Chemical Society, for their support of this work. We are also indebted to Professor W. C. Still for a copy of the MacroModel program.

Supplementary Material Available: Structural report for the organomercurial **23b**, including a description of data collection, atomic coordinates, isotropic thermal parameters, bond lengths, bond angles, and anisotropic thermal parameters, and 300-MHz ^{1}H NMR spectra of **5**, **6**, **8**, **17**, **19-21**, **25a**, and **25b** (20 pages). Ordering information is given on any current masthead page.

Syntheses and Reactions of Silyl Carbamates. 1. Chemoselective Transformation of Amino Protecting Groups via *tert*-Butyldimethylsilyl Carbamates

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The *N*-*tert*-butyldimethylsilyloxycarbonyl group (silyl carbamate) was synthesized from commonly used amino protecting groups such as *N*-*tert*-butoxycarbonyl (Boc) and *N*-benzyloxycarbonyl (Z) by treatment with *tert*-butyldimethylsilyl trifluoromethanesulfonate/2,6-lutidine and *tert*-butyldimethylsilane/$Pd(OAc)_2$, respectively. This novel species, upon activation with fluoride ion, reacts with a variety of electrophiles to give *N*-ester type compounds in high yield. For example, the conversion of *N*-*t*-Boc compounds into their corresponding *N*-Z compounds via a silyl carbamate was accomplished under these mild reaction conditions.

The *N*-trialkylsilyloxycarbonyl group (silyl carbamate) is a species which was first prepared by Breederveld in 1962 by means of insertion of carbon dioxide into an *N*-trialkylsilyl compound (eq 1).[1] This group can be viewed as a masked form of an *N*-carboxylate ion, an extremely unstable species observed during removal of urethane type amino protecting groups under strongly acidic conditions.[2] However, the silyloxycarbonyl species has received little attention from chemists in spite of its considerable synthetic potential. The only other example of the synthesis of a silyl carbamate reported to date is the introduction of this group into partial structures of drugs in order to improve their efficiencies; the preparation in this case involved condensation of trialkylsilanol with an isocyanate (eq 2).[3] No further reports concerning either its reactivity or synthetic potential have appeared since.

$$RNHSiR'_3 + CO_2 \rightarrow RNHCO_2SiR'_3 \quad (1)$$

$$RNCO + R'_3SiOH \rightarrow RNHCO_2SiR'_3 \quad (2)$$

We believed that an *N*-silyloxycarbonyl compound activated by fluoride ion would react with an electrophile to give the corresponding *N*-ester type compound. Our attention was focused on the synthesis of a silyl carbamate from commonly used urethane type amino protecting groups such as *N*-*tert*-butoxycarbonyl (*t*-Boc) and *N*-benzyloxycarbonyl (Z), both representative amino protecting groups used for amino acids, amino sugars, peptides, and alkaloids.[4] We detail below new methods for the synthesis of *tert*-butyldimethylsilyl carbamate from *N*-Z and *N*-*t*-Boc groups and its conversion into amines and various *N*-ester type compounds (eq 3) (i.e., *N*-*t*-Boc group into *N*-Z group via silyl carbamate).[5]

$$RNHCO_2R^1 \longrightarrow [RNHCO_2^-] \longrightarrow RNHCO_2SiR^2_3 \xrightarrow{R^3X} RNHCO_2R^3 \quad (3)$$
$$\downarrow$$
$$RNH_2$$

Results and Discussion

Synthesis of *tert*-Butyldimethylsilyl Carbamate from the *N*-*tert*-Butoxycarbonyl (*t*-Boc) Group. The *N*-*t*-Boc group is stable to a variety of chemical transformations, especially under basic conditions, due to its sterically bulky nature, but is easily removed under acidic conditions.[4] Recently, several groups have reported efficient methods for the deprotection of the *N*-*t*-Boc group by the use of trimethylsilyl perchlorate (Me_3SiClO_4),[6] trimethylsilyl iodide (Me_3SiI),[7] and trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf).[8] Since these methods were used only for removal of the *t*-Boc group under strongly acidic conditions, the putative *N*-$CO_2Si(CH_3)_3$ intermediate could not be detected (eq 4).

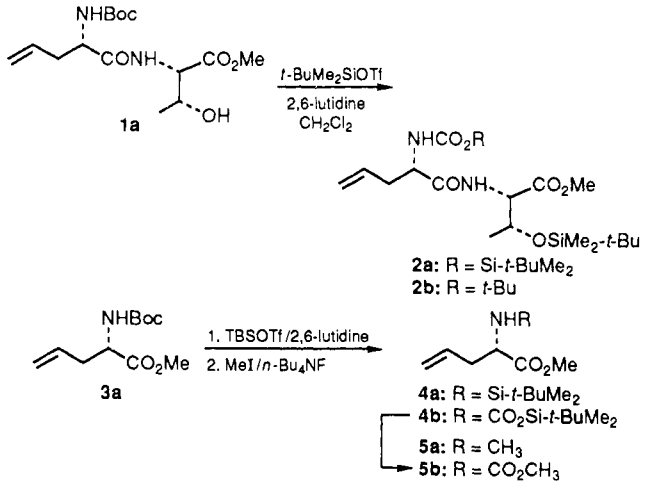
$$RNHCO_2\text{-}t\text{-}Bu \xrightarrow{Me_3SiX} [RNHCO_2SiMe_3] \rightarrow RNH_2HX \quad (4)$$
$$X = I, OTf, ClO_4$$

During the course of our studies on the synthesis of biologically active peptides,[9] we found that *tert*-butyldimethylsilyl trifluoromethanesulfonate (*t*-$BuMe_2SiOTf$), a powerful silylating reagent of a hydroxyl group,[10] in the presence of 2,6-lutidine can be used to effect the transformation of the *t*-Boc group into the *N*-*tert*-butyldimethylsilyloxycarbonyl group (**1a**-**2a**). The ^{1}H NMR ($CDCl_3$) data of **2a** [δ 0.90 (s, 9 H), 0.84 (s, 9 H), 0.25 (s,

(1) Breederveld, H. *Recl. Trav. Chim. Pays-Bas* **1962**, *81*, 276.
(2) Tamm, J. P.; Heath, W. F.; Merrifield, R. B. *Tetrahedron Lett.* **1982**, *23*, 4435.
(3) Chiu, F. T.; Chang, H. Y.; Ozkan, G.; Zon, G.; Fichter, K. C.; Philips, L. R. *J. Pharm. Sci.* **1982**, *71*, 542.
(4) (a) Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*; Springer-Verlag: Berlin, 1984; pp 7 and 151. (b) Greene, Y. W. *Protective Group in Organic Synthesis*; Wiley: New York, 1982; pp 232 and 239.
(5) Parts of this work were published in preliminary reports: (a) Sakaitani, M.; Ohfune, Y. *Tetrahedron Lett.* **1985**, *26*, 5543. (b) Sakaitani, M.; Kurokawa, N.; Ohfune, Y. *Tetrahedron Lett.* **1986**, *27*, 3753.
(6) Vorbrüggen, H.; Krolikiewicz, K. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 818.
(7) Lott, R. S.; Chauhan, V. S.; Stammer, C. H. *J. Chem. Soc., Chem. Commun.* **1979**, 495.
(8) Hamada, Y.; Kato, S.; Shioiri, T. *Tetrahedron Lett.* **1985**, *26*, 3223.
(9) Kurokawa, N.; Ohfune, Y. *J. Am. Chem. Soc.* **1986**, *108*, 6043.
(10) Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.

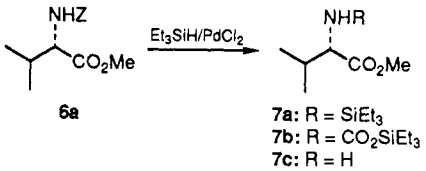
0022-3263/90/1955-0870$02.50/0

3 H), 0.24 (s, 3 H), 0.04 (s, 3 H), −0.03 (s, 3 H)] clearly indicated that the *tert*-butyl group of **1a**[11] is replaced by the *tert*-butyldimethylsilyl group. However, it is not obvious whether this product possesses an NHSi-*t*-$BuMe_2$ or an $NHCO_2Si$-*t*-$BuMe_2$ group. The MS (EI method) data of **2a** showed ion peak at 458, which corresponds molecular formula $C_{22}H_{46}N_2O_4Si_2$ to be NHSi-*t*-$BuMe_2$ **2a**, but this peak could be either M^+ or $M^+ - CO_2$. To confirm that the structure **2a** possesses the $NHCO_2Si$-*t*-$BuMe_2$ group, *t*-Boc-allylglycine methyl ester **3a** was chosen as a structurally simple model.[12] Initial conversion of **3a** into its silylated compound and subsequent reaction with an electrophile such as methyl iodide would provide either an *N*-methyl or an *N*-methoxycarbonyl compound (**5a** or **5b**). Thus, treatment of **3a** with 1.5 equiv of *t*-$BuMe_2SiOTf$ and 2 equiv of 2,6-lutidine in CH_2Cl_2 gave silyl compound **4a** or **4b** as the sole product. Then, methylation was carried out using excess CH_3I in the presence of 1 equiv of tetrabutylammonium fluoride (*n*-Bu_4NF). As a result, the reaction did not give the N-methylated compound **5a** but instead gave the *N*-methoxycarbonyl compound **5b**: ^1H NMR ($CDCl_3$) δ 3.73 (s, 3 H), 3.68 (s, 3 H); MS (EI method) m/z 188 $(M + H)^+$. Accordingly, the structures of the silylated compounds were confirmed to be **2a** and **4b** with an $NHCO_2Si$-*t*-$BuMe_2$ moiety. These results prompted us to further investigate the reactivity and synthetic potential of silyl carbamates.



The *tert*-butyldimethylsilyloxycarbonyl compounds **2a** and **4b** can be isolated by an extractive workup and stored at ambient temperature. This group can be removed under mildly acidic conditions or by the fluoride ion treatment to give a deprotected free amine (vide infra). The silyl carbamates were used for the next reaction without further purification because partial cleavage of the silyloxycarbonyl group was accompanied by moisture or SiO_2 column chromatography. Mild and chemoselective properties of this reaction are described in the aftermentioned section. For the elucidation of the general aspects for the synthesis of silyl carbamates, the solvent and reaction temperature were first examined. Usually, the reaction is carried out under argon atmosphere and is complete within 10 min at room temperature using CH_2Cl_2 as the solvent. Mostly, this process is quantitative, and the homogeneity of the product is ascertained by the ^1H NMR analysis. A small excess of *t*-$BuMe_2SiOTf$ (1.5 equiv) in the presence of 2,6-lutidine or triethylamine (2.0 equiv) is necessary to complete the reaction. In the absence of base, the reaction was sluggish and gave the corresponding amine as a trifluoromethanesulfonic acid salt. The use of ether type solvent (tetrahydrofuran, ether, etc.) or the reaction at low temperature (below 10 °C) resulted in a decrease in yields: the products were composed of a mixture of unreacted starting material and silyl carbamate. The hydroxyl group of **1a** can be converted selectively into *tert*-butyldimethylsilyl ether **2b** when the reaction was conducted at 0 °C.

Synthesis of *tert*-Butyldimethylsilyl Carbamate from *N*-Benzyloxycarbonyl (Z) and *N*-Allyloxycarbonyl Groups (Alloc). It is well known that the *N*-Z group exhibits contrasting chemical properties as compared to the *N*-*t*-Boc group as an amino protective group (stable under acidic conditions that cleave *N*-*t*-Boc) and is removed under very strongly acidic conditions (HBr/acetic acid, HF, etc.) or hydrogenation conditions (H_2/Pd–C).[4] Previously, Birkofer et al. reported a novel method for the removal of the Z group using triethylsilane (Et_3SiH) in the presence of a Pd(II) catalyst. They suggested that this reaction proceeds through the $RNHSiEt_3$ intermediate **7a**.[13]



(5)

By repeating their procedure, however, we found the formation of the *N*-triethylsilyloxycarbonyl ($RNHCO_2SiEt_3$) compound **7b** in which the benzyl group was replaced by the triethylsilyl group.[14] Since **7b** was found to be unstable and partly cleaved under usual workup conditions giving an amine **7c**, we studied the synthesis of the more stable *N*-*tert*-butyldimethylsilyloxycarbonyl compound from the *N*-Z compound. This was achieved successfully by the use of 1.5 equiv of *tert*-butyldimethylsilane (*t*-$BuMe_2SiH$)[15] in the presence of 0.05 equiv of palladium(II) acetate ($Pd(OAc)_2$) and 0.15 equiv of triethylamine. Other catalysts such as $PdCl_2$, $PdCl_2(Ph_3P)_2$, $PdCl_2(CH_3CN)_2$, $NiCl_2$, $RuCl_2(Ph_3P)_3$, and $RhCl(Ph_3P)_3$ were not as effective and the yields were reduced. Examples of the synthesis of *tert*-butyldimethylsilyl carbamates from *N*-Z compounds are shown in Table I. Essentially, the reaction conditions are neutral and the chemoselectivity of this transformation is very high. Although benzyl ethers are stable to the conditions, benzyl esters are not (see, **3d** and **3f**).[16]

Recently, several groups reported an efficient method for the removal of the *N*-allyloxycarbonyl (Alloc) group[17] using Pd(II) catalyst.[18] From this group, the silyl carbamates were prepared, efficiently, in the same reaction conditions as above, in quantitative yield.

(11) Prepared by the condensation of *N*-*t*-Boc-L-allylglycine pyridine thiol ester with *O*-(*tert*-butyldimethylsilyl)-L-threonine using 2 equiv of 1-(trimethylsilyl)imidazole (TMSIm) in dimethylformamide.[9]

(12) Preparation of N-protected allylglycine derivatives, see: Ohfune, Y.; Nishio, N. *Tetrahedron Lett.* **1984**, *25*, 4133.

(13) Birkofer, L.; Bierstein, E.; Ritter, F. *Chem. Ber.* **1961**, *94*, 821.

(14) In this case, M^+, which is in accord with the molecular formula of $C_{13}H_{27}NO_4Si$, was clearly observed; MS (EI method) m/z 290 $(M + H)^+$.

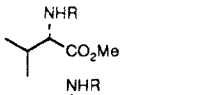
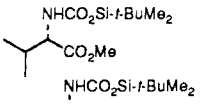
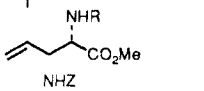
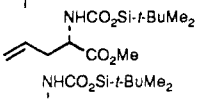
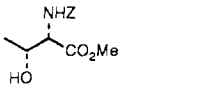
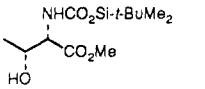
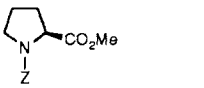
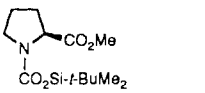
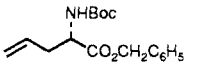
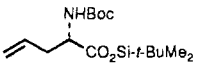
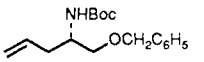
(15) Barton, T. J.; Tully, C. R. *J. Org. Chem.* **1978**, *43*, 3649.

(16) Limitation of this method was encountered during deprotection of *N*-Z group from the sulfur containing amino acid such as *N*-Z-methionine methyl ester. Treatment with $Et_3SiH/Pd(OAc)_2$ gave methionine methyl ester in poor yield as that of the hydrogenation conditions (H_2/Pd–C).[4]

(17) Stevens, C. M.; Watanabe, R. *J. Am. Chem. Soc.* **1950**, *72*, 725.

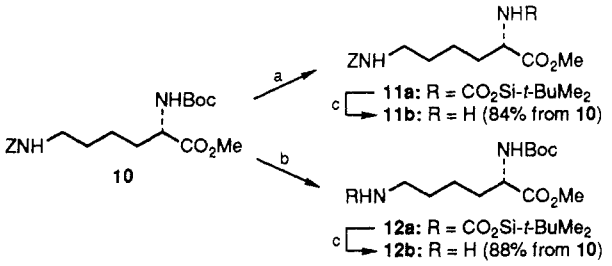
(18) (a) Minami, I.; Ohashi, Y.; Tsuji, J. *Tetrahedron Lett.* **1985**, *26*, 2449. (b) Guibe, F.; Dangles, O.; Balavoine, G. *Tetrahedron Lett.* **1986**, *27*, 2365. (c) Hayakawa, Y.; Kato, H.; Uchida, M. Kajino, H.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 2400.

Table I. Synthesis of *tert*-Butyldimethylsilyl Carbamate from *N*-Benzyloxycarbonyl (Z) and *N*-Allyloxycarbonyl (Alloc) Compounds

substrate		product[a,b] (yield)	
	**6a**: R = Z **6b**: R = Alloc		**7d** (100% from **6a,b**)
	**3b**: R = Z **3c**: R = Alloc		**4b** (62% from **3b**[c] and 100% from **3c**)
	**8a**		**8b** (100%)
	**9a**		**9b** (100%)
	**3d**		**3e** (95%)[d]
	**3f**	no reaction	(0%)

[a] All reactions were carried out using 1.5 equiv of t-$BuMe_2SiH$, 0.05 equiv of $Pd(OAc)_2$, and 0.15 equiv of Et_3N in CH_2Cl_2 at room temperature. [b] The homogeneity of the products were ascertained by the ^1H NMR analysis. [c] Recovery of the starting material (**3b**, 38%; **3f**, 100%). [d] Isolated yield by column chromatography on SiO_2.

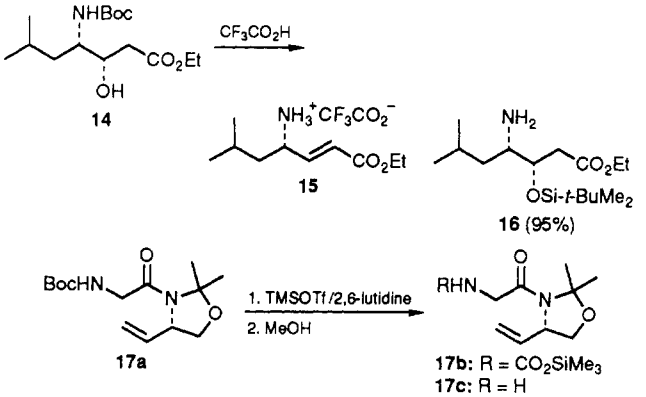
In addition, selective conversion of N^{α}-Boc-N^{ϵ}-Z-L-lysine methyl ester **10** into either N^{α}-silyloxycarbonyl-N^{ϵ}-Z **11a** or N^{α}-Boc-N^{ϵ}-silyloxycarbonyl **12a** was accomplished by the use of t-$BuMe_2SiOTf$ or t-$BuMe_2SiH/Pd(OAc)_2$, respectively, in high yield.



(a) t-$BuMe_2SiOTf$, 2,6-lutidine; (b) t-$BuMe_2SiH$, $Pd(OAc)_2$; (c) n-Bu_4NF

Removal of the Urethane-Type Protective Groups via Silyl Carbamate. Removal of the *N-tert*-butyldimethylsilyloxycarbonyl group prepared from *N*-*t*-Boc or *N*-Z group can be effected by the treatment with n-Bu_4NF (1.0 equiv, room temperature, 1 h) followed by quenching with aqueous ammonium chloride to give an amine in high yields (eq 3, b). Successive treatment of *N*-*t*-Boc-phenylalanine methyl ester **13a** with above conditions gave phenylalanine methyl ester **13b** in 92% yield.[19] As a representative example, N^{α}-Boc-N^{ϵ}-Z-L-lysine methyl ester **10** was selectively converted into the N^{α}-free amine **11b** (84%) or N^{ϵ}-free amine **12b** (88%) via the silyl carbamates **11a** or **12a**.[19] The removal of the *N*-*t*-Boc group of **14**, which is a synthetic intermediate of statine,[20] was carried out by the present method and gave desired **16** in 95% yield, while usual method (CF_3CO_2H) was accompanied by a β-elimination of the hydroxyl group to give **15**.[21]

It is noted that chemoselective removal of an *N*-*t*-Boc group from the Boc-acetonide **17a** to the acetonide **17c** was carried out efficiently by the use of 1.5 equiv of trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf) in the presence of 2.0 equiv of 2,6-lutidine in CH_2Cl_2 at room temperature for 15 min. After workup, the resultant trimethylsilyloxycarbonyl group of **17b** was removed by dissolving in methanol to give free amine **17c** in quantitative yield. The acetonide group of **17a** was completely unchanged.[22] The use of Me_3SiOTf may be superior to that of t-$BuMe_2SiOTf$ when deprotection of the *N*-*t*-Boc group is required.



Interconversion of the Urethane-Type Amino Protective Groups via *tert*-Butyldimethylsilyl Carbamate. Alkylcarbamates have been used not only for urethane-type amino protecting groups but also involved as partial structures in biologically important substances for medicines and agrochemicals such as diperodon (local anesthetic).[23,24] Silyl carbamates could be potentially useful intermediates for the synthesis of a variety of urethane-type compounds, since fluoride ion treatment can generate an activated species which can react with an electrophile to give *N*-ester type compounds (eq 3, c, and eq 6). n-Bu_4NF was found to be the most effective fluoride ion source by comparison with other reagents such as KF, CsF, etc.

The synthesis of the *N*-alkoxycarbonyl compounds from several *N-tert*-butyldimethylsilyl carbamates are summa-

(19) Amines prepared from the corresponding silyl carbamates were identified with the commercially available materials: **13b** from Peptide Institute Inc., Osaka, and **11b** and **12b** from Kokusan Chemical Works Co., Tokyo.

(20) Synthesis of statine, see: Sakaitani, M.; Ohfune, Y. *J. Am. Chem. Soc.*, in press.

(21) Rich, D. H.; Sun, E. T.; Boparai, A. B. *J. Org. Chem.* **1978**, *43*, 3624.

(22) Yamanoi, K.; Ohfune, Y.; Watanabe, K.; Li. P. N.; Takeuchi, H. *Tetrahedron Lett.* **1988**, *29*, 1181.

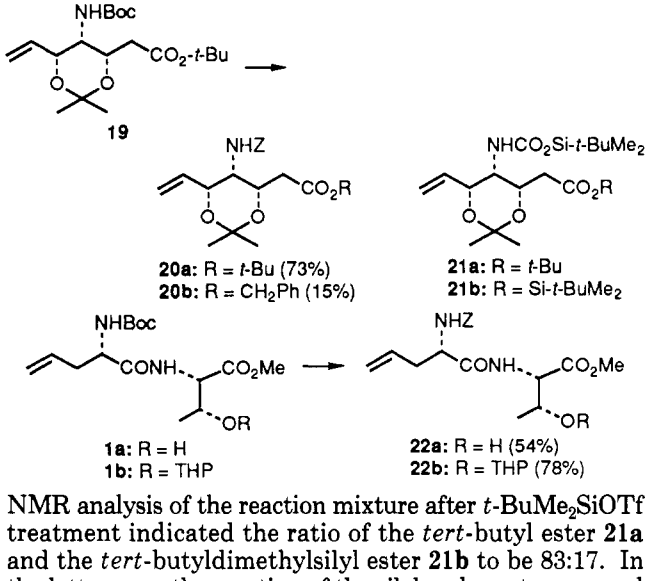
(23) Methods for the preparation of carbamates, see: Sandler, S. R.; Karo, W. *Organic Functional Group Preparations*, 2nd ed.; Academic Press: Orlando, 1986; Vol. II, pp 260 and 274.

(24) Cook, E. S.; Rider, T. H. *J. Pharmacol.* **1938**, *64*, 1.

$$RNHCO_2Si\text{-}t\text{-}BuMe_2 \xrightarrow{F^-} [RNHCO_2Si(F^-)\text{-}t\text{-}BuMe_2] \xrightarrow{R'X} RNHCO_2R' \quad (6)$$

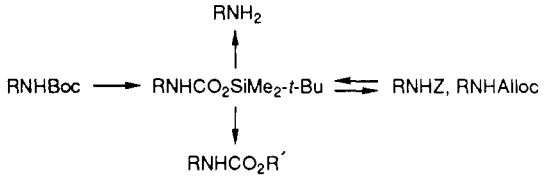
rized in Table II. In all cases the silyl carbamates, prepared from *N*-*t*-Boc compound with *t*-$BuMe_2SiOTf$/2,6-lutidine, was immediately treated with an alkyl halide in the presence of *n*-Bu_4NF at 0 °C for 1 h to give the corresponding alkoxycarbonyl derivative in excellent yield. The reactions using methyl iodide, allyl bromide, and ethyl iodide as the electrophiles gave the corresponding *N*-methoxycarbonyl, *N*-allyloxycarbonyl, and *N*-ethoxycarbonyl compounds, respectively, in high yields. It was of interest to test the conversion of the *N*-*t*-Boc group into the *N*-Z group via a silyl carbamate. The reaction of several silyl carbamates with benzyl bromide proceeded smoothly to give the corresponding *N*-benzyloxycarbonyl (Z) derivatives (entries 3, 4, 8–10) in good yields. Thus conversion of the *N*-*t*-Boc group into the *N*-Z group via a silyl carbamate was achieved.[25] Next, we turned our attention to the synthesis of *tert*-butyl carbamate from a silyl carbamate since this transformation makes the conversion of the *N*-Z group into the *N*-*t*-Boc group possible. Therefore, the reaction of a silyl carbamate with a secondary or a tertiary alkyl halide was examined. Initially, *N*-(*tert*-butyldimethylsilyloxycarbonyl)-L-valine methyl ester was treated with isopropyl iodide to yield (isopropyloxycarbonyl)-L-valine methyl ester **6e** (entry 6) in 46% yield. However, the desired *tert*-butyl carbamate could not be obtained by reaction with *tert*-butyl iodide due probably to steric bulkiness of the electrophile (entry 7).[26]

For additional examples, the present reaction was studied using the acetonide **19**[12] and the dipeptide **1**. In the former case, the *N*-Z derivative **20a** was obtained in 73% yield together with its benzyl ester **20b** (15%) derived from an intermediary *tert*-butyldimethylsilyl ester **21b**: ^1H



NMR analysis of the reaction mixture after *t*-$BuMe_2SiOTf$ treatment indicated the ratio of the *tert*-butyl ester **21a** and the *tert*-butyldimethylsilyl ester **21b** to be 83:17. In the latter case, the reaction of the silyl carbamate prepared from **1a** gave **22a** in 54% yield. The yield was improved by protecting its hydroxyl group with tetrahydropyranyl (THP) group (78%).

Conclusion. The synthesis of *tert*-butyldimethylsilyl carbamate from *N*-*t*-Boc and *N*-Z groups, representative amino protecting groups, was accomplished by the use of *t*-$BuMe_2SiOTf$/2,6-lutidine or *t*-$BuMe_2SiH$/Pd(II) systems. The silyl group can be removed under the neutral conditions to give amines in an inorganic salt free form, and was transformed to the corresponding urethane type groups such as *N*-Z group by treatment with an alkyl halide in the presence of *n*-Bu_4NF. These conversions are summarized as follows.



Experimental Section

Melting points are uncorrected. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on one of the following instruments: Hitachi R-20B, JEOL FX 100, and Nicolet NT-360. Chemical shifts are reported as δ values in ppm relative to $CHCl_3$ (7.26) in $CDCl_3$. Infrared (IR) spectra were measured on Hitachi 270–30 infrared spectrophotometer. Mass spectra were obtained on a Hitachi M-80B spectrometer for electron-impact (EI) ionization. All *N*-*t*-Boc and *N*-Z-L-amino acids except allylglycine were obtained from Peptide Institute, Inc., Osaka, or Kokusan Chemical Works Co., Tokyo. The corresponding methyl ester were prepared by the esterification with diazomethane (CH_2N_2) and purified by column chromatography on silica gel. *N*-*t*-Boc-DL-allylglycine methyl ester was prepared from DL-allylglycine, available from Sigma Chemical Co., in the usual manner; (1) di-*tert*-butyl dicarbonate (Boc_2O)/triethylamine in dioxane/H_2O = 1/1 and (2) esterification with CH_2N_2 in ether. The *tert*-butyldimethylsilyl carbamates after workup were used for next step without further purification.

General Procedure for the Synthesis of *tert*-Butyldimethylsilyl Carbamates from *N*-*tert*-Butoxycarbonyl (Boc) Compounds (Procedure I). *N*-(*tert*-Butyldimethylsilyloxycarbonyl)-DL-allylglycine Methyl Ester (4b). To a stirred solution of *N*-*t*-Boc-DL-allylglycine methyl ester **3a** (183 mg, 0.8 mmol) and 2,6-lutidine (186 μL, 1.6 mmol) in dry CH_2Cl_2 (1.5 mL) at room temperature was added dropwise *tert*-butyldimethylsilyl trifluoromethanesulfonate (*t*-$BuMe_2SiOTf$; 275 μL, 1.2 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 then brine, dried ($MgSO_4$), and concentrated in vacuo to give **4b** (260 mg): oil; IR (neat) 3464, 3372, 2964, 2940, 2900, 2864, 1750, 1706, 1646, 1504 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 5.70 (m, 1 H), 5.12 (m, 3 H), 4.38 (m, 1 H), 3.74 (s, 3 H), 2.52 (m, 2 H), 0.93 (s, 9 H), 0.25 (s, 6 H); MS (EI method) *m*/*z* 288 $(M + H)^+$, 272, 244, 228.

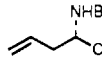
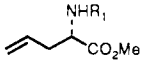
***N*-(*tert*-Butyldimethylsilyloxycarbonyl)-L-allylglycyl-*O*-(*tert*-butyldimethylsilyl)-L-threonine Methyl Ester (2a).** Treatment of **1a** (24.0 mg, 0.07 mmol) with 2,6-lutidine (24 μL, 0.07 mmol) and *t*-$BuMe_2SiOTf$ (41 μL, 0.18 mmol) in CH_2Cl_2 (0.5 mL) according to procedure I gave **2b** (43.3 mg): oil; IR (neat) 3452, 3328, 2960, 2940, 2904, 2864, 1758, 1686, 1518 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 6.54 (d, 1 H, *J* = 9 Hz), 5.81 (ddt, 1 H, *J* = 17, 10, 7 Hz), 5.30 (d, 1 H, *J* = 8 Hz), 5.14 (br d, 1 H, *J* = 17 Hz), 5.12 (br d, 1 H, *J* = 10 Hz), 4.48 (m, 2 H), 4.14 (dt, 1 H, *J* = 8, 7 Hz), 3.70 (s, 3 H), 2.53 (m, 2 H), 1.14 (d, 3 H, *J* = 7 Hz), 0.91 (s, 9 H), 0.84 (s, 9 H), 0.25 (s, 6 H), 0.04 (s, 3 H), −0.02 (s, 3 H); MS (EI method) *m*/*z* 458 $(M - CO_2)^+$, 445, 417, 401, 313.

***N*-(*tert*-Butoxycarbonyl)-L-allylglycyl-*O*-(*tert*-butyldimethylsilyl)-L-threonine Methyl Ester (2b).** To a stirred solution of **1a** (500 mg, 1.52 mmol) and 2,6-lutidine (353 μL, 3.04 mmol) in dry CH_2Cl_2 (3.0 mL) at 0 °C was added dropwise *t*-$BuMe_2SiOTf$ (523 μL, 2.28 mmol). The reaction mixture was stirred at 0 °C for 15 min, quenched with saturated aqueous

(25) In comparison of optical rotation of the products with authentic materials,[a] only slight racemization was accompanied during these transformation. **6a**: $[\alpha]^{30}_D$ −19.4° (*c* 1.0, MeOH) (lit. $[\alpha]^{20}_D$ −21.9°). **9a**: $[\alpha]^{30}_D$ −62.0° (*c* 1.0, MeOH) (lit. $[\alpha]^{20}_D$ −64.0°). **13c**: $[\alpha]^{30}_D$ −14.9° (*c* 1.0, MeOH) (lit. $[\alpha]^{19}_D$ −17.1°). **18b**: $[\alpha]^{30}_D$ −32.6° (*c* 1.0, MeOH) (lit. $[\alpha]^{20}_D$ −35.6°). (a) Yamada, T.; Isono, N.; Inui, A.; Miyazawa, T.; Kuwata, S.; Watanabe, H. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1897.

(26) For a one-pot conversion of the *N*-Z group into the *N*-*t*-Boc group via an amine, see: Sakaitani, M.; Hori, K.; Ohfune, Y. *Tetrahedron Lett.* **1988**, *29*, 2983.

Table II. Conversion of *N*-*t*-Boc Compounds into *N*-Alkyloxycarbonyl Compounds via *tert*-Butyldimethylsilyl Carbamates[a]

entry	substrate	RX	product	% yield[b]
				
1	**3a**	MeI	R_1 = CO_2Me (**5b**)	84
2	**3a**	$C_6H_5CH_2Br$	R_1 = $CO_2CH_2C_6H_5$ (Z) (**3b**)	82
3	**3a**	CH_2=$CHCH_2Br$	R_1 = CO_2CH_2CH=CH_2 (**3c**)	88
4	Boc-L-Val-OMe (**6c**)	$C_6H_5CH_2Br$	Z-L-Val-OMe (**6a**)	85
5	**6c**	EtI	EtO_2C-L-Val-OMe (**6d**)	83
6	**6c**	*i*-PrI	*i*-PrO_2C-L-Val-OMe (**6e**)	46
7	**6c**	*t*-BuI	Boc-L-Val-OMe (**6f**)	0
8	Boc-L-Pro-OMe (**9c**)	$C_6H_5CH_2Br$	Z-L-Pro-OMe (**9a**)	61
9	Boc-L-Phe-OMe (**13a**)	$C_6H_5CH_2Br$	Z-L-Phe-OMe (**13c**)	78
10	Boc-L-Met-OMe (**18a**)	$C_6H_5CH_2Br$	Z-L-Met-OMe (**18b**)	75

[a] All reactions were carried out in two steps: (1) 1.5 equiv of *t*-$BuMe_2SiOTf$, 2 equiv of 2,6-lutidine, CH_2Cl_2, room temperature, and (2) 2 equiv of alkyl halide (RX), 1.0 equiv of 1 M solution of *n*-Bu_4NF, THF, 0 °C, 1 h. [b] Isolated yield (2 steps).

ammonium chloride solution, and extracted with ether several times. The combined organic phase was washed with H_2O and then brine, dried ($MgSO_4$), 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 *O*-silyl ester **2b** (652 mg, 97%): colorless needles; mp 64.0–65.0°C (hexane); IR (neat) 3452, 3336, 2964, 2948, 2864, 1758, 1720, 1688, 1510 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 6.60 (d, 1 H, J = 9 Hz), 5.80 (ddt, 1 H, J = 17, 10, 7 Hz), 5.16 (br d, 1 H, J = 17 Hz), 5.12 (br d, 1 H, J = 10 Hz), 5.04 (d, 1 H, J = 8 Hz), 4.48 (m, 2 H), 4.11 (dt, 1 H, J = 8, 7 Hz), 3.68 (s, 3 H), 2.53 (m, 2 H), 1.43 (s, 9 H), 1.14 (d, 3 H, J = 7 Hz), 0.84 (s, 9 H), 0.03 (s, 3 H), –0.02 (s, 3 H). Anal. Calcd for $C_{21}H_{40}O_6N_2Si$: C, 56.73; H, 9.07; N, 6.30. Found: C, 56.67; H, 9.09; N, 6.33.

***N*-(Triethylsilyloxycarbonyl)-L-valine Methyl Ester (7b).** A suspension of **6a** (265 mg, 1.0 mmol), triethylsilane (640 μL, 4.0 mmol), triethylamine (100 μL, 0.7 mmol), and $PdCl_2$ (50 mg, 0.3 mmol) in CH_2Cl_2 (5 mL) was heated at reflux for 3 h. The reaction mixture was quenched with saturated aqueous ammonium chloride solution and extracted with ether several times. The combined organic phase was washed with H_2O and then brine, dried ($MgSO_4$), and concentrated in vacuo to give **7b** (290 mg): oil; IR (neat) 3380, 2964, 2884, 1750, 1704, 1506 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.26 (d, 1 H, J = 8 Hz), 4.20 (dd, 1 H, J = 8, 5 Hz), 3.70 (s, 3 H), 2.20 (m, 1 H), 0.4–1.3 (m, 21 H); MS (EI method) m/z 290 $(M + H)^+$, 260, 230, 216.

General Procedure for the Synthesis of *tert*-Butyldimethylsilyl Carbamates from *N*-Benzyloxycarbonyl (Z) Compounds (Procedure II). *N*-(*tert*-Butyldimethylsilyloxycarbonyl)-L-valine Methyl Ester (7d). A suspension of *tert*-butyldimethylsilane (*t*-$BuMe_2SiH$; 280 μL, 1.7 mmol), palladium acetate ($Pd(OAc)_2$; 13 mg, 0.06 mmol) and triethylamine (25 μL, 0.18 mmol) in dry CH_2Cl_2 (2.0 mL) at room temperature was stired for 15 min. To the reaction mixture was added a solution of *N*-Z-L-valine methyl ester **6a** (300 mg, 1.1 mmol) in CH_2Cl_2 (2.0 mL). The suspension was stirred for 8 h. The reaction mixture was quenched with saturated aqueous ammonium chloride solution and extracted with ether several times. The combined organic phase was washed with H_2O and then brine, dried ($MgSO_4$), and concentrated in vacuo to give **7d** (342 mg, 100%): oil; IR (neat) 3380, 2968, 2864, 1748, 1716, 1506 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.20 (d, 1 H, J = 10 Hz), 4.21 (dd, 1 H, J = 10, 4 Hz), 3.72 (s, 3 H), 2.10 (m, 1 H), 0.98 (d, 3 H, J = 7 Hz), 0.94 (s, 9 H), 0.92 (d, 3 H, J = 7 Hz), 0.25 (s, 6 H); MS (EI method) m/z 290 $(M + H)^+$, 274, 258, 232, 188, 160.

The same compound was also obtained (207 mg, 100%) from 154 mg (0.72 mmol) of *N*-(allyloxycarbonyl)-L-valine methyl ester **6b** by the treatment with *t*-$BuMe_2SiH$ (179 μL, 1.1 mmol), $Pd(OAc)_2$ (8.0 mg, 0.04 mmol), and triethylamine (15 μL, 0.11 mmol) according to procedure II.

***N*-(*tert*-Butyldimethylsilyloxycarbonyl)-DL-allylglycine Methyl Ester (4b).** Treatment of **3b** (192 mg, 0.73 mmol) with *t*-$BuMe_2SiH$ (182 μL, 1.1 mmol), $Pd(OAc)_2$ (8.0 mg, 0.04 mmol), and triethylamine (15 μL, 0.11 mmol) according to procedure II gave a mixture of silyl carbamate **4b** and starting **3b** (203 mg, the yield of **4b** was determined by the ^1H NMR analysis to be 62%). The mixture was further treated with column chromatography on SiO_2 (elution with 50% ether/hexane), and the unreacted **3b** was recovered (73 mg, 38%). Silyl carbamate **4b** was also obtained (184 mg, 100%) from **3c** (150 mg, 0.75 mmol) by the treatment with *t*-$BuMe_2SiH$ (187 μL, 1.1 mmol), $Pd(OAc)_2$ (8.0 mg, 0.04 mmol), and triethylamine (16 μL, 0.12 mmol) according to procedure II. In this case, none of the starting material was recovered.

***N*-(*tert*-Butyldimethylsilyloxycarbonyl)-L-threonine Methyl Ester (8b).** Treatment of **8a** (200 mg, 0.75 mmol) with *t*-$BuMe_2SiH$ (186 μL, 1.1 mmol), $Pd(OAc)_2$ (8.0 mg, 0.04 mmol), and triethylamine (15 μL, 0.11 mmol) according to procedure II gave **8b** (215 mg, 100%): oil; IR (neat) 3460, 2960, 2940, 2896, 2864, 1758, 1706, 1518 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.60 (d, 1 H, J = 9 Hz), 4.0–4.4 (m, 2 H), 3.68 (s, 3 H), 3.15 (br s, 1 H), 1.20 (d, 3 H, J = 7 Hz), 0.91 (s, 9 H), 0.23 (s, 6 H); MS (EI method) m/z 292 $(M + H)^+$, 274, 247, 235, 215.

***N*-(*tert*-Butyldimethylsilyloxycarbonyl)-L-proline Methyl Ester (9b).** Treatment of **9a** (210 mg, 0.80 mmol) with *t*-$BuMe_2SiH$ (199 μL, 1.2 mmol), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol), and triethylamine (17 μL, 0.12 mmol) according to procedure II gave **9b** (20 mg, 100%): oil; IR (neat) 3500, 2960, 2892, 2864, 1754, 1694, 1466 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 4.30 (m, 1 H), 3.65 (m, 3 H), 3.45 (m, 2 H), 2.00 (m, 4 H), 0.90 (m, 9 H), 0.25 (s, 6 H); MS (EI method) m/z 272 $(M - Me)^+$, 231, 228, 186.

***N*-(*tert*-Butoxycarbonyl)-DL-allylglycine *tert*-Butyldimethylsilyl Ester (3e).** Treatment of **3d** (149 mg, 0.55 mmol) with *t*-$BuMe_2SiH$ (137 μL, 0.83 mmol), $Pd(OAc)_2$ (6.0 mg, 0.03 mmol), and triethylamine (12 μL, 0.09 mmol) according to procedure II gave **3e** (182 mg, 95%): oil; IR (neat) 3460, 3360, 2960, 2940, 2855, 1718, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.62 (ddd, 1 H, J = 15, 10, 6 Hz) 5.05 (m, 3 H), 4.30 (dd, 1 H, J = 9, 8 Hz), 2.52 (m, 2 H), 1.43 (s, 9 H), 0.95 (s, 9 H), 0.29 (s, 6 H); MS (EI method) m/z 330 $(M + H)^+$, 306, 258, 216, 188.

***N*$^{\alpha}$-(*tert*-Butyldimethylsilyloxycarbonyl)-*N*$^{\epsilon}$-(benzyloxycarbonyl)-L-lysine Methyl Ester (11a).** Treatment of **10** (191.0 mg, 0.48 mmol) with 2,6-lutidine (113 μL, 0.97 mmol) and *t*-$BuMe_2SiOTf$ (167 μL, 0.73 mmol) according to procedure I gave **11a** (238 mg): oil; IR (neat) 3352, 2960, 2864, 1750, 1708, 1526 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.35 (s, 5 H), 5.24 (d, 1 H, J = 7 Hz), 5.08 (s, 2 H), 4.80 (br s, 1 H), 4.18 (m, 1 H), 3.74 (s, 3 H), 3.10 (td, 2 H, J = 7, 7 Hz), 1.2–2.0 (m, 6 H), 0.94 (s, 9 H), 0.27 (s, 6 H); MS (EI method) m/z 452 $(M)^+$, 395, 378, 352.

***N*$^{\alpha}$-(*tert*-Butoxycarbonyl)-*N*$^{\epsilon}$-(*tert*-butyldimethylsilyloxycarbonyl)-L-lysine Methyl Ester (12a).** Treatment of **10** (100 mg, 0.25 mmol) with *t*-$BuMe_2SiH$ (63 μL, 0.38 mmol), $Pd(OAc)_2$ (6.0 mg, 0.03 mmol), and triethylamine (12 μL, 0.09 mmol) according to procedure II gave **12a** (96 mg): oil; IR (neat) 3368, 2940, 2864, 1748, 1704, 1520 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.10 (d, 1 H, J = 8 Hz), 4.85 (m, 1 H), 4.25 (m, 1 H), 3.72 (s, 3 H), 3.13 (m, 2 H), 1.46 (s, 9 H), 1.1–2.0 (m, 6 H), 0.94 (s, 9 H), 0.27 (s, 6 H); MS (EI method) m/z 419 $(M + H)^+$, 363, 345, 305, 287, 242.

General Procedure for the Removal of the *tert*-Butyldimethylsilyloxycarbonyl Group (Procedure III). L-Phenylalanine Methyl Ester (13b). To a stirred solution of *N*-(*tert*-butyldimethylsilyloxycarbonyl)-L-phenylalanine methyl ester (187 mg, 0.5 mmol), prepared from **13a** according to procedure I, in THF (1.0 mL) at room temperature was added tet-

rabutylammonium fluoride (500 μL, 1 M solution in THF, 0.5 mmol). The reaction mixture was stirred for 1 h, quenched with saturated aqueous ammonium chloride solution, and extracted with $CHCl_3$ several times. The combined organic phase was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give **13b** (84 mg, 93%): oil; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.22 (s, 5 H), 3.70 (s, 3 H), 3.70 (m, 1 H), 3.12 (dd, 1 H, J = 14, 5 Hz), 2.80 (dd, 1 H, J = 14, 8 Hz), 1.60 (s, 2 H); MS (EI method) m/z 180 $(M + H)^+$.[19]

N^{ϵ}-(Benzyloxycarbonyl)-L-lysine Methyl Ester (11b). Treatment of **11a** (238 mg, 0.48 mmol) with 480 μL (0.48 mmol) of tetrabutylammonium fluoride solution in THF (2.0 mL) according to procedure III gave **11b** (120 mg, 84%): oil; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.32 (s, 5 H), 4.84 (br s, 1 H), 4.07 (s, 2 H), 3.70 (s, 3 H), 3.40 (m, 1 H), 3.17 (dt, 2 H, J = 6, 6 Hz), 1.2–1.9 (m, 8 H).[19]

N^{α}-(*tert*-Butoxycarbonyl)-L-lysine Methyl Ester (12b). Treatment of **12a** (320 mg, 0.73 mmol) with 730 μL (0.73 mmol) of tetrabutylammonium fluoride solution in THF (3.0 mL) according to procedure III gave **12b** (167 mg, 88%): oil; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.02 (d, 1 H, J = 8 Hz), 4.18 (dt, 1 H, J = 8, 7 Hz), 3.74 (s, 3 H), 2.68 (m, 2 H), 1.2–1.9 (m, 8 H), 1.45 (s, 9 H).[19]

(3*S*,4*S*)-4-Amino-6-methyl-3-(*tert*-butyldimethylsilyloxy)heptanoic Acid Ethyl Ester ((3*S*,4*S*)-*O*-(*tert*-Butyldimethylsilyloxy)statine Ethyl Ester) (16). Treatment of *N*-*t*-Boc statine ethyl ester **14** (1.0 g, 3.3 mmol) with 2,6-lutidine (1.57 mL, 13.2 mmol) and *t*-$BuMe_2SiOTf$ (2.27 mL, 9.9 mmol) in CH_2Cl_2 (10 mL) according to procedure I gave (3*S*,4*S*)-*N*-(*tert*-butyldimethylsilyloxycarbonyl)-4-amino-6-methyl-3-(*tert*-butyldimethylsilyloxy)heptanoic acid ethyl ester (1.20 g): oil; IR (neat) 3250, 2964, 2936, 2864, 1742, 1696, 1472 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 4.67 (d, 1 H, J = 9 Hz), 4.18 (m, 1 H), 4.11 (q, 2 H, J = 7 Hz), 3.70 (m, 1 H), 2.46 (m, 2 H), 1.2–1.8 (m, 3 H), 1.28 (t, 3 H, J = 7 Hz), 0.93 (s, 9 H), 0.92 (d, 3 H, J = 7 Hz), 0.88 (d, 3 H, J = 7 Hz), 0.87 (s, 9 H), 0.25 (s, 6 H), 0.08 (s, 3 H), 0.04 (s, 3 H). Treatment of this compound (138 mg, 0.26 mmol) with 260 μL (0.26 mmol) of tetrabutylammonium fluoride solution according to procedure III gave **16** (77 mg, 95%): oil: IR (neat) 2960, 2936, 2864, 1740, 1472, 1372 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 4.12 (q, 2 H, J = 7 Hz), 4.00 (m, 1 H), 2.72 (m, 1 H), 2.65 (dd, 1 H, J = 15, 7 Hz), 2.39 (dd, 1 H, J = 15, 7 Hz), 1.2–1.9 (m, 3 H), 1.44 (br s, 2 H), 1.25 (t, 3 H, J = 7 Hz), 0.93 (d, 3 H, J = 7 Hz), 0.88 (s, 9 H), 0.87 (d, 3 H, J = 7 Hz), 0.08 (s, 3 H), 0.05 (s, 3 H).

General Procedure for the Syntheses of Alkyl Carbamates (Procedure IV). *N*-(Methoxycarbonyl)-DL-allylglycine Methyl Ester (5b). To a stirred solution of **4b** (170 mg, 0.59 mmol) in dry THF (3 mL) at 0 °C was added successively methyl iodide (74 μL, 1.18 mmol) and tetrabutylammonium fluoride solution (0.59 mL, 1 M solution in THF, 0.59 mmol). The reaction mixture was stirred for 1 h, quenched with saturated aqueous ammonium chloride solution, and extracted with ether 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 25% ether in hexane) gave **5b** (93 mg, 84%): oil; IR (neat) 3456, 3020, 2964, 1726, 1512 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.65 (ddt, 1 H, J = 18, 10, 7 Hz), 5.24 (m, 1 H), 5.08 (m, 2 H), 4.40 (dt, 1 H, J = 8, 7 Hz), 3.73 (s, 3 H), 3.65 (s, 3 H), 2.50 (m, 2 H); MS (EI method) m/z 188 $(M + H)^+$, 147, 128. Anal. Calcd for $C_8H_{13}O_4N$: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.40; H, 7.07; N, 7.59.

***N*-(Benzyloxycarbonyl)-DL-allylglycine Methyl Ester (3b).** Treatment of **4b** (185 mg, 0.57 mmol) with benzyl bromide (135 μL, 1.14 mmol) and 680 μL (1 M solution in THF, 0.68 mmol) of tetrabutylammonium fluoride in THF (1.0 mL) according to procedure IV gave **3b** (131 mg, 88%): oil; IR (neat) 3356, 2960, 1750, 1730, 1530 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.30 (s, 5 H), 5.60 (ddd, 1 H, J = 17, 10, 7 Hz), 4.8–5.2 (m, 3 H), 5.08 (s, 2 H), 4.43 (dt, 1 H, J = 8, 7 Hz), 3.69 (s, 3 H), 2.52 (m, 2 H); MS (EI method) m/z 263 $(M)^+$, 222, 204, 178, 160, identical in all respects with those of authentic **3b**.

***N*-(Allyloxycarbonyl)-DL-allylglycine Methyl Ester (3c).** Treatment of **4b** (170 mg, 0.49 mmol) with allyl bromide (86 μL, 0.99 mmol) and 590 μL (1 M solution in THF, 0.59 mmol) of tetrabutylammonium fluoride in THF (1.0 mL) according to procedure IV gave **3c** (86 mg, 82%): oil; IR (neat) 3352, 2960, 1732, 1648, 1532, cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 4.8–6.2 (m, 7 H), 4.03 (ddd, 2 H, J = 6, 2, 2 Hz), 4.34 (m, 1 H), 3.70 (s, 3 H), 2.52 (m, 2 H); MS (EI method) m/z 214 $(M + H)^+$, 173, 155, 129. Anal. Calcd for $C_{10}H_{15}O_4N$: C, 56.33; H, 7.09; N, 6.57. Found: C, 56.67; H, 7.23; N, 6.65.

***N*-(Benzyloxycarbonyl)-L-valine Methyl Ester (6a).** Treatment of **6c** (115.5 mg, 0.5 mmol) with 2,6-lutidine (116 μL, 1.0 mmol) and *t*-$BuMe_2SiOTf$ (172 μL, 0.75 mmol) in CH_2Cl_2 (1 mL) according to procedure I gave **7d** (153 mg), identical in all respects with those obtained previously from *N*-Z-L-valine methyl ester **6a**. Treatment of **7d** (130 mg, 0.42 mmol) with benzyl bromide (101 μL, 0.84 mmol) and 500 μL (1 M solution, 0.50 mmol) of tetrabutylammonium fluoride in THF (1.0 mL) according to procedure IV gave **6a** (95 mg, 85%): oil; IR (neat) 3360, 2972, 1728, 1522 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.60 (s, 5 H), 5.45 (d, 1 H, J = 9 Hz), 5.08 (s, 2 H), 4.25 (dd, 1 H, J = 9, 5 Hz), 3.68 (s, 3 H), 2.05 (m, 1 H), 0.95 (d, 3 H, J = 7 Hz), 0.90 (d, 3 H, J = 7 Hz); MS (EI method) m/z 265 $(M)^+$, 222, 207, 163, which was identical in all respects with those of authentic **6a**.[25]

***N*-(Ethoxycarbonyl)-L-valine Methyl Ester (6d).** Treatment of **7d** (300 mg, 0.84 mmol) with ethyl iodide (134 μL, 1.68 mmol) and 1.01 mL (1 M solution, 1.01 mmol) of tetrabutylammonium fluoride in THF (3.0 mL) according to procedure IV gave **6d** (141 mg, 83%): oil; IR (neat) 3364, 2972, 1728, 1530 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.20 (d, 1 H, J = 9 Hz), 4.20 (dd, 1 H, J = 9, 4 Hz), 4.08 (q, 2 H, J = 7 Hz), 3.69 (s, 3 H), 2.10 (m, 1 H), 1.10 (t, 3 H, J = 7 Hz), 0.92 (d, 3 H, J = 7 Hz), 0.84 (d, 3 H, J = 7 Hz). Anal. Calcd for $C_9H_{17}O_4N$: C, 53.19; H, 8.43; N, 6.89. Found: C, 53.42; H, 8.48; N, 6.92.

***N*-(Isopropyloxycarbonyl)-L-valine Methyl Ester (6e).** Treatment of **7d** (330 mg, 0.89 mmol) with isopropyl iodide (179 μL, 1.98 mmol) and 1.07 mL (1 M solution in THF, 1.07 mmol) of tetrabutylammonium fluoride in THF (3.0 mL) according to procedure IV gave **6e** (88 mg, 46%): oil; IR (neat) 3368, 2980, 1750, 1724, 1528 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.10 (d, 1 H, J = 9 Hz), 4.87 (qq, 1 H, J = 7, 7 Hz), 4.24 (dd, 1 H, J = 9, 5 Hz), 3.73 (s, 3 H), 2.10 (m, 2 H), 1.22 (d, 6 H, J = 6 Hz), 0.94 (d, 3 H, J = 7 Hz), 0.87 (d, 3 H, J = 7 Hz). Anal. Calcd for $C_{10}H_{19}O_4N$: C, 55.28; H, 8.81; N, 6.45. Found: C, 55.67; H, 8.82; N, 6.54.

***N*-(Benzyloxycarbonyl)-L-proline Methyl Ester (9a).** Treatment of **9c** (114.5 mg, 0.5 mmol) with 2,6-lutidine (116 μL, 1.0 mmol) and *t*-$BuMe_2SiOTf$ (172 μL, 0.75 mmol) according to procedure I gave **9b** (153.1 mg), which was completely identical with **9b** prepared from **9a** according to procedure II. Treatment of **9b** (146 mg, 0.48 mmol) with benzyl bromide (114 μL, 0.96 mmol) and 580 μL (1 M solution in THF, 0.58 mmol) of tetrabutylammonium fluoride in THF (1.0 mL) according to procedure IV gave 9a (94 mg, 75%): oil; IR (neat) 2960, 2888, 1750, 1708 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.28 (br s, 5 H), 5.10 (m, 2 H), 4.35 (m, 1 H), 3.60 (m, 5 H), 2.00 (m, 4 H); MS (EI method) m/z 263 $(M)^+$.[25]

***N*-(Benzyloxycarbonyl)-L-phenylalanine Methyl Ester (13c).** Treatment of **13a** (139.5 mg, 0.5 mmol) with 2,6-lutidine (116 μL, 1.0 mmol) and *t*-$BuMe_2SiOTf$ (172 μL, 0.75 mmol) according to procedure I gave *N*-(*tert*-butyldimethylsilyloxycarbonyl)-L-phenylalanine methyl ester (173.5 mg): oil; IR (neat) 3400, 2960, 2940, 2864, 1748, 1706, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.20 (m, 5 H), 5.20 (d, 1 H, J = 8 Hz), 4.30 (dt, 1 H, J = 8, 6 Hz), 3.73 (s, 3 H), 3.12 (m, 2 H), 0.94 (s, 9 H), 0.27 (s, 6 H); MS (EI method) m/z 322 $(M - Me)^+$, 308, 236, 208, 162. This was treated with benzyl bromide (119 μL, 1.00 mmol) and 600 μL (1 M solution in THF, 0.60 mmol) of tetrabutylammonium fluoride in THF (1 mL) according to procedure IV to give **13c** (122 mg, 78%): oil; IR (neat) 3356, 3036, 2960, 1750, 1726, 1518 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.29 (s, 5 H), 7.18 (m, 5 H), 5.30 (d, 1 H), J = 9 Hz), 5.06 (s, 2 H), 4.63 (m, 1 H), 3.66 (s, 3 H), 3.08 (d, 2 H, J = 6 Hz); MS (EI method) m/z 313 $(M)^+$, 270, 254, 210, 181.[25]

***N*-(Benzyloxycarbonyl)-L-methionine Methyl Ester (18b).** Treatment of **18a** (131.5 mg, 0.5 mmol) with 2,6-lutidine (116 μL, 1.0 mmol) and *t*-$BuMe_2SiOTf$ (172 μL, 0.75 mmol) according to procedure I gave *N*-(*tert*-butyldimethylsilyloxycarbonyl)-L-methionine methyl ester (145.9 mg): oil; IR (neat) 3368, 2960,

2940, 2864, 1748, 1704, 1516 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.48 (d, 1 H, J = 9 Hz), 4.38 (dt, 1 H, J = 9, 7 Hz), 3.71 (s, 3 H), 2.50 (m, 2 H), 2.10 (m, 2 H), 2.09 (s, 3 H), 0.92 (s, 9 H), 0.25 (s, 6 H); MS (EI method) m/z 321 $(M + H)^+$, 306, 264, 220. This was treated with benzyl bromide (60 μL, 0.50 mmol) and 450 μL (1 M solution in THF, 0.45 mmol) of tetrabutylammonium fluoride in THF (1.0 mL) according to procedure IV to give **18b** (91 mg, 61%): oil; IR (neat) 3348, 2960, 2924, 1726, 1532 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.30 (s, 5 H), 5.40 (m, 1 H), 5.08 (s, 2 H), 4.50 (m, 1 H), 3.70 (s, 3 H), 2.50 (m, 2 H), 2.06 (s, 3 H), 1.7–2.2 (m, 2 H).[25]

(4*S,5*R**,6*R**)-*N*-(Benzyloxycarbonyl)-5-amino-2,2-dimethyl-6-vinyl-1,3-dioxane-4-acetic Acid *tert*-Butyl Ester (20a).** Treatment of **19** (40.8 mg, 0.11 mmol) with 2,6-lutidine (26 μL, 0.22 mmol) and t-$BuMe_2SiOTf$ (38 μL, 0.16 mmol) in CH_2Cl_2 (0.5 mL) according to procedure I gave **21a** (45.8 mg): oil; IR (neat) 2985, 2940, 2860, 1734, 1718, 1506 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.76 (ddd, 1 H, J = 17, 10, 4 Hz), 5.32 (ddd, 1 H, J = 17, 2, 2 Hz), 5.21 (ddd, 1 H, J = 10, 2, 2 Hz), 4.84 (d, 1 H, J = 9 Hz), 4.50 (m, 1 H), 3.80 (m, 2 H), 2.58 (m, 2 H), 1.43 (s, 9 H), 1.40 (s, 3 H), 1.33 (s, 3 H), 0.90 (s, 9 H), 0.22 (s, 6 H); MS (EI method) m/z 430 $(M + H)^+$, 414, 386, 358, 316, 258, together with **21b** (**21a**:**21b** = 83:17). Treatment of this mixture (43 mg, 0.10 mmol) with benzyl bromide (24 μL, 0.20 mmol) and 105 μL (1 M solution in THF, 0.15 mmol) of tetrabutylammonium fluoride in THF (1.0 mL) according to procedure IV gave **20a** (30 mg, 73%): colorless prisms; mp 42–43 °C (hexane); IR (neat) 3470, 2988, 2900, 1732, 1506 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.33 (s, 5 H), 5.76 (ddd, 1 H, J = 17, 10, 4 Hz), 5.30 (ddd, 1 H, J = 17, 2, 2 Hz), 5.24 (d, 1 H, J = 9 Hz), 5.15 (ddd, 1 H, J = 10, 2, 2 Hz), 5.08 (s, 2 H), 4.52 (m, 1 H), 4.39 (dd, 1 H, J = 7, 2 Hz), 3.69 (ddd, 1 H, J = 10, 2, 2 Hz), 2.40 (d, 2 H, J = 7 Hz) 1.50 (s, 3 H), 1.44 (s, 9 H), 1.40 (s, 3 H); MS (EI method) m/z 406 $(M + H)^+$, 390, 382, 350, 334. Anal. Calcd for $C_{22}H_{31}O_6N$: C, 65.17; H, 7.71; N, 3.45. Found: C, 64.84; H, 7.63; N, 3.49.

N-Z-5-amino-2,2-dimethyl-6-vinyl-1,3-dioxane-4-acetic acid benzyl ester (**20b**) was byproduced (7 mg, 15%). **20b**: oil; IR (neat) 3468, 3360, 3040, 2996, 2948, 1728, 1652, 1506 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.34 (s, 5 H), 7.32 (s, 5 H), 5.74 (ddd, 1 H, J = 17, 10, 4 Hz), 5.28 (ddd, 1 H, J = 17, 2, 2 Hz), 5.16 (ddd, 1 H, J = 10, 2, 2 Hz), 5.13 (s, 2 H), 5.06 (s, 2 H), 5.05 (d, 1 H, J = 8 Hz), 4.52 (m, 1 H), 4.45 (dd, 1 H, J = 7, 2 Hz), 3.70 (ddd, 1 H, J = 10, 2, 2 Hz), 2.54 (d, 2 H, J = 7 Hz) 1.44 (s, 3 H), 1.38 (s, 3 H); MS (EI method) m/z 424 $(M - Me)^+$, 325, 234. Anal. Calcd for $C_{25}H_{29}O_6N$: C, 68.32; H, 6.65; N, 3.19. Found: C, 68.18; H, 6.61; N, 3.26.

***N*-(Benzyloxycarbonyl)-L-allylglycyl-L-threonine Methyl Ester (22a).** Treatment of **2a** (43 mg, 0.07 mmol) with benzyl bromide (25 μL, 0.21 mmol) and 140 μL (1 M solution in THF, 0.14 mmol) of tetrabutylammonium fluoride in THF (1.0 mL) according to procedure IV gave **22a** (14 mg, 54%): colorless needles; mp 104–106 °C (hexane); IR (neat) 3440, 3020, 2970, 1730, 1686, 1504 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.32 (s, 5 H), 6.96 (d, 1 H, J = 9 Hz), 5.75 (ddt, 1 H, J = 17, 10, 7 Hz), 5.52 (d, 1 H, J = 8 Hz), 5.12 (br d, 1 H, J = 17 Hz), 5.12 (br d, 1 H, J = 10 Hz), 5.08 (s, 2 H), 4.58 (dd, 1 H, J = 8, 3 Hz), 4.32 (m, 2 H), 3.72 (s, 3 H), 2.90 (br s, 1 H), 2.51 (m, 2 H), 1.16 (d, 3 H, J = 7 Hz); MS (EI method) m/z 364 $(M)^+$, 346, 333, 320, 305, 279. Anal. Calcd for $C_{18}H_{24}O_6N_2$: C, 59.33; H, 6.64; N, 7.69. Found: C, 59.10; H, 6.60; N, 7.69.

***N*-(Benzyloxycarbonyl)-L-allylglycyl-*O*-(tetrahydropyranyl)-L-threonine Methyl Ester (22b).** Treatment of **1b** (37.0 mg, 0.09 mmol) with 2,6-lutidine (21 μL, 0.18 mmol) and t-$BuMe_2SiOTf$ (31 μL, 0.14 mmol) in CH_2Cl_2 (0.5 mL) according to procedure I gave *N*-(*tert*-butyldimethylsilyloxycarbonyl)-L-allylglycyl-*O*-(tetrahydropyranyl)-L-threonine methyl ester (45.8 mg): oil; IR (neat) 3330, 2944, 2864, 1758, 1680, 1520 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 6.70 (m, 1 H), 5.70 (m, 1 H), 5.35 (m, 1 H), 5.14 (br d, 1 H, J = 17 Hz), 5.10 (br d, 1 H, J = 10 Hz), 4.0–4.6 (m, 4 H), 3.70 (s, 3 H), 3.46 (m, 1 H), 2.53 (m, 2 H), 1.50 (m, 6 H), 1.19 (m, 3 H), 0.91 (s, 9 H), 0.24 (s, 6 H); MS (EI method) m/z 472 $(M)^+$, 457, 431, 415, 371, 344. This was treated with benzyl bromide (21 μL, 0.18 mmol) and 110 μL (1 M solution in THF, 0.11 mmol) of tetrabutylammonium fluoride in THF (1.0 mL) according to procedure IV to give **22b** (31 mg, 78%): oil; IR (neat) 3450, 3020, 2990, 2960, 2860, 1750, 1726, 1684, 1504 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.34 (s, 5 H), 6.72 (m, 1 H), 5.80 (ddt, 1 H, J = 16, 10, 7 Hz), 5.40 (m, 1 H), 5.15 (br d, 1 H, J = 16 Hz), 5.15 (br d, 1 H, J = 10 Hz), 5.10 (s, 2 H), 4.2–4.7 (m, 5 H), 3.2–4.0 (m, 2 H), 3.71 (s, 3 H), 2.55 (m, 2 H), 1.52 (m, 6 H), 1.10 (m, 3 H); MS (EI method) m/z 448 $(M)^+$, 407, 364, 347, 320. Anal. Calcd for $C_{23}H_{32}O_7N_2$: C, 61.59; H, 7.19; N, 6.25. Found: C, 61.82; H, 7.35; N, 6.30.

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Registry No. **1a**, 101817-49-6; **1b**, 101817-50-9; **2a**, 101817-51-0; **2b**, 108543-86-8; **3a**, 106928-50-1; **3b**, 106928-49-8; **3c**, 106928-48-7; **3d**, 124097-05-8; **3e**, 124097-06-9; **4b**, 106928-46-5; **5b**, 106928-47-6; **6a**, 24210-19-3; **6b**, 110761-03-0; **6c**, 58561-04-9; **6d**, 63079-75-4; **6e**, 124021-52-9; **7b**, 124021-50-7; **7d**, 101817-56-5; **8a**, 57224-63-2; **8b**, 110761-05-2; **9a**, 5211-23-4; **9b**, 110761-01-8; **9c**, 59936-29-7; **10**, 73548-77-3; **11a**, 108634-98-6; **11b**, 24498-31-5; **12a**, 108634-97-5; **12b**, 55757-60-3; **13a**, 51987-73-6; **13b**, 2577-90-4; **13c**, 35909-92-3; **14**, 67010-43-9; **16**, 124021-51-8; **18a**, 33900-24-2; **18b**, 56762-93-7; **19**, 101756-79-0; **20a**, 124150-03-4; **20b**, 124150-04-5; **21a**, 124150-02-3; **21b**, 124021-53-0; **22a**, 101841-44-5; **22b**, 101817-52-1; t-$BuMe_2SiOTf$, 69739-34-0; Et_3SiH, 617-86-7; t-$BuMe_2SiH$, 29681-57-0; t-$BuMe_2SiO_2C$-Phe-OMe, 107897-41-6; (3*S*,4*S*)-t-$BuMe_2SiO_2CNHCH(i\text{-}Bu)CH(OSiMe_2Bu\text{-}t)CH_2COOEt$, 124042-12-2; $BrCH_2CH{=}CH_2$, 106-95-6; EtI, 75-03-6; *i*-PrI, 75-30-9; t-$BuMe_2SiO_2C$-Met-OMe, 110761-07-4; t-$BuMe_2SiO_2C$-L-$NHCH(CH_2CH{=}CH_2)CO$-L-Thr(THP)-OMe, 110761-06-3; $PhCH_2Br$, 100-39-0.