Highly Diastereoselective Conjugate Addition of Lithium Dialkylamides to α,β-Unsaturated Esters Having a Chiral Center at the γ-Position

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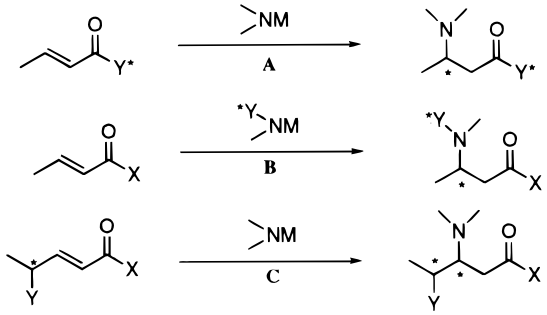
The conjugate addition of lithium amides **2** to *tert*-butyl 4-(OR)-substituted-2-pentenoates **1** produced a mixture of the *syn*- and *anti*-amino esters (**3** and **4**) in high yields. Sterically bulky OR groups, such as trityloxy and *tert*-butyldiphenylsilyloxy, gave the syn diastereomer **3** either exclusively or predominantly. The *syn*-selectivity may be explained by a modified Felkin−Anh model. The use of *tert*-butyldimethylsilyloxy as an OR group afforded a nearly 1:1 mixture of diastereoisomers, and the use of the smallest MeO group produced a 63:37 mixture of the *syn* **3** and *anti* isomer **4**. The presence of Me group at the α-position (C-2 position) of the enoate enhanced the *syn* diastereoselectivity up to 100%; the conjugate addition to *tert*-butyl 4-methoxy-2-methyl-2-pentenoate (**17**) gave the *syn*-isomer **18** exclusively. This enhancement may be explained by the combination of chelation and allylic strain model **19** in which the smallest H orients inside to avoid an allylic strain. A phenyl group at the γ-position enhanced the *anti* selectivity in the case of γ-alkoxy-α,β-enoates such as isopropyl 4-[(*tert*-butyldimethylsilyl)oxy]-4-phenyl-2-butenoate (**20**), and in the case of γ-alkyl-α,β-enoates such as *tert*-butyl 4-phenyl-2-pentenoate (**27**).

β-Amino acids are synthetic precursors of β-lactams and are also present in certain peptides. In this respect, enantioselective synthesis of β-amino acids is becoming an important and challenging synthetic problem. Among several methods for the synthesis of optically active β-amino acids, the conjugate addition of amine nucleophiles to α,β-unsaturated carbonyl compounds is one of the most popular and useful procedures.[1]

There are three possible ways for asymmetric induction in the conjugate addition of amine nucleophiles to Michael acceptors (Scheme 1): (1) the use of chiral auxiliaries Y* (process A); (2) the use of chiral amine nucleophiles Y*NM (process B); (3) the use of γ-chiral-α,β-unsaturated esters (process C). The chiral auxiliary method (A) has been studied widely and deeply,[2] and a high level of enantioselectivity has been accomplished. More recently, the conjugate addition of chiral lithium amides (B) was studied by Davies,[3] Hawkins,[4] Enders,[5] and our group,[6] and very high asymmetric induction has been achieved. However, little was known about the

Scheme 1



diastereoselectivity of 1,2-asymmetric induction in the conjugate addition of metal amides to α,β-unsaturated esters having a chiral center at the γ-position. We report how to enhance the 1,2-asymmetric induction and how to control the diastereoselectivity in the process C.

Result and Discussion

Before we started to investigate the diastereoselectivity of 1,2-asymmetric induction in the conjugate addition of metal amides, the addition of amines,[7] alkoxides,[8] and carbon nucleophiles[9] to α,β-enoates bearing a chiral center at the γ-position had been reported. The syn-selectivity was reported previously for the conjugate addition of benzylamine[7a,b] and various alkoxides[8] to

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(1) For review articles; (a) Cole, D. C. *Tetrahedron* **1994**, *50*, 9517. (b) Juaristi, E.; Quintana, D.; Escalante, J. *Aldrichim. Acta* **1994**, *27(1)*, 3. (c) Cardillo, G.; Tomasini, C. *Chem. Soc. Rev.* **1996**, 117.

(2) (a) d'Angelo, J.; Maddaluno, J. *J. Am. Chem. Soc.* **1986**, *108*, 8112. (b) Yamamoto,Y.; Asao, N.; Uyehara, T. *J. Am. Chem. Soc.* **1992**, *114*, 5427. (c) Mezrhab, B.; Dumas, F.; d'Angero, J.; Riche, C. *J. Org. Chem.* **1994**, *59*, 500. (d) Asao, N.; Uyehara, T.; Tsukada, N.; Yamamoto, Y.; *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2103. (e) Dumas, F.; Mezrhab, B.; d'Angelo, J. *J. Org. Chem.* **1996**, *61*, 2293.

(3) (a) Davies, S. G.; Ichihara, O. *Tetrahedron Asymmetry* **1991**, *2*, 183. (b) Davies, S. G.; Ichihara, O.; Walters, I. A. S. *Synlett* **1993**, 461. (c) Davies, S. G.; Garrido, N. M.; Ichihara, O.; Walters, I. A. S. *J. Chem. Soc., Chem. Commun.* **1993**, 1153. (d) Bunnage, M. E.; Davies, S. G.; Goodwin, C. J. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1375. (e) Davies, S. G.; Ichihara, O.; Walters, I. A. S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1141. (f) Costello, J. F.; Davies, S. G.; Ichihara, O. *Tetrahedron Asymmetry* **1994**, *5*, 1999. (g) Bunnage, M. E.; Burke, A. J.; Davies, S. G.; Goodwin, C. J. *Tetrahedron Asymmetry* **1995**, *6*, 165. (h) Davies, S. G.; Fenwick, D. R. *J. Chem. Soc., Chem. Commun.* **1995**, 1109.

(4) (a) Hawkins, J. M.; Fu, G. C. *J. Org. Chem.* **1986**, *51*, 2820. (b) Rudolf, K.; Hawkins, J. M.; Loncharich, J.; Houk, K. N. *J. Org. Chem.* **1988**, *53*, 3879. (c) Hawkins, J. M.; Lewis, T. A. *J. Org. Chem.* **1992**, *57*, 2114. (d) Hawkins, J. M.; Lewis, T. A. *J. Org. Chem.* **1994**, *59*, 649.

(5) (a) Enders, D.; Bettray, W.; Raabe, G.; Runsink, J *Synthesis* **1994**, 1322. (b) Enders, D.; Walh, H.; Bettray, W. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 455.

(6) (a) Asao, N.; Tsukada, N.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1993**, 1660. (b) Tsukada, N.; Shimada, T.; Gyoung, Y. S.; Asao, N.; Yamamoto, Y. *J. Org. Chem.* **1995**, *60*, 143.

(7) (a) Matsunaga, H.; Sakamaki, T.; Nagaoka, H.; Yamada, Y. *Tetrahedron Lett.* **1983**, *24*, 3009. (b) Dondoni, A.; Boscarato, A.; Marra, A. *Synlett* **1993**, 256. (c) For the addition to 5-alkoxy-2(5*H*)-furanones, de Lange, B.; van Bolhuis, F.; Feringa, B. L. *Tetrahedron* **1989**, *45*, 6799. (d) For the addition to 2-(hydroxyalkyl)propenoates, Perlmutter, P.; Tabone, M. *Tetrahedron Lett.* **1988**, *29*, 949. (e) Asao, N.; Shimada, T.; Tsukada, N.; Yamamoto, Y. *Tetrahedron Lett.* **1994**, *35*, 8425. (f) Hausermann, U. A.; Linden, A.; Song, J.; Hesse, M. *Helv. Chim. Acta* **1996**, *79*, 1995.

(8) Mulzer, J.; Kappert, M.; Huttner, G.; Jibril, I. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 704.

(9) For the most recent article, Yamamoto, Y.; Chounan, Y.; Nishii, S.; Ibuka, T.; Kitahara, H. *J. Am. Chem. Soc.* **1992**, *114*, 7652, and references cited therein.

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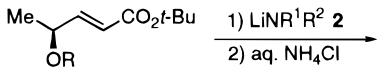
Table 1. Diastereoselectivity on the Conjugate Addition of 2 to 1

entry	enoates **1**	lithium amides **2**	diastereomer ratio *syn*-**3**:*anti*-**4**	total yield (isolated)/%
1	**1a**	**2a**	54:46	91
2	**1b**	**2a**	89:11	99
3	**1c**	**2a**	90:10	95
4	**1c**	**2b**	30:70	79
5	**1d**	**2a**	~100:−	77
6	**1e**	**2b**	63:37	83

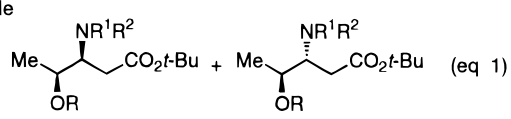
acyclic α,β-enoates and their derivatives. A more complex situation holds for the addition of organometallic reagents (carbon nucleophiles) to acyclic γ-alkoxy-α,β-enoates and enones;[9] the anti-selectivity has been observed frequently with organocopper reagents, but in certain cases organolithium and copper reagents have reacted with syn-selectivity. During our investigation, it was reported that the Michael addition of chiral γ-amino-substituted-α,β-unsaturated esters with nitrogen nucleophiles of the type $Me_3SiNHOSiMe_3$ and MeNHOH proceeded diastereoselectively.[10]

We first investigated the diastereoselectivity on the addition of lithium amides $LiNR^1R^2$ **2** to γ-silyloxy and alkoxy-α,β-unsaturated esters **1** (eq 1). The results are summarized in Table 1. The reaction of *tert*-butyldi-



1a; R = *t*-BuMe$_2$Si
1b; R = *t*-BuPh$_2$Si
1c; R = *i*-Pr$_3$Si
1d; R = Ph$_3$C
1e; R = Me

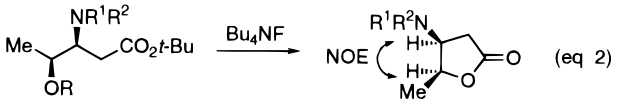
2a; R^1 = SiMe$_3$, R^2 = CH_2Ph
2b; $R^1 = R^2 = CH_2Ph$



3	**4**
3a; R = *t*-BuMe$_2$Si, R^1 = H, R^2 = CH_2Ph	**4a**; R = *t*-BuMe$_2$Si, R^1 = H, R^2 = CH_2Ph
3b; R = *t*-BuPh$_2$Si, R^1 = H, R^2 = CH_2Ph	**4b**; R = *t*-BuPh$_2$Si, R^1 = H, R^2 = CH_2Ph
3c; R = *i*-Pr$_3$Si, R^1 = H, R^2 = CH_2Ph	**4c**; R = *i*-Pr$_3$Si, R^1 = H, R^2 = CH_2Ph
3d; R = *i*-Pr$_3$Si, $R^1 = R^2 = CH_2Ph$	**4d**; R = *i*-Pr$_3$Si, $R^1 = R^2 = CH_2Ph$
3e; R = Ph$_3$C, R^1 = H, R^2 = CH_2Ph	**4e**; R = Ph$_3$C, R^1 = H, R^2 = CH_2Ph
3f; R = Me, $R^1 = R^2 = CH_2Ph$	**4f**; R = Me, $R^1 = R^2 = CH_2Ph$

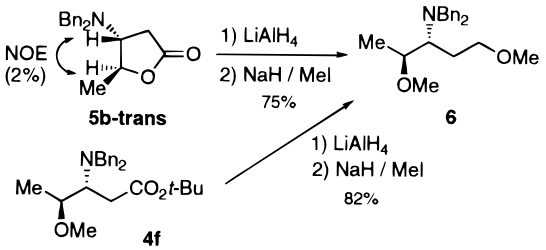
methylsilyl (TBDMS)-protected enoate **1a** with lithium benzyl(trimethylsilyl)amide **2a**[2b,d] gave an approximate 1:1 mixture of the *syn*-**3a** and *anti*-**4a** diastereomers (entry 1). The *syn*-diastereoselectivity increased to 89−90% with sterically bulkier *tert*-butyldiphenylsilyl **1b** and triisopropylsilyl protected enoate **1c** (entries 2 and 3). Chemical yields were very high in the reactions with **1b** and **1c**. The *syn*-diastereoselectivity reached to ~100% using the trityloxy derivative **1d** although the chemical yield decreased to 77% (entry 5). It is clear from these experiments that an increase of steric bulk at the OR group produces high *syn*-diastereoselectivity.

The *syn*-stereochemistry was confirmed by converting the *syn*-adduct **3a**, upon treatment with Bu_4NF, into the cis γ-butyrolactone **5a**; NOE effects were observed between the hydrogen at the β-position and that of the γ-position. A similar method was used for the structural determination of **3b**−**d** (eq 2). The ester group of **4f** was reduced by $LiAlH_4$, and the resulting alcohol was methylated with NaH/MeI, giving **6** in good yield. Desilylation of **4d** followed by lactonization, as mentioned above, gave **5b-trans**. The reduction of **5b-trans** with $LiAlH_4$ gave the corresponding diol, which was methylated with NaH/MeI in 75% yield. The spectroscopic data of the resulting dimethyl ether was completely identical to those of **6**, indicating the *anti*-stereochemistry of **4f**. **3e** was



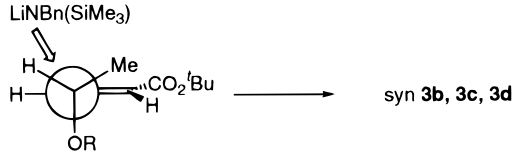
3a : R = Si(*t*-Bu)Me$_2$
R^1 = H, R^2 = Bn
3d : R = *i*-Pr$_3$Si
$R^1 = R^2$ = Bn

5a : R^1 = H, R^2 = Bn (71%)
NOE: 5%
5b-cis : $R^1 = R^2$ = Bn (71%)
NOE: 10%



converted to **7** in 77% yield by the three-component coupling (TCC) procedure.[6,7e] Treatment of **7** with Et-MgBr gave **8** in 81% yield. Detritylation of **8** gave **9** in 96% yield. Treatment of **9** with PPh_3/CCl_4 gave **10** in good yield. The TCC method was used for **3b**, giving **11** in 75% yield. Treatment of **11** with CF_3CO_2H followed by PPh_3/2,2′-dipyridyl disulfide gave **12** in 88% yield. Desilylation of **12** gave **13** in 77% yield. The reaction of **13** with PPh_3/CCl_4 afforded **14** in 92% yield. The acetyl group of **14** was removed, and the OH group was protected with TBDMSCl. The spectroscopic data of the resulting TBDMS derivative were completely identical to those of **10**, indicating the *syn*-stereochemistry of **3e** (Scheme 2).

The *syn*-selectivity for **1b**−**d** can be accounted for by a modified Felkin−Anh model **15**, in which OR group becomes anti, Me orients inside, and the nucleophile **2a** attacks from the less hindered outside position, as shown by the arrow. The coordination of lithium amide **2a** to



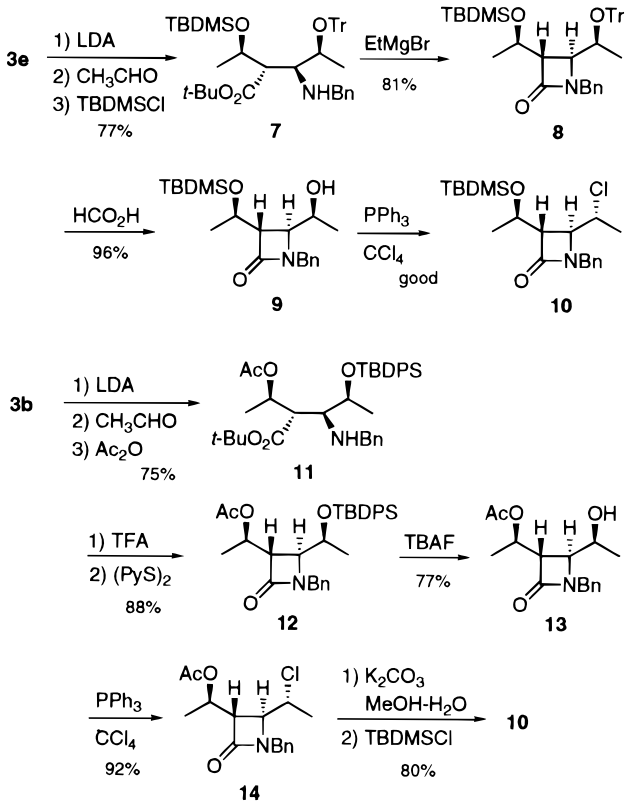
15
for **1b, 1c, 1d**

an oxygen atom of the OR group followed by delivery of the nitrogen nucleophile from the side of OR would not take place; the chelation-controlled delivery of nucleophile **2a** is not conceivable due to the presence of sterically very bulky silyloxy groups[11] in addition to the

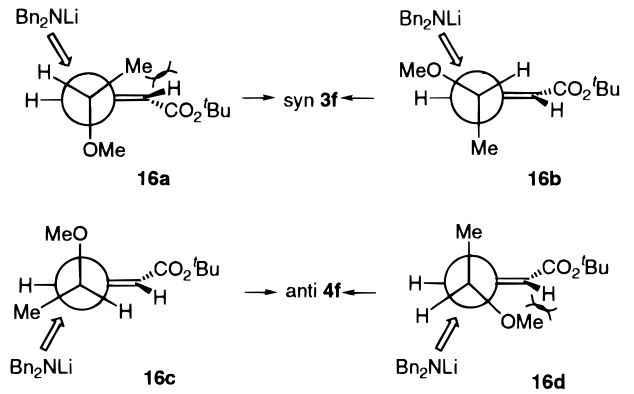
(10) Reetz, M. T.; Röhrig, D.; Harms, K.; Frenking, G. *Tetrahedron Lett.* **1994**, *35*, 8765.

(11) Guanti, G.; Banfi, L.; Narisano, E. *Tetrahedron Lett.* **1991**, *32*, 6939, and references cited therein.

Scheme 2

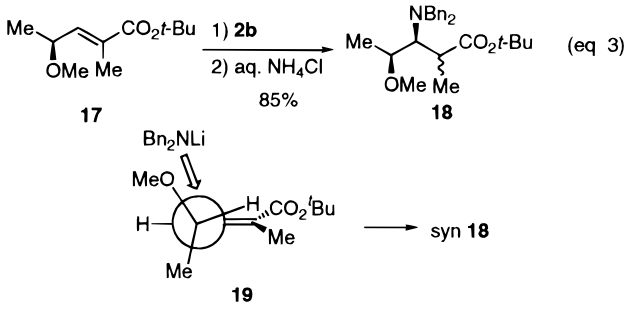


Scheme 3



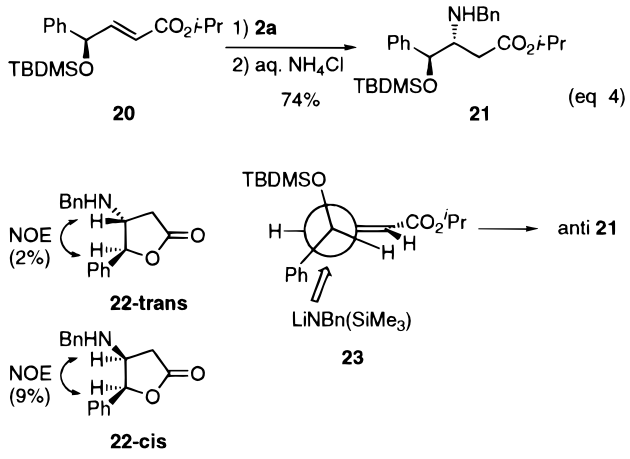
soft nature of the nucleophile. The addition of lithium dibenzylamide **2b** to **1c** afforded a 30:70 mixture of **3d** and **4d** in 79% yield, indicating that the diastereoselectivity depended very much upon the structural difference of lithium amide reagents, either **2a** or **2b** (entry 3 vs 4). Although the precise reason for the *anti*-preference is not clear, the participation of a chelation model is conceivable in the case of **2b** because of its hard characteristics in comparison with **2a**. Very interestingly, the reaction of γ-methoxy-substituted enoate **1e** with lithium dibenzylamide **2b** gave a 63:37 mixture of the *syn*-**3f** and *anti*-**4f** diastereomers in 83% yield (entry 6). Among four possible transition state geometries (Scheme 3), **16d** would be most unfavorable due to the allylic strain between OMe and vinylic hydrogen group, and due to the presence of the Me group at the *anti*-position.[12] Perhaps **16b** would be most favorable owing to both the chelation factor and minimum allylic strain, the presence of a small methyl group at the outside position, and the *anti* OMe. In the case of **16a**, OMe is anti and this is stereoelectronically satisfactory, but there is allylic strain between the inside Me and an olefinic hydrogen. In the case of **16c** there is steric repulsion between the incoming reagent and Me group. Therefore, the reason for the *syn*-preference in the case of **1e** is presumably due to both allylic strain and chelation factor.

To reduce ambiguous factors encountered when we considered probable transition state geometries in **16**, the addition to the α-methyl-substituted enoate **17** was investigated. Interestingly, the reaction of **17** with **2b** gave the *syn*-diastereomer **18** exclusively in 85% yield (eq 3). No *anti*-isomer was detected. A 1:1 mixture of



diastereoisomers concerning the α-position to ester group was obtained, although the stereochemistry at the α-position was not determined. The *syn*-stereochemistry of **18** was determined in the following way. Treatment of **3f** with LDA/MeI gave a 1:1 diastereomeric mixture of the corresponding α-methylated products (**X** and **Y**). Each isomer was separated by a silica gel column chromatography. The spectroscopic data of **X** and **Y** were identical to those of two diastereomers (**18a** and **18b**) separated from **18**. It is now clear that the reaction proceeds through **19**, in which the allylic strain is minimized, leading to the *syn*-isomer **18** exclusively. Furthermore, the above result suggests that chelation-controlled delivery of **2b** is involved in the reaction of **17**.

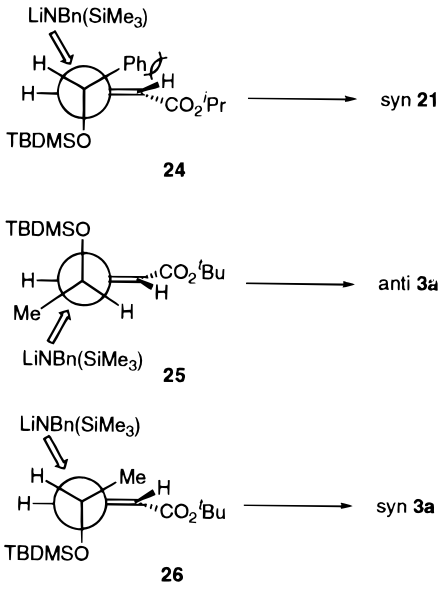
Next, we investigated the reaction of γ-phenyl-substituted enoate **20** in order to determine the effect of a substituent other than Me at the γ-position. The reaction of **20** with **2a** gave exclusively the *anti*-diastereoisomer **21** in 74% yield, with no detection of the *syn*-diastereoisomer (eq 4). Not only isopropyl ester **20**, but also ethyl and *tert*-butyl ester derivatives produced, upon treatment with **2a**, the corresponding *anti*-diastereoisomers exclu-



(12) (a) Anh, N. T.; Eisenstein, O. *Nouv. J. Chem.* **1977**, *1*, 61. (b) Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 3353. (c) Wong, S. S.; Paddon-Row, M. N. *J. Chem. Soc., Chem. Commun.* **1990**, 456.

(13) Yamamoto, Y.; Nishii, S.; Maruyama, K.; Komatsu, T.; Ito, W. *J. Am. Chem. Soc.* **1986**, *108*, 7778.

Scheme 4

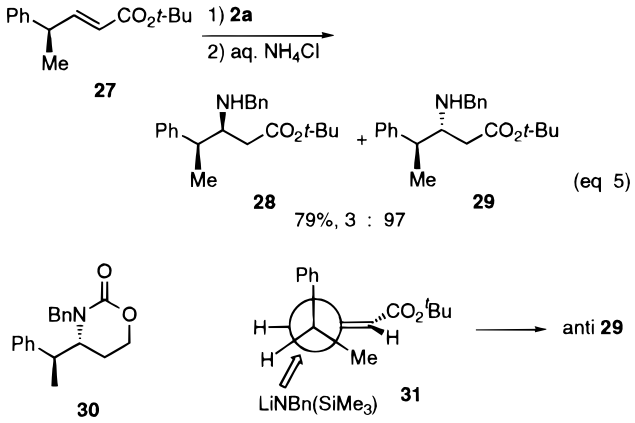


sively although chemical yields were lower than reactions of **20**. The *anti*-stereochemistry of **21** was determined by the similar method as mentioned above. Treatment of **21** with Bu_4NF gave trans-lactone (**22-trans**). The thermal reaction of **20** with benzylamine gave a 2:1 mixture of *syn*- and *anti*-(**21**) adducts. The *syn*-adduct was converted to the corresponding cis-lactone (**22-cis**). NOE effects (9%) between the hydrogens at the β-position and that of the γ-position were observed for **22-cis**, but NOE effects of **22-trans** were less than 2%. The *anti*-diastereoselectivity can be explained by an allylic strain model **23**. It should be noted that the reaction of **1a** (OTBDMS and Me substituent at the γ-position) with **2a** gave about 1:1 mixture of *syn*- and *anti*-diastereomers (entry 1, Table 1). The phenyl substituent enhanced the *anti*-selectivity dramatically. A possible explanation for this difference is as follows (Scheme 4). A serious steric repulsion (allylic strain) would arise between vinylic hydrogen and the phenyl group in the transition state geometry **24** which produces the *syn*-diastereomer. Accordingly, the reaction of **20** would proceed through **23** to afford the *anti*-diastereomer **21**. On the other hand, the steric repulsion between the Me group and vinylic hydrogen would be not so serious, and thus the reaction of **1a** would proceed through both transition state geometries **26** and **25**.

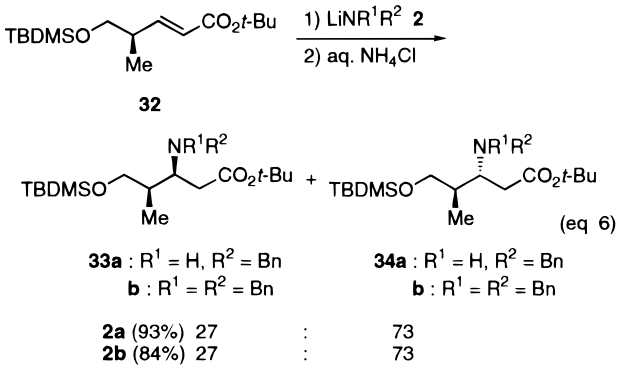
Finally, we investigated the diastereoselectivity in the reaction of enoates substituted with Ph and Me, and with Me and CH_2OTBDMS, at the γ-position. The reaction of **27** with **2a** gave a 3:97 mixture of *syn*-**28** and *anti*-**29** diastereomers in 79% yield (eq 5).

The *anti*-stereochemistry of **29** was confirmed by converting it, upon treatment with $LiAlH_4$ followed by cyclization with TCF (trichloromethyl chloroformate), into the cyclic carbamate **30**. The configuration and stereochemistry of **30** were reported previously (see Experimental Section).[13] The very high *anti*-selectivity is a reflection of a modified Felkin−Anh model **31** in which hydrogen orients outside, small Me group orients inside, and the bulky and electron-withdrawing phenyl group becomes anti. It is clear that not only an appropriate OR substituent at the γ-position but also a stereoelectronically suitable substituent (such as phenyl) produces high 1,2-asymmetric induction.

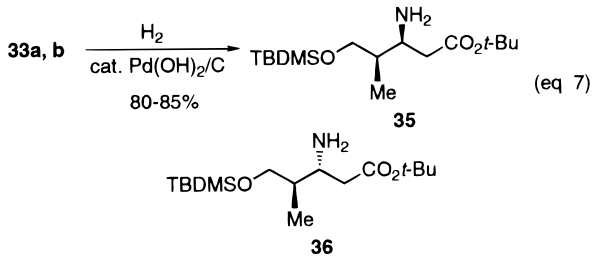
The reaction of **32** with **2a** gave a 27:73 mixture of *syn*-**33a** and *anti*-**34a** diastereomers in 93% yield. The



conjugate addition of **2b** to **32** afforded a 27:73 mixture of *syn*-**33b** and *anti*-**34b** diastereomers in 84% yield (eq 6). The *syn*-configurations of **33a** and **33b** were deter-

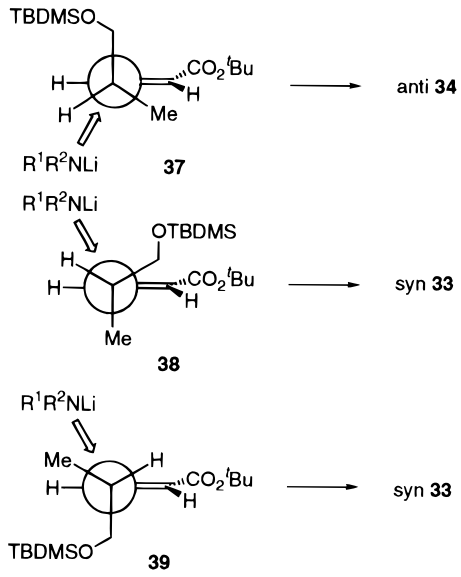


mined by converting them into the reduction product **35** via hydrogenation with catalytic $Pd(OH)_2/C$. The spectroscopic data of **35** were completely identical to those of authentic **35**,[6b] indicating the *syn* stereochemistry of **33a** and **33b**. Similarly, the *anti*-configurations of **34a** and **34b** were determined by converting them into the **36** (eq 7). The predominant formation of the *anti*-isomer **34** can



be explained by a modified Felkin−Anh model **37** (Scheme 5). Relatively low *anti*-selectivity is a reflection of weaker stereoelectronic influence of the CH_2OTBDMS group, in comparison with phenyl group in **31**, upon occupation at the anti position. Perhaps, other transition state geometries such as **38** and **39**, which lead to the *syn*-isomer **33**, would intervene in the reaction of **32**. Although relatively low diastereoselectivities were observed for the conjugate addition of achiral lithium amide reagents **2a** and **2b** to **32**, the use of certain chiral reagents lead to very high asymmetric induction. For example, the reaction of **32** with lithium *N*-benzyl-*N*-((*R*)-phenylethyl)-amide gave the *syn*-diastereomer with essentially 100% de and the reaction with lithium *N*-benzyl-*N*-((*S*)-phenylethyl)amide gave the *anti*-diastereomer exclusively.[6b] Similarly, the addition of lithiated (*R*)-3,5-dihydro-4*H*-dinapth[2,1-*c*:1′,2′-*e*]azepine to **32** afforded 100% de.[4c]

Scheme 5



Accordingly, the asymmetric induction at the β-position of **32** is controlled completely by the chirality of the lithium amide reagents, and the effect of the chirality at the γ-carbon upon the asymmetric induction is very small.

Conclusion

Sterically bulky OR group at the γ-position of enoates, such as trityloxy and *tert*-butyldiphenylsilyloxy, produces a *syn*-diastereoisomer either exclusively or very predominantly. The *syn*-selectivity can be explained by a modified Felkin−Anh model **15**. The reaction of **1e** with lithium dibenzylamide **2b** gives a 63:37 mixture of the *syn*-**3f** and *anti*-**4f** isomer, but the presence of Me group at the α-position of enoate enhances the *syn*-diastereoselectivity up to 100%. This enhancement can be explained by the allylic strain in the transition state geometry. A phenyl group at the γ-position enhances the *anti*-diastereoselectivity in the case of γ-alkoxy-α,β-enoates, and in the case of γ-alkyl-α,β-enoates.

Experimental Section

(*E*)-*tert*-Butyl 4-((*tert*-Butyldimethylsilyl)oxy)-2-pentenoate (1a). To a CH_2Cl_2 (50 mL) solution of ethyl lactate (5.7 mL, 50 mmol) at 0 °C were added imidazole (4.1 g, 60 mmol) and TBDMSCl (8.3 g, 55 mmol), and the mixture was stirred overnight at room temperature. Water (50 mL) was added, and the mixture was extracted with CH_2Cl_2, washed with brine, dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was dissolved in toluene (50 mL), and a 1.5 M toluene solution of DIBAL (iBu$_2$AlH, 33 mL, 50 mmol) was added dropwise in 15 min at −78 °C under argon atmosphere. The mixture was stirred for 80 min, and water (27 mL) was added slowly. The mixture was stirred overnight at room temperature, dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was used for further manipulation without purification. To a suspension of NaH (1.5 g, 37 mmol, 60% in mineral oil) in *n*-hexane (70 mL) at 0 °C under argon atmosphere was added trimethyl phosphonoacetate (7.2 mL, 44 mmol), and the mixture was stirred for 30 min. An *n*-hexane (20 mL) solution of the oil obtained above was added. The resulting mixture was stirred for 15 min at 0 °C and stirred for 1 h at room temperature. Addition of 100 mL of H_2O, extraction with ether, washing with brine, drying with anhydrous $MgSO_4$, concentration under reduced pressure, and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 20/1) gave the *E*- and *Z*-methyl ester (4.70 g, 39%, E/Z = 84/16). To a THF (30 mL) solution of 2-methyl-2-propanol (3.8 mL, 40 mmol) under argon atmosphere at 0 °C was added dropwise in 10 min a 1.65 M *n*-hexane solution of *n*-BuLi (17 mL, 28 mmol). The mixture was stirred for 1 h, and a THF (15 mL) solution of *E*-methyl ester (3.4 g, 13.9 mmol) was added and stirred overnight. The mixture was further stirred for 2 h at room temperature. Addition of excess aqueous saturated NH_4Cl, extraction with ether, washing with brine, drying with anhydrous $MgSO_4$, concentration under reduced pressure, and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 10/1) afforded **1a** (3.40 g, 86%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.82 (dd, J = 4.4, 15.3 Hz, 1H), 5.88 (dd, J = 1.9, 15.3 Hz, 1H), 4.43 (ddq, J = 1.9, 4.4, 6.4 Hz, 1H), 1.49 (s, 9H), 1.25 (d, J = 6.4 Hz, 3H), 0.91 (s, 9H), 0.07 (s, 6H); IR (neat) 2978−2858, 1716, 1367, 1302, 1258, 1153 cm^{-1}. Anal. Calcd for $C_{15}H_{30}O_3Si$ (286.49): C, 62.89; H, 10.55. Found: C, 62.72; H, 10.42.

(*E*)-*tert*-Butyl 4-((*tert*-Butyldiphenylsilyl)oxy)-2-pentenoate (1b). **1b** was prepared from ethyl lactate and Ph_2(tBu)SiCl as described above for **1a** (56% yield from ethyl lactate). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.71−7.32 (m, 10H), 6.78 (dd, J = 5.0, 16.0 Hz, 1H), 5.86 (dd, J = 1.5, 16.0 Hz, 1H), 4.43 (ddq, J = 1.5, 5.0, 6.5 Hz, 1H), 1.48 (s, 9H), 1.13 (d, J = 6.5 Hz, 3H), 1.08 (s, 9H); IR (CCl_4) 3200−2885, 1723, 1380, 1314, 1168 cm^{-1}. Anal. Calcd for $C_{25}H_{34}O_3Si$ (410.63): C, 73.13; H, 8.35. Found: C, 72.85; H, 8.22.

(*E*)-*tert*-Butyl 4-((Triisopropylsilyl)oxy)-2-pentenoate (1c). **1c** was prepared from ethyl lactate and iPr$_3$SiCl as described above for **1a** (58% yield from ethyl lactate). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.82 (dd, J = 4.7, 15.6 Hz, 1H), 5.90 (dd, J = 1.8, 15.6 Hz, 1H), 4.54 (ddq, J = 1.8, 4.7, 6.3 Hz, 1H), 1.48 (s, 9H), 1.28 (d, J = 6.3 Hz, 3H), 1.06 (br s, 21H); IR (neat) 2963−2868, 1717, 1367, 1300, 1153, 1094 cm^{-1}. Anal. Calcd for $C_{18}H_{36}O_3Si$ (328.57): C, 65.80; H, 11.04. Found: C, 65.86; H, 11.27.

(4*S*)-(*E*)-*tert*-Butyl 4-(Trityloxy)-2-pentenoate (1d). To a CH_2Cl_2 (80 mL) solution of (*S*)-ethyl lactate (11.3 mL, 100 mmol) under argon atmosphere were added triethylamine (20.9 mL, 150 mmol), 4-(dimethylamino)pyridine (0.49 g, 0.004 mmol), and trityl chloride (27.0 g, 110 mmol), and the mixture was refluxed for 25 h and then cooled to room temperature. Addition of excess H_2O, extraction with CH_2Cl_2, washing with brine, drying with anhydrous Na_2SO_4, concentration under reduced pressure, and filtration through silica gel (using ethyl acetate as a eluent) gave a crude product, which was used for further manipulation as described above for **1a** (80% yield from ethyl lactate). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.51−7.16 (m, 15H), 6.36 (dd, J = 6.2, 15.4 Hz, 1H), 5.30 (dd, J = 1.3, 15.4 Hz, 1H), 4.19 (ddq, J = 1.3, 6.2, 6.6 Hz, 1H), 1.41 (s, 9H), 1.10 (d, J = 6.6 Hz, 3H); IR (CCl_4) 3012−2780, 1725, 1460, 1319, 1306, 1163 cm^{-1}; $[\alpha]^{24}_D$ −43.4° (c 1.00, $CHCl_3$). Anal. Calcd for $C_{28}H_{30}O_3$ (414.55): C, 81.13; H, 7.29. Found: C, 80.88; H, 7.53.

(*E*)-*tert*-Butyl 4-Methoxy-2-pentenoate (1e). To a suspension of NaH (3.6 g, 120 mmol, 60% in mineral oil) in THF (130 mL) at 0 °C under argon atmosphere was added ethyl lactate (11.3 mL, 100 mmol), and the mixture was stirred for 30 min. MeI (9.3 mL, 120 mmol) was added, and the resulting mixture was stirred for 4 h at room temperature. Addition of excess aqueous saturated NH_4Cl, extraction with ether, washing with brine, drying with anhydrous $MgSO_4$, and concentration under reduced pressure gave a crude product, which was used for further manipulation as described above for **1a** (46% yield from ethyl lactate). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.72 (dd, J = 6.2, 15.7 Hz, 1H), 5,89 (dd, J = 1.1, 15.7 Hz, 1H), 3.89 (ddq, J = 1.1, 6.2, 6.6 Hz, 1H), 3.31 (s, 9H), 1.27 (d, J = 6.6 Hz, 3H) ; IR (neat) 2980−2824, 1717, 1367, 1302, 1259, 1153 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O_3$ (186.25): C, 64.49; H, 9.74. Found: C, 64,58; H, 9.58.

General Procedure for the Conjugate Addition of 2a or 2b to α,β-Unsaturated Enones 1a−e, 17, 20, 27, and 32.[6b] To a THF (20 mL) solution of a dialkylamine (4.2 mmol) under argon atmosphere at −78 °C was added dropwise a 1.65 M *n*-hexane solution of *n*-BuLi (4.1 mmol). The mixture was stirred for 30 min. A THF (3 mL) solution of the α,β-unsaturated enone (2.0 mmol) was added, and the resulting

mixture was stirred for 1.5 h. Addition of excess aqueous saturated NH_4Cl, extraction with ether, washing with brine, drying with anhydrous Na_2SO_4, concentration under reduced pressure, and purification with silica gel column chromatography (using *n*-hexane/ethyl acetate as an eluent) gave the adducts. The reaction of **1a** with **2a**: 91% yield, **3a**/**4a** = 54/46. The reaction of **1b** with **2a**: 99% yield, **3b**/**4b** = 89/11. The reaction of **1c** with **2a**: 95% yield, **3c**/**4c** = 90/10. The reaction of **1c** with **2b**: 79% yield, **3d**/**4d** = 30/70. The reaction of **1d** with **2a**: 77% yield, **3e**/**4e** = 100/0. The reaction of **1e** with **2b**: 83% yield, **3f**/**4f** = 63/37. The reaction of **17** with **2b**: 85% yield, only **18** (1:1 mixture of diastereomers concerning the α-position to ester group). The reaction of **20** with **2a**: 74% yield, only **21**. The reaction of **27** with **2a**: 79% yield, **28**/**29** = 3/97. The reaction of **32** with **2a**: 93% yield, **33a**/**34a** = 27/73. The reaction of **32** with **2b**: 93% yield, **33b**/**34b** = 27/73.

(3*S,4*S**)-*tert*-Butyl 3-(*N*-Benzylamino)-4-((*tert*-butyldimethylsilyl)oxy)pentanoate (3a).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.36−7.18 (m, 5H), 3.90 (dq, J = 4.5, 6.1 Hz, 1H), 3.87 (d, J = 13.1 Hz, 1H), 3.77 (d, J = 13.1 Hz, 1H), 2.96 (ddd, J = 4.5, 5.2, 7.2 Hz, 1H), 2.48 (dd, J = 5.0, 15.0 Hz, 1H), 2.29 (dd, J = 7.2, 15.0 Hz, 1H), 1.44 (s, 9H), 1.14 (d, J = 6.1 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H); IR (neat) 2976−2857, 1727, 1367, 1257, 1153 cm^{-1}. Anal. Calcd for $C_{22}H_{39}NO_3Si$ (393.65): C, 67.13; H, 9.99; N, 3.56. Found: C, 67.02; H, 10.08; N, 3.56.

(3*S,4*S**)-*tert*-Butyl 3-(*N*-Benzylamino)-4-((*tert*-butyldiphenylsilyl)oxy)pentanoate (3b).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.69−7.16 (m, 15H), 3.96 (dq, J = 6.0, 6.0 Hz, 1H), 3.57 (d, J = 13.0 Hz, 1H), 3.50 (d, J = 13.0 Hz, 1H), 3.04 (ddd, J = 3.8, 6.0, 9.0 Hz, 1H), 2.68 (dd, J = 3.8, 15.1 Hz, 1H), 2.22 (dd, J = 9.0, 15.1 Hz, 1H), 1.42 (s, 9H), 1.04 (s, 9H), 1.02 (d, J = 6.0 Hz, 3H); IR (neat) 2975−2857, 1727, 1367, 1154, 1147, 1111 cm^{-1}. Anal. Calcd for $C_{32}H_{43}NO_3Si$ (517.79): C, 74.23; H, 8.37; N, 2.71. Found: C, 74.16; H, 8.32; N, 2.71.

(3*S,4*S**)-*tert*-Butyl 3-(*N*-Benzylamino)-4-((triisopropylsilyl)oxy)pentanoate (3c).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35−7.18 (m, 5H), 4.07 (dq, J = 4.2, 6.1 Hz, 1H), 3.84 (d, J = 13.2 Hz, 1H), 3.78 (d, J = 13.2 Hz, 1H), 3.08 (ddd, J = 3.8, 4.2, 8.7 Hz, 1H), 2.63 (dd, J = 3.8, 15.4 Hz, 1H), 2.18 (dd, J = 8.7, 15.4 Hz, 1H), 1.44 (s, 9H), 1.14 (d, J = 6.1 Hz, 3H), 1.04 (br s, 21H); IR (neat) 2965−2867, 1729, 1367, 1157, 1102 cm^{-1}. Anal. Calcd for $C_{25}H_{45}NO_3Si$ (435.73): C, 68.91; H, 10.41; N, 3.21. Found: C, 69.00; H, 10.44; N, 3.34.

(3*S,4*S**)-*tert*-Butyl 3-(*N*,*N*-Dibenzylamino)-4-((triisopropylsilyl)oxy)pentanoate (3d).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.34−7.11 (m, 10H), 4.13 (dq, J = 5.7, 6.2 Hz, 1H), 3.72, 3.65 (2d, J = 13.9 Hz, each 2H), 3.11 (ddd, J = 4.8, 5.7, 7.6 Hz, 1H), 2.63 (dd, J = 4.8, 15.0 Hz, 1H), 2.55 (dd, J = 7.6, 15.0 Hz, 1H), 1.48 (s, 9H), 1.15 (d, J = 6.2 Hz, 3H), 1.05 (bs, 21H); IR (neat) 2943−2866, 1728, 1454, 1367, 1256, 1157 cm^{-1}. Anal. Calcd for $C_{32}H_{51}NO_3Si$ (525.85): C, 73.09; H, 9.78; N, 2.66. Found: C, 73.31; H, 10.02; N, 2.72.

(3*S*,4*S*)-*tert*-Butyl 3-(*N*-Benzylamino)-4-(trityloxy)pentanoate (3e). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.51−7.10 (m, 20H), 3.73 (dq, J = 3.6, 6.1 Hz, 1H), 3.41 (s, 2H), 2.76 (dd, J = 2.8, 15.6 Hz, 1H), 2.72 (ddd, J = 2.8, 3.6, 10.6 Hz, 1H), 2.16 (dd, J = 10.6, 15.6 Hz, 1H), 1.42 (s, 9H), 0.81 (d, J = 6.1 Hz, 3H); IR (neat) 3086−2874, 1732, 1488, 1367, 1281, 1148 cm^{-1}; $[\alpha]^{24}_D$ −8.88° (*c* 1.00, $CHCl_3$). Anal. Calcd for $C_{35}H_{39}NO_3$ (521.70): C, 80.58; H, 7.53; N, 2.68. Found: C, 80.37; H, 7.78; N, 2.71.

(3*S,4*S**)-*tert*-Butyl 3-(*N*,*N*-Dibenzylamino)-4-methoxypentanoate (3f).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35−7.20 (m, 10H), 3.98 (d, J = 13.9 Hz, 2H), 3.38 (dq, J = 6.2, 6.6 Hz, 1H), 3.23 (s, 3H), 3.06 (ddd, J = 4.8, 6.6, 14.8 Hz, 1H), 2.62 (dd, J = 4.8, 14.6 Hz, 1H), 2.27 (dd, J = 8.0, 14.6 Hz, 1H), 1.44 (s, 9H), 1.11 (d, J = 6.2 Hz, 3H); IR (neat) 2976−2820, 1728, 1454, 1366, 1256, 1161, 1128 cm^{-1}. Anal. Calcd for $C_{24}H_{33}NO_3$ (383.53): C, 75.16; H, 8.67; N, 3.65. Found: C, 75.30; H, 8.90; N, 3.70.

(3*R,4*S**)-*tert*-Butyl 3-(*N*-Benzylamino)-4-((*tert*-butyldimethylsilyl)oxy)pentanoate (4a).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35−7.18 (m, 5H), 3.97 (dq, J = 3.9, 6.2 Hz, 1H), 3.79 (s, 2H), 2.97 (ddd, J = 3.9, 6.0, 7.3 Hz, 1H), 2.38 (dd, J = 6.0, 14.7 Hz, 1H), 2.32 (dd, J = 7.3, 14.7 Hz, 1H), 1.45 (s, 9H), 1.14 (d, J = 6.2 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); IR (neat) 2976−2857, 1728, 1367, 1257, 1154, 1097 cm^{-1}. Anal. Calcd for $C_{22}H_{39}NO_3Si$ (393.65): C, 67.13; H, 9.99; N, 3.56. Found: C, 66.76; H, 10.05; N, 3.58.

(3*R,4*S**)-*tert*-Butyl 3-(*N*-Benzylamino)-4-((*tert*-butyldiphenylsilyl)oxy)pentanoate (4b).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.68−7.18 (m, 15H), 4.01 (dq, J = 2.8, 6.4 Hz, 1H), 3.69 (s, 2H), 3.03 (dt, J = 2.8, 6.5 Hz, 1H), 2.38 (d, J = 6.5 Hz, 2H), 1.39 (s, 9H), 1.04 (s, 9H), 1.01 (d, J = 6.4 Hz, 3H); IR (neat) 3070−2857, 1727, 1427, 1367, 1153 cm^{-1}. Anal. Calcd for $C_{32}H_{43}NO_3Si$ (517.79): C, 74.23; H, 8.37; N, 2.71. Found: C, 74.23; H, 8.21; N, 3.02.

(3*R,4*S**)-*tert*-Butyl 3-(*N*-Benzylamino)-4-((triisopropylsilyl)oxy)pentanoate (4c).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.36−7.18 (m, 5H), 4.11 (dq, J = 3.2, 6.2 Hz, 1H), 3.80 (s, 2H), 3.11 (ddd, J = 3.2, 6.2, 7.3 Hz, 1H), 2.41 (dd, J = 7.3, 14.6 Hz, 1H), 2.30 (dd, J = 6.2, 14.6 Hz, 1H), 1.45 (s, 9H), 1.19 (d, J = 6.2 Hz, 3H), 1.05 (br s, 21H); IR (neat) 2964−2867, 1728, 1463, 1384, 1367, 1154, 1100 cm^{-1}. Anal. Calcd for $C_{25}H_{45}NO_3Si$ (435.73): C, 68.91; H, 10.41; N, 3.21. Found: C, 68.88; H, 9.98; N, 3.10.

(3*R,4*S**)-*tert*-Butyl 3-(*N*,*N*-Dibenzylamino)-4-((triisopropylsilyl)oxy)pentanoate (4d).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.39−7.15 (m, 10H), 4.02 (d, J = 13.6 Hz, 1H), 3.98 (dq, J = 6.2, 6.2 Hz, 1H), 3.40 (d, J = 13.6 Hz, 1H), 3.03 (ddd, J = 5.9, 6.2, 7.3 Hz, 1H), 2.75 (dd, J = 7.3, 15.0 Hz, 1H), 2.61 (dd, J = 5.9, 15.0 Hz, 1H), 1.46 (s, 9H), 1.20 (d, J = 6.2 Hz, 3H), 0.98 (bs, 21H); IR (neat) 2943−2866, 1726, 1454, 1376, 1150, 1099 cm^{-1}. Anal. Calcd for $C_{32}H_{51}NO_3Si$ (525.85): C, 73.09; H, 9.78; N, 2.66. Found: C, 72.73; H, 10.03; N, 2.70.

(3*R,4*S**)-*tert*-Butyl 3-(*N*-Benzylamino)-4-methoxypentanoate (4f).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.38−7.19 (m, 10H), 3.98 (d, J = 13.7 Hz, 2H), 3.36 (d, J = 13.7 Hz, 2H), 3.32 (dq, J = 5.3, 6.6 Hz, 1H), 3.24 (s, 3H), 3.04 (dt, J = 5.3, 6.7 Hz, 1H), 2.58 (d, J = 6.7Hz, 2H), 1.44 (s, 9H), 1.15 (d, J = 6.6 Hz, 3H) ; IR (neat) 2976−2822, 1724, 1367, 1256, 1148, 1103 cm^{-1}. Anal. Calcd for $C_{24}H_{33}NO_3$ (383.53): C, 75.16; H, 8.67; N, 3.65. Found: C, 75.46; H, 9.01; N, 3.75.

(3*S,4*S**)-3-(*N*-Benzylamino)-4-methyl-4-butanolide (5a).** To a THF (2 mL) solution of **3b** (67.3 mg, 0.13 mmol) under argon atmosphere at 0 °C was added dropwise a 1.0 M THF solution of tetrabutylammonium fluoride (0.26 mL, 0.26 mmol), and the mixture was stirred for overnight at room temperature. Addition of excess aqueous saturated NH_4Cl, extraction with ether, washing with brine, drying with anhydrous $MgSO_4$, concentration under reduced pressure, and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 10/1) gave **5a** (19 mg, 71%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.37−7.24 (m, 5H), 4.67 (dq, J = 6.5, 5.6 Hz, 1H), 3.84 (d, J = 13.0 Hz, 1H), 3.72 (d, J = 13.0 Hz, 1H), 3.56 (ddd, J = 6.9, 5.6, 5.3 Hz, 1H), 2.66 (dd, J = 17.0, 6.9 Hz, 1H), 2.48 (dd, J = 17.0, 5.3 Hz, 1H), 1.51 (broad s, 1H), 1.39 (d, J = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 175.29, 139.28, 128.63, 128.03, 127.43, 81.88, 60.32, 51.90, 36.12, 19.50; IR (neat) 3330, 3040−2860, 1770, 1180, 1150 cm^{-1}.

(3*R,4*S**)-3-(*N*,*N*-Dibenzylamino)-4-methyl-4-butanolide (5b-trans). 5b-trans** was prepared from **4d** as described above for **5a** (78% yield). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.33−7.19 (m, 10H), 4.60 (dq, J = 5.9, 5.9 Hz, 1H), 3.72, 3.48 (2d, J = 13.9 Hz, each 2H), 3.33 (ddd, I = 6.0, 7.0, 8.1 Hz, 1H), 2.65 (dd, J = 7.0, 19.0 Hz, 1H), 2.57 (dd, J = 8.1, 19.0 Hz, 1H), 1.31 (d, J = 6.6 Hz, 3H); IR (neat) 2976−2806, 1782, 1495, 1454, 1379, 1175 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_2$ (295.38): C, 77.26; H, 7.17; N, 4.74. Found: C, 76.91; H, 7.47; N, 4.66.

(3*S,4*S**)-3-(*N*,*N*-Dibenzylamino)-4-methyl-4-butanolide (5b-cis). 5b-cis** was prepared from **3d** as described above for **5a** (71% yield). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.38−7.22 (m, 10H), 4.68 (dq, J = 6.5, 6.5 Hz, 1H), 3.71 (d, J = 14.1, 2H), 3.56 (ddd, J = 6.5, 8.0, 4.8 Hz, 1H), 3.47 (d, I = 14.1 Hz, 2H), 2.69 (dd, J = 4.8, 18.0 Hz, 1H), 2.44 (dd, J = 8.1, 18.0 Hz, 1H), 1.55 (d, J = 6.5 Hz, 3H).

(3*R,4*S**)-3-(*N*,*N*-Dibenzylamino)-1,4-dimethoxypentane (6).** To an ether (10 mL) solution of **3f** (84 mg, 0.22 mmol) was added $LiAlH_4$ (17 mg, 0.44 mmol) at 0 °C, and the mixture was stirred for 2 h. Water (17 μL) and 15% aqueous NaOH (17 μL) was added, and the mixture was dried with

anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was used for further manipulation. To a suspension of NaH (53 mg, 1.32 mmol, 60% in mineral oil) in THF (5 mL) at 0 °C under argon atmosphere was added a THF (2 mL) solution of the oil obtained above, and the mixture was stirred for 30 min at room temperature. MeI (70 μL, 1.1 mmol) was added and the resulting mixture was stirred for 12 h. Addition of excess aqueous saturated NH_4Cl, extraction with ether, washing with brine, drying with anhydrous $MgSO_4$, concentration under reduced pressure, and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 8/1) gave **6** (58 mg, 82%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.34−7.17 (m, 10H), 3.77, 3.52 (2d, J = 13.9 Hz, each 2H), 3.48 (dq, J = 4.8, 6.2 Hz, 1H), 3.42 (dd, J = 1.5, 7.0 Hz, 1H), 3.30 (s, 3H), 3.24 (s, 3H), 2.53 (ddd, J = 4.8, 4.8, 7.7 Hz, 1H), 1.82 (dddd, J = 1.5, 2.0, 4.8, 13.9 Hz, 1H), 1.60 (dddd, J = 1.5, 2.0, 4.8, 13.9 Hz, 1H), 1.09 (d, J = 6.2 Hz, 3H); IR (neat) 2970−2822, 1495, 1454, 1371, 1117, 1086 cm^{-1}. Anal. Calcd for $C_{21}H_{29}NO_2$ (327.47): C, 77.03; H, 8.93; N, 4.28. Found: C, 76.74; H, 8.80; N, 4.26.

(2*S*,3*S*,4*S*)-*tert*-Butyl 3-(*N*-Benzylamino)-4-(trityloxy)-2-[(*R*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl]pentanoate (7). To a THF (50 mL) solution of a *N*-benzyl(trimethylsilyl)-amine (4.1 mL, 21 mmol) under argon atmosphere at −78 °C was added dropwise a 1.76 M *n*-hexane solution of *n*-BuLi (11 mL, 20 mmol). The mixture was stirred for 30 min, and a THF (10 mL) solution of **1d** (5.0 g, 12 mmol) was added at −78 °C. After 1.5 h, MeOH (0.89 mL, 22 mmol) was added, and the mixture was stirred for 20 min at −78 °C. To this mixture under argon was added slowly in 10 min a THF (40 mL) solution of LDA (100 mmol) precooled at −78 °C. After 20 min, a 5 M THF solution of acetaldehyde (30 mL, 150 mmol) was added slowly. The mixture was stirred for 1.5 h at −78 °C. The mixture was quenched with excess aqueous saturated NH_4Cl, extracted with ether, washed with brine, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 mL), and imidazole (1.2 g, 17 mmol) and TBDMSCl (3.0 g, 20 mmol) were added at 0 °C. The mixture was stirred overnight at room temperature. Water (20 mL) was added, and the mixture was extracted with CH_2Cl_2, washed with brine, dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. Purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 10/1) gave **7** (6.3 g, 77%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.51−7.14 (m, 20H), 4.26 (d, J = 6.0, 6.6 Hz, 1H), 3.74 (dq, J = 3.5, 6.0 Hz, 1H), 3.44 (s, 2H), 2.98 (dd, J = 5.0, 6.6 Hz, 1H), 2.86 (dd, J = 3.5, 5.0 Hz, 1H), 1.42 (s, 9H), 1.22 (d, J = 6.0 Hz, 3H), 0.91 (s, 9H), 0.76 (d, J = 6.6 Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H); IR (CCl_4) 2980−2885, 1732, 1462, 1382, 1260, 1167, 1102 cm^{-1}; $[\alpha]^{20}_D$ +2.80° (*c* 0.995, $CHCl_3$). Anal. Calcd for $C_{43}H_{57}NO_4Si$ (680.02): C, 75.95; H, 8.45; N, 2.06. Found: C, 76.27; H, 8.81; N, 2.10.

(3*S*,4*S*)-1-*N*-Benzyl-3-[(*R*)-1-((*tert*-Butyldimethylsilyl)oxy)ethyl]-4-[(*S*)-1-(trityloxy)ethyl]-2-azetidinone (8). To a THF (15 mL) solution of **7** (0.43 g, 0.63 mmol) under argon atmosphere at 0 °C was added 0.9 M THF solution of EtMgBr (2.1 mL, 1.9 mmol), and the mixture was stirred for 2 h. Addition of excess aqueous saturated NH_4Cl, extraction with ether, washing with brine, drying with anhydrous Na_2SO_4, concentration under reduced pressure, and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 5/1) gave **8** (0.31 g, 81%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.40−7.08 (m, 20H), 4.24 (s, 2H), 4.22 (dq, J = 3.5, 6.2 Hz, 1H), 3.51 (dd, J = 3.5, 2.2 Hz, 1H), 3.46 (dq, J = 3.5, 6.2 Hz, 1H), 2.96 (dd, J = 2.2, 3.5 Hz, 1H), 1.14 (d, J = 6.2 Hz, 3H), 0.85 (s, 9H), 0.70 (d, J = 6.2 Hz, 3H), 0.06 (s, 3H), 0.02 (s, 3H); IR (CCl_4) 3062−2856, 1736, 1448, 1252, 1219, 1198, 1074 cm^{-1}; $[\alpha]^{20}_D$ −12.1° (*c* 0.60, $CHCl_3$). Anal. Calcd for $C_{39}H_{47}NO_3Si$ (605.90): C, 77.31; H, 7.82; N, 2.31. Found: C, 76.92; H, 7.81; N, 2.35.

(3*S*,4*S*)-1-*N*-Benzyl-3-[(*R*)-1-((*tert*-Butyldimethylsilyl)oxy)ethyl]-4-[(*S*)-1-hydroxyethyl]-2-azetidinone (9). To a ether (4 mL) solution of **8** (0.31 g, 0.51 mmol) at room temperature was added HCO_2H (6 mL), and the mixture was stirred for 7 min. Addition of ether, quenching with aqueous saturated $NaHCO_3$, extraction with ether, washing with brine, drying with anhydrous Na_2SO_4, concentration under reduced pressure, and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 1/1) gave **9** (0.18 g, 96%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35−7.27 (m, 5H), 4.56 (d, J = 15.2 Hz, 1H), 4.39 (d, J = 15.2Hz, 1H), 4.16 (dq, J = 5.4, 6.2 Hz, 1H), 3.73 (dq, J = 7.2, 6.4 Hz, 1H), 3.48 (dd, J = 7.2, 2.2 Hz, 1H), 2.79 (dd, J = 5.4, 2.2 Hz, 1H), 1.24 (d, J = 6.2 Hz, 3H), 1.13 (d, J = 6.4 Hz, 3H), 0.86 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); IR (neat) 3595, 3448, 2990−2870, 1770, 1471, 1392, 1267, 1149, 1058 cm^{-1}; $[\alpha]^{20}_D$ −12.1° (*c* 1.03, $CHCl_3$). Anal. Calcd for $C_{20}H_{33}NO_3Si$ (363.58): C, 66.07; H, 9.15; N, 3.85. Found: C, 65.67; H, 9.20; N, 3.86.

(3*S*,4*S*)-1-*N*-Benzyl-3-[(*R*)-1-((*tert*-Butyldimethylsilyl)oxy)ethyl]-4-[(*R*)-1-chloroethyl]-2-azetidinone (10). Synthesis of **10** from **9**: To a CCl_4 (8 mL) solution of **9** (0.15 g, 0.41 mmol) was added PPh_3 (0.31 g, 1.2 mmol), and the mixture was refluxed for 24 h under argon atmosphere. Concentration under reduced pressure gave **10** in good yield. Synthesis of **10** from **14**: To a MeOH (2 mL) and water (2 mL) solution of **14** (0.36 g, 1.15 mmol) was added K_2CO_3 (0.5 g), and the mixture was stirred for 2 h. The mixture was quenched with water, extracted with ether, washed with brine, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (2 mL), and imidazole (0.09 g, 1.3 mmol) and TBDMSCl (0.18 g, 1.2 mmol) were added at 0 °C, and the mixture was stirred overnight at room temperature. Water was added, and the mixture was extracted with CH_2Cl_2, washed with brine, dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. Purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 5/1) gave **10** (0.35 g, 80%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.38−7.26 (m, 5H), 4.71 (d, J = 15.0 Hz, 1H), 4.21 (dq, J = 6.0, 6.4 Hz, 1H), 4.15 (d, J = 15.0 Hz, 1H), 4.12 (m, 1H), 3.70 (dd, J = 2.0, 3.2 Hz, 1H), 3.07 (dd, J = 6.4, 2.0 Hz, 1H), 1.43 (d, J = 6.9 Hz, 3H), 1.23 (d, J = 6.0 Hz, 3H), 0.86 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H); IR (CCl_4) 3042−2870, 1772, 1470, 1415, 1392, 1264, 1159, 1076 cm^{-1}; $[\alpha]^{23}_D$ −8.38° (*c* 1.01, $CHCl_3$). Anal. Calcd for $C_{20}H_{32}ClNO_2Si$ (382.02): C, 62.88; H, 8.44; N, 3.67. Found: C, 62.86; H, 8.43; N, 3.69.

(2*S*,3*S*,4*S*)-*tert*-Butyl 3-(*N*-Benzylamino)-4-((*tert*-butyldiphenylsilyl)oxy)-2-[(*R*)-1-((*tert*-butyldimethylsilyl)oxy)ethyl]pentanoate (11). TCC reaction of **3b** (2.05 g, 5.0 mmol) as described above for **7** gave the aldol adduct. To a pyridine (30 mL) solution of the aldol adduct was added acetic anhydride (15 mL) at 0 °C, and the mixture was stirred for 1 h at room temperature. Concentration under reduced pressure and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 15/1) gave **11** (2.28 g, 75%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.70−7.15 (m, 15H), 5.29 (dq, J = 8.0, 6.5 Hz, 1H), 4.02 (dq, J = 5.0, 6.0 Hz, 1H), 3.66 (d, J = 15.5 Hz, 1H), 3.61 (d, J = 15.5 Hz, 1H), 3.01 (dd, J = 8.0, 5.0 Hz, 1H), 2.91 (dd, J = 5.0, 5.0 Hz, 1H), 1.93 (s, 3H), 1.45 (s, 9H), 1.29 (d, J = 6.5 Hz, 3H), 1.05 (s, 9H), 1.04 (d, J = 6.0 Hz, 3H); IR (CCl_4) 3100−2890, 1755, 1475, 1422, 1408, 1387, 1255, 1170, 1126, 1090 cm^{-1}; $[\alpha]^{20}_D$ −8.66° (*c* 1.01, $CHCl_3$); HRMS (EI) calcd for $C_{36}H_{49}NO_5Si$ (603.3380), found 603.3380. Anal. Calcd for $C_{36}H_{49}NO_5Si$ (603.88): C, 71.60; H, 8.18; N, 2.32. Found: C, 71.37; H, 8.37; N, 2.49.

(3*S*,4*S*)-1-*N*-Benzyl-3-[(*R*)-1-(acetyloxy)ethyl]-4-[(*S*)-1-((*tert*-butyldiphenylsilyl)oxy)ethyl]-2-azetidinone (12). To a CH_2Cl_2 (25 mL) solution of **11** (1.81 g, 3.0 mmol) was added trifluoroacetic acid (20 mL), and the mixture was stirred for overnight at room temperature. The mixture was quenched with aqueous saturated $NaHCO_3$, extracted with CH_2Cl_2, washed with brine, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was dissolved in acetonitrile (100 mL), PPh_3 (1.57 g, 6.0 mmol) and 2,2′-dipyridyl disulfide (1.32 g, 6.0 mmol) were added, and the mixture was refluxed for 10 h. The mixture was concentrated under reduced pressure. Purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 2/1) gave **12** (1.41 g, 88%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.66−7.18 (m, 15H), 5.13 (dq, J = 6.0, 7.3 Hz, 1H), 4.75 (d, J = 15.0 Hz, 1H), 4.08 (d, J = 15.0 Hz, 1H), 3.99 (dq, J = 4.2, 6.3 Hz, 1H), 3.47 (dd, J = 2.0, 4.2 Hz, 1H), 3.08 (dd, J = 2.0, 6.0 Hz, 1H), 1.90 (s, 3H), 1.20 (d, J = 6.3 Hz, 3H), 1.05 (s, 9H), 0.97 (d, J = 6.3 Hz, 3H); IR (neat) 3100−2890, 1745, 1246, 1111 cm^{-1}; $[\alpha]^{21}_D$ +38.6°

(*c* 0.965, $CHCl_3$). Anal. Calcd for $C_{32}H_{39}NO_4Si$ (529.76): C, 72.55; H, 7.42; N, 2.64. Found: C, 72.29; H, 7.38; N, 2.72.

(3*S*,4*S*)-1-*N*-Benzyl-3-[(*R*)-1-(acetyloxy)ethyl]-4-[(*S*)-1-hydroxyethyl]-2-azetidinone (13). To a THF (10 mL) solution of **12** (1.36 g, 2.57 mmol) under argon atmosphere at 0 °C was added dropwise a 1.0 M THF solution of tetrabutylammonium fluoride (5.13 mL, 5.13 mmol), and the mixture was stirred for 4 h at room temperature. Addition of water, extraction with ether, washing with brine, drying with anhydrous Na_2SO_4, concentration under reduced pressure, and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 1/1) gave **13** (0.58 g, 77%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.37−7.23 (m, 5H), 5.14 (dq, J = 6.5, 7.5 Hz, 1H), 4.62 (d, J = 15.0 Hz, 1H), 4.35 (d, J = 15.0 Hz, 1H), 3.77 (dq, J = 8.0, 6.5 Hz, 1H), 3.31 (dd, J = 2.2, 8.0 Hz, 1H), 2.91 (dd, J = 2.2, 7.5 Hz, 1H), 1.95 (s, 3H), 1.34 (d, J = 6.5 Hz, 3H), 1.14 (d, J = 6.5 Hz, 3H); IR (CCl_4) 3375, 2978−2933, 1740, 1711, 1437, 1242, 1144 cm^{-1}; $[\alpha]^{26}_D$ +65.6° (*c* 1.00, $CHCl_3$). Anal. Calcd for $C_{16}H_{21}NO_4$ (291.35): C, 65.96; H, 7.27; N, 4.81. Found: C, 65.92; H, 7.22; N, 4.93.

(3*S*,4*S*)-1-*N*-Benzyl-3-[(*R*)-1-(acetyloxy)ethyl]-4-[(*R*)-1-chloroethyl]-2-azetidinone (14). 14 was prepared from **13** as described above for **10** (92% yield). Colorless solid: ^{1}H NMR ($CDCl_3$) δ 7.40−7.24 (m, 5H), 5.21 (dq, J = 7.2, 6.5 Hz, 1H), 4.85 (d, J = 15.3 Hz, 1H), 4.14 (dq, J = 6.8, 3.5 Hz, 1H), 3.99 (d, J = 15.3 Hz, 1H), 3.57 (dd, J = 2.0, 3.5 Hz, 1H), 3.26 (dd, J = 7.2, 2.0 Hz, 1H), 1.99 (s, 3H), 1.45 (d, J = 6.8 Hz, 3H), 1.38 (d, J = 6.5 Hz, 3H); IR (CCl_4) 3067−2876, 1767, 1454, 1381, 1236, 1177, 1132 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{20}ClNO_3$ (309.1132), found 309.1123. Anal. Calcd for $C_{16}H_{20}ClNO_3$ (309.80): C, 62.03; H, 6.51; N,4.52. Found: C, 61.58; H, 6.37; N, 4.45.

(*E*)-*tert*-Butyl 4-Methoxy-2-methyl-2-pentenoate (17). To a benzene (180 mL) solution of crude 2-methoxypropanal (ca. 3.2 g, 37 mmol) which was prepared from ethyl lactate and MeI as described above for **1e** was added 2-methyl-2-(triphenyphosphoranylidene)acetic acid *tert*-butyl ester, and the mixture was refluxed for overnight. After concentration under reduced pressure, the residue was dissolved in *n*-hexane (20 mL) and ether (20 mL). Filtration, concentration under reduced pressure and purification with column chromatography (silica gel, *n*-hexane/ethyl acetate, 15/1) gave **17** (2.0 g, 27% from ethyl lactate). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.51 (dq, J = 1.5, 8.6 Hz, 1H), 4.12 (dq, J = 6.6, 8.6 Hz, 1H), 3.28 (s, 3H), 1.83 (d, J = 1.5 Hz, 3H), 1.54 (s, 9H), 1.25 (d, J = 6.6 Hz, 3H); IR (neat) 2989−2750, 1722, 1367, 1342, 1143 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O_3$ (200.28): C, 65.97; H, 10.07. Found: C, 66.08; H, 10.10.

(3*S,4*S**)-*tert*-Butyl 3-(*N*,*N*-Dibenzylamino)-4-methoxy-2-methyl-2-pentanoate (18a).** White solid: ^{1}H NMR ($CDCl_3$) δ 7.35−7.15 (m, 10H), 3.89, 3.72 (2d, J = 13.2 Hz, each 2H), 3.54 (dq, J = 4.2, 6.0 Hz, 1H), 3.25 (s, 3H), 2.95 (dq, J = 6.6, 8.6 Hz, 1H), 2.85 (dd, J = 4.2, 8.6 Hz, 1H), 1.49 (s, 9H), 1.10 (d, J = 6.0 Hz, 3H), 1.05 (d, J = 6.6 Hz., 3H); IR (KBr) 2976−2794, 1716, 1494, 1440, 1365, 1340, 1145, 1107 cm^{-1}. Anal. Calcd for $C_{25}H_{35}NO_3$ (397.56): C, 75.53; H, 8.87; N, 3.52. Found: C, 75.54; H, 9.05; N, 3.58.

Another Diastereomer (18b). White solid: ^{1}H NMR ($CDCl_3$) δ 7.33−7.16 (m, 10H), 3.98, 3.78 (2d, J = 13.5 Hz, each 2H), 3.40 (dq, J = 3.3, 6.2 Hz, 1H), 3.19 (s, 3H), 2.99 (dq, J = 6.6, 9.5 Hz, 1H), 2.83 (dd, J = 3.3, 9.5 Hz, 1H), 1.41 (s, 9H), 1.26 (d, J = 6.6Hz, 3H), 1.12 (d,J = 6.2 Hz, 3H); IR (KBr) 2976−2878, 1720, 1440, 1367, 1148 cm^{-1}. Anal. Calcd for $C_{25}H_{35}NO_3$ (397.56): C, 75.53; H, 8.87; N, 3.52. Found: C, 75.94; H, 9.22; N, 3.63.

(*E*)-Isopropyl 4-((*tert*-butyldimethylsilyl)oxy)-4-phenyl-2-butenoate (20). To a THF (200 mL) solution of benzaldehyde (9.7 mL, 95 mmol) at −78 °C under argon atmosphere was added dropwise 0.98 M THF solution of vinylmagnesium bromide (80 mL, 78.4 mmol) in 30 min. The mixture was stirred for 1 h. Addition of 1 N HCl (200 mL), extraction with ether, washing with brine, drying with anhydrous Na_2SO_4, concentration under reduced pressure, and distillation gave the product (7.0 g, 67%: bp 74 °C/4 mmHg). To a CH_2Cl_2 (250 mL) solution of the oil obtained above at 0 °C were added imidazole (6.8 g, 100 mmol) and TBDMSCl (9.0 g, 60 mmol), and the mixture was stirred for 4 h at room temperature. Addition of water (250 mL), extraction with CH_2Cl_2, washing with brine, drying with anhydrous $MgSO_4$, concentration under reduced pressure, and distillation gave the product (11.9 g, 92%: bp 46 °C/0.7 mmHg). To a MeOH (400 mL) solution of the oil obtained above at −78 °C was bubbled ozone until the color of the solution turned blue. Excess of ozone was removed by bubbling of argon at −78 °C. After the color disppeared, Me_2S (7.5 mL) was added, and the mixture was allowed to warm to room temperature and concentrated under reduced pressure. Ether and water were added, and the mixture was extracted with ether, washed with three times of water and brine, dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was used for further manipulation without purification as described above for **1a**, and *i*-PrOH was used instead of *t*-BuOH at the final step (22% yield from benzaldehyde). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35−7.27 (m, 5H), 6.93 (dd, J = 4.5, 15.2 Hz, 1H), 6.06 (dd, J = 1.7, 15.2 Hz, 1H), 5.30 (dd, J = 1.7, 4.5 Hz, 1H), 5.03 (septet, J = 6.3 Hz, 1H), 1.24 (d, J = 6.3 Hz, 6H), 0.91 (s, 9H), 0.07 (s, 3H), −0.04 (s, 3H); IR (CCl_4) 3000−2856, 1720, 1656, 1280, 1169 cm^{-1}. Anal. Calcd for $C_{19}H_{30}O_3Si$ (334.53): C, 68.22; H, 9.04. Found: C, 68.05; H, 9.42.

(3*R,4*S**)-Isopropyl 3-(*N*-benzylamino)-4-((*tert*-butyldimethylsilyl)oxy)-4-phenylpentanoate (21).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35−7.18 (m, 10H), 4.96 (qq, J = 6.2, 6.2 Hz, 1H), 4.86 (d, J = 4.3 Hz, 1H), 3.77 (s, 2H), 3.18 (ddd, J = 4.3, 5.0, 8.2 Hz, 1H), 2.43 (dd, J = 5.0, 15.3 Hz, 1H), 2.37 (dd, J = 8.2, 15.3 Hz, 1H), 1.20 (d, J = 6.2 Hz, 3H), 1.18 (d, J = 6.2 Hz, 3H), 0.90 (s, 9H), 0.05 (s, 3H), −0.18 (s, 3H); IR (neat) 2982−2858, 1719, 1472, 1375, 1256, 1107 cm^{-1}. Anal. Calcd for $C_{26}H_{39}NO_3Si$ (441.69): C, 70.70; H, 8.90; N, 3.17. Found: C, 70.70; H, 8.78; N, 3.38.

(3*R,4*S**)-3-(*N*-Benzylamino)-4-phenyl-4-butanolide (22-trans). 22-trans** was prepared from **21** as described above for **5a** (52% yield). Colorless needles: mp 76.2−76.7 °C; ^{1}H NMR ($CDCl_3$) δ 7.41−7.25 (m, 10H), 5.25 (d, J = 5.1 Hz, 1H), 3.82 (d, J = 13.5 Hz, 1H), 3.78 (d, J = 13.5 Hz, 1H), 3.54 (ddd, J = 7.1, 6.5, 5.1 Hz, 1H), 2.83 (dd, J = 17.0, 7.1 Hz, 1H), 2.47 (dd, J = 17.0, 6.5 Hz, 1H), 1.60 (broad s, 1H); ^{13}C NMR ($CDCl_3$) δ 175.00, 139.13, 137.77, 128.84, 128.68, 128.60, 127.98, 127.44, 125.61, 84.04, 61.88, 51.94, 36.02; IR ($CHCl_3$) 3335, 1775, 1165, 1140 cm^{-1}. HRMS calcd for $C_{17}H_{17}NO_2$ (267.1259), found 267.1249.

(3*S,4*S**)-3-(*N*-Benzylamino)-4-phenyl-4-butanolide (22-cis).** To a EtOH (2 mL) solution of **20** (0.33 g, 1.0 mmol) was added benzylamine (0.30 mL, 2.8 mmol), and the mixture was stirred for 50 h at 50 °C. Concentration under reduced pressure, and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 15/1) gave **21** (0.35 g, 79%, syn/anti = 2/1). **22-cis** was prepared from *syn*-**21** as described above for **5a** (78% yield). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.43−7.06 (m, 10H), 5.58 (d, J = 4.9 Hz, 1H), 3.73 (ddd, J = 3.0, 4.9, 6.0 Hz, 1H), 3.63 (d, J = 13.8 Hz, 1H), 3.47 (d, J = 13.8 Hz, 1H), 2.77 (dd, J = 16.0, 6.0 Hz, 1H), 2.61 (dd, J = 16.0, 3.0 Hz, 1H), 1.02 (broad s, 1H); ^{13}C NMR ($CDCl_3$) δ 175.67, 139.25, 134.29, 128.74, 128.70, 128.47, 127.76, 127.19, 125.15, 83.83, 56.87, 50.00, 36.48; IR ($CHCl_3$) 3330, 1780, 1195, 1160 cm^{-1}.

(*E*)-*tert*-Butyl 4-Phenyl-2-pentenoate (27). To a benzene (20 mL) solution of D,L-2-phenylpropionaldehyde (1.25 mL, 9.41 mmol) at 0 °C was added dropwise (triphenylphosphoranylidene)acetic acid *tert*-butyl ester (3.22 g, 8.56 mmol). The mixture was stirred for 30 min at 0 °C, stirred for 35 min at room temperature, refluxed for 2.5 h, and then cooled to room temperature. After concentration under reduced pressure, purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 30/1) gave **27** (1.62 g, 82%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.44−7.17 (m, 5H), 7.00 (dd, J = 6.5, 15.3 Hz, 1H), 5.72 (dd, J = 1.8, 15.3 Hz, 1H), 3.58 (ddq, J = 1.8, 6.5, 7.0 Hz, 1H), 1.47 (s, 9H), 1.42 (d, J = 7.0 Hz, 3H); IR (neat) 2980−2933, 1713, 1649, 1368, 1316, 1290, 1154 cm^{-1}. HRMS (EI) calcd for $C_{15}H_{20}O_2$ (232.1463), found 232.1466. Anal. Calcd for $C_{15}H_{20}O_2$ (232.32): C, 77.55; H, 8.68. Found: C, 77.26; H, 8.71.

(3*S,4*S**)-*tert*-Butyl 3-(*N*-Benzylamino)-4-phenylpentanoate (28).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.34−7.15 (m, 10H), 3.82 (d, J = 12.7 Hz, 1H), 3.74 (d, J = 12.7 Hz, 1H),

3.17 (ddd, J = 4.9, 6.7, 8.1 Hz, 1H), 2.97 (dq, J = 6.7, 7.0 Hz, 1H), 2.34 (dd, J = 4.9, 15.0 Hz, 1H), 2.12 (dd, J = 8.1, 15.0 Hz, 1H), 1.42 (s, 9H), 1.35 (d, J = 7.0 Hz, 3H); IR (CCl_4) 3086−2876, 1726, 1495, 1454, 1367, 1256, 1153 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{29}NO_2$ (339.2198), found 339.2163. Anal. Calcd for $C_{22}H_{29}NO_2$ (339.48): C, 77.84; H, 8.61; N, 4.13. Found: C, 77.33; H, 8.45; N, 4.05.

(3*R,4*S**)-*tert*-Butyl 3-(*N*-Benzylamino)-4-phenylpentanoate (29).** Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.33−7.16 (m, 10H), 3.78 (d, J = 13.0 Hz, 1H), 3.68 (d, J = 13.0 Hz, 1H), 3.17 (ddd, J = 6.0, 6.7, 6.8 Hz, 1H), 2.97 (dq, J = 6.7, 7.1 Hz, 1H), 2.37 (dd, J = 6.8, 15.2 Hz, 1H), 2.31 (dd, J = 6.0, 15.2 Hz, 1H), 1.45 (s, 9H), 1.29 (d, J = 7.1 Hz, 3H); IR (CCl_4) 3080−2830, 1728, 1603, 1454, 1367, 1153 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{29}NO_2$ (339.2198), found 339.2175. Anal. Calcd for $C_{22}H_{29}NO_2$ (339.48): C, 77.84; H, 8.61; N, 4.13. Found: C, 77.36; H, 8.43; N, 4.17.

(4*R)-Perhydro-3-benzyl-4-((*S**)-1-phenylethyl)-1,3-oxazin-2-one (30).** To an ether (5 mL) solution of **29** (130 mg, 0.47 mmol) at 0 °C was added $LiAlH_4$ (100 mg), and the mixture was stirred for overnight at room temperature. Water (0.4 mL) and 15% aqueous NaOH (0.1 mL) were added, and the mixture was dried with anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (5 mL), and trichloromethyl chloroformate (0.1 mL) and iPr$_2$NEt were added to the solution at room temperature, and the mixture was stirred for 2 h. After low bp materials were removed under reduced pressure, 5 mL of benzene was added. The mixture was refluxed for overnight and then cooled to room temperature. Concentration under reduced pressure and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 10/1) gave **30** (30.6 mg, 25%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.37−7.08 (m, 10H), 5.15 (d, J = 15.1 Hz, 1H), 4.40−4.30 (m, 1H), 4.24−4.15 (m, 1H), 3.36−3.21 (m, 2H), 3.22 (d, J = 15.1 Hz, 1H), 1.83−1.68 (m, 1H), 1.99 (m, 1H), 1.63 (m, 1H), 1.26(d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 154.83, 142.44, 136.98, 128.75, 128.69, 128.12, 127.68, 127.66, 127.11, 64.22, 50.08, 49.93, 40.25, 23.92, 14.31.

Another approach of **30** via the reaction which was already reported about diastereoselectivity:[13] To a CH_2Cl_2 (5 mL) solution of the carbamate, which was obtained from allylation of *N*-(2-phenylpropylidene)benzylamine followed by treatment with $ClCO_2Me/K_2CO_3$ (4:1 mixture of diastereomers), at −78 °C was bubbled ozone until the color of the solution turned blue. Excess of ozone was removed by bubbling of argon at −78 °C. After the color disappeared, Me_2S (0.2 mL) was added, and the mixture was allowed to warm to room temperature and concentrated under reduced pressure. The residue was dissolved in MeOH (3 mL), and sodium borohydride (100 mg) was added at room temperature. Water (10 mL) was added. The mixture was extracted with ether, washed with brine, dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was dissolved in THF (5 mL). Potassium *tert*-butoxide (50 mg) was added at room temperature, and the mixture was stirred for 3 h. Ether (20 mL) and aqueous saturated NH_4Cl/brine (1/1) were added. Extraction with ether, washing with brine, drying with anhydrous $MgSO_4$, concentration under reduced pressure, and purification with column chromatography (silica gel; *n*-hexane/ethyl acetate, 15/1) gave **30** as a 4:1 mixture of diastereomers (21.1 mg, 18%). **Diastereomer of 30**: Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.39−7.08 (m, 10H), 5.53 (d, J = 14.9 Hz, 1H), 4.13 (d, J = 14.9 Hz, 1H), 4.08 (ddd, J = 11.7, 5.8, 2.8 Hz, 1H), 3.95 (ddd, J = 11.7, 11.5, 4.5 Hz, 1H), 3.42 (ddd, J = 7.5, 5.4, 3.0 Hz, 1H), 3.25 (dq, J = 7.5, 7.1 Hz, 1H), 1.83−1.68 (m, 1H), 1.65−1.56 (m, 1H), 1.41 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 154.23, 142.35, 137.05, 128.92, 128.81, 128.14, 127.78, 127.29, 127.18, 64.16, 57.82, 52.32, 41.49, 24.27, 18.98; IR ($CHCl_3$) 1680, 1490, 1455, 705 cm^{-1}. HRMS (EI) calcd for $C_{19}H_{21}NO_2$ (295.1572), found 295.1568.

(3*S*,4*R*)-*tert*-Butyl 3-(*N*-Benzylamino)-5-((*tert*-butyldimethylsilyl)oxy)-4-methylpentanoate (33a). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35−7.20 (m, 5H), 3.82 (d, J = 12.9 Hz, 1H), 3.74 (d, J = 12.9 Hz, 1H), 3.64 (dd, J = 6.3, 9.9 Hz, 1H), 3.52 (dd, J = 5.8, 9.9 Hz, 1H), 3.13 (m, 1H), 2.41 (dd, J = 6.2, 17.0 Hz, 1H), 2.36 (dd, J = 7.2, 17.0 Hz, 1H), 1.86 (m, 1H), 1.44 (s, 9H), 0.90 (d, J = 7.0 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 6H); IR (CCl_4) 2957−2856, 1728, 1471, 1367, 1255, 1153 cm^{-1}; $[\alpha]^{24}_D$ +3.46° (c 1.07, CCl_4). Anal. Calcd for $C_{23}H_{41}NO_3Si$ (407.67): C, 67.76; H, 10.14; N, 3.44. Found: C, 67.90; H, 9.95; N, 3.55.

(3*S*,4*R*)-*tert*-Butyl 3-(*N*,*N*-Dibenzylamino)-5-((*tert*-butyldimethylsilyl)oxy)-4-methylpentanoate (33b). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.39−7.23 (m, 10H), 3.79 (d, J = 14.0 Hz, 2H), 3.50 (dd, J = 4.3, 9.9 Hz, 1H), 3.41 (d, J = 14.0 Hz, 1H), 3.36 (dd, J = 7.6, 9.9 Hz, 1H), 3.06 (m, 1H), 2.63 (dd, J = 4.6, 15.1 Hz, 1H), 2.39 (dd, J = 7.3, 15.1 Hz, 1H), 1.85 (m, 1H), 1.48 (s, 9H), 1.04 (d, J = 6.6 Hz, 3H), 0.86 (s, 9H), 0.01 (s, 6H); IR ($CHCl_3$) 3009−2856, 1714, 1454, 1367, 1198, 1088 cm^{-1}; $[\alpha]^{23}_D$ +0.495° (c 2.03, $CHCl_3$). Anal. Calcd for $C_{30}H_{47}NO_3Si$ (497.80): C, 72.39; H, 9.52; N, 2.81. Found: C, 72.10; H, 9.59; N, 2.73.

(3*R*,4*R*)-*tert*-Butyl 3-(*N*-Benzylamino)-5-((*tert*-butyldimethylsilyl)oxy)-4-methylpentanoate (34a). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35−7.20 (m, 5H), 3.77 (s, 2H), 3.56 (d, J = 6.1 Hz, 1H), 3.09 (m, 1H), 2.43 (dd, J = 4.1, 15.0 Hz, 1H), 2.24 (dd, J = 8.5, 15.0 Hz, 1H), 1.93 (m, 1H), 1.43 (s, 9H), 0.88 (d, J = 6.9 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 6H); IR (CCl_4) 2957−2856, 1728, 1471, 1367, 1255, 1151 cm^{-1}; $[\alpha]^{24}_D$ −1.75° (c 1.03, CCl_4). Anal. Calcd for $C_{23}H_{41}NO_3Si$ (407.67): C, 67.76; H, 10.14; N, 3.44. Found: C, 67.67; H, 10.05; N, 3.40.

(3*R*,4*R*)-*tert*-Butyl 3-(*N*,*N*-dibenzylamino)-5-((*tert*-butyldimethylsilyl)oxy)-4-methylpentanoate (34b). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.36−7.20 (m, 10H), 3.97 (dd, J = 4.5, 10.0 Hz, 2H), 3.73 (d, J = 13.5 Hz, 2H), 3.42 (d, J = 13.5 Hz, 2H), 3.08 (dd, J = 8.0, 10.0 Hz, 1H), 3.05 (ddd, J = 4.5, 7.5, 13.0 Hz, 1H), 2.65 (dd, J = 4.5, 15.5 Hz, 1H), 2.29 (dd, J = 7.5, 15.5 Hz, 1H), 1.95 (m, 1H), 1.47 (s, 9H), 0.90 (s, 9H), 0.87 (d, J = 6.5 Hz, 3H), 0.02 (s, 6H); IR ($CHCl_3$) 3064−2856, 1713, 1454, 1367, 1159 cm^{-1}; $[\alpha]^{22}_D$ −2.66° (c 2.10, $CHCl_3$). Anal. Calcd for $C_{30}H_{47}NO_3Si$ (497.80): C, 72.39; H, 9.52; N, 2.81. Found: C, 72.35; H, 9.58; N, 2.72.

(3*S*,4*R*)-*tert*-Butyl 3-Amino-5-((*tert*-butyldimethylsilyl)oxy)-4-methylpentanoate (35). To an ethyl acetate (3 mL) solution of **33a** or **33b** (0.3 mmol) was added Pearlman catalyst ($Pd(OH)_2$/C, 47 mg), and the mixture was stirred vigorously for 24 h under H_2 atomosphere. Filtration through Celite, concentration under reduced pressure, and purification with column chromatography (silica gel; ethyl acetate) gave **35** (80−85%). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 3.58 (dd, J = 6.7, 10.1 Hz, 1H), 3.54 (dd, J = 5.5, 10.1 Hz, 1H), 3.32 (ddd, J = 4.0, 4.3, 9.1 Hz, 1H), 2.36 (dd, J = 15.0, 4.3 Hz, 1H), 2.24 (dd, J = 15.0, 9.1 Hz, 1H), 1.66 (m, 1H), 1.45 (s, 9H), 0.89 (s, 9H), 0.87 (d, J = 7.1 Hz, 3H), 0.05 (s, 6H); IR (CCl_4) 3410, 3020−2850, 1740, 1467, 1379, 1260, 1157 cm^{-1}; $[\alpha]^{24}_D$ −6.43° (c 1.68, $CHCl_3$). Anal. Calcd for $C_{16}H_{35}NO_3Si$ (317.53): C, 60.52; H, 11.11; N, 4.41. Found: C, 60.22; H, 11.18; N, 4.33.

(3*R*,4*R*)-*tert*-Butyl 3-Amino-5-((*tert*-butyldimethylsilyl)oxy)-4-methylpentanoate (36). 36 was prepared from **34a** or **34b** as described above for **35** (80−85% yield). Colorless oil: ^{1}H NMR ($CDCl_3$) δ 3.61 (dd, J = 5.5, 10.4 Hz, 1H), 3.55 (dd, J = 5.8, 10.4 Hz, 1H), 3.18 (ddd, J = 3.3, 5.7, 9.6 Hz, 1H), 2.45 (dd, J = 3.3, 15.5 Hz, 1H), 2.19 (dd, J = 9.6, 15.5 Hz, 1H), 1.66 (m, 1H), 1.65 (br s, 2H), 1.46 (s, 9H), 0.89 (s, 9H), 0.89 (d, J = 6.8 Hz, 3H), 0.05 (s, 6H); IR (CCl_4) 3365, 2980−2860, 1738, 1465, 1373, 1260, 1157 cm^{-1}; $[\alpha]^{24}_D$ +13.4° (c 1.68, $CHCl_3$). Anal. Calcd for $C_{16}H_{35}NO_3Si$ (317.53): C, 60.52; H, 11.11; N, 4.41. Found: C, 60.32; H, 11.10; N, 4.42.

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