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Stereoselective synthesis of (−)-diospongins A and B and their stereoisomers at C-5

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J.U. dedicates this paper to Professor Yoshito Kishi on the occasion of his 70th birthday

Abstract—Antiosteoporotic diarylheptanoids (−)-diospongins A (**1**) and B (**2**) were synthesized stereoselectively. The key steps in the synthesis include a stereospecific Pd^{II}-catalyzed cyclization of chiral 1,5,7-trihydroxy-2-heptenes, **6a** and **6b**, to form *cis* and *trans* tetrahydropyran rings and a regioselective Wacker oxidation of β-(tetrahydro-2*H*-pyran-2-yl)styrenes, **5a** and **5b**. Their C-5 epimers **3** and **4** were also synthesized.
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1. Introduction

1,7-Diarylheptanoids including curcuminoids are a class of secondary plant metabolite and have been found in rhizomes of the Zingiberaceae family of plants.[1] Although 1,7-diarylheptanoids are relatively simple molecules, they exhibit various biological and pharmacological activities, such as anti-oxidant activity,[2] anti-cancer activity,[3] inhibitory activity on nitric oxide production,[4] anti-inflammatory activity,[5] and DPPH-radical scavenging activity,[2b] and so on.[6] Particularly, cyclic 1,7-diarylheptanoids have been receiving considerable attention.[7,8] Diospongins A (**1**) and B (**2**) are cyclic 1,7-diarylheptanoids, as shown in Figure 1, that were isolated from rhizomes of *Dioscorea spongiosa* in 2004 by Kadota and co-workers.[9] Diospongins A and B possess 2,6-*cis* and 2,6-*trans* tetrahydro-2*H*-pyran rings, respectively, and these rings are assumed to be formed by an intramolecular cyclization of 5,7-dihydroxy-1,7-diphenyl-2-hepten-1-one, in their biosynthesis. Although both compounds indicate an inhibitory activity against bone resorption induced by parathyroid hormone in a bone organ culture, diospongin B shows more potent antiosteoporotic activity than that of diospongin A due to their different configurations of tetrahydropyran rings. Recently, the synthesis of diospongin B has been reported by three groups.[8,10] We have been interested in studies of the synthesis of cyclic 1,7-diarylheptanoids as well as their biological activities not only because of their antiosteoporotic activity but also because of their inhibitory activity against nitric oxide production. In this paper, we report the total synthesis of diospongins A, B, and their C-5 epimers, **3** and **4**.

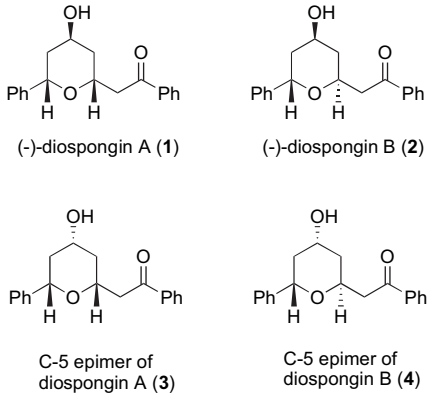

Figure 1. Diospongins A, B and their C-5 epimers.

Our retrosynthetic plan for **1** and **2** is outlined in Scheme 1. The key steps involve a stereospecific construction of chiral *cis* and *trans* tetrahydropyran rings of **5a** and **5b** from **6** by a Pd^{II}-catalyzed 1,3-chirality transfer reaction[11] and a regioselective Wacker oxidation of **5a** and **5b** to **1** and **2**. Acyclic precursors **6a** and **6b** could be derived by an enantioselective reduction of enone **7**, which is readily prepared from the chiral homoallylalcohol **8**[12] by the standard transformation steps.

2. Results and discussion

The synthesis of **7** is shown in Scheme 2. We commenced the synthesis from the known aldehyde **9**,[13] which was derived readily from ethyl (*R*)-(−)-mandelate. Since a simple

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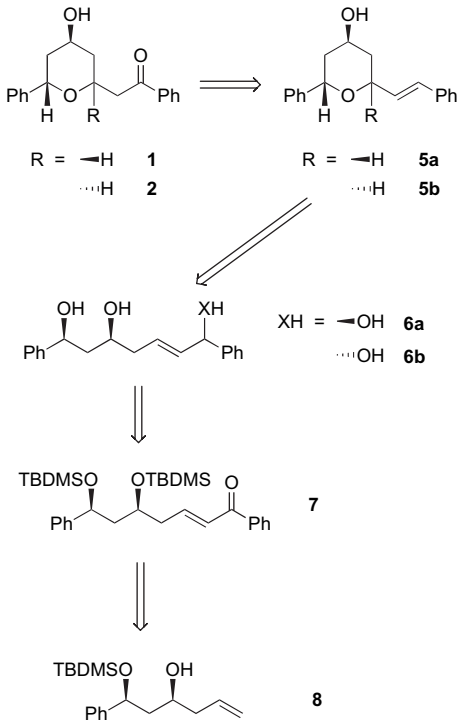
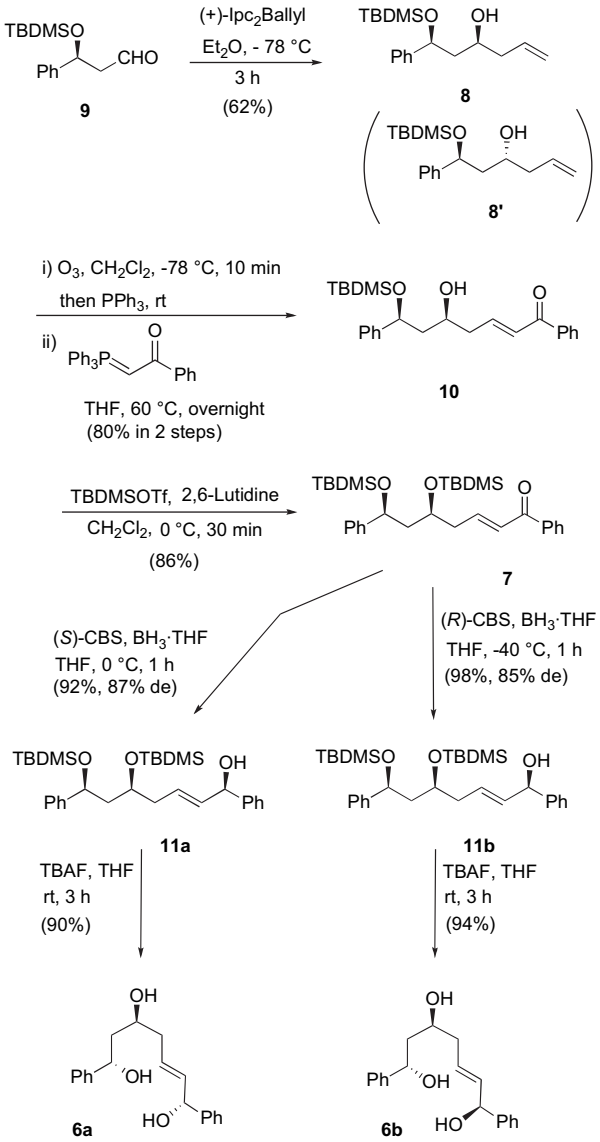


Scheme 1. Retrosynthesis of (−)-Diospongins A and B.

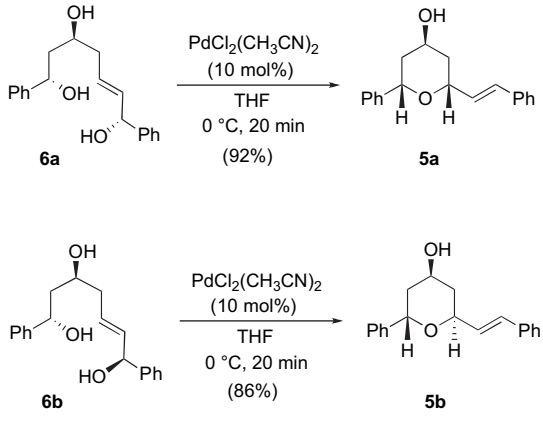
allylation of **9** with non-chiral allylation reagents gave *anti* alcohol **8′**, usually as a major product,[14] enantioselective allylation must be employed in order to obtain the desired *syn* alcohol **8**. Therefore, we chose Brown's chiral allylborane reagent, (+)-Ipc$_2$Ballyl,[15] and compound **8** was obtained in 62% yield along with diastereoisomer **8′** in 14% yield.[16] Oxidative cleavage of the alkenyl bond with ozone followed by Wittig reaction with phosphorane[17] gave enone **10** in 80% yield in two steps. Finally, silylation of the hydroxy group afforded α,β-unsaturated ketone **7** in 86% yield.

Diastereoselective reductions of α,β-unsaturated ketone **7** were performed by using an enantioselective reducing reagent. As shown in Scheme 2, treatment of **7** with an (*S*)-CBS reagent,[18] at 0 °C in THF gave the corresponding (*R*)-allylic alcohol **11a** in 92% yield with 87% de,[19] which was successively deprotected with TBAF in THF to afford triol **6a** in 90% yield. Meanwhile, the reduction of **7** with a (*R*)-CBS reagent[18] gave **11b** in 98% yield with 85% de[19] and the deprotection of silyl ether afforded triol **6b** in 94% yield. With triols in hand, Pd^{II}-catalyzed cyclizations were examined. When triol **6a** containing 7% of **6b** was treated with 10 mol % of $PdCl_2(CH_3CN)_2$ in THF at 0 °C, the desired *cis*-(*E*)-tetrahydropyran **5a** was obtained in 92% yield along with **5b** in 6% yield. Meanwhile, under the same conditions, triol **6b** containing 8% of **6a** gave the desired *trans*-(*E*)-tetrahydropyran **5b** in 86% yield and **5a** in 5% yield. The structures of **5a** and **5b** were confirmed by the NOE experiments with ^{1}H NMR, as shown in Figure 2. An NOE was observed with two axial protons at C-2 and C-6 on the tetrahydropyran ring in the spectrum of **5a**. On the other hand, an NOE was observed with C-2 phenyl protons and C-6 axial proton in that of **5b**. Both cyclizations took place stereospecifically through the intramolecular *syn*-S_N2' mechanism, which we reported previously (Scheme 3).[11]



Scheme 2. Preparation of precursors **6a** and **6b**.

Regioselective introduction of the carbonyl group was accomplished by Wacker oxidation as shown in Scheme 4. Wacker oxidation of **5a** was very slow under the standard procedure.[20] In fact, treatment of alkene **5a** with 50 mol %



Scheme 3. Pd^{II}-catalyzed stereospecific formations of *cis* and *trans* tetrahydropyran rings.

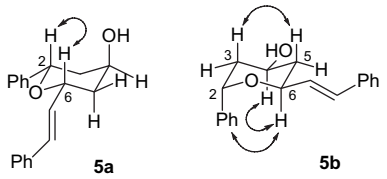
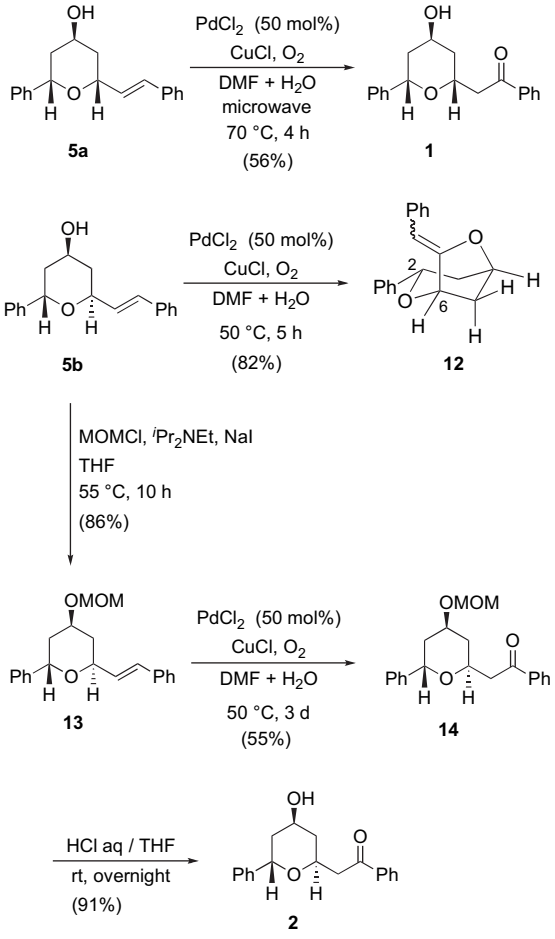


Figure 2. Stereochemistry of **5a** and **5b**.

of $PdCl_2$ and CuCl in a mixture of H_2O and DMF at 50 °C for 3 days provided the desired compound **1** only in 37% yield along with 50% recovery of the starting material. However, the reaction was accelerated by microwave irradiation at 70 °C for 4 h to give the desired **1** in 56% yield along with the starting material in 27% yield. All of the spectra of synthetic **1** were completely in accordance with those of natural (−)-diospongin A.[9]

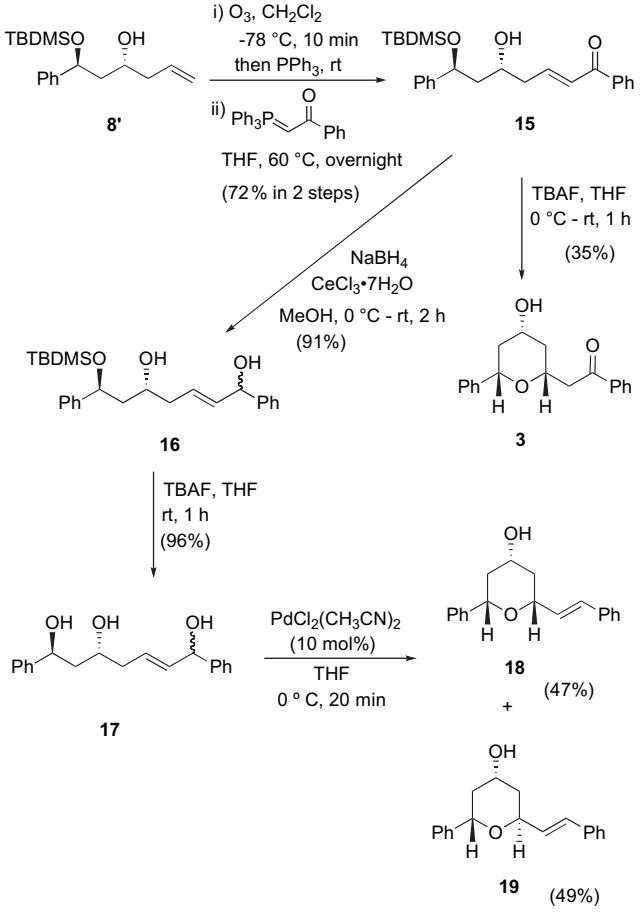


Scheme 4. Synthesis of **1** and **2**.

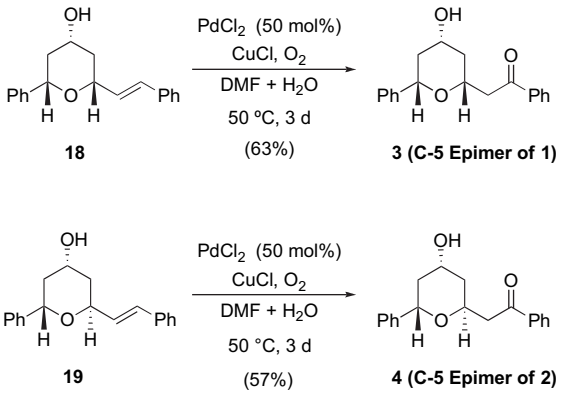
In contrast, the reaction of **5b** under the above conditions without microwave irradiation proceeded faster at 50 °C but, surprisingly, gave unexpected bicyclic compound **12** in 82% yield instead of the desired ketone **2**. We assumed that the intramolecular Wacker reaction took place instead of the intermolecular Wacker reaction. That is, a nucleophilic attack of the hydroxy group located at the cis position with the styryl group occurred on the Pd π-complex of **5b** to form **12**.[21] Therefore, the hydroxy group of **5b** should be protected. After protection of the hydroxy group as a MOM-ether, compound **13** was subjected to Wacker oxidation. Although the conditions under microwave irradiation again gave **12** exclusively, the desired *trans* hydropyran **14** was obtained in 55% yield under general Wacker oxidation conditions at 50 °C for 3 days. Finally, deprotection of MOM-ether with aq. HCl gave the desired **2** in 91% yield. The spectra of synthetic **2** were in accordance with those of natural (−)-diospongin B. The specific rotations of synthetic **1** ($[\alpha]_D^{25}$ −21.4 (*c* 0.8, $CHCl_3$)) and **2** ($[\alpha]_D^{25}$ −22.5 (*c* 0.6, $CHCl_3$)) were in agreement with the data of natural (−)-diospongin A ($[\alpha]_D^{25}$ −21.2 (*c* 0.8, $CHCl_3$)) and (−)-diospongin B ($[\alpha]_D^{25}$ −23.4 (*c* 0.6, $CHCl_3$)).

We were also interested in the synthesis of C-5 epimers **3** and **4** for the following reasons: i) elucidation of the structure and activity relationship of the C-5 hydroxy group and ii) identification of the wrong structure of diospongin A prepared in Chandrasekhar's report.[8a,10] Initially, we assumed that they might obtain C-5 epimer of diospongin A. Our synthesis of **3** and **4** is shown in Schemes 5 and 6.

Compound **8′**, obtained by the reaction of **9** with (−)-Ipc_2-Ballyl, was ozonized and the resulting aldehyde was treated with benzoylmethylidenephosphorane to give enone **15** in 72% yield in two steps in a similar manner to that described for **10**. When **15** was treated with *n*-Bu_4NF, compound **3** was obtained directly in 35% yield. Although an intramolecular Michael reaction of hydroxy nucleophile to enone is more straightforward for obtaining **3**, the reaction was not clean



Scheme 5. Synthesis of **18** and **19**.



Scheme 6. Synthesis of **3** and **4**.

and only gave a thermodynamically favorable cis isomer. No trans isomer **4** was detected in the complex mixture. Nonstereoselective reduction of **15** gave **16** in 91% yield, which was successively treated with *n*-Bu_4NF to afford diastereomeric mixtures of triols **17** in 96% yield. Pd-catalyzed cyclization of **17** in THF at 0 °C gave **18** in 47% yield and **19** in 49% yield. The cis and trans structures were determined by NOE experiments in the manner similar to that described for the case of **5a** and **5b**. Direct Wacker oxidation of **18** gave **3** in 63% yield and 17% recovery of the starting material. In this case, since all three substituent groups on the tetrahydropyran ring were located at equatorial positions, no intramolecular reaction occurred. Therefore, protection of the hydroxy group was unnecessary in contrast to the synthesis of diospongin B. Compound **19** was also oxidized to **4** under the same conditions in 57% yield and a recovery of **19** in 25% yield. We carefully compared the spectroscopic data of **3** and **4** with those in Ref. 8a. None of them were in accordance with those in their report. Therefore, their synthetic product is still mysterious.

3. Conclusions

In summary, the total syntheses of diospongins A and B were achieved in seven steps and nine steps, respectively, from the common intermediate **8**. It is noteworthy that intramolecular Pd^{II}-catalyzed cyclizations are potentially useful for the stereospecific formation of oxacyclic natural products possessing *cis* and *trans* tetrahydropyran rings. Their stereoisomers **3** and **4** were also prepared in short steps. Syntheses of additional analogs and their biological tests are currently underway.

4. Experimental

4.1. Asymmetric allylation of 9, preparation of (4*S*,6*S*)- and (4*R*,6*S*)-6-(*tert*-butyldimethylsilyl)oxy-4-hydroxy-6-phenyl-1-hexene (8) and (8′)

To a stirred solution of (−)-*B*-methoxydiisopinocamphenyl borane (360 mg, 1.1 mmol) in Et_2O (8 mL) at −78 °C was slowly added allylmagnesium bromide (1.1 mL, 1 M solution in ether) and the reaction mixture was stirred for 15 min at −78 °C and for 1 h at room temperature forming (+)-*B*-allyldiisopinocamphenyl borane in situ. After the addition of a solution of **9** (200 mg, 0.75 mmol) in Et_2O (6 mL), the reaction mixture was stirred for 3 h at −78 °C. Then, methanol (5 mL) and 8-hydroxyisoquinoline (220 mg, 1.5 mmol) were added to the mixture at the same temperature, and the mixture was allowed to warm up to room temperature. The reaction mixture was stirred for an additional 6 h. Water was added and the mixture was extracted with EtOAc. The 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 4% EtOAc in hexane gave **8** (143 mg) in 62% yield and **8′** (32 mg) in 14% yield eluted with 6% EtOAc in hexane. Compound **8**: colorless oil; $[\alpha]_D^{25}$ −64.1 (*c* 1.1, $CHCl_3$); R_f=0.30 (10% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.25 (m, 5H), 5.82 (m, 1H), 5.51–5.05 (m, 2H), 4.88 (dd, 1H, *J*=9.3, 4.4 Hz), 3.84 (m, 1H), 3.41 (br s, 1H), 2.3–2.15 (m, 2H), 1.87 (dt, 1H, *J*=14.4, 9.2 Hz), 1.76 (ddd, 1H, *J*=14.4, 4.4, 2.5 Hz), 0.89 (s, 9H), 0.04 (s, 3H), −0.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 134.7, 128.3, 127.5, 126.0, 117.5, 76.4, 70.5, 46.6, 42.0, 25.8, 18.0, −4.4, −5.1; IR (film, cm^{-1}) 3454, 2929, 2857, 1256, 836; MS (FAB) *m*/*z* 307 (M+H$^+$). HRMS calcd for $C_{18}H_{31}O_2Si$ (M+H$^+$): 307.2093; found: *m*/*z* 307.2101. Compound **8′**: Colorless oil; $[\alpha]_D^{22}$ −57.3 (*c* 1.2, $CHCl_3$); R_f=0.29 (10% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.22 (m, 5H), 5.76 (m, 1H), 5.10–5.02 (m, 3H), 3.83 (m, 1H), 3.06 (d, 1H, *J*=2.4 Hz), 2.27–2,15 (m, 2H), 1.90–1.72 (m, 2H), 0.90 (s, 9H), 0.07 (s, 3H), −0.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.3, 134.8, 128.2, 127.0, 125.7, 117.4, 73.4, 67.3, 45.7, 42.1, 25.8, 18.1, −4.7, −5.2; IR (film, cm^{-1}) 3475, 2929, 2857, 1256, 837; MS (FAB) *m*/*z* 307 (M+H$^+$). HRMS calcd for $C_{18}H_{31}O_2Si$ (M+H$^+$): 307.2093; found: *m*/*z* 307.2102. When (+)-*B*-methoxydiisopinocamphenyl borane was used instead of (−)-*B*-methoxydiisopinocamphenyl borane, **8** and **8′** were obtained in a 13:87 ratio.

4.2. (5*S*,7*S*)-7-(*tert*-Butyldimethylsilyl)oxy-5-hydroxy-1,7-diphenyl-2-hepten-1-one (10)

To a stirred solution of **8** (130 mg, 0.42 mmol) in dry CH_2Cl_2 (8 mL) was bubbled a stream of ozone at −78 °C for 10 min. An excess of ozone was removed by bubbling with an argon gas through the reaction mixture for 5–10 min, and after the addition of PPh_3 (222 mg, 0.848 mmol) the reaction mixture was stirred for 2 h at room temperature. After removal of solvent, the mixture was dissolved in dry THF (8 mL) and (phenacylmethylene)triphenylphosphorane (242 mg, 0.636 mmol) was added. The resulting mixture was stirred at 60 °C overnight. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 10% EtOAc in hexane gave **10** (140 mg) in 80% yield. Colorless oil; $[\alpha]_D^{23}$ −41.2 (*c* 1.01, $CHCl_3$); R_f=0.5 (20% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (dd, 2H, *J*=7.0, 1.5 Hz), 7.50 (tt, 1H, *J*=7.3, 1.5 Hz), 7.40 (td, 2H, *J*=7.0, 1.3 Hz), 7.30–7.22 (m, 5H), 7.01 (dt, 1H, *J*=15.4, 6.9 Hz), 6.90 (d, 1H, *J*=15.4 Hz), 4.87 (dd, 1H, *J*=9.5, 4.0 Hz), 4.01 (dddd, 1H, *J*=6.2, 5.9, 3.7, 2.0 Hz), 3.60 (1H, br), 2.47 (ddd, 1H, *J*=15.9, 6.9, 6.2 Hz), 2.43 (ddd, 1H, *J*=15.9, 6.9, 3.7 Hz), 1.89 (ddd, 1H, *J*=14.5, 9.5, 5.9 Hz), 1.75 (ddd, 1H, *J*=14.5, 4.0, 2.0 Hz), 0.84 (s, 9H), −0.01 (s, 3H), −0.28 (s, 3H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 190.5, 145.3, 144.4, 132.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.6, 126.0, 76.6, 70.3, 46.7, 40.9, 25.8, 18.0, −4.4, −5.1; IR (film, cm^{-1}) 3457, 2929, 2856, 1670, 1620, 1253, 837, 778, 700; MS (FAB) *m/z* 433 (M+Na$^+$). HRMS calcd for $C_{25}H_{34}O_3SiNa$ (M+Na$^+$): 433.2175; found: *m/z* 433.2168.

4.3. (5*S*,7*S*)-5,7-Di-(*tert*-butyldimethylsilyl)oxy-1,7-diphenyl-2-hepten-1-one (7)

To a mixture of **10** (130 mg, 0.32 mmol) and 2,6-lutidine (0.11 mL, 0.95 mmol) in dry CH_2Cl_2 (3.2 mL) was added TBDMSOTf (0.11 mL, 0.47 mmol) at 0 °C and the mixture was stirred for 30 min at the same temperature. The reaction mixture was quenched with water and extracted with CH_2Cl_2. Organic layer was washed with water and dried over $MgSO_4$. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 5% EtOAc in hexane gave **7** (143 mg) in 86% yield. Colorless oil; $[\alpha]_D^{22}$ −42.1 (*c* 1.0, $CHCl_3$); R_f=0.62 (20% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (dd, 2H, *J*=7.0, 1.5 Hz), 7.57 (tt, 1H, *J*=7.5, 1.5 Hz), 7.53 (td, 2H, *J*=7.0, 1.5 Hz), 7.33–7.20 (m, 5H), 7.06 (dt, 1H, *J*=15.4, 6.8 Hz), 6.91 (d, 1H, *J*=15.4 Hz), 4.76 (dd, 1H, *J*=8.4, 4.4 Hz), 3.97 (dddd, 1H, *J*=8.4, 6.8, 4.4, 2.0 Hz), 2.65 (dddd, 1H, *J*=14.1, 6.8, 2.0, 1.1 Hz), 2.47 (ddd, 1H, *J*=14.1, 6.8, 1.1 Hz), 2.01 (ddd, 1H, *J*=13.7, 8.4, 4.4 Hz), 1.79 (ddd, 1H, *J*=13.7, 8.4, 4.4 Hz), 0.89 (s, 9H), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H), 0.01 (s, 3H), −0.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.7, 146.7, 145.1, 137.9, 132.5, 128.5, 128.4, 128.2, 128.1, 127.2, 125.9, 72.4, 68.5, 48.5, 40.3, 25.8, 18.1, 18.0, −4.4, −4.5, −4.5, −4.9; IR (film, cm^{-1}) 2954, 2929, 1672, 1624, 1255, 1090; MS (FAB) *m/z* 547 (M+Na$^+$). HRMS calcd for $C_{31}H_{48}O_3Si_2Na$ (M+Na$^+$): 547.3040; found: *m/z* 547.3046.

4.4. Reduction of ketone 7 with (*S*)- and (*R*)-CBS reagents: preparation of 11 and 11′

To a stirred solution of (*S*)-2-methyl-CBS-oxazaborolidine (0.17 mL, 1 M solution in toluene, 0.17 mmol) in dry THF (3 mL) was added $BH_3\cdot$THF (0.17 mL, 1 M solution in toluene, 0.17 mmol). After 30 min, a solution of **7** (75 mg, 0.14 mmol) in dry THF (2 mL) was added to the mixture at 0 °C. The reaction mixture was stirred for 1 h at 0 °C. Evaporation of the solvent and purification of the residue by column chromatography on silica gel eluted with 10% EtOAc in hexane gave (1*R*)-isomer **11** (69.3 mg) in 92% yield with 87% de. Colorless oil; $[\alpha]_D^{22}$ −49.0 (*c* 0.55, $CHCl_3$); R_f=0.28 (10% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.17 (m, 10H), 5.78 (ddd, 1H, *J*=15.4, 6.0, 5.9 Hz), 5.69 (dd, 1H, *J*=15.4, 5.9 Hz), 5.19 (d, 1H, *J*=5.9 Hz), 4.68 (dd, 1H, *J*=8.3, 4.8 Hz), 3.82 (ddd, 1H, *J*=8.3, 6.0, 5.9 Hz), 2.38 (dt, 1H, *J*=13.9, 5.9 Hz), 2.23 (dt, 1H, *J*=13.9, 6.0 Hz), 1.92 (ddd, 1H, *J*=13.9, 8.3, 4.8 Hz), 1.83 (br, 1H), 1.74 (ddd, 1H, *J*=13.9, 7.7, 4.8 Hz), 0.88 (s, 9H), 0.86 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H), −0.01 (s, 3H), −0.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.4, 143.1, 134.7, 128.8, 128.4, 128.1, 127.5, 127.1, 126.2, 126.0, 75.2, 72.4, 69.1, 48.3, 39.5, 25.9, 25.8, 18.1(2C), −4.3, −4.5(2C), −4.9; IR (film, cm^{-1}) 3367, 2928, 2856, 1254, 1091, 836, 775; MS (FAB) *m/z* 549 (M+Na$^+$). HRMS calcd for $C_{31}H_{50}O_3Si_2Na$ (M+Na$^+$): 549.3196; found: *m/z* 549.3201. When (*R*)-CBS reagent was employed instead of (*S*)-CBS reagent and the reaction was conducted at −40 °C for 1 h, (1*S*)-isomer **11′** was obtained in 98% yield with 85% de. Colorless oil; $[\alpha]_D^{22}$ −20.6 (*c* 1.10, $CHCl_3$); R_f=0.28 (10% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.16 (m, 10H), 5.77 (dd, 1H, *J*=15.4, 6.2 Hz), 5.72 (dt, 1H, *J*=15.4, 5.9 Hz), 5.19 (d, 1H, *J*=6.2 Hz), 4.64 (dd, 1H, *J*=8.4, 4.8 Hz), 3.85 (ddd, 1H, *J*=8.4, 6.6, 5.9 Hz), 2.40 (dt, 1H, *J*=14.3, 5.9 Hz), 2.22 (ddd, 1H, *J*=14.3, 6.6, 5.9 Hz), 1.89 (ddd, 1H, *J*=14.0, 8.4, 4.8 Hz), 1.83 (br, 1H), 1.70 (ddd, 1H, *J*=14.0, 7.7, 4.8 Hz), 0.87 (s, 18H), 0.33 (s, 3H), 0.01 (s, 3H), −0.00 (s, 3H), −0.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.3, 143.1, 134.8, 128.8, 128.5, 128.1, 127.5, 127.0, 126.2, 125.9, 75.2, 72.4, 68.9, 48.1, 39.3, 25.9, 25.8, 18.1 (2C), −4.4, −4.5, −4.5, −5.0; IR (film, cm^{-1}) 3349, 2954, 2928, 2886, 1255, 1091, 836; MS (FAB) *m/z* 549 (M+Na$^+$). HRMS calcd for $C_{31}H_{50}O_3Si_2Na$ (M+Na$^+$): 549.3196; found: *m/z* 549.3191.

The diastereomeric ratios of **11** and **11′** were determined by chiral HPLC using DAICEL CHIRALCEL OD-H column. Eluant: hexane/2-propanol (98:2), flow rate: 0.5 mL/min, detection: 254 nm, retention time: 13.4 min (**11**, 1*R*-isomer) 19.7 min (**11′**, 1*S*-isomer).

4.5. (1*R*,5*S*,7*S*)- and (1*S*,5*S*,7*S*)-1,5,7-Trihydroxy-1,7-diphenyl-2-heptene (6a) and (6b)

A mixture of **11a** (32 mg, 0.06 mmol) and an excess of TBAF (0.9 mL of a 1.0 M solution in THF) were stirred in THF (1.5 mL) at room temperature for 3 h. The reaction mixture was diluted with water, and extracted with EtOAc. The organic extract was washed with brine and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluted with EtOAc to give **6a** (16.3 mg) in 90% yield. Colorless oil; $[\alpha]_D^{21}$ −29.6 (*c* 0.94, $CHCl_3$); R_f=0.2 (50% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.25 (m, 10H), 5.78–5.70 (m, 2H), 5.15 (m, 1H), 4.9 (dd, 1H, *J*=9.4, 3.3 Hz), 3.96 (m, 1H), 3.90–3.60 (br, 1H), 2.35–2.14 (m, 2H), 1.90–1.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2, 142.9, 136.0, 128.5, 128.4, 127.6, 127.5, 127.5, 126.1, 125.6, 75.0, 74.9, 71.6, 44.9, 40.8; IR (film, cm^{-1}) 3348, 2918, 1453, 1088; MS (FAB) *m/z* 321 (M+Na$^+$). HRMS calcd for $C_{19}H_{22}O_3Na$ (M+Na$^+$): 321.1467; found *m/z* 321.1461. Compound **6b** was obtained in 94% yield via **11b** by the same manner described for **6a**. Colorless oil; $[\alpha]_D^{21}$ −22.6 (*c* 0.53, $CHCl_3$); R_f=0.2 (50% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.24 (m, 10H), 5.78–5.72 (m, 2H), 5.12 (m, 1H), 4.85 (dd, 1H, *J*=9.5, 3.5 Hz), 3.93 (m, 1H), 2.23–2.16 (m, 2H), 1.86–1.71 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.1, 142.9, 135.7, 128.4, 127.5, 127.4, 127.1, 126.2, 126.1, 125.6, 74.7, 74.6, 71.6, 44.7, 40.3; IR (film, cm^{-1}) 3349, 2915, 1453, 1063; MS (FAB) *m/z* 321 (M+Na$^+$). HRMS calcd for $C_{19}H_{22}O_3Na$ (M+Na$^+$): 321.1467; found *m/z* 321.1458.

4.6. General procedure for Pd-catalyzed cyclization

A mixture of **6a**, **6b** or **17** (0.1 mmol) and 10 mol % of $PdCl_2(CH_3CN)_2$ (2.6 mg, 0.01 mmol) was stirred in dry THF (3.3 mL) at 0 °C for 20 min. Evaporation of the solvent and purification of the residue by column chromatography

on silica gel eluted with 10% EtOAc in hexane gave the corresponding tetrahydropyran.

4.6.1. Compound 5a. Compound **5a** was obtained in 92% yield from **6a**. White amorphous solid; $[\alpha]_D^{21}$ −6.5 (*c* 0.73, $CHCl_3$); R_f=0.6 (35% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.19 (m, 10H), 6.83 (d, 1H, *J*=16.0 Hz), 6.28 (dd, 1H, *J*=16.0, 5.9 Hz), 4.99 (dd, 1H, *J*=11.5, 2.5 Hz), 4.70 (m, 1H), 4.41 (quint, 1H, *J*=3.0 Hz), 1.98–1.75 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7, 137.0, 130.4, 130.2, 128.5, 128.3, 127.5, 127.4, 126.5, 126.0, 73.7, 72.6, 64.8, 40.5, 38.7; IR (film, cm^{-1}) 3320, 2948, 2853, 1450, 1060, 748; MS (FAB) *m/z* 303 (M+Na$^+$). HRMS calcd for $C_{19}H_{20}O_2Na$ (M+Na$^+$): 303.1361; found: *m/z* 303.1352.

4.6.2. Compound 5b. Compound **5b** was obtained from **6b** in 86% yield. White amorphous solid; $[\alpha]_D^{22}$ −82.8 (*c* 0.65, $CHCl_3$); R_f=0.48 (35% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48–7.21 (m, 10H), 6.66 (dd, 1H, *J*=15.9, 1.1 Hz), 6.39 (dd, 1H, *J*=15.9, 5.7 Hz), 5.30 (t, 1H, *J*=4.4 Hz), 4.28 (dddd, 1H, *J*=9.2, 5.7, 4.8, 1.1 Hz), 4.07 (dddd, 1H, *J*=9.2, 9.1, 4.4, 4.0 Hz), 2.54 (ddd, 1H, *J*=14.4, 4.4, 4.0 Hz), 2.09 (ddd, 1H, *J*=12.8, 4.8, 4.0 Hz), 1.96 (ddd, 1H, *J*=14.4, 9.1, 4.4 Hz), 1.63 (dt, 1H, *J*=12.8, 9.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6, 136.8, 130.5, 129.9, 128.6, 128.5, 127.6, 127.2, 126.5, 126.3, 72.0, 70.5, 64.6, 40.4, 36.9; IR (KBr, cm^{-1}) 3364, 2944, 1492, 1477, 1046, 968; MS (FAB) *m/z* 303 (M+Na$^+$). HRMS calcd for $C_{19}H_{20}O_2Na$ (M+Na$^+$): 303.1361; found: *m/z* 303.1352.

4.6.3. Compounds 18 and 19. Compound **17** gave **18** in 47% yield and **19** in 49% yield, after purification of the residue by column chromatography on silica gel eluted with 50% CH_2Cl_2 in hexane. Compound **18**: white amorphous solid; $[\alpha]_D^{23}$ −5.8 (*c* 1.00, $CHCl_3$); R_f=0.38 (CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.19 (m, 10H), 6.65 (d, 1H, *J*= 16.0 Hz), 6.29 (dd, 1H, *J*=16.0, 5.8 Hz), 4.47 (dd, 1H, *J*= 11.0, 1.5 Hz), 4.21 (ddt, 1H, *J*=11.2, 5.8, 1.5 Hz), 4.04 (dddd, 1H, *J*=11.0, 10.8, 6.4, 4.6 Hz), 2.26–2.14 (m, 2H), 1.68 (br s, 1H), 1.16–1.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.8, 136.7, 130.5, 129.5, 128.5, 128.4, 127.6(2C), 126.5, 126.0, 77.7, 76.4, 68.4, 42.8, 41.1; IR (film, cm^{-1}) 3321, 2923, 1450, 1058, 747; MS (FAB) *m/z* 303 (M+Na$^+$). HRMS calcd for $C_{19}H_{20}O_2Na$ (M+Na$^+$): 303.1361; found: *m/z* 303.1353. Compound **19**: light yellow amorphous solid; $[\alpha]_D^{24}$ −30.9 (*c* 1.05, $CHCl_3$); R_f=0.28 (CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$+TMS) δ 7.41–7.23 (m, 10H), 6.65 (dd, 1H, *J*=16.3, 1.8 Hz), 6.36 (dd, 1H, *J*=16.3, 4.2 Hz), 4.97 (m, 1H), 4.74 (dd, 1H, *J*=11.4, 2.2 Hz), 4.17 (dddd, 1H, *J*=11.2, 11.1, 6.6, 4.4 Hz), 2.27 (ddd, 1H, *J*=12.8, 4.2, 2.0 Hz), 2.17 (ddd, 1H, *J*=12.2, 4.4, 2.2 Hz), 1.88 (ddd, 1H, *J*=12.8, 11.2, 5.9 Hz), 1.69–1.62 (br, 1H), 1.62 (dd, 1H, *J*=12.2, 11.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.0, 136.5, 132.0, 129.2, 128.6, 128.4, 127.8, 127.6, 126.4, 126.0, 73.2, 71.8, 64.9, 43.2, 37.7; IR (film, cm^{-1}) 3314, 2922, 1671, 1449, 1051; MS (FAB) *m/z* 303 (M+Na$^+$). HRMS calcd for $C_{19}H_{20}O_2Na$ (M+Na$^+$): 303.1361; found: *m/z* 303.1354.

4.7. General procedure of Wacker oxidation

A mixture of alkene (0.05 mmol), $PdCl_2$ (4.4 mg, 0.025 mmol), and CuCl (7.4 mg, 0.075 mmol) in DMF (0.6 mL) and H_2O (0.6 mL) was stirred at 50 °C for 3 days under an oxygen atomosphere. Evaporation of the solvent under vacuo and purification of the residue by column chromatography on silica gel eluted with 20% EtOAc in hexane gave phenyl ketone.

4.7.1. Compound 1. Compound **1** was obtained from **5a** in 37% yield along with a recovery of **5a** in 50% yield. Colorless amorphous solid; $[\alpha]_D^{24}$ −21.4 (*c* 0.8, $CHCl_3$); R_f=0.35 (40% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (dd, 2H, *J*=7.5, 1.5 Hz), 7.55 (tt, 1H, *J*=7.1, 1.5 Hz) 7.45 (td, 2H, *J*=7.5, 1.3 Hz), 7.31–7.22 (m, 5H), 4.95 (dd, 1H, *J*=11.9, 2.0 Hz), 4.65 (dddd, 1H, *J*=11.5, 6.8, 5.8, 2.0 Hz), 4.37 (q, 1H, *J*=3.0 Hz), 3.41 (dd, 1H, *J*=15.9, 6.8 Hz), 3.06 (dd, 1H, *J*=15.9, 5.8 Hz), 1.97 (ddd, 1H, *J*=13.8, 3.0, 2.0 Hz), 1.94 (ddd, 1H, *J*=13.8, 3.0, 2.0 Hz), 1.76 (ddd, 1H, *J*=13.8, 11.9, 3.0 Hz), 1.75–1.67 (br, 1H), 1.68 (ddd, 1H, *J*=13.8, 11.5, 3.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3, 142.6, 137.3, 133.0, 128.5, 128.3, 128.2, 127.2, 126.8, 73.8, 66.0, 64.6, 45.1, 40.0, 38.4; IR (KBr, cm^{-1}) 3329, 2922, 1680, 1451, 1062; MS (EI) *m/z* 296 (M$^+$). HRMS calcd for $C_{19}H_{20}O_3$ (M$^+$): 296.1412; found: *m/z* 296.1414. Under a microwave in sealed tube at 70 °C for 4 h, the reaction of **5a** gave **1** in 56% yield and 27% recovery of **5a**.

4.7.2. Compound 14. Compound **14** was obtained from **13** in 55% yield along with a recovery of **13** in 35% yield. Colorless oil; $[\alpha]_D^{21}$ 28.9 (*c* 0.79, $CHCl_3$); R_f=0.24 (15% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (dd, 2H, *J*=7.2, 1.8 Hz), 7.57 (tt, 1H, *J*=7.7, 1.9 Hz), 7.46 (t, 2H, *J*=7.5 Hz), 7.36–7.22 (m, 5H), 5.16 (t, 1H, *J*=4.4 Hz), 4.70 (s, 2H), 4.24 (dddd, 1H, *J*=9.4, 7.1, 5.8, 3.1 Hz), 3.91 (dddd, 1H, *J*=9.7, 9.4, 4.3, 3.8 Hz), 3.44 (dd, 1H, *J*=15.9, 7.1 Hz), 3.38 (s, 3H), 3.21 (dd, 1H, *J*=15.9, 5.8 Hz), 2.52 (ddd, 1H, *J*=13.4, 4.4, 3.8 Hz), 2.10 (ddd, 1H, *J*=12.8, 3.8, 3.12 Hz), 1.98 (ddd, 1H, *J*=13.4, 9.7, 4.9 Hz), 1.59 (dt, 1H, *J*=12.8, 9.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.2, 140.3, 137.0, 133.1, 128.6, 128.5, 128.2, 127.1, 126.3, 94.9, 72.3, 69.5, 67.1, 55.3, 44.6, 37.5, 34.4; IR (film, cm^{-1}) 2929, 1685, 1448, 1037, 754; MS (FAB) *m/z* 341 (M+H$^+$). HRMS calcd for $C_{21}H_{25}O_4$ (M+H$^+$): 341.1753; found: *m/z* 341.1745.

4.7.3. Compound 3. Compound **3** was obtained from **18** in 63% yield along with a recovery of **18** in 17% yield. White amorphous solid; $[\alpha]_D^{25}$ −11.6 (*c* 0.54, $CHCl_3$); R_f=0.23 (30% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, 2H, *J*=7.2 Hz), 7.53 (t, 1H, *J*=7.3 Hz), 7.46 (t, 2H, *J*=7.5 Hz), 7.35–7.17 (m, 5H), 4.39 (dd, 1H, *J*=11.5, 1.8 Hz), 4.15 (dddd, 1H, *J*=11.2, 6.6, 6.0, 4.8 Hz), 4.02 (dddd, 1H, *J*=11.0, 10.8, 6.4, 4.4 Hz), 3.46 (dd, 1H, *J*=16.5, 6.0 Hz), 3.08 (dd, 1H, *J*=16.5, 6.6 Hz), 2.22–2.17 (m, 2H), 1.59 (br, 1H), 1.54–1.22 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0, 141.7, 137.2, 133.2, 128.5, 128.3, 128.2, 127.5, 125.9, 77.5, 72.5, 68.2, 44.8, 42.5, 40.9; IR (film, cm^{-1}) 3408, 2920, 1684, 1449, 1063, 754; MS (FAB) *m/z* 297 (M+H$^+$). HRMS calcd for $C_{19}H_{21}O_3$ (M+H$^+$): 297.1491; found: *m/z* 297.1496.

4.7.4. Compound 4. Compound **4** was obtained from **19** in 57% yield along with a recovery of **19** in 25% yield. Amorphous solid; $[\alpha]_D^{25}$ 9.0 (*c* 0.39, $CHCl_3$); R_f=0.19 (30% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, 2H, *J*=7.3 Hz), 7.58 (t, 1H, *J*=7.5 Hz), 7.47 (t, 2H, *J*=7.7 Hz), 7.35–7.26 (m, 5H), 4.89 (m, 1H), 4.74 (dd,

1H, J=10.8, 2.5 Hz), 4.23 (dddd, 1H, J=10.6, 10.2, 5.9, 4.4 Hz), 3.49 (dd, 1H, J=15.4, 6.2 Hz), 3.32 (dd, 1H, J=15.4, 7.8 Hz), 2.25 (dm, 1H, J=12.8 Hz), 2.08 (dm, 1H, J=13.2 Hz), 1.83 (ddd, 1H, J=13.2, 10.6, 5.5 Hz), 1.69 (dd, 1H, J=12.7, 10.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 141.6, 136.9, 133.3, 128.7, 128.4, 128.2, 127.6, 126.1, 71.8, 69.7, 64.7, 41.9, 41.3, 37.6; IR (film, cm^{-1}) 3398, 2924, 1718, 1495, 1055, 749; MS (FAB) m/z 297 (M+H$^+$). HRMS calcd for $C_{19}H_{21}O_3$ (M+H$^+$): 297.1491; found: m/z 297.1483.

4.8. The reaction of 5b under the Wacker oxidation conditions

A mixture of **5b** (12 mg, 0.042 mmol), $PdCl_2$ (3.8 mg, 0.021 mmol), and CuCl (6.4 mg, 0.064 mmol) in DMF (0.8 mL) and H_2O (0.8 mL) was stirred at 50 °C for 5 h under an oxygen atmosphere. Evaporation of the solvent and purification of the residual oil by column chromatography on silica gel eluted with 10% EtOAc in hexane gave **12** (9.8 mg) in 82% yield. White amorphous solid; $[\alpha]_D^{25}$ −165.1(c 0.51, $CHCl_3$); R_f=0.73 (25% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, 2H, J=7.1 Hz), 7.40–7.27 (m, 7H), 7.16 (t, 1H, J=7.3 Hz), 5.63 (s, 1H), 5.08 (t, 1H, J=5.0 Hz), 5.02 (dd, 1H, J=10.9, 4.1 Hz), 4.81 (m, 1H), 2.22 (dm, 1H, J=13.5 Hz), 2.15 (d, 1H, J=11.5 Hz), 2.08 (m, 1H), 1.81 (dd, 1H, J=13.5, 11.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6, 135.8, 128.4, 128.3, 128.1, 127.7, 126.1, 125.9, 101.0, 78.4, 77.8, 77.2, 72.5, 39.9, 38.4; MS (EI) m/z 278 (M$^+$). HRMS calcd for $C_{19}H_{18}O_2$ (M$^+$): 278.1307; found: m/z 278.1298.

4.9. Preparation of 13

To the stirred solution of **5b** (30 mg, 0.107 mmol) in THF (2 mL) was added *N,N*-diisopropylethylamine (0.112 mL, 0.642 mmol), MOMCl (0.064 mL, 0.856 mmol), and sodium iodide (19.2 mg, 0.128 mmol) at room temperature. The mixture was heated at 50 °C for 10 h. After the solvent was removed under vacuum, the reaction mixture was diluted with water and extracted with EtOAc. The extract was washed with brine and dried over $MgSO_4$. Evaporation of the solvent and purification of the residual oil by column chromatography on silica gel eluted with 10% EtOAc in hexane gave **13** (30 mg) in 86% yield. Colorless oil; $[\alpha]_D^{22}$ −24.1 (c 0.9, $CHCl_3$); R_f=0.44 (15% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47–7.21 (m, 10H), 6.64 (d, 1H, J=15.9 Hz), 6.38 (dd, 1H, J=15.9, 5.9 Hz), 5.29 (t, 1H, J=4.4 Hz), 4.74 (s, 2H), 4.26 (ddd, 1H, J=9.4, 5.9, 4.6 Hz), 3.96 (dddd, 1H, J=9.7, 9.3, 4.0, 3.8 Hz), 3.41 (s, 3H), 2.55 (ddd, 1H, J=13.4, 4.0, 3.8 Hz), 2.10 (ddd, 1H, J=12.7, 4.6, 4.0 Hz), 2.04 (ddd, 1H, J=13.4, 9.7, 5.1 Hz), 1.70 (dt, 1H, J=12.7, 9.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6, 136.8, 130.4, 129.9, 128.6, 128.5, 127.5, 127.1, 126.4, 126.3, 94.9, 72.2, 70.7, 69.7, 55.4, 37.8, 34.5; IR (KBr, cm^{-1}) 2927, 1448, 1037; MS (FAB) m/z 347 (M+Na$^+$). HRMS calcd for $C_{21}H_{24}O_3Na$ (M+Na$^+$): 347.1623; found: m/z 347.1616.

4.10. Preparation of 2

A mixture of **14** (19 mg, 0.056 mmol) and 30% HCl (1 mL) was stirred in THF (3 mL) at room temperature overnight. Then, water was added to the mixture and the reaction mixture was neutralized with aq $NaHCO_3$ and extracted with EtOAc. The organic extract was washed with 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 gave **2** (15 mg) in 91% yield. Colorless amorphous solid; $[\alpha]_D^{25}$ −22.5 (c 0.6, $CHCl_3$); R_f=0.25 (40% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (dd, 2H, J=7.7, 1.5 Hz), 7.57 (tt, 1H, J=7.2, 1.5 Hz), 7.45 (td, 2H, J=7.7, 1.5 Hz), 7.38–7.21 (m, 5H), 5.19 (t, 1H, J=4.2 Hz), 4.23 (dddd, 1H, J=9.5 6.9, 5.8, 3.0 Hz), 4.02 (dddd, 1H, J=9.7, 9.5, 5.1, 3.8 Hz), 3.45 (dd, 1H, J=15.8, 6.9 Hz), 3.19 (dd, 1H, J=15.8, 5.8 Hz), 2.51 (ddd, 1H, J=13.2, 4.2, 3.8 Hz), 2.05 (ddd, 1H, J=12.4, 5.1, 3.0 Hz), 1.92 (ddd, 1H, J=13.2, 9.7, 4.2 Hz), 1.50 (dt, 1H, J=12.4, 9.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4, 140.2, 137.2, 133.2, 128.6, 128.5, 128.3, 127.1, 126.3, 72.3, 67.0, 64.2, 44.6, 40.1, 36.7; IR (KBr, cm^{-1}) 3327, 2920, 1680, 1451, 1062; MS (FAB) m/z 297 (M+H$^+$). HRMS calcd for $C_{19}H_{21}O_3$ (M+H$^+$): 297.1491; found: m/z 297.1483.

4.10.1. (5*R*,7*S*)-7-(*tert*-Butyldimethylsilyl)oxy-5-hydroxy-1,7-diphenyl-2-hepten-1-one (15). Compound **8′** gave **15** in 72% yield by the same two-step procedure described for **10**. Colorless oil; $[\alpha]_D^{22}$ −36.6 (c 1.01, $CHCl_3$); R_f=0.52 (20% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (dd, 2H, J=7.0, 1.6 Hz), 7.5 (t, 1H, J=7.2 Hz), 7.45 (t, 2H, J=7.5 Hz), 7.36–7.28 (m, 5H), 6.99 (dt, 1H, J=15.4, 6.8 Hz), 6.85 (d, 1H, J=15.4 Hz), 5.11 (m, 1H), 3.99 (m, 1H), 2.52–2.35 (m, 2H), 1.91 (ddd, 1H, J=14.2, 9.6, 5.2 Hz), 1.83 (ddd, 1H, J=14.2, 5.6, 2.4 Hz), 0.92 (s, 9H), 0.08 (s, 3H), −0.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.6, 145.6, 143.7, 137.7, 132.6, 128.5, 128.4, 128.2, 127.9, 127.2, 125.6, 73.4, 67.0, 45.5, 40.9, 25.7, 18.1, −4.8, −5.3; IR (film, cm^{-1}) 3458, 3027, 2929, 1669, 1620, 1256, 836; MS (FAB) m/z 433 (M+Na$^+$). HRMS calcd for $C_{25}H_{34}O_3SiNa$ (M+Na$^+$): 433.2175; found: m/z 433.2183.

4.10.2. A mixture of (1*R*,5*R*,7*S*)- and (1*S*,5*R*,7*S*)-7-(*tert*-butyldimethylsilyl)oxy-1,5-dihydroxy-1,7-diphenyl-2-heptene (16). To a stirred solution of **15** (140 mg, 0.34 mmol) in methanol (3.2 mL) were added $CeCl_3\cdot 7H_2O$ (159 mg, 0.43 mmol) and $NaBH_4$ (18 mg, 0.47 mmol) at 0 °C. After the addition, reaction mixture was warmed up to room temperature and stirred for 2 h. The mixture was quenched with 0.5 N HCl (20 mL) and extracted with EtOAc. The 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 50% EtOAc in hexane gave **16** (128 mg) as a 1:1 diastereomeric mixture in 91% yield. Colorless oil; R_f=0.19 (20% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.17 (m, 10H), 6.40 (d, 1H, J=14.8 Hz), 6.19–6.08 (m, 1H), 5.07 (m, 1H), 4.56 (m, 1/2H), 4.46 (m, 1/2H), 4.12–4.01 (m, 1H), 2.04–1.65 (m, 4H), 0.88 (d, 9H), −0.05 (d, 3H), −0.13 (d, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7 (1/2C), 143.6 (1/2C), 136.9 (1/2C), 136.8 (1/2C), 132.1 (1/2C), 132.0 (1/2C), 129.6 (1/2C), 129.4 (1/2C), 128.4, 128.2 (1/2C), 128.1 (1/2C), 127.4, 127.2 (1/2C), 127.1 (1/2C), 126.4, 125.6 (1/2C), 125.6 (1/2C), 73.7 (1/2C), 73.6 (1/2C), 72.9 (1/2C), 70.1 (1/2C), 69.3 (1/2C),

66.1 (1/2C), 46.1 (1/2C), 45.5 (1/2C), 43.8 (1/2C), 42.9 (1/2C), 25.8 (3C), 18.1, −4.8, −5.2 (1/2C), −5.3 (1/2C); IR (film, cm^{-1}) 3415, 2928, 2856, 1255, 1065, 836, 778; MS (FAB) *m/z* 435 ($M+Na^+$). HRMS calcd for $C_{25}H_{36}O_3SiNa$ ($M+Na^+$): 435.2332; found: *m/z* 435.2327.

4.10.3. Preparation of triol 17. To a solution of **16** (115 mg, 0.28 mmol) in THF (4 mL) was added TBAF (2.2 mL of a 1.0 M solution in THF, 2.2 mmol) at room temperature. The reaction mixture was stirred for 1 h. After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluted with 80% EtOAc in hexane to give **17** (80 mg) in 96% yield. Colorless oil; R_f=0.22 (50% EtOAc in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.23 (m, 10H), 6.60 (d, 1/2H, *J*=15.8 Hz), 6.57 (d, 1/2H, *J*=15.8 Hz), 6.25 (dd, 1/2H, *J*=15.8, 5.9 Hz), 6.00 (d, 1/2H, *J*=15.8, 5.9 Hz), 5.09–5.05 (m, 1H), 4.65 (m, 1/2H), 4.54 (m, 1/2H), 4.29–4.22 (m, 1H), 3.90–3.60 (br, 3H), 2.13–1.65 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4, 136.6 (1/2C), 136.5 (1/2C), 131.7 (1/2C), 131.6 (1/2C), 130.1 (1/2C), 130.0 (1/2C), 128.6 (1/2C), 128.5 (1/2C), 128.4 (1/2C), 128.4 (1/2C), 127.7 (1/2C), 127.6 (1/2C), 127.4 (1/2C), 127.3 (1/2C), 126.5, 125.6 (1/2C), 125.5 (1/2C), 73.6 (1/2C), 71.6 (1/2C), 71.5 (1/2C), 70.4 (1/2C), 70.0 (1/2C), 66.5 (1/2C), 45.0 (1/2C), 44.8 (1/2C), 42.9 (1/2C), 42.5 (1/2C); IR (film, cm^{-1}) 3365, 2926, 1493, 1059; MS (FAB) *m/z* 321 ($M+Na^+$). HRMS calcd for $C_{19}H_{22}O_3Na$ ($M+Na^+$): 321.1467; found: *m/z* 321.1461.

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