Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 62 (2006) 9237–9246

Highly enantioselective hydrogenation of exocyclic double bond of *N*-tosyloxazolidinones catalyzed by a neutral rhodium complex and its synthetic applications

Zengming Shen, Xiyan Lu* and Aiwen Lei

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

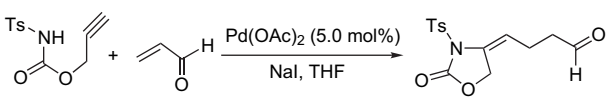
Received 15 May 2006; revised 6 July 2006; accepted 7 July 2006
Available online 7 August 2006

Abstract—A highly enantioselective synthesis of optically active *N*-tosyl-4-alkyl-1,3-oxazolidin-2-ones based on the asymmetric hydrogenation of the trisubstituted exocyclic double bond of *N*-tosyl-4-alkylidene-1,3-oxazolidin-2-ones under the catalysis of neutral $[Rh(COD)Cl]_2$ (COD=1,5-cyclooctadiene) and (*S*)-(+)-DTBM-SEGPHOS was developed. The utility of this highly enantioselective reaction was exemplified by the synthesis of optically active amino acids, amino alcohols, and piperidine derivatives.

1. Introduction

Amino acids,[1] amino alcohols,[2] and piperidine derivatives[3] are compounds of immense interest in nature and importance for the pharmaceutical industry. In addition to their biological importance, they are widely used as catalysts or chiral ligands in many organic or transition-metal catalyzed transformations.[2–5] Thus to develop a synthetic method of experimental simplicity and high generality for these amino acids, amino alcohols, and piperidine derivatives is a challenge for organic chemists.

In our previous work, *N*-tosyloxazolidinones with a trisubstituted exocyclic double bond were conveniently synthesized under the catalysis of the Pd(II) species (Scheme 1).[6] The asymmetric hydrogenation of the trisubstituted exocyclic double bond will afford homochiral *N*-tosyl-4-alkyl-1,3-oxazolidin-2-ones, which can be used as the intermediates for the synthesis of homochiral amino acids, amino alcohols, and piperidine derivatives.



Scheme 1. Synthesis of *N*-tosyl-4-alkylidene-1,3-oxazolidin-2-ones.

However, the asymmetric hydrogenation of the trisubstituted exocyclic double bond of *N*-tosyl-4-alkylidene-1,3-oxazolidin-2-ones has not been reported in the literatures.[7–11] Dixneuf reported the enantioselective hydrogenation of *N*-acyl-4-methylene-1,3-oxazolidin-2-ones catalyzed by a chiral BINAP–Ru complex with 99% ee,[10] but the exocyclic double bond in their substrates is disubstituted, not trisubstituted, and the substituent on the nitrogen atom is an acyl group rather than a tosyl group. Herein, we wish to report the enantioselective hydrogenation of the trisubstituted exocyclic double bond of *N*-tosyloxazolidinones to the optically active *N*-tosyl-4-alkyl-1,3-oxazolidin-2-ones with high enantioselectivity and its application for synthesizing the optically active amino acids, amino alcohols, and piperidine derivatives.

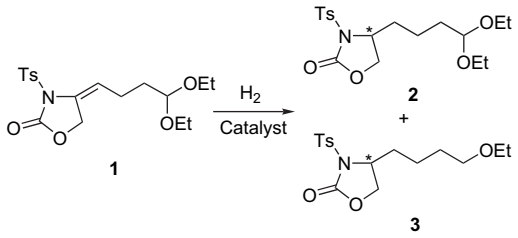
2. Results and discussion

Initially, *N*-tosyloxazolidinone (**1**) was used as the substrate for the asymmetric hydrogenation. Nearly no reaction occurred using chiral BINAP–Ru(II) complexes as the catalyst (Table 1, entries 1–3). Using the cationic $[Rh(COD)_2]OTf$ and (*S*)-BINAP as the catalyst, the hydrogenation of compound **1** only afforded unexpected product **3** (Table 1, entries 4 and 5) in which not only the exocyclic double bond was hydrogenated, but also the acetal group was transformed to an ether with the cleavage of one of the ethoxy groups. Similar phenomena were observed using the cationic $[Rh(COD)_2]BF_4$ and (*R*)-(−)-DTBM-SEGPHOS (Table 1, entry 11). This implied that the cationic Rh catalysts exhibited higher catalytic activities for hydrogenation, but gave

Keywords: Enantioselective hydrogenation; Exocyclic double bonds; *N*-Tosyloxazolidinones; Rhodium complex.
* Corresponding author. Tel.: +86 21 54925158; fax: +86 21 64166128; e-mail: xylu@mail.sioc.ac.cn

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.07.024

Table 1. Hydrogenation of *N*-tosyl-4-alkylidene-1,3-oxazolidin-2-ones catalyzed by different metal complexes[a]



Entry	Metal species	Solvent	Yield(%)[b]/ee(%)[c]	
			2	**3**
1[d]	[RuCl((*S*)-BINAP)(PhH)]Cl	EtOH	4/58	—
2[d]	$[NH_2Et_2][\{RuCl((S)\text{-BINAP})\}_2(\mu\text{-}Cl)_3]$	CH_2Cl_2	—	—
3[d]	$[NH_2Et_2][\{RuCl((S)\text{-BINAP})\}_2(\mu\text{-}Cl)_3]$	EtOH	—	—
4[e]	$[Rh(COD)_2]OTf$	CH_2Cl_2	—	35/20
5[e]	$[Rh(COD)_2]OTf$	Toluene	—	29/12
6[f]	$[Rh(COD)Cl]_2$	EtOH	47/16	—
7[f]	$[Rh(COD)Cl]_2$	CH_2Cl_2	40/43	—
8[g]	$[Rh(COD)Cl]_2$	CH_2Cl_2	90/43	—
9[g]	$[Rh(COD)Cl]_2$	Toluene	92/29	—
10[g]	$[Ir(COD)Cl]_2$	CH_2Cl_2	67/30	—
11[e]	$[Rh(COD)_2]BF_4$	CH_2Cl_2	—	40/5

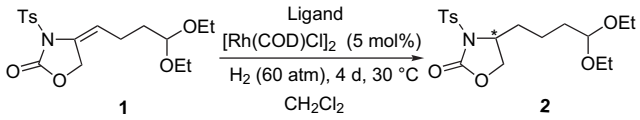
[a] Using (*S*)-BINAP (entries 4–10) and (*R*)-(−)-DTBM-SEGPHOS[13] (entry 11) as ligand.
[b] Isolated yield.
[c] ee values were determined by HPLC.
[d] Conditions: H_2 (100 atm), 50 °C, 2 days, substrate/catalyst=33/1 (entry 1), substrate/catalyst=50/1 (entries 2 and 3).
[e] Conditions: H_2 (60 atm), 30 °C, 4 days, substrate/catalysts/ligand=10/0.96/1.
[f] Conditions: H_2 (30 atm), 30 °C, 2.6 days, substrate/metal species/ligand=20/1/2.2.
[g] Conditions: H_2 (60 atm), 30 °C, 4 days, substrate/metal species/ligand=20/1/2.2.

low ee values.[12] Fortunately, the hydrogenation of compound **1** using the catalyst generated in situ from neutral $[Rh(COD)Cl]_2$ and (*S*)-BINAP gave the expected product **2** in medium yield (Table 1, entries 6 and 7). When the pressure of hydrogen was increased to 60 atm and the reaction time was prolonged to 4 days, the yield was increased to 90% in CH_2Cl_2 and 92% in toluene (Table 1, entries 8 and 9). The ee value was higher in CH_2Cl_2 (43% ee) (Table 1, entry 8). A similar result was obtained using the combination of neutral $[Ir(COD)Cl]_2$ and (*S*)-BINAP (Table 1, entry 10).

Different chiral ligands were tried for screening to improve the enantioselectivity of product **2** using $[Rh(COD)Cl]_2$ as the catalyst precursor under the typical conditions of H_2 (60 atm) at 30 °C in CH_2Cl_2 for 4 days. The use of (−)-DIOP,[14] (*S*,*S*)-BPPM,[15] (*R*, S_P)-**4**,[16] and (*S*)-**5**[17] as ligands gave low yields and ee values (Table 2, entries 1–4). Using (*R*)-tol-BINAP, (*S*)-H_8-BINAP,[18] and (*S*)-SEGPHOS[13] as ligands, the yields were excellent but with medium ee values (Table 2, entries 5–7). Fortunately, excellent enantioselectivity (93% ee) was observed for the combination of $[Rh(COD)Cl]_2$ and (*R*)-(−)-DTBM-SEGPHOS,[13] which exhibits higher steric hindrance and electron-rich properties, but the yield was still not satisfactory (Table 2, entry 8; Scheme 2).

Finally, nearly quantitative yield (99%) and high enantioselectivity (92% ee) were obtained when toluene was used

Table 2. Asymmetric hydrogenation of *N*-tosyloxazolidinone with different chiral ligands[a]



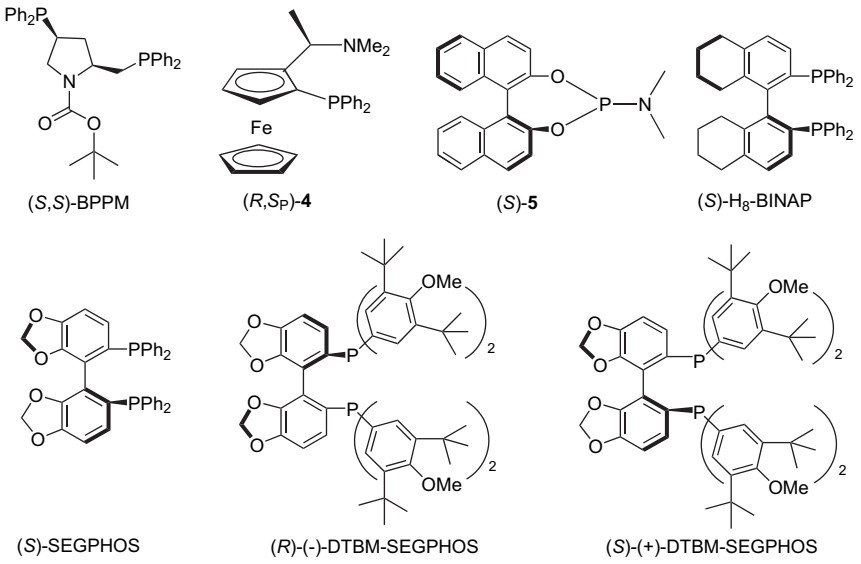
Entry	Ligand	Yield (%)[b]	ee (%)[c]
1	(−)-DIOP	47	7 (+)
2	(*S*,*S*)-BPPM	9	—
3	(*R*, S_P)-**4**	9	16 (−)
4[d]	(*S*)-**5**	Trace	—
5	(*R*)-Tol-BINAP	86	47 (−)
6[e]	(*S*)-H_8-BINAP	91	42 (+)
7[e]	(*S*)-SEGPHOS	99	53 (+)
8[e]	(*R*)-(−)-DTBM-SEGPHOS	52	93 (−)

[a] Reactions were carried out in dry and oxygen-free CH_2Cl_2 with substrate (0.013 M)/metal species/ligand=20/1/2.2 at 30 °C under 60 atm hydrogen pressure during 4 days.
[b] Isolated yield.
[c] ee values were determined by HPLC. The sign of optical rotation was shown in the parenthesis.
[d] Substrate (0.013 M)/metal species/ligand=20/1/4.2.
[e] Substrate (0.1 mmol, 0.026 M).

as the solvent instead of CH_2Cl_2 (Table 3, entry 1). When the amount of catalyst was decreased to 0.5 mol %, excellent enantioselectivity (97% ee) was achieved (Table 3, entry 2).

With this good result in hand, the asymmetric hydrogenation of different kinds of exocyclic double bonds was tried (Table 4). Most of the substrates gave high yield,[19] but the enantioselectivity of the reaction appeared relatively sensitive to the structure of the substrates. (1) Compounds **1** and **6a** gave the highest enantioselectivity. The terminal olefin in (*E*)-**6a** or the acetal group in **1** is possible to coordinate with the metal atom of the catalyst, making the asymmetric hydrogenation of (*E*)-**6a** and **1** more efficient (Table 3, entry 2; Table 4, entry 1). (2) The configuration of exocyclic double bond showed an important effect on the enantioselectivity of the asymmetric hydrogenation (Table 4, entries 1–3, compare (*E*)-**6a**, (*E*)-**6b**, and (*Z*)-**6c**). (3) The bulkiness of the neighboring group of the exocyclic double bond could also influence the enantioselectivity (Table 4, compare entries 4–6). *N*-Acyl-4-methylene-1,3-oxazolidin-2-one (**6f**) could be hydrogenated under our reaction conditions with excellent yield and satisfactory enantioselectivity (Table 4, entry 7).

The result of the high enantioselectivity of the hydrogenation of the exocyclic double bonds encouraged us to use the homochiral oxazolidinones as a synthon for synthesizing optically active compounds. Lysine is considered as an indispensable amino acid for growth of animals.[20] While several methods for synthesizing L-lysine have been reported,[21] a convenient method with high efficiency is still a challenge especially a method for the synthesis of both enantiomers by simply changing the configuration of the chiral ligand. Thus, natural lysine derivative was selected as the first target as shown in Scheme 3. According to our previous work,[6] 4-alkylidene-*N*-tosyloxazolidinone (**10**) can be selectively prepared from compound **9** and acrolein by a Pd(II) catalyzed reaction. Subsequent treatment of **10** with triethyl orthoformate in the presence of a catalytic amount of *p*-toluenesulfonic acid (PTSA) led to *N*-tosyloxazolidinone (**1**) in 88% yield. The enantioselective hydrogenation of



Scheme 2. Chiral ligands for asymmetric hydrogenation.

Table 3. Asymmetric hydrogenation of **1** leading to **2**[a]

Entry	[Rh(COD)Cl]$_2$ (mol %)	(*R*)-(−)-DTBM-SEGPHOS (mol %)	Yield (%)[b]	ee (%)[c]
1[d]	5	10	99	92
2[e]	0.5	1.0	100	97

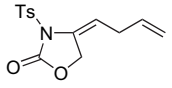
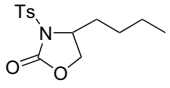
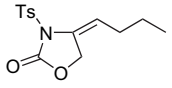
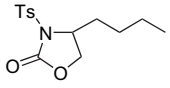
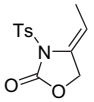
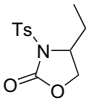
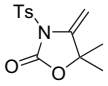
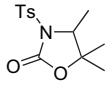
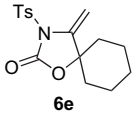
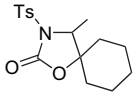
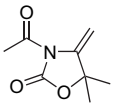
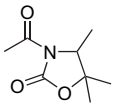
[a] Conditions: H_2 (60 atm), toluene, 30 °C, 4 days.
[b] Isolated yield.
[c] ee values were determined by HPLC.
[d] Substrate (0.1 mmol, 0.026 M).
[e] Substrate (14.4 mmol, 0.13 M).

compound **1**, using (*S*)-(+)-DTBM-SEGPHOS as ligand, gave chiral saturated *N*-tosyloxazolidinone (**2**) in quantitative yield with 97% ee. The lysine derivative **14** was finally achieved by further transformations. Compound **14** was characterized as the L-lysine derivative by comparison with the natural lysine derivative.[21d] The enantiomeric excess of compound **14** was measured by converting **14** to its methyl ester **15** (98% ee). The D-lysine derivative was also obtained by a similar route with 99% ee, when (*R*)-(−)-DTBM-SEGPHOS was used as the ligand in the hydrogenation reaction.

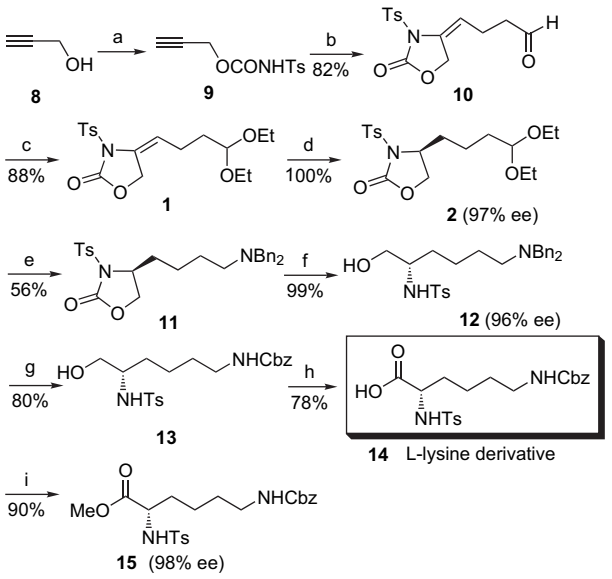
Similarly, the method was extended to the synthesis of natural L-norleucine derivative as shown in Scheme 4. The asymmetric hydrogenation of compound **6a** with (*S*)-(+)-DTBM-SEGPHOS as ligand was the key reaction and gave compound **7a** in quantitative yield with 99% ee. It was converted to the L-norleucine derivative **17** by further transformations. The absolute configuration and enantiomeric excess of compound **17** were determined by its methyl ester **18** (98% ee).[22]

The development of methods for the asymmetric synthesis of piperidines remains an area of considerable interest due to the presence of this heterocyclic ring in a large number of biologically important compounds.[3] Using chiral *N*-tosyloxazolidinone (**2**) (97% ee), the *N*-tosyl-L-pipecolic acid (**22**) and *N*-tosyl-(*R*)-α-pipecoline (**25**) could be easily synthesized as shown in Scheme 5. The absolute configuration and ee value of **22** were determined after esterification[23]

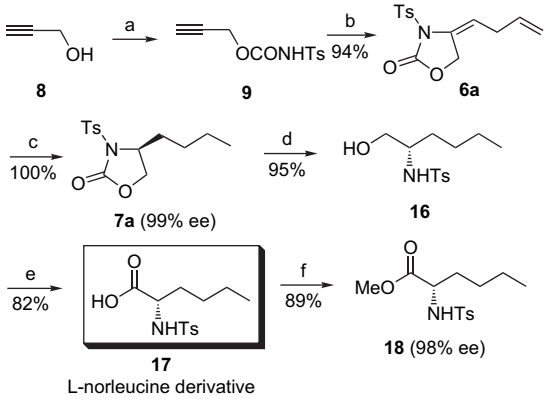
Table 4. Asymmetric hydrogenation of exocyclic double bonds[a]

Entry	Substrate	Product	Yield (%)[b]	ee (%)[c]
1	 **6a**	 **7a**	100	99 (+)
2	 **6b**	 **7a**	100	92 (+)
3	 **6c**	 **7c**	97	27 (−)
4	 **6d**	 **7d**	96	87 (−)
5	 **6e**	 **7e**	100	81 (−)
6	 **6f**	 **7f**	97	39 (+)
7	 **6g**	 **7g**	96	80 (−)

[a] Reaction conditions: substrate (0.26 mmol, 0.13 M), [Rh(COD)Cl]$_2$ (0.5 mol %), (*S*)-(+)-DTBM-SEGPHOS (1 mol %), H_2 (60 atm), toluene, 30 °C, 4 days.
[b] Isolated yield.
[c] ee values were determined by HPLC and the sign of optical rotation was shown in the parenthesis.



Scheme 3. Synthesis of natural L-lysine derivative **14**. (a) TsNCO, THF; (b) $Pd(OAc)_2$, LiBr, acrolein; (c) *p*-TsOH·H_2O, $HC(OEt)_3$; (d) $[Rh(COD)Cl]_2$ (0.5 mol %), (*S*)-(+)-DTBM-SEGPHOS (1 mol %), toluene, H_2 (60 atm), 30 °C, 4 days; (e) (i) THF/HCl (2 N) (3/1); (ii) Et_3N; (iii) Bn_2NH, $NaBH_3CN$; (f) LiOH·H_2O, THF/H_2O (3/1); (g) (i) $Pd(OH)_2$/C (20%), MeOH, H_2 (1 atm); (ii) Cbz-Cl, K_2CO_3, THF/H_2O; (h) Jones' reagent, acetone; (i) MeOH, *p*-TsOH (cat.), benzene, reflux.



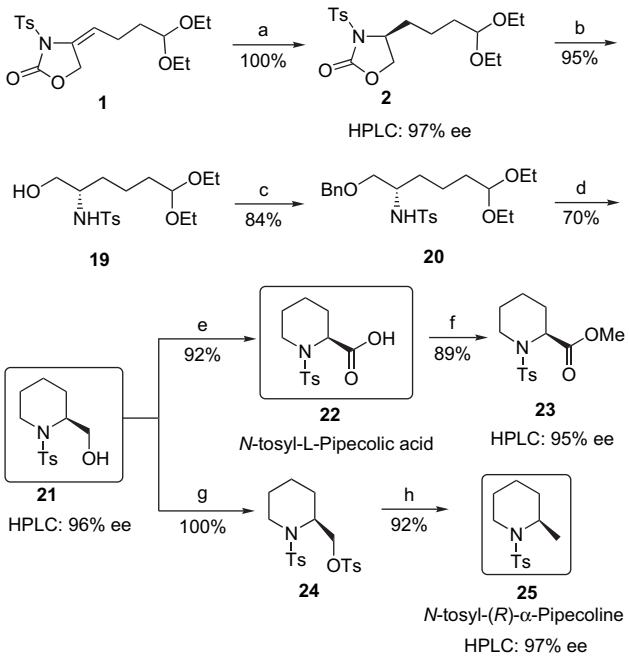
Scheme 4. Synthesis of natural L-norleucine derivative **17**. (a) TsNCO, THF; (b) $Pd(OAc)_2$, LiBr, Et_3N, 3-bromo-propene; (c) $[Rh(COD)Cl]_2$ (0.5 mol %), (*S*)-(+)-DTBM-SEGPHOS (1 mol %), toluene, H_2 (60 atm), 30 °C, 4 days; (d) LiOH·H_2O, THF/H_2O (3/1); (e) Jones' reagent, acetone; (f) MeOH, *p*-TsOH (cat.), benzene, reflux.

and the absolute configuration of **25** (97% ee) was determined by comparison with the literature.[24]

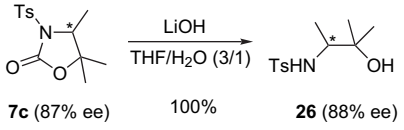
Homochiral oxazolidinones could be also converted to homochiral *N*-tosylamino alcohols in quantitative yield with retention of configuration by hydrolysis under basic condition, for example, **12**, **16**, **19**, and **26** (Scheme 6), which could be used as chiral ligands or their precursors.[2,5]

3. Conclusion

The asymmetric hydrogenation of the trisubstituted or disubstituted exocyclic double bond of *N*-tosyloxazolidinones was achieved under the catalysis of neutral $[Rh(COD)Cl]_2$ and (*S*)-(+)-DTBM-SEGPHOS with nearly quantitative yield and high enantioselectivity. This method provided a novel way to prepare chiral *N*-tosyloxazolidinones with high enantiomeric excess. The advantage and the utility of this reaction were exemplified by the synthesis of the amino acids, amino alcohols, and piperidine derivatives.



Scheme 5. Synthesis of natural piperidine derivatives. (a) $[Rh(COD)Cl]_2$ (0.5 mol %), (*S*)-(+)-DTBM-SEGPHOS (1 mol %), toluene, H_2 (60 atm), 30 °C, 4 days; (b) LiOH·H_2O, THF/H_2O (3/1); (c) NaH, BnBr, THF, −40 °C to 0 °C; (d) (i) *p*-TsOH, MeOH; (ii) Pd/C (10%), H_2 (1 atm), EtOH, rt; (e) Jones' reagent, acetone; (f) MeOH, *p*-TsOH (cat.), benzene, reflux; (g) TsCl, Et_3N, DMAP (cat.), CH_2Cl_2, rt; (h) $LiAlH_4$, Et_2O, reflux.



Scheme 6. Synthesis of *N*-tosylamino alcohols.

4. Experimental

4.1. General

NMR spectra were recorded on a Varian Mercury Vx 300 spectrometer. Infrared spectra were obtained on a Bio-Rad FTS-185 machine. Mass spectra were recorded on Agilent 5973 or Agilent 1100 machine. The optical rotation was measured on a Perkin–Elmer 341 polarimeter and the enantiomeric excesses were determined after separation of the enantiomers by HPLC on a Perkin–Elmer (785A, 200 IC Pump) or Waters (515 Pump, 2487 λ Dual Absorbance Detector) instrument. Elemental analyses were carried out on Elementar Vario EL instruments. All solvents were dried and distilled before use according to the standard methods. All melting points were uncorrected.

4.2. Synthesis of *N*-tosyl-4-alkylidene-1,3-oxazolidin-2-ones

4.2.1. (*E*)-*N*-Tosyl-4-(4′,4′-diethoxybutylidene)-1,3-oxazolidin-2-one (1). To a solution of **10**[6] (3.26 g, 20 mmol) in ethanol (70 mL) was added triethyl orthoformate (3 g, 20 mmol). The mixture was stirred over night in the presence of a catalytic amount of *p*-toluenesulfonic acid (274 mg, 1.4 mmol) at room temperature. After addition of saturated $NaHCO_3$ solution (30 mL), the reaction mixture was extracted with ethyl acetate (3×30 mL). The combined organic extracts were dried (anhydrous sodium sulfate), filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=6/1 (v/v)) to give white solid **1** in 88% yield, mp 76–77 °C (recrystallization from petroleum ether/dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (t, J=7.2 Hz, 6H), 1.74–1.78 (m, 2H), 1.97–1.99 (m, 2H), 2.46 (s, 3H), 3.42–3.59 (m, 2H), 3.59–3.69 (m, 2H), 4.47 (t, J=5.4 Hz, 1H), 4.81–4.82 (m, 2H), 5.93 (tt, J=8.1, 3.0 Hz, 1H), 7.36 (d, J=7.8 Hz, 2H), 7.93 (d, J=7.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.24, 21.66, 22.11, 32.66, 61.06, 65.65, 101.57, 106.79, 127.96, 127.99, 129.79, 134.25, 146.01, 151.90; IR (KBr): ν 2970, 2929, 1805, 1789, 1694, 1598, 1368, 1166, 1062 cm^{-1}; EIMS *m*/*z*: 337 ([M−OEt]$^+$), 266, 228, 182, 155, 154, 138, 129, 103, 91, 85. Anal. Calcd for $C_{18}H_{25}NO_6S$: C, 56.38; H, 6.57; N, 3.65. Found: C, 56.17; H, 6.68; N, 3.47.

4.2.2. (*E*)-*N*-Tosyl-4-(but-3′-enylidene)-1,3-oxazolidin-2-one (6a). To a solution of *p*-toluenesulfonyl isocyanate (3.1 mL, 20.4 mmol) in THF (255 mL) was added propargyl alcohol (1 mL, 17 mmol) under nitrogen. After the mixture was stirred for 1 h at room temperature, triethylamine (2.35 mL, 17 mmol) was added to the mixture. A solution of allyl bromide (14.7 mL, 170 mmol), LiBr (3.0 g, 34 mol), and $Pd(OAc)_2$ (5 mol %, 190.4 mg) in THF (85 mL) was added to the mixture over 4 h at room temperature and stirred at the same temperature for additional 4.5 h. The solvent was evaporated and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=4/1 (v/v)) to give white solid **6a** in 94% yield, mp 84–86 °C (recrystallization from petroleum ether/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 2.67 (dd, J=6.9, 6.9 Hz, 2H), 4.79 (s, 2H), 5.05 (d, J=13.5 Hz, 2H), 5.72–5.85 (m, 1H), 5.97–6.04 (m, 1H), 7.35 (d, J=8.1 Hz, 2H), 7.93 (d, J=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 30.6, 65.5, 104.6, 115.8, 128.0, 129.0, 129.8, 134.2, 134.4, 146.1, 151.8; IR (KBr): ν 2900, 1805, 1790, 1693, 1596, 1383, 1354, 1194, 1181, 1063, 678, 543 cm^{-1}; ESIMS *m*/*z*: 294 (M+H$^+$), 311 (M+NH$_4^+$). HRMS Calcd for $C_{14}H_{15}NO_4S$: 293.0722. Found: 293.0714.

4.2.3. (*E*)-*N*-Tosyl-4-butylidene-1,3-oxazolidin-2-one (6b). To a solution of **6a** (500 mg, 1.7 mmol) in EtOH (87 mL) was added Pd/C (5%, 32 mg). The mixture was stirred under H_2 (1 atm) for 3 h at room temperature. The solvent was evaporated and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=50/1 to 20/1 (v/v)) to give white solid **6b** in 59% yield, mp 84–85 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, J=7.5 Hz, 3H), 1.41–1.53 (m, 2H), 1.84–1.92 (m, 2H), 2.46 (s, 3H), 4.78–4.80 (m, 2H), 5.90–5.97 (m, 1H), 7.36 (d, J=8.7 Hz, 2H), 7.93 (d, J=8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 21.7, 22.4, 28.9, 65.7, 107.8, 127.6, 128.0, 129.8, 134.3, 146.0, 152.0; IR (KBr): ν 2964, 1803, 1679, 1594, 1366, 1180 cm^{-1}; ESIMS *m*/*z*: 296 (M+H$^+$). HRMS Calcd for [$C_{14}H_{17}NO_4S$+Na$^+$]: 318.0776. Found: 318.0766.

4.2.4. Compounds 6c,[25] 6d,[25] 6e,[26] 6f,[25] and 6g.[10a] The above compounds were synthesized according to the literature procedure.

4.3. Typical procedure for the enantioselective hydrogenation of exocyclic double bonds of oxazolidinones

4.3.1. (*S*)-*N*-Tosyl-4-(4′,4′-diethoxybutyl)-1,3-oxazolidin-2-one (2). In a nitrogen-filled glove box, $[Rh(COD)Cl]_2$[27] (0.5 mol %, 1.3 mg) and (*S*)-(+)-DTBM-SEGPHOS[13] (1 mol %, 6.1 mg) dissolved in dry and oxygen-free toluene (4 mL) were stirred for 30 min at room temperature in a glass tube. Compound **1** (200 mg, 0.52 mmol) was added to the mixture. The glass tube was transferred to a stainless steel autoclave in the glove box. After the autoclave was displaced with hydrogen three times, it was pressurized with hydrogen (60 atm) and stirred at 30 °C for 4 days. The solvent was evaporated and the residue was purified by means of column chromatography over silica gel (petroleum ether/ethyl acetate=6/1 to 4/1 (v/v)) to give colorless oil (*S*)-**2** in 100% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, J=7.2 Hz, 3H), 1.20 (t, J=7.0 Hz, 3H), 1.22–1.45 (m, 2H), 1.51–1.72 (m, 2H), 1.75–1.90 (m, 1H), 1.90–2.07 (m, 1H), 2.45 (s, 3H), 3.40–3.57 (m, 2H), 3.57–3.70 (m, 2H), 4.08 (dd, J=9.0, 3.3 Hz, 1H), 4.37–5.00 (m, 3H), 7.35 (d, J=8.1 Hz, 2H), 7.95 (d, J=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.2, 18.7, 21.6, 33.0, 33.3, 57.0, 61.2, 61.4, 67.3, 102.3, 128.2, 129.6, 134.9, 145.4, 152.1; IR (film): ν 2976, 2875, 1785, 1597, 1372, 1173, 666 cm^{-1}; EIMS *m*/*z*: 385 (M$^+$), 340, 184, 155, 140, 103, 91, 85, 75, 47. HRMS Calcd for $C_{16}H_{22}NO_5S$ ([M−OEt]$^+$): 340.1288. Found: 340.1240; HPLC analysis: 97% ee (DAICEL CHIRALCEL AD-H, eluent, hexane/2-propanol=90/10, flow rate 0.6 mL min^{-1}, detection 225 nm light), t_R of major-isomer 20.86 min and that of minor-isomer 27.88 min; $[\alpha]_D^{20}$ +44.5 (*c* 1.12, $CHCl_3$).

4.3.2. *N*-Tosyl-4-(4′-ethoxybutyl)-1,3-oxazolidin-2-one (3). Oil (yield: 40%) (Table 1, entry 11). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, J=7.2 Hz, 3H), 1.23–1.46 (m, 2H), 1.47–1.68 (m, 2H), 1.75–1.89 (m, 1H), 1.90–2.05 (m, 1H), 2.45 (s, 3H), 3.35–3.40 (m, 2H), 3.45 (q, J=7.2 Hz, 2H), 4.08 (dd, J=8.7, 3.3 Hz, 1H), 4.37 (dd, J=8.4, 8.4 Hz, 1H), 4.44–4.52 (m, 1H), 7.35 (d, J=8.4 Hz, 2H), 7.95 (d, J=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.2, 20.5, 21.7, 29.3, 33.4, 57.2, 66.2, 67.5, 69.9, 128.4, 129.7, 135.1, 145.5, 152.2; IR (film): ν 1786, 1597, 1371, 1173, 666 cm^{-1}; EIMS *m*/*z*: 342 (M+H$^+$), 186, 155, 142, 140, 108, 91, 65, 59. Anal. Calcd for $C_{16}H_{23}NO_5S$: C, 56.29; H, 6.79; N, 4.10. Found: C, 56.34; H, 6.92; N, 3.96; HPLC analysis: 5% ee (DAICEL CHIRALCEL AD-H, eluent, hexane/2-propanol=90/10, flow rate 0.6 mL min^{-1}, detection 225 nm light), t_R of major-isomer 13.37 min and that of minor-isomer 16.39 min.

4.3.3. (+)-*N*-Tosyl-4-butyl-1,3-oxazolidin-2-one (7a). White solid (yield: 99%), mp 100–101 °C. ^{1}H NMR

(300 MHz, $CDCl_3$) δ 0.87 (t, J=7.5 Hz, 3H), 1.10–1.38 (m, 4H), 1.80–1.95 (m, 2H), 2.45 (s, 3H), 4.06 (dd, J=3.3, 8.4 Hz, 1H), 4.37 (dd, J=8.4, 8.4 Hz, 1H), 4.45–4.48 (m, 1H), 7.35 (d, J=8.1 Hz, 2H), 7.96 (d, J=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 21.6, 22.2, 25.4, 33.2, 57.2, 67.5, 128.2, 129.6, 135.0, 145.4, 152.2; IR (KBr): ν 2962, 2927, 2854, 1778, 1596, 1486, 1395, 1363, 1174, 1148, 1091, 820, 667, 608, 547 cm^{-1}; ESIMS m/z: 298 ($M+H^+$), 315 ($M+NH_4^+$). Anal. Calcd for $C_{14}H_{19}NO_4S$: C, 56.55; H, 6.44; N, 4.71. Found: C, 56.30; H, 6.37; N, 4.99; HPLC analysis: 99% ee (DAICEL CHIRALCEL OJ, eluent, hexane/2-propanol=70/30, flow rate 0.7 mL min^{-1}, detection 230 nm light), t_R of minor-isomer 19.13 min and that of major-isomer 26.79 min; $[\alpha]_D^{20}$ +54.9 (c 1.03, $CHCl_3$).

4.3.4. (−)-*N*-Tosyl-4-ethyl-1,3-oxazolidin-2-one (7c). White solid (yield: 97%), mp 87–89 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J=7.2 Hz, 3H), 1.82–2.01 (m, 2H), 2.45 (s, 3H), 4.08 (dd, J=3.3, 8.7 Hz, 1H), 4.38 (dd, J=8.7, 8.7 Hz, 1H), 4.43–4.50 (m, 1H), 7.35 (d, J=8.4 Hz, 2H), 7.96 (d, J=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.5, 21.6, 26.4, 57.9, 67.0, 128.3, 129.7, 135.0, 145.5, 152.3; IR (KBr): ν 1766, 1597, 1373, 1175, 1111, 815, 664, 545 cm^{-1}; ESIMS m/z: 270 ($M+H^+$), 287 ($M+NH_4^+$). Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.52; H, 5.61; N, 5.20. Found: C, 53.72; H, 5.60; N, 5.15; HPLC analysis: 27% ee (DAICEL CHIRALPAK AD-H, eluent, hexane/2-propanol=90/10, flow rate 0.8 mL min^{-1}, detection 230 nm light), t_R of major-isomer 21.71 min and that of minor-isomer 32.54 min; $[\alpha]_D^{20}$ −10.7 (c 1.01, $CHCl_3$).

4.3.5. (−)-*N*-Tosyl-4,5,5-trimethyl-1,3-oxazolidin-2-one (7d). White solid (yield: 96%), mp 99–102 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (d, J=4.8 Hz, 3H), 1.40 (s, 3H), 1.42 (s, 3H), 2.45 (s, 3H), 4.14 (q, J=4.8 Hz, 1H), 7.35 (d, J=8.4 Hz, 2H), 7.95 (d, J=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.4, 21.4, 21.6, 27.4, 62.2, 82.3, 128.1, 129.6, 135.1, 145.3, 151.1; IR (KBr): ν 1774, 1596, 1359, 1330, 1278, 1171, 1160, 1131, 1089, 818, 728, 663, 581, 549 cm^{-1}; ESIMS m/z: 284 ($M+H^+$), 301 ($M+NH_4^+$). Anal. Calcd for $C_{13}H_{17}NO_4S$: C, 55.11; H, 6.05; N, 4.94. Found: C, 55.28; H, 6.05; N, 4.90; HPLC analysis: 87% ee (DAICEL CHIRALPAK AD-H, eluent, hexane/2-propanol=90/10, flow rate 0.8 mL min^{-1}, detection 230 nm light), t_R of minor-isomer 12.04 min and that of major-isomer 13.38 min; $[\alpha]_D^{20}$ −25.7 (c 1.11, $CHCl_3$).

4.3.6. (−)-*N*-Tosyl-4-methyl-1-oxa-3-aza-spiro[4,5]-decan-2-one (7e). White solid (yield: 100%), mp 85–87 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (d, J=6.6 Hz, 3H), 1.26–1.82 (m, 10H), 2.45 (s, 3H), 4.14 (q, J=6.6 Hz, 1H), 7.34 (d, J=8.4 Hz, 2H), 7.95 (d, J=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.7, 21.6, 21.8, 22.0, 24.7, 30.4, 36.1, 61.6, 83.5, 128.2, 129.7, 135.3, 145.2, 151.1; IR (KBr): ν 1768, 1598, 1370, 1359, 1174, 1124, 1029, 603, 548 cm^{-1}; ESIMS m/z: 324 ($M+H^+$), 341 ($M+NH_4^+$). Anal. Calcd for $C_{16}H_{21}NO_4S$: C, 59.42; H, 6.52; N, 4.33. Found: C, 59.67; H, 6.74; N, 4.13; HPLC analysis: 81% ee (DAICEL CHIRALCEL OJ-H, eluent, hexane/2-propanol=90/10, flow rate 0.8 mL min^{-1}, detection 230 nm light), t_R of major-isomer 18.71 min and that of minor-isomer 23.04 min; $[\alpha]_D^{20}$ −27.4 (c 1.0, $CHCl_3$).

4.3.7. (+)-*N*-Tosyl-4-methyl-1,3-oxazolidin-2-one (7f). White solid (yield: 97%), mp 94–97 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (d, J=6.3 Hz, 3H), 2.45 (s, 3H), 3.93 (dd, J=8.4, 3.6 Hz, 1H), 4.43 (dd, J=8.4, 8.4 Hz, 1H), 4.53–4.60 (m, 1H), 7.36 (d, J=8.4 Hz, 2H), 7.94 (d, J=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.5, 21.6, 53.5, 69.5, 128.3, 129.7, 135.0, 145.5, 152.0; IR (KBr): ν 1783, 1596, 1363, 1170, 664, 546 cm^{-1}; ESIMS m/z: 256 ($M+H^+$), 273 ($M+NH_4^+$). Anal. Calcd for $C_{11}H_{13}NO_4S$: C, 51.75; H, 5.13; N, 5.49. Found: C, 51.96; H, 5.19; N, 5.33; HPLC analysis: 39% ee (DAICEL CHIRALPAK AD-H, eluent, hexane/2-propanol=90/10, flow rate 0.8 mL min^{-1}, detection 230 nm light), t_R of minor-isomer 18.13 min and that of major-isomer 23.21 min; $[\alpha]_D^{20}$ +14.7 (c 1.04, $CHCl_3$).

4.3.8. (−)-*N*-Acetyl-4,5,5-trimethyl-1,3-oxazolidin-2-one (7g). White solid (yield: 96%), mp 39–40 °C (lit.[10a] mp 42 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (d, J=6.5 Hz, 3H), 1.41 (s, 3H), 1.43 (s, 3H), 2.52 (s, 3H), 4.17 (q, J=6.5 Hz, 1H); IR (KBr): ν 1762, 1702 cm^{-1}; ESIMS m/z: 171, 127, 114, 101, 84, 70, 59, 43, 39; HPLC analysis: 80% ee (DAICEL CHIRALCEL OJ-H, eluent, hexane/2-propanol=90/10, flow rate 0.8 mL min^{-1}, detection 200 nm light), t_R of major-isomer 9.04 min and that of minor-isomer 10.13 min; $[\alpha]_D^{20}$ −51.4 (c 0.54, EtOH).

4.4. Synthesis of L-lysine

4.4.1. (*S*)-*N*-Tosyl-4-((4′-dibenzylamino)butyl)-1,3-oxazolidin-2-one (11). To a solution of THF (31 mL) and 2 N HCl (7.6 mL) was added (*S*)-**2** (2.52 g, 6.6 mmol) at room temperature and the mixture was stirred for 30 min at room temperature. After triethylamine (2.4 mL, 17.2 mmol) was introduced via a syringe and stirred for 5 min at 0 °C, dibenzylamine (1.3 mL, 6.6 mmol) was added to the mixture and the reaction mixture was stirred for 10 min at 0 °C. Then, sodium cyanoborohydride (411.3 mg, 6.6 mmol) was added in one portion at 0 °C. The reaction mixture was stirred for 8 h at room temperature and then poured into 2 N HCl (pH=2) at 0 °C. Concentrated NaOH solution was added to the mixture at 0 °C to make the solution basic (pH=12). Then, saturated NaCl solution (30 mL) was added and the reaction mixture was extracted with ethyl acetate (3×30 mL). The combined organic extracts were washed with brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate/Et_3N=80/10/1 to 100/20/1 (v/v/v)) to give white solid (*S*)-**11** in 56% yield, mp 88–90 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20–1.30 (m, 2H), 1.42–1.50 (m, 2H), 1.63–1.79 (m, 2H), 2.35 (t, J=6.9 Hz, 2H), 2.41 (s, 3H), 3.48 (d, J=13.5 Hz, 2H), 3.53 (d, J=13.5 Hz, 2H), 3.95 (dd, J=8.4, 3.3 Hz, 1H), 4.31 (dd, J=8.4, 8.4 Hz, 1H), 4.38–4.41 (m, 1H), 7.21–7.34 (m, 12H), 7.90 (d, J=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 21.5, 26.5, 33.0, 52.6, 57.0, 58.2, 67.3, 126.7, 128.08, 128.13, 128.6, 129.6, 134.9, 139.6, 145.3, 152.1; IR (KBr): ν 2943, 2799, 1786, 1598, 1494, 1390, 1174, 1091, 911, 666 cm^{-1}; EIMS m/z: 492 (M^+), 210, 181, 155, 91, 65, 43. Anal. Calcd for $C_{28}H_{32}N_2O_4S$: C, 68.27; H, 6.55; N, 5.69. Found: C, 68.01; H, 6.53; N, 5.58; $[\alpha]_D^{20}$ +38.4 (c 1.01, $CHCl_3$).

4.4.2. (2*S*)-6-Dibenzylamino-2-tosylaminohexanol (12). To a solution of (*S*)-**11** (1.7 g, 3.5 mmol) in THF (48 mL)

and water (16 mL) was added lithium hydroxide (308.7 mg, 7.3 mmol) at room temperature. The mixture was stirred for 9 h. After addition of saturated NH_4Cl solution (30 mL), the reaction mixture was extracted with ethyl acetate (3×30 mL). The combined organic extracts were washed with brine (2×20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=2/1 (v/v)) to give colorless oil (*S*)-**12** in 99% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00–1.35 (m, 6H), 1.87–1.93 (br, 1H), 2.27 (t, *J*=6.9 Hz, 2H), 2.39 (s, 3H), 3.11–3.20 (m, 1H), 3.37–3.57 (m, 6H), 4.52 (d, *J*=8.4 Hz, 1H), 7.23–7.33 (m, 12H), 7.74 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 22.9, 26.5, 31.3, 52.6, 55.6, 58.3, 64.8, 126.8, 127.1, 128.2, 128.8, 129.7, 137.5, 139.8, 143.5; IR (film): ν 3502, 3282, 2941, 2798, 1600, 1495, 1453, 1029 cm^{-1}; EIMS *m*/*z*: 466 (M^+), 435, 375, 311, 210, 181, 155, 91, 65. HRMS Calcd for $C_{27}H_{34}N_2O_3S$: 466.2290. Found: 466.2319; HPLC analysis: 96% ee (KROMASIL DMB, eluent, hexane/2-propanol=95/5, flow rate 1 mL min^{-1}, detection 230 nm light), t_R of major-isomer 18.46 min and that of minor-isomer 20.04 min; $[\alpha]_D^{20}$ −3.1 (*c* 1.15, $CHCl_3$).

4.4.3. (2*S*)-2-Tosylamino-6-benzyloxycarbonylaminohexanol (13). To a solution of (*S*)-**12** (1.6 g, 3.3 mmol) in methanol (155 mL) was added $Pd(OH)_2$/C (20%, 1.1 g). The mixture was stirred for 8.5 h under hydrogen (1 atm) at room temperature. The solution was filtered and the filtrate was evaporated under reduced pressure to afford a crude product, which was dissolved in THF (63 mL) and water (47 mL) containing potassium carbonate (1.36 g, 9.9 mmol). Cbz-Cl (0.7 mL, 5.0 mmol) was added to the mixture via a syringe over 15 min period at 0 °C and stirred over night at room temperature. After the addition of brine (30 mL), the reaction mixture was extracted with ethyl acetate (3×30 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate) to give white solid (*S*)-**13** in 80% yield, mp 88–90 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06–1.53 (m, 6H), 2.43 (s, 3H), 2.49 (t, *J*=6.0 Hz, 1H), 3.08 (dt, *J*=6.3, 6.3 Hz, 2H), 3.19–3.30 (m, 1H), 3.45–3.48 (m, 2H), 4.81–4.83 (br, 1H), 5.10 (s, 2H), 5.22 (d, *J*=7.8 Hz, 1H), 7.26–7.37 (m, 7H), 7.75 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.48, 21.69, 29.43, 30.67, 39.96, 55.28, 64.42, 66.73, 127.02, 128.07, 128.12, 128.50, 129.65, 136.40, 137.61, 143.44, 156.78; IR (KBr): ν 3522, 3349, 3275, 2939, 1685, 1546, 1164, 1087, 686, 570 cm^{-1}; ESIMS *m*/*z*: 421 ($M+H^+$). Anal. Calcd for $C_{21}H_{28}N_2O_5S$: C, 59.98; H, 6.71; N, 6.66. Found: C, 59.97; H, 7.00; N, 6.66; $[\alpha]_D^{20}$ +9.2 (*c* 0.85, $CHCl_3$).

4.4.4. *N*-Tosyl-*N*′-benzyloxycarbonyl-L-lysine (14). To a solution of Jones' reagent (2.69 M, 14.7 mL) in acetone (27 mL) was added a solution of (*S*)-**13** (673 mg, 1.6 mmol) in acetone (15 mL) via a dropping funnel over 30 min at 0 °C and the resulting mixture was stirred for 8 h at room temperature. After the addition of isopropanol (10 mL), the solvent was evaporated under reduced pressure and the brine (30 mL) was added. The aqueous solution was extracted with ethyl acetate (3×30 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=3/1 to 1/2 (v/v)) to give white solid (*S*)-**14** in 78% yield, mp 120–121 °C (recrystallization from benzene) (lit.[21] mp 121–122 °C (benzene)). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.10–1.30 (m, 4H), 1.42–1.60 (m, 2H), 2.35 (s, 3H), 2.82–2.87 (m, 2H), 3.55–3.60 (m, 1H), 4.99 (s, 2H), 7.20–7.24 (m, 1H), 7.30–7.40 (m, 6H), 7.63 (d, *J*=8.1 Hz, 2H); IR (KBr): ν 3381, 3265, 2862, 1740, 1653, 1456, 566 cm^{-1}; ESIMS *m*/*z*: 435 ($M+H^+$), 452 ($M+NH_4^+$). Anal. Calcd for $C_{21}H_{26}N_2O_6S$: C, 58.05; H, 6.03; N, 6.45. Found: C, 58.04; H, 6.09; N, 6.29; $[\alpha]_D^{20}$ +13.0 (*c* 2.32, MeOH) (recrystallization from benzene) (lit.[21] $[\alpha]_D^{23}$ +13.5 (*c* 2.2, MeOH)).

4.4.5. *N*-Tosyl-*N*′-benzyloxycarbonyl-L-lysine methyl ester (15). Compound (*S*)-**14** (recrystallization from benzene) (150 mg, 0.35 mmol) was dissolved in methanol (1.5 mL) containing *p*-toluenesulfonic acid (15 mg). The solution was slowly distilled during 6 h; more methanol–benzene being added as required. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate. The solution was washed successively with 10% aqueous sodium hydrogen carbonate, water, dried, and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel (petroleum ether/ethyl acetate=2/1 (v/v)) to give white solid (*S*)-**15** in 90% yield, mp 76–78 °C (recrystallization from petroleum ether/ethyl acetate) (lit.[28] mp 80–81 °C (recrystallization from benzene/light petroleum)). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25–1.50 (m, 4H), 1.61–1.75 (m, 2H), 2.41 (s, 3H), 3.15 (dt, *J*=6.3, 6.3 Hz, 2H), 3.48 (s, 3H), 3.85–3.92 (m, 1H), 4.70–4.80 (br, 1H), 5.10 (s, 2H), 5.48 (d, *J*=8.4 Hz, 1H), 7.26–7.37 (m, 7H), 7.70 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 21.9, 29.0, 32.5, 40.4, 52.3, 55.4, 66.5, 127.1, 127.96, 127.99, 128.4, 129.5, 136.5, 143.6, 156.4, 172.0; IR (KBr): ν 3350, 3271, 2951, 2859, 1739, 1687, 1546 cm^{-1}; ESIMS *m*/*z*: 449 ($M+H^+$), 466 ($M+NH_4^+$); HPLC analysis: 98% ee (DAICEL CHIRALPAK AD-H, eluent, hexane/2-propanol=83/17, flow rate 0.7 mL min^{-1}, detection 225 nm light), t_R of minor-isomer 56.88 min and that of major-isomer 66.29 min; $[\alpha]_D^{20}$ +19.7 (*c* 4.59, $CHCl_3$).

4.5. Synthesis of L-norleucine

4.5.1. (*S*)-2-(Tosylamino)hexanol (16). Compound **16** was synthesized from **7a** similar to the synthesis of (*S*)-**12**. Compound (*S*)-**16**: white solid (yield: 95%), mp 81–83 °C (recrystallization from petroleum ether/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.75 (t, *J*=6.6 Hz, 3H), 0.95–1.20 (m, 4H), 1.25–2.03 (m, 2H), 2.32 (t, *J*=5.7 Hz, 1H), 2.43 (s, 3H), 3.21–3.23 (m, 1H), 3.46–3.60 (m, 2H), 4.97 (d, *J*=7.5 Hz, 1H), 7.31 (d, *J*=8.1 Hz, 2H), 7.78 (d, *J*=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 21.4, 22.2, 27.6, 31.2, 55.6, 64.7, 127.1, 129.6, 137.6, 143.4; IR (KBr): ν 3560, 3501, 3278, 2957, 2931, 1599, 1425, 1335, 1163, 1152, 1087, 1055, 674, 554 cm^{-1}; ESIMS *m*/*z*: 272 ($M+H^+$), 289 ($M+NH_4^+$). Anal. Calcd for $C_{13}H_{21}NO_3S$: C, 57.54; H, 7.80; N, 5.16. Found: C, 57.57; H, 7.61; N, 5.11; $[\alpha]_D^{20}$ −19.9 (*c* 1.1, MeOH).

4.5.2. *N*-Tosyl-L-norleucine (17). Compound **17** was synthesized from **16** similar to the synthesis of (*S*)-**14**. Compound (*S*)-**17**: white solid (yield: 82%), mp 113–115 °C

(recrystallization from benzene). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (t, J=7.2 Hz, 3H), 1.22–1.31 (m, 4H), 1.58–1.78 (m, 2H), 2.41 (s, 3H), 3.89–3.96 (m, 1H), 4.00–4.72 (br, 1H), 5.13 (d, J=9.3 Hz, 1H), 7.27 (d, J=8.1 Hz, 2H), 7.72 (d, J=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 21.4, 21.9, 26.8, 32.6, 55.3, 127.1, 129.6, 136.5, 143.8, 177.0; IR (KBr): ν 3246, 2950, 2870, 1716, 1415, 1324, 1170, 1094, 811, 689, 574 cm^{-1}; ESIMS m/z: 286 (M+H$^+$), 303 (M+NH$_4^+$). Anal. Calcd for $C_{13}H_{19}NO_4S$: C, 54.72; H, 6.71; N, 4.91. Found: C, 54.86; H, 6.57; N, 4.86; $[\alpha]_D^{20}$ +6.7 (c 1.96, MeOH).

4.5.3. Methyl (L)-2-(tosylamino)hexanoate (18). Compound **18** was synthesized similar to the synthesis of (*S*)-**15**. Compound (*S*)-**18**: white solid (yield: 89%), mp 46–48 °C (recrystallization from petroleum ether/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, J=7.2 Hz, 3H), 1.22–1.34 (m, 4H), 1.57–1.75 (m, 2H), 2.42 (s, 3H), 3.49 (s, 3H), 3.87–3.94 (m, 1H), 5.07 (d, J=9.0 Hz, 1H), 7.30 (d, J=8.1 Hz, 2H), 7.73 (d, J=8.1 Hz, 2H); IR (KBr): ν 3268, 2958, 2858, 1743, 1598, 1459, 1345, 1166, 1089, 819, 671, 574, 556 cm^{-1}; ESIMS m/z: 300 (M+H$^+$), 317 (M+NH$_4^+$); HPLC analysis: 98% ee (DAICEL CHIRALCEL OD, eluent, hexane/2-propanol = 95/5, flow rate 0.7 mL min^{-1}, detection 225 nm light), t_R of minor-isomer 22.87 min and that of major-isomer 26.13 min; $[\alpha]_D^{20}$ −11 (c 2.01, EtOH) (lit.[22] $[\alpha]_D^{20}$ −12 (c 2.0, EtOH)).

4.6. Synthesis of *N*-tosyl-L-pipecolic acid and *N*-tosyl-(*R*)-α-pipecoline

4.6.1. (2*S*)-2-Tosylamino-6,6-diethoxyhexanol (19). Compound **19** was synthesized from (*S*)-**2** similar to (*S*)-**12**. Compound (*S*)-**19**: oil (yield: 95%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18 (t, J=6.9 Hz, 6H), 1.21–1.49 (m, 6H), 2.36 (t, J=5.7 Hz, 1H), 2.43 (s, 3H), 3.21–3.25 (m, 1H), 3.25–3.61 (m, 6H), 4.33 (t, J=6.0 Hz, 1H), 5.07 (d, J=7.8 Hz, 1H), 7.31 (d, J=8.1 Hz, 2H), 7.77 (d, J=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.2, 20.7, 21.4, 31.1, 33.0, 55.4, 60.9, 61.0, 64.3, 102.4, 126.9, 129.5, 137.6, 143.2; IR (KBr): ν 3471, 3284, 2976, 2931, 2879, 1599, 1326, 1160 cm^{-1}; EIMS m/z: 282 ([M−CH$_2$OH–C$_2$H$_5$OH]$^+$), 268, 238, 155, 103, 91, 85, 57, 47, 41. HRMS Calcd for $C_{16}H_{26}NO_4S$ ([M−HOCH$_2$]$^+$): 328.1582. Found: 328.1565; $[\alpha]_D^{20}$ −5.3 (c 0.85, EtOH).

4.6.2. (*S*)-2-Tosylamino-6,6-diethoxyhexanol benzyl ether (20). Sodium hydride (293.8 mg of 60% dispersion in mineral oil, 7.34 mmol) was added to a stirred solution of (*S*)-**19** (1.28 g, 3.6 mmol) in dry THF (6 mL) at −40 °C and the mixture was stirred for 30 min with warming to 0 °C. To the above mixture at 0 °C was added dropwise benzyl bromide (0.44 mL, 3.6 mmol) and the mixture was stirred for 2 h. The reaction was quenched with saturated NH_4Cl solution (15 mL) and stirred for 10 min at 0 °C. The mixture was extracted with EtOAc and the extract was washed with brine twice and dried over $MgSO_4$. Concentration under reduced pressure gave a residue, which was purified by chromatography on silica gel (petroleum ether/ethyl acetate) to give colorless oil (*S*)-**20** (84%, 1.34 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.182 (t, J=7.5 Hz, 3H), 1.184 (t, J=7.2 Hz, 3H), 1.25–1.40 (m, 2H), 1.47–1.60 (m, 4H), 2.41 (s, 3H), 3.19–3.23 (m, 1H), 3.29–3.35 (m, 2H), 3.35–3.52 (m, 2H), 3.57–3.63 (m, 2H), 4.34 (s, 2H), 4.37 (t, J=5.4 Hz, 1H), 4.78 (d, J=8.1 Hz, 1H), 7.19–7.34 (m, 7H), 7.70 (d, J=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.2, 20.6, 21.3, 32.1, 33.1, 53.3, 60.9, 71.0, 72.9, 102.5, 126.8, 127.4, 127.5, 128.1, 129.3, 137.6, 137.9, 142.9; IR (KBr): ν 3280, 2976, 2871, 1599, 1455, 1332, 1162, 1093, 666 cm^{-1}; EIMS m/z: 358 ([M−CH$_3$C$_6$H$_4$]$^+$), 282, 248, 202, 155, 103, 91, 85, 57, 47. Anal. Calcd for $C_{24}H_{35}NO_5S$: C, 64.11; H, 7.85; N, 3.12. Found: C, 64.19; H, 8.07; N, 3.06; $[\alpha]_D^{20}$ −12.1 (c 1.5, EtOH).

4.6.3. (*S*)-*N*-Tosyl-2-hydroxymethylpiperidine (21). To a solution of (*S*)-**20** (1.3 g, 2.9 mmol) in THF (23 mL) was added *p*-toluenesulfonic acid (1.1 g, 5.8 mmol). The mixture was stirred for 32 h at room temperature. The reaction was quenched with saturated $NaHCO_3$ solution (30 mL) and stirred for 10 min at 0 °C. The mixture was extracted with EtOAc and the extract was washed twice with brine and dried over $MgSO_4$. Concentration under reduced pressure gave a residue, which was hydrogenated (H_2, 1 atm) in dry EtOH (80 mL) under the catalysis of Pd/C (10%) (40%, 2.12 g) for 2.5 days at room temperature. The reaction mixture was filtrated. The filtrate was concentrated under reduced pressure and then purified by chromatography on silica gel (petroleum ether/ethyl acetate=4/1 to 2/1 (v/v)) to give colorless oil (*S*)-**21** (70%, 545 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24–1.66 (m, 6H), 2.00–2.05 (m, 1H), 2.43 (s, 3H), 3.10 (dt, J=2.7, 13.8 Hz, 1H), 3.54–3.60 (m, 1H), 3.79–3.90 (m, 2H), 3.99–4.00 (m, 1H), 7.30 (d, J=8.1 Hz, 2H), 7.75 (d, J=8.1 Hz, 2H); IR (KBr): ν 3520, 2942, 1598, 1447, 1328, 1156, 1094, 658, 549 cm^{-1}; EIMS m/z: 270 (M+H)$^+$, 238, 155, 91, 65, 55; HPLC analysis: 97% ee (DAICEL CHIRALCEL OJ-H, eluent, hexane/2-propanol=80/20, flow rate 0.8 mL min^{-1}, detection 230 nm light), t_R of minor-isomer 9.18 min and that of major-isomer 9.99 min; $[\alpha]_D^{20}$ −45.0 (c 0.27, EtOH).

4.6.4. *N*-Tosyl-L-pipecolic acid (22). This compound was synthesized from (*S*)-**21** similar to (*S*)-**14**. Compound (*S*)-**22**: oil (yield: 92%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24–1.53 (m, 2H), 1.61–1.81 (m, 3H), 2.13–2.18 (m, 1H), 2.42 (s, 3H), 3.20 (dt, J=2.7, 12.3 Hz, 1H), 3.72–3.76 (m, 1H), 4.76 (d, J=4.5 Hz, 1H), 6.80–7.30 (br, 1H), 7.28 (d, J=8.1 Hz, 2H), 7.69 (d, J=8.1 Hz, 2H); IR (KBr): ν 2964, 2949, 2882, 2861, 1714, 1361, 1336, 1160 cm^{-1}; ESIMS m/z: 284 (M+H$^+$), 301 (M+NH$_4^+$); $[\alpha]_D^{20}$ −24.3 (c 1.0, EtOH).

4.6.5. Methyl *N*-tosyl-L-pipecolate (23). This compound was synthesized similar to (*S*)-**15**. Compound (*S*)-**23**: oil (yield: 89%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23–1.52 (m, 2H), 1.61–1.70 (m, 3H), 2.08–2.13 (m, 1H), 2.42 (s, 3H), 3.20 (dt, J=2.4, 12.0 Hz, 1H), 3.54 (s, 3H), 3.73–3.78 (m, 1H), 4.74 (d, J=5.1 Hz, 1H), 7.27 (d, J=8.4 Hz, 2H), 7.66 (d, J=8.4 Hz, 2H); IR (KBr): ν 2949, 1731, 1596, 1338, 1154, 943, 586 cm^{-1}; EIMS m/z: 297 (M$^+$), 239, 155, 142, 139, 91, 82, 65, 55, 41; HPLC analysis: 95% ee (DAICEL CHIRALPAK AD-H, eluent, hexane/2-propanol=100/0.01, flow rate 0.7 mL min^{-1}, detection 254 nm light), t_R of major-isomer 37.79 min and that of minor-isomer 40.71 min; $[\alpha]_D^{20}$ −40.5 (c 0.65, MeOH) (lit.[23] $[\alpha]_D^{20}$ −37.2 (c 0.62, MeOH)).

4.6.6. (*S*)-*N*-Tosyl-*O*-tosyl-2-hydroxymethylpiperidine[29] (24). Alcohol **21** (299 mg, 1.1 mmol) was added to a solution of triethylamine (0.76 mL, 5.5 mmol) and DMAP (16 mg) in CH_2Cl_2 (60 mL). Then the toluene-*p*-sulfonyl chloride (419.5 mg, 2.2 mmol) dissolved in CH_2Cl_2 (20 mL) was added dropwise to the mixture under ice-water cooling during 1 h. After the resulting mixture was stirred at ambient temperature overnight, it was diluted with CH_2Cl_2 (20 mL), washed with water (10 mL) and brine (10 mL), then dried and evaporated. The residue was subjected to column chromatography on silica gel (petroleum ether/ethyl acetate=4/1 (v/v)) to give oil (*S*)-**24** in 87% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22–1.52 (m, 5H), 1.72 (m, 1H), 2.42 (s, 3H), 2.47 (s, 3H), 2.83 (t, J=14.4 Hz, 1H), 3.70 (m, 1H), 4.00–4.13 (m, 2H), 4.24–4.27 (m, 1H), 7.26 (d, J=7.6 Hz, 2H), 7.35 (d, J=8.1 Hz, 2H), 7.67 (d, J=7.6 Hz, 2H), 7.75 (d, J=8.1 Hz, 2H); IR (KBr): ν 2947, 2868, 1598, 1363, 1191, 1178, 1095, 977, 816, 553 cm^{-1}; ESIMS *m*/*z*: 424 (M+H$^+$), 441 (M+NH$_4^+$); $[\alpha]_D^{20}$ −54.63 (*c* 1.2, EtOH) (lit.[29] $[\alpha]_D^{23}$ +55 (*c* 0.8, EtOH)).

4.6.7. *N*-Tosyl-(*R*)-α-pipecoline[24] (25). An ether (3 mL) solution of (*S*)-**24** was added to a suspension of $LiAlH_4$ (8.4 mg, 0.22 mmol) in Et_2O (3 mL) at 0 °C. The reaction mixture was stirred at room temperature for 10 min and then refluxed for 24 h after hydrolysis by successive addition of 0.3 mL of water, 0.3 mL of 15% NaOH, and 0.9 mL of water, the precipitate formed was filtered off. The filtrate was washed with aqueous $NaHCO_3$ and saturated NaCl and dried over sodium sulfate. The solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=5/1 (v/v)) to give white solid (*R*)-**25** in 92% yield, mp 61–62 °C (recrystallization from petroleum ether/ethyl acetate) (lit.[24] mp 68–70 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (d, J=7.2 Hz, 3H), 1.25–1.61 (m, 6H), 2.42 (s, 3H), 2.97 (dt, J_1=1.6, J_2=12.6 Hz, 1H), 3.70 (dd, J_1=3.5, J_2=12.6 Hz, 1H), 4.21–4.26 (m, 1H), 7.27 (d, J=8.1 Hz, 2H), 7.70 (d, J=8.1 Hz, 2H); IR (KBr): ν 2925, 1597, 1328, 1164, 1093, 822, 600 cm^{-1}; EIMS *m*/*z*: 253 (M$^+$), 238, 239, 155, 91, 65, 56, 55, 41; HPLC analysis: 97% ee (DAICEL CHIRALCEL OJ-H, eluent, hexane/2-propanol=98/2, flow rate 0.7 mL min^{-1}, detection 230 nm light), t_R of minor-isomer 22.71 min and that of major-isomer 28.29 min; $[\alpha]_D^{20}$ −39.3 (*c* 0.85, EtOH) (lit.[24] $[\alpha]_D^{20}$ +41.0 (*c* 0.98, EtOH)).

4.7. Synthesis of optically active amino alcohol derivatives

4.7.1. (+)-*N*-Tosyl-2-methyl-3-aminobutan-2-ol (26). This compound was synthesized from **7c** similar to (*S*)-**12**. Compound (+)-**26**: white solid (quantitative yield), mp 83–85 °C (recrystallization from petroleum ether/ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (d, J=6.9 Hz, 3H), 1.15 (s, 3H), 1.17 (s, 3H), 1.86 (s, 1H), 2.43 (s, 3H), 3.17 (dq, J=8.1, 6.9 Hz, 1H), 4.67 (d, J=8.1 Hz, 1H), 7.31 (d, J=8.4 Hz, 2H), 7.77 (d, J=8.4 Hz, 2H); IR (KBr): ν 3495, 3288, 2989, 1597, 1334, 1153, 1085, 666, 543 cm^{-1}; ESIMS (ESI) *m*/*z*: 258 (M+H$^+$), 275 (M+NH$_4^+$); HPLC analysis: 88% ee (DAICEL CHIRALPAK AD, eluent, hexane/2-propanol=70/30, flow rate 0.7 mL min^{-1}, detection 230 nm light), t_R of minor-isomer 23.21 min and that of major-isomer 31.63 min; $[\alpha]_D^{20}$ +34.3 (*c* 0.54, MeOH).

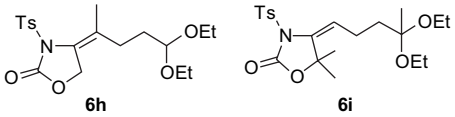
Acknowledgements

The Major State Basic Research Program (Grant no. G2000077502-A). We thank the National Natural Sciences Foundation of China and Chinese Academy of Sciences for the financial support. We thank Professor Zhaoguo Zhang, Professor Kuilin Ding, and Professor Xuelong Hou for the chiral ligands and their precursors.

References and notes

1. (a) For a review on synthetic methods of α-amino acids, see: Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1539; (b) Williams, R. H. *Synthesis of Optically Active α-Amino Acids*; Pergamon: New York, NY, 1989; (c) Schollkopf, U. *Top. Curr. Chem.* **1983**, *109*, 65; (d) Wagner, I.; Musso, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 816.
2. Bergmeier, S. C. *Tetrahedron* **2000**, *56*, 2561.
3. For reviews, see: (a) Laschat, S.; Dickner, T. *Synthesis* **2000**, *13*, 1781; (b) Buffat, M. G. P. *Tetrahedron* **2004**, *60*, 1701; (c) Baliah, V.; Jeyraman, R.; Chandrasekaran, L. *Chem. Rev.* **1983**, *83*, 379; (d) Bates, R. W.; Sa-Ei, L. *Tetrahedron* **2002**, *58*, 5957; (e) Notz, W.; Tanaka, F.; Barbas, C. F., III. *Acc. Chem. Res.* **2004**, *37*, 580.
4. Coppola, D. M.; Schuster, H. F. *Asymmetric Synthesis: Construction of Chiral Molecules Using Amino Acids*; Wiley: New York, NY, 1987.
5. (a) Xu, Z.; Wang, R.; Xu, J.; Da, C.; Yan, W.; Chen, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 5747; (b) Xu, Z.; Chen, C.; Xu, J.; Miao, M.; Yan, W.; Wang, R. *Org. Lett.* **2004**, *6*, 1193.
6. Lei, A.; Lu, X. *Org. Lett.* **2000**, *2*, 2699.
7. Ohta, T.; Miyake, T.; Seido, N.; Kumobayashi, H.; Takaya, H. *J. Org. Chem.* **1995**, *60*, 357.
8. Yue, T. Y.; Nugent, W. A. *J. Am. Chem. Soc.* **2002**, *124*, 13692.
9. Gendre, P. L.; Braun, T.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* **1996**, *61*, 8453.
10. (a) Gendre, P. L.; Thominot, P.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* **1998**, *63*, 1806; (b) Gendre, P. L.; Jérôme, F.; Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1998**, 533.
11. Chung, J. Y.; Zhao, D.; Hughes, D. L.; McNamara, J. M.; Grabowski, E. J.; Reider, P. J. *Tetrahedron Lett.* **1995**, *36*, 7379.
12. The similar phenomena for the asymmetric hydrogenation of geraniol and nerol were reported by Noyori and co-workers. Inoue, S.-I.; Osada, M.; Koyano, K.; Takaya, H.; Noyori, R. *Chem. Lett.* **1985**, 1007.
13. Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264.
14. Kagan, H. B.; Dang, T.-P. *J. Am. Chem. Soc.* **1972**, *94*, 6429.
15. Baker, G. L.; Fritschel, S. J.; Stille, J. R.; Stille, J. K. *J. Org. Chem.* **1981**, *46*, 2954.
16. 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.
17. Arnold, L. A.; Imbos, R.; Mandoli, A.; de Vries, A. H. M.; Naasz, R.; Feringa, B. L. *Tetrahedron* **2000**, *56*, 2865.
18. Zhang, X.; Mashima, K.; Koyano, K.; Sayo, N.; Kumobayashi, H.; Akutogawa, S.; Takaya, H. *Tetrahedron Lett.* **1991**, *32*, 7283.

19. It should be pointed out that **6h** and **6i** were not hydrogenated under the typical conditions (Table 4).



6h **6i**

20. (a) Greenstein, J. P.; Winitz, M. *Chemistry of the Amino Acids*; Wiley: New York, NY, 1961; (b) Friedman, M. *Absorption and Utilization of Amino Acids*; CRC: Boca Raton, FL, 1989.
21. (a) Klabunovskii, E. I.; Karpeiskaya, E. I.; Levitina, E. S.; Godunova, L. F.; Kaigorodova, L. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1985**, 2157; (b) Fasth, K.-J.; Hörnfeldt, K.; Lángström, B. *Acta Chem. Scand.* **1995**, *49*, 301; (c) Siebum, A. H. G.; Tsang, R. K. F.; van der Steen, R.; Raap, J.; Lugtenburg, J. *Eur. J. Org. Chem.* **2004**, 4391; (d) Kjer, A.; Larsen, P. O. *Acta Chem. Scand.* **1961**, *15*, 750.
22. The absolute configuration of compound **18** was also assigned as L, namely *S* by comparison with the optical rotation of literature: (a) Bajgrowicz, J. A.; Hallaoui, A. E.; Jacquier, R.; Pigière, C.; Viallefont, P. *Tetrahedron* **1985**, *41*, 1833; (b) Bajgrowicz, J. A.; Hallaoui, A. E.; Jacquier, R.; Pigière, C.; Viallefont, P. *Tetrahedron Lett.* **1984**, *25*, 2759.
23. The absolute configuration of compound **23** ($[\alpha]_D^{20}$ −40.5 (*c* 0.65, MeOH)) was assigned as L, namely *S* by comparison with the optical rotation of literature (lit. $[\alpha]_D^{23}$ −37.2 (*c* 0.62, MeOH)): Iwata, M.; Kuzuhara, H. *Chem. Lett.* **1985**, 1941.
24. The absolute configuration of compound **25** ($[\alpha]_D^{20}$ −39.3 (*c* 0.85, EtOH)) was assigned *R* by comparison with the optical rotation of literature (lit. $[\alpha]_D^{20}$ +41.0 (*c* 0.98, EtOH)): Ripperger, H.; Schreiber, K. *Tetrahedron* **1965**, *21*, 1485.
25. Tamaru, Y.; Kimura, M.; Tanaka, S.; Kure, S.; Yoshida, Z. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2838.
26. Kimura, M.; Kure, S.; Yoshida, Z.; Tanaka, S.; Fugami, K.; Tamaru, Y. *Tetrahedron Lett.* **1990**, *31*, 4887.
27. Giordano, G.; Crabtree, R. H. *Inorg. Synth.* **1979**, *19*, 218.
28. (a) Barrass, B. C.; Elmove, D. T. *J. Chem. Soc.* **1957**, 4830; (b) Irving, C. C.; Gutmann, H. R. *J. Org. Chem.* **1959**, *24*, 1979.
29. Knight, D. W.; Lewis, N.; Share, A. C.; Haigh, D. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3673.