Supporting Information

Catalytic Enantioselective Addition of Cyclic β-Ketoesters with Activated Olefins and N-Boc Imines Using Chiral C_2-Symmetric Cationic *N*-Heterocyclic Carbenes (NHCs) Pd^{2+} Diaqua Complexes

*Zhen Liu and Min Shi**

State Key Laboratory of Organometallic Chemistry,

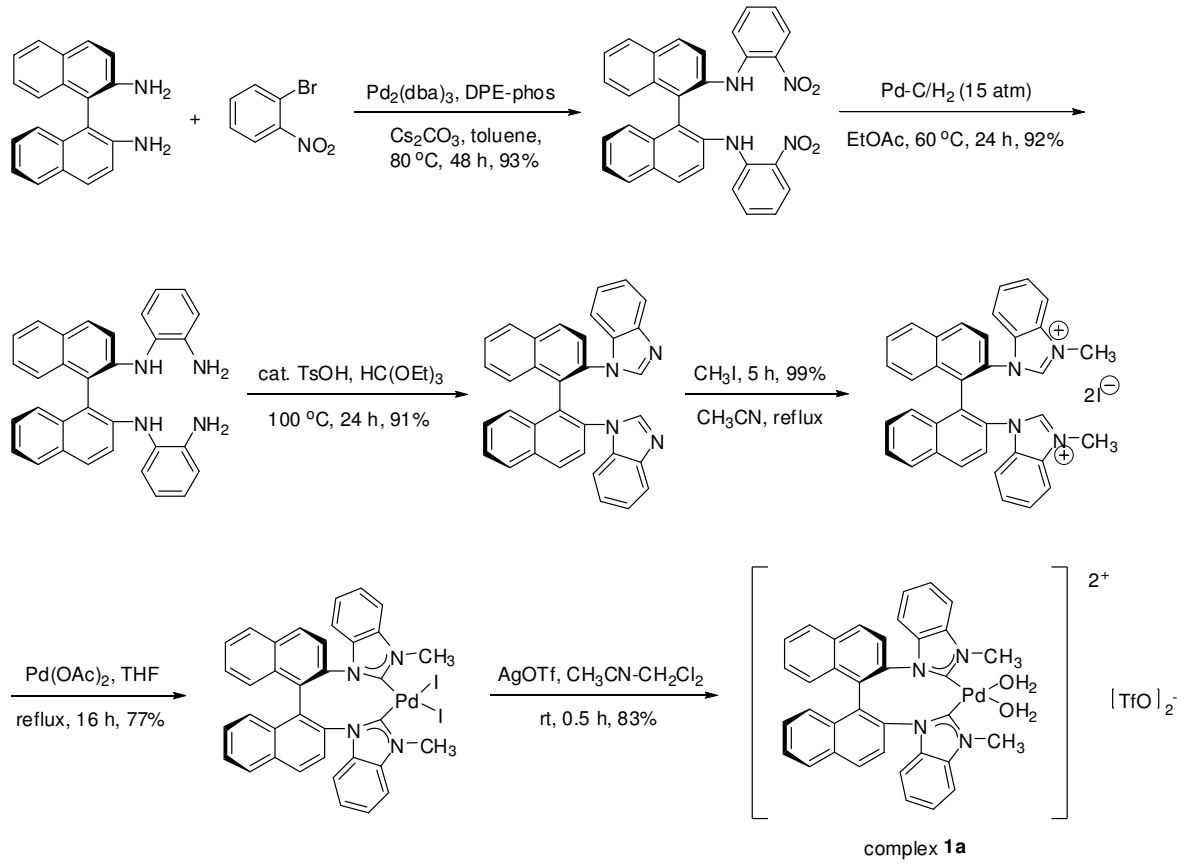
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences,

345 lingling Road, Shanghai 200032, China, Fax: 86-21-64166128. Mshi@mail.sioc.ac.cn

General Remarks: MP was obtained with a Yanagimoto micro melting point apparatus and is uncorrected. Optical rotations were determined in a solution of $CHCl_3$ or CH_2Cl_2 at 20 ^oC by using a Perkin-Elmer-241 MC polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. Infrared spectra were measured on a spectrometer. Unless noted, ^1H NMR spectra were recorded for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; ^{19}F NMR spectra were recorded at 376 MHz for a solution in $CDCl_3$ with $CFCl_3$ as the external reference. *J*-values are in Hz. Mass spectra were recorded with a HP-5989 instrument and HRMS was measured by a Finnigan MA+ mass spectrometer. Organic solvents used were dried by standard methods when necessary. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai $60F_{254}$ silica gel coated plates. Flash column chromatography was carried out using 300-400 mesh silica gel at increased pressure. All reactions were performed under argon using standard Schlenk techniques. The optical purities of adducts were determined by HPLC analysis using a chiral stationary phase column (column, Daicel Co. Chiralcel AS, AD and OD).

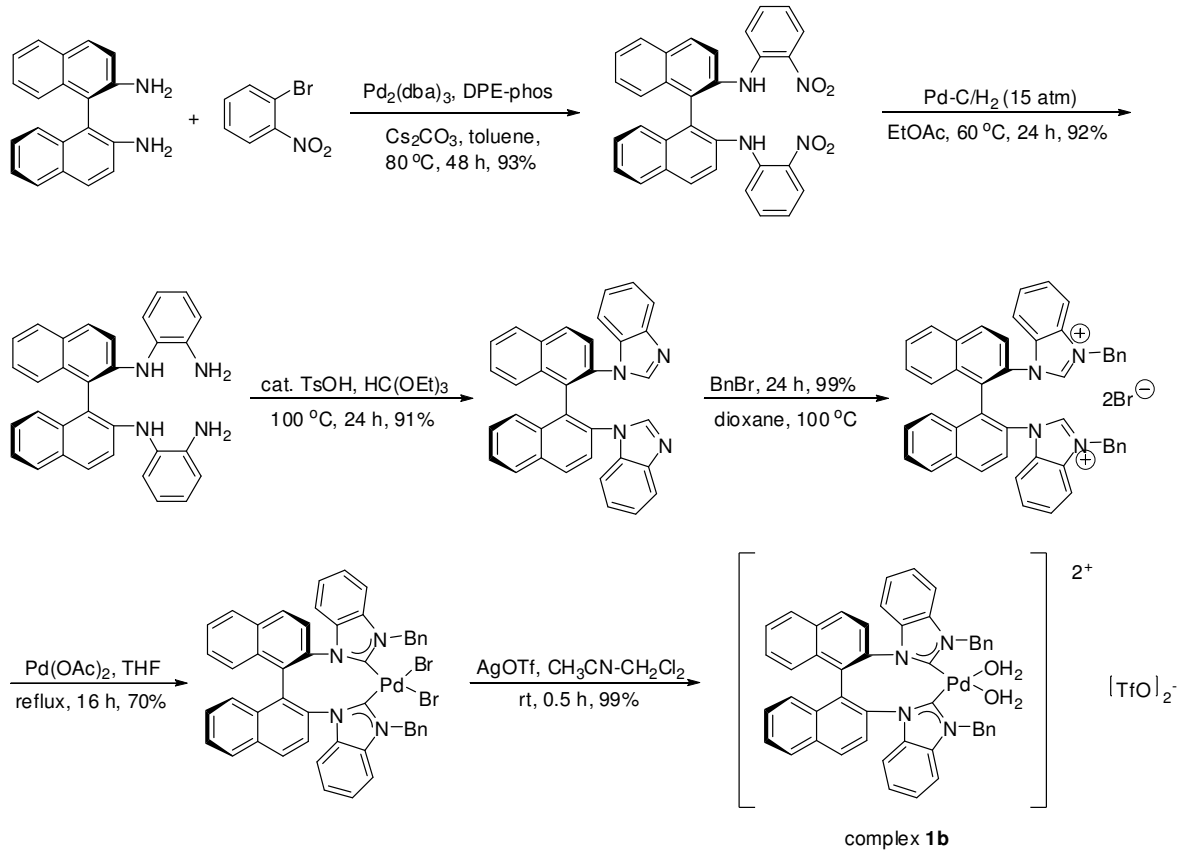
C_2-Symmetric Cationic *N*-Heterocyclic Carbenes (NHCs) Pd^{2+} Diaquo Complexes **1a** and **1b** were prepared according to our previously reported procedure.[1]

General Procedure for the Synthesis of *C*2-Symmetric *N*-Heterocarbene Palladium Diaqua Complexes **1a**

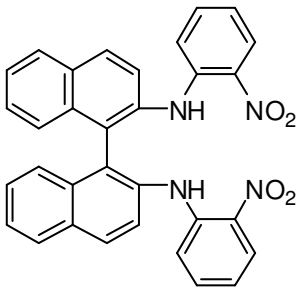


complex **1a**

General Procedure for the Synthesis of *C*2-Symmetric *N*-Heterocarbene Palladium Diaqua Complexes **1b**



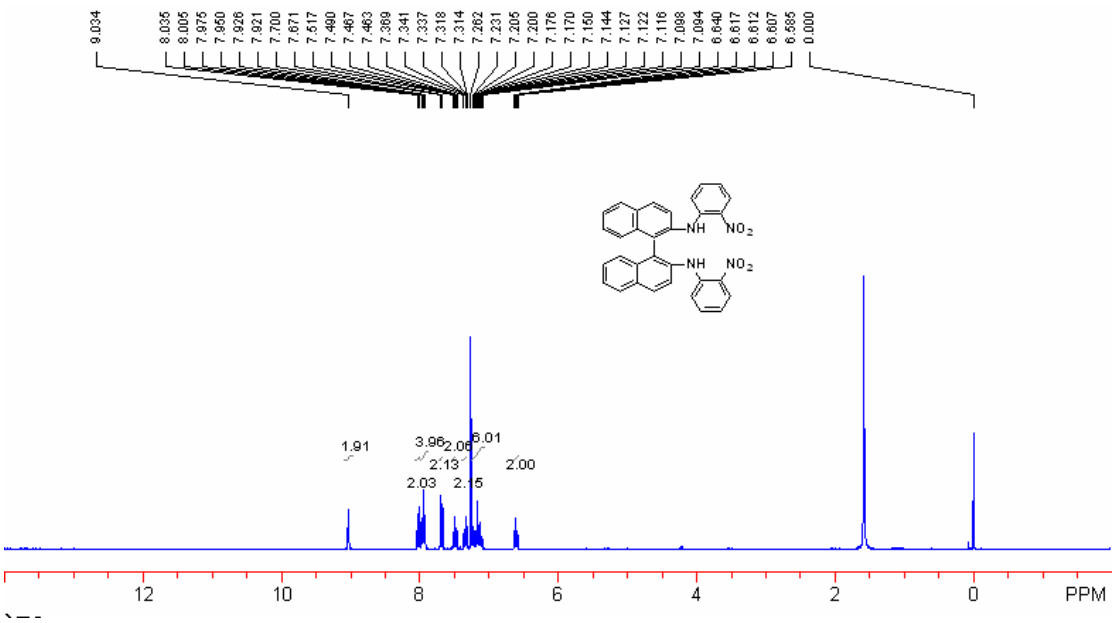
complex **1b**

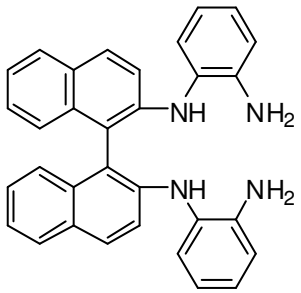


Synthesis of *N2,N2'*-Bis-(2-nitro-phenyl)-[1,1']binaphthalenyl-2,2'-diamine.

Under argon atmosphere, a mixture of 1,1'-binaphthalenyl-2,2'-diamine (200 mg, 0.7 mmol), 2-bromonitrobenzene (426 mg, 2.11 mmol), $Pd_2(dba)_3$ (17 mg, 0.018 mmol), DPE-phos (28 mg, 0.053 mmol), and Cs_2CO_3 (732 mg, 2.25 mmol) was stirred in anhydrous toluene (6.0 mL) at 80 ^oC for 48 h. After the reaction mixture was cooled to room temperature, the reaction was quenched by addition of 14 mL of H_2O. The organic compound was extracted with EtOAc (2.0 x 40 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced

pressure and the residue was purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate = 10/1) to give **1** as a red solid; Yield: 345 mg (93%). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 6.58-6.64 (2H, m, Ar), 7.09-7.26 (6H, m, Ar), 7.31-7.37 (2H, m, Ar), 7.46-7.52 (2H, m, Ar), 7.69 (2H, d, *J* = 8.7 Hz, Ar), 7.92-7.98 (4H, m, Ar), 8.02 (2H, d, *J* = 9.0 Hz, Ar), 9.03 (2H, s, NH). This is a known compound. Its spectroscopic data are consistent with those reported in the literature.[1]

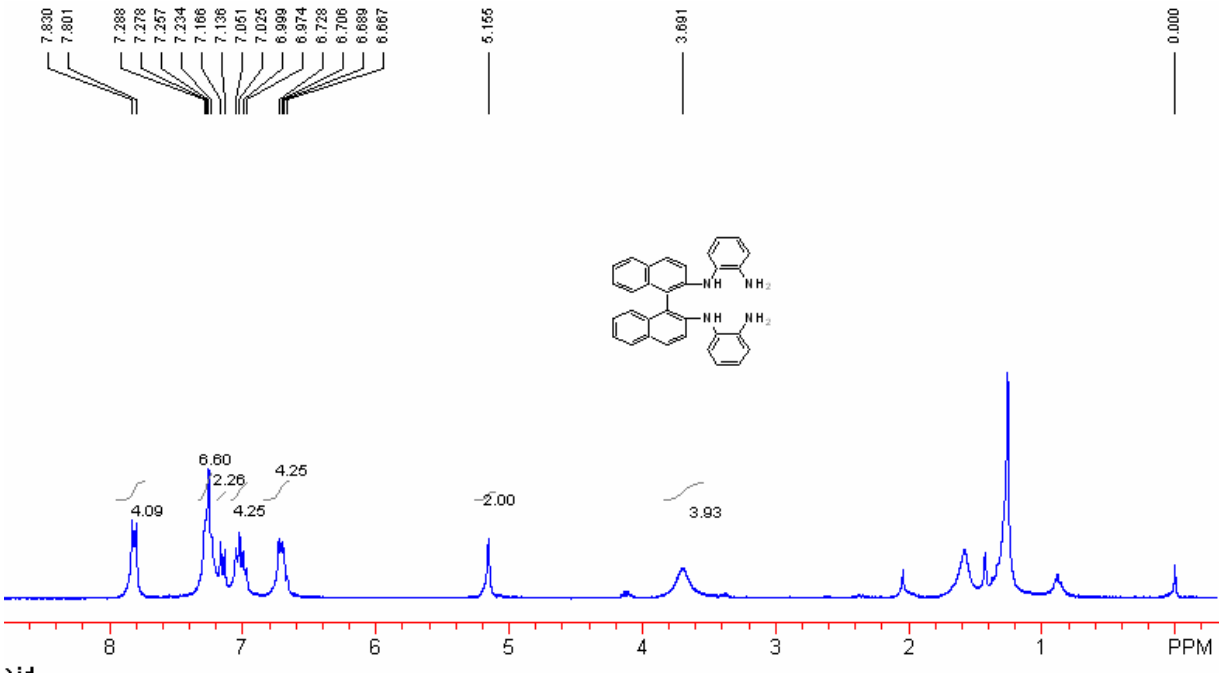


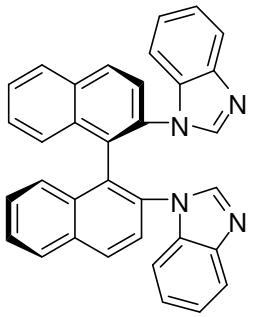


Synthesis of *N2,N2'*-Bis-(2-amino-phenyl)-[1,1']binaphthalenyl-2,2'-diamine.

A mixture of ***N2,N2'*-Bis-(2-nitro-phenyl)-[1,1']binaphthalenyl-2,2'-diamine** (3.0 g, 5.7 mmol), 10% Pd-C (510 mg) in solution of EtOAc (400 mL) were stirred under H_2 atmosphere (15 atm) at 60 ^{o}C for 24 h. After cooling to room temperature, Pd-C was removed by filtration.

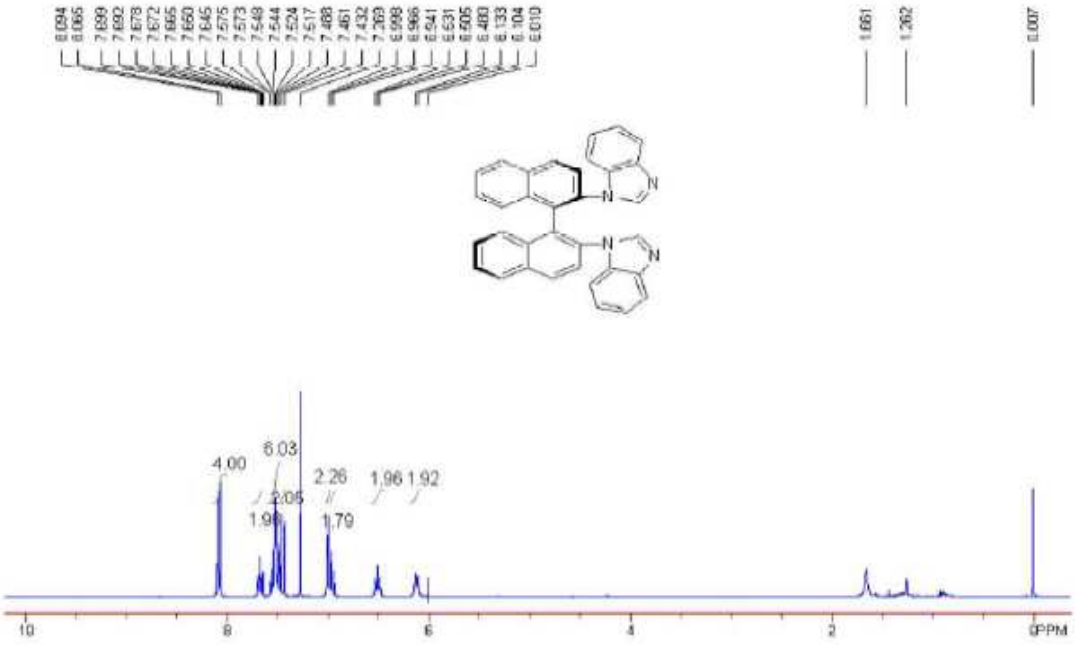
The solvent was evaporated under reduced pressure. The residue was purified by a silica gel flash column chromatography (eluent: hexane/ethyl acetate = 1/1) to give ***N2,N2'*-Bis-(2-amino-phenyl)-[1,1']binaphthalenyl-2,2'-diamine** as a white solid; Yield: 2.43 g (92%). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 3.69 (4H, br, NH_2), 5.16 (2H, br, NH), 6.67-6.73 (4H, m, Ar), 6.97-7.05 (4H, m, Ar), 7.15 (2H, d, J = 9.0 Hz, Ar), 7.23-7.29 (6H, m, Ar), 7.80-7.83 (4H, m, Ar). This is a known compound. Its spectroscopic data are consistent with those reported in the literature.[1]





2,2'-di(1*H*-benzo[*d*]imidazol-1-yl)-1,1'-binaphthyl. The ***N2,N2'*-Bis-(2-amino-phenyl)-[1,1']binaphthalenyl-2,2'-diamine** (237 mg, 0.50 mmol) and

triethyl orthoformate [$HC(OC_2H_5)_3$] (5.0 mL) containing a little TsOH were heated at 100 ^oC for 3 h. After the excess amount of triethyl orthoformate was removed under reduced pressure, the residue was purified by a silica gel flash column chromatography (eluent: petroleum ether/ethyl acetate, 2/3) to give **2,2'-di(1*H*-benzo[*d*]imidazol-1-yl)-1,1'-binaphthyl** as a white solid; Yield: 221 mg (91%). White solid; m.p. 294.5-294.8 ^oC; $[\alpha]^{20}_D$ = +516.7 (*c* 0.97, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 8.08 (4H, d, *J* = 8.7 Hz), 7.70-7.65 (2H, m), 7.58-7.49 (6H, m), 7.45 (2H, d, *J* = 8.7 Hz), 7.00 (2H, s), 6.97-6.94 (2H, m), 6.51 (2H, t, *J* = 7.5 Hz), 6.12 (2H, d, *J* = 8.7 Hz). This is a known compound. Its spectroscopic data are consistent with those reported in the literature.[1]



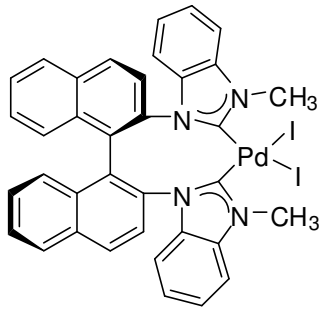
General procedure for the synthesis of the imidazolium salts.

2,2'-di(1*H*-benzo[*d*]imidazol-1-yl)-1,1'-binaphthyl (485 mg, 0.4 mmol) and RX (0.5 mmol) (R = CH_3, Bn; X = I, Br) in dioxane (10 mL) were stirred under reflux for 5~24 h. After cooling to room temperature, volatiles were removed under reduced pressure and the obtained

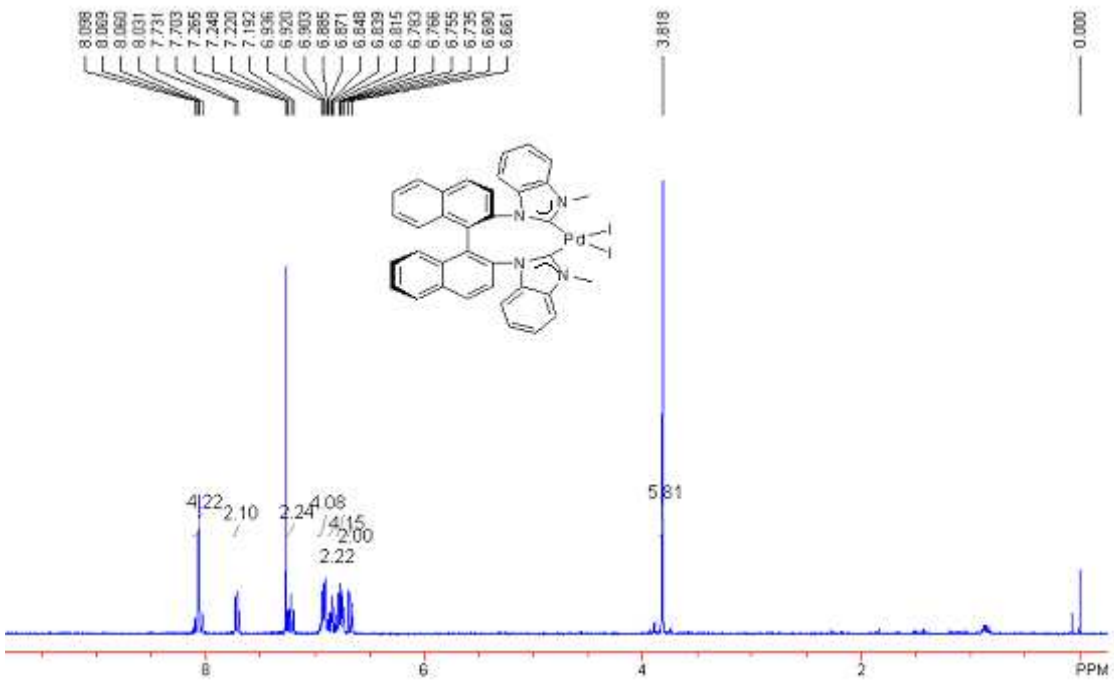
solid compound was used for the next reaction without any further purification.

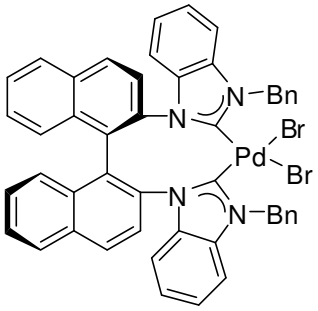
General procedure of the synthesis of the NHC-Pd(II) complexes.

Imidazolium salts (0.2 mmol) and $Pd(OAc)_2$ (44.8 mg, 0.2 mmol) was refluxed in THF (10 mL) for 16~30 h. The volatiles were then removed under reduced pressure and the residue was purified by a silica gel flash column chromatography (eluent: petroleum ether/EtOAc, 2/1 to 0/1) to give **NHC-Pd(II) complexes** as yellow solid.

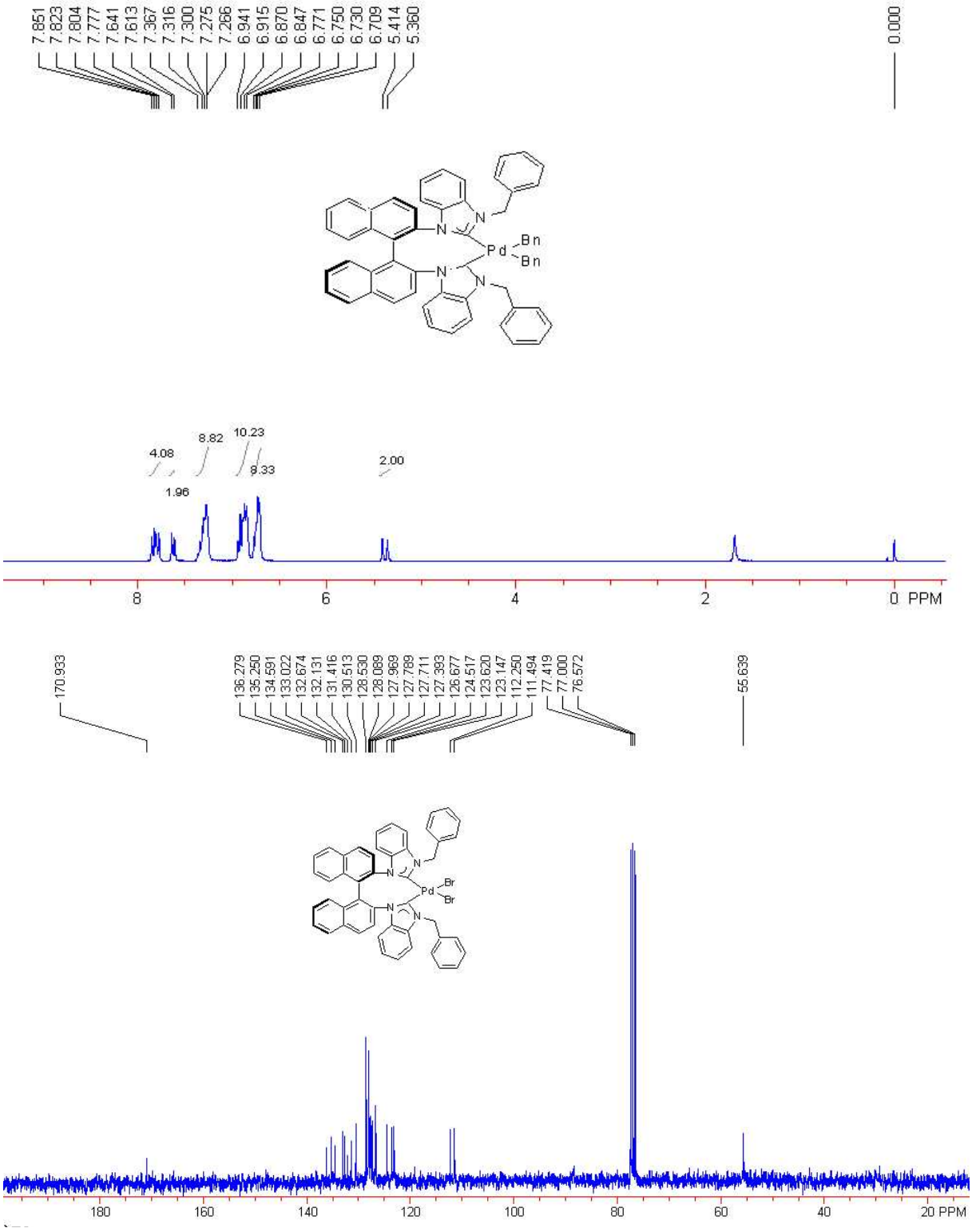


NHC-Pd(II)-I complex: Yellow solid; m.p. > 300 ^{o}C (dec.); $[\alpha]^{20}_{D}$ = +270.0 (*c* 0.086, CHCl3); ^{1}H NMR (300 MHz, CDCl3, TMS): δ 8.10-8.03 (m, 4H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.25-7.19 (m, 2H), 6.94-6.87 (m, 4H), 6.85-6.82 (m, 2H), 6.78-6.74 (m, 4H), 6.68 (d, *J* = 8.7 Hz, 2H), 3.82 (s, 6H). This is a known compound. Its spectroscopic data are consistent with those reported in the literature.[1]





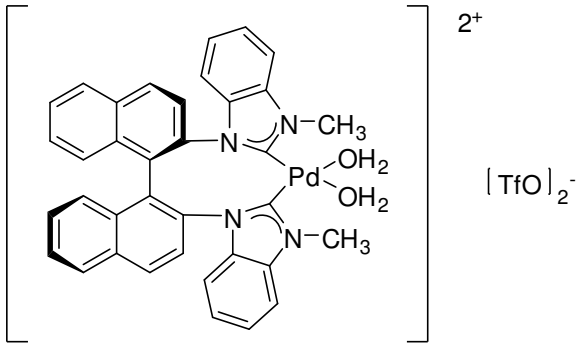
NHC-Pd(II)-Br complex: Pale-yellow solid; m.p. > 300 ^{o}C (Dec.); $[\alpha]^{20}_{D}$ = +45.0 (*c* 0.245, $CHCl_3$); IR (CH_2Cl_2) ν 2961, 2926, 2855, 1261, 1101, 1032, 804 cm-1; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.30-7.25 (m, 6H), 6.94-6.84 (m, 10H), 6.77-6.70 (m, 8H), 5.39 (d, *J* = 16.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 170.9, 136.3, 135.3, 134.6, 133.0, 132.7, 132.1, 131.4, 130.5, 128.5, 128.1, 127.9, 127.8, 127.7, 127.4, 126.7, 124.5, 123.6, 123.1, 112.3, 111.5, 55.6. HRMS (ESI) Calcd. For [$C_{48}H_{34}Br_2N_4$Pd-Br] requires 851.1002. Found: 851.0491 [M+-Br]. Anal. Calcd. For $C_{48}H_{34}Br_2N_4Pd$: C, 61.79; H, 3.67; N, 6.00%. Found: C, 61.27; H: 3.89; N, 5.81%.



General procedure for the synthesis of cationic NHC-Pd^{2+} diaqua complexes 1a-b.

NHC-Pd(II)-X complexes (0.20 mmol) was suspended in a mixture of CH_2Cl_2 (15 mL) and

CH_3CN (5.0 mL). Then, AgOTf (108 mg, 0.42 mmol) was added and the mixture was stirred at room temperature for 10 min. The resulting suspension was filtered from the precipitated AgX (X = Br or I) through the celite and the solvent was removed under reduced pressure to give **1a-b** as white powder.



complex **1a**

Cationic NHC-Pd^{2+} diaqua complex 1a. White solid (this compound contains some amount of petroleum ether, which can not be completely removed); m.p. 289 ^{o}C (Dec.); $[\alpha]^{20}_{D}$ = +43.0 (*c* 0.315, $CHCl_3$); IR (CH_2Cl_2) ν 3223, 2925, 2847, 1580, 1511, 1395, 1290, 1168, 1029, 744 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.14 (s, 4H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.28 (m, 2H), 7.05-6.91 (m, 8H), 6.84-6.77 (m, 4H), 3.93 (s, 6H), 2.16 (br 4H). ^{19}F NMR (282 MHz, $CDCl_3$, CF_3CO_2H): δ -83.8 (s); MS (ESI) m/z 769.1 [M+-2H_2O-OTf], 696.1 [M+-2OTf+K], Anal. Calcd. For $C_{38}H_{30}F_6N_4O_8PdS_2 \cdot H_2O$: C, 46.90; H, 3.31; N, 5.76%. Found: C, 46.91; H, 3.41; N, 5.53%.


8.142
7.773
7.746
7.303
7.279
7.265
7.255
7.052
7.040
7.029
7.021
7.006
6.998
6.941
6.914
6.857
6.834
6.815
6.807
6.799
6.770
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3.934
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2.147
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0.904
0.883
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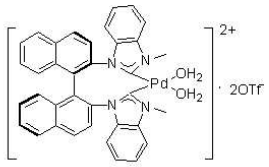
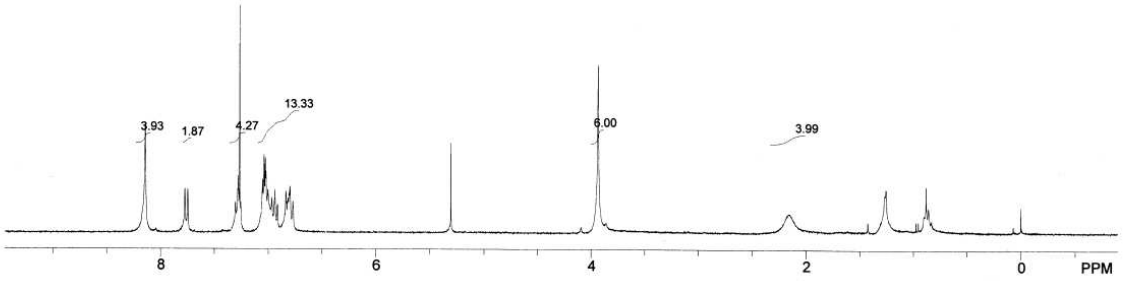
0.000


2+
Pd
OH2
OH2
· 2OTf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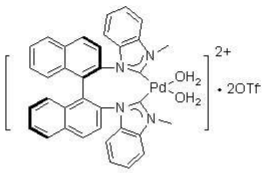
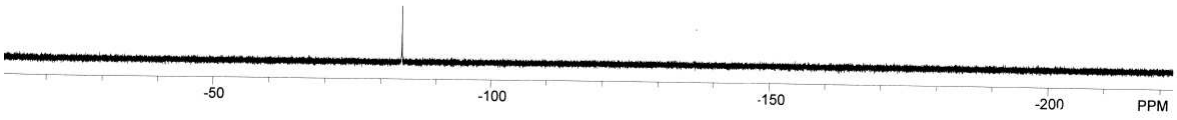
3.99
8
6
4
2
0
PPM


-83.840


2+
Pd
OH2
OH2
• 2OTf

5a


-50
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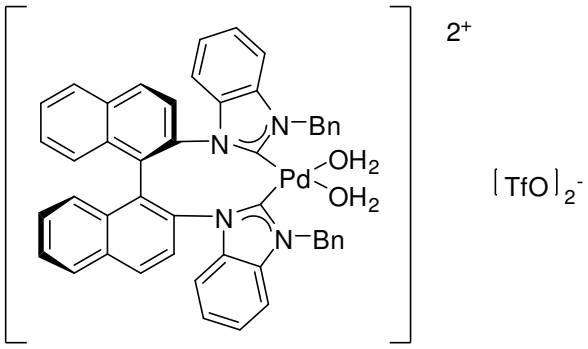
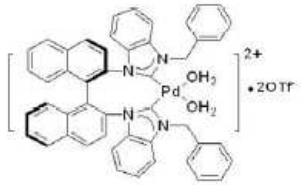
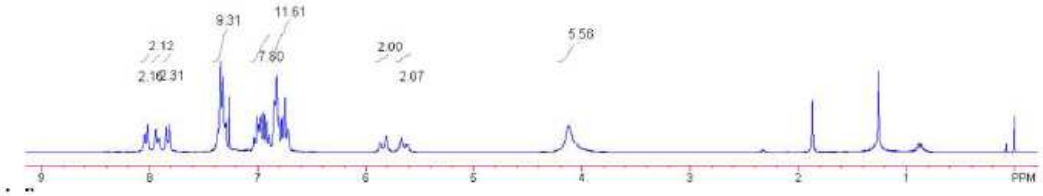
-150
-200
PPM

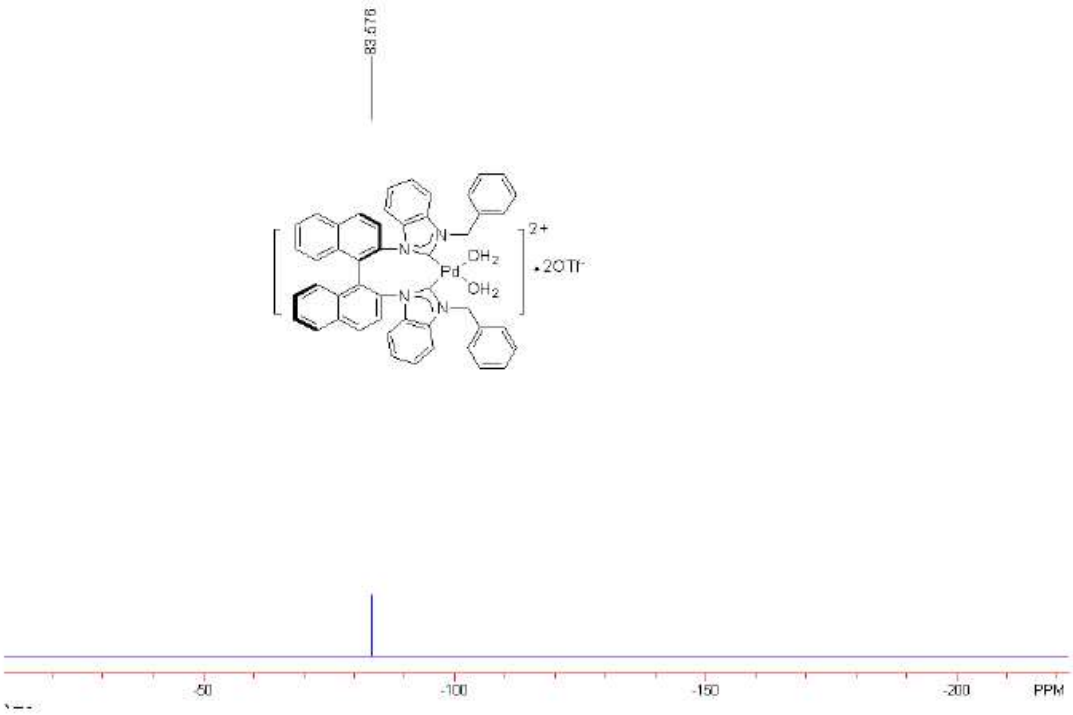


complex **1b**

Cationic NHC-Pd^{2+} diaqua complex 1b. White solid (this compound contains some amount of petroleum ether, whcih can not be completely removed); m.p. 259 ^{o}C (Dec.); $[\alpha]^{20}_{D}$ = +66.0 (*c* 0.220, $CHCl_3$); IR (CH_2Cl_2) ν 2956, 2924, 2854, 1464, 1379, 1250, 1177, 1030, 745 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.03 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 8.7 Hz, 2H), 7.83 (d, *J* = 8.1 Hz, 2H), 7.35-7.28 (m, 8H), 7.03-6.89 (m, 6H), 6.84-6.71 (m, 10H), 5.84 (d, *J* = 16.2 Hz, 2H), 5.65 (d, *J* = 16.2 Hz, 2H), 4.13 (br s, >4H, coordinated and free H_2O). ^{19}F NMR (282 MHz, $CDCl_3$, CF_3CO_2H): δ -83.6 (s); HRMS (ESI) Calcd. For [$C_{50}H_{38}F_6O_8N_4PdS_2-2H_2O$-OTf-H] requires 920.1260. Found: 920.1221 [M+-2H_2O-OTf-H].



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• 2OTf
Pd
OH2
OH2
-50
-100
-150
-200
PPM

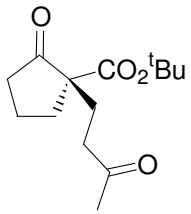
General Procedure for the Catalytic Enantioselective Addition of *β*-Ketoester 2a to Activated Olefins Using C_2-Symmetric Cationic *N*-Heterocyclic Carbenes (NHCs) Pd^{2+} Diaqua Complexes

In a dried Schlenk tube, catalyst (0.01 mmol, **1a** 9.6 mg; **1b** 11 mg), activated olefins (0.4 mmol, 28 mg-53 mg), *β*-Ketoester **2a** (0.2 mmol, 37 mg), 4A MS (50 mg) were dissolved in solvent (0.5 mL) under argon atmosphere. The solution was stirred at the appointed temperature. After the reaction was completed (monitored by TLC), the solvent was removed under vacuum and the residue was purified by flash column chromatography on silica gel eluted with ethyl acetate/petroleum ether (1:20, v/v) to afford the products.

General Procedure for the Catalytic Enantioselective Addition of *β*-Ketoesters to N-Boc Imines Using C_2-Symmetric Cationic *N*-Heterocyclic Carbenes (NHCs) Pd^{2+} Diaqua Complexes

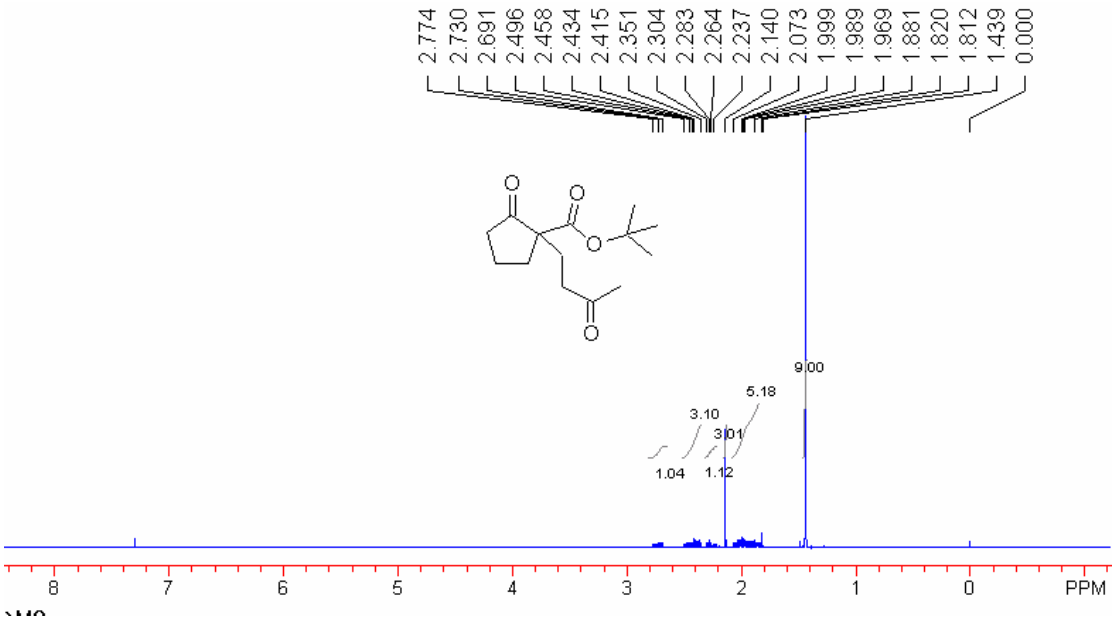
In a dried Schlenk tube, catalyst (0.01 mmol, **1a** 9.6 mg; **1b** 11 mg), N-Boc Imines (0.4 mmol, 82 mg-109 mg), *β*-Ketoesters (0.2 mmol, **2a** 37 mg; **2b** 40 mg) were dissolved in CH_2Cl_2 (1.0 mL) under argon atmosphere. The solution was stirred at room temperature. After the reaction was completed (monitored by TLC), the solvent was removed under vacuum and the residue was purified by flash column chromatography on silica gel eluted with ethyl acetate/petroleum ether (1:20, v/v) to afford the products.

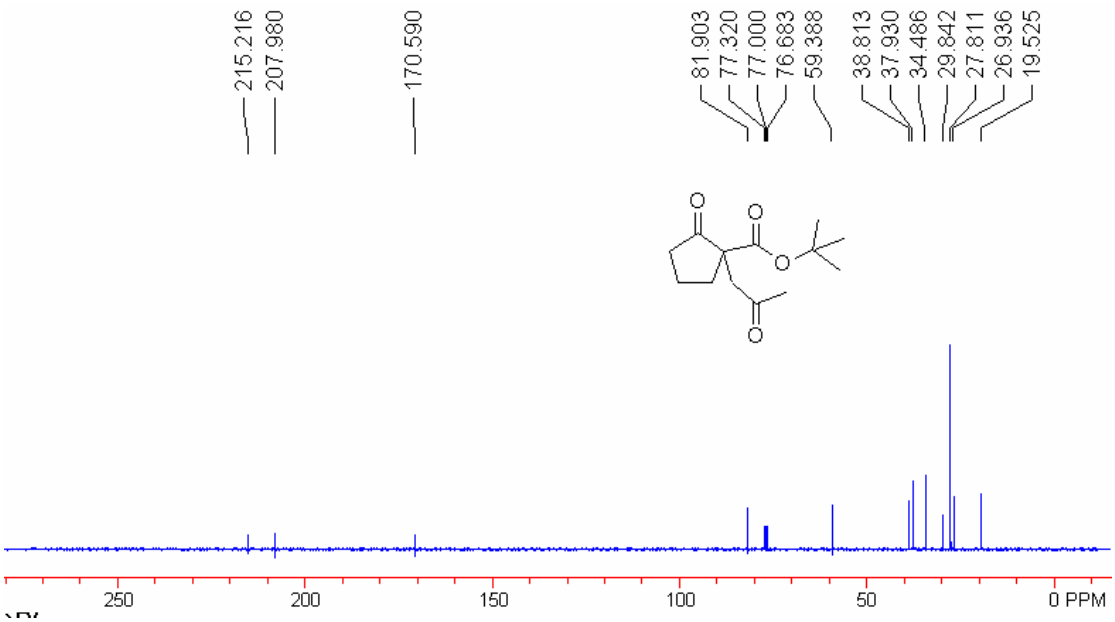
Analytical Data of the Products

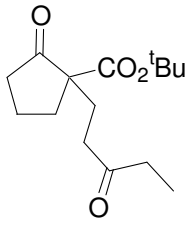


(*S*)-**3a**

(*S*)-2-Oxo-1-(3-oxo-butyl)-cyclopentanecarboxylic acid tert-butyl ester **3a**: This is a known compound.[2a] ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.44 (9H, s), 1.81-2.07 (5H, m), 2.14 (3H, s), 2.22-2.30 (1H, m), 2.35-2.50 (3H, m), 2.69-2.77 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.5, 26.9, 27.8, 29.8, 34.5, 37.9, 38.8, 59.4, 81.9, 170.6, 208.0, 215.2; HPLC (Daicel AS column, hexanes:^{i}PrOH = 95:5, 0.7 mL/min, λ = 230 nm, t_{major} = 17.0 min, t_{minor} = 15.1 min.), 71% ee; $[\alpha]^{20}_{D}$ = -5.2 (c 0.92, $CHCl_3$); Yield: 98%.

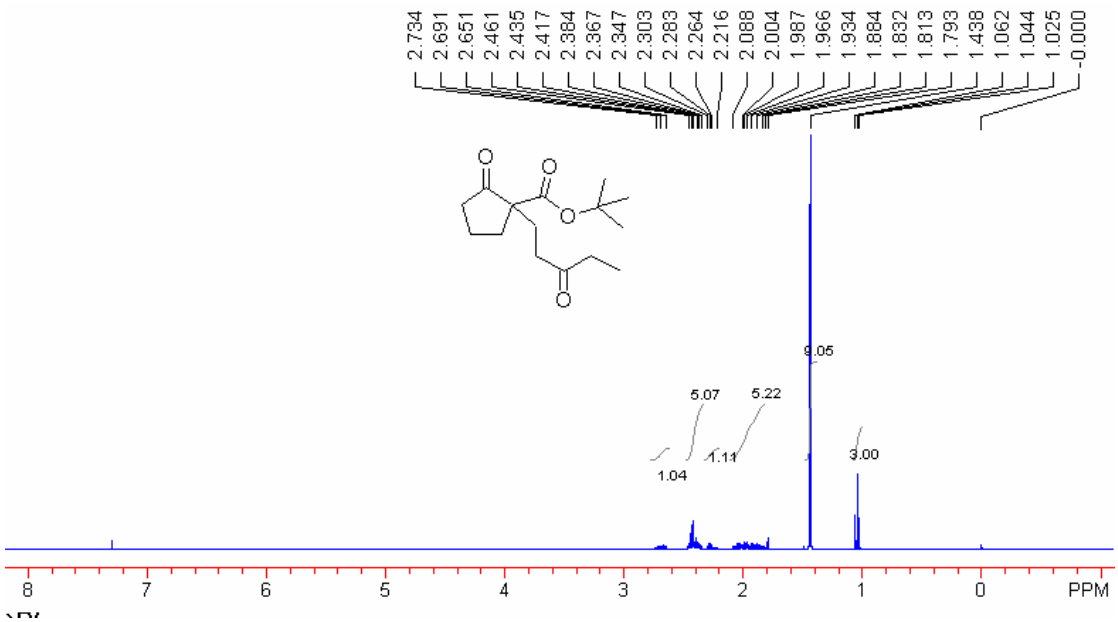


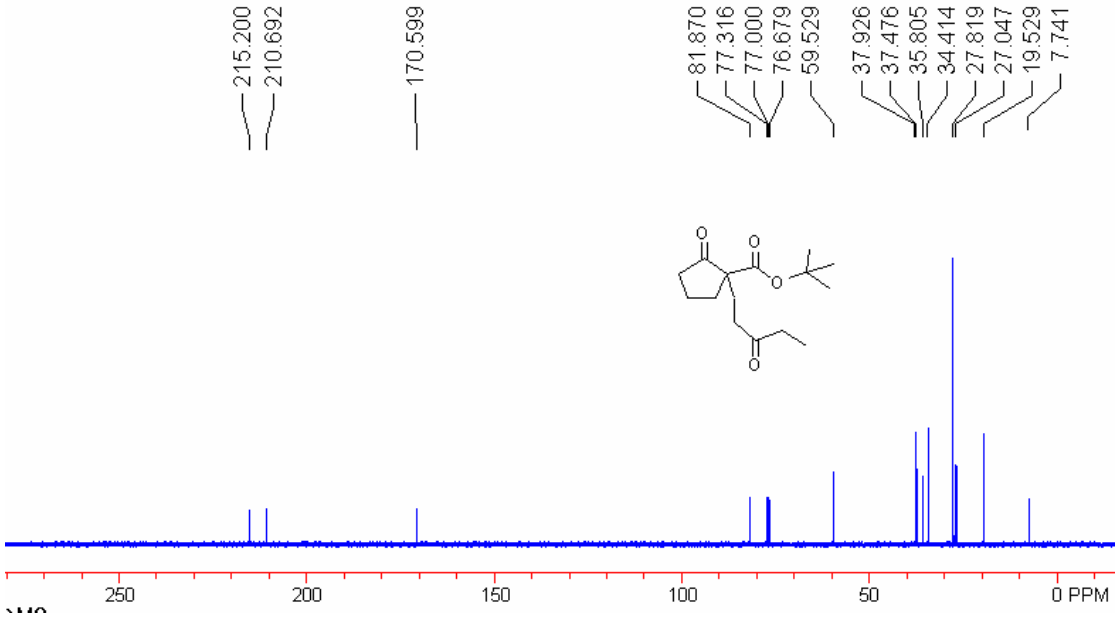


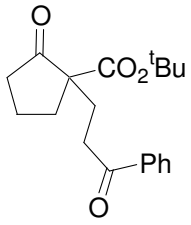


3b

2-Oxo-1-(3-oxo-pentyl)-cyclopentanecarboxylic acid tert-butyl ester **3b**: This is a known compound.[2a] ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.04 (3H, t, J = 7.2 Hz), 1.44 (9H, s), 1.79-2.09 (5H, m), 2.22-2.30 (1H, m), 2.35-2.46 (5H, m), 2.65-2.73 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 7.7, 19.5, 27.0, 27.8, 34.4, 35.8, 37.5, 37.9, 59.5, 81.9, 170.6, 210.7, 215.2; HPLC (Daicel AS column, hexanes:^{i}PrOH = 95:5, 0.7 mL/min, λ = 230 nm, t_{major} = 13.0 min, t_{minor} = 11.3 min.), 19% ee; $[\alpha]^{20}_{D}$ = -2.5 (c 1.6, $CHCl_3$); Yield: 91%.



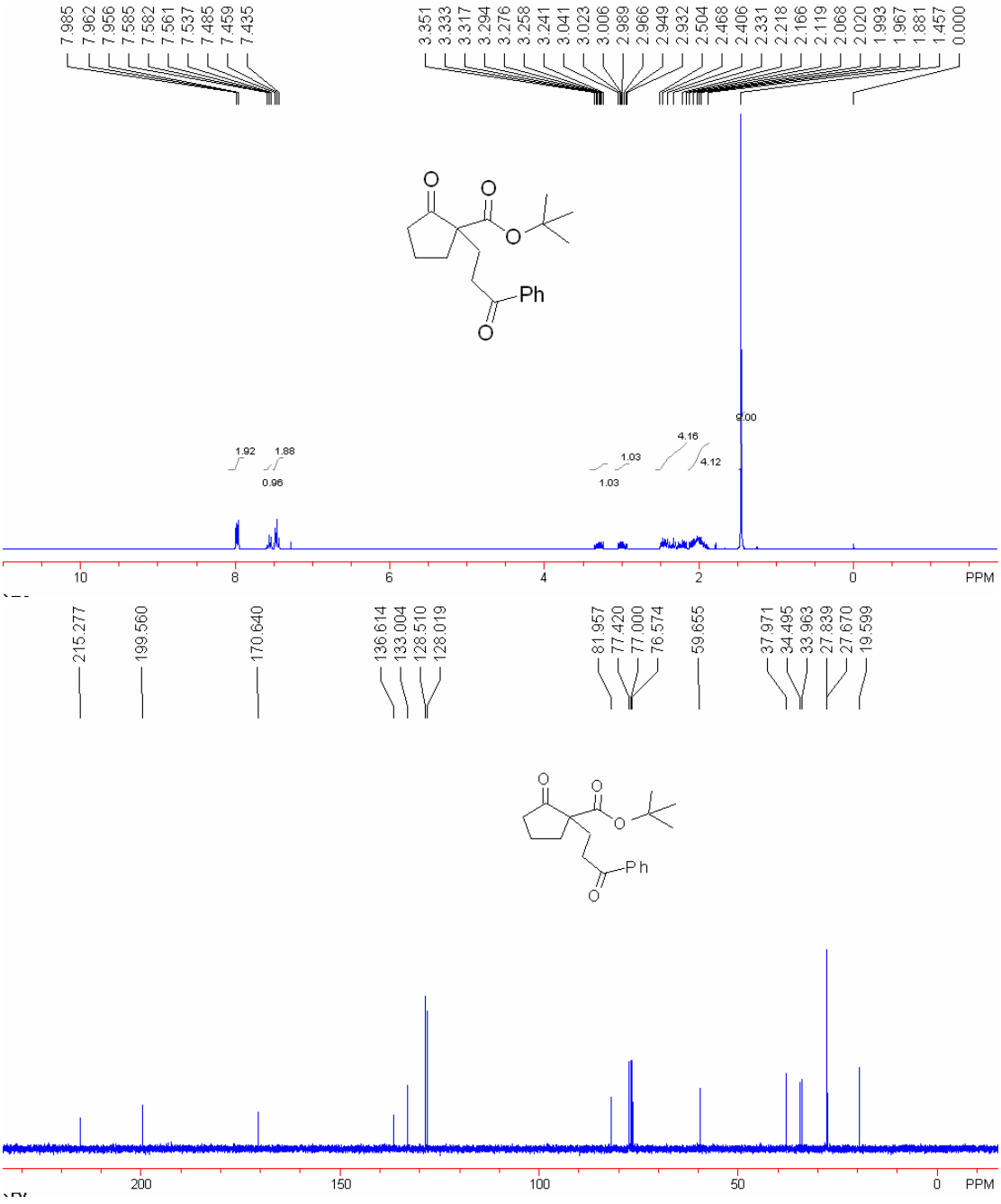


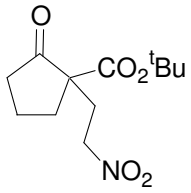


3c

2-Oxo-1-(3-oxo-3-phenylpropyl)-cyclopentanecarboxylic acid tert-butyl ester **3c**: white solid; M.p. 79-80^{o}C; IR (KBr) ν 2975, 1747, 1722, 1687, 1449, 1369, 1255, 1145, 1001, 846, 741, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.46 (9H, s), 1.88-2.12 (4H, m), 2.17-2.50

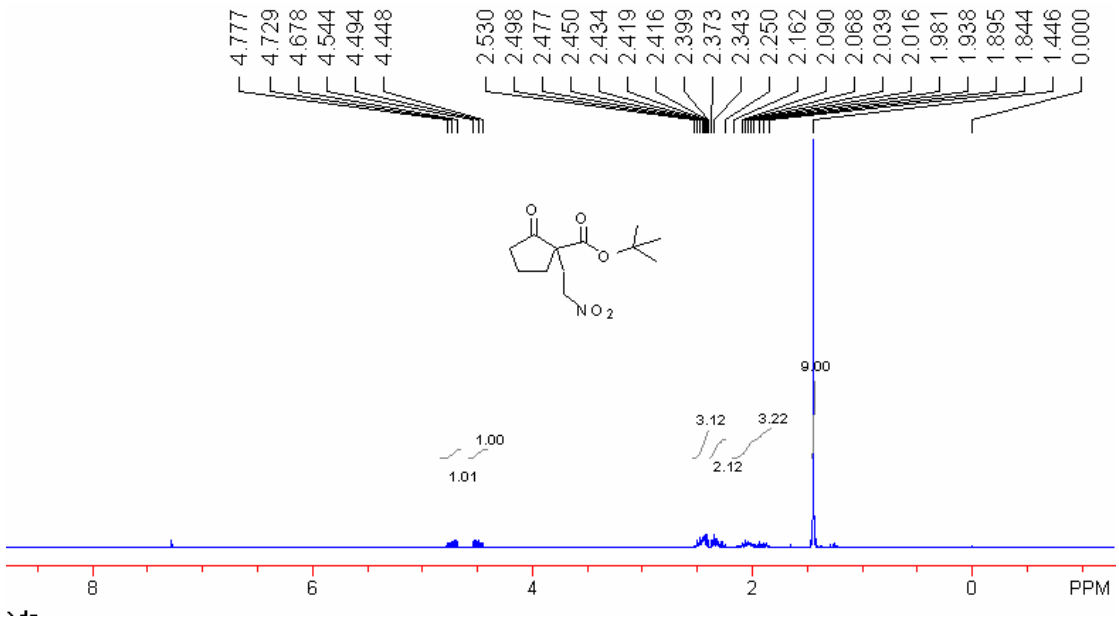
(4H, m), 2.93-3.04 (1H, m), 3.24-3.35 (1H, m), 7.44-7.48 (2H, m), 7.54-7.58 (1H, m), 7.96-7.98 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 19.6, 27.7, 27.8, 34.0, 34.5, 38.0, 59.7, 82.0, 128.0, 128.5, 133.0, 136.6, 170.6, 200.0, 215.3; MS (ESI) *m/e* 339 (M^++23, 100); HRMS (ESI) Calcd. for $C_{19}H_{24}O_4Na^+$ requires 339.1572, Found 339.1567; HPLC (Daicel AS column, hexanes:^{i}PrOH = 95:5, 0.7 mL/min, λ = 230 nm, t_{major} = 18.6 min, t_{minor} = 15.9 min.), 0% ee ; Yield: 93%.

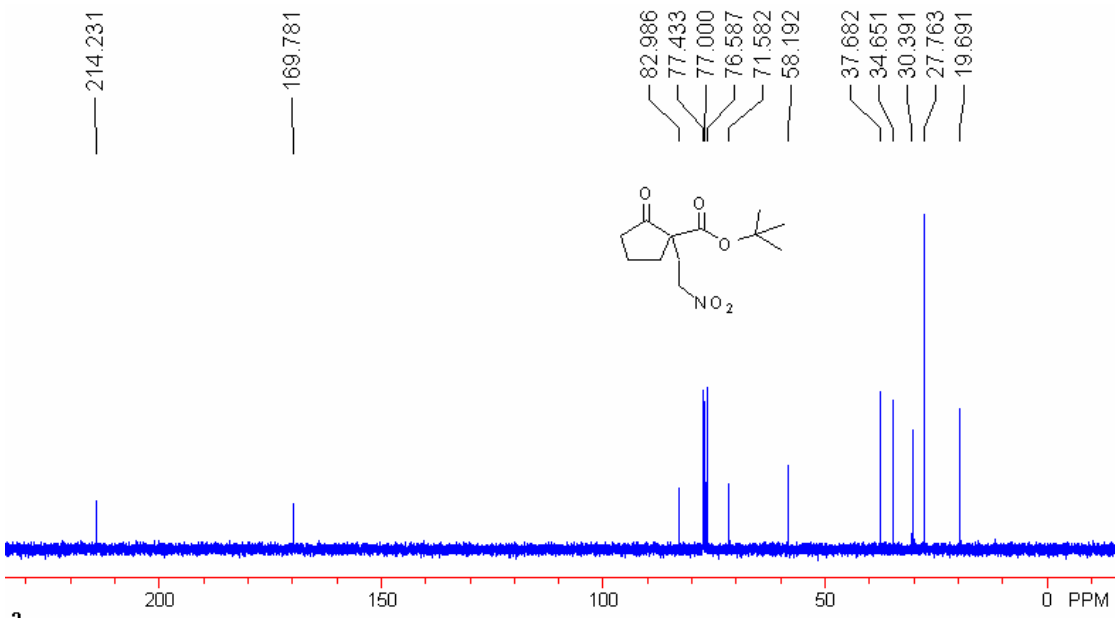


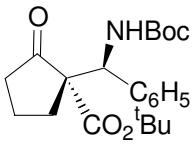


3d

1-(2-Nitro-ethyl)-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **3d**: Colorless oil; IR (KBr) ν 2977, 1748, 1722, 1555, 1454, 1370, 1256, 1149, 844 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.45 (9H, s), 1.84-2.16 (3H, m), 2.25-2.37 (2H, m), 2.40-2.53 (3H, m), 4.45-4.54 (1H, m), 4.68-4.78 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 19.7, 27.8, 30.4, 34.7, 37.7, 58.2, 71.6, 83.0, 169.8, 214.2; MS (ESI) *m/e* 280 (M^++23, 100); HRMS (ESI) Calcd. for $C_{12}H_{19}NO_5Na^+$ requires 280.1161, Found 280.1155; HPLC (Daicel AS column, hexanes:^{i}PrOH = 95:5, 0.7 mL/min, λ = 230 nm, t_{major} = 20.4 min, t_{minor} = 18.5 min.), 38% ee; $[\alpha]^{20}_{D}$ = -2.1 (c 0.75, CH_2Cl_2); Yield: 90%.

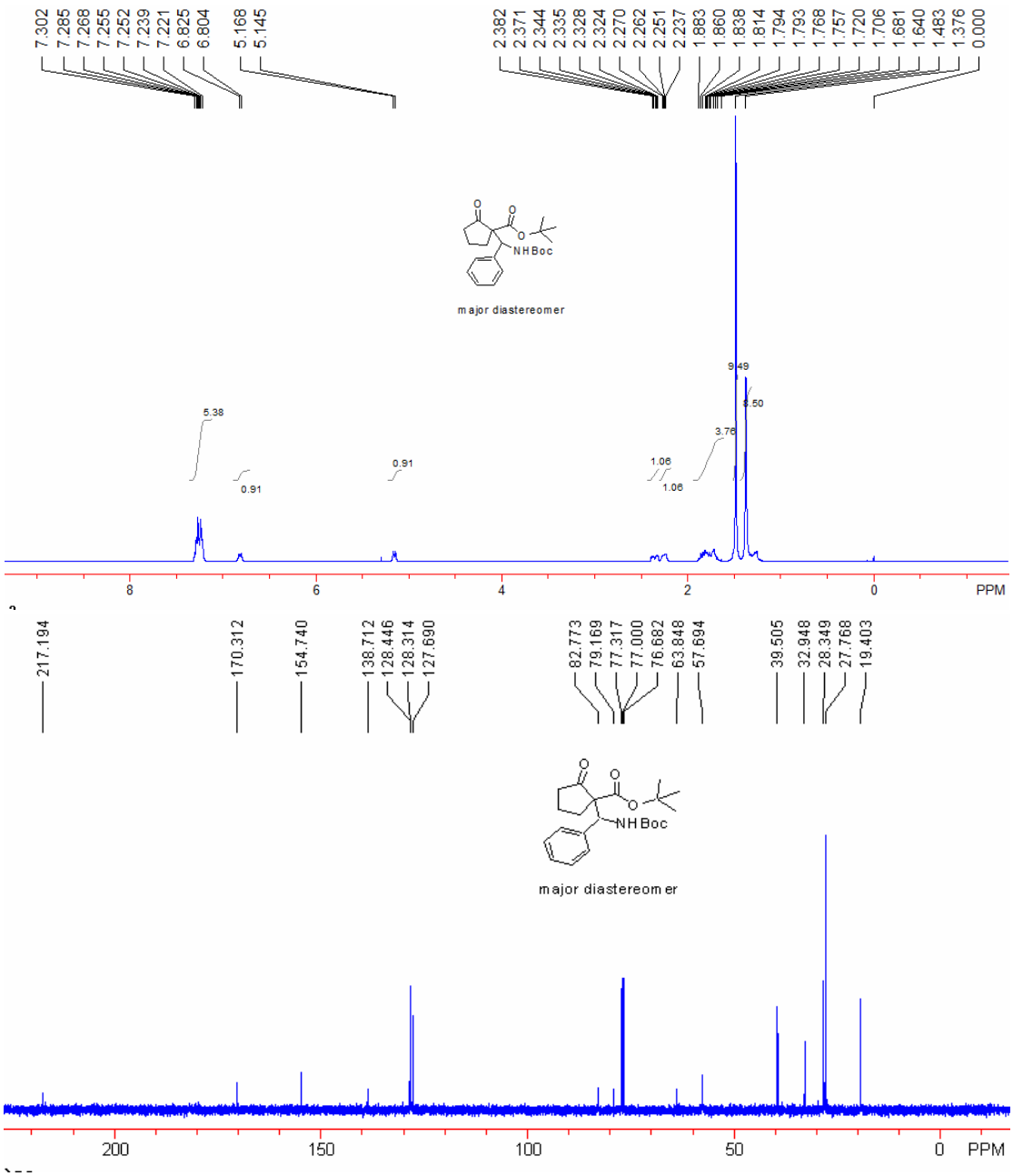


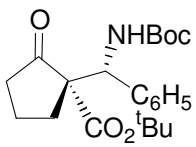




(*S, S*)-**4a**

(*S*,*S*)-1-(tert-Butoxycarbonylaminophenylmethyl)-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4a**: anti diastereomer. This is a known compound.[2b] ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.38 (9H, s), 1.48 (9H, s), 1.64-1.88 (4H, m), 2.24-2.27 (1H, m), 2.32-2.38 (1H, m), 5.16 (1H, d, *J* = 9.2 Hz), 6.81 (1H, d, *J* = 9.2 Hz), 7.22-7.30 (5H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.4, 27.8, 28.3, 32.9, 39.5, 57.7, 63.8, 79.2, 82.8, 127.7, 128.3, 128.4, 138.7, 154.7, 170.3, 217.2; HPLC (Daicel AD column, hexanes:^{i}PrOH = 19:1, 1.0 mL/min, λ = 254 nm, t_{major} = 8.3 min, t_{minor} = 21.0 min.), 80% ee; $[\alpha]^{20}_{D}$ = -7.3 (c 1.0, CH_2Cl_2); Yield: 72%.

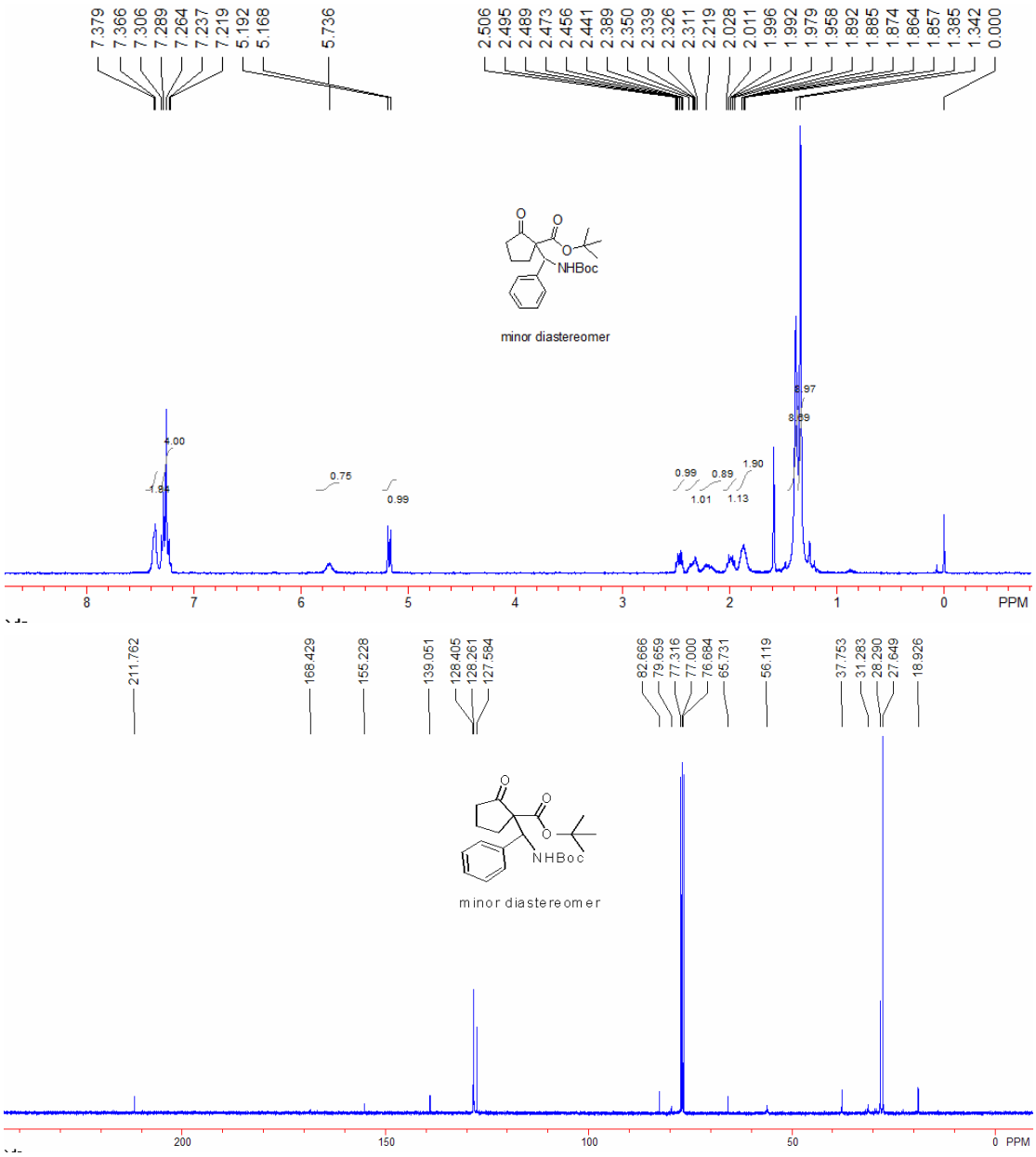


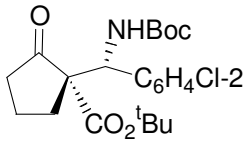


syn diastereomer-**4a**

1-(tert-Butoxycarbonylaminophenylmethyl)-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4a**: syn diastereomer. This is a known compound.[2b] ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.34 (9H, s), 1.38 (9H, s), 1.86-1.89 (2H, m), 1.96-2.03 (1H, m), 2.22 (1H, brs), 2.31-2.39

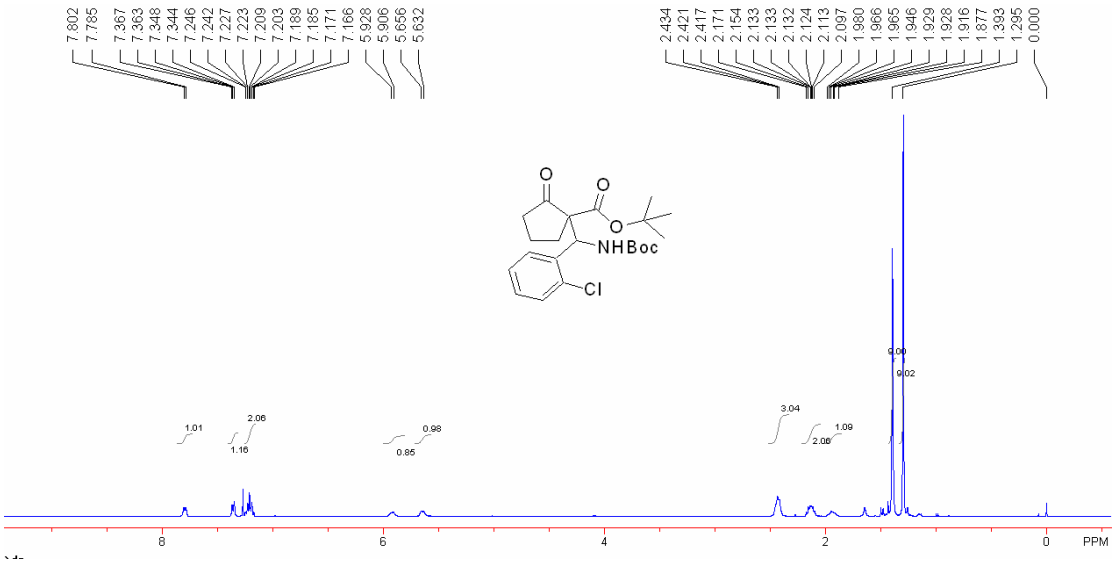
(1H, m), 2.44-2.51 (1H, m), 5.18 (1H, d, J = 9.6 Hz), 5.74 (1H, brs), 7.22-7.31 (3H, m), 7.37-7.38 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 18.9, 27.6, 28.3, 31.3, 37.8, 56.1, 65.7, 79.7, 82.7, 127.6, 128.3, 128.4, 139.1, 155.2, 168.4, 211.8; HPLC (Daicel AD column, hexanes:^{i}PrOH = 19:1, 1.0 mL/min, λ = 254 nm, t_{major} = 24.9 min, t_{minor} = 10.2 min.), 51% ee; $[\alpha]^{20}_{D}$ = -2.9 (c 0.75, CH_2Cl_2); Yield: 19%.

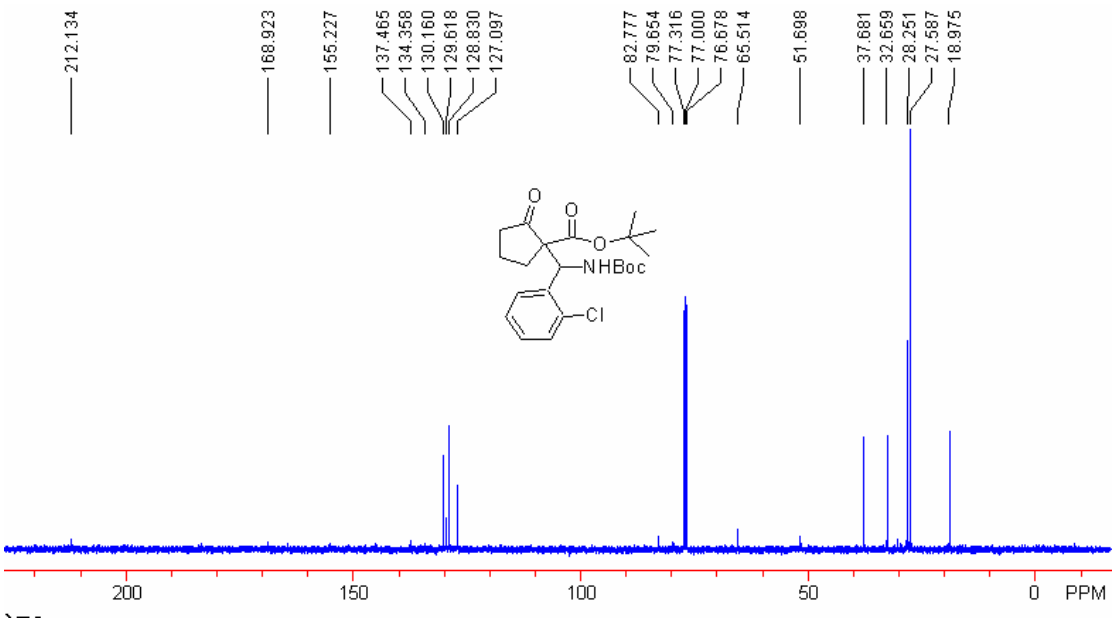


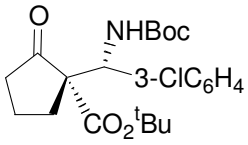


4b

1-[tert-Butoxycarbonylamino-(2-chlorophenyl)methyl]-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4b**: Colorless oil; IR (KBr) ν 2958, 2925, 2854, 1752, 1724, 1490, 1462, 1368, 1274, 1245, 1153, 1039, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.30 (9H, s), 1.39 (9H, s), 1.88-1.98 (1H, m), 2.10-2.17 (2H, m), 2.42-2.43 (3H, m), 5.64 (1H, d, *J* = 9.6 Hz), 5.92 (1H, d, *J* = 9.6 Hz), 7.17-7.25 (2H, m), 7.34-7.37 (1H, m), 7.79 (1H, d, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.0, 27.6, 28.3, 32.7, 37.7, 51.7, 65.5, 79.7, 82.8, 127.1, 128.8, 129.6, 130.2, 134.4, 137.5, 155.2, 168.9, 212.1; MS (ESI) *m/e* 446 (M^++23, 100); HRMS (ESI) Calcd. for $C_{22}H_{30}ClNO_5Na^+$ requires 446.1710, Found 446.1705; (Daicel OD column, hexanes:^{i}PrOH = 99:1, 0.7 mL/min, λ = 214 nm, t_{major} = 50.7 min, t_{minor} = 46.7 min.), 73% ee; $[\alpha]^{20}_D$ = -7.6 (c 0.86, CH_2Cl_2); Yield: 80%.

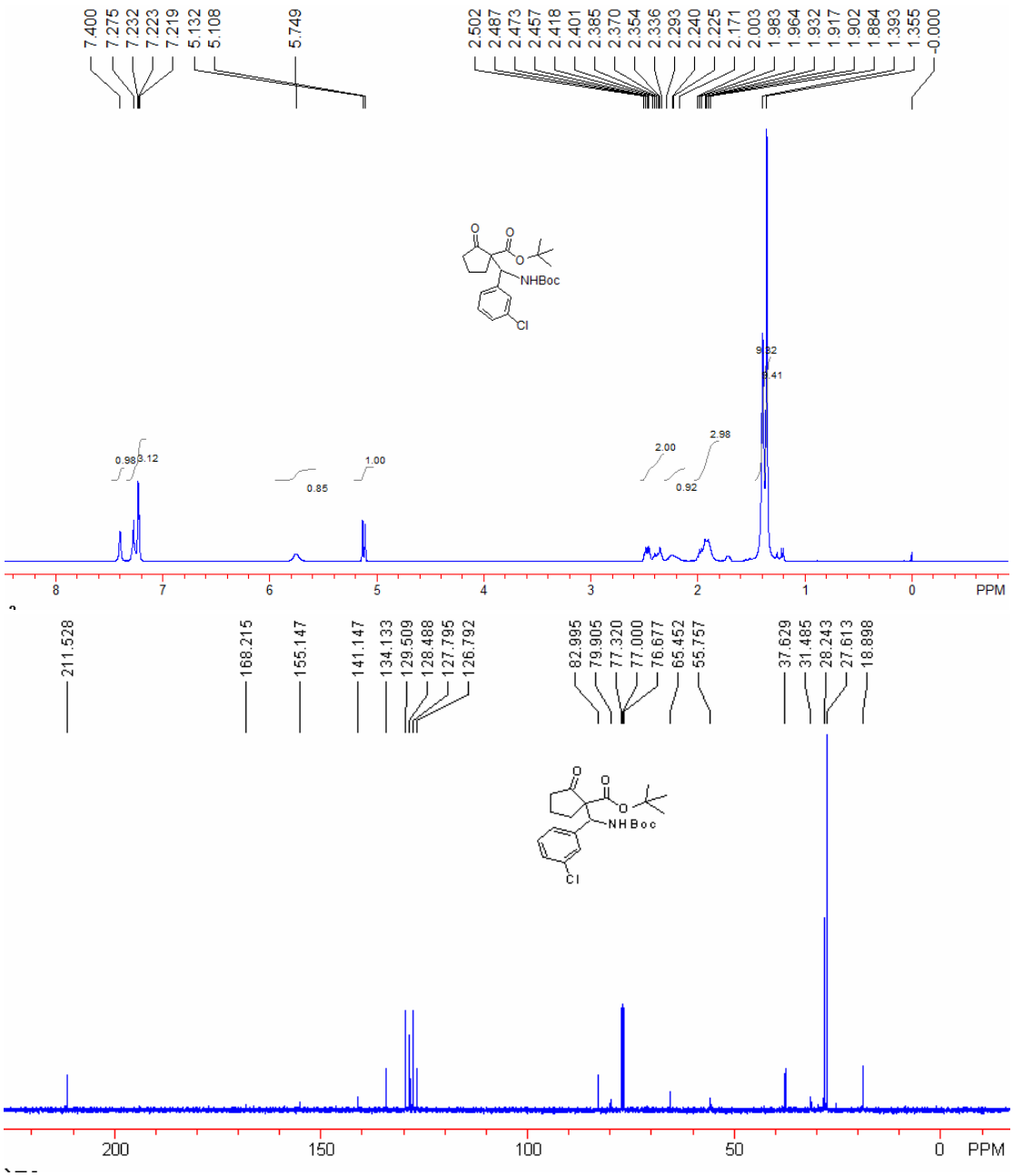


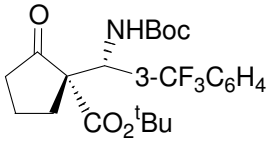




4c

1-[tert-Butoxycarbonylamino-(3-chlorophenyl)methyl]-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4c**: Colorless oil; IR (KBr) ν 2977, 2374, 1749, 1720, 1491, 1248, 1155, 1048, 786 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.36 (9H, s), 1.39 (9H, s), 1.88-2.00 (3H, m), 2.17-2.29 (1H, m), 2.34-2.50 (2H, m), 5.12 (1H, d, *J* = 9.6 Hz), 5.75 (1H, brs), 7.22-7.28 (3H, m), 7.40 (1H, brs); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 18.9, 27.6, 28.2, 31.5, 37.6, 55.8, 65.5, 79.9, 83.0, 126.8, 127.8, 128.5, 129.5, 134.1, 141.1, 155.1, 168.2, 211.5; MS (ESI) *m/e* 446 (M^++23, 100); HRMS (ESI) Calcd. for $C_{22}H_{30}ClNO_5Na^+$ requires 446.1710, Found 446.1705; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 17.7 min, t_{minor} = 5.7 min.), 91% ee; $[\alpha]^{20}_{D}$ = -8.3 (c 0.9, CH_2Cl_2); Yield: 95%.

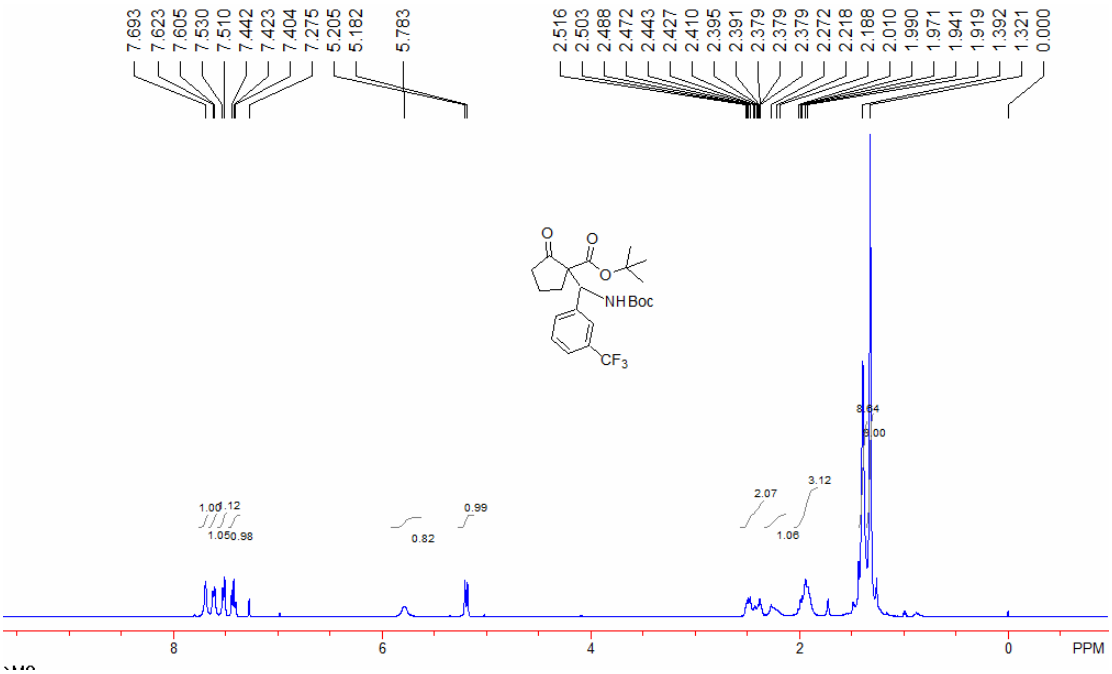


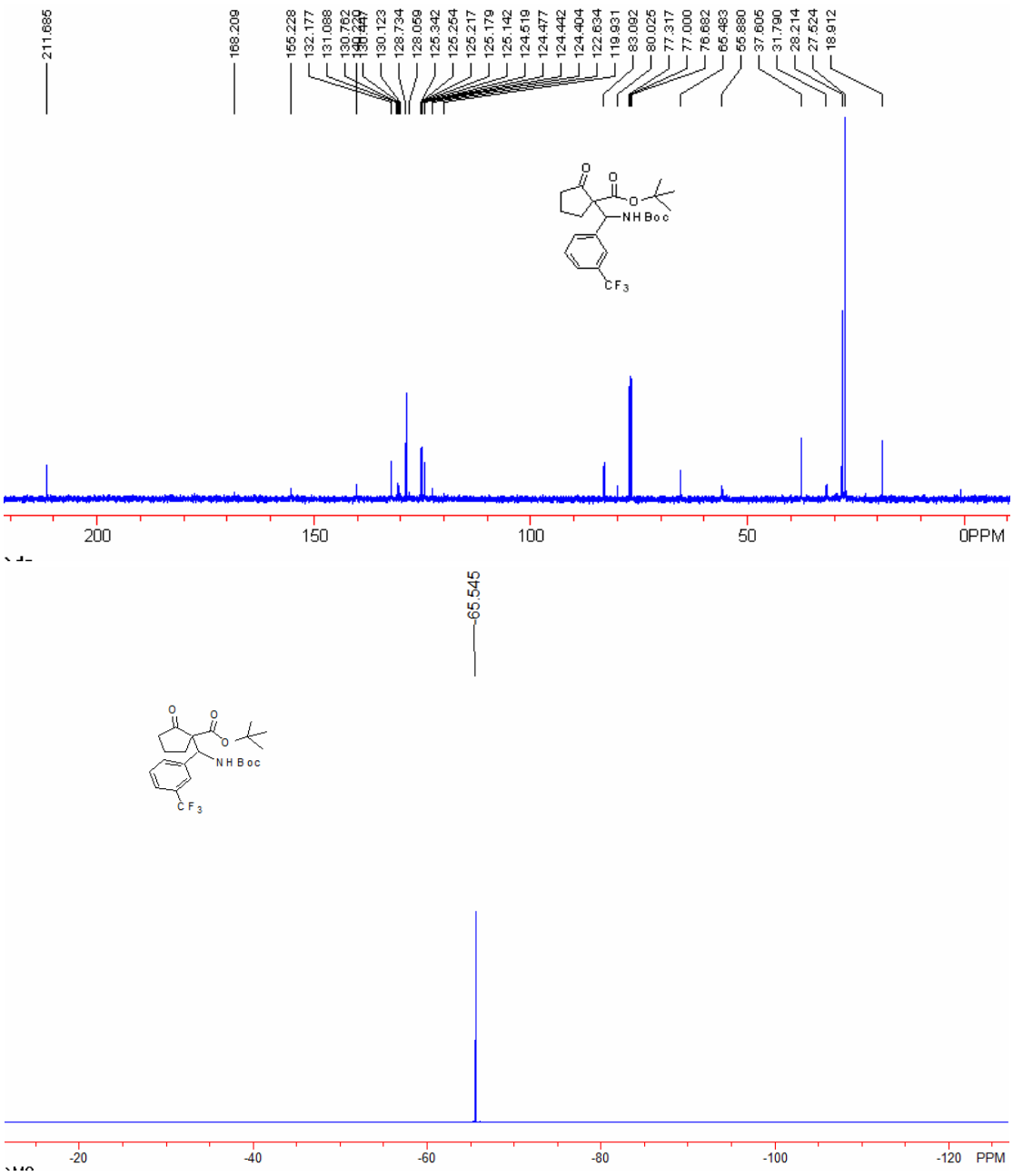


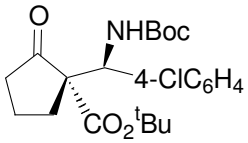
4d

1-[tert-Butoxycarbonylamino-(3-trifluoromethylphenyl)methyl]-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4d**: Colorless oil; IR (KBr) ν 2978, 2931, 1748, 1715, 1495, 1329, 1249, 1164, 1127, 951, 706 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.32 (9H, s), 1.39 (9H, s),

1.92-2.01 (3H, m), 2.19-2.27 (1H, m), 2.38-2.52 (2H, m), 5.19 (1H, d, J = 9.2 Hz), 5.78 (1H, brs), 7.42 (1H, t, J = 7.6 Hz), 7.52 (1H, d, J = 8.0 Hz), 7.61 (1H, d, J = 7.2 Hz), 7.69 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 18.9, 27.5, 28.2, 31.8, 37.6, 55.9, 65.5, 80.0, 83.1, 124.0 (q, J = 270.8 Hz), 124.5 (q, J = 3.8 Hz), 125.2 (q, J = 3.8 Hz), 128.7, 130.6 (q, J = 32.2 Hz), 132.2, 140.2, 155.2, 168.2, 211.7; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ -65.54; MS (ESI) *m/e* 480 (M^++23, 100); HRMS (ESI) Calcd. for $C_{23}H_{30}F_3NO_5Na^+$ requires 480.1974, Found 480.1968; (Daicel AD column, hexanes:^{i}PrOH = 98:2, 0.7 mL/min, λ = 230 nm, t_{major} = 33.4 .min, t_{minor} = 16.9 min.), 94% ee; $[\alpha]^{20}_D$ = -9.4 (c 2.0, CH_2Cl_2); Yield: 90%.



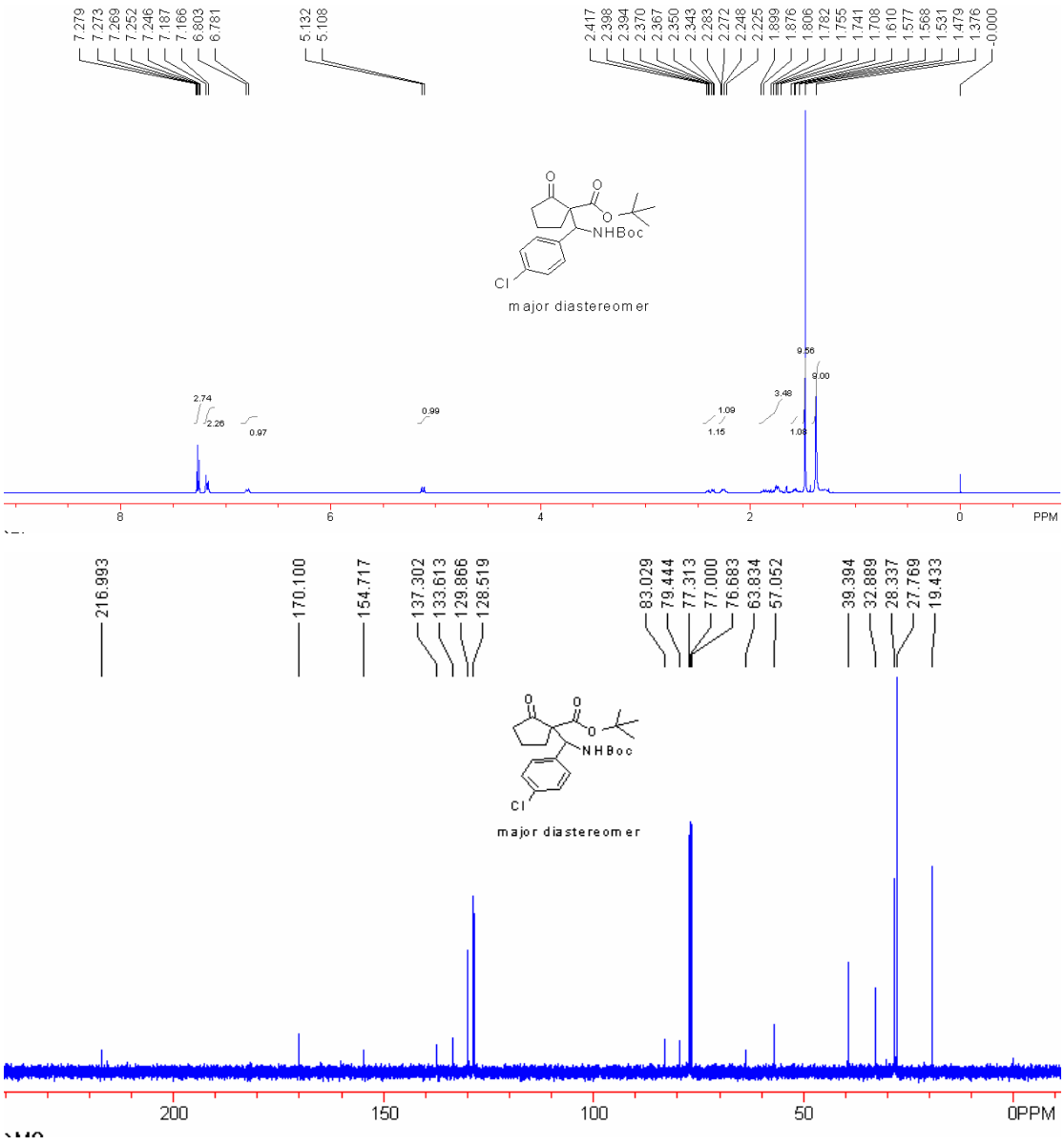


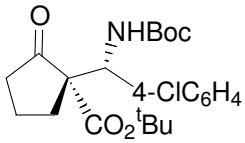


(*S, S*)-**4e**

(*S*,*S*)-1-[tert-Butoxycarbonylamino-(4-chlorophenyl)methyl]-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4e**: anti diastereomer. white solid: M.p. 124-125 ^{o}C; IR (KBr) ν 2980, 2926, 1727, 1710, 1492, 1244, 1155, 1090, 879, 764 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS):

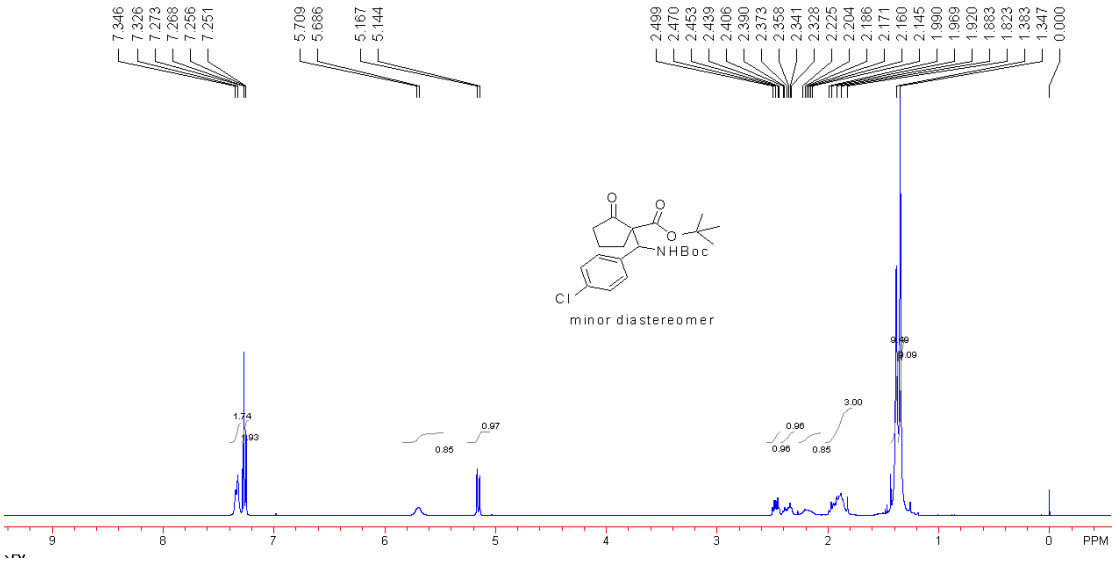
δ 1.38 (9H, s), 1.48 (9H, s), 1.53-1.61 (1H, m), 1.71-1.90 (3H, m), 2.22-2.28 (1H, m), 2.34-2.42 (1H, m), 5.12 (1H, d, *J* = 9.6 Hz), 6.79 (1H, d, *J* = 9.6 Hz), 7.17-7.19 (2H, m), 7.25-7.28 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.4, 27.8, 28.3, 32.9, 39.4, 57.1, 63.8, 79.4, 83.0, 128.5, 129.9, 133.6, 137.3, 154.7, 170.1, 217.0; MS (ESI) *m/e* 446 (M^++23, 70); HRMS (ESI) Calcd. for $C_{22}H_{30}ClNO_5Na^+$ requires 446.1710, Found 446.1705; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 8.7 min, t_{minor} = 20.5 min.), 90% ee; $[\alpha]^{20}_D$ = -5.4 (c 0.15, CH_2Cl_2); Yield: 61%.

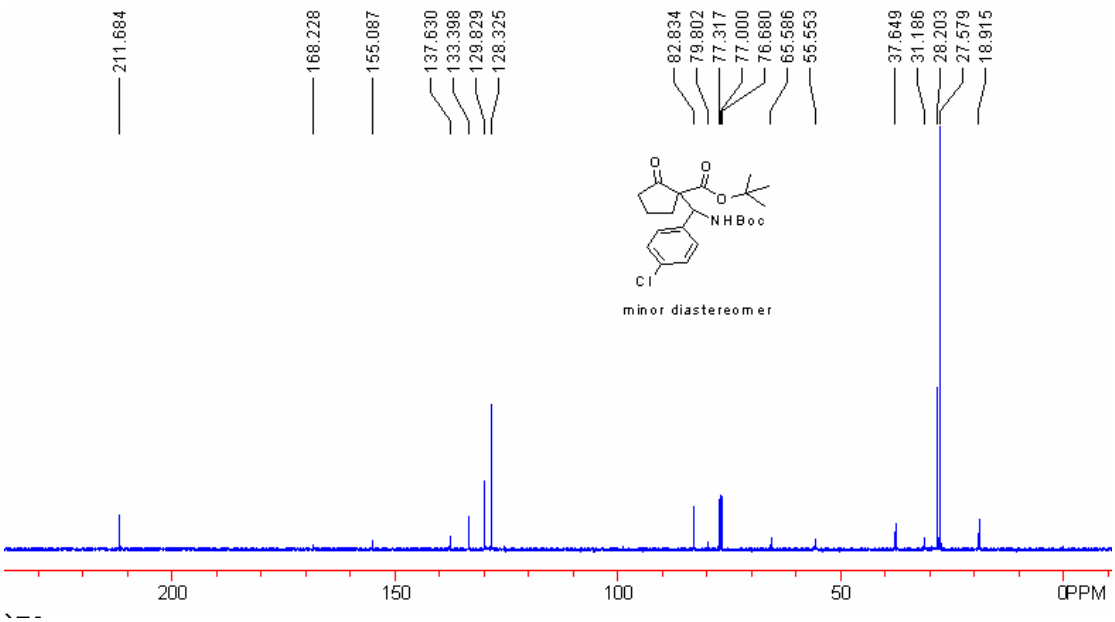


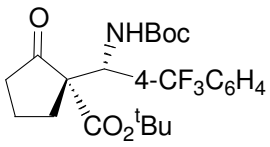


syn diastereomer-**4e**

1-[tert-Butoxycarbonylamino-(4-chloro-phenyl)-methyl]-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4e**: syn diastereomer. white solid: M.p. 125-126 ^{o}C; IR (KBr) ν 2976, 2926, 2854, 1750, 1720, 1492, 1368, 1247, 1154, 1120, 1015, 841 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.35 (9H, s), 1.38 (9H, s), 1.82-1.99 (3H, m), 2.14-2.22 (1H, m), 2.33-2.41 (1H, m), 2.44-2.50 (1H, m), 5.16 (1H, d, *J* = 9.2 Hz), 5.70 (1H, d, *J* = 9.2 Hz), 7.25-7.27 (2H, m), 7.33-7.35 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 18.9, 27.6, 28.2, 31.2, 37.6, 55.6, 65.6, 79.8, 82.8, 128.3, 129.8, 133.4, 137.6, 155.1, 168.2, 211.7; MS (ESI) *m/e* 446 (M^++23, 20); HRMS (ESI) Calcd. for $C_{22}H_{30}ClNO_5Na^+$ requires 446.1710, Found 446.1705; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 6.0 min, t_{minor} = 7.1 min.), 56% ee; $[\alpha]^{20}_{D}$ = -5.2 (c 0.78, CH_2Cl_2); Yield: 30%.

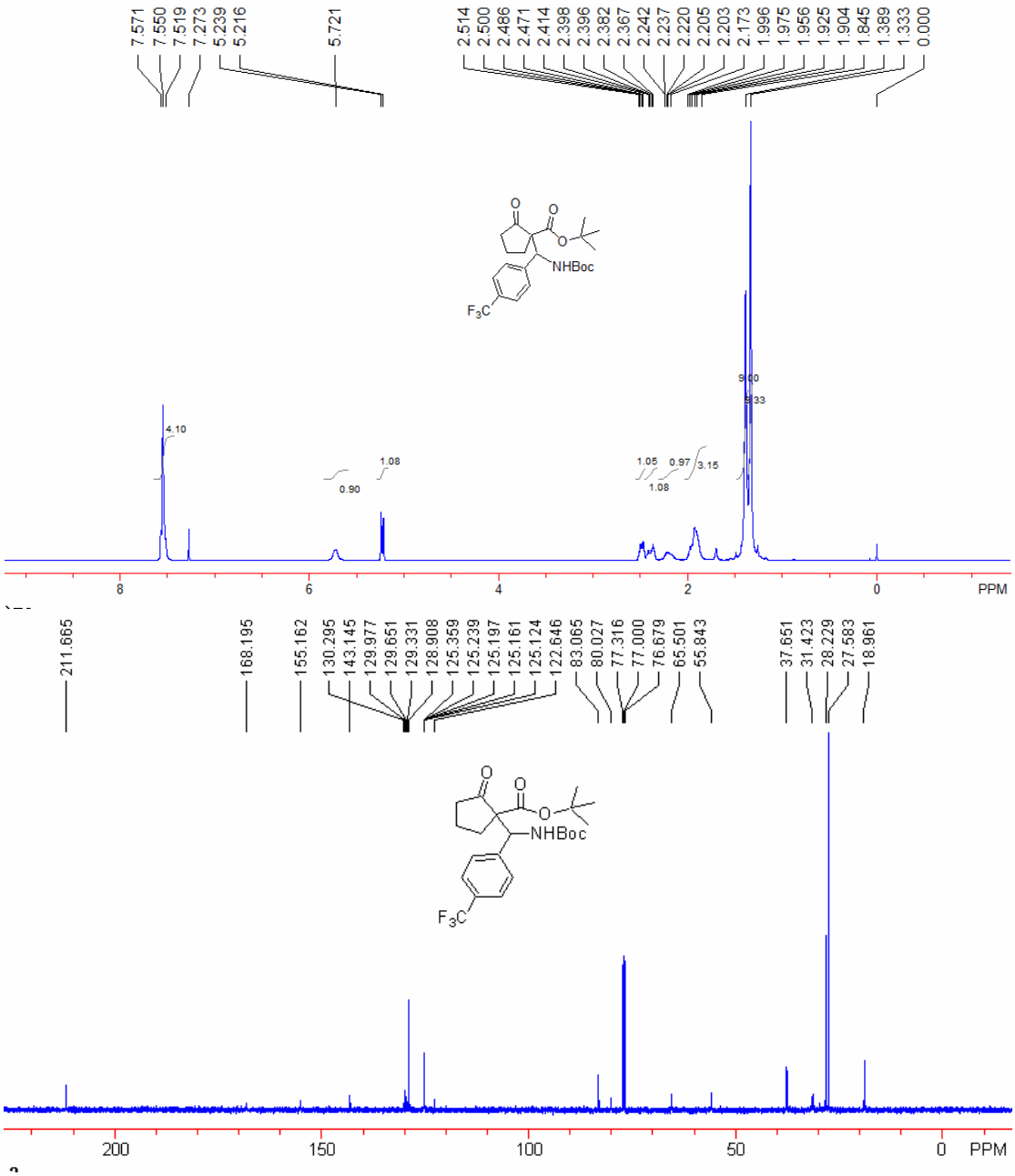






4f

1-[tert-Butoxycarbonylamino-(4-trifluoromethylphenyl)methyl]-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4f**: Colorless oil; IR (KBr) ν 2979, 2933, 1749, 1721, 1509, 1491, 1326, 1246, 1165, 1125, 1069, 847 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.33 (9H, s), 1.39 (9H, s), 1.84-2.00 (3H, m), 2.17-2.24 (1H, m), 2.37-2.41 (1H, m), 2.47-2.51 (1H, m), 5.23 (1H, d, *J* = 9.2 Hz), 5.72 (1H, brs), 7.52-7.57 (4H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.0, 27.6, 28.2, 31.4, 37.7, 55.8, 65.5, 80.0, 83.1, 124.0 (q, *J* = 271.3 Hz), 125.2 (q, *J* = 3.8 Hz), 128.9, 129.8 (q, *J* = 32.1 Hz), 143.1, 155.2, 168.2, 211.7; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ -65.56; MS (ESI) *m/e* 480 (M^++23, 30); HRMS (ESI) Calcd. for $C_{23}H_{30}F_3NO_5Na^+$ requires 480.1974, Found 480.1968; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 25.3 min, t_{minor} = 7.0 min.), 95% ee; $[\alpha]^{20}_D$ = -6.6 (c 0.8, CH_2Cl_2); Yield: 90%.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7.519
7.273
5.239
5.216
5.721
2.514
2.500
2.486
2.471
2.414
2.398
2.396
2.382
2.367
2.242
2.237
2.220
2.205
2.203
2.173
1.996
1.975
1.956
1.925
1.904
1.845
1.389
1.333
0.000
NHBoc
F3C
4.10
0.90
1.08
1.05
0.97
3.15
1.08
9.60
8.33
8
6
4
2
0
PPM
211.665
168.195
155.162
130.295
143.145
129.977
129.651
129.331
128.908
125.359
125.239
125.197
125.161
125.124
122.646
83.065
80.027
77.316
77.000
76.679
65.501
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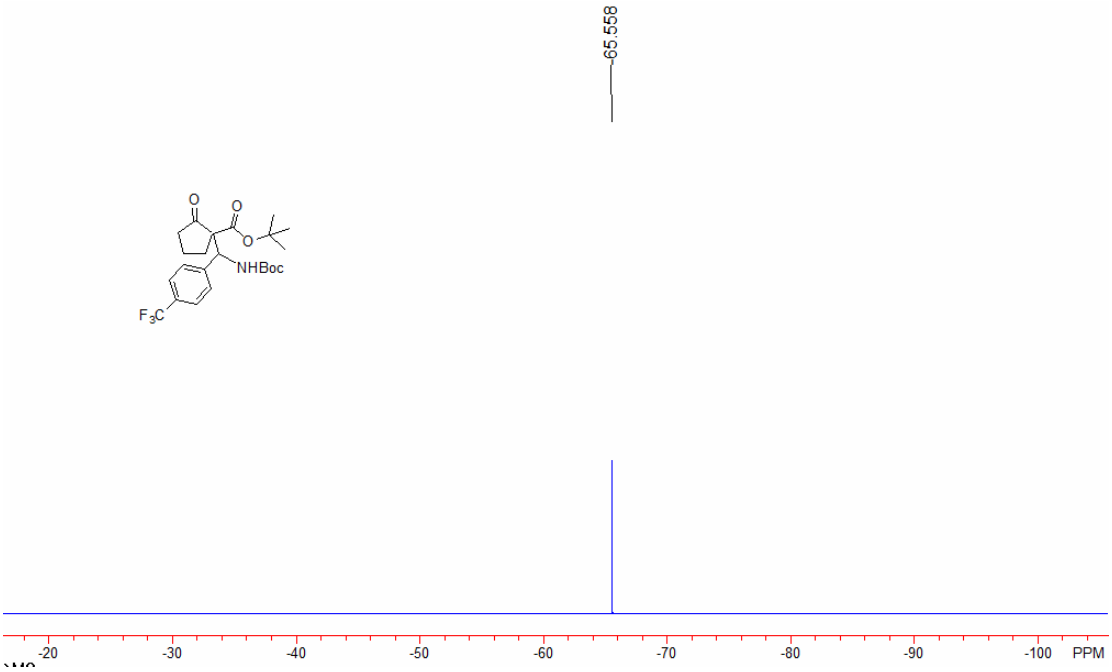
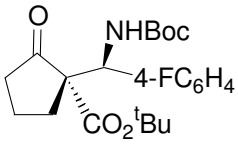
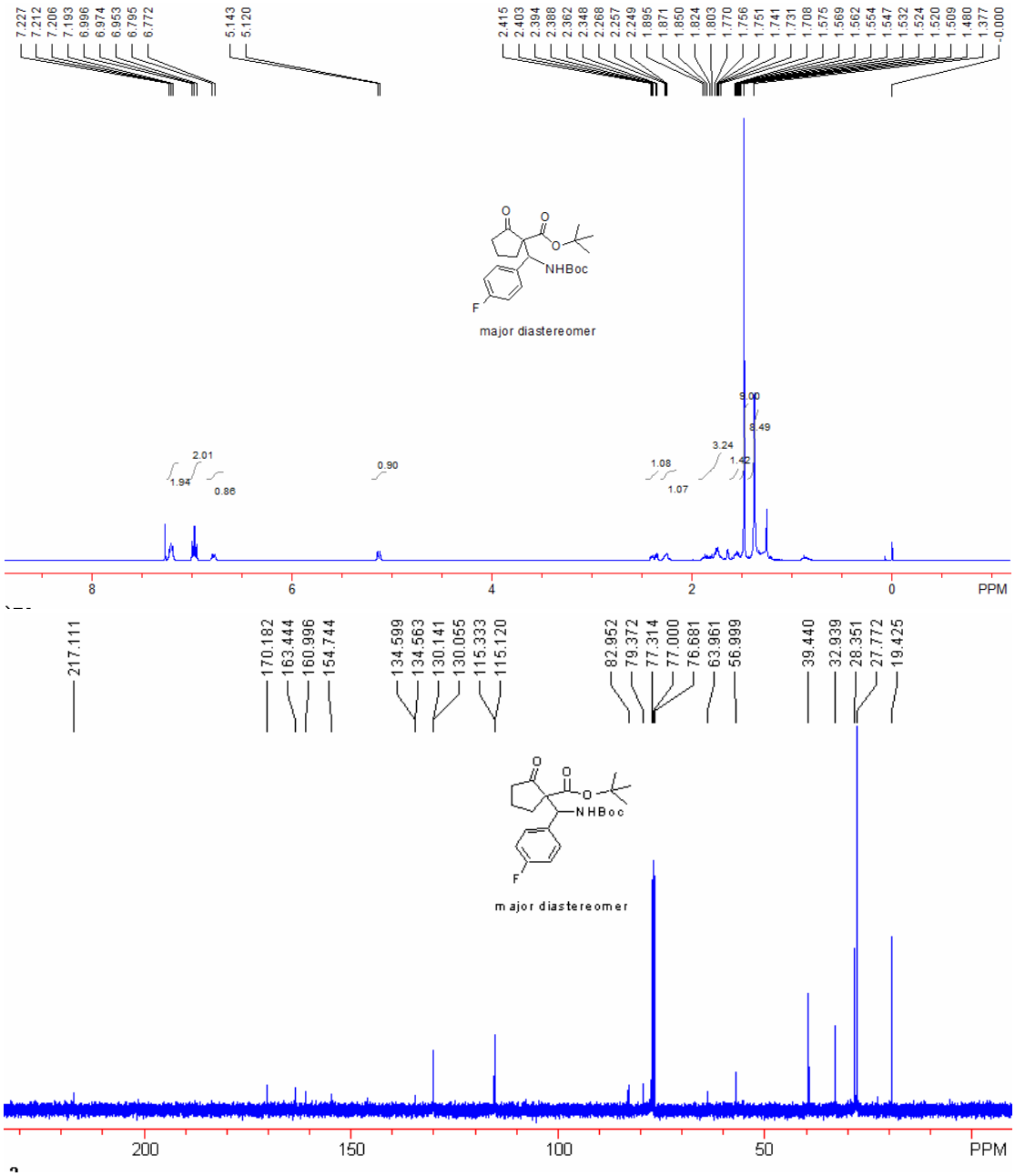
28.229
27.583
18.961
NHBoc
F3C
200
150
100
50
0
PPM





(*S, S*)-**4g**

(*S*,*S*)-1-[tert-Butoxycarbonylamino-(4-fluorophenyl)methyl]-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4g**: anti diastereomer. Colorless oil; IR (KBr) ν 2978, 2933, 1750, 1720, 1510, 1369, 1248, 1160, 1119, 1048, 844 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.38 (9H, s), 1.48 (9H, s), 1.51-1.58 (1H, m), 1.71-1.90 (3H, m), 2.25-2.27 (1H, m), 2.35-2.42 (1H, m), 5.13 (1H, d, *J* = 9.2 Hz), 6.78 (1H, d, *J* = 9.2 Hz), 6.97 (2H, t, *J* = 8.8 Hz), 7.19-7.23 (2H, m). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.4, 27.8, 28.4, 32.9, 39.4, 57.0, 64.0, 79.4, 83.0, 115.2 (d, *J* = 21.3 Hz), 130.1 (d, *J* = 8.6 Hz), 134.6 (d, *J* = 3.6 Hz), 154.7, 162.2 (d, *J* = 244.8 Hz), 170.2, 217.1. ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ -114.63. MS (ESI) *m/e* 430 (M^++23, 30); HRMS (ESI) Calcd. for $C_{22}H_{30}FNO_5Na^+$ requires 430.2006, Found 430.2000; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 6.6 min, t_{minor} = 13.4 min.), 83% ee; $[\alpha]^{20}_{D}$ = -6.0 (c 0.32, CH_2Cl_2); Yield: 61%.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7.212
7.206
7.193
6.996
6.974
6.953
6.795
6.772
5.143
5.120
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2.394
2.388
2.362
2.348
2.268
2.257
2.249
1.895
1.871
1.850
1.824
1.803
1.770
1.756
1.751
1.741
1.731
1.708
1.575
1.569
1.562
1.554
1.547
1.532
1.524
1.520
1.509
1.480
1.377
0.000
NHBoc
F
major diastereomer
9.00
8.49
3.24
2.01
1.94
0.86
0.90
1.08
1.07
1.42
8
6
4
2
0
PPM
217.111
170.182
163.444
160.996
154.744
134.599
134.563
130.141
130.055
115.333
115.120
82.952
79.372
77.314
77.000
76.681
63.961
56.999
39.440
32.939
28.351
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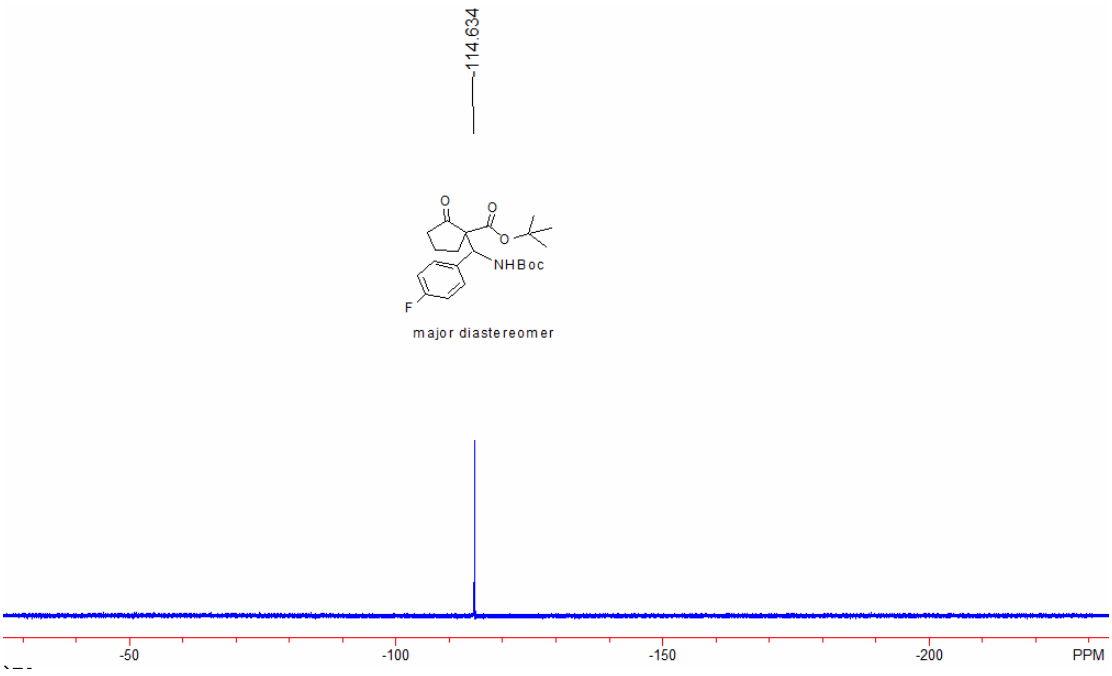
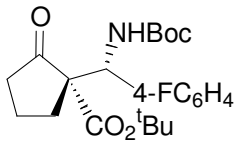
NHBoc
F
major diastereomer
200
150
100
50
PPM

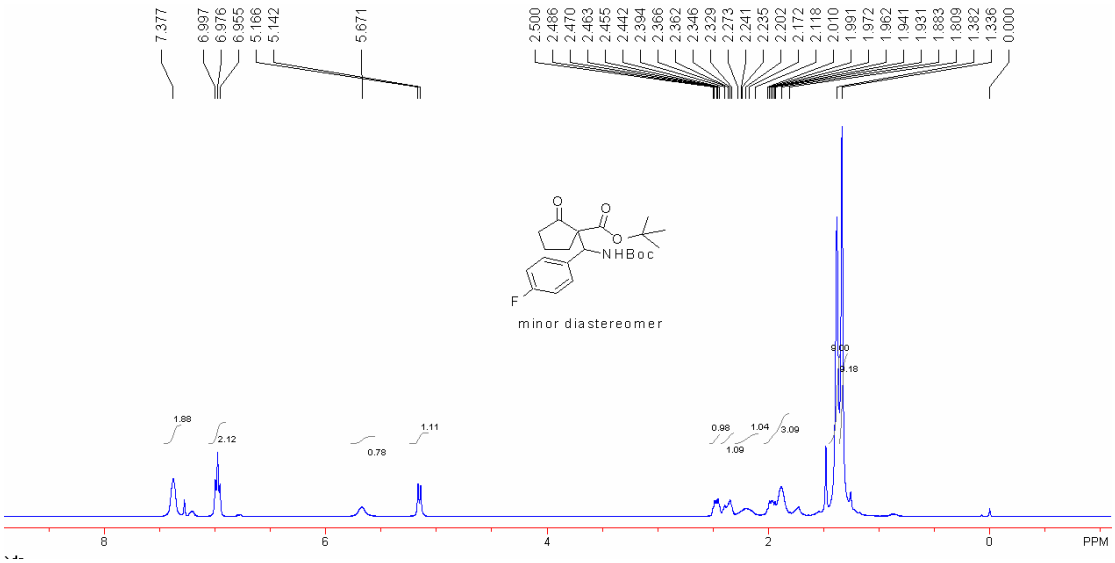


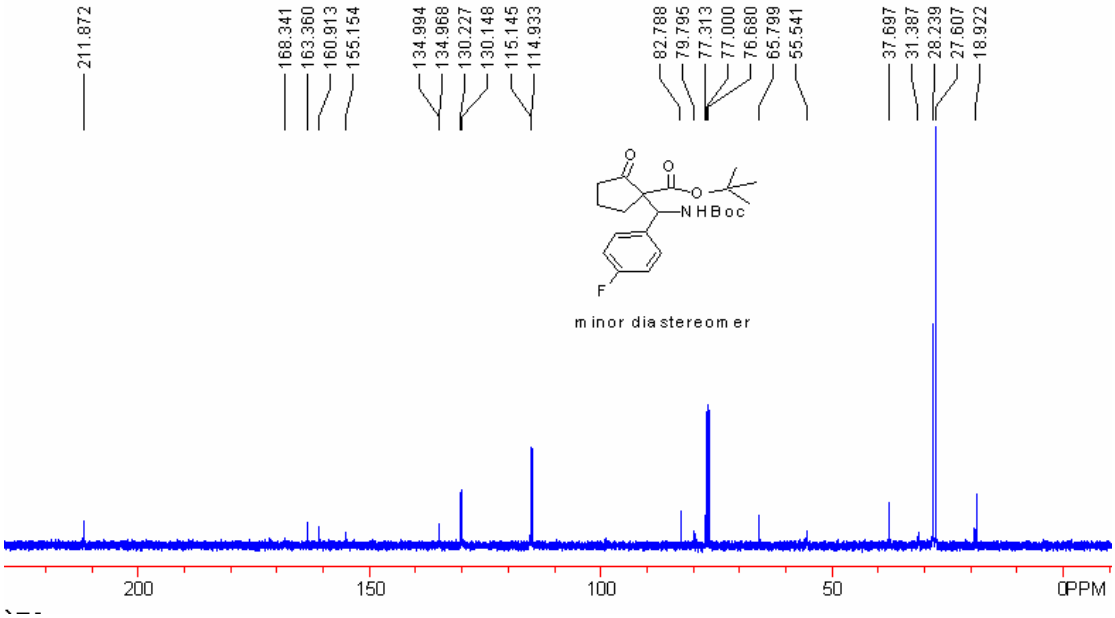


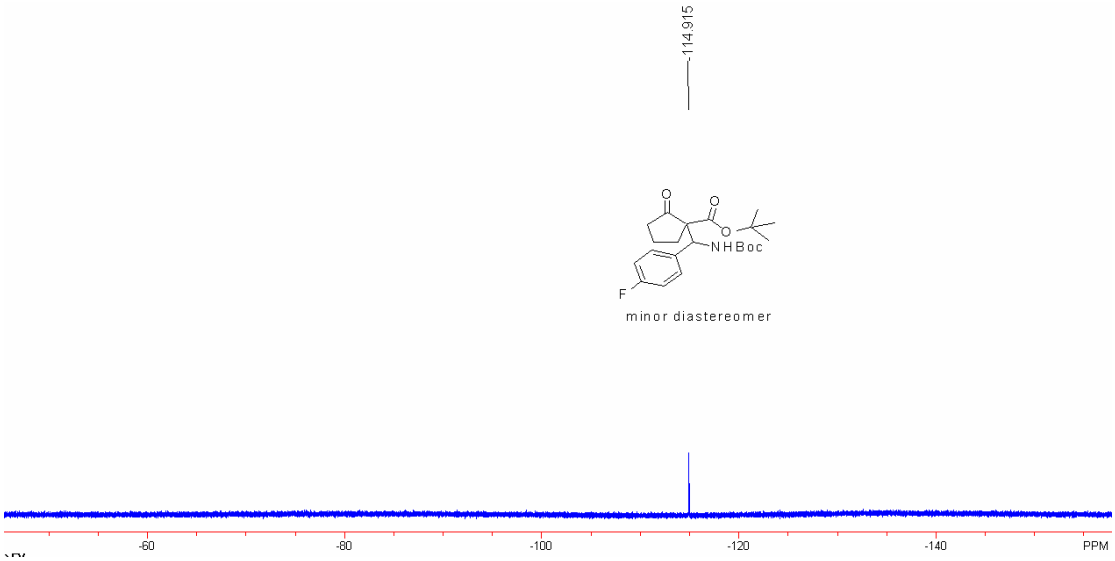
syn diastereomer-**4g**

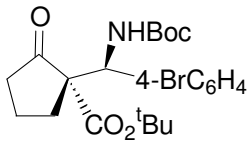
1-[tert-Butoxycarbonylamino-(4-fluorophenyl)methyl]-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4g**: syn diastereomer. Colorless oil; IR (KBr) ν 2955, 2924, 2854, 1745, 1723, 1462, 1377, 1237, 1158, 722 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.34 (9H, s), 1.38 (9H, s), 1.81-2.01 (3H, m), 2.12-2.27 (1H, m), 2.33-2.39 (1H, m), 2.44-2.50 (1H, m), 5.15 (1H, d, *J* = 9.6 Hz), 5.67 (1H, brs), 6.98 (2H, t, *J* = 8.4 Hz), 7.38 (2H, brs); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 18.9, 27.6, 28.2, 31.4, 37.7, 55.5, 65.8, 79.8, 82.8, 115.0 (d, *J* = 21.2 Hz), 130.2 (d, *J* = 7.9 Hz), 135.0 (d, *J* = 2.6 Hz), 155.2, 162.1 (d, *J* = 244.7 Hz), 168.3, 211.9; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ -114.92; MS (ESI) *m/e* 430 (M^++23, 100); HRMS (ESI) Calcd. for $C_{22}H_{30}FNO_5Na^+$ requires 430.2006, Found 430.2000; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 19.9 min, t_{minor} = 6.6 min.), 48% ee;

$[\alpha]^{20}_{D}$ = -5.3 (c 0.5, CH_2Cl_2); Yield: 31%.



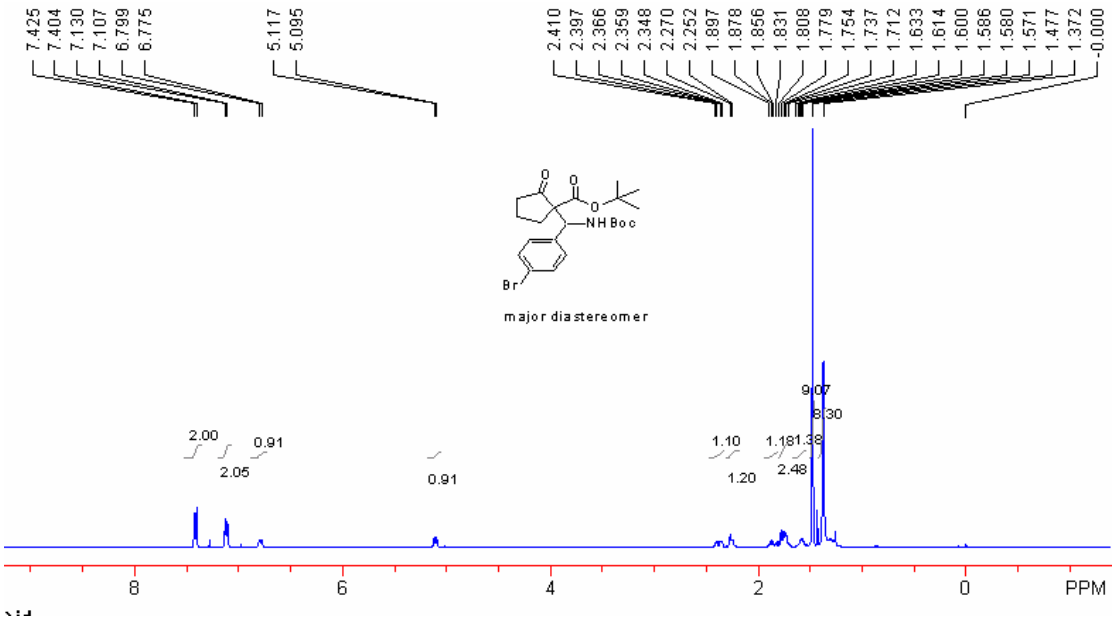


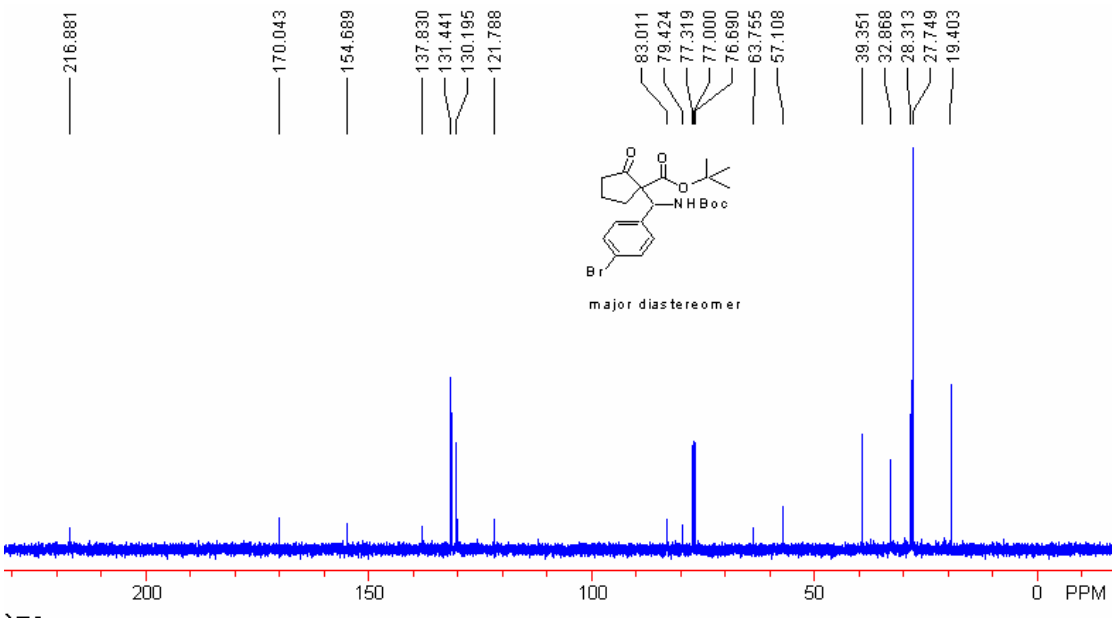


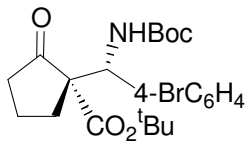


(*S, S*)-**4h**

(*S*,*S*)-1-[(4-Bromo-phenyl)-tert-butoxycarbonylamino-methyl]-2-oxo-cyclopentanecarboxylic acid tert-buty l ester **4h**: anti diastereomer. white solid: M.p. 135-136 ^{o}C; IR (KBr) ν 2975, 2931, 1746, 1715, 1489, 1368, 1244, 1156, 1074, 1008, 911, 878, 744 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.37 (9H, s), 1.48 (9H, s), 1.57-1.63 (1H, m), 1.71-1.78 (2H, m), 1.81-1.90 (1H, m), 2.25-2.27 (1H, m), 2.35-2.41 (1H, m), 5.11 (1H, d, *J* = 8.8 Hz), 6.79 (1H, d, *J* = 8.8 Hz), 7.12 (2H, d, *J* = 9.2 Hz), 7.41 (2H, d, *J* = 9.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.4, 27.7, 28.3, 32.9, 39.4, 57.1, 63.8, 79.4, 83.0, 121.8, 130.2, 131.4, 137.8, 154.7, 170.0, 216.9; MS (ESI) *m/e* 490 (M^++23, 100); HRMS (ESI) Calcd. for $C_{22}H_{30}BrNO_5Na^+$ requires 490.1205, Found 490.1200; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 8.3 min, t_{minor} = 21.7 min.), 70% ee; $[\alpha]^{20}_{D}$ = +4 (c 0.19, CH_2Cl_2); Yield: 59%.

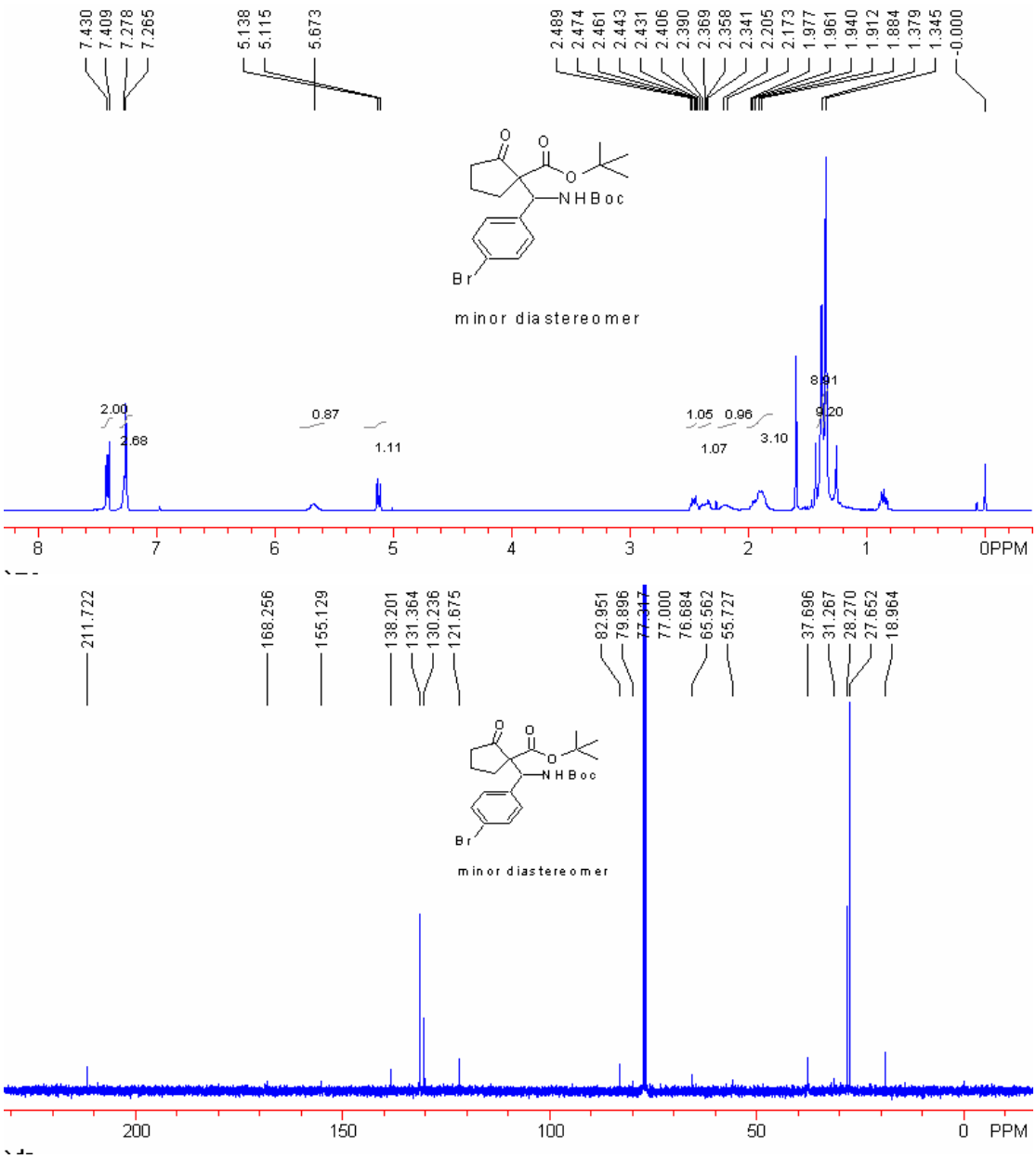


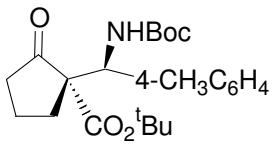




syn diastereomer-**4h**

1-[(4-Bromophenyl)-tert-butoxycarbonylaminomethyl]-2-oxo-cyclopentanecarboxylic acid tert-buty l ester **4h**: syn diastereomer. white solid: M.p. 134-135 ^{o}C; IR (KBr) ν 2970, 2854, 1748, 1715, 1538, 1462, 1377, 1244, 1154, 1028, 1018, 751 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.34 (9H, s), 1.38 (9H, s), 1.88-1.98 (3H, m), 2.17-2.20 (1H, m), 2.34-2.41 (1H, m), 2.43-2.49 (1H, m), 5.13 (1H, d, *J* = 9.2 Hz), 5.67 (1H, brs), 7.27 (2H, d, *J* = 8.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.0, 27.7, 28.3, 31.3, 37.7, 55.7, 65.6, 79.9, 83.0, 121.7, 130.2, 131.4, 138.2, 155.1, 168.3, 211.7; MS (ESI) *m/e* 490 (M^++23, 80); HRMS (ESI) Calcd. for $C_{22}H_{30}BrNO_5Na^+$ requires 490.1205, Found 490.1200; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 32.8 min, t_{minor} = 8.0 min.), 76% ee; $[\alpha]^{20}_{D}$ = -8.1 (c 0.91, CH_2Cl_2); Yield: 30%.

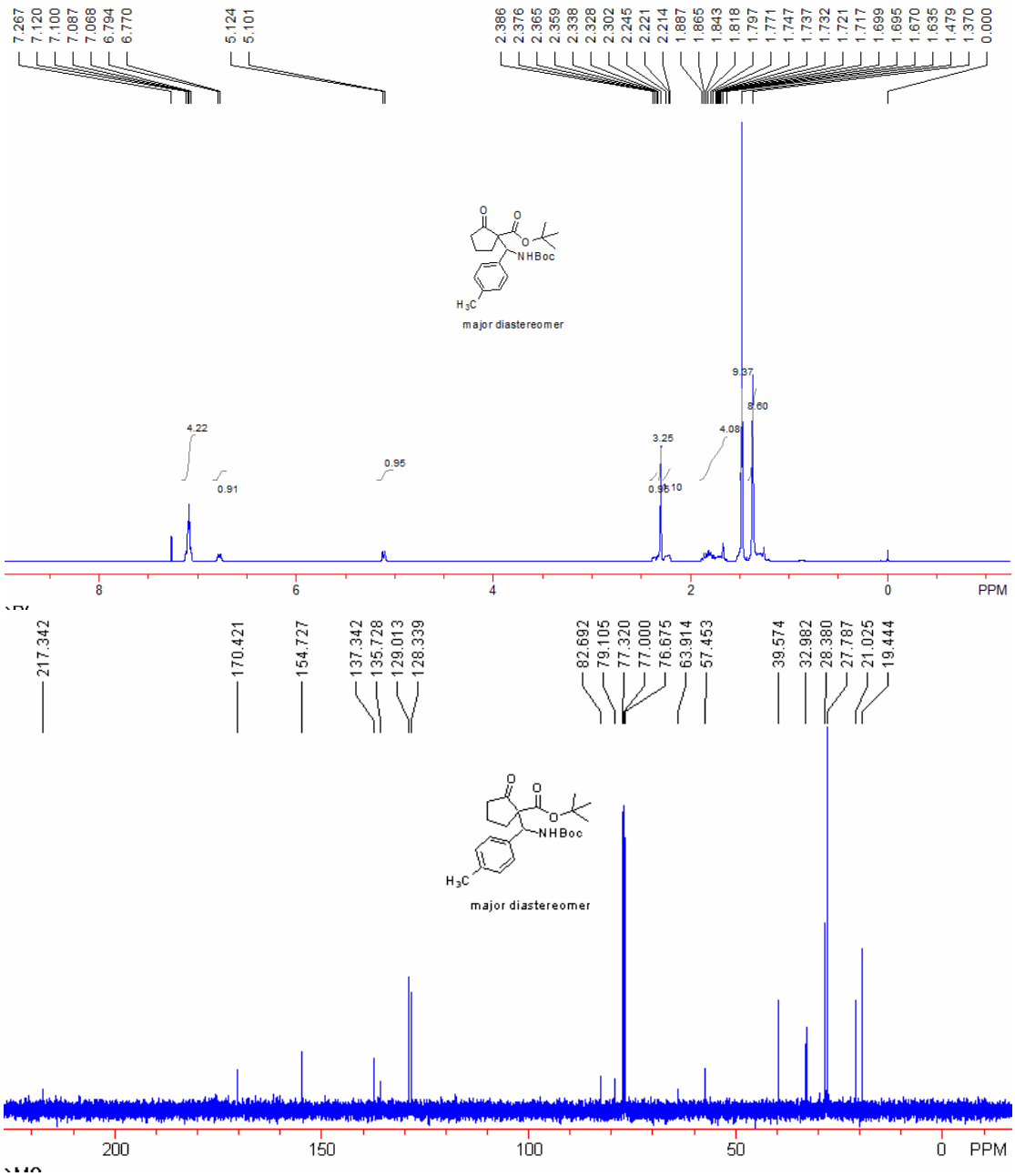


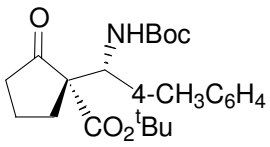


(*S, S*)-**4i**

(*S*,*S*)-1-(tert-Butoxycarbonylamino-p-tolyl-methyl)-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4i**: anti diastereomer. This is a known compound.[2b] ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.37 (9H, s), 1.48 (9H, s), 1.64-1.89 (4H, m), 2.21-2.24 (1H, m), 2.30 (3H, s), 2.33-2.39 (1H, m), 5.11 (1H, d, *J* = 9.2 Hz), 6.78 (1H, d, *J* = 9.2 Hz), 7.07-7.12 (4H, m); ^{13}C

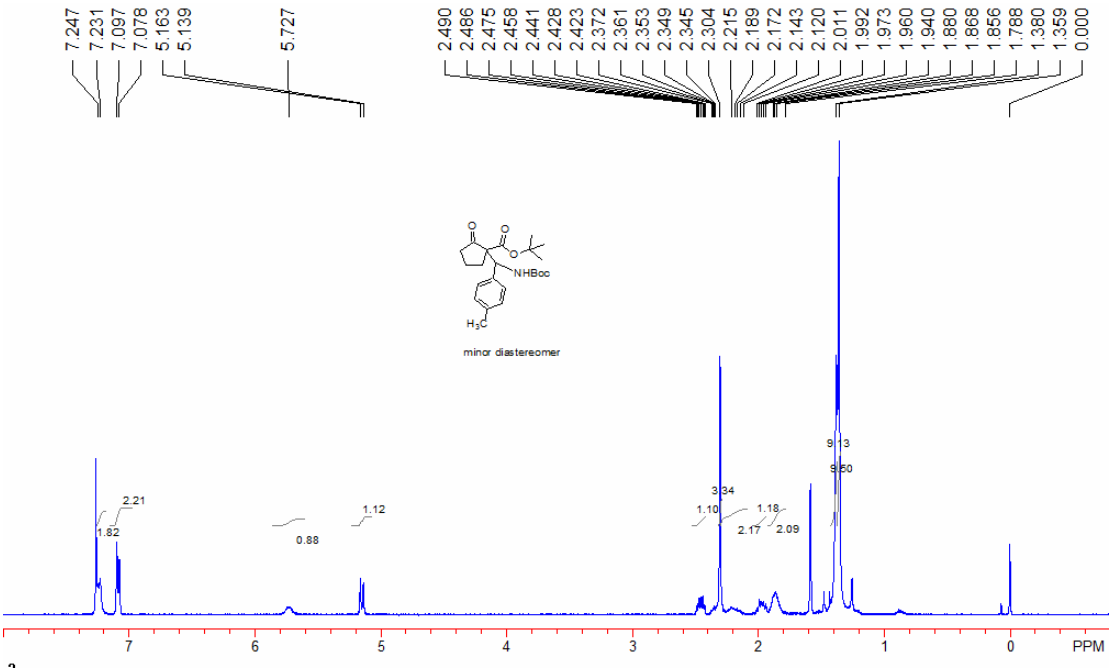
NMR ($CDCl_3$, 100 MHz, TMS): δ 19.4, 21.0, 27.8, 28.4, 33.0, 39.6, 57.5, 63.9, 79.1, 82.7, 128.3, 129.0, 135.7, 137.3, 154.7, 170.4, 217.3; HPLC (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 6.4 min, t_{minor} = 14.3 min.), 80% ee; $[\alpha]^{20}_{D}$ = +8.1 (c 0.75, CH_2Cl_2); Yield: 60%.

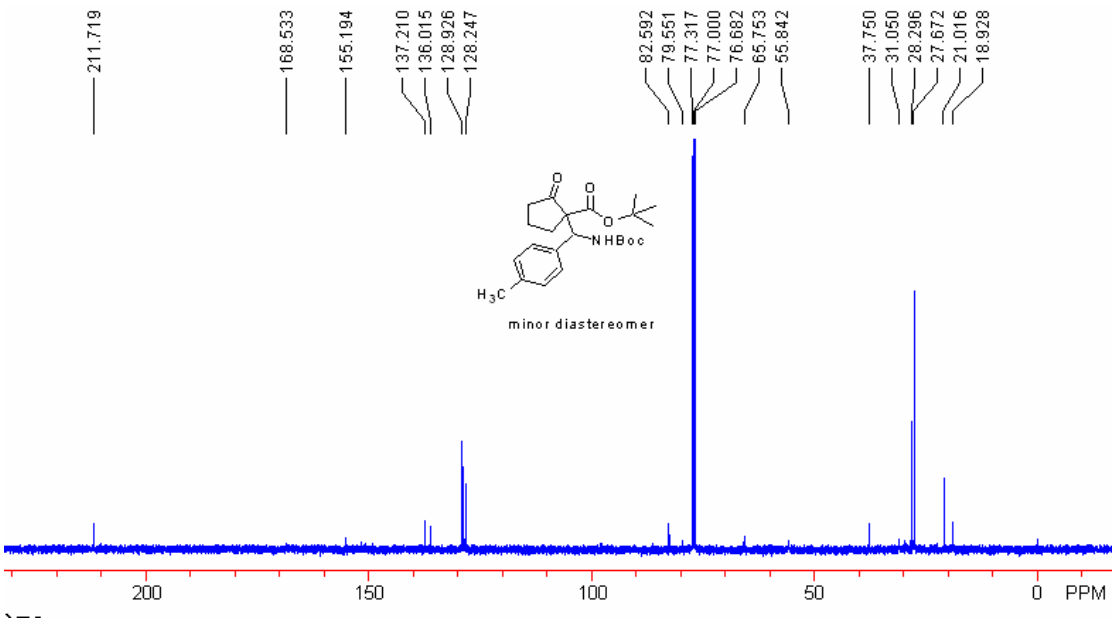


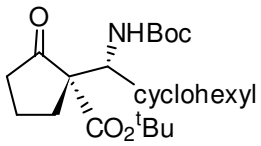


syn diastereomer-**4i**

1-(tert-Butoxycarbonylamino-p-tolylmethyl)-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4i**: syn diastereomer. This is a known compound.[2b] ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.36 (9H, s), 1.38 (9H, s), 1.79-1.88 (2H, m), 1.94-2.01 (1H, m), 2.12-2.37 (2H, m), 2.30 (3H, s), 2.42-2.49 (1H, m), 5.15 (1H, d, *J* = 9.6 Hz), 5.73 (1H, brs), 7.09 (2H, d, *J* = 7.6 Hz), 7.24 (2H, d, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 18.9, 21.0, 27.7, 28.3, 31.0, 37.8, 55.8, 65.8, 79.6, 82.6, 128.2, 128.9, 136.0, 137.2, 155.2, 168.5, 211.7; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 18.0 min, t_{minor} = 7.0 min.), 77% ee; $[\alpha]^{20}_{D}$ = -7.6 (c 0.2, CH_2Cl_2); Yield: 31%.

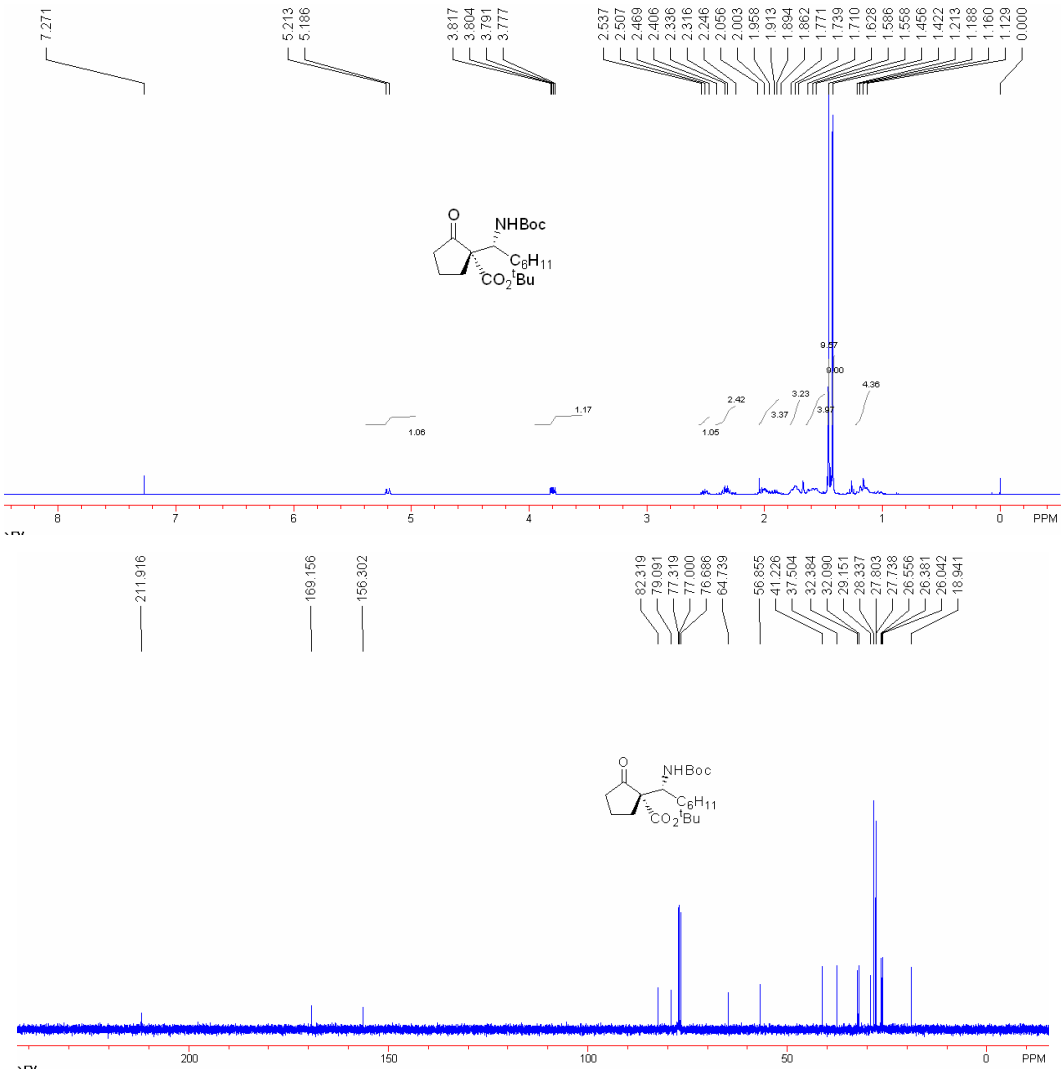


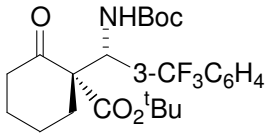




4j

1-(tert-Butoxycarbonylamino-cyclohexyl-methyl)-2-oxo-cyclopentanecarboxylic acid tert-butyl ester **4j**: colorless oil; IR (KBr) ν 2929, 1716, 1495, 1368, 1250, 1155, 779, 736 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.13-1.21 (4H, m), 1.42 (9H, s), 1.46 (9H, s), 1.56-1.63 (4H, m), 1.71-1.77 (3H, m), 1.86-2.06 (3H, m), 2.25-2.41 (2H, m), 2.47-2.54 (1H, m), 3.80 (1H, dd, J_1 = 5.2 Hz, J_2 = 10.4 Hz), 5.20 (1H, d, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 18.9, 26.0, 26.4, 26.6, 27.7, 27.8, 28.3, 29.2, 32.1, 32.4, 37.5, 41.2, 56.9, 64.7, 79.1, 82.3, 156.3, 169.2, 211.9; MS (ESI) *m/e* 418 (M^++23, 100); HRMS (ESI) Calcd. for $C_{22}H_{37}NO_5Na^+$ requires 418.2569, Found 418.2564; (Daicel PC-2 column, hexanes:^{i}PrOH = 80:20, 0.7 mL/min, λ = 214 nm, t_{major} = 5.2 min, t_{minor} = 4.7 min.), 96% ee; $[\alpha]^{20}_D$ = +45 (c 0.3, CH_2Cl_2); Yield: 92%.

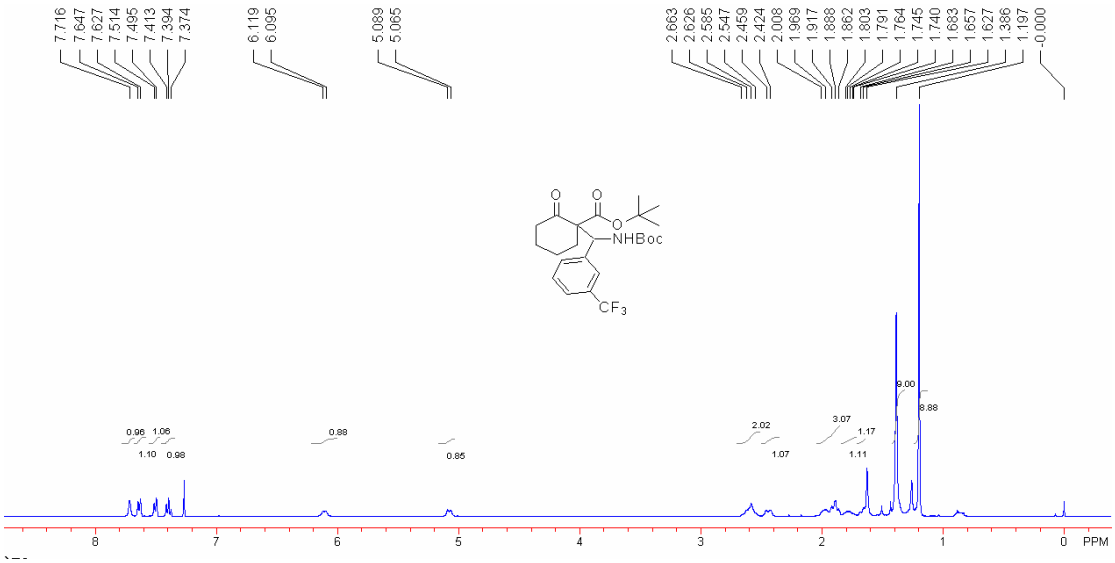


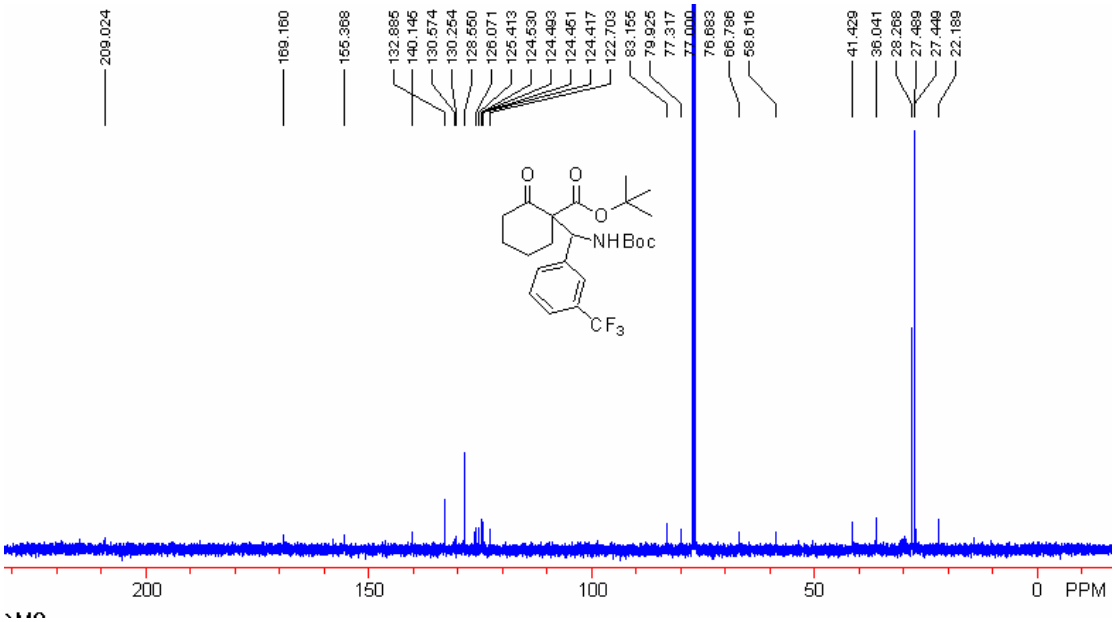


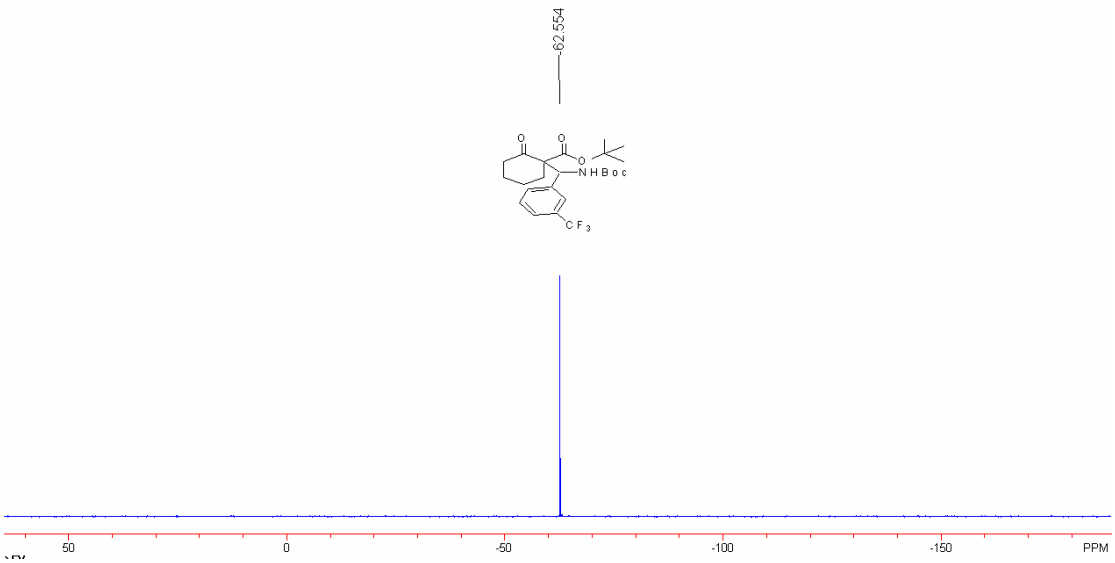
4k

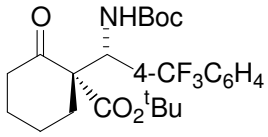
1-[tert-Butoxycarbonylamino-(3-trifluoromethylphenyl)methyl]-2-oxo-cyclohexanecarboxylic acid tert-butyl ester **4k**: colorless oil; IR (KBr) ν 2955, 2854, 1727, 1462, 1377, 1168, 1030, 722 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.20 (9H, s), 1.39 (9H, s), 1.63-1.68 (1H, m), 1.74-1.80 (1H, m), 1.86-2.01 (3H, m), 2.42-2.46 (1H, m), 2.55-2.66 (2H, m), 5.08 (1H, d, *J* = 9.6 Hz), 6.11 (1H, d, *J* = 9.6 Hz), 7.39 (1H, t, *J* = 8.0 Hz), 7.50 (1H, d, *J* = 7.6 Hz), 7.64 (1H, d, *J* = 8.0 Hz), 7.72 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 22.2, 27.4, 27.5, 28.3, 36.0,

41.4, 58.6, 66.8, 79.9, 83.2, 124.1 (q, J = 271.0 Hz), 124.5 (q, J = 3.8 Hz), 126.1 (q, J = 3.8 Hz), 128.6, 130.4 (q, J = 32.0 Hz), 132.9, 140.1, 155.4, 169.2, 209.0; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ -62.55; MS (ESI) *m/e* 494 (M^++23, 100); HRMS (ESI) Calcd. for $C_{24}H_{32}F_3NO_5Na^+$ requires 494.2130, Found 494.2125; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 7.2 min, t_{minor} = 6.6 min.), 88% ee; $[\alpha]^{20}_D$ = -7.4 (c 0.12, CH_2Cl_2); Yield: 85%.



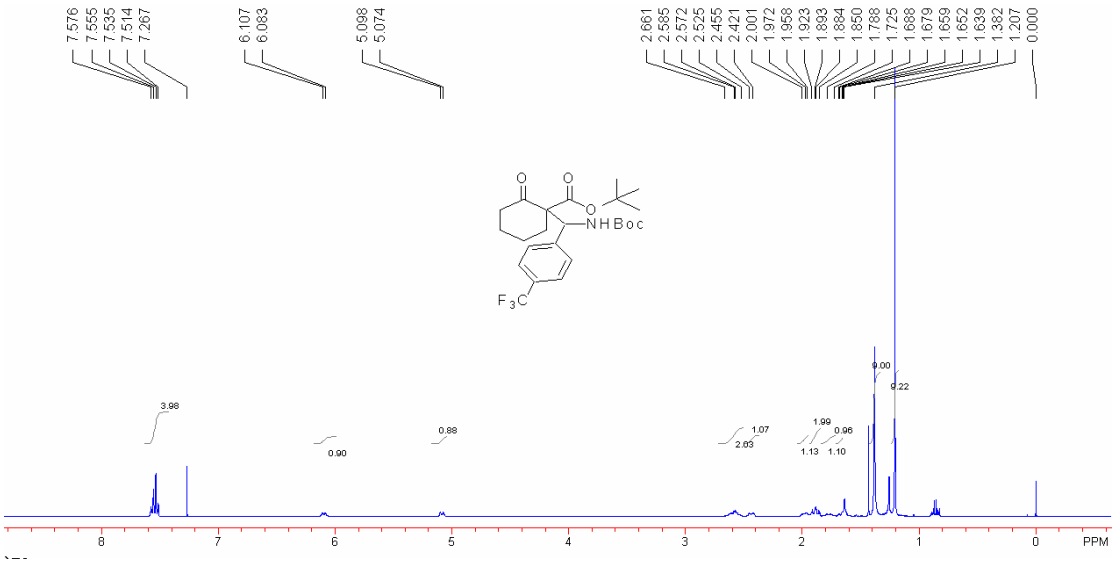


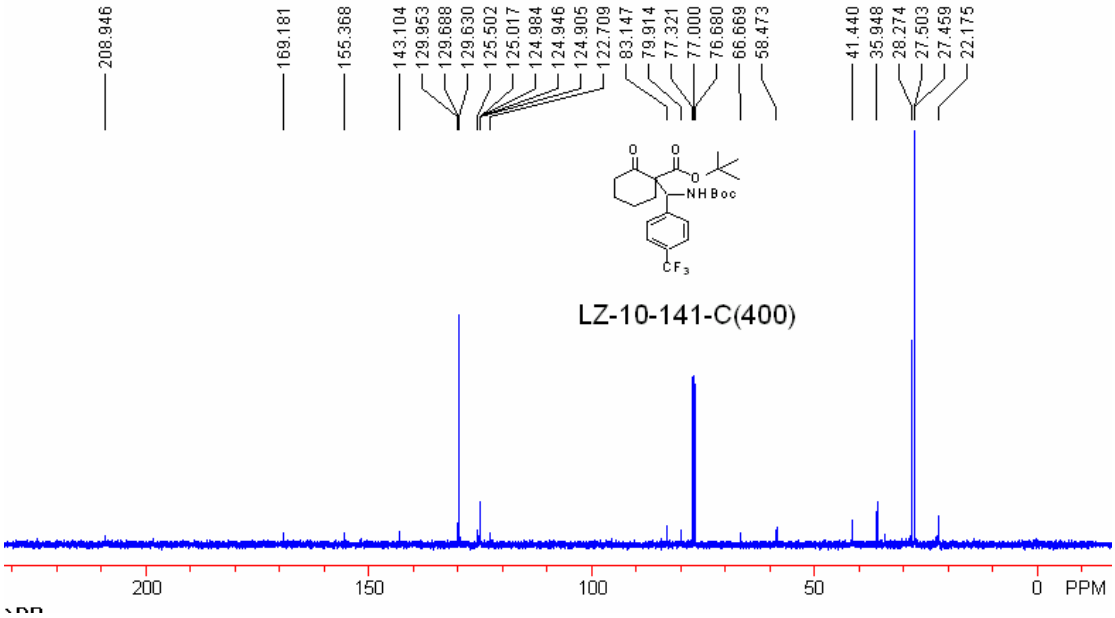


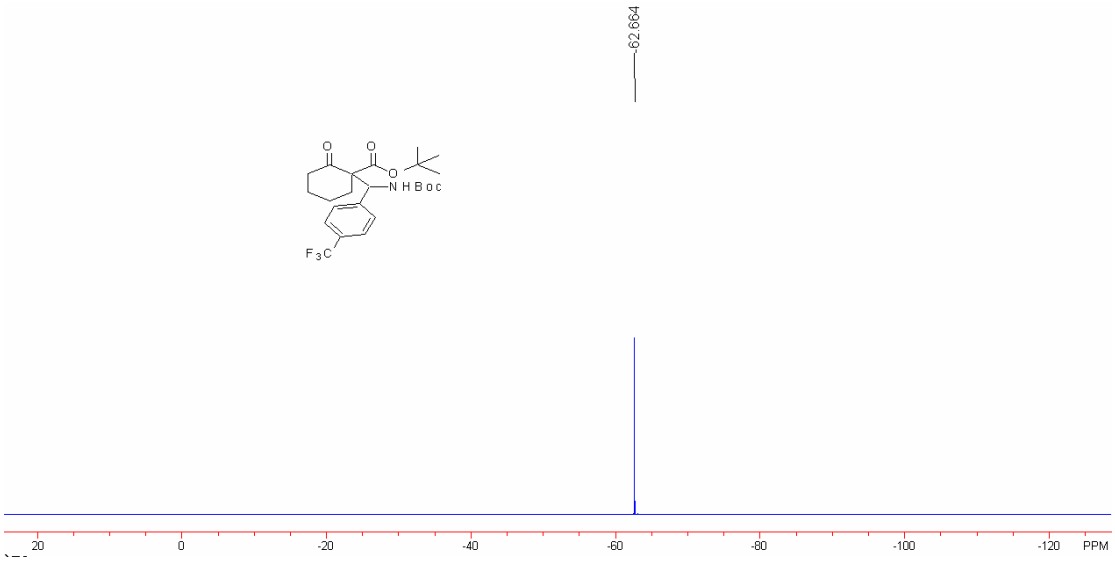


4l

1-[tert-Butoxycarbonylamino-(4-trifluoromethylphenyl)methyl]-2-oxo-cyclohexanecarboxylic acid tert-butyl ester **4l**: colorless oil; IR (KBr) ν 2955, 2924, 2854, 1741, 1723, 1460, 1377, 1168, 722 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.21 (9H, s), 1.38 (9H, s), 1.64-1.69 (1H, m), 1.73-1.79 (1H, m), 1.85-1.92 (2H, m), 1.96-2.00 (1H, m), 2.42-2.46 (1H, m), 2.52-2.66 (2H, m), 5.09 (1H, d, *J* = 9.6 Hz), 6.10 (1H, d, *J* = 9.6 Hz), 7.51-7.58 (4H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 22.2, 27.46, 27.50, 28.3, 36.0, 41.4, 58.5, 66.7, 79.9, 83.1, 124.1 (q, *J* = 279.3 Hz), 125.0 (q, *J* = 3.7 Hz), 129.7, 129.8 (q, *J* = 32.3 Hz), 143.1, 155.4, 169.2, 209.0; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ -62.66; MS (ESI) *m/e* 494 (M^++23, 100); HRMS (ESI) Calcd. for $C_{24}H_{32}F_3NO_5Na^+$ requires 494.2130, Found 494.2125; (Daicel AD column, hexanes:^{i}PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_{major} = 9.4 min, t_{minor} = 8.1 min.), 80% ee; $[\alpha]^{20}_D$ = -5.0 (c 0.5, CH_2Cl_2); Yield: 79%.


7.576
7.555
7.535
7.514
7.267
6.107
6.083
5.098
5.074
2.661
2.585
2.572
2.525
2.455
2.421
2.001
1.972
1.958
1.923
1.893
1.884
1.850
1.788
1.725
1.688
1.679
1.659
1.652
1.639
1.382
1.207
0.000
NHBoc
F3C
3.98
0.90
0.88
1.07
2.03
1.99
1.13
0.96
1.10
9.00
9.22
8
7
6
5
4
3
2
1
0
PPM


208.946
169.181
155.368
143.104
129.953
129.688
129.630
125.502
125.017
124.984
124.946
124.905
122.709
83.147
79.914
77.321
77.000
76.680
66.669
58.473
41.440
35.948
28.274
27.503
27.459
22.175
NHBoc
CF3
LZ-10-141-C(400)
200
150
100
50
0
PPM

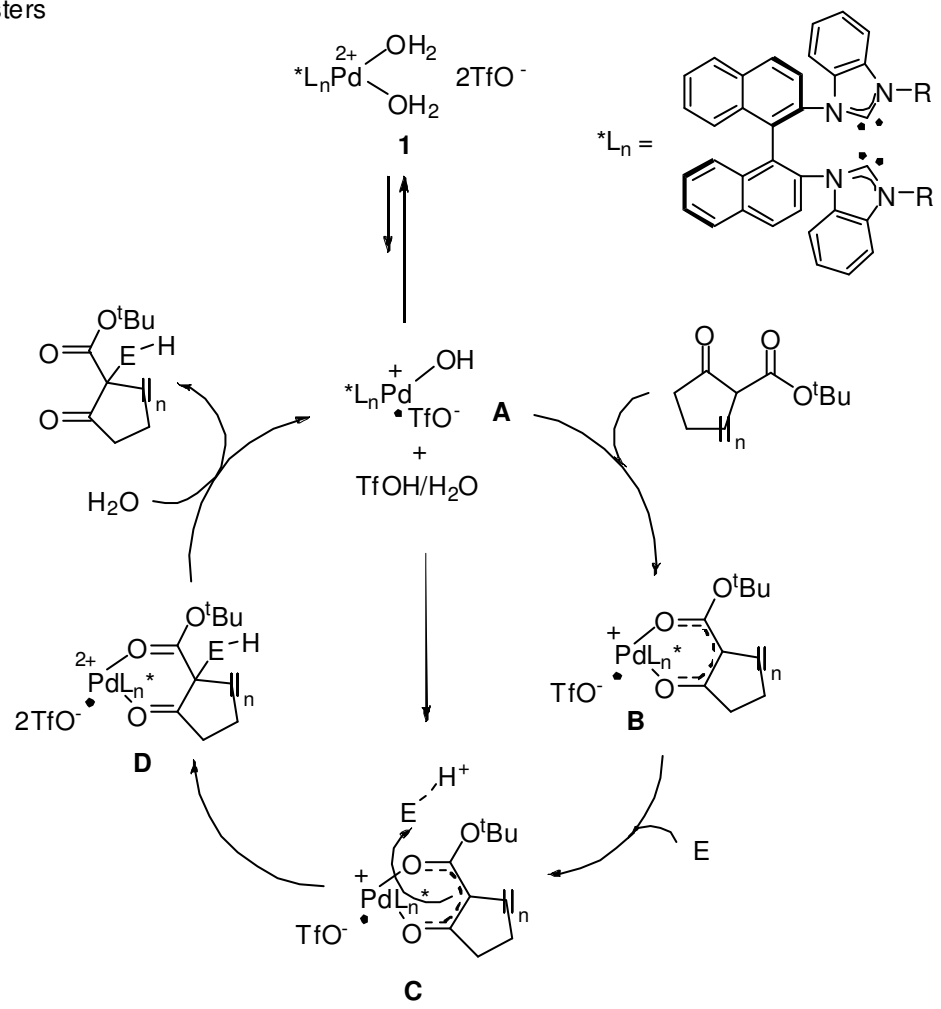

62.664
NHBoc
F3C
20
0
-20
-40
-60
-80
-100
-120
PPM

References

(1) For the papers of our group on the chiral NHC-Pd(II) complexes, see: (a) Chen, T.; Jiang, J. J.; Xu. Q.; Shi, M. *Org. Lett.* **2007**, *9*, 865. (b) Ma, G. N.; Zhang, T.; Shi, M. *Org. Lett.* **2009**, *11*, 875. (c) Duan, W. L.; Shi, M.; Rong, G.-B. *Chem. Commun.* **2003**, 2916. (d) Shi, M.; Duan, W. L. *Appl. Organomet. Chem.* **2005**, *19*, 40.

(2) (a) Hamashima, Y.; Hotta, D.; Umebayashi, N.; Tsuchiya, Y.; Suzuki, T.; Sodeoka, M. *Adv. Synth. Catal.* **2005**, *347*, 1576. (b) Hamashima, Y.; Sasamoto, N.; Hotta, D.; Somei, H.; Umebayashi, N.; Sodeoka, M. *Angew. Chem. Int. Ed.* **2005**, *44*, 1525.

Scheme SI-1. Proposed Mechanism for the Catalytic Enantioselective Addition of β-Ketoesters

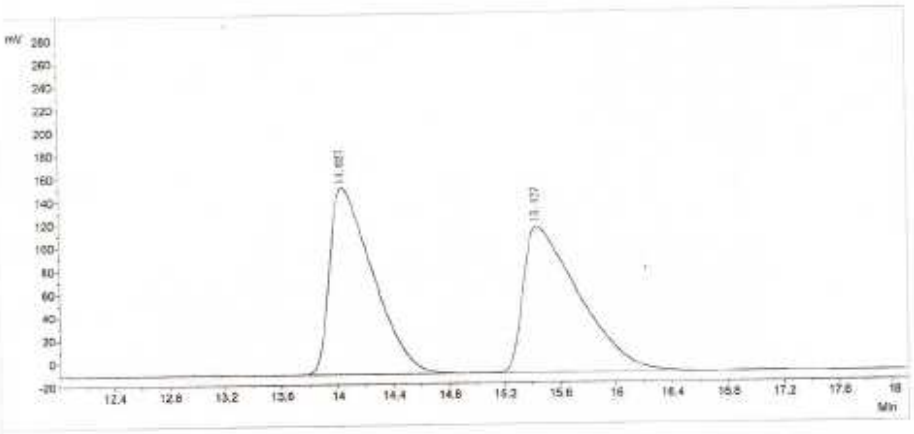


HPLC Data of the Products

HPLC REPORT

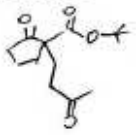
Sample Name:lz-16-Orac as 95.che
Time:11:13
column:
Velocity:

Date:2008-10-30
Method:
the mobile phase:
the detection wavelength:



No.	PeakNo	R.Time	PeakHeight	PeakArea	PerCent
1	1	14.027	160025.2	3481819.5	49.6284
2	2	15.427	125345.6	3533960.8	50.3716
Total			285370.8	7015780.3	100.0000

racemate

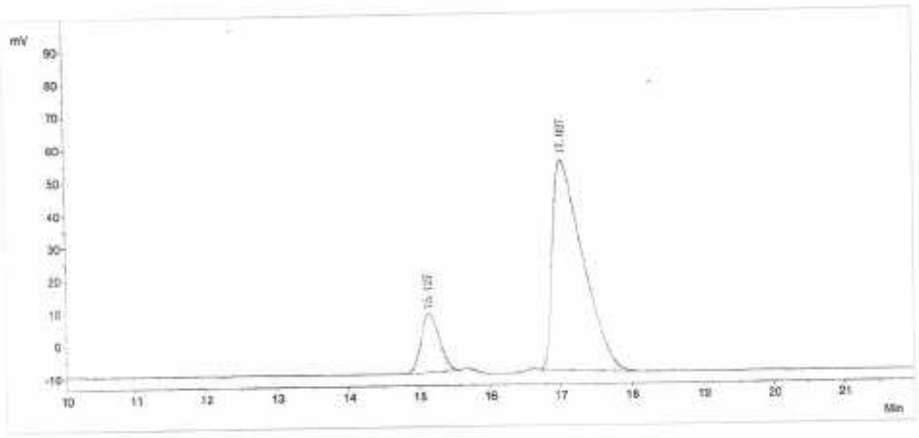


AS-H, hexane/iproH = 95/5, 0.7 mL/min, 230 nm

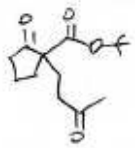
HPLC REPORT

Sample Name:lz-16-1-b.che
Time:14:23
column:
Velocity:

Date:2008-12-12
Method:
the mobile phase:
the detection wavelength:



No	PeakNo	R.Time	PeakHeight	PeakArea	PerCent
1	1	15.127	17572.2	316163.8	14.3272
2	2	17.027	64270.6	1890567.4	85.6728
Total			81842.8	2206731.2	100.0000



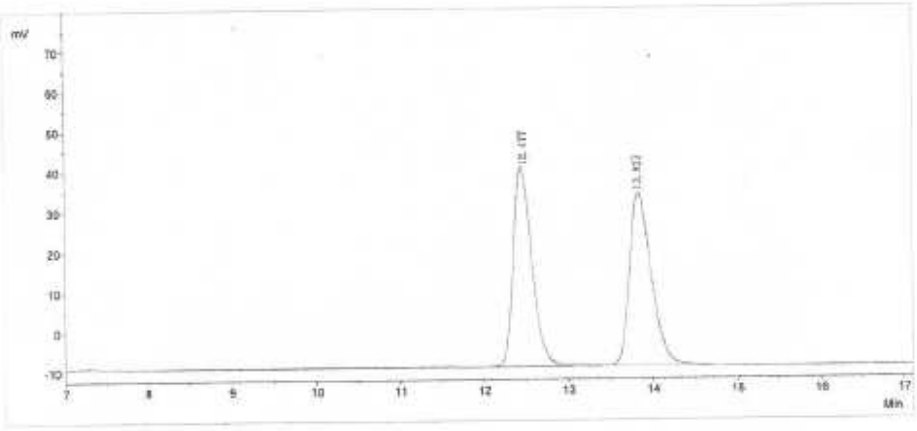
ee = 71%

AS-H, hexane/iproH = 95/5, 0.7 mL/mm, 230 nm

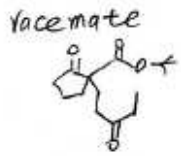
HPLC REPORT

Sample Name:lz-9-44-0rac as 95.che
Time:21:02
column:
Velocity:

Date:2009-02-07
Method:
the mobile phase:
the detection wavelength:



No.	PeakNo	R Time	PeakHeight	PeakArea	PerCent
1	1	12.477	48697.7	773308.7	50.0911
2	2	13.827	42377.3	770496.9	49.9089
Total			91075.0	1543805.6	100.0000

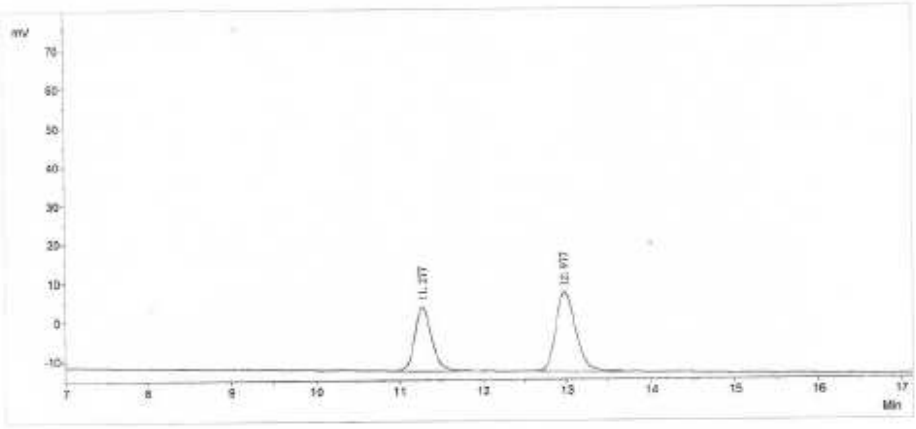


AS-H, hexane/ iproH = 95/5, 0.7 mL/min, 230 nm

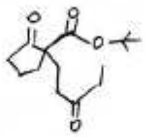
HPLC REPORT

Sample Name:lz-9-44-1.che
Time:15:32
column:
Velocity:

Date:2009-02-15
Method:
the mobile phase:
the detection wavelength:



No.	PeakNo	R.Time	PeakHeight	PeakArea	PerCent
1	1	11.277	16414.2	229156.6	40.4137
2	2	12.977	20391.9	337870.7	59.5863
Total			36806.1	567027.3	100.0000



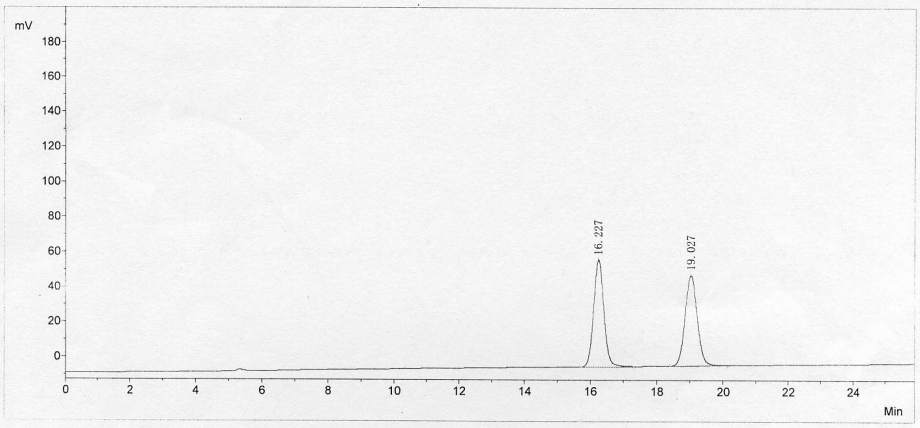
ee = 19%

As-H, hexane/iproH = 95/5, 0.7 mL/min, 230nm

HPLC REPORT

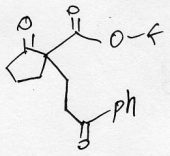
Sample Name:lz-9-56-0rac as 95.che
Time:18:17
column: AS-H
Velocity: 0.7

Date:2009-02-13
Method:
the mobile phase: 95
the detection wavelength: 230



No.	PeakNo	R.Time	PeakHeight	PeakArea	PerCent
1	1	16.227	60954.3	1317683.5	49.8614
2	2	19.027	51858.8	1325010.2	50.1386
Total			112813.1	2642693.7	100.0000

racemate

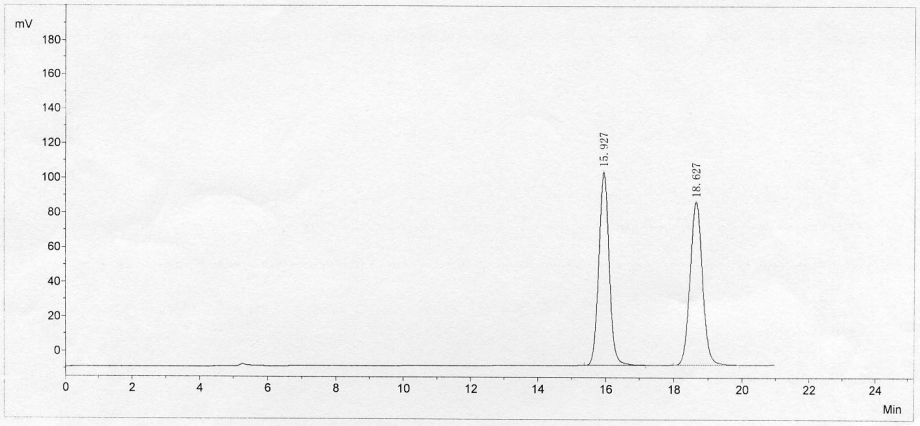


AS-H, hexane/iproH = 95/5, 0.7 mL/min, 230 nm

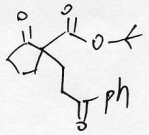
HPLC REPORT

Sample Name:lz-9-56-1.che
Time:18:46
column:
Velocity:

Date:2009-02-13
Method:
the mobile phase:
the detection wavelength:



No.	PeakNo	R.Time	PeakHeight	PeakArea	PerCent
1	1	15.927	111311.9	2364375.0	49.7223
2	2	18.627	93836.0	2390784.1	50.2777
Total			205147.9	4755159.1	100.0000



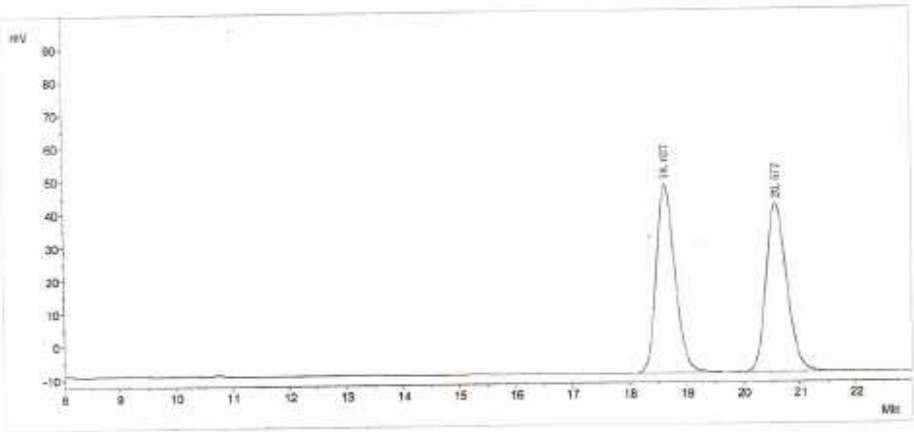
ee = 0

AS-H, hexane/iproH = 95/5, 0.7mL/min, 230nm

HPLC REPORT

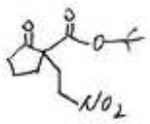
Sample Name:lz-9-45-Orac as 95.che
Time:19:56
column:
Velocity:

Date:2009-02-07
Method:
the mobile phase:
the detection wavelength:



No.	PeakNo	R.Time	PeakHeight	PeakArea	PerCent
1	1	18.627	56593.6	1291939.5	50.1164
2	2	20.677	50497.2	1285938.6	49.8836
Total			107090.8	2577878.1	100.0000

Racemate

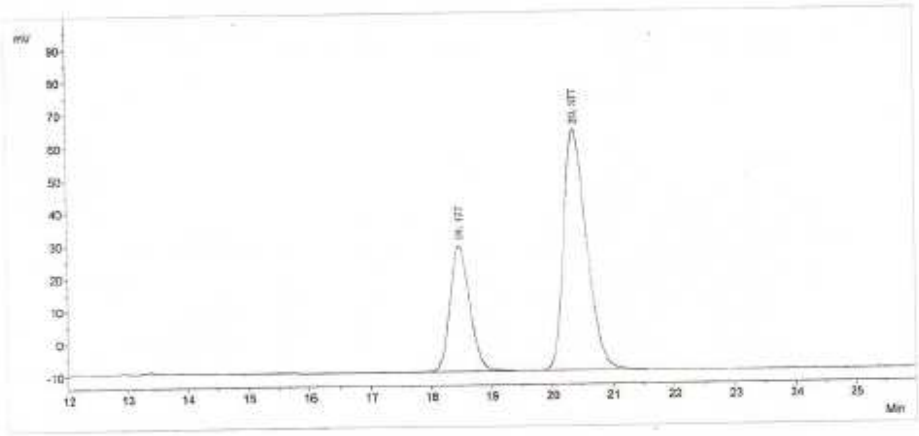


AS-H, hexane/iproH = 95/5, 0.7 mL/min, 230 nm

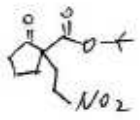
HPLC REPORT

Sample Name:lx-9-45-1.che
Time:20:20
column:
Velocity:

Date:2009-02-07
Method:
the mobile phase:
the detection wavelength:



No.	PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	1	18.477	38416.5	871022.3	31.1810
2	2	20.377	73479.0	1922415.0	68.8190
Total			111895.5	2793438.3	100.0000

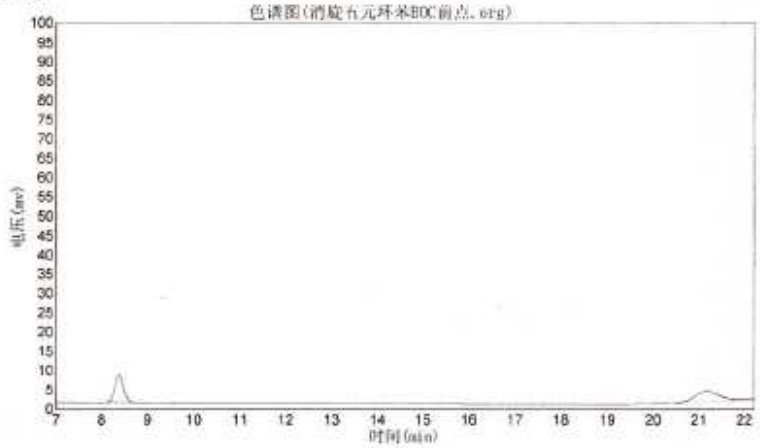


ee = 38%

As-H, hexane/iproH = 95/5, 0.7mL/min, 230nm

积分方法:面积归一法

色谱图(消旋五元环苯BOC前点. erg)

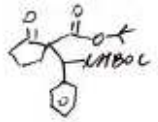


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.383	7145.776	90262.695	50.1470
2		21.165	2551.629	89733.414	49.8530
总计			9697.405	179996.109	100.0000

Racemate

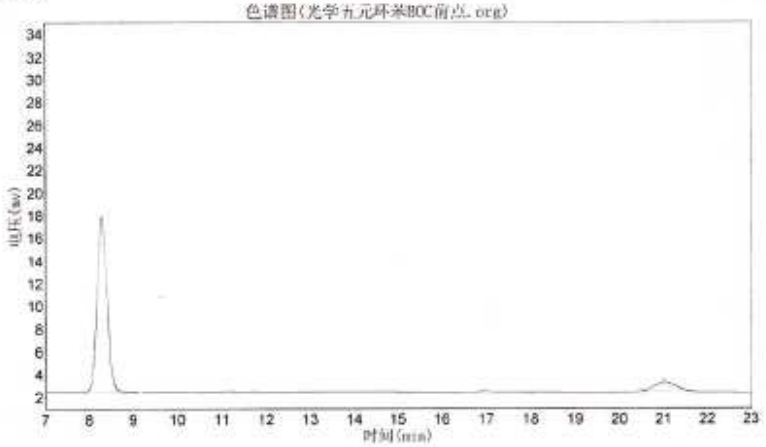
Major diastereomer



AD-H, hexane/iproH = 19/1, 1.0ml L/min, 254nm

积分方法：面积归一法

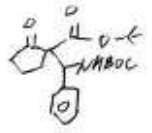
色谱图(光学五元环苯BOC前点.org)



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.290	15265.709	237074.609	89.9196
2		21.012	803.322	26577.133	10.0804
总计			16069.031	263651.742	100.0000

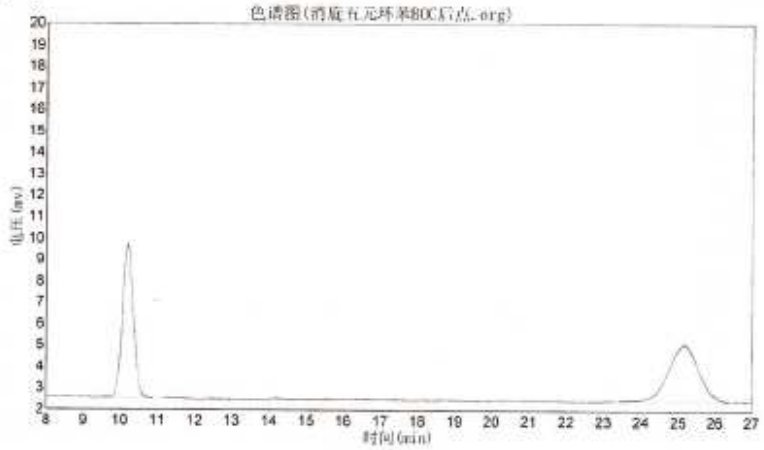
Major diastereomer



ee = 80 %

AD-H, hexane/iproH = 19/1, 1.0 mL/min, 254 nm

积分方法：面积归一法

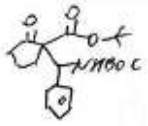


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		10.202	7105.447	147362.766	49.6222
2		25.147	2614.574	149606.703	50.3778
总计			9720.021	296969.469	100.0000

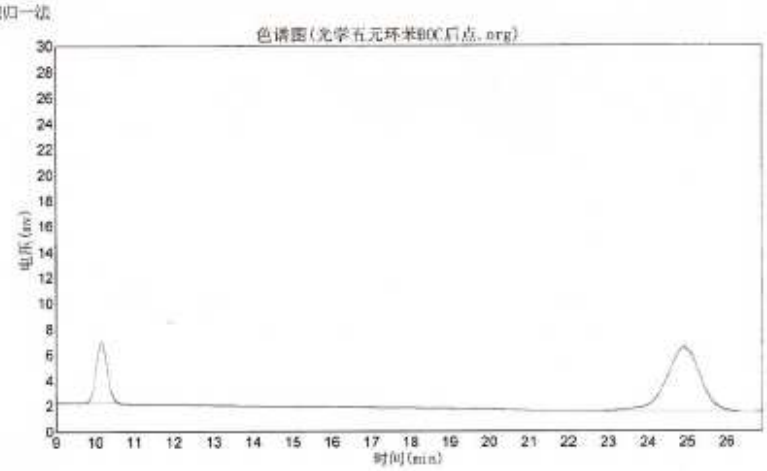
yace mate

Minor diastereomer



AD-H, hexane/iproH = 19/1, 1.0mL/min, 254nm

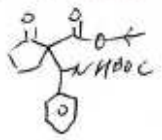
积分方法：面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		10.167	4690.000	93773.508	24.5759
2		24.925	4885.527	287792.656	75.4240
总计			9575.527	381566.164	100.0000

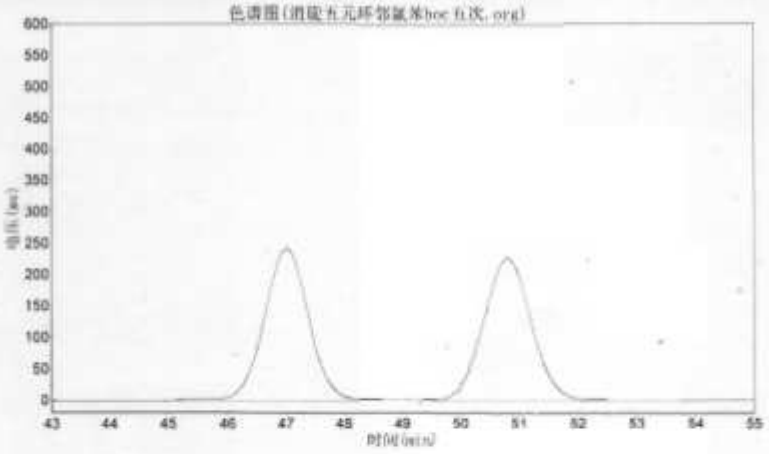
Minor diastereomer



ee = 51 %

AD-H, hexane/iproH = 19/1, 1.0mL/min, 254nm

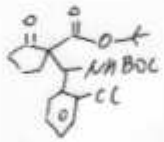
积分方法:面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		47.012	240819.531	12760868.000	50.0701
2		50.803	224914.844	12725121.000	49.9299
总计			465734.375	25485989.000	100.0000

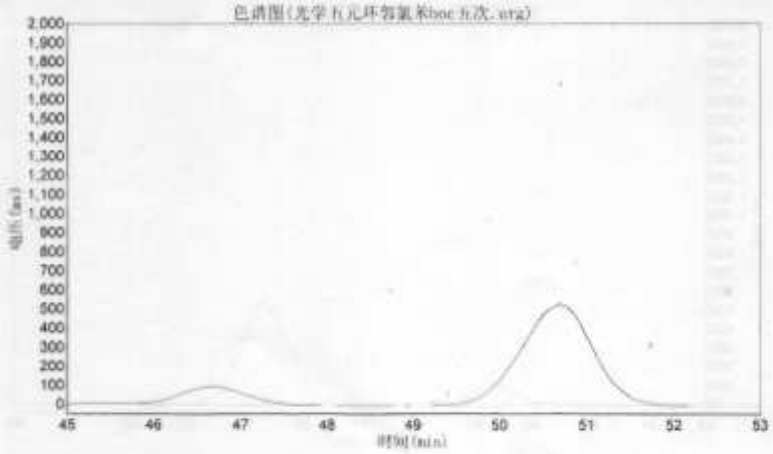
racemate



OD-H, hexane/iprOH = 99/1, 0.7mL/min, 214 nm

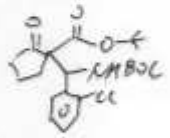
积分方法：面积归一法

色谱图(光学五元环邻氯苯boc五次.org)



分析结果表

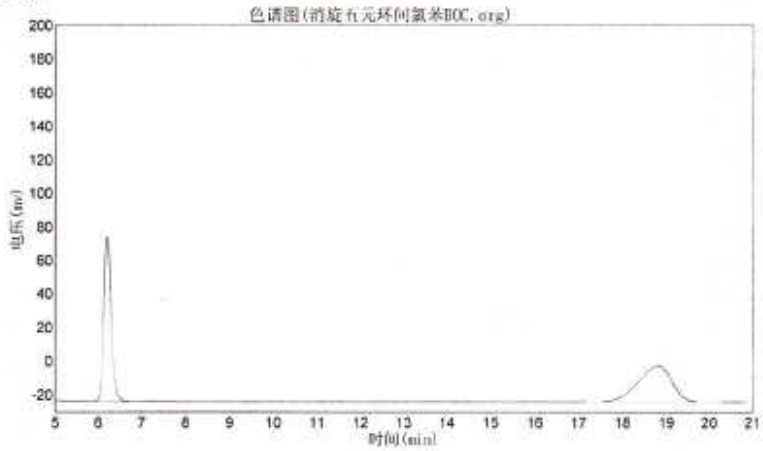
峰号	峰名	保留时间	峰高	峰面积	含量
1		46.673	90810.109	4710964.000	13.3920
2		50.695	527491.875	30466364.000	86.6080
总计			618301.984	35177318.000	100.0000



ee = 73%

OD-H, hexane/iproH = 99/1, 0.7 mL/min, 214nm

积分方法:面积归一法

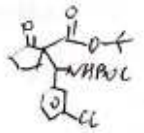


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.215	96729.398	1150628.375	49.9615
2		18.832	21405.744	1152401.625	50.0385
总计			118135.143	2303030.000	100.0000

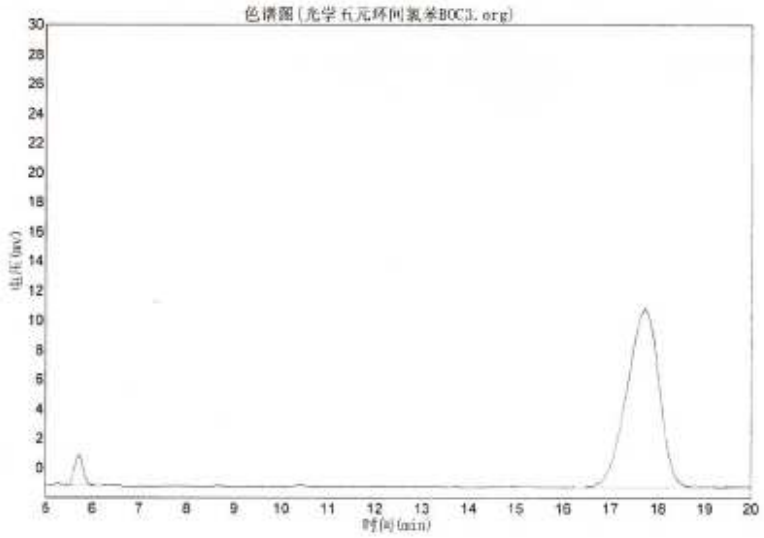
racemate

Major diastereomer



AD-H, hexane/iproH = 90/10, 1.0mL/min, 254nm

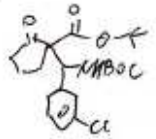
积分方法：面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		5.713	2019.662	26298.678	4.3900
2		17.723	12017.466	572753.563	95.6100
总计			14037.128	599052.240	100.0000

Major diastereomer

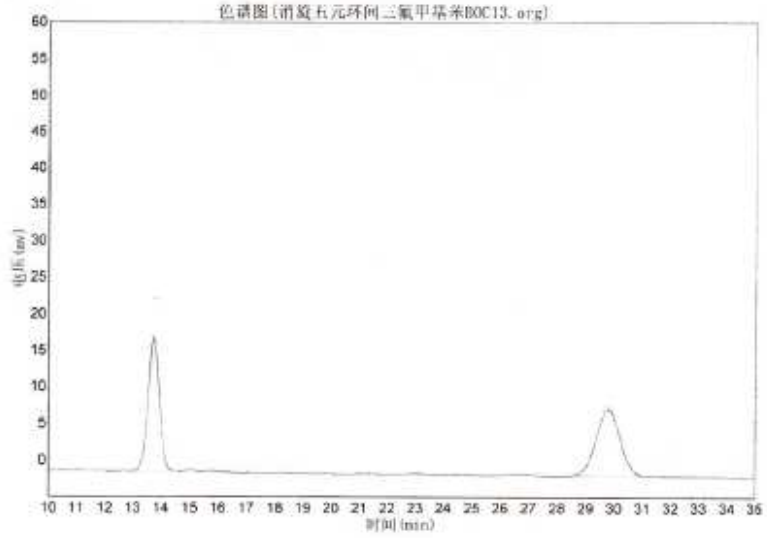


ee = 91%

AD-H, hexane/iproH= 90/10, 1.0 mL/min, 254 nm

积分方法：面积归一法

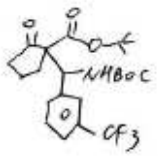
色谱图(消旋五元环例二氟甲基苯BOC13.org)



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		13.742	17978.225	509864.344	49.5255
2		29.802	8946.100	519634.781	50.4745
总计			26924.324	1029499.125	100.0000

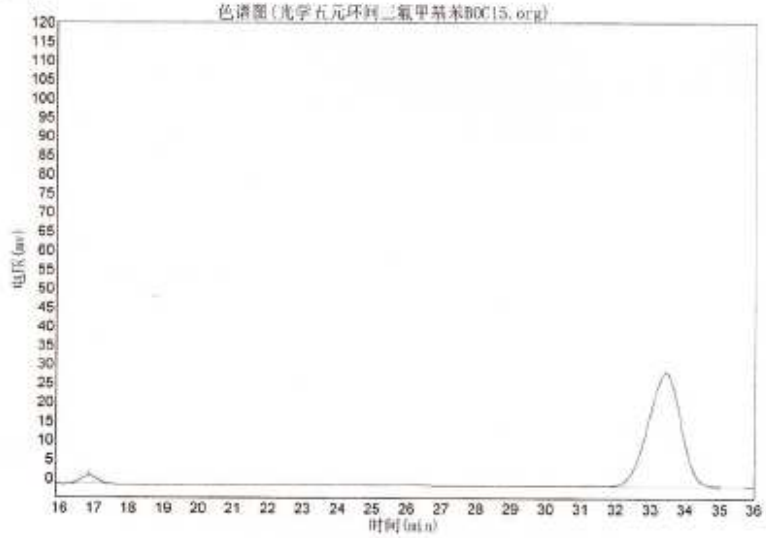
racemate Major diastereomer



AD-H, hexane/iproH = 98/2, 0.7 mL/mM, 230 nM

积分方法：面积归一法

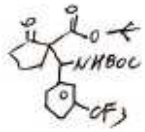
色谱图（光学五元环到二氟甲基苯BOC15.org）



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		16.873	2066.567	62591.188	3.1102
2		33.430	29662.994	1949869.125	96.8898
总计			31729.561	2012460.313	100.0000

major diastereomer

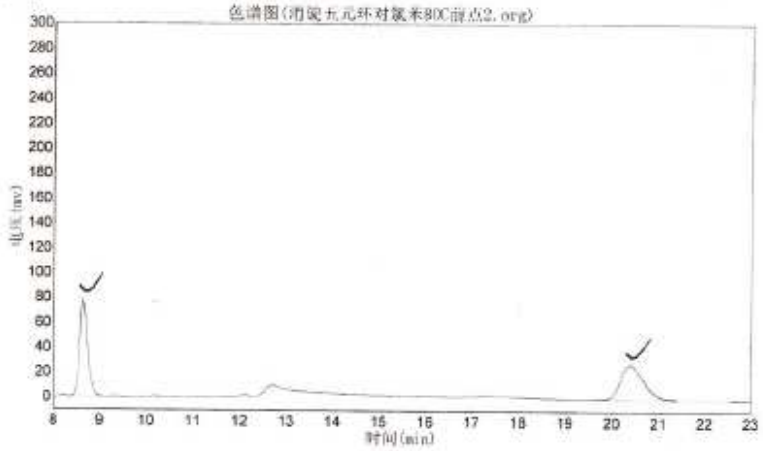


ee= 94%

AD-H, hexane/iproH = 98/2, 0.7mL/mm, 230nm

积分方法:面积归一法

色谱图(消氮五元环对氯苯80C前点2.org)

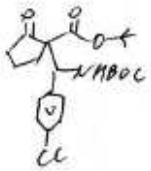


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.635	75927.938	952673.375	49.9626
2		20.388	27783.912	954098.375	50.0374
总计			103711.850	1906771.750	100.0000

Race mate

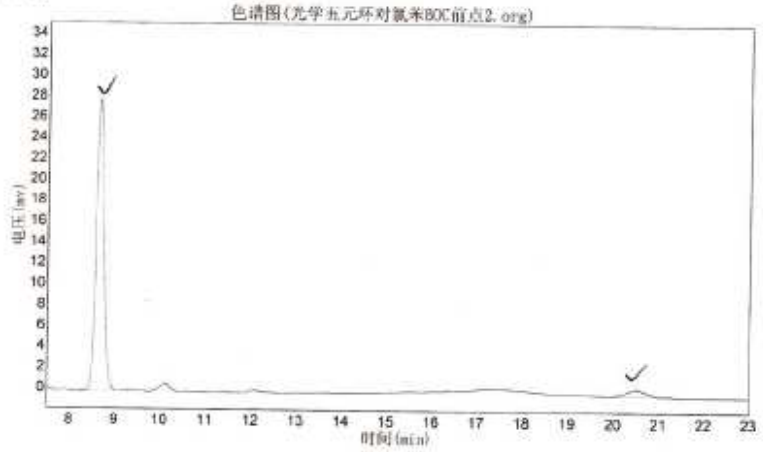
major diastereomer



AD-H, hexane/iprOH = 90/10, 1.0mL/min, 254nM

积分方法：面积归一法

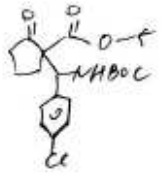
色谱图(光学五元环对氯苯BOC前点2.org)



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.652	27833.912	339997.656	95.1689
2		20.490	616.590	17259.402	4.8311
总计			28450.502	357257.059	100.0000

major diastereomer

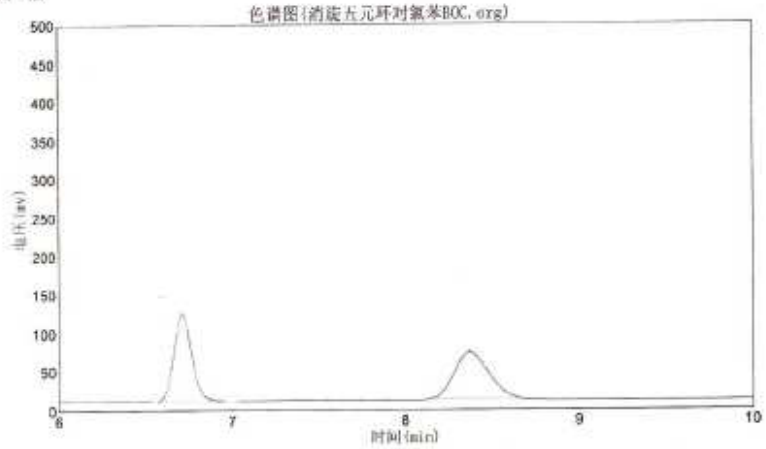


ee = 90%

AD-H, hexane/iproH = 90/10, 1.0mL/min, 254nm

积分方法:面积归一法

色谱图(消旋五元环对氯苯BOC.org)

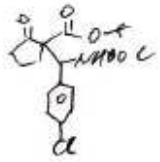


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.715	112284.711	796917.500	49.8911
2		8.372	59069.207	800397.375	50.1089
总计			171353.918	1597314.875	100.0000

racemate

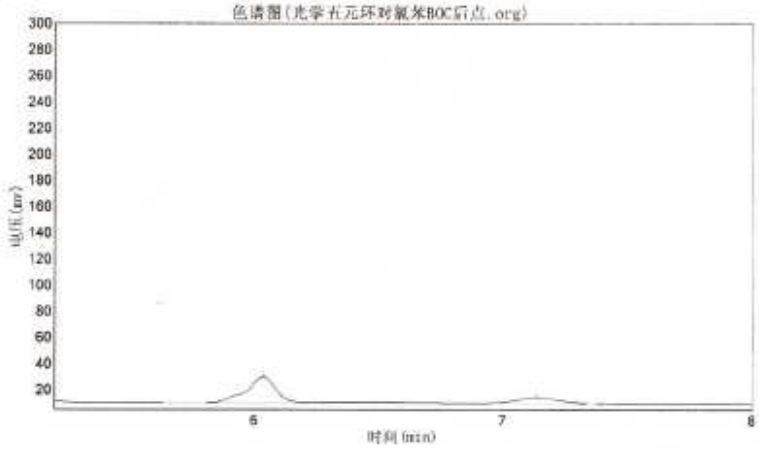
minor diastereomer



AD-H, hexane/iproH = 90/10, 1.0mL/min, 254nm

积分方法:面积归一法

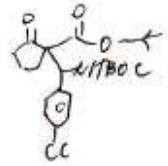
色谱图(光学五元环对氯苯BOC后点.org)



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.038	19926.621	168394.078	78.2081
2		7.137	4247.899	46921.324	21.7919
总计			24174.521	215315.402	100.0000

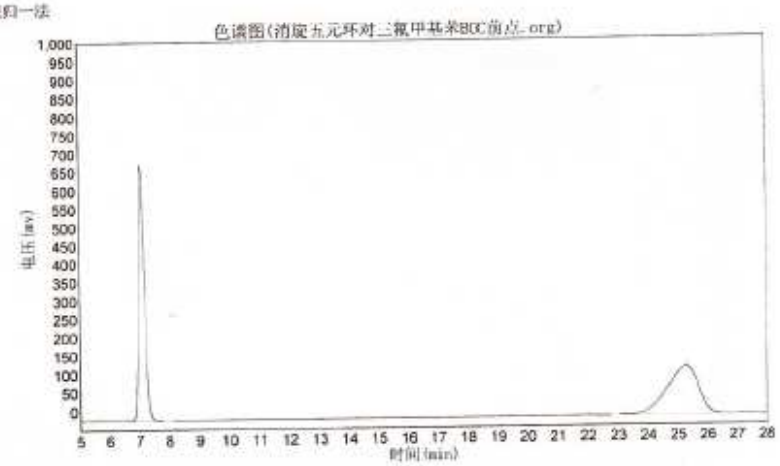
minor diastereomer



ee = 56 %

AD-H, hexane/iprOH= 90/10, 1.0mL/min, 254nm

积分方法:面积归一法

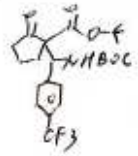


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.090	692410.250	9553631.000	50.1237
2		25.290	129936.672	9506459.000	49.8763
总计			822346.922	19060090.000	100.0000

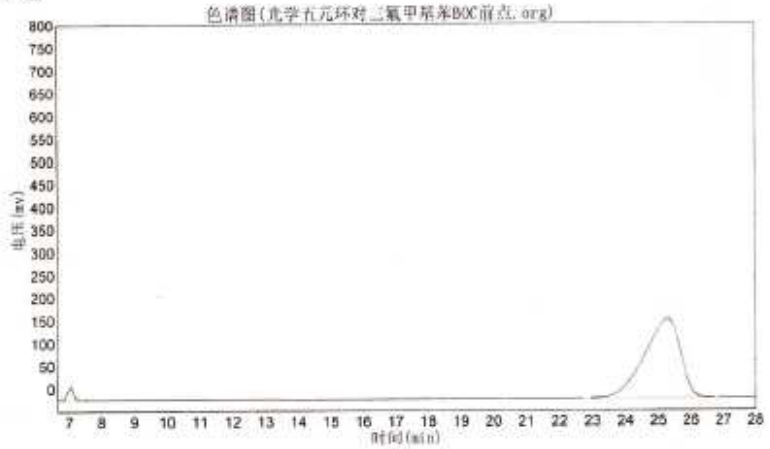
Yate mate

Major diastereomer



AD-H, hexane/ipOH = 90/10, 1.0mL/min, 254nm

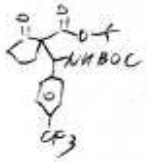
积分方法:面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.042	26893.242	364466.000	2.6753
2		25.297	173445.656	13258704.000	97.3247
总计			200338.898	13623170.000	100.0000

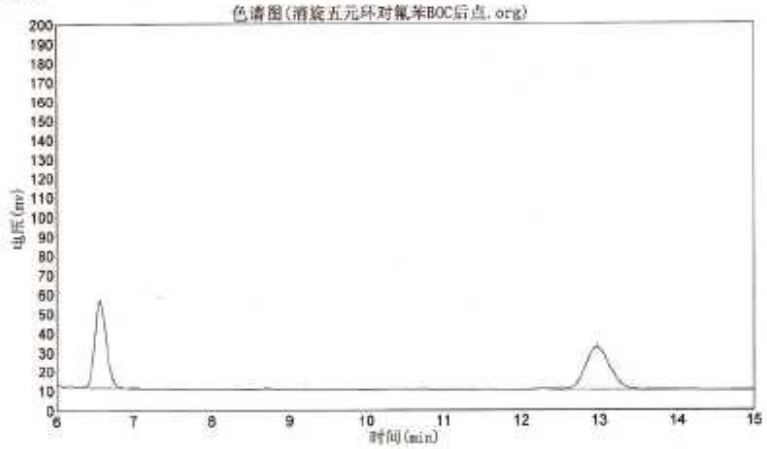
major diastereomer



ee = 95 %

AD-H, hexane/iproH = 90/10, 1.0 mL/mM, 254nm

积分方法:面积归一法

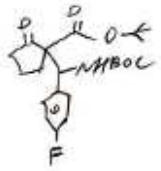


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.565	44655.961	463286.281	49.7047
2		12.967	21683.592	468791.375	50.2953
总计			66339.553	932077.656	100.0000

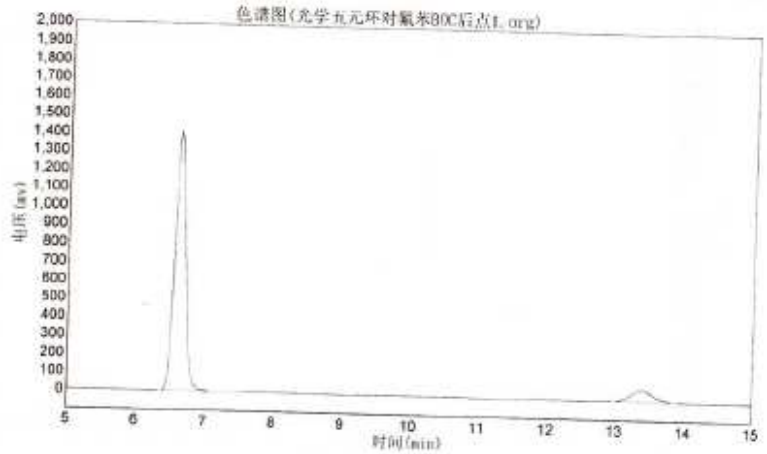
racemate

Major diastereomer



AD-H, hexane/iproH = 90/10, 1.0mL/min, 254nm

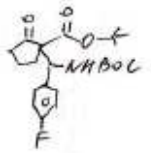
积分方法:面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.615	1394673.750	14989925.000	91.3484
2		13.385	62062.020	1419696.125	8.6516
总计			1456735.770	16409621.125	100.0000

Major diastereomer

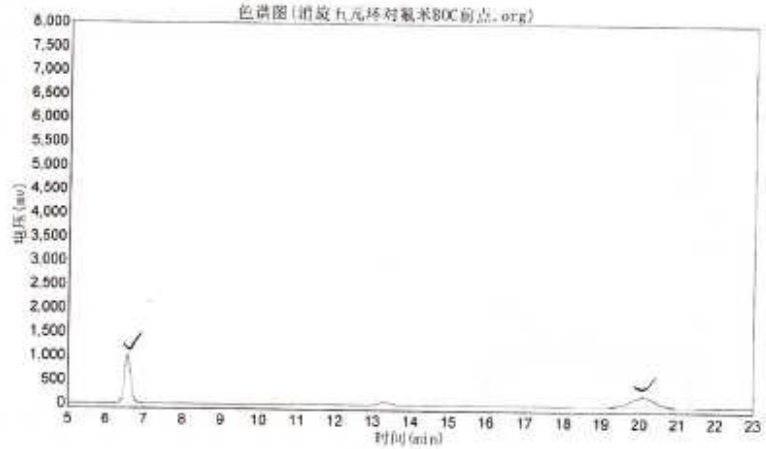


ee = 83 %

AD-H, hexane/iproH = 90/10, 1.0 mL/mM, 254nM

积分方法：面积归一法

色谱图(消旋九元环对氟苯BOC前点.org)

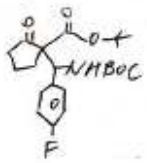


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.568	949185.625	10438009.000	50.7018
2		20.112	207953.656	10149060.000	49.2982
总计			1157139.281	20587069.000	100.0000

Racemate

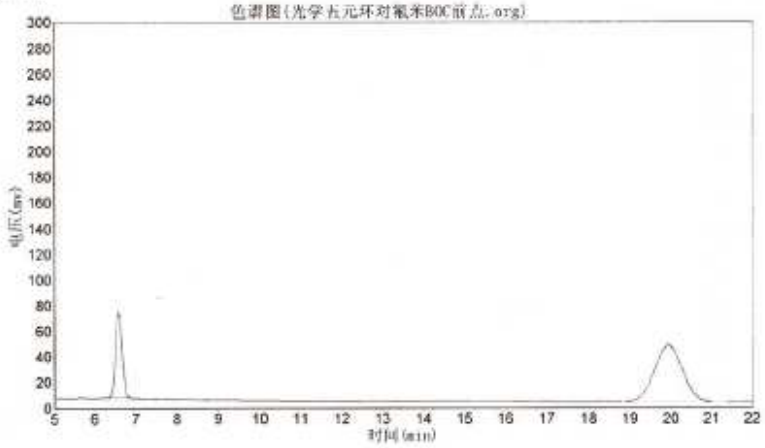
Minor diastereomer



AD-H, hexane/iproH = 90/10, 1.0mL/min, 254nm

积分方法:面积归一法

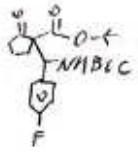
色谱图(光学五元环对氟苯BOC前点.org)



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.578	65912.430	733343.875	26.0323
2		19.943	43779.313	2083714.250	73.9677
总计			109691.742	2817058.125	100.0000

Minor diastereomer

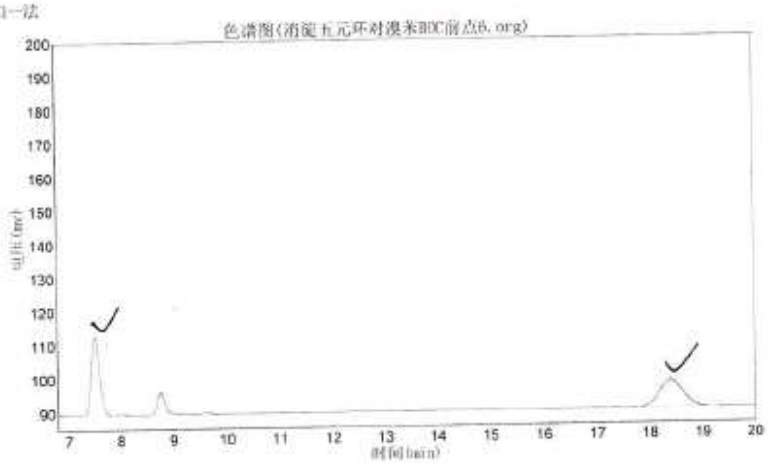


ee= 48%

AD-H, hexane/iproH= 90/10, 1.0 mL/min, 254nm

积分方法:面积归一法

色谱图(消旋五元环对溴苯BOC前点6.org)

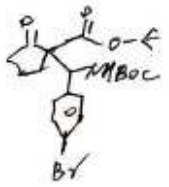


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.517	22899.316	249422.828	50.1396
2		18.388	7890.893	248033.813	49.8604
总计			30790.209	497456.641	100.0000

racemate

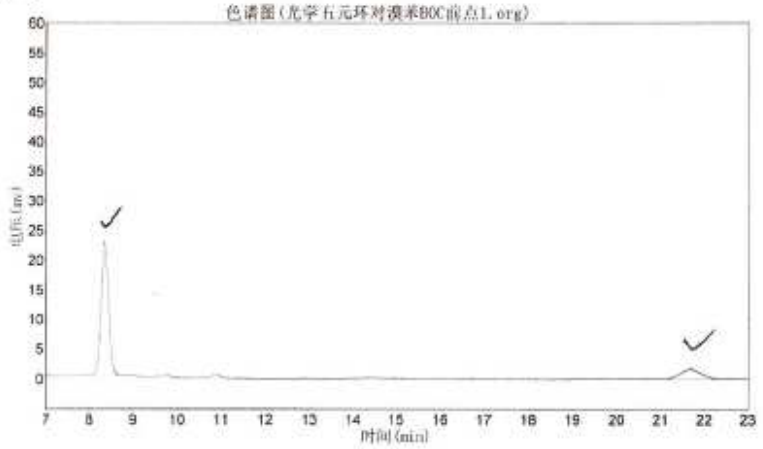
major diastereomer



AD-H, hexane/iproH = 90/10, 1.0mL/min, 254 nm

积分方法：面积归一法

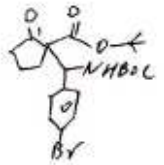
色谱图（光学五元环对溴苯BOC前点1.org）



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.347	22499.354	267536.688	85.1488
2		21.687	1480.005	46662.422	14.8512
总计			23979.358	314199.109	100.0000

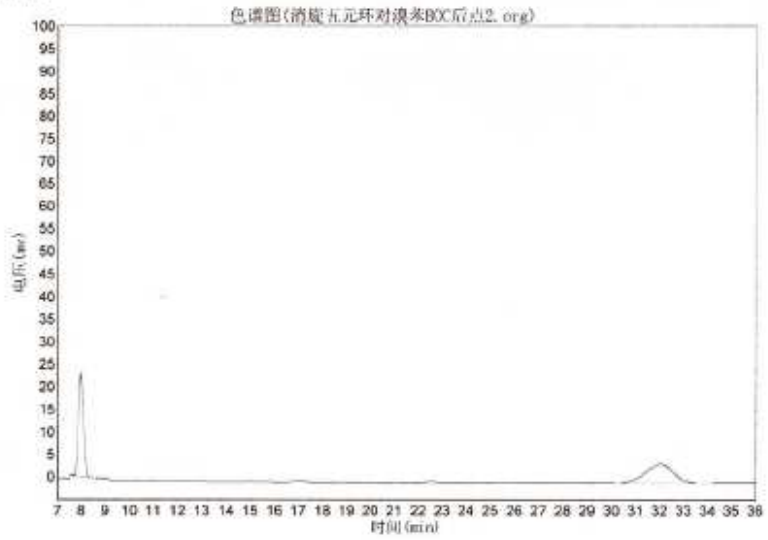
major diastereomer



ee = 70%

AD-H, hexane/iproH = 90/10, 1.0mL/mM, 254nM

积分方法：面积归一法

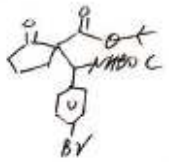


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.972	22643.281	333064.094	49.6289
2		32.037	4151.181	338044.906	50.3711
总计			26794.462	671109.000	100.0000

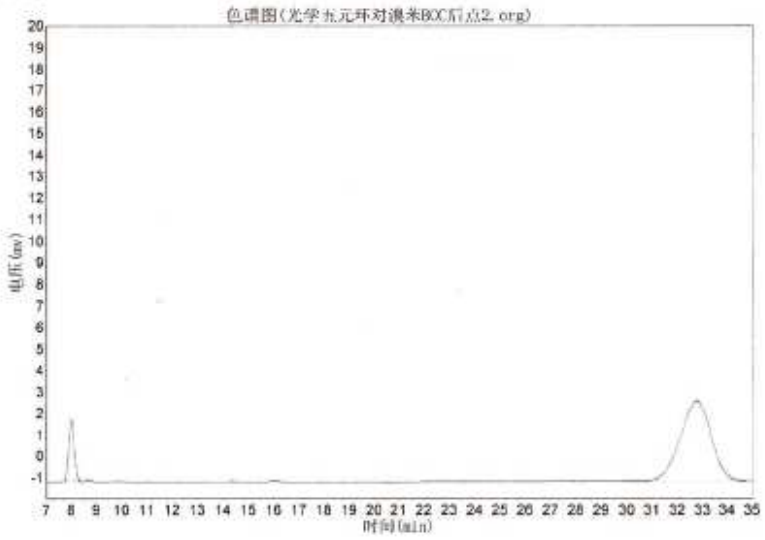
racemate

minor diastereomer



AD-H, hexane/iproH = 90/10, 1.0mL/mm, 254nm

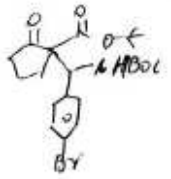
积分方法：面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.020	2792.911	42708.875	11.7858
2		32.802	3699.000	319665.781	88.2142
总计			6491.911	362374.656	100.0000

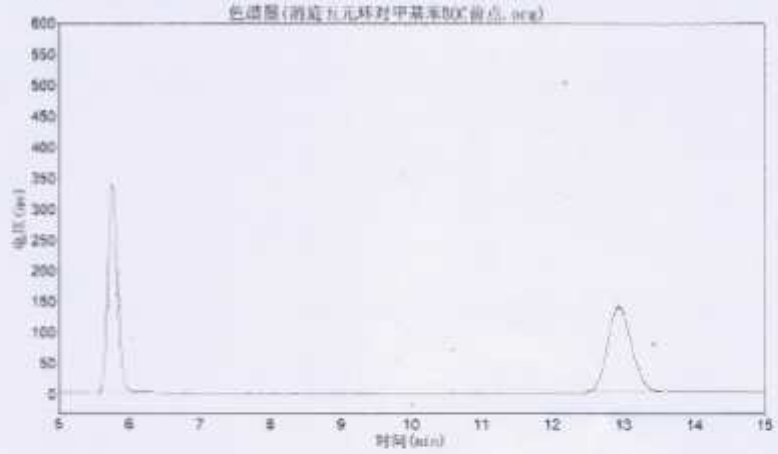
minor diastereomer



ee= 76 %

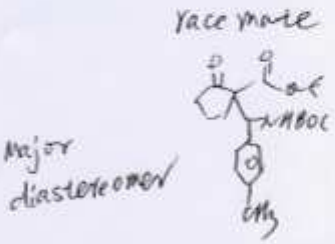
AD-H, hexane/iPrOH=90/10, 1.0mL/min, 254nm

积分方法：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		5.767	333980.750	3145729.000	49.5277
2		12.933	137916.828	3205719.500	50.4723
总计			471906.578	6351448.500	100.0000

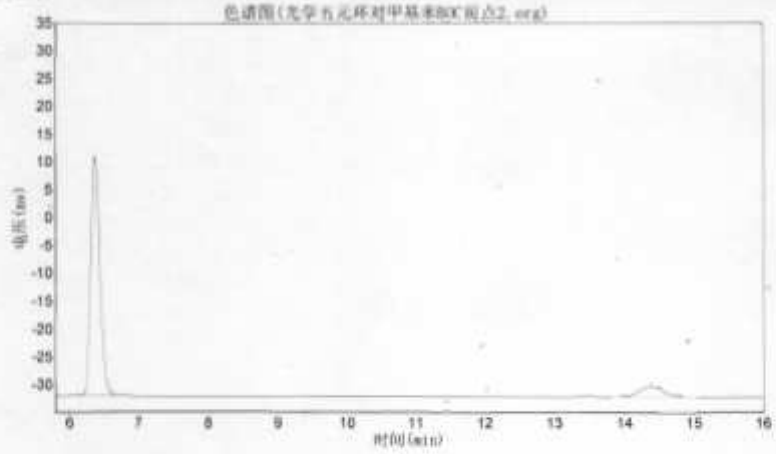


Yace mate

AD-H, hexane/iproH = 90/10, 1.0mL/min, 254nm

积分方法：面积归一法

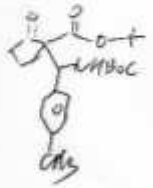
色谱图(光学五元环对甲基苯BOC胺占2.org)



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.377	42538.230	392755.531	89.9501
2		14.383	1852.921	43881.539	10.0499
总计			44391.151	436637.070	100.0000

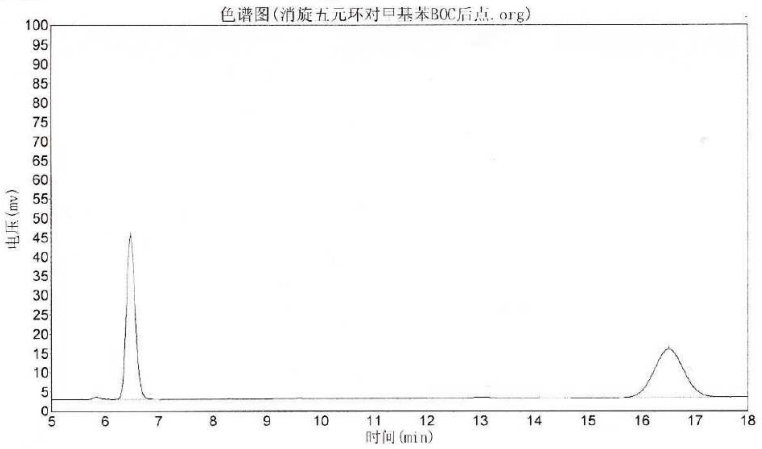
Major diastereomer



ee = 80 %

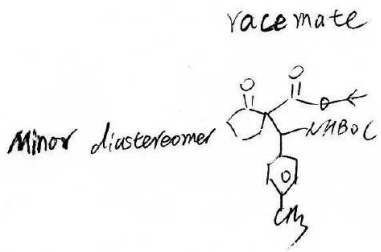
AD-H, hexane/ iproH =90/10, 1.0mL/min, 254nm

积分方法：面积归一法



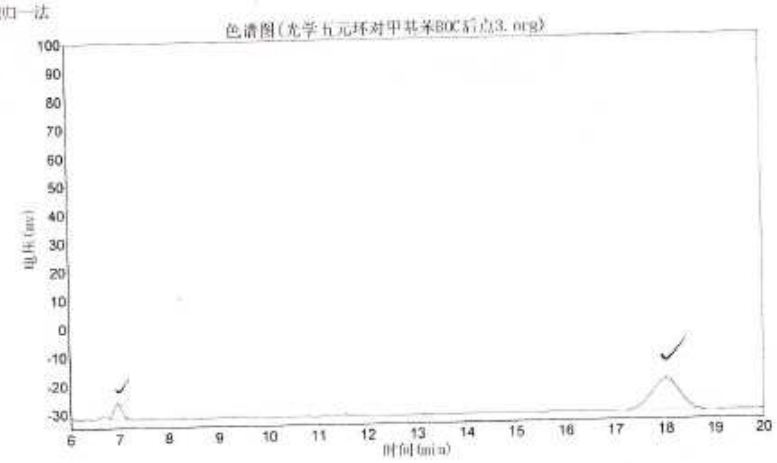
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.477	42404.375	482117.219	50.1058
2		16.503	12398.068	480081.156	49.8942
总计			54802.443	962198.375	100.0000



AD-H, hexane/iproH = 90/10, 1.0mL/min, 254nM

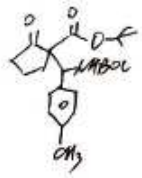
积分方法：面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.958	5407.743	58547.906	11.7069
2		18.025	10952.478	441564.750	88.2931
总计			16360.221	500112.656	100.0000

minor diastereomer

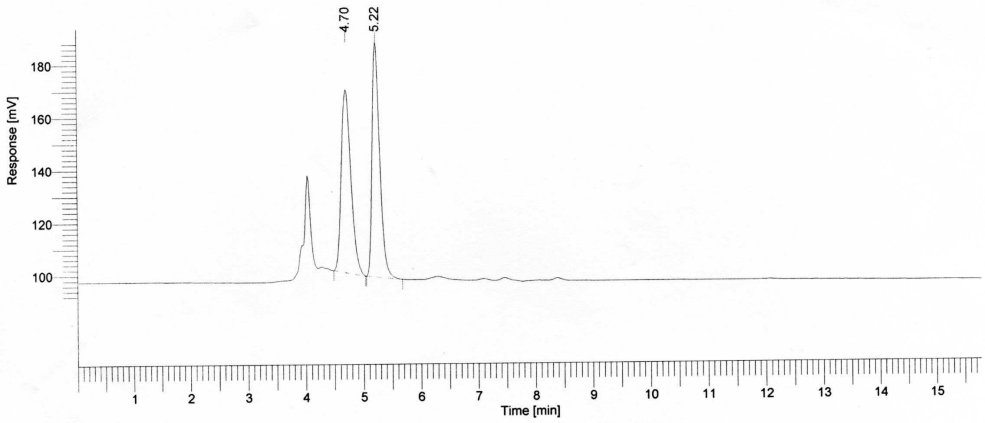


ee = 77%

AD-H, hexane/iproH = 90/10, 1.0 mL/min, 254 nm

Software Version	: 6.3.1.0504	Date	: 2009-11-17 9:05:58
Sample Name	: LZ-11-70-0+-	Data Acquisition Time	: 2009-11-17 8:48:21
Instrument Name	: NCI901	Channel	: A
Rack/Vial	: 0/0	Operator	: manager
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 1		

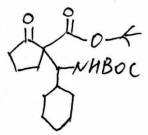
Result File :
Sequence File : D:\2009011017-.seq



HPLC REPORT

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1		4.704	807040.32	69675.26	49.655	BB
2		5.222	818249.32	89321.55	50.345	*BB
			1625289.64	158996.80	1e+02	

racemate

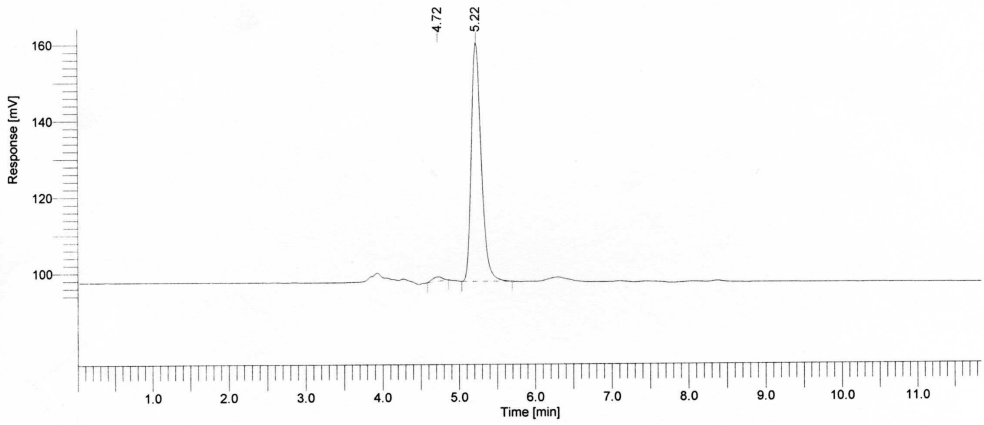


Phenomenex Cellulose-2, hexane/iproH = 80/20, 0.7 mL/mm,

214 nm

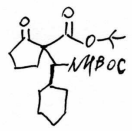
Software Version : 6.3.1.0504		Date	: 2009-11-17 9:32:13
Sample Name : LZ-11-70-1		Data Acquisition Time	: 2009-11-17 9:10:52
Instrument Name : NCI901		Channel	: A
Rack/Vial : 0/0		Operator	: manager
Sample Amount : 1.000000		Dilution Factor	: 1.000000
Cycle : 1			

Result File :
Sequence File : D:\2009011017-.seq



HPLC REPORT

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1		4.723	10526.31	1159.64	1.815	*BB
2		5.222	569532.81	62808.74	98.185	*BB
			580059.12	63968.38	1e+02	

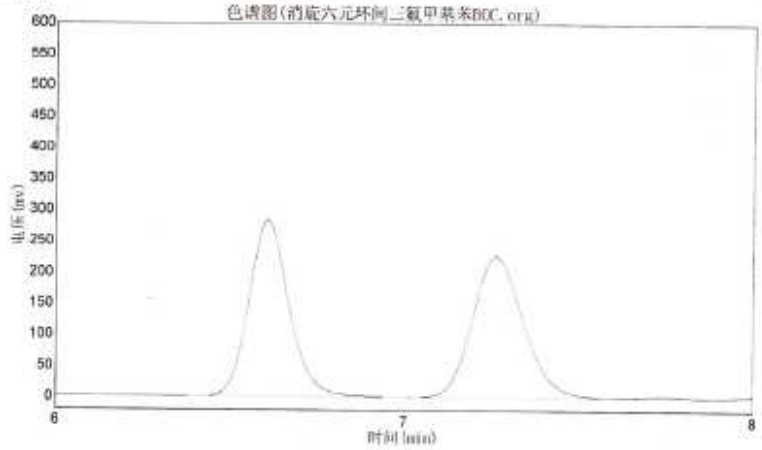


ee = 96%

phenomenex Cellulose-2, hexane/iproH = 80/20,
0.7 mL/min, 214nM

积分方法：面积归一法

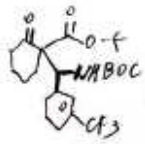
色谱图(消旋六元环酮二氟甲基苯BOC.org)



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.607	282584.125	2280272.000	49.5454
2		7.265	226870.906	2322114.500	50.4546
总计			509455.031	4602386.500	100.0000

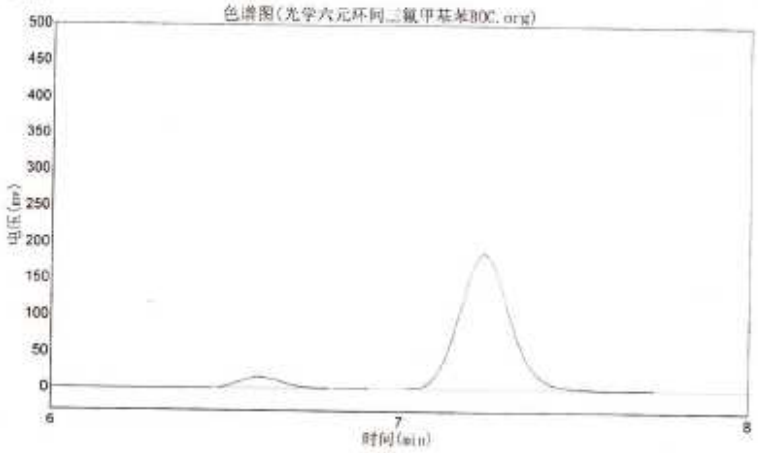
racemate

Major diastereomer 

ee = 0

AD-H, hexane/iPrOH = 90/10, 1.0mL/min, 254nm

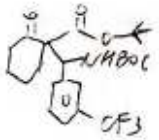
积分方法:面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.598	14550.105	123001.344	6.1048
2		7.242	185632.234	1891839.625	93.8952
总计			200182.340	2014840.969	100.0000

major diastereomer

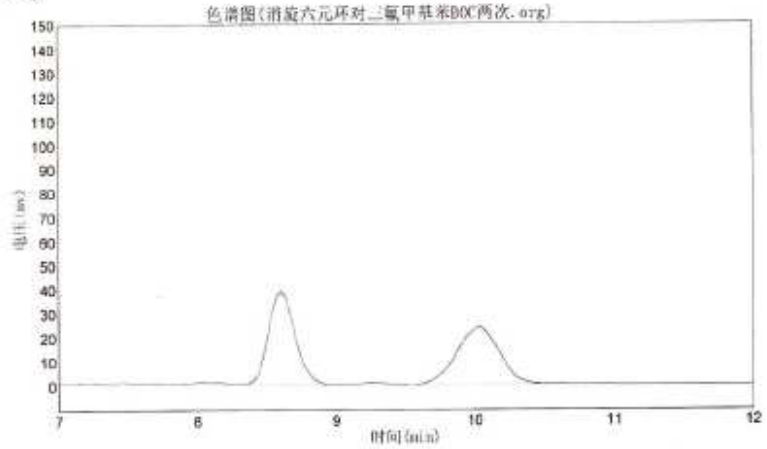


ee = 88%

AD-H, hexane/iproH = 90/10, 1.0mL/min, 254nm

积分方法:面积归一法

色谱图(消旋六元环对三氟甲基苯BOC两次.org)

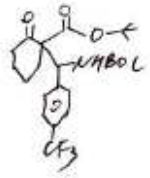


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.602	37778.348	499136.906	50.4273
2		10.033	23279.471	490677.344	49.5727
总计			61057.818	989814.250	100.0000

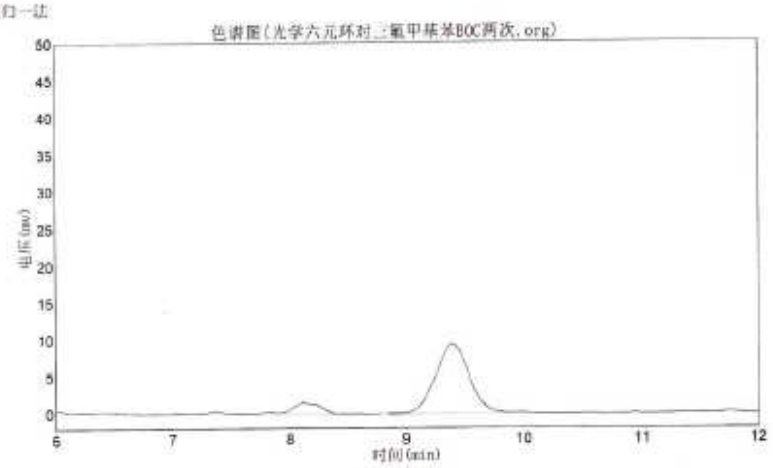
racemate

major diastereomer



AD-H, hexane/iprOH = 90/10, 1.0mL/min, 254nm

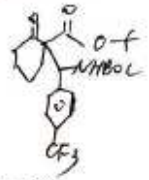
积分方法:面积归一法



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.115	1321.702	20408.037	10.0634
2		9.392	9261.204	182387.141	89.9366
总计			10582.906	202795.178	100.0000

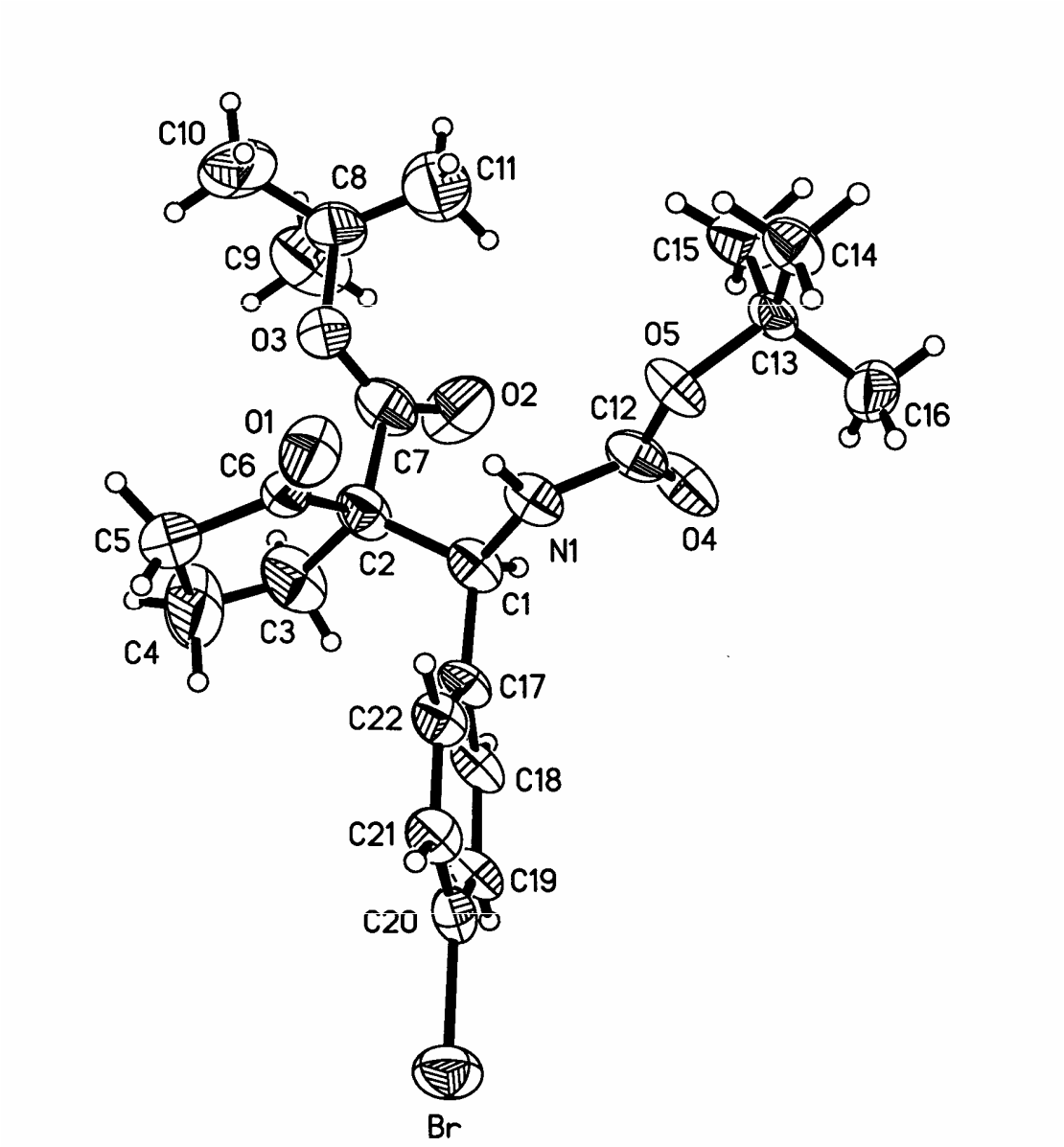
Major diastereomer



ee= 80%

AD-H, hexane/ipoH = 90/10, 1.0mL/min, 254nm

X-ray Crystal Structure of major product of 4h



The crystal data of major product of **4h** have been deposited in CCDC with number 741415. Empirical Formula: $C_{22}H_{30}BrNO_5$; Formula Weight: 468.38; Crystal size: 0.279 x 0.256 x 0.245; Crystal Color, Habit: colorless, prismatic; Crystal System: Monoclinic; Lattice Type: Primitive; Lattice Parameters: a = 9.9053(17)Å, b = 11.2911(18)Å, c = 11.0981(19)Å, $\alpha = 90^o$, $\beta = 109.586(3)^o$, $\gamma = 90^o$, V = 1169.4(3)Å^3; Space group: P2(1); Z = 2; D_{calc} = 1.330 g/cm^3; F_{000} = 488; R1 = 0.0671, wR2 = 0.1623. Diffractometer: Rigaku AFC7R.

Table 1. Crystal data and structure refinement for cd29379.

Identification code	cd29379
Empirical formula	C22 H30 Br N O5
Formula weight	468.38
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 9.9053(17) A alpha = 90 deg. b = 11.2911(18) A beta = 109.586(3) deg. c = 11.0981(19) A gamma = 90 deg.
Volume	1169.4(3) A^3
Z, Calculated density	2, 1.330 Mg/m^3
Absorption coefficient	1.788 mm^-1
F(000)	488
Crystal size	0.279 x 0.256 x 0.245 mm
Theta range for data collection	1.95 to 25.49 deg.
Limiting indices	-11<=h<=11, -13<=k<=7, -13<=l<=11
Reflections collected / unique	6167 / 3660 [R(int) = 0.0575]
Completeness to theta = 25.49	100.0 %
Absorption correction	Empirical
Max. and min. transmission	1.00000 and 0.75495
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3660 / 4 / 272
Goodness-of-fit on F^2	0.842
Final R indices [I>2sigma(I)]	R1 = 0.0671, wR2 = 0.1623
R indices (all data)	R1 = 0.1195, wR2 = 0.1978
Absolute structure parameter	0.03(2)
Largest diff. peak and hole	0.422 and -0.336 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for cd29379.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Br	7334(1)	10623(1)	1522(1)	97(1)
N(1)	3217(9)	5924(6)	2117(7)	66(2)
O(1)	784(8)	6941(9)	237(8)	105(3)
O(2)	1654(9)	6230(10)	4217(9)	133(4)
O(3)	-299(8)	6416(7)	2487(8)	85(2)
O(4)	4544(9)	4902(6)	3901(6)	95(2)
O(5)	3549(8)	3997(5)	1985(6)	73(2)
C(1)	3256(10)	7002(8)	2712(9)	63(2)
C(2)	1722(11)	7466(9)	2520(10)	79(3)
C(3)	1631(17)	8702(10)	3062(13)	112(4)
C(4)	948(19)	9465(12)	1943(16)	132(11)
C(5)	196(14)	8839(12)	772(14)	128(5)
C(6)	869(10)	7632(9)	1070(13)	82(3)
C(7)	957(16)	6604(10)	3160(12)	87(3)
C(8)	-1212(11)	5603(15)	3069(11)	100(3)
C(9)	-1306(17)	6277(13)	4254(14)	146(6)
C(10)	-2648(13)	5767(19)	2022(14)	156(7)
C(11)	-601(16)	4495(15)	3341(18)	156(7)
C(12)	3805(12)	4907(10)	2781(10)	72(3)
C(13)	3834(10)	2786(8)	2490(9)	62(3)
C(14)	3398(11)	2036(8)	1292(9)	75(3)
C(15)	2917(13)	2505(11)	3298(11)	103(4)
C(16)	5414(12)	2688(12)	3278(13)	99(4)
C(17)	4217(10)	7909(8)	2370(8)	58(2)
C(18)	5103(12)	8637(8)	3307(9)	65(3)
C(19)	6046(11)	9410(8)	3119(8)	65(3)
C(20)	6091(10)	9545(8)	1880(9)	68(3)
C(21)	5157(11)	8868(8)	903(9)	67(2)
C(22)	4242(10)	8069(8)	1164(8)	62(2)

Table 3. Bond lengths [A] and angles [deg] for cd29379.

Br-C(20)	1.867(10)
N(1)-C(1)	1.379(11)
N(1)-C(12)	1.384(13)
N(1)-H(1A)	0.83(2)
O(1)-C(6)	1.190(12)
O(2)-C(7)	1.221(13)
O(3)-C(7)	1.235(14)
O(3)-C(8)	1.571(13)
O(4)-C(12)	1.213(10)
O(5)-C(12)	1.323(12)
O(5)-C(13)	1.470(11)
C(1)-C(17)	1.531(13)
C(1)-C(2)	1.552(13)
C(1)-H(1)	0.9800
C(2)-C(3)	1.535(14)
C(2)-C(7)	1.545(14)
C(2)-C(6)	1.558(16)
C(3)-C(4)	1.476(15)
C(3)-H(3A)	0.9700
C(3)-H(3B)	0.9700
C(4)-C(5)	1.448(14)
C(4)-H(4A)	0.9700
C(4)-H(4B)	0.9700
C(5)-C(6)	1.504(16)
C(5)-H(5A)	0.9700
C(5)-H(5B)	0.9700
C(8)-C(11)	1.378(19)
C(8)-C(10)	1.516(15)
C(8)-C(9)	1.549(18)
C(9)-H(9A)	0.9600
C(9)-H(9B)	0.9600
C(9)-H(9C)	0.9600
C(10)-H(10A)	0.9600
C(10)-H(10B)	0.9600
C(10)-H(10C)	0.9600
C(11)-H(11A)	0.9600
C(11)-H(11B)	0.9600
C(11)-H(11C)	0.9600
C(13)-C(15)	1.508(14)
C(13)-C(14)	1.513(13)
C(13)-C(16)	1.520(14)
C(14)-H(14A)	0.9600
C(14)-H(14B)	0.9600
C(14)-H(14C)	0.9600
C(15)-H(15A)	0.9600
C(15)-H(15B)	0.9600
C(15)-H(15C)	0.9600
C(16)-H(16A)	0.9600
C(16)-H(16B)	0.9600
C(16)-H(16C)	0.9600
C(17)-C(22)	1.359(11)
C(17)-C(18)	1.384(13)
C(18)-C(19)	1.345(13)
C(18)-H(18)	0.9300
C(19)-C(20)	1.398(11)
C(19)-H(19)	0.9300
C(20)-C(21)	1.394(13)
C(21)-C(22)	1.377(12)
C(21)-H(21)	0.9300
C(22)-H(22)	0.9300
C(1)-N(1)-C(12)	122.5(8)
C(1)-N(1)-H(1A)	114(8)
C(12)-N(1)-H(1A)	118(8)
C(7)-O(3)-C(8)	117.0(9)
C(12)-O(5)-C(13)	119.9(7)
N(1)-C(1)-C(17)	113.0(7)
N(1)-C(1)-C(2)	111.3(8)

C(17)-C(1)-C(2)	113.7(8)
N(1)-C(1)-H(1)	106.1
C(17)-C(1)-H(1)	106.1
C(2)-C(1)-H(1)	106.1
C(3)-C(2)-C(7)	106.9(8)
C(3)-C(2)-C(1)	115.9(10)
C(7)-C(2)-C(1)	109.4(9)
C(3)-C(2)-C(6)	102.3(9)
C(7)-C(2)-C(6)	111.7(10)
C(1)-C(2)-C(6)	110.5(8)
C(4)-C(3)-C(2)	105.8(10)
C(4)-C(3)-H(3A)	110.6
C(2)-C(3)-H(3A)	110.6
C(4)-C(3)-H(3B)	110.6
C(2)-C(3)-H(3B)	110.6
H(3A)-C(3)-H(3B)	108.7
C(5)-C(4)-C(3)	115.0(12)
C(5)-C(4)-H(4A)	108.5
C(3)-C(4)-H(4A)	108.5
C(5)-C(4)-H(4B)	108.5
C(3)-C(4)-H(4B)	108.5
H(4A)-C(4)-H(4B)	107.5
C(4)-C(5)-C(6)	100.9(11)
C(4)-C(5)-H(5A)	111.6
C(6)-C(5)-H(5A)	111.6
C(4)-C(5)-H(5B)	111.6
C(6)-C(5)-H(5B)	111.6
H(5A)-C(5)-H(5B)	109.4
O(1)-C(6)-C(5)	120.8(12)
O(1)-C(6)-C(2)	126.6(10)
C(5)-C(6)-C(2)	112.5(11)
O(2)-C(7)-O(3)	130.7(11)
O(2)-C(7)-C(2)	117.0(12)
O(3)-C(7)-C(2)	112.4(10)
C(11)-C(8)-C(10)	120.6(16)
C(11)-C(8)-C(9)	114.0(13)
C(10)-C(8)-C(9)	106.4(13)
C(11)-C(8)-O(3)	110.5(10)
C(10)-C(8)-O(3)	97.8(9)
C(9)-C(8)-O(3)	105.5(11)
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(8)-C(10)-H(10A)	109.5
C(8)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(8)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(8)-C(11)-H(11A)	109.5
C(8)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(8)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
O(4)-C(12)-O(5)	126.6(10)
O(4)-C(12)-N(1)	123.5(10)
O(5)-C(12)-N(1)	109.6(8)
O(5)-C(13)-C(15)	110.2(8)
O(5)-C(13)-C(14)	102.9(7)
C(15)-C(13)-C(14)	110.7(8)
O(5)-C(13)-C(16)	108.4(9)
C(15)-C(13)-C(16)	110.7(9)
C(14)-C(13)-C(16)	113.6(8)
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5

H(14B)-C(14)-H(14C)	109.5
C(13)-C(15)-H(15A)	109.5
C(13)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(13)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(13)-C(16)-H(16A)	109.5
C(13)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
C(13)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5
C(22)-C(17)-C(18)	116.5(8)
C(22)-C(17)-C(1)	123.5(8)
C(18)-C(17)-C(1)	120.1(8)
C(19)-C(18)-C(17)	124.5(9)
C(19)-C(18)-H(18)	117.7
C(17)-C(18)-H(18)	117.7
C(18)-C(19)-C(20)	118.4(9)
C(18)-C(19)-H(19)	120.8
C(20)-C(19)-H(19)	120.8
C(21)-C(20)-C(19)	118.3(9)
C(21)-C(20)-Br	120.3(7)
C(19)-C(20)-Br	121.4(8)
C(22)-C(21)-C(20)	120.5(8)
C(22)-C(21)-H(21)	119.7
C(20)-C(21)-H(21)	119.7
C(17)-C(22)-C(21)	121.6(9)
C(17)-C(22)-H(22)	119.2
C(21)-C(22)-H(22)	119.2

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for cd29379. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Br	104(1)	87(1)	121(1)	0(1)	66(1)	-13(1)
N(1)	96(6)	56(6)	49(5)	-2(4)	28(5)	-7(4)
O(1)	88(6)	116(7)	101(6)	-10(5)	19(5)	13(5)
O(2)	99(6)	199(11)	100(6)	55(6)	30(5)	-12(6)
O(3)	72(5)	77(5)	106(5)	11(4)	30(4)	-1(4)
O(4)	168(8)	51(4)	59(4)	2(3)	30(5)	-5(4)
O(5)	124(6)	39(4)	58(4)	1(3)	34(4)	0(4)
C(1)	96(7)	51(6)	52(5)	-11(4)	39(5)	3(5)
C(2)	100(8)	59(6)	99(8)	6(6)	62(7)	9(6)
C(3)	156(12)	71(8)	147(11)	-20(8)	100(10)	22(8)
C(4)	112(14)	71(11)	181(2)	-48(14)	-37(15)	30(9)
C(5)	81(9)	95(10)	188(15)	21(10)	17(9)	-11(8)
C(6)	57(6)	49(7)	136(11)	-5(7)	27(7)	-1(5)
C(7)	122(11)	78(8)	68(7)	18(6)	42(7)	-6(7)
C(8)	92(7)	95(9)	136(9)	33(10)	69(7)	-9(10)
C(9)	202(16)	125(12)	175(13)	-1(10)	150(13)	-7(10)
C(10)	102(10)	176(17)	192(13)	66(16)	54(10)	-45(12)
C(11)	129(13)	130(15)	236(19)	43(14)	95(13)	8(11)
C(12)	108(9)	59(7)	57(7)	9(6)	38(6)	-13(6)
C(13)	77(7)	44(5)	72(6)	20(5)	35(5)	3(5)
C(14)	104(8)	55(6)	79(7)	-5(5)	47(6)	0(5)
C(15)	137(10)	79(8)	113(9)	-12(7)	69(8)	-27(7)
C(16)	71(8)	85(9)	123(10)	-32(8)	6(7)	5(6)
C(17)	85(7)	44(6)	57(6)	5(5)	39(5)	-2(5)
C(18)	109(9)	39(6)	51(6)	4(5)	33(6)	3(6)
C(19)	98(7)	43(5)	55(6)	2(4)	26(5)	0(5)
C(20)	77(7)	57(6)	72(6)	13(5)	26(5)	20(5)
C(21)	85(7)	61(6)	68(6)	0(5)	44(6)	6(5)
C(22)	82(6)	51(6)	66(6)	-12(4)	43(5)	4(5)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for cd29379.

	x	y	z	U(eq)
H(1)	3697	6851	3631	76
H(3A)	1059	8680	3621	134
H(3B)	2579	8994	3544	134
H(4A)	275	9987	2144	143
H(4B)	1680	9957	1797	143
H(5A)	370	9193	41	154
H(5B)	-827	8810	616	154
H(9A)	-2052	5939	4516	219
H(9B)	-1515	7096	4040	219
H(9C)	-408	6214	4939	219
H(10A)	-2599	5458	1232	233
H(10B)	-2881	6594	1924	233
H(10C)	-3374	5351	2248	233
H(11A)	-1134	4027	3748	234
H(11B)	372	4570	3903	234
H(11C)	-616	4116	2563	234
H(14A)	2407	2177	811	113
H(14B)	3533	1214	1522	113
H(14C)	3976	2242	780	113
H(15A)	3232	2968	4067	154
H(15B)	2999	1679	3512	154
H(15C)	1935	2690	2827	154
H(16A)	5980	2823	2738	149
H(16B)	5611	1911	3645	149
H(16C)	5651	3269	3948	149
H(18)	5042	8588	4124	77
H(19)	6653	9845	3796	78
H(21)	5152	8957	68	80
H(22)	3625	7627	498	74
H(1A)	2550(60)	5850(110)	1420(50)	90(40)

Table 6. Torsion angles [deg] for cd29379.

C(12)-N(1)-C(1)-C(17)	112.1(10)
C(12)-N(1)-C(1)-C(2)	-118.5(10)
N(1)-C(1)-C(2)-C(3)	-175.8(9)
C(17)-C(1)-C(2)-C(3)	-46.9(12)
N(1)-C(1)-C(2)-C(7)	63.3(11)
C(17)-C(1)-C(2)-C(7)	-167.8(9)
N(1)-C(1)-C(2)-C(6)	-60.1(10)
C(17)-C(1)-C(2)-C(6)	68.8(10)
C(7)-C(2)-C(3)-C(4)	-124.2(13)
C(1)-C(2)-C(3)-C(4)	113.5(14)
C(6)-C(2)-C(3)-C(4)	-6.7(14)
C(2)-C(3)-C(4)-C(5)	18(2)
C(3)-C(4)-C(5)-C(6)	-20(2)
C(4)-C(5)-C(6)-O(1)	-161.9(13)
C(4)-C(5)-C(6)-C(2)	14.4(15)
C(3)-C(2)-C(6)-O(1)	171.1(11)
C(7)-C(2)-C(6)-O(1)	-74.9(14)
C(1)-C(2)-C(6)-O(1)	47.2(14)
C(3)-C(2)-C(6)-C(5)	-4.9(12)
C(7)-C(2)-C(6)-C(5)	109.1(10)
C(1)-C(2)-C(6)-C(5)	-128.8(9)
C(8)-O(3)-C(7)-O(2)	3(2)
C(8)-O(3)-C(7)-C(2)	-177.0(10)
C(3)-C(2)-C(7)-O(2)	-83.0(14)
C(1)-C(2)-C(7)-O(2)	43.3(13)
C(6)-C(2)-C(7)-O(2)	165.9(10)
C(3)-C(2)-C(7)-O(3)	96.7(12)
C(1)-C(2)-C(7)-O(3)	-137.1(10)
C(6)-C(2)-C(7)-O(3)	-14.4(13)
C(7)-O(3)-C(8)-C(11)	-60.2(17)
C(7)-O(3)-C(8)-C(10)	172.9(12)
C(7)-O(3)-C(8)-C(9)	63.4(14)
C(13)-O(5)-C(12)-O(4)	17.2(16)
C(13)-O(5)-C(12)-N(1)	-169.0(8)
C(1)-N(1)-C(12)-O(4)	-9.2(16)
C(1)-N(1)-C(12)-O(5)	176.7(9)
C(12)-O(5)-C(13)-C(15)	61.5(12)
C(12)-O(5)-C(13)-C(14)	179.6(9)
C(12)-O(5)-C(13)-C(16)	-59.7(11)
N(1)-C(1)-C(17)-C(22)	42.7(13)
C(2)-C(1)-C(17)-C(22)	-85.4(11)
N(1)-C(1)-C(17)-C(18)	-138.5(9)
C(2)-C(1)-C(17)-C(18)	93.3(11)
C(22)-C(17)-C(18)-C(19)	-5.3(15)
C(1)-C(17)-C(18)-C(19)	175.9(9)
C(17)-C(18)-C(19)-C(20)	3.7(15)
C(18)-C(19)-C(20)-C(21)	-0.1(13)
C(18)-C(19)-C(20)-Br	178.6(7)
C(19)-C(20)-C(21)-C(22)	-1.5(13)
Br-C(20)-C(21)-C(22)	179.7(7)
C(18)-C(17)-C(22)-C(21)	3.4(13)
C(1)-C(17)-C(22)-C(21)	-177.9(9)
C(20)-C(21)-C(22)-C(17)	-0.2(13)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for cd29379 [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(18)-H(18)...O(4)#1	0.93	2.56	3.322(12)	139.0
N(1)-H(1A)...O(1)	0.83(2)	2.18(8)	2.847(12)	137(10)

Symmetry transformations used to generate equivalent atoms:
#1 -x+1,y+1/2,-z+1