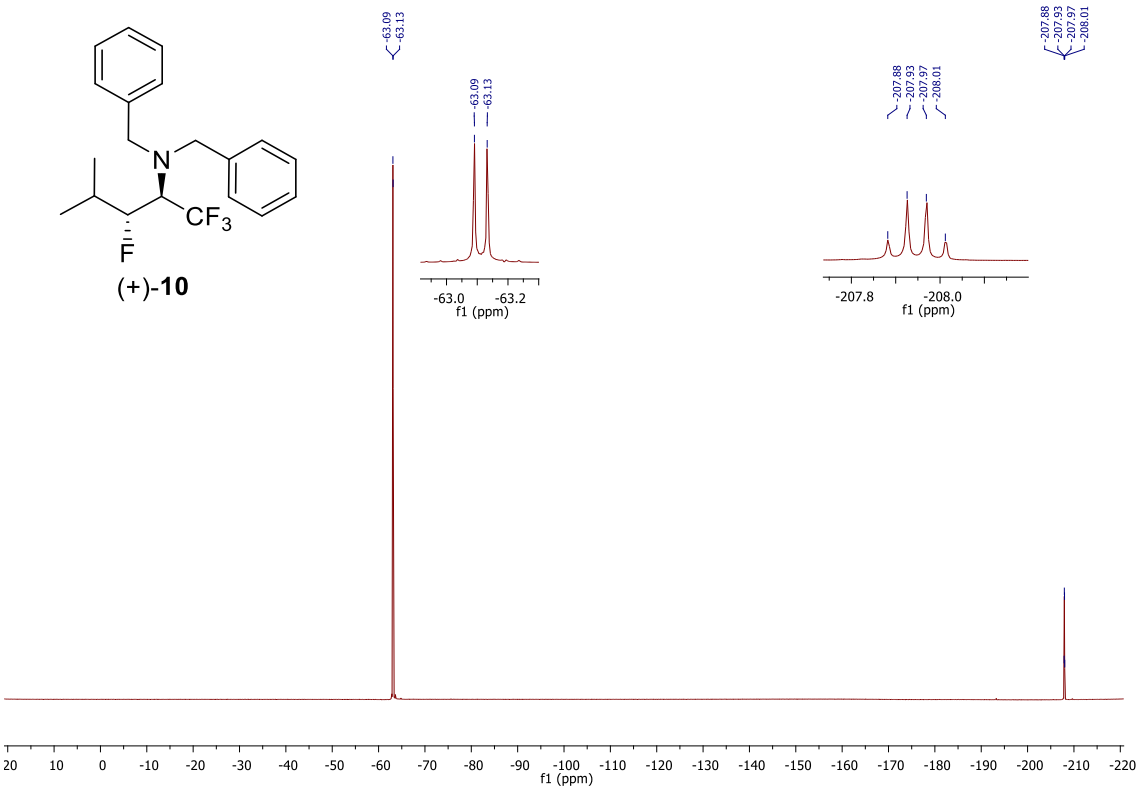
^{1}H NMR, 400 MHz, $CDCl_3$



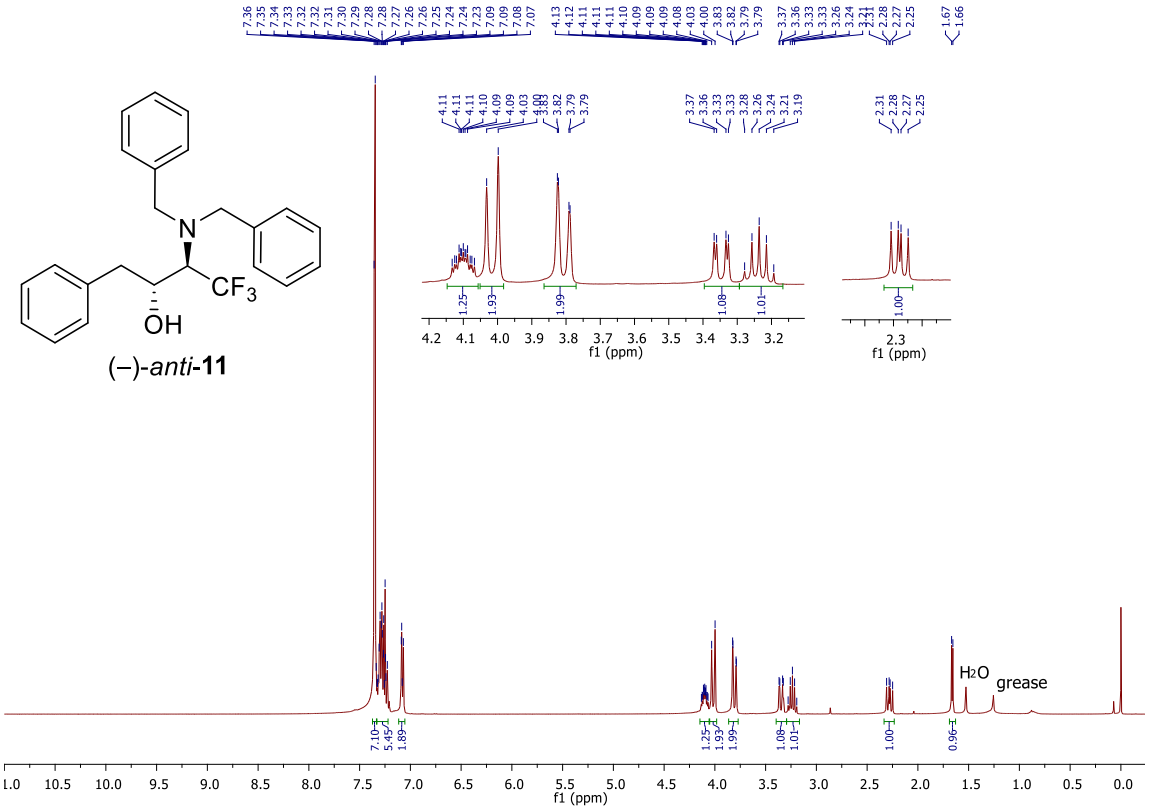
^{13}C NMR, 100 MHz, $CDCl_3$



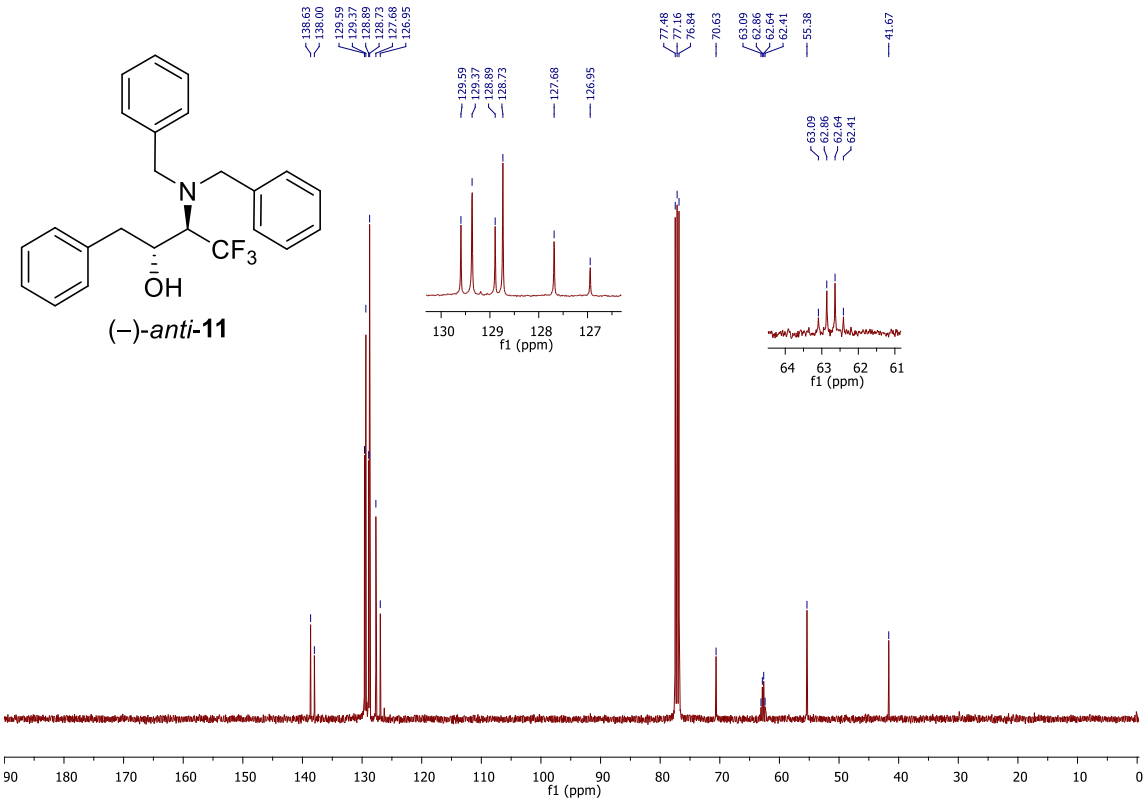
^{19}F NMR, 376 MHz, $CDCl_3$



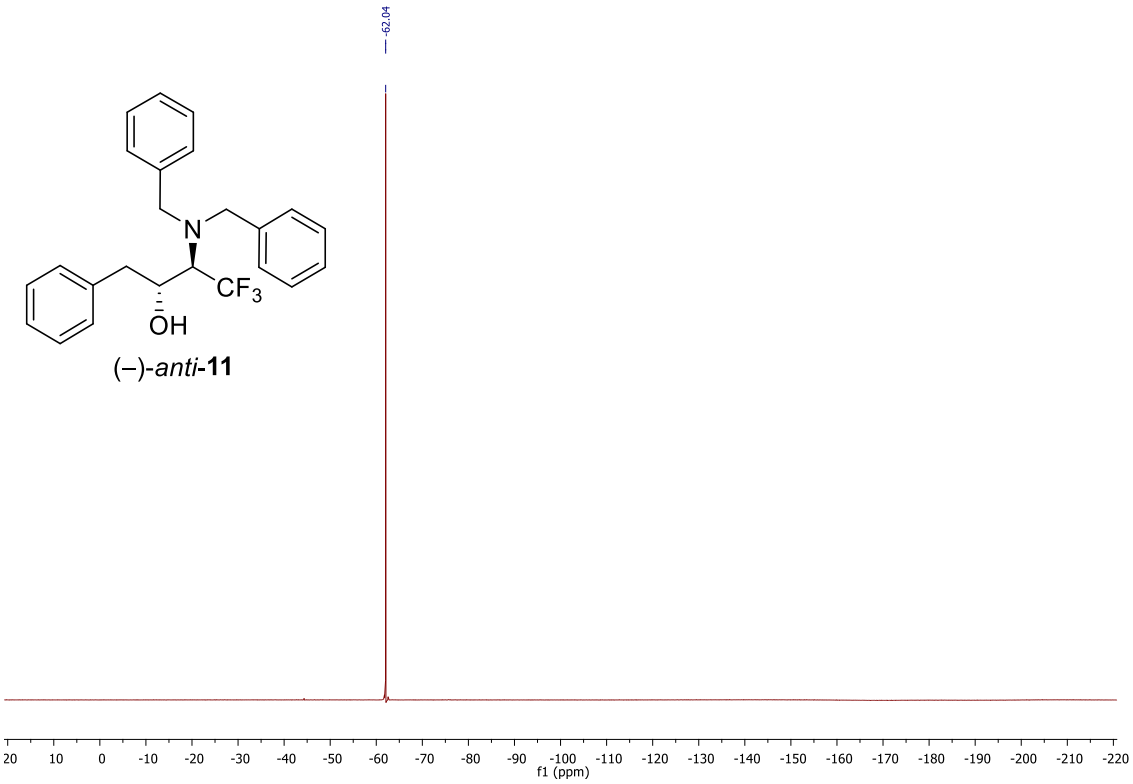
^{1}H NMR, 400 MHz, $CDCl_3$



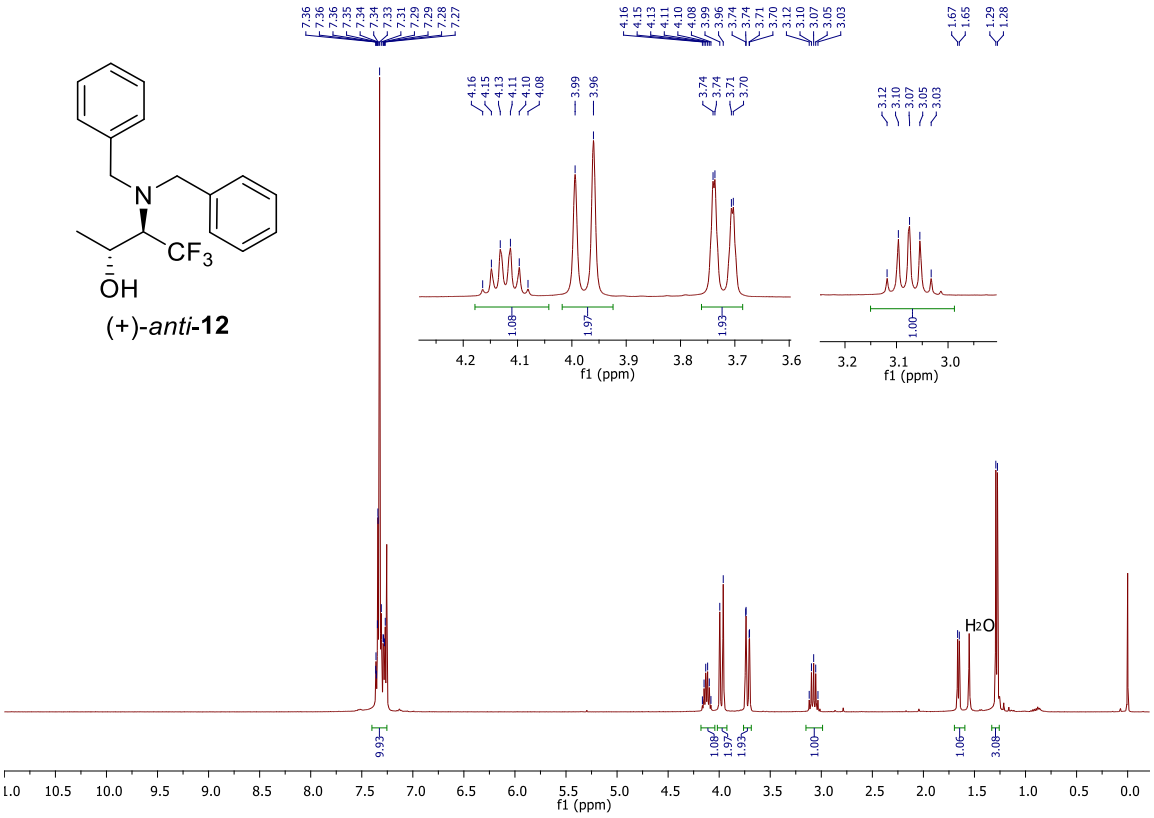
^{13}C NMR, 100 MHz, $CDCl_3$



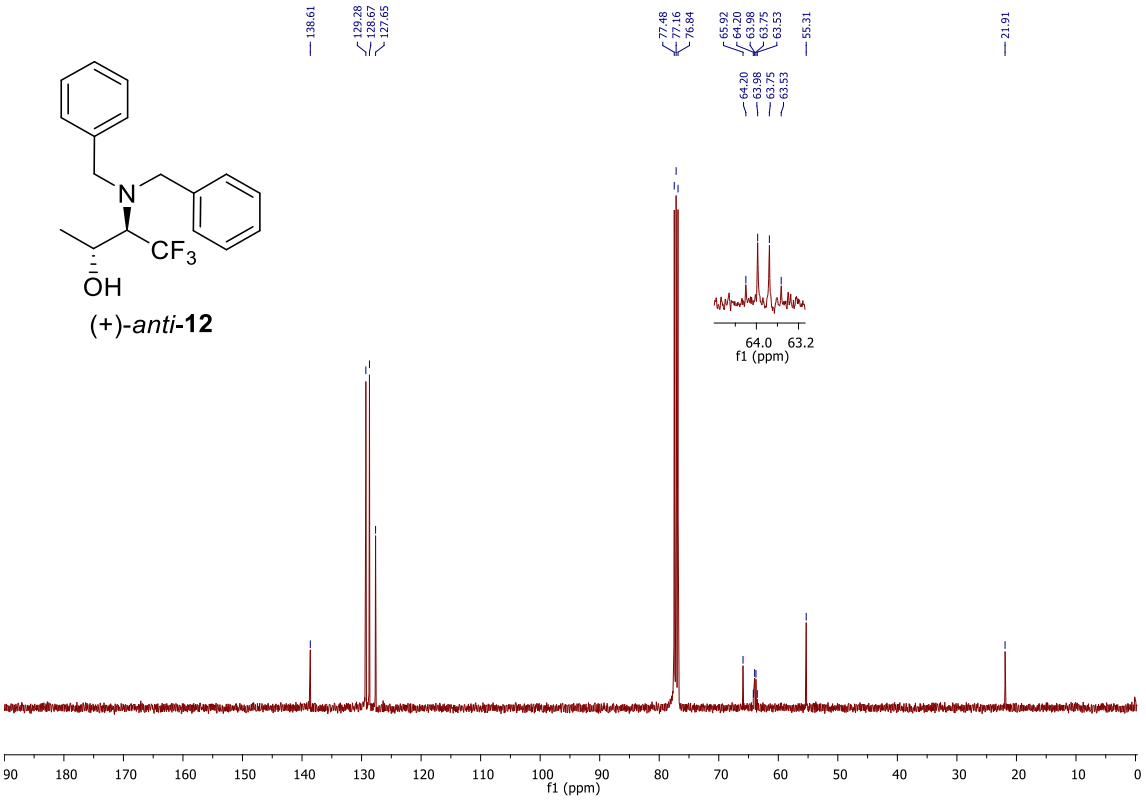
^{19}F NMR, 376 MHz, $CDCl_3$



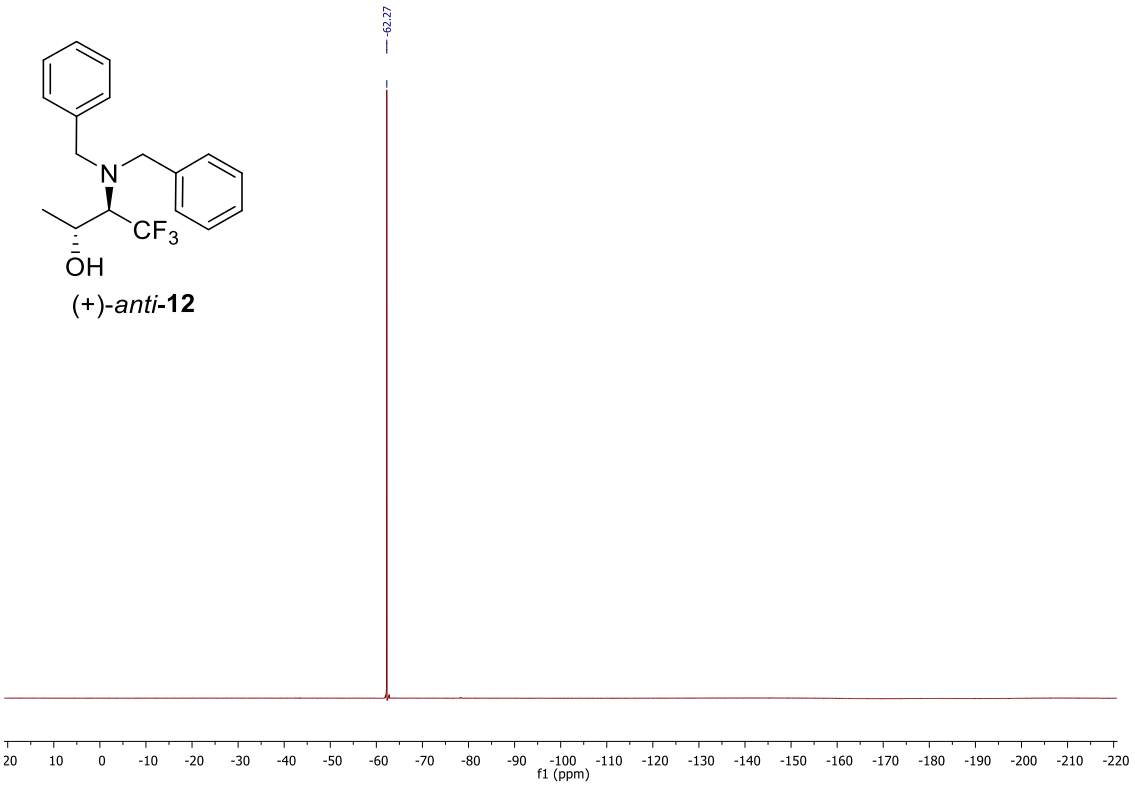
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

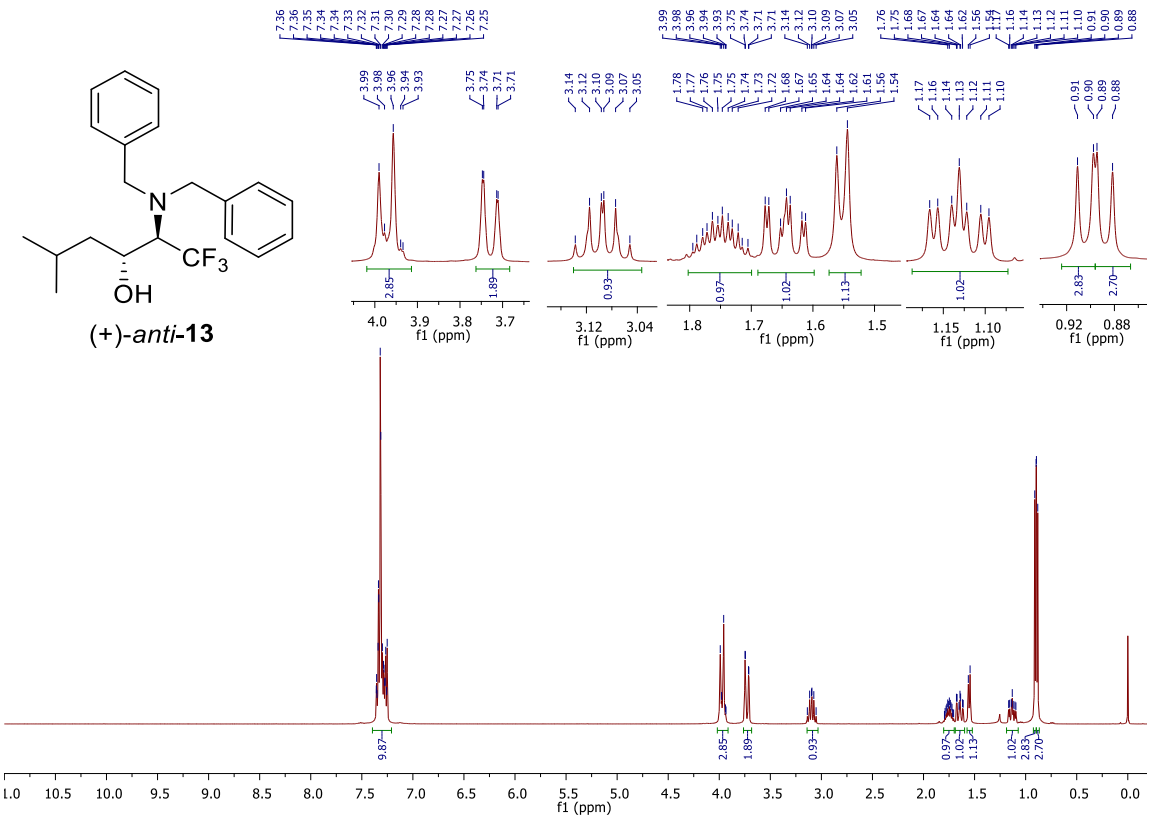


^{19}F NMR, 376 MHz, $CDCl_3$

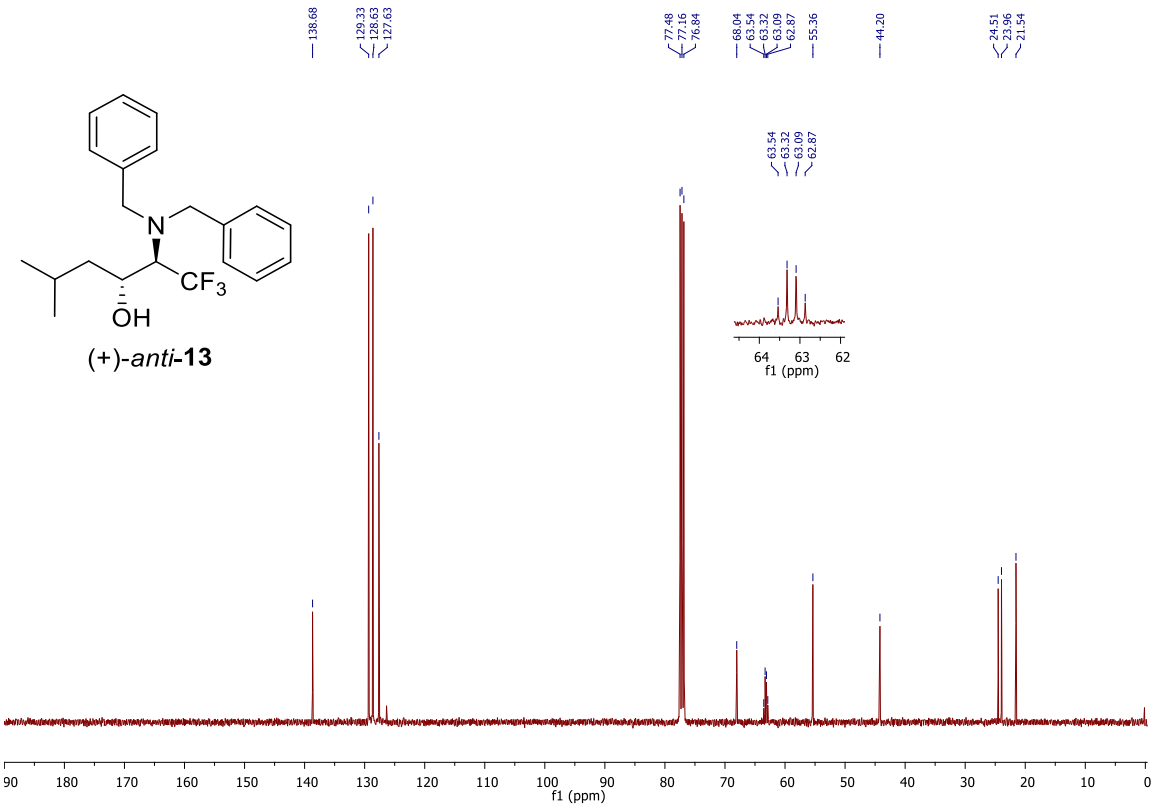


(+)-*anti*-**12**

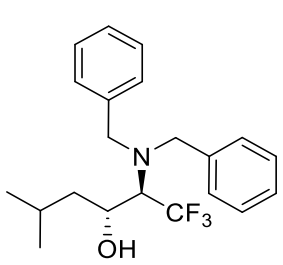
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

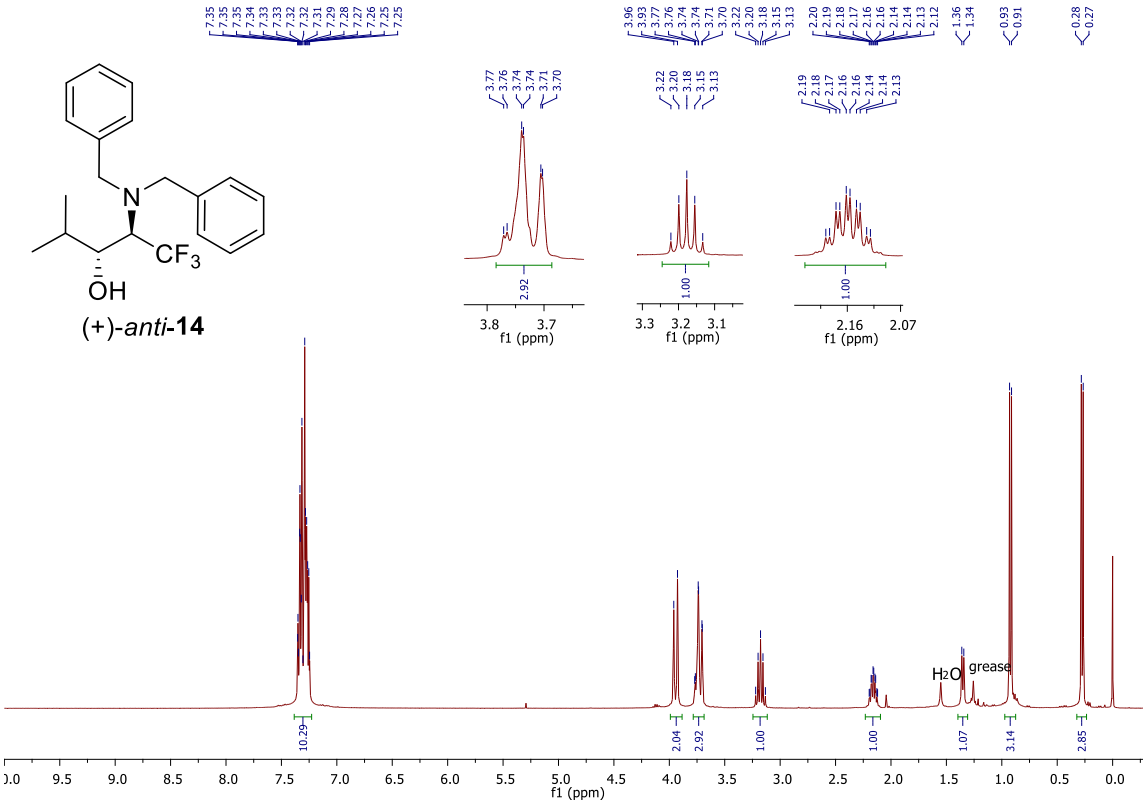


^{19}F NMR, 376 MHz, $CDCl_3$

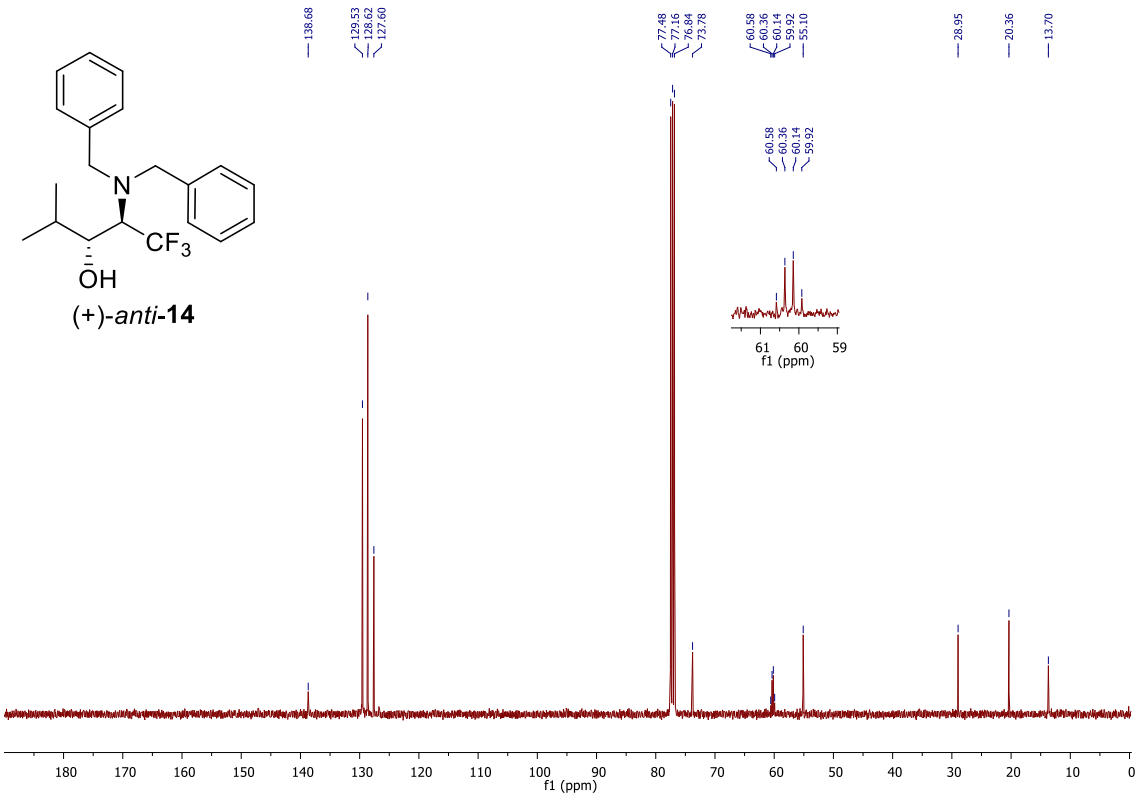


(+)-*anti*-**13**

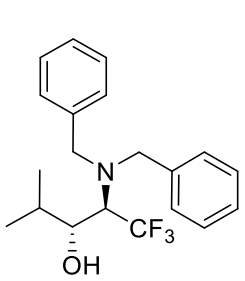
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

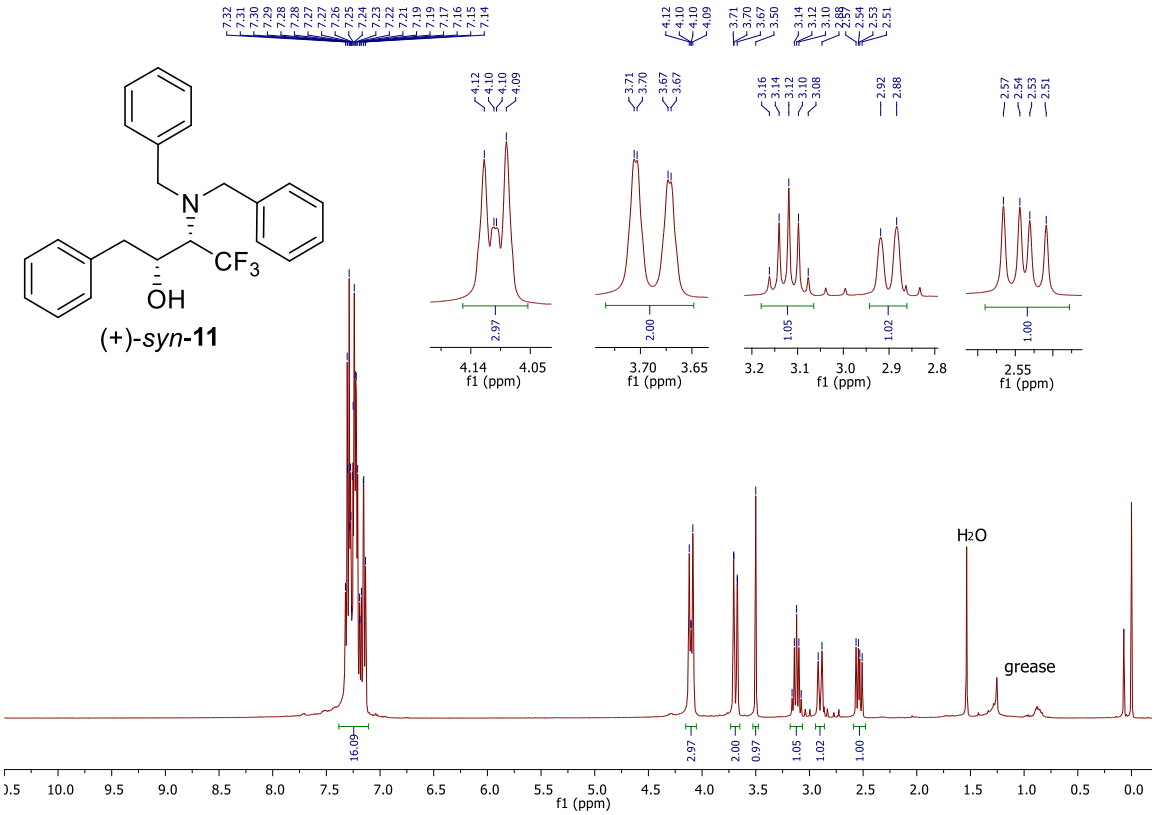


^{19}F NMR, 376 MHz, $CDCl_3$

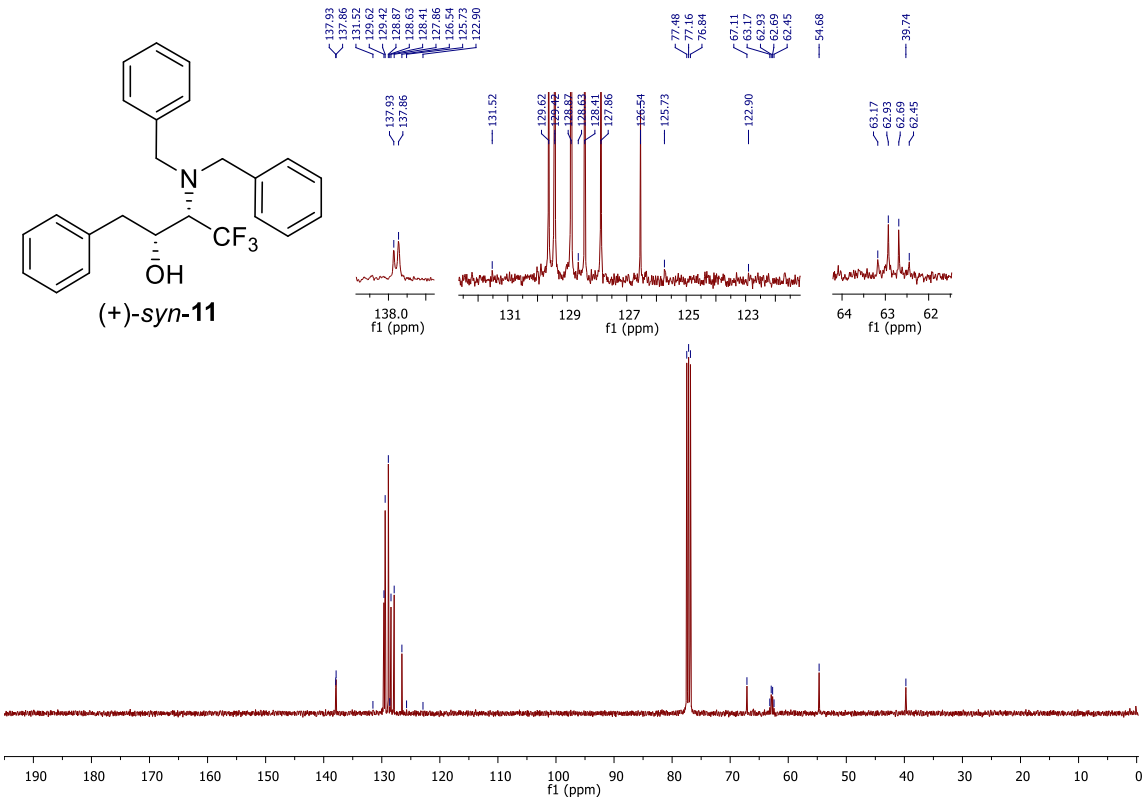


(+)-*anti*-**14**

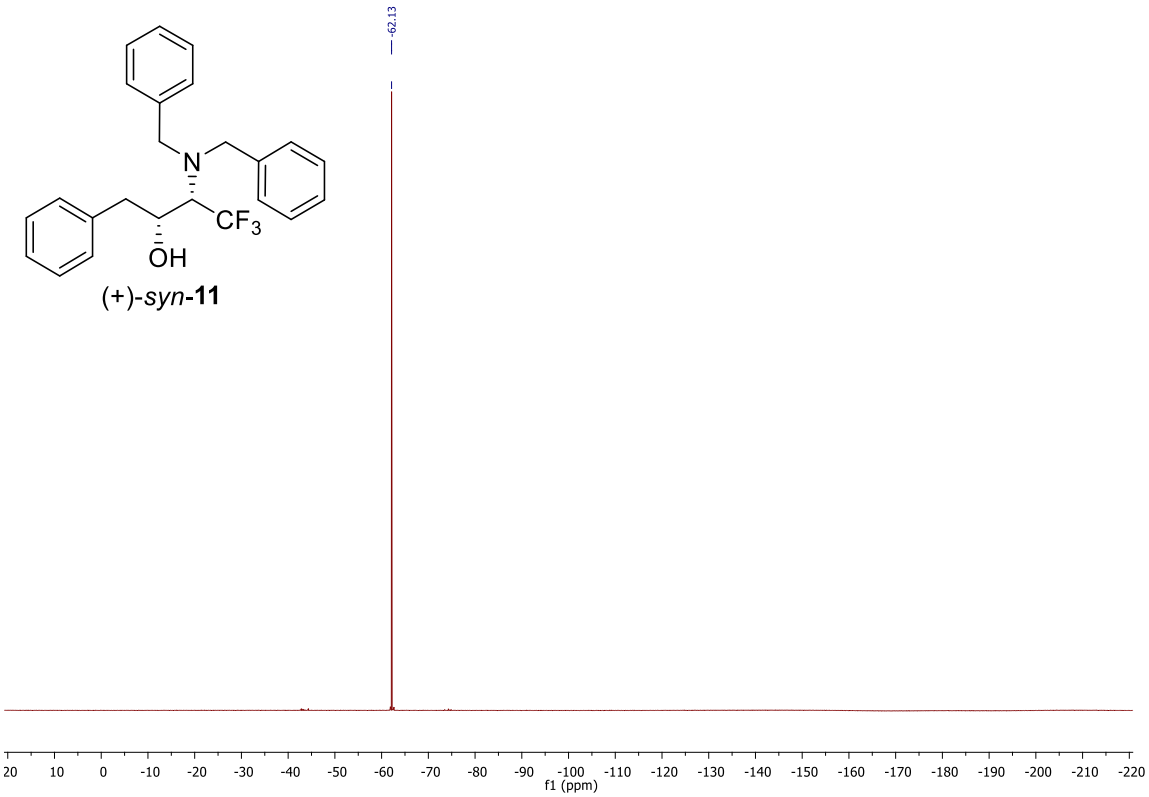
^{1}H NMR, 400 MHz, $CDCl_3$



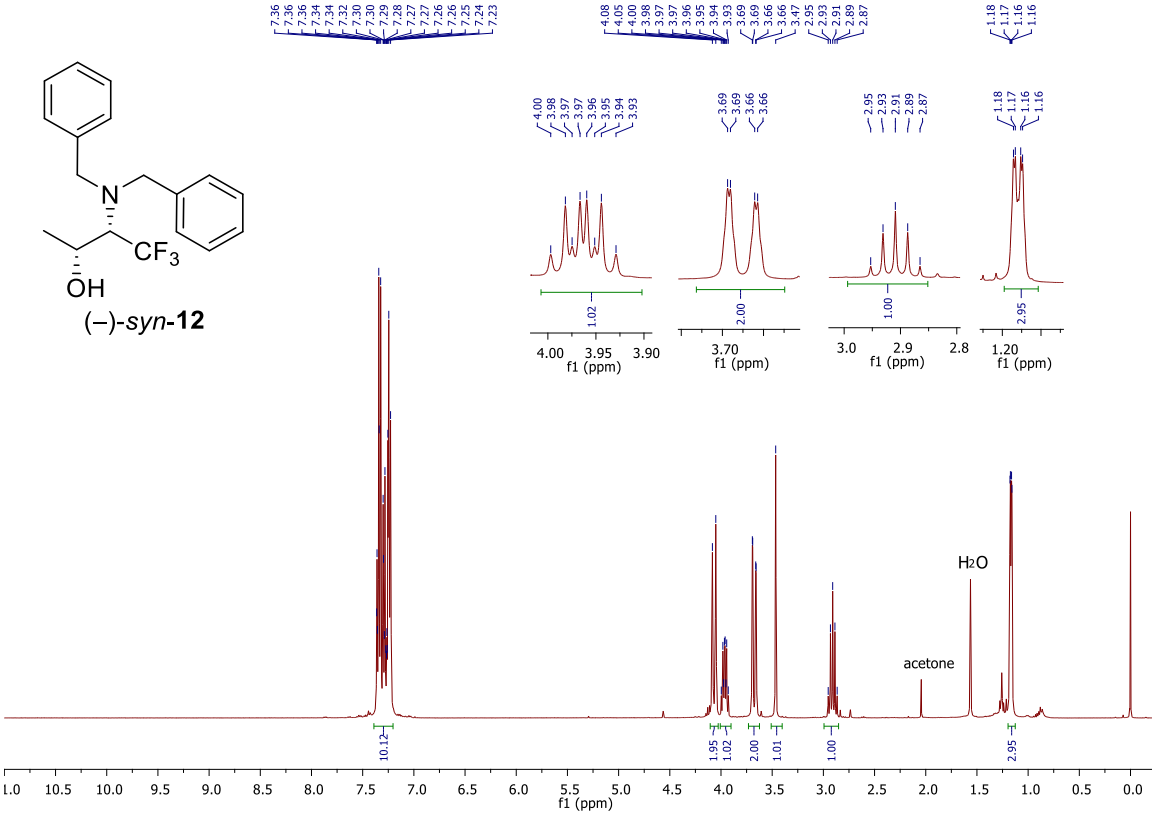
^{13}C NMR, 100 MHz, $CDCl_3$



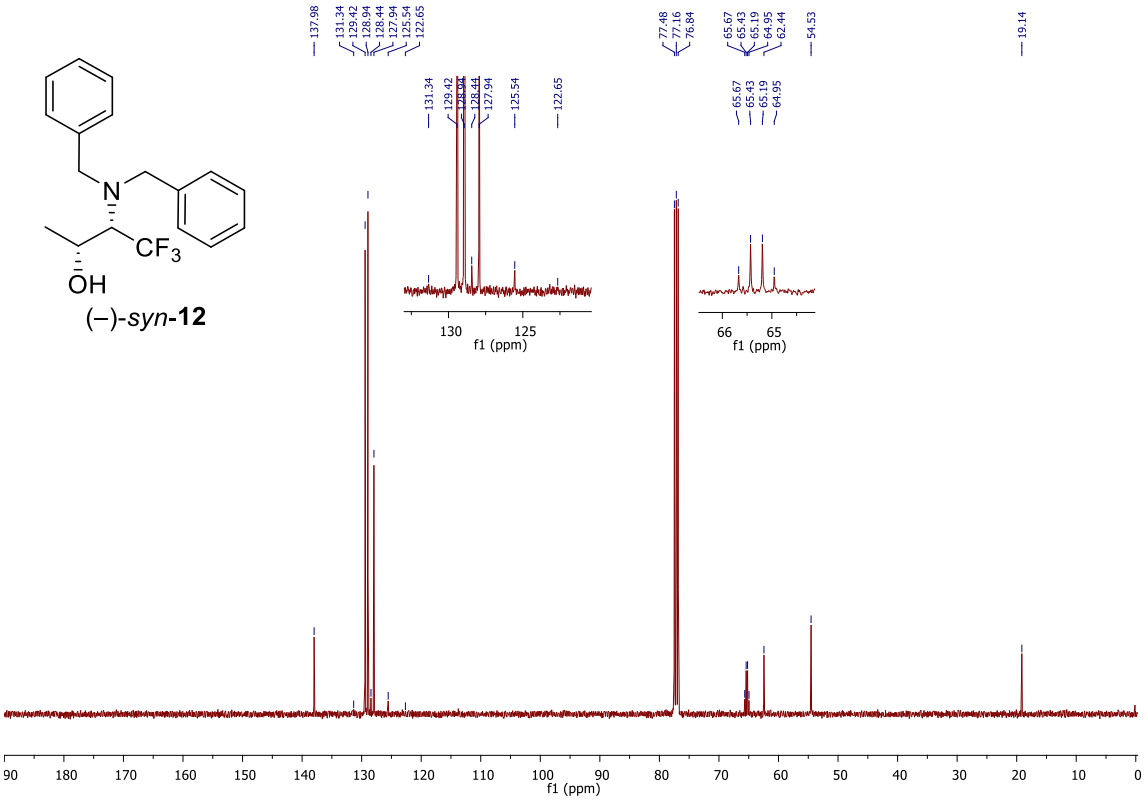
^{19}F NMR, 376 MHz, $CDCl_3$



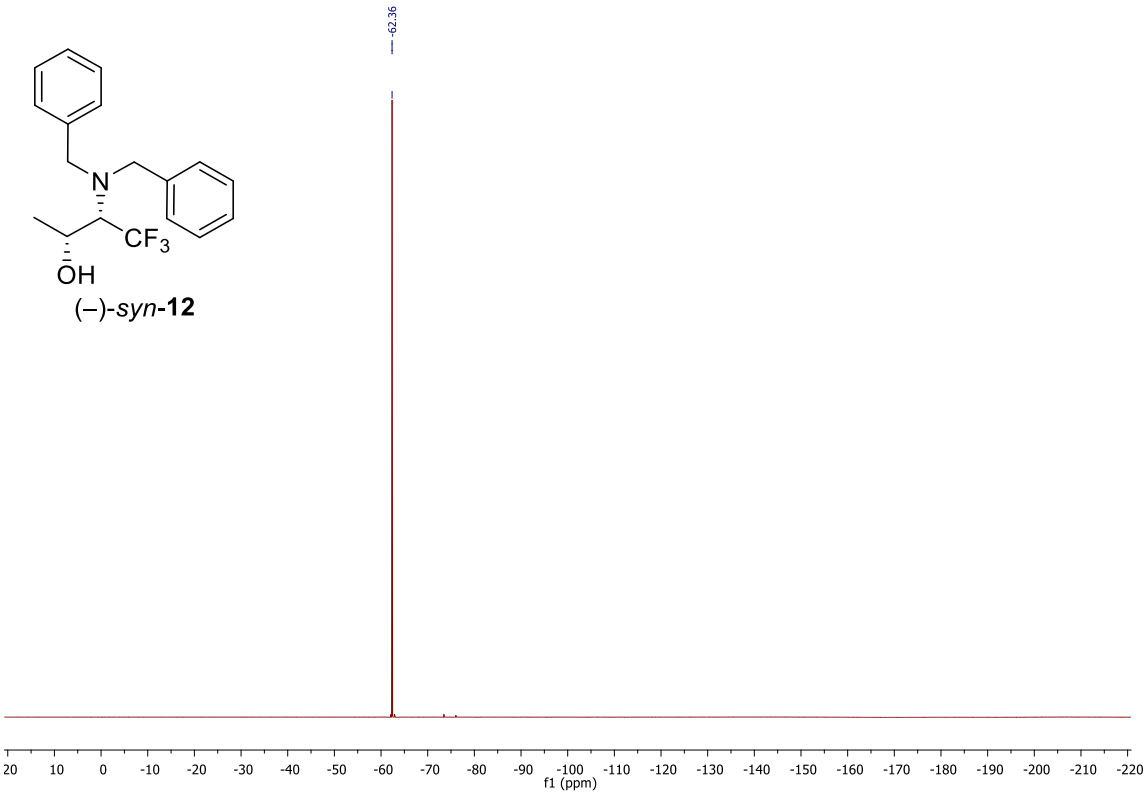
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

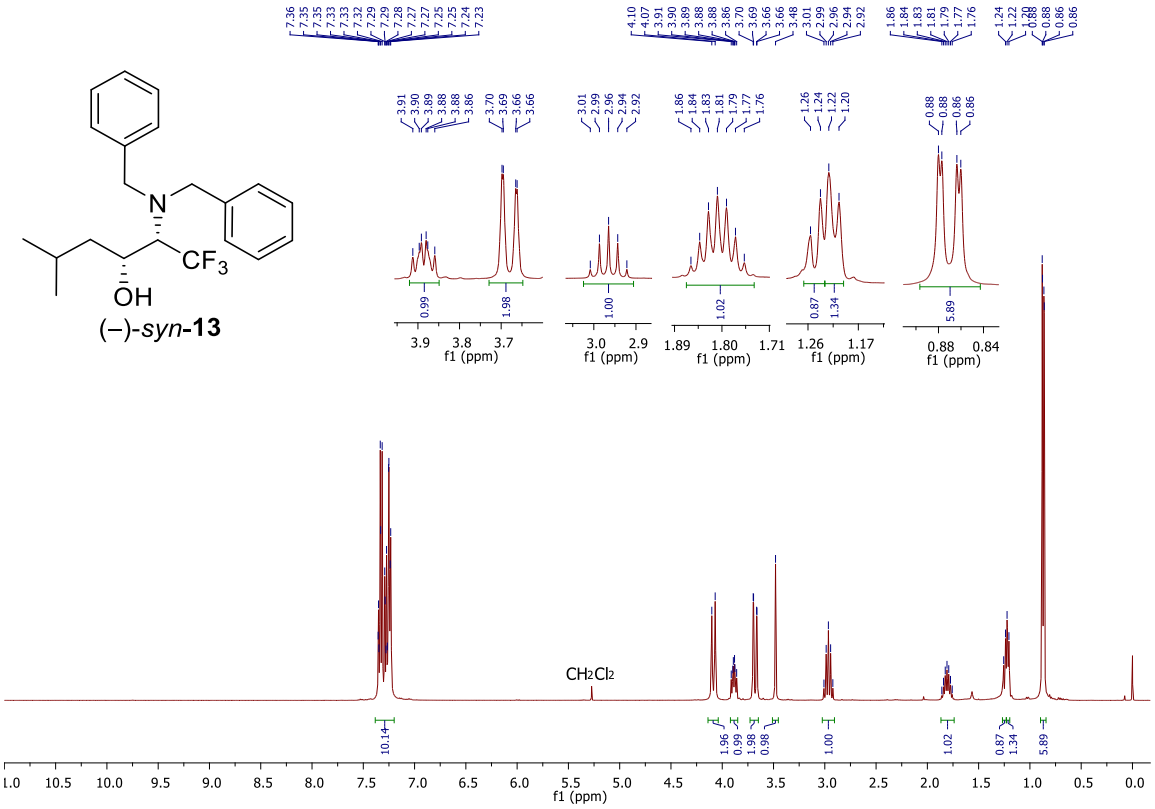


^{19}F NMR, 376 MHz, $CDCl_3$

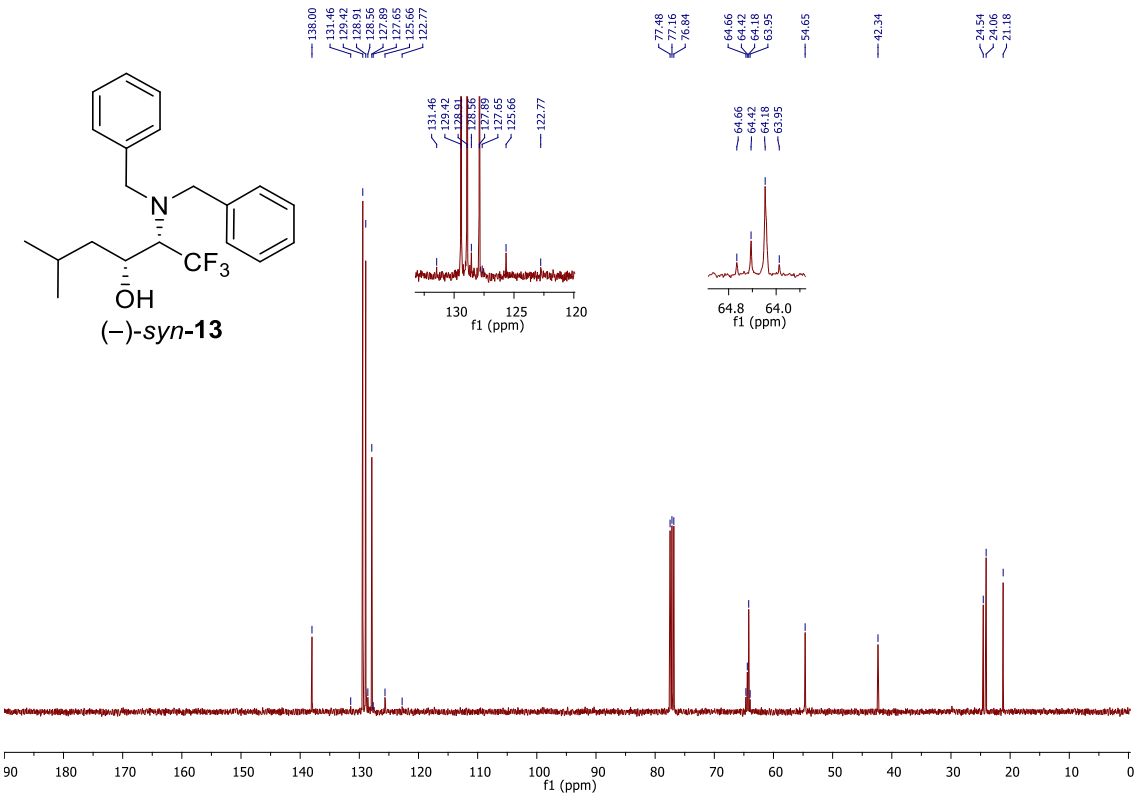


(–)-*syn*-**12**

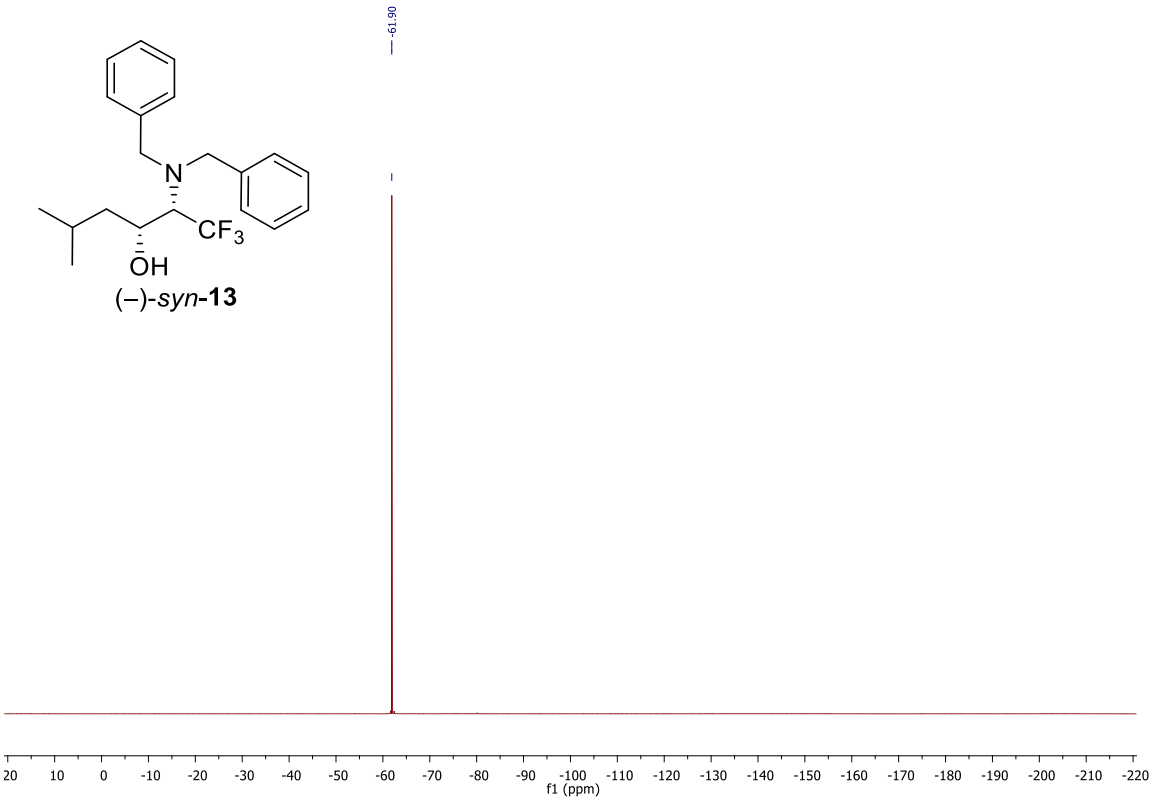
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

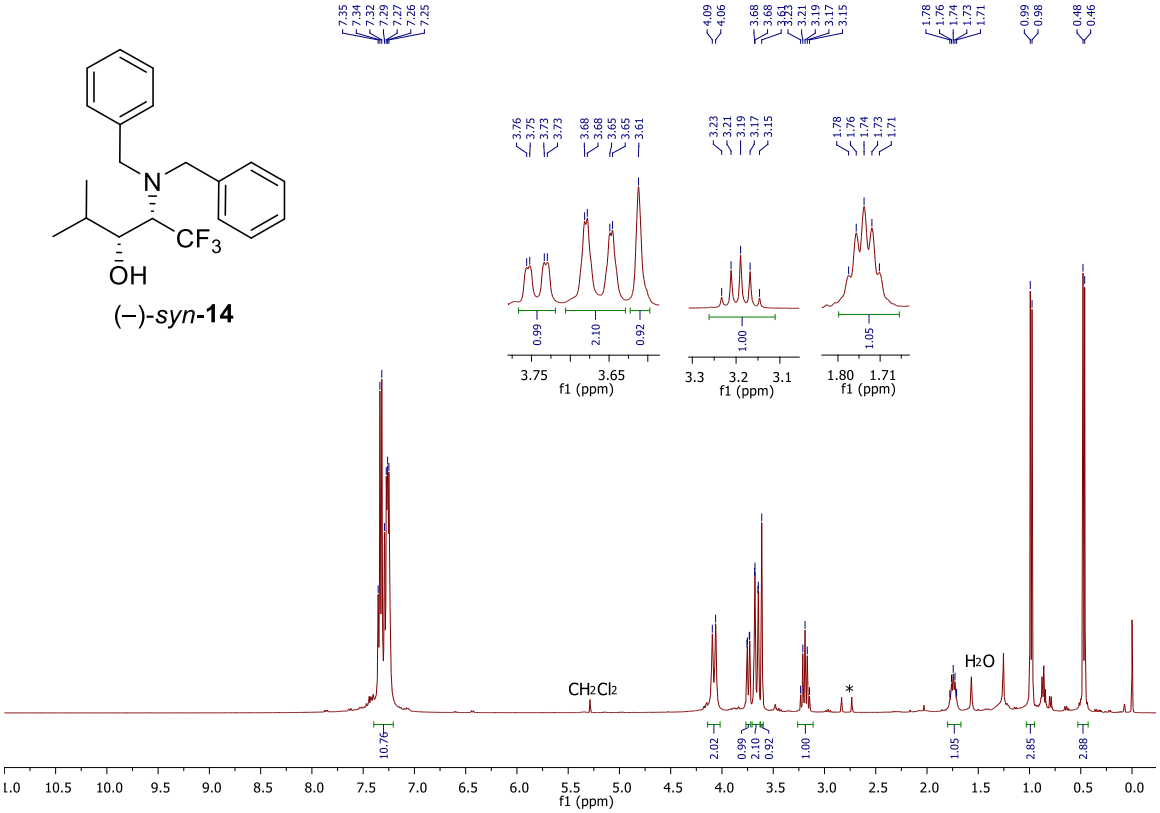


^{19}F NMR, 376 MHz, $CDCl_3$

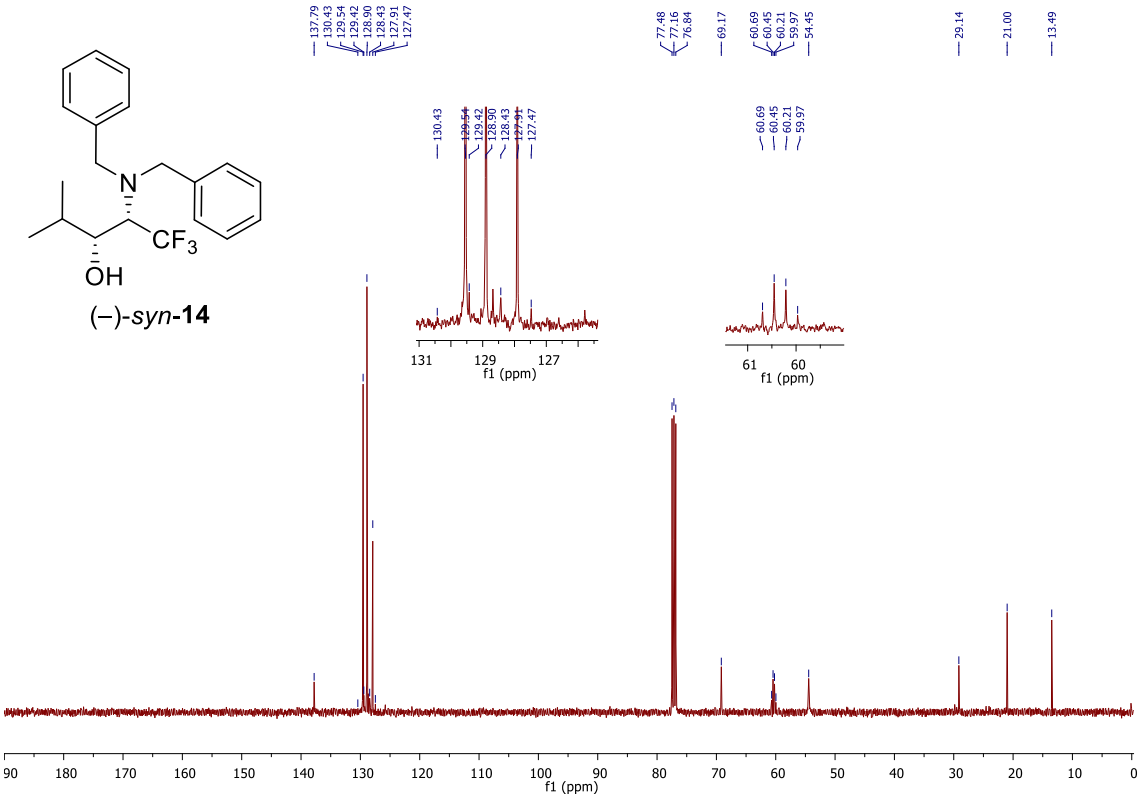


(–)-*syn*-**13**

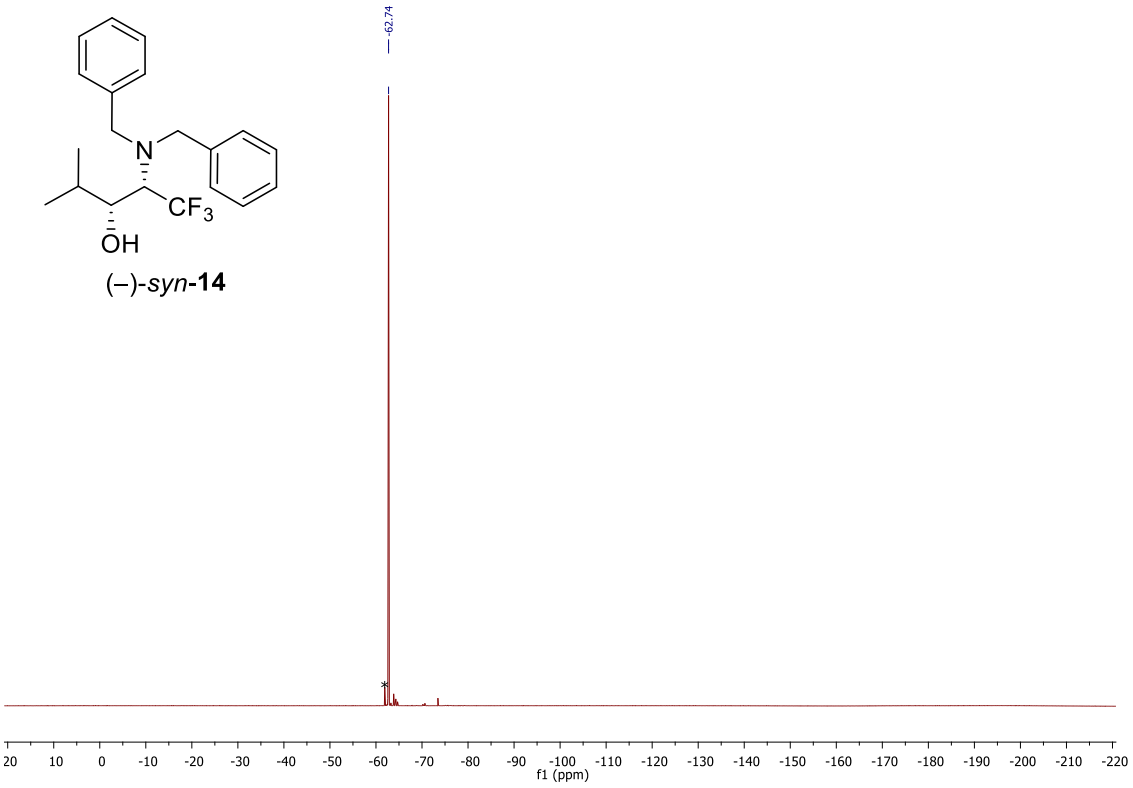
^{1}H NMR, 400 MHz, $CDCl_3$ [contains one impurity (*)]



^{13}C NMR, 100 MHz, $CDCl_3$

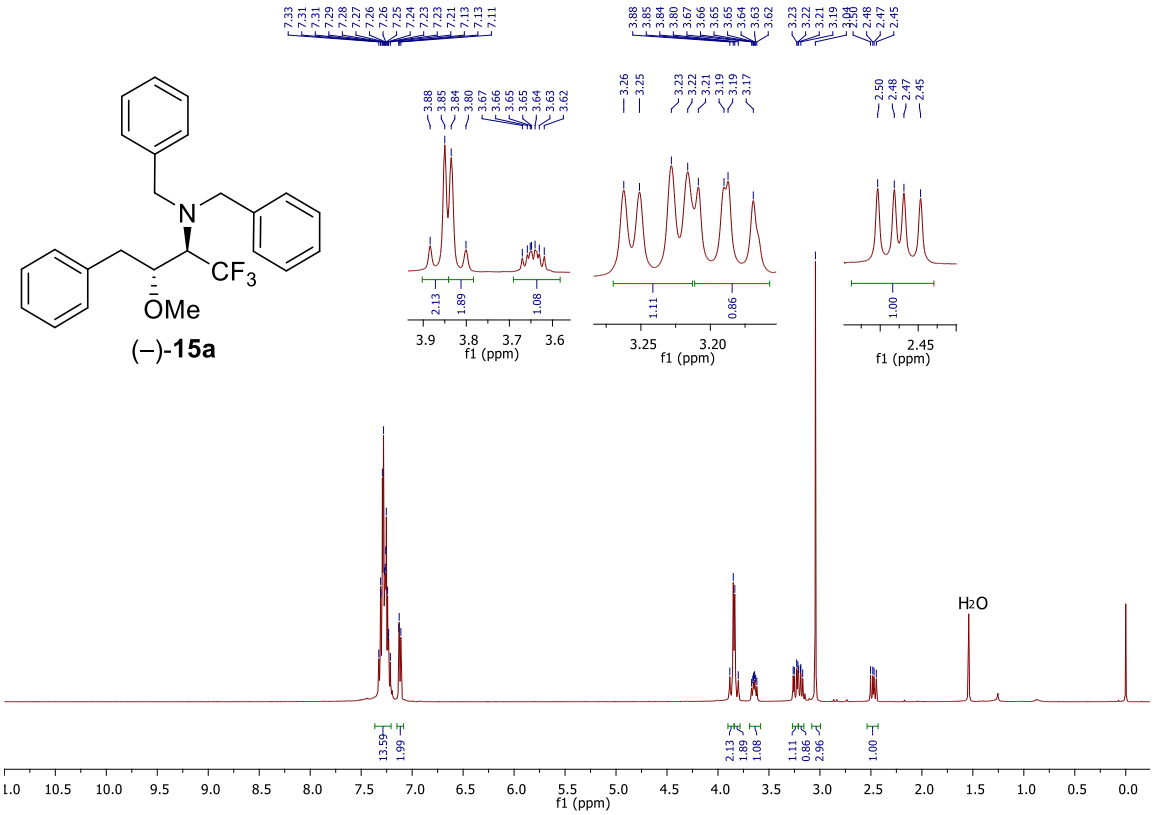


^{19}F NMR, 376 MHz, $CDCl_3$ [contains some impurities (*)]

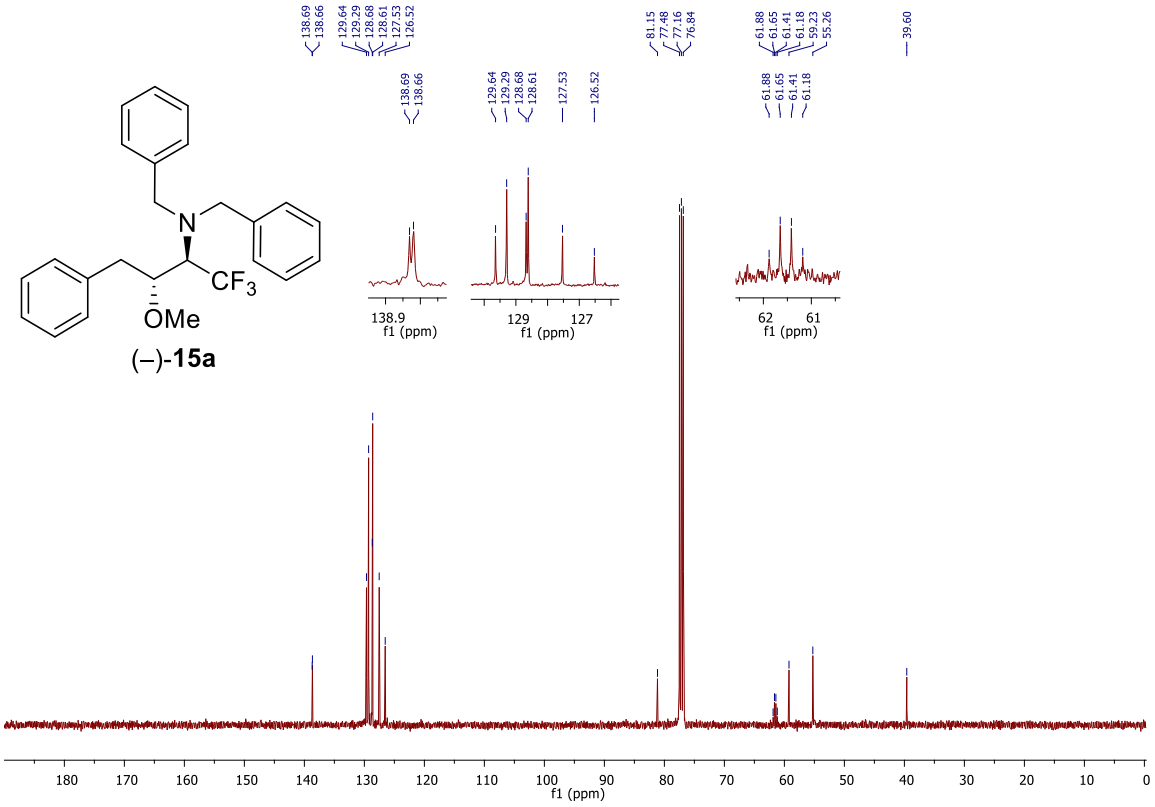


(–)-*syn*-**14**

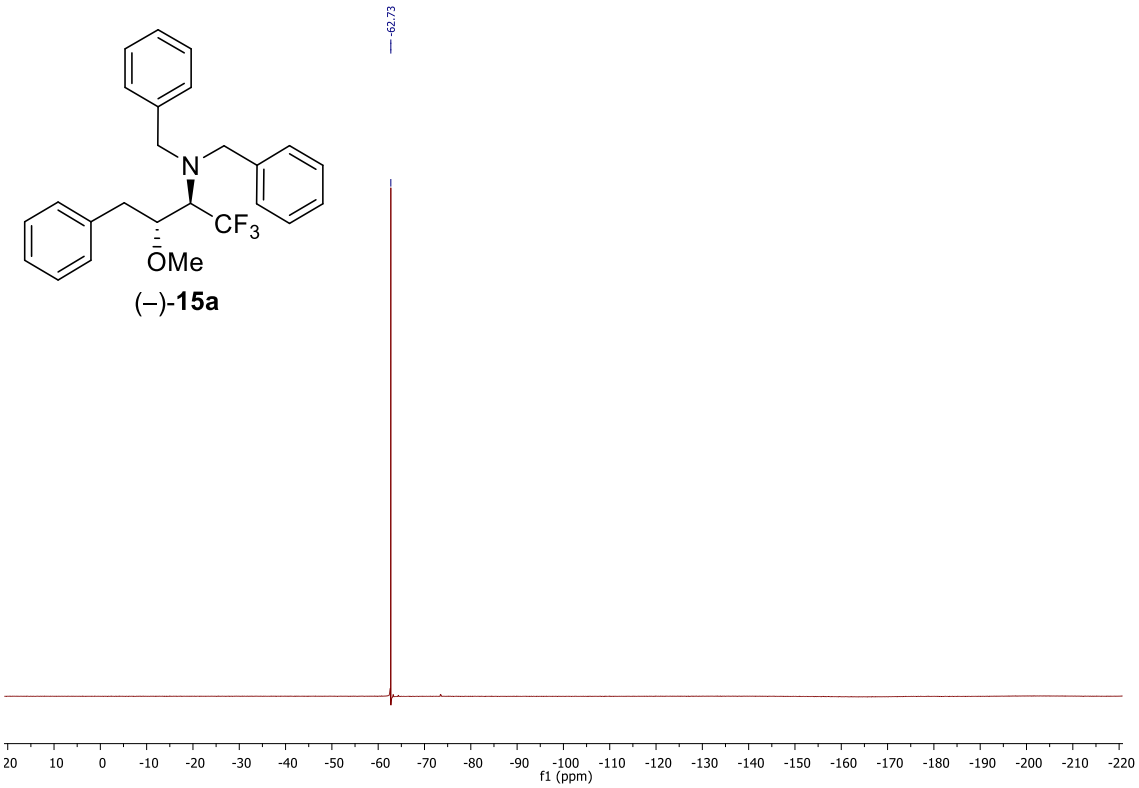
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

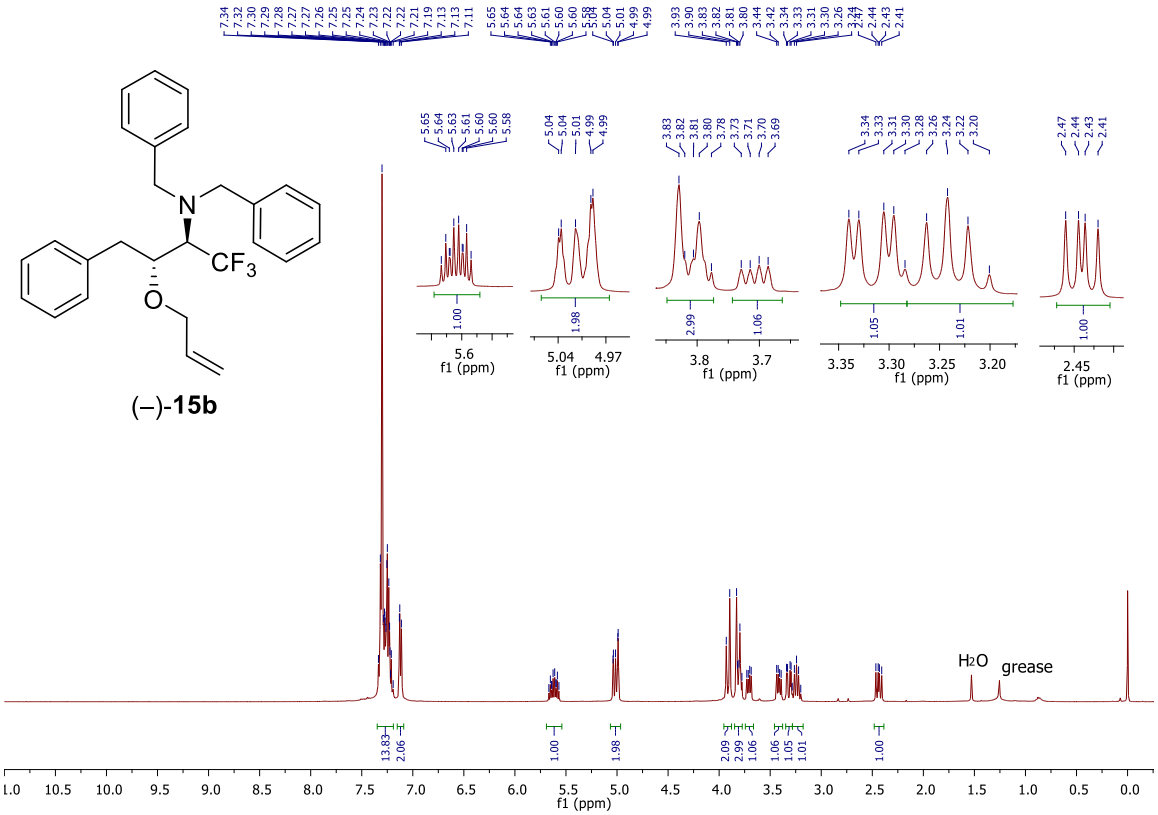


^{19}F NMR, 376 MHz, $CDCl_3$

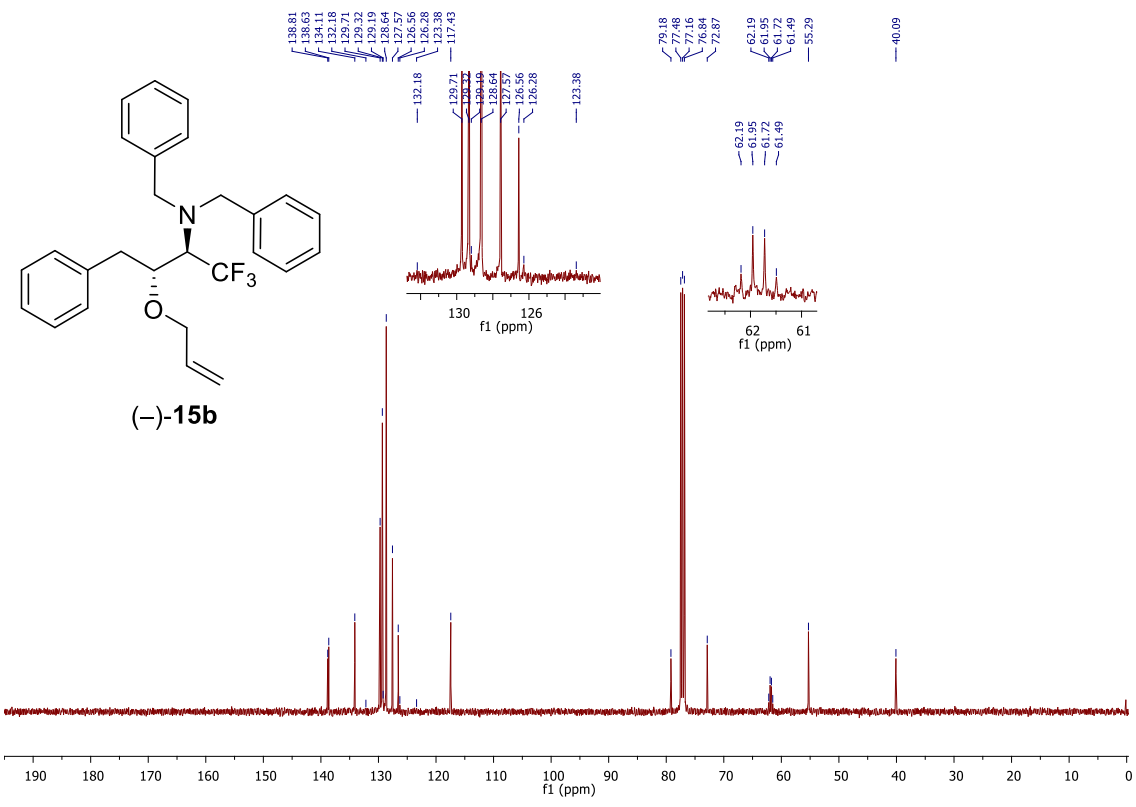


(–)-**15a**

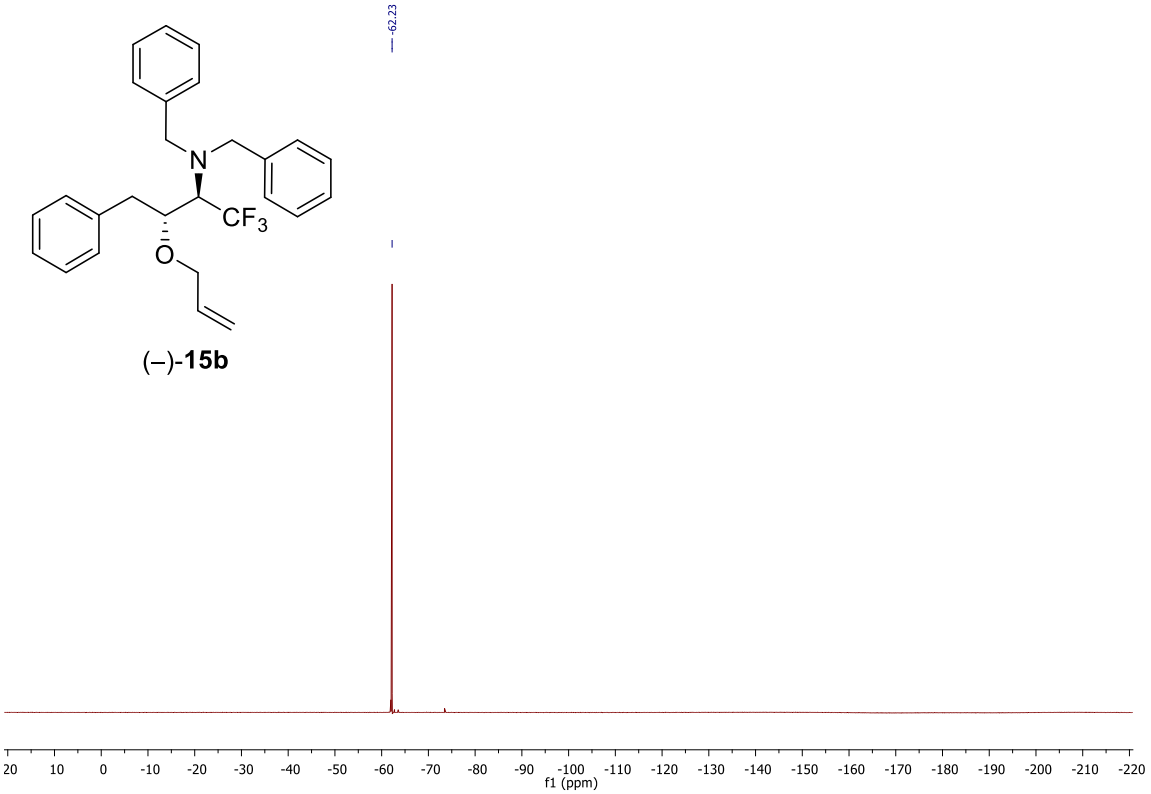
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

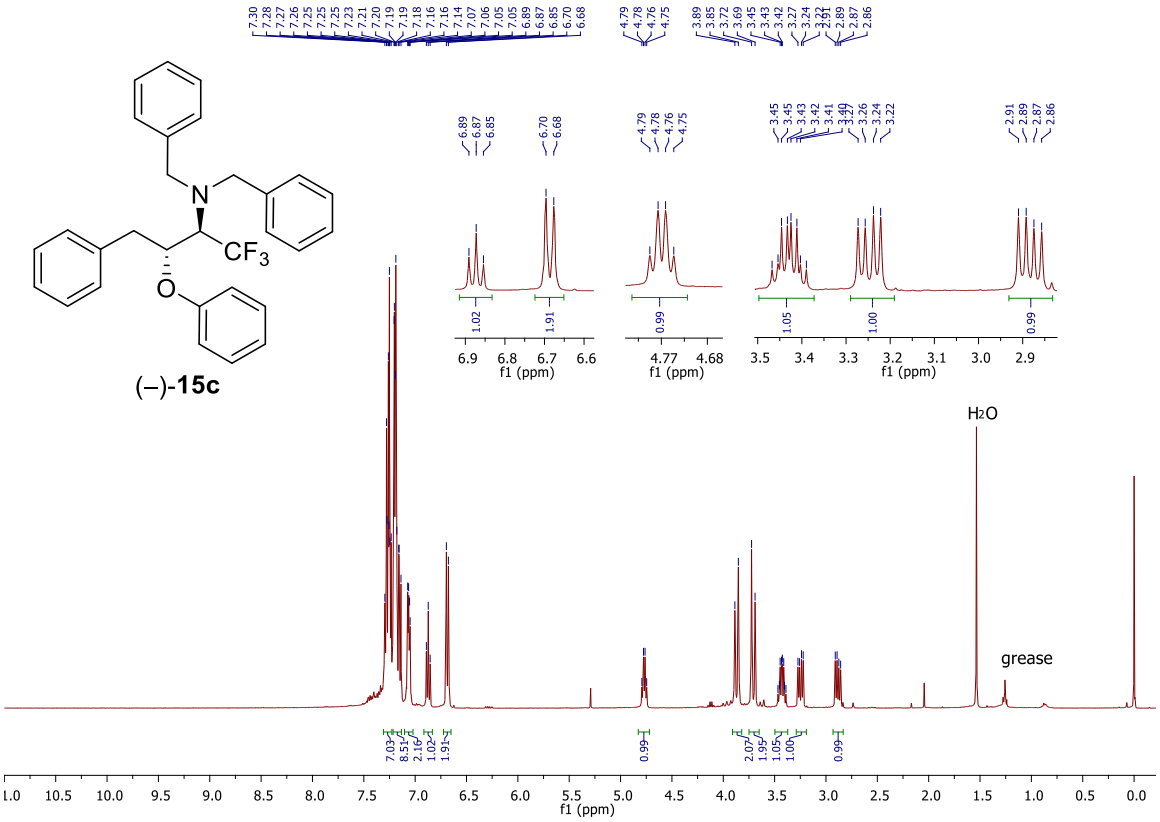


^{19}F NMR, 376 MHz, $CDCl_3$

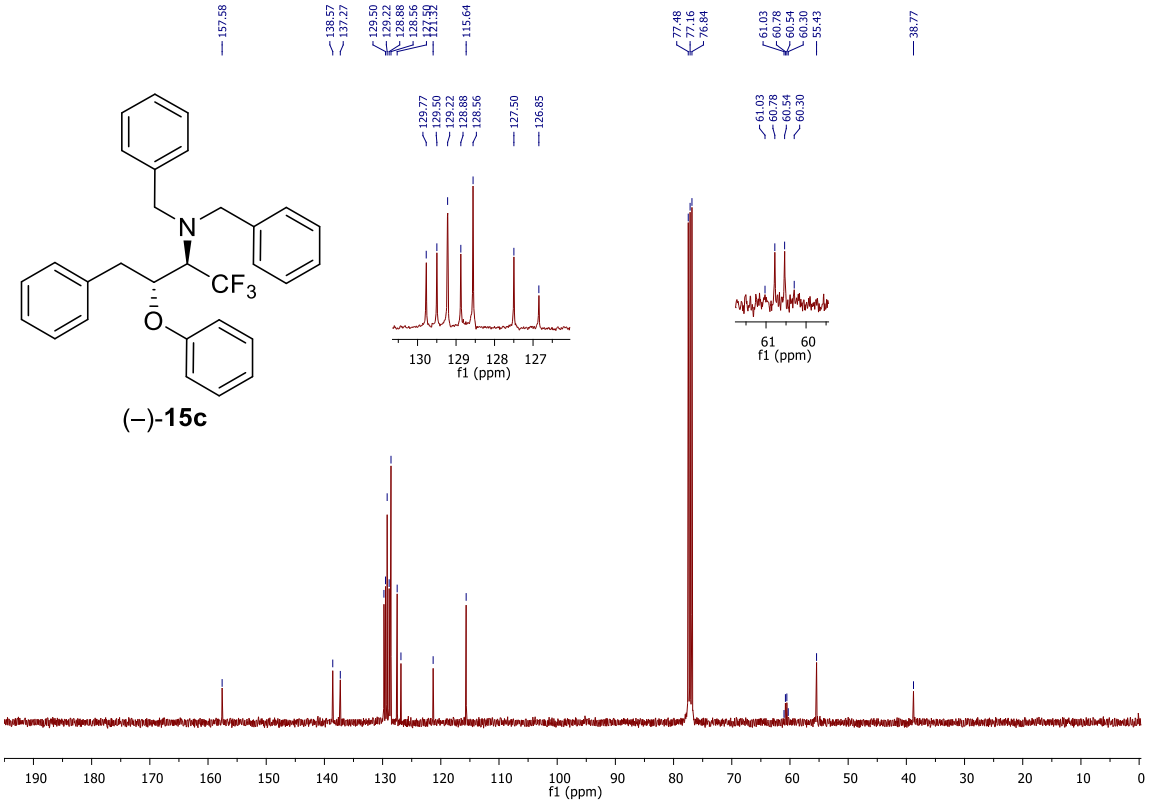


(–)-**15b**

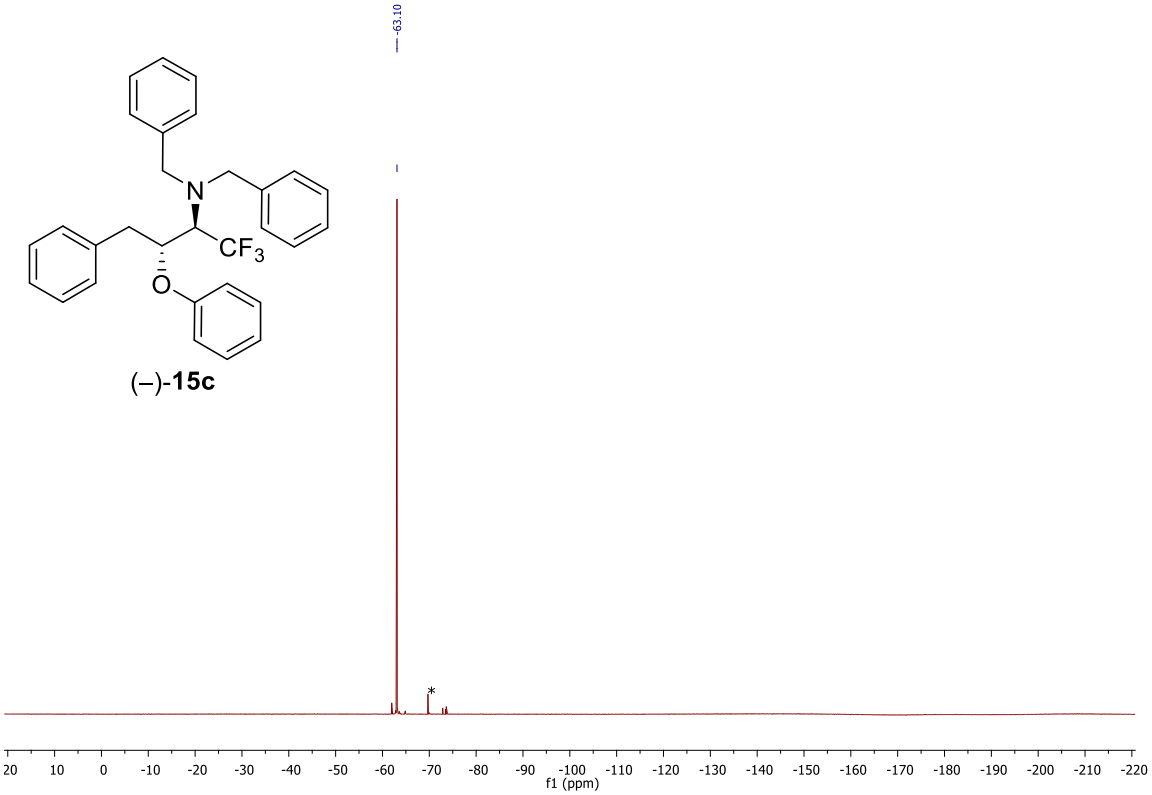
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

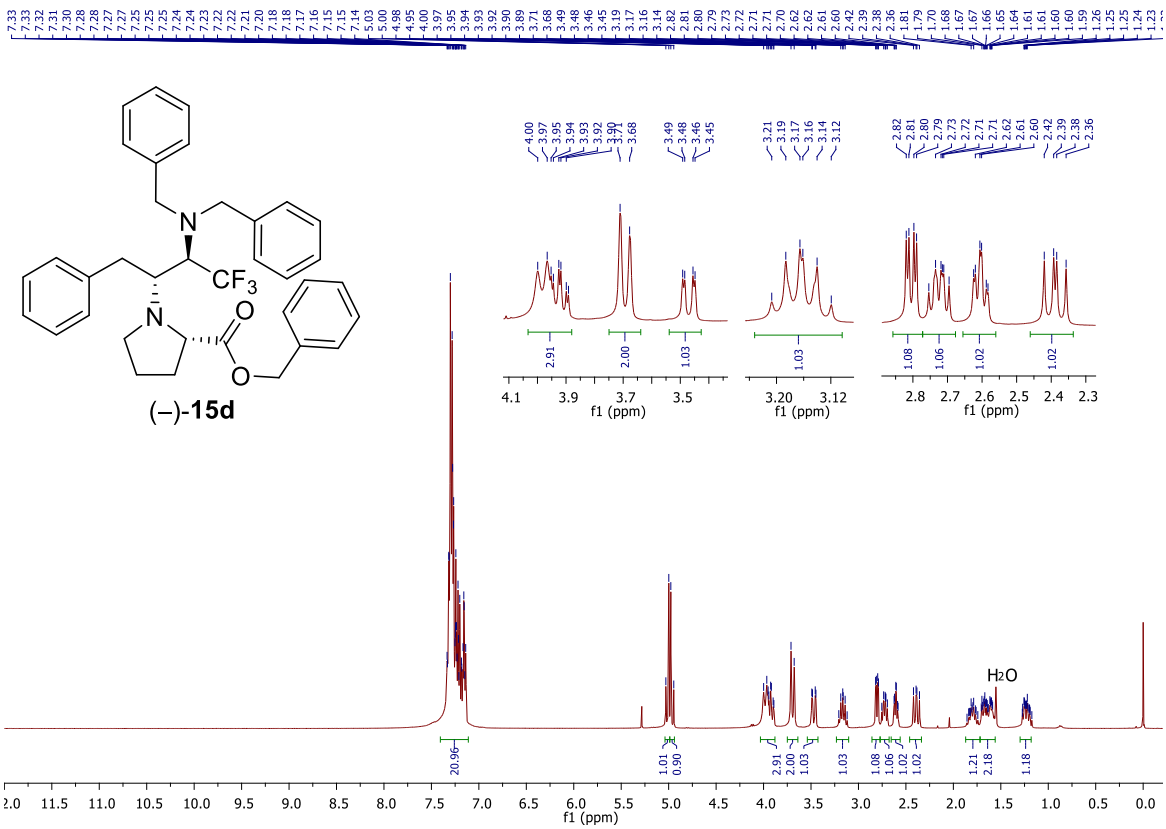


^{19}F NMR, 376 MHz, $CDCl_3$ [contains some impurities (*)]

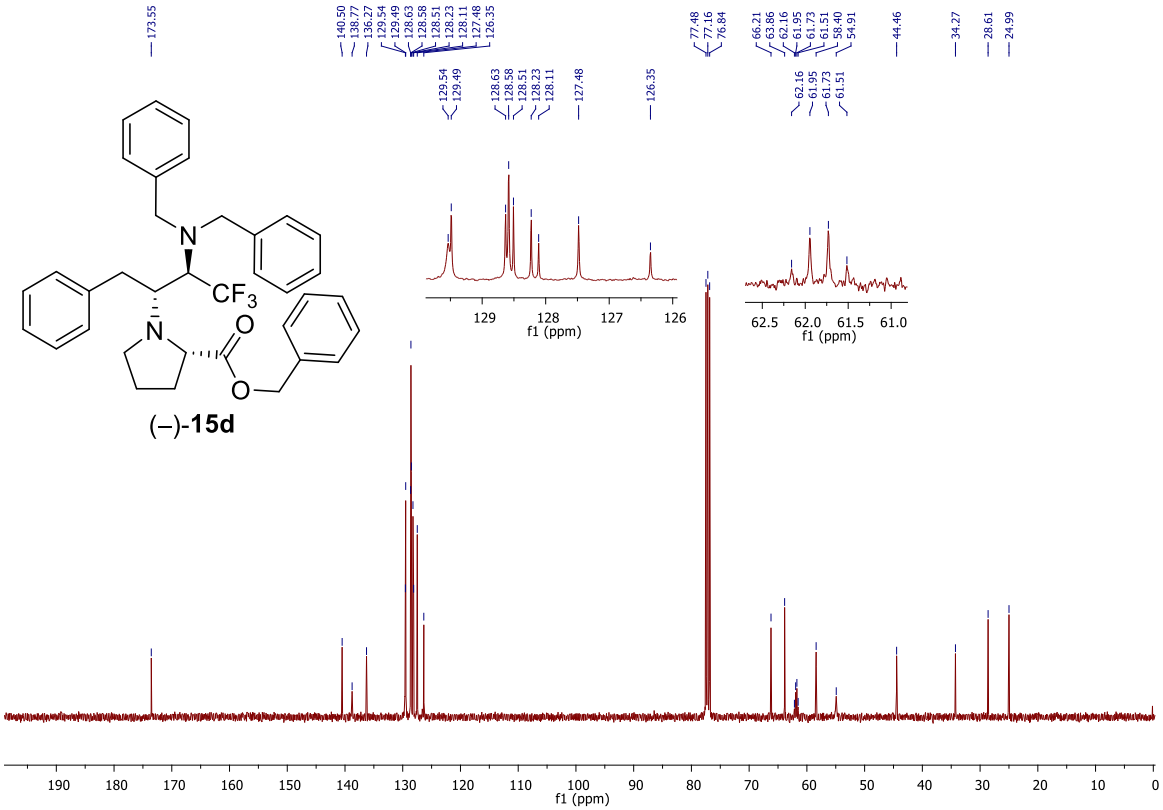


(–)-**15c**

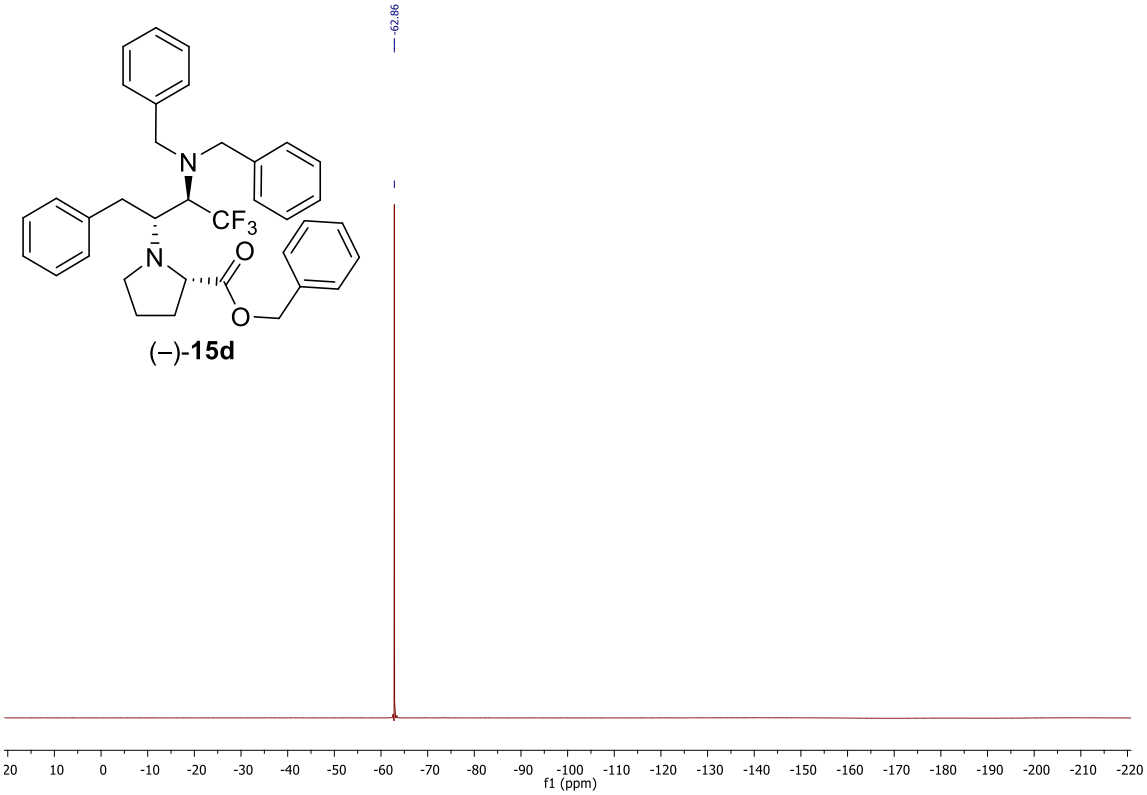
^{1}H NMR, 400 MHz, $CDCl_3$



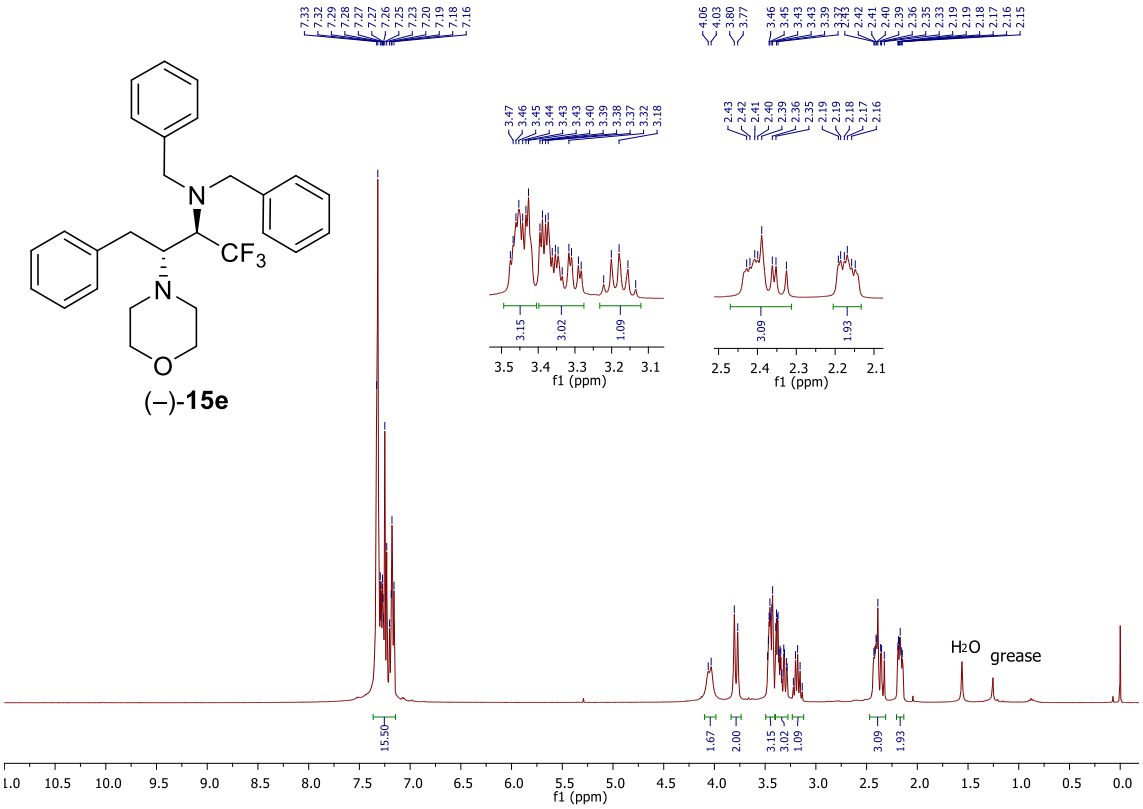
^{13}C NMR, 100 MHz, $CDCl_3$



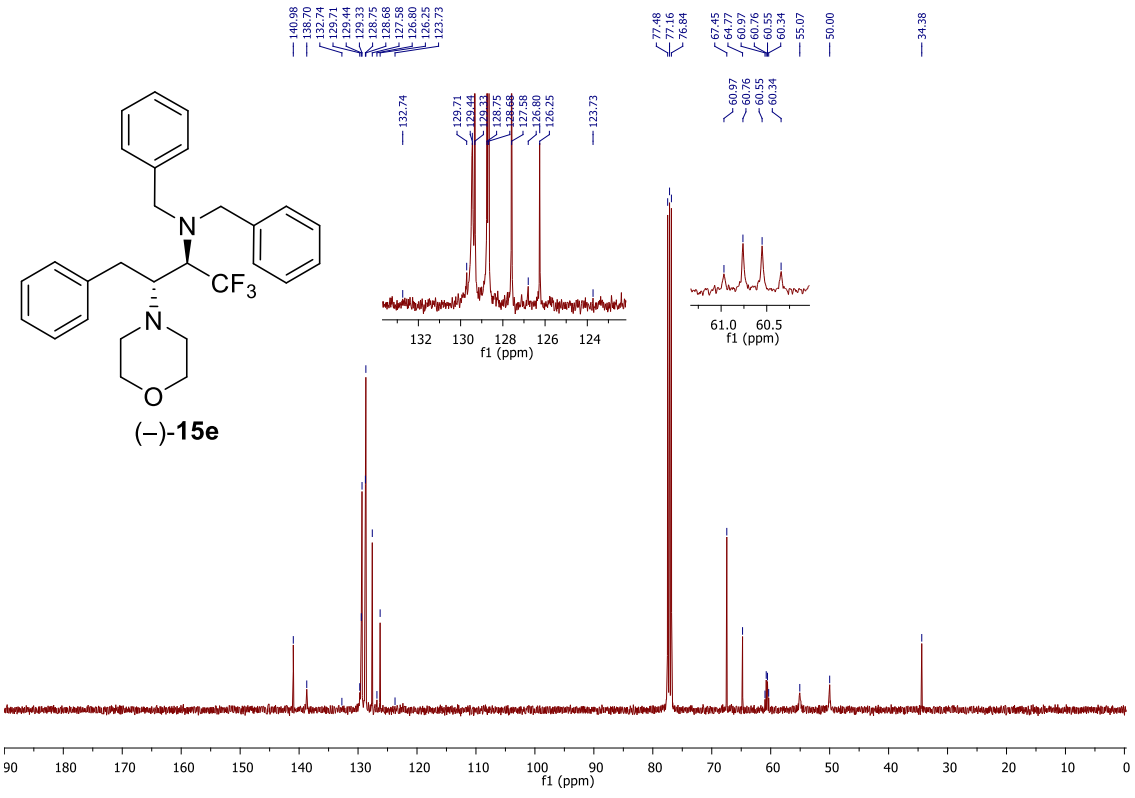
^{19}F NMR, 376 MHz, $CDCl_3$



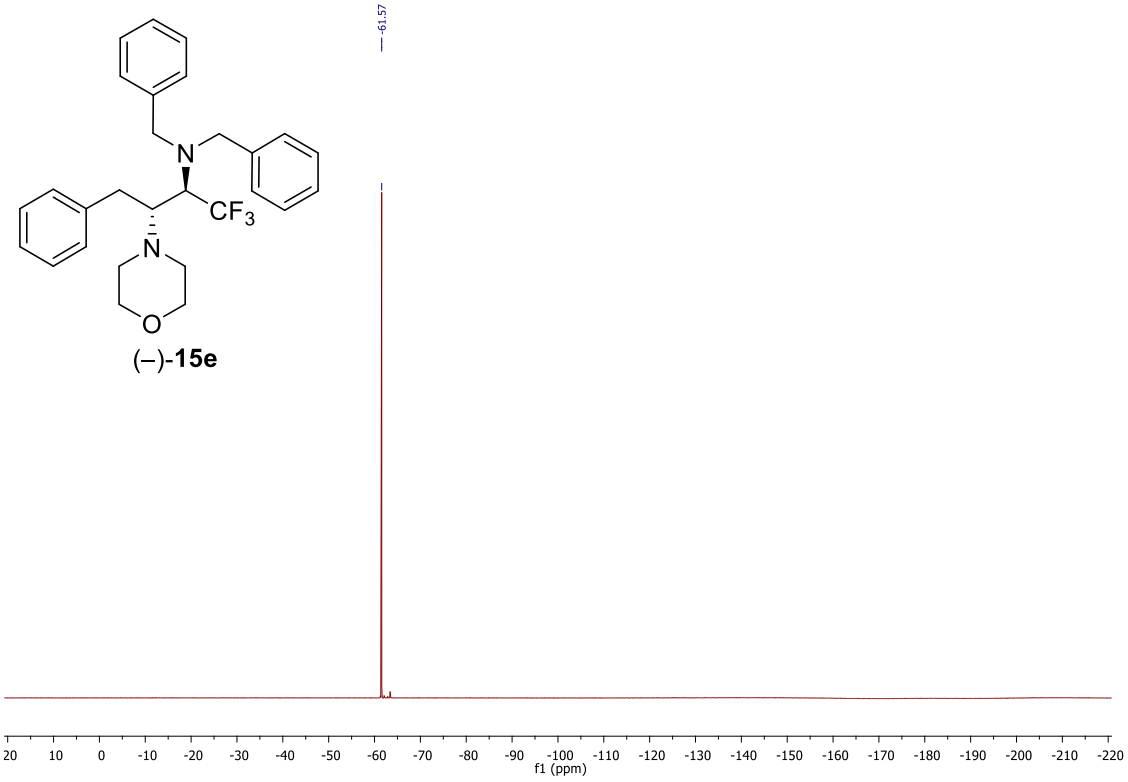
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

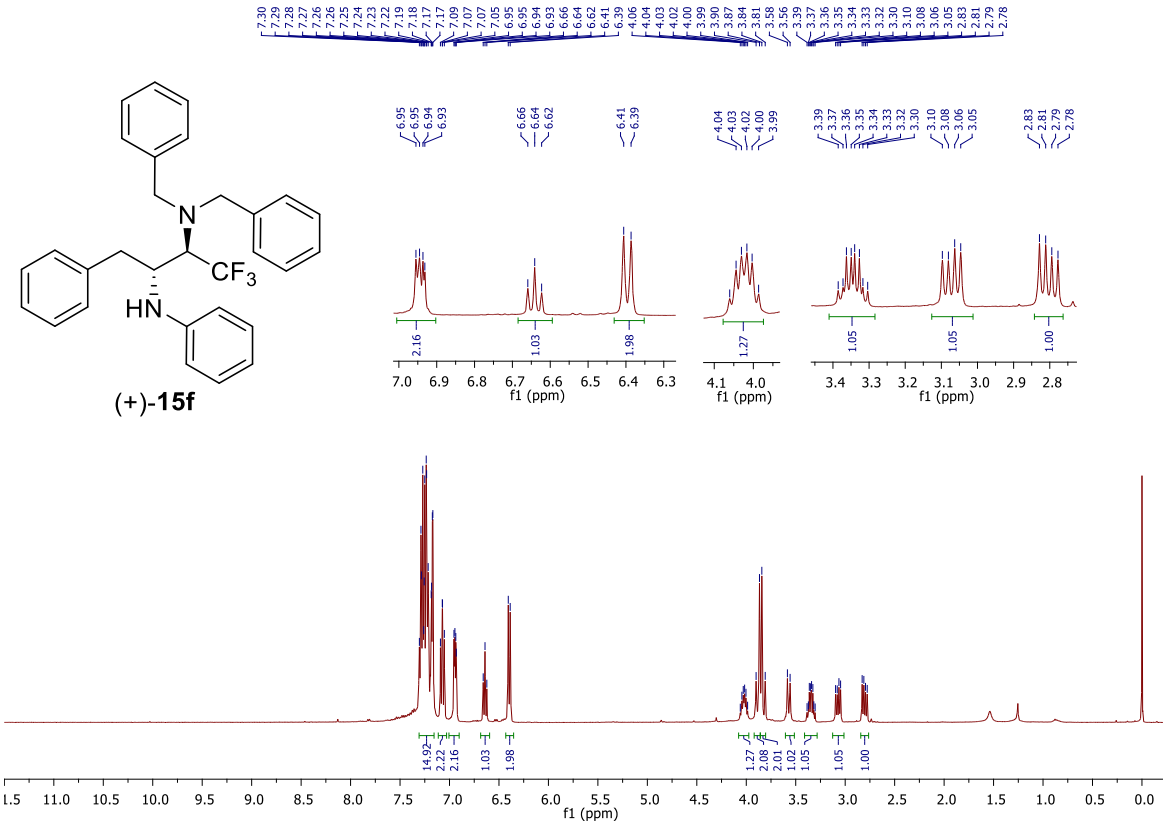


^{19}F NMR, 376 MHz, $CDCl_3$

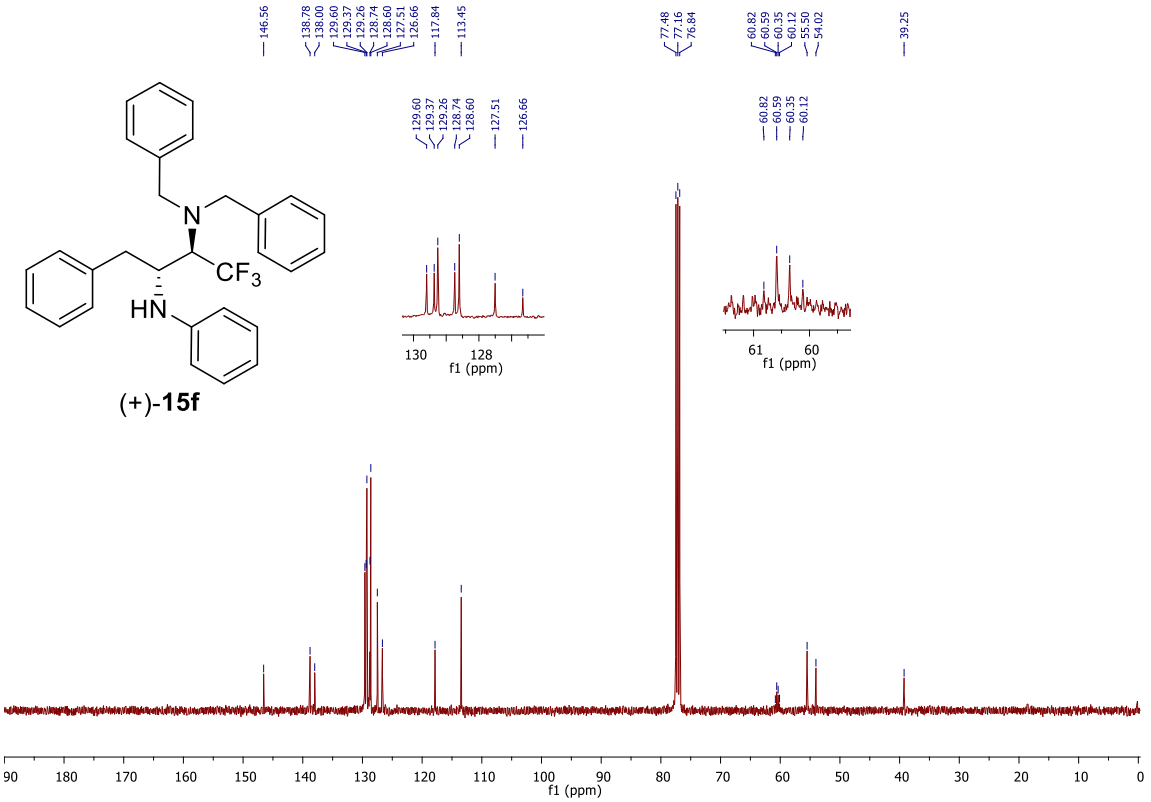


(–)-**15e**

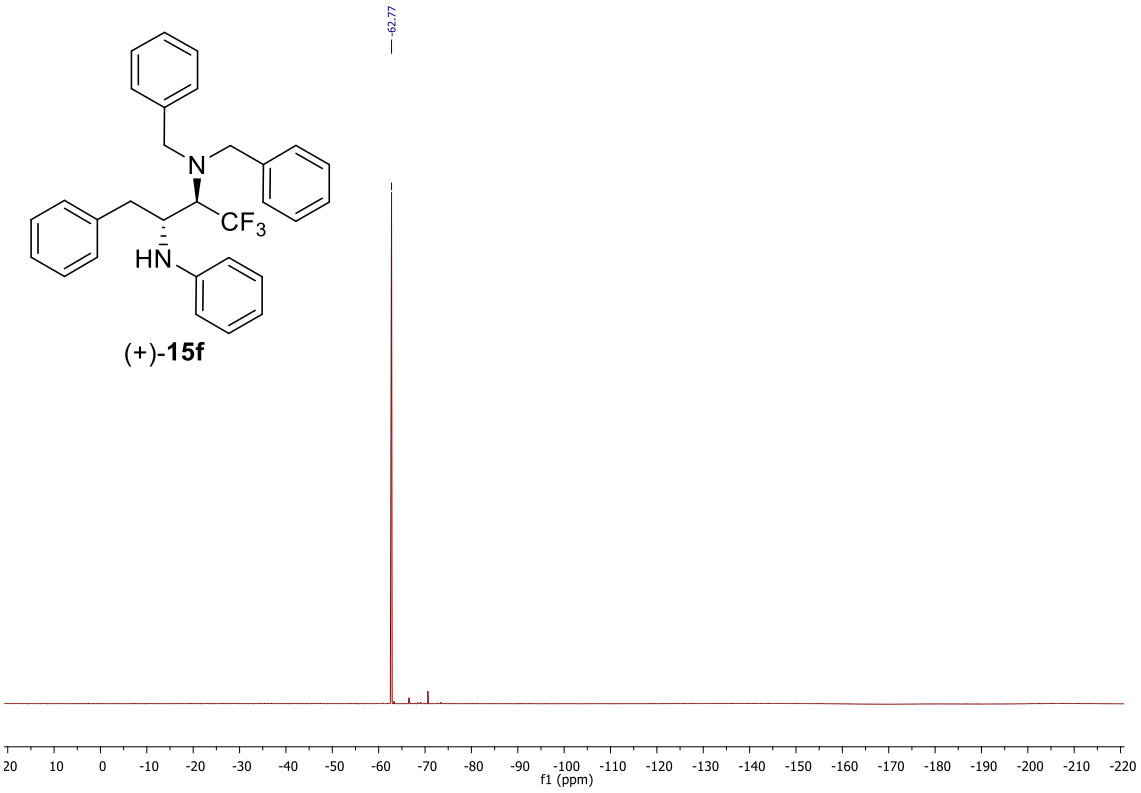
^{1}H NMR, 400 MHz, $CDCl_3$



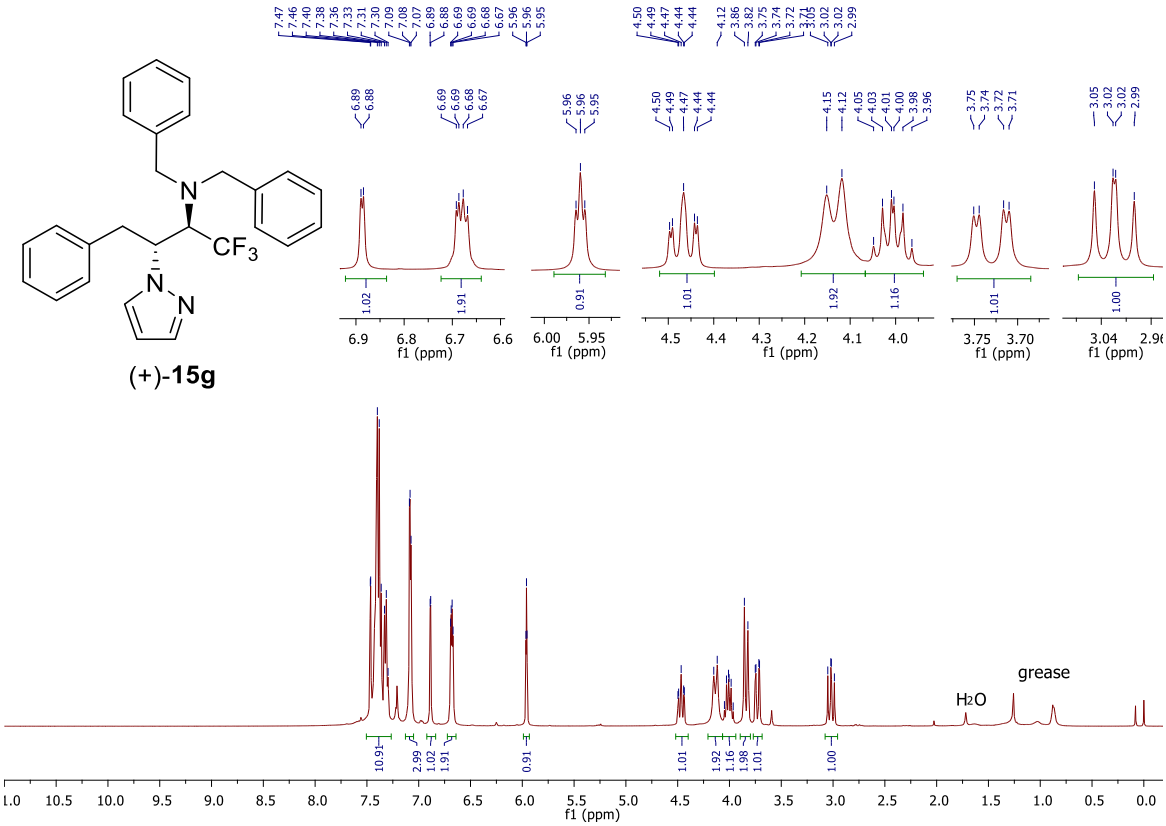
^{13}C NMR, 100 MHz, $CDCl_3$



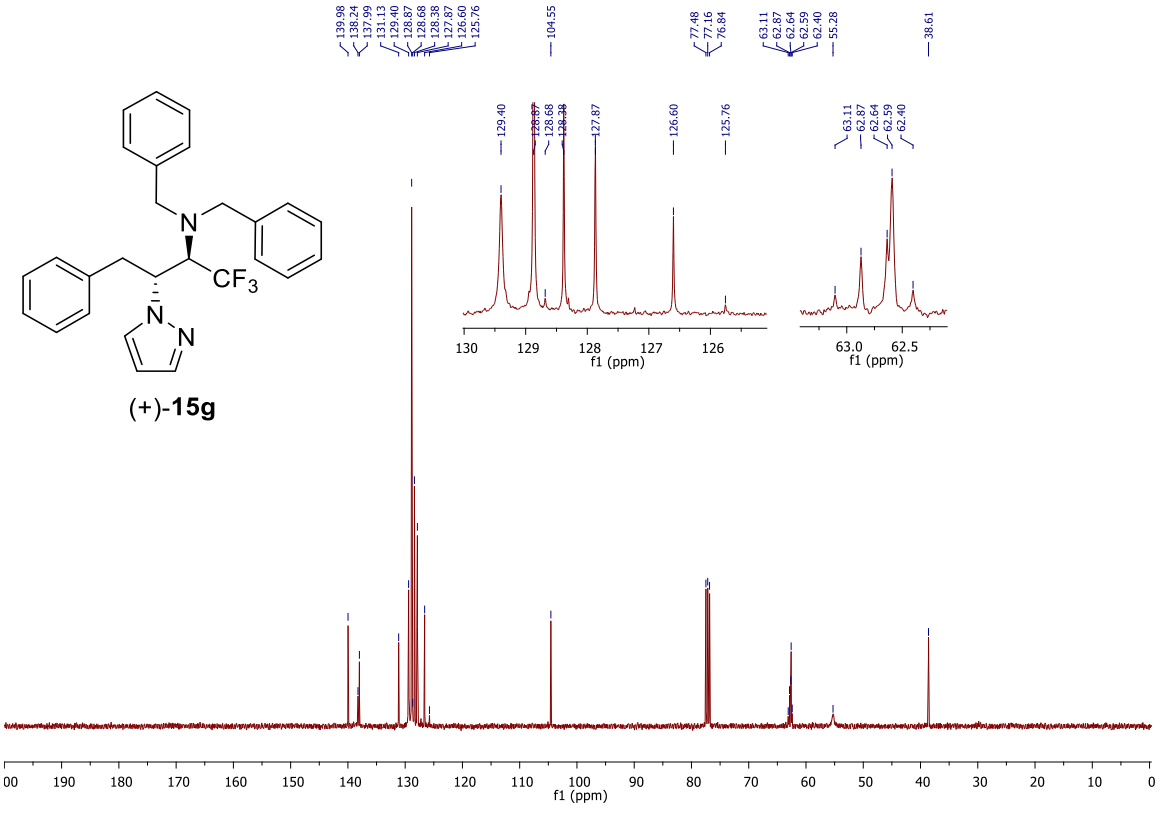
^{19}F NMR, 376 MHz, $CDCl_3$



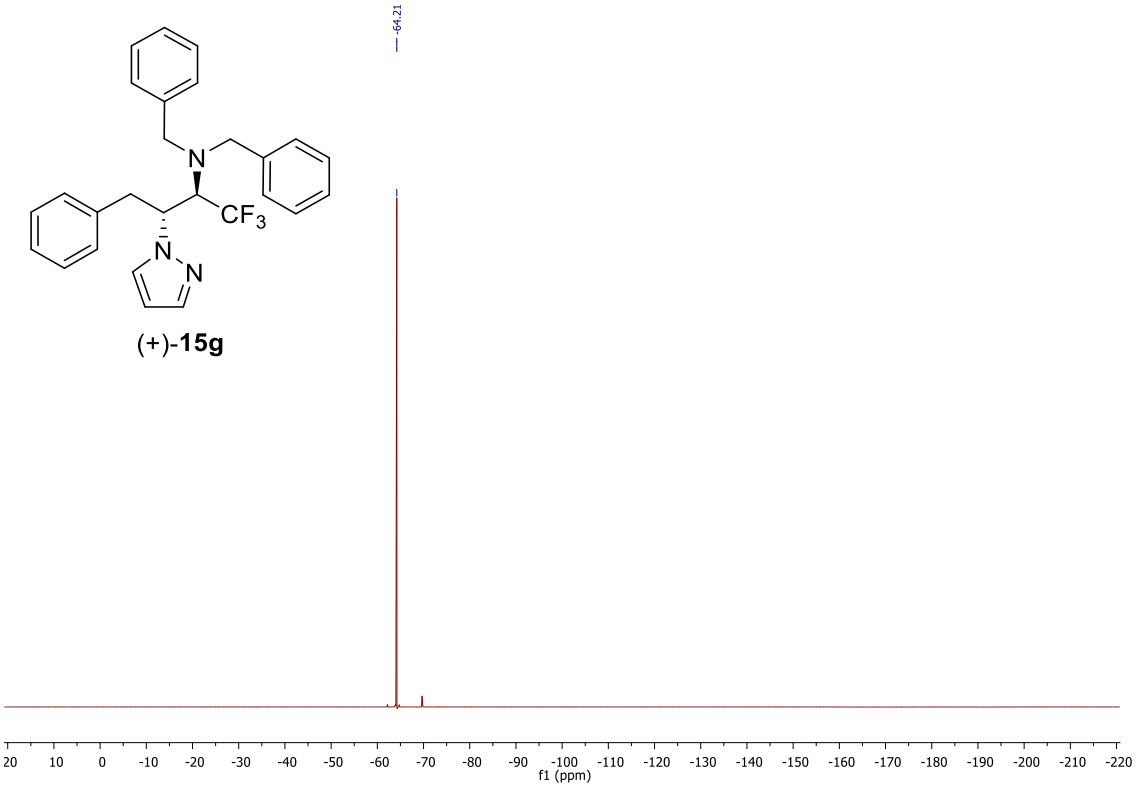
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

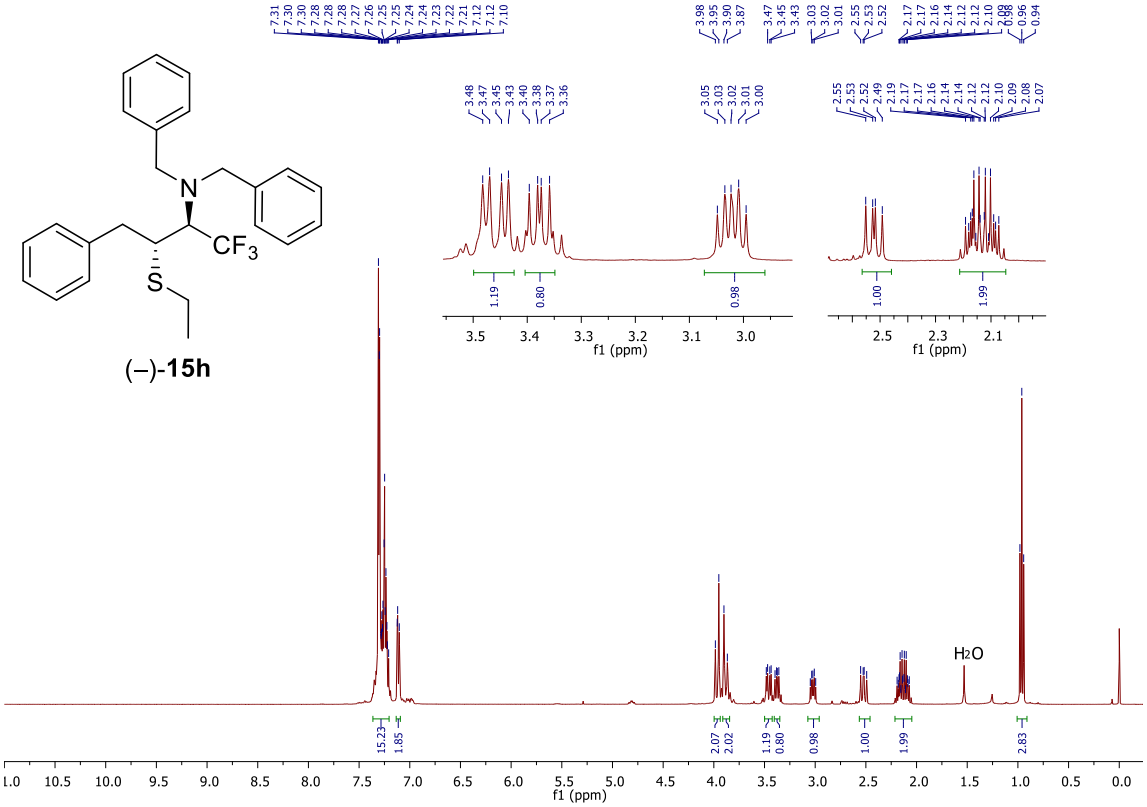


^{19}F NMR, 376 MHz, $CDCl_3$

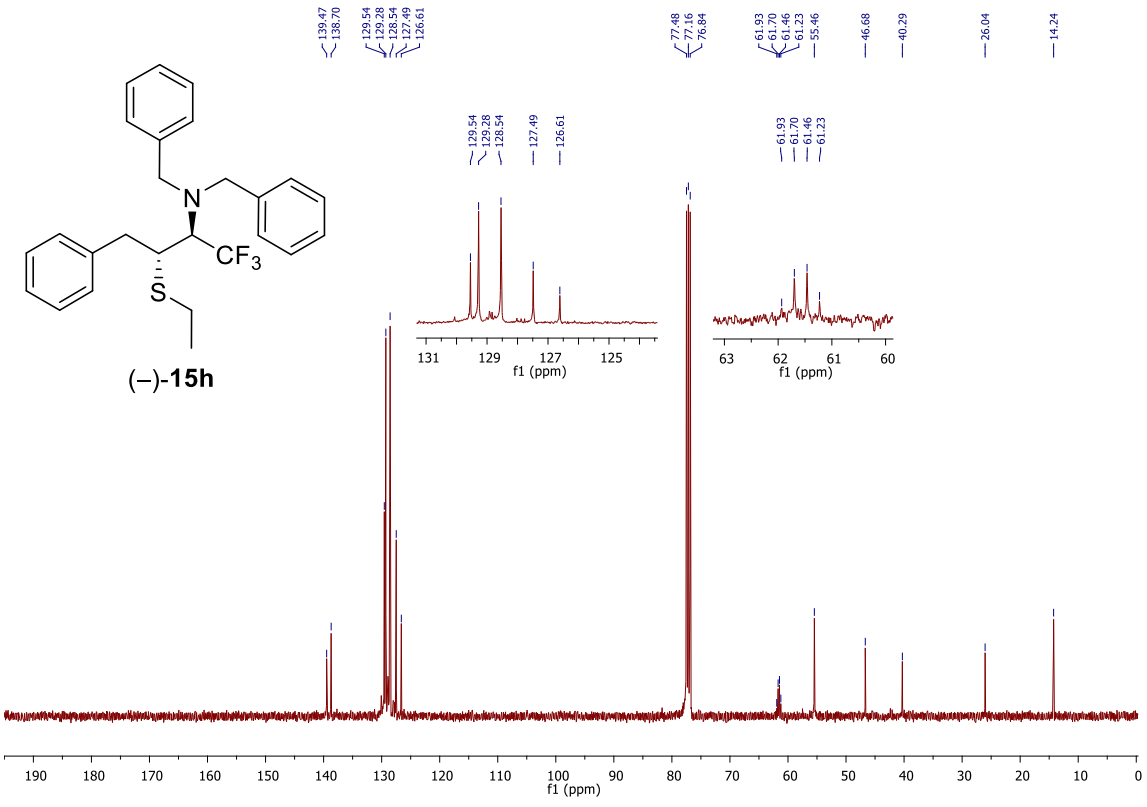


(+)-**15g**

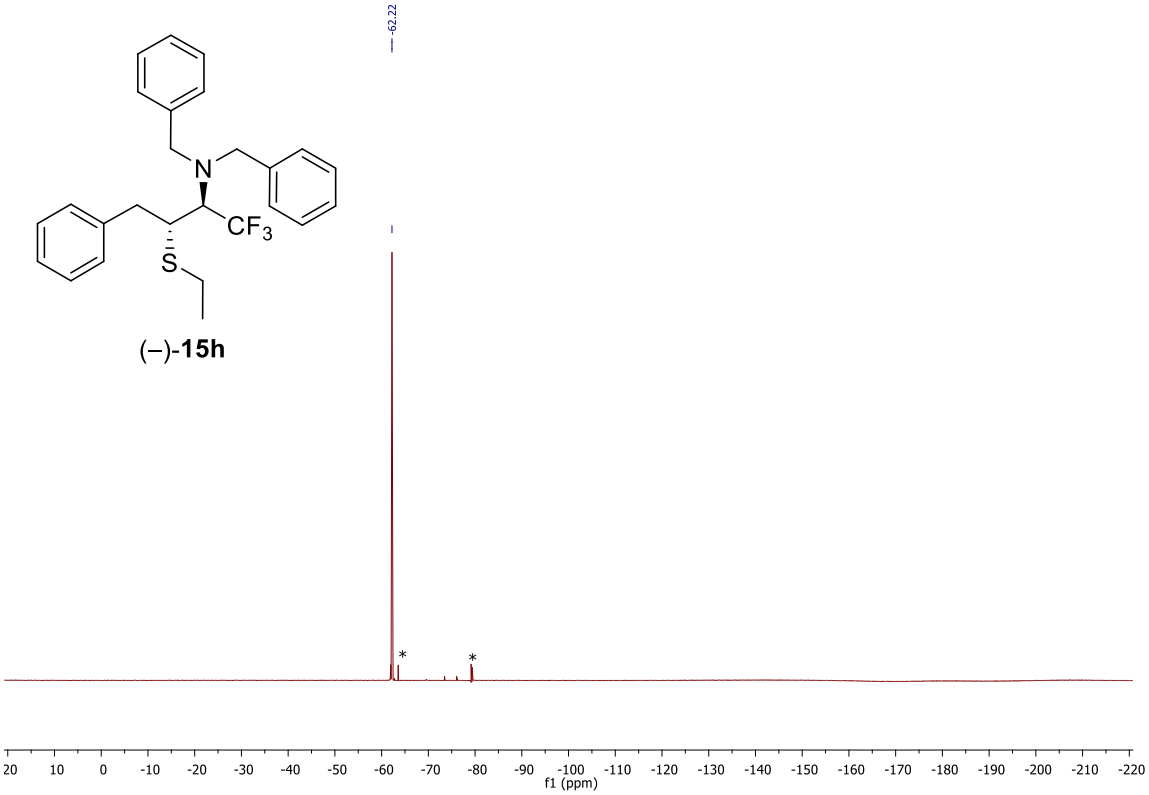
^{1}H NMR, 400 MHz, $CDCl_3$



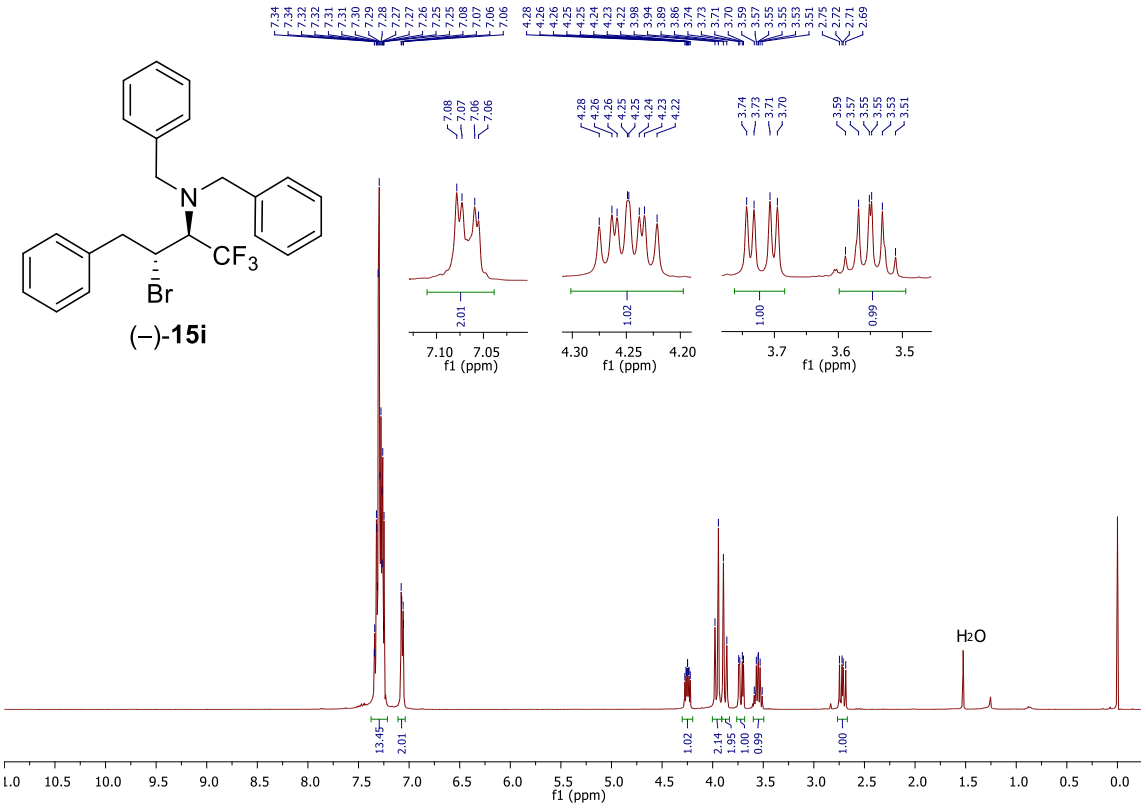
^{13}C NMR, 100 MHz, $CDCl_3$



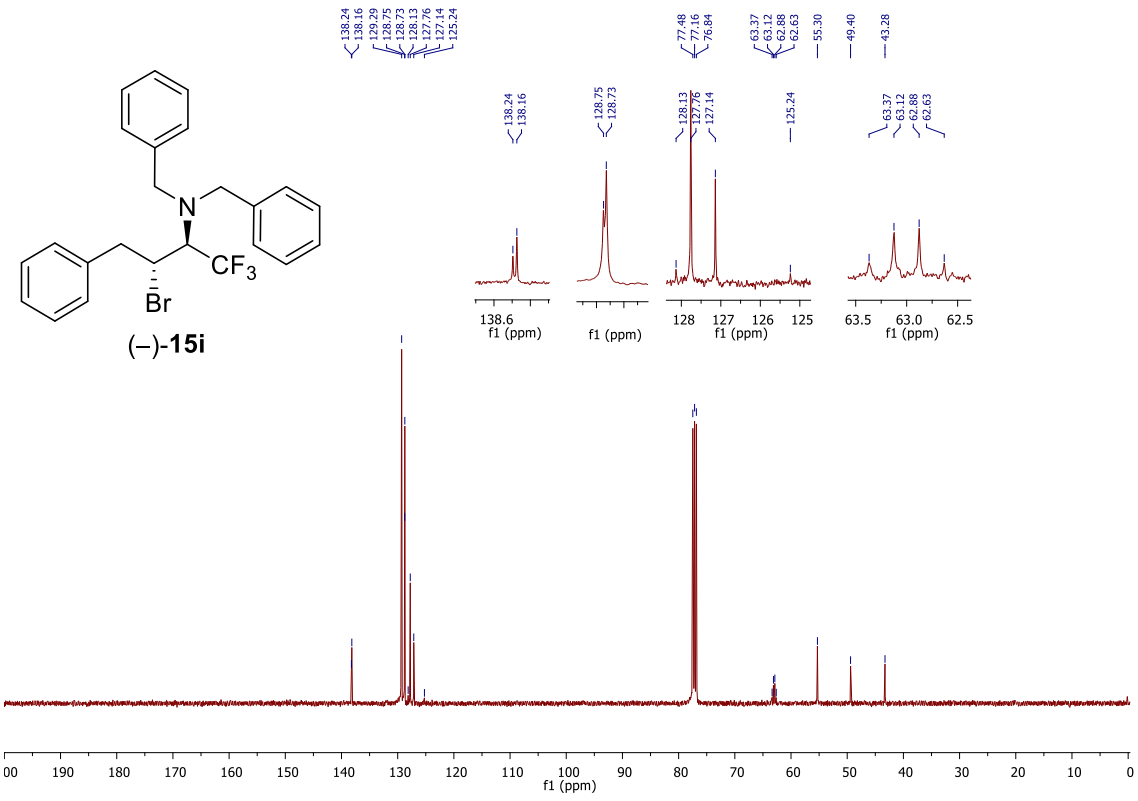
^{19}F NMR, 376 MHz, $CDCl_3$ [contains some impurities (*)]



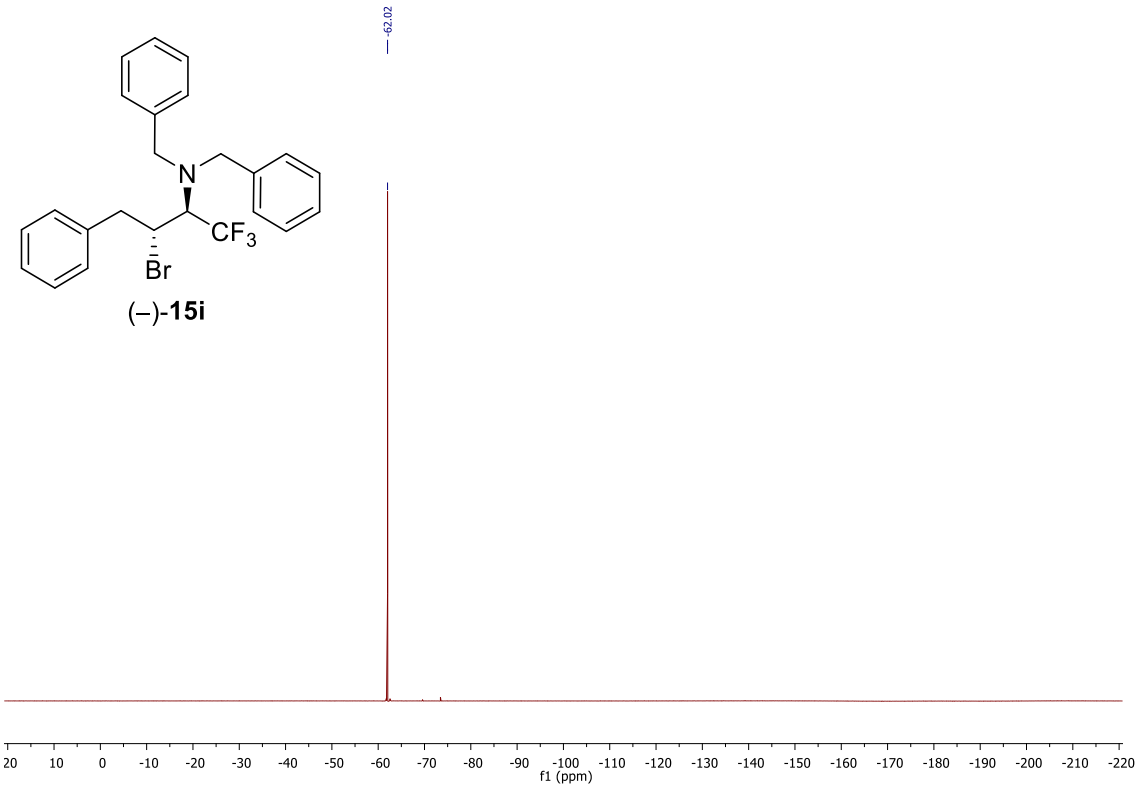
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

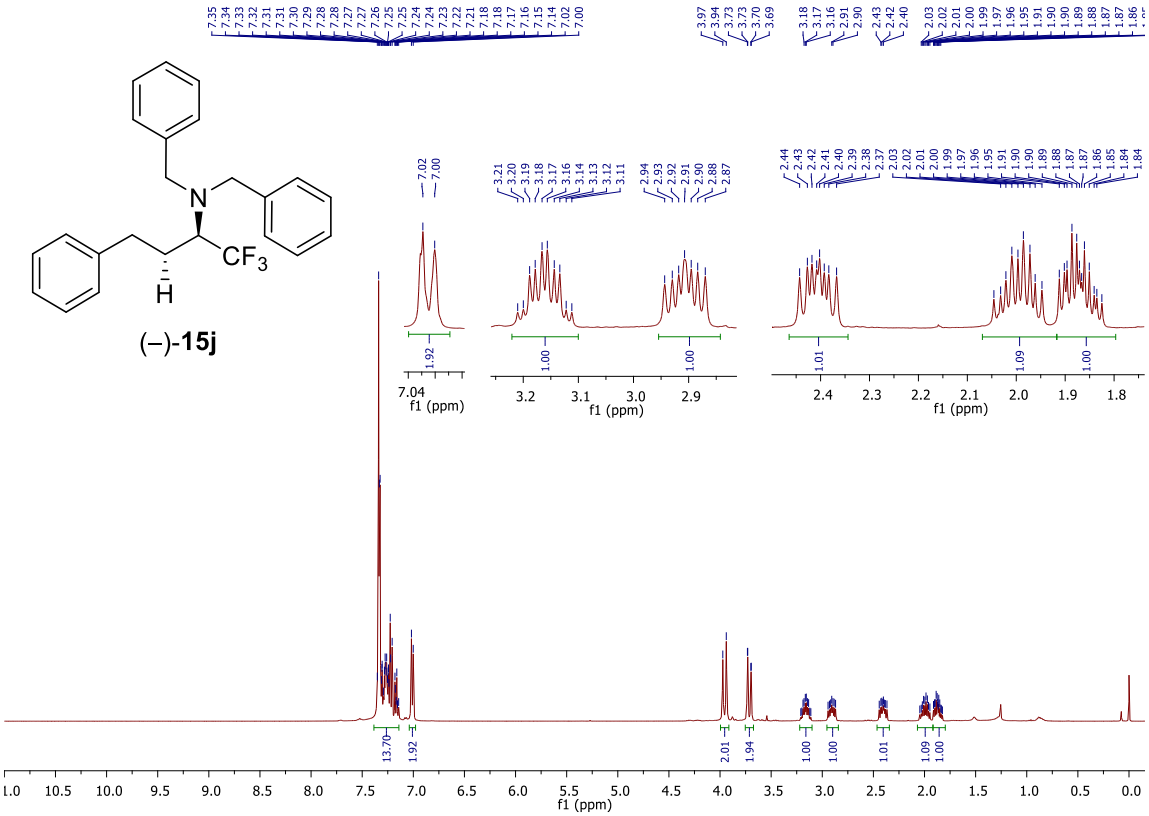


^{19}F NMR, 376 MHz, $CDCl_3$

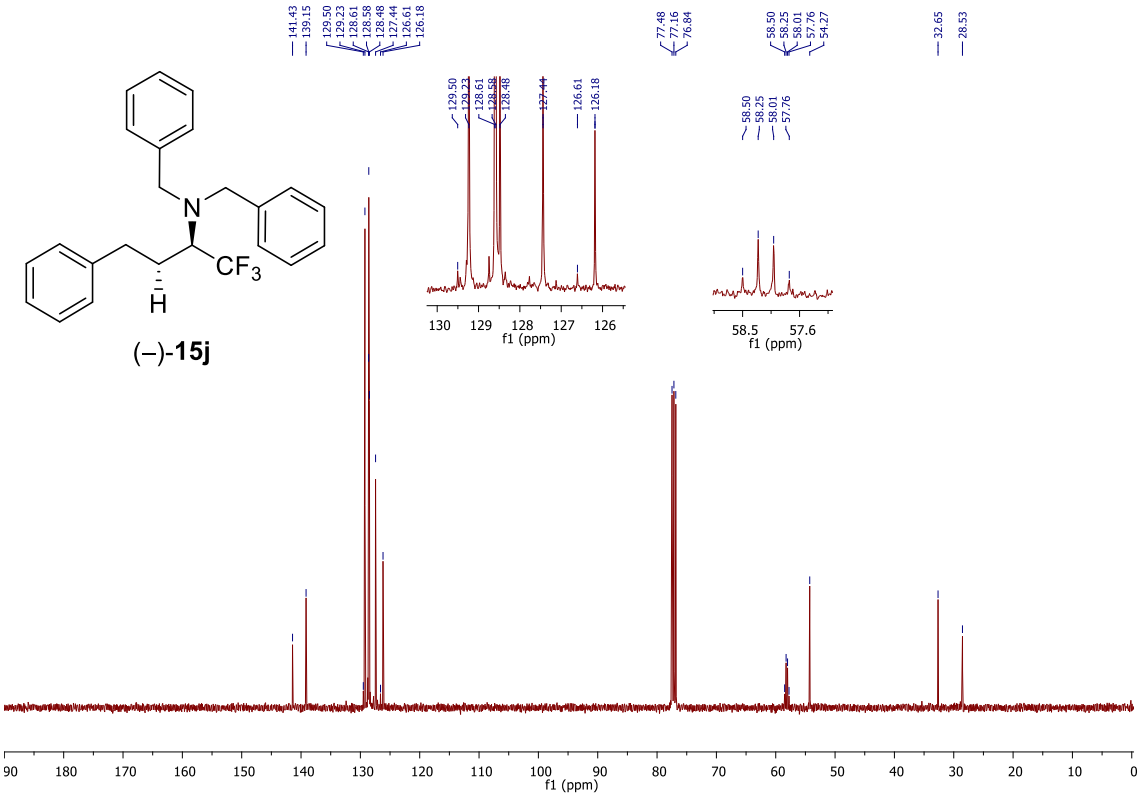


(–)-**15i**

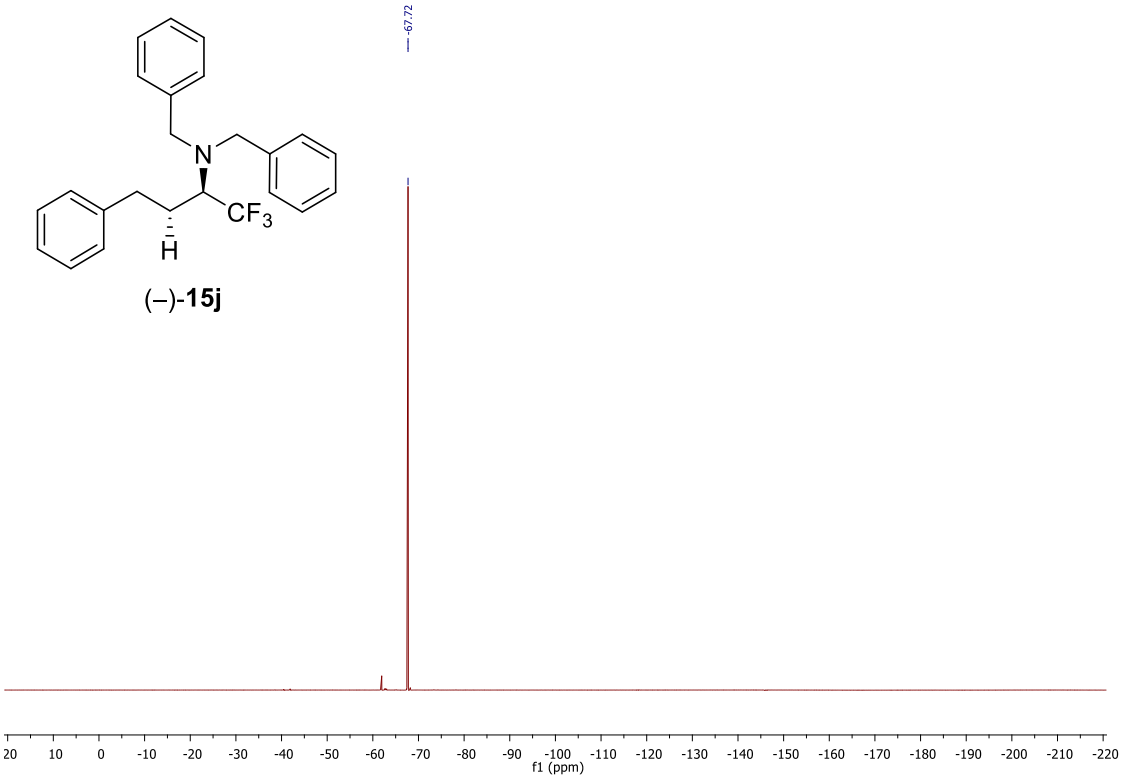
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

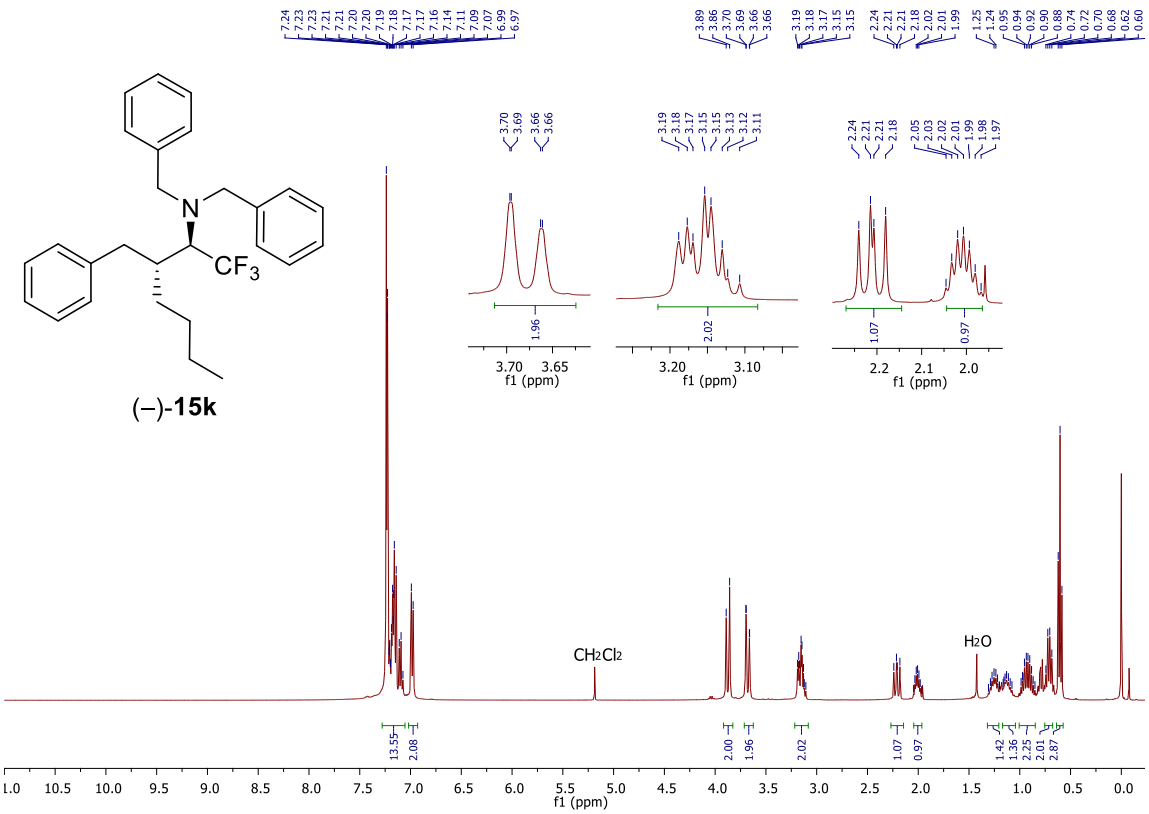


^{19}F NMR, 376 MHz, $CDCl_3$

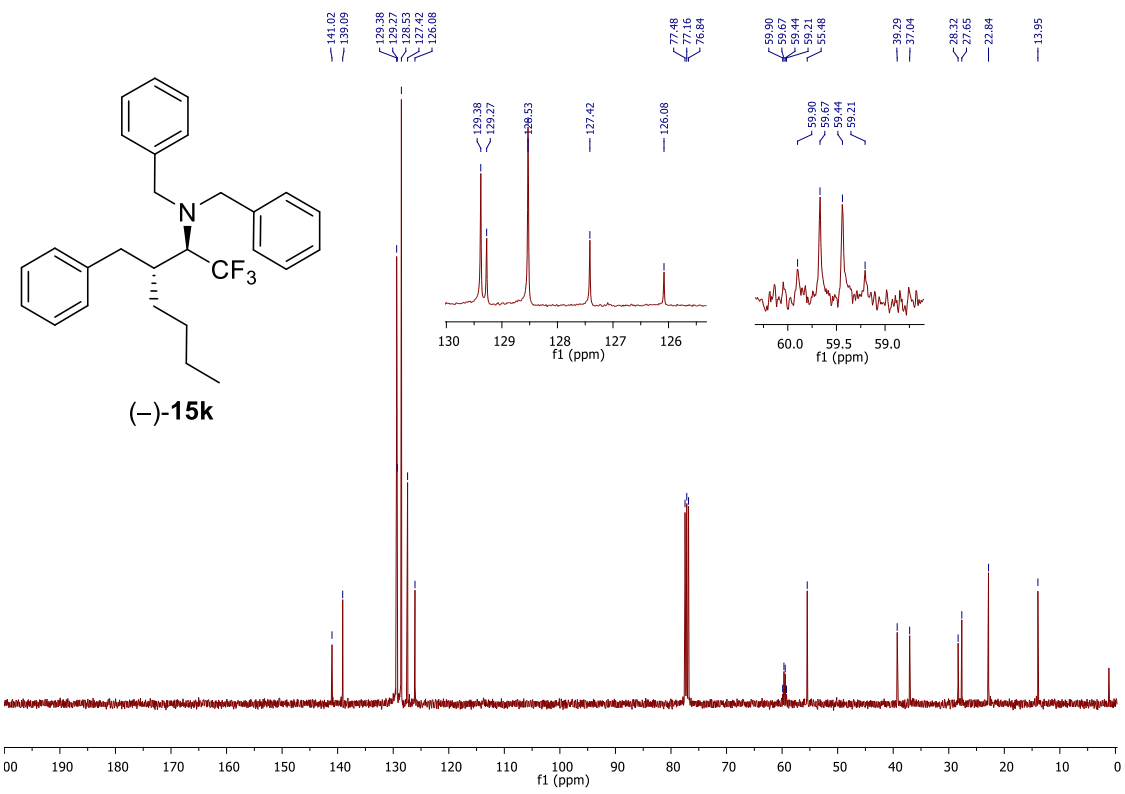


(–)-**15j**

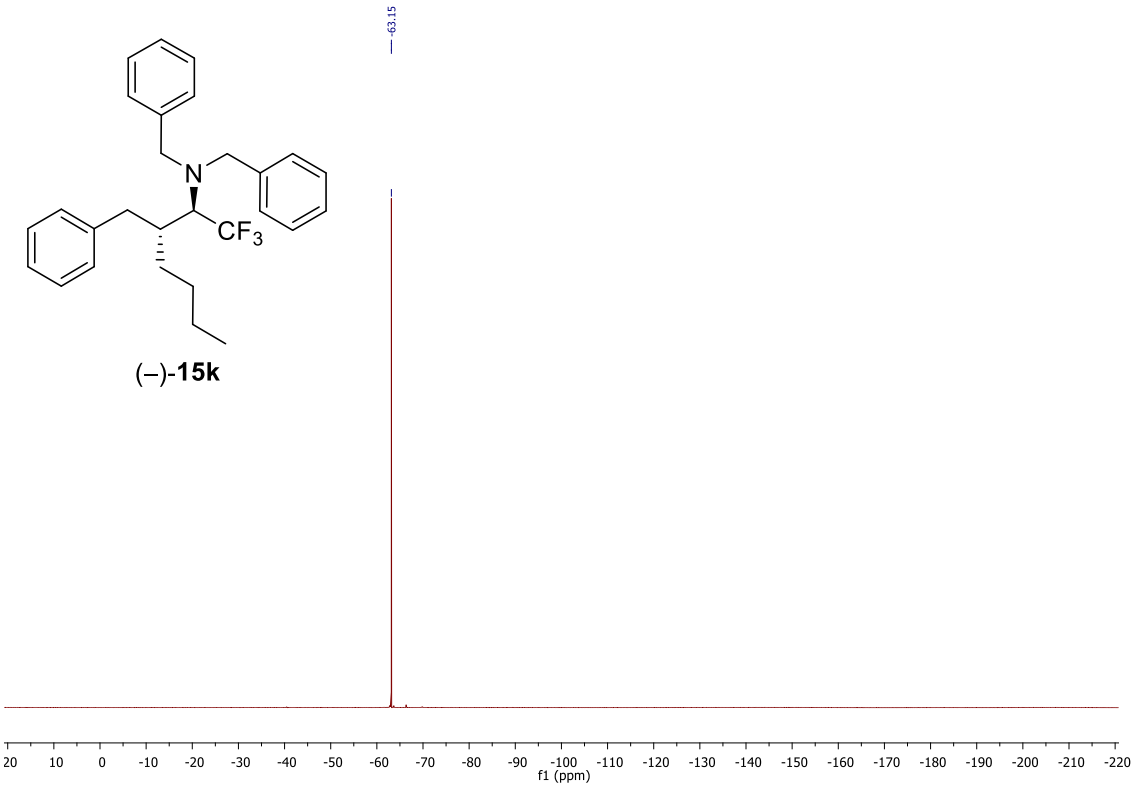
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

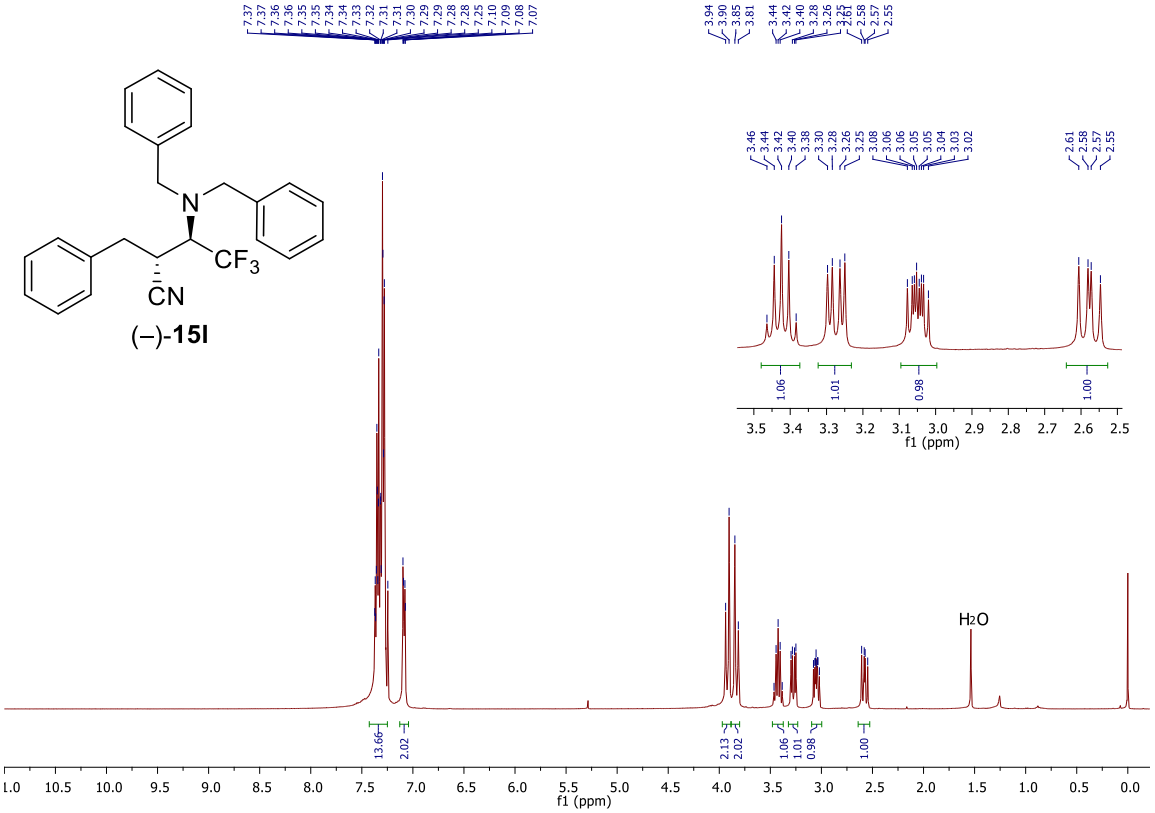


^{19}F NMR, 376 MHz, $CDCl_3$

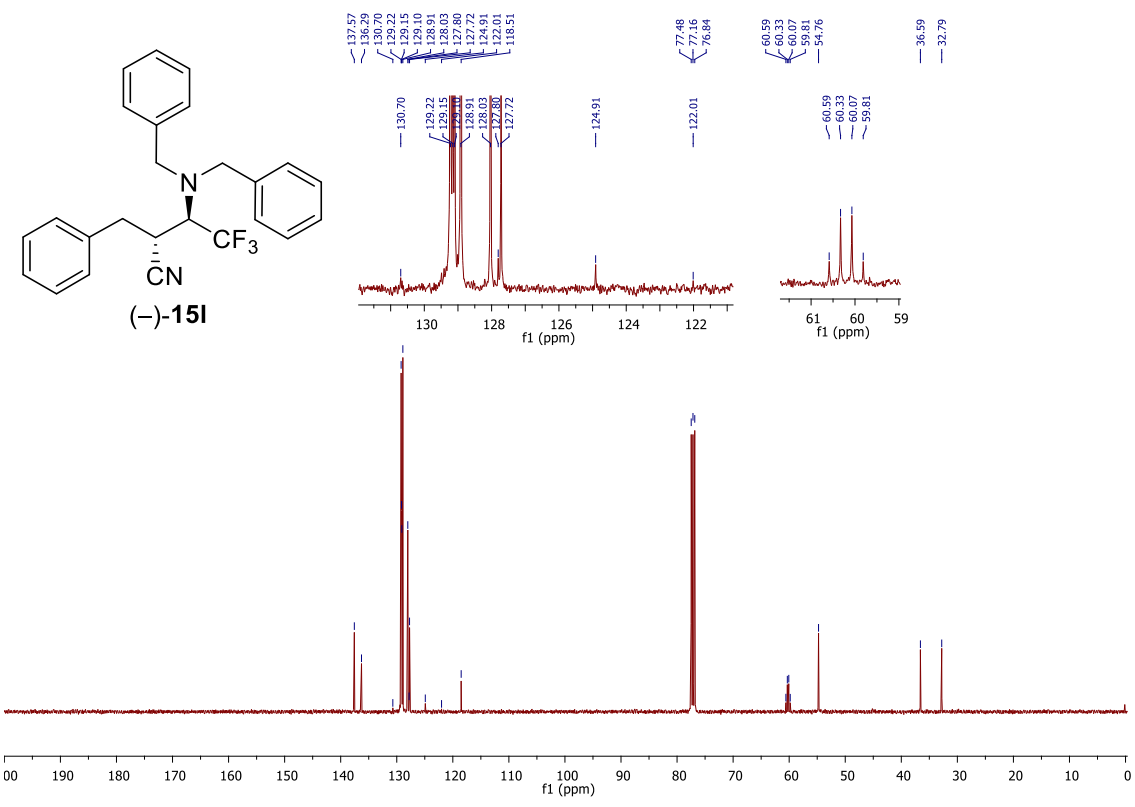


(–)-**15k**

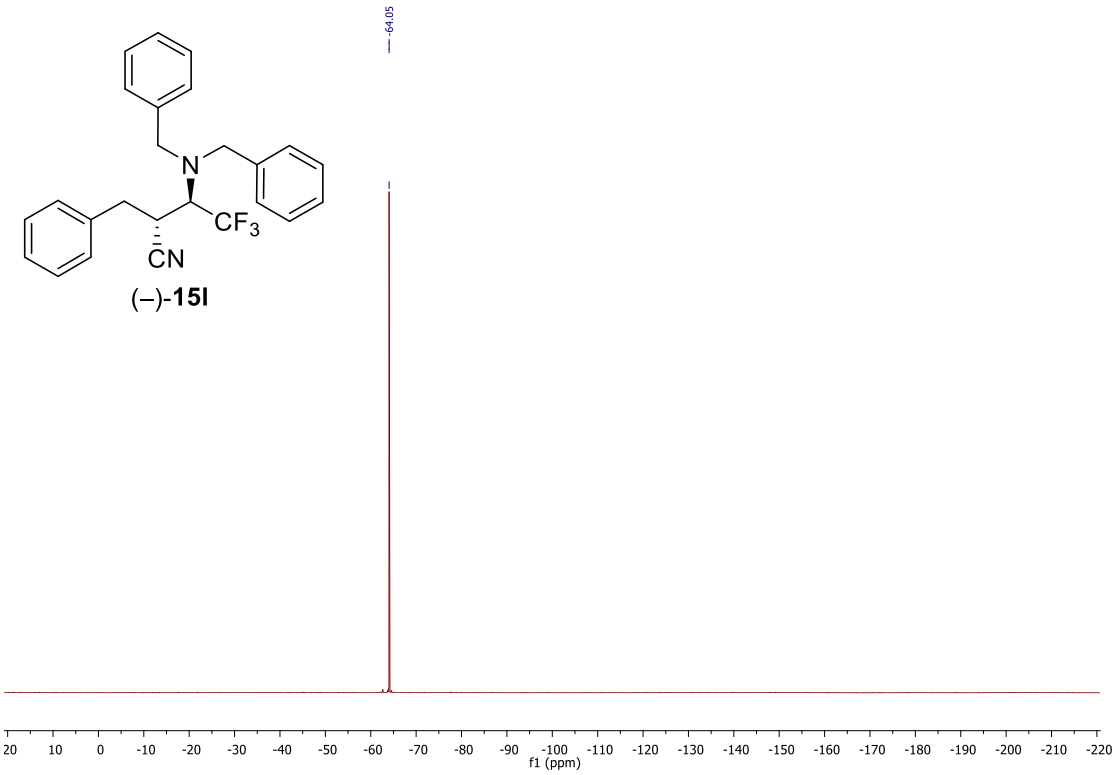
^{1}H NMR, 400 MHz, $CDCl_3$



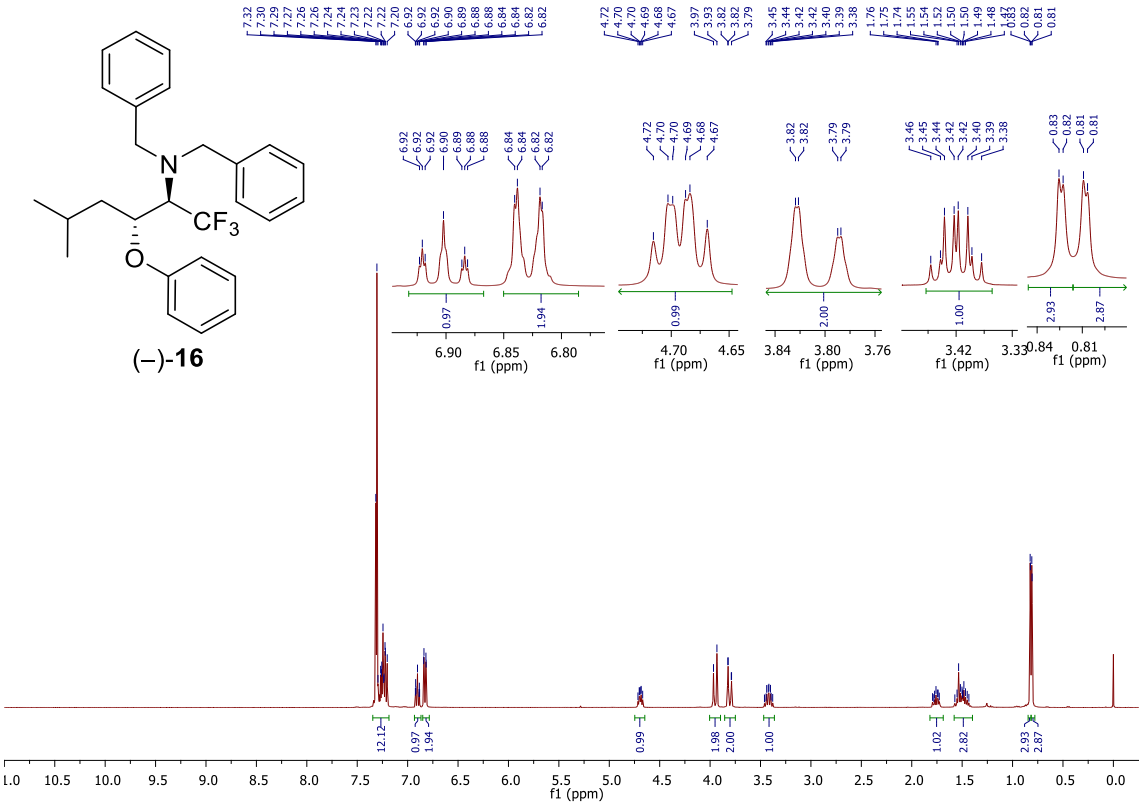
^{13}C NMR, 100 MHz, $CDCl_3$



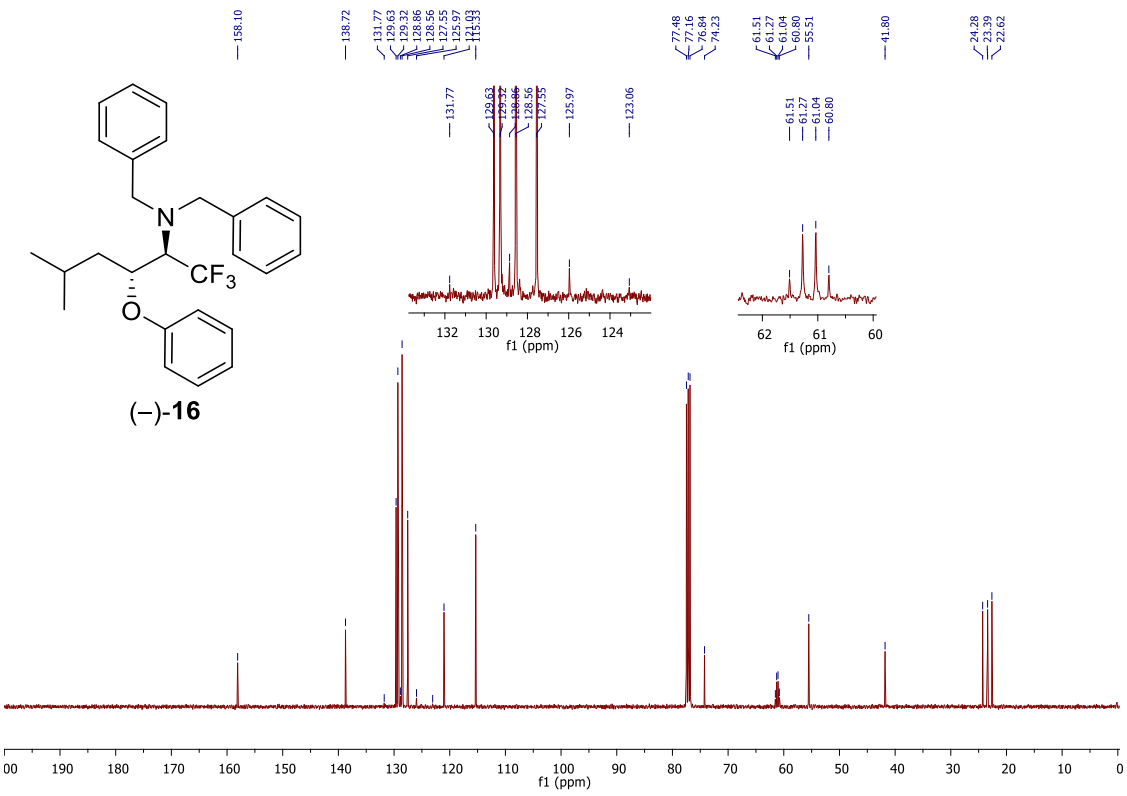
^{19}F NMR, 376 MHz, $CDCl_3$



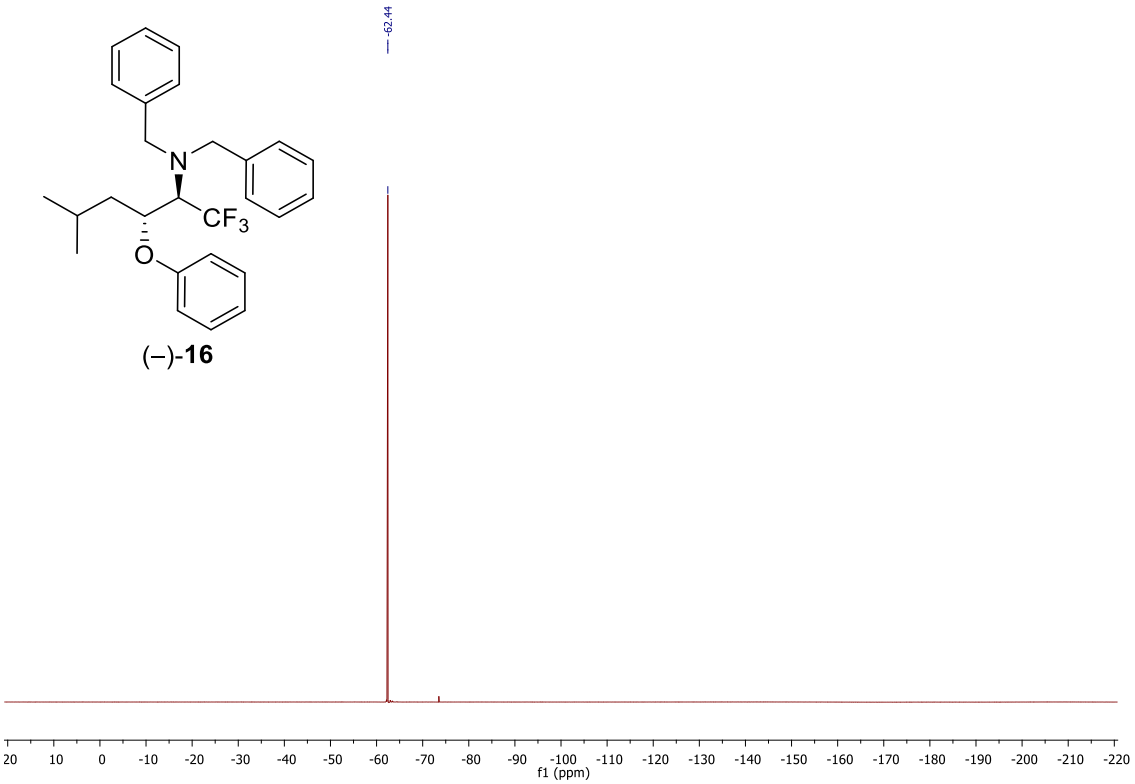
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

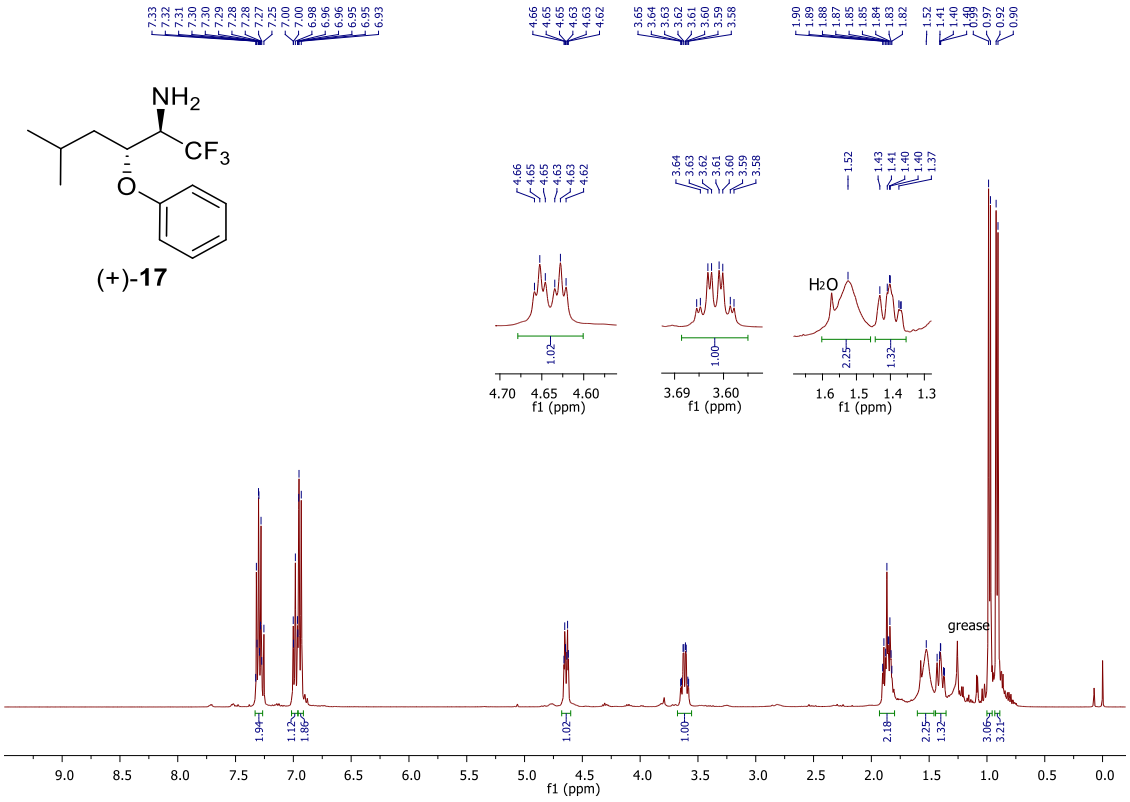


^{19}F NMR, 376 MHz, $CDCl_3$

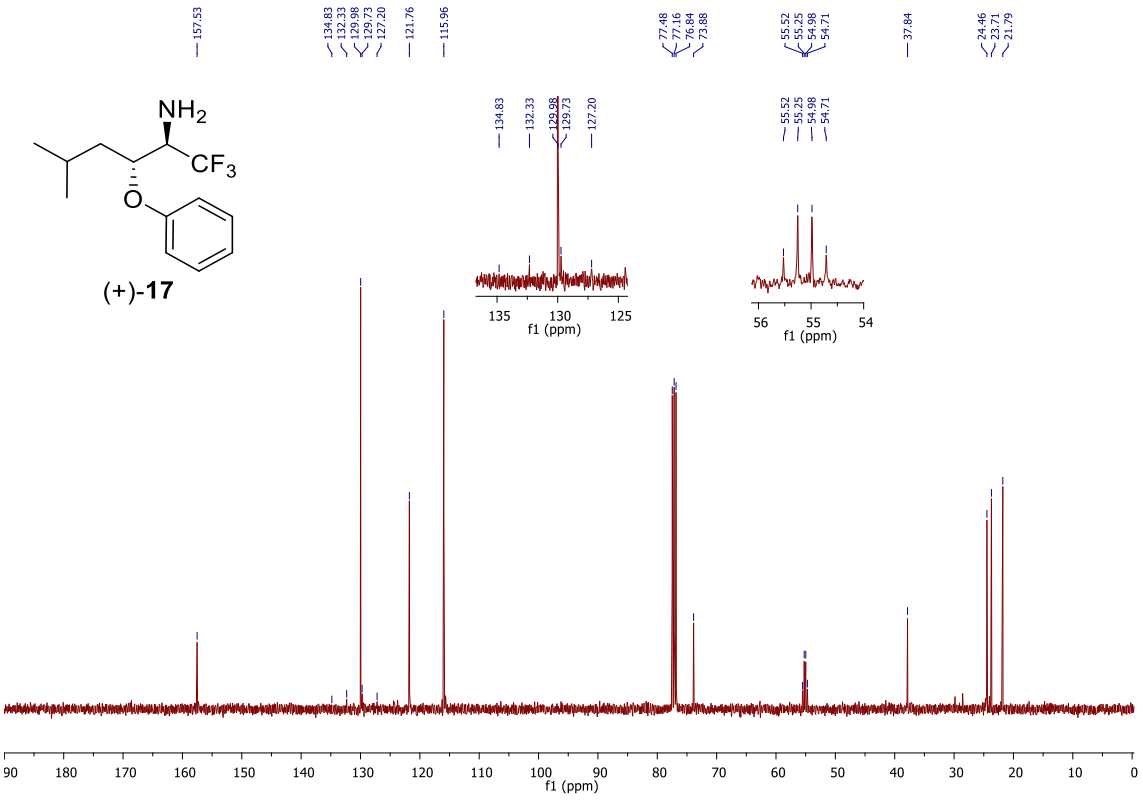


(–)-**16**

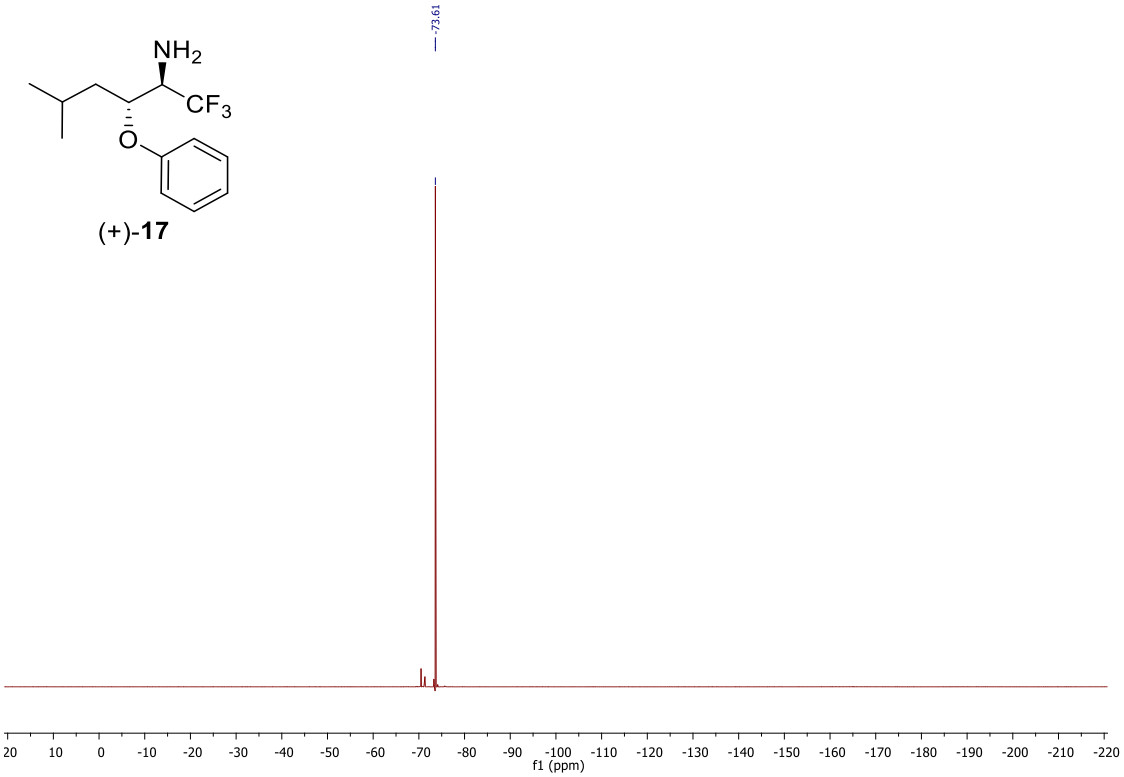
^{1}H NMR, 400 MHz, $CDCl_3$



^{13}C NMR, 100 MHz, $CDCl_3$

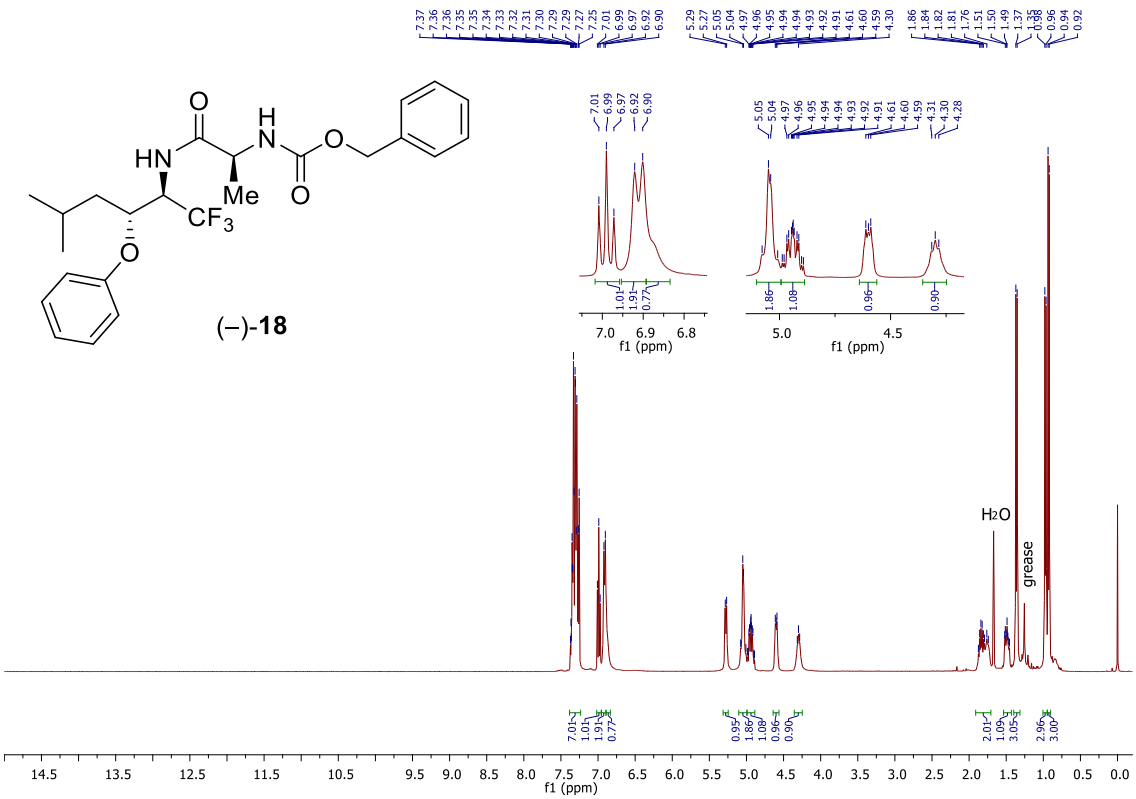


^{19}F NMR, 376 MHz, $CDCl_3$

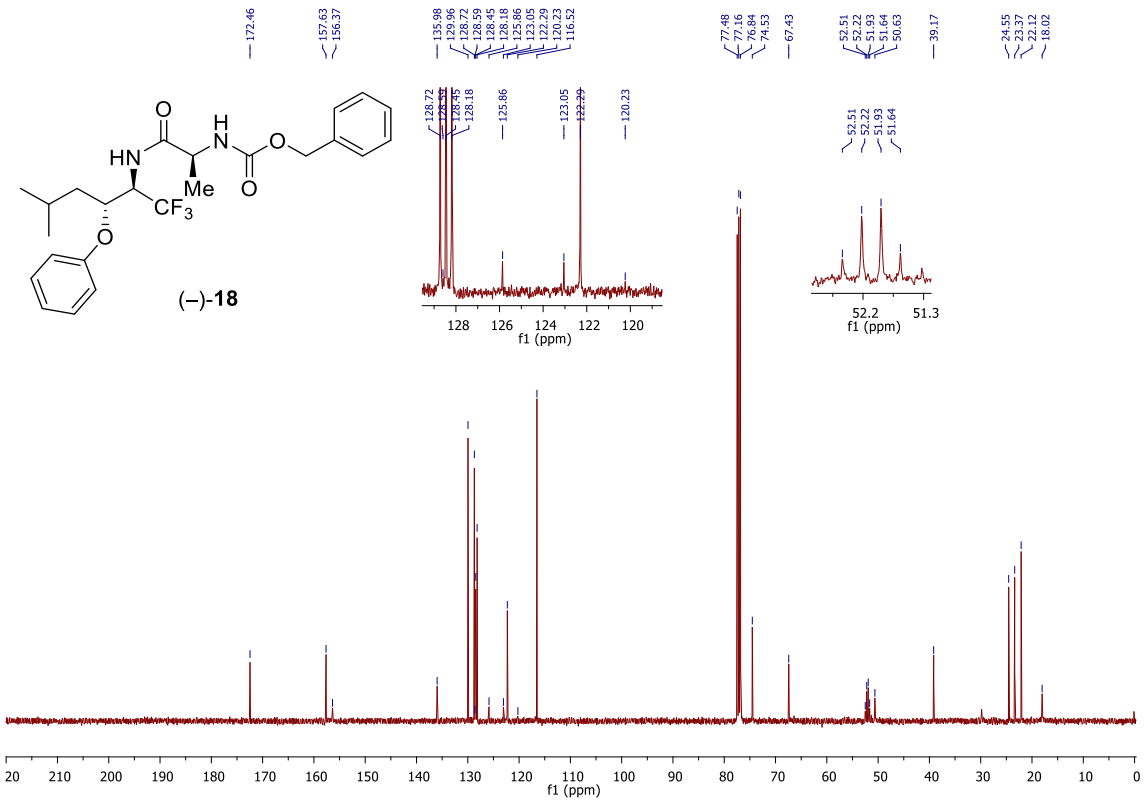


(+)-**17**

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



^{13}C NMR, 100 MHz, $CDCl_3$



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