6,7,9,10,17,18,20,21-Octahydro-53,53,59,59-tetramethyl-43,66-(methanoxy[1,4]benzenomethano[1,4]benzenoxymethano)-2,13-(iminomethano-[1,4]benzeno[1,4]benzenomethanimino[1,3]benzenomethanoxy[1,4]-benzenomethano[1,4]benzenoxymethano[1,3]benzeneiminomethano[1,4]-benzeno[1,4]benzenoxymethanimino)dibenzo[*b*,*k*][1,4,7,10,13,16]hexaoxacyclooctadecin (Cylindrical Macrotricyclic Receptor 1). A solution of diamide **11** (567 mg, 0.32 mmol) in THF (40 mL) was added to a suspension of $LiAlH_4$ (606 mg, 16 mmol) in THF (30 mL) under an argon atmosphere. The reaction mixture was heated under reflux for 12 h and then cooled to 0 °C, and a saturated $MgSO_4$ solution (200 mL) was added drop by drop to the solution. The THF layer was separated by decantation, and the residue was washed with ether (4 × 100 mL). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (25 mL). The solution was washed with water, dried over $MgSO_4$, and concentrated. The crude product was purified by alumina column chromatography (eluent CH_2Cl_2) to give pure **1**: 202 mg, 44%; mp 263-264 °C; IR (KBr) 3450, 1510 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, 8 H, J = 8.0 Hz), 7.37 (d, 4 H, J = 8.0 Hz), 7.36 (d, 4 H, J = 8.0 Hz), 7.01 (d, 8 H, J = 8.8 Hz), 6.73 (d, 8 H, J = 8.8 Hz), 6.68 (d, 2 H, J = 8.2 Hz), 6.66 (s, 2 H), 6.58 (s, 4 H), 6.24 (d, 2 H, J = 2.4 Hz), 6.13 (dd, 2 H, J = 2.4 Hz, 8.2 Hz), 4.95 (s, 8 H), 4.34 (s, 8 H), 4.08-4.02 (m, 8 H), 3.96-3.88 (m, 8 H), 1.56 (s, 12 H); HRMS (FAB) m/e for $C_{94}H_{92}N_4O_{10}$ calcd 1436.6813, found 1436.6980. Anal. Calcd for $C_{94}H_{92}N_4O_{10}\cdot 4H_2O$: C, 74.78; H, 6.68; N, 3.71. Found: C, 75.02; H, 6.55; N, 3.48.

Typical Procedure for the Measurement of K_s'. Freshly purified (alumina TLC; developing solvent, CH_2Cl_2 containing 2% methanol) macrotricyclic receptor **1** (84.5 mg) was dissolved in a $CDCl_3/CD_3OD$ (4/1, v/v) mixed solvent and diluted to 2.00 mL (29.4 mM solution). (3-Phenylpropyl)ammonium picrate (**2a**; 39.4 mg) was also dissolved in a $CDCl_3/CD_3OD$ (4/1, v/v) mixed solvent and diluted to 1.00 mL (108.1 mM solution). A 25.0-μL portion of the standard solution of the substrate was added to each of ten NMR sample tubes and then one each of 0.00-, 30.0-, 50.0-, 70.0-, 90.0-, 110.0-, 130.0-, 150.0-, 170.0-, and 190.0-μL portions of the standard solution of the receptor were added, one to each tube. Every mixture was diluted to 600 μL by the addition of a $CDCl_3/CD_3OD$ (4/1, v/v) mixed solvent, and the ^1H NMR was measured on a JEOL GX-400 instrument. The difference between the chemical shifts in the presence and in the absence of the receptor was plotted for both the ammonium α-methylene and the benzyl protons of **2a**. This curve was fitted to eq 1 with the SALS program[12] on HITAC M-680/M-682H computers.

Acknowledgment. We thank Dr. Hiroshi Nakazawa and Masayuki Nagase of Sumitomo Chemical Co., Ltd., for the measurement of high-resolution mass spectra. This work was supported by the Grant-in-Aid for Scientific Research (No. 62216006, 63107001) from the Ministry of Education, Science and Culture, Japan.

Registry No. 1, 106509-04-0; **1/2a** 1:1 complex, 124400-87-9; **1/2b** 1:1 complex, 124400-89-1; **1/2c** 1:1 complex, 106527-63-3; **1/2d** 1:1 complex, 124400-91-5; **1/2e** 1:1 complex, 124400-93-7; **1/2f** 1:1 complex, 124400-95-9; **1/2g** 1:1 complex, 124400-97-1; **2a**, 124400-86-8; **2b**, 124400-88-0; **2c**, 106527-62-2; **2d**, 124400-90-4; **2e**, 124400-92-6; **2f**, 124400-94-8; **2g**, 124400-96-0; **3**, 31406-52-7; **4**, 97350-55-5; **5**, 106508-97-8; **6**, 106508-99-0; **7**, 106509-03-9; **8**, 106508-98-9; **9**, 106509-00-6; **9** diacid, 106509-01-7; **10**, 106509-02-8; **11**, 106527-61-1; **12** (m = 3), 1070-62-8; **12** (m = 4), 626-86-8; **12** (m = 5), 33018-91-6; **12** (m = 6), 14113-01-0; **12** (m = 7), 1593-55-1; **13** (m = 3), 1501-05-9; **13** (m = 4), 4144-62-1; **13** (m = 5), 7472-43-7; **13** (m = 6), 24314-23-6; **13** (m = 7), 53702-23-1; **14** (m = 3), 36603-28-8; **14** (m = 4), 31274-14-3; **14** (m = 5), 107416-06-8; **14** (m = 6), 124400-98-2; **14** (m = 7), 124400-99-3; **15a**, 582-22-9; **15b**, 13214-66-9; **15c**, 17734-21-3; **15d**, 17734-20-2; **15e**, 17734-22-4; **15f**, 17734-23-5; **15g**, 117534-09-5; picric acid, 88-89-1.

Syntheses and Reactions of Silyl Carbamates. 2. A New Mode of Cyclic Carbamate Formation from *tert*-Butyldimethylsilyl Carbamate

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Contribution from the Suntory Institute for Bioorganic Research, Shimamoto-cho, Mishima-gun, Osaka 618, Japan. *Received June 2, 1989*

Abstract: Stereoselective construction of 1,2 and 1,3 amino hydroxyl systems was achieved by the intramolecular trapping of the *N-tert*-butyldimethylsilyloxycarbonyl species (silyl carbamate) activated by fluoride ion. The reaction of the silyl carbamate with 1,2-syn mesylate **3** gave the 1,2-anti cyclic carbamate **7**, exclusively, with complete inversion of the original stereochemistry of the leaving group. On the other hand, AgF- or AgF/Pd(II)-assisted cyclic carbamate formation from the (chloromethyl)homoallylamines **13b-17b** and (chloromethyl)allylamines **24b-27b** provided desired cyclic carbamates **19a-23a**, and **7**, **8**, and **29a-31a**, respectively, in an $S_{cN'}$ manner. During the formation of **19a-23a**, moderate 1,3-syn stereoselectivity was observed. High 1,2-syn stereoselectivity was accomplished by using AgF/Pd(II) system in the five-membered cyclic carbamate formation. These results were applied to the syntheses of statine **32** and its related amino acid **33**, efficiently.

Recently, 1,2 and 1,3 amino hydroxyl systems have received much attention from synthetic chemists due to their presence in a variety of natural products. Since unusual amino acids possessing the above mentioned moieties are widely distributed in biologically important peptides, development of efficient synthetic methods and application of these methods to the syntheses of such amino acids are currently of importance.[1,2] Recently, we reported the synthesis of the *N-tert*-butyldimethylsilyloxycarbonyl group (silyl carbamate)[3] from the most common urethane-type amino-protecting groups such as *N-tert*-butoxycarbonyl (*N-t*-Boc) and *N*-benzyloxycarbonyl (*N*-Z).[4] Owing to its high reactivity the silyl carbamate can be viewed as an *N-carboxylate ion equivalent*, which can be converted into several urethane-type groups by intermolecular reaction with an electrophile in the presence of fluoride ion.[3] Thus, it was considered that *intramolecular* trapping of this reactive species would provide a stereoselective method for

(1) Hunt, S. In *Chemistry and Biochemistry of the Amino Acids*; Barrett, G. C., Ed.; Chapman: London, 1985; pp 55-138.
(2) For reviews, see: (a) Wagner, I.; Musso, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 816. (b) Ohfune, Y.; Kurokawa, N. *J. Syn. Org. Chem., Jpn.* **1986**, *44*, 647. (c) Coppola, G. M.; Shuster, H. F. *Asymmetric Synthesis. Construction of Chiral Molecule Using Amino Acids*; Wiley: New York, 1987.
(3) (a) Sakaitani, M.; Ohfune, Y. *Tetrahedron Lett.* **1985**, *26*, 5543. (b) Sakaitani, M.; Kurokawa, N.; Ohfune, Y. *Tetrahedron Lett.* **1986**, *27*, 3753. (c) For details of the syntheses of *tert*-butyldimethylsilyl carbamate, see: Sakaitani, M.; Ohfune, Y. *J. Org. Chem.*, in press.
(4) (a) Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*; Springer: Berlin, 1984; pp 7, 151. (b) Greene, T. W. *Protective Groups in Organic Synthesis*; Wiley: New York, 1982; pp 232, 239.

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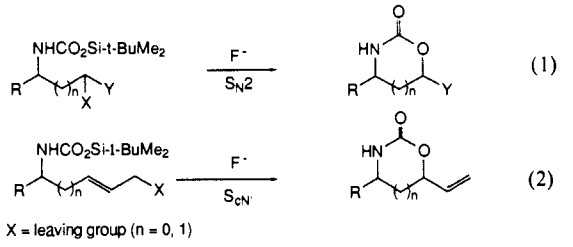
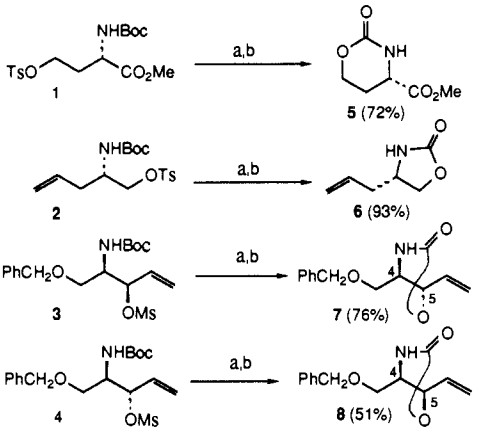
the synthesis of the above mentioned amino hydroxyl systems.[5] As shown in eq 1, the activated species generated by fluoride ion may displace a leaving group on the same substrate to give the cyclic carbamate with inversion (internal S_N2). On the other hand, trapping of this species with allyl halide at an sp^2 carbon ($S_{cN'}$)[6] is also of interest since relative asymmetry from an amino chiral center could be induced (eq 2).[7] We detail here new methods for the cyclic carbamate formation and its application to the synthesis of statine and its related amino acid.[8,9]



Results and Discussion

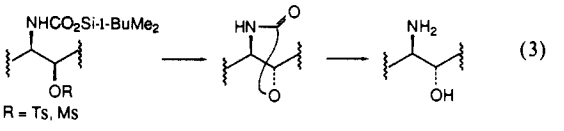
Internal S_N2 Cyclic Carbamate Formation. Although numerous methods have recently been reported for the synthesis of the 1,2-syn (threo) amino hydroxyl system,[9,10] only a limited number of methods are available for the 1,2-anti (erythro) relationship.[11] The use of the Mitsunobu method for the inversion of the hydroxyl group stereochemistry is effective for the synthesis of the 1,2-anti amino hydroxyl system from the 1,2-syn derivative.[12] However, this system has some limitations due to the steric and/or stereoelectronic reasons of the amino substituent (vide infra). The silyl carbamate activated by fluoride ion has enough nucleophilicity to react with an alkyl or an allyl halide.[3] Trapping of this reactive species in an intramolecular manner may provide cyclic carbamate

Scheme I[a]



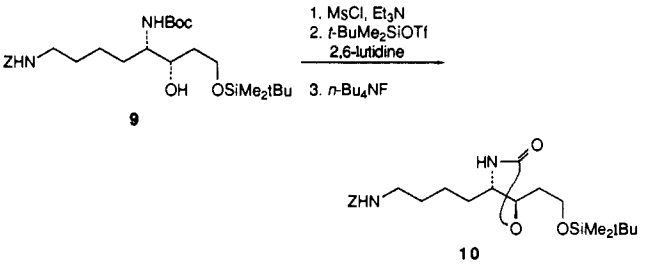
[a] Reagents and conditions: (a) 1.5 equiv of *t*-$BuMe_2SiOTf$, 2.0 equiv of 2,6-lutidine, CH_2Cl_2, room temperature, 15 min; (b) 1.5 equiv of *n*-Bu_4NF, THF, 0 °C, 1 h.

accompanied by an inversion of the original stereochemistry of the leaving group (eq 3).



Initially, the tosylate **1**[13] was chosen as the substrate. Treatment of **1** with 1.5 equiv of *tert*-butyldimethylsilyl trifluoromethanesulfonate (*t*-$BuMe_2SiOTf$) and 2 equiv of 2,6-lutidine in CH_2Cl_2 at room temperature gave its corresponding *N*-silyloxycarbonylated **1**, which upon treatment with 1.0 equiv of tetrabutylammonium fluoride (*n*-Bu_4NF) in tetrahydrofuran (THF) at 0 °C furnished the cyclic carbamate **5** in good yield. This result prompted us to examine the cyclic carbamate formation from the 1,2-syn mesylate **3**.[13,14] Treatment of **3** in the same manner as above gave the 1,2-anti cyclic carbamate **7**, exclusively. This result clearly indicates that the reaction proceeded stereospecifically to give cyclic carbamate **7** in which the original stereochemistry of the hydroxyl group was completely inverted. Furthermore, the reaction of the 1,2-anti mesylate **4**[13,14] gave the cyclic carbamate **8** with a 1,2-syn stereochemistry.

The structures of these carbamates **7** and **8** were elucidated by comparison of their ^1H NMR chemical shifts at 4-H and 5-H with those of the related compounds (see, Table IV). Thus, interconversion of both 1,2-syn and -anti amino hydroxyl systems was accomplished (Scheme I). The significant synthetic potential of this method was demonstrated by the key conversion of **9** into the 1,2-anti carbamate **10**, where the Mitsunobu procedure was not effective probably due to the presence of the sterically bulky *N-tert*-butoxycarbonyl group.[15] Treatment of **9** with 1 equiv of *n*-Bu_4NF in THF at 0 °C for 1 h gave the desired **10**, stereospecifically, in 93% yield.



$S_{cN'}$ Cyclic Carbamate Formation. Intramolecular trapping of the activated silyloxycarbonyl group with a trigonal carbon is of

(5) For the intramolecular electrophilic 2-oxazolidone formation from N-substituted allyl- or homoallylamines, see: (a) Parker, K. A.; O'Fee, R. *J. Am. Chem. Soc.* **1983**, *105*, 654. (b) Wang, Y. F.; Izawa, T.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1982**, *104*, 6465. (c) Overman, L. E.; McCready, R. J. *Tetrahedron Lett.* **1982**, *23*, 4887. (d) Takano, S.; Hatakeyama, S. *Heterocycles* **1982**, *19*, 1243. (e) Georges, M.; Mackay, D.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1982**, *104*, 1101. (f) Pauls, H. W.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1980**, *102*, 3956.

(6) Stork, G.; Schoofs, A. R. *J. Am. Chem. Soc.* **1979**, *101*, 5081.

(7) Parts of this work were published a preliminary report: Sakaitani, M.; Ohfune, Y. *Tetrahedron Lett.* **1987**, *28*, 3987.

(8) Statine: (a) Umezawa, H.; Aoyagi, T.; Morishima, H.; Matsuzaki, M.; Hamada, H.; Takeuchi, T. *J. Antibiot.* **1970**, *23*, 2569. For a review, see: (b) Rich, D. H. In *Proteinase Inhibitors*; Barrett, A. J., Salvesen, G., Eds.; Elsevier: New York, 1986; p 179. (3*S*,4*S*)-4-Amino-3-hydroxy-5-phenylpentanoic acid (AHPPA): (c) Omura, S.; Inamura, N.; Kawakita, K.; Mori, Y.; Yamazaki, Y.; Masuma, R.; Takahashi, Y.; Tanaka, H.; Huang, L.-Y.; Woodruff, H. B. *J. Antibiot.* **1986**, *39*, 1079. Synthesis of AHPPA: (d) Rich, D. H.; Sun, E. T.; Ulm, E. *J. Med. Chem.* **1980**, *23*, 27. (e) Rittle, K. E.; Homnick, C. F.; Ponticello, G. S.; Evans, B. E. *J. Org. Chem.* **1982**, *47*, 3016.

(9) For recent syntheses of statine and its analogues, see: (a) Nishi, T.; Kitamura, M.; Ohkuma, T.; Noyori, R. *Tetrahedron Lett.* **1988**, *29*, 6327. (b) Devant, R. M.; Radunz, H.-E. *Tetrahedron Lett.* **1988**, *29*, 2307. (c) Raddatz, P.; Radunz, H.-E.; Schneider, G.; Schwarz, H. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 426. (d) Maibaum, J.; Rich, D. H. *J. Org. Chem.* **1988**, *53*, 869. (e) Schuda, P. F.; Greenlee, W. J.; Chakravarty, P. K.; Eskola, P. J. *J. Org. Chem.* **1988**, *53*, 873. (f) Schostarez, H. J. *J. Org. Chem.* **1988**, *53*, 3628. (g) Kano, S.; Yuasa, Y.; Yokomatsu, T.; Shibuya, S. *J. Org. Chem.* **1988**, *53*, 3865. (h) Jouin, P.; Castro, B. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1177. (i) Harris, B. D.; Bhat, K. L.; Joullie, M. M. *Tetrahedron Lett.* **1987**, *28*, 2837. (j) Lubell, W. D.; Rapoport, H. *J. Am. Chem. Soc.* **1987**, *109*, 236. (k) Kano, S.; Yokomatsu, T.; Iwasawa, H.; Shibuya, S. *Chem. Lett.* **1987**, 1531. (l) Kano, S.; Yokomatsu, T.; Iwasawa, H.; Shibuya, S. *Tetrahedron Lett.* **1987**, *28*, 6331. (m) Andrew, R. G.; Conrow, R. E.; Elliott, J. D.; Johnson, W. S.; Ramezani, S. *Tetrahedron Lett.* **1987**, *28*, 6535. (n) Sham, H. L.; Rempel, C. A.; Stein, H.; Cohen, J. *J. Chem. Soc., Chem. Commun.* **1987**, 683. (o) Kogen, H.; Nishi, T. *J. Chem. Soc., Chem. Commun.* **1987**, 311. (p) Hanson, G. J.; Baran, J. S.; Lindberg, T. *Tetrahedron Lett.* **1986**, *27*, 3577. (q) Woo, P. W. K. *Tetrahedron Lett.* **1985**, *26*, 2973. Other references are cited therein.

(10) For a review of α-amino aldehydes, see: Jurczak, J.; Gołębiowski, A. *Chem. Rev.* **1989**, *89*, 149. Asymmetric glycine enolate aldol approaches: (a) Evans, D. A.; Weber, A. E. *J. Am. Chem. Soc.* **1986**, *108*, 6757. (b) Schöllkopf, U.; Nozulak, J.; Grauert, M. *Synthesis* **1985**, 55. (c) Nakatsuka, T.; Miwa, T.; Mukaiyama, T. *Chem. Lett.* **1981**, 279.

(11) (a) Evans, D. A.; Sjogren, E. B.; Weber, A. E.; Conn, R. E. *Tetrahedron Lett.* **1987**, *28*, 39. (b) Kurokawa, N.; Ohfune, Y. *J. Am. Chem. Soc.* **1986**, *108*, 6041.

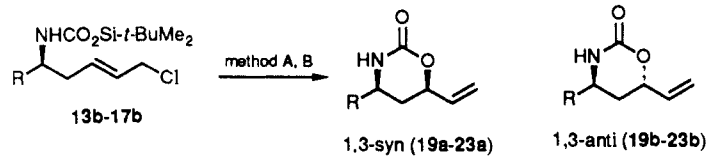
(12) For a review, see: Mitsunobu, O. *Synthesis* **1981**, 1.

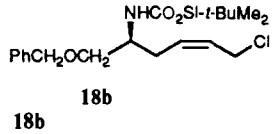
(13) For details of the preparation of this compound, see the supplementary material.

(14) Ohfune, Y.; Nishio, H. *Tetrahedron Lett.* **1984**, *25*, 4133.

(15) Hori, K.; Ohfune, Y. *J. Org. Chem.* **1988**, *53*, 3886.

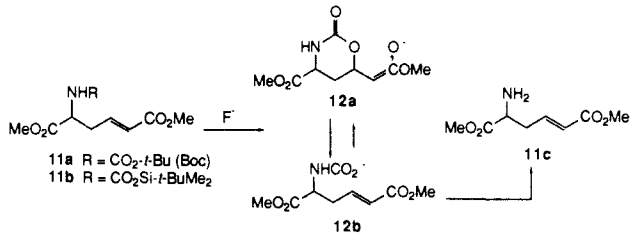
Table I. AgF- (Method A) and AgF/Pd(II)- (Method B) Assisted $S_{cN'}$ Cyclic Carbamate Formation of (Chloromethyl)homoallylamines[a]



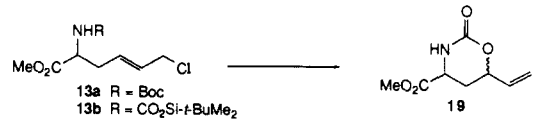
entry	R	method[b,c]	yield,[d] %	product ratio (syn/anti)[e]
1	CO_2Me **13b**	A	63	**19a/19b** = 3/2
2	CO_2CH_2Ph **14b**	A	53	**20a/20b** = 4/3
3	CH_2OCH_2Ph **15b**	A	63	**21a/21b** = 4/1
4	$CH(CH_3)_2$ **16b**	A	63	**22a/22b** = 4/1
5	CH_2Ph **17b**	A	65	**23a/23b** = 4/1
6	CO_2Me **13b**	B	72	**19a/19b** = 1/1
7	CO_2CH_2Ph **14b**	B	53	**20a/20b** = 1/1
8	CH_2OCH_2Ph **15b**	B	70	**21a/21b** = 1/1
9	$CH(CH_3)_2$ **16b**	B	65	**22a/22b** = 3/2
10	CH_2Ph **17b**	B	50	**23a/23b** = 3/2
11	 **18b**	A	0	
12	**18b**	B	0	

[a] Prepared from the corresponding *N*-*t*-Boc **13a–18a**[13] with *t*-$BuMe_2SiOTf$/2,6-lutidine. [b] Method A: 2 equiv of AgF, CH_3CN, room temperature, 15–24 h. [c] Method B: 2 equiv of AgF, 0.1 equiv of allylpalladium(II) chloride dimer, 0.3 equiv of Ph_3P, CH_3CN, room temperature, 3–8 h. [d] Isolated yield. [e] Ratio determined by ^1H NMR or HPLC analysis.

interest. Our initial attempt was to trap this reactive species by a Michael acceptor such as an α,β-unsaturated ester of **11**.[16,17] However, exclusive formation of the amine **11c** was observed by the fluoride ion treatment of the silyl carbamate **11b** (*n*-Bu_4NF, CsF, etc). It is assumed that the reaction underwent initial 1,4-addition to give carbamate **12a**, which subsequently equilibrated to **12b** from which decarboxylation gave **11c**.



Therefore, our attention was turned to the use of an allyl halide as an acceptor of *N*-carboxylate ion species in an $S_{cN'}$ manner (eq 2, $n = 1$).[6] In this case, AgF was our first choice since both chlorine and silicon atoms can be activated by this reagent. Thus, allyl chloride **13b**, prepared from *N*-*t*-Boc **13a**[13] with *t*-$BuMe_2SiOTf$ and 2,6-lutidine, was treated with 2 equiv of AgF in CH_3CN at room temperature for 24 h to give the desired **19** in 63% yield.



For the elucidation of general aspects of this reaction, other reagents and reaction conditions were examined at first. These results are summarized by the following points. (1) No cyclic carbamate **19** with *n*-Bu_4NF/THF without AgF was detected; (2) the use of silver trifluoromethanesulfonate (AgOTf) or silver tetrafluoroborate ($AgBF_4$) reduced the yields (8% with AgOTf/2,6-lutidine/THF, reflux; and 21% with $AgBF_4$/2,6-lutidine/THF); and (3) the use of *N*-*t*-Boc **13a** (without prior

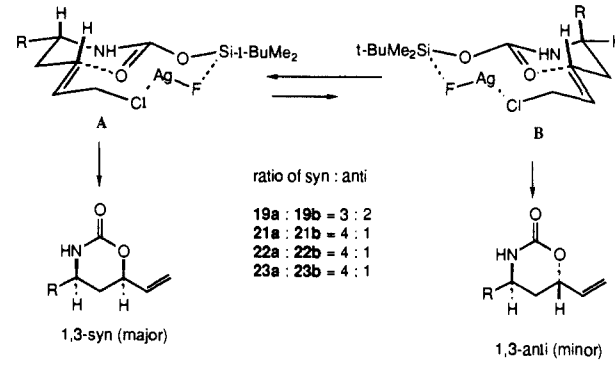


Figure 1.

t-$BuMe_2SiOTf$ treatment) decreased the yield (11% with AgF/CH_3CN, reflux, 20 h). Therefore, it is concluded that the use of AgF is the best choice for the preparation of cyclic carbamate from silyl carbamates.

In addition to the above results, trapping of the activated species with π-allylpalladium complex[18] generated from the allyl chloride moiety of **13b** is of interest. Thus, 0.1 equiv of π-allylpalladium(II) chloride dimer and 0.3 equiv of triphenylphosphine were added to the above reaction medium (**13b** → **19**). Significant rate enhancement (room temperature, 3 h) and increased yield (70%) were observed. To explain the general applicability of the AgF- (method A) and AgF/Pd(II)- (method B) assisted cyclic carbamate formation and its stereochemical outcome, (chloromethyl)homoallylamines **14b–18b**[13] were employed for these reactions (Table I).

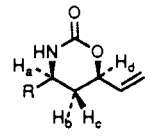
Results of the six-membered cyclic carbamate formation of **13b–18b** were characterized by the following points: (1) cyclic carbamates were produced from the (*E*)-allyl chlorides **13b–17b** in good yield; (2) cyclic carbamate **21** could not be obtained from the (*Z*)-allyl chloride **18b** (entries 11 and 12); (3) moderate stereoselectivity for the formation of 1,3-syn cyclic carbamate was observed by the use of method A (entries 3–5); and (4) in contrast to method A, it is surprising that the stereoselectivity was not observed by the use of method B (entries 6–10). From (1)–(3), it is suggested that the reaction using method A proceeds through

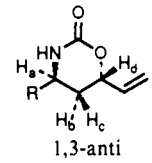
(16) Prepared from *N*-*t*-Boc-allylglycine methyl ester[14] in two steps: (1) ozone, MeOH, −78 °C and $(CH_3)_2S$, room temperature; (2) Ph_3PCHCO_2Me, benzene.

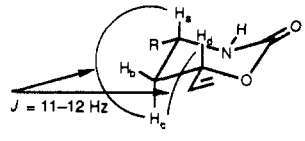
(17) Successful intramolecular Michael addition from O-carbamates, see: Hirama, M.; Shigemoto, T.; Ito, S. *J. Org. Chem.* **1987**, *52*, 3342.

(18) (a) Trost, B. M. *J. Organomet. Chem.* **1986**, *300*, 263. (b) Tsuji, J. *J. Organomet. Chem.* **1986**, *300*, 281.

Table II. ^1H NMR ($CDCl_3$) Chemical Shifts and Coupling Constants of 6-Vinyltetrahydro-1,3-oxazin-2-ones

	R	H_b δ, ppm	H_c δ, ppm	coupling const, Hz J_{a-b}	J_{a-c}	J_{b-d}	J_{c-d}
 1,3-syn	CO_2Me **19a**	2.43	1.86	5	11	3	11
	CH_2OCH_2Ph **21a**	2.01	1.48	5	12	3	12
	$CH(CH_3)_2$ **22a**	1.96	1.44	5	12	3	12
	CH_2Ph **23a**	2.06	1.60	4	11	4	11

	R	H_b and H_c δ, ppm
 1,3-anti	CO_2Me **19b**	2.18 (m, 2 H)
	CH_2OCH_2Ph **21b**	1.87 (m, 2 H)
	$CH(CH_3)_2$ **22b**	1.85 (m, 2 H)
	CH_2Ph **23b**	1.90 (m, 2 H)



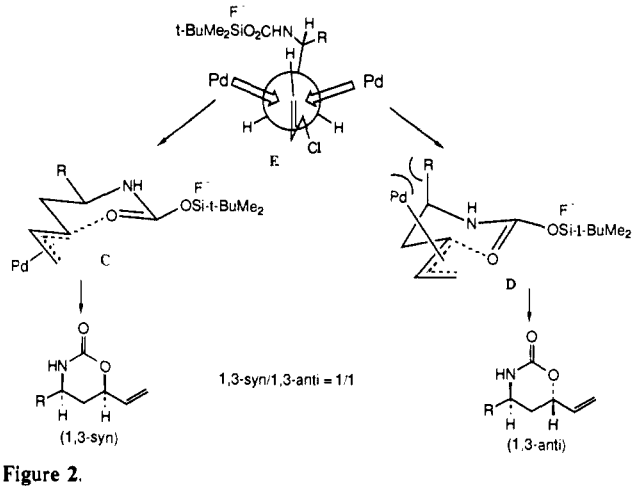
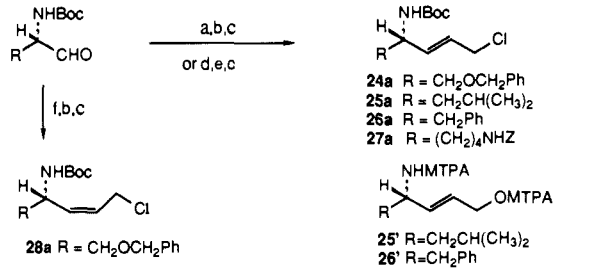


Figure 2.

the cyclic transition state A or B where AgF chelates both with a silicon and with a chlorine atom: since the cyclic transition state from **18b** with a *Z* double bond involving AgF is much higher in energy than that for the *E* derivatives, the rate of side reactions, such as desilylation followed by decarboxylation which gives free amine, is much faster than that of the cyclic carbamate formation.[19,20] 1,3-Syn isomers may be produced in favor of the thermodynamically more stable A (Figure 1). In entries 1 and 2, decreased steric bulkiness by the ester group of **13b** and **14b** may be one of the reasons why the stereoselectivity was reduced.

On the other hand, it is assumed by the consideration of (4) that the use of method B led to an initial dissociation of AgF and subsequent formation of π-allylpalladium intermediates C and D, or E (Figure 2). Although there appears to be a different stability between the transition-state structures, C and D, the product ratio was 1:1. Therefore, we propose that the rate-determining step involves formation of a π-allyl–Pd complex, proceeding via an acyclic model E where the direction of palladium attack to the substrate has an almost even possibility from either side, and that subsequent cyclization occurs in a fast step via

Scheme II[a]



[a] Reagents and conditions: (a) $Ph_3P{=}CHCO_2Et$, benzene, 40 °C; (b) *i*-Bu_2AlH, $BF_3{\cdot}Et_2O$, THF, −78 °C; (c) *N*-chlorosuccinimide (NCS), Ph_3P, CH_2Cl_2, 0 °C; (d) $Ph_3PCHCHO$, benzene, 40 °C; (e) $LiAlH(O\text{-}t\text{-}Bu)_3$, THF, −30 °C; (f) $(CF_3CH_2O)_2P(O)CH_2CO_2Me$, NaH, 18-crown-6, THF, −78 °C.

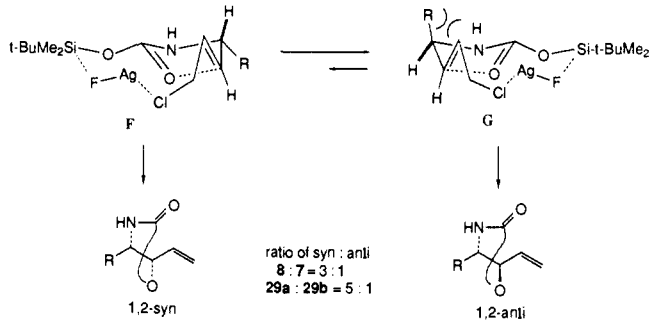


Figure 3.

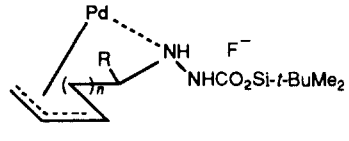
transition-state structures similar to C and D (no equilibrium between C and D).[21]

The stereochemistry of the cyclic carbamates obtained above was elucidated by the ^1H NMR data, as shown in Table II. The large *J* values ($J_{H_a-H_c} = J_{H_c-H_d}$ = 11–12 Hz) observed in all major isomers by method A (entries 1–4, Table I) clearly indicate that

(19) The reaction of **18b** using both methods, A and B, was sluggish and the products were composed of a mixture of polar and unidentifiable compounds that might be produced by an inter- and/or intramolecular reaction of the resulting amine with allyl chloride or other reactive species. A small amount of free amine derived from **18b** was isolated in these cases. On the other hand, the reaction in CH_3CN under reflux gave a complex mixture and the amine could not be detected. We believe that the side reactions in all cases are mainly due to an initial cleavage of the Si–O bond, activated by fluoride ion, followed by a decarboxylation prior to attack to the leaving group under the reaction conditions or by adventitious moisture. Such side reactions would reduce the yields.

(20) The reaction of allyl chloride (i.e., **13b**) with allylpalladium chloride dimer in the absence of AgF was found to be extremely slow by monitoring with TLC. Therefore, it is suggested that both activation of the silicon atom by fluoride ion and formation of π-allylpalladium complex are important to accelerate the reaction rate in producing cyclic carbamates.

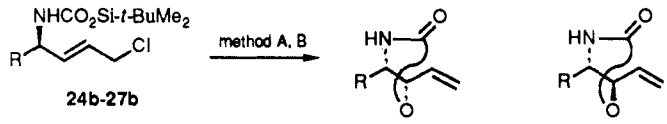
(21) It is assumed that the AgF/Pd(II) reactions from the *Z* allyl chlorides, **18b** and **20b**, involve the transition state (i) in which nitrogen chelates



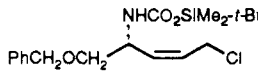
i (*n* = 0,1)

to palladium (internal Lewis acid to nitrogen, which accelerates decarboxylation) resulting in the formation of their corresponding amines. From the *E* isomers, such internal delivery of Lewis acid cannot occur.[a] (a) Trost, B. M.; Verhoeven, T. R. *Comprehensive Organometallic Chemistry*; Sir Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.: Pergamon Press: Oxford, U.K., 1982; pp 799.

Table III. AgF- (Method A) and AgF/Pd(II)- (Method B) Assisted $S_{cN'}$ Cyclic Carbamate Formation of (Chloromethyl)allylamines[a]

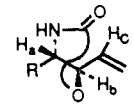
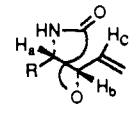


24b-27b 1,2-syn (8, 29a-31a) 1,2-anti (29b-31b)

entry	R	method[b,c]	yield,[d] %	product ratio (syn/anti)[e]
1	CH_2OCH_2Ph **24b**	A	55	**8**/**7** = 3/1
2	$CH_2CH(CH_3)_2$ **25b**	A	81	**29a**/**29b** = 5/1
3	CH_2OCH_2Ph **24b**	B	72	**8**/**7** = 8/1
4	$CH_2CH(CH_3)_2$ **25b**	B	76	**29a**/**29b** = 15/1
5	CH_2Ph **26b**	B	70	**30a**/**30b** = 10/1
6	$(CH_2)_4NHZ$ **27b**	B	53	**31a**/**31b** = 40/1
7	 **28b**	A	0	
8	**28b**	B	9	**8**/**7** = 8/1

[a] Prepared from the corresponding *N*-*t*-Boc **24a-28a**. [b] Method A: 2 equiv of AgF, CH_3CN, room temperature, 15-24 h. [c] Method B: 2 equiv of AgF, 0.1 equiv of allylpalladium(II) chloride dimer, 0.3 equiv of Ph_3P, CH_3CN, room temperature, 3-8 h. [d] Isolated yield. [e] Ratio determined by ^1H NMR or HPLC.

Table IV. ^1H NMR ($CDCl_3$) Chemical Shifts and Coupling Constants of 5-Vinyl-2-oxazolidinones

	R	H_a δ, ppm	H_b δ, ppm	J_{a-b}, Hz	NOE, %
 1,2-syn (trans)	CH_2OCH_2Ph **8**	3.68	4.68	7	
	$CH_2CH(CH_3)_2$ **29a**	3.58	4.50	7	6 (H_a-H_c)
	CH_2Ph **30a**	3.77	4.64	6	
	$(CH_2)_4NHZ$ **31a**	3.50	4.52	6	0 (H_a-H_b)
 1,2-anti (cis)	CH_2OCH_2Ph **7**	4.02	5.08	8	
	$CH_2CH(CH_3)_2$ **29b**	3.94	5.01	7	0 (H_a-H_c)
	CH_2Ph **30b**	4.08	5.08	7	
	$(CH_2)_4NHZ$ **31b**	3.83	5.03	6	6.8 (H_a-H_b)

19a-23a possess the assigned structure with 1,3-syn (cis) substituents.

The five-membered cyclic carbamate formations of the (chloromethyl)allylamines **24b-28b**, prepared from α-amino aldehydes[22,23] as shown in Scheme II by the same methods as above, were next examined. These results are summarized in Table III. In the case of AgF-assisted reactions (method A), moderate yields and 1,2-syn (threo) selectivity were observed (entries 1 and 2). On the other hand, the use of AgF in the presence of Pd(II) catalyst (method B) showed a significant rate enhancement and improvement of the yields. Moreover, in contrast to the results obtained in the six-membered cyclic carbamate formation, an increase in a 1,2-syn (threo) selectivity was observed. Especially, high stereoselectivity was encountered in entries 4-6 in which a bulky substituent is placed at the carbon bearing the amino group.

Five-membered cyclic carbamate formation is thought to arise from hypothetical cyclic intermediate F or G, which resembles that of the six-membered case (Figure 3). Due to the presence of a severe 1,2 steric interaction in the transition-state structure G, the reaction may proceed via a thermodynamically more favored F, resulting in the predominant formation of the 1,2-syn isomer. Desired cyclic carbamate was not produced from the (*Z*)-allylamine **28b** with method A due probably to its high-energy transition-state structure, as mentioned in the six-membered case.[19,20]

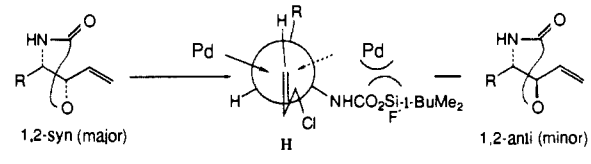


Figure 4.

On the other hand, by adding Pd(II) catalyst, a Felkin-Anh type transition-state model H resembling the thermodynamically favored ground-state conformation[24,25] was proposed to elucidate the greater 1,2-syn selectivity. In this model, it is assumed that initial Pd(II) attack to the less hindered side (rate-determining step) followed by participation of the activated silyloxycarbonyl group (stereocontrol by the allylic chiral center) results in the predominant formation of 1,2-syn adduct (Figure 4). In addition, it is noted that the reaction of (*Z*)-allylamine **28b** using method B produced cyclic carbamate to give **8** and **7** (8%, 8:1). This may be due to an initial isomerization of the *Z* double bond into *E*, which consequently cyclizes to give **8** and **7**.[21]

The structures of the cyclic carbamates in Table III were elucidated by comparison of their ^1H NMR chemical shifts of H_a and H_b of each compound with those of related compounds (Table IV);[26] the H_a and H_b signals of the 1,2-syn carbamates

(22) Yasumasa, H.; Shioiri, T. *Chem. Pharm. Bull.* **1982**, *30*, 1921.

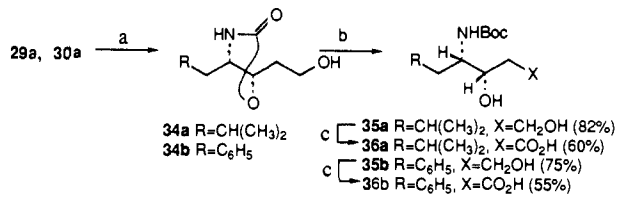
(23) No racemization during this process was confirmed by converting allyl alcohols to the corresponding *N*,*O*-bis-(+)-MTPA amide esters.[a] ^1H NMR data indicated their homogeneity: (4*S*)-*N*,*O*-bis-(+)-MTPA-4-amino-6-methyl-2-heptenol (**25'**): oil; ^1H NMR ($CDCl_3$) δ 7.3-7.6 (m, 10 H), 6.62 (d, 1 H, *J* = 9 Hz), 5.67 (m, 2 H), 4.77 (m, 2 H), 4.57 (m, 1 H), 3.53 (q, 3 H, *J* = 1 Hz), 3.42 (q, 3 H, *J* = 1 Hz), 1.3-1.7 (m, 3 H), 0.93 (d, 6 H, *J* = 7 Hz). The methoxy groups of its diastereomer appeared at δ 3.55 (q, 3 H, *J* = 1 Hz) and 3.38 (q, 3 H, *J* = 1 Hz). (4*S*)-*N*,*O*-bis-(+)-MTPA-4-amino-5-phenyl-2-pentanol (**26'**): oil; ^1H NMR ($CDCl_3$) δ 7.30 (m, 15 H), 6.58 (d, 1 H, *J* = 9 Hz), 5.65 (m, 2 H), 4.86 (m, 1 H), 4.72 (d, 2 H, *J* = 7 Hz), 3.50 (q, 3 H, *J* = 1 Hz), 3.18 (q, 3 H, *J* = 1 Hz), 2.87 (m, 2 H). (a) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(24) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61.

(25) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

(26) The significant difference of *J* values ($J_{H_a-H_b}$) observed between 1,2-syn (trans) and 1,2-anti (cis) 2-oxazolidone systems was used for the structure determination of these systems.[a] However, only slight differences of *J* values observed in these studies, maybe due to the allylic nature of the H_a position. (a) Futagawa, S.; Inui, T.; Shiba, T. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3308.

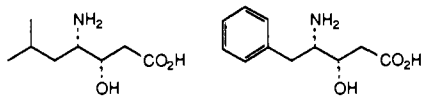
Scheme III[a]



[a] Reagents and conditions: (a) (1) 9-BBN, THF, room temperature, (2) 6 N NaOH, 30% H_2O_2; (b) (1) $Ba(OH)_2$, EtOH, reflux; (2) Boc_2O, Et_3N, THF, room temperature; (c) PtO_2, O_2, dioxane/H_2O = 1/3, 50 °C.

appeared 0.3–0.5 ppm upfield relative to those of the anti isomers. A NOE (6%) was observed between H_a and H_c in **29a** indicating a trans relationship of the vinyl and R substituents on the 2-oxazolidone ring: the major isomers having 1,2-syn stereochemistry were further proven by converting several derivatives into the corresponding natural amino acids as described in the following section.

Stereoselective Synthesis of Statine and Its Related Amino Acid. In recent studies concerning renin inhibition, the pepstatine family of peptide-related inhibitors have been expected to be potential antihypertensive medicinal agents.[8] Statine (**32**) and (3*S*,4*S*)-



32 statine **33** AHPPA

4-amino-3-hydroxy-5-phenylpentanoic acid (**33**; AHPPA) are the key constituent amino acids of these peptides. Although much attention has focused on the syntheses of statine and AHPPA,[8,9] only a limited number of methods provide the stereoselective construction of these key vicinal amino hydroxyl systems.

Since the AgF/Pd(II)-assisted $S_{cN'}$ five-membered cyclic carbamate formation was proven to be an extremely effective method for the synthesis of vicinal amino hydroxyl systems with the requisite 1,2-syn stereochemistry, this method was applied to the syntheses of statine and its related amino acid, AHPPA (**33**). Thus, the cyclic carbamates **29a** and **30a**, prepared stereoselectively in the previous section, are the intermediates that possess appropriate functionalities and carbon frameworks corresponding to these amino acids, respectively. Conversion of these intermediates to the target amino acids is as follows. Hydroboration of **29a** using 9-borabicyclo[3.3.1]nonane (9-BBN) and subsequent oxidation (NaOH, 30% H_2O_2) gave the primary alcohol **34a**. Hydrolysis of the cyclic carbamate of **34a** with $Ba(OH)_2$ followed by protection of the resulting amine with di-*tert*-butyl dicarbonate (Boc_2O) furnished N-protected diol **35a** in 82% yield from **29a**. The primary hydroxyl group of **35a** was selectively oxidized[27] by the use of PtO_2/O_2 to give *N*-*t*-Boc-statine (**36a**; 60%, 27% overall yield from *N*-*t*-Boc-L-isoleucinal): mp 118–120 °C, $[\alpha]^{34}_D$ −38.5° (*c* 1.0, MeOH). *N*-*t*-Boc-AHPPA **36b** was prepared in the same manner as above (19% overall yield from *N*-*t*-Boc-L-phenylalaninal): mp 151–152 °C, $[\alpha]^{30}_D$ −37.5° (*c* 1.0, MeOH). These synthetic materials showed spectroscopic as well as physical constants completely identical with those reported.[8d,8e]

Conclusion. *Intramolecular* trapping of the *tert*-butyldimethylsilyl carbamate activated by fluoride ion was studied. In the internal S_N2 reactions, complete inversion of the original hydroxyl group stereochemistry was observed. On the other hand, AgF- and AgF/Pd(II)-assisted $S_{cN'}$ cyclic carbamate formation was accomplished by the use of (chloromethyl)homoallylamines and (chloromethyl)allylamines. These results provide new methods for the stereoselective construction of 1,2 and 1,3 amino hydroxyl systems. Application of the present studies was demonstrated by the synthesis of several biologically important unusual amino acids.

(27) Maurer, P. J.; Takahata, H.; Rapoport, H. *J. Am. Chem. Soc.* **1984**, *106*, 1095.

Experimental Section

Melting points are uncorrected. ^1H NMR spectra were recorded on one of the following instruments: JEOL FX 100, Nicolet NT-360, or General Electric GN-500. Chemical shifts are reported as δ values in ppm relative to $CHCl_3$ (7.26) in $CDCl_3$. IR spectra were measured on an Hitachi 270-30 infrared spectrophotometer. Mass spectra were obtained on a Hitachi M-80B spectrometer for electron impact (EI) ionization and secondary ionization mass spectrometry (SIMS). Optical rotations were taken on a Perkin-Elmer 241 polarimeter. All reactions were monitored by thin-layer chromatography, carried on 2 × 5 cm precoated TLC plates (silica gel 60F-254; layer thickness, 0.25 mm) manufactured by Merck, with UV light (254 nm), ninhydrin, or $KMnO_4$ solution (0.5 g dissolved in 100 mL of water). Silica gel (Merck 60, 70–230 mesh) was used for column chromatography. Medium-pressure liquid chromatography (MPLC) was carried out by LiChroprep Si 60 lobar column sizes A, B, and C (Merck). High-performance liquid chromatography (HPLC) was performed with Develosil ODS-5 (Nomura Chemical). All reactions were carried out under an argon atmosphere. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials unless otherwise stated.

4-(Methoxycarbonyl)tetrahydro-1,3-oxazin-2-one (5). To a stirred solution of **1** (149 mg, 0.38 mmol) and 2,6-lutidine (88 μL, 0.76 mmol) in dry CH_2Cl_2 (1 mL) at room temperature was added dropwise *tert*-butyldimethylsilyl trifluoromethanesulfonate (*t*-$BuMe_2SiOTf$; 131 μL, 0.57 mmol). The reaction mixture was stirred for 15 min, quenched with saturated aqueous ammonium chloride solution, and extracted with ether several times. The combined organic phase was washed with H_2O and brine, dried ($MgSO_4$), and concentrated in vacuo to give *N*-(*tert*-butyldimethylsilyloxycarbonyl)-*O*-(*p*-tolylsulfonyl)-L-homoserine methyl ester (180 mg; **procedure I** for the preparation of *tert*-butyldimethylsilyl carbamate).[3]

The resulting silyl carbamate was treated with 380 mL [1 M solution in tetrahydrofuran (THF), 0.38 mmol] of tetrabutylammonium fluoride in THF (2 mL) at 0 °C for 1 h and quenched with saturated aqueous ammonium chloride solution. The mixture was extracted with ethyl acetate (EtOAc) several times. The combined organic phase was washed with H_2O and then brine, dried ($MgSO_4$), and concentrated in vacuo to give the crude product, which upon purification by column chromatography on silica gel (elution with 50% EtOAc in ether) gave **5** (44 mg, 72%): colorless prisms; mp 92–93 °C (EtOAc); IR (neat) 3296, 2964, 1740, 1716 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 6.66 (br s, 1 H), 4.30 (t, 2 H, J = 6 Hz), 4.22 (m, 1 H), 3.80 (s, 3 H), 2.0–2.5 (m, 2 H); MS (EI method), m/z 159 $(M)^+$, 115, 100. Anal. Calcd for $C_6H_9O_4N$: C, 45.28; H, 5.70; N, 8.80. Found: C, 45.34; H, 5.68; N, 8.78.

4-(2-Allyl)-2-oxazolidinone (6). *N*-(*tert*-Butyldimethylsilyloxycarbonyl)-2-amino-1-(*p*-tolylsulfonyloxy)-4-pentene was prepared from **2** (2.44 g, 6.9 mmol) according to procedure I. The resulting silyl carbamate in THF (20 mL) was treated at 0 °C with 10.5 mL (1 M solution in THF, 10.5 mmol) of tetrabutylammonium fluoride. The reaction mixture was stirred for 1 h and extracted with EtOAc several times. The combined organic phase was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give an oily residue, which upon purification by column chromatography on silica gel (elution with 10% EtOAc in ether) gave **6** (811 mg, 93%): oil; IR (neat) 3292, 2984, 2920, 1750, 1646 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 6.71 (br s, 1 H), 5.72 (ddt, 1 H, J = 18, 10, 7 Hz), 5.17 (dd, 1 H, J = 10, 2 Hz), 5.14 (dd, 1 H, J = 18, 2 Hz), 4.47 (dd, 1 H, J = 8, 8 Hz), 4.05 (d, 1 H, J = 8 Hz), 4.00 (m, 1 H), 2.34 (dd, 2 H, J = 7, 7 Hz); MS (EI method), m/z 128 $(M)^+$, 87. Anal. Calcd for $C_6H_9O_2N$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.73; H, 7.22; N, 10.99.

(4*R,5*S**)-4-(Benzyloxymethyl)-5-vinyl-2-oxazolidinone (7).** (2*R**,3*R**)-*N*-(*tert*-Butyldimethylsilyloxycarbonyl)-2-amino-1-(benzyloxy)-3-(methylsulfonyloxy)-4-pentene, prepared from **3**[13,14] (83 mg, 0.22 mmol) according to procedure I, was treated with 330 μL (1 M solution in THF, 0.33 mmol) of tetrabutylammonium fluoride at 0 °C for 1 h. The reaction mixture was extracted with EtOAc several times. The combined organic phase was washed with H_2O and then brine, dried ($MgSO_4$), and concentrated in vacuo to give the crude product, which upon purification by column chromatography on silica gel (elution with ether) gave **7** (38 mg, 76%): oil; IR (neat) 3296, 2872, 1758 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.35 (m, 5 H), 5.85 (ddd, 1 H, J = 17, 10, 7 Hz), 5.48 (ddd, 1 H, J = 17, 2, 2 Hz), 5.46 (br s, 1 H), 5.33 (ddd, 1 H, J = 10, 2, 2 Hz), 5.08 (dddd, 1 H, J = 8, 7, 2, 2 Hz), 4.51 (s, 2 H), 4.02 (ddd, 1 H, J = 8, 8, 5 Hz), 3.42 (m, 2 H). Anal. Calcd for $C_{13}H_{15}O_3N$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.26; H, 6.51; N, 6.01.

(4*R,5*R**)-4-(Benzyloxymethyl)-5-vinyl-2-oxazolidinone (8).** (2*R**,3*S**)-*N*-(*tert*-Butyldimethylsilyloxycarbonyl)-2-amino-1-(benzyloxy)-3-(methylsulfonyloxy)-4-pentene, prepared from **4**[13,14] (99 mg, 0.26 mmol) according to procedure I, was treated with 520 μL (1 M solution

in THF, 0.52 mmol) of tetrabutylammonium fluoride in THF (1 mL) at 0 °C for 1 h. The reaction mixture was extracted with EtOAc several times. The combined organic phase was washed with H_2O and then brine, dried ($MgSO_4$), and concentrated in vacuo to give the crude product, which upon purification by column chromatography on silica gel (elution with ether) gave **8** (32 mg, 53% in two steps): oil; IR (neat) 3288, 2872, 1758 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.36 (s, 5 H), 6.10 (br s, 1 H), 5.91 (ddd, 1 H, J = 17, 11, 7 Hz), 5.36 (ddd, 1 H, J = 17, 2, 2 Hz), 5.28 (ddd, 1 H, J = 11, 2, 2 Hz), 4.68 (dddd, 1 H, J = 7, 7, 2, 2 Hz), 4.55 (s, 2 H), 3.68 (dddd, 1 H, J = 7, 7, 7, 2 Hz), 3.49 (m, 2 H). Anal. Calcd for $C_{13}H_{15}O_3N$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.94; H, 6.41; N, 5.87.

General Procedure for AgF-Assisted Cyclic Carbamate Formation (Method A). 4-(Methoxycarbonyl)-6-vinyltetrahydro-1,3-oxazin-2-one (19a and 19b). *N*-(*tert*-Butyldimethylsilyloxycarbonyl)-2-amino-6-chloro-4-hexenoic acid methyl ester (**13b**) was prepared from **13a** (150 mg, 0.54 mmol) according to procedure 1. To a suspension of AgF (82 mg, 0.65 mmol) in CH_3CN (1 mL) at room temperature was added a solution of **13b** in CH_3CN (1 mL). The reaction mixture was stirred at room temperature for 18 h and filtered. The filtrate was concentrated in vacuo to give the crude product, which upon purification by column chromatography on silica gel (elution with 10% MeOH in $CHCl_3$) gave a mixture of **19a** (1,3-syn) and **19b** (1,3-anti) (63 mg, 63%; **19a/19b** = 3/2): oil; IR (neat) 3296, 2960, 1740, 1716 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 6.2–6.7 (m, 1 H), 5.6–6.0 (m, 1 H), 5.2–5.5 (m, 2 H), 4.6–4.9 (m, 1 H), 4.0–4.3 (m, 1 H), 3.80 (s, 3 H), 1.6–2.6 (m, 2 H); MS (EI method), m/z 185 $(M)^+$, 126. Anal. Calcd for $C_8H_{11}O_4N$: C, 51.89; H, 5.99; N, 7.56. Found: C, 51.89; H, 6.04; N, 7.59. The diastereomeric ratio was determined by ^1H NMR analysis [δ 6.58 (br s)/6.26 (br s) = 3/2], since this mixture could not be separated by SiO_2 column chromatography. The stereochemistries of these compounds were elucidated by their 500-MHz ^1H NMR data: signals of C-5 methylene protons of the major isomer appeared at δ 2.43 (5βH, $J_{4-5\beta}$ = 5 Hz, $J_{5\beta-6}$ = 3 Hz) and 1.86 (5αH, $J_{4-5\alpha}$ = $J_{5\alpha-6}$ = 11 Hz) indicating this to be syn-**19a**, while signals of the minor isomer appeared at δ 2.18 (m, 2 H) (see Table II).

General Procedure for AgF/Pd(II)-Assisted Cyclic Carbamate Formation (Method B). 4-(Methoxycarbonyl)-6-vinyltetrahydro-1,3-oxazin-2-one (19a and 19b). To a suspension of AgF (130 mg, 1.02 mmol), PPh_3 (30 mg, 0.11 mmol), and allylpalladium(II) chloride dimer (10 mg, 0.03 mmol) in CH_3CN (1 mL) at room temperature was added a solution of **13b** (181 mg, 0.51 mmol) in CH_3CN (1 mL), prepared from **13a** according to procedure 1. The reaction mixture was stirred at room temperature for 15 h and filtered. The filtrate was concentrated in vacuo to give the crude product, which upon purification by column chromatography on silica gel (elution with 10% MeOH in chloroform) gave a mixture of **19a** and **19b** (68 mg, 72%; **19a/19b** = 1/1).

4-(Benzyloxycarbonyl)-6-vinyltetrahydro-1,3-oxazin-2-one (20a and 20b). Treatment of **14b** (105 mg, 0.26 mmol) with AgF (51 mg, 0.39 mmol) in CH_3CN (2 mL) according to method A gave a mixture of **20a** (1,3-syn) and **20b** (1,3-anti) (36 mg, 53%; **20a/20b** = 4/3): oil; IR (neat) 3280, 1760, 1716 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.36 (s, 5 H), 5.6–7.1 (m, 2 H), 5.2–5.5 (m, 2 H), 5.20 (s, 2 H), 4.8 (m, 1 H), 4.20 (m, 1 H), 1.6–2.6 (m, 2 H). Anal. Calcd for $C_{14}H_{15}O_4N$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.36; H, 5.80; N, 5.33. The ratio of this mixture was determined by ^1H NMR analysis: **20a** [δ 5.47 (ddd)]/**20b** [5.43 (ddd)] = 4/3.

These compounds were also prepared by using method B: Treatment of **14b** (145 mg, 0.34 mmol) with AgF (85 mg, 0.67 mmol), PPh_3 (21 mg, 0.08 mmol), and allylpalladium chloride dimer (7 mg, 0.02 mmol) gave a mixture of **20a** and **20b** (47 mg, 53%; **20a/20b** = 1/1).

4-(Benzyloxymethyl)-6-vinyltetrahydro-1,3-oxazin-2-one (21a and 21b). Treatment of **15b** (86 mg, 0.22 mmol) with AgF (44 mg, 0.35 mmol) in CH_3CN (2 mL) according to method A gave a mixture of **21a** (1,3-syn) and **21b** (1,3-anti) (62 mg, 63%; **21a/21b** = 4/1). The diastereomeric ratio was determined by HPLC analysis [Develosil ODS-5, elution with MeOH/H_2O = 1/1 (2 mL/min), detected by UV monitor (240 nm). Retention time: **21a**, 42.2 min; **21b**, 38.7 min]. Major isomer **21a** was separated from its diastereomer **21b** by recrystallization. **21a**: colorless leaflets (hexane); mp 77–78 °C; IR (neat) 3256, 2920, 2872, 1706 cm^{-1}; ^1H NMR ($CDCl_3$, 500 Hz) δ 7.36 (s, 5 H), 5.90 (ddd, 1 H, J = 17, 10, 6 Hz), 5.62 (br s, 1 H), 5.19 (ddd, 1 H, J = 17, 2, 2 Hz), 5.16 (ddd, 1 H, J = 10, 2, 2 Hz), 4.75 (ddddd, 1 H, J = 12, 6, 3, 2, 2 Hz), 4.55 (s, 2 H), 3.80 (dddd, 1 H, J = 12, 9, 5, 4 Hz), 3.57 (dd, 1 H, J = 9, 4 Hz), 3.29 (dd, 1 H, J = 9, 9 Hz), 2.01 (dddd, 1 H, J = 14, 5, 3, 2 Hz), 1.48 (ddd, 1 H, J = 14, 12, 12 Hz). Anal. Calcd for $C_{14}H_{17}O_3N$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.83; H, 6.93; N, 5.68.

Pure 1,3-anti isomer **21b** was obtained by HPLC (Develosil ODS-5, 50% MeOH in H_2O) in semipreparative scale. **21b**: oil; IR (neat) 3300, 2990, 2960, 1712 cm^{-1}; ^1H NMR ($CDCl_3$, 500 Hz) δ 7.34 (s, 5 H), 5.88 (ddd, 1 H, J = 17, 12, 5 Hz), 5.50 (br s, 1 H), 5.36 (ddd, 1 H, J = 17, 2, 2 Hz), 5.29 (ddd, 1 H, J = 12, 2, 2 Hz), 4.89 (ddddd, 1 H, J = 10, 5, 2, 2, 2 Hz), 4.54 (s, 2 H), 3.73 (m, 1 H), 3.52 (dd, 1 H, J = 9, 5 Hz), 3.36 (dd, 1 H, J = 9, 9 Hz), 1.87 (dd, 2 H, J = 6, 5 Hz).

Preparation of these compounds was also carried out by using method B: Treatment of **15b** (141 mg, 0.36 mmol) with AgF (92 mg, 0.72 mmol), PPh_3 (21 mg, 0.08 mmol), and allylpalladium chloride dimer (7 mg, 0.02 mmol) gave a mixture of **21a** and **21b** (62 mg, 70%; **21a/21b** = 1/1).

4-Isopropyl-6-vinyltetrahydro-1,3-oxazin-2-one (22a and 22b). Treatment of **16b** (120 mg, 0.37 mmol) with AgF (96 mg, 0.75 mmol) in CH_3CN (3 mL) according to method A gave a mixture of **22a** (1,3-syn) and **22b** (1,3-anti) (40 mg, 63%; **22a/22b** = 4/1). The diastereomeric ratio was determined by HPLC analysis [Develosil ODS-5, elution with MeOH/H_2O = 60/40 (1 mL/min), detected by UV monitor (220 nm). Retention time: **22a**, 31.0 min; **22b**, 25.0 min]. Major isomer **22a** was separated from its diastereomer **22b** by recrystallization. **22a**: colorless prisms (ether); mp 142–143 °C; IR (neat) 3252, 3128, 2972, 1700 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.90 (ddd, 1 H, J = 17, 10, 6 Hz), 5.55 (br s, 1 H), 5.36 (ddd, 1 H, J = 10, 2, 2 Hz), 4.68 (ddddd, 1 H, J = 12, 6, 3, 2, 2 Hz), 3.32 (ddd, 1 H, J = 11, 6, 5 Hz), 1.96 (dddd, 1 H, J = 13, 5, 3, 2 Hz), 1.60 (m, 1 H), 1.44 (ddd, 1 H, J = 13, 12, 11 Hz), 0.97 (d, 3 H, J = 7 Hz), 0.95 (d, 3 H, J = 7 Hz). Anal. Calcd for $C_9H_{15}O_2N$: C, 63.88; H, 8.28; N, 8.93. Found: C, 63.87; H, 8.30; N, 8.99.

These compounds were also prepared by using method B: Treatment of **16b** (272 mg, 0.64 mmol) with AgF (163 mg, 1.28 mmol), PPh_3 (67 mg, 0.25 mmol), and allylpalladium chloride dimer (23 mg, 0.06 mmol) gave a mixture of **22a** and **22b** (70 mg, 65%; **22a/22b** = 3/2).

4-Benzyl-6-vinyltetrahydro-1,3-oxazin-2-one (23a and 23b). Treatment of **17b** (296 mg, 0.72 mmol) with AgF (183 mg, 1.44 mmol) in CH_3CN (4 mL) according to method A gave a mixture of **23a** (1,3-syn) and **23b** (1,3-anti) (102 mg, 65%; **23a/23b** = 4/1). The diastereomeric ratio was determined by HPLC analysis [Develosil ODS-5, elution with MeOH/H_2O = 60/40 (1 mL/min), detected by UV monitor (220 nm). Retention time: **23a**, 24.0 min; **23b**, 22.0 min]. Major isomer **23a** was separated from its diastereomer by recrystallization. **23a**: colorless needles (ether/hexane); mp 102–105 °C; IR (neat) 3264, 2932, 1712, 1600, 1496 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.30 (m, 5 H), 5.96 (br s, 1 H), 5.80 (ddd, 1 H, J = 17, 10, 5 Hz), 5.40 (ddd, 1 H, J = 17, 1, 1 Hz), 5.26 (ddd, 1 H, J = 10, 1, 1 Hz), 4.72 (ddddd, 1 H, J = 11, 6, 1, 1, 1 Hz), 3.78 (dddd, 1 H, J = 11, 7, 7, 4 Hz), 2.83 (d, 2 H, J = 7 Hz), 2.06 (ddddd, 1 H, J = 14, 4, 4, 1, 1 Hz), 1.60 (ddd, 1 H, J = 14, 11, 11 Hz). Anal. Calcd for $C_{13}H_{15}O_2N$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.62; H, 6.95; N, 6.46. Minor isomer **23b** was separated by HPLC (Develosil ODS-5, elution with 60% MeOH in H_2O). **23b**: colorless prisms; mp 125–131 °C (ether/hexane); IR (neat) 3256, 2932, 1706, 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.1–7.4 (m, 5 H), 5.87 (ddd, 1 H, J = 18, 10, 4 Hz), 5.2–5.4 (m, 2 H), 5.20 (d, 1 H, J = 6 Hz), 4.92 (m, 1 H), 3.65 (m, 1 H), 2.88 (dd, 1 H, J = 14, 6 Hz), 2.70 (dd, 1 H, J = 14, 8 Hz), 1.92 (m, 2 H).

Preparation of these compounds was also carried out by using method B: Treatment of **17b** (387 mg, 0.94 mmol) with AgF (239 mg, 1.88 mmol), PPh_3 (99 mg, 0.38 mmol), and allylpalladium chloride dimer (34 mg, 0.09 mmol) gave a mixture of **23a** and **23b** (101 mg, 50%; **23a/23b** = 3/2).

Preparation of (2*R*)-*N*-(*tert*-Butoxycarbonyl)-2-amino-1-(benzyloxy)-5-chloro-3-pentene (24a). Ozone was passed through the solution of (2*R*)-*N*-*t*-Boc-2-amino-1-(benzyloxy)-3-butene (5.0 g, 18.1 mmol) in MeOH (200 mL) at −78 °C until the solution became slightly blue. Excess ozone was displaced by passing a stream of O_2 (solution became colorless), and $(CH_3)_2S$ (10 mL) was added at −78 °C with stirring. The reaction mixture was allowed to stand at room temperature for 18 h and concentrated in vacuo to give an oily residue, which upon purification by column chromatography on silica gel (elution with 30% ether in hexane) gave an aldehyde (3.8 g, 75%): oil; IR (neat) 3360, 3036, 2984, 2936, 2872, 2736, 1740, 1714, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 9.48 (s, 1 H), 7.22 (s, 5 H), 5.49 (d, 1 H, J = 8 Hz), 4.42 (s, 2 H), 4.25 (m, 1 H), 3.88 (dd, 1 H, J = 10, 4 Hz), 3.60 (dd, 1 H, J = 10, 5 Hz), 1.44 (s, 9 H).

To a stirred solution of the resulting aldehyde (500 mg, 1.8 mmol) in dry benzene (10 mL) was added (formylmethylene)triphenylphosphorane (Ph_3P=CHCHO, 817 mg, 2.7 mmol) at 40 °C. After being stirred at 40 °C for 2 h, the reaction mixture was directly subjected to column chromatography on silica gel (elution with 30% ether in hexane) to give α,β-unsaturated aldehyde (310 mg, 57%): oil; IR (neat) 3350, 2984, 2932, 1720, 1696, 1646, 1516 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 9.58 (dd, 1 H, J = 8, 2 Hz), 7.34 (s, 5 H), 6.0–7.3 (m, 2 H), 5.01 (d, 1 H, J = 8 Hz), 4.2–4.8 (m, 1 H), 4.55 (s, 2 H), 3.60 (m, 2 H), 1.48 (s, 9 H).

Lithium tri-*tert*-butoxyaluminohydride [$LiAlH(O\text{-}t\text{-}Bu)_3$, 300 mg, 1.2 mmol] was dissolved in dry THF (10 mL) and then the solution was cooled to −78 °C. To this solution was added a solution of the resulting α,β-unsaturated aldehyde (310 mg, 1.0 mmol) in dry THF (3 mL). The reaction mixture was warmed slowly to −30 °C, stirred at the same temperature for 2 h, and quenched with MeOH (1 mL). To the reaction mixture was added successively ether (50 mL), H_2O (3 mL), and $MgSO_4$ (20 g). The suspension was stirred at room temperature for 30 min and filtered. The filtrate was concentrated in vacuo to give an oily residue, which upon purification by a column chromatography on silica gel (elution with 75% ether in hexane) gave an allyl alcohol (208 mg, 67%): oil; IR (neat) 3348, 2984, 2936, 2868, 1698, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.33 (s, 5 H), 5.77 (m, 2 H), 4.95 (d, 1 H, J = 8 Hz), 4.53 (s, 2 H), 4.34 (m, 1 H), 4.13 (m, 2 H), 3.53 (m, 2 H), 2.00 (m, 1 H), 1.48 (s, 9 H).

To a stirred solution of the resulting allyl alcohol (289 mg, 0.94 mmol) in dry CH_2Cl_2 (20 mL) were added portionwise triphenylphosphine (492 mg, 1.87 mmol) and *N*-chlorosuccinimide (188 mg, 1.41 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and concentrated in vacuo to give the crude product, which upon purification by a column chromatography on silica gel (elution with 20% ether in hexane) gave **24a** (260 mg, 85%): oil; IR (neat) 3370, 2984, 2936, 2868, 1712, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.35 (s, 5 H), 5.83 (m, 2 H), 4.92 (d, 1 H, J = 8 Hz), 4.54 (s, 2 H), 4.32 (m, 1 H), 4.08 (m, 2 H), 3.55 (m, 2 H), 1.48 (s, 9 H). Anal. Calcd for $C_{17}H_{24}O_3NCl$: C, 62.67; H, 7.42; N, 4.30. Found: C, 62.56; H, 7.54; N, 4.24.

4-(Benzyloxymethyl)-5-vinyl-2-oxazolidinone (8 and 7). *N*-(*tert*-Butyldimethylsilyloxycarbonyl)-2-amino-1-(benzyloxy)-5-chloro-3-pentene (**24b**; 155 mg, 0.37 mmol), prepared from **24a** according to procedure I and treated with AgF (70 mg, 0.55 mmol) in CH_3CN (2 mL) according to method A, gave a mixture of **8** (1,3-syn) and **7** (1,3-anti) (47 mg, 55%; **8**/**7** = 3/1). Cyclic carbamates, thus obtained, showed spectroscopic data completely identical with those of **8** and **7**, prepared from **4** and **3**, respectively. These compounds were also prepared by using method B: Treatment of **24b** (231 mg, 0.54 mmol) with AgF (138 mg, 1.10 mmol), PPh_3 (29 mg, 0.11 mmol), and allylpalladium chloride dimer (10 mg, 0.03 mmol) gave a mixture of **8** and **7** (91 mg, 72%; **8**/**7** = 8/1).

Preparation of (4*S*)-*N*-(*tert*-Butoxycarbonyl)-4-amino-6-methyl-2-hepten-1-ol. To a solution of *N*-*t*-Boc-L-leucinal[22] [(3.0 g, 14.0 mmol; $[\alpha]^{30}_D$ −26.0° (*c* 1.0, MeOH)] in benzene (50 mL) at 40 °C was added [(ethoxycarbonyl)methylene]triphenylphosphorane ($Ph_3P{=}CHCO_2Et$; 7.3 g, 21 mmol). The reaction mixture was stirred at 40 °C for 30 min and concentrated under reduced pressure to give an oily residue, which upon purification by column chromatography on silica gel (elution with 50% ether in hexane) gave (4*S*)-*N*-*t*-Boc-4-amino-6-methyl-2-heptenoic acid ethyl ester (3.8 g) as an oil. The resulting α,β-unsaturated ester was reduced immediately to avoid racemization. To a solution of thus obtained ester (3.8 g, 13.3 mmol) in CH_2Cl_2 (100 mL) at −78 °C was added 1.64 mL (13.3 mmol) of boron trifluoride etherate.[28] The resulting mixture was stirred at −78 °C for 15 min. To this solution was added 40.2 mL (40.2 mmol) of diisobutylaluminum hydride ($i\text{-}Bu_2AlH$; 1 M solution in hexane). The reaction mixture was stirred at −78 °C for an additional 2 h, quenched by the addition of 6.9 mL (121.0 mmol) of acetic acid and 5 mL of H_2O, diluted with 100 mL of ether, and dried ($MgSO_4$). The resulting suspension was filtered. The filtrate was concentrated in vacuo to give an oily residue, which upon purification by column chromatography on silica gel (elution with 67% ether in hexane) gave the title compound (2.8 g, 84% from *N*-*t*-Boc-leucinal): colorless prisms; mp 82–83 °C (hexane); $[\alpha]^{30}_D$ −22.0° (*c* 1.0, MeOH); IR (neat) 3336, 2964, 2940, 2875, 1694, 1534 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.65 (m, 2 H), 4.80 (d, 1 H, J = 8 Hz), 4.08 (m, 2 H), 3.60 (m, 1 H), 3.36 (m, 1 H), 1.45 (s, 9 H), 1.1–1.8 (m, 3 H), 0.93 (d, 6 H, J = 7 Hz); MS (EI method), m/z 244 $(M + H)^+$, 188, 186, 170. Anal. Calcd for $C_{13}H_{25}O_3N$: C, 64.17; H, 10.35; N, 5.76. Found: C, 64.07; H, 10.35; N, 5.73.

(4*S*)-*N*-(*tert*-Butoxycarbonyl)-4-amino-1-chloro-6-methyl-2-heptene (25a). To a solution of (4*S*)-*N*-(*tert*-butoxycarbonyl)-4-amino-6-methyl-2-hepten-1-ol (2.3 g, 9.3 mmol) and triphenylphosphine (4.9 g, 18.6 mmol) in CH_2Cl_2 (50 mL) at 0 °C was added *N*-chlorosuccinimide (1.9 g, 14.0 mmol). The reaction mixture was stirred at 0 °C for 1 h and concentrated under reduced pressure to give an oily residue, which upon purification by column chromatography on silica gel (elution with 30% ether in hexane) gave **25a**: oil; $[\alpha]^{28}_D$ −27.7° (*c* 1.0, MeOH): IR (neat) 3348, 2964, 2940, 2876, 1698, 1522 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.65 (m, 2 H), 4.59 (d, 1 H, J = 8 Hz), 4.15 (m, 1 H), 4.00 (m, 2 H), 1.44 (s, 9 H), 1.1–1.8 (m, 3 H), 0.91 (d, 6 H, J = 7 Hz); MS (EI method), m/z 204 $(M - t\text{-}Bu)^+$, 170, 148. Anal. Calcd for $C_{13}H_{24}O_2NCl$: C, 59.64; H, 9.24; N, 5.35. Found: C, 59.68; H, 9.27; N, 5.53.

4-Isobutyl-5-vinyl-2-oxazolidinone [(4*S*,5*S*)-29a and (4*S*,5*R*)-29b]. *N*-(*tert*-Butyldimethylsilyloxycarbonyl)-4-amino-1-chloro-6-methyl-2-heptene (**25b**; 700 mg, 2.0 mmol), prepared from **25a** (530 mg, 2.0 mmol) according to procedure I and treated with AgF (381 mg, 0.30 mmol) in CH_3CN (6 mL) according to method A, gave a mixture of diastereomers **29a** and **29b**, which were separated by medium-pressure column chromatography on silica gel (elution with 50% ether in hexane). Less polar 1,2-syn cyclic carbamates **29a**: (230 mg, 67%): oil; $[\alpha]^{34}_D$ −76.4° (*c* 1.0, MeOH); IR (neat) 3280, 2964, 2936, 2876, 1760 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 6.67 (br s, 1 H), 5.88 (ddd, 1 H, J = 17, 10, 7 Hz), 5.37 (ddd, 1 H, J = 17, 2, 1 Hz), 5.28 (ddd, 1 H, J = 10, 2, 1 Hz), 4.50 (dd, 1 H, J = 7, 7 Hz), 3.58 (dtd, 1 H, J = 7, 6, 1 Hz), 1.2–1.9 (m, 3 H), 0.92 (d, 3 H, J = 7 Hz), 0.91 (d, 3 H, J = 7 Hz); MS (EI method), m/z 169 $(M)^+$, 141, 125. Anal. Calcd for $C_9H_{15}O_2N$: C, 63.88; H, 8.87; N, 8.28. Found: C, 63.98; H, 9.07; N, 8.16. More polar 1,2-anti isomer **29b**: (47 mg, 14%); colorless needles; mp 55–57 °C (hexane); $[\alpha]^{34}_D$ −27.5° (*c* 1.0, MeOH); IR (neat) 3272, 2964, 1754 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 5.90 (br s, 1 H), 5.87 (ddd, 1 H, J = 17, 10, 7 Hz), 5.40 (ddd, 1 H, J = 17, 2, 1 Hz), 5.36 (ddd, 1 H, J = 10, 2, 1 Hz), 5.01 (dd, 1 H, J = 7, 7 Hz), 3.94 (ddd, 1 H, J = 10, 7, 5 Hz), 1.2–1.8 (m, 3 H), 0.95 (d, 3 H, J = 7 Hz), 0.88 (d, 3 H, J = 7 Hz). Anal. Calcd for $C_9H_{15}O_2N$: C, 63.88; H, 8.87; N, 8.28. Found: C, 63.97; H, 8.98; N, 8.38.

AgF/Pd(II)-assisted cyclic carbamate formation of the silyl carbamate **25b** was carried out according to method B: Treatment of **25b** (500 mg, 1.34 mmol) with AgF (340 mg, 2.68 mmol), PPh_3 (30 mg, 0.11 mmol), and allylpalladium chloride dimer (10 mg, 0.03 mmol) gave a mixture of **29a** and **29b** (171 mg, 76%; **29a**/**29b** = 15/1).

Preparation of (4*S*)-*N*-(*tert*-Butoxycarbonyl)-4-amino-5-phenyl-2-penten-1-ol. To a solution of *N*-*t*-Boc-L-phenylalanal[22] [2.0 g, 8.0 mmol; $[\alpha]^{33}_D$ −26.7° (*c* 1.0, MeOH)] in benzene (30 mL) at 30 °C was added $Ph_3P{=}CHCO_2Et$ (4.0 g, 12.0 mmol). The reaction mixture was stirred at 30 °C for 30 min and concentrated in vacuo to give an oily residue, which upon purification by column chromatography on silica gel (elution with 50% ether in hexane) gave α,β-unsaturated ester (2.5 g): oil. The resulting α,β-unsaturated ester was reduced immediately, to avoid racemization.

To a solution of (4*S*)-*N*-*t*-Boc-4-amino-5-phenyl-2-pentenoic acid ethyl ester (4.1 g, 12.8 mmol) in CH_2Cl_2 (60 mL) at −78 °C was added boron trifluoride etherate (1.70 mL, 13.8 mmol) and the resulting mixture was stirred at −78 °C for 15 min. To this solution was added 38.4 mL (38.4 mmol) of $i\text{-}Bu_2AlH$ (1 M solution in hexane). The reaction mixture was stirred at −78 °C for an additional 2 h, quenched by the successive addition of acetic acid (7.0 mL, 122.8 mmol) and H_2O (5 mL), diluted with ether (100 mL), and dried ($MgSO_4$). The resulting suspension was filtered and the filtrate was concentrated in vacuo to give the crude product, which upon purification by column chromatography on silica gel (elution with 75% ether in hexane) gave the title compound (2.79 g, 78%): colorless needles; mp 96–97 °C (ether/hexane); $[\alpha]^{29}_D$ −4.8° (*c* 1.0, MeOH); IR (neat) 3360, 2970, 2930, 1696, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.20 (m, 5 H), 5.67 (m, 2 H), 4.24 (m, 2 H), 4.08 (br s, 2 H), 2.82 (d, 2 H, J = 7 Hz), 1.87 (br s, 1 H), 1.40 (s, 9 H); MS (EI method), m/z 206, 186, 130. Anal. Calcd for $C_{16}H_{23}O_3N$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.06; H, 8.33; N, 5.03.

(4*S*)-*N*-(*tert*-Butoxycarbonyl)-4-amino-1-chloro-5-phenyl-2-pentane (26a). To a solution of (4*S*)-*N*-(*tert*-butoxycarbonyl)-4-amino-5-phenyl-2-penten-1-ol (1.21 g, 4.4 mmol) and triphenylphosphine (2.3 g, 8.7 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added *N*-chlorosuccinimide 882 mg (6.6 mmol). The reaction mixture was stirred at 0 °C for 1 h and concentrated in vacuo to give an oily residue, which upon purification by column chromatography on silica gel (elution with 30% ether in hexane) gave **26a** (1.20 g, 93%): colorless prisms; mp 68–69 °C (hexane); $[\alpha]^{33}_D$ −6.0° (*c* 1.0, MeOH); IR (neat) 3376, 2988, 1684, 1522 cm^{-1}; ^1H NMR ($CDCl_3$, 100 Mz) δ 7.25 (m, 5 H), 5.70 (m, 2 H), 4.24 (br s, 2 H), 4.01 (m, 2 H), 2.84 (m, 2 H), 1.43 (s, 9 H); MS (EI method), m/z 204, 178, 160, 148. Anal. Calcd for $C_{16}H_{22}O_2NCl$: C, 64.97; H, 7.50; N, 4.74. Found: C, 64.95; H, 7.50; N, 4.72.

4-Benzyl-5-vinyl-2-oxazolidinone [(4*S*,5*S*)-30a and (4*S*,5*R*)-30b]. *N*-(*tert*-Butyldimethylsilyloxycarbonyl)-4-amino-1-chloro-5-phenyl-2-pentene (**26b**; 1.07 g, 2.57 mmol), prepared from **26a** (760 mg, 2.57 mmol) according to procedure I and treated with AgF (653 mg, 5.14 mmol), Ph_3P (137 mg, 0.52 mmol), and allylpalladium chloride dimer (47 mg, 0.13 mmol) in CH_3CN (6 mL) according to method B, gave a mixture of **30a** and **30b** (365 mg, 70%; **30a**/**30b** = 10/1). Recrystallization of this mixture from ether and hexane gave pure **30a**: colorless needles; mp 71–72 °C; $[\alpha]^{34}_D$ −53.1° (*c* 1.0, MeOH); IR (neat) 3276, 2944, 1742, 1498 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.27 (m, 5 H), 6.62 (br s, 1 H), 5.73 (ddd, 1 H, J = 16, 10, 7 Hz), 5.20 (dd, 1 H, J =

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16, 1 Hz), 5.16 (dd, 1 H, J = 10, 1 Hz), 4.64 (dd, 1 H, J = 6, 6 Hz), 3.77 (dt, 1 H, J = 7, 7 Hz), 2.86 (d, 2 H, J = 7 Hz); MS (EI method), m/z 203 $(M)^+$, 160, 128, 112. Anal. Calcd for $C_{12}H_{13}O_2N$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.96; H, 6.32; N, 6.92.

Preparation of (4*S*)-N^8-(Benzyloxycarbonyl)-N^4-(*tert*-butoxycarbonyl)-4,8-diamino-1-chloro-2-octene (27a). To a solution of N^{ϵ}-Z-N^{α}-*t*-Boc-L-lysinal[15] (2.2 g, 6.0 mmol) in benzene (30 mL) at room temperature was added $Ph_3P{=}CHCO_2Me$ (3.0 g, 9.0 mmol). The reaction mixture was stirred at room temperature for 16 h and concentrated in vacuo to give an oily residue, which upon purification by column chromatography on silica gel (elution with 50% ether in hexane) gave α,β-unsaturated ester (2.13 g, 84%): oil. To a solution of α,β-unsaturated ester (536 mg, 1.28 mmol) in CH_2Cl_2 (5 mL) at −78 °C was added boron trifluoride etherate (346 μL, 2.81 mmol) and the resulting mixture was stirred at −78 °C for 15 min. To this solution was added 3.83 mL (3.83 mmol) of *i*-Bu_2AlH (1 M solution in hexane). The reaction mixture was stirred at −78 °C for an additional 1 h, quenched with acetic acid (700 μL, 122.8 mmol), and warmed to room temperature. After an addition of 10% tartaric acid (10 mL), the reaction mixture was extracted with CH_2Cl_2 several times. The combined organic phase was washed with aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo to give the crude product, which upon purification by column chromatography on silica gel (elution with 75% ether in hexane) gave (4*S*)-N^8-(benzyloxycarbonyl)-N^4-(*tert*-butoxycarbonyl)-4,8-diamino-2-octene-1-ol (424 mg, 85%): oil; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.34 (s, 5 H), 5.65 (m, 2 H), 5.08 (s, 2 H), 4.10 (m, 2 H), 3.16 (m, 2 H), 1.44 (s, 9 H).

To a solution of the allyl alcohol (423 mg, 1.08 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added *N*-chlorosuccinimide (187 mg, 1.4 mmol). The reaction mixture was stirred at 0 °C for 1 h and concentrated in vacuo to give an oily residue, which upon purification by column chromatography on silica gel (elution with 30% ether in hexane) gave **27a** (443 mg, 100%): oil; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.32 (s, 5 H), 5.70 (m, 2 H), 5.08 (s, 2 H), 4.76 (br s, 1 H), 4.48 (br d, 1 H), 4.10 (br s, 1 H), 4.04 (m, 2 H), 3.20 (m, 2 H), 1.40 (s, 9 H).

4-[[(*N*-Benzyloxycarbonyl)amino]butyl]-5-vinyl-2-oxazolidinone [(4*S*,5*S*)-31a and (4*S*,5*R*)-31b]. Treatment of *N*-*tert*-butyldimethylsilyloxycarbonyl **27b**, prepared from **27a** (774 mg, 1.89 mmol) according to procedure 1, with AgF (479 mg, 3.77 mmol), Ph_3P (99 mg, 0.38 mmol), and allylpalladium chloride dimer (34 mg, 0.094 mmol) in CH_3CN (4 mL) and CH_2Cl_2 (2 mL) according to method B gave a mixture of **31a** and **31b** (322 mg, 54%; **31a**/**31b** = 40/1). These products were separated by medium-pressure chromatography (elution with ethyl acetate/benzene = 1/1). **31a**: oil; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.35 (m, 5 H), 6.35 (br s, 1 H), 5.86 (ddd, 1 H, J = 6, 10, 17 Hz), 5.18–5.45 (m, 2 H), 5.10 (s, 2 H), 4.98 (br s, 1 H), 4.52 (dd, 1 H, J = 6, 6 Hz), 3.50 (ddd, 1 H, J = 6, 6, 6 Hz), 3.20 (m, 2 H), 1.30–1.70 (6 H, m). **31b**: oil; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.35 (m, 5 H), 5.90 (br s, 1 H), 5.86 (ddd, 1 H, J = 7, 10, 17 Hz), 5.18–5.45 (m, 2 H), 4.98 (br s, 1 H), 4.52 (dd, 1 H, J = 6, 6 Hz), 3.83 (ddd, 1 H, J = 7, 8, 8 Hz), 3.20 (m, 2 H), 1.20–1.70 (m, 6 H).

(3*S*,4*S*)-*N*-(*tert*-Butoxycarbonyl)-4-amino-1,3-dihydroxy-6-methylheptane (35a). To a solution of **29a** (59.0 mg, 0.35 mmol) in THF (3 mL) at room temperature was added 9-borabicyclo[3.3.1]nonane (9-BBN; 2.1 mL, 0.5 M solution in hexane, 1.05 mmol). The reaction mixture was stirred for 20 h. To the mixture were added, successively, EtOH (640 μL), 6 N NaOH (215 μL), and 30% H_2O_2 (426 μL). The mixture was heated at 50 °C for 1 h, cooled to room temperature, and extracted with EtOAc several times. The combined organic phase was washed with H_2O and brine, dried ($MgSO_4$), and concentrated in vacuo to give crude **34a**, which was subjected to the subsequent reaction without purification. The crude **34a** was dissolved in a mixture of EtOH (30 mL) and saturated aqueous barium hydroxide (6 mL). The mixture was refluxed with stirring for 15 h and filtered. Ethanol in the filtrate was removed under reduced pressure. The aqueous solution was diluted with 50 mL of H_2O and subjected to a column of Dowex-50W×4 ion-exchange resin (elution with 28% NH_3). The eluent was concentrated in vacuo and the residue was dissolved in THF (5 mL). To this solution was added triethylamine (50 μL, 0.35 mmol) and di-*tert*-butyl dicarbonate (Boc_2O; 122 μL, 0.53 mmol). The reaction mixture was stirred for 20 h and concentrated in vacuo to give an oily residue, which upon column chromatography on silica gel (elution with 15% EtOAc in ether) gave protected amino diol **35a** (75 mg, 82%): oil; $[\alpha]^{29}_D$ −40.2° (*c* 1.0, MeOH); IR (neat) 3396, 2964, 2880, 1688, 1518 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 4.82 (d, 1 H, J = 9 Hz), 3.4–3.9 (m, 5 H), 3.24 (br s, 1 H), 1.2–1.8 (m, 3 H), 1.44 (s, 9 H), 0.90 (d, 6 H, J = 7 Hz); MS (EI method), m/z 262 $(M + H)^+$, 206, 186, 130. Anal. Calcd for $C_{13}H_{27}O_4N$: C, 59.74; H, 10.41; N, 5.36. Found: C, 59.74; H, 10.41; N, 5.38.

(3*S*,4*S*)-*N*-(*tert*-Butoxycarbonyl)-4-amino-1,3-dihydroxy-5-phenylpentane (35b). The synthesis of **35b** was carried out by the same procedure as above (**29a** → **35a**) starting from the cyclic carbamate **30a** (107.5 mg, 0.53 mmol) to give *N*-*t*-Boc-aminodiol **35b** (117.6 mg, 75%): colorless needles; mp 106–108 °C (ether/hexane); $[\alpha]^{29}_D$ −38.2° (*c* 1.0, MeOH); IR (neat) 3404, 2984, 2940, 1688, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.25 (s, 5 H), 5.02 (d, 1 H, J = 9 Hz), 3.80 (m, 5 H), 2.88 (d, 2 H, J = 7 Hz), 2.80 (m, 1 H), 1.5–2.1 (m, 2 H), 1.40 (s, 9 H); MS (EI method), m/z 222, 204, 164, 148. Anal. Calcd for $C_{16}H_{25}O_4N$: C, 65.06; H, 8.53; N, 4.74. Found: C, 65.07; H, 8.51; N, 4.80.

(3*S*,4*S*)-*N*-(*tert*-Butoxycarbonyl)-4-amino-3-hydroxy-6-methylheptanoic acid (*N*-*t*-Boc-statine) (36a). To a suspension of PtO_2 (55 mg, 0.24 mmol), which was reduced primarily with H_2 (1 atm) for 30 min, in H_2O (3 mL) was added a solution of **35a** (63 mg, 0.24 mmol) in dioxane (2 mL). Oxygen gas was passed through this mixture at 55 °C for 30 h. Filtration of the reaction mixture followed by addition of $NaHCO_3$ powder into the filtrate afforded a fairly basic solution (pH 8), which was washed with EtOAc, and the aqueous layer was adjusted to pH 3 with 10% HCl. The resulting solution was extracted with EtOAc several times. The combined organic phase was dried ($MgSO_4$) and evaporated in vacuo to give *N*-*t*-Boc-statine (**36a**; 40 mg, 60%): colorless needles; mp 118–120 °C (*i*-PrOH), $[\alpha]^{34}_D$ −38.4° (*c* 1.0, MeOH); IR (neat) 3350, 2968, 1716, 1700, 1514 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.20 (br s, 2 H), 4.97 (d, 1 H, J = 9 Hz), 4.02 (m, 1 H), 3.64 (m, 1 H), 2.54 (d, 2 H, J = 7 Hz), 1.2–1.9 (m, 5 H), 1.46 (s, 9 H), 0.93 (d, 6 H, J = 7 Hz); MS (EI method), m/z 202, 186, 130, which were in accord with those of an authentic sample.[8d]

(3*S*,4*S*)-*N*-(*tert*-Butoxycarbonyl)-4-amino-3-hydroxy-5-phenylpentanoic acid (*N*-*t*-Boc-AHPPA) (36b). The synthesis of **36b** was carried out by the same procedure as above (**35a** → **36a**) starting from **35b** (76.5 mg, 0.26 mmol) to give *N*-*t*-Boc-AHPPA (**36b**; 44.4 mg, 55%): colorless needles (*i*-PrOH); mp 151–152 °C; $[\alpha]^{30}_D$ −37.5° (*c* 1.0, MeOH); IR (neat) 3348, 2984, 2936, 1714, 1516 cm^{-1}; ^1H NMR ($CDCl_3/CD_3OD$ = 10/1, 100 MHz) δ 7.17 (s, 5 H), 3.90 (m, 1 H), 3.70 (m, 1 H), 2.79 (d, 2 H, J = 7 Hz), 2.36 (m, 2 H), 1.31 (s, 9 H); MS (EI method), m/z 253 $(M + H - t\text{-Bu})^+$, 236, 218, 162. Anal. Calcd for $C_{16}H_{23}O_5N$: C, 62.12; H, 7.49; N, 4.53. Found: C, 61.81; H, 7.43; N, 4.57. The synthetic *N*-*t*-Boc-AHPPA (**36b**) was identical in all respects with those of authentic sample.[8e]

Acknowledgment. We thank Professor Koji Nakanishi, Director of the Suntory Institute for Bioorganic Research, for his continued encouragement. We thank Dr. Glen Spears, Research Associate of this Institute, for reviewing the manuscript. This work was supported in part by a grant-in-aid from the Ministry of Education, Science and Culture, Japan.

Supplementary Material Available: Detailed experimental procedures and spectral data for compounds **1–4**, **13a–18a**, and **28a** (18 pages). Ordering information is given on any current masthead page.