## ***SUPPORTING INFORMATION***

***Title:*** Tripeptide-Catalyzed Asymmmetric Aldol Reaction of Trifluoromethylated Aromatic Keotnes with Acetone

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**Content**



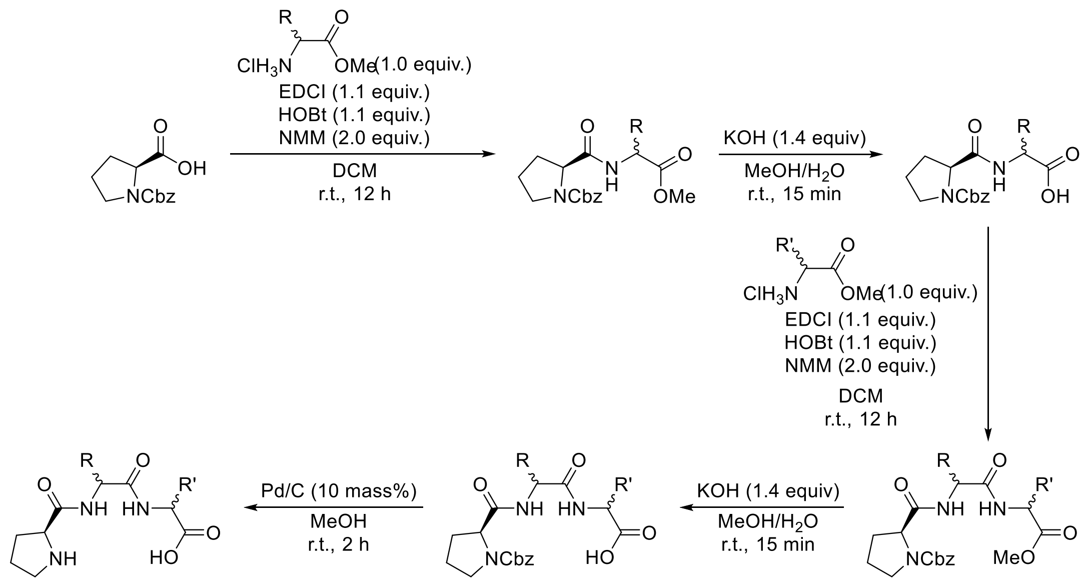
## 1. General

Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 40-50 μm. NMR spectra were recorded on a JEOL JNM-ECA600 spectrometer (1H, 600 MHz; 13C, 150 MHz). Chemical shifts of $^{1}$H NMR and $^{13}$C NMR signals reported δ ppm referenced to the solvent, an internal $SiMe_4$ or Sodium 3-(Trimethylsilyl)-1-propanesulfonate. HRMS were obtained at an ionization potential of 70 eV with a JEOL JMS-T100GCV spectrometer. Melting points were measured on AS ONE ATM-01 melting-point apparatus. Optical rotations were measured by JASCO P-1010 Polarimeter. HPLC analysis were performed with Daicel Chiralpak AD-H column (25 cm × 4.6 mm × 5 μm), Chiralpak OD-H column (25 cm × 4.6 mm × 5 μm) and Chiralpak AS-H column (25 cm × 4.6 mm × 5 μm). Absolute configurations of aldol adducts **4a**–**4f**, and **4i** were determined by comparison between **4a**–**4f**'s, and **4i's** optical rotation and previous reported optical rotation.[1]

## 2. Materials

All reagents and solvents were purchased from commercial sources and used without purification. Amino ester hydrochlorides were synthesised by the literature methods.[2] **1g**, **1h**, and **1j** were synthesised by previously reported method.[3]

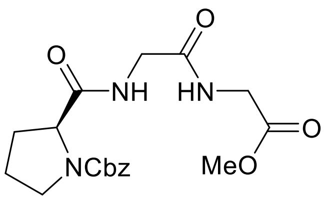
## 3. Preparation of the tripeptide catalysts




**Condensation between Cbz-Pro-OH and amino ester hydrochloride:** To a solution of Cbz-Pro-OH (20.0 mmol, 4.985 g) in $CH_2Cl_2$ (100 mL), Amino ester hydrochloride (20.0 mmol), HOBt (22.0 mmol, 2.973g), EDCI (22 mmol, 3.9 mL) and NMM (40 mmol, 4.4 mL) was added at 0 °C. The reaction mixture was stirred at room temperature for 12 h. The resulting mixture was concentrated under reduced pressure and was diluted by ethyl acetate. The mixture was washed with saturated aqueous $NaHCO_3$ (100 mL), 1M $HCl_{aq}$ (100 mL) and brine. The Organic phase was dried over $Na_2SO_4$. After removal of solvent under reduced pressure, the crude was purified through column chromatography on silica gel using *n*-hexane/ethyl acetate as eluent to give corresponding Cbz-protected dipeptide esters.

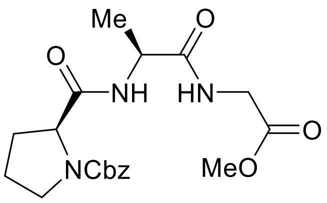
**Hydrolysis of Cbz-protected peptide esters:** To a solution of Cbz-protected peptide-esters (15.0 mmol) in MeOH (60 mL) and $H_2O$ (30 mL), KOH (21.0 mmol, 1.168 g) was added at room temperature. The reaction mixture was stirred at room temperature for 15 min and the resulting mixture was concentrated under reduced pressure. The mixture was extracted with ethyl acetate. To the aqueous phase, 1M $HCl_{aq}$ was added until pH 3. The aqueous phase was extracted with ethyl acetate. The organic phase was washed with brine and was dried over $Na_2SO_4$. After the removal of solvent under reduced pressure, corresponding Cbz-protected peptide was obtained.

**Condensation of between Cbz-protected dipeptide and amino ester hydrochloride:** To a solution of Cbz-protected dipeptide (10.0 mmol) in $CH_2Cl_2$ (100 mL), Amino ester hydrochloride (10.0 mmol), HOBt (11.0 mmol, 1.483g), EDCI (11 mmol, 2.0 mL) and NMM (20 mmol, 2.2 mL) was added at 0 °C. The reaction mixture was stirred at room temperature for 12 h. The resulting mixture was concentrated under reduced pressure and was diluted by ethyl acetate. The mixture was washed with saturated aqueous $NaHCO_3$ (50 mL), 1M $HCl_{aq}$ (50 mL) and brine. The Organic phase was dried over $Na_2SO_4$. After removal of solvent under reduced pressure, the crude was purified through column chromatography on silica gel using $CHCl_3$/MeOH as eluent to give corresponding Cbz-protected tripeptide esters.




**Cbz-Pro-Gly-Gly-OMe**

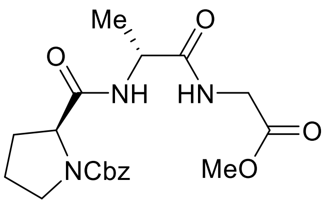
71% yield, $^1$H NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 7.93 (1H, s), 7.83 (1H, s), 7.37-7.27 (5H, m), 5.09 (1H, d, *J* = 12.9 Hz), 5.06 (1H, d, *J* = 12.9 Hz), 4.30-4.20 (1H, m), 3.86 (2H, d, *J* = 5.8 Hz), 3.78 (1H, dd, *J* = 16.7, 5.8 Hz), 3.73 (1H, dd, *J* = 16.7, 5.3 Hz), 3.65 (3H, s), 3.53-3.42 (2H, m), 2.18-2.10 (1H, m), 1.97-1.87 (2H, m), 1.86-1.78 (1H, m). $^{13}$C NMR (150 MHz, DMSO-$d_6$, VT 100 °C) δ: 172.2, 169.9, 169.1, 154.3, 137.0, 128.2, 127.5, 127.2, 66.1, 60.1, 51.5, 46.8, 42.1, 40.7, 30.3, 23.5. HRMS (EI): *m/z* cald for $C_{18}H_{23}N_3O_6$[$M^+$]: 377.1587; found: 377.1564. m.p. 104-105 °C; $[\alpha]_D^{30}$ = -28.2 (c = 0.11 in MeOH)




**Cbz-Pro-Ala-Gly-OMe**

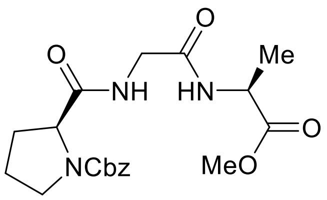
90% yield, $^1$H NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 7.85 (1H, s), 7.75 (1H, s), 7.36-7.28 (5H, m), 5.08 (1H, d, *J* = 12.9 Hz), 5.04 (1H, d, *J* = 12.9 Hz), 4.36-4.31 (1H, m), 4.28 (1H, dd, *J* = 8.6, 3.4 Hz), 3.90-3.80 (2H, m), 3.65 (3H, s), 3.49-3.41 (2H, m), 2.16-2.09 (1H, m), 1.95-1.86 (2H, m), 1.85-1.78 (1H, m), 1.28-1.19 (3H, m). $^{13}$C NMR (150 MHz, DMSO-$d_6$, VT 100 °C) δ: 172.5, 171.7, 170.0, 154.3, 137.1, 128.2, 127.6, 127.2, 66.1, 59.8, 51.5, 48.2, 46.9, 40.8, 30.3, 23.4, 17.8. HRMS (EI): *m/z* cald for $C_{19}H_{25}N_3O_6$[$M^+$]:

391.1743; found: 391.1771. m.p. 124-125 °C; $[\alpha]_D^{22}$ = -85.5 (c = 0.42 in MeOH)



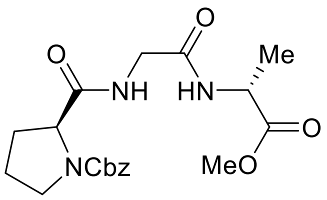

**Cbz-Pro-D-Ala-Gly-OMe**

85% yield, $^1$H NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 7.88 (1H, s), 7.80 (1H, s), 7.39-7.27 (5H, m), 5.07 (2H, s), 4.37-4.32 (1H, m), 4.26 (1H, dd, *J* = 8.2, 3.4 Hz), 3.83 (2H, d, *J* = 5.8 Hz), 3.64 (3H, s), 3.53-3.42 (2H, m), 2.17-2.10 (1H, m), 1.95-1.86 (2H, m), 1.85-1.78 (1H, m), 1.24 (3H, d, *J* = 7.2 Hz). $^{13}$C NMR (150 MHz, DMSO-$d_6$, VT 100 °C) δ: 172.4, 171.7, 169.9, 154.4, 137.1, 128.2, 127.6, 127.2, 66.1, 60.1, 51.5, 48.2, 46.9, 40.8, 30.3, 23.6, 17.9. HRMS (EI): *m/z* cald for $C_{19}H_{25}N_3O_6[M^+]$: 391.1743; found: 391.1718. $[\alpha]_D^{23}$ = 5.1 (c = 0.16 in MeOH)



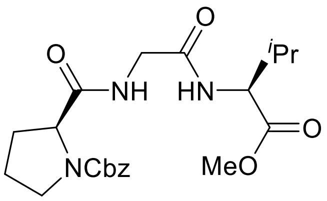

**Cbz-Pro-Gly-Ala-OMe**

82% yield, $^1$H NMR (600MHz, DMSO-$d_6$, VT 100 °C) δ: 7.93 (1H, s), 7.79 (1H, s), 7.37-7.28 (5H, m), 5.10 (1H, d, *J* = 12.9 Hz), 5.06 (1H, d, *J* = 12.9 Hz), 4.36-4.32 (1H, m), 4.27-4.25 (1H, m), 3.79-3.69 (2H, m), 3.65 (3H, s), 3.51-3.42 (2H, m), 2.18-2.10 (1H, m), 1.95-1.88 (2H, m), 1.85-1.79 (1H, m), 1.30 (3H, d, *J* = 7.2 Hz). $^{13}$C NMR (150 MHz, DMSO-$d_6$, VT 100 °C) δ: 172.1, 171.7, 168.0, 153.7, 136.5, 127.7, 127.0, 126.7, 65.5, 59.6, 51.1, 47.1, 46.3, 41.6, 29.7, 23.0, 16.6. HRMS (EI): *m/z* cald for $C_{19}H_{25}N_3O_6[M^+]$: 391.1743; found: 391.1743. $[\alpha]_D^{30}$ = -46.2 (c = 0.43 in MeOH)



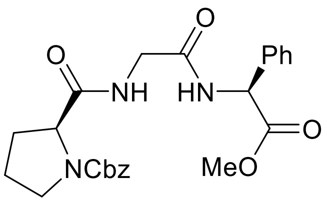

**Cbz-Pro-Gly-D-Ala-OMe**

89% yield, $^1$H NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 7.90 (1H, s), 7.80 (1H, s), 7.37-7.28 (5H, m), 5.10 (1H, d, *J* = 12.7 Hz), 5.06 (1H, d, *J* = 12.7 Hz), 4.37-4.32 (1H, m), 4.27-4.24 (1H, m), 3.74 (2H, d, *J* = 5.8 Hz), 3.64 (3H, s), 3.53-3.48 (1H, m), 3.47-3.43 (1H, m), 2.17-2.11 (1H, m), 1.95-1.87 (2H, m), 1.85-1.79 (1H, m), 1.31 (3H, d, *J* = 7.2 Hz). $^{13}$C NMR (150 MHz, DMSO-$d_6$, VT 100 °C) δ: 172.1, 171.6, 168.0, 153.8, 136.5, 127.7, 127.0, 126.7, 65.6, 59.7, 51.2, 47.1, 46.3, 41.6, 29.8, 23.0, 16.6. HRMS (EI): *m/z* cald for $C_{19}H_{25}N_3O_6[M^+]$: 391.1743; found: 391.1720. m.p. 132-133 °C; $[\alpha]_D^{30}$ = 47.5 (c = 0.43 in MeOH)




**Cbz-Pro-Gly-Val-OMe**

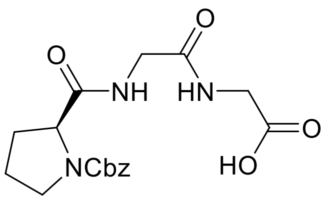
88% yield, $^1$H NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 7.94 (1H, s), 7.62 (1H, s), 7.36-7.29 (5H, m), 5.10 (1H, d, *J* = 12.9 Hz), 5.06 (1H, d, *J* = 12.9 Hz), 4.35-4.19 (2H, m), 3.82-3.74 (2H, m), 3.66 (3H, s), 3.53-3.43 (2H, m), 2.17-2.11 (1H, m), 2.09-2.02 (1H, m), 1.95-1.88 (2H, m), 1.86-1.80 (1H, m), 0.90 (3H, d, J = 1.7 Hz), 0.89 (3H, d, *J* = 1.7 Hz). $^{13}$C NMR (150 MHz, DMSO-$d_6$, VT 100 °C) δ: 172.4, 171.6, 169.0, 154.3, 137.1, 128.3, 127.6, 127.2, 66.1, 60.1, 57.5, 51.4, 46.9, 42.3, 30.2, 23.5, 18.7, 18.1. HRMS (EI): *m/z* cald for $C_{21}H_{29}N_3O_6[M^+]$: 419.2056; found: 419.2072. $[\alpha]_D^{25}$ = -53.6 (c = 0.60 in MeOH)




**Cbz-Pro-Gly-Phg-OMe**

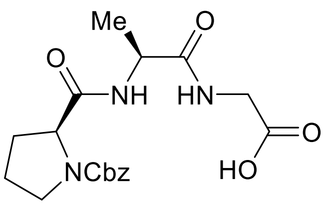
96% yield, $^1$H NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 8.26 (1H, s), 7.94 (1H, s), 7.39-7.28 (10H, m), 5.49 (1H, d, *J* = 7.6 Hz), 5.05 (1H, d, *J* = 12.7 Hz), 4.99 (1H, d, *J* = 12.7 Hz), 4.27 (1H, dd, *J* = 8.4, 3.3 Hz), 3.85 (1H, dd, *J* = 16.6, 5.7 Hz), 3.79 (1H, dd, *J* = 16.6, 5.7 Hz), 3.66 (3H, s), 3.54-3.41 (2H, m), 2.17-2.10 (1H, m), 1.94-1.86 (2H, m), 1.85-1.78 (1H, m). $^{13}$C NMR (150 MHz, DMSO-$d_6$, 100 °C) δ: 172.3, 170.7, 168.7, 154.3, 137.1, 136.5, 128.6, 128.2, 128.1, 127.6, 127.5, 127.2, 66.0, 60.1, 56.3, 52.1, 46.8, 42.1, 30.4, 23.5. HRMS (EI): *m/z* cald for $C_{24}H_{27}N_3O_6[M^+]$: 453.1900; found: 453.1892. m.p. 137-138 °C; $[\alpha]_D^{25}$ = 35.9 (c = 0.54 in MeOH)

**Hydrolysis of Cbz-protected peptide esters:** To a solution of Cbz-protected peptide-esters (5.0 mmol) in MeOH (40 mL) and $H_2O$ (20 mL), KOH (7.0 mmol, 39.3 mg) was added at room temperature. The reaction mixture was stirred at room temperature for 15 min and the resulting mixture was concentrated under reduced pressure. The mixture was extracted with ethyl acetate. To the aqueous phase, 1M $HCl_{aq}$ was added until pH = 3. The aqueous phase was extracted with ethyl acetate. The organic phase was washed with brine and was dried over $Na_2SO_4$. After the removal of solvent under reduced pressure, corresponding Cbz-protected peptide was obtained.



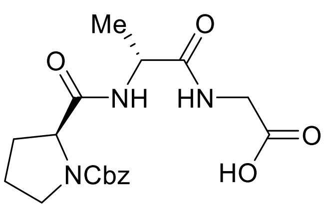
**Cbz-Pro-Gly-Gly-OH**

80% yield, $^1$H NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 12.18 (1H, br s), 7.91 (1H, s), 7.70 (1H, s), 7.36-7.29 (5H, m), 5.09 (1H, d, *J* = 12.6 Hz), 5.05 (1H, d, *J* = 12.6 Hz), 4.28-4.24 (1H, m), 3.82-3.69 (4H, m), 3.51-3.41 (2H, m), 2.18-2.10 (1H, m), 1.97-1.87 (2H, m), 1.85-1.79 (1H, m). $^{13}$C NMR (150 MHz, DMSO-$d_6$, VT 100 °C) δ: 171.7, 170.1, 168.4, 153.8, 136.5, 127.7, 127.0, 126.7, 65.6, 59.6, 46.3, 41.6, 40.3, 29.8, 23.0. HRMS (EI): *m/z* cald for $C_{17}H_{21}N_3O_6$[$M^+$]: 363.1430; found: 363.1443. m.p. 69-70 °C; $[\alpha]_D^{29}$ = -43.2 (c = 0.17 in MeOH)



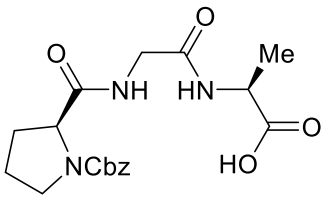
**Cbz-Pro-Ala-Gly-OH**

82% yield, $^1$H NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 12.10 (1H, br s), 7.76 (1H, s), 7.72 (1H, s), 7.36-7.29 (5H, m), 5.08 (1H, d, *J* = 12.4 Hz), 5.04 (1H, d, *J* = 12.4 Hz), 4.36-4.31 (1H, m), 4.28 (1H, d, *J* = 6.4 Hz), 3.80 (1H, dd, *J* = 17.2, 5.5 Hz), 3.75 (1H, dd, *J* = 17.2, 5.5 Hz), 3.49-3.41 (2H, m), 2.20-2.07 (1H, m), 1.98-1.85 (2H, m), 1.83-1.77 (1H, m), 1.21 (3H, s). $^{13}$C NMR (150 MHz, DMSO-$d_6$, VT 100 °C) δ: 172.3, 171.6, 170.6, 154.2, 137.1, 128.2, 127.6, 127.2, 66.0, 59.8, 48.2, 46.9, 40.9, 30.4, 23.4, 17.9. HRMS (EI): *m/z* cald for $C_{18}H_{23}N_3O_6$ [$M^+$]: 377.1587; found: 377.1579. m.p. 66-67 °C; $[\alpha]_D^{23}$ = -88.7 (c = 0.077 in MeOH)



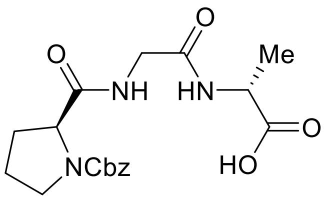
**Cbz-Pro-D-Ala-Gly-OH**

38% yield, $^1$H NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 12.18 (1H, br s), 7.77 (2H, s), 7.40-7.25 (5H, m), 5.07 (2H, s), 4.36-4.31 (1H, m), 4.26 (1H, dd, *J* = 7.9, 2.4 Hz), 3.75 (2H, d, *J* = 6.2 Hz), 3.50-3.41 (2H, m), 2.17-2.08 (1H, m), 1.99-1.86 (2H, m), 1.84-1.78 (1H, m), 1.24 (3H, d, *J* = 6.9 Hz). $^{13}$C NMR (150 MHz, DMSO-d$_6$, VT 100 °C) δ: 172.2, 171.6, 170.5, 154.3, 137.0, 128.2, 127.5, 127.2, 66.1, 60.1, 48.2, 46.9, 40.9, 30.3, 23.6, 17.9. HRMS (EI): *m/z* cald for $C_{18}H_{23}N_3O_6$ [M$^+$]: 377.1587; found: 377.1587. m.p. 211-212 °C; $[\alpha]_D^{24}$ = -9.4 (c = 0.16 in MeOH)



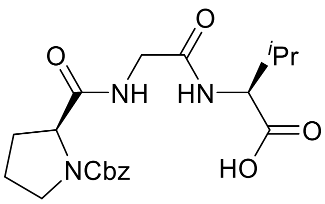

**Cbz-Pro-Gly-Ala-OH**

64% yield, $^1$H NMR (600 MHz, DMSO-d$_6$, VT 100 °C) δ: 12.12 (1H, br s), 7.92 (1H, s), 7.64 (1H, s), 7.36-7.29 (5H, m), 5.09 (1H, d, *J* = 12.8 Hz), 5.05 (1H, d, *J* = 12.8 Hz), 4.30-4.24 (2H, m), 3.75 (1H, dd, *J* = 16.4, 6.0 Hz), 3.70 (1H, dd, *J* = 16.4, 5.4 Hz), 3.51-3.41 (2H, m), 2.18-2.10 (1H, m), 2.00-1.88 (2H, m), 1.87-1.79 (1H, m), 1.29 (3H, d, *J* = 7.3 Hz). $^{13}$C NMR (150 MHz, DMSO-d$_6$, VT 100 °C) δ: 172.9, 171.6, 167.8, 153.7, 136.5, 127.7, 127.0, 126.7, 65.5, 59.6, 47.1, 46.3, 41.6, 29.8, 23.0, 16.9. HRMS (EI): *m/z* cald for $C_{10}H_{16}N_3O_4$[M$^+$-Cbz]: 242.1141; found: 242.1127. m.p. 70-72 °C; $[\alpha]_D^{29}$ = -57.5 (c = 0.12 in MeOH)



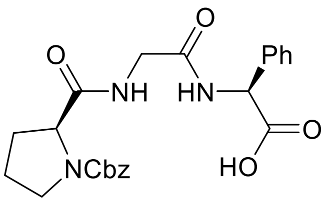

**Cbz-Pro-Gly-D-Ala-OH**

74% yield, $^1$H NMR (600 MHz, DMSO-d$_6$, VT 100 °C) δ: 12.17 (1H, br s), 7.90 (1H, s), 7.66 (1H, s), 7.40-7.25 (5H, m), 5.10 (1H, d, *J* = 12.8 Hz), 5.05 (1H, d, *J* = 12.8 Hz), 4.30-4.23 (2H, m), 3.76-3.69 (2H, m), 3.52-3.47 (1H, m), 3.46-3.42 (1H, m), 2.17-2.11 (1H, m), 1.99-1.87 (2H, m), 1.86-1.78 (1H, m), 1.30 (3H, d, *J* = 6.9 Hz). $^{13}$C NMR (150 MHz, DMSO-d$_6$, VT 100 °C) δ: 173.4, 172.2, 168.3, 154.3, 137.0, 128.2, 127.5, 127.2, 66.1, 60.2, 47.6, 46.8, 42.2, 30.3, 23.5, 17.4. HRMS (EI): *m/z* cald for $C_{18}H_{23}N_3O_6$[M$^+$]: 377.1587; found: 377.1567. m.p. 74-75 °C; $[\alpha]_D^{29}$ = -34.9 (c = 0.12 in MeOH)




**Cbz-Pro-Gly-Val-OH**

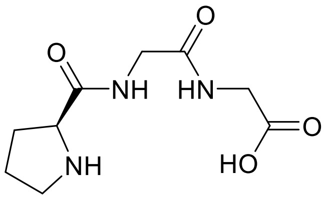
28% yield, $^{1}H$ NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 12.26 (1H, br s), 7.95 (1H, s), 7.46 (1H, s), 7.37-7.27 (5H, m), 5.09 (1H, d, *J* = 13.1 Hz), 5.05 (1H, d, *J* = 13.1 Hz), 4.27 (1H, dd, *J* = 8.6, 3.1 Hz), 4.19 (1H, dd, *J* = 8.3, 5.5 Hz), 3.79 (1H, dd, *J* = 16.4, 6.2 Hz), 3.74 (1H, dd, *J* = 16.4, 5.9 Hz), 3.52-3.40 (2H, m), 2.17-2.03 (2H, m), 1.95-1.87 (2H, m), 1.86-1.79 (1H, m), 0.91 (3H, d, *J* = 5.5 Hz), 0.90 (3H, d, *J* = 5.5 Hz).$^{13}C$ NMR (150MHz, DMSO-$d_6$, VT 100 °C) δ: 172.4, 168.8, 154.3, 137.1, 128.3, 127.6, 127.3, 66.1, 60.1, 57.3, 46.9, 42.4, 30.1, 23.5, 18.9, 17.9. HRMS (EI): *m/z* cald for $C_{20}H_{27}N_3O_6$ [$M^+$]: 405.1900; found: 405.1898. m.p. 71-72 °C; $[\alpha]_D^{24}$ = -41.0 (c = 0.26 in MeOH)




**Cbz-Pro-Gly-Phg-OH**

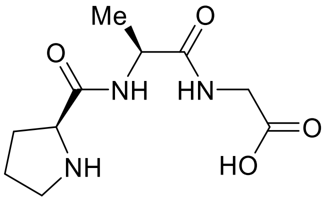
90% yield, $^{1}H$ NMR (600 MHz, DMSO-$d_6$, VT 100 °C) δ: 12.53 (1H, br s), 8.11 (1H, s), 7.94 (1H, s), 7.41-7.13 (10H, m), 5.40 (1H, t, *J* = 6.5 Hz), 5.10-4.98 (2H, m), 4.26 (1H, t, *J* = 4.5 Hz), 3.83 (2H, dd, *J* = 16.7, 5.2 Hz), 3.77 (2H, dd, *J* = 16.7, 5.5 Hz), 3.53-3.35 (2H, m), 2.17-2.10 (1H, m), 1.95-1.78 (3H, m). $^{13}C$ NMR (150MHz, DMSO-$d_6$, VT 100 °C) δ: 172.4, 171.4, 168.5, 154.3, 137.4, 137.4, 137.1, 128.9, 128.4, 128.3, 128.1, 127.8, 127.6, 127.4, 127.3, 125.2, 66.1, 60.2, 56.3, 46.9, 42.3, 30.4, 23.5. HRMS (EI): *m/z* cald for $C_{23}H_{25}N_3O_6$ [$M^+$]: 439.1743; found: 439.1753. m.p. 79-80 °C; $[\alpha]_D^{25}$ = -15.8 (c = 0.87 in MeOH)

**Deprotection of Cbz of Cbz-protected tipeptide:** To a solution of Cbz-protected tripeptide (2 mmol) in MeOH (30 mL), 10% Pd/C was added at room temperature. After stirred under hydrogen (1 atm) for 2 h at room temperature, The resulting mixture was filtered. After the removal of solvent under reduced pressure, corresponding tripeptide was obtained.



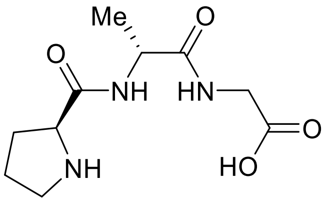
**H-Pro-Gly-Gly-OH (3a)**

85% yield, $^{1}$H NMR (600 MHz, $D_2O$) δ: 4.46 (1H, dd, *J* = 8.6, 6.9 Hz), 4.07 (1H, d, *J* = 16.8 Hz), 3.99 (1H, d, *J* = 16.8 Hz), 3.81 (1H, d, *J* = 17.2 Hz), 3.77 (1H, d, *J* = 17.2 Hz), 3.47-3.37 (2H, m), 2.50-2.43 (1H, m), 2.15-2.04 (3H, m). $^{13}$C NMR (150 MHz, $D_2O$) δ: 178.8, 173.3, 172.9, 62.5, 49.1, 45.7, 45.2, 32.2, 26.5. HRMS (EI): *m/z* cald for $C_9H_{15}N_3O_4[M^+]$: 229.1063; found: 229.1058. m.p. 114-116 °C; $[\alpha]_D^{28}$ = -16.2 (c = 0.53 in $H_2O$)



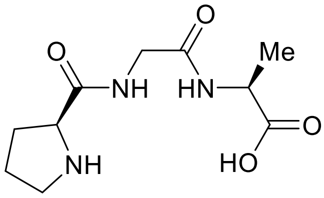
**H-Pro-Ala-Gly-OH (3b)**

49% yield, $^{1}$H NMR (600MHz, $D_2O$) δ: 4.45-4.37 (2H, m), 3.78 (1H, d, *J* = 17.4 Hz), 3.74 (1H, d, *J* = 17.4 Hz), 3.46-3.34 (2H, m), 2.50-2.41 (1H, m), 2.11-2.04 (3H, m), 1.42 (3H, d, *J* = 7.2 Hz). $^{13}$C NMR (150 MHz, $D_2O$) δ: 178.9, 176.7, 172.0, 62.3, 52.6, 49.2, 46.0, 32.4, 26.5, 19.3. HRMS (EI): *m/z* cald for $C_{10}H_{17}N_3O_4[M^+]$: 243.1219; found: 243.1209. m.p. 237-238 °C; $[\alpha]_D^{25}$ = -66.6 (c = 0.13 in $H_2O$)



**H-Pro-D-Ala-Gly-OH (3c)**

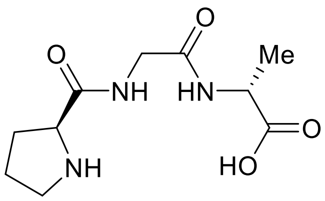
99% yield, $^{1}$H NMR (600 MHz, $D_2O$) δ: 4.45-4.37 (2H, m), 3.78 (1H, d, *J* = 17.4 Hz), 3.74 (1H, d, *J* = 17.4 Hz), 3.46-3.34 (2H, m), 2.50-2.41 (1H, m), 2.11-2.04 (3H, m), 1.42 (3H, d, *J* = 7.2 Hz). $^{13}$C NMR (150 MHz, $D_2O$) δ: 179.0, 176.8, 172.1, 62.4, 52.6, 49.2, 46.0, 32.3, 26.5, 19.4. HRMS (EI): *m/z* cald for $C_{10}H_{17}N_3O_4[M^+]$: 243.1219; found: 243.1207. m.p. 241-242 °C; $[\alpha]_D^{25}$ = 13.2 (c = 0.13 in $H_2O$)



**H-Pro-Gly-Ala-OH (3d)**

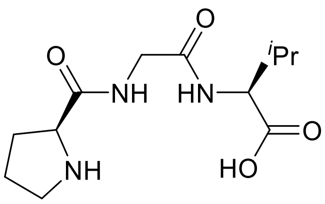
99% yield, $^{1}$H NMR (600 MHz, $D_2O$) δ: 4.45 (1H, dd, *J* = 8.8, 6.7 Hz), 4.15 (1H, q, *J* = 7.4 Hz), 4.02 (1H, d, *J* = 16.5 Hz), 3.98 (1H, d, *J* = 16.5 Hz), 3.48-3.37 (2H, m), 2.50-2.44 (1H, m), 2.15-2.05 (3H, m), 1.33 (3H, d, *J* = 7.4 Hz). $^{13}$C NMR (150 MHz, $D_2O$) δ: 182.6, 172.9, 172.4, 62.5, 53.7, 49.1, 45.2, 32.3, 26.5, 20.1. HRMS (EI): *m/z* cald for

$C_{10}H_{18}N_3O_4$[M$^+$+H]: 244.1297; found: 244.1284. m.p. 147-148 °C; $[\alpha]_D^{27}$ = -44.9 (c = 0.21 in $H_2O$)



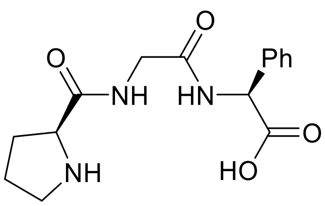

**H-Pro-Gly-D-Ala-OH (3e)**

93% yield, $^1$H NMR (600 MHz, $D_2O$) δ: 4.45 (1H, t, *J* = 7.4 Hz), 4.17 (1H, q, *J* = 7.2 Hz), 4.04 (1H, d, *J* = 17.2 Hz), 3.97 (1H, d, *J* = 17.2 Hz), 3.47-3.37 (2H, m), 2.50-2.43 (1H, m), 2.14-2.05 (3H, m), 1.34 (3H, d, *J* = 7.2 Hz). $^{13}$C NMR (150 MHz, $D_2O$) δ: 182.3, 172.8, 172.5, 62.5, 53.5, 49.1, 45.1, 32.2, 26.5, 20.0. HRMS (EI): *m/z* cald for $C_{10}H_{18}N_3O_4$[M$^+$]: 243.1220; found: 243.1219. m.p. 126-128 °C; $[\alpha]_D^{27}$ = 6.0 (c = 0.45 in $H_2O$)




**H-Pro-Gly-Val-OH (3f)**

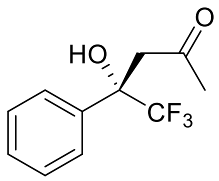
99% yield, $^1$H NMR (600 MHz, $D_2O$) δ: 4.45 (1H, t, *J* = 7.9 Hz), 4.14 (1H, d, *J* = 4.8 Hz), 4.07 (1H, d, *J* = 16.8 Hz), 4.02 (1H, d, *J* = 16.8 Hz), 3.56-3.37 (2H, m), 2.52-2.42 (1H, m), 2.17-2.05 (4H, m), 0.93 (3H, d, *J* = 7.0 Hz), 0.90 (3H, d, *J* = 7.0 Hz). $^{13}$C NMR (150 MHz, $D_2O$) δ: 180.2, 173.1, 172.8, 62.8, 62.5, 49.2, 45.1, 33.0, 32.3, 26.5, 21.4, 19.9. HRMS (EI): *m/z* cald for $C_{12}H_{21}N_3O_4$[M$^+$]: 271.1532; found: 271.1558. m.p. 154-155 °C; $[\alpha]_D^{25}$ = -40.1 (c = 0.52 in $H_2O$)



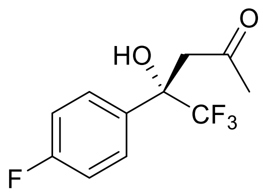

**H-Pro-Gly-Phg-OH (3g)**

92% yield, $^1$H NMR (600 MHz, $D_2O$) δ: 7.43-7.36 (5H, m), 5.21 (1H, s), 4.44 (1H, t, *J* = 7.7 Hz), 4.02 (2H, s), 3.50-3.33 (2H, m), 2.49-2.43 (1H, m), 2.14-2.00 (3H, m). $^{13}$C NMR (150 MHz, $D_2O$) δ: 178.7, 172.8, 172.4, 140.6, 131.6, 130.9, 129.9, 62.5, 62.0, 49.1, 45.2, 32.3, 26.5. HRMS (EI): *m/z* cald for $C_{15}H_{19}N_3O_4$[M$^+$]: 305.1376; found: 305.1360. m.p. 181-182 °C; $[\alpha]_D^{25}$ = 3.4 (c = 0.34 in $H_2O$)

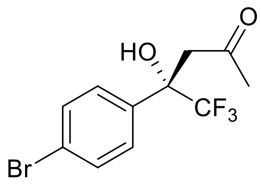
**4. General procedure for tripeptide-catalyzed asymmetric aldol reaction of trifluoromethlyated aromatic ketones:** A mixture of tripeptide (10 μmol) and acetone (2 mmol, 0.15 mL) was stirred at -40 °C for 10 min. To the resulting mixture, trifluoromethylated aromatic ketones (0.1 mmol) was added. The mixture was stirred at -40 °C for 36 h and then was filtrated to remove catalyst. the mixture was concentrated under reduced pressure. Preparative thin layer chromatography on silica gel using hexane/dichororomethane = 80/20 gave the aldol adduct. The enantiomeric excess of aldol adduct was determined by chiral HPLC.



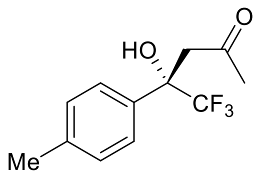

**(*S*)-4-hydroxy-4-phenyl-5,5,5-trifluoropentan-2-one (4a).** 71% yield, $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.56 (2H, d, *J* = 7.2 Hz), 7.41-7.35 (3H, m), 5.43 (1H, s), 3.37 (1H, d, *J* = 17.0 Hz), 3.21 (1H, d, *J* = 17.0 Hz), 2.21 (3H, s). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 208.9, 137.4, 128.8, 128.4, 126.1, 124.4 (q, *J* = 284.6 Hz), 76.0 (q, *J* = 28.9 Hz), 45.1, 32.1. HRMS (EI): *m/z* cald for $C_{11}H_{11}F_3O_2[M^+]$: 232.0711; found: 232.0698. m.p. 57 °C; $[\alpha]_D^{24}$ = 18.6 (c = 0.27 in $CHCl_3$), HPLC (DAICEL CHIRALPAK OD-H, *n*-hexane /$^i$PrOH = 90/10, 1.0 mL/min, 210 nm, 35 °C) minor enantiomer t = 6.1 min, major enantiomer t = 8.5 min.



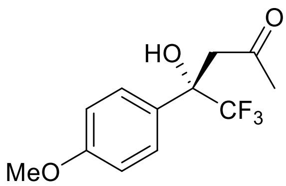

**(*S*)-4-(4-fluorophenyl)-4-hydroxy-5,5,5-trifluoropentan-2-one (4b).** 81% yield, $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.54 (2H, dd, *J* = 8.8, 5.3 Hz), 7.10-7.06 (2H, m), 5.50 (1H, s), 3.31 (1H, d, *J* = 17.2 Hz), 3.21 (1H, d, *J* = 17.2 Hz), 2.22 (3H, s). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 209.2, 163.3 (d, *J* = 248.4 Hz), 133.7, 128.5 (d, *J* = 8.7 Hz), 124.7 (q, *J* = 284.6 Hz), 115.8 (d, *J* = 21.7 Hz), 76.1 (q, *J* = 29.4 Hz), 45.4, 32.5. HRMS (EI): *m/z* cald for $C_{11}H_{10}F_4O_2[M^+]$: 250.0617; found: 250.0624. m.p. 58-59 °C; $[\alpha]_D^{25}$ = 18.5 (c = 0.43 in $CHCl_3$), HPLC (DAICEL CHIRALPAK OD-H, *n*-hexane /$^i$PrOH = 99/1, 1.0 mL/min, 210 nm, 35 °C) minor enantiomer t = 14.8 min, major enantiomer t = 16.0 min.



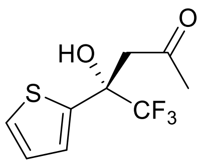
**(*S*)-4-(4-bromophenyl)-4-hydroxy-5,5,5-trifluoropentan-2-one (4c).** 80% yield, $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.53 (2H, d, *J* = 8.6 Hz), 7.43 (2H, d, *J* = 8.6 Hz), 5.50 (1H, s), 3.30 (1H, d, *J* = 17.2 Hz), 3.20 (1H, d, *J* = 17.2 Hz), 2.21 (3H, s). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 208.7, 136.5, 131.6, 127.9, 124.1 (q, *J* = 284.6 Hz), 123.2, 75.8 (q, *J* = 29.9 Hz), 44.8, 32.0. HRMS (EI): *m/z* cald for $C_{11}H_{10}BrF_3O_2[M^+]$: 309.9816; found: 309.9827. m.p. 89-90 °C; $[\alpha]_D^{24}$ = 17.2 (c = 0.18 in $CHCl_3$), HPLC (DAICEL CHIRALPAK OD-H, *n*-hexane /$^i$PrOH = 99/1, 1.0 mL/min, 210 nm, 35 °C) minor enantiomer t = 18.4 min, major enantiomer t = 21.4 min.



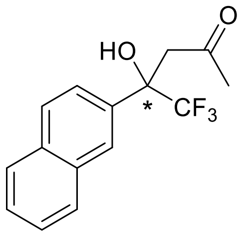
**(*S*)-4-(4-methylphenyl)-4-hydroxy-5,5,5-trifluoropentan-2-one (4d)** 26% yield, $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.44 (2H, d, *J* = 8.1 Hz), 7.20 (2H, d, *J* = 8.1 Hz), 5.38 (1H, s), 3.36 (1H, d, *J* = 17.2 Hz), 3.18 (1H, d, *J* = 17.2 Hz), 2.35 (3H, s), 2.20 (3H, s). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 209.4, 139.1, 134.8, 129.6, 126.4, 124.9 (q, *J* = 284.6 Hz), 76.3 (q, *J* = 29.4 Hz), 45.5, 32.5, 21.4. HRMS (EI): *m/z* cald for $C_{12}H_{13}F_3O_2[M^+]$: 246.0868; found: 246.0844. m.p. 66-67 °C; $[\alpha]_D^{25}$ = 14.0 (c = 0.050 in $CHCl_3$), HPLC (DAICEL CHIRALPAK OD-H, *n*-hexane /$^i$PrOH = 99/1, 1.0 mL/min, 210 nm, 35 °C) minor enantiomer t = 12.9 min, major enantiomer t = 15.8 min.



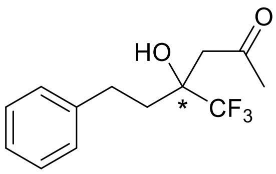
**(*S*)-4-(4-methyoxyphenyl)-4-hydroxy-5,5,5-trifluoropentan-2-one (4e)** 12% yield, $^1$H NMR (600 MHz, $CDCl_3$) δ: 7.47 (2H, d, *J* = 8.1 Hz), 6.91 (2H, d, *J* = 8.1 Hz), 5.39 (1H, s), 3.80 (3H, s), 3.34 (1H, d, *J* = 17.0 Hz), 3.16 (1H, d, *J* = 17.0 Hz), 2.19 (3H, s). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 209.0, 159.8, 129.3, 127.4, 124.5 (q, *J* = 285.0 Hz), 113.8, 76.0, 75.5 (q, *J* = 28.9 Hz), 55.2, 45.0, 32.1. HRMS (EI): *m/z* cald for $C_{12}H_{13}F_3O_3[M^+]$: 262.0817; found: 262.0792. m.p. 53-54 °C; $[\alpha]_D^{25}$ = 24.0 (c = 0.055 in $CHCl_3$), HPLC (DAICEL CHIRALPAK OD-H, *n*-hexane /$^i$PrOH = 97/3, 0.5 mL/min, 210 nm, 35 °C) minor enantiomer t = 23.0 min, major enantiomer t = 24.1 min.



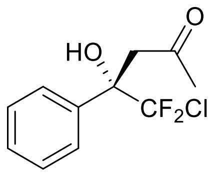
**(*S*)-4-(thiophen-2-yl)-4-hydroxy-5,5,5-trifluoropentan-2-one (4f)** 18% yield, $^{1}$H NMR (600 MHz, $CDCl_3$) δ: 7.34-7.31 (1H, m), 7.10 (1H, d, *J* = 3.4 Hz), 7.02-6.99 (1H, m), 5.90 (1H, s), 3.32 (1H, d, *J* = 17.2 Hz), 3.14 (1H, d, *J* = 17.2 Hz), 2.21 (3H, s). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 209.4, 142.0, 127.6, 126.9, 126.1, 124.1 (q, *J* = 285.1 Hz), 75.8 (q, *J* = 30.3 Hz), 46.0, 32.4. HRMS (EI): *m/z* cald for $C_9H_9F_3O_2S_1$[$M^+$]: 238.0275; found: 238.0254. $[\alpha]_D^{27}$ = 17.8 (c = 0.050 in $CHCl_3$), HPLC (DAICEL CHIRALPAK OD-H, *n*-hexane /$^{i}$PrOH = 90/10, 0.5 mL/min, 235 nm, 35 °C) minor enantiomer t = 14.2 min, major enantiomer t = 14.7 min.



**4-(naphthalene-2-yl)-4-hydroxy-5,5,5-trifluoropentan-2-one (4g)** 73% yield, $^{1}$H NMR (600 MHz, $CDCl_3$) δ: 8.16 (1H, s), 7.93-7.87 (3H, m), 7.69 (1H, d, *J* = 8.6 Hz), 7.56-7.53 (2H, m), 5.73 (1H, s), 3.48 (1H, d, *J* = 16.8 Hz), 3.30 (1H, d, *J* = 16.8 Hz), 2.18 (3H, s). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 209.0, 134.7, 133.1, 132.8, 128.4, 128.2, 127.4, 126.7, 126.4, 126.0, 124.6 (q, *J* = 284.7 Hz), 123.2, 76.1 (q, *J* = 29.4 Hz), 45.0, 31.8. HRMS (EI): *m/z* cald for $C_{15}H_{13}F_3O_2$[$M^+$]: 282.0868; found: 282.0841. $[\alpha]_D^{27}$ = 10.0 (c = 0.21 in $CHCl_3$), HPLC (DAICEL CHIRALPAK OD-H, *n*-hexane /$^{i}$PrOH = 90/10, 1.0 mL/min, 210 nm, 35 °C) minor enantiomer t = 7.2 min, major enantiomer t = 10.2 min.



**4-hydroxy-4-(2-phenylethyl)-5,5,5-trifluoropentan-2-one (4h).** 21% yield, $^{1}$H NMR (600 MHz, $CDCl_3$) δ: 7.34-7.30 (2H, m), 7.25-7.20 (3H, m), 5.54 (1H, s), 2.94 (1H, d, *J* = 16.8 Hz), 2.84 (1H, td, *J* = 12.9, 4.9 Hz), 2.73 (1H, td, *J* = 12.9, 4.9 Hz), 2.68 (1H, d, *J* = 16.8 Hz), 2.26 (3H, s), 2.14-2.06 (1H, m), 1.92 (1H, td, *J* = 12.9, 4.9 Hz). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 210.4, 141.2, 128.7, 128.5, 126.3, 126.1 (q, *J* = 287.1 Hz), 75.2 (q, *J* = 27.5 Hz), 42.6, 36.9, 32.1, 29.1. HRMS (EI): *m/z* cald for $C_{13}H_{15}F_3O_2$[$M^+$]: 260.1024; found: 260.9994. $[\alpha]_D^{26}$ = -8.5 (c = 0.060 in $CHCl_3$), HPLC (DAICEL CHIRALPAK OD-H, *n*-hexane /$^{i}$PrOH = 90/10, 0.5 mL/min, 210 nm, 35 °C) minor enantiomer t = 14.5 min, major enantiomer t = 15.3 min.




**(*S*)-4-hydroxy-4-phenyl-5-chloro-5,5-difluoropentan-2-one (4j).** 42% yield, $^{1}$H NMR (600 MHz, $CDCl_3$) δ: 7.65 (2H, d, *J* = 7.9 Hz), 7.46-7.40 (3H, m), 5.66 (1H, br s), 3.52 (1H, d, *J* = 17.0 Hz), 3.30 (1H, d, *J* = 17.0 Hz), 2.22 (3H, s). $^{13}$C NMR (150 MHz, $CDCl_3$) δ: 209.4, 138.1, 130.3 (t, *J* = 299.1 Hz), 128.9, 128.4, 126.7, 79.6 (t, *J* = 25.3 Hz), 45.6, 32.2. HRMS (EI): *m/z* cald for $C_{11}H_{11}ClF_2O_2$[$M^+$]: 248.0416; found: 248.0406. m.p. 68-69 °C; $[\alpha]_D^{27}$ = 41.8 (c = 0.040 in $CHCl_3$), HPLC (DAICEL CHIRALPAK OD-H, *n*-hexane /$^i$PrOH = 95/5, 1.0 mL/min, 210 nm, 35 °C) minor enantiomer t = 7.9 min, major enantiomer t = 10.5 min.

## 5. Computational Details

All calculations were performed using Gaussian 03 and 09 program suite.[2 3] Geometries were fully optimized at the B3LYP/6-31G(d,p) level. Frequency calculations were performed with structures characterized as transition states based on the observed number of imaginary frequencies, and thermodynamic corrections at 298 K and 1 atm were also calculated at the same level of theory. The electronic energies were then improved by the ωB97XD/def-TZVPP[4] single-point calculations, which took the solvent effects of acetone into account by using the SMD solvation model.[5] Gibbs energies in solution can be obtained from adding the gas-phase Gibbs energy corrections of the solute (the B3LYP/6-31G(d,p)) to the single-point energies (the ωB97XD/def-TZVPP). we confirmed that TS-(*S*) and TS-(*R*) were connected by the minimum energy path to the corresponding prereaction complexes and products.

## 6. Reference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2. T. E. kristensen, K. Vestli, F. K. Hansen, T. Hansen, *Eur. J. Org. Chem.* 2009, 5185.

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Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

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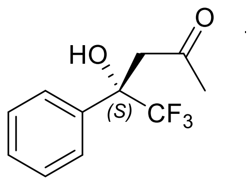
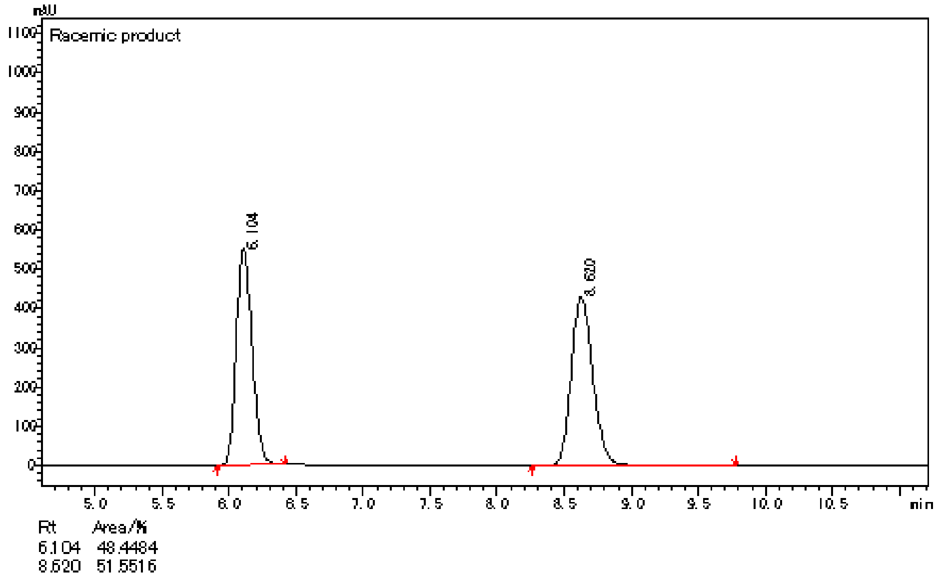
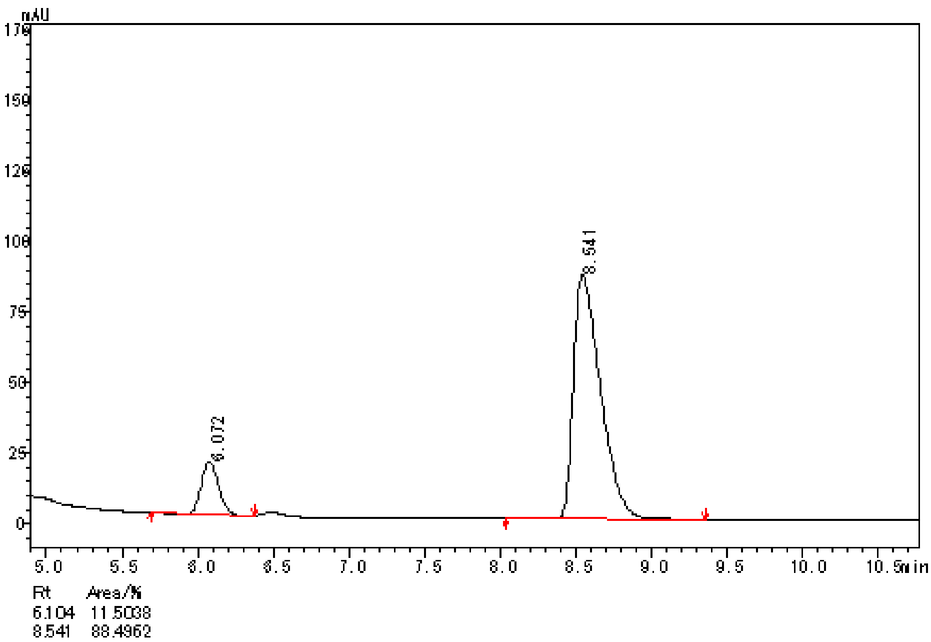
## 7. Copy of HPLC spectra

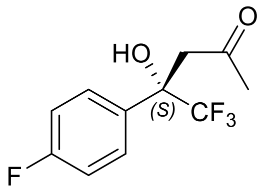


**4a**, 75% *ee*

DAICEL CHIRALPAK OD-H, *n*-hexane /$^{i}$PrOH = 90/10, 1.0 mL/min, 210 nm, 35 °C

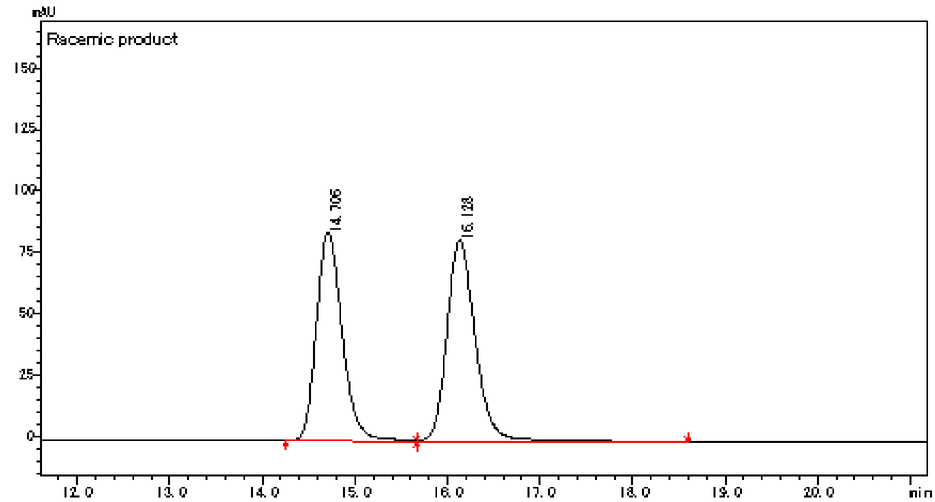


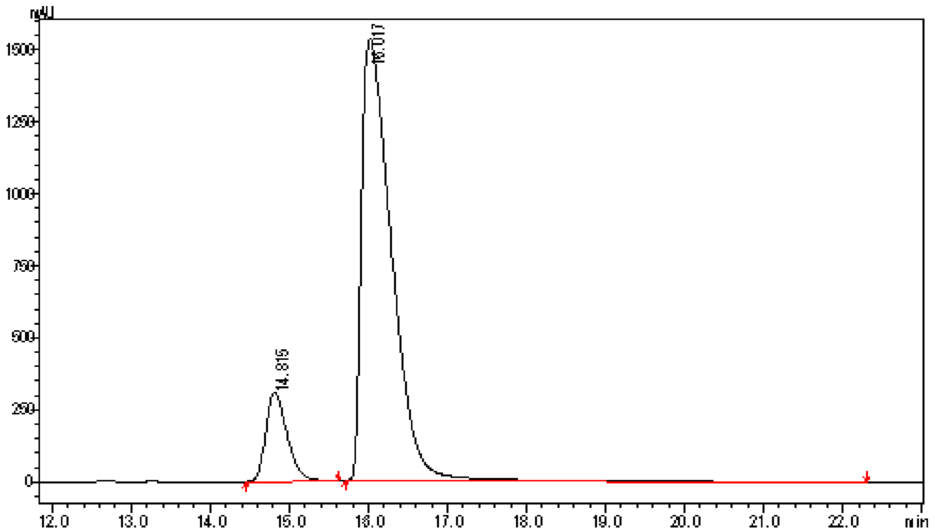



**4b**, 75% *ee*

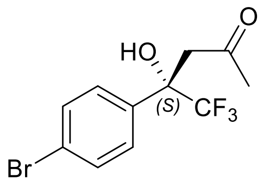
DAICEL CHIRALPAK OD-H, *n*-hexane /$^{i}$PrOH = 99/1, 1.0 mL/min, 210 nm, 35 °C




| Rt | Area/% |
|---|---|
| 14.706 | 48.5132 |
| 16.128 | 51.4868 |

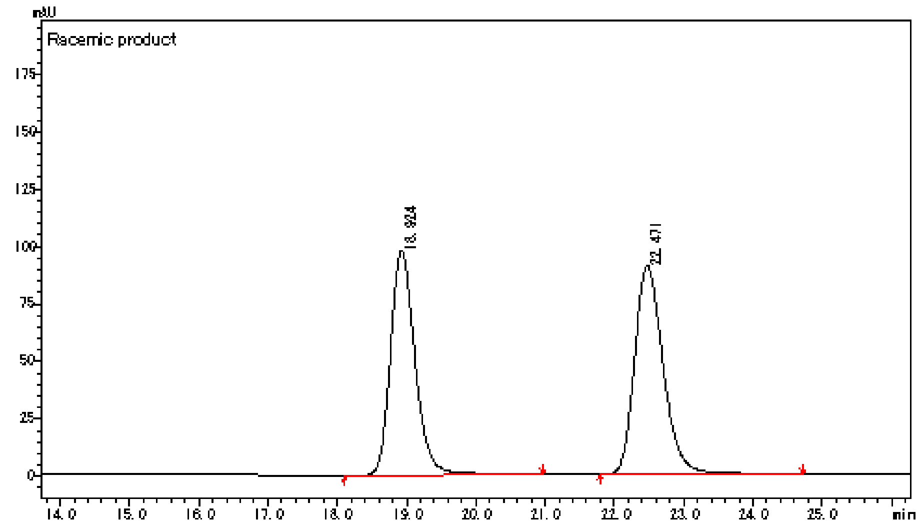



| Rt | Area/% |
|---|---|
| 14.815 | 12.3733 |
| 16.017 | 87.6267 |

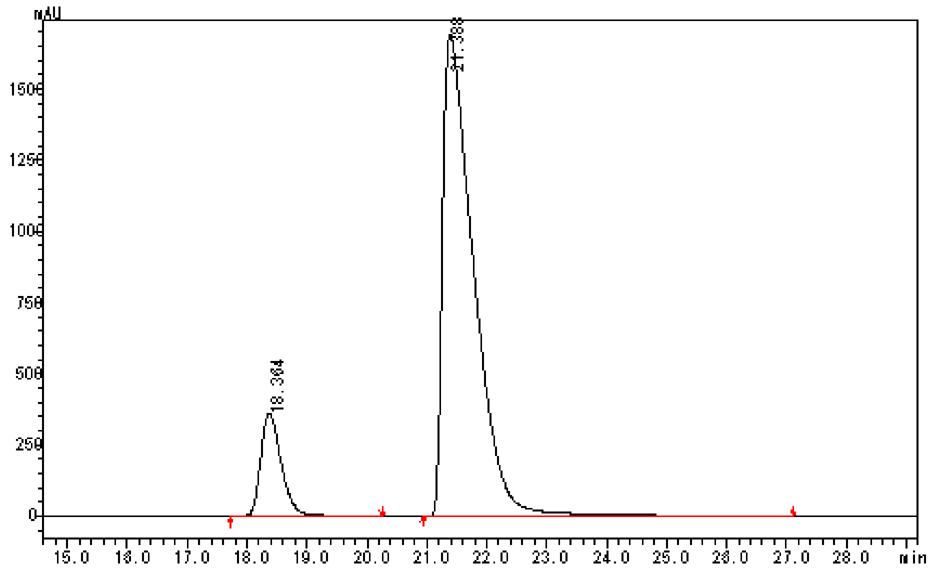



**4c**, 75% *ee*

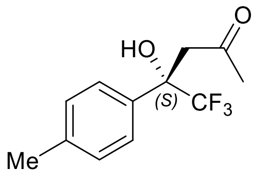
DAICEL CHIRALPAK OD-H, *n*-hexane /$^{i}$PrOH = 99/1, 1.0 mL/min, 210 nm, 35 °C




| Rt | Area/% |
|---|---|
| 18.924 | 48.0525 |
| 22.471 | 51.9475 |

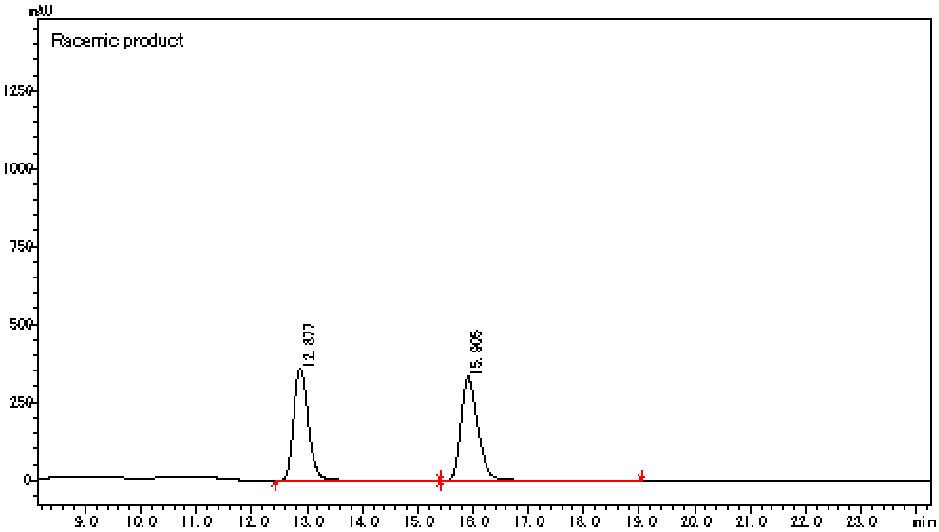



| Rt | Area/% |
|---|---|
| 18.364 | 12.3940 |
| 21.368 | 87.6060 |

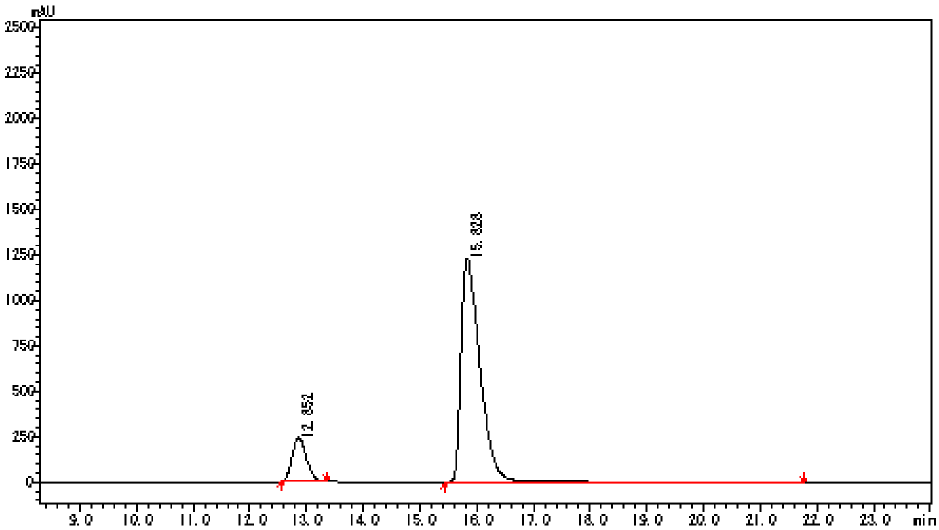



**4d**, 75% *ee*

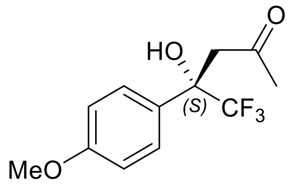
DAICEL CHIRALPAK OD-H, *n*-hexane /$^{i}$PrOH = 99/1, 1.0 mL/min, 210 nm, 35 °C




| Rt | Area/% |
|---|---|
| 12.877 | 48.2936 |
| 15.905 | 51.7061 |

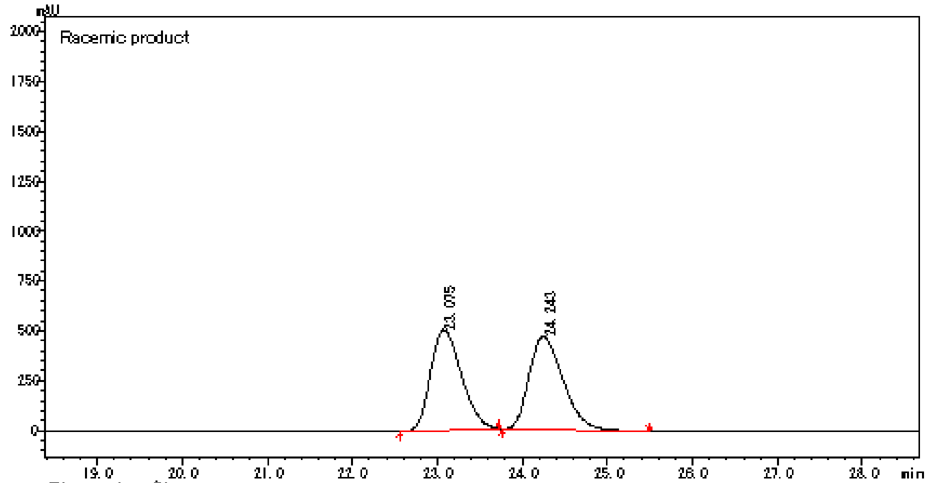



| Rt | Area/% |
|---|---|
| 12.852 | 12.7331 |
| 15.828 | 87.2669 |

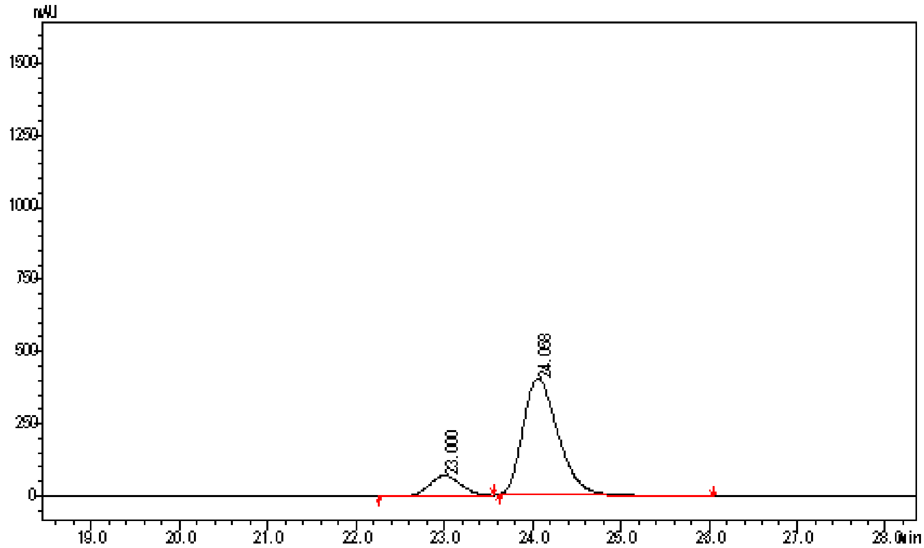


**4e**, 74% *ee*

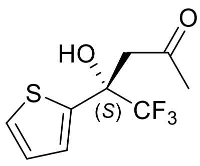
DAICEL CHIRALPAK OD-H, *n*-hexane /$^i$PrOH = 97/3, 0.5 mL/min, 210 nm, 35 °C




| Rt | Area/% |
| --- | --- |
| 23.075 | 49.6661 |
| 24.243 | 51.3339 |

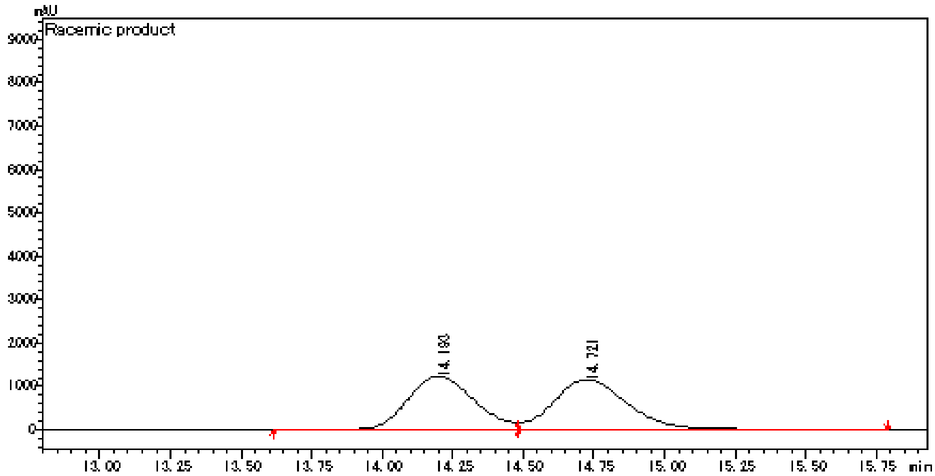



| Rt | Area/% |
| --- | --- |
| 23.000 | 13.1894 |
| 24.058 | 86.8106 |

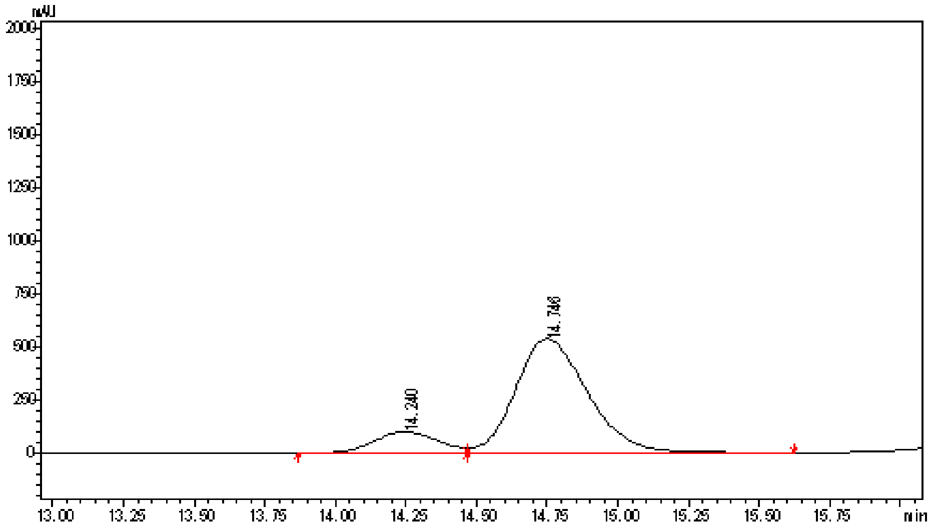



**4f**, 71% *ee*

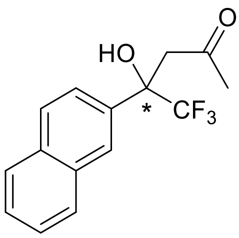
DAICEL CHIRALPAK OD-H, *n*-hexane /$^i$PrOH = 90/10, 0.5 mL/min, 235 nm, 35 °C




| Rt | Area/% |
|---|---|
| 14.193 | 49.1452 |
| 14.721 | 50.8549 |

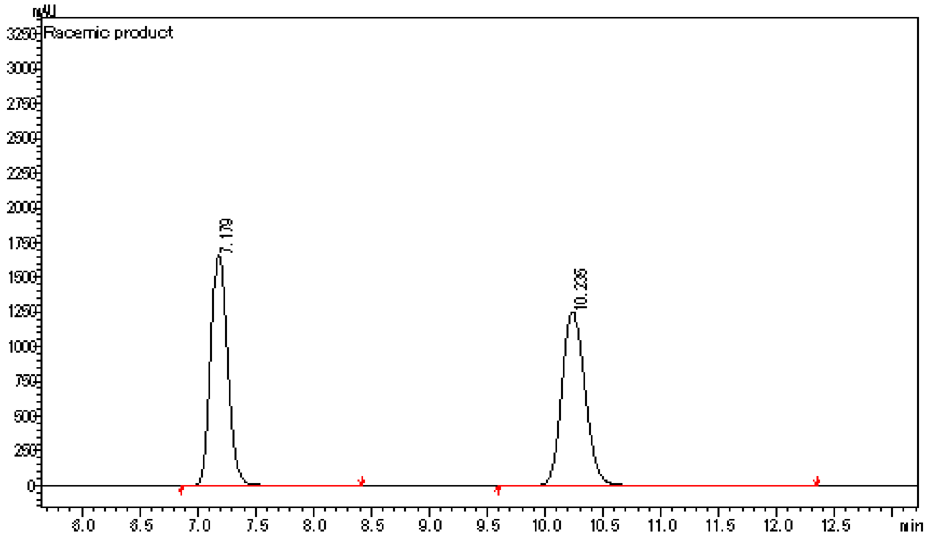



| Rt | Area/% |
|---|---|
| 14.240 | 14.3171 |
| 14.746 | 85.6829 |

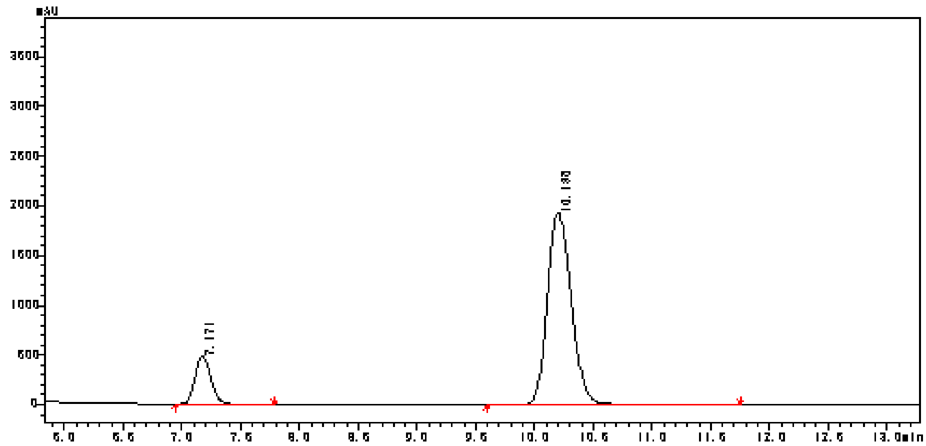



**4g**, 71% *ee*

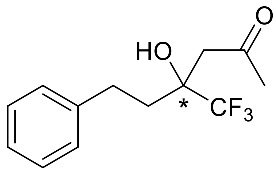
DAICEL CHIRALPAK OD-H, *n*-hexane /$^{i}$PrOH = 90/10, 1.0 mL/min, 210 nm, 35 °C




| Rt | Area/% |
|---|---|
| 7.179 | 49.1159 |
| 10.235 | 50.8841 |

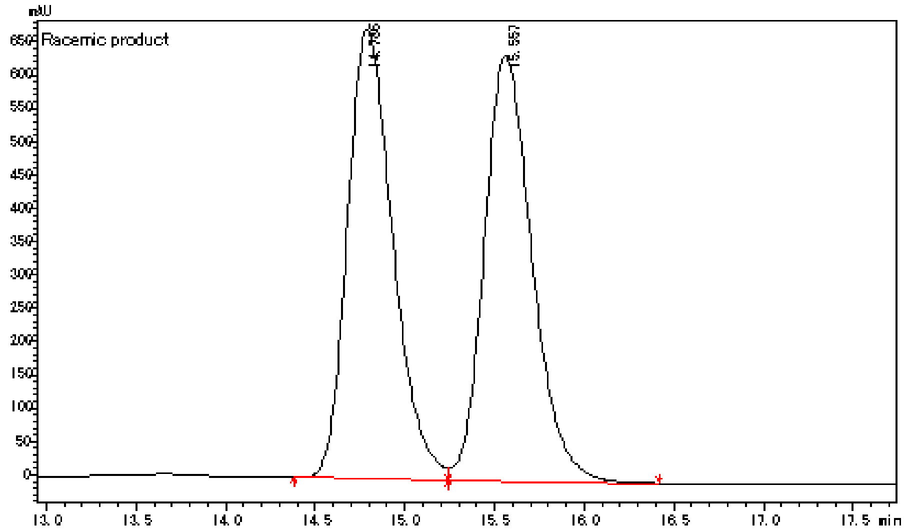



| Rt | Area/% |
|---|---|
| 7.171 | 14.3096 |
| 10.198 | 85.6914 |

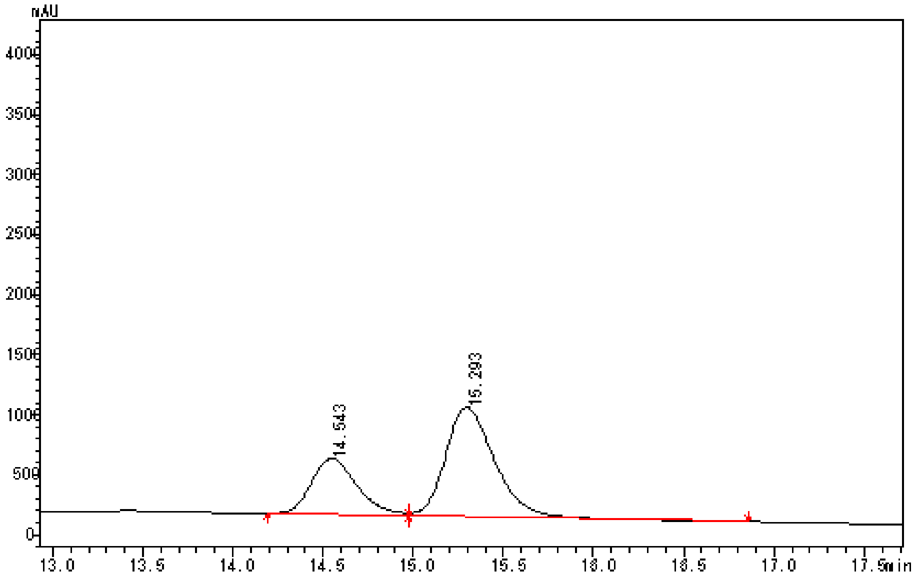



**4h**, 36% *ee*

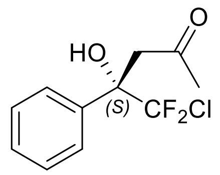
DAICEL CHIRALPAK OD-H, *n*-hexane /$^{i}$PrOH = 90/10, 0.5 mL/min, 210 nm, 35 °C




| Rt | area/% |
|---|---|
| 14.786 | 50.0648 |
| 15.557 | 49.9352 |

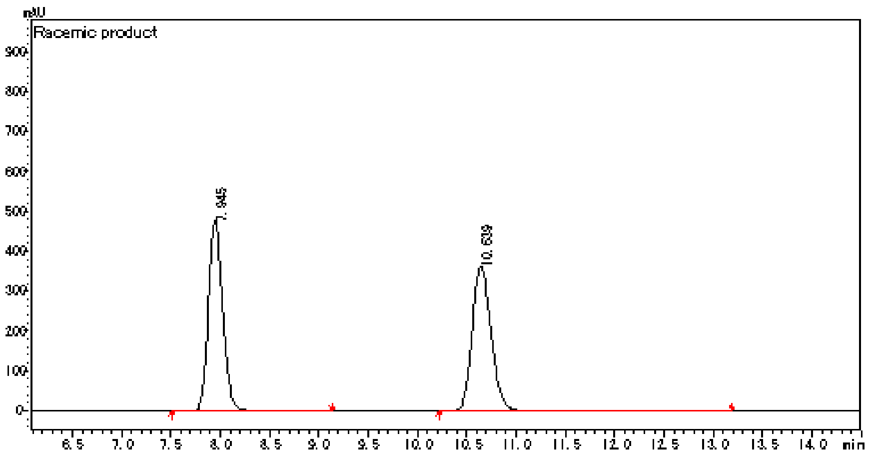



| Rt | area/% |
|---|---|
| 14.548 | 31.8282 |
| 15.298 | 68.1718 |

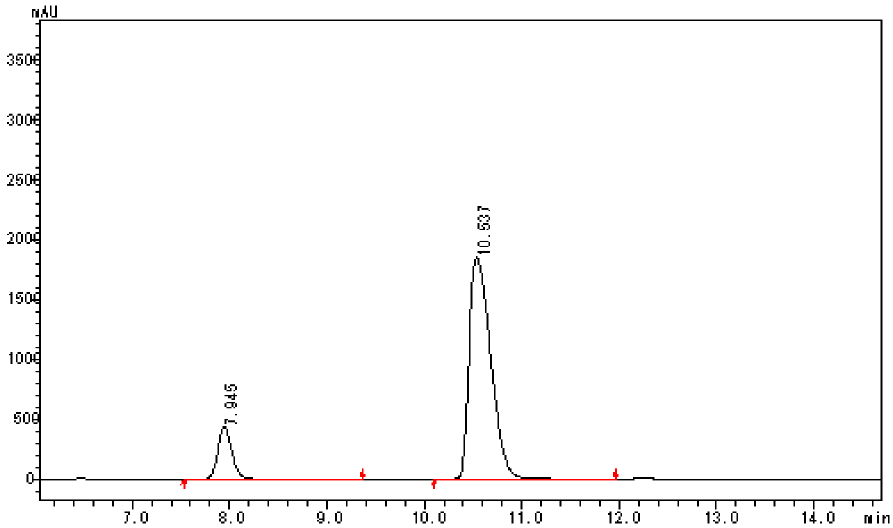


**4i**, 73% *ee*

DAICEL CHIRALPAK OD-H, *n*- hexane /$^{i}$PrOH = 95/5, 1.0 mL/min, 210 nm, 35 °C

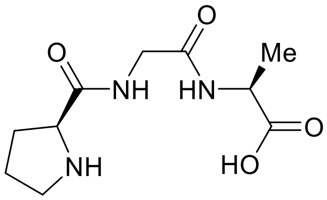



| Rt | Area/% |
|---|---|
| 7.945 | 49.7956 |
| 10.639 | 50.2044 |

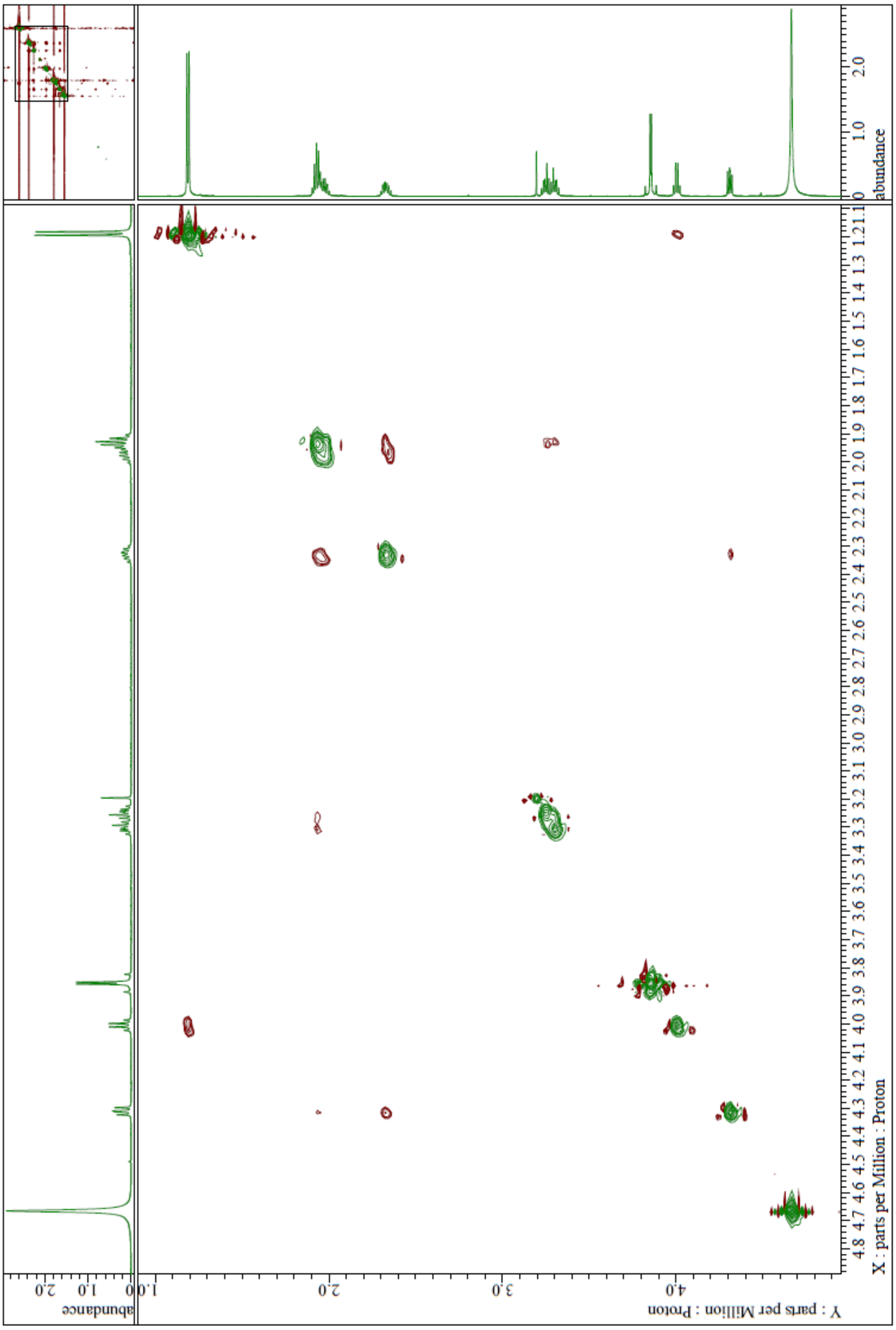



| Rt | Area/% |
|---|---|
| 7.945 | 13.3881 |
| 10.537 | 86.6119 |

## 8. Copy of NOESY spectra




H-Pro-Gly-Ala-OH (**3d**)



## 7. Geometries and Cartesian Coordinatess

TS-(S)

E = -1655.84617063 a.u.

(B3LYP/6-31G(d',p'))

182.9 i cm-1

E = -1656.04155582 a.u.

(SMD/ωB97XD/def-TZVPP)

| | | | |
|---|---|---|---|
| H | -0.283019 | 1.168360 | 0.000000 |
| N | -1.225706 | 0.917820 | -0.294320 |
| C | -1.905092 | -0.064365 | 0.346641 |
| C | -1.869347 | 1.814467 | -1.245234 |
| O | -3.047792 | -0.413803 | 0.093891 |
| C | -1.154622 | -0.783880 | 1.500120 |
| N | 0.220565 | -0.303340 | 1.757191 |
| C | -1.878193 | -0.517818 | 2.834361 |
| C | 0.264171 | 0.571312 | 2.963497 |
| C | -1.208856 | 0.769214 | 3.335934 |
| H | -1.152578 | -1.847944 | 1.248538 |
| H | -2.955404 | -0.433145 | 2.677820 |
| H | -1.690400 | -1.348452 | 3.526038 |
| H | -1.607820 | 1.646378 | 2.814959 |
| H | 0.771220 | 1.510408 | 2.745775 |
| H | 0.820110 | 0.041825 | 3.750477 |
| H | -1.335502 | 0.932475 | 4.409781 |
| C | 1.317988 | -0.727654 | 1.114578 |
| C | 2.570973 | -0.140551 | 1.349096 |
| C | 1.160552 | -1.791595 | 0.058401 |
| H | 2.733281 | 0.392957 | 2.278307 |
| H | 3.438866 | -0.661991 | 0.961222 |
| H | 0.372227 | -1.542688 | -0.657757 |
| H | 2.094935 | -1.917703 | -0.489686 |
| H | 0.901202 | -2.749808 | 0.527495 |
| H | -2.892774 | 1.468312 | -1.398851 |
| C | -1.915881 | 3.229867 | -0.642417 |
| H | -1.328386 | 1.802585 | -2.200710 |
| N | -0.764362 | 3.956403 | -0.811827 |
| O | -2.880176 | 3.642887 | -0.021202 |
| H | 0.050538 | 3.464144 | -1.152267 |
| C | -0.530952 | 5.211890 | -0.091768 |
| C | -0.610507 | 5.037868 | 1.446287 |
| O | -0.046573 | 3.911583 | 1.943512 |
| O | -1.077390 | 5.868476 | 2.178543 |
| H | 0.386275 | 3.365406 | 1.252155 |
| C | 2.492498 | 1.675043 | 0.180800 |
| O | 1.339208 | 2.177075 | 0.340539 |
| C | 2.683040 | 1.079244 | -1.243516 |
| H | 0.517088 | 5.473642 | -0.298058 |
| C | -1.429166 | 6.354571 | -0.568198 |
| C | 3.701183 | 2.341470 | 0.791384 |
| C | 5.022349 | 1.968508 | 0.489387 |
| C | 3.484899 | 3.391027 | 1.699050 |
| C | 4.561383 | 4.049762 | 2.290709 |
| C | 6.095501 | 2.634661 | 1.079402 |
| C | 5.870976 | 3.674859 | 1.983493 |
| H | 2.470309 | 3.694353 | 1.935323 |
| H | 4.374391 | 4.861636 | 2.989336 |
| H | 5.220951 | 1.162716 | -0.208195 |
| H | 7.111501 | 2.337596 | 0.830798 |
| H | 6.710512 | 4.190270 | 2.443637 |
| F | 3.616193 | 0.105803 | -1.357494 |
| F | 1.526400 | 0.563240 | -1.701791 |
| F | 3.038059 | 2.069057 | -2.087946 |
| H | -1.280797 | 6.520775 | -1.640157 |
| H | -2.476835 | 6.110696 | -0.382025 |
| H | -1.183871 | 7.269519 | -0.023047 |
| H | -1.183871 | 7.269519 | -0.023047 |

TS-(R)

E = -1655.84878107 a.u.

(B3LYP/6-31G(d',p'))

200.4 i cm-1

E = -1656.03987447 a.u.

(SMD/ωB97XD/def-TZVPP)

| | | | |
|---|---|---|---|
| H | -0.283019 | 1.168360 | 0.000000 |
| N | -1.225706 | 0.917820 | -0.294320 |
| C | -1.905092 | -0.064365 | 0.346641 |
| C | -1.869347 | 1.814467 | -1.245234 |
| O | -3.047792 | -0.413803 | 0.093891 |
| C | -1.154622 | -0.783880 | 1.500120 |
| N | 0.220565 | -0.303340 | 1.757191 |
| C | -1.878193 | -0.517818 | 2.834361 |
| C | 0.264171 | 0.571312 | 2.963497 |
| C | -1.208856 | 0.769214 | 3.335934 |
| H | -1.152578 | -1.847944 | 1.248538 |
| H | -2.955404 | -0.433145 | 2.677820 |
| H | -1.690400 | -1.348452 | 3.526038 |
| H | -1.607820 | 1.646378 | 2.814959 |
| H | 0.771220 | 1.510408 | 2.745775 |
| H | 0.820110 | 0.041825 | 3.750477 |
| H | -1.335502 | 0.932475 | 4.409781 |
| C | 1.317988 | -0.727654 | 1.114578 |
| C | 2.570973 | -0.140551 | 1.349096 |
| C | 1.160552 | -1.791595 | 0.058401 |
| H | 2.733281 | 0.392957 | 2.278307 |

| | | | |
|---|---|---|---|
| H | 3.438866 | -0.661991 | 0.961222 |
| H | 0.372227 | -1.542688 | -0.657757 |
| H | 2.094935 | -1.917703 | -0.489686 |
| H | 0.901202 | -2.749808 | 0.527495 |
| H | -2.892774 | 1.468312 | -1.398851 |
| C | -1.915881 | 3.229867 | -0.642417 |
| H | -1.328386 | 1.802585 | -2.200710 |
| N | -0.764362 | 3.956403 | -0.811827 |
| O | -2.880176 | 3.642887 | -0.021202 |
| H | 0.050538 | 3.464144 | -1.152267 |
| C | -0.530952 | 5.211890 | -0.091768 |
| C | -0.610507 | 5.037868 | 1.446287 |
| O | -0.046573 | 3.911583 | 1.943512 |
| O | -1.077390 | 5.868476 | 2.178543 |
| H | 0.386275 | 3.365406 | 1.252155 |
| C | 2.492498 | 1.675043 | 0.180800 |
| O | 1.339208 | 2.177075 | 0.340539 |
| C | 2.683040 | 1.079244 | -1.243516 |
| H | 0.517088 | 5.473642 | -0.298058 |
| C | -1.429166 | 6.354571 | -0.568198 |
| C | 3.701183 | 2.341470 | 0.791384 |
| C | 5.022349 | 1.968508 | 0.489387 |
| C | 3.484899 | 3.391027 | 1.699050 |
| C | 4.561383 | 4.049762 | 2.290709 |
| C | 6.095501 | 2.634661 | 1.079402 |
| C | 5.870976 | 3.674859 | 1.983493 |
| H | 2.470309 | 3.694353 | 1.935323 |
| H | 4.374391 | 4.861636 | 2.989336 |
| H | 5.220951 | 1.162716 | -0.208195 |
| H | 7.111501 | 2.337596 | 0.830798 |
| H | 6.710512 | 4.190270 | 2.443637 |
| F | 3.616193 | 0.105803 | -1.357494 |
| F | 1.526400 | 0.563240 | -1.701791 |
| F | 3.038059 | 2.069057 | -2.087946 |
| H | -1.280797 | 6.520775 | -1.640157 |
| H | -2.476835 | 6.110696 | -0.382025 |
| H | -1.183871 | 7.269519 | -0.023047 |