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STEREOSELECTIVE APPROACH TOWARD OPHIODILACTONES BASED ON AN INTRAMOLECULAR [2 + 2] CYCLOADDITION REACTION[†]

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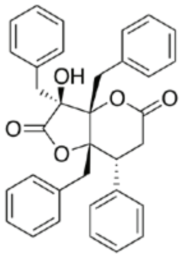
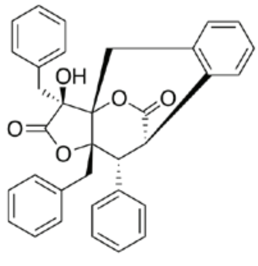
Abstract – The highly enantio- and diastereoselective synthesis of a promising precursor of ophiodilactones A and B, tetrameric phenylpropanoids isolated from the ophiuroid *Ophiocoma scolopendrina*, is described. The synthesis involves an organocatalytic asymmetric Michael reaction, intramolecular [2 + 2] cycloaddition of a ketene to an alkene, Baeyer-Villiger oxidation, and construction of the C2 quaternary center as major transformations.

INTRODUCTION

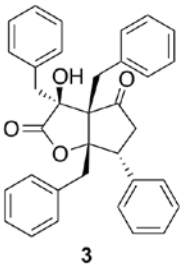
Ophiodilactones A (**1**) and B (**2**) are new tetrameric phenylpropanoids isolated from *Ophiocoma scolopendrina*, a tropical and subtropical ophiuroid widely distributed in the Indo-Pacific, and exhibit moderate cytotoxic activity against P388 murine leukemia cells with IC_{50} values of 5.0 and 2.2 μgmL^{-1}, respectively.[1] These compounds possess characteristic compact structures consisting of a fused γ-lactone/δ-lactone skeleton with four phenyl groups and four or five contiguous stereogenic centers containing three quaternary centers. Their unique highly substituted dilactone structures and biological activities prompted us to investigate the synthesis of ophiodilactones,[2] resulting in our recent achievement of the first total synthesis.[3] During that time, we also studied an alternative approach based on intramolecular [2 + 2] cycloaddition of a ketene to an alkene.



ophiodilactone A (**1**)



ophiodilactone B (**2**)



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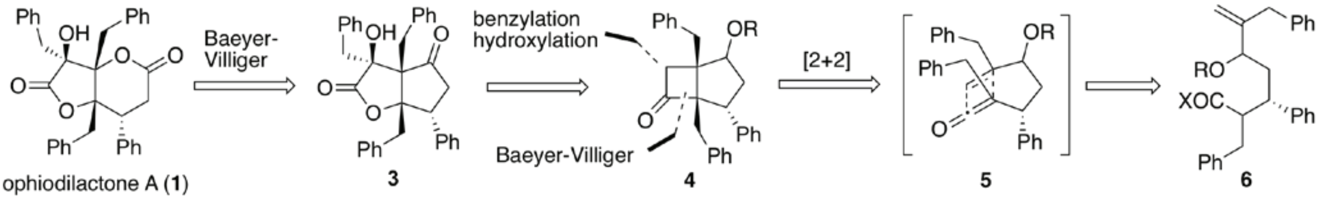
[†] Dedicated with respect to Professor Isao Kuwajima on the occasion of his 77th birthday

We report here the highly stereoselective synthesis of keto lactone **3**, a promising precursor of ophiodilactones.

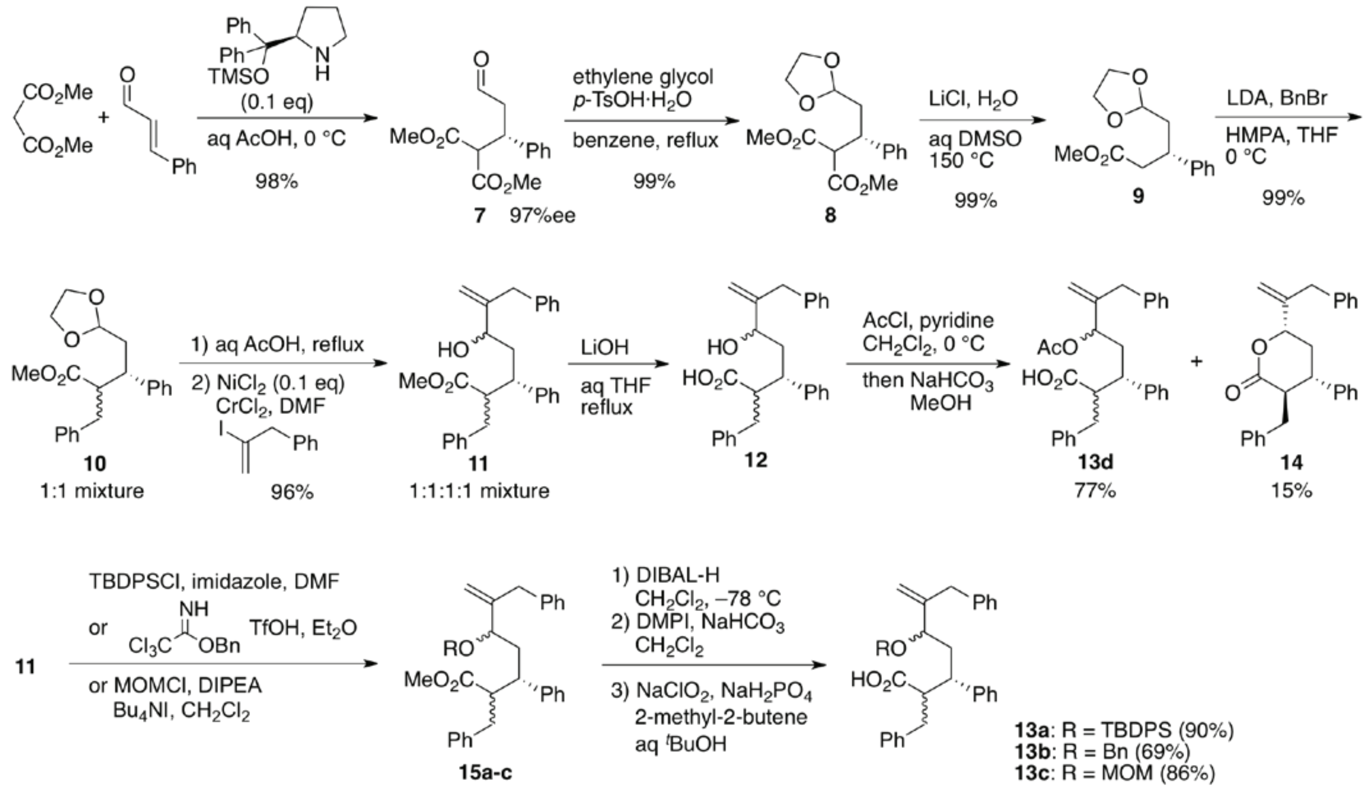
RESULTS AND DISCUSSION

Ophiodilactone A (**1**) can be directly transformed to ophiodilactone B (**2**) by $Cu(OAc)_2$-mediated radical cyclization.[3] We therefore focused on the synthesis of **1**. Based on a Baeyer-Villiger oxidation, we envisioned ketone **3** as a precursor which would be accessible from cyclobutanone **4** through another Baeyer-Villiger oxidation and stereoselective benzylation followed by hydroxylation by taking advantage of the rigid bicylic skeleton. To access **4** we considered intramolecular [2 + 2] cycloaddition of ketene **5** which could be in situ generated from **6**. Although such cycloaddition reactions are well documented,[4] the reactions giving products with four contiguous stereogenic centers involving two adjacent quaternary centers at junctures have been rarely investigated.[5] One of key issues of this approach is therefore the feasibility and diastereoselectivity of the [2 + 2] cycloaddition step.



Scheme 1. Retrosynthetic analysis of ophiodilactone A

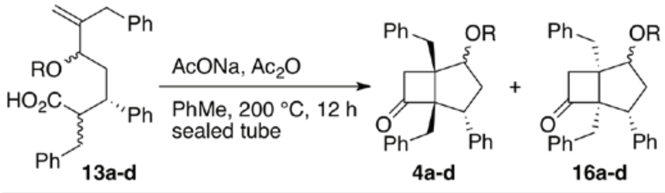
Scheme 2 illustrates the synthesis of the compounds corresponding to **6**. Thus, organocatalytic asymmetric Michael addition[6] of dimethyl malonate to cinnamaldehyde afforded aldehyde **7** of 97% ee in 98% yield. Acetalization of **7** and Krapcho decarboxylation[7] of **8** gave **9**, which was then benzylated in the presence of lithium diisopropylamide to provide ester **10** as a 1:1 epimeric mixture in excellent overall yield. After acidic hydrolysis of **10**, the resulting aldehyde was directly subjected to Nozaki-Hiyama-Kishi reaction[8] with (2-iodoallyl)benzene[9] to afford alcohol **11** as an inseparable 1:1:1:1 diastereoisomeric mixture. For the next [2 + 2] cycloaddition, we then attempted to prepare TBDPS ether **13a**, Bn ether **13b**, and MOM ether **13c** by protection of the hydroxy group followed by saponification. However, the protected compounds **15a-c** turned out to be unexpectedly stable under saponification conditions and no reactions occurred. Compounds **13a-c** were eventually obtained by a three-step sequence involving DIBAL-H reduction, Dess-Martin oxidation, and Pinnick-Kraus oxidation in good overall yields. On the other hand, **11** underwent saponification without difficulty to give carboxylic acid **12**, which was acetylated to provide acetate **13d** and δ-lactone **14** in 77% and 15% yields, respectively. The ^1H NMR spectrum revealed **14** to be a single stereoisomer with all equatorial substituents.



Scheme 2. Synthesis of carboxylic acids **13a-d**

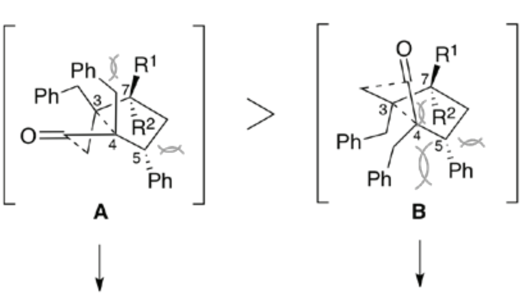
The crucial [2 + 2] cycloaddition was then examined with four carboxylic acids **13a-d**. When the acid chlorides, prepared from **13a-d** using oxalyl chloride, were treated with triethylamine in boiling toluene, the desired cycloaddition products were not produced at all. On the other hand, as seen in Table 1, when **13a-d** were heated in acetic anhydride[10] in the presence of NaOAc at 200 °C for 12 h, cycloadditions of the ketenes, in situ generated from the corresponding mixed anhydrides, took place to provide the cyclized products.[11] Among the substrates examined, acetoxy derivative **13d** gave the most satisfying result and **4d** was obtained as a 1.7:1 mixture in 91% yield (entry 4).

Table 1. [2 + 2] Cycloaddition reactions



Entry	Substrate	Yield (%)^a (α:β)^b 4a-d	16a-d
1	**13a** (R = TBDPS)	49 (1:2.3)	11 (β only)
2	**13b** (R = Bn)	36 (1:1.8)	7 (β only)
3	**13c** (R = MOM)	66 (1:2.0)	0
4	**13d** (R = Ac)	91 (1.7:1)	0

^{a} Isolated yield. ^{b} The ratio was determined by ^{1}H NMR.

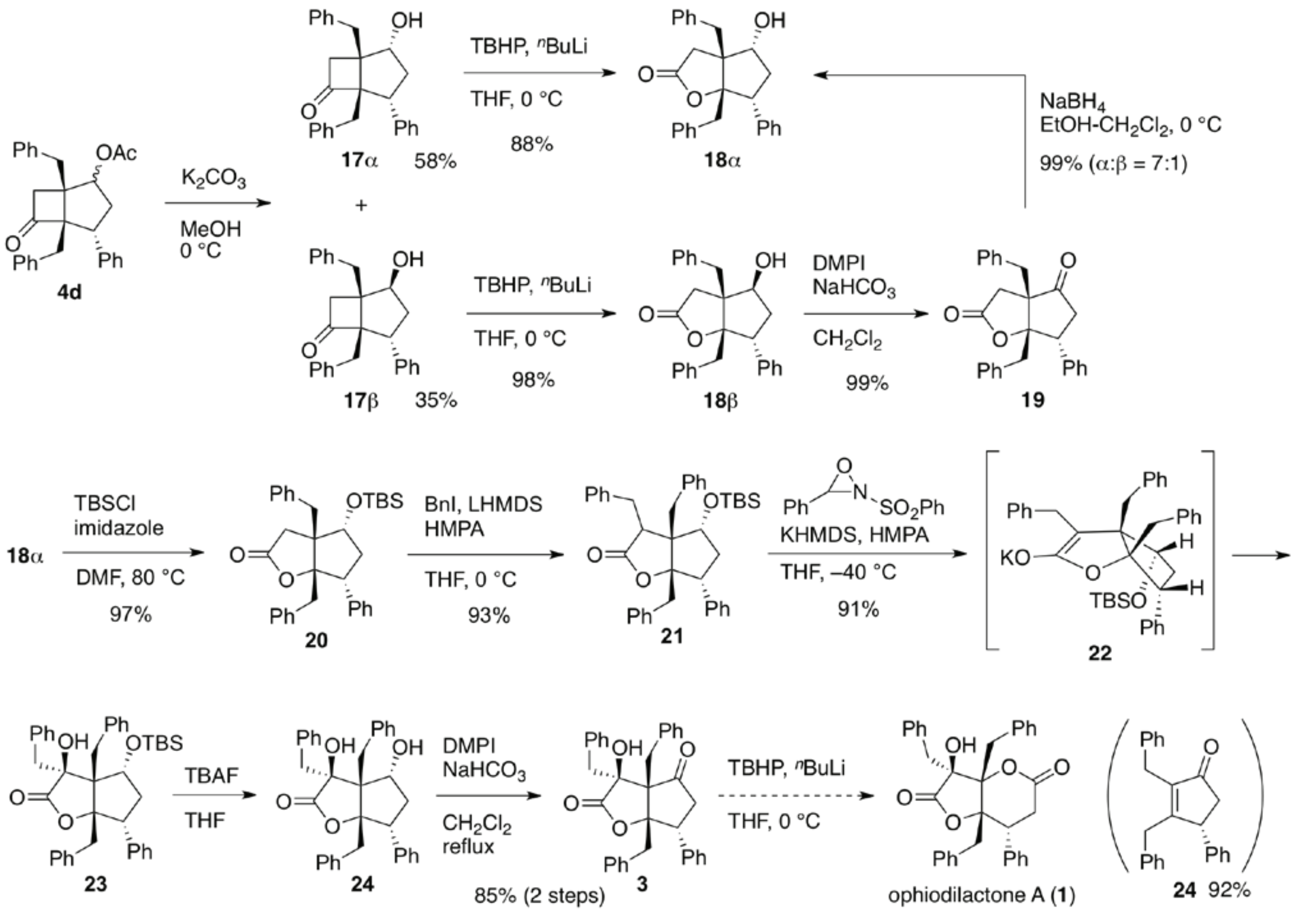


4a-d α: R^1 = H, R^2 = OR
4a-d β: R^1 = OR, R^2 = H

16a-d α: R^1 = H, R^2 = OR
16a-d β: R^1 = OR, R^2 = H

The stereochemical outcomes can be explained by assuming transition states **A** and **B**,[12] the latter of which would be largely disfavored by the steric repulsion between the C4 benzyl and C5 phenyl groups. However, as OR group on the C7 position is bulkier, the energy difference between **A** and **B** becomes smaller leading to the formation of **16β** as well as **4α** and **4**β because the steric interactions between C7 and C3 substituents become serious (entries 1 and 2).

With the desired cyclobutanone **4d** in hand, we then attempted to synthesize ophiodilactone A (**1**) starting from the Baeyer-Villiger oxidation[13] (Scheme 3). Methanolysis of **4d** afforded **17α** and **17β** in 58% and 35% yields, respectively. Baeyer-Villiger oxidation of **17α** was first examined using *m*CPBA under various conditions but no reaction occurred. However, we gratifyingly found that when **17α** was treated with lithium *tert*-butyl peroxide in THF at 0 °C, γ-lactone **18α** was obtained in 88% yield. This procedure again effectively worked for **17β** to produce γ-lactone **18β** in 98% yield, which was converted to **18α** via **19** by Dess-Martin oxidation followed by $NaBH_4$ reduction in good yield. At this stage, the stereostructure of **18α** was confirmed by its X-ray crystallographic analysis.[14] After protection of the hydroxy group of **18α** as its TBS ether **20**, the stereoselective introduction of benzyl and hydroxy groups at the C2 position was then examined.



Scheme 3. Synthesis of keto lactone **3**

Thus, the lithium enolate generated from **20** was reacted with benzyl iodide in THF-HMPA at 0 °C afforded benzylated compound **21** in 93% yield. Compound **21** was then converted to the potassium enolate and reacted with the Davis reagent[15] in THF-HMPA at –40 °C to cleanly give alcohol **23** as a single diastereoisomer in 91% yield. The observed high stereoselectivity can be explained by the convex face attack of the Davis reagent to enolate **22**. Successive desilylation of **23** and Dess-Martin oxidation of **24** gave keto lactone **3**, the stereostructure of which was confirmed by the X-ray analysis of its acetate.[16] The final Baeyer-Villiger oxidation was then examined using lithium *tert*-butyl peroxide as mentioned for the oxidation of **17α**. However, ophiodilactone A (**1**) was not produced but cyclopentenone **25** was formed by base-promoted retro-aldol followed by E1cb elimination. After protection of the hydroxy group of **24** as its acetate and MOM ether, their Baeyer-Villiger oxidations were also examined but no reaction occurred possibly for steric reasons.

In conclusion, we have developed a highly enantio- and diastereoselective route to keto lactone **3**, a promising precursor of ophiodilactones A (**1**) and B (**2**), which proceeds through an organocatalytic Michael addtion, intramolecular [2 + 2] cycloaddition, Baeyer-Villiger oxidation, and stereoselective construction of the C2 quaternary center by benzylation followed by hydroxylation. The remaining task toward the total synthesis of ophiodilactone A (**1**) is the only construction of the δ-lactone ring structure, which is currently under investigation.

EXPERIMENTAL

Where appropriate, reactions were performed in flame-dried glassware under argon atmosphere. All extracts were dried over $MgSO_4$ and concentrated by rotary evaporation below 30 °C at 25 Torr unless otherwise noted. Commercial reagents and solvents were used as supplied with following exceptions. Benzene, *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), dichloromethane (CH_2Cl_2), ethyl acetate (AcOEt), hexamethyldisilazane (HMDS), hexamethylphosphoric triamide (HMPA), hexane, toluene, and triethylamine were distilled from CaH_2. Thin layer chromatography (TLC) was performed using precoated silica gel plates (0.2 or 0.5 mm thickness). Column chromatography was performed using silica gel (particle size 100-210 mm (regular), 40-50 mm (flash)). Optical rotations were recorded on a digital polarimeter at ambient temperature. Infrared spectra were measured on a Fourier transform infrared spectrometer. ^{1}H NMR (400 and 500 MHz) and ^{13}C NMR (100 and 125 MHz) spectra were measured using $CDCl_3$ or CD_3OD as solvent, and chemical shifts are reported as δ values in ppm based on internal $CHCl_3$ (7.26 ppm, ^{1}H; 77.0 ppm, ^{13}C), MeOH (3.31 ppm, ^{1}H; 49.2 ppm, ^{13}C). MS and HRMS spectra were taken in EI or FAB mode.

(*S*)-Dimethyl 2-(3-Oxo-1-phenylpropyl)malonate (7). To an ice-cooled solution of cinnamaldehyde (264 mg, 2.0 mmol), (*R*)-2-(diphenyl((trimethylsilyl)oxy)methyl)pyrrolidine (32 mg, 0.10 mmol), and acetic acid (12 μL, 0.20 mmol) in H_2O (0.5 mL) was added dimethyl malonate (132 mg, 1.0 mmol). After being stirred at 0 °C for 1 day, the mixture was diluted with AcOEt, washed with saturated $NaHCO_3$ and brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 10 g, hexane/AcOEt = 5:1) gave **7** (258 mg, 98%) as a yellow oil: $[\alpha]_D^{26}$ +32.1 (*c* 0.850, $CHCl_3$) (lit.[17] $[\alpha]_D^{23}$ +29.8 (c. 0.56, $CHCl_3$), 97% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.31-7.20 (m, 5H), 4.06-4.00 (m, 1H), 3.76-3.74 (m, 4H), 3.50 (s, 3H), 2.93-2.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 168.3, 167.8, 139.7, 128.7, 127.9, 127.5, 57.2, 52.7, 52.4, 47.2, 39.4; FTIR (neat) 2954, 1755, 1740, 1725, 1435, 1254 cm^{-1}; MS (EI) *m/z* 43 (100), 105, 132, 236, 264 (M^+); HRMS (EI) calcd for $C_{14}H_{16}O_5$ (M^+) 264.0987, found 264.0998; HPLC: 97% ee, Chiralcel OJ-H, hexane/*i*-PrOH = 7:3, 25 °C, 5 μL, 1.0 mL/min, 210 nm, t_R = 12.6 min (minor), t_R = 16.3 min (major).

(*S*)-Dimethyl (2-(1,3-Dioxolan-2-yl)-1-phenylethyl)malonate (8). A solution of **7** (150 mg, 0.570 mmol), ethylene glycol (0.317 mL, 5.70 mmol), and *p*-toluenesulfonic acid (1 mg, 0.0057 mmol) in benzene (3 mL) was heated under reflux using a Dean-Stark apparatus for 7 h. The mixture was cooled to room temperature, diluted with AcOEt, washed with saturated $NaHCO_3$ and brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 8 g, hexane/AcOEt = 4:1) gave **8** (173 mg, 99%) as a yellow oil: $[\alpha]_D^{26}$ –9.1 (*c* 0.950, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.19 (m, 5H), 4.51 (dd, *J* = 7.5, 2.8 Hz, 1H), 3.95-3.87 (m, 2H), 3.76-3.64 (m, 7H), 3.44 (s, 3H), 2.12 (td, *J* = 12.1 Hz, 2.7 Hz, 1H), 1.97-1.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 167.9, 140.0, 128.4, 128.2, 127.1, 102.4, 64.7, 64.6, 58.1, 52.6, 52.2, 41.5, 37.8; FTIR (neat) 2954, 1736, 1435, 1250, 1138 cm^{-1}; MS (EI) *m/z* 73 (100), 169, 230, 308 (M^+); HRMS (EI) calcd for $C_{16}H_{20}O_6$ (M^+) 308.1252, found 308.1244.

(*S*)-Methyl 4-(1,3-Dioxolan-2-yl)-3-phenylbutanoate (9). A solution of **8** (2.50 g, 8.11 mmol), LiCl (687 mg, 16.2 mmol), and H_2O (0.146 mL, 8.11 mmol) in DMSO (80 mL) was heated at 150 °C for 7 h. The mixture was cooled to room temperature, diluted with Et_2O, washed with saturated NH4Cl and brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 100 g, hexane/AcOEt = 4:1) gave **9** (2.00 g, 99%) as a yellow oil: $[\alpha]_D^{26}$ –15.1 (*c* 0.600, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.18 (m, 5H), 4.62 (dd, *J* = 6.8, 3.4 Hz, 1H), 3.97-3.90 (m, 2H), 3.81-3.73 (m, 2H), 3.57 (s, 3H), 3.42-3.35 (m, 1H), 2.75 (dd, *J* = 15.4, 6.8 Hz, 1H), 2.62 (dd, *J* = 15.4, 8.3 Hz, 1H), 2.08-2.02 (m, 1H), 1.97-1.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 143.2, 128.5, 127.4, 126.7, 102.8, 64.8, 64.7, 51.5, 41.4, 40.0, 38.0; FTIR (neat) 2952, 1738, 1140, 1030 cm^{-1}; MS (EI) *m/z* 43, 73 (100), 104, 172, 250 (M^+); HRMS (EI) calcd for $C_{14}H_{18}O_4$ (M^+) 250.1202, found 250.1205.

(2*RS*,3*S*)-Methyl 2-Benzyl-4-(1,3-dioxolan-2-yl)-3-phenylbutanoate (10) (1:1 mixture). To a solution of diisopropylamine (1.2 mL, 8.40 mmol) was added *n*-butyllithium (2.69 M in hexane, 3.0 mL, 8.00 mmol) at –78 °C, and the mixture was stirred at 0 °C for 15 min. HMPA (2.8 mL, 16.0 mmol) was added and the mixture was stirred at 0 °C for 15 min. This mixture was cooled to –78 °C and a solution of **9**

(1.00 g, 4.00 mmol) in THF (15 mL) was added and then benzyl bromide (0.52 mL, 4.40 mmol) was added after stirring at –78 °C for 1 h. The mixture was warmed to 0 °C and stirred for 4 h. The reaction was quenched with saturated NH_4Cl (4 mL) and the mixture was extracted with AcOEt. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 120 g, hexane/AcOEt = 4:1) to give **10** (1.35 g, 99%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.11 (m, 9H), 6.98-6.96 (m, 1H), 4.55 (dd, *J* = 6.0, 4.0 Hz, 0.5 x 1H), 4.44 (dd, *J* = 7.9, 2.5 Hz, 0.5 x 1H), 3.94-3.85 (m, 2H), 3.80-3.67 (m, 2H), 3.55 (s, 0.5 x 3H), 3.24 (s, 0.5 x 3H), 3.15 (td, *J* = 11.0, 3.2 Hz, 1H), 3.03-2.86 (m, 2H), 2.67 (dd, *J* = 13.4, 11.5 Hz, 0.5 x 1H), 2.49 (dd, *J* = 13.6, 3.8 Hz, 0.5 x 1H), 2.20-2.09 (m, 1.5H), 1.82-1.76 (m, 0.5 x 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 173.9, 141.4, 139.2, 128.8,128.5, 128.3, 128.3, 128.3, 128.2, 128.2, 127.0,126.8, 126.3, 126.2, 102.7, 102.6, 64.8, 64.7, 64.7, 64.7, 54.8, 54.3, 51.4, 51.0, 44.6, 44.3, 38.6, 37.2, 37.1, 36.3; FTIR (neat) 2950, 1732, 1139 cm^{-1}; MS (EI) *m/z* 43 (100), 73, 163, 262, 340 (M^+); HRMS (EI) calcd for $C_{21}H_{24}O_4$ (M^+) 340.1676, found 340.1677.

(2*RS*,3*S*,5*RS*)-Methyl 2,6-Dibenzyl-5-hydroxy-3-phenylhept-6-enoate (11) (1:1:1:1 mixture). A solution of **9** (13.5 g, 39.7 mmol) in 50% aq acetic acid (120 mL) was heated at 90 °C for 16 h. The mixture was cooled to room temperature and extracted with AcOEt. The extract was washed with saturated $NaHCO_3$ and brine, dried, and concentrated to give the correspondingaldehyde (12.0 g), which was used for the next reaction without purification.

Crude aldehyde (12.0 g) and (2-iodoallyl)benzene[9] (12.6 g, 51.6 mmol) were dissolved in degassed DMF (200 mL), and $NiCl_2$ (504 mg, 3.97 mmol) and $CrCl_2$ (16.3 g, 159 mmol) were added at 0 °C. After being stirred at room temperature for 2 h, the mixture was diluted with AcOEt, washed with saturated NH4Cl and brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 1 kg, hexane/AcOEt = 4:1) gave **11** (15.8 g, 96%, 2 steps) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.01 (m, 12H), 6.98-6.93 (m, 3H), 5.08 (s, 0.25 x 1 H), 5.03 (s, 0.25 x 1 H), 4.93 (s, 0.5 x 1H), 4.75 (s, 0.25 x 1 H), 4.71 (s, 0.25 x 1 H), 4.67 (s, 0.5 x 1H), 3.85-3.11 (m, 6H), 2.97-2.40 (m, 4H), 2.06-1.46 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 175.1, 174.0, 152.0, 151.8, 149.8, 149.7, 141.8, 141.5, 141.5, 141.2, 140.5, 139.3, 139.2, 139.0, 139.0, 137.4, 129.4, 129.2, 129.0, 129.0, 128.8, 128.8, 128.7, 128.7, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.0, 127.0, 126.9, 126.8, 126.7, 126.3, 126.2, 126.2, 126.2, 126.1, 126.1, 126.1, 126.0, 124.5, 119.7, 114.3, 114.1, 111.1, 110.9, 102.6, 74.8, 73.7, 73.7, 71.3, 71.1, 64.6, 64.6, 54.9, 54.8, 54.7, 54.4, 53.9, 51.3, 50.9, 50.9, 45.4, 45.2, 45.2, 45.0, 44.9, 44.6, 40.7, 40.1, 39.5, 39.4, 39.3, 37.8, 34.5, 37.4, 37.3, 37.0, 36.9, 36.4, 36.0, 13.9; FTIR (neat) 3471, 3027, 1731, 1446, 1162 cm^{-1}; MS (EI) *m/z* 73 (100), 163, 278, 414 (M^+); HRMS (EI) calcd for $C_{28}H_{30}O_3$ (M^+) 414.2185, found 414.2175.

(2*RS*,3*S*,5*RS*)-Methyl 2,6-Dibenzyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-phenylhept-6-enoate (15a) (diastereoisomeric mixture). To a solution of **11** (90 mg, 0.217 mmol) in DMF (0.2 mL) were added *tert*-butyldiphenylchlorosilane (0.28 mL, 1.08 mmol) and imidazole (148 mg, 2.17 mmol) at room temperature. After being stirred at room temperature for 2 h, the mixture was diluted with AcOEt, washed with 1 M HCl (2 mL), saturated $NaHCO_3$, and brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 6 g, hexane/AcOEt = 40:1) gave **15a** (123 mg, 87%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-6.61 (m, 25H), 4.87, 4.84, 4.47, 4.44, 4.42, 4.35 (6 x s, 2H), 4.02-3.85 (m, 1H), 3.56-3.16 (m, 3H), 2.99-2.51 (m, 3H), 2.23-1.89 (m, 2H), 1.07-0.90 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 174.9, 174.8, 173.9, 150.7, 148.8, 148.4, 142.1, 142.0, 140.6, 140.4, 139.5, 139.5, 139.4, 139.3, 138.8, 136.2, 136.2, 136.2, 136.2, 136.1, 136.1, 135.9, 135.9, 135.9, 135.8, 135.8, 134.4, 134.3, 134.2, 133.6, 133.6, 130.0, 129.7, 129.6, 129.5, 129.5, 129.4, 128.9, 128.9, 128.7, 128.7, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 127.4, 127.4, 127.3, 126.5, 126.5, 126.3, 126.1, 126.1, 126.0, 125.8, 125.8, 114.6, 114.5, 112.6, 78.4, 77.2, 75.8, 75.0, 55.3, 55.2, 54.8, 51.3, 51.3, 51.2, 50.9, 44.9, 44.8, 44.8, 44.5, 44.3, 41.7, 39.0, 37.8, 37.3, 37.2, 37.0, 36.0, 35.6, 35.1, 27.1, 27.0, 27.0, 26.9, 26.5, 19.4, 19.3, 19.2, 12.8; FTIR (neat) 2947, 1734, 1108 cm^{-1}; MS (EI) *m/z* 199 (100), 471, 595, 652 (M^+); HRMS (EI) calcd for $C_{44}H_{48}O_3Si$ (M^+) 652.3380, found 652.3387.

(2*RS*,3*S*,5*RS*)-Methyl 2,6-dibenzyl-5-(benzyloxy)-3-phenylhept-6-enoate (15b) (diastereoisomeric mixture). To a solution of **11** (90 mg, 0.217 mmol) and benzyl trichloroacetimidate (0.080 mL, 0.435 mmol) in Et_2O (0.8 mL) was added trifluoromethanesulfonic acid (10 μL, 0.109 mmol) at room temperature. After stirring at room temperature for 2 h, the reaction was quenched with 1 M HCl (2 mL) and the mixture was extracted with AcOEt. The extract was washed saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed (SiO_2 6 g, hexane/AcOEt = 20:1) to give **15b** (107 mg, 97%) as acolorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-6.91 (m, 20H), 5.15-4.30 (m, 4H), 4.06-3.39 (m, 5H), 3.32-3.02 (m, 3H), 2.93-2.42 (m, 2H), 2.30-1.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 175.0, 174.6, 174.0, 161.9, 148.7, 141.9, 141.3, 141.2, 139.4, 139.3, 139.3, 139.2, 139.1, 138.6, 138.3, 136.3, 136.2, 131.2, 130.9, 129.8, 129.5, 129.3, 129.3, 129.2, 129.1, 128.9, 128.9, 128.8, 128.8, 128.8, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.4, 127.4, 127.3, 127.3, 126.9, 126.7, 126.6, 126.5, 126.4, 126.2, 126.2, 126.1, 126.1, 126.0, 126.0, 125.9, 116.7, 116.3, 112.6, 81.4, 81.0, 78.2, 69.9, 69.9, 69.8, 69.6, 69.5, 54.9, 54.7, 54.7, 54.3, 54.0, 52.7, 51.3, 51.2, 51.2, 50.9, 50.8, 45.2, 45.2, 45.0, 44.6, 43.0, 41.4, 40.1, 38.6, 37.5, 37.4, 36.9, 36.5, 36.3, 36.0, 35.6, 13.9; FTIR (neat) 3027, 1730, 1492 1454, 1159 cm^{-1}; MS (EI) *m/z* 91 (100), 233, 396, 471, 504 (M^+); HRMS (EI) calcd for $C_{35}H_{36}O_3$ (M^+) 504.2669, found 504.2673.

(2*RS*,3*S*,5*RS*)-Methyl 2,6-Dibenzyl-5-(methoxymethoxy)-3-phenylhept-6-enoate (15c) (diastereoisomeric mixture). To an ice-cooled solution of **11** (100 mg, 0.241 mmol) in CH_2Cl_2 (2 mL) were added *N,N*-diisopropylethylamine (0.21 mL, 1.21 mmol), chloromethyl methyl ether (92 μL, 1.21 mmol), and tetra-*n*-butylammonium iodide (446 mg, 1.21 mmol). After being stirred at room temperature for 2 h, the mixture was diluted with AcOEt, wahed with 1 M HCl, saturated $NaHCO_3$ and brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 6 g, hexane/AcOEt = 7:1) gave **15c** (108 mg, 97%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-6.95 (m, 15H), 4.99, 4.94, 4.84, 4.76, 4.73, 4.68 (6 x s, 2H), 4.65-4.30 (m, 2H), 3.89-3.51 (m, 3H), 3.39-3.16 (m, 6H), 3.09-2.80 (m, 2H), 2.74-2.40 (m, 1H), 2.26-1.67 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 174.9, 174.1, 174.0, 148.8, 146.3, 141.8, 141.1, 141.0, 139.3, 139.3, 139.2, 139.1, 139.0, 129.7, 129.5, 129.2, 129.2, 129.0, 129.0, 128.9, 128.7, 128.5, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.0, 127.4, 127.0, 126.9, 126.8, 126.8, 126.7, 126.4, 126.2, 126.2, 126.1, 126.1, 126.0, 117.1, 117.0, 113.3, 94.5, 94.5, 94.1, 93.6, 93.4, 80.1, 78.1, 78.0, 77.2, 77.1, 56.0, 55.9, 55.4, 55.2, 55.2, 55.1, 55.0, 54.5, 54.2, 51.3, 51.3, 51.0, 50.9, 45.3, 45.2, 45.1, 45.0, 44.9, 44.5, 39.8, 38.8, 38.3, 37.3, 37.2, 36.4, 36.0, 35.5, 13.1, 11.6; FTIR (neat) 2945, 1734, 1157, 1093, 1032 cm^{-1}; MS (EI) *m/z* 91 (100), 163, 396, 458 (M^+); HRMS (EI) calcd for $C_{30}H_{34}O_4$ (M^+) 458.2455, found 458.2458.

(2*RS*,3*S*,5*RS*)-2,6-Dibenzyl-5-((*tert*-butyldiphenylsilyl)oxy)-3-phenylhept-6-enoic Acid (13a) (diastereoisomeric mixture). To a solution of **15a** (110 mg, 0.169 mmol) in CH_2Cl_2 (2 mL) was added DIBAL-H (1.02 M in hexane, 0.38 mL, 0.388 mmol) at –78 °C. After stirring at –78 °C for 3 h, the reaction was quenched with saturated Rochelle salt (2 mL) and the mixture was extracted with AcOEt. The extrct was washed with brine, dried, concentrated, and chromatographed (SiO_2 6 g, hexane/AcOEt = 10:1) to give the corresponding alcohol (100 mg, 95%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-6.67 (m, 25H), 4.88, 4.76, 4.47, 4.42, 4.40 (5 x s, 2H), 4.14-3.93 (m, 1H), 3.52-2.87 (m, 5H), 2.53-2.33 (m, 2H), 2.17-1.76 (m, 4H), 1.06-0.90 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9, 148.8, 148.6, 142.9, 142.8, 141.8, 141.7, 141.1, 141.0, 140.9, 139.8, 139.6, 139.6, 139.1, 137.9, 136.2, 136.1, 136.0, 136.0, 135.9, 134.8, 134.5, 134.4, 133.8, 133.5, 129.8, 129.6, 129.5, 129.5, 129.5, 129.4, 129.1, 129.0, 129.0, 128.9, 128.7, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 127.5, 127.4, 127.4, 127.4, 127.3, 127.3, 127.3, 126.7, 126.2, 126.0, 126.0, 126.0, 125.9, 125.9, 125.8, 114.3, 112.8, 78.8, 76.1, 75.8, 62.2, 62.0, 61.6, 48.9, 48.6, 48.5, 48.4, 48.3, 42.4, 41.9, 41.9, 41.7, 40.2, 39.0, 37.9, 37.6, 37.5, 36.2, 36.0, 35.2, 34.9, 34.4, 34.2, 27.0, 27.0, 19.4, 19.3, 19.3, 12.7; FTIR (neat) 3457, 2932, 1107, 1045 cm^{-1}; MS (FAB) *m/z* 91 (100), 135, 199, 625 (M^{+1}); HRMS (FAB) calcd for $C_{43}H_{48}O_2Si$ (M^+) 624.3400, found 624.3376.

To an ice-cooled solution of the alcohol (100 mg, 0.160 mmol) in CH_2Cl_2 (2 mL) were added $NaHCO_3$ (70 mg, 0.801 mmol) and Dess-Martin periodinane (136 mg, 0.320 mmol). After being stirred at room temperature for 1 h, the mixture was diluted with AcOEt, washed with 50% $Na_2S_2O_3$, saturated $NaHCO_3$, and brine, dried, and concentrated to give the corresponding aldehyde as a yellow oil which was used for the next reaction without purification.

Crude aldehyde thus obtained was dissolved in *tert*-BuOH (1.2 mL) and H_2O (0.6 mL), NaH_2PO_4 (77 mg, 0.641 mmol), $NaClO_2$ (58 mg, 0.641 mmol), and 2-methyl-2-butene (0.36 mL, 3.20 mmol) were added at 0 °C. After being stirred at 0 °C for 1 h, the mixture was diluted with AcOEt, washed with saturated $NaHCO_3$ and brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 6 g, hexane/AcOEt = 7:1) gave **13a** (101 mg, 98%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-6.61 (m, 25H), 4.88, 4.85, 4.48, 4.46, 4.42, 4.37 (6 x s, 2H), 4.05-3.73 (m, 1H), 3.56-3.15 (m, 1H), 3.00-2.85 (m, 1H), 2.80-2.29 (m, 4H), 2.21-1.86 (m, 2H), 1.05-1.00 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.4, 150.8, 148.9, 148.4, 141.5, 140.3, 140.0, 139.5, 139.4, 139.2, 139.1, 138.9, 138.8, 137.6, 136.3, 136.2, 136.0, 136.0, 135.9, 135.9, 134.8, 134.4, 134.3, 134.2, 134.1, 134.1, 133.7, 133.6, 133.6, 133.6, 130.0, 129.8, 129.7, 129.5, 129.5, 129.4, 128.9, 128.9, 128.8, 128.7, 128.7, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.8, 127.7, 127.6, 127.5, 127.5, 127.4, 127.4, 127.4, 127.3, 127.3, 126.5, 126.3, 126.2, 126.1, 126.0, 125.9, 125.8, 114.6, 114.5, 112.5, 77.7, 75.7, 74.7, 54.9, 54.9, 54.4, 44.5, 43.9, 41.8, 40.5, 38.1, 36.8, 36.6, 36.0, 35.2, 34.9, 27.1, 27.0, 27.0, 27.0, 26.9, 21.0, 19.4, 19.3, 19.3, 19.2, 19.2, 14.2, 13.0, 11.4; FTIR (neat) 3060, 3030, 2933, 2848, 1706, 1107 cm^{-1}; MS (FAB) *m/z* 91 (100), 135, 199, 639 (M^{+1}); HRMS (FAB) calcd for $C_{43}H_{46}O_3Si$ (M$^+$) 638.3231, found 638.3245.

(2*RS*,3*S*,5*RS*)-2,6-Dibenzyl-5-(benzyloxy)-3-phenylhept-6-enoic Acid (13b) (diastereoisomeric mixture). Compound **15b** (100 mg, 0.198 mmol) was reduced with DIBAL-H in the same manner as described for the reduction of **15a** to give the corresponding alcohol (72.4 mg, 77%) as a colorless oil after column chromatography (SiO_2 6 g, hexane/AcOEt = 10:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-6.87 (m, 20H), 5.03-4.35 (m, 3H), 4.08-3.86 (m, 3H), 3.65-3.31 (m, 4H), 2.94-2.31 (m, 2H), 2.19-1.72 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 148.8, 147.0, 143.7, 141.3, 141.0, 140.8, 140.7, 139.4, 139.3, 139.1, 138.4, 138.3, 138.1, 131.4, 130.6, 130.5, 129.6, 129.6, 129.3, 129.1, 129.0, 128.9, 128.9, 128.8, 128.8, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.4, 127.4, 126.9, 126.4, 126.3, 126.3, 126.2, 126.1, 125.9, 125.9, 125.9, 125.8, 125.7, 115.9, 112.6, 81.6, 81.0, 78.9, 70.2, 70.0, 62.1, 61.5, 60.9, 51.4, 48.3, 48.2, 47.8, 47.7, 43.0, 42.5, 42.0, 41.5, 39.3, 38.8, 38.7, 36.5, 36.3, 36.0, 35.0, 34.9, 34.4, 14.2, 14.0; FTIR (neat) 3423, 3025, 2946, 1058, 1492, 1450 cm^{-1}; MS (EI) *m/z* 91 (100), 233, 368, 458, 476 (M$^+$); HRMS (EI) calcd for $C_{34}H_{36}O_2$ (M$^+$) 476.2702, found 476.2688.

The alcohol (70 mg, 0.147 mmol) was subjected to Dess-Martin oxidation followed by Pinnick-Kraus oxidation in the same manner as described for the synthesis of **13a** to give **13b** (66.0 mg, 92%) as a colorless oil after column chromatography (SiO_2 6 g, hexane/AcOEt = 6:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-6.91 (m, 20H), 5.03, 4.90, 4.83, 4.81, 4.74, 4.63 (6 x s, 2H), 4.10-3.50 (m, 3H), 3.42-2.40 (m, 6H), 2.31-1.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.8, 148.6, 147.0, 141.6, 141.0, 140.7, 139.1, 139.1, 139.0, 138.9, 138.5, 138.3, 136.8, 129.9, 129.8, 129.5, 129.4, 129.3, 129.1, 128.9, 128.8, 128.7, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.5, 127.4, 127.0, 126.8, 126.7, 126.3, 126.2, 126.2, 126.0, 116.1, 112.6, 80.7, 78.1, 76.8, 70.1, 70.0, 69.9, 69.9, 69.8, 54.5, 53.0, 44.9, 44.8, 44.1, 41.5, 40.0, 38.8, 38.6, 37.4, 37.1, 36.8, 35.6; FTIR (neat) 3060, 3027, 2924, 1706, 1449 cm^{-1}; MS (EI) *m/z* 91 (100), 233, 382, 471, 504 (M$^+$); HRMS (EI) calcd for $C_{34}H_{34}O_3$ (M$^+$) 490.2504, found 490.2500.

(2*RS*,3*S*,5*RS*)-2,6-Dibenzyl-5-(methoxymethoxy)-3-phenylhept-6-enoic acid (13c) (diastereoisomeric mixture). Compound **15c** (100 mg, 0.218 mmol) was reduced with DIBAL-H in the same manner as described for the reduction of **15a** to give the corresponding alcohol (86.5 mg, 92%) as a colorless oil after column chromatography (SiO_2 6 g, hexane/AcOEt = 4:1): ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.03 (m, 15H), 5.00-4.38 (m, 4H), 3.92-3.56 (m, 1H), 3.43-3.11 (m, 7H), 2.88-1.79 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 146.6, 146.4, 143.1, 142.7, 142.6, 142.4, 141.2, 141.0, 140.8, 140.7, 139.3, 139.2, 139.0, 137.2, 129.5, 129.5, 129.2, 129.1, 129.0, 129.0, 129.0, 128.9, 128.7, 128.7, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.0, 127.5, 126.6, 126.5, 126.5, 126.4, 126.1, 125.9, 125.8, 125.8, 125.7, 116.7, 116.4, 113.5, 113.4, 94.3, 93.9, 93.7, 93.6, 80.5, 80.4, 78.5, 78.4, 77.7, 62.4, 62.0, 61.3, 61.1, 56.1, 56.0, 55.4, 55.3, 55.2, 48.7, 48.5, 48.4, 48.3, 48.2, 43.1, 42.6, 42.5, 41.6, 38.6, 38.4, 38.3, 37.6, 36.7, 36.4, 36.2, 35.8, 34.9, 34.8, 34.7, 34.4, 13.1, 12.2, 11.9; FTIR (neat) 3446, 2932, 1090, 1034 cm^{-1}; MS (EI) *m/z* 91 (100), 368, 398, 430 (M$^+$); HRMS (EI) calcd for $C_{29}H_{34}O_3$ (M$^+$) 430.2517, found 430.2526.

The alcohol (80 mg, 0.186 mmol) was subjected to Dess-Martin oxidation followed by Pinnick-Kraus oxidation in the same manner as described for the synthesis of **13a** to give **13c** (79.3 mg, 96%) as a colorless oil after column chromatography (SiO_2 6 g, hexane/AcOEt = 1:1): ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-6.94 (m, 15H), 4.97-4.33 (m, 4H), 3.89-3.60 (m, 1H), 3.35-3.04 (m, 6H), 2.86-2.48 (m, 3H), 2.24-1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.4, 179.8, 179.1, 148.7, 148.7, 146.4, 146.3, 141.4, 140.8, 140.5, 139.1, 139.1, 139.0, 138.9, 137.4, 137.2, 134.9, 129.7, 129.5, 129.3, 129.2, 129.0, 129.0, 128.9, 128.8, 128.8, 128.7, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.5, 127.1, 127.0, 126.7, 126.4, 126.3, 126.3, 126.1, 126.0, 126.0, 117.1, 116.8, 113.4, 94.5, 94.3, 94.1, 93.6, 93.4, 78.0, 77.3, 56.0, 55.9, 55.4, 55.3, 55.3, 55.2, 54.9, 54.7, 53.4, 44.9, 44.6, 44.1, 39.7, 38.7, 38.4, 38.2, 37.2, 37.0, 36.9, 36.8, 36.5, 35.9, 35.6, 35.5, 35.4, 13.1, 11.6; FTIR (neat) 3053, 3030, 2941, 1707, 1151, 1031 cm^{-1}; MS (EI) *m/z* 91 (100), 382, 412, 444 (M$^+$); HRMS (EI) calcd for $C_{29}H_{32}O_4$ (M$^+$) 444.2294, found 444.2287.

(2*RS*,3*S*,5*RS*)-5-Acetoxy-2,6-dibenzyl-3-phenylhept-6-enoic Acid (13d) and (3*R*,4*S*,6*S*)-3-Benzyl-4-phenyl-6-(3-phenylprop-1-en-2-yl)tetrahydro-2*H*-pyran-2-one (14). A solution of **11** (3.7 g, 8.90 mmol) and LiOH (1.1 g, 26.8 mmol) in 50% aq THF (50 mL) was heated at 80 °C for 12 h. The mixture was cooled in an ice bath, acidified with 1 M HCl (30 mL), and extracted with AcOEt. The extract was washed with brine, dried, and concentrated to give hydroxy acid **12** which was used for the next reaction without purification.

To an ice-cooled solution of crude hydroxy acid **12** thus obtained in CH_2Cl_2 (80 mL) were added pyridine (2.66 mL, 33.0 mmol) and acetyl chloride (1.76 mL, 24.7 mmol), and the mixture was stirred at room temperature for 2 h. The mixture was then cooled to 0 °C, and $NaHCO_3$ (3.59 g, 41.2 mmol) and MeOH (20 mL) were added. After being stirred at room temperature for 1 h, the mixture was diluted with AcOEt and acidified with 1 M HCl (30 mL). The organic layer was washed with saturated $NaHCO_3$ (10 mL) and brine, dried, concentrated, and chromatographed (SiO_2 150 g, hexane/AcOEt = 6:1 to 1:1) to give **13d** (2.81 g, 77%) and **14** (501 mg, 15%).

13d: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-6.96 (m, 15H), 5.00-4.70 (m, 2H), 3.71-3.62 (m, 1H), 3.43-3.17 (m, 2H), 3.00-2.76 (m, 2H), 2.66-2.57 (m, 1H), 2.51-2.39 (m, 1H), 2.22-1.66 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.4, 180.2, 180.0, 171.8, 170.0, 170.0, 147.6, 147.5, 145.2, 140.6, 140.3, 140.2, 140.2, 138.8, 138.7, 138.7, 138.5, 138.4, 136.9, 133.7, 130.4, 129.3, 129.1, 129.0, 129.0, 128.9, 128.9, 128.8, 128.8, 128.7, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.3, 127.2, 127.1, 126.8, 126.5, 126.4, 126.2, 126.1, 126.0, 123.9, 122.0, 116.4, 113.1, 112.7, 110.3, 109.7, 78.5, 75.7, 74.1, 73.8, 54.9, 54.7, 54.4, 53.8, 51.6, 45.1, 44.8, 44.8, 44.3, 42.5, 39.6, 39.6, 38.4, 37.6, 37.4, 37.1, 37.0, 36.9, 36.3, 35.9, 35.8, 29.9, 21.2, 21.1, 20.8, 20.7, 14.0, 12.4; FTIR (neat) 3027, 2924, 1736, 1708, 1239 cm^{-1}; MS (EI) *m/z* 91 (100), 143, 233, 382, 442 (M^+); HRMS (EI) calcd for $C_{29}H_{30}O_4$ (M^+) 442.2155, found 442.2166.

14: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.08 (m, 15H), 5.14 (m, 1H), 4.82 (m, 1H), 4.49 (dd, *J* = 11.7 Hz, 2.4 Hz, 1H), 3.48 (d, *J* = 15.6 Hz, 1H), 3.40 (dd, *J* = 14.2 Hz, 3.9 Hz, 1H), 3.35 (d, *J* = 15.6 Hz, 1H), 3.09-3.04 (m, 1H), 2.87 (td, *J* = 12.2 Hz, 3.4 Hz, 1H), 2.65 (dd, *J* = 14.2 Hz, 5.4 Hz, 1H), 1.99 (dt, *J* = 14.2 Hz, 2.9 Hz, 1H), 1.91-1.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 146.2, 142.2, 138.3, 138.2, 129.7, 129.2, 129.0, 128.4, 128.4, 127.3, 127.3, 126.6, 126.4, 114.0, 81.0, 48.4, 41.6, 38.4, 37.2, 34.5; FTIR (neat) 3027, 2923, 1725, 1108 cm^{-1}; MS (EI) *m/z* 63 (100), 78, 234, 382 (M^+); HRMS (EI) calcd for $C_{27}H_{26}O_2$ (M^+) 382.1938 found 382.1944.

General Procedure for [2 + 2] Cycloaddition Reactions of Compounds 13a-d. Compound **13a-d** (1.0 mmol), NaOAc (82 mg, 1.0 mmol), acetic anhydride (0.47 mL, 5.0 mmol) and toluene (10 mL) were placed in a sealed tube, and the mixture was heated at 200 °C for 12 h. The mixture was cooled to room temperature and diluted with AcOEt, washed with saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed.

Reaction of 13a. 4aα (15 mg, 15%), **4aβ** (33 mg, 34%), and **16a** (11 mg, 11%) were obtained from **13a** (100 mg, 0.157 mmol) after column chromatography (SiO_2 5 g, hexane/AcOEt = 40:1).

4aα: colorless oil; $[\alpha]_D^{26}$ +4.7 (*c* 0.705, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.53 (m, 4H), 7.44-7.00 (m, 19H), 6.76-6.74 (m, 2H), 4.51 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.59 (d, *J* = 18.6 Hz, 1H), 3.11 (d, *J* = 15.0 Hz, 1H), 3.03 (d, *J* = 15.0 Hz, 1H), 2.99 (s, 2H), 2.87 (q, *J* = 6.8 Hz, 1H), 2.79 (d, *J* = 18.6 Hz, 1H), 2.04-1.93 (m, 2H), 0.98 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.3, 138.1, 138.0, 136.9, 135.8, 135.8, 134.1, 133.6, 130.2, 130.2, 129.7, 128.6, 128.4, 128.0, 127.7, 127.6, 127.5, 126.6, 126.2, 77.6, 77.2, 50.4, 48.6, 48.1, 39.8, 39.3, 36.7, 27.0, 19.3; FTIR (neat) 2932, 1768, 1111 cm^{-1}; MS (FAB) *m/z* 91, 135 (100), 199, 621 (M^{+1}); HRMS (FAB) calcd for $C_{43}H_{44}O_2Si$ (M^+) 621.3188, found 621.3188.

4aβ: colorless oil; $[\alpha]_D^{25}$ +116.1 (*c* 1.500, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 6.8 Hz, 2H), 7.57 (d, *J* = 6.8 Hz, 2H), 7.44-7.19 (m, 16H), 7.07-7.06 (m, 3H), 6.63-6.62 (m, 2H), 4.42 (d, *J* = 2.8 Hz, 1H), 3.95 (d, *J* = 14.2 Hz, 1H), 3.74-3.69 (m, 1H), 3.18 (d, *J* = 14.8 Hz, 1H), 3.08 (d, *J* = 14.8 Hz, 1H), 2.81 (d, *J* = 18.4 Hz, 1H), 2.73 (d, *J* = 14.2 Hz, 1H), 2.55 (d, *J* = 18.4 Hz, 1H), 2.15 (dd, *J* = 14.0 Hz, 6.8 Hz, 1H), 2.03 (td, *J* = 14.0 Hz, 3.2 Hz, 1H), 1.12 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.1,. 139.2, 138.8, 137.2, 136.2, 135.8, 134.6, 133.0, 130.8, 129.9, 129.7, 129.6, 128.4, 128.3, 128.2, 127.8, 127.8, 127.5, 126.4, 126.3, 126.2, 79.6, 79.0, 52.4, 50.7, 50.0, 40.1, 35.8, 34.7, 27.4, 19.4; FTIR (neat) 2932, 1764, 1106, 1066 cm^{-1}; MS (FAB) *m/z* 91, 135 (100), 199, 621 (M^{+1}); HRMS (FAB) calcd for $C_{43}H_{44}O_2Si$ (M^+) 621.3188, found 621.3188.

16a: colorless oil; $[\alpha]_D^{26}$ -43.8 (*c* 0.540, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.00 (m, 21H), 6.78-6.75 (m, 2H), 6.55-6.53 (m, 2H), 4.73 (dd, *J* = 9.2 Hz, 6.4 Hz, 1H), 3.59 (d, *J* = 18.0 Hz, 1H), 3.24 (dd, *J* = 7.6 Hz, 3.2 Hz, 1H), 3.15 (d, *J* = 14.4 Hz, 1H), 2.98 (d, *J* = 14.4 Hz, 1H), 2.95 (d, *J* = 18.0 Hz, 1H), 2.82 (d, *J* = 14.4 Hz, 1H), 2.76 (d, *J* = 14.4 Hz, 1H), 1.98-1.88 (m, 1H), 1.81-1.75 (m, 1H), 0.99 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.6, 141.2, 137.9, 136.8, 135.9, 135.8, 134.1, 133.3, 130.5, 130.0, 129.7, 129.6, 128.8 128.4, 128.1, 127.6, 127.4, 126.4, 126.2, 126.1, 77.6, 76.9, 50.4, 49.3, 47.6, 40.5, 40.1, 34.5, 26.9, 19.2; FTIR (neat) 2932, 1771, 1107 cm^{-1}; MS (EI) *m/z* 69 (100), 199, 397, 421, 620 (M^+); HRMS (FAB) calcd for $C_{43}H_{44}O_2Si$ (M^+) 620.3125, found 620.3139.

Reaction of 13b. 4bα (7.6 mg, 13%), **4bβ** (13.2 mg, 23%), and **16b** (4.0 mg, 7%) were obtained from **13b** (60 mg, 0.122 mmol) after column chromatography (SiO_2 5 g, hexane/AcOEt = 20:1).

4bα: colorless oil; $[\alpha]_D^{24}$ +11.2 (*c* 0.425, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.16 (m, 16H), 7.00-6.98 (m, 2H), 6.91-6.89 (m, 2H), 4.28 (d, *J* = 11.4 Hz, 1H), 4.14-4.09 (m, 1H), 4.13 (d, *J* = 11.4 Hz, 1H), 3.46 (d, *J* = 18.6 Hz, 1H), 3.15-3.02 (m, 5H), 2.83 (d, *J* = 18.6 Hz, 1H), 2.48-2.41 (m, 1H), 2.04-1.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.6, 138.5, 138.2, 137.0, 130.6, 129.7, 128.8, 128.2, 128.1, 128.0, 127.9, 127.4, 127.3, 126.8, 126.4, 126.3, 83.4, 71.4, 51.2, 48.8, 47.3, 41.8, 37.0, 36.6, 30.9; FTIR (neat) 3028, 1767, 1111 cm^{-1}; MS (FAB) *m/z* 91 (100), 274, 339, 472 (M^+); HRMS (FAB) calcd for $C_{34}H_{32}O_2$ (M^+) 472.2404, found 472.2403.

4bβ: colorless oil; $[\alpha]_D^{25}$ +54.3 (*c* 0.700, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.16 (m, 18H), 6.84-6.82 (m, 2H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.42 (d, *J* = 11.6 Hz, 1H), 3.91 (d, *J* = 3.3 Hz, 1H), 3.74-3.69 (m, 1H), 3.73 (d, *J* = 13.0 Hz, 1H), 3.14 (d, *J* = 15.6 Hz, 1H), 3.08 (d, *J* = 15.6 Hz, 1H), 3.07 (d, *J* = 19.0 Hz, 1H), 2.67 (d, *J* = 19.0 Hz, 1H), 2.62 (d, *J* = 13.0 Hz, 1H), 2.44 (dd, *J* = 14.0 Hz, 6.7 Hz, 1H), 2.17 (td, *J* = 14.0 Hz, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.1, 138.9, 138.7, 138.4, 137.1, 130.7, 129.8, 128.6, 128.5, 128.4, 128.1, 127.9, 127.6, 127.4, 126.8, 126.3, 126.3, 83.5, 78.9, 70.3, 53.1, 50.5, 49.8, 35.7, 34.9, 34.3, 30.9; FTIR (neat) 3028, 1767, 1500, 1455 cm^{-1}; MS (FAB) *m/z* 91 (100), 256, 339, 472 (M^+); HRMS (FAB) calcd for $C_{34}H_{32}O_2$ (M^+) 472.2387, found 472.2403.

16b: colorless oil; $[\alpha]_D^{24}$ -45.4 (*c* 0.200, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-6.85 (m, 20H), 4.49 (dd, *J* = 9.8 Hz, 7.0 Hz, 1H), 4.19 (d, *J* = 11.4 Hz, 1H), 4.04 (d, *J* = 11.4 Hz, 1H), 3.52 (d, *J* = 18.0 Hz, 1H), 3.36 (d, *J* = 6.0 Hz, 1H), 3.26 (d, *J* = 13.6 Hz, 1H), 3.16 (d, *J* = 13.6 Hz, 1H), 3.02 (d, *J* = 18.0 Hz, 1H), 2.87, 2.24-2.18 (m, 1H), 2.00-1.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.6, 142.0, 138.4, 138.3, 136.7, 130.2, 129.8, 129.2, 129.0, 128.8, 128.7, 128.5, 128.4, 128.2, 128.1, 128.1, 128.0, 128.0, 127.8, 127.8, 127.4, 127.3, 126.6, 126.5, 83.5, 77.6, 77.2, 71.4, 51.7, 48.2, 48.2, 42.0, 37.9, 34.2; FTIR (neat) 3028, 1769, 1096 cm^{-1}; MS (FAB) *m/z* 91 (100), 303, 381, 472 (M^+); HRMS (FAB) calcd for $C_{34}H_{32}O_2$ (M^+) 472.2404, found 472.2403.

Reaction of 13c. A 1:2 inseparable mixture of **4cα** and **4cβ** (44.6 mg, 66%) was obtained from **13c** (70 mg, 0.158 mmol) after column chromatography (SiO_2 5 g, hexane/AcOEt = 10:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.15 (m, 13 x 2/3H + 13 x 1/3H), 7.02-7.00 (m, 2 x 1/3H), 6.85-6.82 (m, 2 x 2/3H), 4.79 (d, *J* = 6.8 Hz, 1 x 2/3H), 4.55 (d, *J* = 6.8 Hz, 1x 2/3H), 4.11 (s, 2 x 1/3H), 4.07 (dd, *J* = 10.4 Hz, 6.7 Hz, 1 x 1/3H), 4.01 (d, *J* = 2.9 Hz, 1 x 2/3H), 3.62 (dd, *J* = 13.4 Hz, 6.6 Hz, 1 x 2/3H), 3.60 (d, *J* = 13.7 Hz, 1 x 2/3H), 3.43 (d, *J* = 18.6 Hz, 1 x 1/3H), 3.32 (s, 3 x 2/3H), 3.14 (s, 3 x 1/3H), 3.11-3.00 (m, 2 x 2/3H + 5 x 1/3H), 3.03 (d, *J* = 18.4 Hz, 1 x 2/3H), 2.86 (d, *J* = 18.6 Hz, 1 x 1/3H), 2.71 (d, *J* = 18.4 Hz, 1 x 2/3H), 2.65 (d, *J* = 13.7 Hz, 1 x 2/3H), 2.50-2.45 (m, 1 x 1/3H), 2.43 (dd, *J* = 14.0 Hz, 6.6 Hz, 1 x 2/3H), 2.22 (td, *J* = 14.0 Hz, 3.2 Hz, 1 x 2/3H), 2.10-2.01 (m, 1 x 1/3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.4, 210.9, 139.0, 138.7, 138.3, 138.1, 137.2, 136.9, 130.7, 130.5, 129.6, 129.5, 128.7, 128.5, 128.4, 128.1, 128.0, 127.9, 127.9, 126.8, 126.7, 126.4, 126.4, 126.3, 126.2, 96.8, 96.4, 83.5, 83.1, 79.4, 78.4, 56.0, 55.5, 53.3, 51.3, 50.6, 49.9, 48.9, 47.2, 41.7, 38.6, 36.8, 36.4, 35.6, 35.6; FTIR (neat) 2933, 1766, 1044 cm^{-1}; MS (FAB) *m/z* 91, 231, 322 (100), 426 (M^+); HRMS (FAB) calcd for $C_{29}H_{30}O_3$ (M^+) 426.2190, found 426.2195.

Reaction of 13d. A 1.7:1 mixture of **4dα** and **4dβ** (2.44 g, 91%) was obtained from **13d** (2.80 g, 6.33 mmol) after column chromatography (SiO_2 200 g, hexane/AcOEt = 6:1). Pure **4dα** and **4dβ** were obtained for data collection by preparative TLC (hexane/AcOEt = 4:1).

4dα: colorless oil; $[\alpha]_D^{23}$ +28.7 (*c* 0.880, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.13 (m, 13H), 7.00-6.96 (m, 2H), 5.34 (dd, *J* = 10.2 Hz, 6.6 Hz, 1H), 3.23 (d, *J* = 18.8 Hz, 1H), 3.21-3.16 (m, 1H), 3.14 (d, *J* = 15.2 Hz, 1H), 3.05-2.96 (m, 1H), 3.04 (d, *J* = 15.2 Hz, 1H), 2.57-2.50 (m, 1H), 1.98-1.91 (m, 1H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.1, 170.3, 137.6, 137.4, 136.6, 130.6, 129.3, 128.7, 128.3, 128.2, 128.0, 127.0, 126.6, 126.5, 78.6, 77.8, 51.1, 48.4, 46.0, 41.8, 36.3, 36.2, 20.4; FTIR (neat) 3030, 1768, 1734, 1243, 1044 cm^{-1}; MS (EI) *m/z* 91, 231, 322 (100), 382, 424 (M^+); HRMS (EI) calcd for $C_{29}H_{28}O_3$ (M^+) 424.2048, found 424.2038.

4dβ: colorless oil; $[\alpha]_D^{23}$ +108.1 (*c* 0.860, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.18 (m, 11H), 7.10-7.08 (m, 2H), 6.89-6.86 (m, 2H), 5.12 (d, *J* = 3.6 Hz, 1H), 3.56 (dd, *J* = 13.4 Hz, 7.0 Hz), 3.48 (d, *J* = 13.8 Hz, 1H), 3.16 (d, *J* = 15.4 Hz, 1H), 3.10 (d, *J* = 15.4 Hz, 1H), 3.08 (d, *J* = 18.6 Hz, 1H), 2.76 (d, *J* = 18.6 Hz, 1H), 2.73 (d, *J* = 13.8 Hz, 1H), 2.38 (td, *J* = 14.0 Hz, 3.6 Hz, 1H), 2.25 (dd, *J* = 15.0 Hz, 7.0 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.8, 169.8, 137.9, 137.8, 136.9, 130.8, 129.2, 128.7, 128.5, 128.1, 128.0, 127.0, 126.8, 126.5, 79.8, 79.1, 53.2, 50.1, 49.2, 37.3, 36.0, 35.3, 21.4; FTIR (neat) 3031, 1766, 1738, 1242 cm^{-1}; MS (EI) *m/z* 91, 231, 322 (100), 424 (M^+); HRMS (EI) calcd for $C_{29}H_{28}O_3$ (M^+) 424.2047, found 424.2039.

(1*S*,2*R*,4*R*,5*S*)-1,5-Dibenzyl-2-hydroxy-4-phenylbicyclo[3.2.0]heptan-6-one (17α) and (1*S*,2*S*,4*R*,5*S*)-1,5-Dibenzyl-2-hydroxy-4-phenylbicyclo[3.2.0]heptan-6-one (17β). Compound **4d** (2.5 g, 5.89 mmol) was dissolved in CH_2Cl_2 (20 mL), and MeOH (40 mL) and K_2CO_3 (669 mg, 6,48 mmol) were added at room temperature. After being heated at 60 °C for 2 h, the mixture was cooled to room temperature, diluted with AcOEt, washed with brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 200g, $CHCl_3$) gave **17α** (1.31 g, 58%) and **17β** (779 mg, 35%).

17α: yellow oil; $[\alpha]_D^{28}$ +67.1 (*c* 3.000, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.17 (m, 13H), 7.00-6.99 (m, 2H), 4.53-4.50 (m, 1H), 3.35 (d, *J* = 18.4 Hz, 1H), 3.13 (d, *J* = 15.0 Hz, 1H), 3.13-3.09 (m, 1H), 3.04 (d, *J* = 13.2 Hz, 1H), 3.01 (d, *J* = 15.0 Hz, 1H), 2.96 (d, *J* = 13.2 Hz, 1H), 2.36-2.31 (m, 1H), 2.05 (dd, *J* = 13.2 Hz, 12.0 Hz, 1H), 0.63 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.7, 138.0, 137.8, 137.0, 130.5, 129.3, 128.8, 128.7, 128.1, 127.9, 127.2, 127.0, 126.4, 79.6, 77.1, 49.9, 48.1, 47.5, 41.8, 38.2, 36.5; FTIR (neat) 3552, 3029, 1757, 1492, 1454 cm^{-1}; MS (EI) *m/z* 91, 249 (100), 291, 340, 382 (M^+); HRMS (EI) calcd for $C_{27}H_{26}O_2$ (M^+) 382.1942, found 382.1933.

17β: colorless oil; $[\alpha]_D^{28}$ +55.2 (*c* 1.800, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.14 (m, 13H), 6.85-6.83 (m, 2H), 4.20 (s, 1H), 3.72 (dd, *J* = 13.6 Hz, 6.7 Hz, 1H), 3.59 (d, *J* = 13.6 Hz, 1H), 3.11 (s, 2H), 3.00 (d, *J* = 18.2 Hz, 1H), 2.65 (d, *J* = 18.2 Hz, 1H), 2.62 (d, *J* = 13.6 Hz, 1H), 2.35 (td, *J* = 13.6 Hz, 3.6 Hz, 1H), 2.11 (dd, *J* = 14.2 Hz, 6.7 Hz, 1H), 1.68 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9, 138.7, 138.6, 137.2, 130.7, 130.1, 129.7, 128.5, 128.1, 127.9, 126.7, 126.5, 126.3, 79.3, 76.4, 53.0, 50.8, 50.5, 40.4, 35.8, 35.8; FTIR (neat) 3500, 3028, 1761, 1500, 1446 cm^{-1}; MS (EI) *m*/*z* 91, 249 (100), 340, 382 (M$^+$); HRMS (EI) calcd for $C_{27}H_{26}O_2$ (M$^+$) 382.1942, found 382.1033.

(3a*R*,4*R*,6*R*,6a*S*)-3a,6a-Dibenzyl-4-hydroxy-6-phenylhexahydro-2*H*-cyclopenta[*b*]furan-2-one (18α). To a solution of *tert*-butyl hydroperoxide (4.07 M in toluene, 0.71 mL, 2.88 mmol) in THF (5 mL) was added n-butyllithium (2.69 M in hexane, 0.97 mL, 2.62 mmol) at –78 °C, and the mixture was stirred at –78 °C for 30 min. The resulting solution of lithium *tert*-butyl peroxide was then added to a solution of **17α** (500 mg, 1.31 mmol) in THF (7 mL) at 0 °C, and the mixture was stirred at 0 °C for 4 h. The mixture was diluted with AcOEt, washed with 1 M HCl, $NaHCO_3$, and brine, dried, concentrated, and chromatographed (SiO_2 10 g, hexane/AcOEt = 4:1) to give **18α** (461 mg, 88%) as colorless needles: $[\alpha]_D^{27}$ -44.3 (*c* 0.900, $CHCl_3$); mp 172-173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.19 (m, 13H), 7.09 (d, *J* = 6.4 Hz, 1H), 4.32-4.27 (m, 1H), 3.30 (d, *J* = 12.8 Hz, 1H), 3.16 (d, *J* = 15.0 Hz, 1H), 3.05 (dd, *J* = 13.7 Hz, 5.8 Hz, 1H), 2.90 (d, *J* = 15.0 Hz, 1H), 2.73 (d, *J* = 12.8 Hz, 1H), 2.72 (d, *J* = 17.4 Hz, 1H), 2.39-2.33 (m, 1H), 2.07 (td, *J* = 13.2 Hz, 9.8 Hz, 1H), 1.84 (d, *J* = 17.4 Hz, 1H), 0.95 (d, *J* = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 136.8, 135.0, 130.9, 129.8, 129.3, 128.9, 128.4, 128.3, 127.4, 127.2, 127.0, 96.7, 75.0, 54.8, 50.4, 42.1, 39.2, 37.5, 36.1; FTIR (neat) 3464, 3027, 1766, 1182, 1083 cm^{-1}; MS (EI) *m*/*z* 91 (100), 149, 264, 398 (M$^+$); HRMS (EI) calcd for $C_{27}H_{26}O_3$ (M$^+$) 398.1881, found 398.1880.

(3a*R*,4*S*,6*R*,6a*S*)-3a,6a-Dibenzyl-4-hydroxy-6-phenylhexahydro-2*H*-cyclopenta[*b*]furan-2-one (18β). Compound **17β** (500 mg, 1.31 mmol) was subjected to Baeyer-Villiger oxidation in the same manner as described for the reaction of **17α** to give **18β** (510 mg, 98%) as a white powder: $[\alpha]_D^{24}$ +11.3 (*c* 0.770, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.10 (m, 13H), 6.77-6.75 (m, 2H), 4.08 (s, 1H), 3.68 (dd, *J* = 13.1 Hz, 6.9 Hz, 1H), 3.58 (d, *J* = 13.4 Hz, 1H), 3.23 (s, 2H), 2.72 (d, *J* = 18.6 Hz, 1H), 2.71 (d, *J* = 14.2 Hz, 1H), 2.28-2.20 (m, 2H), 2.04 (dd, *J* = 14.0 Hz, 7.2 Hz, 1H), 1.86 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 137.8, 137.7, 135.9, 131.0, 130.2, 129.6, 128.6, 128.1, 127.8, 126.8, 126.6, 96.8, 75.7, 57.6, 51.8, 42.3, 39.8, 39.4, 36.2; FTIR (neat) 3465, 3028, 1754, 1257, 1204, 1015 cm^{-1}; MS (EI) *m*/*z* 91 (100), 264, 382, 398 (M$^+$); HRMS (EI) calcd for $C_{27}H_{26}O_3$ (M$^+$) 398.1872, found 398.1762.

(3a*S*,6*R*,6a*S*)-3a,6a-Dibenzyl-6-phenyltetrahydro-2*H*-cyclopenta[*b*]furan-2,4(5*H*)-dione (19). To a solution of **18β** (450 mg, 1.13 mmol) in CH_2Cl_2 (12 mL) were added $NaHCO_3$ (492 mg, 5.65 mmol) and Dess-Martin periodinane (958 mg, 2.26 mmol) at room temperature. After stirring at room temperature for 1 h, the reaction was quenched with 50% $Na_2S_2O_3$ (10 mL) and the mixture was extracted with AcOEt. The extract was was washed with saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed (SiO_2 20 g, hexane/AcOEt = 10:1) to give **19** (443 mg, 99%) as a white powder: $[\alpha]_D^{24}$ +1.8 (*c* 2.040, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.21 (m, 15H), 3.31 (d, *J* = 13.9 Hz, 1H), 3.25 (d, *J* = 14.8 Hz, 1H), 3.19 (d, *J* = 14.8 Hz, 1H), 3.12 (d, *J* = 13.9 Hz, 1H), 2.93 (dd, *J* = 11.6 Hz, 9.7 Hz, 1H), 2.73-2.56 (m, 2H), 2.49 (d, *J* = 17.3 Hz, 1H), 1.60 (d, *J* = 17.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

217.7, 173.4, 136.0, 135.2, 133.9, 130.8, 129.7, 129.6, 128.8, 128.7, 128.5, 127.8, 127.7, 127.6, 94.9, 62.2, 48.5, 42.6, 39.0, 38.8, 36.1; FTIR (neat) 3029, 1785, 1745, 1166 cm^{-1}; MS (EI) *m/z* 91 (100), 264, 305, 382 (M$^+$); HRMS (EI) calcd for $C_{27}H_{24}O_3$ (M$^+$) 396.1725, found 396.1725.

Reduction of Compound 19. To an ice-cooled solution of **19** (400 mg, 1.01 mmol) in CH_2Cl_2 (5 mL) were added EtOH (5 mL) and $NaBH_4$ (29 mg, 0.757 mmol). After stirring at 0 °C for 12 h, the reaction was quenched with saturated NH_4Cl (10 mL) and the mixture was extracted with AcOEt. The extraxt was washed with saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed (SiO_2 50 g, hexane/AcOEt = 4:1) to give **18α** (351 mg, 87%) and **18β** (50 mg, 12%).

(3a*R*,4*R*,6*R*,6a*S*)-3a,6a-Dibenzyl-4-((*tert*-butyldimethylsilyl)oxy)-6-phenylhexahydro-2*H*-cyclopenta[*b*]furan-2-one (20). A solution of **18α** (1.0 g, 2.51 mmol), *tert*-butyldimethylchlorosilane (757 mg, 5.02 mmol), imidazole (683 mg, 10.4 mmol) in DMF (5 mL) was heated at 80 °C for 22 h. The mixture was cooled to room temperature, diluted with AcOEt, washed with 1 M HCl (15 mL), saturated $NaHCO_3$, and brine, dried, and concentrated. Purification of the residue by flash column chromatography (SiO_2 50 g, hexane/AcOEt = 9:1) gave **20** (1.25 g, 97%) as a colorless oil: $[\alpha]_D^{24}$ +1.8 (*c* 0.750, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 6.8 Hz, 2H), 7.37-7.20 (m, 11H), 7.03 (d, *J* = 6.4 Hz, 2H), 4.17 (t, *J* = 7.3 Hz, 1H), 3.41 (d, *J* = 13.3 Hz, 1H), 3.11-3.06 (m, 2H), 2.85 (d, *J* = 14.9 Hz, 1H), 2.67 (d, *J* = 16.4 Hz, 1H), 2.63 (d, *J* = 13.3 Hz, 1H), 2.50-2.43 (m, 1H), 2.06-1.98 (m, 1H), 1.67 (d, *J* = 16.4 Hz, 1H), 0.63 (s, 9H), -0.16 (s, 3H), -0.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 137.6, 136.8, 135.1, 130.9, 129.8, 129.7, 128.6, 128.4, 128.3, 127.3, 126.9, 126.9, 96.5, 74.4, 56.2, 50.8, 41.2, 40.9, 39.1, 37.0, 25.5, 17.7, -4.3, -6.1; FTIR (neat) 2930, 1776, 1109 cm^{-1}; MS (FAB) *m/z* 91 (100), 135, 382, 512 (M$^+$); HRMS (FAB) calcd for $C_{33}H_{40}O_3Si$ (M$^+$) 512.2720, found 512.2698.

(3a*R*,4*R*,6*R*,6a*S*)-3,3a,6a-Tribenzyl-4-((*tert*-butyldimethylsilyl)oxy)-6-phenylhexahydro-2*H*-cyclopenta[*b*]furan-2-one (21). To a degassed solution of **20** (1.2 g, 2.34 mmol) in THF (15 mL) was added lithium hexamethyldisilazide (1.0 M in THF, 7.0 mL, 7.0 mmol) at 0 °C, and the mixture was stirred at 0 °C for 1 h. HMPA (2.45 mL, 14.1 mmol) was added and the mixture was stirred for 30 min at 0 °C. Benzyl iodide (0.440 mL, 3.51 mmol) was then added and stirring was continued at 0 °C for 1.5 h. The reaction was quenched with 1 M HCl (10 mL) and the mixture was extracted with AcOEt. The extract was washed with saturated $NaHCO_3$ and brine, dried, concentrated, purified by flash column chromatography (SiO_2 50 g, hexane/AcOEt = 10:1) to give **21** (1.31 g, 93%) as a colorless oil: $[\alpha]_D^{26}$ –61.9 (*c* 1.000, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.8 Hz, 2H), 7.33-7.11 (m, 11H), 6.91 (d, *J* = 7.6 Hz, 2H), 4.14 (dd, *J* = 7.1 Hz, 4.2 Hz, 1H), 3.78 (dd, *J* = 11.1 Hz, 3.8 Hz, 1H), 3.59 (d, *J* = 15.9 Hz, 1H), 3.14 (d, *J* = 14.9 Hz, 1H), 3.02-2.07 (m, 1H), 2.96 (d, *J* = 14.9 Hz, 1H), 2.90 (d, *J* = 15.9 Hz, 1H), 2.35 (dd, *J* = 14.4 Hz, 3.9 Hz, 1H), 2.32-2.26 (m, 1H), 2.02-1.93 (m, 1H), 1.29-1.22 (m, 1H), 0.83 (s, 9H), -0.11 (s, 3H), -0.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 139.5, 137.5, 136.7, 135.9, 131.4, 129.9, 129.6, 128.8, 128.6, 128.5, 128.3, 128.0, 127.3, 127.1, 126.6, 126.1, 96.0, 75.7, 57.3, 50.7, 43.5, 40.2, 39.4, 38.4, 32.3, 25.9, 17.9, -3.5, -5.9; FTIR (neat) 2952, 1766, 1111 cm^{-1}; MS (EI) *m/z* 91 (100), 231, 321, 545, 602 (M$^+$); HRMS (EI) calcd for $C_{40}H_{46}O_3Si$ (M$^+$) 602.3212, found 602.3207.

(3*S*,3a*S*,4*R*,6*R*,6a*S*)-3,3a,6a-Tribenzyl-4-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-6-phenylhexahydro-2*H*-cyclopenta[*b*]furan-2-one (23). To a solution of **21** (1.30 g, 2.16 mmol) in THF (10 mL) was added potassium hexamethyldisilazide (0.5 M in toluene, 8.6 mL, 4.3 mmol) at 0 °C, the mixture was stirred at 0 °C for 1 h. HMPA (1.5 mL, 8.63 mmol) was added and the mixture was stirred for 30 min at 0 °C and cooled to –78 °C. Phenyl-2-(phenylsulfonyl)oxaziridine (Davis reagent) (1.70 g, 6.47 mmol) was then added and stirring was continued at –40 °C for 9 h. The reaction was quenched with 1 M HCl (10 mL) and the mixture was extracted with AcOEt. The extract was washed with saturated $NaHCO_3$ and brine, dried, concentrated, chromatographed (SiO_2 50 g, hexane/AcOEt = 20:1) to give **23** (1.21 g, 91%) as a colorless oil: $[\alpha]_D^{25}$ –53.2 (*c* 1.800, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.2 Hz, 2H), 7.49-7.26 (m, 8H), 7.10 (d, *J* = 6.8 Hz, 2H), 7.09-6.92 (m, 8H), 4.81 (d, *J* = 4.4 Hz, 1H), 3.90 (d, *J* = 14.4 Hz, 1H), 3.71 (d, *J* = 13.6 Hz, 1H), 3.62 (d, *J* = 14.0 Hz, 1H), 3.45 (dd, *J* = 11.8 Hz, 4.4 Hz, 1H), 2.96 (d, *J* = 14.4 Hz, 1H), 2.86 (td, *J* = 12.2 Hz, 5.2 Hz, 1H), 2.63 (d, *J* = 13.6 Hz, 1H), 2.46 (d, *J* = 14.0 Hz, 1H), 2.36 (s, 1H), 1.99 (dd, *J* = 14.8 Hz, 4.4 Hz, 1H), 0.97 (s, 9H), 0.05(s, 3H), -0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 140.7, 136.8, 136.4, 134.2, 132.3, 131.6, 130.8, 130.4, 128.6, 128.4, 127.6, 127.4, 127.3, 127.0, 126.3, 125.3, 97.6, 65.2, 51.5, 43.7, 43.6, 37.6, 33.7, 26.3, 18.3, 0.00, -3.0, -5.4; FTIR (neat) 3534, 2934, 1773, 1500, 1455, 1265, 1182, 1000 cm^{-1}; MS (FAB) *m/z* 91 (100), 247, 323, 619 (M$^+$+1), HRMS (EI) calcd for $C_{40}H_{46}O_4Si$ (M$^+$) 618.3233, found 618.3281.

(3*S*,3a*S*,6*R*,6a*S*)-3,3a,6a-Tribenzyl-3-hydroxy-6-phenyltetrahydro-2*H*-cyclopenta[*b*]furan-2,4(5*H*)-dione (3). To an ice-cooled solution of **23** (50 mg, 0.081 mmol) in THF (1 mL) was added tetra-*n*-butylammonium fluoride (1.0 M in THF, 0.12 mL, 0.12 mmol). After being stirred at room temperature for 3 h, the mixture was diluted with AcOEt, washed with 1 M HCl, saturated $NaHCO_3$, and brine, dried, and concentrated to give **24** (40.2 mg).

To a solution of **24** (40 mg) in CH_2Cl_2 (2 mL) were added $NaHCO_3$ (41 mg, 0.476 mmol) and Dess-Martin periodinane (135 mg, 0.317 mmol) at room temperature. The mixture was heated under reflux for 3.3 h, cooled to room temperature, diluted with AcOEt, washed with saturated $Na_2S_2O_3$, saturated $NaHCO_3$ and brine, dried, and concentrated. Purification by flash column chromatography (SiO_2 5 g, hexane/AcOEt = 8:1) to give **3** (34.3 mg, 85%) as a white powder: $[\alpha]_D^{25}$ +51.7 (*c* 2.25 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.1 Hz, 2H), 7.42-7.30 (m, 8H), 7.08-7.01 (m, 3H), 6.95-6.86 (m, 5H), 6.72 (d, *J* = 6.8 Hz, 1H), 3.87 (d, *J* = 14.4 Hz, 1H), 3.44 (d, *J* = 14.7 Hz, 1H), 3.39 (d, *J* = 14.2 Hz, 1H), 3.31 (d, *J* = 14.2 Hz, 1H), 3.19 (d, *J* = 14.4 Hz, 1H), 3.08 (d, *J* = 14.7 Hz, 1H), 2.63 (dd, *J* = 17.0 Hz, 12.4 Hz, 1H), 2.54-2.42 (m, 2H), 2.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.3, 174.6, 136.4, 135.3, 134.5, 132.1, 130.8, 130.7, 129.5, 128.7, 128.5, 128.4, 127.6, 127.4, 127.2, 126.2, 94.0, 68.3, 48.9, 45.9, 40.1, 38.2, 33.0; FTIR (neat) 3520, 3030, 1779, 1742, 1500, 1455, 1258, 1197, 1167, 1000 cm^{-1}; MS (EI) *m/z* 91, 131, 339 (100), 411, 502 (M$^+$); HRMS (EI) calcd for $C_{34}H_{30}O_4$ (M$^+$) 502.2134, found 502.2133.

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SUPPORTING INFORMATION

X-Ray crystallographic data of **18α** and the acetate of **3**, and ^{1}H and ^{13}C NMR spectra for all new compounds are available.

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