JOC The Journal of Organic Chemistry

ARTICLE

pubs.acs.org/joc

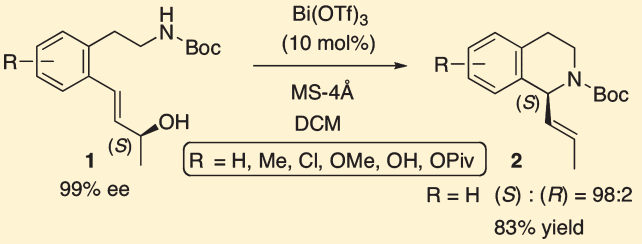
# Synthesis of Chiral 1-Substituted Tetrahydroisoquinolines by the Intramolecular 1,3-Chirality Transfer Reaction Catalyzed by $Bi(OTf)_3$

Nobuyuki Kawai,* Ryuzou Abe, Mika Matsuda, and Jun'ichi Uenishi

Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto 607-8412, Japan

Supporting Information

**ABSTRACT:** The intramolecular 1,3-chirality transfer reaction of chiral amino alcohols **1** with 99% ee was developed to construct chiral 1-substituted tetrahydroisoquinoline **2**. $Bi(OTf)_3$ (10 mol %)-catalyzed cyclization of **1** (R = H) afforded (*S*)-1-(*E*)-propenyl tetrahydroisoquinoline **2** (R = H) in 83% yield with a ratio of 98:2. The stereochemistry at the newly formed chiral center was produced by a *syn* $S_N2'$-type process. In this reaction, the substituent on the benzene ring of **1** significantly affected the reactivities and selectivities. A plausible reaction mechanism was proposed.

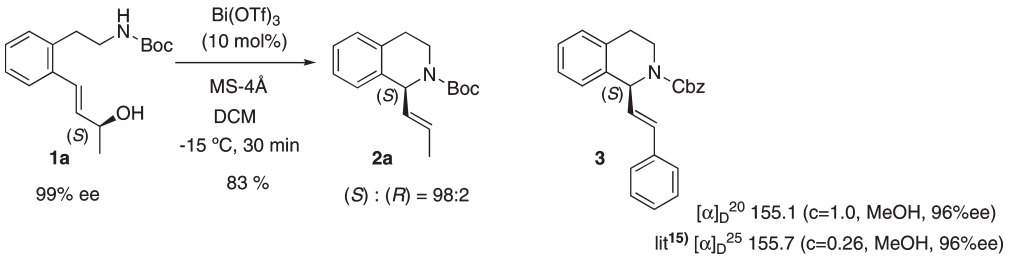



1,2,3,4-Tetrahydroisoquinolines, especially 1-substituted tetrahydroisoquinolines, are compounds of great interest due to their biological and pharmacological properties.[1] For instance, 1-methyl- and 1-phenyl tetrahydroisoquinoline are involved in the treatment of Parkinson's and other nervous disorders,[1d] and derivatives with methoxy or hydroxy substituents at the 6 and/or 7 position comprise the widest group of naturally occurring alkaloids.[2] Preparation of these compounds has received much attention, especially with regard to efforts directed at asymmetric synthesis.[3−10] The most important synthetic methods are the Pictet−Spengler cyclization,[4] the reduction of 1-substituted 3,4-dihydroisoquinolines,[5] α-alkylation of chiral formamidines,[6] and organolithium additions to imines.[7] These methods allow the synthesis of enantioenriched 1-substituted tetrahydroisoquinolines in two steps: cyclization and creation of a stereocenter, although only the asymmetric Pictet−Spengler reaction creates the stereogenic carbon at C-1 simultaneously with the ring closure. Furthermore the alternative reported synthetic methods of enantioenriched 1-substituted tetrahydroisoquinolines in one step include intramolecular aminoselenation with chiral selenium compounds,[8] asymmetric allylic amination catalyzed by Pd(0) complex,[9] and an enantioselective aza-Michael reaction.[10] These methods still need improvement with regard to the selectivity of chiral induction.

Direct amino substitution of alcohols has emerged as an attractive area of research because this approach is considered more efficient.[11,12] Although there are many catalysts for direct allylic aminations or amino substitutions of allylic alcohols reported in the literature, only a few reports involve chiral transfer with a chiral secondary allylic alcohol as a substrate.[12e,12g,13] In several examples, the racemic amine and amide were afforded by passing through the cationic intermediate, except for a few reports[13] dealing with $PdCl_2$-$(CH_3CN)_2$ or [P(*t*-Bu)$_2$*o*-biphenyl]AuCl-$AgSbF_6$ as a catalyst.

Since strict stereocontrol ring formation is desired, we have designed a new stereocontrolled synthesis of 1-substituted tetrahydroisoquinoline by an intramolecular $S_N2'$-type reaction, in which the attack of an amino nucleophile onto the prochiral carbon of olefin in an *exo-trig* fashion results in the formation of a tetrahydroisoquinoline ring. Stereoselective 1,3-chirality transfer might be expected in either a *syn*-$S_N2'$- or *anti*-$S_N2'$-type process intramolecularly. Recently, we have found and communicated

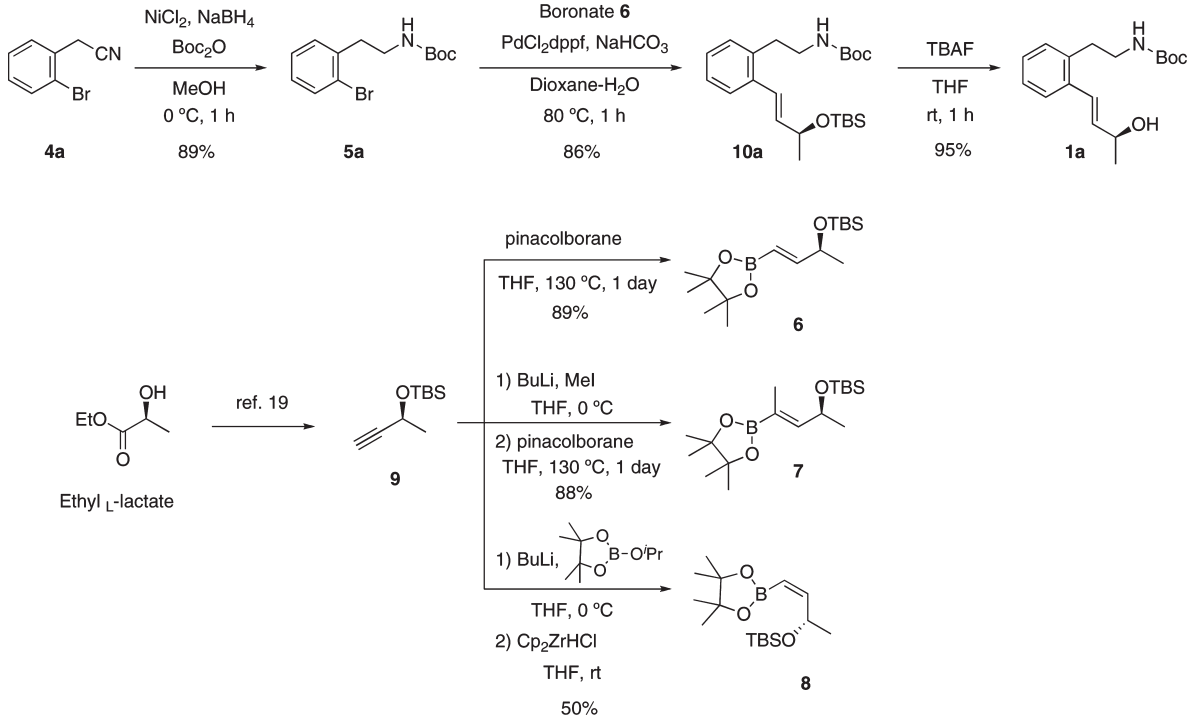
**Scheme 1. $Bi(OTf)_3$-Catalyzed Cyclization via 1,3-Chirality Transfer**




**Received:** December 15, 2010
**Published:** February 28, 2011

 © 2011 American Chemical Society 

**Scheme 2. Synthesis of the Precursors**

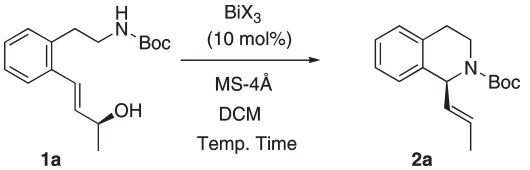



that $Bi(OTf)_3$ is an efficient catalyst in the stereoselective cyclization of substrate possessing a chiral allylic alcohol **1a** conjugated with a benzene ring to afford the (*S*)-1-(*E*)-propenyl tetrahydroisoquinoline **2a** in 83% yield with a ratio of 98:2.[14] (Scheme 1) The absolute configuration of **2a** was determined to be *S* by conversion to known compound **3**,[15] followed by a comparison of the specific rotation on the sign. In our previous communication, we have a few examples. The reactions were then studied in more depth, and we report herein a detailed study of the $Bi(OTf)_3$-catalyzed intramolecular 1,3-chirality transfer reaction with a broad scope. In particular, the effect of the substituent on the benzene ring of **1** was examined in the reaction to establish it as an efficient methodology for the synthetic application of naturally occurring alkaloids.

## RESULTS AND DISCUSSION

**Preparation of Cyclization Precursors.** Scheme 2 shows the synthesis of the cyclization precursor **1a** as a general synthesis. The chiral allylic alcohol moiety has been introduced by the Suzuki coupling reaction of **5a**[16] and boronate **6**.[17] We began the synthesis from 2-(*o*-bromophenyl)acetonitrile **4a**[18] prepared from benzyl bromide by cyanation in DMSO. Reduction of the nitrile with $NaBH_4$ and a catalytic amount of $NiCl_2$ in MeOH followed by protection of the resultant amine with $Boc_2O$ gave **5a** in 89% yield. The (*E*)-alkenyl boronate **6** was prepared by hydroboration of the chiral alkyne **9**[19] with pinacolborane in 89% yield. (*E*)-Trisubstituted alkenylboronate **7** and (*Z*)-alkenyl boronate **8**[20] were also prepared. The homologation of **9** with BuLi and MeI, followed by the hydroboration, gave **7** in 88% yield in 2 steps. The treatment of **9** with BuLi and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane followed by the hydrozirconation of the resultant alkynylboronate gave **8** in 50% yield in 2 steps. The cross-coupling reaction of **5a** and **6** proceeded in the presence of 5 mol % of $PdCl_2(dppf)$ as a catalyst and $NaHCO_3$ in aqueous solution and produced **10a** in 86% yield. Deprotection of **10a** with TBAF in THF afforded the alcohol **1a** in 95% yield.

**Table 1. Optimization of Reaction Conditions**



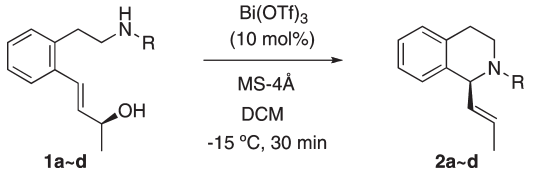

| entry | X | temp (°C) | time (h) | yield (%) | ratio (*S*:*R*)[a] |
|---|---|---|---|---|---|
| 1 | Cl | −15 | 0.5 | 85 | 82:18 |
| 2 | Br | −15 | 2 | 0 | |
| 3 | OTf | −15 | 0.5 | 83 | 98:2 |
| 4 | OTf | 0 | 0.1 | 82 | 94:6 |
| 5 | OTf | −50 | 12 | 64 | 96:4 |
| 6[b] | OTf | −15 | 0.5 | 63 | 96:4 |
| 7[b,c] | OTf | −15 | 0.5 | 49 | 96:4 |

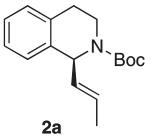
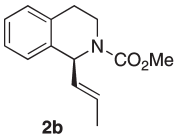
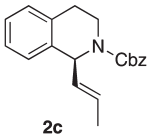
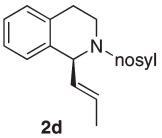
[a] Determined by HPLC. [b] In the absence of MS-4 Å. [c] $H_2O$ (30 mol %) was added before the addition of the solution of **1a**.

**Bi-Catalyzed Cyclizations.** The effect of the counteranion was examined in Bi(III)-catalyzed cyclization of **1a** in Table 1. In the presence of MS-4 Å, $BiCl_3$ completed the reaction at −15 °C in 30 min to afford **2a** in 85% yield with a ratio of 82:18 (entry 1). By contrast, the softer bromide counteranion did not promote the reaction at −15 °C (entry 2). In entry 3, $Bi(OTf)_3$ proved to be the most efficient catalyst in the high 1,3-chiraity transfer. The temperature effect was examined in the $Bi(OTf)_3$-catalyzed cyclization. At 0 °C, the reaction was completed within 5 min to afford **2a** in 82%


dx.doi.org/10.1021/jo102452d |*J. Org. Chem.* 2011, 76, 2102–2114

**Table 2. Substituent Effect on the Amino Group**




| Product |  |  |  |  |
|---|---|---|---|---|
| | 2a | 2b | 2c | 2d |
| Yield (%) | 83 | 65 | 67 | 91 |
| Ratio; (*S*) : (*R*) | 98:2 | 90:10 | 89:11 | 70:30 |

yield along with a slight loss of selectivity (94:6) (entry 4). The reaction took much longer at −50 °C, leading to a lower yield of **2a**, and no significant increase in the selectivity was observed in entry 5. The addition of MS-4 Å was very important to complete the reaction and obtain **2a** in high yield by comparison of entries 3 and 6. In entry 7, the addition of 30 mol % of $H_2O$ in $Bi(OTf)_3$ to generate TfOH resulted in a low yield of **2a**.

Under the optimized conditions, the scope of the reaction with respect to the amide substrate was examined with catalyst (Table 2). The methyl and benzyl carbamate were less reactive for the cyclization than the Boc group, and the cyclized products **2b** and **2c** were obtained in 65% and 67% yield with ratios of 90:10 and 89:11, respectively. When the sulfonamide with a nitro substituent, a nosyl group, was used, the reaction was completed within 30 min, and the corresponding product **2d** was obtained in 91% yield with a 70:30 ratio. Neither the PMB amine nor the pivaloyl amide cyclized at all, and starting materials were recovered.

Several precursors that were substituted at the *para* position relative to the alkenyl substituent on the benzene ring were used in the $Bi(OTf)_3$-catalyzed cyclization under the following conditions: 10 mol % of $Bi(OTf)_3$ with MS-4 Å in DCM at −15 or −20 °C. The cyclizations proceeded smoothly, within 5 min, and the methyl substituent **2e** and chloro substituent **2f** were obtained in 71% and 88% yields, respectively, with high 1,3-chirality transfer (Table 3). The **2g** substituted with a methoxy group, which is a more electron-donating group than a methyl group, was obtained in quantitative yield. However, non-1,3-chirality transfer was observed. The cyclization of hydroxy-substituted **1h** was promoted by $Bi(OTf)_3$ and resulted in no selectivity. In contrast, the reaction of the methoxy substituent at the *meta* position relative to the alkenyl substituent on the benzene ring was completed at −15 °C in 2.3 h, and **2i** was obtained in 82% yield with high 1,3-chirality transfer (95:5). The cyclizations of the *m*-chloro substituent required 2 days at 0 °C to go to completion to give **2j** in 68% yield with a ratio of 93:7. These results indicate that a mesomeric effect enhanced the reactivity and selectivity. The methyl substituent at the *ortho* position relative to the alkenyl substituent on the benzene ring was examined. However, the reaction did not take place at −15 °C, requiring warming to room temperature, and **2k** was obtained in 74% yield with a significant loss of selectivity (77:23). The substituent effect on the allylic alcohol was examined with **1l** at −15 °C, and the corresponding product **2l** possessing a quaternary carbon was obtained in 60% yield with a ratio of 74:26.

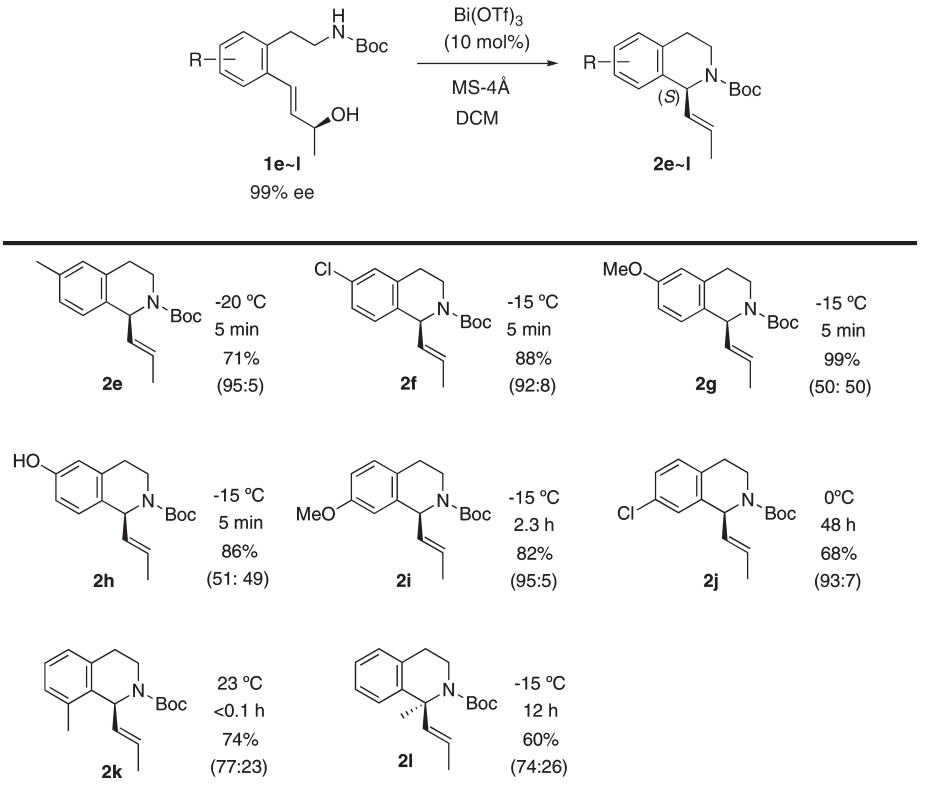
Further studies were designed to test the effects of substitution on the allylic alcohol moiety and to clarify the reaction mechanism (Scheme 3). When *cis*-olefin **1m** was subjected to the reaction conditions, the reaction was far more sluggish, even after 1 day at room temperature with 50 mol % of $Bi(OTf)_3$, giving only low yield of ***ent*-2a** with a ratio of 29:71. Surprisingly, on the acetate **1n**, the cyclization did not take place at −15 °C within 0.5 h. When the reaction was performed at 0 °C, the corresponding product **1a** was obtained in 91% yield with a ratio of 64:36. It is noteworthy that the hydroxy group of allylic alcohol plays an important role in the cyclization.

**Mechanism of the Cyclization.** The stereochemical outcome of the Bi(III)-catalyzed amination of the **1** is characteristic of a concerted $S_N2'$-type substitution.[21] On the basis of the results, $BiBr_3$, a soft Lewis acid, did not catalyze the reaction due to the low stability of the carbonyl complexes. In contrast, $BiCl_3$ and especially $Bi(OTf)_3$, in which the Lewis acidity of bismuth is amplified by three strong electron-withdrawing groups, are strong and relative hard, effective Lewis acids. Therefore, the mechanism for the intramolecular Bi(III)-catalyzed amination of allyl alcohols involving $\pi$-activation of the allylic C═C bond was found to be at odds with the high oxophilicity of $Bi(OTf)_3$. Rather, a mechanism involving $\sigma$-activation of the hydroxyl group appears to be more in line with the pronounced $\sigma$-acidity of the cationic Bi(III) complexes. Thus, as shown in Figure 1, the coordination of $Bi(OTf)_3$ with the hydroxy group of allyl alcohol followed by elimination of TfOH formed the complex II. Bi of the complex II coordinates the carbonyl group of Boc to determine the face selectivity, followed by *syn* $S_N2'$-type cyclization to afford **2a** along with $Bi(OH)(OTf)_2$. Finally, $Bi(OTf)_3$ would be regenerated from TfOH and $Bi(OH)(OTf)_2$ by the assistance of MS-4 Å.

No coordination between Bi and the carbonyl group led to ***ent*-2a** via an *anti* $S_N2'$-type process with a ratio similar to that of **2a**. The possibility that $Bi(OTf)_3$ coordinates function of both the hydroxy group and the carbonyl group at the same time for a concerted mechanism based on the crystalline structure of a


dx.doi.org/10.1021/jo102452d |*J. Org. Chem.* 2011, 76, 2102–2114

**Table 3. Scope and limitation**



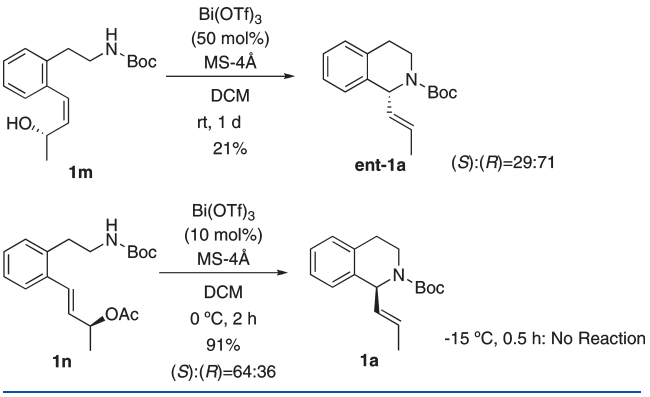

nonahydrate of $Bi(OTf)_3$[22] established by Dubac cannot be ruled out. The Bi atom has a negative charge in the complex **I** and cannot coordinate with the carbonyl group of Boc.[23] The coordination ability of the oxygen atom of the carbonyl group with Bi atom can be considered as the nucleophilicity of those of carbamates from the results in Table 2. The $^t$Bu ester (Boc) has nucleophilicity higher than that of Bn ester (Cbz) and methyl ester (methyl carbamate).[24]

A possible mechanism can be proposed for the observed poor 1,3-chirality transfer in the cyclizations of **1k**−**1n** in Figure 2. The steric hindrance between the methyl group (or the benzylic proton) and the vinyl proton in possible two conformations **A** (and **B**) prevented the coordination between Bi and the carbonyl group in the cyclizations of **1k** (and **1l**). In the same way, the cyclization of the (*Z*)-isomer **1m** has been attributed to the strong steric hindrance between the allylic proton and the benzylic proton (or the aromatic proton). (**C**) In the cyclization of the acetate **1n**, the 14-membered chelating complex **D** was assumed to be formed on the basis of the reduced reactivity and selectivity.[25] The low stereocontrolled cyclization via *syn* and *anti* attack has been attributed to the flexibility of the 14-membered chelating complex.

A plausible mechanism can be proposed for the observed poor 1,3-chirality transfer in the cyclization of **1g** (Scheme 4). There could be a cascade of electrons, moving from the methoxy substituent to the coordinated hydroxy group with $Bi(OTf)_3$. This would cause an elimination of the hydroxy group and lead to no stereoselective ring closure.

**Synthesis of the Chiral Oxygen-Substituted Tetrahydroisoquinoline at the 6 Position.** For the application to natural product synthesis, additional reaction conditions of **1g** were examined, as shown in Table 4. In entries 1 and 2, the effects of reaction temperature were examined. At −40 °C, the reaction completed after 45 min and the product **2g** was obtained in 96% yield with a ratio of 75:25 (entry 1). A further decrease to −78 °C resulted in no improvement in the selectivity (entry 2). Toluene was used as a solvent in entry 3, and cyclization of **1g** at −40 °C proceeded to give **2g** in 34% yield with a ratio of 70:30. When the 10 mol % of pyridine (entry 4) was added in the mixtures of catalyst and MS-4 Å in DCM followed by addition of the solution of **1g** in DCM, the product **2g** was obtained in 81% yield with ratios of 75:25.[25]

**Scheme 3. Cyclizations of (*Z*) Isomer and the Acetate Derivative**





dx.doi.org/10.1021/jo102452d |*J. Org. Chem.* 2011, 76, 2102–2114

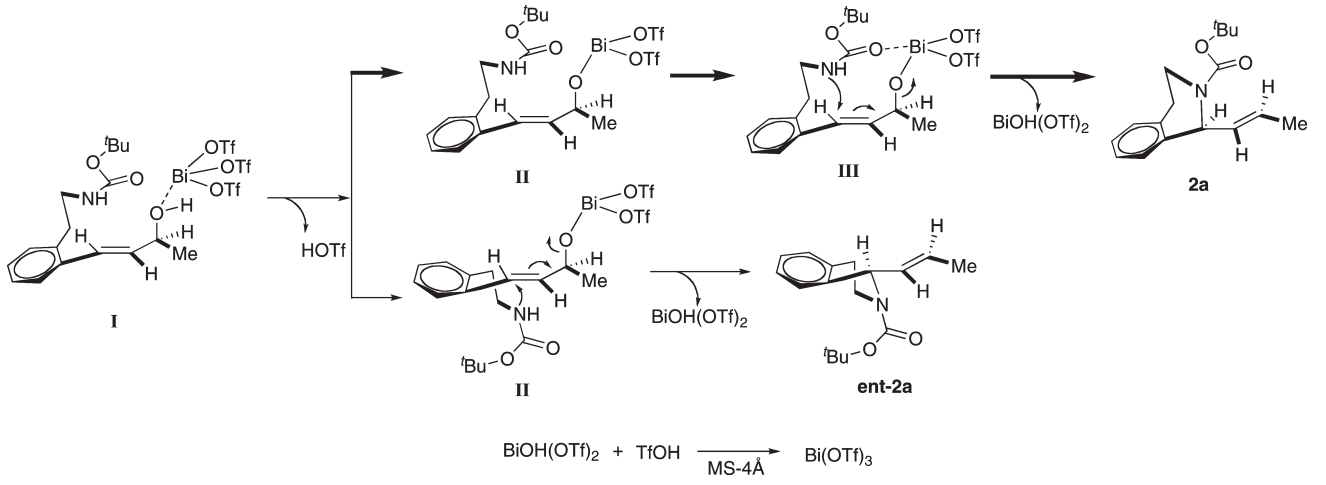



**Figure 1.** Plausible mechanism of the cyclization.

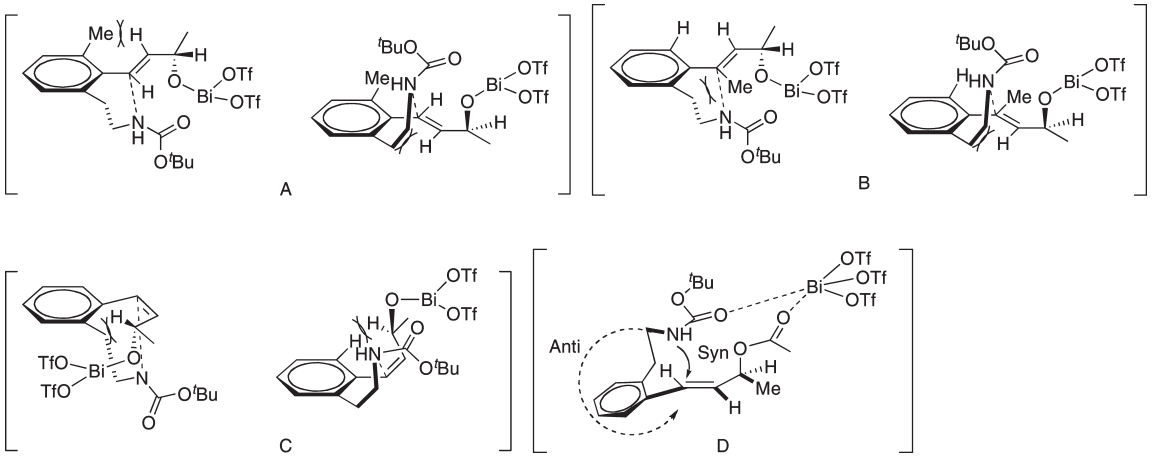
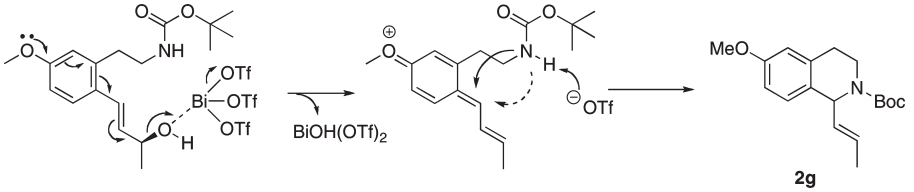



**Figure 2.** Consideration of the selectivity on the transition states **A** (on **1k**), **B** (on **1l**), **C** (on **1m**), and **D** (on **1n**).

**Scheme 4. Rationalization for the Enhancement of the Reactivity and Selectivity by *p*-Methoxy Substituent**




Next, the effects of the counterion were examined. With 10 mol % of $BiCl_3$, the cyclization proceeded at −40 °C to afford **2g** in 56% yield with nonchiral transfer in entry 5. The combination of $Bi(OTf)_3$ and $KPF_6$ resulted in a nonimprovement in chiral transfer with 56% yield in entry 6.

Although high 1,3-chirality transfer was not achieved, the focus was to establish a methodology for the synthesis of oxygen-substituted 1-propenyl tetrahydroisoquinoline at the 6 position in a suitable optically pure form. Pivaloyl ester **1i** was chosen as a possible solution to the present substitution problem. A few comments concerning the choice of this particular pivaloyl ester are in order. First, the ester substituent is electron-withdrawing. Second, the bulky *t*-Bu group may minimize the potential of the oxygen lone pairs of the carbonyl group for chelation with Bi. Finally, the ester is suitable as a protective group of phenol derivative for the synthetic applications.

Removal of a methyl group of **4g**[26] with $BBr_3$ in DCM followed by esterification of the resultant phenol gave **4o** in 84% yield in 2 steps (Scheme 5), After 3 general steps [(1) reduction of nitrile and protection; (2) Suzuki coupling; (3) desilylation] were conducted, the precursor **1o** was prepared in 60% yield in 3 steps. With the precursor **1o** in hand, the cyclization reaction was examined. Although Bi-catalyzed cyclization of **1o** proceeded to completion at −15 °C much slower than that of **1g**, high 1,3-chirality transfer


dx.doi.org/10.1021/jo102452d |*J. Org. Chem.* 2011, 76, 2102–2114

was achieved. After 7 h, the ester **2o** was obtained in 81% yield with a ratio of 93:7.

## CONCLUSION

We have described $Bi(OTf)_3$-catalyzed chiral synthesis of 1-substituted tetrahydroisoquinolines from chiral amino allyl alcohol via a 1,3-chirality transfer process. The stereochemistry at the newly formed chiral center is produced by a *syn* $S_N2'$-type process. In this reaction, the substituent on the benzene ring of **1** significantly affected the reactivities and selectivities. The precursor substituted with a methoxy group at the *para* position relative to the alkenyl substituent on the benzene ring gave the corresponding **2g** in 99% yield with a loss of chirality transfer on the $Bi(OTf)_3$-catalyzed cyclization under the optimized conditions. The replacement of a methoxy group with a pivaloyl ester achieved high 1,3-chirality transfer in the reaction to afford the oxygen-substituted tetrahydrohydroisoquinoline derivatives, which are observed in natural products and biologically important products. The reaction mechanism has been proposed to be an attractive interaction based on the intermediary Bi complex coordination of the hydroxy group and the carbonyl group.

## EXPERIMENTAL SECTION

### Synthesis of the Precursor

**Reduction of Nitrile and the Protection of the Resultant Amine.** To a stirred solution of cyanide **4** (35.7 mmol) in MeOH (350 mL) were added $(Boc)_2O$ (15.6 g, 71.6 mmol), $NiCl_2 \cdot 6H_2O$ (941 mg, 3.93 mmol), and $NaBH_4$ (7.0 g, 189 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 1.5 h and treated with $Et_2NH$ (4.3 mL, 71.6 mmol). The mixture was stirred for 0.5 h and evaporated. To the residue were added EtOAc and saturated aqueous $NH_4Cl$, the aqueous layer was extracted with EtOAc 3 times, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and evaporated. Purification of the residue by column chromatography on silica gel or distillation gave **5**. Yields: **5a** (89%), **5b** (68%) $ClCO_2Me$ was added instead of $Boc_2O$, **5c** (65%) CbzCl was added instead of $Boc_2O$, **5d** (65%) *o*-nitrobenzensulfonyl chloride was added instead of $Boc_2O$, **5e** (80%), **5f** (69%), **5g** (61%), **5h** (60%), **5i** (58%), **5j** (61%), **5k** (68%), **5o** (73%).

The cyanide **4** was prepared from the corresponding bromide by cyanation in the literature.[17] **4a**,[17] **4e**,[27] **4f**,[28] **4g**,[26] **4h**,[29] **4i**,[30] **4j**,[31] and **4k**[32] had been reported previously.

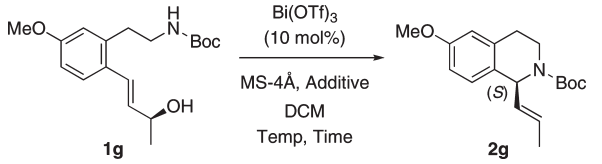
Compounds **5a**,[16] **5b**,[33] and **5c**[34] had been reported previously, and their identities were confirmed by comparison of their spectroscopic data with the reported data. Characterization data for the new compounds **5d**, **5e**, **5f**, **5g**, **5h**, **5i**, **5j**, **5k**, and **5o** are shown below.

*N-Nosyl-N-[2-(2-bromophenyl)ethyl]amine* (***5d***). Colorless oil, $R_f$ = 0.32 (20% EtOAc in hexane); $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.45 (d, $J$ = 8.0 Hz, 1H), 7.20−7.09 (m, 8H), 5.00 (s, 2H), 4.78−4.72 (m, 1H), 3.41−3.37 (m, 2H), 2.89 (t, $J$ = 7.0 Hz, 1H), 2.73 (t, $J$ = 7.0 Hz, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 136.8, 133.8, 133.5, 133.0, 132.8, 131.2, 131.0, 128.7, 127.7, 126.3, 125.4, 124.4, 43.2, 36.5; IR (neat, $cm^{-1}$) 3019, 2927, 1541, 1416, 1360, 1215, 1168, 1074; MS $m/z$ 385 ($M + H^+$); HRMS (CI) calcd for $C_{14}H_{14}BrN_2O_4S$ $m/z$ 384.9857, found: 384.9865.

*N-Boc-N-[2-(2-bromo-5-methyl-phenyl)ethyl]amine* (***5e***). White solid, $R_f$ = 0.46 (20% EtOAc in hexane); mp 71−72 °C; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 7.40 (d, $J$ = 8.1 Hz, 1H), 7.04 (s, 1H), 6.90 (d, $J$ = 8.1 Hz, 1H), 4.59 (brs, 1H), 3.39−3.35 (m, 2H), 2.92−2.28 (m, 2H), 2.28 (s, 3H), 1.44 (s, 9H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 155.8, 137.9, 137.4, 132.5, 131.8, 128.9, 121.1, 79.2, 40.3, 36.2, 28.4, 20.8; IR (KBr, $cm^{-1}$) 3359, 2989, 1685, 1526, 1465, 1394, 1366, 1278, 1250, 1167, 1025; MS $m/z$ 313 ($M^+$); HRMS (EI) calcd for $C_{14}H_{20}BrNO_2$ $m/z$ 313.0677, found 313.0685. Anal. Calcd for $C_{14}H_{20}BrNO_2$: C, 53.51; H, 6.42; N, 4.46. Found: C, 53.41; H, 6.43; N, 4.34.

*N-Boc-N-[2-(2-bromo-5-chloro-phenyl)ethyl]amine* (***5f***). White solid, $R_f$ = 0.51 (20% EtOAc in hexane); mp 70−71 °C; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 7.46 (d, $J$ = 8.5 Hz, 1H), 7.21 (d, $J$ = 2.5 Hz, 1H), 7.07 (dd, $J$ = 8.5, 2.5 Hz, 1H), 4.59 (br, 1H), 3.38 (td, $J$ = 6.5, 6.5 Hz, 2H), 2.92 (t, $J$ = 6.5 Hz, 2 H), 1.43 (s, 9H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 155.8, 140.2, 133.9, 133.3, 130.9, 128.2, 122.4, 79.4, 39.9, 36.3, 28.3; IR (KBr, $cm^{-1}$) 3583, 3019, 2400, 1709, 1508, 1464, 1367, 1216, 1168, 1100, 1030; MS $m/z$ 333 ($M^+$); HRMS (EI) calcd for $C_{13}H_{17}BrClNO_2$ $m/z$ 333.0131, found 333.0135. Anal. Calcd for $C_{13}H_{17}BrClNO_2$: C, 46.66; H, 5.12; N, 4.19. Found: C, 46.39; H, 4.95; N, 4.01.

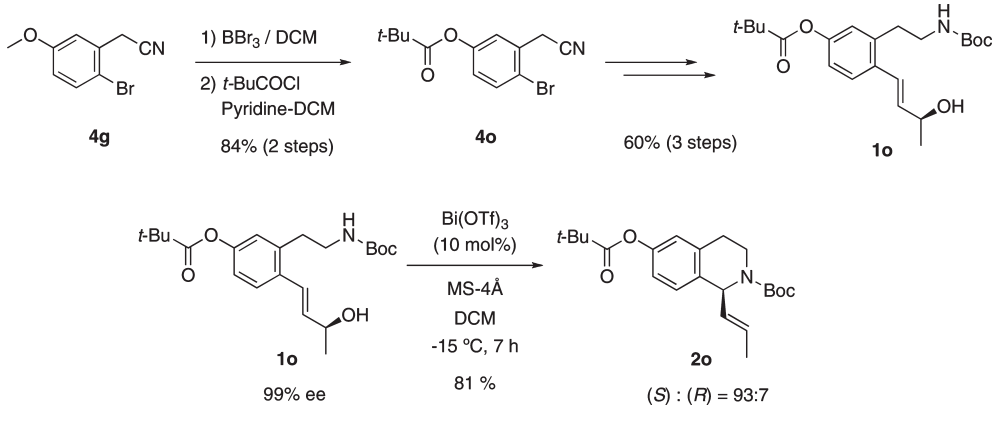
**Table 4. Cyclization of 1g under Several Conditions**




| entry | additive[a] | temp (°C) | time (h) | yield (%) | ratio (*S*:*R*)[b] |
|---|---|---|---|---|---|
| 1 | | −40 | 0.8 | 96 | 75:25 |
| 2 | | −78 | 0.1 | 40 | 74:26 |
| 3[c] | | −40 | 4 | 34 | 70:30 |
| 4 | pyridine | −20 | 0.5 | 81 | 75:25 |
| 5[d] | | −40 | 1.2 | 56 | 56:44 |
| 6 | $KPF_6$[e] | −15 | 2.5 | 56 | 71:29 |

[a] 10 mol %. [b] Determined by HPLC. [c] Toluene was used as a solvent. [d] $BiCl_3$ was used. [e] $Bi(OTf)_2PF_6$ was formed in situ.[12e]

**Scheme 5. Preparation of Pivaloyl Ester 1o and the Cyclization**





dx.doi.org/10.1021/jo102452d |*J. Org. Chem.* 2011, 76, 2102–2114

*N-Boc-N-[2-(2-bromo-5-methoxy-phenyl)ethyl]amine (**5g**).* White solid, $R_f$ = 0.32 (20% EtOAc in hexane); mp 88−90 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.41 (d, $J$ = 8.8 Hz, 1H), 6.77 (d, $J$ = 2.8 Hz, 1H), 6.66 (dd, $J$ = 8.8, 2.8 Hz, 1H), 4.61 (brs, 1H), 3.77 (s, 3H), 3.30−3.45 (m, 2H), 2.90 (t, $J$ = 7.0 Hz, 2H), 1.43 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 158.9, 155.8, 139.3, 133.3, 116.4, 115.0, 114.0, 79.3, 55.4, 40.2, 36.6, 28.4; IR (KBr, $cm^{-1}$) 3335, 2971, 1686, 1543, 1477, 1244, 1172; MS $m/z$; 329 ($M^+$); HRMS (EI) calcd for $C_{14}H_{20}BrNO_3$ $m/z$ 329.0626, found 329.0624. Anal. Calcd for $C_{14}H_{20}BrNO_3$: C, 50.92; H, 6.10; N, 4.24. Found: C, 51.21; H, 6.11; N, 4.39.

*N-Boc-N-[2-(2-bromo-5-hydroxy-phenyl)ethyl]amine (**5h**).* White solid, $R_f$ = 0.15 (20% EtOAc in hexane); mp 83−85 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.33 (d, $J$ = 8.6 Hz, 1H), 6.78 (s, 1H), 6.63 (dd, $J$ = 8.6, 2.6 Hz, 1H), 4.77 (brs, 1H), 3.39−3.34 (m, 2H), 2.86−2.83 (m, 2H), 1.43 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 156.4, 155.9, 139.0, 133.5, 117.8, 115.7, 114.2, 79.9, 40.2, 36.3, 28.4; IR (KBr, $cm^{-1}$) 3332, 2977, 2932, 1681, 1593, 1575, 1517, 1472, 1394, 1367, 1290, 1246, 1165, 1056; MS $m/z$; 315 ($M^+$); HRMS (EI) calcd for $C_{13}H_{18}BrNO_3$ $m/z$ 315.0469, found 315.0466. Anal. Calcd for $C_{13}H_{18}BrNO_3$: C, 49.38; H, 5.74; N, 4.43. Found: C, 49.66; H, 5.94; N, 4.52.

*N-Boc-N-[2-(2-bromo-4-methoxy-phenyl)ethyl]amine (**5i**).* Colorless oil, $R_f$ = 0.32 (20% EtOAc in hexane); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.12 (d, $J$ = 8.4 Hz, 1H), 7.09 (d, $J$ = 2.4 Hz, 1H), 6.80 (dd, $J$ = 8.4, 2.4 Hz, 1H), 4.58 (brs, 1H), 3.78 (s, 3H), 3.35 (td, $J$ = 6.7, 6.7 Hz, 2H), 2.88 (t, $J$ = 6.7 Hz, 2H), 1.43 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 158.7, 155.9, 131.3, 124.6, 118.0, 113.6, 113.6, 79.2, 55.5, 40.5, 35.4, 28.4; IR (neat, $cm^{-1}$) 3361, 2976, 1705, 1605, 1567, 1495, 1455, 1441, 1391, 1365, 1340, 1245, 1172, 1038; MS $m/z$ 329 ($M^+$); HRMS (EI) calcd for $C_{14}H_{20}BrNO_3$ $m/z$ 329.0626, found 329.0621.

*N-Boc-N-[2-(2-bromo-4-chloro-phenyl)ethyl]amine (**5j**).* White solid, $R_f$ = 0.5 (20% EtOAc in hexane); mp 36−38 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.55 (d, $J$ = 2.0 Hz, 1H), 7.22 (dd, $J$ = 8.1, 2.0 Hz, 1H), 7.15 (d, $J$ = 8.1 Hz, 1H), 4.59 (brs, 1H), 3.40-3.25 (m, 2H), 2.95−2.85 (m, 2H), 1.42 (s, 9H); 13C NMR (CDCl3, 125 MHz) $\delta$ 155.8, 137.0, 132.9, 132.4, 131.6, 127.7, 124.8, 79.3, 40.1, 35.8, 28.4; IR (KBr, $cm^{-1}$) 3454, 3018, 2979, 2933, 2400, 1708, 1507, 1471, 1392, 1367, 1216, 1168, 1103, 1038; MS $m/z$ 333 ($M^+$); HRMS (EI) calcd for $C_{13}H_{17}BrClNO_2$ $m/z$ 333.0131, found 333.0135. Anal. Calcd for $C_{13}H_{17}BrClNO_2$: C, 46.66; H, 5.12; N, 4.19. Found: C, 46.39; H, 4.95; N, 4.01.

*N-Boc-N-[2-(2-bromo-3-methyl-phenyl)ethyl]amine (**5k**).* White solid, $R_f$ = 0.5 (20% EtOAc in hexane); mp 77−78 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.13 (dd, $J$ = 7.5, 7.5 Hz, 1H), 7.11 (d, $J$ = 7.5 Hz, 1H), 7.05 (d, $J$ = 7.5 Hz, 1H), 4.59 (brs, 1H), 3.40−3.39 (m, 2H), 2.99−2.97 (m, 2H), 2.42 (s, 3H), 1.43 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 155.9, 138.8, 138.7, 129.1, 128.4, 127.3, 126.9, 79.2, 40.2, 37.1, 28.4, 24.0; IR ($CHCl_3$, $cm^{-1}$) 3453, 3017, 2979, 1708, 1509, 1392, 1366, 1216, 1169, 1025; MS $m/z$ 313 ($M^+$); HRMS (EI) calcd for $C_{14}H_{20}BrNO_2$ $m/z$ 313.0677, found 313.0685. Anal. Calcd for $C_{14}H_{20}BrNO_2$: C, 53.51; H, 6.42; N, 4.46. Found: C, 53.60; H, 6.40; N, 4.42.

*N-Boc-N-[2-(2-bromo-5-pivaroyloxy-phenyl)ethyl]amine (**5o**).* White solid, $R_f$ = 0.45 (20% EtOAc in hexane); mp 110−111 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.52 (d, $J$ = 8.5 Hz, 1H), 6.93 (s, 1H), 6.83 (d, $J$ = 8.5 Hz, 1H), 4.63 (s, 1H), 3.38−3.36 (m, 2H), 3.00−2.90 (m, 2H), 1.43 (s, 9H), 1.34 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 176.7, 155.8, 150.3, 139.7, 133.4, 124.0, 121.4, 120.7, 79.3, 40.0, 39.1, 36.3, 28.4, 27.1; IR ($CHCl_3$, $cm^{-1}$) 2977, 1749, 1703, 1508, 1469, 1366, 1269, 1157, 1119, 1025; MS $m/z$ 399 ($M^+$); HRMS (EI) calcd for $C_{18}H_{25}BrNO_4$ $m/z$ 399.1045, found 399.1049. Anal. Calcd for $C_{18}H_{26}BrNO_4$: C, 54.01; H, 6.55; N, 3.50. Found: C, 53.87; H, 6.77; N, 3.35.

*4-Bromo-3-(cyanomethyl)phenyl Pivalate (**4o**).* To a stirred solution of cyanide **4h** (3.62 g, 17 mmol) in DCM (250 mL) were added pyridine (4.95 mL, 61.2 mmol) and pivaloyl chloride (4.95 mL, 61.2 mmol) at 0 °C. The mixture was stirred at room temperature for 1 day. The resulting mixture was treated with satd $NH_4Cl$ aq. The aqueous layer was extracted with EtOAc 3 times. The combined organic extracts were washed with brine and dried over $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography using hexane/EtOAc (9:1) as the eluent gave **4o** (5.01 g, 99%). Colorless solid. $R_f$ = 0.32 (20% EtOAc in hexane); mp 70−71 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.59 (d, $J$ = 8.7 Hz, 1H), 7.26 (d, $J$ = 2.7 Hz, 1H), 6.96 (dd, $J$ = 8.7, 2.7 Hz, 1H), 3.83 (s, 1H), 1.36 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 176.6, 150.8, 133.8, 131.0, 123.3, 123.0, 119.6, 116.5, 39.2, 27.0, 24.9; IR (neat, $cm^{-1}$) 2976 2936, 2874, 2253, 1806, 1754, 1713, 1604, 1578, 1470, 1366, 1271, 1157, 1113, 1028; MS $m/z$ 295 ($M^+$); HRMS (EI) calcd for $C_{13}H_{14}BrNO_2$ $m/z$ 295.0207, found 295.0205. Anal. Calcd for $C_{13}H_{14}BrNO_2$: C, 52.72; H, 4.76; N, 4.73. Found: C, 52.49; H, 4.69; N, 4.50.

*(2S)-(E)-2-(tert-Butyldimethylsilyloxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-ene (**6**).* In sealed tube, to the solution of **9** (5.58 g, 30.3 mmol) in THF (4 mL) was added fresh pinacolborolane (4.87 mL, 33.3 mmol) at room temperature. The mixture was stirred at 130 °C for 1 day. The resulting mixture was treated with satd $NH_4Cl$ aq and extracted with EtOAc 3 times. The combined organic extracts were washed with brine and dried over $MgSO_4$. Concentration and purification of the residue by column chromatography using hexane/EtOAc (17:3) as the eluent gave **6** (8.41 g, 89%). Colorless oil, $[\alpha]^{20}_D$ 3.19 ($c$ 0.95, $CHCl_3$). Other than optical rotation, the physical properties of (+)-**6** matched those reported for (±)-**6** in the literature.[17]

*(2S)-(E)-2-(tert-Butyldimethylsilyloxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-3-ene (**7**).* To the solution of **9** (1.2 g, 6.5 mmol) in THF (30 mL) was added 1.58 M solution of BuLi in hexane (4.7 mL, 7.5 mmol) at 0 °C. The mixture was stirred at 0 °C for 10 min and treated with MeI (1.2 mL, 19.7 mmol). The reaction mixture was stirred at room temperature for 1 h and quenched with satd $NH_4Cl$ aq. The aqueous layer was extracted with $Et_2O$, and the organic extract was washed with $H_2O$ and brine, dried over $MgSO_4$, and concentrated in vaccuo. The crude product was conducted to the next hydroboration reaction, the same procedure as for **6**, without further purification. After workup, purification of the residue by column chromatography using hexane/EtOAc (40:1) as an eluent gave **7** (1.86 g, 88%). Colorless oil, $R_f$ = 0.63 (10% $Et_2O$ in hexane); $[\alpha]^{20}_D$ −9.1 ($c$ 0.97, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.25 (1H, dd, $J$ = 8.0, 1.5 Hz), 4.65 (1H, d, $J$ = 8.0, 6.5 Hz), 1.67 (3H, d, $J$ = 1.5 Hz), 1.26 (6H, s), 1.25 (6H, s), 1.17 (3H, d, $J$ = 6.5 Hz), 0.87 (9H, s), 0.03 (3H, s), 0.01 (3H, s); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 150.4, 139.5, 137.9, 83.2, 65.6, 25.9, 24.9, 24.5, 23.5, 18.2, 13.9, −4.5, −4.7; IR (neat, $cm^{-1}$) 3433, 1637, 1215, 1140, 754; MS (EI$^+$) $m/z$ 326 ($M^+$). HRMS calcd for $C_{17}H_{35}BO_3Si$ ($M^+$) $m/z$ 326.2448, found 326.2446.

*(2S)-(Z)-2-(tert-Butyldimethylsilyloxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-ene (**8**).* To the solution of **9** (258 mg, 1.4 mmol) in $Et_2O$ (1.4 mL) was added 1.58 M solution of BuLi in hexane (0.8 mL, 1.4 mmol) at −78 °C. The mixture was stirred at −78 °C for 30 min and treated with the solution of 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborane (265 mg, 1.4 mmol) in $Et_2O$. The reaction mixture was stirred at −78 °C for 4.5 h and quenched with 1 N HCl aq. The aqueous layer was extracted with $Et_2O$, and the organic extract was washed with brine, dried over $MgSO_4$, and concentrated in vaccuo. The crude product was conducted to the next reaction without further purification.

To the solution of $Cp_2ZrCl(H)$ (376 mg, 1.46 mmol) in THF (2.4 mL) was added the solution of the crude product in THF (2.4 mL). The reaction mixture was stirred for 1 h and treated with dist $H_2O$ (1 mL). The mixture was stirred for 10 h and concentrated in vaccuo. The residue was extracted with $Et_2O$, and the organic extract was washed with brine, dried, concentrated. Purification of the residue by column chromatography on silica gel using hexane/EtOAc (40:1) as an eluent gave **8** (225 mg, 50%). Colorless oil, $R_f$ = 0.71 (10% $Et_2O$ in hexane); $[\alpha]^{20}_D$ 40.5 ($c$ 0.27, $CHCl_3$). Other than optical rotation, the physical properties of (+)-**8** matched those reported for (±)-**8** in the literature.[20]

**Suzuki Cross-Coupling.** To the mixture of **5** (2.24 mmol), $NaHCO_3$ (933 mg, 11 mmol), and **6** (2.9 mmol) in 1,4-dioxane (30 mL) and $H_2O$ (12 mL) was added $PdCl_2$(dppf) (91.5 mg, 0.11 mmol). The reaction mixture was stirred at 80 °C for 2 h and quenched with $H_2O$. The aqueous layer was extracted with EtOAc, and the organic extract was washed with brine, dried over $MgSO_4$, and concentrated in vaccuo. Purification by column chromatography on silica gel using 5% EtOAc in hexane as an eluent gave **10**. Yields: **10a** (86%), **10b** (84%), **10c** (75%), **10d** (64%), **10e** (76%), **10f** (67%), **10g** (78%), **10h** (68%), **10i** (78%), **10j** (84%), **10k** (53%), **10l** (87%),[35] **10m**,[36] **10o** (84%).

*(3S)-(E)-N-Boc-N-[2-[2-(3-tert-butyldimethylsilyloxy-1-butenyl)phenyl]-ethyl]amine (**10a**).* Colorless oil, $R_f$ = 0.38 (10% EtOAc in hexane); $[\alpha]^{20}_D$ −19.3 (*c* 1.10, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.46 (1H, dd, *J* = 7.2, 2.4 Hz), 7.25- 7.15 (2H, m), 7.10 (1H, dd, *J* = 6.4, 2.4 Hz), 6.80 (1H, d, *J* = 15.6 Hz), 6.13 (1H, dd, *J* = 15.6, 5.1 Hz), 5.58 (1H, s), 4.51 (1H, qdd, *J* = 6.4, 5.1, 1.3 Hz), 3.48−3.41 (2H, m), 2.89 (2H, t, *J* = 6.8 Hz), 1.31 (3H, d, *J* = 6.4 Hz), 1.14 (9H, s), 0.94 (9H, s), 0.11 (3H, s), 0.09 (3H, s); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 155.8, 136.8, 136.3, 136.2, 130.0, 127.4, 126.8, 126.3, 124.9, 79.1, 69.3, 41.1, 33.4, 28.4, 25.9, 24.6, 18.3, −4.6, −4.7; IR (neat, $cm^{-1}$) 3454, 2930, 1707, 1507, 908, 732; MS ($EI^+$) *m*/*z* 405 ($M^+$); HRMS calcd for $C_{23}H_{39}NO_3Si$ ($M^+$) *m*/*z* 405.2699, found 405.2703.

*(3S)-(E)-N-Methoxycarbonyl-N-[2-[2-(3-tert-butyldimethylsilyloxy-1-butenyl)phenyl]ethyl]amine (**10b**).* Colorless oil, $R_f$ = 0.65 (30% EtOAc in hexane); $[\alpha]^{20}_D$ −22.0 (*c* 0.67, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.45 (1H, dd, *J* = 6.7, 1.8 Hz), 7.22−7.17 (2H, m), 7.13 (1H, d, *J* = 6.7 Hz), 6.78 (1H, d, *J* = 15.3 Hz), 6.12 (1H, dd, *J* = 15.3, 5.5 Hz), 4.67 (1H, s), 4.50 (1H, qd, *J* = 6.1, 5.5 Hz), 3.66 (3H, s), 3.40−3.37 (2H, m), 2.87−2.89 (2H, m), 1.31 (3H, d, *J* = 6.1 Hz), 0.93 (9H, s), 0.11 (3H, s), 0.09 (3H, s); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 156.9, 136.9, 136.3, 136.0, 130.0, 127.4, 126.9, 126.3, 124.8, 69.3, 52.0, 41.6, 33.5, 25.9, 24.6, 18.3, −4.6, −4.7; IR (neat, $cm^{-1}$) 3451, 1711, 1516, 910, 733; MS ($CI^+$) *m*/*z* 364 ($M + H^+$); HRMS calcd for $C_{20}H_{34}NO_3Si$ ($M + H^+$) *m*/*z* 364.2308, found 364.2300.

*(3S)-(E)-N-Cbz-N-[2-[2-(3-tert-butyldimethylsilyloxy-1-butenyl)-phenyl]ethyl]amine (**10c**).* Colorless oil, $R_f$ = 0.63 (20% EtOAc in hexane); $[\alpha]^{20}_D$ −81.3 (*c* 0.06, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.40 (1H, d, *J* = 7.3 Hz), 7.36−7.32 (5H, m), 7.22−7.16 (2H, m), 7.11 (1H, d, *J* = 7.1 Hz), 6.78 (1H, d, *J* = 15.3 Hz), 6.11 (1H, dd, *J* = 15.3, 5.5 Hz), 5.10 (2H, s), 4.74 (1H, bs), 4.49 (1H, d, *J* = 6.1, 5.5 Hz), 3.41−3.40 (2H, m), 2.90 (2H, bs), 1.30 (3H, d, *J* = 6.1 Hz), 0.93 (9H, s), 0.10 (3H, s), 0.08 (3H, s); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 156.3, 136.91, 136.9, 136.3, 135.9, 130.0, 128.51, 128.5, 128.1, 127.4, 126.9, 126.4, 124.8, 69.3, 66.6, 41.6, 33.4, 25.9, 24.6, 18.3, −4.6, −4.7; IR (neat, $cm^{-1}$) 3423, 1646, 1518, 1145, 967, 752; MS ($CI^+$) *m*/*z* 440 ($M + H^+$); HRMS calcd for $C_{26}H_{38}NO_3Si$ ($M + H^+$) *m*/*z* 440.2621, found 440.2629.

*(3S)-(E)-N-Nosyl-N-[2-[2-(3-tert-butyldimethylsilyloxy-1-butenyl)phenyl]-ethyl]amine (**10d**).* Colorless oil, $R_f$ = 0.40 (30% EtOAc in hexane); $[\alpha]^{20}_D$ −10.5 (*c* 0.19, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.08−8.06 (1H, m), 7.82 (1H, dd, *J* = 6.1, 3.7 Hz), 7.70 (2H, dd, *J* = 5.5, 3.7 Hz), 7.37 (1H, d, *J* = 7.3 Hz), 7.18−7.10 (2H, m), 7.04 (1H, d, *J* = 6.7 Hz), 6.69 (1H, d, *J* = 15.3 Hz), 6.06 (1H, dd, *J* = 15.3, 4.9 Hz), 5.32 (1H, s), 4.46 (1H, qd, *J* = 6.7, 4.9 Hz), 3.33−3.29 (2H, m), 2.91−2.94 (2H, m), 1.27 (3H, d, *J* = 6.7 Hz), 0.92 (9H, s), 0.09 (3H, s), 0.07 (3H, s); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 147.8, 137.3, 136.3, 134.5, 133.8, 133.4, 132.8, 130.9, 130.0, 127.5, 127.3, 126.5, 125.4, 124.4, 69.1, 44.2, 33.6, 25.8, 24.6, 18.2, −4.6, −4.7; IR (neat, $cm^{-1}$) 3434, 2956, 2253, 1640, 1543, 1362, 1169, 907, 732. MS ($EI^+$) *m*/*z* 490 ($M^+$); HRMS calcd for $C_{24}H_{34}N_2O_5SSi$ ($M^+$) *m*/*z* 490.1957, found 490.1965.

*(3S)-(E)-N-Boc-[2-[2-(3-tert-butyldimethylsilyloxy-1-butenyl)-5-methylphenyl]ethyl]amine (**10e**).* Colorless oil. $R_f$ = 0.30 (10% EtOAc in hexane); $[\alpha]^{22}_D$ −26.5 (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.35 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 6.96 (s, 1H), 6.74 (d, *J* = 15.6 Hz, 1H), 6.07 (dd, *J* = 15.6, 5.2 Hz, 1H), 4.53 (br, 1H), 4.48 (dqd, *J* = 6.4, 6.4, 1.2 Hz, 1H), 3.32−3.30 (m, 2H), 2.84−2.83 (m, 2H), 2.31 (s, 3H), 1.44 (s, 9H), 1.30 (d, *J* = 5.6 Hz, 3H), 0.93 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 155.8, 137.1, 136.0, 135.8, 133.4, 130.8, 127.6, 126.2, 124.8, 79.0, 69.4, 41.2, 33.3, 28.4, 25.9, 24.7, 21.0, 18.3, −4.6, −4.7; IR (neat, $cm^{-1}$) 3361, 2929, 2857, 1708, 1613, 1504, 1462, 1390, 1365, 1252, 1173, 1077; MS *m*/*z* 419 ($M^+$); HRMS (EI) calcd for $C_{24}H_{41}NO_3Si$ *m*/*z* 419.2856, found 419.2860.

*(3S)-(E)-N-Boc-N-[2-[2-(3-tert-butyldimethylsilyloxy-1-butenyl)-5-chlorophenyl]ethyl]amine (**10f**).* Colorless oil. $R_f$ = 0.31 (10% EtOAc in hexane); $[\alpha]_D^{22}$ −17.9 (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.36 (d, *J* = 8.2 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 7.12 (s, 1H), 6.72 (d, *J* = 15.6 Hz, 1H), 6.09 (dd, *J* = 15.6, 5.5 Hz, 1H), 4.53 (br, 1H), 4.48 (dq, *J* = 6.0, 6.0 Hz, 1H), 3.30−3.29 (m, 2H), 2.84-2.83 (m, 2H), 1.44 (s, 9H), 1.30 (d, *J* = 5.5 Hz, 3H), 0.93 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); $^{13}$C NMR (CDCl3, 100 MHz) $\delta$ 155.7, 138.0, 137.3, 134.8, 132.8, 129.8, 127.6, 126.9, 123.9, 79.3, 69.1, 40.9, 33.3, 28.4, 25.8, 24.5, 18.2, −4.6, −4.7; IR (neat, $cm^{-1}$) 3361, 2956, 2929, 2857, 1707, 1594, 1507, 1479, 1391, 1366, 1252, 1172, 1094; MS *m*/*z* 439 ($M^+$); HRMS (EI) calcd for $C_{23}H_{38}NO_3Si$ *m*/*z* 439.2309, found: 439.2318.

*(3S)-(E)-N-Boc-N-[2-[2-(3-tert-butyldimethylsilyloxy-1-butenyl)-5-methoxyphenyl]ethyl]amine (**10g**).* Colorless oil. $R_f$ = 0.30 (10% EtOAc in hexane); $[\alpha]^{22}_D$ −2.0 (c 1.0, $C_6H_6$); $^1$H NMR (400 MHz, $C_6D_6$) $\delta$ 7.38 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 15.6 Hz, 1H), 6.68 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.66 (d, *J* = 2.8 Hz, 1H), 6.06 (dd, *J* = 15.6, 6.0 Hz, 1H), 4.47 (dq, *J* = 6.4, 6.0 Hz, 1H), 4.12 (brs, 1H), 3.34 (s, 3H), 3.21-3.18 (m, 2H), 2.75-2.68 (m, 2H), 1.43 (s, 9H), 1.33 (d, *J* = 6.4 Hz, 3H), 1.03 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H); 13C NMR (100 MHz, C6D6) $\delta$ 160.2, 156.3, 138.9, 135.5, 129.8, 128.9, 126.1, 116.2, 113.6, 79.1, 70.8, 55.4, 42.3, 34.9, 29.1, 26.7, 25.7, 19.0, −5.2, −5.5; IR (neat, $cm^{-1}$) 3367, 2930, 1713, 1607, 1501, 1390, 1365, 1255, 1171, 1096; MS *m*/*z* 435 ($M^+$); HRMS (EI) calcd for $C_{24}H_{41}NO_4Si$ *m*/*z* 435.2805, found: 435.2797.

*(3S)-(E)-N-Boc-N-[2-[2-(3-tert-butyldimethylsilyloxy-1-butenyl)-5-hydroxyphenyl]ethyl]amine (**10h**).* Colorless oil. $R_f$ = 0.18 (20% EtOAc in hexane); $[\alpha]^{22}_D$ −20.8 (*c* 0.67, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.72 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.31 (d, *J* = 8.5 Hz, 1H), 6.82 (s, 1H), 6.66 (s, 1H), 6.65 (d, *J* = 15.5 Hz, 1H), 5.98 (dd, *J* = 15.5, 5.5 Hz, 1H), 4.66 (s, 1H), 4.46 (qd, *J* = 6.5, 5.5 Hz, 1H), 3.35−3.22 (m, 2H), 2.82−2.71 (m, 2H), 1.44 (s, 9H), 1.29 (d, *J* = 6.5 Hz, 3H), 0.92 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 156.2, 155.7, 137.6, 134.6, 127.6, 124.6, 116.5, 114.2, 79.6, 69.5, 60.5, 41.2, 33.4, 28.4, 25.9, 24.7, 18.3, −4.6, −4.7; IR (neat, $cm^{-1}$) 3352, 2955, 2930, 2885, 2857, 1682, 1607, 1577, 1504, 1461, 1393, 1367, 1252, 1165, 1095; MS *m*/*z* 421 ($M^+$); HRMS (EI) calcd for $C_{23}H_{39}NO_4Si$ *m*/*z* 421.2648, found 421.2655.

*(3S)-(E)-N-Boc-N-[2-[2-[3-(tert-butyldimethylsilyloxy)but-1-enyl]-4-methoxyphenyl]ethyl]amine (**10i**).* Colorless oil. $R_f$ = 0.30 (10% EtOAc in hexane); $[\alpha]^{22}_D$ −22.2 (*c* 1.0, CHCl3); 1H NMR (CDCl3, 500 MHz) $\delta$ 7.05 (d, *J* = 8.2 Hz, 1H), 6.98 (d, *J* = 2.5 Hz, 1H), 6.75 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.74 (d, *J* = 15.6 Hz, 1H), 6.11 (dd, *J* = 15.6, 5.3 Hz, 1H), 4.49 (dt, *J* = 6.4, 5.3 Hz, 1H), 4.49 (br, 1H), 3.81 (s, 3H), 3.29-3.27 (m, 2H), 2.81−2.80 (m, 2H), 1.43 (s, 9H), 1.31 (d, *J* = 6.4 Hz, 3H), 0.93 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); $^{13}$C NMR (125 MHz, CDCl3) $\delta$ 158.4, 155.8, 137.3, 136.8, 131.1, 128.6, 125.0, 113.0, 111.4, 79.1, 69.2, 55.3, 41.4, 32.6, 28.4, 25.9, 24.6, 18.3, −4.6, −4.7; IR (neat, $cm^{-1}$) 3374, 2930, 2857, 1712, 1606, 1573, 1497, 1390, 1365, 1251, 1168, 1044 ; MS *m*/*z* 435 ($M^+$); HRMS (EI) calcd for C24H41NO4Si m/z 435.2805, found: 435.2802.

*(3S)-(E)-N-Boc-N-[2-[2-[3-(tert-butyldimethylsilyloxy)but-1-enyl]-4-chlorophenyl]ethyl]amine (**10j**).* Colorless oil. $R_f$ = 0.30 (10% EtOAc in hexane); $[\alpha]^{22}_D$ −63.1 (*c* 1.0, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.41 (s, 1H), 7.14 (d, *J* = 7.0 Hz, 1H), 7.06 (d, *J* = 7.0 Hz, 1H), 6.73 (d, *J* = 15.0 Hz, 1H), 6.13 (dd, *J* = 15.0, 4.5 Hz, 1H), 4.49 (brs, 1H), 3.34−3.20 (m, 2H), 2.88−2.75 (m, 2H), 1.43 (s, 9H), 1.30 (d, *J* = 5.5 Hz, 3H), 0.93 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 155.7, 138.0, 138.0, 134.7, 132.5, 131.4, 127.2, 126.1, 123.8, 79.3, 69.0, 41.0, 32.9, 28.4, 25.9, 24.5, 18.3, −4.7, −4.7; IR (neat, $cm^{-1}$) 3359, 2955, 2929, 2857, 1706, 1507, 1480, 1390, 1365, 1251, 1170, 1089; MS *m*/*z*


dx.doi.org/10.1021/jo102452d |*J. Org. Chem.* 2011, 76, 2102–2114

439 ($M^+$); HRMS (EI) calcd for $C_{23}H_{38}ClNO_3Si$ $m/z$ 439.2309, found 439.2314.

*(3S)-(E)-N-Boc-N-[2-[2-[3-(tert-butyldimethylsilyloxy)but-1-enyl]-3-methylphenyl]ethyl]amine (**10k**).* Colorless oil. $R_f$ = 0.30 (10% EtOAc in hexane); $[\alpha]^{22}_D$ −19.0 (*c* 0.26, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.09 (dd, *J* = 7.3, 6.1 Hz, 1H), 7.07 (d, *J* = 6.1 Hz, 1H), 7.03 (d, *J* = 7.3 Hz, 1H), 6.51 (d, *J* = 16.5 Hz, 1H), 5.70 (dd, *J* = 16.5, 5.115 Hz, 1H), 4.51−4.47 (m, 2H), 3.31−3.30 (m, 2H), 2.83−2.80 (m, 2H), 2.28 (s, 3H), 1.43 (s, 9H), 1.32 (d, *J* = 6.1 Hz, 3H), 0.93 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 155.8, 140.0, 139.3, 136.8, 136.4, 128.3, 127.2, 126.6, 124.8, 77.2, 69.3, 41.0, 33.8, 28.4, 25.9, 24.7, 21.1, 18.3, −4.7, −4.8; IR (neat, $cm^{-1}$) 3369, 2928, 2857, 2360, 1707, 1507, 1462, 1391, 1365, 1252, 1172, 1081, 1003; MS $m/z$ 419 ($M^+$); HRMS (EI) calcd for $C_{24}H_{41}N_3OSi$ $m/z$ 419.2856, found 419.2851.

*(4S)-(E)-N-Boc-N-[2-[2-(4-tert-butyldimethylsilyloxy-2-pentenyl)phenyl]ethyl]amine (**10l**).* Colorless oil. $R_f$ = 0.25 (10% EtOAc in hexane); $[\alpha]^{20}_D$ −12.6 (*c* 0.26, $CHCl_3$); $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.19−7.14 (3H, m), 7.04 ($^1$H, m), 5.33 (1H, dq, *J* = 8.2, 1.2 Hz), 4.67 (1H, dq, *J* = 8.2, 6.3 Hz), 4.50 (1H, bs), 3.34−3.31 (2H, m), 2.77 (2H, t, *J* = 7.0 Hz), 1.93 (3H, d, *J* = 1.2 Hz), 1.42 (9H, s), 1.27 (3H, d, *J* = 6.3 Hz), 0.90 (9H, s), 0.10 (3H, s), 0.09 (3H, s); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 155.7, 145.1, 135.6, 135.4, 133.7, 129.5, 128.5, 126.9, 126.3, 79.1, 66.0, 41.5, 33.1, 28.4, 25.9, 24.4, 19.1, 18.2, −4.5, −4.6; IR (neat, $cm^{-1}$) 3453, 1642, 1508, 903, 725; MS ($EI^+$) $m/z$ 419 ($M^+$); HRMS calcd for $C_{24}H_{41}NO_3Si$ ($M^+$) $m/z$ 419.2856, found 419.2851.

*(3S)-(E)-N-Boc-N-[2-[2-[3-(tert-butyldimethylsilyloxy)but-1-enyl]-5-pivaroyloxyphenyl]ethyl]amine (**10o**).* Colorless oil. $R_f$ = 0.30 (10% EtOAc in hexane); $[\alpha]^{22}_D$ −17.4 (*c* 1.0, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.43 (d, *J* = 8.0 Hz, 1H), 6.90 (dd, *J* = 8.0, 2.5 Hz, 1H), 6.83 (d, *J* = 2.5 Hz, 1H), 6.73 (d, *J* = 15.5 Hz, 1H), 6.29 (dd, *J* = 15.5, 5.5 Hz, 1H), 4.55 (br, 1H), 4.48 (dq, *J* = 6.5, 5.5 Hz, 1H), 3.31−3.28 (m, 2H), 2.86−2.85 (m, 2H), 1.44 (s, 9H), 1.35 (s, 9H), 1.30 (d, *J* = 6.5 Hz, 3H), 0.93 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 177.0, 155.8, 150.2, 137.5, 136.9, 133.9, 127.3, 124.3, 122.7, 119.9, 77.2, 69.3, 40.9, 39.0, 33.3, 28.4, 27.1, 25.9, 24.6, 18.3, −4.6, −4.7; IR (neat, $cm^{-1}$): 3401, 2973, 2931, 2857, 1753, 1713, 1605, 1508, 1393, 1366, 1250, 1157, 1121; MS $m/z$ 505 ($M^+$); HRMS (EI) calcd for $C_{28}H_{47}NO_5Si$ $m/z$ 505.3223, found 505.3229.

**Desilylation of TBS Ether.** To the solution of **10** (10 mmol) was added a 1.0 M solution of TBAF (11 mL, 11 mmol) in THF. The reaction mixture was stirred and treated with $H_2O$. The aqueous layer was extracted with EtOAc, and the organic extract was washed with brine, dried over $MgSO_4$, and concentrated in vaccuo. Purification by column chromatography on silica gel gave **1**. Yields: **1a** (95%), **1b** (80%), **1c** (81%), **1d** (96%), **1e** (91%), **1f** (98%), **1g** (92%), **1h** (90%), **1i** (99%), **1j** (91%), **1k** (95%), **1l** (95%), **1m** (39% in 2steps), **1o** (97%).

*(3S)-(E)-N-Boc-N-[2-[2-(3-hydroxy-1-butenyl)phenyl]ethyl]amine (**1a**).* Colorless solid. $R_f$ = 0.12 (30% EtOAc in hexane); mp 60−62 °C; $[\alpha]^{22}_D$ +20.7 (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.44 (dd, *J* = 6.6 2.4 Hz, 1H), 7.20-7.12 (m, 2H), 7.11 (dd, *J* = 6.6, 2.4 Hz, 1H), 6.95 (d, *J* = 15.9 Hz, 1H), 6.16 (dd, *J* = 15.9, 5.5 Hz, 1H), 5.80 (s, 1H), 4.54 (qd, *J* = 6.2, 5.5 Hz, 1H), 3.43-3.35 (m, 2H), 2.95-2.80 (m, 2H), 1.27 (s, 1H), 1.38 (d, *J* = 6.2 Hz, 3H), 1.16 (s, 9H); $^{13}$C NMR (CDCl3, 125 MHz) $\delta$ 155.9, 136.4, 136.2, 129.8, 127.4, 126.915, 126.913, 126.42, 79.5, 68.5, 41.3, 34.5, 28.4, 23.3; IR (neat, $cm^{-1}$) 3357, 2975, 2930, 1693, 1613, 1515, 1455, 1392, 1366, 1252, 1171, 1056; MS $m/z$ 306 ($M^+$); HRMS (EI) calcd for $C_{18}H_{28}NO_3$ $m/z$ 306.2069, found 306.2061. Anal. Calcd for $C_{18}H_{28}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 71.08; H, 9.18; N, 4.43.

*(3S)-(E)-N-Methoxycarbonyl-N-[2-[2-(3-hydroxy-1-butenyl)phenyl]-ethyl]amine (**1b**).* Colorless oil. $R_f$ = 0.10 (30% EtOAc in hexane); $[\alpha]_D^{22}$ 27.3 (c 0.91, $CHCl_3$); $^1$H-NMR (500 MHz, CDCl3) $\delta$ 7.43 (1H, d, *J* = 6.7 Hz), 7.17-7.22 (2H, m), 7.12 (1H, dd, *J* = 8.5, 1.8 Hz), 6.92 (1H, d, *J* = 15.3 Hz), 6.15 (1H, dd, *J* = 15.3, 5.5 Hz), 4.89 (1H, s), 4.52 (1H, qd, *J* = 6.7, 5.5 Hz), 3.66 (3H, s), 3.30-3.35 (2H, m), 2.89 (2H, t, *J* = 7.3 Hz), 1.37 (3H, d, *J* = 6.7 Hz); $^{13}$C-NMR (125 MHz, CDCl3) $\delta$ 157.1, 136.5, 136.5, 136.1, 130.0, 127.6, 127.0, 126.4, 126.4, 68.6, 52.2, 41.8, 34.3, 23.2; IR (neat, $cm^{-1}$) 3441, 1696, 1524, 1260, 908, 730; MS ($EI^+$) $m/z$ 249 ($M^+$); HRMS calcd for $C_{14}H_{19}NO_3$ ($M^+$) $m/z$ 249.1365, found 249.1371.

*(3S)-(E)-N-Cbz-N-[2-[2-(3-hydroxy-1-butenyl)phenyl]ethyl]amine (**1c**).* Colorless solid. $R_f$ = 0.17 (30% EtOAc in hexane); mp 41−42 °C; $[\alpha]^{20}_D$ 0.86 (*c* 0.78, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.43 (1H, dd, *J* = 6.7, 1.8 Hz), 7.37−7.31 (5H, m), 7.23−7.17 (2H, m), 7.14−7.09 (1H, m), 6.93 (1H, d, *J* = 15.9 Hz), 6.15 (1H, dd, *J* = 15.9, 5.5 Hz), 5.10 (2H, s), 5.00 (1H, bs), 4.52 (1H, qd, *J* = 6.7, 5.5 Hz), 3.40−3.29 (2H, m), 2.91−2.88 (2H, m), 1.37 (3H, d, *J* = 6.7 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 156.4, 136.5, 136.4, 136.3, 135.9, 129.8, 128.51, 128.1, 127.5, 127.0, 126.4, 126.2, 68.5, 66.7, 41.7, 34.2, 23.2; IR (neat, $cm^{-1}$) 3419, 1646, 1524, 1250, 1139; MS ($EI^+$) $m/z$ 325 ($M^+$); HRMS calcd for $C_{20}H_{23}NO_3$ ($M^+$) $m/z$ 325.1678, found 325.1681. Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.96; H, 7.07; N, 4.38.

*(3S)-(E)-N-Nosyl-N-[2-[2-(3-hydroxy-1-butenyl)phenyl]ethyl]amine (**1d**).* Colorless oil. $R_f$ = 0.07 (30% EtOAc in hexane); $[\alpha]^{20}_D$ 3.3 (*c* 0.2, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.11−8.09 (1H, m), 7.84−7.81 (1H, m), 7.72−7.70 (2H, m), 7.40 (1H, d, *J* = 7.3 Hz), 7.20−7.14 (2H, m), 7.06 (1H, d, *J* = 7.3 Hz), 6.81 (1H, d, *J* = 15.3 Hz), 6.13 (1H, dd, *J* = 15.3, 6.1 Hz), 5.43 (1H, t, *J* = 6.1 Hz), 4.51 (1H, qd, *J* = 6.7, 6.1 Hz), 3.32−3.28 (2H, m), 2.90- 3.00 (2H, m), 1.37 (3H, d, *J* = 6.7 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 147.8, 136.6, 136.2, 134.9, 133.9, 133.4, 132.9, 130.8, 129.9, 127.8, 127.4, 126.6, 126.1, 125.4, 68.8, 44.5, 33.9, 23.4; IR (neat, $cm^{-1}$) 3358, 2971, 1639, 1539, 1362, 1162, 730; MS (FAB) $m/z$ 399 ($M + Na^+$); HRMS calcd for $C_{18}H_{20}N_2O_5SNa$ ($M + Na^+$) $m/z$ 399.0991, found 399.0987.

*(3S)-(E)-N-Boc-N-[2-[2-(3-hydroxybut-1-enyl)-5-methylphenyl]-ethyl]amine (**1e**).* Colorless solid. $R_f$ = 0.17 (30% EtOAc in hexane); mp 60−62 °C; $[\alpha]^{22}_D$ 20.7 (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.33 (d, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.94 (s, 1H), 6.90 (d, *J* = 15.5 Hz, 1H), 6.10 (dd, *J* = 15.5, 5.5 Hz, 1H), 4.73 (br, 1H), 4.55−4.48 (m, 1H), 3.26−3.24 (m, 2H), 2.84−2.82 (m, 3H), 2.31 (s, 3H), 1.44 (s, 9H), 1.36 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 156.0, 137.2, 136.1, 135.6, 133.6, 130.6, 127.6, 126.3, 79.5, 77.2, 68.6, 41.4, 34.4, 28.4, 23.2, 21.0; IR (neat, $cm^{-1}$) 3357, 2975, 2930, 1693, 1613, 1515, 1455, 1392, 1366, 1252, 1171, 1056; MS ($EI^+$) $m/z$ 306 ($M^+$); HRMS calcd for $C_{18}H_{28}NO_3$ ($M^+$) $m/z$ 306.2069, found 306.2061. Anal. Calcd for $C_{18}H_{28}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 71.08; H, 9.18; N, 4.43.

*(3S)-(E)-N-Boc-N-[2-[5-chloro-2-(3-hydroxybut-1-enyl)-phenyl]ethyl]-amine (**1f**).* White solid. $R_f$ = 0.17 (30% EtOAc in hexane); mp 84−86 °C; $[\alpha]^{22}_D$ +19.8 (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.34 (d, *J* = 8.1 Hz, 1H), 7.16 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.10 (d, *J* = 1.8 Hz, 1H), 6.88 (d, *J* = 15.6 Hz, 1H), 6.12 (dd, *J* = 15.6, 5.2 Hz, 1H), 4.78 (brs, 1H), 4.51 (brs, 1H), 3.24−3.22 (m, 2H), 3.05 (brs, 1H), 2.82 (t, *J* = 7.0 Hz, 2H), 1.43 (s, 9H), 1.36 (d, *J* = 5.2 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 156.0, 138.0, 137.0, 135.1, 132.8, 130.0, 127.7, 127.0, 125.2, 79.7, 68.3, 41.0, 34.4, 28.4, 23.1; IR (KBr, $cm^{-1}$) 3855, 3753, 3651, 3366, 2975, 1686, 1534, 1459, 1367, 1274, 1173; MS $m/z$ 325 ($M^+$); HRMS (EI) calcd for $C_{17}H_{24}ClNO_3$ $m/z$ 325.1445, found 325.1436. Anal. Calcd for $C_{17}H_{24}ClNO_3$: C, 62.67; H, 7.42; N, 4.30. Found: C, 62.95; H, 7.42; N, 4.34.

*(3S)-(E)-N-Boc-N-[2-[2-(3-hydroxybut-1-enyl)-5-methoxyphenyl]-ethyl]amine (**1g**).* White solid. $R_f$ = 0.17 (30% EtOAc in hexane); mp 97−98 °C; $[\alpha]^{22}_D$ +21.0 (*c* 1.0, $C_6H_6$); $^1$H NMR (400 MHz, $C_6D_6$) $\delta$ 7.33 (d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 15.6 Hz, 1H), 6.68 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.65 (d, *J* = 2.8 Hz, 1H), 6.07 (dd, *J* = 15.6, 5.6 Hz, 1H), 4.51 (td, *J* = 5.6 Hz, 1H), 4.40−4.47 (m, 1H), 3.36 (s, 3H), 3.15−3.08 (m, 2H), 2.68−2.64 (m, 2H), 1.39 (s, 9H), 1.38 (d, *J* = 5.6 Hz, 3H); $^{13}$C NMR (125 MHz, $C_6D_6$) $\delta$ 160.2, 156.8, 138.8, 136.1, 130.3, 128.5, 126.5, 116.3,

113.3, 79.6, 69.2, 55.4, 42.3, 35.6, 29.1, 24.4; IR (KBr, $cm^{-1}$) 3378, 2972, 1686, 1535, 1366, 1281, 1162; MS $m/z$ 321 ($M^+$); HRMS (EI) calcd for $C_{18}H_{27}NO_4$ $m/z$ 321.1940, found 321.1944. Anal. Calcd for $C_{18}H_{27}NO_4$: C, 67.27; H, 8.47; N, 4.36. Found: C, 67.53; H, 8.33; N, 4.33.

*(3S)-(E)-N-Boc-N-[2-[2-(3-hydroxybut-1-enyl)-5-hydroxyphenyl]-ethyl]amine (**1h**).* White solid. $R_f$ = 0.30 (50% EtOAc in hexane); mp 98−100 °C; $[\alpha]^{22}_D$ +17.9 (*c* 1.0, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.25 (d, *J* = 8.2 Hz, 1H), 6.77 (d, *J* = 15.7 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 1H), 6.61 (s, 1H), 5.99 (dd, *J* = 15.7, 6.2 Hz, 1H), 4.83 (brs, 1H), 4.53−4.38 (m, 1H), 3.32−3.15 (m, 2H), 2.80−2.70 (m, 2H), 1.42 (s, 9H), 1.36 (d, *J* = 6.4 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 156.3, 155.9, 137.7, 133.8, 128.2, 127.7, 126.3, 116.5, 114.2, 79.8, 68.9, 41.2, 34.1, 28.4, 23.2; IR (KBr, $cm^{-1}$) 3352, 3018, 2978, 1692, 1607, 1577, 1504, 1455, 1394, 1367, 1251, 1215, 1164, 1096; MS $m/z$ 307 ($M^+$); HRMS (EI) calcd for $C_{17}H_{25}NO_4$ $m/z$ 307.1783, found 307.1791. Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.71; H, 8.00; N, 4.58.

*(3S)-(E)-N-Boc-N-[2-[2-(3-hydroxybut-1-enyl)-4-methoxyphenyl]-ethyl]amine (**1i**).* Colorless oil. $R_f$ = 0.17 (30% EtOAc in hexane); $[\alpha]^{22}_D$ +11.7 (*c* 1.0, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.03 (d, *J* = 8.4 Hz, 1H), 6.96 (d, *J* = 1.7 Hz, 1H), 6.92 (d, *J* = 15.7 Hz, 1H), 6.75 (dd, *J* = 8.4 Hz, 1H), 6.14 (dd, *J* = 15.7, 5.5 Hz, 1H), 4.69 (br, 1H), 4.52 (br, 1H), 3.81 (s, 3H), 3.22−3.21 (m, 2H), 2.80 (br, 1H), 2.82−2.79 (m, 2H), 1.44 (s, 9H), 1.38 (d, *J* = 5.5 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 158.5, 156.0, 137.6, 136.6, 130.8, 128.6, 126.4, 113.2, 111.5, 79.5, 68.5, 55.3, 41.6, 33.8, 28.4, 23.2; IR (neat, $cm^{-1}$) 3362, 2974, 1693, 1606, 1496, 1365, 1252, 1166, 1040; MS $m/z$ 321 ($M^+$); HRMS (EI) calcd for $C_{18}H_{27}NO_4$ $m/z$ 321.1940, found 321.1947.

*(3S)-(E)-N-Boc-N-[2-[4-chloro-2-(3-hydroxybut-1-enyl)-phenyl]-ethyl]amine (**1j**).* Colorless oil. $R_f$ = 0.17 (30% EtOAc in hexane); $[\alpha]^{22}_D$ +11.0 (*c* 0.84, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.40 (s, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.91 (d, *J* = 15.5 Hz, 1H), 6.16 (dd, *J* = 15.5, 5.0 Hz, 1H), 4.70 (brs, 1H), 4.53 (brs, 1H), 3.25−3.18 (m, 2H), 2.88 (brs, 1H), 2.84−2.82 (m, 2H), 1.44 (s, 9H), 1.37 (d, *J* = 6.5 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 156.0, 138.3, 137.7, 134.6, 132.6, 131.1, 127.3, 126.3, 125.2, 79.7, 68.3, 41.2, 34.1, 28.4, 23.1; IR (neat, $cm^{-1}$) 3376, 2976, 2931, 1686, 1593, 1523, 1481, 1392, 1366, 1250, 1167, 1054; MS $m/z$ 325 ($M^+$); HRMS (EI) calcd for $C_{17}H_{24}ClNO_3$ $m/z$ 325.1445, found 325.1451.

*(3S)-(E)-N-Boc-N-[2-[2-(3-hydroxybut-1-enyl)-3-methylphenyl]ethyl]-amine (**1k**).* Colorless oil. $R_f$ = 0.17 (30% EtOAc in hexane); $[\alpha]^{22}_D$ −3.3 (*c* 0.54, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.08 (dd, *J* = 6.3, 6.3 Hz, 1H), 7.06 (dd, *J* = 6.3, 2.1 Hz, 1H), 6.99 (dd, *J* = 6.3, 2.1 Hz, 1H), 6.62 (d, *J* = 16.2 Hz, 1H), 5.80 (dd, *J* = 16.2, 6.8 Hz, 1H), 4.82 (brs, 1H), 4.51 (dq, *J* = 6.8, 6.3 Hz, 1H), 3.83 (brs, 1H), 3.19 (dd, *J* = 8.7, 7.2 Hz, 2H), 2.91−2.74 (m, 2H), 2.26 (s, 3H), 1.44 (s, 9H), 1.38 (d, *J* = 6.3 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 156.1, 139.8, 137.4, 136.5, 136.3, 128.3, 127.2, 126.8, 126.2, 79.7, 68.8, 41.3, 35.4, 28.4, 22.9, 20.6; IR (neat, $cm^{-1}$) 3350, 2974, 1691, 1519, 1365, 1252, 1171; MS $m/z$ 305 ($M^+$); HRMS (EI) calcd for $C_{18}H_{27}NO_3$ $m/z$ 305.1991, found 305.1986.

*(3S)-(E)-N-Boc-N-[2-[2-(3-hydroxy-1-pentenyl)phenyl]ethyl]amine (**1l**).* Colorless oil. $R_f$ = 0.17 (30% EtOAc in hexane); $[\alpha]^{20}_D$ 6.9 (*c* 1.54, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.19−7.14 (3H, m), 7.10−7.09 (1H, m), 5.42 (1H, d, *J* = 8.5 Hz), 4.79−4.75 (2H, m), 3.32−3.29 (1H, m), 3.15−3.11 (1H, m), 2.82−2.76 (2H, m), 2.02 (3H, s), 1.43 (9H, s), 1.32 (3H, d, *J* = 6.7 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 156.1, 145.2, 135.8, 135.3, 134.3, 129.8, 126.9, 126.4, 79.7, 64.3, 42.3, 34.7, 28.4, 23.0, 19.1; IR (neat, $cm^{-1}$) 3419, 1687, 1519, 1171; MS (EI$^+$) $m/z$ 305 ($M^+$); HRMS calcd for $C_{18}H_{27}NO_3$ $m/z$ 305.1991, found 305.1999.

*(3S)-(Z)-N-Boc-N-[2-[2-(3-hydroxy-1-butenyl)phenyl]ethyl]amine (**1m**).* Colorless oil. $R_f$ = 0.16 (30% EtOAc in hexane); $[\alpha]^{20}_D$ −72.5 (*c* 0.13, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.16−7.21 (3H, m), 7.09 (1H, d, *J* = 6.7 Hz), 6.56 (1H, d, *J* = 11.0 Hz), 5.79 (1H, t, *J* = 10.4 Hz), 4.58−4.51 (2H, m), 3.47−3.41 (1H, m), 3.26−3.18 (1H, m), 2.90−2.87 (1H, m), 2.70−2.66 (1H, m), 1.36 (9H, s), 1.32 (3H, d, *J* = 5.5 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 155.9, 137.3, 136.8, 136.2, 129.9, 129.8, 128.0, 127.5, 126.2, 79.6, 63.7, 40.9, 34.3, 28.3, 23.2; IR (neat, $cm^{-1}$) 3420, 1732, 1652; MS (FAB) $m/z$ 292 ($M^+$); HRMS calcd for $C_{17}H_{26}NO_3$ ($M + H^+$) $m/z$ 292.1913, found 292.1910.

*(3S)-(E)-N-Boc-N-[2-[2-(3-acetoxy-1-butenyl)phenyl]ethyl]amine (**1n**).* To a solution of **1a** (12.0 mg, 41 $\mu$mol) in pyridine (0.5 mL) was added $Ac_2O$ (7.8 $\mu$L, 82 $\mu$mol). The resultant mixture was stirred at room temperature for 1 h, and DMAP (0.5 mg, 4.1 $\mu$mol) was added. After stirring for 20 min, the solution was concentrated. Purification of the residue by thin layer chromatography on silica gel eluted with 70% EtOAc in hexane gave **1n** (12.4 mg, 90%) as a colorless oil. $R_f$ = 0.58 (20% EtOAc in hexane); $[\alpha]^{20}_D$ −59.6 (*c* 0.97, $CHCl_3$); $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.46-7.42 (1H, m), 7.24-7.13 (3H, m), 6.89 (1H, d, *J* = 15.6 Hz), 6.04 (1H, dd, *J* = 15.6, 6.9 Hz), 5.51 (1H, dq, *J* = 6.9, 6.5 Hz), 3.33-3.26 (2 H, m), 2.89-2.84 (2H, m), 2.08 (3H, s), 1.43 (9H, s), 1.42 (3H, d, *J* = 6.5 Hz), 7.13−7.24 (3H, m), 7.42 (1H, m); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 170.4, 155.8, 136.6, 135.6, 131.0, 130.0, 129.2, 128.0, 126.8, 126.3, 79.1, 71.3, 41.2, 33.6, 28.4, 21.4, 20.4; IR (neat, $cm^{-1}$) 3450, 1707, 1646, 1508, 1215, 754, 669; MS (EI$^+$) $m/z$ 333 ($M^+$); HRMS calcd for $C_{19}H_{27}NO_4$ $m/z$ 333.1940, found 333.1944.

*(3S)-(E)-N-Boc-N-[2-[2-(3-hydroxybut-1-enyl)-5-pivaroyloxy-phenyl]-ethyl]amine (**1o**).* White crystal, $R_f$ = 0.20 (30% EtOAc in hexane); mp 90−93 °C; $[\alpha]^{22}_D$ +14.8 (*c* 0.1, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.40 (d, *J* = 8.4 Hz, 1H), 6.89 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.88 (d, *J* = 15.5 Hz, 1H), 6.82 (d, *J* = 2.3 Hz, 1H), 6.10 (dd, *J* = 15.5, 6.4 Hz, 1H), 4.80 (brs, 1H), 4.54−4.45 (m, 1H), 3.27−3.20 (m, 2H), 3.20 (brs, 1H), 2.88−2.80 (m, 2H), 1.43 (s, 9H), 1.35 (d, *J* = 6.4 Hz, 3H), 1.34 (s, 9H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 177.0, 156.0, 150.2, 137.5, 136.6, 134.1, 127.4, 125.6, 122.5, 119.9, 79.5, 68.4, 41.1, 39.0, 34.4, 28.4, 27.1, 23.2; IR (neat, $cm^{-1}$) 3452, 2978, 2933, 2874, 1745, 1698, 1605, 1511, 1458, 1395, 1367, 1276, 1242, 1216, 1157, 1124, 1056, 1030; MS $m/z$ 391 ($M^+$); HRMS (EI) calcd for $C_{22}H_{33}NO_5$ $m/z$ 391.2358, found 391.2352. Anal. Calcd for $C_{22}H_{33}NO_5$: C, 67.49; H, 8.50; N, 3.58. Found: C, 67.28; H, 8.33; N, 3.50.

**Bi(OTf)$_3$-Catalyzed Cyclization.** To the mixture of $Bi(OTf)_3$ (10.4 mg, 16 $\mu$mol) and MS-4 Å (94 mg) in DCM (1.6 mL) was added the solution of **1** (0.16 mmol) in DCM (1.4 mL) at −15 °C. The reaction mixture was stirred and quenched with satd $NaHCO_3$ aq, the aqueous layer was extracted with EtOAc, and the organic extract was washed with brine, dried over $MgSO_4$, and concentrated in vaccuo. Purification of the residue by column chromatography on $SiO_2$ gave **2**. Yields: **2a** (83%) from **1a**, **2b** (65%), **2c** (67%), **2d** (91%), **2e** (71%), **2f** (88%), **2g** (99%), **2h** (86%), **2i** (82%), **2j** (68%), **2k** (74%), **2l** (60%), **2a** (91%) from **1n**, **2o** (81%).

Determination of ee by HPLC:

**2a**: (Daicel Chiralcel AD-H, n-hexane/ isopropanol = 95/5, flow rate 0.5 mL/min, *T* = 20 °C, 254 nm): $t_R$ = 9.7 min (minor), $t_S$ = 12.5 min (major)

**2b**: (Daicel Chiralcel OD-H, n-hexane/ isopropanol = 90/10, flow rate 0.5 mL/min, *T* = 20 °C, 254 nm): $t_S$ = 10.5 min (major), $t_R$ = 14.5 min (minor),

**2c**: (Daicel Chiralcel OD-H, n-hexane/ isopropanol = 90/10, flow rate 0.5 mL/min, *T* = 20 °C, 254 nm): $t_S$ = 11.9 min (major), $t_R$ = 15.7 min (minor)

**2d**: (Daicel Chiralcel OD-H, n-hexane/ isopropanol = 90/10, flow rate 0.5 mL/min, *T* = 20 °C, 254 nm): $t_S$ = 35.6 min (major), $t_R$ = 47.9 min (minor)

**2e**: (Daicel Chiralcel AD-H, n-hexane/ isopropanol = 95/5, flow rate 0.3 mL/min, *T* = 20 °C, 254 nm): $t_R$ = 17.8 min (minor), $t_S$ = 27.3 min (major)

**2f**: (Daicel Chiralcel AD-H, n-hexane/ isopropanol = 95/5, flow rate 0.3 mL/min, *T* = 20 °C, 254 nm): $t_R$ = 15.4 min (minor), $t_S$ = 20.2 min (major)

**2g**: (Daicel Chiralcel AD-H, n-hexane/ isopropanol = 95/5, flow rate 0.5 mL/min, *T* = 20 °C, 254 nm): $t_R$ = 11.0 min (minor), $t_S$ = 17.0 min (major)

**2h**: (Daicel Chiralcel AD-H, n-hexane/ isopropanol = 95/5, flow rate 0.5 mL/min, $T$ = 20 °C, 254 nm): $t_R$ = 39.1 min (minor), $t_S$ = 55.9 min (major)

**2i**: (Daicel Chiralcel AD-H, n-hexane/ isopropanol = 95/5, flow rate 0.5 mL/min, $T$ = 20 °C, 254 nm): $t_R$ = 13.5 min (minor), $t_S$ = 17.1 min (major)

**2j**: (Daicel Chiralcel AD-H, n-hexane/ isopropanol = 98.8/1.3, flow rate 0.5 mL/min, $T$ = 20 °C, 254 nm): $t_R$ = 18.4 min (minor), $t_S$ = 21.0 min (major)

**2k**: (Daicel Chiralcel OD-H, n-hexane/ isopropanol = 99/1, flow rate 1.0 mL/min, $T$ = 20 °C, 254 nm): $t_S$ = 4.6 min (major), $t_R$ = 6.3 min (minor),

**2l**: (Daicel Chiralcel AD-H, n-hexane/ isopropanol = 95/5, flow rate 0.5 mL/min, $T$ = 20 °C, 254 nm): $t_R$ = 13.4 min (minor), $t_S$ = 16.6 min (major)

**2o**: (Daicel Chiralcel AD-H, n-hexane/ isopropanol = 95/5, flow rate 0.5 mL/min, $T$ = 20 °C, 254 nm): $t_R$ = 9.7 min (minor), $t_S$ = 11.7 min (major)

*(1S)-(E)-N-Boc-1-(1-propenyl)-tetrahydroisoquinoline* (***2a***). Colorless solid. $R_f$ = 0.63 (20% EtOAc in hexane); mp 41−42 °C; $[\alpha]^{20}_D$ 151.9 ($c$ 0.95, $CHCl_3$);. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.19−7.11 (4H, m), 5.62−5.47 (3H, m), 4.12 (1H, brs), 3.20 (1H, brs), 2.94−2.85 (1H, m), 2.75−2.70 (1H, m), 1.68 (3H, d, $J$ = 6.1 Hz), 1.48 (9H, s); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 154.6, 135.8, 134.6, 130.9, 128.8, 127.9, 127.0, 126.4, 125.9, 79.6, 56.5, 37.6, 28.8, 28.5, 17.6; IR (neat, cm$^{-1}$) 2977, 2250, 1682, 1164, 909, 735; MS (EI$^+$) $m/z$ 273 ($M^+$); HRMS calcd for $C_{17}H_{23}NO_2$ ($M^+$) $m/z$ 273.1729, found 273.1720. Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.95; H, 8.30; N, 5.13.

*(1S)-(E)-Methyl-1-(1-propenyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate* (***2b***). Colorless oil. $R_f$ = 0.63 (20% EtOAc in hexane); $[\alpha]^{20}_D$ 137.4 ($c$ 0.46, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.19−7.10 (4H, m), 5.64−5.52 (3H, m), 4.10 (1H, bs), 3.74 (3H, s), 3.28 (1H, bs), 2.96−2.91 (1H, m), 2.75−2.71 (1H, m), 1.68 (3H, d, $J$ = 5.8 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 155.9, 135.6, 134.4, 130.7, 128.8, 127.9, 127.5, 126.6, 126.0, 56.2, 52.6, 38.2, 28.6, 17.6; IR (neat, cm$^{-1}$) 3588, 2952, 1702, 1534, 1446, 1122, 963, 765. MS (EI$^+$) $m/z$ 231 ($M^+$); HRMS calcd for $C_{14}H_{17}NO_2$ ($M^+$) $m/z$ 231.1259, found 231.1253.

*(1S)-(E)-N-Cbz-1-(1-propenyl)-tetrahydroisoquinoline* (***2c***). Colorless oil. $R_f$ = 0.63 (20% EtOAc in hexane); $[\alpha]^{20}_D$ 102.4 ($c$ 0.96, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.37−7.30 (5H, m), 7.19−7.11 (4H, m), 5.62−5.57 (3H, m), 5.19−5.13 (2H, m), 4.20−4.00 (1H, m), 3.30−3.27 (1H, m), 2.95−2.91 (1H, m), 2.79−2.70 (1H, m), 1.66 (3H, d, $J$ = 9.7 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 155.2, 136.8, 135.4, 134.3, 130.5, 128.7, 128.4, 128.2, 127.9, 127.8, 127.5, 126.6, 126.0, 67.0, 56.3, 38.2, 28.6, 17.6; IR (neat, cm$^{-1}$) 3433, 2086, 1643; MS (EI$^+$) $m/z$ 307 ($M^+$); HRMS calcd for $C_{20}H_{21}NO_2$ ($M^+$) $m/z$ 307.1576, found 307.1572.

*(1S)-(E)-N-Nosyl-1-(1-propenyl)-tetrahydroisoquinoline* (***2d***). Colorless oil. $R_f$ = 0.33 (30% EtOAc in hexane); $[\alpha]^{20}_D$ 128.1 ($c$ 0.13, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.04−7.97 (1H, m), 7.70−7.59 (3H, m), 7.20−7.17 (2H, m), 7.11−7.05 (2H, m), 5.61−5.57 (1H, m), 5.50 (1H, d, $J$ = 6.7 Hz), 5.43−5.37 (1H, m), 4.04−3.96 (1H, m), 3.51−3.46 (1H, m), 2.92−2.87 (1H, m), 2.78−2.71 (1H, m), 1.58 (3H, d, $J$ = 6.7); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 147.9, 134.3, 134.2, 133.2, 131.5, 130.7, 130.0, 129.6, 129.0, 128.3, 127.9, 127.0, 126.1, 124.1, 58.2, 39.8, 28.4, 17.6; IR (neat, cm$^{-1}$) 3499, 1664, 1541, 1371, 1163, 966, 755; MS (EI+) $m/z$ 358 (M+); HRMS calcd for $C_{18}H_{18}N_2O_4S$ (M+) $m/z$ 358.0987, found 358.0982.

*(1S)-(E)-N-Boc-6-methyl-1-(1-propenyl)-tetrahydroisoquinoline* (***2e***). Colorless oil. $R_f$ = 0.63 (20% EtOAc in hexane); $[\alpha]^{22}_D$ +126.4 ($c$ 0.6, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.01 (s, 1H), 7.00 (s, 1H), 6.95 (s, 1H), 5.59 (dd, $J$ = 15.0, 5.1 Hz, 1H), 5.50 (dq, $J$ = 15.0, 6.1 Hz, 1H), 5.55−5.35 (m, 1H), 4.20−3.90 (m, 1H), 3.30−3.10 (m, 1H), 2.95−2.80 (m, 1H), 2.65−2.73 (m, 1H), 2.31 (s, 3H), 1.68 (d, $J$ = 6.1 Hz, 3H), 1.49 (s, 9H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 154.67, 136.02, 134.48, 132.86, 131.02, 129.27, 127.70, 126.80, 126.77, 79.55, 56.26, 37.41, 28.75, 28.48, 20.9, 17.6; IR (neat, cm$^{-1}$) 2973, 2928, 1695, 1415, 1364, 1335, 1290, 1253, 1234, 1167, 1133, 1097, 1040; MS $m/z$; 287 ($M^+$); HRMS (EI) calcd for $C_{18}H_{25}NO_2$ $m/z$ 287.1878, found 287.1885.

*(1S)-(E)-N-Boc-6-chloro-1-(1-propenyl)-tetrahydroisoquinoline* (***2f***). Colorless oil. $R_f$ = 0.63 (20% EtOAc in hexane); $[\alpha]^{22}_D$ +117 ($c$ 0.3, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.14 (dd, $J$ = 8.2, 2.1 Hz, 1H), 7.13 (s, 1H), 7.03 (d, $J$ = 8.2 Hz, 1H), 5.56 (dd, $J$ = 15.4, 5.2 Hz, 1H), 5.47 (dq, $J$ = 15.4, 6.1 Hz, 1H), 5.65−5.30 (m, 1H), 4.10 (brs, 1H), 3.14 (brs, 1H), 2.90−2.83 (m, 1H), 2.70−2.65 (m, 1H), 1.68 (d, $J$ = 6.1 Hz, 3H), 1.48 (s, 9H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 154.5, 136.6, 134.3, 132.0, 130.5, 129.4, 128.6, 127.7, 126.1, 79.9, 55.7, 37.1, 28.7, 28.5, 17.6; IR (neat, cm$^{-1}$) 3019, 1684, 1420, 1366, 1216, 1162; MS $m/z$; 307 ($M^+$); HRMS (EI) calcd for $C_{17}H_{22}ClNO_2$ $m/z$ 307.1339, found 307.1336.

*(1S)-(E)-N-Boc-6-methoxy-1-(1-propenyl)-tetrahydroisoquinoline* (***2g***). Colorless oil. $R_f$ = 0.63 (20% EtOAc in hexane); $[\alpha]^{22}_D$ +62.0 ($c$ 0.4, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.02 (d, $J$ = 8.4 Hz, 1H), 6.75 (dd, $J$ = 8.4, 2.4 Hz, 1H), 6.65 (d, $J$ = 2.4 Hz, 1H), 5.58 (dd, $J$ = 14.6, 5.3 Hz, 1H), 5.48 (dq, $J$ = 14.6, 6.1 Hz, 1H), 5.45 (brs, 1H), 4.12 (brs, 1H), 3.78 (s, 3H), 3.17 (brs, 1H), 2.95−2.80 (m, 1H), 2.68 (dt, $J$ = 16.0, 3.5 Hz, 1H), 1.68 (d, $J$ = 6.1 Hz, 3H), 1.48 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 158.0, 154.6, 135.8, 131.1, 128.9, 128.0, 126.7, 113.1, 112.3, 79.5, 55.9, 55.1, 37.2, 29.1, 28.4, 17.5; IR ($CHCl_3$, cm$^{-1}$) 2974, 2932, 2836, 1694, 1612, 1581, 1503, 1454, 1416, 1364, 1335, 1287, 1239, 1164, 1121, 1096, 1040; MS $m/z$ 303 ($M^+$); HRMS (EI) calcd for $C_{18}H_{25}NO_3$ $m/z$ 303.1834, found 303.1841.

*(1S)-(E)-N-Boc-6-hydroxy-1-(1-propenyl)-tetrahydroisoquinoline* (***2h***). Colorless oil. $R_f$ = 0.23 (20% EtOAc in hexane); $[\alpha]^{22}_D$ −0.31 ($c$ 0.42, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.87 (d, $J$ = 8.3 Hz, 1H), 6.60 (brd, $J$ = 8.3 Hz, 1H), 6.53 (d, $J$ = 2.0 Hz, 1H), 5.53−5.23 (m, 3H), 4.0 (brs, 1H), 3.08 (brs, 1H), 2.78−2.70 (m, 1H), 2.55 (dt, $J$ = 15.8, 4.1 Hz, 1H), 1.60 (d, $J$ = 6.2 Hz, 3H), 1.41 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 154.9, 154.4, 136.2, 131.1, 129.2, 127.8, 127.0, 115.0, 113.6, 80.0, 56.3, 37.5, 29.0, 28.6, 17.7; IR ($CHCl_3$, cm$^{-1}$) 3399, 1650, 1427, 1161; MS $m/z$ 290 (M + H)$^+$; HRMS (CI) calcd for $C_{17}H_{24}NO_3$ $m/z$ 290.1756, found 290.1764.

*(1S)-(E)-N-Boc-7-methoxy-1-(1-propenyl)-tetrahydroisoquinoline* (***2i***). Colorless solid. $R_f$ = 0.64 (20% EtOAc in hexane); mp 87−88 °C; $[\alpha]^{22}_D$ +129.7 ($c$ 0.315, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.03 (d, $J$ = 8.4 Hz, 1H), 6.74 (dd, $J$ = 8.4, 2.6 Hz, 1H), 6.65 (d, $J$ = 2.6 Hz, 1H), 5.59 (dd, $J$ = 15.0, 5.3 Hz, 1H), 5.52 (dq, $J$ = 15.0, 6.0 Hz, 1H), 5.55−5.30 (m, 1H), 4.20−3.95 (m, 1H), 3.78 (s, 3H), 3.25−3.05 (m, 1H), 2.90−2.88 (m, 1H), 2.65 (dt, $J$ = 15.7, 3.6 Hz, 1H), 1.68 (d, $J$ = 6.0 Hz, 3H), 1.48 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 157.7, 154.7, 137.0, 130.7, 130.0, 127.2, 126.8, 112.8, 79.6, 56.7, 55.3, 37.6, 28.5, 28.0, 17.6; IR (neat, cm$^{-1}$) 3595, 3006, 2977, 2933, 1686, 1613, 1580, 1504, 1454, 1420, 1365, 1318, 1250, 1168, 1123, 1099, 1040 cm$^{-1}$; MS $m/z$ 303 ($M^+$); HRMS calcd for $C_{18}H_{25}NO_3$ $m/z$ 303.1834, found 303.1840. Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 70.95; H, 8.46; N, 4.5.

*(1S)-(E)-N-Boc-7-chloro-1-(1-propenyl)-tetrahydroisoquinoline* (***2j***). Colorless oil. $R_f$ = 0.64 (20% EtOAc in hexane); $[\alpha]^{22}_D$ +148.1 ($c$ 0.64, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.12 (d, $J$ = 8.1 Hz, 1H), 7.10 (s, 1H), 7.04 (d, $J$ = 8.1 Hz, 1H), 5.59−5.48 (m, 1H), 5.55−5.51 (m, 1H), 5.55−5.35 (m, 1H), 4.12 (brs, 1H), 3.13 (brs, 1H), 2.88−2.81 (m, 1H), 2.69−2.66 (m, 1H), 1.70 (d, $J$ = 5.2 Hz, 3H), 1.48 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 154.5, 137.7, 133.1, 131.5, 130.2, 130.1, 127.9, 127.8, 126.7, 79.9, 55.7, 37.4, 28.5, 28.3, 17.6; IR (neat, cm$^{-1}$) 2975, 2930, 1696, 1600, 1486, 1454, 1416, 1365, 1339, 1312, 1290, 1247, 1233, 1192, 1128, 1100, 1041; MS $m/z$ 307 ($M^+$); HRMS (EI) calcd for $C_{17}H_{22}ClNO_2$ $m/z$ 307.1339, found 307.1333.

*(1S)-(E)-N-Boc-8-methyl-1-(1-propenyl)-tetrahydroisoquinoline* (***2k***). Colorless oil. $R_f$ = 0.75 (30% EtOAc in hexane); $[\alpha]^{22}_D$ +140.0 ($c$ 0.4, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$); the compound exists as a mixture (1.12:1) of carbamate rotamers; signals corresponding to the major rotamer: $\delta$ 7.10 (d, $J$ = 13.5 Hz, 1H), 7.01 (dd, $J$ = 13.5, 7.5 Hz, 1H), 6.97 (d, $J$ = 13.5 Hz, 1H), 5.75 (brs, 1H), 5.25 (dq, $J$ = 13.0, 7.0 Hz, 1H),

3.81−3.72 (m, 1H), 3.45−3.25 (m, 1H), 2.95−2.72 (m, 2H), 2.26 (s, 3H), 1.65 (brd, $J$ = 7.0 Hz, 3H), 1.49 (s, 9H); representative signals corresponding to the minor rotamer: $\delta$ 7.09 (d, $J$ = 13.5 Hz, 1H), 7.01 (dd, $J$ = 13.5, 7.5 Hz, 1H), 6.97 (d, $J$ = 13.5 Hz, 1H), 5.60−5.50 (m, 1H), 5.25 (dq, $J$ = 13.0, 7.0 Hz, 1H), 3.98−3.90 (m, 1H), 3.45−3.25 (m, 1H), 2.95−2.72 (m, 2H), 2.24 (s, 3H), 1.65 (brd, $J$ = 7.0 Hz, 3H), 1.48 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) signals corresponding to both rotamer: $\delta$ 154.8, 154.7, 135.4, 134.8, 134.7, 135.0, 134.3, 129.5, 129.3, 128.1, 127.8, 127.6, 126.6, 126.5, 126.2, 79.7, 79.5, 53.7, 52.6, 38.9, 37.5, 28.7, 28.6, 28.5, 19.00, 18.99, 17.6; IR ($CHCl_3$, cm$^{-1}$) 3019, 2360, 2340, 1684, 1216, 1164, 1117; MS $m/z$ 287 ($M^+$); HRMS (EI) calcd for $C_{18}H_{25}NO_2$ $m/z$ 287.1885, found 287.1881.

*(1S)-(E)-N-Boc-1-(1-methyl-1-propenyl)-tetrahydroisoquinoline* (**2l**). Colorless oil. $R_f$ = 0.75 (30% EtOAc in hexane); $[\alpha]^{20}_D$ 13.7 ($c$ 0.71, $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.20−7.15 (2H, m), 7.06−7.12 (2H, m), 5.67 (1H, d, $J$ = 15.9 Hz), 5.57−5.48 (1H, m), 3.78−3.64 (2H, m), 2.85−2.82 (2H, m), 1.75 (3H, s), 1.72−1.71 (3H, m), 1.47 (9H, s); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 155.6, 142.3, 138.2, 135.0, 128.2, 128.0, 126.2, 125.8, 121.6, 79.8, 61.5, 41.2, 30.4, 28.5, 26.8, 17.7; IR (neat, cm$^{-1}$) 2979, 1671, 1166, 912, 742; MS (EI$^+$) $m/z$ 287 ($M^+$); HRMS calcd for $C_{18}H_{25}NO_2$ ($M^+$) $m/z$ 287.1885, found 287.1877.

*(1S)-(E)-N-Boc-6-pivaroyloxy-1-(1-propenyl)-tetrahydroisoquinoline* (**2o**). Colorless oil. $R_f$ = 0.64 (20% EtOAc in hexane); $[\alpha]^{22}_D$ +125 ($c$ 0.3, $CHCl_3$); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.10 (d, $J$ = 8.3 Hz, 1H), 6.86 (dd, $J$ = 8.3, 2.3 Hz, 1H), 6.82 (d, $J$ = 2.3 Hz, 1H), 5.56 (dd, $J$ = 15.4, 5.2 Hz, 1H), 5.48 (dq, $J$ = 15.4, 6.1 Hz, 1H), 5.51−5.42 (m, 1H), 4.12 (brs, 1H), 3.15 (brs, 1H), 2.93−2.83 (m, 1H), 2.71−2.67 (m, 1H), 1.67 (d, $J$ = 6.1 Hz, 3H), 1.48 (s, 9H), 1.34 (s, 9H); $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$ 177.2, 154.6, 149.4, 136.1, 133.2, 130.7, 129.0, 127.4, 121.4, 119.2, 79.8, 56.2, 39.0, 37.3, 28.8, 28.5, 27.1, 17.6; IR (neat, cm$^{-1}$) 3017, 2977, 1747, 1685, 1478, 1420, 1366, 1337, 1280, 1217, 1148, 1118, 1030; MS (EI$^+$) $m/z$ 373 ($M^+$); HRMS calcd for $C_{22}H_{31}NO_4$ ($M^+$) $m/z$ 373.2253, found 373.2246.

## ■ ASSOCIATED CONTENT

**Ⓢ Supporting Information.** Copies of the $^1$H and/or $^{13}$C NMR spectra for compounds **1a**−**1o**, **2a**−**2l**, **2o**, **4o**, **5d**−**5k**, **5o**, **7**, **10a**−**10l**, and **10o**. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

**Corresponding Author**
*kawai@mb.kyoto-phu.ac.jp

## ■ ACKNOWLEDGMENT

Research (no. 22790023 and 21590030) from the Ministry of Education, Culture, Sports, Science and Technology (MEXT), and Japan Society for the Promotion of Science (JSPS).

## ■ REFERENCES

(1) Agonism of the $\beta$-adrenoceptor: (a) Nikulin, V. I.; Rakov, I. M.; De Los Angeles, J. E.; Mehta, R. C.; Boyd, L. Y.; Feller, D. R.; Miller, D. D. *Bioorg. Med. Chem.* **2006**, *14*, 1684–1697. Antagonism of the D1 and NMDA receptor:(b) Gao, M.; Kong, D.; Clearfield, A.; Zheng, Q.-H. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2229–2233 and reference therein. Inhibition of α-glucosidase:(c) Takada, K.; Uehara, T.; Nakao, Y.; Matsunaga, S.; van Soest, R. W. M.; Fusetani, N. *J. Am. Chem. Soc.* **2004**, *126*, 187–193. (d) Nagatsu, T. *Neurosci. Res.* **1997**, *29*, 99–111 and references therein.

(2) (a) Battersby, A. R.; Binks, R.; Huxtable, R. *Tetrahedron Lett.* **1968**, *9*, 6111–6115.(b) Lundström, J. In *The Alkaloids*; Brossi, A., Ed.; Academic Press: NewYork, 1983; Vol. 21, p 312. (c) Kenneth, W. B. *Nat. Prod. Rep.* **2003**, *20*, 342–365.

(3) For reviews: Chrzanowska, M.; Rozwadowska, M. D. *Chem. Rev.* **2004**, *104*, 3341–3370.

(4) (a) Pictet, A.; Spengler, T. *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 2030–2036.(b) Whaley, W. M.; Govindachari, T. R. *Organic Reactions*; John Wiley & Sons: New York, 1951; Vol. 6, p 151. For recent reviews: (c) Cox, E. D.; Cook, J. M. *Chem. Rev.* **1995**, *95*, 1797–1842. (d) Larghi, E. L.; Amongero, M.; Bracca, A-B. J.; Kaufman, T. S. *ARKIVOC* **2005**, *xii*, 98–153.

(5) (a) Polniaszek, R. P.; Kaufman, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 4859–4863. (b) Polniaszek, R. P.; Dillard, L. W. *Tetrahedron Lett.* **1990**, *31*, 797–800. (c) Comins, D. L.; Badawi, M. M. *Heterocycles* **1991**, *32*, 1869–1873.

(6) (a) Meyers, A. I.; Dickman, D. A. *J. Am. Chem. Soc.* **1987**, *109*, 1263–1265. (b) Meyers, A. I.; Warmus, J. S.; Gonzá lez, M. A.; Guiles, J.; Akahane, A. *Tetrahedron Lett.* **1991**, *32*, 5509–5512. (c) Meyers, A. I. *Tetrahedron* **1992**, *48*, 2589–2612.

(7) Wünsch, B.; Nerdinger, S. *Eur. J. Org. Chem.* **1998**, 711–718.

(8) Wirth, T.; Fragale, G. *Synthesis* **1998**, 162–166.

(9) Ito, K.; Akashi, S.; Saito, B.; Katsuki, T. *Synlett* **2003**, 1809–1812.

(10) Takasu, K.; Maiti, S.; Ihara, M. *Heterocycles* **2003**, *59*, 51–55.

(11) For a review of allylic amination: (a) Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689–1708. For a recent review of palladium-catalyzed C−N bond formation from alcohol:(b) Muzart, J. *Tetrahedron* **2005**, *61*, 4179–4212. A review of the palladium-catalyzed activation of allylic alcohols:(c) Tamaru, Y. *Eur. J. Org. Chem.* **2005**, 2647–2656. Recent examples of the palladium-catalyzed activation of allylic alcohols: (d) Nishikata, T.; Lipshutz, B. H. *Org. Lett.* **2009**, *11*, 2377–2379. (e) Shue, Y.-J.; Yang, S.-C.; Lai, H.-C. *Tetrahedron Lett.* **2003**, *44*, 1481–1485. Asymmetric amination:(f) Yamashita, Y.; Gospalarathnam, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 7508–7509. Review of Pd(II)-catalyzed reaction:(g) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285–2309. (h) Tietze, L. F.; IIa, H.; Bell, H. P. *Chem. Rev.* **2004**, *104*, 3453–3516.

(12) For other recent examples of direct substitution of allylic alcohol with amine or amide, iodine as a catalyst: (a) Wu, W.; Rao, W.; Er, Y. Q.; Loh, K.; Poh, C. Y.; Chan, P. W. H. *Tetrahedron Lett.* **2008**, *49*, 2620–2624. (b) Motokura, K.; Nakagiri, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Jitukawa, K.; Kaneda, K. *Org. Lett.* **2006**, *8*, 4617–4620. (c) Yadav, J. S.; Subba Reddy, B. V.; Srinivasa Rao, T.; Krishna, B. B. M.; Narayana Kumar, G. G. K. S. *Chem. Lett.* **2007**, *36*, 1472–1473. (d) Shirakawa, S.; Shimizu, S. *Synlett* **2008**, 1539–1542. (e) Qin, H.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 409–413. (f) Kothandaraman, P.; Foo, S. J.; Chan, P. W. H. *J. Org. Chem.* **2009**, *74*, 5947–5952. (g) Wang, G.-W.; Shen, Y.-B.; Wu, X.-L. *Eur. J. Org. Chem.* **2008**, 4367–4371. (h) Yang, H.; Fang, L.; Zhang, M.; Zhu, C. *Eur. J. Org. Chem.* **2009**, 666–672.

(13) (a) Mukherjee, P.; Widenhoefer, R. A. *Org. Lett.* **2010**, *12*, 1184–1187. (b) Hirai, Y.; Nagatsu, M. *Chem. Lett.* **1994**, 21–22. (c) Hande, S. M.; Kawai, N.; Uenishi, J. *J. Org. Chem.* **2009**, *74*, 244–253.

(14) Kawai, N.; Abe, R.; Uenishi, J. *Tetrahedron Lett.* **2009**, *50*, 6580–6583.

(15) Wang, S.; Seto, C. T. *Org. Lett.* **2006**, *8*, 3979–3982.

(16) Yang, Bryant H.; Buchwald, Stephen L. *Org. Lett.* **1999**, *1*, 35–37.

(17) Movassaghi, M.; Hunt, D. K.; Tjandra, M. *J. Am. Chem. Soc.* **2006**, *128*, 8126–8127.

(18) Adamczyk, M.; Watt, D. S.; Netzel, D. A. *J. Org. Chem.* **1984**, *49*, 4226–4237.

(19) Ku, Y. −Y.; Patel, R. R.; Elisseou, E. M.; Sawick, D. P. *Tetrahedron Lett.* **1995**, *36*, 2733–2736.

(20) As a racemic form. See: Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990–4991.

(21) Magrid, R, M. *Tetrahedron* **1980**, *36*, 1901–1930.

(22) (a) Frank, W.; Reiss, G. J.; Schneider, J. *Angew. Chem., Int. Ed.* **1995**, *34*, 2416–2417. See also a review of $Bi(OTf)_3$:(b) Gaspard-Iloughmane, H.; Le Roux, C. *Eur. J. Org. Chem.* **2004**, 2517–2532.

(c) Gaspard-Iloughmane, H.; Le Roux, C. In *Acid Catalysis in Modern Organic Synthesis*; Yamamoto, H., Ishihara, K, Eds.; John Wiley & Sons: Weinheim, Germany, 2008; pp 551−588.

(23) Notably, Boyer has proposed a σ-activation pathway for chlorination and elimination and etherification of allyl alcohols with Bi(III) halides on the basis of HSAB principle. See: Keramane, E, M.; Boyer, B.; Roque, J.-P. *Tetrahedron.* **2001**, *57*, 1909–1916.

(24) For a review of the reactivity of the N-Boc protecting group: Agami, C.; Couty, F. *Tetrahedron.* **2002**, *58*, 2701–2724.

(25) In this case, there is no possibility to generate TfOH. This result including the effect of desiccant in Table 1 supports that the active species of catalyst might be Bi(III) even if the possibility of TfOH as a catalyst can not be ruled out. The formation of carbocation can not be ruled out in the cyclization of **1n**. In Table 4 (entry 4), pyridine was added for the acid scavenger or inducement the attenuation in Lewis acidity.

(26) Muratake, H.; Natsume, M. *Tetrahedron* **2006**, *62*, 7056–7070.

(27) Shishikura, J.; Inoue, M.; Ogiyama, T.; Yonezawa, K.; Yamaki, S.; Yokoyama, K.; Kakimoto, S.; Okada, H. PCT Int. Appl. WO 2008143263, 2008.

(28) Moser, P.; Sallmann, A.; Wiesenberg, I. *J. Med. Chem.* **1990**, *33*, 2358–68.

(29) Erdelmeier, I.; Chaudiere, J.; Moutet, M.; Yadan, J.-C. PCT Int. Appl. WO 9527706, 1995.

(30) Ito, K.; Tanaka, H.; Shibata, M. *Heterocycles* **1978**, *9*, 485–491.

(31) Petigara, R. B.; Yale, H. L. *J. Heterocycl. Chem.* **1974**, *11*, 331–337.

(32) Kim, Y. H.; Lee, H.; Kim, Y. J.; Kim, B. T.; Heo, J.-N. *J. Org. Chem.* **2008**, *73*, 495–501.

(33) Baudoin, B.; Evers, M.; Genevois-Borella, A.; Karlsson, A.; Malleron, J.-L.; Mathieu, M. PCT Int. Appl. WO 2009044019, 2009.

(34) Kubo, T.; Katoh, C.; Yamada, K.; Okano, K.; Tokuyama, H.; Fukuyama, T. *Tetrahedron* **2008**, *64*, 11230–11236.

(35) Boronate **7** was used.

(36) Boronate **8** was used. Without purification, the crude product was conducted to the next reaction.