JOC Article

Synthesis of Chiral Nonracemic 1-(2-Pyridinyl)ethylamines: Stereospecific Introduction of Amino Function onto the 2-Pyridinylmethyl Carbon Center

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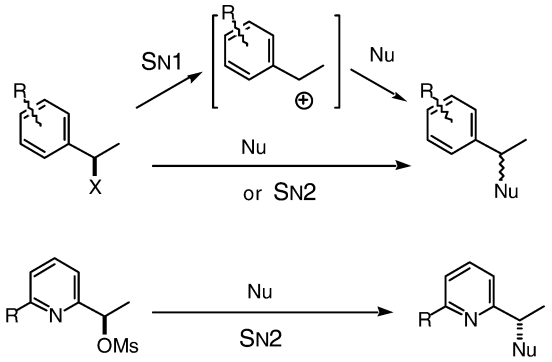
Stereospecific substitutions of optically pure 1-(pyridinyl)ethyl methanesulfonates with various amines are described. The reaction of (*R*)- or (*S*)-1-(2-pyridinyl)ethyl methanesulfonate with primary amines, including amino acid esters, gives *N*-substituted (*S*)- or (*R*)-1-(2-pyridinyl)ethylamines (**4**) with inversion of the configuration. Secondary cyclic amines are also reacted with (*R*)-**2** to give the corresponding substituted amines (**5**) in excellent yields. Optically pure and *meso* triamine ligands having two pyridine rings, (*S*,*S*)-**4f** and *meso*-**4f**, (*S*,*S*)-**9e**, (*S*,*R*)-**9e**, and (*S*,*S*)-**9f**, have been prepared in stereochemically pure form by this method. Not only the substitution reaction of optically active **2** but also that of 1-(4-pyridinyl)ethyl and 1-(3-pyridinyl)ethyl methanesulfonates **11** and **14** take place stereospecifcally with inversion of the chiral center.

Introduction

Although nucleophilic substitution reaction on the benzylic position has been extensively investigated in aromatic systems,[1] there have been few studies of that on the pyridinylmethyl position.[2] The nucleophilic substitution reaction of 1-(phenyl)ethyl halide occurs mostly through an S_N1 process along with a partial S_N2 process.[1a,b] Therefore, this substitution does not take place stereospecifically except in limited cases in which a strong electron-withdrawing group is attached on the aromatic ring.[1e] On the other hand, we have recently reported that perfect stereospecific substitution occurred in the case of 1-(2-pyridinyl)ethyl methanesulfonate with an inversion of the configuration through an S_N2 process. Optically pure 1-(2-pyridinyl)ethylamines were obtained when chiral nonracemic methanesulfonate derivatives were used for the reaction (Scheme 1).[3] Since chiral nonracemic pyridine derivatives have become important as ligands in modern asymmetric synthesis as well as molecular recognition chemistry,[4] it will be valuable to synthesize pure chiral nonracemic pyridine derivatives. In this paper, we report in detail substitution reactions at the pyridinylmethyl position with amine nucleophiles, in-

SCHEME 1



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(2) (a) Chelucci, G.; Cabras, M. A.; Saba, A. *Tetrahedron*: *Asymmetry* **1994**, *5*, 1973−1978. (b) Jiang, Q.; Plew, D. V.; Murtuza, S.; Zhang, X. *Tetrahedron Lett.* **1996**, *37*, 797−800. (c) Haviv, F.; DeNet, R. W.; Michaels, R. J.; Ratajczyk, J. D.; Carter, G. W.; Young, P. R. *J. Med. Chem.* **1983**, *26*, 218−222. (d) Kostik, E. L.; Abiko, A.; Oku, A. *J. Org. Chem.* **2001**, *66*, 1638−1646. (e) Jiang, Q.; Plew, D. V.; Murtuza, S.; Zhang, X. *Tetrahedron Lett.* **1996**, *37*, 797−800.

(3) (a) Uenishi, J.; Takagi, T.; Ueno, T.; Hiraoka, T.; Yonemitsu, O.; Tsukube, H. *Synlett* **1999**, 41−44. (b) Uenishi, J.; Hiraoka, T.; Yuyama, K.; Yonemitsu, O. *Heterocycles* **2000**, *52*, 719−732. (c) Uenishi, J.; Hamada.; Takagi, T.; Yonemitsu, O. *Heterocycles* **2001**, *53*, 735−746. (d) Uenishi, J.; Hamada, M. *Tetrahedron*: *Asymmetry* **2001**, *21*, 2999−3006.

(4) (a) Chelucci, G.; Orru, G.; Pinna, G. A. *Tetrahedron* **2003**, *59*, 9471−9515. (b) Fletcher, N. C. *J. Chem. Soc., Perkin Trans. 1* **2002**, 19831−1842. (c) Soai, K.; Sato, I. *Viva Origino* **2002**, *30*, 186−198. (d) Vancheesan, S.; Jesudurai, D. *Catalysis* **2002**, 311−337. (e) Chelucci, G.; Thummel, R. P. *Chem. Rev.* **2002**, *102*, 3129−3170. (f) Nishiyama, H. *Enantiomer* **1999**, *4*, 569−574. (g) Mamula, O.; von Zelewsky, A. *Coord. Chem. Rev.* **2003**, *242*, 87−95.

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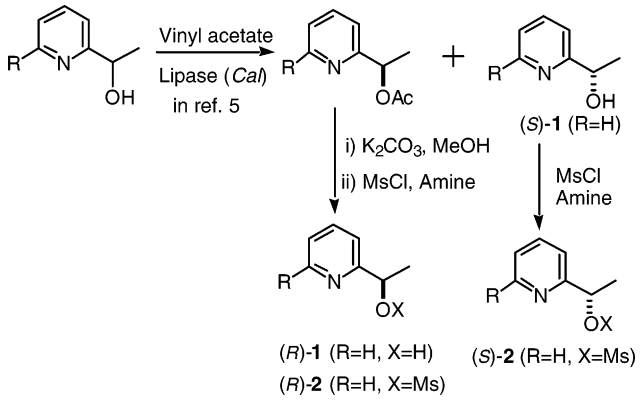
SCHEME 2



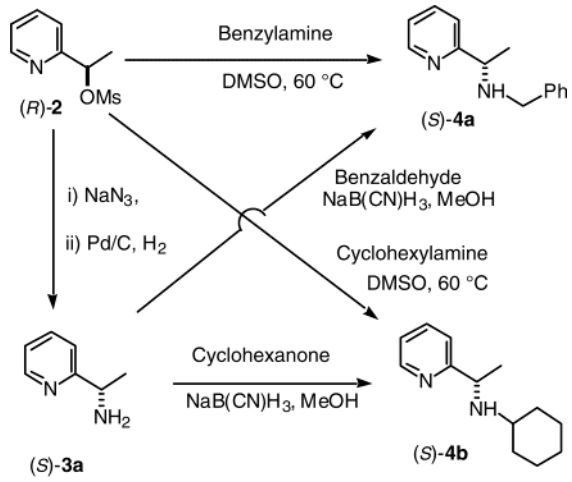
cluding amino acid esters and preparation of a variety of chiral nonracemic 1-(pyridinyl)ethylamines.

Results and Discussion

We previously reported that lipase-catalyzed kinetic acetylation of racemic 1-(2-pyridinyl)ethanols by vinyl acetate gave optically pure (*R*)-1-(2-pyridinyl)ethyl acetates and recovery of (*S*)-1-(2-pyridinyl)ethanols.[5] (*R*)-1-(2-Pyridinyl)ethanols were derived by methanolysis of the resulting acetates quantitatively. Mesylation of the optically pure alcohols (*R*)-**1** (R = H) and (*S*)-**1** (R = H) with methanesulfonyl chloride in the presence of either triethylamine or DMAP gave the corresponding methanesulfonates (*R*)-**2** (R = H) and (*S*)-**2** (R = H) in quantitative yields with retention of the configuration (Scheme 2).[3b] These mesylates could be purified by silica gel column chromatography. Although they become red in color after 1 day, they can be used for the next reaction. The red-colored substance increases gradually upon storage for long periods of time and is assumed to be a dimer of pyridinium salt due to its solubility in water. If that is the case, the mesylate can be purified easily by silica gel chromatography.

Treatment of compound (*R*)-**2** with an excess of benzylamine in DMSO at 60 °C for 3 h gave (*S*)-*N*-benzyl-*N*-1-(2-pyridinyl)ethylamine (*S*)-**4a** in 93% yield. The reaction with cyclohexylamine gave (*S*)-**4b** in 76% yield. The stereochemistry of the products was confirmed to be of the (*S*)-configuration by subsequent independent syntheses shown in Scheme 3. Thus, reductive amination of benzaldehyde with the known (*S*)-1-(2-pyridinyl)ethylamine (*S*)-**3a**,[6] which was also derived by the substitution reaction of (*R*)-**2** with sodium azide and successive reduction of the resulted azide,[3b] gave (*S*)-**4a** in 75% yield. In the same manner, the reaction of (*S*)-**3a** with cyclohexanone afforded (*S*)-**4b** in 84% yield. On the other hand, starting from (*S*)-**2**, the same sequence of the reactions gave their enantiomers, (*R*)-**3a**, (*R*)-**4a**, and (*R*)-**4b**, respectively. The optical purity of the products was determined to be over 95% ee by a chiral HPLC experiment. Since the ee value of **4a** or **4b** was equal to that of the original starting material, (*R*)-**2** or (*S*)-**2**, the reaction was proved to occur stereospecifically via an S_N2 process.

SCHEME 3



However, it is noted that the mesylate should not be used without purification, because the chloride is partially formed in some cases as a secondary product by substitution of the mesylate with the resulted triethylamine hydrochloride and contaminates the crude product. Since the chloride has a stereochemistry opposite to that of the mesylate, the substitution reaction using the crude mesylate results in a decrease in the overall enantiomeric purity of the desired enantiomer. In fact, a lower ee value was observed in the same substitution reaction in some cases when crude mesylate was used.[7] Although the chloride was produced in a longer reaction time, very little chloride was formed when the mesylation was completed in a short time by the use of an excess of reagents at 0 °C.

DMSO was found to be the best solvent for this substitution reaction. When the reaction of (*R*)-**2** with benzylamine was carried out in other solvents such as HMPA, EtOH, acetonitrile, and DMF at 60 °C for 3 h, the reactions were clean but yields of (*S*)-**4a** did not exceed 50−60%. In comparison, when the reaction was conducted in benzene or THF, the yield was poor.

Although the reaction proceeded very well in DMSO, removal of DMSO from the amine product was sometimes troublesome. It requires high-vacuum conditions or gel permeation HPLC separation. In such cases, acetonitrile is an alternative solvent. Although the reaction in acetonitrile was 3−6 times slower than that in DMSO, purification of the product was much easier than in the case of using DMSO. In addition, the reaction proceeded cleanly even at a temperature over 60 °C, and, more importantly, the chiral center was not racemized at all in DMSO and acetonitrile. Therefore, acetonitrile is a solvent suitable for obtaining polar amine products.

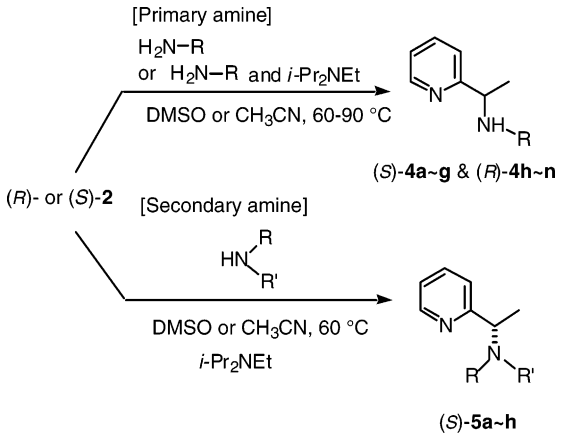
The mesylate (*R*)-**2** reacted with primary as well as secondary amines as shown in Scheme 4. The results obtained by using various primary amines, including

(5) Uenishi, J.; Hiraoka, T.; Hata, S.; Nishiwaki, K.; Yonemitsu, O.; Nakamura, K.; Tsukube, H. *J. Org. Chem.* **1998**, *63*, 2481−2487.

(6) Previous reports for the synthesis of nonracemic 1-(2-pyridinylethyl)amine: (a) Brunner, H.; Fisch, H. *J. Organomet. Chem.* **1987**, *335*, 1−14. (b) Michelsen, K. *Acta Chem. Scand.* **1974**, A *28*, 428−434.. (c) Cervinka, O.; Belovsky, O.; Rejmanova, P. *Coll. Czech. Chem. Comm.* **1973**, *38*, 1358−1363. (d) Mi, A.; Xiao, X.; Wu, L.; Jiang, Y. *Synth. Commun.* **1991**, *21*, 2207−2212.

(7) When the crude mesylate was used for the substitution with azide anion, the ee values were reported to be 66−92% in ref 2a and also were confirmed by our hands. However, the reaction gave the product with excellent ee (>95%) as long as we used the purified mesylate.

SCHEME 4



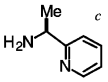
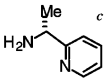
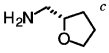
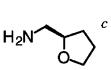
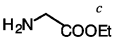
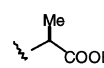
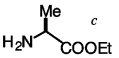
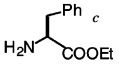
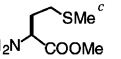
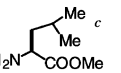
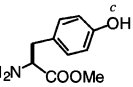
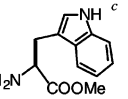
amino acid esters, are summarized in Table 1. The reaction with primary amines was fast and was complete within 1 h. The reaction with aniline gave (*S*)-**4c** in 79% yield, and that with bulky adamantylamine gave (*S*)-**4d** in 83% yield (entries 3 and 4). Chiral nonracemic amines such as (*S*)- and (*R*)-1-(phenyl)ethylamines reacted without epimerization to give (*S*,*S*)-**4e** and (*S*,*R*)-**4e** in 82 and 90% yields, respectively (entries 5 and 6). Since the proton NMR spectrum of the crude product indicated a single diastereomer, the reaction was confirmed to proceed stereospecifically. Similarly, the reaction of (*R*)-**2** with (*S*)-1-(2-pyridinyl)ethylamine ((*S*)-**3a**) gave (*S*,*S*)-*N*,*N*-bis[1-(2-pyridinyl)ethyl]amine ((*S*,*S*)-**4f**) in 86% yield (entry 7). However, that with (*R*)-**3a** gave *meso*-*N*,*N*-bis-1-(2-pyridinyl)ethylamine (*meso*-**4f**) in 87% yield (entry 8). The reaction with 2-furylmethylamines efficiently gave the corresponding amines, (*S*,*S*)-**4g** and (*S*,*R*)-**4g,** in 62 and 64% yields, respectively (entries 9 and 10).

The reaction of (*S*)-**2** with amino acid ester gave *N*-1-(2-pyridinyl)ethyl-substituted amino acid ester. The results obtained by using seven amino acid esters are listed in entries 11−17. The reaction with glycine ethyl ester gave (*R*)-**4h** in 77% yield. Although other L-amino acid esters are good substrates, the reactions caused partial racemization of the amino acid ester unit. For example, the reaction with L-alanine ethyl ester at 90 °C gave *N*-[1-(2-pyridinyl)ethyl]alanine ester (*R*)-**4i** containing 20% of the other diastereomer due to the epimerization of the chiral center in the amino acid ester unit. This minor diastereomer was identified with the major product yielded by the reaction of (*R*)-**2** with L-alanine ethyl ester. Better diastereomeric ratios were obtained at 60 °C with longer reaction times (entries 14−17).

As shown in Table 2, cyclic secondary amines also reacted with (*R*)-**2** to give (aminoethyl)pyridines (*S*)-**5a**−**i** in excellent yields. The reaction with (*R*)- and (*S*)-prolinols gave (*S*,*S*)-**5h** and (*S*,*R*)-**5i** as single stereoisomers in 86 and 87% yields, respectively (entries 8 and 9). However, acyclic secondary amines reacted poorly. For example, the reaction of (*R*)-**2** with diethylamine gave only 35% yield even with a prolonged reaction time or at an elevated temperature.[8]

(8) New optically pure (*R*,*R*)- and (*R*,*S*)-*N*-2-pyridinylmethyl-*N*,*N*-bis-[1-(2-pyridinyl)ethyl]amines for luminescent lanthanide complexes were prepared by this method, see: Yamada, T.; Shinoda, S.; Sugimoto, H.; Uenishi, J.; Tsukube, H. *Inorg. Chem.*. **2003**, *42*, 7932−7937.

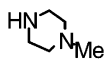
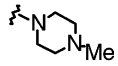
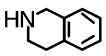
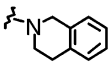
TABLE 1. Stereospecific Substitution of (*R*)- and (*S*)-2 with Nonchiral and Chiral Nonracemic Primary Amines

entry	conf. of mesylate	amine H_2N−R	time (h)	product	R	yield[a] (%)
1	*R*		0.4[b]	(*S*)-**4a**		93
2	*R*		0.3[b]	(*S*)-**4b**		76
3	*R*	H_2N−Ph	0.3[b]	(*S*)-**4c**		79
4	*R*	H_2N−adamantyl	0.3[b]	(*S*)-**4d**		83
5	*R*		1.0[b]	(*S*,*S*)-**4e**		82
6	*R*		0.5[b]	(*S*,*R*)-**4e**		90
7	*R*		0.4[d]	(*S*,*S*)-**4f**		86
8	*R*		0.1[d]	*meso*-**4f**		87
9	*R*		0.1[d]	(*S*,*S*)-**4g**		62
10	*R*		0.3[d]	(*S*,*R*)-**4g**		64
11	*S*		22[e]	(*R*)-**4h**		77
12	*S*		13[e]	(*R*)-**4i**[f]		72
13	*S*		23[e]	(*R*)-**4j**[g]		83
14	*S*		37[d]	(*R*)-**4k**[h]		65
15	*S*		37[d]	(*R*)-**4l**[i]		57
16	*S*		63[d]	(*R*)-**4m**[h]		74
17	*S*		42[d]	(*R*)-**4n**[j]		70

[a] Isolated yield. [b] DMSO was used as a solvent. [c] *i*-Pr_2NEt was used as a base. [d] CH_3CN was used as a solvent at 60 °C. [e] CH_3CN was used as a solvent at 90 °C. [f] Dr (diastereomeric ratio) = 4:1. [g] Dr = 4.4:1. [h] Dr = 12:1. [i] Dr = 13:1. [j] Dr = 14:1.

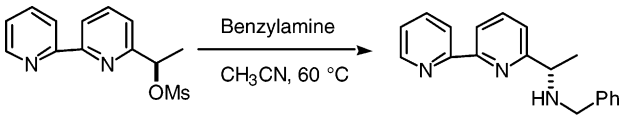
2,2′-Bipyridine and 2,2′:6′,2″-terpyridine are important ligands in coordination chemistry as well as organometallic chemistry.[4d,e] However, optically pure 1-(2,2′-bipyridinyl)ethylamine derivatives have not been synthesized so far. Optically pure 6-[1-(*N*-benzylamino)ethyl]-2,2′-bipyridine (*S*)-**7** was prepared in 57% yield from optically pure 6-(1-hydroxyethyl)-2,2′-bipyridinyl methanesulfonate

TABLE 2. Stereospecific Substitution of (*R*)-2 with Nonchiral and Chiral Nonchiral Secondary Amines

entry	amine HNRR'	time (h)	product	R	yield [a] (%)
1		0.4 [b]	(*S*)-**5a**		79
2		0.3 [b]	(*S*)-**5b**		76
3		0.3 [b]	(*S*)-**5c**		79
4		0.3 [b]	(*S*)-**5d**		83
5		0.3 [b]	(*S*)-**5e**		73
6		1.0 [b]	(*S*)-**5f**		82
7		0.5 [b]	(*S*)-**5g**		90
8		0.4 [c,d]	(*S,S*)-**5h**		86
9		0.1 [c,d]	(*S,R*)-**5h**		87

[a] Isolated yield. [b] DMSO was used as a solvent. [c] CH_3CN was used as a solvent. [d] *i*-Pr_2NEt was used as a base.

SCHEME 5

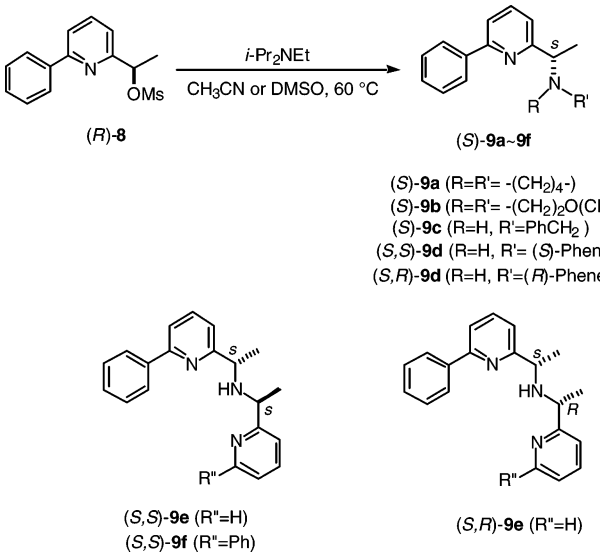


(*R*)-**6** (*S*)-**7**

(*R*)-**6**[3b] in the same manner as described for the substitution reaction of (*R*)-**2** (Scheme 6).

More complex chiral pyridines have been prepared by the same method. Syntheses of 6-phenyl-substituted pyridines **9a**−**f** are shown in Scheme 6. When mesylate (*R*)-**8**, which was prepared from 1-[2-(6-phenylpyridinyl)]-ethanol,[3d] was treated with pyrrolidine, piperidine, and benzylamine, (*S*)-**9a**, (*S*)-**9b**, and (*S*)-**9c** were obtained in 65, 71, and 90% yields, respectively. Similarly, the reaction of (*R*)-**8** with (*S*)- and (*R*)-1-(phenyl)ethylamines gave (*S,S*)-**9d** and (*S,R*)-**9d** in 48 and 61% yields, respectively. No diastereoisomer was detected in the NMR spectra of the crude products of (*S,S*)-**9d**. Triamines (*S,S*)-**9e** and (*S,R*)-**9e** were obtained by substitution reaction with (*S*)- and (*R*)-1-(2-pyridinyl)ethylamines in 60 and 69% yields, respectively. Since they are not separable by chromatographic techniques, including HPLC, the stereospecific synthesis of (*S,S*)-**9e** and (*S,R*)-**9e** is valuable. Substitution with (*S*)-1-[2-(6-phenylpyridinyl)]ethylamine gave an optically active C_2-symmetric triamine ligand (*S,S*)-**9f** in 37% yield. Since they are triamine ligands

SCHEME 6



having two pyridine units beside the chiral secondary ethylamine, they are expected to behave as host molecules.[9]

All the results suggest that the substitution reaction proceeded via the S_N2 process. That is, the product was obtained with perfect inversion of the stereocenter. However, it is known that S_N1 and S_N2 reactions compete in the case of 1-(phenyl)ethyl halide due to the stability of the benzylic cation.[1] An electron-withdrawing group substituted on the aromatic ring enhances the S_N2 process, while an electron-donating group stabilizes the benzylic cation to suppress it. In the case of a 2-pyridinyl or 4-pyridinylmethyl group, the corresponding benzylic cation was destabilized by not only the electron-withdrawing property but also the reverse resonance effect of the pyridine ring. Since the S_N1 process is unfavorable in these cases, the S_N2 reaction occurs in the reactions of 1-(2-pyridinyl)ethyl methanesulfonate and 1-(4-pyridinyl)ethyl methanesulfonate. In fact, displacement of (*R*)-1-(4-pyridinyl)ethanol (*R*)-**10**[10] with piperidine took place via its methanesulfonate (*R*)-**11** stereospecifically to give optically pure *N*-1-(4-pyridinyl)ethylpiperidine (*S*)-**12** in 84% yield with an inversion of the stereochemistry (Scheme 7).

Since the 1-(3-pyridinyl)ethyl cation generated from 1-(3-pyridinyl)ethyl methanesulfonate (*R*)-**14** is stabilized by the resonance effect of the pyridine ring, it is hydrolyzed quite easily on a silica gel column.[11] Therefore, 1-(3-pyridinyl)ethyl methanesulfonate (*R*)-**14** was obtained with difficulty in pure form[12] and substituted amines were obtained in poor yields with some loss of enantiomeric purity. However, after the mesylation, the resulting ammonium chloride salt was removed by filtration, and the quickly condensed filtrate was subjected to substitu-

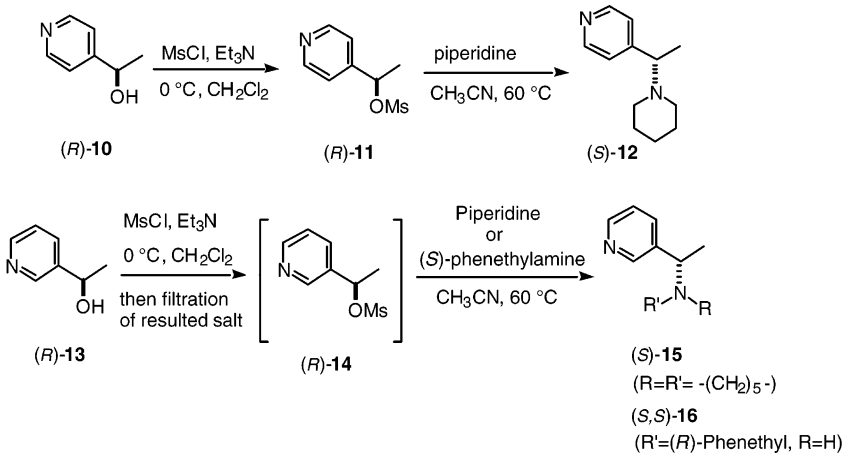
(9) Complex formations with some metals are in progress in our laboratory.

(10) Literature for the synthesis of nonracemic 1-(3- and 4-pyridinyl)ethanols: (a) Ziffer, H.; Kawai, K.-i.; Kasai, M.; Imura, M.; Froussios, C. *J. Org. Chem.* **1983**, *48*, 3017−3021. (b) Laumen, K.; Schneider, M. P. *J. Chem. Soc., Chem. Commun.* **1988**, 598−600.

(11) Since the hydrolyzed product (*R*)-1-(3-pyridinyl)ethanol was found to be 60% ee, S_N2 and S_N1 processes were in competition.

(12) Aqueous workup or purification by silica gel chromatography gave a mixture of mesylate and hydrolyzed product.

SCHEME 7



tion reaction with piperidine to give *N*-1-(3-pyridinyl)-ethylpiperidine (*S*)-**15** in 69% yield from (*R*)-**13**. As long as these processes were handled quickly, the ee value could be maintained over 90%. As an additional example, the reaction with optically pure (*S*)-1-(phenyl)ethylamine gave (*S*,*S*)-**16** in 40% yield using this recipe. The stereochemical results were confirmed by chiral HPLC and also by the fact that the formation of a diastereomer of (*S*,*S*)-**16** was found to be less than 5% in the NMR spectrum. These results clearly indicated that the substitution took place mostly via the S_N2 process, even with (3-pyridinyl)-ethyl methanesulfonate.

Conclusion

In conclusion, stereospecific substitutions of 1-(pyridinyl)ethyl methanesulfonates with amines were achieved. When chiral nonracemic 1-(pyridinyl)ethanol was used, the corresponding chiral nonracemic 1-(pyridinyl)ethylamine was obtained with inversion of the chiral center. This methodology is general and useful for the preparation of not only simple 1-(2-pyridinyl)ethylamines but also of more complex 1-(2-pyridinyl)ethylamines such as **9**. Construction of multiple chiral complexity of pyridine containing triamine ligands will be reported in due course.

Experimental Section

General Substitution Reaction of (*R*)-2 with Various Primary Amines. A mixture of (*R*)-**2** (201 mg, 1 mmol), the corresponding primary amine (1.5−2.5 mmol) listed in Table 1, and diisopropylethylamine (5 mmol) was heated at 60 °C in DMSO or acetonitrile (2−5 mL). The reaction mixture was quenched with water and extracted with EtOAc or with CH_2Cl_2. If necessary, the mixture was made basic by aq Na_2CO_3 and extracted. The organic extract was washed with brine and dried over $MgSO_4$. The crude product was purified by silica gel column chromatography eluted with a mixture of EtOAc and hexane or EtOAc containing 1−5% Et_3N. Note for the experiment: When the product is less polar and easily separable from DMSO, DMSO is recommended. When the primary amine is cheap, an excess of the amine can be used instead of diisopropylethylamine. DMAP can be used instead of diisopropylethylamine when the product amine is less polar and easily separable from DMAP.

(*S*)-*N*-Benzyl-*N*-[1-(2-pyridinyl)ethyl]amine ((*S*)-4a): oil; R_f = 0.45 (EtOAc); $[\alpha]^{27}_D$ −45 (*c* 1.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (d, *J* = 6.7 Hz, 3H), 2.10−2.26 (br, 1H), 3.64 (ABq, *J* = 7.9, 14.4 Hz, 2H), 3.92 (q, *J* = 6.7 Hz, 1H), 7.16 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 7.20−7.30 (m, 5H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.65 (td, *J* = 7.6, 1.8 Hz, 1H), 8.58 (dm, *J* = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.6, 51.5, 58.4, 121.1, 121.8, 126.7, 128.0 (2C), 128.1 (2C), 136.4, 140.0, 149.1, 164.1; LRMS (FAB) 213 (M^+ + H); HRMS (FAB) calcd for $C_{14}H_{17}N_2$ 213.1392 (M^+ + H), found 213.1408.

(*S*)-*N*-Cyclohexyl-*N*-[1-(2-pyridinyl)ethyl]amine ((*S*)-4b): oil; R_f = 0.13 (EtOAc); $[\alpha]^{27}_D$ −75 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00−1.23 (m, 5H), 1.37 (d, *J* = 6.7 Hz, 3H), 1.58−1.80 (m, 3H), 1.90−2.05 (br, 1H), 2.10−2.30 (m, 3H), 4.05 (q, *J* = 6.7 Hz, 1H), 7.14 (dd, *J* = 7.2, 4.8 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.64 (td, *J* = 6.7 and 1.7 Hz, 1H), 8.55 (d, *J* = 5.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4, 24.9, 25.2, 26.1, 33.2, 34.3, 54.1, 55.7, 121.2, 121.7, 136.4, 149.2, 165.2; LRMS (FAB) 205 (M^+ + H); HRMS (FAB) calcd for $C_{13}H_{21}N_2$ 205.1705 (M^+ + H), found 205.1686.

(*S*)-*N*-Phenyl-*N*-[1-(2-pyridinyl)ethyl]amine ((*S*)-4c): needles; mp 76−77 °C (hexane); R_f = 0.42 (20% EtOAc in hexane); $[\alpha]^{27}_D$ +4 (*c* 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54 (d, *J* = 6.6 Hz, 3H), 4.45 (br s, 1H), 4.61 (q, *J* = 6.6 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 2H), 6.65 (t, *J* = 7.3 Hz, 1H), 7.07−7.14 (m, 3H), 7.33 (d, *J* = 7.7 Hz, 1H), 7.58 (td, *J* = 7.7 and 1.8 Hz, 1H), 8.56 (dm, *J* = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.1, 54.7, 113.3 (2C), 117.3, 120.2, 121.9 (2C), 129.1, 136.8, 147.0, 149.2, 163.8; LRMS (EI, rel intensity %) 198 (M^+, 28), 183 (base), 167 (6), 120 (41); HRMS (EI) calcd for $C_{13}H_{14}N_2$ 198.1157 (M^+), found 198.1159.

(*S*)-*N*-Adamantyl-*N*-[1-(2-pyridinyl)ethyl]amine ((*S*)-4d): oil; R_f = 0.18 (EtOAc); $[\alpha]^{25}_D$ −34 (*c* 1.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (d, *J* = 6.8 Hz, 3H), 1.40−1.70 (m, 13H), 1.93−2.10 (m, 3H), 4.15 (q, *J* = 6.8 Hz, 1H), 7.09 (ddd, *J* = 7.2, 4.3, 1.3 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.61 (dd, *J* = 7.6, 1.8 Hz, 1H), 8.49 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.1, 29.5 (3C), 36.6 (3C), 43.6 (3C), 51.3, 51.7, 120.9, 121.3, 136.2, 148.5, 163.0; LRMS (FAB) 257 (M^+ + H); HRMS (FAB) calcd for $C_{17}H_{25}N_2$ 257.2018 (M^+ + H), found 257.2001.

(*S*,*S*)-*N*-[1-(Phenyl)ethyl]-*N*-[1-(2-pyridinyl)ethyl]-amine ((*S*,*S*)-4e): oil; R_f = 0.20 (EtOAc); $[\alpha]^{25}_D$ −167 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, *J* = 6.6 Hz, 3H), 1.30 (d, *J* = 6.7 Hz, 3H), 2.10−2.50 (br, 1H), 3.43 (q, *J* = 6.6 Hz, 1H), 3.45 (q, *J* = 6.7 Hz, 1H), 7.05 (d, *J* = 7.7 Hz, 1H), 7.15 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.20−7.35 (m, 5H), 7.63 (td, *J* = 7.7, 1.6 Hz, 1H), 8.60 (d, *J* = 4.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4, 25.1, 55.6, 56.1, 121.8, 121.9, 126.8 (2C), 128.3 and 128.3 (2C), 136.2, 145.6, 149.6, 164.7; LRMS (FAB) 227 (M^+ + H); HRMS (FAB) calcd for $C_{15}H_{19}N_2$ 227.1548 (M^+ + H), found 227.1538.

***N*-[(*R*)-1-(Phenyl)ethyl]-*N*-[(*S*)-1-(2-pyridinyl)ethyl]-amine ((*S*,*R*)-4e):** oil; R_f = 0.20 (EtOAc); $[\alpha]^{25}_D$ −7 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (d, *J* = 6.6 Hz, 3H), 1.39 (d, *J* = 6.6 Hz, 3H), 2.21 (br s, 1H), 3.80 (q, *J* = 6.6 Hz,

1H), 3.86 (q, J = 6.6 Hz, 1H), 7.05 (dd, J = 7.5, 4.8 Hz, 1H), 7.17 (d, J = 7.5 Hz, 1H), 7.18−7.30 (m, 5H), 7.56 (td, J = 7.7, 1.6 Hz, 1H), 8.54 (dm, J = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 23.5, 55.0, 56.0, 121.1, 121.6, 126.6 (2C), 126.7, 128.2 (2C), 136.2, 145.5, 149.1, 164.4; LRMS (FAB) 227 (M^+ + H); HRMS (FAB) calcd for $C_{15}H_{19}N_2$ 227.1548 (M^+ + H), found 227.1545.

(*S,S*)-*N,N*-Bis[1-(2-pyridinyl)ethyl]amine ((*S,S*)-4f): oil; R_f = 0.30 (5% Et_3N in EtOAc); $[\alpha]^{24}_D$ −178 (*c* 2.0, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (d, J = 6.7 Hz, 6H), 2.20−2.30 (br, 1H), 3.61 (q, J = 6.7 Hz, 2H), 7.13 (ddd, J = 7.4, 5.4, 1.1 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 7.64 (td, J = 7.7, 1.8 Hz, 2H), 8.55 (d, J = 4.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (2C), 56.9 (2C), 121.2 (2C), 121.8 (2C), 136.4 (2C), 149.2 (2C), 164.5 (2C); LRMS (FAB) 228 (M^+ + H); HRMS (FAB) calcd for $C_{14}H_{18}N_3$ 228.1501 (M^+ + H), found 228.1518.

***meso*-*N,N*-Bis[1-(2-pyridinyl)ethyl]amine (*meso*-4f):** oil; R_f = 0.30 (5% Et_3N in EtOAc); $[\alpha]^{25}_D$ ±0 (*c* 2.0, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (d, J = 6.7 Hz, 6H), 2.65−2.75 (br, 1H), 3.87 (q, J = 6.7 Hz, 2H), 7.05 (ddd, J = 7.7, 5.1, 1.2 Hz, 2H), 7.19 (d, J = 7.7 Hz, 2H), 7.51 (td, J = 7.7, 1.8 Hz, 2H), 8.46 (dm, J = 5.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.1 (2C), 56.4 (2C), 120.9 (2C), 121.6 (2C), 138.6 (2C), 148.8 (2C), 164.3 (2C); LRMS (FAB) 228 (M^+ + H); HRMS (FAB) calcd for $C_{14}H_{18}N_3$ 228.1501 (M^+ + H), found 228.1486.

***N*-[(*S*)-1-(2-Pyridinyl)ethyl]-*N*-[(*S*)-tetrahydrofurfuryl]-amine ((*S,S*)-4g):** oil; R_f = 0.59 (10% Et_3N in EtOAc); $[\alpha]^{27}_D$ −12 (*c* 2.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (d, J = 6.6 Hz, 3H), 1.49 (m, 1H), 1.81−1.99 (m, 3H), 2.47 (dd, J = 11.7 and 4.0 Hz, 1H), 2.59 (dd, J = 11.7 and 7.9 Hz, 1H), 3.74 (dt, J = 8.6, 6.8 Hz, 1H), 3.84 (dt, J = 8.2, 6.6 Hz, 1H), 3.89 (ABq, J = 11.6, 6.6 Hz, 1H), 3.95 (qd, J = 7.0, 4.0 Hz, 1H), 7.14 (ddd, J = 7.7, 4.8, 1.2 Hz, 1H), 7.38 (d, J = 7.9 Hz, 1H), 7.65 (td, J = 7.7, 1.8 Hz, 1H), 8.57 (dm, J = 4.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9, 25.6, 29.3, 52.5, 59.8, 67.8, 78.7, 120.8, 121.7, 136.4, 149.0, 164.8; LRMS (EI, rel intensity %) 206 (M^+, 2), 135 (base), 107 (93); HRMS (EI) calcd for $C_{12}H_{18}N_2O$ 206.1419 (M^+), found 206.1416.

***N*-[(*S*)-1-(2-Pyridinyl)ethyl]-*N*-[(*R*)-tetrahydrofurfuryl]-amine ((*S,R*)-4g):** oil; R_f = 0.59 (10% Et_3N in EtOAc); $[\alpha]^{24}_D$ −34 (*c* 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (d, J = 6.6 Hz, 3H), 1.53 (m, 1H), 1.80−1.96 (m, 3H), 2.19 (br s, 1H), 2.46 (dd, J = 12.1, 7.7 Hz, 1H), 2.62 (dd, J = 12.1, 4.0 Hz, 1H), 3.73 (dt, J = 8.4, 6.6 Hz, 1H), 3.81 (dt, J = 8.1, 6.6 Hz, 1H), 3.90 (q, J = 6.6 Hz, 1H), 4.01 (ABq d, J_{AB} = 12.2 Hz, J_A = 7.3, 3.7 Hz, J_B = 7.0, 3.7 Hz, 1H), 7.13 (ddd, J = 7.3, 4.8, 1.1 Hz, 1H), 7.34 (d, J = 7.7 Hz, 1H), 7.64 (td, J = 7.7 and 1.8 Hz, 1H), 8.55 (dm, J = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9, 25.7, 29.1, 52.0, 59.4, 67.8, 78.3, 120.7, 121.8, 136.5, 149.2, 164.8; LRMS (EI, rel intensity %) 206 (M^+, 2), 135 (base), 107 (56); HRMS (EI) calcd for $C_{12}H_{18}N_2O$ 206.1419 (M^+), found 206.1408.

(*R*)-*N*-[1-(2-Pyridinyl)ethyl]glycine Ethyl Ester ((*R*)-4h): yellow oil; R_f = 0.23 (EtOAc); $[\alpha]^{26}_D$ −59 (*c* 1.8, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, J = 7.1 Hz, 3H), 1.43 (d, J = 6.6 Hz, 3H), 2.05 (br s, 1H,), 3.30 (ABq, J = 17 Hz, 2H), 3.91 (q, J = 6,6 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 7.16 (dd, J = 7.7, 4.8 Hz, 1H), 7.35 (d, J = 7.7 Hz, 1H), 7.66 (td, J = 7.7, 1.7 Hz, 1H), 8.55 (d, J = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.5, 48.7, 58.7, 60.5, 120.8, 121.9, 136.4, 149.0, 163.4, 172.0; IR (neat) 1740 cm^{-1}, 3325 cm^{-1}; LRMS (FAB) 209 (M^+ + H); HRMS (FAB) calcd for $C_{11}H_{17}N_2O_2$ 209.1290 (M^+ + H), found 209.1293.

(*R*)-[*N*-1-(2-Pyridinyl)ethyl]-L-alanine Ethyl Ester ((*R*)-4i): dr (diastereomeric ratio) 80% (4:1); yellow oil; R_f = 0.27 (EtOAc); $[\alpha]^{26}_D$ +4.5 (*c* 2.8, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (t, J = 7.1 Hz, 3H), 1.33 (d, J = 6.9 Hz, 3H), 1.41 (d, J = 6.7 Hz, 3H), 2.00−2.30 (br, 1H), 3.36 (q, J = 6,9 Hz, 1H), 3.94 (q, J = 6.7 Hz, 1H,), 4.07 (q, J = 7.1 Hz, 2H), 7.16 (dd, J = 7.7, 4.9 Hz, 1H), 7.31 (d, J = 7.7 Hz, 1H), 7.65 (td, J = 7.7, 1.8 Hz, 1H), 8.56 (d, J = 4.9 Hz, 1H), minor D-isomer δ 1.26 (d, J = 7.0 Hz, 3H), 1.27 (t, J = 7.0 Hz, 3H), 1.38 (d, J = 6.7 Hz, 3H), 2.06 (br s, 1H), 3.13 (q, J = 7.0 Hz, 1H), 3.85 (q, J = 6.7 Hz, 1H), 4.16 (q, J = 7.0 Hz, 1H), 4.17 (q, J = 7.0 Hz, 1H), 7.15 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H), 7.40 (d, J = 7.7 Hz, 1H), 7.66 (td, J = 7.7, 1.8 Hz, 1H), 8.54 (d, J = 4.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 18.7, 22.1, 54.0, 56.7, 60.5, 120.8, 121.9, 136.4, 149.1, 163.7, 175.1, minor D-isomer δ 14.1, 19.6, 23.8, 54.6, 58.1, 60.5, 120.7, 121.9, 136.5, 149.1, 164.2, 175.9; IR (neat) 1735, 3325 cm^{-1}; LRMS (FAB) 223 (M^+ + H); HRMS (FAB) calcd for $C_{12}H_{19}N_2O_2$ 223.1446 (M^+ + H), found 223.1464.

(*R*)-*N*-[1-(2-Pyridinyl)ethyl]-L-phenylalanine Ethyl Ester ((*R*)-4j): dr 81.5% (4.4:1); yellow oil; R_f = 0.47 (60% EtOAc in hexane); $[\alpha]^{26}_D$ −37 (*c* 3.8, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (t, J = 7.1 Hz, 3H), 1.36 (d, J = 6.6 Hz, 3H), 2.10 (br s, 1H), 2.94 (dd, J = 13.0, 7.4 Hz, 1H), 3.03 (dd, J = 13, 6.3 Hz, 1H), 3.56 (dd, J = 7.4, 6.3 Hz, 1H), 3.90 (q, J = 6.6 Hz, 1H), 3.91 (dq, J = 7.1, 1.3 Hz, 2H), 6.19 (td, J = 7.7, 1.7 Hz, 1H), 7.11−7.30 (m, 7H), 8.53 (d, J = 5.0 Hz, 1H), minor D-isomer δ 1.17 (t, J = 7.10 Hz, 3H), 1.33 (d, J = 6.7 Hz, 3H), 2.05 (br s, 1H), 2.88 (dd, J = 13.3, 8.1 Hz, 1H), 2.93 (dd, J = 13.3, 6.0 Hz, 1H), 3.81 (q, J = 6.7 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 7.02−7.29 (m, 7H), 7.48 (td, J = 7.7, 1.8 Hz, 1H), 8.45 (d, J = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 21.9, 39.5, 57.5, 60.3, 60.8, 120.9, 121.9, 126.4, 128.2 (2C), 129.2 (2C), 136.4, 137.3, 148.9, 163.8, 174.1, minor D-isomer δ 13.9, 23.5, 39.9, 58.1, 60.4, 60.8, 1203, 121.6, 128.0 (2C), 129.2 (2C), 136.3, 137.3, 148.8, 164.1, 174.6; IR (neat) 1730, 3320 cm^{-1}; LRMS (FAB) 299 (M^+ + H); HRMS (FAB) calcd for $C_{18}H_{23}N_2O_2$ 299.1759 (M^+ + H), found 299.1776.

(*R*)-*N*-[1-(2-Pyridinyl)ethyl]-L-methionine Ethyl Ester ((*R*)-4k): dr 92.3% (12:1); yellow oil; R_f = 0.38 (60% EtOAc in hexane); $[\alpha]^{27}_D$ −10.5 (*c* 1.8, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (t, J = 7.1 Hz, 3H), 1.40 (d, J = 6.7 Hz, 3H), 1.86−1.97 (m, 2H), 2.00−2.30 (br, 1H), 2.10 (s, 3H), 2.58−2.64 (m, 2H), 3.44 (t, J = 5.7 Hz, 1H), 3.88 (q, J = 6.7 Hz, 1H), 4.04 (qd, J = 7.1, 1.6 Hz, 2H), 7.15 (dd, J = 7.1, 4.9 Hz, 1H), 7.29 (d, J = 7.7 Hz, 1H), 7.64 (td, J = 7.7, 1.7 Hz, 1H), 8.55 (d, J = 4.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 15.3, 21.9, 30.3, 32.6, 57.5, 58.0, 60.7, 120.9, 121.9, 136.4, 149.1, 163.8, 174.7; IR (neat) 1730, 3320 cm^{-1}; LRMS (FAB) 283 (M^+ + H); HRMS (FAB) calcd for $C_{14}H_{23}N_2O_2S$ 283.1480 (M^+ + H), found 283.1468.

(*R*)-*N*-[1-(2-Pyridinyl)ethyl]-L-leucine Ethyl Ester ((*R*)-4l): dr 92.9% (13:1); yellow oil; R_f = 0.46 (50% EtOAc in hexane); $[\alpha]^{27}_D$ −13 (*c* 1.1, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 6.5 Hz, 3H), 1.39 (d, J = 6.6 Hz, 3H), 1.51 (dd, J = 7.1, 7.0 Hz, 2H), 1.72 (ddq, J = 13.0, 6.6, 6.5 Hz, 1H), 1.90−2.30 (br, 1H), 3.40 (dd, J = 7.2, 7.1 Hz, 1H), 3.55 (s, 3H), 3.87 (q, J = 6.6 Hz, 1H), 7.14 (dd, J = 7.1, 4.9 Hz, 1H), 7.45 (d, J = 7.7 Hz, 1H), 7.68 (td, J = 7.7, 1.7 Hz, 1H), 8.53 (d, J = 4.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 22.4, 22.5, 24.7, 42.8, 51.4, 57.7, 57.8, 120.9, 121.9, 136.4, 149.0, 163.9, 176.0; IR (neat) 1738, 3320 cm^{-1}; LRMS (FAB) 251 (M^+ + H); HRMS (FAB) calcd for $C_{14}H_{23}N_2O_2$ 251.1759 (M^+ + H), found 251.1751.

(*R*)-*N*-[1-(2-Pyridinyl)ethyl]-L-tyrosine Methyl Ester ((*R*)-4m): dr 92.3% (12:1); yellow oil; R_f = 0.3 (80% EtOAc in hexane); $[\alpha]^{24}_D$ −36 (*c* 3.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (d, J = 6.6 Hz, 3H), 2.90 (d, J = 6.7 Hz, 2H), 3.46 (s, 3H), 3.52 (t, J = 6.7 Hz, 1H), 3.95 (q, J = 6.6 Hz, 1H), 6.71 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 8.4 Hz, 2H), 7.18 (dd, J = 7.3, 4.9 Hz, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.67 (td, J = 7.7, 1.7 Hz, 1H), 8.50 (d, J = 4.9 Hz, 1H). Two protons for NH and OH were not observed. ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.0, 38.4, 51.5, 57.5, 61.0, 115.5 (2C), 121.4, 122.4, 127.8, 130.1 (2C), 137.2, 148.4, 155.6, 163.6, 174.7; IR (neat) 1735, 3320 cm^{-1}; LRMS (FAB) 301 (M^+ + H); HRMS (FAB) calcd for $C_{17}H_{21}N_2O_3$ 301.1552 (M^+ + H), found 301.1566.

(*R*)-*N*-[1-(2-Pyridinyl)ethyl]-l-tryptophan Methyl Ester ((*R*)-4n): dr 93.3% (14:1); yellow oil; R_f = 0.30 (80% EtOAc in hexane); $[\alpha]^{25}_D$ −39 (*c* 2.9, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (d, J = 6.7 Hz, 3H), 2.30−2.50 (br s, 1H), 3.18 (d, J =

6.6 Hz, 2H), 3.45 (s, 3H), 3.68 (t, J = 6.6 Hz, 1H), 3.94 (q, J = 6.7 Hz, 1H), 7.05−7.20 (m, 4H), 7.28 (d, J = 8.1 Hz, 1H), 7.34 (d, J = 7.7 Hz, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.61 (td, J = 7.7, 1.8 Hz, 1H,), 8.11 (br, 1H), 8.52 (d, J = 4.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.9, 28.9, 51.5, 57.6, 59.9, 110.7, 111.1, 118.5, 119.1, 121.1, 121.7, 120.0, 122.9, 127.4, 136.1, 136.5, 148.9, 163.7, 175.0; IR (neat) 1730, 3400 cm^{-1}; LRMS (FAB) 324 (M^+ + H); HRMS (FAB) calcd for $C_{19}H_{22}N_3O_2$ 324.1730 (M^+ + H), found 324.1695.

Reactions with Secondary Amine. The reaction was carried out under conditions similar to those described for the synthesis of (*S*)-**4** except that 4−6 equiv of amine should be used in the absence of diisopropylethylamine.

(*S*)-*N*-[1-(2-Pyridinyl)ethyl]pyrrolidine ((*S*)-5a): oil; R_f = 0.47 (5% Et_3N in EtOAc); $[\alpha]^{25}_D$ −62 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (d, J = 6.6 Hz, 3H), 1.73−1.83 (m, 4H), 2.35−2.48 (m, 2H), 2.57−2.68 (m, 2H), 3.40 (q, J = 6.6 Hz, 1H), 7.14 (ddd, J = 7.2, 4.9, 1.2 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.64 (td, J = 7.7, 1.8 Hz, 1H), 8.53 (dm, J = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 23.4 (2C), 52.6 (2C), 67.2, 121.5, 121.9, 136.5, 148.9, 164.4; LRMS (FAB) 177 (M^+ + H); HRMS (FAB) calcd for $C_{11}H_{17}N_2$ 177.1392 (M^+ + H), found 177.1381.

(*S*)-*N*-[1-(2-Pyridinyl)ethyl]piperidine ((*S*)-5b): oil; R_f = 0.41 (5% Et_3N in EtOAc); $[\alpha]^{25}_D$ −34 (*c* 2.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (d, J = 6.7 Hz, 3H), 1.35−1.42 (m, 2H), 1.52−1.61 (m, 4H), 2.30−2.39 (m, 2H), 2.42−2.54 (m, 2H), 3.55 (q, J = 6.7 Hz, 1H), 7.10 (ddd, J = 6.7 4.9 1.2 Hz, 1H), 7.40 (dd, J = 7.3, 1.1 Hz, 1H), 7.62 (td, J = 7.7, 1.8 Hz, 1H), 8.54 (d, J = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.9, 24.5, 26.1 (2C), 51.4 (2C), 66.1, 121.6, 121.8, 136.0, 148.7, 163.7; LRMS (FAB) 191 (M^+ + H); HRMS (FAB) calcd for $C_{12}H_{19}N_2$ 191.1548 (M^+ + H), found 191.1522.

(*S*)-*N*-[1-(2-Pyridinyl)ethyl]morpholine ((*S*)-5c): oil; R_f = 0.30 (EtOAc); $[\alpha]^{25}_D$ −54 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.42 (d, J = 6.8 Hz, 3H), 2.40−2.45 (m, 2H), 2.60−2.65 (m, 2H), 3.51 (q, J = 6.8 Hz, 1H), 3.73 (t, J = 4.8 Hz, 4H), 7.15 (ddd, J = 7.7, 4.8, 1.8 Hz, 1H), 7.38 (d, J = 7.7 Hz, 1H), 7.65 (td, J = 7.7, 1.8 Hz, 1H), 8.55 (d, J = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.1, 51.0 (2C), 66.7, 66.9 (2C), 122.0 and 122.0, 136.4, 149.0, 162.3; LRMS (FAB) 193 (M^+ + H); HRMS (FAB) calcd for $C_{11}H_{17}N_2O$ 193.1341 (M^+ + H), found 193.1371.

(*S*)-*N*-[1-(2-Pyridinyl)ethyl]thiomorpholine ((*S*)-5d): oil; R_f = 0.20 (EtOAc); $[\alpha]^{25}_D$ −18 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (d, J = 6.8 Hz, 3H), 2.64−2.70 (m, 4H), 2.71−2.82 (m, 4H), 3.71 (q, J = 6.8 Hz, 1H), 7.14 (ddd, J = 7.3, 4.9, 1.2 Hz, 1H), 7.38 (d, J = 7.7 Hz, 1H), 7.63 (td, J = 7.7, 1.8 Hz, 1H), 8.55 (d, J = 3.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.2, 28.2 (2C), 52.0 (2C), 66.1, 121.8, 122.1, 136.1, 148.9, 162.5; LRMS (FAB) 209 (M^+ + H); HRMS (FAB) calcd for $C_{11}H_{17}N_2S$ 209.1112 (M^+ + H), found 209.1128.

(*S*)-*N*-Methyl-*N*′-[1-(2-pyridinyl)ethyl]piperadine ((*S*)-5e): oil; R_f = 0.50 (50% MeOH in EtOAc); $[\alpha]^{25}_D$ −39 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (d, J = 6.9 Hz, 3H), 2.21 (s, 3H), 2.30−2.50 (m, 8H), 3.54 (q, J = 6.7 Hz, 1H), 7.14 (ddd, J = 7.6, 5.0, 1.8 Hz, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.61 (td, J = 7.6, 1.6 Hz, 1H), 8.54 (dm, J = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3 45.9 (2C), 50.3, 55.2 (2C), 66.2, 121.8, 121.9, 136.2, 148.9, 163.2; LRMS (FAB) 206 (M^+ + H); HRMS (FAB) calcd for $C_{12}H_{20}N_3$ 206.1657 (M^+ + H), found 206.1681.

(*S*)-*N*-[1-(2-Pyridinyl)ethyl]-1,2,3,4-tetrahydroquinoline ((*S*)-5f): oil; R_f = 0.40 (20% EtOAc in hexane); $[\alpha]^{25}_D$ −71 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.66 (d, J = 6.8 Hz, 3H), 1.80−2.00 (m, 2H), 2.76−2.81 (m, 2H), 3.10−3.20 (m, 1H), 3.30−3.40 (m, 1H), 5.09 (q, J = 6.8 Hz, 1H), 6.56 (t, J = 7.5 Hz, 1H), 6.58 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 7.4 Hz, 2H), 7.14 (dd, J = 7.5, 4.8 Hz, 1H), 7.28 (d, J = 7.7 Hz, 1H), 7.59 (td, J = 7.7, 1.7 Hz, 1H), 8.60 (dm, J = 4.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.1, 22.4, 28.4, 43.2, 57.5, 110.9, 115.7, 121.2, 121.7, 122.9, 127.1, 129.2, 136.5, 145.3, 149.2, 162.5; LRMS (FAB) 239 (M^+ + H); HRMS (FAB) calcd for $C_{16}H_{19}N_2$ 239.1542 (M^+ + H), found 239.1558.

(*S*)-*N*-[1-(2-Pyridinyl)ethyl]-1,2,3,4-tetrahydroisoquinoline ((*S*)-5g): oil; R_f = 0.42 (70% EtOAc in hexane); $[\alpha]^{25}_D$ −4 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.48 (d, J = 6.7 Hz, 3H), 2.66−2.87 (m, 4H), 3.60 (d, J = 14.8 Hz, 1H), 3.76 (q, J = 6.7 Hz, 1H), 3.85 (d, J = 14.8 Hz, 1H), 6.96−7.10 (m, 4H), 7.14 (ddd, J = 7.4, 4.9, 1.3 Hz, 1H), 7.45 (dd, J = 7.8, 1.1 Hz, 1H), 7.62 (td, J = 7.7, 1.8 Hz, 1H), 8.54 (ddd, J = 5.5, 1.6, 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 29.3, 47.9, 53.3, 65.8, 121.7, 121.9, 125.4, 125.9, 126.6, 128.5, 134.4, 135.0, 136.4, 148.8, 163.6; LRMS (FAB) 239 (M^+ + H); HRMS (FAB) calcd for $C_{16}H_{19}N_2$ 239.1542 (M^+ + H), found 239.1559.

(*S*)-2-(Hydroxymethyl)-*N*-[(*S*)-1-(2-pyridinyl)ethyl]pyrrolidine ((*S,S*)-5h): oil; R_f = 0.20 (EtOAc); $[\alpha]^{25}_D$ −17 (*c* 1.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.49 (d, J = 6.8 Hz, 3H), 1.60−1.83 (m, 4H), 2.50 (m, 1H), 2.92−3.05 (m, 2H), 3.46 (dd, J = 10.0, 4.0 Hz, 1H), 3.62 (dd, J = 10.0, 4.0 Hz, 1H), 3.95−4.05 (br, 1H), 4.10 (q, J = 6.8 Hz, 1H), 7.16 (ddd, J = 7.6, 5.1, 1.1 Hz, 1H), 7.30 (d, J = 7.7 Hz, 1H), 7.66 (t, J = 7.7 Hz, 1H), 8.55 (dm, J = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 23.4, 28.7, 50.4, 60.4, 61.5, 64.2, 121.9, 122.0, 136.2, 148.6, 162.0; LRMS (FAB) 207 (M^+ + H); HRMS (FAB) calcd for $C_{12}H_{19}N_2O$ 207.1497 (M^+ + H), found 207.1481.

(*R*)-2-(Hydroxymethyl)-*N*-[(*S*)-1-(2-pyridinyl)ethyl]pyrrolidine ((*S,R*)-5h): oil; R_f = 0.20 (EtOAc); $[\alpha]^{25}_D$ −20 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (d, J = 6.8 Hz, 3H), 1.68−1.95 (m, 4H), 2.65 (m, 1H), 2.90−3.00 (m, 2H), 3.16 (dd, J = 10.0, 4.2 Hz, 1H), 3.20 (dd, 10.0, 4.2 Hz, 1H), 3.40−3.52 (br, 1H), 3.95 (q, J = 6.8 Hz, 1H), 7.16 (ddd, J = 6.8, 5.4, 1.1 Hz, 1H), 7.34 (d, J = 7.7 Hz, 1H), 7.65 (t, J = 7.7 Hz, 1H), 8.54 (dm, J = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.6, 24.0, 28.7, 48.7, 61.9, 62.4, 63.5, 121.7, 122.0, 136.4, 148.8, 163.7; LRMS (FAB) 207 (M^+ + H); HRMS (FAB) calcd for $C_{12}H_{19}N_2O$ 207.1497 (M^+ + H), found 207.1509.

(*S*)-*N*-Benzyl-*N*-{1-[6-(2,2′bipyridinyl)]ethyl}amine ((*S*)-7): oil; R_f = 0.44 (5% Et_3N in EtOAc); $[\alpha]^{22}_D$ −71 (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46 (d, J = 6.6 Hz, 3H), 2.09 (br, 1H), 3.69 (s, 2H), 3.99 (q, J = 6.6 Hz, 1H), 7.20−7.38 (m, 7H), 7.79 (t, J = 7.7 Hz, 1H), 7.81 (td, J = 7.1, 1.8 Hz, 1H), 8.28 (d, J = 7.7 Hz, 1H), 8.48 (d, J = 7.9 Hz, 1H), 8.68 (dm, J = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.1, 51.8, 58.6, 119.1, 121.2, 121.4, 123.6, 126.8, 128.2 (2C), 128.3 (2C), 136.8, 137.3, 140.6 149.1, 155.5, 156.4, 163.8; LRMS (FAB) 290 (M^+ + H); HRMS (FAB) calcd for $C_{19}H_{20}N_3$ 290.1657 (M^+ + H), found 290.1654.

Preparation of (*R*)-[2-(6-Phenylpyridinyl)]ethyl Methanesulfonate ((*R*)-8): To a mixture of (*R*)-[2-(6-phenylpyridinyl)]ethanol (199 mg, 1 mmol), Et_3N (506 mg, 5 mmol), and DMAP (24 mg, 0.2 mmol) in CH_2Cl_2 (5 mL) was added methanesulfonyl chloride (229 mg, 2 mmol) dropwise at 0 °C. After the mixture was stirred for 30 min at the same temperature, water was added and the mixture was extracted with EtOAc. The extract was washed with brine and dried over $MgSO_4$. Solvent was removed, and the residual oil was chromatographed on silica gel eluted with 15% EtOAc in hexane to give mesylate (*R*)-**8** (247 mg) in 89% yield: oil; R_f = 0.20 (EtOAc); $[\alpha]^{25}_D$ +52.0 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (d, J = 6.7 Hz, 3H), 1.74−1.81 (m, 4H), 2.42−2.52 (m, 2H), 2.61−2.70 (m, 2H), 3.55 (q, J = 6.7 Hz, 1H), 7.35−7.48 (m, 4H), 7.40−7.51 (m, 4H), 7.72 (d, J = 7.7 Hz, 1H), 7.81 (t, J = 7.7 Hz, 1H), 8.01−8.05 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 38.8, 81.1, 118.9, 120.0, 126.9 (2C), 128.8 (2C), 129.3, 137.9, 138.6, 156.9, 158.0; LRMS (EI) 277 (M^+); HRMS (EI) calcd for $C_{14}H_{15}NO_3$ 277.0772 (M^+), found 277.0773.

(*S*)-*N*-{1-[2-(6-Phenylpyridinyl)]ethyl}pyrrolidine ((*S*)-9a): oil; R_f = 0.20 (EtOAc); $[\alpha]^{25}_D$ +52.0 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (d, J = 6.7 Hz, 3H), 1.74−1.81 (m, 4H), 2.42−2.52 (m, 2H), 2.61−2.70 (m, 2H), 3.55 (q, J = 6.7 Hz, 1H), 7.35−7.48 (m, 4H), 7.56 (dd, J = 7.2, 1.1 Hz, 1H), 7.70 (t, J = 7.7 Hz, 1H), 8.01 (dm, J = 6.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 23.3 (2C), 52.4 (2C), 67.2, 118.6, 119.6,

126.9 (2C), 128.5 (2C), 137.0, 139.6, 156.2, 164.5; LRMS (FAB) 253 ($M^+ + H$); HRMS (FAB) calcd for $C_{17}H_{20}N_2$ 253.1705 ($M^+ + H$), found 253.1730.

(*S*)-*N*-{1-[2-(6-Phenylpyridinyl)]ethyl}morpholine ((*S*)-9b): oil; $R_f = 0.32$ (EtOAc); $[\alpha]^{25}_D$ +48.3 (*c* 1.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.42 (d, $J = 6.8$ Hz, 3H), 2.40−2.52 (m, 2H), 2.55−2.66 (m, 2H), 3.70 (q, $J = 6.8$ Hz, 1H), 3.73 (t, $J = 4.7$ Hz), 7.33−7.48 (m, 4H), 7.55 (dd, $J = 7.7$, 1.1 Hz, 1H), 7.63 (t, $J = 7.7$ Hz, 1H), 8.01 (dm, $J = 7.8$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.0, 50.8 (2C), 66.5, 67.2 (2C), 118.5, 120.0, 126.8 (2C), 128.5 (2C), 128.6, 136.9, 139.5, 156.3, 162.8; LRMS (FAB) 269 ($M^+ + H$); HRMS (FAB) calcd for $C_{18}H_{22}N_2$ 269.1654 ($M^+ + H$), found 269.1653.

(*S*)-*N*-Benzyl-*N*-{1-[2-(6-phenylpyridinyl)]ethyl}amine ((*S*)-9c): oil; $R_f = 0.30$ (EtOAc); $[\alpha]^{25}_D$ −70 (*c* 1.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.46 (d, $J = 6.7$ Hz, 3H), 2.05−2.45 (br, 1H), 3.70 (dd, $J = 5.7$, 3.0 Hz, 2H), 3.98 (q, $J = 6.7$ Hz, 1H), 7.30−7.52 (m, 10H), 7.62 (dd, $J = 7.2$, 1.1 Hz, 1H), 7.72 (t, $J = 7.7$ Hz, 1H), 8.04 (dm, $J = 6.9$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.0, 51.8, 58.6, 118.5, 119.7, 126.8, 126.9, 128.2 (2C), 128.3 (2C), 128.6 (2C), 128.8 (2C), 137.1, 139.5, 140.5, 156.7, 164.2; LRMS (FAB) 289 ($M^+ + H$); HRMS (FAB) calcd for $C_{20}H_{21}N_2$ 289.1747 ($M^+ + H$), found 289.1713.

(*S,S*)-*N*-1-(Phenyl)ethyl-*N*-{1-[2-(6-phenylpyridinyl)]ethyl}amine ((*S,S*)-9d): oil; $R_f = 0.30$ (40% EtOAc in hexane); $[\alpha]^{25}_D$ −181 (*c* 0.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (d, $J = 6.6$ Hz, 3H), 1.35 (d, $J = 6.8$ Hz, 3H), 3.54 (q, $J = 6.6$ Hz, 1H), 3.65 (q, $J = 6.8$ Hz, 3H), 7.01 (d, $J = 7.2$ Hz, 1H), 7.23−7.38 (m, 5H), 7.42−7.54 (m, 3H), 7.61 (d, $J = 7.7$ Hz, 1H), 7.69 (t, $J = 7.7$ Hz, 1H), 8.06 (dm, $J = 7.0$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.6, 25.3, 55.6, 56.2, 118.3, 120.2, 126.7, 126.8 and 126.8, 126.9, 128.3 and 128.3, 128.6 and 128.6, 128.8 and 128.8, 136.8, 139.5, 145.7, 156.7, 164.2; LRMS (FAB) 303 ($M^+ + H$); HRMS (FAB) calcd for $C_{21}H_{23}N_2$ 303.1861 ($M^+ + H$), found 303.1855.

***N*-[(*R*)-1-(Phenyl)ethyl]-*N*-{(*S*)-1-[2-(6-phenylpyridinyl)]ethyl}amine ((*S,R*)-9d):** oil; $R_f = 0.31$ (40% EtOAc); $[\alpha]^{25}_D$ −71 (*c* 0.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (d, $J = 6.5$ Hz, 3H), 1.41 (d, $J = 6.6$ Hz, 3H), 3.80 (q, $J = 6.5$ Hz, 1H), 3.91 (q, $J = 6.6$ Hz, 3H), 7.12 (d, $J = 7.3$ Hz, 1H), 7.20−7.32 (m, 5H), 7.38−7.48 (m, 3H), 7.55 (d, $J = 7.7$ Hz, 1H), 7.69 (t, $J = 7.7$ Hz, 1H), 8.06 (dm, $J = 7.0$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.0, 23.3, 55.1, 56.0, 118.2, 119.6, 126.7 and 126.7 (2C), 126.8, 128.3 (2C), 128.6 (2C), 128.7 (2C), 137.0, 139.5, 145.8, 156.4, 164.1; LRMS (FAB) 303 ($M^+ + H$); HRMS (FAB) calcd for $C_{21}H_{23}N_2$ 303.1861 ($M^+ + H$), found 303.1833.

***N*-{(*S*)-1-[2-(6-Phenylpyridinyl)]}-*N*-[(*S*)-1-(2-pyridinyl)ethyl]amine ((*S,S*)-9e):** oil; $R_f = 0.38$ (2% Et_3N in AcOEt); $[\alpha]^{23}_D$ −163 (*c* 1.45, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (d $J = 7.0$ Hz, 3H), 1.38 (d, $J = 7.3$ Hz, 3H), 2.55 (br s, 1H), 3.70 (quint, $J = 7.0$ Hz, 2H), 7.14 (ddd, $J = 7.3$, 4.8, 1.1 Hz, 1H), 7.19 (d, $J = 7.3$ Hz, 1H), 7.34−7.48 (m, 4H), 7.56−7.71 (m, 3H), 8.02 (dm, $J = 7.0$ Hz, 2H), 8.55 (dt, $J = 4.8$, 0.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.7 (2C), 57.1, 57.2, 118.5, 119.8, 121.3, 121.8, 126.9, 128.6 (2C), 128.7 (2C), 136.4, 137.0, 139.7, 149.2, 156.6, 164.5, 165.1; LRMS (FAB) 304 ($M^+ + H$); HRMS (FAB) calcd for $C_{20}H_{22}N_3$ 304.1814 ($M^+ + H$), found 304.1808.

***N*-{(*S*)-1-[2-(6-Phenylpyridinyl)]}-*N*-[(*R*)-1-(2-pyridinyl)ethyl]amine ((*S,R*)-9e):** oil; $R_f = 0.38$ (2% Et_3N in AcOEt); $[\alpha]^{25}_D$ −23 (*c* 1.75, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.45 (d, $J = 6.6$ Hz, 3H), 1.48 (d, $J = 6.6$ Hz, 3H), 2.62 (br s, 1H), 3.96 (q, $J = 6.6$ Hz, 1H), 4.00 (q, $J = 6.6$ Hz, 1H), 7.05 (ddd, $J = 7.3$, 4.8 and 1.1 Hz, 1H), 7.16 (d, $J = 7.3$ Hz, 1H), 7.24 (d, $J = 7.7$ Hz, 1H), 7.36−7.54 (m, 5H), 7.60 (t, $J = 7.3$ Hz, 1H), 7.99 (dm, $J = 6.6$ Hz, 2H), 8.50 (dm, $J = 4.8$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3 (2C), 56.7 (2C), 118.3, 119.2, 120.9, 121.6, 126.9, 128.5 (2C), 128.6 (2C), 136.2, 136.9, 139.5, 149.0, 156.3, 164.2, 164.7; LRMS (FAB) 304 ($M^+ + H$); HRMS (FAB) calcd for $C_{20}H_{21}N_3$ 303.1735 (M^+), found 303.1741.

(*S,S*)-*N,N′*-Bis[1-(6-phenyl-2-pyridinyl)ethyl]amine ((*S,S*)-9f): oil, $R_f = 0.37$ (40% EtOAc in hexane); $[\alpha]^{25}_D$ −198.0 (*c* 1.4, $CHCl_3$); $R_f = 0.4$ (80% EtOAc in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 1.42 (d, $J = 6.8$ Hz, 6H), 2.35−2.60 (br, 1H), 3.80 (q, $J = 6.7$ Hz, 2H), 7.29 (d, $J = 7.7$ Hz, 2H), 7.35−7.50 (m, 6H), 7.58 (dd, $J = 7.7$ and 1.1 Hz, 2H), 7.71 (t, $J = 7.7$ Hz, 2H), 8.00 (dm, $J = 8.4$ Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9 (2C), 57.2 (2C), 118.5 (2C), 119.7 (2C), 126.9 (4C), 128.6 (4C), 128.7 (2C), 137.0 (2C), 139.7 (2C), 156.6 (2C), 164.7 (2C); LRMS (FAB) 380 ($M^+ + H$); HRMS (FAB) calcd for $C_{26}H_{26}N_3$ 380.2212 ($M^+ + H$), found 380.2104.

(*R*)-1-(4-Pyridinyl)ethyl Methanesulfonate ((*R*)-11). To an ice-cooled solution of 1-(4-pyridinyl)ethanol[10] (1.7 g, 13.8 mmol) and triethylamine (6.98 g, 69 mmol) in CH_2Cl_2 (100 mL) was added MsCl (4.74 g, 41 mmol) dropwise. After the mixture was stirred for 20 min at the same temperature, the mixture was quenched with aq $NaHCO_3$ and extracted with CH_2Cl_2. The extract was washed with water and brine and dried over $MgSO_4$. The crude product was purified by silica gel column chromatography eluted with 60% EtOAc in hexane to give (*R*)-**11** (2.16 g) in 78% yield: oil; $R_f = 0.38$ (EtOAc); $[\alpha]^{22}_D$ −2 (*c* 0.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.71 (d, $J = 6.6$ Hz, 3H), 2.93 (s, 3H), 5.71 (q, $J = 6.6$ Hz, 1H), 7.31 (d, $J = 5.7$ Hz, 2H), 8.65 (d, $J = 5.7$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.2, 38.9, 78.0, 120.5 (2C), 150.4 (2C); IR (neat) 1359, 1192 cm^{-1}; LRMS (EI, rel intensity %) 201 (M^+, 24), 122 (57), 106 (base); HRMS (EI) calcd for $C_8H_{11}N_3$ 201.0459 (M^+), found 201.0455.

(*S*)-*N*-[1-(4-Pyridinyl)ethyl]piperidine ((*S*)-12). A mixture of (*R*)-**11** (40 mg, 0.2 mmol) and piperidine (2 mmol) in acetonitrile (1 mL) was heated at 60 °C for 2.5 h. Aqueous $NaHCO_3$ and EtOAc were added to the mixture. The organic layer was washed with water and brine and dried over $MgSO_4$. The crude product was purified by silica gel column chromatography eluted with EtOAc and EtOAc containing 10% Et_3N to give (*S*)-**12** (32 mg) in 84% yield: oil; $R_f = 0.43$ (EtOAc); $[\alpha]^{27}_D$ −16 (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (d, $J = 6.8$ Hz, 3H), 1.40 (quint, $J = 5.3$ Hz, 2H), 1.56 (quint, $J = 5.3$ Hz, 4H), 2.27−2.43 (m, 4H), 3.41 (q, $J = 6.8$ Hz, 1H), 7.25 (d, $J = 5.7$ Hz, 2H), 8.52 (d, $J = 5.7$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 24.5, 26.2 (2C), 51.4 (2C), 64.1, 122.9 (2C), 149.7 (2C), 153.3; LRMS (EI, rel intensity %) 190 (M^+, 11), 175 (base), 112 (66), 106 (21); HRMS (EI) calcd $C_{12}H_{18}NO_3S$ 190.1470 (M^+), found 190.1471.

Mesylation and Substitution Reaction for the Synthesis of (*S*)-15 and (*S,R*)-16. To an ice-cooled solution of 1-(3-pyridinyl)ethanol[10] (100 mg, 0.8 mmol) and triethylamine (404 mg, 4 mmol) in CH_2Cl_2 was added MsCl (275 mg, 2.4 mmol) dropwise. After the mixture was stirred for 40 min at the same temperature, a 1:1 mixture of anhydrous ether and pentane (12 mL) was added. The forming salts were removed by suction under an Ar atmosphere. The filtrate was condensed, and the residual oil was subjected to use for the next reaction directly. The oily mesylate (*R*)-**14** was dissolved in acetonitrile (4 mL), to which solution piperidine (8 mmol) was added for the synthesis of (*S*)-**15** or diisopropylethylamine (1.03 g, 8 mmol) and (*R*)-1-phenethylamine (2 mmol) were added for that of (*S,R*)-**16**. The whole mixture was heated at 60 °C for 1 or 21 h, respectively. Aqueous $NaHCO_3$ was added to the mixture, and the mixture was extracted with EtOAc for (*S*)-**15** and CH_2Cl_2 for (*S,R*)-**16**. Organic extract was washed with water and brine and dried over $MgSO_4$. Solvent was removed, and the residual oil was purified by chromatography on silica gel eluted with EtOAc and 10% Et_3N in EtOAc for (*S*)-**15** and 50% EtOAc in hexane for (*S,R*)-**16**. (*S*)-**15** and (*S,R*)-**16** were obtained in 69 and 40% yields, respectively.

(*S*)-*N*-[1-(3-Pyridinyl)ethyl]piperidine ((*S*)-15): oil; $R_f = 0.43$ (5% Et_3N in EtOAc); $[\alpha]^{26}_D$ +14 (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.39 (d, $J = 6.6$ Hz, 3H), 1.37−1.43 (m, 2H), 2.32−2.43 (m, 4H), 3.48 (q, $J = 6.6$ Hz, 1H), 7.25 (dd, $J = 7.7$, 4.4 Hz, 1H), 7.66 (d, $J = 7.7$ Hz, 1H), 8.48 (d, $J = 4.4$ Hz, 1H), 8.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 24.5, 26.1 (2C), 51.2 (2C), 62.5, 123.2, 135.1, 139.1, 148.2, 149.5.

LRMS (FAB) 191 ($M^+ + H$); HRMS (FAB) calcd $C_{12}H_{19}N_2$ 191.1548 ($M^+ + H$), found 191.1542.

(*S*)-*N*-[1-(3-Pyridinyl)ethyl]-*N*-[(*S*)-1-phenethy]amine ((*S*,*R*)-16): oil; $R_f = 0.47$ (EtOAc); $[\alpha]^{24}_D$ −167 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (d, $J = 6.6$ Hz, 3H), 1.28 (d, $J = 6.6$ Hz, 3H), 1.67 (br s, 1H), 3.45 (q, $J = 6.6$ Hz, 1H), 3.54 (q, $J = 6.6$ Hz, 1H), 7.17−7.36 (m, 6H), 7.61 (d, $J = 7.7$ Hz, 1H), 8.41 (d, $J = 1.6$ Hz, 1H), 8.50 (dd, $J = 4.8$, 1.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7 (2C), 52.7, 55.2, 123.5, 126.4 (2C), 126.9, 128.5 (2C), 134.2, 140.7, 145.2, 148.4, 148.9; MS (FAB) 227 ($M^+ + H$); HRMS (FAB) calcd $C_{15}H_{19}N_2$ 227.1548 ($M^+ + H$), found 227.1541.

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Supporting Information Available: Copies of the ^{1}H and/or ^{13}C NMR spectra for compounds (*S*)-**4a**, (*S*)-**4b**, (*S*)-**4c**, (*S*)-**4d**, (*S*,*S*)-**4e**, (*S*,*R*)-**4e**, (*S*,*S*)-**4f**, *meso*-**4f**, (*S*,*S*)-**4g**, (*S*,*R*)-**4g**, (*R*)-**4h**, (*R*)-**4i**, (*R*)-**4j**, (*R*)-**4k**, (*R*)-**4l**, (*R*)-**4m**, (*R*)-**4n**, (*S*)-**5a**, (*S*)-**5b**, (*S*)-**5c**, (*S*)-**5d**, (*S*)-**5e**, (*S*)-**5f**, (*S*)-**5g**, (*S*,*S*)-**5h**, (*S*,*R*)-**5h**, (*R*)-**7**, (*S*)-**9a**, (*S*)-**9b**, (*S*)-**9c**, (*S*,*S*)-**9d**, (*S*,*R*)-**9d**, (*S*,*S*)-**9e**, (*S*,*R*)-**9e**, (*S*,*S*)-**9f**, (*R*)-**11**, (*S*)-**12**, (*S*)-**15**, and (*S*)-**16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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