Chinese Journal of Chemistry, **2004**, *22*, 727—731 **Article**

Diastereoselective Synthesis of Chiral Pyrrolidine and Piperidine Ring Systems

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A diastereoselective method for the synthesis of chiral pyrrolidine and piperidine ring containing compounds was described. The protocol of bromination followed by aminocyclization furnishes an easily handled while highly efficient procedure for the intramolecular amidation of an isolated double bond. High diastereomeric excess was observed in this synthetic procedure.

Keywords diastereoselective, pyrrolidine, piperidine, aminocyclization

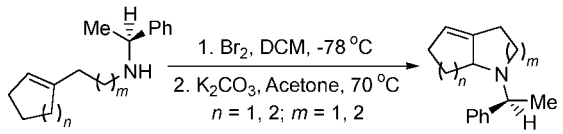
Introduction

Pyrrolidine and piperidine containing substructures are present in a large class of biologically active natural products as well as numerous therapeutic agents.[1] Synthesis of these nitrogen heterocyclic ring system has long attracted considerable interests from the synthetic community.[2] Recent trends have been directed towards the asymmetric construction of the chiral substituted pyrrolidine and piperidine ring systems.[3] As part of our efforts in pursuit of efficient while flexible strategy towards the synthesis of biologically active natural alkaloids, we recently disclosed a facile method for the synthesis of the core of hexahydroindole and octahydroquinoline ring systems.[4] The bromination followed by aminocyclization furnishes a general procedure for the intramolecular haloamidation of an isolated double bond. The method described by us is easy to handle, efficient and most of all, the protocol is highly useful for the diastereoselective synthesis of chiral pyrrolidine and piperidine ring containing subunits with chiral amines, *R*- or *S*-methylphenylamine, being incorporated (Scheme 1). To further demonstrate the utility of this protocol to the asymmetric synthesis of substituted pyrrolidine and piperidine ring systems, a few more examples were conducted and the results are summarized and reported herein in detail.

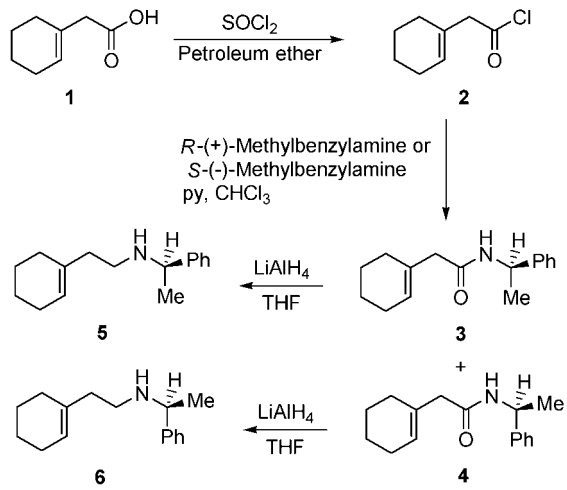
Results and discussion

The initial stage for our research is to synthesize chiral secondary amines that incorporate a double bond. Compound **1** was prepared by following procedure reported in the literature.[5] Procedures leading to chiral secondary amines are either by reduction of amides as shown in Scheme 2 or by reduction of imines as depicted in Scheme 3. Acid **1** was thus reacted with $SOCl_2$ in petroleum ether to afford acyl chloride **2** which was immediately treated with *R*-(+)-methyl benzylamine or *S*-(−)-methylbenzylamine to afford amides **3** and **4** respectively. Reduction of amides **3** and **4** with lithium aluminium hydride in tetrahydrofuran led to secondary

Scheme 1 Formation of enantiomeric pure pyrrolidine and piperidine ring system



Scheme 2 Preparation of secondary amines by reduction of amides



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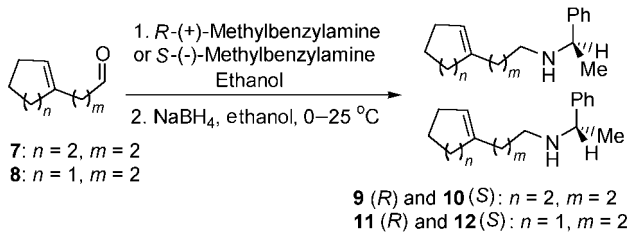
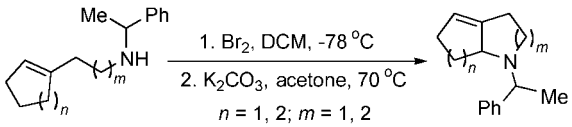
Scheme 3 Preparation of secondary amines by reduction of imines

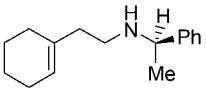
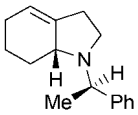
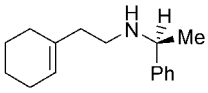
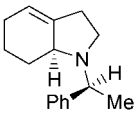
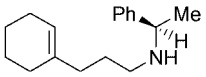
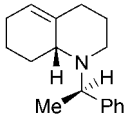
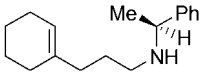
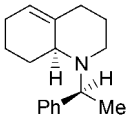
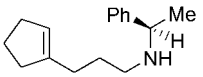
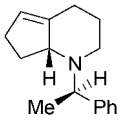
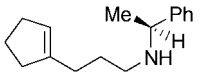
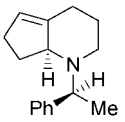


amines **5** and **6**. For compounds **9** to **12**, aldehydes **7** and **8**, prepared by following procedure reported in literature,[6] were treated with chiral amines, *R*-(+)-methylbenzylamine and *S*-(−)-methylbenzylamine, to generate corresponding imines. The resulting imines were reduced by sodium borohydride in ethanol to afford secondary amines **9**, **10**, **11** and **12**.

After obtaining chiral secondary amines, bromination followed by aminocyclization was carried out (see general procedure in experimental section). To our delight, good yields were obtained with excellent diastereoselectivities (see Table 1). Although two diastereoisomers were expected for either *R*- or *S*- secondary amines employed, only one (absolute configuration unassigned) stereoisomer was isolated. Utilization of *R* or *S*-secondary amines afforded cyclization product with identical spectrum (NMR, IR), however, with opposite optical rotation, thus providing a facile method to obtain both stereoisomers of the enantiomeric pair. The diastereomeric excess was determined by chiral HPLC. High diastereomeric excess ($de \geqslant 98\%$) was observed for all substrates used in this research. The double bond was retained in the final products thus rendering this protocol valuable for the synthesis of highly functional piperidine and pyrrolidine ring systems. It is noteworthy that the double bond was formed only in the original carbocyclic ring.

Table 1 Diastereoselective aminocyclization to form chiral pyrrolidine and piperidine ring system

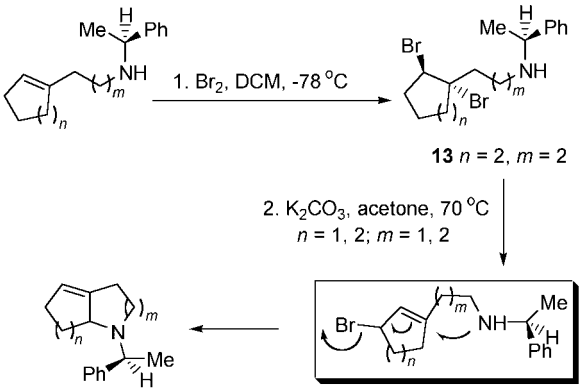


Entry	Secondary amine	Product [a]	Yield [b]/%	*de* [c]/%	$[\alpha]_D^{25}$
1			70	99	+5.4 (*c* 1.50, $CHCl_3$)
2			71	99	−6.1 (*c* 1.30, $CHCl_3$)
3			74	99	−23.7 (*c* 1.28, $CHCl_3$)
4			83	99	+23.4 (*c* 1.05, $CHCl_3$)
5			74	98	+8.0 (*c* 1.20, $CHCl_3$)
6			72	99	−9.2 (*c* 1.54, $CHCl_3$)

[a] The absolute configuration for the newly formed chiral centre was not determined. [b] Yields represented isolated ones based on secondary amine. [c] Diastereomeric excess (*de*%) was determined by chiral HPLC by using Chiralpak AD-RH [Amylose tri(3,5-dimethylphenylcarbamate) coated on 5 nm silica gel substrate] column.

Although we did not isolate the allylic intermediate as depicted in Scheme 4, the high diastereomeric excess as well as the position of the final double bond observed strongly suggested that the pathway of the key cyclization step was through an allylic bromide intermediate. Dibromide **13** was isolated after addition of bromine and it was fully characterized by spectrum means. Treatment of dibromide **13** with potassium carbonate in either DMF or acetone afforded the desire piperidine ring system in good yield with high diastereoselectivity (Scheme 4).

Scheme 4 Pathway for aminocyclization



Conclusion

In summary, a simple while highly diastereoselective method for the synthesis of enantiomerically pure pyrrolidine and piperidine ring containing heterocycles was developed. A plausible pathway was also provided. Utilization of this protocol for the synthesis of natural alkaloid Lycorine is currently underway in our laboratory.

Experimental

General experimental

Infrared (IR) spectra (ν_{max}) were recorded on a Perkin-Elmer 1800 Fourier Transform Infrared spectrophotometer in KBr plates. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker Avance 300 spectrometer at 300 MHz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker Avance 300 spectrometer at 75 MHz. HRMS was recorded on an AutoSpec3090 spectrometer. Chemical shifts are reported as δ values in parts per million (ppm) relative to tetramethylsilane (TMS) for all recorded NMR spectra. Low resolution mass spectra were recorded on a Finnigan Trace 2000 GC-MS spectrometer. Optical rotation was recorded on a Perkin-Elmer 341 polarimeter. Starting materials and reagents used in reactions were obtained commercially from Acros, Aldrich, Fluka and used without purification, unless otherwise indicated.

Synthesis of the chiral secondary amines

Cyclohexen-1-yl-acetylchloride (2) To the solution of compound **1** (700 mg, 5 mmol) in petroleum ether (20 mL) was added $SOCl_2$ (714 mg, 6 mmol). After being stirred at room temperature for 2 h, the mixture was heated to 60 ℃ for 1 h. The petroleum ether and excess $SOCl_2$ were removed under reduced pressure. The crude product was used immediately in the next step without further purification.

2-(Cyclohexen-1-yl)-*N*-(1-phenylethyl)-acetamide (3) Pyridine (790 mg, 10 mmol) in $CHCl_3$ (2 mL) was added to a solution of compound **2** in $CHCl_3$ (15 mL) at 0 ℃. To the resulting mixture, a solution of *R*-(+)- methylbenzylamine (605 mg, 5 mmol) in $CHCl_3$ (5 mL) was added and the mixture was stirred for 2 h at room temperature. The mixture was then heated to 70 ℃ for 1 h and quenched by 2 mol • L^{-1} HCl (3.5 mL). After dilution with water (50 mL), the mixture was extracted with $CHCl_3$ (3×10 mL). The combined organic phases were washed by water and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was filtered through a short column of silica gel to afford compound **3** (1.03 g) as colorless oil. The oil was directly used for reduction without further purification. Physical data of compound **3** are as follows. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.31—7.08 (m, 5H), 6.03 (brs, 1H), 5.52 (brs, 1H), 5.05 (q, J=6.9 Hz, 1H), 2.78 (s, 2H), 1.95 (brs, 2H), 1.86 (brs, 2H), 1.63—1.40 (m, 4H), 1.37 (d, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.20, 143.37, 133.02, 128.63, 127.26, 126.67, 126.03, 48.48, 46.37, 28.37, 25.36, 22.80, 22.03, 21.84; IR (film) ν: 3313, 1645, 1539, 1446, 1245, 1131, 757, 701 cm^{-1}; MS *m/z* (%): 243 (M^+, 10), 228 (1), 120 (8), 105 (100), 77 (17); ESI-HRMS calcd for $C_{16}H_{22}NO$ (M^++1) 244.1696, found 244.1700. Similar procedure also led to the preparation of compound **4**, colorless oil.

(+)-*N*-[2-(Cyclohexen-1-yl)-ethyl]-*N*-(1-phenylethyl)-amine (5) Lithium aluminium hydride (158 mg, 4 mmol) was dissolved in THF (15 mL). To this mixture, a solution of compound **3** (972 mg, 4 mmol) in THF (5 mL) was added at 0 ℃ and the resulting mixture was then stirred at 70 ℃ for 6 h. A solution of KOH (672 mg, 12 mmol) in water (4 mL) was added at 0 ℃ and the mixture was stirred for 30 min at room temperature. After dilution with water (50 mL), the mixture was extracted with Et_2O (3×20 mL). After removal of the solvent, the residue was chromatographed on silica gel [*V*(petroleum ether) : *V*(EtOAc)=10/1] to give compound **5** (733 mg, 80%) as colorless oil. $[\alpha]_D^{25}$ +29.4 (*c* 1.57, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.38—7.20 (m, 5H,), 5.43 (brs, 1H), 3.74 (q, J=6.6 Hz, 1H), 2.62—2.43 (m, 2H), 2.11 (t, J=6.7 Hz, 2H), 2.01—1.90 (m, 2H), 1.85—1.78 (m, 2H), 1.61—1.45 (m, 5H), 1.34 (d, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 146.26, 135.89, 128.76, 127.19, 126.92, 123.08, 58.62, 45.74, 38.74, 28.44, 25.63, 24.68, 23.32, 22.87; IR (film) ν: 3302, 1647, 1492, 1449, 1130, 760, 700 cm^{-1}; MS *m/z* (%): 229

(M^+, 1), 214 (1), 134 (81), 105 (100), 91 (8), 77 (21); ESI-HRMS calcd for $C_{16}H_{24}N$ (M^+ + 1) 230.1903, found 230.1902.

(−)-*N*-[2-(Cyclohexen-1-yl)-ethyl]-*N*-(1-phenylethyl)-amine (6) Compound **6** was obtained (81%) as colorless oil by the procedure as described above for compound **5**. $[\alpha]_D^{25}$ −30.0 (*c* 1.48, $CHCl_3$). Other data were identical to those of compound **5**.

(+)-*N*-[3-(Cyclohexen-1-yl)-propyl]-*N*-(1-phenylethyl)-amine (9) To the solution of compound **7** (542 mg, 4 mmol) in EtOH (15 mL) was added a solution of *R*-(+)-methylbenzylamine (605 mg, 5 mmol) in EtOH (5 mL) at room temperature and the resulting mixture was stirred at 40 ℃ for 5 h under nitrogen. The mixture was cooled to 0 ℃ and $NaBH_4$ (190 mg, 5 mmol) was added in small portion over a period of 20 min. The resulting mixture was stirred at 0 ℃ for 30 min. The solvent was removed under reduced pressure. The residue was diluted with Et_2O (40 mL) and washed with water and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel [*V*(petroleum ether) : *V*(EtOAc)=12/1→10/1] to afford compound **9** (802 mg, 66%) as colorless oil. $[\alpha]_D^{25}$ +37.2 (*c* 1.45, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40—7.18 (m, 5H), 5.36 (brs, 1H), 3.75 (q, *J*=6.6 Hz, 1H), 2.52—2.32 (m, 2H), 2.01—1.82 (m, 6H), 1.75—1.42 (m, 7H), 1.35 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 146.01, 137.60, 128.50, 126.92, 126.69, 121.09, 58.43, 47.70, 35.90, 28.34, 28.25, 25.36, 24.48, 23.12, 22.69; IR (film) *v*: 1602, 1491, 1448, 1132, 760, 700 cm^{-1}; MS *m/z* (%): 243 (M^+, 3), 228 (15), 147 (28), 134 (23), 105 (100), 91 (10), 77 (13); ESI-HRMS calcd for $C_{17}H_{26}N$ (M^++1) 244.2060, found 244.2058.

(−)-*N*-[3-(Cyclohexen-1-yl)-propyl]-*N*-(1-phenylethyl)-amine (10) Similar procedure led to compound **10** (67%), a colorless oil. $[\alpha]_D^{25}$ −36.5 (*c* 1.15, $CHCl_3$). Other data were identical to those of compound **9**.

(+)-*N*-[3-(Cyclopenten-1-yl)-propyl]-*N*-(1-phenylethyl)-amine (11) To the solution of compound **8** (372 mg, 3 mmol) in EtOH (15 mL) was added dropwise *R*-(+)-methylbenzylamine (436 mg, 3.6 mmol) in EtOH (5 mL) at room temperature and the reaction mixture was stirred at 40 ℃ for 5 h under nitrogen. The resulting mixture was cooled to 0 ℃ and then added $NaBH_4$ (114 mg, 3 mmol) in portions. The resulting mixture was stirred at 0 ℃ for 30 min. The solution was evaporated under reduced pressure. The residue was diluted with Et_2O and the solution was washed with water and dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, the residue was chromatographed on silica gel [*V*(petroleum ether) : *V*(EtOAc) = 12/1] to afford compound **11** (447 mg, 65%) as colorless oil. $[\alpha]_D^{25}$ + 39.2 (*c* 1.08, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.30—7.10 (m, 5H), 5.22 (brs, 1H), 3.67 (q, *J*=6.6 Hz, 1H), 2.48—2.28 (m, 2H), 2.21—2.04 (m, 4H), 1.98 (t, *J* =7.4 Hz, 2H), 1.82—1.70 (m, 2H), 1.61—1.30 (m, 3H), 1.27 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.83, 143.37, 127.35, 125.98, 125.51, 122.35, 57.28, 46.64, 33.98, 31.37, 27.90, 27.33, 23.34, 22.39; IR (film) *v*: 3316, 1602, 1491, 1449, 1129, 760, 700 cm^{-1}; MS *m/z* (%): 229 (M^+, 7), 214 (23), 147 (15), 134 (32), 105 (100), 91 (13), 79 (27), 67 (20); ESI-HRMS calcd for $C_{16}H_{24}N$ (M^++1) 230.1903, found 230.1900.

(−)-*N*-[3-(Cyclopenten-1-yl)-propyl]-*N*-(1-phenylethyl)-amine (12) Compound **12**, colorless oil, was similarly prepared (66%) as described for compound **11**. $[\alpha]_D^{25}$ −38.6 (*c* 1.24, $CHCl_3$). Other data were identical to those of compound **11**.

General procedure for aminocyclization

Chiral secondary amine (1.0 mmol) in dichloromethane (10 mL) was stirred under nitrogen at –78 ℃ for 5 min. Dry bromine (1.2 mmol, pre-washed with concentrated sulfuric acid) in dichloromethane (2 mL) was added dropwise under nitrogen at –78 ℃ over a period of 5 min. The resulting mixture was then stirred at –78 ℃ for 10 min. The dichloromethane was removed under reduced pressure and acetone (10 mL) or DMF (6 mL) was then added together with K_2CO_3 (414 mg, 3 mmol). The resulting mixture was heated to 50 ℃ under nitrogen. The reaction was monitored by thin-layer chromatography. After removal of the solvent, the residue was diluted with water (10 mL) and extracted with dichloromethane (3 × 10 mL). The organic phases were combined and washed with water and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was chromatographed on silica gel [petroleum ether-EtOAc] to afford the enantiomerically pure products.

1-(1-Phenylethyl)-2,3,5,6,7,7a-hexahydroindole Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.29 (dd, *J*=1.5, 8.3 Hz, 2H), 7.20 (ddd, *J*=1.5, 8.1, 8.3 Hz, 2H), 7.15 (dd, *J*=1.5, 8.1 Hz, 1H), 5.32 (brs, 1H), 3.57 (q, *J*=6.7 Hz, 1H), 2.98 (m, 1H), 2.63 (m, 1H), 2.40—2.25 (m, 3H), 1.86 (m, 2H), 1.57 (m, 1H), 1.31 (d, *J*=6.7 Hz, 3H), 1.31—1.10 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.56, 139.89, 127.01, 126.66, 125.73, 117.60, 62.73, 61.19, 47.59, 28.61, 26.71, 23.93, 19.86, 17.70; IR (film) *v*: 1601, 1492, 1451, 1370, 1279, 1128, 762, 699 cm^{-1}; MS *m/z* (%): 227 (M^+, 15), 212 (17), 199 (52), 122 (25), 105 (100), 95 (84), 91 (23), 77 (31); ESI-HRMS calcd for $C_{16}H_{22}N$ (M^++1) 228.1752, found 228.1760. For other data see Table 1.

1-(1-Phenylethyl)-1,2,3,4,6,7,8,8a-octahydroquinoline Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.39 (d, *J*=7.5 Hz, 2H), 7.22 (dd, *J*=7.1, 7.5 Hz, 2H), 7.13 (d, *J*=7.1 Hz, 1H), 5.41 (brs, 1H), 4.32 (q, *J*=6.7 Hz, 1H), 3.01 (m, 1H), 2.40 (d, *J*=11.2 Hz, 1H), 2.25—1.85 (m, 6H), 1.75 (m, 1H), 1.65—1.20 (m, 4H), 1.20 (d, *J*=6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.88, 137.88, 128.05, 127.93, 126.29, 121.78, 57.79, 53.92, 45.25, 34.85, 29.18, 26.85, 25.66, 21.82, 7.80; IR (film) *v*: 1601, 1493, 1446, 1139, 777, 697 cm^{-1}; MS *m/z* (%): 241 (M^+, 2), 213 (26), 136 (13), 109 (98), 105 (100), 94 (10), 91 (25), 79 (47), 77 (44), 67 (16), 53 (10),

41 (20); ESI-HRMS calcd for $C_{17}H_{24}N$ (M^++1) 242.1904, found 242.1908. For other data see Table 1.

4-Aza-4-(1-phenylethyl)-3,3a,4,5,6,7-hexahydro-2*H*-indene Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.39 (d, J=7.2 Hz, 2H), 7.23 (dd, J=0, 7.2 Hz, 2H), 7.16 (d, J=7.0 Hz, 1H), 5.32 (brs, 1H), 3.99 (q, J=6.7 Hz, 1H), 3.43 (m, 1H), 2.54—2.05 (m, 6H), 1.90—1.22 (m, 4H), 1.26 (d, J=6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.32, 142.01, 126.80, 126.79, 125.28, 121.13, 64.78, 55.08, 43.52, 30.14, 28.71, 26.33, 24.94, 7.52; IR (film) v: 1493, 1448, 1378, 1259, 1017, 801, 697 cm^{-1}; MS *m/z* (%): 227 (M^+, 47), 226 (24), 212 (38), 123 (35), 122 (74), 108 (24), 105 (100), 95 (23), 91 (21), 79 (47), 77 (37); ESI-HRMS calcd for $C_{16}H_{22}N$ (M^++1) 228.1760, found 228.1752. For other data see Table 1.

***N*-[3-(1,2-Dibromocyclohexyl)-propyl]-*N*-(1-phenylethyl)-amine (13)** To the solution of compound **9** (121.5 mg, 0.5 mmol) and $NaHCO_3$ (84 mg, 1 mmol) in DCM (15 mL) was added dropwise Br_2 (176 mg, 1.1 mmol) in DCM (5 mL) at –78 ℃. The reaction mixture was stirred at the same temperature for 10 mins. After being warmed to room temperature, the reaction mixture was extracted with DCM. After evaporation of solvent under reduced pressure, the residue was chromatographed on silica gel [DCM-acetone, 50/1] to afford compond **13** 175 mg (87%) as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.38—7.24 (m, 5H), 4.63 (brs, 1H), 3.79 (q, J=6.6 Hz, 1H), 2.65—2.42 (m, 3H), 2.11—1.71 (m, 10H), 1.70—1.40 (m, 2H), 1.38 (d, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.68, 127.39, 125.83, 125.55, 75.10, 58.26, 57.11, 46.36, 34.81, 30.82, 23.86, 23.79, 23.31, 21.19, 19.43; IR (film) v: 3319, 1651, 1492, 1450, 1182, 761, 700 cm^{-1}; MS (FAB^+) *m/z* (%): 406 (24), 404 (54), 402 (M^++1, 34), 324 (12), 322 (14), 308 (6), 254 (15), 244 (100), 242 (86), 240 (30), 226 (21), 147 (36), 134 (72), 120 (22), 105 (100); ESI-HRMS calcd for $C_{17}H_{26}Br_2N$ (M^++1) 402.0407, found 402.0433.

References

1 (a) Lewis, J. R. *Nat. Prod. Rep*. **2001**, *18*, 95.
(b) O'Hagen, D. *Nat. Prod. Rep*. **2000**, *17*, 435.
(c) Watson, P. S.; Jiang, B.; Scott, B. *Org. Lett*. **2000**, *2*, 3679.
(d) Gogfraid, T.; Miller, R.; Wibo, M. *Pharmacol. Rev*. **1986**, *38*, 32.

2 For representative papers on the pyrrolidine series, see:
(a) Xu, Y. Z.; Choi, J.; Calaza, M. I.; Turner, S. C.; Rapoport, H. *J. Org. Chem*. **1999**, *64*, 4069.
(b) Turner, S. C.; Zhai, H.; Rapoport, H. *J. Org. Chem*. **2000**, *65*, 861.
(c) Knight, D. W.; Salter, R. *Tetrahedron Lett*. **1999**, *40*, 5915.

3 For representative papers on the piperidine series, see:
(a) Takahata, H.; Kubota, M.; Ikota, N. *J. Org. Chem*. **1999**, *64*, 8594.
(b) Kumareswaran, R.; Balasubramanian, T.; Hassner, A. *Tetrahedron Lett*. **2000**, *41*, 8157.
(c) Agammi, C.; Couty, F.; Evano, G. *Tetrahedron: Asymmetry* **2000**, *11*, 4639.
(d) Eskici, M.; Gallagher, T. *Synlett* **2000**, 1360.
(e) Willis, J. C.; Bellosta, V.; Bouzbouz, S. *Synlett* **2000**, 1461.
(f) Lindstrom, S.; Ripa, L.; Halberg, A. *Org. Lett*. **2000**, *2*, 2291.
(g) Cossy, J.; Pevet, I.; Mever, C. *Synlett* **2000**, 122.

4 For reviews on asymmetric synthesis of the pyrrolidine and piperidine derivatives, see:
(a) Bailey, P. D.; Millwood, P. A.; Smith, P. D. *J. Chem. Soc., Chem. Commun*. **1998**, 633.
(b) Dickner, S. T. *Synthesis* **2000**, 1781.
(c) Clark, A. J. *Chem. Soc. Rev*. **2002**, *31*, 1.

5 Shao, Z.-H.; Chen, J.-B.; Tu, Y.-Q.; Li, L.; Zhang, H.-B. *Chem. Commun*. **2003**, 1918.

6 Ruppert, J. F.; White, J. D. *J. Org. Chem*. **1974**, *39*, 269.

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