Supporting Information

Stereoselective and Regioselective Intramolecular Friedel-Crafts Reaction of Aziridinium Ions for Synthesis of 4-Substituted Tetrahydroisoquinolines

Hyun-Soon Chong* and Yunwei Chen

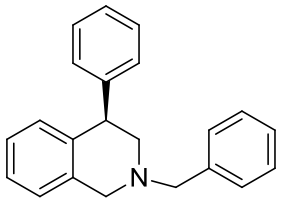
Chemistry Division, Department of Biological and Chemical Sciences,
Illinois Institute of Technology, Chicago, IL.

Table of Contents

General Information: ^{1}H and ^{13}C NMR spectra were obtained using a Bruker 300 instrument and chemical shifts are reported in ppm on the δ scale relative to TMS or solvent. Electrospray iodization (ESI) high resolution mass spectra (HRMS) were obtained on JEOL double sector JMS-AX505HA mass spectrometer (University of Notre Dame, IN). Analytical chiral HPLC was performed on an Agilent 1200 (Agilent, Santa Clara, CA) equipped with a diode array detector and a chiralpak column (4.6 x 150 mm, 80Å). Optical rotation was determined using JASCO P-2000 polarimeter. All reagents were purchased from Sigma-Aldrich (St. Louis, MO) and used as received unless otherwise noted. All solvents for chromatography were purchased from VWR (Radnor, PA).

General procedure for Friedel-Crafts reaction: To the suspension of $AlCl_3$ (2.2 equiv) in toluene (1 mL), secondary β-amino halide **1**, **2**, or **3** (1 equiv) in toluene (2 mL) was added dropwise over 10 to 20 min at 0 ^{o}C. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2h while monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature and quenched by H_2O (10 mL). The reaction mixture was extracted with ethyl acetate (2 × 10 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (60-230 mesh) with 1%-1.5% ethyl acetate in hexanes to afford the desired product **5**. Enatiomeric excess of **5** (50 µL, 1 mg of sample in 10 mL of hexanes) was determined by chiral HPLC (Chiralpak® AD-H, isocratic, 230 nm, 22 ^{o}C) using the following chromatographic conditions: method A (3/97 = *i*-PrOH/Hexanes at a flow rate of 1 mL/min); method B (1/99 = *i*-PrOH/Hexanes at a flow rate of 1 mL/min); method C (1/99 = *i*-PrOH/Hexanes at a flow rate of 0.5 mL/min); method D (0.4/99.6 = *i*-PrOH/Hexanes at a flow rate of 1 mL/min).

Table 1. Synthesis of THIQ analogues (R)-5a and (R)-5b



(R)-5a

(Table 1, entry 1)

(4R)-2-Benzyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline((R)-5a). To the suspension of $AlCl_3$ (38.6 mg, 0.29 mmol) in toluene (1 mL), **(R)-1a** (50 mg, 0.13 mmol) in toluene (2 mL) was added dropwise over 15 min at 0 ^oC. The reaction was complete after addition of **(R)-1a.** After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure **(R)-5a** (31.5 mg, 81.0%). ^1H NMR ($CDCl_3$, 300 MHz) δ 2.70 (dd, J = 11.4, 7.8 Hz, 1H), 3.10 (dd, J = 11.7, 5.4 Hz, 1H), 3.70 (s, 2H), 3.77 (dd, J = 18.3, 15.3 Hz, 2H), 4.28 (dd, J = 6.6, 6.6 Hz, 1H), 6.92 (d, J = 6 Hz, 1H), 7.07-7.33 (m, 14H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 45.9 (d), 56.5 (t), 59.3 (t), 62.6 (t), 126.0 (d), 126.3 (d), 126.4 (d), 127.1 (d), 128.2 (d), 128.3 (d), 128.9 (d), 129.2 (d), 129.6 (d), 135.4 (s), 137.6 (s), 138.3 (s), 145.0 (s). $[\alpha]^{26}_D$ = – 29.5° (c = 2.3, $CHCl_3$). HRMS (ESI) Calcd for $C_{22}H_{22}N$ $[M + H]^+$ *m/z* 300.1747. Found: $[M + H]^+$ *m/z* 300.1738. HPLC (method A), t_R = 3.0 min (R, major) and 2.3 min (S, minor), 71% ee.

(Table 1, entry 2)

To the suspension of $AlCl_3$ (23.2mg, 0.17mmol) in toluene (1 mL), **(R)-1a** (30 mg, 0.079 mmol) in toluene (2 mL) was added dropwise over 10 min at – 70 ^oC. The reaction mixture was kept at -70 ^oC for 30 min. Then the reaction mixture was slowly warmed to

– 20 ^{o}C over 15 min. The reaction was kept at –20 ^{o}C for 15 min. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure **(R)-5a** (11.7 mg, 49.5%).

$[\alpha]^{26}_{D}$ = – 40.5° (*c* = 0.59, $CHCl_3$). HPLC (method A), 79% ee.

(Table 1, entry 3)

To the suspension of $AlCl_3$ (19.5mg, 0.15 mmol) in toluene (1 mL), **(R)-1a** (25.2 mg, 0.066 mmol) in toluene (2 mL) was added dropwise over 10 min at – 20 ^{o}C. The reaction mixture was kept at -20 ^{o}C for 15 min. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure **(R)-5a** (10.8 mg, 54.7%).

$[\alpha]^{26}_{D}$ = – 38.8° (*c* = 0.54, $CHCl_3$). HPLC (method A), 70% ee.

(Table 1, entry 4)

To the suspension of $AlCl_3$ (43.7 mg, 0.33 mmol) in toluene (1 mL), **(R)-2a** (50 mg, 0.15 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^{o}C. The reaction was complete after addition of **(R)-2a**. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure **(R)-5a** (33.6 mg, 75%).

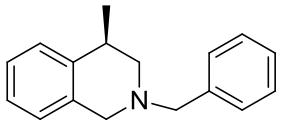
$[\alpha]^{26}_{D}$ = – 30.2° (*c* = 1.03, $CHCl_3$). HPLC (method A), 63% ee.

(Table 1, entry 5)

To the suspension of $AlCl_3$ (34.4 mg, 0.26 mmol) in toluene (1 mL), **(R)-3a** (50 mg, 0.12 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^{o}C. The reaction was complete after addition of **(R)-3a.** After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford

pure **(R)-5a** (25.9 mg, 72%). $[\alpha]^{26}_{D} = -31.1°$ (*c* = 1.3, $CHCl_3$).

HPLC (method A), 61% ee.

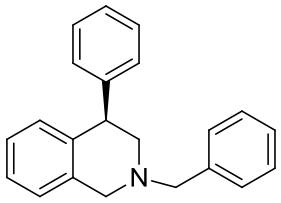


(R)-5b

(Table 1, entry 7)

(4R)-2-benzyl-4-methyl-1,2,3,4-tetrahydroisoquinoline ((R)-5b). To the suspension of $AlCl_3$ (35.2 mg, 0.264 mmol) in toluene (1 mL), **(R)-1b** (38.2 mg, 0.12 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^{o}C. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60–230 mesh) with 1% ethyl acetate in hexanes to afford desired (R)-**5b** (25.5 mg, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.33 (d, *J* = 6.9 Hz, 3H), 2.45 (dd, *J* = 11.4, 6.3 Hz, 1H), 2.82 (dd, *J* = 11.1, 4.8 Hz, 1H), 3.02-3.09 (m, 1H), 3.59-3.75 (m, 4H), 7.01 (d, *J* = 7.5 Hz, 1H), 7.10-7.32 (m, 4H), 7.36 (dd, *J* = 6.9, 6.9 Hz, 2H), 7.44 (d, *J* = 6.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 21.0 (q), 33.2 (d), 56.9 (t), 58.1 (t), 62.9 (t), 125.6 (d), 126.3 (d), 126.5 (d), 127.1 (d), 127.7 (d), 128.3 (d), 129.0 (d), 134.7 (s), 138.7 (s), 139,9 (s). $[\alpha]^{26}_{D}$ = + 24.5^{o} (*c* = 1.3, $CHCl_3$). HRMS (ESI) Calcd for $C_{17}H_{20}N$ $[M + H]^+$ *m/z* 238.1590. Found: $[M + H]^+$ *m/z* 238.1601. HPLC (method A), t_R = 2.3 min (S, minor) and 3.1 min (R, major), 97.0% ee.

Effect of Catalyst on the formation of (R)-5a and (S)-5b (Table 2)



(R)-5a

(Table 2, entry 1)

See the result described above (Table 1, entry 1)

(Table 2, entry 2)

To the suspension of $FeBr_3$ (85.6 mg, 0.29 mmol) in toluene (1 mL), **(R)-1a** (50 mg, 0.13 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The reaction was complete after addition of **(R)-1a**. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford **(R)-5a** (23 mg, 59.2%). $[\alpha]^{26}_D = -32.1°$ (*c* = 1.4, $CHCl_3$). HPLC (method A), 83% ee.

(Table 2, entry 3)

To the suspension of $InCl_3$ (63.3 mg, 0.29 mmol) in toluene (1 mL), **(R)-1a** (50 mg, 0.13 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The reaction was stirred at room temperature for 20 h and quenched by H_2O (10 mL). After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure product **(R)-5a** (30.2 mg, 77.7%).

$[\alpha]^{26}_D = -40.1^o$ (*c* = 1.0, $CHCl_3$). HPLC (method A), 77.0% ee.

(Table 2, entry 4)

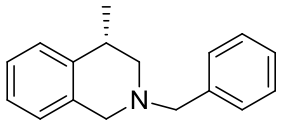
To the solution of $TiCl_4$ (290 μL, 0.29 mmol, 1M solution in toluene) in toluene (1 mL), **(R)-1a** (50 mg, 0.13 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC.

The reaction was stirred at room temperature for 15 h and quenched by H_2O (10 mL). After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure product **(R)-5a** (28 mg, 72%). $[\alpha]^{26}_D = -42.5^o$ (*c* = 0.7, $CHCl_3$). HPLC (method A), 81% ee.

(Table 2, entry 5)

To the suspension of $SnCl_4$ (75.5 mg, 0.29 mmol) in toluene (1 mL), **(R)-1a** (50 mg, 0.13 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The reaction mixture was slowly warmed to room temperature. The reaction was complete after 2.5 h stirring at room temperature and quenched by H_2O (10 mL). After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure product **(R)-5a** (11.2 mg, 29%).

$[\alpha]^{26}_D = -51.4°$ (*c* = 0.8, $CHCl_3$). HPLC (method A), 81% ee.

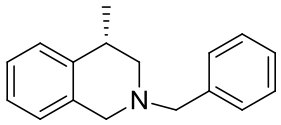


(S)-5b

(Table 2, entry 6)

(4S)-2-Benzyl-4-methyl-1,2,3,4-tetrahydroisoquinoline ((S)-5b). To the suspension of $AlCl_3$ (46.9 mg, 0.35 mmol) in toluene (1 mL), secondary β-amino bromide **(S)-1b** (50 mg, 0.16 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1% ethyl acetate in hexanes to afford desired **(S)-5b** (35.2 mg, 93%). ^1H and ^{13}C NMR data are identical to **(R)-5b**.

$[\alpha]^{26}_{D} = -15.8°$ (c = 1.26, $CHCl_3$). HPLC (method A), t_R = 2.2 min (S, major) and 2.7 min (R, minor), 96.9% ee.



(S)-5b

(Table 2, entry 7)

To the suspension of $FeBr_3$ (103 mg, 0.35 mmol) in toluene (1 mL) and molecular sieves (4 beads), **(S)-1b** (50 mg, 0.16 mmol) in toluene (2 mL) was added dropwise over 5 min at 0 ^{o}C. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux overnight. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.0% ethyl acetate in hexanes to afford **(S)-5b** (9.6 mg, 25.3%).

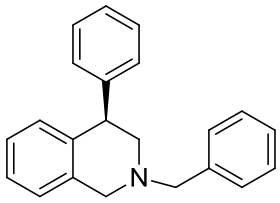
$[\alpha]^{26}_{D} = -13.8^{o}$ (c = 0.3, $CHCl_3$). HPLC (method A), 85% ee.

(Table 2, entry 8)

To the suspension of $InCl_3$ (77.4 mg, 0.35 mmol) in toluene (1 mL) and molecular sieves (4 beads), **(S)-1b** (50 mg, 0.16 mmol) in toluene (2 mL) was added dropwise over 15 min at 0 ^{o}C. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 4 days. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.0% ethyl acetate in hexanes and then was purified by prep-TLC with 5% ethyl acetate in hexanes to afford pure product **(S)-5b** (8.5 mg, 22.4%).

$[\alpha]^{26}_{D} = -15.3^{o}$ (c = 0.6, $CHCl_3$). HPLC (method A), 97% ee.

Effect of solvents on the formation of THIQ analogues (R)-5a and (S)-5b (Table 3)



(R)-5a

(Table 3, entry 1)

See the result described above (Table 1, entry 1)

(Table 3, entry 2)

To the suspension of $AlCl_3$ (38 mg, 0.29 mmol) in benzene (1 mL), **(R)-1a** (50 mg, 0.13 mmol) in benzene (2 mL) was added dropwise over 10 min at 0 ^oC. The reaction was complete after addition of **(R)-1a**. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure product **(R)-5a** (31.6 mg, 81.3%).

$[\alpha]^{26}_D = -26.5^o$ (*c* = 1.3, $CHCl_3$). HPLC (method A), 58.9% ee.

(Table 3, entry 3)

To the suspension of $AlCl_3$ (38.6 mg, 0.29 mmol) in *p*-xylene (1 mL), **(R)-1a** (50 mg, 0.13 mmol) in *p*-xylene (2 mL) was added dropwise over 10 min at 0 ^oC and then warmed to room temperature The reaction was complete after warming up to room temperature (~10 min). After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure product **(R)-5a** (26.8 mg, 70%). $[\alpha]^{26}_D = -39.0^o$ (*c* = 1.1, $CHCl_3$). HPLC (method A), 69% ee.

(Table 3, entry 4)

To the suspension of $AlCl_3$ (38.6 mg, 0.29 mmol) in 1,2-dichloroethane (1 mL), **(R)-1a** (50 mg, 0.13 mmol) in 1,2-dichloroethane (2 mL) was added dropwise over 15 min at 0 ^oC. The reaction was complete after addition of **(R)-1a.** After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure product **(R)-5a** (37 mg, 95.2%).

$[\alpha]^{26}_D = -34.6°$ (*c* = 1.1, $CHCl_3$). HPLC (method A), 77.9% ee.

(Table 3, entry 5)

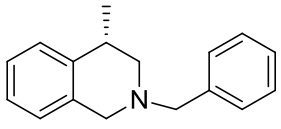
To the suspension of $AlCl_3$ (23 mg, 0.17 mmol) in CH_2Cl_2 (1 mL), **(R)-1a** (30 mg, 0.079 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 10 min at 0 ^oC. The reaction was complete after addition of **(R)-1a**. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure pure product **(R)-5a** (21.4 mg, 90.6%).

$[\alpha]^{26}_D = -34.4^o$ (*c* = 1.0, $CHCl_3$). HPLC (method A), 75% ee.

(Table 3, entry 6)

To the suspension of $AlCl_3$ (23 mg, 0.17 mmol) in $CHCl_3$ (1 mL), **(R)-1a** (30 mg, 0.079 mmol) in $CHCl_3$ (2 mL) was added dropwise over 10 min at 0 ^oC. The reaction was complete after addition of **(R)-1a**. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure pure product **(R)-5a** (22.2 mg, 94%).

$[\alpha]^{26}_D = -32.5^o$ (*c* = 1.0, $CHCl_3$). HPLC (method A), 62% ee.



(S)-5b

(Table 3, entry 10)

See the result in (Table 2, entry 6).

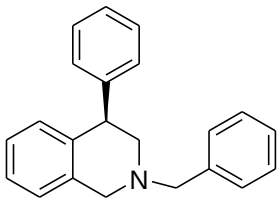
(Table 3, entry 11)

To the suspension of $AlCl_3$ (46.9 mg, 0.35 mmol) in benzene (1 mL), **(S)-1b** (50 mg, 0.16 mmol) in benzene (2 mL) was added dropwise over 10 min at 0 ^oC. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1% ethyl acetate in hexanes to afford pure product pure product **(S)-5b** (33.1 mg, 87.3%). $[\alpha]^{26}_D = -19.2^o$ (*c* = 0.9, $CHCl_3$). HPLC (method A), >99% ee.

(Table 3, entry 12)

To the suspension of $AlCl_3$ (46.7 mg, 0.35 mmol) in *p*-xylene (1 mL) and molecular sieves (4 beads), **(S)-1b** (50 mg, 0.16 mmol) in *p*-xylene (2 mL) was added dropwise over 15 min at room temperature and kept stirring for 2 h and then heated to reflux for 40 min. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1% ethyl acetate in hexanes pure product **(S)-5b** (27.8 mg, 73%). $[\alpha]^{26}_D = -22.9^o$ (*c* = 1.0, $CHCl_3$). HPLC (method A), 98.3% ee.

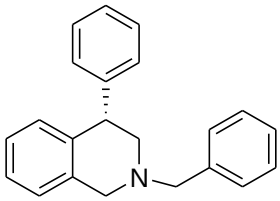
Table 4. Substrate scope for the synthesis of various THIQ analogues 5



(R)-5a

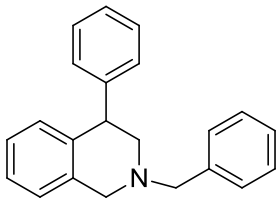
(Table 4, entry 1)

See the result described above (Table 1, entry 1)



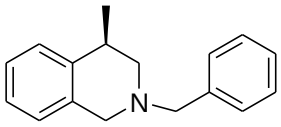
(S)-5a

(4S)-2-Benzyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline ((S)-5a). To the suspension of $AlCl_3$ (38.6 mg, 0.29 mmol) in toluene (1 mL), **(S)-1a** (50 mg, 0.13 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The reaction was complete after addition of **(S)-1a**. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure product **(S)-5a** (30.8 mg, 79.2%). $[\alpha]^{26}_D$ = + 38.6° (*c* = 2.1, $CHCl_3$). HPLC (method A), 76% ee.



(rac)-5a

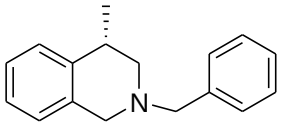
2-Benzyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline((rac)-5a). To the suspension of $AlCl_3$ (38.6 mg, 0.29 mmol) in toluene (1 mL), **(rac)-1a** (50 mg, 0.13 mmol) in toluene (2 mL) was added dropwise over 15 min at 0 ^oC. The reaction was complete after addition of **(rac)-1a.** After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.5% ethyl acetate in hexanes to afford pure **(rac)-5a** (30.7 mg, 79%). ^1H and ^{13}C NMR data are identical to **(R)-5a**.



(R)-5b

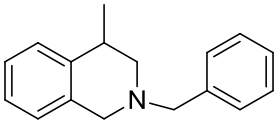
(Table 4, entry 2)

See the result described above (Table 1, entry 7)



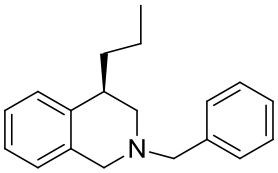
(S)-5b

See the result described above (Table 2, entry 6)



(rac)-5b

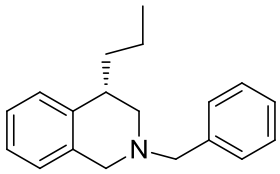
2-benzyl-4-methyl-1,2,3,4-tetrahydroisoquinoline (rac-5b). To the suspension of $AlCl_3$ (46.9 mg, 0.35 mmol) in toluene (1 mL), **(rac)-1b** (50 mg, 0.16 mmol) in toluene (2 mL) was added dropwise over 15 min at 0 ^{o}C. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1% ethyl acetate in hexanes to afford desired **(rac)-5b** (27.4 mg, 72%). ^{1}H and ^{13}C NMR data are identical to **(R)-5b**.



(R)-5c

(Table 4, entry 3)

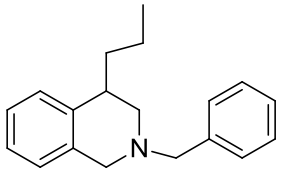
(4R)-2-Benzyl-4-propyl-1,2,3,4-tetrahydroisoquinoline ((R)-5c). To the suspension of $AlCl_3$ (42.4 mg, 0.32 mmol) in toluene (1 mL), **(R)-1c** (50 mg, 0.144 mmol) in toluene (2 mL) was added dropwise over 15 min at 0 ^oC. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.0% ethyl acetate in hexanes to afford desired **(R)-5c** (30 mg, 78.5%). ^1H NMR ($CDCl_3$, 300 MHz) δ 0.92 (t, J = 7.2 Hz, 3H), 1.24-1.36 (m, 1 H), 1.62-1.82 (m, 3H), 2.61 (dd, J = 11.4, 4.5 Hz, 1H), 2.70 (dd, J = 11.4, 4.2 Hz, 1H), 2.77-2.83 (m, 1H), 3.51 (d, J = 15.0 Hz, 1H), 3.60 (d, J = 13.2 Hz, 1H), 3.76 (d, J = 13.5 Hz, 2H), 7.00 (d, J = 7.2 Hz, 1H), 7.08-7.14 (m, 1H), 7.17 (d, J = 7.2 Hz, 2H), 7.28-7.31 (m, 1H), 7.35 (dd, J = 7.5, 7.5 Hz, 2H), 7.41 (d, J = 6.9 Hz, 2H);. HRMS (ESI) Calcd for $C_{19}H_{24}N$ $[M + H]^+$ *m/z* 266.1903. Found: $[M + H]^+$ *m/z* 266.1905. $[\alpha]^{26}_D$ = + 12.7^o (c = 0.8, $CHCl_3$). HPLC (method A), t_R = 2.1 min (S, minor) and 2.6 min (R, major), >99% ee.



(S)-5c

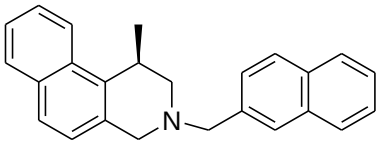
(4S)-2-Benzyl-4-propyl-1,2,3,4-tetrahydroisoquinoline ((S)-5c). To the suspension of $AlCl_3$ (42.4 mg, 0.32 mmol) in toluene (1 mL), **(S)-1c** (50 mg, 0.144 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.0% ethyl acetate in hexanes to afford desired **(S)-5c** (25 mg, 65.5%). ^1H NMR and ^{13}C NMR are identical to those of **(R)-5c**. $[\alpha]^{26}_D$ = – 12.9^o (c = 1.2, $CHCl_3$).

HPLC (method A), t_R = 2.2 min (S, major) and 2.6 min (R, minor), >99% ee.



(rac)-5c

2-Benzyl-4-propyl-1,2,3,4-tetrahydroisoquinoline ((rac)-5c). To the suspension of $AlCl_3$ (42.2 mg, 0.32 mmol) in toluene (1 mL), **(rac)-1c** (50 mg, 0.144 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.0% ethyl acetate in hexanes to afford desired **(rac)-5c** (23.5 mg, 61%). ^1H and ^{13}C NMR data are identical to those of **(R)-5c**.

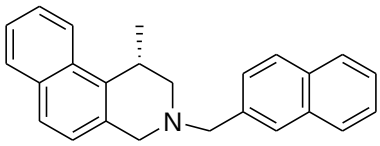


(R)-5d

(Table 4, entry 4)

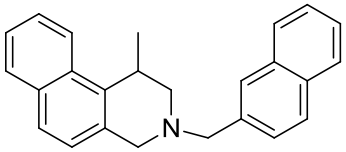
(1R)-1-Methyl-3-(naphthalen-2-ylmethyl)-1H,2H,3H,4H-benzo[f]isoquinoline ((R)-5d). To the suspension of $AlCl_3$ (35.2 mg, 0.264 mmol) in toluene (1 mL), **(R)-1d** (50 mg, 0.12 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 0.5% ethyl acetate in hexanes to afford desired **(R)-5d** (19.6 mg, 48.6%). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.56 (d, J = 6.9 Hz, 3H), 2.66 (dd, J = 11.1, 3.6 Hz, 1H), 3.00 (d, J = 11.1 Hz, 1H), 3.48-3.58 (m, 1H), 3.59 (d, J = 15.6 Hz, 1H),

3.83 (d, *J* = 13.2 Hz, 1H), 4.00 (d, *J* = 13.2 Hz, 1H), 4.10 (d, *J* = 15.6 Hz, 1H), 7.11 (d, *J* = 8.7 Hz, 1H), 7.42-7.55 (m, 4H), 7.65 (dd, *J* = 9.3, 9.3 Hz, 2H), 7.81-7.88 (m, 5H), 8.02 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 21.7 (q), 30.7 (d), 57.1 (t), 57.3 (t), 123.3 (d), 124.8 (d), 125.3 (d), 125.6 (d), 125.9 (d), 126.0 (d), 126.2 (d), 127.3 (d), 127.4 (d), 127.7 (d), 127.8 (d), 128.7 (d), 131.5 (s), 131.6 (s), 132.7 (s), 132.9 (s), 133.4 (s), 135.0 (s), 136.6 (s). $[\alpha]^{26}_D$ = + 84.2^o (*c* = 0.6, $CHCl_3$). HRMS (ESI) Calcd for $C_{25}H_{24}N$ $[M + H]^+$ *m/z* 338.1903. Found: $[M + H]^+$ *m/z* 338.1920. HPLC (method B), t_R = 6.9 min (S, minor) and 6.0 min (R, major), >99% ee.



(S)-5d

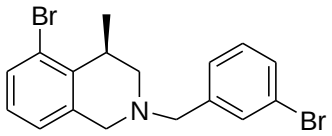
(1S)-1-Methyl-3-(naphthalen-2-ylmethyl)-1H,2H,3H,4H-benzo[f]isoquinoline ((S)-5d). To the suspension of $AlCl_3$ (35 mg, 0.26 mmol) in toluene (1 mL), **(S)-1d** (50 mg, 0.120 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^{o}C. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 0.5% ethyl acetate in hexanes to afford desired **(S)-5d** (21.5 mg, 53.1%). ^{1}H and ^{13}C NMR data are identical to those of **(R)-5d.** $[\alpha]^{26}_D$ = – 93.1^o (*c* = 0.9, $CHCl_3$). HPLC (method B), t_R = 6.9 min (S, major) and 6.0 min (R, minor), >99% ee.



(rac)-5d

1-Methyl-3-(naphthalen-2-ylmethyl)-1H,2H,3H,4H-benzo[f]isoquinoline ((rac)-5d).

To the suspension of $AlCl_3$ (35.4 mg, 0.26 mmol) in toluene (1 mL), **(rac)-1d** (50 mg, 0.12 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 0.5% ethyl acetate in hexanes to afford desired **(rac)-5d** (28.4 mg, 70%). ^1H and ^{13}C NMR data are identical to those of **(R)-5d**.

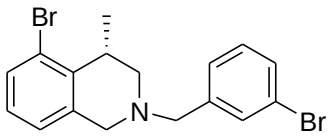


(R)-5e

(Table 4, entry 5)

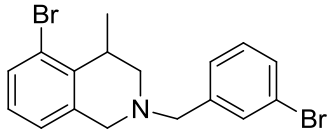
(4R)-5-Bromo-2-[(3-bromophenyl)methyl]-4-methyl-1,2,3,4-tetrahydroisoquinoline ((R)-5e). To the suspension of $AlCl_3$ (30.9 mg, 0.23 mmol) in toluene (1 mL), **(R)-1e** (50 mg, 0.11 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 ^oC. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.0% ethyl acetate in hexanes to afford desired **(R)-5e** (23.5 mg, 54%). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.40 (d, J = 6.6 Hz, 3H), 2.49 (dd, J = 11.1, 3.3 Hz, 1H), 2.80 (d, J = 11.1 Hz, 1H), 3.08-3.10 (m, 1H), 3.33 (d, J = 15.0 Hz, 1H), 3.63 (dd, J = 30.6, 13.5 Hz, 2H), 3.90 (d, J = 15.0 Hz, 1H), 6.94 (d, J = 6.6 Hz, 1H), 6.99 (dd, J = 7.8, 7.8 Hz, 1H), 7.21 (dd, J = 7.8, 7.8 Hz, 2H), 7.35 (d, J = 7.8 Hz, 1H), 7.39-7.42 (m, 1H), 7.58 (s, 1H);^{13}C NMR ($CDCl_3$, 300 MHz) δ 20.5 (q), 34.5 (d), 56.2 (t), 57.0 (t), 62.1 (t), 122.5 (s), 124.8 (s), 125.8 (d), 127.1 (d), 127.4 (d), 130.2 (d), 130.4 (d), 130.8 (d), 131.8 (d), 136.8 (s), 138.8 (s), 141.9 (s). HRMS (ESI) Calcd for $C_{17}H_{18}Br_2N$ $[M + H]^+$

m/z 393.9801. Found: $[M + H]^+$ *m/z* 393.9819. $[\alpha]^{26}_D$ = + 27° (*c* = 1.0, $CHCl_3$). HPLC (method C), t_R = 4.5 min (S, minor) and 4.7 min (R, major), 77.8% ee.



(S)-5e

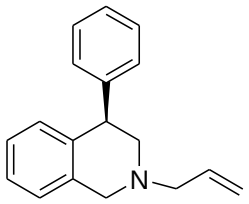
(4S)-5-Bromo-2-[(3-bromophenyl)methyl]-4-methyl-1,2,3,4-tetrahydroisoquinoline ((S)-5e). To the suspension of $AlCl_3$ (15.1 mg, 0.11 mmol) in toluene (1 mL), **(S)-1e** (24.5 mg, 0.05 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 °C. The resulting reaction mixture was gradually warm to room temperature over 2 h and then was heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.0% ethyl acetate in hexanes to afford crude product which was further purified by prep-TLC with hexanes to provide pure product **(S)-5e** (10.1 mg, 51%). ^1H and ^{13}C NMR data are identical to those of **(R)-5e**. $[\alpha]^{26}_D$ = – 35.5° (*c* = 0.5, $CHCl_3$). HPLC (method C), t_R = 4.5 min (S, major) and 4.7 min (R, minor), 86.2% ee.



(rac)-5e

5-Bromo-2-[(3-bromophenyl)methyl]-4-methyl-1,2,3,4-tetrahydroisoquinoline ((rac)-5e). To the suspension of $AlCl_3$ (30.9 mg, 0.23 mmol) in toluene (1 mL), **(rac)-1e** (50 mg, 0.11 mmol) in toluene (2 mL) was added dropwise over 10 min at 0 °C. The resulting reaction mixture was gradually warm to room temperature over 2 h and then was heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography

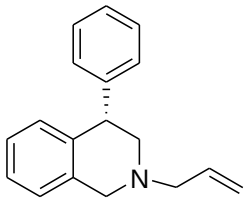
on silica gel (60-230 mesh) with 1.0% ethyl acetate in hexanes to afford crude product which was further purified by prep-TLC with hexanes to provide pure product **(rac)-5e** (19.4 mg, 45%). ^{1}H and ^{13}C NMR data are identical to those of **(R)-5e**.



(*R*)-**5f**

(Table 4, entry 6)

(4R)-4-phenyl-2-(prop-2-en-1-yl)-1,2,3,4-tetrahydroisoquinoline ((R)-5f). To the suspension of $AlCl_3$ (44.5 mg, 0.33 mmol) in DCE (1 mL), secondary β-amino bromide (50 mg, 0.15 mmol) in DCE (2 mL) was added dropwise over 15 min at $0^{o}C$. The reaction was done after addition of the bromide and was quenched by H_2O (10mL) and then extracted with ethyl acetate (10mL X 2). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to provide crude product which was purified by column chromatography on silica gel (60-220mesh) with 5% ethyl acetate in hexanes to afford pure product (15.4 mg, 41%). $[\alpha]^{26}_{D} = -4.8^{\circ}$ (*c* = 1.0, $CHCl_3$). HPLC (method D), $t_R = 3.8$ min (S, minor) and 4.6 min (R, major), 18.6% ee.

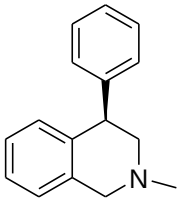


(S)-5f

(4S)-4-Phenyl-2-(prop-2-en-1-yl)-1,2,3,4-tetrahydroisoquinoline ((S)-5f). To the suspension of $AlCl_3$ (44.5 mg, 0.33 mmol) in 1,2-dichloroethane (1 mL), **(S)-1f** (50 mg, 0.15 mmol) in 1,2-dichloroethane (2 mL) was added dropwise over 15 min at 0 ^{o}C. The

reaction was complete after addition of **(S)-1f.** After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 5% ethyl acetate in hexanes to afford **(S)-5f** (13.6 mg, 36%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.60 (dd, J = 11.7, 9.0 Hz, 1H), 3.11-3.15 (m, 1H), 3.18 (d, J = 6.6 Hz, 2H), 3.67 (d, J = 15.0 Hz, 1H), 3.85 (d, J = 15.0 Hz, 1H), 4.28 (dd, J = 6.0, 6.0 Hz, 1H), 5.16-5.25 (m, 2H), 5.85-5.98 (m, 1H), 6.87 (d, J = 7.5 Hz, 1H), 7.05-7.33 (m, 8H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 45.9 (d), 56.5 (t), 59.5 (t), 61.2 (t), 117.9 (t), 126.0 (d), 126.3 (d), 126.4 (d), 126.5 (d), 128.3 (d), 129.2 (d), 135.1 (d), 135.2 (d), 137.6 (s), 144.7 (s). HRMS (ESI) Calcd for $C_{18}H_{20}N$ [M + H]$^+$ *m/z* 250.1590. Found: [M + H]$^+$ *m/z* 250.1582.

$[\alpha]^{26}_D$ = + 12.4^o (*c* = 0.65, $CHCl_3$). HPLC (method D), t_R = 3.8 min (S, major) and 4.6 min (R, minor), 46.9% ee.



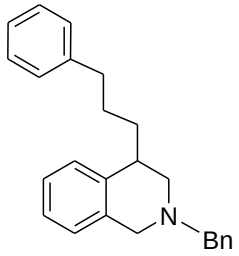
(*R*)-**5g**

(Table 4, entry 7)

(4R)-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline ((R)-5g). To the suspension of $AlCl_3$ (29 mg, 0.22 mmol) in DCE (1 mL), secondary β-amino bromide **1g** (30 mg, 0.1 mmol) in DCE (1 mL) was added dropwise over 10 min at -20 ^{o}C. The reaction mixture was slowly warm to -10 ^{o}C over 10min. After which period, the reaction was done and was quenched by H_2O (10mL) and then extracted with ethyl acetate (10 mL x 2). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to provide pure (**R)-5g** (15.1 mg, 68%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.46 (s, 3H), 2.60 (dd, J = 11.4, 9.0 Hz, 1H), 3.09 (dd, J = 12.3, 6.4 Hz, 1H), 3.65 (d, J = 14.7 Hz, 1H), 3.82 (d, J = 14.7 Hz, 1H),

4.32 (dd, J = 6.3, 6.3 Hz, 1H), 6.88 (d, J = 7.5 Hz, 1H), 7.05-7.36 (m, 8H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 45.7 (q), 45.8 (d), 58.3 (t), 61.6 (t), 125.9 (d), 126.1 (d), 126.2 (d), 126.4 (d), 129.1 (d), 129.4 (d), 129.6 (d), 134.9 (s), 137.0 (s), 144.5 (s). HRMS (ESI) Calcd for $C_{16}H_{17}N$ $[M + H]^+$ m/z 224.1434. Found: $[M + H]^+$ m/z 224.1387.

$[\alpha]^{26}_D = -1.3^\circ$ (c = 0.78, $CHCl_3$). HPLC (method B), t_R = 2.9 min (S, minor) and 3.2 min (R, major), 2.1% ee. **(S)-5g** was reported in the literature.[1] $[\alpha]^{26}_D = +17.2^\circ$ (c = 0.80, $CHCl_3$).

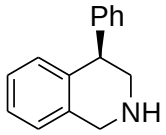


(*rac*)-**5h**

(Scheme 4)

2-Benzyl-4-(3-phenylpropyl)-1,2,3,4-tetrahydroisoquinoline ((rac)-5h). To the suspension of $AlCl_3$ (34.7 mg, 0.26 mmol) in toluene (1 mL), **1h** (50 mg, 0.118 mmol) in toluene (2 mL) was added dropwise over 15 min at 0 ^oC. The resulting reaction mixture was gradually warmed to room temperature over 2 h and then heated to reflux for 2 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 1.0% ethyl acetate in hexanes to afford pure product (rac)-**5h** (26.7 mg, 66.3%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ1.57-1.65 (m, 2H), 1.69-1.90 (m, 2H), 2.57-2.64 (m, 3H), 2.69-2.75 (m, 1H), 2.78-2.84 (m, 1H), 3.54 (dd, J = 17.7, 13.2 Hz, 2H), 3.77 (dd, J = 15.0, 4.2 Hz, 2H), 7.00 (d, J = 6.9 Hz, 1H), 7.09-7.22 (m, 6H), 7.27-7.42 (m, 7H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 29.4 (t), 35.8 (t), 36.2 (t), 38.6 (d), 54.2 (t), 56.8 (t), 62.9 (t), 125.6 (d), 125.7 (d), 126.1 (d), 126.4 (d), 127.1 (d), 128.3 (d), 128.5 (d), 129.0

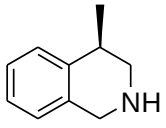
(d), 135.0 (s), 138.8 (s), 139.2 (s), 142.6 (s). HRMS (ESI) Calcd for $C_{25}H_{27}N$ $[M + H]^+$ *m/z* 342.2216. Found: $[M + H]^+$ *m/z* 342.2215.



(R)-7a

Scheme 1

(4R)-4-phenyl-1,2,3,4-tetrahydroisoquinoline (7a).[2] To a solution of **(R)-5a** (63 mg, 0.21 mmol) in anhydrous methanol (3 mL), 10% Pd/C (63 mg) and ammonia formate (133 mg, 2.1 mmol) were added sequentially. The reaction mixture was stirred at room temperature for 3 h and then heated to reflux for 10 min. The resulting mixture was filtered through celite and evaporated to dryness. The residue was treated with saturated $NaHCO_3$ (5 mL) and extracted with $CHCl_3$ (2 × 5 mL). The organic layer was washed with H_2O (2 × 5 mL). The organic layer was dried over $MgSO_4$ and evaporated to dryness. The residue was purified by prep-TLC using 10% ethyl acetate in hexane to give pure product **(R)-7a** (15.7 mg, 35%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.06 (br, 1H) 3.11 (dd, *J* = 12.9, 6.3 Hz, 1H), 3.42 (dd, *J* = 12.9, 6.3 Hz, 1H), 4.13 (dd, *J* = 24.9, 17.1 Hz, 2H), 6.92 (d, *J* = 7.5 Hz, 1H), 7.1-7.33 (m, 8H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 44.9 (d), 48.5 (t), 52.3 (t), 125.9 (d), 126.3 (d), 126.4 (d), 128.5 (d), 128.9 (d), 130.3 (d), 136.3 (s), 137.4 (s), 144.9 (s). $[\alpha]^{26}_D$ = + 4.4° (*c* = 0.8, $CHCl_3$). Lit.[2] $[\alpha]^{26}_D$ = + 11.1° (*c* = 0.73, CH_3OH).



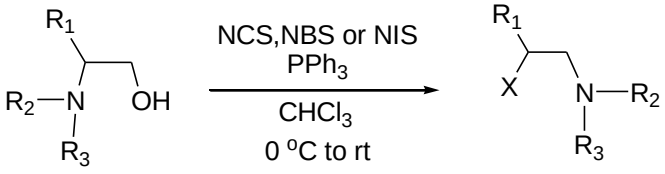
(R)-7b

Scheme 1

(4R)-4-methyl-1,2,3,4-tetrahydroisoquinoline (7b).[3] To a solution of **(R)-5b** (15 mg, 0.063 mmol) in anhydrous methanol (2 mL), 10% Pd/C (15 mg) and ammonia formate (39.9 mg, 0.63 mmol) were added sequentially. The reaction mixture was stirred at room temperature for 3 h and then heated to reflux for 10 min. The resulting mixture was filtered through celite and evaporated to dryness. The residue was treated with saturated $NaHCO_3$ (5 mL) and extracted with $CHCl_3$ (2 × 5 mL). The organic layer was washed with H_2O (2 × 5 mL). The organic layer was dried over MgSO4 and evaporated to dryness. The residue was purified by prep-TLC using 10% ethyl acetate in hexane to give pure product (R)-**7b** (4.5 mg, 48.6%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.29 (d, J = 6.6 Hz, 3H), 1.88 (br, 1H), 2.78-2.90 (m, 2H), 3.22 (dd, J = 12.3, 4.5 Hz, 1H), 4.01 (s, 2H), 7.00 (d, J = 7.2 Hz, 1H), 7.10-7.26 (m, 3H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 20.6 (q), 32.1 (d), 48.8 (t), 51.1 (t), 125.7 (d), 126.0 (d), 126.3 (d), 128.2 (d), 135.6 (s), 140.1 (s).

$[\alpha]^{26}_D$ = + 21.4° (c = 0.1, $CHCl_3$). Lit.[3] $[\alpha]^{26}_D$ = + 47.2° (c = 0.5, $CHCl_3$).

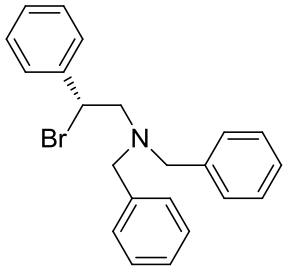
Synthesis of β-haloamines (Scheme 2)



(R)-**8** or (S)-**8** (R)-**1**-**3** or (S)-**1**-**3**

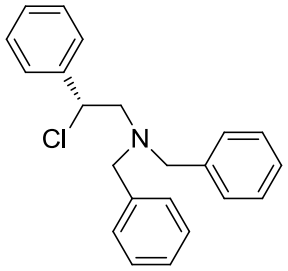
General procedure for synthesis of secondary β-amino halide 1, 2 and 3. To a solution of *N*,*N*-dialkylated alcohol **8** (1 equiv) and triphenyl phosphine (1.2 equiv) in $CHCl_3$ was added NCS, NBS or NIS (1.2 equiv) portionwise at 0 °C over 10 min. The resulting mixture was stirred for 4 h while being maintained at 0 °C. The ice bath was removed,

and the reaction mixture was warmed to room temperature and stirred for 1 h and evaporated to dryness. The residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5-10% ethyl acetate in hexanes.



(R)-1a

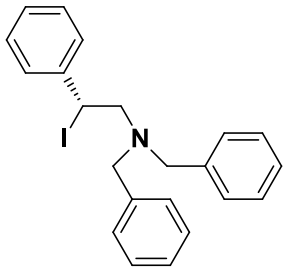
Dibenzyl[(2R)-2-bromo-2-phenylethyl]amine ((R)-1a). To a solution of **(S)-8a**[4] (200 mg, 0.63 mmol) and PPh_3 (199.1 mg, 0.76 mmol) in $CHCl_3$ (10 mL) was added NBS (135.3 mg, 0.76 mmol) portionwise at 0 °C over 20 min. After the work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(R)-1a** (150 mg, 62.3%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.22 (d, J = 7.6 Hz, 2H), 3.61(dd, J = 41.4, 13.5 Hz, 4H), 4.91 (dd, J = 7.6, 7.6 Hz, 1H), 7.19-7.31 (m, 15H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 52.7 (d), 58.9 (t), 61.6 (t), 127.1 (d), 128.1 (d), 128.3 (d), 128.3 (d), 128.5 (d), 129.0 (d), 139.0 (s), 140.1 (s). $[\alpha]^{26}_D = -60.0^o$ (c = 1.0, $CHCl_3$). HRMS (ESI) Calcd for $C_{22}H_{24}NO$ $[M - Br + H_2O]^+$ *m/z* 318.4321. Found: $[M - Br + H_2O]^+$ *m/z* 318.1870.



(R)-2a

Dibenzyl[(2R)-2-chloro-2-phenylethyl]amine ((R)-2a). To a solution of **(S)-8a**[4] (165 mg, 0.52 mmol) and PPh_3 (162.4 mg, 0.62 mmol) in $CHCl_3$ (5 mL) at 0 ^oC was added NCS (85 mg, 0.62 mmol). After 1 h at 0 ^oC, additional 0.4 equiv of PPh_3 (55.0 mg, 0.21 mmol) and NCS (27.8 mg, 0.21 mmol) was added. After the work-up, the residue was purified by silica gel column chromatography eluted with 5% ethyl acetate in hexanes to afford **(R)-2a** (44.5 mg, 25%) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.12 (d, J = 7.3 Hz, 2H), 3.65 (dd, J = 40.1, 13.6 Hz, 4H), 4.85 (dd, J = 7.4, 7.4 Hz, 1H), 7.23-7.37 (m, 15H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 59.0 (t), 61.1 (d), 61.9 (t), 127.1 (d), 127.6 (d), 128.3 (d), 128.6 (d), 128.9 (d), 129.2 (d), 139.0 (s), 140.4 (s).

$[\alpha]^{26}_D = -47.3^o$ (c = 1.0, $CHCl_3$). HRMS (ESI) Calcd for $C_{22}H_{24}NO$ $[M - Cl + H_2O]^+$ *m/z* 318.4321. Found: $[M - Br + H_2O]^+$ *m/z* 318.1865.

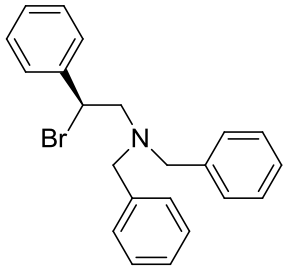


(R)-3a

Dibenzyl[(2R)-2-iodo-2-phenylethyl]amine ((R)-3a). To a solution of **(S)-8a**[4] (250 mg, 0.79 mmol) and PPh_3 (248.9 mg, 0.95 mmol) in $CHCl_3$ (7 mL) at 0 ^oC was added NIS (212.7 mg, 0.95 mmol). After 1 h at 0 ^oC, additional 0.4 equiv of PPh_3 (82.8 mg, 0.32 mmol) and NIS (71.7 mg 0.32 mmol) was added. After the work-up, the residue was purified by silica gel column chromatography eluted with 5% ethyl acetate in hexanes to afford **(R)-3a** (202.2 mg, 60%) as a yellow oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.21 (dd, J = 13.8, 9.0 Hz, 1H), 3.36 (dd, J = 13.5, 6.6 Hz, 1H), 3.67 (dd, J = 31.2, 13.5 Hz, 4H),

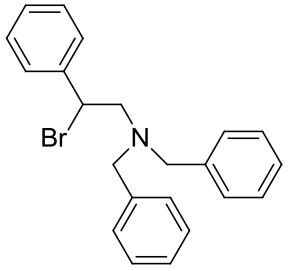
5.22 (dd, J = 8.8, 6.8 Hz, 1H), 7.25-7.43 (m, 15H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 32.5 (d), 58.7 (t), 63.0 (t), 128.1 (d), 128.6 (d), 128.7 (d), 128.8 (d), 129.2 (d), 129.3 (d), 139.0 (s), 142.3 (s).

$[\alpha]^{26}_D = -85.7^o$ (c = 1.0, $CHCl_3$). HRMS (ESI) Calcd for $C_{22}H_{24}NO$ [M - Br + H_2O]$^+$ *m/z* 318.4321. Found: [M – I + H_2O]$^+$ *m/z* 318.1881.



(S)-1a

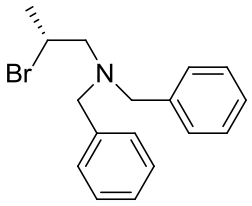
Dibenzyl[(2S)-2-bromo-2-phenylethyl]amine ((S)-1a). General procedure was followed. To a solution of **(R)-8a**[5] (160 mg, 0.5 mmol) and PPh_3 (159 mg, 0.61 mmol) in $CHCl_3$ (10 mL) was added NBS (108 mg, 0.61 mmol) portionwise at 0 °C over 20 min. After the work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(S)-1a** (104 mg, 55%).^{1}H and ^{13}C NMR are identical to those of (**R**)-**1a**. $[\alpha]^{26}_D = +51.0^o$ (c = 1.0, $CHCl_3$).



(rac)-1a

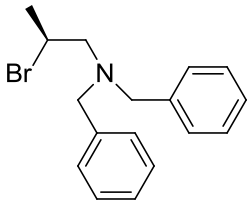
Dibenzyl(2-bromo-2-phenylethyl)amine ((rac)-1a). General procedure was followed. To a solution of **(rac)-8a**[6] (500 mg, 1.58 mmol) and PPh_3 (620 mg, 2.36 mmol) in $CHCl_3$ (10 mL) was added NBS (421 mg, 2.36 mmol) portionwise at 0 °C over 20 min. After the

work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure (rac)-**1a** (400 mg, 66%).[1]H and [13]C NMR data are identical to those of **(R)-1a.**



(R)-1b

Dibenzyl[(2R)-2-bromopropyl]amine ((R)-1b).[7] To a solution of (S)-**8b**[8] (2 g, 7.8 mmol) and PPh_3 (2.46 g, 9.4 mmol) in $CHCl_3$ (30 mL) at 0 ^oC was added NBS (1.68 g, 9.4 mmol). After the work-up, the residue was purified by silica gel column chromatography eluted with 5% ethyl acetate in hexanes to afford **(R)-1b** (1.9 g, 76%) as a white solid. ^1H NMR ($CDCl_3$, 300 MHz) δ1.65 (d, J = 6.6 Hz, 3H), 2.73 (dd, J = 13.5, 8.1 Hz, 1H), 2.92 (dd, J = 13.2, 6.0 Hz, 1H), 3.65 (dd, J = 35.7, 13.5 Hz, 4H), 4.07-4.14 (m, 1H), 7.26-7.42 (m, 10H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 24.0 (q), 47.9 (d), 59.1 (t), 62.7 (t), 127.2 (d), 128.3 (d), 129.0 (d), 139.1 (s). $[\alpha]^{26}_D$ = + 18.9^o (c = 1.0, $CHCl_3$).

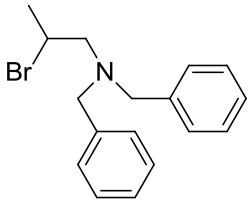


(S)-1b

Dibenzyl[(2S)-2-bromopropyl]amine ((S)-1b).[9] To a solution of **(R)-8b**[10] (536mg, 2.1 mmol) and PPh_3 (661 mg, 2.5 mmol) in $CHCl_3$ (10 mL) at 0 ^oC was added NBS (445 mg, 2.5 mmol). After the work-up, the residue was purified by silica gel column chromatography eluted with 5% ethyl acetate in hexanes to afford **(S)-1b** (500 mg, 76%)

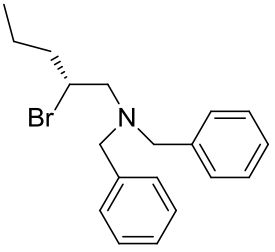
as a white solid. ^{1}H and ^{13}C NMR data are identical to those of **(R)-1b**.

$[\alpha]^{26}_{D} = -16.2^{o}$ (c = 1.0, $CHCl_3$).



(rac)-1b

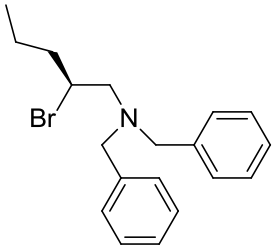
Dibenzyl(2-bromopropyl)amine ((rac)-1b). To a solution of **(rac)-8b** (974 mg, 3.8 mmol) and PPh_3 (1.2 g, 4.6 mmol) in $CHCl_3$ (25 mL) at 0 ^{o}C was added NBS (819 mg, 4.6 mmol). After the work-up, the residue was purified by silica gel column chromatography eluted with 5% ethyl acetate in hexanes to afford (rac)-**1b** (840 mg, 69.5%) as a white solid. ^{1}H and ^{13}C NMR data are identical to **(R)-1b**.



(R)-1c

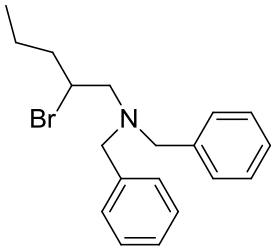
Dibenzyl[(2R)-2-bromopentyl]amine ((R)-1c). To a solution of **(S)-8c**[11] (95 mg, 0.34 mmol) and PPh_3 (89 mg, 0.34 mmol) in $CHCl_3$ (3 mL) at 0 ^{o}C was added NBS (60.5 mg, 0.34 mmol). After the work-up, the residue was purified by silica gel column chromatography eluted with 5% ethyl acetate in hexanes to afford **(R)-1c** (52.9 mg, 45%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 7.4 Hz, 3H), 1.26-1.45 (m, 3H), 1.46-1.64 (m, 1H), 1.89-1.97 (m, 1H), 2.78-2.94 (m, 2H), 3.67 (dd, J = 33.0, 13.5 Hz, 4H), 4.00-4.05 (m, 1H), 7.25-7.41 (m, 10H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 13.5 (q),

20.3 (t), 38.2 (t), 54.8 (d), 59.2 (t), 61.4 (t), 127.2 (d), 128.3 (d), 129.0 (d), 139.1 (s). $[\alpha]^{26}_{D}$ = + 16.0^{o} (*c* = 1.0, $CHCl_3$). HRMS (ESI) Calcd for $C_{19}H_{26}NO$ $[M - Br + H_2O]^+$ *m/z* 284.4158. Found: $[M - Br + H_2O]^+$ *m/z* 284.2027.



(S)-1c

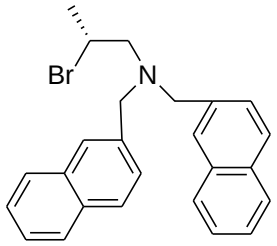
Dibenzyl[(2S)-2-bromopentyl]amine ((S)-1c). General procedure was followed. To a solution of **(R)-8c** (214 mg, 0.76 mmol) and PPh_3 (238 mg, 0.91 mmol) in $CHCl_3$ (7 mL) was added NBS (162 mg, 0.91 mmol) portionwise at 0 °C over 20 min. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(S)-1c** (138 mg, 52%). ^{1}H and ^{13}C NMR data are identical to those of **(R)-1c**. $[\alpha]^{26}_{D}$ = – 14.5^{o} (*c* = 1.0, $CHCl_3$).



(rac)-1c

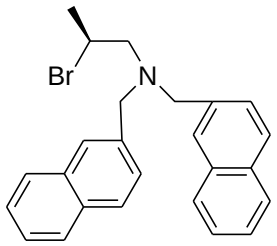
Dibenzyl(2-bromopentyl)amine ((rac)-1c). General procedure was followed. To a solution of **(rac)-8c** (300 mg, 1.06 mmol) and PPh_3 (416.6 mg, 1.59 mmol) in $CHCl_3$ (10 mL) was added NBS (283 mg, 1.59 mmol) portionwise at 0 °C over 20 min. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(rac)-1c** (150 mg, 40.9%). ^{1}H and

^{13}C NMR data are identical to those of **(R)-1c.**



(R)-1d

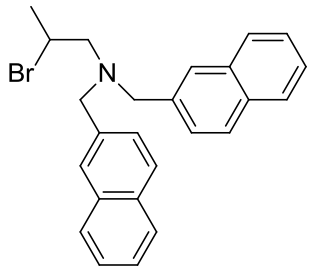
[(2R)-2-Bromopropyl]bis(naphthalen-2-ylmethyl)amine ((R)-1d). To a solution of **(S)-8d** (284 mg, 0.80 mmol) and PPh_3 (251 mg, 0.96 mmol) in $CHCl_3$ (7 mL) was added NBS (170 mg, 0.96 mmol) portionwise at 0 °C over 20 min. After the work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(R)-1d** (241 mg, 72%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.65 (d, J = 6.6 Hz, 3H), 2.81 (dd, J = 13.5, 7.8 Hz, 1H), 3.07 (dd, J = 13.2, 6.3 Hz, 1H), 3.83 (dd, J = 30.6, 13.5 Hz, 4H), 4.13-4.20 (m, 1H), 7.45-7.54 (m, 4H), 7.62 (d, J = 8.4 Hz, 2H), 7.81 (s, 2H), 7.84-7.88 (m, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 24.0 (q), 47.9 (d), 59.4 (t), 62.7 (t), 125.7 (d), 126.1 (t), 127.3 (d), 127.6 (d), 127.7 (d), 128.1 (d), 132.9 (s), 133.3 (s), 136.7 (s). $[\alpha]^{26}_D = -5.4^o$ (c = 1.0, $CHCl_3$). HRMS (ESI) Calcd for $C_{25}H_{26}NO$ $[M - Br + H_2O]^+$ m/z 356.4800. Found: $[M - Br + H_2O]^+$ m/z 356.2006.



(S)-1d

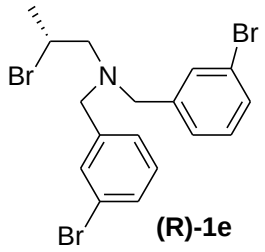
[(2S)-2-Bromopropyl]bis(naphthalen-2-ylmethyl)amine ((S)-1d). To a solution of **(R)-**

8d (78 mg, 0.22 mmol) and PPh_3 (86.3 mg, 0.33 mmol) in $CHCl_3$ (1 mL) was added NBS (58.8 mg, 0.33 mmol) portionwise at 0 °C over 10 min. After the work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(S)-1d** (37 mg, 40%). ^1H and ^{13}C NMR data are identical to those of **(R)-1d**. $[\alpha]^{26}_D = +5.2^o$ (*c* = 1.0, $CHCl_3$).



(rac)-1d

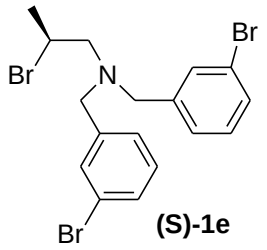
(2-Bromopropyl)bis(naphthalen-2-ylmethyl)amine ((rac)-1d). To a solution of **(rac)-8d** (680 mg, 1.9 mmol) and PPh_3 (602 mg, 2.3 mmol) in $CHCl_3$ (8 mL) was added NBS (409 mg, 2.3 mmol) portionwise at 0 °C over 10 min. After the work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(rac)-1d** (523 mg, 65.9%). ^1H and ^{13}C NMR data are identical to those of **(R)-1d**.



(R)-1e

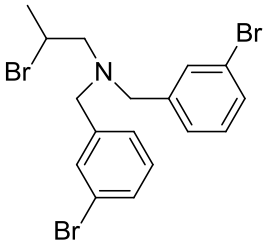
Bis[(3-bromophenyl)methyl][(2R)-2-bromopropyl]amine ((R)-1e). To a solution of **(S)-8e** (509 mg, 1.2 mmol) and PPh_3 (378 mg, 1.4 mmol) in $CHCl_3$ (7 mL) was added NBS (249 mg, 1.4 mmol) portionwise at 0 °C over 20 min. After the work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5%

ethyl acetate in hexanes to afford pure **(R)-1e** (466 mg, 82%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.64 (d, J = 6.6 Hz, 3H), 2.67 (dd, J = 13.5, 7.2 Hz, 1H), 2.86 (dd, J = 13.5, 6.9 Hz, 1H), 3.58 (dd, J = 18.9, 13.8 Hz, 4H), 4.09 (dd, J = 13.8, 6.9 Hz, 1H), 7.18 (dd, J = 7.5, 7.5 Hz, 2H), 7.33 (d, J = 7.5 Hz, 2H), 7.40 (d, J = 7.8 Hz, 2H), 7.51 (s, 2H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 24.0 (q), 47.3 (d), 58.41 (t), 62.5 (t), 122.5 (s), 127.5 (d), 130.0 (d), 130.3 (d), 131.9 (d), 141.2 (s). $[\alpha]^{26}_{D}$ = + 1.1^{o} (c = 1.0, $CHCl_3$). HRMS (ESI) Calcd for $C_{17}H_{20}Br_2NO$ $[M - Br + H_2O]^+$ *m/z* 414.1548. Found: $[M - Br + H_2O]^+$ *m/z* 414.9917.



(S)-1e

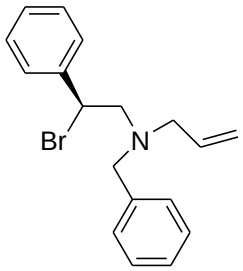
Bis[(3-bromophenyl)methyl][(2S)-2-bromopropyl]amine ((S)-1e). To a solution of **(R)-8e** (92 mg, 0.22 mmol) and PPh_3 (87.6 mg, 0.33 mmol) in $CHCl_3$ (1 mL) was added NBS (59.5 mg, 0.33 mmol) portionwise at 0 °C over 5 min. After the work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(S)-1e** (77 mg, 73.5%). ^{1}H and ^{13}C NMR data are identical to those of **(R)-1e**. $[\alpha]^{26}_{D}$ = – 1.6^{o} (c = 1.0, $CHCl_3$).



(rac)-1e

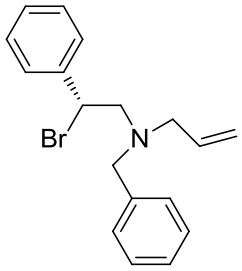
Bis[(3-bromophenyl)methyl](2-bromopropyl)amine ((rac)-1e). To a solution of **(rac)-**

8e (200 mg, 0.48 mmol) and PPh_3 (152 mg, 0.58 mmol) in $CHCl_3$ (5 mL) was added NBS (103.4 mg, 0.58 mmol) portionwise at 0 °C over 10 min. After the work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(rac)-1e** (142 mg, 62.1%). ^1H and ^{13}C NMR data are identical to those of **(R)-1e**.



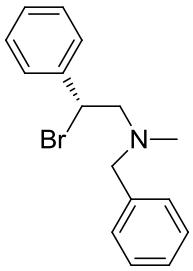
(S)-1f

Benzyl[(2S)-2-bromo-2-phenylethyl](prop-2-en-1-yl)amine ((S)-1f). To a solution of **(R)-8f** (150 mg, 0.56 mmol) and PPh_3 (175.5 mg, 0.67 mmol) in $CHCl_3$ (6 mL) was added NBS (119.9 mg, 0.67 mmol) portionwise at 0 °C over 20 min. After the work-up, the residue was purified *via* column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(S)-1f** (108.7 mg, 59%). ^1H NMR ($CDCl_3$, 300 MHz) δ 3.13 (dd, J = 6.3, 0.9 Hz, 2H), 3.24 (dd, J = 6.9, 5.4 Hz, 2H), 3.66 (dd, J = 27.0, 13.5 Hz, 2H), 4.98 (dd, J = 8.1, 7.2 Hz, 1H), 4.96-5.22 (m, 2H), 5.75-5.88 (m, 1H), 7.21-7.42 (m, 10H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 53.1 (d), 57.3 (t), 58.8 (t), 61.4 (t), 117.8 (t), 128.1 (d), 128.2 (d), 128.3 (d), 128.5 (d), 128.7 (d), 128.9 (d), 135.4 (d), 139.1 (s), 140.8 (s). $[\alpha]^{26}_D$ = + 88.6^o (c = 0.5, $CHCl_3$). HRMS (ESI) Calcd for $C_{18}H_{22}NO$ [M – Br + H_2O]$^+$ *m/z* 268.3734. Found: [M – Br + H_2O]$^+$ *m/z* 268.1724.



(R)-1f

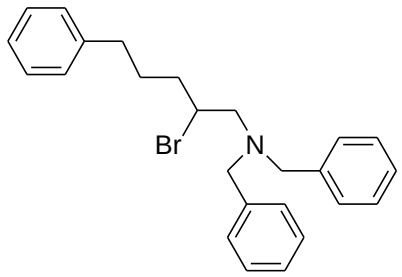
Benzyl[(2R)-2-bromo-2-phenylethyl](prop-2-en-1-yl)amine ((R)-1f). To a solution of **(S)-8f (**150 mg, 0.56 mmol) and PPh_3 (178.2 mg, 0.68 mmol) in $CHCl_3$ (6 mL) was added NBS (121.04 mg, 0.68 mmol) portionwise at 0 °C over 20 min. The resulting mixture was stirred for 4 h while being maintained at 0 °C. The ice bath was removed, and the reaction mixture was warmed to room temperature and stirred for 1 h and evaporated to dryness. The residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% EtOAc in hexanes to afford **(R)-1f** (89.2 mg, 48.5%). $[\alpha]^{26}_{D} = -41.0$ (*c* = 1.0, $CHCl_3$). ^{1}H and ^{13}C NMR data of **(R)-1f** are identical to those of **(S)-1f.**



(R)-1g

Benzyl[(2R)-2-bromo-2-phenylethyl]methylamine ((R)-1g). To a solution of **(S)-8g** (140 mg, 0.16 mmol) and PPh_3 (183.4 mg, 0.70 mmol) in $CHCl_3$ (10mL) was added NBS (124.6 mg, 0.70 mmol) portionwise at 0 °C over 20 min. The resulting mixture was stirred for 4 h while being maintained at 0 °C. The ice bath was removed, and the reaction mixture was warmed to room temperature and stirred for 1 h and evaporated to

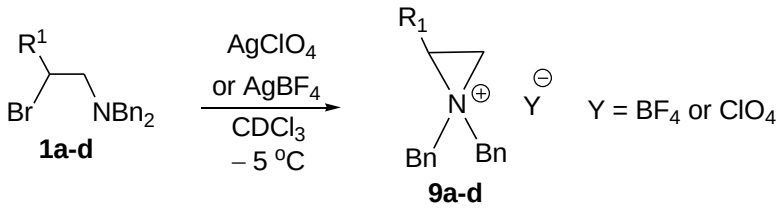
dryness. The residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% EtOAc in hexanes to afford pure **(R)-1g** (75 mg, 43%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.28 (s, 3H), 3.04-3.20 (m, 2H), 3.58 (dd, J = 15.2, 14.0 Hz, 2H), 5.04 (dd, J = 6.7, 6.7 Hz, 1H), 7.20-7.39 (m, 10H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 42.5 (q), 52.5 (d), 62.4 (t), 64.5 (t), 127.1 (d), 127.9 (d), 128.2 (d), 128.4 (d), 128.7 (d), 129.0 (d), 138.6 (s), 140.7 (s). $[\alpha]^{26}_{D} = -47.2$ (c = 1.0, $CHCl_3$).



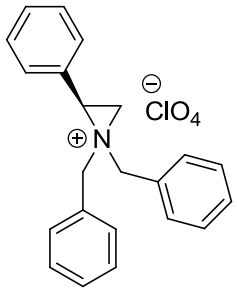
1h

Dibenzyl(2-bromo-5-phenylpentyl)amine (1h). To a solution of **(rac)-8h** (200 mg, 0.56 mmol) and PPh_3 (175.1 mg, 0.67 mmol) in CH_3CN (5 mL) was added NBS (118.58 mg, 0.67 mmol) portionwise at 0 °C over 20 min. After the work-up, the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **(rac)-1h** (140 mg, 60%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.60-1.70 (m, 2H), 1.82-1.89 (m, 1H), 2.06-2.14 (m, 1H), 2.61-2.65 (m, 2H), 2.81-3.00 (m, 2H), 3.64 (dd, J = 42.0, 13.5 Hz, 4H), 4.03-4.05 (m, 1H). 7.21-7.38 (m, 15H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 28.8 (t), 35.2 (t), 35.5 (t), 54.7 (d), 59.3 (t), 61.5 (t), 125.9 (d), 127.2 (d), 128.4 (d), 128.5 (d), 129.1 (d), 139.1 (s), 142.0 (s). HRMS (ESI) Calcd for $C_{25}H_{30}NO$ $[M - Br + H_2O]^+$ m/z 360.5118. Found: $[M - Br + H_2O]^+$ m/z 360.2337.

Synthesis and characterization of optically active aziridinium ions (Scheme 2)



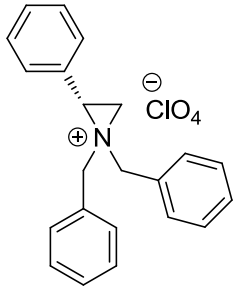
General synthesis of aziridinium ions 9. To a stirred solution of β-amino bromide **1a-d** in $CDCl_3$ at -5 °C was added silver perchlorate (5 equiv), silver tetrafluoroborate (1 equiv) or silver triflate (5 equiv). The resulting mixture was continuously stirred at – 5 °C, while the reaction progress was monitored using TLC. After completion of the reaction, silver bromide was filtered. The aziridinium ions obtained was characterized by ^{1}H and ^{13}C NMR and optical rotation.



(S)-9aa

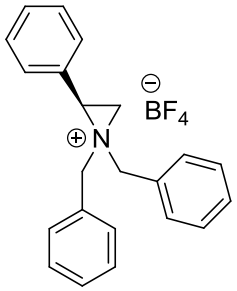
(S)-1,1-Dibenzyl-2-phenylaziridinium perchlorate ((S)-9aa). The general procedure was followed for the reaction of **(R)-1a** (50 mg, 0.13 mmol) and $AgClO_4$ (136.2 mg, 0.66 mmol) in $CDCl_3$ (1 mL) for 15 min. After completion of the reaction, silver bromide was filtered, and the filtrate was immediately characterized by ^{1}H and ^{13}C NMR and optical rotation. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.55 (d, J = 14.5 Hz, 1H), 3.83 (dd, J = 8.3, 4.9 Hz, 1H), 3.95 (d, J = 14.5 Hz, 1H), 4.02 (dd, J = 7.7, 5.0 Hz, 1H), 4.38 (d, J = 13.5 Hz, 1H), 4.60 (d, J = 13.5 Hz, 1H), 4.85 (dd, J = 8.2, 8.2 Hz, 1H), 7.13-7.26 (m, 2H), 7.36-7.44 (m, 13H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 42.0 (t), 53.6 (d), 56.3 (t), 61.5 (t), 125.1

(s), 128.7 (s), 129.0 (s), 129.6 (d), 129.7 (d), 129.8 (d), 129.9 (d), 130.2 (d), 130.9 (d), 131.3 (d), 131.5 (s), 131.7 (s). $[\alpha]^{26}_{D}$ = + 20.3^{o} (*c* = 1.1, $CDCl_3$).



(R)-9aa

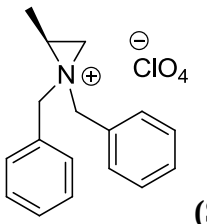
(R)-1,1-Dibenzyl-2-phenylaziridinium perchlorate ((R)-9aa). The general procedure was followed for the reaction of **(S)-1a** (50 mg, 0.13 mmol) and $AgClO_4$ (136.2 mg, 0.66 mmol) in $CDCl_3$ (1 mL) for 15 min. After completion of the reaction, silver bromide was filtered, and the filtrate was immediately characterized by ^{1}H and ^{13}C NMR and optical rotation. $[\alpha]^{26}_{D}$ = – 22.1^{o} (*c* = 0.82, $CDCl_3$). ^{1}H and ^{13}C NMR data of **(R)-9aa** are identical to those of **(S)-9aa.**



(S)-9ab

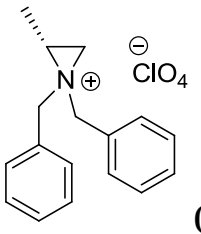
(S)-1,1-Dibenzyl-2-phenylaziridinium tetrafluoroborate ((S)-9ab). The general procedure was followed for the reaction of **(R)-1a** (50 mg, 0.13 mmol) and $AgBF_4$ (25.6 mg, 0.13 mmol) in $CDCl_3$ (1 mL) for 15 min. After completion of the reaction, silver bromide was filtered, and the filtrate was immediately characterized by ^{1}H and ^{13}C NMR and optical rotation. $[\alpha]^{26}_{D}$ = + 24.8^{o} (*c* = 1.0, $CDCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.54 (d, *J* = 14.5 Hz, 1H), 3.80 (dd, *J* = 8.2, 4.8 Hz, 1H), 3.88-4.05 (m, 2H), 4.34 (d, *J* =

13.5 Hz, 1H), 4.68 (d, *J* = 13.5 Hz, 1H), 4.82 (dd, *J* = 8.1, 8.1 Hz, 1H), 7.13-7.18 (m, 2H), 7.36-7.43 (m, 13H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 42.0 (t), 53.5 (d), 56.2 (t), 61.4 (t), 125.2 (s), 128.7 (s), 128.9 (s), 129.7 (d), 129.8 (d), 129.9 (d), 130.1 (d), 130.8 (d), 131.2 (d), 131.6 (d). ^{1}H and ^{13}C NMR data of **(S)-9ab** are almost identical to those of **(S)-9aa.**



(S)-9ba

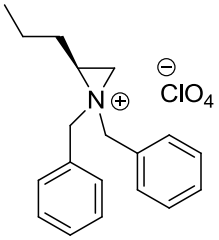
(S)-1,1-Dibenzyl-2-methylaziridinium perchlorate ((S)-9ba). The general procedure was followed for the reaction of **(R)-1b** (40 mg, 0.13 mmol) and $AgClO_4$ (130.2 mg, 0.63 mmol) in $CDCl_3$ (0.8 mL) for 5 min. After completion of the reaction, silver bromide was filtered, and the filtrate was evaporated and dried *in vacuo*. The residue was characterized by ^{1}H and ^{13}C NMR and optical rotation. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.80 (d, *J* = 6.1 Hz, 3H), 3.21 (dd, *J* = 8.2, 3.7 Hz, 1H), 3.31 (dd, *J* = 7.4, 3.8 Hz, 1H), 3.54-3.61 (m, 1H), 4.18 (dd, *J* = 18.8, 13.9 Hz, 2H), 4.39 (dd, *J* = 13.7, 9.4 Hz, 2H), 7.22 (d, *J* = 6.4 Hz, 2H), 7.28-7.49 (m, 8H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 11.9 (q), 43.0 (t), 47.9 (d), 56.3 (t), 61.1 (t), 128.1 (s), 129.1 (s), 129.6 (d), 129.7 (d), 130.1 (d), 130.2 (d), 130.6 (d), 131.0 (d). $[\alpha]^{26}_{D}$ = + 17.2° (*c* = 1.3, $CHCl_3$).



(R)-9ba

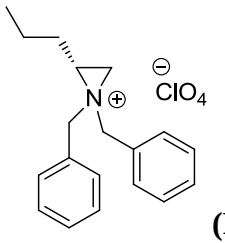
(R)-1,1-Dibenzyl-2-methylaziridinium perchlorate ((R)-9ba). The general procedure was followed for the reaction of **(S)-1b** (40 mg, 0.13 mmol) and $AgClO_4$ (130.2 mg, 0.63

mmol) in $CDCl_3$ (0.8 mL) for 5 min. After completion of the reaction, silver bromide was filtered, and the filtrate was evaporated and dried *in vacuo*. The residue was characterized by ^1H and ^{13}C NMR and optical rotation. $[\alpha]^{26}_D = -19.4°$ (c = 0.93, $CHCl_3$). ^1H and ^{13}C NMR data of **(R)-9ba** are identical to those of **(S)-9ba.**



(S)-9ca

(2S)-1,1-Dibenzyl-2-propylaziridin-1-ium perchlorate ((S)-9ca). The general procedure was followed for the reaction of **(R)-1c** (30 mg, 0.088 mmol) and $AgClO_4$ (89 mg, 0.43 mmol) in $CDCl_3$ (0.8 mL) for 5 min. After completion of the reaction, silver bromide was filtered, and the filtrate was evaporated and dried *in vacuo*. The residue was characterized by ^1H and ^{13}C NMR and optical rotation. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.95 (t, J = 7.3 Hz, 3H), 1.47-1.54 (m, 2H), 1.87-1.92 (m, 1H), 2.17-2.24 (m, 1H), 3.26-3.46 (m, 2H), 3.45-3.65 (m, 1H), 4.16 (dd, J = 13.8, 6.7 Hz, 2H), 4.41 (dd, J = 13.6, 10.8 Hz, 2H), 7.19-7.32 (m, 2H), 7.32-7.54 (m, 8H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 13.5 (q), 20.0 (t), 28.2 (t), 43.4 (t), 51.6 (d), 56.2 (t), 61.4 (t), 128.4 (s), 129.1 (s), 129.6 (d), 129.8 (d), 130.0 (d), 130.3 (d), 130.7 (d), 131.0 (d). $[\alpha]^{26}_D = +20.1°$ (c = 1.1, $CHCl_3$).

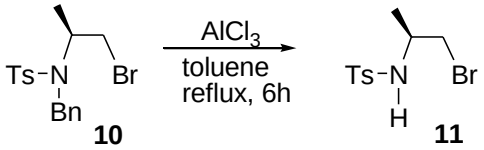


(R)-9ca

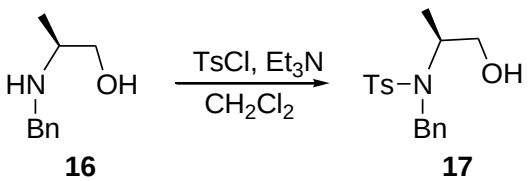
(2R)-1,1-Dibenzyl-2-propylaziridin-1-ium perchlorate ((R)-9ca). The general procedure was followed for the reaction of **(S)-1c** (30 mg, 0.088 mmol) and $AgClO_4$ (89

mg, 0.43 mmol) in $CDCl_3$ (0.8 mL) for 5 min. After completion of the reaction, silver bromide was filtered, and the filtrate was evaporated and dried *in vacuo*. The residue was characterized by ^1H and ^{13}C NMR and optical rotation. $[\alpha]^{26}_D = -24.8°$ (c = 0.89, $CHCl_3$). ^1H and ^{13}C NMR data of **(S)-9ca** are almost identical to those of **(S)-9ca.**

Lewis acid-promoted debenzylation of β-amino bromide 10 (Scheme 3)



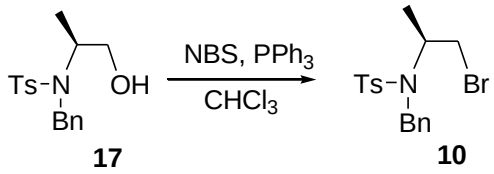
***N*-[(2S)-1-Bromopropan-2-yl]-4-methylbenzene-1-sulfonamide (11).** To the suspension of $AlCl_3$ (19.2 mg, 0.14 mmol) in toluene (1 mL), β-amino bromide **10** (25 mg, 0.065 mmol) in toluene (2 mL) was added dropwise over 15 min at 0 ^oC. The resulting reaction mixture was gradually warm to room temperature over 2 h and then was heated to reflux for 6 h. After the work-up, the residue was purified by column chromatography on silica gel (60-230 mesh) with 15% ethyl acetate in hexanes to afford **11** (18.5 mg, 97.5%). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17 (d, J = 6.6 Hz, 3H), 2.43 (s, 3H), 3.33-3.38 (m, 2H), 3.58-3.62 (m, 1H), 4.87 (d, J = 8.1 Hz, 1H), 7.32 (d, J = 8.3 Hz, 2H), 7.78 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 20.1 (q), 21.6 (q), 39.3 (t), 49.4 (d), 127.0 (d), 129.8 (d), 137.6 (s), 143.7 (s). $[\alpha]^{26}_D = -33.6$ (c = 0.8, $CHCl_3$). HRMS (ESI) Calcd for $C_{10}H_{14}BrNNaO_2S$ $[M + Na]^+$ *m/z* 313.9821. Found: $[M + Na]^+$ *m/z* 313.9856.



(2S)-*N*-Benzyl-1-hydroxy-S-(4-methylphenyl)propane-2-sulfonamido (17).[12] To a

solution of **16**[13] (120 mg, 0.73 mmol) and triethylamine (88.9 mg, 0.88 mmol) in CH_2Cl_2 (5 mL) at 0 ^oC was added tosyl chloride (152.5 mg, 0.8 mmol) portionwise in over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 30% ethyl acetate in hexanes to afford **17** (172.5 mg, 74%). ^1H NMR ($CDCl_3$, 300 MHz) δ 0.91 (d, J = 6.9 Hz, 3H), 1.75 (t, J = 6.3 Hz, 1H), 2.44 (s, 3H), 3.27 (t, J = 6.3 Hz, 2H), 3.99-4.06 (m, 1H), 4.16 (d, J = 15.6 Hz, 1H), 4.67 (d, J = 15.6 Hz, 1H), 7.25-7.36 (m, 5H), 7.42 (d, J = 6.9 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 14.1 (q), 21.6 (q), 47.5 (t), 56.0 (d), 64.8 (t), 127.1 (d), 127.8 (d), 127.9 (d), 128.8 (d), 129.8 (d), 137.7 (s), 138.1 (s), 143.5 (s).

$[\alpha]^{26}_D$ = + 33.5 (c = 0.6, $CHCl_3$).

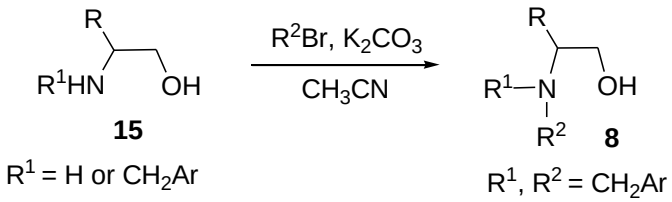


17 **10**

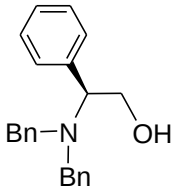
***N*-Benzyl-*N*-[(2S)-1-bromopropan-2-yl]-4-methylbenzene-1-sulfonamide (10)**. To a solution of **17**[12] (150 mg, 0.47 mmol) and PPh_3 (146.7 mg, 0.56 mmol) in $CHCl_3$ (5 mL) was added NBS (100.4 mg, 0.56 mmol) portionwise at 0 °C over 20 min. The resulting mixture was stirred for 4 h while being maintained at 0 °C. The ice bath was removed, and the reaction mixture was warmed to room temperature and stirred for 2 d and evaporated to dryness. The residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% ethyl acetate in hexanes to afford pure **10** (76.5 mg, 42.6%). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.15 (d, J = 6.9Hz, 3H), 2.44 (s, 3H), 2.88 (t, J = 9.9 Hz, 1H), 3.30 (dd, J = 9.9, 5.4Hz, 1H), 4.10-4.14 (m, 1H), 4.18 (d, J = 15.6Hz, 1H), 4.62 (d, J = 15.6 Hz, 1H), 7.26-7.39 (m, 7H), 7.73 (d, J = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 16.6 (q), 21.6 (q), 35.6 (t), 48.0 (t), 55.6 (d), 127.1 (d), 128.0 (d), 128.2 (d),

128.7 (d), 129.8 (d), 137.6 (s), 137.7 (s), 143.5 (s). $[\alpha]^{26}_{D} = -21.9^{o}$ (*c* = 1.0, $CHCl_3$). HRMS (ESI) Calcd for $C_{17}H_{20}BrNNaO_2S$ $[M + Na]^+$ *m/z* 404.0290. Found: $[M + Na]^+$ *m/z* 404.0320.

<u>Synthesis of β-amino alcohols 8</u> (Scheme 2)



General Procedure for synthesis of *N,N*-bisubstituted β-amino alcohols 8. To a solution of **15 (**1 equiv) and K_2CO_3 (2.2 equiv) in CH_3CN (15 mL) at 0 ^{o}C was added dropwise a solution of an alkylating agent (2.2 equiv) in CH_3CN (5 mL) over 20 min. The mixture was allowed to room temperature and stirred for 24 h and filtered. The filtrate was subject to evaporation *in vacuo*, and the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 5-10% ethyl acetate in hexanes to afford pure **8**.

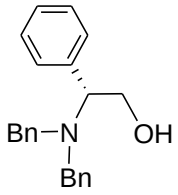


(S)-8a

(2S)-2-(Dibenzylamino)-2-phenylethan-1-ol ((S)-8a).[4] To a solution of **(S)-15a** (2 g, 14.6 mmol) and K_2CO_3 (4.2 g, 30.6 mmol) in CH_3CN (15 mL) at 0 ^{o}C was added dropwise a solution of benzyl bromide (5.1 g, 29.9 mmol) in CH_3CN (2 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 5% ethyl acetate in hexanes to afford **(S)-8a** (2.5 g, 54%).

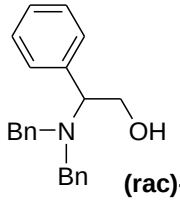
$[\alpha]^{26}_{D} = +136.9°$ (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.12 (br, 1H), 3.20 (d,

J = 13.2 Hz, 2H), 3.66-3.69 (m, 1H), 3.96-4.00 (m, 3H), 4.20 (dd, *J* = 10.5, 10.5 Hz, 1H), 7.32-7.47 (m, 15H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 53.6 (t), 60.5 (t), 63.1 (d), 127.4 (d). 128.1 (d), 128.5 (d), 128.7 (d), 129.1 (d), 129.4 (d), 135.1 (s), 139.2 (s).



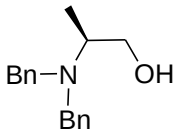
(R)-8a

(2R)-2-(Dibenzylamino)-2-phenylethan-1-ol ((R)-8a).[5] To a solution of (R)-**15a** (1.58 g, 11.5 mmol) and K_2CO_3 (2.68 g, 25.3 mmol) in CH_3CN (15 mL) at 0 ^oC was added dropwise a solution of benzyl bromide (4.04 g, 29.9 mmol) in CH_3CN (5 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 5% ethyl acetate in hexanes to afford **(R)-13a** (1.2 g, 32.9%). $[\alpha]^{26}_D$ = – 128.6° (*c* = 1.0, $CHCl_3$). ^{1}H and ^{13}C NMR data of **(R)-8a** are essentially identical to **(S)-8a**.



(rac)-8a

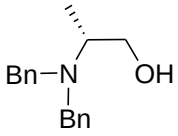
2-(Dibenzylamino)-2-phenylethan-1-ol ((rac)-8a).[6] To a solution of (rac)-**15a** (700 mg, 5.1 mmol) and K_2CO_3 (1.55 g, 11.2 mmol) in CH_3CN (2 mL) at 0 ^oC was added dropwise a solution of benzyl bromide (1.74 g, 10.2 mmol) in CH_3CN (3 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 5% ethyl acetate in hexanes to afford **(rac)-13a** (911 mg, 56%). ^{1}H and ^{13}C NMR are identical to those of **(S)-8a**.



(S)-8b

(2S)-2-(Dibenzylamino)propan-1-ol ((S)-8b).[8] To a solution of **(S)-15b** (2.5 g, 34 mmol) and K_2CO_3 (5.64 g, 40.8 mmol) in CH_3CN (15 mL) at 0 ^oC was added dropwise a solution of benzyl bromide (6.98 g, 40.8 mmol) in CH_3CN (5mL) over 20 min After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(S)-8b** (5.99 g, 69.1%).

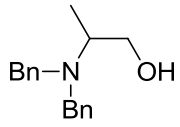
$[\alpha]^{26}_D$ = + 109.0° (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.01 (d, *J* = 6.6 Hz, 3H), 2.99-3.06 (m, 1H), 3.20 (br, 1H), 3.39 (d, *J* = 13.2 Hz, 3H), 3.50 (dd, *J* = 10.2, 10.2 Hz, 1H), 3.86 (d, *J* = 13.2 Hz, 2H), 7.28-7.34 (m, 10H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 8.7 (q), 53.0 (t), 54.2 (d), 62.8 (t), 127.3 (d), 128.5 (d), 129.0 (d), 139.3 (s).



(R)-8b

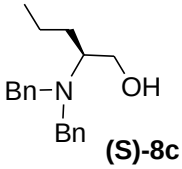
(2R)-2-(Dibenzylamino)propan-1-ol ((R)-8b).[10] To a solution of **(R)-15b** (530 mg, 7.1 mmol) and K_2CO_3 (2.0 g, 15 mmol) in CH_3CN (13 mL) at 0 ^oC was added dropwise a solution of benzyl bromide (2.5 g, 14.6 mmol) in CH_3CN (2 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(R)-8b** (1.6 g, 88.3%).

$[\alpha]^{26}_D$ = – 86.4° (*c* = 1.0, $CHCl_3$). ^1H and ^{13}C NMR data of **(R)-8b** are essentially identical to those of **(S)-8b**.



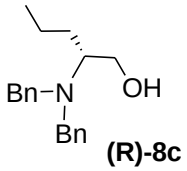
(rac)-8b

2-(Dibenzylamino)propan-1-ol ((rac)-8b). To a solution of **(rac)-15b** (1.0 g, 13.3 mmol) and K_2CO_3 (3.9 g, 27.9 mmol) in CH_3CN (20 mL) at 0 ^oC was added dropwise a solution of benzyl bromide (4.6 g, 27.3 mmol) in CH_3CN (15 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(rac)-8b** (2.0 g, 60%). ^1H and ^{13}C NMR are essentially identical to those of **(S)-8b**.



(S)-8c

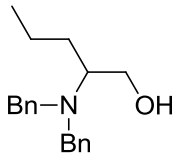
(2S)-2-(Dibenzylamino)pentan-1-ol ((S)-8c).[11] To a solution of **(S)-15c** (45.6 mg, 0.44 mmol) and K_2CO_3 (135.24 mg, 0.98 mmol) in CH_3CN (2 mL) at 0 ^oC was added dropwise a solution of benzyl bromide (153.9 mg, 0.9 mmol) in CH_3CN (1 mL) over 10 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(S)-8c** (99 mg, 80%). $[\alpha]^{26}_D$ = + 82.0° (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 0.96 (t, *J* = 6.9 Hz, 3H), 1.19-1.38 (m, 3H), 1.69-1.74 (m, 1H), 2.80-2.83 (m, 1H), 3.23 (br, 1H), 3.40-3.53 (m, 4H), 3.84 (d, *J* = 13.2 Hz, 2H), 7.24-7.36 (m, 10 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 14.5 (q), 20.4 (t), 27.2 (t), 53.2 (t), 58.7 (d), 60.9 (t), 127.4 (d), 128.5 (d), 129.1 (d), 139.4 (s).



(R)-8c

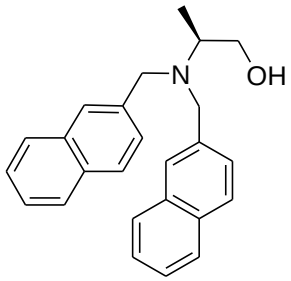
(2R)-2-(Dibenzylamino)pentan-1-ol ((R)-8c). To a solution of **(R)-15c** (197 mg, 1.9 mmol) and K_2CO_3 (554 mg, 4.0 mmol) in CH_3CN (4 mL) at 0 ^oC was added dropwise a solution of benzyl bromide (666 mg, 3.9 mmol) in CH_3CN (2 mL) over 10 min. After the work-up, the crude mixture was purified via chromatography on silica gel (60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(R)-8c** (490 mg, 91%).

$[\alpha]^{26}_D$ = – 82.7° (*c* = 1.0, $CHCl_3$). ^1H and ^{13}C NMR data of **(R)-8c** are essentially identical to those of **(S)-8c**.



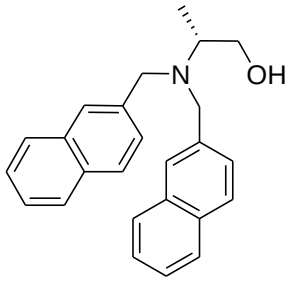
(rac)-8c

2-(Dibenzylamino)pentan-1-ol ((rac)-8c). To a solution of **(rac)-15c** (500 mg, 4.85 mmol) and K_2CO_3 (1.5 g, 10.7 mmol) in CH_3CN (6 mL) at 0 ^oC was added dropwise a solution of benzyl bromide (1.66 g, 9.7 mmol) in CH_3CN (4 mL) over 10 min. After the work-up, the crude mixture was purified via chromatography on silica gel (60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(rac)-8c** (952 mg, 69.4%). ^1H and ^{13}C NMR data of **(rac)-8c** are identical to those of **(S)-8c**.



(S)-8d

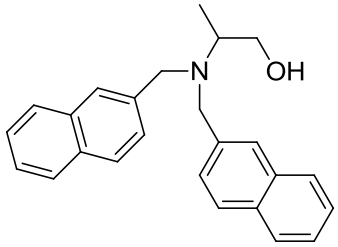
(2S)-2-[Bis(naphthalen-2-ylmethyl)amino]propan-1-ol ((S)-8d). To a solution of **(S)-15d** (288 mg, 3.8 mmol) and K_2CO_3 (1.2 g, 8.4 mmol) in CH_2Cl_2 (4 mL) at 0 ^oC was added dropwise a solution of 2-bromomethyl naphthalene (1.68 g, 7.6 mmol) in CH_2Cl_2 (2 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(S)-8d** (600 mg, 50%). $[\alpha]^{26}_D = -48.0°$ (*c* = 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.07 (d, *J* = 6.6 Hz, 3H), 3.05-3.12 (m, 1H), 3.19 (br, 1H), 3.34-3.39 (m, 1H), 3.58 (d, *J* = 13.2 Hz, 2H), 4.03 (d, *J* = 13.2 Hz, 2H), 7.44-7.52 (m, 6H), 7.74 (s, 2H), 7.80-7.85 (m, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 8.8 (q), 53.2 (t), 54.2 (d), 62.8 (t), 125.8 (d), 126.1 (d), 127.0 (d), 127.6 (d), 127.8 (d), 127.9 (d), 128.5 (d), 132.8 (s), 133.3 (s), 136.8 (s). HRMS (ESI) Calcd for $C_{25}H_{26}NO$ $[M + H]^+$ *m/z* 356.2009. Found: $[M + H]^+$ *m/z* 356.2017.



(R)-8d

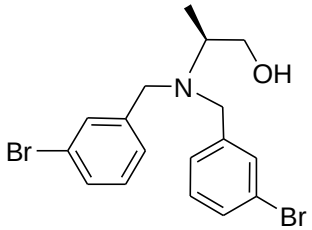
(2R)-2-[Bis(naphthalen-2-ylmethyl)amino]propan-1-ol ((R)-8d). To a solution of **(R)-15d** (42 mg, 0.56 mmol) and K_2CO_3 (170 mg, 1.23 mmol) in CH_3CN (1 mL) at 0 ^oC was added dropwise a solution of 2-bromomethyl naphthalene (272 mg, 1.23 mmol) in

CH_3CN (1 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(R)-8d** (84 mg, 42%). $[\alpha]^{26}_D$ = + 41.8° (*c* = 1.0, $CHCl_3$). ^1H and ^{13}C NMR data of **(R)-8d** are identical to those of **(S)-8d**.



(rac)-8d

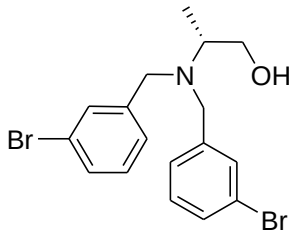
2-[Bis(naphthalen-2-ylmethyl)amino]propan-1-ol ((rac)-8d). To a solution of **(rac)-15d** (808 mg, 10.8 mmol) and K_2CO_3 (3.1 g, 22.6 mmol) in CH_3CN (10 mL) at 0 ^oC was added dropwise a solution of 2-bromomethyl naphthalene (4.88 g, 22.1 mmol) in CH_3CN (10 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(rac)-8d** (1.7 g, 44.3%). ^1H and ^{13}C NMR are identical to those of (S)-**8d**.



(S)-8e

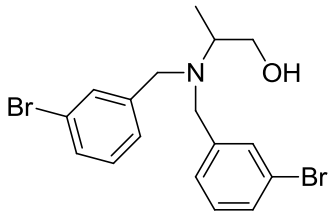
(2S)-2-{Bis[(3-bromophenyl)methyl]amino}propan-1-ol ((S)-8e). To a solution of **(S)-15e** (207 mg, 2.8 mmol) and K_2CO_3 (800 mg, 5.8 mmol) in CH_3CN (5 mL) at 0 ^oC was added dropwise a solution of 3-bromobenzyl bromide (1.4 g, 5.7 mmol) in CH_3CN (2 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel

(60-230 mesh) eluted with 15% ethyl acetate in hexanes to afford **(S)-8e** (814 mg, 70%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.99 (d, J = 6.6 Hz, 3H), 2.77 (br, 1H), 2.93-3.00 (m, 1H), 3.38 (d, J = 13.5 Hz, 2H), 3.46 (dd, J = 21.0, 10.8 Hz, 2H), 3.76 (d, J = 13.5 Hz, 2H), 7.16-7.24 (m, 4H), 7.36-7.40 (m, 4H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 9.0 (q), 52.8 (t), 54.9 (d), 62.9 (t), 122.6 (s), 127.5 (d), 130.2 (d), 130.5 (d), 132.0 (d), 141.5 (s). $[\alpha]^{26}_D$ = + 43.8° (c = 1.0, $CHCl_3$). HRMS (ESI) Calcd for $C_{17}H_{19}Br_2NO$ $[M]^+$ *m/z* 413.1469. Found: $[M]^+$ *m/z* 413.9880.



(R)-8e

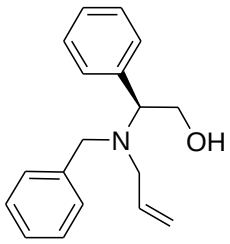
(2R)-2-{Bis[(3-bromophenyl)methyl]amino}propan-1-ol ((R)-8e). To a solution of **(R)-15e** (41 mg, 0.55 mmol) and K_2CO_3 (166 mg, 1.2 mmol) in CH_3CN (1 mL) at 0 ^{o}C was added dropwise a solution of 3-bromobenzyl bromide (300 mg, 1.2 mmol) in CH_3CN (1mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 5% ethyl acetate in hexanes to afford **(R)-8e** (100 mg, 44%). ^{1}H and ^{13}C NMR are identical to **(S)-8e**. $[\alpha]^{26}_D$ = – 41.2° (c = 1.0, $CHCl_3$).



(rac)-8e

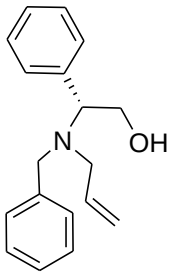
2-{Bis[(3-bromophenyl)methyl]amino}propan-1-ol ((rac)-8e). To a solution of **(rac)-15e** (219 mg, 2.9 mmol) and K_2CO_3 (846 mg, 6.1 mmol) in CH_3CN (5 mL) at 0 ^{o}C was

added dropwise a solution of 3-bromobenzyl bromide (1.49 g, 5.9 mmol) in CH_3CN (2 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 5% ethyl acetate in hexanes to afford **(rac)-8e** (740 mg, 61.8%). ^1H and ^{13}C NMR are identical to **(S)-8e.**



(S)-8f

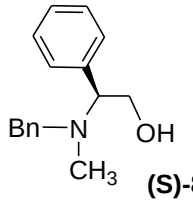
(2S)-2-[Benzyl(prop-2-en-1-yl)amino]-2-phenylethan-1-ol ((S)-8f). To a solution of **(S)-15f** (250 mg, 1.1 mmol) and Na_2CO_3 (140 mg, 1.32 mmol) in CH_3CN (6 mL) at 0 ^oC was added dropwise a solution of allyl bromide (159.7 mg, 1.32 mmol) in CH_3CN (2 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 5% ethyl acetate in hexanes to afford **(S)-8f** (177.5 mg, 60%). ^1H NMR ($CDCl_3$, 300 MHz) δ 2.84(dd, J = 14.1, 8.4 Hz, 1H), 3.16(d, J = 13.8 Hz, 2H), 3.41-3.47 (m, 1H), 3.68 (dd, J = 9.0, 3.6 Hz, 1H), 3.97-4.16 (m, 3H), 5.22-5.30 (m, 2H), 5.86-5.91 (m, 1H), 7.27-7.47 (m, 10H);^{13}C NMR ($CDCl_3$, 300 MHz) δ 52.6 (t), 53.6 (t), 60.6 (t), 63.5 (d), 118.1 (t), 127.3 (d), 128.0 (d), 128.4 (d), 128.6 (d), 128.8 (d), 128.9 (d), 129.2 (d), 135.6 (s), 136.5 (d), 139.3 (s). $[\alpha]^{26}_D$ = + 134.9 (c = 1.0, $CHCl_3$). HRMS (ESI) Calcd for $C_{18}H_{22}NO$ $[M + H]^+$ *m/z* 268.1696. Found: $[M + H]^+$ *m/z* 268.1710.



(R)-8f

(2R)-2-[benzyl(prop-2-en-1-yl)amino]-2-phenylethan-1-ol ((R)-8f). To a stirred solution of **(R)-15f** (250 mg, 1.10 mmol) in CH_3CN (3 mL) was added K_2CO_3 (227.7 mg, 1.65 mmol) at 0 ^oC. Then the solution of allyl bromide (263.5 mg, 1.65 mmol) in CH_3CN (2 mL) at 0 ^oC was added dropwise. The reaction mixture was gradually warmed to RT and stirred for 24 h while the reaction progress was continuously monitored using TLC. The reaction mixture was filtered and concentrated *in vacuo*. The crude *N*-benzyl, *N*-methyl amino alcohol was purified via column chromatography on silica gel (60-230 mesh) eluted with 10% Ethyl acetate in hexanes to afford pure diakylated amino alcohol (184 mg, 62.5%). $[\alpha]^{26}_D = -99.9$ (c = 2.1, $CHCl_3$).

^1H and ^{13}C NMR data of **(R)-8f** are essentially identical to those of **(S)-8f**.



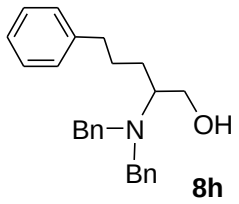
(S)-8g

(2S)-2-[benzyl(methyl)amino]-2-phenylethan-1-ol ((S)-8g).[14] To a stirred solution of **15g**[15] (250 mg, 1.10 mmol) in CH_3CN (5 mL) was added Na_2CO_3 (140 mg, 1.32 mmol) at 0 ^oC. Then the solution of dimethyl sulfate (166.5 mg, 1.32 mmol) in CH_3CN (3 mL) at 0 ^oC was added dropwise. The reaction mixture was gradually warmed to RT and stirred for 24 h while the reaction progress was continuously monitored using TLC. The reaction mixture was filtered and concentrated *in vacuo*. The crude *N*-benzy, *N*-methyl amino alcohol was purified via column chromatography on silica gel (60-230 mesh) eluted with 15% Ethyl acetate in hexanes to afford pure diakylated amino alcohol (154.4 mg, 60%).

^1H NMR ($CDCl_3$, 300 MHz) δ 2.18 (s, 3H), 3.27 (br, 1H), 3.40 (d, J = 13.2 Hz, 1H),

3.65-3.76 (m, 2H), 3.90 (dd, *J* = 9.6, 5.1 Hz, 1H), 4.11 (dd, *J* = 9.9, 9.9 Hz, 1H), 7.28-7.46 (m, 10H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 36.8 (q), 58.5 (t), 60.7 (t), 68.1 (d), 127.1 (d), 128.0 (d), 128.3 (d), 128.4 (d), 128.9 (d), 129.1 (d), 135.3 (s), 138.9 (s).

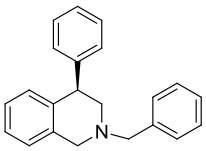
$[\alpha]^{26}_{D}$ = + 7.6 (c = 1.0 $CHCl_3$).



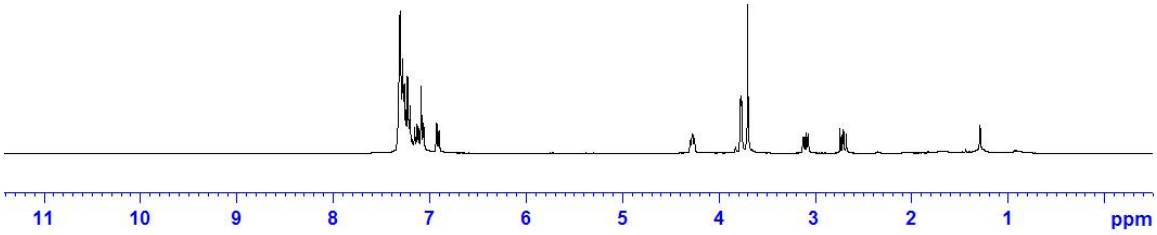
8h

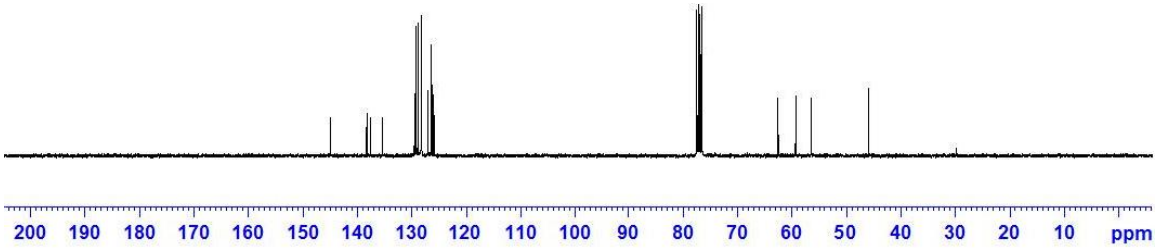
2-(Dibenzylamino)-5-phenylpentan-1-ol (8h). To a solution of **15h** (200 mg, 1.1 mmol) and K_2CO_3 (339 mg, 2.46 mmol) in CH_3CN (4 mL) at 0 ^{o}C was added dropwise a solution of benzyl bromide (420 mg, 2.5 mmol) in CH_3CN (1 mL) over 20 min. After the work-up, the residue was purified via chromatography on silica gel (60-230 mesh) eluted with 5% ethyl acetate in hexanes to afford **8h** (400 mg, 100%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.29-1.33 (m, 1H), 1.60-1.71 (m, 2H), 1.76-1.83 (m, 1H), 2.66 (dd, *J* = 7.5, 7.5 Hz, 2H), 2.84-2.88 (m, 1H), 3.44 (d, *J* = 13.5 Hz, 2H), 3.50-3.58 (m, 1H), 3.84 (d, *J* = 13.5 Hz, 2H), 7.20-7.37 (m, 15H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 24.7 (t), 28.8 (t), 36.1 (t), 53.3 (t), 59.1 (d), 61.0 (t), 126.0 (d), 127.3 (d), 128.4 (d), 128.5 (d), 128.6 (d), 128.8 (d), 129.1 (d), 139.3 (s), 142.0 (s). HRMS (ESI) Calcd for $C_{25}H_{30}NO$ $[M + H]^+$ *m/z* 360.2322. Found: $[M + H]^+$ *m/z* 360.2350.

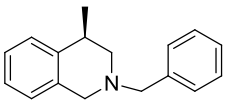
^{1}H and ^{13}C NMR spectra of THIQ analogues 5



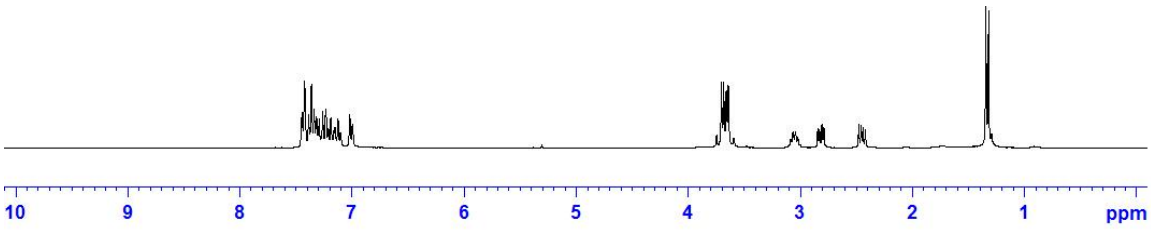
(R)-5a

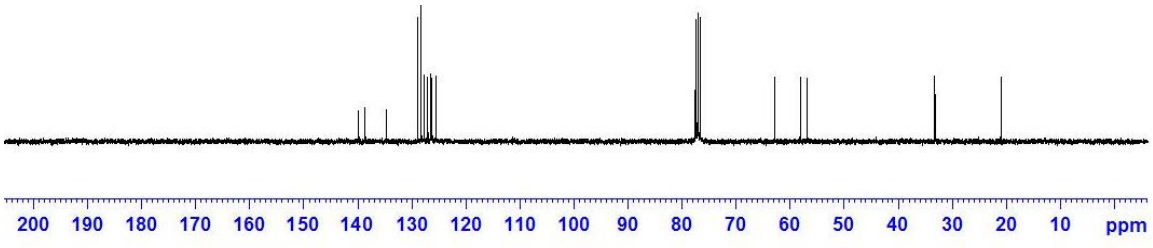


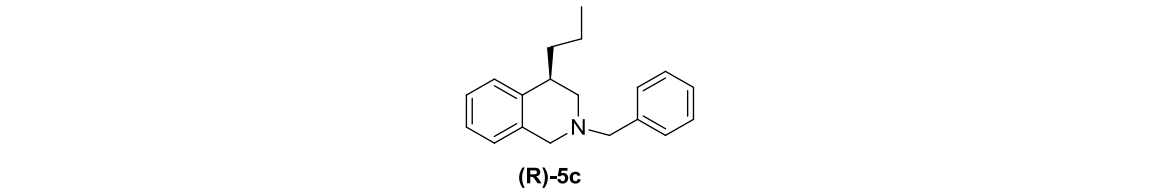




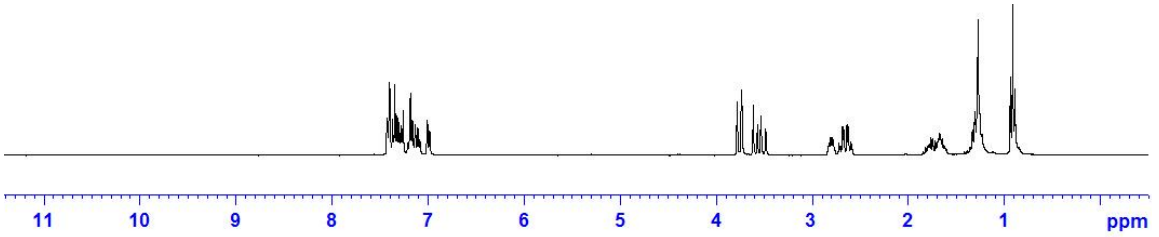
(R)-5b

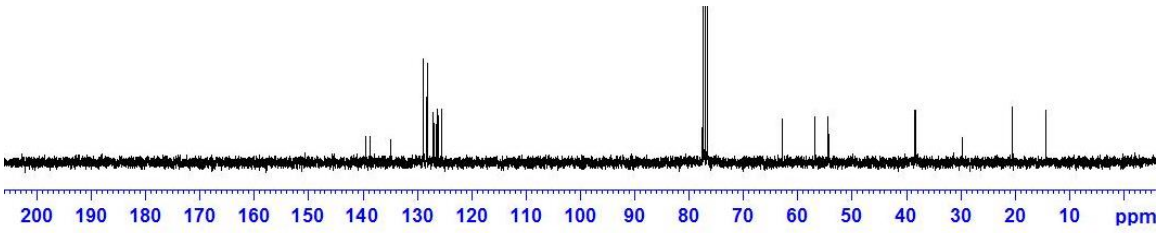


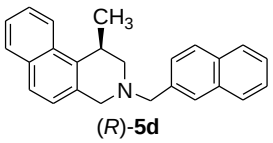




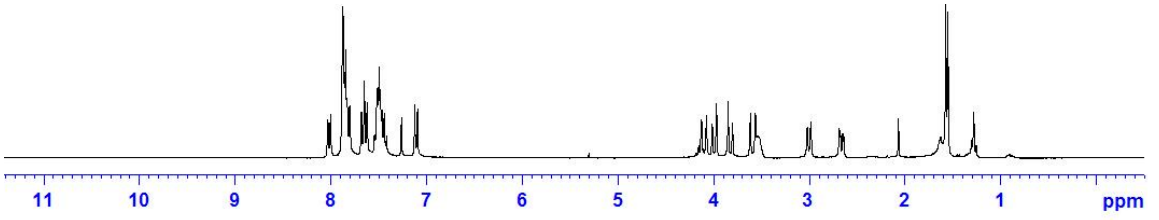
(R)-5c

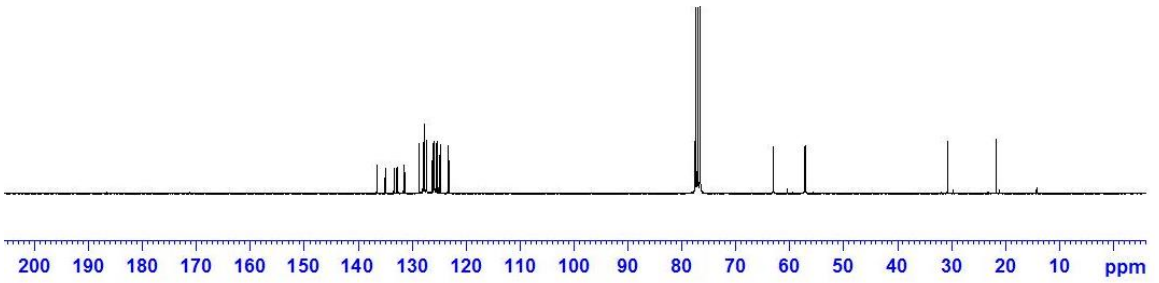

11 10 9 8 7 6 5 4 3 2 1 ppm

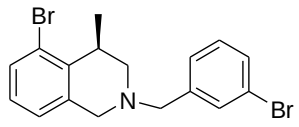

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


CH3
N

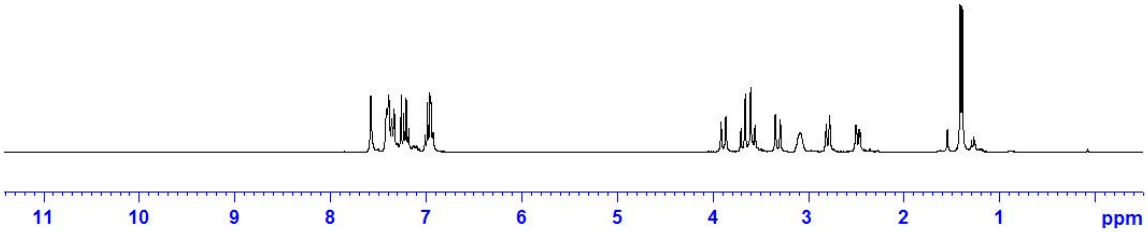
(*R*)-**5d**

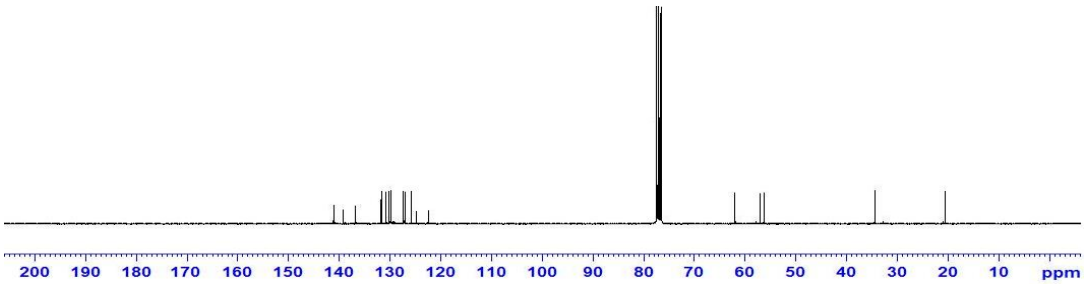

11 10 9 8 7 6 5 4 3 2 1 ppm

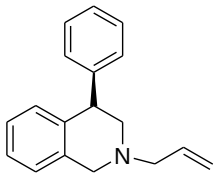

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Br
N
Br

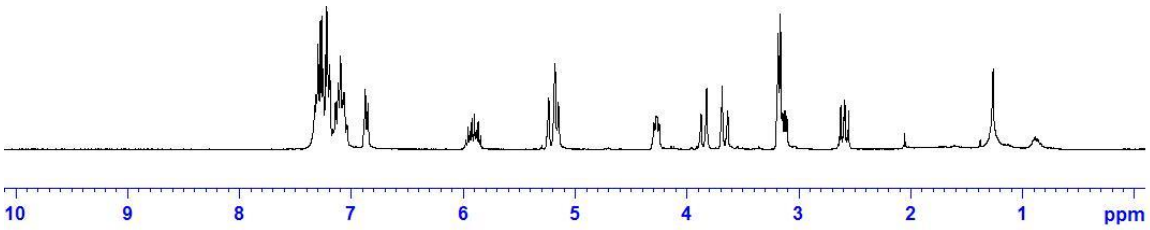
(R)-5e

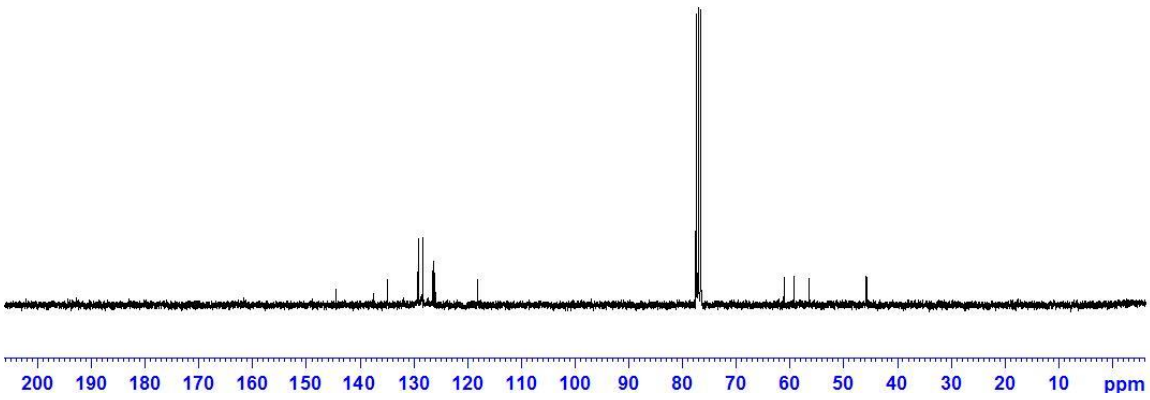

11 10 9 8 7 6 5 4 3 2 1 ppm

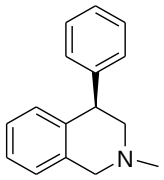

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


N

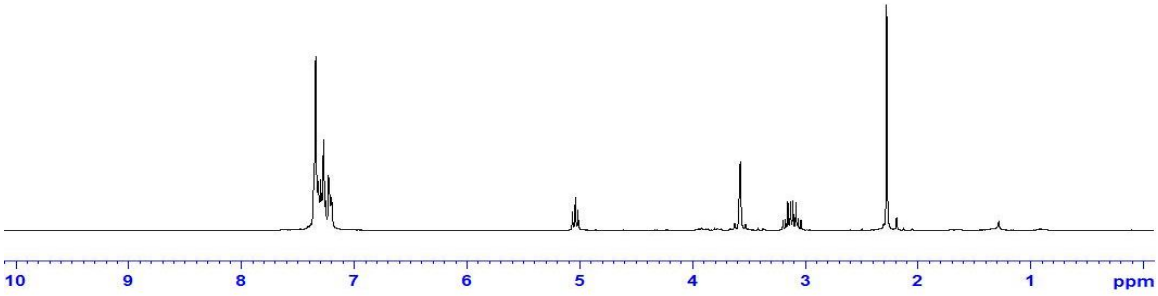
(R)-5f

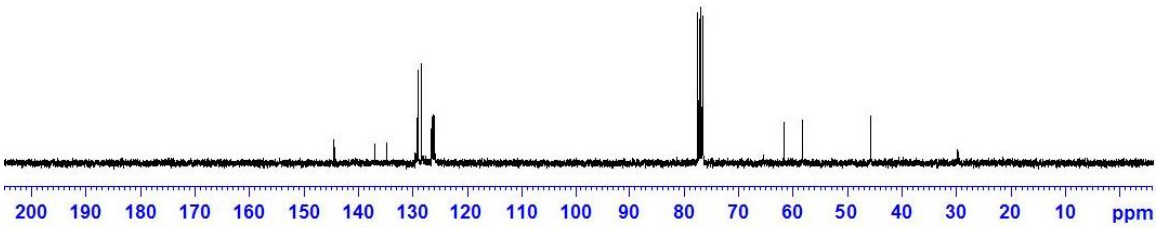

10 9 8 7 6 5 4 3 2 1 ppm

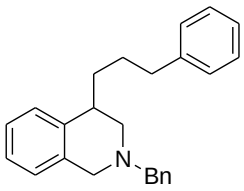

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



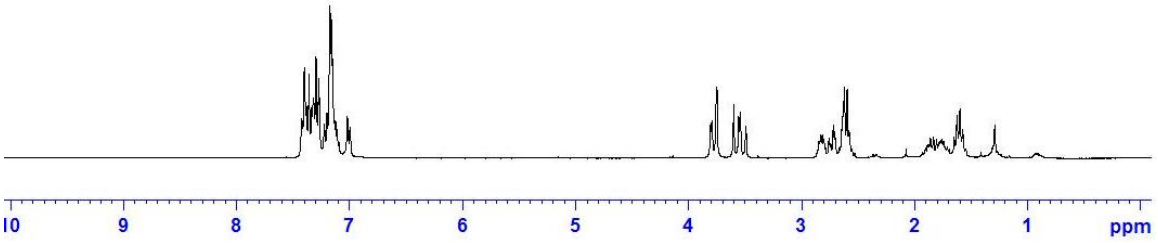
(R)-**5g**

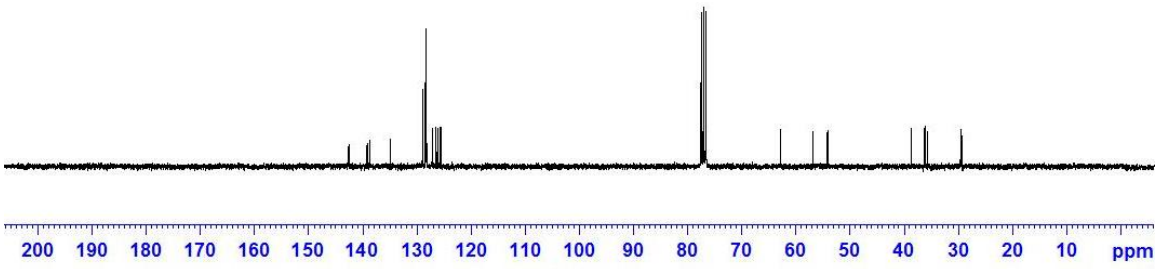

10 9 8 7 6 5 4 3 2 1 ppm


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

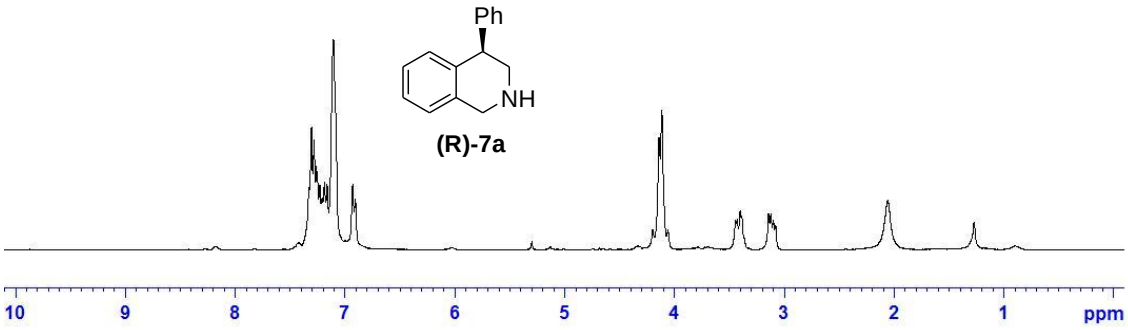

N
Bn

(rac)-5h

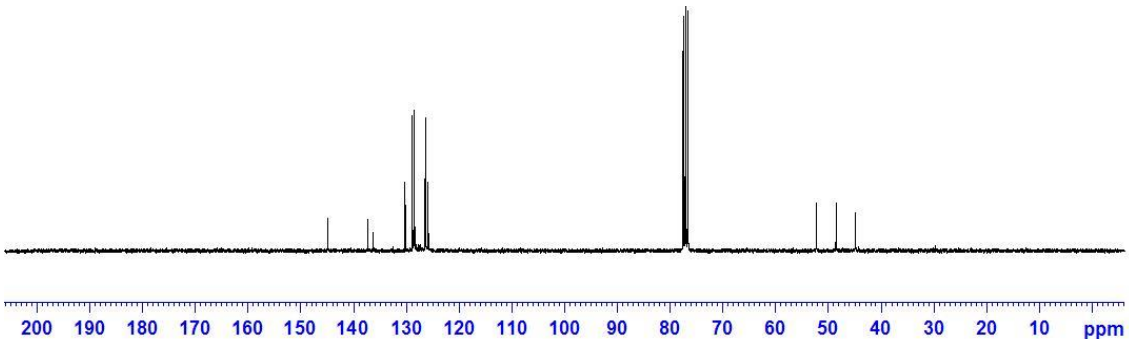

10 9 8 7 6 5 4 3 2 1 ppm

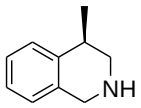

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

^{1}H and ^{13}C NMR spectra of THIQs 7

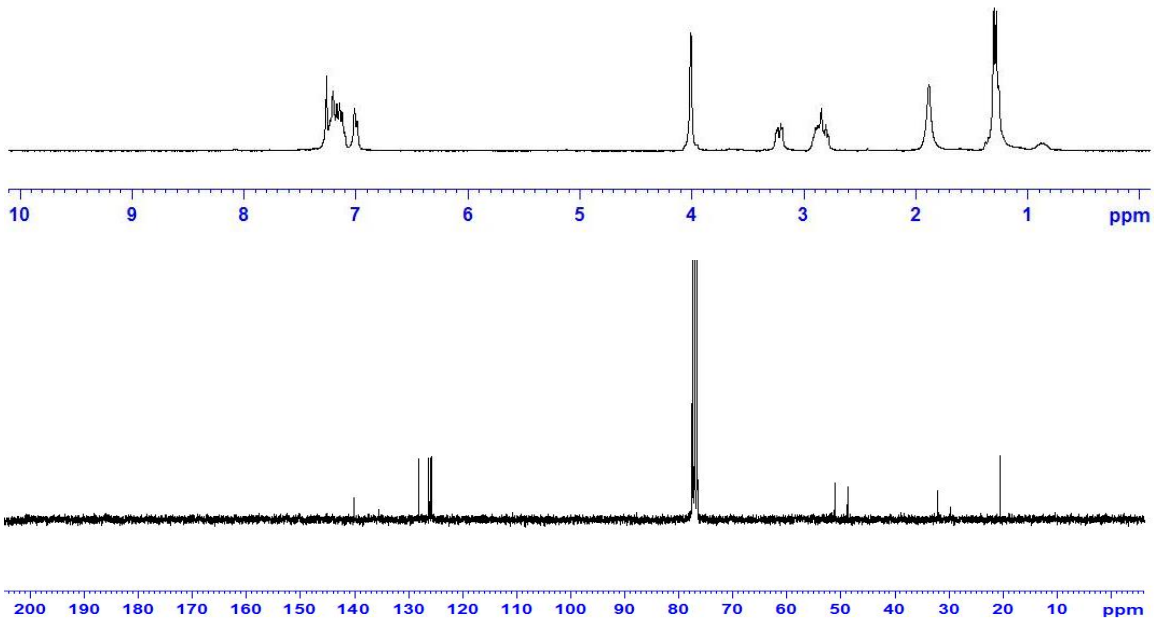


(R)-7a

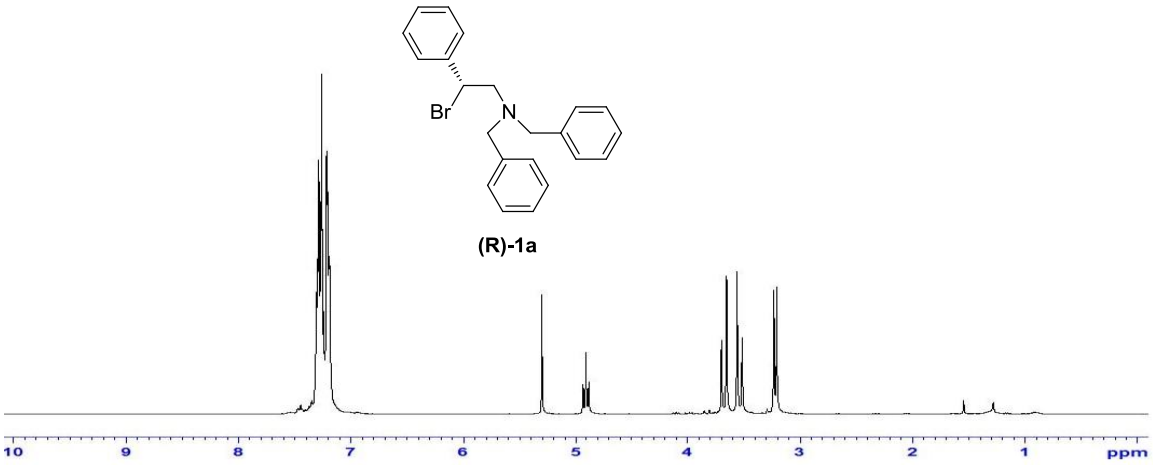




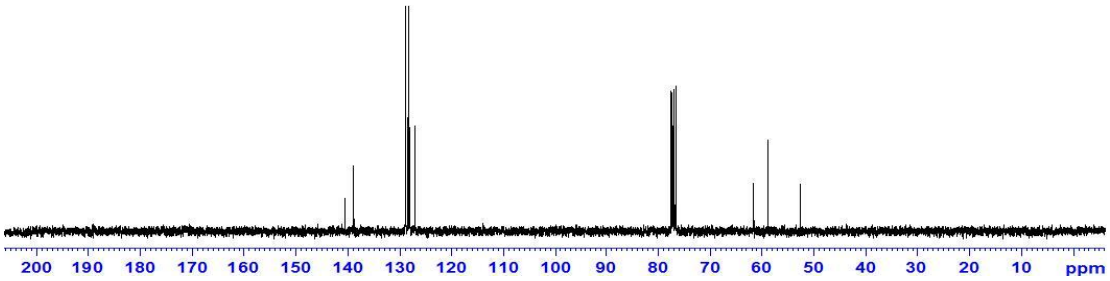
(R)-7b

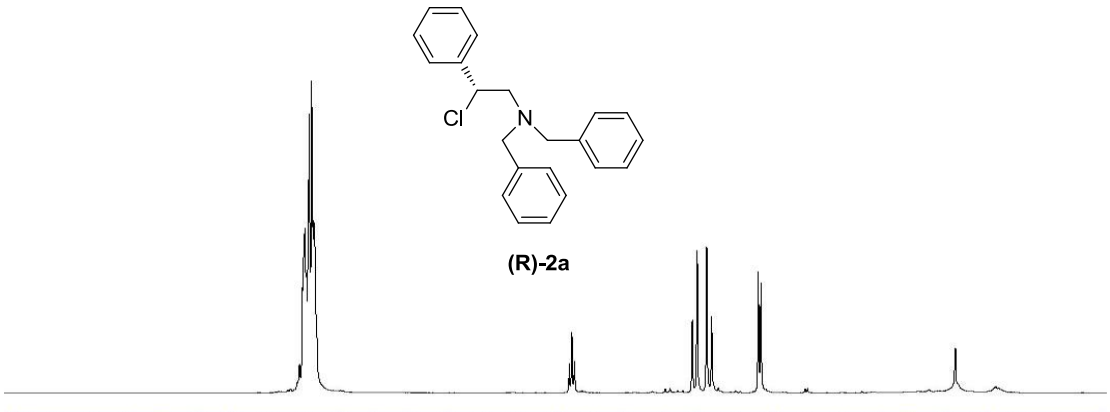


^{1}H and ^{13}C NMR spectra of substituted β-haloamines 1, 2, 3, 10, and 11

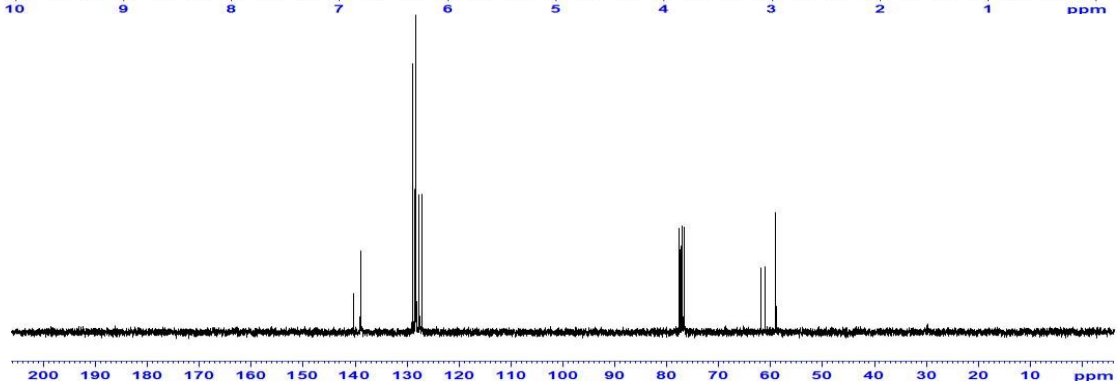


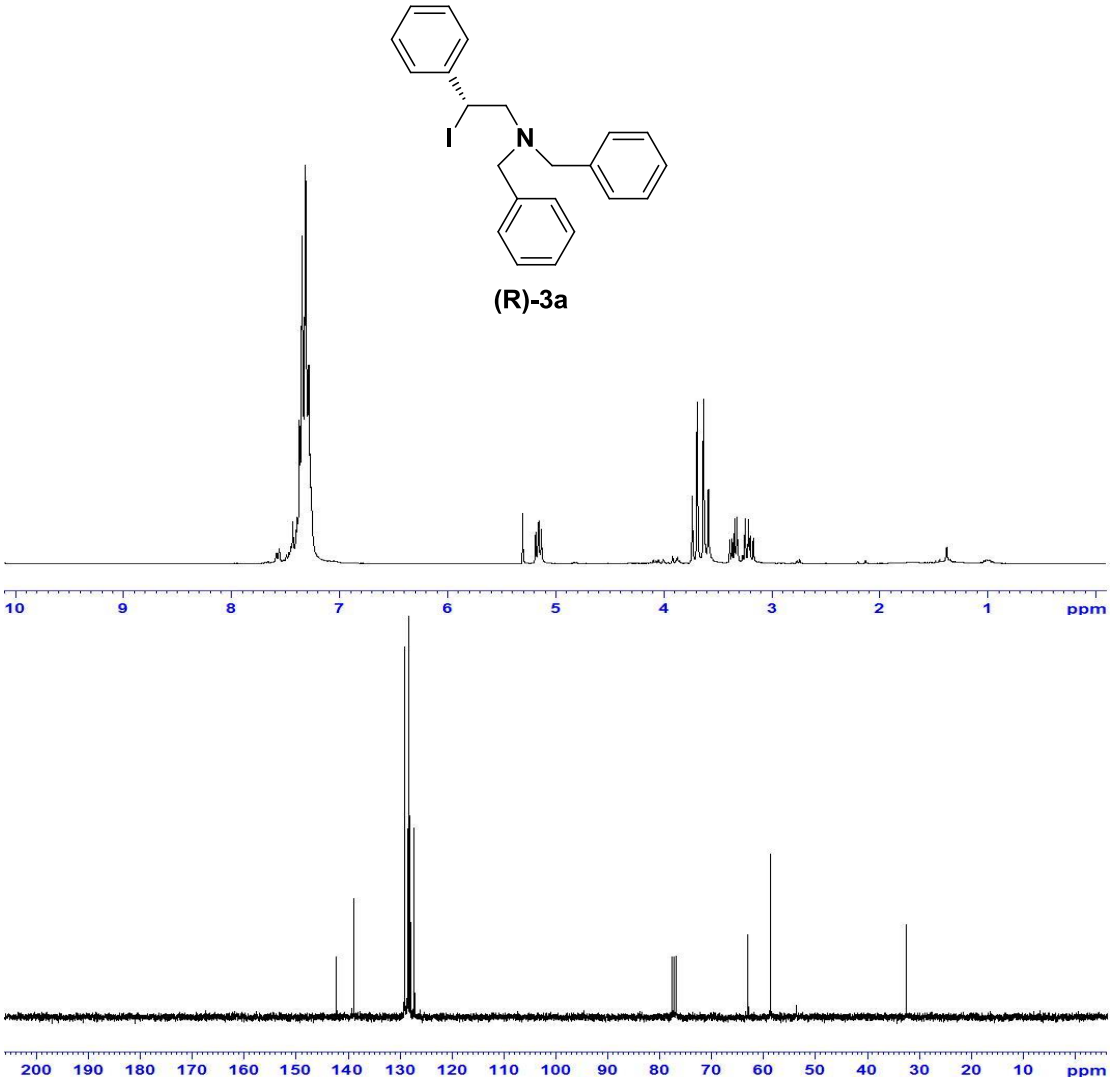
(R)-1a

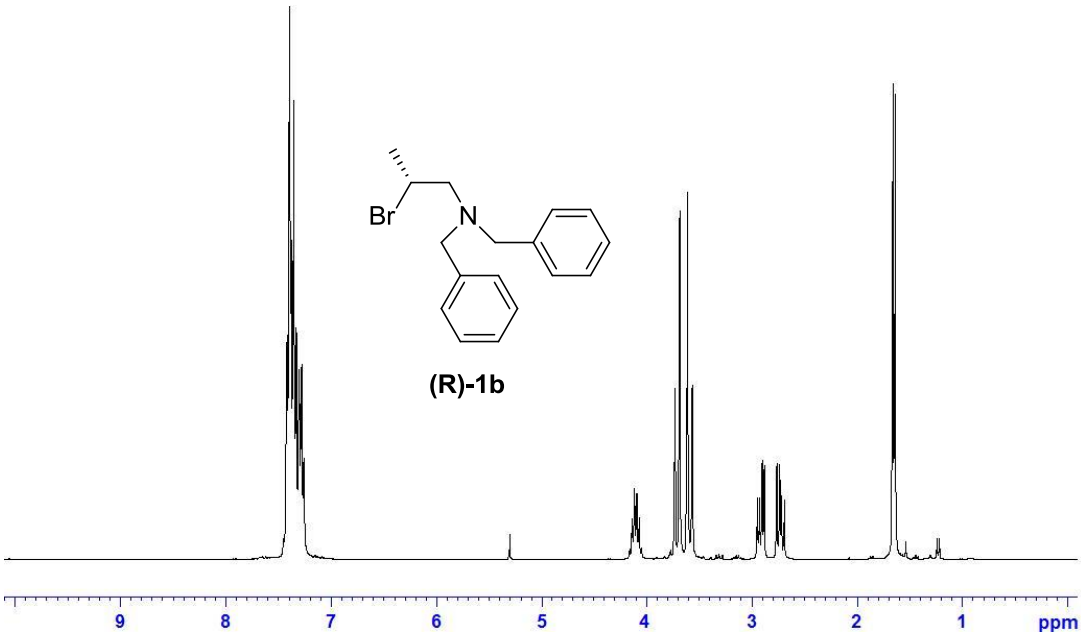


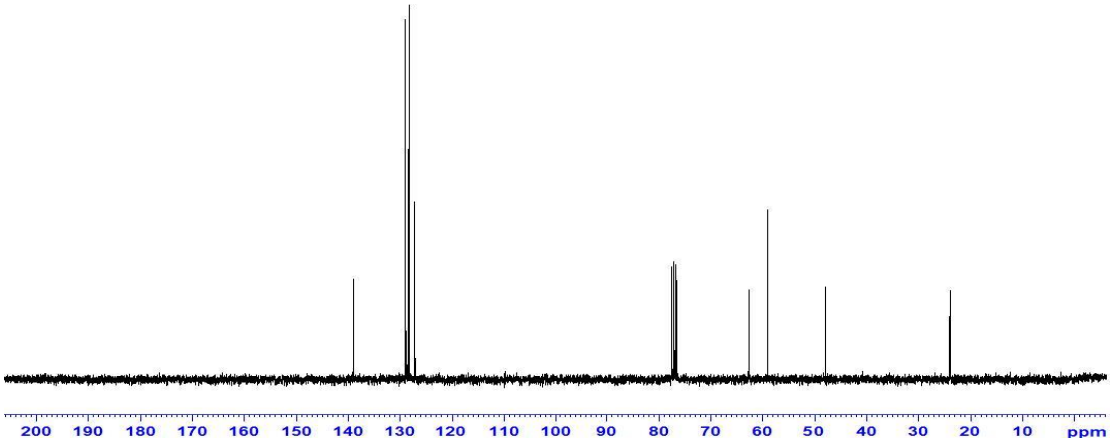


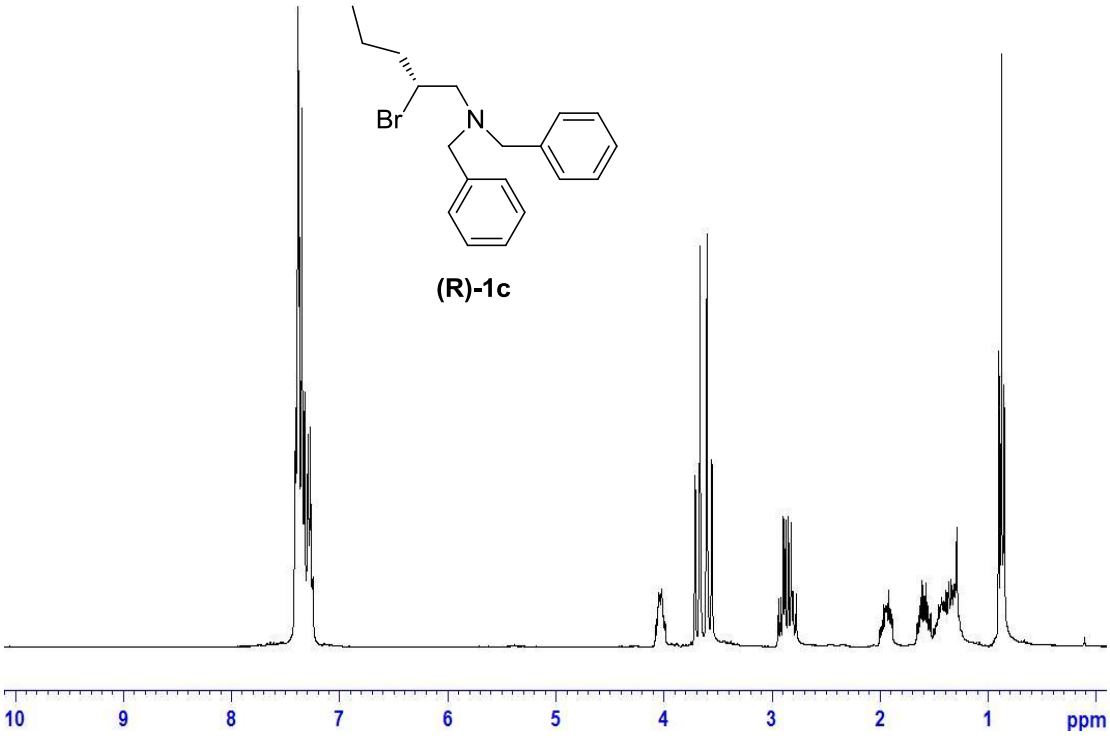
(R)-2a



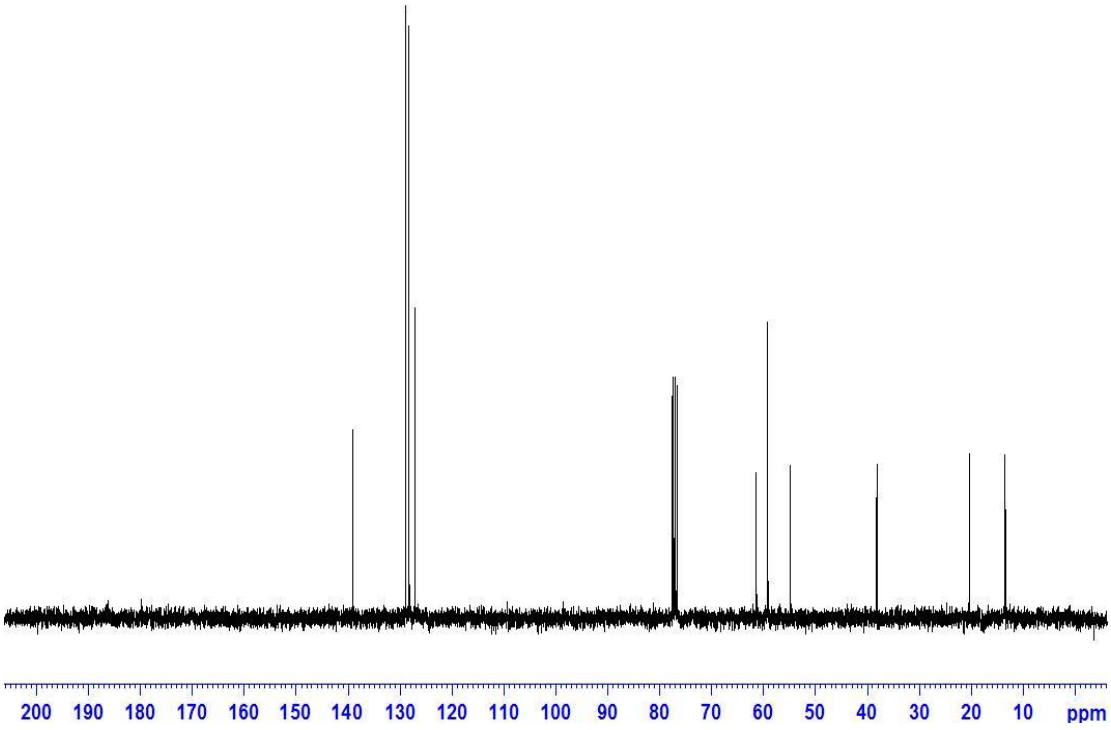

I
N
(R)-3a
10
9
8
7
6
5
4
3
2
1
ppm
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

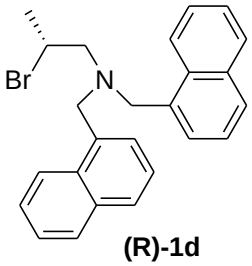

Br
N
(R)-1b
9
8
7
6
5
4
3
2
1
ppm


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

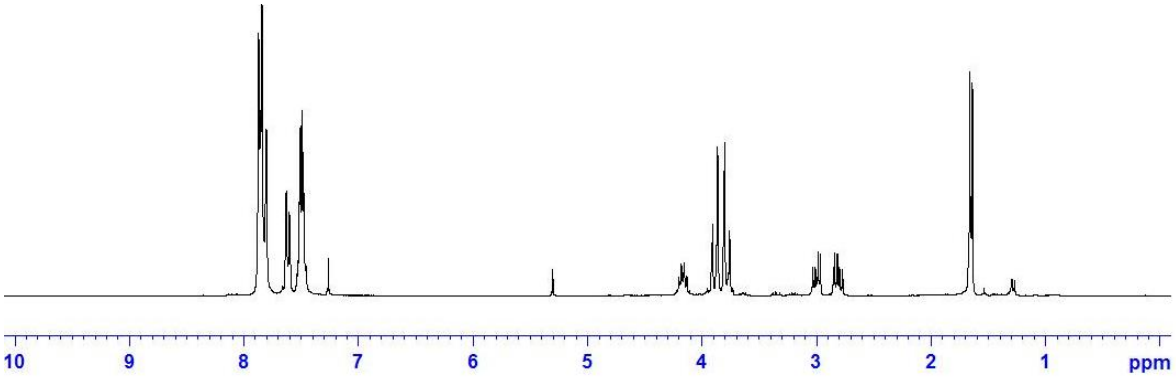

Br
N
10 9 8 7 6 5 4 3 2 1 ppm

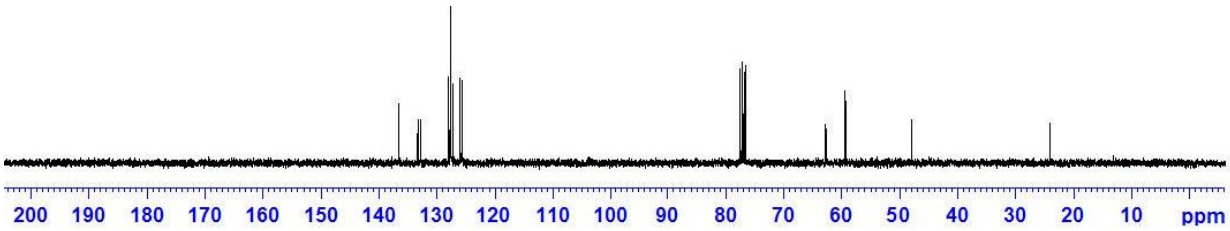
(R)-1c

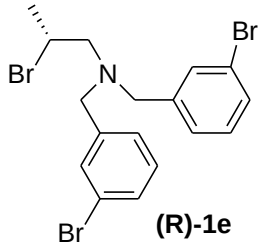

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Br
N

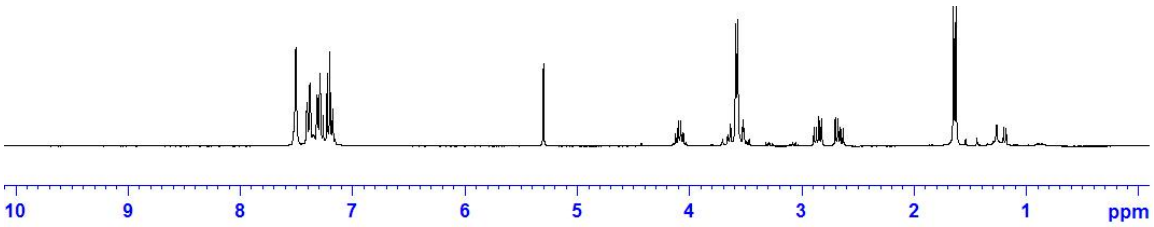
(R)-1d

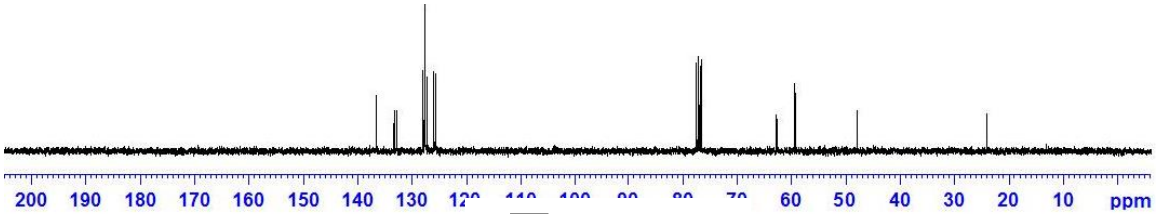

10 9 8 7 6 5 4 3 2 1 ppm

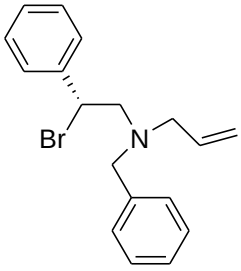

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Br
Br
N
Br

(R)-1e

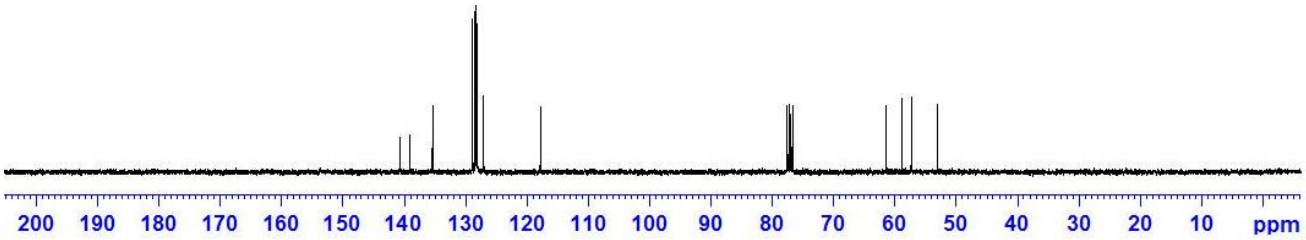

10 9 8 7 6 5 4 3 2 1 ppm

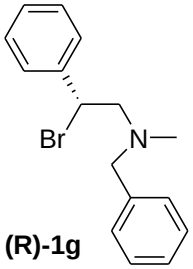

200 190 180 170 160 150 140 130 60 50 40 30 20 10 ppm


Br
N

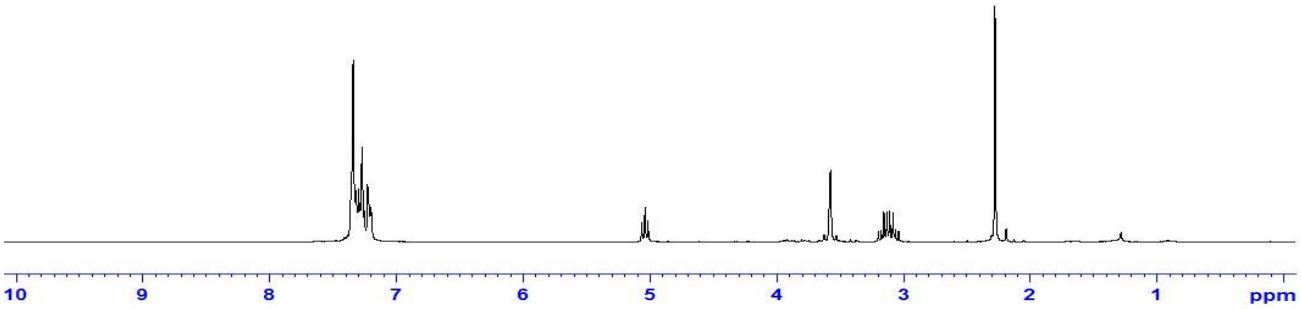
(R)-1f

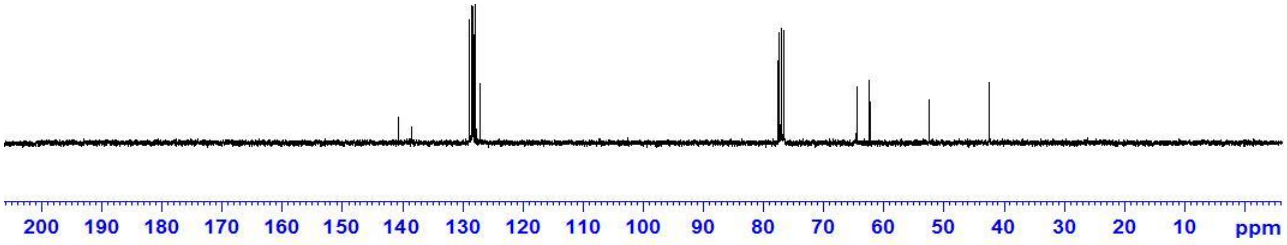
10 9 8 7 6 5 4 3 2 1 ppm

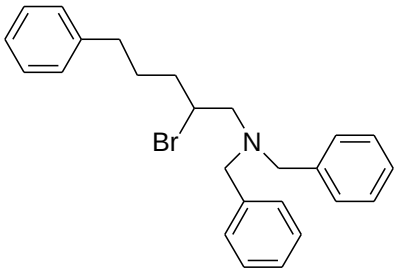

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Br
N

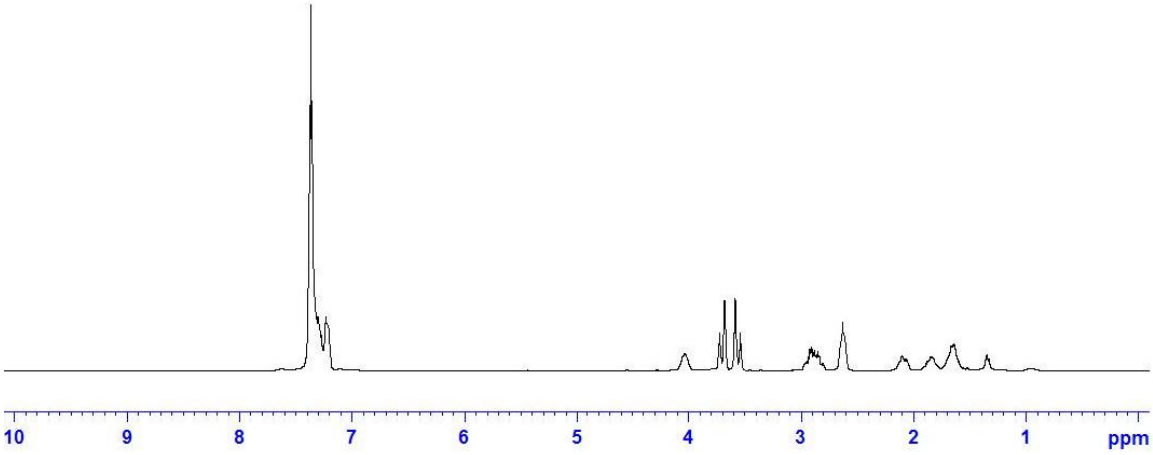
(R)-1g

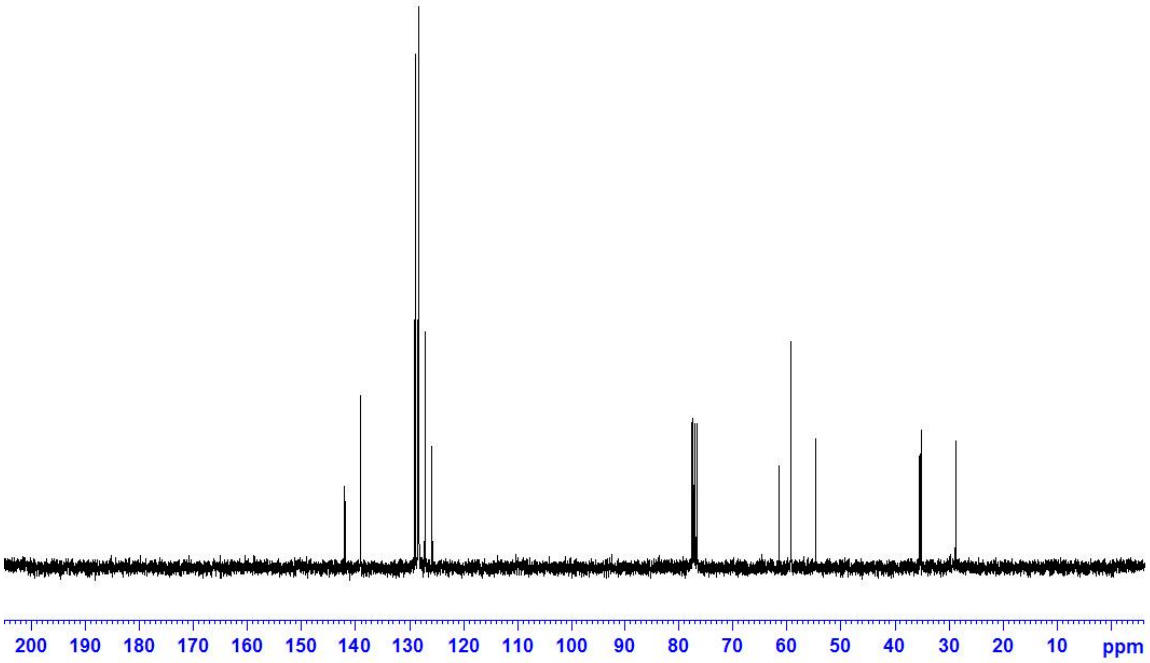

10 9 8 7 6 5 4 3 2 1 ppm

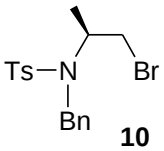

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Br
N

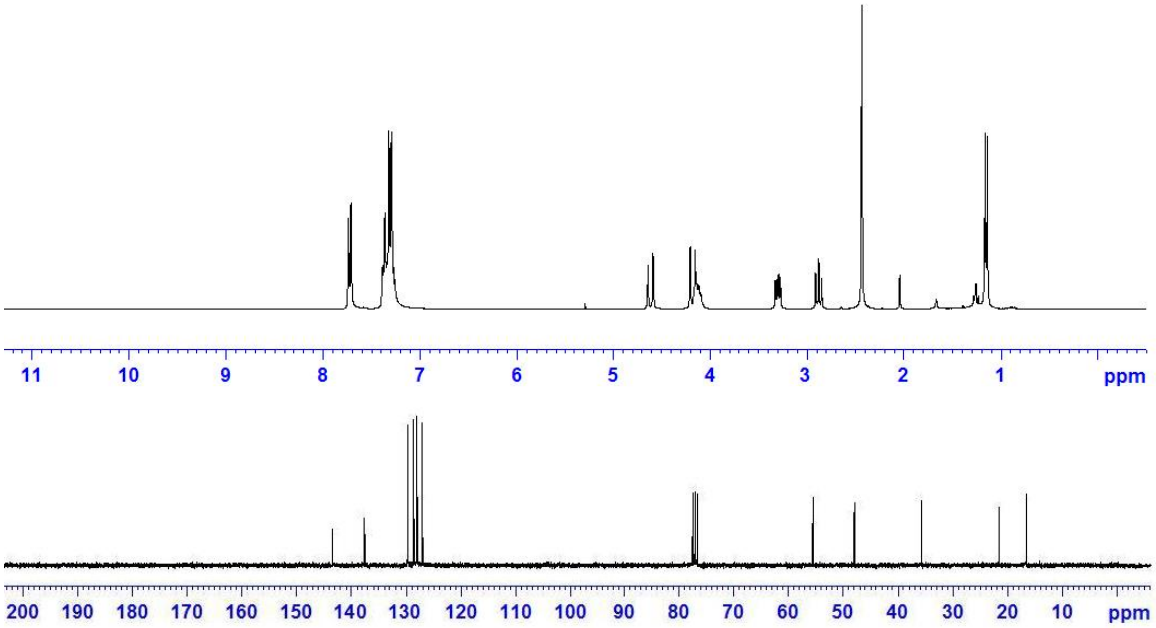
(*rac*)-1h

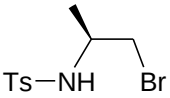

10
9
8
7
6
5
4
3
2
1
ppm


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

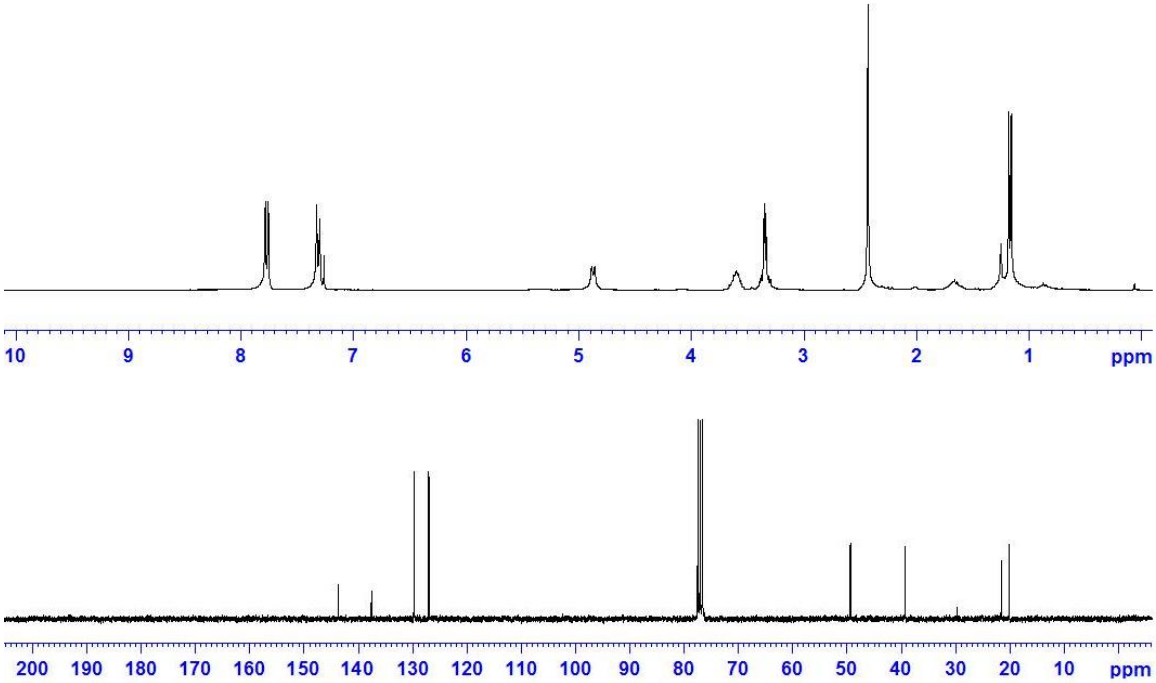

Ts—N
Br
Bn

10

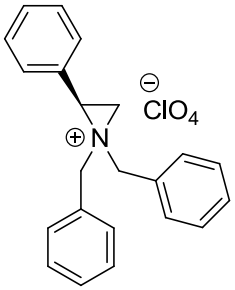

11 10 9 8 7 6 5 4 3 2 1 ppm
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Ts—NH
Br

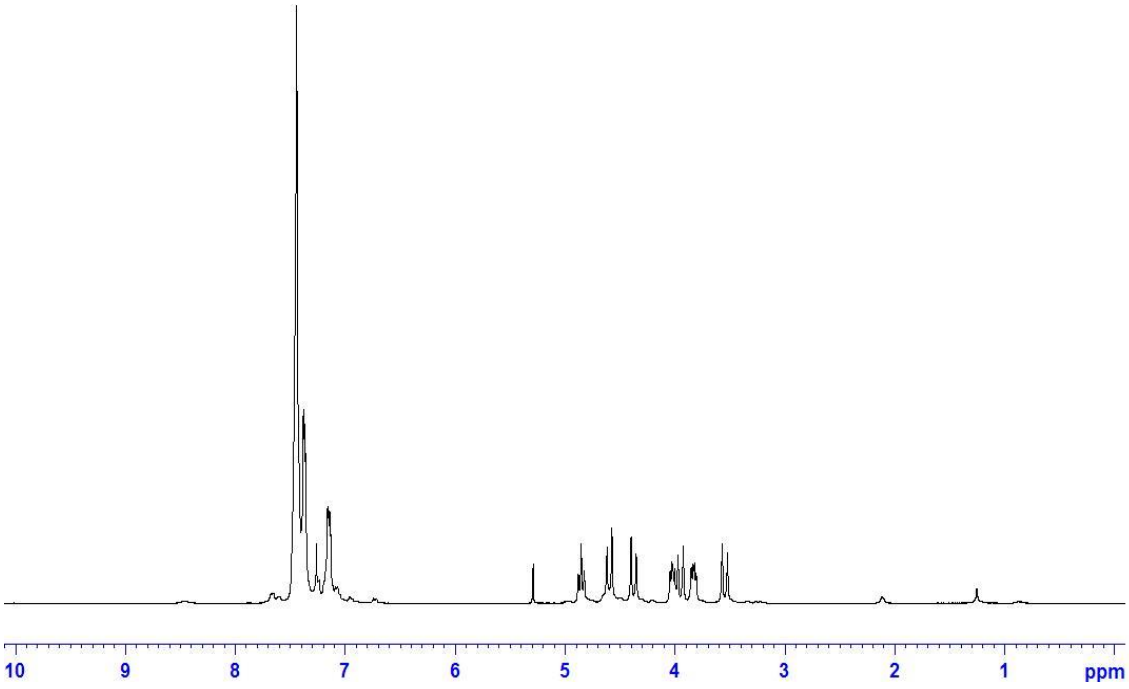
11

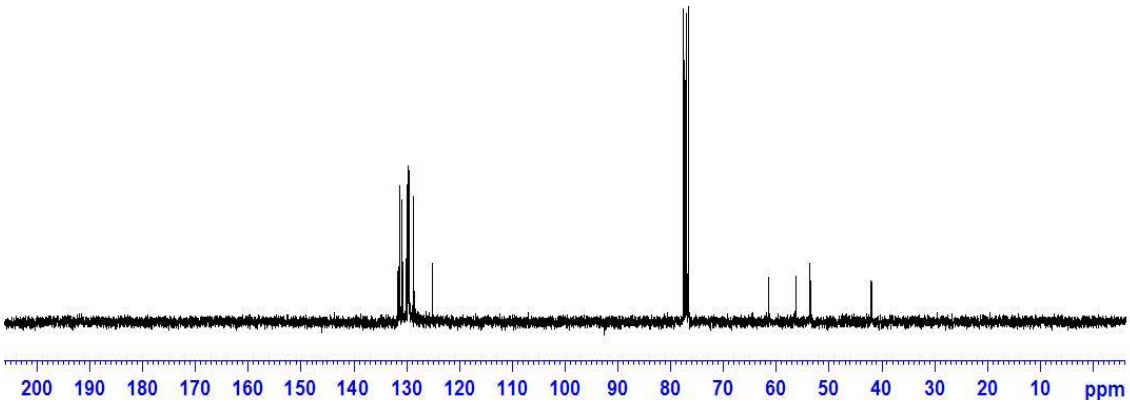

10 9 8 7 6 5 4 3 2 1 ppm
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

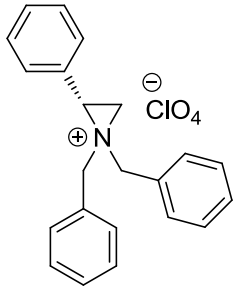
^{1}H and ^{13}C NMR spectra of Aziridinium ions 9



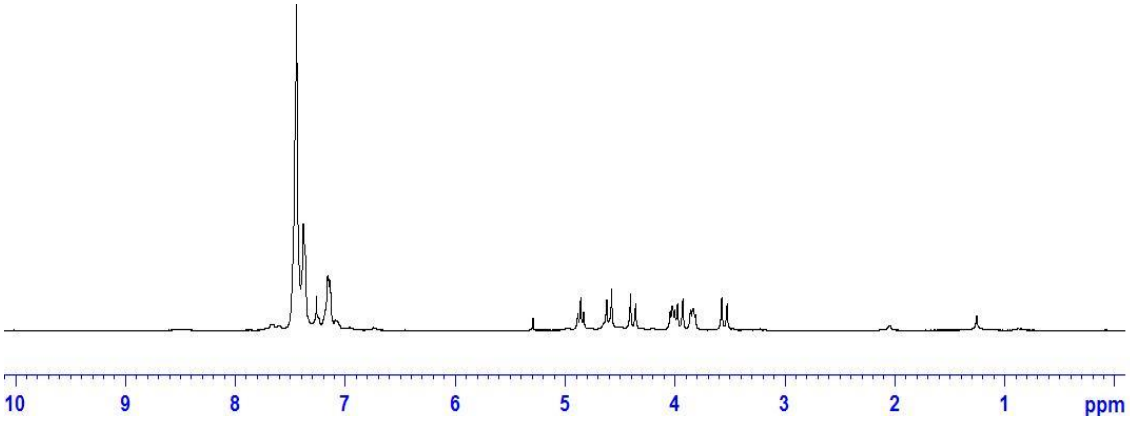
(S)-9aa

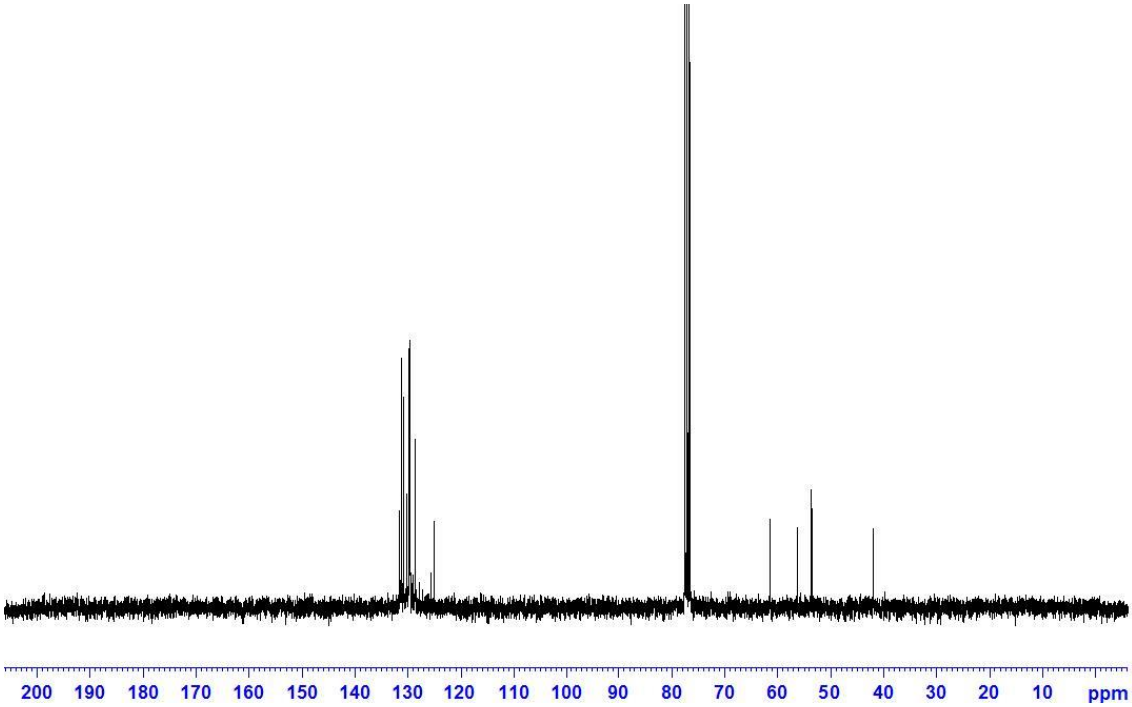


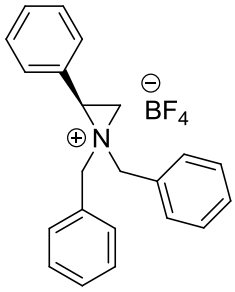



ClO4
N

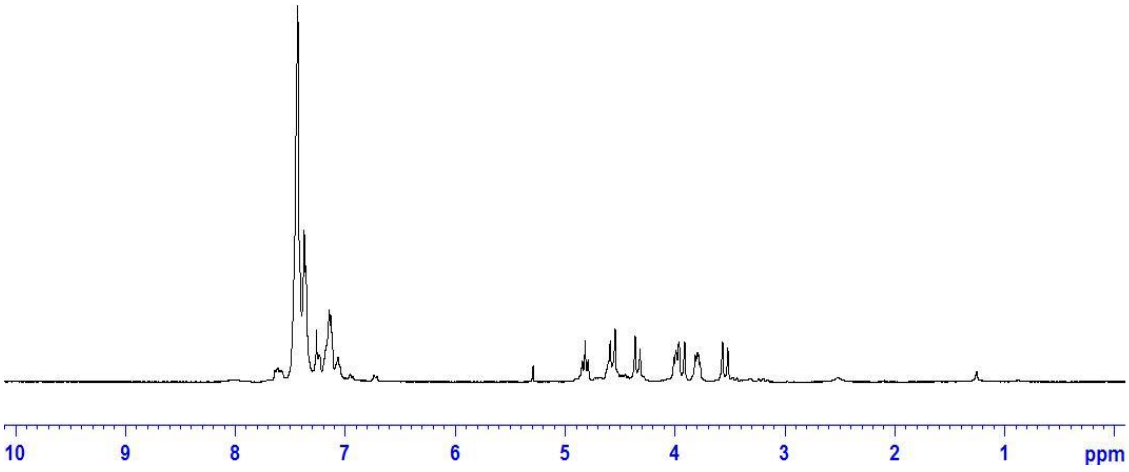
(R)-9aa

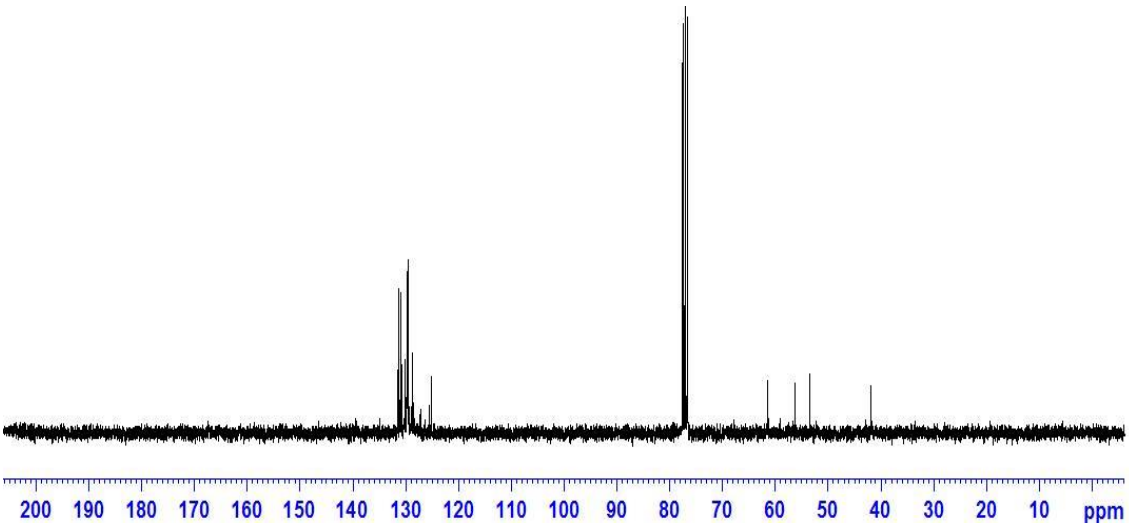

10
9
8
7
6
5
4
3
2
1
ppm

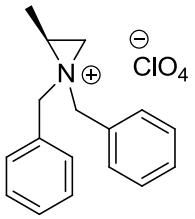

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


BF4
N

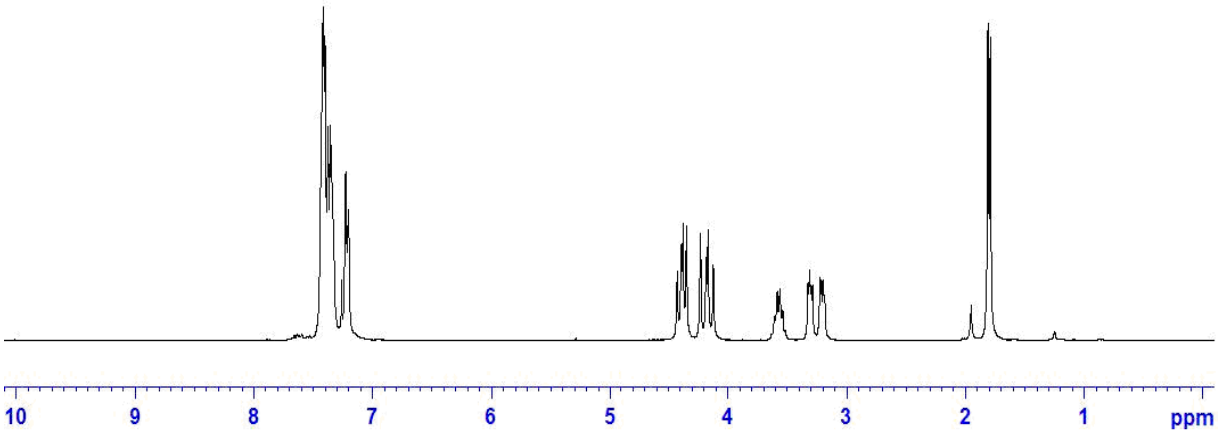
(S)-9ab

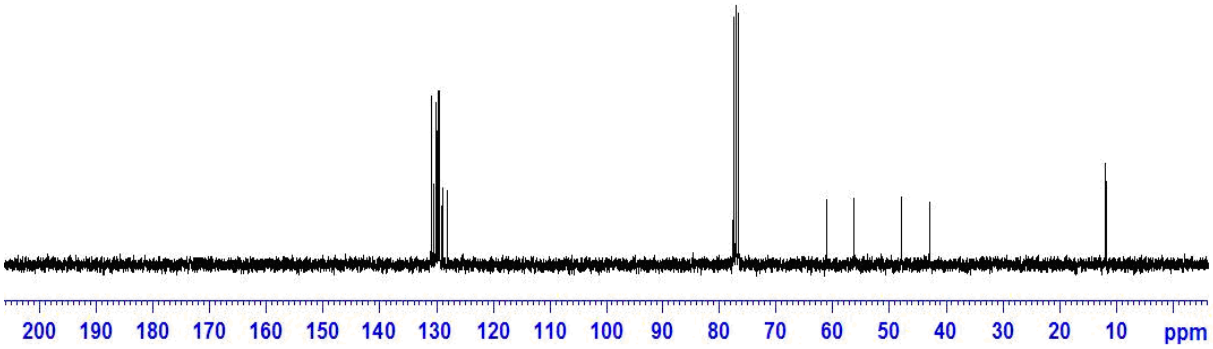

10
9
8
7
6
5
4
3
2
1
ppm

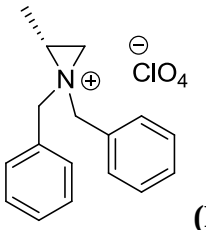

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


N
ClO4

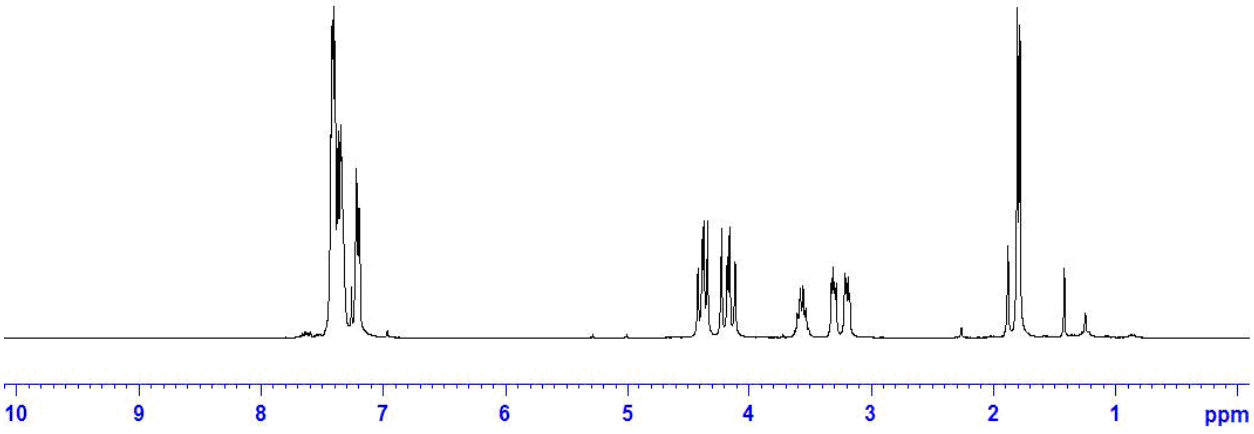
(S)-9ba

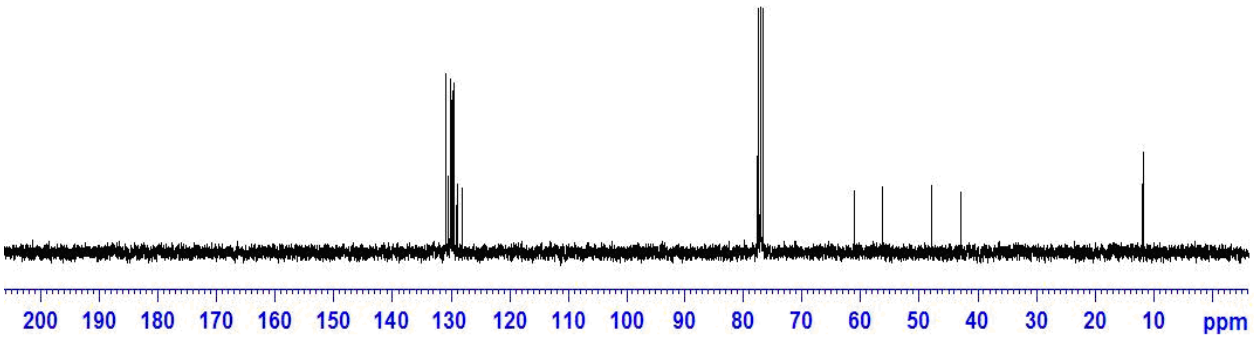

10
9
8
7
6
5
4
3
2
1
ppm

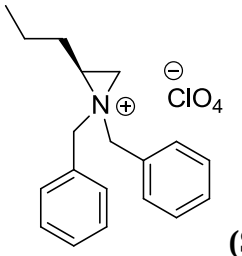

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


ClO4

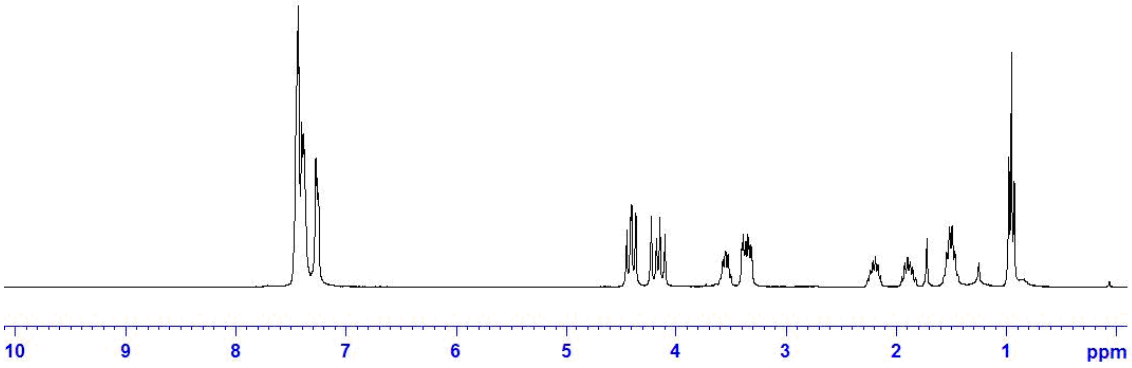
(R)-9ba

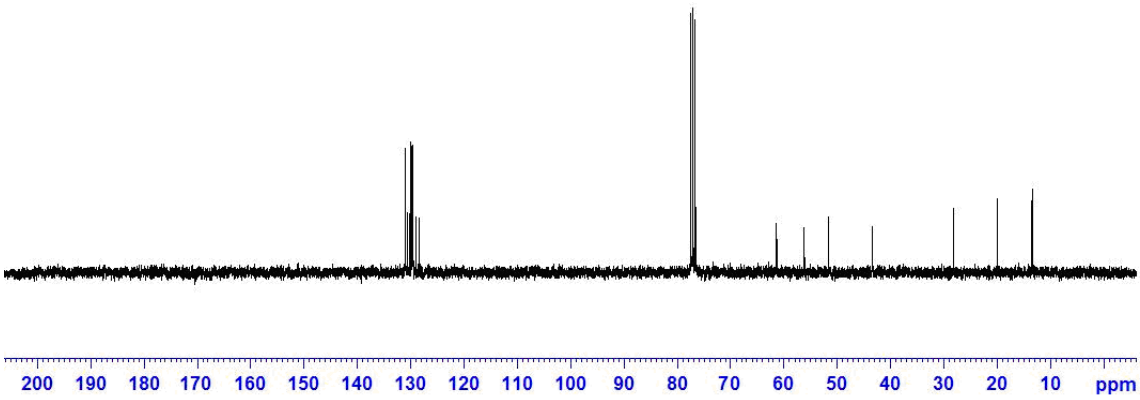

10
9
8
7
6
5
4
3
2
1
ppm

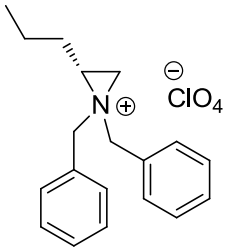

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


ClO4

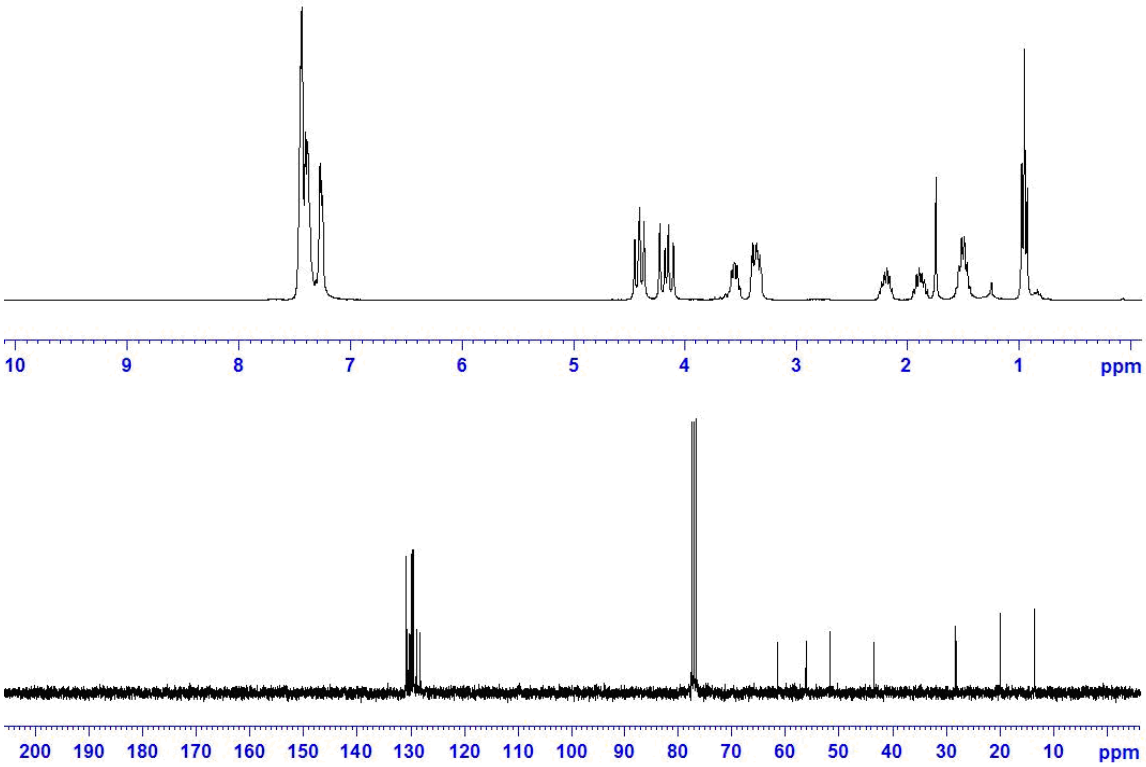
(S)-9ca


10
9
8
7
6
5
4
3
2
1
ppm

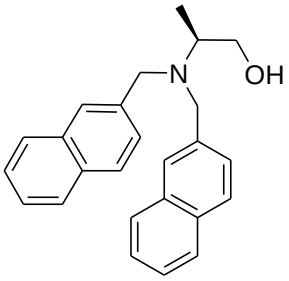

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


N
ClO4

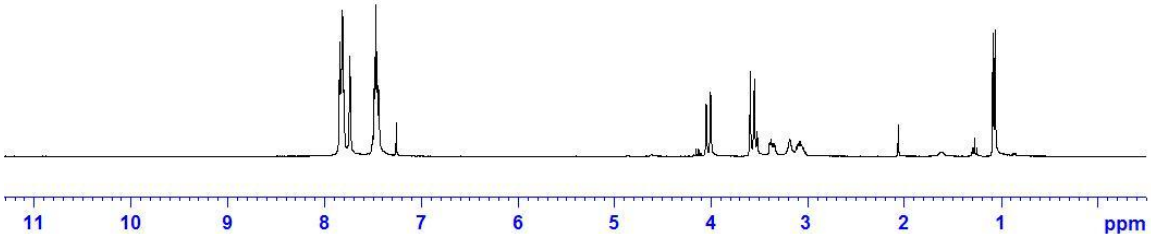
(R)-9ca

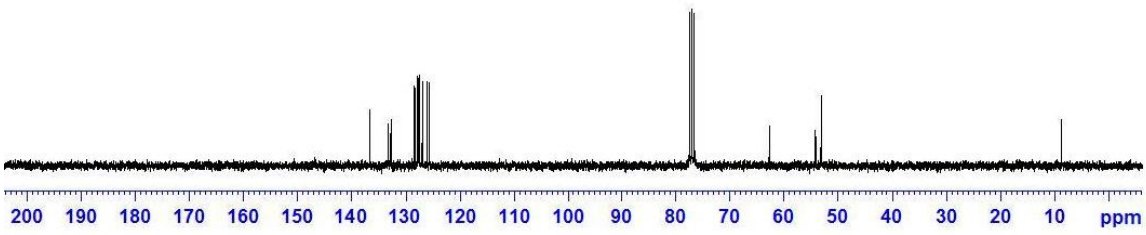

10
9
8
7
6
5
4
3
2
1
ppm
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

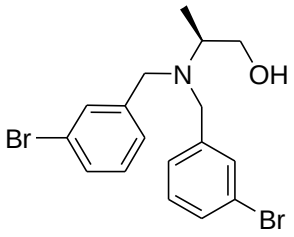
^{1}H and ^{13}C NMR spectra of β-amino alcohols 8



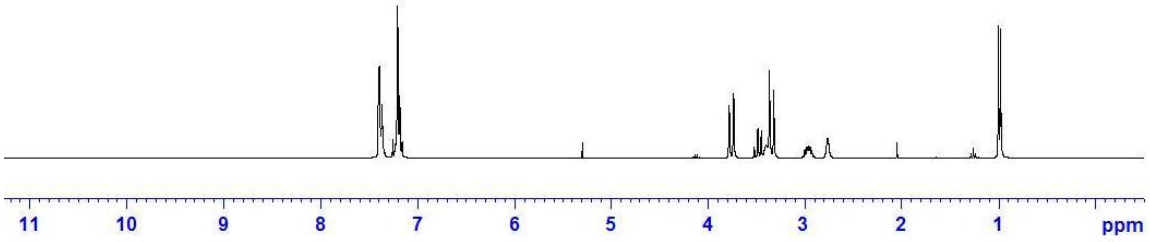
(S)-8d

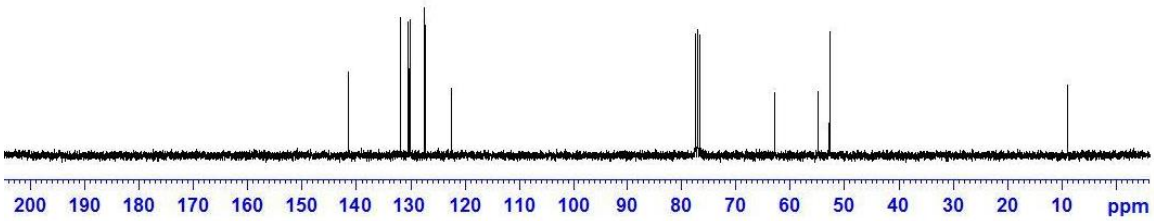


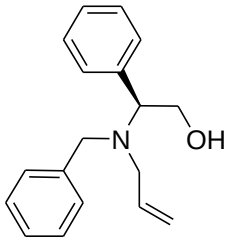



N
OH
Br
Br

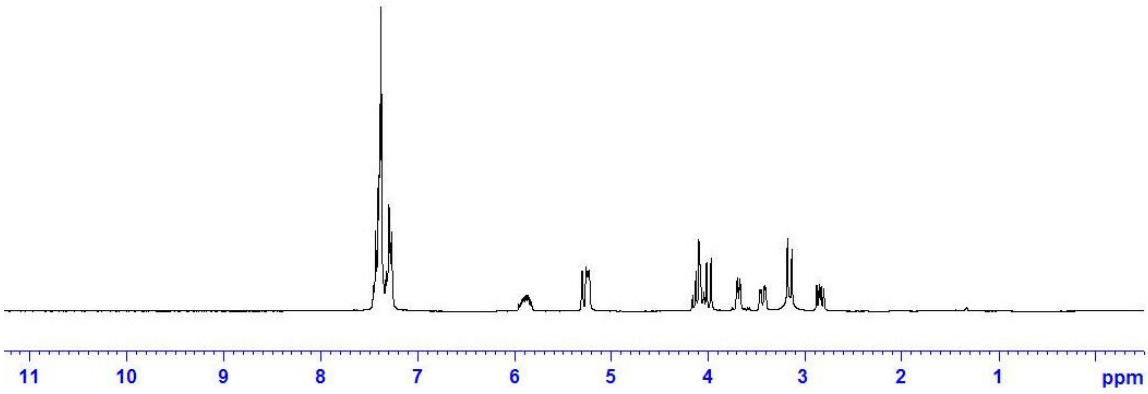
(S)-8e

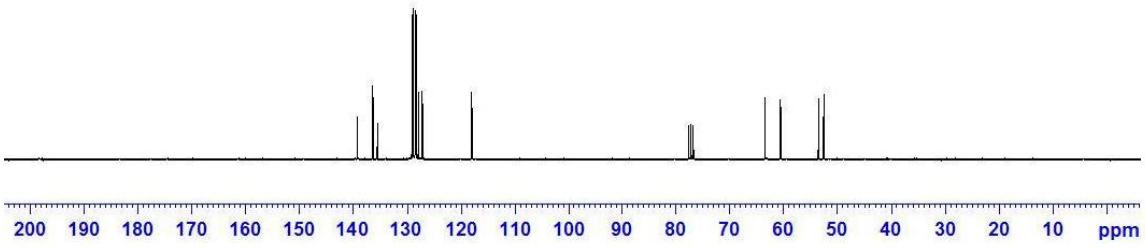

11
10
9
8
7
6
5
4
3
2
1
ppm

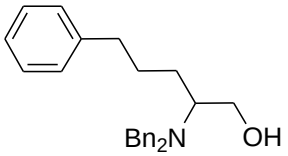

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


N
OH

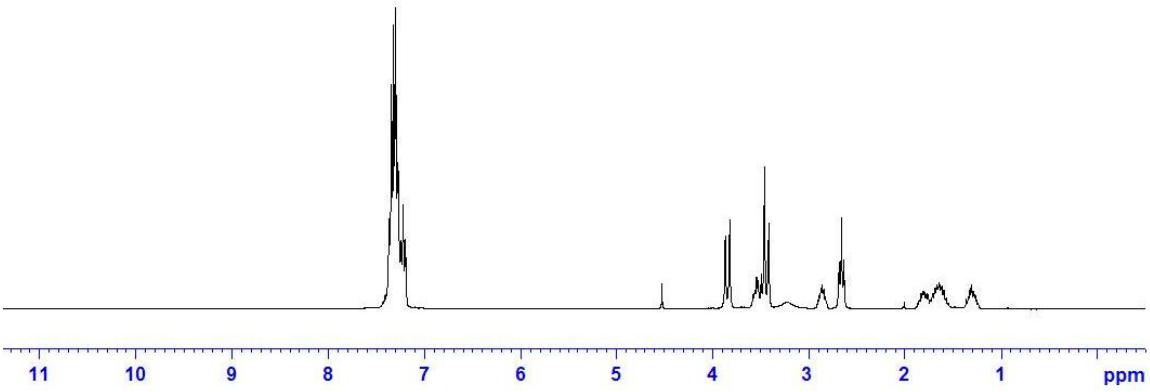
(S)-8f

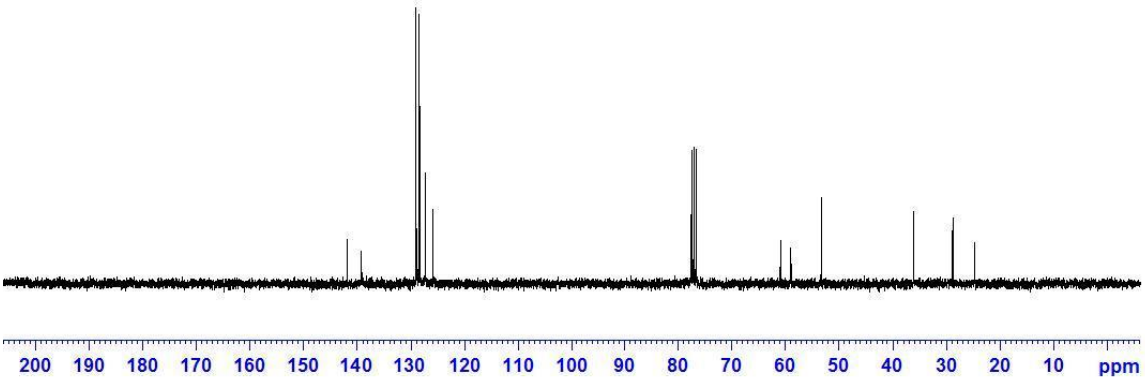

11
10
9
8
7
6
5
4
3
2
1
ppm


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

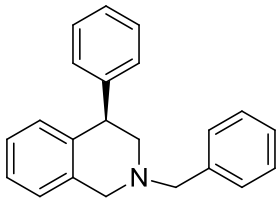

Bn2N
OH

8h


11
10
9
8
7
6
5
4
3
2
1
ppm

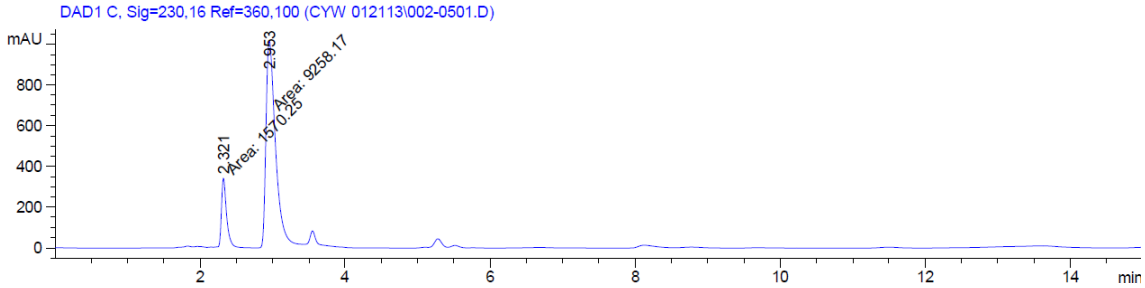

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Chiral HPLC chromatograms of THIQ analogues 5



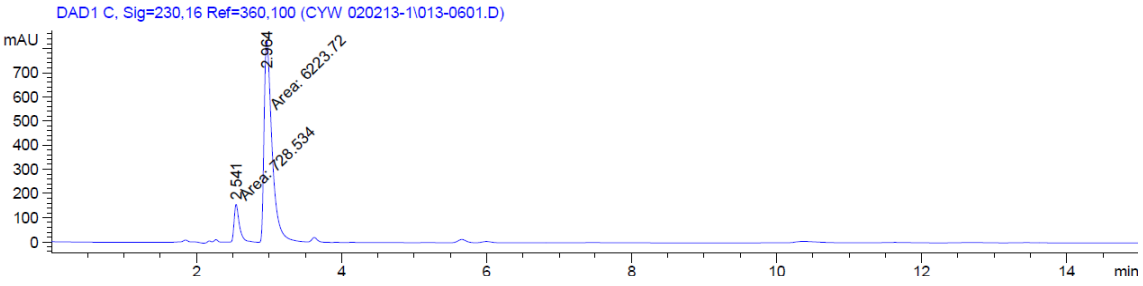
(R)-5a

(Table 1, entry 1, temp: 0 °C, 71% ee)



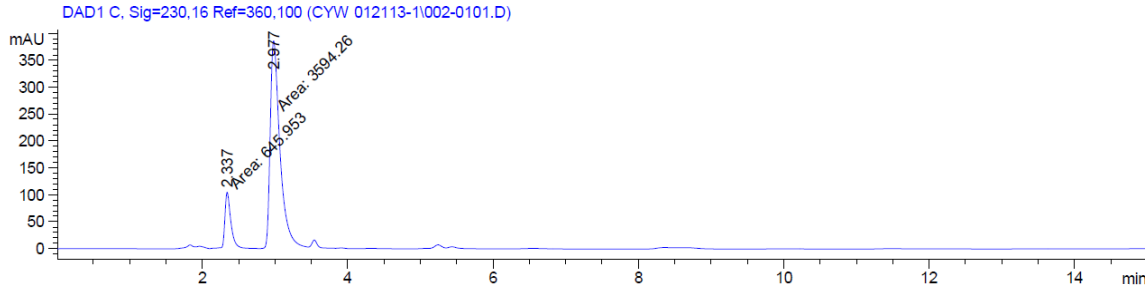
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.321	MM	0.0775	1570.25269	337.68329	14.5012
2	2.953	MM	0.1511	9258.16797	1020.87604	85.4988

(Table 1, entry 2, temp: – 70 °C to – 20 °C, 79% ee)



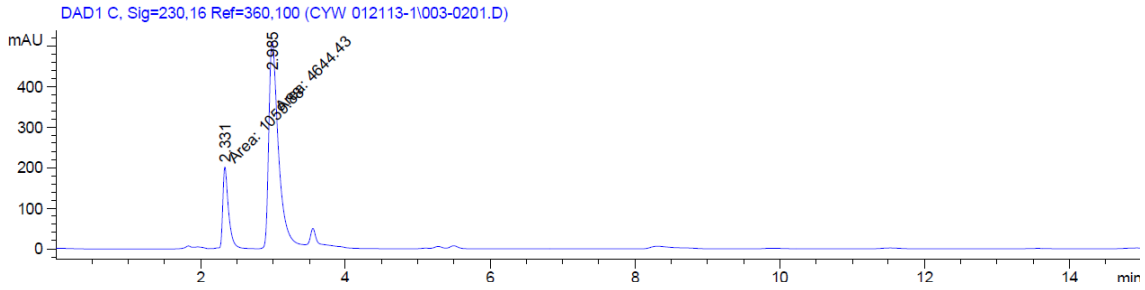
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.541	MM	0.0785	728.53448	154.67966	10.4791
2	2.964	MM	0.1238	6223.72461	837.79950	89.5209

(Table 1, entry 3, temp: – 20 °C, 70% ee)



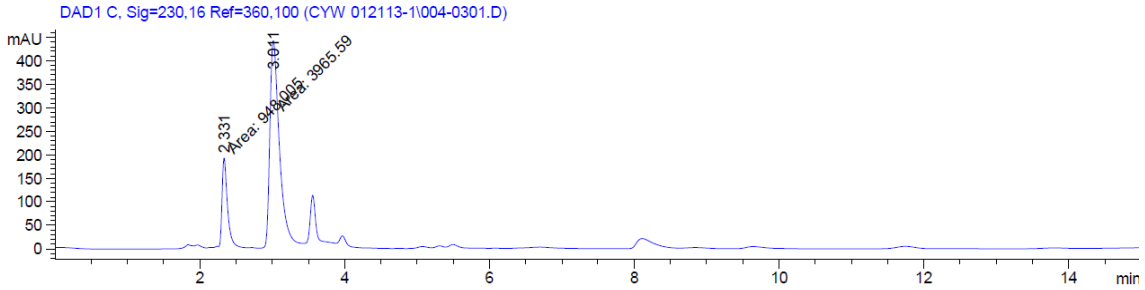
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.337	MM	0.0995	645.95313	108.14835	15.2340
2	2.977	MM	0.1548	3594.26123	387.06531	84.7660

(Table 1, entry 4, temp: 0 °C, 63% ee)

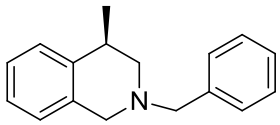


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.331	MM	0.0881	1059.87646	200.44795	18.5803
2	2.985	MM	0.1521	4644.43115	508.86456	81.4197

(Table 1, entry 5, temp: 0 °C, 61% ee)

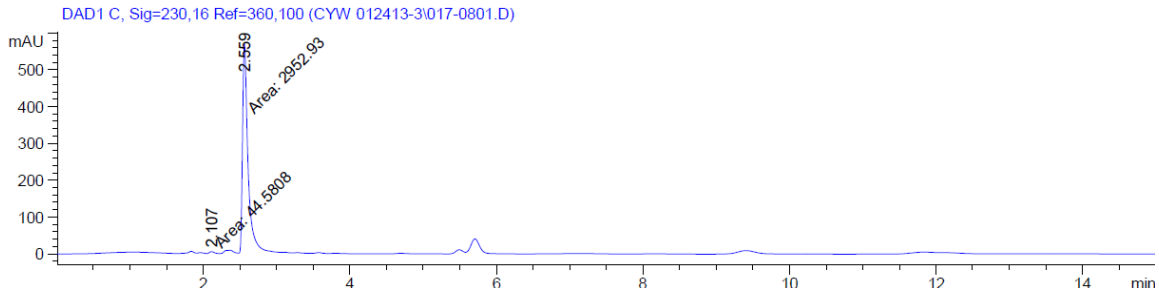


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.331	MM	0.0835	948.00537	189.20534	19.2935
2	3.011	MM	0.1506	3965.59424	438.92996	80.7065



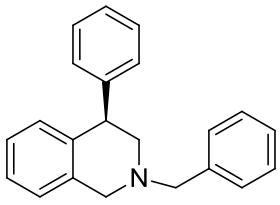
(R)-5b

(Table 1, entry 7, temp: 0 ^{o}C to reflux, 97.0% ee)



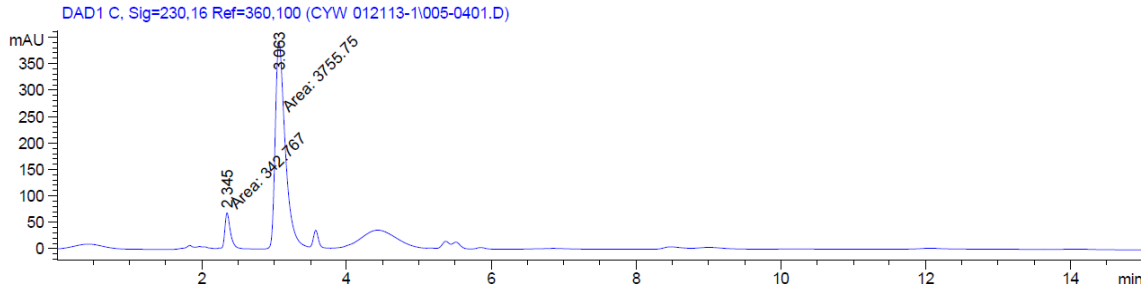
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.107	MM	0.0856	44.58078	8.67560	1.4873
2	2.559	MM	0.0858	2952.93457	573.34760	98.5127

<u>Catalyst effect on the synthesis of (R)-5a (Table 2)</u>



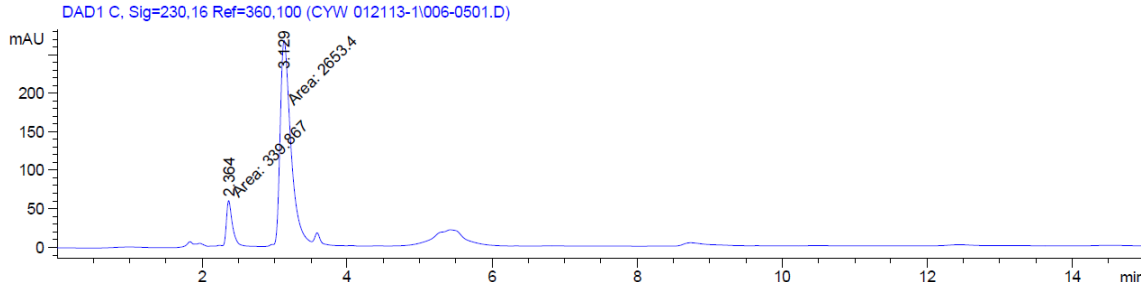
(R)-5a

(Table 2, entry 2, $FeBr_3$, 83% ee)



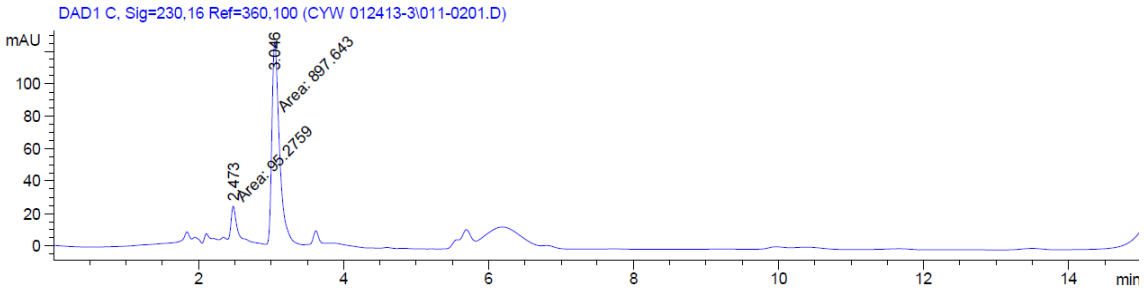
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.345	MM	0.0849	342.76675	67.27968	8.3632
2	3.063	MM	0.1598	3755.74707	391.77582	91.6368

(Table 2, entry 3, $InCl_3$, 77% ee)



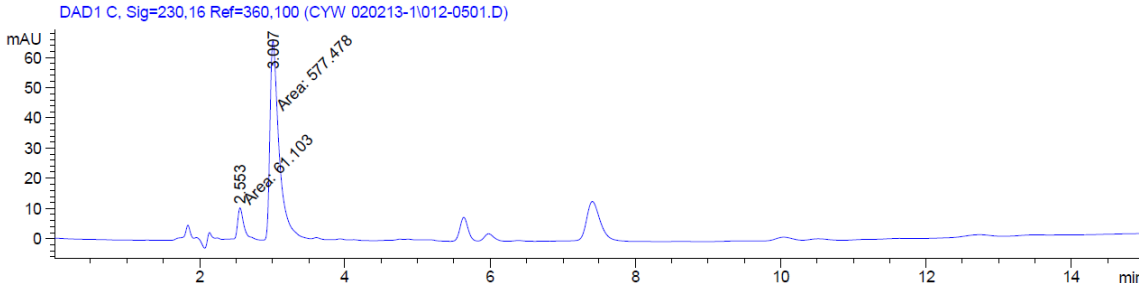
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.364	MM	0.0948	339.86703	59.76844	11.3544
2	3.129	MM	0.1674	2653.40283	264.24896	88.6456

(Table 2, entry 4, $TiCl_4$, 81% ee)



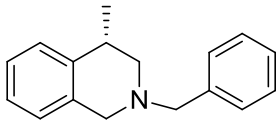
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.473	MM	0.0763	95.27595	20.81837	9.5955
2	3.046	MM	0.1193	897.64337	125.40724	90.4045

(Table 2, entry 5, $SnCl_4$, 81% ee)



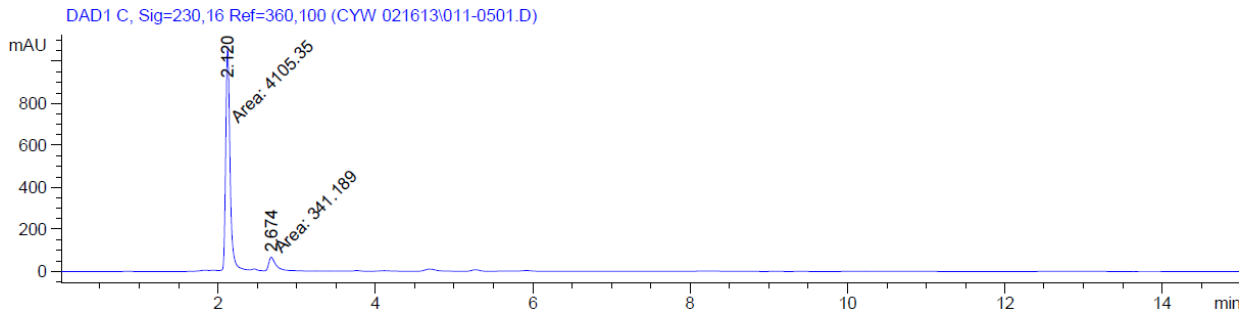
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.553	MM	0.0969	61.10302	10.51288	9.5686
2	3.007	MM	0.1459	577.47833	65.94612	90.4314

Effect of catalyst on the synthesis of (S)-5b (Table 2)



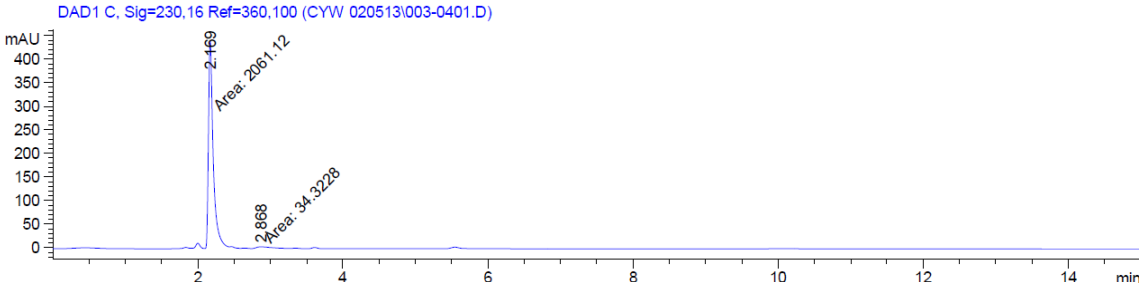
(S)-5b

(Table 2, entry 7, $FeBr_3$, 85% ee)



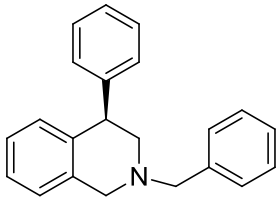
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.120	MM	0.0635	4105.35010	1078.04407	92.3269
2	2.674	MM	0.0835	341.18890	68.13349	7.6731

(Table 2, entry 8, $InCl_3$, 97% ee)



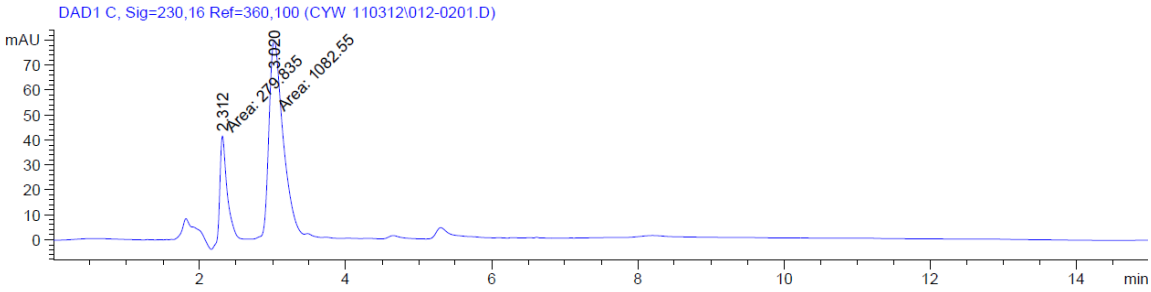
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.169	MM	0.0767	2061.11646	447.71838	98.3620
2	2.868	MM	0.1734	34.32275	3.29979	1.6380

Effect of solvent on the synthesis of (R)-5a (Table 3)



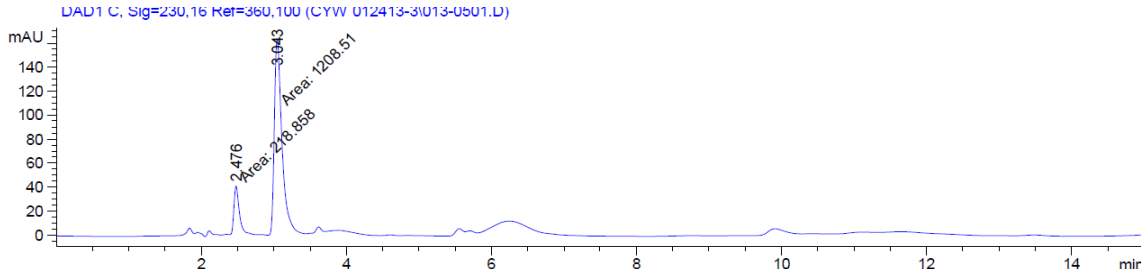
(R)-5a

(Table 3, entry 2, Benzene, 59% ee)



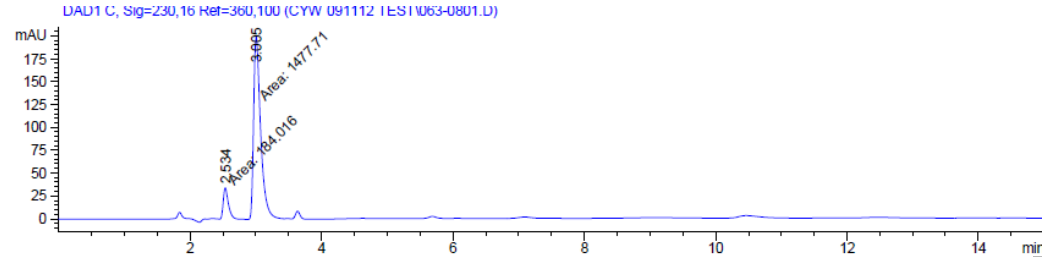
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.312	MM	0.1117	279.83545	41.76924	20.5402
2	3.020	MM	0.2266	1082.54529	79.62730	79.4598

(Table 3, entry 3, *p*-xylene, 69% ee)



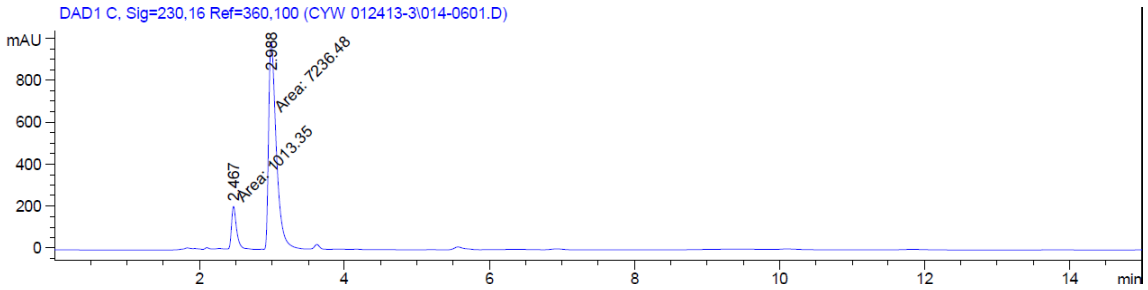
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.476	MM	0.0867	218.85783	42.08460	15.3329
2	3.043	MM	0.1224	1208.51392	164.55754	84.6671

(Table 3, entry 4, $(CH_2Cl_2)_2$, 78% ee)



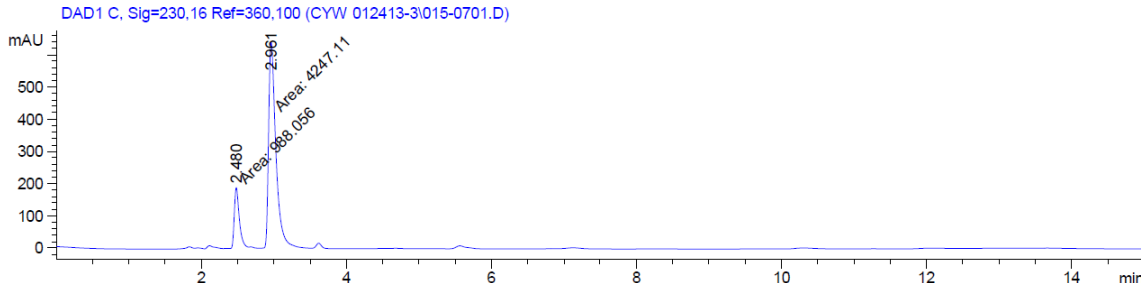
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.534	MM	0.0892	184.01639	34.38907	11.0738
2	3.005	MM	0.1229	1477.70984	200.47089	88.9262

(Table 3, entry 5, CH_2Cl_2, 75% ee)



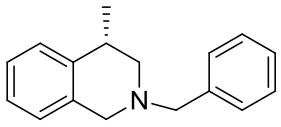
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.467	MM	0.0802	1013.35077	210.57399	12.2833
2	2.988	MM	0.1204	7236.47900	1002.09631	87.7167

(Table 3, entry 6, $CHCl_3$, 62% ee)



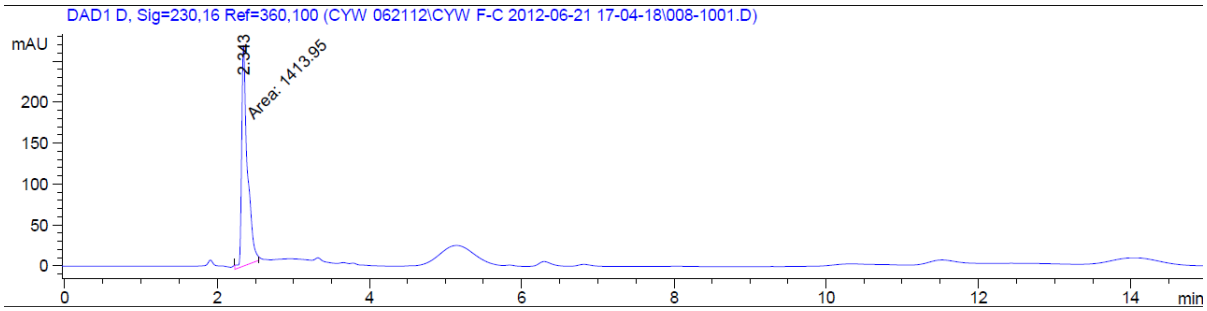
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.480	MM	0.0837	988.05609	196.62846	18.8734
2	2.961	MM	0.1112	4247.11084	636.60175	81.1266

<u>Solvent effect on the synthesis of (S)-5b (Table 3)</u>



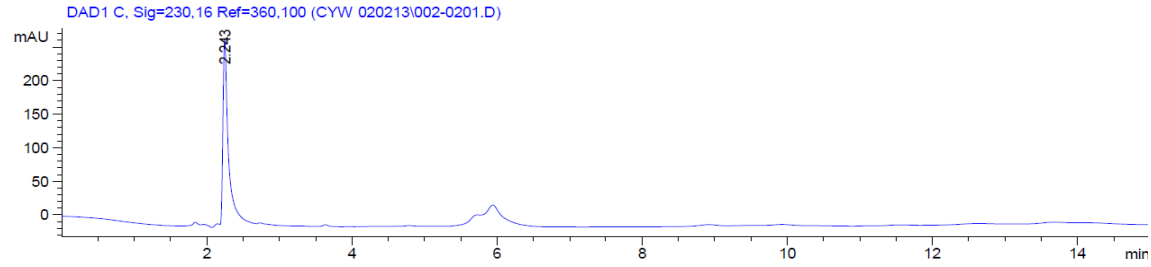
(S)-5b

(Table 3, entry 11, Benzene, >99% ee)



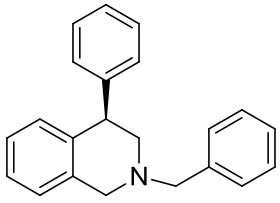
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.343	MM	0.0867	1413.95300	271.96436	100.0000

(Table 3, entry 12, *p*-xylene, 98.3% ee)



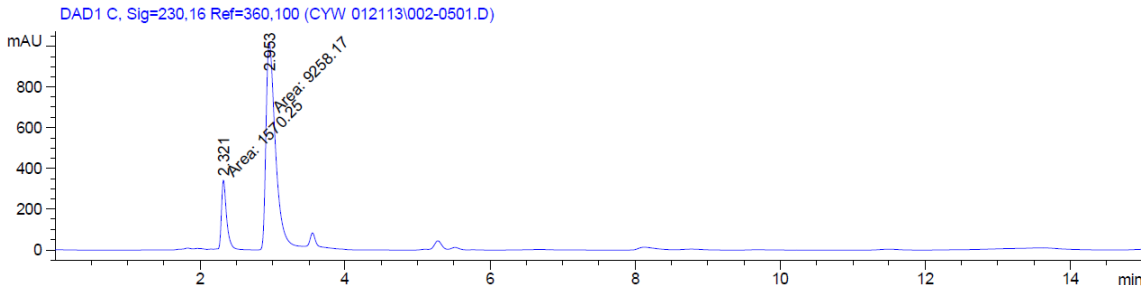
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.243	MM	0.0876	1465.42590	278.96753	99.1263
2	2.731	MM	0.0879	12.91653	2.44846	0.8737

Table 4. Substrate scope

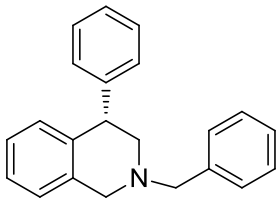


(R)-5a

(Table 4, entry 1, 71% ee)

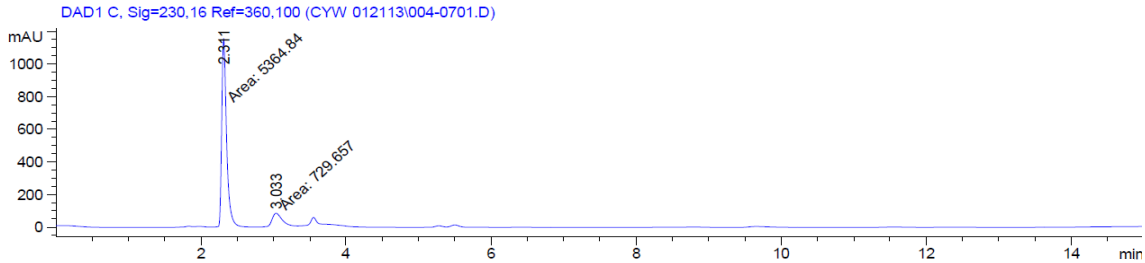


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.321	MM	0.0775	1570.25269	337.68329	14.5012
2	2.953	MM	0.1511	9258.16797	1020.87604	85.4988

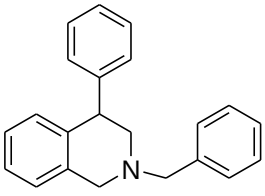


(S)-5a

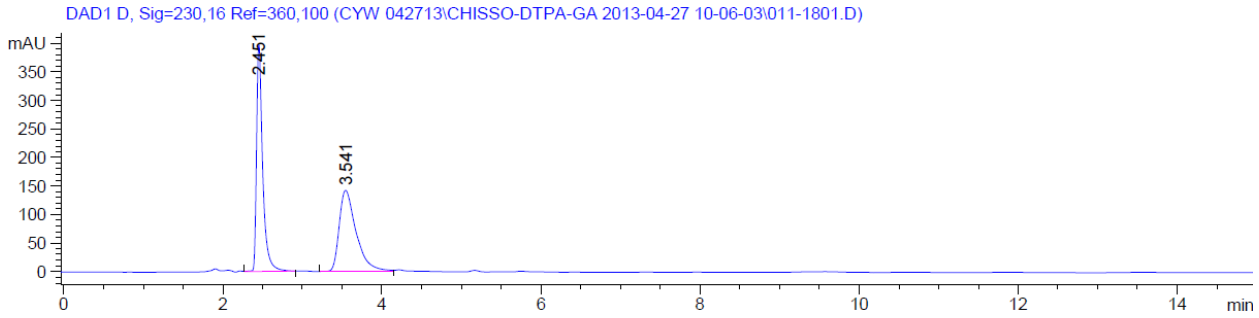
(76% ee)



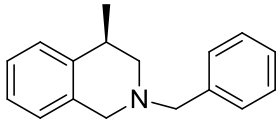
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.311	MM	0.0771	5364.84180	1159.46667	88.0276
2	3.033	MM	0.1489	729.65656	81.67146	11.9724



(rac)-**5a**

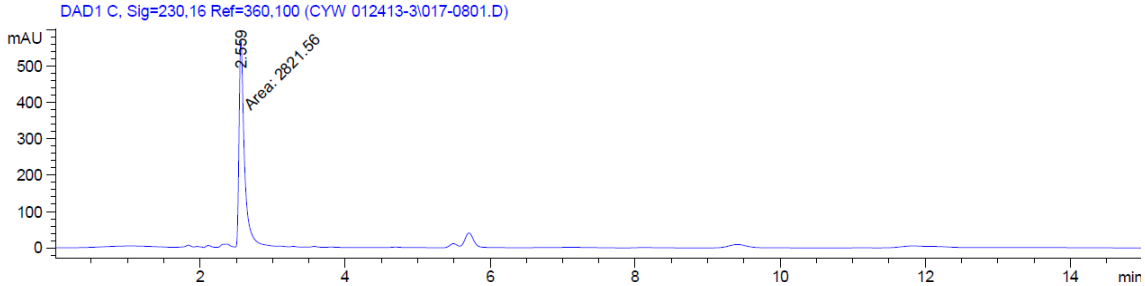


t_R = 2.5 min (S-isomer), 3.5 min (R-isomer)

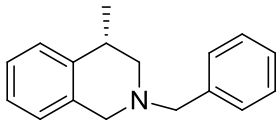


(R)-5b

(Table 4, entry 2, 97.0% ee)

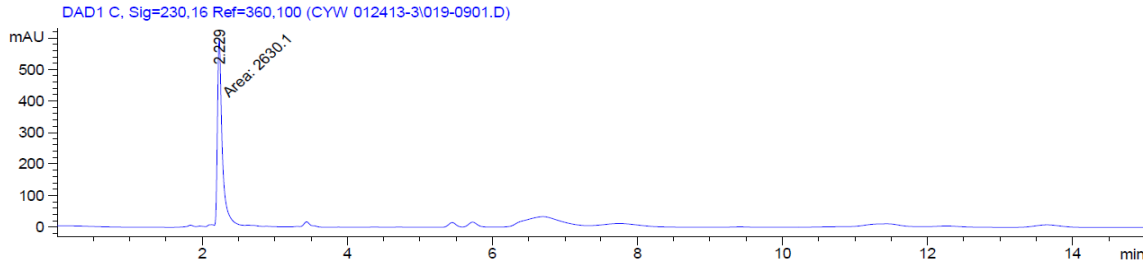


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.107	MM	0.0856	44.58078	8.67560	1.4873
2	2.559	MM	0.0858	2952.93457	573.34760	98.5127

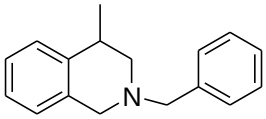


(S)-5b

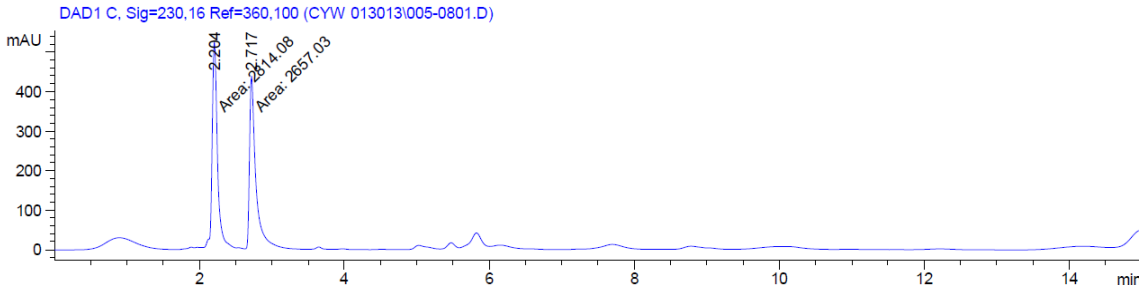
(96.9% ee)



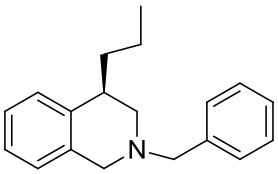
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.229	MM	0.0787	2844.25903	602.23199	98.4300
2	2.629	MM	0.1652	45.36733	4.57738	1.5700



(rac)-**5b**

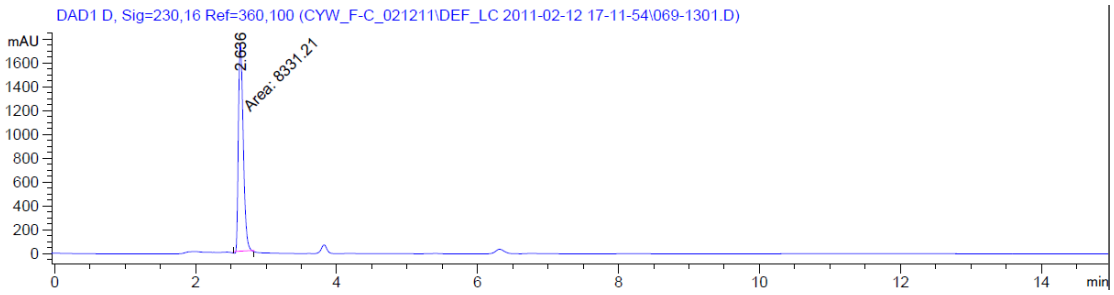


t_R = 2.2 min (S-isomer), 2.7 min (R-isomer)

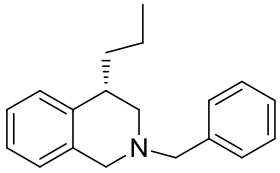


(R)-5c

(Table 4, entry 3, >99% ee)

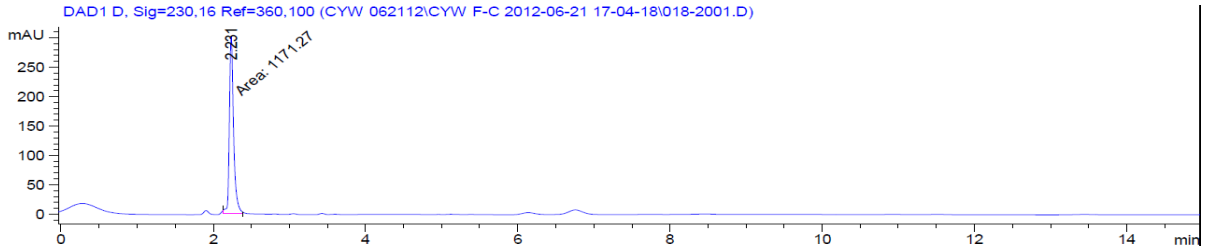


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.636	MM	0.0791	8331.21191	1755.75012	100.0000

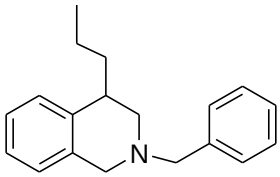


(S)-5c

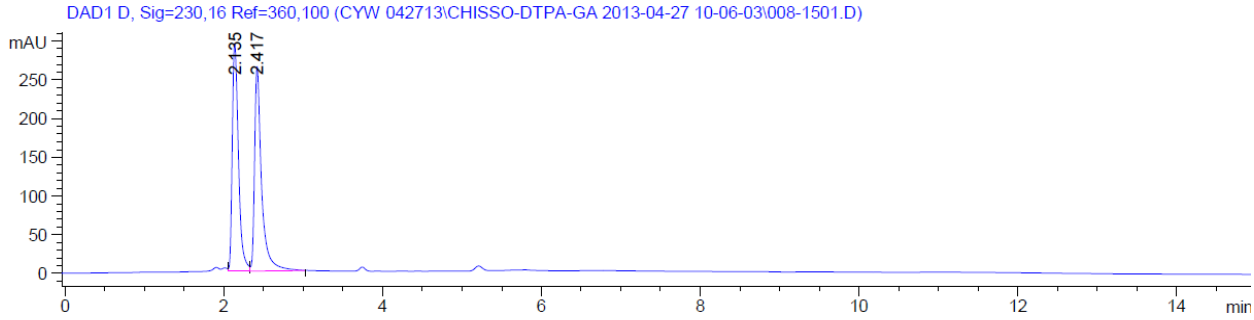
(>99% ee)



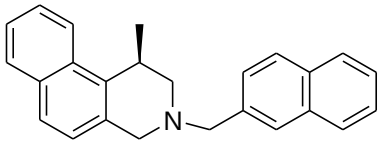
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.231	MM	0.0638	1171.26965	306.17804	100.0000



(rac)-**5c**

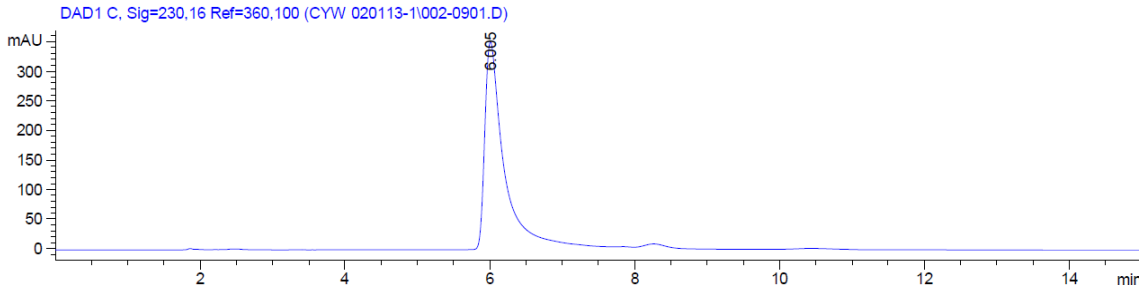


t_R = 2.1 (S-isomer), t_R = 2.4 (R-isomer)

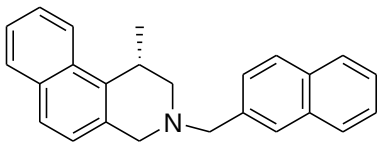


(R)-5d

(Table 4, entry 4, >99% ee)

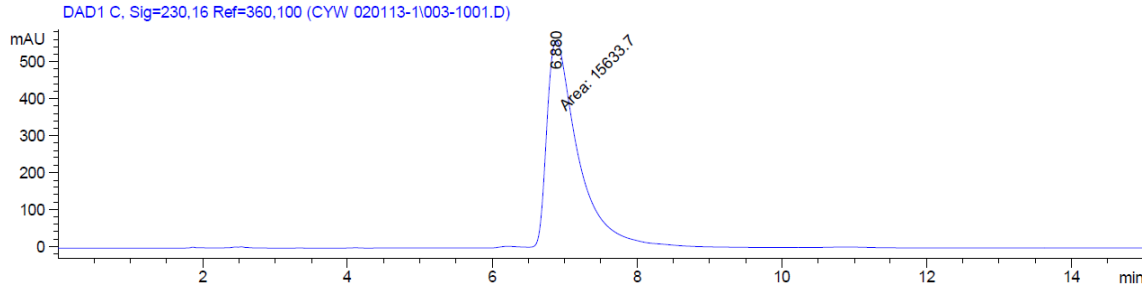


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.005	BB	0.2642	6493.06250	350.36359	100.0000



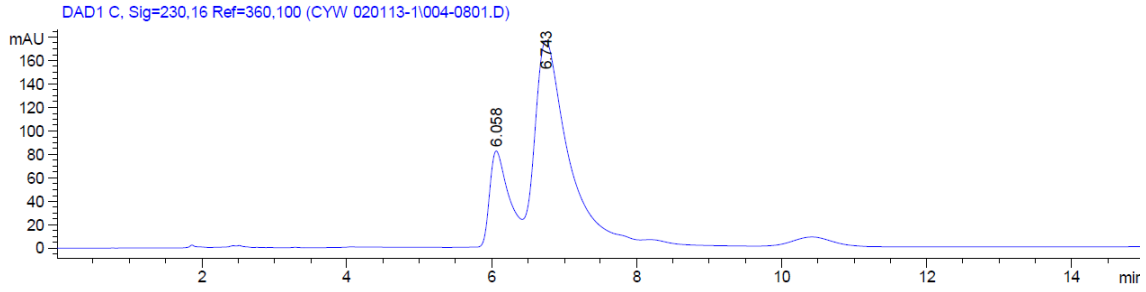
(S)-5d

(>99% ee)

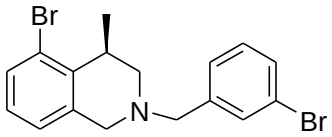


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.880	MM	0.4734	1.56337e4	550.38269	100.0000

Chiral HPLC of a mixture of (R)-5d and (S)-5d (co-injection of the R and S isomer)

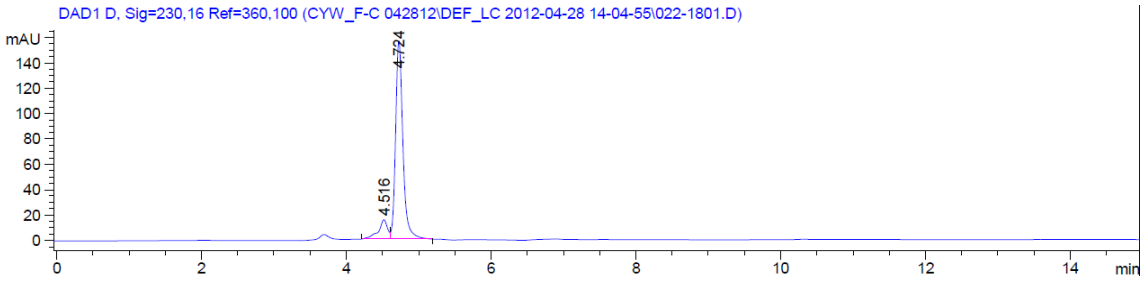


t_R = 6.1 min (R-isomer), 6.7 min (S-isomer)

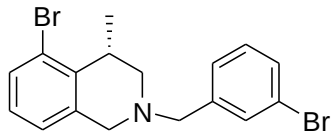


(R)-5e

(Table 4, entry 5, 78% ee)

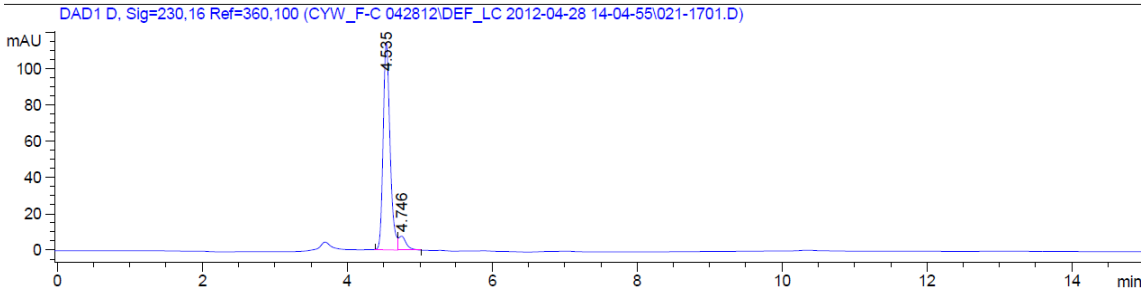


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.516	BV	0.1286	138.01517	15.40079	11.0906
2	4.724	VB	0.1063	1106.42126	156.92093	88.9094



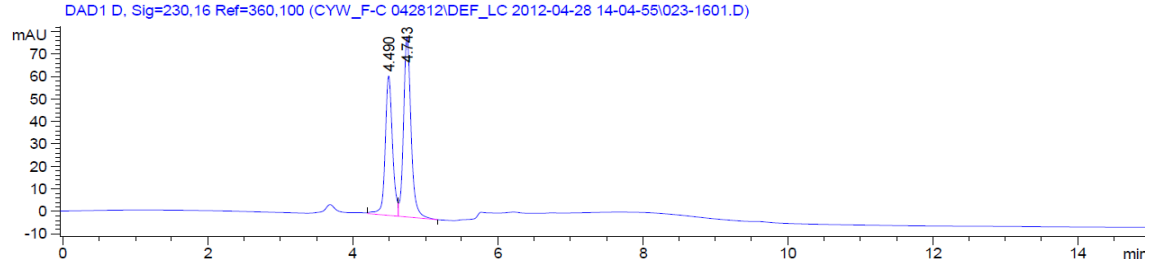
(S)-5e

(86% ee)

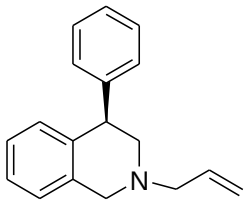


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.535	BV	0.1013	758.66046	114.55817	93.0818
2	4.746	VB	0.1052	56.38690	7.72517	6.9182

Chiral HPLC of a mixture of (R)-5e and (S)-5e (co-injection of the R and S isomer)

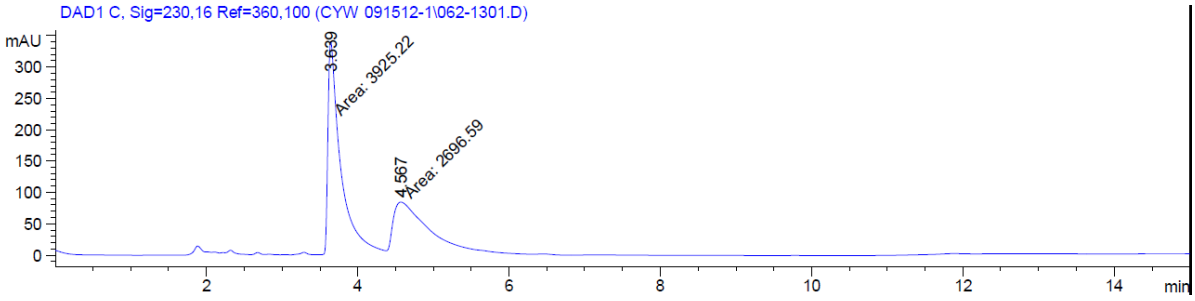


t_R = 4.5 min (S-isomer), 4.7 min (R-isomer)

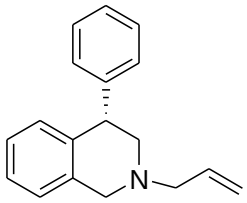


(R)-5f

(Table 4, entry 6, 18.6% ee)

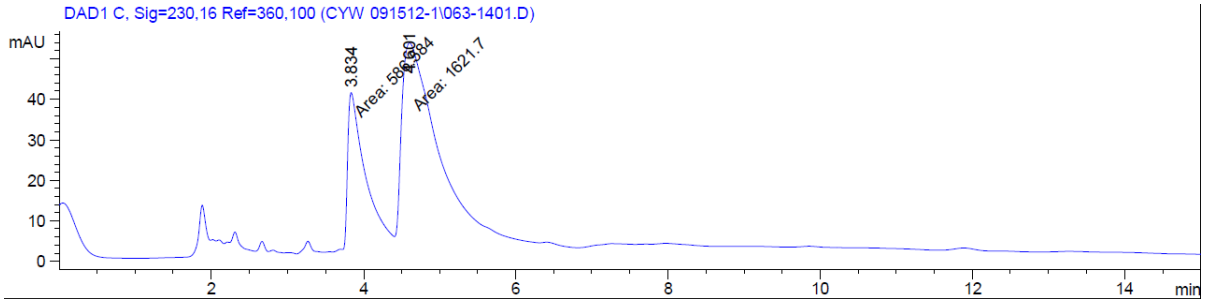


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.639	MM	0.1933	3925.22437	338.47012	59.2772
2	4.567	MM	0.5493	2696.58545	81.82365	40.7228

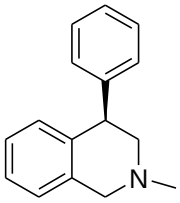


(S)-5f

(46.9% ee)

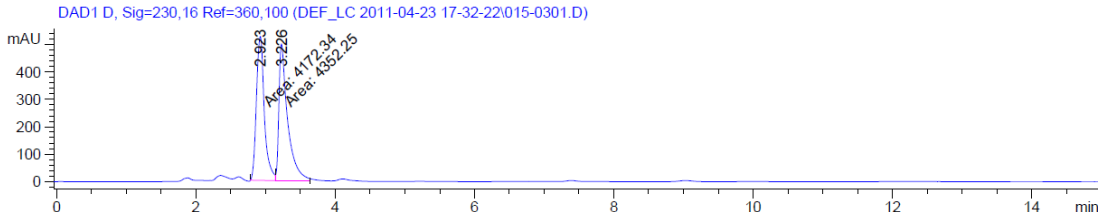


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.834	MM	0.2555	586.58435	38.26030	26.5629
2	4.601	MM	0.5578	1621.70105	48.45588	73.4371



(R)-5g

(Table 4, entry 7, 2.1% ee)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.923	MM	0.1323	4172.33887	525.67554	48.9447
2	3.226	MM	0.1449	4352.25195	500.44461	51.0553

Reference

1. Philippe, N.; Levacher, V.; Dupas, G.; Quéguiner, G.; Bourguignon, J. *Org. Lett.* **2000**, *2*, 2185.

2. Kihara, M.; Ikeuchi, M.; Adachi, S.; Nagao, Y.; Moritoki, H.; Yamaguchi, M, Taira, Z. *Chem. Pharm. Bull.* **1995**, *43*, 1543.

3. Pedrosa, R.; Andrés, C.; Iglesias, J. M.; Obeso, M. A. *Tetrahedron* **2001**, *57*, 4005.

4. Schwerdtfeger, J.; Kolczewski, S.; Weber, B.; Frohlich, R.; Hoppe, D. *Synthesis* **1999**, *9*, 1573. (not clear)

5. Metro, T-X.; Appenzeller, J.; Pardo, D. G.; Cossy, J. *Org. Lett.* **2006**, *8*, 3509.

6. Meguro, M.; Asao, N.; Yamamoto, Y. *J. Chem. Soc., Perkin Trans. I* **1994**, 2597

7. Dakanali, M.; Tsikalas, G. K.; Krautscheid, H.; Katerinopoulos, H. E. *Tetrahedron Letts.* **2008**, *49*, 1648.

8. A. J. M. van Beijnen, R. J. M. Nolte, A. J. Naaktgeboren, J. W. Zwikker, W. Drenth, A. M. F. Hezemans. Macromolecules. 1983, 16, 1679.

9. Nagle, A. S.; Salvatore, R. N.; Chong, B.D.; Jung, K. W. *Tetrahedron Letts.* **2000**, *41*, 3011.

10. Hanessian, S.; Parthasarathy, S.; Mauduit, M.; Payza, K. *J. Med. Chem.* **2003**, *46*, 34

11. Gmeiner, P.; Kaertner, A. *Synthesis* **1995**, *1*, 83.

12. Jurczak, J.; Gryko, D.; Kobrzycka, E.; Gruza, H.; Prokopowiczit, P *Tetrahedron*. **1998**, *54*, 6051.

13. Ranganathan, R. S.; Pillai, R. K.; Raju, N.; Fan, H.; Nguyen, H.; Tweedle, M. F.; Desreux, J. F.; Jacques, V. *Inorg. Chem.* **2002**, *41*, 6846.

14. Wu, H-F.; Lin, W-B.; Xia, L-Z.; Luo, Y-Z.; Chen, X-Z.; Li, G-Y.; Zhang, G-L.; Pan, X-F. *Helv. Chim. Acta.* **2009**, 92, 677.

15. Linzaga, I.; Escalante, J.; Munoz, M.; Juaristi, E. *Tetrahedron* **2002**, *58*, 8973