Dehydrooligopeptides. XVII. Practical Syntheses of All of the Diastereomers of *N*,*N*-Protected 2,3-Diaminobutanoic Acids from L- and D-Threonine Derivatives[1)]

Yutaka Nakamura, Miki Hirai, Kenji Tamotsu, Yasuchika Yonezawa, and Chung-gi Shin*

Laboratory of Organic Chemistry, Faculty of Technology, Kanagawa University, Rokkakubashi, Kanagawa-ku, Yokohama 221

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Syntheses of all of the diastereomers of 2,3-diaminobutanoic acids, found in some peptide antibiotics and toxins, were accomplished. The four isomers were derived mainly through two pathways including S_N2 inversions of the β-substituent of L- or D-threonine derivatives. The various protecting groups and effective nucleophiles for the S_N2 inversion were examined.

Some kinds of peptide antibiotics and toxins comprise one or more diastereomers of 2,3-diaminobutanoic acid (H-Dab-OH) and another unusual α-amino acid, such as an α-dehydroamino acid. For example, it is wellknown that both lavendomycin[2)] and antrimycins[3)] (cirratiomycins),[4)] produced by *Streptomyces* (*St.*) *lavendulea* and *St. xanthocidicus MGl25-CFl* (*St. cirratus 248-Sg2*), respectively, contain a (2*S*,3*S*)-Dab-OH residue, amphomycin,[5)] produced by *St. canus*, and so on,[6)] as well as a (2*S*,3*S*)- and/or (2*S*,3*R*)-Dab-OH residue. Convenient syntheses of (2*S*,3*S*)- and (2*S*,3*R*)-Dab-OH derivatives[7)] from L-allothreonine and L-threonine, respectively, as well as those of the abovementioned lavendomycin and antrimycin Dv, were recently reported by Schmidt et al.[8—10)] However, there has been no report concerning a synthetic study of the other diastereomers, (2*R*,3*S*)- and (2*R*,3*R*)-Dab-OH.

During the course of the total synthesis of eight kinds of antrimycins[1)] we have also briefly reported on the synthesis of (2*S*,3*S*)-N^2-Boc-N^3-Cbz-Dab-OH (**1a**) (Cbz=benzyloxycarbonyl) from *N*-*t*-butoxycarbonyl-L-threonine (Boc-L-Thr-OH) (**2a**).[1,11)] Here, we wish to report in detail on a few synthetic pathways for **1a** and the other three diastereomers (N^2,N^3-diprotected (2*R*,3*R*)-, (2*S*,3*R*)-, and (2*R*,3*S*)-Dab-OH (**1b**, **1c**, and **1d**)) from Boc-L- and D-Thr-OH (**2a** and **2b**).

The configurational structures of the four diastereomers of N^2,N^3-diprotected Dab-OH (**1**) are illustrated in Fig. 1.

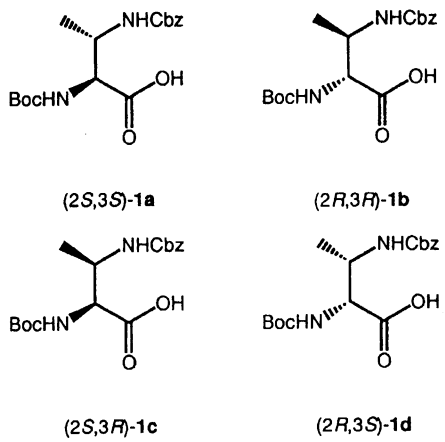


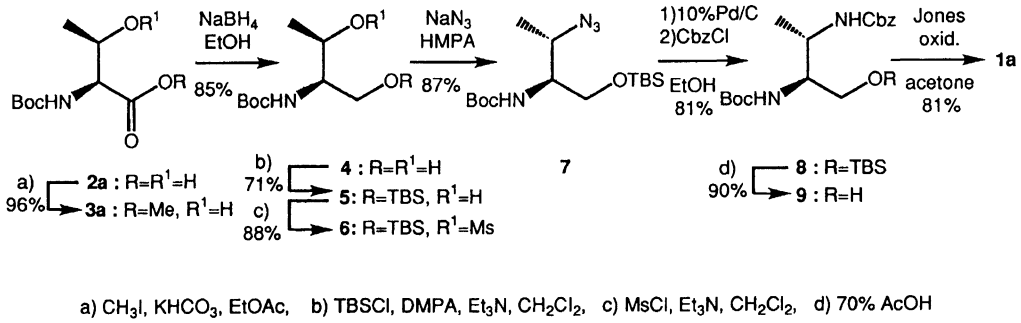
Fig. 1.

Results and Discussion

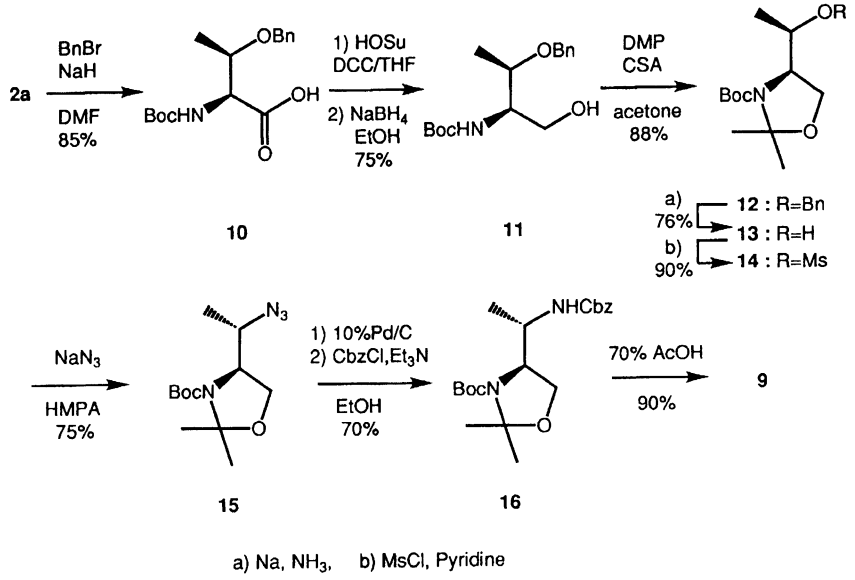
Syntheses of (2*S*,3*S*)- and (2*R*,3*R*)-Diaminobutanoic Acids (1a and 1b). To establish a general synthetic method, the syntheses of (2*S*,3*S*)- and (2*R*,3*R*)-Dab-OH (**1a** and **1b**) from **2a** and **2b**, respectively, were studied variously, and successfully developed, as shown in Schemes 1, 2, 3, and 4.

First of all, the esterification of **2a** with CH_3I in the presence of $KHCO_3$, followed by a reduction of the formed Boc-L-Thr-OMe (**3a**) with $NaBH_4$, gave the starting material (2*R*,3*R*)-2-(Boc-amino)butane-1,3-diol (**4**). The selective protection of the primary hydroxyl group of **4** with *t*-butyldimethylsilyl chloride (TBSCl) in the presence of 4-dimethylaminopyridine (DMAP) and Et_3N gave the corresponding *t*-butyldimethylsilyl (TBS)oxybutanol (**5**). Furthermore, mesylation of the secondary hydroxyl group of **5** with methanesulfonyl chloride (MsCl) in the presence of Et_3N gave the O^1,O^3-diprotected butane-1,3-diol (**6**).

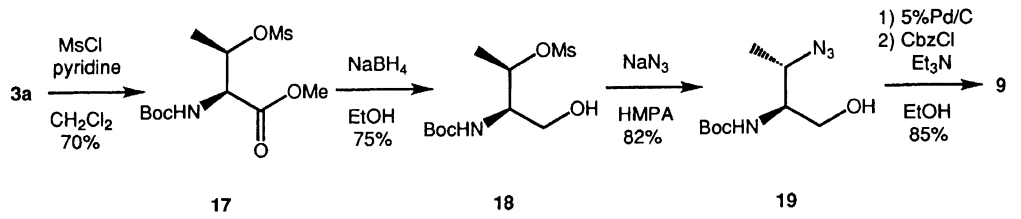
Subsequently, the reaction of **6** with NaN_3 in hexa-



Scheme 1.



Scheme 2.

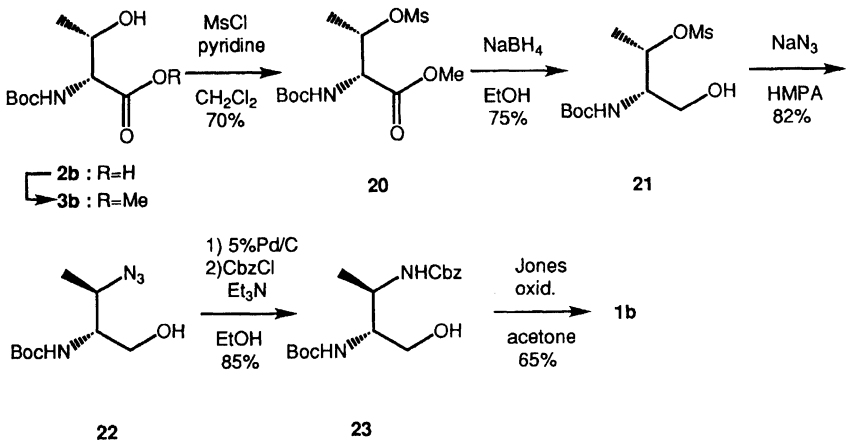


Scheme 3.

methylphosphoric triamide (HMPA) in the presence of 15-crown-5 was achieved to give the expected (2*S*,3*S*)-3-azido-2-(Boc-amino)-1-butanol (**7**). The catalytic hydrogenolysis of the azido group of **7** with 10% Pd/C, followed by acylation with CbzCl in the presence of Et_3N, gave the corresponding N^2,N^3-diprotected (2*S*,3*S*)-2,3-diamino-1-butanol (**8**). Finally, deprotection of the TBS group with 70% AcOH and then Jones oxidation of the corresponding *O*-free diaminobutanol (**9**) obtained gave the expected **1a** in 81% yield (Scheme 1).

In addition, alternative routes for the synthesis of **1a** from **2a** were also studied in the following manner.

The protection of **2a** with benzyl bromide (BnBr) in dimethylformamide (DMF) in the presence of NaH gave Boc-L-Thr(Bn)-OH (**10**), which was then reduced with $NaBH_4$ to give the corresponding (2*R*,3*R*)-3-benzyloxy-2-(Boc-amino)-1-butanol (**11**). The subsequent conversion of **11** with 2,2-dimethoxypropane (DMP) in the presence of *dl*-camphor-10-sulfonic acid (CSA) gave (*R*)-4-[(*R*)-1-(benzyloxy)ethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (**12**). Then, the deprotection of the benzyl group alone by a Birch reduction gave the corresponding 4-(1-hydroxyethyl) derivative (**13**). Mesylation of **13** with MsCl gave (*R*)-4-[(*R*)-1-(mesyloxy)-ethyl] derivative (**14**), which was reacted with NaN_3 to give the (*S*)-4-[(*S*)-1-azidoethyl] derivative (**15**). Subsequently, as in the case of **7**, consecutive hydrogenolysis and acylation of **15** gave the corresponding 4-[1-(Cbz-amino)ethyl]-1,3-oxazolidine derivative (**16**). Finally, deprotection of the isopropylidene group of **16** by treating with 70% AcOH gave **9** in 90% yield, as shown in Scheme 2.



Scheme 4.

By comparing the above two routes with respect to the yields and the reaction steps, the first synthetic method is thought to be preferable to the second method via **12**. To further shorten the synthetic pathway to **1a**, and to simplify the procedures, the first method was extensively modified. Namely, the mesylation of **3a** with MsCl gave Boc-L-Thr(Ms)-OMe (**17**),[12] which was immediately reduced with $NaBH_4$ to give the corresponding 3-mesyloxy-1-butanol (**18**). Even though no protecting group was used to the 1-hydroxyl group of **18**, the desirable substitution with NaN_3 took place beautifully to give 3-azido-1-butanol (**19**) in 82% yield. Finally, as in the case of **7**, the successive hydrogenolysis and acylation of **19** gave **9** in only four steps from **3a** (Scheme 3).

From the above results, the third improved synthetic method can be said to be significantly simple and more practical. In effect, as shown in Scheme 4, the enantiomer (2*R*,3*R*)-Dab-OH (**1b**) was also readily synthesized in good overall yield from **2b** via successive Boc-D-Thr(Ms)-OMe (**20**), (2*S*,3*S*)-3-mesyloxy (**21**)-, (2*R*,3*R*)-3-azido (**22**)-, and (2*R*,3*R*)-3-(Cbz-amino)-1-butanol (**23**) in four steps.

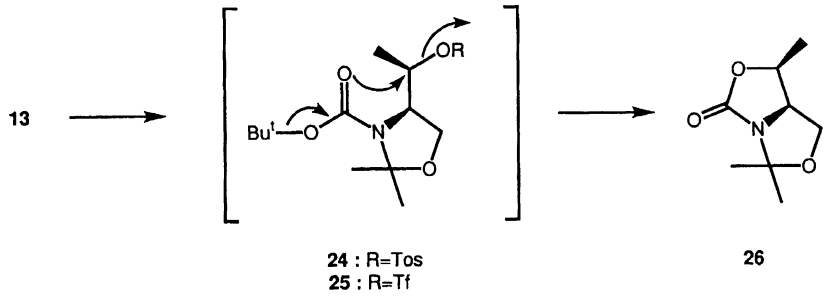
Consequently, by comparing the above three synthetic methods for **1**, it can be seen that the third method is the most available. However, in the syntheses of (2*S*,3*R*)- and (2*R*,3*S*)-Dab-OH (**1c** and **1d**), the second method using the 1,3-oxazolidine derivative was found to be effective.

Syntheses of (2*S*,3*R*)- and (2*R*,3*S*)-Diaminobutanoic Acids (1c and 1d). For the synthesis of **1c** and **1d** from **2a** and **2b**, a double inversion at the C-3 position is necessary. However, all attempts using (2*R*,3*R*)-**18** and (2*S*,3*S*)-**21** were unsuccessful. Therefore, the above-mentioned second method was applied to the syntheses of **1c** and **1d**.

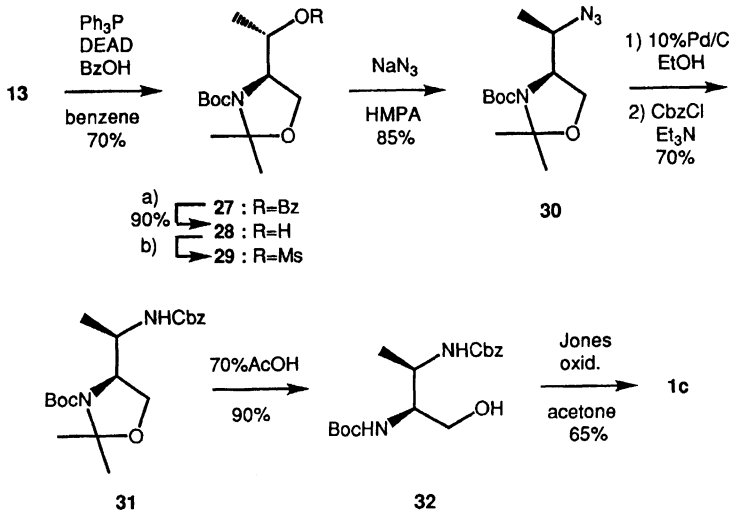
First, since trifluoromesyl (Tf) and tosyl (Tos) groups are more electron-attractive than the Ms group, the TfO and TosO groups as the leaving group in **13** were thought to be superior to the mesyloxy (MsO) group. However, attempts to isolate the corresponding tosylate (**24**) and triflate (**25**), derived by sulfonations of **13** with toluenesulfonyl chloride (TosCl) and trifluoromethanesulfonic acid anhydride (Tf_2O), respectively, were unsuccessful. Namely, the formed intermediates, **24** and **25**, were very labile, and undesirable intramolecular substitution-cyclization occurred either immediately or gradually to give unstable oxazolo[3,4-*c*]oxazole (**26**). The structure and reaction mechanism could be understood based on the spectral data (IR and ^1H NMR) and the recently reported literature,[13] as shown in Scheme 5.

Consequently, direct substitution of the hydroxyl group of **13** by using the other nucleophile was examined, and was successful in the following ways. According to Scheme 6, the reaction of **13** with BzOH in the presence of triphenylphosphine (Ph_3P) and diethyl azodicarboxylate (DEAD)[14] gave the corresponding (*R*)-4-[(*S*)-1-benzoyloxy)ethyl] (**27**). Subsequent deprotection of the benzoyl group with K_2CO_3 gave the corresponding (*R*)-4-[(*S*)-1-(hydroxy)ethyl] derivative (**28**). Furthermore, mesylation of **28** with MsCl and a subsequent inversion reaction of the mesyloxy derivative (**29**) with NaN_3 gave the expected (*S*)-4-[(*R*)-1-azidoethyl] derivative (**30**). Then, the hydrogenolysis of the azido group of **30** with 10% Pd/C, followed by acylation with CbzCl, gave the (*S*)-4-[(*R*)-1-(Cbz-amino)ethyl] derivative (**31**), which was further deprotected with 70% AcOH into **32**, and finally oxidized to give the expected (2*S*,3*R*)-Dab-OH (**1c**).

Quite similarly as in the case of **1c** from **2a**, the enantiomer (2*R*,3*S*)-Dab-OH (**1d**) was also synthesized from Boc-D-Thr(Bn)-OH (**33**) via successive (2*S*,3*S*)-2-(Boc-amino)-3-benzyloxy-1-butanol (**34**), (*S*)-4-[(*S*)-1-(benzyloxy)ethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (**35**), the corresponding (*S*)-4-[(*S*)-1-(hydroxy)ethyl] (**36**)-, (*S*)-4-[(*R*)-1-(benzoyloxy)ethyl] (**37**)-, (*S*)-4-[(*R*)-1-(hydroxy)ethyl] (**38**)-, (*S*)-4-[(*R*)-1-(mesyloxy)ethyl] (**39**)-, (*R*)-4-[(*S*)-1-azidoethyl] (**40**)-, and (*R*)-4-[(*S*)-1-(Cbz-amino)ethyl]-1,3-oxazolidine (**41**) and final N^2,N^3-diprotected-(2*R*,3*S*)-2,3-diamino-1-butanol derivatives (**42**) in good yields, respectively



Scheme 5.



Scheme 6.

(Scheme 7).

The melting points, elemental analyses, and specific rotations of the four diastereomers of the diaminobutanol derivatives (**9**, **23**, **32**, **42**) and **1a**—**d** are summarized in Tables 1 and 2.

In conclusion, we believe that the practical synthetic method for all Dab diastereomers is sufficiently applicable to the synthesis of other α,β-diamino acids, and is useful for the studying of the correlation between the structure and the bioactivity of the peptides containing an appropriate diamino acid residue.

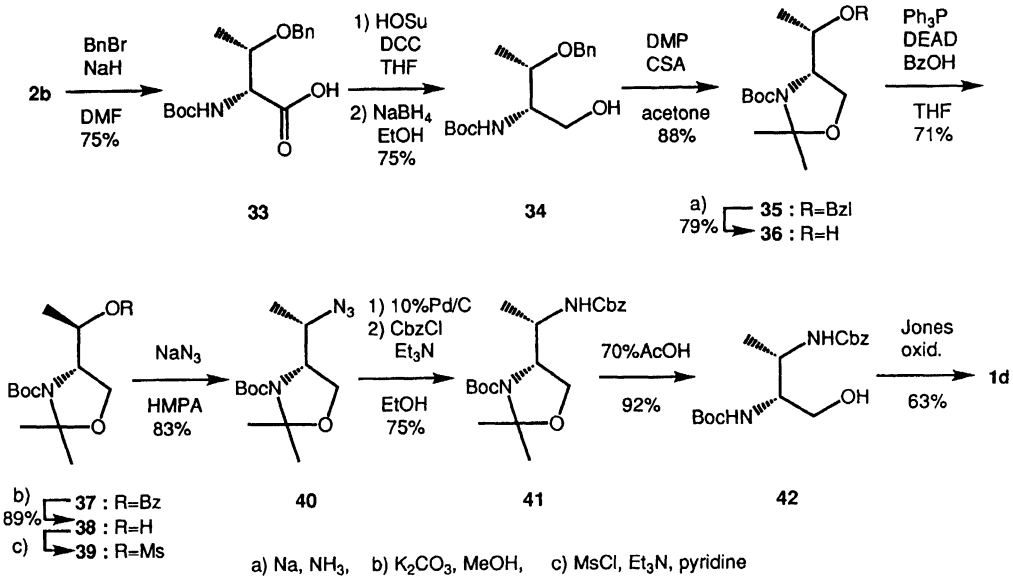
Experimental

The melting points were determined using a Yamato (Model Mp-21) micro-melting point apparatus, and were uncorrected. The IR spectra were recorded using a Hitachi EPI-G2 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured with JEOL EX90 and FX 200 spectrometers in $CDCl_3$ and DMSO-d_6 with tetramethylsilane as the internal standard. The optical rotations were measured with a DIP-4 polarimeter (Japan Spectroscopic Co., Ltd).

Starting Materials. Boc-L-Thr-OH (**2a**) and Boc-D-Thr-OH (**2b**) were purchased from Nippon Rikagaku Yakuhin Co., Ltd.

Boc-L- and D-Thr-OMe (3a and 3b). To a solution of **2a** or **2b** (1.00 g, 45.6 mmol) in DMF (70 ml) was added $KHCO_3$ (9.14 g, 91.2 mmol), followed by the addition of CH_3I (4.6 ml, 73.0 mmol). After stirring for 5 h at room temperature, the reaction mixture was poured into water (200 ml) and extracted with ethyl acetate (3×30 ml). The combined extracts were washed with brine (3×10 ml), and then dried over anhydrous Na_2SO_4. The concentration in vacuo gave a syrupy **3a** or **3b**, which was used in the next reaction without purification.

(2*R*,3*R*)-2-(*t*-Butoxycarbonyl)aminobutane-1,3-diol (4) from 2a. A solution of **2a** (2.0 g, 9.1 mmol), *N*-hydroxysuccinimide (HOSu) (1.16 g, 10.0 mmol) and dicyclohexylcarbodiimide (DCC) (2.07 g, 10.0 mmol) in THF (15 ml) was stirred at 0 °C for 1 h, and then at room temperature for 5 h. The deposited DCC urea was filtered off, and the filtrate was concentrated in vacuo. To a solution of the residue in THF (20 ml), a suspension of $NaBH_4$ (1.04 g, 27.4 mmol) in EtOH (5 ml) was added; the reaction mixture was then stirred for 30 min at 0 °C, quenched by adding saturated aqueous NH_4Cl (30 ml) and concentrated in vacuo. The obtained residue was extracted with $CHCl_3$ (3×20 ml). The combined extracts were washed with brine (2×20 ml) and dried over anhydrous Na_2SO_4. The concentration in vacuo gave a crude syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (2:1 v/v) to give **4** as a colorless syrup. Yield 96%. $[\alpha]_D^{25}$ +1.6° (*c* 1.20, MeOH). IR (KBr) 3400, 1690, 1527 cm^{-1}. ^{1}H NMR δ=1.21 (d, 3H, J=6.2 Hz), 1.45 (s, 9H), 3.40—4.40 (m, 6H), 5.44



Scheme 7.

Table 1. N^2,N^3-Diprotected 2,3-Diamino-1-butanol Derivatives (**9**, **23**, **32**, **42**)

Compound No.	Mp[a] °C	Found/%[b] C	H	N	$[\alpha]_D$[c] °
9 (2*S*, 3*S*)	129—131	60.12	7.86	8.23	−9.8 (*c* 0.9)
23 (2*R*, 3*R*)	130—131	60.09	7.60	8.09	+10.1 (*c* 0.5)
32 (2*S*, 3*R*)	93—95	60.07	7.60	8.17	+27.3 (*c* 1.7)
42 (2*R*, 3*S*)	93—95	60.03	7.86	8.26	−25.4 (*c* 1.6)

a) Colorless needles from a mixture of hexane and EtOAc. b) Calcd for $C_{17}H_{26}N_2O_5$: C, 60.34; H, 7.74; N, 8.28%. c) Measured in MeOH at 25—26 °C.

Table 2. N^2,N^3-Diprotected 2,3-Diaminobutanoic Acid (**1**)

Compound No.	Mp[a] °C	Found/%[b] C	H	N	$[\alpha]_D$[c] °
1a (2*S*, 3*S*)	112—113	57.82	6.83	7.96	−21.0 (*c* 0.3)
1b (2*R*, 3*R*)	112—113	57.97	6.74	7.88	+21.1 (*c* 1.0)
1c (2*S*, 3*R*)	190—191	57.60	6.26	7.69	+11.6 (*c* 1.5)
1d (2*R*, 3*S*)	190—191	57.52	6.85	7.88	−11.8 (*c* 1.5)

a) Colorless needles from a mixture of hexane and EtOAc. b) Calcd for $C_{17}H_{24}N_2O_6$: C, 57.94; H, 6.87; N, 7.95%. c) Measured in MeOH at 25—26 °C.

(br d, 1H, NH). Found: C, 52.63; H, 9.34; N, 6.46%. Calcd for $C_9H_{19}NO_4$: C, 52.66; H, 9.33; N, 6.82%.

1,3-Diol (4) from 3a. To a solution of **3a** (2.0 g, 8.6 mmol) in EtOH (15 ml) was added $NaBH_4$ (0.65 g, 17 mmol) at 0 °C. After this was stirred for 1.5 h, the resulting mixture was returned to room temperature for 1.5 h, and quenched by adding a saturated aqueous NH_4Cl solution (50 ml). After removing the organic solvent in vacuo, the obtained residue was extracted with EtOAc (3×10 ml). The combined extracts were washed three times with brine (3×20 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave a syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (2:1 v/v) to give **4**. Yield 85%.

(2*R*,3*R*)-2-(*t*-Butoxycarbonyl)amino-1-(*t*-butyldimethyl)siloxy-3-butanol (5). To a solution of **4** (1.0 g, 4.9 mmol), Et_3N (0.82 ml, 5.9 mmol) and DMAP (30 mg, 0.24 mmol) in CH_2Cl_2 (10 ml) were added TBSCl (0.74 g, 4.9 mmol). After this was stirred for 6 h at room temperature, the reaction mixture was diluted with $CHCl_3$ (20 ml). The resultant solution was washed with water (2×10 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave a colorless syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (4:1 v/v) to give **5** as a colorless syrup. Yield 71%. The syrup crystallized gradually. Mp 68—70 °C. $[\alpha]_D^{25}$ −16.4° (*c* 1.48, MeOH). IR (KBr) 3458, 1692, 1503 cm^{-1}. ^1H NMR δ=0.08 (s, 6H), 0.90 (s, 9H), 1.19 (d, 3H), 1.45 (s, 9H), 3.30 (br d, 1H), 3.85 (dq, 1H), 3.85 (dABq, 2H), 4.15 (ddq, 1H, J=6.4 and 2.0 Hz), 5.18 (br d, 1H, J=8.1 Hz). Found: C, 56.08; H, 10.70; N, 4.36%. Calcd for $C_{15}H_{33}NO_4Si$: C, 56.39; H, 10.41; N, 4.39%.

(2*R*,3*R*)-2-(*t*-Butoxycarbonyl)amino-1-(*t*-butyldimethyl)siloxy-3-(methylsulfonyloxy)butane (6). To a solution of **5** (0.60 g, 1.9 mmol) and Et_3N (0.32 ml, 2.3 mmol) in CH_2Cl_2 (6 ml) was added MsCl (0.15 ml, 1.9 mmol) at 0 °C. After this was stirred for 4 h at room temperature, the reaction mixture was added to $CHCl_3$ (20 ml). The resultant solution was washed with water (2×10 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave a syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (4:1 v/v) to give **6** as a colorless syrup. Yield 88%. $[\alpha]_D^{25}$ −2.0° (*c* 1.20, MeOH). IR (KBr) 3400, 1740, 1530 cm^{-1}. ^1H NMR δ=0.08 (s, 6H), 0.92 (s, 9H), 1.45 (s, 9H), 1.48 (d, 3H), 3.03 (s, 3H), 3.63—3.75 (m, 3H), 4.74 (br d, 1H), 5.03 (dq, 1H, J=3.5 Hz). Found: C, 47.09; H, 8.89; N, 3.66%. Calcd for $C_{16}H_{35}NO_6SSi \cdot 1/2H_2O$: C, 47.26; H, 8.92; N, 3.44%.

(2*S*,3*S*)-3-Azido-2-(*t*-butoxycarbonyl)amino-1-(*t*-butyldimethyl)siloxybutane (7). To a solution of **6** (0.40 g, 1.0 mmol) and 15-crown-5 (0.23 g, 1.0 mmol) in HMPA (1.5 ml) was added NaN_3 (0.33 g, 5.1 mmol) at 55

°C. After this was stirred for 3 h, the reaction mixture was added to EtOAc (30 ml). The resultant solution was washed with brine (10 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave an oily residue, which was purified on a silica-gel column using a mixture of hexane and EtOAc (15:1 v/v) to give **7** as a colorless oil. Yield 87%. $[\alpha]_D^{25}$ +13.6° (*c* 0.75, MeOH). IR (KBr) 2098, 1722, 1503 cm^{-1}. ^1H NMR δ=0.03 (s, 6H), 0.83 (s, 9H), 1.25 (d, 3H, J=6.4 Hz), 1.38 (s, 9H), 3.46—3.86 (m, 4H), 4.74 (br d, 1H). Found: C, 51.93; H, 9.48; N, 15.97%. Calcd for $C_{15}H_{32}N_4O_3Si$: C, 52.29; H, 9.36; N, 16.27%.

(2*S*, 3*S*)- 3- (Benzyloxycarbonyl)amino- 2- (*t*- butoxycarbonyl)amino-1-(*t*-butyldimethyl)siloxybutane (8). A solution of **7** (0.50 g, 1.5 mmol) in EtOH (5 ml) was hydrogenolyzed catalytically with 10% Pd/C (0.1 g) for 2 h at room temperature. After removing the catalyst, the filtrate was stirred together with Et_3N (0.26 ml, 1.9 mmol) and benzyl chloroformate (0.25 ml, 1.7 mmol) for 1 h at room temperature, and then concentrated in vacuo. The obtained residue was dissolved in $CHCl_3$ (30 ml) and washed with saturated aqueous $NaHCO_3$ (10 ml), and then brine (2×10 ml), and finally dried over anhydrous Na_2SO_4. Concentration in vacuo gave crude crystals, which were purified on a silica-gel column using a mixture of hexane and EtOAc (4:1 v/v) to give colorless crystals. Recrystallization from hexane gave **8** as colorless needles. Yield 81%. Mp 96—98 °C. $[\alpha]_D^{25}$ −17.1° (*c* 1.31, MeOH). IR (KBr) 3358, 1686, 1533 cm^{-1}. ^1H NMR δ=0.07 (s, 6H), 0.90 (s, 9H), 1.20 (d, 3H, J=6.8 Hz), 1.44 (s, 9H), 3.50—4.09 (m, 4H), 5.04 (br d, 1H), 5.10 (s, 2H), 5.87 (br d, 1H), 7.36 (s, 5H). Found: C, 60.78; H, 9.25; N, 6.14%. Calcd for $C_{23}H_{40}N_2O_5Si$: C, 61.03; H, 8.91; N, 6.19%.

(2*S*,3*S*)-3-(Benzyloxycarbonyl)amino-2-(*t*-butoxycarbonyl)amino-1-butanol (9). A solution of **8** (0.50 g, 1.1 mmol) in 70% AcOH (10 ml) was stirred for 12 h at room temperature, and then concentrated in vacuo to give colorless crystals. Recrystallization from a mixture of hexane and EtOAc gave **9** as a colorless needles. Yield 90%. IR (KBr) 3352, 1689, 1542 cm^{-1}. ^1H NMR δ=1.24 (d, 3H, J=7.0 Hz), 1.43 (s, 9H), 3.27—3.80 (m, 5H), 5.11 (s, 2H), 5.12 (br d, 1H), 5.22 (br d, 1H), 7.35 (s, 5H).

(2*S*,3*S*)-3-(Benzyloxycarbonyl)amino-2-(*t*-butoxycarbonyl)aminobutanoic Acid (1a). A solution of **9** (0.60 g, 1.8 mmol) in acetone (30 ml) was treated with Jones reagent, with stirring, at 0 °C for 1 h, then quenched with 2-propanol (3 ml). The deposited precipitates were filtered off, and the filtrate was added to saturated aqueous $NaHCO_3$ (30 ml). After removing the organic solvent in vacuo, the aqueous solution was washed with diethyl ether (2×15 ml) and then acidified to pH 4 with citric acid, and extracted with EtOAc (3×20 ml). The combined extracts were washed with brine (3×10 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave colorless crystals, which were recrystallized from a mixture of hexane and EtOAc to give **1a** as a colorless needles. IR (KBr) 3500, 3340, 1695, 1530 cm^{-1}. 200 MHz ^1H NMR (DMSO-d_6) δ=1.02 (d, 3H, J=6.8 Hz), 1.38 (s, 9H), 3.97 (m, 1H), 4.16 (dd, 1H, J=8.8 and 6.3 Hz), 5.01 (s, 2H), 6.94 (br d, 1H, J=8.8 Hz), 7.21 (br d, 1H, J=8.3 Hz), 7.33 (s, 5H). 200 MHz ^{13}C NMR (DMSO-d_6) δ=16.2, 28.2, 47.4, 57.2, 65.2, 78.3, 127.5, 127.7, 128.4, 137.2, 155.4, 155.7, 172.2.

Boc-L-Thr(Bn)-OH (10). To a solution of **2a** (5.0 g, 22 mmol) in DMF (80 ml) was added NaH (55% dispersion in mineral oil, 2.1 g, 48 mmol), with stirring, at −15 °C. After this was stirred for 2 h, benzyl bromide (2.9 ml, 24 mmol) was further added to the mixture, and the resulting mixture was stirred at room temperature for 5 h. The reaction mixture was poured into water (100 ml) and washed with diethyl ether (2×50 ml). The aqueous solution was acidified with citric acid and extracted with EtOAc (3×50 ml). The combined extracts were washed with brine (3×30 ml), and then dried over anhydrous Na_2SO_4. Concentration in vacuo gave a residual syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (2:1 v/v) to give a colorless syrup. After the syrup gradually crystallized, the crystals were recrystallized from a mixture of hexane and EtOAc to give colorless prisms. Yield 85%. Mp 112—114 °C. $[\alpha]_D^{25}$ +15.8° (*c* 1.10, MeOH). Lit,[15] Mp 115—116 °C. $[\alpha]_D$ +15.8° (*c* 1.1, MeOH).

(2*R*,3*R*)-3-Benzyloxy-2-(*t*-butoxycarbonyl)amino-1-butanol (11). A solution of **10** (3.0 g, 9.7 mmol), HOSu (1.2 g, 10.70 mmol), and DCC (2.2 g, 11 mmol) in THF (30 ml) was stirred at 0 °C for 30 min and at room temperature for 6 h. The deposited DCC urea was filtered off, and the filtrate was concentrated in vacuo. The obtained residue was dissolved in THF (30 ml), and then treated with a suspension of $NaBH_4$ (0.70 g, 19 mmol) in EtOH (10 ml) at 0 °C. After this, it was stirred for 30 min, and the resulting mixture was quenched by adding saturated aqueous NH_4Cl (20 ml). Evaporation of the organic solvent in vacuo gave a residue, which was extracted with $CHCl_3$ (3×20 ml). The combined extracts were washed with brine (2×20 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave a syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (2:1 v/v) to give **11** as a colorless syrup. Yield 75%. $[\alpha]_D^{26}$ +8.6° (*c* 1.20, MeOH). IR (KBr) 3348, 1698, 1503 cm^{-1}. ^1H NMR δ=1.22 (d, 3H), 1.44 (s, 9H), 3.16 (br s, 1H), 3.48—3.74 (m, 3H), 3.84 (dq, 1H, J=2.5 and 6.0 Hz), 4.30 and 4.60 (ABq, 2H, J=12.0 Hz), 5.09 (br s, 1H), 7.27 (s, 5H). Found: C, 64.79; H, 8.52; N, 4.93%. Calcd for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53; N, 4.74%.

(*R*)-4-[(*R*)-1-(Benzyloxy)ethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (12). After a solution of **11** (2.0 g, 6.1 mmol), *dl*-camphor-10-sulfonic acid (40 mg) and 2,2-dimethoxypropane (10 ml) in acetone (20 ml) had been stirred for 6 h at room temperature, it was neutralized with Et_3N. The reaction mixture was then evaporated, and the residue was purified on a silica-gel column using a mixture of hexane and EtOAc (5:1 v/v) to give **12** as a colorless syrup. Yield 88%. $[\alpha]_D^{25}$ −13.4° (*c* 1.60, MeOH). IR (KBr) 2936, 1700, 1456 cm^{-1}. ^1H NMR δ=1.18 (d, 3H, J=5.5 Hz), 1.41 (s, 3H), 1.44 (s, 9H), 1.60 (s, 3H), 3.80—4.28 (m, 4H), 4.58 (s, 2H), 7.25 (s, 5H). Found: C, 67.96; H, 8.72; N, 4.19%. Calcd for $C_{19}H_{29}NO_4$: C, 68.03; H, 8.71; N, 4.18%.

(*R*)-3-*t*-Butoxycarbonyl-2,2-dimethyl-4-[(*R*)-1-hydroxyethyl]-1,3-oxazolidine (13). To a solution of **12** (3.2 g, 9.7 mmol) in NH_3 (60 ml) was added Na (ca. 3.3 g) with stirring at −78 °C. After this was stirred for 1 h, excess NH_4Cl was added. The resulting mixture was allowed to stand at room temperature until the dissolved NH_3 disappeared. The reaction mixture was first dissolved in EtOAc (150 ml) and washed with brine (3×40 ml), and then dried over anhydrous Na_2SO_4. Concentration in vacuo

gave a residual syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (4 : 1 v/v) to give colorless crystals. Recrystallization from a mixture of hexane and EtOAc gave **13** as colorless prisms. Yield 76%. Mp 88—89 °C. $[\alpha]_D^{24}$ −16.1° (*c* 1.40, MeOH). IR (KBr) 3442, 1698, 1458 cm^{-1}. ^1H NMR δ=1.19 (d, 3H, J=6.0 Hz), 1.48 (s, 12H), 1.59 (s, 3H), 3.72—4.36 (m, 5H). Found: C, 59.13; H, 9.44; N, 5.75%. Calcd for $C_{12}H_{23}NO_4$: C, 58.75; H, 9.45; N, 5.71%.

(*R*)-3-*t*-Butoxycarbonyl-2,2-dimethyl-4-[(*R*)-1-(methylsulfonyloxy)ethyl]-1,3-oxazolidine (14). To a solution of **13** (1.0 g, 4.1 mmol) in CH_2Cl_2 (10 ml) was added MsCl (0.63 ml, 8.1 mmol) and Et_3N (1.15 ml, 8.1 mmol) with stirring at −10 °C. After this was stirred for 5 min, the reaction mixture was added to diethyl ether (40 ml). The resultant solution was washed with brine (20 ml), 10% citric acid (20 ml), saturated aqueous $NaHCO_3$ (20 ml) and then brine (20 ml), and finally dried over anhydrous Na_2SO_4. Concentration in vacuo gave colorless crystals, which were recrystallized from hexane to give **14** as colorless needles. Yield 90%. Mp 80—82 °C. $[\alpha]_D^{25}$ +3.2° (*c* 1.0, MeOH). IR (KBr) 1698, 1365, 1176, 912 cm^{-1}. 200 MHz ^1H NMR (65 °C) δ=1.39 (d, 3H, J=6.8 Hz), 1.45 (s, 3H), 1.49 (s, 9H), 1.59 (s, 3H), 3.00 (s, 3H), 3.60—3.75 (m, 1H), 3.93—4.19 (m, 2H), 5.01—5.20 (m, 1H). Found: C, 48.51; H, 7.51; N, 4.21%. Calcd for $C_{13}H_{25}NO_6S$: C, 48.24; H, 7.73; N, 4.33%.

(*S*)-4-[(*S*)-1-Azidoethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (15). A solution of **14** (1.8 g, 5.5 mmol), NaN_3 (2.0 g, 31 mmol) and 15-crown-5 (0.2 ml) in HMPA (1 ml) was stirred for 5 h at 70 °C. Excess NaN_3 was filtered off and the filtrate was evaporated in vacuo. The residue was purified on a silica-gel column using a mixture of hexane and EtOAc (10 : 1 v/v) to give **15** as a colorless syrup. Yield 75%. $[\alpha]_D^{25.5}$ +33.3° (*c* 2.10, MeOH). IR (KBr) 2104, 1698 cm^{-1}. 200 MHz ^1H NMR (65 °C) δ=1.21 (d, 3H, J=6.8 Hz), 1.49 (s, 12H), 1.60 (s, 3H), 3.75—3.97 (m, 4H). Found: C, 53.42; H, 8.33; N, 20.94%. Calcd for $C_{12}H_{22}N_4O_3$: C, 53.31; H, 8.20; N, 20.73%.

(*S*)-4-[(*S*)-1-(Benzyloxycarbonylamino)ethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (16). A solution of **15** (1.0 g, 3.2 mmol) in EtOH (20 ml) was treated catalytically with 10% Pd/C (100 mg) at room temperature for 6 h. After removing the catalyst, Et_3N (0.57 ml, 4.1 mmol) and benzyl chloroformate (0.65 ml, 3.5 mmol) were added to the resultant solution. After this was stirred for 1 h at room temperature, the reaction mixture was concentrated in vacuo. The residue was dissolved in $CHCl_3$ (50 ml) and washed with saturated aqueous $NaHCO_3$ (20 ml), and then brine (2×20 ml), and finally dried over anhydrous Na_2SO_4. Concentration in vacuo gave crude crystals, which were recrystallized from a mixture of hexane and EtOAc to give **16** as colorless needles. Yield 70%. Mp 88—89 °C. $[\alpha]_D^{24}$ +72.1° (*c* 1.21, MeOH). IR (KBr) 3352, 1701, 1527 cm^{-1}. ^1H NMR δ=1.22 (d, 3H, J=6.1 Hz), 1.44 (s, 9H), 1.48 (s, 3H), 1.55 (s, 3H), 3.65—4.15 (m, 4H), 5.08 (s, 2H), 5.88 (br d, 1H), 7.32 (s, 5H). Found: C, 63.35; H, 7.81; N, 7.31%. Calcd for $C_{20}H_{30}N_2O_5$: C, 63.47; H, 7.99; N, 7.40%.

Compound 9 from 16. A solution of **16** (1.0 g, 2.6 mmol) in 70% AcOH (20 ml) was stirred at room temperature for 12 h. The reaction mixture was concentrated in vacuo to give colorless crystals. Recrystallization from a mixture of hexane and EtOAc gave **9** as colorless needles. Yield 90%.

Boc-L-Thr(Ms)-OMe (17). To a solution of **3a** (4.0 g, 17 mmol) and pyridine (14 ml, 17 mmol) in CH_2Cl_2 (30 ml) was added MsCl (1.5 ml, 19 mmol) with stirring at 0 °C. After this was stirred for 1 h and at room temperature for 3 h, the reaction mixture was washed with 0.5 M HCl (2×20 ml, M=mol dm^{-3}), and then brine (3×20 ml), and finally dried over anhydrous Na_2SO_4. Concentration in vacuo gave an oil, which was used to next reaction without purification. Yield about 70%. IR (KBr) 1716, 1515, 1368 cm^{-1}. ^1H NMR δ=1.22 (d, 3H, J=6.1 Hz), 1.47 (s, 9H), 2.98 (s, 3H), 3.79 (s, 3H), 4.51 (dd, 1H), 5.13—5.44 (m, 2H).

(2*R*,3*R*)-2-(*t*-Butoxycarbonyl)amino-3-(methylsulfonyloxy)butanol (18). To a solution of **17** (3.0 g, 9.6 mmol) in EtOH (20 ml) was added $NaBH_4$ (0.73 g, 19 mmol) at 0 °C. After this was stirred for 1 h and at room temperature for 1.5 h, the reaction mixture was quenched by adding aqueous NH_4Cl (50 ml). Evaporation of organic solvent gave a residue, which was extracted with EtOAc (3×50 ml). The combined extracts were washed with brine (3×30 ml) and dried over anhydrous Na_2SO_4. Concentration in vacuo gave a syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (2 : 1 v/v) to give **18** as a colorless syrup. Yield 75%. $[\alpha]_D^{25.5}$ +5.6° (*c* 1.10, MeOH). IR (KBr) 3400, 1704, 1521, 1368 cm^{-1}. ^1H NMR δ=1.22 (d, 3H, J=6.1 Hz), 1.44 (s, 9H), 2.52 (br s, 1H), 3.07 (s, 3H), 3.68 (d, 2H), 3.96 (ddd, 1H), 4.91 (br d, 1H), 5.09 (dq, 1H). Found: C, 42.44; H, 7.38; N, 5.08%. Calcd for $C_{10}H_{21}NO_6S$: C, 42.39; H, 7.47; N, 4.94%.

(2*S*,3*S*)-3-Azido-2-(*t*-butoxycarbonyl)amino-1-butanol (19). Similarly as in the case of **15**, the azidation of **18** was carried out to give a syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (5 : 1 v/v) to give **19** as a colorless syrup. Yield 82%. $[\alpha]_D^{18}$ +41.1° (*c* 0.80, MeOH). IR (KBr) 3370, 2110, 1701, 1515 cm^{-1}. ^1H NMR δ=1.22 (d, 3H, J=6.6 Hz), 1.46 (s, 9H), 2.53 (br s, 1H), 3.48—3.91 (m, 4H), 5.18 (br d, 1H). Found: C, 46.75; H, 7.75; N, 23.81%. Calcd for $C_9H_{18}N_4O_3$: C, 46.95; H, 7.88; N, 24.33%.

Compound 9 from 19. Similarly as in the case of **9** from **8**, the catalytic hydrogenolysis of **19** with 5% Pd/C, and then acylation with CbzCl were carried out to give **9**. Yield 85%.

Boc-D-Thr(Ms)-OMe (20). Similarly as in the case of **17**, the mesylation of **3b** with MsCl was performed to give **20** (75%) as a colorless syrup, which was used in the next reaction without further purification.

(2*S*,3*S*)-2-(*t*-Butoxycarbonyl)amino-3-(methylsulfonyl)oxy-1-butanol (21). Similarly as in the case of **18**, the reduction of **20** with $NaBH_4$ was performed to give **21** (75%) as a colorless syrup, which was used in the next reaction without further purification.

(2*R*,3*R*)-3-Azido-2-(*t*-butoxycarbonyl)amino-1-butanol (22). Similarly as in the case of **19**, the azidation of **21** with NaN_3 was carried out to give **22** as a colorless syrup. Yield 80%. $[\alpha]_D^{19}$ −43.6° (*c* 0.90, MeOH). Found: C, 46.78; H, 7.79; N, 24.25%. Calcd for $C_9H_{18}N_2O_3$: C, 46.95; H, 7.88; N, 24.33%.

(2*R*,3*R*)-3-(Benzyloxycarbonyl)amino-2-(*t*-butoxycarbonyl)amino-1-butanol (23). Similarly as in the case of **9** from **19**, the catalytic hydrogenolysis of **22** with

5% Pd/C and the acylation with CbzCl were performed to give colorless crystals. Recrystallization from a mixture of hexane and EtOAc gave **23** as colorless needles. Yield 85%.

(2*R*, 3*R*)- 3- (Benzyloxycarbonyl)amino- 2- (*t*- butoxycarbonyl)aminobutanoic Acid (1b). Similarly as in the case of **1a**, the Jones oxidation of **23** was performed to give **1b** as colorless needles. Yield 65%.

(4*S*,5*R*)-4,8,8-Trimethyl-1-aza-3,7-dioxabicyclo-[3.3.0]octan-2-one (26). To a solution of **13** (0.1 g, 0.6 mmol) in CH_2Cl_2 (2 ml) was added pyridine (0.43 ml, 5.5 mmol) and Tf_2O or TosCl (0.50 mmol) under cooling. After this was stirred for 30 min and at room temperature for 3 h, the reaction mixture was dissolved in $CHCl_3$ (15 ml) and washed successively with 0.5 M-HCl (2×10 ml) and brine (10 ml), and then dried over anhydrous Na_2SO_4. Concentration in vacuo gave a syrup, which was purified on a silica-gel column using a mixture of hexane and EtOAc (2 : 1 v/v) to give **26** as an unstable colorless syrup. Yield 70%. IR (KBr) 2986, 1758, 1392 cm^{-1}. ^1H NMR δ=1.36 (d, 3H, Me), 1.70 (s, 3H, Me), 3.42 (s, 3H, Me), 3.74 (dd, 1H, H-4b), 3.93 (dd, 1H, H-4a, J=9.0 Hz), 4.36 (ddd, 1H, H-5, J=6.1 and 8.0 Hz), 4.67 (dq, 1H, H-6, J=6.0 and 8.0 Hz).

(*R*)- 4- [(*S*)- 1- (Benzoyloxy)ethyl]- 3- *t*- butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (27). To a solution of **13** (2.0 g, 8.2 mmol) in THF (20 ml) was added a solution of Ph_3P (6.85 g, 26.1 mmol) in THF (10 ml) and benzoic acid (5.0 g, 40.9 mmol) in benzene (20 ml) at 0 °C. After this was stirred for 8 min, a solution of diethyl azodicarboxylate (6.4 ml, 40.6 mmol) in THF (10 ml) was added to the resulting solution. After it was stirred for an additional 10 min and allowed to stand at room temperature for 5 h, the reaction mixture was added to EtOAc (50 ml). The resultant solution was washed with 10% citric acid (3×30 ml), then with saturated aqueous $NaHCO_3$ (3×30 ml) and finally with brine (3×30 ml). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified on a silica-gel column using a mixture of $CHCl_3$ and acetone (7 : 1 v/v) to give **27** as a colorless syrup. Yield 70%. $[\alpha]_D^{25}$ +2.6° (*c* 1.0, MeOH). IR (KBr) 2980, 2978, 1701, 1695 cm^{-1}. ^1H NMR δ=1.43 (d, 3H, J=6.6 Hz), 1.59 (s, 15H), 3.92—4.52 (m, 3H), 5.62 (dq, 1H), 7.34—8.44 (m, 5H). Found: C, 65.19; H, 7.77; N, 3.90%. Calcd for $C_{19}H_{27}NO_5$: C, 65.31; H, 7.79; N, 4.01%.

(*R*)-3-*t*-Butoxycarbonyl-2,2-dimethyl-4-[(*S*)-1-hydroxyethyl]-1,3-oxazolidine (28). To a solution of **27** (2.0 g, 5.7 mmol) in MeOH (15 ml) was added K_2CO_3 (1.4 g, 10.1 mmol) at room temperature. After this was stirred for 12 h, the excess K_2CO_3 was filtered off and the filtrate was concentrated in vacuo. The residue was purified on a silica-gel column using a mixture of hexane and EtOAc (4 : 1 v/v) to give **28** as a colorless syrup. Yield 90%. $[\alpha]_D^{24}$ +36.2° (*c* 1.15, MeOH). IR (KBr) 3466, 1698, 1515 cm^{-1}. ^1H NMR δ=1.16 (d, 3H, J=4.4 Hz), 1.50 (s, 12H), 1.58 (s, 3H), 3.75—4.27 (m, 5H). Found: C, 58.31; H, 9.32; N, 5.60%. Calcd for $C_{12}H_{23}NO_4$: C, 58.75; H, 9.45; N, 5.71%.

(*R*)- 3- *t*- Butoxycarbonyl- 2, 2- dimethyl- 4- [(*S*)- 1- (methylsulfonyl)ethyl]-1,3-oxazolidine (29). Similarly as in the case of **14**, the mesylation of **28** was performed to give **29**, which was used in the next reaction without purification. 200 MHz ^1H NMR (65 °C) δ=1.40 (d, 3H, J=6.4 Hz), 1.45 (s, 3H), 1.49 (s, 9H), 1.58 (s, 3H), 2.98 (s, 3H), 3.93—4.07 (m, 3H), 5.04—5.19 (m, 1H).

(*S*)-4-[(*R*)-1-Azidoethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (30). Similarly as in the case of **15**, the azidation of **29** was carried out to give **30** as a colorless syrup. Yield 85%. $[\alpha]_D^{25.5}$ −0.9° (*c* 2.0, MeOH). IR (KBr) 2980, 2116, 1704 cm^{-1}. 200 MHz ^1H NMR (65 °C) δ=1.21 (d, 3H, J=6.8 Hz), 1.47 (s, 12H), 1.49 (s, 9H), 1.59 (s, 3H), 3.76—4.22 (m, 4H). Found: C, 53.60; H, 8.24; N, 20.44%. Calcd for $C_{12}H_{32}N_4O_3$: C, 53.32; H, 8.20; N, 20.73%.

(*S*)-4-[(*R*)-1-(Benzyloxycarbonylamino)ethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (31). Similarly as in the case of **16**, the successive hydrogenolysis of **30** and acylation with CbzCl was performed to give **31** as a colorless syrup. Yield 70%. $[\alpha]_D^{25.5}$ +1.4° (*c* 1.10, MeOH). IR (KBr) 3352, 1701, 1527 cm^{-1}. ^1H NMR δ=1.22 (d, 3H, J=6.1 Hz), 1.44 (s, 9H), 1.48 (s, 3H), 1.55 (s, 3H), 3.65—4.14 (m, 4H), 5.08 (s, 2H), 5.88 (br d, 1H), 7.37 (s, 5H). Found: C, 63.66; H, 8.11; N, 7.31%. Calcd for $C_{20}H_{30}N_2O_5$: C, 63.47; H, 7.99; N, 7.40%.

(2*S*, 3*R*)- 3- (Benzyloxycarbonyl)amino- 2- (*t*- butoxycarbonyl)amino-1-butanol (32). Similarly as in the case of **9** from **16**, the deprotection of **31** with 70% AcOH was performed to give **32** as colorless needles. Yield 90%. IR (KBr) 3478, 1695, 1668, 1548 cm^{-1}. ^1H NMR δ=1.20 (d, 3H, J=6.8 Hz), 1.41 (s, 9H), 3.22—4.07 (m, 5H), 5.08 (s, 2H), 5.14 (br d, 1H, NH), 5.79 (br d, 1H, NH), 7.39 (s, 5H).

(2*S*, 3*R*)- 3- (Benzyloxycarbonyl)amino- 2- (*t*- butoxycarbonyl)aminobutanoic Acid (1c). Similarly as in the case of **1a**, the oxidation of **32** was performed to give **1c** as colorless needles. Yield 65%. IR (KBr) 3382, 2974, 1695, 1599, 1518 cm^{-1}. 200 MHz ^1H NMR (DMSO-d_6) δ=1.07 (d, 3H, J=6.4 Hz), 1.38 (s, 9H), 3.97—4.20 (m, 2H), 5.00 (s, 2H), 6.89 (br d, 1H, NH), 6.72 (br d, 1H, NH), 7.17 (br d, 1H, J=9.7 Hz), 7.33 (s, 5H). 200 MHz ^{13}C NMR (DMSO-d_6) δ=18.4, 28.2, 47.7, 57.8, 65.4, 78.5, 127.7, 127.9, 128.4, 137.1, 155.5, 155.9, 172.1.

Boc-D-Thr(Bn)-OH (33). Similarly as in the case of **10**, the benzylation of **2b** was performed to give **33** as colorless prisms. Yield 87%.

(2*S*,3*R*)-3-Benzyloxy-2-(*t*-butoxycarbonyl)aminobutanol (34). Similarly as in the case of **11**, the reduction of **33** was performed to give **34** as colorless syrup. Yield 75%. Found: C, 64.80; H, 8.60; N, 4.78%. Calcd for $C_{16}H_{25}NO_4$: C, 65.05; H, 8.53; N, 4.74%.

(*S*)-4-[(*S*)-1-(Benzyloxy)ethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (35). Similarly as in the case of **12**, the acetonation of **34** was carried out to give **35** as a colorless syrup. Yield 88%. $[\alpha]_D^{25}$ −13.4° (*c* 1.60, MeOH). Found: C, 67.68; H, 8.64; N, 4.09%. Calcd for $C_{19}H_{29}NO_4$: C, 68.03; H, 8.71; N, 4.18%.

(*S*)-3-*t*-Butoxycarbonyl-4-[(*S*)-1-hydroxyethyl]-2,2-dimethyl-1,3-oxazolidine (36). Similarly as in the case of **13**, the debenzylation of **35** was performed to give **36** as a colorless syrup. Yield 79%. $[\alpha]_D^{26}$ −11.9° (*c* 1.19, MeOH). Found: C, 58.75; H, 9.45; N, 5.78%. Calcd for $C_{12}H_{23}NO_4$: C, 58.75; H, 9.45; N, 5.71%.

(*S*)-4-[(*R*)-1-(Benzyloxy)ethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (37). Similarly as in the case of **27**, the benzylation of **36** was performed to give **37** as a colorless syrup. Yield 71%. $[\alpha]_D^{25}$ +2.6° (*c* 1.0, MeOH). Found: C, 65.55; H, 7.83; N, 3.95%. Calcd for $C_{19}H_{27}NO_4$: C, 65.31; H, 7.79; N, 4.01%.

(*S*)-3-*t*-Butoxycarbonyl-2,2-dimethyl-4-[(*R*)-1-hydroxyethyl]-1,3-oxazolidine (38). Similarly as in the case of **28**, the hydrolysis of **37** was performed to give **38** as a colorless syrup. Yield 89%. $[\alpha]_D^{24}$ −39.4° (*c* 1.33, MeOH). Found: C, 58.59; H, 9.35; N, 5.48%. Calcd for $C_{12}H_{23}NO_4$: C, 58.75; H, 9.45; N, 5.71%.

(*S*)-3-*t*-Butoxycarbonyl-2,2-dimethyl-4-[(*R*)-1-(methanesulfonyloxy)ethyl]-1,3-oxazolidine (39). Similarly as in the case of **29**, the mesylation of **38** was carried out to give **39**, which was used to next reaction without purification.

(*R*)-4-[(*S*)-1-Azidoethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (40). Similarly as in the case of **30**, the azidation of **39** was carried out to give **40** as a colorless syrup. Yield 83%. $[\alpha]_D^{25.5}$ −0.9° (*c* 2.0, MeOH). Found: C, 53.39; H, 7.76; N, 21.01%. Calcd for $C_{12}H_{22}N_4O_3$: C, 53.32; H, 8.20; N, 20.73%.

(*R*)-4-[(*S*)-1-(Benzyloxycarbonylamino)ethyl]-3-*t*-butoxycarbonyl-2,2-dimethyl-1,3-oxazolidine (41). Similarly as in the case of **31**, the successive hydrogenolysis of **40** and acylation with CbzCl was performed to give **41** as a colorless syrup. Yield 75%. $[\alpha]_D^{25.5}$ +1.4° (*c* 1.10, MeOH). Found: C, 63.24; H, 8.07; N, 6.94%. Calcd for $C_{20}H_{30}N_2O_5$: C, 63.47; H, 7.99; N, 7.40%.

(2*R*, 3*S*)-3-(Benzyloxycarbonyl)amino-2-(*t*-butoxycarbonyl)amino-1-butanol (42). Similarly as in the case of **32**, the deprotection of **41** with 70% AcOH was performed to give **42** as colorless needles. Yield 92%.

(2*R*, 3*S*)-3-(Benzyloxycarbonyl)amino-2-(*t*-butoxycarbonyl)aminobutanoic Acid (1d). Similarly as in the case of **1c**, the oxidation of **42** was performed to give **1d** as colorless needles. Yield 63%.

References

1) Part XVI: Y. Nakamura, A. Ito, and C. Shin, *Bull. Chem. Soc. Jpn.*, **67**, 2151 (1994).
2) T. Komori, M. Ezaki, E. Kino, M. Kohsaka, H. Aoki, and H. Imanaka, *J. Antibiot.*, **38**, 691 (1985).
3) N. Shimada, K. Morimoto, H. Naganawa, T. Takita, M. Hamada, K. Maeda, T. Takeuchi, and H. Umezawa, *J. Antibiot.*, **34**, 1613 (1981).
4) T. Shiroza, N. Ebisawa, K. Furihata, T. Endo, H. Seto, and N. Otake, *Agric. Biol. Chem.*, **46**, 865 (1982).
5) M. Bodanszky, G. F. Sigler, and A. Bodanszky, *J. Am. Chem. Soc.*, **95**, 2352 (1973).
6) E. Atherton and J. Meienhofer, *Hoppe-Seyler's Z. Physiol. Chem.*, **354**, 689 (1973); J. H. Martin and W. K. Hausmann, *J. Am. Chem. Soc.*, **82**, 2079 (1960).
7) U. Schmidt, K. Mundinger, B. Riedl, G. Haas, and R. Lau, *Synthesis*, **1992**, 1201.
8) U. Schmidt, K. Mundinger, R. Mangold, and A. Lieberknecht, *J. Chem. Soc., Chem. Commun.*, **1990**, 1216.
9) U. Schmidt and B. Riedl, *J. Chem. Soc., Chem. Commun.*, **1992**, 1186.
10) U. Schmidt and B. Riedl, *Synthesis*, **1993**, 815.
11) Y. Nakamura and C. Shin, *Chem. Lett.*, **1992**, 49.
12) K. Sato, S. Saijo, and K. Kotera, *Chem. Pharm. Bull.*, **33**, 1342 (1985).
13) M. A. Lago, T. Samanen, and J. D. Elliott, *J. Org. Chem.*, **57**, 3493 (1992).
14) O. Mitsunobu, *Synthesis*, **1979**, 1.
15) T. Takaya, Y. Kishida, and S. Sakakibara, *J. Chromatogr.*, **215**, 297 (1992).