Novel Small Organic Molecules for Highly Enantioselective Direct Aldol Reaction

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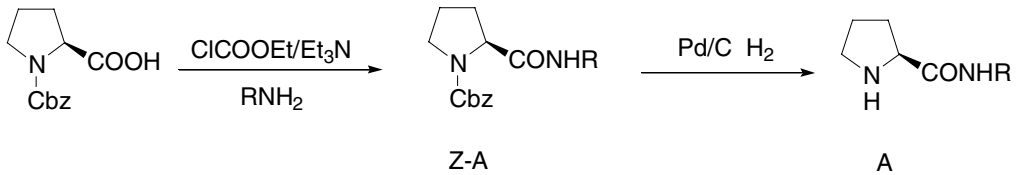
(Supporting information)

General: NMR spectra were recorded on a Brucker-300 MHz spectrometer. Elemental analysis was carried out using Carlo Erba-1106 Analyzer. Optical rotations were measured on a Perkin-Elmer 241 Polarimeter at = 589 nm. FT-ICRMS spectra were recorded on P-SIMS-Gly of Bruker Daltonics.Inc.. HPLC analysis was performed on Waters-Breeze (2487 Dual λ Absorbance Detector and 1525 Binary HPLC Pump). Chiralpak AS, AD and OJ columns were purchased from Daicel Chemical Industries, LTD. Chiral GC analysis was performed on VARIAN CP-3380 with a CP CHIPASIL-DEX column. Acetone was dried over anhydrous K_2CO_3. Hexane and ethyl acetate for column chromatography were distilled before use.

Materials: All starting materials were purchased from Acros and used directly.

The typical procedure for the preparation of 1a-2b



Z-A A

Typical procedure for the synthesis of Z-A: ***N***-Carbobenzyloxy-L-proline (2.0 g, 8.0 mmol) and TEA

(0.81 g, 8.0 mmol) were dissolved in THF (30 mL). The solution was cooled down to 0°C. To the solution was added ethylchloroformate (0.88 g, 8.0 mmol) dropwise for 15 min. After the solution was stirred for 30 min, amine (8.0 mmol) was added for 15 min. The resulting solution was stirred at 0 °C for 1 h and at room temperature for another 16 h, and then refluxed for 3 h. After cooled down to room temperature, the solution was diluted with ethyl acetate. After filtration and removal of solvent under reduced pressure, the residue was purified through column chromatography on silica gel (eluent: hexane: ethyl acetate = 2:1) to give Z-**A** .

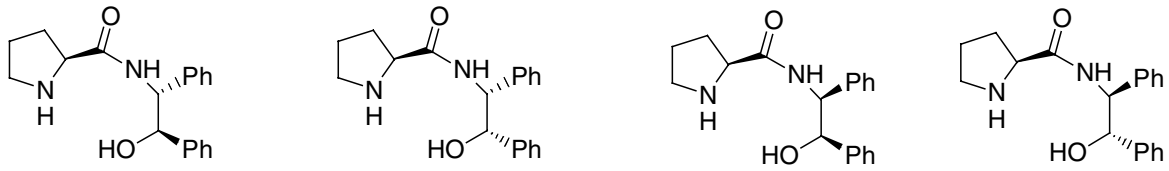
Typical procedure for the synthesis of A: Compounds Z-**A** (1.0 g), 5% Pd/C (0.1 g) and methanol (30 ml) were mixed in a 100 mL two-neck flask. After stirred under hydrogen (1 atm) for 1 h, the solution was filtered. Removal of solvent, the resulting residue was purified through column chromatography on silica gel (eluent: hexane: ethyl acetate = 2:1) to give **A**.

(2*S*,1'*R*)-Pyrrolidine-2-carboxylic acid (1-benzyl-2-hydroxy-ethyl)- amide (1a) Yield: 79% mp 136.9-138.7 ^{0}C; [ ]$^{20}_D$= -16.6 (c= 0.48, CH_3CH_2OH); ^{1}HNMR (300 MHz,$CDCl_3$) (ppm) 1.65-1.72 (m, 2H), 1.94-2.15 (m, 3H), 1.87 (m, 1H), 2.11 (m, 1H),2.52 (br, 1H) 2.80-2.97 (m, 4H), 3.60-3.75 (m, 3H), 4.02 (m, 1H), 7.21-7.34 (m, 5H), 7.87 (br, 1H); ^{13}CNMR (75 MHz, $CDCl_3$) (ppm) 25.9, 30.7, 36.9, 47.0, 53.5, 60.4, 65.1, 126.5, 128.4, 129.1, 137.7, 175.8. HRMS (FT-ICRMS) exact mass calcd for $(C_{14}H_{20}N_2O_2 + H)^+$ requires m/z 249.1603, found m/z 249.1585.

(2*S*,1'*S*)-Pyrrolidine-2-carboxylic acid (1-benzyl-2-hydroxy-ethyl)- amide (2a): Yield: 82% mp 104.4-105.9 ^{0}C; [ ]$^{25}_D$= -63.0 (c= 0.5, CH_3CH_2OH); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 1.43 (m, 2H), 1.56 (m, 3H), 1.71 (m, 1H), 2.00 (m, 1H), 2.78 (m, 1H), 2.88-2.95 (m, 2H), 3.60-3.76 (m, 3H), 4.12 (m, 1H), 7.11-7.33 (m, 5H), 7.87 (br, 1H); ^{13}CNMR (75 MHz, $CDCl_3$) (ppm) 26.7, 31.4, 37.9, 47.9, 53.9, 61.2, 66.5, 127.4, 129.3, 130.0, 138.5, 177.2; MS (ESI): 249.2 (MH^+). HRMS (FT-ICRMS) exact mass calcd for $(C_{14}H_{20}N_2O_2 + H)^+$ requires m/z 249.1603, found m/z 249.1598.

(2*S*,1'*R*)-Pyrrolidine-2-carboxylic acid (1-isopropyl-2-hydroxy-ethyl)-amide (1b): Yield: 85%; mp 106.4-108.6^{0}C; [ ]$^{20}_D$= -25.1 (c= 0.47, CH_3CH_2OH); ^{1}HNMR (300 MHz,$CDCl_3$) (ppm) 0.95 (m, 6H), 1.70-1.76 (m, 2H), 1.93 (m, 2H), 2.12 (m, 1H), 2.56 (br, 1H), 2.90-3.01 (m, 2H), , 3.62 (m, 2H), 3.73 (m, 2H), 7.90 (br, 1H); ^{13}CNMR (75 MHz, $CDCl_3$) (ppm) 18.4, 19.4, 26.0, 28.9, 30.8, 47.1, 57.6, 60.4, 64.5, 176.2. HRMS (FT-ICRMS) exact mass calcd for $(C_{10}H_{20}N_2O_2 + H)^+$ requires 201.1603, found m/z 201.1590.

.**(2*S*,1'*S*)-Pyrrolidine-2-carboxylic acid (1-isopropyl-2-hydroxy-ethyl)-amide (2b):** Yield: 94%; mp 79.2-82.8 ^{0}C; [ ]$^{25}_D$= -83.4 (c= 1.1, CH_3CH_2OH); ^{1}HNMR (300 MHz,$CDCl_3$) (ppm) 0.93 (m, 6H), 1.72 (m, 2H), 1.92 (m, 2H), 2.20 (m, 1H), 2.70 (br, 1H), 2.90-3.11 (m, 2H), 3.60-3.80 (m, 4H), 7.92 (br, 1H); ^{13}CNMR (75 MHz, $CDCl_3$) (ppm)19.2, 20.5, 27.1, 29.8, 31.6, 48.1, 58.0, 61.4, 65.6, 177.4; HRMS (FT-ICRMS) exact mass calcd for $(C_{10}H_{20}N_2O_2 + H)^+$ requires 201.1603, found m/z 201.1591.



3a **3b** **3c** **3d**

Preparation and characterization of 3a: *N*-Carbobenzyloxy-L-proline (2.0 g, 8.0 mmol) and TEA (0.81 g, 8.0 mmol) were dissolved in THF (30ml). The solution was cooled down to 0°C. To the solution was added ethylchloroformate (0.88 g, 8.0 mmol) dropwise for 15 min. After the solution was stirred for 30 min, (1*R*,2*R*)-2-amino-1,2-diphenyl-ethanol (1.7 g, 8.0 mmol) was added for 15 min. The resulting solution was stirred at 0 °C for 1 h and at room temperature for 16 h, and refluxed for 3 h. After the solution was cooled down to room temperature, the solution was washed with ethyl acetate, and filtered. After the solvent was evaporated to dryness, the residue was purified through column chromatography on a silica gel (eluent: hexane: ethyl acetate= 2:1) to give Z-**3a.**

Compounds Z-**3a** (1.0 g), 5% Pd/C (0.1 g) and methanol (30 ml) were put in a 100 ml two-neck flask. The solution was stirred under hydrogen at 50 ^{0}C for 2h, and filtered on Celite to remove any solids, then evaporated to dryness to give pure **3a**.

(2*S*,1'*S*,2'*R*)-Pyrrolidine-2-carboxylic acid (2-hydroxy-1,2-diphenyl-ethyl)-amide (3a):Yield: 82% mp 183.8-186.4 ^{0}C (Dec); [ ]$^{23}_D$= -29.2 (c= 0.5, CH_3CH_2OH); ^{1}HMNR (300 MHz, CD_3OD) (ppm) 1.51-1.65 (m,3H), 2.95 (m, 1H), 3.65 (m, 1H), 4.99 (d, *J*= 4.2 Hz, 1H), 5.08 (d, *J*= 4.2 Hz, 1H), 7.20-7.40 (m, 10H); ^{13}CNMR (75 MHz, $CDCl_3$) (ppm) 25.9, 30.5, 47.1, 59.0, 60.4, 77.1, 126.0, 126.9, 127.4, 127.5, 127.9, 128.5, 139.3, 140.7, 175.5. HRMS (FT-ICRMS) exact mass calcd for $(C_{19}H_{22}N_2O_2 + H)^+$ requires m/z 311.1760, found m/z 311.1750.

(2*S*,1'*R*,2'*R*)-Pyrrolidine-2-carboxylic acid (2-hydroxy-1,2-diphenyl-ethyl)-amide (3b):

N-Carbobenzyloxy-L-proline (2.0 g, 8.0mmol) and TEA (0.81 g, 8.0 mmol) were dissolved in THF (30 mL). The solution was cooled down to 0°C. To the solution was added ethylchloroformate (0.88 g, 8.0 mmol) dropwise for 15 min. After the solution was stirred for 30 min, (1S,2R)-2-amino-1,2-diphenyl-ethanol (1.7 g, 8.0 mmol) was added for 15 min. The resulting solution was stirred at 0 °C for 1 h and at room temperature for 16 h, and then refluxed for 3 h. After the solution was cooled down to room temperature, the solution was washed with ethyl acetate. After filtered, the solvent was evaporated and the residue was recrystallized from ethanol to give pure Z-**3b**

Compounds Z-**3b** (1.0 g), 5% Pd/C (0.1 g) and methanol (30 mL) were put in a 100 ml two neck flask. The solution was stirred under hydrogen (1 atm) at 50 ^{0}C for 2 h. After filtered, the solvent was evaporated to provide pure **3b**. Yield: 70% mp 201.1-203.6 ^{0}C (Dec); $[\ ]^{23}_D$= -28.4 (c= 0.49 CH_3OH); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 1.61-1.68 (m,2H), 1.87 (m, 1H), 2.09 (m, 1H), 2.82 (m, 1H), 2.96 (m, 1H), 3.69 (m, 1H), 4.98 (d, *J*=4.8 Hz, 1H),.5.32(m, 1H), 7.05-7.32 (m, 10H), 8.35 (br, 1H); ^{13}CNMR (75 MHz, $CDCl_3$) (ppm) 26.0, 30.6, 47.1, 59.1, 60.3, 126.9, 127.4, 127.6, 127.7, 128.2, 137.8, 139.5, 175.6. HRMS (FT-ICRMS) exact mass calcd for $(C_{19}H_{22}N_2O_2 + H)^+$ requires m/z 311.1760, found m/z 311.1758 (MH^+)

The procedure for the synthesis of 3c is similar as 3b

(2*S*,1'*R*,2'*S*)-Pyrrolidine-2-carboxylic acid (2-hydroxy-1,2-diphenyl-ethyl)-amide (3c): Yield: 74% mp 141.7-144.8 ^{0}C; $[\ ]^{22}_D$= -23.8 (c= 0.52, CH_3CH_2OH); ^{1}HNMR (300 MHz, CD_3OD) (ppm) 1.37 (m,1H), 1.56 (m, 1H), 1.66 (m, 1H), 1.93 (m, 1H), 2.93 (m, 1H), 3.64 (m, 1H), 4.94 (d, *J*= 6.9 Hz, 1H), 5.16 (d, *J*= 6.9 Hz, 1H), 7.26 (m, 10H); ^{13}CNMR (75 MHz, CD_3OD) (ppm) 25.9, 31.2, 47.3, 59.3, 60.9, 76.8, 127.6, 127.8, 128.1, 128.44, 128.47, 128.5, 140.0, 142.2, 174.2. HRMS (FT-ICRMS) exact mass calcd for $(C_{19}H_{22}N_2O_2 + H)^+$ requires m/z 311.1760, found m/z 311.1751 (MH^+)

The procedure for the synthesis of 3d is similar as 3b.

(2*S*,1'*S*,2'*S*)-Pyrrolidine-2-carboxylic acid (2-hydroxy-1,2-diphenyl- ethyl)-amide (3d): Yield: 80% mp 66.9-70.7 ^{0}C; $[\ ]^{25}_D$= -23.75 (c= 2.0, CH_3CH_2OH); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 1.60-1.67 (m,2H), 1.76 (m, 1H), 2.04(m, 1H), 2.50(br, 2H), 2.85-2.98 (m, 2H), 3.65 (m, 1H), 4.96 (d, *J*=5.1Hz, 1H), 5.09 (m, 1H), 7.18-7.31 (m, 10H),8.49(d, *J*=5.8Hz 1H); ^{13}CNMR (75 MHz, $CDCl_3$) (ppm) 25.1, 30.5, 47.26, 59.7, 60.4, 77.7, 126.3, 126.9, 127.52, 127.54, 128.0, 128.5, 139.4, 141.0, 175.8; HRMS (FT-ICRMS) exact mass calcd for $(C_{19}H_{22}N_2O_2 + H)^+$ requires m/z 311.1760, found m/z 311.1751.

General procedure for aldol reaction: To a mixture of anhydrous acetone (1 mL) was added the corresponding aldehyde (0.5 mmol) and L-proline derivative (20 mol %) and the resulting mixture was stirred at –25 ^{o}C for 24-48 h. The reaction mixture was treated with saturated ammonium chloride solution, the layers were separated, and the aqueous layer was extracted with ethyl acetate, dried over anhydrous $MgSO_4$. After removal of solvent, the residue was purified through flash column chromatography on a silica gel (eluent: hexane: ethyl acetate =1: 3) to give the pure adducts.

4-Hydroxy-4-(4'-nitrophenyl)-butan-2-one (4a)[2]: Yield: 66%; [ ]$^{18}_{D}$= +61.6 (c= 0.51, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 2.21 (s, 3H), 2.83 (m, 2H), 3.56 (d, *J* = 3.2 Hz, 1H), 5.25 (m, 1H), 7.52 (d, *J*= 7.0 Hz, 2H), 8.20 (d, *J* = 7.0 Hz, 2H). Enantiomeric excess: 93%, determined by HPLC (Daicel Chiralpak AS-H, i-PrOH/ Hexane=30/ 70), UV 254nm, flow rate 1.0 mL/min. *R*-isomer, t_R 13.0min and *S*-isomer, t_R 16.3 min.

4-Hydroxy-4-(4'-bromophenyl)-butan-2-one (4b)[2]: Yield: 77%; [ ]$^{18}_{D}$= +53.3 (c= 0.42, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 2.20 (s, 3H), 2.82 (m, 2H), 3.40 (d, *J* = 3.0 Hz, 1H), 5.12 (m, 1H), 7.24 (d, *J*= 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H). Enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak AS-H, i-PrOH/ Hexane=15/ 85), UV 262nm, flow rate 1.0 mL/min. *R*-isomer, t_R 11.4 min and *S*-isomer, t_R 13.7 min.

4-Hydroxy-4-(4'-chlorophenyl)-butan-2-one (4c): Yield: 75%; [ ]$^{18}_{D}$=+62.7 (c= 0.48, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 2.18(s,1H), 2.82(m,1H), 3.46(br,1H) 5.11(m,1H), 7.29(m,4H); Enantiomeric excess: 93%, determined by HPLC (Daicel Chiralpak AS-H, i-PrOH/ Hexane=10/ 90), UV 254nm, flow rate 1.0 mL/min. *R*-isomer, t_R 14.1 min and *S*-isomer, t_R 17.6 min.

4-Hydroxy-4-(2'-chlorophenyl)-butan-2-one (4d)[2]: Yield: 83%; [ ]$^{18}_{D}$= +97.0 (c= 0.34, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) (ppm) 2.22 (s, 3H), 2.64-3.03 (m, 2H), 3.61 (br, 1H), 5.56 (m, 1H), 7.19-7.34 (m, 3H), 7.64 (t, 1H). Enantiomeric excess: 85%, determined by HPLC (Daicel Chiralpak AS-H, i-PrOH/ Hexane=8/ 92), UV 262nm, flow rate 1.0 mL/min. *R*-isomer, t_R 17.9 min and *S*-isomer, t_R 12.5 min.

4-Hydroxy-4-phenyl-butan-2-one (4e): Yield: 51%; [ ]$^{20}_{D}$= +60.0 (c= 0.67, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 2.21 (s, 3H), 2.87 (m, 2H), 3.32 (d, *J* = 3.0 Hz, 1H), 5.17 (m, 1H), 7.27-7.38 (m,

5H. Enantiomeric excess: 83%, determined by HPLC (Daicel Chiralpak AS-H, i-PrOH/ Hexane=15/ 85), UV 257nm, flow rate 1.0 mL/min. *R*-isomer, t_R 11.2 min and *S*-isomer, t_R 12.5 min.

(4*R*)-4-(1-Naphthyl)-4-hydroxy-2-butanone (4f): Yield: 76%; $[\ ]^{20}_{D}$= +74.3 (c= 0.48, $CHCl_3$); ^{1}HNMR (300MHz, $CDCl_3$) (ppm) 2.24 (s, 3H), 3.00 (m, 1H), 3.45 (d, *J* = 3.3 Hz, 1H), 5. 97 (t 1H) 7.47-7.54 (m, 3H), 7.71 (d, *J*= 10.2 Hz, 1H), 7.81 (d, *J*= 11.4 Hz, 1H), 7.88 (m, 1H) 8.00 (m, 1H); Enantiomeric excess: 81%, determined by HPLC (Daicel Chiralpak AS-H, i-PrOH/ Hexane=15/ 85), UV 243nm, flow rate 1.0 mL/min. *R*-isomer, t_R 12.6 min and *S*-isomer, t_R 13.8 min.

4-(2-Naphthyl)-4-hydroxy-2-butanone (4g): Yield: 93%; $[\ ]^{18}_{D}$= +58.8 (c= 0.5, $CHCl_3$); HNMR (300 MHz, $CDCl_3$) (ppm) 2.21 (s, 3H), 2.95 (m, 2H), 3.44 (bs, 1H), 5.34 (m,1H), 7.45 (m, H), 7.82 (m, 4H); Enantiomeric excess: 84%, determined by HPLC (Daicel Chiralpak AS-H, i-PrOH/ Hexane=15/ 85), UV 257nm, flow rate 1.0 mL/min. *R*-isomer, t_R 19.8 min and *S*-isomer, t_R 22.1 min

4-Hydroxy-4-(4-methylphenyl)-butan-2-one (4h): Yield: 48%; $[\ ]^{20}_{D}$= +57.1 (c= 0.35, $CHCl_3$); ^{1}HNMR (300MHz, $CDCl_3$) (ppm) 2.20 (s, 3H), 2.35 (s, 1H) 2.77-2.88 (m, 2H), 3.32 (s, 1H), 5.25 (d, *J*=8.7 Hz, 2H), 7.17 (d, *J*= 7.8Hz, 2H) 7.26 (d, *J*= 7.8Hz, 2H); Enantiomeric excess: 84%, determined by HPLC (Daicel Chiralpak, AS-H, i-PrOH /Hexane=15/ 85), UV 257nm, flow rate 1.0 mL/min. *R*-isomer, t_R 10.1 min and *S*-isomer, t_R 12.4 min.

4-Hydroxy-4-(3'-nitro-phenyl)-butan-2-one (4i): Yield: 63%; $[\ ]^{20}_{D}$= +62.1 (c= 0.35, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 2.23 (s, 3H), 2.89 (t, 2H), 3.70 (br, 1H), 5.52 (m, 1H), 7.53 (t, 1H), 7.71 (d, *J*= 7.5 Hz, 1H), 8.13 (m,1H) 8.24 (s,1H); Enantiomeric excess: 87%, determined by HPLC (Daicel Chiralpak OJ-H, i-PrOH/ Hexane= 20/ 80), UV 254nm flow rate 1.0 mL/min. *R*-isomer, t_R 17.3 min and *S*-isomer, t_R 19.9 min.

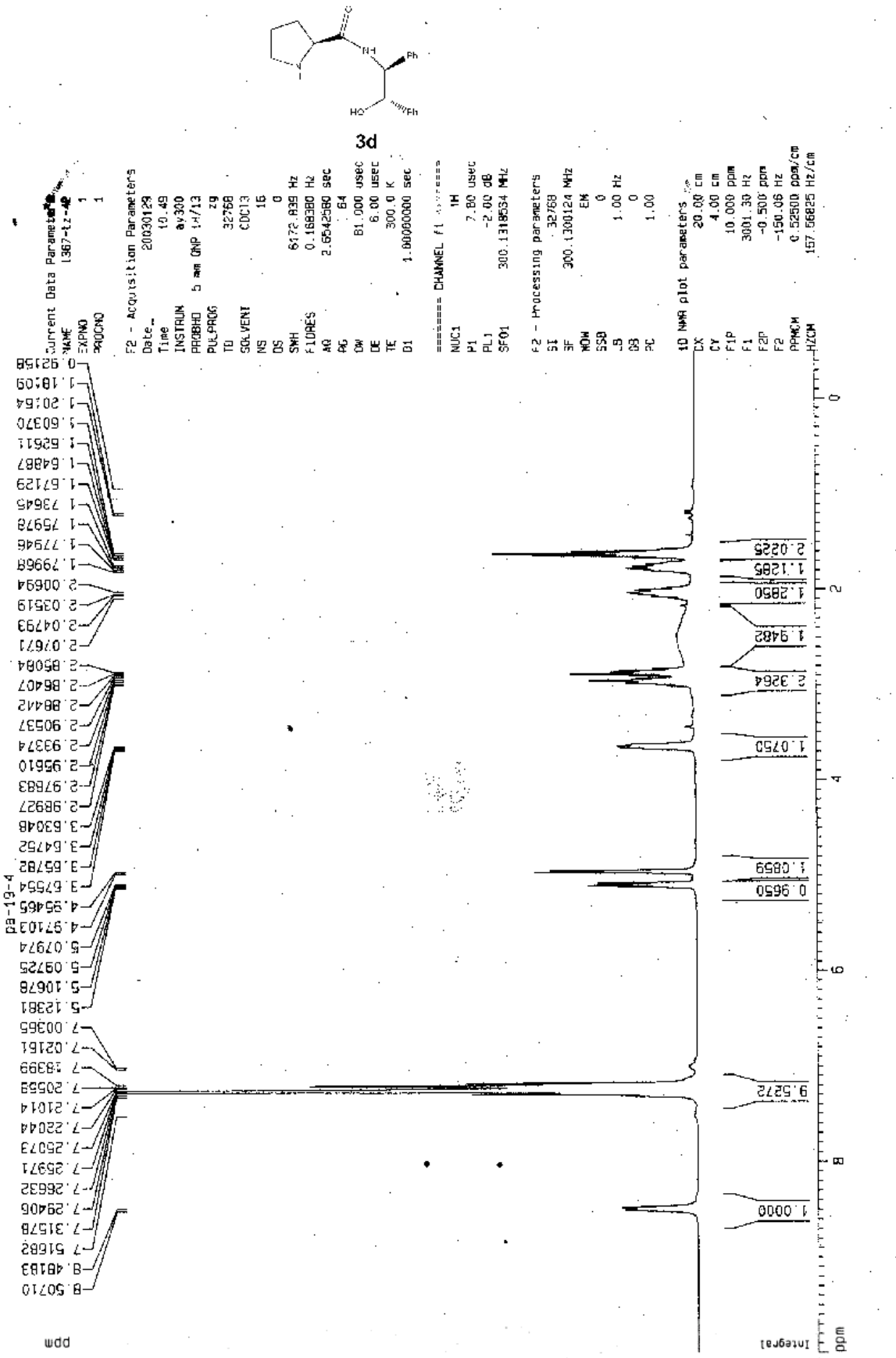
(4*R*)-4-(Cyclohexyl)-4-hydroxy-2-butanone (4j): Yield: 85%; $[\ ]^{18}_{D}$=+45.9 (c= 0.24, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 0.97-1.25 (m, 6H), 1.62-1.77 (m, 5H), 2.18 (s, 3H), 2.55 (m, 2H), 2.89 (bs, 1H), 3.80 (m 1H); Enantiomeric excess: 97%, determined by HPLC (Daicel Chiralpak AD, i-PrOH/ Hexane= 10/ 90), UV 280nm flow rate 1.0 mL/min. *R*-isomer, t_R 6.1 min and *S*-isomer, t_R 7.0 min.

4-Hydroxy-5-methyl-hexan-2-one (4k): Yield: 43%; [ ]$^{18}_{D}$= +77.6 (c= 0.51, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 0.90 (d, *J*=6.6Hz, 1H) ,1.11(m, 1H), 1.43 (m, 1H),1.77 (m, 1H), 2.17 (s, 1H), 2.56 (m, 2H), 2.97 (br, 1H), 4.11(m, 1H); Enantiomeric excess: 98%, determined by HPLC (Daicel Chiralpak AD, i-PrOH/ Hexane= 3/ 97), UV 280nm flow rate 1.0 mL/min. *R*-isomer, t_R 9.1 min and *S*-isomer, t_R 10.0 min.

4-Hydroxy-5,5-dimethyl-hexan-2-one (4l): Yield: 51%; [ ]$^{18}_{D}$= +75.5 (c= 0.38, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 0.91(s,1H), 2.52-2.66 (m,2H), 3.77(m,1H); Enantiomeric excess: >99%, determined by HPLC (Daicel Chiralpak AD, i-PrOH/ Hexane= 3/ 97), UV 280nm flow rate 1.0 mL/min.*R*-isomer, t_R 7.4 min and *S*-isomer, t_R 8.8 min.

4-Hydroxy-heptan-2-one (4m): Yield: 17%; ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 0.93 (m, 1H), 1.34-1.51(m, 2H) 2.18 (s, 3H) 2.60 (m, 1H) 2.97(br, 1H) 4.08 (m, 1H); Enantiomeric excess: 87%, determined by chiral GC analysis (CP CHIRASIL-DEX), Inject Temp 240 ^{0}C ,Column Temp 110 ^{0}C, FID Oven Temp 260 ^{0}C, Inlet Pressure 10 Psi. *R*-isomer, t_R 5.7 min and *S*-isomer, t_R 5.9 min.

4-Hydroxy-octan-2-one (4n): Yield: 12%; ^{1}HNMR (300 MHz, $CDCl_3$) (ppm) 0.82 (t, *J*= 7.2 Hz, 1H), 1.22-1.40(m, 4H) 2.10 (s, 3H) 2.46-2.58 (m, 2H) 2.88(br, 1H) 3.95 (m, 1H); Enantiomeric excess: 87%, determined by chiral GC analysis (CP CHIRASIL-DEX), Inject Temp 240 ^{0}C ,Column Temp 120 ^{0}C, FID Oven Temp 260 ^{0}C, Inlet Pressure 10 Psi. *R*-isomer, t_R 6.0 min and *S*-isomer, t_R 6.2 min.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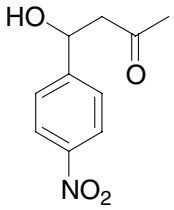

(**4a**)-Racemic

ulas

Project Name: Waters
Reported by User: System

Breeze

SAMPLE INFORMATION

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Injection Volume:	20.00 ul	Date Processed:	11/26/02 12:28:45 PM
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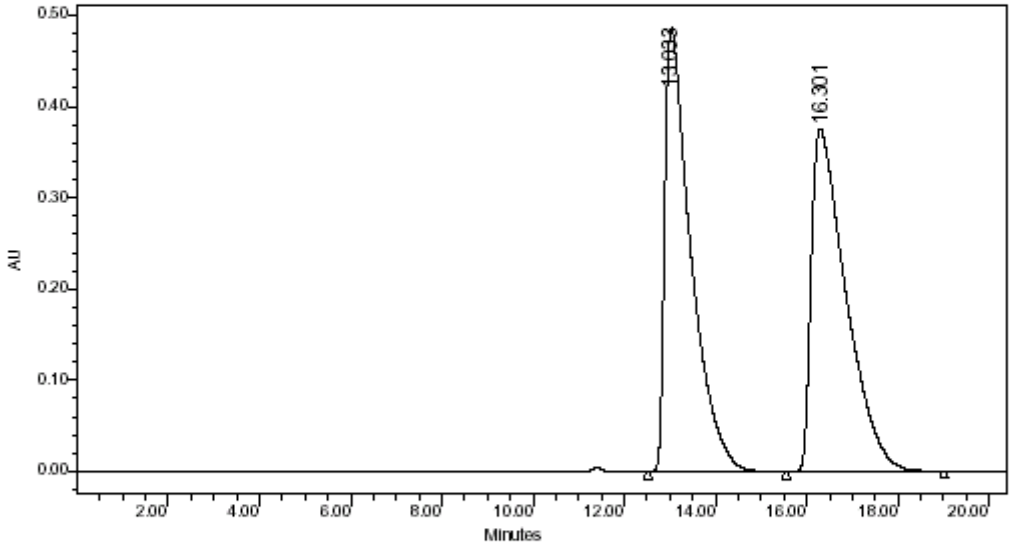
Sampling Rate:	1.00 per sec	Sample Set Name:	

Sample Values
Used in Calculations



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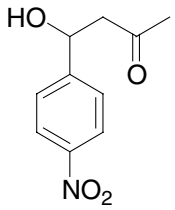
2	16.301	Unknown	19784997	50.65	375013	43.55	BB	208	15.550	19.033

	Baseline Start (min)	Baseline End (min)	Slope (V/sec)	Offset (V)
1	12.533	15.550	3.707475e-005	-4.430724e-004



(**4a**), 93% ee

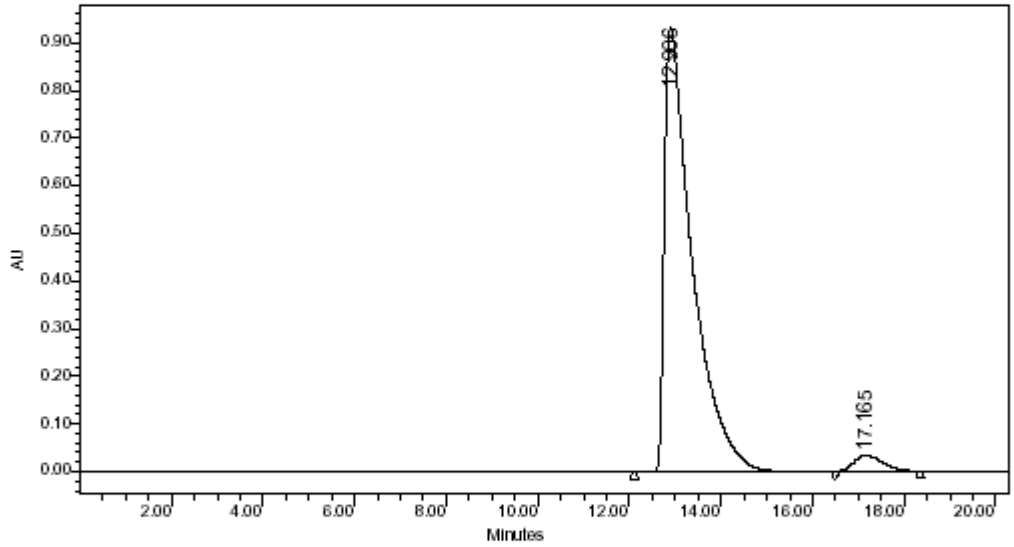
ulas
Project Name: Waters
Reported by User: System

Breeze

SAMPLE INFORMATION

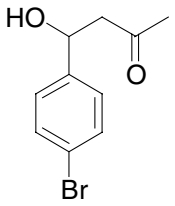
Sample Name:	tz-89	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	11/26/02 11:24:42 AM
Vial:	1	Acq. Method:	30
Injection #:	2	Processed By:	System
Injection Volume:	20.00 ul	Date Processed:	11/26/02 11:56:54 AM
Run Time:	40.00 Minutes	Channel Name:	2487Channel 1
Sampling Rate:	1.00 per sec	Sample Set Name:	

Sample Values
Used in Calculations



	RT (min)	Peak Type	Area (V*sec)	% Area	Height (V)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	12.906	Unknown	39247715	96.33	931362	96.44	bv	263	12.117	16.500
2	17.165	Unknown	1493391	3.67	34336	3.56	vb	112	16.500	18.367

	Baseline Start (min)	Baseline End (min)	Slope (V/sec)	Offset (V)
1	12.117	18.367	1.074371e-004	-1.302841e-003



(**4b**)-racemic

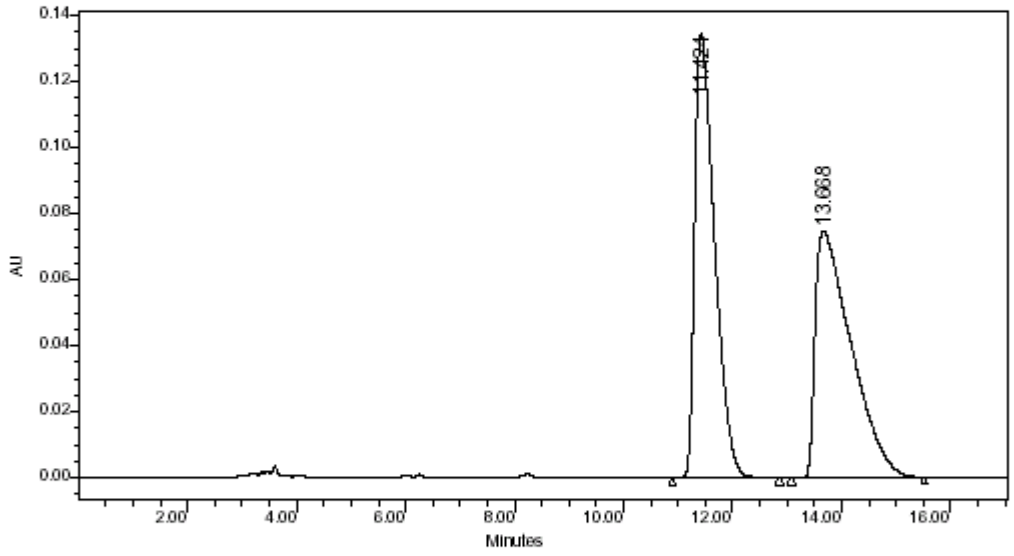
ulas
Project Name: Waters
Reported by User: System

Breeze

SAMPLE INFORMATION

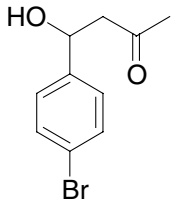
Sample Name:	tz--Br-0.	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	12/9/02 1:51:54 PM
Vial:	1	Acq. Method:	15
Injection #:	2	Processed By:	System
Injection Volume:	20.00 ul	Date Processed:	12/9/02 2:09:35 PM
Run Time:	50.00 Minutes	Channel Name:	2487Channel 1
Sampling Rate:	1.00 per sec	Sample Set Name:	

Sample Values
Used in Calculations



	RT (min)	Peak Type	Area (V*sec)	% Area	Height (V)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	11.424	Unknown	3396586	49.87	134505	64.26	BB	118	10.900	12.867
2	13.668	Unknown	3414883	50.13	74793	35.74	BB	146	13.083	15.533

	Baseline Start (min)	Baseline End (min)	Slope (V/sec)	Offset (V)
1	10.900	12.867	-2.715547e-005	3.601292e-004



(**4b**), 90% ee

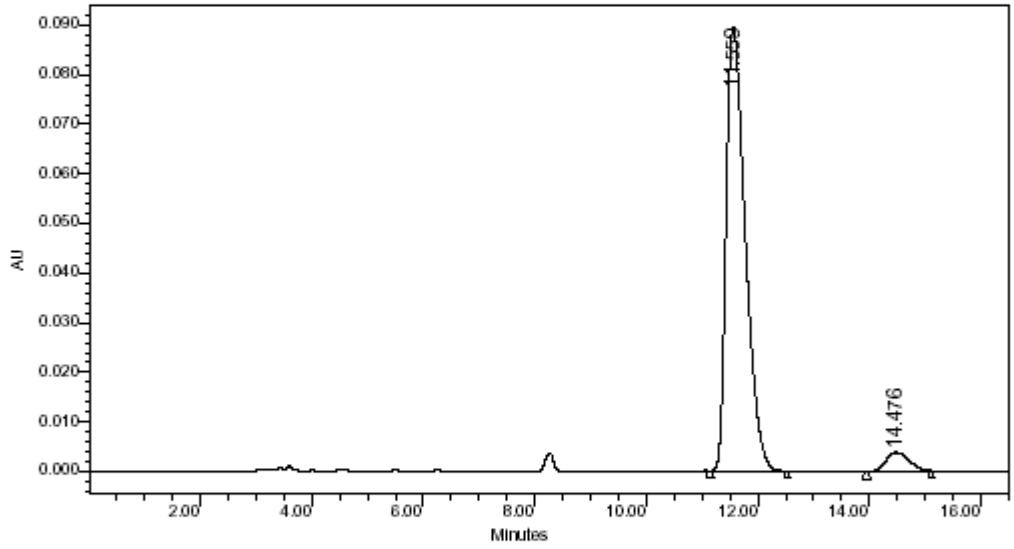
ulas
Project Name: Waters
Reported by User: System

Breeze

SAMPLE INFORMATION

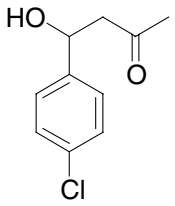
Sample Name:	tz--Br-TT-12	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	12/9/02 2:10:57 PM
Vial:	1	Acq. Method:	15
Injection #:	3	Processed By:	System
Injection Volume:	20.00 ul	Date Processed:	12/9/02 4:11:13 PM
Run Time:	50.00 Minutes	Channel Name:	2487Channel 1
Sampling Rate:	1.00 per sec	Sample Set Name:	

Sample Values
Used in Calculations



	RT (min)	Peak Type	Area (V*sec)	% Area	Height (V)	% Height	Integration Type	Points Across Peak	Start Time (min)	End Time (min)
1	11.559	Unknown	2116173	95.12	89424	95.92	BB	82	11.150	12.533
2	14.476	Unknown	108592	4.88	3799	4.08	Bb	69	13.950	15.117

	Baseline Start (min)	Baseline End (min)	Slope (V/sec)	Offset (V)
1	11.150	12.533	-4.570742e-005	6.769897e-004



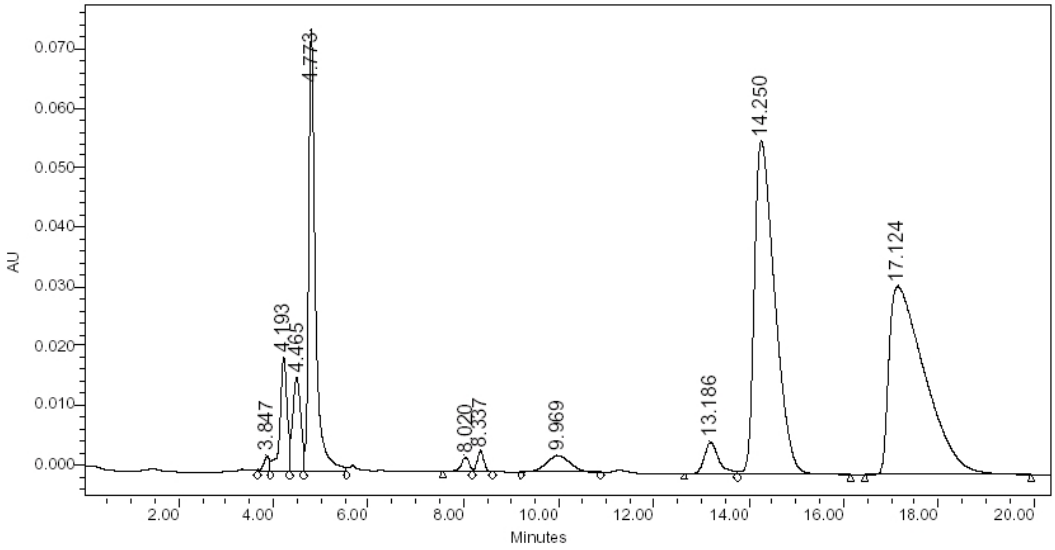
(**4c**)-racemic

ulas
Project Name: Defaults
Reported by User: System

Breeze

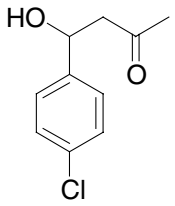
SAMPLE INFORMATION

Sample Name:	TZ-140	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	2/6/03 10:56:54 AM
Vial:	1	Acq. Method:	100A
Injection #:	1	Date Processed:	2/6/03 11:24:35 AM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	3.847	26093	0.55	2687	1.25
2	4.193	202944	4.26	19303	8.99
3	4.465	186396	3.91	15981	7.45
4	4.773	739187	15.51	74804	34.86
5	8.020	29277	0.61	2499	1.16
6	8.337	34094	0.72	3534	1.65
7	9.969	102990	2.16	2825	1.32
8	13.186	113015	2.37	5278	2.46
9	14.250	1667600	34.99	56050	26.12
10	17.124	1664871	34.93	31642	14.74

Report Method: Untitled Printed 11:41:04 AM 2/6/03 Page: 1 of 1



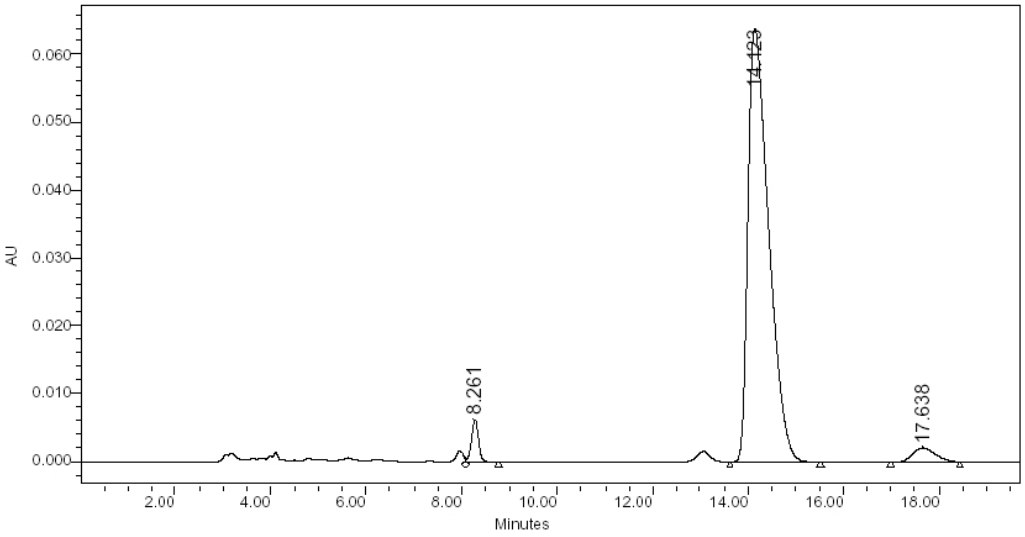
(**4c**), 93% ee

ulas
Project Name: Defaults
Reported by User: System

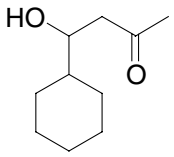
Breeze

SAMPLE INFORMATION

Sample Name:	TZ-141	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	2/6/03 11:20:25 AM
Vial:	1	Acq. Method:	100A
Injection #:	2	Date Processed:	2/6/03 11:40:14 AM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	8.261	62263	3.03	6229	8.61
2	14.123	1921152	93.64	64040	88.52
3	17.638	68299	3.33	2079	2.87



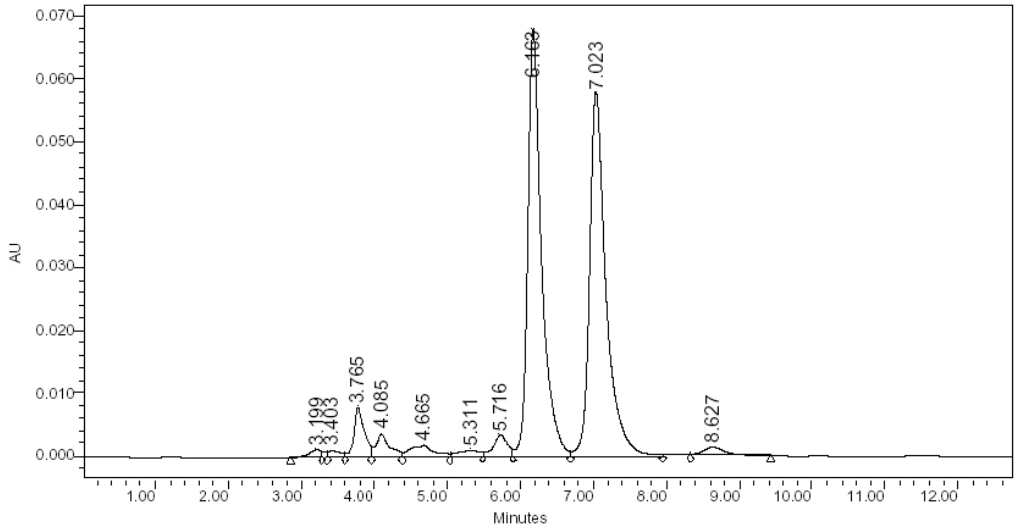
(**4j**)- racemic

ulas
Project Name: Defaults
Reported by User: System

Breeze

SAMPLE INFORMATION

Sample Name:	TT-80-0.	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	1/17/03 10:06:03 AM
Vial:	1	Acq. Method:	10
Injection #:	2	Date Processed:	1/17/03 10:32:48 AM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	3.199	14776	0.70	1314	0.89
2	3.403	12855	0.61	1082	0.73
3	3.765	78599	3.75	7891	5.33
4	4.085	47610	2.27	3642	2.46
5	4.665	42723	2.04	1912	1.29
6	5.311	22410	1.07	1086	0.73
7	5.716	47772	2.28	3476	2.35
8	6.163	892686	42.55	68188	46.04
9	7.023	905273	43.15	58077	39.22
10	8.627	33172	1.58	1427	0.96

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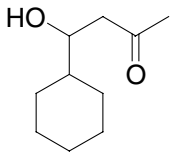


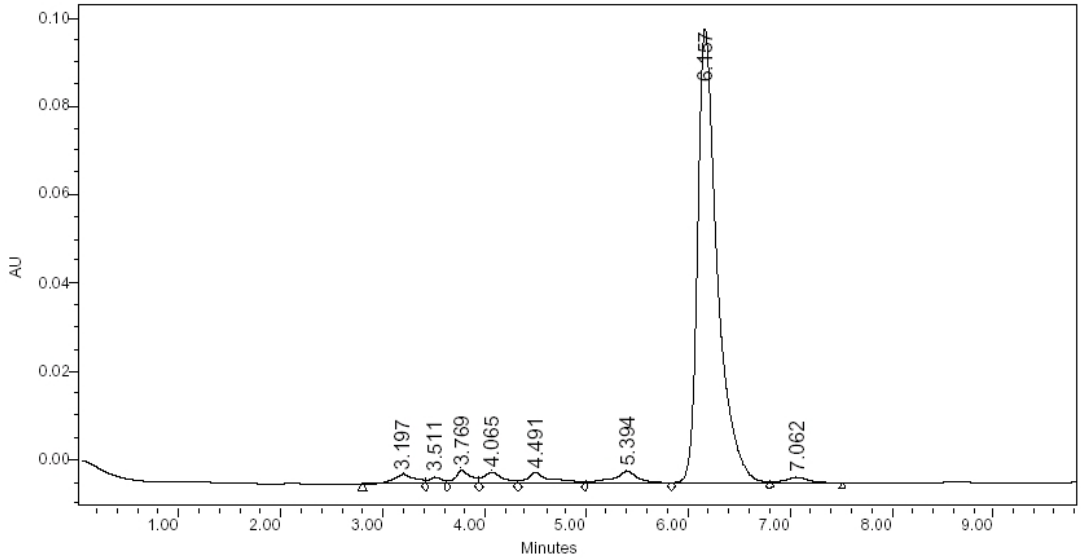
(**4j**) 97% ee

ulas
Project Name: Defaults
Reported by User: System

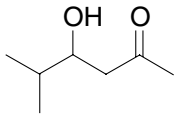
Breeze

SAMPLE INFORMATION

Sample Name:	TT-82	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	1/17/03 10:51:30 AM
Vial:	1	Acq. Method:	10
Injection #:	5	Date Processed:	1/17/03 11:01:24 AM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	3.197	32664	2.03	2182	1.83
2	3.511	13543	0.84	1463	1.23
3	3.769	33714	2.10	3094	2.60
4	4.065	34268	2.13	2613	2.20
5	4.491	42080	2.62	2496	2.10
6	5.394	48703	3.03	2664	2.24
7	6.157	1379364	85.89	103172	86.74
8	7.062	21547	1.34	1265	1.06

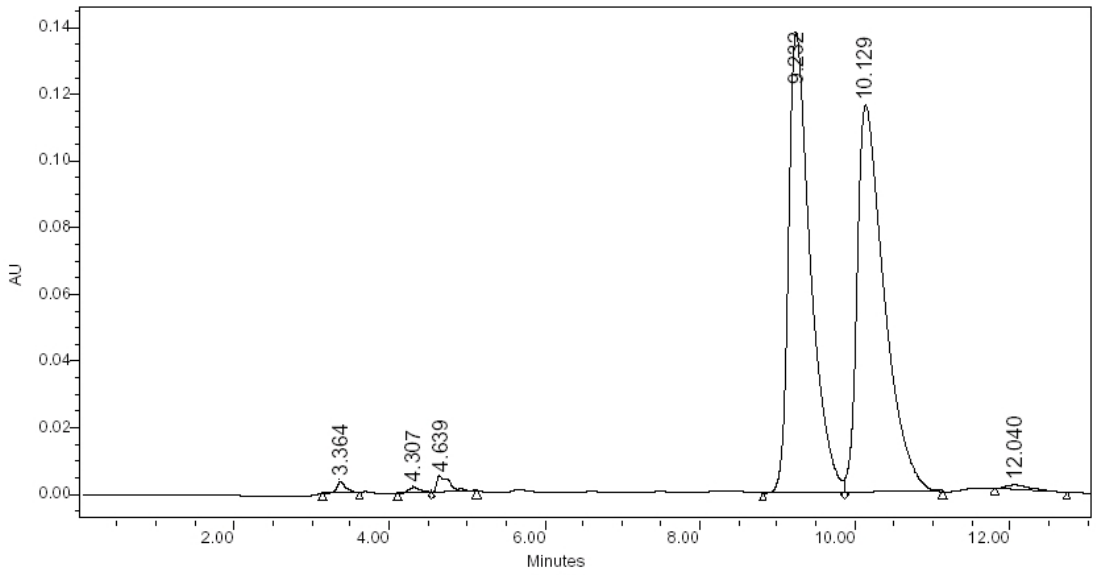


(**4k**)-racemic

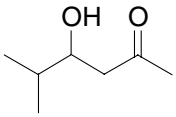
ulas
Project Name: Defaults
Reported by User: System

SAMPLE INFORMATION

Sample Name:	TZ-90Unk.	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	1/20/03 12:56:20 PM
Vial:	1	Acq. Method:	3uv280
Injection #:	1	Date Processed:	1/20/03 1:28:13 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	3.364	26252	0.46	3450	1.30
2	4.307	22782	0.40	1905	0.72
3	4.639	63174	1.11	5158	1.94
4	9.232	2709062	47.80	138219	51.93
5	10.129	2812165	49.62	116031	43.59
6	12.040	34209	0.60	1417	0.53

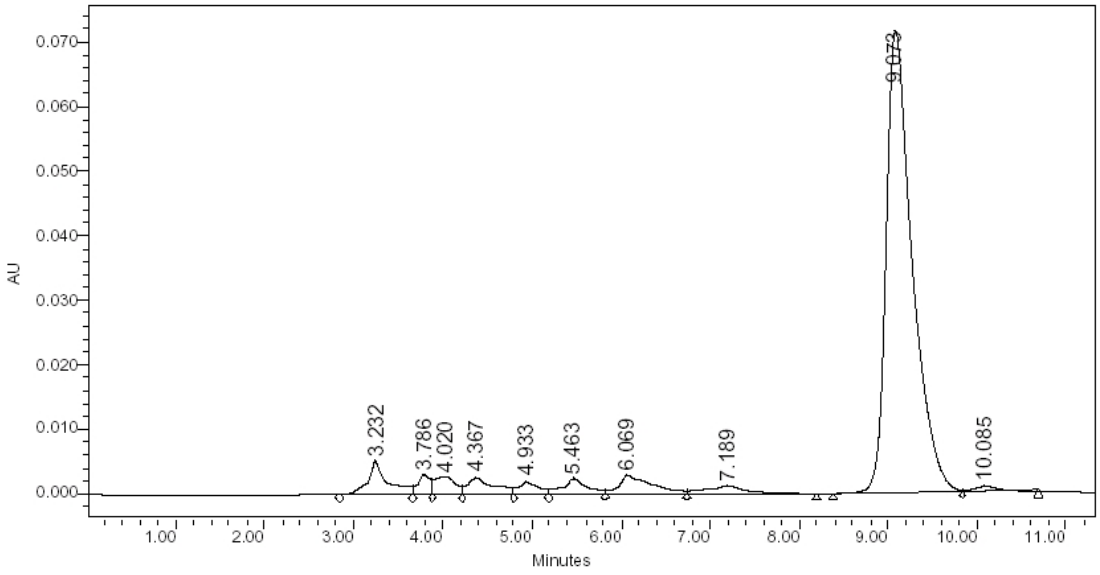


(**4k**) 98% ee

ulas
Project Name: Defaults
Reported by User: System

SAMPLE INFORMATION

Sample Name:	TZ-91	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	1/20/03 1:26:02 PM
Vial:	1	Acq. Method:	3uv280
Injection #:	3	Date Processed:	1/20/03 1:38:36 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	3.232	82551	4.39	5153	5.44
2	3.786	30071	1.60	3084	3.26
3	4.020	43439	2.31	2734	2.89
4	4.367	54886	2.92	2545	2.69
5	4.933	28968	1.54	1866	1.97
6	5.463	46504	2.47	2425	2.56
7	6.069	75586	4.02	2956	3.12
8	7.189	42076	2.24	1296	1.37
9	9.073	1458137	77.54	71790	75.79
10	10.085	18251	0.97	873	0.92

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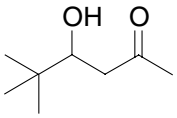


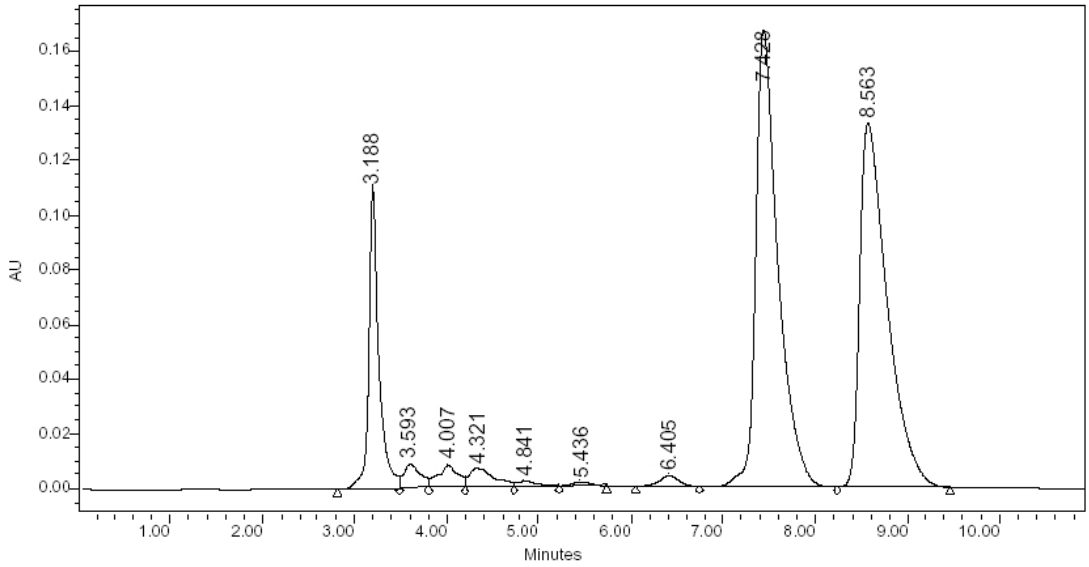
(**4l**)-racemic

ulas
Project Name: Defaults
Reported by User: System

Breeze

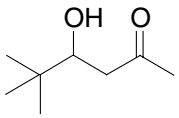
SAMPLE INFORMATION

Sample Name:	TZ-160.	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	1/29/03 4:16:10 PM
Vial:	1	Acq. Method:	3uv280
Injection #:	6	Date Processed:	1/30/03 9:57:41 AM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	3.188	830539	12.01	110749	24.93
2	3.593	115884	1.68	9139	2.06
3	4.007	131178	1.90	8481	1.91
4	4.321	135598	1.96	7132	1.61
5	4.841	37118	0.54	2358	0.53
6	5.436	27667	0.40	1777	0.40
7	6.405	64470	0.93	4116	0.93
8	7.428	2813219	40.69	167371	37.67
9	8.563	2758218	39.89	133185	29.98

Report Method: Untitled Printed 10:36:02 AM1/30/03 Page: 1 of 1



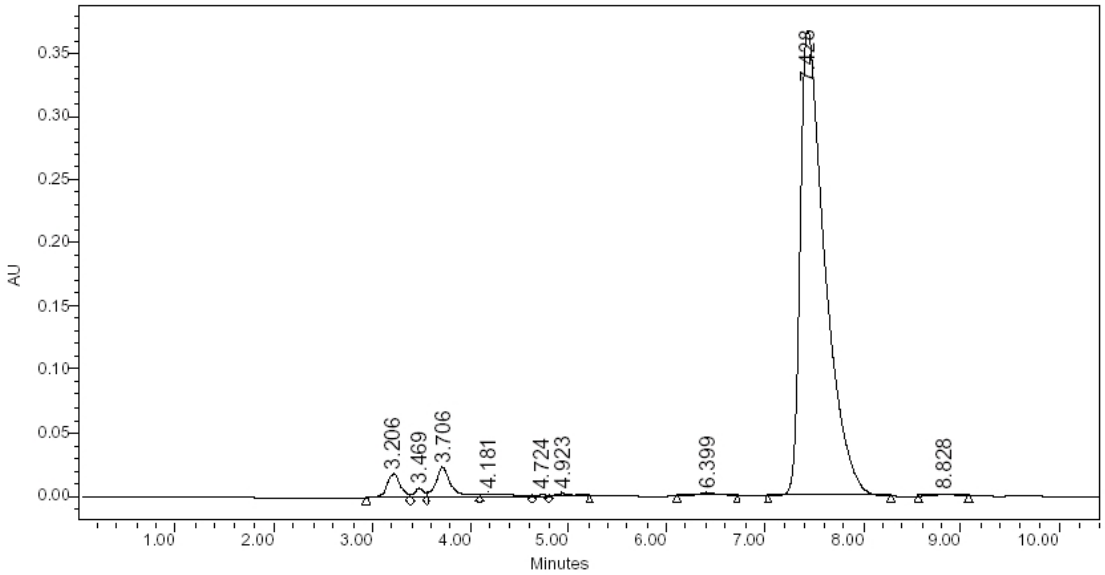
(**4l**) 99% ee

ulas
Project Name: Defaults
Reported by User: System

Breeze

SAMPLE INFORMATION

Sample Name:	TZ-161.	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	1/30/03 9:26:28 AM
Vial:	1	Acq. Method:	3uv280
Injection #:	1	Date Processed:	1/30/03 9:40:17 AM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	3.206	176491	2.51	18279	4.28
2	3.469	47706	0.68	7058	1.65
3	3.706	255443	3.63	23529	5.51
4	4.181	50173	0.71	2038	0.48
5	4.724	10941	0.16	1225	0.29
6	4.923	24839	0.35	2165	0.51
7	6.399	33436	0.48	2654	0.62
8	7.428	6413902	91.21	368376	86.33
9	8.828	19244	0.27	1360	0.32

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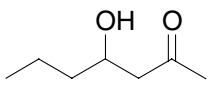


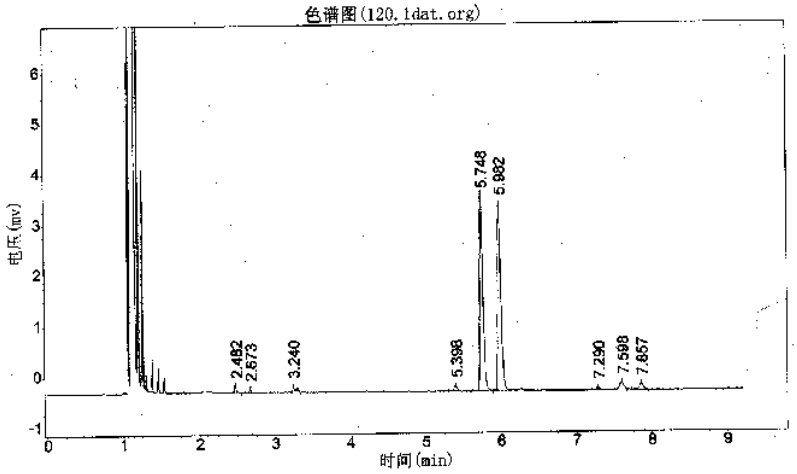
(4m)-racemic

N2000 数据工作站 1

实验时间：2003-03-10,9:22:47
谱图文件:D:\1367\唐卓\2003.03.10\120.1dat.org

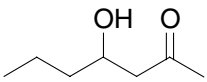
报告时间：2003-03-12,13:49:40
计算方法:面积归一法

色谱图(120.1dat.org)



分析结果表

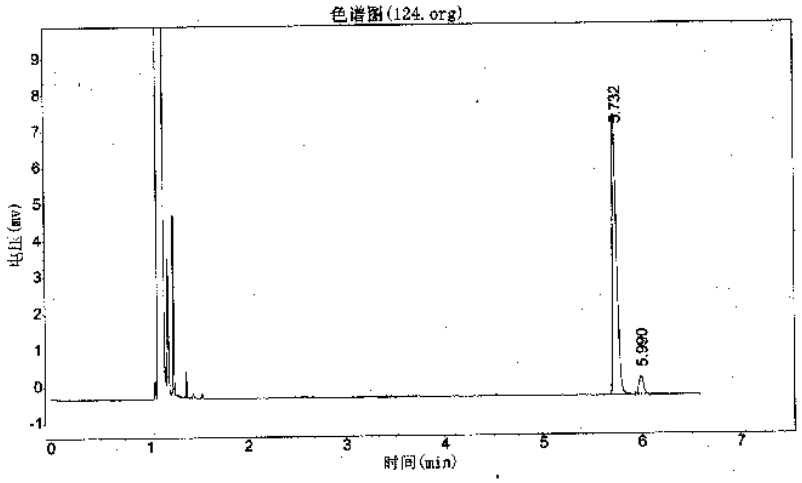
峰号	峰名	保留时间(RT, min)	峰高 Height	峰面积 Area	含量 % Area
1		2.482	150.154	248.450	0.9893
2		2.673	51.308	97.550	0.3881
3		3.240	96.429	383.500	1.5271
4		5.398	103.400	330.200	1.3148
5		5.748	3911.188	11400.800	45.3977
6		5.982	3671.778	11401.100	45.3989
7		7.290	49.524	182.050	0.7249
8		7.598	140.900	556.700	2.2168
9		7.857	120.333	512.800	2.0420
总计			8295.013	25113.149	100.0000



4m 87% ee

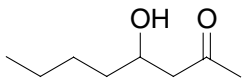
实验时间：2003-03-10,9:22:47
谱图文件:D:\1367\唐卓\2003.03.10\124.org

报告时间：2003-03-12,13:52:45
计算方法:面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		5.732	7487.750	22754.625	93.6204
2		5.990	499.292	1550.575	6.3796
总计			7987.042	24305.200	100.0000



(4n)-racemic

N2000 数据工作站 1

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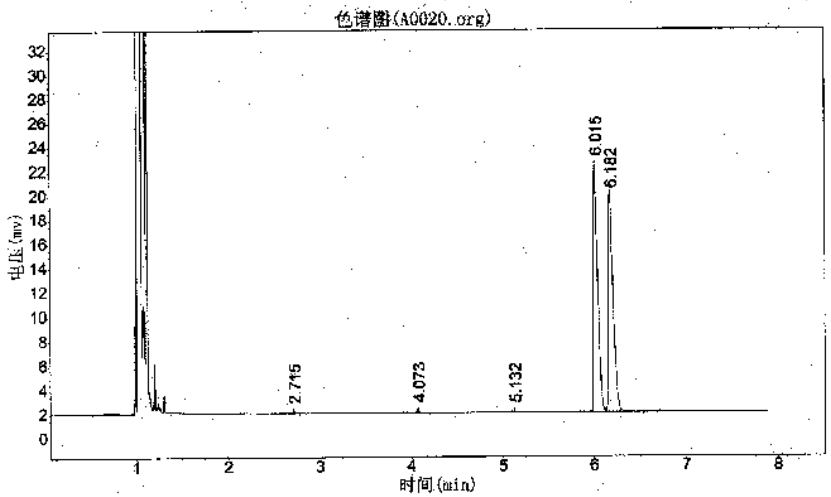
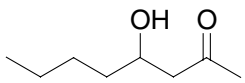
计算方法:面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		2.715	51.216	324.550	0.2500
2		4.073	106.448	319.850	0.2464
3		5.132	41.143	109.400	0.0843
4		6.015	20172.383	64355.105	49.5814
5		6.182	17930.324	64687.895	49.8378
总计			38301.514	129796.800	100.0000



(4n) 86% ee

实验时间：2003-02-24,10:32:45 报告时间：2003-03-12,13:56:18
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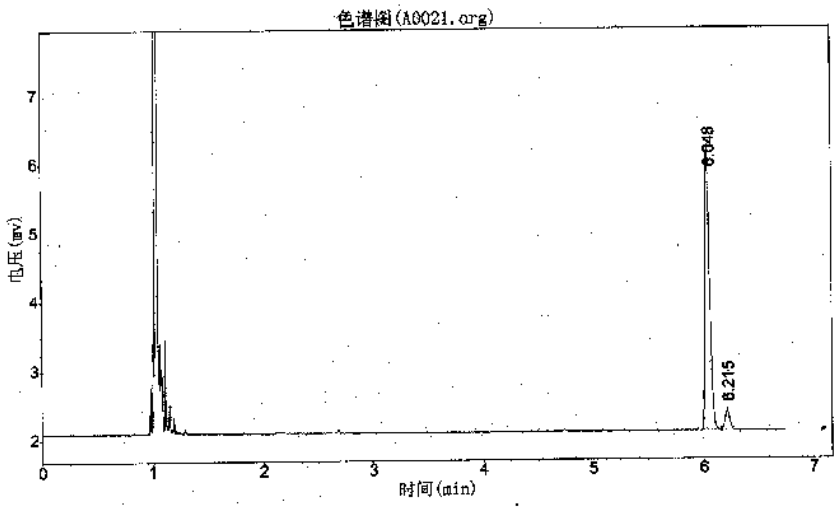

分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.048	3967.522	12125.348	93.2024
2		8.215	262.391	884.352	6.7976
总计			4229.913	13009.700	100.0000

Calculations:

Transition state geometries for the aldol reaction of benzaldehyde with acetone catalyzed by **3d:**

Calculations were performed using the Gaussian 98 Program.[3] Geometries were optimized by the Hartree-Fock method with the 6-31G* basis set and energies were further evaluated with the B3LYP/ 6-31G** method.[4]

The resulting Z-matrix for the two transition structures **TS1** and **TS2**, as well as the total energies are the follows:

Structure of **TS1**:

C						
N	1	1.478259				
C	2	1.470643	1	111.535694		
C	3	1.534105	2	102.726629	1	-18.959757
C	4	1.528336	3	103.070632	2	34.918845
C	3	1.534329	2	116.131033	1	101.713701
O	6	1.204588	3	116.767732	2	169.650086
N	6	1.334317	3	118.128003	2	-12.183091
C	8	1.459204	6	120.560648	3	178.377591
C	9	1.552064	8	109.293758	6	-152.835696
O	10	1.397230	9	110.128042	8	46.675975
C	2	1.310448	1	122.885195	5	179.528346
C	12	1.413034	2	121.896067	1	-8.155880
C	13	1.936933	12	100.746965	2	-88.235265
O	14	1.269959	13	110.680921	12	39.671722
C	12	1.504950	2	118.762154	1	179.797088
C	9	1.522052	8	111.253186	6	82.158132
C	17	1.386589	9	120.690498	8	-125.648804
C	18	1.386879	17	120.818918	9	-179.263721
C	19	1.383614	18	120.206318	17	-0.128545
C	20	1.386949	19	119.499381	18	-0.110859
C	21	1.383935	20	120.097914	19	0.101806
C	10	1.518329	9	111.152075	8	167.709171

C	23	1.391069	10	120.069430	9	-84.587315
C	24	1.383800	23	120.596045	10	179.367845
C	25	1.386857	24	120.262101	23	0.150354
C	26	1.383562	25	119.517316	24	0.146646
C	27	1.386875	26	120.114801	25	-0.131128
C	14	1.511860	13	100.036197	12	165.379580
C	29	1.389672	14	121.144536	13	74.649535
C	30	1.384162	29	120.634360	14	178.924718
C	31	1.386578	30	119.961427	29	-0.179195
C	32	1.385726	31	119.683985	30	-0.422433
C	33	1.385570	32	120.251798	31	0.330698
H	8	1.002735	6	119.714262	3	9.729167
H	11	0.957700	10	107.334635	9	-86.736520
H	14	1.091465	13	95.275608	12	-82.334548
H	13	1.076519	12	114.641509	2	159.839664
H	9	1.080832	8	107.063882	6	-36.362688
H	10	1.085880	9	108.404347	8	-73.062204
H	3	1.078590	2	110.658186	1	-137.712385
H	4	1.085418	3	109.248789	2	-82.483884
H	4	1.080130	3	111.431416	2	157.765151
H	1	1.077160	2	109.664948	12	57.898322
H	1	1.084477	2	108.791540	12	-61.481411
H	5	1.083384	4	110.261273	3	79.779716
H	5	1.082728	4	113.012600	3	-159.298504
H	13	1.073990	12	117.182349	2	23.742007
H	16	1.079602	12	110.155128	2	-179.797232
H	16	1.084787	12	109.983925	2	60.624005
H	16	1.083719	12	111.274842	2	-59.499390
H	18	1.074967	17	119.497555	9	1.084936
H	19	1.075555	18	119.691513	17	-179.877815
H	20	1.075612	19	120.286781	18	-179.919682
H	21	1.075950	20	120.067386	19	-179.898719
H	22	1.076413	21	119.413160	20	-179.666517

H	24	1.073924	23	119.330167	10	-1.756530
H	25	1.075884	24	119.732953	23	179.801648
H	26	1.075722	25	120.228403	24	179.823931
H	27	1.075684	26	120.167696	25	179.643157
H	28	1.075534	27	119.461889	26	179.991570
H	30	1.077196	29	119.793749	14	-0.620139
H	31	1.075615	30	119.939627	29	-179.784775
H	32	1.075524	31	120.111656	30	-179.822909
H	33	1.075800	32	119.932532	31	-179.077915
H	34	1.073235	33	120.896045	32	-178.336856

E(HF/6-31G*) = **-1450.26084 a.u.**

E(B3LYP/6-31G**//HF/6-31G*) = **-1459.55176 a.u.**

Structure of **TS2**:

C						
N	1	1.476516				
C	2	1.472322	1	111.229006		
C	3	1.532771	2	102.424035	1	-21.535754
C	4	1.528700	3	102.781201	2	36.741685
C	3	1.535878	2	116.331827	1	98.667393
O	6	1.205049	3	116.345653	2	174.671401
N	6	1.332748	3	118.229209	2	-6.945854
C	8	1.458747	6	120.885051	3	176.540828
C	9	1.553449	8	109.451001	6	-141.183524
O	10	1.397797	9	109.967213	8	45.297059
C	2	1.306397	1	122.934878	5	-179.599669
C	12	1.422896	2	122.207448	1	-5.570958
C	13	1.927338	12	101.666588	2	-85.699210
O	14	1.274763	13	111.397428	12	5.646536
C	12	1.502403	2	118.867914	1	-178.524011
C	9	1.521375	8	111.142538	6	93.576173
C	17	1.386608	9	120.719976	8	-125.220567

C	18	1.387390	17	120.804821	9	-179.716102
C	19	1.383322	18	120.193996	17	-0.082861
C	20	1.387389	19	119.513599	18	-0.073861
C	21	1.383611	20	120.123316	19	0.053924
C	10	1.517776	9	111.061845	8	166.270085
C	23	1.391221	10	120.133690	9	-83.948288
C	24	1.383728	23	120.587839	10	179.304802
C	25	1.387001	24	120.264023	23	0.102410
C	26	1.383520	25	119.522661	24	0.151790
C	27	1.386997	26	120.109237	25	-0.101258
C	14	1.514629	13	102.327271	12	-122.659996
C	29	1.386888	14	120.963869	13	113.173895
C	30	1.388190	29	120.366631	14	178.742036
C	31	1.383381	30	120.420301	29	-0.480485
C	32	1.388239	31	119.558503	30	-0.327529
C	33	1.381973	32	119.917793	31	0.434761
H	8	1.003674	6	119.967011	3	8.890176
H	11	0.957459	10	107.021781	9	-84.918001
H	13	1.075096	12	113.191309	2	159.259452
H	9	1.079502	8	106.557457	6	-24.769979
H	10	1.084908	9	108.564898	8	-74.264987
H	3	1.078721	2	110.435791	1	-140.465760
H	4	1.085486	3	109.396034	2	-80.648847
H	4	1.079578	3	111.360062	2	159.354800
H	1	1.079663	2	109.745772	12	58.823441
H	1	1.083463	2	109.001326	12	-60.355837
H	5	1.083514	4	110.287401	3	79.269741
H	5	1.082596	4	113.118896	3	-159.700821
H	13	1.076950	12	116.053712	2	27.377881
H	16	1.079051	12	109.964039	2	174.261222
H	16	1.083066	12	110.404117	2	54.578371
H	16	1.085069	12	110.570420	2	-65.760680
H	14	1.090207	13	93.824566	12	125.935362

H	18	1.075143	17	119.512782	9	0.501247
H	19	1.075578	18	119.695536	17	-179.911154
H	20	1.075615	19	120.283475	18	-179.961543
H	21	1.075943	20	120.048032	19	-179.989702
H	22	1.076557	21	119.479713	20	-179.755774
H	24	1.074008	23	119.327735	10	-1.751066
H	25	1.075890	24	119.734018	23	179.799830
H	26	1.075738	25	120.223949	24	179.849169
H	27	1.075708	26	120.166311	25	179.653718
H	28	1.075605	27	119.486364	26	179.931087
H	30	1.071997	29	119.860559	14	0.116020
H	31	1.075595	30	119.550803	29	-179.874041
H	32	1.075527	31	120.278179	30	-179.728159
H	33	1.075741	32	120.113098	31	-179.199371
H	34	1.077523	33	119.508781	32	-179.660393

E(HF/6-31G*) = **-**1450.25698 a.u.

E(B3LYP/6-31G**//HF/6-31G*) = **-**1459.54693 a.u.

Reference:

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