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# Asymmetric synthesis of $\beta^{2,3}$-amino acids by InI–Pd(0)-promoted metalation and addition of chiral 2-vinylaziridines

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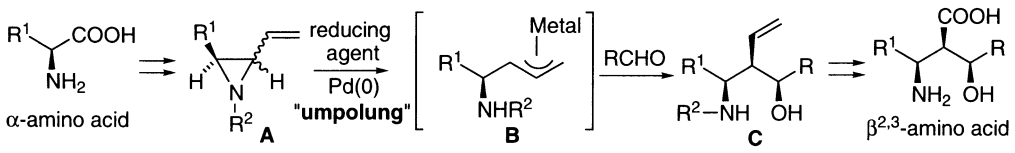
**Abstract**—The reaction of optically active 3-alkyl-2-vinylaziridines with various aldehydes in the presence of InI and $Pd(PPh_3)_4$ gives rise to chiral *syn*,*syn*-2-vinyl-1,3-amino alcohols possessing three contiguous chiral centers stereoselectively. The ratio of the *syn*,*syn*-isomer to the other three isomers is significantly affected by the C3-substituents of aziridines as well as the alkyl groups of aldehydes. In addition, the obtained 1,3-aminoalcohols can be converted into biologically important $\beta^{2,3}$-amino acid derivatives. 

## 1. Introduction

Due to their very high reactivity and ability to function as carbon electrophiles, vinylaziridines and their analogues have been used as intermediates for the synthesis of azinomycin, β-lactams, (*R*)-(−)-dysidazirine, azacycles such as 2,6-disubstituted tetrahydropyridines, indolizidine alkaloids, pyrrolizidine alkaloids, and 3,7-disubstituted tetrahydroazepinone.[1] In the course of our studies on chiral aziridines, we have developed several unique syntheses and reactions of 2-alkenylaziridines such as Pd(0)-catalyzed isomerization of *trans*-isomers into *cis*-ones and organocopper-mediated *anti*-$S_N2'$ substitution, aimed at stereoselective synthesis of alkene dipeptide isosteres.[2] In contrast to the reactions of aziridines used as electrophiles, there are few reactions where 2-alkenylaziridines were employed as nucleophiles.[3] Recently, several umpolung reactions of allylic alcohol derivatives and vinylic epoxides with various reducing agents via the π-allylpalladium complexes have been developed.[4] Therefore, anticipating a dramatic increase in their synthetic versatility, we started to explore an efficient synthetic method of chiral allylmetals bearing an amino group at the δ-position from 2-alkenylaziridines with a reducing agent and a Pd(0) catalyst. If the reaction of the resultant allylmetals with aldehydes proceeds regio- and stereoselectively (**A**→**C**), $\beta^{2,3}$-amino acid derivatives, which are very important compounds as peptidomimetics, could be easily prepared from α-amino acids as shown in Scheme 1. Herein, we describe in detail an InI/Pd(0)-mediated allylation of aldehydes with the *N*-activated vinylaziridines **1**, which proceeds with regio- and stereoselectivity to provide the *syn*,*syn*-2-vinyl-1,3-amino alcohols **2a** and **5a**–**7a** in good yield, and transformation of the obtained products into $\beta^{2,3}$-amino acid derivatives.[5]

## 2. Results and discussion

Diastereoselective addition of chiral allylmetals possessing a stereogenic center at the δ-position with aldehydes plays an important role in stereoselective synthesis, since contiguous stereogenic centers can be created in a single operations and the resulting homoallylic alcohols can be used for further chemical transformation into various types of natural and synthetic compounds.[6,7] Although there are numerous reports concerning the preparation and utilization of 4-hydroxy- or 4-alkoxyallyl metals,[7] few




**Scheme 1.** General synthetic strategy of $\beta^{2,3}$-amino acids from α-amino acids.

*Keywords*: vinylaziridines; $\beta^{2,3}$-amino acids; metalation.

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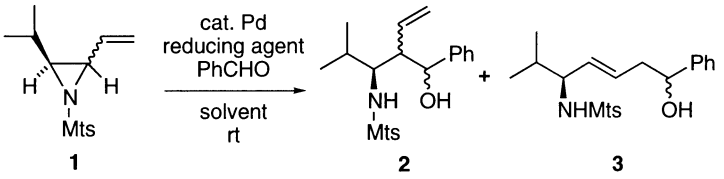



**Scheme 2.**

**Table 1.** Synthesis of 2-vinyl-1,3-amino alcohols **2** from 2-vinylaziridine **1** with various reducing agents

| Entry | Reaction conditions | Yield[a] (%) (**2**–**3**) |
|---|---|---|
| 1 | $Et_2Zn$, $Pd(PPh_3)_4$, THF, 2 h | 16:17 |
| 2 | $SnCl_2$, $PdCl_2(CH_3CN)_2$, DMF/$H_2O$, 23 h | 32:0 |
| 3 | $Et_3B$, $Pd(PPh_3)_4$, THF, 8 h | – |
| 4 | InI (2), $Pd(PPh_3)_4$ (5), THF, 6 h | 83:3 |

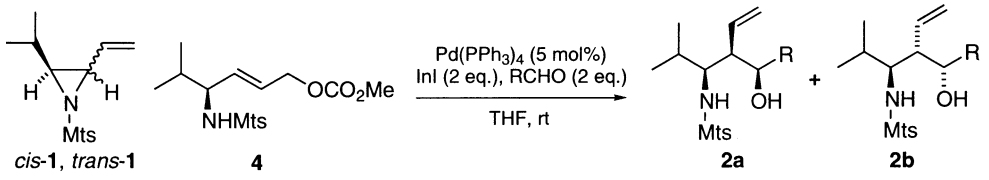
All reactions were carried out with 2 equiv. of benzaldehyde in the presence of palladium catalyst and reducing agent at room temperature.
[a] Isolated yields.

reactions of chiral allylmetals bearing an amino group at the δ-position have been reported.[8] We have already found that *trans*-*N*-activated 2-vinylaziridines were efficiently isomerized into the corresponding *cis*-isomers via a π-allylpalladium complex by the reaction with a catalytic amount of $Pd(PPh_3)_4$.[2d] Then we examined various reducing agents for the Pd(0)-promoted metalation of optically active 3-alkyl-2-vinylaziridines **1** and the subsequent nucleophilic addition with several aldehydes.

The synthesis of β-amino acids has attracted considerable attention in recent years.[9] Among various substituted β-amino acids, β′-hydroxy derivatives constitute an important class of molecules with interesting chemical and biological properties due to their similarity to serine and other unusual amino acids.

## 2.1. Synthesis of *N*-Mts-2-vinyl-1,3-amino alcohols from *N*-Mts-2-vinylaziridines

It is known that a strong electron-withdrawing protecting group on the nitrogen atom is required for the Pd-catalyzed ring-opening of aziridines. Hence, we chose a 2,4,6-trimethylbenzenesulfonyl (Mts) group for that purpose. The requisite *N*-arylsulfonylated 2,3-*trans*- and 2,3-*cis*-3-alkyl-2-vinylaziridines *trans*-**1** and *cis*-**1** were prepared from natural α-amino acids with high optical purity according to our recently published procedures.[2d] We initially examined the umpolung reaction for generating the desired allylmetal reagent from **1**. The reactions of **1** and benzaldehyde (2 equiv.) were carried out at room temperature using various reducing agents (2–3 equiv.) and a catalytic amount of a Pd-catalyst under argon atmosphere (Scheme 2). The representative results are shown in Table 1. It is revealed that the reactivity of the allylmetal reagent bearing an amino group at the δ-position is strongly affected by the reducing reagent employed. When $Et_2Zn$[4a] was used as a reducing agent (entry 1), the desired 1,3-amino alcohols **2** were obtained as minor products together with 1,5-amino alcohols **3**. A similar reaction of **1** with $SnCl_2$[4b] produced **2** without other products, but the yield of **2** was low due to decomposition of the starting material (entry 2). Although addition of $Et_3B$[4c] resulted in a complex mixture of products, the choice of InI[4d] as a reducing agent promoted the transmetalation and nucleophilic addition with benzaldehyde to give **2** in 83% yield (entries 3 and 4).

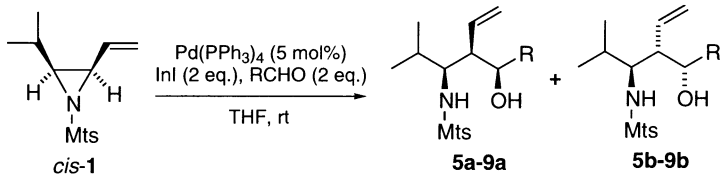



**Scheme 3.**

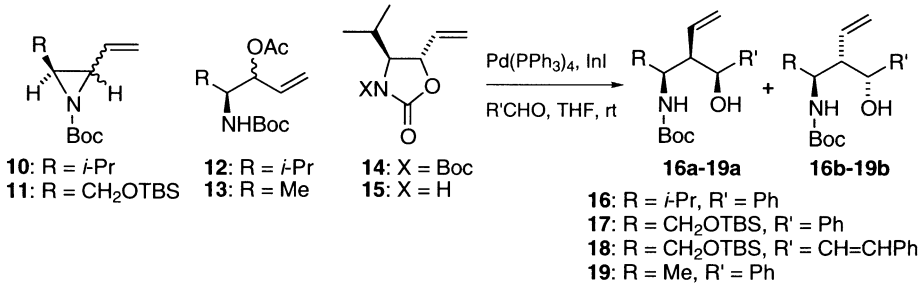
**Table 2.** The InI–Pd(0)-mediated allylation of 2-vinyl-aziridines **1** and allylic carbonate **4** with various aldehydes

| Entry | Substrate | Aldehyde R (RCHO) | Reaction time (h) | Yield[a] (%) | Ratio[b] (**a**–**b**–others) |
|---|---|---|---|---|---|
| 1 | *trans*-**1** | Ph | 6 | **2** (76) | 89:11:0 |
| 2 | *cis*-**1** | Ph | 5 | **2** (88) | 90:10:0 |
| 3 | **4** | Ph | 7 (40°C) | **2** (52) | 85:15:0 |
| 4 | *cis*-**1** | *p*-$MeOC_6H_4$ | 26 | **5** (86) | 90:10:0 |
| 5 | *cis*-**1** | *p*-$ClC_6H_4$ | 3 | **6** (77) | 91:9:0 |
| 6 | *cis*-**1** | *i*-Pr | 23 | **7** (88) | 93:7:0 |
| 7 | *cis*-**1** | Et | 2 | **8** (80) | 51:14:35 |
| 8 | *cis*-**1** | Me | 1 | **9** (92) | 38:25:37 |

All reactions were carried out with 2 equiv. of aldehyde in the presence of $Pd(PPh_3)_4$ (5 mol%) and InI (2 equiv.) in dry THF at room temperature.
[a] Total yields.
[b] Calculated from isolated yield.




**Scheme 4.** **5**: R=*p*-MeOC$_6$H$_4$, **6**: R=*p*-ClC$_6$H$_4$, **7**: R=*i*-Pr, **8**: R=Et, **9**: R=Me.




**Scheme 5.**

Having established the conditions for giving **2**, we next examined the effect of the C-2 chirality of **1** on diastereoselectivity (**2a/2b**) (Scheme 3). Treatment of *cis*-**1** and *trans*-**1** with benzaldehyde in the presence of InI and Pd(PPh$_3$)$_4$ gave the same *syn*,*syn*-1,3-amino alcohols **2a** as a major product in a similar ratio of **2a/2b** (Table 2, entries 1 and 2). In addition, although reaction of the methyl carbonate **4**,[2a] bearing no chirality on the C2 position, proceeded slowly even if at 40°C, similar results were obtained except for the moderate yield (entry 3). From these results, it is revealed that the allylation of these compounds proceeds via the same intermediate, and the stereoselectivity is only affected by the substituent of the C3 position, but not that of the C2 position. These facts are reasonable by considering that the isomerization of *trans*-**1** and *cis*-**1** proceeds quickly via a π-allylmetal complex. Therefore, the following reactions were carried out with the 2,3-*cis*-vinylaziridines. We next investigated the Pd-mediated allylation with several aldehydes (Scheme 4). As shown in Table 2 (entries 4–8), all entries afforded the *syn*,*syn*-1,3-amino alcohols **5a**–**9a** as a major product among four possible diastereomers, irrespective of aromatic aldehydes having an electron-withdrawing or electron-donating group on the aromatic ring and aliphatic ones. In this reaction, the substituents of the aldehydes play an important role on the selectivity. Whereas the bulky substituents such as aryl and secondary alkyl groups tend to afford the *syn*,*syn*-adducts with good diastereoselectivity, the reactions with propionaldehyde and acetaldehyde gave rise to the four diastereomers with low to moderate selectivity. This result is in sharp contrast to that of allyltitanium reagents, where another *syn*,*anti*-diastereomer was obtained predominantly and the diastereoselectivity dramatically changed depending on the aldehydes employed.[8c] In particular, the Ti-mediated reaction with aryl aldehyde resulted in poor stereoselectivity. Furthermore, the reaction rate of the In-mediated allylation was significantly influenced by the substituents of the aldehydes. The electron-donating and/or bulky substituents tend to retard the allylation reaction (entries 4 and 6).

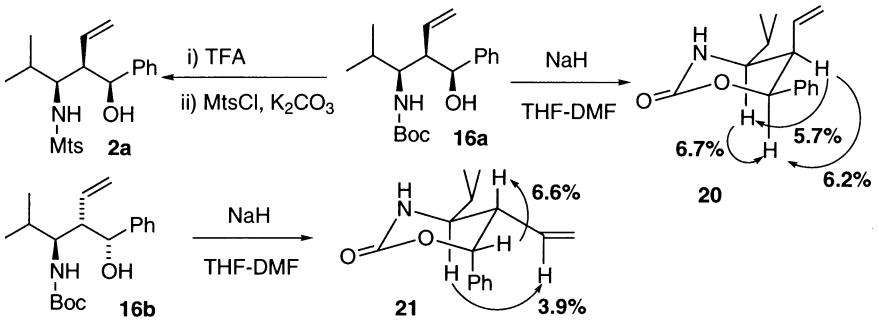
## 2.2. Synthesis of *N*-Boc-2-vinyl-1,3-amino alcohols from *N*-Boc-2-vinylaziridines and their applications

It would be desirable to employ a Boc group for protection of the amino moiety in place of the Mts group. Therefore, we next examined the umpolung of the *N*-Boc-aziridines **10** and **11**, *N*-Boc-allylic acetates **12** and **13**,[2f] and oxazolidinones **14** and **15**[10] under identical transmetalation conditions (Scheme 5). The reaction of **10** and **11** with benzaldehyde gave the corresponding *N*-Boc-*syn*,*syn*-1,3-amino alcohols **16a** and **17a** as a major product with a little bit lower yield than that of the *N*-Mts-aziridine **1** (Table 3, entries 1 and 2). Furthermore, the same treatment of **11** with cinnamaldehyde resulted in lesser diastereoselectivity (entry 3). On the other hand, on employing the acetate **12** and *N*-Boc-oxazolidinone **14** as a substrate, both the chemical yield and diastereoselectivity of **16a** were increased (entries 4 and 6). In contrast, unprotected oxazolidinone **15** afforded none of the desired 1,3-amino alcohols. Comparison with the diastereoselectivity obtained from the reactions of **10**, **11** and **12**, **13** (entries 1–2, 4 and 5) revealed that bulkiness of the alkyl group (R) of the substrates would be crucial to achieve good diastereoselectivity.

**Table 3.** The InI–Pd(0)-mediated allylation of 2-vinyl-aziridines **10** and **11**, allylic acetates **12** and **13**, and carbonate **14**

| Entry | Substrate | Aldehyde R′ (R′CHO) | Yield[a] (%) | Ratio[b] (**a**–**b**) |
|---|---|---|---|---|
| 1 | **10** | Ph | **16** (51) | 90:10 |
| 2 | **11** | Ph | **17** (58) | 88:12 |
| 3 | **11** | PhCH=CH | **18** (51) | 69:31 |
| 4 | **12** | Ph | **16** (84) | 93:7 |
| 5 | **13** | Ph | **19** (55) | 80:20 |
| 6 | **14** | Ph | **16** (89) | 93:7 |

All reactions were carried out with 2 equiv. of aldehyde in the presence of Pd(PPh$_3$)$_4$ (5 mol%) and InI (2 equiv.) in dry THF at room temperature.
[a] Total yields.
[b] Calculated from isolated yield.




**Scheme 6.**

The configuration at the newly created stereocenters of the major and minor diastereomers **16a** and **16b** was determined by the chemical transformation and NOE experiment (Scheme 6). Namely, treatment of **16a** and **16b** with NaH afforded the tetrahydro-1,3-oxazin-2-ones **20** and **21**, which were analyzed by NOE difference spectroscopy. In **20**, the strong interaction between H-1 and H-3 (6.7%), H-1 and H-2 (6.2%), and H-2 and H-3 (5.7%) clearly indicated the *syn*,*syn*-configuration. Similarly, in **21**, the distinct interaction between H-1 and H-2 (6.6%), and H-3 and vinyl proton (3.9%) clearly indicated the *syn*,*anti*-configuration. The stereochemistry of the major *N*-Mts adduct **2a** was confirmed by conversion of the assigned major product **16a** into **2a**. The other diastereomers were deduced by comparison of their TLC behavior and $^1$H NMR spectra with that of **16a** and **16b**.

The stereoselectivity attained in the allylation reaction can be explained reasonably by consideration of the three transition states (**A**–**C**, Fig. 1).[7c,11] The six-membered chair-like T.S.-models **A** where the most sterically demanding alkyl moiety ($R^1$) is located at the *anti*-position, seem to be the most favorable according to the Felkin–Ahn model. However, a similar six-membered boat-like T.S.-model **B**, where the allylindium reagents possess (*Z*)-configuration and coordinate to the amido group, could not be ruled out. In practice, we could not find any differences between the reaction of **10** and **12** via the T.S.-models **A** and **B** depending on the allylindium intermediates bearing neutral and anionic species of the *N*-protecting groups, in terms of stereoselectivity and reaction rate. In any event, both T.S. models gave the *syn*,*syn*-1,3-amino alcohols as a major product. On the contrary, when the aziridine and allylic acetate bearing a smaller alkyl group such as **11** and **13** was used for the allylation, another six-membered chair-like T.S.-model **C**, where the amino moiety ($NHR^2$) is located at the *anti*-position, would gradually prevailed, resulting in low stereoselectivity.

Finally, we transformed the obtained *syn*,*syn*-1,3-amino alcohols into β-amino-β′-hydroxycarboxylic acid derivatives, which are versatile intermediates for unnatural amino acids, β-lactams, and β-lactones (Scheme 7). Ozonolysis of the alcohols **2a**, **5a** and **6a**, followed by reduction with dimethyl sulfide to afford the aldehydes, which were subjected to the $NaClO_2$ oxidation, gave the corresponding carboxylic acids in good yield. After esterification with $TMSCHN_2$, the methyl β-amino-β′-hydroxyesters **22**–**24** were obtained in 58–89% yields from the alcohols **2a**, **5a** and **6a**.

## 3. Conclusion

In conclusion, we have demonstrated a novel utility of *N*-activated 2-vinylaziridines as a precursor of chiral

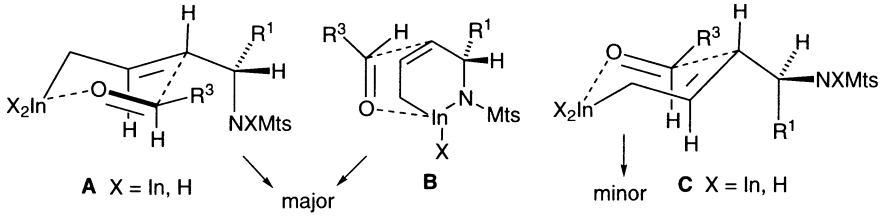
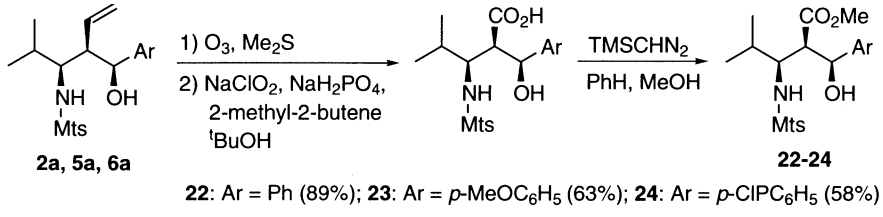



**Figure 1.** Plausible transition state model (**A**, **B** and **C**).




**Scheme 7.**

allylmetals by umpolung with an indium(I) salt in the presence of a Pd(0) catalyst. The allylindium reagents bearing a protected amino group (Mts and Boc) possess a different character from the reported allyltitanium[8c,d] and allenylindium reagents[8a,b] in terms of stereochemistry of the major products (**2a** vs. **2b**) and the stereodetermined chiral centers (C-2 vs C-3), respectively.

## 4. Experimental

### 4.1. General

Melting points are uncorrected. $^1$H NMR spectra were recorded in $CDCl_3$ using a JEOL EX-500 spectrometer. Chemical shift are reported in parts per million downfield from internal $Me_4Si$. Nominal (LR-MS) and exact mass (HRMS) spectra were recorded on a JEOL JMS-01SG-2 or JMS-HX/HX 110A mass spectrometer. Optical rotations were measured in $CHCl_3$ with a JASCO DIP-360 digital polarimeter. For flash chromatography, silica gel 60 H (silica gel for thin-layer chromatography, Merck) was employed.

**4.1.1. Alcohol 2.** Table 1, entry 1. To a stirred solution of **1** (40.0 mg, 0.136 mmol), $Pd(PPh_3)_4$ (8 mg, 6.8 μmol) and benzaldehyde (27.7 μl, 0.273 mmol) in dry THF (1 ml) was added a 1.1 M toluene solution of $En_2Zn$ (0.25 ml, 0.273 mmol) under an argon atmosphere, and the mixture was stirred for 2 h at room temperature. After quenching with 0.1N HCl, the resulting mixture was extracted with AcOEt. The extract was washed with water and brine, and dried over $MgSO_4$. The filtrate was concentrated in vacuo, and the obtained residue was purified by flash chromatography over silica gel with hexane–AcOEt (6:1) gave the γ-adduct **2** (9.0 mg, 16%) and α-adduct **3** (9.5 mg, 17%) as diastereomixtures. Entry 2. To a stirred solution of **1** (15.0 mg, 0.051 mmol), $PdCl_2(CH_3CN)_2$ (1.0 mg, 3.0 μmol) and benzaldehyde (11 mg, 0.102 mmol) in a mixture of DMF (0.3 ml) and water (0.1 ml) was added $SnCl_2$ (29 mg, 0.15 mmol) under an argon atmosphere, and the mixture was stirred at room temperature for 23 h. After quenching with 0.1N HCl, the resulting mixture was extracted with AcOEt. The extract was washed with water and brine, and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with hexane–AcOEt (7:1) gave the diastereomeric γ-adduct **2** (6.3 mg, 32%) as the sole product. Entry 4. To a stirred solution of **1** (15 mg, 0.051 mmol), $Pd(PPh_3)_4$ (3.0 mg, 2.6 μmol) and InI (25 mg, 0.10 mmol) in dry THF (0.5 ml) under an argon atmosphere was added a solution of benzaldehyde (11 mg, 0.10 mmol) in dry THF (0.5 ml), and the mixture was stirred at room temperature for 7 h. After 0.1N HCl was added to the mixture, the resulting mixture was extracted with ether. The extract was washed with water and brine, and dried over $MgSO_4$. The filtrate was concentrated in vacuo, and the obtained residue was purified by flash chromatography over silica gel with hexane–AcOEt (7:1) to give **3** (0.6 mg, 3%) and **2** (17 mg, 83%) as diastereomeric mixture.

**4.1.2. *syn*,*syn*-Alcohol 2a.** Table 2, entry 1. To a stirred solution of *trans*-**1** (85.0 mg, 0.290 mmol), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol) and InI (140 mg, 0.579 mmol) in dry THF (1 ml) under an argon atmosphere was added a solution of benzaldehyde (59 μl, 0.58 mmol) in dry THF (1 ml), and the mixture was stirred at room temperature for 6 h. The same workup procedure as described for **2** (Table 1, entry 4) gave **2b** (9.8 mg, 8%) and **2a** (79 mg, 68%). Entry 2. The same treatment of *cis*-**1** (40 mg, 0.136 mmol) as described above (entry 1) gave **2b** (5.0 mg, 9%) and **2a** (43 mg, 79%). Entry 3. The same treatment of **4** (43.0 mg, 0.116 mmol) as described above (entry 1) except for the reaction temperature (at 40°C for 7 h) gave **2b** (3.5 mg, 8%) and **2a** (21 mg, 44%). **2a**. Colorless crystals from $Et_2O$–hexane. Mp 108–110°C; $[\alpha]_D^{28}=-48.1$ (*c* 1.44, $CHCl_3$); $^1$H NMR ($CDCl_3$, 270 MHz) δ: 0.62 (d, *J*=6.8 Hz, 6H), 1.57 (m, 1H), 2.28 (d, *J*=2.7 Hz, 1H), 2.30 (s, 3H), 2.55 (ddd, *J*=3.2, 7.0, 10.0 Hz, 1H), 2.62 (s, 6H), 3.16 (ddd, *J*=3.2, 5.4, 9.8 Hz, 1H), 4.50 (d, *J*=9.8 Hz, 1H), 4.60 (dd, *J*=2.7, 7.0 Hz, 1H), 5.13 (dd, *J*=1.6, 17.3 Hz, 1H), 5.32 (dd, *J*=1.6, 10.0 Hz, 1H), 5.87 (dt, *J*=10.0, 17.3 Hz, 1H), 6.95 (s, 2H), 7.17–7.35 (m, 5H); $^{13}$C NMR ($CDCl_3$, 67.8 MHz) δ: 18.3, 19.2, 21.1, 23.4, 32.7, 53.6, 59.4, 74.9, 121.9, 127.4, 128.0, 128.4, 132.2. 134.9, 135.7, 138.7, 142.2; LRMS (FAB) *m*/*z* 402 ($MH^+$), 400, 384, 254 (100), 183, 119; HRMS (FAB) *m*/*z* calcd. for $C_{23}H_{32}NO_3S$ ($MH^+$) 402.2103; found: 402.2107. **2b**. A colorless oil; $[\alpha]_D^{34}=-41.9$ (*c* 0.983, $CHCl_3$); $^1$H NMR ($CDCl_3$, 270 MHz) δ: 0.43 (d, *J*=7.0 Hz, 3H), 0.76 (d, *J*=7.0 Hz, 3H), 1.91 (dqq, *J*=2.7, 7.0, 7.0 Hz, 1H), 2.26 (dt, *J*=2.4, 9.2 Hz, 1H), 2.30 (s, 3H), 2.65 (s, 6H), 3.28 (d, *J*=4.6 Hz, 1H), 3.39 (dt, *J*=3.0, 9.7 Hz, 1H), 4.60 (dd, *J*=1.6, 17.0 Hz, 1H), 4.84 (d, *J*=10.3 Hz, 1H), 4.90 (dd, *J*=1.6, 10.3 Hz, 1H), 5.22 (dd, *J*=3.2, 4.3 Hz, 1H), 5.67 (dt, *J*=10.0, 17.0 Hz, 1H), 6.95 (s, 2H), 7.17–7.32 (m, 5H); LRMS (FAB) *m*/*z* 402 ($MH^+$), 400 (100), 198; HRMS (FAB) *m*/*z* calcd. for $C_{23}H_{30}NO_3S$ ($M-H^-$) 400.1946; found: 400.1951.

**4.1.3. *syn*,*syn*-Alcohol 5a.** Table 2, entry 4. To a stirred solution of *cis*-**1** (45.0 mg, 0.153 mmol), $Pd(PPh_3)_4$ (9.0 mg, 7.7 μmol) and InI (74 mg, 0.31 mmol) in dry THF (1 ml) under an argon atmosphere was added a solution of *p*-anisaldehyde (37 μl, 0.31 mmol) in dry THF (0.5 ml), and the mixture was stirred at room temperature for 26 h. The same workup and flash chromatography over silica gel with hexane–AcOEt (5:1) gave **5b** as a diastereomixture (5.8 mg, 9%) and **5a** (51 mg, 77%). **5a**. Colorless crystals from $Et_2O$–hexane. Mp 105–107°C; $[\alpha]_D^{29}=-43.1$ (*c* 0.35, $CHCl_3$); $^1$H NMR ($CDCl_3$, 270 MHz) δ: 0.62 (d, *J*=6.8 Hz, 6H), 1.55 (m, 1H), 2.18 (d, *J*=2.4 Hz, 1H), 2.30 (s, 3H), 2.54 (m, 1H), 2.61 (s, 6H), 3.10 (ddd, *J*=2.7, 5.4, 10.0 Hz, 1H), 3.80 (s, 3H), 4.48–4.53 (m, 2H), 5.17 (dd, *J*=1.6, 17.0 Hz, 1H), 5.36 (dd, *J*=1.6, 10.3 Hz, 1H), 5.87 (dt, *J*=10.3, 17.0 Hz, 1H), 6.82 (d, *J*=8.6 Hz, 2H), 6.95 (s, 2H), 7.11 (d, *J*=8.6 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 67.8 MHz) δ: 18.5, 19.2, 21.3, 23.4, 32.8, 53.5, 55.5, 59.2, 74.3, 113.8, 121.9, 128.7, 132.2, 134.2, 135.2, 135.8, 138.7, 142.2, 159.4. Anal. calcd for $C_{24}H_{33}NO_4S$: C, 66.79; H, 7.71; N, 3.25. Found: C, 66.90; H, 7.68; N, 3.19.

**4.1.4. *syn*,*syn*-Alcohol 6a.** Table 2, entry 5. To a stirred solution of *cis*-**1** (45.0 mg, 0.153 mmol), $Pd(PPh_3)_4$ (9.0 mg, 7.7 μmol) and InI (74 mg, 0.31 mmol) in dry THF (1 ml) was added a solution of *p*-chlorobenzaldehyde (43 mg, 0.31 mmol) in dry THF (0.5 ml) under an argon

atmosphere, and the mixture was stirred at room temperature for 3 h. The same workup and flash chromatography over silica gel with hexane–AcOEt (4:1) gave **6b** (4.5 mg, 7%) and **6a** (47 mg, 70%). **6a**. Yellow crystals from $Et_2O$–hexane. Mp 140°C; $[\alpha]_D^{29}=-53.9$ (*c* 0.34, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$: 0.60 (d, *J*=4.6 Hz, 3H), 0.63 (d, *J*=4.6 Hz, 3H), 1.55 (dqq, *J*=5.4, 4.6, 4.6 Hz, 1H), 2.30 (s, 3H), 2.44–2.52 (m, 2H), 2.61 (s, 6H), 3.15 (ddd, *J*=3.0, 5.4, 9.7 Hz, 1H), 4.53 (d, *J*=9.7 Hz, 1H), 4.65 (d, *J*=6.5 Hz, 1H), 5.09 (dd, *J*=1.6, 17.3 Hz, 1H), 5.20 (dd, *J*=1.6, 10.3 Hz, 1H), 5.87 (dt, *J*=17.3, 10.3 Hz, 1H), 6.95 (s, 2H), 7.15–7.29 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 67.8 MHz) $\delta$: 18.4, 19.3, 21.1, 23.4, 32.7, 53.7, 59.6, 74.3, 122.2, 128.5, 128.8, 132.2, 133.6, 134.3, 135.6, 138.6, 140.8, 142.3. Anal. calcd for $C_{23}H_{30}NO_3S$: C, 63.36; H, 6.94; N, 3.21. Found: C, 63.10; H, 6.92; N, 3.07. **6b**. A colorless oil. $[\alpha]_D^{33}=-41.2$ (*c* 0.42, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$: 0.36 (d, *J*=7.0 Hz, 3H), 0.73 (d, *J*=7.0 Hz, 3H), 1.89 (dqq, *J*=2.7, 7.0, 7.0 Hz, 1H), 2.19 (dt, *J*=2.4, 10.3 Hz, 1H), 2.30 (s, 3H), 2.66 (s, 6H), 3.41 (dt, *J*=2.7, 10.3 Hz, 1H), 3.52 (d, *J*=5.1 Hz, 1H), 4.58 (dd, *J*=1.6, 17.3 Hz, 1H), 4.76 (d, *J*=10.3 Hz, 1H), 4.91 (dd, *J*=1.6, 10.3 Hz, 1H), 5.26 (dd, *J*=2.4, 5.1 Hz, 1H), 5.63 (dt, *J*=10.3, 17.3 Hz, 1H), 6.96 (s, 2H), 7.17–7.27 (m, 4H); LRMS (FAB) *m/z* 436 ($MH^+$), 434 (100), 198, 168, 153; HRMS (FAB) *m/z* calcld. for $C_{23}H_{29}ClNO_3S$ ($M-H^-$) 434.1557; found: 434.1556.

**4.1.5. *syn*,*syn*-Alcohol 7a.** Table 2, entry 6. To a stirred solution of *cis*-**1** (45.0 mg, 0.153 mmol), $Pd(PPh_3)_4$ (9.0 mg, 7.7 μmol) and InI (74 mg, 0.31 mmol) in dry THF (1 ml) was added a solution of isobutylaldehyde (29 μl, 0.31 mmol) in dry THF (0.5 ml) under an argon atmosphere, and the mixture was stirred at room temperature for 23 h. The same workup and flash chromatography over silica gel with hexane–AcOEt (5:1) gave **7b** (3.5 mg, 6%) and **7a** (46 mg, 82%). **7a**. Orange crystals from $Et_2O$–hexane. Mp 100–105°C; $[\alpha]_D^{30}=-35.2$ (*c* 0.29, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$: 0.72 (d, *J*=7.0 Hz, 3H), 0.78 (d, *J*=7.0 Hz, 3H), 0.83 (d, *J*=7.0 Hz, 3H), 0.89 (d, *J*=7.0 Hz, 3H), 1.61 (m, 1H), 1.73 (m, 1H), 1.77 (d, *J*=4.9 Hz, 1H), 2.29 (s, 3H), 2.35 (dt, *J*=5.4, 10.3 Hz, 1H), 2.64 (s, 6H), 3.07 (dt, *J*=4.9, 6.2 Hz, 1H), 3.40 (dt, *J*=5.4, 9.2 Hz, 1H), 4.39 (d, *J*=9.2 Hz, 1H), 5.13 (dd, *J*=1.6, 17.0 Hz, 1H), 5.22 (dd, *J*=1.6, 10.3 Hz, 1H), 5.67 (dt, *J*=10.3, 17.0 Hz, 1H), 6.93 (s, 2H); $^{13}C$ NMR ($CDCl_3$, 67.8 MHz) $\delta$: 17.4, 18.1, 19.4, 20.0, 21.1, 23.4, 30.9, 31.8, 49.3, 60.4, 77.0, 120.5, 132.1, 134.9, 136.2, 138.4, 142.0. Anal. calcd for $C_{20}H_{33}NO_3S$: C, 65.36; H, 9.05; N, 3.81. Found: C, 64.90; H, 8.82; N, 3.68. **7b**. A colorless oil; $[\alpha]_D^{30}=-28.1$ (*c* 0.401, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$: 0.41 (d, *J*=7.0 Hz, 3H), 0.73 (d, *J*=6.8 Hz, 3H), 0.80 (d, *J*=6.8 Hz, 3H), 0.98 (d, *J*=6.5 Hz, 3H), 1.63 (dqq, *J*=6.8, 6.8, 9.6 Hz, 1H), 1.88 (dqq, *J*=3.4, 6.5, 7.0 Hz, 1H), 2.21 (dt, *J*=1.6, 10.0 Hz, 1H), 2.92 (s, 3H), 2.65 (s, 6H), 2.98 (d, *J*=5.3 Hz, 1H), 3.37 (dt, *J*=3.4, 10.0 Hz, 1H), 3.43 (ddd, *J*=1.6, 5.3, 9.6 Hz, 1H), 4.62 (d, *J*=10.0 Hz, 1H), 5.04 (dd, *J*=1.9, 17.0 Hz, 1H), 5.09 (dd, *J*=1.9, 10.0 Hz,1H), 5.69 (dt, *J*=10.0, 17.0 Hz, 1H), 6.94 (s, 2H); LRMS (FAB) *m/z* 368 ($MH^+$) 350, 254, 252, 183, 151, 119 (100); HRMS (FAB) *m/z* calcd for $C_{20}H_{34}NO_3S$ ($MH^+$) 368.2259; found: 368.2250.

**4.1.6. *syn*,*syn*-Alcohol 8a.** Table 2, entry 7. To a stirred solution of *cis*-**1** (13.8 mg, 0.047 mmol), $Pd(PPh_3)_4$ (2.7 mg, 2.4 μmol) and InI (23 mg, 0.094 mmol) in dry THF (1 ml) was added a solution of propionaldehyde (6.8 μl, 0.094 mmol) in dry THF (0.5 ml) under an argon atmosphere, and the mixture was stirred at room temperature for 2 h. The same workup and flash chromatography over silica gel with hexane–AcOEt (4:1) gave a mixture of **8b** and other isomer (3.2 mg, 19%, 3:2) and a mixture of **8a** and other isomer (10.1 mg, 61%, 2:1). **8a**. $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$: 0.61 (d, *J*=6.7 Hz, 1.02H), 0.72–0.88 (m, 7.98H), 0.88–2.0 (m, 3H), 2.18 (m, 1H), 2.29 (s, 3H), 2.64 (s, 2.04H), 2.66 (s, 3.96H), 3.38 (m, 1.32H), 3.44 (m, 0.34H), 3.57 (m, 0.34H), 4.44 (d, *J*=9.2 Hz, 0.66H), 4.94 (d, *J*=10.1 Hz, 0.34H), 5.02–5.28 (m, 2H), 5.54 (ddd, *J*=10.1, 10.4, 17.1 Hz, 0.34H), 5.69 (ddd, *J*=10.1, 10.1, 17.4 Hz, 0.66H), 6.93 (s, 2H); LRMS (FAB) *m/z* 354 ($MH^+$, 45), 336, 254, 119 (100). **8b**. $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$: 0.36 (d, *J*=7.1 Hz, 1.8H), 0.54 (d, *J*=6.7 Hz, 1.2H), 0.71 (d, *J*=7.0 Hz, 1.8H), 0.79 (d, *J*=6.7 Hz, 1.2H), 0.92 (m, 3H), 1.2–1.7 (m, 2.4H), 1.86 (m, 0.6H), 1.98 (m, 0.6H), 2.25 (m, 0.4H), 2.29 (s, 3H), 2.64 (s, 2.4H), 2.65 (s, 3.6H), 3.10 (d, *J*=5.2 Hz, 0.6H), 3.18 (d, *J*=4.9 Hz, 0.4H), 3.37 (ddd, *J*=3.1, 9.8, 9.8 Hz, 0.6H), 3.44 (m, 0.4H), 3.54 (m, 0.4H), 3.93 (m, 0.6H), 4.49 (d, *J*=10.1 Hz, 0.4H), 4.58 (d, *J*=10.1 Hz, 0.6H), 4.9–5.3 (m, 2H), 5.55 (ddd, *J*=9.8, 10.4, 17.4 Hz, 0.4H), 5.67 (ddd, *J*=10.1, 10.4, 17.4 Hz, 0.6H), 6.94 (s, 2H); LRMS (FAB) *m/z* 354 ($MH^+$, 56), 336, 254, 119 (100).

**4.1.7. *syn*,*syn*-Alcohol 9a.** Table 2, entry 8. To a stirred solution of *cis*-**1** (38.6 mg, 0.132 mmol), $Pd(PPh_3)_4$ (7.6 mg, 6.6 μmol) and InI (64 mg, 0.26 mmol) in dry THF (1 ml) was added a solution of acetaldehyde (15 μl, 0.26 mmol) in dry THF (0.5 ml) under an argon atmosphere, and the mixture was stirred at room temperature for 1 h. The same workup and flash chromatography over silica gel with hexane–AcOEt (5:1) gave a mixture of **9b** and other isomer (15.0 mg, 34%, 2.2:1) and a mixture of **9a** and other isomer (26.1 mg, 58%, 1.4:1). **9a**+isomer. $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$: 0.58, 0.75, 0.76, 0.78, 1.08, 1.10 (each d, *J*=7.0, 6.7, 7.1, 7.3, 6.1, 5.8 Hz, total 9H), 1.70 and 1.81 (each m, total 1H), 2.09 (ddd, *J*=4.9, 4.9, 9.8 Hz, 0.58H), 2.16 (ddd, *J*=7.3, 7.3, 9.8 Hz, 0.42H), 2.29 (s, 3H), 2.64 and 2.65 (each s, total 6H), 3.34 and 3.39 (each m, total 1H), 3.66 and 3.89 (each m, total 1H), 4.49 (d, *J*=9.5 Hz, 0.58H), 5.01 (d, *J*=9.8 Hz, 0.42H), 5.05–5.35 (m, total 2H), 5.53 (ddd, *J*=10.1, 10.1, 17.1 Hz, 0.58H), 5.71 (ddd, *J*=10.1, 10.1, 17.1 Hz, 0.42H), 6.93 (s, 2H); LRMS (FAB) *m/z* 340 ($MH^+$, 100), 254, 119. **9b**+isomer. $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$: 0.32 (d, *J*=6.8 Hz, 1.98H), 0.51 (d, *J*=10.2 Hz, 1.02H), 0.70 (d, *J*=7.0 Hz, 1.98H), 0.78 (d, *J*=6.8 Hz, 1.02H), 1.14 (d, *J*=6.8 Hz, 1.98H), 1.15 (d, *J*=6.4 Hz, 1.02H), 1.53 (m, 0.34H), 1.85 (m, 0.66H), 1.90 (ddd, *J*=1.9, 9.8, 10.1 Hz, 1H), 2.19 (ddd, *J*=2.4, 9.5, 9.8 Hz, 1H), 2.29 (s, 3H), 2.63 (s, 2.04H), 2.65 (s, 3.96H), 3.34 (ddd, *J*=3.1, 10.1, 10.1 Hz, 0.66H), 3.42 (m, 0.34H), 3.89 (m, 0.66H), 4.36 (m, 0.34H), 4.54 (d, *J*=10.1 Hz, 0.34H), 4.68 (d, *J*=10.1 Hz, 0.66H), 4.95–5.25 (m, 2H), 5.57 (ddd, *J*=10.1, 10.1, 17.4 Hz, 0.34H), 5.68 (ddd, *J*=10.1, 10.1, 17.4 Hz, 0.66H), 6.94 (s, 2H); LRMS (FAB) *m/z* 340 ($MH^+$, 100), 254, 119.

**4.1.8. Boc-Aziridine 10.** To a stirred solution of (3*RS*,4*S*)-4-

[*N*-(*tert*-butoxycarbonyl)amino]-5-methylhexene-3-ol (340 mg, 0.1.48 mmol) in THF (4 ml) were added $PPh_3$ (468 mg, 1.78 mmol) and diethyl azodicarboxylate (40% solution in toluene, 807 ml, 1.78 mmol) at 0°C, and the mixture was stirred for 5 h. The mixture was concentrated in vacuo to give an oily residue, which was purified by $SiO_2$ flash chromatography. Elution with hexane–AcOEt (5:1) gave **10** (175 mg, 56%). **10** (*cis–trans*=6:1). A colorless oil; $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$: 0.88 (d, *J*=6.8 Hz, 18/7H), 0.98 (d, *J*=6.8 Hz, 3/7H), 1.06 (d, *J*=6.8 Hz, 3/7H), 1.13 (d, *J*=6.8 Hz, 18/7H), 1.3–1.5 (m, 1H), 1.45 (s, 9H), 2.16 (dd, *J*=9.6, 6.8 Hz, 6/7H), 2.22 (dd, *J*=7.7, 6.1 Hz, 1/7H), 2.80 (dd, *J*=7.6, 3.2 Hz, 1/7H), 2.98 (t, *J*=6.8 Hz, 6/7H), 5.24–5.30 (m, 1H), 5.39–5.47 (m, 1H), 5.67 (m, 1H). Anal. calcd for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63. Found: C, 67.95; H, 10.16; N, 6.37.

**4.1.9. Boc-Aziridine 11.** The same treatment of (3*RS*,4*S*)-4-[*N*-(*tert*-butoxycarbonyl)amino]-5-*tert*-butyldimethylsiloxypenten-3-ol (200 mg, 0.603 mmol) as described for **10** gave **11** (143 mg, 76%). **11** (*cis–trans*=6:1). A colorless oil; $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$: 0.06 (s, 3H), 0.07 (s, 3H), 0.90 (s, 9H), 1.45 (s, 9H), 2.57 (dt, *J*=4.5, 3.0 Hz, 1/7H), 2.71 (dt, *J*=6.5, 5.4 Hz, 6/7H), 2.94 (m, 1/7H), 3.03 (t, *J*=6.5 Hz, 6/7H), 3.53 (dd, *J*=8.5, 6.5 Hz, 6/7H), 3.69 (dd, *J*=11.3, 4.9 Hz, 1/7H), 3.80 (dd, *J*=8.5, 5.4 Hz, 6/7H), 3.89 (dd, *J*=11.3, 4.0 Hz, 1/7H), 5.26–5.31 (m, 1H), 5.38–5.48 (m, 1H), 5.69 (ddd, *J*=16.7, 10.3, 6.5 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 67.8 MHz) $\delta$ (major): −4.8, −4.5, 18.5, 26.1, 28.1, 42.8, 44.3, 61.2, 81.5, 119.8, 131.9, 162.3; LRMS (FAB) *m*/*z* 314 ($MH^+$), 258, 200, 73 (100); HRMS (FAB), *m*/*z* calcd. for $C_{16}H_{32}NO_3Si$ ($MH^+$) 314.2152, found: 314.2165.

**4.1.10. Acetate 12.** To a stirred solution of (3*RS*,4*S*)-4-[*N*-(*tert*-butoxycarbonyl)amino]-5-methylhexen-3-ol (500 mg, 2.18 mmol) in $CH_2Cl_2$ (1 ml) were added pyridine (4.4 ml), DMAP (13 mg, 0.11 mmol) and $Ac_2O$ (2.0 ml, 21.8 mmol), and the mixture was stirred at room temperature for 1 h. After quenching with citric acid, the mixture was extracted with ether. The extract was washed with water, a saturated $NaHCO_3$ solution and brine, and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with hexane–AcOEt (8:1) gave **12** (425 mg, 72%). **12** (*syn–anti*=6:1). A colorless oil; $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$: 0.89 (d, *J*=6.5 Hz, 3/7H), 0.92 (d, *J*=7.2 Hz, 18/7H), 0.95 (d, *J*=7.2 Hz, 18/7H), 0.99 (d, *J*=6.5 Hz, 3/7H), 1.44 (s, 9H), 1.71 (m, 1H), 2.07 (s, 3/7H), 2.09 (s, 18/7H), 3.37 (m, 1/7H), 3.55 (ddd, *J*=10.9, 7.2, 3.9 Hz, 6/7H), 3.70 (m, 1/7H), 4.37 (d, *J*=10.5 Hz, 1/7H), 4.58 (d, *J*=10.3 Hz, 6/7H), 5.1–5.6 (m, 3H), 5.6–6.0 (m, 1H); $^{13}$C NMR ($CDCl_3$, 67.8 MHz) $\delta$ (major): 18.4, 20.1, 21.2, 28.6, 30.0, 58.5, 74.6, 79.4, 118.0, 134.4, 156.3, 170.2; LRMS (FAB), *m*/*z* 272 ($MH^+$), 216, 172, 156 (100); HRMS (FAB), *m*/*z* calcd. for $C_{14}H_{26}NO_4$ ($MH^+$) 272.1862, found: 272.1857.

**4.1.11. Oxazolidinone 14.** To a stirred solution of a mixture of (4*R*,5*S*)- and (4*R*,5*R*)-4-isopropyl-5-vinyloxazolidin-2-one **15** (140 mg, 0.902 mmol) in THF (3 ml) were added $Et_3N$ (137 μl, 0.992 mmol), DMAP (110 mg, 0.902 mmol) and $Boc_2O$ (216 mg, 0.992 mmol), and the resulting mixture was stirred at room temperature for 15 h. After the mixture was concentrated in vacuo and the residue was extracted with ether, the extract was washed with a 10% citric acid solution, a saturated $NaHCO_3$ solution and brine, and then dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with hexane–AcOEt (5:1) gave **14** (166 mg, 72%) and *cis*-adduct (24 mg, 10%). **14**. A colorless oil; $[\alpha]_D^{17}=-21.9$ (*c* 0.366, $CHCl_3$); $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$: 0.94 (d, *J*=7.0 Hz, 3H), 0.96 (d, *J*=7.0 Hz, 3H), 1.54 (s, 9H), 2.29 (dq, *J*=7.0, 4.1 Hz, 1H), 3.89 (dd, *J*=4.1, 3.0 Hz, 1H), 4.46 (dd, *J*=5.5, 3.0 Hz, 1H), 5.31 (d, *J*=10.3 Hz, 1H), 5.41 (d, *J*=16.7 Hz, 1H), 5.85 (ddd, *J*=16.7, 10.3, 5.5 Hz, 1H). LRMS (FAB) *m*/*z* 256 ($MH^+$), 200 (100); HRMS (FAB), *m*/*z* calcd. for $C_{13}H_{22}NO_4$ ($MH^+$) 256.1549, found: 256.1557.

**4.1.12. *syn*,*syn*-Alcohol 16a.** Table 3, entry 1. The same treatment of **10** (40.0 mg, 0.189 mmol) and benzaldehyde (29 μl, 0.31 mmol) as described for **2a** afforded the oily residue, which was purified by $SiO_2$ flash chromatography with hexane–AcOEt (5:1) gave **16b** (3.2 mg, 5%) and **16a** (28 mg, 46%). Entry 4. The same treatment of **12** (60.0 mg, 0.221 mmol) and benzaldehyde (50 μl, 0.44 mmol) as described above gave **16b** (4.2 mg, 6%) and **16a** (55 mg, 78%). Entry 6. The same treatment of **14** (48.0 mg, 0.188 mmol) and benzaldehyde (38 μl, 0.38 mmol) as described above gave **16b** (3.8 mg, 6%) and **16a** (50 mg, 83%). **16a**. A colorless oil; $[\alpha]_D^{26}=-88.8$ (*c* 0.965, $CHCl_3$); $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$: 0.82 (d, *J*=6.8 Hz, 6H), 1.46 (s, 9H), 1.61 (dqq, *J*=6.8, 6.8, 7.8 Hz, 1H), 2.58 (ddd, *J*=3.0, 6.5, 10.0 Hz, 1H), 2.82 (br, 1H), 3.33 (ddd, *J*=3.0, 7.8, 10.0 Hz, 1H), 4.42 (d, *J*=10.0 Hz, 1H), 4.73 (d, *J*=6.5 Hz, 1H), 5.06 (dd, *J*=1.6, 17.3 Hz, 1H), 5.26 (dd, *J*=1.6, 10.0 Hz, 1H), 5.81 (dt, *J*=10.0, 17.3 Hz, 1H), 7.23–7.35 (m, 5H); $^{13}$C NMR ($CDCl_3$, 67.8 MHz) $\delta$: 18.6, 19.9, 28.6, 32.0, 54.2, 57.0, 75.5, 79.5, 120.7, 127.1, 127.7, 128.3, 134.2, 142.7, 156.4; LRMS (FAB) *m*/*z* 320 ($MH^+$), 246, 116 (100); HRMS (FAB) *m*/*z* calcd for $C_{19}H_{30}NO_3$ ($MH^+$) 320.2225; found: 320.2214. **16b**. A colorless oil; $[\alpha]_D^{33}=-35.6$ (*c* 0.358, $CHCl_3$); $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$: 0.80 (d, *J*=6.8 Hz, 3H), 0.98 (d, *J*=6.8 Hz, 3H), 1.47 (s, 9H), 2.06 (dqq, *J*=3.0, 6.8, 6.8 Hz, 1H), 2.18 (dt, *J*=1.9, 10.4 Hz, 1H), 3.77 (dt, *J*=1.9, 10.4 Hz, 1H), 4.27 (d, *J*=4.3 Hz, 1H), 4.56 (dd, *J*=1.9, 17.3 Hz, 1H), 4.63 (d, *J*=10.4 Hz, 1H), 4.89 (dd, *J*=1.9, 10.4 Hz, 1H), 4.94 (m, 1H), 5.69 (dt, *J*=10.4, 17.3 Hz, 1H), 7.15–7.32 (m, 5H); LRMS (FAB) *m*/*z* 320 ($MH^+$), 246, 116 (100); HRMS (FAB) *m*/*z* calcd for $C_{19}H_{30}NO_3$ ($MH^+$) 320.2225; found: 320.2235.

**4.1.13. *syn*,*syn*-Alcohol 17a.** Table 3, entry 2. The same treatment of **9** (111 mg, 0.354 mmol) and benzaldehyde (72 μl, 0.71 mmol) as described for **2a** afforded the oily residue, which was purified by $SiO_2$ flash chromatography with hexane–AcOEt (5:1) to give **17b** as a diastereomixture (10.4 mg, 7%) and **17a** as a single isomer (76 mg, 51%). **17a**. A colorless oil; $[\alpha]_D^{32}=-15.9$ (*c* 0.508, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 0.02 (s, 3H), 0.04 (s, 3H), 0.88 (s, 9H), 1.44 (s, 9H), 2.70 (m, 1H), 3.20 (br, 1H), 3.50 (m, 1H), 3.64 (m, 1H), 3.75 (m, 1H), 4.67 (m, 1H), 4.87 (br, 1H), 4.96 (d, *J*=16.5 Hz, 1H), 5.16 (d, *J*=10.0 Hz, 1H), 5.84 (dt, *J*=10.0, 16.5 Hz, 1H), 7.24–7.32 (m, 5H); LRMS (FAB) *m*/*z* 422 ($MH^+$), 322, 308, 218 (100); HRMS (FAB) *m*/*z* calcd. for $C_{23}H_{40}NO_4Si$ ($MH^+$) 422.2727; found: 422.2721.

**4.1.14. *syn*,*syn*-Alcohol 18a.** Table 3, entry 3. The same treatment of **11** (65 mg, 0.207 mmol; *cis*–*trans*=7:1) and *trans*-cinnamaldehyde (39 μl, 0.31 mmol) as described for **2a** afforded the oily residue, which was purified by $SiO_2$ flash chromatography with hexane–AcOEt (7:1) to give **18b** as a diastereomixture (10 mg, 11%) and **18a** as a single isomer (32 mg, 35%). **18a**. A colorless oil; $[\alpha]_D^{19}=+22.3$ (*c* 1.47, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 270 MHz) δ: 0.08 (s, 6H), 0.91 (s, 9H), 1.44 (s, 9H), 2.56 (ddd, *J*=4.8, 4.8, 10.0 Hz, 1H), 3.60 (dd, *J*=5.1, 10.0 Hz, 1H), 3.74 (dd, *J*=4.0, 10.0 Hz, 1H), 3.92 (m, 1H), 4.45 (dd, *J*=4.8, 6.2 Hz, 1H), 4.68 (br d, *J*=8.1 Hz, 1H), 5.17 (d, *J*=17.1 Hz, 1H), 5.26 (d, *J*=10.0 Hz, 1H), 5.86 (td, *J*=10.0, 17.1 Hz, 1H), 6.23 (dd, *J*=6.2, 15.9 Hz, 1H), 6.61 (d, *J*=15.9 Hz, 1H), 7.20–7.39 (m, 5H); $^{13}C$ NMR ($CDCl_3$, 67.8 MHz) δ: −4.8, −4.5, 18.4, 26.1, 28.6, 51.8, 53.1, 63.6, 72.5, 79.9, 120.1, 126.8, 127.7, 128.7, 130.7, 131.0, 134.2, 137.2, 156.0; LRMS (CI) *m/z* 448 ($MH^+$), 446, 374, 346, 294 (100); HRMS (CI) *m/z* calcd for $C_{25}H_{42}NO_4Si$ ($MH^+$) 448.2883; found: 448.2866.

**4.1.15. *syn*,*syn*-Alcohol 19a.** Table 3, entry 5. The same treatment of **13** (39 mg, 0.160 mmol) and benzaldehyde (33 μl, 0.32 mmol) as described for **2a** afforded the oily residue, which was purified by $SiO_2$ flash chromatography with hexane–AcOEt (5:1) to give **19b** as a diastereomixture (4.9 mg, 11%) and **19a** as a single isomer (21 mg, 44%). **19a**. A colorless oil; $[\alpha]_D^{21}=-68.8$ (*c* 1.61, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 500 MHz) δ: 1.08 (d, *J*=6.4 Hz, 3H), 1.45 (s, 9H), 2.30 (ddd, *J*=3.4, 6.4, 9.8 Hz, 1H), 2.69 (br s, 1H), 3.78 (br s, 1H), 4.38 (br s, 1H), 4.82 (br s, 1H), 5.05 (d, *J*=17.4 Hz, 1H), 5.28 (d, *J*=9.8 Hz, 1H), 5.84 (td, *J*=9.8, 17.4 Hz, 1H), 7.24–7.43 (m, 5H); LRMS (FAB) *m/z* 292 ($MH^+$), 236, 218, 154, 88 (100); HRMS (FAB) *m/z* calcd for $C_{17}H_{26}NO_3$ ($MH^+$) 292.1913; found: 292.1921.

**4.1.16. Oxazinone 20.** To a stirred suspension of NaH (60% suspension, 2.0 mg, 0.046 mmol) in DMF (0.5 ml) was added a solution of **16a** (9.7 mg, 0.030 mmol) in THF (1 ml) at 0°C under an argon atmosphere, and the mixture was stirred at room temperature for 3 h. After quenched with a 10% citric acid solution, the mixture was extracted with AcOEt. The extract was washed with a saturated $NaHCO_3$ solution, water and brine, and dried over $MgSO_4$. Usual workup followed by flash chromatography with hexane–AcOEt (1:1) gave **20** (5.4 mg, 72%). **20**. Colorless crystals from $Et_2O$–hexane. Mp 154–156°C; $[\alpha]_D^{32}=-43.1$ (*c* 0.252, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 500 MHz) δ: 0.92 (d, *J*=6.4 Hz, 3H), 1.04 (d, *J*=6.7 Hz, 3H), 1.65 (qqd, *J*=6.4, 6.7, 10.5 Hz, 1H), 2.73 (ddd, *J*=1.8, 3.6, 10.5 Hz, 1H), 3.33 (dd, *J*=3.6, 10.5 Hz, 1H), 4.76 (dd, *J*=1.3, 17.0 Hz, 1H), 5.11 (dd, *J*=1.3, 10.5 Hz, 1H), 5.42 (br s, 1H), 5.49 (d, *J*=1.8 Hz, 1H), 5.67 (ddd, *J*=10.5, 10.5, 17.0 Hz, 1H), 7.26–7.35 (m, 5H); LRMS (FAB) *m/z* 246 ($MH^+$), 116 (100); HRMS (FAB) *m/z* calcd for $C_{15}H_{20}NO_2$ ($MH^+$) 246.1494; found: 246.1497.

**4.1.17. Oxazinone 21.** The same treatment of **16b** (9.0 mg, 0.0282 mmol) as described for **20** and purification by $SiO_2$ column chromatography with hexane–AcOEt (3:1) gave **21** (3.3 mg, 48%). **21**. A colorless oil; $[\alpha]_D^{32}=-32.6$ (*c* 0.291, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 500 MHz) δ: 1.01 (d, *J*=6.8 Hz, 6H), 1.86 (sepd, *J*=6.8, 6.7 Hz, 1H), 2.82 (ddd, *J*=3.3, 5.8, 8.8 Hz), 3.07 (ddd, *J*=2.1, 5.8, 6.7 Hz, 1H), 5.11 (d, *J*=17.1 Hz, 1H), 5.16 (d, *J*=10.4 Hz, 1H), 5.41 (d, *J*=3.3 Hz, 1H), 5.47 (ddd, *J*=8.8, 10.4, 17.1 Hz, 1H), 5.67 (br s, 1H), 7.25–7.40 (m, 5H); LRMS (FAB) *m/z* 246 ($MH^+$), 149, 116 (100); HRMS (FAB) *m/z* calcd for $C_{15}H_{20}NO_2$ ($MH^+$) 246.1494; found: 246.1491.

**4.1.18. Ester 22.** A solution of **2a** (10 mg, 0.025 mmol) in a mixture of MeOH (2 ml) and $CH_2Cl_2$ (1 ml) was treated with a stream $O_3/O_2$ at −78°C until blue color persisted. After the solution was purged with $O_2$ to remove excess $O_3$, $Me_2S$ (5.5 μl, 0.074 mmol) was added and the mixture was stirred at −78°C for 0.5 h and then at room temperature for 1 h. The mixture was concentrated in vacuo and the residue was used for the following reaction. To a solution of the crude aldehyde and 2-methyl-2-butene (5.0 μl, 0.10 mmol) in *t*-BuOH (1 ml) was added a solution of $NaClO_2$ (4.5 mg, 0.050 mmol) and $NaH_2PO_4$ (7.5 mg, 0.062 mmol) in water, and the resulting mixture was stirred vigorously for 40 min. After addition of a 10% HCl solution for acidification, the mixture was extracted with $CHCl_3$ and the organic layer was dried over $Na_2SO_4$ and concentrated in vacuo. The residue was dissolved in a mixture of benzene–MeOH (4:1, 1.25 ml) and $TMSCHN_2$ (10% solution in *n*-hexane, 77 ml, 0.068 mmol) was added to the solution, and the mixture was stirred at room temperature for 1 h. After concentration in vacuo, the residue was purified by column chromatography over silica gel with hexane–AcOEt (5:1) to give **22** (9.6 mg, 89%). **22**. A colorless oil; $[\alpha]_D^{15}=-44.6$ (*c* 0.552, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 270 MHz) δ: 0.72 (d, *J*=7.0 Hz, 6H), 1.83 (dq, *J*=5.4, 7.0 Hz, 1H), 2.31 (s, 3H), 2.47 (d, *J*=5.1 Hz, 1H), 2.63 (s, 6H), 3.03 (dd, *J*=3.2, 8.6 Hz, 1H), 3.22 (ddd, *J*=3.2, 5.4, 8.8 Hz, 1H), 3.68 (s, 3H), 4.71 (dd, *J*=4.3, 8.6 Hz, 1H), 6.17 (d, *J*=8.8 Hz, 1H), 6.97 (s, 2H), 7.00–7.04 (m, 2H), 7.26–7.30 (m, 3H); $^{13}C$ NMR ($CDCl_3$, 67.8 MHz) δ: 17.6, 18.8, 21.1, 23.1, 32.9, 51.6, 52.4, 58.1, 74.2, 126.9, 128.8, 128.9, 132.1, 137.0, 138.3, 141.0, 141.8, 174.9; LRMS (FAB) *m/z*, 434 ($MH^+$), 254 (100); HRMS (FAB) *m/z* calcd for $C_{23}H_{32}NO_5S$ ($MH^+$) 434.2002, found: 434.2009.

**4.1.19. Ester 23.** The same treatment of **5a** (9.3 mg, 0.022 mmol) as described for **22** gave the crude product, which was purified by column chromatography over silica gel with hexane–AcOEt (3:1) to give **23** (6.3 mg, 63%). **23**: A colorless oil; $[\alpha]_D^{16}=-39.4$ (*c* 0.360, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 270 MHz) δ: 0.72 (d, *J*=6.8 Hz, 6H), 1.79 (dq, *J*=5.4, 6.8 Hz, 1H), 2.23 (d, *J*=4.6 Hz, 1H), 2.32 (s, 3H), 2.63 (s, 6H), 3.00 (dd, *J*=3.0, 9.3 Hz, 1H), 3.16 (ddd, *J*=3.0, 5.4, 8.6 Hz, 1H), 3.71 (s, 3H), 3.81 (s, 3H), 4.66 (dd, *J*=4.6, 9.3 Hz, 1H), 6.25 (d, *J*=8.6 Hz, 1H), 6.78–6.82 (m, 2H), 6.90–6.97 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 67.8 MHz) δ: 17.5, 19.0, 21.1, 23.1, 33.1, 51.4, 52.5, 55.5, 58.1, 73.9, 114.2, 128.3, 132.1, 133.0, 137.0, 138.3, 139.4, 141.8, 175.1; LRMS (FAB) *m/z* 464 ($MH^+$), 254 (100), 154; LRMS (FAB) *m/z* calcd for $C_{24}H_{34}NO_6S$ ($MH^+$) 464.2106, found: 464.2112.

**4.1.20. Ester 24.** The same treatment of **6a** (9.8 mg, 0.023 mmol) as described for **22** gave the crude product, which was purified by column chromatography over silica gel with hexane–AcOEt (5:1) to give **24** (6.1 mg, 58%). **24**: A colorless oil; $[\alpha]_D^{17}=-55.3$ (*c* 0.235, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 270 MHz) δ: 0.70 (d, *J*=6.8 Hz, 3H), 0.71 (d,

$J$=6.8 Hz, 3H), 1.77 (dqq, $J$=5.4, 6.8, 6.8 Hz, 1H), 2.31 (s, 3H), 2.63 (s, 6H), 2.97 (dd, $J$=3.2, 8.4 Hz, 1H), 3.23 (ddd, $J$=3.2, 5.4, 8.6 Hz, 1H), 3.68 (s, 3H), 4.79 (dd, $J$=5.0, 8.4 Hz, 1H), 6.15 (d, $J$=8.6 Hz, 1H), 6.96 (s, 2H), 7.03–7.07 (m, 2H), 7.26–7.30 (m, 2H); $^{13}$C NMR ($CDCl_3$, 67.8 MHz) $\delta$: 17.8, 18.8, 21.1, 23.1, 32.7, 51.9, 52.5, 58.2 73.5, 128.3 129.0, 132.1, 134.4, 136.8, 138.3, 139.7, 141.9, 174.6; LRMS (FAB) $m/z$ 468 ($MH^+$), 254 (100), 119; HRMS (FAB) $m/z$ calcd for $C_{23}H_{31}ClNO_5S$ ($MH^+$) 468.1611, found: 468.1592.

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