

## STEREOSPECIFIC SUBSTITUTION OF 1-(2-PYRIDINYL)-ETHYL METHANESULFONATE WITH *S*- AND *O*-NUCLEOPHILES

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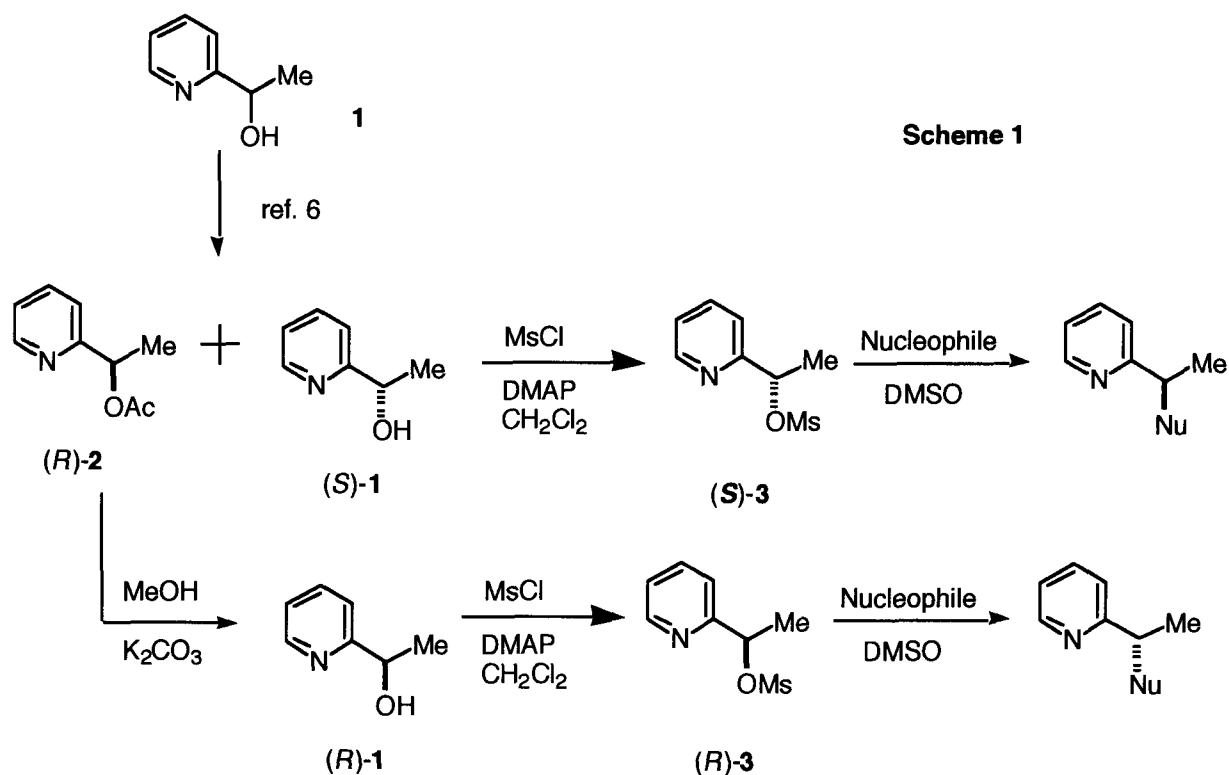
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**Abstract**-Nucleophilic substitution reactions of (*S*)- and (*R*)-1-(2-pyridinyl)ethyl methanesulfonate with *S*- and *O*-nucleophiles are described. The reaction of *S*-nucleophiles, such as aryl- and alkylthiols, and thioacetic acid, gave substituted sulfide and thioacetate with inversion of the configurations. For the reaction of *O*-nucleophiles, sodium phenoxides gave aryl ethers in good yields stereospecifically, but sodium alkoxide gave complex mixtures including racemic alkyl ether. Reactions with sodium carboxylate afforded the corresponding ester stereospecifically.

### INTRODUCTION

Chiral ligands have become important not only for asymmetric reactions but also for molecular recognitions of chiral molecules.<sup>1</sup> An enormous number of chiral amine ligands have reported so far,<sup>2</sup> and a pyridine unit has been widely used as a functional part for the chiral ligands.<sup>3</sup> However, a few preparations of chiral pyridines in which the chiral center is located directly on the pyridine ring have been reported.<sup>4</sup> Synthesis of such a chiral pyridine is of our interest.<sup>5</sup> Recently, we have reported lipase-catalyzed kinetic acetylation of 1-(2-pyridinyl)ethanols with a highly enantiomeric excess,<sup>6</sup> and stereospecific replacement of the chiral alcohol with some nitrogen and sulfur nucleophiles *via* its methanesulfonate.<sup>7</sup> Since the substitution reaction of (*S*)- and (*R*)-1-(2-pyridinyl)ethyl methanesulfonates ((*S*)- and (*R*)-**3**) was found to proceed with an inversion of the configuration, this reaction has offered a novel method for preparing optically active pyridine derivatives. In this paper, we report the details of stereospecific substitutions of optically pure (*S*)- and (*R*)-**3** with sulfur nucleophiles and an additional result with oxygen nucleophiles.



### Starting Materials

Highly optically pure (*S*)-1-(2-pyridinyl)ethanol ((*S*)-1) and (*R*)-1-(2-pyridinyl)ethyl acetate ((*R*)-2) were obtained by the lipase-catalyzed kinetic acetylation of 1-(2-pyridinyl)ethanol with vinyl acetate.<sup>6</sup> Methanolysis of (*R*)-1-(2-pyridinyl)ethyl acetate provided optically pure (*R*)-1-(2-pyridinyl)ethanol ((*R*)-1) quantitatively. In this reaction sequence, both (*S*)- and (*R*)-1 are available in preparative scales. Mesylation of both enantiomers was performed by treating the alcohols with an excess of methanesulfonyl chloride in methylene chloride in the presence of DMAP to give (*S*)- and (*R*)-3 in 85-95% yields.<sup>7</sup> The mesylate is fairly stable in refrigerator and decomposing gradually at room temperature, though its color became red after removal of solvents.

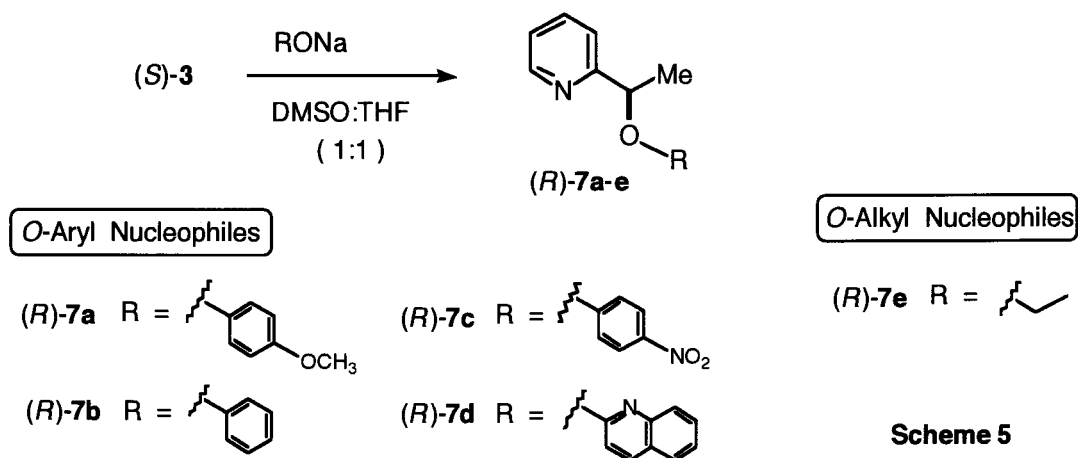
### Substitution Reaction with *S*-Nucleophiles

When (*S*)-3 was treated with thiophenol in DMSO in the presence of triethylamine at room temperature, sulfide ((*R*)-4a) was obtained in 87% yield. The optical purity was determined to be 98% ee by HPLC using a chiral column (Chiralcel OJ). In the same manner, reactions with pyridine-2-thiol and pyrimidine-2-thiol gave the corresponding sulfides, ((*R*)-4b and (*R*)-4c) in 76 and 87% yields, respectively. However, the reaction with quinoline-2-thiol gave (*R*)-4d in poor yield. When NaH was used instead of an amine base in a mixture of DMSO and THF, the chemical yield was dramatically improved to 86%. When the obtained (*R*)-4d was retreated under the same conditions in a mixture of DMSO and THF in the presence of sodium salt of quinoline-2-thiol, the specific rotation ( $[\alpha]_D^{25} +607^\circ$ ) of (*R*)-4d did not change even after 12 h. This result suggested that epimerization did not occur under these reaction conditions. The poor reactivity of cyclohexanethiol and dodecanethiol with amine bases was also improved by the use of their sodium salts.



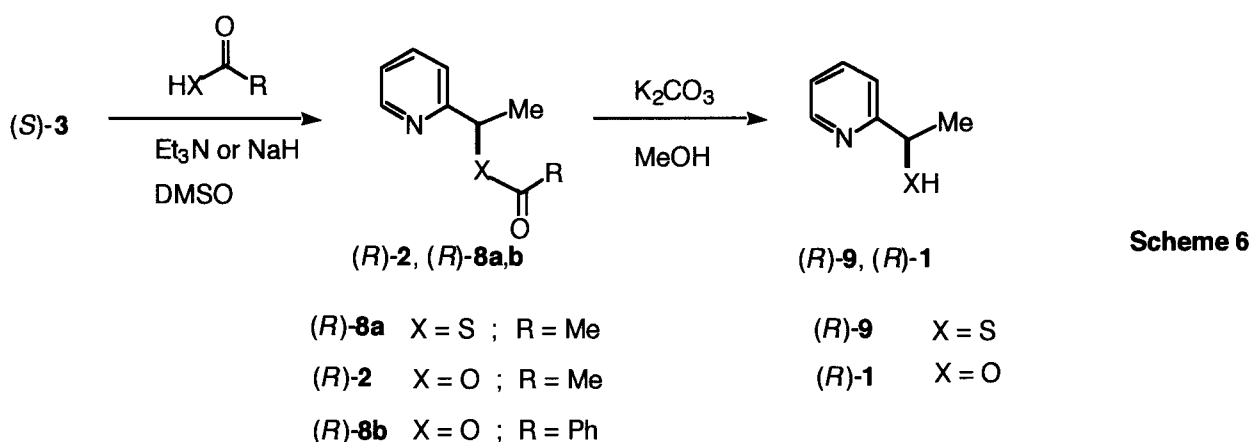
### Substitution Reaction with *O*-Nucleophiles

Next, we examined the substitution reactions with phenols and alcohols. The reaction of (*S*)-**3** with sodium salt of *p*-methoxyphenol at 60° C for 1 h gave anisyl ether ((*R*)-**7a**) in 96% yield. Under the same conditions, the reaction with sodium phenoxide gave (*R*)-**7b** in 92% yield. On the other hand, sodium salt of *p*-nitrophenol was less reactive and gave (*R*)-**7c** in only 48% yield along with 30% recovery of the starting mesylate. These results suggested that nucleophilicity was important and an electron-withdrawing group on the aromatic ring reduced the reaction rate. In fact, amine bases did not work at all. Sodium salt of 2-quinolinol also reacted with (*S*)-**3** to give (*R*)-**7d** in 60% yield. We tried to determine the ee value of (*R*)-**7a-d** by HPLC but without success. Since the specific rotation values of (*R*)-**7a** and (*R*)-**7b**,  $[\alpha]_D^{25} +7.5^\circ$  and  $-17.0^\circ$ , were not changed when they were treated with sodium phenoxide in DMSO for 6 h, it was assumed that an epimerization at the chiral carbon center did not take place in the reaction process. Considering this result and the complete inversion of the chiral center in the cases with nitrogen nucleophiles as well as sulfur nucleophiles, it was thought that the reaction with phenoxide would proceed stereospecifically with inversion of the configuration. Although *O*-substitution worked well for a phenol-type hydroxy group, the substitution reaction with alkoxides gave complex mixtures including alcohol (**1**). The reaction of (*S*)-**3** with sodium ethoxide gave **7e** only in 12% yield, which showed  $[\alpha]_D^{25} -3^\circ$  (*c* 0.50, in CHCl<sub>3</sub>). Since the authentic material for (*R*)-**7e**, prepared from (*R*)-**1** with ethyl iodide independently, showed  $[\alpha]_D^{25} -75^\circ$  (*c* 0.70, in CHCl<sub>3</sub>), compound (**7e**) was almost racemized in the reaction. The major product in the reaction was (*R*)-**1**, which was presumably formed by hydrolysis of methanesulfonate ester.

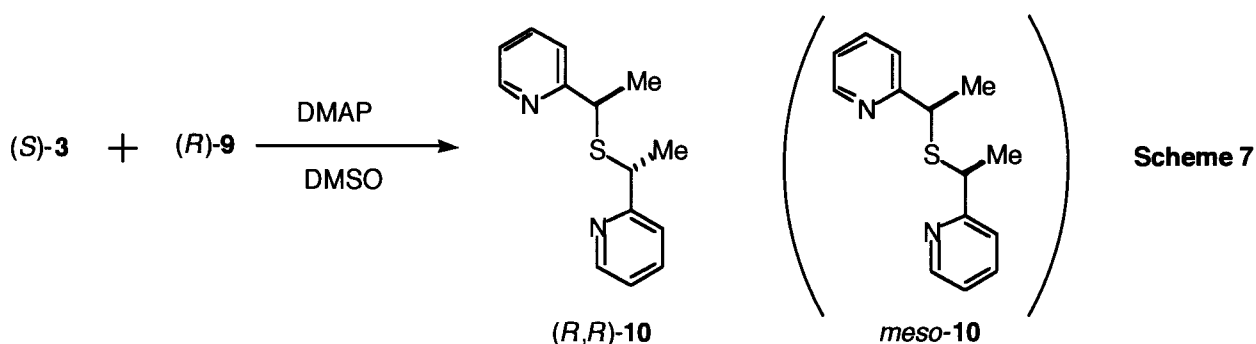


### Substitution Reaction with *S*- and *O*-Carboxylate

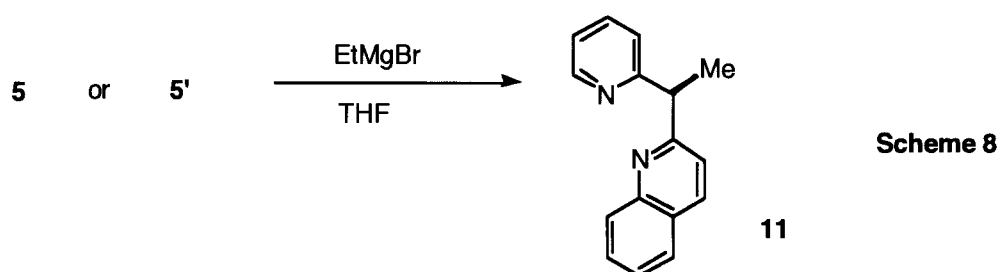
If the substitution reaction of *S*- or *O*-carboxylate anion with **3** can also take place with inversion of the chiral center, stereochemically inverted 1-(2-pyridinyl)ethanethiol or 1-(2-pyridinyl)ethanol would be attained after hydrolysis of the products. Indeed, the reaction of (*S*)-**3** with thioacetic acid in the presence of triethylamine gave thioester ((*R*)-**8a**) in 80% yield. Methanolysis of the ester gave (*R*)-1-(2-pyridinyl)ethanethiol ((*R*)-**9**) in 51% yield. In the same manner, the reaction of potassium acetate and benzoate gave (*R*)-**2** and (*R*)-**8b** in 71% and 87% yields, respectively. Hydrolysis of (*R*)-**2** afforded (*R*)-**1**, which possessed nearly 98% of ee.



When sodium salt of (*R*)-**9** was treated with (*S*)-**3** in DMSO, sulfide (**10**) was obtained in 72% yield. The specific rotation showed  $[\alpha]_D^{25} +404^\circ$  (*c* 2.78, in  $\text{CHCl}_3$ ), and no *meso* isomer was found in the crude mixture of the nmr spectrum. The formation of this single and optically active diastereomer apparently indicated that the newly formed chiral center has an (*R*)-configuration. The results supported the notion that the substitution reaction also occurs through an  $\text{S}_{\text{N}}2$  replacement mechanism.



Finally, in the relation of our previous work in sulfoxide chemistry,<sup>8</sup> chiral sulfoxides (**5** and **5'**) were subjected to ligand coupling reaction.<sup>9</sup> Treatment of **5** with ethylmagnesium bromide in THF at room temperature gave 1-(2-pyridinyl)-1-(2-quinolinyl)ethane (**11**) in 30% yield. The reaction of **5'** also gave the same product in 45% yield. The products have the same specific rotation,  $[\alpha]_D^{27} +11^\circ$  (*c* 0.54, in  $\text{CHCl}_3$ ). The stereochemistry of **11** was assumed to have an (*R*)-configuration, because it has been established that ligand coupling reactions of sulfoxide proceed with retention of the configuration.<sup>10</sup> The product (**11**) is quite interesting for a ligand having no heteroatom substituent on the tertiary chiral carbon center located between 2-quinoline and 2-pyridine rings.



In conclusion, optically pure pyridinyl sulfides, aryl ethers, and esters can be prepared by the substitution reaction of optically active 1-(2-pyridinyl)ethyl methanesulfonate with *S*- and *O*-nucleophiles. These new

## EXPERIMENTAL

<sup>1</sup>H NMR were recorded on JEOL LA-500 and 300 (500 and 300 MHz) and Varian Gemini-300 (300 MHz) spectrometers in CDCl<sub>3</sub> with tetramethylsilane as an internal standard. MS spectra were obtained on JASCO JMS-MS700, JMS-GC mate, and JMS-SX 102A QQ instruments. IR spectra were recorded on JASCO FT/IR-230 and 410 instruments. All air- or moisture-sensitive reactions were carried out in flame-dried glassware under Ar or N<sub>2</sub> atmosphere. THF was distilled freshly over sodium/benzophenone ketyl under nitrogen atmosphere, and DMSO was dried over CaH<sub>2</sub>, and they were distilled before the use. Thin layer chromatography (TLC) was performed with Merck 60F<sub>254</sub> precoated silica gel plates. Column chromatography was carried out using Merck silica gel 60 (70-230 mesh) for gravity column.

**Substitution Reaction with *S*-Nucleophiles. Method A;** To a stirred solution of (*S*)- or (*R*)-**3** (1 mmol) and triethylamine (606 mg, 6 mmol) in DMSO (6.8 mL) was added thiol (2 mmol) at rt. After 40 min, the mixture was quenched with saturated NaHCO<sub>3</sub> (6 mL) and extracted with Et<sub>2</sub>O (150 mL). The organic layer was separated and washed with water and brine, then dried over MgSO<sub>4</sub> and concentrated. The residual oil was purified by column chromatography on silica gel eluted with a mixture of EtOAc and hexane. The eluents were 10% EtOAc in hexane for **4a**, 30% for **4b**, and 50% for **4c**. **Method B;** To a stirred suspension of NaH (60% in mineral oil, 80 mg, 2 mmol) in DMSO-THF (1 : 1, 4.8 mL) was added thiol (2 mmol) at rt. After evolution of hydrogen gas was stopped, the mixture was added to a stirred solution of (*S*)- or (*R*)-**3** (1 mmol) in DMSO (2.2 mL) at the same temperature. The mixture was then stirred for 30 min to 7 h at rt or 60 °C and Et<sub>2</sub>O (150 mL) was added to the reaction mixture. The mixture was washed with saturated aq. NaHCO<sub>3</sub>, water and brine, and dried over MgSO<sub>4</sub>. The solvent was removed and the residual oil was purified by column chromatography on silica gel eluted with a mixture of EtOAc and hexane. The eluents were 5% for **4d**, **4e**, and **4f**, and 20% for **4g**.

**Phenyl (*R*)-1-(2-pyridinyl)ethyl sulfide (4a).** (Method A) Yield 87% as an oil. *R*<sub>f</sub> = 0.56 (30% EtOAc in hexane); [α]<sub>D</sub><sup>27</sup> +207° (*c* 1.59, CHCl<sub>3</sub>); <sup>1</sup>H NMR (300 MHz) δ 1.67 (3H, d, *J* = 7.0 Hz, -CHCH<sub>3</sub>), 4.50 (1H, q, *J* = 7.0 Hz, -CHCH<sub>3</sub>), 7.11 (1H, ddd, *J* = 7.3, 5.0, 0.9 Hz, Ar-*H*), 7.15-7.33 (6H, m), 7.57 (1H, td, *J* = 7.7, 1.8 Hz, Ar-*H*), 8.52 (1H, dm, *J* = 4.0 Hz, Ar-*H*); <sup>13</sup>C NMR (75 MHz) δ 21.0, 49.1, 121.6, 121.9, 126.9, 128.6, 131.9, 134.7, 136.5, 149.1, 162.2; MS (EI) *m/z* 215 (M<sup>+</sup>); HRMS (EI) *m/z* Calcd for C<sub>13</sub>H<sub>13</sub>NS: 215.0768 (M<sup>+</sup>). Found: 215.0783.

**2-Pyridinyl (*R*)-1-(2-pyridinyl)ethyl sulfide (4b).** (Method A) Yield 76% as an oil. *R*<sub>f</sub> = 0.37 (20% EtOAc in hexane); [α]<sub>D</sub><sup>19</sup> +319° (*c* 1.44, CHCl<sub>3</sub>); <sup>1</sup>H NMR (300 MHz) δ 1.78 (3H, d, *J* = 7.0 Hz, -CHCH<sub>3</sub>), 5.23 (1H, q, *J* = 7.1 Hz, -CHCH<sub>3</sub>), 6.96 (1H, ddd, *J* = 7.3, 5.0, 1.1 Hz, Ar-*H*), 7.15 (2H, d, *J* = 7.3 Hz, Ar-*H*), 7.45 (2H, d, *J* = 7.5 Hz, Ar-*H*), 7.63 (1H, td, *J* = 7.7, 1.8 Hz, Ar-*H*), 8.50 (2H, d, *J* = 4.9 Hz, Ar-*H*), 8.59 (1H, dm, *J* = 4.0 Hz, Ar-*H*); <sup>13</sup>C NMR (75 MHz) δ 21.4, 44.8, 119.5, 121.9, 121.9, 122.5, 135.9, 136.5, 149.3, 149.3,

158.6, 162.3; MS (EI)  $m/z$  216 ( $M^+$ ); HRMS (EI)  $m/z$  Calcd for  $C_{12}H_{12}N_2S$ : 216.0722 ( $M^+$ ). Found: 216.0681.

**2-Pyrimidinyl (*R*)-1-(2-Pyridinyl)ethyl sulfide (4c).** (Method A) Yield 87% as an oil.  $R_f$  = 0.37 (20% EtOAc in hexane);  $[\alpha]_D^{27}$  +289° ( $c$  2.01,  $CHCl_3$ );  $^1H$  NMR (300 MHz)  $\delta$  1.81 (3H, d,  $J$  = 7.1 Hz,  $-CHCH_3$ ), 5.20 (1H, q,  $J$  = 7.1 Hz,  $-CHCH_3$ ), 6.94 (1H, t,  $J$  = 4.9 Hz, Ar-*H*), 7.16 (1H, ddd,  $J$  = 7.5, 4.9, 1.1 Hz, Ar-*H*), 7.47 (1H, d,  $J$  = 7.9 Hz, Ar-*H*), 7.63 (1H, td,  $J$  = 7.7, 1.8 Hz, Ar-*H*), 8.50 (2H, d,  $J$  = 4.9 Hz, Ar-*H*), 8.59 (1H, dm,  $J$  = 4.0 Hz, Ar-*H*);  $^{13}C$  NMR (75 MHz)  $\delta$  21.2, 45.5, 116.3, 121.8, 121.9, 136.5, 149.2, 157.1, 161.8, 171.9; MS (EI)  $m/z$  217 ( $M^+$ ); HRMS (EI)  $m/z$  Calcd for  $C_{11}H_{11}N_3S$ : 217.0673 ( $M^+$ ). Found: 217.0704.

**2-Quinolinylnyl (*R*)-1-(2-pyridinyl)ethyl sulfide (4d).** (Method B) Yield 86% as an oil.  $R_f$  = 0.62 (30% EtOAc in hexane);  $[\alpha]_D^{24}$  +607° ( $c$  1.53,  $CHCl_3$ );  $^1H$  NMR (300 MHz)  $\delta$  1.86 (3H, d,  $J$  = 7.2 Hz,  $-CHCH_3$ ), 5.54 (1H, q,  $J$  = 7.2 Hz,  $-CHCH_3$ ), 7.11 (1H, ddd,  $J$  = 6.7, 4.9, 2.1 Hz, Ar-*H*), 7.16 (1H, d,  $J$  = 8.7 Hz, Ar-*H*), 7.40 (1H, td,  $J$  = 7.0, 1.2 Hz, Ar-*H*), 7.52–7.65 (3H, m, Ar-*H*), 7.67 (1H, d,  $J$  = 7.7 Hz, Ar-*H*) 7.82 (1H, d,  $J$  = 7.7 Hz, Ar-*H*), 7.95 (1H, d,  $J$  = 8.4 Hz, Ar-*H*), 8.59 (1H, dm,  $J$  = 4.6 Hz, Ar-*H*);  $^{13}C$  NMR (75 MHz)  $\delta$  20.7, 43.9, 120.4, 121.5, 121.9, 124.7, 125.5, 127.1, 127.4, 129.1, 134.9, 136.0, 147.7, 148.8, 158.3, 162.0; MS (EI)  $m/z$  266 ( $M^+$ ); HRMS (EI)  $m/z$  Calcd for  $C_{16}H_{14}N_2S$ : 266.0877 ( $M^+$ ). Found: 266.0897.

**Cyclohexyl (*R*)-1-(2-pyridinyl)ethyl sulfide (4e).** (Method B) Yield 76% as an oil.  $R_f$  = 0.33 (10% EtOAc in hexane);  $[\alpha]_D^{27}$  +151° ( $c$  1.78,  $CHCl_3$ );  $^1H$  NMR (500 MHz)  $\delta$  1.20–2.10 (10H, m), 1.58 (3H, d,  $J$  = 7.2 Hz,  $-CHCH_3$ ), 2.35–2.55 (1H, m), 4.18 (1H, q,  $J$  = 7.1 Hz,  $-CHCH_3$ ), 7.13 (1H, ddd,  $J$  = 7.4, 4.9, 1.2 Hz, Ar-*H*), 7.43 (1H, td,  $J$  = 7.9, 0.9 Hz, Ar-*H*), 7.65 (1H, td,  $J$  = 7.5, 1.8 Hz, Ar-*H*) 8.50 (1H, ddd,  $J$  = 5.0, 1.8, 0.9 Hz, Ar-*H*);  $^{13}C$  NMR (125 MHz)  $\delta$  21.8, 25.8, 25.9, 26.0, 33.5, 33.9, 43.0, 44.3, 121.4, 121.8, 136.7, 148.8, 164.1; MS (FAB)  $m/z$  222 ( $M^+ + H$ ); HRMS (FAB)  $m/z$  Calcd for  $C_{13}H_{20}NS$ : 222.1316 ( $M^+ + H$ ). Found: 222.1293.

**Dodecanyl (*R*)-1-(2-pyridinyl)ethyl sulfide (4f).** (Method B) Yield 76% as an oil.  $R_f$  = 0.31 (5% EtOAc in hexane);  $[\alpha]_D^{26}$  +105° ( $c$  1.82,  $CHCl_3$ );  $^1H$  NMR (300 MHz)  $\delta$  0.55 (3H, t,  $J$  = 6.5 Hz) 1.11–1.34 (18H, m), 1.36–1.51 (2H, m), 1.59 (3H, d,  $J$  = 7.1 Hz,  $-CHCH_3$ ), 2.05–2.44 (2H, m), 4.06 (1H, q,  $J$  = 7.1 Hz,  $-CHCH_3$ ), 7.12 (1H, ddd,  $J$  = 7.5, 5.0, 1.2 Hz, Ar-*H*), 7.39 (1H, d,  $J$  = 7.9 Hz, Ar-*H*), 7.63 (1H, td,  $J$  = 7.7, 1.9 Hz, Ar-*H*) 8.49 (1H, d,  $J$  = 5.0 Hz, Ar-*H*);  $^{13}C$  NMR (75 MHz)  $\delta$  14.1, 21.1, 22.6, 28.8, 29.1, 29.3, 29.4, 29.4, 29.5, 29.6, 29.6, 31.9, 32.1, 45.7, 121.4, 121.8, 136.6, 148.8, 163.6; MS (FAB)  $m/z$  308 ( $M^+ + H$ ); HRMS (FAB)  $m/z$  Calcd for  $C_{19}H_{34}NS$ : 308.2412 ( $M^+$ ). Found: 308.2382.

**Ethyl (*R*)-2-[(*t*-butoxycarbonyl)amino]-3-[(*R*)-1-(2-pyridinyl)ethyl]thiopropanate (4g).** (Method B) Yield 47% as an oil.  $R_f$  = 0.29 (30% EtOAc in hexane);  $[\alpha]_D^{27}$  +100° ( $c$  1.90,  $CHCl_3$ );  $^1H$  NMR (300 MHz)  $\delta$  1.27 (3H, tm,  $J$  = 7.2 Hz,  $-CH_2CH_3$ ) 1.44 (9H, s, *t*-Bu), 1.60 (3H, d,  $J$  = 7.2 Hz,  $-CHCH_3$ ), 2.82 (2H, m), 4.05–4.20 (2H, m,  $-OCH_2CH_3$ ), 4.17 (1H, q,  $J$  = 7.2 Hz,  $-CHCH_3$ ), 4.43 (1H, br q,  $J$  = 5.3 Hz), 5.56 (1H, m), 7.17 (1H, dd,  $J$  = 5.0, 0.7 Hz, Ar-*H*), 7.36 (1H, d,  $J$  = 7.9 Hz, Ar-*H*), 7.67 (1H, td,  $J$  = 7.7, 1.7 Hz, Ar-*H*) 8.55 (1H, d,  $J$  = 5.0 Hz, Ar-*H*);  $^{13}C$  NMR (75 MHz)  $\delta$  14.1, 20.8, 28.2, 33.3, 45.8, 53.5, 61.5, 79.8, 121.4, 122.2, 136.9, 149.0, 155.2, 162.5, 171.0; IR (neat) 1755, 1720  $cm^{-1}$ . MS (EI)  $m/z$  354 ( $M^+$ ); HRMS (EI)  $m/z$  Calcd for  $C_{17}H_{26}N_2O_4S$ : 354.1613 ( $M^+$ ). Found: 354.1608.

**2-Quinolinylnyl (*R*)-1-(2-pyridinyl)ethyl sulfoxide, (5) and (5').** To a stirred solution of (*R*)-4d (100 mg, 0.38 mmol) in  $CHCl_3$  (8 mL) was added *m*CPBA (98 mg, 85% activity, 0.48 mmol) little by little at rt. The

reaction mixture was stirred for 1 h, and then quenched with saturated aq.  $\text{NaHCO}_3$  (1.5 mL). The mixture was extracted with  $\text{CHCl}_3$  (80 mL), and washed with water and brine, and dried over  $\text{MgSO}_4$ . The solvent was removed and the residual oil was purified by column chromatography on silica gel eluted with 30% EtOAc in hexane to give **5** (30 mg, 28%), **5'** (30 mg, 28%), and sulfone (15 mg, 13%). **5** oil;  $R_f = 0.56$  (50% EtOAc in hexane);  $[\alpha]_D^{27} -130^\circ$  ( $c$  1.30,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (300 MHz)  $\delta$  1.55 (3H, d,  $J = 7.3$  Hz,  $-\text{CHCH}_3$ ), 4.62 (1H, q,  $J = 7.2$  Hz,  $-\text{CHCH}_3$ ), 7.24 (1H, dd,  $J = 6.5, 2.8$  Hz, Ar- $H$ ), 7.37 (1H, d,  $J = 7.7$  Hz, Ar- $H$ ), 7.66 (2H, m, Ar- $H$ ), 7.79 (1H, td,  $J = 8.4, 1.5$  Hz, Ar- $H$ ), 7.91 (2H, m, Ar- $H$ ), 8.08 (1H, d,  $J = 8.4$  Hz, Ar- $H$ ), 8.34 (1H, d,  $J = 8.4$  Hz, Ar- $H$ ), 8.57 (1H, d,  $J = 4.4$  Hz, Ar- $H$ );  $^{13}\text{C NMR}$  (75 MHz)  $\delta$  10.5, 66.1, 116.5, 122.9, 123.3, 127.8, 127.9, 128.1, 129.4, 130.6, 136.6, 137.7, 147.4, 149.6, 156.5, 163.3; IR (neat)  $1046\text{ cm}^{-1}$ . **5'** colorless crystals, mp  $87\text{--}88^\circ\text{C}$  (hexane:EtOAc, 9:1);  $R_f = 0.44$  (50% EtOAc in hexane);  $[\alpha]_D^{27} +457^\circ$  ( $c$  1.10,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (300 MHz)  $\delta$  1.88 (3H, d,  $J = 7.2$  Hz,  $-\text{CHCH}_3$ ), 5.22 (1H, q,  $J = 7.3$  Hz,  $-\text{CHCH}_3$ ), 7.22 (1H, ddd,  $J = 7.4, 5.0, 0.9$  Hz, Ar- $H$ ), 7.29 (1H, d,  $J = 8.6$  Hz, Ar- $H$ ), 7.56 (1H, d,  $J = 7.7$  Hz, Ar- $H$ ), 7.69 (2H, dd,  $J = 7.9, 1.8$  Hz, Ar- $H$ ), 7.80-7.94 (3H, m, Ar- $H$ ), 8.22 (1H, d,  $J = 8.6$  Hz, Ar- $H$ ), 8.44 (1H, d,  $J = 4.2$  Hz, Ar- $H$ );  $^{13}\text{C NMR}$  (75 MHz)  $\delta$  14.3, 65.2, 115.9, 122.6, 123.8, 127.7, 128.1, 129.4, 130.5, 135.8, 137.3, 147.1, 148.8, 154.3, 163.2; IR (neat)  $1057\text{ cm}^{-1}$ ; MS (FAB)  $m/z$  283 ( $\text{M}^+\text{+H}$ ); HRMS (FAB)  $m/z$  Calcd for  $\text{C}_{16}\text{H}_{15}\text{N}_2\text{OS}$ : 283.0826 ( $\text{M}^+\text{+H}$ ). Found: 283.0899. Sulfone colorless crystals, mp  $114\text{--}5^\circ\text{C}$  (methanol);  $R_f = 0.82$  (50% EtOAc in hexane);  $[\alpha]_D^{25} +36^\circ$  ( $c$  1.43,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (300 MHz)  $\delta$  1.87 (3H, d,  $J = 7.2$  Hz,  $-\text{CHCH}_3$ ), 5.22 (1H, q,  $J = 7.3$  Hz,  $-\text{CHCH}_3$ ), 7.22 (1H, ddd,  $J = 7.4, 5.0, 0.9$  Hz, Ar- $H$ ), 7.56 (1H, d,  $J = 7.7$  Hz, Ar- $H$ ), 7.69 (2H, dd,  $J = 7.9, 1.8$  Hz, Ar- $H$ ), 7.80-7.94 (3H, m, Ar- $H$ ), 8.21 (1H, d,  $J = 8.2$  Hz, Ar- $H$ ), 8.28 (1H, d,  $J = 8.7$  Hz, Ar- $H$ ), 8.42 (1H, d,  $J = 3.7$  Hz, Ar- $H$ );  $^{13}\text{C NMR}$  (75 MHz)  $\delta$  13.3, 64.2, 118.7, 123.5, 124.9, 127.7, 129.3, 130.3, 131.1, 136.9, 138.2, 147.3, 149.1, 153.1, 155.5, 168.3; IR (KBr)  $1298, 1137\text{ cm}^{-1}$ .

**1-(2-Pyridinyl)ethyl thiocyanate (6)**. To a stirred solution of (*S*)-**3** (50 mg, 0.25 mmol) in DMSO (1.0 mL) was added sodium thiocyanate (162 mg, 1.99 mmol) at rt. The mixture was stirred for 30 min at  $60^\circ\text{C}$ . The reaction mixture was diluted with  $\text{Et}_2\text{O}$  (80 mL) and washed with water and brine, then dried over  $\text{MgSO}_4$  and concentrated. The residual oil was purified by column chromatography on silica gel eluted with 20% EtOAc in hexane to give **6** (15 mg, 37%) as an oil.  $R_f = 0.65$  (50% EtOAc in hexane);  $^1\text{H NMR}$  (300 MHz)  $\delta$  1.91 (3H, d,  $J = 7.0$  Hz,  $-\text{CHCH}_3$ ), 4.70 (1H, q,  $J = 7.0$  Hz,  $-\text{CHCH}_3$ ), 7.28 (1H, ddd,  $J = 7.5, 4.9, 1.0$  Hz, Ar- $H$ ), 7.35 (1H, d,  $J = 7.9$  Hz, Ar- $H$ ), 7.74 (1H, td,  $J = 7.7, 1.8$  Hz, Ar- $H$ ), 8.59 (1H, d,  $J = 4.8$  Hz, Ar- $H$ );  $^{13}\text{C NMR}$  (75 MHz)  $\delta$  21.2, 49.5, 111.8, 120.9, 123.0, 136.8, 149.3, 157.5; IR (neat)  $2168\text{ cm}^{-1}$ ; MS (EI)  $m/z$  164 ( $\text{M}^+$ ); HRMS (EI)  $m/z$  Calcd for  $\text{C}_8\text{H}_8\text{N}_2\text{S}$ : 164.0408 ( $\text{M}^+$ ). Found: 164.0376.

**Substitution Reaction with O-Nucleophiles**. To a stirred solution of (*S*)-**3** (202 mg, 1 mmol) in DMSO (2.2 mL) was added sodium salt (2 mmol) of phenol or alcohol in DMSO-THF (1 : 1, 6.0 mL), generated from NaH and phenol or alcohol, at rt. The mixture was continued for 30 min to 20 h at  $60^\circ\text{C}$ . After cooling, it was diluted with  $\text{Et}_2\text{O}$  (150 mL) and washed with saturated aq.  $\text{NaHCO}_3$ , water and brine. The organic layer was dried over  $\text{MgSO}_4$  and concentrated. The residual oil was purified by column chromatography on silica gel eluted with a mixture of EtOAc and hexane. The eluents were 30% EtOAc in hexane for **7a** and



**7b**, 15% for **7c**, and 10% for **7d**.

**4-Methoxyphenyl (R)-1-(2-pyridinyl)ethyl ether (7a)**. Yield 96% as an oil.  $R_f = 0.45$  (30% EtOAc in hexane);  $[\alpha]_D^{26} +7.5^\circ$  ( $c$  3.00,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (300 MHz)  $\delta$  1.66 (3H, d,  $J = 6.6$  Hz,  $-\text{CHCH}_3$ ), 3.79 (3H, s,  $\text{OCH}_3$ ), 5.35 (1H, q,  $J = 6.6$  Hz,  $-\text{CHCH}_3$ ), 6.72-6.82 (4H, m, Ar-H), 7.20 (1H, t,  $J = 4.9$  Hz, Ar-H), 7.45 (1H, d,  $J = 8.1$  Hz, Ar-H), 7.67 (1H, td,  $J = 7.7, 1.7$  Hz, Ar-H) 8.57 (1H, d,  $J = 3.7$  Hz, Ar-H);  $^{13}\text{C NMR}$  (75 MHz)  $\delta$  22.6, 55.5, 77.4, 114.4, 116.5, 119.8, 122.2, 136.9, 148.8, 151.7, 153.7, 162.6; MS (EI)  $m/z$  229 ( $M^+$ ); HRMS (EI)  $m/z$  Calcd for  $\text{C}_{14}\text{H}_{15}\text{NO}_2$ : 229.1103 ( $M^+$ ). Found: 229.1097.

**Phenyl (R)-1-(2-pyridinyl)ethyl ether (7b)**. Yield 92% as an oil.  $R_f = 0.46$  (30% EtOAc in hexane);  $[\alpha]_D^{27} -17^\circ$  ( $c$  1.8,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (300 MHz)  $\delta$  1.68 (3H, d,  $J = 6.5$  Hz,  $-\text{CHCH}_3$ ), 6.89 (1H, q,  $J = 6.5$  Hz,  $-\text{CHCH}_3$ ), 6.85-6.91 (3H, m, Ar-H), 7.17-7.22 (3H, m, Ar-H), 7.44 (1H, d,  $J = 8.0$  Hz, Ar-H), 7.66 (1H, td,  $J = 7.7, 1.8$  Hz, Ar-H) 8.58 (1H, d,  $J = 4.9$  Hz, Ar-H);  $^{13}\text{C NMR}$  (75 MHz)  $\delta$  22.7, 76.7, 115.5, 119.8, 120.7, 122.3, 129.4, 137.1, 148.8, 157.6, 162.5; MS (EI)  $m/z$  199 ( $M^+$ ); HRMS (EI)  $m/z$  Calcd for  $\text{C}_{13}\text{H}_{13}\text{NO}$ : 199.0997 ( $M^+$ ). Found: 199.0998.

**4-Nitrophenyl (R)-1-(2-pyridinyl)ethyl ether (7c)**. Yield 48% as an oil.  $R_f = 0.37$  (30% EtOAc in hexane);  $[\alpha]_D^{26} +36^\circ$  ( $c$  1.70,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (300 MHz)  $\delta$  1.74 (3H, d,  $J = 6.5$  Hz,  $-\text{CHCH}_3$ ), 5.52 (1H, q,  $J = 6.5$  Hz,  $-\text{CHCH}_3$ ), 6.94 (2H, d,  $J = 9.2$  Hz, Ar-H), 7.23 (1H, dd,  $J = 7.3, 4.9$  Hz, Ar-H), 7.38 (1H, d,  $J = 8.1$  Hz, Ar-H), 7.69 (1H, td,  $J = 7.7, 1.5$  Hz, Ar-H), 8.11 (2H, d,  $J = 9.2$  Hz, Ar-H), 8.33 (1H, d,  $J = 4.9$  Hz, Ar-H);  $^{13}\text{C NMR}$  (75 MHz)  $\delta$  22.5, 77.9, 115.5, 119.6, 122.9, 125.7, 137.3, 141.4, 149.1, 160.8, 162.7; IR (neat) 1515, 1342  $\text{cm}^{-1}$ ; MS (EI)  $m/z$  244 ( $M^+$ ); HRMS (EI)  $m/z$  Calcd for  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_3$ : 244.0848 ( $M^+$ ). Found: 244.0852.

**2-Quinolinyl (R)-1-(2-pyridinyl)ethyl ether (7d)**. Yield 60% as an oil.  $R_f = 0.68$  (50% EtOAc in hexane);  $[\alpha]_D^{24} +219^\circ$  ( $c$  1.23,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (300 MHz)  $\delta$  1.76 (3H, d,  $J = 6.6$  Hz,  $-\text{CHCH}_3$ ), 6.54 (1H, q,  $J = 6.6$  Hz,  $-\text{CHCH}_3$ ), 6.99 (1H, d,  $J = 8.8$  Hz, Ar-H), 7.13 (1H, dd,  $J = 6.8, 4.5$  Hz, Ar-H), 7.31 (1H, d,  $J = 7.0$  Hz, Ar-H), 7.48 (1H, d,  $J = 7.0$  Hz, Ar-H), 7.52-7.67 (3H, m, Ar-H), 7.75 (1H, d,  $J = 8.4$  Hz, Ar-H), 7.96 (1H, d,  $J = 8.8$  Hz, Ar-H) 8.59 (1H, d,  $J = 4.8$  Hz, Ar-H);  $^{13}\text{C NMR}$  (75 MHz)  $\delta$  21.1, 73.5, 113.2, 120.5, 122.1, 123.9, 125.1, 127.3, 128.3, 129.3, 136.5, 138.7, 146.4, 149.1, 161.0, 162.0; MS (EI)  $m/z$  250 ( $M^+$ ); HRMS (EI)  $m/z$  Calcd for  $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}$ : 250.1106 ( $M^+$ ). Found: 250.1119.

**(R)-1-(2-Pyridinyl)ethyl thioacetate (8a)**. To a stirred solution of (*S*)- **3** (202 mg, 1.00 mmol) and triethylamine (610 mg, 6.02 mmol) in DMSO (6.7 mL) was added thioacetic acid (149 mg, 6.02 mmol) at rt. The mixture was stirred for 2.5 h at the same temperature and quenched with saturated aq.  $\text{NaHCO}_3$ . The mixture was extracted with  $\text{Et}_2\text{O}$ . The organic layer was washed with water and brine, then dried over  $\text{MgSO}_4$  and concentrated. The residual oil was purified by column chromatography on silica gel eluted with 10% EtOAc in hexane to give (*R*)-**8a** (145 mg, 80%) as an oil.  $R_f = 0.56$  (30% EtOAc in hexane);  $[\alpha]_D^{25} +253^\circ$  ( $c$  2.03,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (300 MHz)  $\delta$  1.69 (3H, d,  $J = 7.2$  Hz,  $-\text{CHCH}_3$ ), 2.32 (3H, s,  $\text{C(O)CH}_3$ ), 4.83 (1H, q,  $J = 7.2$  Hz,  $-\text{CHCH}_3$ ), 7.16 (1H, ddd,  $J = 7.5, 4.9, 1.0$  Hz, Ar-H), 7.32 (1H, d,  $J = 7.7$  Hz, Ar-H), 7.63 (1H, td,  $J = 7.7, 1.8$  Hz, Ar-H), 8.57 (1H, dt,  $J = 4.7, 0.9$  Hz, Ar-H);  $^{13}\text{C NMR}$  (75 MHz)  $\delta$  21.0, 30.4, 44.5, 122.0, 122.2, 136.7, 149.5, 161.2, 195.1; IR (neat) 1692  $\text{cm}^{-1}$ ; MS (EI)  $m/z$  181 ( $M^+$ ); HRMS (EI)  $m/z$  Calcd for  $\text{C}_9\text{H}_{11}\text{NOS}$ : 181.0561 ( $M^+$ ). Found: 181.0581.

**(R)-1-(2-Pyridinyl)ethanethiol (9).** To a stirred solution of (*R*)-**8a** (101 mg, 0.56 mmol) in methanol (2.0 mL) was added anhydrous  $K_2CO_3$  (308 mg, 2.23 mmol) at rt. The mixture was stirred for 20 min at the same temperature. The reaction mixture was concentrated and the residue was extracted with EtOAc. The organic extract was washed with water and brine, dried over  $MgSO_4$  and concentrated. The residual oil was chromatographed on silica gel eluted with 20% EtOAc in hexane to give (*R*)-**9** (39 mg, 51%) as an oil. *Rf* = 0.28 (50% EtOAc in hexane);  $[\alpha]_D^{27} +236^\circ$  (*c* 2.00,  $CHCl_3$ );  $^1H$  NMR (300 MHz)  $\delta$  1.73 (3H, d, *J* = 6.9 Hz,  $-CHCH_3$ ), 2.55 (1H, d, *J* = 6.8 Hz, *SH*), 4.25 (1H, q, *J* = 6.9 Hz,  $-CHCH_3$ ), 7.15 (1H, td, *J* = 4.3, 1.1 Hz, *Ar-H*), 7.34 (1H, d, *J* = 8.1 Hz, *Ar-H*), 7.65 (1H, td, *J* = 7.7, 1.9 Hz, *Ar-H*), 8.54 (1H, d, *J* = 4.4 Hz, *Ar-H*);  $^{13}C$  NMR (75 MHz)  $\delta$  19.2, 51.1, 121.9, 122.0, 136.0, 149.0, 160.7; MS (EI) *m/z* 139 ( $M^+$ ); HRMS (EI) *m/z* Calcd for  $C_7H_9NS$ : 139.0455 ( $M^+$ ). Found: 139.0433.

**Substitution Reaction with Potassium Carboxylates.** To a stirred solution of (*S*)-**3** (202 mg, 1 mmol) and 18-crown-*O*-6 (240 mg, 1 mmol) in DMSO (2 mL) was added potassium acetate or benzoate (10 mmol) at rt. The mixture was stirred for 1 h at 60 °C and diluted with  $Et_2O$  (100 ml). The mixture was then washed with water and brine, then dried over  $MgSO_4$  and concentrated. The residual oil was purified by column chromatography on silica gel eluted with 30% EtOAc in hexane.

**(R)-1-(2-Pyridinyl)ethyl acetate (2).** Yield 71% as an oil.  $[\alpha]_D^{24} +99^\circ$  (*c* 1.43,  $CHCl_3$ ). All the spectroscopic data were consistent with those reported in ref. 6.

**(R)-1-(2-Pyridinyl)ethyl benzoate (8b).** Yield 87% as an oil. *Rf* = 0.48 (30% EtOAc in hexane);  $[\alpha]_D^{25} -39^\circ$  (*c* 1.90,  $CHCl_3$ );  $^1H$  NMR (300 MHz)  $\delta$  1.75 (3H, d, *J* = 6.6 Hz,  $-CHCH_3$ ), 6.17 (1H, q, *J* = 6.6 Hz,  $-CHCH_3$ ), 7.22 (1H, dd, *J* = 7.4, 1.5 Hz, *Ar-H*), 7.43-7.48 (3H, m, *Ar-H*), 7.54-7.60 (1H, m, *Ar-H*), 7.67-7.73 (1H, m, *Ar-H*), 8.11 (2H, d, *J* = 7.0 Hz, *Ar-H*), 8.62 (1H, d, *J* = 4.9 Hz, *Ar-H*);  $^{13}C$  NMR (75 MHz)  $\delta$  20.7, 73.6, 120.2, 122.6, 128.3, 129.6, 130.1, 133.0, 136.7, 149.2, 160.4, 165.7; IR (neat) 1725, 1235, 1073  $cm^{-1}$ ; MS (FAB) *m/z* 228 ( $M^+ + H$ ); HRMS (FAB) *m/z* Calcd for  $C_{14}H_{14}NO_2$ : 228.1025 ( $M^+ + H$ ). Found: 228.1029.

**(R, R)-Di[1-(2-pyridinyl)ethyl] sulfide (10).** The reaction of (*S*)-**3** (69 mg, 0.34 mmol) with (*R*)-**9** (75 mg, 0.50 mmol) was carried out under the same conditions described for the preparation of **4** by method A. The reaction completed for 1.5 h at rt. Purification was performed by column chromatography on silica gel eluted with 20% EtOAc in hexane. (*R, R*)-**10** (60 mg) was obtained in 72% yield. Oil. *Rf* = 0.35 (20% EtOAc in hexane);  $[\alpha]_D^{27} +404^\circ$  (*c* 2.78,  $CHCl_3$ );  $^1H$  NMR (300 MHz)  $\delta$  1.45 (6H, d, *J* = 7.2 Hz,  $-CHCH_3$ ), 3.84 (2H, q, *J* = 7.2 Hz,  $-CHCH_3$ ), 7.11 (2H, ddd, *J* = 7.7, 5.0, 1.0 Hz, *Ar-H*), 7.32 (2H, dd, *J* = 7.7, 1.0 Hz, *Ar-H*), 7.61 (2H, td, *J* = 7.7, 1.8 Hz, *Ar-H*), 8.51 (2H, dd, *J* = 5.0, 1.8 Hz, *Ar-H*);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  20.7, 44.7, 121.3, 121.5, 1336.3, 148.6, 162.8; MS (EI) *m/z* 244 ( $M^+$ ); HRMS (EI) *m/z* Calcd for  $C_{14}H_{16}N_2S$ : 244.1033 ( $M^+$ ). Found: 244.1047.

**(R)-1-(2-Pyridinyl)-1-(2-quinolinyl)ethane (11).** To a stirred solution of **5'** (216 mg, 0.765 mmol) in anhydrous THF (7.7 mL) was added ethylmagnesium bromide (1.15 mL, 1.02M THF solution) at 0°C. Then, cooling bath was removed and the reaction was continued for 3 h at rt. An ice water and sat.  $NH_4Cl$  were added and the mixture was extracted with  $CH_2Cl_2$ . The extract was washed with water and brine, and dried

over  $\text{MgSO}_4$ . After evaporation of the solvent, the residual oil was purified by silica gel column chromatography eluted with 80% EtOAc in hexane to give **11** (78 mg, 45%). Oil.  $R_f = 0.51$  (80% EtOAc in hexane);  $[\alpha]_D^{27} +11^\circ$  ( $c$  0.54,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (500 MHz)  $\delta$  1.86 (3H, d,  $J = 7.2$  Hz), 4.68 (1H, q,  $J = 7.2$  Hz), 7.12 (1H, ddd,  $J = 7.7, 5.0, 1.1$  Hz), 7.32 (1H, d,  $J = 7.7$  Hz), 7.41 (1H, d,  $J = 8.5$  Hz), 7.49 (1H, ddd,  $J = 8.1, 7.0, 1.1$  Hz), 7.58 (1H, td,  $J = 7.7, 1.7$  Hz), 7.69 (1H, ddd,  $J = 8.5, 7.0, 1.7$  Hz), 7.76 (1H, dd,  $J = 8.1, 0.9$  Hz), 8.05 (1H, d,  $J = 8.5$  Hz), 8.10 (1H, d,  $J = 8.5$  Hz), 8.58 (1H, ddd,  $J = 5.0, 1.7, 0.9$  Hz);  $^{13}\text{C NMR}$  (125 MHz)  $\delta$  19.7, 50.6, 120.8, 121.5, 122.9, 126.0, 127.0, 127.4, 129.1, 129.3, 136.4, 136.5, 147.6, 149.2, 163.4, 164.1. Anal. Calcd for  $\text{C}_{16}\text{H}_{14}\text{N}_2$ : C, 82.02, H, 6.02, N, 11.96. Found: C, 81.71, H, 6.02, N, 11.77.

## ACKNOWLEDGMENTS

This work was supported by a Special Grant for Cooperative Research administered by the Japan Private School Promotion Foundation. Financial support from the hoh-ansha foundation was greatly acknowledged. We thank Mr. Daisuke Mukai for assistance with the preparation of several materials.

## REFERENCES

1. Asymmetric reaction; E. N. Jacobsen, A. Pfaltz, and H. Yamamoto, Eds. 'Comprehensive Asymmetric Catalysis, Vol I-III, Springer-Verlag Inc., Berlin, 1999; G. Helmchen, R. W. Hoffmann, J. Mulzer, and E. Schaumann, Eds. 'Stereo-selective Synthesis, Georg Thieme Verlag, Stuttgart, 1996. Molecular Recognition; J. M. Lehn, Ed. in Chief, 'Comprehensive Supramolecular Chemistry, Elsevier Science Ltd. 1996.
2. H. Brunner and W. Zettlmeier, 'Handbook of Enantioselective Catalysts, Products and Catalysts', VCH, Weinheim, 1993, Vol. I; H. Brunner and W. Zettlmeier, 'Handbook of Enantioselective Catalysts, Ligands', VCH, Weinheim, 1993, Vol. II.
3. H. Zhang, F. Xue, T. C. W. Mak, and K. S. Chan, *J. Org. Chem.*, 1996, **61**, 8002; A. H. M. de Vries, R. P. Hof, D. Staal, R. P. Kellogg, and B. L. Feringa, *Tetrahedron: Asymmetry*, 1997, **8**, 1539; H. Brunner and P. Bublak, *Synthesis*, 1995, 36, and their previous series of 'Enantioselective Catalysis'; G. Chelucci, *Tetrahedron: Asymmetry*, 1995, **6**, 811 and references cited therein; P. Scrimin, P. Tecilla, and U. Tonellato, *J. Org. Chem.*, 1994, **59**, 4194; M. Ishizaki, K. Fujita, M. Shimamoto, and O. Hoshino, *Tetrahedron: Asymmetry*, 1994, **5**, 411; S. Conti, M. Falorni, G. Giacomelli, and F. Soccolini, *Tetrahedron*, 1992, **48**, 8993; H. Nishiyama, M. Kondo, T. Nakamura, and K. Itoh, *Organometallics*, 1991, **10**, 500; C. Bolm, M. Zehnder, and D. Bur, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 205; *Angew. Chem.*, 1990, **102**, 206.
4. C. Bolm, M. Ewald, M. Felder, and G. Schlingloff, *Chem. Ber.*, 1992, **125**, 1169; K. Soai, S. Niwa, and T. Kobayashi, *J. Chem. Soc., Chem. Commun.*, 1987, 801; R. Seemayer and M. P. Scheneider, *Tetrahedron: Asymmetry*, 1992, **3**, 827; S. Cossu, S. Conti, G. Giacomelli, and M. Falorni, *Synthesis*, 1994, 1429.
5. H. Tsukube, S. Shinoda, J. Uenishi, T. Hiraoka, N. Kojima, and O. Yonemitsu, *J. Org. Chem.*, 1998, **63**, 3884; J. Uenishi, T. Ueno, S. Hata, K. Nishiwaki, T. Tanaka, S. Wakabayashi, and S. Oae, *Het-*

- erocycles*, 1999, **50**, 341; H. Tsukube, J. Uenishi, N. Kojima, and O. Yonemitsu, *Tetrahedron Lett.*, 1995, **36**, 2257.
6. J. Uenishi, T. Hiraoka, S. Hata, K. Nishiwaki, O. Yonemitsu, K. Nakamura, and H. Tsukube, *J. Org. Chem.*, 1998, **63**, 2481; J. Uenishi, K. Nishiwaki, S. Hata, and K. Nakamura, *Tetrahedron Lett.*, 1994, **35**, 7973.
  7. J. Uenishi, T. Takagi, T. Ueno, T. Hiraoka, O. Yonemitsu, and H. Tsukube, *Synlett*, 1999, 41; J. Uenishi, T. Hiraoka, K. Yuyama, and O. Yonemitsu, *Heterocycles*, 2000, **52**, 719.
  8. S. Oae, T. Takeda, J. Uenishi, and S. Wakabayashi, *Phosphorus, Sulfur and Silicon*, 1996, **115**, 179; J. Uenishi, A. Yamamoto, T. Takeda, S. Wakabayashi, and S. Oae, *Heteroatom Chem.*, 1992, **3**, 73; S. Wakabayashi, Y. Kiyohara, S. Kameda, J. Uenishi, and S. Oae, *Heteroatom Chem.*, 1990, **1**, 225.
  9. S. Oae, *Croat. Chim. Acta*, 1986, **59**, 129; S. Oae, *Rev. Heteroatom Chem.*, 1988, **1**, 304; S. Oae and N. Furukawa, *Adv. Heterocyclic Chem.*, 1990, **48**, 1.
  10. J.-P. Finet, 'Ligand Coupling Reactions with Heteroatomic Compounds, Pergamon (An Imprint of Elsevier Science), Oxford, UK, 1998; S. Oae and Y. Uchida, *Acc. Chem. Res.*, 1991, **24**, 225.

Received, 31st May, 2000