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Syntheses of the AB and EFGH ring segments of gambierol

Isao Kadota,[a] Chie Kadowaki,[b] Choul-Hong Park,[b] Hiroyoshi Takamura,[b] Kumi Sato,[b] Philip W. H. Chan,[b] Stephan Thorand[b] and Yoshinori Yamamoto[b,*]

[a]*Research Center for Sustainable Materials Engineering, Institute of Multidisciplinary Research for Advanced Materials, Tohoku University, Sendai 980-8578, Japan*

[b]*Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980-8578, Japan*

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Abstract—Stereocontrolled syntheses of the AB and EFGH ring systems of gambierol (**1**) are described. The two key intermediates **3** and **55**, representing the AB and EFGH ring frameworks, were prepared from 2-deoxy-D-ribose via linear sequences. Brown's asymmetric allylboration and the intramolecular hetero-Michael reaction were successfully applied to the construction of the A ring moiety. Synthesis of the EFGH ring segment **55** was achieved by the SmI_2 mediated reductive cyclization, constructing the EF ring bearing two 1,3-diaxial methyl groups, and the palladium catalyzed coupling of enol triflate and zinc bishomoenolate, making the GH ring moiety. Attempted convergent approaches toward the EFGH ring framework are also described.

1. Introduction

Gambierol (**1**), which has a 6,6,6,6,7,6,6,7-polycyclic ether skeleton including 18 stereocenters and a triene side chain, was isolated from the cultured cells of *Gambierdiscus toxicus* by Yasumoto in 1993.[1] The compound shows significant toxicity against mice (LD_{50} 50 μg/kg), and the symptoms resemble those caused by ciguatoxins inferring the possibility that it is also implicated in ciguatera poisoning.[2] In the course of our synthetic effort towards gambierol, we synthesized the AB, E, and H ring segments in 1998,[3,4] based on the absolute stereochemistry proposed by Yasumoto and co-workers in 1993.[1] However, later on in 1999, they revised the absolute stereochemistry;[2] it is now believed to be the opposite to that reported in 1993. Accordingly, we undertook to synthesize those segments having the correct absolute stereochemistry. Scheme 1 shows our new synthetic strategy for the convergent synthesis of **1**. The polycyclic ether framework of **1** would be constructed from **2** via oxidation of the C–C triple bond to an α-diketone, selective removal of the TBS protective groups, and subsequent reductive cyclization of the resulting hydroxy ketone.[5] Retrosynthetic disassembly of the alkyne **2** based on a retro-acetylide-triflate coupling[6] furnished the AB ring segment **3** and the EFGH ring segment **4**. It was thought that the later compound **4** would be derived from the carboxylic acid **5** and the alcohol **6** via an esterification followed by an olefin metathesis.[7] Based on the retrosynthetic analysis of Scheme 1, we tested the first generation route toward gambierol (**1**) as described below.[8]

2. Synthesis of the AB ring segment

Protection of the known starting material **7**[9] with TBSCl followed by ozonolysis gave the aldehyde **8** in 99% yield (Scheme 2). Brown's asymmetric allylboration of **8** using allyldiisopinocampheylborane derived from (+)-pinene afforded the homoallylic alcohol **9** as the sole product in 92% yield.[10,11] Deprotection of the silyloxy group of **9** using TBAF and ozonolysis followed by Wittig reaction gave the α,β-unsaturated ester **10** in 94% yield. The cyclization precursor **10** was then subjected to an intramolecular hetero-Michael reaction. Thus, treatment of **10** with K_2CO_3 in THF/MeOH gave a 92:8 mixture of the desired bicyclic compound **11** and its diastereoisomer in 78% combined yield.[12] The stereochemistry of the major product **11** was unambiguously confirmed by NOE experiments on the corresponding acetate derivative **12** as shown in Fig. 1.

Further chain elongation and introduction of an alkynyl group are shown in Scheme 3. Protection of the hydroxy group of **11** with TIPSOTf followed by reduction of the ester group of **13** with $LiAlH_4$ gave the alcohol **14** in 94% yield. One carbon elongation of the hydroxymethyl group of **14** was achieved in the following way. Swern oxidation and subsequent Wittig reaction of the resulting aldehyde with $Ph_3P{=}CH_2$ gave the corresponding one carbon elongated olefin, which was converted to the alcohol **15** through hydroboration in 85% yield. Benzyl protection of the

Keywords: stereocontrolled synthesis; AB and EFGH ring segments; gambierol; polycyclic ether.

* Corresponding author. Tel.: +81-22-2176581; fax: +81-22-2176784; e-mail: yoshi@yamamoto1.chem.tohoku.ac.jp

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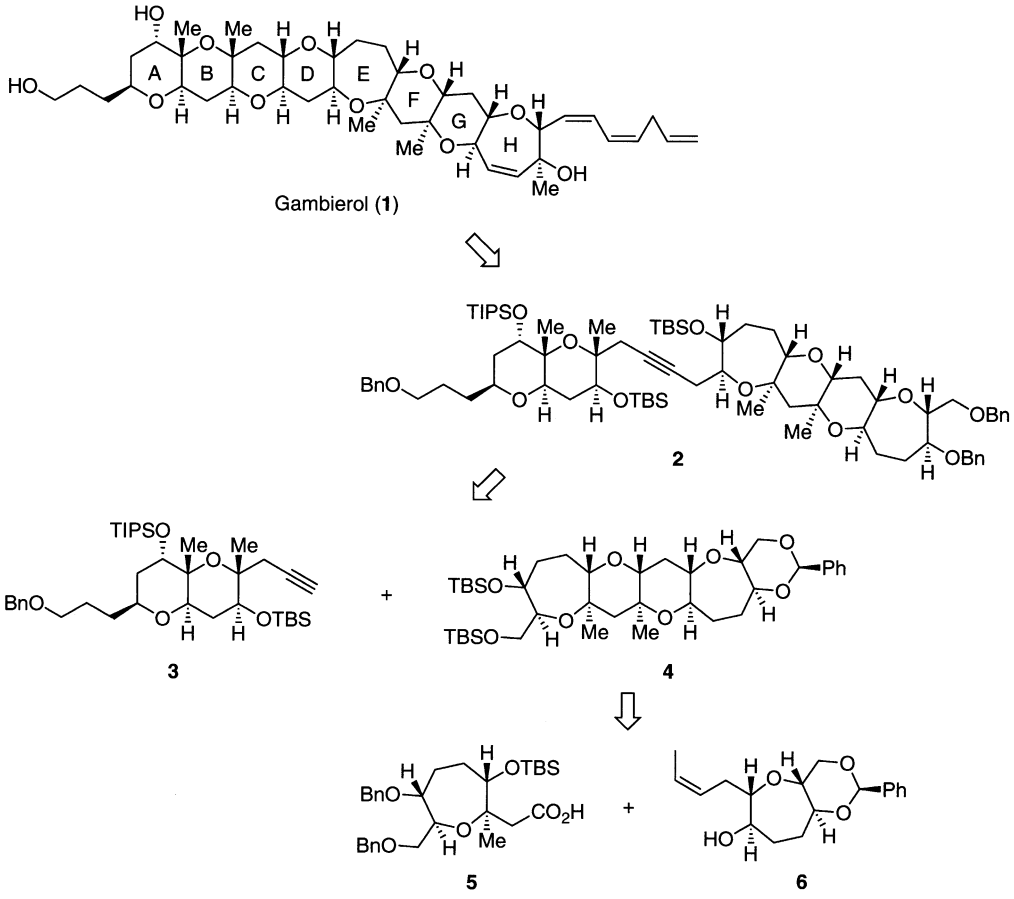
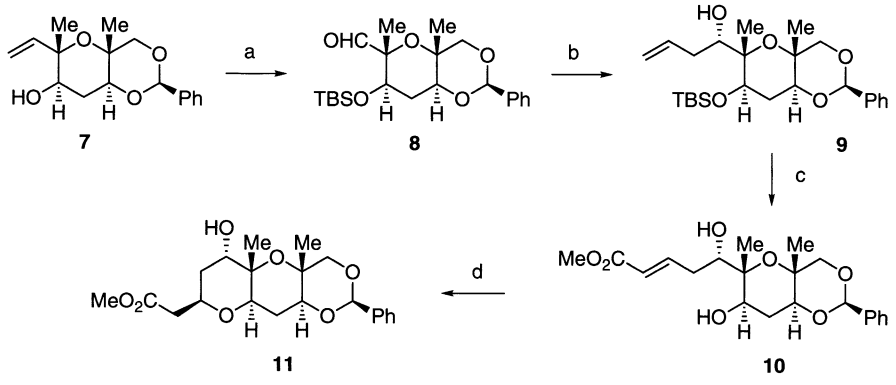


Scheme 1. Retrosynthesis of gambierol (**1**).



Scheme 2. (a) (i) TBSOTf, 2,6-lutidine, CH_2Cl_2, 40°C, 100%; (ii) O_3, CH_2Cl_2/MeOH, −78°C, then PPh_3, −78°C to rt, 99%; (b) $^{d}Ipc_2B$-allyl, ether, −78°C; H_2O_2, NaOH, rt, 92%; (c) (i) TBAF, THF, rt, 100%; (ii) O_3, CH_2Cl_2/MeOH, −78°C, then PPh_3, −78°C to rt, 99%; (iii) $Ph_3P{=}CHCO_2Me$, CH_2Cl_2, rt, 95%; (d) K_2CO_3, THF/MeOH, 40°C, 78% (92:8).

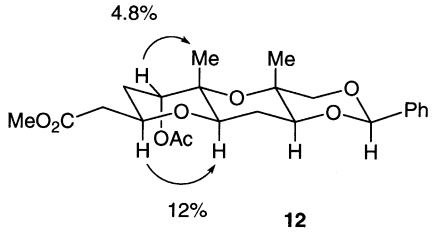
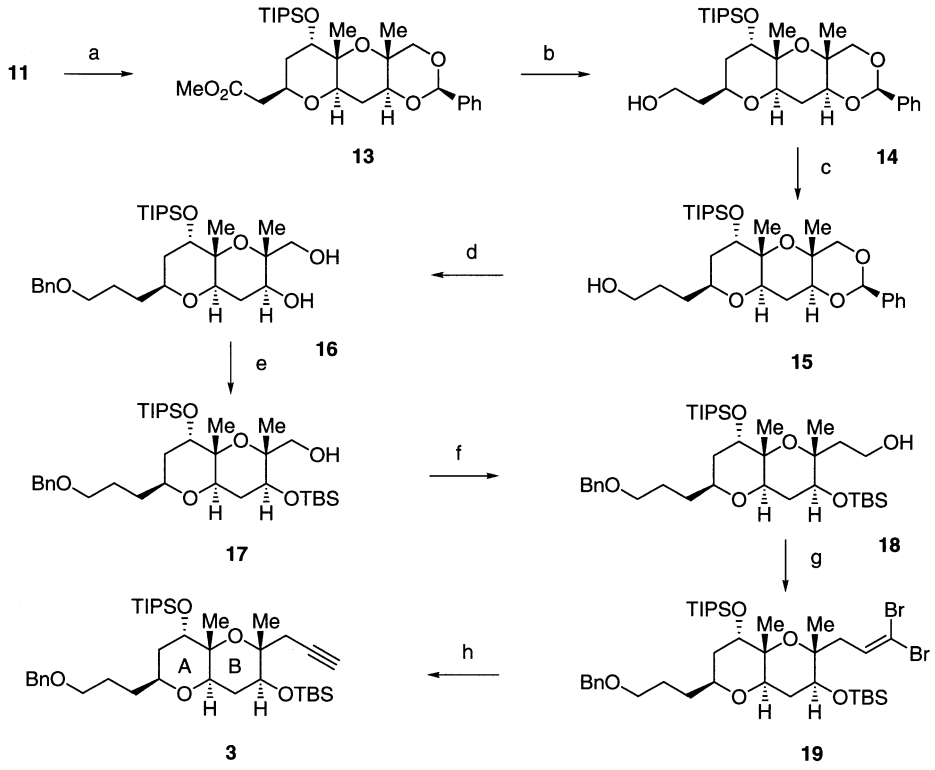


Figure 1. Observed NOEs are shown by arrows.

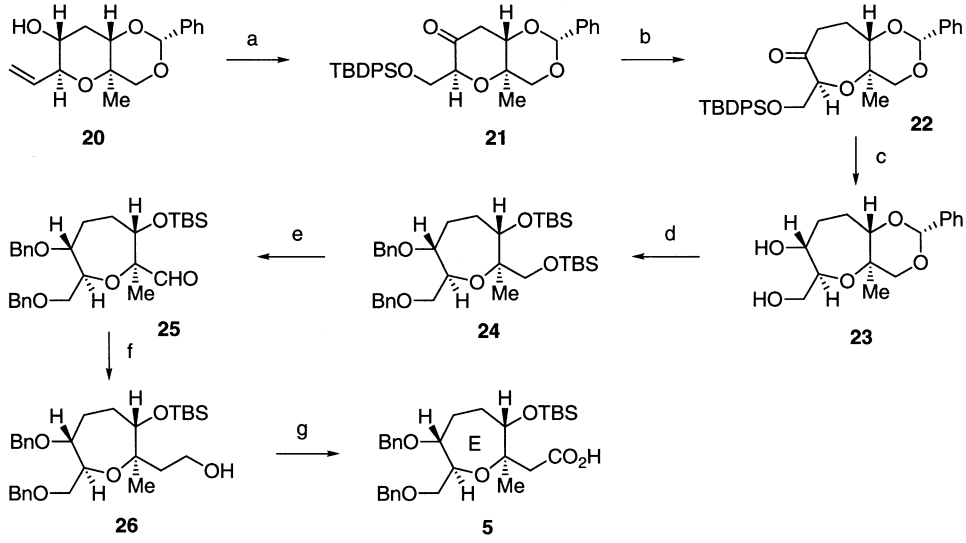
hydroxy group of **15** followed by removal of the benzylidene acetal using catalytic CSA in MeOH furnished the diol **16** in 99% yield. Protection of **16** as a bis-TBS ether followed by selective deprotection of the primary silyloxy group gave **17** in 76% yield. Swern oxidation, Wittig reaction, and hydroboration afforded the alcohol **18** in 72% yield. Conversion of **18** to the alkyne **3** was performed by oxidation with SO_3·py/DMSO/Et_3N, reaction with CBr_4/PPh_3, followed by treatment of the resulting dibromoolefin **19** with *n*-BuLi.[13] The yield of **3** from **18** was 88%.



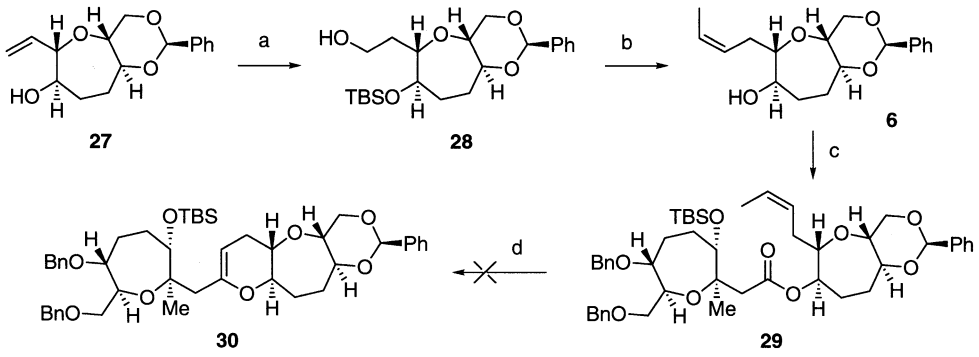
Scheme 3. (a) TIPSOTf, 2,6-lutidine, DMF, 60°C, 98%; (b) $LiAlH_4$, ether, 0°C, 96%; (c) (i) $(COCl)_2$, DMSO, CH_2Cl_2, −78°C, then Et_3N, −78°C to rt; (ii) $Ph_3P^+CH_3Br^-$, NaHMDS, THF, 0°C, 90% (2 steps); (iii) (*c*-Hex)$_2$BH, 0°C, then 30% H_2O_2, 3N NaOH, 0°C to rt, 94%; (d) (i) BnBr, KH, THF, 60°C; (ii) CSA, MeOH, rt, 99% (2 steps); (e) (i) TBSOTf, 2,6-lutidine, CH_2Cl_2, rt; (ii) CSA, MeOH/CH_2Cl_2, rt, 76% (2 steps); (f) (i) $(COCl)_2$, DMSO, CH_2Cl_2, −78°C, then Et_3N, −78°C to rt; (ii) $Ph_3P^+CH_3Br^-$, NaHMDS, THF, 40°C, 97% (2 steps); (iii) $BH_3{\cdot}SMe_2$, 0°C, then 30% H_2O_2, 3N NaOH, 0°C to rt, 74%; (g) (i) $SO_3{\cdot}py$, DMSO, Et_3N, CH_2Cl_2, 0°C, 91%; (ii) CBr_4, PPh_3, CH_2Cl_2, 0°C, 97%; (h) *n*-BuLi, THF, −78°C, 99%.

3. Attempted convergent approaches toward the EFGH ring framework

We next examined the convergent synthesis of the EFGH ring segment **4**. The E ring moiety was constructed in stereoselective manner by using Mori's ring expansion methodology as shown in Scheme 4. The starting material **20**, prepared from 2-deoxy-D-ribose via the hydroxy epoxide cyclization,[9] was converted to the ketone **21** in 62% yield via ozonolysis, reductive work up, selective



Scheme 4. (a) (i) O_3, MeOH, −78°C, then $NaBH_4$, −78°C to rt, 78%; (ii) TBDPSCl, imidazole, DMF, rt, 86%; (iii) $(COCl)_2$, DMSO, CH_2Cl_2, −78°C, then Et_3N, −78°C to rt, 93%; (b) (i) $TMSCHN_2$, $BF_3{\cdot}OEt_2$, CH_2Cl_2, −78°C; (ii) PPTS, MeOH, rt, 74% (2 steps); (c) (i) TBAF, THF, rt, 89%; (ii) $Me_4NBH(OAc)_3$, CH_3CN/AcOH, −20°C, 89%; (d) (i) BnBr, KH, THF, 0°C to rt, 68%; (ii) conc. HCl, MeOH, rt, 86%; (iii) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0°C to rt, 98%; (e) (i) CSA, MeOH, 0°C, 89%; (ii) $(COCl)_2$, DMSO, CH_2Cl_2, −78°C, then Et_3N, −78°C to rt, 93%; (f) (i) $Ph_3P^+CH_3Br^-$, NaHMDS, THF, 0°C, 33%; (ii) (*c*-Hex)$_2$BH, THF, 0°C, then 30% H_2O_2, 3N NaOH, 93%; (g) (i) Dess–Martin periodinane, CH_2Cl_2, rt; (ii) $NaClO_2$, 2-methyl-2-butene, NaH_2PO_4, *t*-BuOH/H_2O, rt, 91% (2 steps).

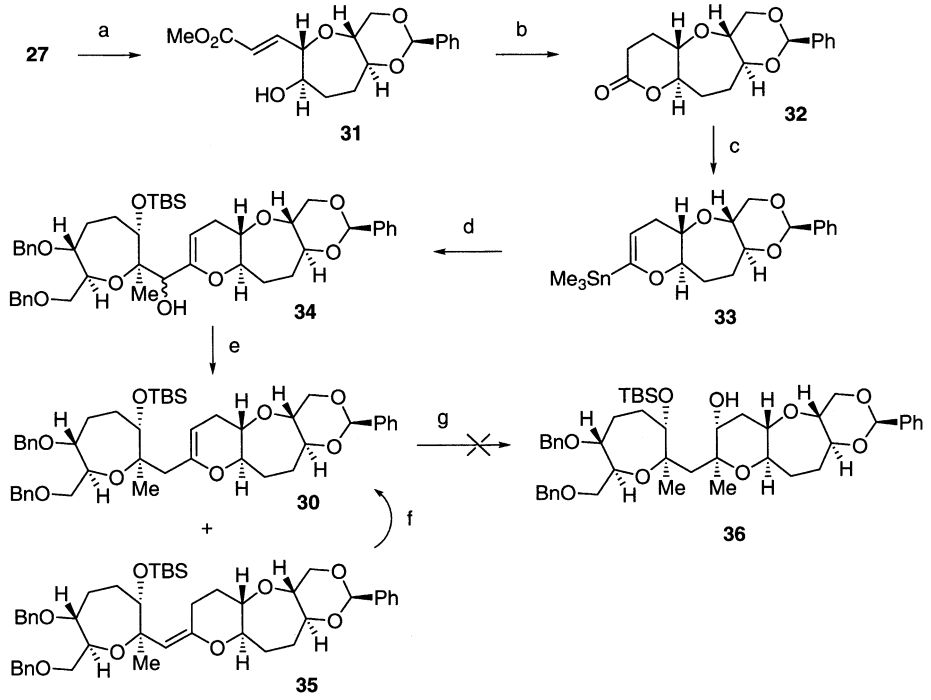


Scheme 5. (a) (i) TBSCl, imidazole, DMF, 50°C, 96%; (ii) (*c*-Hex)$_2$BH, THF, 0°C, then 30% H_2O_2, 3N NaOH, 99%; (b) (i) $(COCl)_2$, DMSO, CH_2Cl_2, −78°C, then Et_3N, −78°C to rt; (ii) $Ph_3P^+CH_2CH_3Br^-$, NaHMDS, THF, 0°C, 65% (2 steps); (iii) TBAF, THF, rt, 99%; (c) **5**, DCC, DMAP, CSA, CH_2Cl_2, rt, 45%; (d) Tebbe reagent or Cp_2TiMe_2, THF, rt to 65°C.

protection of the resulting primary alcohol, and Swern oxidation. Treatment of **21** with $TMSCHN_2$ and $BF_3{\cdot}OEt_2$ followed by the hydrolysis of the resulting silyl enol ether gave the 7-membered cyclic ketone **22** in 74% yield.[14] Desilylation and subsequent stereoselective reduction of the resulting β-hydroxy ketone afforded the diol **23** as the sole product in 89% yield.[15] Benzyl protection of **23**, hydrolysis of the benzylidene acetal, and TBS protection gave the bis-TBS ether **24** in 57% yield. Selective deprotection of the primary silyloxy group followed by Swern oxidation gave the aldehyde **25** in 83% yield. One carbon chain elongation of **25** was performed by Wittig reaction followed by hydroboration to give the alcohol **26** in 31% yield. Dess–Martin oxidation of **26**,[16] followed by the treatment of the resulting aldehyde with $NaClO_2$, gave the carboxylic acid **5** in 91% yield.

TBS protection of **27**[3c] followed by hydroboration afforded **28** in 95% yield (Scheme 5). The alcohol **28** was converted to the olefin **6** in 64% yield via Swern oxidation, Wittig reaction, and desilylation. DCC coupling of **6** with **5** gave the ester **29** in 45% yield. The coupling product **29** was then subjected to the metathesis reaction reported by Nicolaou.[7] However, all attempts to effect cyclization of **29** resulted in failure and none of **30** was obtained.

Scheme 6 shows an alternative approach towards the EFGH ring framework via the intermediate **30**. The compound **27** was converted to **31** in quantitative yield via ozonolysis and Wittig reaction. Hydrogenation of **31** followed by lactonization gave the lactone **32** in 77% yield. Treatment of **32** with KHMDS and $PhNTf_2$ gave the corresponding ketene acetal triflate,[17] which was converted to the vinylstannane



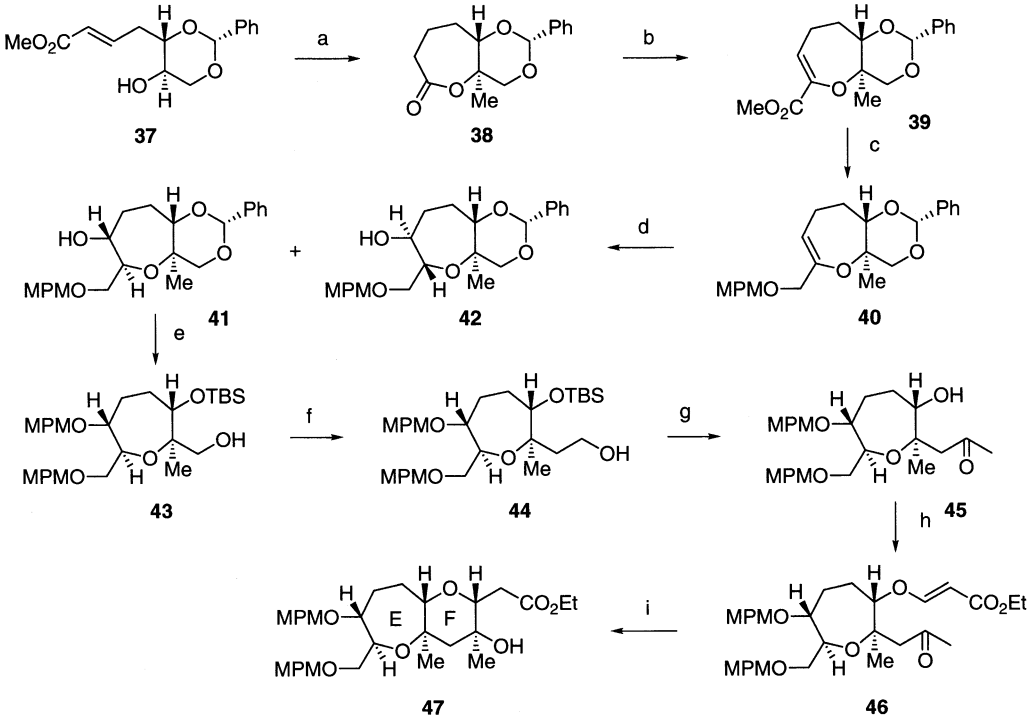
Scheme 6. (a) (i) O_3, CH_2Cl_2, −78°C, then Ph_3P, −78°C to rt; (iii) $Ph_3P{=}CH_2CO_2Me$, 100% (2 steps); (b) (i) H_2, Pd/C, EtOAc, rt, 98%; (ii) *p*-TsOH, benzene, reflux, 79%; (c) (i) KHMDS, $PhNTf_2$, HMPA, THF, −78°C to rt, 70%; (ii) $(Me_3Sn)_2$, LiCl, $Pd(PPh_3)_4$, THF, reflux, 81%; (d) *n*-BuLi, THF, −78°C, then **25**, 97%; (e) (i) KH, CS_2, THF, rt, then MeI, 95%; (ii) *n*-Bu_3SnH, AIBN, benzene, 85°C, 64% of **30** and 11% of **35**; (f) $RuCl_2(PPh_3)_3$, benzene, 80°C, 61%; (g) (i) dimethyldioxirane, CH_2Cl_2, −65°C; (ii) Me_3Al, CH_2Cl_2, −78°C to rt.

33 in 57% yield by the palladium catalyzed coupling with $(Me_3Sn)_2$.[18] The vinylstannane **33** was then subjected to condensation with the aldehyde **25** under the conditions reported by Nicolaou. Thus, the metal exchange with *n*-BuLi and addition of the aldehyde **25** gave the coupling product **34** as a mixture of diastereoisomers in 97% yield.[19] Barton deoxygenation of **34** gave an 85:15 mixture of **30** and the *exo*-olefin **35** in 75% combined yield.[20] The later compound was converted to the desired enol ether **30** by heating with $RuCl_2(PPh_3)_3$ in 61% yield.[19] Again, however, all attempts to introduce a methyl group into the olefin of **30** using the Rainier's protocol failed.[21] Finally, therefore, we decided to abandon the convergent construction of **4** and to seek a linear approach to the EFGH ring framework.

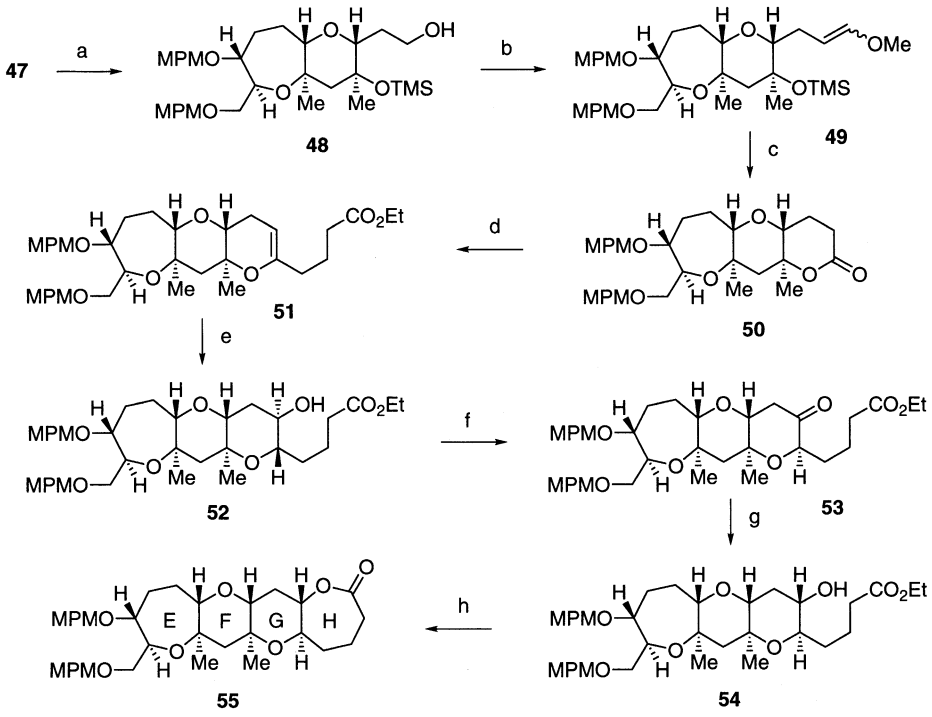
4. Synthesis of the EFGH ring segment

Scheme 7 describes the synthesis of the EF ring segment. The starting material **37**,[22] derived from 2-deoxy-D-ribose, was converted into **38** in 67% yield by hydrogenation, Swern oxidation, methylation, hydrolysis, and Yamaguchi lactonization.[23] The ketene acetal triflate derived from the lactone **38** was subjected to the palladium catalyzed carbonylation to give **39** in 92% yield.[24] DIBALH reduction of the ester **39** followed by MPM protection gave **40** in 99% yield. Hydroboration of the enol ether **40** with $BH_3{\cdot}SMe_2$ gave a 3:2 mixture of the desired alcohol **41** and its stereoisomer **42** in 89% yield. Protection of **41** with MPMCl, hydrolysis of the benzylidene acetal, protection of the resulting diol as a bis-TBS ether, and selective removal of the primarly TBS group afforded **43** in 57% yield. One carbon elongation of the hydroxymethyl group of **43** was achieved by Swern oxidation and subsequent Wittig reaction of the resulting aldehyde followed by hydroboration to give alcohol **44** in 77% yield. Swern oxidation followed by the addition of MeMgBr to the resulting aldehyde gave the corresponding methyl carbinol, which was oxidized under Swern conditions, giving the methyl ketone **45** upon desilylation, in 66% yield. Construction of the F ring including 1,3-diaxial methyl groups was carried out by the Nakata protocol.[25] Thus, treatment of the alcohol **45** with ethyl propiolate and 4-methylmorphorine gave the acrylate **46**, which was then subjected to the SmI_2 mediated reductive cyclization to give the bicycle **47** as a single stereoisomer in 97% yield.

Construction of the EFGH ring system is shown in Scheme 8. Protection of the hydroxy group of **47** with TMS/imidazole followed by reduction of the ester with $LiAlH_4$ gave the alcohol **48** in quantitative yield. Swern oxidation of **48** followed by Wittig reaction gave the enol ether **49** in 64% yield. After hydrolysis, the resulting aldehyde was oxidized to the corresponding hydroxy carboxylic acid, which was allowed to cyclize under Yamaguchi conditions to give **50** in 74% yield. Treatment of the lactone **50** with $PhNTf_2$ and KHMDS gave the corresponding ketene acetal triflate, which was allowed to react with $IZn(CH_2)_3CO_2Et$ in the presence of $Pd(PPh_3)_4$ to afford **51** in 87% yield.[4c,26,27] Unfortunately, hydroboration of the



Scheme 7. (a) (i) H_2, 5% Pd/C, EtOAc, 98%; (ii) $(COCl)_2$, DMSO, CH_2Cl_2, −78°C, then Et_3N, −78°C to rt; (iii) Me_3Al, CH_2Cl_2, −20°C, 70% (2 steps); (iv) LiOH, THF/H_2O, rt, 100%; (v) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, rt, then DMAP, benzene, rt, 98%; (b) (i) $PhNTf_2$, KHMDS, HMPA, THF, −78°C; (ii) CO, Et_3N, $Pd(PPh_3)_4$, MeOH, rt, 92% (2 steps); (c) (i) DIBALH, CH_2Cl_2, −78°C, 99%; (ii) MPMCl, KH, THF, 0°C to rt, 95%; (d) BH_3SMe_2, THF, 0°C to rt, then 30% H_2O_2, 3N NaOH, 0°C, 53% of **41**, 36% of **42**; (e) (i) MPMCl, KH, THF, 0°C to rt, 77%; (ii) CSA, CH_2Cl_2/MeOH, rt, 84%; (iii) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0°C to rt, 96%; (iv) CSA, CH_2Cl_2/MeOH, 0°C, 91%; (f) (i) $(COCl)_2$, DMSO, CH_2Cl_2, −78°C, then Et_3N, −78°C to rt, 95%; (ii) $Ph_3P^+CH_3Br^-$, NaHMDS, THF, 0 to rt, 96%; (iii) $(c\text{-Hex})_2BH$, 0°C, then H_2O_2, 3N NaOH, 0°C, 84%; (g) (i) $(COCl)_2$, DMSO, CH_2Cl_2, −78°C, then Et_3N, −78°C to rt, 86%; (ii) MeMgI, ether, 0°C; (iii) $(COCl)_2$, DMSO, CH_2Cl_2, −78°C, then Et_3N, −78°C to rt, 89% (2 steps); (iv) TBAF, THF, rt, 86%; (h) ethyl propiolate, 4-methylmorphorine, CH_2Cl_2, rt, 100%; (i) SmI_2, MeOH, THF, 0°C, 97%.



Scheme 8. (a) (i) TMS/imidazole, CH_2Cl_2, rt; (ii) $LiAlH_4$, ether, 0°C, 100% (2 steps). (b) (i) SO_3·py, DMSO, Et_3N, CH_2Cl_2, rt, 87%; (ii) $Ph_3P^+CH_2OMeCl^-$, NaHMDS, THF, −78°C to rt, 74%; (c) (i) CSA, CH_3CN/H_2O, rt, 83%; (ii) $NaClO_2$, 2-methyl-2-butene, NaH_2PO_4, *t*-BuOH/H_2O, rt; (iii) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, rt, then DMAP, benzene, rt, 89% (2 steps); (d) (i) $PhNTf_2$, KHMDS, HMPA, THF, −78°C; (ii) $IZn(CH_2)_3CO_2Et$, $Pd(PPh_3)_4$, benzene, rt, 87% (2 steps); (e) BH_3·SMe_2, THF, 0°C, then 30% H_2O_2, satd $NaHCO_3$, 94%; (f) (i) Dess–Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt; (ii) DBU, toluene, rt, 64% (2 steps); (g) $NaBH_4$, CH_2Cl_2/MeOH, −78°C, 98%; (h) (i) LiOH, THF/H_2O, 40°C; (ii) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, rt, then DMAP, benzene, rt, 76% (2 steps).

enol ether **51** gave the undesired stereoisomer **52** as the sole product, although the yield was quantitative. Stereoisomerization of **52** was performed by the following steps; Dess–Martin oxidation of **52** followed by treatment with DBU gave **53** in 64% yield, and then reduction of the ketone **53** with $NaBH_4$ gave the desired alcohol **54** as a single stereoisomer in 98% yield. Hydrolysis of the ester followed by Yamaguchi lactonization gave the EFGH ring segment **55** in 76% yield. The stereochemistry of **55** was unambiguously confirmed by ^1H NMR analysis and NOE experiments as shown in Fig. 2.

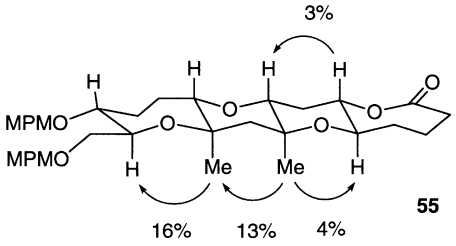


Figure 2. Observed NOEs are shown by arrows.

5. Conclusion

Synthesis of the AB ring segment **3**, having absolute stereochemistry corresponding to natural gambierol **1**, was achieved from 2-deoxy-D-ribose. Brown's asymmetric allylboration and the intramolecular hetero-Michael reaction were successfully applied to the construction of the A ring moiety. Although a significant number of convergent approaches toward the EFGH ring framework were examined, all attempts resulted in failure, forcing us to take a linear strategy for the target molecule. Finally, the construction of the EFGH ring segment **55** was achieved by 40 steps from 2-deoxy-D-ribose in 1.9% total yield. The SmI_2 mediated reductive cyclization was successfully applied to the construction of the EF ring bearing two 1,3-diaxial methyl groups. The palladium catalyzed coupling of enol triflate and zinc bishomoenolate was very effective and efficient for synthesizing the GH ring moiety. Further studies toward the total synthesis of gambierol are now in progress in our laboratories.

6. Experimental

6.1. General procedure

All reactions involving air- and/or moisture-sensitive materials were carried out under argon with dry solvents purchased from Wako or Kanto chemicals. On workup, extracts were dried over $MgSO_4$. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm Merck silica gel plates (60F-254). Column chromatography was performed with Kanto Chemical silica gel (60N, spherical, neutral, particle size 0.100–0.210 mm). Yields refer to chromatographically and spectroscopically homogeneous materials.

Chemical shifts are reported in delta (δ) units relative to

tetramethylsilane or to the singlet at 7.26 ppm for chloroform. Coupling constants are reported in hertz (Hz).

6.1.1. Aldehyde 8. To a stirred solution of alcohol **7** (5.0 g, 17.2 mmol) and 2,6-lutidine (6.0 ml, 51.7 mmol) in CH_2Cl_2 (170 ml) at 0°C was added TBSOTf (7.88 ml, 34.4 mmol) dropwise, and the mixture was stirred at room temperature. After 1 h, the reaction mixture was quenched with MeOH, diluted with ether, then washed with satd $NaHCO_3$ and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 10:1) to give the silyl ether (7.1 g, quantitative): colorless oil; R_f=0.45 (hexane/EtOAc, 10:1); IR (neat) 1471, 1095 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.53–7.42 (m, 5H), 6.01 (dd, J=12.7, 7.0 Hz, 1H), 5.70 (s, 1H), 5.39 (dd, J=12.7, 0.7 Hz, 1H), 5.31 (dd, J=7.0, 0.7 Hz, 1H), 4.06 (d, J=9.9 Hz, 1H), 3.78 (m, 1H), 2.12 (m, 2H), 1.70 (s, 3H), 1.49 (s, 3H), 1.01 (s, 9H), 0.23 (s, 3H), 0.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.5, 137.6, 129.1, 128.4, 126.3, 112.6, 103.0, 80.3, 78.5, 74.7, 68.9, 31.3, 25.7, 21.2, 19.1, 17.8, −4.1, −4.9.

A solution of the silyl ether (5.0 g, 12.3 mmol) in CH_2Cl_2 (60 ml) and MeOH (60 ml) was cooled to −78°C. After passing ozonized oxygen until color of the solution changed to blue, PPh_3 (6.48 g, 24.7 mmol) was added and the mixture was stirred for 30 min at room temperature. The reaction mixture was concentrated and purified by chromatography (hexane/EtOAc, 10:1) to give the aldehyde **8** (4.9 g, 99%): colorless oil; R_f=0.20 (hexane/EtOAc, 10:1); $[\alpha]^{24}_D$=−1.8° (*c* 1.00, $CHCl_3$); IR (neat) 2947, 1741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.39 (s, 1H), 7.35–7.20 (m, 5H), 5.57 (s, 1H), 4.03 (dd, J=9.4, 5.8 Hz, 1H), 3.95 (d, J=9.9 Hz, 1H), 3.66–3.58 (m, 2H), 2.18–2.12 (m, 1H), 1.98 (ddd, J=12.3, 12.3, 9.4 Hz, 1H), 1.60 (s, 3H), 1.38 (s, 3H), 0.97 (s, 9H), 0.08 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.6, 137.2, 129.2, 128.3, 126.2, 102.9, 81.9, 79.2, 76.6, 69.2, 67.8, 30.8, 25.5, 18.8, 17.7, 17.5, −4.4, −5.2; HRMS (EI) calcd for $C_{22}H_{34}O_5Si$ 406.2174, found 406.2176.

6.1.2. Homoallylic alcohol 9. To a stirred solution of aldehyde **8** (5.0 g, 12.3 mmol) in ether (110 ml) at −78°C was added dropwise a solution of allyldiisopinocamphenylborane (117 ml, 0.21 M in pentane) over 14 min. After stirring for 5 h at the same temperature, the mixture was quenched with MeOH. H_2O_2 (30 ml, 30% in H_2O) and aqueous NaOH (29 ml, 3N in H_2O) were added to the reaction mixture at 0°C and the mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with ethyl acetate, then washed with satd NH_4Cl and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 20:1) to give the homoallylic alcohol **9** (5.08 g, 92%): colorless oil; R_f=0.39 (hexane/EtOAc, 4:1); $[\alpha]^{24}_D$=+1.5° (*c* 1.07, $CHCl_3$); IR (neat) 3600–3200, 1641 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.91 (m, 1H), 5.55 (s, 1H), 5.10 (m, 2H), 4.05 (dd, J=11, 5.1 Hz, 1H), 3.88 (d, J=9.9 Hz, 1H), 3.49–3.34 (m, 3H), 2.55 (m, 1H), 2.41 (dd, J=14.5, 6.2 Hz, 1H), 2.21–1.91 (m, 3H), 1.45 (s, 3H), 1.35 (s, 3H), 0.87 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.4, 136.4, 129.2, 128.4, 126.3, 116.5, 103.1, 80.1, 78.0, 76.6, 71.7, 68.8, 35.7, 31.1, 25.7, 18.9, 18.85, 17.9, −3.1, −4.7; HRMS (EI) calcd for $C_{25}H_{39}O_5Si$ (M−H) 447.2567, found 447.2610.

6.1.3. Unsaturated ester 10. To a stirred solution of **9** (14.1 g, 31.5 mmol) in THF (300 ml) at 0°C was added TBAF (38 ml, 1 M in THF, 38 mmol). After 0.5 h, the reaction mixture was concentrated and subjected to chromatography (hexane/EtOAc, 2:1) to give the diol (10.5 g, 100%): colorless oil; R_f=0.57 (hexane/EtOAc, 1:1); $[\alpha]^{24}_D$=−4.6° (*c* 0.11, $CHCl_3$); IR (neat) 3600–3200, 1155 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.78 (m, 1H), 5.53 (s, 1H), 5.20–5.10 (m, 2H), 3.84 (dd, J=11.4, 4.8 Hz, 1H), 3.81 (d, J=9.7 Hz, 1H), 3.69 (s, 1H), 3.49 (m, 3H), 2.84 (s, 1H), 2.53 (m, 1H), 2.12–1.85 (m, 3H), 1.51 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.4, 135.2, 129.0, 128.2, 126.2, 118.3, 102.8, 80.3, 79.7, 77.6, 76.6, 74.8, 68.8, 35.4, 28.9, 18.8, 15.9; HRMS, calcd for $C_{19}H_{26}O_5$ (M) 334.1780, found 334.1781.

A solution of the diol (10.5 g, 31.5 mmol) in CH_2Cl_2 (150 ml) and MeOH (150 ml) was treated with ozone at −78°C until the solution turned to blue. The mixture was treated with triphenylphosphine (24.8 g, 94.5 mmol) and stirred at 25°C for 1 h. Concentration and chromatography (hexane/EtOAc, 1:1) gave the hemiacetal (10.5 g, 99%): white solid; R_f=0.19 (hexane/EtOAc, 1:1); IR (neat) 3600–3200, 1452 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.59 (s, 1H), 5.14 (d, J=3.7 Hz, 1H), 4.43 (m, 1H), 3.94–3.52 (m, 4H), 2.10 (m, 4H), 1.64 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 129.3, 128.4, 126.3, 103.3, 92.5, 82.6, 77.2, 76.4, 71.6, 71.4, 33.9, 26.5, 20.5, 20.0, 18.6.

To a solution of the hemiacetal (10.5 g, 31.2 mmol) in CH_2Cl_2 (300 ml) was added methyl triphenylphosphoranylideneacetate (52.2 g, 156 mmol) at room temperature and the mixture was stirred for 12 h at 40°C. The reaction mixture was concentrated and diluted with hexane. The resulting solid was filtered off and the filtrate was concentrated. The residue was purified by chromatography (hexane/EtOAc, 1:1) to give α,β-unsaturated ester **10** (11.9 g, 95%): colorless oil; R_f=0.36 (hexane/EtOAc, 1:1); $[\alpha]^{24}_D$=+14.2° (*c* 0.45, $CHCl_3$); IR (neat) 3600–3200, 1728 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 6.98 (ddd, J=15.2, 9.0, 7.0 Hz, 1H), 5.94 (d, J=15.2 Hz, 1H), 5.55 (s, 1H), 3.88 (m, 1H), 3.82 (d, J=10.3 Hz, 1H), 3.73 (s, 3H), 3.64–3.48 (m, 4H), 3.02 (m, 1H), 2.67 (m, 1H), 2.24 (m, 1H), 2.17–1.86 (m, 2H), 1.53 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 146.4, 137.4, 129.2, 128.4, 126.3, 123.5, 103.0, 80.2, 79.6, 77.8, 74.6, 69.1, 51.6, 34.3, 29.3, 18.9, 16.1; HRMS (EI) calcd for $C_{21}H_{28}O_7$ (M^+) 392.1835, found 392.1839.

6.1.4. Ester 11. To a solution of **10** (12.8 g, 32.7 mmol) in THF (15 ml) and MeOH (15 ml) was added K_2CO_3 (90 mg, 0.66 mmol). After stirring for 5 h at 40°C, the reaction mixture was diluted with ether, then washed with satd NH_4Cl, water, and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 10:1) to give **11** (10.0 g, 78%): colorless oil; R_f=0.39 (hexane/EtOAc, 5:1); $[\alpha]^{24}_D$=+4.9° (*c* 0.41, $CHCl_3$); IR (neat) 3600–3200, 1732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.52 (s, 1H), 4.25 (m, 1H),

3.91 (dd, J=12.0, 4.0 Hz, 1H), 3.81 (d, J=9.7 Hz, 1H), 3.7 (bs, 1H), 3.64 (s, 3H), 3.58 (dd, J=12.0, 4.0 Hz, 1H), 3.52 (d, J=9.9 Hz, 1H), 2.63 (bs, 1H), 2.51 (dd, J=15.2, 7.3 Hz, 1H), 2.37 (dd, J=15.2, 5.3 Hz, 1H), 2.07–1.81 (m, 4H), 1.56 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 137.2, 128.9, 128.1, 126.1, 102.8, 81.8, 76.1, 76.0, 73.4, 71.1, 70.8, 70.7, 70.5, 51.5, 40.1, 34.7, 26.5, 20.0, 19.5; HRMS (EI) calcd for $C_{21}H_{28}O_7$ (M^+) 392.1835, found 392.1838.

6.1.5. Acetate 12. This material was prepared from **11** with standard acetylation conditions. **12**: colorless oil; R_f=0.38 (hexane/EtOAc, 2:1); IR (neat) 1732 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.56 (s, 1H), 5.56 (t, J=2.8 Hz, 1H), 4.21 (m, 1H), 3.90 (dd, J=11.7, 4.0 Hz, 1H), 3.85 (d, J=9.9 Hz, 1H), 3.70 (s, 3H), 3.60 (dd, J=11.7, 3.7 Hz, 1H), 3.42 (d, J=10.0 Hz, 1H), 2.57 (dd, J=15.8, 7.7 Hz, 1H), 2.21 (dd, J=15.7, 5.0 Hz, 1H), 2.21 (s, 3H), 2.15–1.94 (m, 3H), 1.78 (m, 1H), 1.57 (s, 3H), 1.42 (s, 3H).

6.1.6. TIPS ether 13. To a stirred solution of alcohol **11** (3.3 g, 8.4 mmol) and 2,6-lutidine (4.9 ml, 42 mmol) in DMF (85 ml) at 0°C was added TIPSOTf (9.9 ml, 37 mmol). After stirring for 13 h at 60°C, the mixture was diluted with ether, then washed with satd NH_4Cl, water, and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 10:1) to give **13** (4.5 g, 98%): colorless oil; R_f=0.22 (hexane/EtOAc, 10:1); $[\alpha]^{24}_D$=+8.6° (c 1.06, $CHCl_3$); IR (neat) 1743 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.51 (s, 1H), 4.29 (m, 1H), 4.03 (dd J=12.0, 4.0 Hz, 1H), 3.92 (m, 1H), 3.76 (d, J=9.7 Hz, 1H), 3.65 (s, 3H), 3.63 (m, 2H), 2.58 (dd, J=15.0, 7.0 Hz, 1H), 2.37 (dd, J=15.0, 6.0 Hz, 1H), 2.10–1.86 (m, 3H), 1.71 (dt, J=14.0, 2.8 Hz, 1H), 1.56 (s, 3H), 1.32 (s, 3H), 1.09 (brs, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 137.6, 129.0, 128.3, 126.3, 103.1, 81.9, 76.5, 76.3, 73.4, 71.9, 70.8, 70.5, 51.6, 40.5, 38.1, 27.1, 20.6, 18.2, 18.2, 12.4; HRMS (EI) calcd for $C_{30}H_{48}O_7Si$ (M^+) 548.3169, found 548.3173.

6.1.7. Alcohol 14. To a suspension of $LiAlH_4$ (100 mg, 2.64 mmol) in ether (15 ml) at 0°C was added a solution of **13** (1.45 g, 2.64 mmol) in ether (10 ml). After stirring for 1 h, the mixture was diluted with ether and quenched with brine. The resulting white precipitate was filtered off, and the filtrate was concentrated. The crude product was purified by chromatography (hexane/EtOAc, 4:1) to give **14** (1.31 g, 96%): colorless oil; R_f=0.12 (hexane/EtOAc, 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.53 (s, 1H), 4.16–4.07 (m, 1H), 4.05 (dd, J=11.9, 4.2 Hz, 1H), 3.94 (brs, 1H), 3.84–3.74 (m, 3H), 3.67–3.60 (m, 2H), 2.56 (t, J=5.1 Hz, 1H), 2.07–1.90 (m, 3H), 1.78–1.60 (m, 3H), 1.58 (s, 3H), 1.37 (s, 3H), 1.09 (brs, 21H).

6.1.8. Alcohol 15. To a solution of DMSO (920 μl, 13 mmol) in CH_2Cl_2 (20 ml) at −78°C was added $(COCl)_2$ (930 μl, 10.7 mmol), and the mixture was stirred for 10 min at the same temperature. A solution of **14** (3.1 g, 5.92 mmol) in CH_2Cl_2 (40 ml) was added to the resulting mixture, and the stirring was continued for 1.5 h. Triethylamine (4.1 ml, 29.6 mmol) was added, and the mixture was allowed to warm to room temperature with stirring. The mixture was diluted with ether, then washed with satd NH_4Cl, water, and brine. The organic layer was concentrated to give the crude aldehyde.

To a stirred suspension of methyltriphenylphosphonium bromide (3.2 g, 8.9 mmol) in THF (20 ml) at 0°C was added NaHMDS (8.9 ml, 1.0 M in THF, 8.9 mmol), and the resulting mixture was stirred for 10 min at the same temperature. A solution of the aldehyde obtained above in THF (30 ml) was added to the mixture, and the stirring was continued for 1 h. The reaction was quenched with water, and the mixture was extracted with ether. The organic layer was washed with brine, dried, and concentrated. The residue was diluted with hexane, and the resulting solid was filtered off. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 10:1) to give the olefin (2.8 g, 90%): colorless oil; R_f=0.42 (hexane/EtOAc, 10:1); $[\alpha]^{24}_D$=+28.5° (c 0.74, $CHCl_3$); IR (neat) 2943, 1641 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.78 (m, 1H), 5.53 (s, 1H), 5.06 (m, 2H), 4.02 (dd, J=12.0, 4.0 Hz, 1H), 3.92 (m, 1H), 3.88 (m, 1H), 3.77 (d, J=10.0 Hz, 1H), 3.63 (dd, J=15.6, 4.0 Hz, 1H), 3.63 (s, 1H), 2.33 (m, 1H), 2.17 (m, 1H), 2.12–1.75 (m, 3H), 1.65 (dt, J=14.3, 2.9 Hz, 1H), 1.58 (s, 3H), 1.33 (s, 3H), 1.10 (brs, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 134.3, 129.1, 128.3, 126.3, 117.0, 103.2, 103.0, 82.1, 76.8, 73.7, 73.4, 72.0, 70.4, 39.8, 38.0, 27.2, 20.6, 18.2, 12.4; HRMS (EI) calcd for $C_{30}H_{48}O_5Si$ (M^+) 516.3271, found 516.3287.

To a solution of cyclohexene (1.6 ml, 16 mmol) in THF (20 ml) at 0°C was added BH_3·SMe (710 μl, 8.0 mmol), and the mixture was stirred for 20 min at the same temperature. A solution of the olefin obtained above (2.76 g, 5.3 mmol) in THF (30 ml) was added, and the stirring was continued for 0.5 h. Aqueous 3N NaOH (18 ml, 54 mmol) and 30% H_2O_2 (2 ml, 64 mmol) were added. After stirring for 1 h at room temperature, the mixture was extracted with ether. The organic layer was washed with aqueous $Na_2S_2O_3$ and brine. Concentration and chromatography (hexane/EtOAc, 5:1) gave **15** (2.68 g, 94%): colorless oil; R_f=0.21 (hexane/EtOAc, 3:1); $[\alpha]^{24}_D$=+4.09° (c 0.21, $CHCl_3$); IR (neat) 360–3200, 1654 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.52 (s, 1H), 4.03 (dd, J=11.7, 4.2 Hz, 1H), 3.93 (m, 1H), 3.87 (m, 1H), 3.77 (d, J=9.9 Hz, 1H), 3.63 (m, 4H), 2.06 (m, 1H), 1.97 (d, J=11.7 Hz, 1H), 1.88 (m, 6H), 1.57 (s, 3H), 1.34 (s, 3H), 1.10 (s, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5, 129.0, 128.3, 126.3, 103.0, 81.9, 76.7, 76.3, 74.4, 73.3, 72.0, 70.4, 62.8, 38.7, 32.4, 29.2, 27.1, 20.6, 18.2, 12.4; HRMS (EI) calcd for $C_{30}H_{50}O_6Si$ (M^+) 534.3376, found 534.3349.

6.1.9. Diol 16. To a stirred suspension of KH (1.38 g of a suspension in mineral oil, 12.1 mmol, prewashed with hexane) in THF (50 ml) at 0°C was added a solution of **15** (5.4 g, 10.1 mmol) in THF (50 ml). After 40 min, benzyl bromide (1.8 ml, 15.1 mmol) was added, and the mixture was stirred for 14 h at room temperature. The reaction was quenched with MeOH at 0°C, and the mixture was diluted with ether and washed with water and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 20:1) to give the benzyl ether (6.28 g, 100%): colorless oil; R_f=0.37 (hexane/EtOAc, 20:1); $[\alpha]^{24}_D$=+8.78° (c 0.56, $CHCl_3$); IR (neat) 1641 cm^{-1}; ^{1}H

NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.52 (s, 1H), 4.48 (s, 2H), 3.99 (dd, J=11.7, 4.8 Hz, 1H), 3.91 (s, 1H), 3.84 (m, 1H), 3.77 (d, J=12.5 Hz, 1H), 3.61 (m, 2H), 3.46 (m, 2H), 2.05–1.38 (m, 8H), 1.57 (s, 3H), 1.32 (s, 3H), 1.04 (s, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 137.7, 129.1, 128.3, 127.6, 127.5, 126.3, 103.2, 82.1, 76.6, 76.4, 74.0, 73.3, 73.0, 72.1, 70.4, 70.3, 38.7, 32.3, 27.3, 25.9, 20.8, 20.6, 18.3, 18.3, 12.5.

To a mixture of the benzyl ether (5.8 g, 9.3 mmol) in MeOH (70 ml) and CH_2Cl_2 (30 ml) at 0°C was added camphorsulfonic acid (0.43 g, 1.9 mmol), and the mixture was stirred for 22 h at room temperature. The reaction mixture was quenched with triethylamine, concentrated and purified by chromatography (hexane/EtOAc, 2:1) to give **16** (4.95 g, 99%): colorless oil; R_f=0.34 (hexane/EtOAc, 2:1); IR (neat) 3600–3200, 1465 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 4.49 (s, 2H), 3.94 (dd, J=11.7, 4.8 Hz, 1H), 3.94 (m, 1H), 3.81 (m, 1H), 3.74 (dd, J=12.5, 3.5 Hz, 1H), 3.63–3.32 (m, 4H), 2.58 (brs, 2H), 2.05–1.38 (m, 8H), 1.25 (s, 3H), 1.19 (s, 3H), 1.07 (s, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 128.3, 128.2, 127.6, 127.5, 127.5, 77.8, 75.0, 73.2, 72.9, 72.5, 71.7, 70.2, 67.9, 37.9, 32.2, 30.2, 25.8, 19.4, 18.1, 18.0, 12.7.

6.1.10. TBS ether 17. To a mixture of **16** (4.96 g, 9.2 mmol) and 2,6-lutidine (4.33 ml, 37.1 mmol) in CH_2Cl_2 (100 ml) at 0°C was added TBSOTf (5.5 ml, 23.9 mmol). After stirring for 1 h at room temperature, the mixture was quenched with MeOH at 0°C, diluted with ether, then washed with satd $NaHCO_3$ and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 20:1) to give the bis-silyl ether (6.92 g, 98%): colorless oil; R_f=0.25 (hexane/EtOAc, 20:1); IR (neat) 1641 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 4.49 (s, 2H), 3.88 (m, 1H), 3.78 (m, 1H), 3.75 (dd, J=12.3, 4.2 Hz, 1H), 3.54–3.36 (m, 5H), 1.94–1.40 (m, 8H), 1.21 (s, 3H), 1.20 (s, 3H), 1.07 (s, 21H), 0.87 (s, 9H), 0.85 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H), 0.02 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.3, 127.6, 127.5, 79.2, 74.3, 73.0, 72.2, 71.7, 71.4, 71.0, 70.4, 38.4, 32.3, 31.4, 26.0, 25.7, 19.5, 19.3, 18.4, 18.3, 17.8, 12.5, −3.9, −5.1, −5.3, −5.6.

To a mixture of the bis-silyl ether (6.37 g, 8.32 mmol) in CH_2Cl_2 (20 ml) and MeOH (60 ml) at 0°C was added CSA (0.39 g, 1.7 mmol). After stirring for 18 h at the same temperature, the mixture was quenched with triethylamine, concentrated, and purified by chromatography (hexane/EtOAc, 10:1) gave **17** (4.18 g, 77%): colorless oil; R_f=0.32 (hexane/EtOAc, 10:1); IR (neat) 3600–3200, 1463 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 4.48 (s, 2H), 3.99 (dd, J=11.2, 5.3 Hz, 1H), 3.94 (m, 1H), 3.80 (m, 1H), 3.69 (dd, J=12.1, 4.0 Hz, 1H), 3.46 (m, 2H), 3.27 (m, 2H), 2.41 (dd, J=9.0, 3.7 Hz, 1H), 1.91–1.34 (m, 8H), 1.24 (s, 3H), 1.12 (s, 3H), 1.07 (s, 21H), 0.85 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 128.3, 127.6, 127.5, 78.6, 74.7, 73.1, 72.9, 72.6, 71.4, 70.3, 67.9, 67.5, 37.9, 32.3, 30.8, 25.8, 25.7, 20.0, 19.3, 18.1, 18.0, 17.8, 12.7, 12.5, −4.1, −5.2.

6.1.11. Alcohol 18. To a solution of DMSO (56 μl, 0.78 mmol) in CH_2Cl_2 (2 ml) at −78°C was added $(COCl)_2$ (56 μl, 0.64 mmol), and the mixture was stirred for 10 min at the same temperature. A solution of **17** (232 mg, 0.36 mmol) in CH_2Cl_2 (1.5 ml) was added to the resulting mixture, and the stirring was continued for 1 h. Triethylamine (250 μl, 1.78 mmol) was added, and the mixture was allowed to warm to room temperature with stirring. The mixture was diluted with ether, then washed with satd NH_4Cl, water, and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 10:1) to give the aldehyde (232 mg, 100%): colorless oil; R_f=0.37 (hexane/EtOAc, 10:1); IR (neat) 1726 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.47 (s, 1H), 7.35–7.24 (m, 5H), 4.49 (s, 2H), 3.96 (m, 2H), 3.80 (m, 1H), 3.76 (dd, J=12.5, 4.8 Hz, 1H), 3.46 (m, 2H), 2.07 (m, 1H), 1.80–1.43 (m, 7H), 1.30 (s, 3H), 1.26 (s, 3H), 1.07 (s, 21H), 0.85 (s, 9H), 0.06 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.7, 138.5, 127.6, 127.5, 81.9, 75.4, 73.0, 72.3, 70.4, 70.3, 67.6, 38.3, 32.3, 31.3, 25.9, 25.7, 19.7, 18.2, 18.2, 17.2, 17.9, 12.6, 0.00, −4.4, −5.1; HRMS (EI) calcd for $C_{27}H_{43}O_6Si$ (M−$C_6H_{21}Si$) 491.2825, found 491.2829.

To a stirred suspension of methyltriphenylphosphonium bromide (420 mg, 1.17 mmol) in THF (4 ml) at 0°C was added NaHMDS (1.2 ml, 1.0 M in THF, 1.2 mmol), and the resulting mixture was stirred for 10 min at the same temperature. A solution of the aldehyde (378 mg, 0.58 mmol) in THF (2 ml) was added to the mixture, and the mixture was stirred for 0.5 h at 40°C. The reaction was quenched with water, and the mixture was extracted with ether. The organic layer was washed with brine, dried, and concentrated. The residue was diluted with hexane, and the resulting solid was filtered off. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 20:1) to give the olefin (2.8 g, 90%): colorless oil; R_f=0.45 (hexane/EtOAc, 20:1); IR (neat) 1647 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.85 (dd, J=17.6, 11.0 Hz, 1H), 5.14 (dd, J=17.6, 1.2 Hz, 1H), 4.97 (dd, J=11.0, 1.5 Hz, 1H), 4.49 (s, 2H), 3.90 (m, 1H), 3.84 (dd, J=12.5, 4.4 Hz, 1H), 3.83 (m, 1H), 3.59 (dd, J=10.5, 5.0 Hz, 1H), 3.47 (m, 2H), 1.94–1.43 (m, 8H), 1.30 (s, 3H), 1.25 (s, 3H), 1.07 (s, 21H), 0.85 (s, 9H), 0.05 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 138.6, 128.3, 127.6, 127.5, 112.5, 78.3, 74.8, 73.6, 73.1, 72.9, 72.4, 71.2, 70.4, 38.4, 32.3, 31.6, 25.9, 25.8, 20.9, 19.9, 18.3, 17.9, 12.6, −4.1, −4.9.

A stirred solution of the olefin (406 mg, 0.63 mmol) in THF (7 ml) at 0°C was added BH_3·SMe_2 (89 μl, 1.0 mmol). After stirring for 1 h at the same temperature, the reaction mixture was treated with 3N NaOH (2.1 ml, 6.3 mmol) and 30% H_2O_2 (2.2 ml, 7.6 mmol), and the mixture was stirred for another 1 h. The reaction mixture was diluted with ether, washed with satd aqueous Na_2SO_3 and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 10:1) to give **18** (309 mg, 74%): colorless oil; R_f=0.42 (hexane/EtOAc, 5:1); IR (neat) 3600–3200, 1463 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.26 (m, 5H), 4.50 (s, 2H), 3.92 (m, 1H), 3.88 (m, 2H), 3.81 (dd, J=11.7, 4.6 Hz, 1H), 3.73 (m, 1H), 3.57 (dd, J=10.6, 5.1 Hz, 1H), 3.48 (m, 2H), 2.85 (bs, 1H), 1.91–1.45 (m, 10H), 1.31 (s, 3H), 1.23 (s, 3H), 1.11 (s, 21H), 0.86 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 138.6, 128.4, 127.6, 127.5, 80.4, 75.6, 74.7, 73.2, 73.0, 72.5, 71.1, 70.3, 59.5, 43.4, 38.4, 32.3, 31.0, 25.9, 25.7, 21.1, 19.4, 18.4, 18.3, 17.8, 13.0, −3.8, −5.0; HRMS (EI) calcd for $C_{37}H_{68}O_6Si_2$ (M^+) 664.4550, found 664.4554.

6.1.12. Dibromoolefin 19. To a mixture of **18** (273 mg, 0.41 mmol), DMSO (1 ml), and triethylamine (290 μl, 2.0 mmol) in CH_2Cl_2 (4 ml) at 0°C was added sulfur trioxide pyridine complex (260 mg, 1.6 mmol). After stirring for 2 h, the reaction mixture was diluted with ether, then washed with satd NH_4Cl and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 10:1) to give the aldehyde (247 mg, 91%): colorless oil; R_f=0.38 (hexane/EtOAc, 10:1); IR (neat) 1724 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.89 (t, J=3.1 Hz, 1H), 7.36–7.26 (m, 5H), 4.49 (s, 2H), 3.93 (m, 1H), 3.83 (dd, J=12.1, 4.3 Hz, 2H), 3.55 (dd, J=10.8, 4.9 Hz, 1H), 3.48 (m, 2H), 2.45 (dd, J=15.5, 3.4 Hz, 1H), 2.35 (bd, J=14.5 Hz, 1H), 1.92–1.45 (m, 8H), 1.36 (s, 3H), 1.25 (s, 3H), 1.05 (s, 21H), 0.85 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 203.8, 138.5, 128.4, 127.6, 127.5, 77.6, 77.2, 75.5, 74.7, 73.3, 73.0, 72.2, 71.2, 70.3, 55.2, 38.4, 32.3, 31.0, 30.3, 29.7, 25.9, 25.7, 22.7, 22.1, 19.4, 18.2, 18.2, 17.8, 12.6, −3.8, −5.1.

To stirred solution of CBr_4 (227 mg, 0.68 mmol) in CH_2Cl_2 (1 ml) at 0°C was added triphenylphosphine (359 mg, 1.4 mmol). After 5 min, a solution of the aldehyde (113 mg, 0.17 mmol) in CH_2Cl_2 (1 ml) was added. After stirring for 10 min, the mixture was diluted with CH_2Cl_2 and washed with brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 10:1) to give **19** (135 mg, 97%): colorless oil; R_f=0.45 (hexane/EtOAc, 10:1); ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.20 (m, 5H), 6.61 (m, 1H), 4.48 (s, 2H), 3.90 (m, 1H), 3.81 (m, 1H), 3.76 (dd, J=12.1, 4.2 Hz, 1H), 3.45 (m, 3H), 2.44 (dd, J=15.4, 8.7 Hz, 1H), 1.87–1.38 (m, 8H), 1.19 (s, 3H), 1.17 (s, 3H), 1.06 (s, 21H), 0.87 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 135.9, 128.3, 127.6, 127.5, 88.8, 77.8, 75.2, 74.5, 73.2, 72.9, 72.2, 71.3, 70.3, 46.3, 38.4, 32.3, 31.3, 25.9, 25.7, 21.5, 19.3, 18.3, 18.2, 17.8, 12.7, −3.8, −5.1.

6.1.13. Alkyne 3. To a stirred solution of olefin **19** (225 mg, 0.27 mmol) in THF (3 ml) at −78°C was added *n*-butyllitium (0.36 ml, 1.6 M in hexane, 0.58 mmol), and the mixture was stirred for 0.5 h at the same temperature. The mixture was allowed to warm to 0°C, quenched with satd NH_4Cl, and extracted with ether. The organic layer was washed with brine (0.5 ml), concentrated, and purified by chromatography (hexane/EtOAc, 10:1) to give the acetylene **3** (184 g, quantitative yield): colorless oil; R_f=0.46 (hexane/EtOAc, 10:1); $[\alpha]^{24}_D$=+49.0° (c 0.50, $CHCl_3$); IR (neat) 2120, 1463 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.22 (m, 5H), 4.48 (s, 2H), 3.91 (s, 1H), 3.83 (m, 1H), 3.76 (dd, J=12.1, 4.2 Hz, 1H), 3.46 (m, 3H), 2.45 (dd, J=16.3, 2.8 Hz, 1H), 2.45 (dd, J=16.3, 2.8 Hz, 1H), 2.10 (d, J=16.2 Hz, 1H), 1.90 (t, J=2.0 Hz, 1H), 1.88–1.38 (m, 7H), 1.32 (s, 3H), 1.26 (s, 3H), 1.05 (s, 21H), 0.85 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 128.3, 127.6, 127.5, 81.7, 77.7, 75.0, 74.2, 73.2, 72.9, 71.3, 69.7, 65.8, 38.4, 32.9, 32.3, 31.6, 31.4, 25.9, 25.7, 22.6, 21.4, 19.2, 18.4, 18.3, 17.8, 15.2, 14.1, 12.5, −3.9, −5.1; HRMS (EI) calcd for $C_{35}H_{59}O_5Si_2$ ($M-C_3H_7$) 615.3901, found 615.3905.

6.1.14. Ester 29. A stirred solution of the carboxylic acid **5** (159 mg, 0.30 mmol), alcohol **6** (110 mg, 0.30 mmol), DMAP (11 mg, 0.09 mmol) and CSA (21 mg, 0.09 mmol) in CH_2Cl_2 (3 ml) at 25°C was treated with DCC (93 mg, 0.45 mmol). After 5 h, the reaction mixture was diluted with ether and filtered through a Celite pad. The filtrate was concentration and purified by chromatography (hexane/EtOAc, 10:1) to afford **29** (109 mg, 45%): colorless oil; R_f=0.29 (hexane/EtOAc, 10:1); ^1H NMR (300 MHz, $CDCl_3$) δ 7.51–7.46 (m, 2H), 7.38–7.22 (m, 13H), 5.56 (m, 1H), 5.45 (s, 1H), 5.42 (m, 1H), 4.97 (m, 1H), 4.51 (s, 2H), 4.50 (d, J=11.7 Hz, 1H), 4.35 (d, J=11.7 Hz, 1H), 4.23 (m, 1H), 3.92 (m, 2H), 3.67–3.40 (m, 7H), 2.53 (m, 2H), 2.25 (m, 2H), 2.02–1.60 (m, 6H), 1.61 (d, J=6.6 Hz, 3H), 1.56 (s, 2H), 1.37 (s, 3H), 0.90 (s, 9H), 0.069 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 138.7, 137.8, 128.9, 128.2, 127.6, 127.5, 127.5, 127.4, 127.3, 126.5, 126.2, 125.5, 100.9, 83.6, 81.6, 79.9, 79.6, 78.5, 76.4, 76.0, 75.8, 74.9, 74.7, 74.0, 73.2, 72.1, 70.9, 69.6, 45.9, 32.0, 27.0, 25.9, 25.0, 24.1, 18.0, 18.0, 13.0, −4.2, −5.0.

6.1.15. Vinylatannane 33. A solution of **32** (992 mg, 3.26 mmol) and HMPA (1.14 ml, 6.58 mmol) in THF (30 ml) was treated with KHMDS (13 ml, 0.5 M in toluene, 6.6 mmol) at −78°C. After stirring at −78°C for 2 h, $PhNTf_2$ (2.37 g, 6.58 mmol) was added, and the mixture was allowed to warm to 25°C. After further stirring at 25°C for 1 h, the reaction was quenched with water (containing 1% of triethylamine), and the mixture was extracted with ether. The organic layer was washed with brine, concentrated, and subjected to chromatography (pentane/ether, 10:1–5:1 containing 1% triethylamine) to give the enol triflate (995 mg, 70%): colorless oil; R_f=0.17 (hexane/EtOAc, 10:1); ^1H NMR (300 MHz, C_6D_6) δ 7.62 (d, J=6.8 Hz, 2H), 7.23–7.09 (m, 3H), 5.18 (s, 1H), 4.14 (dd, J=5.0, 2.6 Hz, 1H), 4.09 (m, 1H), 3.40–3.27 (m, 2H), 3.13 (m, 2H), 2.90 (ddd, J=9.3, 9.3, 6.2 Hz, 1H), 1.84–1.54 (m, 6H).

A mixture of the enol triflate (995 mg, 2.28 mmol), hexamethylditin (1.10 ml, 3.30 mmol), $Pd(PPh_3)_4$ (94 mg, 0.08 mmol) and lithium chloride (763 mg, 18 mmol) in THF (20 ml) was heated at 80°C for 5 h. The resulting brown suspension was diluted with ether, filtered through a Celite pad. The filtrate was concentrated and subjected to chromatography (hexane/ether, 300:1–5:1, containing 1% triethylamine) to provide **33** (833 mg, 81%): colorless oil; R_f=0.20 (hexane/ether, 10:1); ^1H NMR (300 MHz, C_6D_6) δ 7.64–7.59 (m, 2H), 7.22–7.08 (m, 3H), 5.25 (s, 1H), 4.68 (m, 1H), 4.20 (dd, J=8.8, 2.9 Hz, 1H), 3.51–3.28 (m, 5H), 2.28–2.10 (m, 2H), 2.04–1.83 (m, 4H), 0.19 (dd, J=27.0, 27.0 Hz, 9H); ^{13}C NMR (75 MHz, C_6D_6) δ 162.4, 138.8, 128.8, 128.2, 126.8, 109.9, 101.3, 82.4, 80.0, 78.9, 75.3, 70.0, 31.3, 29.8, 29.1, −9.79.

6.1.16. Alcohol 34. A solution of azeotropically dried **33** (400 mg, 0.89 mmol) in THF (8.0 ml) was treated dropwise at −78°C with *n*-BuLi (0.52 ml, 1.67 M in *n*-hexane, 0.83 mmol). After stirring at −78°C for 20 min, a solution

of azeotropically dried aldehyde **25** (237 mg, 0.48 mmol) in THF (2.0 ml) was added dropwise. After stirring for another 2 h at −78°C, the mixture was quenched with MeOH at this temperature. The reaction mixture was allowed to warm up to room temperature, diluted with ether, and washed with brine. The organic layer was concentrated and subjected to chromatography (hexane/EtOAc, 10:1–1:1, containing 1% triethylamine) to afford **34** (289 mg, 77%) as a mixture of diastereomers. **34** (major isomer): colorless oil; R_f=0.27 (hexane/EtOAc, 2:1); ^{1}H NMR (300 MHz, C_6D_6) δ 7.63 (d, J=6.2 Hz, 2H), 7.35–7.04 (m, 13H), 5.26 (s, 1H), 4.82 (bdd, J=2.4, 2.4 Hz, 1H), 4.53–4.28 (m, 6H), 4.18 (bd, J=8.1 Hz, 2H), 4.07 (s, 1H), 3.71 (bd, J=10.1 Hz, 1H), 3.59 (dd, J=9.6, 6.3 Hz, 1H), 3.54–3.30 (m, 8H), 2.30–1.77 (m, 8H), 1.47 (s, 3H), 0.96 (s, 9H), 0.065 (d, J=6.2 Hz, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 153.4, 139.5, 139.4, 138.8, 128.9, 128.5, 128.3, 127.8, 127.6, 127.5, 126.7, 101.4, 97.5, 82.7, 82.3, 79.7, 79.1, 78.8, 77.2, 75.4, 74.0, 73.5, 72.5, 71.5, 69.9, 29.9, 29.5, 29.0, 27.5, 26.2, 18.4, 17.5, −4.08, −4.82.

6.1.17. Enol ether 30. A solution of alcohol **34** (13 mg, 0.017 mmol) in ether (1.0 ml) was treated with KH (19 mg of 35% in mineral oil, prewashed with hexane, 0.17 mmol) and carbon disulfide (5 μl, 0.083 mmol), and the mixture was stirred 2 h at 25°C. The reaction mixture was quenched with methyl iodide (20 μl, 0.33 mmol), diluted with ether, then washed with satd NH_4Cl and brine. The organic layer was concentrated to afford the xanthate (13.8 mg, 95%) which was used directly for the next step.

A mixture of xanthate (39 mg, 0.045 mmol), Bu_3SnH (60 μl, 0.023 mmol) and AIBN (1 mg) in benzene (3 ml) was heated at 80°C for 30 min. The mixture was concentrated and subjected to chromatography (hexane/EtOAc, 10:1–4:1, containing 1% triethylamine) to give **30** (22 mg, 64%) and **35** (3.9 mg, 11%).

Compound **30**: colorless oil; R_f=0.46 (hexane/EtOAc, 4:1); ^{1}H NMR (300 MHz, C_6D_6) δ 7.24 (d, J=7.0 Hz, 2H), 7.36 (d, J=7.3 Hz, 2H), 7.29 (d, J=7.4 Hz, 2H), 7.22–7.07 (m, 9H), 5.27 (s, 1H), 4.50 (d, J=11.7 Hz, 1H), 4.95 (s, 2H), 4.48–4.46 (m, 1H), 4.35 (d, J=11.7 Hz, 1H), 4.31–4.20 (m, 2H), 4.09 (bd, J=5.0 Hz, 1H), 3.78 (dd, J=9.9, 2.6 Hz, 1H), 3.68 (dd, J=9.9, 6.2 Hz, 1H), 3.58–3.30 (m, 6H), 2.39 (s, 2H), 2.22–1.60 (m, 8H), 1.50 (s, 3H), 1.42–1.20 (m, 2H), 0.99 (s, 9H), 0.051 (s, 6H); ^{13}C NMR (75.45 MHz, C_6D_6) δ 152.2, 139.6, 138.8, 128.9, 128.5, 127.8, 127.6, 127.5, 127.4, 101.4, 98.0, 82.3, 80.3, 79.6, 79.2, 78.8, 76.2, 75.4, 75.3, 73.4, 72.8, 71.4, 70.0, 45.3, 30.2, 29.7, 29.1, 26.2, 26.0, 25.9, 19.4, 18.3, −4.13, −4.80; HRMS (EI) calcd for $C_{46}H_{62}O_8Si$ (M^+) 770.4210, found 770.4178.

Compound **35**: colorless oil; R_f=0.34 (hexane/EtOAc, 4:1); IR (neat) 3032, 1682 cm^{-1}; $[\alpha]^{21}_D$=−1.97° (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, C_6D_6) δ 7.67 (d, J=7.0 Hz, 2H), 7.38 (d, J=6.8 Hz, 2H), 7.24–7.03 (m, 11H), 5.27 (s, 1H), 4.81 (s, 1H), 4.60–4.39 (m, 5H), 4.34 (d, J=7.0 Hz, 1H), 4.20 (dd, J=10.6, 4.7 Hz, 1H), 3.89 (dd, J=10.1, 2.4 Hz, 1H), 3.76 (dd, J=10.1, 6.0 Hz, 1H), 3.62 (ddd, J=14.5, 5.5, 3.7 Hz, 1H), 3.48–3.22 (m, 5H), 2.96 (ddd, J=14.6, 5.1, 4.2 Hz, 1H), 2.13–1.64 (m, 8H), 1.78 (s, 3H), 1.44–1.16 (m, 3H), 1.04 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (75.45 MHz, C_6D_6) δ 149.0, 139.8, 138.7, 128.9, 128.4, 128.3, 127.8, 127.6, 127.4, 127.3, 126.7, 115.7, 101.2, 81.3, 81.3, 80.6, 79.6, 79.3, 76.4, 74.6, 74.5, 73.4, 72.8, 71.6, 69.8, 30.3, 30.1, 29.3, 28.8, 27.1, 26.2, 21.3, 18.5, −4.19, −4.66; HRMS (EI) calcd for $C_{46}H_{62}O_8Si$ (M^+) 770.4210, found 770.4192.

6.1.18. Conversion of 35 to 30. To a solution of **35** (68 mg, 0.088 mmol) in benzene (8 ml) was added $RuCl_2(PPh_3)_3$ (85 mg, 0.089 mmol) at 25°C. After stirring for 3 days at 80°C, the mixture was filtered through a silica gel pad using ether as an eluent. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 10:1–4:1, containing 1% triethylamine) to give **30** (41.6 mg, 61%).

6.1.19. Lactone 38. A mixture of **37** (32.0 g, 115 mmol) and 5% Pd/C (1.0 g) in EtOAc (500 ml) was vigorously stirred under hydrogen atmosphere at room temperature. After 10 h, the catalyst was filtered off. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 1:1) to give the saturated ester (31.5 g, 98%): colorless oil; R_f=0.44 (hexane/EtOAc, 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.27 (m, 5H), 5.45 (s, 1H), 4.23 (dd, J=9.7, 3.8 Hz, 1H), 3.70–3.50 (m, 3H), 3.64 (s, 3H), 2.46 (d, J=4.4 Hz, 1H), 2.37 (t, J=7.0 Hz, 2H), 1.96–1.53 (m, 4H).

To a solution of DMSO (510 μl, 7.2 mmol) in CH_2Cl_2 (10 ml) at −78°C was added $(COCl)_2$ (470 μl, 5.4 mmol), and the mixture was stirred for 0.5 h at the same temperature. A solution of the ester (1.0 g, 3.6 mmol) in CH_2Cl_2 (5 ml) was added to the resulting mixture, and the stirring was continued for 1 h. Triethylamine (2.5 ml, 18 mmol) was added, and the mixture was allowed to warm to room temperature with stirring. The mixture was diluted with ether, then washed with satd NH_4Cl, water, and brine. The organic layer was concentrated to give the crude ketone which was used for next reaction without purification.

To a mixture of the ketone in CH_2Cl_2 (15 ml) at −15°C was added $AlMe_3$ (4.4 ml, 0.98 M in hexane, 4.3 mmol). After stirring at the same temperature for 2 h, the mixture was quenched with MeOH and brine. The resulting white precipitate was removed by filtration through a Celite pad. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 2:1) to give the methylcarbinol (742 mg, 70%): colorless oil; R_f=0.21 (hexane/EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.27 (m, 5H), 5.46 (s, 1H), 4.10 (dd, J=14.1, 7.1 Hz, 1H), 3.87 (d, J=10.6 Hz, 1H), 3.70–3.52 (m, 1H), 3.64 (s, 3H), 3.55 (d, J=10.6 Hz, 1H), 2.36 (t, J=6.9 Hz, 2H), 2.00–1.47 (m, 4H), 1.35 (s, 3H).

To a mixture of the methyl ester (2.25 g, 7.64 mmol) in THF (20 ml) and H_2O (10 ml) was added $LiOH{\cdot}H_2O$ (482 mg, 11.5 mmol), and the mixture was stirred at 40°C for 1 h. The mixture was cooled to 0°C, acidified by 1N HCl, and extracted with EtOAc. The organic layer was concentrated to give the crude carboxylic acid which was used for next step without purification.

To a mixture of the carboxylic acid obtained above in THF

(50 ml) at 0°C were added triethylamine (1.6 ml, 11.5 mmol) and 2,4,6-trichlorobenzoyl chloride (1.9 ml, 12.2 mmol). After stirring at the same temperature for 1 h, the reaction mixture was diluted with benzene (300 ml) and added to a solution of DMAP (1.9 g, 15.3 mmol) in benzene (150 ml) at room temperature. After 1 h, the mixture was filtered through a Celite pad, concentrated, and purified by chromatography (hexane/EtOAc, 1:1) to give **38** (1.97 g, 98%): colorless oil; R_f=0.47 (hexane/EtOAc, 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.28 (m, 5H), 5.46 (s, 1H), 4.00 (d, J=11.0 Hz, 1H), 3.77 (dd, J=11.0, 3.8 Hz, 1H), 3.73 (d, J=11.0 Hz, 1H), 2.78 (dd, J=15.6, 5.9 Hz, 1H), 2.55 (ddd, J=13.5, 13.5, 2.3 Hz, 1H), 2.06–1.65 (m, 4H), 1.64 (s, 3H).

6.1.20. Ester 39. To a stirred solution of **38** (2.8 g, 10.7 mmol), $PhNTf_2$ (7.5 g, 21 mmol), and DMPU (3.9 ml, 32 mmol) in THF (200 ml) at −78°C was added KHMDS (39 ml, 0.7 M in toluene, 27 mmol). After stirring for 0.5 h, the reaction mixture was quenched with H_2O and extracted with ether. The organic layer was washed with brine and concentrated to give the crude enol triflate which was used for next reaction without purification.

A mixture of the enol triflate obtained above, Et_3N (6.0 ml, 43 mmol), $Pd(PPh_3)_4$ (250 mg, 0.21 mmol), and MeOH (17 ml, 430 mmol) in DMF (50 ml) was stirred at room temperature under the carbon monoxide atmosphere. After 13 h, the mixture was filtered through a silica gel pad. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 4:1) to give **39** (3.0 g, 92%): colorless oil; R_f=0.40 (hexane/EtOAc, 4:1); ^{1}H NMR (300 MHz, C_6D_6) δ 7.58–7.54 (m, 2H), 7.25–7.10 (m, 3H), 6.45 (dd, J=9.2, 3.8 Hz, 1H), 5.34 (s, 1H), 4.18 (d, J=10.5 Hz, 1H), 3.74 (d, J=10.5 Hz, 1H), 3.48 (dd, J=11.2, 3.8 Hz, 1H), 3.37 (s, 3H), 1.90–1.40 (m, 4H).

6.1.21. MPM ether 40. To a mixture of **39** (4.51 g, 14.8 mmol) in CH_2Cl_2 (150 ml) at −78°C was added DIBALH (33 ml, 1.0 M in CH_2Cl_2, 33 mmol), and the mixture was stirred at the same temperature for 0.5 h. The mixture was quenched with MeOH and brine, and the resulting white precipitate was removed by filtration through a Celite pad. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 2:1) to give the allylic alcohol (4.06 g, 99%): colorless oil; R_f=0.27 (hexane/EtOAc, 2:1); ^{1}H NMR (300 MHz, C_6D_6) δ 7.58–7.54 (m, 2H), 7.25–7.10 (m, 3H), 5.38 (s, 1H), 4.95 (dd, J=8.8, 3.3 Hz, 1H), 3.95 (d, J=10.6 Hz, 1H), 3.71 (m, 2H), 3.69 (d, J=10.6 Hz, 1H), 3.61 (m, 1H), 2.00–1.50 (m, 4H).

To a stirred suspension of KH (3.2 g of a suspension in mineral oil, 27.4 mmol, prewashed with hexane) in THF (70 ml) at 0°C were added MPMCl (3.7 ml, 27.4 mmol) and a solution of the alcohol obtained above (3.78 g, 13.7 mmol) in THF (40 ml), and the mixture was stirred at room temperature for 1 h. The reaction was quenched with MeOH at 0°C, diluted with ether, then washed with water and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 10:1–2:1) to give **40** (5.43 g, 100%): colorless oil; R_f=0.08 (hexane/EtOAc, 10:1); ^{1}H NMR (300 MHz, C_6D_6) δ 7.63–7.56 (m, 2H), 7.23–7.19 (m, 5H), 6.83–6.75 (m, 2H), 5.39 (s, 1H), 5.32 (dd, J=9.0, 3.3 Hz, 1H), 4.35 (s, 2H), 4.00 (d, J=10.5 Hz, 1H), 3.79–3.68 (m, 2H), 3.64–3.58 (m, 1H), 3.34 (s, 3H), 1.90–1.40 (m, 4H).

6.1.22. Alcohol 41. To a solution of **40** (5.91 g, 14.9 mmol) in THF (100 ml) at 0°C was added $BH_3{\cdot}SMe_2$ (2.8 ml, 29.8 mmol), and the mixture was stirred at the same temperature for 2 h. An aqueous solution of NaOH (1N, 50 ml) and 30% H_2O_2 (10 ml) were added, and the mixture was stirred at room temperature for 0.5 h. The mixture was extracted with ether. The organic layer was washed with saturated aqueous Na_2SO_3 and brine, then concentrated. The residue was purified by chromatography (hexane/EtOAc, 2:1) to give **41** (3.28 g, 53%) and **42** (2.25 g, 36%).

Compound **41**: colorless oil; R_f=0.24 (hexane/EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.40 (m, 2H), 7.30–7.25 (m, 3H), 7.20 (d, J=8.6 Hz, 2H), 6.81 (d, J=8.6 Hz, 2H), 5.38 (s, 1H), 4.45 (d, J=11.7 Hz, 1H), 4.38 (d, J=11.7 Hz, 1H), 3.90 (m, 1H), 3.80–3.70 (m, 2H), 3.75 (s, 3H), 3.54–3.45 (m, 3H), 3.34 (dd, J=9.5, 6.4 Hz, 1H), 2.47 (brs, 1H), 2.00–1.65 (m, 4H).

Compound **42**: colorless oil; R_f=0.18 (hexane/EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.40 (m, 2H), 7.30–7.25 (m, 3H), 7.19 (d, J=8.6 Hz, 2H), 6.82 (d, J=8.6 Hz, 2H), 5.39 (s, 1H), 4.46 (d, J=11.5 Hz, 1H), 4.40 (d, J=11.5 Hz, 1H), 3.92 (dd, J=10.8, 4.1 Hz, 1H), 3.75–3.40 (m, 6H), 3.74 (s, 3H), 2.75 (brs, 1H), 2.00–1.50 (m, 4H).

6.1.23. TBS ether 43. To a stirred suspension of KH (32 mg of a suspension in mineral oil, 0.28 mmol, prewashed with hexane) in THF (1 ml) at 0°C were added MPMCl (38 μl, 0.28 mmol) and a solution of **41** (58 mg, 0.14 mmol) in THF (1.5 ml), and the mixture was stirred at room temperature for 1 h. The reaction was quenched with MeOH at 0°C, diluted with ether, then washed with water and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 4:1) to give the bis-MPM ether (58 mg, 77%): colorless oil; R_f=0.21 (hexane/EtOAc, 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.40 (m, 2H), 7.30–7.25 (m, 3H), 7.23 (d, J=8.6 Hz, 2H), 7.17 (d, J=8.6 Hz, 2H), 6.80 (d, J=8.6 Hz, 2H), 6.76 (d, J=8.6 Hz, 2H), 5.40 (s, 1H), 4.40 (s, 2H), 4.36 (d, J=11.5 Hz, 1H), 4.25 (d, J=11.5 Hz, 1H), 3.99 (m, 1H), 3.75 (d, J=10.3 Hz, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 3.64 (m, 1H), 3.55 (d, J=10.3 Hz, 1H), 3.46 (dd, J=11.6, 3.7 Hz, 1H), 3.35 (dd, J=9.9, 5.1 Hz, 1H), 3.24 (dd, J=9.9, 5.9 Hz, 1H), 2.02–1.93 (m, 2H), 1.67–1.46 (m, 2H), 1.44 (s, 3H).

To a mixture of the MPM ether obtained above (3.37 g, 6.3 mmol) in MeOH (100 ml) and CH_2Cl_2 (20 ml) was added camphorsulfonic acid (732 mg, 3.15 mmol). After stirring at room temperature for 27 h, the mixture was quenched with triethylamine, concentrated, and purified by chromatography (hexane/EtOAc, 1:1–0:1) to give the diol (2.36 g, 84%): colorless crystal; R_f=0.47 (EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J=8.6 Hz, 2H), 7.19 (d, J=8.6 Hz, 2H), 6.90 (d, J=8.6 Hz, 2H), 6.87 (d, J=8.6 Hz, 2H), 4.51–4.40 (m, 3H), 4.26 (d, J=11.4 Hz, 1H), 3.90–3.40 (m, 6H), 3.82 (s, 6H), 2.10–1.65 (m, 4H), 1.28 (s, 3H).

To a mixture of the diol obtained above (2.36 g, 5.29 mmol)

in CH_2Cl_2 (60 ml) at 0°C were added 2,6-lutidine (1.9 ml, 15.9 mmol) and TBSOTf (2.9 ml, 12.7 mmol), and the mixture was stirred at room temperature for 1.5 h. The mixture was quenched with MeOH, diluted with ether, then washed with satd $NaHCO_3$ and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 8:1) to give the bis-TBS ether (3.44 g, 96%): colorless oil; R_f=0.23 (hexane/EtOAc, 8:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, J=8.6 Hz, 2H), 7.13 (d, J=8.6 Hz, 2H), 6.80 (d, J=8.6 Hz, 2H), 6.77 (d, J=8.6 Hz, 2H), 4.51–4.40 (m, 3H), 4.30 (d, J=11.2 Hz, 1H), 4.00 (m, 1H), 3.81 (m, 1H), 3.75 (s, 6H), 3.53 (dd, J=10.3, 2.8 Hz, 1H), 3.45 (dd, J=10.2, 5.5 Hz, 1H), 3.34–3.26 (m, 3H), 1.90–1.65 (m, 4H), 0.87 (s, 9H), 0.85 (s, 9H), −0.01 (s, 9H), −0.03 (s, 3H).

To a mixture of the bis-TBS ether (3.44 g, 5.1 mmol) in MeOH (40 ml) and CH_2Cl_2 (14 ml) at 0°C was added camphorsulfonic acid (273 mg, 1.02 mmol). After stirring at 0°C for 1.5 h, the mixture was quenched with triethylamine, diluted with ether, then washed with water and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 4:1) to give **43** (2.59 g, 91%): colorless crystal; R_f=0.15 (hexane/EtOAc, 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J=8.6 Hz, 2H), 7.11 (d, J=8.6 Hz, 2H), 6.84 (d, J=8.6 Hz, 2H), 6.81 (d, J=8.6 Hz, 2H), 4.45 (d, J=11.7 Hz, 1H), 4.43 (d, J=11.2 Hz, 1H), 4.38 (d, J=11.7 Hz, 1H), 4.23 (d, J=11.2 Hz, 1H), 3.81–3.75 (m, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.58 (dd, J=10.1, 3.1 Hz, 1H), 3.43–3.32 (m, 5H), 2.27 (brs, 1H), 1.92–1.80 (m, 2H), 1.65–1.47 (m, 2H), 1.18 (s, 3H), 0.84 (s, 9H), 0.01 (s, 3H), −0.02 (s, 3H).

6.1.24. Alcohol 44. To a solution of DMSO (76 μl, 1.07 mmol) in CH_2Cl_2 (5 ml) at −78°C was added $(COCl)_2$ (76 μl, 0.87 mmol), and the mixture was stirred for 10 min at the same temperature. A solution of **43** (272 mg, 0.49 mmol) in CH_2Cl_2 (2 ml) was added to the resulting mixture, and the stirring was continued for 1 h. Triethylamine (340 μl, 2.43 mmol) was added, and the mixture was allowed to warm to room temperature with stirring. The mixture was diluted with ether, then washed with satd NH_4Cl, water, and brine. The organic layer was concentrated to give the crude aldehyde which was used for next reaction without purification.

To a stirred suspension of methyltriphenylphosphonium bromide (433 mg, 1.21 mmol) in THF (5 ml) at 0°C was added dropwise NaHMDS (1.20 ml, 1.0 M in THF, 1.20 mmol). After stirring for 10 min, a solution of the crude aldehyde in THF (2 ml) was added, and the mixture was stirred for another 1 h. The reaction mixture was quenched with acetone, diluted with ether, then washed with water and brine. The organic layer was concentrated and diluted with hexane. The resulting solid was filtered off. The filtrate was concentrated and purified by column chromatography (hexane/EtOAc, 4:1) to give the olefin (245.7 mg, 91%): colorless oil; R_f=0.46 (hexane/EtOAc, 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.16 (m, 4H), 6.88–6.81 (m, 4H), 5.86 (dd, J=17.3, 10.8 Hz, 1H), 5.27 (dd, J=17.2, 1.8 Hz, 1H), 5.02 (dd, J=10.7, 1.8 Hz, 1H), 4.54–4.44 (m, 3H), 4.34 (d, J=11.2 Hz, 1H), 4.01 (m, 1H), 3.80 (s, 6H), 3.70 (m, 1H), 3.63–3.37 (m, 3H), 1.94–1.58 (m, 4H), 1.26 (s, 3H), 0.91 (s, 9H), 0.040 (s, 6H); ^{13}C NMR (75.45 MHz, $CDCl_3$) δ 158.9, 158.8, 144.3, 131.0, 131.0, 129.1, 129.0, 113.6, 113.5, 112.5, 80.3, 78.5, 76.9, 74.4, 72.8, 71.6, 70.8, 55.2, 25.9, 25.4, 25.3, 19.6, 18.1, −4.38, −5.12.

To a mixture of cyclohexene (100 μl, 1.00 mmol) in THF (0.2 ml) at 0°C was added BH_3·SMe_2 (48 μl, 0.50 mmol), and the mixture was stirred for 15 min at the same temperature. A solution of the olefin (180 mg, 323 μmol) in THF (1.0 ml) was added dropwise. After 30 min, the reaction mixture was treated with 3N NaOH (0.5 ml, 1.5 mmol) and 30% H_2O_2 (0.5 ml). The cooling bath was removed, and the reaction mixture was stirred for another 30 min. The reaction mixture was diluted with ether and washed with brine. The organic layer was concentrated and purified by chromatography (hexane/ether, 2:1–1:1) to afford **44** (155.9 mg, 84%): colorless oil; R_f=0.14 (hexane/ether, 1:1); IR (neat) 3600–3200, 1612 cm^{-1}; $[\alpha]^{24}_D$=−20.4° (c 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, J=8.6 Hz, 2H), 7.15 (d, J=8.6 Hz, 2H), 6.87 (d, J=8.6 Hz, 2H), 6.84 (d, J=8.6 Hz, 2H), 4.45 (m, 3H), 4.22 (d, J=11.4 Hz, 1H), 3.96–3.47 (m, 4H), 3.79 (s, 6H), 3.44–3.27 (m, 1H), 1.94–1.50 (m, 6H), 1.25 (s, 3H), 0.86 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, CDCl3) δ 159.1, 130.4, 130.3, 129.4, 129.2, 113.7, 82.8, 78.8, 77.6, 74.2, 72.7, 71.1, 70.5, 59.4, 55.2, 42.2, 35.5, 26.3, 25.8, 25.4, 17.9, 16.2, −4.11, −5.03; HRMS (EI) calcd for C24H41O6Si (M−C8H9O) 453.2672, found 453.2680.

6.1.25. Ketone 45. To a mixture of DMSO (430 μl, 6.05 mmol) in CH_2Cl_2 (20 ml) at −78°C was added $(COCl)_2$ (430 μl, 4.94 mmol), and the mixture was stirred at the same temperature. After 10 min, a solution of alcohol **44** (1.38 g, 2.40 mmol) was added dropwise. After stirring for 1.5 h, triethylamine (1.70 ml, 12.2 mmol) was added, and the reaction mixture was allowed to warm to room temperature. The mixture was diluted with ether, then washed with satd NH_4Cl, and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 2:1) to give the aldehyde (1.18 g, 86%): colorless oil; R_f=0.26 (hexane/EtOAc, 4:1); IR (neat) 1720 cm^{-1}; $[\alpha]^{24}_D$=−12.8° (c 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.86 (dd, J=2.9, 2.9 Hz, 1H), 7.22 (d, J=8.6 Hz, 2H), 7.19 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 6.84 (d, J=8.6 Hz, 2H), 4.44 (m, 3H), 4.28 (d, J=11.1 Hz, 1H), 3.90–3.68 (m, 1H), 3.80 (s, 6H), 3.58–3.36 (m, 4H), 2.49 (dd, J=15.1, 2.4 Hz, 1H), 2.42 (dd, J=15.1, 3.3 Hz, 1H), 1.98–1.52 (m, 4H), 1.33 (s, 3H), 0.88 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 159.0, 130.4, 130.5, 129.2, 129.1, 113.7, 80.0, 78.5, 77.8, 74.7, 72.8, 71.6, 70.6, 55.2, 54.3, 26.2, 25.8, 25.1, 17.9, 17.5, −4.12, −5.00; HRMS (EI) calcd for $C_{24}H_{39}O_6Si$ (M−C_8H_9O) 451.2516, found 451.2534.

To a stirred solution of aldehyde (1.18 g, 2.06 mmol) in ether (20 ml) at 0°C was added MeMgI (4.3 ml, 1.0 M in THF, 3.54 mmol). After stirring for 0.5 h, the reaction was quenched with aqueous saturated NH_4Cl, and the mixture was extracted with ether. The organic layer was washed with brine and concentrated to give the crude alcohol.

To a solution of DMSO (0.33 ml, 4.64 mmol) in CH_2Cl_2

(5 ml) at −78°C was added $(COCl)_2$ (330 μl, 3.80 mmol), and the mixture was stirred at the same temperature. After 10 min, a solution of the alcohol obtained above in CH_2Cl_2 (15 ml) was added dropwise. After stirring for 1.5 h, triethylamine (1.48 ml, 10.6 mmol) was added, and the reaction mixture was allowed to warm to room temperature. The mixture was diluted with ether, then washed with satd NH_4Cl, and brine. The organic layer was concentrated to give the crude ketone: colorless oil; R_f=0.23 (hexane/EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*=8.6 Hz, 2H), 7.17 (d, *J*=8.6 Hz, 2H), 6.86 (d, *J*=8.6 Hz, 2H), 6.84 (d, *J*=8.6 Hz, 2H), 4.44 (m, 3H), 4.27 (d, *J*=11.4 Hz, 1H), 3.80 (m, 1H), 3.80 (s, 6H), 3.68 (m, 1H), 3.50–3.38 (m, 3H), 2.62 (d, *J*=12.7 Hz, 1H), 2.45 (d, *J*=12.7 Hz, 1H), 2.19 (s, 3H), 1.94–1.56 (m, 4H), 1.25 (s, 3H), 0.88 (s, 9H), 0.06 (s, 6H).

To a stirred solution of the crude ketone in THF (10 ml) at room temperature was added TBAF (2.5 ml, 1.0 M in THF, 2.5 mmol). After stirring for 16 h, the reaction mixture was diluted with EtOAc and washed with brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 4:1–1:1) to give **45** (810 mg, 81%): colorless oil; R_f=0.26 (hexane/EtOAc, 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*=8.6 Hz, 2H), 7.17 (d, *J*=8.6 Hz, 2H), 6.86 (d, *J*=8.6 Hz, 2H), 6.84 (d, *J*=8.6 Hz, 2H), 4.50–4.38 (m, 3H), 4.23 (d, *J*=11.2 Hz, 1H), 3.84 (m, 1H), 3.80 (s, 3H), 3.80 (s, 3H), 3.62–3.50 (m, 2H), 3.41–3.37 (m, 2H), 2.73 (d, *J*=12.7 Hz, 1H), 2.65 (d, *J*=12.7 Hz, 1H), 2.63 (m, 1H), 2.21 (s, 3H), 2.00–1.86 (m, 2H), 1.72–1.58 (m, 3H), 1.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.0, 159.0, 130.4, 130.3, 129.2, 129.2, 113.7, 113.6, 80.0, 77.6, 74.0, 72.7, 71.7, 70.4, 55.3, 55.2, 32.7, 26.2, 25.1, 16.1.

6.1.26. Ester 46. To a stirred solution of **45** (810 mg, 1.71 mmol) in CH_2Cl_2 (8 ml) at room temperature were added *N*-methylmorphorine (0.38 ml, 3.42 mmol) and ethyl propiolate (0.35 ml, 3.42 mmol). After stirring at 30°C for 16 h, the reaction mixture was diluted with EtOAc and washed with brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 4:1–2:1) to give **46** (978 mg, 100%): colorless oil; R_f=0.47 (hexane/EtOAc, 1:1); IR (neat) 1706 cm^{-1}; $[\alpha]^{27}_D$=−7.67° (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, *J*=12.5 Hz, 1H), 7.22 (d, *J*=8.6 Hz, 2H), 7.15 (d, *J*=8.6 Hz, 2H), 6.86 (d, *J*=8.6 Hz, 2H), 6.83 (d, *J*=8.6 Hz, 2H), 5.26 (d, *J*=12.5 Hz, 1H), 4.48–4.37 (m, 3H), 4.27 (d, *J*=11.2 Hz, 1H), 4.15 (q, *J*=7.1 Hz, 2H), 4.03 (dd, *J*=10.4, 2.7 Hz, 1H), 3.82 (m, 1H), 3.80 (s, 3H), 3.80 (s, 3H), 3.53–3.36 (m, 3H), 2.67 (d, *J*=12.7 Hz, 1H), 2.50 (d, *J*=12.7 Hz, 1H), 2.19 (s, 3H), 2.02–1.64 (m, 4H), 1.31 (s, 3H), 1.26 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.8, 167.8, 161.6, 159.1, 159.1, 130.2, 129.3, 129.2, 113.7, 113.7, 98.2, 86.9, 78.8, 74.6, 72.8, 71.4, 70.8, 59.8, 55.2, 53.2, 33.0, 24.8, 22.7, 17.3, 14.3; HRMS (EI) calcd for $C_{24}H_{33}O_7$ (M−$C_8H_9O_2$) 449.2176, found 449.2197.

6.1.27. Alcohol 47. To a stirred solution of **46** (978 mg, 1.71 mmol) and MeOH (210 μl, 5.13 mmol) in THF (17 ml) at 0°C was added SmI_2 (52 ml, 0.1 M in THF, 5.2 mmol). After stirring at 0°C for 15 min, the reaction mixture was diluted with EtOAc, then washed with saturated aqueous $Na_2S_2O_3$ and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 2:1–1:1) to give **47** (950 mg, 97%): colorless crystal; R_f=0.40 (hexane/EtOAc, 1:1); IR (neat) 3600–3200, 1732 cm^{-1}; $[\alpha]^{27}_D$=−11.0° (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*=8.6 Hz, 2H), 7.18 (d, *J*=8.6 Hz, 2H), 6.87 (d, *J*=8.6 Hz, 2H), 6.83 (d, *J*=8.6 Hz, 2H), 4.47 (s, 2H), 4.43 (d, *J*=11.7 Hz, 1H), 4.33 (d, *J*=11.7 Hz, 1H), 4.16 (q, *J*=7.2 Hz, 2H), 3.99 (m, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.71–3.63 (m, 2H), 3.42 (dd, *J*=9.9, 5.3 Hz, 1H), 3.28 (dd, *J*=9.9, 6.2 Hz, 1H), 3.14 (dd, *J*=11.6, 3.6 Hz, 1H), 2.65 (dd, *J*=15.6, 3.9 Hz, 1H), 2.40 (dd, *J*=15.6, 9.3 Hz, 1H), 2.02–1.72 (m, 3H), 1.68–1.52 (m, 3H), 1.39 (s, 3H), 1.27 (t, *J*=7.2 Hz, 3H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 159.1, 130.7, 130.4, 129.2, 128.9, 113.7, 113.6, 86.8, 82.8, 78.3, 76.3, 75.5, 72.9, 72.3, 70.3, 70.0, 60.6, 56.0, 55.3, 35.0, 29.7, 24.9, 23.3, 23.2, 15.5, 14.2; HRMS (EI) calcd for $C_{24}H_{35}O_8$ (M−C_8H_9O) 451.2330, found 451.2302.

6.1.28. TMS ether 48. A stirred solution of alcohol **47** (18 mg, 0.031 mmol) in CH_2Cl_2 (0.5 ml) at 25°C was treated with 1-(trimethylsilyl)imidazole (0.1 ml, 0.68 mmol). After stirring for 16 h, the mixture was quenched with MeOH and concentrated to give the silyl ether (21 mg, 100%): colorless oil; R_f=0.31 (hexane/EtOAc, 4:1); IR (neat) 1738 cm^{-1}; $[\alpha]^{27}_D$=−8.22° (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*=8.6 Hz, 2H), 7.19 (d, *J*=8.6 Hz, 2H), 6.87 (d, *J*=8.6 Hz, 2H), 6.83 (d, *J*=8.6 Hz, 2H), 4.48 (s, 2H), 4.43 (d, *J*=11.7 Hz, 1H), 4.30 (d, *J*=11.7 Hz, 1H), 4.16 (m, 2H), 3.98 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.70 (dd, *J*=10.3, 2.6 Hz, 1H), 3.66 (m, 1H), 3.42 (dd, *J*=9.9, 5.3 Hz, 1H), 3.29 (dd, *J*=9.9, 6.4 Hz, 1H), 3.17 (dd, *J*=11.8, 3.7 Hz, 1H), 2.60 (dd, *J*=15.4, 2.6 Hz, 1H), 2.30 (dd, *J*=15.4, 10.5 Hz, 1H), 2.00–1.75 (m, 4H), 1.64–1.48 (m, 2H), 1.37 (s, 3H), 1.26 (t, *J*=7.2 Hz, 3H), 1.26 (s, 3H), 0.106 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 159.1, 158.9, 130.7, 130.5, 129.2, 128.9, 113.7, 113.6, 86.8, 83.1, 78.3, 76.2, 75.5, 73.1, 72.8, 72.3, 69.9, 60.4, 55.7, 55.2, 34.5, 24.9, 24.5, 23.2, 15.8, 14.2, 2.65; HRMS (EI) calcd for $C_{34}H_{49}O_9Si$ (M−CH_3) 629.3146, found 629.3142.

To a suspension of $LiAlH_4$ (73.4 mg, 1.78 mmol) in ether (15 ml) at 0°C was added a solution of the silyl ether (1.15 g, 1.78 mmol) in Et_2O (5 ml). After stirring at 0°C for 0.5 h, the reaction mixture was quenched with MeOH and brine, and the resulting white precipitate was removed by filtration through a Celite pad. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 2:1) to give **48** (1.07 g, 100%): colorless oil; R_f=0.31 (hexane/EtOAc, 2:1); IR (neat) 3600–3200 cm^{-1}; $[\alpha]^{28}_D$=−9.91° (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J*=8.6 Hz, 2H), 7.19 (d, *J*=8.6 Hz, 2H), 6.87 (d, *J*=8.6 Hz, 2H), 6.83 (d, *J*=8.6 Hz, 2H), 4.48 (s, 2H), 4.43 (d, *J*=11.4 Hz, 1H), 4.32 (d, *J*=11.4 Hz, 1H), 4.00 (m, 1H), 3.82 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.77 (m, 1H), 3.67 (m, 1H), 3.42 (dd, *J*=9.9, 5.2 Hz, 1H), 3.35 (dd, *J*=9.8, 2.9 Hz, 1H), 3.29 (dd, *J*=9.9, 6.4 Hz, 1H), 3.16 (dd, *J*=11.9, 3.7 Hz, 1H), 1.98–1.92 (m, 2H), 1.90–1.79 (m, 2H), 1.66 (m, 1H), 1.60 (m, 1H), 1.51 (m, 1H), 1.38 (s, 3H), 1.29 (s, 3H), 0.12 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 159.0, 130.7, 130.5, 129.2, 128.9, 113.7, 113.7, 87.4, 86.7, 78.3, 76.3, 75.3, 73.7, 72.9, 72.3, 70.0, 62.6, 55.9, 55.2, 30.8, 25.0, 24.6, 23.6, 15.7, 2.67; HRMS

(EI) calcd for $C_{25}H_{41}O_7Si$ (M−C_8H_9O) 481.2619, found 481.2605.

6.1.29. Enol ether 49. To a stirred mixture of **48** (181 mg, 0.30 mmol), DMSO (0.3 ml), and triethylamine (250 μl, 1.80 mmol) in CH_2Cl_2 (3 ml) at 0°C was added sulfur trioxide/pyridine complex (143 mg, 0.90 mmol). After stirring at 25°C for 3.5 h, the reaction mixture was diluted with ether and washed with satd NH_4Cl. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 4:1) to give the aldehyde (153 mg, 85%): colorless oil; R_f=0.29 (hexane/EtOAc, 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.74 (dd, *J*=2.4, 2.4 Hz, 1H), 7.23 (d, *J*=8.6 Hz, 2H), 7.19 (d, *J*=8.6 Hz, 2H), 6.87 (d, *J*=8.6 Hz, 2H), 6.83 (d, *J*=8.6 Hz, 2H), 4.48 (s, 2H), 4.45 (d, *J*=11.3 Hz, 1H), 4.32 (d, *J*=11.3 Hz, 1H), 3.99 (dd, *J*=4.6, 4.6 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.74 (dd, *J*=9.2, 4.6 Hz, 1H), 3.67 (m, 1H), 3.42 (dd, *J*=9.9, 5.3 Hz, 1H), 3.29 (dd, *J*=9.8, 6.5 Hz, 1H), 3.18 (dd, *J*=11.7, 3.5 Hz, 1H), 2.58 (ddd, *J*=15.4, 3.3, 3.3 Hz, 1H), 2.43 (ddd, *J*=15.4, 9.1, 2.1 Hz, 1H), 2.20–1.75 (m, 4H), 1.64–1.48 (m, 2H), 1.38 (s, 3H), 1.27 (s, 3H), 0.10 (s, 9H).

To a stirred solution of methoxymethyltriphenylphosphonium chloride (318 mg, 0.90 mmol) in THF (1 ml) at −78°C was added NaHMDS (0.9 ml, 1.0 M solution in THF, 0.9 mmol). After stirring for 30 min, a solution of the aldehyde (153 mg) in THF (1.5 ml) was added, and the mixture was stirred at room temperature for 1 h. The reaction mixture was quenched with water and extracted with ether. The organic layer was washed with brine and concentrated. The residue was diluted with hexane, and the resulting solid was filtered off. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 10:1–4:1) to give **49** (104 mg, 74%): colorless oil; R_f=0.34 (hexane/EtOAc, 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, *J*=8.6 Hz, 2H), 7.20 (d, *J*=8.6 Hz, 2H), 6.87 (d, *J*=8.6 Hz, 2H), 6.82 (d, *J*=8.6 Hz, 2H), 6.34 (d, *J*=12.6 Hz, 1H), 4.85 (ddd, *J*=13.4, 6.7, 6.7 Hz, 1H), 4.48 (s, 2H), 4.43 (d, *J*=11.7 Hz, 1H), 4.29 (d, *J*=11.7 Hz, 1H), 3.99 (bdd, *J*=4.9, 4.9 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.67 (m, 1H), 3.52 (s, 3H), 3.42 (dd, *J*=9.9, 5.3 Hz, 1H), 3.66 (m, 1H), 3.42 (dd, *J*=9.9, 5.3 Hz, 1H), 3.29 (dd, *J*=9.9, 6.4 Hz, 1H), 3.30 (dd, *J*=9.9, 6.2 Hz, 1H), 3.08 (bd, *J*=8.1 Hz, 2H), 2.20 (m, 1H), 2.50–1.80 (m, 5H), 1.68–1.42 (m, 2H), 1.37 (s, 3H), 1.26 (s, 3H), 0.109 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 158.9, 147.8, 130.8, 130.5, 129.2, 128.9, 113.7, 113.6, 100.7, 87.5, 86.7, 78.4, 76.1, 75.6, 73.9, 72.8, 72.3, 69.9, 56.1, 55.9, 55.2, 29.7, 26.8, 25.0, 24.3, 15.8, 2.72.

6.1.30. Lactone 50. To a mixture of **49** (104 mg, 0.16 mmol) in wet CH_3CN (1.2 ml) was added CSA (2.3 mg, 0.01 mmol). After stirring at room temperature for 1.5 h, the reaction was quenched with triethylamine. The mixture was concentrated and purified by chromatography (hexane/EtOAc, 1:1–1:4) to give the aldehyde (74.5 mg, 83%): colorless oil; R_f=0.16 (hexane/EtOAc=1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.24 (d, *J*=8.6 Hz, 2H), 7.20 (d, *J*=8.6 Hz, 2H), 6.87 (d, *J*=8.6 Hz, 2H), 6.82 (d, *J*=8.6 Hz, 2H), 4.46 (s, 2H), 4.43 (d, *J*=11.6 Hz, 1H), 4.38 (d, *J*=11.6 Hz, 1H), 3.99 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.67 (m, 1H), 3.41 (dd, *J*=9.9, 5.2 Hz, 1H), 3.28 (dd, *J*=9.9, 6.1 Hz, 1H), 3.09 (dd, *J*=10.5, 1.7 Hz, 1H), 3.04 (dd, *J*=11.9, 3.8 Hz, 1H), 2.60 (dddd, *J*=17.4, 7.3, 7.3, 1.8 Hz, 1H), 2.55 (dddd, *J*=17.4, 17.4, 7.3, 7.3 Hz, 1H), 2.10–1.39 (m, 8H), 1.38 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.2, 159.4, 159.3, 131.0, 130.8, 129.6, 129.3, 114.0, 114.0, 87.1, 86.0, 78.6, 76.6, 75.9, 73.2, 72.7, 71.0, 70.3, 56.2, 55.6, 41.8, 25.2, 23.8, 23.4, 21.9, 15.8.

To a mixture of the aldehyde (75 mg, 0.14 mmol) in *t*-BuOH/H_2O (2:1, 0.8 ml) at room temperature were added 2-methyl-2-butene (64 μl, 0.6 mmol), NaH_2PO_4 (58 mg, 0.48 mmol), and sodium chlorite (55 mg, 0.48 mmol). After vigorous stirring for 1 h, the reaction mixture was diluted with EtOAc and washed with brine. The organic layer was concentrated to give the crude carboxylic acid.

To a mixture of the carboxylic acid obtained above in THF (0.4 ml) at 0°C were added triethylamine (30 μl, 0.22 mol) and 2,4,6-trichlorobenzoyl chloride (35 μl, 0.22 mmol). After stirring at room temperature for 1.5 h, the reaction mixture was diluted with benzene (2 ml) and added to a solution of DMAP (35 mg, 0.29 mmol) in benzene (2 ml). After 40 min, the mixture was concentrated, diluted with EtOAc, and filtered through a Celite pad. The filtrate was purified by chromatography (hexane/EtOAc, 2:1) to give **50** (66 mg, 89%): colorless crystal; R_f=0.40 (hexane/EtOAc, 1:1); IR (neat) 1732 cm^{-1}; $[\alpha]^{26}_D$=−35.4° (*c* 1.475, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*=8.6 Hz, 2H), 7.19 (d, *J*=8.6 Hz, 2H), 6.86 (d, *J*=8.6 Hz, 2H), 6.83 (d, *J*=8.6 Hz, 2H), 4.47 (s, 2H), 4.43 (d, *J*=11.6 Hz, 1H), 4.37 (d, *J*=11.6 Hz, 1H), 4.02 (m, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.69 (brd, *J*=5.2 Hz, 1H), 3.52 (dd, *J*=12.5, 5.2 Hz, 1H), 3.43 (dd, *J*=10.0, 5.2 Hz, 1H), 3.30 (dd, *J*=10.2, 6.7 Hz, 1H), 3.24 (dd, *J*=11.7, 3.4 Hz, 1H), 2.86–2.61 (m, 2H), 2.11–1.80 (m, 3H), 1.66 (m, 1H), 1.51 (m, 1H), 1.47 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 159.1, 159.0, 130.5, 130.3, 129.2, 128.9, 113.7, 113.6, 88.0, 78.6, 78.5, 78.1, 76.5, 75.3, 72.9, 72.2, 70.1, 55.2, 52.2, 28.2, 25.1, 23.1, 22.8, 20.8, 16.1; HRMS (EI) calcd for $C_{23}H_{31}O_7$ (M−C_8H_9O) 419.2070, found 419.2078.

6.1.31. Ester 51. To a stirred solution of **50** (281 mg, 0.52 mmol), $PhNTf_2$ (372 mg, 1.04 mmol), and DMPU (190 μl, 1.04 mmol) in THF (5 ml) at −78°C was added KHMDS (2.1 ml, 0.5 M in toluene, 1.05 mmol). After stirring for 0.5 h, the reaction mixture was quenched with water containing 1% triethylamine and allowed to warm up to room temperature. The mixture was diluted with ether and washed with brine. The organic layer was concentrated to give the crude enol triflate: light yellow crystal; R_f=0.40 (hexane/EtOAc, 2:1); ^{1}H NMR (300 MHz, C_6D_6) δ 7.20 (d, *J*=8.6 Hz, 2H), 7.19 (d, *J*=8.6 Hz, 2H), 6.81 (d, *J*=8.6 Hz, 2H), 6.79 (d, *J*=8.6 Hz, 2H), 4.36 (s, 3H), 4.33 (s, 3H), 4.15 (m, 2H), 3.80 (d, *J*=5.3 Hz, 1H), 3.49 (dd, *J*=9.4, 4.6 Hz, 1H), 3.30 (s, 3H), 3.29 (s, 3H), 3.26 (m, 1H), 3.10 (dd, *J*=11.0, 5.7 Hz, 1H), 2.97 (dd, *J*=11.7, 3.5 Hz, 1H), 2.08–1.56 (m, 6H), 1.39 (m, 2H), 1.38 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 159.8, 159.7, 147.9, 131.1, 130.8, 129.5, 129.4, 119.1(q), 114.1,

114.0, 88.3, 86.5, 79.7, 78.3, 77.7, 76.9, 75.6, 73.2, 72.6, 70.3, 54.7, 52.0, 25.3, 23.6, 23.1, 17.5, 16.3.

To a suspension of Zn–Cu couple (688 mg, 10.4 mmol) in benzene (3 ml) and DMA (1.5 ml) was added ethyl 3-iodobutyrate (650 μl, 5.2 mmol). The mixture was stirred at 90°C for 4 h and cooled to 25°C. A solution of the enol triflate obtained above in benzene (1.5 ml) and a solution of $Pd(PPh_3)_4$ (150 mg, 0.13 mmol) in benzene (1 ml) were added successively. After stirring at room temperature for 2 h, the reaction mixture was filtered through a silica gel pad. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 10:1–4:1, containing 1% triethylamine) to afford **51** (290 mg, 87%): colorless crystal; R_f=0.20 (hexane/EtOAc, 4:1); ^{1}H NMR (300 MHz, C_6D_6) δ 7.20 (d, J=8.6 Hz, 2H), 7.19 (d, J=8.6 Hz, 2H), 6.80 (d, J=8.6 Hz, 2H), 6.78 (d, J=8.6 Hz, 2H), 4.35 (s, 4H), 4.30 (bd, J=3.8 Hz, 1H), 4.21 (bdd, J=5.5, 5.5 Hz, 1H), 3.94 (q, J=7.2 Hz, 2H), 3.81 (bd, J=5.5 Hz, 1H), 3.51 (dd, J=9.5, 4.7 Hz, 1H), 3.43 (dd, J=11.0, 5.9 Hz, 1H), 3.31 (s, 3H), 3.30 (s, 3H), 3.19 (dd, J=11.9, 3.5 Hz, 1H), 2.22–1.68 (m, 12H), 1.55 (s, 3H), 1.52–1.26 (m, 2H), 1.21 (s, 3H), 0.94 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 172.8, 159.7, 159.6, 151.0, 131.2, 131.0, 129.5, 129.4, 114.1, 114.0, 88.3, 79.6, 78.6, 76.9, 76.1, 74.0, 73.2, 72.8, 70.2, 60.0, 54.7, 53.3, 33.6, 33.5, 25.5, 24.6, 23.9, 22.8, 18.4, 16.6, 14.3; HRMS (EI) calcd for $C_{29}H_{40}O_8$ (M−C_8H_9O) 517.2802, found 517.2800.

6.1.32. Alcohol 52. To a stirred solution of **51** (24 mg, 0.038 mmol) in THF (0.3 ml) at 0°C was added BH_3·SMe_2 (4.6 μl, 0.049 mmol), and the mixture was stirred at the same temperature for 1.5 h. Satd $NaHCO_3$ (1.5 ml) and 30% hydrogen peroxide (75 μl) were added at 0°C, and the mixture was stirred at room temperature for 0.5 h. The reaction mixture was diluted with EtOAc, then washed with satd $Na_2S_2O_3$ and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 1:1) to give **52** (23 mg, 94%): colorless crystal; R_f=0.23 (hexane/EtOAc, 1:1); ^{1}H NMR (300 MHz, C_6D_6) δ 7.20 (d, J=8.6 Hz, 2H), 7.19 (d, J=8.6 Hz, 2H), 6.80 (d, J=8.6 Hz, 2H), 6.78 (d, J=8.6 Hz, 2H), 4.36 (s, 4H), 4.20 (bdd, J=5.3, 5.3 Hz, 1H), 3.95 (q, J=7.2 Hz, 2H), 3.84–3.79 (m, 1H), 3.76 (dd, J=11.7, 6.4 Hz, 1H), 3.63–3.50 (m, 3H), 3.32 (m, 1H), 3.30 (s, 3H), 3.29 (s, 3H), 3.18 (dd, J=11.8, 3.3 Hz, 1H), 2.24–2.12 (m, 6H), 1.92–1.67 (m, 3H), 1.52 (s, 3H), 1.40–1.24 (m, 3H), 1.18 (s, 3H), 0.95 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 173.3, 159.7, 159.6, 131.3, 131.0, 129.5, 129.4, 114.1, 114.0, 88.6, 78.6, 77.7, 76.8, 76.0, 74.8, 73.2, 72.9, 71.9, 70.3, 68.0, 60.0, 34.2, 33.5, 33.1, 25.7, 25.0, 24.0, 20.9, 16.7, 14.3; HRMS (EI) calcd for $C_{29}H_{41}O_9$ (M−C_8H_9O) 535.2908, found 535.2942.

6.1.33. Ketone 53. To a solution of **52** (180 mg, 0.27 mmol) in CH_2Cl_2 (3 ml) at room temperature was added Dess–Martin periodinate (300 mg, 0.71 mmol) and $NaHCO_3$ (150 mg, 1.79 mmol), and the mixture was stirred for 0.5 h. Aqueous saturated solution of $NaHCO_3$ and $Na_2S_2O_3$ (1:1, 5 ml) was added, and the mixture was vigorously stirred for 15 min. The mixture was extracted with ether. The organic layer was washed with aqueous saturated $NaHCO_3$ and brine, then concentrated to give the crude ketone: colorless crystal; R_f=0.23 (hexane/EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J=8.6 Hz, 2H), 7.20 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 6.83 (d, J=8.6 Hz, 2H), 4.48 (s, 2H), 4.47 (d, J=11.7 Hz, 1H), 4.35 (d, J=11.7 Hz, 1H), 4.12 (q, J=7.1 Hz, 2H), 4.06–3.98 (m, 2H), 3.84 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.69 (m, 1H), 3.43 (dd, J=9.9, 4.9 Hz, 1H), 3.31 (dd, J=9.9, 6.2 Hz, 1H), 3.21 (dd, J=11.7, 3.7 Hz, 1H), 2.44 (dd, J=10.7, 8.4 Hz, 1H), 2.36–2.25 (m, 3H), 2.05–1.40 (m, 10H), 1.44 (s, 3H), 1.31 (s, 3H), 1.25 (t, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.8, 173.4, 159.1, 158.9, 130.6, 130.4, 129.2, 128.9, 113.7, 113.6, 87.5, 78.8, 78.2, 76.4, 75.4, 73.0, 72.5, 72.4, 70.0, 60.2, 55.2, 53.3, 39.8, 34.0, 32.7, 25.2, 23.2, 21.1, 20.9, 16.3, 14.2.

To a solution of the crude ketone obtained above in toluene (5 ml) was added DBU (400 μl, 2.73 mmol). After stirring at room temperature for 0.5 h, the reaction mixture was diluted with EtOAc, then washed with saturated aqueous NH_4Cl and brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 2:1) to give **53** (113 mg, 64%): colorless solid; R_f=0.29 (hexane/EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J=8.6 Hz, 2H), 7.20 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 6.83 (d, J=8.6 Hz, 2H), 4.48 (s, 2H), 4.43 (d, J=11.5 Hz, 1H), 4.32 (d, J=11.5 Hz, 1H), 4.12 (q, J=7.1 Hz, 2H), 4.03 (bs, 2H), 3.84–3.79 (m, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 3.70 (bs, 1H), 3.57 (dd, J=13.2, 5.7 Hz, 1H), 3.44 (dd, J=9.9, 5.2 Hz, 1H), 3.31 (dd, J=9.7, 6.4 Hz, 1H), 3.24 (dd, J=11.5, 3.3 Hz, 1H), 2.74 (dd, J=17.6, 5.5 Hz, 1H), 2.44 (dd, J=17.6, 13.4 Hz, 1H), 2.41–2.24 (m, 3H), 2.05–1.46 (m, 7H), 1.50 (s, 3H), 1.31 (s, 3H), 1.25 (t, J=7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.9, 173.3, 159.1, 159.0, 130.6, 130.4, 129.3, 128.9, 113.7, 113.7, 87.9, 78.7, 78.2, 77.2, 76.4, 75.6, 73.0, 72.4, 72.1, 70.1, 60.3, 55.3, 53.1, 41.1, 34.1, 31.2, 30.3, 25.3, 23.2, 20.6, 16.8, 16.7, 14.2.

6.1.34. Alcohol 54. To a solution of **53** (113 mg, 0.17 mmol) in MeOH (2 ml) and CH_2Cl_2 (2 ml) at −78°C was added $NaBH_4$ (15 mg, 0.40 mmol), and the mixture was stirred at −78°C for 2 h. The reaction mixture was diluted with EtOAc and washed with brine. The organic layer was concentrated and purified by chromatography (hexane/EtOAc, 1:1) to give **54** (111 mg, 98%): colorless oil; R_f=0.26 (hexane/EtOAc, 1:1); IR (neat) 3600–3200, 1736 cm^{-1}; $[\alpha]^{25}_D$=−4.97° (c 0.78, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J=8.6 Hz, 2H), 7.19 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 6.83 (d, J=8.6 Hz, 2H), 4.47 (s, 2H), 4.46 (d, J=11.9 Hz, 1H), 4.32 (d, J=11.9 Hz, 1H), 4.12 (q, J=7.1 Hz, 2H), 4.00 (m, 1H), 3.81 (m, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.67 (m, 1H), 3.48–3.36 (m, 2H), 3.30 (dd, J=9.9, 6.3 Hz, 2H), 3.19 (dd, J=11.8, 3.3 Hz, 1H), 3.10 (dd, J=12.7, 3.3 Hz, 1H), 2.31 (dd, J=6.9, 6.9 Hz, 2H), 2.10–1.38 (m, 12H), 1.47 (s, 3H), 1.26 (s, 3H), 1.25 (dd, J=9.0, 9.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 158.9, 158.8, 130.5, 130.3, 129.1, 128.8, 113.5, 88.6, 80.8, 78.0, 76.2, 75.8, 72.9, 72.3, 71.8, 70.5, 69.9, 60.1, 55.0, 53.6, 34.1, 33.6, 31.4, 25.4, 23.2, 20.6, 17.0, 17.0, 16.6, 14.1; HRMS (EI) calcd for $C_{29}H_{43}O_9$ (M−C_8H_9O) 535.2907, found 535.2913.

6.1.35. Lactone 55. To a solution of **54** (29 mg, 0.045 mmol) in THF/H_2O (2:1, 0.8 ml) was added

$LiOH{\cdot}H_2O$ (3.5 mg, 0.084 mmol). After stirring at 40°C for 1 h, the mixture was acidified with 1 M HCl to pH 2 and extracted with EtOAc. The organic layer was concentrated to give the crude carboxylic acid: colorless crystal; R_f=0.23 (EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, J=8.6 Hz, 2H), 7.19 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 6.82 (d, J=8.6 Hz, 2H), 4.47 (s, 2H), 4.45 (d, J=11.2 Hz, 1H), 4.32 (d, J=11.2 Hz, 1H), 4.00 (brs, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.78 (m, 1H), 3.66 (bs, 1H), 3.41 (m, 2H), 3.31 (dd, J=15.6, 6.1 Hz, 1H), 3.19 (d, J=9.2 Hz, 1H), 3.08 (d, J=11.2 Hz, 1H), 2.36 (m, 2H), 2.17–1.36 (m, 13H), 1.47 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.6, 159.0, 158.9, 130.6, 130.4, 129.2, 128.9, 113.7, 113.6, 88.7, 80.8, 78.2, 76.8, 76.3, 75.9, 73.0, 72.4, 72.1, 70.8, 70.1, 55.2, 53.6, 33.8, 33.6, 31.4, 25.5, 23.3, 20.5, 17.1, 16.7.

To a mixture of the carboxylic acid obtained above in THF (0.4 ml) at 0°C were added triethylamine (20 μl, 0.14 mmol) and 2,4,6-trichlorobenzoyl chloride (24 μl, 0.15 mmol). After stirring at room temperature for 2 h, the reaction mixture was diluted with benzene (2 ml) and added to a solution of DMAP (22 mg, 0.18 mmol) in benzene (2 ml). After 0.5 h, the mixture was concentrated, diluted with EtOAc, and filtered through a Celite pad. The filtrate was purified by chromatography (hexane/EtOAc, 2:1) to give **55** (21 mg, 76%): colorless crystal; mp 155°C (hexane/CH_2Cl_2); R_f=0.26 (hexane/EtOAc, 1:1); $[\alpha]^{25}_D$=−31.2° (c 0.99, $CHCl_3$); IR (KBr) 1755 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, J=8.6 Hz, 2H), 7.19 (d, J=8.6 Hz, 2H), 6.86 (d, J=8.6 Hz, 2H), 6.83 (d, J=8.6 Hz, 2H), 4.47 (s, 2H), 4.46 (d, J=11.8 Hz, 1H), 4.37 (d, J=11.8 Hz, 1H), 4.13 (ddd, J=10.4, 10.4, 5.1 Hz, 1H), 4.00 (bs, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.68 (bs, 1H), 3.61 (ddd, J=9.3, 9.3, 3.3 Hz, 1H), 3.42 (dd, J=9.8, 5.0 Hz, 1H), 3.29 (dd, J=9.7, 6.3 Hz, 1H), 3.19 (dd, J=11.8, 3.3 Hz, 1H), 3.13 (dd, J=13.2, 3.5 Hz, 1H), 2.68 (dd, J=13.5, 7.0 Hz, 1H), 2.55 (dd, J=13.6, 13.6 Hz, 1H), 2.26 (m, 1H), 2.12 (bd, J=13.2 Hz, 1H), 2.03–1.82 (m, 4H), 1.75–1.48 (m, 6H), 1.47 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 159.1, 159.0, 130.6, 130.5, 129.2, 128.9, 113.7, 113.7, 88.8, 79.7, 78.2, 77.8, 76.4, 75.8, 73.0, 72.4, 71.9, 70.4, 70.1, 55.2, 53.4, 36.0, 34.4, 30.7, 25.4, 23.3, 20.6, 17.0, 16.6; HRMS (EI) calcd for $C_{27}H_{37}O_8$ ($M-C_8H_9O$) 489.2488, found 489.2499.

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