RING OPENING OF OPTICALLY ACTIVE *CIS*-DISUBSTITUTED AZIRIDINO ALCOHOLS: AN ENANTIODIVERGENT SYNTHESIS OF FUNCTIONALIZED AMINO ALCOHOL DERIVATIVES#

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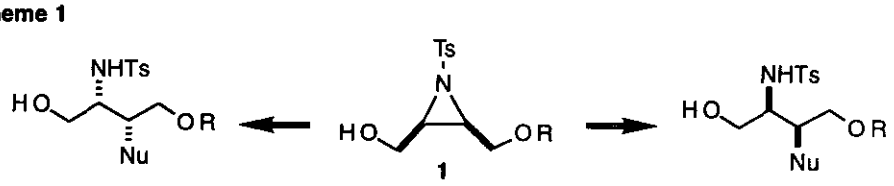
Abstract-Ring-opening reactions of optically active *cis*-disubstituted aziridino alcohols have been investigated. Regio- and stereo-selective ring opening took place with internal and external nucleophiles. Unusual amino acids derivatives (**14**) and (**15**), the key synthetic intermediates for bestatin and related peptides, have been prepared.

Ring opening of aziridines has been extensively studied since it provides a convenient entry to stereoselective preparation of functionalized amino compounds which have great potential and versatility as chiral building blocks, auxiliaries, and ligands.[1] This paper focuses on ring opening of optically active *cis*-disubstituted aziridino alcohols.[2] The characteristic feature of the reaction is its enantiodivergency (Scheme 1). Due to the hidden symmetric nature of **1**, both enantiomers of amino alcohol derivatives are obtainable from **1** simply by controlling the regiochemistry of alcohol-protection. Ring-opening reactions of **1** by intramolecular and intermolecular nucleophilic attack and its application to the synthesis of biologically active peptides are described.[3]

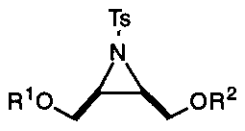
Scheme 1



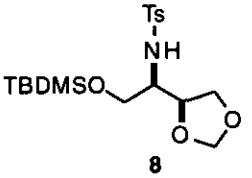
Intramolecular Ring Opening of Aziridines

Optically active (≥95% ee) aziridine (**2**) was obtained by enzymatic transesterification of **3**.[4] Silylation of **2** with *tert*-butyldimethylsilyl (TBDMS) chloride followed by removal of acetyl group afforded **4** in 94% yield. Treatment of **4** with formaldehyde in the presence of cesium carbonate furnished **8** as a sole product in 88% yield *via* nucleophilic attack of the hydroxide anion of the hemiacetal formed *in situ*.[5] On treatment with bases, **4** was converted into epoxide (**9**) *via* intramolecular S_N2 displacement by the hydroxide anion. Bases such as BnOLi, *t*-BuOLi, and *n*-BuLi were effective for the transformation of **4**, affording **9** in 88, 71, and 68% yield, respectively. Ring opening with nitrogen nucleophile was also accomplished. Aziridino alcohol (**5**) was first converted to the benzylurethane derivative (**6**) on treatment with benzyl isocyanate, which was then treated with *t*-BuOK to yield the cyclic urethane (**10**) in 74% overall yield.[6] Formation of a five-membered ring rather than a six-membered one was evident from its ir spectrum [ν_{max} ($CHCl_3$) 1745 cm^{-1}]. Thus, regio- and stereo-controlled ring-opening of aziridino alcohols (**4**) and (**5**) was achieved with internal oxygen- and nitrogen-nucleophiles. Compounds (**8**) and (**9**) can be used as chiral building blocks for the synthesis of unusual amino acids derivatives which contain *threo* β-amino alcohol moiety (*vide infra*).

Next we investigated enantiodivergency of the present process. Optically active aziridine (**7**), the enantiomer of **5**, was prepared from **2** in 89% overall yield through the following sequence: i) ethoxyethylation of the hydroxy group of **2**, ii) hydrolysis of the acetate, iii) silylation of the resulting alcohol, and iv) removal of the ethoxyethyl group. Successful preparation of an enantiomeric pair (**5** and **7**) assures the enantiodivergency of the process. For example, **11**, the enantiomer of **10**, was obtained from



2 : R^1=H, R^2=Ac
3 : R^1= R^2=Ac
4 : R^1=TBDMS, R^2=H
5 : R^1=TBDPS, R^2=H
6 : R^1=TBDPS, R^2=CONHBn
7 : R^1=H, R^2=TBDPS



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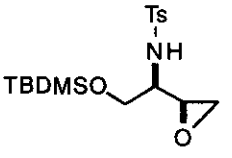

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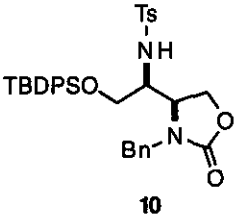

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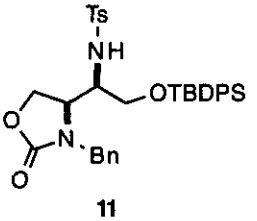

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7 in 82% yield through the same procedure as employed for the transformation of **5** to **10**. Enantiomeric pair of the chiral diamine derivatives (**10**) and (**11**), is expected to be potentially useful chiral ligands in asymmetric synthesis.[7]

Intermolecular Ring Opening of Aziridines

Ring-opening of **4** *via* intermolecular nucleophilic attack was examined with a variety of nucleophiles. Nitrogen-, chlorine-, carbon-, and sulfur-nucleophiles were effective. The results are compiled in Table 1. Reaction of **4** with aniline without catalyst afforded the ring-opened products, (**12a**) and (**13a**), in 54% and 23% yield, respectively (entry 1). Use of the corresponding lithium amide gave better regio-selectivity in the ring-opening reaction, though chemical yield was decreased (entry 2). Both sodium azide and trimethylsilyl azide showed poor regioselectivity (~2:1) in the reaction with **4** (entries 3 and 4). Introduction of chlorine was achieved with high regioselectivity using diethylaluminum chloride, affording **12c** in 41% yield (entry 5). Reactions of lithium phenylacetylide and lithium phenylthiolate with **4** furnished **12d** and **12e**, respectively, in a highly regioselective manner (entries 6 and 7). Generally, organolithium and organoaluminum reagent showed high regioselectivity. These observations suggest that the ring-opening reactions proceed *via* initial coordination of the reagent with the hydroxy group of **4**,[8] followed by intramolecular delivery of the nucleophile to the proximal carbon center. Slight decrease in the regioselectivity in the presence of HMPA (entry 8) is compatible with the rationale.

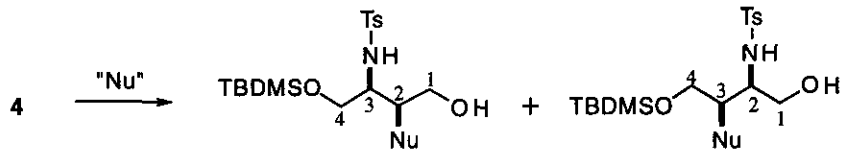


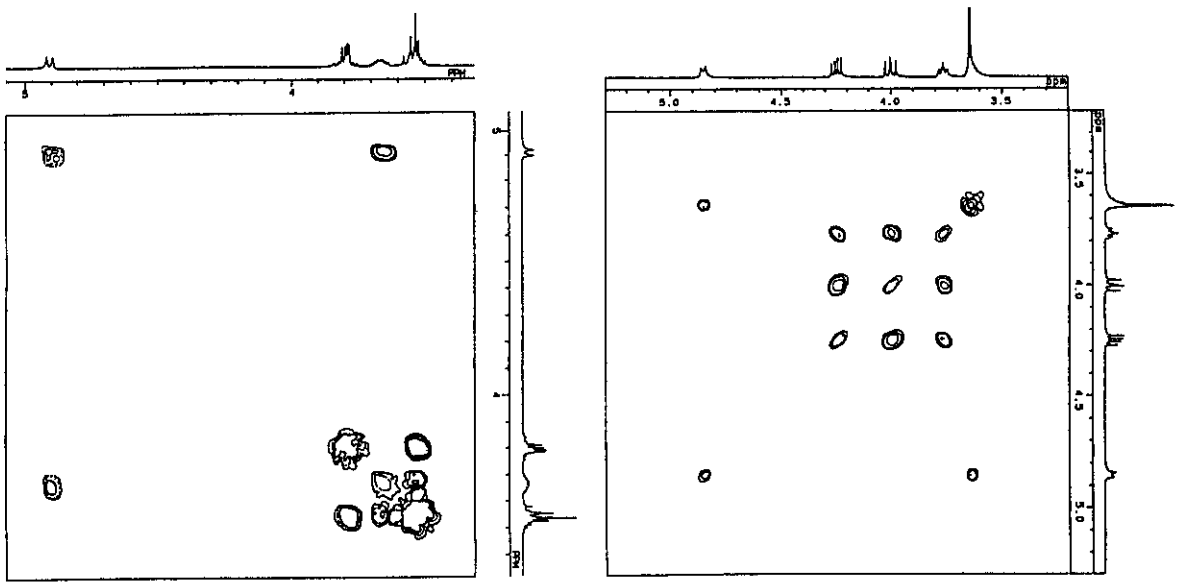
Table 1. Nucleophilic Ring Opening of **4**

entry	Nu	conditions	products (yield, %)
1	PhNH	$PhNH_2$, naet, room temperature, 4 days	**12a** (54), **13a** (23)
2	PhNH	$PhNH_2$, *n*-BuLi, THF, room temperature, overnight	**12a** (43), **13a** (7)
3	N_3	NaN_3, DMF, 50 °C, 2 h	**12b** (60), **13b** (27)
4	N_3	$TMSN_3$, EtOH, DMF, 80 °C, 6 h	**12b** (45), **13b** (22)
5	Cl	Et_2AlCl, CH_2Cl_2, reflux, 2 days	**12c** (41)[a], **13c** *b*
6	Ph-C≡C	Ph-C≡CH, *n*-BuLi, THF, room temperature, 4 h	**12d** (62), **13d** (<8)
7	PhS	PhSH, *n*-BuLi, THF, 0 °C, 30 min	**12e** (81), **13e** (2)
8	PhS	PhSH, *n*-BuLi, THF, HMPA, 0 °C, 30 min	**12e** (87), **13e** (10)

a) 20% of **4** was recovered. b) Not detected.

Structural determination of the regioisomers (**12**) and (**13**) was accomplished by investigation of their ^{1}H-^{1}H COSY spectra. For example, in the case of **12e** (Figure 1a), methylene protons (δ 3.51~3.58, m) adjacent to the methine bearing a TsNH group were readily distinguished from the methylene protons (δ 3.78, 3.82, two dd) adjacent to the SPh-bearing methine based on their correlations with the characteristic TsN*H* signals (δ 4.91, br d). In the acetate of **12e** (Figure 1b), the former methylene protons appeared at

Figure 1. ^{1}H-^{1}H COSY spectra of **12e** and the acetate of **12e**.



(a) ^{1}H-^{1}H COSY spectrum of **12e**.

(b) ^{1}H-^{1}H COSY spectrum of the acetate of **12e**.

Table 2. Selected ^{1}H-nmr chemical shifts of **12**, **13** and their acetates[a]

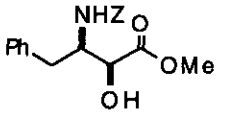
entry	compound	C_1-H	C_1-H (acetate)[b]	Δδ C_1-H[c]	C_4-H	C_4-H (acetate)[d]	Δδ C_4-H[e]
1	**12b**	3.68, 3.72	4.01[f]	0.33, 0.29	3.37, 3.41	3.41, 3.52	0.04, 0.11
2	**12c**	3.75, 3.84	3.93, 4.16	0.18, 0.32	3.31, 3.47	3.49, 3.59	0.18, 0.12
3	**12d**	3.75, 3.81	3.77, 4.16	0.02, 0.35	3.44, 3.55	3.59, 3.70	0.15, 0.15
4	**12e**	3.78, 3.82	4.00, 4.25	0.22, 0.43	3.55[f]	3.63[f]	0.08
5	**13a**	3.16, 3.73[f]	4.06, 4.25	0.90, 0.52	3.73[f], 3.99	3.73[f]	0.0, -0.26

a) 400 or 200 MHz ^{1}H-nmr measured in $CDCl_3$. Chemical shifts are expressed by ppm downfield from tetramethylsilane as an internal standard (δ-value). b) Chemical shift of C_1-H of the corresponding acetate. c) δ (C_1-H (acetate)) - δ (C_1-H) ppm. d) Chemical shift of C_4-H of the corresponding acetate. e) δ (C_4-H (acetate)) - δ (C_4-H) ppm. Negative values indicate high field shift. f) Chemical shift of the center of the multiplet signal.

δ 3.60~3.66 (m) and the latter at δ 4.00 (dd) and 4.25 (dd). Acetylation caused < 0.1 ppm down-field shift in the former methylene protons whereas 0.22~0.43 ppm down-field shift was observed in the latter. These observations indicate that the methylene group adjacent to the SPh-bearing methine has hydroxy group as a substituent. Accordingly, the structure of **12e** was determined as shown. In a similar manner, regioisomeric structures of **12a-d** and **13a-d** were determined. Selected ^{1}H-nmr data of methylene protons of **12, 13** and their acetates are shown in Table 2.

Synthesis of Intermediates for Biologically Active Peptides

We have shown that optically active *threo* β-amino alcohol derivatives such as **8** and **9** could be prepared by the ring opening of **4**. Besides, the process was proved to be essentially enantiodivergent. The present strategy was applied to the synthesis of biologically active peptides. As target molecules, we chose a pseudo-enantiomeric pair of *threo* β-amino alcohol derivatives, methyl (2*S*, 3*R*)-3-{*N*-(benzyloxycarbonyl)amino}-2-hydroxy-4-phenylbutanoate (**14**) and (3*S*, 4*S*)-4-{*N*-(*tert*-butoxycarbonyl)amino}-3-hydroxy-5-phenylpentanoic acid [(3*S*, 4*S*)-Boc-AHPPA] (**15**). Compound (**14**) is a key synthetic intermediate for bestatin[9b,d] which is a specific inhibitor of aminopeptidase B and is known to show antitumor activity through activation of immune system.[9c] Another *threo* β-amino alcohol derivative (**15**) is a key synthetic intermediate for the potent pepsin-inhibitory peptide.[10a] AHPPA is also a constituent of the potent renin-inhibitor, ahpatinin G.[10b,11]



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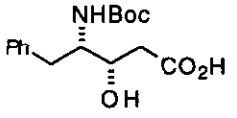

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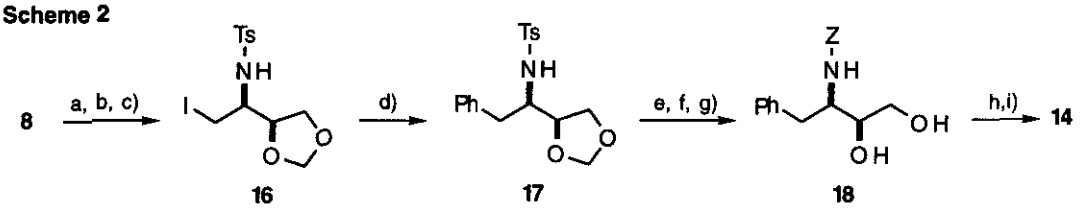
Synthesis of **14** started with **8** (Scheme 2). The OTBDMS group of **8** was converted into iodine in 80% yield through a three-step sequence involving removal of the silyl protecting group, tosylation, and substitution with an iodide ion. Treatment of **16** with diphenylcopperlithium afforded **17** in a high yield. Conversion of **17** to **18** was accomplished by removing the tosyl group and the methylene acetal of **17**, followed by benzyloxycarbonylation of the resulting dihydroxy amine. Selective oxidation of the primary hydroxyl group of **18** in the presence of the secondary one was achieved by means of molecular oxygen

oxidation catalyzed by platinum oxide.[12] Esterification of the resulting α-hydroxy acid afforded a 75% yield of **14**, mp 99-100 °C, $[\alpha]_{577}$ + 83° (*c* 0.74, MeOH) {*lit.*,[9d] mp 94-95 °C and $[\alpha]_{578}$ + 82° (*c* 0.81, MeOH)}. The spectral data were identical with those reported.[9d]

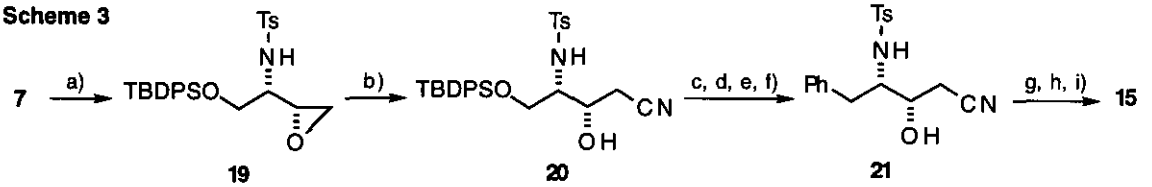
Scheme 2



a) Bu_4NF / THF, b) TsCl / Py, c) NaI / acetone, 80% (3 steps), d) Ph_2CuLi / THF, 97%, e) Na / NH_3, f) HBr / MeOH, g) Z-Cl, $NaHCO_3$ / MeOH-H_2O, 71% (3 steps), h) O_2, PtO_2 / H_2O, i) CH_2N_2 / THF, 75% (2 steps)

Synthesis of **15** utilized the aziridine-epoxide conversion (Scheme 3). Aziridino alcohol (**7**) was treated with *t*-BuOLi to afford epoxide (**19**) in 95% yield. Nucleophilic ring opening of **19** by a cyanide ion with the aid of lithium perchlorate[13] proceeded regioselectively to give **20** in 95% yield. Conversion of the OTBDPS group into a phenyl group was performed by the four-step sequence similar to that employed for the conversion of **8** to **17**, affording **21** in 55% overall yield. Hydrolysis of the cyano group of **21**, and removal of the tosyl group followed by *t*-butoxycarbonylation furnished **15**, mp 147-149 °C, $[\alpha]_D^{20}$ - 39° (*c* 0.38, MeOH) {*lit.*,[10a] mp 148-148.5 °C, $[\alpha]_D^{20}$ - 37° (*c* 1.1, MeOH)}. The spectral data were identical with thosereported.[10a]

Scheme 3



a) *t*-BuOLi / HMPA-THF, 95%, b) KCN, $LiClO_4$, / MeCN, 95%, c) Bu_4NF / THF, d) TsCl / Py, e) NaI / acetone, f) Ph_2CuLi / THF, 55% (4 steps), g) NaOH / H_2O_2 -H_2O, h) Na / NH_3, i) $(Boc)_2O$, NaOH / dioxane-H_2O, 40% (3 steps)

ACKNOWLEDGEMENT

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EXPERIMENTAL SECTION

General. Melting points were measured using a Yanagimoto Micro Melting Point Apparatus and were uncorrected. Nmr spectra were obtained with a Varian Gemini 200 (200 MHz) or a JEOL JNM-GX400 (400 MHz) or JEOL JNM-A400 (400 MHz) spectrometer, chemical shifts being given in ppm units (tetramethylsilane or chloroform as internal standards, indicating 0 or 7.24 ppm, respectively). Ir spectra were recorded with a JACSO A-202 or a PERKIN ELMER 1720-X diffracting grating infrared spectrophotometer. Specific rotation was measured with a Horiba SEPA-200 automatic digital polarimeter or Perkin-Elmer Model 241 polarimeter. Mass spectra were recorded with a JEOL JMS-DX300 mass spectrometer. Tlc analyses and preparative tlc were performed on commercial glass plates bearing 0.25-mm layer and 0.5-mm layer of Merck Kiesel-gel 60 F_{254}, respectively. Silica gel column chromatography was carried out with Wakogel C-200 or Nacalai tesque silica gel 60 (150-325 mesh). Tetrahydrofuran (THF), ether, and toluene were distilled over benzophenone ketyl before each use. Dichloromethane, acetonirile, and hexamethyphophoric triamide (HMPA) were distilled from calcium hydride. Dimethylformamide (DMF) was distilled from phosphorous pentoxide under reduced pressure.

(2*S*, 3*R*)-2-*tert*-Butyldimethylsilyloxymethyl-3-hydroxymethyl-*N*-tosylaziridine (4) : To a solution of **2** (745 mg, 2.5 mmol) in dichloromethane (25 ml) cooled at 0 °C, were added triethylamine (1.0 ml, 7.2 mmol), *t*-butyldimethylsilyl chloride (0.90 g, 6.0 mmol), and 4-dimethylaminopyridide (30 mg, 0.25 mmol). After stirring at room temperature for 1 h, the mixture was poured into water and extracted with ether. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was dissolved in methanol (25 ml) and treated with potassium carbonate (414 mg, 3.0 mmol) at 0 °C for 15 min. The mixture was poured into water and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 3) to afford **4** (867 mg, 94% yield) as a colorless oil: $[\alpha]_D^{22}$ - 12.2° (*c* 1.4, $CHCl_3$); ^{1}H-nmr (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.8 Hz, 2H), 3.89 (dd, *J* = 11.7, 5.9 Hz, 1H), 3.74 (dd, *J* = 12.1, 5.9 Hz, 1H), 3.66 (dd, *J* = 12.1, 6.2 Hz, 1H), 3.61 (dd, *J* = 11.4, 6.6 Hz, 1H),

3.13~3.04 (m, 2H), 2.44 (s, 3H), 0.84 (s, 9H), 0.023 (s, 3H), 0.019 (s, 3H); ir ($CHCl_3$) ν 3500, 3030, 2950, 2850, 1600, 1470, 1330, 1090, 840, cm^{-1}. Anal. Calcd for $C_{17}H_{29}NO_4SSi$: C, 54.95; H, 7.87; N, 3.77. Found: C, 54.67; H, 8.06; N, 3.73.

(2*S*, 3*R*)-2-*tert*-Butyldiphenylsilyloxymethyl-3-hydroxymethyl-*N*-tosylaziridine (5): To a solution of **2** (198 mg, 0.66 mmol) in DMF (2 ml) cooled at 0 °C, were added imidazole (54 mg, 0.79 mmol) and *t*-butyldiphenyllsilyl chloride (0.20 ml, 0.77 mmol). After stirring for 30 min, the mixture was poured into water and extracted with ether. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. Four fifths of the residue was dissolved in methanol (2.5 ml) and treated with potassium carbonate (76 mg, 0.55 mmol) at 0 °C for 15 min. The mixture was poured into water and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 3) to afford **5** (215 mg, 93% yield) as a colorless oil: $[\alpha]_D^{19}$ - 23 ° (*c* 0.95, $CHCl_3$); ^{1}H-nmr (200 MHz) δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.60~7.24 (m, 12H), 4.59 (qd, *J* = 6.0, 5.5 Hz, 1H), 3.70 (d, *J* = 5.5 Hz, 2H), 3.62~3.19 (m, 6H), 3.18~3.04 (m, 2H), 2.38 (s, 3H), 1.14 (dd, *J* = 5.5, 2.9 Hz, 3H), 1.07 (t, *J* = 7.4 Hz, 3H), 0.97 (s, 9H); ir ($CHCl_3$) ν 3080~2860, 1730, 1600, 1430, 1330, 1240, 1160, 1140, 1110, 1090, 1055, 945, 700 cm^{-1}. Anal. Calcd for $C_{31}H_{41}NO_5SSi$: C, 65.57; H, 7.28; N, 2.47. Found: C, 65.50; H, 7.42; N, 2.41.

(2*S*, 3*R*)-3-Benzylcarbamoyloxymethyl-2-*tert*-butyldiphenylsilyloxymethyl-*N*-tosylaziridine (6): To a solution of **5** (130 mg, 0.26 mmol) in toluene (1.3 ml), were added *N,N*-diisopropylethylamine (68 μl, 0.39 mmol) and benzyl isocyanate (34 μl, 0.31 mmol). After stirring 4 h at 50 °C, the mixture was warmed at 80 °C and stirred for additional 4 h. The mixture was poured into water and extracted with ether. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 4) to afford **6** (134 mg, 85% yield) as a colorless oil: ^{1}H-Nmr (200 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.61~7.20 (m, 17H), 4.78 (bt, *J* = 5.8 Hz, 1H), 4.29 (d, *J* = 5.9 Hz, 2H), 4.19 (dd, *J* = 12.0, 4.3 Hz, 1H), 3.92 (dd, *J* = 12.2, 7.0 Hz, 1H), 3.76 (dd, *J* = 11.6, 6.3 Hz, 1H), 3.66 (dd, *J* = 11.6, 5.2 Hz, 1H), 3.20~3.10 (m, 2H), 2.31 (s, 3H), 0.98 (s, 9H). Anal. Calcd for $C_{35}H_{40}N_2O_5SSi$: C, 66.85; H, 6.41; N, 4.45. Found: C, 66.38; H, 6.51; N, 4.39.

(2*R*, 3*S*)-2-*tert*-Butyldiphenylsilyloxymethyl-3-hydroxymethyl-*N*-tosylaziridine (7): A solution of **2** (2.00 g, 6.8 mmol) in dichloromethane (20 ml) was treated with ethyl vinyl ether (6.50 ml, 68

mmol) and *p*-toluenesulfinic acid (~2 mg) overnight at room temperature. The reaction mixture was poured into saturated aq $NaHCO_3$ solution and extracted with ethyl acetate. The organic phase was washed with saturated NaCl aq solution, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (twice, ethyl acetate : hexane = 1 : 2, then dichloromethane) to afford (2*R*, 3*S*)-2-acetoxymethyl-3-(1-ethoxyethyloxymethyl)-*N*-tosylaziridine (2.50 g, quant) as a colorless oil: $[\alpha]_D^{19}$ - 25° (*c* 1.7, $CHCl_3$); ^{1}H-nmr (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 4.66 (quint., *J* = 5.5 Hz, 1H), 4.21 (ddd, *J* = 12.1, 4.8, 3.5 Hz, 1H), 4.01 (ddd, *J* = 12.1, 7.3, 2.8 Hz, 1H), 3.60 (d, *J* = 5.9 Hz, 1H), 3.60 (ddd, *J* = 92.9, 11.0, 5.9 Hz, 1H), 3.53 (qdd, *J* = 7.0, 4.8, 4.8 Hz, 1H), 3.38 (qdd, *J* = 9.5, 7.0, 2.2 Hz, 1H), 3,17~3.07 (m, 2H), 2.45 (s, 3H), 1.92 (d, *J* = 3.3 Hz, 3H), 1.22 (dd, *J* = 8.3, 5.5 Hz, 3H), 1.15 (dt, *J* = 7.0, 1,1 Hz, 3H); ir ($CHCl_3$) ν 3030, 2980, 2930, 1740, 1600, 1440, 1370, 1330, 1160, 1130, 1090, 1040 cm^{-1}. Aanl. Calcd for $C_{17}H_{25}NO_6S$: C, 54.97; H, 6.78; N, 3.77. Found: C, 54.93; H, 6.92; N, 3.85. The 1-ethoxyethyl ether (2.30 g, 6.2 mmol) was dissolved in methanol (25 ml) and treated with K_2CO_3 (1.03 g, 7.5 mmol) at 0 °C for 15 min. The reaction mixture was poured into water and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 2 : 3) to afford (2*S*, 3*R*)-2-(1-ethoxyethyloxymethyl)-3-hydroxymethyl-*N*-tosylaziridine (2.00 g, 99% yield) as a colorless oil: $[\alpha]_D^{19}$ - 14° (*c* 1.2, $CHCl_3$); ^{1}H-nmr (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 4.68 (qd, *J* = 29.3, 5.5 Hz, 1H), 3.81~3.70 (m, 2H), 3.64 (dd, *J* = 12.1, 5.9 Hz, 1H), 3.58~3.45 (m, 2H), 3.40 (qdd, *J* = 9.0, 7.0, 2.2 Hz, 1H), 3.13~3.05 (m, 2H), 2.44 (s, 3H), 1.24 (dd, *J* = 8.8, 5.5 Hz, 3H), 1.16 (t, *J* = 7.0 Hz, 3H); ir ($CHCl_3$) ν 3490, 3030, 3010, 2980, 2940, 2890, 1600, 1445, 1380, 1330, 1160, 1130, 1090, 1050 cm^{-1}. Aanl. Calcd for $C_{15}H_{23}NO_5S$: C, 54.69; H, 7.04; N, 4.25. Found: C, 54.55; H, 7.13; N, 4.23. The alcohol (1.90 g, 5.8 mmol) was dissolved in DMF (20 ml) and treated with triethylamine (1.20 ml, 8.7 mmol), *t*-butyldiphenylsilyl chloride (1.80 ml, 6.9 mmol), and 4-dimethylaminopyridine (71 mg, 0.58 mmol) at 0 °C. After stirring overnight at room temperature, the reaction mixture was poured into saturated aq NH_4Cl solution and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 9) to afford (2*R*, 3*S*)-2-*tert*-butyldiphenylsilyloxymethyl-3-(1-ethoxyethyloxymethyl)-*N*-tosylaziridine (3.30 g, 99% yield) as a colorless oil: $[\alpha]_D^{20}$ + 14° (*c* 1.1, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 2H),

7.60~7.24 (m, 12H), 4.59 (qd, J = 6.0, 5.5 Hz, 1H), 3.70 (d, J = 5.5 Hz, 2H), 3.62~3.19 (m, 6H), 3.18~3.04 (m, 2H), 2.38 (s, 3H), 1.14 (dd, J = 5.5, 2.9 Hz, 3H), 1.07 (t, J = 7.4 Hz, 3H), 0.97 (s, 9H); ir ($CHCl_3$) ν 3080, 2860, 1730, 1600, 1430, 1330, 1240, 1160, 1140, 1110, 1090, 1055, 945, 700 cm^{-1}. Aanl. Calcd for $C_{31}H_{41}NO_5SSi$: C, 65.57; H, 7.28; N, 2.47. Found: C, 65.50; H, 7.42; N, 2.41. The silyl ether (3.20 g, 5.6mmol) was dissolved in THF (30 ml) and treated with 0.5 M aq HCl solution (3.0 ml) at 0 °C for 15 h. The reaction mixture was poured into saturated aq $NaHCO_3$ solution and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 3) to afford **7** (2.60 g, 95% yield) as a colorless oil: $[\alpha]_D^{20}$ + 22° (*c* 1.1, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 2H), 7.60~7.34 (m, 12H), 3.81 (dd, J = 11.4, 5.6 Hz, 1H), 3.65 (dd, J = 11.7, 5.6 Hz, 1H), 3.64 (d, J = 6.1 Hz, 2H), 3.18~3.05 (m, 2H), 2.39 (s, 3H), 0.98 (s, 9H); ir ($CHCl_3$) ν 3590, 3490, 3080~2860, 1710, 1600, 1475, 1465, 1430, 1330, 1160, 1115, 1090, 705 cm^{-1}. Aanl. Calcd for $C_{27}H_{33}NO_4SSi$: C, 65.42; H, 6.71; N, 2.83. Found: C, 65.32; H, 6.86; N, 2.71.

(*S*)-5-[(*S*)-2-*tert*-Butyldimethylsilyloxy-1-(*N*-tosylamino)ethyl]-1,3-dioxolane (8): A mixture of **4** (2.65 g, 7.1 mmol), paraformaldehyde (537 mg, 14 mmol), and cesium carbonate (1.18 g, 3.6 mmol) in acetonitrile (30 ml) was stirred overnight at room temperature. The mixture was poured into water and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 6) to afford **8** (2.51 g, 88% yield) as a colorless oil: $[\alpha]_D^{20}$ -35° (*c* 1.5, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.3 Hz, 2H), 4.90 (s, 1H), 4.88 (d, J = 8.2 Hz, 1H), 4.69 (s, 1H), 4.22 (ddd, J = 7.1, 5.9, 3.5 Hz, 1H), 3.75 (dd, J = 8.4, 7.0 Hz, 1H), 3.60~3.42 (m, 3H), 3.29~3.17 (m, 1H), 2.40 (s, 3H), 0.81 (s, 9H), -0.04 (s, 6H); ir ($CHCl_3$) ν 3390, 3030, 2950, 2930, 2850, 1600, 1470, 1410, 1340, 1260, 1160, 1080, 940, 840cm^{-1}. Anal. Calcd for $C_{18}H_{31}NO_5SSi$: C, 53.84; H, 7.78; N, 3.49. Found: C, 53.69; H, 7.86; N, 3.37.

(*S*)-2-[(*S*)-2-*tert*-Butyldimethylsilyloxy-1-(*N*-tosylamino)ethyl]oxirane (9): Butyllithium (1.56 M in hexane, 0.43 ml, 0.67 mmol) was added to a solution of benzyl alcohol (72 μl, 0.70 mmol) in THF-HMPA (5:1, 1.2 ml) at 0 °C. After stirring for 10 min, and the mixture was added to a solution of **4** (50 mg, 0.14 mmol) in THF-HMPA (5:1, 1.2 ml) which had been cooled at -78 °C. After stirring for 1 h, the mixture was warmed to 0 °C and stirred for additional 2 h. The resulting mixture was poured into water and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over

Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 2) to afford **9** (44 mg, 88% yield) as a colorless oil: $[\alpha]_D^{20}$ - 33° (*c* 1.2, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 7.9 Hz, 2H), 4.81 (d, *J* = 7.3 Hz, 1H), 3.56~3.43 (m, 3H), 3.15~3.10 (m, 1H), 2.64 (t, *J* = 4.5 Hz, 1H), 2.53 (dd, *J* = 4.7, 2.7 Hz, 1H), 2.39 (s, 3H), 0.81 (s, 9H), -0.04 (s, 3H), -0.05 (s, 3H); ir ($CHCl_3$) ν 3380, 3030, 2950, 2860, 1600, 1340, 1160, 1090, 840, 660 cm^{-1}; HRms Calcd for $C_{16}H_{26}NO_4SSi$ (M^+ - CH_3), 356.1352, found *m/z* 356.1353.

(*S*)-4-[(*S*)-2-*tert*-Butyldimethylsilyloxy-1-(*N*-tosylamino)ethyl]-3-benzyl-1,3-oxazolidine-2-one and its (*R*, *R*)-isomer (10 and 11) : A solution of **6** (39 mg, 0.065 mmol) and potassium *t*-butoxide (15 mg, 0.13 mmol) in THF (0.4 ml) was stirred overnight at 0 °C. The mixture was poured into water and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative tlc (ethyl acetate : hexane = 1 : 2) to afford **10** (34 mg, 87% yield) as a colorless oil: $[\alpha]_D^{22}$ +48° (*c* 1.7, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.48~7.14 (m, 19H), 5.1 (d, *J* = 5.1 Hz, 1H), 4.52 (d, *J* = 15.0 Hz, 1H), 4.27 (dd, *J* = 4.4, 8.6 Hz, 1H), 4.12~3.92 (m, 2H), 3.79 (d, *J* = 15.1 Hz, 1H), 3.49 (dd, *J* = 10.7, 5.0 Hz, 1H), 3.28~3.12 (m, 2H), 2.42 (s, 3H), 0.97 (s, 9H); ir ($CHCl_3$) ν 3320, 3020, 2930, 2850, 1745, 1600, 1420, 1160, 1110, 1090, 700cm^{-1}; HRms Calcd for $C_{35}H_{40}N_2O_5SSi$ (M^+), 628.2427, found *m/z* 628.2415.

The (*R*, *R*)-isomer (**11**) prepared from **7** in 82% yield through the same procedure as employed for the conversion of **5** to **10**, showed $[\alpha]_D^{22}$ - 47° (*c* 1.5, $CHCl_3$).

(2*S*, 3*S*)-4-*tert*-Butyldimethylsilyloxy-2-phenylamino-3-tosylamino-1-butanol (12a) and (2*R*, 3*R*)-4-*tert*-Butyldimethylsilyloxy-3-phenylamino-2-tosylamino-1-butanol (13a) : Butyllithium (1.55 M in hexane, 0.18 ml, 0.28 mmol) was added to a solution of aniline (26 μl, 0.28 mmol) in THF (0.5 ml) at 0 °C and the mixture was stirred for 10 min. To the mixture, was added a solution of **4** (53 mg, 0,41 mmol) in THF (0.3 ml) and the resulting mixture was stirred overnight at 0 °C. The mixture was poured into water and extracted with ether. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative tlc (twice; ethyl acetate : hexane = 1 : 3, then dichloromethane) to afford **12a** (27 mg, 43% yield) and **13a** (5.1 mg, 7% yield), respectively. **12a**: colorless needles: mp 130-131 °C (hexane); $[\alpha]_D^{21}$ + 26 ° (*c* 0.7, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.15 (dd, *J* =

8.4, 7.4 Hz, 2H), 6.73 (t, J = 7.4 Hz, 1H), 6.60 (d, J = 7.6 Hz, 2H), 5.09 (d, J = 8.4 Hz, 1H), 3.85~3.5 (m, 5H), 3.32 (dd, J = 10.3, 5.7 Hz, 1H), 2.45 (s, 3H), 0.86 (s, 9H), -0.03 (s, 6H); ir (KBr) ν 3470, 3400, 3150, 2960, 2940, 2900, 2870, 1600, 1530, 1500, 1320, 1250, 1160, 1090, 840cm^{-1}. Anal. Calcd for $C_{23}H_{36}N_2O_4SSi$: C, 59.45; H, 7.81; N, 6.03. Found: C, 59.38; H, 8.01; N, 6.07. **13a**: colorless needles: mp 122-123 °C (hexane); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.77 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 7.4 Hz, 1H), 7.18 (d, J = 7.6 Hz, 1H), 6.76 (t, J = 7.5 Hz, 1H), 6.62 (d, J = 7.6 Hz, 2H), 5.60 (d, J = 7.0 Hz, 1H), 3.99 (dd, J = 12.5, 4.0 Hz, 1H), 3.79~3.66 (m, 3H), 3.45~3.36 (m, 1H), 3.16 (dd, J = 12.2, 4.2 Hz, 1H), 2.42 (s, 3H), 0.91 (s, 9H), 0.09 (s, 6H); ir (KBr) ν 3370, 2960, 2940, 1600, 1510, 1460, 1400, 1340, 1260, 1160, 1090, 1020, 840cm^{-1}. Anal. Calcd for $C_{23}H_{36}N_2O_4SSi$: C, 59.45; H, 7.81; N, 6.03. Found: C, 59.21; H, 7.85; N, 6.01. **Acetate of 13a**: colorless oil: ^{1}H-Nmr (200 MHz, $CDCl_3$) δ 7.77 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.19 (dd, J = 8.6, 7.4 Hz, 2H), 6.75 (t, J = 7.4 Hz, 1H), 6.58 (d, J = 5.4 Hz, 2H), 5.31 (d, J = 5.5 Hz, 1H), 4.25 (dd, J = 12.1, 6.2 Hz, 1H), 4.06 (dd, J = 12.1, 3.5 Hz, 1H), 3.83~3.62 (m, 4H), 2.43 (s, 3H), 1.80 (s, 3H), 0.89 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H).

(2*S*, 3*S*)-2-Azido-4-*tert*-butyldimethylsilyloxy-3-*N*-tosylamino-1-butanol (12b) and **(2*R*, 3*R*)-3-Azido-4-*tert*-butyldimethylsilyloxy-2-*N*-tosylamino-1-butanol (13b)** : A mixture of **4** (55 mg, 0.15 mmol) and sodium azide (12 mg, 0.18 mmol) in DMF (0.5 ml) was stirred at 50 °C for 2 h. The mixture was poured into water and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative tlc (ethyl acetate : hexane = 1 : 2) to afford **12b** (39 mg, 60% yield) and **13b** (16 mg, 27% yield), respectively. **12b**: colorless oil; $[\alpha]_D^{21}$ - 8.6 ° (*c* 1.4, $CHCl_3$); ^{1}H-nmr (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 4.81 (d, J = 9.5 Hz, 1H), 3.82 (td, J = 6.6, 2.9 Hz, 1H), 3.72 (dd, J = 11.5, 6.6 Hz, 1H), 3.68 (dd, J = 11.5, 6.6 Hz, 1H), 3.54~3.48 (m, 1H), 3.41 (dd, J = 10.0, 7.6 Hz, 1H), 3.37 (dd, J = 10.0, 5.2 Hz, 1H), 2.44 (s, 3H), 0.83 (s, 9H), -0.04 (s, 6H); ir ($CHCl_3$) ν 3530, 3380, 3030, 2950, 2860, 2110, 1600, 1470, 1420, 1340, 1260, 1160, 1090, 840, 660 cm^{-1}; HRms Calcd for $C_{16}H_{27}N_4O_4SSi$ (M^+ - CH_3), 399.1522, found *m/z* 399.1551. **Acetate of 12b**: colorless oil: ^{1}H-Nmr (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 4.75 (d, J = 8.8 Hz, 1H), 4.06~3.96 (m, 3H), 3.52 (dd, J = 9.5, 4.0 Hz, 1H), 3.41 (dd, J = 9.5, 8.4 Hz, 1H), 3.41~3.36 (m, 1H), 2.43 (s, 3H), 2.05 (s, 3H), 0.85 (s, 9H), 0.01 (s, 3H), 0.006 (s, 3H). **13b**: colorless oil; $[\alpha]_D^{21}$ - 5.2 ° (*c* 1.6, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.73 (d, J = 8.3 Hz, 2H), 7.30

(d, J = 8.1 Hz, 2H), 5.10 (d, J = 7.7 Hz, 1H), 3.71~3.51 (m, 4H), 3.39~3.25 (m, 2H), 2.41 (s, 3H), 0.84 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H); ir ($CHCl_3$) ν 3380, 3030, 2930, 2860, 2110, 1600, 1470, 1410, 1340, 1260, 1160, 1090, 840, 670 cm^{-1}; *HRms Calcd for* $C_{16}H_{27}N_4O_4SSi$ (M^+-CH_3), 399.1522, found *m/z* 399.1507.

(2*S*, 3*R*)-4-*tert*-Butyldimethylsilyloxy-2-chloro-3-*N*-tosylamino-1-butanol (12c) : Diethylaluminum chloride (1.0 M in hexane, 0.26 ml, 0.26 mmol) was added to a solution of **4** (64 mg, 0.17 mmol) in dichloromethane (1.7 ml) at -45 °C. The mixture was warmed to room temperature and stirred overnight, then heated at reflux for additional 2 days. The mixture was poured into 5% aq HCl solution and extracted with ethyl acetate. The organic phase was washed successively with saturated aq $NaHCO_3$ solution and saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative tlc (ethyl acetate : hexane = 1 : 2) to afford **12c** (28 mg, 41% yield). The regioisomer (**13c**) was not detected in the reaction residue. **12c**: colorless needles: mp 91-92 °C (hexane); $[\alpha]_D^{20}$ - 17 ° (*c* 0.7, $CHCl_3$); ^{1}H-nmr (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 4.81 (d, J = 9.5 Hz, 1H), 4.27 (ddd, J = 8.8, 5.9, 2.6 Hz, 1H), 3.84 (dd, J = 12.1, 8.8 Hz, 1H), 3.75 (dd, J = 12.1, 5.9 Hz, 1H), 3.80~3.73 (m, 1H), 3.47 (dd, J = 9.9, 8.8 Hz, 1H), 3.31 (dd, J = 9.9, 4.8 Hz, 1H), 2.44 (s, 3H), 0.81 (s, 9H), -0.06 (s, 3H), -0.07 (s, 3H); ir (KBr) ν 3350, 3100, 2880, 2850, 2780, 1630, 1500, 1440, 1350, 1180, 1120, 1090, 960, 880, 790, 720, 680cm^{-1}. Anal. Calcd for $C_{17}H_{30}NO_4ClSSi$: C, 50.04; H, 7.41; N, 3.43. Found: C, 49.97; H, 7.51; N, 3.39. **Acetate of 12c**: colorless oil: ^{1}H-Nmr (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 4.77 (d, J = 9.5 Hz, 1H), 4.41 (td, J = 7.0, 2.2 Hz, 1H), 4.16 (dd, J = 11.5, 6.8 Hz, 1H), 3.93 (dd, J = 11.5, 7.1 Hz, 1H), 3.68~3.62 (m, 1H), 3.59 (dd, J = 9.9, 4.4 Hz, 1H), 3.49 (dd, J = 9.9, 9.2 Hz, 1H), 2.44 (s, 3H), 2.00 (s, 3H), 0.85 (s, 9H), 0.01 (s, 3H), 0.007 (s, 3H); ir ($CHCl_3$) ν 3376, 3030, 2956, 2931, 2859, 1746, 1599, 1344, 1228, 1161, 1093, 839, 669 cm^{-1}.

(3*S*, 4*S*)-5-*tert*-Butyldimethylsilyloxy-3-hydroxymethyl-1-phenyl-4-*N*-tosylamino-1-pentyne (12d) and (3*R*, 4*R*)-4-*tert*-Butyldimethylsilyloxymethyl-5-hydroxy-1-phenyl-4-*N*-tosylamino-1-pentyne (13d): Butyllithium (1.55 M in hexane, 0.25 ml, 0.40 mmol) was added to a solution of phenylacetylene (43 μl, 0.39 mmol) in THF (0.4 ml) at -78 °C and the mixture was warmed to 0 °C and stirred for 1 h. To the solution, was added a solution of **4** (50 mg, 0.20 mmol) in THF (0.3 ml) at -78 °C. After stirring for 4 h at the same temperature, the mixture was poured into saturated aq NH_4Cl solution and extracted with ether. The organic phase was washed with saturated aq NaCl solution, dried

over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative tlc (ethyl acetate : hexane = 1 : 3) to afford **12d** (38 mg, 62% yield). The regioisomer (**13d**) could not be purified completely (~8% yield) and the structure was determined by its ^{1}H-nmr spectrum. **12d**: colorless needles; $[\alpha]_D^{20}$ - 75 ° (*c* 0.6, $CHCl_3$); mp 120-121 °C (hexane); ^{1}H-nmr (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.39~7.27 (m, 7H), 4.85 (d, *J* = 9.6 Hz, 1H), 3.81 (dd, *J* = 11.5, 9.2 Hz, 1H), 3.75 (dd, *J* = 11.5, 5.5 Hz, 1H), 3.68~3.62 (m, 1H), 3.55 (dd, *J* = 9.9, 8.4 Hz, 1H), 3.44 (dd, *J* = 9.9, 4.8 Hz, 1H), 3.20 (ddd, *J* = 9.2, 5.5, 3.3 Hz, 1H), 2.42 (s, 3H), 0.82 (s, 9H), -0.04 (s, 3H), -0.05 (s, 3H); ir (KBr) ν 3350, 3100, 2880, 2850, 2830, 2790, 1640, 1520, 1500, 1380, 1360, 1280, 1190, 1160, 1120, 1080, 880, 770 cm^{-1}. Anal. Calcd for $C_{25}H_{35}NO_4SSi$: C, 63.39; H, 7.45; N, 2.96. Found: C, 63.26; H, 7.50; N, 2.90. **Acetate of 12d**: colorless oil: ^{1}H-Nmr (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.39~7.28 (m, 7H), 4.82 (d, *J* = 9.2 Hz, 1H), 4.16 (dd, *J* = 11.0, 5.9 Hz, 1H), 3.77 (dd, *J* = 11.0, 9.2 Hz, 1H), 3.70 (dd, *J* = 9.5, 4.0 Hz, 1H), 3.59 (t, *J* = 9.5 Hz, 1H), 3.56~3.50 (m, 1H), 3.40 (ddd, *J* = 9.2, 5.9, 2.9 Hz, 1H), 2.42 (s, 3H), 1.97 (s, 3H), 0.87 (s, 9H), 0.041 (*s*, 3H), 0.038 (s, 3H); ir ($CHCl_3$) ν 3371, 3030, 2956, 2931, 2859, 1739, 1599, 1340, 1226, 1093, 839 cm^{-1}. **13d**: ^{1}H-Nmr (200 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.33 (m, 7), 5.20 (d, *J* = 8.9 Hz, 1H), 4.10 (ddd, *J* = 7.7, 6.0, 1.8 Hz, 1H), 3.88 (dd, *J* = 10.4, 4.2 Hz, 1H), 3.79 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.57~3.48 (m, 1H), 2.49 (dd, *J* = 16.8, 6.0 Hz, 1H), 2.35 (s, 3), 2.30 (dd, *J* = 16.8, 7.8 Hz, 1H), 0.89 (s, 9H), 0.07 (s, 6H).

(2*S*, 3*R*)-4-*tert*-Butyldimethylsilyloxy-2-phenylthio-3-*N*-tosylamino-1-butanol (12e) and (2*S*, 3*R*)-4-*tert*-Butyldimethylsilyloxy-3-phenylthio-2-*N*-tosylamino-1-butanol (13e): Butyllithium (1.59 M in hexane, 0.24 ml , 0.38 mmol) was added to a solution of benzenethiol (40 μl , 0.38 mmol) in THF (0.4 ml) at 0 °C and the mixture was stirred for 1 h. To the solution, was added a solution of **4** (59 mg, 0.16 mmol) in THF (0.4 ml) at 0 °C. After stirring for 30 min, the mixture was poured into water and extracted with ether. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative tlc (ethyl acetate : hexane = 1 : 4) to afford **12e** (64 mg, 81% yield) and **13e** (1.6 mg, 2% yield), respectively. **12e**: colorless needles: mp 148-149 °C (ether); $[\alpha]_D^{21}$ + 34 ° (*c* 0.8, $CHCl_3$); ^{1}H-nmr (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.1 Hz, 2H), 7.39~7.20 (m, 7H), 4.91 (d, *J* = 9.2 Hz, 1H), 3.82 (dd, *J* = 12.1, 8.1 Hz, 1H), 3.78 (dd, *J* = 12.1, 5.9 Hz, 1H), 3.69~3.64 (m, 1H), 3.58~3.51 (m, 3H), 2.43 (s, 3H), 0.78 (s, 9H), -0.10 (s, 3H), -0.13 (s, 3H); ir (KBr) ν 3450, 3130, 2950, 2930, 2900, 2850, 1600, 1580, 1470, 1320, 1160, 1120, 1090, 1010, 910, 840, 670 cm^{-1}. Anal. Calcd for $C_{23}H_{35}NO_4S_2Si$: C, 57.34; H,

7.32; N, 2.91. Found: C, 57.35; H, 7.29; N, 3.06. **Acetate of 12e**: colorless oil: ^{1}H-Nmr (200 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.44~7.39 (m, 2H), 7.30~7.26 (m, 5H), 4.85 (d, *J* = 8.4 Hz, 1H), 4.25 (dd, *J* = 11.4, 6.3 Hz, 1H), 4.00 (dd, *J* = 11.4, 8.3 Hz, 1H), 3.77 (ddd, *J* = 8.3, 6.2, 2.1 Hz, 1H), 3.66~3.60 (m, 3H), 2.42 (s, 3H), 1.97 (s, 3H), 0.80 (s, 9H), -0.04 (s, 3H), -0.09 (s, 3H); ir ($CHCl_3$) ν 3364, 3030, 2956, 2931, 2859, 1741, 1599, 1341, 1228, 1161, 1093, 839 cm^{-1}. **13e**: colorless oil: ^{1}H-Nmr (200 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.3 Hz, 2H), 7.36~7.21 (m, 7H), 5.67 (d, *J* = 7.3 Hz, 1H), 4.15 (dd, *J* = 11.2, 2.4 Hz, 1H), 4.00 (dd, *J* = 11.9, 2.4 Hz, 1H), 3.86 (dd, *J* = 11.2, 5.2 Hz, 1H), 3.57~3.49 (m, 1H), 3.40~3.31 (m, 1H), 3.14 (dd, *J* = 11.4, 5.2 Hz, 1H), 2.40 (s, 3H), 0.91 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H).

(*S*)-5-[(*S*)-2-Iodo-1-(*N*-tosylamino)ethyl]-1,3-dioxolane (16): Tetrabutylammonium fluoride (1.0 M in THF, 9.3 ml, 9.3 mmol) was added to a solution of **5** (2.50 g, 6.2 mmol) in THF (100 ml) at 0 °C and the mixture was stirred for 1 h. The mixture was poured into water and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 1) to afford (*S*)-5-[(*S*)-2-hydroxy-1-(*N*-tosylamino)ethyl]-1,3-dioxolane (1.60 g, 91% yield): colorless needles: mp 101-102 °C (ether); $[\alpha]_D^{20}$ - 14° (*c* 1.0, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 5.32 (d, *J* = 7.7 Hz, 1H), 4.95 (s, 1H), 4.74 (s, 1H), 4.20 (ddd, *J* = 7.0, 5.7, 3.5 Hz, 1H), 3.82 (dd, *J* = 8.7, 7.0 Hz, 1H), 3.71~3.63 (m, 2H), 3.58~3.45 (b, 1H), 3.36~3.25 (m, 1H), 2.43 (s, 3H); ir (KBr) ν 3450, 3330, 3190, 2910, 1600, 1460, 1320, 1160, 1080, 930, 810, 670 cm^{-1}. Anal. Calcd for $C_{12}H_{17}NO_5S$: C, 50.16; H, 5.96; N, 4.87. Found: C, 50.09; H, 6.05; N, 4.81. The alcohol was dissolved in pyridine (25 ml) and treated with *p*-toluenesulfonyl chloride (5.30 g, 28 mmol) overnight at room temperature. The mixture was poured into 1 M aq HCl solution and extracted with ethyl acetate. The organic phase was washed successively with saturated aq $NaHCO_3$ solution and saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 2) to afford (*S*)-5-[(*S*)-2-tosyl-1-(*N*-tosylamino)ethyl]-1,3-dioxolane (2.30 g, 92% yield): colorless needles: mp 127-128 °C (ether); $[\alpha]_D^{20}$ - 73° (*c* 1.0, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.3 Hz, 4H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.99 (d, *J* = 7.8 Hz, 1H), 4.94 (s, 1H), 4.63 (s, 1H), 4.19 (ddd, *J* = 7.4, 5.2, 2.5 Hz, 1H), 4.01 (s, 1H), 3.97 (d, *J* = 2.3 Hz, 1H), 3.72 (dd, *J* = 8.8, 7.3 Hz, 1H), 3.51 (ddd, *J* = 14.0, 7.7, 2.6 Hz, 1H), 3.39 (dd, *J* = 8.8, 5.3 Hz, 1H), 2.46 (s, 3H), 2.44 (s, 3H); ir (KBr) ν 3270, 2950, 2880, 1600, 1440,

1360, 1180, 1160, 1090, 980, 840, 820, 670 cm^{-1}. Anal. Calcd for $C_{19}H_{23}NO_7S_2$: C, 51.69; H, 5.25; N, 3.17. Found: C, 51.63; H, 5.26; N, 3.02. The sulfonate was dissolved in acetone (40 ml) and treated with sodium iodide (3.90 g, 26 mmol) under reflux for 2 h. The mixture was poured into 1% aq $Na_2S_2O_3$ solution and extracted with ethyl acetate. The organic phase was washed successively with saturated aq $NaHCO_3$ solution and saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 2) to afford **16** (2.00 g, 96% yield): colorless needles: mp 81-83 °C (ether); $[\alpha]_D^{20}$ - 17° (*c* 1.2, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 5.14 (d, *J* = 8.1 Hz, 1H), 4.99 (s, 1H), 4.67 (s, 1H), 4.36 (ddd, *J* = 7.3, 5.1, 2.2 Hz, 1H), 3.74 (dd, *J* = 8.4, 7.3 Hz, 1H), 3.43~3.11 (m, 4H), 2.42 (s, 3H); ir ($CHCl_3$) ν 3380, 3030, 2930, 2860, 1600, 1410, 1340, 1160, 1090, 940, 670 cm^{-1}; HRms Calcd for $C_{12}H_{16}NO_4IS$ (M^+) 396.9843. Found 396.9803.

(*S*)-5-[(*S*)-2-Phenyl-1-(*N*-tosylamino)ethyl]-1,3-dioxolane (17): Phenyllithium (1.0 M sol in cyclohexane-ether, 23.3 ml, 23.3 mmol) was added to a suspension of cuprous iodide (2.20 g, 11.3 mmol) in THF (10 ml) at 0 °C. After stirring for 10 min, the mixture was cooled at -78 °C and treated with a solution of **16** (448 mg, 1.1 mmol) in THF (10 ml). The resulting mixture was gradually warmed to room temperature and stirred for 2 h. The mixture was poured into aq NH_4Cl solution and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 3) to afford **17** (383 mg, 97% yield): colorless needles: mp 102-103 °C (ether); $[\alpha]_D^{21}$ + 33° (*c* 1.1, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.27~7.18 (m, 3H), 7.09~7.04 (m, 2H), 5.05 (s, 1H), 4.96 (d, *J* = 8.4 Hz, 1H), 4.72 (s, 1H), 3.95 (td, *J* = 6.5, 2.4 Hz, 1H), 3.68 (dd, *J* = 8.5, 7.7 Hz, 1H), 3.60 (dd, *J* = 8.4, 6.2 Hz, 1H), 3.53~3.40 (m, 1H), 2.85 (dd, *J* = 13.5, 9.2 Hz, 1H), 2.71 (dd, *J* = 13.4, 5.9 Hz, 1H), 2.42 (s, 3H); ir (KBr) ν 3300, 2870, 1600, 1490, 1450, 1410, 1160, 1080, 940, 660 cm^{-1}. Anal. Calcd for $C_{18}H_{21}NO_4S$: C, 62.23; H, 6.09; N, 4.03. Found: C, 62.07; H, 6.15; N, 4.21.

(2*S*, 3*R*)-3-Benzyloxycarbonylamino-2-hydroxy-4-phenyl-1-butanol (18): A solution of **17** (58 mg, 0.17 mmol) in THF (1.0 ml) was added to a solution of sodium (33 mg, 1.4 mmol) in liquid ammonia (10 ml) at -78 °C. After addition of additional sodium (24 mg, 1.0 mmol), the mixture was stirred for 30 min and then quenched with solid NH_4Cl. After ammonia was evaporated, the residue was dissolved in 1 M aq NaOH solution and extracted with dichloromethane-ethanol (5:1). The organic phase

was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was dissolved in methanol (1.0 ml) and treated with 30% HBr in acetic acid under reflux of methanol overnight. The mixture was concentrated *in vacuo* and the residue was dissolved in water-methanol (1 : 4, 2.5 ml) and neutralized with solid $NaHCO_3$. To the mixture, was added solid $NaHCO_3$ (72 mg, mmol) and benzyloxycarbonyl chloride (0.12 ml, mmol). After stirring overnight at room temperature, the mixture was poured into saturated aq NaCl solution and extracted with dichloromethane-ethanol (5:1). The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 1) to afford **18** (38 mg, 71% yield): colorless needles: mp 88-89 °C (ether); $[\alpha]_D^{20}$ + 35° (*c* 1.0, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.36~7.18 (m, 10H), 5.29 (d, *J* = 9.2 Hz, 1H), 5.03 (s, 2H), 4.96 (d, *J* = 8.4 Hz, 1H), 4.72 (s, 1H), 3.95 (q, *J* = 6.5, 2.4 Hz, 1H), 3.68~3.42 (m, 3H), 3.06 (br s, 2H), 2.88 (d, *J* = 7.6 Hz, 2H); ir (KBr) ν 3370, 3250, 2940, 1690, 1520, 1450, 1250, 1050, 730, 690 cm^{-1}. Anal. Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.48; H, 6.67; N, 4.40.

Methyl (2*S*, 3*R*)-3-{*N*-(Benzyloxycarbonyl)amino}-2-hydroxy-4-phenylbutanoate (14): A suspension of platinum(IV) oxide (61 mg, 0.27 mmol) in water (0.5 ml) was stirred under hydrogen atmosphere at room temperature for 1 h. After replacing the hydrogen atmosphere by oxygen, solid $NaHCO_3$ (15 mg, 0.18 mmol) and **18** (50 mg, 0.16 mmol) were added to the mixture and the resulting suspension was stirred for 2 days at room temperature. The mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was dissolved in 1 M aq HCl solution and extracted successively with dichloromethane and ethyl acetate. The combined organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was dissolved in THF (1.0 ml) and treated with diazomethane at 0 °C. After concentration of the reaction mixture, the residue was purified by preparative tlc (ethyl acetate : hexane = 1 : 2) to afford **14** (40 mg, 75% yield): colorless needles: mp 99-100 °C (ethyl acetate-hexane) (*lit.*,[9d] mp 94-95 °C, $[\alpha]_{577}^{21}$ + 90° (*c* 0.8, MeOH){*lit.*,[9d] $[\alpha]_{578}^{25}$ + 82° (*c* 0.8, MeOH)}; ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.35~7.23 (m, 10H), 5.11 (d, *J* = 9.9 Hz, 1H), 5.04 (s, 2H), 4.33 (dd, *J* = 17.1, 8.8 Hz, 1H), 4.09 (dd, *J* = 4.0, 1.5 Hz, 1H), 3.71 (s, 3H), 3.20 (d, *J* = 4.1 Hz, 1H), 2.99~2.87 (m, 2H); ir (KBr) ν 3450, 3400, 1740, 1690, 1520, 1450, 1240, 1100, 1040, 750, 700 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.35; H, 6.24; N, 4.09.

(*R*)-2-[(*R*)-2-*tert*-Butyldiphenylsilyloxy-1-(*N*-tosylamino)ethyl]oxirane (19): Alcohol (**7**) (2.50 g, 5.1 mmol) was treated by the same procedure as employed for the conversion of **4** to **6** to furnish

19 (2.40 g, 95% yield): colorless oil; ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.68~7.18 (m, 14H), 4.77 (d, *J* = 4.5 Hz, 1H), 3.62~3.52 (m, 3H), 3.25~3.21 (m, 1H), 2.68 (t, *J* = 4.7 Hz, 1H), 2.59 (dd, J = 2.7, 4.7 Hz, 1H), 2.39 (s, 3H), 1.02 (s, 9H); ir ($CHCl_3$) ν 3380, 3080, 3040, 2960, 2940, 1730, 1600, 1590, 1470, 1430, 1340, 1250, 1160, 1110, 1090, 900, 820, 700 cm^{-1}. Anal. Calcd for $C_{27}H_{33}NO_4SSi$: C, 65.42; H, 6.71; N, 2.83. Found: C, 65.20; H, 6.76; N, 2.83.

(3*S*, 4*S*)-5-*tert*-Butyldiphenylsilyloxy-3-hydroxy-4-(*N*-tosylamino)pentanenitrile (20): A solution of **19** (2.18g, 4.4 mmol) in acetonitrile (20 ml) was treated with potassium cyanide (430 mg, 6.6 mmol) and lithium perchlorate (702 mg, 6.6 mmol) overnight at room temperature. The reaction mixture was poured into saturated aq NaCl solution and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 3) to afford **20** (2.19 g, 95% yield): colorless needles: mp 171-172 °C (ether); $[\alpha]_D^{20}$ + 35° (*c* 1.0, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.57~7.37 (m, 10H), 5.12 (d, *J* = 9.1 Hz, 1H), 4.30~4.20 (m, 1H), 3.60 (dd, *J* = 10.5, 3.8 Hz, 1H), 3.52 (dd, *J* = 10.5, 5.3 Hz, 1H), 3.35~3.25 (m, 1H), 3.00 (s, 1H), 2.49 (dd, *J* = 16.7, 7.5 Hz, 1H), 2.40 (s, 3H), 2.34 (dd, *J* = 16.6, 5.5 Hz, 1H), 1.02 (s, 9H); ir ($CHCl_3$) ν 3500, 3380, 3030, 2940, 2860, 2250, 1735, 1600, 1430, 1340, 1250, 1160, 1120, 910, 820, 705 cm^{-1}. Aanl. Calcd for $C_{28}H_{34}N_2O_4SSi$: C, 64.34; H, 6.56; N, 5.36. Found: C, 64.16; H, 6.73; N, 5.16.

(3*S*, 4*S*)-3-Hydroxy-5-phenyl-4-(*N*-tosylamino)pentanenitrile (21): A solution of **20** (1.90 g, 3.6 mmol) in THF (20 ml) was treated with tetrabutylammonium fluoride (1.0 M sol in THF, 4.30 ml, 4.3 mmol) at 0 °C for 30 min. The reaction mixture was poured into saturated aq NH_4Cl solution and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 4) to afford (3*S*, 4*S*)-3,5-dihydroxy-4-(*N*-tosylamino)pentanenitrile (911 mg, 89% yield): colorless needles: mp 157-158 °C (chloroform); $[\alpha]_D^{20}$ + 38° (*c* 1.2, MeOH); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 7.9 Hz, 2H), 4.13 (ddd, *J* = 7.7, 5.8, 2.1 Hz, 1H), 3.52~3.17 (m, 3H), 2.62 (dd, *J* = 16.8, 8.0 Hz, 1H), 2.50 (dd, *J* = 16.8, 5.6 Hz), 2.43 (s, 3H); ir (KBr) ν 3500, 3240, 2970~2890, 2250, 1595, 1440, 1315, 1290, 1150, 960, 910, 820, 680 cm^{-1}. Aanl. Calcd for $C_{12}H_{16}N_2O_4S$: C, 50.69; H, 5.67; N, 9.85. Found: C, 50.45; H, 5.68; N, 9.72. The alcohol (716 mg, 2.5 mmol) in pyridine (3.0 ml) and treated with *p*-toluenesulfonyl chloride (2.34 g, 12. 6 mmol) at 0 °C for

1 h. The reaction mixture was poured into diluted aq HCl solution and extracted with ethyl acetate. The organic phase was washed successively with saturated aq $NaHCO_3$ solution and saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 2 : 3) to afford (3*S*, 4*S*)-3-hydroxy-5-tosyloxy-4-(*N*-tosylamino)pentanenitrile (934 mg, 85% yield): colorless needles: mp 130-132 °C (ether); $[\alpha]_D^{17}$ + 31° (*c* 1.0, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.70 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.28 (d, *J* = 9.5 Hz, 1H), 4.26~4.17 (m, 1H), 4.00 (dd, *J* = 10.3, 8.8 Hz, 1H), 3.86 (dd, *J* = 10.3, 5.0 Hz, 1H), 3.56~3.44 (m, 1H), 3.33 (d, *J* = 5.5 Hz, 1H), 2.54 (d, *J* = 8.4 Hz), 2.47 (s, 3H), 2.44 (s, 3H), 2.27 (dd, *J* = 16.8, 5.0 Hz, 1H); ir (KBr) ν 3300, 2930, 2260, 1600, 1495, 1450, 1340, 1160, 1090, 980, 820, 670 cm^{-1}. Aanl. Calcd for $C_{19}H_{22}N_2O_6S_2$: C, 52.04; H, 5.06; N, 6.39. Found: C, 51.77; H, 5.03; N, 6.20. The tosylate (876 mg, 2.0 mmol) was dissolved in acetone (10 ml) and treated with sodium iodide (1.50 g, 10 mmol) at 0 °C and then at 40 °C for 3 h. The reaction mixture was poured into 1% aq $Na_2S_2O_3$ solution and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 2 : 3) to afford (3*S*, 4*R*)-3-hydroxy-5-iodo-4-(*N*-tosylamino)pentanenitrile (744 mg, 95% yield): colorless needles: mp 116-117 °C (ether); $[\alpha]_D^{20}$ - 29° (*c* 1.0, $CHCl_3$); ^{1}H-nmr (200 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 2H), 5.66 (d, *J* = 8.2 Hz, 1H), 4.47~4.41 (m, 1H), 3.42 (br s, 1H), 3.18 (t, *J* = 9.9 Hz, 1H), 2.93 (dd, *J* = 10.2, 4.2 Hz, 1H), 2.65 (dd, *J* = 16.9, 8.4 Hz, 1H), 2.45 (s, 3H), 2.42 (dd, *J* = 16.8, 4.5 Hz, 1H); ir (KBr) ν 3420, 3290, 2930, 2260, 1600, 1420, 1340, 1160, 1090, 1060, 905, 815, 680 cm^{-1}. Aanl. Calcd for $C_{12}H_{15}N_2O_3Si$ • 1/4 Et_2O: C, 37.83; H, 4.27; N, 6.79. Found: C, 37.91; H, 4.24; N, 6.66. Phenyllithium (1.68 M sol in cyclohexane-ether, 6.2 ml, 10. 4 mmol) was added to a suspension of cuprous bromide (747 mg, 5.2 mmol) in THF (8.0 ml) at 0 °C. After stirring for 10 min, the mixture was cooled at -78 °C and treated with the iodide obtained above (206 mg, 0,52 mmol) in THF (2.0 ml). The resulting mixture was stirred for 1 h at -78 °C, then at 0 °C for 1 h. The mixture was poured into saturated aq NH_4OH solution and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (ethyl acetate : hexane = 1 : 1) to afford **21** (174 mg, 78% yield): colorless needles: mp 159-160 °C ($CHCl_3$-hexane); $[\alpha]_D^{20}$ - 76° (*c* 1.1, $CHCl_3$); ^{1}H-nmr (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.21~7.14 (m, 3H), 6.96~6.94 (m, 2H),

5.23 (d, J = 9.2 Hz, 1H), 3.87 (br s, 1H), 3.46~3.39 (m, 1H), 3.14 (d, J = 5.9 Hz, 1H), 2.80 (dd, J = 13.6, 9.2 Hz, 1H), 2.71 (dd, J = 17.2, 8.8 Hz, 1H), 2.50 (dd, J = 13.6, 6.2 Hz, 1H), 2.46 (dd, J = 17.9, 4.9 Hz, 1H), 2.42 (s, 3H); ir (KBr) ν 3430, 3300, 2930, 2260, 1600, 1490, 1430, 1320, 1150, 1060, 980, 920 cm^{-1}. Aanl. Calcd for $C_{18}H_{20}N_2O_3S$: C, 62.77; H, 5.85; N, 8.13. Found: C, 62.81; H, 5.87; N, 8.05.

(3*S*, 4*S*)-4-{*N*-(*tert*-Butoxycarbonyl)amino}-3-hydroxy-5-phenylpentanoic Acid (15): The nitrile (**21**)(72mg,0.21 mmol) was dissolved in 20 % aq NaOH solution (2.5 ml) and treated with 30% aq H_2O_2 solution (1.0 ml) for 1 h at room temperature, and the mixture was heated at reflux for 2 h. The warm reaction mixture was immediately poured into 40% aq H_3PO_4 solution and extracted with ethyl acetate under salting out. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative tlc (dichloromethane : acetone : acetic acid = 72 : 12 : 1) to afford (3*S*, 4*S*)-3-hydroxy-5-phenyl-4-(*N*-tosylamino)pentanoic acid (62 mg, 85% yield): colorless needles: mp 169-170 °C ($CHCl_3$); $[\alpha]_D^{19}$ - 40° (*c* 1.1, MeOH); ^{1}H-nmr (400 MHz, CD_3OD) δ 7.59 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.13~7.07 (m, 3H), 6.98~6.96 (m, 2H), 3.98 (ddd, J = 7.7, 5.5, 2.2 Hz, 1H), 3.45 (td, J = 7.7, 2.2 Hz, 1H), 2.86 (dd, J = 13.6, 9.2 Hz, 1H), 2.48 (s, 1H), 2.47 (d, J = 2.9 Hz, 1H), 2.39 (s, 3H), 2.35 (dd, J = 13.2, 7.0 Hz, 1H). Aanl. Calcd for $C_{18}H_{21}NO_5S$: C, 59.49; H, 5.82; N, 3.85. Found: C, 59.16; H, 5.95; N, 3.81. A solution of the acid (62 mg, 0.17 mmol) in THF (0.5 ml) was added to a solution of sodium (30 mg, 1.3 mmol) in liquid ammonia (10 ml) at -78 °C. After addition of additional sodium (28 mg, 1.2 mmol), the reaction mixture was stirred for 3 h at the same temperature, then quenched with solid NH_4Cl. After evaporation of liquid ammonia, the residue was dissolved in distilled water, desalted (Asahi Kasei Micro Acilizer S1), and lyophilized to afford the crude product (26 mg): ^{1}H-Nmr (200 MHz, D_2O, H_2O as internal standard (4.72 ppm)) δ 7.32 ~ 7.21 (m, 5H), 4.01 ~ 3.93 (m, 1H), 3.49 ~ 3.39 (m, 1H), 3.05 (dd, J = 14.4, 5.5 Hz, 1H), 2.76 (dd, J = 14.4, 9.4 Hz, 1H), 2.52 (dd, J = 15.4, 5.1 Hz, 1H), 2.36 (dd, J = 15.4, 7.4 Hz, 1H). The crude residue was dissolved in water-dioxane (1 : 1, 1.3 ml) and treated with 1M aq NaOH solution (0.15 ml) and di-*tert*-butyl dicarbonate (40 μl, mmol) at 0 °C. After stirring for 1 h at room temperature, additional 1 M aq NaOH solution (0.15 ml) and di-*tert*-butyl dicarbonate (40 μl, mmol) were added and the resulting mixture was stirred for 2 h. The mixture was acidified with 5% aq $KHSO_4$ solution and extracted with ethyl acetate. The organic phase was washed with saturated aq NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative tlc (dichloromethane:acetone:acetic acid =

72:12:1) to afford **15** (25 mg, 47% overall yield): colorless needles: mp 147-149 °C ($CHCl_3$) (*lit.*,[10a] mp 148-148.5 °C) ; $[\alpha]_D^{20}$ - 39° (*c* 0.4, MeOH){*lit.*,[10a] $[\alpha]_D^{20}$ - 37° (*c* 1.1, MeOH)}; ^{1}H-nmr (400 MHz, $CDCl_3$: CD_3OD=10 : 1) δ 7.26 (s, 5H), 4.01 ~ 3.97 (br d, 1H), 2.88 (d, *J* = 7.3 Hz, 2H) 2.60 ~ 2.35 (m, 2H), 1.39 (s, 9H). Aanl. Calcd for $C_{16}H_{23}NO_5 \cdot 1/3\ H_2O$: C, 60.94; H, 7.56; N, 4.44. Found: C, 60.93; H, 7.53; N, 4.68.

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Dedicated to the late Professor Yoshio Ban.

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