A Catalytic Enantioselective Access to Optically Active 2-Imidazoline from *N*-Sulfonylimines and Isocyanoacetates

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Optically active 2-imidazolines are not only widespread in natural products but are also useful intermediates for the synthesis of biologically active molecules.[1] Chiral 2-imidazolines as versatile chiral building blocks, chiral auxiliaries, and chiral ligands have attracted considerable recent interest.[2] Especially, chiral 2,3-diamino acids, which could be easily obtained from chiral 2-imidazolines, are a constituent of several antibiotics as well as other biologically active compounds.[3] The general approaches to optically active 2-imidazoline usually started from chiral amino acids or optically active 1,2-diamines. These methods included the use of a stoichiometric amount of chiral reagents or chiral starting materals.[4] Recently, a catalytic stereoselective synthesis of 2-imidazoline has been reported. The Ru(II)-catalyzed aldol reaction of isocyanoacetate with *N*-sulfonylimines gave t*rans*-2-imidazolines stereoselectively,[5] whereas an Au(I) complex catalyzed analogous reaction afforded *cis*-2-imidazoline as the major product.[6] However, to the best of our knowledge, a catalytic enantioselective access to optically active 2-imidazoline by a similar approach has not been reported. Here, we wish to describe an efficient asymmetric synthesis from *N*-sulfonylimines with isocyanoacetate to give optically active 2-imidazolines in high yields and moderate to high ee values (Scheme 1).

In recent years, chemists have shown great interest in using chiral ferrocenes as ligands of transition metal complexes in asymmetric catalysis, and successful results have been obtained in several asymmetric reactions.[7] In 1986, Hayashi and Ito[8a] et al. reported an elegant asymmetric synthesis of oxazoline by using a gold(I) complex catalyzed aldol reaction in the presence of chiral ferrocenylphosphine ligands. The reaction of methyl isocyanoacetate (**5b**) with aldehydes catalyzed by bis(cyclohexyl isocyanide)gold(I) tetrafluoroborate (**3**) and chiral ferrocenylphosphine (**2**) showed high enantioselectivity with enantiomeric excesses as high as 97−99%. To probe the ability of the gold(I) catalyst (**3**) with chiral ferrocene ligand (**2**) to induce the enantioselectivity in a similar reaction, we examined the reaction of imine under identical conditions. On treatment of methyl isocyanoacetate (**5b**) with *N*-tosyl-*p*-chlorobenzaldimine (**4a**) in the presence of **3** and **2**, the ee values of *cis*- and *trans*-2-imidazoline (67:33) obtained were only 14% and 25%, respectively. Interestingly, when the neutral gold(I) complex Me_2SAuCl (**1**) with chiral ferrocenylphosphine (**2**) was used as catalyst, the asymmetric induction of this reaction of **5b** with **4a** could be brought to good levels.

A typical procedure is illustrated by the synthesis of **6b** (Scheme 1). The catalytic system was prepared in situ by mixing Me_2SAuCl (**1**) and chiral ferrocenylphosphine (**2**) together. A mixture of **4b** and **5a** (1:1) was allowed to react in the presence of 0.5 mol % catalyst in CH_2Cl_2 at 25 °C for 20 h to afford 2-imidazoline in quantitative yield after simple treatment. A 96:4 ratio of *cis*/*trans* isomers was obtained on the basis of the ^1H NMR spectrum of the crude product (**6b**), and the enantiomeric excess of the *cis*- and *trans*-2-imidazolines was determined to be 74% and 26%, respectively, by HPLC analysis. The initial ee value of 74% for *cis*-**6b** could be easily raised to 99% by a single recrystallization from THF/*n*-hexane. The optically pure *cis*-2-imidazoline (**6b**) was converted to **7b** by hydrolysis. The absolute configuration of **7b** was determined to be 2*R*,3*R* by X-ray crystallography as shown in ref 9. Thus, the absolute configuration of *cis*-**6b** was assigned as (4*R*,5*R*)-4-(ethoxycarbonyl)-5-*p*-bromophenyl)-1-*N*-tosyl-2-imidazoline.

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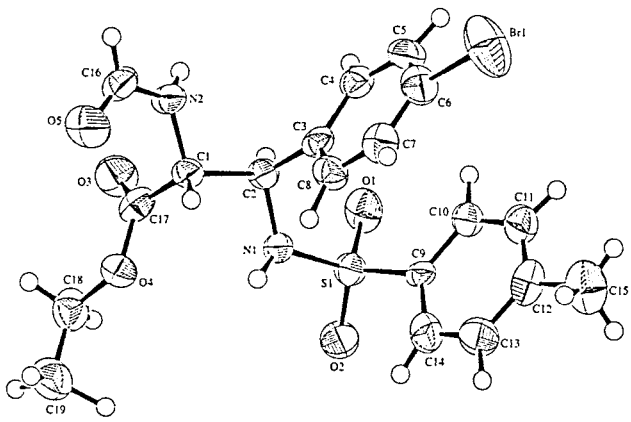
(9) Single-crystal X-ray structure of **7b**:



10.1021/jo980949s CCC: $18.00
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Scheme 1

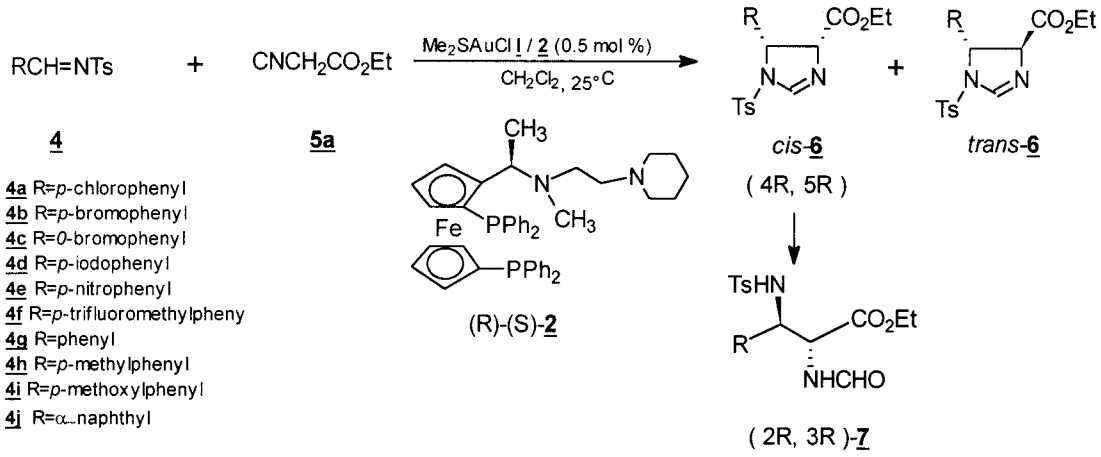

Table 1. Reaction of *N*-Sulfonylimines 4 with Ethyl Isocyanoacetate 5a Catalyzed by Chiral Ferrocenylphosphine (2)−Me_2SAuCl Complex[a]

no.	R	time (h)	ratio[b] of *cis*/*trans*	*cis*-**6** (%)[c]	*cis*-**6** (% ee)[d] (confign)	*trans*-**6** (% ee)[d]
1	*p*-ClPh	24	>96:4	91	60 (4*R*,5*R*)	
2	*p*-BrPh	20	>96:4	90	74 (4*R*,5*R*)	26
3	*0*−BrPh	20	85:15	76	72 (4*R*,5*R*)	25
4	*p*-IPh	20	96:4	86	88 (4*R*,5*R*)	
5	*p*-NO_2Ph	24	94:6	84	62 (4*R*,5*R*)	27
6	*p*-CF_3Ph	20	90:10	82	46 (4*R*,5*R*)	
7	Ph	24	92:8	85	61 (4*R*,5*R*)	32
8	*p*-CH_3Ph	34	96:4	88	47 (4*R*,5*R*)	15
9	*p*-CH_3OPh	48	96:4	89	58 (4*R*,5*R*)	
10	α-naphthyl	48	92:8	79	58 (4*R*,5*R*)	28

[a] The reaction was carried out in CH_2Cl_2 at 25 °C for 20−48 h. **4**/**5**/catalyst = 1/1/0.005. [b] Determined by ^{1}H NMR analysis before isolations. [c] Isolated yields. [d] Determined by HPLC analysis using a chiral OD or AD column.

We found that the enantioselectivity was not affected by the electronic property of the substituents on phenyl ring of imine. For example, although *p*-CF_3 group is a stronger withdrawing group than *p*-CH_3 group (Table 1, entries 6 and 8), the ee values of **6f** and **6g** are almost the same. However, as we can see from Table 1, the same reaction of *N*-tosyl *p*-Cl-, *p*-Br-, and *p*-I-benzaldimine gave ee values of 60, 74, and 88%, respectively. It appears that the larger substituent in the phenyl group gives a higher enantioselectivity. On the other hand, the alkyl group R in the ester group (-COOR, R = Me (**5b**), Et (**5a**), *i*-Pr (**5c**)) on the isocyanoacetate could also affect both *trans*/*cis* selectivity and enantioselectivity of the products. In the case of the reaction of **4a** with **5b**, **5a**, and **5c**, *cis*/*trans* ratios of 91:9, >96:4, and 93:7 were given respectively with the corresponding ee values of 49%, 60%, and 66%. The better results were obtained in the use of **5a** or **5c** with imine (**4**) in the present conditions.

We have shown that gold complexes **1** and **3** gave different enantioselectivity in the reaction with imines by using the same chiral ferrocenyl ligand (**2**). The results listed in Table 2 indicated that **1** and **3** behave differently in reactions with aldehyde and imine. For the reaction with aldehyde, the combination of **3** and **2** gave better results than that of **1** and **2**, showing higher stereoselectivity and higher ee values with shorter reaction time. For instance, the reaction of **5b** with *p*-chlorobenzaldehyde provided *trans*-2-oxazoline with an ee value of 94% ([α] = +274°, lit.[8b] +273°) in 24 h (entry 1). When Me_2-SAuCl (**1**) was used instead of **3**, we found that the ee value of *trans*-2-oxazoline decreased to 83% with the longer reaction time (entry 4). On the contrary, for the reactions with imines, **1** and **2** are a better combination than that of **3** and **2**. The ee values of *cis*-2-imidazoline were obviously increased from 14% and 37% (entries 2 and 3) to 49% and 74% (entries 5 and 6), respectively.

In general, the isocyanide is a stronger coordinating ligand with gold(I) than thioether. Thioether is supposed to be displaced by phosphine ligands more easily in the present reactions. However, we also found that the neutral gold(I) complex AuCl(c-HexNC) with ligand **2** shows an enantioselectivity as good as the **1** + **2** system for the reaction of **4a** and **5a** (*cis*-**6a**: $[\alpha]^{20}_D$ −175°). Togni and Pastor[10] reported a crystal structure of neutral gold(I)−chiral aminoferrocenylphosphine and suggested that there were a similar transition state structure in the stereoselective step in the presence of neutral and cationic gold(I) complexes for the aldol reaction of aldehydes. However, the changes in the enantioselectivity listed in Table 2 cannot be explained using the same transition state. We also noticed that a different chemical shift in ^{31}P NMR spectrum were observed in the two catalytic systems. Up to now, we cannot rationalize the above result in a reasonable explanation.

In summary, a catalytic enantioselective reaction of *N*-sulfonylimines with isocyanoacetates has been achieved by using chiral Me_2SAuCl−ferrocenylphophine catalyst. The mildness of the reaction conditions, the simplicity of the procedure, and rather high ee values, from which a optically pure *cis*-2-imidazoline could be easily obtained by a single recrystallization, will offer a convenient and efficient method for the synthesis of the optically pure 2, 3-diamino acids and other useful optically active derivatives. Further investigation is now in progress.

Experimental Section

Materials and General Methods. ^{1}H NMR spectra were recorded in $CDCl_3$ at 300 MHz. All *N*-sulfonylimines **4**,[11] isocyanoacetates **5**,[12] and Au(I) complexes[13] were prepared according to literature methods. Ferrocenylphosphine **2** was prepared according to the reported procedure.[8b,14] THF and *n*-hexane were refluxed with sodium and then freshly distilled.

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Table 2. Reaction of *p*-Cl-benzaldehyde and *N*-Sulfonylimine with Isocyanoacetate 5 Catalyzed by Au(I) Complexes 1 and 3[a]

no.	substrate	Au(I) complex	time (h)	ratio[b] of *cis*/*trans*	product (ee %)[c]
1	*p*-ClPhCHO/$CNCH_2CO_2Me$ (**5b**)	**3**	24	5/95	*trans*-2-oxazoline (94)
2	*p*-ClPhCH=NTs (**4a**)/**5b**	**3**	55	67/33	*cis*-2-imidazoline (14) *trans*-2-imidazoline (25)
3	*p*-BrPhCH=NTs (**4b**)/$CNCH_2CO_2Et$ (**5a**)	**3**	55	90/10	*cis*-2-imidazoline (37)
4	*p*-ClPhCHO/**5b**	**1**	50	17/83	*trans*-2-oxazoline (83)
5	*p*-ClPhCH=NTs (**4a**)/**5b**	**1**	24	88/12	*cis*-2-imidazoline (49)
6	*p*-BrPhCH=NTs (**4b**)/**5a**	**1**	20	96/4	*cis*-2-imidazoline (74)

[a] The reaction was carried out in CH_2Cl_2 at 25 °C. [b] Determined by ^1H NMR analysis before isolations. [c] Determined by HPLC analysis using a chiral OD column.

Dichloromethane was distilled immediately prior to use from CaH_2 under nitrogen. All melting points are uncorrected.

General Procedure for the Me_2SAuCl−Ferrocenylphosphine Catalyzed Reaction of *N*-Sulfonylimines (4) with Ethyl Isocyanoacetate (5a). A mixture of Me_2SAuCl (**1**, 1.2 mg, 0.004 mmol) and chiral ligand (**2**, 2.4 mg, 0.0033 mmol) in 4 mL of CH_2Cl_2 was stirred for 15 min, and then to the resultant solution were added sequentially 195 mg of **4a** (0.66 mmol) and 75−80 mg of **5a** (0.66−0.70 mmol). The reaction mixture was stirred under nitrogen at 25 °C for 20−24 h until **4a** was not detected by silica TLC. After removal of the catalyst by filtration, the solvent was removed under vacuum to give a crude *trans*/*cis* mixture of 2-imidazoline, which was isolated by preparative TLC (petroleum ether (60−90 °C):ethyl acetate:dichloromethame = 4:2:1) to give *cis*-(4*R*,5*R*)-2-imidazoline (**6a**). The enantiomeric excess of *cis*-**6a** was determined by HPLC analysis, and the *cis*/*trans* ratio was determined by using ^1H NMR spectra of the crude product. The chemical yield of *cis*/*trans*-2-imidazoline was nearly quantitative. The yields of *cis*-2-imidazolines are listed in Table 1.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-(4-chlorophenyl)-1-*N*-tosyl-2-imidazoline (*cis*-6a): 91% yield; $[\alpha]^{20}_D$ −182° (*c* 1.00, THF 60% ee (determined by HPLC analysis using a CHIRALCEL OD column: 25 cm × 0.46 cm i.d.; eluent, 15% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (+)-**6a** t_R = 19.667 min, (−)-**6a** t_R = 26.320 min). The optically pure *cis*-2-imidazoline was obtained from the filtrate by recrystallization in THF/*n*-hexane in 40% yield and 99% ee: mp 139.5−140 °C; $[\alpha]^{20}_D$ −298° (*c* 1.00, THF); ^1H NMR ($CDCl_3$/TMS) δ 0.80 (t, 3 H), 2.39 (s, 3 H), 3.54−3.77 (m, 2 H), 5.11 (d, *J* = 11.28 Hz, 1 H), 5.18 (d, *J* = 11.28 Hz, 1 H), 6.92 (d, *J* = 8.32 Hz, 2 H), 7.05 (d, *J* = 8.32 Hz, 2 H), 7.12 (d, *J* = 8.06 Hz, 2 H), 7.38 (d, *J* = 8.06 Hz, 2 H), 7.75 (s, 1H); IR 1750 cm^{-1}, 1610 cm^{-1}; MS *m*/*z* 406 (M^+ + 1, 4), 333 (13), 251 (100), 178 (3), 155 (30), 91 (74). Anal. Calcd for $C_{19}H_{19}ClN_2O_4S$: C, 56.08; H, 4.70; N, 6.88. Found: C, 56.24; H, 4.74; N, 6.69.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-(4-bromophenyl)-1-*N*-tosyl-2-imidazoline (*cis*-6b): 90% yield; $[\alpha]^{20}_D$ −192° (*c* 1.01, THF); 74% ee (determined by HPLC analysis using a CHIRALCEL OD column: 25 cm × 0.46 cm i.d.; eluent, 20% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (+)-**6b** t_R = 24.390 min, (−)-**6b** t_R = 30.177 min). The optically pure *cis*-2-imidazoline was obtained from the filtrate by the recrystallization in THF/*n*-hexane in 37% yield and 99% ee: mp 143.5−144 °C; $[\alpha]^{20}_D$ −259° (*c* 1.00, THF); ^1H NMR ($CDCl_3$/TMS) δ 0.82 (t, 3 H), 2.41 (s, 3 H), 3.59−3.77 (m, 2 H), 5.11 (d, *J* = 11.35 Hz, 1 H), 5.18 (d, *J* = 11.35 Hz, 1 H), 6.87 (d, *J* = 8.39 Hz, 2 H), 7.16 (d, *J* = 8.21 Hz, 2 H), 7.21 (d, *J* = 8.39 Hz, 2 H), 7.39 (d, *J* = 8.21 Hz, 2 H), 7.75 (s, 1H); IR 1751 cm^{-1}, 1610 cm^{-1}; MS *m*/*z* 451 (M^+, 20), 378 (5), 155 (24), 91 (64). Anal. Calcd for $C_{19}H_{19}BrN_2O_4S$: C, 50.56; H, 4.24; N, 6.20. Found: C, 50.38; H, 4.18; N, 6.04.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-(2-bromophenyl)-1-*N*-tosyl-2-imidazoline (*cis*-6c): 76% yield; mp 128−130 °C; $[\alpha]^{20}_D$ −298° (*c* 1.05, THF); 72% ee (determined by HPLC analysis using a CHIRALCEL OD column: 25 cm × 0.46 cm i.d.; eluent, 20% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (−)-**6c** t_R = 16.860 min, (+)-**6c** t_R = 21.387); ^1H NMR ($CDCl_3$/TMS) δ 0.82 (t, 3 H), 2.43 (s, 3 H), 3.47−3.55 (m, 1 H), 3.65−3.71 (m, 1H), 5.18 (dd, *J* = 11.35, 1.82 Hz, 1 H), 5.47 (d, *J* = 11.35 Hz, 1 H), 7.09−7.21 (m, 3 H), 7.28 (d, *J* = 8.30 Hz, 2 H), 7.48−7.51 (m, 1H), 7.60 (d, = 8.06 Hz, 2 H), 7.79 (d, *J* = 1.77 Hz, 1H); IR 1751 cm^{-1}, 1610 cm^{-1}; MS *m*/*z* 451 (M^+, 8), 378 (5), 155 (28), 91 (63). Anal. Calcd for $C_{19}H_{19}BrN_2O_4S$: C, 50.56; H, 4.24; N, 6.20. Found: C, 50.29; H, 4.16; N, 6.02.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-(4-iodophenyl)-1-*N*-tosyl-2-imidazoline (*cis*-6d): 86% yield; mp 130−131.5 °C; $[\alpha]^{20}_D$ −207° (*c* 1.00, THF); 88% ee (determined by HPLC analysis using a CHIRALCEL OD column: 25 cm × 0.46 cm i.d.; eluent, 20% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (+)-**6d** t_R = 20.513 min, (−)-**6d** t_R = 27.100); ^1H NMR ($CDCl_3$/TMS) δ 0.81 (t, 3 H), 2.43 (s, 3 H), 3.63−3.74 (m, 2 H), 5.10 (d, *J* = 11.12 Hz, 1 H),5.20 (d, *J* = 11.12 Hz, 1 H), 6.73 (d, *J* = 8.10 Hz, 2 H), 7.15 (d, *J* = 8.10 Hz, 2 H), 7.37−7.42 (m, 4 H), 7.77 (s, 1H); IR 1751 cm^{-1}, 1610 cm^{-1}; MS *m*/*z* 498 (M^+ + 1, 8), 425 (7), 342 (100), 270 (2), 155 (18). Anal. Calcd for $C_{19}H_{19}IN_2O_4S$: C, 45.79; H, 3.84; N, 5.62. Found: C, 45.77; H, 3.59; N, 5.36.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-(4-nitrophenyl)-1-*N*-tosyl-2-imidazoline (*cis*-6e): 84% yield; mp 118−120 °C; $[\alpha]^{20}_D$ −233° (*c* 1.00, THF); 62% ee (determined by HPLC analysis using a CHIRALPKA AD column: 25 cm × 0.46 cm i.d.; eluent, 40% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (−)-**6e** t_R = 38.963 min, (+)-**6e** t_R = 53.017); ^1H NMR ($CDCl_3$/TMS) δ 0.82 (t, 3 H), 2.41 (s, 3 H), 3.52−3.60 (m, 1 H), 3.70−3.78 (m, 1H), 5.17 (d, *J* = 11.59 Hz, 1 H), 5.25 (d, *J* = 11.59 Hz, 1 H), 7.17−7.27 (m, 4 H), 7.47 (d, *J* = 8.12 Hz, 2 H), 7.79 (s, 1 H), 8.01 (d, *J* = 8.51 Hz, 2 H); IR 1738 cm^{-1}, 1628 cm^{-1}; MS *m*/*z* 417 (M^+ + 1, 26), 344 (18), 262 (88), 155 (65), 91 (100). Anal. Calcd for $C_{19}H_{19}N_3O_6S$: C, 54.67; H, 4.58; N, 10.07. Found: C, 54.53; H, 4.61; N, 10.04.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-(4-trifluoromethylphenyl)-1-*N*-tosyl-2-imidazoline (*cis*-6f): 82% yield; mp 130−132 °C; $[\alpha]^{20}_D$ −149° (*c* 1.00, THF); 46% ee (determined by HPLC analysis using a CHIRALCEL OD column: 25 cm × 0.46 cm i.d.; eluent, 20% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (+)-**6f** t_R = 16.080 min, (−)-**6f** t_R = 21.720); ^1H NMR ($CDCl_3$/TMS) δ 0.76 (t, 3 H), 2.37 (s, 3 H), 3.54−3.60 (m, 1 H), 3.67−3.73 (m, 1H), 5.24 (s, 2 H), 7.09−7.16 (m, 4 H), 7.32−7.41 (m, 4H), 7.79 (s, 1H); IR 1752 cm^{-1}, 1610 cm^{-1}; MS *m*/*z* 440 (M^+ + 1, 42), 367 (18), 285 (100), 212 (2), 155 (53), 91 (97). Anal. Calcd for $C_{20}H_{19}F_3N_2O_4S$: C, 54.54; H, 4.34; N, 6.36. Found: C, 54.26; H, 4.12; N, 6.57.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-phenyl-1-*N*-tosyl-2-imidazoline (*cis*-6g): 85% yield; mp 152−154 °C; $[\alpha]^{20}_D$ −175° (*c* 1.02, THF); 61% ee (determined by HPLC analysis using a CHIRALPAK AD column: 25 cm × 0.46 cm i.d.; eluent, 20% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (−)-**6g** t_R = 22.513 min, (+)-**6g** t_R = 35.180); ^1H NMR ($CDCl_3$/TMS) δ 0.75 (t, 3 H), 2.37 (s, 3 H), 3.49−3.55 (m, 1 H), 3.65−3.68 (m, 1 H), 5.17 (s, 2 H), 7.00 (d, *J* = 7.10 Hz, 2 H), 7.07−7.18 (m, 5 H), 7.40 (d, *J* = 8.19 Hz, 2 H), 7.76 (s, 1 H); IR 1749 cm^{-1}, 1614 cm^{-1}; MS *m*/*z* 372 (M^+ + 1, 21), 299 (18), 217 (100), 155 (28), 91 (78). Anal. Calcd for $C_{19}H_{20}N_2O_4S$: C, 61.27; H, 5.41; N, 7.52. Found: C, 61.09; H, 5.59; N, 7.32.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-(4-methylphenyl)-1-*N*-tosyl-2-imidazoline (*cis*-6h): 88% yield; mp 130−132 °C; $[\alpha]^{20}_D$ −160° (*c* 1.00, THF); 47% ee (determined by HPLC analysis using a CHIRALCEL OD column: 25 cm × 0.46 cm i.d.; eluent, 20% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (+)-**6h** t_R = 15.610 min, (−)-**6h** t_R = 21.730); ^1H NMR ($CDCl_3$/TMS) δ 0.78 (t, 3 H),

(14) (a) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, N.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M.; Yamamoto, K.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138. (b) Hayashi, T.; Yamazaki, A. *J. Organomet. Chem.* **1991**, *413*, 295.

2.25 (s, 3 H), 2.38 (s, 3 H), 3.58−3.69 (m, 2 H), 5.14 (s, 2 H), 6.89 (s, 4 H), 7.12 (d, J = 8.07 Hz, 2 H), 7.05 (d, J = 8.07 Hz, 2 H), 7.75 (s, 1 H); IR 1753 cm^{-1}, 1609 cm^{-1}; MS m/z 386 ($M^+ + 1$, 42), 313 (11), 231 (100), 155 (20), 91 (63). Anal. Calcd for $C_{20}H_{22}N_2O_4S$: C, 62.15; H, 5.73; N, 7.25. Found: C, 62.06; H, 5.62; N, 7.15.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-(4-methoxylphenyl)-1-*N*-tosyl-2-imidazoline (*cis*-6i): 89% yield; mp 119−120 °C; $[\alpha]^{20}_D$ −170° (*c* 1.00, THF); 58% ee (determined by HPLC analysis using a CHIRALCEL OD column: 25 cm × 0.46 cm i.d.; eluent, 20% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (+)-**6i** t_R = 21.567 min, (−)-**6i** t_R = 28.007); ^{1}H NMR ($CDCl_3$/TMS) δ 0.75 (t, 3 H), 2.33 (s, 3 H), 3.49−3.57 (m, 1 H), 3.62−3.73 (m, 1 H), 3.68 (s, 3 H), 5.10 (s, 2 H), 6.55 (d, J = 8.57 Hz, 2 H), 6.86 (d, J = 8.57 Hz, 2 H), 7.08 (d, J = 8.20 Hz, 2 H), 7.34 (d, J = 8.20 Hz, 2 H), 7.70 (s, 1H); IR 1730 cm^{-1}, 1611 cm^{-1}; MS m/z 402 ($M^+ + 1$, 4), 329 (8), 247 (95), 174 (6), 155 (9), 91 (49). Anal. Calcd for $C_{20}H_{22}N_2O_5S$: C, 59.68; H, 5.51; N, 6.96. Found: C, 59.60; H, 5.54; N, 6.63.

(4*R*,5*R*)-*cis*-4-(Ethoxycarbonyl)-5-(α-naphthyl)-1-*N*-tosyl-2-imidazoline (*cis*-6j): 79% yield; mp 151−153 °C; $[\alpha]^{20}_D$ −227° (*c* 1.00, THF); 58% ee (determined by HPLC analysis using a CHIRALCEL OD column: 25 cm × 0.46 cm i.d.; eluent, 10% *i*-PrOH in hexane; flow rate, 0.7 mL/min, (−)-**6j** t_R = 41.050 min, (+)-**6j** t_R = 47.157); ^{1}H NMR ($CDCl_3$/TMS) δ 0.21 (t, 3 H), 2.39 (s, 3 H), 3.02−3.10 (m, 1 H), 3.34−3.49 (m, 1H), 5.39 (d, J = 11.43 Hz, 1 H), 5.96 (d, J = 11.43 Hz, 1 H), 7.18−7.93 (m, 12H); IR 1738 cm^{-1}, 1630 cm^{-1}; MS m/z 422 ($M^+ + 1$, 10), 349 (7), 267 (100), 194 (15), 155 (16), 91 (34). Anal. Calcd for $C_{23}H_{22}N_2O_4S$: C, 65.38; H, 5.25; N, 6.63. Found: C, 65.06; H, 5.41; N, 6.63.

Typical Procedure for the Gram Scale: 5.8 mg (0.019 mmol) of **1** and 12.1 mg (0.016 mmol) of **2** in 15 mL of CH_2Cl_2 were stirred for 15 min, and then to the mixture were added 980 mg of **4a** (3.34 mmol) and 388 mg of **5a** (3.43 mmol). The mixture was stirred under nitrogen at 25 °C for 24 h until **4a** was not detected by silica TLC. Removal of the catalyst by filtration through silica and evaporation of the solvent under vacuum gave a *cis*/*trans* mixture (90:10) of 2-imidazoline quantitatively. The *cis* isomer was isolated by column chromatography over silica gel eluting with petroleum ether (60−90 °C)−ethyl acetate−dichloromethame (4:2:1) to give 60% ee of *cis*-(4*R*,5*R*)-2-imidazoline **6a** (1.12 g) in 82% yield, $[\alpha]^{20}_D$ −185° (*c* 1.005, THF). The optically pure *cis*-**6a** (99% ee) was obtained in 39% yield from the filtrate by the recrystallization in THF/hexane (12 mL/24 mL): mp 139−139.5 °C; $[\alpha]^{20}_D$ −311° (*c* 1.05, THF).

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Supporting Information Available: X-ray structural analysis of **7b**. This material is available free of charge via the Internet at http://acs.org.

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