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Palladium-Catalyzed Stereospecific Synthesis of 2,6-Disubstituted Tetrahydropyrans: 1,3-Chirality Transfer by an Intramolecular Oxypalladation Reaction

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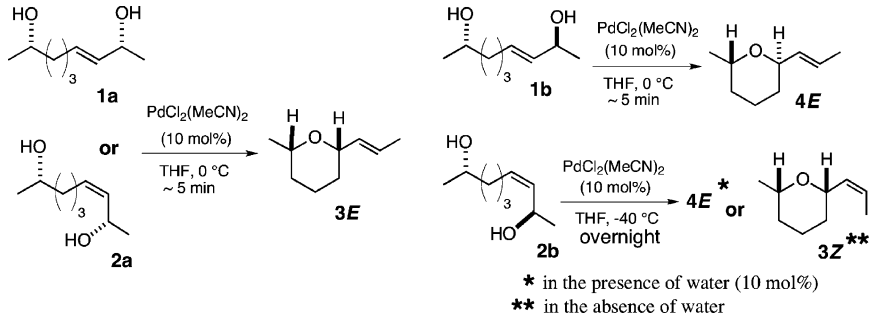

$PdCl_2(CH_3CN)_2$ (10 mol %) catalyzed reactions of non-3-ene-2,8-diols **1** and **2** gave 2,6-disubstituted tetrahydropyrans **3** and **4** in excellent yields with high diastereoselectivities (>20:1). Intramolecular cyclizations of the hydroxy nucleophile to the chiral allylic alcohol take place efficiently under mild conditions. A new stereogenic center is generated on the tetrahydropyran ring by 1,3-chirality transfer from the chiral allylic alcohol via a *syn*-SN2′ type process. Cis tetrahydropyran **3***E* was formed from *syn*-2,8-diols **1a** and **2a**, and trans tetrahydropyran **4***E* was formed from *anti*-2,8-diol **1b**, stereospecifically. Cis tetrahydropyran bearing a cis alkene **3***Z* was obtained from **2b** at −40 °C, while **4***E* was formed from **2b** in the presence of catalytic amount of water at −40 °C. The face selectivity of these cyclizations can be rationalized by taking a favorable conformation of the intermediary Pd π-complex with allylic alcohols, escaping the allylic strain and 1,3-diaxial interactions. A stereocontrolled synthesis of optically pure 2-alkenyl-6-methyltetrahydropyran **17** was achieved efficently in four steps from 6-silyloxy-1-heptyne **13** with an aldehyde and included asymmetric alkynylation, partial reduction of alkyne, deprotection of the silyl group, and the stereospecific cyclization.

Introduction

The synthesis of substituted tetrahydropyrans remains a topic of considerable interest due to the prevalence of these structures in natural products and biologically active compounds. Tetra- and dihydropyrans bearing substituents at the 2- and/or 6-positions on the ring are often observed in a large number of biologically important natural products such as phorboxazole,[1a] zampanolide,[1b] lasonolide,[1c] ratjadone,[1d] leucascandrolide,[1e] swinholides,[1f] misakinolides,[1g] sorangicin A,[1h] scytophycins,[1i] and laulimalide.[1j] The cis or trans configuration of the 2,6-substituents on the hydropyran ring can affect the three-dimensional molecular shape as well as the biological activity in these natural products. Therefore, stereocontrolled synthesis of 2,6-disubstituted tetra- and dihydropyrans is an important task for the synthesis of these natural products.[2] In fact, considerable efforts have been devoted to the development of efficient and stereoselective methods, including a hetero-Diels−Alder reaction of dienes and aldehydes,[3] an intramolecular hetero-Michael-type reaction,[4] an alkylation of oxonium ion,[5] and others,[6] some of which are shown in Figure 1.

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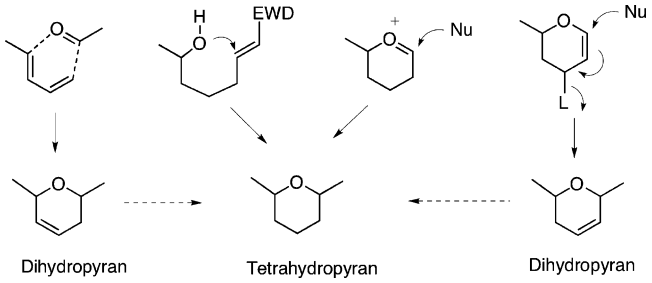
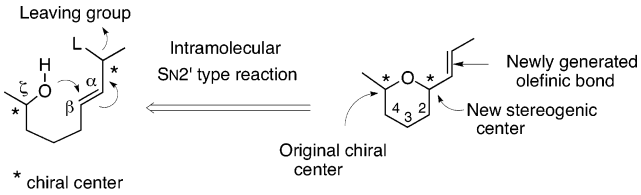


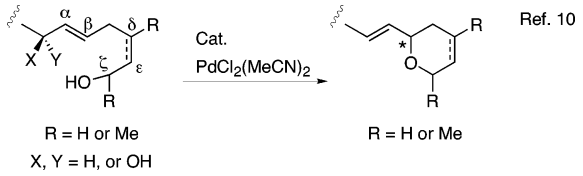
FIGURE 1. Synthesis of 2,6-disubstituted tetra- and dihydropyran rings.

The stereochemistry of newly generated chiral centers has been controlled by intermolecular and intramolecular reactions, in which total conformational stability of the ring and stereoelectronic effect of the hydropyran ring have been large factors for the stereocontrol. Since strict stereocontrol ring-formation is desired, we have designed a new stereocontrolled synthesis of hydropyrans by an intramolecular SN2′ type reaction as described in Scheme 1, in which an attack of oxygen nucleophile onto the diastereotopic carbon of olefin in an exo trigonal fashion results in the formation of a tetrahydropyran ring. A stereospecific 1,3-chirality transfer might be expected in either a *syn*-SN2′ or *anti*-SN2′ process intramolecularly. Although we have examined ionic SN2′ cyclizations based on this idea, unsatisfied stereoselective results have been obtained by *anti*-SN2′ and SN1′ reactions.[7] Therefore, we have started the study of Pd-catalyzed tetrahydropyran synthesis.

SCHEME 1. Synthesis of 2,6-Disubstituted Tetrahydropyran by Intramolecular SN2′ Type Reaction



SCHEME 2



A nucleophilic attack of heteroatoms on Pd π-complexes, as well as π-allyl Pd complexes, is well-known in Pd-catalyzed reactions,[8] and Pd^{II}-promoted intramolecular ring formation leading to oxygen heterocycles has been documented well.[8,9] We have recently reported some Pd^{II}-catalyzed hydropyran formation reactions[10] in which intramolecular $PdCl_2$-catalyzed cyclization took place stereospecifically and gave 3,6-dihydro-[*2H*]pyrans from ζ-hydroxy-$\alpha,\beta,\delta,\epsilon$-unsaturated alcohol and tetrahydropyrans from ζ-hydroxy-α,β-unsaturated alcohols via an SN2′-type reaction as shown in Scheme 2.

In this paper, we report full accounts of the stereochemical results in the Pd^{II}-catalyzed cyclization reactions of ζ-hydroxy allylic alcohols and a new stereospecific synthetic method for 2,6-disubstituted tetrahydropyrans.

Results and Discussion

Preparation of Non-3-ene-2,8-diols. Four optically pure non-3-ene-2,8-diols, **1a**, **1b**, **2a**, and **2b**, that possess an *E*- or *Z*-olefinic bonds with an *R*- or *S*-chiral center on the allylic part were chosen as precursors for the cyclization. When these diols are cyclized, four kinds of stereoisomeric tetrahydropyrans, **3***E*, **3***Z*, **4***E*, and **4***Z*, can be formed. These structures are shown in Figure 2.

The synthesis of **1a**,**b** and **2a**,**b** is shown in Scheme 3. In our previous communication, we used lipase-catalyzed kinetic acetylation reactions for the preparation of ζ-hydroxy and allylic hydroxy chiral centers of **1a** and **1b**.[10a] In this study, we have improved the method for preparation of ζ-hydroxy chiral center by using a ring-opening reaction of a chiral epoxide with a Grignard reagent.

The addition of a copper reagent, generated from 4-bromo-1-butene, to (*S*)-propylene oxide gave (*S*)-1-hepten-6-ol **5**[11] in

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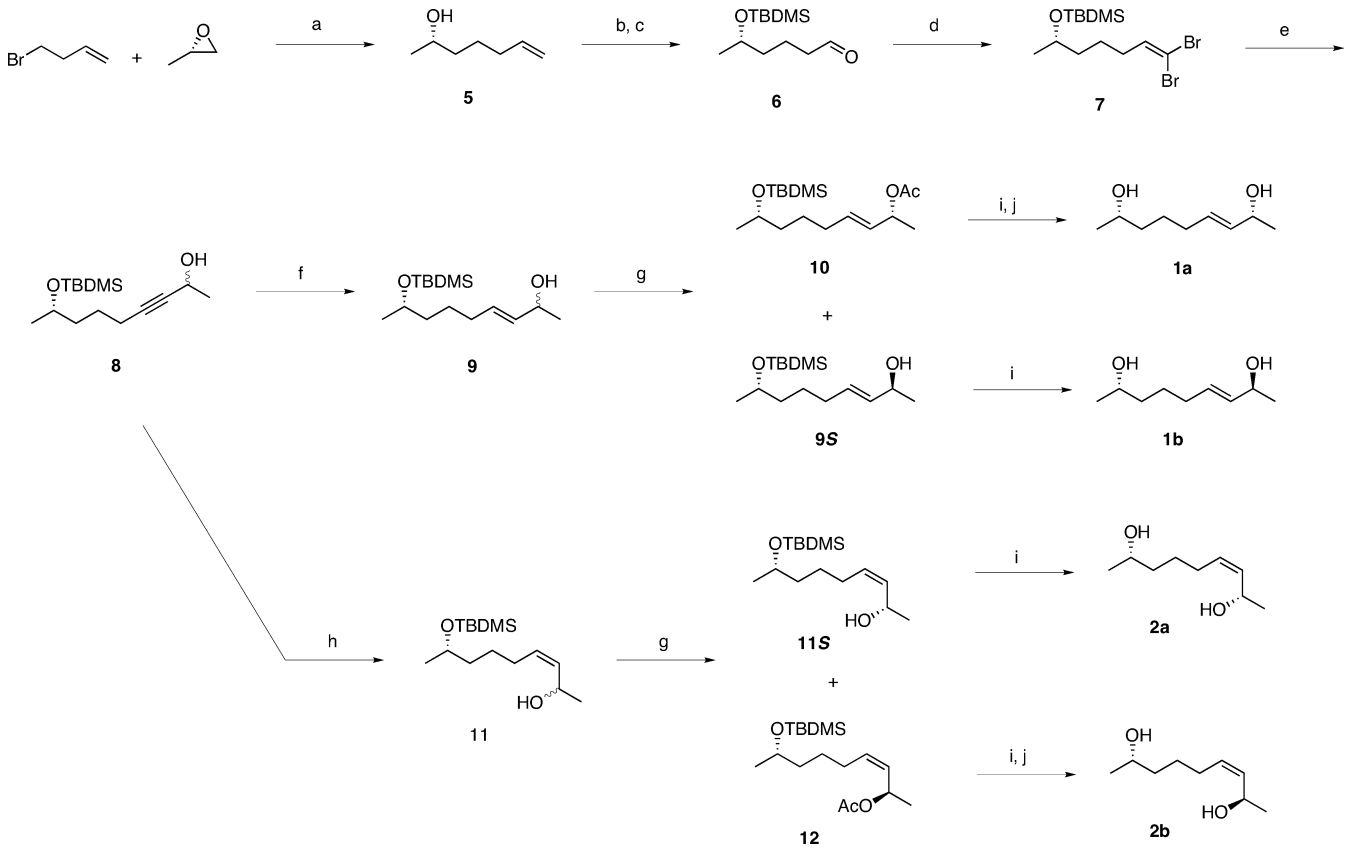
SCHEME 3 [a]



[a] Reagents and conditions: (a) Mg, CuCN, THF, Et_2O, 12 h, 0 °C (90%); (b) TBDMSCl, imidazole, DMF, 30 min, rt (85%); (c) O_3, CH_2Cl_2, 1 h, −78 °C then Ph_3P (90%); (d) CBr_4, PPh_3, NEt_3, CH_2Cl_2, 15 h, 0 °C (89%); (e) *n*-BuLi, THF, −78 °C then acetaldehyde, 2 h, −78 to 0 °C (90%); (f) Red-al, THF, reflux, 2 h (quant); (g) *Ca*l, vinyl acetate, MS 4 Å, *i*-Pr_2O, 1.5−12 h, rt (**10**: 45%, **9***S*: 48%, **11***S*: 39%, **12**: 47%); (h) H_2, Lindlar's catalyst, 4 h, rt (95%); (i) TBAF, THF, 41 h, rt; (j) K_2CO_3, MeOH, 2 h, rt (**1a**: 87% in 2 steps, **1b**: 88%, **2a**: 92%, **2b**: 74% in 2 steps).

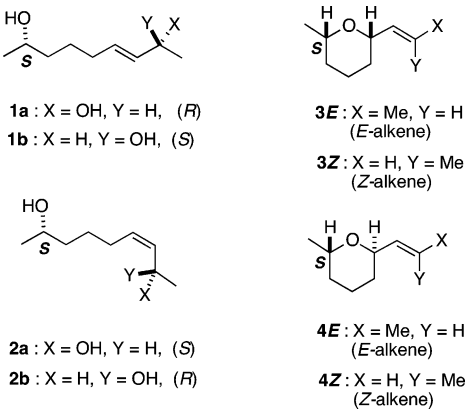


FIGURE 2. (*E*)- and (*Z*)-non-3-ene-2,8-diols and **(***E*)- and (*Z*)-6-methyl-2-propenyltetraydropyrans.

90% yield. After the protection of alcohol with TBDMSCl, ozonolysis of the terminal olefin gave the aldehyde **6**[12] in 77% yield in two steps. Wittig reaction of **6** in the presence of triethylamine gave 1,1-dibromo-1-alkene **7** in 89% yield. The reaction of alkynyllithium, generated from **7** with 2 equiv of BuLi, with acetaldehyde gave propargyl alcohol **8** in 92% yield as a 1:1 diastereomeric mixture. A partial reduction of the alkynyl bond with Red-al afforded (*E*)-allylic alcohol **9** in a quantitative yield. The diastereomeric alcohols **9** were subjected to lipase-catalyzed kinetic acetylation by *Candida antarctica* lipase (*Ca*l) with vinyl acetate.[13] An (*R*)-acetate **10** was obtained in 45% yield with >98% de, and (*S*)-alcohol **9***S* was recovered in 48% yield with >98% de. Desilylation of **10** with TBAF, followed by methanolysis, gave diol **1a** in 87% yield in two steps. Diol **1b** was obtained from **9***S* in 88% yield by treatment with TBAF. For the preparation of **2a** and **2b**, hydrogenation of **8** in the presence of Lindlar's catalyst gave (*Z*)-allylic alcohol **11** in 95% yield. A *Ca*l-catalyzed kinetic acetylation of alcohol **11** with vinyl acetate in a manner similar to that described above gave (*R*)-acetate **12** in 39% yield with >98% de along with an (*S*)-alcohol **11***S* in 47% yield with >98% de. Diol **2a** was obtained in 92% yield from **11***S*, and **2b** was obtained in 74% yield in two steps in the same manner as described for **1a** and **1b**.

Pd-Catalyzed Cyclizations. When diol **1a** was treated with 10 mol % of $PdCl_2(MeCN)_2$ in THF at 0 °C for 5 min, *cis*-(*E*)-tetrahydropyran **3***E*[14] was obtained as a single stereoisomer

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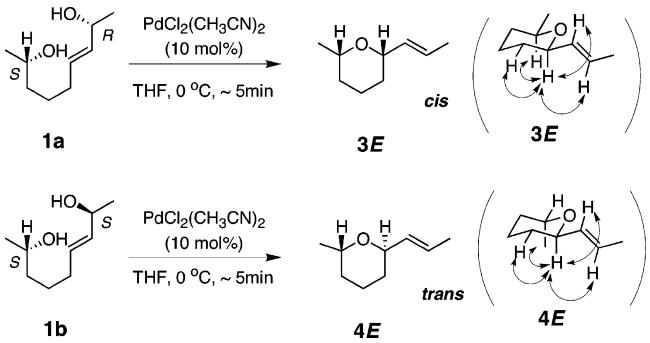
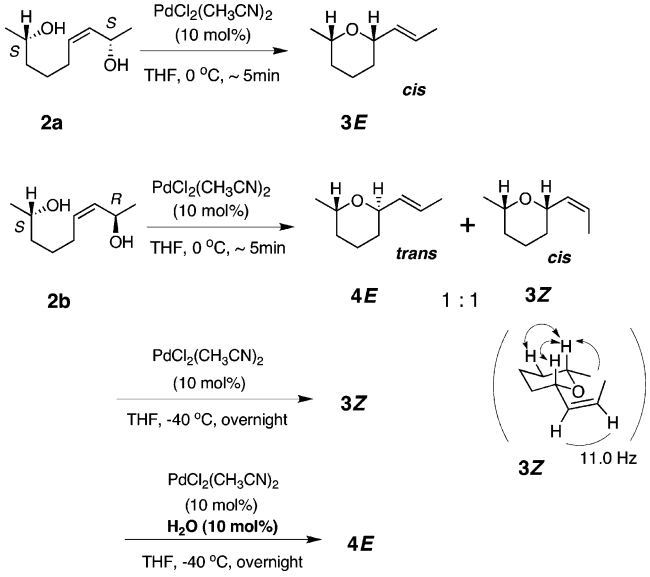
SCHEME 4



SCHEME 5



in 72% yield.[15] Meanwhile, under the same conditions **1b** gave *trans*-(*E*)-tetrahydropyran **4***E* as a single isomer in 79% yield.[15] The structures were confirmed by NOE experiments with ^{1}H NMR, and the relations are shown in Scheme 4. Although both reactions seemed to proceed very smoothly in THF at 0 °C based on the TLC analysis, the chemical yields of **3** and **4** after isolation appeared to be less than the actual yields due to their volatile characters. In fact, later as shown in Scheme 6, the nonvolatile tetrahydropyran **17** was obtained in 95% yield in the cyclization of **16**. The results indicate that the 1,3-chirality transfer from the chiral center of the starting allylic alcohol to the newly generated chiral center on the tetrahydropyran ring is perfectly controlled. In this conversion, a *syn*-SN2′ type cyclization takes place stereospecifically in a 6-exo-trigonal fashion promoted by a Pd^{II} catalyst.[16,17]

Under the same conditions, the cyclization of the (*Z*)-diol **2a** also proceeded smoothly to give *cis*-(*E*)-tetrahydropyran **3***E* as a single stereoisomer in 76% yield.[15] In contrast, treatment of **2b** with $PdCl_2(MeCN)_2$ under the same reaction conditions gave a rather disappointing result. The expected *trans*-(*E*)-tetrahydropyran **4***E* was obtained along with *cis*-(*Z*)-tetrahydropyran **3***Z* as a 1:1 mixture in a combined yield of 78%.[15] The structure of **3***Z* was identified by NOE experiments. When excess LiCl was added in the reaction of **2b**, cyclization did not occur. The reaction rate became much slower below −70 °C. However, when the reaction was conducted at −40 °C, *cis*-(*Z*)-tetrahydropyran **3***Z* was obtained in 77% yield exclusively. More surprisingly, when the reaction was performed in the presence of 10 mol % of H_2O at −40 °C, *trans*-(*E*)-tetrahydropyran **4***E* was obtained as a single isomer in 72% yield. On the other hand, the reaction in the presence of an excess of H_2O (1 equiv or more) gave a mixture of **3***Z* and **4***E* with moderate to poor selectivity. An addition of 10 mol % of water for the reaction of **2a** at −40 °C gave **3***E* as a single stereoisomer in 72% yield. The relative reaction rates of **1a**, **1b**, **2a**, and **2b** were examined. When the reactions were conducted at −15 °C in THF in the presence of 2.5 mol % of $PdCl_2(CH_3CN)_2$, cyclizations of **1a** and **1b** were complete in 40 and 70 min, respectively. On the other hand, reactions of **2a** and **2b** were not completed even after 3 h under the same conditions. Approximately 90% of **2a** and 70% of **2b** were consumed to lead to the cyclized products after 3 h. These results indicate that the relative rates are **1a** > **1b** ≫ **2a** > **2b**. On the basis of the stereochemical outcome and the relative rate studies, we should now consider the reaction mechanism.

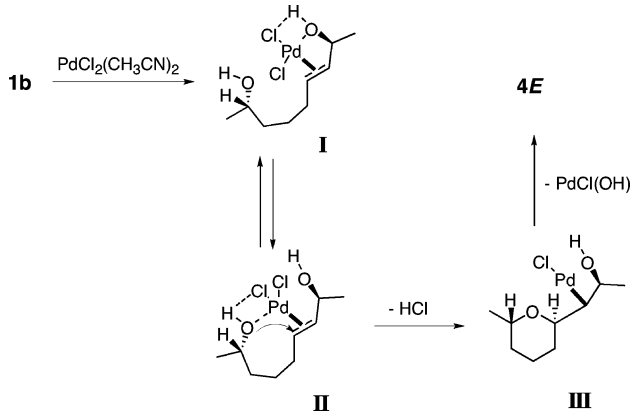


FIGURE 3.

Mechanism and Origin of Stereoselectivity in Reactions of Pd^{II}-Catalyzed Cyclization. The mechanism of oxypalladation has been extensively studied.[8,9,18] A chloride ion plays a role for the stereocontrol in the intermolecular reactions. However, we did not observed any chloride ion effect in the intramolecular cyclization, and thus a reaction mechanism via chloride intermediate in the above cyclizations has been eliminated.[18] On the basis of our experimental results, we can propose its reaction mechanism as shown in Figure 3.

When a Pd π-complex is formed by a coordination of $PdCl_2$ with the allylic alcohol, one of the π-faces of the olefinic bond may be recognized with an assistance of the adjacent chiral hydroxy group, which generates a π-complex **I** preferentially. In this complex, Pd locates on the syn-face side to the hydroxy

(15) The quantitative conversion was observed in an NMR tube experiment. Since products **3** and **4** are volatile liquids, some technical loss occurs during the workup and purification process in the above scale of the reaction.

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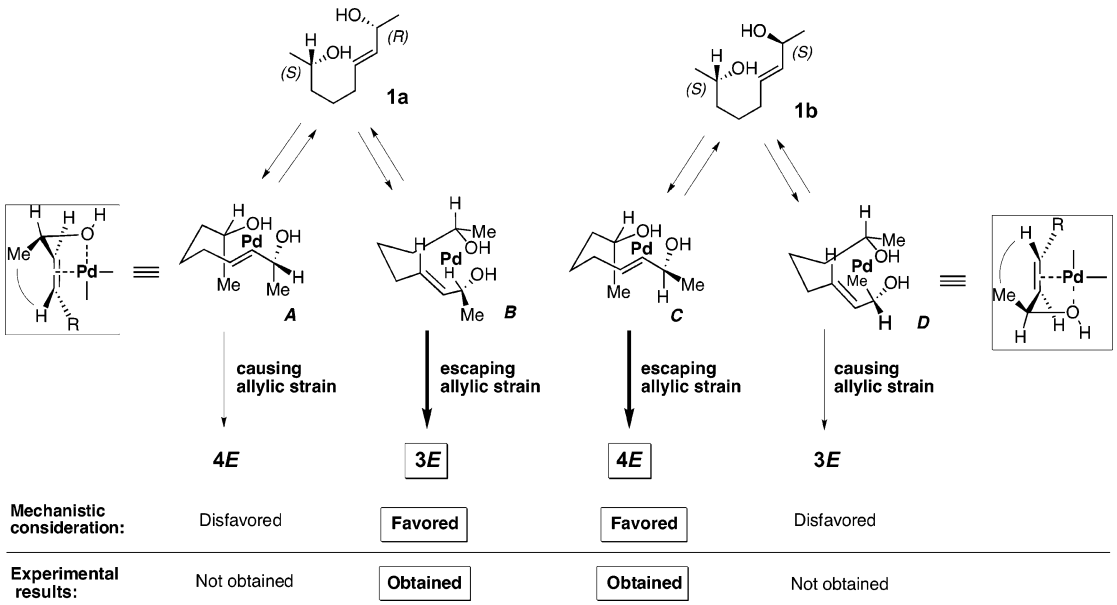


FIGURE 4.

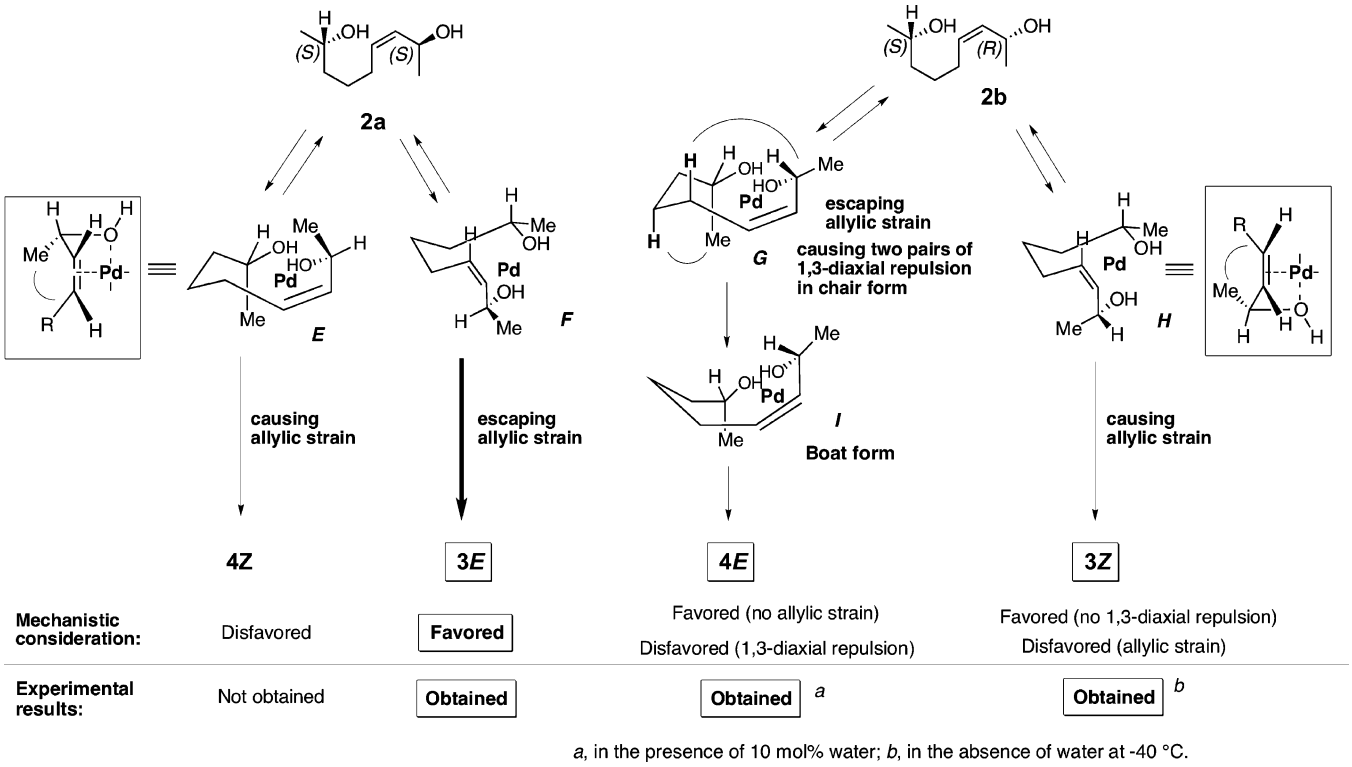


FIGURE 5.

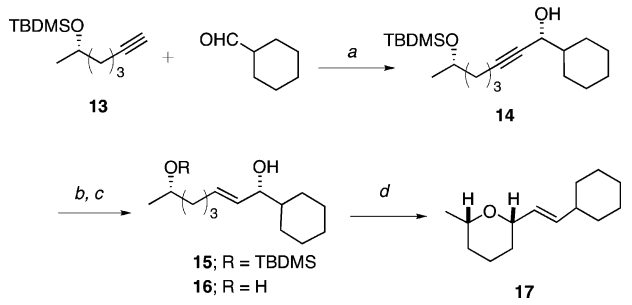
group. This complex may be present in equilibrium with complex **II** by a ligand exchange of the hydroxy function of the ζ-alcohol. A *syn*-attack of this hydroxy nucleophile onto the electrophilic carbon in **II** occurs intramolecularly from the same side of the Pd-complex in a 6-exo-trigonal fashion to give a σ-Pd complex **III**.[19] Subsequently, *syn*-elimination of PdCl(OH) generates tetrahydropyran bearing an (*E*)-olefinic substituent. In the catalytic cycle, PdCl(OH) may promote the reaction by itself or regenerate $PdCl_2$ by the reaction with HCl.

It should be noted that this Pd^{II}-catalyzed intramolecular Heck-type reaction of allylic alcohol proceeds very smoothly without any oxidant.

On the basis of the stereochemical outcome, plausible reaction paths from **1a** and **1b** are proposed in Figure 4. For the arrangement of the Pd complex in the reaction of **1a** and **1b**, the initial π-complexes **A** and **B** from **1a** and **C** and **D** from **1b** are available and could react. The conformations **A** and **C** lead

(19) The recent intramolecular syn-oxypalladation in 5-exo trigonal type cyclization reaction via palladium(II) species, see: (a) Hayashi, T.; Yamasaki, K.; Mimura, M.; Uozumi, Y. *J. Am. Chem. Soc.* **2004**, *126*, 3036−3037. (b) Trend, R. M.; Ramtohul, Y. K.; Stoltz B. M. *J. Am. Chem. Soc.* **2005**, *127*, 17778−17788.

SCHEME 6 [a]



[a] Reagents and conditions: (a) Zn(OTf) $_2$, (+)-*N*-methylephedrine, Et_3N, toluene, rt, 3 h (96%); (b) Red-al, THF, reflux, 20 min (96%); (c) TBAF, THF, rt, overnight (94%); (d) 10 mol % of $PdCl_2(CH_3CN)_2$, THF, 0 °C, 35 min (95%).

to the 2,6-trans product **4***E*, whereas the conformations **B** and **D** lead to the 2,6-cis product **3***E*. Although the π-complexes **A** and **D** possess an unfavorable allylic strain in their conformations, the π-complexes **B** and **C** do not. Therefore, the cyclization of **1a** and **1b** proceeds through the more likely conformations **B** and **C** to give the *cis*-pyran **3***E* and the *trans*-pyran **4***Z*, respectively, as a single product.

In the cyclization of (*Z*)-diol **2a**, the favorable intermediate **F**, void of the allylic strain in the two conformations **E** and **F**, afforded **3***E* exclusively. On the other hand, as the stereochemical results show, the mechanism is more complicated in the reaction of **2b**. The reaction at room temperature gave a mixture of **3***Z* and 4*E*. Although the intermediate **G** is a conformation void of the allylic strain, two pairs of severe 1,3-diaxial repulsive interactions might be anticipated in the chair form. On the other hand, the intermediate **H** has an allylic strain between the terminal methyl group and the (*Z*)-substituent on the olefinic bond. For this reason, no preferable conformation may be present for the cyclization of **2b**. The formation of **4***E* might take place through a boat-form intermediate like **I**. Though the effect of water in the preferential formation of **4***E* is not clear yet, it might assist the boat conformation or any other intermediate. For the formation of **3***Z*, it is interesting that low temperature, in the absence of a trace of water, allows the cyclization. We are not able to explain this phenomena rationally at this stage.

General Synthesis of 2,6-Dialkyl-Substituted Tetrahydropyran. The stereospecific ring formation might be useful for the general synthesis of 2,6-disubstituted tetrahydropyrans. Carreira's asymmetric alkynylation of cyclohexanecarboxaldehyde with (*S*)-6-silyloxy-1-heptyne **13**[20] in the presence of (+)-*N*-methylephedrine gave the (*R*)-propargyl alcohol **14** in 96% yield with a 98:2 diastereomeric ratio.[21] Partial reduction to allylic alcohol by Red-al followed by deprotection of the silyl group gave the diol **16** in 90% yield in 2 steps. Finally, treatment of **16** with 10 mol % of $PdCl_2(CH_3CN)_2$ gave the (*Z*,2*S*,6*R*)-6-methyl-2-(2-cyclohexyl-1-ethenyl)tetrahydropyran **17** in 95% yield. This reaction sequence presents a flexible and new synthetic method for the synthesis 2,6-disubstituted tetrahydropyrans.

(20) Drian, C. L.; Greene, A. E. *J. Am. Chem. Soc.* **1982**, *104*, 5473−5483.

(21) Carreira's asymmetric addition reaction of alkyne to aldehyde. Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 1806−1807.

3. Conclusion

We have described $PdCl_2$-catalyzed stereospecific synthesis of 2,6-substituted tetrahydropyrans in good yields with excellent diastereoselectivities (>20:1). The important features of this reaction are the following: (i) the face-selective formation of the initial Pd^{II} π-complex can be controlled by the chiral center of the allylic alcohol, (ii) elimination of PdCl(OH) regenerates $PdCl_2$ or itself promotes the catalytic cycle, (iii) the reaction proceeds under mild conditions via a *syn*-SN2′ type process, (iv) the stereochemistry of the product is perfectly controlled, and (v) water plays an important role in the formation of **4***E* from **2b**. We have realized the asymmetric synthesis of cis 2,6-substituted tetrahydropyran **17** from a hydroxyalkyne and an aldehyde.

Experimental Section

(5*S*)-5-(*tert*-Butyldimethylsilyloxy)-1-hexanal (6).[12] To a solution of **5**[11] (1.21 g, 10.6 mmol) and imidazole (1.46 g, 21.4 mmol) in DMF (80 mL) was added TBDMSCl (2.42 g, 16.1 mmol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C and allowed to warm to room temperature. The reaction mixture was quenched with water and extracted with Et_2O. The organic extracts were washed with brine and dried ($MgSO_4$). Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with hexane gave (6*S*)-6-(*tert*-butyldimethylsilyloxy)-1-heptene (2.07 g, 85%). After this compound (483 mg, 2.11 mmol) was dissolved in CH_2Cl_2 (10 mL), a dilute stream of O_3 in O_2 was bubbled into the solution at −78 °C until the colorless solution became a persistent blue color. Then, PPh_3 (1.11 g, 4.22 mmol) was added, and the reaction was warmed to room temperature under an Ar atmosphere. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with CH_2Cl_2 gave **6** (437 mg, 90%): colorless oil; $[\alpha]^{24}_D$ +18.0 (*c* 1.04, $CHCl_3$); R_f 0.65 (CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (t, 1H, J = 1.8 Hz), 3.78 (m, 1H), 2.43 (td, 2H, J = 7.3, 1.8 Hz), 1.50−1.78 (m, 2H), 1.39−1.47 (m, 2H), 1.13 (d, 3H, J = 6.1 Hz), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H).

(6*S*)-6-(*tert*-Butyldimethylsilyloxy)-1,1-dibromo-1-heptene (7). To a solution of CBr_4 (1.04 g, 3.14 mmol) in CH_2Cl_2 (3 mL) was added dropwise a solution of PPh_3 (1.65 g, 6.28 mmol) in CH_2Cl_2 (1 mL) at 0 °C. After the mixture was stirred for 15 min, NEt_3 (1.76 mL, 12.6 mmol) was added, and the solution was stirred for an additional 10 min. Then, a solution of **6** (362 mg, 1.57 mmol) in CH_2Cl_2 (1 mL) was added, and the reaction mixture was stirred for 10 h at room temperature. The mixture was quenched with a saturated $NaHCO_3$ solution and extracted 3 times (hexane). The combined organic extracts were washed with brine and dried ($MgSO_4$). Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with hexane gave **7** (537 mg, 89%): colorless oil; $[\alpha]^{24}_D$ +8.7 (*c* 1.01, $CHCl_3$); R_f 0.26 (hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.38 (t, 1H, J = 7.3 Hz), 3.78 (m, 1H), 2.06−2.17 (m, 2H), 1.37−1.54 (m, 4H), 1.12 (d, 3H, J = 6.2 Hz), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 88.6, 68.2, 38.9, 33.0, 25.9, 23.9, 23.8, 18.1, −4.4, −4.7; IR (film, cm^{-1}) 2928, 2857, 1623, 1462, 1373, 1254, 1188, 1139, 1096, 1036, 835, 774; MS (CI) *m*/*z* 385 (M + H^+). HRMS calcd for $C_{13}H_{27}Br_2OSi$ (M + H^+) 385.0197, found *m*/*z* 385.0193.

(2*S*,8*S*)- and (2*R*,8*S*)-8-(*tert*-Butyldimethylsilyloxy)non-3-yn-2-ol (8). To a solution of **7** (846 mg, 2.20 mmol) in THF (1.8 mL) was added *n*-BuLi (1.68 mL of a 2.6 M solution in hexane, 4.37 mmol) at −78 °C. The mixture was stirred for 3 h before an addition of freshly distilled acetaldehyde (3.67 mL, 65.7 mmol). The reaction mixture was stirred for 0.5 h after removal of the cooling bath. The mixture was quenched with water (80 mL) and extracted (Et_2O). The organic extract was washed with brine and dried ($MgSO_4$). Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 15% Et_2O in hexane gave

8 (539 mg, 90%): colorless oil; R_f 0.72 (30% Et_2O in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 4.50 (qt, 1H, J = 6.6, 1.8 Hz), 3.80 (m, 1H), 2.17−2.25 (m, 2H), 1.75 (s, 1H), 1.49−1.58 (m, 4H), 1.42 (d, 3H, J = 6.6 Hz), 1.12 (d, 3H, J = 6.2 Hz), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 84.5, 82.4, 68.2, 58.6, 38.7, 25.9, 24.8, 24.7, 23.7, 18.7, 18.1, −4.4, −4.7; IR (film, cm^{-1}) 3358, 2930, 2858, 2247, 1462, 1373, 1254, 1137, 1090, 899, 836, 774; MS (CI) m/z 271 (M + H^+). HRMS calcd for $C_{15}H_{31}O_2Si$ (M + H^+) 271.2093, found m/z 271.2089.

(*E*,2*S*,8*S*)- and (*E*,2*R*,8*S*)-8-(*tert*-Butyldimethylsilyloxy)non-3-en-2-ol (9). To a stirred solution of **8** (20 mg, 0.074 mmol) in THF (1 mL) was added Red-Al (0.089 mL of a 65% solution in toluene, 0.29 mmol) at 0 °C. The mixture was refluxed for 2 h and quenched with water and extracted (ether). The organic extracts was washed with brine and dried ($MgSO_4$). Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 15% Et_2O in hexane gave **9** (20.4 mg) in quantitative yield: colorless oil; R_f 0.10 (10% EtOAc in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.62 (dt, 1H, J = 15.4, 6.4 Hz), 5.49 (ddt, 1H, J = 15.4, 6.2, 1.3 Hz), 4.25 (dq, 1H, J = 6.4, 6.4 Hz), 3.77 (m, 1H), 1.97−2.04 (m, 2H), 1.31−1.49 (m, 4H), 1.25 (s, 1H), 1.24 (d, 3H, J = 6.2 Hz), 1.10 (d, 3H, J = 6.1 Hz), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.3, 130.9, 68.9, 68.4, 39.1, 32.1, 25.9, 25.3, 23.8, 23.4, 18.1, −4.4, −4.7; IR (film, cm^{-1}) 3347, 2929, 2857, 1461, 1373, 1254, 1134, 1059, 968, 835, 774; MS (FAB) m/z 295 (M + Na^+). HRMS calcd for $C_{15}H_{32}O_2SiNa$ (M + Na^+) 295.2069, found m/z 295.2076.

(*Z*,2*S*,8*S*)- and (*Z*,2*R*,8*S*)-8-(*tert*-Butyldimethylsilyloxy)non-3-en-2-ol (11). To a solution of **8** (400 mg, 1.48 mmol) in a mixture of EtOAc:pyridine:1-hexene (10:1:1, 1 mL) was added Lindlar's catalyst (5% of Pd, poisoned with lead, 40 mg). The reaction mixture was stirred for 4 h under a H_2 atmosphere and filtered through a Celite pad. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel eluted with 50% Et_2O in hexane gave **11** (384 mg, 95%): colorless oil; R_f 0.65 (70% Et_2O in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.41 (m, 2H), 4.64 (dqm, 1H, J = 6.2, 1.1 Hz), 3.77 (m, 1H), 2.04−2.12 (m, 2H), 1.56 (s, 1H), 1.31−1.50 (m, 4H), 1.24 (d, 3H, J = 6.4 Hz), 1.11 (d, 3H, J = 6.0 Hz), 0.88 (s, 9H), 0.04 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.9, 133.8, 131.2, 122.0, 68.5 (**11*S***) and 68.4 (**11*R***), 63.9, 39.2, 27.6, 25.9, 25.8, 23.9 (**11*S***), and 23.8 (**11*R***), 23.6, 18.1, −4.4, −4.7; IR (film, cm^{-1}) 3349, 2929, 1656, 1462, 1373, 1254, 1188, 1135, 1032, 923, 836, 807, 774; MS (CI) m/z 273 (M + H^+). HRMS calcd for $C_{15}H_{33}O_2Si$ (M + H^+) 273.2250, found m/z 273.2254.

Lipase-Catalyzed Kinetic Acetylation of 9 and 11. To a solution of **9** or **11** (3.0 mmol) in diisopropyl ether (50 mL) were added MS 4 Å (592 mg), *Ca*l (238 mg), and vinyl acetate (1.34 mL, 14.6 mmol) at room temperature. The mixture was stirred for 1.5 h and filtered through a Celite pad. After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluted with 20% EtOAc in hexane for acetates **10** and **12** and with EtOAc for alcohols **9*S*** and **11*S***. The physical and spectroscopic data for **10** and **12** are described as follows. **10**: colorless oil; $[\alpha]^{27}_D$ +53.5 (*c* 1.00, $CHCl_3$); R_f 0.68 (20% EtOAc in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.68 (dt, 1H, J = 15.4, 6.4), 5.45 (ddt, 1H, J = 15.4, 6.6, 1.5 Hz), 5.30 (dq, 1H, J = 6.4, 6.4 Hz), 3.77 (m, 1H), 2.03 (s, 3H), 1.98−2.07 (m, 2H), 1.33−1.50 (m, 4H), 1.28 (d, 3H, J = 6.4 Hz), 1.11 (d, 3H, J = 6.1 Hz), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 133.1, 129.5, 71.0, 68.3, 39.0, 32.1, 25.8, 24.9, 23.7, 21.4, 20.3, 18.1, −4.4, −4.7; IR (film, cm^{-1}) 2930, 2857, 1740, 1461, 1371, 1240, 1136, 1043, 968, 835, 774; MS (CI) m/z 315 (M + H^+). HRMS calcd for $C_{17}H_{35}O_3Si$ (M + H^+) 315.2355, found m/z 315.2360. **12**: colorless oil; $[\alpha]^{27}_D$ −0.76 (*c* 1.04, $CHCl_3$); R_f 0.85 (60% Et_2O in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.62 (dq, 1H, 8.4, 6.6 Hz), 5.47 (dt, 1H, J = 10.6, 7.3 Hz), 5.36 (ddt, 1H, J = 11.0, 8.8, 1.1 Hz), 3.77 (m, 1H), 2.03−2.17 (m, 2H), 2.01 (s, 3H), 1.34−1.47 (m, 4H), 1.27 (d, 3H, J = 6.6 Hz), 1.11 (d, 3H, J = 6.2 Hz), 0.88 (s, 9H), 0.04 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 133.0, 129.4, 68.4, 67.0, 39.2, 27.7, 25.9, 25.7, 23.8, 21.3, 20.9, 18.1, −4.4, −4.8; IR (film, cm^{-1}) 2930, 2858, 1739, 1462, 1371, 1243, 1133, 1087, 1041, 949, 836, 774; MS (CI) m/z 315 (M + H^+). HRMS calcd for $C_{17}H_{35}O_3Si$ (M + H^+) 315.2355, found m/z 315.2360. The spectroscopic data of **9*S*** and **11*S*** are described in the synthesis of racemic mixtures above. The specific rotations are $[\alpha]^{27}_D$ +6.3 (*c* 1.00, $CHCl_3$) for **9*S*** and $[\alpha]^{26}_D$ +9.6 (*c* 1.11, $CHCl_3$) for **11*S***.

Preparation of 1b and 2a. To a solution of **9*S*** or **11*S*** (1.0 mmol) in THF (2 mL) was added TBAF (8.1 mL of a 1.0 M solution in THF, 8.1 mmol) at room temperature. The reaction mixture was stirred for 1−2 days and quenched with water, and then extracted with EtOAc. The organic extracts was washed with brine and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluted with EtOAc to give **1b** or **2a**. **1b**: 88%; colorless oil; $[\alpha]^{26}_D$ +1.4 (*c* 1.06, $CHCl_3$); R_f 0.15 (40% EtOAc in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.61 (dt, 1H, J = 15.4, 6.4 Hz), 5.50 (ddt, 1H, J = 15.4, 6.2, 1.1 Hz), 4.24 (dq 1H, J = 6.2, 6.2 Hz), 3.78 (m, 1H), 2.04 (m, 2H), 1.67 (s, 2H), 1.40−1.48 (m, 4H), 1.24 (d, 3H, J = 6.2 Hz), 1.17 (d, 3H, J = 6.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.5, 130.5, 68.8, 67.9, 38.7, 32.0, 25.2, 23.5, 23.4; IR (film, cm^{-1}) 3337, 2968, 2930, 1455, 1371, 1129, 1063, 968, 938, 868; MS (FAB) m/z 181 (M + Na^+). HRMS calcd for $C_9H_{18}O_2Na$ (M + Na^+) 181.1204, found m/z 181.1198. **2a**: 92%; colorless oil; $[\alpha]^{23}_D$ +4.3 (*c* 0.82, $CHCl_3$); R_f 0.22 (90% Et_2O in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.37−5.48 (m, 2H), 4.63 (dq, 1H, J = 7.5, 6.2 Hz), 3.80 (m, 1H), 2.12 (m, 2H), 1.52 (s, 2H), 1.39−1.50 (m, 4H), 1.24 (d, 3H, J = 6.2 Hz), 1.19 (d, 3H, J = 6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.1, 130.8, 67.9, 63.8, 38.7, 27.4, 25.7, 23.6, 23.5; IR (film, cm^{-1}) 3336, 2967, 1656, 1457, 1371, 1314, 1181, 1110, 1058, 1012, 933, 826; MS (FAB) m/z 181 (M + Na^+). HRMS calcd for $C_9H_{18}O_2Na$ (M + Na^+) 181.1204, found m/z 181.1211.

Preparation of 1a and 2b. Deprotections of the silyl group of **10** and **12** were performed by the same procedure described for the desilylation of **9*S*** and **11*S*** except with 60% EtOAc in hexane as an eluent for silica gel column chromatography. The intermediary monoacetate from **10**: colorless oil; $[\alpha]^{26}_D$ +66.7 (*c* 1.02, $CHCl_3$); R_f 0.31 (30% EtOAc in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.54 (dt, 1H, J = 15.4, 6.6 Hz), 5.40 (ddt, 1H, J = 15.4, 6.8, 1.5 Hz), 5.24 (dq, 1H, J = 6.4, 6.4 Hz), 3.73 (m, 1H), 1.98 (s, 3H), 1.94−2.07 (m, 3H), 1.31−1.49 (m, 4H), 1.23 (d, 3H, J = 6.4), 1.12 (d, 3H, J = 6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 132.9, 129.7, 71.1, 67.7, 38.6, 32.0, 25.0, 23.4, 21.3, 20.3; IR (film, cm^{-1}) 3419, 2932, 1735, 1372, 1242, 1041, 949; MS (CI) m/z 201 (M + H^+). HRMS calcd for $C_{11}H_{21}O_3$ (M + H^+) 201.1491, found m/z 201.1492. The intermediary monoacetate from **12**: colorless oil; $[\alpha]^{23}_D$ +6.9 (*c* 0.55, $CHCl_3$); R_f 0.39 (70% Et_2O in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.62 (dq, 1H, J = 8.8, 6.4 Hz), 5.48 (dt, 1H, J = 11.0, 7.5 Hz), 5.35 (ddt, 1H, J = 11.6, 9.0, 1.5 Hz), 3.81 (m, 1H), 2.24 (m, 1H), 2.05 (m, 1H), 2.01 (s, 3H), 1.69 (s, 1H), 1.38−1.53 (m, 4H), 1.27 (d, 3H, J = 6.4 Hz), 1.18 (d, 3H, J = 6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 132.8, 129.5, 67.5, 67.0, 38.6, 27.4, 25.6, 23.5, 21.4, 20.8; IR (film, cm^{-1}) 3427, 2969, 2931, 1737, 1454, 1371, 1244, 1126, 1041, 949, 846; MS (CI) m/z 201 (M + H^+). HRMS calcd for $C_{11}H_{21}O_3$ (M + H^+) 201.1491, found m/z 201.1483. The monoacetates were hydrolyzed by the following conditions: A mixture of monoacetate (1 mmol) and K_2CO_3 (645 mg, 4.67 mmol) in methanol (11 mL) was stirred for 2 h at room temperature. The mixture was quenched with a saturated NH_4Cl solution and extracted (EtOAc). The extract was washed with brine and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluted with EtOAc. **1a**: 87% in 2 steps; colorless oil; $[\alpha]^{25}_D$ +16.5 (*c* 1.05, $CHCl_3$); R_f 0.13 (40% EtOAc in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.63 (dt, 1H, J = 15.4, 6.2 Hz), 5.51 (ddt, 1H, J = 15.4, 6.2, 1.1 Hz), 4.25 (dq 1H, J = 6.4, 6.2 Hz), 3.80 (qm, 1H, J = 6.2 Hz), 2.04 (m, 2H), 1.51 (s, 2H), 1.36−1.50

(m, 4H), 1.25 (d, 3H, $J = 6.2$ Hz), 1.18 (d, 3H, $J = 6.1$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.5, 130.6, 68.9, 68.0, 38.7, 32.0, 25.3, 23.5, 23.4; IR (film, cm^{-1}) 3347, 2968, 2930, 1670, 1455, 1371, 1129, 1063, 968, 939, 869; MS (FAB) *m*/*z* 181 (M + Na$^+$). HRMS calcd for $C_9H_{18}O_2Na$ (M + Na$^+$) 181.1204, found *m*/*z* 181.1210. **2b**: 74% in 2 steps; colorless oil; $[\alpha]^{25}_D$ +16.5 (*c* 1.05, $CHCl_3$); R_f 0.13 (40% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.36−5.47 (m, 2H), 4.63 (dq, 1H, $J = 7.5$, 6.2 Hz), 3.80 (m, 1H), 2.01−2.23 (m, 2H), 1.62 (s, 2H), 1.39−1.54 (m, 4H), 1.24 (d, 3H, $J = 6.4$ Hz), 1.18 (d, 3H, $J = 6.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.1, 130.9, 68.0, 63.8, 38.5, 27.3, 25.8, 23.6, 23.5; IR (film, cm^{-1}) 3348, 2968, 2929, 1656, 1457, 1371, 1314, 1109, 1058, 1011, 929, 826; MS (FAB) *m*/*z* 181 (M + Na$^+$). HRMS calcd for $C_9H_{18}O_2Na$ (M + Na$^+$) 181.1204, found *m*/*z* 181.1209.

General Procedure of Pd-Catalyzed Cyclization of ζ-Hydoxy-α,β-unsaturated Alcohol. A mixture of alcohol **1** or **2** (1 mmol) and $PdCl_2(CH_3CN)_2$ (26.5 mg, 0.1 mmol) was stirred in THF (10 mL) at 0 °C for 5 min. The mixture was diluted with pentane, and precipitates were removed by filtration through a Celite pad. After removal of the solvent, the residue was purified by column chromatography on silica gel eluted with 5% Et_2O in pentane. The physical and spectroscopic data for **3***E*, **4***E*, and **3***Z* are described as follows. **3***E*:[14a,c] colorless oil; $[\alpha]^{24}_D$ +13.6 (*c* 1.20, $CHCl_3$); R_f 0.77 (10% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.69 (dqd, 1H, $J = 15.4$, 6.4, 0.9 Hz), 5.51 (ddq, 1H, $J = 15.4$, 6.6, 1.5 Hz), 3.77 (ddm, 1H, $J = 11.3$, 6.6 Hz), 3.48 (dqd, 1H, $J = 11.0$, 6.2, 1.6 Hz), 1.82 (m, 1H), 1.68 (ddd, 3H, $J = 6.4$, 1.5, 0.7 Hz), 1.46−1.60 (m, 3H), 1.25−1.35 (m, 2H), 1.19 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.7, 126.7, 78.3, 73.7, 33.0, 31.4, 23.5, 22.2, 17.8; IR (film, cm^{-1}) 2932, 1442, 1366, 1320, 1203, 1077, 1036, 963; MS (GC/MS) *m*/*z* 140. **4***E*:[14c] colorless oil; $[\alpha]^{23}_D$ +38.0 (*c* 2.00, $CHCl_3$); R_f 0.70 (10% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.62−5.66 (m, 2H), 4.25−4.29 (m, 1H), 3.91 (dqd, 1H, $J = 7.5$, 6.4, 2.8 Hz), 1.71 (dd, 3H, $J = 6.1$, 1.3 Hz), 1.59−1.68 (m, 4H), 1.19−1.32 (s, 2H), 1.16 (d, 3H, $J = 6.4$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.4, 127.2, 71.9, 67.0, 32.1, 29.6, 20.4, 18.6, 17.9; IR (film, cm^{-1}) 2930, 1444, 1378, 1260, 1038, 803; MS (GC/MS) *m*/*z* 140. **3***Z*:[14b,c] colorless oil; $[\alpha]^{24}_D$ −13.1 (*c* 0.35, $CHCl_3$); R_f 0.60 (5% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52 (dqd, 1H, $J = 11.0$, 7.0, 1.1 Hz), 5.31 (ddq, 1H, $J = 11.0$, 7.7, 1.8 Hz), 4.16 (ddd, 1H, $J = 11.0$, 8.1, 2.2 Hz), 3.49 (dqd, 1H, $J = 11.0$, 6.2, 1.8 Hz), 1.83 (m, 1H), 1.67 (dd, 3H, $J = 6.6$, 1.5 Hz), 1.49−1.59 (m, 3H), 1.21−1.37 (m, 2H), 1.18 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.1, 125.8, 73.8, 73.6, 33.0, 31.3, 23.6, 22.3, 13.4; IR (film, cm^{-1}) 3022, 2932, 2856, 1443, 1365, 1307, 1203, 1183, 1158, 1075, 1049, 989, 961, 927, 875, 808; MS (GC/MS) *m*/*z* 140.

Asymmetric Alkynylation: Preparation of 14. To a stirred suspension of $Zn(OTf)_2$ (73.6 mg, 0.202 mmol, predried overnight at 125 °C under vacuum) and (+)-*N*-methylephedrine (39.6 mg, 0.221 mmol) in dry toluene (0.63 mL) was added Et_3N (30.8 μL, 0.221 mmol) in one portion. After the white slurry was stirred at room temperature for 3 h, alkyne **13** (50 mg, 0.221 mmol) was added. The mixture was stirred for 30 min and quenched with freshly distilled cyclohexanecarboxaldehyde (20.6 mg, 0.184 mmol). After the mixture was stirred for 3 h at room temperature, a saturated NH_4Cl solution was added to the mixture, and it was extracted (Et_2O). The extract was washed with brine and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluted with 25% of Et_2O in hexane to give **14** (59.9 mg, 96%): colorless oil; $[\alpha]^{22}_D$ +10.7 (*c* 0.43, $CHCl_3$) (96% de); R_f 0.34 (25% Et_2O in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4,13 (dt, 1H, $J = 5.9$, 2.0 Hz), 3.80 (m, 1H), 2.19−2.24 (m, 2H), 1.43−1.86 (m, 11H), 1.12 (d, 3H, $J = 6.1$ Hz), 1.03−1.26 (m, 5H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.1, 80.3, 68.1, 67.4, 44.4, 38.8, 28.6, 28.1, 26.4, 25.9, 25.9, 25.0, 23.8, 18.8, 18.1, −4.4, −4.7; IR (film, cm^{-1}) 3389, 2927, 2232, 1450, 1374, 1254, 1187, 1137, 1092, 1024, 893, 836, 774, 661; MS (FAB) *m*/*z* 339 (M + H$^+$). HRMS calcd for $C_{20}H_{39}O_2Si$ (M + H$^+$) 339.2719, found *m*/*z* 339.2713. The enantiomeric purity was deteremined by chiral HPLC after deriving the corresponding benzoate with use of DAICEL CHIRALCEL OD-H. Eluent, hexane/2-propanol (99/1); flow rate, 0.1 mL/min; detection, 254 nm; retention time, 35.8 min (major *R*-isomer), 38.6 min (minor *S*-isomer).

Preparation of 15. To a solution of **14** (37.5 mg, 0.11 mmol) in THF (1.5 mL) was added Red-al (0.17 mL of a solution of 65% in toluene, 0.55 mmol). The mixture was refluxed for 20 min, quenched with a saturated NH_4Cl solution, and then extracted (Et_2O). The extract was washed with brine and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluted with 25% of Et_2O in hexane to give **15** (36.1 mg, 96%): colorless oil; $[\alpha]^{23}_D$ +3.7 (*c* 0.52, $CHCl_3$) (96% de, based on the value obtained for **14**); R_f 0.41 (25% Et_2O in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (dt, 1H, $J = 15.4$, 6.4 Hz), 5.44 (ddt, 1H, $J = 15.4$, 7.2, 1,1 Hz), 3.73−3.81 (m, 2H), 2.03 (q, 2H, $J = 6.6$ Hz), 1.59−1.87 (m, 5H), 1.14−1.57 (m, 9H), 1.11 (d, 3H, $J = 6.1$ Hz), 0.90−1.08 (m, 2H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.8, 131.6, 77.6, 68.4, 43.7, 39.2, 32.2, 28.8, 28.7, 26.6, 26.2, 26.1, 25.9, 25.4, 23.8, 18.1, −4.4, −4.7; IR (film, cm^{-1}) 3366, 2927, 2855, 1450, 1374, 1254, 1135, 1094, 1006, 892, 835, 774; MS (FAB) *m*/*z* 363 (M + Na$^+$) . HRMS calcd for $C_{20}H_{40}O_2SiNa$ (M + Na$^+$) 363.2695, found *m*/*z* 363.2698.

Preparation of 16. To a solution of **15** (19.9 mg, 58.4 μmol) in THF (0.1 mL) was added TBAF (0.47 mL of a 1.0 M solution in THF, 0.47 mmol) at room temperature. The mixture was stirred overnight, quenched with water, and then extracted (EtOAc). After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluted with Et_2O and gave **16** (12.4 mg, 94%): colorless oil; $[\alpha]^{20}_D$ +2.2 (*c* 0.83, $CHCl_3$) (96% de, based on the value obtained for **14**); R_f 0.46 (Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.66 (dt, 1H, $J = 15.2$, 6.4 Hz), 5.46 (ddt, 1H, $J = 15.2$, 7.2, 1.1 Hz), 3.75−3.83 (m, 2H), 2.06 (q, 2H, $J = 6.6$ Hz), 1.64−1.88 (m, 4H), 1.03−1.60 (m, 10H), 1.19 (d, 3H, $J = 6.2$ Hz), 0.83−1.02 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.5, 131.9, 77.6, 68.0, 43.7, 38.8, 32.2, 28.8, 28.7, 26.5, 26.1, 26.0, 25.4, 23.5; IR (film, cm^{-1}) 3366, 2925, 2853, 1667, 1450, 1374, 1308, 1124, 1005, 971, 910, 892, 842, 734; MS (FAB) *m*/*z* 249 (M + Na$^+$). HRMS calcd for $C_{14}H_{26}O_2Na$ (M + Na$^+$) 249.1830, found *m*/*z* 249.1835.

Pd-Catalyzed Cyclization of 16. To a solution of **16** (15 mg, 66 μmol) in THF (0.5 mL) at 0 °C was added a solution of $PdCl_2(CH_3CN)_2$ (1.7 mg, 10 mol %) in THF (0.5 mL). The mixture was stirred for 35 min at 0 °C and diluted with pentane. After filtration through a Celite pad, the filtrate was concentrated. Purification of the residue by column chromatography on silica gel eluted with 5% Et_2O in pentane gave **17** (13.1 mg, 95%): colorless oil; $[\alpha]^{20}_D$ −8.3° (*c* 0.60, $CHCl_3$); R_f 0.61 (5% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.65 (dd, 1H, $J = 16.1$, 6.2 Hz), 5.47 (ddd, 1H, $J = 15.8$, 6.4, 1.1 Hz), 3.82 (ddm, 1H, $J = 10.8$, 6.2 Hz), 3.52 (dqd, 1H, $J = 11.0$, 6.1, 1.8 Hz), 1.48−1.99 (m, 10H), 1.05−1.40 (m, 7H), 1.24 (d, 3H, $J = 6.1$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.4, 128.9, 78.6, 73.6, 40.3, 33.1, 32.7, 31.7, 26.2, 26.1, 23.6, 22.3; IR (film, cm^{-1}) 2925, 2851, 1448, 1366, 1306, 1260, 1201, 1084, 1038, 966, 886, 805; MS (EI) *m*/*z* 208 (M$^+$). HRMS calcd for $C_{14}H_{24}O$ (M$^+$) 208.1827, found *m*/*z* 208.1823.

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Supporting Information Available: Copies of the ^{1}H and/or ^{13}C NMR spectra for compounds **1a**, **1b**, **2a**, **2b**, **3***E*, **4***E*, **3***Z*, **7**, **8**, **9**, **9***S*, **10**, **11**, **11***S*, **12**, **14**, **15**, **16**, and **17**. This material is available free of charge via the Internet at http://pubs.acs.org.

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