Supplementary data

A FLUOROUS PROLINE CATALYST IMMOBILIZED ON TEFLON® FOR HIGHLY STEREOSELECTIVE ASYMMETRIC ALDOL REACTIONS

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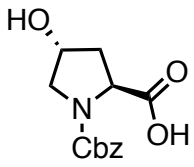
1. **Synthesis of proline catalyst**

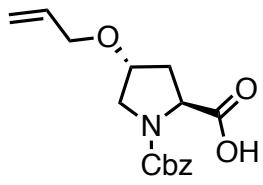
(*2S*,*4R*)-*trans*-*N*-Cbz-4-hydroxyproline[1]



A solution of (*2S*,*4R*)-4-hydroxypyrrolidine-2-carboxylic acid (1.64 g, 12.6 mmol) and sodium carbonate (3.33 g, 31.5 mmol) in H_2O/acetone (14 mL, 6 mL/1 mL v/v) was stirred at 0 °C for 10 min. To the mixture was slowly added benzyloxycarbonyl chloride (2.13 mL, 15.12 mmol). The resulting mixture was warmed to room temperature and stirred for 21 h. The mixture was diluted with water (30 mL) and added 1N HCl until pH = 1-2. The reaction mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : methanol = 5 : 1) to give desired product (3.27 g, 98%).

White solid; m.p. 102.2-102.9 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.36-7.31 (m, 5H), 5.17 (d, *J* = 11.3 Hz, 2H), 4.61-4.51 (m, 2H), 3.67-3.61 (m, 2H), 2.41-2.18 (m, 2H).

(*2S*,*4R*)-4-(Allyloxy)-1-((benzyloxy)carbonyl)pyrrolidine-2-carboxylic acid 2[1]

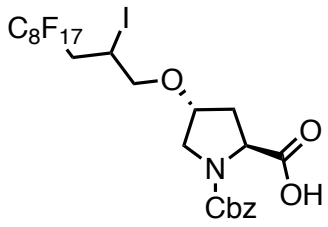


Under N_2 atmosphere, to a solution of (*2S*,*4R*)-*trans*-*N*-Cbz-4-hydroxyproline (2.1 g, 7.9 mmol) in dry-THF (20 mL) was added sodium hydride (60% dispersion in oil, 792 mg, 19.8 mmol) at 0 °C. After warming the reaction mixture to room temperature, allyl bromide (1.8 mL, 20.6 mmol) was added dropwise, and then the mixture was stirred for 41 h. The reaction mixture was quenched with water (17 mL) and added 1N HCl until pH = 1-2. After the addition of ethyl acetate, the organic phase was separated and the aqueous phase was extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated (crude 2.5 g).

Next, a mixture of crude (2.5 g, 7.1 mmol), NaOH (511 mg, 12.9 mmol), H_2O (3 mL), and methanol (3 mL) was stirred at room temperature for 24 h. The reaction mixture was washed with ethyl acetate. The pH of aqueous layer was adjusted to pH = 1-2 by addition of 1N HCl. The solution was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give **2** (1.66 g, 69%).

Colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 9.15 (brs, 1H), 7.35-7.29 (m, 5H), 5.95-5.79 (m, 1H), 5.29-5.07 (m, 4H), 4.55-4.45 (m, 1H), 4.16-4.13 (m, 1H), 3.96 (d, *J* = 5.13 Hz, 2H), 3.75-3.53 (m, 2H), 2.44-2.04 (m, 2H).

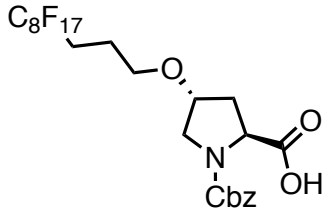
(*2S*,*4R*)-1-((Benzyloxy)carbonyl)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)oxy)pyrrolidine-2-carboxylic acid[1]



After the third freeze-pump-thaw cycle of **2** (3.85 g, 12.6 mmol), a mixture of **2** and $C_8F_{17}I$ (3.43 mL, 13.0 mmol) was heated at 80 °C. AIBN (210 mg, 1.3 mmol) was added to this solution and the mixture was stirred for 48 h. After the addition of 1N HCl and ethyl acetate, The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by FSPE[2)] (methanol : H_2O = 68 : 32) to give desired product (4.85 g, 43%).

Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.74 (brs, 1H), 7.36-7.30 (m, 5H), 5.24-5.13 (m, 2H), 4.57-4.47 (m, 1H), 4.36-4.28 (m, 1H), 4.18-4.17 (m, 1H), 3.86-3.59 (m, 4H), 3.05-2.57 (m, 2H), 2.50-2.12 (m, 2H).

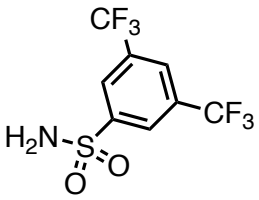
(*2S*,*4R*)-1-((Benzyloxy)carbonyl)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)oxy)pyrrolidine-2-carboxylic acid 3a[1]



A solution of (*2S*,*4R*)-1-((benzyloxy)carbonyl)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-2-iodoundecyl)oxy)pyrrolidine-2-carboxylic acid (652.5 mg, 0.766 mmol), AIBN (12.6 mg, 0.0766 mmol), Hypophosphorous Acid (1.44 mL, 7.66 mmol), and sodium hydrogen carbonate (772.8 mg, 9.19 mmol) in EtOH (10 mL) was stirred at reflux for 4 h. 1N HCl was added to reaction mixture until pH = 1-2. The mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (dichloromethane : methanol = 95 : 5) to give **3** (348.7 mg, 63%).

Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 7.36-7.30 (m, 5H), 5.18-5.13 (m, 2H), 4.53-4.43 (m, 1H), 4.12-4.06 (m, 1H), 3.75-3.45 (m, 4H), 2.35-2.04 (m, 4H), 1.90-1.82 (m, 2H).

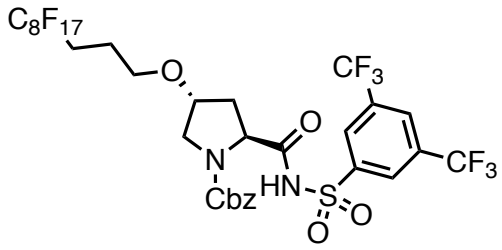
3,5-Bis(trifluoromethyl)benzenesulfonamide[1]



To a solution of 3,5-bis(trifluoromethyl)benzenesulfonyl chloride (2.0 g, 6.4 mmol) in H_2O (10 mL) was added 25% ammonia solution (2.59 mL, 67.5 mmol) at 100 °C and stirred for 2 h. Excess water was separated as the toluene azeotrope. After the addition of 1N HCl, the crude was purified by filtration to give desired product (1.6 g, 85%).

White solid; mp. 182-183 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.39 (s, 2H), 8.09 (s, 1H), 5.07 (s, 2H).

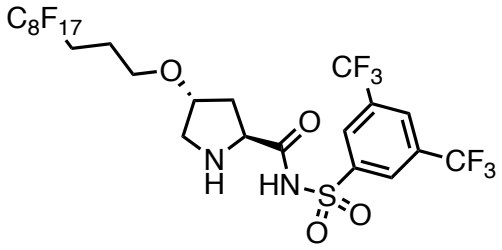
Benzyl(*2S*,*4R*)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)oxy)pyrrolidine-1-carboxylate[1]



Under N_2 atmosphere, EDCI (127 mL, 0.72 mmol) was added dropwise to a solution of **3a** (348.8 mg, 0.48 mmol), 3,5-bis(trifluoromethyl) benzenesulfonamide (209.8 mg, 0.72 mmol), DMAP (19.6 mg, 0.12 mmol), and HOBt (110 mg, 0.72 mmol) in dry- dichloromethane/dry-DMF (15 mL, 2 mL/1 mL v/v) at 0 °C and the mixture was stirred for 10 min. Then the reaction temperature rose to room temperature and the mixture was stirred for further 32 h. 1N HCl was added to reaction mixture until pH = 1-2. The mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 4) to give desired product (400.8 mg, 83%).

Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.53 (s, 2H), 8.12 (s, 1H), 7.37 (s, 5H), 5.26-5.15 (m, 2H), 4.43-4.37 (m, 1H), 4.05-3.99 (m, 1H), 3.63-3.37 (m, 4H), 2.56-2.48 (m, 1H), 2.19-1.99 (m, 3H), 1.86-1.76 (m, 2H).

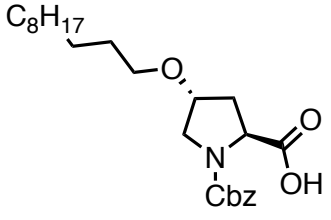
(*2S*,*4R*)-*N*-((3,5-Bis(trifluoromethyl)phenyl)sulfonyl)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)oxy)pyrrolidine-2-carboxamide 1a[1]



Benzyl(*2S*,*4R*)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)oxy)pyrrolidine-1-carboxylate (379.0 mg, 0.38 mmol) and Pd/C (161.76 mg, 0.076 mmol) in methanol (6 mL) was stirred at room temperature for 17 h under H_2 balloon. The Pd/C was removed by filtration through a pad of celite with methanol. The filtrate was concentrated. The crude was purified by silica gel chromatography (dichloromethane : methanol = 19 : 1) to give **1a** (286.3 mg, 88%).

white solid; m.p. 103.8-104.9 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.35 (s, 2H), 7.99 (s, 1H), 4.55-4.48 (m, 1H), 4.20 (s, 1H), 3.62-3.46 (m, 4H), 2.59-2.51 (m, 1H), 2.18-2.02 (m, 3H), 1.85-1.75 (m, 2H).

(2*S*,4*R*)-1-((Benzyloxy)carbonyl)-4-(undecyloxy)pyrrolidine-2-carboxylic acid 3b[1]

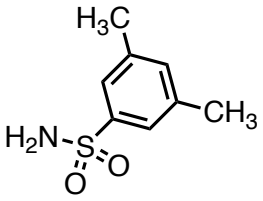


Under N_2 atmosphere, a solution of (*2S*,*4R*)-*trans*-*N*-Cbz-4-hydroxyproline (999.6 mg, 3.8 mmol) in dry-DMF (10 mL) was stirred at 0 °C, then sodium hydride (565.5 mg, 9.4 mmol) was added in two equal portions over a period of 15 min. The reaction mixture was warmed to room temperature and then stirred for further 15 min. 1-Iodododecane (2.2 mL, 9.8 mmol) was added dropwise to the reaction mixture. After being stirred at room temperature for 7 h, the reaction mixture was

quenched with H_2O and added 1N HCl until pH = 1-2. The mixture was extracted with diethyl ether. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : methanol = 20 : 1) to give desired product (1238.3 mg, 78%).

Yellow oil; ^{1}H NMR (270MHz, $CDCl_3$) δ = 7.35-7.29 (m, 5H), 5.17-5.12 (m, 2H), 4.52-4.43 (m, 1H), 4.09-4.04 (m, 1H), 3.72-3.60 (m, 2H), 3.41-3.35 (m, 2H), 2.45-2.09 (m, 2H), 1.55-1.50 (m, 2H), 1.26 (s, 16H), 0.88 (t, *J* = 6.6 Hz, 3H).

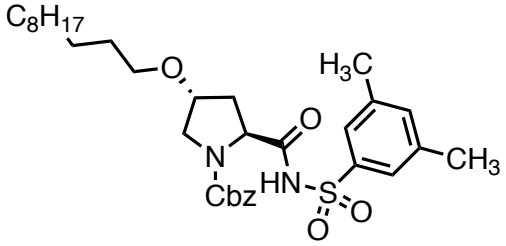
3,5-Dimethylbenzenesulfonamide[1]



To a solution of 3,5- Dimethylbenzenesulfonyl chloride (501 mg, 2.45 mmol) in H_2O (5 mL) was added ammonium hydroxide (3.76 mL, 24.4 mmol) at 100 °C and stirred for 2 h. Excess water was separated as the toluene azeotrope. After the addition of 1 N HCl, the residue was purified by filtration to give desired product (453 mg, quant.).

White solid; m.p. 129-132 °C; 1H NMR (270 MHz, $CDCl_3$); δ = 7.55 (s, 2H), 7.21 (s, 1H), 4.69 (s, 2H), 2.39 (s, 6H).

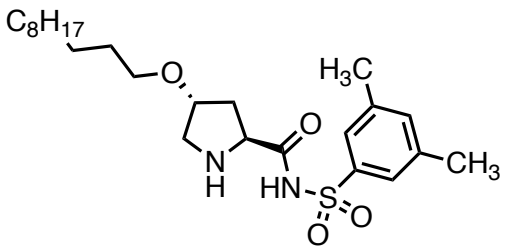
(2*S*,4*R*)-*N*-((3,5-Dimethylphenyl)sulfonyl)-4-(undecyloxy)pyrrolidine-2-carboxamide[1]



Under N_2 atmosphere, EDCI (107 μL, 0.61 mmol) was added dropwise to a solution of **3b** (102 mg, 0.24 mmol), 3,5-Dimethylbenzenesulfonamide (43 mg, 0.23 mmol), and DMAP (89 mg, 0.73 mmol) in *t*-butyl alcohol/1,2-dichloroethane (1 mL, 0.5 mL/0.5 mL v/v) at 0 °C and the mixture was stirred for 10 min. Then the reaction temperature was warmed to room temperature and the mixture was stirred for further 4 h. 1N HCl was added to reaction mixture until pH = 1-2. The mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate) to give desired product (66 mg, 49%).

Yellow oil; ^{1}H NMR (270MHz, $CDCl_3$) δ = 7.61 (s, 2H), 7.30 (s, 5H), 7.13 (s, 1H), 5.14 (q, *J* = 12.4 Hz, 2H), 4.43-4.38 (m, 1H), 4.00-3.97 (m, 1H), 3.50 (brs, 2H), 3.31-3.26 (m, 2H), 2.30-1.96 (m, 8H), 1.45 (brs, 2H), 1.24 (s, 18H), 0.88 (t, *J* = 6.5 Hz, 3H).

(2*S*,4*R*)-*N*-((3,5-Dimethylphenyl)sulfonyl)-4-(undecyloxy)pyrrolidine-2-carboxamide 1b[1]

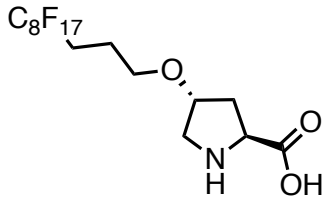


(2*S*,4*R*)-*N*-((3,5-Dimethylphenyl)sulfonyl)-4-(undecyloxy)pyrrolidine-2-carboxamide (44.6 mg, 0.076 mmol) and Pd/C (16.7 mg, 0.016 mmol) in methanol (1.2 mL) was stirred at room temperature for 16 h under H_2 balloon. The Pd/C was removed by filtration through a pad of celite with methanol.

The filtrate was concentrated to give **1b** (32.9 mg, 96%).

Yellow oil; ^{1}H NMR (270MHz, $CDCl_3$) δ = 7.51 (s, 2H), 7.09 (s, 1H), 4.43-4.37 (m, 1H), 4.05 (brs, 1H) 3.69-3.63 (m, 1H), 3.44-3.31 (m, 3H), 2.58-2.46 (m, 1H), 2.34 (s, 6H), 1.99-1.88 (m, 1H), 1.52-1.44 (m, 2H), 1.21 (s, 16H), 0.88 (t, *J* = 6.8 Hz, 3H).

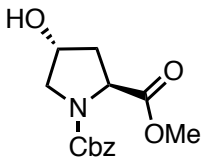
(2*S*,4*R*)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoroundecyl)oxy)pyrrolidine-2-carboxylic acid 1c[2]



3a (1844 mg, 2.54 mmol) and Pd/C (332.9 mg, 0.508 mmol) in methanol (3.80 mL) was stirred at room temperature for 22 h under H_2 balloon. The Pd/C was removed by filtration through a pad of celite with methanol. The filtrate was concentrated. The crude was purified by silica gel chromatography (ethyl acetate : methanol = 8 : 2) to give **1c** (489.1 mg, 32%).

Yellow solid; m.p. 128.8-131.3 °C; ^{1}H NMR (270 MHz, CD_3OD) δ = 4.16-4.14 (m, 1H), 3.80-3.65 (m, 1H), 3.56-3.26 (m, 2H), 2.93-2.88 (m, 2H), 2.53-2.38 (m, 1H), 2.30-2.05 (m, 3H), 1.92-1.82 (m, 2H).

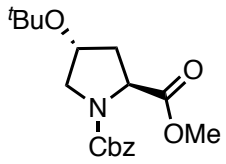
1-Benzyl 2-methyl (2*S*,4*R*)-4-hydroxypyrrolidine-1,2-dicarboxylate[3]



Under N_2 atmosphere, (*2S,4R*)-*trans*-*N*-Cbz-4-hydroxyproline (499.9 mg, 1.89 mmol), methyl iodide (587 μL, 9.42 mmol) and potassium carbonate (528.0 mg, 3.77 mmol) in dry-DMF (3.8 mL) was stirred at room temperature for 16 h. The reaction mixture was diluted with water and was extracted with ethyl acetate. the organic phase was separated and the aqueous phase was extracted with ethyl acetate. The combined organic phase was washed with saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and evaporated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 1) to give desired product (464.4 mg, 88%).

Pink oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33-7.26 (m, 5H), 5.18-4.94 (m, 2H), 4.49-4.39 (m, 2H), 3.71-3.52 (m, 5H), 2.31-2.22(m, 1H), 2.05-1.97 (m, 1H).

1-Benzyl 2-methyl (2*S*,4*R*)-4-(*tert*-butoxy)pyrrolidine-1,2-dicarboxylate[4]

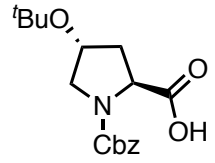


In a 20 mL round bottom flask equipped with a magnetic stirring bar and a condenser coil, $Mg(ClO_4)_2$ (185.4 mg, 0.83 mmol) and 1-benzyl 2-methyl (2*S*,4*R*)-4-hydroxypyrrolidine-1,2-dicarboxylate (464.0 mg, 1.66 mmol) were dissolved in dichloromethane. (3.0 mL). This solution was treated with di-tert-butyl decarbonate (1087.8 mg, 4.98 mmol) in dichloromethane (2.5 mL) and was refluxed while the reaction progress was monitored by TLC. After the mixture was stirred for 46 h, and then the reaction mixture was diluted with water and extracted with dichloromethane. The organic phase was separated and the aqueous phase was extracted with dichloromethane. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, and

the solvent was removed by rotary evaporation. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 2) to give desired product (322.6 mg, 58%).

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37-7.27 (m, 5H), 5.21-5.01 (m, 2H), 4.47-4.40 (m, 1H), 4.33-4.25 (m, 1H), 3.80-3.26 (m, 5H), 2.18-2.04 (m, 2H), 1.17(s, 9H).

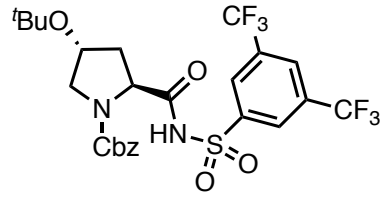
(2*S*,4*R*)-1-((Benzyloxy)carbonyl)-4-(*tert*-butoxy)pyrrolidine-2-carboxylic acid 3f[5]



1-Benzyl 2-methyl (2*S*,4*R*)-4-(*tert*-butoxy)pyrrolidine-1,2-dicarboxylate (161.6 mg, 0.48 mmol) and LiOH·H_2O (28.3 mg, 0.68 mmol) in H_2O/THF (1.9 mL, 1.4 mL/0.5 mL v/v) was stirred at room temperature for 6 h. The reaction mixture was quenched with 1N HCl. The aqueous layer was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4, filtered, and concentrated to give **3f** (158 mg, quant.).

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36-7.29 (m, 5H), 5.21-5.08 (m, 2H), 4.50-4.44 (m, 1H), 4.34-4.29 (m, 1H), 3.78-3.68 (m, 1H), 3.40-3.28 (m, 1H), 2.32-2.12 (m, 2H), 1.18 (s, 9H).

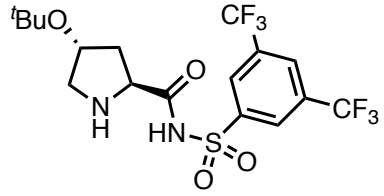
Benzyl (2*S*,4*R*)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)-4-(*tert*-butoxy)pyrrolidine-1-carboxylate



3f (82 mg, 0.26 mmol), DMAP (92.2 mg, 0.77 mmol) and EDCI (112.5 µL, 0.64 mmol) in *t*-butyl alcohol/1,2-dichloroethane (1.2 mL, 0.6 mL/0.6 mL v/v) was stirred at 0 °C for 10 min. 3,5-Bis(trifluoromethyl)benzenesulfonamide (71.1 mg, 0.24 mmol) in *t*-butyl alcohol/1,2-dichloroethane (1.2 mL, 0.6 mL/0.6 mL v/v) was added dropwise to the reaction mixture, and then the mixture was stirred at room temperature for 24 h. 1N HCl was added to reaction mixture until pH = 1-2. The mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 3) to give desired product (85.1 mg, 56%).

Colorless Oil; ^{1}H NMR (400 MHz, CD_3OD) δ = 8.53, (s, 2H), 8.12, (s, 1H), 7.37 (s, 5H), 5.28-5.14 (m, 2H), 4.38-4.35 (m, 1H), 4.23-4.18 (m, 1H), 3.53-3.49 (m, 1H), 3.28-3.24 (m, 1H), 2.51-2.46 (m, 1H), 1.89-1.84 (m, 1H), 1.15 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.88, 157.81, 141.35, 135.53, 128.92, 128.70, 128.56, 128.10, 127.40, 123.76, 121.04, 74.34, 68.85, 68.54, 59.47, 53.22, 34.11, 28.18; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.80; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{25}H_{26}F_6N_2O_6S$ 597.1494, found: 597.1492.

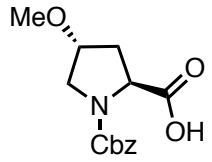
(2*S*,4*R*)-*N*-((3,5-Bis(trifluoromethyl)phenyl)sulfonyl)-4-(*tert*-butoxy)pyrrolidine-2-carboxamide 1e



Benzyl (2*S*,4*R*)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)-4-(*tert*-butoxy)pyrrolidine-1-carboxylate (67.8 mg, 0.11 mmol) and Pd/C (48.2 mg, 0.55 mmol) in methanol (2.3 mL) was stirred at room temperature for 2 h under H_2 balloon. The catalyst was removed by filtration through a pad of celite with methanol. The filtrate was concentrated. The crude was purified by silica gel chromatography (dichloromethane : methanol = 10 : 1) to give **1e** (36.1 mg, 69%).

White Solid; m.p. 42.2-43.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.38 (s, 2H), 7.98 (s, 1H), 4.51 (m, 1H), 4.35 (brs, 1H), 3.69 (dd, *J* = 12 Hz, 4.8 Hz, 1H), 3.33 (d, *J* = 12 Hz, 1H), 2.35-2.29 (m, 1H), 2.11-2.04 (m, 1H), 1.14 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.15, 145.60, 132.32, 131.99, 127.04, 125.19, 121.47, 75.01, 69.76, 62.27, 53.78, 38.36, 28.01; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.75; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{17}H_{20}F_6N_2O_4S$ 463.1126, found: 463.1122.

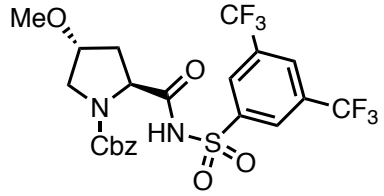
(2*S*,4*R*)-1-((Benzyloxy)carbonyl)-4-methoxypyrrolidine-2-carboxylic acid 3d[6]



Under N_2 atmosphere, a solution of (*2S,4R*)-*trans*-*N*-Cbz-4-hydroxyproline (1000 mg, 3.77 mmol) in dry-THF (10 mL) was stirred at 0 °C, then sodium hydride (301.6 mg, 7.539 mmol) was added. The reaction mixture was warmed to room temperature and then stirred for 10 min. Iodomethane (470 μL, 7.539 mmol) was added dropwise to the reaction mixture. After stirred at room temperature for 18 h, the reaction mixture was quenched with H_2O and added 1N HCl until pH = 1-2. The mixture was extracted with dichloromethane. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 1) to give **3d** (903.8 mg, 86%).

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 11.27 (s, 1H), 7.34-7.26 (m, 5H), 5.19-5.07 (m, 2H), 4.50-4.44 (m, 1H), 4.01-3.98 (m, 1H), 3.77-3.57 (m, 2H), 3.30 (s, 3H), 2.45-2.33 (m, 1H), 2.21-2.10 (m, 1H).

Benzyl (2*S*,4*R*)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)-4-methoxypyrrolidine-1-carboxylate

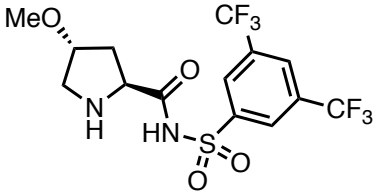


3d (80.3 mg, 0.286 mmol), DMAP (105.4 mg, 0.863 mmol) and EDCI (101 μL, 0.575 mmol) in *t*-butyl alcohol/1,2-dichloroethane (2 mL, 1 mL/1 mL v/v) was stirred at 0 °C for 10 min. 3,5-Bis(trifluoromethyl)benzenesulfonamide (90.0 mg, 0.273 mmol) in *t*-butyl alcohol/1,2-dichloroethane (2 mL, 1 mL/1 mL v/v) was added dropwise to the reaction mixture, and then the mixture was stirred at room temperature for 12 h. 1N HCl was added to reaction mixture until pH = 1-2. The mixture was extracted with ethyl acetate. The organic layer was washed with 1N HCl, saturated aqueous

$NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 3) to give desired product (111.6 mg, 74%).

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.46, (s, 2H), 7.94, (s, 1H), 7.26 (s, 5H), 5.15 (brs, 2H), 4.43 (s, 1H), 3.91 (s, 1H), 3.59-3.20 (m, 5H), 2.29-2.14 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.16, 157.23, 145.20, 135.45, 132.22, 128.52, 127.87, 126.62, 123.90, 121.18, 118.46, 78.41, 77.24, 68.43, 56.59, 51.80, 29.72; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.88; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{22}H_{20}F_6N_2O_6S$ 555.1025, found: 555.1019.

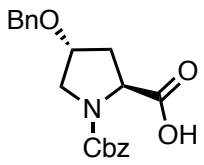
(2*S*,4*R*)-*N*-((3,5-Bis(trifluoromethyl)phenyl)sulfonyl)-4-methoxypyrrolidine-2-carboxamide 1f



Benzyl (*2S,4R*)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)-4-methoxypyrrolidine-1-carboxylate (56.0 mg, 0.101 mmol) and Pd/C (43.0 mg, 0.020 mmol) in methanol (2 mL) was stirred at room temperature for 2 h under H_2 balloon. The Pd/C was removed by filtration through a pad of celite with methanol. The filtrate was concentrated. The crude was purified by silica gel chromatography (chloroform : methanol = 10 : 1) to give **1f** (41.1 mg, 97%).

White solid; m.p. 46.6-46.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.38 (s, 2H), 8.00 (s, 1H), 4.53-4.49 (m, 1H), 4.09 (s, 1H), 3.64 (s, 2H), 3.30 (s, 3H), 2.59-2.54 (m, 1H), 2.02-1.95 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 173.94, 145.45, 127.12, 125.29, 124.17, 121.38, 79.24, 62.14, 56.68, 51.67, 35.35; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.78; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{14}H_{14}F_6N_2O_4S$ 421.0657, found: 421.0653.

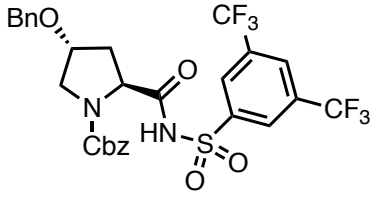
(2*S*,4*R*)-4-(Benzyloxy)-1-((benzyloxy)carbonyl)pyrrolidine-2-carboxylic acid 3e[6]



Under N_2 atmosphere, a solution of (*2S,4R*)-*trans*-*N*-Cbz-4-hydroxyproline (1000 mg, 3.770 mmol) in dry-THF (10 mL) was stirred at 0 °C, then sodium hydride (60% dispersion in oil, 301.6 mg, 7.539 mmol) was added. The reaction mixture was warmed to room temperature and then stirred for 10 min. Benzyl bromide (897 μL, 7.539 mmol) was added dropwise to the reaction mixture. After stirred at room temperature for 18 h, the reaction mixture was quenched with H_2O and added 1N HCl until pH = 1-2. The mixture was extracted with dichloromethane. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 1) to give **3e** (1107.3 mg, 83%).

Colorless Oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.70 (s, 1H), 7.30-7.25 (m, 10H), 5.15-5.05 (m, 2H), 4.55-4.38 (m, 3H), 4.14-4.10 (m, 1H), 3.82-3.57 (m, 2H), 2.42-2.34 (m, 1H), 2.16-2.06 (m, 1H).

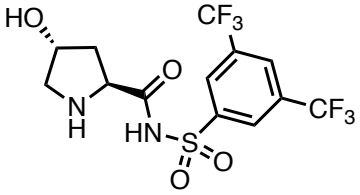
Benzyl (2*S*,4*R*)-4-(benzyloxy)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)pyrrolidine-1-carboxylate



3e (150 mg, 0.42 mmol), DMAP (153.7 mg, 1.27 mmol) and WSCD·HCl (161.7 mg, 0.84 mmol) in *t*-butyl alcohol/1,2-dichloroethane (2.0 mL, 1.0 mL/1.0 mL v/v) was stirred at 0 °C for 10 min. 3,5-Bis(trifluoromethyl)benzenesulfonamide (112.2 mg, 0.38 mmol) in *t*-butyl alcohol/1,2-dichloroethane (2.2 mL, 1.1 mL/1.1 mL v/v) was added dropwise to the reaction mixture, and then the mixture was stirred at room temperature for 15 h. 1N HCl was added to reaction mixture until pH = 1-2. The mixture was extracted with ethyl acetate. The organic layer was washed with 1N HCl, saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 3) to give desired product (238.6 mg, 99%).

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) 8.42 (s, 2H), 7.92 (s, 1H), 7.27-7.18 (m, 10H), 5.10-4.94 (m, 2H), 4.41-4.32 (m, 3H), 4.10 (s, 1H), 3.62-3.46 (m, 2H), 2.23 (brs, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.17, 156.75, 144.63, 137.72, 135.81, 132.16, 131.97, 128.52, 128.21, 127.85, 127.78, 127.63, 125.67, 124.06, 121.18, 118.76, 71.33, 67.88, 62.08, 52.15, 35.26; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.78; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{28}H_{24}F_6N_2O_6S$ 631.1338, found: 631.1338.

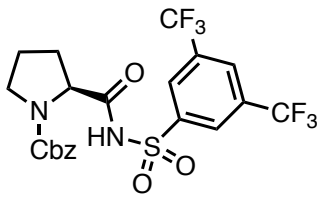
(2*S*,4*R*)-*N*-((3,5-Bis(trifluoromethyl)phenyl)sulfonyl)-4-hydroxypyrrolidine-2-carboxamide 1g



Benzyl (*2S,4R*)-4-(benzyloxy)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)pyrrolidine-1-carboxylate (56.7 mg, 0.090 mmol) and $Pd(OH)_2$ (12.6 mg, 0.018 mmol) in methanol (2 mL) was stirred at 35 °C for 24 h under H_2 balloon. The $Pd(OH)_2$ was removed by filtration through a pad of celite with methanol. The filtrate was concentrated. The crude was purified by silica gel chromatography (chloroform : methanol = 5 : 1) to give **1g** (36.5 mg, 54%).

White solid; m.p. 36.5-37.3 °C; ^{1}H NMR (400 MHz, CD_3OD) δ = 8.36 (s, 2H), 8.03 (s, 1H), 4.39 (t, *J* = 3.6 Hz, 1H), 4.15-4.10 (m, 1H), 3.24-3.20 (m, 1H), 3.10-3.07 (m, 1H), 2.31-2.26 (m, 1H), 1.91-1.84 (m, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ = 173.53, 146.47, 131.25, 127.79, 124.56, 121.71, 69.77, 61.09, 53.32, 38.43; ^{19}F NMR (376 MHz, CD_3OD) δ = -64.10; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{13}H_{12}F_6N_2O_4S$ 407.0500, found: 407.0495.

Benzyl (*S*)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)pyrrolidine-1-carboxylate

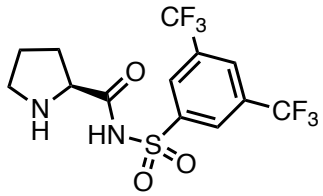


((Benzyloxy)carbonyl)-*L*-proline (100.3 mg, 0.40 mmol), DMAP (146.9 mg, 1.20 mmol) and WSCD·HCl (154.5 mg, 0.80 mmol) in *t*-butyl alcohol/1,2-dichloroethane (2.0 mL, 1.0 mL/1.0 mL v/v) was stirred at 0 °C for 10 min. 3,5-Bis(trifluoromethyl)benzenesulfonamide (111.7 mg, 0.38 mmol) in *t*-butyl alcohol/1,2-dichloroethane (2.0 mL, 1.0 mL/1.0 mL v/v) was added dropwise to the reaction mixture, and then

the mixture was stirred at room temperature for 72 h. 1N HCl was added to reaction mixture until pH = 1-2. The mixture was extracted with ethyl acetate. The organic layer was washed with 1N HCl, saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 3) to give desired product (187.5 mg, 94%).

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.46 (s, 2H), 8.00 (s, 1H), 7.29 (s, 5H), 5.17-5.03 (m, 2H), 4.29 (s, 1H), 3.41 (d, *J* = 8.0 Hz, 2H), 2.28-1.83 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.50, 156.93, 143.24, 135.81, 128.56, 128.30, 128.13, 127.90, 123.92, 121.46, 118.49, 68.01, 61.97, 47.16, 28.20, 24.32; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -62.83; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{21}H_{18}F_6N_2O_5S$ 525.0919, found: 525.0915.

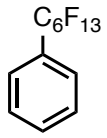
(*S*)-*N*-((3,5-Bis(trifluoromethyl)phenyl)sulfonyl)pyrrolidine-2-carboxamide 1h[7]



Benzyl (*S*)-2-(((3,5-bis(trifluoromethyl)phenyl)sulfonyl)carbamoyl)pyrrolidine-1-carboxylate (256 mg, 0.49 mmol) and Pd/C (208 mg, 0.098 mmol) in methanol (2.44 mL) was stirred at room temperature for 7 h under H_2 balloon. The Pd/C was removed by filtration through a pad of celite with methanol. The filtrate was concentrated to give **1h** (175 mg, 92%).

White solid; m.p. 186.4-186.8 °C; ^{1}H NMR (500 MHz, CD_3OD) δ = 8.36 (s, 2H), 8.03 (s, 1H), 3.93-3.90 (m, 1H), 3.25-3.09 (m, 2H), 2.25-2.18 (m, 1H), 1.96-1.76 (m, 3H).

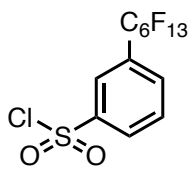
(Perfluorohexyl)benzene 5b[8]



To a suspension of iodobenzene (546 μL, 4.90 mmol) and Cu powder (4.99 g, 78.43 mmol) in dry-DMSO (7.0 ml) was added perfluorohexyl iodide (3.18 mL, 14.71 mmol) under N_2 atmosphere at 120 °C and stirred for 19 h. After the addition of saturated aqueous $Na_2S_2O_3$ solution, Cu powder was removed by filtration through a pad of Celite and washed with diethyl ether. The filtrate was extracted with diethyl ether. The organic phase was separated and the aqueous phase was extracted with diethyl ether. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane) to give **5b** (1494.2 mg, 77%).

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60-7.55 (m, 3H), 7.51-7.48 (m, 2H).

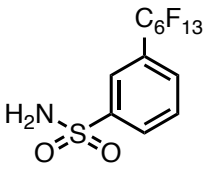
3-(Perfluorohexyl)benzenesulfonyl chloride



5b (200.6 mg, 0.51 mmol) was added to chlorosulfonamide (503 μL, 7.57 mmol) at room temperature. The mixture was stirred at 120 °C for 3 h, and then cooled to room temperature was pippeted cautiously onto ice. The aqueous layer was extracted with diethyl ether. The organic layer was dried over Na_2SO_4, filtered, concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane) to give desired product (112.2 mg, 45%).

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.30-8.28 (m, 2H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 1H).

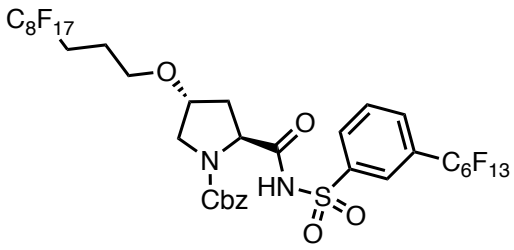
3-(Pq6erfluorohexyl)benzenesulfonamide 6b



In a 50 mL round bottom flask equipped with a magnetic stirring bar and a condenser coil, 3-(Perfluorohexyl)benzenesulfonyl chloride (200.8 mg, 0.51 mmol) was dissolved in THF (2.7 mL). This solution was treated with 25% ammonia solution (756 µL, 5.05 mmol) and was refluxed for 19 h. Excess water was separated as the toluene azeotrope. After the addition of 1N HCl, the suspension was purified by filtration to give **6b** (190.7 g, 80%).

Yellow solid; m.p. 123.2-123.6 °C; ^{1}H NMR (400 MHz, DMSO-d6) δ = 8.17 (d, *J* = 8.0 Hz, 1H), 8.09 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.88 (t, *J* = 8.0 Hz, 1H), 7.63 (s, 2H); ^{13}C NMR (101 MHz, DMSO-d6) δ = 145.21, 130.55, 129.91, 129.79, 127.82, 123.69; ^{19}F NMR (376 MHz, DMSO-d6) δ = -80.11, -109.62, -121.14, -122.44, -125.64; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{12}H_6F_{13}NO_2S$ 475.9990, found: 475.9983.

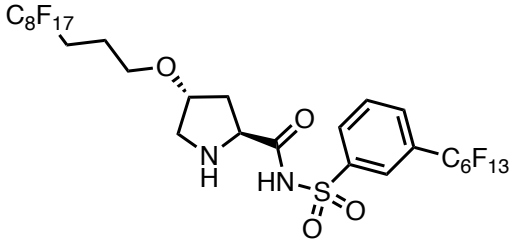
Benzyl (2*S*,4*R*)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)oxy)-2-(((3-(perfluorohexyl)phenyl)sulfonyl)carbamoyl)pyrrolidine-1-carboxylate



3a (127 mg, 0.18 mmol), DMAP (42.1 mg, 0.35 mmol) and EDCI (92.6 µL, 0.53 mmol) in *t*-butyl alcohol/1,2-dichloroethane (0.2 mL, 0.1 mL/0.1 mL v/v) was stirred at 0 °C for 10 min. **6b** (61.2 mg, 0.13 mmol) in *t*-butyl alcohol/1,2-dichloroethane (0.4 mL, 0.2 mL/0.2 mL v/v) was added dropwise to the reaction mixture, and then the mixture was stirred at room temperature for 24 h. 1N HCl was added to reaction mixture until pH = 1-2. The mixture was extracted with ethyl acetate. The organic layer was washed with 1N HCl, saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 3) to give desired product (96.4 mg, 63%).

White solid; 112-113 °C; ^{1}H NMR (400 MHz, CD_3OD) δ = 8.21-8.12 (m, 2H), 7.88-7.80 (m, 1H), 7.75-7.62 (m, 1H), 7.22-7.02 (m, 5H), 4.92-4.62 (m, 2H), 4.22-4.15 (m, 1H), 3.96 (brs, 1H), 3.56-3.36 (m, 4H), 2.30-2.04 (m, 3H), 1.83-1.67 (m, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ = 173.23, 155.06, 140.99, 136.51, 131.54, 129.77, 128.13, 127.76, 127.51, 127.46, 126.90, 126.35, 121.37, 118.81, 118.64, 117.97, 115.39, 114.01, 113.61, 112.58, 112.44, 112.33, 111.50, 111.17, 111.08, 110.04, 76.59, 66.98, 59.51, 59.40, 52.01, 36.32, 27.46, 20.49; ^{19}F NMR (376 MHz, CD_3OD) δ = -82.27, -111.73, -115.29, -122.25, -122.45, -122.49, -122.63, -122.80, -123.66, -124.34, -127.17; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{36}H_{24}F_{30}N_2O_6S$ 1183.0954, found: 1183.0941.

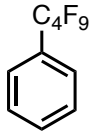
(2*S*,4*R*)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoroundecyl)oxy)-*N*-((3-(perfluorohexyl)phenyl)sulfonyl)pyrrolidine-2-carboxamide 1j



Benzyl (2*S*,4*R*)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)oxy)-2-(((3-(perfluorohexyl)phenyl)sulfonyl)carbamoyl) pyrrolidine-1-carboxylate (23.6 mg, 0.02 mmol) and Pd/C (4.3 mg, 0.004 mmol) in methanol (0.3 mL) was stirred at room temperature for 24 h under H_2 balloon. The Pd/C was removed by filtration through a pad of celite with methanol. The filtrate was concentrated. The crude was purified by recyclization (methanol) to give **1j** (15.0 mg, 71%).

White solid; m.p. 89-90 °C; ^{1}H NMR (500 MHz, CD_3OD) δ = 8.13-8.11 (m, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 4.11 (brs, 1H), 4.03-3.99 (m, 1H), 3.50-3.40 (m, 2H), 3.25-3.21 (m, 2H), 2.48-2.43 (m, 1H), 2.23-2.12 (m, 2H), 1.91-1.75 (m, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ = 172.84, 144.76, 130.99, 129.64, 128.78, 128.61, 125.63, 121.53, 119.58, 118.86, 118.42, 117.65, 117.09, 115.76, 114.72, 113.38, 113.13 110.55, 108.23, 107.34, 106.59, 78.02, 67.12, 61.03, 50.82, 35.02, 27.47, 20.55; ^{19}F NMR (466 MHz, CD_3OD) δ = -82.32, -111.50, -115.26, -122.30, -122.49, -122.61, -122.80, -123.68, -124.33, -127.18; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{28}H_{18}F_{30}N_2O_4S$ 1049.0586, found: 1049.0568.

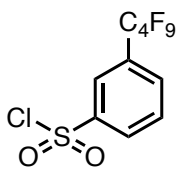
(Perfluorobutyl)benzene 5c[9]



To a suspension of iodobenzene (546 μL, 4.90 mmol) and Cu powder (4.99 g, 78.43 mmol) in dry-DMSO (7.0 ml) was added perfluorobutyl iodide (2.53 mL, 14.71 mmol) under N_2 atmosphere at 120 °C and stirred for 14 h. After the addition of saturated aqueous $Na_2S_2O_3$ solution, Cu powder was removed by filtration through a pad of Celite and washed with diethyl ether. The filtrate was extracted with diethyl ether. The organic phase was separated and the aqueous phase was extracted with diethyl ether. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane) to give **5c** (406.1 mg, 28%).

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60-7.56 (m, 3H), 7.52-7.49 (m, 2H).

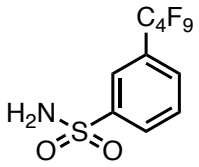
3-(Perfluorobutyl)benzenesulfonyl chloride[10]



5c (299.5 mg, 1.01 mmol) was added to chlorosulfonamide (1.0 mL, 15.20 mmol) at room temperature. The mixture was stirred at 120 °C for 2.5 h, and then cooled to room temperature was pippeted cautiously onto ice. The aqueous layer was extracted with diethyl ether. The organic layer was dried over Na_2SO_4, filtered, concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane) to give desired product (229 mg, 57%).

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.29-8.28 (m, 2H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 7.5 Hz, 1H).

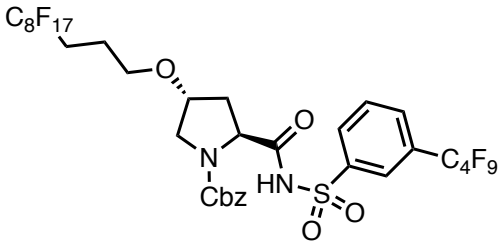
3-(Perfluorobutyl)benzenesulfonamide 6c



In a 50 mL round bottom flask equipped with a magnetic stirring bar and a condenser coil, 3-(perfluorobutyl)benzenesulfonyl chloride (200.0 mg, 0.68 mmol) was dissolved in THF. This solution was treated with 25% ammonia solution (1.01 mL, 6.76 mmol) and was refluxed for 19 h. Excess water was separated as the toluene azeotrope. After the addition of 1N HCl, the suspension was purified by filtration to give **6c** (217.7 mg, 86%).

Yellow solid; m.p. 106.9-107.7 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.17-8.15 (m, 2H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.71 (t, *J* = 8.1 Hz, 1H), 4.88 (brs, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 143.13, 131.05, 130.34, 130.03, 129.88, 125.22 115.94, 115.10, 114.02, 110.44; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -80.86, -110.95, -122.28, -125.40; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{36}H_{24}F_{30}N_2O_6S$ 1183.0954, found: 1183.0941..

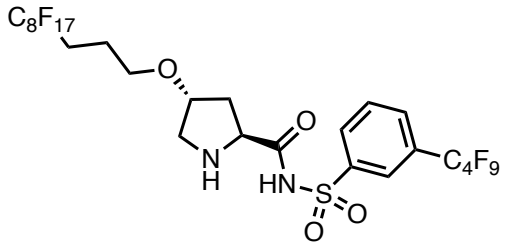
Benzyl (2*S*,4*R*)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)oxy)-2-(((3-(perfluorobutyl)phenyl)sulfonyl)carbamoyl)pyrrolidine-1-carboxylate



3a (102.5 mg, 0.14 mmol), DMAP (51.8 mg, 0.42 mmol) and WSCD·HCl (54.2 mg, 0.28 mmol) in *t*-butyl alcohol/1,2-dichloroethane (0.7 mL, 0.35 mL/0.35 mL v/v) was stirred at 0 °C for 10 min. **6c** (50.4 mg, 0.28 mmol) in *t*-butyl alcohol/1,2-dichloroethane (0.7 mL, 0.35 mL/0.35 mL v/v) was added dropwise to the reaction mixture, and then the mixture was stirred at room temperature for 5 h. 1N HCl was added to reaction mixture until pH = 1-2. The mixture was extracted with ethyl acetate. The organic layer was washed with 1N HCl, saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 3) to give desired product (124.2 mg, 81%).

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.58 (s, 1H), 8.28-8.26 (m, 2H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.37 (s, 5H), 5.24-5.16 (m, 2H), 4.41-4.38 (m, 1H), 4.02-3.98 (m, 1H), 3.59-3.38 (m, 4H), 2.54-2.49 (m, 1H), 2.17-1.96 (m, 3H), 1.84-1.77 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.53, 157.72, 139.87, 135.54, 132.03, 130.31, 130.06, 129.81, 129.59, 128.73, 128.63, 128.20, 127.11, 118.84, 118.61,118.46, 118.27, 118.15, 115.96, 115.74, 115.62, 115.41, 115.06, 114.75, 68.59, 68.41, 67.79, 59.47, 51.58, 32.19, 27.81, 20.92; ^{19}F NMR (376 MHz, $CDCl_3$) δ = -80.64, -80.88, -110.95, -114.17, -121.60, -121.77, -122.29, -122.58, -123.29, -125.40, -125.97; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{34}H_{24}F_{26}N_2O_6S$ 1083.1018, found: 1083.1029.

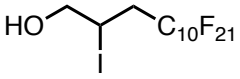
(2*S*,4*R*)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoroundecyl)oxy)-*N*-((3-(perfluorobutyl)phenyl)sulfonyl)pyrrolidine-2-carboxamide 1k



Benzyl (2*S*,4*R*)-4-((4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)oxy)-2-(((3-(perfluorobutyl)phenyl)sulfonyl)carbamoyl) pyrrolidine-1-carboxylate (112.0 mg, 0.10 mmol) and Pd/C (22.0 mg, 0.02 mmol) in methanol (2.1 mL) was stirred at room temperature for 23 h under H_2 balloon. The Pd/C was removed by filtration through a pad of celite with methanol. The filtrate was concentrated. The crude was purified by recyclization (methanol) to give **1k** (64.2 mg, 65%).

White solid; m.p. 28.8-29.6 °C; ^{1}H NMR (500 MHz, CD_3OD) δ = 8.20-8.18 (m, 2H), 7.76 (d, *J* = 10.5 Hz, 1H), 7.68 (t, *J* = 10.0 Hz, 1H), 4.20 (d, *J* = 2.5 Hz, 1H), 4.13-4.09 (m, 1H), 3.58-3.47 (m, 2H), 3.34-3.28 (m, 2H), 2.54 (dd, *J* = 17.5 Hz, *J* = 9.5 Hz, 1H), 2.31-2.18 (m, 2H), 1.96-1.78 (m, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ = 172.86, 144.73, 130.96, 129.35, 128.98, 128.42, 125.59, 121.35, 118.85, 118.58, 116.05, 115.72, 113.18, 111.19, 110.94, 110.53, 108.28, 107.29, 105.60, 77.91, 67.12, 61.10, 50.88, 35.12, 27.48, 20.54; ^{19}F NMR (466 MHz, CD_3OD) δ = -82.29, -82.56, -111.73, -115.29, -122.61, -122.79, -123.50, -123.63, -124.31, -126.62, -127.17; HRMS-DART (*m/z*):$[M+H]^+$ calcd for $C_{26}H_{18}F_{26}N_2O_4S$ 949.0650, found: 949.0659.

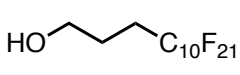
4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Henicosafluoro-2-iodotridecan-1-ol[11]



A stirred solution of allyl alcohol (3.82 µL, 6.811 mmol) and perfluorodecyl iodide (1.1 g, 1.703 mmol) was heated at 90 ◦C under N_2 atmosphere. To this solution was added AIBN (28.0 mg, 0.170 mmol), and the mixture was heated at 90 ◦C for 18h. The reaction mixture was concentrated. The crude was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 3) to give desired product (984.7 mg, 82%).

White solid; m.p. 130-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.46-4.40 (m, 1H), 3.84-3.76 (m, 2H), 3.08-2.69 (m, 2H), 2.02 (t, *J* = 6.4 Hz, 1H).

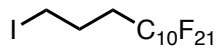
4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-Henicosafluorotridecan-1-ol 7[11]



To a stirred solution of 4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-henicosafluoro-2-iodotridecan-1-ol (984.7 g, 1.399 mmol) in dry toluene (6 mL) at 90 °C under N_2 atmosphere, Bu_3SnH (451 µL, 1.678 mmol) and AIBN (23 mg, 0.140 mmol) were added. After the mixture was subsequently heated at 90 °C for 19 h, the solvent was evaporated. The residue was subjected to column chromatography on silica gel (ethyl acetate : *n*-hexane = 1 : 5) to give desired product (514.4 mg, 64%).

White solid; m.p. 82-83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.74 (t, *J* = 5.6 Hz, 2H), 2.28-2.14 (m, 2H), 1.90-1.83 (m, 2H).

1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-Henicosafluoro-13-iodotridecane 8[12]



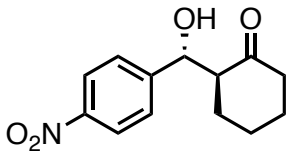
7 (847.7 mg, 1.47 mmol) was added to a solution of triphenylphosphine (694.8 mg, 2.65 mmol) and imidazole (200.2 mg, 2.94 mmol) in diethyl ether/acetonitrile (7.3 mL, 4.4 mL/2.9 mL v/v), and the solution was cooled down to 0 °C. Solid iodine (745.7 mg, 2.94 mmol) wad added in one portion, and the mixture was stirred at this temperature for an additional 10 min, then the reaction mixture was warmed to room temperature and stirred for 5 h. The reaction mixture was diluted with saturated aqueous $Na_2S_2O_3$ solution, and was extracted with ethyl acetate. The organic phase was separated and the aqueous phase was extracted with ethyl acetate. The combined organic phase was washed with saturated aqueous $Na_2S_2O_3$ solution and brine, dried over Na_2SO_4, filtered, concentrated. The crude was purified by silica gel chromatography (*n*-hexane) to give **6** (948.0 mg, 98%).

White solid; m.p. 72-73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.24 (t, *J* = 6.8 Hz, 2H), 2.28 -2.09 (m, 4H).

2. Asymmetric aldol reaction

Table 1, entry 1

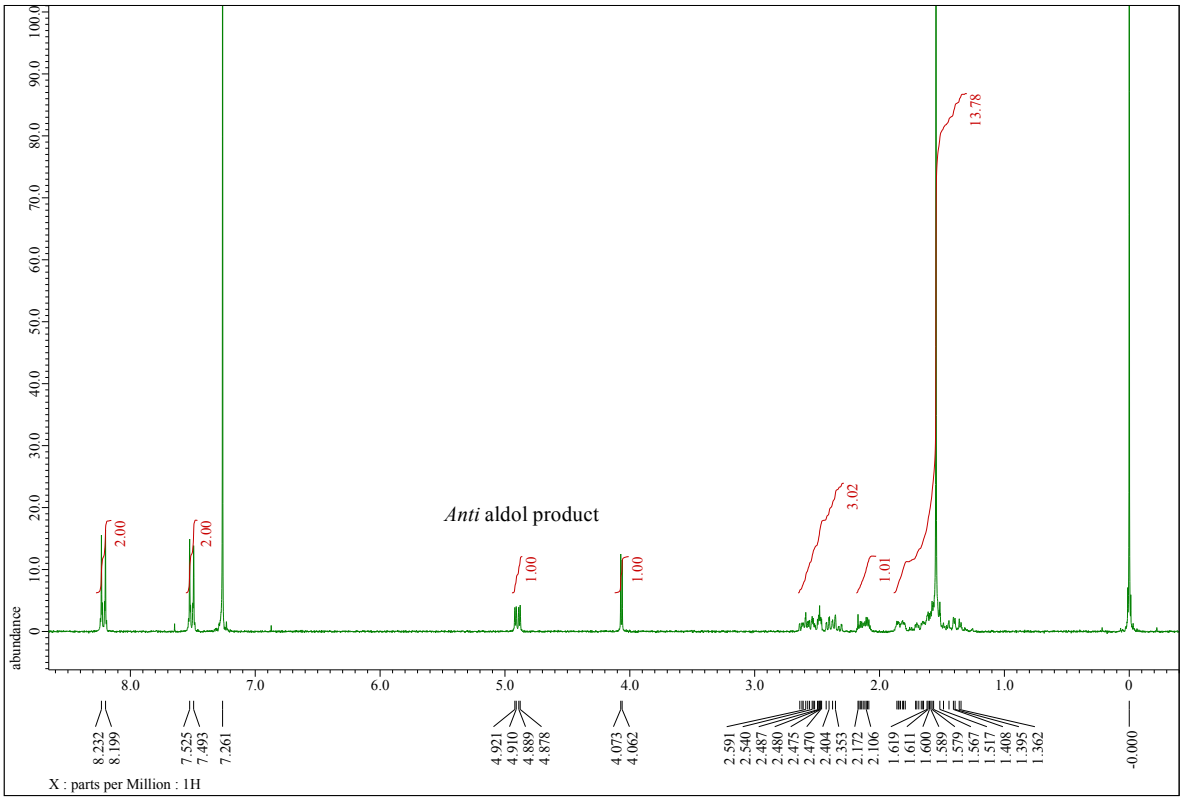
(*S*)-2-((*R*)-Hydroxy(4-nitrophenyl)methyl)cyclohexan-1-one 4a[5)]



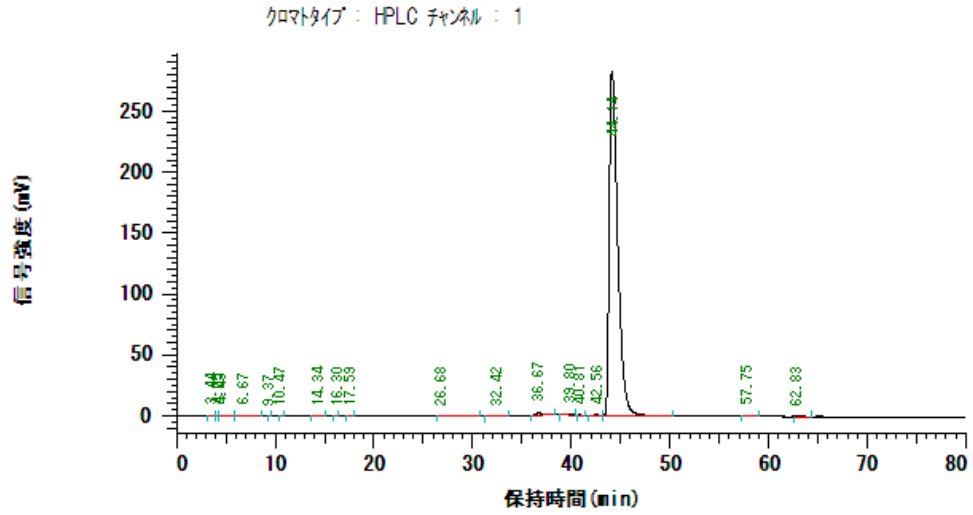
To a solution of **1a** (5.63 mg, 0.0065 mmol) in dry-THF (660 μL) was added cyclohexanone (680 μL, 6.57 mmol) and 4-nitrobenzaldehyde (100.3 mg, 0.66 mmol). After being stirred at room temperature for 96 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : *n*-hexane = 1 : 3) to give 2-(hydroxy(4-nitrophenyl)methyl)cyclohexan-1-one **4a** (143.9 mg, 87%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. *Ee* of the *anti* aldol product was determined *via* HPLC of the crude product after confirming the retention time of each racemic compound.

White solid; m.p. 97.7-98.8 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.22 (d, *J* = 8.9 Hz, 2H), 7.51 (d, *J* = 8.6 Hz, 2H), 4.90 (dd, *J* = 8.6 Hz, 3.0 Hz, 1H), 4.07 (d, *J* = 3.0 Hz, 1H), 2.64-2.31 (m, 3H), 2.17-2.09 (m, 1H), 1.86-1.35 (m, 5H).

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



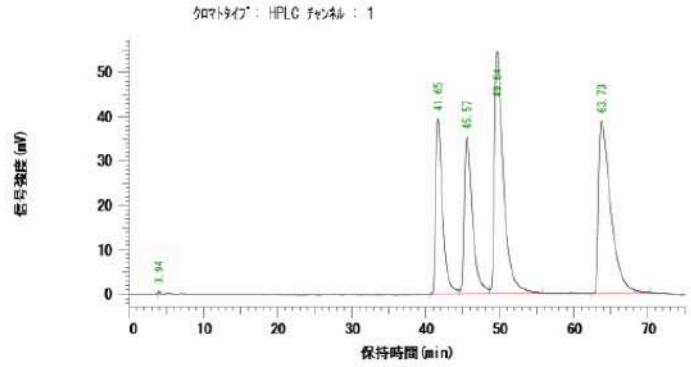
ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1

ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	3.44	6761	0.040	BV
2	4.05	6385	0.038	VV
3	4.43	6897	0.041	VB
4	6.67	13333	0.079	BB
5	9.37	238	0.001	BB
6	10.47	487	0.003	BB
7	14.34	1350	0.008	BB
8	16.30	760	0.004	BB
9	17.59	2117	0.012	BB
10	26.68	3621	0.021	BB
11	32.42	3830	0.023	BB
12	36.67	122086	0.720	BB
13	39.80	22389	0.132	BB
14	40.81	6417	0.038	BB
15	42.56	36638	0.216	BV
16	44.14	16704163	98.465	VB
17	57.75	25522	0.150	BB
18	62.83	1626	0.010	BB
		16964620	100.000	

Yield : 87%, *anti* : *syn* = 100 : 0, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 44.14 min (major), t_R = 62.83 min (minor)]

HPLC analysis of racemic compound (*anti* form + *syn* form)

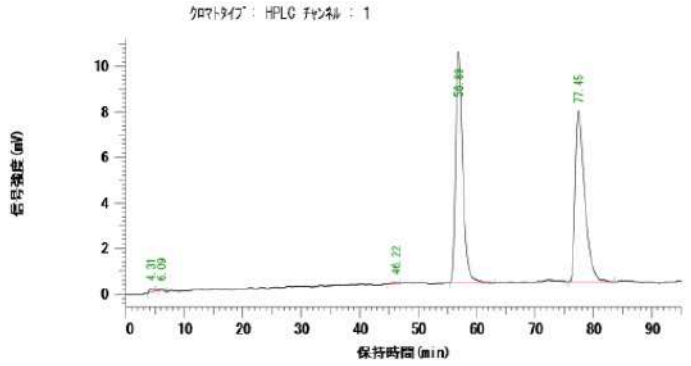


ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ: aldol
ｶﾗﾑ名 : Column
ﾎﾟﾝﾌﾟA(ﾒｲﾝ) : L-2130
ﾎﾟﾝﾌﾟA 溶離液A: iPrOH
ﾎﾟﾝﾌﾟA 溶離液B: Hex
ﾎﾟﾝﾌﾟA 溶離液C:
ﾎﾟﾝﾌﾟA 溶離液D:
ﾒｿｯﾄﾞ作成者:
分析ﾌｧｲﾙｺﾒﾝﾄ:

ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	3.94	9785	0.070	VB
2	41.65	2510898	17.876	BV
3	45.57	2634853	18.759	VV
4	49.64	4530337	32.253	VB
5	63.73	4360248	31.042	BB
		14046121	100.000	

HPLC analysis of racemic compound *(anti* form)

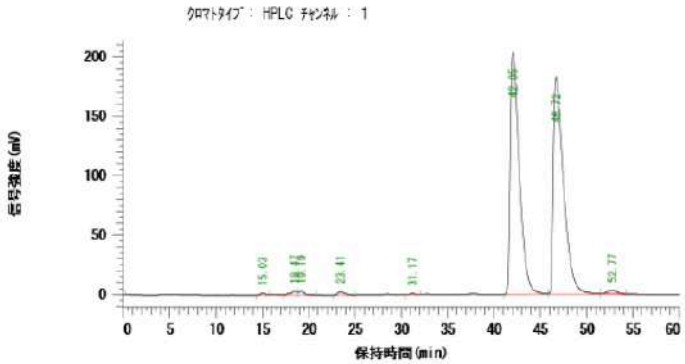


ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ: iProOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名 : Column
ﾎﾟﾝﾌﾟA(ﾒｲﾝ) : L-2130
ﾎﾟﾝﾌﾟA 溶離液A: iPrOH
ﾎﾟﾝﾌﾟA 溶離液B: Hex
ﾎﾟﾝﾌﾟA 溶離液C:
ﾎﾟﾝﾌﾟA 溶離液D:
ﾒｿｯﾄﾞ作成者:
分析ﾌｧｲﾙｺﾒﾝﾄ:

ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	4.31	7093	0.417	BB
2	6.09	5637	0.332	BB
3	46.22	4017	0.236	BB
4	56.89	850386	50.024	BB
5	77.45	832825	48.991	BB
		1699958	100.000	

HPLC analysis of racemic compound (*syn* form)



ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： iPrOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名： Column
ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4
ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：
ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

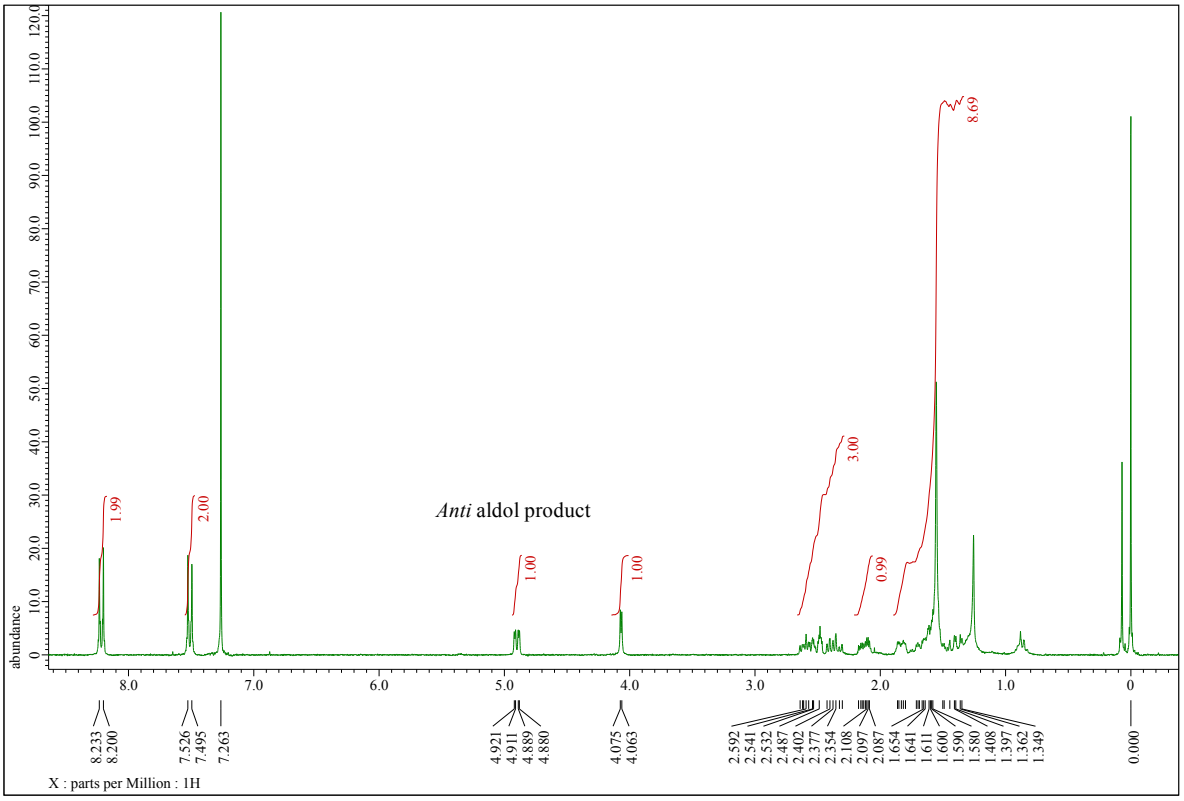
ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	0.01	134	0.000	BB
2	15.03	60905	0.215	BV
3	18.47	149830	0.530	BV
4	19.19	131369	0.464	VB
5	23.41	144566	0.511	BB
6	31.17	38405	0.136	BB
7	42.05	13669428	48.323	BV
8	46.72	13897227	49.128	VV
9	52.77	195972	0.693	TBB
		28287836	100.000	

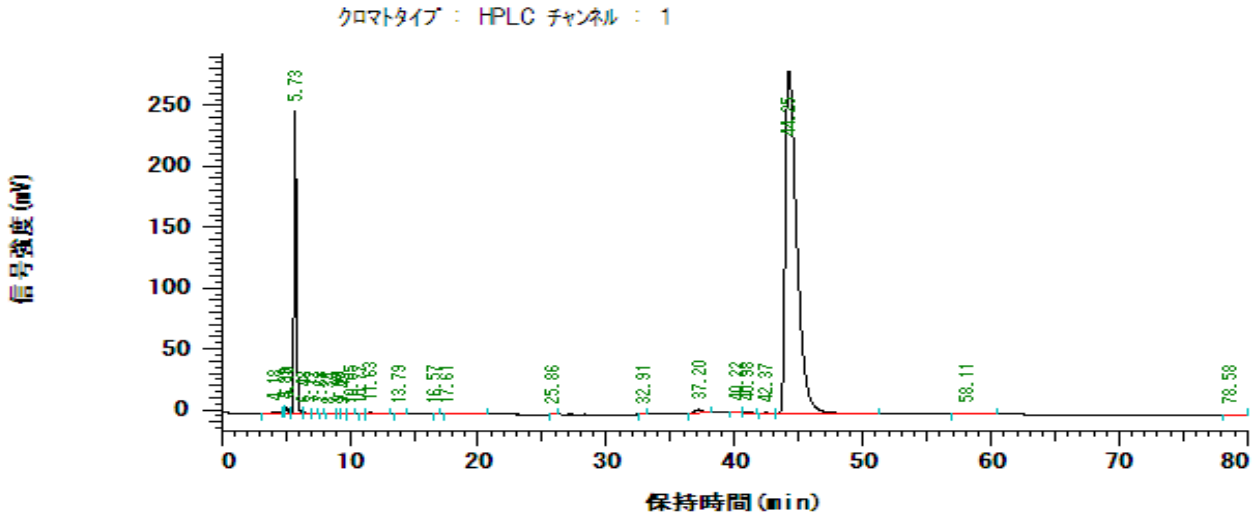
Table 1, entry 2

To a solution of **1a** (5.63 mg, 0.0065 mmol) in H_2O (660 μL) was added cyclohexanone (680 μL, 6.57 mmol) and 4-nitrobenzaldehyde (100.3 mg, 0.66 mmol). After being stirred at room temperature for 168 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (132.7 mg, 81%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. *Ee* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1

ピーク定量 : 面積
定量計算方法 : 面積%

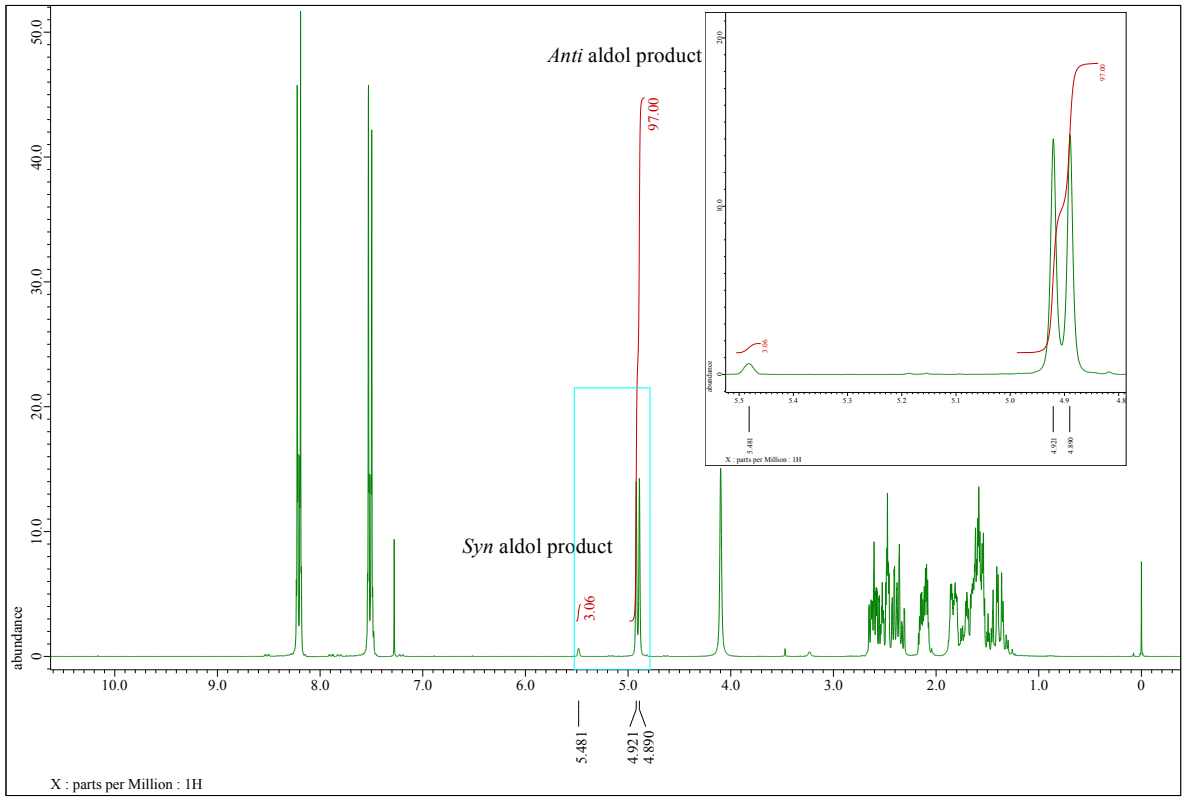
NO	RT	面積	濃度1	BC
1	4.18	105405	0.509	BV
2	4.89	38434	0.186	VV
3	5.10	77497	0.374	VV
4	5.73	2771007	13.379	VV
5	6.48	5345	0.026	TBB
6	7.12	7419	0.036	TBB
7	7.68	1032	0.005	TBB
8	8.34	2183	0.011	BB
9	9.09	3474	0.017	BB
10	9.45	1579	0.008	BB
11	10.05	2475	0.012	BB
12	10.77	990	0.005	BB
13	11.63	39669	0.192	BB
14	13.79	2126	0.010	BB
15	16.57	653	0.003	BB
16	17.61	2151	0.010	BB
17	25.86	677	0.003	BB
18	32.91	506	0.002	BB
19	37.20	143515	0.693	BB
20	40.22	26678	0.129	BV
21	40.98	49642	0.240	VB
22	42.37	22293	0.108	BB
23	44.25	17324851	83.646	BB
24	58.11	80742	0.390	BB
25	78.58	1760	0.008	BB
		20712103	100.000	

Yield : 81%, *anti* : *syn* = 100 : 0, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 44.25 min (major), t_R = 78.58 min (minor)]

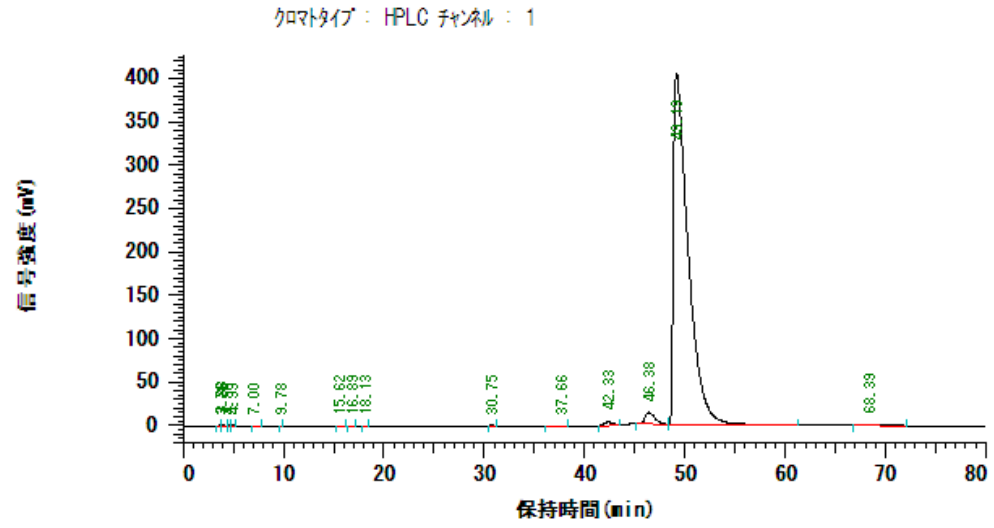
Table 1, entry 3

To a solution of **1a** (5.63 mg, 0.0065 mmol) in dry-toluene (660 µL) was added cyclohexanone (680 µL, 6.57 mmol) and 4-nitrobenzaldehyde (100.1 mg, 0.66 mmol). After being stirred at room temperature for 120 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (152.0 mg, 92%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. *Ee* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1
ピーク定量 : 面積
定量計算方法 : 面積%

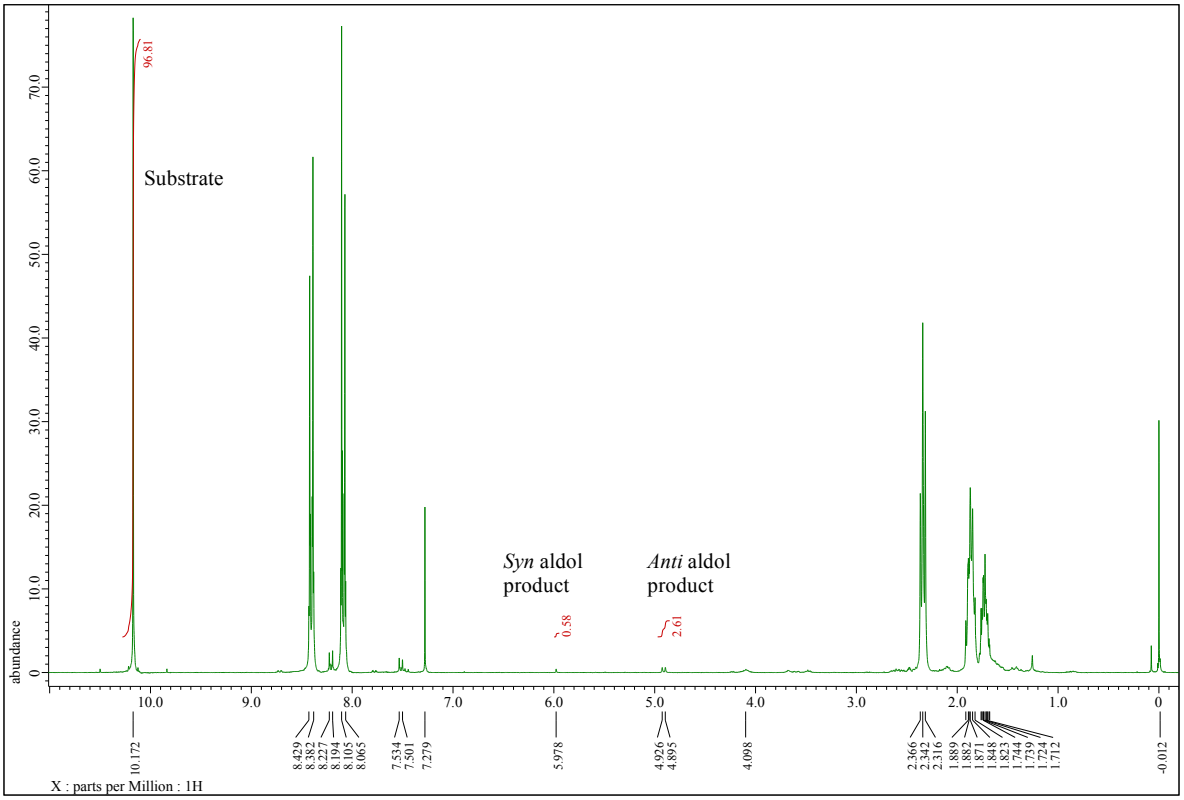
NO	RT	面積	濃度1	BC
1	3.76	4879	0.012	BV
2	3.88	9874	0.023	VB
3	4.50	1410	0.003	TBB
4	4.99	877	0.002	BB
5	7.00	1406	0.003	BB
6	9.78	457	0.001	BB
7	15.62	1921	0.005	BB
8	16.89	893	0.002	BB
9	18.13	1978	0.005	BB
10	30.75	5179	0.012	BB
11	37.66	2994	0.007	BB
12	42.33	203386	0.482	BB
13	46.38	870007	2.063	BB
14	49.19	40923796	97.027	BB
15	68.39	148838	0.353	BB
		42177895	100.000	

Yield : 92%, *anti* : *syn* = 97 : 3, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 49.19 min (major), t_R = 68.39 min (minor)]

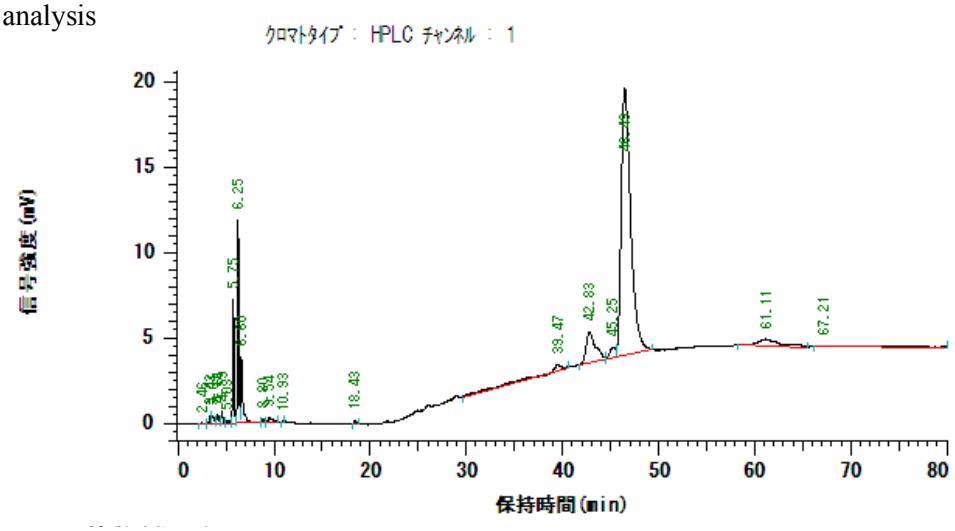
Table 1, entry 4

To a solution of **1a** (5.2 mg, 0.0060 mmol) in dry-MeCN (3.9 mL) was added cyclohexanone (596.2 µL, 5.8 mmol) and 4-nitrobenzaldehyde (87.5 mg, 0.58 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti : syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

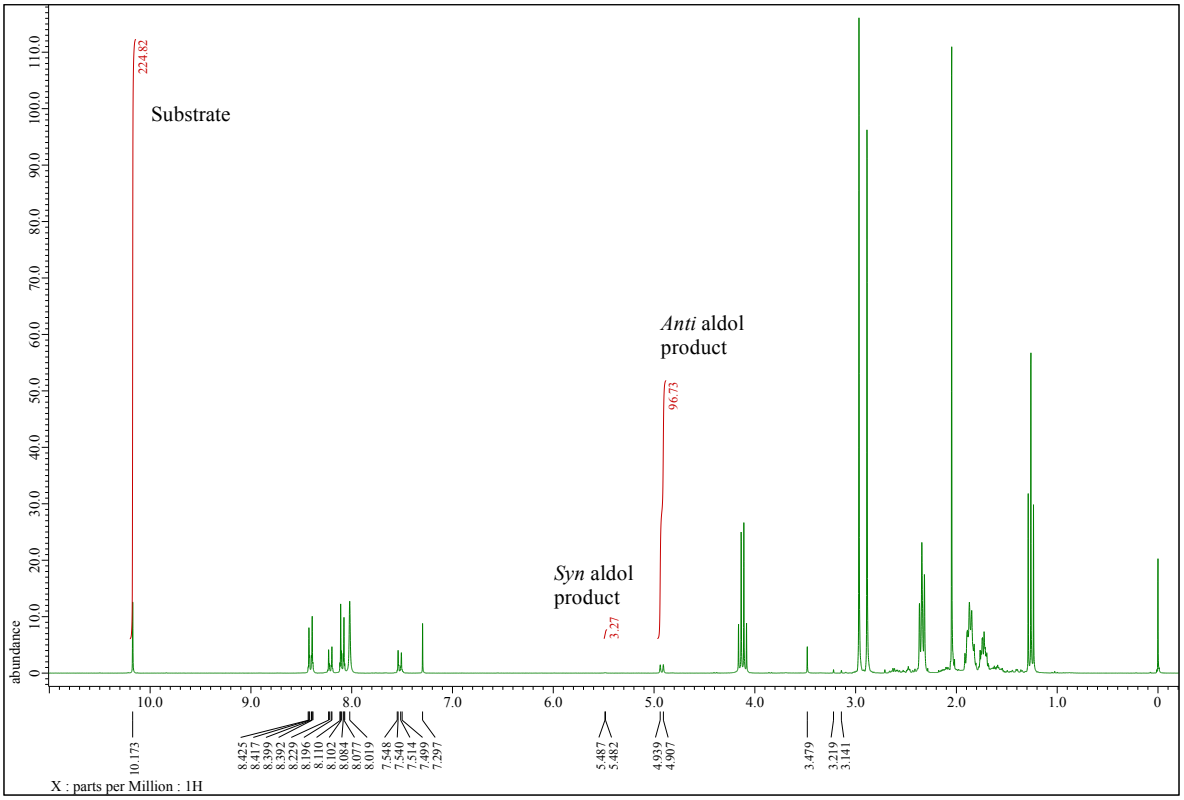
NO	RT	面積	濃度1	BC
1	2.46	1391	0.088	BB
2	3.42	7241	0.459	BV
3	3.61	7476	0.473	VV
4	4.14	9975	0.632	VV
5	4.59	6722	0.426	VB
6	5.03	3699	0.234	BV
7	5.75	68167	4.317	VV
8	6.25	108343	6.861	VV
9	6.60	61946	3.923	VB
10	8.80	2144	0.136	TBB
11	9.54	8762	0.555	BB
12	10.93	363	0.023	BB
13	18.43	3090	0.196	BB
14	39.47	18288	1.158	BB
15	42.83	119537	7.570	BV
16	45.25	23592	1.494	VV
17	46.49	1041206	65.937	VB
18	61.11	68257	4.323	BB
19	67.21	18881	1.196	BB
		1579080	100.000	

Conv. : 3%, *anti* : *syn* = 82 : 18, 88% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 46.49 min (major), t_R = 61.11 min (minor)]

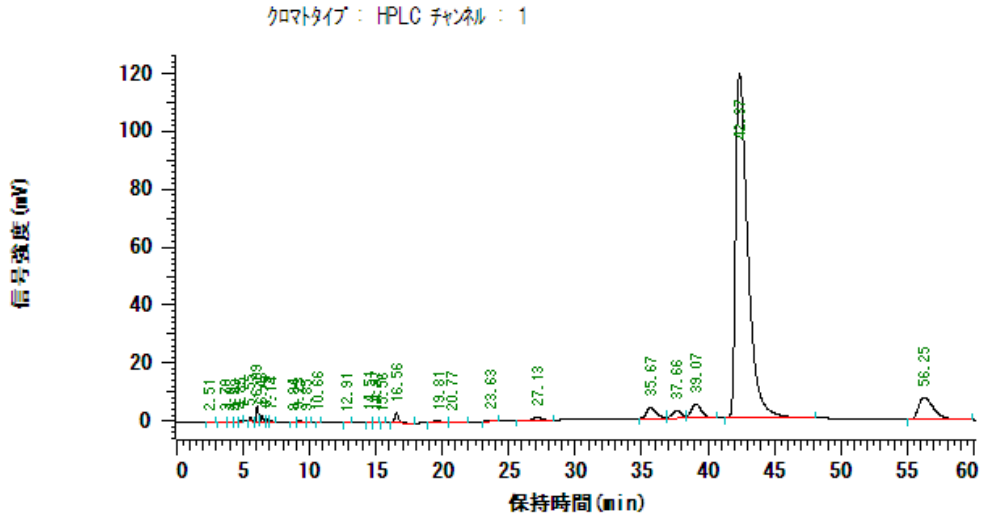
Table 1, entry 5

To a solution of **1a** (5.0 mg, 0.0058 mmol) in dry-DMF (3.9 mL) was added cyclohexanone (596.2 µL, 5.8 mmol) and 4-nitrobenzaldehyde (87.2 mg, 0.58 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti : syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1

ﾋﾟｰｸ定量：面積

定量計算方法：面積%

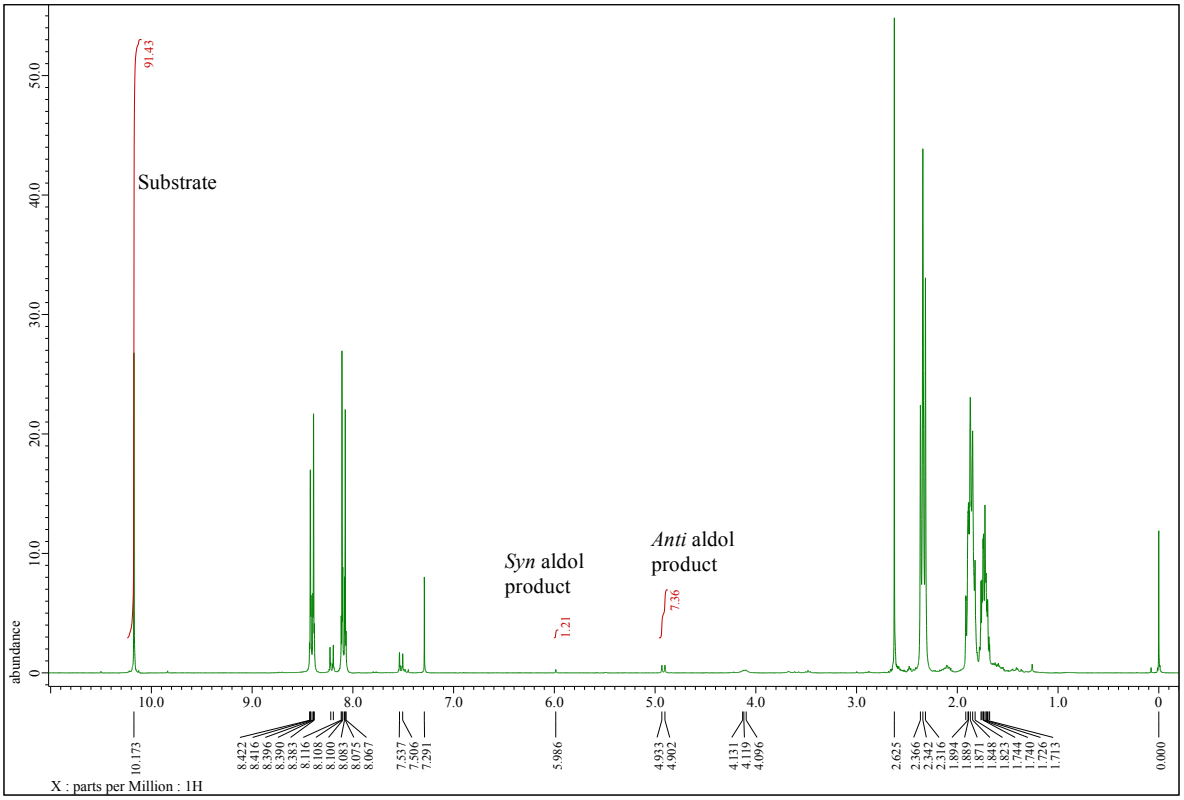
NO	RT	面積	濃度1	BC
1	2.51	1099	0.012	BB
2	3.70	7903	0.088	BV
3	4.03	3703	0.041	VV
4	4.49	2855	0.032	VB
5	4.85	4136	0.046	BB
6	5.55	14878	0.165	BB
7	6.09	49762	0.553	BV
8	6.43	25505	0.283	VV
9	6.79	11749	0.131	VV
10	7.14	11210	0.125	VB
11	8.84	2224	0.025	BV
12	9.23	16797	0.187	VV
13	9.85	2625	0.029	VB
14	10.66	747	0.008	BB
15	12.91	587	0.007	BB
16	14.51	2796	0.031	BB
17	14.97	2548	0.028	BB
18	15.56	268	0.003	BB
19	16.56	67049	0.745	BB
20	19.81	29864	0.332	BV
21	20.77	13708	0.152	VB
22	23.63	7866	0.087	BB
23	27.13	47841	0.531	BB
24	35.67	181216	2.013	BV
25	37.66	121885	1.354	VV
26	39.07	262548	2.916	VB
27	42.37	7496649	83.275	BB
28	56.25	612203	6.801	BB
		9002221	100.000	

Conv. : 31%, *anti* : *syn* = 97 : 3, 85% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 42.37 min (major), t_R = 56.25 min (minor)]

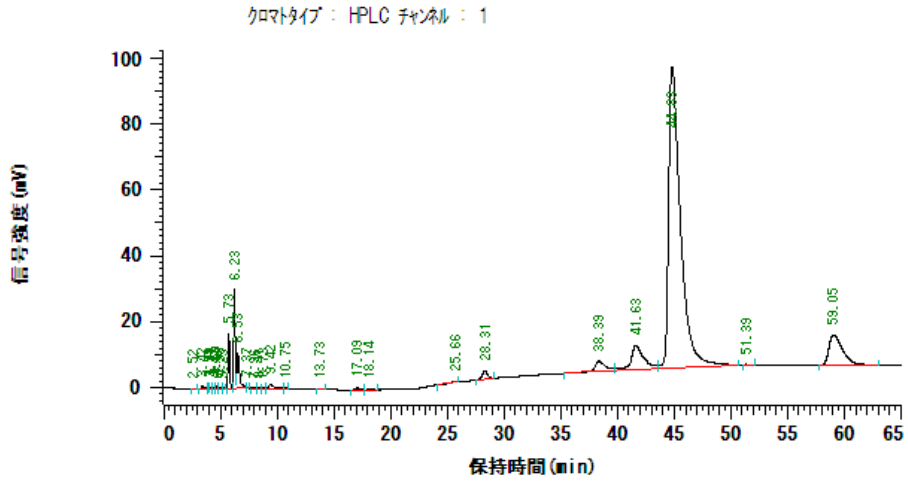
Table 1, entry 6

To a solution of **1a** (5.0 mg, 0.0058 mmol) in dry-DMSO (3.9 mL) was added cyclohexanone (596.2 μL, 5.8 mmol) and 4-nitrobenzaldehyde (87.1 mg, 0.58 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti : syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1
ピーク定量 : 面積
定量計算方法 : 面積%

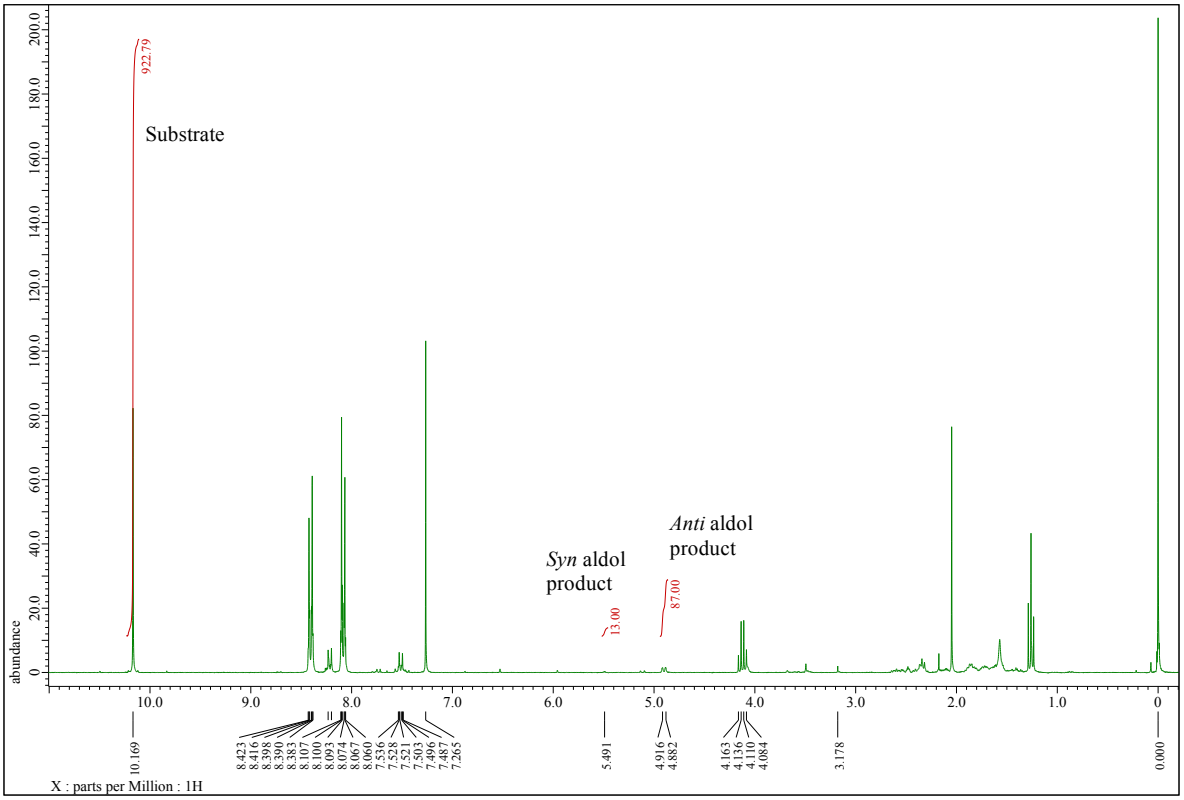
NO	RT	面積	濃度1	BC
1	2.52	1032	0.012	BB
2	3.42	17107	0.192	BV
3	3.99	2935	0.033	VV
4	4.11	5319	0.060	VV
5	4.41	2042	0.023	VV
6	4.59	7375	0.083	VV
7	4.98	4254	0.048	VV
8	5.25	2008	0.023	VB
9	5.73	153289	1.718	BV
10	6.23	268650	3.011	VV
11	6.53	152700	1.711	VB
12	7.37	858	0.010	BB
13	7.96	1533	0.017	BB
14	8.41	878	0.010	BB
15	8.73	4912	0.055	BB
16	9.42	33896	0.380	BB
17	10.75	1236	0.014	BB
18	13.73	648	0.007	BB
19	17.09	12739	0.143	BB
20	18.14	9293	0.104	BB
21	25.66	7292	0.082	BB
22	28.31	76041	0.852	BB
23	38.39	211991	2.376	BV
24	41.63	590835	6.621	VV
25	44.83	6573760	73.666	VB
26	51.39	1424	0.016	BB
27	59.05	779616	8.736	BB
		8923663	100.000	

Conv. : 9%, *anti* : *syn* = 86 : 14, 79% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 44.83 min (major), t_R = 59.05 min (minor)]

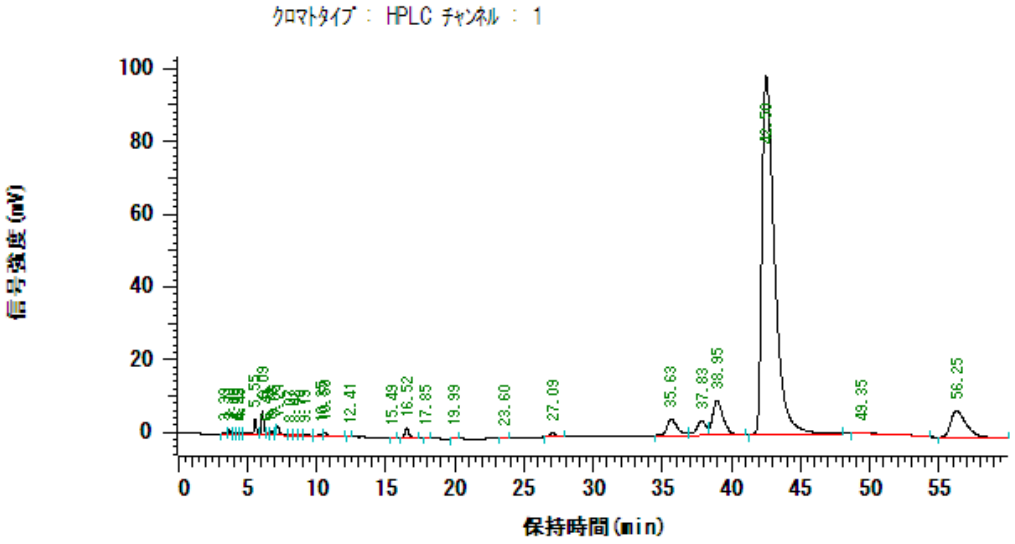
Table 1, entry 7

To a solution of **1a** (4.9 mg, 0.0057 mmol) in dry-MeOH (3.8 mL) was added cyclohexanone (584.3 µL, 5.7 mmol) and 4-nitrobenzaldehyde (85.5 mg, 0.57 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti : syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

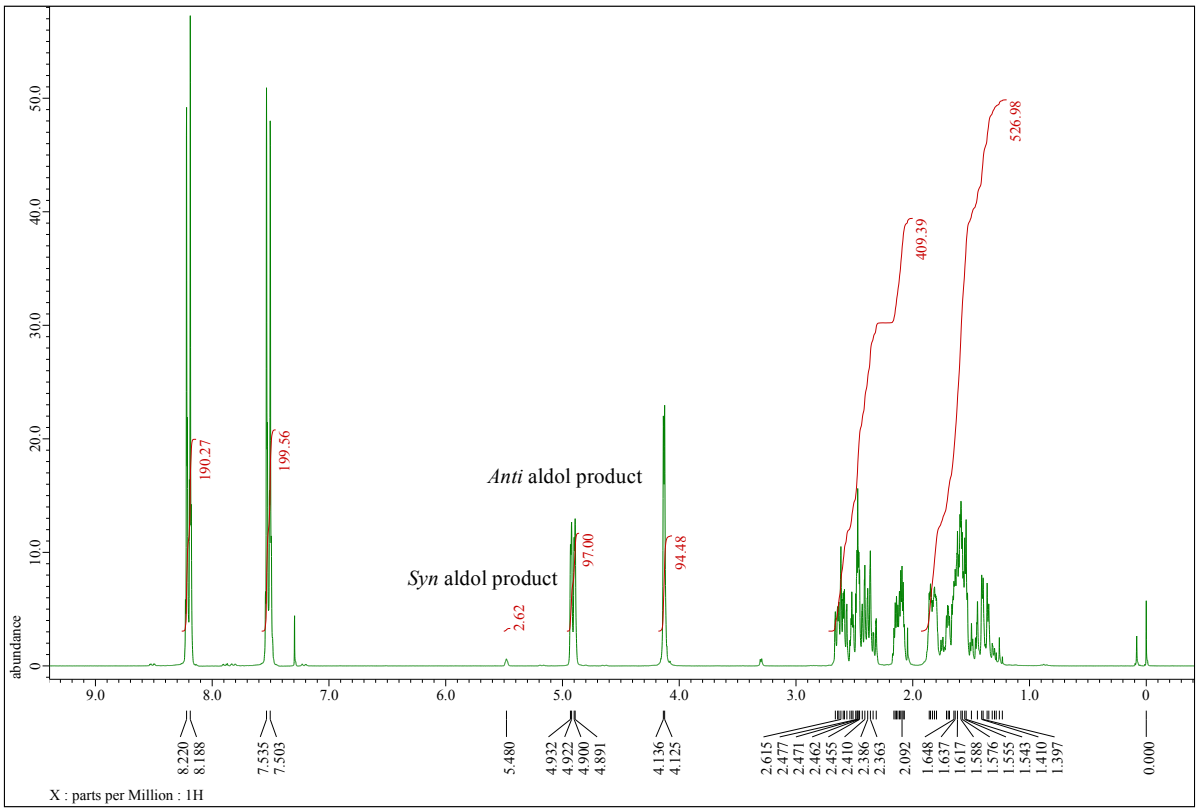
NO	RT	面積	濃度1	BC
1	3.39	6551	0.080	BV
2	3.71	15263	0.186	W
3	4.05	6341	0.077	W
4	4.33	3956	0.048	W
5	4.48	8019	0.098	W
6	5.55	72059	0.880	W
7	6.09	81540	0.996	W
8	6.41	849	0.010	TBB
9	6.78	11969	0.146	W
10	7.05	16294	0.199	W
11	7.21	47763	0.583	W
12	8.07	1234	0.015	TBB
13	8.42	1111	0.014	TBB
14	8.79	1312	0.016	TBB
15	9.15	10103	0.123	W
16	10.35	12808	0.156	W
17	10.59	20223	0.247	VB
18	12.41	775	0.009	BB
19	15.49	1035	0.013	BB
20	16.52	54358	0.664	BB
21	17.85	1205	0.015	BB
22	19.99	3102	0.038	BB
23	23.60	4348	0.053	BB
24	27.09	30185	0.369	BB
25	35.63	227835	2.783	BV
26	37.83	186684	2.280	W
27	38.95	505466	6.175	VB
28	42.50	6205499	75.804	BB
29	49.35	71580	0.874	BB
30	56.25	576771	7.046	BB
		8186238	100.000	

Conv. : 10%, *anti* : *syn* = 87 : 13, 83% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 42.50 min (major), t_R = 56.25 min (minor)]

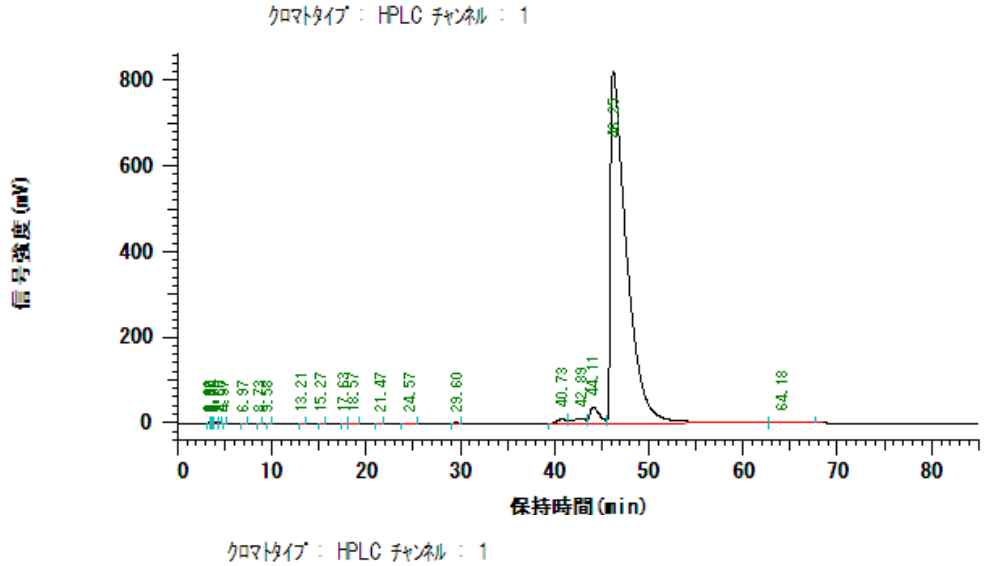
Table 1, entry 8

To a solution of **1a** (56.3 mg, 0.065 mmol) in dry-toluene (660 μL) was added cyclohexanone (680 μL, 6.57 mmol) and 4-nitrobenzaldehyde (100.7 mg, 0.66 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (155.4 mg, 94%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. *Ee* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

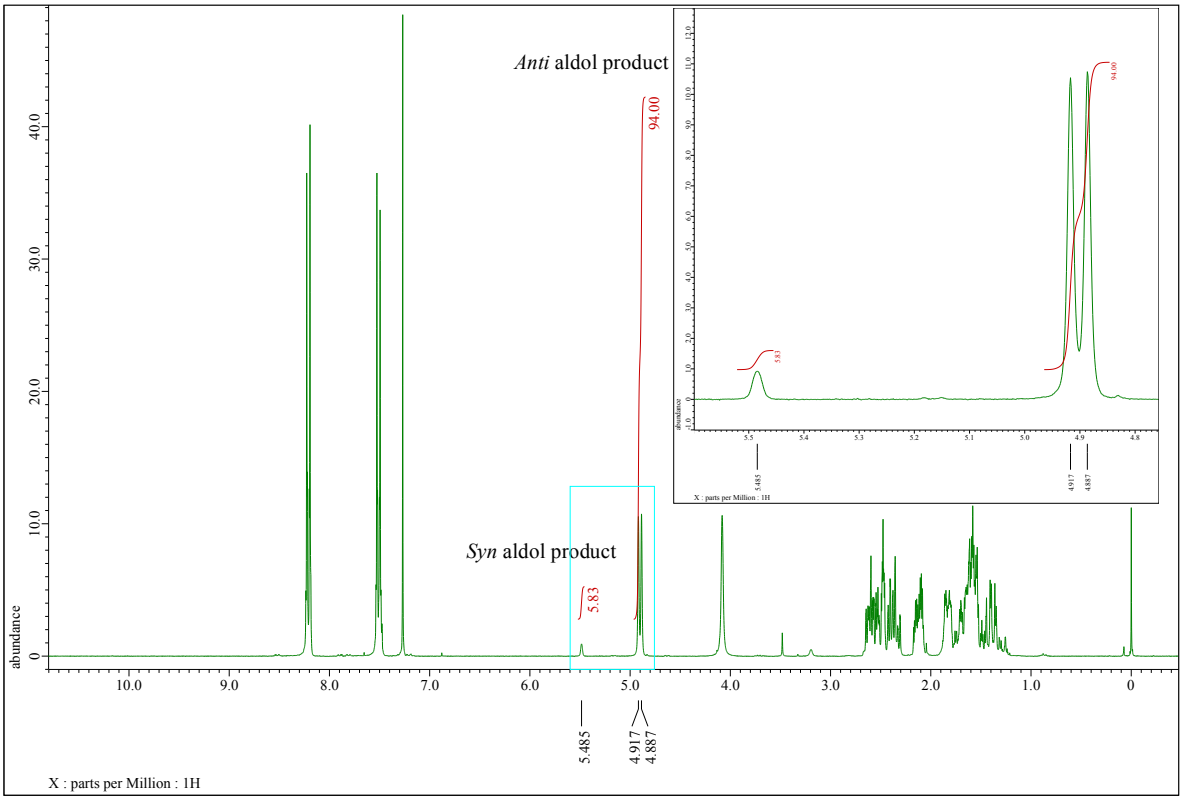
NO	RT	面積	濃度1	BC
1	3.39	8755	0.009	BV
2	3.60	5673	0.006	VV
3	3.74	5708	0.006	VV
4	3.89	13588	0.013	VV
5	4.50	3471	0.003	TBB
6	4.97	626	0.001	BB
7	6.97	2816	0.003	BB
8	8.73	1147	0.001	BB
9	9.58	945	0.001	BB
10	13.21	1016	0.001	BB
11	15.27	464	0.000	BB
12	17.63	1144	0.001	BB
13	18.57	8726	0.009	BB
14	21.47	1328	0.001	BB
15	24.57	8541	0.008	BB
16	29.60	11993	0.012	BB
17	40.73	581566	0.574	BV
18	42.89	949064	0.936	VV
19	44.11	2586198	2.551	VV
20	46.25	96964546	95.638	VV
21	64.18	229817	0.227	TBB
		1.013E+08	100.000	

Yield : 94%, *anti* : *syn* = 97 : 3, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 46.25 min (major), t_R = 64.18 min (minor)]

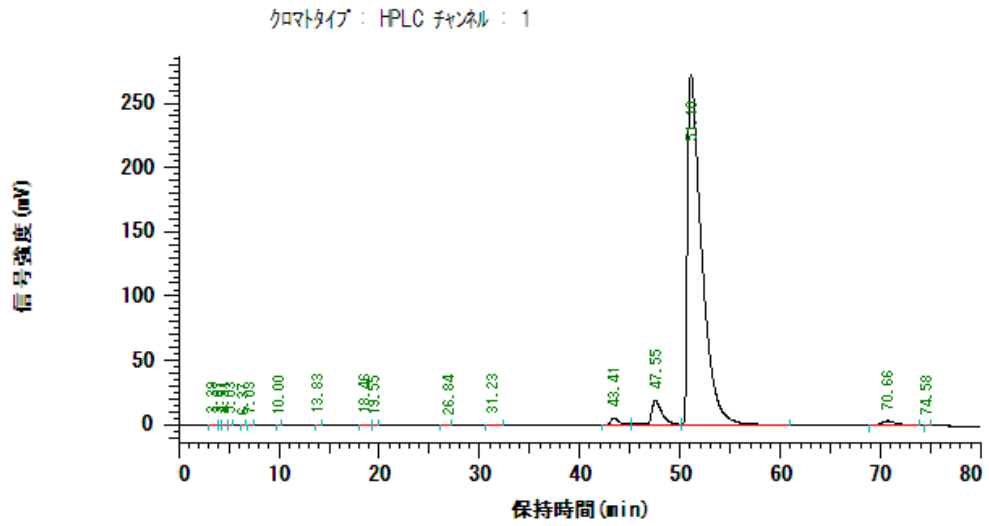
Table 1, entry 9

To a solution of **1a** (43.4 mg, 0.050 mmol) in dry-toluene (240 μL) was added cyclohexanone (176 μL, 1.70 mmol) and 4-nitrobenzaldehyde (25 mg, 0.17 mmol). After being stirred at room temperature for 23 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (42.6 mg, quant.). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. *Ee* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

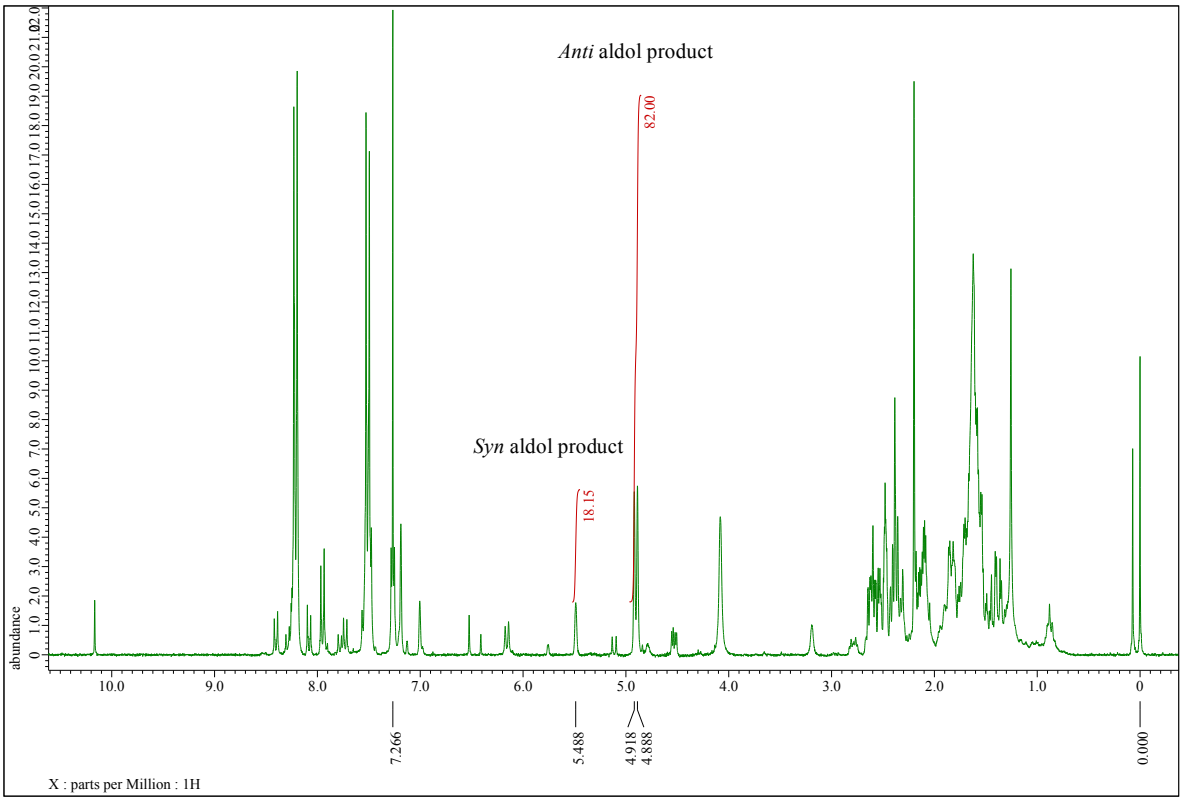
NO	RT	面積	濃度1	BC
1	3.39	14344	0.049	BV
2	3.97	7430	0.026	VV
3	4.51	6976	0.024	VB
4	5.03	1956	0.007	BB
5	6.37	546	0.002	BB
6	7.03	2778	0.010	BB
7	10.00	475	0.002	BB
8	13.83	1502	0.005	BB
9	18.46	12012	0.041	BB
10	19.55	626	0.002	BB
11	26.84	452	0.002	BB
12	31.23	34257	0.118	BB
13	43.41	379105	1.304	BV
14	47.55	1535860	5.284	VV
15	51.10	26670612	91.764	VB
16	70.66	394882	1.359	BB
17	74.58	594	0.002	BB
		29064407	100.000	

Yield : quant., *anti* : *syn* = 94 : 6, 97% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 51.10 min (major), t_R = 70.66 min (minor)]

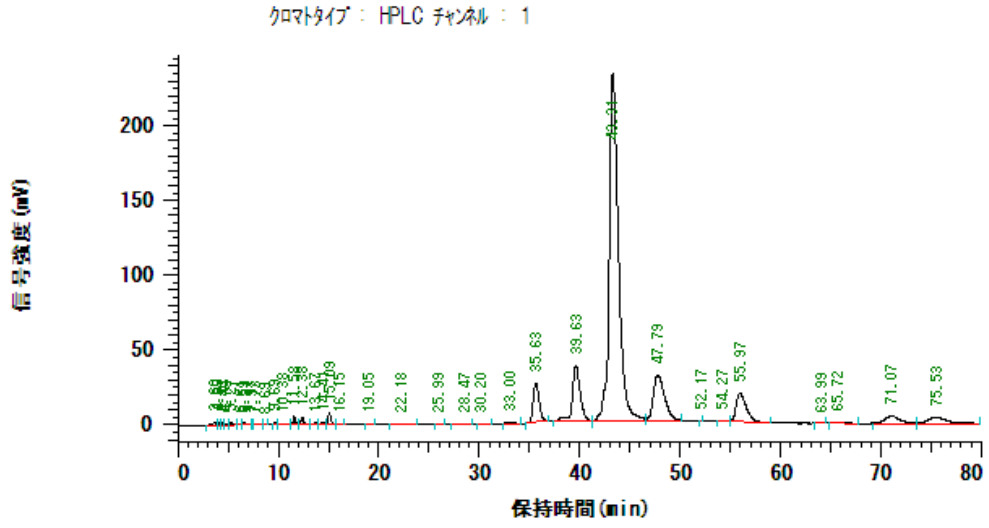
Table 1, entry 10

To a solution of **1b** (6.2 mg, 0.014 mmol) in dry-toluene (200 μL) was added cyclohexanone (150 μL, 1.45 mmol) and 4-nitrobenzaldehyde (25.2 mg, 0.17 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (23.1 mg, 56%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. *Ee* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

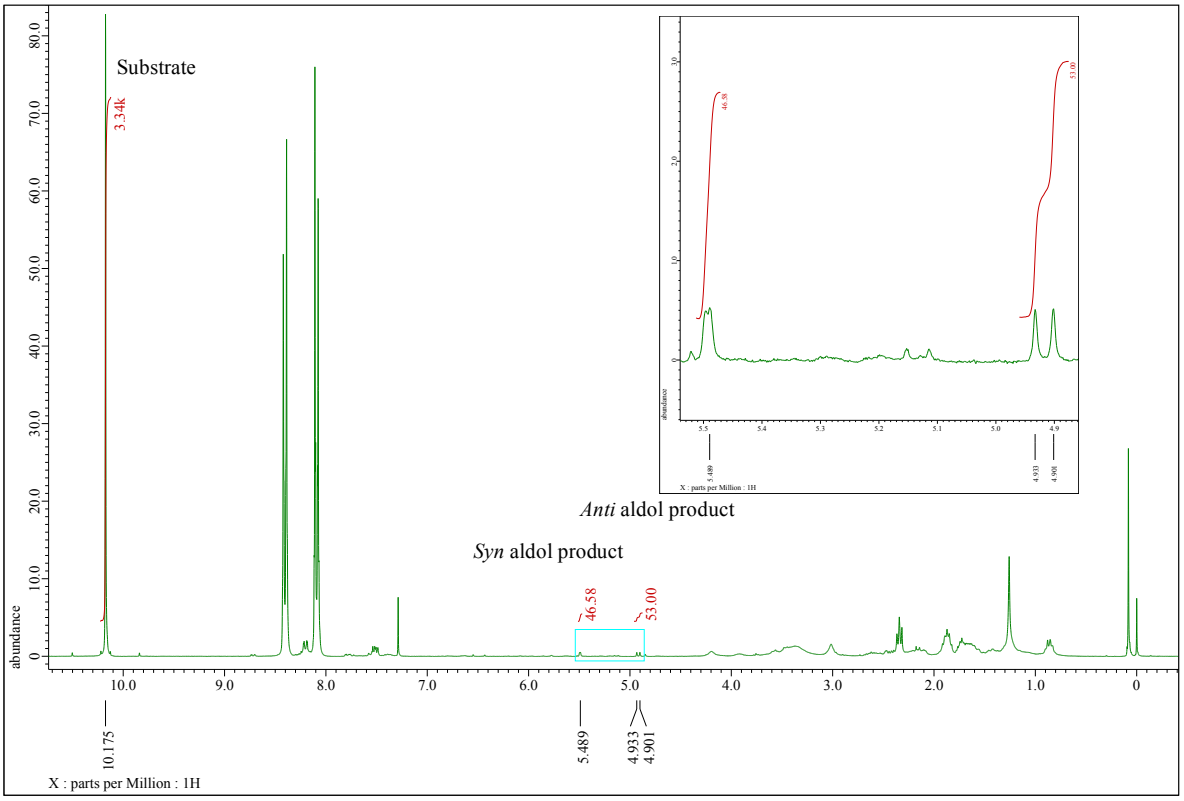
NO	RT	面積	濃度1	BC
1	3.60	38043	0.165	BV
2	4.03	20062	0.087	W
3	4.40	19054	0.083	W
4	4.79	16422	0.071	W
5	5.27	30354	0.132	W
6	6.31	7387	0.032	W
7	6.59	20442	0.089	W
8	7.37	4520	0.020	W
9	7.73	7482	0.032	VB
10	8.69	1866	0.008	BB
11	9.69	17107	0.074	BV
12	10.38	18793	0.082	VB
13	11.58	76971	0.334	BV
14	12.38	79484	0.345	VB
15	13.67	18488	0.080	BB
16	14.41	28735	0.125	BV
17	15.09	154543	0.670	W
18	16.15	5309	0.023	TBB
19	19.05	8568	0.037	BB
20	22.18	25712	0.112	BB
21	25.99	2071	0.009	BB
22	28.47	7835	0.034	BB
23	30.20	4300	0.019	BB
24	33.00	39464	0.171	BB
25	35.63	1070406	4.644	BB
26	39.63	1971022	8.550	BB
27	43.31	14616083	63.406	BV
28	47.79	2309361	10.018	VB
29	52.17	115	0.001	BB
30	54.27	33355	0.145	BV
31	55.97	1308362	5.676	VB
32	63.99	1661	0.007	BB
33	65.72	34740	0.151	BB
34	71.07	511737	2.220	BV
35	75.53	541731	2.350	VB
		23051585	100.000	

Yield : 56%, *anti* : *syn* = 82 : 18, 84% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 43.31 min (major), t_R = 55.97 min (minor)]

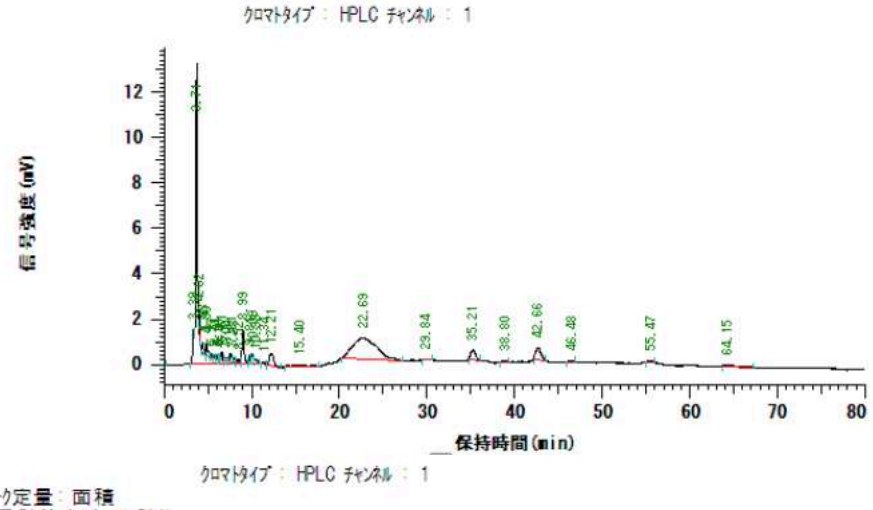
Table 1, entry 11

To a solution of **1c** (25.4 mg, 0.043 mmol) in dry-toluene (430 µL) was added cyclohexanone (450 µL, 4.35 mmol) and 4-nitrobenzaldehyde (64.9 mg, 0.43 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti* : *syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1
ピーク定量 : 面積
定量計算方法 : 面積%

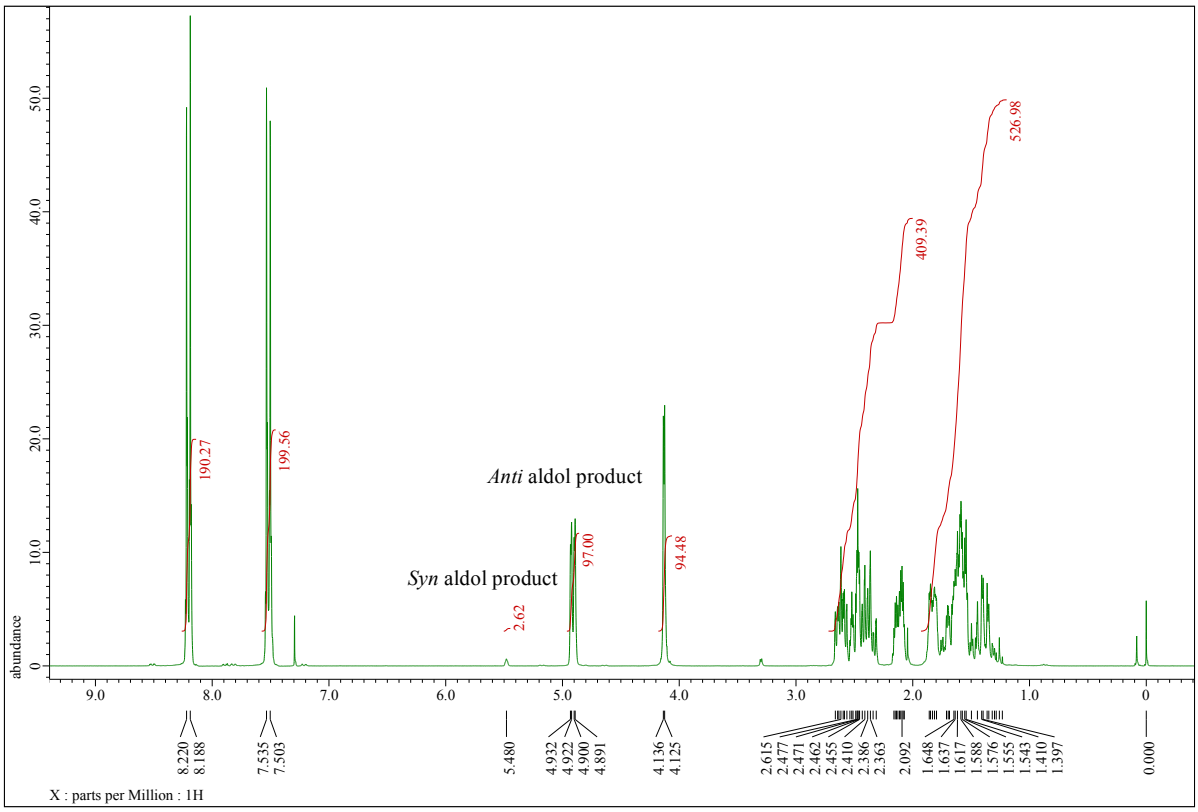
NO	RT	面積	濃度1	BC
1	0.01	125	0.022	BB
2	3.39	17964	3.090	BV
3	3.71	227167	39.075	VV
4	4.02	4450	0.766	TBB
5	4.43	5029	0.865	TBB
6	4.80	8761	1.507	TBB
7	5.37	960	0.165	TBB
8	5.71	1041	0.179	TBB
9	6.01	1479	0.255	TBB
10	6.30	1738	0.299	TBV
11	6.61	3747	0.645	TVB
12	7.00	2900	0.499	TBB
13	7.61	4325	0.744	TBV
14	7.93	1723	0.296	TVB
15	8.52	2099	0.361	TBB
16	8.99	24822	4.270	VV
17	9.81	5200	0.894	VV
18	10.09	5413	0.931	VV
19	10.39	4860	0.836	VB
20	11.34	1390	0.239	BB
21	12.21	18512	3.184	BB
22	15.40	7918	1.362	BB
23	22.69	181659	31.247	BB
24	29.84	711	0.122	BB
25	35.21	14908	2.564	BB
26	38.80	1789	0.308	BB
27	42.66	21502	3.699	BB
28	46.48	1641	0.282	BB
29	55.47	1682	0.289	BB
30	64.15	5830	1.003	BB
		581345	100.000	

Conv. : 3%, *anti* : *syn* = 53 : 47, 85% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 42.66 min (major), t_R = 55.47 min (minor)]

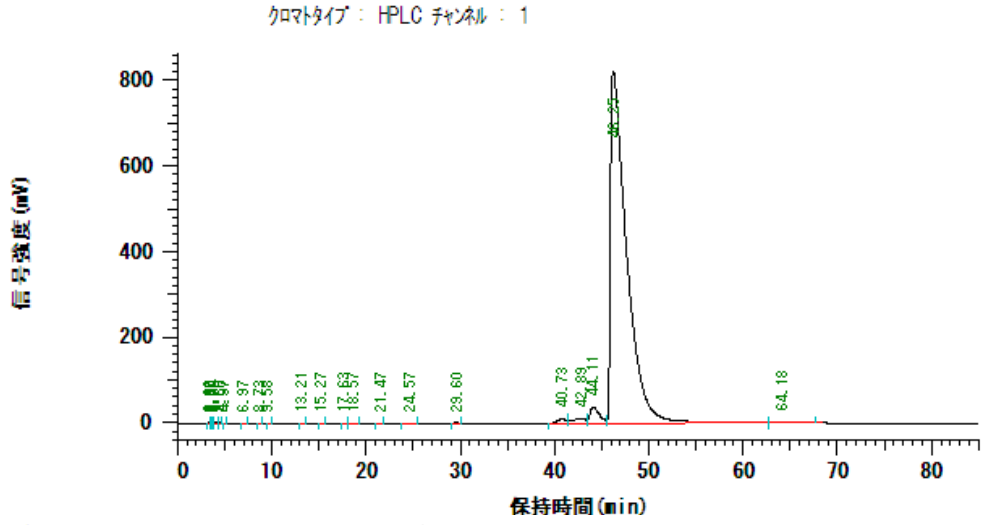
Table 2, entry 1

To a solution of **1a** (56.3 mg, 0.065 mmol) in dry-toluene (660 µL) was added cyclohexanone (680 µL, 6.57 mmol) and 4-nitrobenzaldehyde (100.7 mg, 0.66 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (155.4 mg, 94%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. *Ee* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

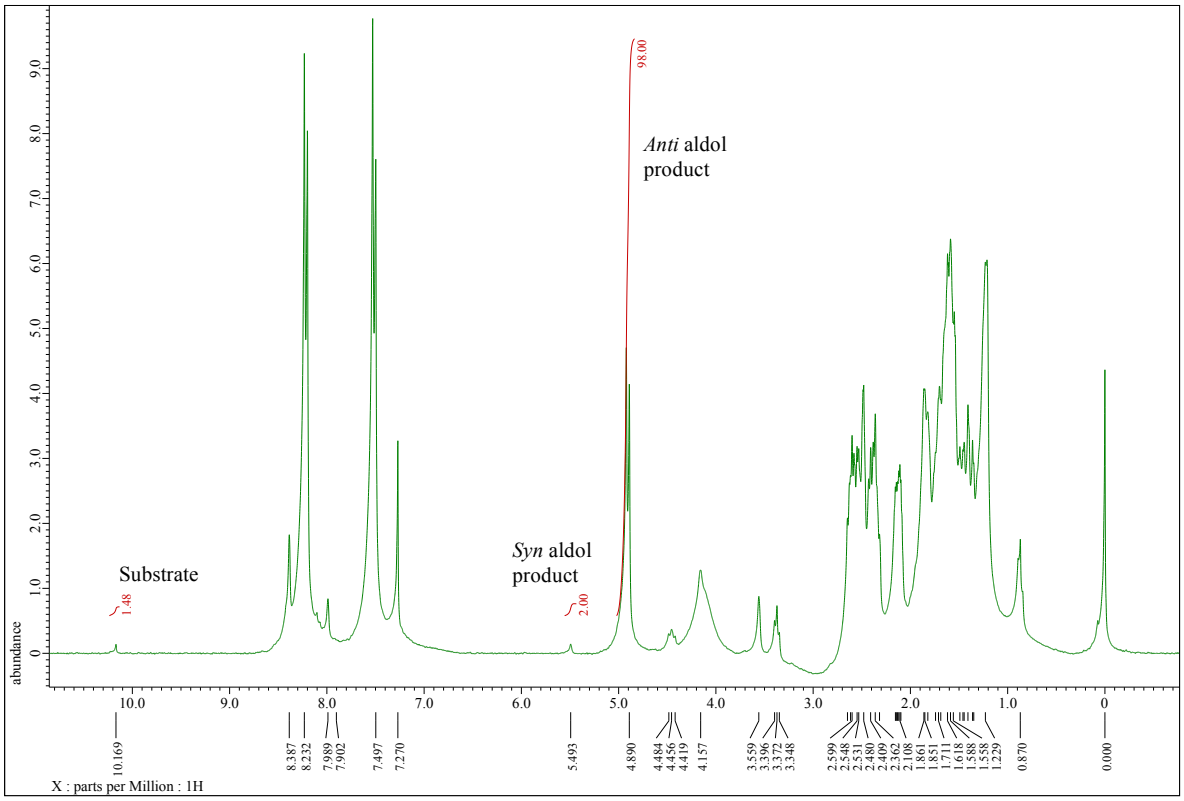
NO	RT	面積	濃度1	BC
1	3.39	8755	0.009	BV
2	3.60	5673	0.006	VV
3	3.74	5708	0.006	VV
4	3.89	13588	0.013	VV
5	4.50	3471	0.003	TBB
6	4.97	626	0.001	BB
7	6.97	2816	0.003	BB
8	8.73	1147	0.001	BB
9	9.58	945	0.001	BB
10	13.21	1016	0.001	BB
11	15.27	464	0.000	BB
12	17.63	1144	0.001	BB
13	18.57	8726	0.009	BB
14	21.47	1328	0.001	BB
15	24.57	8541	0.008	BB
16	29.60	11993	0.012	BB
17	40.73	581566	0.574	BV
18	42.89	949064	0.936	VV
19	44.11	2586198	2.551	VV
20	46.25	96964546	95.638	VV
21	64.18	229817	0.227	TBB
		1.013E+08	100.000	

Yield : 94%, *anti* : *syn* = 97 : 3, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 46.25 min (major), t_R = 64.18 min (minor)]

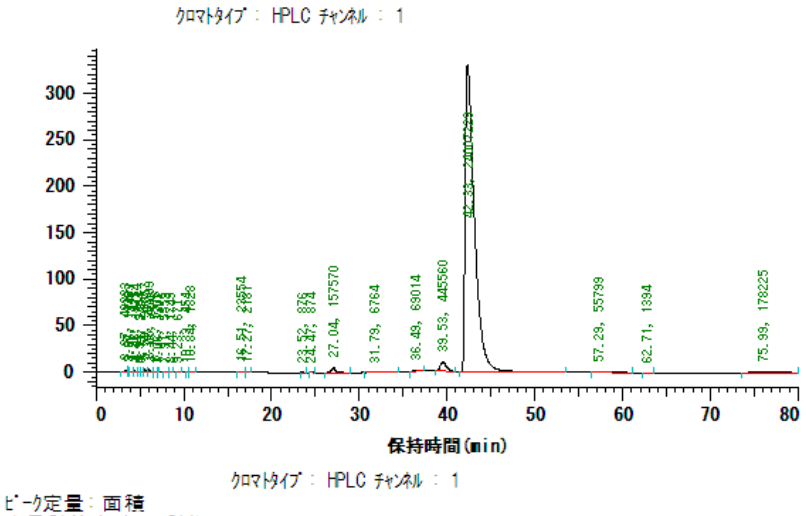
Table 2, entry 2

To a solution of **1d** (15.9 mg, 0.028 mmol) in dry-toluene (0.28 mL) was added cyclohexanone (0.3 mL, 2.8 mmol) and 4-nitrobenzaldehyde (43 mg, 0.28 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti : syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

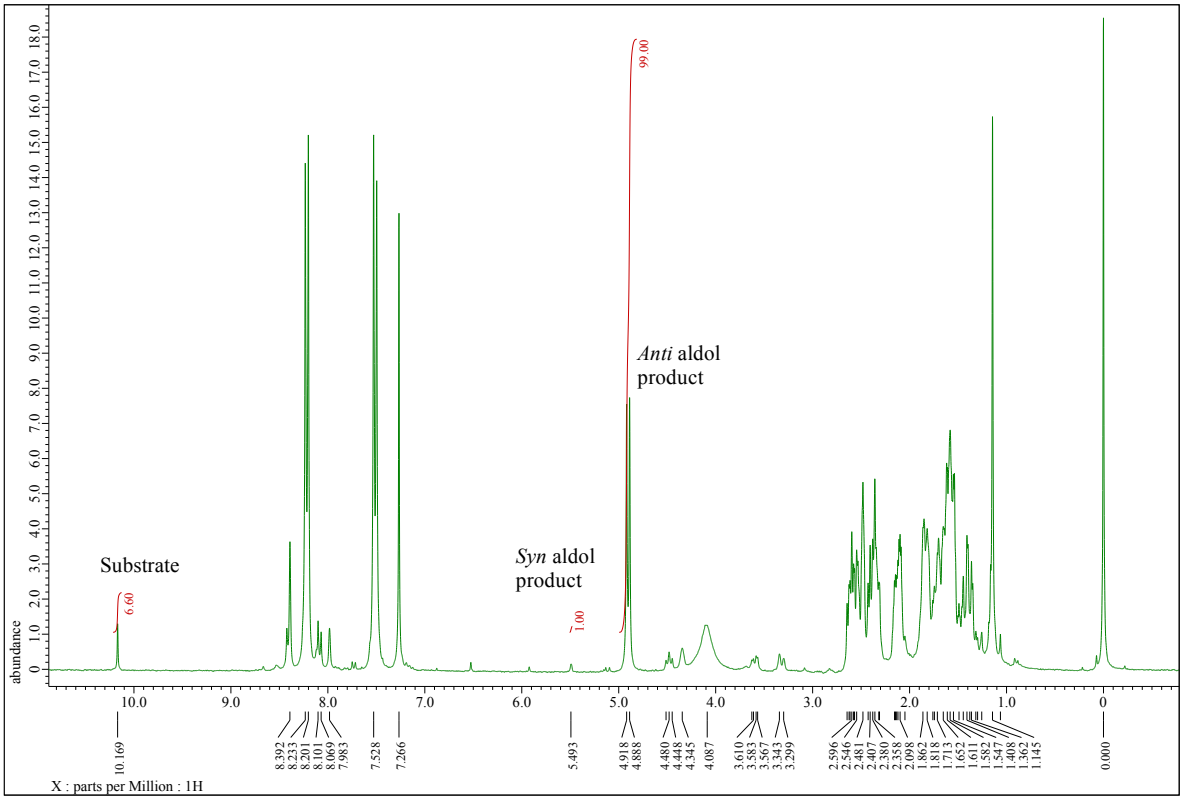
NO	RT	面積	濃度1	BC
1	3.37	49333	0.196	BV
2	3.67	1139	0.005	TBB
3	3.86	13463	0.054	VV
4	4.46	19754	0.079	VV
5	4.91	3344	0.013	VV
6	5.13	2451	0.010	VB
7	5.53	33057	0.132	BV
8	6.05	45099	0.179	VB
9	6.72	5576	0.022	BB
10	7.06	1202	0.005	BB
11	7.91	5559	0.022	BB
12	8.44	1749	0.007	BB
13	9.23	671	0.003	BB
14	10.33	454	0.002	BB
15	10.84	1828	0.007	BB
16	16.51	23554	0.094	BB
17	17.27	2181	0.009	BB
18	23.52	876	0.003	BB
19	24.47	874	0.003	BB
20	27.04	157570	0.627	BB
21	31.79	6764	0.027	BB
22	36.49	69014	0.275	BB
23	39.53	445560	1.773	BB
24	42.33	24007229	95.518	BB
25	57.29	55799	0.222	BB
26	62.71	1394	0.006	BB
27	75.99	178225	0.709	BB
		25133719	100.000	

Conv. : 99%, *anti* : *syn* = 98 : 2, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 42.33 min (major), t_R = 57.29 min (minor)]

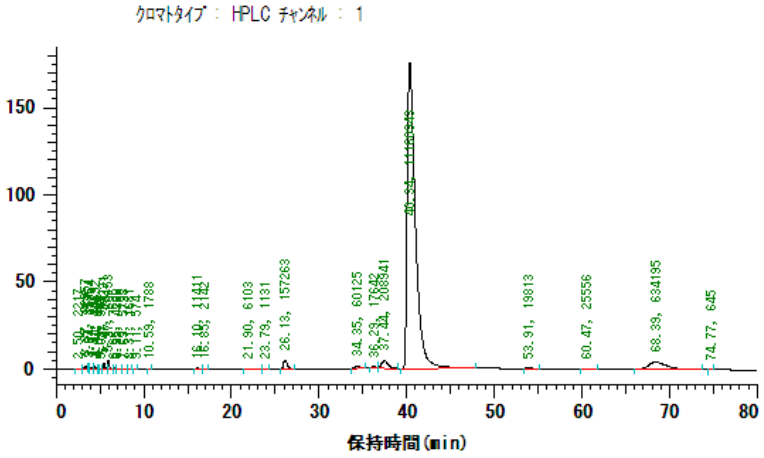
Table 2, entry 3

To a solution of **1e** (17.7 mg, 0.038 mmol) in dry-toluene (0.38 mL) was added cyclohexanone (0.4 mL, 3.8 mmol) and 4-nitrobenzaldehyde (57.9 mg, 0.38 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti : syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1

ピーク定量 : 面積
定量計算方法 : 面積%

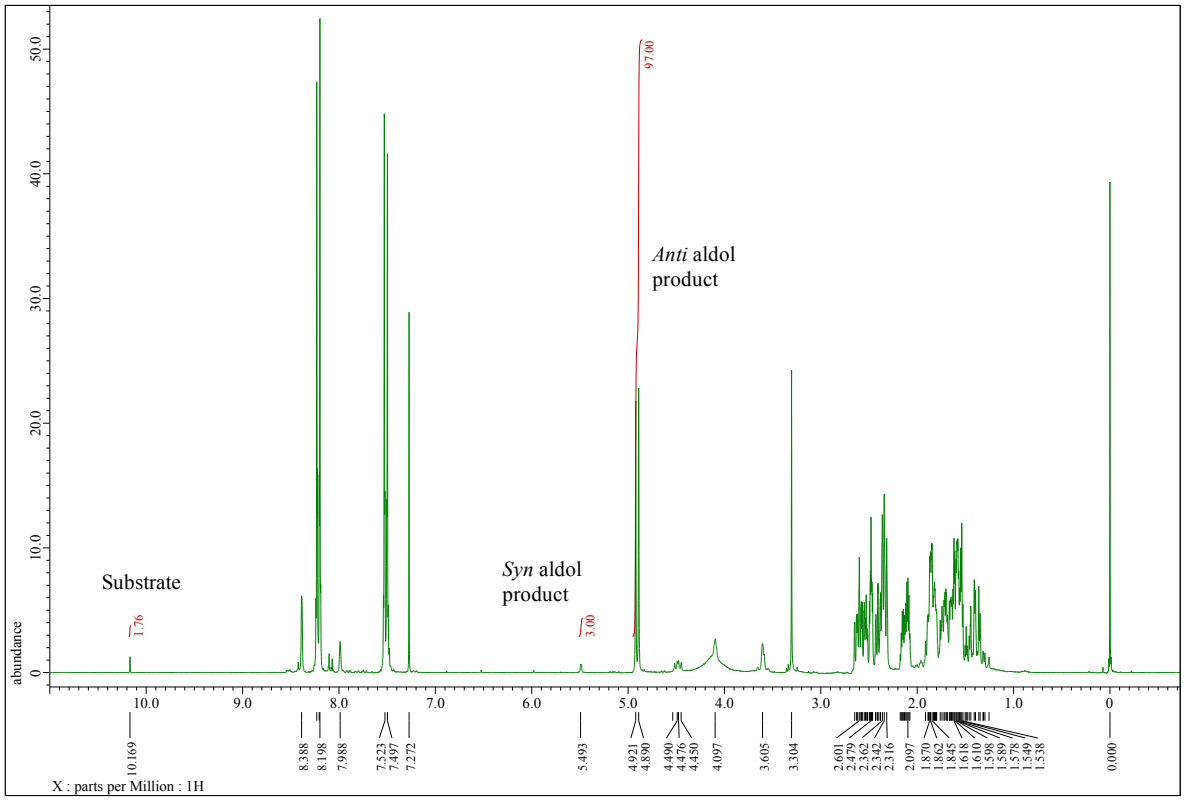
NO	RT	面積	濃度1	BC
1	2.50	2217	0.018	BB
2	3.37	32957	0.263	BV
3	3.67	8576	0.069	W
4	3.84	15854	0.127	W
5	4.44	30692	0.245	W
6	4.81	968	0.008	TBB
7	5.09	943	0.008	TBB
8	5.47	39231	0.313	W
9	5.97	60153	0.480	W
10	6.63	7635	0.061	W
11	6.95	4288	0.034	VB
12	7.69	5798	0.046	BB
13	8.31	1681	0.013	BB
14	9.11	574	0.005	BB
15	10.59	1788	0.014	BB
16	16.10	11411	0.091	BB
17	16.85	2142	0.017	BB
18	21.90	6103	0.049	BB
19	23.79	1131	0.009	BB
20	26.13	157263	1.256	BB
21	34.35	60125	0.480	BB
22	36.29	17642	0.141	BV
23	37.44	208941	1.669	VB
24	40.34	11160943	89.150	BB
25	53.91	19813	0.158	BB
26	60.47	25556	0.204	BB
27	68.39	634195	5.066	BB
28	74.77	645	0.005	BB
		12519265	100.000	

Conv. : 94%, *anti* : *syn* = 99 : 1, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 40.34 min (major), t_R = 53.91 min (minor)]

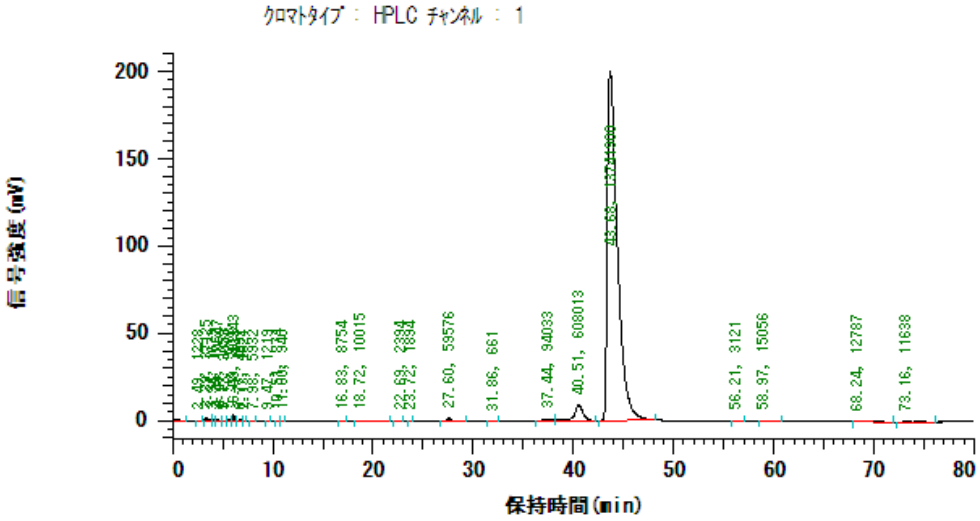
Table 2, entry 4

To a solution of **1f** (17.7 mg, 0.042 mmol) in dry-toluene (0.42 mL) was added cyclohexanone (0.44 mL, 4.2 mmol) and 4-nitrobenzaldehyde (62.6 mg, 0.41 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti : syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

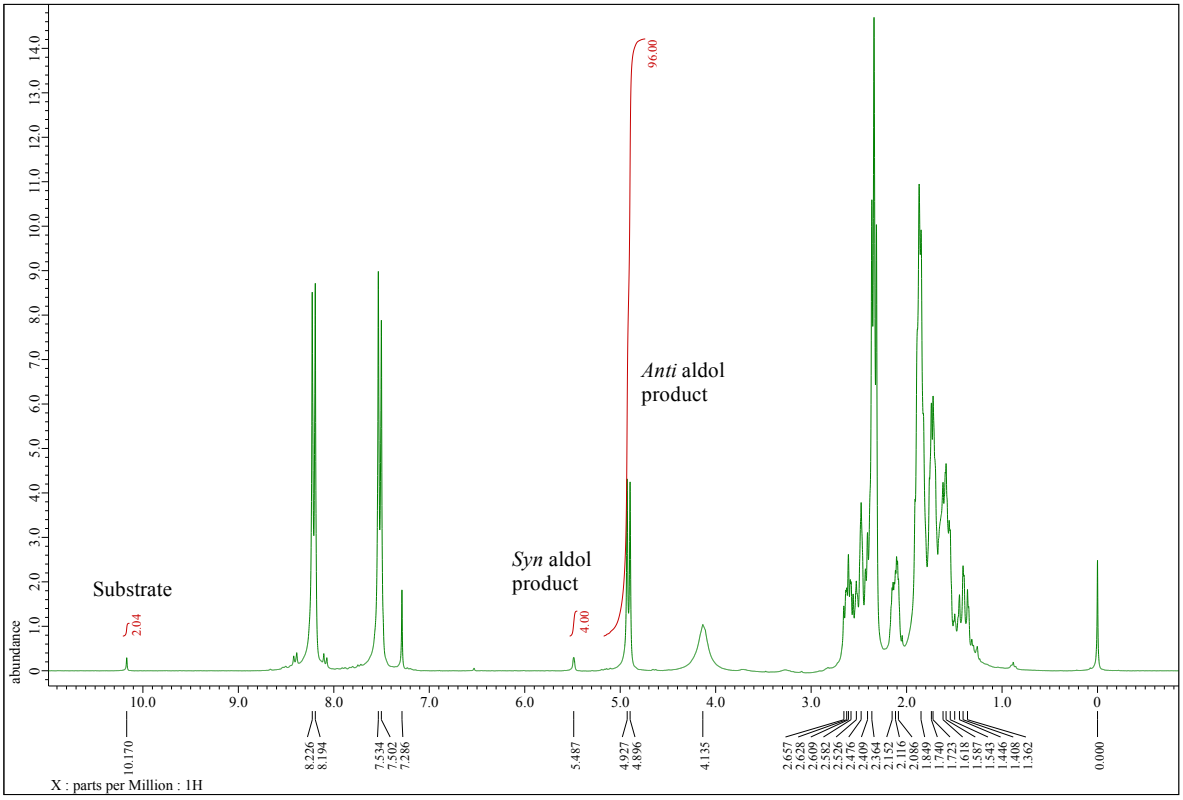
NO	RT	面積	濃度1	BC
1	0.52	5706	0.039	BB
2	2.49	1228	0.008	BB
3	3.39	37125	0.253	BV
4	3.94	1673	0.011	TBB
5	4.49	10547	0.072	VB
6	5.17	3059	0.021	BB
7	5.58	9268	0.063	BB
8	6.08	40343	0.275	BB
9	6.77	4832	0.033	BB
10	7.13	1621	0.011	BB
11	7.98	5932	0.040	BB
12	9.47	1219	0.008	BB
13	10.51	874	0.006	BB
14	11.00	940	0.006	BB
15	16.83	8754	0.060	BB
16	18.72	10015	0.068	BB
17	22.69	2394	0.016	BB
18	23.72	1894	0.013	BB
19	27.60	59576	0.405	BB
20	31.86	661	0.005	BB
21	37.44	94033	0.640	BV
22	40.51	608013	4.138	VB
23	43.68	13741900	93.519	BB
24	56.21	3121	0.021	BB
25	58.97	15056	0.102	BB
26	68.24	12787	0.087	BB
27	73.16	11638	0.079	BB
		14694209	100.000	

Conv. : 98%, *anti* : *syn* = 97 : 3, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 43.68 min (major), t_R = 58.97 min (minor)]

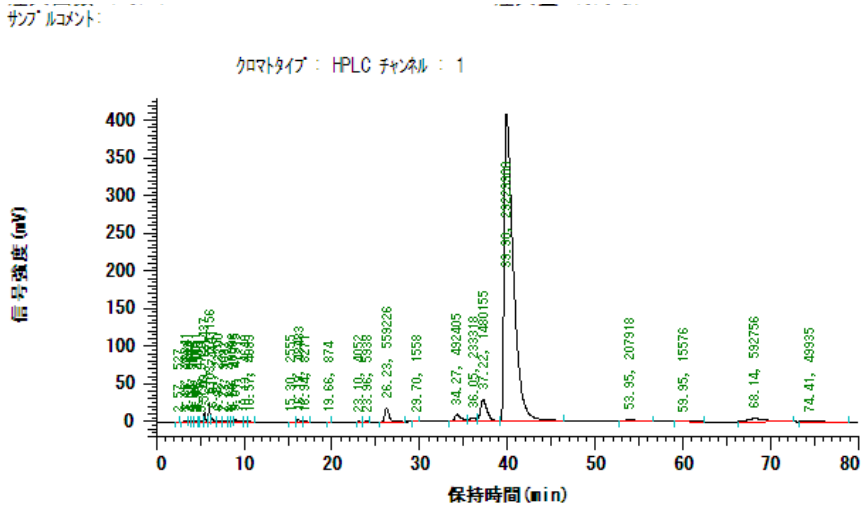
Table 2, entry 5

To a solution of **1g** (17.7 mg, 0.044 mmol) in dry-toluene (0.44 mL) was added cyclohexanone (0.45 mL, 4.4 mmol) and 4-nitrobenzaldehyde (66.0 mg, 0.44 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti : syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

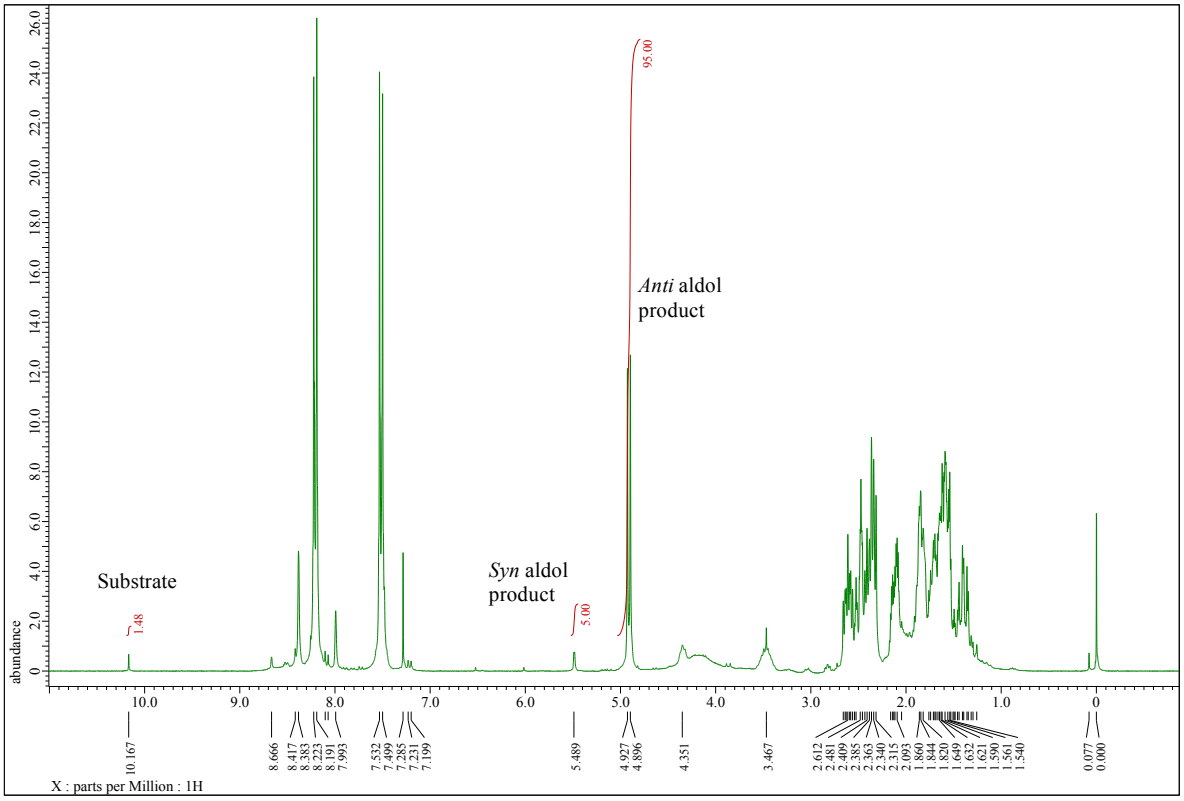
NO	RT	面積	濃度1	BC
1	2.57	527	0.002	BB
2	3.36	23841	0.071	BV
3	3.67	9292	0.028	VV
4	4.04	5504	0.016	VV
5	4.46	17751	0.053	VV
6	4.83	4580	0.014	VV
7	5.11	3720	0.011	VV
8	5.49	121437	0.362	VV
9	6.03	241156	0.719	VV
10	6.31	74191	0.221	VV
11	6.98	23700	0.071	VV
12	7.73	9092	0.027	VV
13	8.32	4778	0.014	VV
14	8.60	28008	0.083	VV
15	9.01	47915	0.143	VV
16	10.13	4640	0.014	VV
17	10.57	4089	0.012	VB
18	15.30	2555	0.008	BB
19	16.19	48483	0.144	BV
20	16.94	8271	0.025	VB
21	19.66	874	0.003	BB
22	23.10	4052	0.012	BB
23	23.96	5938	0.018	BB
24	26.23	559226	1.666	BB
25	29.70	1558	0.005	BB
26	34.27	492405	1.467	BV
27	36.05	233318	0.695	VV
28	37.22	1480155	4.411	VV
29	39.90	29229900	87.105	VB
30	53.95	207918	0.620	BB
31	59.95	15576	0.046	BB
32	68.14	592756	1.766	BB
33	74.41	49935	0.149	BB
		33557141	100.000	

Conv. : 98%, *anti* : *syn* = 96 : 4, 99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 39.90 min (major), t_R = 53.95 min (minor)]

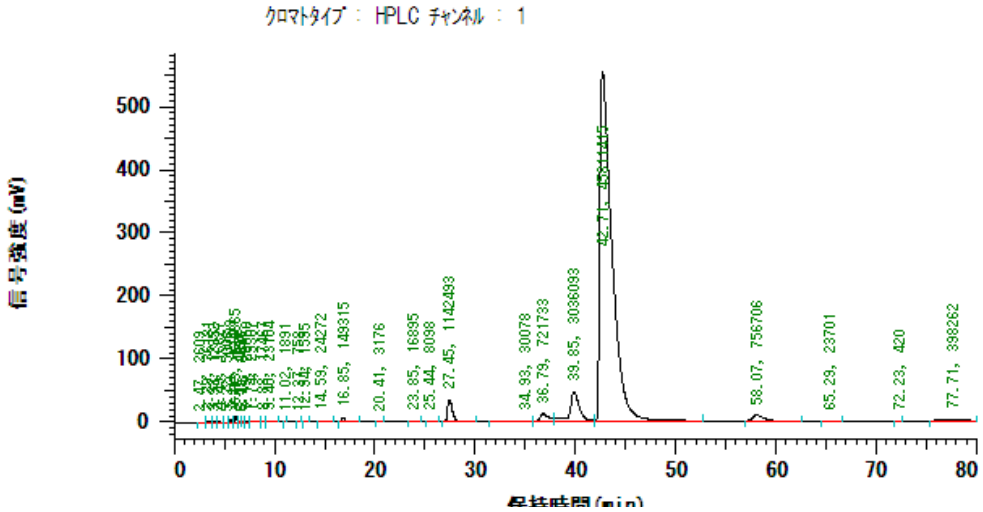
Table 2, entry 6

To a solution of **1h** (15.0 mg, 0.038 mmol) in dry-toluene (0.38 mL) was added cyclohexanone (0.4 mL, 3.8 mmol) and 4-nitrobenzaldehyde (57.5 mg, 0.38 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion and diastereoselectivity (*anti : syn*) were determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ: iPrOH:Hex=4:96 1ml/min
ｶﾗﾑ名 : Column
ﾒｿｯﾄﾞ作成者 :
ﾎﾟﾝﾌﾟA(ﾒｲﾝ) : L-2130
ﾎﾟﾝﾌﾟA 溶離液A: iPrOH
ﾎﾟﾝﾌﾟA 溶離液B: Hex
ﾎﾟﾝﾌﾟA 溶離液C:
ﾎﾟﾝﾌﾟA 溶離液D:
分析ﾌｧｲﾙｺﾒﾝﾄ:

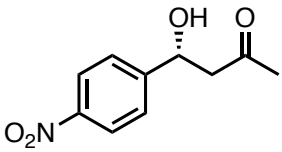
ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法: 面積%

NO	RT	面積	濃度1	BC
1	2.47	2609	0.005	BB
2	3.39	36181	0.069	BV
3	3.93	12952	0.025	VV
4	4.49	16827	0.032	VB
5	5.22	5008	0.010	BV
6	5.63	42088	0.080	VV
7	6.13	124865	0.238	VV
8	6.55	4816	0.009	TBV
9	6.79	3837	0.007	TVB
10	7.15	20950	0.040	VV
11	7.74	25307	0.048	VV
12	8.88	17467	0.033	VV
13	9.40	23104	0.044	VB
14	11.02	1891	0.004	BB
15	12.37	758	0.001	BB
16	12.94	1595	0.003	BB
17	14.59	24272	0.046	BB
18	16.85	149315	0.285	BB
19	20.41	3176	0.006	BB
20	23.85	16895	0.032	BB
21	25.44	8098	0.015	BB
22	27.45	1142493	2.178	BB
23	34.93	30078	0.057	BV
24	36.79	721733	1.376	VV
25	39.85	3036093	5.787	VV
26	42.71	45811415	87.322	VB
27	58.07	756706	1.442	BB
28	65.29	23701	0.045	BB
29	72.23	420	0.001	BB
30	77.71	398262	0.759	BB
		52462912	100.000	

Conv. : 97%, *anti* : *syn* = 95 : 5, 97% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 42.71 min (major), t_R = 58.07 min (minor)]

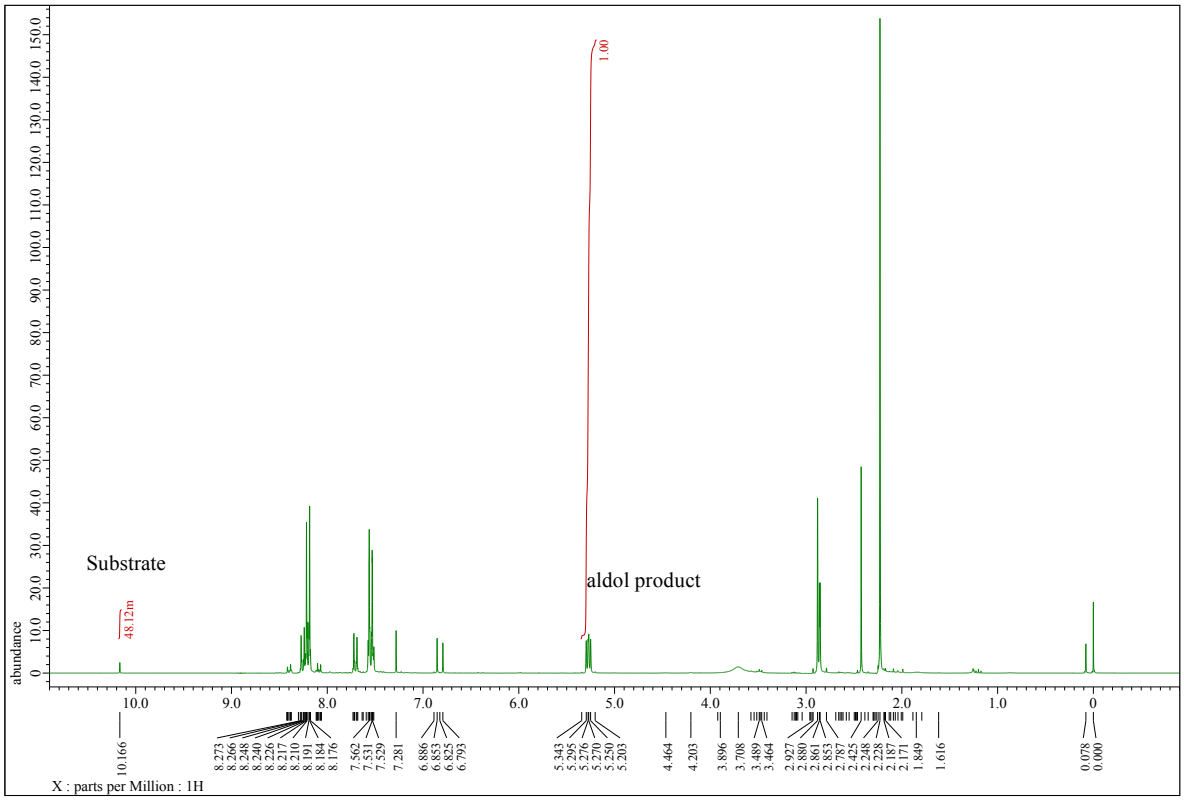
Table 2, entry 7

(*R*)-4-hydroxy-4-(4-nitrophenyl)butan-2-one 4b[13)]

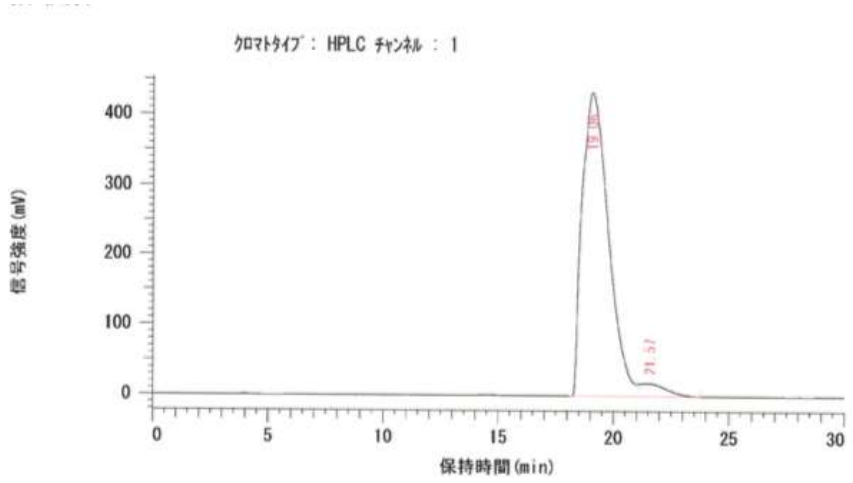


To a solution of **1a** (20.0 mg, 0.023 mmol) in dry-toluene (0.23 mL) was added acetone (459 μL, 6.2 mmol) and 4-nitrobenzaldehyde (34.9 mg, 0.23 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion was determined by ^{1}H NMR of the crude product. E*e* of the aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1

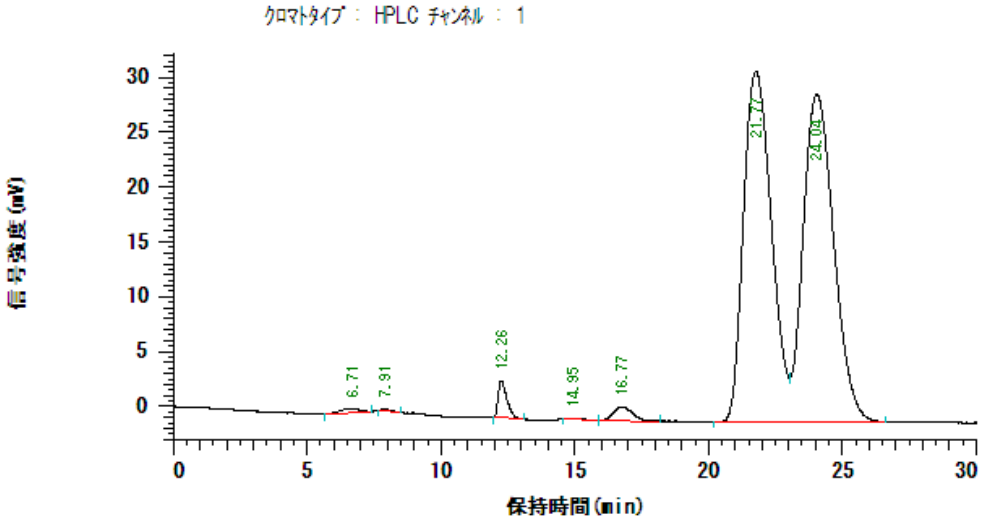
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	19.06	34077253	95.820	MC
2	21.57	1486649	4.180	MC
		35563902	100.000	

ﾚﾎﾟｰﾄﾋﾟｰｸの判定ﾚﾍﾞﾙ： 0

Conv. : 95%, 92% *ee*; The *ee* of aldol product was determined by HPLC. [Daicel chiralcel OJ-3 column, hex : ^{i}PrOH = 80 : 20, flow rate 0.8 mL/min, t_R = 19.06 min (major), t_R = 21.57 min (minor)]

HPLC analysis of racemic compound



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1

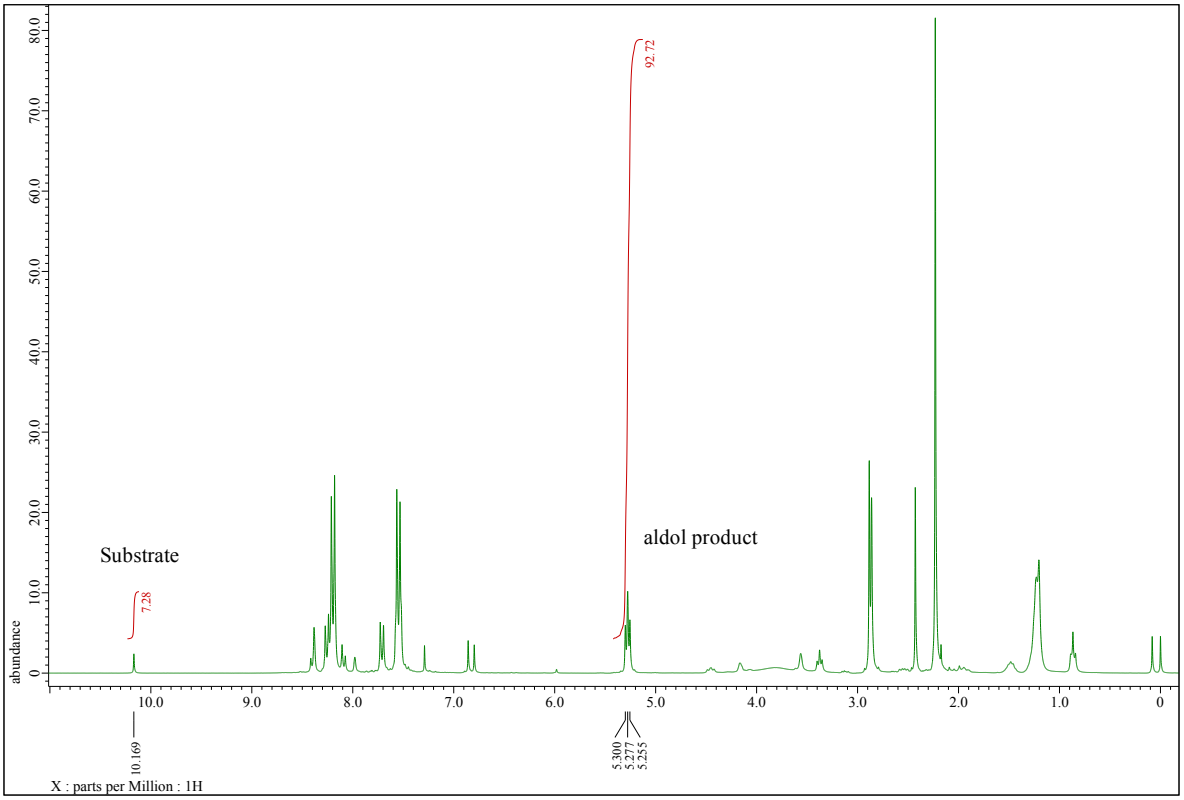
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	6.71	19430	0.400	BB
2	7.91	5315	0.110	BB
3	12.26	76736	1.581	BB
4	14.95	5047	0.104	BB
5	16.77	62973	1.297	BB
6	21.77	2303733	47.459	BV
7	24.04	2380966	49.050	VB
		4854200	100.000	

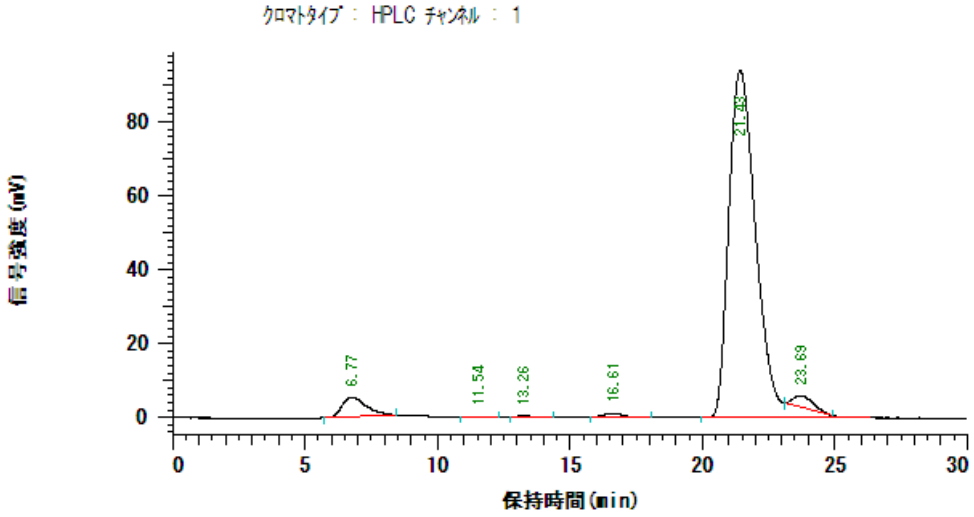
Table 2, entry 8

To a solution of **1d** (14.6 mg, 0.026 mmol) in dry-toluene (0.26 mL) was added acetone (517 µL, 7.0 mmol) and 4-nitrobenzaldehyde (39.2 mg, 0.26 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion was determined by ^{1}H NMR of the crude product. E*e* of the aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

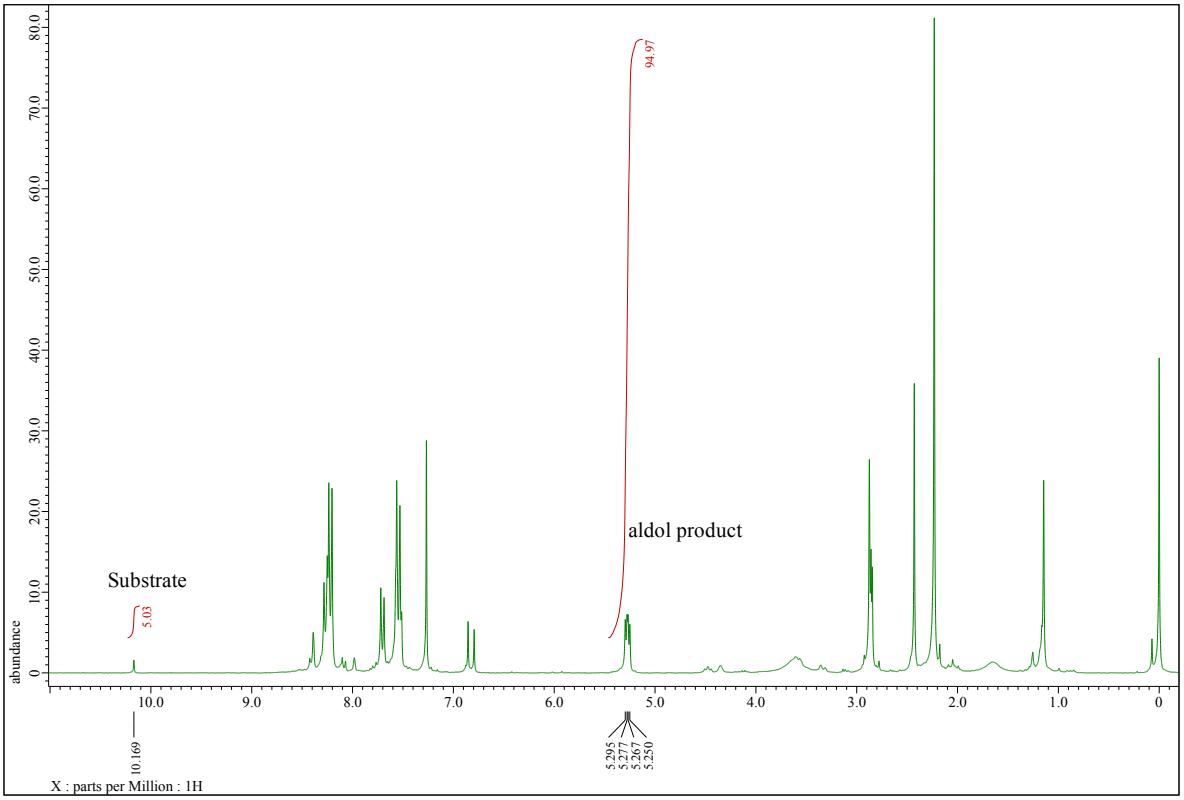
NO	RT	面積	濃度1	BC
1	6.77	332059	4.501	BB
2	11.54	3521	0.048	BB
3	13.26	2933	0.040	BB
4	16.61	55098	0.747	BB
5	21.43	6809729	92.310	BV
6	23.69	173699	2.355	TBB
		7377039	100.000	

Conv. : 93%, 95% *ee*; The *ee* of aldol product was determined by HPLC. [Daicel chiralcel OJ-3 column, hex : ^{i}PrOH = 80 : 20, flow rate 0.8 mL/min, t_R = 21.43 min (major), t_R = 23.69 min (minor)]

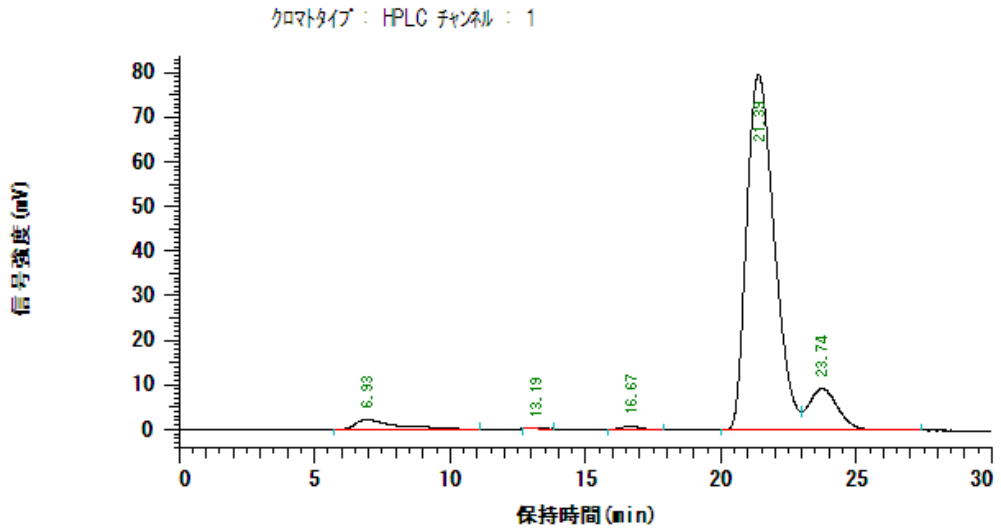
Table 2, entry 9

To a solution of **1e** (18.1 mg, 0.039 mmol) in dry-toluene (0.39 mL) was added acetone (778 µL, 11 mmol) and 4-nitrobenzaldehyde (59.0 mg, 0.39 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion was determined by ^{1}H NMR of the crude product. E*e* of the aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



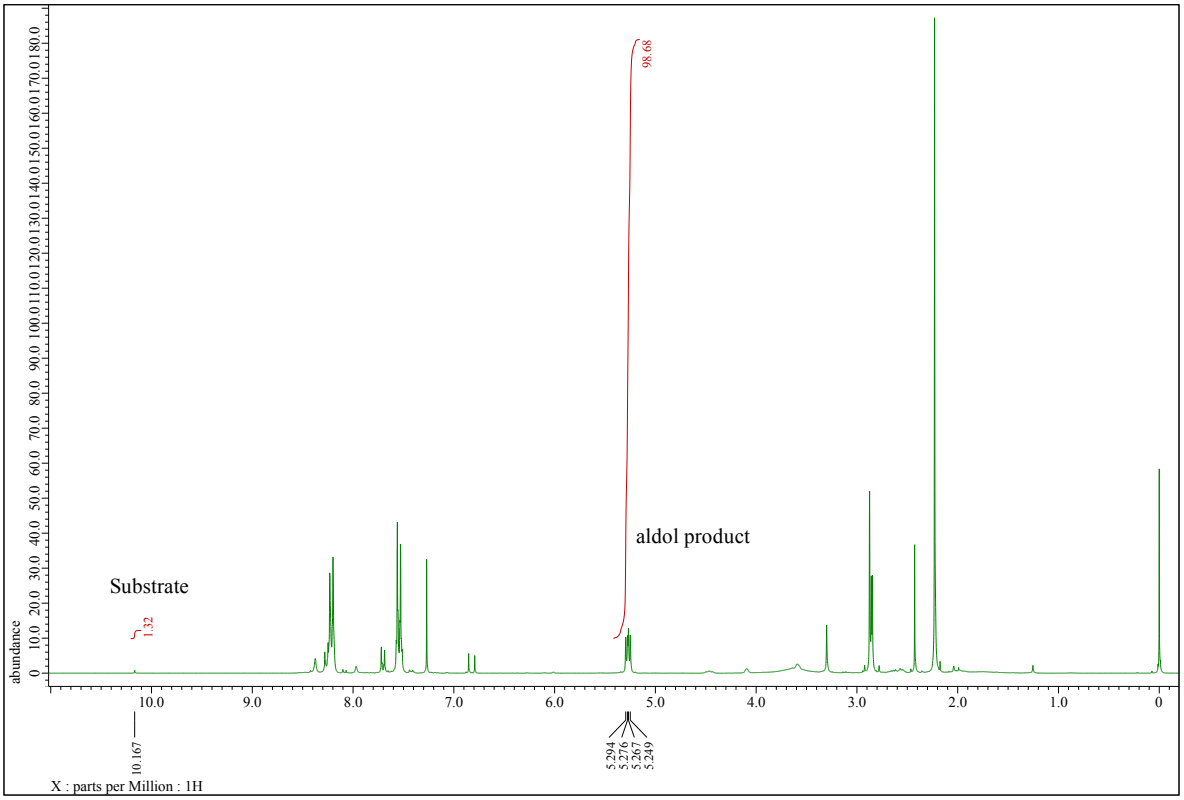
NO	RT	面積	濃度1	BC
1	6.93	237944	3.603	BB
2	13.19	2474	0.037	BB
3	16.67	42703	0.647	BB
4	21.39	5622171	85.133	BV
5	23.74	698666	10.580	VB
		6603958	100.000	

Conv. : 95%, 78% *ee*; The *ee* of aldol product was determined by HPLC. [Daicel chiralcel OJ-3 column, hex : ^{i}PrOH = 80 : 20, flow rate 0.8 mL/min, t_R = 21.39 min (major), t_R = 23.74 min (minor)]

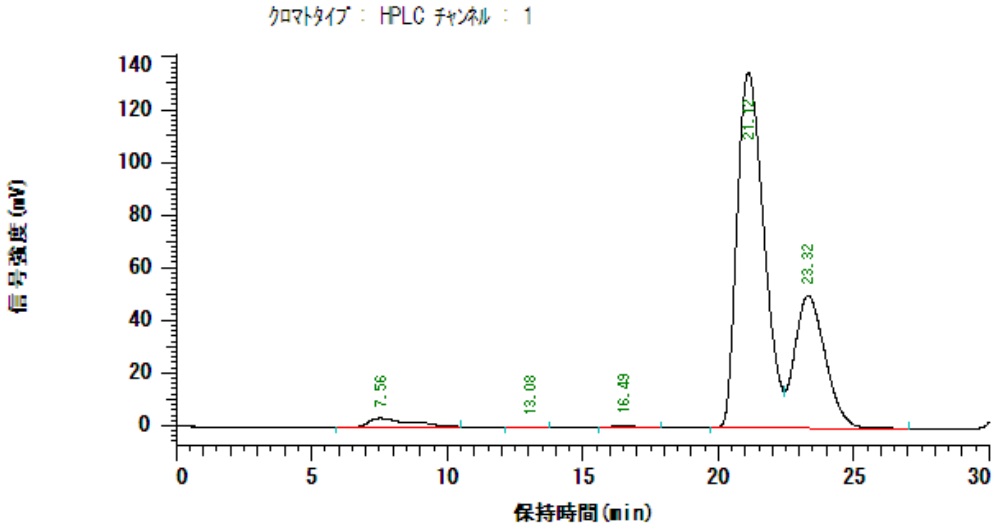
Table 2, entry 10

To a solution of **1f** (19.2 mg, 0.046 mmol) in dry-toluene (0.46 mL) was added acetone (907 µL, 12 mmol) and 4-nitrobenzaldehyde (69.0 mg, 0.46 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion was determined by ^{1}H NMR of the crude product. E*e* of the aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

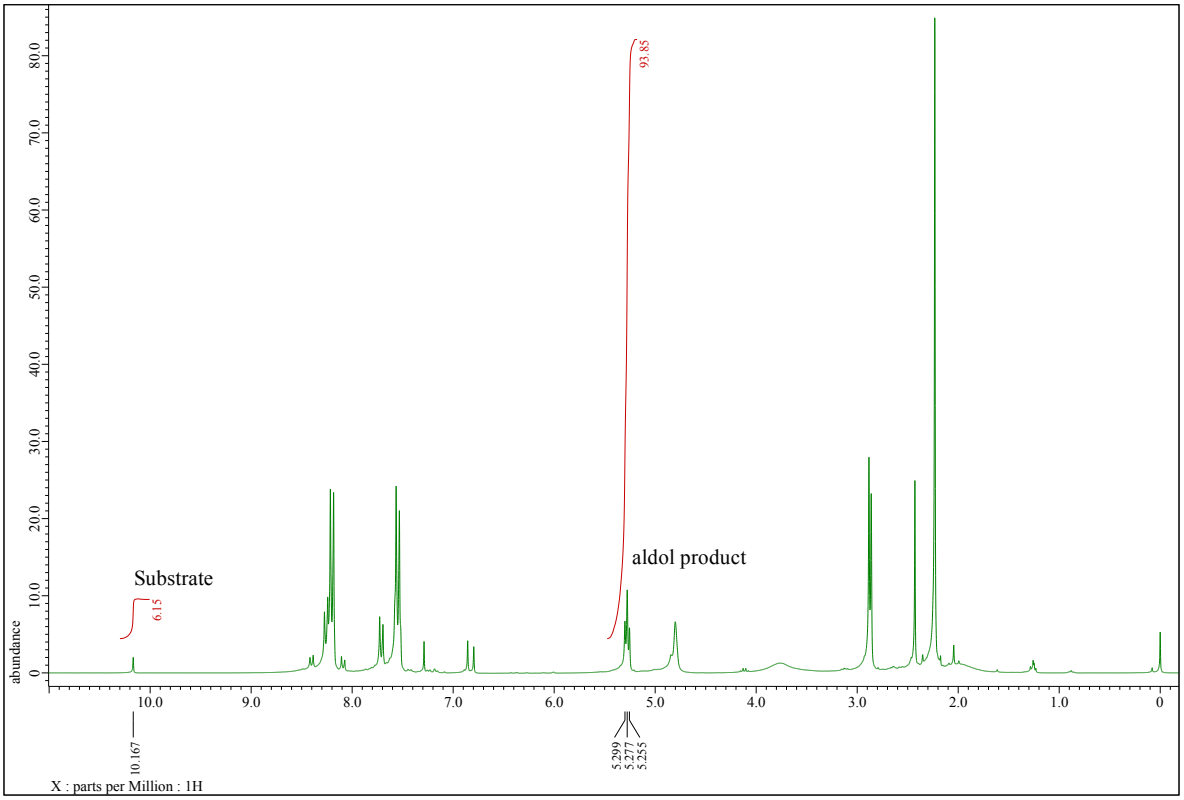
NO	RT	面積	濃度1	BC
1	7.56	355263	2.611	BB
2	13.08	7622	0.056	BB
3	16.49	49436	0.363	BB
4	21.12	9256092	68.018	BV
5	23.32	3939969	28.953	VB
		13608382	100.000	

Conv. : 99%, 40% *ee*; The *ee* of aldol product was determined by HPLC. [Daicel chiralcel OJ-3 column, hex : ^{i}PrOH = 80 : 20, flow rate 0.8 mL/min, t_R = 21.12 min (major), t_R = 23.32 min (minor)]

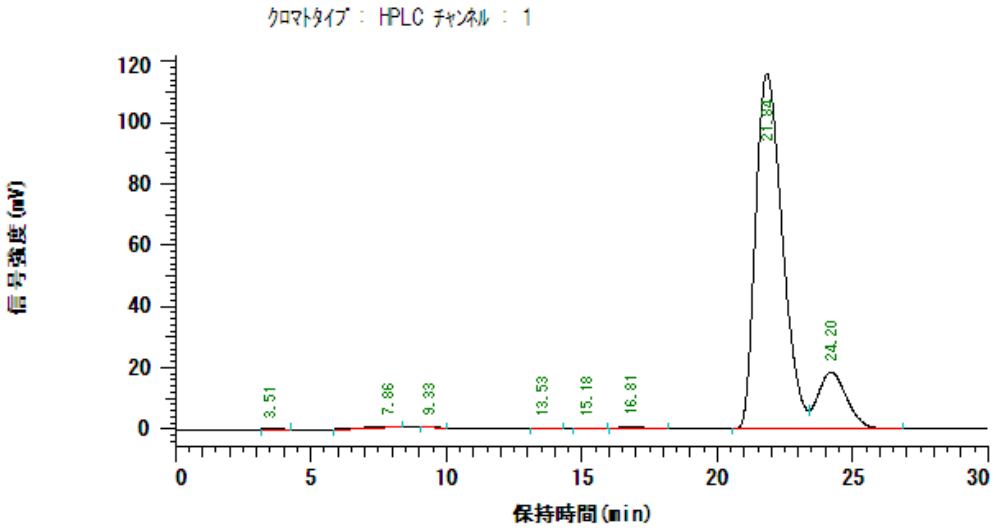
Table 2, entry 11

To a solution of **1g** (16.0 mg, 0.039 mmol) in dry-toluene (0.40 mL) was added acetone (781 µL, 11 mmol) and 4-nitrobenzaldehyde (59.5 mg, 0.39 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion was determined by ^{1}H NMR of the crude product. E*e* of the aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

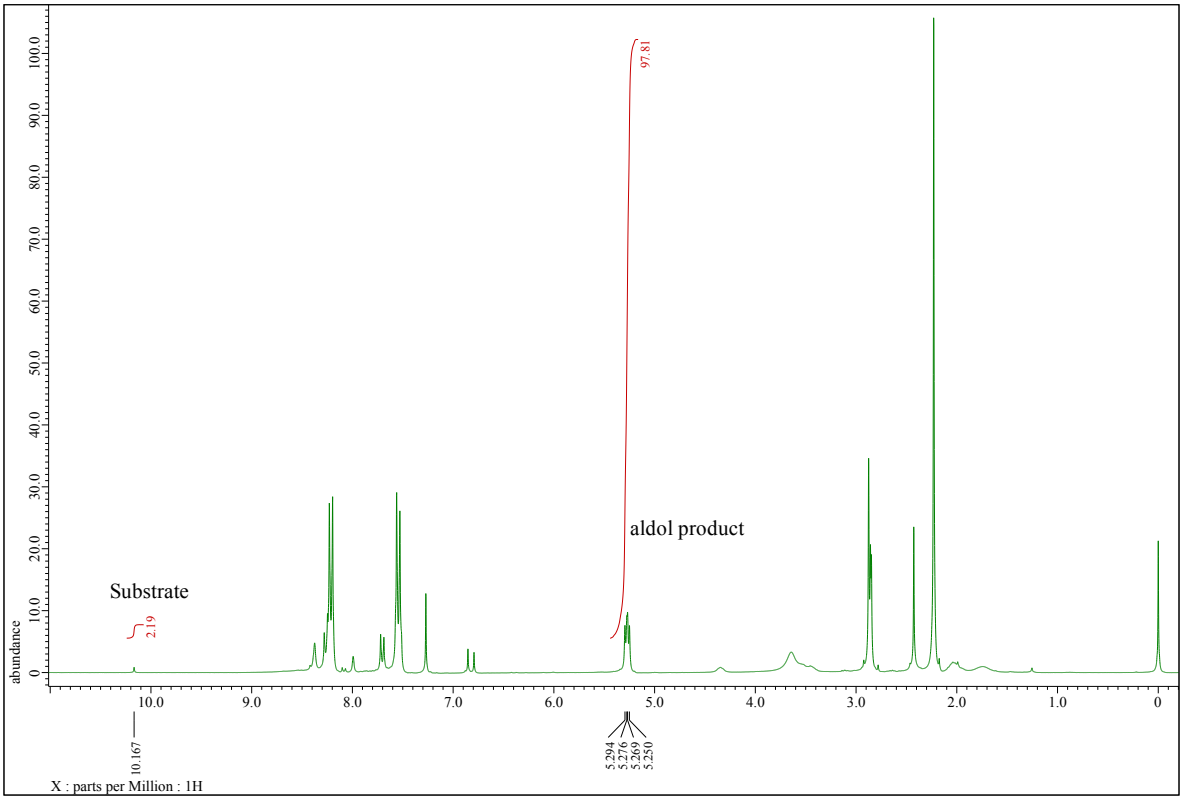
NO	RT	面積	濃度1	BC
1	3.51	1557	0.017	BB
2	7.86	19577	0.208	BB
3	9.33	8541	0.091	BB
4	13.53	2725	0.029	BB
5	15.18	3877	0.041	BB
6	16.81	46791	0.496	BB
7	21.84	7961164	84.473	BV
8	24.20	1380277	14.646	VB
		9424509	100.000	

Conv. : 94%, 70% *ee*; The *ee* of aldol product was determined by HPLC. [Daicel chiralcel OJ-3 column, hex : ^{i}PrOH = 80 : 20, flow rate 0.8 mL/min, t_R = 21.84 min (major), t_R = 24.20 min (minor)]

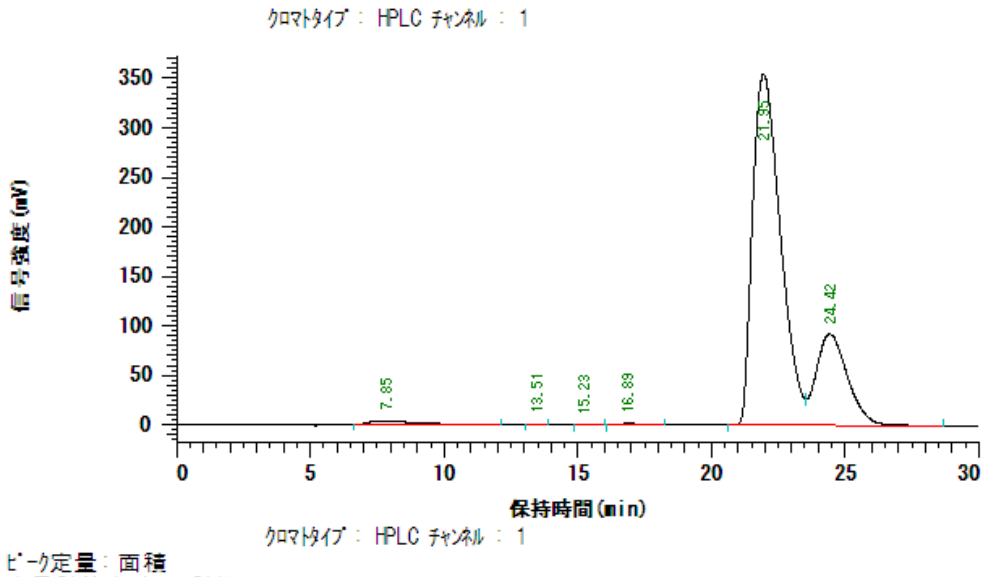
Table 2, entry 12

To a solution of **1h** (13.5 mg, 0.035 mmol) in dry-toluene (0.35 mL) was added acetone (690 μL, 9.3 mmol) and 4-nitrobenzaldehyde (52.4 mg, 0.35 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. Conversion was determined by ^{1}H NMR of the crude product. E*e* of the aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1

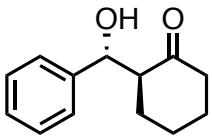
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	7.85	557769	1.650	BB
2	13.51	4194	0.012	BB
3	15.23	4190	0.012	BB
4	16.89	83836	0.248	BB
5	21.95	25646607	75.886	BV
6	24.42	7499540	22.191	VB
		33796136	100.000	

Conv. : 98%, 55% *ee*; The *ee* of aldol product was determined by HPLC. [Daicel chiralcel OJ-3 column, hex : ^{i}PrOH = 80 : 20, flow rate 0.8 mL/min, t_R = 21.95 min (major), t_R = 24.42 min (minor)]

Table 3, entry 1

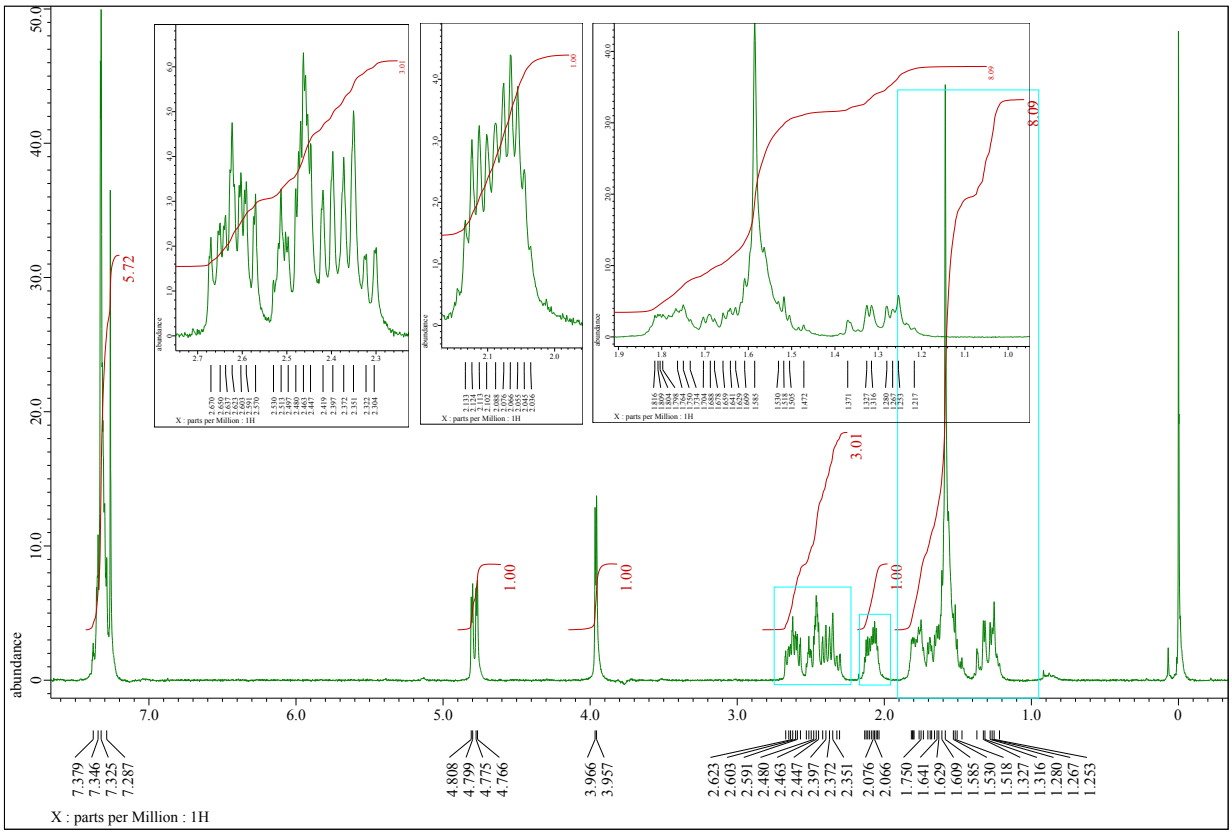
(*S*)-2-((*R*)-hydroxy(phenyl)methyl)cyclohexan-1-one 4c[1)]



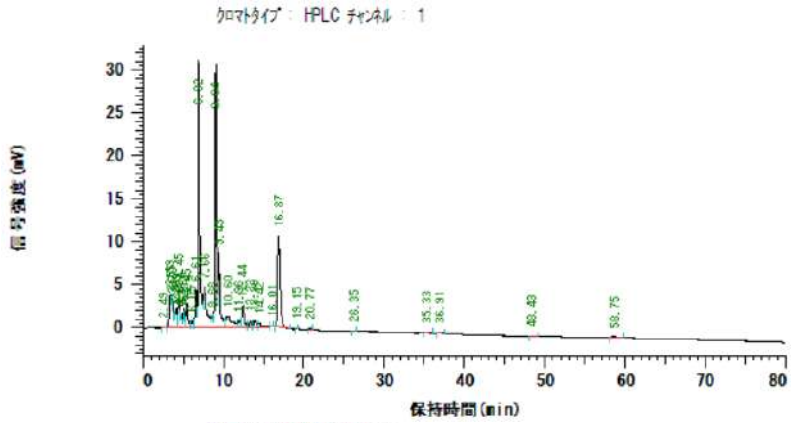
To a solution of **1a** (9.6 mg, 0.0111 mmol) in dry-toluene (110 μL) was added cyclohexanone (115.0 μL, 1.11 mmol) and benzaldehyde (11.28 μL, 0.111 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4c** (9.1 mg, 40%). Diastereoselectivity (*anti* : *syn*) and *ee* of the *anti* aldol product were determined *via* HPLC of the crude product after confirming the retention time of each racemic compound.

Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H), 4.79 (dd, J = 8.9 Hz, 2.4, 1H,), 3.96 (d, J = 2.4 Hz, 1H), 2.67-2.30 (m, 3H), 2.13-2.04 (m, 1H), 1.82-1.22 (m, 5H).

^{1}H NMR, 270 MHz,



HPLC analysis



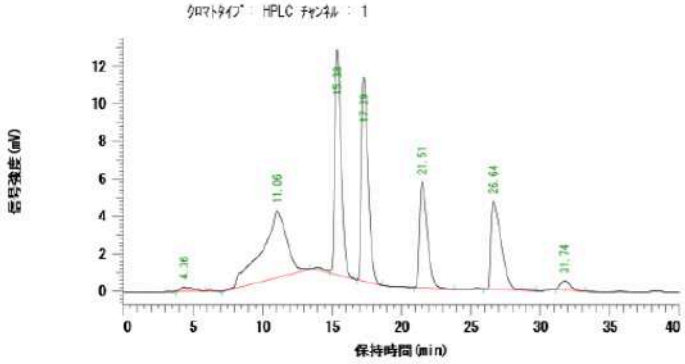
クロマトタイプ : HPLC チャンネル : 1

ピーク定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	2.49	1883	0.100	BB
2	3.39	51767	2.741	BV
3	3.55	25745	1.363	W
4	3.70	27610	1.462	W
5	3.93	10967	0.581	W
6	4.09	28717	1.520	W
7	4.45	69806	3.696	W
8	4.67	854	0.045	TBB
9	4.96	16170	0.856	W
10	5.12	20684	1.095	W
11	5.45	47153	2.496	W
12	6.05	15748	0.834	W
13	6.61	56943	3.015	W
14	6.92	434880	23.024	W
15	7.66	148235	7.848	W
16	8.66	1707	0.090	TBB
17	9.04	372207	19.706	W
18	9.43	141368	7.485	W
19	10.60	58834	3.115	W
20	11.96	15839	0.839	W
21	12.44	52537	2.782	W
22	13.33	13891	0.735	W
23	13.90	13548	0.717	W
24	14.42	13180	0.698	VB
25	16.01	609	0.032	BB
26	16.87	231274	12.244	BB
27	19.15	425	0.023	BB
28	20.77	1933	0.102	BB

Yield : 40%, *anti* : *syn* = 89 : 11, 98% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 11.96 min (*syn* : minor), t_R = 13.90 min (*syn* : major), t_R = 16.87 min (*anti* : major), t_R = 20.77 min (*anti* : minor)]

HPLC analysis of racemic compound (*anti* form + *syn* form)

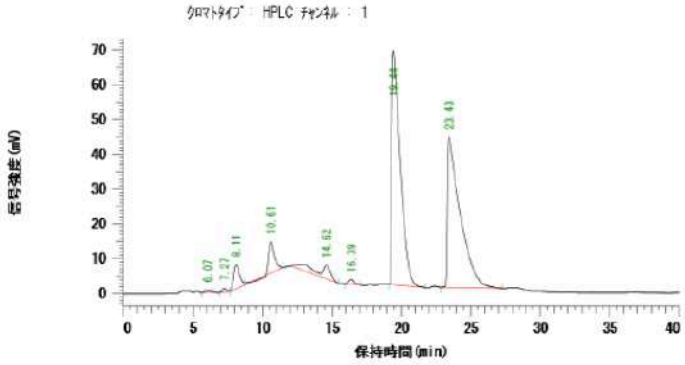


ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： IPrOOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	4.36	15753	0.936	BB
2	11.06	449464	26.715	BB
3	15.38	379186	22.538	VB
4	17.29	364828	21.684	BB
5	21.51	213375	12.682	BB
6	26.64	236933	14.083	BB
7	31.74	22919	1.362	BB
		1682458	100.000	

HPLC analysis of racemic compound (*anti* form)

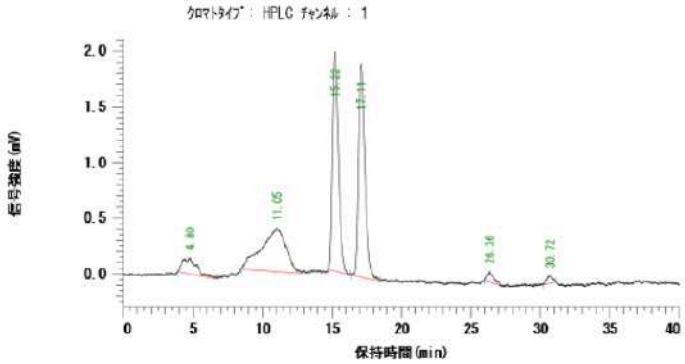


ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： IPrOOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	6.07	17921	0.288	BB
2	7.27	24592	0.395	BB
3	8.11	200824	3.226	BV
4	10.61	249605	4.010	VB
5	14.62	132116	2.122	VB
6	16.39	34007	0.546	BB
7	19.44	2800989	44.997	BB
8	23.43	2764813	44.416	BB
		6224867	100.000	

HPLC analysis of racemic compound *(syn* form)



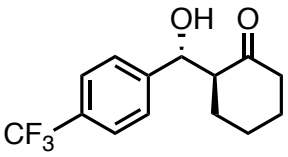
ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ：iPrOOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名：Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)：L-2130
ﾎﾟﾝﾌﾟA 溶離液A：4　　ﾎﾟﾝﾌﾟA 溶離液B：96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ：HPLC ﾁｬﾝﾈﾙ：1
ﾋﾟｰｸ定量：面積
定量計算方法：面積%

NO	RT	面積	濃度1	BC
1	4.80	9450	5.156	BB
2	11.05	47901	26.132	BB
3	15.22	59549	32.486	BB
4	17.11	61641	33.628	BB
5	26.36	2872	1.567	BB
6	30.72	1890	1.031	BB
		183303	100.000	

Table 3, entry 2

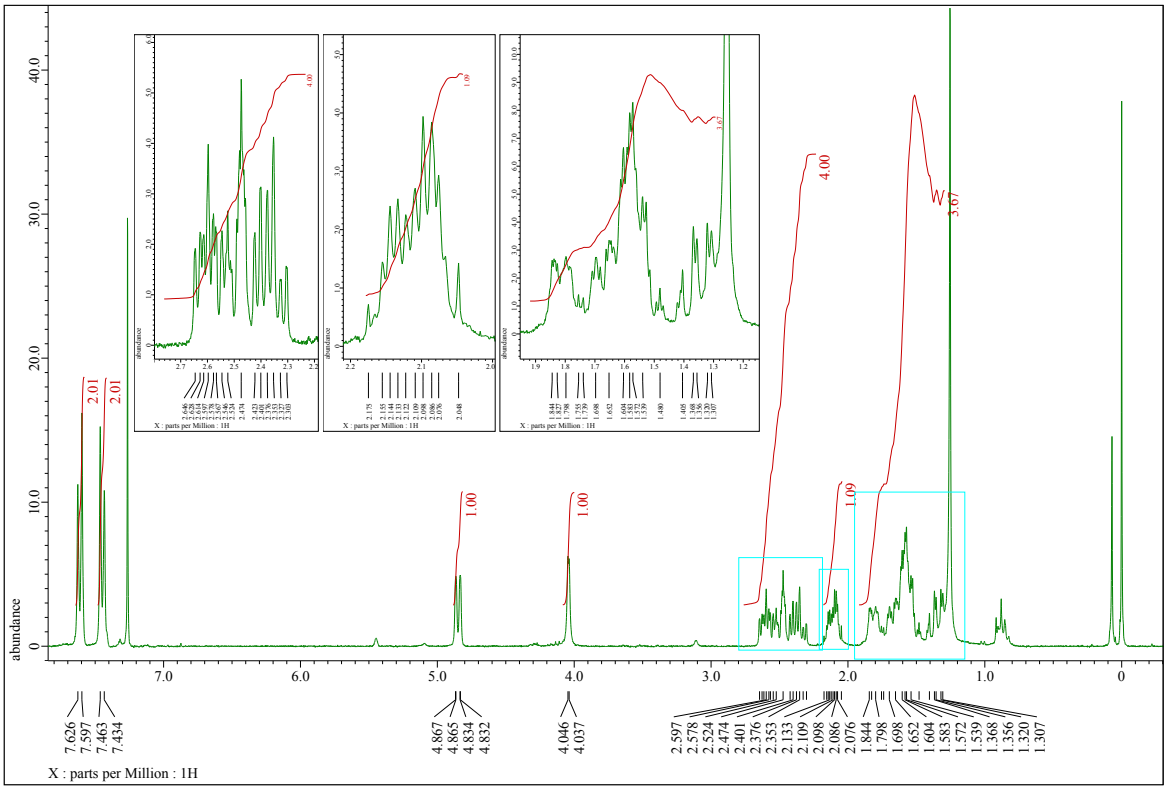
(*S*)-2-((*R*)-hydroxy(4-(trifluoromethyl)phenyl)methyl)cyclohexan-1-one 4d[1)]



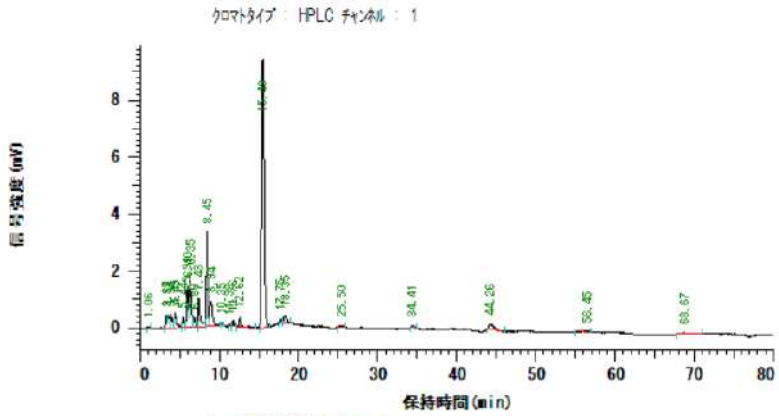
To a solution of **1a** (11.6 mg, 0.0134 mmol) in dry-toluene (140 μL) was added cyclohexanone (140 μL, 1.34 mmol) and p-trifluorobenzaldehyde (23.6 mg, 0.134 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4d** (13.7 mg, 38%). Diastereoselectivity (*anti* : *syn*) and *ee* of the *anti* aldol product were determined *via* HPLC of the crude product after confirming the retention time of each racemic compound.

White solid; m.p. 91.9-92.7 °C; ^{1}H NMR (270 MHz, $CDCl_3$) 7.61 (d, J = 7.8, 2H), 7.45 (d, J = 7.8 Hz, 2H), 4.85 (dd, J = 8.6 Hz, 2.4 Hz, 1H), 4.06 (d, J = 2.7 Hz, 1H), 2.65-2.31 (m, 4H), 2.18-2.05 (m, 1H), 1.84-1.26 (m, 4H).

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



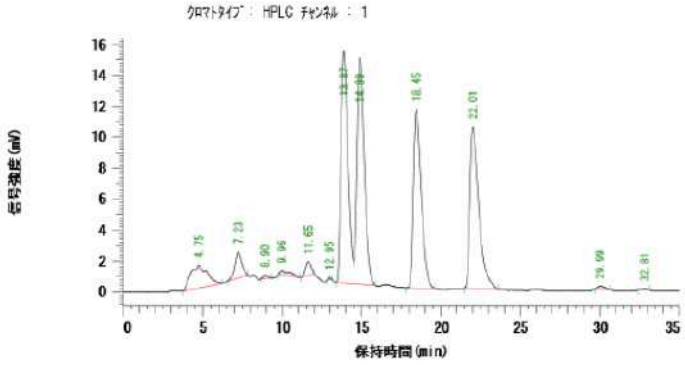
クロマトタイプ : HPLC チャンネル : 1

ピーク定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	1.06	519	0.133	BB
2	3.37	5654	1.451	BV
3	3.58	6423	1.649	VV
4	3.94	6171	1.584	VV
5	4.45	9863	2.532	VB
6	5.44	5454	1.400	BV
7	5.91	10400	2.669	VV
8	6.10	13760	3.532	VV
9	6.35	25366	6.511	VV
10	6.89	5123	1.315	VB
11	7.43	16627	4.268	BV
12	8.45	39007	10.012	VV
13	8.94	18949	4.863	VB
14	10.35	795	0.204	BB
15	11.33	732	0.188	BB
16	11.76	3234	0.830	BB
17	12.62	7957	2.042	BB
18	15.49	188354	48.342	BB
19	17.75	2603	0.668	BV
20	18.35	6867	1.763	VB
21	25.50	2246	0.577	BB
22	34.41	2293	0.589	BB
23	44.26	8037	2.063	BB
24	56.45	821	0.211	BB
25	68.67	2356	0.605	BB

Yield : 38%, *anti* : *syn* = 95 : 5, 93% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 11.76 min (*sun* : major), t_R = 12.62 min (*sun* : minor), t_R = 15.49 min (*anti* : major), t_R = 18.35 min (*anti* : minor)]

HPLC analysis of racemic compound (*anti* form + *syn* form)

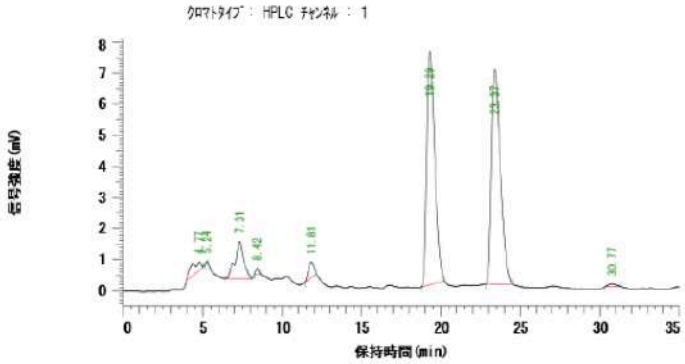


ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： iProOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	4.75	106923	5.365	BB
2	7.23	49381	2.478	BB
3	8.90	3624	0.182	BB
4	9.96	12269	0.616	BB
5	11.65	21873	1.097	BB
6	12.95	1777	0.089	BB
7	13.87	453717	22.764	BV
8	14.89	468601	23.511	VB
9	18.45	394819	19.809	BB
10	22.01	410358	20.589	BB
11	29.99	5983	0.300	BB
12	32.81	1759	0.088	BB
13	36.01	4790	0.240	BB
14	40.17	7294	0.366	BB
15	42.42	2410	0.121	BB
16	74.63	6331	0.318	BB
17	98.72	41204	2.067	BB
		1993113	100.000	

HPLC analysis of racemic compound (*anti* form)

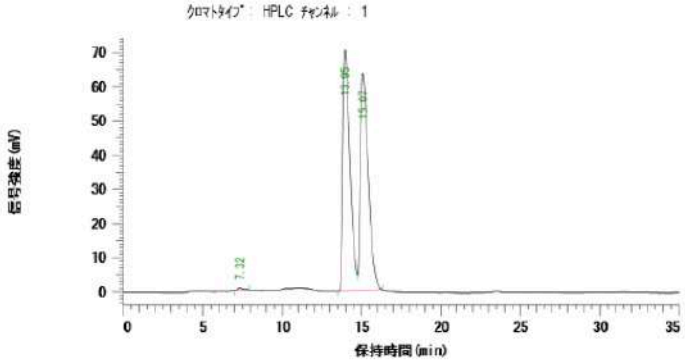


ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： iProOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	4.77	14348	2.312	BB
2	5.24	902	0.145	BB
3	7.31	44633	7.192	BB
4	8.42	2561	0.413	BB
5	11.81	11404	1.838	BB
6	19.29	265885	42.844	BB
7	23.37	275111	44.331	BB
8	30.77	3042	0.490	BB
9	37.51	2694	0.434	BB
		620580	100.000	

HPLC analysis of racemic compound (*syn* form)



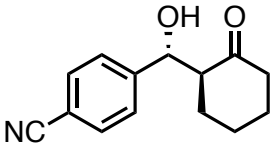
ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： IPrOOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	7.32	17182	0.389	BB
2	13.95	2181055	49.355	BV
3	15.07	2220903	50.256	VB
		4419140	100.000	

Table 3, entry 3

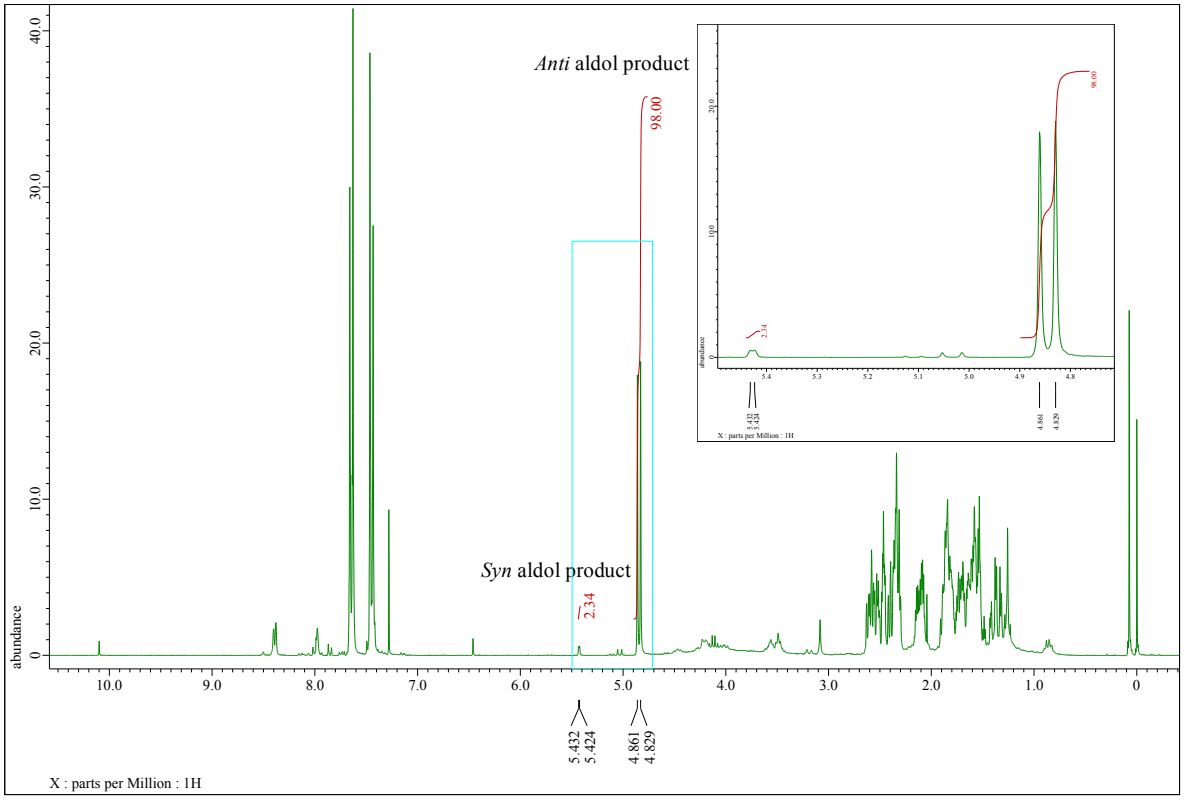
4-((*R*)-hydroxy((*S*)-2-oxocyclohexyl)methyl)benzonitrile 4e[1)]



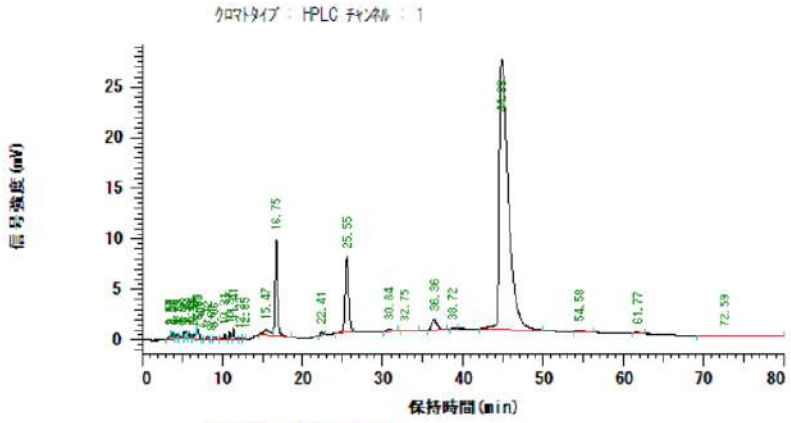
To a solution of **1a** (13.8 mg, 0.0159 mmol) in dry-toluene (160 μL) was added cyclohexanone (165 μL, 1.59 mmol) and p-cyanobenzaldehyde (20.6 mg, 0.159 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4e** (36.4 mg, 100%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. *Ee* of the *anti* aldol product was determined *via* HPLC of the crude product after confirming the retention time of each racemic compound.

Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.65 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.1 Hz, 2H), 4.84 (d, J = 8.4 Hz, 1H), 4.05 (s, 1H), 2.62-2.30 (m, 3H), 2.16-2.05 (m, 1H), 1.86-1.47 (m, 5H).

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis

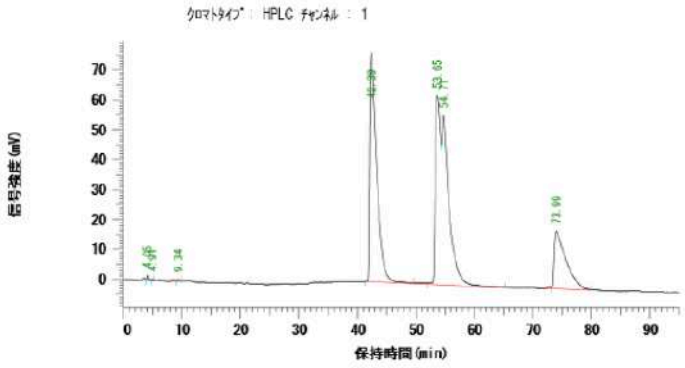


クロマトタイプ : HPLC チャンネル : 1
ピーク定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	3.57	7711	0.281	BV
2	3.69	6524	0.238	VV
3	4.00	4987	0.182	VV
4	4.39	5667	0.207	VV
5	4.73	3451	0.126	VB
6	5.32	8022	0.292	BV
7	5.56	3935	0.143	VB
8	5.88	6755	0.246	BB
9	6.38	9874	0.360	BV
10	6.85	9295	0.339	VV
11	6.99	11818	0.431	VV
12	7.40	1110	0.040	TBB
13	8.12	5931	0.216	BB
14	8.61	637	0.023	BB
15	9.06	6253	0.228	BB
16	10.31	8840	0.322	BB
17	10.97	9475	0.345	BV
18	11.41	15525	0.566	VB
19	12.22	1375	0.050	BB
20	12.85	477	0.017	BB
21	15.47	29165	1.063	BV
22	16.75	200009	7.290	VB
23	22.41	6684	0.244	BB
24	25.55	224938	8.199	BB
25	30.84	8975	0.327	BB
26	32.75	4731	0.172	BB
27	36.36	48968	1.785	BB
28	38.72	1170	0.043	BB
29	44.83	2056542	74.957	BB
30	54.58	9875	0.360	BB
31	61.77	6768	0.247	BB
32	72.59	18132	0.661	BB

Yield : 100%, *anti* : *syn* = 98 : 2, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 36.36 min (syn), t_R = 44.83 min (*anti* : major), t_R = 61.77 min (*anti* : minor)]

HPLC analysis of racemic compound (*anti* form + *syn* form)



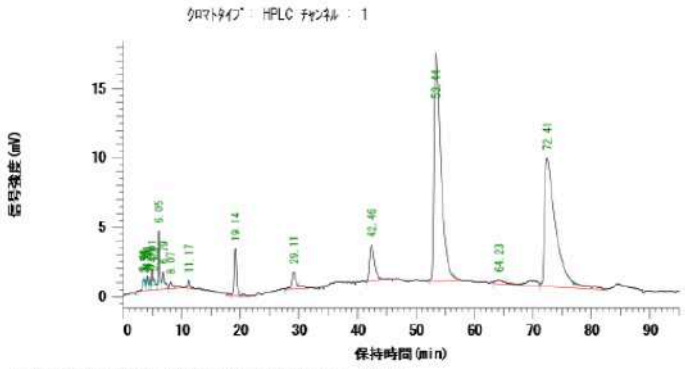
ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： IPrOOH Hex=4 96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	4.05	15512	0.088	BV
2	4.91	4751	0.027	BV
3	9.34	10559	0.060	BB
4	42.39	6148048	34.820	BV
5	53.65	3705581	20.987	VV
6	54.71	5115933	28.974	VB
7	73.99	2656392	15.045	VB
		17656776	100.000	

HPLC analysis of racemic compound (*anti* form : *syn* form = 10 : 1)*

* determined by ^{1}H NMR

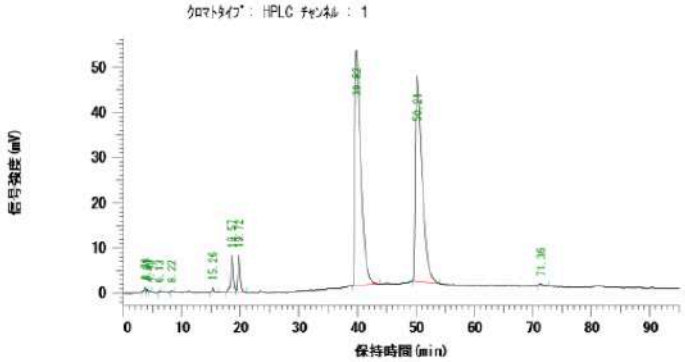


ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： IPrOOH Hex=4 96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	3.41	12498	0.414	BV
2	3.59	5812	0.193	VV
3	3.75	8284	0.275	VV
4	4.01	14494	0.480	VV
5	4.48	15607	0.517	VV
6	4.91	19221	0.637	VV
7	5.23	19865	0.658	VV
8	6.05	57466	1.905	VV
9	6.79	25043	0.830	VV
10	8.07	13347	0.442	BB
11	11.17	7990	0.265	VV
12	19.14	83471	2.766	VB
13	29.11	52880	1.753	BV
14	42.46	146484	4.855	BV
15	53.44	1334703	44.235	VV
16	64.23	25973	0.861	BV
17	72.41	1174130	38.914	BV
		3017268	100.000	

HPLC analysis of racemic compound (*syn* form)



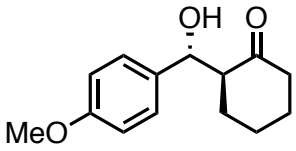
ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ: iProOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名: Column　　ﾒｿｯﾄﾞ作成者:
ﾎﾟﾝﾌﾟA(ﾒｲﾝ): L-2130
ﾎﾟﾝﾌﾟA 溶離液A: 4　　ﾎﾟﾝﾌﾟA 溶離液B: 96
ﾎﾟﾝﾌﾟA 溶離液C:　　ﾎﾟﾝﾌﾟA 溶離液D:
分析ﾌｧｲﾙｺﾒﾝﾄ:

ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量: 面積
定量計算方法: 面積%

NO	RT	面積	濃度1	BC
1	3.73	19014	0.244	BV
2	4.01	6900	0.089	VB
3	4.49	4303	0.055	BB
4	6.13	4226	0.054	BB
5	6.22	4491	0.058	BB
6	15.26	25070	0.322	BB
7	18.57	247038	3.169	BV
8	19.72	235047	3.015	VB
9	39.82	3603462	46.229	BB
10	50.21	3623898	46.492	BB
11	71.36	21299	0.273	BB
		7794748	100.000	

Table 3, entry 4

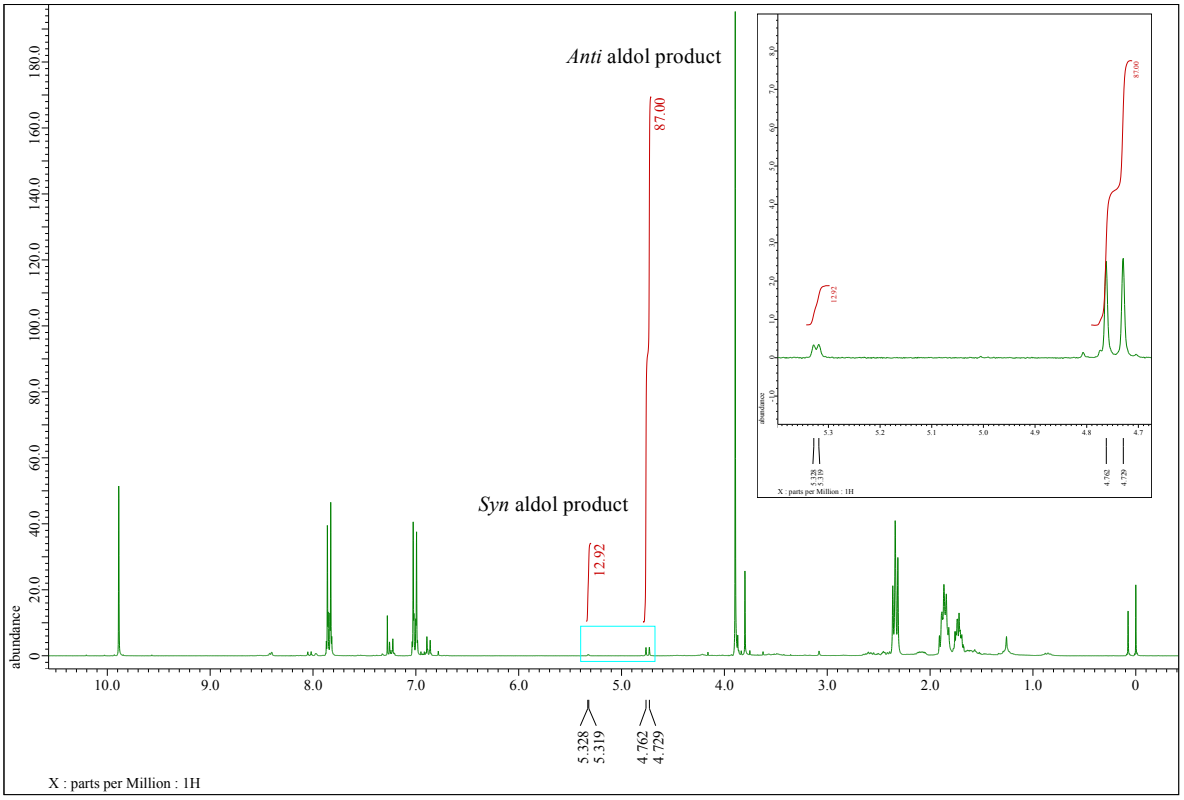
(*S*)-2-((*R*)-hydroxy(4-methoxyphenyl)methyl)cyclohexan-1-one 4f[1)]



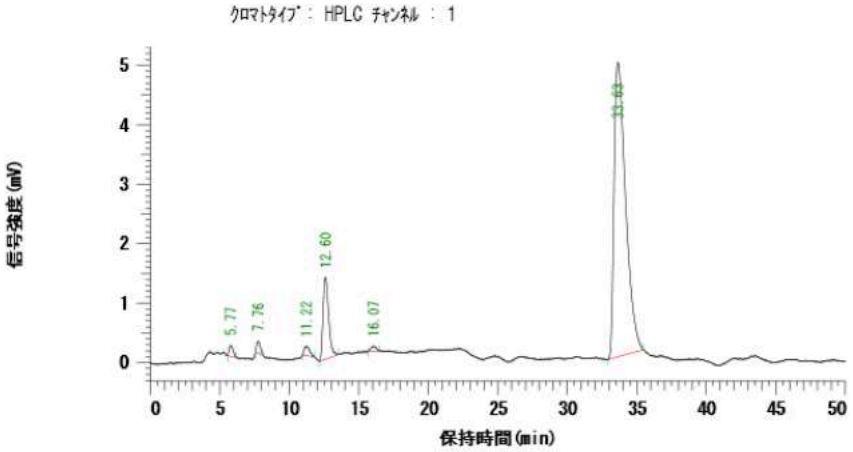
To a solution of **1a** (15.1 mg, 0.017 mmol) in dry-toluene (170 μL) was added cyclohexanone (176 μL, 1.7 mmol) and p-methoxybenzaldehyde (20.7 μL, 0.17 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4f** (6.1 mg, 15%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. *Ee* of the *anti* aldol product was determined *via* HPLC of the purified product (anti form) after confirming the retention time of each racemic compound.

Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.24 (d, J = 8.9 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 4.74 (dd, J = 8.9, 1.9 Hz, 1H), 3.93 (d, J = 2.4 Hz, 1H), 3.80 (s, 3H), 2.64-2.30 (m, 3H), 2.13-2.05 (m, 1H), 1.81-1.23 (m, 5H).

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis

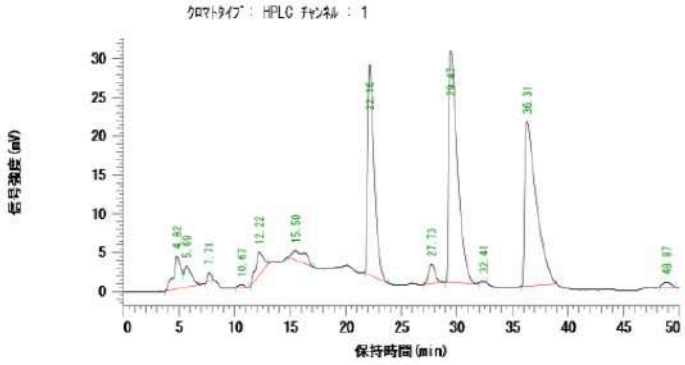


ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	5.77	3587	1.079	BB
2	7.76	3648	1.097	BB
3	11.22	4214	1.267	BB
4	12.60	37928	11.406	BB
5	16.07	2077	0.625	BB
6	33.63	281068	84.526	BB
		332522	100.000	

Yield : 15%, *anti* : *syn* = 87 : 13, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 33.63 min (*anti* : major)]

HPLC analysis of racemic compound (*anti* form + *syn* form)

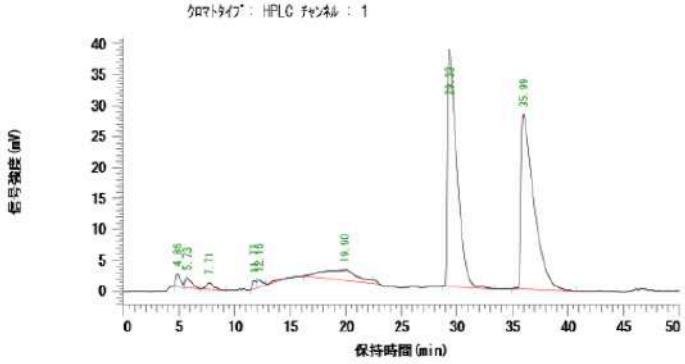


ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： iProOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	4.82	194241	3.877	BV
2	5.69	123223	2.459	VB
3	7.71	22190	0.443	BB
4	10.67	10036	0.200	BB
5	12.22	138577	2.766	BB
6	15.50	116176	2.319	BB
7	22.16	1101155	21.977	BB
8	27.73	103696	2.070	BB
9	29.47	1623622	32.405	BB
10	32.41	5860	0.117	BB
11	36.31	1541561	30.767	BB
12	48.87	30080	0.600	BB
		5010417	100.000	

HPLC analysis of racemic compound *(anti* form)

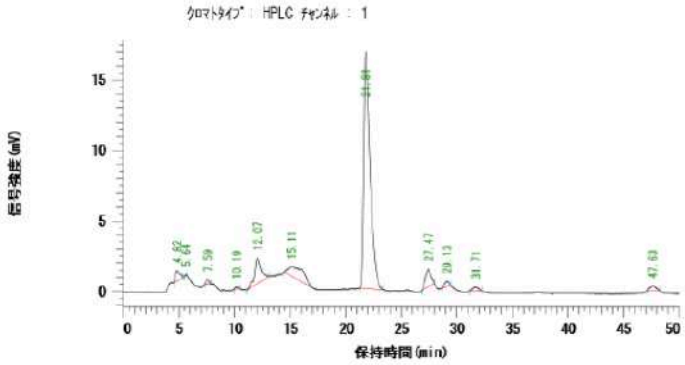


ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： iProOH:Hex=4:96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

NO	RT	面積	濃度1	BC
1	4.86	60535	1.193	BV
2	5.73	66324	1.307	VB
3	7.71	48365	0.953	BB
4	11.77	27574	0.544	BV
5	12.16	40437	0.797	VV
6	19.90	354110	6.980	BV
7	29.33	2235011	44.057	BB
8	35.99	2240589	44.167	BB
		5072945	100.000	

HPLC analysis of racemic compound (*syn* form)*



ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ： IPro0H Hex=4 96 1ml/min 120min
ｶﾗﾑ名： Column　　ﾒｿｯﾄﾞ作成者：
ﾎﾟﾝﾌﾟA(ﾒｲﾝ)： L-2130
ﾎﾟﾝﾌﾟA 溶離液A： 4　　ﾎﾟﾝﾌﾟA 溶離液B： 96
ﾎﾟﾝﾌﾟA 溶離液C：　　ﾎﾟﾝﾌﾟA 溶離液D：
分析ﾌｧｲﾙｺﾒﾝﾄ：

ｸﾛﾏﾄﾀｲﾌﾟ： HPLC ﾁｬﾝﾈﾙ： 1
ﾋﾟｰｸ定量： 面積
定量計算方法： 面積%

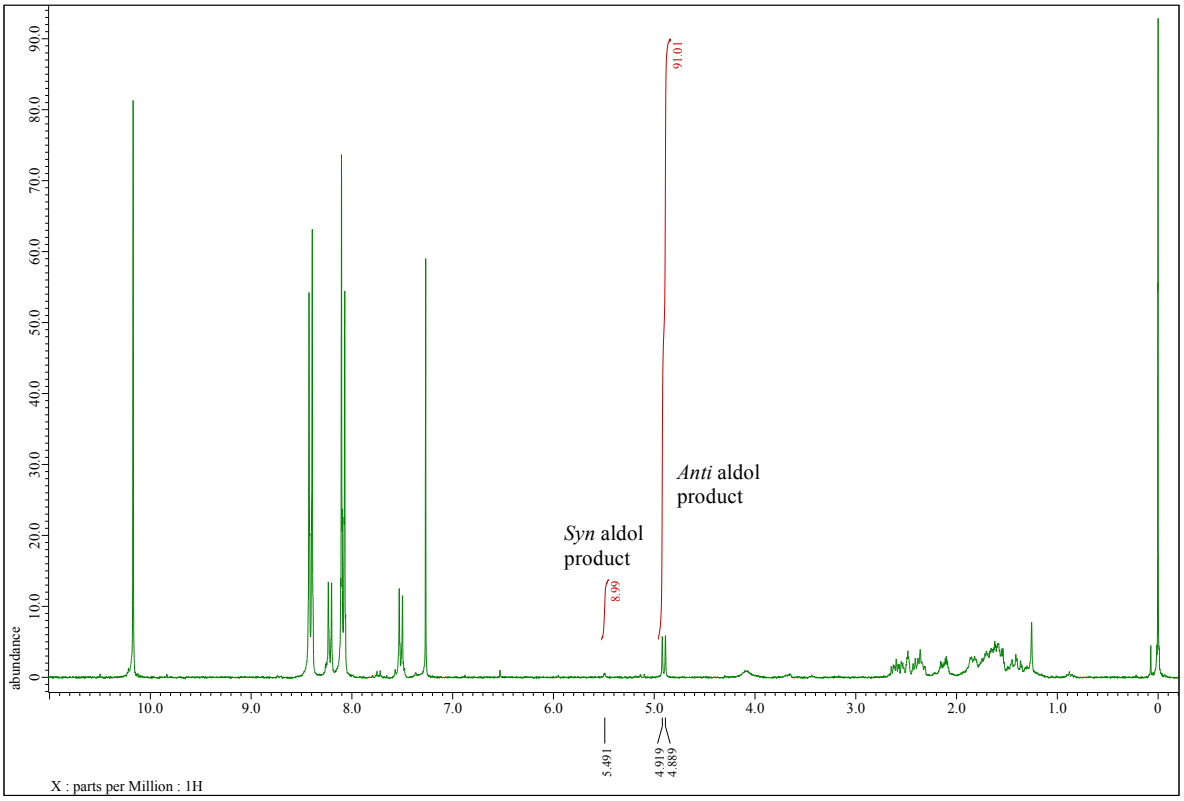
NO	RT	面積	濃度1	BC
1	4.82	18669	1.999	BB
2	5.64	1569	0.168	BB
3	7.59	5227	0.560	BB
4	10.19	3003	0.322	BB
5	12.07	73461	7.864	BB
6	15.11	78525	8.407	BB
7	21.81	679908	72.787	BB
8	27.47	41122	4.402	BB
9	29.13	10794	1.156	BB
10	31.71	10331	1.106	BB
11	47.63	11488	1.230	BB
		934097	100.000	

*_Syn_ form could not be separated to the enantiomers under these conditions.

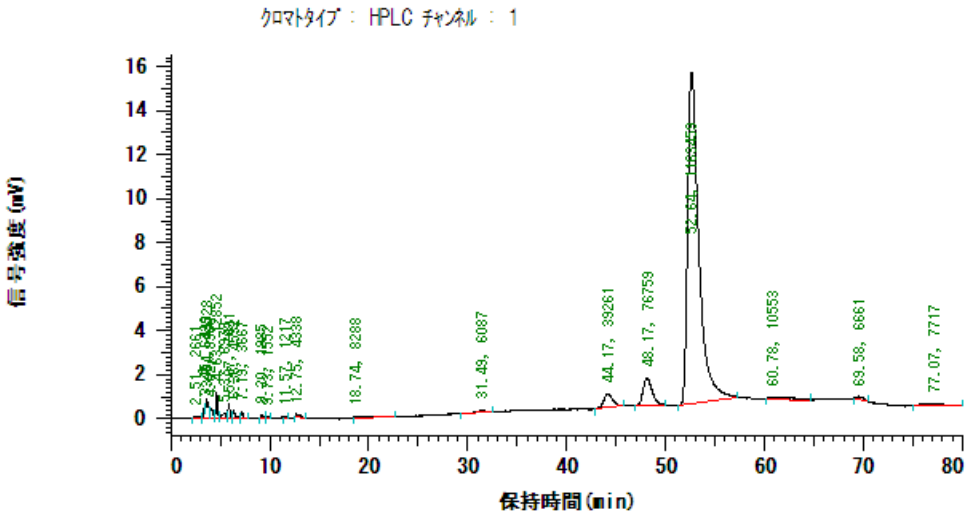
Table 5, entry 1

To a solution of **1i** (10.1 mg, 0.0087 mmol) in dry-toluene (0.087 mL) was added cyclohexanone (90 µL, 0.87 mmol) and 4-nitrobenzaldehyde (13.2 mg, 0.087 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (3.2 mg, 15%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ﾃﾞｰﾀ処理用分析ﾌｧｲﾙ: iPrOH:Hex=4:96 1ml/min
ｶﾗﾑ名 : Column
ﾎﾟﾝﾌﾟA(ﾒｲﾝ) : L-2130
ﾎﾟﾝﾌﾟA 溶離液A: iPrOH
ﾎﾟﾝﾌﾟA 溶離液C:
分析ﾌｧｲﾙｺﾒﾝﾄ:
ﾒｿｯﾄﾞ作成者 :
ﾎﾟﾝﾌﾟA 溶離液B: Hex
ﾎﾟﾝﾌﾟA 溶離液D:

ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1

ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

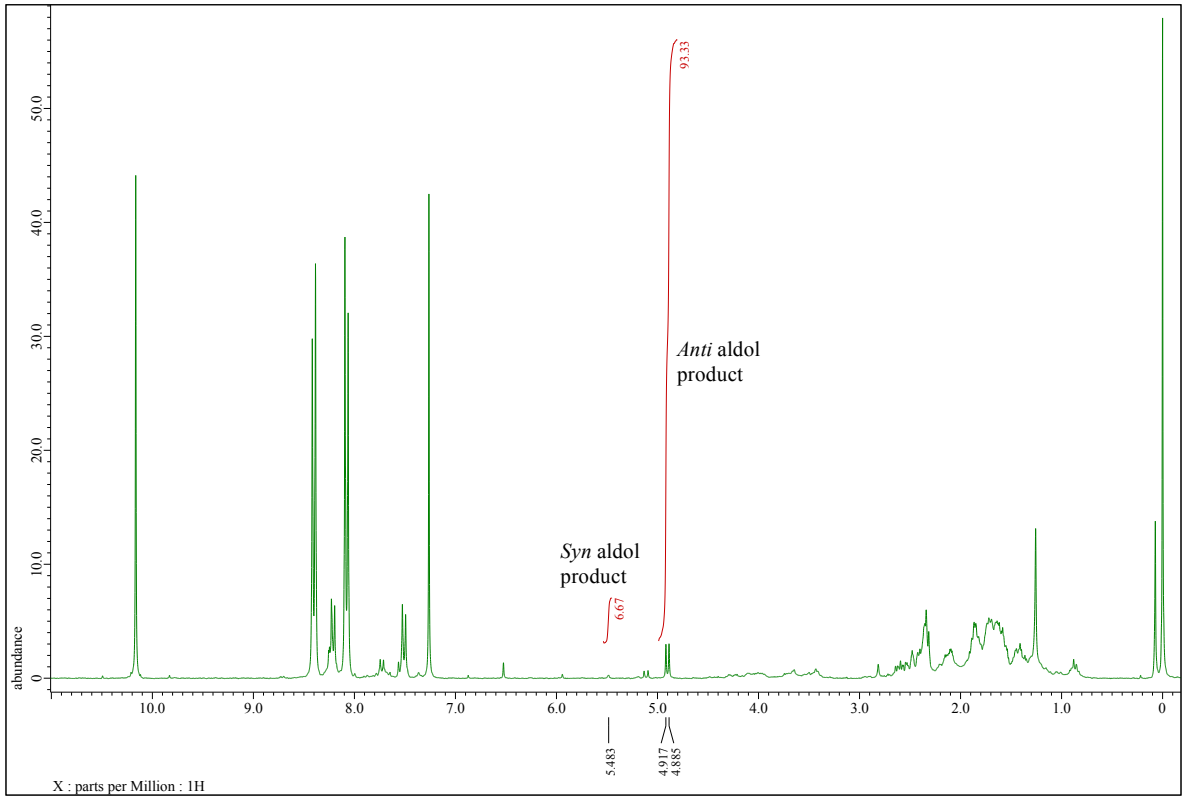
NO	RT	面積	濃度1	BC
1	2.51	2661	0.191	BB
2	3.45	6429	0.461	BV
3	3.64	14528	1.041	VV
4	4.02	8360	0.599	VV
5	4.63	12852	0.921	VV
6	5.37	6979	0.500	VV
7	5.87	7431	0.533	VB
8	6.36	4532	0.325	BB
9	7.19	3667	0.263	BB
10	9.20	1985	0.142	BB
11	9.73	1552	0.111	BB
12	11.57	1217	0.087	BB
13	12.75	4338	0.311	BB
14	18.74	8288	0.594	BB
15	31.49	6087	0.436	BB
16	44.17	39261	2.814	BB
17	48.17	76759	5.501	BB
18	52.64	1163459	83.382	BB
19	60.78	10553	0.756	BB
20	69.58	6661	0.477	BB
21	77.07	7717	0.553	BB
		1395316	100.000	

Yield : 15%, *anti* : *syn* = 91 : 9, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 52.64 min (major), t_R = 69.58 min (minor)]

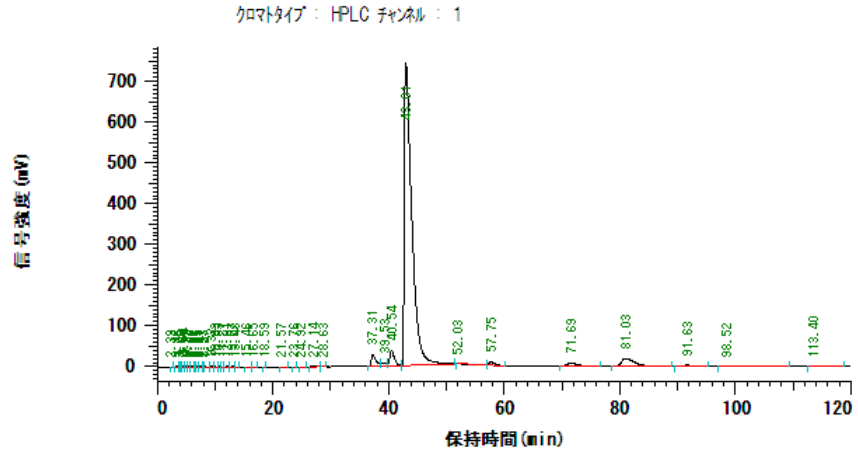
Table 5, entry 2

To a solution of **1i** (5.6 mg, 0.0049 mmol) in dry-toluene (0.049 mL) was added cyclohexanone (152 μL, 1.5 mmol) and 4-nitrobenzaldehyde (7.4 mg, 0.049 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (1.3 mg, 11%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1
ピーク定量 : 面積
定量計算方法 : 面積%

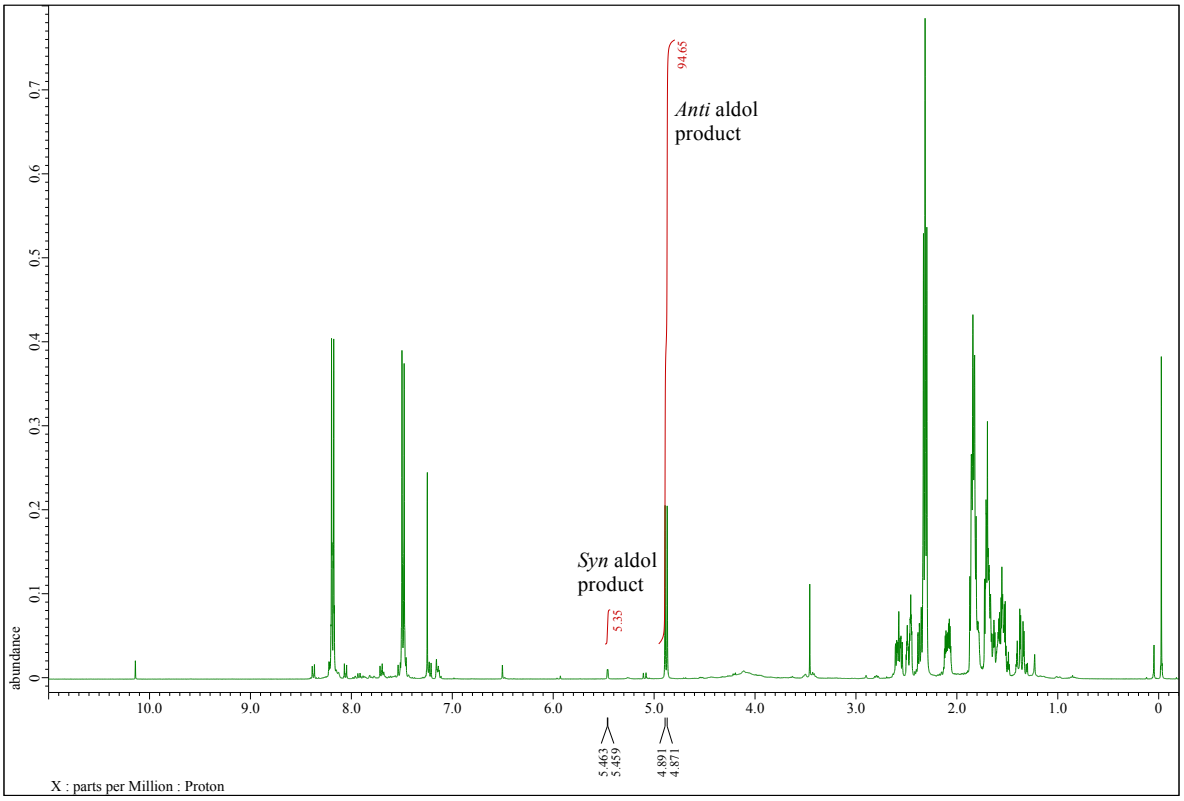
NO	RT	面積	濃度1	BC
1	2.39	653	0.001	BB
2	3.42	20936	0.028	BV
3	3.75	8143	0.011	VV
4	4.09	19355	0.026	VV
5	4.54	22494	0.030	VV
6	4.95	9832	0.013	VV
7	5.22	12269	0.016	VV
8	6.02	13762	0.018	VV
9	6.38	5123	0.007	VV
10	6.85	11517	0.015	VV
11	7.41	18528	0.025	VV
12	7.93	4544	0.006	VV
13	8.27	18885	0.025	VV
14	9.32	35239	0.047	VV
15	10.03	10655	0.014	VV
16	10.63	13753	0.018	VV
17	11.21	4609	0.006	VV
18	12.01	11853	0.016	VB
19	13.07	10339	0.014	BV
20	13.48	5774	0.008	VB
21	15.46	6767	0.009	BV
22	16.65	2834	0.004	VB
23	18.59	516	0.001	BB
24	21.57	6737	0.009	BB
25	23.76	1247	0.002	BB
26	24.92	2717	0.004	BB
27	27.14	37637	0.050	BV
28	28.63	6466	0.009	VB
29	37.31	1554704	2.068	BV
30	39.53	606482	0.807	VV
31	40.54	2041201	2.715	VV
32	43.01	65021854	86.494	VB
33	52.03	236246	0.314	BV
34	57.75	665613	0.885	VB
35	71.69	1023304	1.361	BB
36	81.03	3161942	4.206	BB
37	91.63	428041	0.569	BB
38	98.52	99894	0.133	BB
39	113.40	12703	0.017	BB
		75175168	100.000	

Yield : 11%, *anti* : *syn* = 93 : 7, 89% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 43.01 min (major), t_R = 57.75 min (minor)]

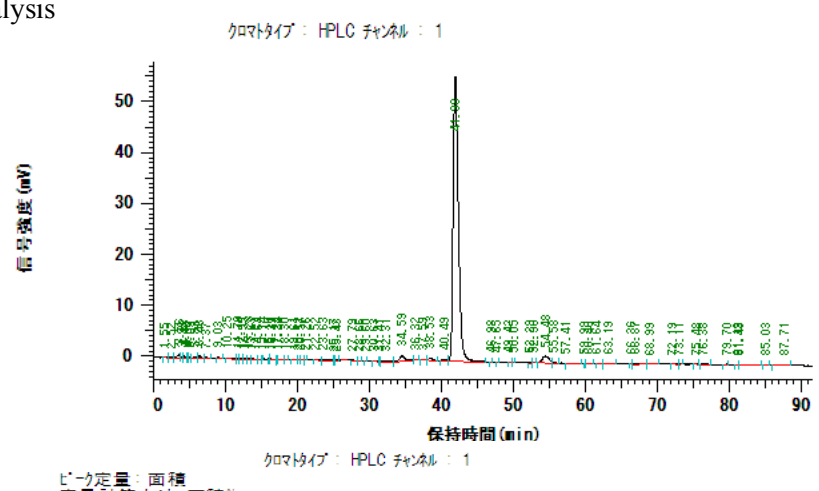
Table 5, entry 3

To a solution of **1j** (6.5 mg, 0.0062 mmol) in dry-toluene (0.062 mL) was added cyclohexanone (64.2 µL, 0.62 mmol) and 4-nitrobenzaldehyde (9.7 mg, 0.062 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (12.9 mg, 83%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

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



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1
ピーク定量 : 面積
定量計算方法 : 面積%

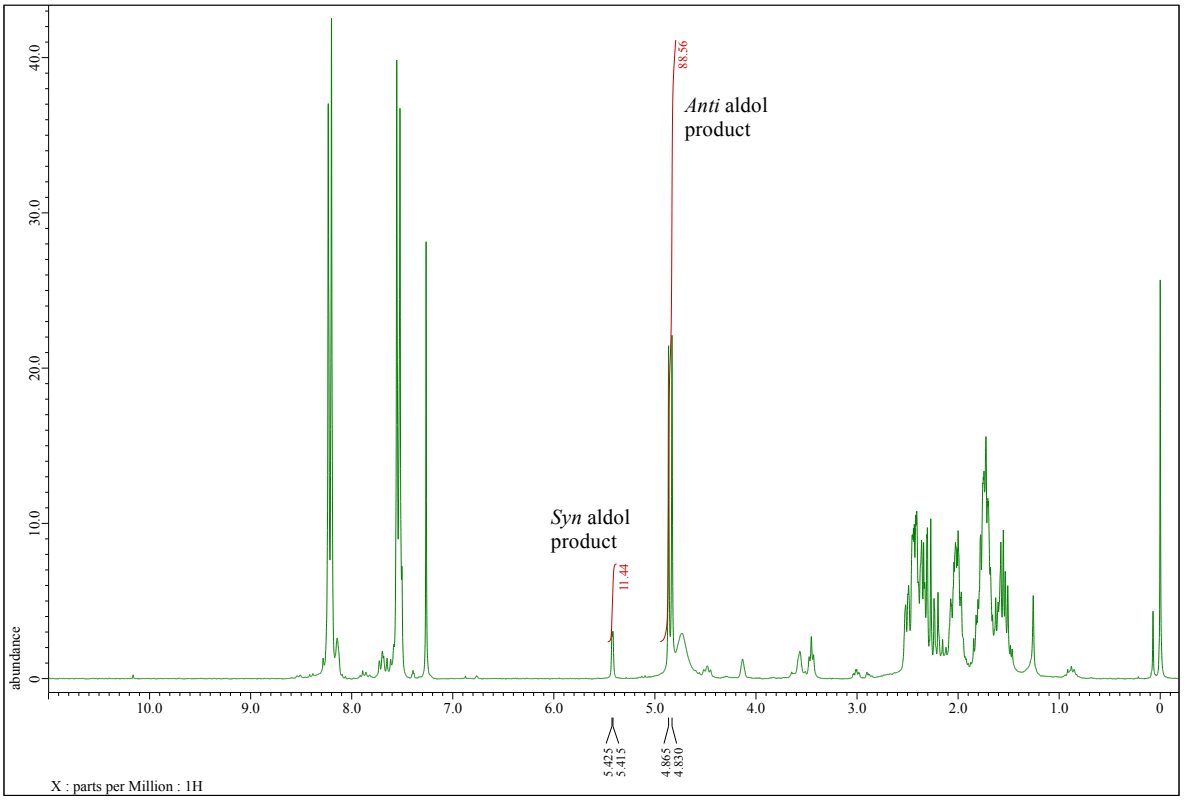
NO	RT	面積	濃度1	BC
1	1.55	1288	0.040	BB
2	2.52	2677	0.083	BB
3	3.56	18338	0.567	BV
4	3.93	5884	0.182	VV
5	4.38	6965	0.215	VV
6	4.80	3975	0.123	VV
7	5.09	4493	0.139	VB
8	5.83	7820	0.242	BV
9	6.48	10448	0.323	VB
10	7.37	2205	0.068	BB
11	9.03	3695	0.114	BB
12	10.25	3319	0.103	BB
13	11.70	1179	0.036	BV
14	12.11	5040	0.156	VV
15	12.55	4078	0.126	VB
16	13.28	7803	0.241	BV
17	13.63	8729	0.270	VB
18	14.64	3406	0.105	BB
19	15.14	600	0.019	BB
20	16.10	641	0.020	BB
21	16.31	5864	0.181	BB
22	17.24	757	0.023	BV
23	17.32	6137	0.190	VV
24	18.30	2964	0.092	VB
25	19.61	2047	0.063	BV
26	20.12	1492	0.046	VB
27	20.57	4214	0.130	BB
28	21.26	1541	0.048	BB
29	22.52	6275	0.194	BB
30	23.63	14320	0.443	BV
31	25.17	1665	0.052	VB
32	25.43	1781	0.055	BB
33	27.79	2855	0.088	BB
34	28.66	810	0.025	BB
35	29.60	393	0.012	BB
36	30.63	8658	0.268	BV
37	31.41	1847	0.057	VB
38	32.31	21458	0.664	BB
39	34.59	62769	1.942	BV
40	36.32	1169	0.036	TBB
41	37.59	2771	0.086	BV
42	38.53	19431	0.601	VB
43	40.49	13772	0.426	BV
44	41.98	2770317	85.699	VB
45	46.98	466	0.014	BB
46	47.65	505	0.016	BB
47	49.42	562	0.017	BB
48	50.05	69	0.002	BB
49	52.29	2825	0.087	BB
50	52.90	941	0.029	BB
51	54.48	82805	2.562	BB
52	55.58	3029	0.094	BB
53	57.41	13396	0.414	BB
54	59.99	606	0.019	BB
55	60.40	4924	0.152	BB
56	61.64	3794	0.117	BB
57	63.19	12872	0.398	BB
58	66.36	1894	0.059	BB
59	66.87	9719	0.301	BB
60	68.99	3227	0.100	BB
61	72.19	1664	0.051	BB
62	73.11	1086	0.034	BB
63	75.48	1529	0.047	BB
64	76.38	832	0.026	BB
65	79.70	1613	0.050	BB
66	81.19	1893	0.059	BB
67	81.43	17591	0.544	BB
68	85.03	1342	0.042	BB
69	87.71	5508	0.170	BB
		3232584	100.000	

Yield : 83%, *anti* : *syn* = 95 : 5, 94% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 41.98 min (major), t_R = 54.48 min (minor)]

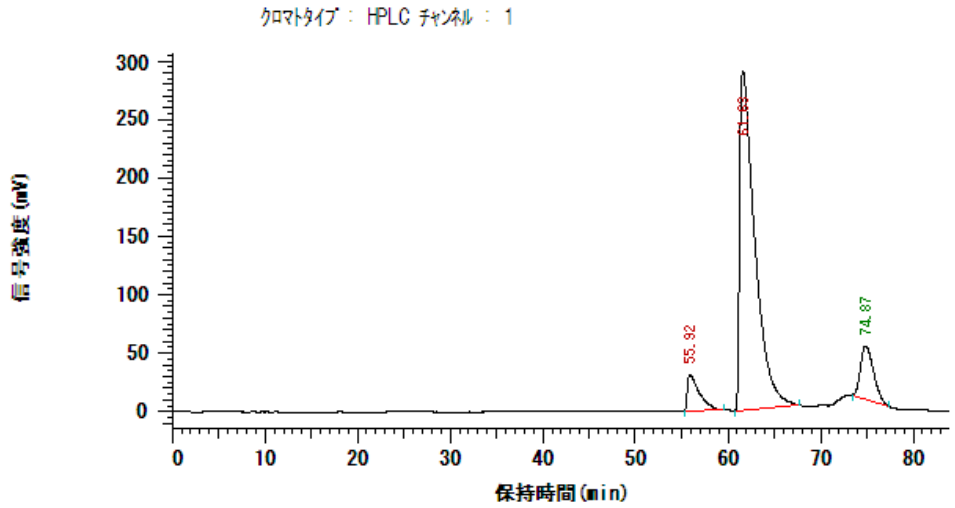
Table 5, entry 4

To a solution of **1k** (10.0 mg, 0.0105 mmol) in dry-toluene (0.105 mL) was added cyclohexanone (109 µL, 1.054 mmol) and 4-nitrobenzaldehyde (15.9 mg, 0.105 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4a** (22.1 mg, 84%). Diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1

ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	55.92	2792007	7.013	MC
2	61.63	32626009	81.956	MC
3	74.87	4391168	11.031	BB
		39809184	100.000	

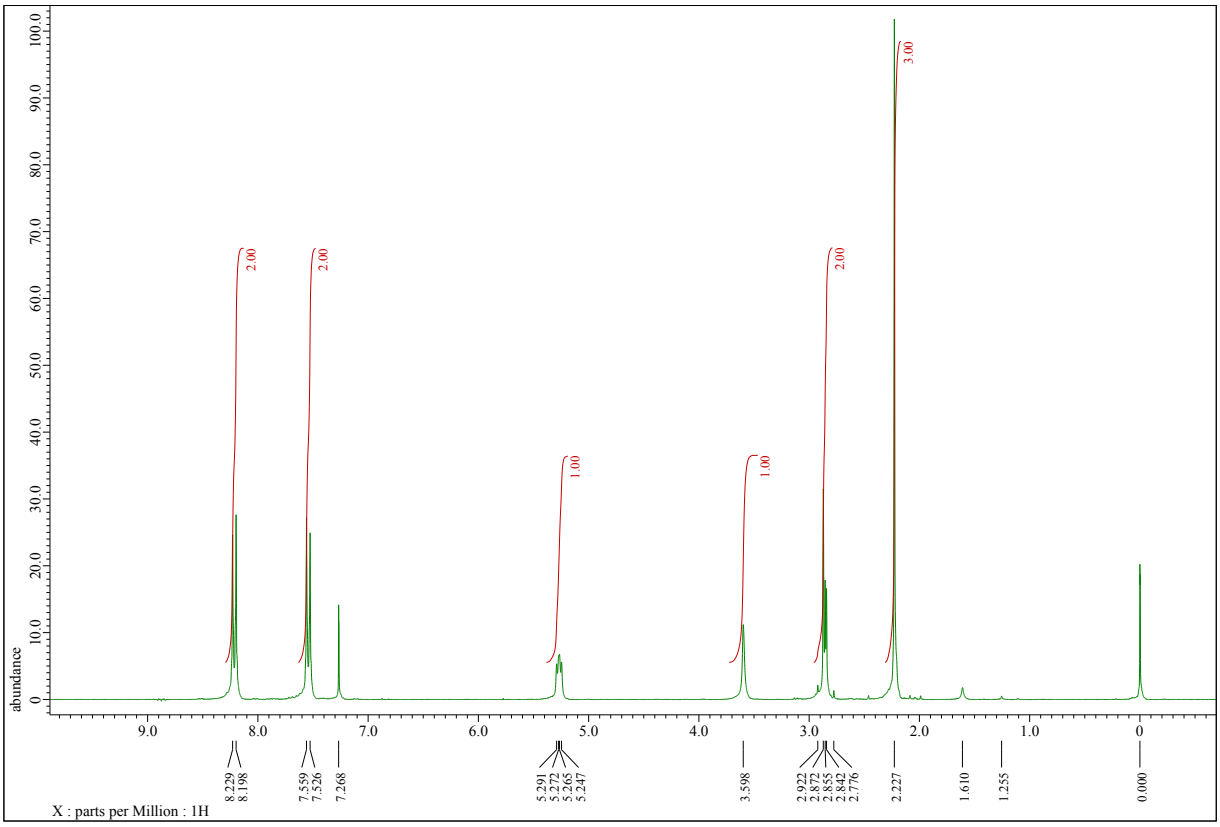
Yield : 84%, *anti* : *syn* = 89 : 11, 76% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 61.63 min (major), t_R = 74.87 min (minor)]

Table 5, entry 5

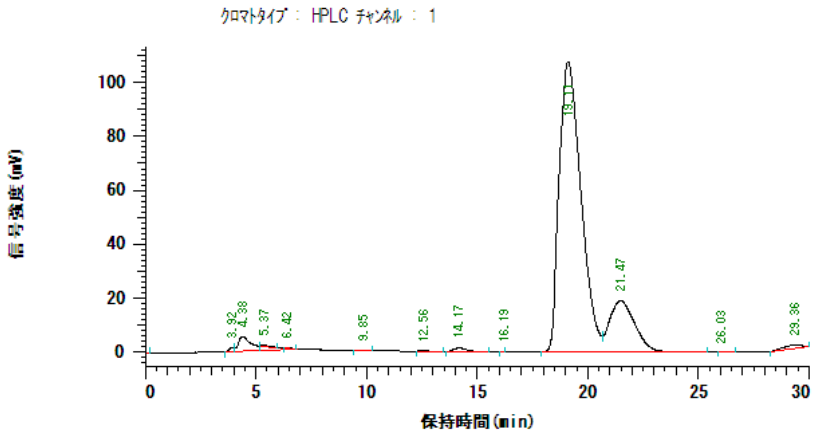
To a solution of **1i** (6.0 mg, 0.0052 mmol) in dry-toluene (0.052 mL) was added acetone (104 μL, 1.4 mmol) and 4-nitrobenzaldehyde (7.9 mg, 0.052 mmol). After being stirred at room temperature for 24 h, the mixture was concentrated. The resulting residue was purified by silica gel chromatography (ethyl acetate : hexane = 1 : 3) to give **4b** (5.3 mg, 49%). E*e* of the aldol product was determined *via* HPLC of the crude product.

White solid; m.p. 58-59 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.21 (d, *J* = 8.4 Hz, 2H), 8.54 (d, *J* = 8.9 Hz, 2H), 5.29-5.25 (m, 1H), 5.60 (s, 1H), 2.92-2.78 (m, 2H), 2.23 (s, 3H).

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



ｸﾛﾏﾄﾀｲﾌﾟ : HPLC ﾁｬﾝﾈﾙ : 1
ﾋﾟｰｸ定量 : 面積
定量計算方法 : 面積%

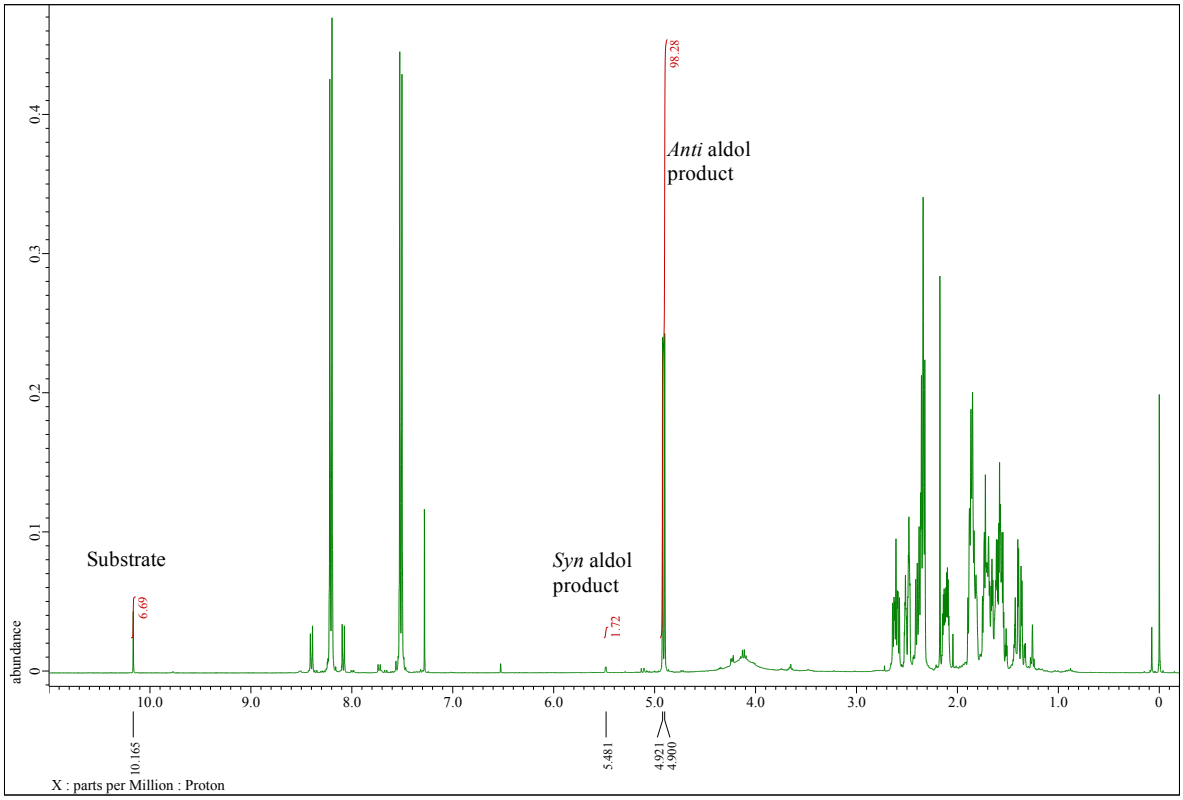
NO	RT	面積	濃度1	BC
1	0.01	128	0.001	BB
2	3.92	24579	0.263	BV
3	4.38	306311	3.283	VV
4	5.37	12831	0.138	TBB
5	6.42	3296	0.035	TBB
6	9.85	3183	0.034	BB
7	12.56	4524	0.048	BB
8	14.17	58475	0.627	BB
9	16.19	108	0.001	BB
10	19.11	7328269	78.549	BV
11	21.47	1506919	16.152	VB
12	26.03	782	0.008	BB
13	29.36	80128	0.859	BB
		9329533	100.000	

Yield : 49%, 66% *ee*; The *ee* of aldol product was determined by HPLC. [Daicel chiralcel OJ-3 column, hex : ^{i}PrOH = 80 : 20, flow rate 0.8 mL/min, t_R = 19.11 min (major), t_R = 21.47 min (minor)]

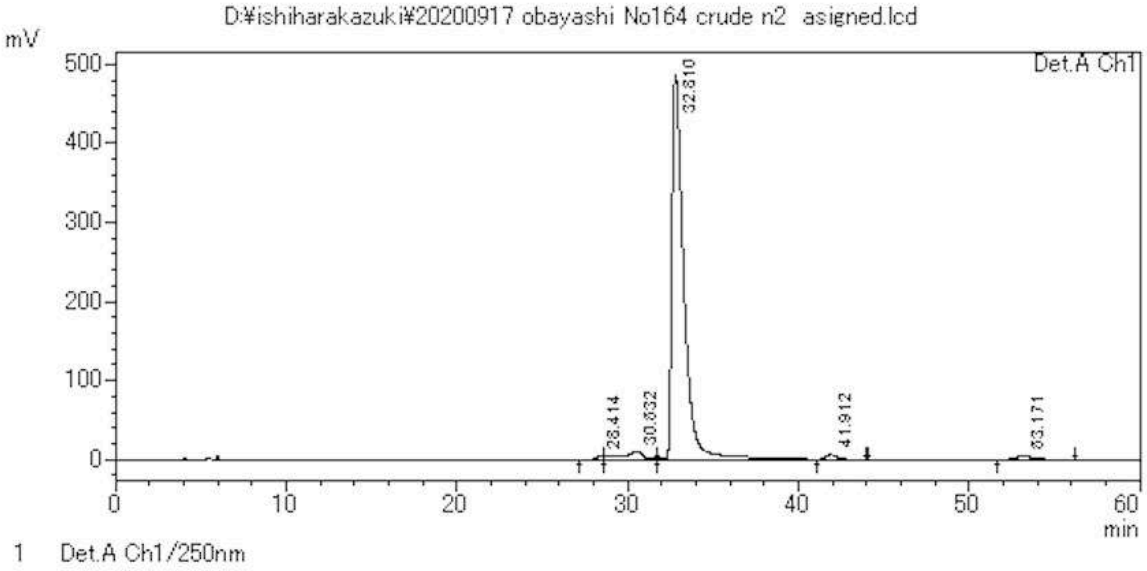
Table 6, entry 1

To a solution of **1l** (20.0 mg, 0.0207 mmol) in dry-toluene (0.2 mL) was added cyclohexanone (214 µL, 2.07 mmol) and 4-nitrobenzaldehyde (31.2 mg, 0.207 mmol). After being stirred at room temperature for 24 h. Ethyl acetate was added to reaction mixture and organic layer was washed with brine. Aqueous layer was extracted with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated. Conversion and diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

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



HPLC analysis



ピークテーブル

検出器A Ch1 250nm

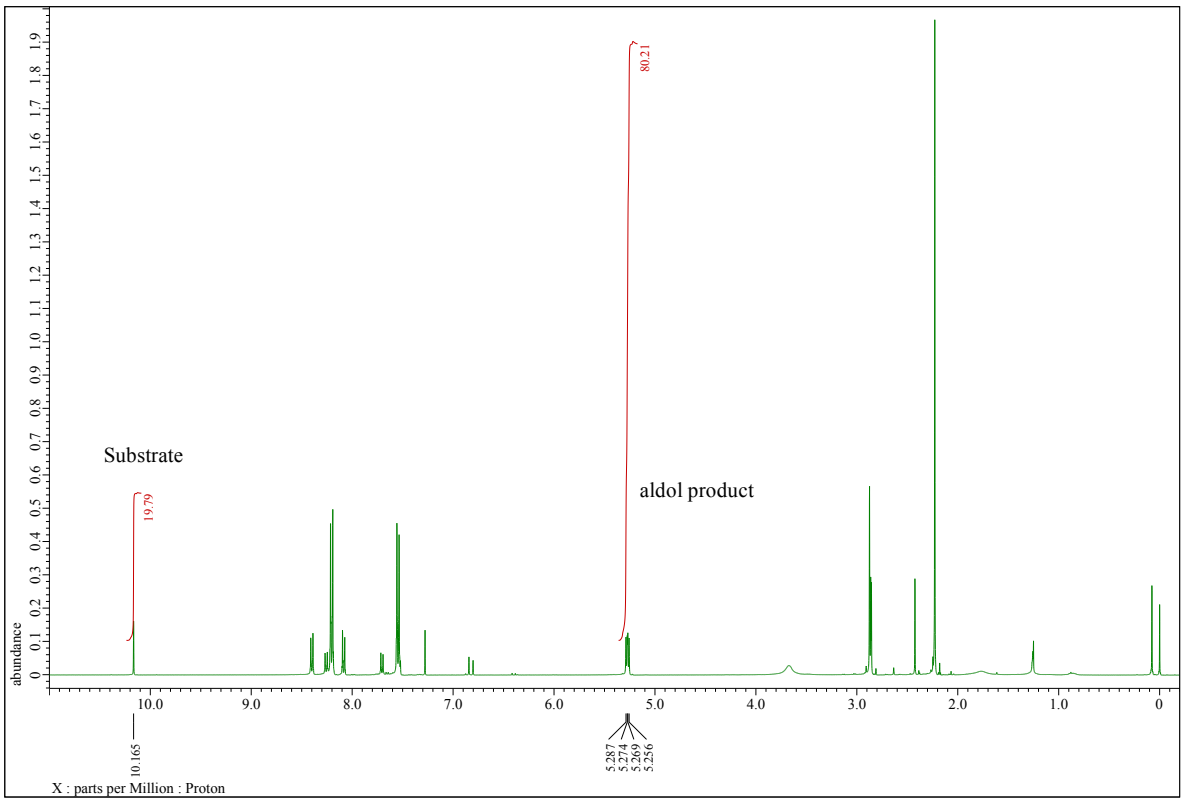
ピーク#	保持時間	面積	高さ	面積%	高さ%
1	28.414	158231	4535	0.610	0.882
2	30.532	1003188	11517	3.864	2.241
3	32.810	24094220	487343	92.815	94.834
4	41.912	295025	5982	1.136	1.164
5	53.171	408652	4514	1.574	0.878
合計		25959316	513891	100.000	100.000

Conv. : 94%, *anti* : *syn* = 98 : 2, 98% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 32.810 min (major), t_R = 41.912 min (minor)]

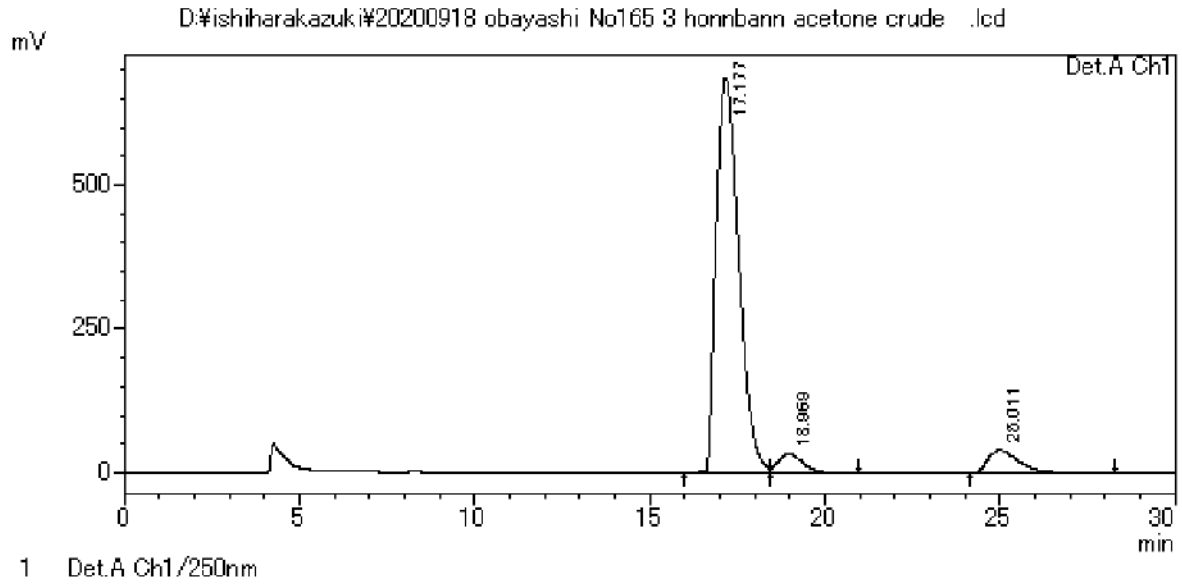
Table 6, entry 2

To a solution of **1l** (20.2 mg, 0.0209 mmol) in dry-toluene (0.2 mL) was added acetone (415 µL, 5.64 mmol) and 4-nitrobenzaldehyde (31.6 mg, 0.209 mmol). After being stirred at room temperature for 24 h. Ethyl acetate was added to reaction mixture and organic layer was washed with brine. Aqueous layer was extracted with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated. Conversion and diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

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



HPLC analysis



ピークテーブル

検出器A Ch1 250nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	17.177	30679509	684677	88.831	90.644
2	18.969	1536155	32340	4.448	4.281
3	25.011	2321165	38327	6.721	5.074
合計		34536828	755344	100.000	100.000

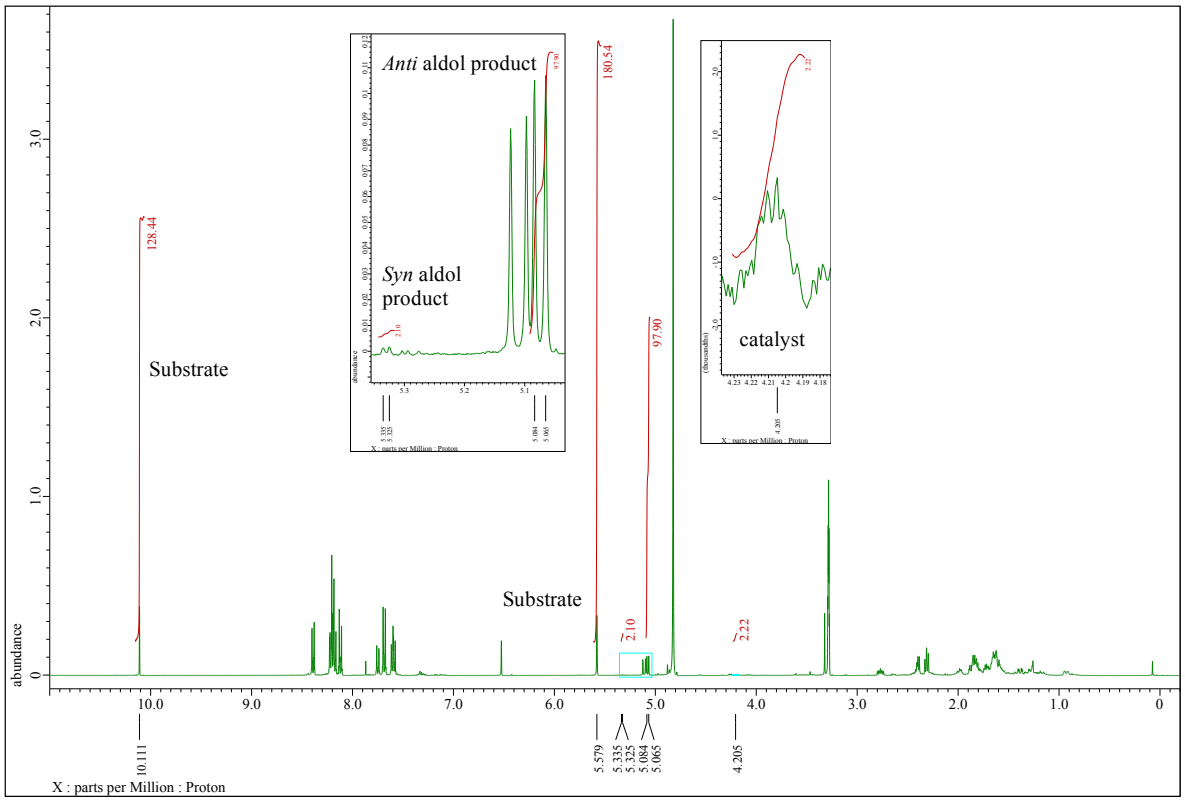
Conv. : 80%, 90% *ee*; The *ee* of product was determined by HPLC. [Daicel chiralcel OJ-3 column, hex : ^{i}PrOH = 80 : 20, flow rate 0.8 mL/min, t_R = 17.177 min (major), t_R = 18.969 min (minor)]

Table 7, entry 1

To a solution of **11** (10.7 mg, 0.0111 mmol) in dry-toluene (332 µL) was added cyclohexanone (115 µL, 1.107 mmol) and 4-nitrobenzaldehyde (16.7 mg, 0.111 mmol). After being stirred at room temperature for 24 h. Teflon® (321 mg) and water (775 µL) were then added, and the mixture was stirred for 15 minutes.

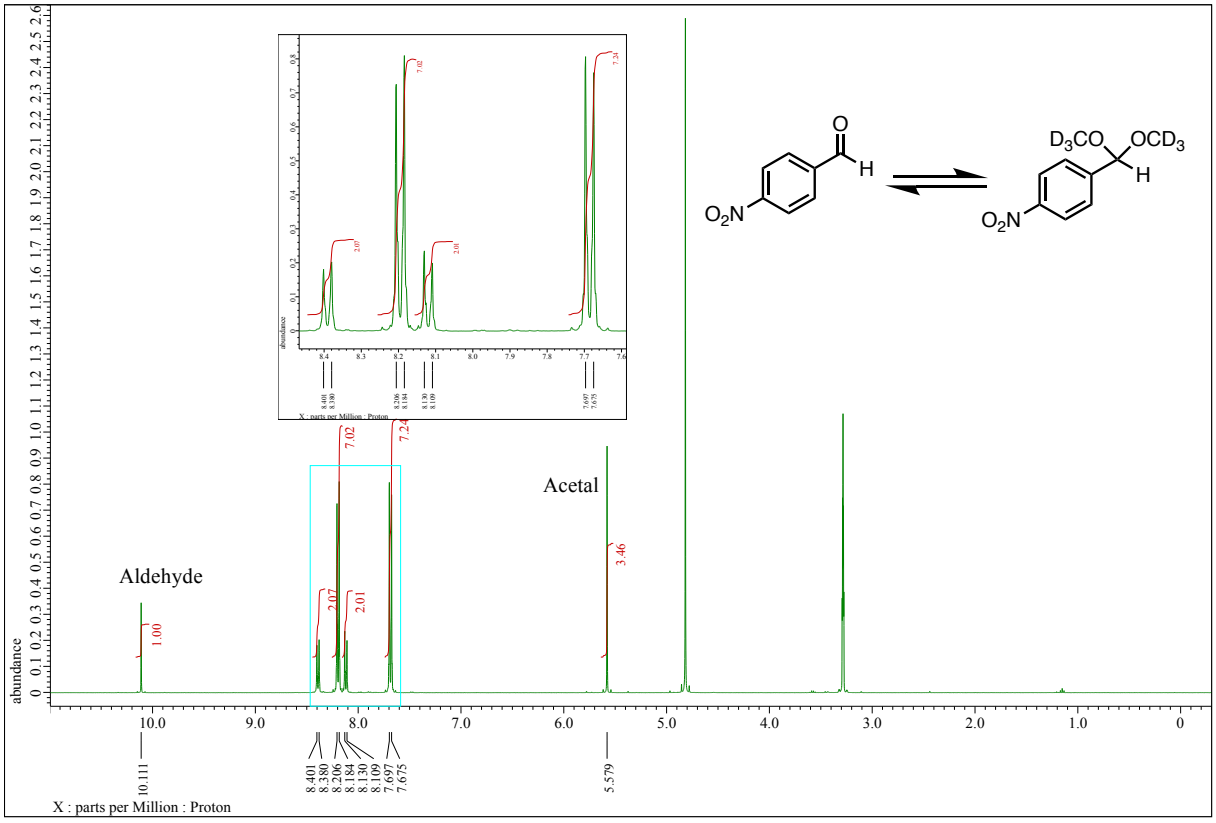
The reaction mixture was then filtered. The filtrate was extracted with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated. Conversion and diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 400 MHz, CD_3OD

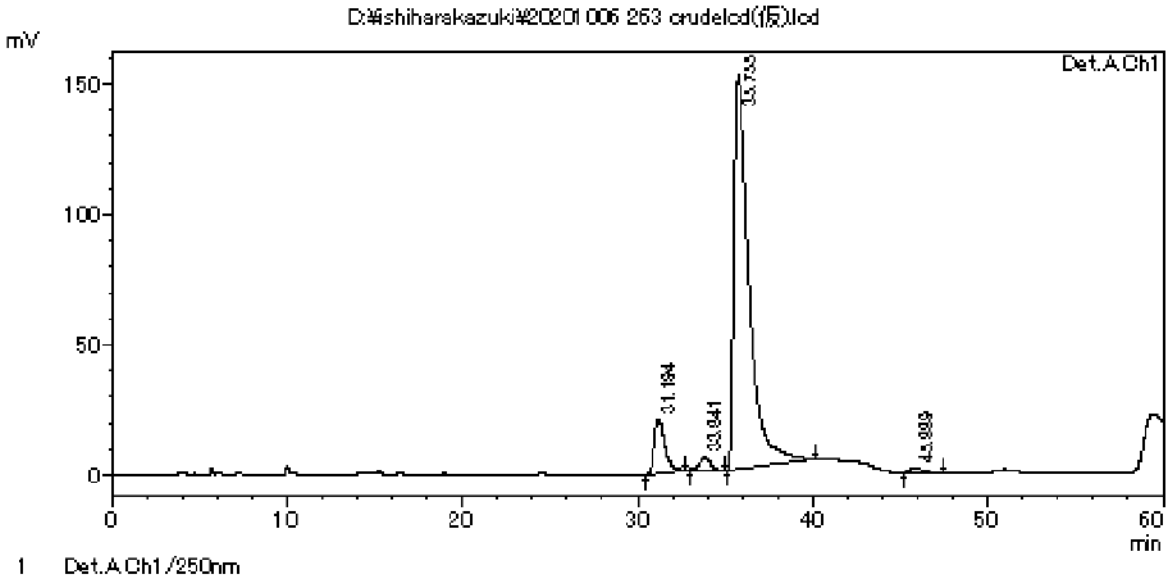


^{1}H NMR spectrum of 4-nitrobenzaldehyde in CD_3OD

^{1}H NMR, 400 MHz, CD_3OD



HPLC analysis



ピークテーブル

検出器A Ch1 250nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	31.194	862148	20757	8.448	11.596
2	33.841	218017	5027	2.136	2.809
3	35.755	9034604	151652	88.528	84.722
4	45.889	90637	1563	0.887	0.873
合計		10205307	179000	100.000	100.000

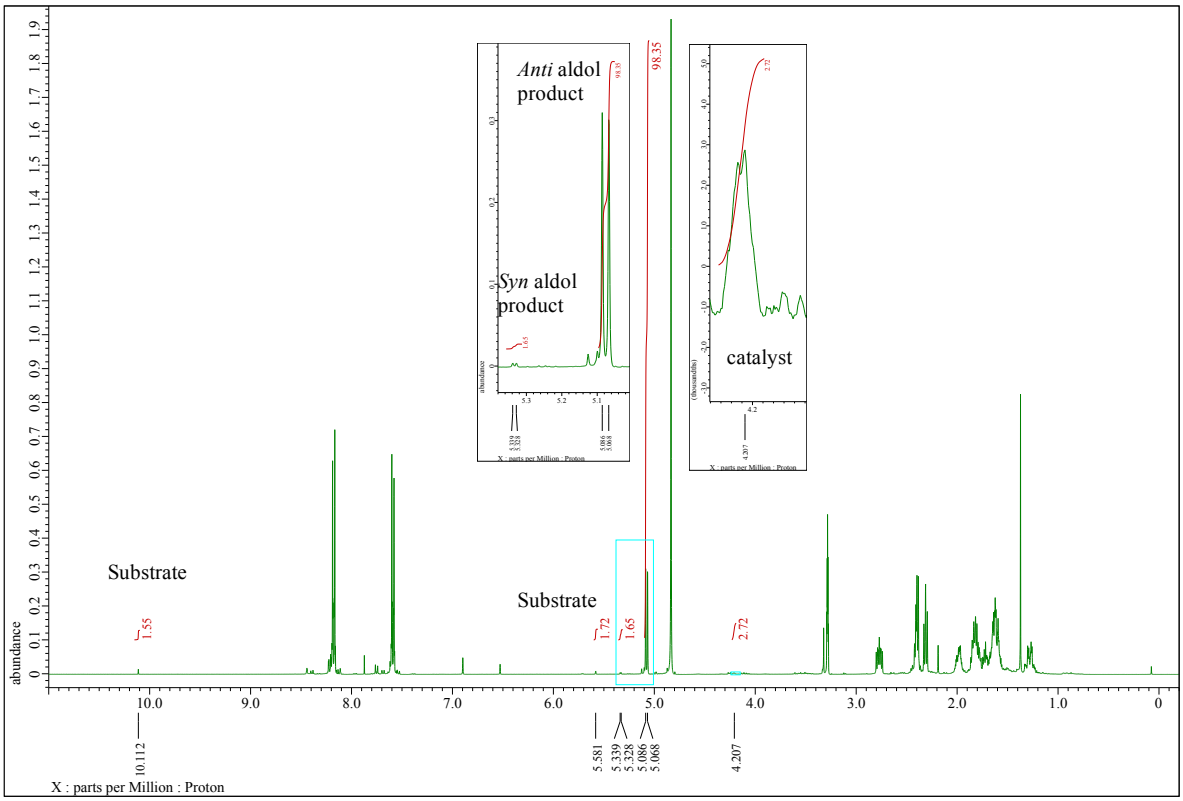
Conv. : 24%, *anti* : *syn* = 98 : 2, 98% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 35.755 min (major), t_R = 45.889 min (minor)]

Table 7, entry 2

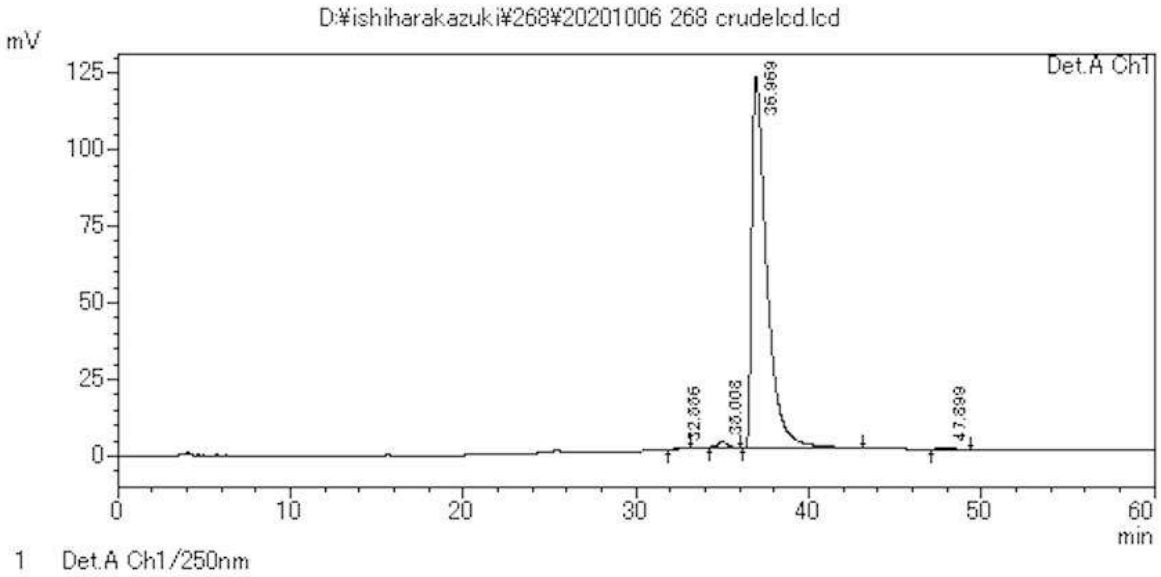
To a solution of **1l** (10.7 mg, 0.0111 mmol) in dry-THF (332 µL) was added cyclohexanone (115 µL, 1.107 mmol) and 4-nitrobenzaldehyde (16.7 mg, 0.111 mmol). After being stirred at room temperature for 24 h. Teflon® (321 mg) and water (775 µL) were then added, and the mixture was stirred for 15 minutes.

The reaction mixture was then filtered. The filtrate was extracted with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated. Conversion and diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 400 MHz, CD_3OD



HPLC analysis



ピークテーブル

検出器A Ch1 250nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	32.556	25041	644	0.334	0.519
2	35.008	81557	1900	1.088	1.530
3	36.969	7366458	121331	98.308	97.689
4	47.899	20195	326	0.270	0.262
合計		7493250	124202	100.000	100.000

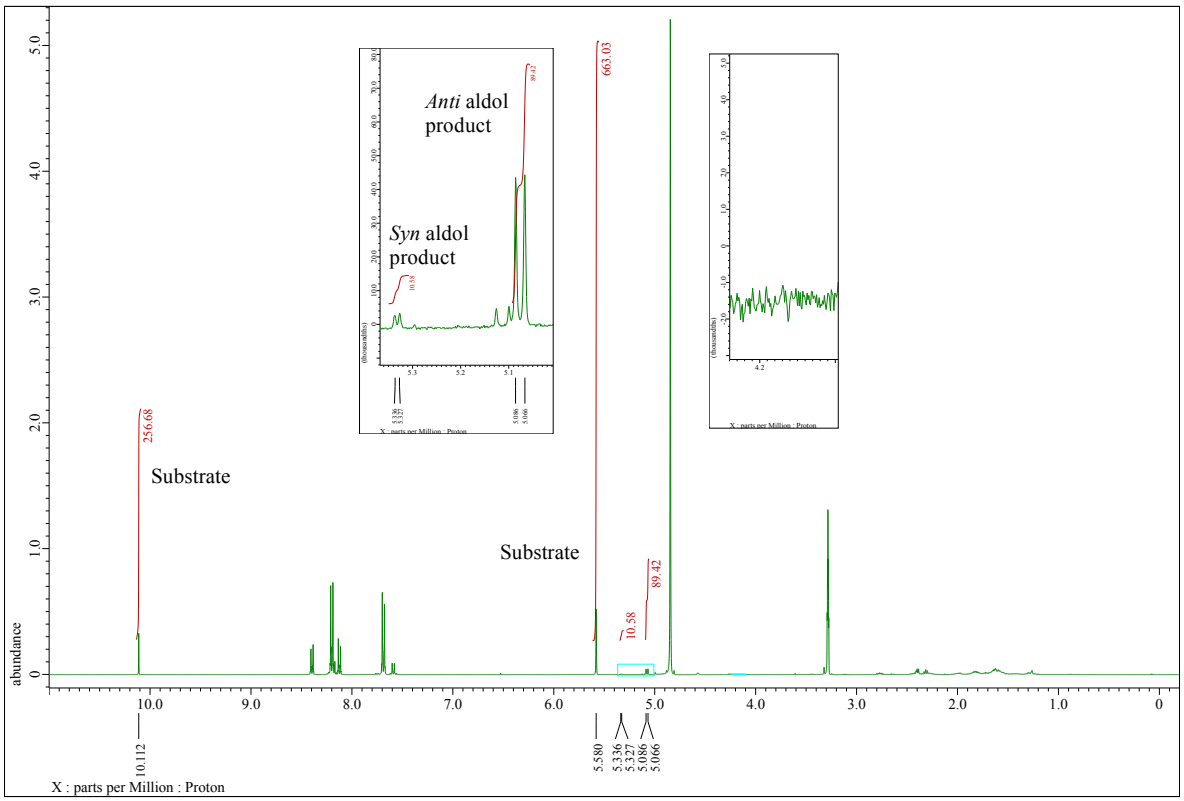
Conv. : 97%, *anti* : *syn* = 98 : 2, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 36.969 min (major), t_R = 47.899 min (minor)]

Table 7, entry 3

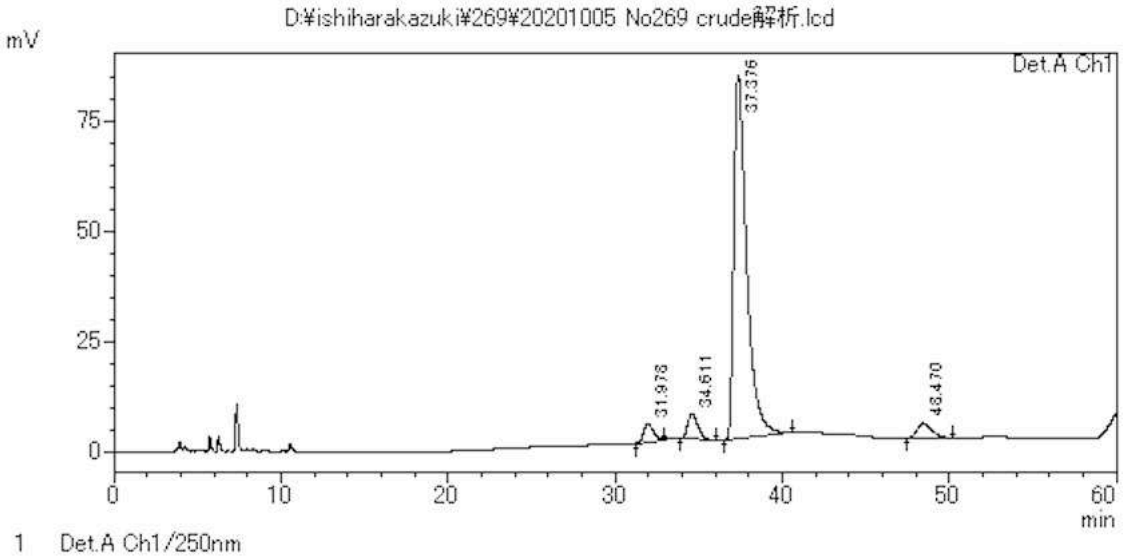
To a solution of **11** (10.7 mg, 0.0111 mmol) in dry-MeOH (332 µL) was added cyclohexanone (115 µL, 1.107 mmol) and 4-nitrobenzaldehyde (16.7 mg, 0.111 mmol). After being stirred at room temperature for 24 h. Teflon® (321 mg) and water (332 µL) were then added, and the mixture was stirred for 15 minutes.

The reaction mixture was then filtered. The filtrate was extracted with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated. Conversion and diastereoselectivity (*anti* : *syn*) was determined by ^{1}H NMR of the crude product. E*e* of the *anti* aldol product was determined *via* HPLC of the crude product.

^{1}H NMR, 400 MHz, CD_3OD



HPLC analysis



ピークテーブル

検出器A Ch1 250nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	31.978	155037	4024	3.078	4.213
2	34.611	249569	5858	4.954	6.134
3	37.376	4414308	82162	87.625	86.026
4	48.470	218797	3465	4.343	3.627
合計		5037711	95508	100.000	100.000

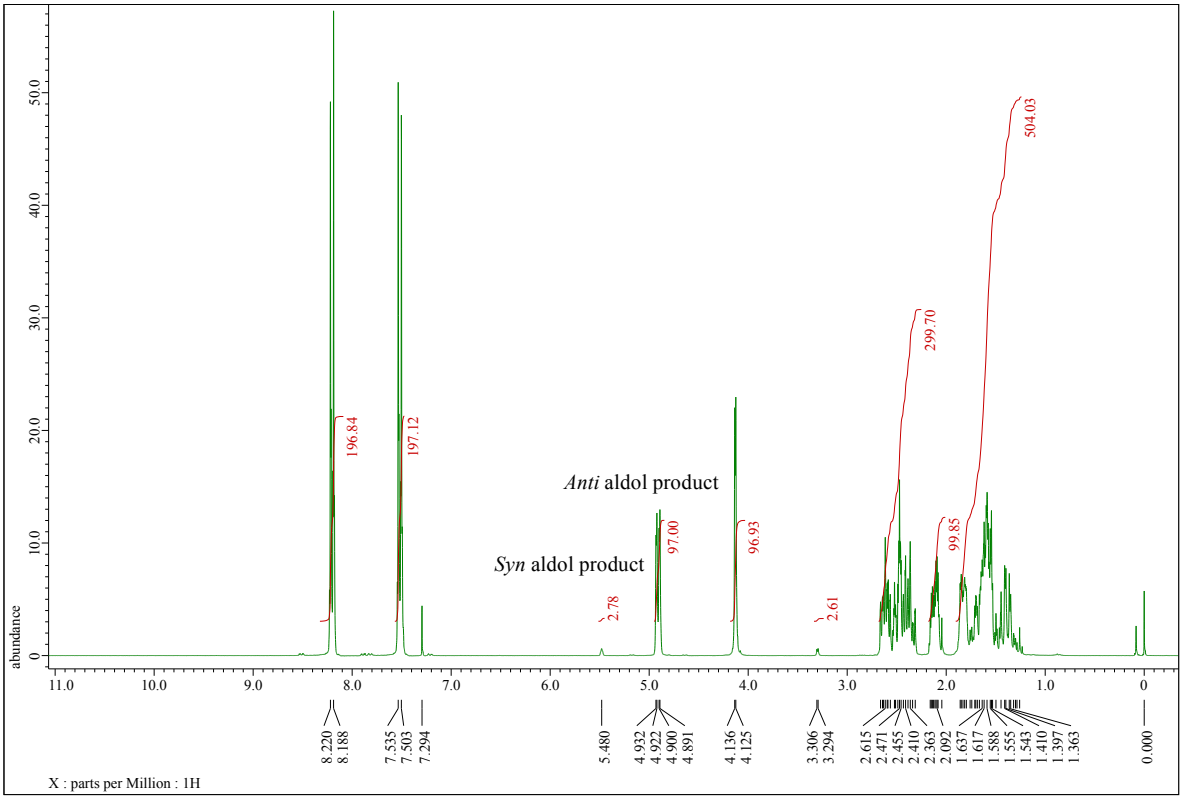
Conv. : 10%, *anti* : *syn* = 89 : 11, 91% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 37.376 min (major), t_R = 48.470 min (minor)]

3. **Reuse of multi-fluorous proline catalyst on FluoroFlash® in the aldol reaction**

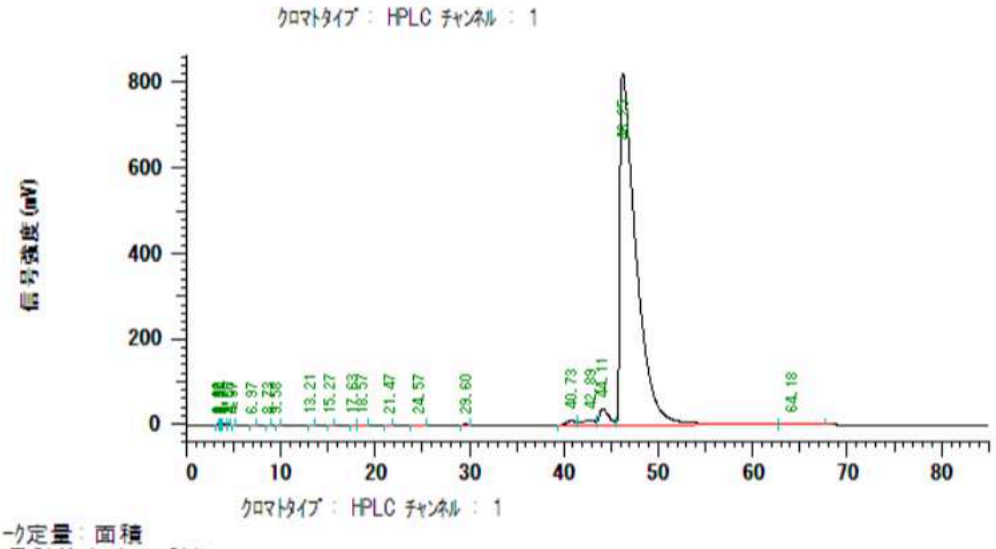
Cyclohexanone (1.03 mL, 10 mmol) and 4-nitrobenzaldehyde (151.1 mg, 1 mmol) were added to a slurry of supported catalyst **1a** on fluorous silica gel (86.6 mg, 0.1 mmol; 2.6 g: fluorous silica gel 30-fold by mass in comparison to the amount of catalyst) in toluene (3 mL). After stirring for 24 h at room temperature, water (3 mL) was added to the mixture. The resulting mixture was filtered through a glass filter 3G4 (diameter : 5-10 µ) and washed with toluene/H_2O (1 : 1 v/v). The filtrate was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The recovered catalyst **1a** was dried and used directly in the next cycle.

Table 4, cycle 1

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



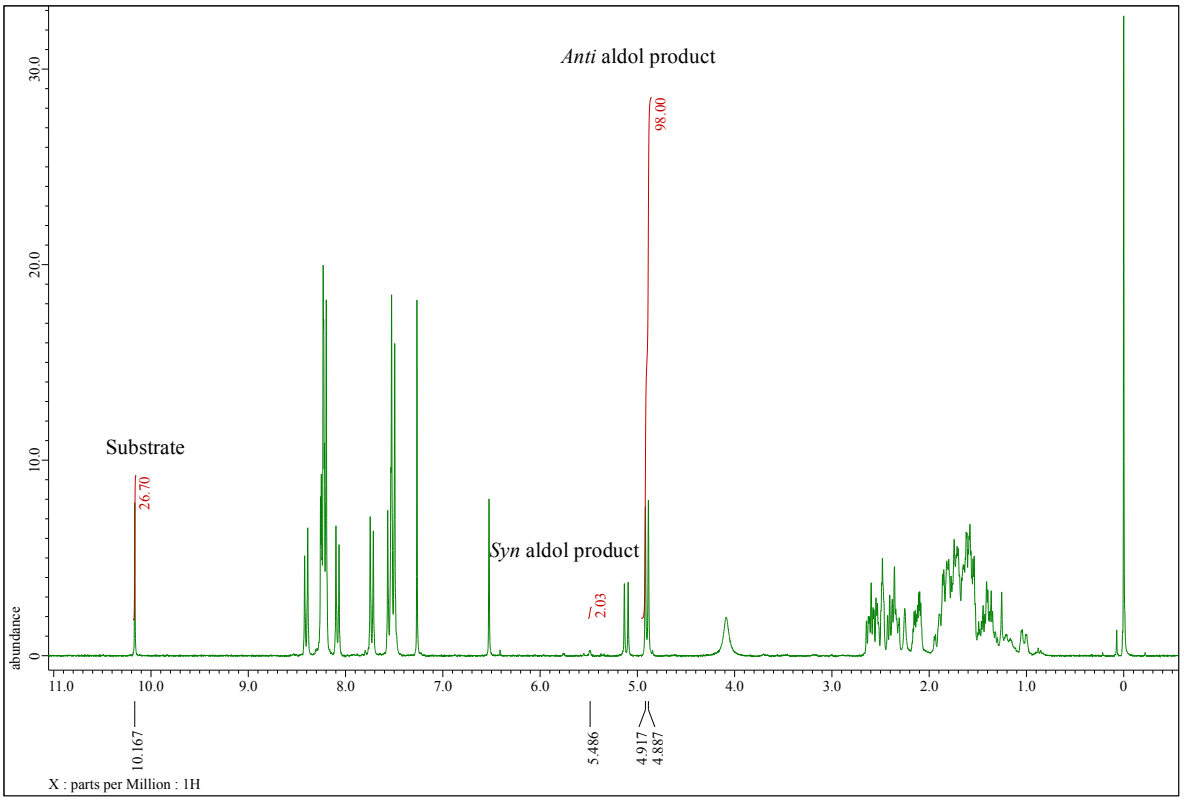
ピーク定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	3.39	8755	0.009	BV
2	3.60	5673	0.006	VV
3	3.74	5708	0.006	VV
4	3.89	13588	0.013	VV
5	4.50	3471	0.003	TBB
6	4.97	626	0.001	BB
7	6.97	2816	0.003	BB
8	8.73	1147	0.001	BB
9	9.58	945	0.001	BB
10	13.21	1016	0.001	BB
11	15.27	464	0.000	BB
12	17.63	1144	0.001	BB
13	18.57	8726	0.009	BB
14	21.47	1328	0.001	BB
15	24.57	8541	0.008	BB
16	29.60	11993	0.012	BB
17	40.73	581566	0.574	BV
18	42.89	949064	0.936	VV
19	44.11	2586198	2.551	VV
20	46.25	96964546	95.638	VV
21	64.18	229817	0.227	TBB

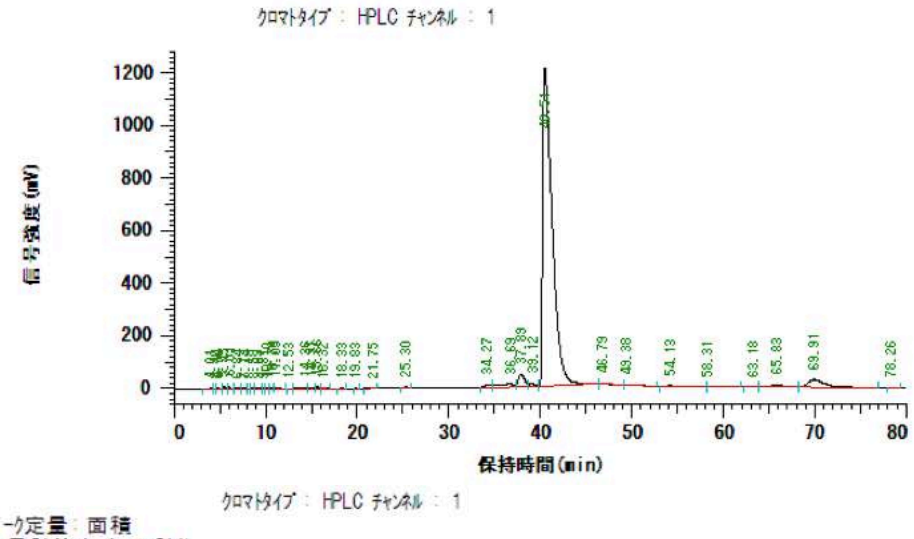
Conv. : 100%, Yield : 94%, *anti* : *syn* = 97 : 3, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 46.25 min (major), t_R = 64.18 min (minor)]

Table 4, cycle 2

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1

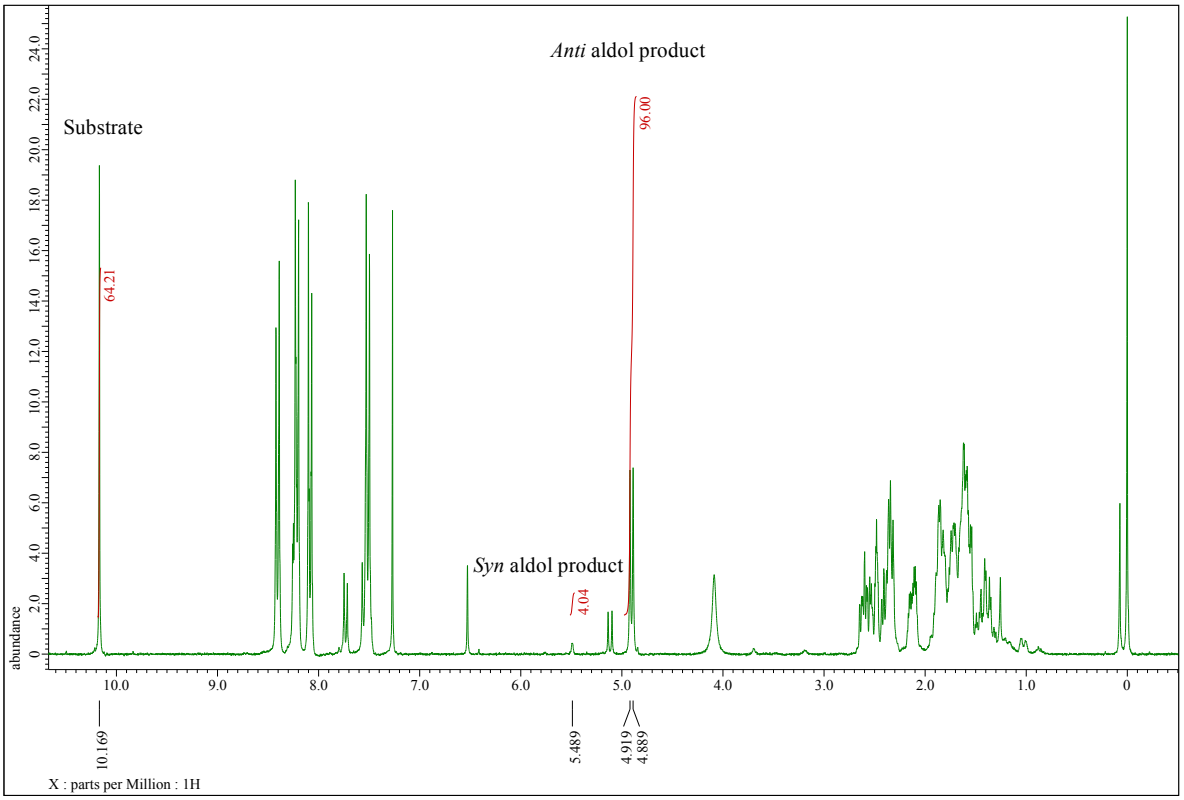
ピーク定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	4.01	24614	0.025	BV
2	4.40	7646	0.008	W
3	4.74	21826	0.022	W
4	5.45	77702	0.080	W
5	6.01	123703	0.127	W
6	6.84	34080	0.035	W
7	7.74	21286	0.022	W
8	8.13	4305	0.004	W
9	8.59	12666	0.013	W
10	9.09	23942	0.025	W
11	9.81	12196	0.013	W
12	10.10	15002	0.015	W
13	10.79	39890	0.041	W
14	11.05	74649	0.077	VB
15	12.53	3750	0.004	BB
16	14.36	149782	0.154	BV
17	14.91	98175	0.101	W
18	15.66	204208	0.210	W
19	16.32	13985	0.014	TBB
20	18.33	7920	0.008	BB
21	19.83	1791	0.002	BB
22	21.75	31806	0.033	BB
23	25.30	111734	0.115	BB
24	34.27	475564	0.489	BV
25	36.69	1186708	1.220	W
26	37.89	2070437	2.128	W
27	39.12	417082	0.429	VB
28	40.51	86291752	88.704	BB
29	46.79	124794	0.128	BV
30	49.38	424307	0.436	VB
31	54.13	406826	0.418	BB
32	58.31	24665	0.025	BB
33	63.18	20724	0.021	BV
34	65.83	1026542	1.055	W
35	69.91	3692276	3.795	VB
36	78.26	2042	0.002	BB

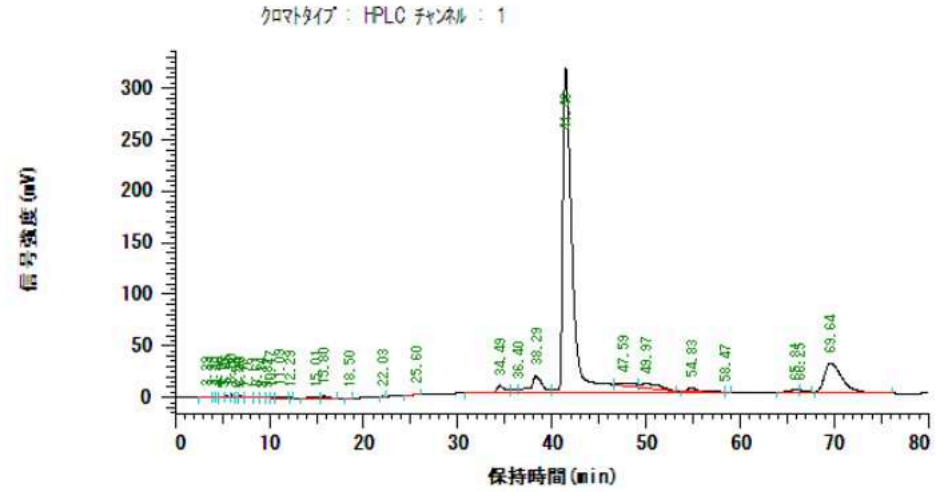
Conv. : 79%, *anti* : *syn* = 98 : 2, >99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 40.51 min (major), t_R = 58.31 min (minor)]

Table 4, cycle 3

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



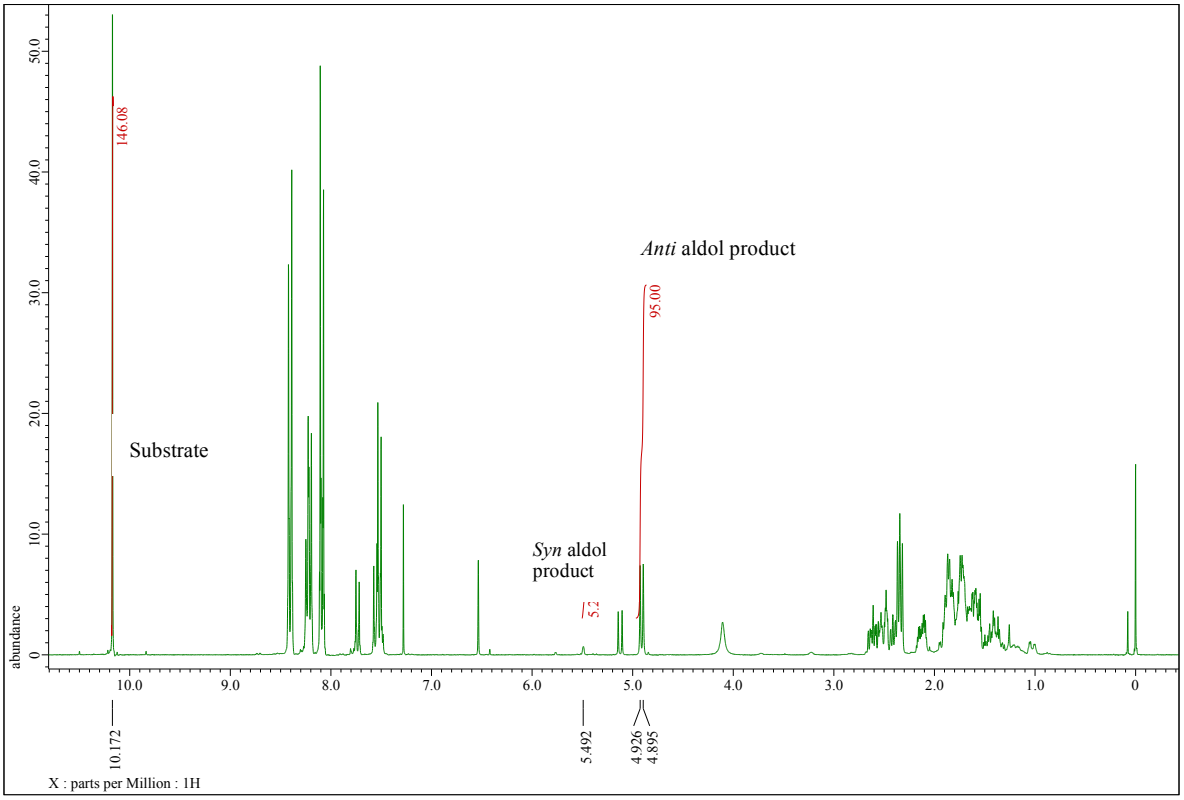
クロマトタイプ : HPLC チャンネル : 1
ピーク定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	3.39	33491	0.111	BV
2	3.99	13123	0.043	W
3	4.40	6284	0.021	VB
4	5.15	12731	0.042	BV
5	5.45	29949	0.099	W
6	6.00	41032	0.136	W
7	6.54	5479	0.018	W
8	6.90	22996	0.076	VB
9	7.76	5617	0.019	BB
10	8.61	14773	0.049	BB
11	9.14	6361	0.021	BB
12	9.82	3475	0.011	BV
13	10.17	3112	0.010	VB
14	11.09	22917	0.076	BB
15	12.29	765	0.003	BB
16	15.01	15313	0.051	BV
17	15.80	47591	0.157	VB
18	18.50	1947	0.006	BB
19	22.03	6968	0.023	BB
20	25.60	35508	0.117	BB
21	34.49	463100	1.531	BV
22	36.40	145370	0.481	W
23	38.29	1381439	4.567	W
24	41.46	23021066	76.108	W
25	47.59	281612	0.931	TBV
26	49.97	600255	1.984	TVB
27	54.83	225227	0.745	TBB
28	58.47	925	0.003	BB
29	65.81	135559	0.448	BV
30	66.25	80073	0.265	VB
31	69.64	3583737	11.848	BB

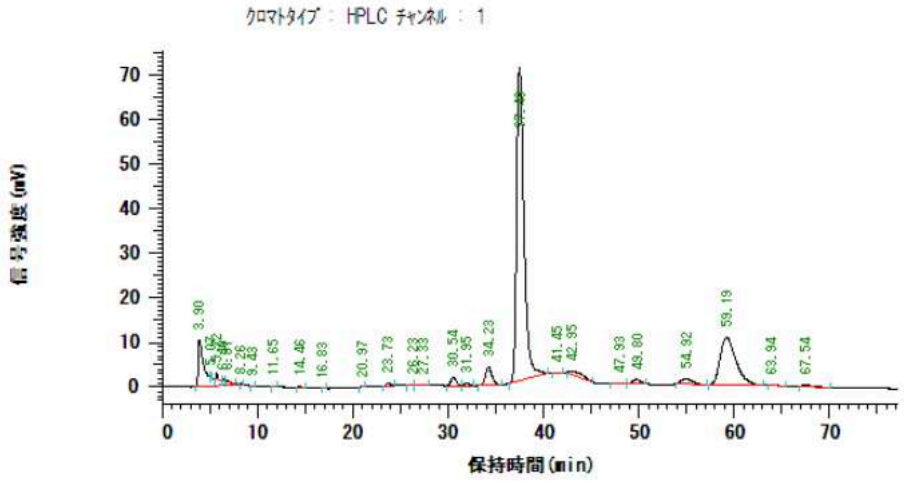
Conv. : 61%, *anti* : *syn* = 96 : 4, 98% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 41.46 min (major), t_R = 54.83 min (minor)]

Table 4, cycle 4

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1

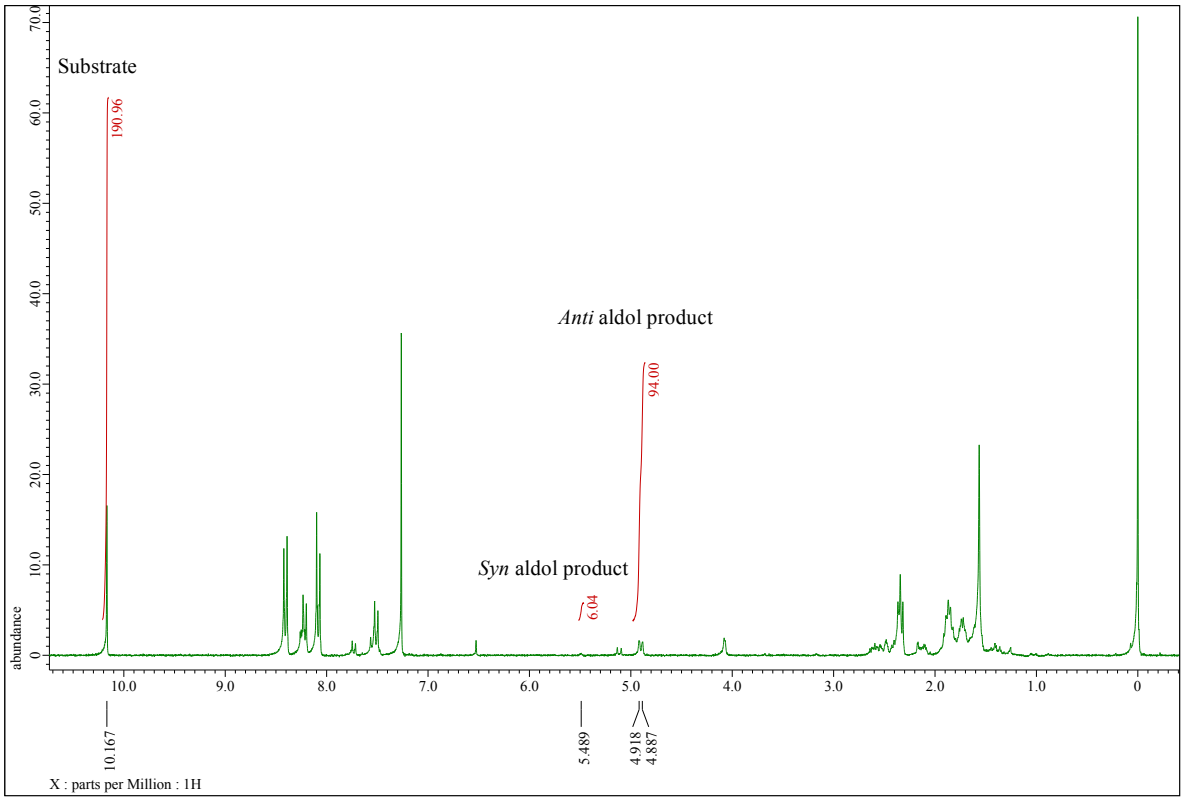
ピーク定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	3.90	556172	9.132	BV
2	5.07	2422	0.040	TBB
3	5.72	15255	0.250	TBB
4	6.40	6127	0.101	TBV
5	6.81	9099	0.149	TVB
6	8.26	1606	0.026	BB
7	9.43	833	0.014	BB
8	11.65	2282	0.037	BB
9	14.46	9271	0.152	BB
10	16.83	697	0.011	BB
11	20.97	2742	0.045	BB
12	23.73	19730	0.324	BB
13	26.23	1554	0.026	BB
14	27.33	2617	0.043	BB
15	30.54	73990	1.215	BB
16	31.95	20487	0.336	BB
17	34.23	187143	3.073	BB
18	37.49	3675340	60.348	BB
19	41.45	3553	0.058	BB
20	42.95	87680	1.440	BB
21	47.93	5375	0.088	BB
22	49.80	53863	0.884	BB
23	54.92	101217	1.662	BB
24	59.19	1215426	19.957	BB
25	63.94	9114	0.150	BB
26	67.54	26643	0.437	BB

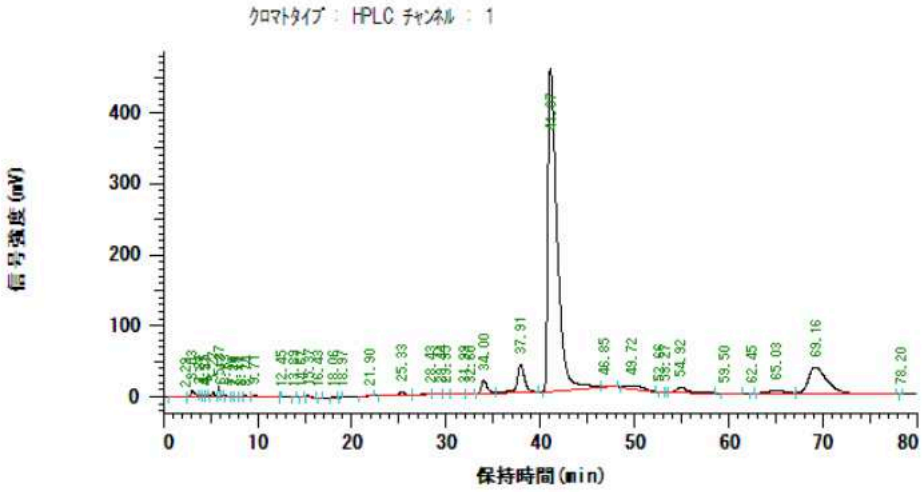
Conv. : 41%, *anti* : *syn* = 95 : 5, 97% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 37.49 min (major), t_R = 49.80 min (minor)]

Table 4, cycle 5

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1

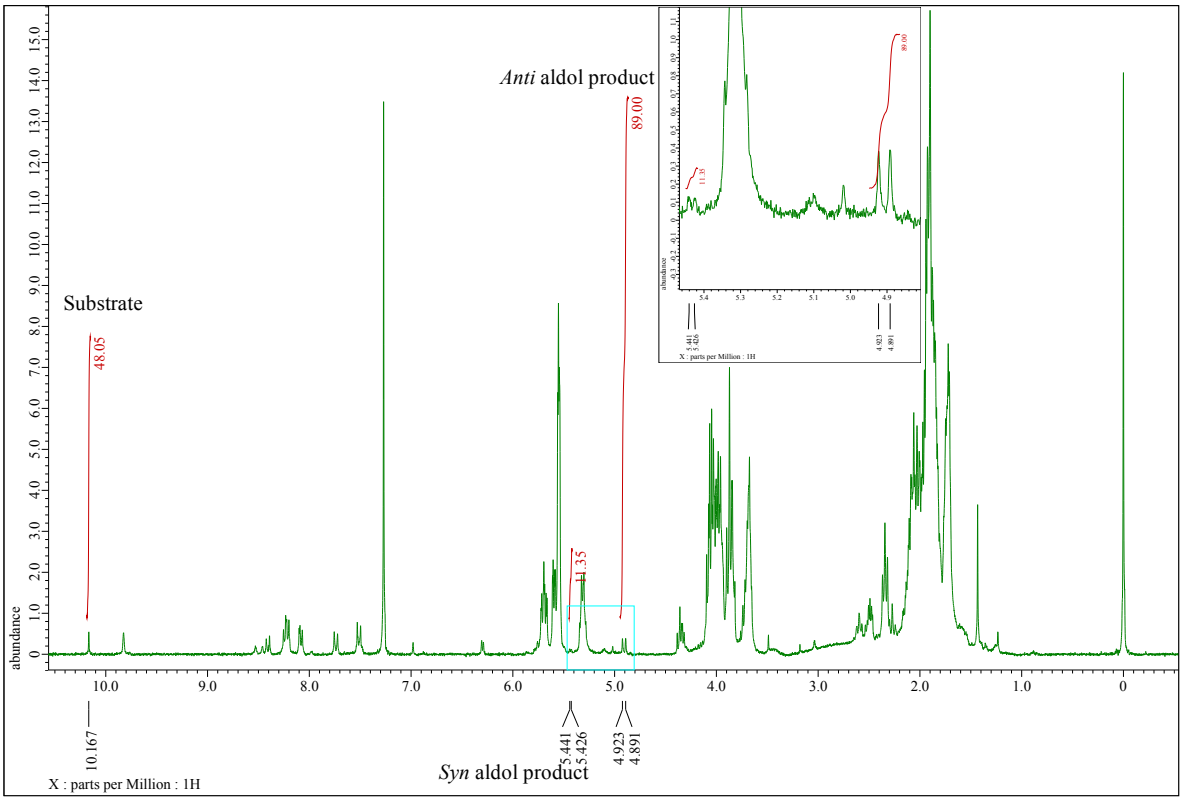
ピーク定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	2.29	11222	0.027	BV
2	3.03	488406	1.171	W
3	3.81	3875	0.009	TBB
4	4.25	11374	0.027	TBB
5	4.51	2099	0.005	TBB
6	5.27	162566	0.390	W
7	5.87	212803	0.510	W
8	6.13	3839	0.009	TBB
9	6.63	77234	0.185	W
10	7.29	26356	0.063	W
11	7.75	26780	0.064	W
12	8.17	26652	0.064	W
13	8.74	52384	0.126	W
14	9.71	104228	0.250	VB
15	12.45	580	0.001	BB
16	13.89	512	0.001	BB
17	14.67	1724	0.004	BB
18	15.37	43770	0.105	BB
19	16.43	901	0.002	BB
20	18.06	5219	0.013	BB
21	18.97	459	0.001	BB
22	21.90	18312	0.044	BB
23	25.33	243234	0.583	BV
24	28.43	100370	0.241	W
25	29.44	44410	0.107	W
26	29.95	31325	0.075	W
27	31.99	31472	0.075	W
28	32.60	10991	0.026	VB
29	34.00	775051	1.859	BV
30	37.91	2088273	5.008	VB
31	41.07	30463946	73.064	BV
32	46.85	32750	0.079	TBB
33	49.72	483559	1.160	BB
34	52.66	3001	0.007	BB
35	53.27	1921	0.005	BV
36	54.92	522738	1.254	VB
37	59.50	7281	0.017	BB
38	62.45	1651	0.004	BB
39	65.03	470801	1.129	BV
40	69.16	5099882	12.231	VB
41	78.20	1023	0.002	BB

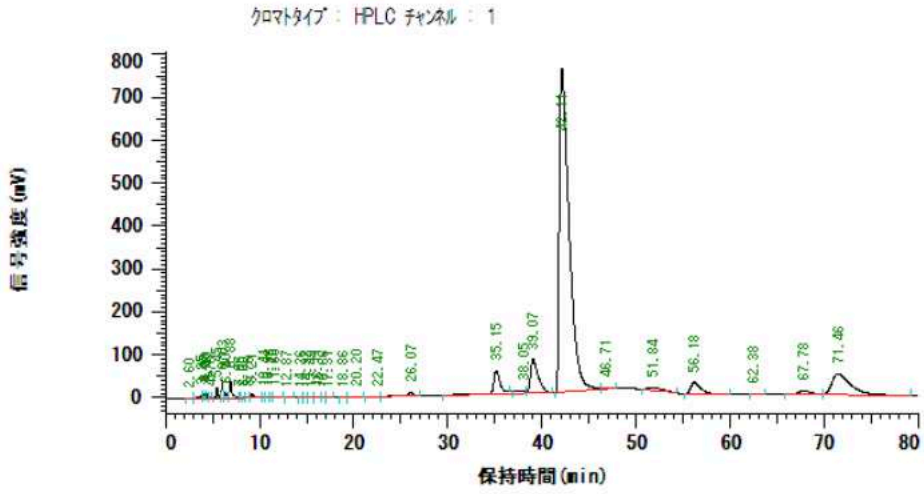
Conv. : 34%, *anti* : *syn* = 94 : 6, 97% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 41.07 min (major), t_R = 54.92 min (minor)]

Table 4, cycle 6

^{1}H NMR, 270 MHz, $CDCl_3$



HPLC analysis



クロマトタイプ : HPLC チャンネル : 1

ピーク定量 : 面積
定量計算方法 : 面積%

NO	RT	面積	濃度1	BC
1	2.60	1910	0.003	BB
2	3.85	76519	0.104	BV
3	4.09	98498	0.134	VV
4	4.30	192773	0.263	VV
5	4.76	4476	0.006	TBB
6	5.45	309911	0.422	VV
7	6.03	403700	0.550	VV
8	6.40	173301	0.236	VV
9	6.88	794997	1.083	VV
10	7.86	2408	0.003	TBB
11	8.20	2251	0.003	TBB
12	8.76	47049	0.064	VV
13	9.21	353032	0.481	VV
14	10.41	3361	0.005	TBV
15	10.93	10165	0.014	TVV
16	11.25	8384	0.011	TVV
17	11.60	19048	0.026	TVB
18	12.87	6673	0.009	TBB
19	14.26	1473	0.002	BB
20	14.92	831	0.001	BB
21	15.42	3247	0.004	BV
22	16.11	55434	0.076	VV
23	16.66	14173	0.019	VV
24	17.31	5632	0.008	VB
25	18.86	17894	0.024	BV
26	20.20	54586	0.074	VB
27	22.47	34594	0.047	BV
28	26.07	328585	0.448	VB
29	35.15	2320224	3.161	BV
30	38.05	437531	0.596	VV
31	39.07	4185232	5.701	VB
32	42.11	53417328	72.767	BV
33	46.71	33954	0.046	TBB
34	51.84	650744	0.886	BB
35	56.18	1858239	2.531	BB
36	62.38	4796	0.007	BB
37	67.78	804846	1.096	BV
38	71.46	6670775	9.087	VB

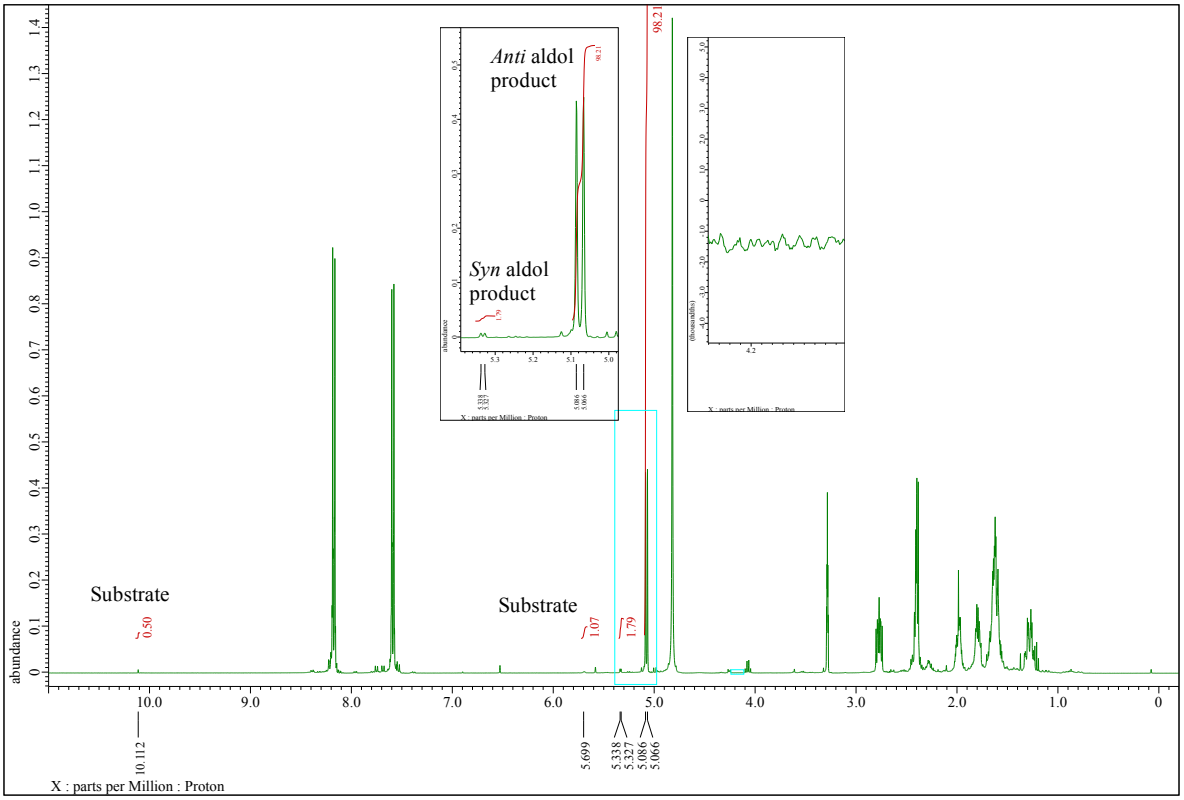
Conv. : 68%, *anti* : *syn* = 89 : 11, 93% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 42.11 min (major), t_R = 56.18 min (minor)]

4. Reuse of multi-fluorous proline catalyst on Teflon® in the aldol reaction

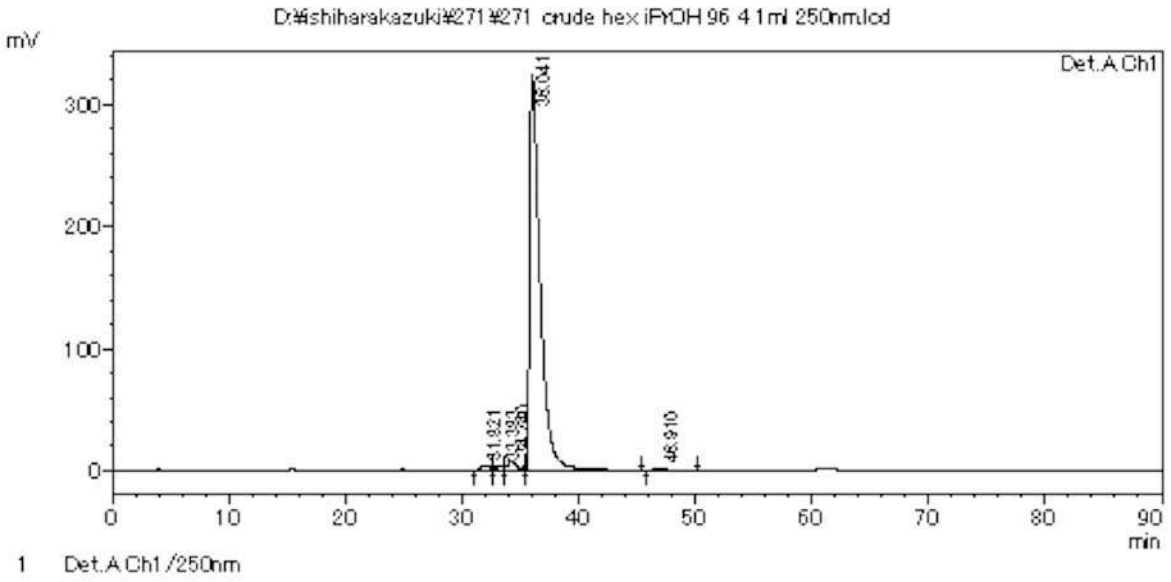
To a solution of **1l** (10.7 mg, 0.0111 mmol) in dry-THF (332 μL) was added cyclohexanone (115 μL, 1.107 mmol) and 4-nitrobenzaldehyde (16.7 mg, 0.111 mmol). After being stirred at room temperature for 24 h. The reaction solvent was then removed, and the residue was dissolved in MeOH (332 μL). Teflon® (321 mg, 30 times the weight of the catalyst) was added, followed by of water (332 μL, the same volume as that of MeOH). The reaction mixture was stirred for 15 min and then filtered. The resulting mixture was filtered through a glass filter 3G4 (diameter : 5-10 μ) and washed with MeOH/H_2O (1 : 1 v/v). The filtrate was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The recovered catalyst **1l** was dried and used directly in the next cycle.

Table 8, cycle 1

^{1}H NMR, 400 MHz, CD_3OH



HPLC analysis



ピークテーブル

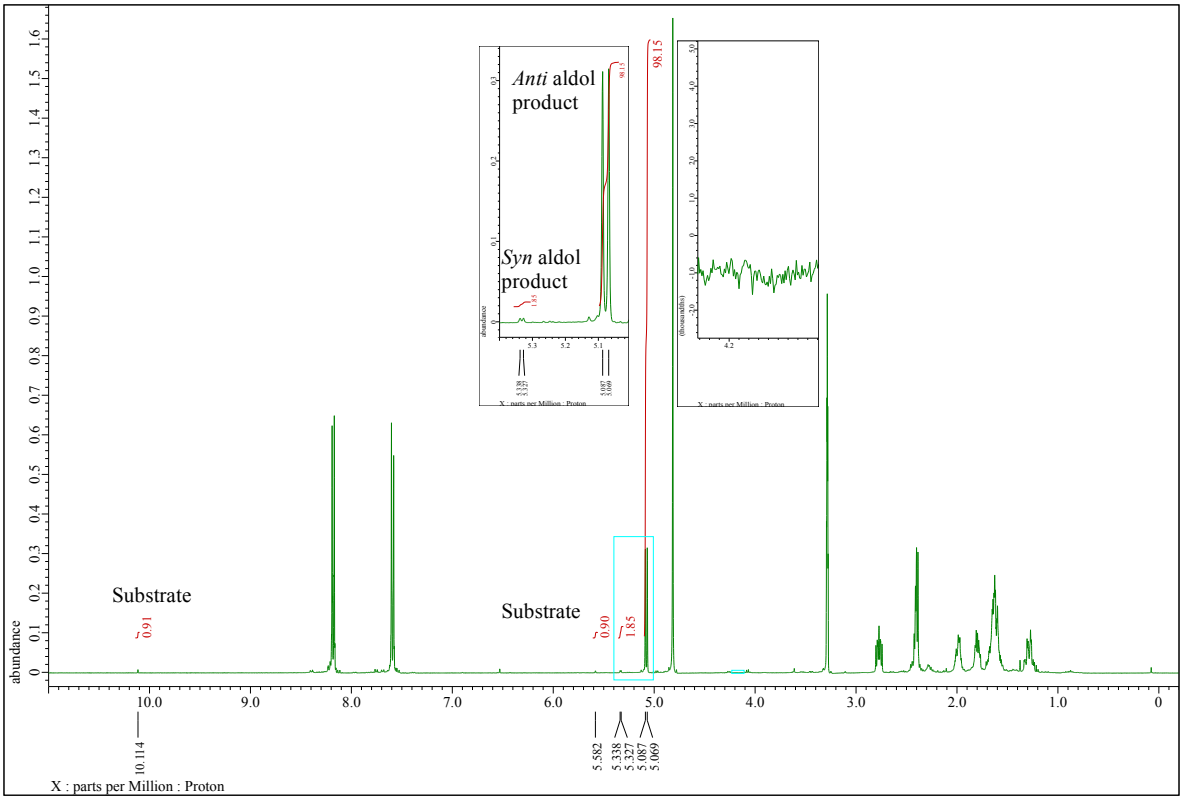
検出器A Ch1 250nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	31.821	256046	4463	1.194	1.306
2	33.383	171404	3176	0.800	0.930
3	34.240	452757	8362	2.112	2.448
4	36.041	20438789	324189	95.336	94.887
5	46.910	119687	1469	0.558	0.430
合計		21438682	341660	100.000	100.000

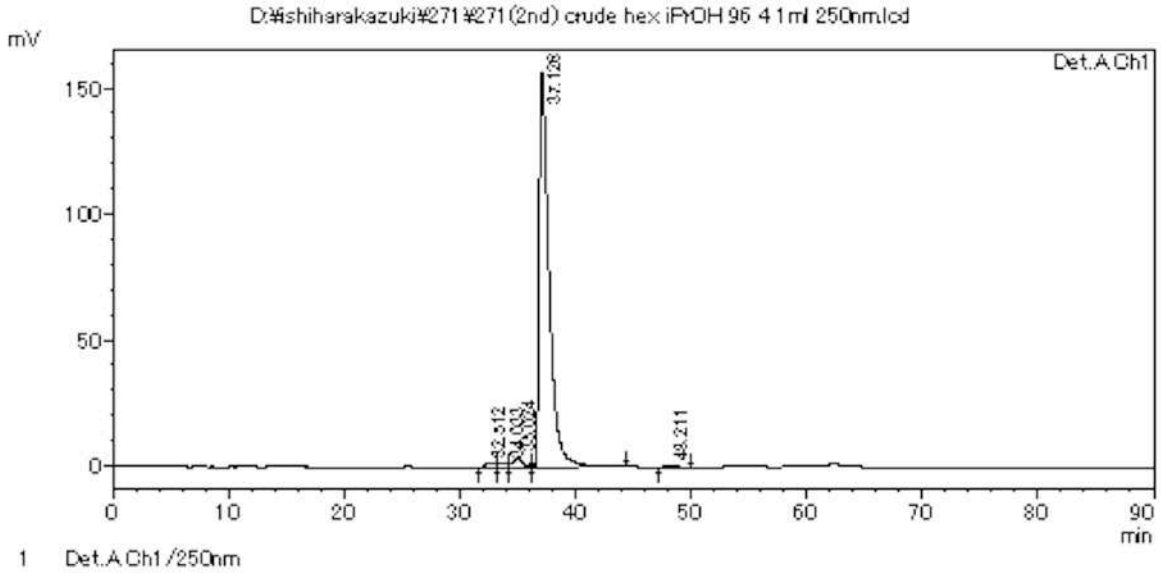
Conv. : 98%, *anti* : *syn* = 98 : 2, 99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 36.041 min (major), t_R = 46.910 min (minor)]

Table 8, cycle 2

^{1}H NMR, 400 MHz, CD_3OH



HPLC analysis



ピークテーブル

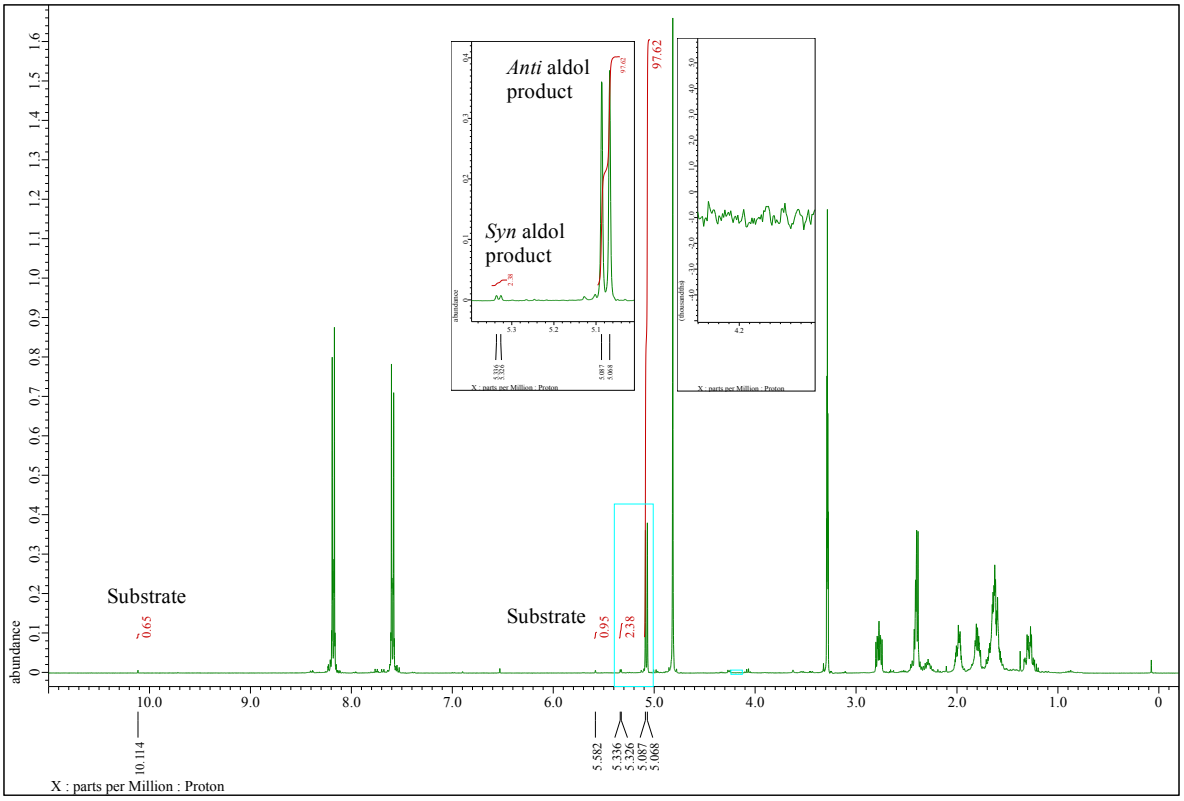
検出器A Ch1 250nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	32.512	89743	1582	0.918	0.966
2	34.033	67697	1189	0.693	0.726
3	35.024	223641	3909	2.288	2.387
4	37.126	9346559	156380	95.636	95.488
5	48.211	45458	710	0.465	0.434
合計		9773098	163769	100.000	100.000

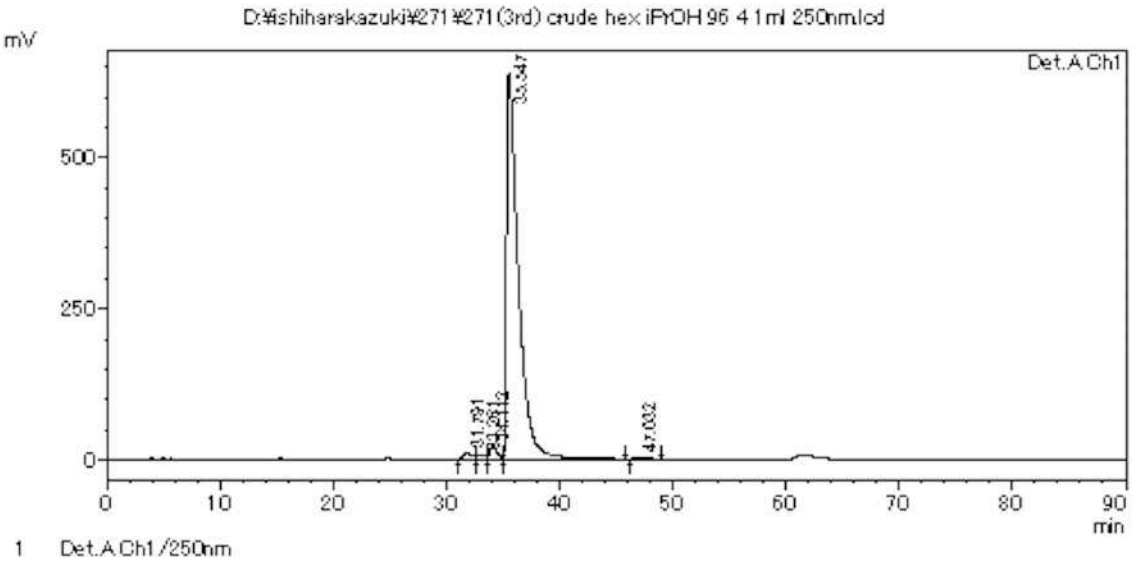
Conv. : 98%, *anti* : *syn* = 98 : 2, 99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 37.126 min (major), t_R = 48.211 min (minor)]

Table 8, cycle 3

^{1}H NMR, 400 MHz, CD_3OH



HPLC analysis



ピークテーブル

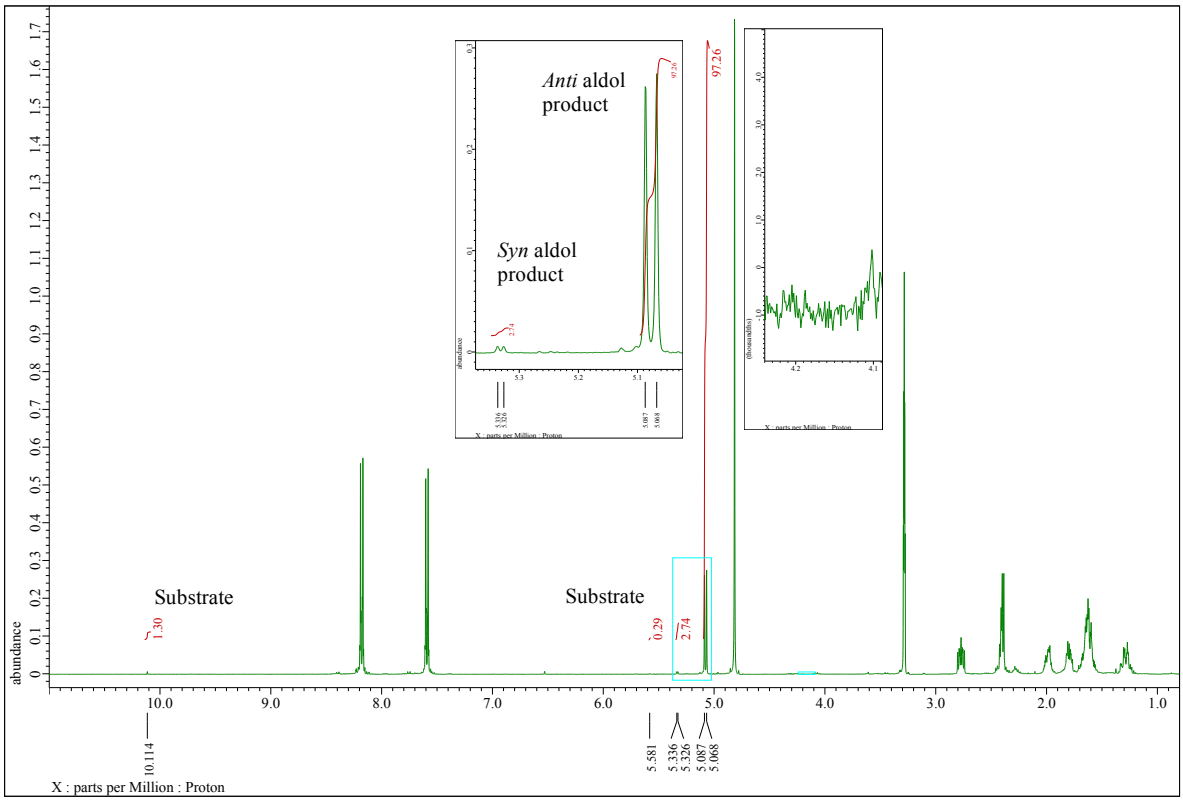
検出器A Ch1 250nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	31.791	563593	9628	1.156	1.409
2	33.261	426707	7612	0.876	1.114
3	34.112	1095120	22325	2.247	3.267
4	35.547	46385303	639528	95.172	93.600
5	47.032	267891	4161	0.550	0.609
合計		48738614	683254	100.000	100.000

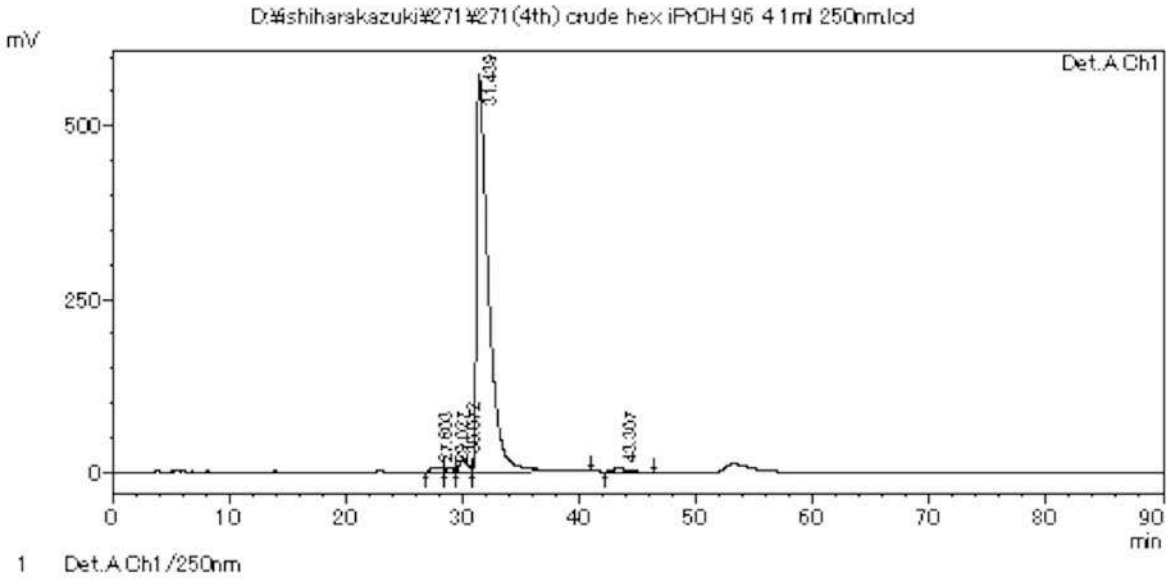
Conv. : 98%, *anti* : *syn* = 97 : 3, 99% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 35.547 min (major), t_R = 47.032 min (minor)]

Table 8, cycle 4

^{1}H NMR, 400 MHz, CD_3OH



HPLC analysis



ピークテーブル

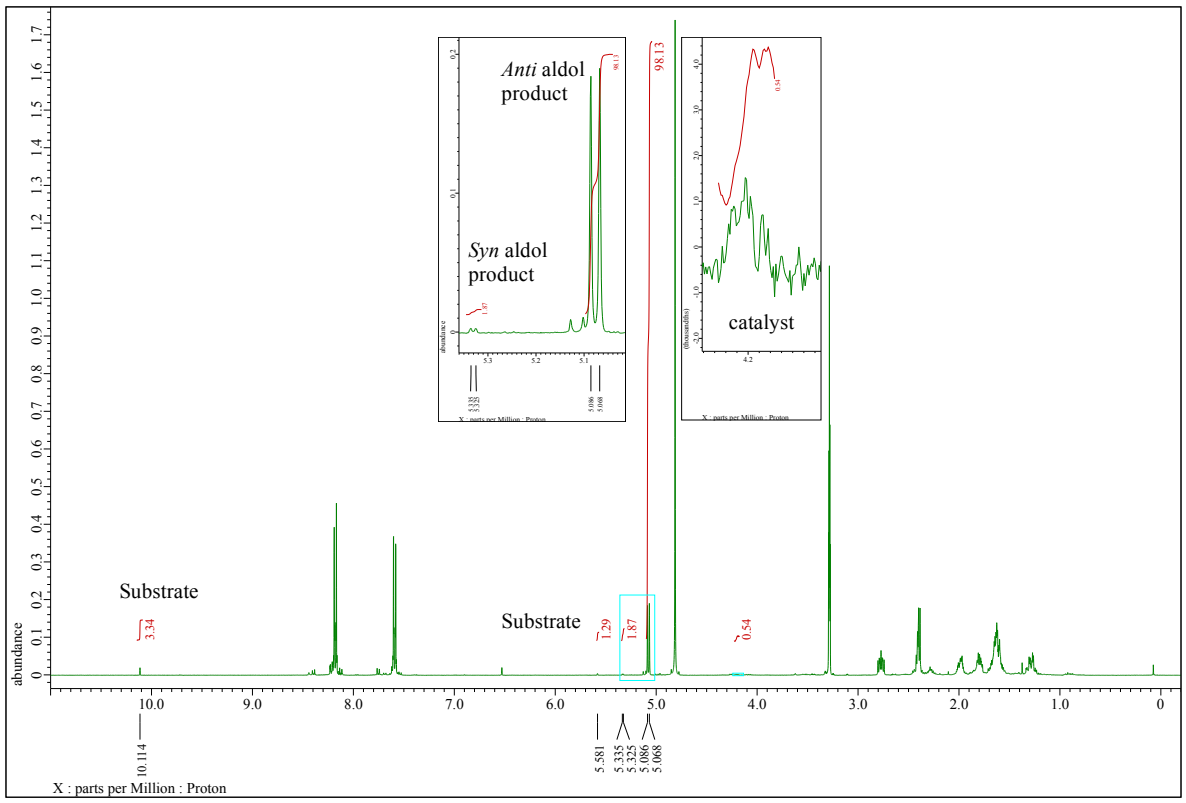
検出器A Ch1 250nm

ピーク#	保持時間	面積	高さ	面積%	高さ%
1	27.603	392930	6934	0.921	1.140
2	29.027	233511	4115	0.548	0.676
3	30.072	856964	17795	2.009	2.925
4	31.439	40796711	574439	95.660	94.418
5	43.307	367603	5119	0.862	0.841
合計		42647719	608402	100.000	100.000

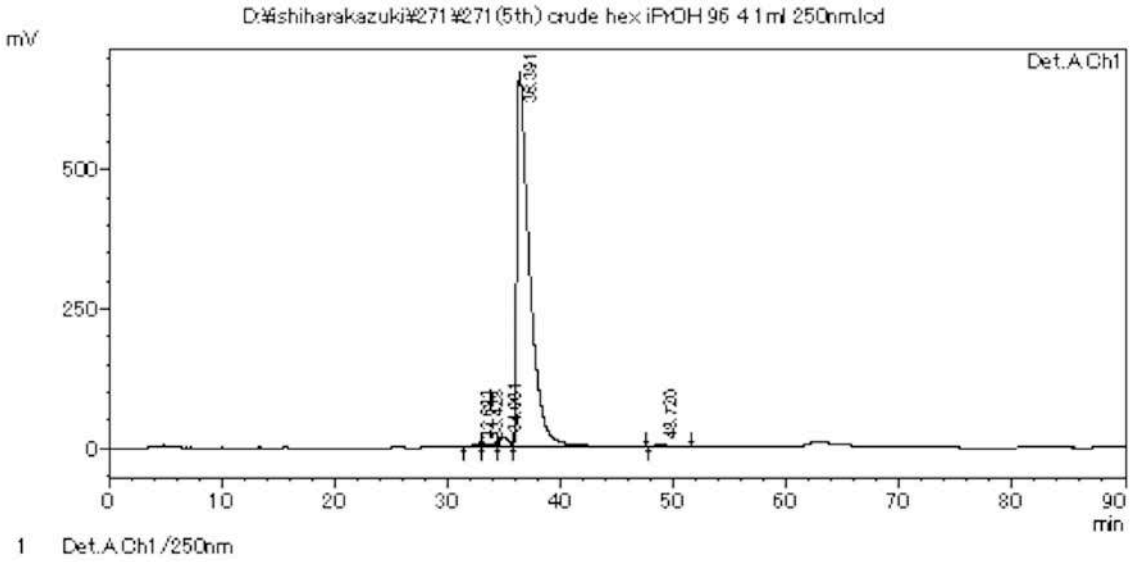
Conv. : 98%, *anti* : *syn* = 97 : 3, 98% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 31.439 min (major), t_R = 43.307 min (minor)]

Table 8, cycle 5

^{1}H NMR, 400 MHz, CD_3OH



HPLC analysis



ピークテーブル

検出器A Ch1 250nm

ピーク番	保持時間	面積	高さ	面積%	高さ%
1	32.683	342191	7310	0.622	1.020
2	33.428	582190	7265	1.058	1.014
3	34.981	965882	19205	1.754	2.681
4	36.391	52674174	675709	95.681	94.317
5	48.720	487307	6938	0.885	0.968
合計		55051744	716427	100.000	100.000

Conv. : 95%, *anti* : *syn* = 98 : 2, 98% *ee*; The *ee* of *anti* aldol product was determined by HPLC. [Daicel chiralpac IB+OD-3 column, hex : ^{i}PrOH = 96 : 4, flow rate 1.0 mL/min, t_R = 36.391 min (major), t_R = 48.720 min (minor)]

5. **References for supporting information**

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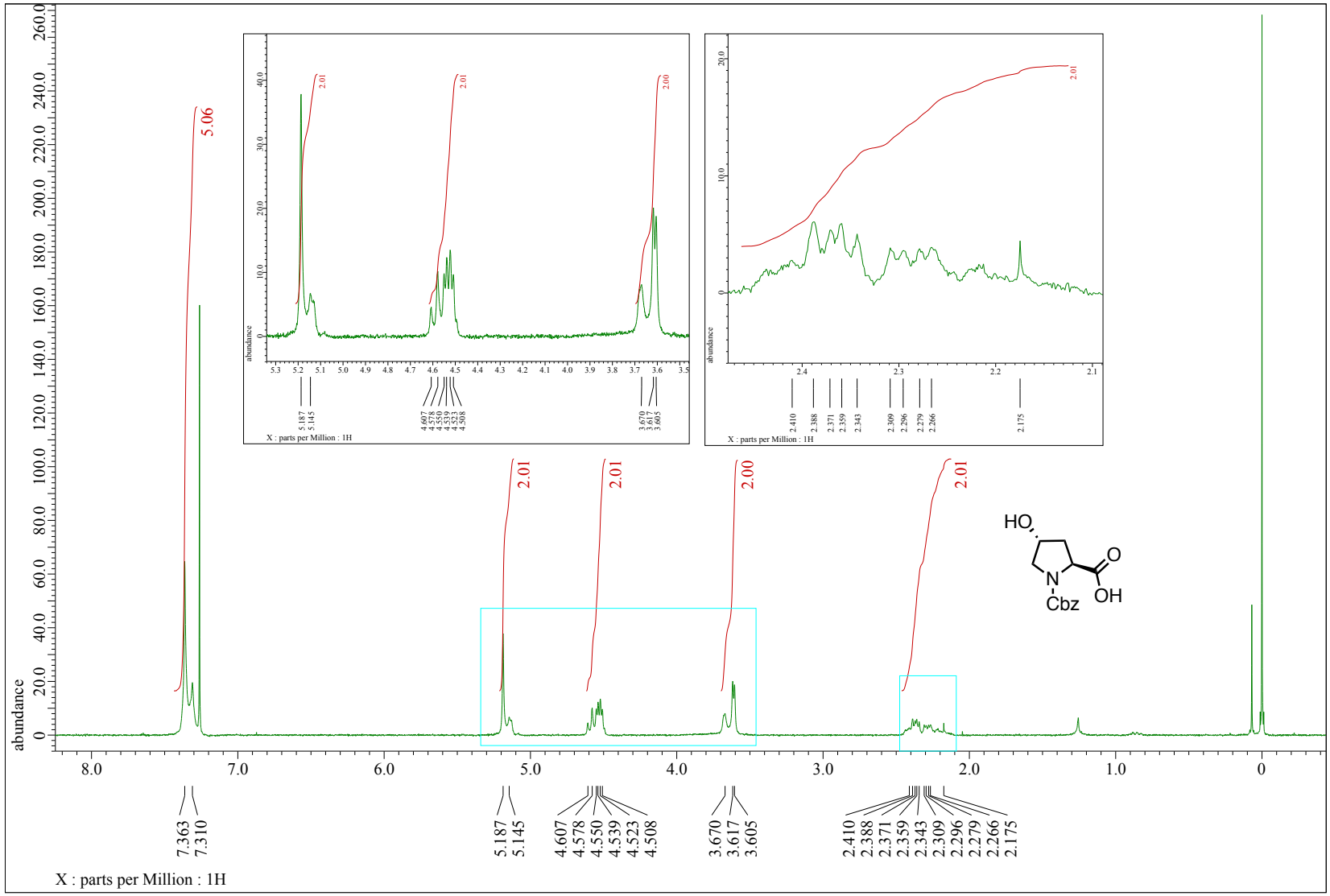
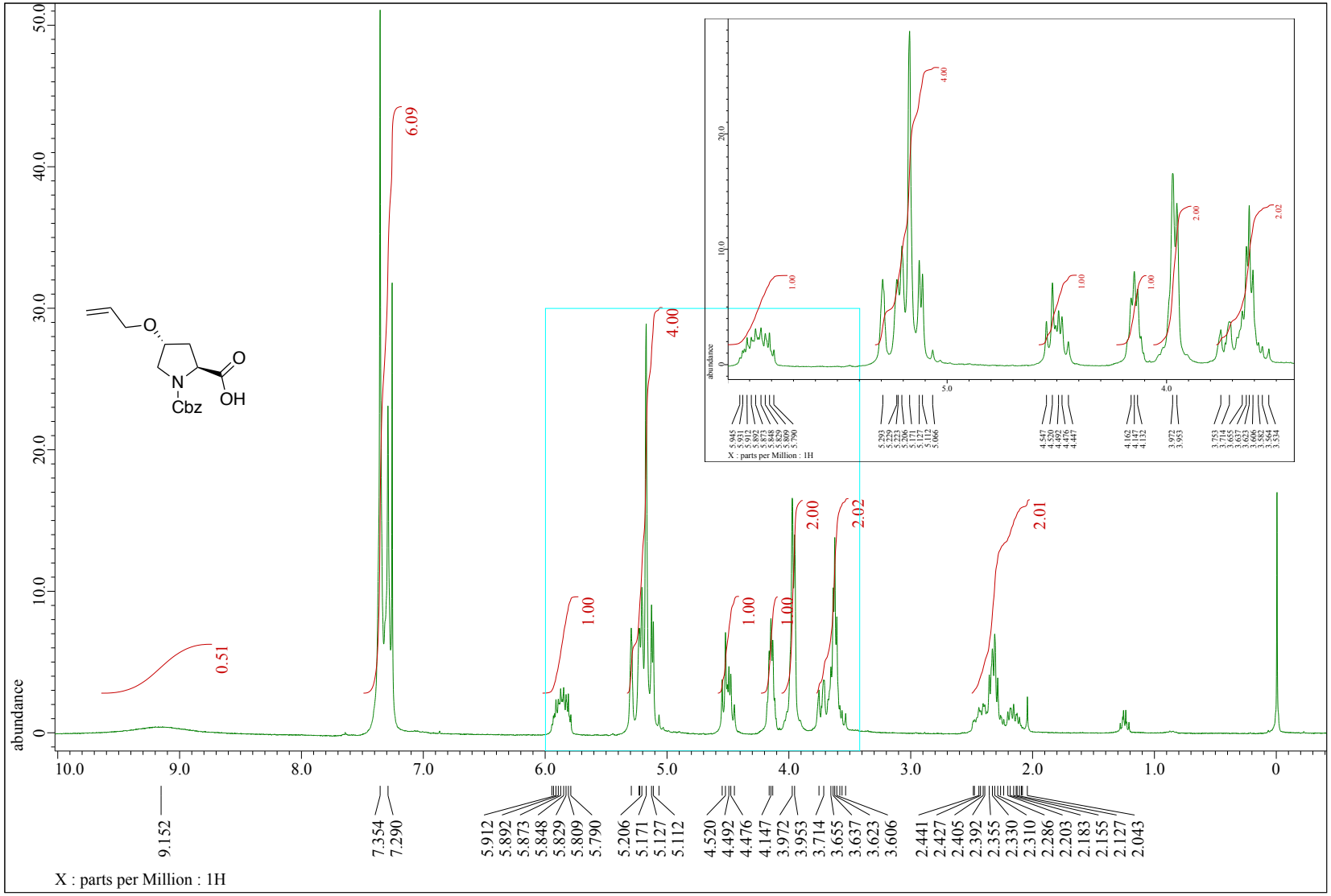
6. **Spectral data for products**

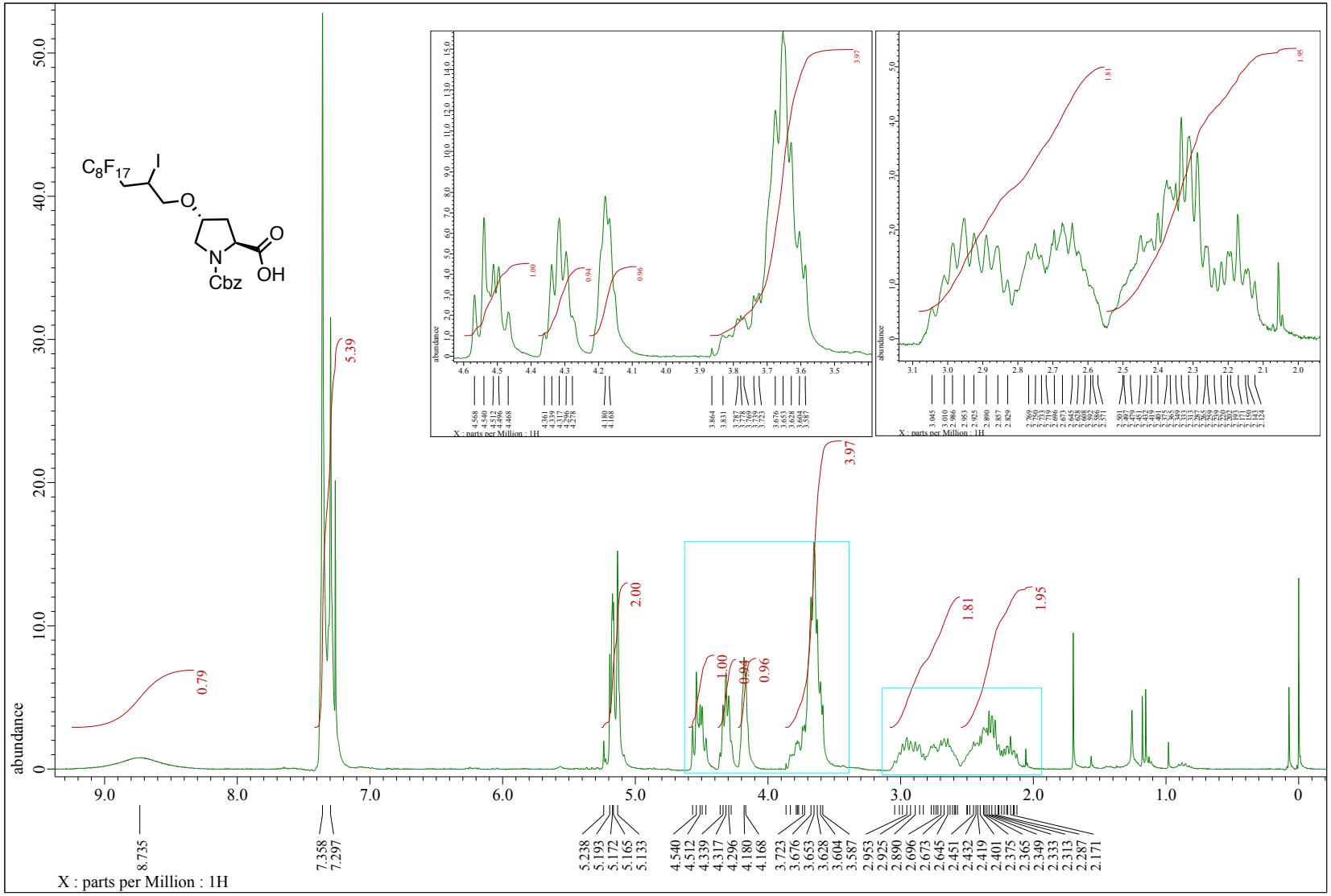
^{1}H NMR, 270 MHz, $CDCl_3$



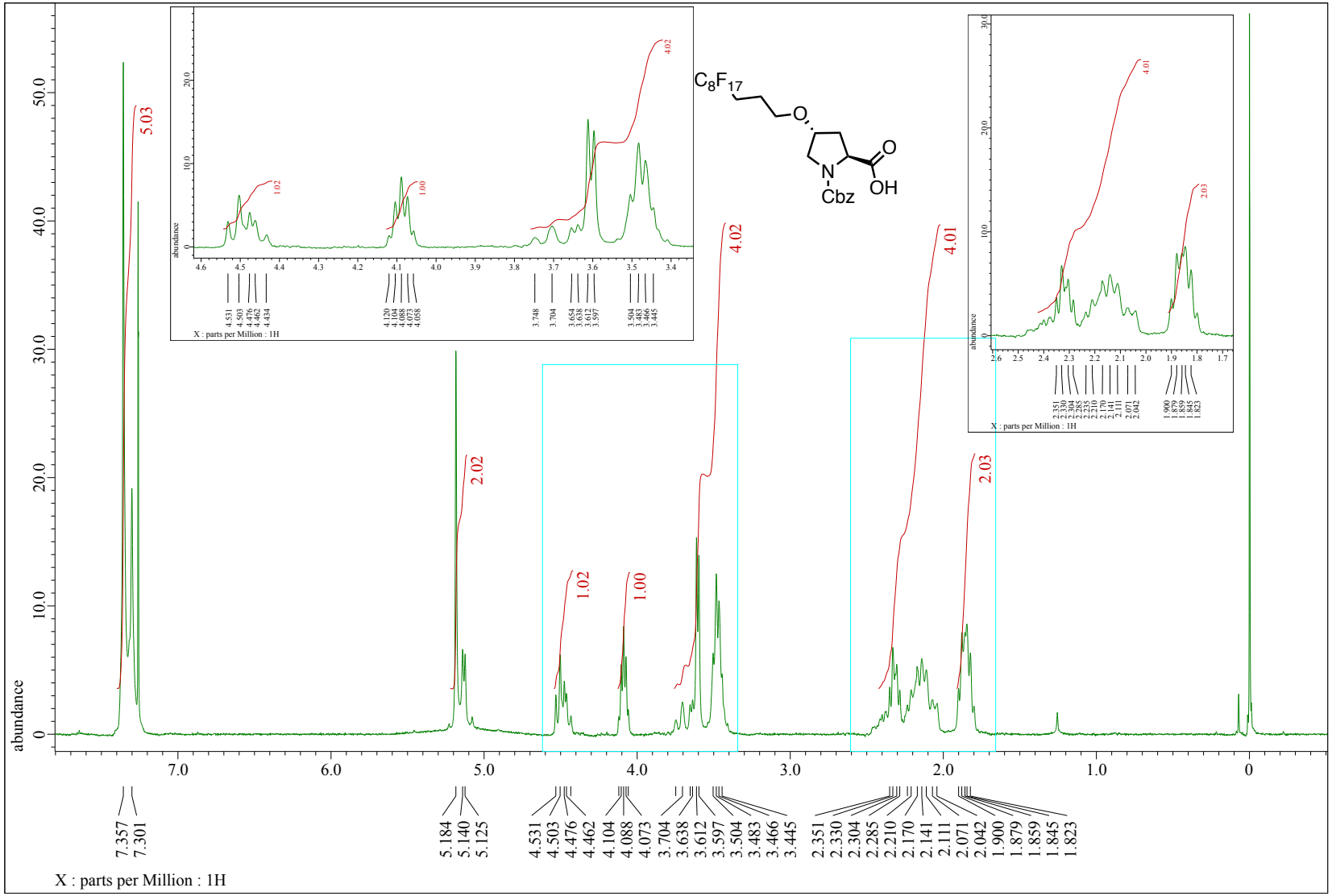
^{1}H NMR, 270 MHz, $CDCl_3$



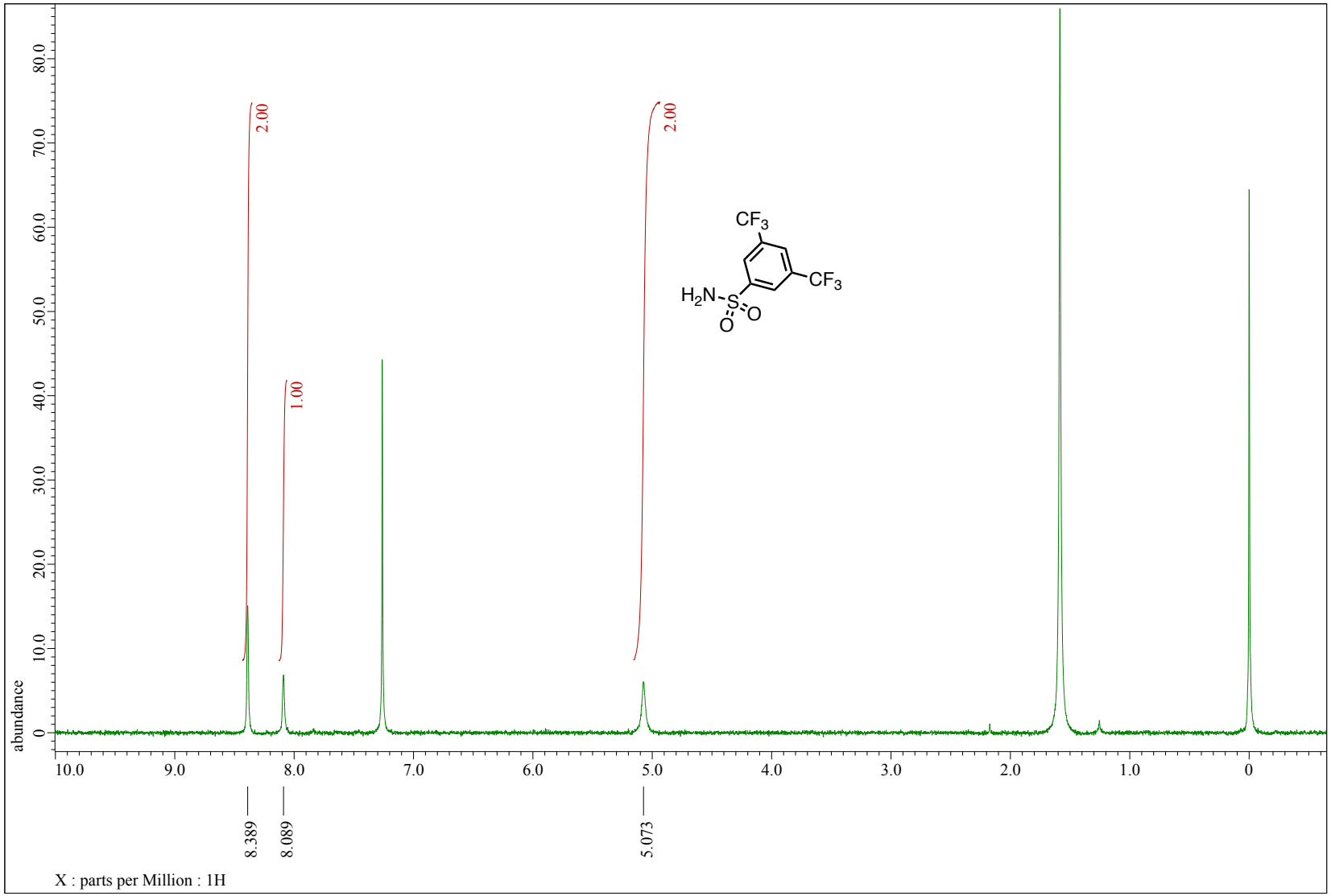
^{1}H NMR, 270 MHz, $CDCl_3$



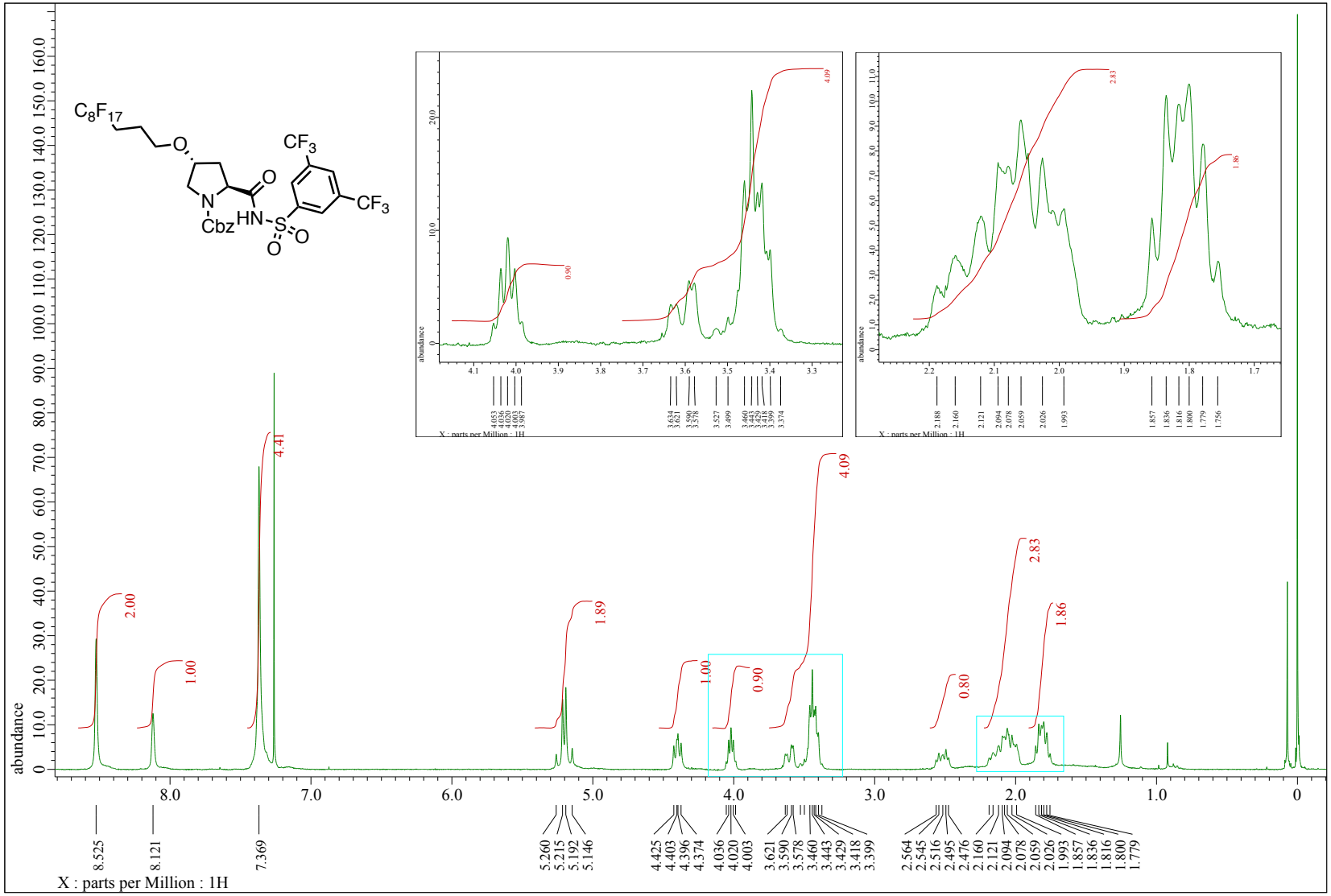
^{1}H NMR, 270 MHz, $CDCl_3$



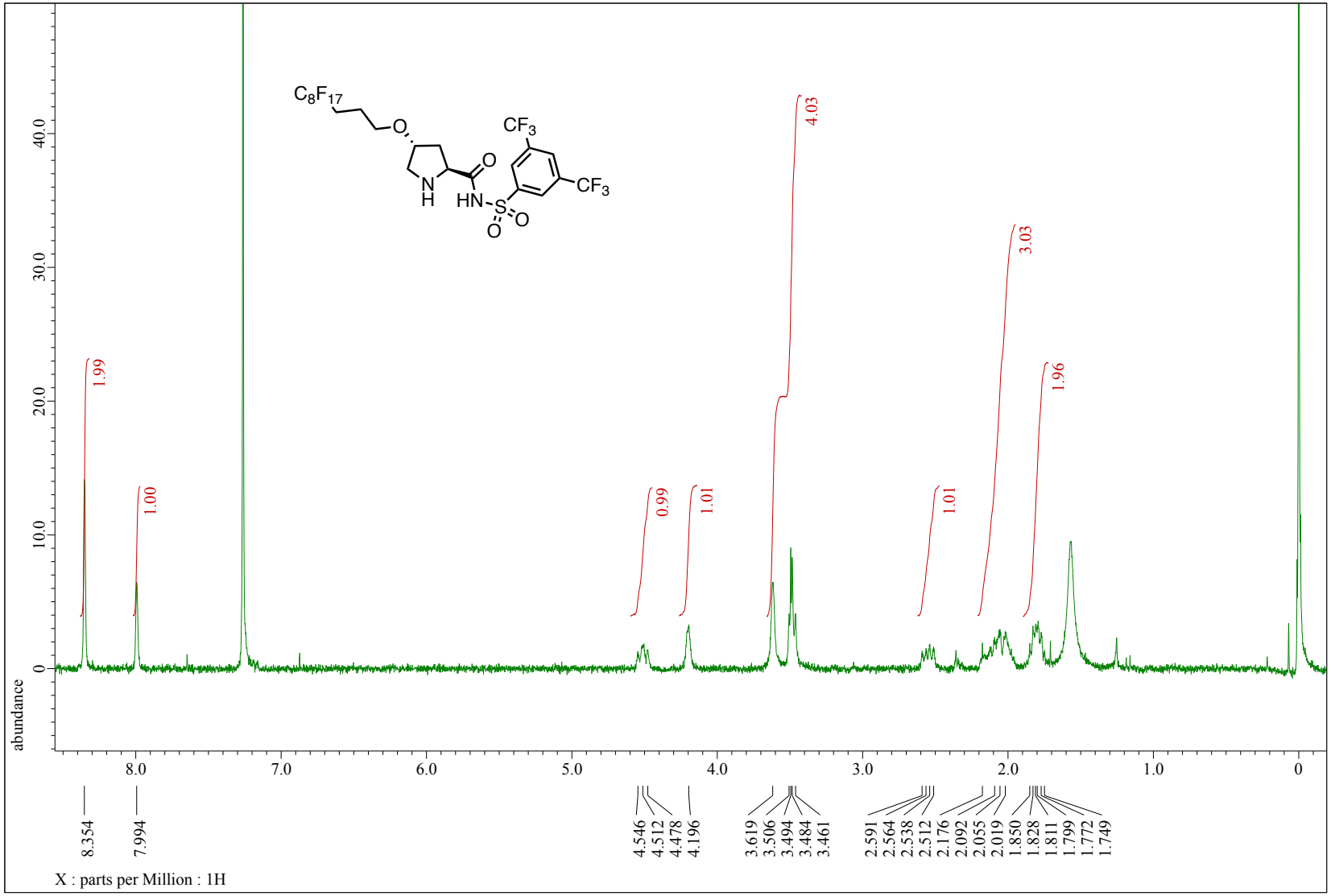
^{1}H NMR, 270 MHz, $CDCl_3$



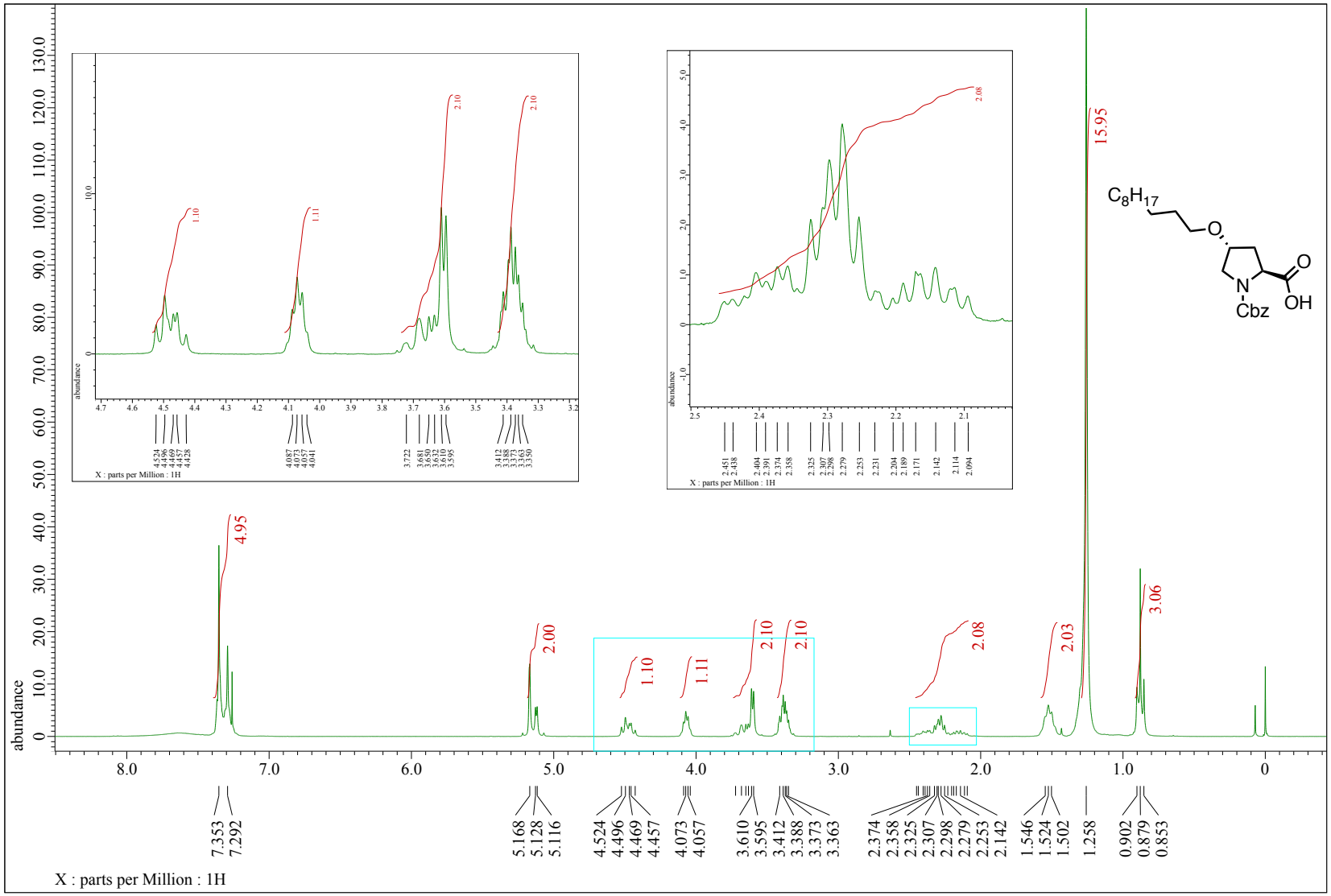
^{1}H NMR, 270 MHz, $CDCl_3$



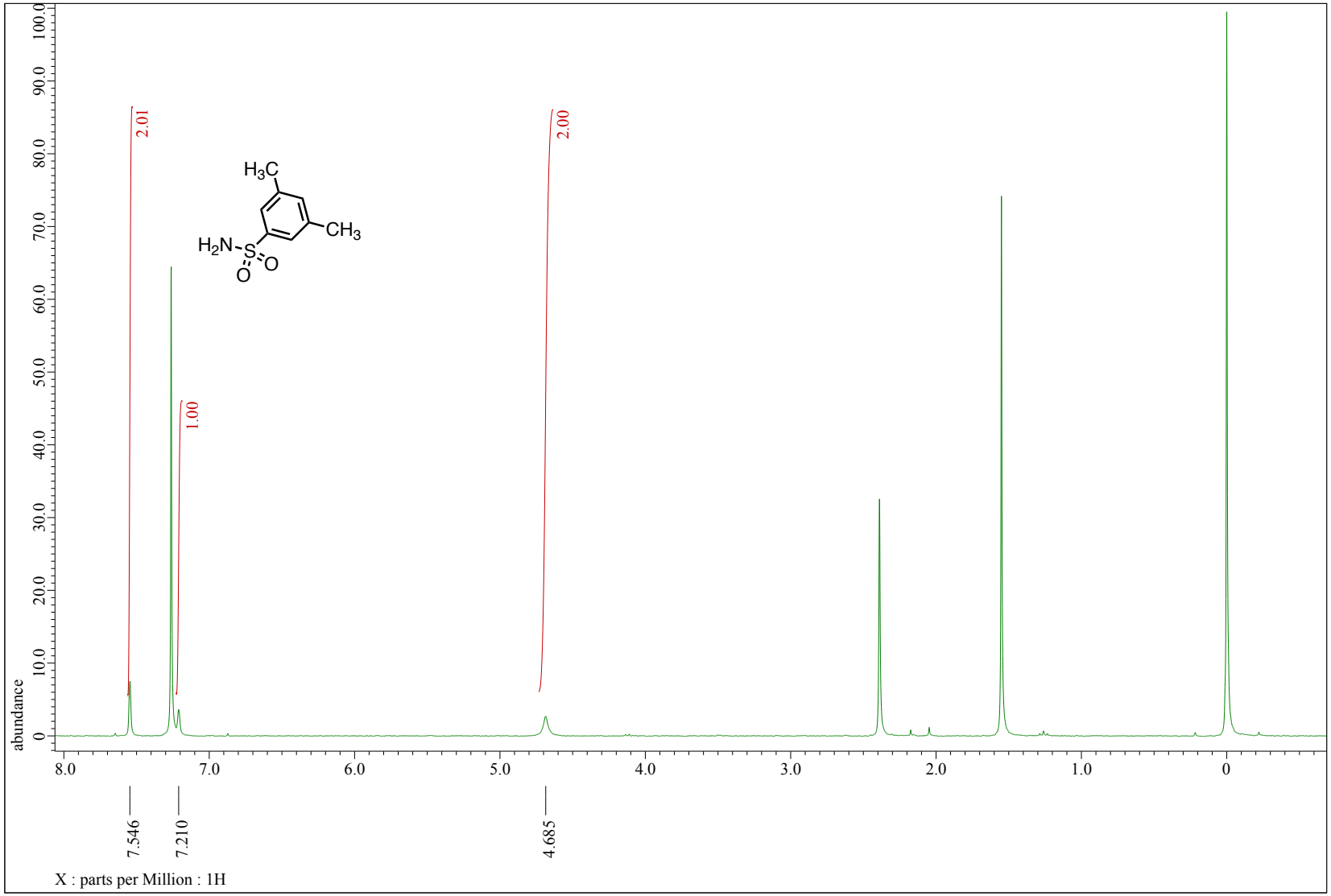
^{1}H NMR, 270 MHz, $CDCl_3$



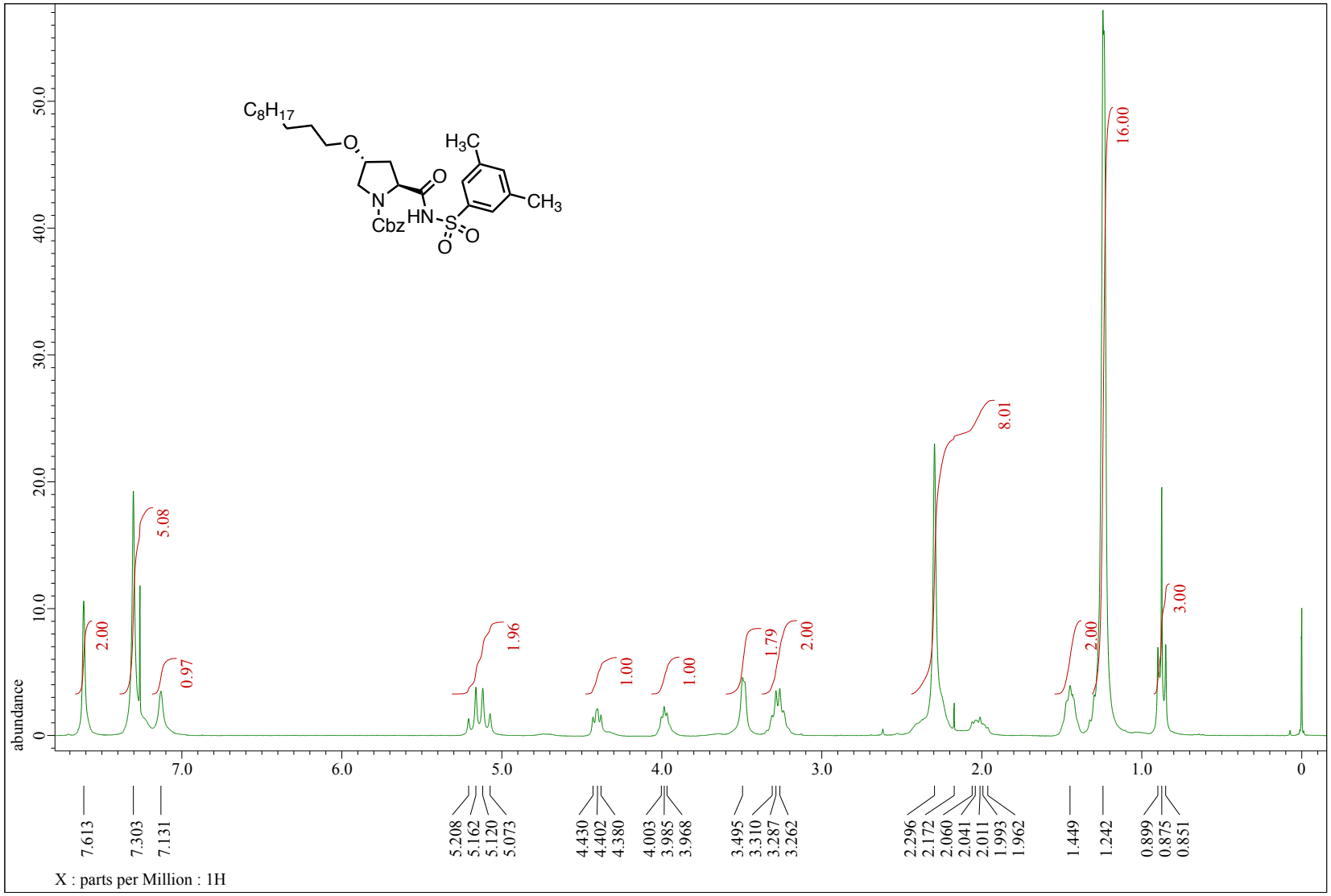
^{1}H NMR, 270 MHz, $CDCl_3$



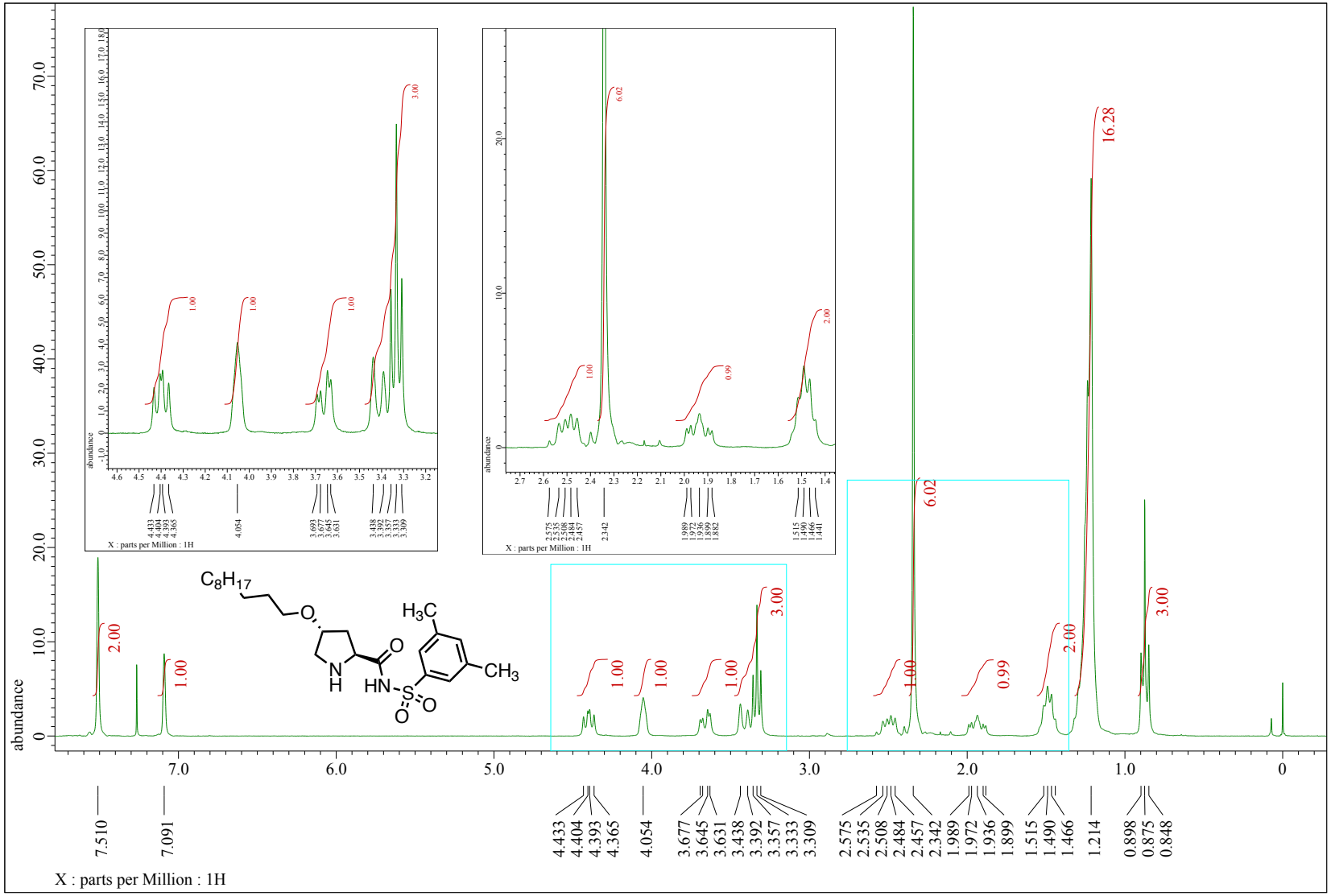
^{1}H NMR, 270 MHz, $CDCl_3$



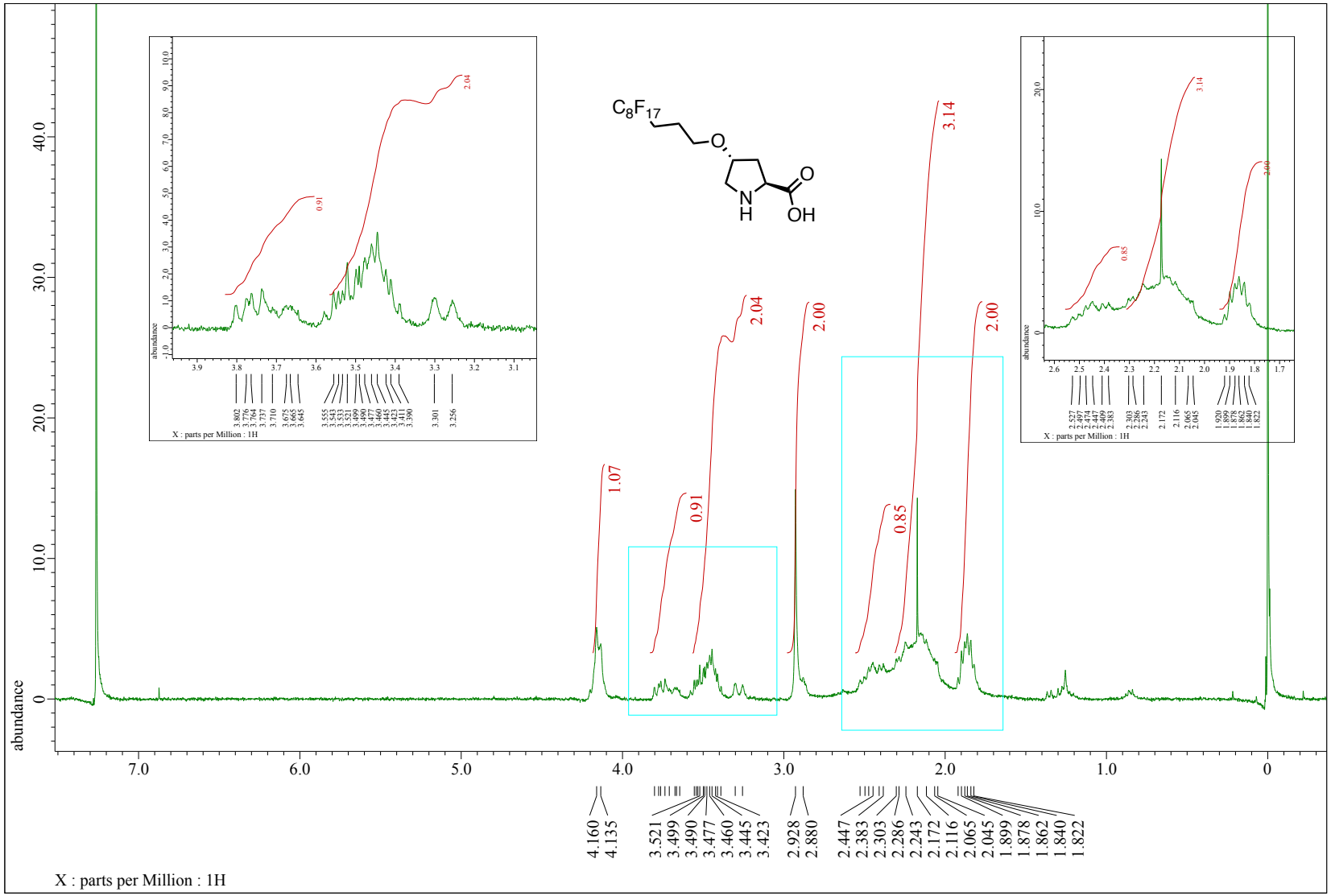
^{1}H NMR, 270 MHz, $CDCl_3$



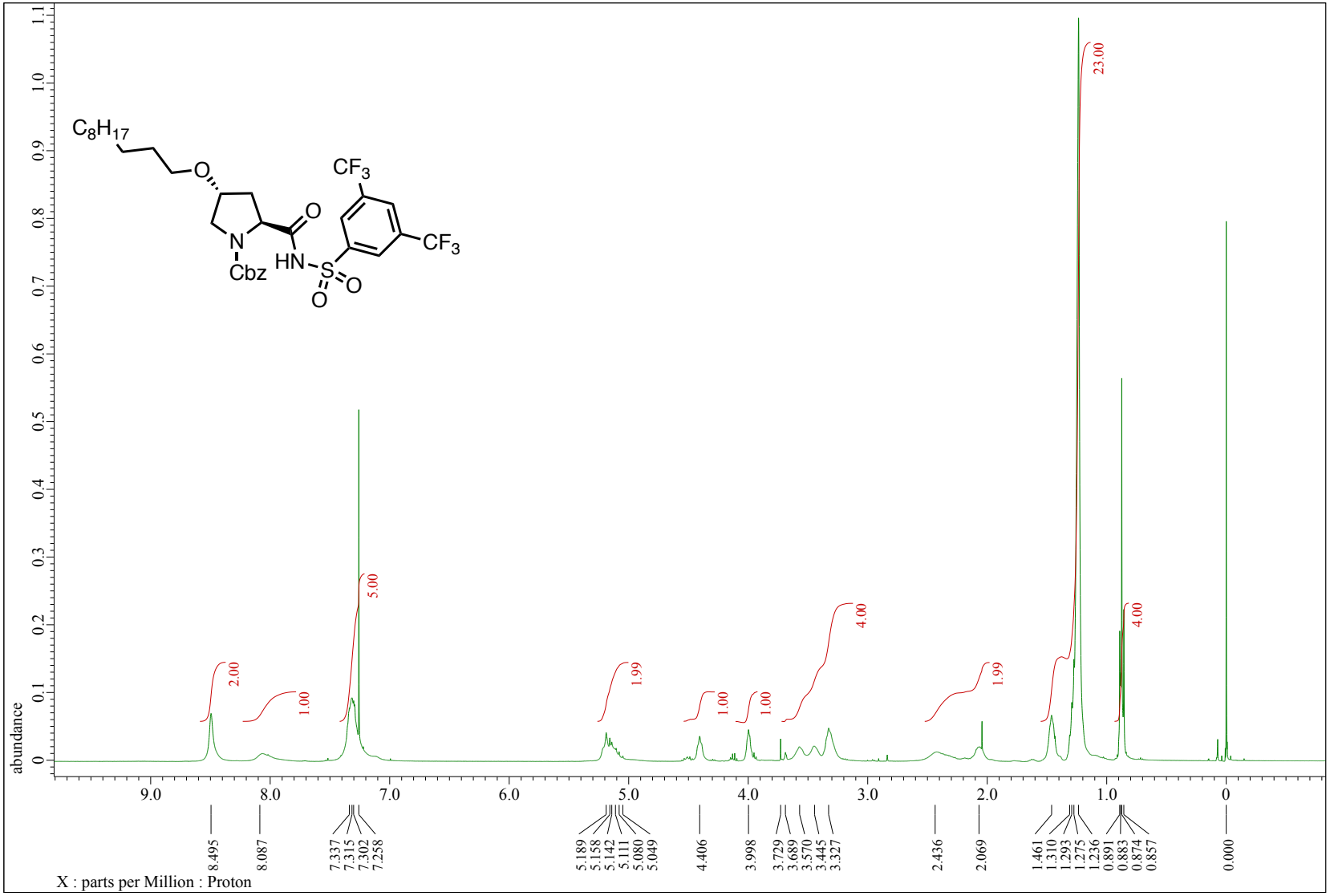
^{1}H NMR, 270 MHz, $CDCl_3$



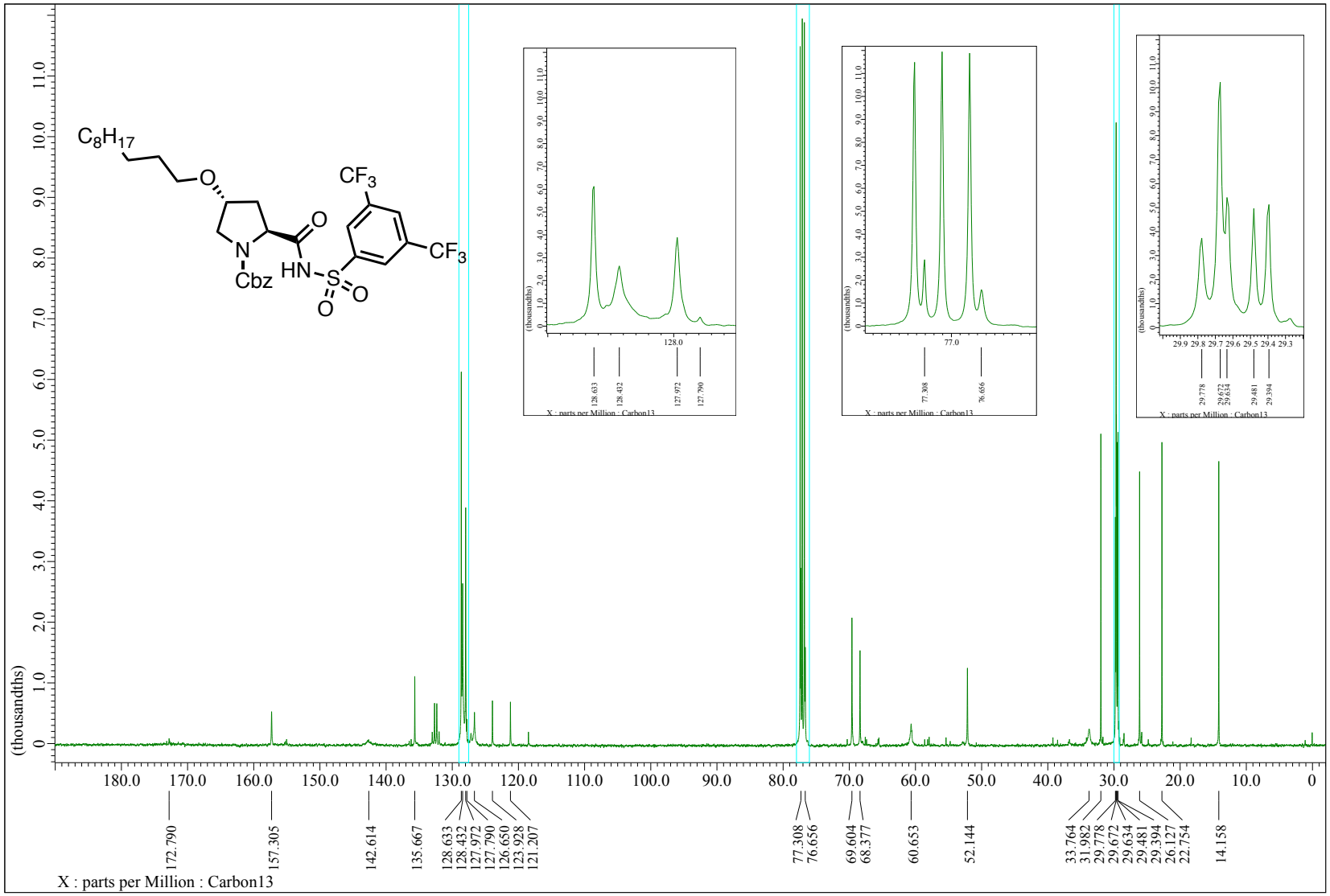
^{1}H NMR, 270 MHz, CD_3OD



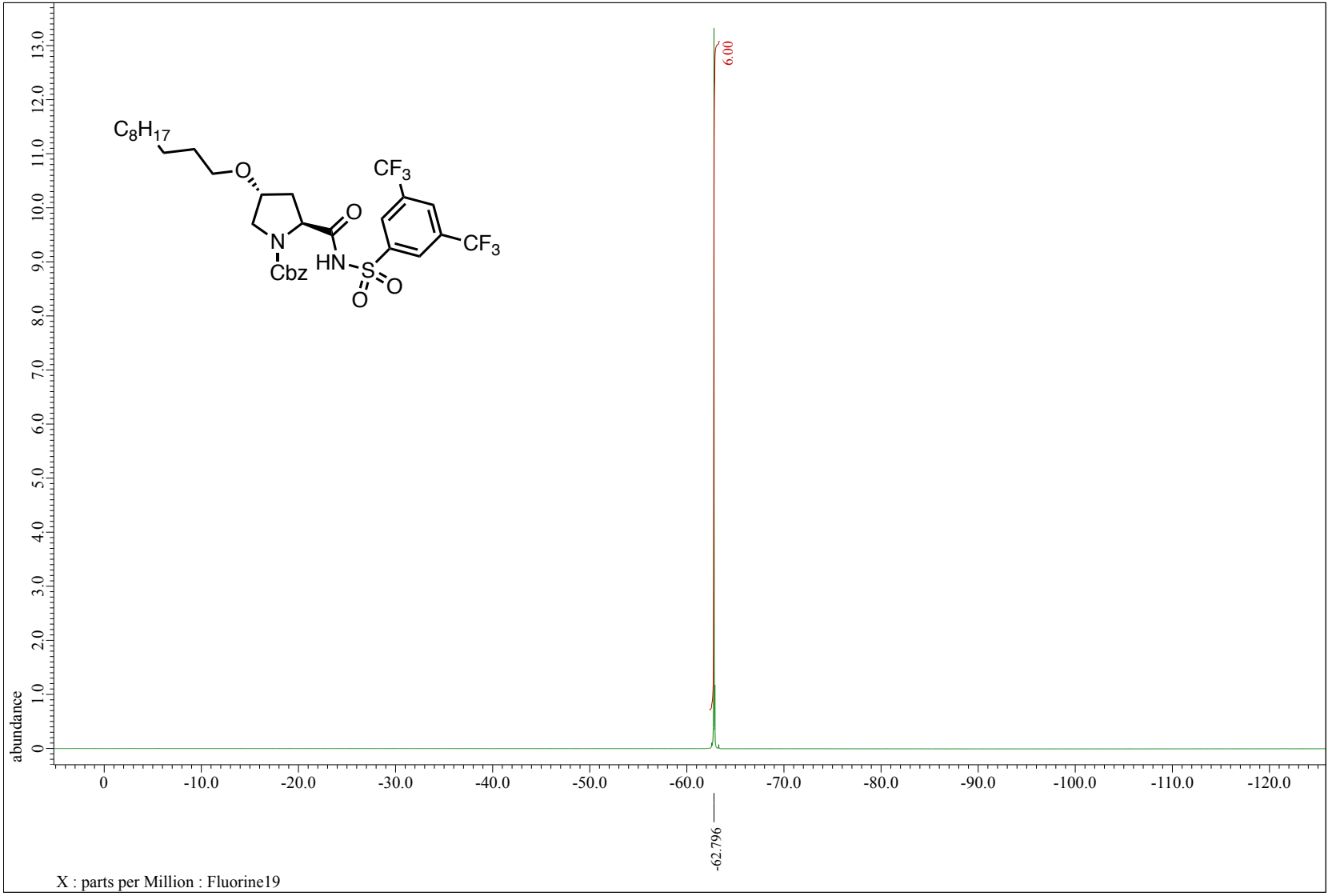
^{1}H NMR, 500 MHz, $CDCl_3$



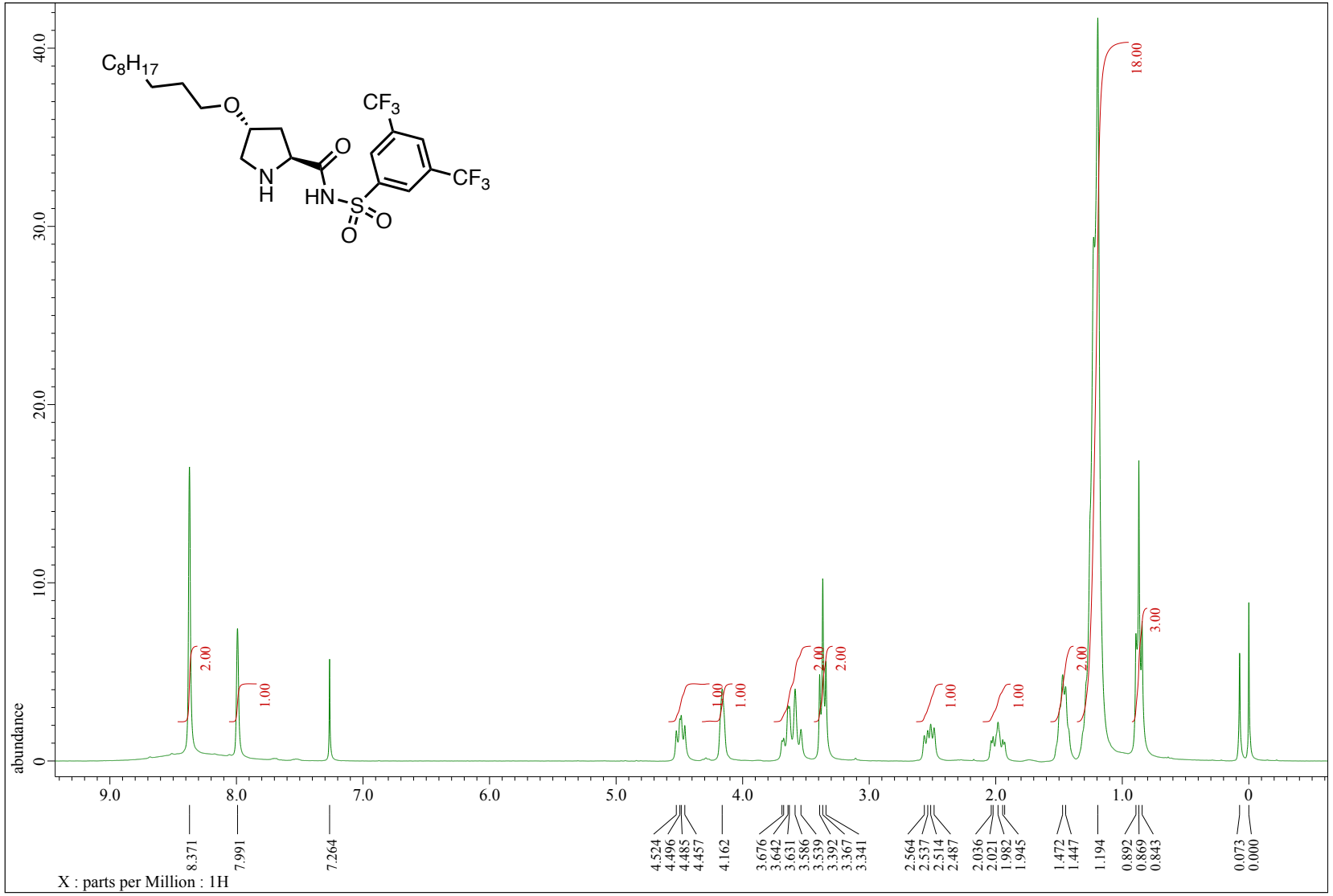
^{13}C NMR, 101 MHz, $CDCl_3$



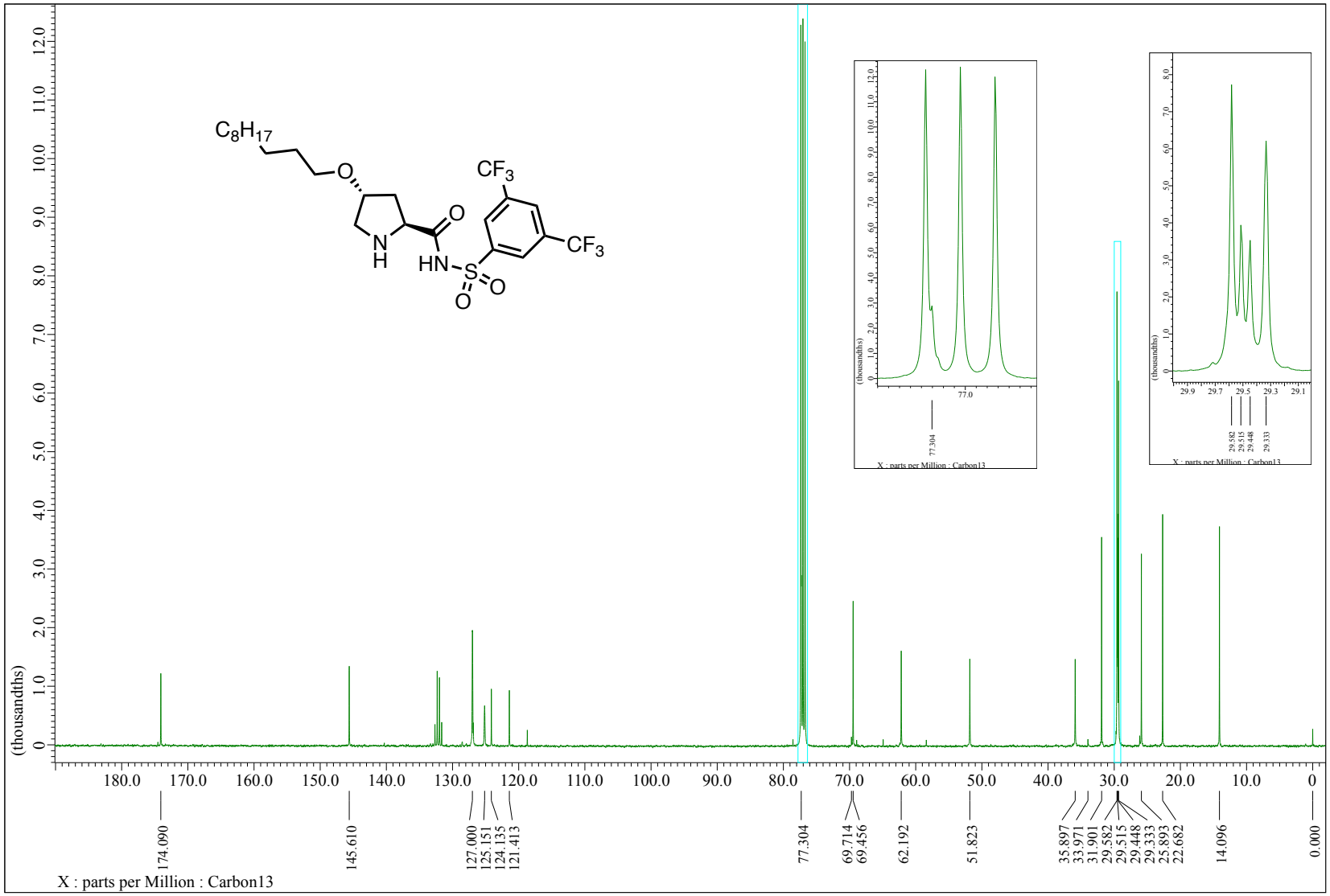
^{19}F NMR, 376 MHz, $CDCl_3$



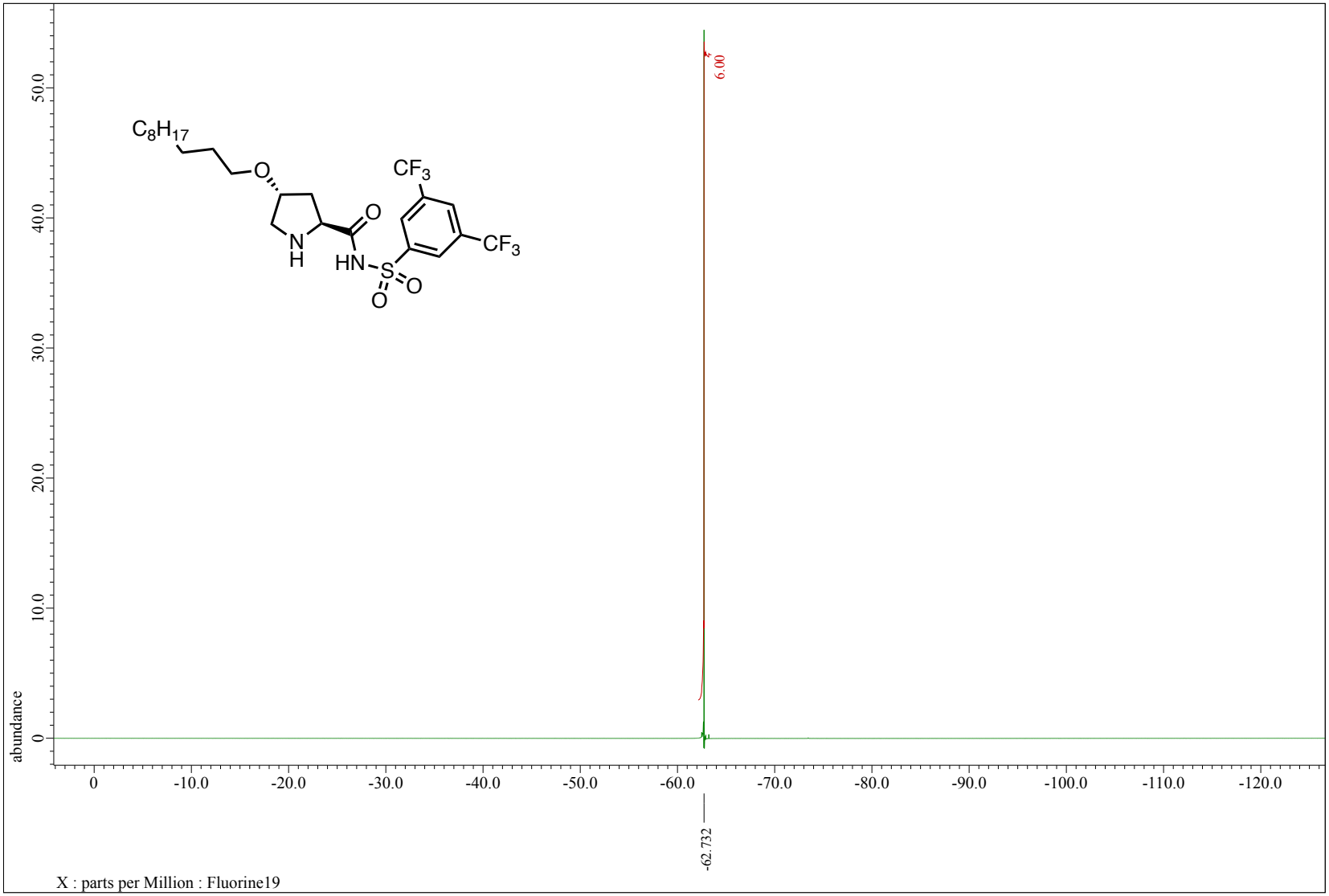
^{1}H NMR, 270 MHz, $CDCl_3$



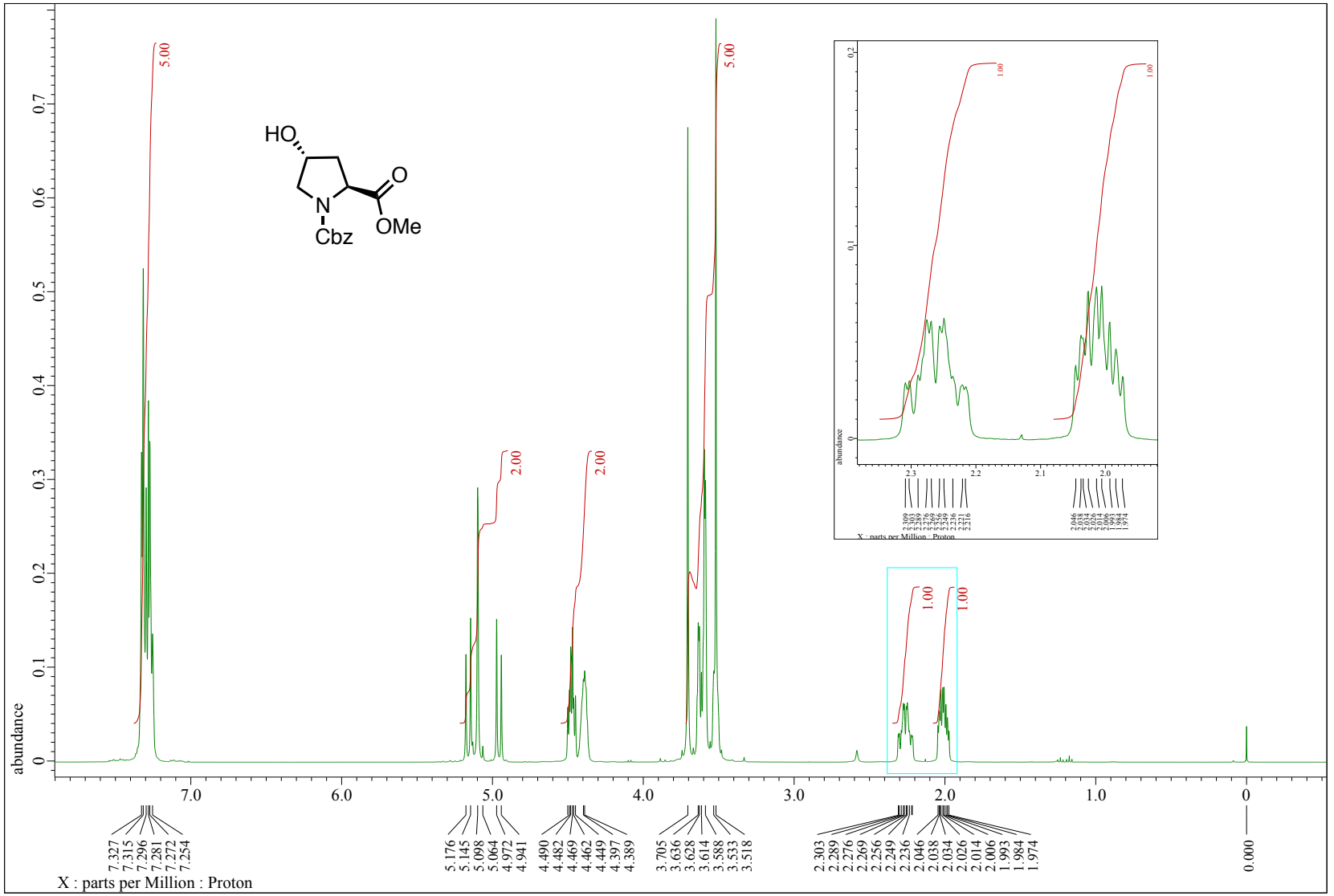
^{13}C NMR, 101 MHz, $CDCl_3$



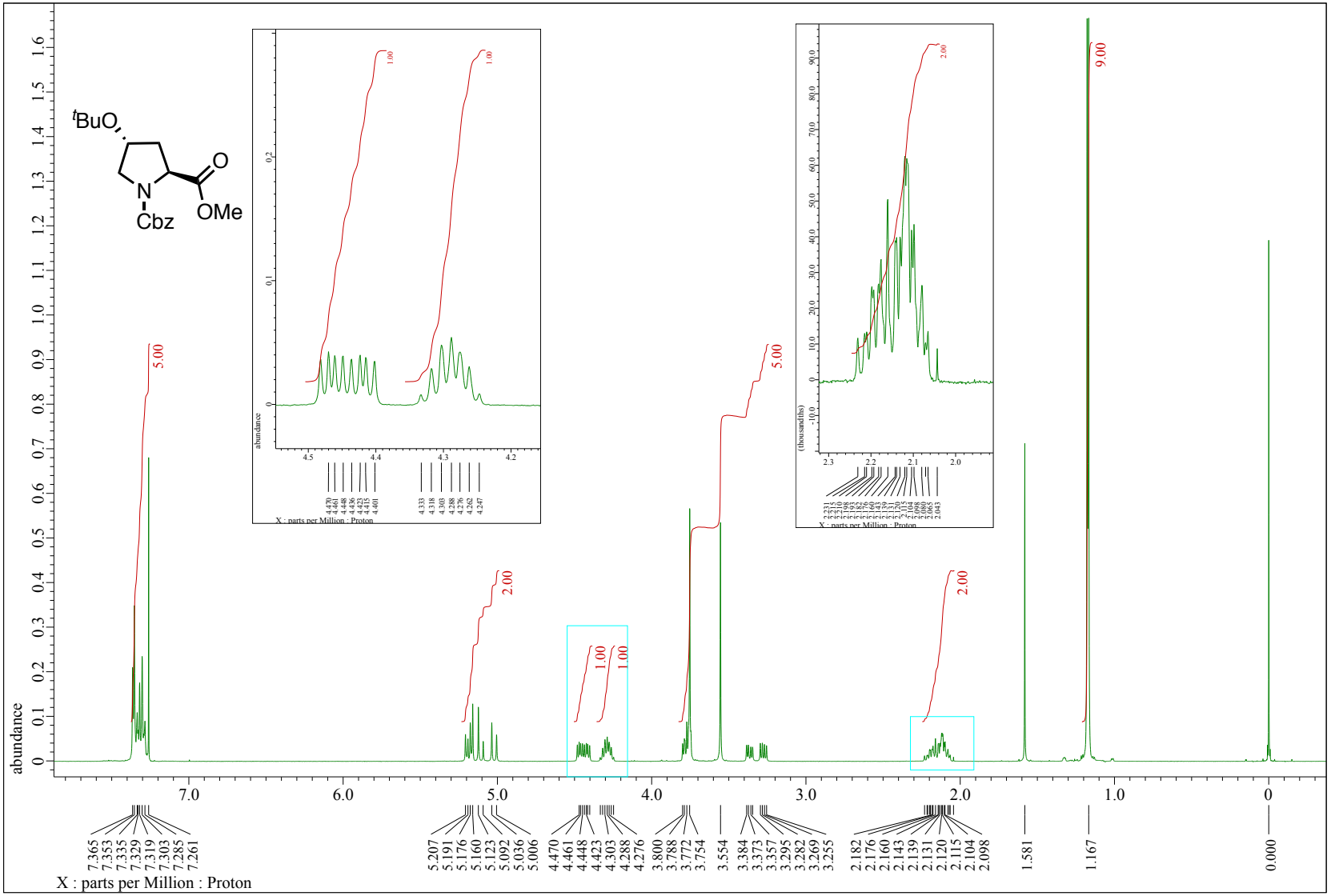
^{19}F NMR, 376 MHz, $CDCl_3$



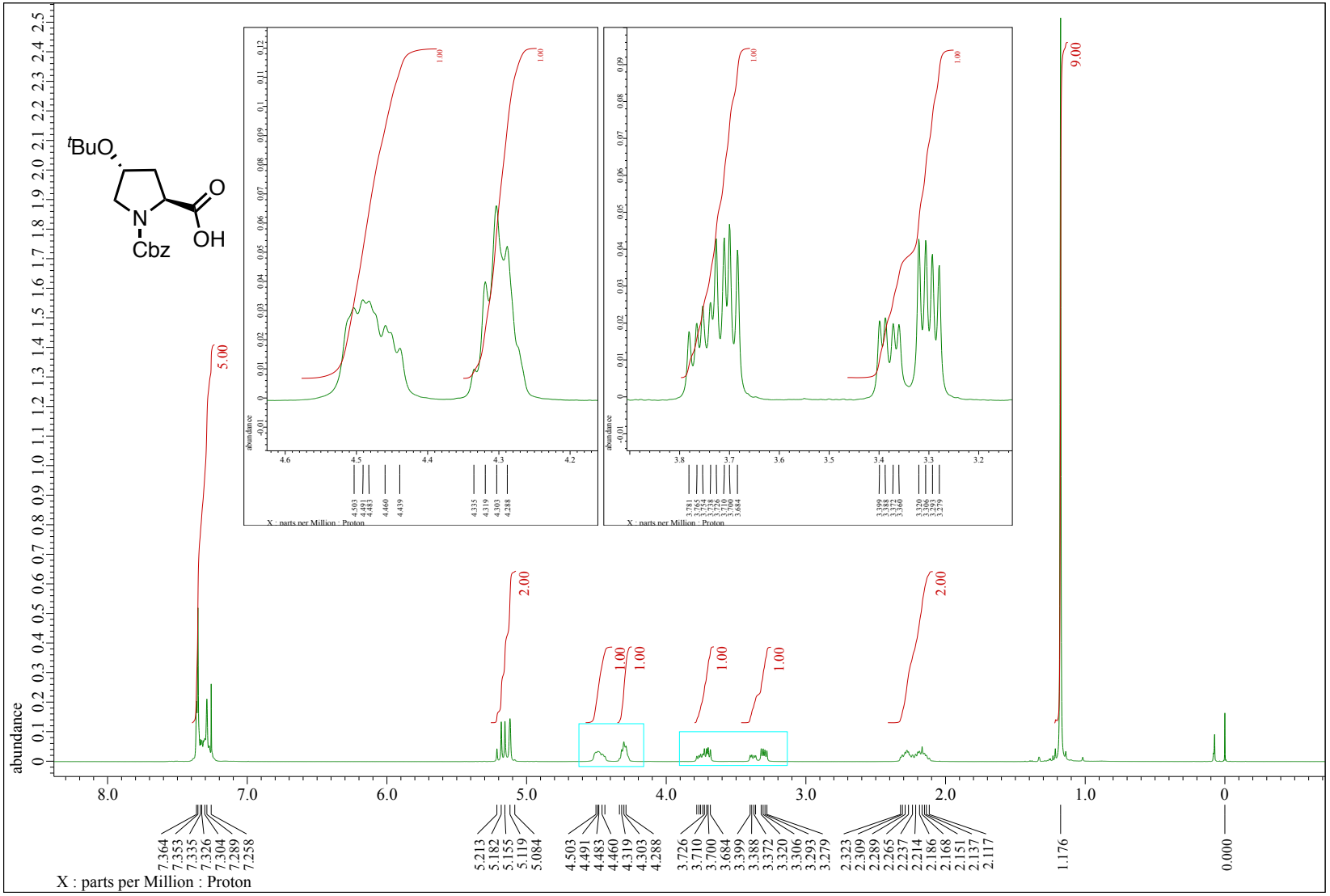
^{1}H NMR, 400 MHz, $CDCl_3$



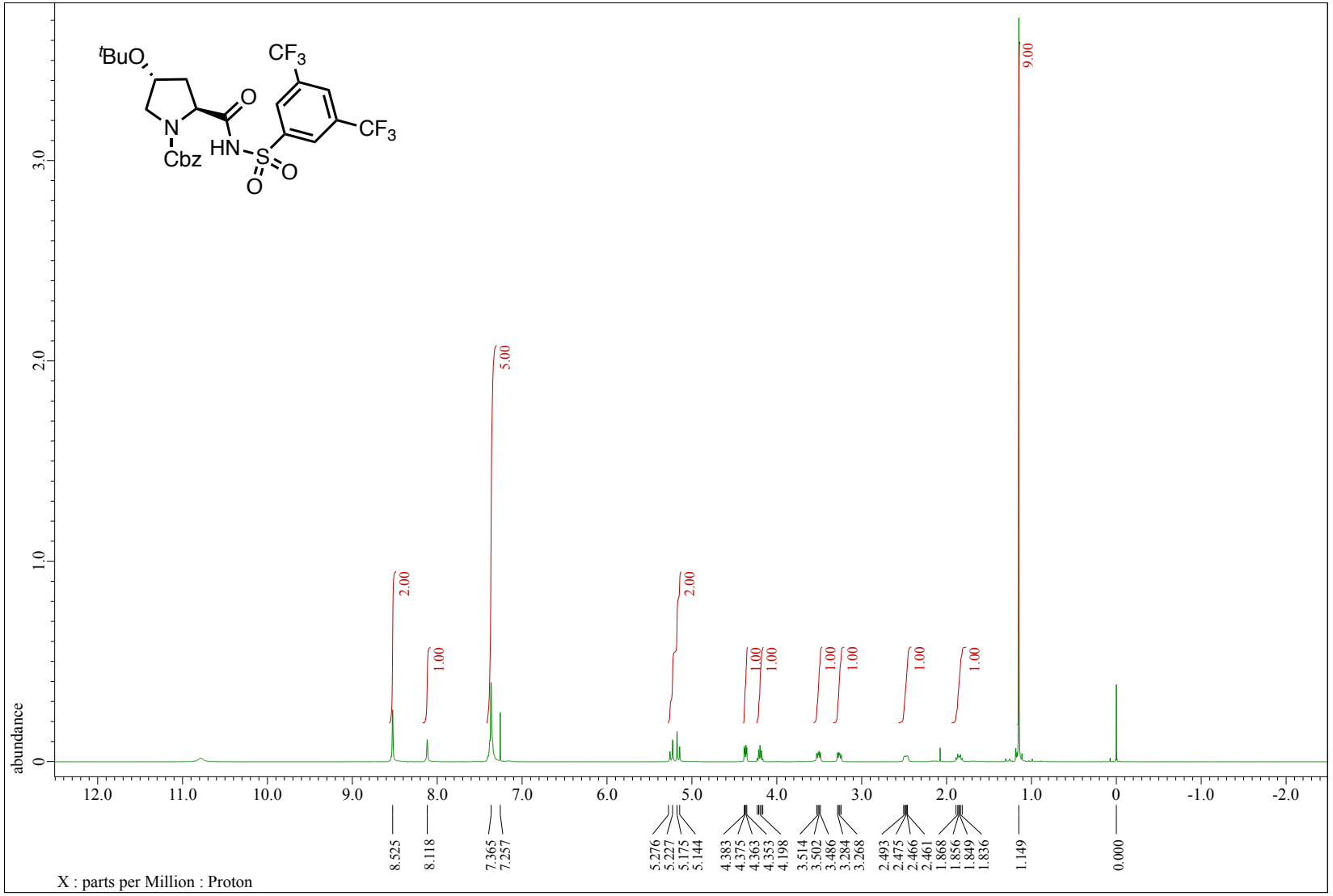
^{1}H NMR, 400 MHz, $CDCl_3$



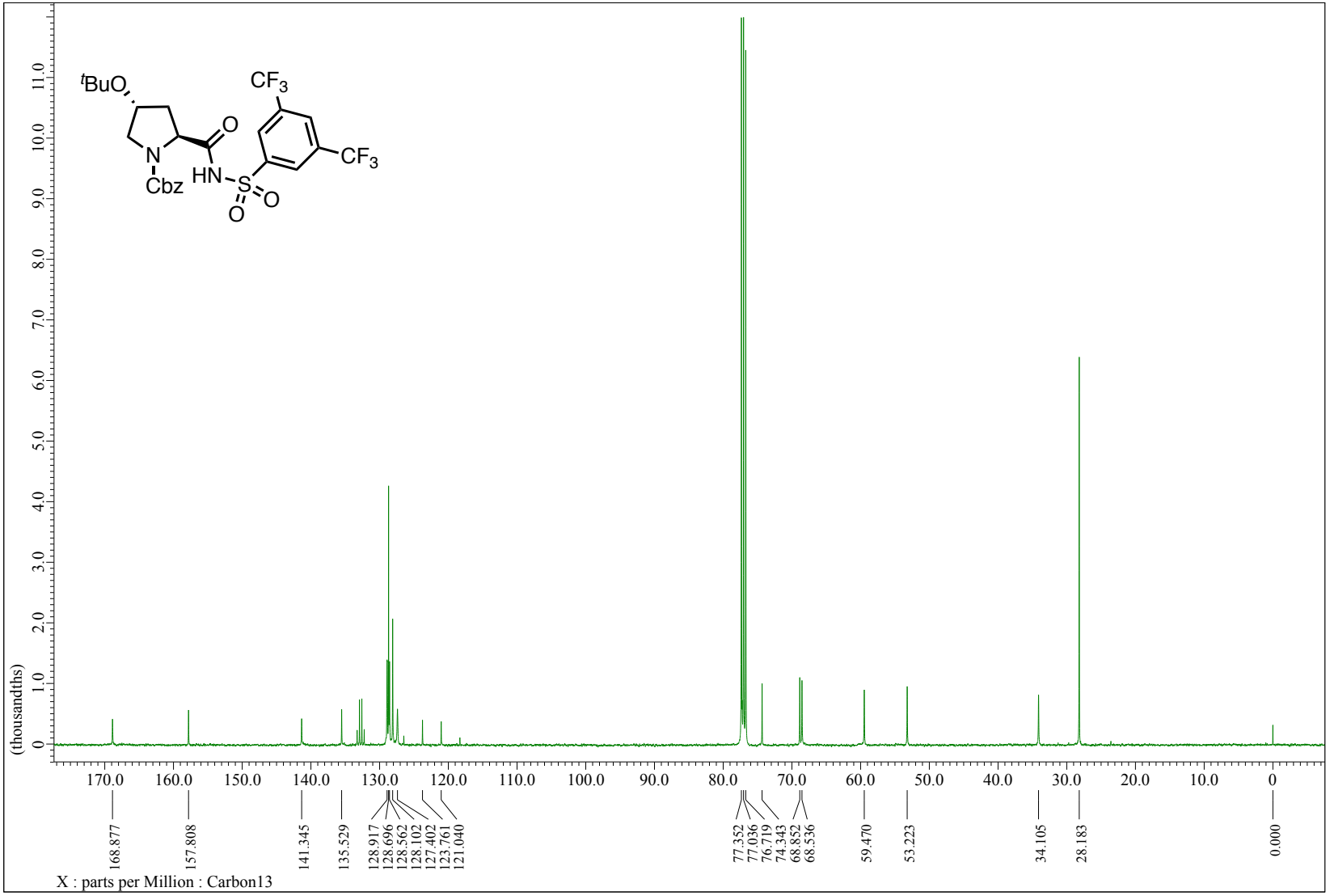
^{1}H NMR, 400 MHz, $CDCl_3$



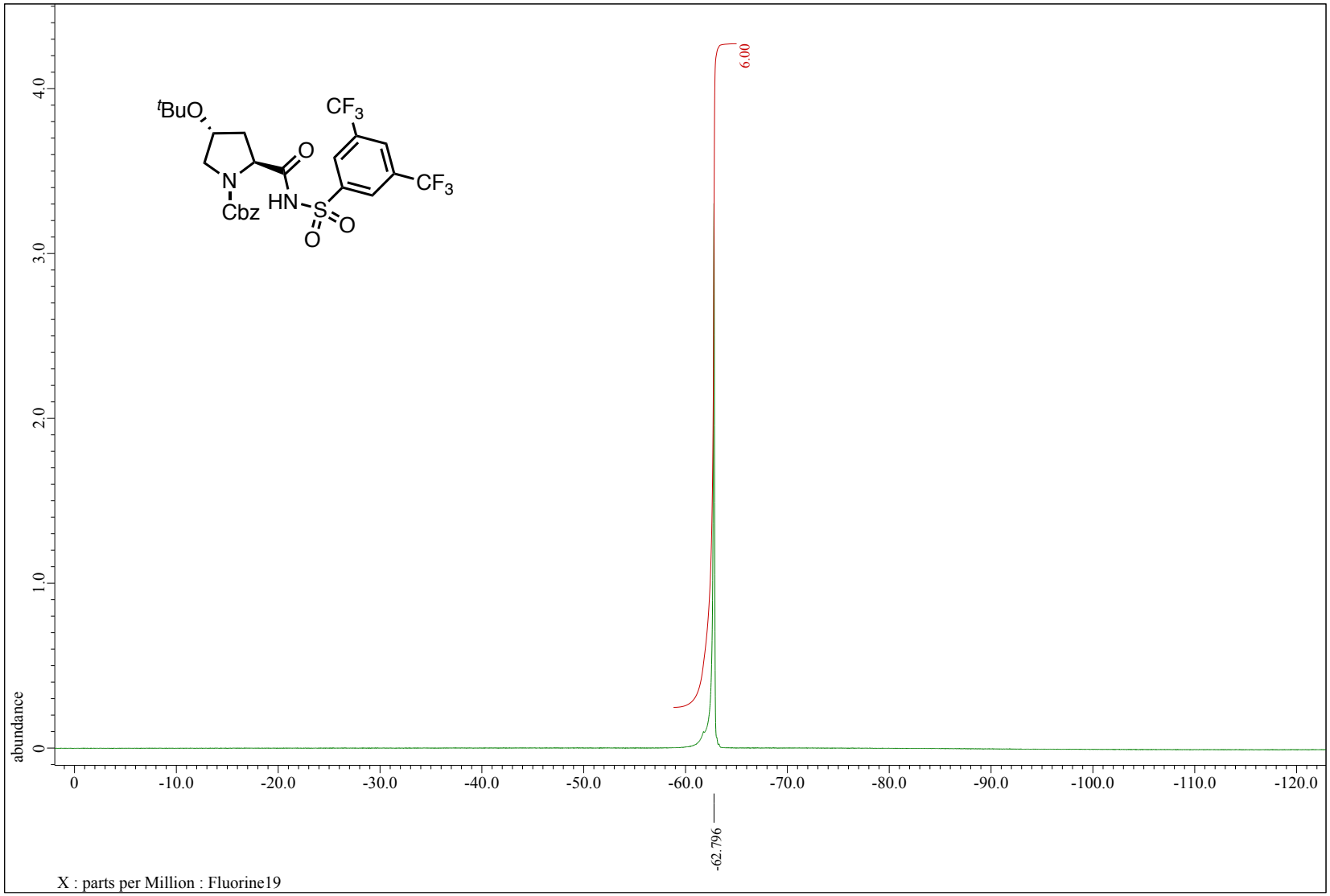
^{1}H NMR, 400 MHz, CD_3OD



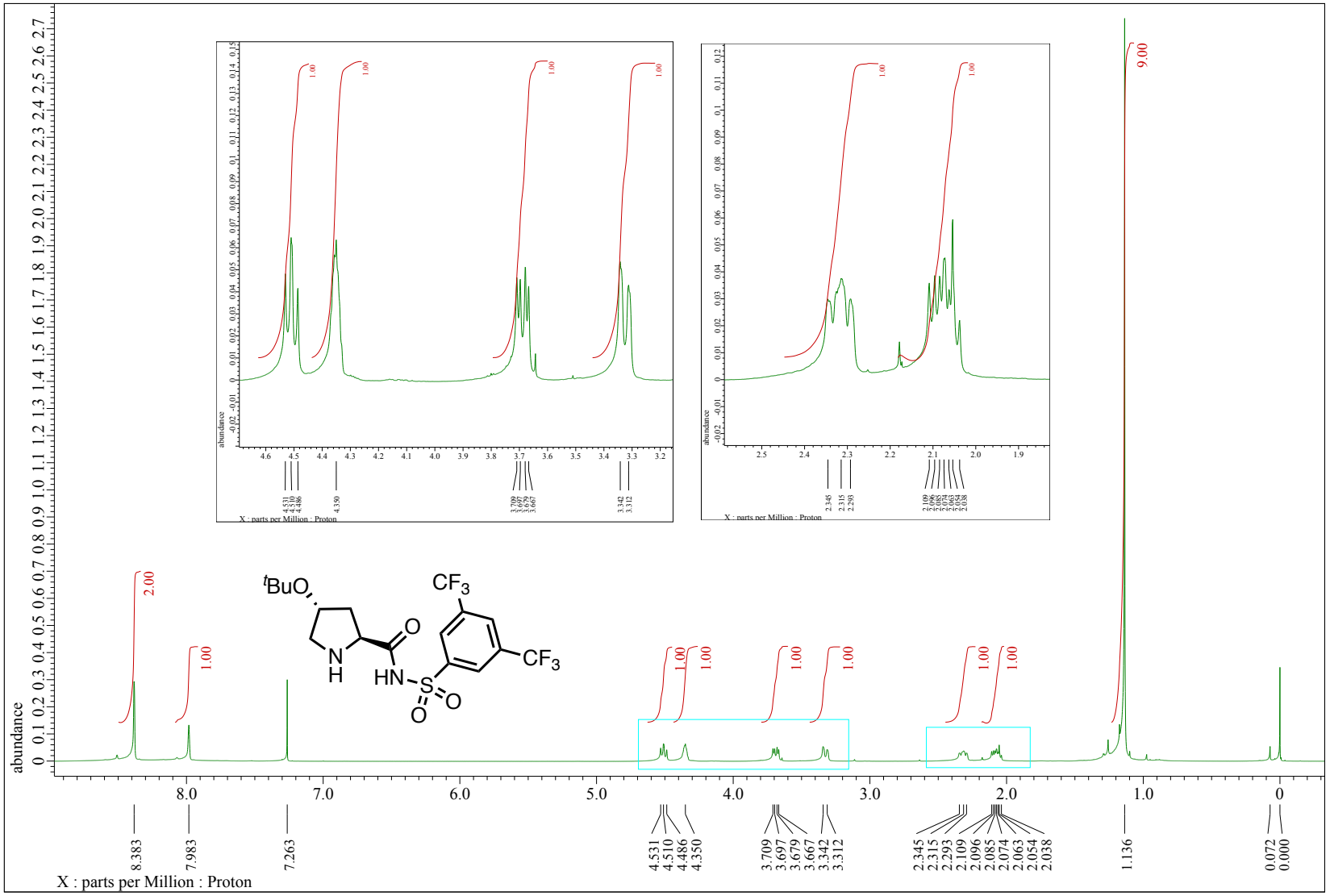
^{13}C NMR, 101 MHz, $CDCl_3$



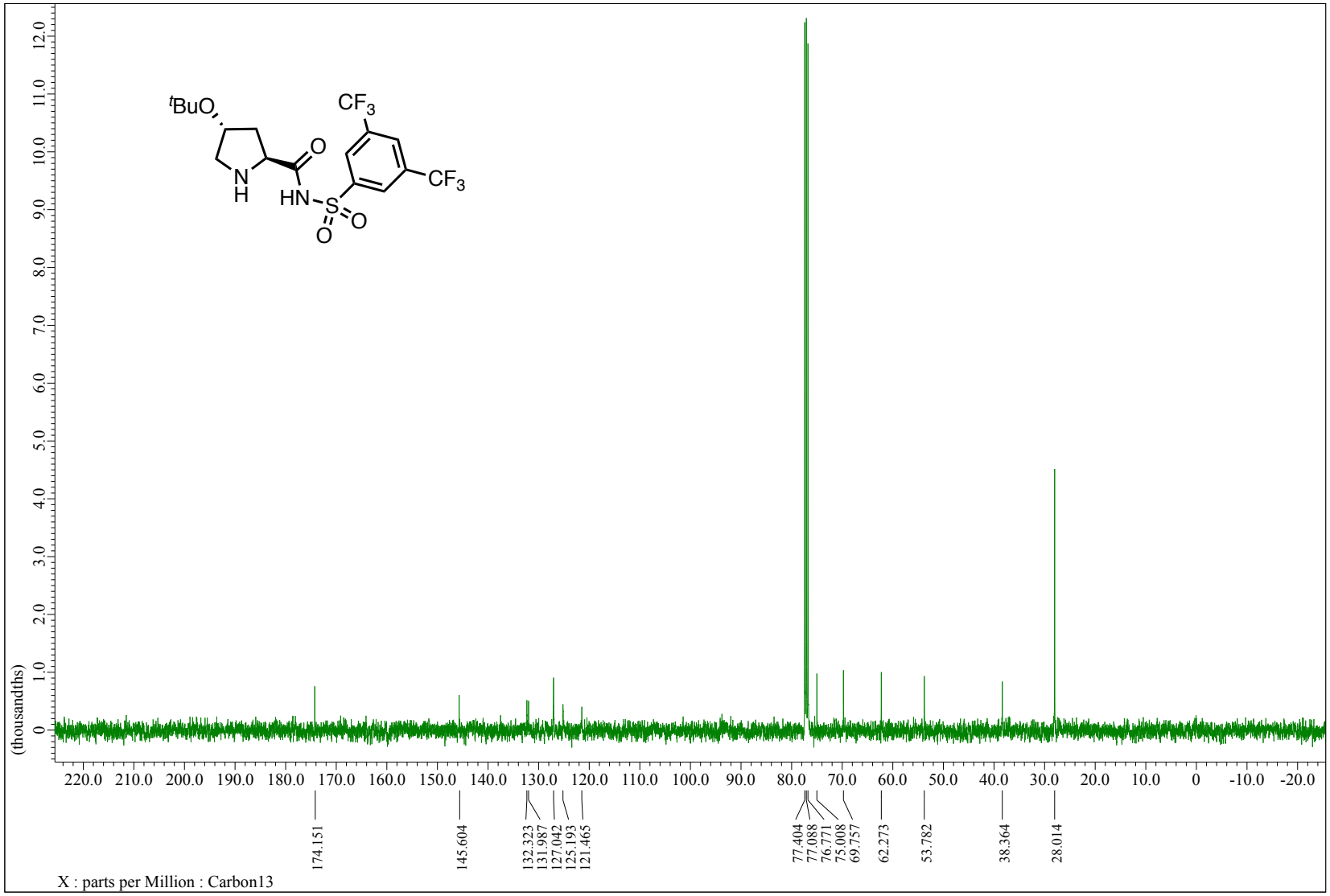
^{19}F NMR, 376 MHz, $CDCl_3$



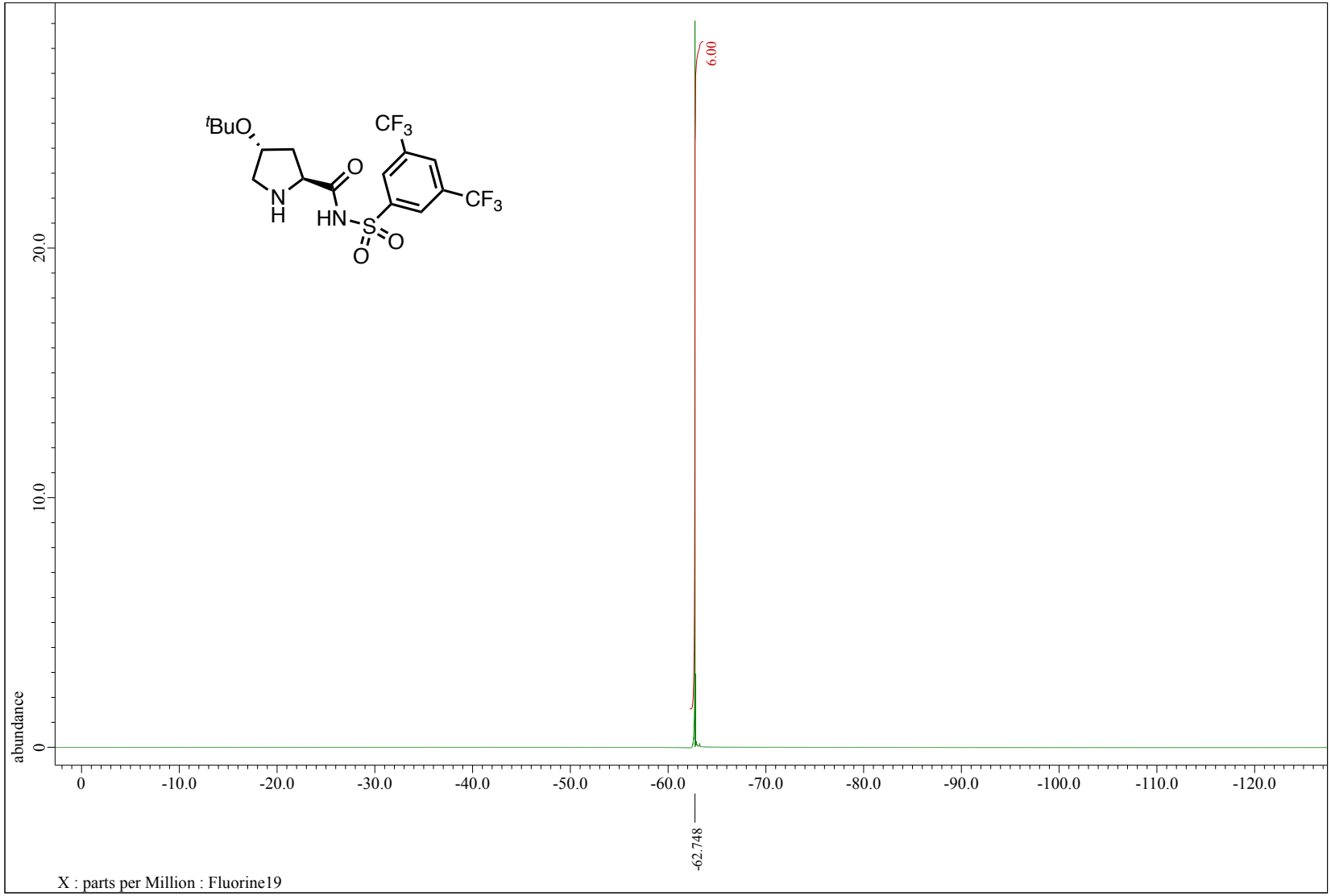
^{1}H NMR, 400 MHz, $CDCl_3$



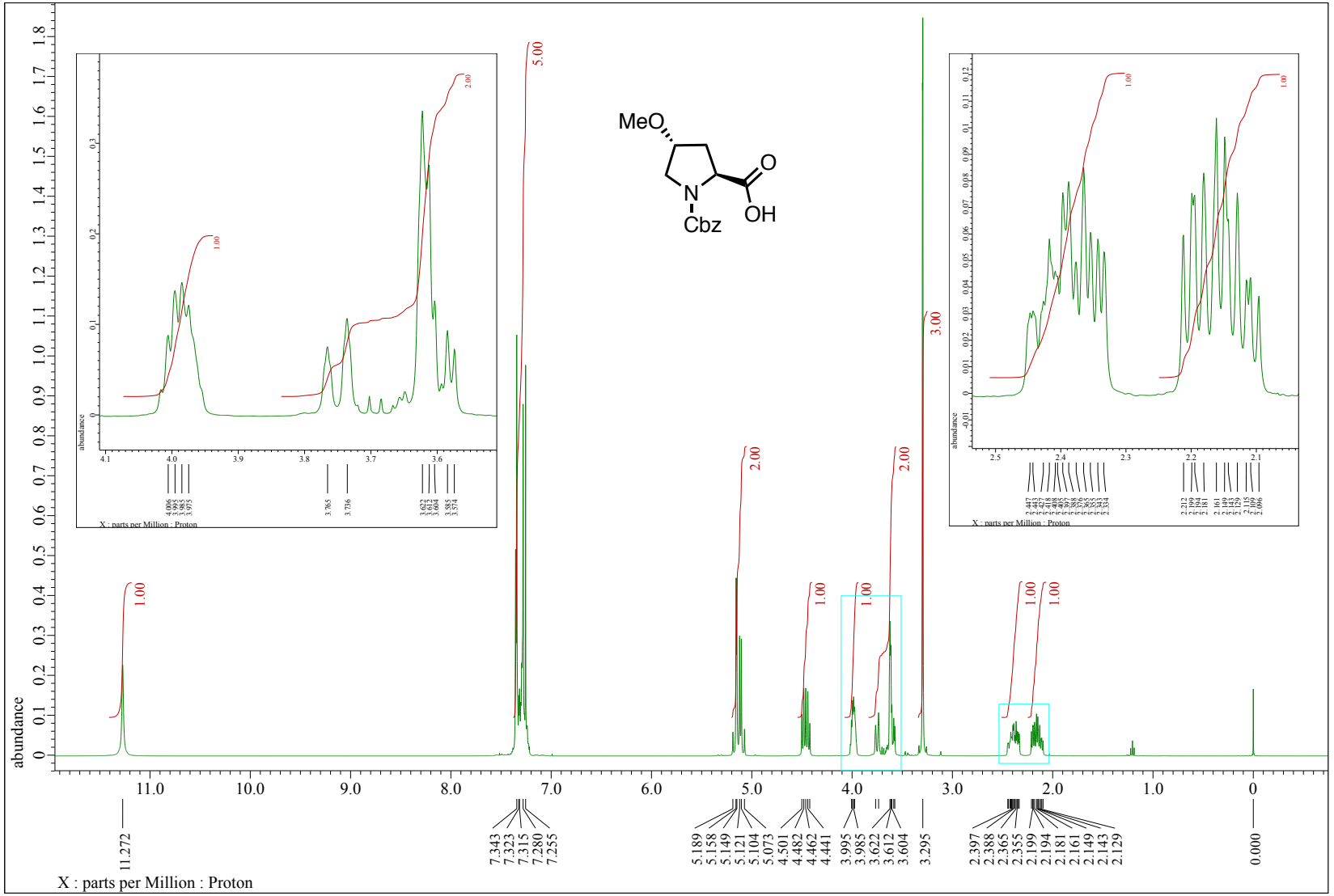
^{13}C NMR, 101 MHz, $CDCl_3$



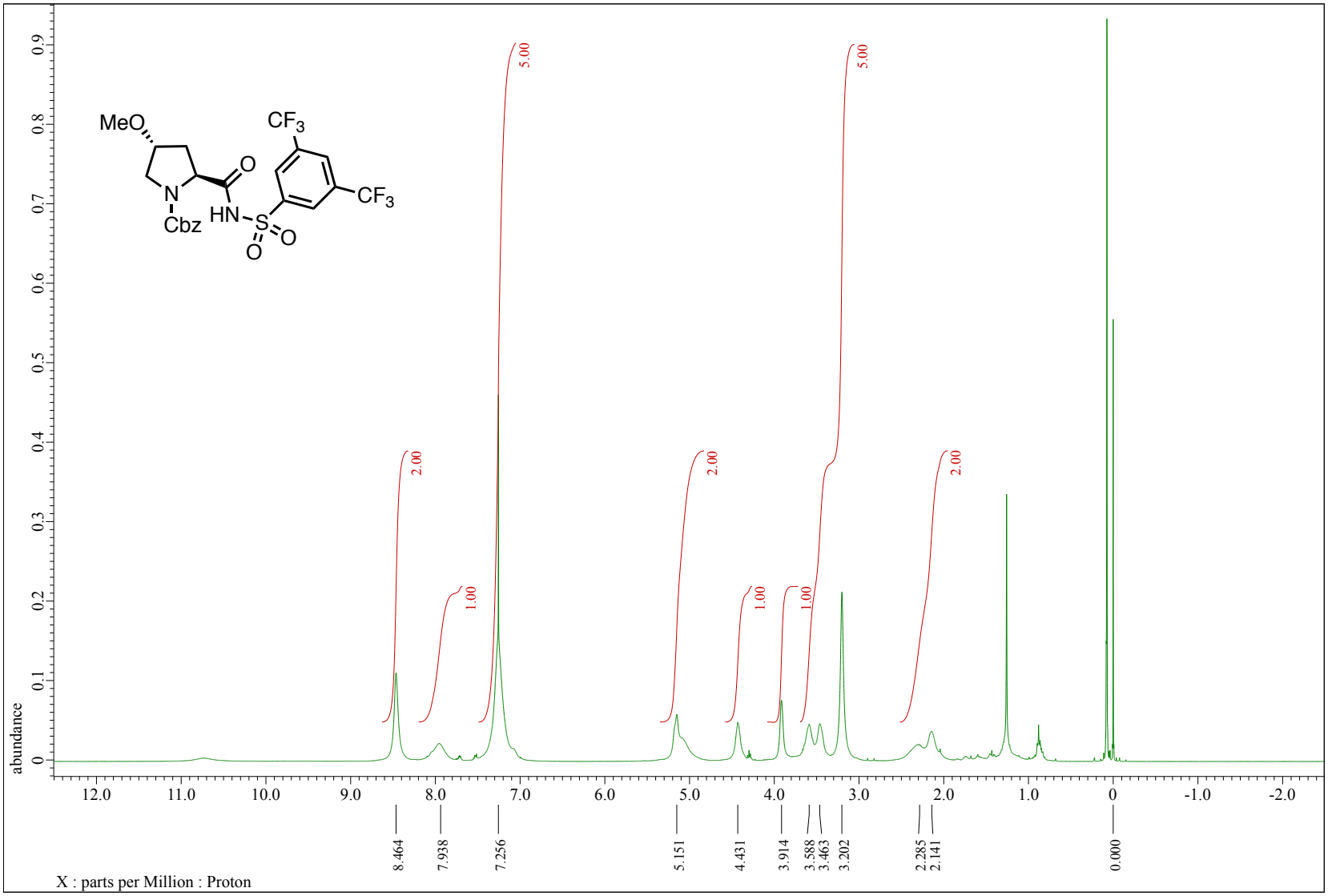
^{19}F NMR, 376 MHz, $CDCl_3$



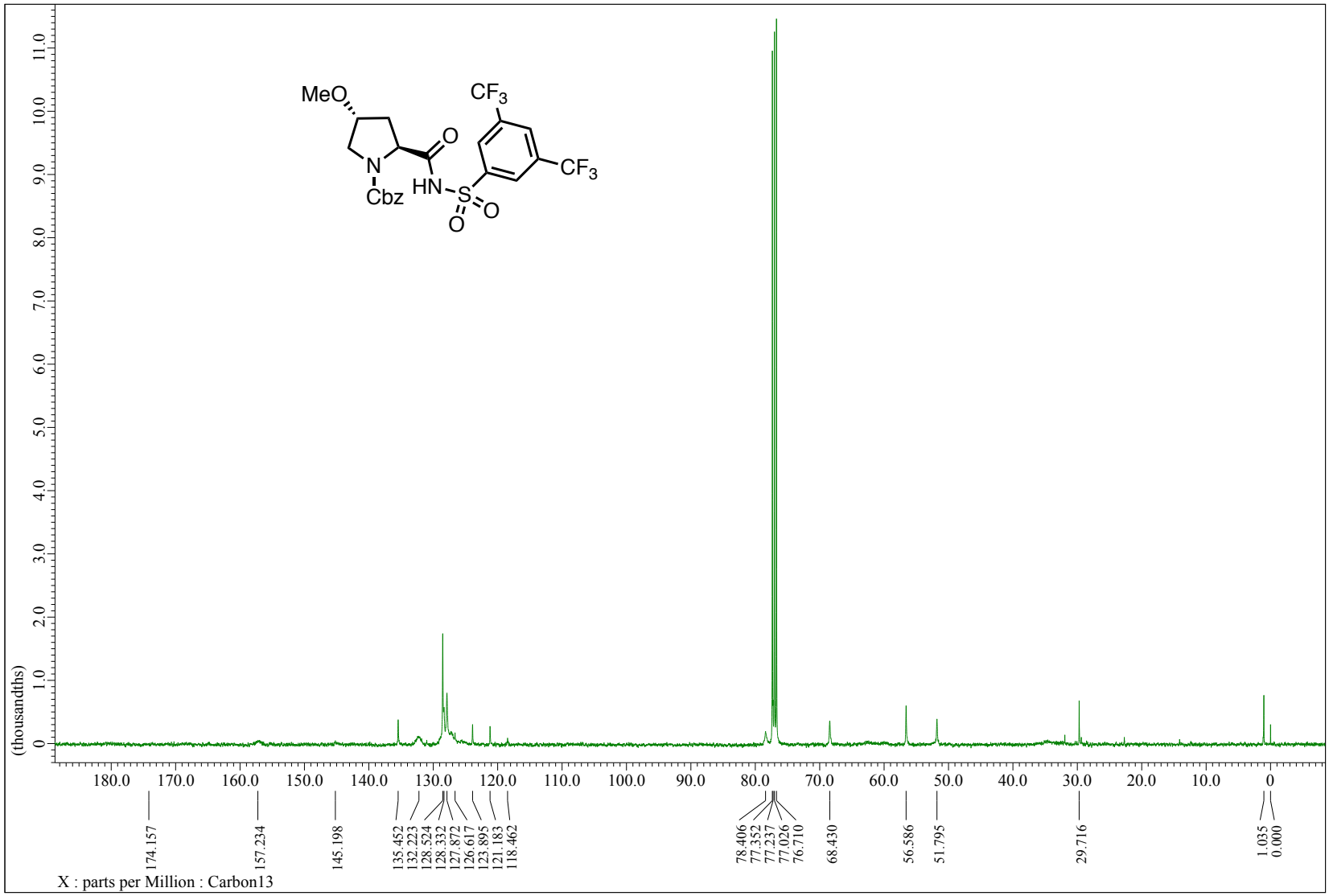
^{1}H NMR, 400 MHz, $CDCl_3$



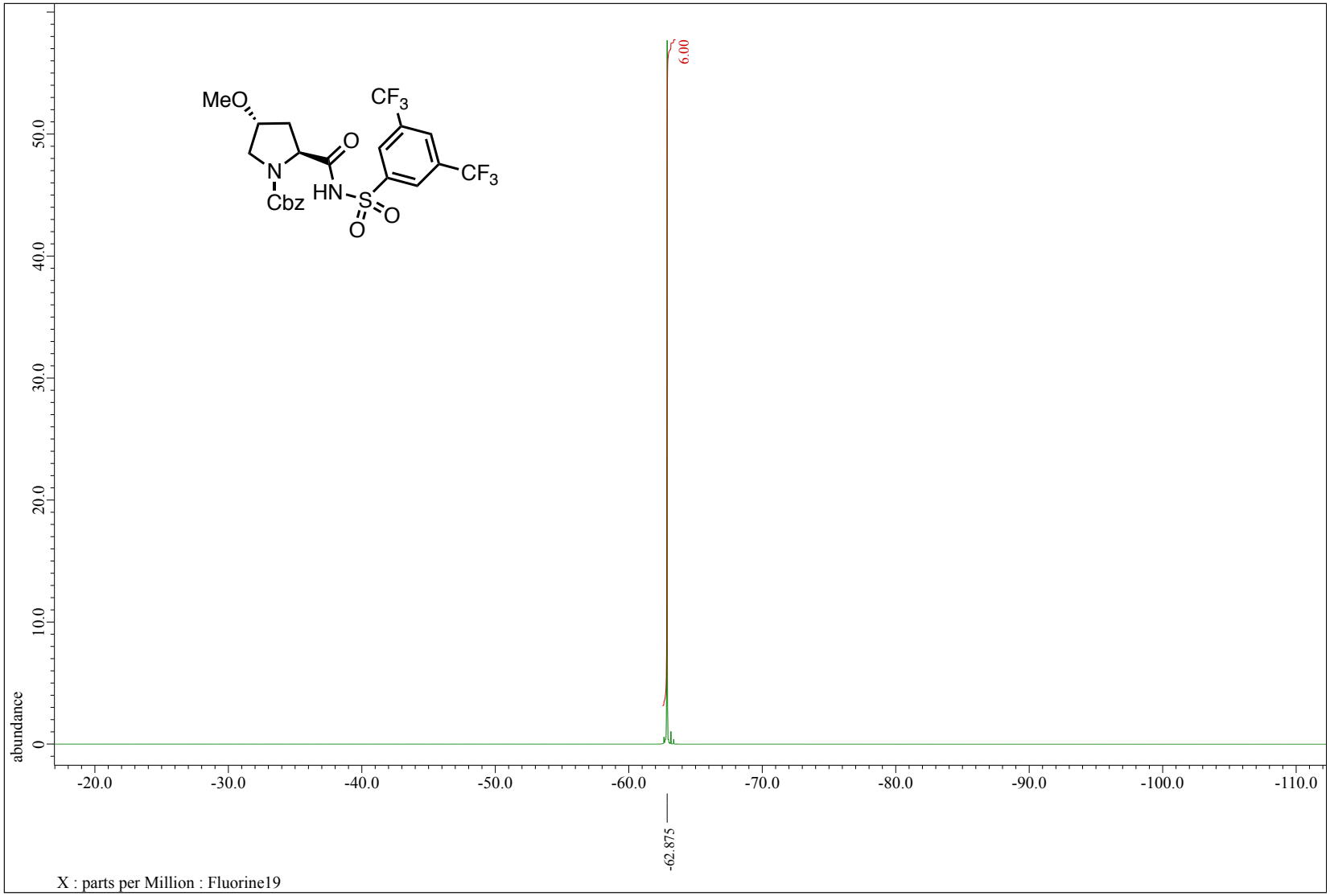
^{1}H NMR, 400 MHz, $CDCl_3$



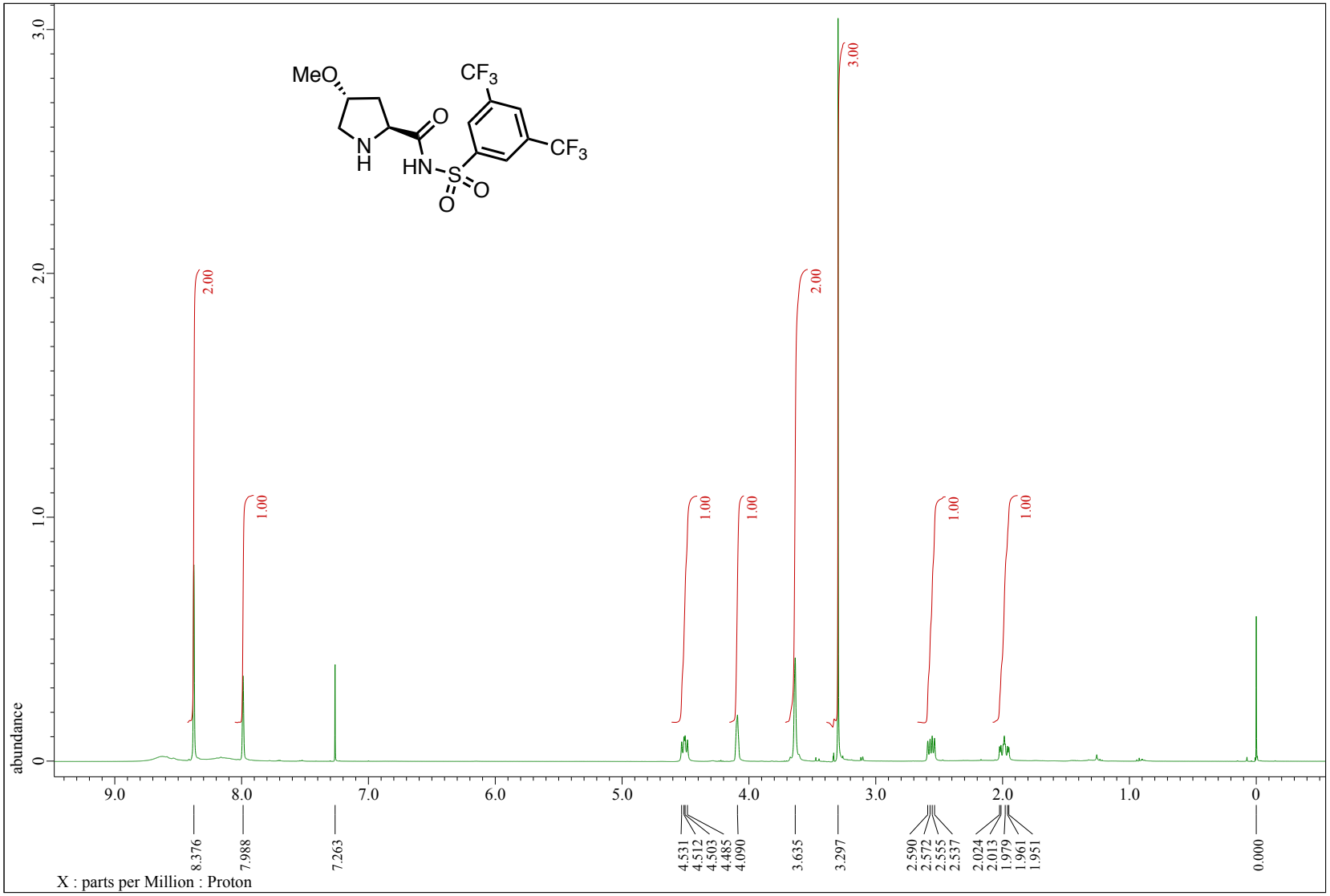
^{13}C NMR, 101 MHz, $CDCl_3$



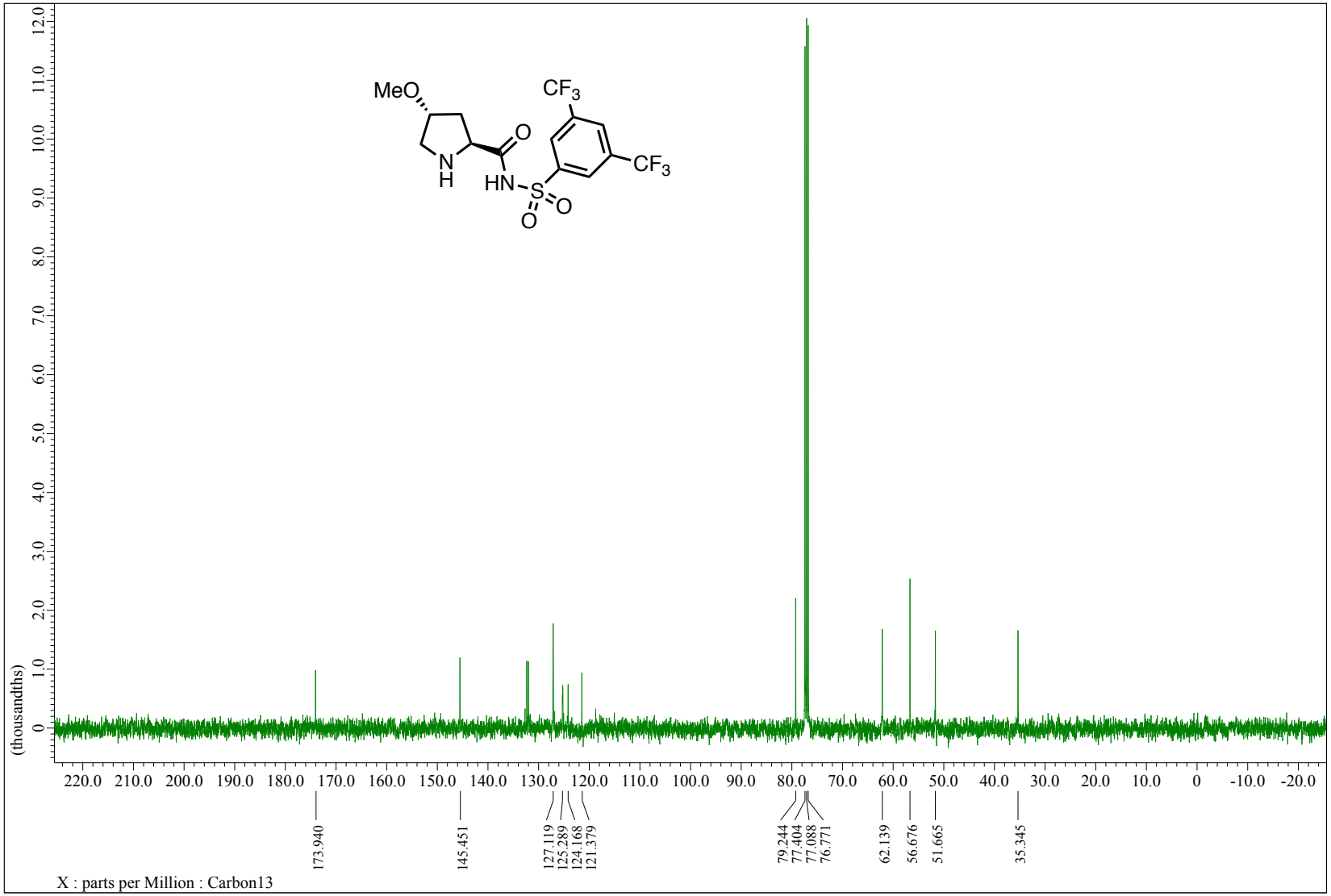
^{19}F NMR, 376 MHz, $CDCl_3$



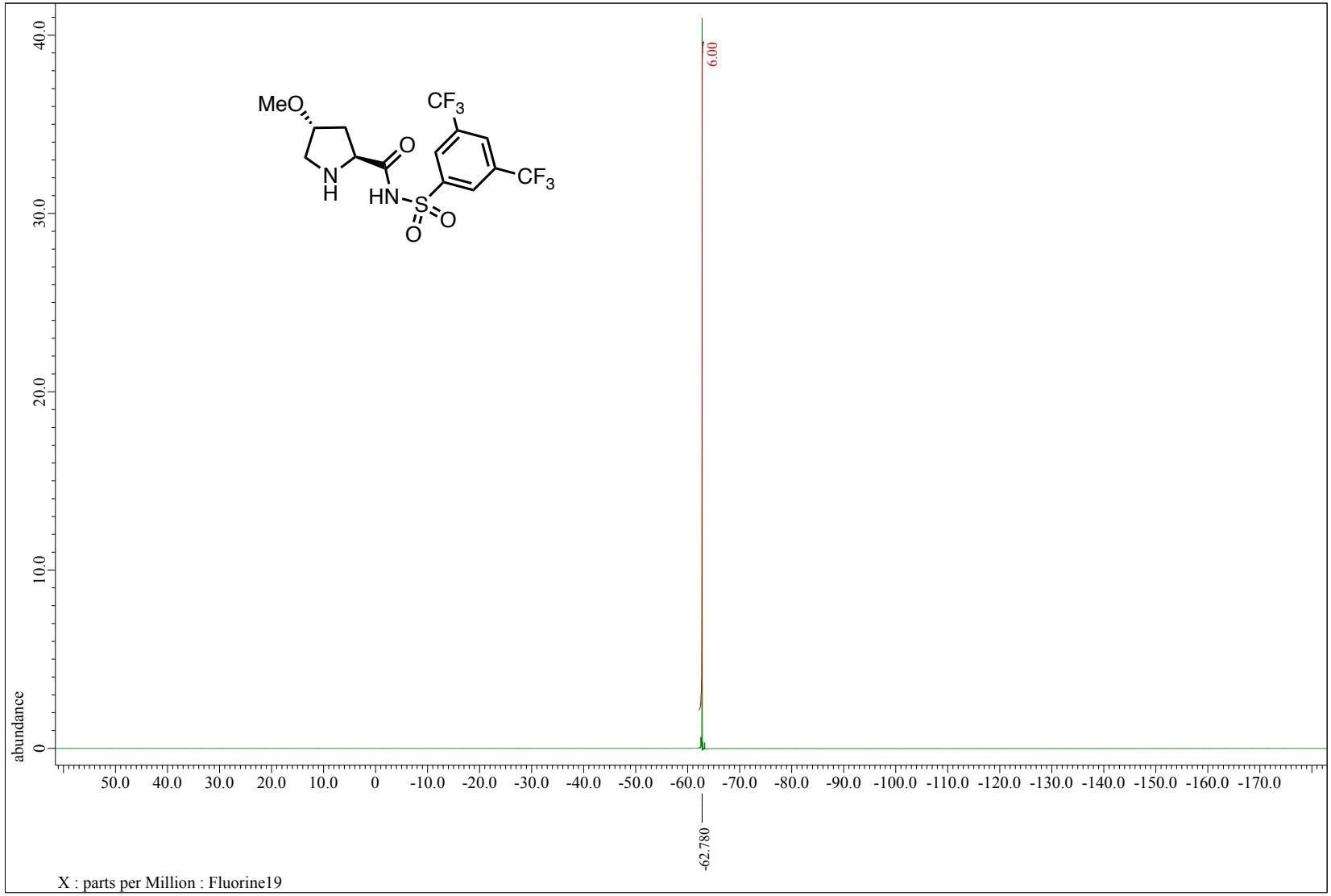
^{1}H NMR, 400 MHz, $CDCl_3$



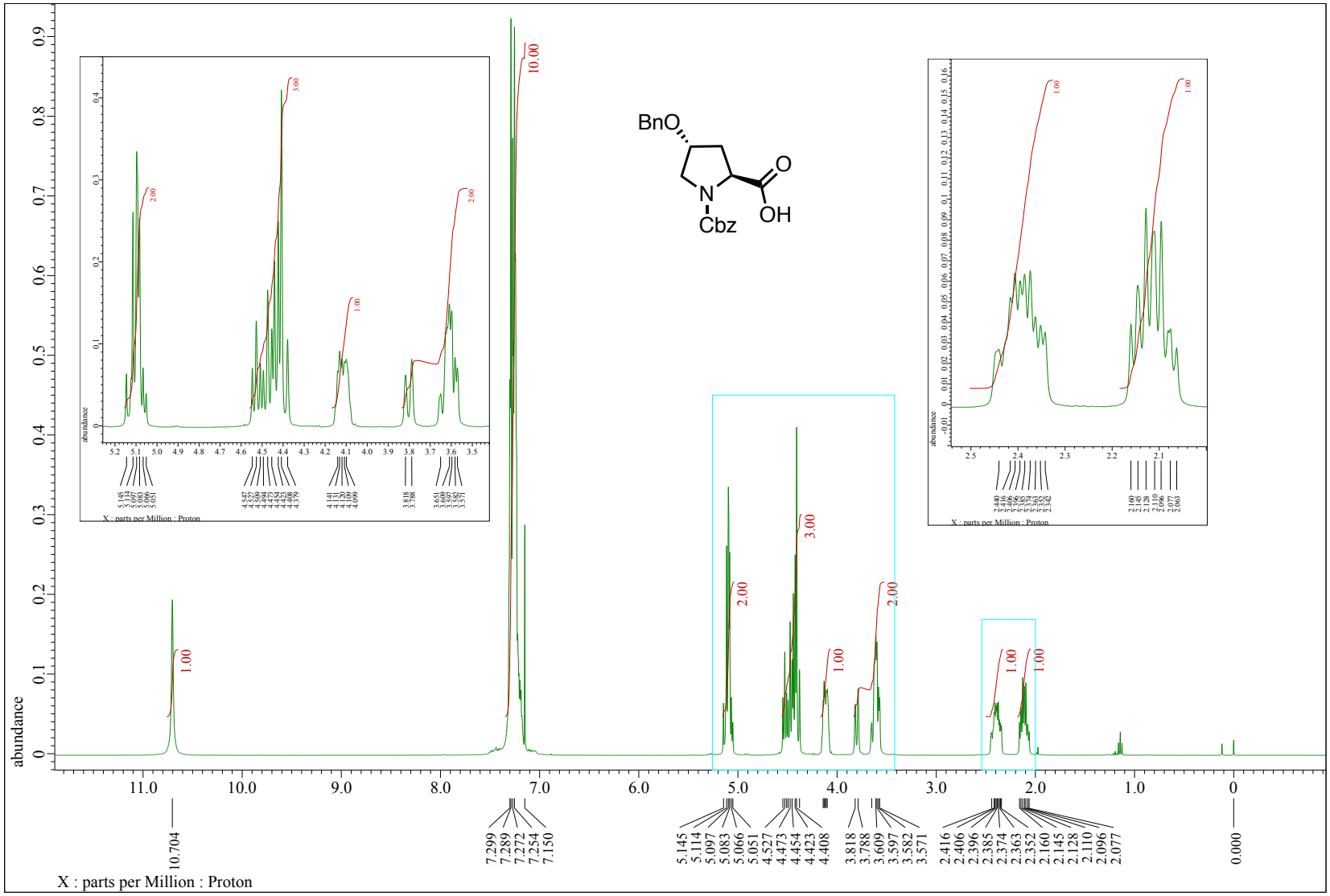
^{13}C NMR, 101 MHz, $CDCl_3$



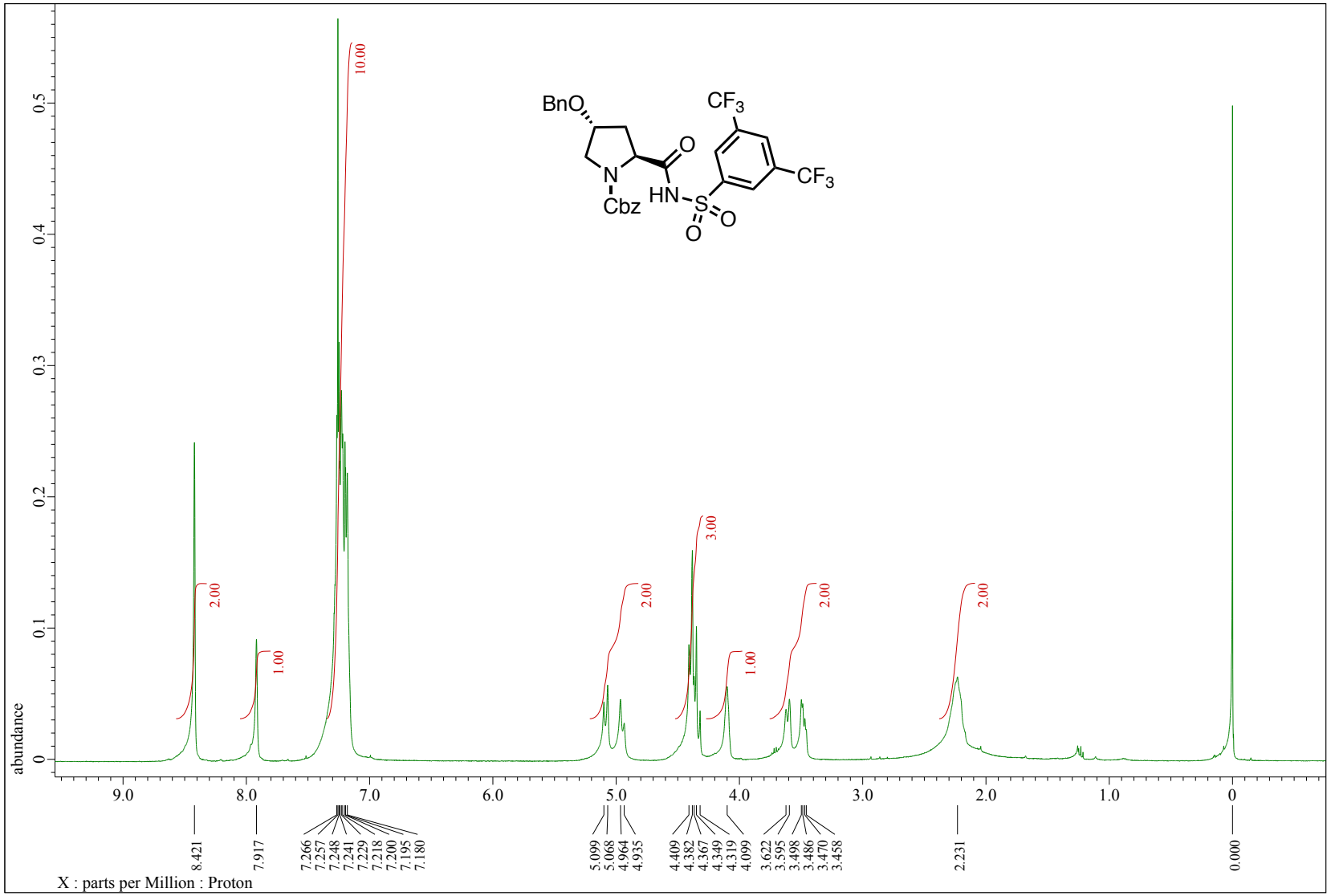
^{19}F NMR, 376 MHz, $CDCl_3$



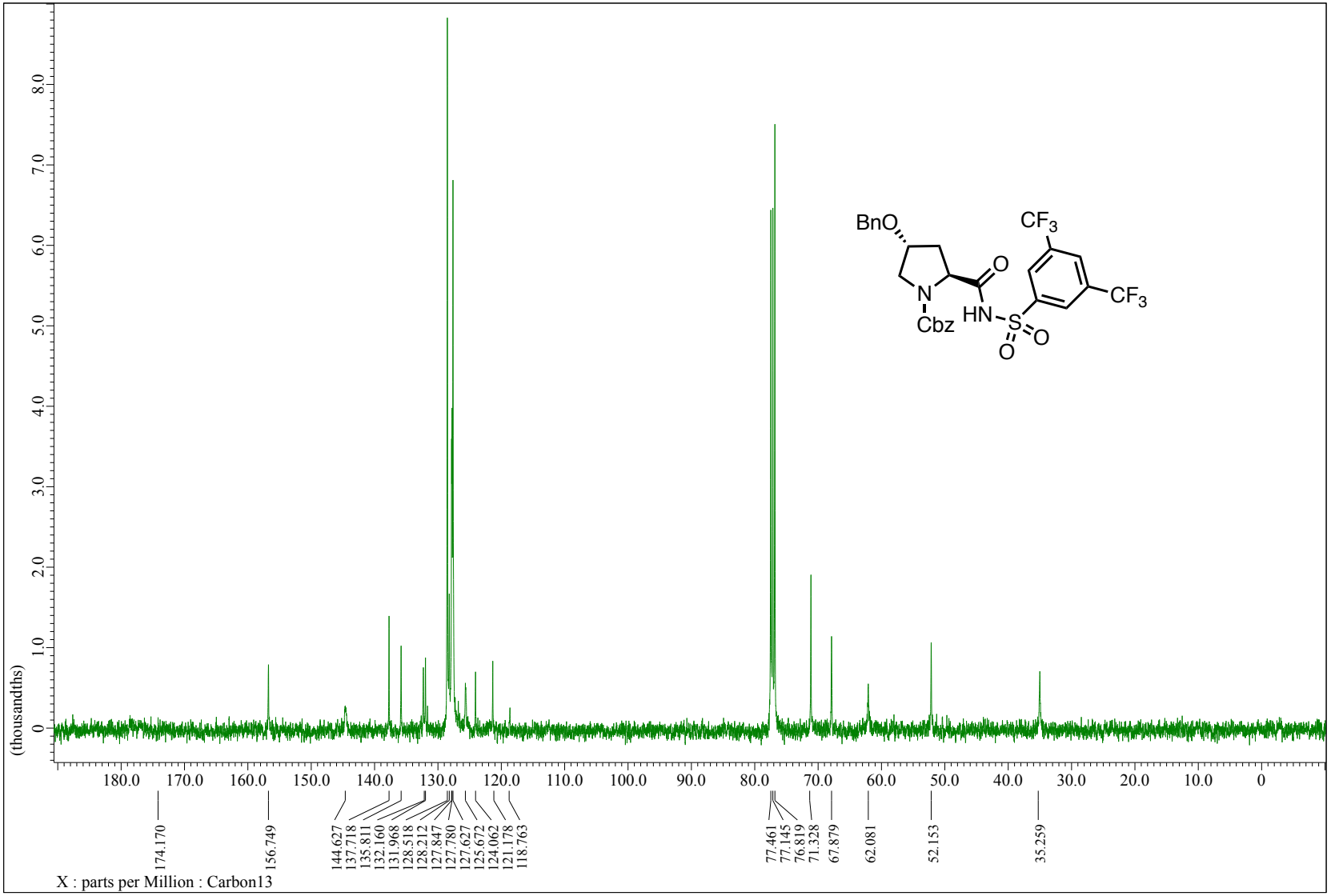
^{1}H NMR, 400 MHz, $CDCl_3$



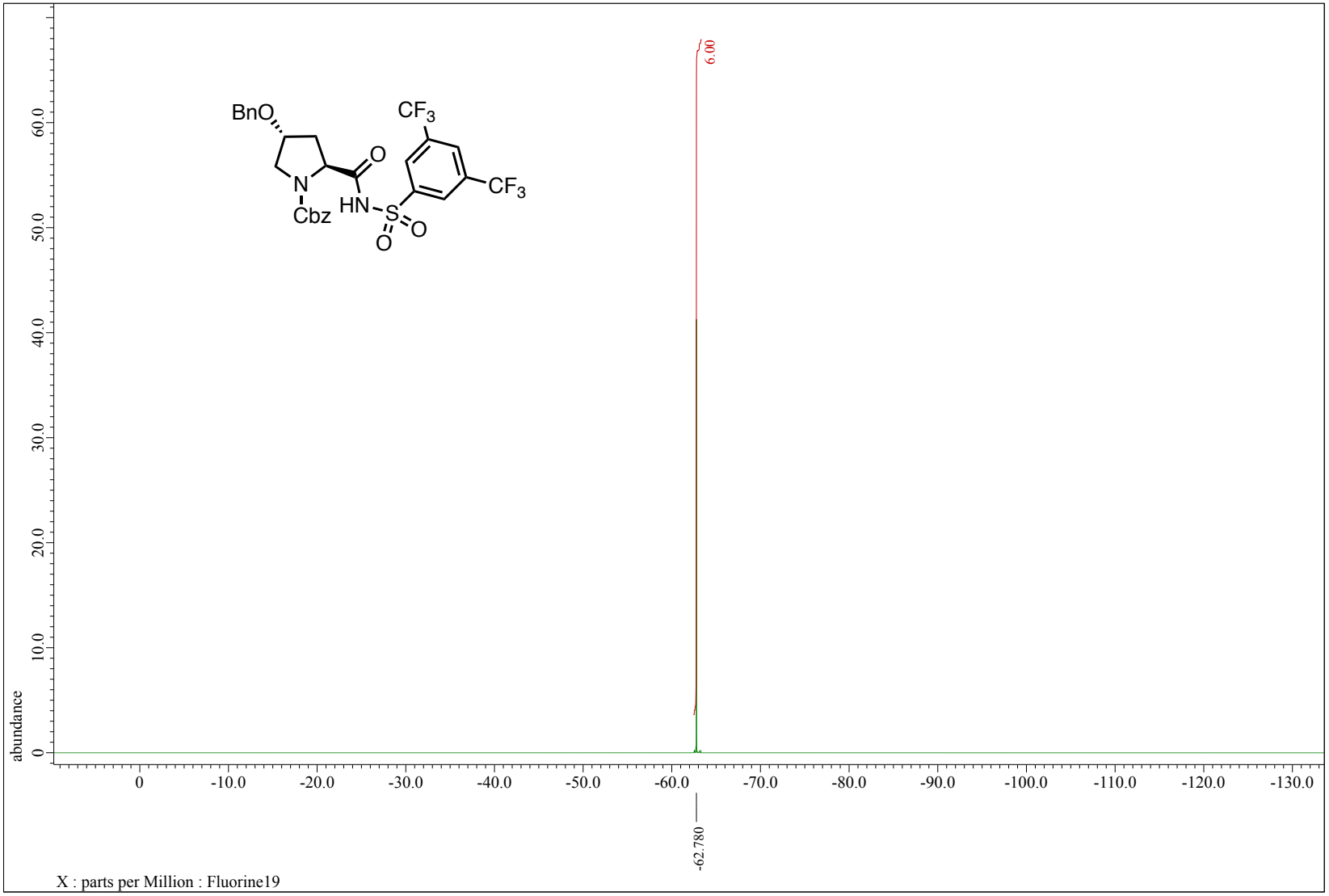
^{1}H NMR, 400 MHz, $CDCl_3$



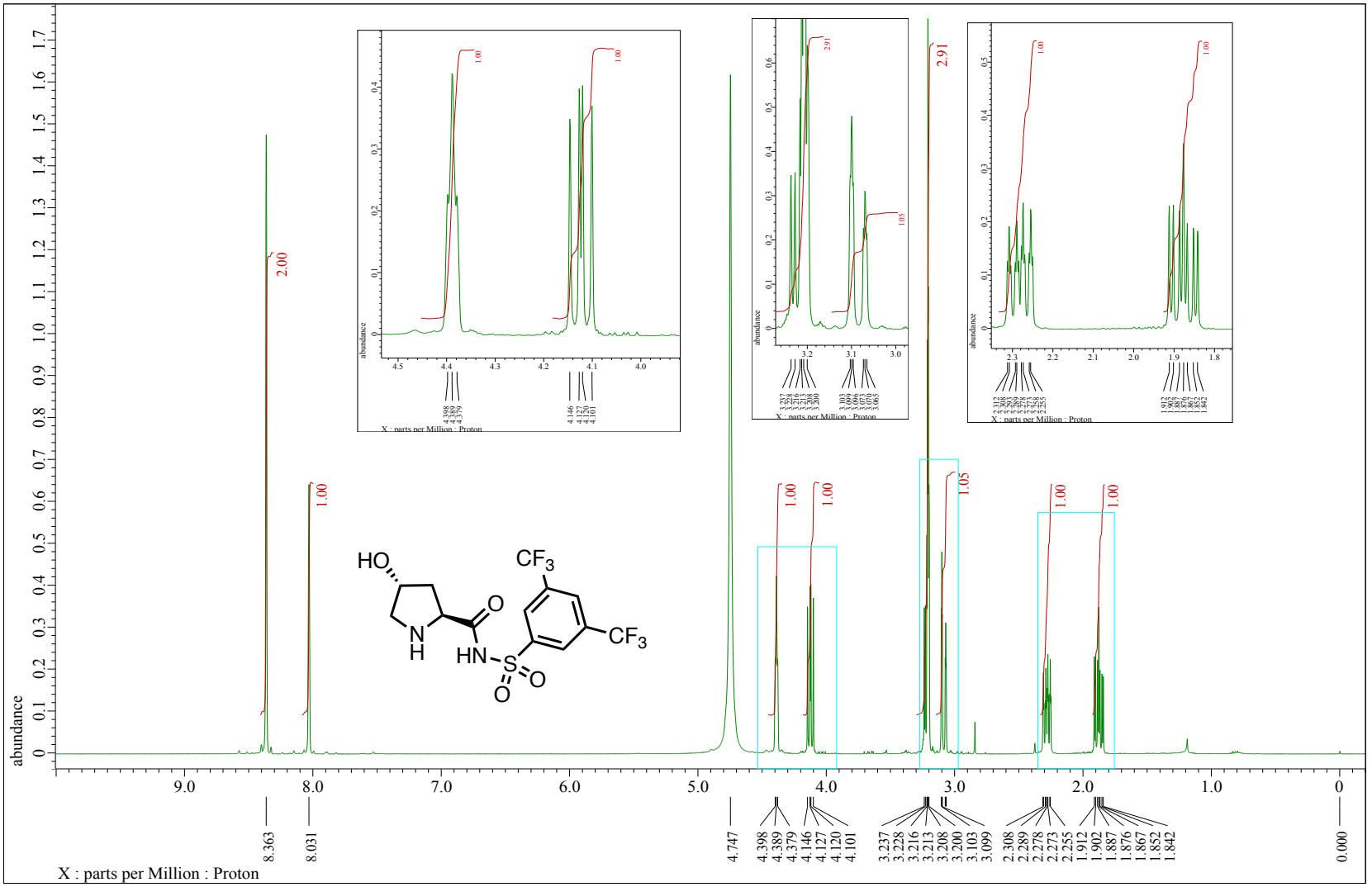
^{13}C NMR, 101 MHz, $CDCl_3$



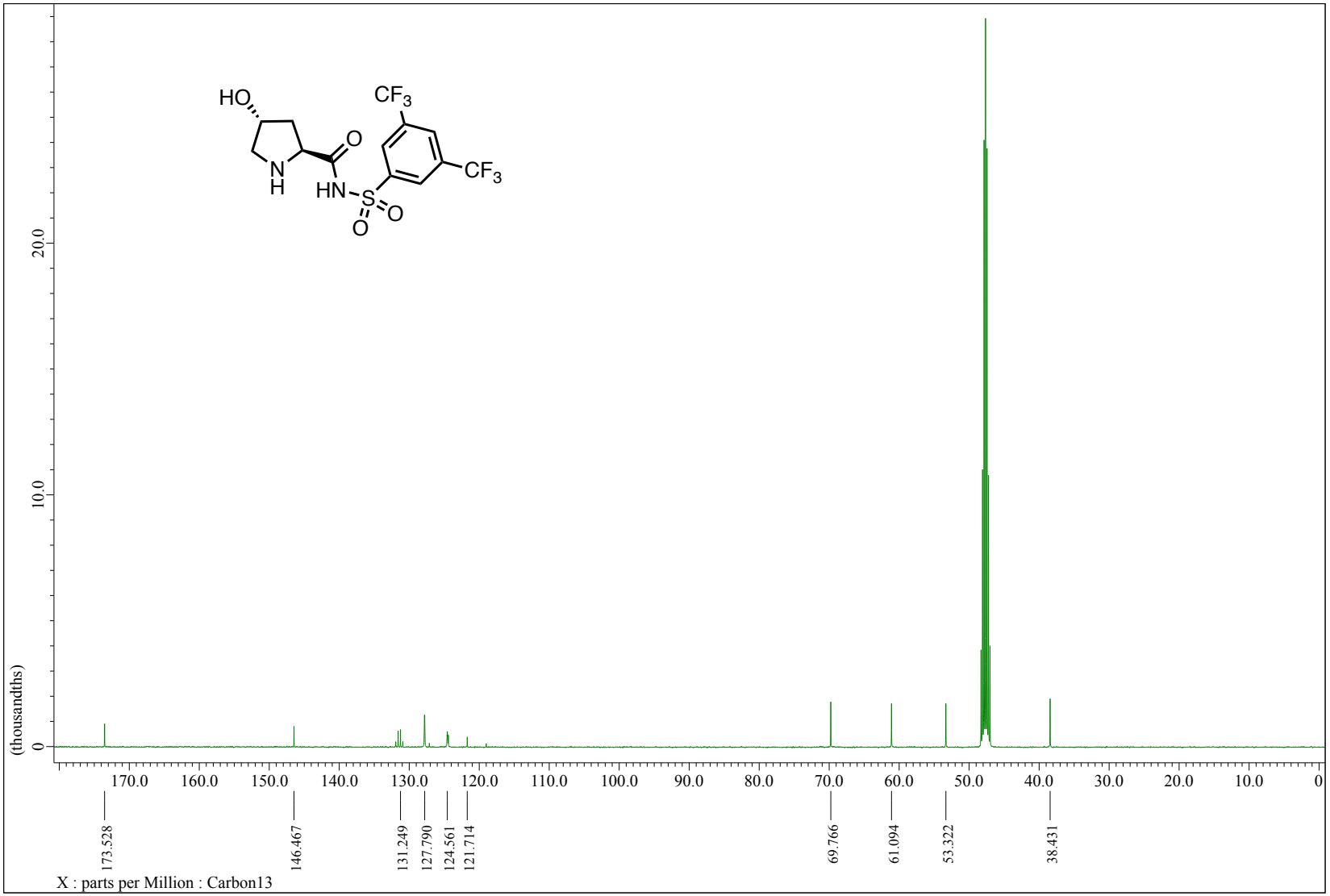
^{19}F NMR, 376 MHz, $CDCl_3$



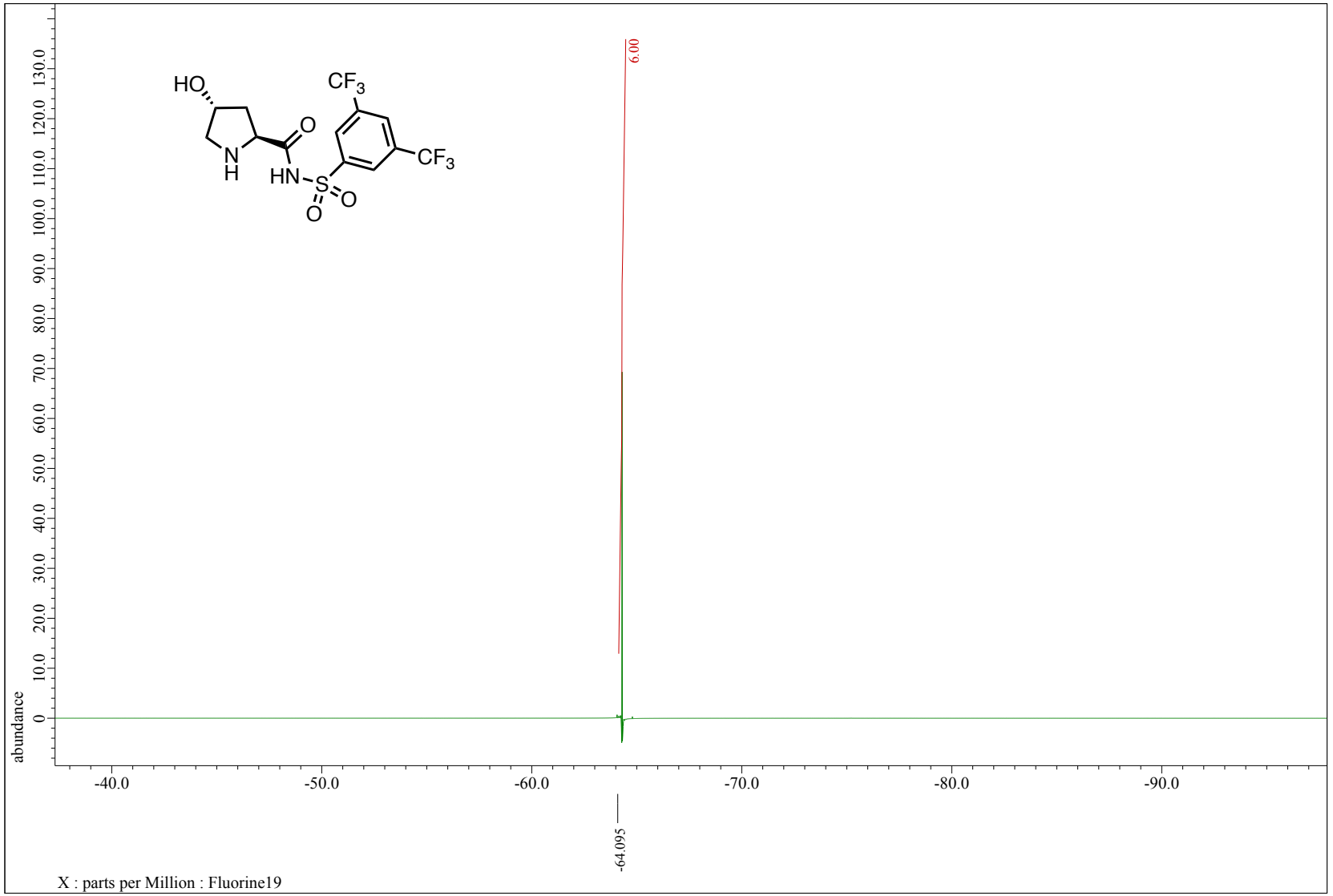
^{1}H NMR, 400 MHz, CD_3OD



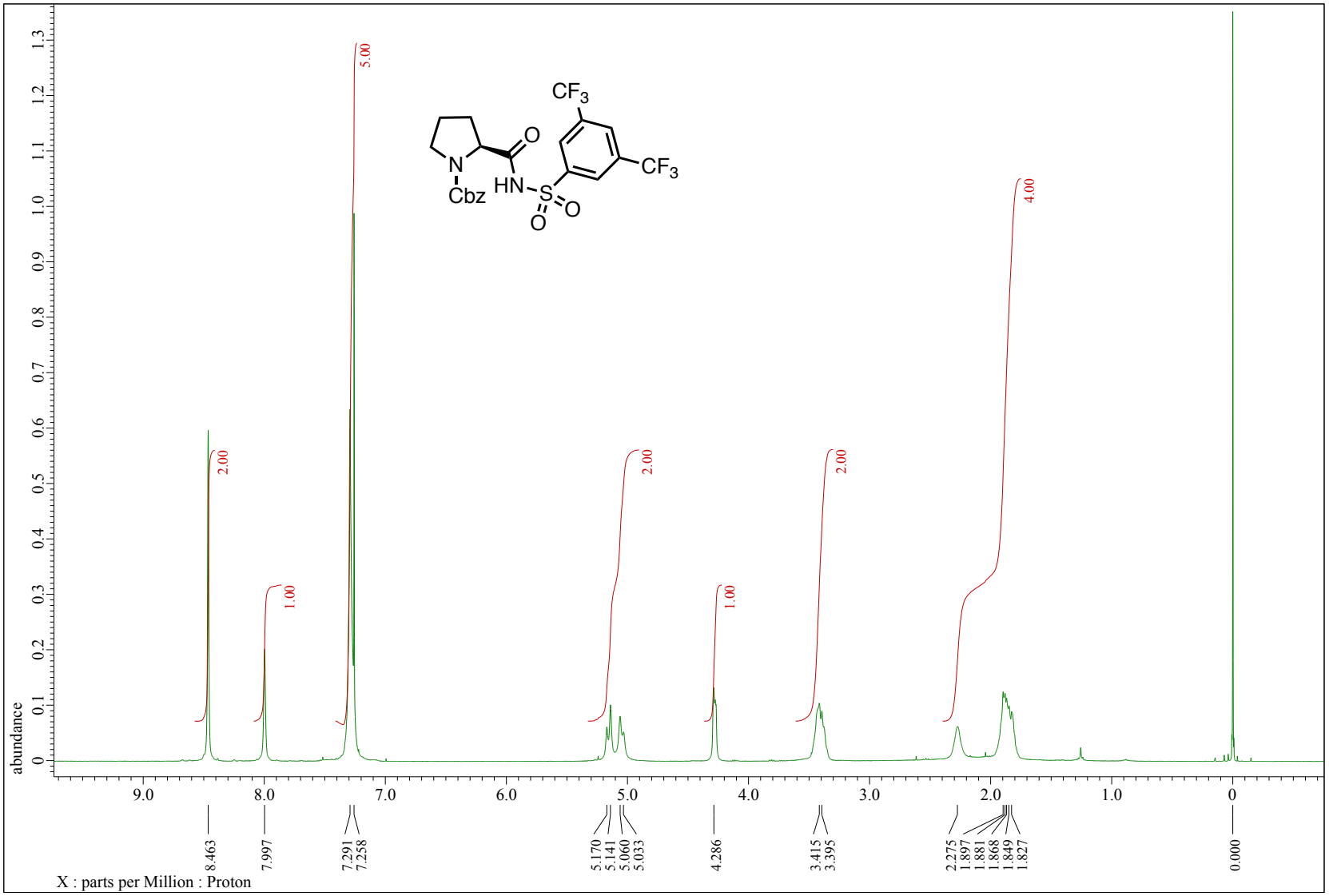
^{13}C NMR, 101 MHz, CD_3OD



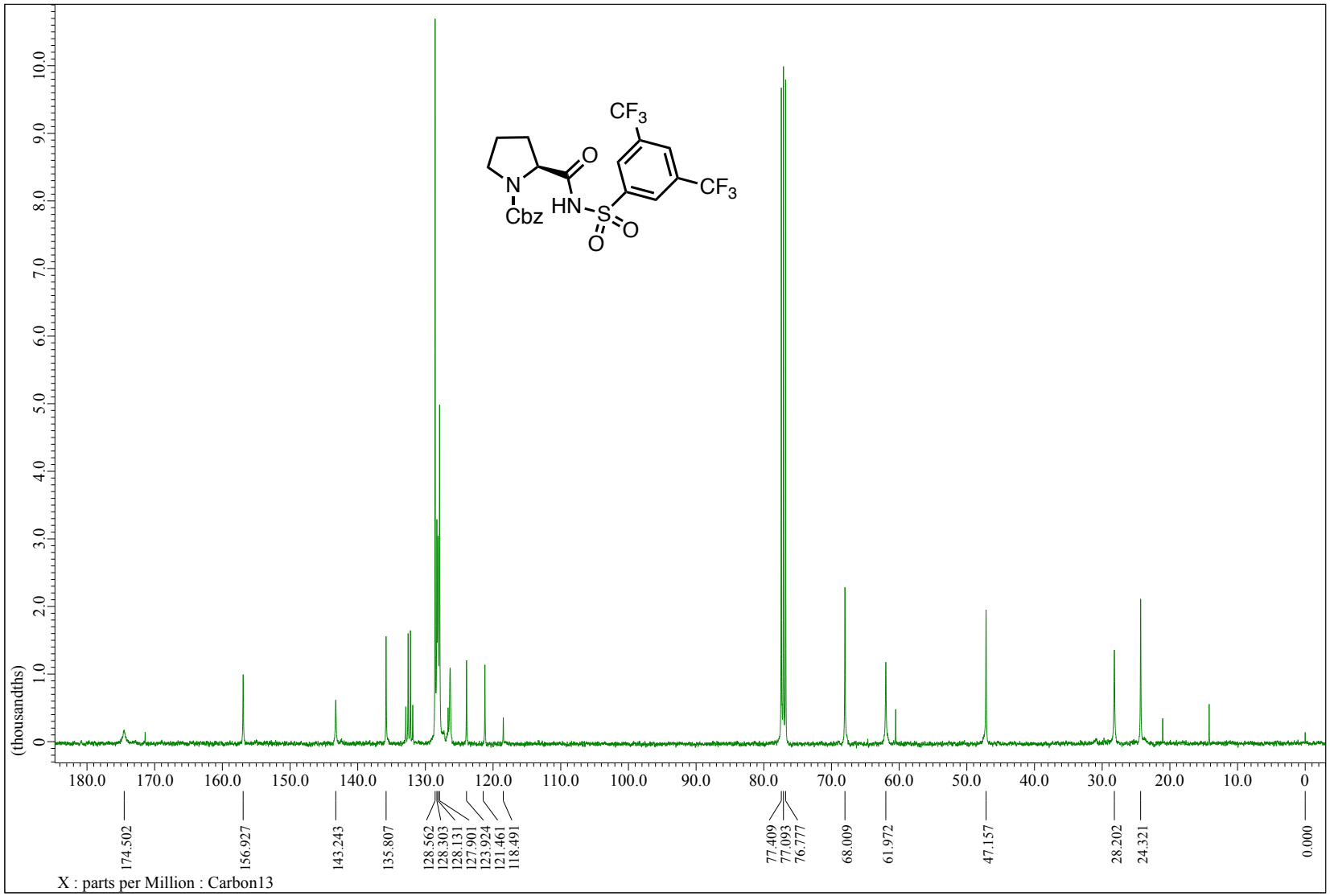
^{19}F NMR, 376 MHz, CD_3OD



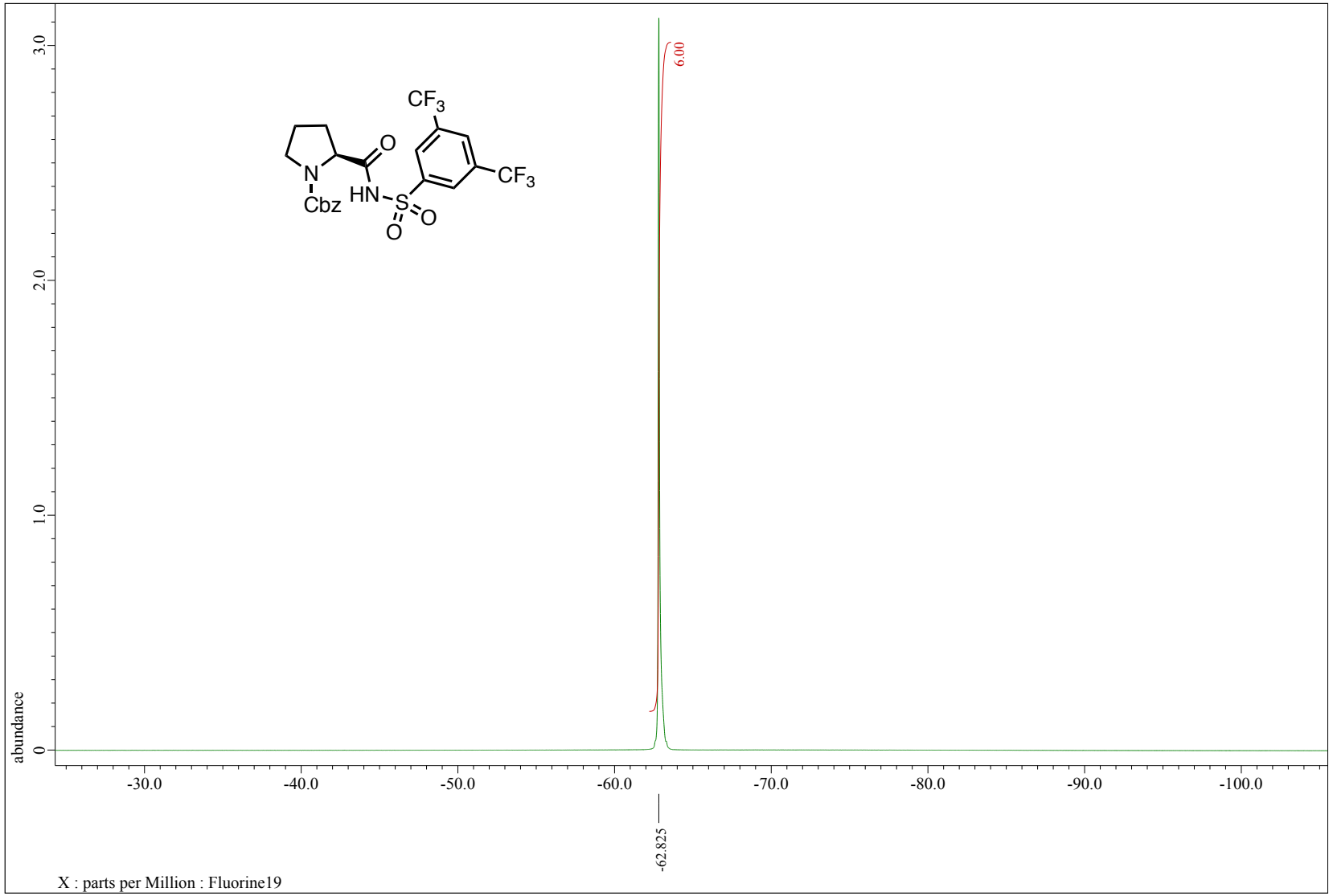
^{1}H NMR, 400 MHz, $CDCl_3$



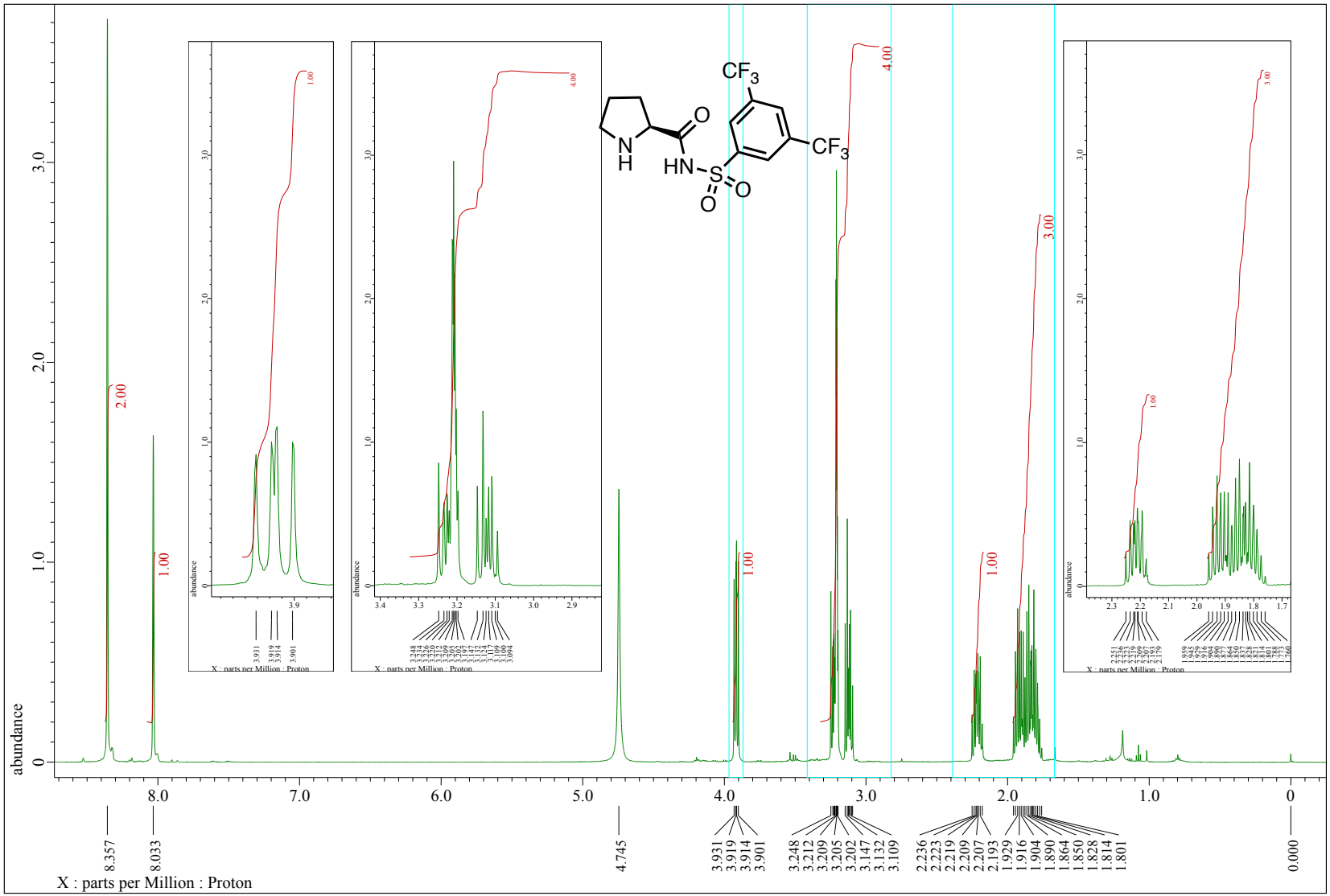
^{13}C NMR, 101 MHz, $CDCl_3$



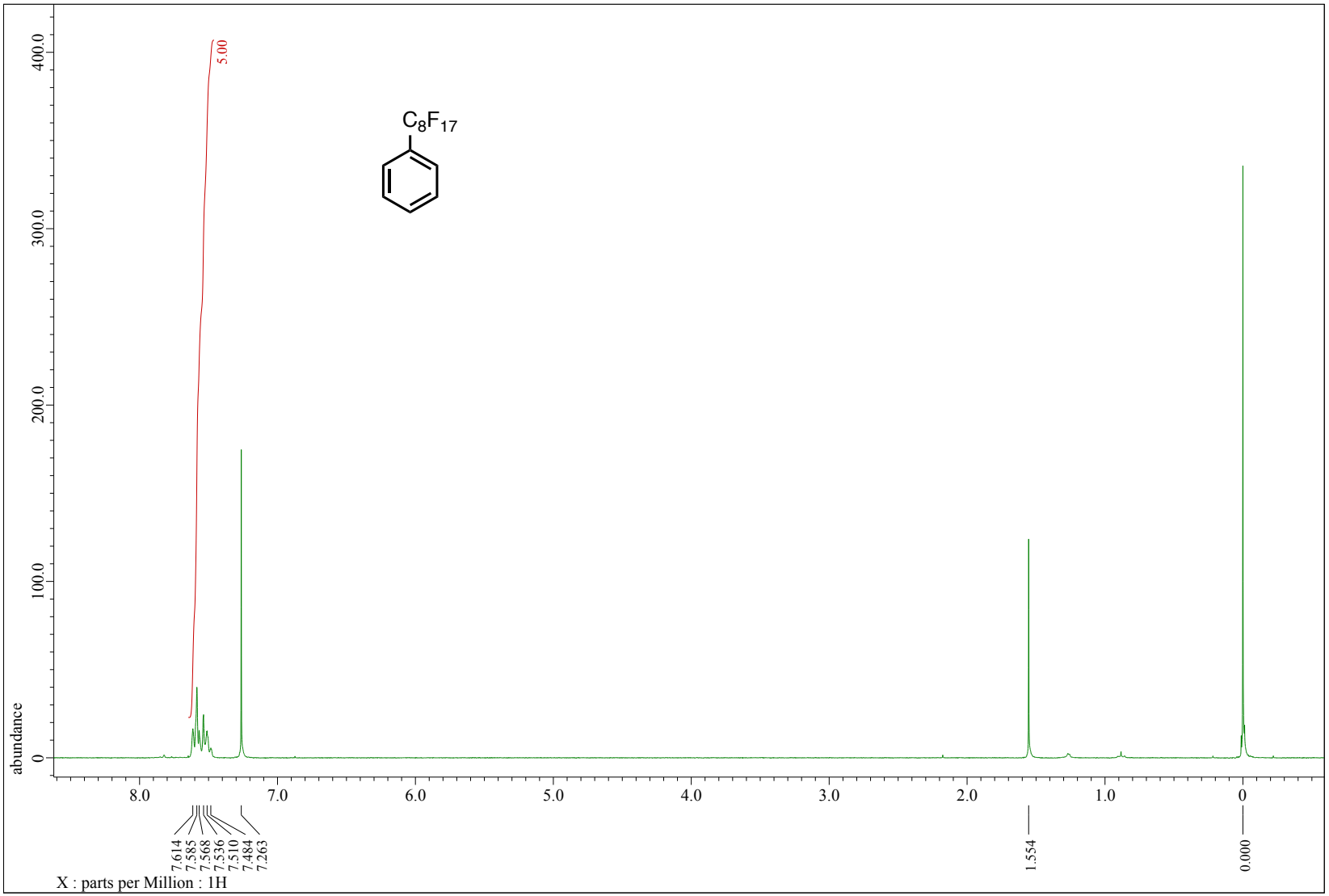
^{19}F NMR, 376 MHz, $CDCl_3$



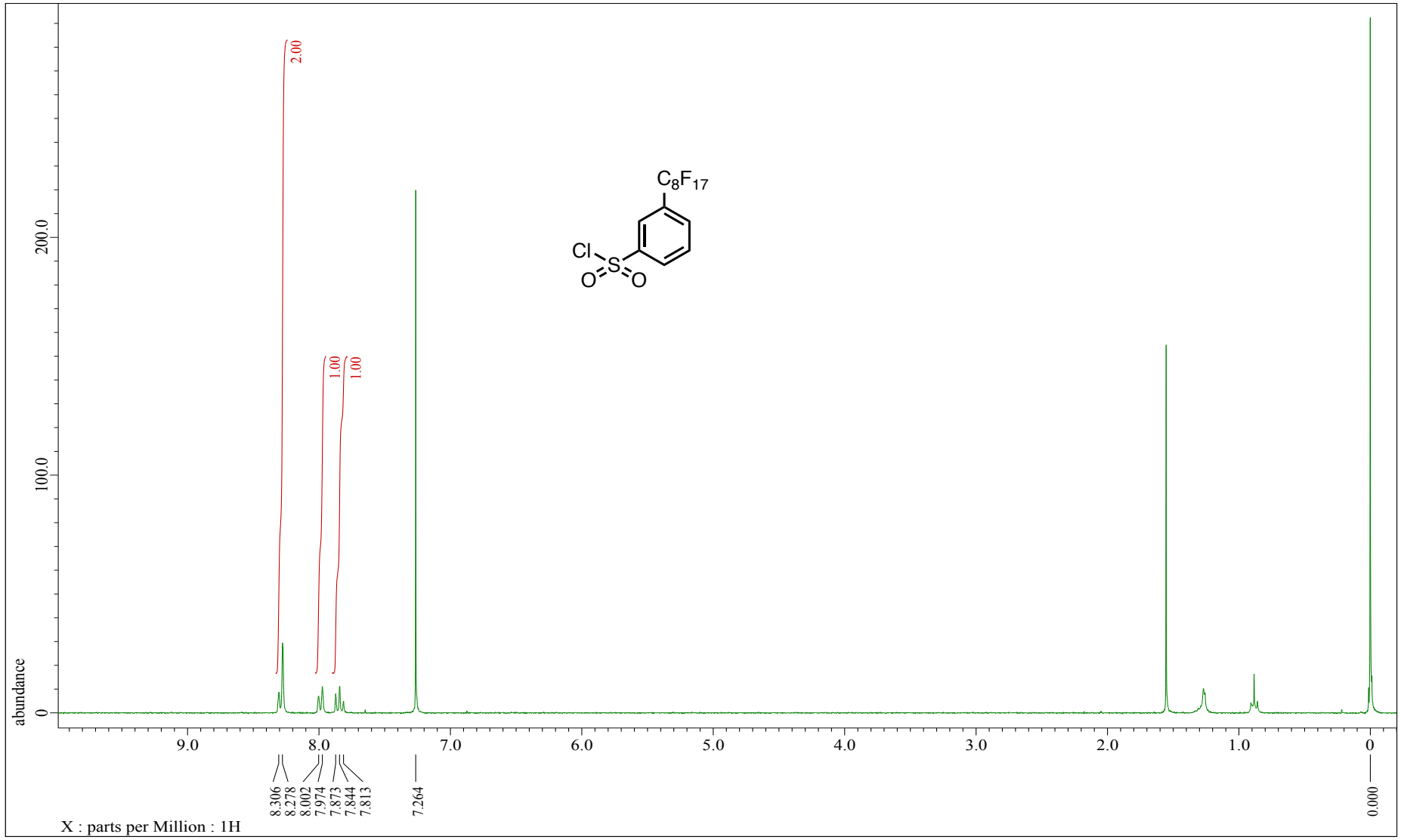
^{1}H NMR, 500 MHz, CD_3OD



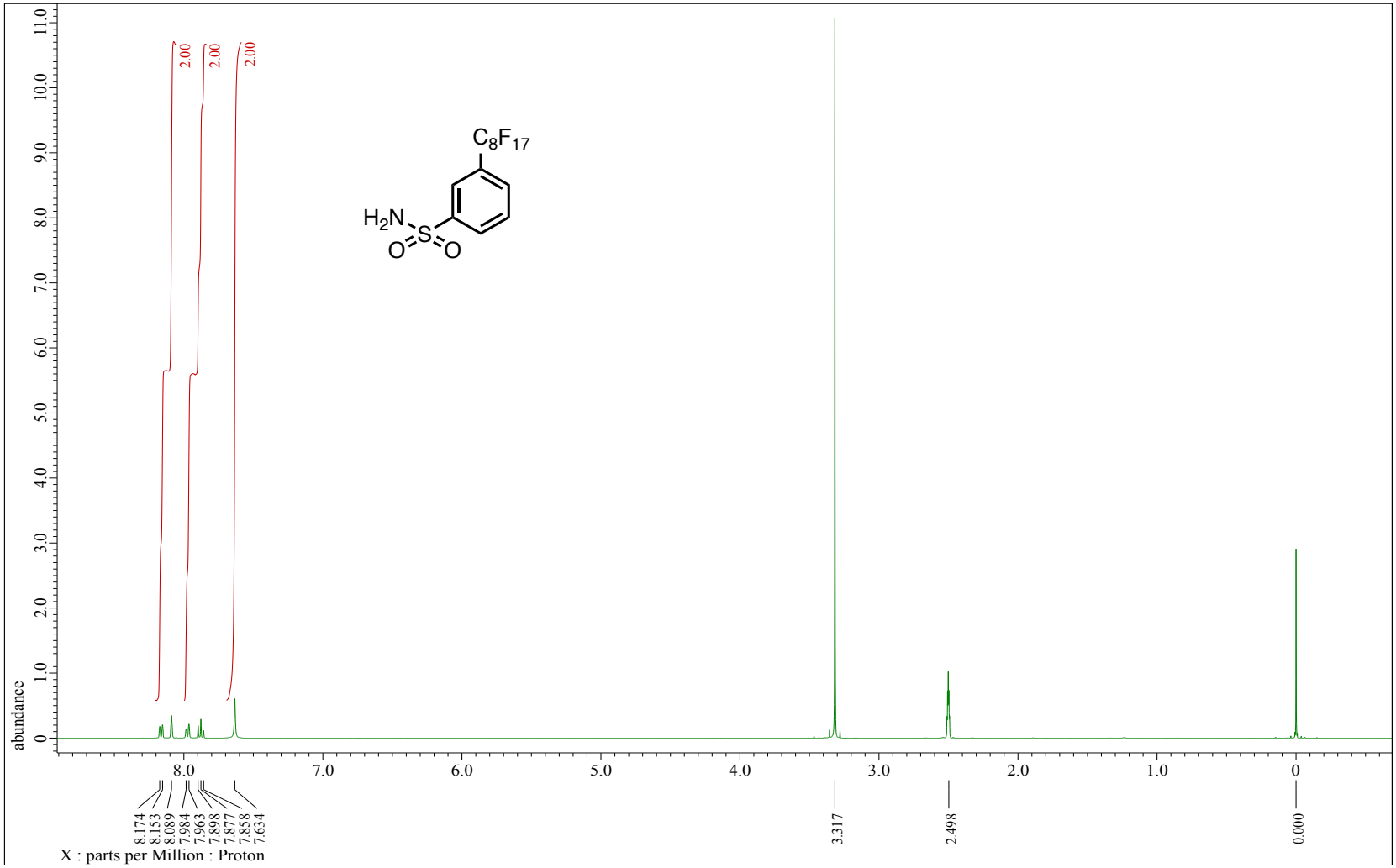
^{1}H NMR, 270 MHz, $CDCl_3$



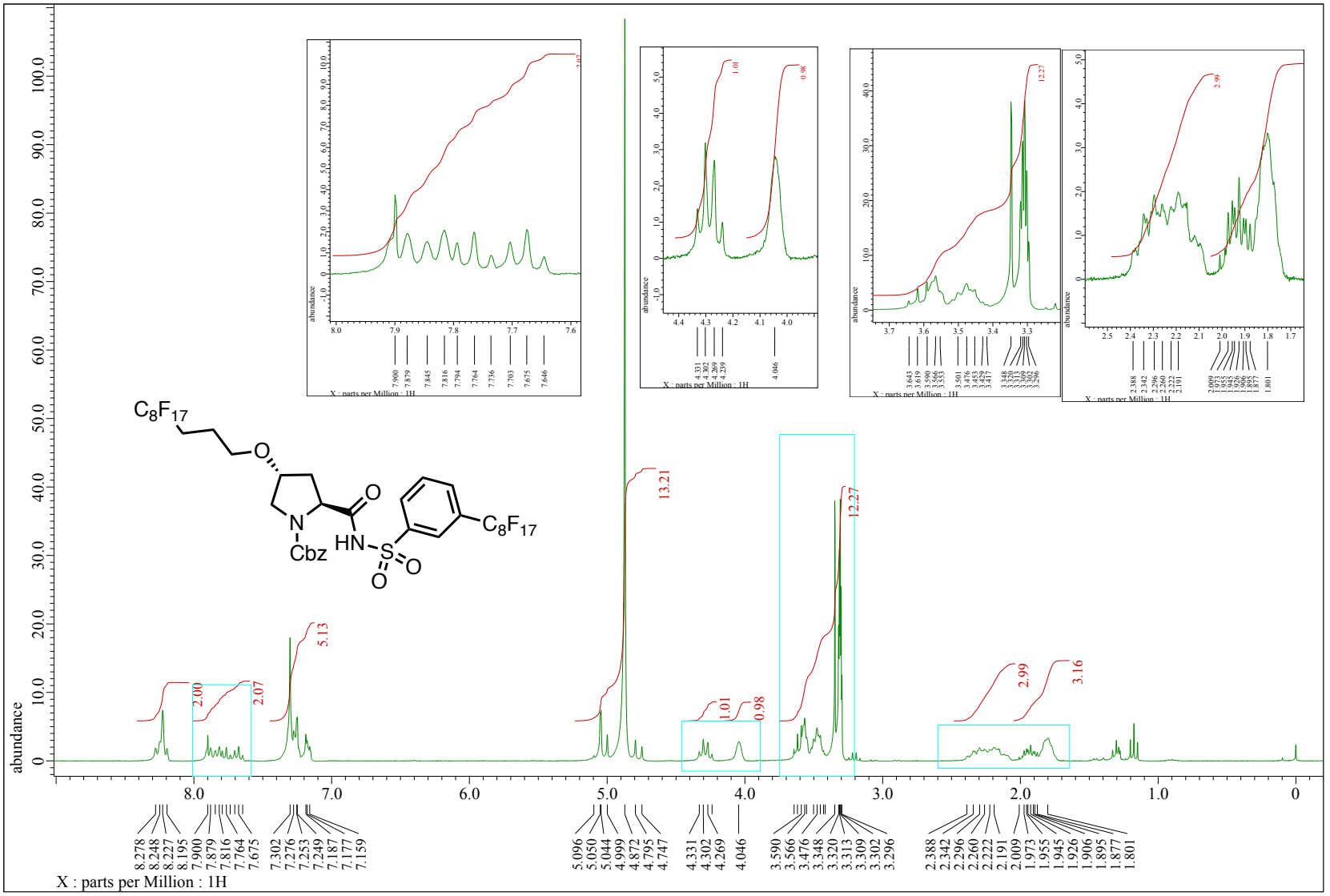
^{1}H NMR, 270 MHz, $CDCl_3$



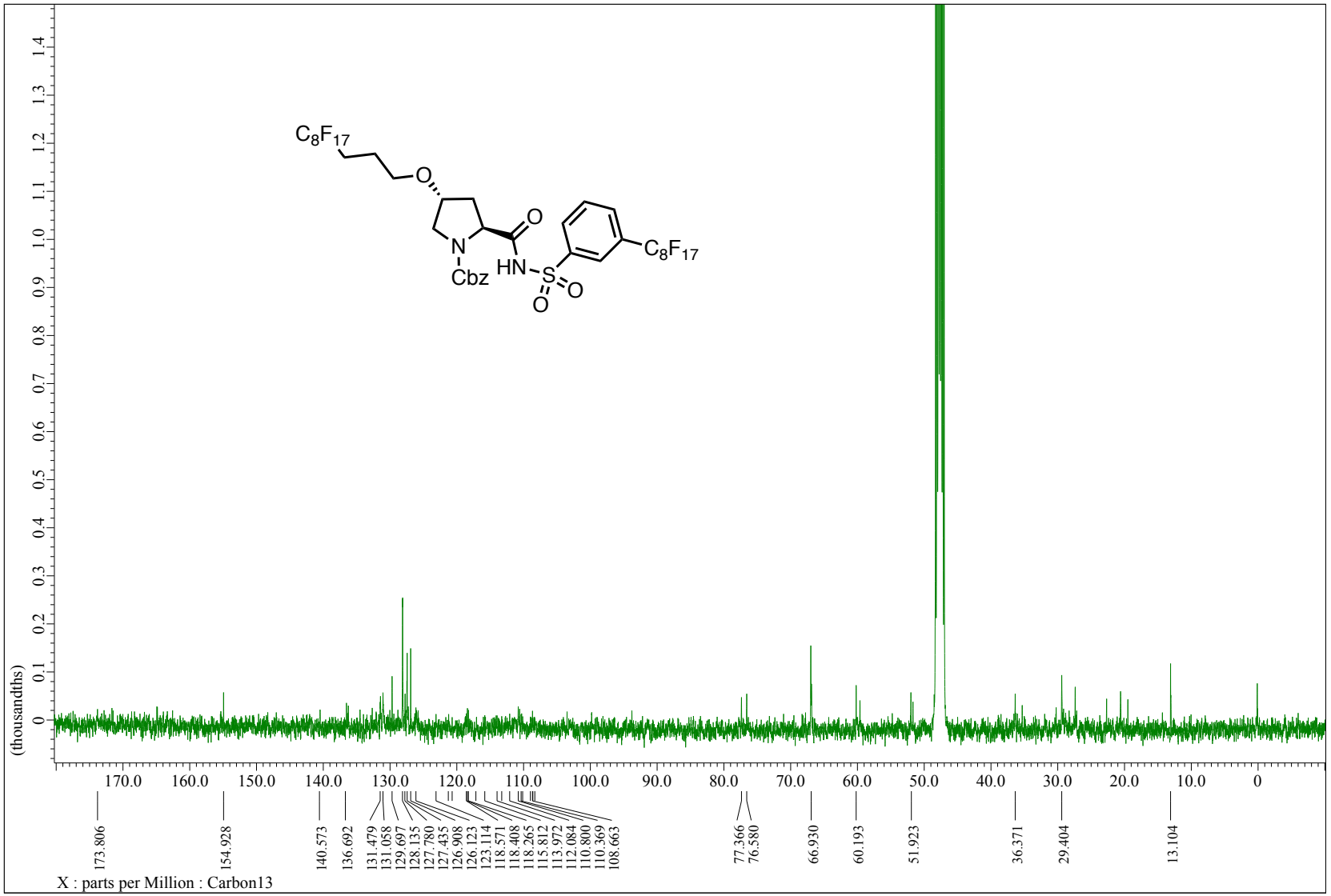
^{1}H NMR, 400 MHz, DMSO-d6



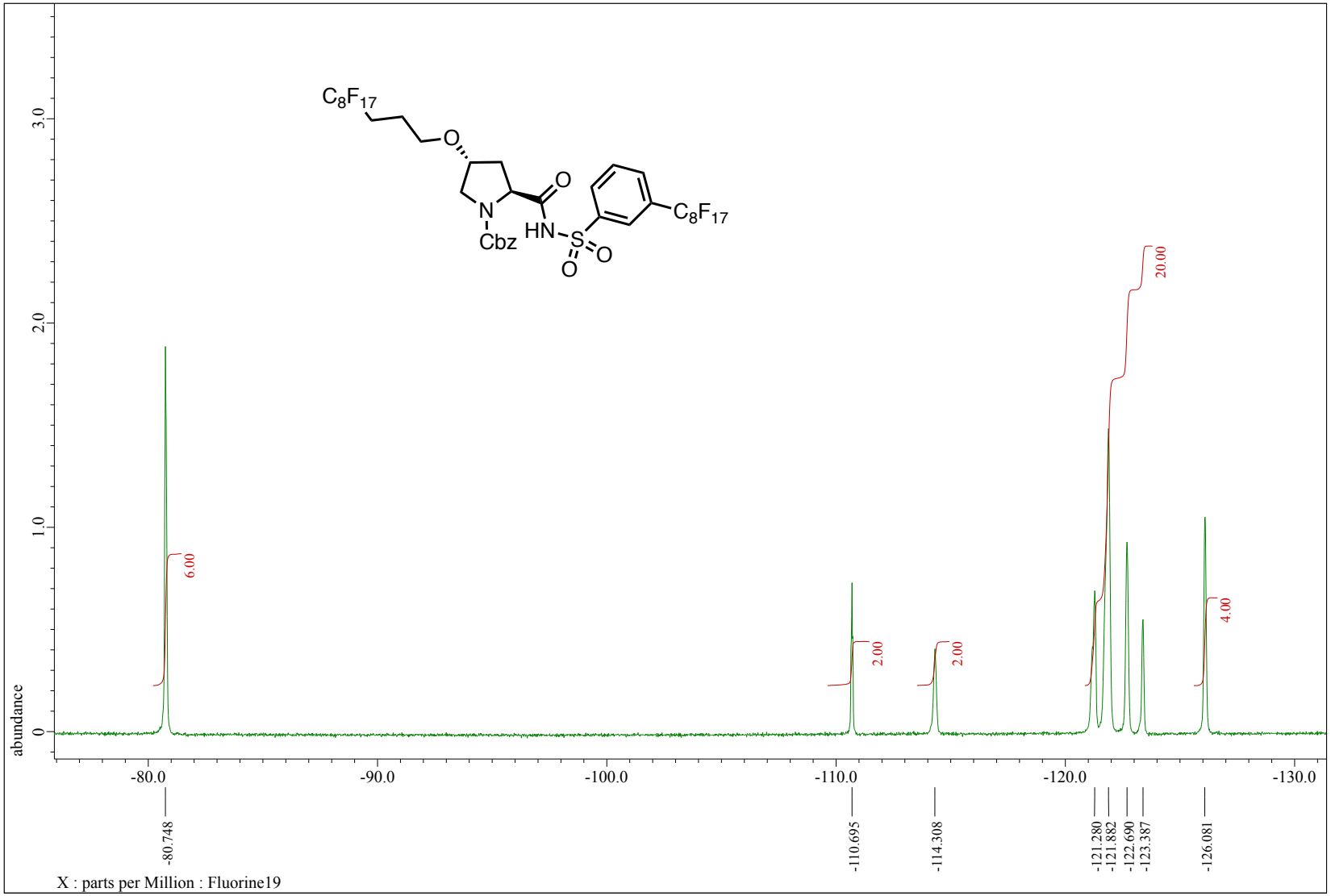
^{1}H NMR, 270 MHz, CD_3OD



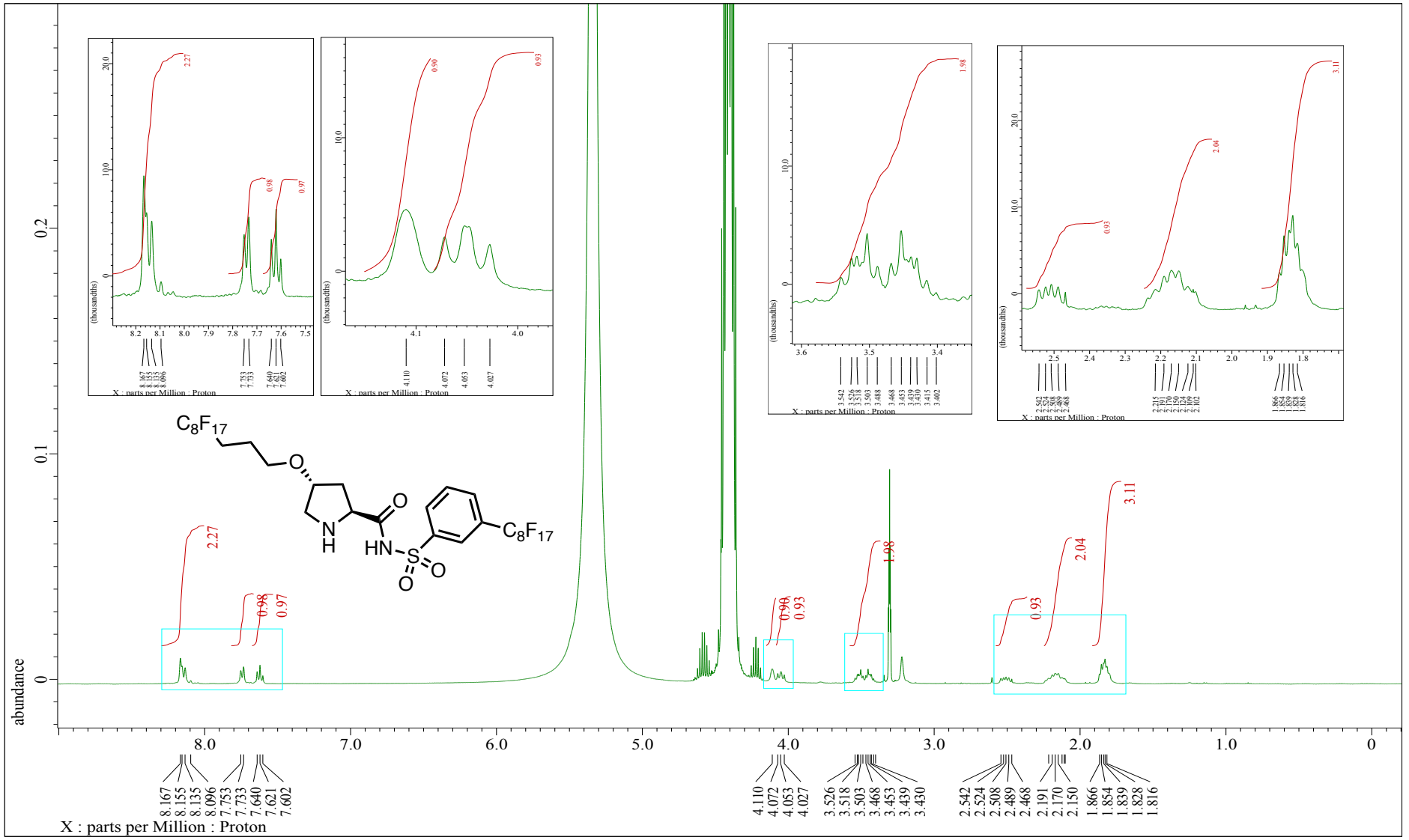
^{13}C NMR, 101 MHz, CD_3OD



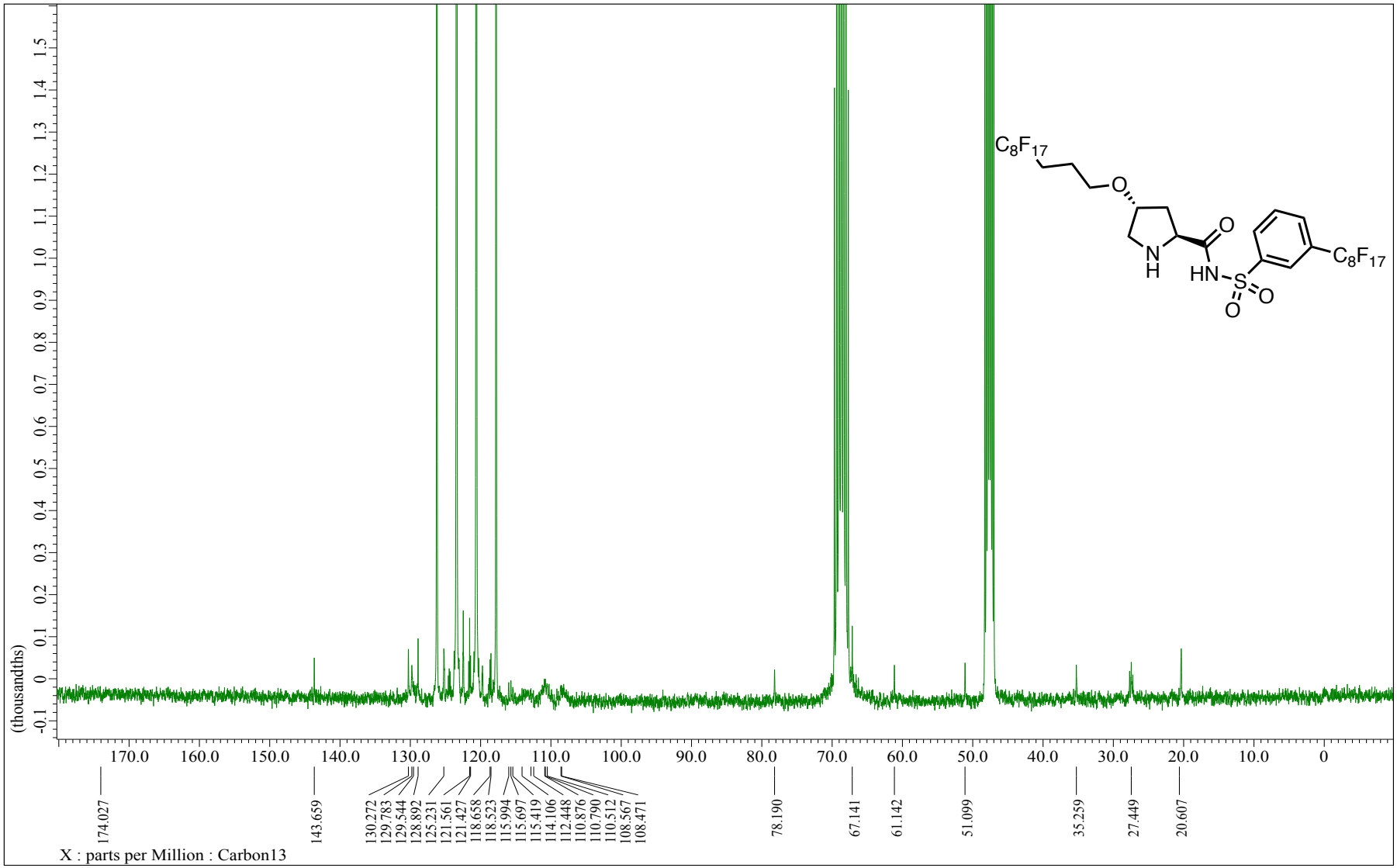
^{19}F NMR, 376 MHz, $CDCl_3$



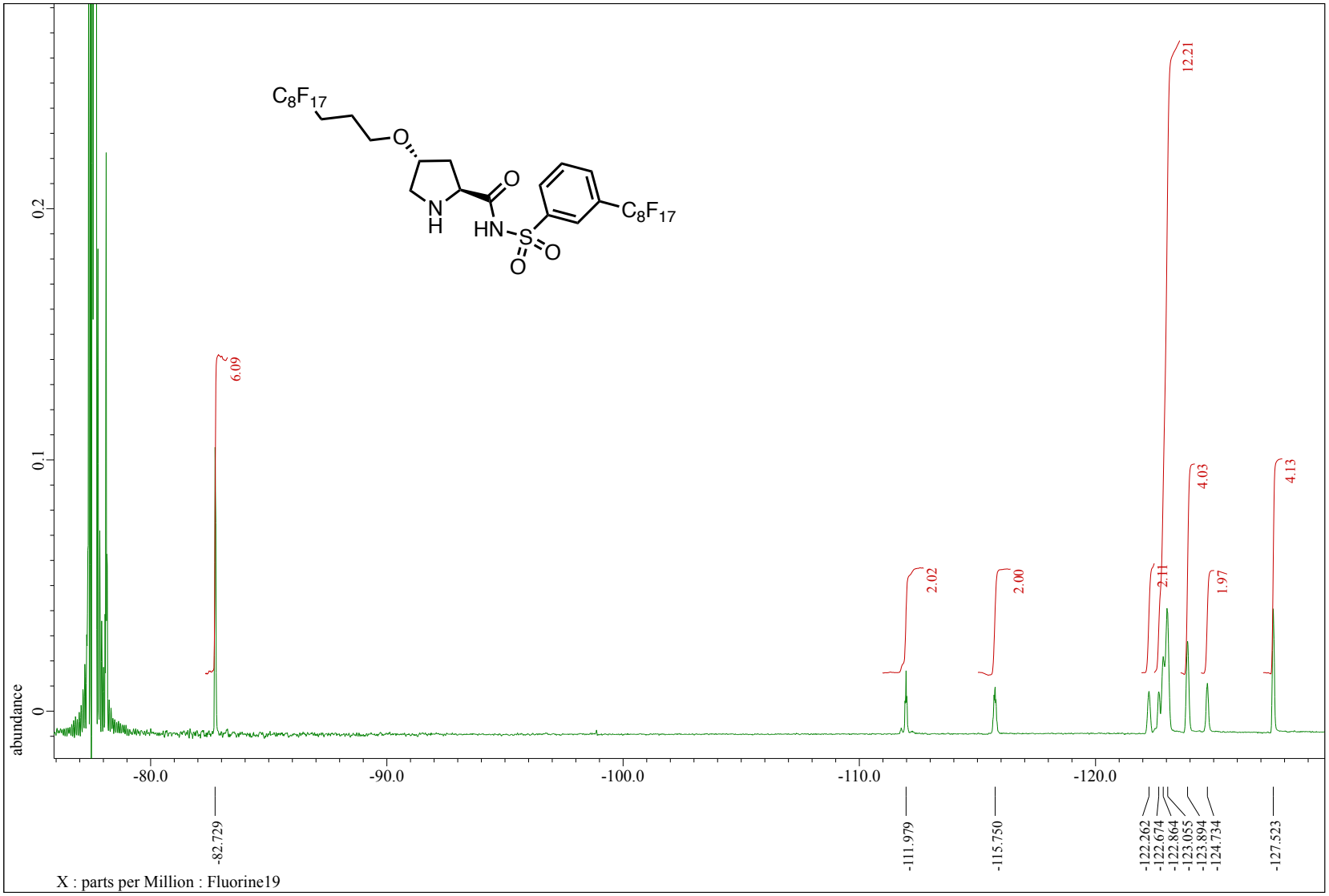
^{1}H NMR, 400 MHz, CD_3OD+Hexafluoroisopropanol



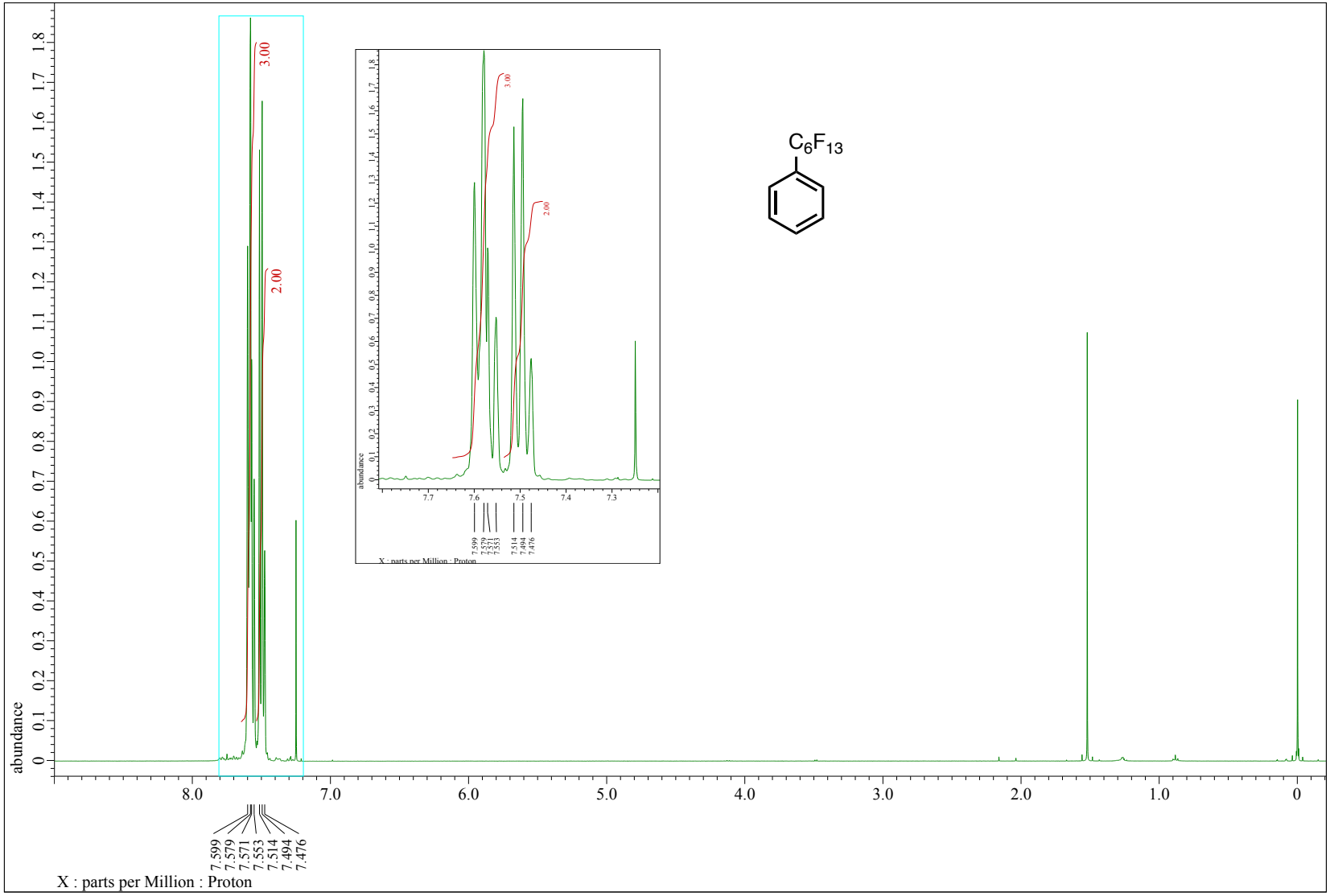
^{13}C NMR, 101 MHz, CD_3OD+Hexfluoroisopropanol



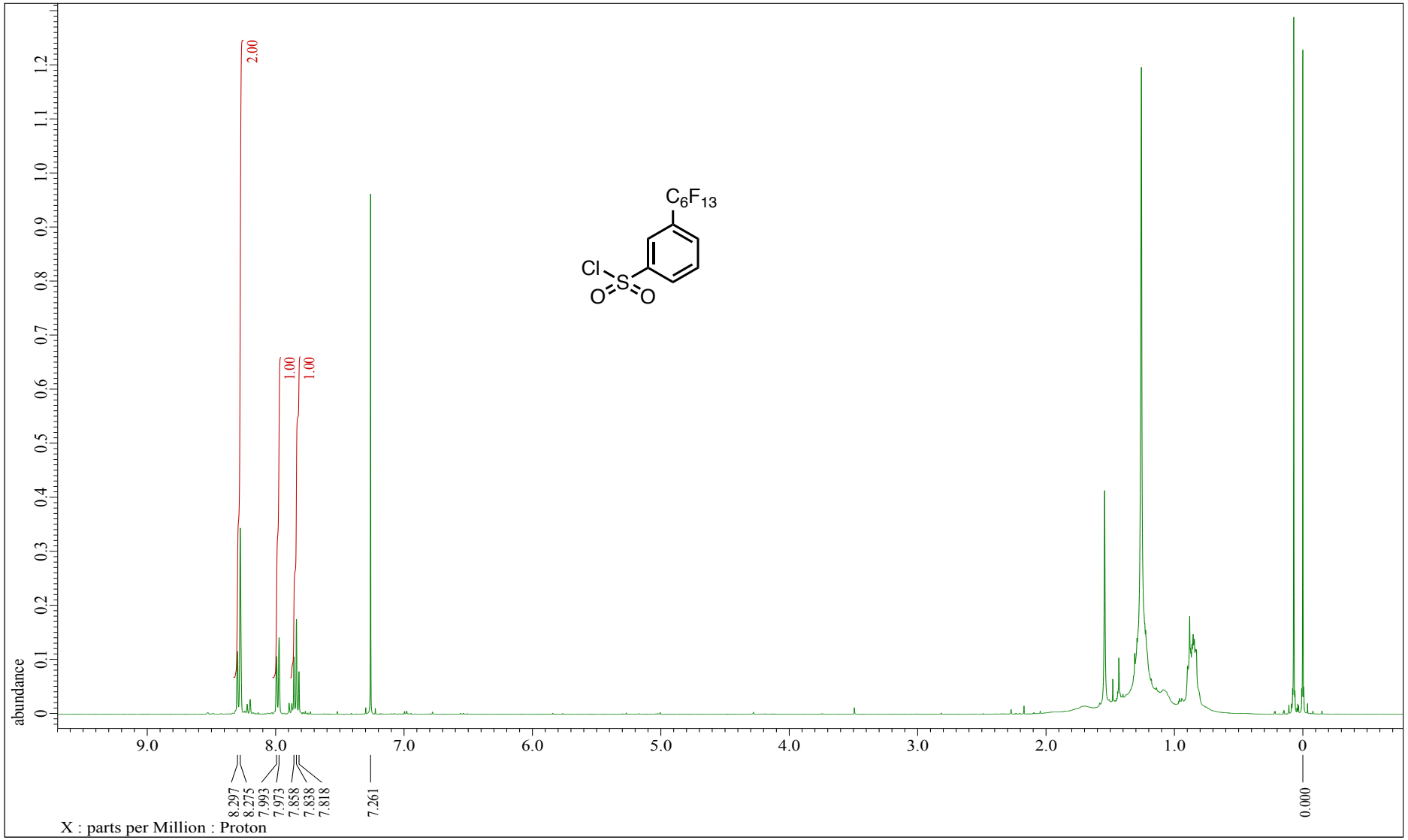
^{19}F NMR, 376 MHz, CD_3OD+Hexfluoroisopropanol



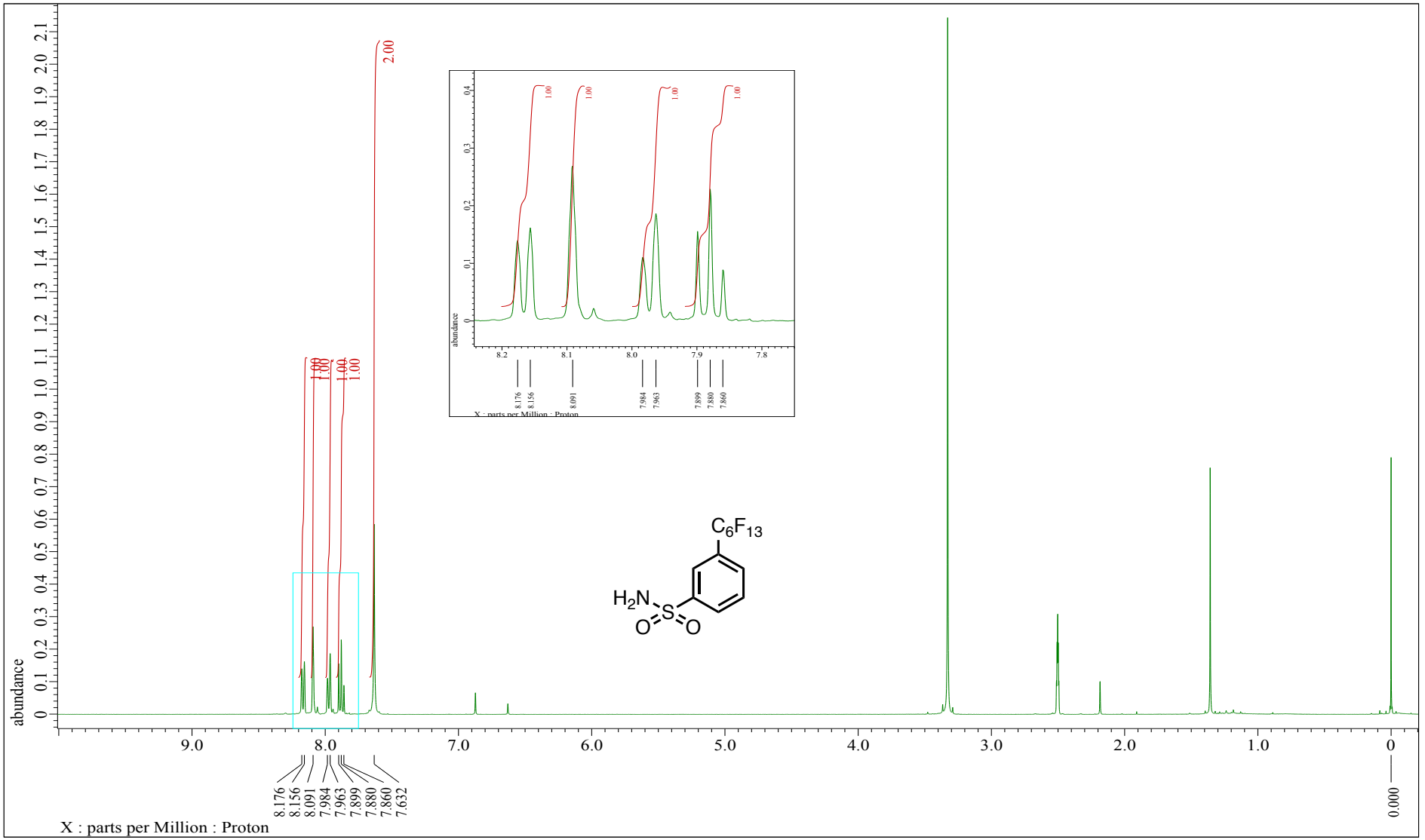
^{1}H NMR, 400 MHz, $CDCl_3$



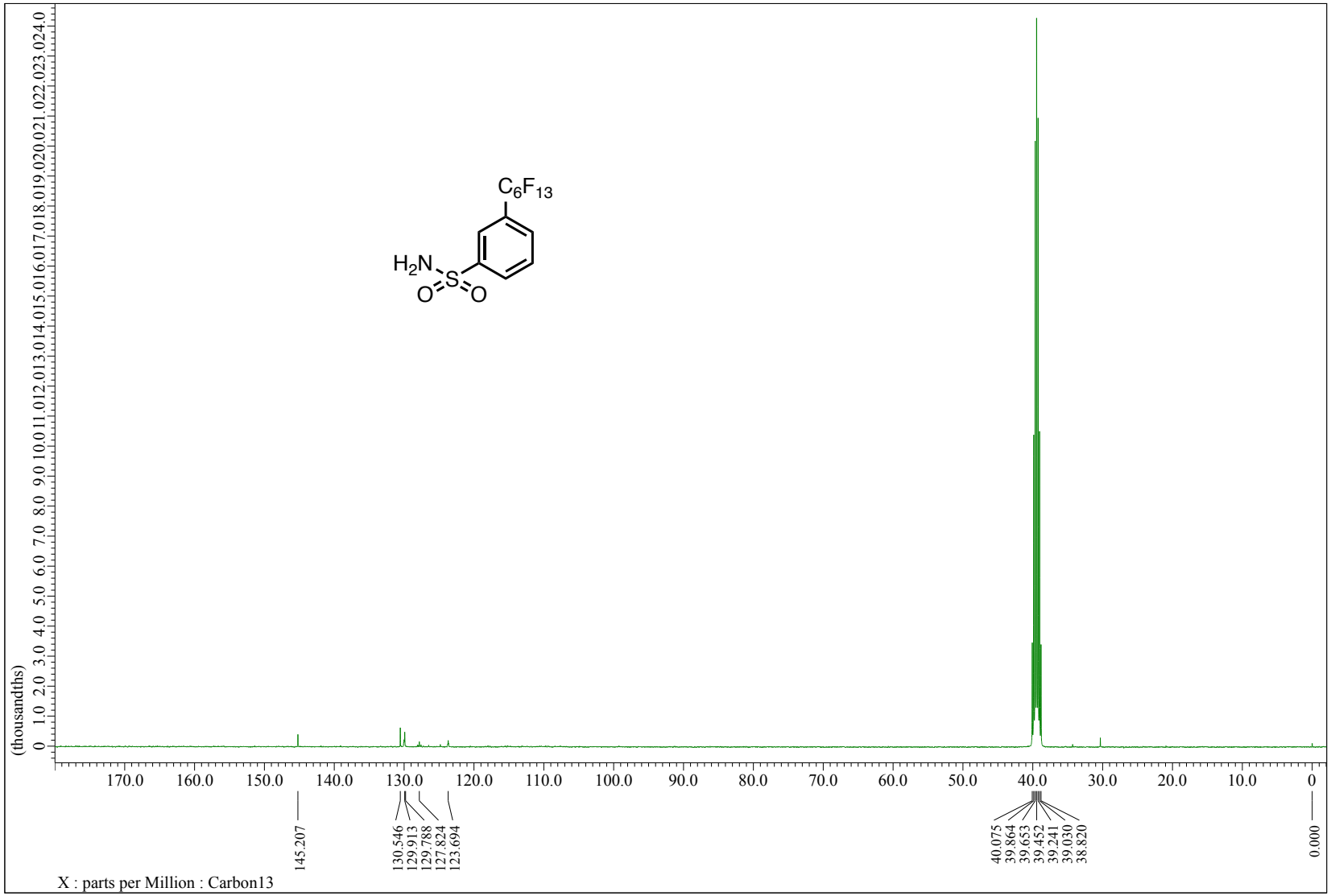
^{1}H NMR, 400 MHz, $CDCl_3$



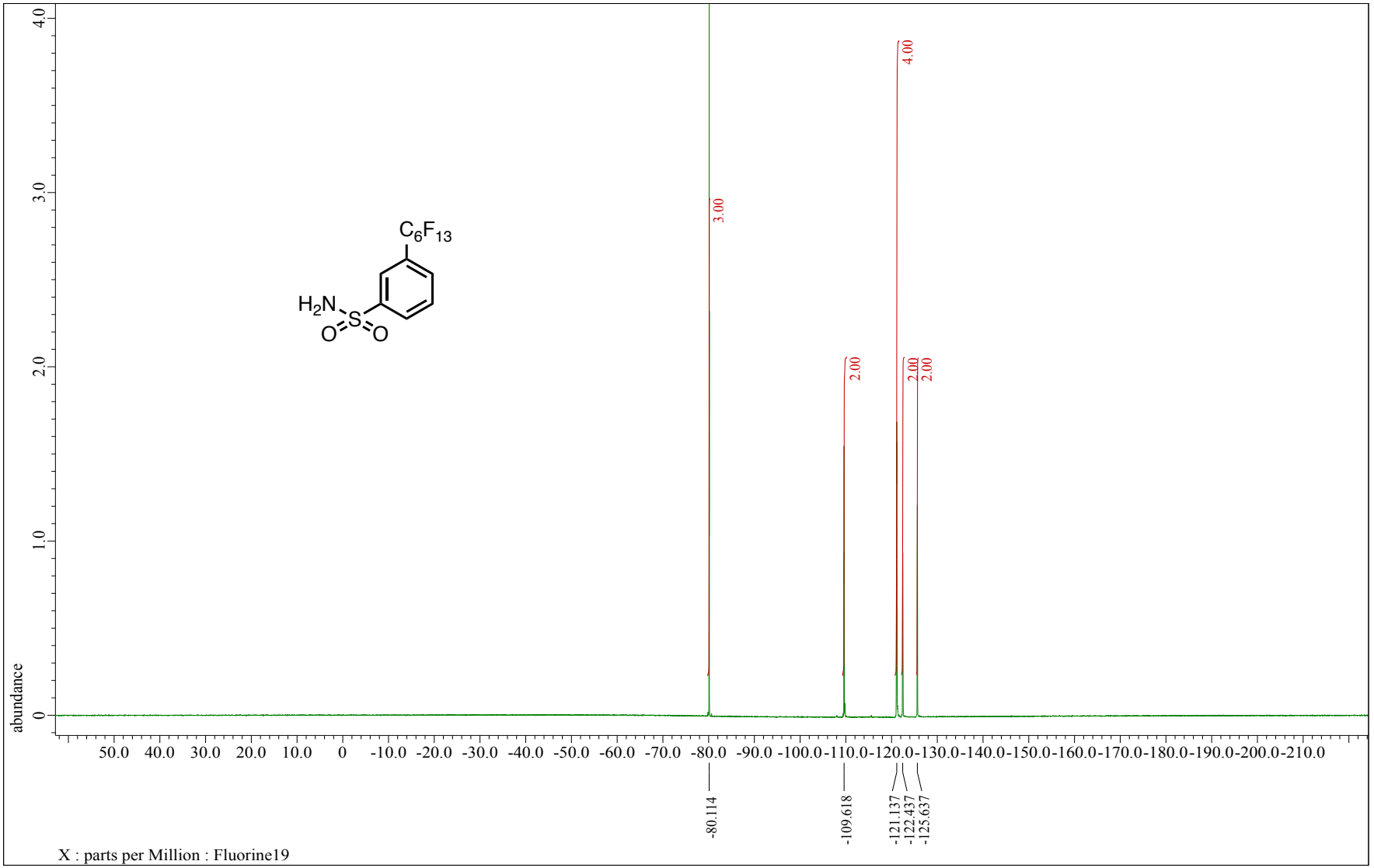
^{1}H NMR, 400 MHz, DMSO-d6



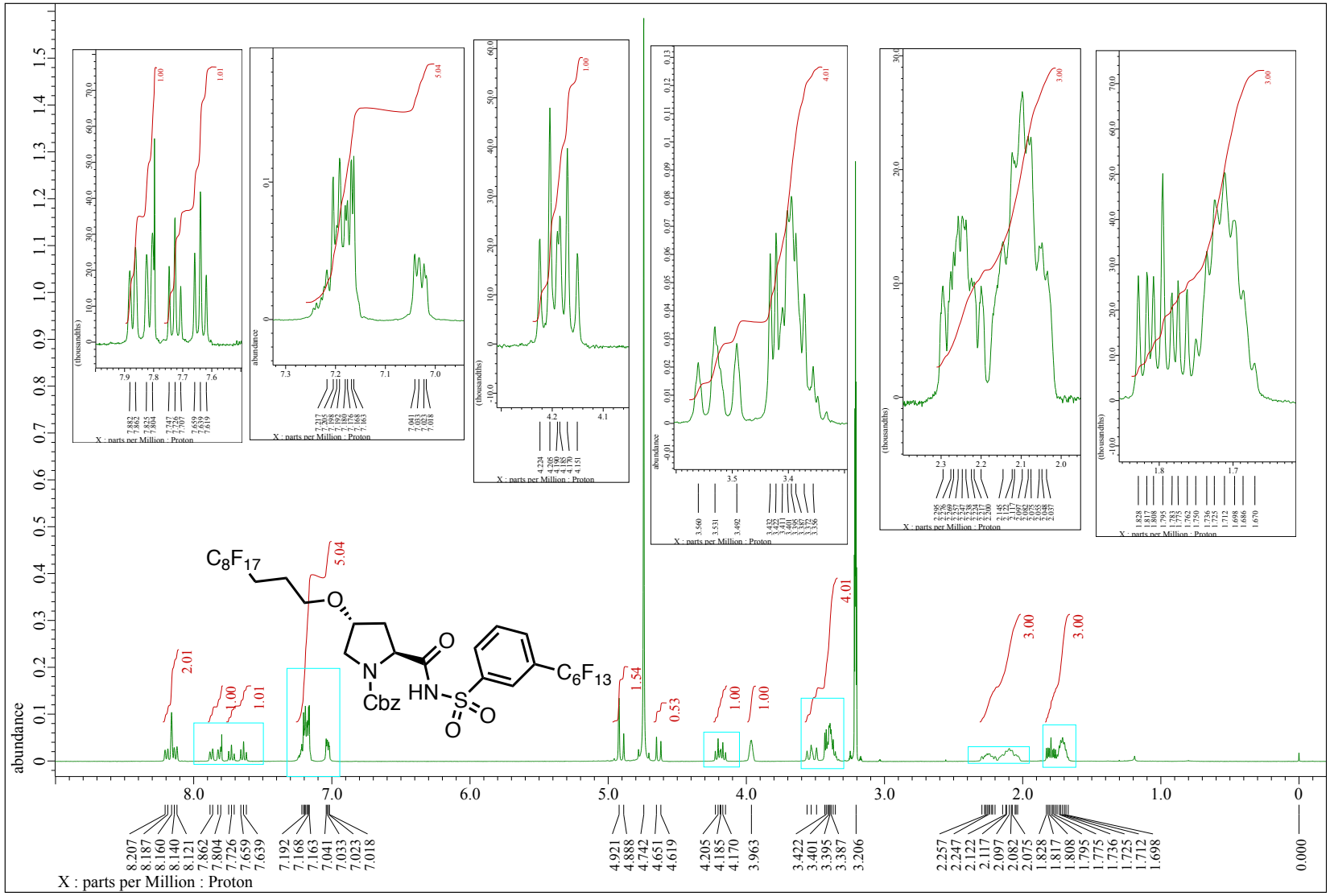
^{13}C NMR, 101 MHz, DMSO-d6



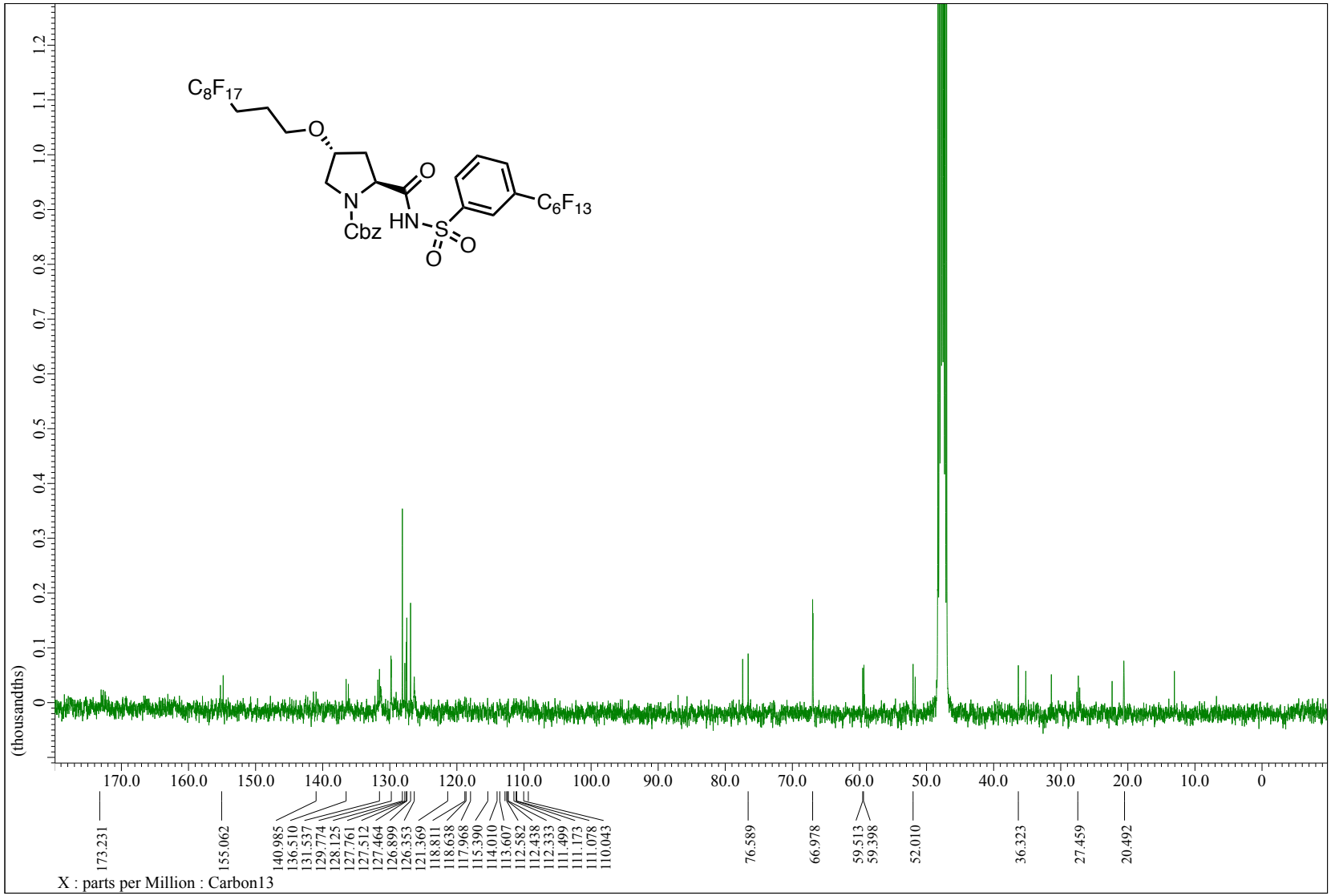
^{19}F NMR, 376 MHz, DMSO-d6



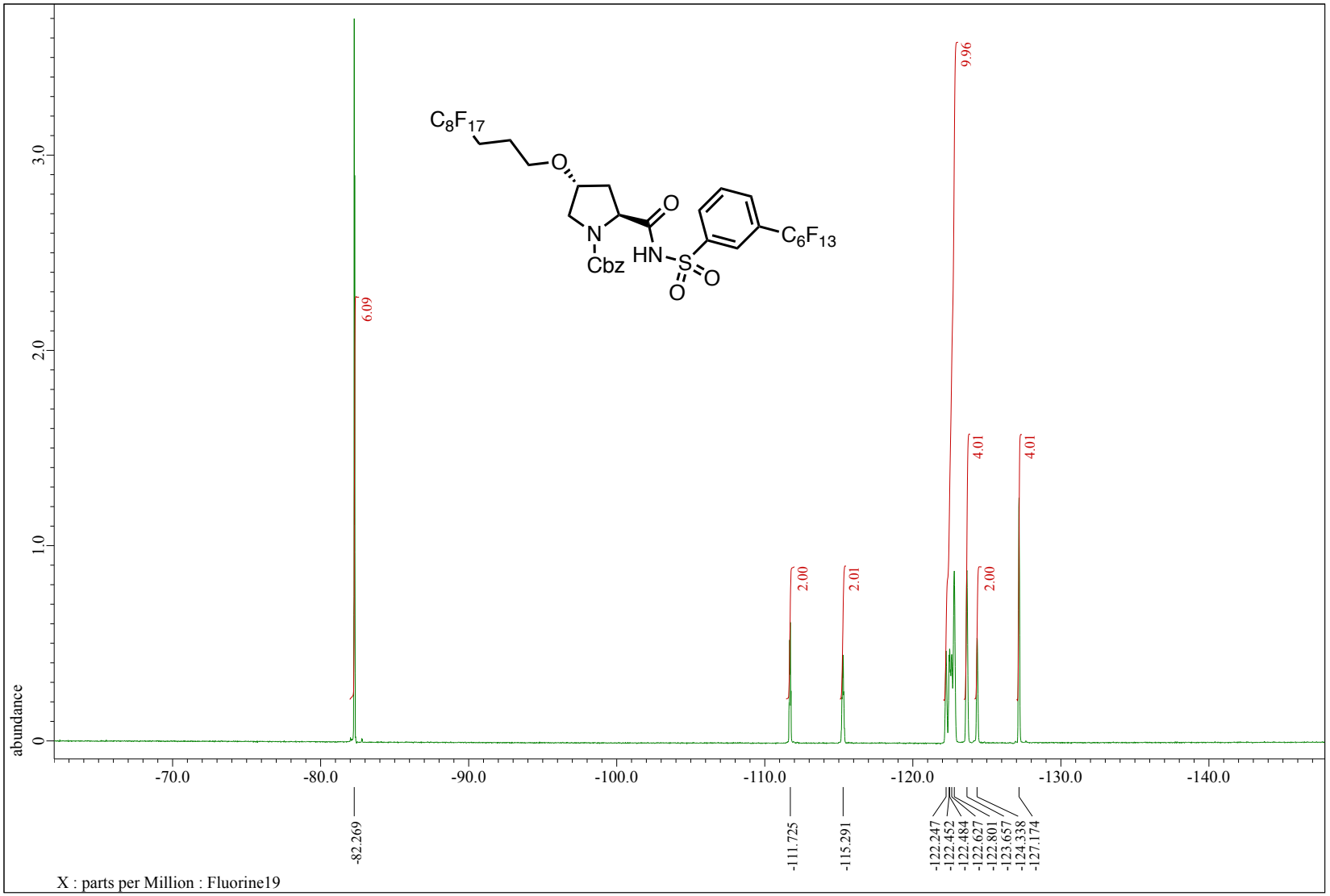
^{1}H NMR, 400 MHz, CD_3OD



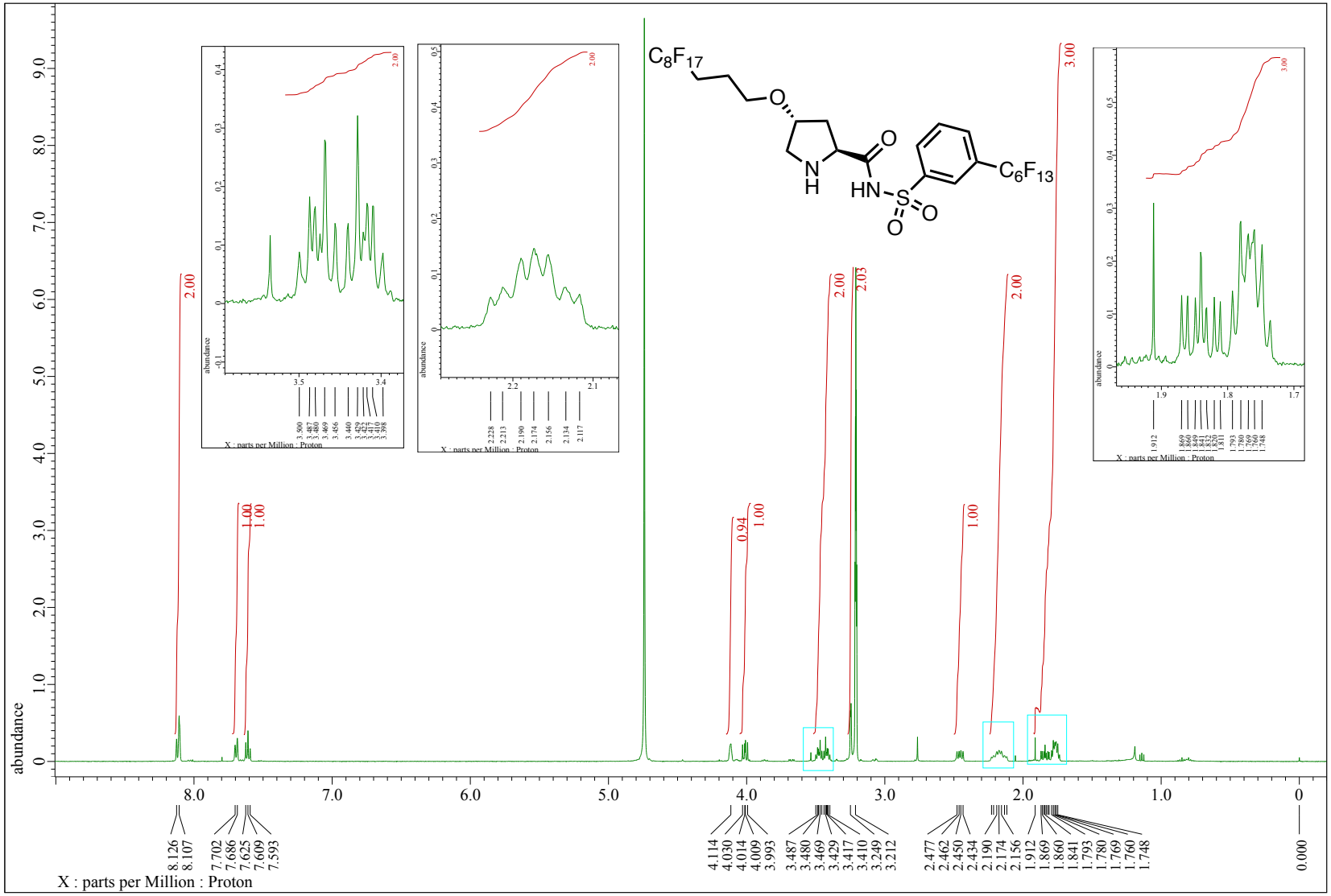
^{13}C NMR, 101 MHz, CD_3OD



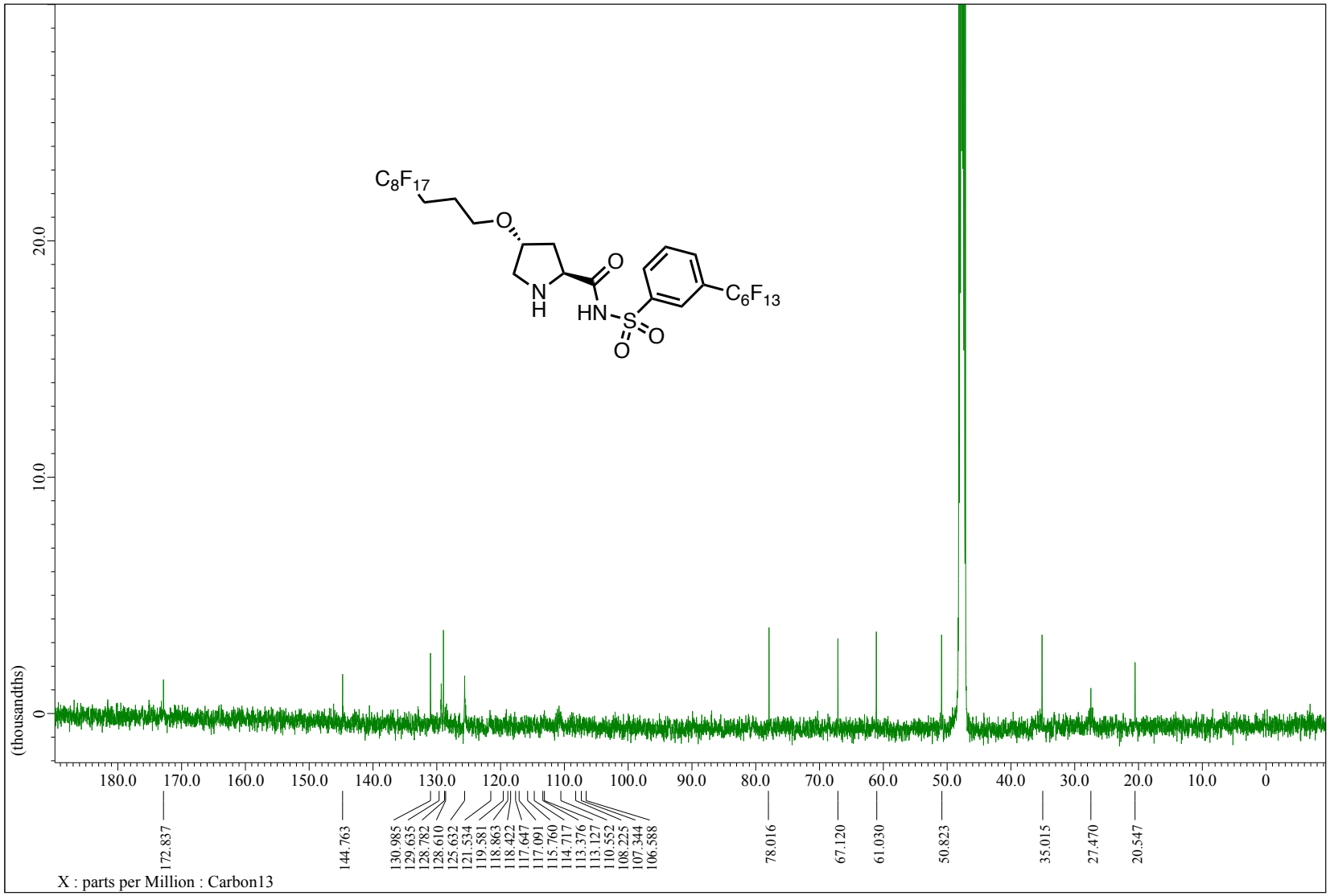
^{19}F NMR, 376 MHz, CD_3OD



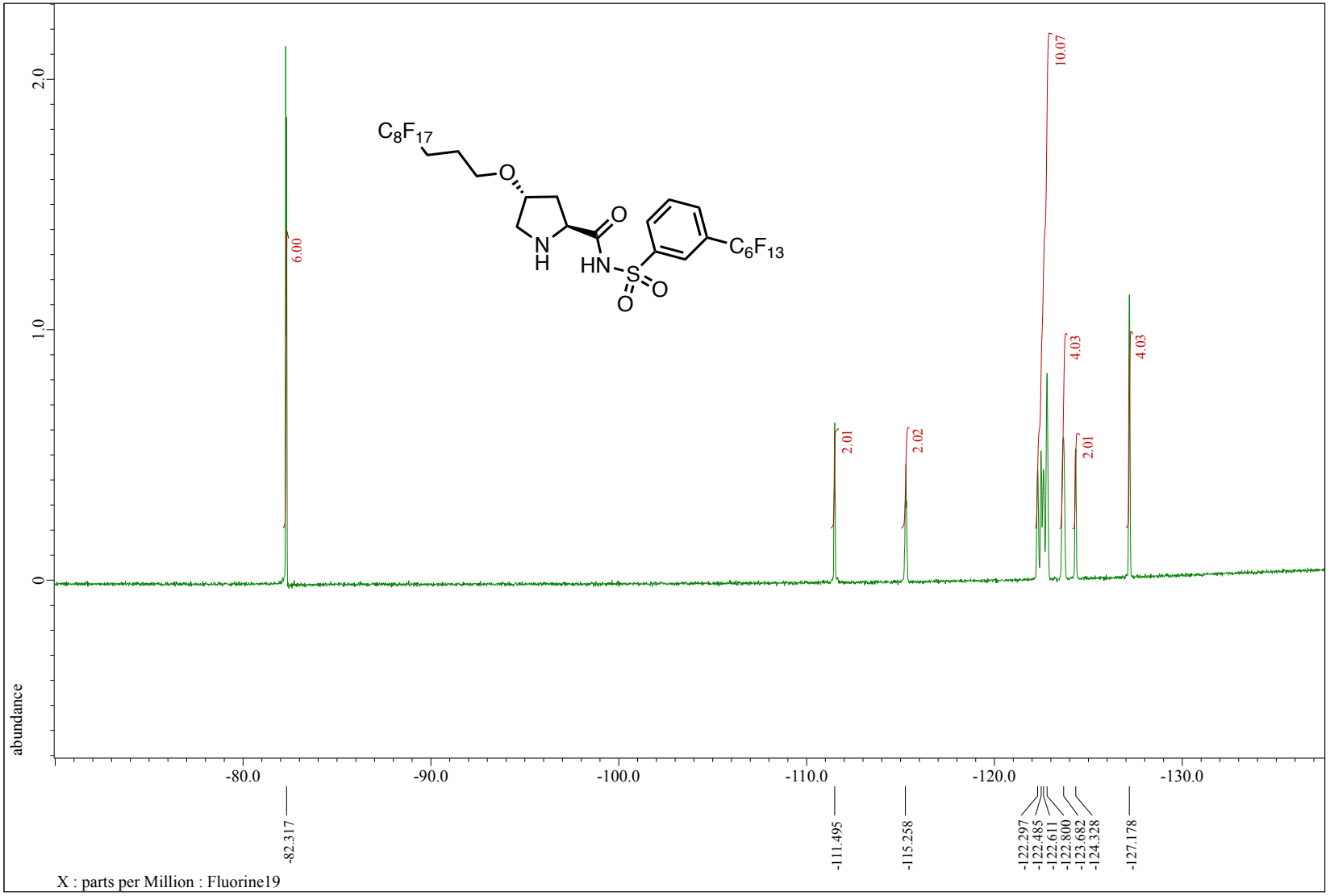
^{1}H NMR, 500 MHz, CD_3OD



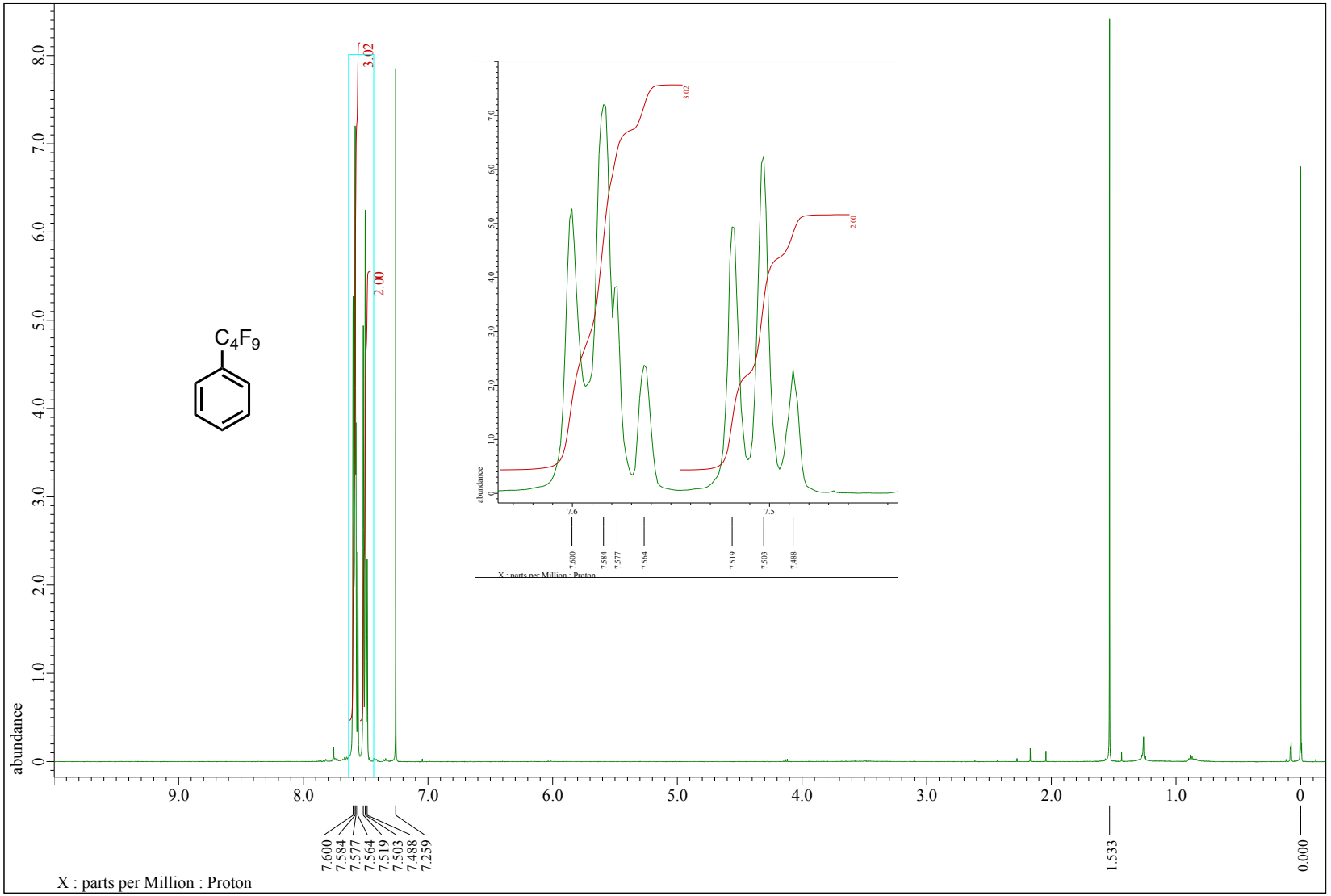
^{13}C NMR, 125 MHz, CD_3OD



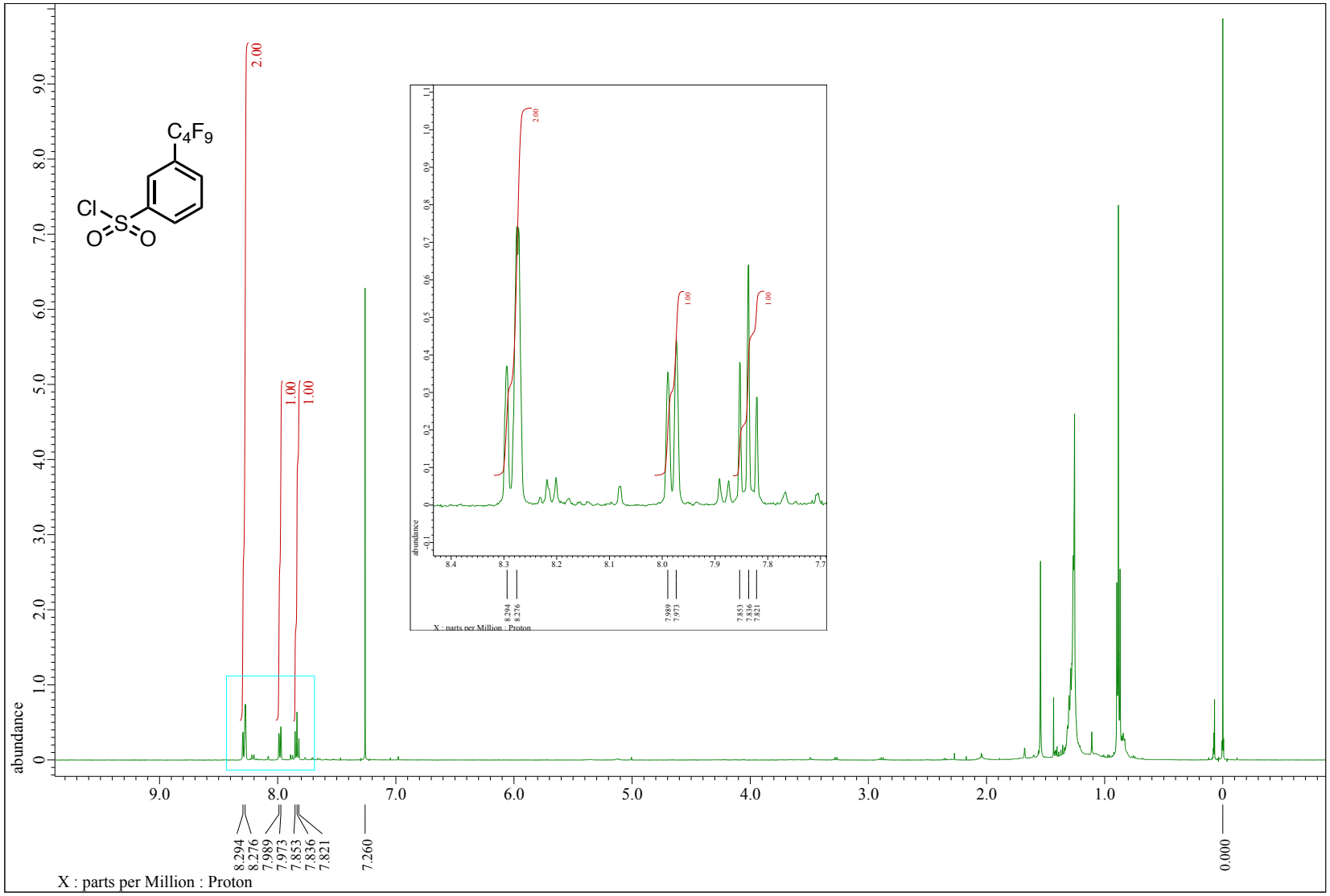
^{19}F NMR, 466 MHz, CD_3OD



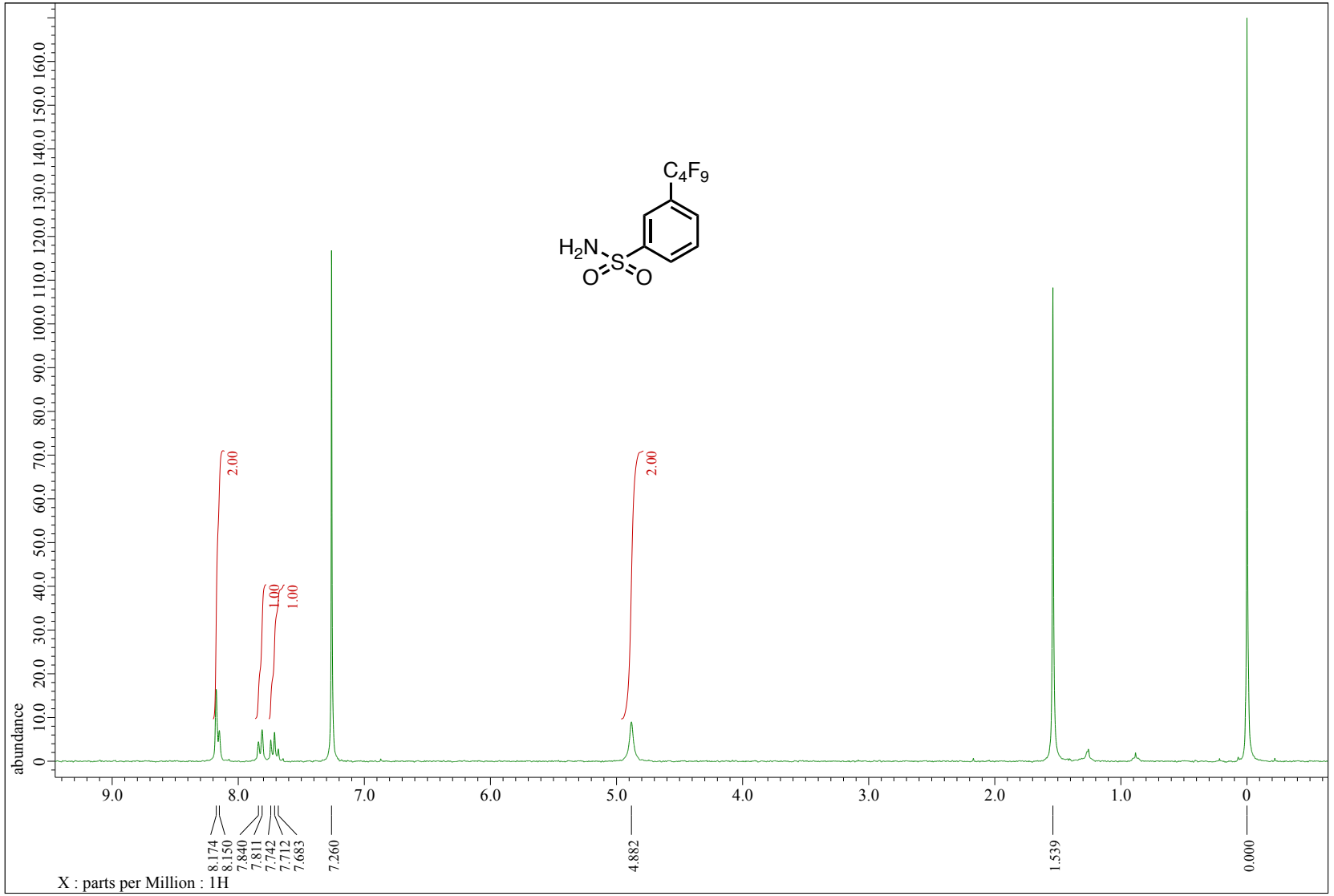
^{1}H NMR, 400 MHz, $CDCl_3$



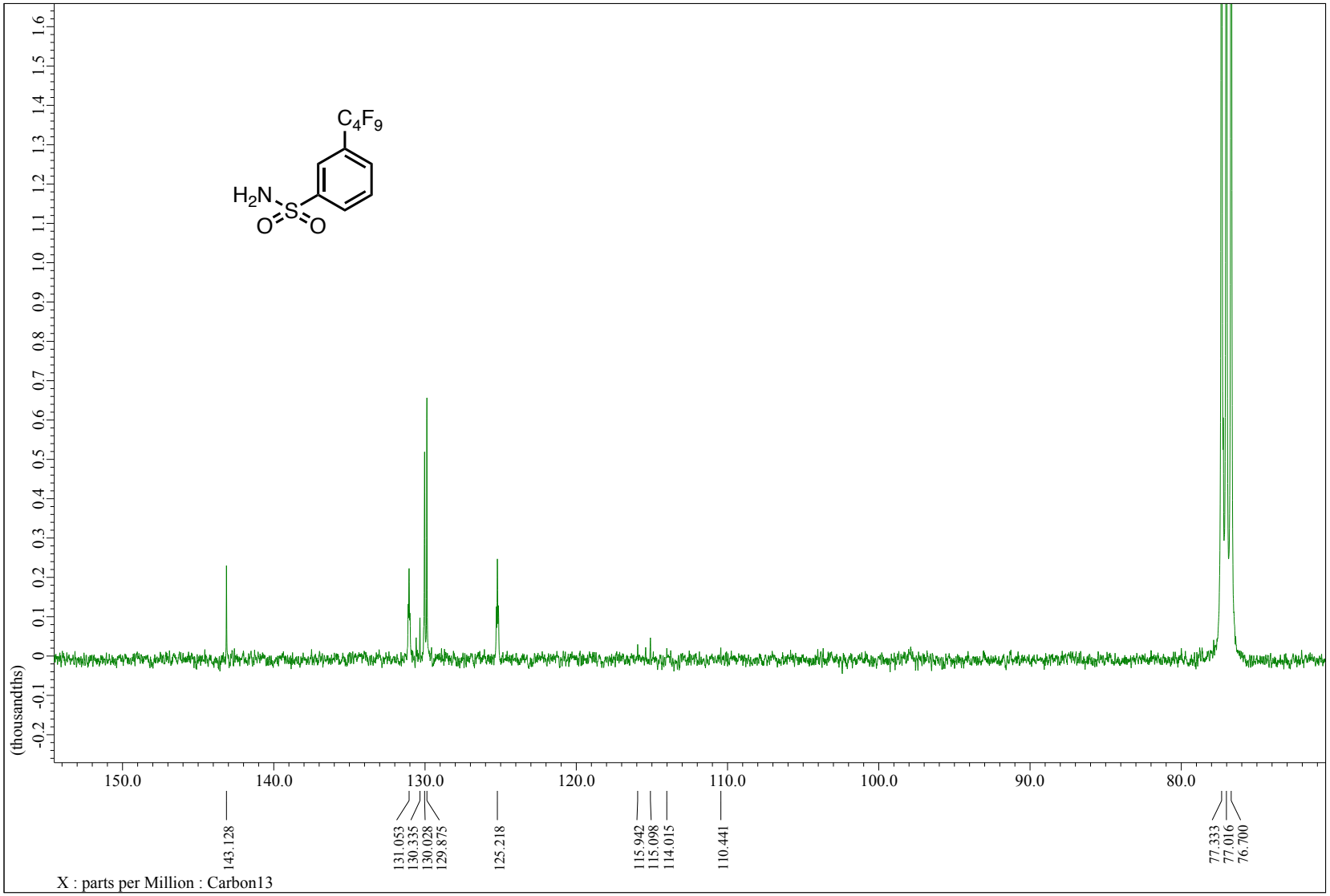
^{1}H NMR, 500 MHz, $CDCl_3$



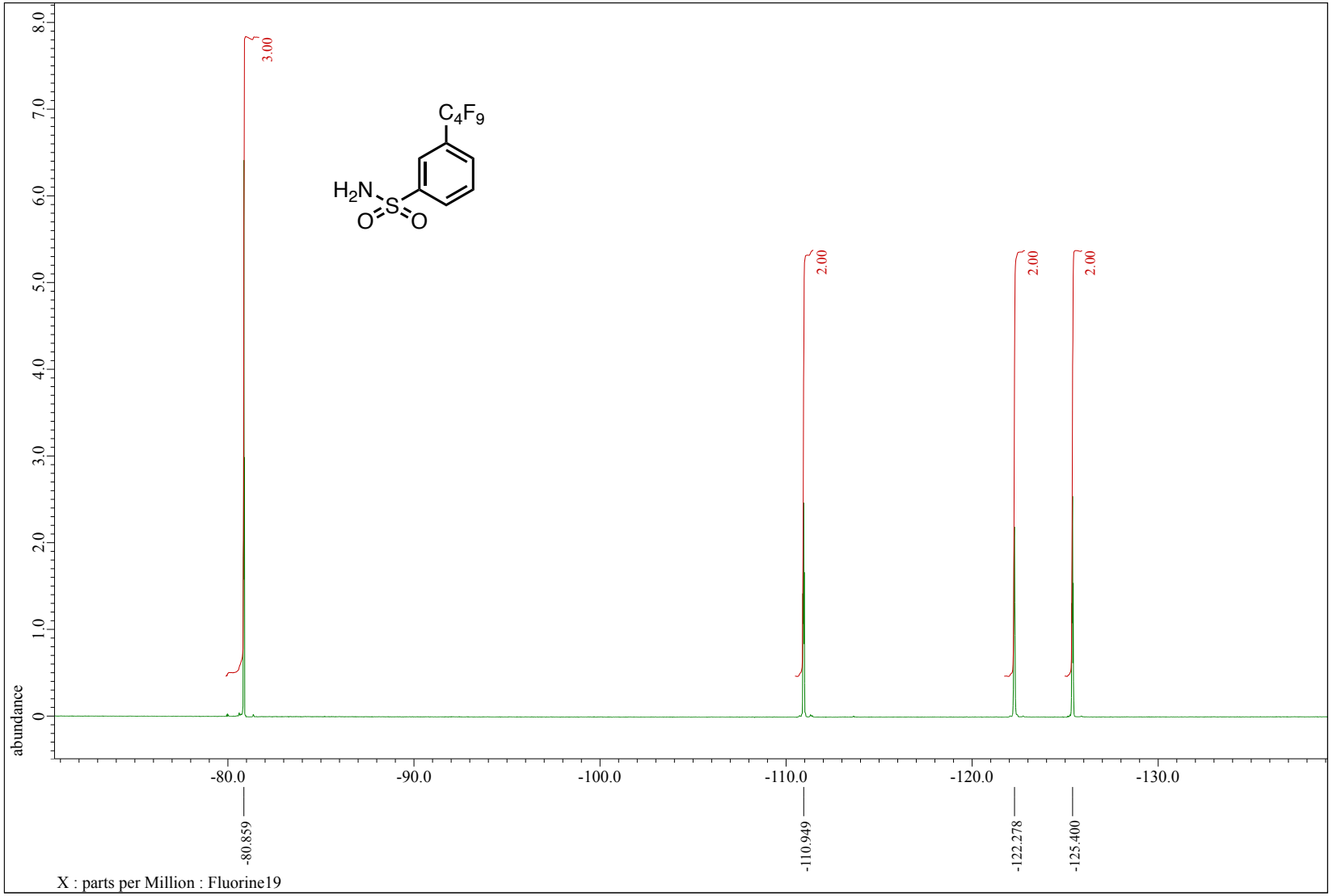
^{1}H NMR, 270 MHz, $CDCl_3$



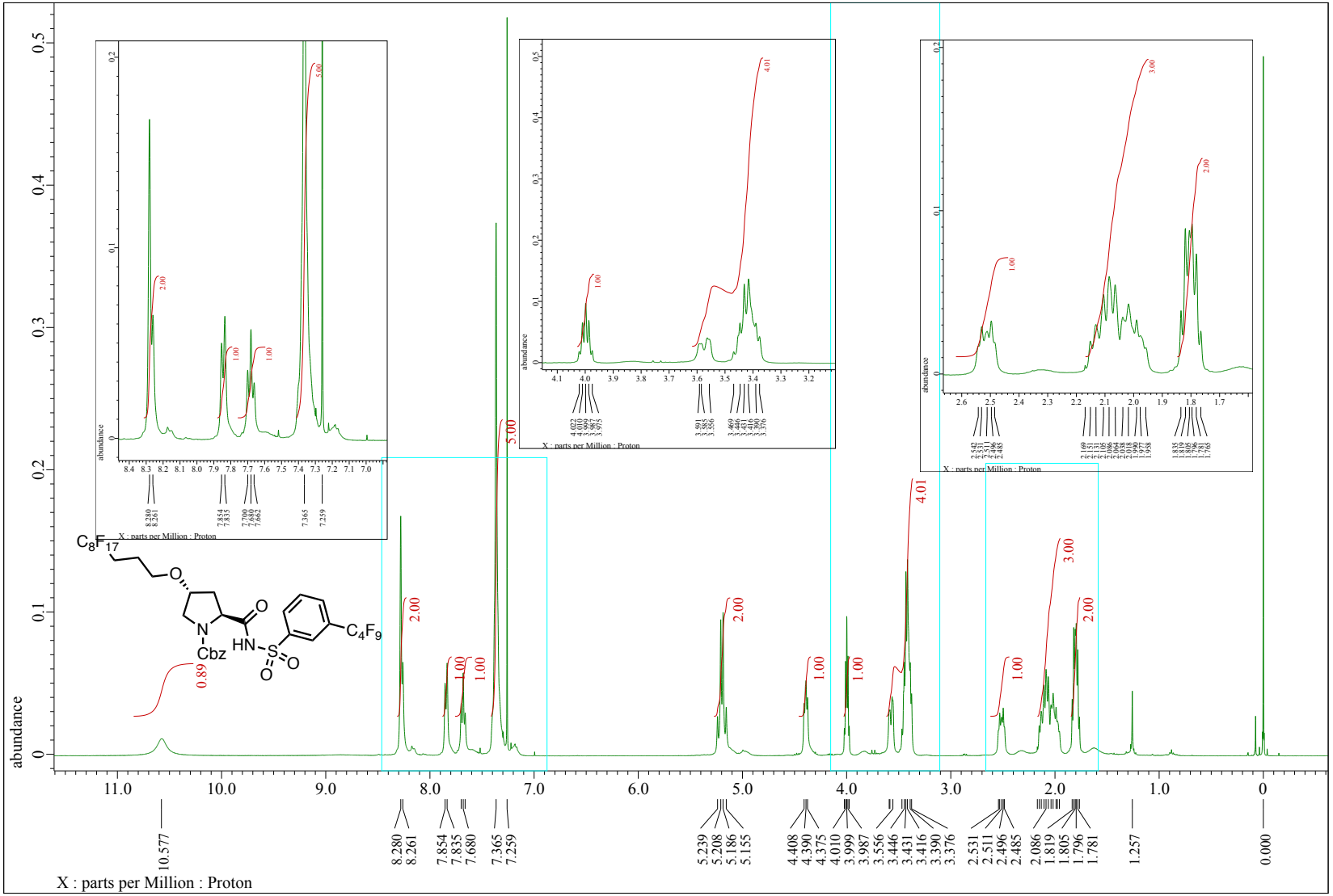
^{13}C NMR, 101 MHz, $CDCl_3$



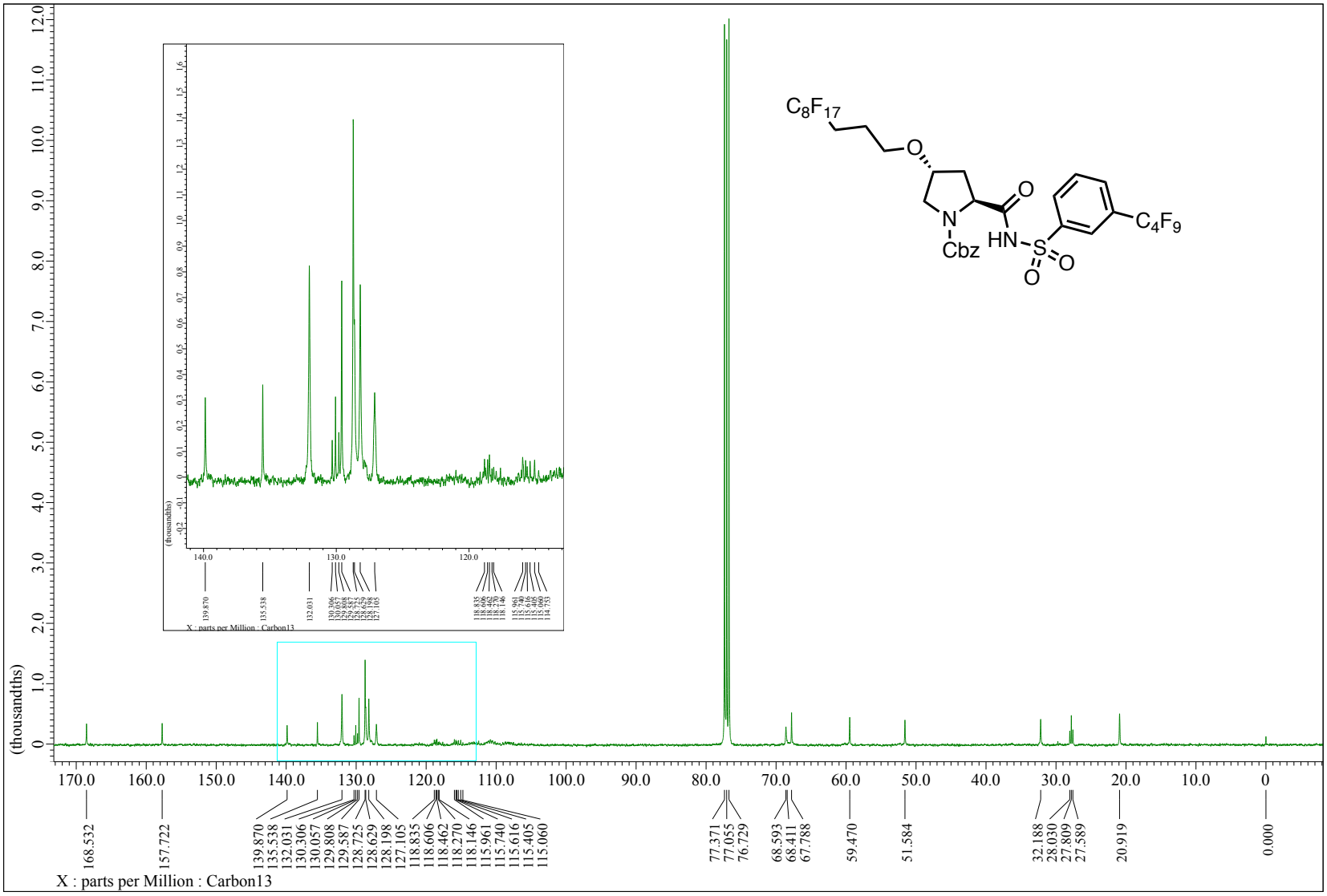
^{19}F NMR, 376 MHz, $CDCl_3$



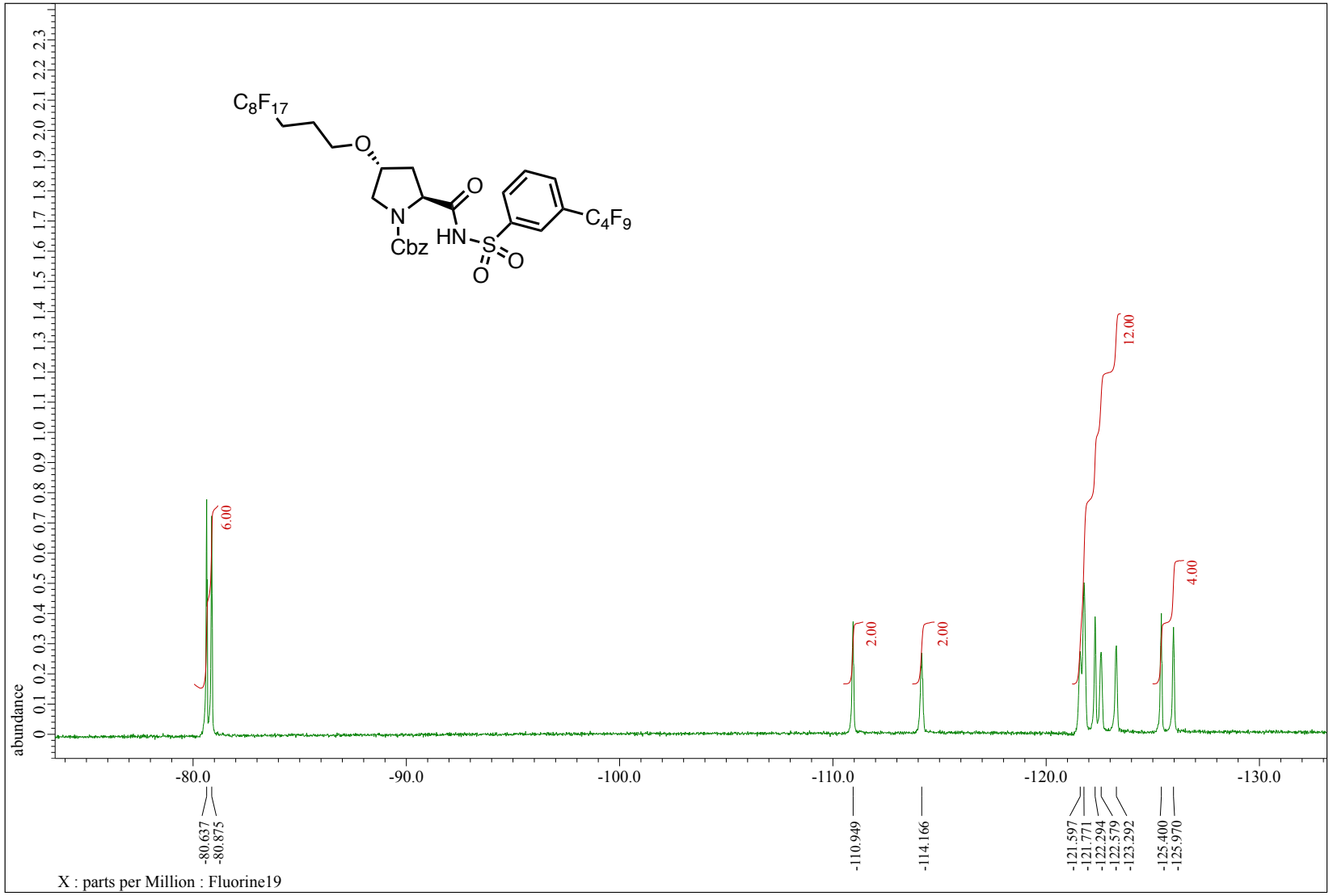
^{1}H NMR, 400 MHz, $CDCl_3$



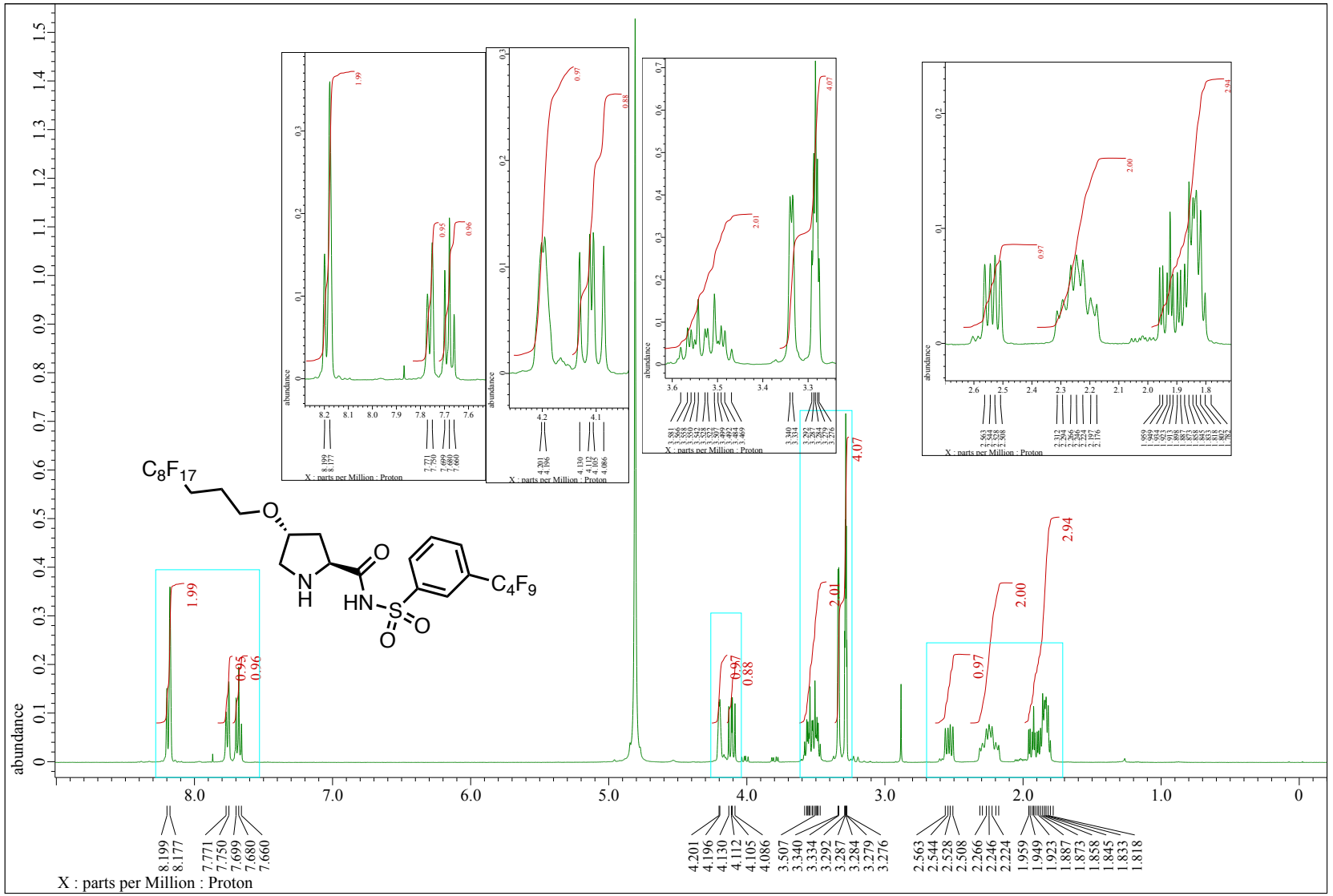
^{13}C NMR, 101 MHz, $CDCl_3$



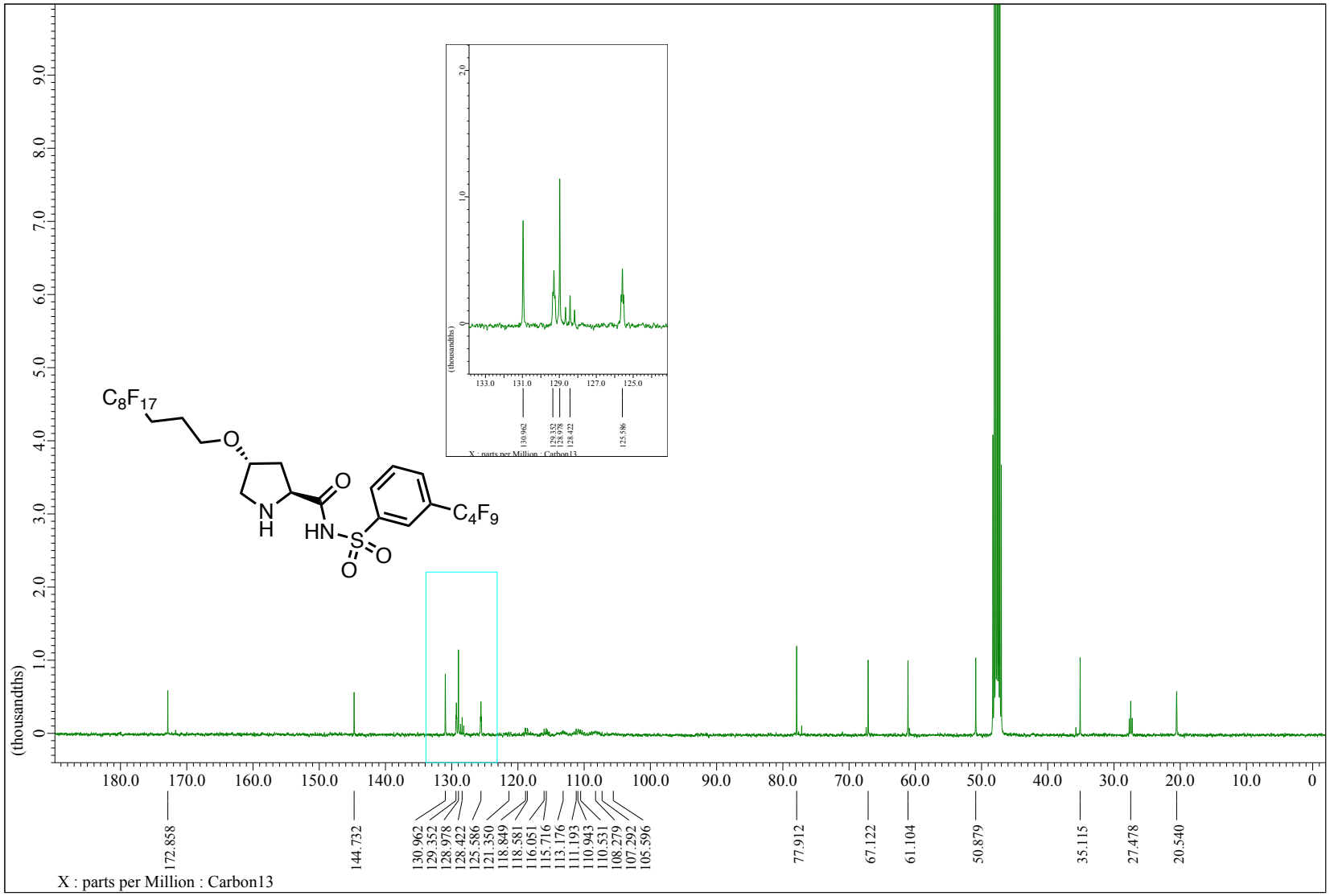
^{19}F NMR, 376 MHz, $CDCl_3$



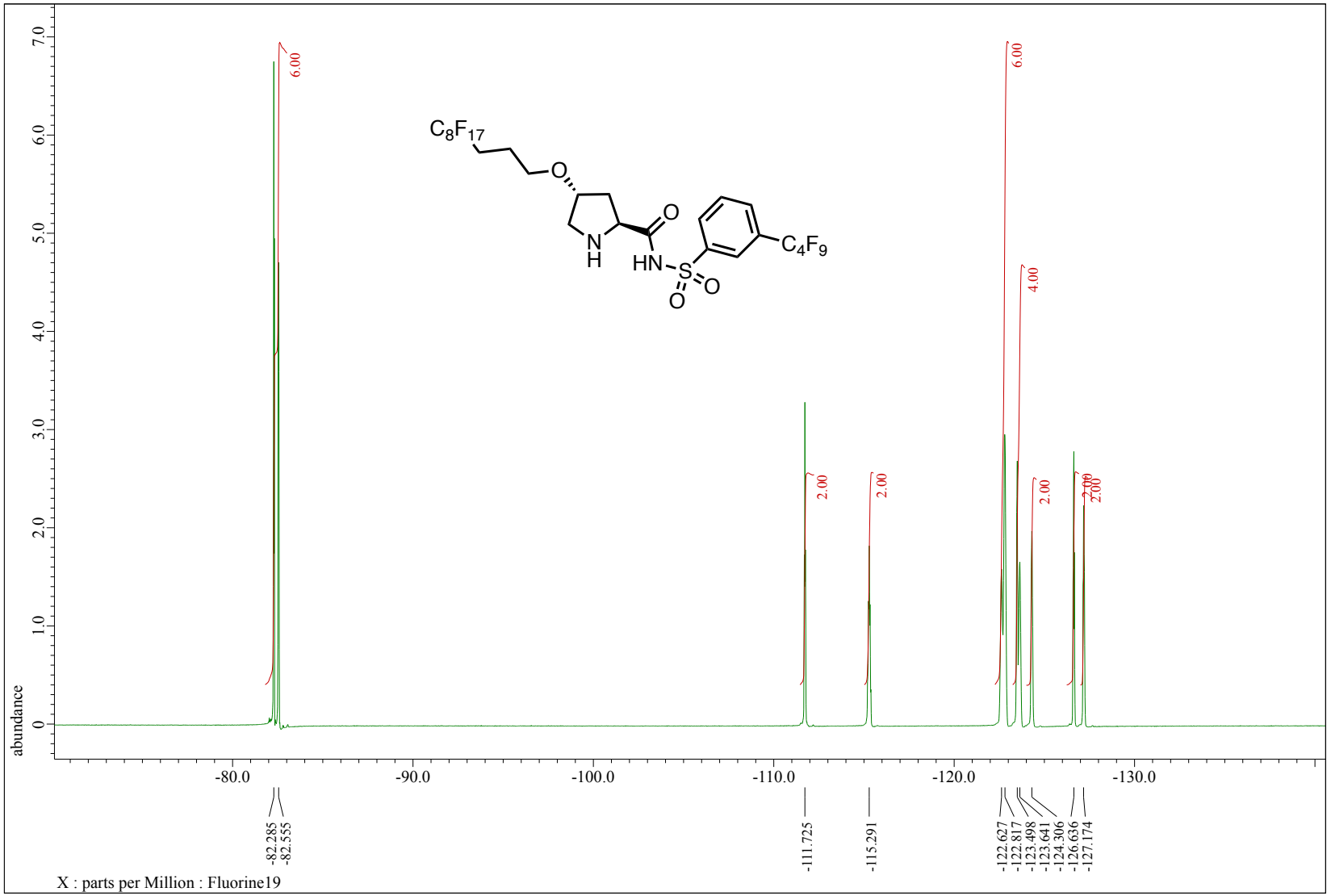
^{1}H NMR, 500 MHz, CD_3OD



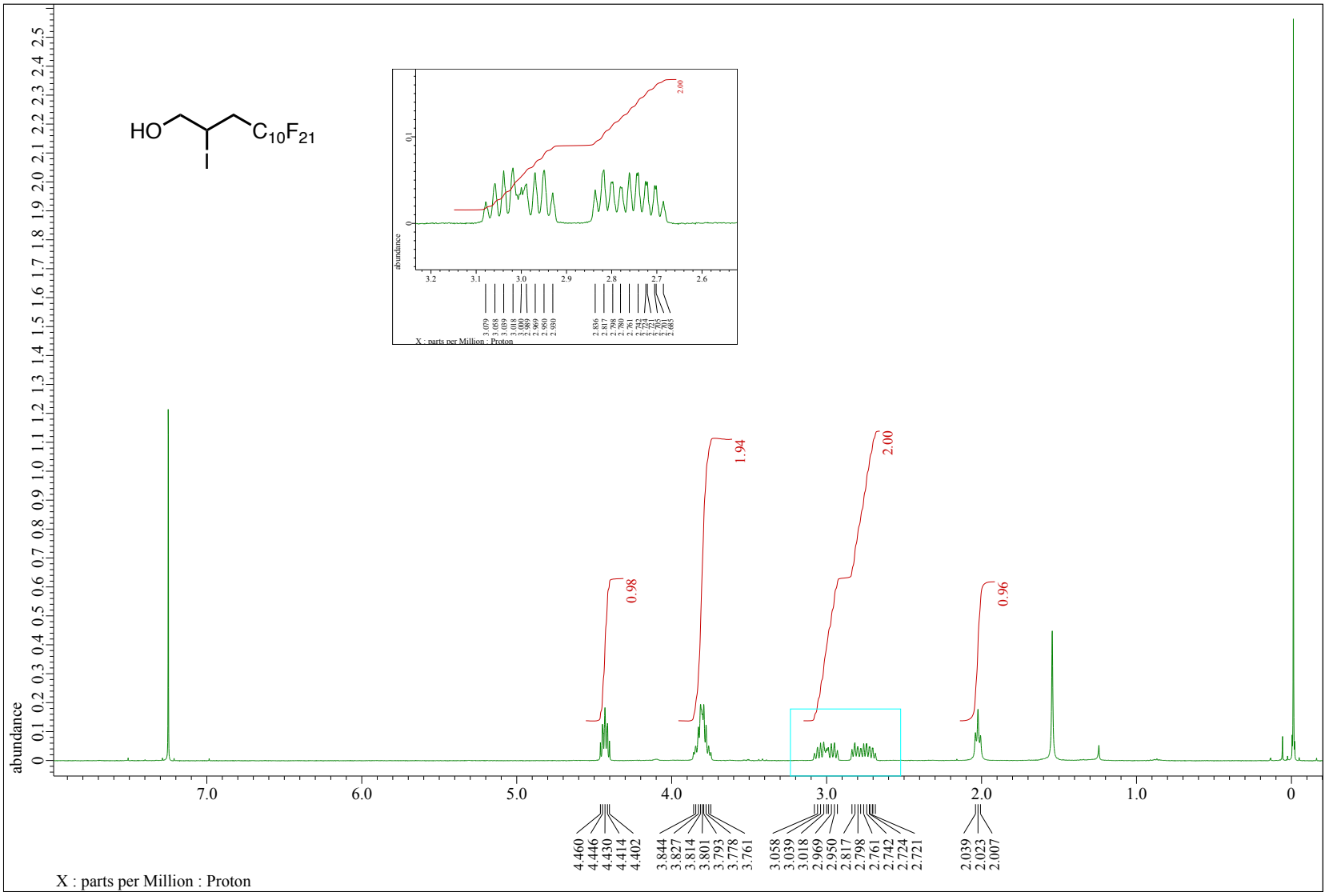
^{13}C NMR, 125 MHz, CD_3OD



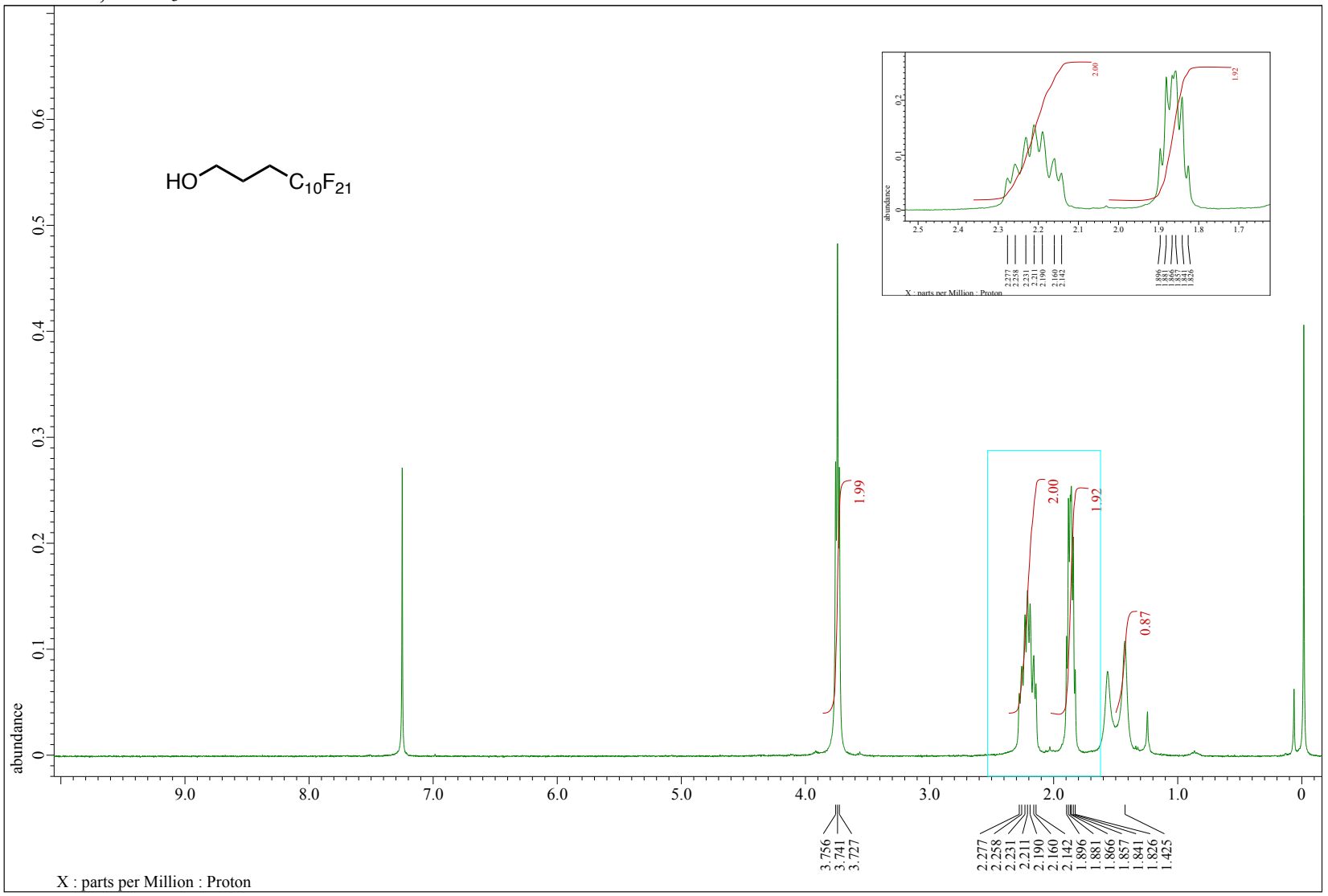
^{19}F NMR, 466 MHz, CD_3OD



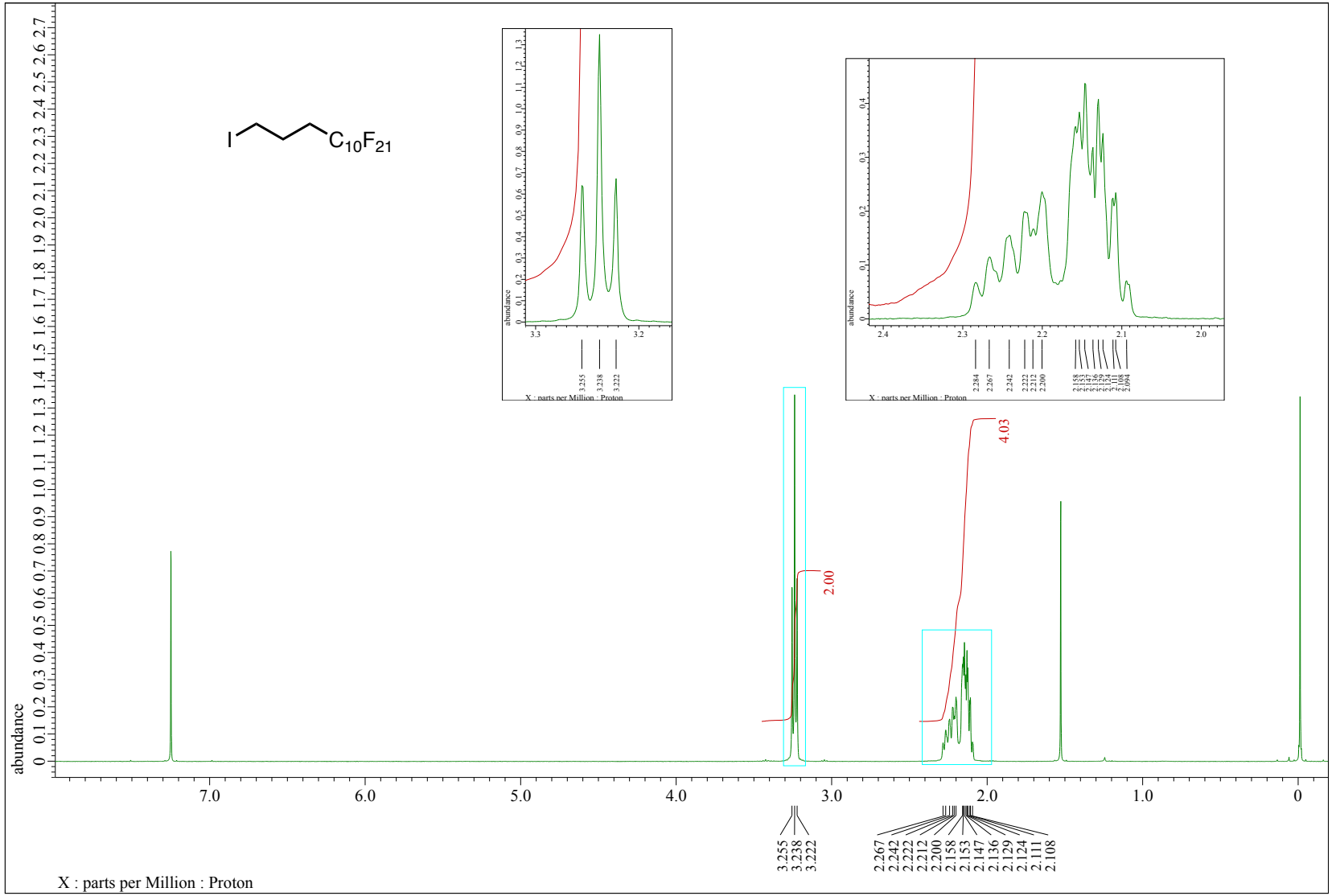
^{1}H NMR, 400 MHz, $CDCl_3$



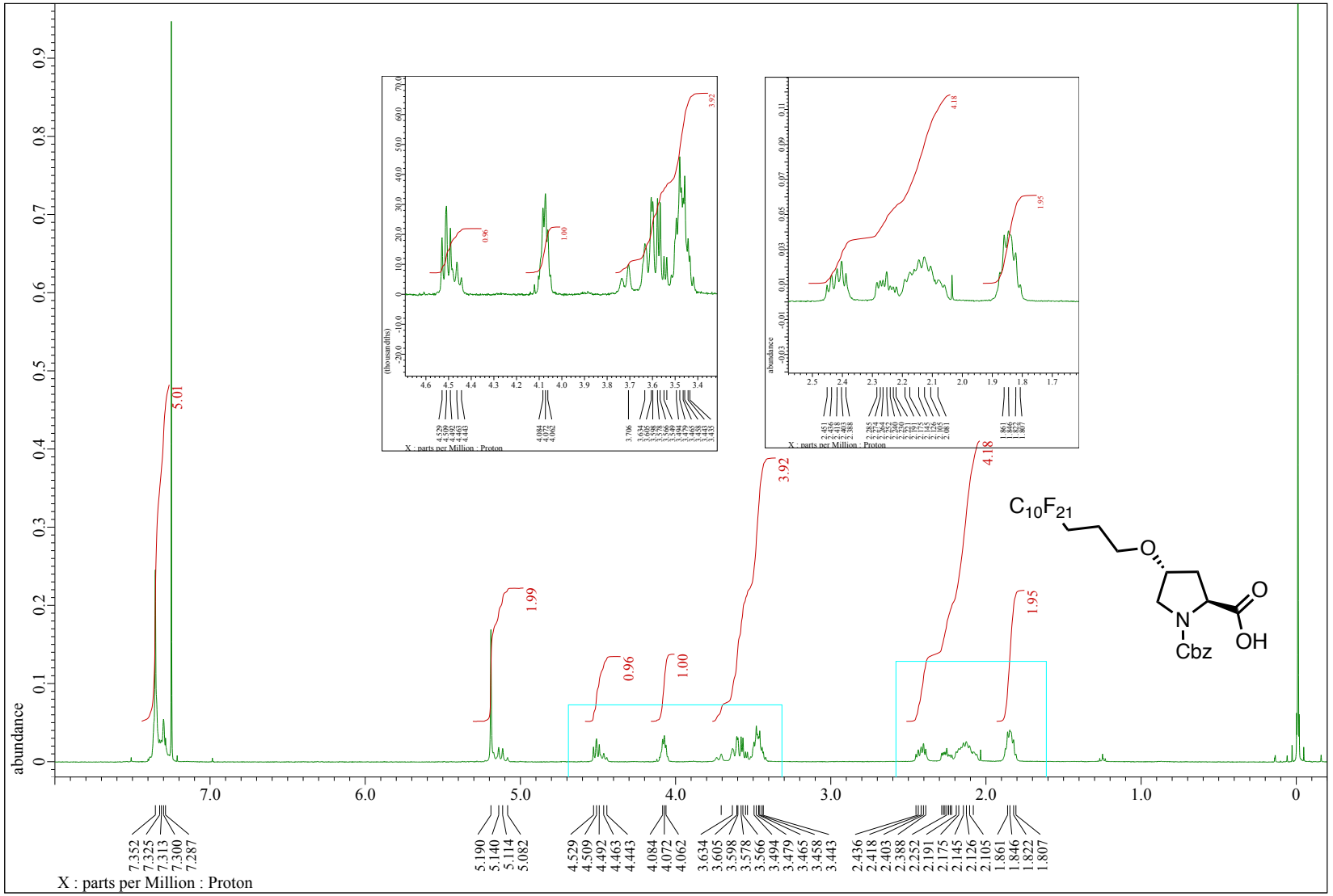
^{1}H NMR, 400 MHz, $CDCl_3$



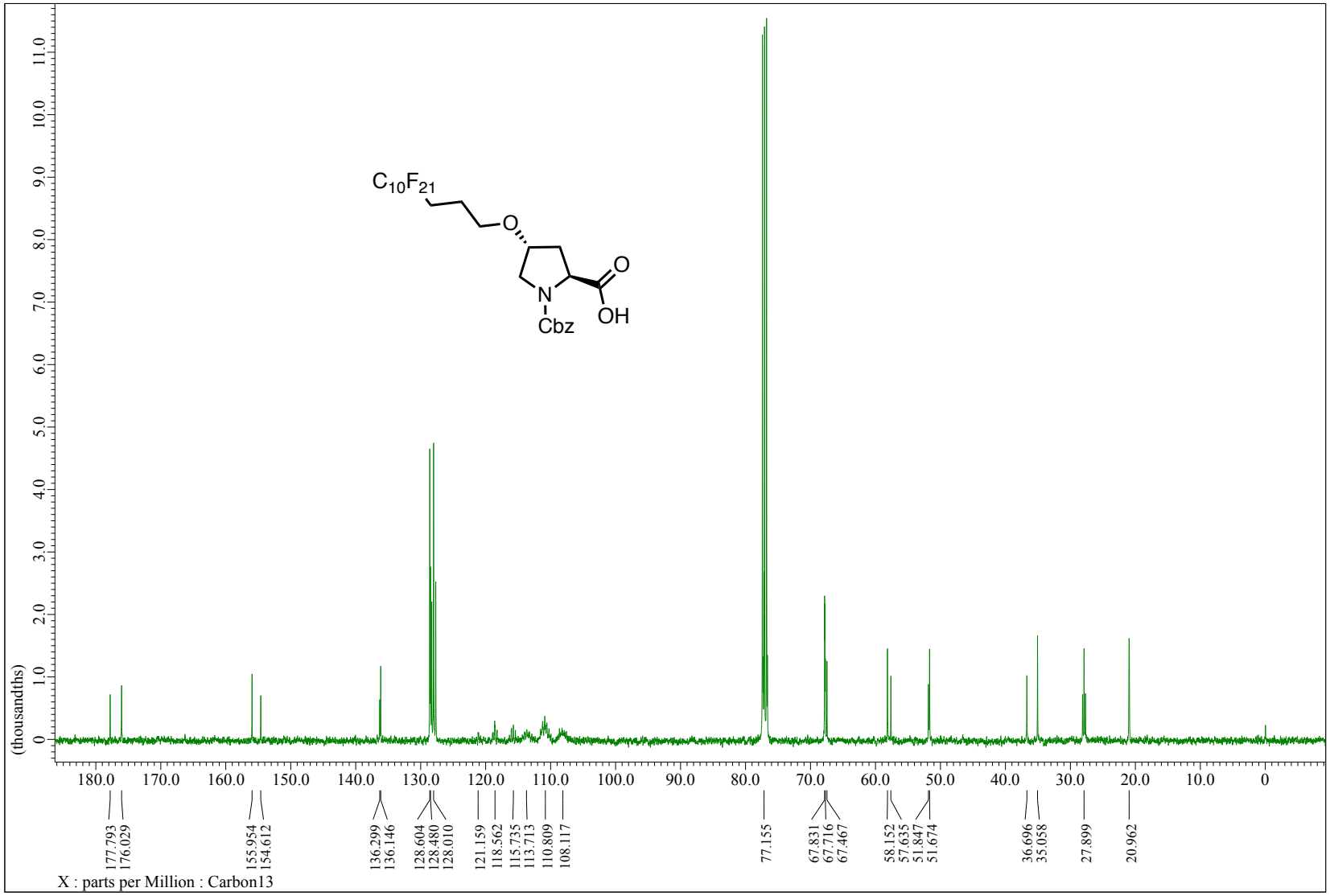
^{1}H NMR, 400 MHz, $CDCl_3$



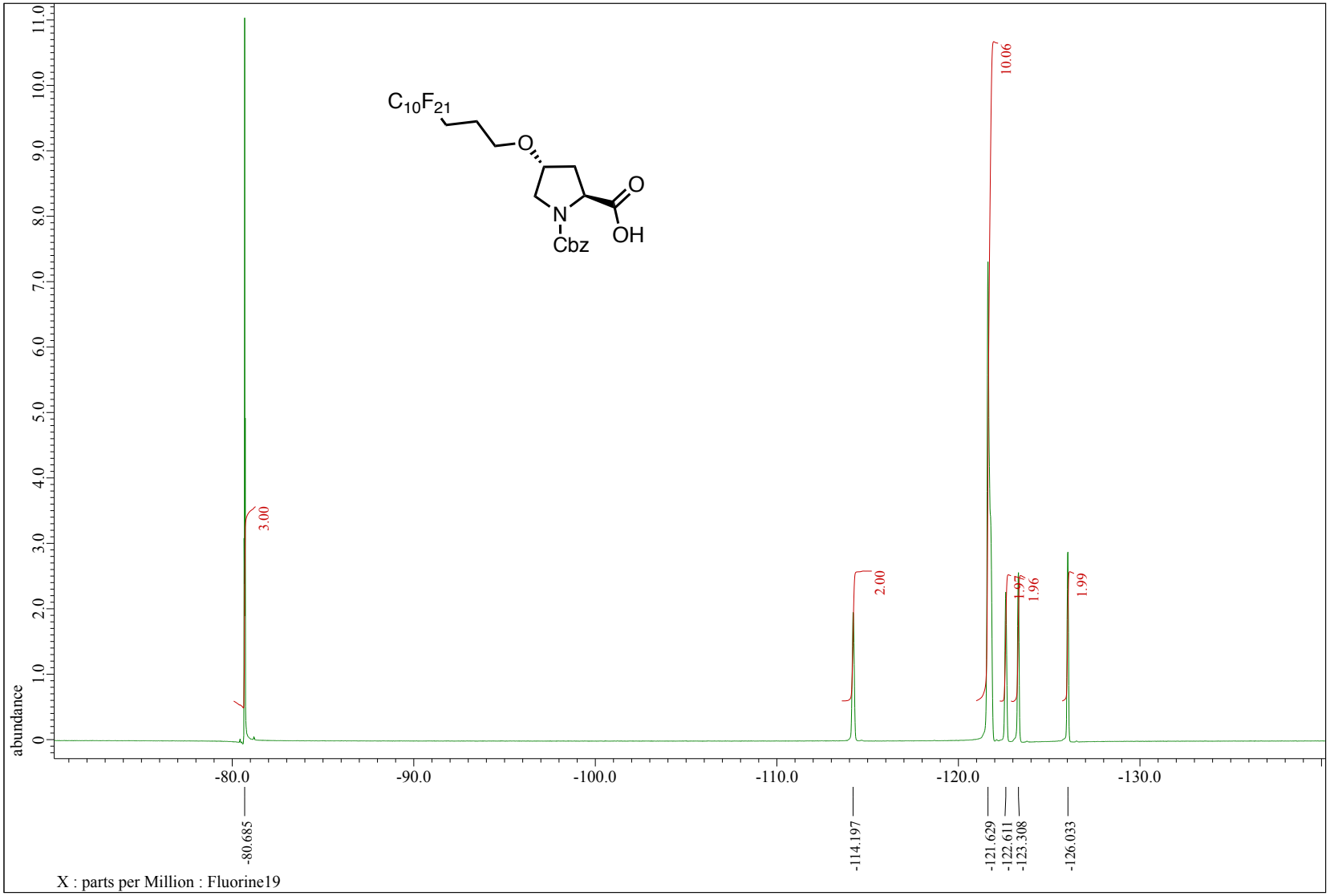
^{1}H NMR, 400 MHz, $CDCl_3$



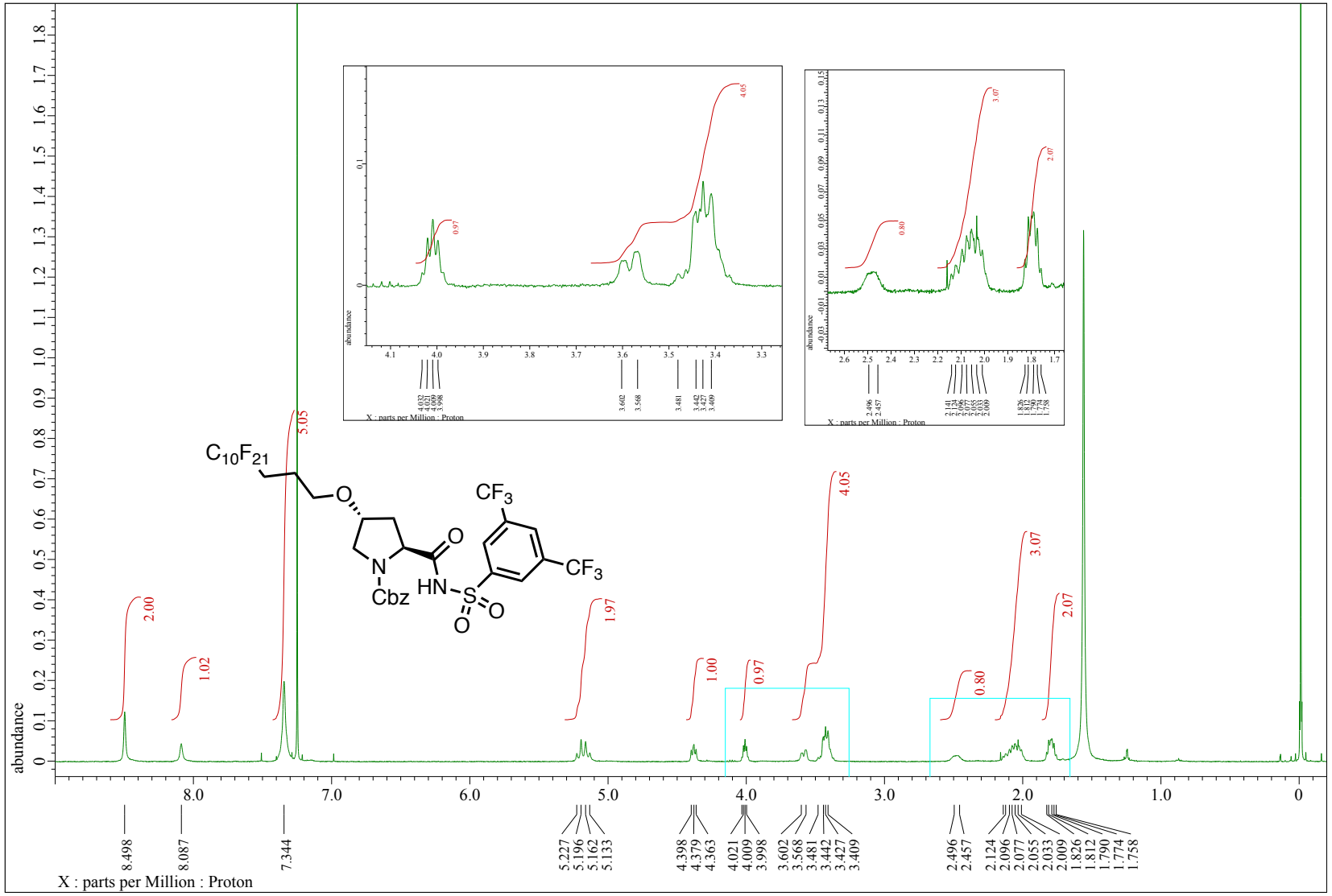
^{13}C NMR, 101 MHz, $CDCl_3$



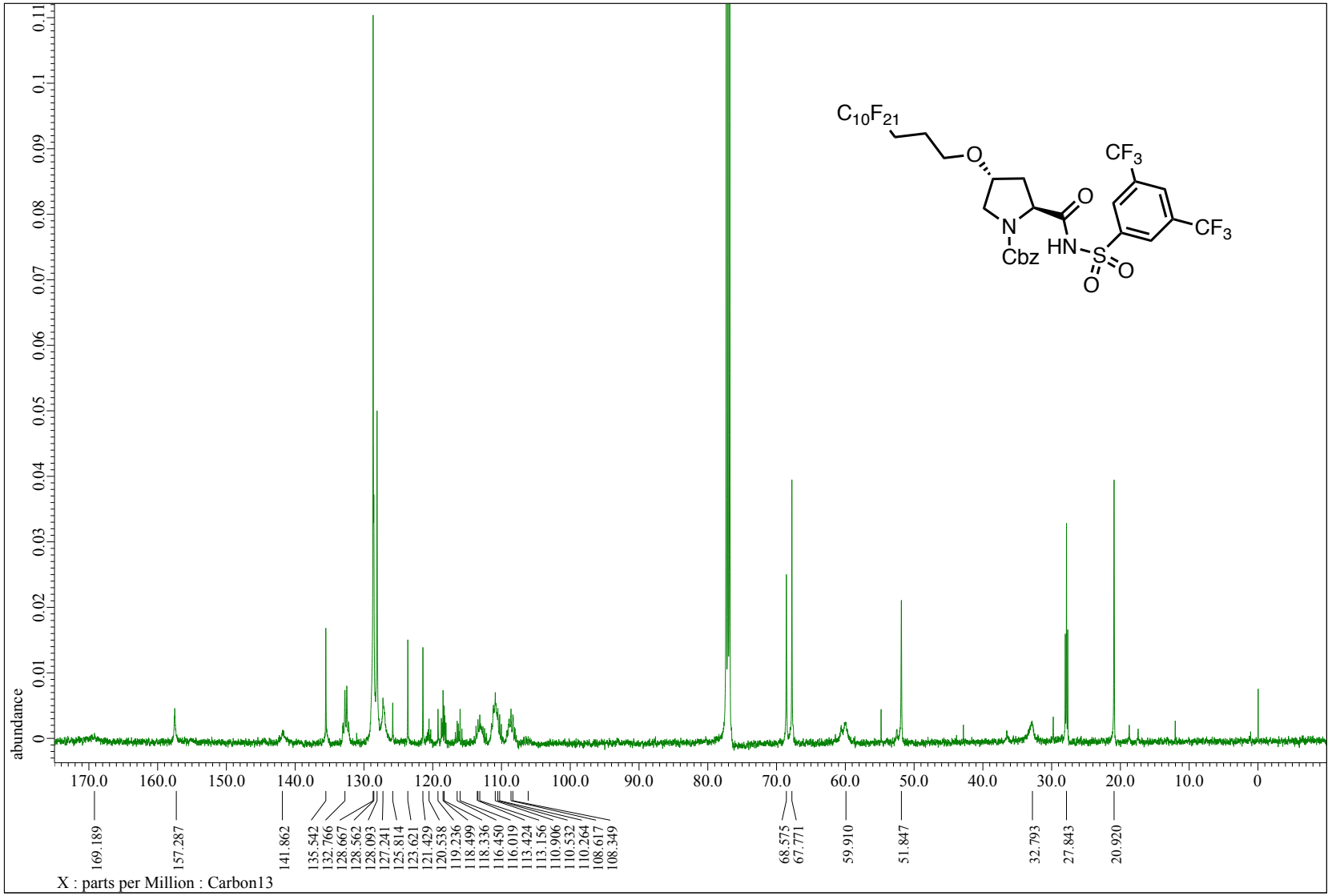
^{19}F NMR, 376 MHz, $CDCl_3$



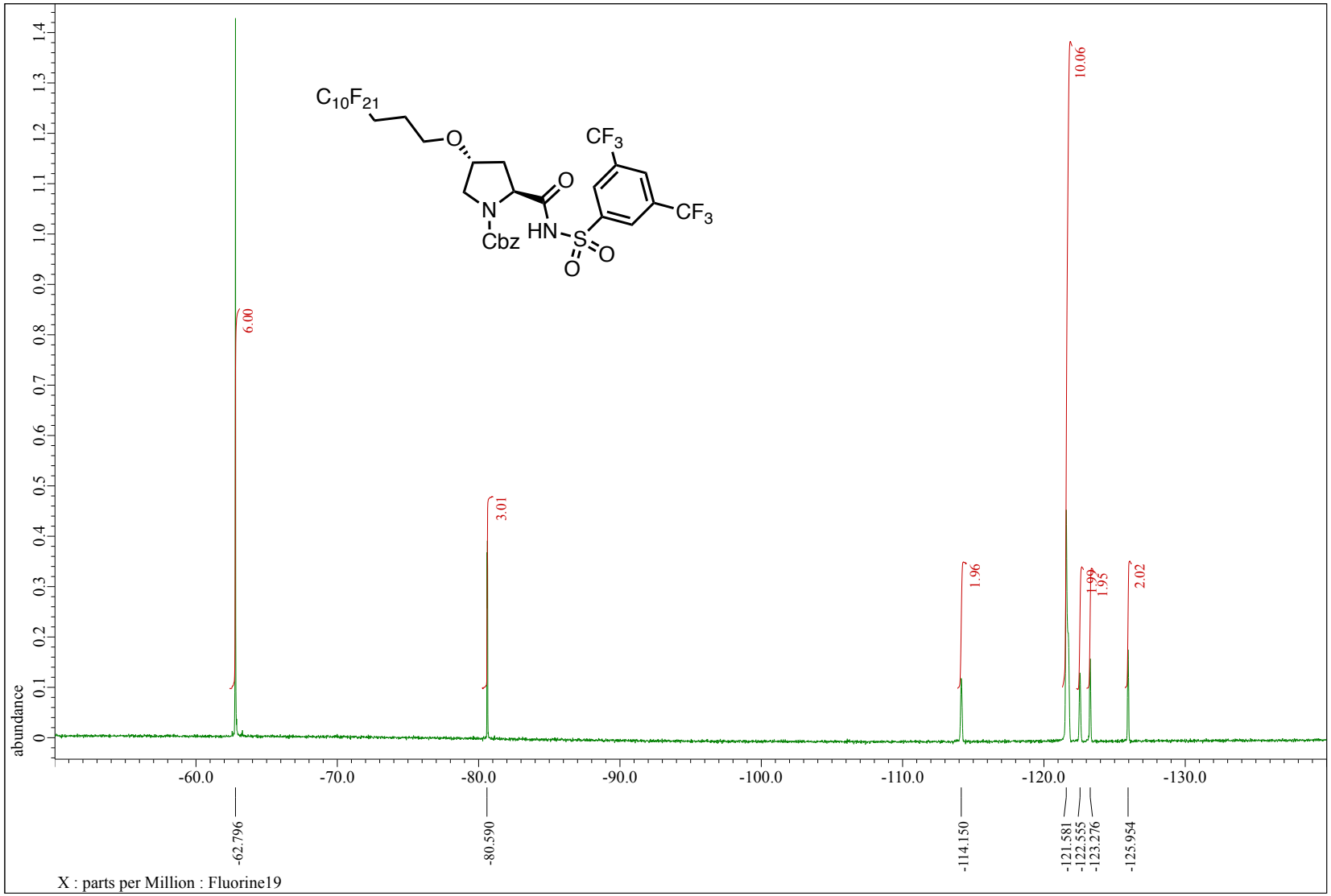
^{1}H NMR, 400 MHz, $CDCl_3$



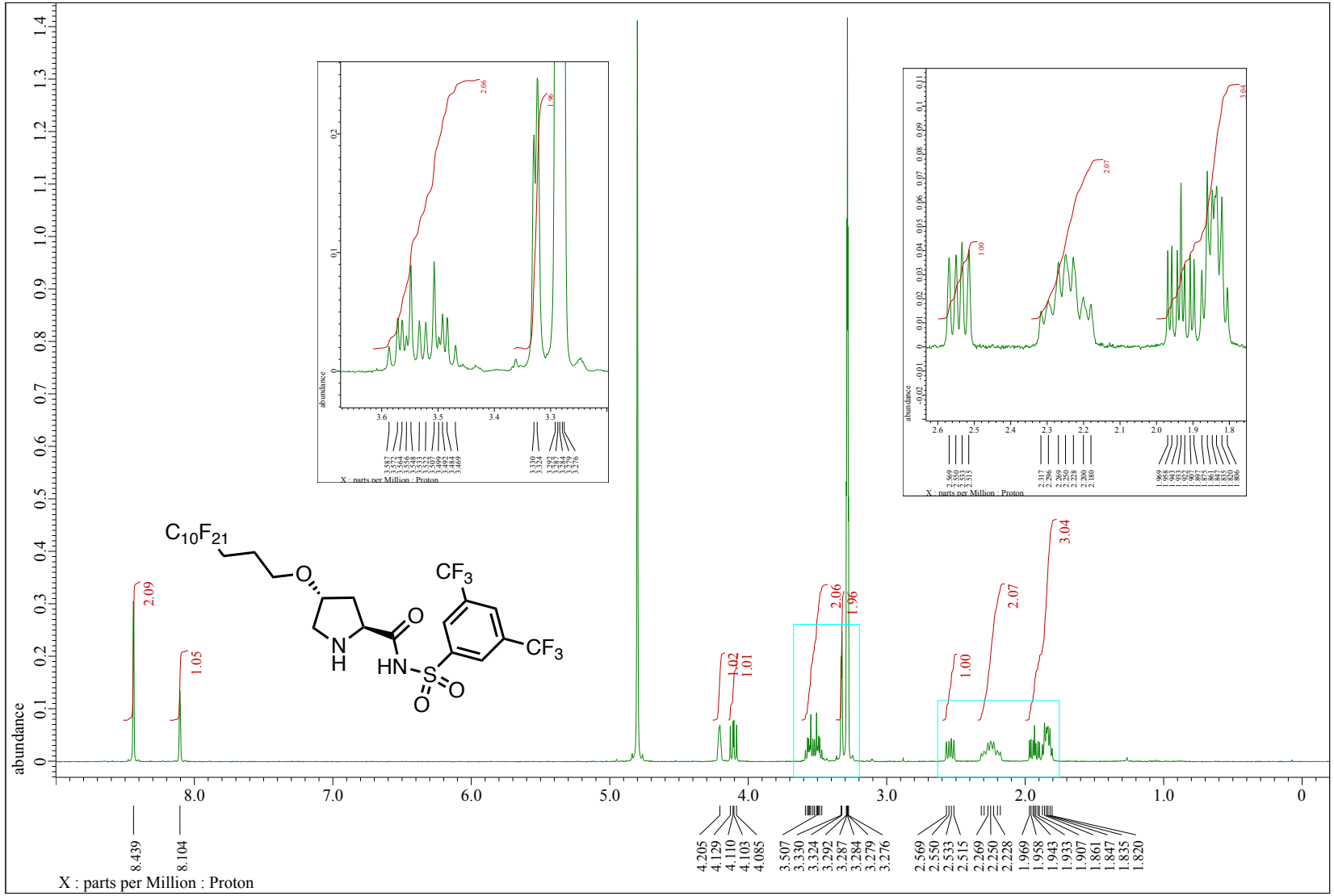
^{13}C NMR, 101 MHz, $CDCl_3$



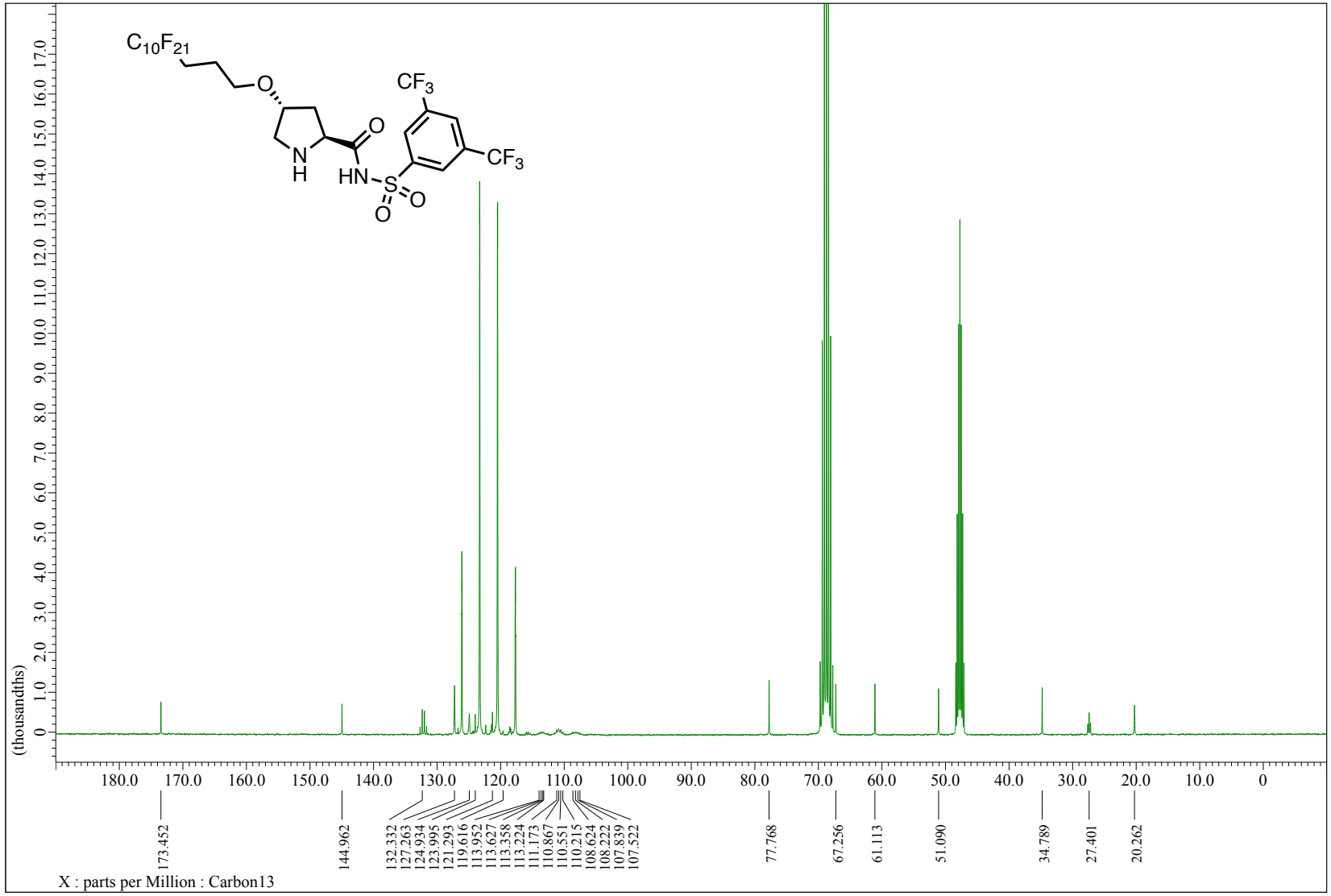
^{19}F NMR, 376 MHz, $CDCl_3$



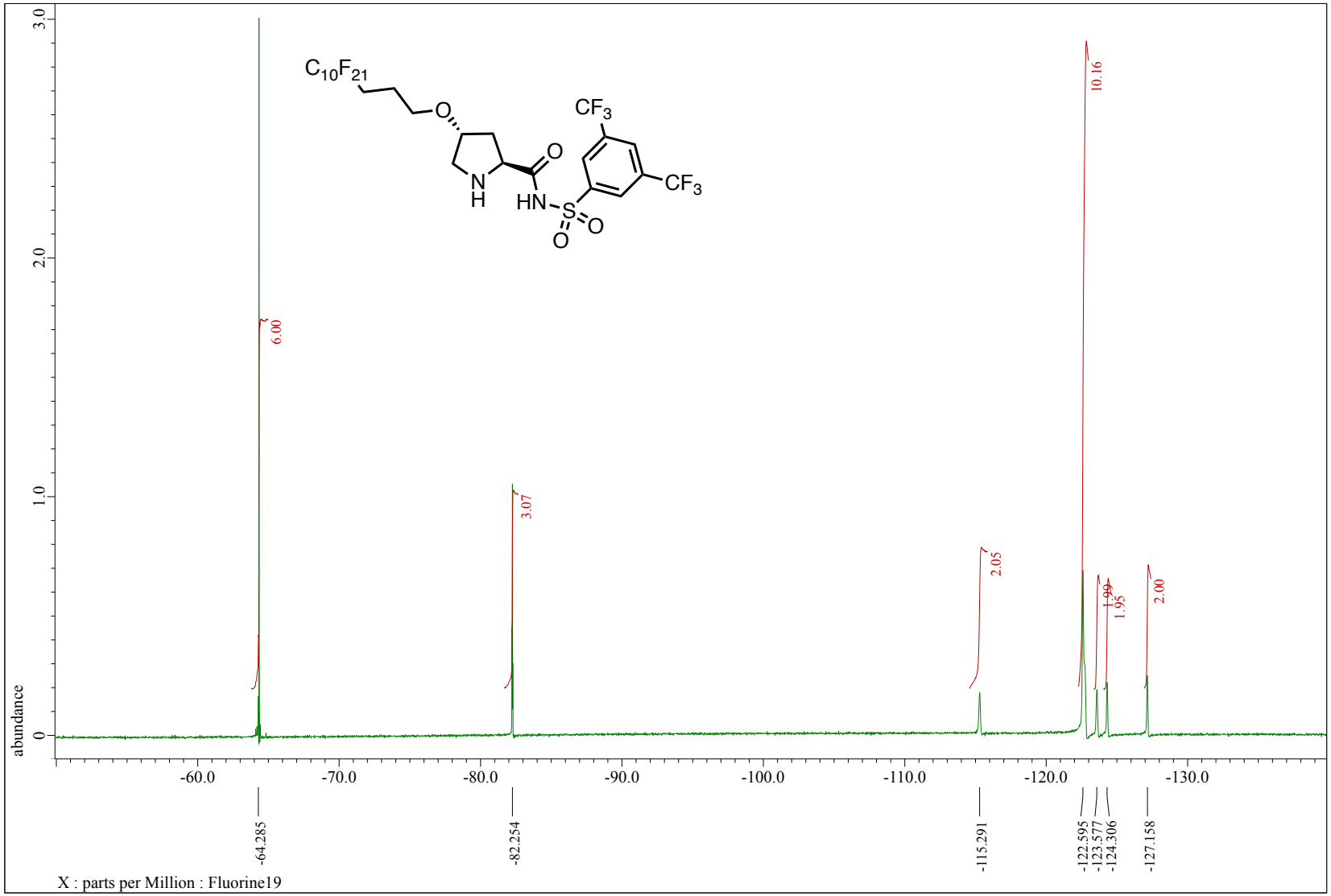
^{1}H NMR, 400 MHz, CD_3OD



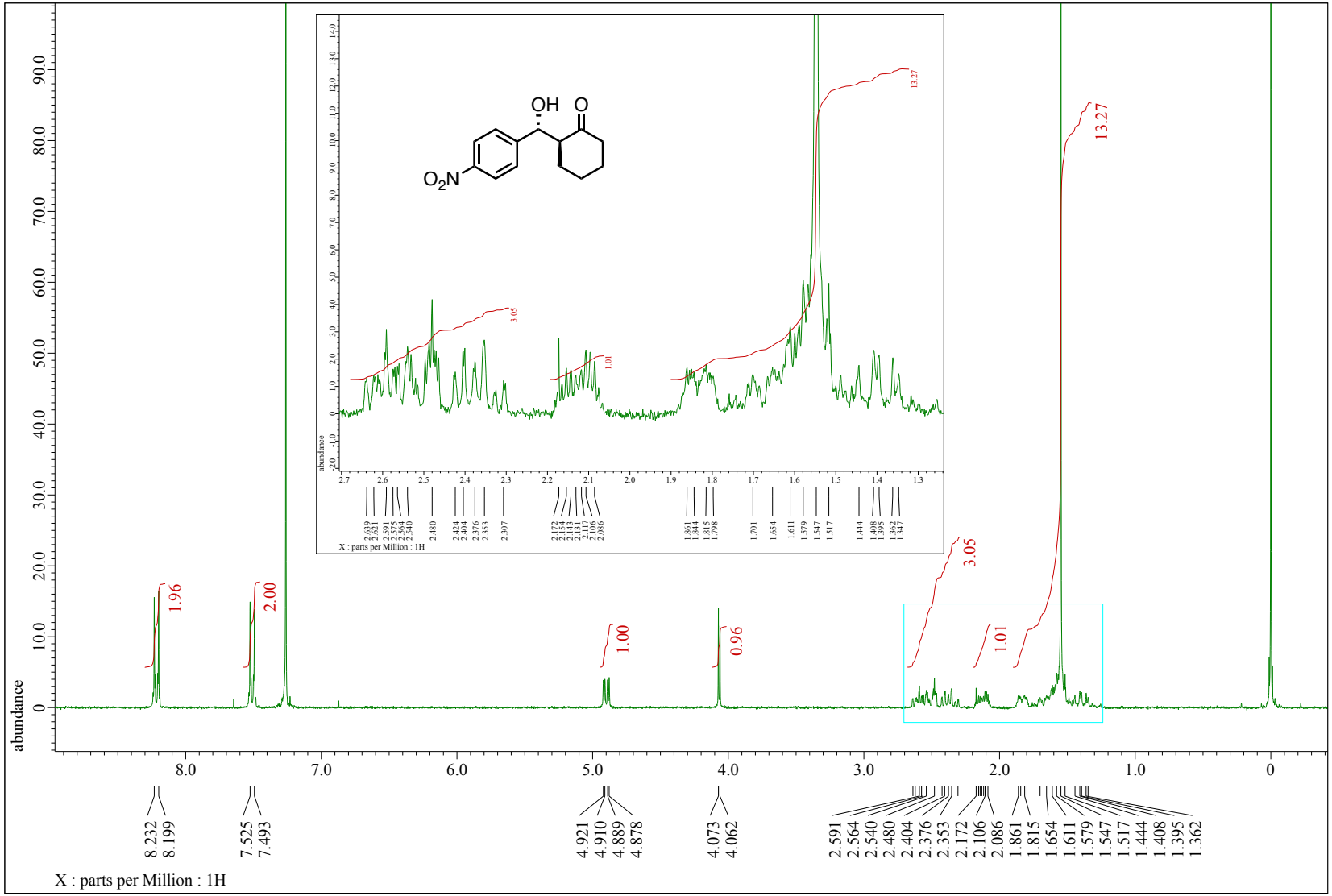
^{13}C NMR, 101 MHz, CD_3OD + Hexafluoroisopropanol



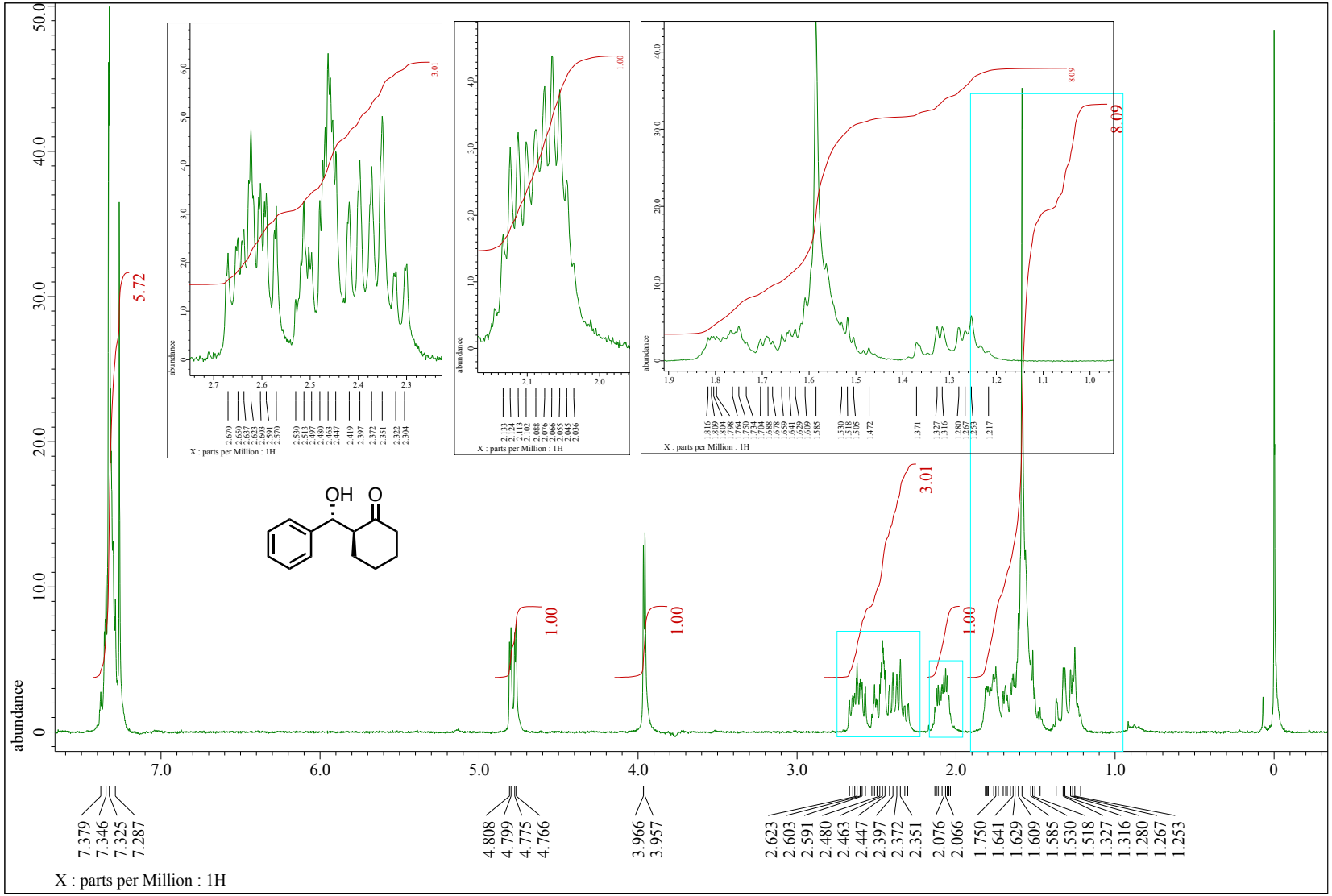
^{19}F NMR, 376 MHz, CD_3OD



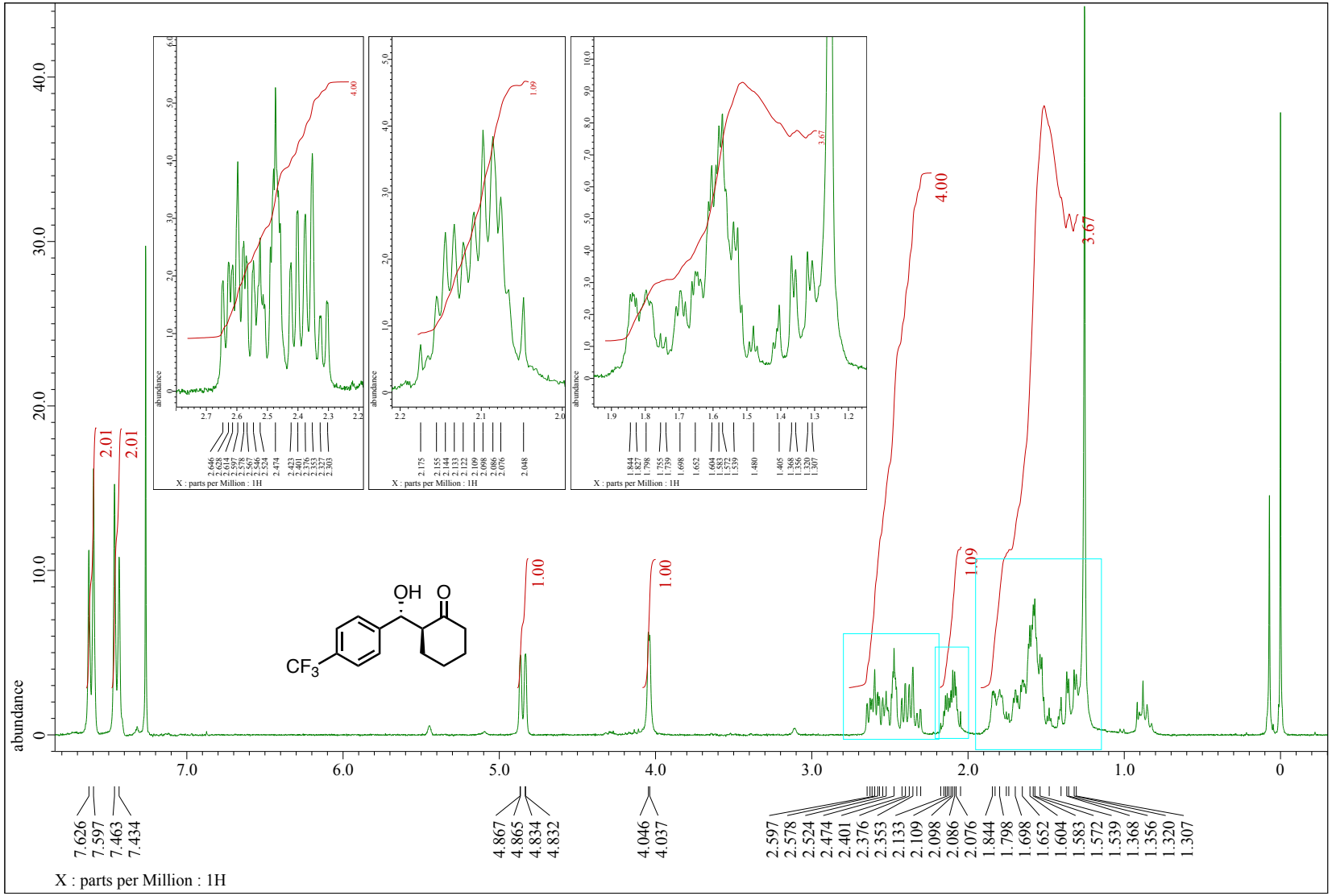
^{1}H NMR, 270 MHz, $CDCl_3$



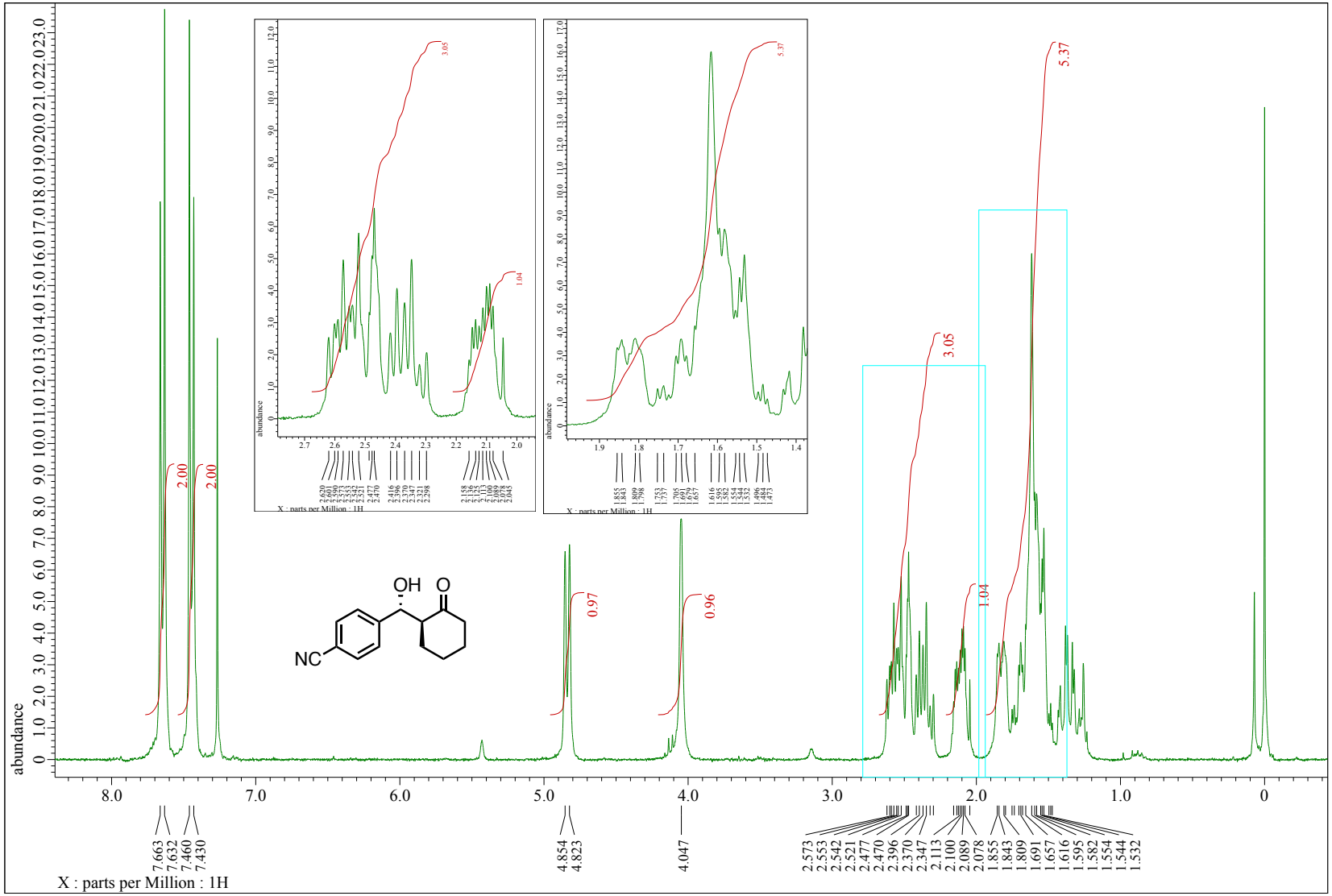
^{1}H NMR, 270 MHz, $CDCl_3$



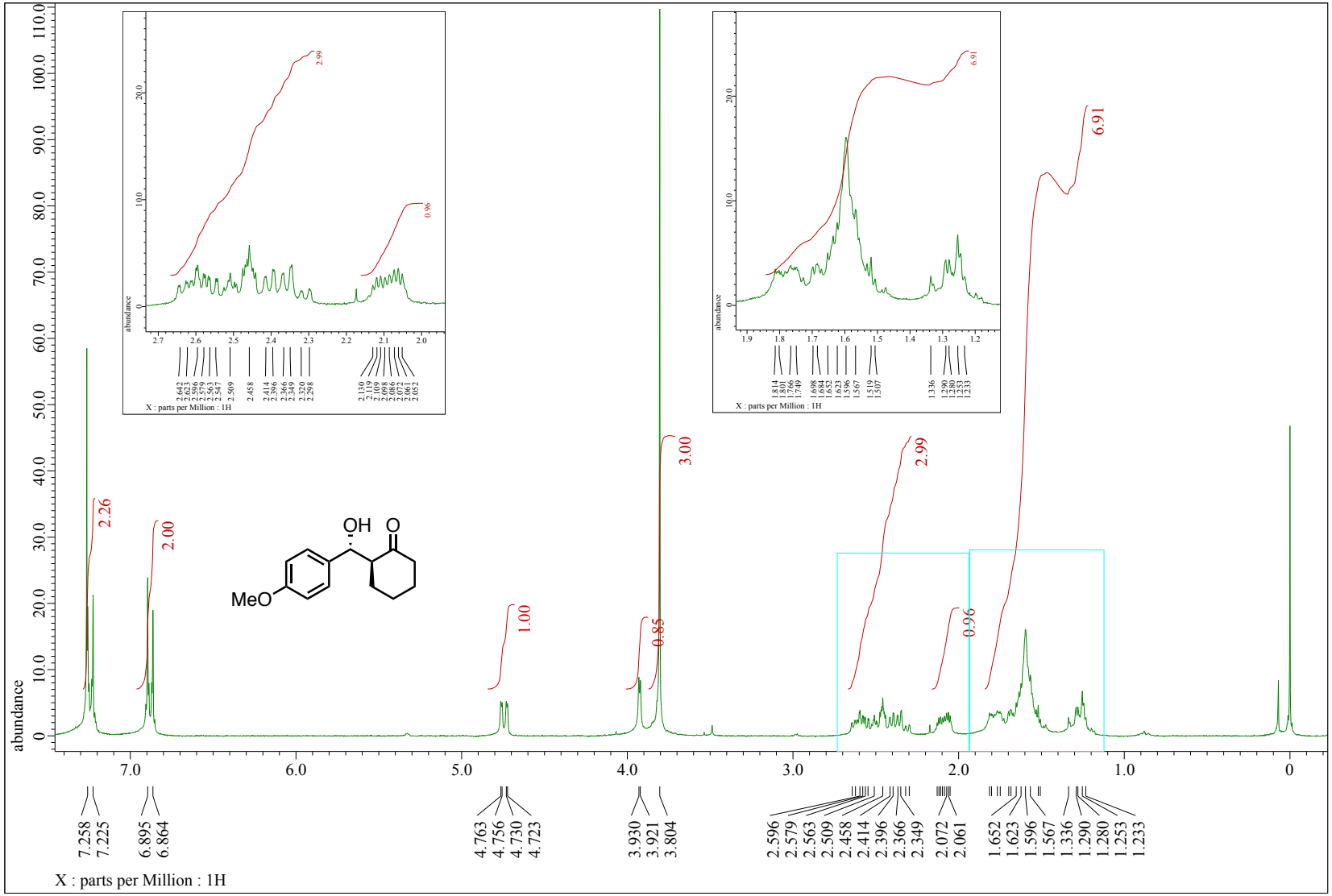
^{1}H NMR, 270 MHz, $CDCl_3$



^{1}H NMR, 270 MHz, $CDCl_3$



^{1}H NMR, 270 MHz, $CDCl_3$



^{1}H NMR, 270 MHz, $CDCl_3$