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# Supporting information

## Asymmetric synthesis of (α*S*)-polyfluoroalkylated *N*-Boc-prolinols by diethyl zinc-induced asymmetric Meerwein-Ponndorf-Verley reduction of perfluoroalkyl *N*-Boc-pyrrolidyl ketones

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**A typical procedure of the preparation of prolinol 2.**

To a hexane (5 ml) solution of (*S*)-*tert*-butyl 2-(2,2,3,3,4,4,5,5,5-nonafluoropentanoyl)pyrrolidine-1-carboxylate (**1a**)[1] (0.4249 g, 1.0183 mmol) in was slowly added a hexane solution of $Et_2Zn$ (5 ml, 5 mmol, 1.0 M hexane solution) at room temperature. After stirring at room temperature for 24 h, the reaction mixture was quenched with 10% HCl (60 ml), extracted with diethyl ether (30 ml X 3), dried over $NaSO_4$, and concentrated under vacuum to give the residue. Purification of the residue by flash chromatography on silica gel with a mixed solution of hexane-$Et_2O$ (v/v = 5/1) gave (*S*)-*tert*-butyl 2-((*S*)-2,2,3,3,4,4,5,5,5-nonafluoro-1-hydroxypentyl)pyrrolidine-1-carboxylate (**2a**) (0.3111 g, 73%, $\alpha R/\alpha S$ = 8/92).

**(*S*)-*tert*-butyl 2-((*S*)-2,2,3,3,4,4,5,5,5-nonafluoro-1-hydroxypentyl)pyrrolidine-1-carboxylate (2a):**

*Rf* 0.18 (hexane/$Et_2O$=5/1); mp 124.7-127.3 °C; $[\alpha]_{589}^{22}$ –2.54° (*c* = 1.02, $CHCl_3$); IR (KBr) 3360 (OH), 1681 (C=O) $cm^{-1}$; HRMS (EI) Found *m/z* 419.1145. Calcd for $C_{14}H_{18}F_9NO_3$: M, 419.1143;
Major/Minor = 61/39;

Major isomer: $^1$H NMR (400 MHz, $CDCl_3$) δ 1.46 (9H, s), 1.67-2.34 (4H, m), 3.28 (1H, t, *J* = 7.2 Hz), 3.55 (1H, br s), 4.20 (1H, s), 4.53 (1H, d, *J* = 21.1 Hz), 5.20 (1H, br s); $^{13}$C NMR (400 MHz, $CDCl_3$) δ 24.6 (s), 25.8 (s), 28.4 (s), 47.0 (s), 57.2 (s), 68.8-69.6 (m), 81.0 (s), 105.6-122.5 (m), 155.0 (s); $^{19}$F NMR (400 MHz, $CDCl_3$) δ –127.3 - –124.8 (3F, m), –123.3 - –122.8 (2F, m), –120.4 - –119.1 (1F, m), –80.9 (3F, t, *J* = 10.0 Hz);

Minor isomer: $^1$H NMR (400 MHz, $CDCl_3$) δ 1.46 (9H, s), 1.67-2.34 (4H, m), 3.26 (1H, t, *J* = 7.4 Hz), 3.65 (1H, br s), 4.10 (1H, s), 4.65 (1H, d, *J* = 20.7 Hz), 5.18 (1H, br s); $^{13}$C NMR (400 MHz, $CDCl_3$) δ 24.5 (s), 27.4 (s), 28.4 (s), 47.7 (s), 59.6 (s), 68.8-69.6 (m), 80.8 (s), 105.6-122.5 (m), 156.4 (s); $^{19}$F NMR (400 MHz, $CDCl_3$) δ –127.3 - –124.8 (3F, m), –123.3 - –122.8 (2F, m), –120.4 - –119.1 (1F, m), –80.9 (3F, t, *J* = 10.0 Hz).

**(*S*)-*tert*-butyl**
**2-((*S*)-1-hydroxy-2,2,3,3,4,4,5,5,6,6,7,7-dodecamethyloctyl)pyrrolidine-1-carboxylate (2b):**

*Rf* 0.18 (hexane/$Et_2O$ = 5/1); mp 135.5-137.2 °C; $[\alpha]_{589}^{22}$ –1.45° (*c* = 1.01, $CHCl_3$); IR (KBr) 3372 (OH), 1674 (C=O) $cm^{-1}$; HRMS (EI) Found *m/z* 519.1086. Calcd for $C_{16}H_{18}F_{13}NO_3$: M, 519.1079;
Major/Minor = 62/38;

Major isomer: $^1$H NMR (400 MHz, $CDCl_3$) δ 1.46 (9H, s), 1.68-2.35 (4H, m), 3.28 (1H, t, *J* = 8.6

[1] Funabiki, K.; Shibata, A.; Iwata, H.; Hatano, K.; Kubota, Y.; Komura, K.; Ebihara, M.; Matsui, M. *J. Org. Chem.* **2008**, *73*, 4694.

Hz), 3.56 (1H, br s), 4.20 (1H, s), 4.52 (1H, d, *J* = 22.0 Hz), 5.21 (1H, br s); $^{13}$C NMR (400 MHz, $CDCl_3$) δ 24.6 (s), 25.8 (s), 28.5 (s), 47.0 (s), 57.2 (s), 68.6-69.9 (m), 80.9 (s), 101.1-119.2 (m), 156.5 (s); $^{19}$F NMR (400 MHz, $CDCl_3$) δ −127.0 - −124.6 (3F, m), −123.1- −122.5 (2F, m), −122.3 - −121.6 (4F, m), −120.1- −118.9 (1F, m), -80.8 (3F, t , *J* = 10.0 Hz);

Minor isomer: $^{1}$H NMR (400 MHz, $CDCl_3$) δ 1.46 (9H, s), 1.68-2.35 (4H, m), 3.26 (1H, t, *J* = 8.6 Hz), 3.56 (1H, br s), 4.10 (1H, s), 4.66 (1H, d, *J* = 19.8 Hz), 5.21 (1H, br s); $^{13}$C NMR (400 MHz, $CDCl_3$) δ 24.5 (s), 27.6 (s), 28.5 (s), 47.7 (s), 59.8 (s), 68.6-69.9 (m), 80.9 (s), 101.1-119.2 (m), 154.9 (s); $^{19}$F NMR (400 MHz, $CDCl_3$) δ −127.0 - −124.6 (3F, m), −123.1 - −122.5 (2F, m), −122.3 - −121.6 (4F, m), −120.1 - −118.9 (1F, m), −80.8 (3F, t , *J* = 10.0 Hz).

**(*S*)-*tert*-butyl 2-((*S*)-2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluoro-1-hydroxynonyl)pyrrolidine-1-carboxylate (2c):**

*Rf* 0.18 (hexane/$Et_2O$ = 5/1); mp 146.3-147.3 °C; $[\alpha]_{589}^{22}$ −0.99° (*c* = 1.00, $CHCl_3$); IR (KBr) 3368 (OH), 1667 (C=O) cm$^{-1}$; HRMS (EI) Found *m/z* 619.1017. Calcd for $C_{18}H_{18}F_{17}NO_3$: M, 619.1015;

Major/Minor = 63/37;

Major isomer: $^{1}$H NMR (400 MHz, methanol-$d_4$) δ 1.46 (9H, s), 1.68-2.32 (4H, m), 3.28 (1H, t, *J* = 8.1 Hz), 3.56 (1H, br s), 4.21 (1H, s), 4.53 (1H, d, *J* = 16.6 Hz), 5.20 (1H, br s); $^{13}$C NMR (400 MHz, acetone-$d_6$) δ 24.7 (s), 25.0 (s), 27.8 (s), 46.6 (s), 56.7 (s), 68.3-69.1 (m), 79.1 (s), 106.3-121.8 (m), 154.4 (s); $^{19}$F NMR (400 MHz, methanol-$d_4$) δ −127.4 - −125.3 (3F, m), −123.7 (2F, s), −123.1 - −121.8 (8F, m), −120.1 - −119.0 (1F, m), −82.3 (3F, t, *J* = 10.5 Hz);

Minor isomer: $^{1}$H NMR (400 MHz, methanol-$d_4$) δ 1.46 (9H, s), 1.68-2.32 (4H, m), 3.26 (1H, t, *J* = 8.1 Hz), 3.56 (1H, br s), 4.11 (1H, s), 4.67 (1H, d, *J* = 18.9 Hz), 5.20 (1H, br s); $^{13}$C NMR (400 MHz, acetone-$d_6$) δ 24.2 (s), 25.6 (s), 27.7 (s), 47.0 (s), 57.2 (s), 66.9-68.1 (m), 78.9 (s), 106.3-121.8 (m), 153.4 (s); $^{19}$F NMR (400 MHz, methanol-$d_4$) δ −127.4 - −125.3 (3F, m), −123.7 (2F, s), −123.1 - −121.8 (8F, m), −120.1 - −119.0 (1F, m), −82.3 (3F, t, *J* = 10.5 Hz).

**(*S*)-*tert*-butyl 2-((*S*)-2,2,2-trifluoro-1-hydroxyethyl)pyrrolidine-1-carboxylate (2d)[1]:**

*Rf* 0.10 ($CH_2Cl_2$); mp 124.2-125.0 °C; $[\alpha]_D^{23}$ -56.8° (*c* = 1.00, $CHCl_3$); IR (KBr) 3326 (OH), 1655 (C=O) cm$^{-1}$; HRMS (FAB) found: *m/z* 270.1324. Calcd for $C_{11}H_{19}F_3NO_3$: M+H, 270.1317; Anal. Calcd for C, 49.07; H, 6.74; N, 5.20. Found: C, 48.98; H, 6.50; N, 5.19.

Major/Minor = 65/35;

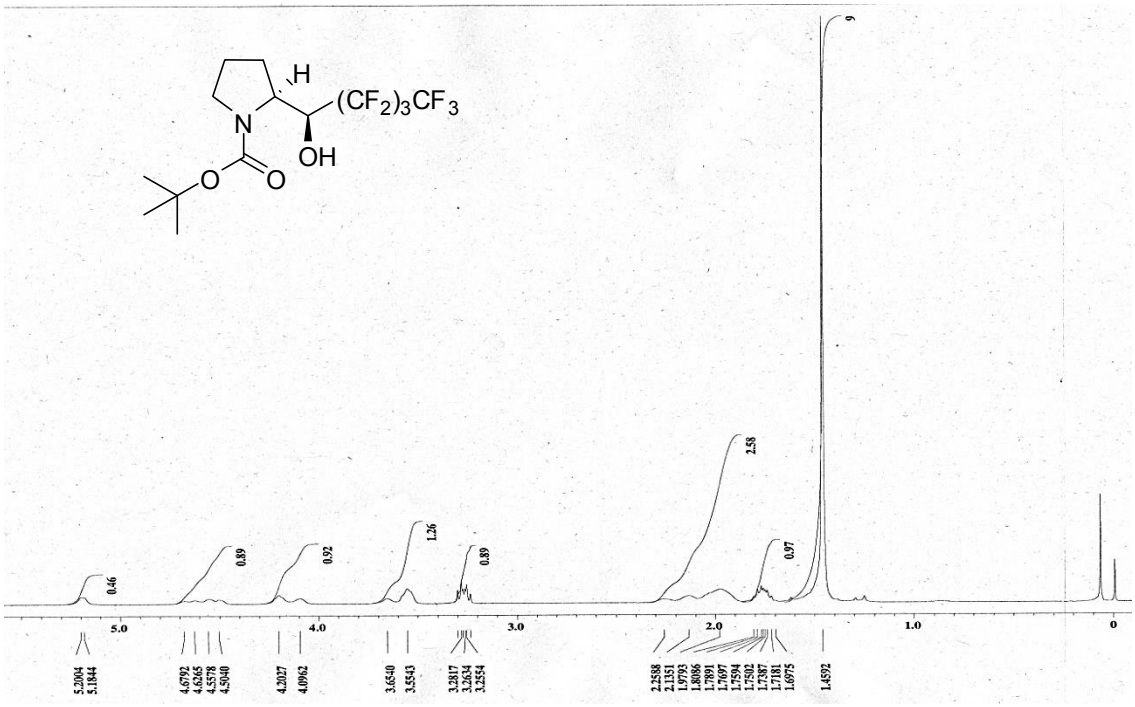
Major isomer: $^{1}$H NMR (400 MHz, $CDCl_3$) δ 1.47 (9H, s), 1.78-2.23 (4H, m), 3.27-3.78 (2H, m), 4.02-4.19 (1H, m), 4.25-4.36 (1H, m), 5.48 (1H, br s); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 24.2 (s), 26.4 (s), 28.2 (s), 47.3 (s), 58.1 (s), 70.5 (quint, *J* = 28.7 Hz), 80.4 (s), 124.8 (q, *J* = 284.3 Hz), 156.1 (s); $^{19}$F NMR (376 MHz, $CDCl_3$) δ −74.8 (3F, d, *J* = 5.7 Hz);

Minor isomer: $^{1}$H NMR (400 MHz, $CDCl_3$) δ 1.47 (9H, s), 1.78-2.23 (4H, m), 3.27-3.78 (2H, m), 4.02-4.19 (1H, m), 4.25-4.36 (1H, m), 5.48 (1H, br s); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 24.2 (s), 25.3 (s), 28.2 (s), 46.3 (s), 56.7 (s), 70.5 (quint, *J* = 28.7 Hz), 80.4 (s), 124.6 (q, *J* = 283.5 Hz), 156.1 (s); $^{19}$F NMR (376 MHz, $CDCl_3$) δ −76.9 (3F, s).

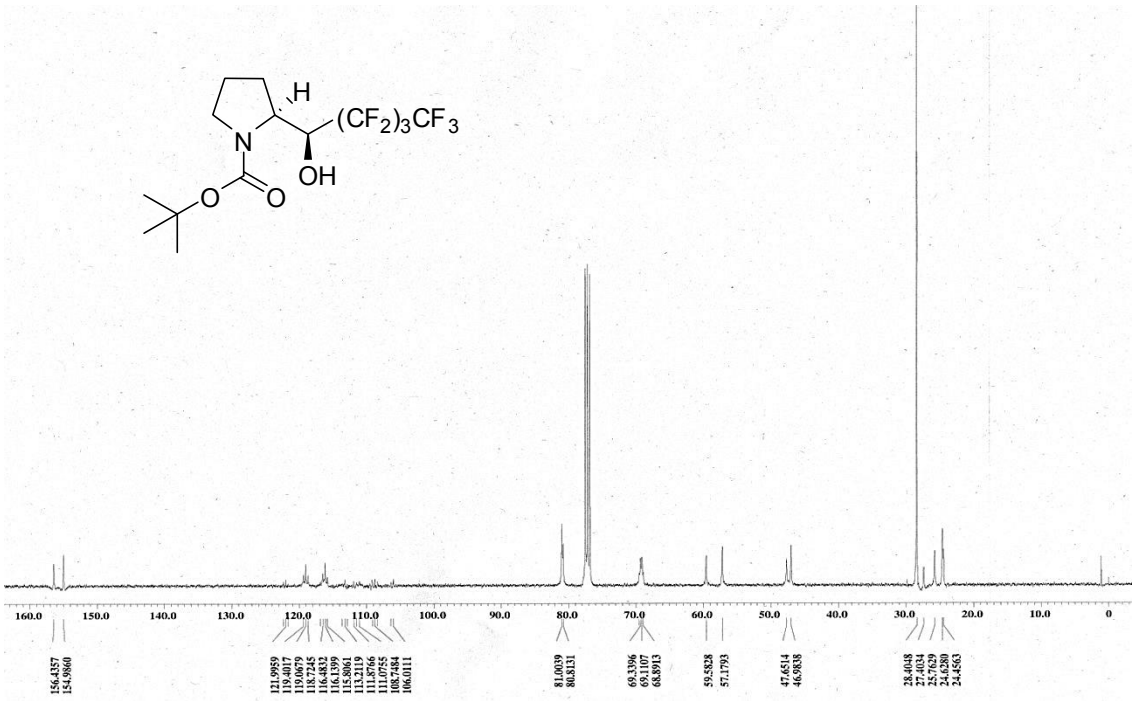
**(1*S*,7a*S*)-1-(perfluorobutyl)tetrahydropyrrolo[1,2-c]oxazol-3(1*H*)-one (3a):** *Rf* 0.13 (hexane/$Et_2O$ = 5/1); mp 104.6–106.0 °C; $[\alpha]_{589}^{25}$ −0.19 (*c* = 1.01, $CHCl_3$); IR (KBr) 1770 (C=O) $cm^{-1}$; HRMS (EI) found: *m/z* 345.0419. Calcd for $C_{10}H_8F_9NO_2$: M, 345.0411; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 1.78-2.11 (3H, m), 2.12-2.33 (1H, m), 3.17-3.38 (1H, m), 3.61 (1H, dt, *J* = 11.2, 8.1 Hz), 3.99-4.16 (1H, m), 5.08 (1H, ddd, *J* = 20.3, 7.9, 3.0 Hz); $^{13}$C NMR (400 MHz, $CDCl_3$) δ 25.97 (s), 26.02 (s), 45.3 (s), 61.0 (s), 70.1 (dd, *J* = 34.4, 21.2 Hz), 107.9-124.11 (m), 58.6 (s); $^{19}$F NMR (400 MHz, $CDCl_3$) δ −126.3 - −125.6 (2F, m), −123.6 - −122.9 (2F, m), −120.2 - −122.8 (2F, m), −80.8 (3F, t, *J* = 9.7 Hz).

**(*S*)-*tert*-butyl 2-((*S*)-2,2,3,3,4,4,5,5,5-nonafluoro-1-hydroxypentyl)pyrrolidine-1-carboxylate (2a)**

$^{1}$H NMR



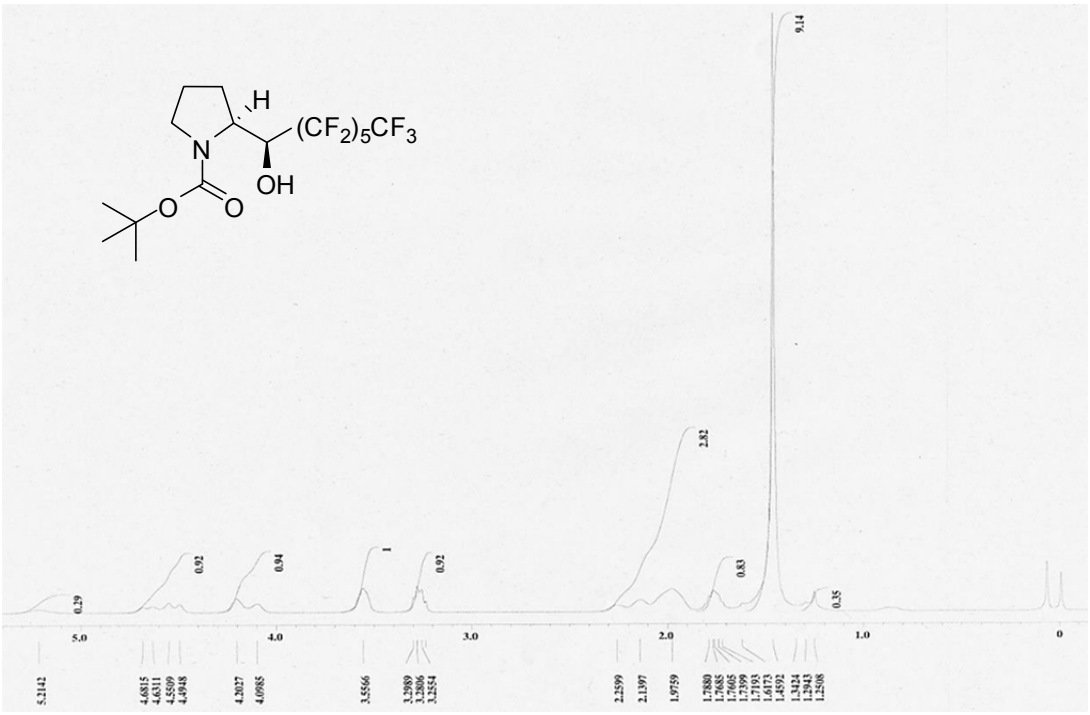

$^{13}$C NMR



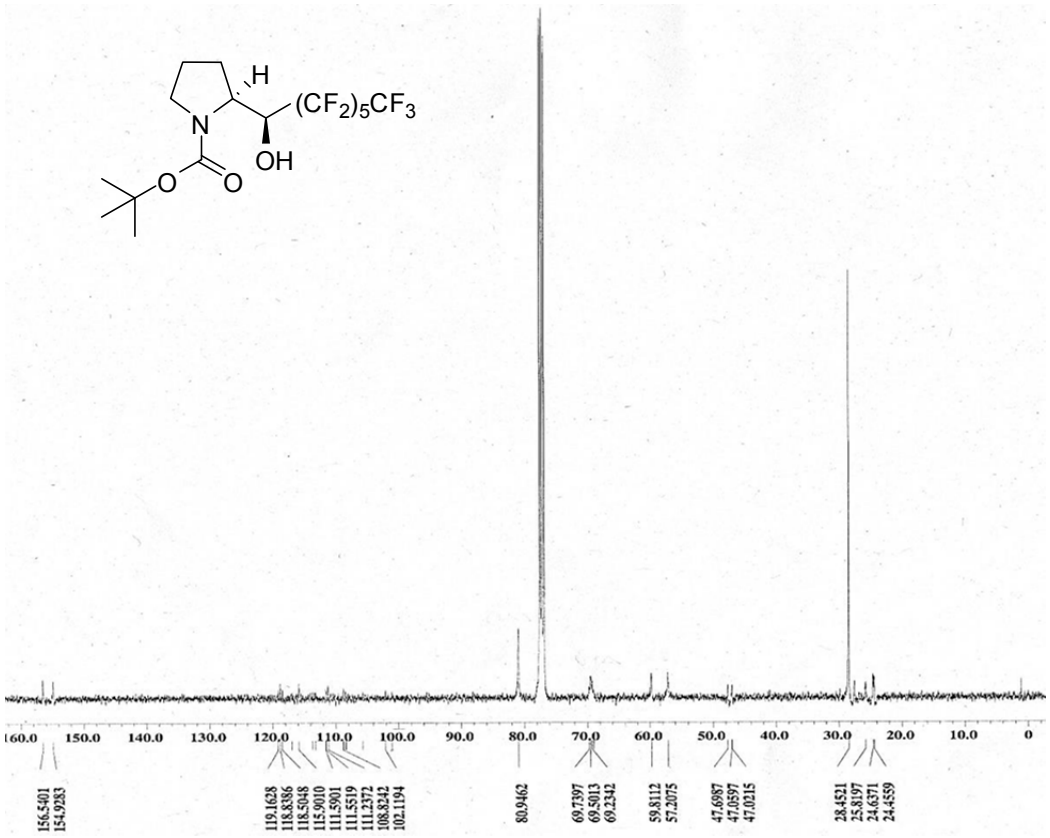
**(*S*)-*tert*-butyl**

**2-((*S*)-1-hydroxy-2,2,3,3,4,4,5,5,6,6,7,7-dodecamethyloctyl)pyrrolidine-1-carboxylate (2b)**

$^{1}$H NMR

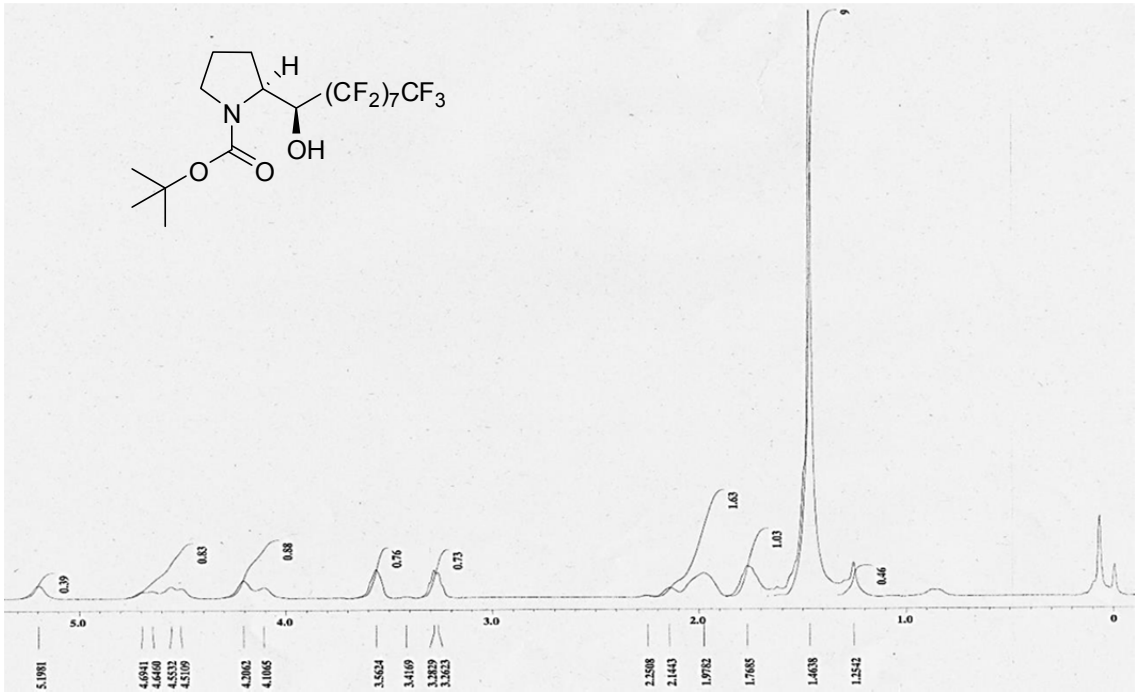



$^{13}$C NMR

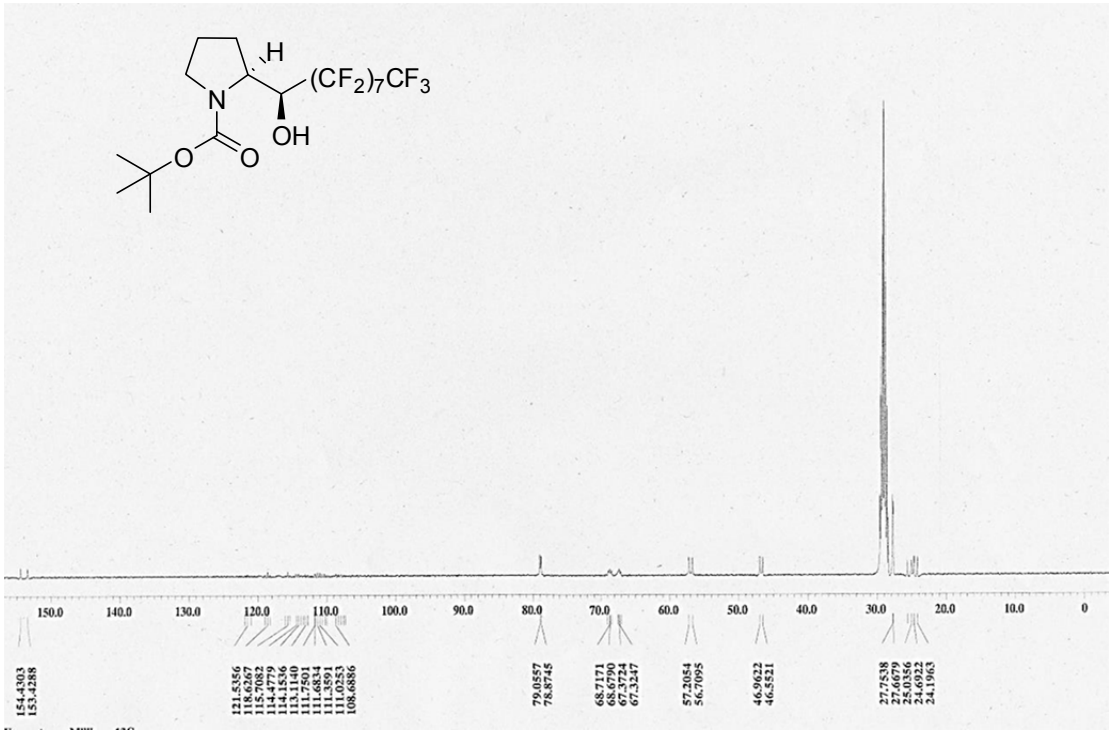


**(*S*)-*tert*-butyl 2-((*S*)-2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluoro-1-hydroxynonyl) pyrrolidine-1-carboxylate (2c)**

$^{1}$H NMR

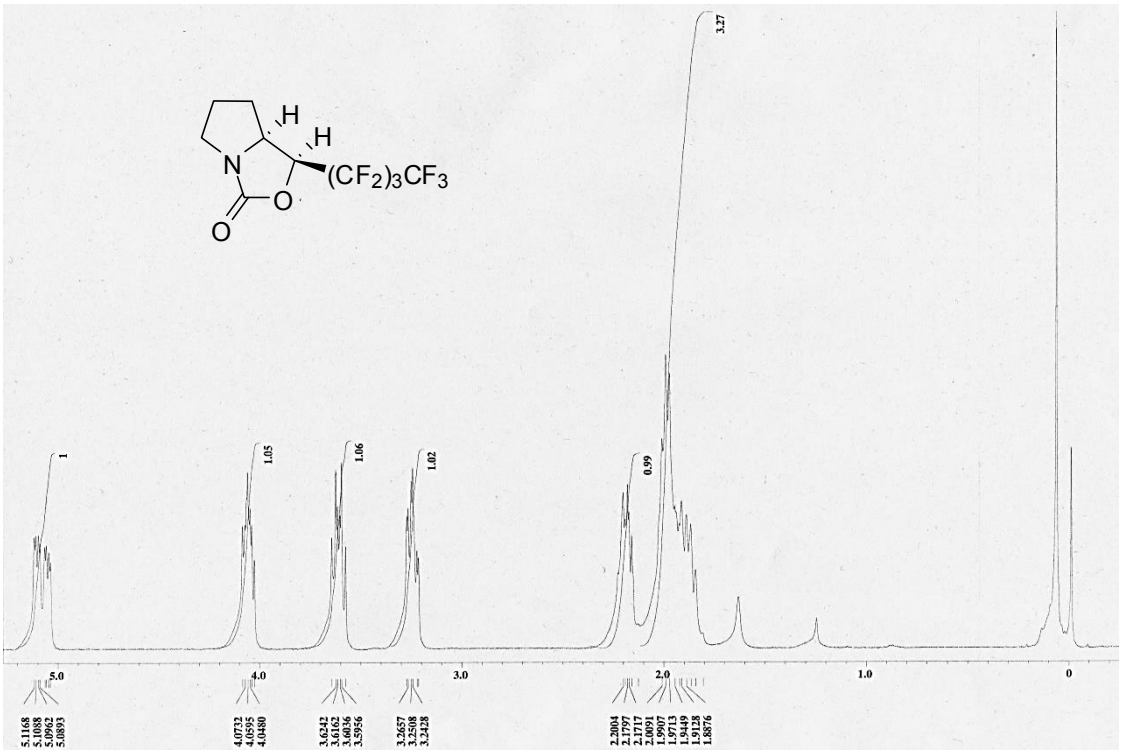



$^{13}$C NMR



**(1*S*,7a*S*)-1-(perfluorobutyl)tetrahydropyrrolo[1,2-c]oxazol-3(1*H*)-one (3a)**

$^{1}$H NMR




$^{13}$C NMR