Highly Diastereoselective Synthesis of 2-Oxazoline-4-carboxylates by Formal [3 + 2] Cycloadditions of a 5-Alkoxyoxazole with α-Alkoxy Aldehydes Catalyzed by Tin(IV) Chloride

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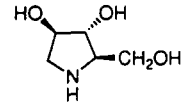
Received November 30, 1993®

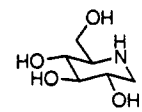
The formal [3 + 2] cycloaddition of 5-methoxy-2-(*p*-methoxyphenyl)oxazole with 2(*S*)-(benzyloxy)-propanal and 2(*S*)-[(*tert*-butyldimethylsilyl)oxy]propanal in the presence of tin(IV) chloride gave *cis*-(4*R*,5*S*,1′*S*)- and *trans*-(4*S*,5*S*,1′*S*)-5-(1′-alkoxyethyl)-4-(methoxycarbonyl)-2-(*p*-methoxyphenyl)-2-oxazolines with high diastereoselectivity (94 and 92% selectivity, respectively). A similar reaction of 5-methoxy-2-(*p*-methoxyphenyl)oxazole with 2,3-di-*O*-benzyl-*D*-glyceraldehyde gave methyl *cis*-(4*S*,5*R*,1′*R*)-2-(*p*-methoxyphenyl)-5-[1′,2′-bis(benzyloxy)ethyl]-2-oxazoline-4-carboxylate with high diastereoselectivity (>95% selectivity), and the latter was easily converted to biologically important chiral 2-amino-1,3,4,5-tetrol derivatives.

Introduction

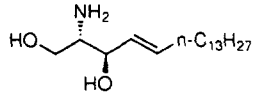
There are many biologically active compounds incorporating chiral *erythro*-2-amino polyol substructures, such as sphingosine and phytosphingosine, which participate in various functions of the central nervous system, and *D*-AB1 and 1-deoxynojirimycin, which show glycosidase inhibitor activity.[1] Optically pure 2-oxazoline-4-carboxylates are useful building blocks for the synthesis of chiral β-hydroxy amino acids, 2-amino 1,3-diols, and their derivatives.[2,3] Recently, we reported the first *cis*-selective syntheses of 5-substituted 2-oxazoline-4-carboxylates by the formal [3 + 2] cycloaddition of 5-alkoxyoxazoles with aldehydes.[4] The reaction of a 5-alkoxyoxazole with a



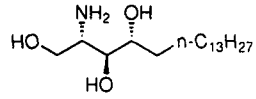
D-AB1



1-Deoxynojirimycin



Sphingosine



Phytosphingosine

chiral α-alkoxy aldehyde is expected to give a 5-(1′-alkoxyalkyl)-substituted 2-oxazoline-4-carboxylate diastereoselectively in an optically pure form by means of chiral induction resulting from the cycloaddition pathway. The establishment of a synthesis of chiral 2-oxazoline-4-carboxylates should be useful for the synthesis of biological active compounds having a chiral amino polyol structure. We now wish to report the diastereoselective synthesis of methyl *cis*- and *trans*-5-(1′-alkoxyalkyl)-2-oxazoline-4-carboxylates by the tin(IV) chloride-catalyzed reaction of 5-methoxy-2-(*p*-methoxyphenyl)oxazole (1) with chiral α-alkoxy aldehydes and the easy transformation of the 2-oxazoline-4-carboxylates to chiral *erythro*-2-amino polyol derivatives.

Results and Discussion

The reaction of oxazole 1 with 2(*S*)-(benzyloxy)propanal[5] in CH_2Cl_2 in the presence of several kinds of Lewis acids gave four diastereomeric 2-oxazoline-4-carboxylates, **2a–d**, in the ratios shown in Table 1 (runs 1–6). Titanium(IV) chloride, boron trifluoride etherate, ethylaluminum dichloride, and catalyst B, which was prepared *in situ* by mixing ethylaluminum dichloride and 2,4,6-tribromophenol, showed unsatisfactory selectivity. However, the reaction catalyzed by tin(IV) chloride (1.0 equiv) at −20 °C for 2 h gave 2-oxazoline-4-carboxylates in high yield (85%) and high diastereoselectivity (**2a:2b:2c:2d** = 94:3:2:1) through predominant *si*-face attack of oxazole 1 on 2(*S*)-(benzyloxy)propanal (run 1). The use of boron trifluoride etherate or ethylaluminum dichloride resulted in an increase of *re*-face attack on the aldehyde in comparison with other Lewis acids that have the ability to chelate. It is interesting to note that catalyst A, which was prepared *in situ* by mixing $AlMe_3$ and binaphthol, rarely showed satisfactory *cis*-selectivity (run 5). This result contrasts with the up to 98% *cis*-selectivity obtained with this catalyst and simple aldehydes.[4]

As described in a previous paper,[4] the tin(IV) chloride-catalyzed reaction of 1 with benzaldehyde and ethyl glyoxylate resulted in *trans*-selectivity due to epimerization of the products under the reaction conditions.[6] In the case of the reaction with 2(*S*)-(benzyloxy)propanal, *cis*-selectivity was observed, which may be attributed to inhibition of epimerization by the formation of a complex

® Abstract published in *Advance ACS Abstracts*, May 15, 1994.

(1) For a review, see: Nishimura, Y. *J. Synth. Org. Chem., Jpn.* **1991**, *49*, 846.

(2) For stereoselective syntheses of *trans*-2-oxazolines and their transformation to β-amino alcohols, see: (a) Matsumoto, K.; Urabe, Y.; Ozaki, Y.; Iwasaki, T.; Miyoshi, M. *Agric. Biol. Chem.* **1975**, *39*, 1869. (b) Matsumoto, K.; Ozaki, Y.; Suzuki, M.; Miyoshi, M. *Agric. Biol. Chem.* **1976**, *40*, 2045. (c) Ozaki, Y.; Matsumoto, K.; Miyoshi, M. *Agric. Biol. Chem.* **1978**, *42*, 1565. (d) Hoppe, D.; Schöllkopf, U. *Liebigs Ann. Chem.* **1972**, *763*, 1.

(3) For enantioselective syntheses of *trans*-2-oxazolines and their transformation to β-amino alcohols, see: (a) Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 645. (b) *Idem. Tetrahedron Lett.* **1987**, *28*, 6215. (c) *Ibid.* **1988**, *29*, 239. (d) Ito, Y; Sawamura, M.; Shirakawa, E.; Hayashizaki, K.; Hayashi, T. *Ibid.* **1988**, *29*, 235. (e) *Idem. Tetrahedron* **1988**, *44*, 5253.

(4) (a) Suga, H.; Shi, X.; Fujieda, H.; Ibata, T. *Tetrahedron Lett.* **1991**, *32*, 6911. (b) Suga, H.; Shi, X.; Ibata, T. *J. Org. Chem.* **1993**, *58*, 7397.

(5) Wuts, P. G. M.; Bigelow, S. S. *J. Org. Chem.* **1983**, *48*, 3489.

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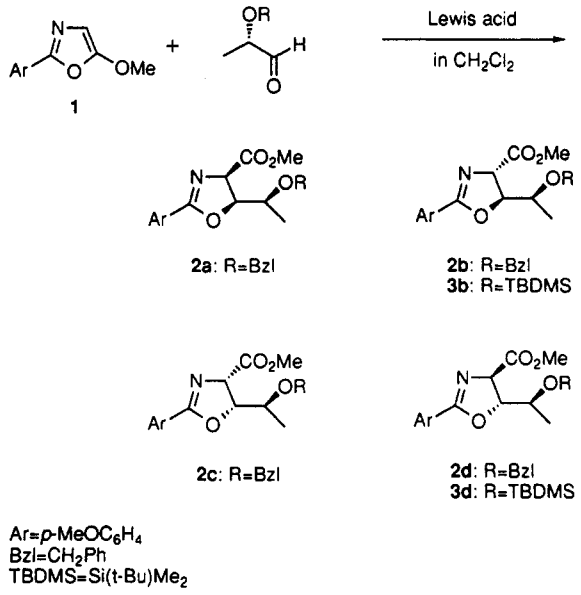
Table 1. Reactions of Oxazole 1 with 2(*S*)-(Benzyloxy)propanal and 2(*S*)-[(*tert*-Butyldimethylsilyl)oxy]propanal[a]

run	R	conditions: Lewis acid	conditions: temp (time)	% yield[b,f]	2a:2b:2c:2d or 3b:3d[b]	*cis*/*trans*	*si*/*re*
1	Bzl	$SnCl_4$	−20 °C (2 h)	85	94:3:2:1	96/4	97/3
2	Bzl	$TiCl_4$	−20 °C (2 h)–0 °C (20 h)	51	47:21:25:7	72/28	68/32
3	Bzl	BF_3·OEt_2	−20 °C (2 h)–0 °C (20 h)	30	4:37:9:50	13/87	41/59
4	Bzl	$EtAlCl_2$	−20 °C (2 h)–0 °C (20 h)	76	6:36:12:46	18/82	42/58
5	Bzl	catalyst A[c]	0 °C (5 h)–rt (50 h)	20	10:36:24:30	34/66	46/54
6	Bzl	catalyst B[d]	0 °C (25 h)	81	10:58:9:23	19/81	68/32
7	TBDMS	$SnCl_4$	0 °C (30 h)	53	92:8	*trans* only	92/8
8	TBDMS	Et_2AlCl	0 °C (25 h)	43	52:48	*trans* only	52/48
9	TBDMS	$EtAlCl_2$	0 °C (25 h)	65	46:54	*trans* only	46/54
10	TBDMS	catalyst B[d]	0 °C (25 h)	41	70:30	*trans* only	70/30
11	TBDMS	catalyst C[e]	0 °C (30 h)	48	71:29	*trans* only	71/29

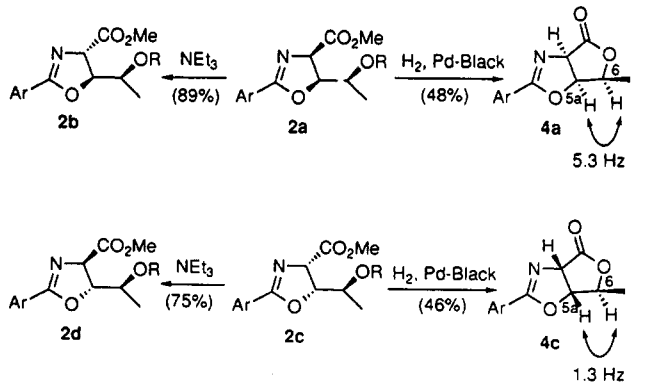
[a] The reaction was carried out in the presence of 1.0 equiv of Lewis acid in CH_2Cl_2 unless otherwise stated. [b] Total yields of adducts. Determined by HPLC analysis. [c] Catalyst A was prepared *in situ* by allowing $AlMe_3$ to react with binaphthol at rt for 1 h; 5.0 equiv of catalyst A was used in a solution of acetonitrile. [d] Catalyst B was prepared *in situ* by mixing equimolar amounts of 2,4,6-tribromophenol and $EtAlCl_2$ at rt for 1.5 h. [e] Catalyst C was prepared *in situ* by allowing $AlMe_3$ to react with 2.0 equiv of 2,4,6-tribromophenol at rt for 1 h. [f] Oxazole 1 was recovered unchanged: run 1, 13%; run 2, 15%; run 3, 59%; run 4, 14%; run 5, 8%; run 6, 10%; run 7, 27%; run 8, 7%; run 9, 9%; run 10, 11%.



of the initially produced 2-oxazoline with tin(IV) chloride. Milky precipitates are deposited in the flask as the reaction proceeds. The tin(IV) chloride-catalyzed reaction of **1** with α-benzyloxy aldehydes is a more effective methodology for the stereoselective synthesis of *cis*-5-aliphatic substituted 2-oxazoline-4-carboxylates than the previously reported catalyst A-catalyzed cycloaddition of 5-alkoxyoxazoles with aliphatic aldehydes.[4]

The reaction of oxazole **1** with 2(*S*)-[(*tert*-butyldimethylsilyl)oxy]propanal in the presence of tin(IV) chloride gave *trans*-2-oxazoline-4-carboxylate **3b** in a highly diastereoselective manner (run 7), instead of the product of *re*-face attack through a Felkin–Anh-type transition state model. In this case, the predominant formation of *trans*-2-oxazolines is probably explained by the epimerization of *cis*-2-oxazolines to thermodynamically more stable *trans*-products under the reaction conditions.[6] Bulky organoaluminum Lewis acids, such as catalysts B and C, gave increased *si*-face selectivity in comparison with diethylaluminum chloride and ethylaluminum dichloride (runs 8–11).[7]

The structures of 2-oxazoline-4-carboxylates **2a–d** were determined as follows. *cis*-2-Oxazolines **2a** and **2c** were converted to the corresponding lactones **4a** and **4c**, respectively, by debenzylation (H_2, Pd-black, AcOH in MeOH) followed by cyclization. The *cis*- and *trans*-geometries (H_{5a}–H_6) of the lactones were established by examination of the ^1H NMR coupling constants. Thus, *cis*-isomer **4a** displayed a coupling constant of J_{5a-6} = 5.3 Hz, whereas *trans*-isomer **4c** displayed a smaller coupling constant (J_{5a-6} = 1.3 Hz). Thereby, **2a** was determined to be *cis*-(4*R*,5*S*,1′*S*)-5-[1′-(benzyloxy)ethyl]-4-(methoxycarbonyl)-2-(*p*-methoxyphenyl)-2-oxazoline by virtue of the fact that the absolute configuration of C-1′ of **2a** is the same as that of the C-2 of the starting 2(*S*)-(benzyloxy)propanal. The optical purity of oxazoline **2a** was 96% ee[8] by HPLC analysis (DAICEL CHIRALPAK AS with 10% *i*-PrOH in hexane (0.5 mL/min)). The structures of *trans*-2-oxazolines **2b** and **2d** were determined by the fact that the epimerization of *cis*-2-oxazolines **2a** and **2c** in the presence of triethylamine in MeCN gave thermodynamically more stable **2b** and **2d**, respectively, through deprotonation at C-4. The structures of oxazolines **3b** and **3d** were determined by the fact that their desilylation products were identical to the debenzylation products of **2b** and **2d**, respectively.



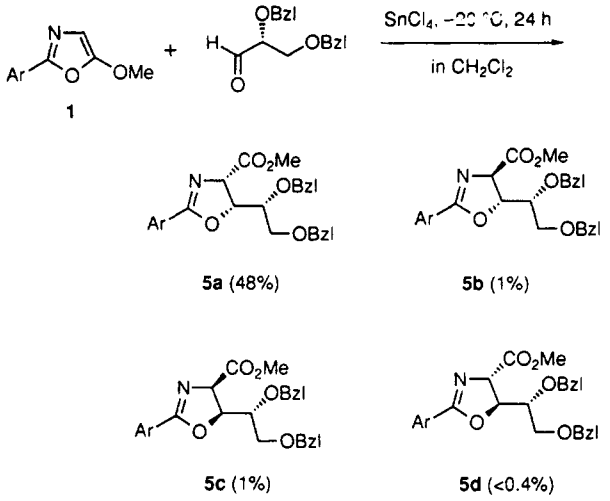
Oxazole **1** undergoes the formal [3 + 2] cycloaddition

(6) Some *cis*-2-oxazoline-4-carboxylates epimerize in the presence of tin(IV) chloride. For example, *cis*-2-(*p*-methoxyphenyl)-5-phenyl-2-oxazoline-4-carboxylate and *cis*-4,5-bis(ethoxycarbonyl)-2-(*p*-methoxyphenyl)-2-oxazoline epimerize to the *trans*-2-oxazoline in the presence of tin(IV) chloride (1.0 equiv).[4]

(7) Bulky organoaluminum reagents, such as methylaluminum bis(2,4,6-tri-*tert*-butylphenoxide), show anti-Cram selectivity: Maruoka, K.; Itoh, T.; Sakurai, M.; Nonoshita, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 3588.

(8) A small degree of racemization occurs, probably during the synthesis of the aldehyde.[5]

with 2,3-di-*O*-benzyl-D-glyceraldehyde[9] in the presence of $SnCl_4$ to give *cis*-2-oxazoline-4-carboxylate **5a** with high diastereoselectivity (**5a**:**5b**:**5c**:**5d** = >95:2:2:<1).[10] This



stereoselectivity of the reaction with this aldehyde is nearly the same as that of the reaction with 2(*S*)-(benzyloxy)-propanal, and a milky precipitate was deposited in the flask as the reaction proceeded. In marked contrast, 2,3-*O*-isopropylidene-D-glyceraldehyde gave less satisfactory results in terms of reactivity and diastereoselectivity.

To demonstrate the synthetic usefulness of this highly diastereoselective reaction, the conversion of 2-oxazoline-4-carboxylate **5a** to an *erythro*-2-amino 1,3,4,5-tetrol derivative was investigated. The treatment of 2-oxazoline **5a** with $LiAlH_4$ at 60 °C in tetrahydrofuran for 5 h gave expected *erythro*-2-amino 1,3,4,5-tetrol derivative **6** in quantitative yield. The benzyl and *p*-methoxyphenylmethyl protecting groups of **7** could be easily removed by Pd-black/$HCO_2^-NH_4^+$ after bis-silylation of **6**. Product **8** was isolated as Boc-8 in 78% overall yield from **5a**. Compounds 8 and Boc-8 are important intermediates for the synthesis of biologically active natural products having the amino polyol substructure, such as *D*-AB1 and 1-deoxynojirimycin, since these natural products have the same absolute configuration as that of 8.

The *cis*-selectivity and the *si*-face selectivity of the reaction could be satisfactorily explained by chelated transition state **A**, which involves the sterically less-hindered synclinal attack of the C4–C5 double bond of oxazole 1 on the aldehyde (Figure 1).[11,12] A transition state like **B** is unfavorable because of steric hindrance. After the nucleophilic attack of the oxazole, zwitterionic intermediate **I** cyclizes to selectively afford *cis*-adducts **2a** and **5a** through the oxazole ring-opening. On the other hand, the *si*-face selectivity of the reaction of 2-(*S*)-[(*tert*-butyldimethylsilyl)oxy]propanal is not fully explained, but the high reactivity of the bidentate coordinating α-alkoxy aldehyde toward the oxazole in comparison with that of

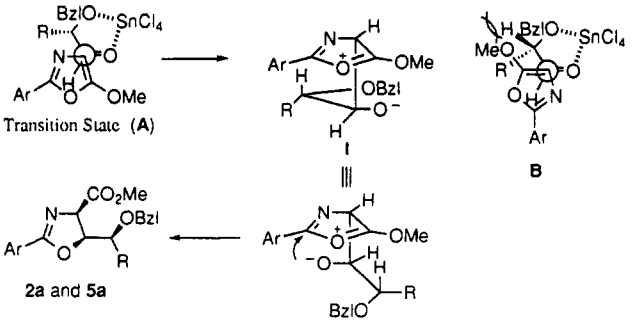
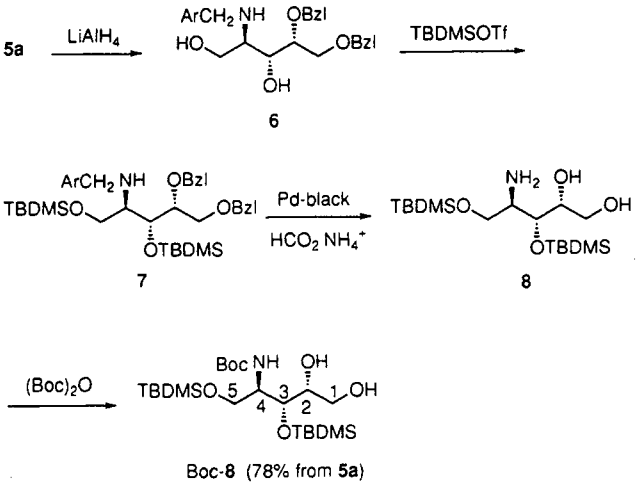


Figure 1. Postulated transition state.



the monodentate cases seems to indicate that the reaction proceeds through chelation control.

In conclusion, the above-described methodology involving the tin(IV) chloride-catalyzed formal [3 + 2] cycloaddition of a 5-alkoxyoxazole with chiral α-benzyloxy aldehydes has the advantages of high *cis*-selectivity, good yield, and the production of optically pure 2-oxazoline-4-carboxylates over the previously reported methylaluminum β-binaphthoxide-catalyzed reaction of an aliphatic aldehyde.[4] Furthermore, the diastereoselectively synthesized 5-(1′-alkoxyalkyl)-substituted 2-oxazoline-4-carboxylate was demonstrated to be a useful building block for the preparation of chiral *erythro*-2-amino polyol derivatives.

Experimental Section

General Procedures. Melting points are uncorrected. ^1H NMR spectra were run at 270 or 500 MHz. ^{13}C NMR spectra were determined at 67.8 or 125.7 MHz. Medium-pressure liquid chromatography was carried out on a column packed with silica gel 60 (Merck, size: 0.040–0.063 mm). HPLC was performed with a Nova-Pak C18 column or a Radial-PAK μ-Porasil column (Waters). All reactions were carried out under an argon atmosphere in dried glassware.

5-Methoxy-2-(*p*-methoxyphenyl)oxazole (1) was synthesized by the method described in the literature.[13] MeCN and CH_2Cl_2 were purified by the methods reported previously.[4] THF was purified by distillation from Na and then from $LiAlH_4$. MeOH was purified by distillation from Mg.

Reaction of Oxazole 1 with 2(*S*)-(Benzyloxy)propanal in the Presence of Tin(IV) Chloride: Formation of Methyl 2-(*p*-Methoxyphenyl)-5-[1′-(benzyloxy)ethyl]-2-oxazoline-4-carboxylates 2a–d. To a solution of oxazole 1 (0.205 g, 1.0 mmol) and 2(*S*)-(benzyloxy)propanal (0.164 g, 1.0 mmol) in CH_2Cl_2 (10 mL) at −20 °C was added tin(IV) chloride (0.12

(9) Beving, H. F. G.; Boren, H. B.; Geregg, P. J. *Acta Chem. Scand.* **1967**, *21*, 2083.

(10) The reaction was performed on a 1-mmol scale to give **5a** in 48% yield (recovered 1; 22%). When the reaction was performed on a 10-mmol scale, 2-oxazoline **5a** was obtained in 61% isolated yield (recovered 1; 26%).

(11) We proposed a similar chelation-type transition state model for $Ti(OR)_2Cl_2$-catalyzed reactions of oxazole 1 with ethyl glyoxylate.[4b]

(12) A similar type of transition state has been proposed for the reactions of enol silanes and ene reactions: (a) Heathcock, C. H.; Davidsen, S. K.; Hug, K. T.; Flippin, L. A. *J. Org. Chem.* **1986**, *51*, 3027. (b) Mikami, K.; Loh, T.-P.; Nakai, T. *Tetrahedron Asymmetry* **1990**, *1*, 13.

(13) Grifanti, M.; Sein, M. L. *Ann. Chim. (Rome)* **1965**, *55*, 578.

mL, 1.0 mmol). The mixture was stirred at the same temperature for 2 h and quenched with a saturated solution of $NaHCO_3$. After the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), the organic layer was dried over anhyd $MgSO_4$, and the solvent was removed under reduced pressure. A crude product obtained was analyzed by HPLC (Nova-Pak C18) using biphenyl as an internal standard. 2-Oxazolines **2a** and **2c** were isolated in this order by medium-pressure liquid chromatography on silica gel with hexane–ethyl acetate (9:1). 2-Oxazolines **2b** and **2d** were obtained by isomerization of **2a** and **2c**, respectively, as described below. The reaction performed using oxazole **1** (2.05 g, 10.0 mmol), 2(*S*)-(benzyloxy)propanal (1.64 g, 10.0 mmol), tin(IV) choloride (1.2 mL, 10.0 mmol), and CH_2Cl_2 gave **2a** (2.65 g, 72% yield), **2c** (0.061 g, 1.6% yield), a mixture of **2b** and **2d** (0.175 g), and unchanged **1** (0.244 g, 12%).

2a: Colorless needles (hexane); mp 64.4–65.6 °C; $[\alpha]^{25}_D = -53.2°$ (c 1.22, THF); IR (KBr) 1719, 1648 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34 (3H, d, J = 6.3 Hz), 3.54 (3H, s), 3.85 (3H, s), 4.05 (1H, dq, J = 4.0, 6.3 Hz), 4.44 (1H, d, J = 12.1 Hz), 4.60 (1H, d, J = 12.1 Hz), 4.82 (1H, dd, J = 10.6, 4.0 Hz), 4.99 (1H, d, J = 10.6 Hz), 6.93 (2H, m), 7.16–7.35 (5H, m), 7.97 (2H, m); ^{13}C NMR ($CDCl_3$) δ 15.9 (q), 52.0 (q), 55.3 (q), 69.5 (d), 70.7 (t), 72.8 (d), 84.9 (d), 113.7, 130.3 (each d), 119.7 (s), 126.7, 127.1, 128.2 (each d), 138.4 (s), 162.4 (s), 165.6 (s), 171.1 (s); MS (EI, rel intensity) m/z 369 (3, M^+), 266 (35), 263 (53), 234 (36), 204 (92), 190 (21), 176 (21), 135 (77), 91 (100). Anal. Found: C, 68.08; H, 6.28; N, 3.78%. Calcd for $C_{21}H_{23}NO_5$: C, 68.27; H, 6.28; N, 3.79%.

2b: Colorless oil; IR (neat) 1740, 1638 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (3H, d, J = 6.3 Hz), 3.68–3.87 (1H, m), 3.79 (3H, s), 4.60 (1H, d, J = 12.0 Hz), 4.68 (1H, d, J = 12.0 Hz), 4.74 (1H, d, J = 7.3 Hz), 4.93 (1H, dd, J = 7.3, 5.1 Hz), 6.90 (2H, m), 7.23–7.39 (5H, m), 7.94 (2H, m); ^{13}C NMR ($CDCl_3$) δ 14.9 (q), 52.7 (q), 70.0 (d), 71.2 (t), 74.3 (d), 84.0 (d), 113.7, 130.4 (each d), 119.5 (s), 127.6, 127.7, 128.4 (each d), 138.2 (s), 162.5 (s), 165.4 (s), and 171.9 (s); MS (EI, rel intensity) m/z 369 (2, M^+), 266 (28), 263 (25), 234 (96), 204 (42), 202 (32), 190 (9), 176 (14), 135 (51), 91 (100). Anal. Found: C, 68.05; H, 6.30; N, 3.87%. Calcd for $C_{21}H_{23}NO_5$: C, 68.27; H, 6.28; N, 3.79%.

2c: Colorless powder (hexane); mp 59.4–60.3 °C; IR (KBr) 1742, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (3H, d, J = 5.9 Hz), 3.52 (3H, s), 3.85 (3H, s), 3.97 (1H, dq, J = 8.3, 5.9 Hz), 4.31 (1H, d, J = 11.6 Hz), 4.60 (1H, d, J = 11.6 Hz), 4.71 (1H, dd, J = 9.9, 8.3 Hz), 5.00 (1H, d, J = 9.9 Hz), 6.91 (2H, m), 7.23–7.39 (5H, m), 7.92 (2H, m); ^{13}C NMR ($CDCl_3$) δ 16.8 (q), 52.0 (q), 55.4 (q), 69.8 (d), 70.2 (t), 73.0 (d), 83.7 (d), 113.7, 130.4 (each d), 119.4 (s), 127.2, 127.5, 128.3 (each d), 138.1 (s), 162.5 (s), 165.8 (s), 171.0 (s); MS (EI, rel intensity) m/z 369 (2, M^+), 266 (52), 263 (46), 234 (43), 204 (56), 190 (17), 176 (31), 135 (54), 91 (100). Anal. Found: C, 68.46; H, 6.42; N, 3.49%. Calcd for $C_{21}H_{23}NO_5$: C, 68.27; H, 6.28; N, 3.79%.

2d: Colorless oil; IR (neat) 1742, 1636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (3H, d, J = 6.6 Hz), 3.74–3.90 (1H, m), 3.80 (3H, s), 3.84 (3H, s), 4.52 (1H, d, J = 12.1 Hz), 4.64 (1H, d, J = 12.1 Hz), 4.81–4.87 (2H, m), 6.91 (2H, m), 7.23–7.36 (5H, m), 7.93 (2H, m); ^{13}C NMR ($CDCl_3$) δ 15.5 (q), 52.7 (q), 55.4 (q), 69.8 (d), 71.3 (t), 74.5 (d), 84.6 (d), 113.7, 130.4 (each d), 119.5 (s, 1-C of Ar), 127.6, 128.3, 130.4 (each d), 138.2 (s), 162.5 (s), 165.3 (s), 172.1 (s); HRMS (EI) found M^+, 369.1576, calcd for $C_{21}H_{23}NO_5$ M^+, 369.1577.

Reaction of Oxazole 1 with 2(*S*)-[(*tert*-Butyldimethylsilyl)oxy]propanal in the Presence of Tin(IV) Chloride: Formation of Methyl 2-(*p*-Methoxyphenyl)-5-[1′-[(*tert*-butyldimethylsilyl)oxy]ethyl]-2-oxazoline-4-carboxylates 3b and 3d. To a solution of oxazole **1** (0.205 g, 1.0 mmol) and 2(*S*)-[(*tert*-butyldimethylsilyl)oxy]propanal (0.188 g, 1.0 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added tin(IV) chloride (0.12 mL, 1.0 mmol). The mixture was stirred at 0 °C for 30 h and quenched with a saturated solution of $NaHCO_3$. After the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), the combined organic layer was dried over anhyd $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product, which was analyzed by HPLC (μ-Porasil) using *m*-nitrophenyl *p*-phenoxyphenyl ketone as an internal standard. 2-Oxazolines **3b** and **3d** were isolated in this order by medium-pressure liquid chromatography on silica gel with hexane–ethyl acetate (97:3). The reaction performed using oxazole **1** (0.205 g, 1.0 mmol), 2(*S*)-[(*tert*-butyldimethylsilyl)oxy]propanal (0.188 g, 1.0 mmol), tin(IV) chloride (0.12 mL, 1.0 mmol), and CH_2Cl_2 (10 mL) for 4.7 h gave **3b** (0.164 g, 42% yield), **3d** (0.009 g, 2% yield), and unchanged **1** (0.035 g, 17%).

3b: Colorless oil: IR (neat) 1745, 1639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06 (3H, s), 0.09 (3H, s), 0.85 (9H, s), 1.21 (3H, d, J = 6.3 Hz), 3.84 (3H, s), 3.86 (3H, s), 4.03 (1H, dq, J = 4.8, 6.3 Hz), 4.67 (1H, d, J = 6.9 Hz), 4.78 (1H, dd, J = 6.9, 4.8 Hz), 6.91 (2H, m), 7.92 (2H, m); ^{13}C NMR ($CDCl_3$) δ −4.9 (q), −4.4 (q), 18.0 (s), 18.5 (q), 25.6 (q), 52.6 (q), 55.4 (q), 68.7 (d), 69.9 (d), 85.0 (d), 113.7, 130.3 (each d), 119.7 (s), 162.4 (s), 165.4 (s), 172.1 (s); MS (EI, rel intensity) m/z 393 (5, M^+), 336 (100), 292 (27), 249 (19), 206 (35), 159 (29), 135 (47), 73 (20). Anal. Found: C, 60.77; H, 7.89; N, 3.49%. Calcd for $C_{20}H_{31}NO_5Si$: C, 61.03; H, 7.94; N, 3.56%.

3d: Colorless oil; IR (neat) 1741, 1641 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.09 (3H, s), 0.04 (3H, s), 0.77 (9H, s), 1.19 (3H, d, J = 6.3 Hz), 3.81 (3H, s), 3.85 (3H, s), 4.19 (1H, dq, J = 3.1, 6.3 Hz), 4.73 (1H, dd, J = 7.3, 3.1 Hz), 4.91 (1H, d, J = 7.3 Hz), 6.90 (2H, m), 7.90 (2H, m); ^{13}C NMR ($CDCl_3$) δ −4.9 (q), −4.5 (q), 17.8 (s), 19.4 (q), 25.5 (q), 52.6 (q), 55.3 (q), 67.9 (d), 68.6 (d), 85.5 (d), 113.6, 130.3 (each d), 119.8 (s), 162.2 (s), 165.0 (s), 172.4 (s); MS (EI, rel intensity) m/z 393 (2, M^+), 336 (100), 292 (24), 234 (16), 206 (16), 159 (38), 135 (27), 73 (15). Anal. Found: C, 60.87; H, 7.87; N, 3.57%. Calcd for $C_{20}H_{31}NO_5Si$: C, 61.03; H, 7.94; N, 3.56%.

Isomerization of 2-Oxazoline 2a. To a solution of **2a** (0.185 g, 0.50 mmol) in MeCN (1 mL) was added Et_3N (0.21 mL, 1.5 mmol). The mixture was refluxed for 27 h. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel with hexane–ethyl acetate (9:1) to give *trans*-2-oxazoline **2b** (0.164 g, 89% yield) together with unchanged 2-oxazoline **2a** (5 mg, 3%).

Isomerization of 2-Oxazoline 2c. To a solution of **2c** (0.063 g, 0.17 mmol) in MeCN (0.8 mL) was added Et_3N (0.12 mL, 0.85 mmol). The mixture was refluxed for 27 h. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel with hexane–ethyl acetate (9:1) to give *trans*-2-oxazoline **2d** (0.047 g, 75%).

Formation of Lactone 4a. 2-Oxazoline **2a** (0.185 g, 0.50 mmol) dissolved in a mixture of AcOH (0.35 mL, 6.1 mmol) and MeOH (10 mL) was treated with Pd-black for 24 h under 10 atm of hydrogen gas. After removal of the catalyst by filtration through Celite, the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel with hexane–ethyl acetate (13:7) to give lactone **4a** (59 mg, 48%): colorless plates (benzene); mp 176.0–178.2 °C; IR (KBr) 1775, 1763, 1641 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.51 (3H, d, J = 6.6 Hz), 3.86 (3H, s), 4.91 (1H, dq, J = 5.3, 6.6 Hz), 5.01 (1H, d, J = 8.3 Hz), 5.27 (1H, dd, J = 5.3, 8.3 Hz), 6.93 (2H, m), 7.95 (2H, m); ^{13}C NMR ($CDCl_3$) δ 15.1 (q), 55.4 (q), 70.8 (d), 79.2 (d), 80.5 (d), 113.9, 130.5 (each d), 118.4 (s), 162.9 (s), 165.7 (s), 173.0 (s); MS (EI, rel intensity) m/z 247 (51, M^+), 203 (8), 175 (16), 135 (100). Anal. Found: C, 63.11; H, 5.30; N, 5.61%. Calcd for $C_{13}H_{13}NO_4$: C, 63.15: H, 5.30; N, 5.66%.

Formation of Lactone 4c. 2-Oxazoline **2c** (13 mg, 35 μmol) was treated in the same manner as lactone **2a**. After removal of the catalyst by filtration through Celite, the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel with hexane–ethyl acetate (13:7) to give lactone **4c** (4 mg, 46% yield): colorless amorphous solid; IR (KBr) 1771, 1633 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.54 (3H, d, J = 6.9 Hz), 3.86 (3H, s), 4.80 (1H, dq, J = 1.3, 6.9 Hz), 4.96 (1H, dd, J = 1.3, 8.3 Hz), 5.96 (1H, d, J = 8.3 Hz), 6.92 (2H, m), 7.93 (2H, m); ^{13}C NMR ($CDCl_3$) δ 20.5, 55.4, 70.1, 82.0, 83.8, 113.91, 130.6, 118.4, 162.9, 165.7, 172.4; HRMS found M^+, 247.0839, calcd for $C_{13}H_{13}NO_4$ M^+, 247.0844. Elemental analysis could not done because of its small quantity.

Debenzylation of 2b. 2-Oxazoline **2b** (15 mg, 41 μmol) dissolved in a mixture of AcOH (29 μL, 0.50 mmol) and MeOH (0.8 mL) was treated with Pd-black for 24 h under 10 atm of hydrogen. After removal of the catalyst by filtration over Celite, the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel with hexane–ethyl acetate (7:3) to give methyl (4*S*,5*S*,1′*S*)-5-[1′-(benzyloxy)ethyl]-2-(*p*-methoxyphenyl)-2-oxazoline-4-carboxylate (4 mg, 35% yield): colorless oil; IR (neat) 3383, 1742, 1636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (3H, d, J = 6.6 Hz), 2.05 (1H, br), 3.82 (3H, s), 3.85 (3H, s), 3.73–3.99 (1H, m), 4.61–4.67 (2H, m), 6.91 (2H, m), 7.94

(2H, m); ^{13}C NMR ($CDCl_3$) δ 18.7 (q), 52.8 (q), 55.4 (q), 68.7 (d), 70.5 (d), 85.6 (d), 113.8, 130.4 (each d), 119.3 (s), 162.6 (s), 165.0 (s), 171.7 (s); HRMS (EI) found M$^+$, 279.1107, calcd for $C_{14}H_{17}NO_5$ M$^+$, 279.1107.

Debenzylation of 2d. 2-Oxazoline **2d** (15 mg, 41 μmol) was debenzylated in the same manner as **2b**. After removal of the catalyst by filtration over Celite, the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel with hexane–ethyl acetate (7:3) to give methyl (4*R*,5*R*,1′*S*)-5-[1′-(benzyloxy)ethyl]-2-(*p*-methoxyphenyl)-2-oxazoline-4-carboxylate (4 mg, 35% yield): colorless oil; IR (neat) 3358, 1742, 1636 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (3H, d, *J* = 6.3 Hz), 1.97 (1H, br), 3.82 (3H, s), 3.85 (3H, s), 4.16 (1H, dq, *J* = 3.8, 6.3 Hz), 4.77 (1H, dd, *J* = 7.6, 3.8 Hz), 4.85 (1H, d, *J* = 7.6 Hz), 6.91 (2H, m), 7.94 (2H, m); ^{13}C NMR ($CDCl_3$) δ 18.0 (q), 52.8 (q), 55.4 (q), 67.6 (d), 69.0 (d), 85.5 (d), 113.8, 130.5 (each d), 119.1 (s), 162.7 (s), 165.2 (s), 172.0 (s); HRMS (EI) found M$^+$, 279.1069, calcd for $C_{14}H_{17}NO_5$ M$^+$, 279.1107.

Desilylation of 3b. To 2-oxazoline **3b** (60 mg, 0.15 mmol) was added 1.0 M solution of tetrabutylammonium fluoride (0.30 mL, 0.30 mmol) in THF at rt. After the mixture stirred for 1.5 h, water was added, and the mixture was extracted by CH_2Cl_2 (10 mL × 3). The combined organic layers were washed with a saturated solution of NH_4Cl and dried over anhyd $MgSO_4$. Removal of the solvent under reduced pressure gave a residue, which was purified by chromatography on silica gel with hexane–ethyl acetate (3:1) to give methyl (4*S*,5*S*,1′*S*)-5-[1′-(benzyloxy)-ethyl]-2-(*p*-methoxyphenyl)-2-oxazoline-4-carboxylate (9 mg, 21% yield).

Desilylation of 3d. Treatment and workup of 2-oxazoline **3d** in the manner described for **3b** gave methyl (4*R*,5*R*,1′*S*)-5-[1′-(benzyloxy)ethyl]-2-(*p*-methoxyphenyl)-2-oxazoline-4-carboxylate (8 mg, 31% yield).

Formation of Methyl 2-(*p*-Methoxyphenyl)-5-[1′,2′-bis(benzyloxy)ethyl]-2-oxazoline-4-carboxylates 5a–d. To a solution of oxazole **1** (0.205 g, 1.0 mmol) and 2,3-di-*O*-benzyl-D-glyceraldehyde (0.270 g, 1.0 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added tin(IV) chloride (0.12 mL, 1.0 mmol). After stirring at −20 °C for 24 h, the mixture was treated with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The organic layer was dried over anhyd $MgSO_4$, and the solvent was removed from the organic solution under reduced pressure. The residue was purified by medium pressure liquid chromatography on silica gel to give **5a** (226 mg, 48% yield), **5b** (5 mg, 1% yield), **5c** (6 mg, 1% yield), and **5d** (<2 mg, <0.4% yield) with hexane–ethyl acetate (37:3). The reaction performed using oxazole **1** (2.05 g, 10.0 mmol), 2,3-di-*O*-benzyl-D-glyceraldehyde (2.70 g, 10.0 mmol), tin(IV) chloride (1.2 mL, 10.0 mmol), and CH_2Cl_2 (100 mL) resulted in a high yield of **5a** (2.91 g, 61% yield) accompanied by unchanged **1** (0.535 g, 26%).

5a: Colorless oil: $[\alpha]^{25}_D$ = +15.4° (*c* 1.75, THF); IR (neat) 1721, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.49 (3H, s), 3.74 (2H, d, *J* = 5.9 Hz), 3.82 (3H, s), 4.20 (1H, dt, *J* = 3.3, 5.9 Hz), 4.51 (1H, d, *J* = 12.0 Hz), 4.55 (1H, d, *J* = 12.8 Hz), 4.57 (1H, d, *J* = 12.8 Hz), 4.68 (1H, d, *J* = 12.0 Hz), 5.02 (1H, d, *J* = 10.6 Hz), 5.12 (1H, dd, *J* = 10.6, 3.3 Hz), 6.90 (2H, m), 7.17–7.36 (10H, m), 7.93 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.0 (q), 55.3 (q), 69.3 (d), 69.4 (t), 73.5 (t), 76.0 (t), 76.0 (d), 81.6 (d), 113.6, 130.3 (each d), 119.7 (s), 126.7, 127.2, 127.7, 128.1, 128.3, 128.4 (each d), 137.9 (s), 138.3 (s), 162.4 (s), 165.4 (s), 171.1 (s); MS (EI, rel intensity) *m*/*z* 476 (1, M$^+$), 354 (14), 266 (14), 263 (30), 234 (11), 204 (6), 176 (9), 151 (16), 135 (60), 91 (100). Anal. Found: C, 70.45; H, 6.19; N, 2.98%. Calcd for $C_{28}H_{29}NO_6$: C, 70.72; H, 6.15; N, 2.95%.

5b: Colorless oil; IR (neat) 1735, 1636 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.74 (3H, s), 3.74–3.85 (3H, m), 3.83 (3H, s), 4.49–4.59 (2H, m), 4.68 (1H, d, *J* = 11.9 Hz), 4.78 (1H, d, *J* = 11.9 Hz), 4.81 (1H, d, *J* = 7.9 Hz), 5.07 (1H, dd, *J* = 7.9, 4.3 Hz), 6.89 (2H, m), 7.25–7.34 (10H, m), 7.90 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.6 (q), 55.4 (q), 69.5 (t), 70.1 (d), 73.1 (t), 73.6 (t), 77.5 (d), 82.0 (d), 113.6, 130.4 (each d), 119.4 (s), 127.0, 127.6, 127.7, 127.78, 127.82, 128.4 (each d), 137.8 (s), 137.9 (s), 162.4 (s), 165.2 (s), 171.7 (s); HRMS (EI) found M$^+$, 475.1984, calcd for $C_{28}H_{29}NO_6$ M$^+$, 475.1995.

5c: Colorless oil; IR (neat) 1741, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.49 (3H, s), 3.74 (1H, dd, *J* = 10.9, 3.3 Hz), 3.85 (3H, s), 3.90 (1H, dd, *J* = 10.9, 3.3 Hz), 4.03–4.09 (1H, m), 4.38 (1H, d, *J* = 11.6 Hz), 4.56 (1H, d, *J* = 12.4 Hz), 4.65 (1H, d, *J* = 12.4 Hz), 4.73 (1H, d, *J* = 11.6 Hz), 4.99 (1H, d, *J* = 9.9 Hz), 5.05 (1H, dd, *J* = 9.9, 7.6 Hz), 6.90 (2H, m), 7.24–7.38 (10H, m), 7.85 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.0 (q), 55.4 (q), 68.6 (t), 69.5 (d), 71.5 (t), 73.4 (t), 76.3 (d), 79.2 (d), 113.7, 130.4 (each d), 119.3 (s), 127.2, 127.5, 127.67, 127.71, 128.3, 128.4 (each d), 138.0 (s), 138.1 (s), 162.5 (s), 165.7 (s), 171.1 (s); HRMS (EI) found M$^+$, 475.2012, calcd for $C_{28}H_{29}NO_6$ M$^+$, 475.1995.

5d: Colorless oil; IR (neat) 1740, 1641 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.61–3.71 (2H, m), 3.72 (3H, s), 3.85 (3H, s), 3.94–4.00 (1H, m), 4.50 (1H, d, *J* = 11.9 Hz), 4.56 (1H, d, *J* = 11.9 Hz), 4.60 (1H, d, *J* = 11.9 Hz), 4.71 (1H, d, *J* = 11.9 Hz), 5.00 (1H, d, *J* = 7.6 Hz), 5.09 (1H, dd, *J* = 7.6, 3.5 Hz), 6.90 (2H, m), 7.24–7.36 (10H, m), 7.89 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.5 (q), 55.4 (q), 69.1 (t), 69.8 (d), 72.8 (t), 73.6 (t), 77.3 (d), 82.1 (d), 113.7, 130.4 (each d), 119.5 (s), 127.66, 127.70, 127.8, 128.3, 128.4 (each d), 137.8 (s), 137.9 (s), 162.4 (s), 165.0 (s), 172.0 (s); HRMS (EI) found M$^+$, 475.2008, calcd for $C_{28}H_{29}NO_6$ M, 475.1995.

4,5-Bis(benzyloxy)-2-[(*p*-methoxyphenyl)methyl]aminopentane-1,3-diol (6). To a suspension of $LiAlH_4$ (0.20 g, 5.2 mmol) in THF (9.8 mL) was added a solution of 2-oxazoline **5a** (0.766 g, 1.6 mmol) in THF (5.2 mL). After the mixture was stirred at rt for 1.5 h and then at 60 °C for 5 h, it was quenched with water (30 mL) at 0 °C and filtered. The filtrate was extracted with CH_2Cl_2 (30 mL × 5) and dried over anhyd $MgSO_4$. After removal of the solvent under reduced pressure, the resulting colorless solid was washed with hexane to give **6** in quantitative yield: Colorless needles (hexane); $[\alpha]^{25}_D$ = −27.4° (c 1.30, THF); mp 101.5–102.8 °C; IR (KBr) 3445, 3387 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.80 (3H, br), 2.75 (1H, dt, *J* = 6.2, 4.6 Hz), 3.64 (1H, dd, *J* = 10.1, 4.6 Hz), 3.65 (1H, d, *J* = 12.8 Hz), 3.69 (1H, dd, *J* = 11.1, 4.7Hz), 3.69 (1H, dd, *J* = 10.1, 4.6 Hz), 3.74 (1H, d, *J* = 12.8 Hz), 3.74 (1H, dd, *J* = 11.1, 4.7 Hz), 3.76 (3H, s), 3.79–3.82 (2H, m), 4.45 (1H, d, *J* = 11.5 Hz), 4.51 (2H, s), 4.68 (1H, d, *J* = 11.5 Hz), 6.81 (2H, m), 7.18 (2H, m), 7.25–7.35 (10H, m); ^{13}C NMR ($CDCl_3$) δ 50.5 (t), 55.3 (q), 58.7 (d), 60.5 (t), 70.1 (t), 72.2 (d), 72.7 (t), 73.6 (t), 77.5 (d), 113.8, 128.5 (each d), 127.7, 127.8, 127.9, 128.0, 128.5, 129.5 (each d), 132.2(s), 137.8 (s), 138.0 (s), 158.8 (s); MS (EI, rel intensity) 452 (2, (M + 1)$^+$), 420 (20), 180 (38), 121 (100), 91 (23). Anal. Found: C, 71.70; H, 7.39; N, 3.17%. Calcd for $C_{27}H_{33}NO_5$: C, 71.82; H, 7.37; N, 3.10%.

***N*-[(*p*-Methoxyphenyl)methyl]-4,5-bis(benzyloxy)-1,3-bis[(*tert*-butyldimethylsilyl)oxy]-2-pentylamine (7).** To a solution of amino diol **6** (0.305 g, 0.68 mmol) in CH_2Cl_2 (2.2 mL) were added 2,6-lutidine (0.40 mL, 3.4 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.47 mL, 2.0 mmol), successively. After the mixture was stirred for 1 h, the organic layer was washed with 20% $NaHSO_4$ and dried over anhyd $MgSO_4$. After removal of the solvent under reduced pressure, the resulting colorless solid was washed with hexane to give **7** in quantitative yield: colorless plate crystals (hexane); mp 63.4–64.6 °C; $[\alpha]^{25}_D$ = −5.7° (c 1.00, THF); IR (KBr) 3419 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ −0.11 (3H, s), 0.06 (3H, s), 0.14 (3H, s), 0.15 (3H, s), 0.81 (9H, s), 0.94 (9H, s), 3.55–3.58 (1H, m), 3.59–3.67 (1H, m), 3.63 (1H, dd, *J* = 10.4, 2.5 Hz), 3.66 (1H, dd, *J* = 10.4, 3.2 Hz), 3.78 (3H, s), 3.83–3.89 (1H, m), 3.99 (1H, dd, *J* = 11.5, 2.8 Hz), 4.13 (1H, dd, *J* = 9.6, 4.1 Hz), 4.16 (1H, dd, *J* = 11.5, 8.7 Hz), 4.39–4.45 (1H, m), 4.44 (1H, d, *J* = 11.6 Hz), 4.53 (1H, d, *J* = 11.6 Hz), 4.59 (2H, s), 6.75 (2H, m), 7.02 (2H, m), 7.23–7.38 (10H, m), 7.78 (1H, br); ^{13}C NMR ($CDCl_3$) δ −5.7 (q), −5.5 (q), −5.1 (q), −5.0 (q), 17.7 (s), 18.1 (s), 25.6 (s), 25.8 (s), 51.8 (t), 55.3 (q), 62.0 (t), 63.6 (d), 65.6 (t), 66.8 (d), 72.4 (t), 74.0 (t), 78.6 (d), 114.5, 128.4, 128.46, 128.54, 128.61, 128.64, 130.9 (each d), 123.2 (s), 135.9 (s), 136.9 (s), and 160.4 (s); MS (EI, rel intensity) *m*/*z* 679 (0.04, M$^+$), 664 (0.2), 622 (9), 620 (10), 586 (9), 586 (9), 534 (26), 426 (17), 294 (70), 121 (100), 91 (29). Compound **7** is too labile to be purified as an analytical sample and was immediately used for further reactions.

4-Amino-3,5-bis[(*tert*-butyldimethylsilyl)oxy]pentane-1,2-diol (8). A suspension of amine **7** (0.196 g, 0.29 mmol), Pd-black (about 0.2 g), and ammonium formate (0.091 g, 1.4 mmol) in MeOH (8 mL) was refluxed for 5 h. After the Pd-black was filtered off, removal of the solvent under reduced pressure gave a residue, to which ether was added. The solid material obtained was filtered off, and the solvent of the filtrate was removed *in vacuo* to give diol **8** (0.108 mg, 99%): colorless oil; IR (neat) 3447, 3159 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.08 (6H, s), 0.10

(6H, s), 0.89 (9H, s), 0.90 (9H, s), 3.64 (1H, dt, J = 4.4, 5.7 Hz), 3.72 (1H, dd, J = 10.3, 5.7 Hz), 3.77 (1H, dd, J = 10.3, 5.7 Hz), 3.87 (1H, dd, J = 11.0, 5.5 Hz), 3.91 (1H, dt, J = 1.8, 5.5 Hz), 3.94 (1H, dd, J = 11.0, 5.5 Hz), 4.02 (1H, dd, J = 4.4, 1.8 Hz), 5.20 (4H, br); ^{13}C NMR ($CDCl_3$) δ −5.9 (q), −5.7 (q), −5.6 (q), 18.07 (s), 18.14 (s), 25.7 (q), 25.8 (q), 56.5 (d), 59.7 (t), 64.6 (t), 68.4 (d), 70.8 (d); HRMS (CI, CH_4) found (M + 1$^+$), 380.2661, calcd for $C_{17}H_{41}NO_4Si_2$ (M + 1$^+$), 380.2644.

N-(*tert*-Butoxycarbonyl)-4-amino-3,5-bis[(*tert*-butyldimethylsilyl)oxy]pentane-1,2-diol (Boc-8). To a solution of amino diol 8 (59 mg, 0.15 mmol) in THF (1 mL) were added Et_3N (42 μL, 0.30 mmol) and di-*tert*-butyl carbonate (43 μL, 0.18 mmol), successively. After the mixture was stirred for 20 h at rt, ether (20 mL) was added to the mixture. The organic solution was washed with 0.5 M hydrochloric acid and a saturated solution of $NaHCO_3$, successively, and then dried over anhyd $MgSO_4$. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel with hexane–ethyl acetate (93:7) to give Boc-8 (59 mg, 78% yield from **5a**): colorless oil; IR (neat) 3439, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.07 (6H, s), 0.08 (6H, s), 0.89 (9H, s), 0.90 (9H, s), 1.45 (9H, s), 3.51–3.55 (1H, m), 3.63–3.76 (5H, m), 4.04 (1H, dd, J = 2.3, 10.2 Hz); ^{13}C NMR ($CDCl_3$) δ −5.54 (q), −5.49 (q), −5.4 (q), 18.3 (s), 25.86 (q), 25.89 (q), 28.3 (q), 53.4 (d), 61.7 (t), 64.1 (t), 69.6 (d), 69.8 (d), 80.2 (s), 157.0 (s); HRMS (CI, CH_4) found (M + 1)$^+$, 480.3189, calcd for $C_{22}H_{50}NO_6Si_2$ (M + 1)$^+$, 480.3214

Acknowledgment. Thanks are due to Mr. H. Moriguchi, Faculty of Engineering, Osaka University, for obtaining the mass spectra. This work was supported in part by a Grant-in-Aid for Scientific Research (No. 03854059) from the Ministry of Education, Science and Culture, Japan.