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A simple and practical access to enantiopure 2,3-diamino acid derivatives

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Abstract

Enantiomerically pure (4*R*,5*R*)- and (4*S*,5*S*)-2-imidazolines **5** were conveniently obtained on a gram scale. These can be converted into enantiopure (2*R*,3*R*)-2,3-diamino ester **6** or 2,3-diamino alcohol **7** by hydrolysis or reduction.

1. Introduction

Recently, much interest has been focused on the synthesis of unnatural and unusual 2,3-diamino acids, since this class of compound has an intrinsic biological activity. For example, 2,3-diaminopropanoic acid is an important structural element of some peptide antibiotics, antifungal dipeptides, and other biologically active compounds.[1] (2*S*,3*S*)- and (2*R*,3*S*)-2,3-Diaminobutanoic acid are present in peptide antibiotics such as aspartocin, glumamycin, lavendomytin, etc.[2] 2,3-Diamino-4-phenylbutanoic acid is a part of aminodeoxybestatin.[3] When an unusual 2,3-diamino acid is incorporated into medicinally-important peptides, it is also expected to modify biological activity in a useful way. Accordingly, the development of a simple and efficient method to produce enantiomerically pure 2,3-diamino acid from readily available starting materials is an important goal.

A number of efficient syntheses of chiral 2,3-diamino acids originated from natural optically-active α-amino acids or from stoichiometrical amounts of chiral reagents. Preparations of 2,3-diaminopropanoic and 2,3-diaminobutanoic acids have been reported from aspartic acid,[4] L-serine[5] and threonine.[6] Rapoport recently provided a method for the synthesis of 4-phenyl-2,3-diaminobutanoic acid by the electrophilic substitution at C-3 of an aspartic acid derivative.[4] A complementary route to 3-substituted 2,3-diamino acids is the diastereoselective addition of Grignard reagents to α-amino nitrones derived from L-serine.[5] In addition, the stereoselective synthesis of 2,3-diaminobutanoic acid from *tert*-butyl

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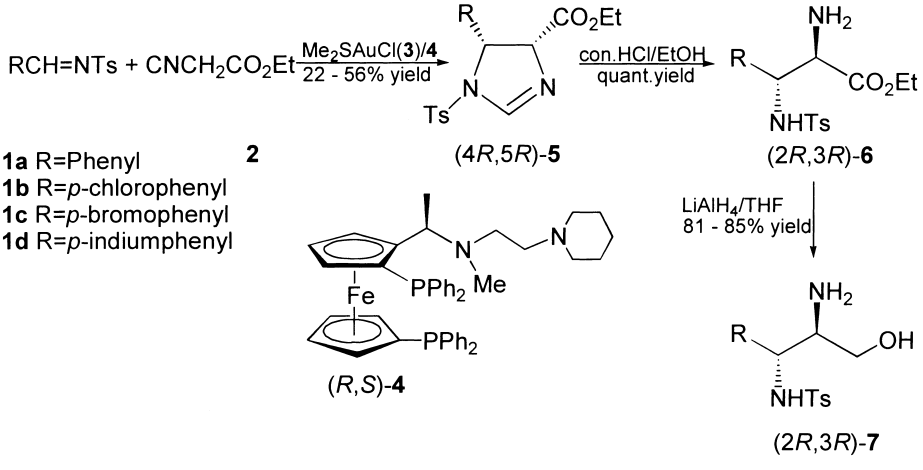
crotonate as the starting material using Sharpless asymmetric aminohydroxylation reaction has been reported in a 42% overall yield.[7] The cycloaddition reaction from (5*S*)-phenylmorpholin-2-one with aromatic imine may afford enantiomerically pure *threo*-(2*S*,3*R*)-3-aryl-2,3-dimino acids in a 36–46% yield.[8] Also, an aminated side chain precursor of the anticancer drug taxol was prepared through the β-lactam synthon method in a 21% yield.[9] It is noteworthy that the first catalytic asymmetric hydrogenation of (*E*)-α, β-bis-(*N*-acylamino)acrylates was reported to provide the corresponding optically active (2*S*,3*R*)-2,3-bis-(*N*-acylamino)carboxylates with 79–82% ee promoted by a rhodium complex bearing the chiral diphosphine ligand TRAP.[10]

All of these methods are either low-yielding or lengthy in terms of steps. Thus, a simple and efficient route to enantiopure 2,3-diamino acids is still of current interest to synthetic organic chemists. Hayashi and Ito et al. have reported an elegant asymmetric synthesis using gold(I) complex catalyzed aldol reaction of aldehydes with isocyanoacetates in the presence of chiral ferrocenylphosphine ligands in 1986.[11] Recently, they developed a similar stereoselective aldol-type reaction of *N*-sulfonylimines with methyl isocyanoacetate catalyzed by gold(I) complexes, which would provide an efficient route to *erythro*-2,3-diamino acids.[12] As a part of our research into the asymmetric synthesis of 2-imidazoline,[13] we have been interested in the synthesis of enantiomerically pure 2,3-diamino acids. Here, we wish to furnish a simple and efficient access to enantiomerically pure 2,3-diamino acid derivatives started from a catalytic asymmetric reaction of *N*-sulfonylimine with isocyanoacetate.

2. Results and discussion

Optically active (4*R*,5*R*)- or (4*S*,5*S*)-2-imidazolines were synthesized in high yield with 46–88% ee values in the presence of catalytic amount of Au(I) complex bearing chiral ferrocenylphosphine.[13] We found that the enantiomerically pure 2-imidazoline with 99% ee can be obtained after a common workup and a single recrystallization in moderate yield. Moreover, catalytic reactions and upgradings can be performed on a gram scale. This provides a practical synthetically-useful method for the preparation of enantiomerically pure 2-imidazoline, an important intermediate in organic synthesis. Enantiomerically pure 2,3-diamino esters were further obtained from enantiomerically pure 2-imidazoline by treatment with conc. HCl in EtOH (Scheme 1). The results are shown in Table 1.



Scheme 1.

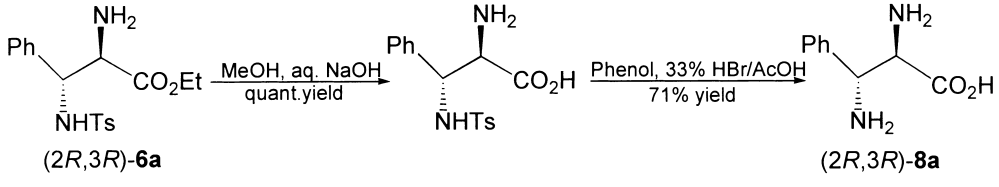
Table 1
Synthesis of enantiomerically pure 2,3-diamino acid derivatives from 2-imidazolines

		cis-**5**		**6**		**7**	
entry	imine	% ee [a] (config.)	yield %[b]	$[\alpha]^{20}_D$ (config.)	yield %[b]	$[\alpha]^{20}_D$ (config.)	yield %[c]
1	1a	99 (4*R*,5*R*)	22	- 25.2 (2*R*,3*R*)	22	- 4.1 (2*R*,3*R*)	83
2	1b	99 (4*R*,5*R*)	32	- 24.6 (2*R*,3*R*)	32	- 3.2 (2*R*, 3*R*)	85
3	1b	97 (4*S*,5*S*)	31	+ 22.6 (2*S*,3*S*)	31		
4	1c	99 (4*R*,5*R*)	49	- 21.4 (2*R*,3*R*)	49	- 3.7 (2*R*,3*R*)	81
5	1c	99 (4S, 5S)	51	+ 20.2 (2S, 3S)	51		
6	1d	96 (4*R*,5*R*)	56	- 19.2 (2*R*,3*R*)	56		

[a] Determined by HPLC analysis using a chiral OD or OA column. [b] Isolated yield based on the *N*-sulfonylimine. [c] Isolated yield based on **6**.

The yield of 2,3-diamino esters obtained was based on the starting material *N*-sulfonylimines including the following procedures: a catalytic enantioselective reaction of *N*-sulfonylimine **1** and isocyanoacetate **2**; purification of *cis*-2-imidazoline **5**, recrystallization of enantiomerically pure *cis*-2-imidazoline, and hydrolysis of optically pure *cis*-2-imidazoline. When (*R*,*S*)-ferrocenylphosphine (*R*,*S*)-**4** was used as a chiral ligand for the catalytic reaction, (2*R*,3*R*)-2,3-diamino esters (2*R*,3*R*)-**6** was obtained. On the contrary, (2*S*,3*S*)-diamino esters (2*S*,3*S*)-**6** was also obtained easily by using (*S*,*R*)-ferrocenylphosphine ligand (*S*,*R*)-**4** (entries 3 and 5).

2,3-Diamino-3-phenylpropanoic acid has been revealed as an alternative to the side chain of taxol for improving the water solubility of that anticancer drug.[9] Removal of the tosyl group from our product, 2,3-diamino ester, was crucial for the synthesis of free 2,3-diamino acids. We found that the tosyl group in 2,3-diamino ester can be easily removed by treatment with phenol in a refluxing solution of 33% HBr/AcOH, followed by addition of water and neutralization with propylene oxide to afford free (2*R*,3*R*)-2,3-diamino acid in 71% yield (Scheme 2).[14]



(2*R*,3*R*)-**6a** (2*R*,3*R*)-**8a**

Scheme 2.

It is well known that chiral amino alcohols are important building blocks for the synthesis of biologically-active molecules and have been extensively used in the asymmetrical reactions as a chiral auxiliary or ligand.[15] The asymmetric synthesis of 1,2-amino alcohols has been extensively reported.[15a,16] However, there have been few reports of asymmetric synthesis to 2,3-diamino alcohols, which may become precursors of new kinds of amino alcohol compounds. Using enantiomerically pure 2,3-diamino esters obtained using our procedure, chiral 2,3-dimino alcohols can be readily obtained by the reduction with $LiAlH_4$/THF at refluxing conditions in high yield as shown in Scheme 1.

In conclusion, we have provided a simple and practical route to 3-aryl-substituted enantiopure 2,3-diamino acid derivatives in good yield, which was started from a catalytic asymmetric reaction of readily available *N*-sulfonylimine and isocyanoacetate.

3. Experimental

A typical procedure for the preparation of *cis*-imidazoline **5c**: a mixture of Me_2SAuCl[17] (**3**, 9.97 mg, 0.034 mmol) and (*R*,*S*)-chiral ferrocenylphosphine[18] (**4**, 20.8 mg, 0.028 mmol) in CH_2Cl_2 (25 mL) was stirred for 15 min under nitrogen. To the solution, 1.95 g (5.77 mmol) of **1b**[19]and 0.66 g (5.87 mmol) of ethyl isocyanoacetate[20] **2**, were added. The mixture was stirred under nitrogen at 25°C for 20 h. After removal of the catalyst by filtration, the solvent was evaporated under vacuum to give a crude *cis*:*trans* (90:10) mixtures of 2-imidazoline. The *cis* isomer was isolated by column chromatography over silica gel eluting with petroleum ether:ethyl acetate:dichloromethane (4:2:1) to give 74% ee of *cis*-(4*R*,5*R*)-2-imidazoline in 78% yield. The optically pure *cis*-**5c** was obtained with 99% ee from the filtrate by the recrystallization in THF:*n*-hexane (16.5 mL:33 mL).

*3.1. (4*R,*5*R*)*-cis-*4-(Ethoxylcarbonyl)-5-phenyl-1*-N-*tosyl-2-imidazoline* ***5a***

Enantiomeric excess: 99% (determined by HPLC analysis using a Chiralpak AD column); mp 145–146°C; $[\alpha]_D^{20}$ −320 (*c* 1.00, THF); ^{1}H NMR ($CDCl_3$/TMS) δ 0.75 (t, 3H), 2.37 (s, 3H), 3.49–3.55 (m, 1H), 3.65–3.68 (m, 1H), 5.17 (s, 2H), 7.00 (d, *J*=7.10 Hz, 2H), 7.07–7.18 (m, 5H), 7.40 (d, *J*=8.19 Hz, 2H), 7.76 (s, 1H); 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.

*3.2. (4*R,*5*R*)*-cis-*4-(Ethoxylcarbonyl)-5-(4-chlorophenyl)-1*-N-*tosyl-2-imidazoline* ***5b***

Enantiomeric excess: 99% (determined by HPLC analysis using a Chiralcel OD column); mp 139–139.5°C; $[\alpha]_D^{20}$ −311 (*c* 1.00, THF); ^{1}H NMR ($CDCl_3$/TMS) δ0.80 (t, 3H), 2.39 (s, 3H), 3.54–3.77 (m, 2H), 5.11 (d, *J*=11.28 Hz, 1H),5.18 (d, *J*=11.28 Hz, 1H), 6.92 (d, *J*=8.32 Hz, 2H), 7.05 (d, *J*=8.32 Hz, 2H), 7.12 (d, *J*=8.06 Hz, 2H), 7.38 (d, *J*=8.06 Hz, 2H), 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.

*3.3. (4*S,*5*S*)*-cis-*4-(Ethoxylcarbonyl)-5-(4-chlorophenyl)-1*-N-*tosyl-2-imidazoline* ***5b***

Enantiomeric excess: 97% (determined by HPLC analysis using a Chiralcel OD column); mp 137–138°C; $[\alpha]_D^{20}$ +298 (*c* 0.99, THF); ^{1}H NMR ($CDCl_3$/TMS) δ 0.82 (t, 3H), 2.40 (s, 3H), 3.62–3.74 (m, 2H), 5.12 (d, *J*=11.36 Hz, 1H), 5.18 (d, *J*=11.36 Hz, 1H), 6.94 (d, *J*=8.53 Hz, 2H), 7.07 (d, *J*=8.53 Hz, 2H), 7.16 (d, *J*=8.34 Hz, 2H), 7.40 (d, *J*=8.34 Hz, 2H), 7.75 (d, *J*=1.90 Hz, 1H). Anal. calcd for $C_{19}H_{19}ClN_2O_4S$: C, 56.08; H, 4.70; N, 6.88. Found: C, 56.06; H, 4.76; N, 6.78.

*3.4. (4*R,*5*R*)*-cis-*4-(Ethoxylcarbonyl)-5-(4-bromophenyl)-1*-N-*tosyl-2-imidazoline* ***5c***

Enantiomeric excess: 99% (determined by HPLC analysis using a Chiralcel OD column); mp 143–143.5°C; $[\alpha]_D^{20}$ −274 (*c* 1.00, THF); ^{1}H NMR ($CDCl_3$/TMS) δ 0.82 (t, 3H), 2.41 (s, 3H), 3.59–3.77

(m, 2H), 5.11 (d, *J*=11.35 Hz, 1H),5.18 (d, *J*=11.35 Hz, 1H), 6.87 (d, *J*=8.39 Hz, 2H), 7.16 (d, *J*=8.21 Hz, 2H), 7.21 (d, *J*=8.39 Hz, 2H), 7.39 (d, *J*=8.21 Hz, 2H), 7.75 (s, 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.

3.5. *(4*S,*5*S*)*-cis-*4-(Ethoxylcarbonyl)-5-(4-bromophenyl)-1*-N-*tosyl-2-imidazoline* ***5c***

Enantiomeric excess: 99% (determined by HPLC analysis using a Chiralcel OD column); mp 142–143°C; $[\alpha]_D^{20}$ +272 (*c* 0.99, THF); ^1H NMR ($CDCl_3$/TMS) δ 0.82 (t, 3H), 2.40 (s, 3H), 3.62–3.75 (m, 2H), 5.11 (d, *J*=11.38 Hz, 1H), 5.19 (dd, J=11.38, 2.11 Hz, 1H), 6.87 (d, *J*=8.48 Hz, 2H), 7.16 (d, *J*=8.39 Hz, 2H), 7.21 (d, *J*=8.48 Hz, 2H), 7.39 (d, *J*=8.39 Hz, 2H), 7.75 (d, *J*=1.96 Hz, 1H). Anal. calcd for $C_{19}H_{19}BrN_2O_4S$: C, 50.56; H, 4.24; N, 6.20. Found: C, 50.56; H, 4.22; N, 6.04.

3.6. *(4*R,*5*R*)*-cis-*4-(Ethoxylcarbonyl)-5-(4-iodophenyl)-1*-N-*tosyl-2-imidazoline* ***5d***

Enantiomeric excess: 96% (determined by HPLC analysis using a Chiralcel OD column); mp 134–135°C; $[\alpha]_D^{20}$ −234 (*c* 1.00, THF); ^1H NMR ($CDCl_3$/TMS) δ 0.81 (t, 3H), 2.43 (s, 3H), 3.63–3.74 (m, 2H), 5.10 (d, *J*=11.12 Hz, 1H), 5.20 (d, *J*=11.12 Hz, 1H), 6.73 (d, *J*=8.10 Hz, 2H), 7.15 (d, *J*=8.10 Hz, 2H), 7.37–7.42 (m, 4H), 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.

3.7. *General procedure for the preparation of 2,3-diamino esters from the hydrolysis of 2-imidazolines*

Compound (4*R*,5*R*)-**5c** (500 mg) was treated with 3.5 mL of conc. HCl in 21 mL of EtOH at 60°C for 4 h. After removal of the EtOH, the residue was added to 20 mL CH_2Cl_2 and neutralized with solid $NaHCO_3$. The solution was dried by Na_2SO_4 and filtration by suction. The filtrate was concentrated and dried under vacuum to give (2*R*,3*R*)-2,3-diamino ester **6c** in quant yield (49% yield based on the *N*-sulfonylimine).

3.8. *Ethyl (2*R,*3*R*)-2-amino-3-(*N-*tosylamino)-3-phenylpropionate* ***6a***

Mp 89–90°C; $[\alpha]_D^{20}$ −25.2 (*c* 1.00, THF); ^1H NMR ($CDCl_3$/TMS) δ1.20 (t, 3H), 1.61 (br, NH), 2.31 (s, 3H), 3.74 (s, 1H), 4.00–4.09 (m, 2H), 4.88 (d, *J*=3.82 Hz, 1H), 6.11 (br, NH), 6.98–7.16 (m, 7H), 7.53 (d, *J*=8.30 Hz, 2H); MS *m/z* 362 (M^+, 100), 260 (36), 155 (34), 91 (62). Anal. calcd for $C_{18}H_{22}N_2O_4S$: C, 59.64; H, 6.11; N, 7.72. Found: C, 59.82; H, 5.86; N, 7.86.

3.9. *Ethyl (2*R,*3*R*)-2-amino-3-(*N-*tosylamino)-3-(4-chlorophenyl)propionate* ***6b***

Mp 107–108°C; $[\alpha]_D^{20}$ −24.6 (*c* 1.00, THF); ^1H NMR ($CDCl_3$/TMS) δ 1.20 (t, 3H), 1.75 (br, NH), 2.34 (s, 3H), 3.77 (s, 1H), 4.03–4.08 (m, 2H), 4.87 (s, 1H), 6.04 (br, NH), 6.93 (d, *J*=8.34 Hz, 2H), 7.05–7.09 (m, 4H), 7.50 (d, *J*=8.15 Hz, 2H); MS *m/z* 396 (M^+, 8), 323 (0.5), 294(93), 155(91), 102(18), 91(100). Anal. calcd for $C_{18}H_{21}N_2O_4SCl$: C, 54.47; H, 5.33; N, 7.06. Found: C, 54.54; H, 5.35; N, 6.97.

3.10. Ethyl (2S, 3S)-2-amino-3-(N-tosylamino)-3-(4-chlorophenyl)propionate **6b**

Mp 105–106°C; $[\alpha]_D^{20}$ +22.6 (*c* 1.00, THF); ^{1}H NMR ($CDCl_3$/TMS) δ 1.12 (t, 3H), 1.60 (br, NH), 2.27 (s, 3H), 3.73 (s, 1H), 3.97–4.00 (m, 2H), 4.78 (s, 1H), 6.05 (br, NH), 6.86 (d, *J*=8.30 Hz, 2H), 6.97–7.02 (m, 4H), 7.20 (d, J=8.10 Hz, 2H). Anal. calcd for $C_{18}H_{21}N_2O_4SCl$: C, 54.47; H, 5.33; N, 7.06. Found: C, 54.52; H, 5.09; N, 6.81.

3.11. Ethyl (2R,3R)-2-amino-3-(N-tosylamino)-3-(4-bromophenyl)propionate **6c**

Mp 91–92°C; $[\alpha]_D^{20}$ −21.4 (*c* 1.00, THF); ^{1}H NMR ($CDCl_3$/TMS) δ 1.22 (t, 3H), 1.78 (br, NH), 2.35 (s, 3H), 3.75 (s, 1H), 4.00–4.11 (m, 2H), 4.84 (s, 1H), 6.15 (br, NH), 6.86 (d, *J*=8.32 Hz, 2H), 7.07 (d, *J*=8.14 Hz, 2H), 7.20 (d, *J*=8.32 Hz, 2H), 7.48 (d, *J*=8.14 Hz, 2H); MS *m/z* 396 (M^+, 8), 323 (0.5), 294 (93), 155 (91), 102 (18), 91 (100). Anal. calcd for $C_{18}H_{21}N_2O_4SBr$: C, 48.98; H, 4.79; N, 6.34. Found: C, 49.02; H, 4.77; N, 6.38.

3.12. Ethyl (2S,3S)-2-amino-3-(N-tosylamino)-3-(4-bromophenyl)propionate **6c**

Mp 89–90°C; $[\alpha]_D^{20}$ +20.2 (*c* 1.00, THF); ^{1}H NMR ($CDCl_3$/TMS) δ 1.13 (t, 3H), 1.75 (br, NH), 2.28 (s, 3H), 3.70 (s, 1H), 3.97–4.00 (m, 2H), 4.78 (s, 1H), 6.05 (br, NH), 6.79 (d, *J*=8.30 Hz, 2H), 7.00 (d, *J*=8.2 Hz, 2H), 7.13 (d, *J*=8.30 Hz, 2H), 7.42 (d, *J*=8.20 Hz, 2H). Anal. calcd for $C_{18}H_{21}N_2O_4SBr$: C, 48.98; H, 4.79; N, 6.34. Found: C, 48.85; H, 4.47; N, 6.15.

3.13. Ethyl (2R,3R)-2-amino-3-(N-tosylamino)-3-(4-iodophenyl)propionate **6d**

Mp 112–113°C; $[\alpha]_D^{20}$ −19.2 (*c* 1.00, THF); ^{1}H NMR ($CDCl_3$/TMS) δ 1.23 (t, 3H), 1.61 (br, NH), 2.37 (s, 3H), 3.73 (s, 1H), 4.01–4.10 (m, 2H), 4.83 (s, 1H), 6.11 (br, NH), 6.73 (d, *J*=8.23 Hz, 2H), 7.07 (d, *J*=8.14 Hz, 2H), 7.40 (d, *J*=8.14 Hz, 2H), 7.48 (d, *J*=8.23 Hz, 2H); MS *m/z* 488 (M^++1, 6), 386 (6), 155 (46), 91 (100). Anal. calcd for $C_{18}H_{21}N_2O_4SI$: C, 44.27; H, 4.33; N, 5.73. Found: C, 44.48; H, 4.39; N, 5.55.

3.14. General reduction procedure with $LiAlH_4$ as follows

Compound (2*R*,3*R*)-**6c** (380 mg) was dissolved in 3 mL THF, and added dropwise to a mixture of 65 mg $LiAlH_4$ in 2 mL of THF at 0°C while stirring. The mixture was refluxed for 5 h, and hydrolyzed at 0°C by slow, successive addition of 0.4 mL H_2O, 0.4 mL 15% NaOH aqueous and 0.8 mL H_2O. The precipitates formed were removed by filtration and washed with a mixture of EtOH:conc. HCl (20:1). The filtrate was concentrated and neutralized with 5% aq. $NaHCO_3$ to form a white solid. The white solid was obtained by filtration, washed with water and Et_2O, and dried under vacuum to give 278 mg of (2*R*,3*R*)-**7c** in an 81% yield.

3.15. (2R,3R)-2-Amino-3-(N-tosylamino)-3-phenylpropanol **7a**

83% Yield; $[\alpha]_D^{20}$ −4.1 (*c* 1.00, EtOH in 0.1 ml conc. HCl); ^{1}H NMR (DMSO-d_6) δ 2.28 (s, 3H), 2.84 (m, 1H), 3.10 (m, 2H), 3.32 (br, OH), 4.27 (d, *J*=5.91 Hz, 1H), 7.10–7.17 (m, 7H), 7.44 (d, *J*=8.27 Hz, 2H); MS *m/z* 320 (M^++1, 4), 260 (1), 155 (6), 91 (36). HRMS calcd for ($C_{15}H_{17}N_2SO_3$, M^+-CH_3): 305.0959; found 305.0938.

3.16. (2R,3R)-2-Amino-3-(N-tosylamino)-3-(4-chlorophenyl)propanol **7b**

85% Yield; $[\alpha]_D^{20}$ −3.2 (*c* 1.00, EtOH in 0.1 mL conc. HCl); ^{1}H NMR (DMSO-d_6) δ 2.30 (s, 3H), 2.84 (m, 1H), 3.10 (m, 2H), 3.33 (br, OH), 4.25 (d, J=5.87 Hz, 1H), 7.07–7.17 (m, 6H), 7.42 (d, *J*=7.96 Hz, 2H); MS *m/z* 354 (M^++1, 20), 294 (1), 155 (6). HRMS calcd for ($C_{16}H_{20}N_2ClSO_3$, M^++1): 355.0883; found 355.0896.

3.17. (2R,3R)-2-Amino-3-(N-tosylamino)-3-(4-bromophenyl)propanol **7c**

81% Yield; $[\alpha]_D^{20}$ −3.7 (*c* 0.97, EtOH in 0.1 mL conc. HCl); ^{1}H NMR (DMSO-d_6) δ 2.31 (s, 3H), 2.84 (m, 1H), 3.10 (m, 2H), 3.32 (br, OH), 4.24 (d, J=5.84 Hz, 1H), 7.02 (d, *J*=8.35 Hz, 2H), 7.15 (d, J=8.13 Hz, 2H), 7.27 (d, J=8.35 Hz, 2H), 7.41 (d, *J*=8.13 Hz, 2H); MS *m/z* 399 (M^++1, 1), 155 (6), 91 (36). HRMS calcd for ($C_{16}H_{20}N_2BrSO_3$, M^++1): 399.0378; found 399.0377.

3.18. (2R,3R)-3-Phenyl-2,3-diamino acid **8a**

71% Yield; mp 192–193°C (dec.); $[\alpha]_D^{20}$ −8.0 (c 0.65, 6 N HCl); ^{1}H NMR (300 MHz/D_2O) δ 3.91 (d, *J*=7.00 Hz, 1H), 4.53 (d, *J*=7.00 Hz, 1H), 7.43–7.55 (m, 5H); ^{13}C NMR (300 MHz/D_2O) δ 58.9, 61.1, 130.1, 131.9, 138.1, 177.7; FAB-MS 181 (M^++1), 164 (M^+−16), 148 (M^+−32).

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References

1. (a) Wang, M.; Gould, S. J. *J. Org. Chem*. **1993**, *58*, 5176. (b) Rane, D. F.; Girijavallabhan, V. M.; Ganguly, A. K.; Pike, R. E.; Saksena, A. K.; McPhall, A. T. *Tetrahedron Lett*. **1993**, *34*, 3201. (c) Baldwin, J. E.; Adlington, R. M.; Birch, D. J. *Tetrahedron Lett*.**1985**, *26*, 5931. (d) Baldwin, J. E.; Adlington, R. M.; Birch, D. J. *J. Chem. Soc., Chem. Commun*. **1985**, 256. (e) Pfammatter, E.; Seebach, D. *Liebigs. Ann. Chem*. **1991**, 1323. (f) Webber, S. E.; Okano, K.; Little, T. L.; Reich, S. H.; Xin, Y.; Fuhrman, S. A.; Matthews, D. A.; Love, R. A.; Hendrickson, T. F.; Patick, A. K.; Meador, J. M.; Ferre, R. A.; Brown, E. L.; Ford, C. E.; Binford, S. L.; Worland, S. T. *J. Med. Chem*. **1998**, *41*, 2786 and references cited therein.
2. (a) Martin, J. H.; Hausmann, W. K. *J. Am. Chem. Soc*. **1960**, *82*, 2079. (b) Inoue, M.; Hitomi, H.; Mizuno, K.; Fujino, M.; Miyake, A.; Nakazawa, K.; Shibata, M.; Kanzaki, T. *Bull. Chem. Soc. Jpn*. **1960**, *33*, 1014. (c) Fujino, M.; Inoue, M.; Veyanagi, J.; Miyake, A. *Bull. Chem. Soc. Jpn*. **1961**, *34*, 740. (d) Inoue, M. *Bull. Chem. Soc. Jpn*. **1961**, *34*, 885. (e) Inoue, M. *Bull. Chem. Soc. Jpn*. **1962**, *35*, 1556. (f) Fujino, M.; Inoue, M.; Ueyangi, J.; Miyake, A. *Bull. Chem. Soc. Jpn*. **1965**, *38*, 515. (g) Uchida, L.; Shigematsu, N.; Ezaki, M.; Hashimoto, M. *Chem. Pharm. Bull*. **1985**, *33*, 3053.
3. Palomo, C.; Aizpurua, J. M.; Cabre, F.; Cuevas, C.; Munt, S.; Odriozola, J. M. *Tetrahedron Lett*. **1994**, *35*, 2725.
4. Dunn, P. J.; Haner, R.; Rapoport, H. *J. Org. Chem*. **1990**, *55*, 5017.
5. Merino, P.; Lanaspa A.; Merchan, F. L.; Tejero, T. *Tetrahedron: Asymmetry* **1998**, *9*, 629.
6. (a) Nakamura, Y.; Shin, C. *Chem. Lett*. **1992**, 49. (b) Nakamura, Y.; Hirai, M.; Tamotsu, K.; Yonezawa, Y.; Shin, C. *Bull. Chem. Soc. Jpn*. **1995**, *68*, 1369. (c) Schmidt, U.; Mundinger, K.; Mangold, R.; Lieberknecht, A. *J. Chem. Soc., Chem. Commun*. **1996**, 1216. (d) Schmidt, U.; Mundinger, K.; Riedi, B.; Haas, G.; Lau, Palomo, C. *Synthesis* **1992**, 1201.
7. Han, H.; Yoon, J.; Janda K. D. *J. Org. Chem*. **1998**, *63*, 2045.
8. Alker, D.; Harwood, L. M.; Williams, C. E. *Tetrahedron Lett*. **1998**, *39*, 475.
9. Moyna, G.; Williams, H. J.; Scott, A. I. *Synth. Commun*. **1997**, *27*, 156.

10. Kuwano, R.; Okuda, S.; Ito, Y. *Tetrahedron: Asymmetry* **1998**, *9*, 2774.
11. Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc*. **1986**, *108*, 6405.
12. Hayashi, T.; Kishi, E.; Soloshonok, V. A.; Uozumi, Y. *Tetrahedron Lett*. **1996**, *37*, 4969.
13. Zhou, X.-T.; Lin, Y.-R.; Dai, L.-X.; Sun, J.; Xia, L.-J.; Tang, M.-H. *J. Org. Chem*. **1999**, *64*, 1331.
14. Jefford, C. W.; McNulty, J. *Helv. Chim. Acta*. **1994**, *77*, 2142.
15. (a) Ager D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev*. **1996**, *96*, 835. (b) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl*. **1991**, 49.
16. (a) Masui, M.; Shioiri, T. *Tetrahedron Lett*. **1998**, *39*, 5195. (b) Masui, M.; Shioiri, T. *Tetrahedron Lett*. **1998**, *39*, 5199. (c) Kim, B. M.; Bae, S. J.; Seomoon, G. *Tetrahedron Lett*. **1998**, *39*, 6921. (d) Laib, T.; Ouazzani, J.; Zhu, J. *Tetrahedron: Asymmetry* **1998**, *9*, 169 and references cited therein. (e) Reddy, K. L.; Sharpless, K. B. *J. Am. Chem. Soc*. **1998**, *120*, 1207 and references cited therein.
17. Bonati, F.; Minghetti, G. *Gazz. Chim. Ital*. **1973**, *103*, 373.
18. Hayashi, T.; Yamazaki, A. *J. Organomet. Chem*. **1991**, *413*, 295.
19. Love, B. E.; Raje, P. S.; Williams II, T. C. *Synlett*, **1994**, 493. (b) Jennings, W. B.; Lovely, C. T. *Tetrahedron Lett*. **1988**, *29*, 3725.
20. Hartman, G. D.; Weinstock, L. M. *Org. Synth*. **1988**, *6*, 620.