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Studies on the Stereoselective Methylation of α-Sulfinyl Carbanions Generated from Three Isomeric Pyridylmethyl *p*-Tolyl Sulfoxides and Benzyl 2-Pyridyl Sulfoxide

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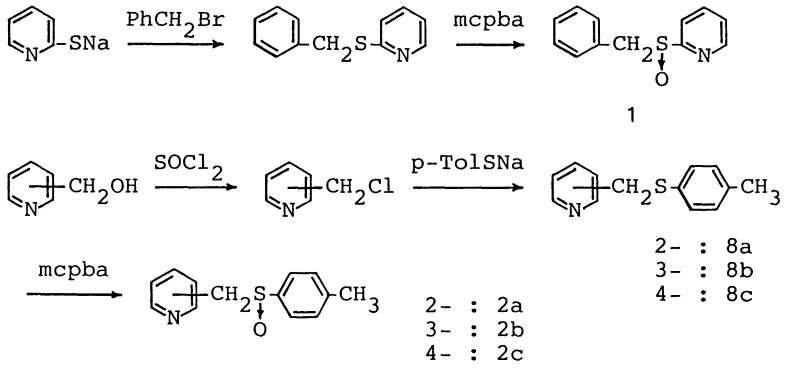
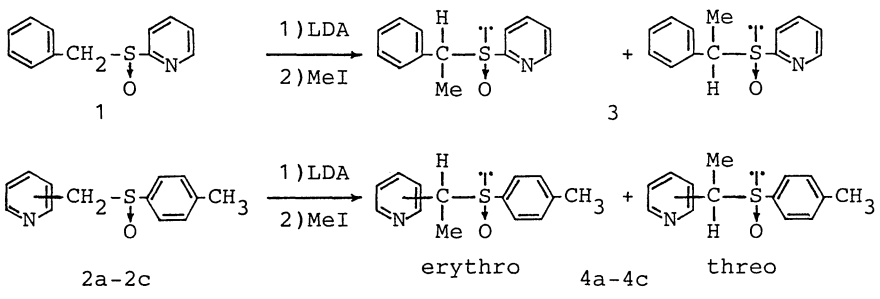
A high stereoselectivity in the methylation of 2-pyridylmethyl *p*-tolyl sulfoxide (**2a**) with lithium diisopropylamide and iodomethane was observed at low temperature. The chelation of Li^+ by both the nitrogen atom in the pyridine ring and the sulfinyl oxygen atom in **2a** promotes the stereoselectivity as compared with isomeric sulfoxides.

Numerous α-sulfinyl carbanions have been extensively studied for organic synthesis.[1] In general, α-methylene protons attached to the sulfinyl group are nonequivalent[2] and, thus, numerous α-sulfinyl carbanions obtained upon treatment with strong bases are diastereotopic and react with simple electrophiles providing two diastereoisomers in different ratios.[3] The sulfoxides bearing a suitable heteroaromatic ring, such as a pyridyl group, may promote the stereoselectivity of the α-carbanion upon treatment with electrophiles by chelating the metallic cation.[4] In order to determine the effect of heterocycles on the stereochemistry of α-sulfinyl carbanions, we prepared benzyl 2-pyridyl sulfoxide (**1**) and three isomeric pyridylmethyl *p*-tolyl sulfoxides (**2a—2c**). We first treated them with lithium diisopropylamide and then with iodomethane in tetrahydrofuran. This paper describes the results on the high stereoselectivity in the methylation of sulfoxide **2a**, as compared to other isomeric sulfoxides at low temperatures, and discusses the structure of the intermediary carbanion attached to the 2-pyridyl group.

Sulfoxides **1**, **2a—2c** were synthesized and their methylation performed by treatment with lithium diisopropylamide, and then with iodomethane, as shown in Schemes 1 and 2. After the usual work-up procedures, both erythro and threo methylated sulfoxides **3**, **4a—4c** were obtained, as shown in Table 1. The structures of the products were determined by ^1H NMR, IR, and elemental analysis. The ratios of the two isomers were determined by either isolation or by calculating the peak area of the methine quartet or methyl doublet protons by 500-MHz ^1H NMR. The results shown in Table 1 reveal the following characteristic points: (1) The four sulfoxides employed in the methylation resulted in the predominant forma-



Scheme 1.



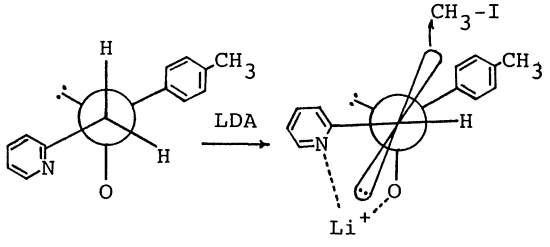
Scheme 2.

Table 1. Reaction of Sulfoxides with Iodomethane

Substrate	Temp/°C	Time/h	Yield/%	Diastereomer ratio (Erythro/Threo)
1	−78	3.0	24	2.4
1	0	3.0	45	1.9
2a	−85	5.0	40	13.0
2a	−78	1.2	89	10.0
2a	−78	3.5	87	9.5
2a	−76	3.0	46	2.3[a]
2a	−72	4.0	68	6.0[b]
2a	−53	3.5	94	4.1
2a	−33	2.5	79	3.1
2a	−22	2.5	88	2.1
2a	−15	2.5	71	1.5
2a	0	1.2	86	1.5
2b	−90	5.0	90	2.8
2b	−78	3.5	—	2.7
2b	−50	3.5	42	2.0
2b	−5	2.5	45	1.4
2c	−80	21.5	No reaction	
2c	−20	3.5	—	1.1

a) In the presence of 12-crown-4 (3.0 equiv). b) In the presence of HMPA (1.0 equiv).

tion of erythro isomers at temperatures as low as −78 °C. However, the selectivities depend on the position of the pyridyl group and the reaction temperature employed. Interestingly, 2-pyridyl derivative **2a** gave the highest stereoselectivity among other isomeric sulfoxides. Analogous methylation of benzyl *p*-tolyl sulfoxide also leads to the preferential formation of erythro isomers, even though the selectivity is 1.5 : 1 (erythro : threo).[5] The high stereoselectivity of **2a** can be rationally explained in terms of the formation of the carbanion generated from **2a** and lithium diisopropylamide in which the lithium cation is strongly chelated by the sulfinyl oxygen, carbanion carbon, and pyridyl nitrogen atoms. Therefore, iodomethane approaches to the carbanion from the opposite site of the chelated side, as shown in Scheme 3.[6] (2) The stereoselectivity of **2a** depends remarkably on the temperature. However, in the case of the reaction of **2b**, the stereoselectivity is rather insensitive to the temperature. This result seems to be consistent with the methylation of **1** or benzyl *p*-tolyl sulfoxide with iodomethane. Meanwhile, sulfoxide **2c** was found to react with iodomethane above −20 °C, though the stereoselectivity was nearly in 1 : 1. Thus, these results seem to indicate that the chelation of Li^+ by the 2-pyridyl group plays an important role in the stereoselectivity. The erythro-to-threo ratio of **2a** shown in Table 1 is reciprocally linearly correlated to the reaction temperature between −90 °C to 0 °C. Thus, the plot of log(threo/erythro) of **2a** against $1/T$ gave a straight line and $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values calculated by the Arrhenius equation of $-R T \ln K_T/K_E = \Delta\Delta H^{\ddagger} - T\Delta\Delta S^{\ddagger}$, where K_T/K_E is the ratio of threo vs. erythro isomers, giving $\Delta\Delta H^{\ddagger}$=11.23 kJ mol^{-1} and $\Delta\Delta S^{\ddagger}$=38.58 J K^{-1} mol^{-1}. On the other hand, the threo/erythro ratio obtained from the reaction of **2b** also gave a linear relationship against $1/T$ to provide $\Delta\Delta H^{\ddagger}$=3.47 kJ mol^{-1} and $\Delta\Delta S^{\ddagger}$=9.96 J K^{-1} mol^{-1}, respectively. These results clearly indicate that the methylation reactions of carbanions derived from **2a** and **2b** proceed via a similar mechanistic process with the erythro preference. However, the stereoselectivity of **2a** depends more on the temperature than that of **2b**. These observations reflect the large differences in the activation parameters, the $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values, of **2a** and **2b** (as described above). These large differences of the $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values between sulfoxides **2a** and **2b** in the methylation reactions suggest that the carbanion once formed from **2a** should be more rigid than that of **2b**, since the Li^+ of **2a** would be strongly chelated at low temperature by both the sulfinyl oxygen and the pyridyl nitrogen atoms, as shown in Scheme 3. These chelated carbanions of **2a** energetically promote the preferential approach of iodomethane from the back side of the carbon atom chelated by Li^+, to form the erythro product **4a**, while the chelation of Li^+ may be weakened by elevating the temperature to reduce the attack of iodomethane from the erythro-side of the carbanion. On the other hand, the carbanion of **2b** has no such rigidness as does that of **2a**, since the pyridyl nitrogen atom is located far from the formation of chelation of the Li^+. Therefore, the carbanion of **2b** has no high stereoselectivity as does the benzyl *p*-tolyl sulfoxide. (3) The effect of

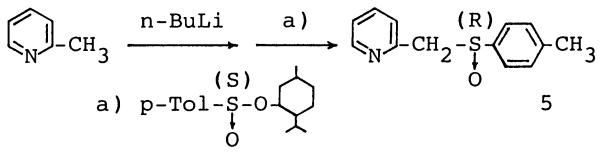


Scheme 3.

the chelation of Li^+ on the reaction was also supported by an experiment carried out in the presence of 12-crown-4 or hexamethylphosphoric triamide. That the isomeric ratio in **2a** decreased down to 2.3 : 1, even at −76 °C, is ascribed to the removal of Li^+ from the chelation site by the crown ether.

In order to confirm the stereochemical process and the absolute configuration of the starting sulfoxide **2a** and the two isomeric products, optically active 2-pyridylmethyl *p*-tolyl sulfoxide (**5**) was prepared according to the Andersen's process starting from *l*-menthyl *p*-toluenesulfinate and 2-pyridylmethyl lithium, as shown in Scheme 4. Optically pure sulfoxide **5** was obtained in 90% yield. The absolute configuration of the sulfoxide **5** was determined by X-ray crystallographic analysis to have an *R* configuration.[7] (*R*)-Sulfoxide **5** was allowed to react with lithium diisopropylamide and iodomethane at −74 °C in a similar manner to that of racemic **2a** to give a mixture of optically active erythro and threo isomers in a total yield of 91%, from which erythro isomer **6** was separated by recrystallization, mp 92—93 °C, $[\alpha]_D^{25}$=+239.7° (*c* 0.70, $CHCl_3$). The configuration of the methylated carbon of erythro isomer **6** was determined from the following chemical procedures. Initially, the optically active erythro isomer **6** was reduced to the corresponding sulfide **7a** with lithium aluminium hydride in ether at 0 °C in 43% yield after purification, $[\alpha]_D^{25}$=+122.2° (*c* 0.70, $CHCl_3$). The optically active sulfide **7b** of known configuration was prepared by the following procedures, as shown in Scheme 5, where the configuration of 1-(2-pyridyl)-ethanol has been determined previously.[8] Since the optical rotation of the sulfide **7a**, thus obtained, shows a positive sign, which coincides with that of the (*R*)-sulfide prepared authentically, as shown in Scheme 5, the absolute configuration of the optically active sulfoxide **6** is determined to be C_RS_R. Therefore, these stereochemical experiments clearly supported the view that the methylation of sulfinyl carbanion of **2a** predominantly gives the erythro isomer **4a**, the configuration of which was tentatively determined by ^1H NMR chemical shifts.

The present investigations indicate that the nitrogen atom located at the γ-position with regard to the sulfinyl group plays an important role in promoting the stereoselectivity of the carbanions with electrophiles.



Scheme 4.

Experimental

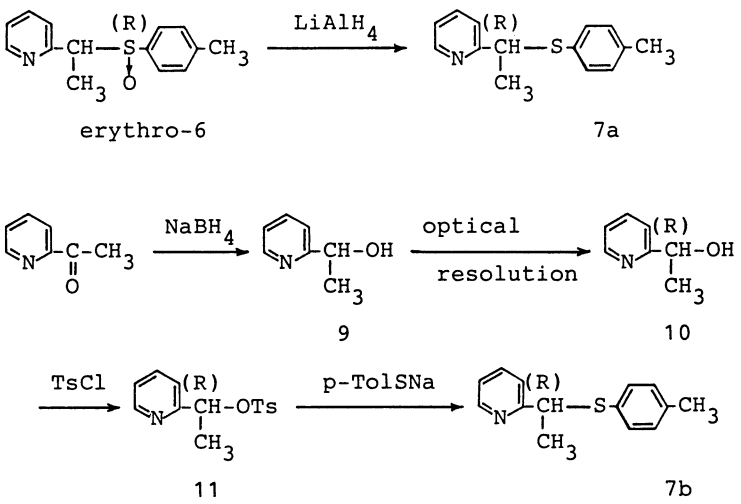
All melting points were uncorrected. IR spectra were recorded on JASCO A-3 spectrometer. ^1H NMR spectra were obtained with Hitachi R-600 or Bruker AM-500. Preparative liquid chromatography was performed on a Japan Analytical Co., Ltd., Model LC-09. All reactions were monitored by thin-layer chromatography (TLC) [Merck Kieselgel 60 F_{254}]. Silica gel used for column chromatography was Wako-gel C-200. Elemental analyses were carried out by Chemical Analysis Center at this University.

All reagents were obtained from Wako Pure Chemical Industries Ltd., Tokyo Kasei Co., Ltd., or Aldrich Chemical Co. The reaction solvents were further purified by general methods.

Benzyl 2-pyridyl sulfoxide (**1**) was prepared according to the known method as shown in Scheme 1.[9] Mp 89—91 °C; ^1H NMR ($CDCl_3$) δ=8.52—8.73 (m, 1H, 6-PyH), 6.83—7.95 (m, 8H, 3,4,5-PyH, ArH), 4.07, 4.37 (ABq, *J*=8 Hz, 2H, CH_2); IR(KBr) 1050 cm^{-1}.

Synthesis of the Sulfoxides. Sulfoxides **2a—2c** and optically active sulfoxide **5** were synthesized by general methods, as illustrated in Schemes 1[10] and 4.[11]

2-Pyridylmethyl *p*-Tolyl Sulfoxide (2a). To a stirred solution of sodium (0.644 g, 28.0 mmol) in ethanol (50 mL) at 0 °C was added dropwise a solution of *p*-toluenethiol (3.41



Scheme 5.

g, 27.5 mmol) in ethanol (50 mL). To this mixture was added dropwise 2-pyridylmethyl chloride (3.51 g, 27.5 mmol); the solution was stirred for 4 h at room temperature. The mixture was then filtrated while removing the solvent under reduced pressure. To the residue was added 50 mL of water; it was then extracted with dichloromethane (3×50 mL). The extracts were dried with anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel; eluent, $CHCl_3$) to give 2-pyridyl *p*-tolyl sulfide (**8a**) in 98% yield as colorless liquid: ^{1}H NMR ($CDCl_3$) δ=8.38—8.62 (m, 1H, 6-PyH), 6.88—7.75 (m, 7H, 3,4,5-PyH, ArH), 4.21 (m, 2H, CH_2), 2.28 (s, 3H, CH_3). To a stirred solution of the sulfide **8a** (5.40 g, 25.1 mmol) in dichloromethane (120 mL) at 0 °C was added *m*-chloroperbenzoic acid (mcpba) (4.75 g, 27.5 mmol) in dichloromethane (200 mL). The mixture was stirred at 0 °C for 1.5 h and treated with anhydrous ammonia. The resulting solid was separated by filtration and the filtrate was evaporated under reduced pressure to afford crude sulfoxide, which was purified by column chromatography (silica gel; eluent, $CHCl_3$) to give sulfoxide **2a** in 74% yield. Recrystallization from benzene gave colorless crystals: mp 93—94 °C; ^{1}H NMR ($CDCl_3$) δ=8.54—8.55 (m, 1H, 6-PyH), 7.18—7.65 (m, 7H, 3,4,5-PyH, ArH), 4.15, 4.22 (ABq, J=13 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3); IR(KBr) 1050 cm^{-1}; Calcd for $C_{13}H_{13}ONS$: C, 67.50; H, 5.78; N, 6.06%. Found: C, 67.67; H, 5.78; N, 5.97%.

3-Pyridylmethyl *p*-Tolyl Sulfoxide (2b). 3-Pyridylmethyl *p*-tolyl sulfide (**8b**) was prepared by the same procedure as **8a**. **8b**: colorless liquid; ^{1}H NMR ($CDCl_3$) δ=8.27—8.48 (m, 2H, 2,6-PyH), 6.87—7.65 (m, 6H, 4,5-PyH, ArH), 4.00 (s, 2H, CH_2), 2.29 (s, 3H, CH_3). To a stirred solution of sulfide **8b** (727 mg, 3.38 mmol) in dichloromethane (15 mL) at 0 °C was added mcpba (640 mg, 3.71 mmol) in dichloromethane (15 mL). After a work-up, sulfoxide **2b** was obtained in 65% yield. Recrystallization from benzene/hexane gave colorless crystals: mp 94—95 °C; ^{1}H NMR($CDCl_3$) δ=8.51—8.53 (m, 1H, 6-PyH), 8.03—8.04 (m, 1H, 2-PyH), 7.21—7.42 (m, 6H, 4,5-PyH, ArH), 3.92, 4.06 (ABq, J=13 Hz, 2H, CH_2), 2.39 (s, 3H, CH_3); IR(KBr) 1035 cm^{-1}; Calcd for $C_{13}H_{13}ONS$: C, 67.50; H, 5.67; N, 6.06%. Found: C, 67.60; H, 5.73; N, 6.07%.

4-Pyridylmethyl *p*-Tolyl Sulfoxide (2c). Similarly, sulfoxide **2c** was obtained in 78% yield. Mp 165—166 °C; ^{1}H NMR ($CDCl_3$) δ=8.48 (d, J=5 Hz, 2H, 2,6-PyH), 7.23—7.27 (m, 4H, ArH), 6.89 (d, J=5 Hz, 2H, 3,5-PyH) 3.93, 4.02 (ABq, J=13 Hz, CH_2), 2.40 (s, 3H, CH_3); IR(KBr) 1040 cm^{-1}; Calcd for $C_{13}H_{13}ONS$: C, 67.50; H, 5.67; N, 6.06%. Found: C, 67.56; H, 5.75; N, 6.03%.

(*R*)-(+)-2-Pyridylmethyl *p*-Tolyl Sulfoxide (5). To a stirred solution of 2-methylpyridine (188 mg, 2.02 mmol) in tetrahydrofuran (THF) (1 mL) at −20 °C was added 1.6 M BuLi (1M=1 mol dm^{-3}) in hexane solution (1.26 mL, 2.02 mmol). The mixture was stirred at room temperature and then cooled to −72 °C. The mixture was then added dropwise to (*S*)-(+)-*l*-menthyl *p*-toluenesulfinate (594 mg, 2.20 mmol) in THF (5 mL) with stirring at −72 °C for 2 h. After hydrolysis and neutralization with 1M HCl, the mixture was extracted with dichloromethane (3×20 mL). The extract was dried with anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel; eluent, $CHCl_3/CH_3CO_2C_2H_5$=1/2) to give sulfoxide **5** in 90% yield. Recrystallization from benzene/hexane gave colorless crystals: mp 104—105 °C; ^{1}H NMR($CDCl_3$) δ=8.54—8.55 (m, 1H, 6-PyH), 7.18—7.65 (m, 3,4,5-PyH, ArH), 4.15, 4.22 (ABq, J=13 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3); IR(KBr) 1050 cm^{-1}; $[\alpha]_D^{25}$=+253.8° (*c* 1.0, $CHCl_3$); Calcd for $C_{13}H_{13}ONS$: C, 67.50; H, 5.66; N, 6.05%. Found: C, 67.52; H, 5.67; N, 5.94%.

Reaction of Sulfoxides with Iodomethane. In a typical run, to a stirred solution of 2-pyridylmethyl *p*-tolyl sulfoxide (**2a**) (150 mg, 0.648 mmol) in THF (7.5 mL) was added a solution of lithium diisopropylamide (LDA) (0.859 mmol) in THF (2.5 mL) under an Ar atmosphere at −78 °C for 0.5 h. To the mixture was added iodomethane (0.2 mL, 3.21 mmol) and the solution was stirred at −78 °C for 1.2 h. After hydrolysis and extraction with dichloromethane (3×30 mL), the extract was dried with anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel; eluent, $CHCl_3/CH_3CO_2C_2H_5$=1/2) to give diastereomeric mixture of 1-(2-pyridyl)-1-(*p*-tolylsulfinyl)ethane (**4a**) in 89% yield. The ratio of isomers **4a** was determined by calculating the peak area of the methine quartet or methyl doublet protons by 500-MHz ^{1}H NMR in $CDCl_3$. The results are summarized in Table 1 and chemical shifts were as follows. **4a**: erythro; δ=8.48—8.50 (m, 1H, 6-PyH), 7.05—7.65 (m, 7H, PyH, ArH), 4.18 (q, J=7 Hz, 1H, CH), 2.37 (s, 3H, Ar-CH_3), 1.55 (d, J=7 Hz, 3H, CH_3). threo; δ=8.53—8.54 (m, 1H, 6-PyH), 7.05—7.65 (m, 7H, 3,4,5-PyH, ArH), 3.99 (q, J=7 Hz, 1H, CH), 2.37 (s, 3H, Ar-CH_3), 1.67 (d, J=7 Hz, 3H, CH_3). **4b:** erythro; δ=8.48—8.49 (m, 1H, 6-PyH), 7.91—7.92 (m, 1H, 2-PyH), 6.83—7.47 (m, 6H, 4,5-PyH, ArH), 3.84 (q, J=7 Hz, 1H, CH), 2.35 (s, 3H, Ar-CH_3), 1.72 (d, J=7 Hz, 3H, CH_3). threo; δ=8.52—8.53 (m, 1H, 6-PyH), 8.13—8.14 (m, 1H, 2-PyH), 6.83—7.47 (m, 6H, 4,5-PyH, ArH), 3.87 (q, J=7 Hz, 1H, CH), 2.38 (s, 3H, Ar-CH_3), 1.65 (d, J=7 Hz, 3H, CH_3). **4c:** erythro; δ=8.45 (d, J=5 Hz, 2H, 2,6-PyH), 7.03—7.27 (m, 4H, ArH), 6.86 (d, J=5 Hz, 2H, 3,5-PyH), 3.81 (q, J=7 Hz, 1H, CH), 2.36 (s, 3H, Ar-CH_3), 1.66 (d, J=7 Hz, 3H, CH_3). threo; δ=8.49 (d, J=5 Hz, 2H, 2,6-PyH), 7.03—7.27(m, 4H, ArH), 6.93 (d, J=5 Hz, 2H, 3,5-PyH), 3.84 (q, J=7 Hz, 1H, CH), 2.37 (s, 3H, Ar-CH_3), 1.63 (d, J=7 Hz, 3H, CH_3).

Absolute Configuration of Optically Active 1-(2-Pyridylmethyl)-1-(*p*-tolylsulfinyl)ethane (6). The absolute configuration of methylated sulfoxide **6** was determined by the following procedure.

Reaction of Optically Active (*R*)-(+)-2-Pyridylmethyl *p*-Tolyl Sulfoxide (5) with Iodomethane. Optically active sulfoxide **5** (500 mg, 2.16 mmol) in THF (25 mL) was treated similarly as **2a** with LDA (2.88 mmol) in THF (2.5 mL), and then with iodomethane (2.8 mL, 44.98 mmol) at −74 °C for 4 h. The reaction mixture was treated with water (20 mL) and extracted with dichloromethane (3×50 mL). After column chromatographic purification (silica gel; eluent, $CHCl_3/CH_3CO_2C_2H_5$=1/2) optically active 1-(2-pyridyl)-1-(*p*-tolylsulfinyl)ethane (**6**) was obtained in 91% yield. The diastereomeric mixture was separated by recrystallization with diisopropyl ether: erythro (main diastereomer): mp 92—93 °C, ^{1}H NMR ($CDCl_3$) δ=8.48—8.50 (m, 1H, 6-PyH), 7.05—7.65 (m, 7H, 3,4,5-PyH, ArH), 4.18 (q, J=7 Hz, 1H, CH), 2.37 (s, 3H, Ar-CH_3), 1.55 (3H, d, J=7 Hz, CH_3). Calcd for $C_{14}H_{15}ONS$: C, 68.53; H, 6.16; N, 5.70%. Found: C, 68.44; H, 6.22; N, 5.67%. $[\alpha]_D^{25}$=+239.7° (*c* 0.7, $CHCl_3$). The enantiomeric excess of the sulfoxide was determined by

^{1}H NMR with Eu(tfc) as a shift reagent to be about 100%. threo: colorless liquid; ^{1}H NMR($CDCl_3$) δ=8.53—8.54 (m, 1H, 6-PyH), 7.05—7.65 (m, 7H, 3,4,5-PyH, ArH), 3.99 (q, J=7 Hz, 1H, CH), 2.37 (s, 3H, Ar-CH_3), 1.67 (d, J=7 Hz, CH_3).

Reduction of *erythro*-6. To a stirred solution of erythro **6** (90 mg, 0.37 mmol) in ether (8 mL) at 0 °C was added lithium alminium hydride (20 mg, 0.53 mmol). The reaction mixture was stirred at 0 °C for 3 h and treated with aqueous ammonia. The resulting solid was separated by filtration and the filtrate was extracted with dichloromethane (3×20 mL). The extract was washed with water (2×50 mL) and dried with anhydrous magnesium sulfate. The solvent was then evaporated under reduced pressure. The residue was purified by preparative liquid chromatography to give 1-(2-pyridyl)-1-(*p*-tolylthio)ethane (**7a**) in 43% yield: colorless liquid; ^{1}H NMR($CDCl_3$) δ=8.38—8.58 (m, 1H, 6-PyH), 6.82—7.73 (m, 7H, 3,4,5-PyH, ArH), 4.44 (q, J=7 Hz, 1H, CH), 2.38 (s, 3H, Ar-CH_3), 1.66 (d, J=7 Hz, 3H, CH_3); $[\alpha]_D^{25}$=+122.2° (*c* 0.7, $CHCl_3$).

Synthesis of Optically Active (*R*)-(+)-1-(2-Pyridyl)-1-(*p*-tolylthio)ethane (7b). 1-(2-Pyridyl)ethanol (**9**) was obtained in 68% yield from the reduction of 2-acetylpyridine with sodium borohydride; bp 103—104 °C/17mmHg (lit,[8] 95 °C/10mmHg; 1 mmHg≈133.322 Pa). A hot solution of **9** (3.3 g, 26.8 mmol) and (2*R*,3*R*)-2,3-*O*-dibenzoyltartaric acid (9.6 g, 26.8 mmol) in ethanol (20 mL) was allowed to slowly cool to room temperature. The resulting crystalline product was recrystallized three times (mp 146—147 °C) with ethanol and treated with aqueous sodium hydroxide to give (*S*)-(−)-1-(2-pyridyl)ethanol (**10**) in 17% yield: $[\alpha]_D^{25}$=−43.1° (*c* 1.9, EtOH); ee=76%.[8] To a stirred solution of **10** (500 mg, 4.06 mmol) in pyridine (20 mL) at 0 °C was added *p*-toluenesulfonyl chloride (775 mg, 4.07 mmol). The mixture was stirred at 0 °C for 6 h and treated with ice-water (40 mL). The mixture was extracted with ether (3×50 mL). The extracts were dried with anhydrous magnesium sulfate and the solvent was evaporated under reduced pressure to afford the corresponding crude tosylate **11**. To a stirred solution of sodium (103 mg, 4.48 mmol) in ethanol (100 mL) was added *p*-toluenethiol (504 mg, 4.06 mmol). The mixture was stirred at room temperature for 10 min; to this was added crude **11**. The mixture was stirred at room temperature for 6 h and filtrated. The filtrate was treated with aqueous sodium hydroxide and extracted with dichloromethane (3×100 mL). The extracts were dried with magnesium sulfate and evaporated under reduced pressure. The residue was purified by column chromatography (silica gel; eluent, $CHCl_3$) to give (*R*)-(+)-1-(2-pyridyl)-1-(*p*-tolylthio)ethane (**7b**) in 11% yield as colorless liquid: ^{1}H NMR ($CDCl_3$) δ=8.38—8.57 (m, 1H, 6-PyH), 6.85—7.73 (m, 7H, 3,4,5-PyH, ArH), 4.43 (q, J=7 Hz, 1H, CH), 2.28 (s, 3H, Ar-CH_3), 1.66 (d, J=7 Hz, 3H, CH_3); $[\alpha]_D^{25}$=+101.5° (*c* 2.1, $CHCl_3$).

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