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Stereochemistry and Mechanistic Study of Intramolecular Pd^{II}-Catalyzed Oxypalladation and 1,3-Chirality-Transfer Reactions

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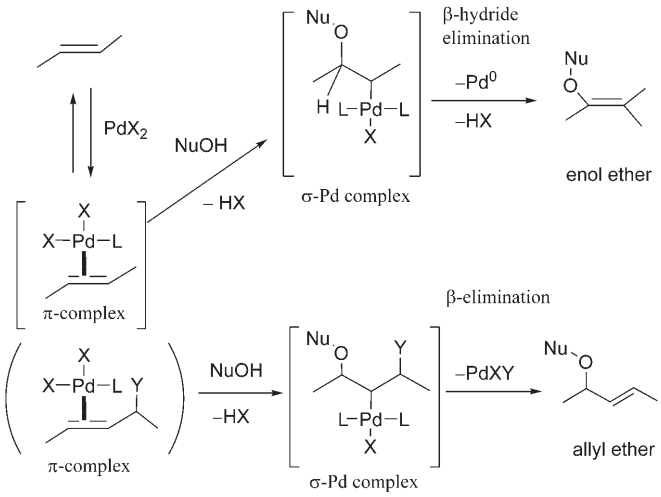
Dedicated to Professor Teruaki Mukaiyama on the occasion of his 80th birthday.

Abstract: Pd^{II}-catalyzed cyclizations of chiral ε-, ζ-, and η-hydroxy-α,β-unsaturated alcohols are described. The reactions took place stereospecifically to give chiral 2,5-disubstituted tetrahydrofurans, 2,6-disubstituted tetrahydropyrans, and 2,7-disubstituted oxepanes, respectively. The chirality of the carbon center of the chiral allylic alcohol is transferred stereospecifically to the carbon center of the newly generated oxacyclic ring. A plausible reaction mechanism involves 1) chiral-allylic-alcohol-induced *syn* facioselective formation of a Pd π-complex, 2) *syn* oxypalladation, and 3) *syn* elimination of PdCl(OH), which provide a rational account for the stereochemical results.

Keywords: chirality transfer · cyclization · oxygen heterocycles · palladium · reaction mechanism

Introduction

Pd^{II}-catalyzed reactions are widely used in organic synthesis and are powerful tools for the construction of complex molecules.[1] The inter- or intramolecular oxypalladation reactions[2] with oxygen nucleophiles such as alcohols or water offer attractive functional-group transformations as well as new synthetic routes to many valuable compounds. This type of reaction (Scheme 1) involves the formation of a Pd π-complex with an alkene in the first step, followed by nucleophilic attack on the Pd-coordinated alkene, leading to a Pd σ-complex by simultaneous elimination of HX. When dehydropalladation (β-hydride elimination) takes place from the intermediate σ-complex, an enol ether is formed. On the other hand, when a potential leaving group, such as a hydroxy group (Y = OH, in Scheme 1), is attached to the carbon atom next to the σ-palladium bond, an allyl ether is formed preferentially. In the former case, an oxidant is required for regeneration of Pd^{II} by the oxidation of Pd^0 to complete the catalytic cycle, but not in the latter case. Although a number of stereochemical investigations of oxypalladation reactions have been made[3] so far, the *syn*-oxypalladation mechanism is proposed in intramolecular reactions[4] as well as intermolecular reactions[2b,3f,i] on the basis of the experimental results.



Scheme 1. Pd^{II}-catalyzed oxypalladation reaction and the formation of enol ether or allyl ether.

According to the mechanism shown in Scheme 1, if the substrate is a chiral allylic alcohol (Y = OH), chirality would be expected to be transferred to the newly generated carbon stereocenter. Indeed, as shown in Scheme 2, we have demonstrated intramolecular Pd^{II}-catalyzed cyclizations of chiral ζ-hydroxy-α,β-unsaturated alcohols with successful 1,3-chir-

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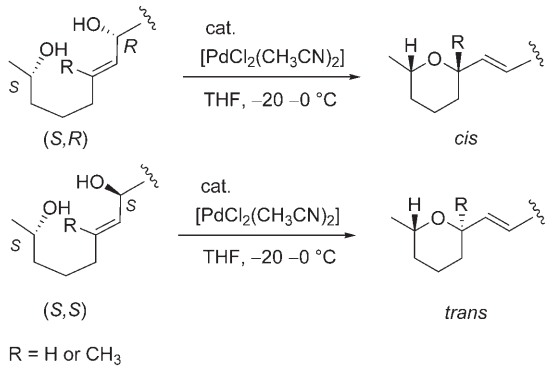
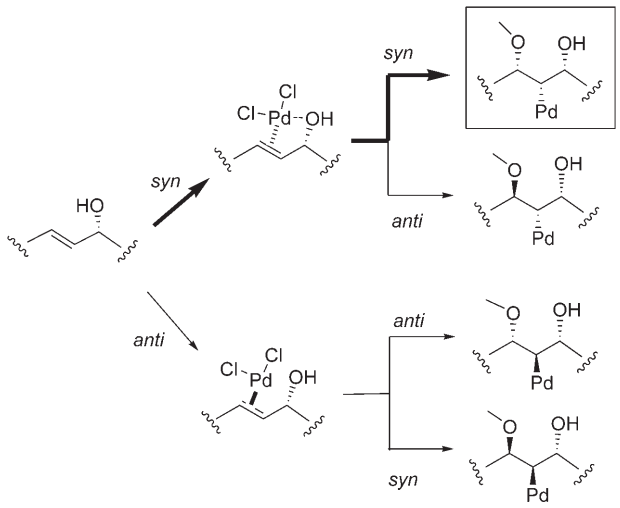


Scheme 2. Pd^{II}-catalyzed cyclizations of chiral ζ-hydroxy-α,β-unsaturated alcohols.

ality transfer, leading stereospecifically to 2,6-di- and 2,2,6-trisubstituted tetrahydropyrans and oxaspiropyrans.[5,6]

To facilitate discussion of the stereochemistry of the oxypalladation, all the possible stereochemical outcomes are described in Scheme 3. First, coordination of Pd^{II} to the allylic

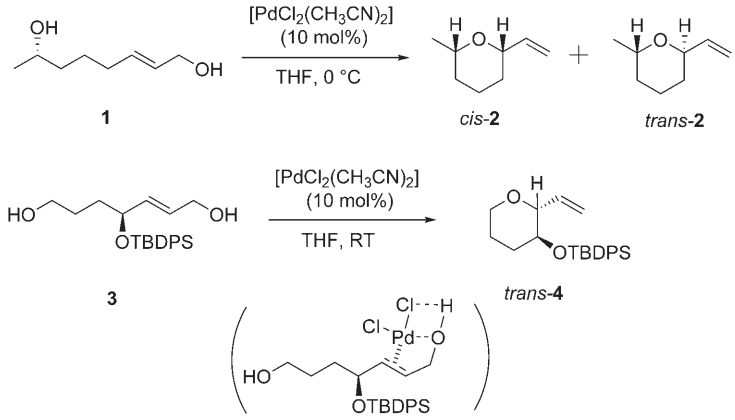


Scheme 3. Reaction pathways of syn- and anti-oxypalladation in chiral allylic alcohol.

alcohol gives *syn*- or *anti*-coordinated complexes with respect to the hydroxy group. Then, the hydroxy nucleophile can attack the two diastereomeric π-complexes in a *syn* or *anti* fashion to provide four possible diastereomers of the Pd σ-complex. When subsequent elimination of PdXY, PdCl(OH) in this case, takes place in a *syn* fashion, chiral *E* and *Z* allyl ethers are formed. On the basis of the results shown in Scheme 2, we propose that the reaction proceeds through the route indicated by bold arrows in Scheme 3. Although other scenarios cannot be ruled out, this "*syn* coordination, *syn* oxypalladation, and *syn* elimination" mechanism rationally accounts for our stereochemical results. However, questions still remain: 1) Regarding the facioselectivity in the formation of the Pd π-complex in the first step, does the adjacent hydroxy group coordinate to Pd^{II} and control the direction of formation of the Pd π-complex? 2) Regarding the direction of the nucleophilic attack in the second step, why does *syn* attack occur dominantly in intramolecular oxypalladation, rather than *anti* attack? 3) Regarding to the stereochemical course of the final step, is *syn* elimination favorable rather than *anti* elimination? Furthermore, are there any exceptions to this observation? The previously studied reactions of chiral ζ-hydroxy-α,β-unsaturated alcohols are definitely stereospecific and give chiral tetrahydropyrans as indicated in Scheme 2. However, as the mechanistic proposal was made on the basis of a limited number of substrates, we have now expanded this study to additional substrates, including some other ζ-hydroxy-α,β-unsaturated alcohols bearing a neighboring substituent, as well as ε- and η-hydroxy-α,β-unsaturated alcohols. Herein we describe more results supporting the "*syn* coordination, *syn* oxypalldation, and *syn* elimination" mechanism and discuss the above-mentioned stereochemical questions for the intramolecular oxypalladation reaction.

Results and Discussion

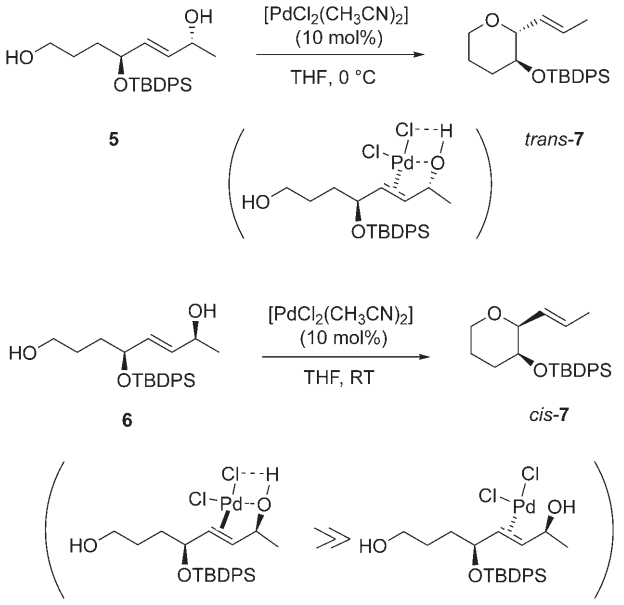
First, we examined the allyl alcohol **1**, which has a hydroxy-substituted stereogenic center at the ζ-position (Scheme 4). Coordination of Pd^{II} may occur on both diastereotopic faces of the alkene to form diastereomeric mixtures of Pd π-complexes. In fact, treatment of **1** with 10 mol% of [$PdCl_2(CH_3CN)_2$] in THF at 0°C gave a 1:1 mixture of *cis*- and *trans*-6-methyl-2-vinyltetrahydropyrans, *cis*-**2** and *trans*-**2**[7] in 85% yield. However, when a *tert*-butyldiphenylsilyloxy (TBDPSO) group was present at the γ-position, the reaction



Scheme 4. Pd^{II}-catalyzed cyclizations of chiral ζ-hydroxy-α,β-unsaturated alcohols. TBDPS = *tert*-butyldiphenylsilyl

of compound **3** under the same conditions took 1.5 h at room temperature to give 2,3-*trans*-**4**[8] in 92% yield as a single stereoisomer, the structure of which was confirmed by NMR spectroscopy. The putative intermediate π-complex shown in parentheses in Scheme 4 would form by coordination of Pd to the alkene *anti* to the TBDPSO group, for steric reasons.

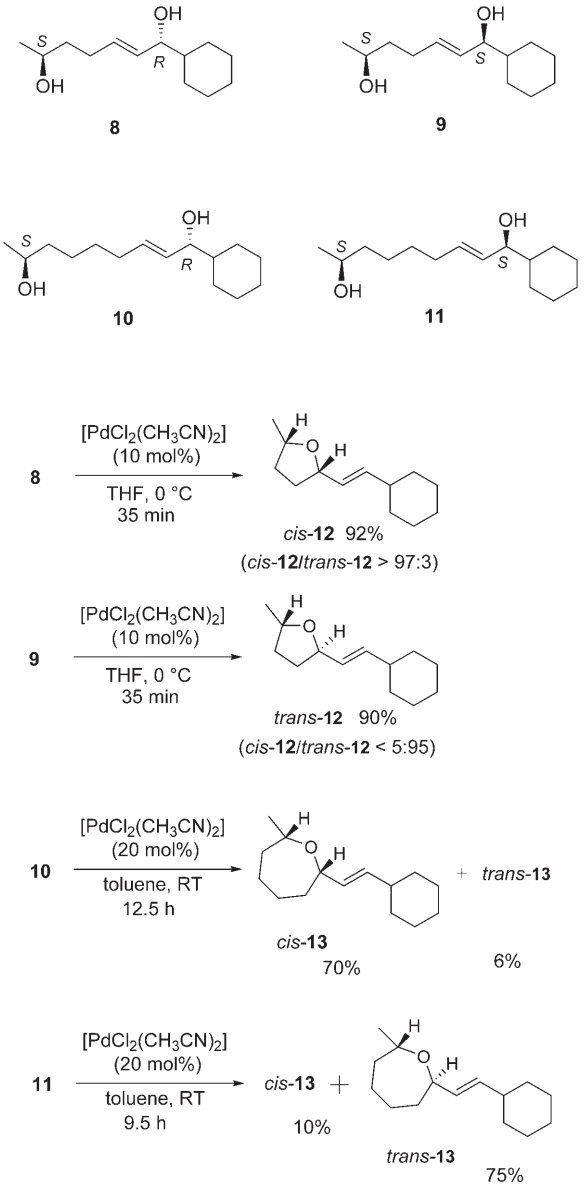
If an additional stereogenic and hydroxy-substituted center exists at the other allylic position, as in substrates **5** and **6** (Scheme 5), the direction of formation of the Pd π-



Scheme 5. Pd^{II}-catalyzed cyclizations of chiral ζ-hydroxy-α,β-unsaturated alcohols.

complex becomes more interesting. In the case of **5**, with the secondary *R* alcohol and (*S*)-OTBDPS groups in an *anti* relationship, both functions should cooperatively effect the diastereoselective formation of the Pd π-complex shown in parentheses in the upper part of Scheme 5. In fact, the reaction of **5** with [$PdCl_2(CH_3CN)_2$] (10 mol%) in THF at 0°C afforded exclusively *trans*-**7** in 93% yield. On the other hand, for substrate **6**, the coordinative effect of the *S* alcohol and the simple steric effect of the (*S*)-OTBDPS group should be incompatible for the formation of the Pd π-complex. In fact, the reaction of **6** took 10 h at room temperature. However, only *cis*-**7** was obtained in 96% yield, strongly suggesting that the secondary allylic hydroxy group plays a more important role in the stereoselective formation of the Pd π-complex,[9] overriding the steric effect of the γ-substituent.

The coordination of the chiral hydroxy-substituted center is critical for the diastereoselective formation of the Pd π-complex, which eventually mediates the 1,3-chirality transfer for the formation of tetrahydropyran rings. If this mechanism can be applied generally, there would be a potential for the formation of other oxaheterocyclic rings. Therefore, we have prepared the ε- and η-hydroxy-α,β-unsaturated alcohols **8–11** and examined the stereochemical outcome of the intramolecular cyclization, in which tetrahydrofurans or oxepanes would be produced (Scheme 6).



Scheme 6. Pd-catalyzed cyclization of chiral ε- and η-hydroxy-α,β-unsaturated alcohols.

When the (1*R*,6*S*)-cyclohexylhept-2-ene-1,6-diol (**8**) was subjected to the cyclization in THF in the presence of [$PdCl_2(CH_3CN)_2$] (10 mol%) at 0°C, the reaction completed in 35 min to give a tetrahydrofuran *cis*-**12** in 92% yield with high selectivity (>97:3 ratio). On the other hand, the reaction of (1*S*,6*S*)-**9** gave the other diastereomer *trans*-**12** in 90% yield with similar selectivity (<5:95 ratio). Their relative configurations were determined by ^{1}H NMR spectroscopy and NOE experiments.

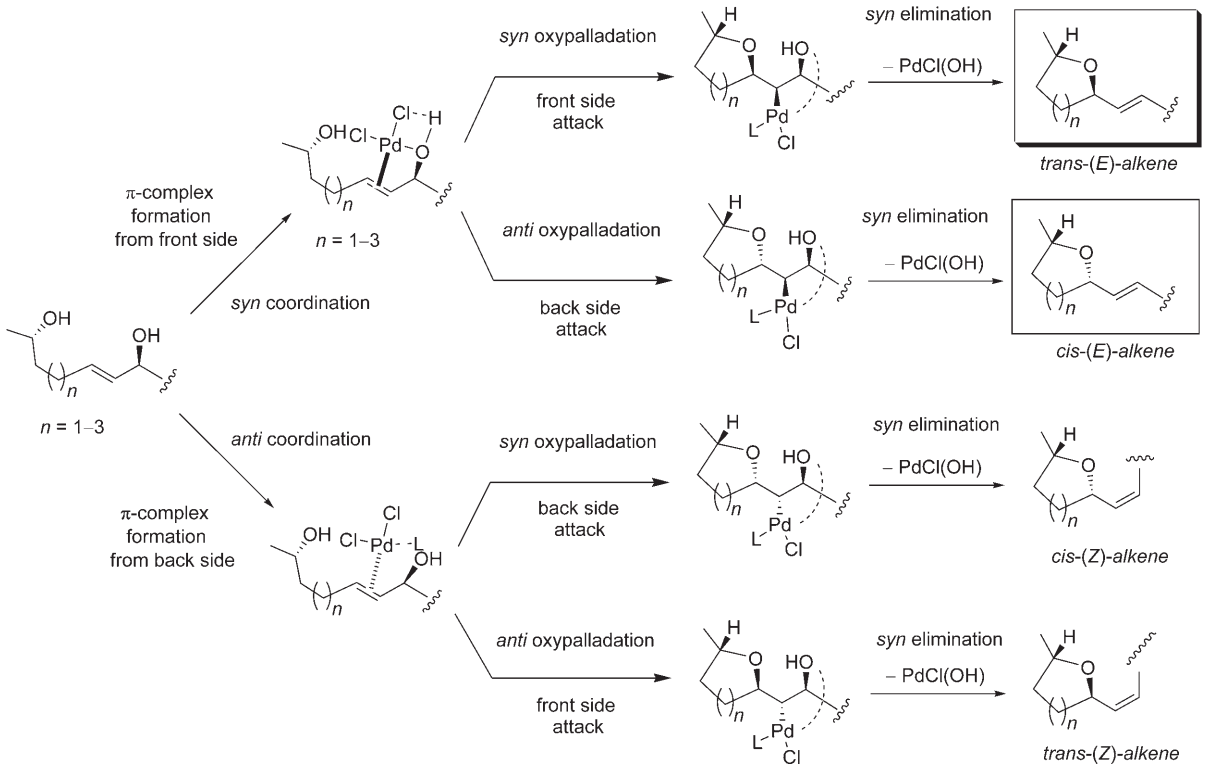
In contrast to the results in the formations of five- and six-membered rings, the reaction of η-hydroxy-α,β-unsatu-

rated alcohols **10** and **11** proceeded slower under the above-mentioned reaction conditions, which gave the desired cyclized product in less than 50% yield after 36 h at room temperature. When the solvent was replaced with toluene and 20 mol% of catalyst was used, the reaction of **10** was completed in 12.5 h at room temperature, and gave *cis*-**13** in 70% yield along with the *trans*-**13** isomer in 6% yield. The formation of the diastereoisomer was unexpected, but similarly the reaction of **11** under the same conditions also gave a mixture of *trans*- and *cis*-**13** in 75% and 10% yields, respectively. These relative configurations were determined by NOE experiments. These results indicate that the cyclizations are highly selective for the formation of five-membered and six-membered rings, but a little less selective for seven-membered-ring formation.

Although the minor isomers were isolated only in the case of the oxepane, we need to discuss the mechanism for the formation of these minor products. The possible reaction pathways in the case of one starting diastereomeric diol is shown in Scheme 7.

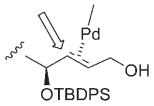
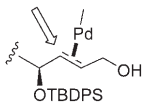
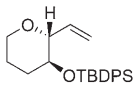
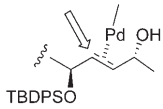
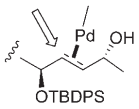
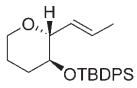
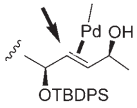
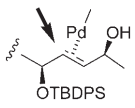
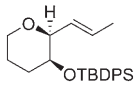
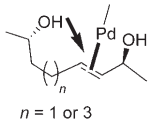
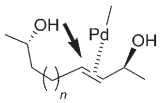
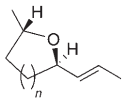
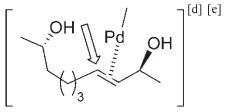
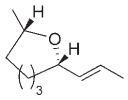
According to our previous results and in line with the initial arguments, the Pd^{II} catalyst coordinates *syn* selectively on the alkene with respect to the chiral allylic alcohol. Furthermore, as shown in the lower half of Scheme 7, if the Pd^{II} catalyst coordinates in an *anti* fashion, and either *syn* or *anti* oxypalladation is followed by *syn* elimination of PdCl(OH), *Z* alkenes would be formed. Since no such products could be detected in the reactions, the *syn* coordination in the first step must be predominant. In the second step, both *syn* and *anti* oxypalladations are possible to give the *all-syn* intermediate (relations of OH, σ-Pd, and ether ring bonds) and/or the *syn–anti* intermediate (*syn* relation between σ-Pd and OH bonds and *anti* relation between σ-Pd and ring bonds). The former isomer would afford a major *trans* oxacyclic product with an *E* alkene, and the latter would give a minor *cis* oxacyclic product with an *E* alkene. This *syn* oxypalladation is compatible with recent mechanistic studies.[4]

Although the above-mentioned mechanism involving the "*syn* coordination, *syn* oxypalladation, and *syn* elimination" pathway is rational, one may remark on the possibility of the "*anti* coordination, *anti* oxypalladation, and *anti* elimination" pathway, which would provide the same product. The key intermediates for both possibilities are depicted in Table 1. The Pd π-complex intermediate for *syn* oxypalladation and *syn* elimination is shown in the left column and that for *anti* oxypalladation and *anti* elimination in the middle column. The directions of the nucleophilic attack of the oxygen atom are indicated with bold arrow from the front side and with empty arrow from the back side. A comparison of these intermediates shows that the pathway of *anti* oxypalladation and *anti* elimination can be ignored for the following reasons: 1) If an *anti* oxypalladation takes place, the resulting σ-Pd complex bears a *syn* hydrogen atom to the σ-Pd bond, which would facilitate β-hydride elimination and lead to the enol ether. The intermediates shown in the middle column in Table 1, entries 2–4 would give a σ-Pd complex with two *syn* hydrogen atoms to give the enol ether or the methyl ketone by β-hydride elimina-



Scheme 7. Stereochemistry and reaction mechanism of 1,3-chirality transfer in intramolecular oxypalladation.

Table 1. Pd π-complexes leading to the cyclized products in *syn* and *anti* oxypalladations.

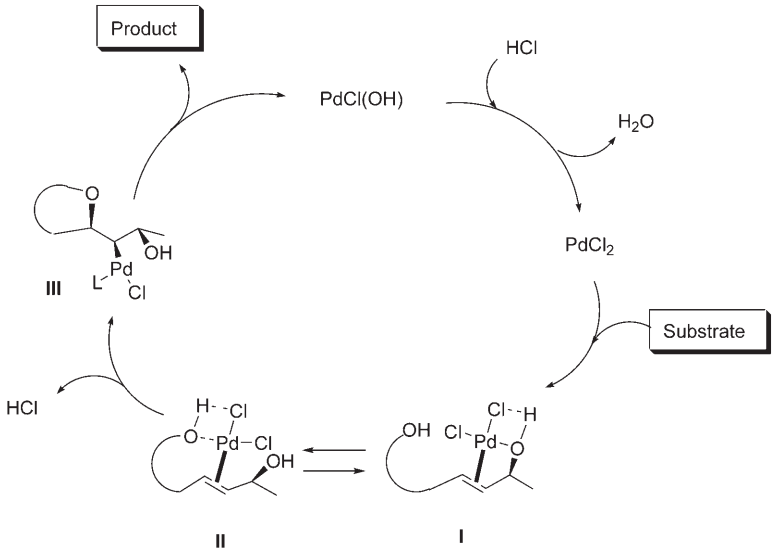
Entry	Starting material	Intermediate *syn* Oxypalladation[a]	Intermediate *anti* Oxypalladation[b]	Product	
1	**3**				*trans*-**4**
2	**5**				*trans*-**7**
3	**6**				*cis*-**7**
4	**9** ($n=1$) or **11** ($n=3$)	 n = 1 or 3			*trans*-**12** ($n=1$) or *trans*-**13**[c] ($n=3$)
			 [d] [e]		*cis*-**13**[f]

[a] Subsequent *syn* elimination leads to the product. [b] Subsequent *anti* elimination leads to the product. [c] Major product from **11**. [d] $n=3$: The reaction pathway to *cis*-**13** in the reaction of **11**. [e] *syn* Oxypalladation followed by *anti* elimination lead to the minor product *cis*-**13**. [f] Minor product from **11**.

tion. However, no such product was obtained in these reactions. 2) If *trans*-**4** is obtained by *anti* oxypalladation and *anti* elimination, the Pd^{II} catalyst must coordinate unusually on the alkene from the same side as the large OTBDPS group in Table 1, entry 1. On the other hand, for the *anti* oxypalladation and *anti* elimination pathway in Table 1, entries 2–4, the Pd^{II} species has to approach the alkenyl face from the opposite side of the hydroxy group against a hydroxy-directed coordination.[9] 3) If we consider the mechanism of minor isomer *cis*-**13** by the *anti* elimination pathway in Table 1, entry 4, *syn* oxypalladation must occur. In this case, the Pd^{II} species should coordinate unfavorably on the opposite side to the hydroxy group, and the OH nucleophile would come from the same side of the Pd π-complex.

We therefore conclude that if the initial coordination of Pd^{II} occurs by the hydroxy-directed arrangement and the *syn* oxypalladation is followed in the second step, then the third *syn* elimination is inevitable.[10]

We propose the mechanism of the catalytic cycle and the stereochemistry for the formation of the major isomer in Scheme 8. The reaction occurs through the hydroxy-group-induced facioselective formation of the π-complex **I**, hydroxy ligand exchange leading to another π-complex **II** in equilibrium, an intramoleular *syn* oxypalladation leading to *all-syn* intermediate **III**, and *syn* elimination as the final step. *syn* Oxypalladation favorably occurs via the hydroxy-coordinated σ-Pd intermediate **II** and is a major pathway for the diastereoselective cyclization. However, how can we explain the formation of the minor

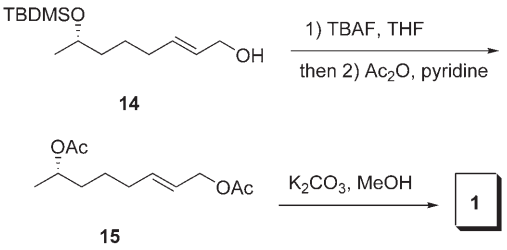


Scheme 8. Catalytic cycle of Pd^{II} in the oxypalladation reaction.

isomer in the case of the seven-membered ring? When the intermediate **II** is less stable than in the case of the five- and six-membered rings in equilibrium with **I**, due to a larger size of its cyclic conformation, a backside attack (*anti* to Pd π-complex) of the hydroxy nucleophile to **I** may occur to some extent partially in the formation of the seven-membered ring. Following this mechanism, a small amount of *anti* oxypalladation can be observed in the formation of oxepane, but not in the case of five- and six-membered rings.

Preparation of Precursors for Pd^{II}-Catalyzed Cyclization

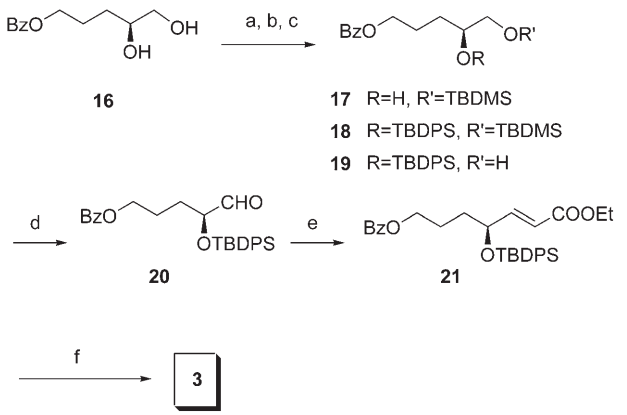
The compound **1** was prepared in three steps from (*S*)-silyloxy-2-heptene-1-ol (**14**)[11] as shown in Scheme 9. Although



Scheme 9. Preparation of **1**.

desilylation with TBAF in THF gave **1**, its purification was rather difficult. Therefore, the crude product was first converted into diacetate **15**. After purification of **15**, methanolysis of the acetates afforded pure **1** in 75% yield from **14**.

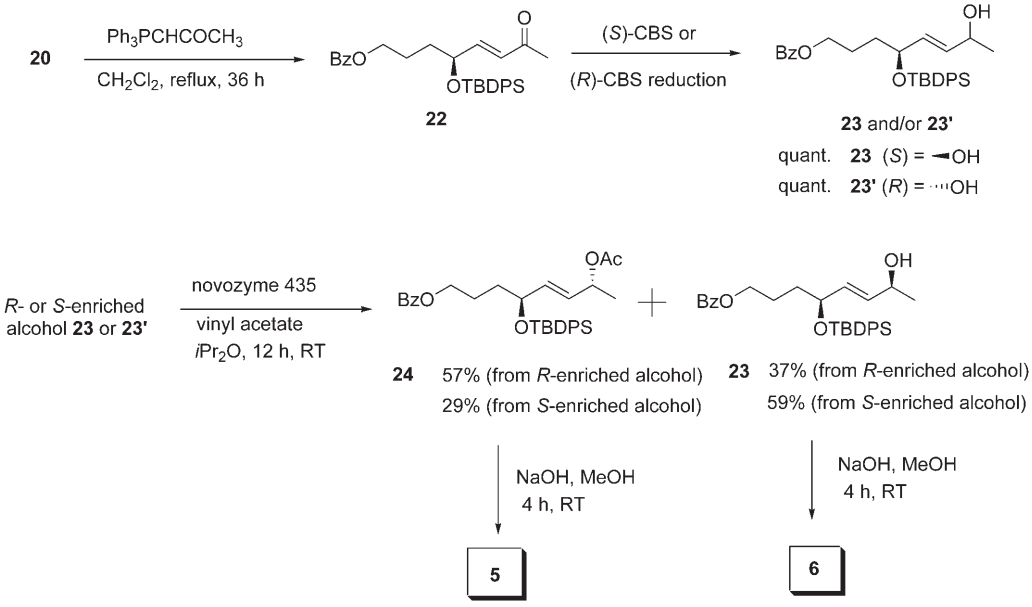
The compound **3** was obtained in six steps from 5-benzoyloxy-1,2-pentanediol (**16**)[12] as shown in Scheme 10. Monoprotection of the primary alcohol function of **16** with TBDMSCl followed by the (second) protection of the secondary alcohol with TBDPSCl gave **18** in 77% yield in two



Scheme 10. Preparation of **3**. Reagents and conditions: a) TBDMSCl, Et_3N, DMAP, CH_2Cl_2, 0 °C, 6 h; b) TBDPSCl, imidazole, DMAP, DMF, 60 °C, 36 h; c) $BF_3{\cdot}OEt_2$, CH_2Cl_2, −5 °C, 17 h; d) Swern oxidation: $(COCl)_2$, DMSO, CH_2Cl_2, −78 °C, then Et_3N; e) NaH, $(EtO)_2POCH_2COOEt$, THF, room temperature, 18 h; f) Red-Al, THF, room temperature, 1 h. Bz = benzoyl; Red-Al = sodium bis(2-methoxyethoxy)aluminum hydride.

steps. Selective deprotection of the TBDMS ether[13] by treatment with $BF_3{\cdot}OEt_2$ afforded **19** in 92% yield. Swern oxidation and subsequent Horner–Wadsworth–Emmons reaction with triethyl phosphonoacetate gave **21** in 88% yield in two steps. Treatment of **21** with excess Red-Al allowed both reduction of the ester and deprotection of the benzoate to give **3** in 90% yield.

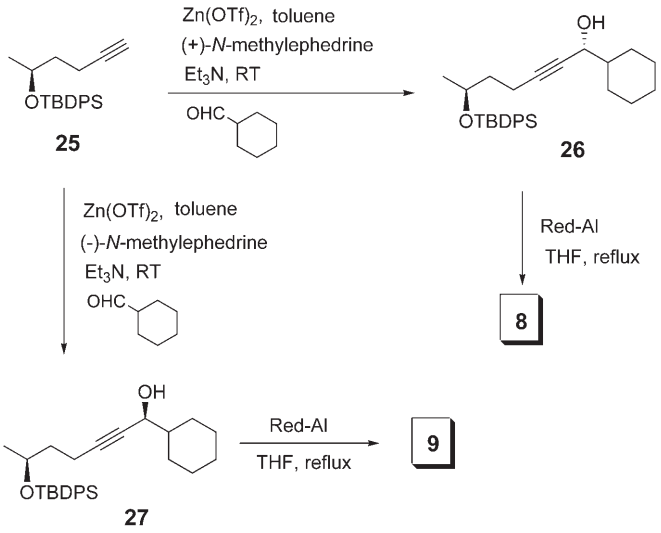
The diols **5** and **6** were synthesized from **20** in four steps (Scheme 11). Wittig reaction of aldehyde **20** with triphenylphosphanylideneacetone in dichloromethane gave **22** in 95% yield. Asymmetric reductions with CBS reagent[14] did not work sufficiently well. The reduction of **22** catalyzed by (*S*)-CBS with BH_3 gave a mixture of **23** and **23'** in excellent yield, but in a 1:1.84 ratio. As this ratio was not satisfactory,



Scheme 11. Preparation of precursors **5** and **6**.

the mixture was subjected to a lipase-catalyzed kinetic acetylation with vinyl acetate and a lipase (novozyme 435)[15] to give acetate (*R*)-**24** in 57% yield and alcohol (*S*)-**23** in 37% yield. On the other hand, the reduction catalyzed by (*R*)-CBS gave an *S*-enriched mixture in a 1.85:1 ratio. Acetylation of the mixture by lipase and vinyl acetate afforded acetate (*R*)-**24** in 29% yield and alcohol (*S*)-**23** in 59% yield. Compounds **5** and **6** were obtained by the hydrolysis of **24** and **23** in 89 and 90% yields, respectively.

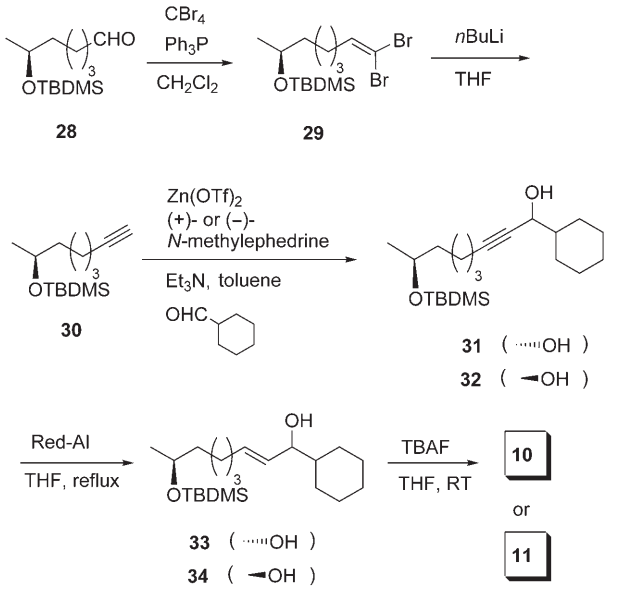
The preparation of **8** and **9** is shown in Scheme 12. A similar approach was followed for the synthesis of the six-membered tetrahydropyrans in which Carreira's asymmetric alkynylation[16] was employed for the introduction of the



Scheme 12. Preparation of precursors **8** and **9**.

chiral secondary alcohol. Alkynylation of cyclohexanecarboxaldehyde with **25**[17] in the presence of (+)-*N*-methylephedrine and $Zn(OTf)_2$ gave chiral propargyl alcohol **26** in 96% yield. The diastereoselectivity was determined to be greater than 99:1 d.r. by chiral HPLC. Partial reduction of the propargyl alcohol and deprotection of the TBDPS group proceeded smoothly in the presence of Red-Al in refluxing THF to give the desired diol **8** in 98% yield. The diastereomer **9** was obtained in two steps through **27**, similarly by replacing the (+)-*N*-methylephedrine to (−)-*N*-methylephedrine in 97 and 70% yields, respectively.

For the synthesis of compounds **10** and **11** (Scheme 13), terminal alkynes **30** is required as the starting material. It was prepared in 73% yield from the known aldehyde **28**[18] by a standard two-step transformation: 1) dibromoalkenylation of **28** with CBr_4 and triphenylphosphine, and then 2) treatment with BuLi (2 equiv). Carreira's asymmetric alkylation of cyclohexanecarboxaldehyde with **30** by the use of (+)-*N*-methylephedrine gave **31** in 95% yield. The diastereomeric ratio was found to be >98:2 determined by chiral HPLC. On the other hand, that with the use of (−)-*N*-methylephedrine gave **32** in 92% yield with 97:3 d.r. Reduction



Scheme 13. Preparation of precursors **10** and **11**.

of **31** with Red-Al followed by desilylation with TBAF afforded **10** in 77% yield over two steps. The same reactions from **32** gave **11** in 69% yield over two steps.

Conclusions

Intramolecular Pd^{II}-catalyzed cyclizations of ζ-hydroxy-α,β-unsaturated alcohols bearing a neighboring substituent, as well as ε- and η-hydroxy-α,β-unsaturated alcohols provided oxacyclic compounds stereospecifically. The chirality of the carbon atom of the allylic alcohol function is transferred to the carbon center on the newly generated oxacyclic ring efficiently. On the basis of the stereochemical results, a plausible mechanism for this cyclization is proposed. Chiral-allylic-alcohol-induced *syn*-facioselective formation of the Pd π-complex initiates the cyclization reaction. Subsequent *syn* oxypalladation followed by *syn* elimination of [PdCl(OH)] occurs favorably to give five-, six-, and seven-membered oxacyclic rings with high stereospecificity. However, partial *anti* oxypalladation take place in the cyclization of η-hydroxy-α,β-unsaturated alcohols to form a minor isomer in 6–10%. This result suggests the possibility of *anti* oxypalladation, even in intramolecular cyclization reactions, if the substrate is designed properly.

Experimental Section

General

Column chromatography was performed on E. Merck silica gel (230–400 mesh). The plate used for TLC is E. Merck precoated silica gel 60 F_{254} (0.25-mm thick). Optical rotations were measured on a JASCO DIP-360 polarimeter. Infrared (IR) spectra were recorded on a JASCO FT/IR-410 spectrometer. NMR spectra were recorded with a JEOL-AL300 (300 MHz for ^1H NMR and 75 MHz for ^{13}C NMR) and a Varian XL-400

(400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR). NMR samples were dissolved in $CDCl_3$, and chemical shifts are reported relative to TMS as internal standard or solvent ($CDCl_3$, 7.26 ppm). Low-resolution and high-resolution mass spectra (Exact FAB-MS) were obtained with a JEOL JMS-SX 102 A instrument. Non-aqueous reactions were carried out in flame-dried glassware under an Ar atmosphere. THF, benzene, and diethyl ether were dried over sodium benzophenone ketyl. CH_2Cl_2 was dried over P_4O_{10}, and toluene was dried over CaH_2. These solvents were distilled freshly before use. (*S*)- and (*R*)-CBS reagents containing (*S*)- and (*R*)-3,3-diphenyl-1-methyltetrahydro-3*H*-pyrrole[1,2-*c*][1,3,2]oxazaborole in 1 M toluene solution were purchased from Aldrich. Novozyme 435 (*Candida antarctica* lipase) was purchased from Novo Nordisk Bioindustry.

Typical Procedure for Pd^{II}-Catalyzed Cyclization

A mixture of diol (0.1 mmol) and $[PdCl_2(CH_3CN)_2]$ (21.6 mg, 0.02 mmol) was stirred in THF (2 mL) at 0 °C. After the reaction was completed, the mixture was diluted with pentane (20–40 mL) and filtered through a celite pad. The filtrate was concentrated and the residue was purified by column chromatography on silica gel to give the corresponding oxacyclic compound. The chemical yield, reaction time, reaction temperature if not at 0 °C, and solvent for column chromatography are indicated in the beginning of the physical and spectroscopic data for the individual compounds.

2:[7] 85 %; reaction time: 20 min; solvent for chromatography: 5 % Et_2O in pentane. Colorless oil as a 1:1 mixture of inseparable *cis* and *trans* isomers; R_f = 0.48 (10 % EtOAc in hexane); ^{1}H NMR (300 MHz): δ = 6.0–5.81 (m, 1H), 5.23 (dm, J = 17.0 Hz, 1/2H), 5.20 (dm, J = 17.6 Hz, 1/2H), 5.18 (dm, J = 10.6 Hz, 1/2H), 5.08 (dm, J = 10.4 Hz, 1/2H), 4.39–4.32 (m, 1/2H), 4.01–3.79 (m 1H), 3.53–3.43 (m, 1/2H), 1.87–1.23 (m, 6H), 1.21 (d, J = 6.4 Hz, 3/2H), 1.16 ppm (d, J = 6.4 Hz, 3/2H); ^{13}C NMR (75 MHz): δ = 139.6 (c), 138.9 (t), 115.6 (t), 114.6 (c), 78.4 (c), 73.7 (c), 72.2 (t), 67.1 (t), 33.0 (c), 32.3 (t), 31.1 (c), 28.9 (t), 23.5 (c), 22.2 (c), 20.6 (t), 18.6 ppm (t).

trans-**4**: 92 %; reaction time: 1.5 h; room temperature; solvent for chromatography: 5 % EtOAc in hexane. Colorless oil; R_f = 0.34 (10 % EtOAc in hexane); $[\alpha]_D^{23}$ = +18.8 (c = 1.2 in $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3071, 2933, 1507, 1428, 1361, 923, 823, 740 cm^{-1}; ^{1}H NMR (300 MHz): δ = 7.69–7.66 (m, 4H), 7.45–7.33 (m, 6H), 5.92 (ddd, J = 17.3, 10.5, 5.8 Hz, 1H), 5.33 (ddd, J = 17.3, 2.0, 1.8 Hz, 1H), 5.17 (ddd, J = 10.5, 2.0, 1.8 Hz, 1H), 3.85 (m, 1H), 3.64 (m, 1H), 3.49–3.31 (m, 2H), 1.79 (m, 1H), 1.54–1.38 (m, 3H), 1.03 ppm (s, 9H); ^{13}C NMR (75 MHz): δ = 136.9, 136.0, 135.9, 134.7, 133.6, 129.6, 129.5, 127.5, 127.3, 117.0, 83.1, 72.2, 67.3, 33.3, 26.9, 25.2, 19.3 ppm; HRMS (CI+): m/z calcd for $C_{23}H_{31}O_2Si$: 367.2093 $[M+H]^+$; found: 367.2102.

trans-**7**: 93 %; reaction time: 4 h; solvent for chromatography: 5 % EtOAc in hexane. Colorless oil; R_f = 0.43 (20 % EtOAc in hexane); $[\alpha]_D^{22}$ = −13.2 (c = 0.93 in $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2932, 2863, 1430, 1109 cm^{-1}; ^{1}H NMR (300 MHz): δ = 7.68–7.64 (m, 4H), 7.45–7.33 (m, 6H), 5.73 (dqd, J = 15.1, 6.8, 0.9 Hz, 1H), 5.44 (ddq, J = 15.3, 7.3, 1.6 Hz, 1H), 3.84–3.79 (m, 1H), 3.56 (t, J = 8.2 Hz, 1H), 3.45–3.29 (m, 2H), 1.84 (m, 1H), 1.64 (dd, J = 6.4, 1.6 Hz, 3H), 1.53–1.38 (m, 3H), 1.02 ppm (s, 9H); ^{13}C NMR (75 MHz): δ = 136.0, 135.9, 134.7, 133.7, 130.3, 129.9, 129.5, 129.4, 127.4, 127.3, 83.5, 71.9, 67.3, 33.3, 26.9, 25.4, 19.2, 17.9 ppm; HRMS (CI+): m/z calcd for $C_{24}H_{33}O_2Si$: 381.2250 $[M+H]^+$; found: 381.2244.

cis-**7**: 96 %; reaction time: 10 h; room temperature; solvent for chromatography: 5 % EtOAc in hexane. Colorless oil; R_f = 0.43 (20 % EtOAc in hexane); $[\alpha]_D^{23}$ = −19.9 (c = 0.81 in $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2932, 1428, 1027, 959, 823, 701 cm^{-1}; ^{1}H NMR (300 MHz): δ = 7.70–7.66 (m, 4H), 7.45–7.33 (m, 6H), 5.70 (dqd, J = 13.8, 6.8, 0.9 Hz, 1H), 5.29 (m, 1H), 3.98 (t, J = 8.8 Hz, 1H), 3.81 (dm, J = 1.8 Hz, 1H), 3.50–3.32 (m, 2H), 1.84–1.76 (ddm, J = 6.9, 1.8 Hz, 4H), 1.55–1.38 (m, 3H), 1.02 ppm (s, 9H); ^{13}C NMR (75 MHz): δ = 136.0, 135.9, 134.8, 133.6, 129.69, 129.60 (2C), 129.4, 127.4, 127.3, 77.5, 72.0, 67.2, 33.3, 26.9, 25.3, 19.2, 13.9 ppm; HRMS (CI+): m/z calcd for $C_{24}H_{33}O_2Si$: 381.2250 $[M+H]^+$; found: 381.2255.

cis-**12**: 92 %; reaction time: 35 min; solvent for chromatography: 3 % Et_2O in hexane. Colorless oil; R_f = 0.33 (3 % EtOAc in hexane); $[\alpha]_D^{21}$ = −1.28 (c = 1.32 in $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2924, 1448, 1375, 1080, 967, 913, 732 cm^{-1}; ^{1}H NMR (300 MHz): δ = 5.59 (dd, J = 15.4, 6.4 Hz, 1H), 5.43 (ddd, J = 15.4, 6.6, 1.1 Hz, 1H), 4.18 (q, J = 7.1 Hz, 1H), 3.95 (tq, J = 6.2, 6.0 Hz, 1H), 2.04 −1.92 (m 3H), 1.72–1.57 (m, 6H), 1.54–1.43 (m, 1H) 1.31–1.00 (m, 5H), 1.25 ppm (d, J = 6.0 Hz, 3H); ^{13}C NMR (75 MHz): δ = 138.7, 128.5, 80.6, 75.3, 40.2, 33.0, 32.7, 32.6, 32.3, 26.1, 26.03 (2C), 21.4 ppm; HRMS (EI+): m/z calcd for $C_{13}H_{22}O$: 194.1671 $[M]^+$; found: 194.1673.

trans-**12**: 90 %; reaction time: 35 min; solvent for chromatography: 3 % Et_2O in hexane. Colorless oil; R_f = 0.33 (3 % EtOAc in hexane); $[\alpha]_D^{21}$ = +12.9 (c = 1.12 in $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2924, 2852, 1448, 1078, 966 cm^{-1}; ^{1}H NMR (300 MHz): δ = 5.57 (dd, J = 15.4, 6.4 Hz, 1H), 5.41 (ddd, J = 15.4, 6.2, 1.1 Hz, 1H), 4.35 (q, J = 7.3 Hz, 1H), 4.12 (tq, J = 6.2, 6.0 Hz, 1H), 2.11–2.02 (m, 2H), 1.97–1.88 (m, 1H), 1.71–1.59 (m, 7H), 1.54–1.41 (m, 1H), 1.32–1.00 (m, 4H), 1.22 ppm (d, J = 6.0 Hz, 3H); ^{13}C NMR (62.5 MHz): δ = 138.3, 128.4, 79.7, 74.9, 40.2, 34.2, 33.3, 32.7, 32.6, 26.1, 26.04 (2C), 21.4 ppm; HRMS (EI+): m/z calcd for $C_{13}H_{22}O$: 194.1671 $[M]^+$; found: 194.1674.

cis- and *trans*-**13**: The reactions were conducted in toluene at room temperature. The reaction from **10** gave *cis*-**13** in 70 % yield and *trans*-**13** in 6 % yield. Reaction time: 12.5 h; solvent for chromatography: 1 % diethyl ether in hexane for *cis*-**13** and 3 % diethyl ether in hexane for *trans*-**13**. The reaction from **11** gave *cis*-**13** in 10 % yield and *trans*-**13** in 75 % yield. Reaction time: 9.5 h. *cis*-**13**: Yellow oil; R_f = 0.41 (3 % EtOAc in hexane); $[\alpha]_D^{22}$ = −14.6 (c = 0.96 in $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2924, 2851, 1448, 1371, 1139, 1101, 968 cm^{-1}; ^{1}H NMR (300 MHz): δ = 5.51 (dd, J = 15.6, 6.0 Hz, 1H), 5.45 (ddd, J = 15.6, 5.5, 0.91 Hz, 1H), 3.93 (m, 1H), 3.71 (m, 1H), 1.91(m, 1H), 1.81–1.49 (m, 13H), 1.30–1.22 (m, 2H), 1.18 (d, J = 6.2 Hz, 3H), 1.14–0.99 ppm (m, 3H); ^{13}C NMR (75 MHz): δ = 135.7, 129.7, 79.6, 75.3, 40.2, 38.0, 36.7, 32.8 (2C), 26.2, 26.1(2C), 25.3, 24.8, 23.1 ppm; HRMS (EI+): m/z calcd for $C_{15}H_{26}O$: 222.1984 $[M]^+$; found: 222.1976. *trans*-**13**: Yellow oil; R_f = 0.34 (3 % EtOAc in hexane); $[\alpha]_D^{22}$ = −7.9 (c = 0.62 in $CHCl_3$); IR (neat): $\tilde{\nu}$ = 2923, 2851, 1448, 1374, 1104, 966 cm^{-1}; ^{1}H NMR (300 MHz): δ = 5.53 (ddd, J = 15.5, 5.5, 0.9 Hz, 1H), 5.46 (ddd, J = 15.7, 4.9, 0.9 Hz, 1H), 4.09 (m, 1H), 3.79 (m, 1H), 1.92 (m, 1H), 1.87–1.60 (m, 9H), 1.52–1.19 (m, 7H), 1.14 (d, J = 6.2 Hz, 3H), 1.12–0.99 ppm (m, 2H); ^{13}C NMR (68 MHz): δ = 136.0, 129.4, 74.7, 69.9, 40.3, 37.9, 35.8, 32.96, 32.94, 27.7, 26.5, 26.2, 26.0 (2C), 22.6 ppm; HRMS (EI+): m/z calcd for $C_{15}H_{26}O$: 222.1984 $[M]^+$; found: 222.1979.

Synthesis of Precursors for the Oxypalladation Reactions

1: TBAF (2.42 mL, 1 M THF solution) was added to a solution of **14**[11] (104 mg, 0.4 mmol) in THF (2.8 mL), and the mixture was stirred at room temperature for 24 h. The solvent was evaporated in vacuo. The residue was dissolved in CH_2Cl_2 (2.5 mL) and treated with acetic anhydride (0.25 mL, 2.4 mmol) and pyridine (0.5 mL) at 0 °C. The mixture was stirred for 5 h at the same temperature, diluted with water (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and condensed. The residual oil was purified by column chromatography on silica gel to give diacetate **15** (81 mg) in 88 % yield. R_f = 0.48 (20 % EtOAc in hexane); ^{1}H NMR (300 MHz): δ = 5.71 (dt, J = 15.5, 6.4 Hz, 1H), 5.58 (ddt, J = 15.2, 6.4, 1.2 Hz, 1H), 4.88 (m, 1H), 4.49 (dd, J = 6.2, 0.9 Hz, 2H), 2.09–1.98 (m, 8H), 1.64–1.32 (m, 4H), 1.19 ppm (d, J = 6.2 Hz, 3H). The diacetate (81 mg) was dissolved in MeOH (2 mL), and K_2CO_3 (150 mg, 1.06 mmol) was added. After the mixture was stirred for 6 h at room temperature, the reaction mixture was filtered through a celite pad. The celite pad was washed with chloroform (2 × 3 mL). The filtrate and chloroform were combined and condensed. The crude product was purified by column chromatography on silica gel eluted with 3 % MeOH in $CHCl_3$ to give **1** (43 mg) in 85 % yield. Yellow oil; R_f = 0.21 (50 % EtOAc in hexane); $[\alpha]_D^{22}$ = +5.2 (c = 1.06 in $CHCl_3$); IR (neat): $\tilde{\nu}$ = 3347, 2931, 1670, 1459, 1374, 1088, 970 cm^{-1}; ^{1}H NMR (300 MHz): δ = 5.72–5.57 (m, 2H), 4.06 (bd, J = 4.4 Hz, 2H), 3.78 (m, 1H), 2.06 (m, 2H), 1.79 (bs, 2H), 1.53–1.36 (m, 4H), 1.17 ppm (d, J = 6.2 Hz, 3H); ^{13}C NMR (75 MHz): δ = 132.7, 129.2, 67.8, 63.5, 38.6,

32.0, 25.1, 23.4 ppm; HRMS (FAB+): *m/z* calcd for $C_8H_{16}O_2Na$: 167.1048 $[M+Na]^+$; found: 167.1040.

17: TBDMSCl (2.52 g, 16.7 mmol) was added to a mixture of (*S*)-4,5-dihydroxypentyl benzoate **16**[12] (3.42 g, 15.25 mmol), DMAP (186 mg, 1.5 mmol), and NEt_3 (10.6 mL, 76.3 mmol) in CH_2Cl_2 (50 mL) at 0 °C. The mixture was stirred for 6 h at the same temperature, quenched with aqueous $NaHSO_4$ (15 mL, 1 M solution) and extracted with Et_2O (3× 20 mL). The combined organic extracts were washed with saturated $NaHCO_3$ and dried over $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 25% EtOAc in hexane afforded **17** (4.23 g) in 83% yield. Colorless oil; R_f=0.42 (30% EtOAc in hexane); $[\alpha]_D^{24}$=+0.18 (*c*=1.08 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3501, 2929, 2857, 1720, 1452, 1275, 1113, 837, 711 cm^{-1}; ^1H NMR (300 MHz): δ=8.03 (dd, *J*=6.9, 1.2 Hz, 2H), 7.54 (tt, *J*=7.3, 1.2 Hz, 1H), 7.42 (td, *J*=7.3, 1.4 Hz, 2H), 4.36 (td, *J*=6.4, 1.2 Hz, 2H), 3.70 (m, 1H), 3.64 (dd, *J*=9.7, 3.3 Hz, 1H), 3.44 (dd, *J*=9.7, 7.1 Hz, 1H), 2.48 (d, *J*=3.4 Hz, 1H), 2.05–1.77 (m, 2H), 1.58 (q, *J*=6.6 Hz, 2H), 0.90 (s, 9H), 0.07 ppm (s, 6H); ^{13}C NMR (75 MHz): δ=166.5, 132.8, 130.3, 129.5, 128.2, 71.3, 67.1, 64.9, 29.2, 25.8, 25.0, 18.2, −5.38, −5.43 ppm; HRMS (FAB+): *m/z* calcd for $C_{18}H_{31}O_4Si$: 339.1991 $[M+H]^+$; found: 339.2000.

18: TBDPSCl (4.16 mL, 16.2 mmol) was added to a stirred solution of **17** (4.23 g, 12.5 mmol), DMAP (917 mg, 7.5 mmol), imidazole (4.25 g, 62.5 mmol) in DMF (72 mL) at room temperature. The reaction mixture was stirred at 60 °C for 36 h, then quenched with water (50 mL), and extracted with Et_2O (3×30 mL). 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 on silica gel eluted with hexane afforded **18** (6.7 g) in 93% yield. Colorless oil; R_f= 0.39 (10% EtOAc in hexane); $[\alpha]_D^{23}$=−2.32 (*c*=1.16 in $CHCl_3$); IR (neat): $\tilde{\nu}$=2955, 2857, 1721, 1274, 1110, 835, 708 cm^{-1}; ^1H NMR (300 MHz): δ=8.03 (dt, *J*=7.7, 0.7 Hz, 2H), 7.70 (dd, *J*=6.9, 0.5 Hz, 4H), 7.56 (td, *J*=7.6, 0.5 Hz, 1H), 7.46–7.34 (m, 8H), 4.25 (td, *J*=6.0, 1.8 Hz, 2H), 3.83 (m, 1H), 3.50 (dd, *J*=9.9, 4.9 Hz, 2H), 1.91–1.59 (m, 4H), 1.09 (s, 9H), 0.82 (s, 9H), −0.05 (s, 3H), −0.10 ppm (s, 3H); ^{13}C NMR (75 MHz): δ=166.5, 135.8 (2C), 134.3, 134.1, 132.7, 130.4, 129.6, 129.54, 129.52, 128.2, 127.5, 127.4, 72.9, 65.8, 65.2, 30.2, 27.0, 25.8, 23.7, 19.3, 18.1, −5.53, −5.55 ppm; HRMS (FAB+): *m/z* calcd for $C_{34}H_{48}O_4Si_2Na$: 599.2989 $[M+Na]^+$; found: 599.2980.

19: $BF_3{\cdot}Et_2O$ (1.3 mL, 10.36 mmol) was added to a solution of **18** (1.2 g, 2.08 mmol) in CH_2Cl_2 (20 mL) at −20 °C, and the reaction mixture was stirred at −5 °C for 17 h. The reaction mixture was then quenched with saturated $NaHCO_3$ (20 mL) and extracted with EtOAc (80 mL). The organic extract was washed with brine and dried over $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 30% Et_2O in hexane afforded **19** (886 mg) in 92% yield. Colorless oil; R_f=0.25 (20% EtOAc in hexane); $[\alpha]_D^{22}$=+28.4 (*c*=1.16 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3486, 2931, 1719, 1275, 1110, 822, 705 cm^{-1}; ^1H NMR (300 MHz): δ=7.99–7.95 (m, 2H), 7.68 (td, *J*=7.8, 1.4 Hz, 4H), 7.55 (tt, *J*=7.3, 1.4 Hz, 1H), 7.44–7.33 (m, 8H), 4.15, (m, 2H), 3.85 (m, 1H), 3.56 (m, 2H), 1.78 (t, *J*=6.2 Hz, 1H), 1.71–1.65 (m, 4H), 1.08 ppm (s, 9H); ^{13}C NMR (75 MHz): δ=166.4, 135.7, 135.6, 133.7, 133.5, 132.7, 130.2, 129.8 (2C), 129.4, 128.2, 127.7, 127.6, 73.4, 65.7, 64.7, 30.1, 27.0, 24.3, 19.3 ppm; HRMS (FAB+): *m/z* calcd for $C_{28}H_{35}O_4Si$: 463.2304 $[M+H]^+$; found: 463.2297.

20: A solution of DMSO (0.22 mL, 3.09 mmol) in CH_2Cl_2 (4 mL) was added dropwise to a solution of $(COCl)_2$ (0.177 mL, 1.54 mmol) in CH_2Cl_2 (4 mL) at −78 °C. The mixture was stirred for an additional 10 min at the same temperature. Then, a solution of **19** (478 mg, 1.03 mmol) in CH_2Cl_2 (7 mL) was added dropwise to the reaction mixture at the same temperature over 15 min. The reaction was continued for an additional 1.5 h at the same temperature. After the addition of NEt_3 (1 mL, 7.23 mmol) to the mixture, the reaction was warmed up to 0 °C and kept at this temperature for 15 min. The reaction mixture was then quenched with saturated NH_4Cl (20 mL) and extracted with EtOAc (60 mL). The organic layer was washed with brine and water and dried over $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 20% EtOAc in hexane afforded **20** (428 mg) in 90% yield. Colorless oil; R_f=0.47 (20% EtOAc in hexane); $[\alpha]_D^{22}$=+5.99 (*c*=1.05 in $CHCl_3$); IR (neat): $\tilde{\nu}$=2958, 1720, 1601, 1428, 1273, 1111, 822, 702 cm^{-1}; ^1H NMR (300 MHz): δ=9.62 (d, *J*=1.2 Hz, 1H), 8.01–7.97 (m, 2H), 7.66–7.61 (m, 4H), 7.56 (tt, *J*= 7.3, 1.2 Hz, 1H), 7.46–7.33 (m, 8H), 4.21 (m, 2H), 4.10 (m, 1H), 1.91–1.71 (m, 4H), 1.12 ppm (s, 9H); ^{13}C NMR (75 MHz): δ=203.4, 166.4, 135.7, 135.6, 132.9, 132.8, 132.7, 130.2, 130.09, 130.07, 129.5, 128.3, 127.8 (2C), 77.4, 64.4, 29.4, 26.9, 23.4, 19.3 ppm; HRMS (EI+): *m/z* calcd for $C_{28}H_{32}O_4Si$: 460.2070 $[M]^+$; found: 460.2063.

21: Triethylphosphonoacetate (495 mg, 2.2 mmol) was added dropwise to a stirred suspension of NaH (48.7 mg, 2 mmol) in THF (5 mL) at 0 °C. The reaction mixture was stirred for 10 min at the same temperature, and then a solution of **20** (780 mg, 1.69 mmol) in THF (4 mL) was added dropwise. The mixture was stirred for 10 min at 0 °C and overnight at room temperature. The mixture was quenched with saturated NH_4Cl (10 mL) and extracted with EtOAc (50 mL). The extract was washed with water and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by chromatography on silica gel eluted with 25% EtOAc in hexane to afford **21** as a yellowish oil (731 mg, 88%); R_f=0.42 (10% EtOAc in hexane); $[\alpha]_D^{23}$=−5.9 (*c*=1.03 in $CHCl_3$); IR (neat): $\tilde{\nu}$= 2958, 1716, 1683, 1428, 1272, 1111, 822, 708 cm^{-1}; ^1H NMR (300 MHz): δ=7.99–7.96 (m, 2H), 7.68–7.53 (m, 5H), 7.45–7.32 (m, 8H), 6.85 (dd, *J*=15.6, 5.1 Hz, 1H), 5.98 (dd, *J*=15.6, 1.2 Hz, 1H), 4.47 (q, *J*=5.1 Hz, 1H), 4.22–4.12 (m, 4H), 1.83–1.58 (m, 4H), 1.29 (t, *J*=7.1 Hz, 3H), 1.10 ppm (s, 9H); ^{13}C NMR (75 MHz): δ=166.4, 166.3, 149.3, 135.78, 135.73, 133.6, 133.2, 132.8, 130.2, 129.87, 129.8, 129.5, 128.2, 127.67, 127.61, 120.8, 71.8, 64.7, 60.3, 33.1, 27.0, 23.2, 19.3, 14.2 ppm; HRMS (CI+): *m/z* calcd for $C_{32}H_{39}O_5Si$: 531.2566 $[M+H]^+$; found: 531.2558.

3: Red-Al (23 μL, 70% solution in toluene) was added dropwise to a solution of **21** (50 mg, 0.094 mmol) in THF (0.4 mL) at room temperature. The reaction was stirred for an additional 1 h, quenched with water (5 mL), and extracted with chloroform (3×5 mL). 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 on silica gel eluted with 1% MeOH in chloroform afforded **3** (32.7 mg) in 90% yield. Colorless oil; R_f=0.24 (40% EtOAc in hexane); $[\alpha]_D^{22}$=−11.8 (*c*=0.94 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3347, 2931, 1472, 1428, 1361, 1110, 822, 741, 702 cm^{-1}; ^1H NMR (300 MHz): δ=7.69–7.64 (m, 4H), 7.46–7.32 (m, 6H), 5.54 (ddt, *J*=15.5, 6.7, 1.2 Hz, 1H), 5.45 (dtd, *J*=15.5, 5.3, 0.7 Hz, 1H), 4.26 (m, 1H), 3.90 (bs, 2H), 3.54 (bs, 2H), 1.67 (bs, 1H), 1.61–1.50 (m, 5H), 1.06 ppm (s, 9H); ^{13}C NMR (75 MHz): δ=136.0, 135.8, 134.3, 134.1, 133.9, 129.68, 129.60, 129.55, 127.54, 127.3, 73.5, 62.9, 62.8, 34.0, 27.7, 27.0, 19.2 ppm; HRMS (FAB+): *m/z* calcd for $C_{23}H_{33}O_3Si$: 385.2199 $[M+H]^+$; found: 385.2206.

22: A mixture of **20** (838 mg, 1.82 mmol) and triphenylphosphoranylidene-2-propanone (1.73 g, 5.45 mmol) in CH_2Cl_2 (18 mL) was heated at reflux for 35 h. The mixture was passed through a short pad of silica gel eluted with 50% EtOAc in hexane. The filtrate was condensed, and the residue was purified by chromatography on silica gel eluted with 25% EtOAc in hexane to give **22** (872 mg) in 95% yield. Yellowish oil; R_f= 0.36 (10% EtOAc in hexane); $[\alpha]_D^{22}$=−7.2 (*c*=1.1 in $CHCl_3$); IR (neat): $\tilde{\nu}$=2958, 1719, 1678, 1428, 1274, 1111, 822, 709 cm^{-1}; ^1H NMR (300 MHz): δ=8.01–7.98 (m, 2H), 7.69–7.61 (m, 4H), 7.55 (td, *J*=7.5, 1.2 Hz, 1H), 7.45–7.32 (m, 8H), 6.62 (dd, *J*=15.9, 5.5 Hz, 1H), 6.11 (dd, *J*=15.9, 0.9 Hz, 1H), 4.48 (q, *J*=7.7 Hz, 1H), 4.24 (td, *J*=6.6, 1.4 Hz, 2H), 2.15 (s, 3H), 1.82–1.67 (m, 4H), 1.15 ppm (s, 9H); ^{13}C NMR (75 MHz): δ=198.1, 166.3, 148.0, 135.7, 135.6, 133.4, 133.2, 132.7, 130.1, 129.86, 129.81, 129.73, 129.4, 128.2, 127.6, 127.5, 72.0, 64.5, 33.3, 27.0, 26.9, 23.4, 19.2 ppm; HRMS (EI+): *m/z* calcd for $C_{31}H_{36}O_4Si$: 500.2383 $[M]^+$; found: 500.2375.

24 and **23**: (*S*)-CBS reagent (59.9 μL, 0.2 mmol) was added to a solution **22** (200 mg, 0.4 mmol) in THF (4 mL) at room temperature. After the mixture was cooled to −10 °C, a solution of $BH_3{\cdot}THF$ complex (114.2 μL, 1.2 mmol in 1 M THF) was added to the mixture, and the reaction mixture was stirred for 30 min at same temperature. The mixture was further stirred at room temperature for 30 min and then quenched with MeOH (0.2 mL). The solvent was removed, and purification of the residue by column chromatography on silica gel eluted with 30% EtOAc in hexane

afforded an oily mixture of **23** and **23′** quantitatively. The ratio was estimated to be 1:1.84 (**23**/**23′**) by ^{1}H NMR spectroscopy. The mixture was subjected to lipase-catalyzed kinetic acetylation. A mixture of **23**, **23′**, vinyl acetate (0.18 mL, 2.0 mmol), 4-Å molecular sieves (80 mg), and novozyme 435 (61 mg, 30% *w*/*w*) was stirred in diisopropyl ether (12 mL) for 12 h at room temperature. The reaction was monitored with TLC until the reaction did not proceed further (50% completion). The solids were filtered off, and the filtrate was condensed. The residue was purified by column chromatography on silica gel eluted with 10% EtOAc in hexane to give acetate (*R*)-**24** (123 mg) in 57% yield and with 25% EtOAc in hexane to give alcohol (*S*)-**23** (74 mg) in 37% yield.

24: Colorless oil; R_f=0.52 (20% EtOAc in hexane); $[\alpha]_D^{22}$=+22.4 (*c*=1.09 in $CHCl_3$); IR (neat): $\tilde{\nu}$=2931, 1721, 1428, 1370, 1272, 1110, 822, 702 cm^{-1}; ^{1}H NMR (300 MHz): δ=8.03–8.0 (m, 2H), 7,69–7.63 (m, 4H), 7.56 (tt, *J*=7.5, 1.2 Hz, 1H), 7.46–7.32 (m, 8H), 5.64 (dd, *J*=15.4, 6.7 Hz, 1H), 5.39 (dd, *J*=15.4, 6.4 Hz, 1H), 5.23 (quint, *J*=6.4 Hz, 1H), 4.23 (m, 3H), 2.0 (s, 3H), 1.80–1.60 (m, 4H), 1.16 (d, *J*=6.4 Hz, 3H), 1.08 ppm (s, 9H); ^{13}C NMR (75 MHz): δ=170.0, 166.4, 135.8, 135.7, 133.99, 133.97, 133.95, 132.7, 130.38, 130.33, 129.6, 129.4 (2C), 128.2, 127.5, 127.3, 73.0, 70.2, 64.8, 34.0, 26.9, 23.8, 21.2, 20.0, 19.2 ppm; HRMS (FAB+): *m*/*z* calcd for $C_{33}H_{40}O_5SiNa$: 567.2543 $[M+Na]^+$; found: 567.2534.

23: Colorless oil; R_f=0.33 (10% EtOAc in hexane); $[\alpha]_D^{23}$=−4.6 (*c*=1.01 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3426, 2960, 1719, 1428, 1389, 1275, 1111, 822, 707 cm^{-1}; ^{1}H NMR (300 MHz): δ=8.04–8.00 (m, 2H), 7.70–7.66 (m, 4H), 7.56 (tt, *J*=7.3, 1.4 Hz, 1H), 7.46–7.32 (m, 8H), 5.51 (ddd, *J*=15.4, 7.1, 0.9 Hz, 1H), 5.36 (ddd, *J*=15.4, 6.4, 0.7 Hz, 1H), 4.26 (m, 3H), 4.07 (quint, *J*=6.4 Hz, 1H), 1.84–1.56 (m, 4H), 1.17–1.08 ppm (m, 12H); ^{13}C NMR (75 MHz): δ=166.5, 135.9, 135.8, 134.8, 134.3, 133.9, 132.7, 132.0, 130.3, 129.6, 129.49, 129.47, 128.2, 127.5, 127.2, 73.2, 68.0, 64.8, 34.0, 26.9, 23.9, 22.7, 19.2 ppm; HRMS (FAB+): *m*/*z* calcd for $C_{31}H_{38}O_4SiNa$: 525.2437 $[M+Na]^+$; found: 525.2431.

On the other hand, when (*R*)-CBS reagent was used instead of (*S*)-CBS reagent in the above reduction, an oily mixture of **23** and **23′** was obtained quantitatively in a 1.85:1 ratio. Lipase-catalyzed kinetic acetylation under the above conditions gave (*R*)-**24** (65 mg) in 29% yield and (*S*)-**23** (118 mg) in 59% yield.

5: A mixture of **24** (110 mg, 0.20 mmol) and powdered NaOH (40.3 mg, 1 mmol) was stirred in methanol (4 mL) at room temperature for 4 h. After evaporation of solvent, the mixture was dissolved in water (12 mL) and extracted with $CHCl_3$ (3×10 mL). The extracts were combined and dried over $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 5% MeOH in $CHCl_3$ afforded **5** (77 mg) in 89% yield. Colorless oil; R_f=0.31 (40% EtOAc in hexane); $[\alpha]_D^{22}$=−12.1 (*c*=0.86 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3347, 2930, 1589, 1428, 1110, 822 cm^{-1}; ^{1}H NMR (300 MHz): δ=7.69–7.64 (m, 4H), 7.45–7.32 (m, 6H), 5.50 (dd, *J*=15.4, 6.7 Hz, 1H,), 5.34 (dd, *J*=15.4, 6.0 Hz, 1H), 4.20 (m, 1H), 4.09 (quint, *J*=6.2 Hz, 1H), 3.51 (t, *J*=5.6 Hz, 2H), 2.04 (bs, 2H), 1.62–1.49 (m, 4H), 1.07 ppm (s, 12H); ^{13}C NMR (75 MHz): δ=135.9, 135.8, 134.7, 134.2, 134.0, 131.8, 129.5, 129.4, 127.4, 127.3, 73.5, 67.9, 62.5, 34.0, 27.6, 26.9, 22.8, 19.2 ppm; HRMS (FAB+): *m*/*z* calcd for $C_{24}H_{34}O_3SiNa$: 421.2175 $[M+Na]^+$; found: 421.2181.

6: The methanolysis of **23** was performed in the same manner described for the preparation of **5**. Compound **6** was obtained in 90% yield. Colorless crystals; m.p. 42–45 °C; R_f=0.31 (40% EtOAc in hexane); $[\alpha]_D^{22}$=−14.7 (*c*=1.04 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3348, 2931, 1427, 1362, 1110, 822, 740, 701 cm^{-1}; ^{1}H NMR (300 MHz): δ=7.69–7.65 (m, 4H), 7.46–7.32 (m, 6H), 5.48 (ddd, *J*=15.4, 7.1, 1.1 Hz, 1H), 5.30 (dd, *J*=15.5, 6.5 Hz, 1H), 4.21 (m, 1H), 4.04 (m, 1H), 3.56 (bs, 2H), 1.69–1.53 (m, 6H), 1.09–1.06 ppm (d, 12H); ^{13}C NMR (75 MHz): δ=136.0, 135.9, 134.7, 134.4, 134.0, 132.3, 129.6, 129.5, 127.5, 127.3, 73.6, 68.1, 62.8, 34.1, 27.9, 26.9, 22.7, 19.2 ppm; HRMS (FAB+): *m*/*z* calcd for $C_{24}H_{34}O_3SiNa$: 421.2175 $[M+Na]^+$; found: 421.2181; elemental analysis: calcd (%) for $C_{24}H_{34}O_3Si$: C 72.32, H, 8.60; found: C 72.02, H, 8.34.

26: Et_3N (0.1 mL, 0.713 mmol) was added in one portion to a stirred suspension of $Zn(OTf)_2$ (237.6 mg, 0.653 mmol, pre-dried overnight at 125 °C under vacuum) and (+)-*N*-methylephedrine (127.7 mg, 0.713 mmol) in dry toluene (2.7 mL) at room temperature. After the resulting white slurry was stirred at room temperature for 3 h, **25**[17] (200 mg, 0.594 mmol) was added. The mixture was stirred for an additional 30 min, and freshly distilled cyclohexanecarboxaldehyde (65 μL, 0.534 mmol) was added. After the mixture was stirred for 5 h at room temperature, a saturated solution of NH_4Cl (10 mL) was added, and the mixture was extracted with Et_2O (50 mL). The organic extract was washed with brine and dried over $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 10% of Et_2O in hexane afforded **26** (255 mg) in 96% yield. Colorless oil; R_f=0.42 (20% EtOAc in hexane); $[\alpha]_D^{25}$=−2.5 (*c*=1.01 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3366, 3071, 3048, 2928, 2855, 1589, 1472, 1449, 1428, 1376, 1260, 1187, 1136, 1109, 1084, 1021, 939, 908, 822, 738, 702 cm^{-1}; ^{1}H NMR (300 MHz): δ=7.70–7.66 (m, 4H), 7.44–7.34 (m, 6H), 4.05 (brs, 1H), 3.97 (tq, *J*=6.0, 5.6 Hz, 1H), 2.28 (dt, *J*=6.2, 1.8 Hz, 2H), 1.77–1.72 (m, 4H), 1.70–1.40 (m, 6H), 1.26–1.10 (m, 4H), 1.05 ppm (s, 12H); ^{13}C NMR (75 MHz): δ=135.87, 135.85, 134.7, 134.2, 129.5, 129.4, 127.5, 127.4, 86.0, 80.1, 68.4, 67.3, 44.2, 38.3, 28.5, 28.1, 27.0, 26.4, 25.9, 25.8, 23.1, 19.2, 14.8 ppm; HRMS (FAB+): *m*/*z* calcd for $C_{29}H_{40}O_2SiNa$: 471.2696 $[M+Na]^+$; found: 471.2703. The diastereoselectivity was confirmed to be >99:1 by HPLC analysis: column: Daicel Chiralcel ODH, solvent: 2-propanol/hexane (2:98), flow rate: 0.1 mL min^{-1}, retention time: 60.4 min (**27**) and 66.8 min (**26**).

8: Red-Al (72 μL, 70% solution in toluene, 0.356 mmol) was added to a solution of **26** (40 mg, 0.089 mmol) in THF (4 mL), and the mixture was heated at reflux for 4 h. After cooling, the reaction mixture was quenched with water (5 mL) and extracted with Et_2O (3×20 mL). 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 on silica gel eluted with 2% MeOH in $CHCl_3$ afforded **8** (18.5 mg) in 98% yield. Colorless oil; R_f=0.24 (40% EtOAc in hexane); $[\alpha]_D^{21}$=+4.1 (*c*=1.01 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3359, 2923, 2852, 1716, 1669, 1449, 1374, 1304, 1127, 1081, 1004, 970, 891, 843, 733 cm^{-1}; ^{1}H NMR (300 MHz): δ=5.60 (dt, *J*=15.4, 6.4 Hz, 1H), 5.51 (dd, *J*=15.4, 7.1 Hz, 1H), 3.86–3.69 (m, 2H), 2.23–2.04 (m, 2H), 1.86–1.67 (m, 4H), 1.62–1.49 (m, 5H), 1.41–1.24 (m, 3H), 1.20–1.16 (m, 4H), 1.01–0.83 ppm (m, 2H); ^{13}C NMR (75 MHz): δ=132.2, 131.9, 77.5, 67.6, 43.6, 38.6, 28.8, 28.65, 28.63, 26.5, 26.1, 26.0, 23.4 ppm; HRMS (FAB+): *m*/*z* calcd for $C_{13}H_{24}O_2Na$: 235.1674 $[M+Na]^+$; found: 235.1680.

27: The reaction of **25** with cyclohexanecarboxaldehyde was performed in the same manner described for the preparation of **26** except for the use of (−)-*N*-methylephedrine instead of (+)-*N*-methylephedrine. Compound **27** was obtained in 97% yield. Colorless oil; R_f=0.42 (20% EtOAc in hexane); $[\alpha]_D^{21}$=+5.1 (*c*=0.74 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3390, 3071, 2927, 2855, 2238, 1589, 1450, 1428, 1376, 1259, 892, 822, 740, 702 cm^{-1}; ^{1}H NMR (300 MHz): δ=7.70–7.67 (m, 4H), 7.45–7.35 (m, 6H), 4.06 (brs, 1H), 3.97 (tq, *J*=6.1, 5.9 Hz, 1H), 2.28 (td, *J*=6.1, 1.8 Hz, 2H), 1.83–1.72 (m, 5H), 1.69–1.39 (m, 5H), 1.30–1.13 (m, 4H), 1.05 ppm (s, 12H); ^{13}C NMR (75 MHz): δ=135.8 (2C), 134.7, 134.2, 129.5, 129.4, 127.5, 127.4, 85.9, 80.1, 68.4, 67.3, 44.2, 38.3, 28.5, 28.1, 26.9, 26.3, 25.9, 25.8, 23.1, 19.2, 14.8 ppm; HRMS (FAB+): *m*/*z* calcd for $C_{29}H_{40}O_2SiNa$: 471.2696 $[M+Na]^+$; found: 471.2690. The diastereoslectivity was confirmed to be 99:1 by HPLC analysis: column: Daicel Chiralcel ODH, solvent: 2-propanol/hexane (2:98), flow rate: 0.1 mL min^{-1}, retention time: 60.4 min (**27**) and 66.8 min (**26**).

9: The reaction of **27** with Red-Al was performed in the same manner described for the preparation of **8**. Compound **9** was obtained in 70% yield. Colorless oil; R_f=0.24 (40% EtOAc in hexane); $[\alpha]_D^{22}$=+4.6 (*c*=1.03 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3366, 2921, 2863, 1665, 1449, 970 cm^{-1}; ^{1}H NMR (300 MHz): δ=5.60 (dt, *J*=15.4, 6.4 Hz, 1H), 5.51 (ddd, *J*=15.4, 6.9, 1.2 Hz, 1H), 3.86–3.75 (m, 2H), 2.24–2.04 (m, 2H), 1.86–1.62 (m, 5H), 1.58–1.41 (m, 4H), 1.37–1.28 (m, 1H), 1.25–1.09 (m, 6H), 1.01–0.88 ppm (m, 2H); ^{13}C NMR (62.5 MHz): δ=132.2, 131.9, 77.5, 67.6, 43.6, 38.5, 28.8, 28.65, 28.61, 26.5, 26.1, 26.0, 23.5 ppm; HRMS (FAB+): *m*/*z* calcd for $C_{13}H_{24}O_2Na$: 235.1674 $[M+Na]^+$; found: 235.1683.

29: A solution of PPh_3 (6 g, 22.8 mmol) in CH_2Cl_2 (7 mL) was added dropwise to a solution of CBr_4 (3.8 g, 11.4 mmol) in CH_2Cl_2 (14 mL) at 0 °C. After the mixture was stirred for 15 min, NEt_3 (6.4 mL, 45.7 mmol) was added, and the mixture was stirred for an additional 10 min at the

same temperature. A solution of (*S*)-6-(*tert*-butyldimethylsilyloxy)heptanal (**28**)[18] (1.4 g, 5.7 mmol) in CH_2Cl_2 (7 mL) was added, the reaction mixture was stirred for 5 h at room temperature, quenched with a saturated solution of $NaHCO_3$ (15 mL), and extracted with hexane (3× 25 mL). 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 on silica gel eluted with hexane afforded **29** (1.82 g) in 80% yield. Colorless oil; R_f=0.34 (1% EtOAc in hexane); $[\alpha]_D^{22}$=+8.9 (c=1.07 in $CHCl_3$); IR (neat): $\tilde{\nu}$=2929, 2857, 1623, 1461, 1374, 1254, 1137, 1100, 1051, 1005, 938, 891, 835, 804, 774, 660 cm^{-1}; ^{1}H NMR (300 MHz): δ=6.38 (t, J=7.3 Hz, 1H), 3.76 (m, 1H), 2.09 (q, J=7.1 Hz, 2H), 1.46–1.25 (m, 6H), 1.11 (d, J=6.0 Hz, 3H), 0.89 (s, 9H), 0.05 ppm (s, 6H); ^{13}C NMR (62.5 MHz): δ=138.7, 68.3, 39.3, 32.9, 27.8, 25.8, 25.2, 23.8, 21.4, 18.1, −4.3, −4.7 ppm; HRMS (CI+): m/z calcd for $C_{14}H_{29}Br_2OSi$: 399.0354 $[M+H]^+$; found: 399.0363.

30: *n*BuLi (6.35 mL, 2.6 M solution in hexane, 9.9 mmol) was added to a solution of **29** (1.8 g, 4.5 mmol) in THF (18 mL) at −78 °C. The mixture was stirred for 1 h at the same temperature, and then quenched with water (30 mL). The mixture was extracted with Et_2O (70 mL). The organic extracts were washed with brine and dried over $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 3% Et_2O in hexane afforded **30** (984 mg) in 91% yield. Colorless oil; R_f=0.36 (3% EtOAc in hexane); $[\alpha]_D^{20}$=+12.9 (c=1.05 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3314, 2930, 2857, 1462, 1375, 1254, 1135, 1099, 1047, 1005, 835, 774 cm^{-1}; ^{1}H NMR (300 MHz): δ=3.77 (m, 1H), 2.19 (td, J=6.9, 2.5 Hz, 2H), 1.93 (t, J=2.5 Hz, 1H), 1.52–1.33 (m, 6H), 1.12 (d, J=6.2 Hz, 3H), 0.88 (s, 9H), 0.04 ppm (s, 6H); ^{13}C NMR (62.5 MHz): δ=84.5, 68.4, 68.1, 39.1, 28.5, 25.8, 24.9, 23.8, 18.4, 18.1, −4.3, −4.7 ppm; HRMS (CI+): m/z calcd for $C_{14}H_{29}OSi$: 241.1988 $[M+H]^+$; found: 241.1982.

31 and **32**: The reaction of **30** with cyclohexanecarboxaldehyde was performed in the same manner described for the preparation of **26** on a 100-mg scale with (+)-*N*-methylephedrine as a chiral ligand to give **31** in 95% yield. The same reaction of **30** with (−)-*N*-methylephedrine instead of (+)-*N*-methylephedrine as a chiral ligand gave **32** in 92% yield. Their diastereoselectivities were determined to be >98:2 d.r. for **31** and >97:3 d.r. for **32** by HPLC analysis: column: Daicel Chiralcel ODH, solvent: 2-propanol/hexane (0.2:98.8), flow rate: 0.1 mL min^{-1}, retention time: 65.1 min (**31**) and 72.8 min (**32**).

31: Colorless oil; R_f=0.36 (20% EtOAc in hexane); $[\alpha]_D^{22}$=+6.7 (c=0.86 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3367, 2927, 2855, 1450, 1375, 1254, 1135, 1097, 1045, 835, 774 cm^{-1}; ^{1}H NMR (300 MHz): δ=4.1 (bs, 1H), 3.77 (m, 1H), 2.21 (td, J=6.6, 1.8 Hz, 2H), 1.85–1.65 (m, 6H), 1.55–1.31 (m, 7H), 1.26–1.01 (m, 8H), 0.88 (s, 9H), 0.04 ppm (s, 6H); ^{13}C NMR (75 MHz): δ= 86.1, 80.1, 68.5, 67.4, 44.3, 39.1, 28.7, 28.5, 28.1, 26.4, 25.9, 25.8 (2C), 25.0, 23.7, 18.7, 18.1, −4.4, −4.7 ppm; HRMS (CI+): m/z calcd for $C_{21}H_{41}O_2Si$: 353.2876 $[M+H]^+$; found: 353.2880.

32: Colorless oil; R_f=0.36 (20% EtOAc in hexane); $[\alpha]_D^{20}$=+10.9 (c= 0.94 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3367, 2928, 2855, 1450, 1375, 1254, 1135, 1097, 1045, 1006, 892, 835, 808, 774 cm^{-1}; ^{1}H NMR (300 MHz): δ=4.12 (brs, 1H), 3.76 (m, 1H), 2.21 (td, J=6.7, 1.6 Hz, 2H), 1.85–1.65 (m, 6H), 1.55–1.34 (m, 7H), 1.31–1.01 (m, 8H), 0.88 (s, 9H), 0.04 ppm (s, 6H); ^{13}C NMR (75 MHz): δ=86.1, 80.2, 68.5, 67.4, 44.3, 39.1, 28.7, 28.5, 28.1, 26.4, 25.9, 25.8 (2C), 25.0, 23.7, 18.7, 18.1, −4.4, −4.7 ppm; HRMS (CI+): m/z calcd for $C_{21}H_{41}O_2Si$: 353.2876 $[M+H]^+$; found: 353.2872.

33: Red-Al (0.29 mL, 70% solution in toluene, 1.47 mmol) was added to a solution of **31** (130 mg, 0.368 mmol) in THF (13 mL), and the mixture was heated at reflux for 3.5 h. The reaction mixture was cooled, quenched with water (10 mL), and extracted with Et_2O (50 mL). The organic extract was washed with brine and dried over $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 10% Et_2O in hexane afforded **33** (115 mg) in 88% yield. Colorless oil; R_f=0.36 (20% EtOAc in hexane); $[\alpha]_D^{21}$=+6.5 (c=0.91 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3366, 2927, 1449, 1253, 1047, 835, 773 cm^{-1}; ^{1}H NMR (300 MHz): δ=5.57 (dt, J=15.4, 6.6 Hz, 1H), 5.46 (dd, J=15.4, 7.3 Hz, 1H), 3.75 (m, 2H), 2.04 (q, J=6.2 Hz, 2H), 1.87–1.63 (m, 5H), 1.42–1.16 (m, 11H), 1.10 (d, J=6.0 Hz, 3H), 1.02–0.91 (m, 2H), 0.88 (s, 9H), 0.03 ppm (s, 6H); ^{13}C NMR (75 MHz): δ=132.8, 131.5, 77.6, 68.5, 43.6, 39.4, 32.2, 29.2, 28.8, 28.6, 26.5, 26.1, 26.0, 25.8, 25.3, 23.7, 18.1, −4.4, −4.7 ppm; HRMS (FAB+): m/z calcd for $C_{21}H_{42}O_2SiNa$: 377.2852 $[M+Na]^+$; found: 377.2845. By the same procedure described for the synthesis of **33**, compound **32** provided **34** in 80% yield. Colorless oil; R_f=0.36 (20% EtOAc in hexane); $[\alpha]_D^{23}$=+11.2 (c=1.05 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3365, 2927, 2855, 1450, 1374, 1254, 1134, 1050, 1004, 969, 890, 835, 774 cm^{-1}; ^{1}H NMR (300 MHz): δ=5.73 (dt, J=15.4, 6.4 Hz, 1H), 5.62 (dd, J=15.2, 7.3 Hz, 1H), 3.91 (m, 2H), 2.19 (q, J=6.7 Hz, 2H), 2.03–1.79 (m, 5H), 1.64–1.29 (m, 11H), 1.26 (d, J=6.0 Hz, 3H), 1.18–1.09 (m, 2H), 1.04 (s, 9H), 0.20 ppm (s, 6H); ^{13}C NMR (75 MHz): δ=132.9, 131.5, 77.7, 68.5, 43.6, 39.5, 32.2, 29.3, 28.8, 28.7, 26.5, 26.1, 26.0, 25.8, 25.3, 23.7, 18.1, −4.4, −4.7 ppm; HRMS (FAB+): m/z calcd for $C_{21}H_{42}O_2SiNa$: 377.2852 $[M+Na]^+$; found: 377.2858.

10: A mixture of **33** (106 mg, 0.298 mmol) and TBAF (1.1 mL, 1.0 M solution in THF, 2.98 mmol) in THF (3.6 mL) was stirred at room temperature for 2 days. Then it was quenched with water (8 mL) and extracted with Et_2O (50 mL). The organic extract was washed with brine and dried over $MgSO_4$. Evaporation of solvent and purification of the residue by column chromatography on silica gel eluted with 80% Et_2O in hexane afforded **10** (63 mg) in 88% yield. Colorless crystals; m.p. 59–61 °C; R_f= 0.33 (40% EtOAc in hexane); $[\alpha]_D^{21}$=+1.9 (c=1.01 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3346, 2922, 2850, 1452 cm^{-1}; ^{1}H NMR (300 MHz): δ=5.57 (dtd, J= 15.7, 6.4, 0.5 Hz, 1H), 5.49 (ddt, J=15.4, 7.3, 0.9 Hz, 1H), 3.76 (m, 2H), 2.06 (q, J=6.4 Hz, 2H), 1.88–1.64 (m, 5H), 1.47–1.23 (m, 11H), 1.18 (d, J=6.2 Hz, 3H), 1.02–0.86 ppm (m, 3H); ^{13}C NMR (62.5 MHz): δ=132.7, 131.6, 77.6, 68.0, 43.6, 39.0, 32.1, 29.1, 28.8, 28.6, 26.5, 26.1, 26.0, 25.2, 23.5 ppm; HRMS (FAB+): m/z calcd for $C_{15}H_{28}O_2Na$: 263.1987 $[M+Na]^+$; found: 263.1980; elemental analysis: calcd (%) for $C_{15}H_{28}O_2$: C 74.95, H, 11.74; found: C 74.63, H, 12.02.

11: Compound **11** was obtained in 86% yield from **34** in the same manner described for the preparation of **10**. Colorless oil; R_f=0.33 (40% EtOAc in hexane); $[\alpha]_D^{22}$=+7.6 (c=0.82 in $CHCl_3$); IR (neat): $\tilde{\nu}$=3355, 2922, 2863, 1669, 1450, 969, 891, 755 cm^{-1}; ^{1}H NMR (300 MHz): δ=5.57 (dt, J=15.5, 6.4 Hz, 1H), 5.48 (ddt, J=15.2, 6.9, 0.9 Hz, 1H), 3.76 (m, 2H), 2.05 (q, J=6.0 Hz, 2H), 1.87–1.63 (m, 5H), 1.51–1.20 (m, 11H), 1.18 (d, J=6.2 Hz, 3H), 1.14–0.88 ppm (m, 3H); ^{13}C NMR (62.5 MHz): δ=132.6, 131.6, 77.6, 68.0, 43.6, 39.0, 32.1, 29.1, 28.8, 28.6, 26.5, 26.1, 26.0, 25.2, 23.4 ppm; HRMS (FAB+): m/z calcd for $C_{15}H_{28}O_2Na$: 263.1987 $[M+Na]^+$; found: 263.1982.

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[1] a) J. Tsuji, *Palladium Reagent and Catalysts: Innovations in Organic Synthesis*, John Willey & Sons, Chichester, **1995**; b) L. S. Hegedus in *Organmetallics in Synthesis* (Ed.: M. Schlosser), John Willey & Sons, Chichester, **2002**, pp. 1123–1217.

[2] a) T. Hosokawa, S.-I. Murahashi in *Handbook of Organopalladium Chemistry for Organic Synthesis* (Ed.: E.-i. Negishi), John Willey & Sons, New York, **2002**, pp. 2141–2192; b) P. M. Henry, in *Handbook of Organopalladium Chemistry for Organic Synthesis* (Ed.: E.-i. Negishi), John Willey & Sons, New York, **2002**, pp. 2119–2139; c) G. Zeni, R. C. Larock, *Chem. Rev.* **2004**, *104*, 2285–2309.

[3] a) H. B. Lee, P. M. Henry, *Can. J. Chem.* **1976**, *54*, 1726–1738; b) D. E. James, L. F. Hines, J. K. Stille, *J. Am. Chem. Soc.* **1976**, *98*, 1806–1809; c) T. Majima, H. Kurosawa, *J. Chem. Soc. Chem. Commun.* **1977**, 610–611; d) J. E. Bäckvall, B. Åkermark, S. O. Ljunggren, *J. Chem. Soc. Chem. Commun.* **1977**, 264–265; e) J. E. Bäckvall, B. Åkermark, S. O. Ljunggren, *J. Am. Chem. Soc.* **1979**, *101*, 2411–2416; f) J. W. Francis, P. M. Henry, *Organometallics* **1991**, *10*, 3498–3503; g) K. Zaw, P. M. Henry, *Organometallics* **1992**, *11*, 2008–2015; h) J. W. Francis, P. M. Henry, *Organometallics* **1992**, *11*,

2832–2836; i) O. Hamed, P. M. Henry, *Organometallics* **1997**, *16*, 4903–4909; j) O. Hamed, C. Thompson, P. M. Henry, *J. Org. Chem.* **1997**, *62*, 7082–7083; k) O. Hamed, P. M. Henry, C. Thompson, *J. Org. Chem.* **1999**, *64*, 7745–7750; l) D. J. Nelson, R. Li, C. Brammer, *J. Am. Chem. Soc.* **2001**, *123*, 1564–1568.

[4] a) J. S. Nakhla, J. W. Kampf, J. P. Wolfe, *J. Am. Chem. Soc.* **2006**, *128*, 2893–2901; b) R. M. Trend, Y. K. Ramtohul, B. M. Stoltz, *J. Am. Chem. Soc.* **2005**, *127*, 17778–17788; c) M. B. Hay, J. P. Wolfe, *J. Am. Chem. Soc.* **2005**, *127*, 16468–16476; d) M. B. Hay, A. R. Hardin, J. P. Wolfe, *J. Org. Chem.* **2005**, *70*, 3099–3107; e) T. Hayashi, K. Yamasaki, M. Mimura, Y. Uozumi, *J. Am. Chem. Soc.* **2004**, *126*, 3036–3037.

[5] a) N. Kawai, J.-M. Lagrange, J. Uenishi, *Eur. J. Org. Chem.* **2007**, 2808–2814; b) N. Kawai, J. M. Lagrange, M. Ohmi, J. Uenishi, *J. Org. Chem.* **2006**, *71*, 4530–4537; c) J. Uenishi, M. Ohmi, A. Ueda, *Tetrahedron: Asymmetry* **2005**, *16*, 1299–1303.

[6] Recent synthesis of oxacyclic compounds catalyzed by $PdCl_2$; a) A. Zawisza, D. Sinou, *Tetrahedron Lett.* **2006**, *47*, 3271–3274; b) A. Zawisza, B. Fenet, D. Sinou, *Eur. J. Org. Chem.* **2007**, 2296–2309.

[7] E. L. Eliel, K. D. Hargrave, K. M. Pietrusiewicz, M. Manoharan, *J. Am. Chem. Soc.* **1982**, *104*, 3635–3643.

[8] M. Miyazawa, Y, Hirose, M. Narantsetseg, H. Yokoyama, S. Yamaguchi, Y, Hirai, *Tetrahedron Lett.* **2004**, *45*, 2883–2886.

[9] Hydroxy group directed coordination of $PdCl_2$ catalyst to allylic alcohol; see ref. [3f-k] and W. Smadja, S. Czernecki, G. Ville, C. Georgoulis, *Organometallics* **1987**, *6*, 166–169.

[10] For example, syn-elimination; U. Hacksell, G. D. Daves, Jr., *Organometallics* **1983**, *2*, 772–775. Anti-elimination was observed but at high Cl ion concentration conditions; see ref. [3 h].

[11] S. Tanimori, Y. Morita, M. Tsubota, M. Nakayama, *Synth. Commun.* **1996**, *26*, 559–567.

[12] L. M. Grubb, B. P. Branchaud, *J. Org. Chem.* **1997**, *62*, 242–243.

[13] C. H. Sugisaki, Y. Ruland, M. Baltas, *Eur. J. Org. Chem.* **2003**, 672–688.

[14] E. J. Corey, C. J. Helal, *Angew. Chem.* **1998**, *110*, 2092–2118; *Angew. Chem. Int. Ed.* **1998**, *37*, 1986–2012.

[15] For a recent review, see: a) K. Nakamura, T. Matsuda, in *Enantiomer Separation: Fundamentals and Practical Methods*, (Ed.: F. Toda), Kluwer, Dordrecht, **2004**, pp. 231–266; b) for allylic alcohols, see: M. Fujii, M. Fukumura, Y. Hori, Y. Hirai, H. Akita, K. Nakamura, K. Toriizuka, Y. Ida, *Tetrahedron: Asymmetry* **2006**, *17*, 2292–2298.

[16] For the asymmetric addition reaction of alkynes to aldehydes, see: D. E. Frantz, R. Fässler, E. M. Carreira, *J. Am. Chem. Soc.* **2000**, *122*, 1806–1807.

[17] J. Mulzer, M. Berger, *J. Org. Chem.* **2004**, *69*, 891–898.

[18] Y. K. Booth, P. Y. Hayes, C. J. Moore, L. K. Lambert, W. Kitching, J. J. De Voss, *Org. Biomol. Chem.* **2007**, *5*, 1111–1117.

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