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Synthetic studies on goniodomin A: convergent assembly of the C15–C36 segment via palladium-catalyzed organostannane–thioester coupling

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ABSTRACT

A stereocontrolled convergent synthesis of the C15–C36 segment of goniodomin A, a potent anti-angiogenic marine polyether macrolide, has been achieved using Stille-type cross-coupling reaction of a vinylstannane and a thioester as a key segment assembly process.

1. Introduction

Goniodomin A (**1**, Fig. 1) is an architecturally complex marine polyether macrolide, which was first isolated as a potent antifungal agent from the dinoflagellate *Alexandrium hiranoi* (formerly *Goniodoma pseudogoniaulax*) collected at the rock pool in Jogashima in Japan by Murakami and his colleagues in 1988.[1] More recently, Moeller and co-workers also reported the isolation of goniodomin A as a cytotoxic constituent from the dinoflagellate *Alexandrium monilatium*.[2] The unique planar structure, containing four *exo*-methylenes, a dihydropyran, a 6,6-spiroacetal, a tetrahydrofuran, and a six-membered hemiacetal embedded in a 36 carbon chain was elucidated by Murakami and co-workers based on NMR studies.[1] We have recently determined the absolute configuration of goniodomin A based on extensive 2D NMR analysis, degradation experiments of the natural sample, synthesis of designed model compounds for NMR spectroscopic comparisons, and correlation with synthetic reference compounds.[3]

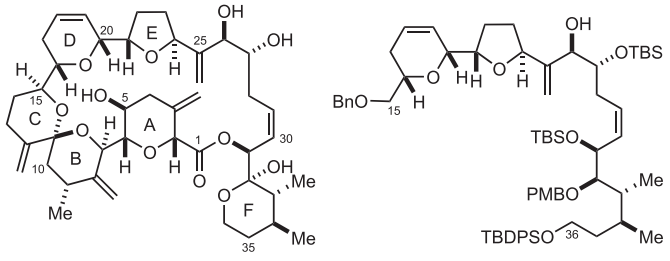

Fig. 1. Structures of goniodomin A (**1**) and the C15–C36 segment **2**.

From the viewpoint of biological properties, goniodomin A has profound effects on reorganization of the actin cytoskeleton. It has been demonstrated that goniodomin A stimulates the actomyosin ATPase activity mediated through binding to and altering the conformation of actin.[4] It has also been reported to induce largely different modulation of actomyosin ATPase activity between ventricular and atrial muscles.[5] Furthermore, goniodomin A has been found to cause morphological changes in 1321N1 human astrocytoma cells by increasing the filamentous actin content in a concentration-dependent manner.[6] It also exhibits anti-angiogenic activity through inhibition of actin reorganization in endothelial cells.[7]

The diverse biological properties and structural complexity of goniodomin A prompted us to initiate studies toward the total synthesis of this natural product.[8] Herein, we report in detail a stereocontrolled convergent assembly of the C15–C36 segment **2** (Fig. 1) of goniodomin A via palladium-catalyzed organostannane–thioester coupling.[9]

2. Results and discussion

2.1. Initial synthetic plan toward the C15–C31 model of goniodomin A

We initially planned a convergent synthesis of the C15–C31 domain **3** as a model for evaluation of segment assembly process and stereocontrolled construction of the C26,C27-diol moiety. Our plan for the synthesis of **3** using Julia–Kocienski reaction[10] is illustrated in Scheme 1. We considered that **3** would be accessible via Julia–Kocienski reaction between the C15–C26 aldehyde **5** and the C27–C31 sulfone **6** followed by Sharpless asymmetric dihydroxylation (AD)[11] of the resultant (*E*)-olefin **4**. We envisaged that the two ether rings of aldehyde **5** would be constructed via 5- and 6-*exo* cyclizations of the respective epoxy alcohols **7** and **8**.

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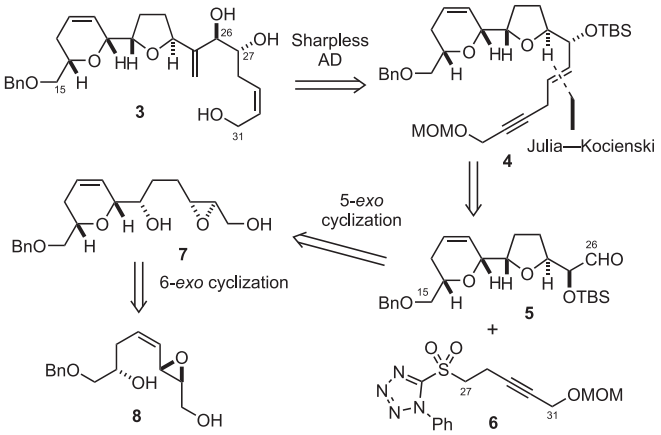
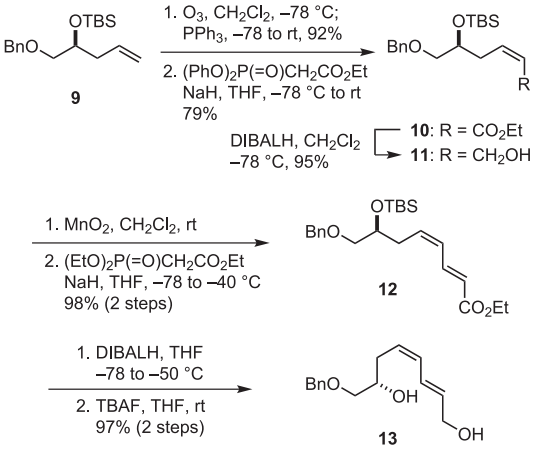


Scheme 1. Initial synthetic plan.

The synthesis of the C15–C26 aldehyde **5** commenced with the known TBS ether **9**,[12] which was derived from benzyl (*S*)-glycidyl ether in two steps (Scheme 2). Ozonolysis of the double bond (92%), followed by homologation using Horner–Wadsworth–Emmons (HWE) reaction of the resultant aldehyde under Ando's conditions,[13] gave (*Z*)-enoate **10** in 79% isolated yield, along with an 8/1 mixture of (*E*)- and (*Z*)-isomers (19%). Reduction of **10** with DIBALH gave allylic alcohol **11** in 95% yield. Oxidation with MnO_2[14] followed by HWE reaction of the resultant aldehyde with ethyl diethylphosphonoacetate led to (*E*,*Z*)-dienoate **12** in 98% yield (two steps). DIBALH reduction and subsequent desilylation afforded diol **13** in 97% yield (two steps).



Scheme 2. Preparation of diol **13**.

We next investigated tandem Sharpless asymmetric epoxidation (AE)[15]/6-*exo* cyclization of **13** as summarized in Table 1. When the reaction was performed under catalytic conditions, the desired dihydropyran **14** was isolated in only 11% yield (entry 1). Although the tandem AE/cyclization could be achieved, the low conversion yield and poor total mass recovery were problematic. Under stoichiometric conditions, the yield of **14** was slightly improved; however, the total mass recovery remained moderate (entry 2). Finally, we found that the desired **14** could be isolated in 88% yield, when the reaction was carried out under stoichiometric conditions using cumyl hydroperoxide (CHP) as an oxidant and worked-up by *n*-Bu_3P and aqueous citric acid (entry 3).[15b]

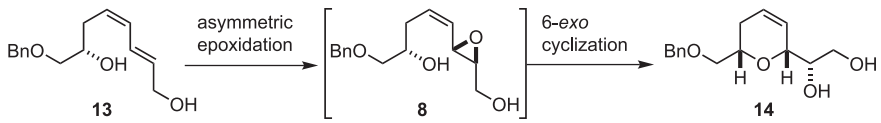
Selective mono-tosylation[16] of **14** (TsCl, Et_3N, *n*-Bu_2SnO) and subsequent treatment with K_2CO_3 in MeOH gave epoxide **15** in high overall yield (Scheme 3). At this stage, the stereochemistry of the D-ring was unambiguously confirmed by an NOE observed between H-16 and H-20 as shown. Copper-catalyzed allylation of **15** followed by acylation gave acetate **16** in 93% yield for the two steps. Chemoselective dihydroxylation of the terminal olefin within **16** was accomplished under the modified AD conditions [AD-mix β, OsO_4, $(DHQD)_2PHAL$][11] to give 1,2-diol **17** as a ca. 4/1 mixture of diastereomers in 77% yield (after one recycle). Oxidative cleavage of 1,2-diol **17** with $NaIO_4/SiO_2$[17] followed by homologation with a Wittig reagent produced (*E*)-enoate **18** in 96% yield for the two steps (*E*/*Z*>20/1). DIBALH reduction provided diol **19**, which was subjected to tandem AE/5-*exo* cyclization to give the DE-ring diol **20** as a ca. 20/1 mixture of diastereomers. After removal of the minor diastereomer by flash chromatography on silica gel, diol **20** was isolated as a single isomer in 84% yield. Bis-silylation of diol **20**, followed by selective cleavage of the primary TBS ether (CSA, MeOH), delivered alcohol **21**. Subsequent oxidation with 2-iodoxybenzoic acid (IBX) gave aldehyde **5**.

The synthesis of sulfone **6** is summarized in Scheme 4. Mitsunobu reaction[18] of 3-butyn-1-ol and 5-mercapto-1-phenyltetrazole gave alkyne **22** (94% yield), which was treated with LDA followed by paraformaldehyde to deliver propargylic alcohol **23** in 66% yield. Molybdenum-catalyzed oxidation to the corresponding sulfone followed by MOM protection of the primary alcohol furnished the desired C27–C31 sulfone **6**.

Julia–Kocienski reaction[10] between aldehyde **5** and sulfone **6** proceeded smoothly by using KHMDS as a base (DME, −75 to 0 °C) to give the desired olefin **4** in 90% yield from **21** (*E*/*Z*=ca. 7/1) (Scheme 5).

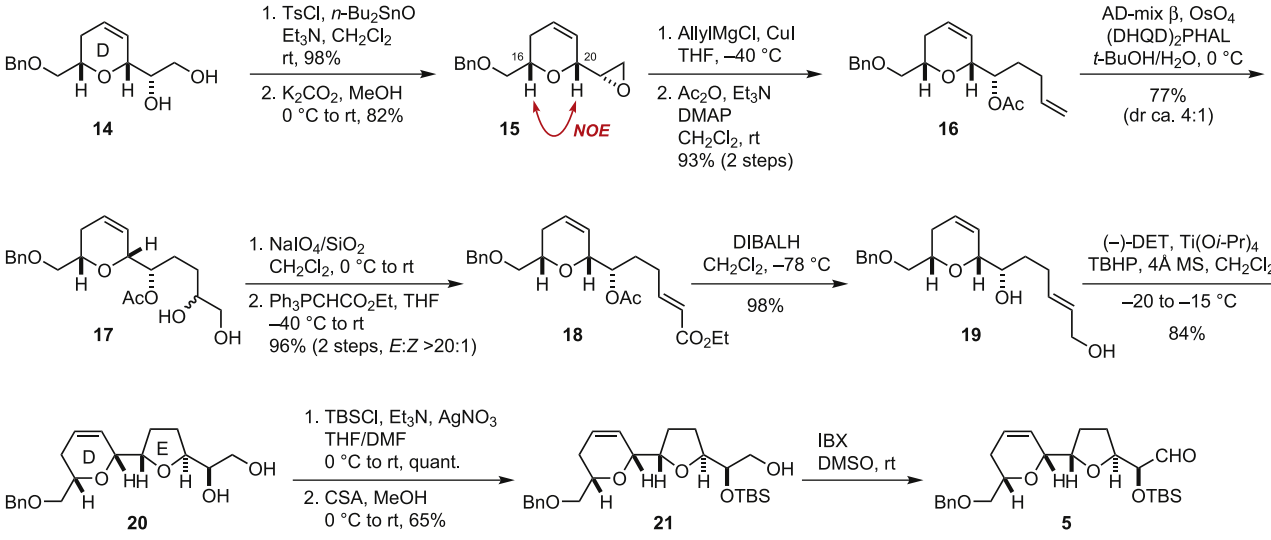
With olefin **4** in hand, we next investigated chemo- and diastereoselective dihydroxylation of **4** as summarized in Table 2. Treatment of **4** with OsO_4 and NMO in *t*-BuOH/H_2O at 0 °C produced the desired diol **24** in only poor yield (<6%) as an inseparable 3.5/1 mixture of diastereomers, along with isomer **25** (43%, *E*/*Z*=ca. 6/1 at C26–C27 olefin) and unreacted olefin **4** (21%, *E*/*Z*=ca. 6/1) (entry 1). To improve the chemoselectivity, we attempted to utilize

Table 1
Investigation of the tandem Sharpless AE/6-*exo* cyclization

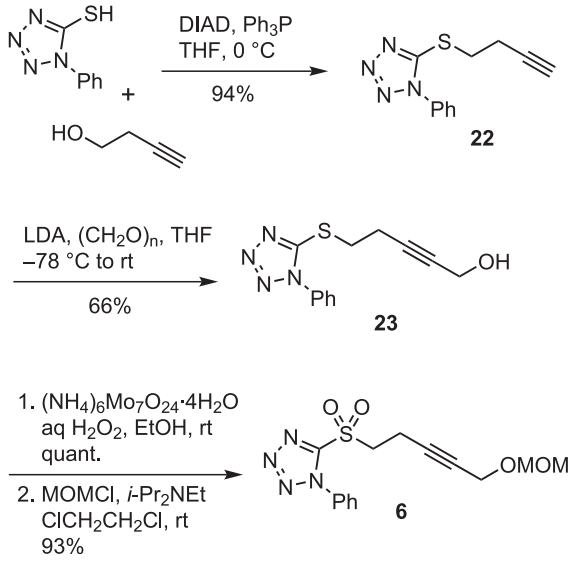


Entry[a]	Reagents and conditions	Work-up	Yield (%)
1	(+)-DET (0.15 equiv), Ti(O*i*-Pr)$_4$ (0.1 equiv) TBHP (1.5 equiv), −20 °C	$Na_2SO_4 \cdot nH_2O$	11 (47[b])
2	(+)-DET (1.5 equiv), Ti(O*i*-Pr)$_4$ (1.2 equiv) TBHP (4.0 equiv), −20 °C	$Na_2SO_4 \cdot nH_2O$	41 (10[b])
3	(+)-DET (1.5 equiv), Ti(O*i*-Pr)$_4$ (1.2 equiv) CHP (4.0 equiv), −25 °C	*n*-Bu_3P; then citric acid, aq acetone	88

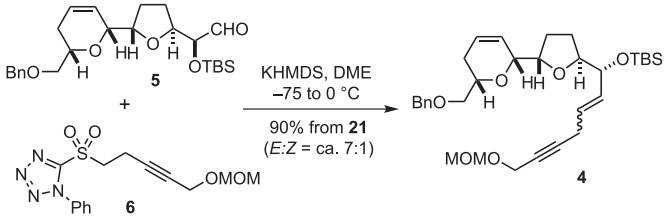
[a] All reactions were performed in the presence of 4 Å molecular sieves in CH_2Cl_2.
[b] Yield of recovered starting material.



Scheme 3. Preparation of aldehyde **5**.



Scheme 4. Synthesis of sulfone **6**.



Scheme 5. Julia–Kocienski reaction of **5** and **6**.

AD conditions.[11,19] Dihydroxylation of **4** under Sharpless AD conditions using $(DHQD)_2PHAL$ as a chiral ligand afforded **24** (12%, dr=ca. 1/1) along with **25** (30%, *E*/*Z*=ca. 4/1) and **4** (18%, *E*/*Z*=ca. 4/1) (entry 2). Switching the chiral ligand to $(DHQD)_2AQN$, known as a moderately superior ligand to $(DHQD)_2PHAL$ for the most of 1,2-disubstituted olefins,[20] was not effective for improving the chemoselectivity of the reaction (entry 3). These results indicated that the C18–C19 olefin is intrinsically more reactive than the C26–C27 olefin. These poor chemo- and diastereoselectivities of the dihydroxylation prompted us to re-design our synthetic approach toward the C15–C31 model **3**.

2.2. Revised synthetic plan for the construction of the C15–C31 model 3

Our revised synthetic strategy toward the construction of the C15–C31 model **3**[21] is shown in Scheme 6. Stereoselective construction of the C26,C27-diol moiety would be achieved by a substrate-controlled reduction of enone **26**. We thought that enone **26** could be assembled by means of palladium(0)-catalyzed, copper(I)-mediated Stille-type cross-coupling[22–24] of the C15–C25 vinylstannane **27** and the C26–C31 thioester **28**.

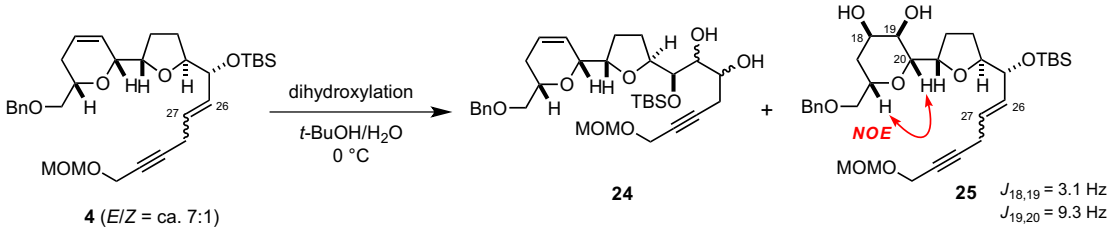
The synthesis of thioester **28** commenced with regioselective epoxide opening[25] of (*S*)-glycidol with an acetylide anion derived from **29** followed by tritylation to give alcohol **30** in 76% yield (two steps) (Scheme 7). Silylation of **30** (TIPSCl, Et_3N, $AgNO_3$, 99%) and selective deprotection of the trityl group (Et_3SiH, $BF_3{\cdot}OEt_2$, 86%) furnished primary alcohol **31**. Partial reduction of the triple bond (H_2, Lindlar catalyst) followed by oxidation using IBX gave aldehyde **32** in 88% yield for the two steps. Oxidation to the corresponding acid and condensation with *p*-toluenethiol using benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate (PyBOP®)[26] afforded thioester **28** in 80% yield (two steps).

The synthesis of vinylstannane **27** is illustrated in Scheme 8. Oxidative cleavage of the 1,2-diol of **20** with $NaIO_4/SiO_2$ and subsequent homologation of the resultant aldehyde with Ohira–Bestmann reagent **33**[27] (K_2CO_3, MeOH) gave alkyne **34** in 95% yield for the two steps. Alkyne **34** was then transformed into vinylstannane **27** in a three-step sequence, including oxymercuration of **34** ($HgSO_4$ in 1% aqueous H_2SO_4, 94%),[28] conversion of the resultant methyl ketone **35** into enol triflate **36** (KHMDS, $PhNTf_2$, 79%), and Stille reaction[29] of **36** with hexamethylditin [$Pd(PPh_3)_4$, LiCl, THF, 70 °C, 90%].

\The stereochemistry of the C21 and C24 stereogenic centers of **27** was assigned through conformational analysis based on NOE experiments and a coupling constant (Fig. 2). The observed NOE between H-20 and H-24 and the absence of an NOE between H-21 and H-24 revealed the 2,5-*trans*-tetrahydrofuran stereochemistry of the E-ring. On the other hand, the coupling constant, $J_{20,21}$=6.8 Hz, which is a typical value for H/H-anti orientation of vicinal oxygenated systems,[30] and an NOE between H-20 and H-24 and the absence of NOEs between H-19 and H-22 methylene protons indicated the C19/C22-anti orientation. Thus, the relative stereochemistry of **27** could be represented as that in Fig. 2.

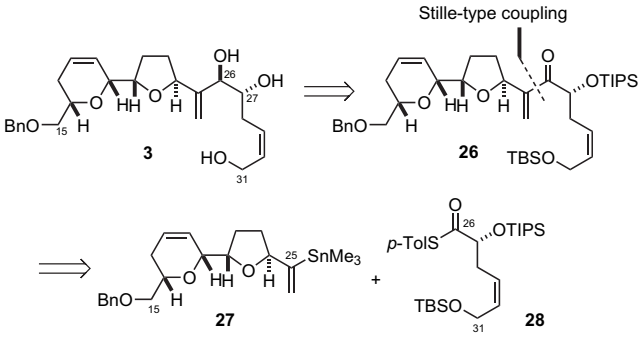
With the requisite segments **27** and **28** in hand, we next investigated the key segment assembly process, and the results are summarized in Table 3. Initially, we performed the Stille-type

Table 2
Investigation of the dihydroxylation

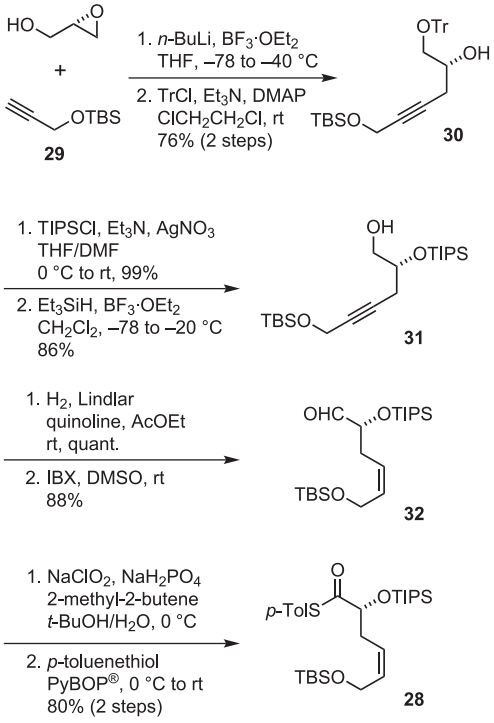


Entry[a]	Reagents	Yield (%)		
		24[b]	**25**[c]	Recovered **4**[c]
1	OsO_4, NMO	<6% (3.5/1)	43% (6/1)	21% (6/1)
2	OsO_4, $(DHQD)_2PHAL$ K_2CO_3, $K_3[Fe(CN)_6]$, $MeSO_2NH_2$	12% (1/1)	30% (4/1)	18% (4/1)
3	OsO_4, $(DHQD)_2AQN$ K_2CO_3, $K_3[Fe(CN)_6]$, $MeSO_2NH_2$	<11% (1/1)	27% (4/1)	17% (3/1)

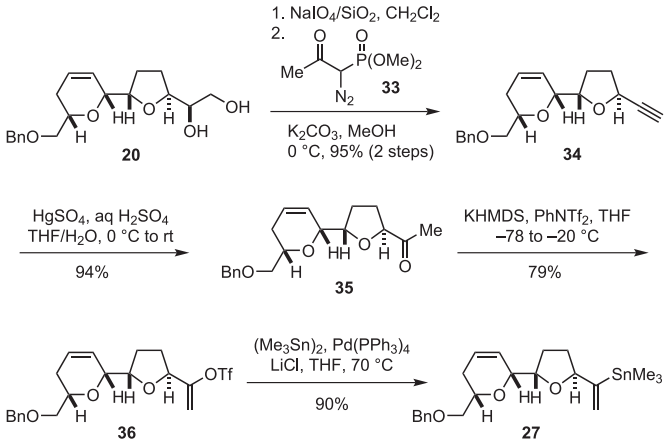
[a] All reaction were performed using **4** as a 7/1 mixture of *E*/*Z* isomers at C26–C27 double bond.
[b] Number in parentheses indicates the ratio of diastereomers (judged by ^1H NMR).
[c] Number in parentheses indicates the ratio of *E*/*Z* isomers (judged by ^1H NMR).



Scheme 6. Revised synthetic plan of the C15–C31 model **3**.



Scheme 7. Synthesis of thioester **28**.



Scheme 8. Synthesis of vinylstannane **27**.

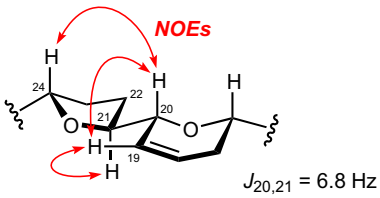
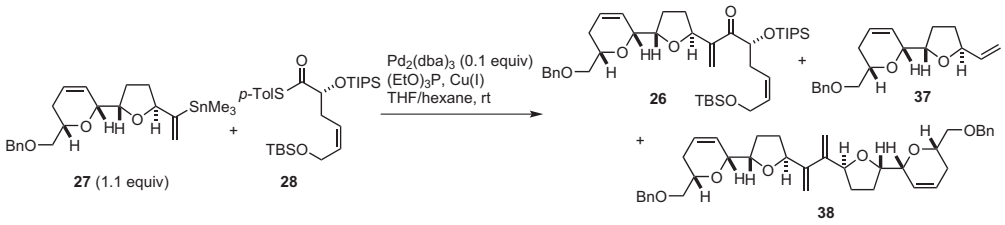


Fig. 2. Key NOEs observed in vinylstannane **27**. No NOE was observed between H-21/H-24 and H-19/H-22.

coupling reaction under Liebeskind conditions[22a] [$Pd_2(dba)_3$, $(EtO)_3P$, copper(I) thiophene-2-carboxylate (CuTC), THF/hexanes (1/2), room temperature, 27 h], but the desired enone **26** was obtained albeit in 22% yield, along with a significant amount of protodestannylation product **37** (62%) (entry 1). Upon changing CuTC to copper(I) diphenylphosphinate (CuDPP),[22a,31] the yield of **26** was dramatically improved to 60% (entry 2).[22b] Further improvement was possible by running the reaction in degassed THF/hexanes to give **26** in 77% yield (entry 3). Finally, we found that the use of a Pd/$(EtO)_3P$ ratio of 1/2 rather than 1/4 accelerated the rate of reaction and led to the formation of **26** in higher yield (entry 4).[32]

Stereoselective 1,2-reduction of enone **26** under Luche conditions[33] ($NaBH_4$, $CeCl_3·7H_2O$, EtOH, −40 °C) afforded the requisite

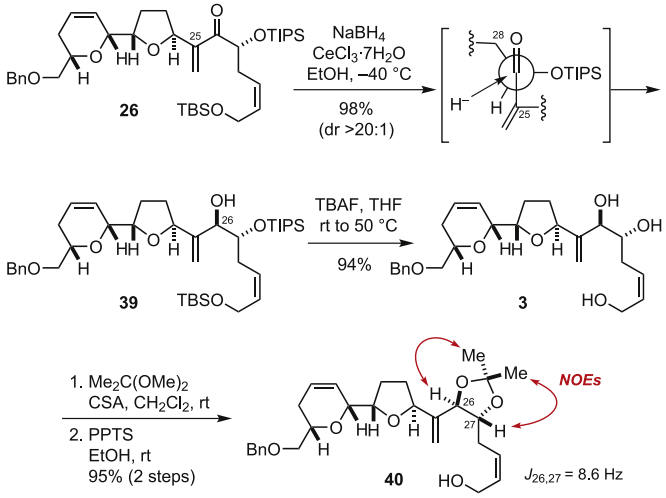
Table 3
Investigation of Stille-type coupling under Liebeskind conditions



Entry	Cu(I) (equiv)	$(EtO)_3P$ (equiv)	Yield (%)		
			26	**37**	**38**
1	CuTC (2.0)	0.8	22	62	Trace
2	CuDPP (2.0)	0.8	60	Trace	ND[a]
3[b]	CuDPP (2.0)	0.8	77	18	<6
4[b]	CuDPP (2.0)	0.4	87	0	<7

[a] ND=Not determined.
[b] Degassed solvents were used.

allylic alcohol **39** in 98% yield with high diastereoselectivity (dr>20/1) (Scheme 9). Subsequent silyl deprotection gave the C15–C31 model compound **3** in 94% yield. The stereochemistry at C26 was confirmed by $J_{26,27}$=8.6 Hz and NOE experiments on the acetonide derivative **40**, which was readily available from **3** in two steps. The stereochemical outcome of this reduction can be rationalized by a Felkin–Ahn model[34] as illustrated in Scheme 9.

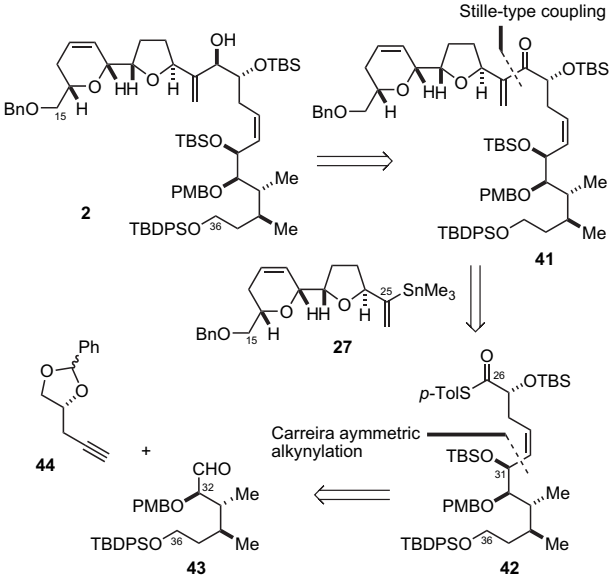


Scheme 9. Synthesis of the C15–C31 model **3**.

2.3. Convergent synthesis of the C15–C36 segment

Having completed the model study, we next investigated the construction of the C15–C36 segment **2**. We considered that **2** would be synthesized via Stille-type coupling of the C15–C25 vinylstannane **27** and the C26–C36 thioester **42** of comparable complexity (Scheme 10). Thioester **42** could be accessed from aldehyde **43** and alkyne **44** via Carreira asymmetric alkynylation[35] to establish the C31 stereogenic center.

The synthesis of thioester **42** commenced with the previously described aldehyde **43**[3] (17/1 diastereomeric mixture at C32) and alkyne **44**, which was readily available from (*S*)-glycidol in three steps (Scheme 11). Carreira asymmetric alkynylation of **43** with **44** under standard conditions [$Zn(OTf)_2$, (+)-*N*-methylephedrine, Et_3N, toluene, room temperature][34] afforded propargylic alcohol **45** as a ca. 10/1 mixture of diastereomers at the C31

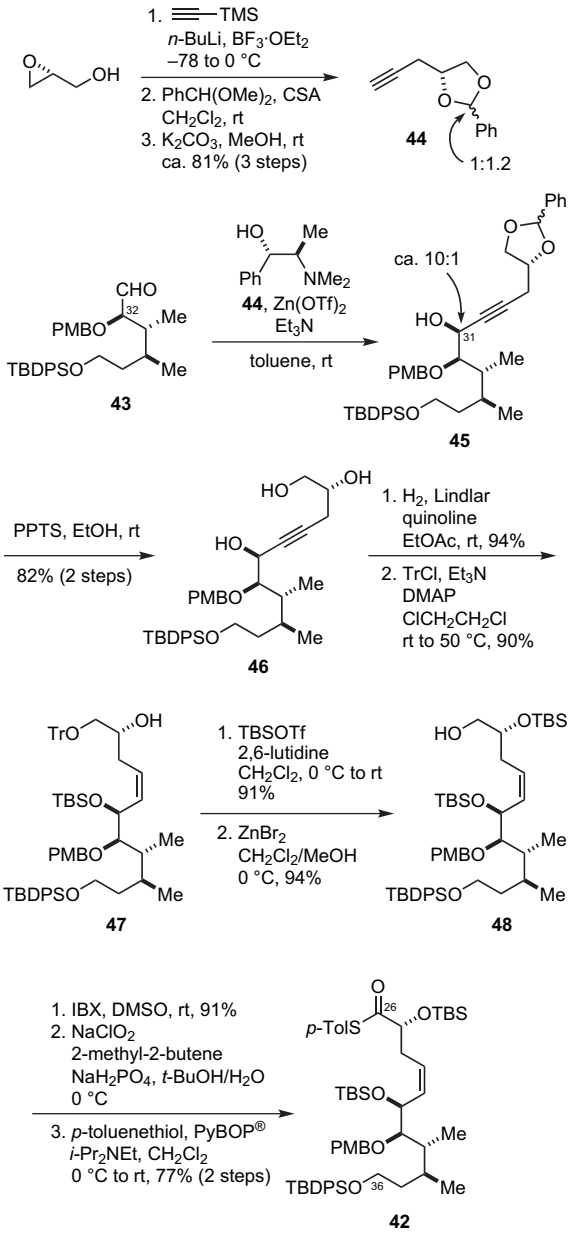


Scheme 10. Synthetic plan for the construction of the C15–C36 segment.

stereogenic center. Subsequent deprotection of the benzylidene acetal (PPTS, EtOH) followed by removal of the minor diastereomer at C31 using flash chromatography on silica gel afforded triol **46** in 82% yield (two steps). Partial reduction of the alkyne and subsequent three-step protective group manipulations led to primary alcohol **48** via **47** in good overall yield. Oxidation of the primary alcohol to the corresponding acid and esterification with *p*-toluenethiol furnished the desired thioester **42** in 70% yield for the three steps.

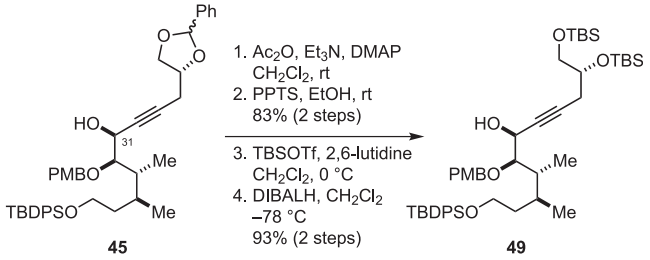
The stereochemistry of the newly generated stereogenic center at C31 was unambiguously confirmed by conversion of **45** into the known compound **49**[3] by a four-step sequence: (1) Ac_2O, Et_3N, DMAP, CH_2Cl_2, room temperature; (2) PPTS, EtOH, room temperature (83%, two steps); (3) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C; (4) DIBALH, CH_2Cl_2, −78 °C (93%, two steps) (Scheme 12).

Coupling of the segments **42** and **27** (1.1 equiv) was efficiently achieved under the optimized conditions [$Pd_2(dba)_3$ (0.1 equiv), $(EtO)_3P$ (0.4 equiv), CuDPP (2.0 equiv), degassed THF/hexanes, room temperature, 6 h] to afford the desired product **41** in 74% yield (95% based on recovered **42**) (Scheme 13). Stereoselective reduction of enone **41** thus obtained under Luche conditions ($NaBH_4$, $CeCl_3\cdot 7H_2O$,

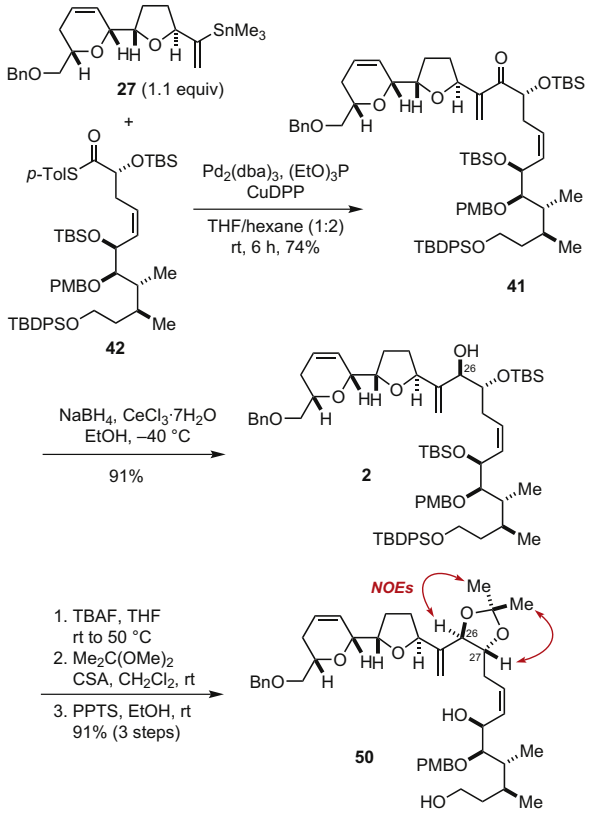


Scheme 11. Synthesis of thioester **42**.

EtOH, −40 °C, 91%) completed the synthesis of the C15–C36 segment **2** as a single diastereomer. The stereochemistry at C26 was unambiguously established by NMR analysis on acetonide **50**, derived from **2** in three steps, on the basis of $J_{26,27}$ value (8.6 Hz) and NOEs observed between H-26, H-27, and acetonide methyl groups, as shown.



Scheme 12. Derivatization of **45** to confirm the C31 stereochemistry.



Scheme 13. Completion of the synthesis of the C15–C36 segment **2**.

3. Conclusion

Although our early efforts toward the C15–C31 model **3** proved to be unsuccessful, we have finally developed a highly convergent and stereocontrolled access to the C15–C36 segment **2**. The key features of the synthesis of the C15–C25 vinylstannane **27** and the C26–C36 thioester **42** include the stereoselective construction of the D- and E-rings using tandem Sharpless asymmetric epoxidation/*exo* cyclization and Carreira asymmetric alkynylation to establish the C31 stereogenic center. Most importantly, palladium-catalyzed, copper(I)-mediated organostannane–thioester coupling enabled an efficient assembly of the advanced segments **27** and **42**, which showcases the versatility of this reaction in complex molecule synthesis. Further studies toward the total synthesis of goniodomin A are currently underway in our laboratory and will be reported in due course.

4. Experimental section

4.1. General remarks

All reactions sensitive to moisture and/or air were carried out under an atmosphere of argon in dry, freshly distilled solvents under anhydrous conditions using oven-dried glassware unless otherwise noted. Anhydrous dichloromethane (CH_2Cl_2) was purchased from Kanto Chemical Co. Inc. and used directly without further drying. Anhydrous tetrahydrofuran, diethyl ether, and toluene were purchased from Wako Pure Chemical Industries, Ltd. and further purified by a Glass Contour solvent purification system under an atmosphere of argon immediately prior to use. Diisopropylamine, triethylamine, 2,6-lutidine, 1,2-dichloroethane, and methanol were distilled from calcium hydride under an atmosphere of argon. Hexamethylphosphoramide (HMPA) was distilled from calcium hydride under reduced pressure. *N*,*N*-Dimethylformamide (DMF) and dimethyl

sulfoxide (DMSO) were distilled from magnesium sulfate under reduced pressure. All other chemicals were purchased at highest commercial grade and used directly. Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F_{254} plates (0.25-mm thickness). Flash column chromatography was carried out using Kanto Chemical silica gel 60N (40–100 mesh, spherical, neutral) or Fuji Silysia silica gel BW-300 (200–400 mesh). Optical rotations were recorded on a JASCO P-1020 digital polarimeter. IR spectra were recorded on a JASCO FT/IR-4100 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity INOVA-500 or JEOL JNM-ECA-600 spectrometer, and chemical shift values are reported in parts per million (δ) downfield from tetramethylsilane with reference to internal residual solvent [^{1}H NMR, $CHCl_3$ (7.24), C_6HD_5 (7.15); ^{13}C NMR, $CDCl_3$ (77.0), C_6D_6 (128.0)] unless otherwise noted. Coupling constants (J) are reported in hertz (Hz). The following abbreviations were used to designate the multiplicities: s=singlet; d=doublet; t=triplet; m=multiplet; br=broad. ESI-TOF mass spectra were measured on a Bruker microTOFfocus spectrometer.

*4.1.1. (Z)-Enoate **10**.* Ozone was bubbled through a solution of TBS ether **9** (7.49 g, 24.4 mmol) in CH_2Cl_2 (122 mL) at −78 °C until a pale blue color was persisted. After oxygen was bubbled through the solution to remove excess ozone, triphenylphosphine (19.2 g, 73.3 mmol) was added to the solution at −78 °C. The resultant solution was allowed to warm to room temperature and stirred at that temperature overnight. The mixture was concentrated under reduced pressure. Purification of the residue by column chromatography (silica gel, EtOAc/hexanes=1/25 to 1/20) gave an aldehyde (6.95 g, 92%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (dd, J=2.5, 2.0 Hz, 1H), 7.36–7.24 (m, 5H), 4.51 (d, J=12.5 Hz, 1H), 4.50 (d, J=12.5 Hz, 1H), 4.34 (m, 1H), 3.48 (dd, J=9.0, 4.5 Hz, 1H), 3.37 (dd, J=9.0, 6.0 Hz, 1H), 2.64 (ddd, J=16.0, 5.5, 2.0 Hz, 1H), 2.56 (ddd, J=16.0, 7.0, 2.5 Hz, 1H), 0.84 (s, 9H), 0.04 (s, 6H).

To a solution of ethyl diphenylphosphonoacetate (2.75 g, 8.59 mmol) in THF (72 mL) at 0 °C was added NaH (ca. 60% in mineral oil, 330 mg, 8.25 mmol). The resultant mixture was stirred at that temperature for 20 min and then cooled to −78 °C. To this mixture was added a solution of the above aldehyde (2.21 g, 7.16 mmol) in THF (4 mL+2×1 mL rinse). The resultant mixture was stirred at −78 °C for 11 h before it was quenched with saturated aqueous NH_4Cl solution. The mixture was diluted with H_2O and the volatiles were removed under reduced pressure. The residue was extracted with EtOAc, and the organic layer was washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/40 to 1/10) gave (*Z*)-enoate **10** (2.15 g, 79%) as a colorless oil, along with a ca. 8/1 mixture of (*E*)- and (*Z*)-isomers (527 mg, 19%). Data for **10**: $[\alpha]_D^{28}$ +4.1 (*c* 3.0, benzene); IR (film) 2954, 2929, 2897, 2856, 1720, 1179, 1096, 835, 777 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.28 (m, 4H), 7.28–7.23 (m, 1H), 6.33 (ddd, J=11.5, 7.5, 7.5 Hz, 1H), 5.81 (ddd, J=11.5, 1.5, 1.5 Hz, 1H), 4.50 (d, J=12.0 Hz, 1H), 4.49 (d, J=12.0 Hz, 1H), 4.14 (q, J=7.0 Hz, 2H), 3.95 (m, 1H), 3.40 (dd, J=9.5, 5.5 Hz, 1H), 3.37 (dd, J=9.5, 5.5 Hz, 1H), 2.96–2.84 (m, 2H), 1.25 (t, J=7.0 Hz, 3H), 0.85 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 146.1, 138.3, 128.3 (×2), 127.55 (×2), 127.46, 121.0, 74.4, 73.3, 70.7, 59.8, 34.2, 25.8 (×3), 18.1, 14.2, −4.5, −4.9; HRMS (ESI) calcd for $C_{21}H_{34}O_4SiNa$ [(M+Na)$^+$] 401.2119, found 401.2126.

*4.1.2. Allylic alcohol **11**.* To a solution of (*Z*)-enoate **10** (25.5 g, 67.3 mmol) in CH_2Cl_2 (670 mL) at −78 °C was added DIBALH (1.03 M solution in hexanes, 137 mL, 141 mmol). The resultant solution was stirred at −78 °C for 40 min before it was quenched with MeOH. Saturated aqueous potassium sodium tartrate solution was added, and the mixture was diluted with EtOAc and vigorously stirred at room temperature until the layers became clear. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography (silica gel, EtOAc/hexanes=1/8) gave allylic alcohol **11** (21.5 g, 95%) as a colorless oil: $[\alpha]_D^{29}$ +3.9 (*c* 2.0, $CHCl_3$); IR (film) 3388, 2953, 2928, 2886, 2856, 1254, 1104, 1007, 835, 776 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.75 (m, 1H), 5.59 (m, 1H), 4.51 (d, J=12.0 Hz, 1H), 4.50 (d, J=12.0 Hz, 1H), 4.12 (m, 2H), 3.86 (m, 1H), 3.40 (dd, J=9.5, 4.7 Hz, 1H), 3.36 (dd, J=9.5, 4.7 Hz, 1H), 2.42–2.28 (m, 2H), 1.84 (br s, 1H), 0.86 (s, 9H), 0.03 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 130.8, 128.8, 128.4 (×2), 127.7 (×2), 127.6, 73.6, 73.4, 70.8, 58.3, 32.6, 25.8 (×3), 18.1, −4.65, −4.68; HRMS (ESI) calcd for $C_{19}H_{32}O_3SiNa$ [(M+Na)$^+$] 359.2013, found 359.2005.

*4.1.3. Dienoate **12**.* To a solution of allylic alcohol **11** (10.75 g, 31.90 mmol) in CH_2Cl_2 (160 mL) was added MnO_2 (27.8 g+27.8 g+19.5 g, 320 mmol+320 mmol+224 mmol) in three portions over a period of 3 h. The resultant mixture was further stirred at room temperature for 1.5 h, at which time TLC analysis showed complete consumption of the starting material. The mixture was filtered through a plug of Celite, and the filtrate was concentrated under reduced pressure. The crude aldehyde was azeotropically dried with benzene twice, and used for the next reaction without purification.

To a solution of ethyl diethylphosphonoacetate (7.96 mL, 40.0 mmol) in THF (107 mL) at 0 °C was added NaH (ca. 60% in mineral oil, 1.53 g, 38.3 mmol). The resultant mixture was stirred at 0 °C for 30 min and cooled to −78 °C. To the mixture was added a solution of the above crude aldehyde in THF (10 mL+2×5 mL rinse). The resultant mixture was allowed to warm to −40 °C, and stirred for 10 h before it was quenched with saturated aqueous NH_4Cl solution. The mixture was diluted with H_2O, and the volatiles were concentrated under reduced pressure. The residual aqueous layer was extracted with EtOAc, and the organic layer was washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/40 to 1/10) gave dienoate **12** (12.63 g, 98% for the two steps) as a colorless oil: $[\alpha]_D^{29}$ +14.6 (*c* 1.0, $CHCl_3$); IR (film) 2954, 2928, 2898, 2856, 1715, 1637, 1266, 1173, 1130, 835, 777 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (dd, J=15.5, 12.0 Hz, 1H), 7.38–7.22 (m, 5H), 6.19 (dd, J=12.0, 12.0 Hz, 1H), 5.90 (m, 1H), 5.85 (d, J=15.5 Hz, 1H), 4.49 (d, J=12.5 Hz, 1H), 4.49 (d, J=12.5 Hz, 1H), 4.18 (q, J=7.3 Hz, 2H), 3.91 (m, 1H), 3.39 (dd, J=9.5, 5.5 Hz, 1H), 3.33 (dd, J=9.5, 6.0 Hz, 1H), 2.58–2.47 (m, 2H), 1.27 (t, J=7.3 Hz, 3H), 0.84 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 139.5, 138.2, 136.9, 128.33, 128.31 (×2), 127.6 (×2), 127.5, 121.7, 73.9, 73.4, 70.8, 60.2, 33.5, 25.8 (×3), 18.1, 14.3, −4.6, −4.8; HRMS (ESI) calcd for $C_{23}H_{36}O_4SiNa$ [(M+Na)$^+$] 427.2275, found 427.2259.

*4.1.4. Diol **13**.* To a solution of dienoate **12** (2.20 g, 5.43 mmol) in THF (55 mL) at −78 °C was added dropwise DIBALH (1.02 M solution in hexanes, 16.0 mL, 16.3 mmol). The resultant solution was allowed to warm to −50 °C and stirred for 30 min before it was quenched with MeOH. Saturated aqueous potassium sodium tartrate solution was added, and the mixture was diluted with EtOAc and vigorously stirred at room temperature until the layers became clear. The mixture was concentrated under reduced pressure to remove volatiles, and the residual aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude alcohol was azeotropically dried with benzene twice and used for the next reaction without purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 6.51 (ddd, J=15.5, 10.5, 1.3 Hz, 1H), 6.07 (dd, J=11.0, 10.5 Hz, 1H), 5.79 (ddd, J=15.5, 6.0, 6.0 Hz, 1H), 5.50 (ddd,

J=11.0, 8.0, 7.5 Hz, 1H), 4.51 (d, J=12.0 Hz, 1H), 4.48 (d, J=12.0 Hz, 1H), 4.14 (m, 2H), 3.87 (ddd, J=11.0, 5.5, 5.5 Hz, 1H), 3.39 (dd, J=9.5, 5.5 Hz, 1H), 3.35 (dd, J=9.5, 6.0 Hz, 1H), 2.48–2.35 (m, 2H), 1.28 (dd, J=6.0, 6.0 Hz, 1H), 0.85 (s, 9H), 0.03 (s, 3H), 0.03 (s, 3H).

To a solution of the above crude alcohol in THF (18 mL) at 0 °C was added TBAF (1.0 M solution in THF, 8.2 mL, 8.2 mmol). The resultant solution was stirred at room temperature for 13 h before saturated aqueous NH_4Cl solution was added. The organic layer was concentrated under reduced pressure, and the residual aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/8 to 1/0) gave diol **13** (1.31 g, 97% for the two steps) as a colorless oil: $[\alpha]_D^{28}$ −3.5 (c 1.0, $CHCl_3$); IR (film) 3377, 3027, 2905, 2862, 1454, 1087, 988 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.25 (m, 5H), 6.50 (ddd, J=15.0, 11.0, 1.3 Hz, 1H), 6.11 (dd, J=11.0, 11.0 Hz, 1H), 5.82 (ddd, J=15.0, 5.5, 5.5 Hz, 1H), 5.46 (m, 1H), 4.53 (d, J=12.0 Hz, 1H), 4.52 (d, J=12.0 Hz, 1H), 4.16 (m, 2H), 3.87 (ddd, J=12.5, 6.5, 3.0 Hz, 1H), 3.50 (dd, J=9.0, 3.0 Hz, 1H), 3.37 (dd, J=9.0, 3.0, 1H), 2.44 (br s, 1H), 2.45–2.34 (m, 2H), 1.70 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 132.9, 130.3, 128.4 (×2), 127.8, 127.7 (×2), 127.2, 126.1, 73.7, 73.4, 70.2, 63.3, 31.7; HRMS (ESI) calcd for $C_{15}H_{20}O_3Na$ [(M+Na)$^+$] 271.1305, found 271.1303.

*4.1.5. Dihydropyran **14**.* To a suspension of (+)-diethyl tartrate (2.31 mL, 13.5 mmol) and 4 Å molecular sieves (3.34 g) in CH_2Cl_2 (90 mL) at −40 °C was added dropwise Ti(O*i*-Pr)$_4$ (3.19 mL, 10.8 mmol). The resultant mixture was stirred at −40 °C for 30 min. Cumyl hydroperoxide (80 wt %, 6.63 mL, 35.9 mmol) was added dropwise, and the resultant mixture was stirred at −40 °C for 30 min. To the mixture was added a solution of diol **13** (2.21 g, 8.91 mmol) in CH_2Cl_2 (5 mL+2×1 mL rinse). The resultant mixture was allowed to warm to −25 °C, and stirred for 9 h before it was quenched with tri-*n*-butylphosphine (7.80 mL, 31.3 mmol). Citric acid (3.08 g, 16.0 mmol) in acetone/H_2O (9/1, v/v, ca. 30 mL) was added, and the resultant mixture was stirred at room temperature for 1.5 h. The mixture was filtered through a plug of Celite, and the Celite bed was washed successively with CH_2Cl_2, EtOAc, and acetone. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=2/3 to 1/1) to give dihydropyran **14** (2.07 g, 88%) as a colorless oil: $[\alpha]_D^{27}$ −30.9 (c 1.0, $CHCl_3$); IR (film) 3398, 3032, 2865, 1454, 1367, 1186, 1085, 739, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.25 (m, 5H), 5.92 (m, 1H), 5.68 (m, 1H), 4.55 (d, J=12.5 Hz 1H), 4.54 (d, J=12.5 Hz 1H), 4.32 (br s, 1H), 3.79 (m, 1H), 3.74 (dd, J=11.0, 5.0 Hz, 1H), 3.63 (dd, J=11.0, 4.0 Hz, 1H), 3.61 (m, 1H), 3.52–3.45 (m, 2H), 3.07 (br s, 2H), 2.14 (m, 1H), 1.97 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 128.4 (×2), 127.71, 127.68 (×2), 126.3, 125.9, 77.1, 73.4, 73.2, 72.9, 72.6, 63.1, 27.3; HRMS (ESI) calcd for $C_{15}H_{20}O_4Na$ [(M+Na)$^+$] 287.1254, found 287.1251.

*4.1.6. Epoxide **15**.* To a solution of dihydropyran **14** (207 mg, 784 μmol), di-*n*-butyltin oxide (4.0 mg, 16 μmol), and TsCl (157 mg, 823 μmol) in CH_2Cl_2 (7.80 mL) at room temperature was added triethylamine (114 μL, 821 μmol). The resultant solution was stirred at room temperature for 12 h, and additional portions of triethylamine (33.0 μL, 273 μmol) and TsCl (45.0 mg, 236 μmol) were added. The resultant solution was stirred for 110 min before it was quenched with H_2O. The mixture was extracted with CH_2Cl_2, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/3) gave a monotosylate (323 mg, 98%) as a pale yellow oil: $[\alpha]_D^{27}$ −17.4 (c 1.0, $CHCl_3$); IR (film) 3419, 2863, 1597, 1454, 1359, 1189, 984 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81–7.75 (m, 2H), 7.35–7.25 (m, 7H), 5.89 (m, 1H), 5.69 (m, 1H), 4.53 (d, J=12.5 Hz, 1H), 4.51 (d, J=12.5 Hz, 1H), 4.22 (dd, J=10.5, 6.5 Hz, 1H), 4.20 (br s, 1H), 4.07 (dd, J=10.5, 6.5 Hz, 1H), 3.82–3.72 (m, 2H), 3.48 (dd, J=10.5, 6.5 Hz, 1H), 3.41 (dd, J=10.5, 4.3 Hz, 1H), 2.56 (br s, 1H), 2.41 (s, 3H), 2.00 (m, 1H), 1.92 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 138.1, 132.7, 129.8 (×2), 128.4 (×2), 127.9 (×2), 127.7, 127.6 (×2), 126.5, 125.4, 75.1, 73.3, 73.1, 72.7, 71.7, 71.1, 27.4, 21.6; HRMS (ESI) calcd for $C_{22}H_{26}O_6S_1Na$ [(M+Na)$^+$] 441.1342, found 441.1349.

To a solution of the above monotosylate (323 mg, 771 μmol) in MeOH (2.6 mL) at room temperature was added K_2CO_3 (128 mg, 927 μmol). The resultant solution was stirred at room temperature for 4 h. The mixture was filtered through a plug of Celite, and the filtrate was concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/5) gave epoxide **15** (156 mg, 82%) as a colorless oil: $[\alpha]_D^{28}$ +10.1 (c 1.0, benzene); IR (film) 3033, 2995, 2923, 2895, 2861, 1253, 1091, 740, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.92 (m, 1H), 5.76 (m, 1H), 4.60 (d, J=12.0 Hz, 1H), 4.54 (d, J=12.0 Hz, 1H), 3.92 (br s, 1H), 3.81 (ddd, J=10.5, 6.0, 4.0 Hz, 1H), 3.56 (dd, J=10.5, 6.0 Hz, 1H), 3.47 (dd, J=10.5, 4.0 Hz, 1H), 2.95 (ddd, J=6.5, 3.5, 2.0 Hz, 1H), 2.81 (dd, J=5.0, 3.5 Hz, 1H), 2.73 (dd, J=5.0, 2.0 Hz, 1H), 2.09 (m, 1H), 1.95 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 128.4 (×2), 127.7 (×2), 127.6, 126.2, 125.8, 75.4, 73.4, 72.9, 72.8, 53.4, 46.1, 27.5; HRMS (ESI) calcd for $C_{15}H_{18}O_3Na$ [(M+Na)$^+$] 269.1148, found 269.1148.

*4.1.7. Acetate **16**.* To a suspension of CuI (23.0 mg, 121 μmol) in THF (4.10 mL) at −40 °C was added dropwise allylmagnesium chloride (2.0 M solution in THF, 1.83 mL, 3.66 mmol). The mixture was stirred at −40 °C for 30 min. To the mixture was added dropwise a solution of epoxide **15** (300 mg, 1.22 mmol) in THF (1 mL+2×0.5 mL rinse) via cannula. The resultant solution was stirred at −40 °C for 1.5 h before it was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude alcohol was used for the next reaction without purification: ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.94 (m, 1H), 5.82 (dddd, J=17.0, 10.5, 7.0, 7.0 Hz, 1H), 5.67 (ddd, J=9.5, 1.5, 1.5 Hz, 1H), 5.03 (dd, J=17.0, 1.5 Hz, 1H), 4.95 (br d, J=10.5 Hz, 1H), 4.60 (d, J=12.0 Hz, 1H), 4.55 (d, J=12.0 Hz, 1H), 4.18 (br s, 1H), 3.86 (ddd, J=9.0, 6.5, 3.5 Hz, 1H), 3.74 (ddd, J=9.0, 3.5, 3.5 Hz, 1H), 3.54 (dd, J=10.5, 6.5 Hz, 1H), 3.46 (dd, J=10.5, 3.5 Hz, 1H), 2.28 (m, 1H), 2.16–2.00 (m, 3H), 1.93 (m, 1H), 1.62–1.52 (m, 2H).

To a solution of the above crude alcohol in CH_2Cl_2 (4.1 mL) at room temperature were added successively triethylamine (678 μL, 4.88 mmol), acetic anhydride (345 μL, 3.65 mmol), and DMAP (30.0 mg, 246 μmol). The resultant solution was stirred at room temperature for 2.5 h before it was concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/8) gave acetate **16** (376 mg, 93% for the two steps) as a colorless oil: $[\alpha]_D^{27}$ −33.9 (c 1.0, $CHCl_3$); IR (film) 3064, 3033, 2921, 2858, 1740, 1373, 1236, 1095 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.24 (m, 5H), 5.89 (m, 1H), 5.78 (dddd, J=17.0, 10.3, 6.5, 6.5 Hz, 1H), 5.59 (ddd, J=10.5, 1.5, 1.5 Hz, 1H), 4.99 (dd, J=17.0, 1.5 Hz, 1H), 4.95 (dd, J=10.3, 1.5 Hz, 1H), 4.89 (ddd, J=9.0, 3.9, 3.8 Hz, 1H), 4.60 (d, J=12.0 Hz, 1H), 4.57 (d, J=12.0 Hz, 1H), 4.28 (br s, 1H), 3.79 (m, 1H), 3.56 (dd, J=10.7, 6.5 Hz, 1H), 3.46 (dd, J=10.7, 4.0 Hz, 1H), 2.16–1.90 (m, 4H), 2.06 (s, 3H), 1.83–1.66 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 138.4, 137.9, 128.3 (×2), 127.6 (×2), 127.5, 126.2, 126.1, 114.9, 75.6, 75.0, 73.3, 73.1, 72.9, 29.7, 28.3, 27.7, 21.2; HRMS (ESI) calcd for $C_{20}H_{26}O_4Na$ [(M+Na)$^+$] 353.1723, found 353.1725.

*4.1.8. 1,2-Diol **17**.* To a solution of acetate **16** (4.21 g, 12.8 mmol) and $(DHQD)_2PHAL$ (298 mg, 383 μmol) in *t*-BuOH/H_2O (1/1, v/v, 64 mL) at 0 °C were added AD-mix β (17.9 g) and OsO_4 (39.3 mM solution in

t-BuOH, 3.25 mL, 128 μmol). The resultant mixture was stirred at 0 °C for 21 h, and an additional portion of OsO_4 (39.3 mM solution in *t*-BuOH, 1.63 mL, 64.1 μmol) was added. The mixture was stirred at 0 °C for 4 h before it was quenched with saturated aqueous $Na_2S_2O_3$ solution. The mixture was extracted with EtOAc, and the organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/5 to 5/1) gave 1,2-diol **17** (2.71 g, 58% yield, dr=ca. 4/1 by ^{1}H NMR) as a colorless oil, along with recovered **16** (1.48 g). Recovered **16** was contaminated with some impurities. To a solution of the recovered **16** (1.48 g, ca. 4.38 mmol) and $(DHQD)_2PHAL$ (137 mg, 176 μmol) in *t*-BuOH/H_2O (1/1, v/v, 14.6 mL) at 0 °C were added AD-mix β (6.13 g) and OsO_4 (39.3 mM solution in *t*-BuOH, 1.67 mL, 65.6 μmol). After the mixture was stirred at 0 °C for 11 h, *tert*-butyl methyl ether (3.8 mL) was added and the mixture was stirred for 7 h. To the mixture was added an additional amount of OsO_4 (39.3 mM solution in *t*-BuOH, 1.67 mL, 65.6 μmol). The resultant mixture was stirred at 0 °C for 17 h and then room temperature for 10 h before it was quenched with saturated aqueous $Na_2S_2O_3$ solution. The mixture was extracted with EtOAc, and the organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/5 to 5/1) gave an additional 1,2-diol **17** (886 mg, ca. 55%, dr=ca. 4/1). Total yield: 3.60 g, 77%. Data for **17**: $[\alpha]_D^{28}$ −21.7 (*c* 1.0, $CHCl_3$); IR (film) 3421, 2927, 2863, 1734, 1374, 1244, 1092 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, major isomer) δ 7.35–7.24 (m, 5H), 5.88 (m, 1H), 5.59 (ddd, *J*=10.5, 1.0, 1.0 Hz, 1H), 4.85 (ddd, *J*=9.0, 4.4, 4.2 Hz, 1H), 4.58 (d, *J*=12.0 Hz, 1H), 4.54 (d, *J*=12.0 Hz, 1H), 4.25 (br s, 1H), 3.79 (ddd, *J*=10.5, 7.5, 4.0 Hz, 1H), 3.63 (br s, 1H), 3.58–3.52 (m, 2H), 3.45 (dd, *J*=10.0, 4.0 Hz, 1H), 3.35 (dd, *J*=10.5, 7.5 Hz, 1H), 2.84 (br s, 1H), 2.49 (br s, 1H), 2.05 (s, 3H), 2.13 (m, 1H), 1.92 (m, 1H), 1.81 (m, 1H), 1.73 (m, 1H), 1.48 (m, 1H), 1.37 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, major isomer) δ 170.9, 138.1, 128.3 (×2), 127.7 (×2), 127.6, 126.1, 126.0, 75.5, 75.3, 73.3, 73.0, 72.8, 71.9, 66.6, 28.7, 27.5, 25.3, 21.2; HRMS (ESI) calcd for $C_{20}H_{28}O_6Na$ [(M+Na)$^+$] 387.1778, found 387.1780.

*4.1.9. Enoate **18**.* To a solution of 1,2-diol **17** (2.67 g, 7.34 mmol, ca. 4/1 mixture of diastereomers) in CH_2Cl_2 (70 mL) at 0 °C was added $NaIO_4$ on SiO_2 (17.7 g, ca. 12.1 mmol). The resultant mixture was allowed to warm to room temperature and stirred for 40 min. The mixture was filtered through a sintered glass funnel, and the filtrate was concentrated under reduced pressure. The crude aldehyde was azeotropically dried with benzene and used immediately in the next reaction without purification.

To a solution of the above aldehyde in THF (37 mL) at −40 °C was added ethyl (triphenylphosphoranylidene)acetate (5.11 g, 14.7 mmol). The resultant solution was stirred at −40 °C for 50 min and allowed to warm to room temperature. The mixture was stirred at room temperature for 13 h before it was concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/7 to 1/1) gave enoate **18** (2.83 g, 96% for the two steps, *E*/*Z*>20/1) as a colorless oil: $[\alpha]_D^{26}$ −16.0 (*c* 1.0, $CHCl_3$); IR (film) 2927, 2900, 2859, 1737, 1717, 1653, 1369, 1236, 1094, 1044 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 6.92 (ddd, *J*=15.5, 7.0, 7.0 Hz, 1H), 5.89 (m, 1H), 5.79 (d, *J*=15.5 Hz, 1H), 5.57 (m, 1H), 4.85 (ddd, *J*=8.5, 4.0, 4.0 Hz, 1H), 4.60 (d, *J*=12.0 Hz, 1H), 5.56 (d, *J*=12.0 Hz, 1H), 4.27 (br s, 1H), 4.15 (q, *J*=7.0 Hz, 2H), 3.78 (m, 1H), 3.55 (dd, *J*=10.0, 6.5 Hz, 1H), 3.46 (dd, *J*=10.0, 4.5 Hz, 1H), 2.30–2.14 (m, 2H), 2.06 (s, 3H), 2.06–1.86 (m, 2H), 1.85–1.74 (m, 2H), 1.26 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 166.6, 148.2, 138.3, 128.3 (×2), 127.6 (×2), 127.5, 126.4, 125.9, 121.6, 75.4, 74.9, 73.3, 73.1, 72.8, 60.2, 28.3, 27.6, 27.5, 21.1, 14.2; HRMS (ESI) calcd for $C_{23}H_{30}O_6Na$ [(M+Na)$^+$] 425.1935, found 425.1928.

*4.1.10. Diol **19**.* To a solution of enoate **18** (19.8 mg, 49.3 μmol) in CH_2Cl_2 (1 mL) at −78 °C was added dropwise DIBALH (1.02 M solution in hexanes, 217 μL, 221 μmol). The resultant solution was stirred at −78 °C for 20 min before it was quenched with saturated aqueous potassium sodium tartrate solution. The mixture was diluted with EtOAc and vigorously stirred at room temperature until the layers became clear. The mixture was extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/2 to 2/1) gave diol **19** (15.4 mg, 98%, *E*/*Z*>20/1) as a colorless oil: $[\alpha]_D^{28}$ −4.5 (*c* 1.0, $CHCl_3$); IR (film) 3397, 3033, 2911, 2859, 1450, 1362, 1183, 1088, 1006, 967, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.91 (m, 1H), 5.71–5.60 (m, 3H), 4.58 (d, *J*=12.5 Hz, 1H), 4.54 (d, *J*=12.5 Hz, 1H), 4.16 (br s, 1H), 4.06–4.00 (m, 2H), 3.84 (m, 1H), 3.70 (m, 1H), 3.53 (dd, *J*=10.0, 6.5 Hz, 1H), 3.46 (dd, *J*=10.0, 4.0 Hz, 1H), 2.46 (br s, 1H), 2.27 (m, 1H), 2.11 (m, 1H), 2.04 (m, 1H), 1.91 (m, 1H), 1.83 (br s, 1H), 1.61–1.47 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 132.4, 129.5, 128.4 (×2), 127.7 (×2), 127.6, 126.4, 125.6, 77.8, 73.3, 73.0, 72.9, 72.6, 63.5, 31.2, 28.6, 27.6; HRMS (ESI) calcd for $C_{19}H_{26}O_4Na$ [(M+Na)$^+$] 341.1723, found 341.1728.

*4.1.11. DE-ring diol **20**.* To a suspension of (−)-diethyl tartrate (4.58 g, 22.2 mmol) and 4 Å molecular sieves (4.70 g) in CH_2Cl_2 (54 mL) at −30 °C was added dropwise Ti(O*i*-Pr)$_4$ (5.69 mL, 19.2 mmol). The resultant mixture was stirred at that temperature for 30 min. TBHP (5.0 M solution in isooctane, 11.8 mL, 59.0 mmol) was added dropwise, and the resultant mixture was stirred at −30 °C for 40 min. To the mixture was added dropwise a solution of diol **19** (4.71 g, 14.8 mmol) in CH_2Cl_2 (15 mL+5 mL rinse) via cannula. The resultant mixture was allowed to warm to −15 °C and stirred at that temperature for 44 h. Citric acid (5.68 g, 29.6 mmol) in acetone/H_2O (3/1, v/v, 30 mL) was added, and the resultant mixture was stirred at room temperature for 3 h. The mixture was filtered through a plug of Celite, and the Celite bed was washed successively with EtOAc and acetone. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=2/3 to 3/2 to 3/1) to give DE-ring diol **20** (4.44 g) as a mixture of diastereomers and some minor impurities. Further purification by flash column chromatography (silica gel, $CHCl_3$/acetone=8/1 to 2/1) gave the DE-ring diol **20** (4.14 g, 84%): $[\alpha]_D^{28}$ −17.2 (*c* 1.0, $CHCl_3$); IR (film) 3398, 3028, 2869, 1454, 1362, 1067, 737, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.24 (m, 5H), 5.86 (m, 1H), 5.70 (ddd, *J*=10.5, 1.3, 1.3 Hz, 1H), 4.58 (d, *J*=12.0 Hz, 1H), 4.56 (d, *J*=12.0 Hz, 1H), 4.15 (br s, 1H), 4.00–3.91 (m, 2H), 3.80 (m, 1H), 3.73–3.63 (m, 2H), 3.59 (dd, *J*=12.0, 6.5 Hz, 1H), 3.54 (dd, *J*=10.3, 4.0 Hz, 1H), 3.46 (dd, *J*=10.3, 4.5 Hz, 1H), 2.59 (br s, 2H), 2.09–1.85 (m, 5H), 1.81 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.3, 128.3 (×2), 127.61 (×2), 127.58, 126.9, 125.4, 81.3, 80.6, 76.8, 73.3, 73.1, 73.0 (×2), 63.8, 27.7, 27.2, 27.1; HRMS (ESI) calcd for $C_{19}H_{26}O_5Na$ [(M+Na)$^+$] 357.1673, found 357.1659.

*4.1.12. Primary alcohol **21**.* To a solution of diol **20** (73.3 mg, 219 μmol) and triethylamine (285 μL, 1.98 mmol) in THF (2.2 mL) at 0 °C was added $AgNO_3$ (168 mg, 989 μmol). After 45 min, TBSCl (149 mg, 989 μmol) was added and the resultant mixture was stirred at room temperature for 15 h. The solution was filtered through a plug of Celite into saturated aqueous $NaHCO_3$ solution, and the filtrate was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/30) gave bis-TBS ether (123 mg, quant.) as a colorless oil: $[\alpha]_D^{25}$ −15.4 (*c* 1.0, $CHCl_3$); IR (film) 3033, 2953, 2928, 2886, 2857, 1472, 1462, 1388, 1254, 1078,

836, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.83 (m, 1H), 5.78 (br d, J=10.0 Hz, 1H), 4.60 (d, J=12.0 Hz, 1H), 4.57 (d, J=12.0 Hz, 1H), 4.10–4.02 (m, 2H), 3.85–3.76 (m, 3H), 3.55 (dd, J=10.3, 5.8 Hz, 1H), 3.50–3.43 (m, 3H), 2.08–1.78 (m, 6H), 0.86 (s, 9H), 0.85 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H), 0.01 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.5, 128.3 (×2), 128.0, 127.6 (×2), 127.5, 124.7, 81.2, 80.2, 77.0, 74.5, 73.4, 73.1 (×2), 65.6, 28.2, 27.9, 26.0 (×3), 25.9 (×3), 25.3, 18.3, 18.1, −4.5, −4.6, −5.4, −5.5; HRMS (ESI) calcd for $C_{31}H_{54}O_5Si_2Na$ [$(M+Na)^+$] 585.3402, found 585.3410.

To a solution of the above bis-TBS ether (491 mg, 872 μmol) in MeOH/CH_2Cl_2 (1/3, v/v, 4.36 mL) at 0 °C was added CSA (20.3 mg, 87.4 μmol). The resultant solution was stirred at 0 °C for 50 min and then at room temperature for 100 min. The reaction was quenched with triethylamine, and the mixture was concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/5 then $CHCl_3$/acetone=2/1) gave primary alcohol **21** (254 mg, 65%) as a colorless oil, along with unreacted bis-TBS ether (123 mg, 25%) and diol **20** (28.9 mg, 10%). Data for **21**: $[\alpha]_D^{24}$ −11.6 (*c* 1.0, $CHCl_3$); IR (film) 3446, 2952, 2927, 2883, 2856, 1457, 1362, 1253, 1186, 836, 777, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.85 (m, 1H), 5.74 (br d, J=10.5 Hz, 1H), 4.60 (d, J=12.0 Hz, 1H), 4.57 (d, J=12.0 Hz, 1H), 4.08 (br s, 1H), 3.97 (dd, J=13.3, 6.3 Hz, 1H), 3.86 (dd, J=13.0, 6.5 Hz, 1H), 3.79 (m, 1H), 3.64 (dd, J=10.0, 5.5 Hz, 1H), 3.62–3.54 (m, 2H), 3.54 (dd, J=10.5, 6.5 Hz, 1H), 3.47 (dd, J=10.5, 4.0 Hz, 1H), 2.36 (br s, 1H), 2.08–1.84 (m, 5H), 1.76 (m, 1H), 0.87 (s, 9H), 0.073 (s, 3H), 0.067 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.5, 128.3 (×2) 127.55 (×2), 127.51, 127.48, 125.1, 81.8, 81.3, 77.0, 73.9, 73.3, 73.04, 73.03, 65.7, 28.4, 27.8, 27.4, 25.8 (×3), 18.0, −4.5, −4.6; HRMS (ESI) calcd for $C_{25}H_{40}O_5SiNa$ [$(M+Na)^+$] 471.2537, found 471.2547.

4.1.13. Alkyne ***22***. To a solution of 3-butyn-1-ol (737 mg, 10.5 mmol), 5-mercapto-1-phenyltetrazole (2.81 g, 15.8 mmol), and PPh_3 (4.14 g. 15.8 mmol) in THF (35.0 mL) at 0 °C was added diisopropyl azodicarboxylate (ca. 1.9 M in toluene, 8.31 mL, 15.8 mmol). The resultant solution was stirred at 0 °C for 1.5 h before it was quenched with saturated aqueous $NaHCO_3$ solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/9 to 1/5) gave alkyne **22** (2.28 g, 94%) as a colorless oil: IR (film) 3291, 3064, 1596, 1498, 1413, 1387, 1280, 1242, 761, 693 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.58–7.50 (m, 5H), 3.51 (t, J=6.9 Hz, 2H), 2.79 (td, J=6.9, 2.4 Hz, 2H), 2.04 (d, J=2.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.7, 133.5, 130.2, 129.8 (×2), 123.8 (×2), 81.1, 70.6, 32.1, 19.3; HRMS (ESI) calcd for $C_{11}H_{11}N_4S$ [$(M+H)^+$] 231.0699, found 231.0695.

4.1.14. Propargylic alcohol ***23***. To a solution of diisopropylamine (419 μL, 2.99 mmol) in THF (1.0 mL) was added *n*-BuLi (2.69 M solution in hexanes, 952 μL, 2.56 mmol) at 0 °C. The solution was stirred at that temperature for 1 h. To the solution was added a solution of alkyne **22** (490 mg, 2.13 mmol) in THF (5.0 mL) at −78 °C. The resultant solution was stirred at −78 °C for 45 min. To the solution was added paraformaldehyde (96 mg, 3.20 mmol) in one portion, and the resultant mixture was allowed to warm to room temperature over 30 min. The reaction was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/2 to 2/1) gave propargylic alcohol **23** (364 mg, 66%) as a colorless oil: IR (film) 3397, 2914, 2865, 1596, 1498, 1413, 1388, 1015, 762, 694 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.58–7.50 (m, 5H), 4.21 (t, J=2.0 Hz, 2H), 3.50 (t, J=6.8 Hz, 2H), 2.82 (tt, J=6.8, 2.0 Hz, 2H), 1.61 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.8, 133.5, 130.2, 129.8 (×2), 123.8 (×2), 82.9, 80.7, 51.1, 32.2, 19.6; HRMS (ESI) calcd for $C_{12}H_{13}N_4OS$ [$(M+H)^+$] 261.0805, found 261.0804.

4.1.15. Sulfone ***6***. To a solution of propargylic alcohol **23** (347 mg, 1.33 mmol) in EtOH (13.3 mL) at room temperature was added an ice cooled solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (165 mg, 134 μmol) in 30% aqueous H_2O_2 (756 μL). The resultant solution was stirred at room temperature for 31 h before it was diluted with H_2O. The volatiles were removed under reduced pressure. The residue was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=2/3 to 1/1 to 2/1) gave a sulfone (393 mg, quant.) as a colorless oil: IR (film) 3420, 2983, 2923, 2870, 1497, 1354, 1151, 1016, 765, 690, 536 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.68–7.58 (m, 5H), 4.15 (t, J=2.1 Hz, 2H), 3.87 (t, J=7.3 Hz, 2H), 2.91 (tt, J=7.3, 2.1 Hz, 2H), 1.82 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.1, 132.8, 131.6, 129.7 (×2), 125.2 (×2), 81.6, 79.7, 54.5, 50.9, 13.6; HRMS (ESI) calcd for $C_{12}H_{12}N_4O_3SNa$ [$(M+Na)^+$] 315.0522, found 315.0517.

To a solution of the above sulfone (383 mg, 1.31 mmol) and *i*-Pr_2NEt (685 μL, 3.93 mmol) in 1,2-dichloroethane (1.31 mL) at 0 °C was added MOMCl (149 μL, 1.96 mmol). The resultant mixture was stirred at room temperature for 5 h. Additional portions of *i*-Pr_2NEt (228 μL, 1.31 mmol) and MOMCl (100 μL, 1.32 mmol) were added, and the stirring was continued at room temperature for 2 h before it was quenched with saturated aqueous $NaHCO_3$ solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/2 to 1/1) gave sulfone **6** (401 mg, 93%) as a colorless oil: IR (film) 3067, 2948, 2825, 1497, 1354, 1150, 1100, 1045, 921, 765, 690 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.68–7.56 (m, 5H), 4,63 (s, 2H), 4.11 (t, J=2.5 Hz, 2H), 3.87 (t, J=7.6 Hz, 2H), 3.34 (s, 3H), 2.91 (tt, J=7.6, 2.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.1, 132.9, 131.5, 129.7 (×2), 125.1 (×2), 94.8, 80.2, 79.0, 55.6, 54.4, 54.2, 13.6; HRMS (ESI) calcd for $C_{14}H_{16}N_4O_4SNa$ [$(M+Na)^+$] 359.0784, found 359.0775.

4.1.16. Olefin ***4***. To a solution of primary alcohol **21** (221 mg, 493 μmol) in DMSO (4.90 mL) at room temperature was added IBX (282 mg, 986 μmol). The resultant solution was stirred at room temperature for 3 h before it was quenched with a 1/1 mixture of saturated aqueous $NaHCO_3$ solution and saturated aqueous $Na_2S_2O_3$ solution. The mixture was extracted with diethyl ether, and the organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure gave aldehyde **5** (223 mg), which was azeotropically dried with benzene and used immediately in the next reaction without purification: ^1H NMR (500 MHz, $CDCl_3$) δ 9.62 (d, J=1.0 Hz, 1H), 7.35–7.24 (m, 5H), 5.85 (m, 1H), 5.72 (m, 1H), 4.60 (d, J=12.5 Hz, 1H), 4.57 (d, J=12.5 Hz, 1H), 4.25 (dd, J=11.0, 6.5 Hz, 1H), 4.13–4.07 (m, 2H), 3.91 (dd, J=12.0, 6.0 Hz, 1H), 3.79 (ddd, J=10.0, 4.0, 4.0 Hz, 1H), 3.54 (dd, J=10.0, 6.0 Hz, 1H), 3.46 (dd, J=10.0, 4.5 Hz, 1H), 2.08–1.84 (m, 6H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H).

To a solution of sulfone **6** (191 mg, 568 μmol) in DME (3.0 mL) at −65 °C was added KHMDS (0.5 M solution in toluene, 1.13 mL, 565 μmol). The resultant solution was cooled to −75 °C and stirred at that temperature for 30 min. To the solution was added a solution of the above aldehyde in DME (1.0 mL+2×0.45 mL rinse), and the resultant solution was allowed to warm to 0 °C slowly. The solution was stirred for additional 3 h, and then the reaction was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica

gel, EtOAc/hexanes=1/5) gave olefin **4** (247 mg, 90% from **21**, *E*/*Z*=ca. 7/1 judged by ^{1}H NMR) as a colorless oil: $[\alpha]_D^{26}$ −13.2 (*c* 1.0, $CHCl_3$); IR (film) 2952, 2928, 2886, 2856, 1462, 1361, 1253, 1150, 1099, 1074, 1047, 836, 776 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, major isomer) δ 7.35–7.24 (m, 5H), 5.83 (m, 1H), 5.76 (m, 1H), 5.66–5.57 (m, 2H), 4.68 (s, 2H), 4.60 (d, *J*=12.0 Hz, 1H), 4.56 (d, *J*=12.0 Hz, 1H), 4.23 (dd, *J*=3.5, 3.5 Hz, 1H), 4.20 (t, *J*=2.0 Hz, 2H), 4.06 (br s, 1H), 3.93 (m, 1H), 3.87 (dd, *J*=12.0, 6.0 Hz, 1H), 3.79 (m, 1H), 3.55 (dd, *J*=10.0, 6.0 Hz, 1H), 3.47 (dd, *J*=10.0, 4.3 Hz, 1H), 3.36 (s, 3H), 2.96 (br s, 1H), 2.08–1.76 (m, 7H), 0.87 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, major isomer) δ 138.5, 132.4, 128.3 (×2), 127.8, 127.6 (×2), 127.5, 124.80, 124.78, 94.6, 83.8, 82.9, 81.7, 77.4, 77.1, 74.4, 73.3, 73.07, 73.05, 55.5, 54.6, 27.9, 27.8, 25.9 (×3), 25.4, 21.7, 18.2, −4.5, −4.7; HRMS (ESI) calcd for $C_{32}H_{48}O_6SiNa$ [(M+Na)$^+$] 579.3112, found 579.3116.

4.1.17. Trityl ether ***30***. To a solution of alkyne **29** (1.00 g, 5.87 mmol) in THF (15 mL) at −78 °C was added *n*-BuLi (2.76 M solution in hexanes, 2.06 mL, 5.69 mmol). After stirring for 20 min, $BF_3\cdot OEt_2$ (2.11 mL, 5.60 mmol) was added, and the resultant solution was stirred for additional 25 min. To the solution was added a solution of (*S*)-glycidol (145 mg, 1.96 mmol) in THF (3.6 mL+1 mL rinse), and the resultant solution was allowed to warm to −40 °C. The solution was stirred for additional 20 min before it was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=2/3) gave a diol (405 mg), which was contaminated with some impurities. This material was used for the next reaction without further purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.27 (t, *J*=2.5 Hz, 2H), 3.83 (m, 1H), 3.71 (dd, *J*=11.0, 3.5 Hz, 1H), 3.55 (dd, *J*=11.0, 6.0 Hz, 1H), 2.82 (br s, 1H), 2.54 (br s, 1H), 2.47–2.42 (m, 2H), 0.88 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 81.2, 80.8, 70.3, 65.5, 51.9, 25.8 (×3), 23.8, 18.3, −5.2 (×2).

To a solution of the above diol (405 mg, ca. 1.66 mmol) in 1,2-dichloroethane (1.66 mL) at room temperature were added triethylamine (692 μL, 4.97 mmol), TrCl (690 mg, 2.48 mmol), and DMAP (20 mg, 164 μmol), and the resultant solution was stirred at room temperature for 9.5 h. The resultant mixture was concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/25 to 1/20 to 1/10) gave trityl ether **30** (726 mg, 76% for the two steps) as a colorless viscous oil: $[\alpha]_D^{26}$ −5.8 (*c* 1.0, $CHCl_3$); IR (film) 3447, 3059, 3033, 2953, 2928, 2857, 1597, 1491, 1448, 1254, 1142, 1076, 837, 776, 706 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.39 (m, 6H), 7.32–7.26 (m, 6H), 7.22 (m, 3H), 4.22 (t, *J*=2.0 Hz, 2H), 3.87 (m, 1H), 3.23 (dd, *J*=9.0, 4.0 Hz, 1H), 3.19 (dd, *J*=9.0, 6.0 Hz, 1H), 2.52–2.42 (m, 2H), 2.31 (d, *J*=5.0 Hz, 1H), 0.87 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0 (×3), 128.9 (×6), 128.1 (×6), 127.4 (×3), 87.0, 81.3, 81.1, 69.6, 66.4, 52.1, 26.1 (×3), 24.5, 18.5, −4.9 (×2); HRMS (ESI) calcd for $C_{31}H_{38}O_3SiNa$ [(M+Na)$^+$] 509.2482, found 509.2486.

4.1.18. Primary alcohol ***31***. To a solution of trityl ether **30** (388 mg, 797 μmol) and triethylamine (554 μL, 3.98 mmol) in THF/DMF (2/1, v/v, 6.0 mL) at 0 °C was added $AgNO_3$ (338 mg, 1.99 mmol). After stirring for 10 min, TIPSCl (426 μL, 1.99 mmol) was added, and the resultant solution was stirred at room temperature for 12 h. The solution was filtered through a plug of Celite into saturated aqueous $NaHCO_3$ solution, and the filtrate was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/30) gave a TIPS ether (509 mg, 99%) as a colorless oil: $[\alpha]_D^{25}$ −9.7 (*c* 1.0, $CHCl_3$); IR (film) 3059, 2942, 2895, 2865, 1490, 1463, 1448, 1254, 1077, 1000, 837, 705 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.32 (m, 6H), 7.28–7.24 (m, 6H), 7.20 (m, 3H), 4.19 (t, *J*=2.0 Hz, 2H), 3.99 (m, 1H), 3.17 (dd, *J*=9.5, 6.5 Hz, 1H), 3.15 (dd, *J*=9.5, 4.0 Hz, 1H), 2.69 (m, 1H), 2.50 (m, 1H), 1.00–0.93 (m, 21H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.1 (×3), 128.8 (×6), 127.7 (×6), 126.8 (×3), 86.4, 82.0, 80.1, 70.6, 66.3, 51.9, 25.9 (×3), 25.4, 18.3, 18.0 (×6), 12.4 (×3), −5.14, −5.16; HRMS (ESI) calcd for $C_{40}H_{58}O_3Si_2Na$ [(M+Na)$^+$] 665.3817, found 665.3820.

To a solution of the above TIPS ether (434 mg, 674 μmol) in CH_2Cl_2 (3.4 mL) at −78 °C were added Et_3SiH (327 μL, 2.02 mmol) and $BF_3\cdot OEt_2$ (166 μL, 1.35 mmol). The resultant solution was gradually warmed to −20 °C over 80 min. The solution was stirred at that temperature for additional 2 h before it was quenched with saturated aqueous $NaHCO_3$ solution. The mixture was extracted with CH_2Cl_2, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/25 to 1/10) gave primary alcohol **31** (233 mg, 86%) as a colorless viscous oil: $[\alpha]_D^{27}$ −15.1 (*c* 1.0, $CHCl_3$); IR (film) 3445, 2944, 2893, 2866, 1464, 1362, 1254, 1143, 1115, 1081, 837 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.26 (t, *J*=2.0 Hz, 2H), 3.98 (m, 1H), 3.73–3.62 (m, 2H), 2.53 (ddt, *J*=16.5, 9.0, 2.0 Hz, 1H), 2.41 (m, 1H), 1.92 (br t, *J*=6.0 Hz, 1H), 1.10–1.02 (m, 21H), 0.88 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 81.2, 80.8, 71.4, 65.3, 51.9, 25.8 (×3), 24.1, 18.3, 18.01 (×3), 18.00 (×3), 12.3 (×3), −5.2 (×2); HRMS (ESI) calcd for $C_{21}H_{44}O_3Si_2Na$ [(M+Na)$^+$] 423.2721, found 423.2737.

4.1.19. Thioester ***28***. To a solution of primary alcohol **31** (143 mg, 356 μmol) in EtOAc (1.78 mL) were added quinoline (10.5 μL, 88.9 μmol) and Pd/$CaCO_3$ poisoned with Pb (2.9 mg). The resultant mixture was vigorously stirred under an atmosphere of hydrogen at room temperature for 2 h. The mixture was filtered through a plug of Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=1/30) to give an olefin (145 mg, quant.) as a colorless oil: $[\alpha]_D^{27}$ −15.6 (*c* 1.0, $CHCl_3$); IR (film) 3448, 2944, 2891, 2866, 1464, 1254, 1094, 1065, 882, 837, 776, 679 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.65 (m, 1H), 5.51 (m, 1H), 4.22 (dd, *J*=12.0, 7.0 Hz, 1H), 4.17 (dd, *J*=12.0, 6.0 Hz, 1H), 3.90 (m, 1H), 3.53 (ddd, *J*=11.0, 5.5, 5.5 Hz, 1H), 3.46 (ddd, *J*=11.0, 7.0, 4.5 Hz, 1H), 2.44 (dd, *J*=7.5, 5.5 Hz, 1H), 2.43–2.32 (m, 2H), 1.10–1.02 (m, 21H), 0.88 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.2, 127.0, 72.1, 64.9, 59.0, 32.0, 25.9 (×3), 18.4, 18.1 (×6), 12.4 (×3), −5.16, −5.24; HRMS (ESI) calcd for $C_{21}H_{46}O_3Si_2Na$ [(M+Na)$^+$] 425.2878, found 425.2873.

To a solution of the above olefin (263 mg, 653 μmol) in DMSO (2.2 mL) at room temperature was added IBX (374 mg, 1.31 mmol). The resultant solution was stirred at room temperature for 4 h before it was quenched with a 1/1 mixture of saturated aqueous $NaHCO_3$ solution and saturated aqueous $Na_2S_2O_3$ solution. The mixture was extracted with diethyl ether, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/40 to 1/20) gave aldehyde **32** (230 mg, 88%) as a colorless oil, which was used in the next reaction without further purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (d, *J*=2.0 Hz, 1H), 5.63 (m, 1H), 5.48 (m, 1H), 4.24–4.14 (m, 2H), 4.10 (dt, *J*=6.0, 2.0 Hz, 1H), 2.51–2.36 (m, 2H), 1.13–1.02 (m, 21H), 0.87 (s, 9H), 0.04 (s, 6H).

To a solution of the above aldehyde **32** (230 mg, 575 μmol), 2-methyl-2-butene (609 μL, 5.75 mmol), and NaH_2PO_4 (207 mg, 1.73 mmol) in *t*-BuOH/H_2O (5/1, v/v, 5.75 mL) at 0 °C was added $NaClO_2$ (78.0 mg, 862 μmol). The resultant mixture was stirred at 0 °C for 50 min before it was quenched with H_2O. The mixture was acidified with 0.1 M HCl solution (pH 3) and extracted with $CHCl_3$, and the organic layer was washed with brine, dried over Na_2SO_4,

filtered, and concentrated under reduced pressure. The crude acid was azeotropically dried with benzene and used immediately in the next reaction without purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.69 (m, 1H), 5.47 (m, 1H), 4.47 (dd, J=5.5, 3.5 Hz, 1H), 4.21 (m, 1H), 4.16 (m, 1H), 2.66 (ddd, J=13.5, 8.5, 3.5 Hz, 1H), 2.49 (ddd, J=13.5, 6.5, 5.5 Hz, 1H), 1.18–1.05 (m, 21H), 0.87 (s, 9H), 0.04 (s, 6H).

To a solution of the above crude acid, i-Pr_2NEt (120 μL, 689 μmol), and p-toluenethiol (79 mg, 636 μmol) in DMF (5.8 mL) at 0 °C was added PyBOP® (329 mg, 632 μmol). The resultant solution was allowed to warm to room temperature and stirred for 8 h. The reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with EtOAc, and the combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/80 to 1/40) gave thioester **28** (240 mg, 80% for the two steps) as a colorless oil: $[\alpha]_D^{28}$ +49.2 (*c* 1.0, $CHCl_3$); IR (film) 2946, 2892, 2867, 1701, 1494, 1463, 1253, 1132, 1090, 882, 837, 806, 776, 684 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24–7.16 (m, 4H), 5.67 (m, 1H), 5.58 (m, 1H), 4.48 (dd, J=6.0, 4.0 Hz, 1H), 4.24–4.11 (m, 2H), 2.63 (ddd, J=13.5, 7.5, 4.0 Hz, 1H), 2.51 (m, 1H), 2.35 (s, 3H), 1.24–1.08 (m, 21H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 203.1, 139.3, 134.6 (×2), 132.8, 129.9 (×2), 124.5, 123.4, 78.3, 59.5, 34.5, 25.9 (×3), 21.3, 18.3, 18.04 (×3), 18.02 (×3), 12.4 (×3), −5.2 (×2); HRMS (ESI) calcd for $C_{28}H_{50}O_3SSi_2Na$ [(M+Na)$^+$] 545.2911, found 545.2931.

4.1.20. Alkyne ***34****.* To a solution of diol **20** (112.6 mg, 337 μmol) in CH_2Cl_2 (3.4 mL) at 0 °C was added $NaIO_4$ on SiO_2 (673 mg, ca. 460 μmol). The resultant mixture was allowed to warm to room temperature and stirred for 60 min. An additional portion of $NaIO_4$ on SiO_2 (135 mg, ca. 92.0 μmol) was added, and the stirring was continued for 20 min. The mixture was filtered through a sintered glass funnel, and the filtrate was concentrated under reduced pressure. The crude aldehyde was used immediately in the next reaction without purification.

To a solution of the above aldehyde in MeOH (1.7 mL) at 0 °C were added Ohira–Bestmann reagent **33** (76.0 μL, 507 μmol) and K_2CO_3 (116 mg, 841 μmol). The resultant solution was stirred at 0 °C for 1.5 h before it was diluted with diethyl ether. The mixture was extracted with diethyl ether, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/20) gave alkyne **34** (95.0 mg, 95% for the two steps) as a colorless oil: $[\alpha]_D^{26}$ −21.4 (*c* 0.5, $CHCl_3$); IR (film) 3289, 3032, 2889, 2862, 1093, 1062, 737, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.87 (m, 1H), 5.72 (m, 1H), 4.70 (ddd, J=6.5, 4.5, 1.8 Hz, 1H), 4.59 (d, J=12.0 Hz, 1H), 4.55 (d, J=12.0 Hz, 1H), 4.14 (m, 1H), 4.06 (ddd, J=7.5, 5.5, 5.5 Hz, 1H), 3.80 (m, 1H), 3.55 (dd, J=10.3, 5.8 Hz, 1H), 3.46 (dd, J=10.3, 4.3 Hz, 1H), 2.40 (d, J=1.8 Hz, 1H), 2.17 (m, 1H), 2.13–2.00 (m, 2H), 1.95–1.90 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 128.4 (×2), 127.60 (×2), 127.55, 127.1, 125.5, 83.7, 81.0, 76.6, 73.3, 73.0, 72.9, 72.5, 68.5, 33.2, 27.8, 26.5; HRMS (ESI) calcd for $C_{19}H_{22}O_3Na$ [(M+Na)$^+$] 321.1461, found 321.1450.

4.1.21. Methyl ketone ***35****.* To a solution of alkyne **34** (46.3 mg, 155 μmol) in THF/H_2O (2/1, v/v, 1.5 mL) at 0 °C was added saturated solution of $HgSO_4$ in 1% aqueous H_2SO_4 (683 μL). The resultant mixture was allowed to warm to room temperature and stirred for 4 h. The mixture was cooled to 0 °C and quenched with saturated aqueous $NaHCO_3$ solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/5) gave methyl ketone **35** (46.1 mg, 94%) as a colorless oil: $[\alpha]_D^{26}$ −43.3 (*c* 1.0, $CHCl_3$); IR (film) 3032, 2889, 2862, 1715, 1454, 1355, 1186, 1077, 738, 698 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.32–7.27 (m, 2H), 7.21–7.16 (m, 2H), 7.10 (m, 1H), 5.77 (ddd, J=10.0, 1.5, 1.5 Hz, 1H), 5.67 (m, 1H), 4.40 (d, J=15.0 Hz, 1H), 4.37 (d, J=15.0 Hz, 1H), 4.22 (dd, J=7.0, 7.0 Hz, 1H), 4.04 (br s, 1H), 3.90 (dd, J=12.5, 6.3 Hz, 1H), 3.71 (m, 1H), 3.44 (dd, J=10.3, 5.5 Hz, 1H), 3.30 (dd, J=10.3, 4.8 Hz, 1H), 1.94 (m, 1H), 1.87 (s, 3H), 1.84 (m, 1H), 1.80–1.57 (m, 4H); ^{13}C NMR (125 MHz, C_6D_6) δ 208.9, 139.2, 128.5 (×2), 127.9, 127.69 (×2), 127.67, 125.4, 84.5, 82.6, 77.3, 73.33, 73.30, 73.28, 28.9, 28.2, 27.5, 25.3; HRMS (ESI) calcd for $C_{19}H_{24}O_4Na$ [(M+Na)$^+$] 339.1567, found 339.1558.

4.1.22. Enol triflate ***36****.* To a solution of KHMDS (0.5 M solution in toluene, 1.51 mL, 753 μmol) in THF (4.6 mL) at −78 °C was added dropwise a solution of methyl ketone **35** (226 mg, 708 μmol) in THF (1 mL+2×0.5 mL rinse) via cannula. The resultant solution was allowed to warm to −40 °C. After being stirred for 15 min, the solution was cooled to −78 °C, and a solution of $PhNTf_2$ (282 mg, 790 μmol) in THF (0.57 mL) was added via cannula. The resultant solution was allowed to warm to −20 °C and stirred at that temperature for 20 min. The solution was cooled to −78 °C and quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, hexanes then EtOAc/hexanes=1/10) gave enol triflate **36** (251 mg, 79%) as a colorless oil: $[\alpha]_D^{27}$ −12.9 (*c* 1.0, benzene); IR (film) 3033, 2894, 2861, 1670, 1419, 1212, 1142, 1079, 933 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.32–7.26 (m, 2H), 7.21–7.16 (m, 2H), 7.10 (m, 1H), 5.69–5.60 (m, 2H), 4.80 (d, J=3.0 Hz, 1H), 4.68 (d, J=3.0 Hz, 1H), 4.38 (d, J=12.5 Hz, 1H), 4.37 (d, J=12.5 Hz, 1H), 4.35 (m, 1H), 4.03 (m, 1H), 3.93 (dd, J=12.0, 6.0 Hz, 1H), 3.69 (m, 1H), 3.43 (dd, J=10.5, 6.0 Hz, 1H), 3.29 (dd, J=10.5, 4.5 Hz, 1H), 1.91 (m, 1H), 1.80–1.70 (m, 3H), 1.67 (m, 1H), 1.55 (m, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 155.9, 139.1, 128.5 (×2), 128.3, 127.7 (×2), 127.6, 125.5, 119.1 (q, J_{C-F}=320 Hz), 103.7, 82.4, 77.7, 77.2, 73.34, 73.30, 73.2, 30.0, 28.1, 27.0; HRMS (ESI) calcd for $C_{20}H_{23}F_3O_6SNa$ [(M+Na)$^+$] 471.1060, found 471.1047.

4.1.23. Vinylstannane ***27****.* To a solution of enol triflate **36** (34.7 mg, 77.5 μmol) in THF (1.48 mL) at room temperature were added successively LiCl (32.8 mg, 774 μmol), $Pd(PPh_3)_4$ (8.9 mg, 7.7 μmol), and hexamethylditin (48.1 μL, 232 μmol). After stirring at room temperature for 1 h, the solution was warmed to 70 °C and stirred for 3 h. The mixture was cooled to room temperature, diluted with diethyl ether, and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, hexanes then EtOAc/hexanes=1/20 to 1/10) to give vinylstannane **27** (32.4 mg, 90%) as a colorless oil: $[\alpha]_D^{28}$ −18.6 (*c* 1.0, benzene); IR (film) 3033, 2975, 2934, 2908, 2893, 2860, 1456, 1185, 1093, 1061, 917, 767, 696, 526 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.34–7.29 (m, 2H), 7.23–7.16 (m, 2H), 7.11 (m, 1H), 5.97 (ddd, J=10.5, 1.3, 1.3 Hz, 1H), 5.76 (m, 1H), 5.69 (m, 1H), 5.29 (m, 1H), 4.59 (m, 1H), 4.43 (d, J=12.2 Hz, 1H), 4.40 (d, J=12.2 Hz, 1H), 4.07 (br s, 1H), 3.98 (dd, J=14.2, 6.8 Hz, 1H), 3.76 (m, 1H), 3.49 (dd, J=9.8, 5.9 Hz, 1H), 3.34 (dd, J=9.8, 4.4 Hz, 1H), 2.03–1.89 (m, 3H), 1.83 (m, 1H), 1.72 (m, 1H), 1.49 (dddd, J=9.3, 9.3, 9.3, 9.3 Hz, 1H), 0.24 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 159.0, 139.3, 128.7, 128.5 (×2), 127.7 (×2), 127.6, 125.0, 122.4, 85.9, 81.6, 78.1, 73.43, 73.41, 73.3, 34.0, 29.2, 28.3, −8.7 (×3); HRMS (ESI) calcd for $C_{22}H_{32}O_3SnNa$ [(M+Na)$^+$] 487.1270, found 487.1280.

4.1.24. Copper(I) diphenylphosphinate (CuDPP). Suspension of Cu_2O (822 mg, 5.75 mmol) and diphenylphosphinic acid (2.50 g, 11.5 mmol) in degassed toluene (28 mL) was refluxed for 20 h with azeotropical removal of water using a Dean–Stark apparatus. The reaction mixture was cooled to room temperature, and the

resultant solid was filtered under a stream of argon. The resultant powder was washed successively with degassed toluene, dry diethyl ether, and dry hexanes and then dried under reduced pressure to give copper(I) diphenylphosphinate (2.97 g, 92%) as a light tan powder. This powder was active enough for coupling reaction: IR (KBr) 3073, 1590, 1484, 1437, 1129, 1040 cm^{-1}.

4.1.25. Enone ***26***. To a suspension of thioester **28** (21.8 mg, 41.7 μmol), copper(I) diphenylphosphinate (23.4 mg, 83.4 μmol), and $Pd_2(dba)_3$ (3.80 mg, 4.15 μmol) in hexane (200 μL, degassed) at room temperature was added a portion (100 μL, 16.7 μmol) of a stock solution of triethylphosphite (28.6 μL) in THF (0.97 mL, degassed). After stirring for 25 min, a solution of vinylstannane **27** (21.4 mg, 46.2 μmol) in THF/hexanes (1/2, v/v, 300 μL+234 μL rinse, degassed) was added, and the resultant ocherous suspension was stirred at room temperature for 2 h. The mixture was diluted with hexane and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, benzene to EtOAc/hexanes=10/1 to 5/1) to give enone **26** (25.3 mg, 87%) as a colorless oil, along with homo-coupling product **38** (1.8 mg, ca. 7%, contaminated with some impurities. Data for **26**: $[\alpha]_D^{27}$ −17.9 (*c* 1.0, $CHCl_3$); IR (film) 2945, 2982, 2865, 1686, 1668, 1463, 1254, 1093, 837, 777, 682 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 6.30 (s, 1H), 6.16 (s, 1H), 5.87 (m, 1H), 5.79 (br d, *J*=10.0 Hz, 1H), 5.59 (ddd, *J*=11.5, 6.5, 6.0 Hz, 1H), 5.40 (m, 1H), 4.77 (dd, *J*=14.0, 7.0 Hz, 1H), 4.74 (dd, *J*=14.0, 7.0 Hz, 1H), 4.60 (d, *J*=12.0 Hz, 1H), 4.56 (d, *J*=12.0 Hz, 1H), 4.18–4.10 (m, 3H), 4.00 (dd, *J*=13.0, 6.5 Hz, 1H), 3.81 (m, 1H), 3.56 (dd, *J*=10.5, 6.0 Hz, 1H), 3.47 (dd, *J*=10.5, 5.0 Hz, 1H), 2.52 (m, 1H), 2.47–2.30 (m, 2H), 2.05 (m, 1H), 2.00–1.85 (m, 3H), 1.49 (ddd, *J*=15.5, 15.5, 8.0 Hz, 1H), 1.08–0.98 (m, 21H), 0.86 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.6, 147.4, 138.5, 132.4, 128.3 (×2), 127.6 (×2), 127.5, 127.4, 125.2, 124.8, 123.9, 81.4, 77.5, 76.8, 76.1, 73.4, 73.1, 73.0, 59.4, 34.8, 32.7, 27.9, 27.2, 25.9 (×3), 18.3, 17.96 (×3), 17.94 (×3), 12.2 (×3), −5.2 (×2); HRMS (ESI) calcd for $C_{40}H_{66}O_6Si_2Na$ [$(M+Na)^+$] 721.4290, found 721.4304.

4.1.26. Allylic alcohol ***39***. To a solution of enone **26** (14.2 mg, 20.3 μmol) in EtOH (1.0 mL) was added $CeCl_3 \cdot 7H_2O$ (11.4 mg, 30.6 μmol). After stirring at room temperature for 20 min, the resultant solution was cooled to −40 °C and treated with $NaBH_4$ (0.92 mg, 24.3 μmol) in one portion. The resultant mixture was stirred at that temperature for 1.5 h before it was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/10) gave allylic alcohol **39** (14.0 mg, 98%, dr>20/1 judged by ^1H NMR) as a colorless oil: $[\alpha]_D^{25}$ −12.2 (*c* 1.0, $CHCl_3$); IR (film) 3502, 2928, 2892, 2865, 1463, 1254, 1090, 1066, 837, 776, 679 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.85 (m, 1H), 5.80 (br d, *J*=10.5 Hz, 1H), 5.60 (m, 1H), 5.47 (m, 1H), 5.22 (s, 1H), 5.12 (s, 1H), 4.60 (d, *J*=12.0 Hz, 1H), 4.56 (d, *J*=12.0 Hz, 1H), 4.43 (dd, *J*=7.0, 7.0 Hz, 1H), 4.22–4.16 (m, 2H), 4.06 (br s, 1H), 3.98 (ddd, *J*=8.0, 4.0, 4.0 Hz, 1H), 3.96–3.87 (m, 2H), 3.79 (m, 1H), 3.55 (dd, *J*=11.0, 6.0 Hz, 1H), 3.46 (dd, *J*=10.0, 4.5 Hz, 1H), 2.85 (d, *J*=7.5 Hz, 1H), 2.47 (ddd, *J*=15.0, 8.0, 8.0 Hz, 1H), 2.21 (m, 1H), 2.15–1.88 (m, 5H), 1.73 (m, 1H), 1.18–0.98 (m, 21H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.4, 138.5, 132.2, 128.3 (×2), 127.8, 127.6 (×2), 127.5, 125.4, 124.9, 110.6, 81.0, 79.7, 77.1, 73.7, 73.38, 73.36, 73.1 (×2), 59.6, 32.6, 31.7, 27.9, 27.5, 25.9 (×3), 18.3, 18.19 (×3), 18.14 (×3), 12.8 (×3), −5.17, −5.19; HRMS (ESI) calcd for $C_{40}H_{68}O_6Si_2Na$ [$(M+Na)^+$] 723.4447, found 723.4474.

4.1.27. C15–C31 model ***3***. To a solution of allylic alcohol **39** (13.8 mg, 19.7 μmol) in THF (400 μL) at room temperature was added TBAF (1.0 M solution in THF, 59 μL, 59 μmol). The resultant solution was stirred at room temperature for 2 h and then at 50 °C for 30 min. The mixture was cooled to room temperature and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=2/1 to 1/0) gave C15–C31 model **3** (8.0 mg, 94%, dr>20/1) as a colorless oil: $[\alpha]_D^{27}$ −30.5 (*c* 0.8, $CHCl_3$); IR (film) 3394, 3030, 2917, 2866, 1455, 1065, 933, 738, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.34–7.30 (m, 4H), 7.27 (m, 1H), 5.92–5.83 (m, 2H), 5.68 (dddd, *J*=10.3, 2.8, 1.4, 1.4, 1H), 5.62 (ddd, *J*=10.3, 8.2, 7.9 Hz, 1H), 5.18 (m, 2H), 4.60 (d, *J*=12.4 Hz, 1H), 4.56 (d, *J*=12.4 Hz, 1H), 4.54 (br dd, *J*=8.6, 5.9 Hz, 1H), 4.19 (m, 1H), 4.11 (ddd, *J*=12.4, 7.3, 0.7 Hz, 1H), 4.06 (dd, *J*=12.4, 7.3 Hz, 1H), 4.03 (ddd, *J*=12.7, 7.3, 5.5 Hz, 1H), 3.96 (d, *J*=5.9 Hz, 1H), 3.81 (dddd, *J*=10.3, 6.5, 4.1, 3.8 Hz, 1H), 3.76 (dd, *J*=11.7, 5.9 Hz, 1H), 3.54 (dd, *J*=10.7, 6.5 Hz, 1H), 3.46 (dd, *J*=10.7, 4.1 Hz, 1H), 2.34–2.28 (m, 2H), 2.13 (m, 1H), 2.09–1.99 (m, 2H), 1.99–1.91 (m, 2H), 1.86 (dddd, *J*=11.7, 9.2, 8.9, 8.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.7, 138.3, 131.3, 129.1, 128.4 (×2), 127.6 (×3), 126.7, 125.8, 113.8, 81.3, 80.6, 76.8, 76.7, 73.4, 73.0, 72.9, 71.9, 57.5, 31.4, 31.0, 27.7, 26.9; HRMS (ESI) calcd for $C_{25}H_{34}O_6Na$ [$(M+Na)^+$] 453.2248, found 453.2234.

4.1.28. Acetonide ***40***. To a solution of triol **3** (7.9 mg, 18 μmol) in CH_2Cl_2 (370 μL) at room temperature were added 2,2-dimethoxypropane (23 μL, 190 μmol) and CSA (0.43 mg, 1.9 μmol). The resultant solution was stirred at room temperature for 0.5 h before it was quenched with saturated aqueous $NaHCO_3$ solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude acetonide (9.0 mg) was contaminated with the corresponding 2-methoxy-2-propyl ether, and thus used in the next reaction without purification.

To a solution of the crude acetonide (9.0 mg) in EtOH (370 μL) at 0 °C was added pyridinium *p*-toluenesulfonate (0.46 mg, 1.8 μmol). The resultant solution was allowed to warm to room temperature and stirred for 5 min before it was quenched with triethylamine (excess). The mixture was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=3/2) to give acetonide **40** (8.2 mg, 95% for the two steps, dr>20/1) as a colorless oil: $[\alpha]_D^{24}$ −19.3 (*c* 0.9, $CHCl_3$); IR (film) 3445, 3029, 2983, 2867, 1455, 1370, 1165, 1091, 1056, 698 cm^{-1}; ^1H NMR (600 MHz, C_6D_6) δ 7.33–7.29 (m, 2H), 7.21–7.17 (m, 2H), 7.10 (m, 1H), 5.84–5.77 (m, 2H), 5.68 (dddd, *J*=10.3, 5.9, 2.4, 1.7 Hz, 1H), 5.62 (m, 1H), 5.39 (dd, *J*=1.4, 1.4 Hz, 1H), 5.27 (br dd, *J*=6.8, 6.5 Hz, 1H), 4.54 (m, 1H), 4.42 (d, *J*=12.4 Hz, 1H), 4.39 (d, *J*=12.4 Hz, 1H), 4.16 (m, 1H), 4.13 (d, *J*=8.6 Hz, 1H), 4.11 (dd, *J*=13.0, 6.9 Hz, 1H), 4.04 (dd, *J*=13.1, 6.9 Hz, 1H), 4.00 (m, 1H), 3.94 (ddd, *J*=8.6, 7.6, 2.4 Hz, 1H), 3.76 (m, 1H), 3.47 (dd, *J*=10.3, 6.2 Hz, 1H), 3.32 (dd, *J*=10.3, 4.4 Hz, 1H), 2.40 (dddd, *J*=14.4, 7.2, 3.1, 1.4 Hz, 1H), 2.28 (m, 1H), 2.00–1.90 (m, 5H), 1.72–1.65 (m, 2H), 1.38 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 147.3, 139.2, 132.4, 128.5 (×2), 128.3, 127.7 (×2), 127.66, 127.64, 125.3, 111.7, 108.4, 81.6, 81.5, 80.3, 79.8, 77.6, 73.39, 73.36, 73.31, 58.1, 32.5, 29.9, 28.2, 27.8, 27.3, 27.0; HRMS (ESI) calcd for $C_{28}H_{38}O_6Na$ [$(M+Na)^+$] 493.2561, found 493.2562.

4.1.29. Alkyne ***44***. To a solution of trimethylsilylacetylene (2.00 mL, 14.2 mmol) in THF (25 mL) at −78 °C was added *n*-BuLi (2.69 M solution in hexanes, 5.10 mL, 13.7 mmol). After stirring at −78 °C for 20 min, $BF_3 \cdot OEt_2$ (1.69 mL, 13.7 mmol) was added. After 40 min, to the mixture was added dropwise a solution of (*S*)-glycidol (351 mg, 4.74 mmol) in THF (1 mL+2×0.5 mL rinse) via cannula. The resultant solution was allowed to warm to 0 °C and stirred for further 20 min before it was quenched with saturated aqueous $NaHCO_3$ solution. The organic layer was concentrated under reduced pressure, and the residue was extracted with EtOAc, washed with brine, dried over

Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude diol (776 mg), which was used in the next reaction without purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.85 (m, 1H), 3.72 (dd, J=11.5, 3.5 Hz, 1H), 3.57 (dd, J=11.5, 6.5 Hz, 1H), 2.47 (dd, J=16.5, 6.5 Hz, 1H), 2.44 (dd, J=16.5, 6.5 Hz, 1H), 2.09 (br s, 2H), 0.13 (s, 9H).

To a solution of the above diol (776 mg) in CH_2Cl_2 (15.6 mL) were added benzaldehyde dimethylacetal (1.42 mL, 9.47 mmol) and CSA (55.0 mg, 237 μmol). The resultant solution was stirred at room temperature for 3 h before it was quenched with triethylamine. The mixture was concentrated under reduced pressure to give a crude benzylidene acetal, which was used in the next reaction without purification.

To a solution of the above crude benzylidene acetal in MeOH (9.4 mL) was added K_2CO_3 (1.55 g, 11.2 mmol). The resultant solution was stirred at room temperature for 1 h before it was diluted with EtOAc. The organic layer was washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, hexanes then diethyl ether/hexanes=1/6) gave alkyne **44** (741 mg, ca. 81% for the three steps, dr=ca. 1.2/1) as a colorless oil, which was contaminated with ca. 5.5 mol % of benzaldehyde (judged by ^{1}H NMR). This mixture was used in the next reaction without further purification. Analytical sample (ca. 1.1/1 mixture of diastereomers) was obtained by further purification by preparative HPLC. Data for **44**: $[\alpha]_D^{26}$ −51.1 (c 1.0, $CHCl_3$); IR (film) 3290, 3035, 2881, 1478, 1401, 1220, 1091, 1070, 1026, 971, 759, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52–7.42 (m, 2H), 7.40–7.34 (m, 3H), 5.98 (s, 0.48H), 5.80 (s, 0.52H), 4.44–4.35 (m, 1H), 4.30 (dd, J=8.5, 6.5 Hz, 0.48H), 4.15 (dd, J=8.0, 7.0 Hz, 0.52H), 4.00 (dd, J=8.0, 5.0 Hz, 0.52H), 3.88 (dd, J=8.5, 7.0 Hz, 0.48H), 2.66–2.59 (m, 1H), 2.59–2.50 (m, 1H), 2.10–1.96 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ; 137.7, 137.1, 129.5, 129.2, 128.4 (×2), 128.3 (×2), 126.7 (×2), 126.4 (×2), 104.6, 103.9, 79.6, 79.4, 74.6, 74.0, 70.6, 70.3, 69.9, 69.6, 23.9, 23.2; HRMS (ESI) calcd for $C_{12}H_{12}O_2Na$ [(M+Na)$^+$] 211.0730, found 211.0722.

*4.1.30. Triol **46**.* To a suspension of $Zn(OTf)_2$ [755 mg, 2.08 mmol, dried under vacuum (2 mm Hg) at 60–80 °C for 20 min immediately prior to use] and (+)-*N*-methylephedrine (406 mg, 2.27 mmol) in toluene (1 mL) was added triethylamine (316 μL, 2.27 mmol). The resulting mixture was stirred at room temperature for 2 h 40 min. A solution of alkyne **44** (356 mg, ca. 1.89 mmol) in toluene (0.5 mL) was added dropwise via cannula. After stirring for 45 min, a solution of aldehyde **43** (453 mg, 873 μmol) in toluene (300 μL+2×200 μL rinse) was added dropwise via cannula. The resultant mixture was stirred at room temperature for 12 h before it was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with diethyl ether, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/10 to 1/3.5) gave propargylic alcohol **45** (561 mg) as a ca. 1/1.3/11/13 mixture of diastereomers, which was contaminated with some impurities. The mixture was used in the next reaction without further purification: ^{1}H NMR (500 MHz, $CDCl_3$, for the major two diastereomers) δ 7.68–7.62 (m, 4H), 7.45–7.31 (m, 11H), 7.25–7.21 (m, 2H), 6.83–6.78 (m, 2H), 5.92 (s, 0.48H), 5.75 (s, 0.52H), 4.70–4.66 (m, 1H), 4.57–4.53 (m, 1H), 4.47–4.42 (m, 1H), 4.37–4.27 (m, 1H), 4.22 (dd, J=8.5, 6.0 Hz, 0.48H), 4.06 (dd, J=8.5, 6.5 Hz, 0.52H), 3.95 (dd J=8.5, 5.0 Hz, 0.52H), 3.82 (dd, J=8.5, 7.0 Hz, 0.48H), 3.76 (s, 1.56H), 3.75 (s, 1.44H), 3.73–3.62 (m, 2H), 3.42–3.36 (m, 1H), 2.74–2.58 (m, 1H), 2.58–2.46 (m, 1H), 2.29–2.22 (m, 1H), 2.21–2.12 (m, 1H), 1.86–1.76 (m, 1H), 1.60–1.51 (m,1H), 1.50–1.41 (m, 1H), 1.02 (s, 9H), 0.78–0.68 (m, 6H).

To a solution of the above propargylic alcohol **45** (561 mg) in EtOH (7.9 mL) at room temperature was added pyridinium *p*-toluenesulfonate (80.0 mg, 319 μmol). The resultant solution was stirred at room temperature for 4.5 h before it was quenched with triethylamine (221 μL, 1.59 mmol). The mixture was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=2/3 to 2/1) to give triol **46** (441 mg, 82% for the two steps) as a colorless oil: $[\alpha]_D^{28}$ +29.3 (c 1.0, $CHCl_3$); IR (film) 3386, 2961, 2931, 2861, 1514, 1248, 1111, 1087, 1036, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68–7.62 (m, 4H), 7.42–7.32 (m, 6H), 7.26–7.21 (m, 2H), 6.84–6.80 (m, 2H), 4.69 (d, J=11.0 Hz, 1H), 4.56 (d, J=11.0 Hz, 1H) 4.43 (br d, J=5.5 Hz, 1H), 3.76 (s, 3H), 3.76–3.64 (m, 3H), 3.61 (br d, J=12.5 Hz, 1H), 3.48 (dd, J=11.5, 6.0 Hz, 1H), 3.40 (dd, J=10.0, 3.3 Hz, 1H), 2.59 (br s, 1H), 2.45–2.80 (m, 2H), 2.25 (d, J=8.5 Hz, 1H), 2.16 (m, 1H), 1.92 (br s, 1H), 1.78 (m, 1H), 1.55 (m, 1H), 1.46 (m, 1H), 1.02 (s, 9H), 0.74 (d, J=7.5 Hz, 3H), 0.71 (d, J=6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 135.6 (×2), 135.5 (×2), 134.00, 133.97, 130.5, 129.54 (×2), 129.51 (×2), 127.6 (×4), 113.9 (×2), 84.1, 82.8, 80.9, 74.7, 70.1, 65.4, 64.9, 62.5, 55.2, 39.3, 38.3, 28.2, 26.8 (×3), 23.9, 19.2, 13.8, 10.0; HRMS (ESI) calcd for $C_{37}H_{50}O_6SiNa$ [(M+Na)$^+$] 641.3269, found 641.3270.

*4.1.31. Trityl ether **47**.* To a solution of triol **46** (124 mg, 200 μmol) in EtOAc (1 mL) were added quinoline (6.1 μL, 50 μmol) and Pd/$CaCO_3$ poisoned with Pb (12.4 mg). The resultant suspension was stirred vigorously under an atmosphere of hydrogen at room temperature for 13 h. The mixture was filtered through a plug of Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=1/1 to 2/1) to give a (*Z*)-alkene (117 mg, 94%) as a colorless oil: $[\alpha]_D^{28}$ −7.5 (c 1.0, $CHCl_3$); IR (film) 3377, 2958, 2931, 2857, 1514, 1248, 1111, 1091, 1037, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68–7.63 (m, 4H), 7.43–7.37 (m, 2H), 7.37–7.32 (m, 4H), 7.26–7.21 (m, 2H), 6.84–6.80 (m, 2H), 5.83 (dd, J=10.0, 10.0 Hz, 1H), 5.59 (ddd, J=10.0, 10.0, 6.5 Hz, 1H), 4.62 (d, J=11.5 Hz, 1H) 4.57 (d, J=11.5 Hz, 1H), 4.51 (dd, J=8.5, 3.0 Hz, 1H), 3.76 (s, 3H), 3.75–3.62 (m, 3H), 3.61–3.48 (m, 2H), 3.45 (dd, J=8.5, 3.3 Hz, 1H), 2.62 (br s, 3H), 2.48 (ddd, J=14.0, 9.5, 7.0 Hz, 1H), 2.24 (m, 1H), 2.16 (m, 1H), 1.59 (m, 1H), 1.51 (m, 1H), 1.44 (m, 1H), 1.01 (s, 9H), 0.76 (d, J=8.0 Hz, 3H), 0.67 (d, J=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 135.6 (×2), 135.5 (×2), 134.00, 133.98, 130.8, 130.7, 129.50, 129.49, 129.35 (×2), 129.2, 127.6 (×4), 113.8 (×2), 84.3, 74.8, 71.0, 68.1, 64.9, 62.5, 55.2, 38.7, 38.3, 31.9, 28.3, 26.8 (×3), 19.1, 14.0, 10.2; HRMS (ESI) calcd for $C_{37}H_{52}O_6SiNa$ [(M+Na)$^+$] 643.3425, found 643.3434.

To a solution of the above (*Z*)-alkene (70.8 mg, 114 μmol) in 1,2-dichloroethane (290 μL) at 0 °C were added triethylamine (47.6 μL, 343 μmol), TrCl (41.2 mg, 148 μmol), and DMAP (1.4 mg, 11 μmol), and the resultant solution was stirred at room temperature for 1.5 h. The reaction mixture was diluted with 1,2-dichloroethane (850 μL) and stirred at 50 °C for 10 h. Additional portions of triethylamine (111 μL, 799 μmol) and TrCl (41.2 mg, 148 μmol) were added, and the stirring was continued at 50 °C for further 17 h. The mixture was cooled to room temperature, quenched with H_2O, and neutralized with 5% aqueous citric acid (pH=ca. 7). The mixture was extracted with CH_2Cl_2, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/10 to 1/7 to 1/5) gave trityl ether **47** (89.0 mg, 90%) as a colorless viscous oil: $[\alpha]_D^{28}$ +16.0 (c 1.0, $CHCl_3$); IR (film) 3410, 3068, 2957, 2930, 2858, 1513, 1248, 1110, 1089, 1035, 763, 745, 703, 505 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67–7.62 (m, 4H), 7.44–7.39 (m, 6H), 7.39–7.32 (m, 6H), 7.31–7.25 (m, 6H), 7.25–7.19 (m, 5H), 6.82–6.78 (m, 2H), 5.77 (t, J=9.5 Hz, 1H), 5.50 (m, 1H), 4.62 (d, J=11.0 Hz, 1H) 4.57 (d, J=11.0 Hz, 1H), 4.44 (dd, J=9.0, 2.5 Hz, 1H), 3.84 (q, J=5.5 Hz, 1H), 3.75 (s, 3H), 3.71–3.60 (m, 2H), 3.41 (dd, J=8.5,

3.0 Hz, 1H), 3.15–3.07 (m, 2H), 2.51 (br s, 2H), 2.40 (ddd, *J*=14.0, 8.5, 5.0 Hz, 1H), 2.24 (ddd, *J*=14.0, 6.0, 6.0 Hz, 1H), 2.15 (m, 1H), 1.57–1.38 (m, 3H), 1.01 (s, 9H), 0.73 (d, *J*=7.0 Hz, 3H), 0.64 (d, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 143.8 (×3), 135.6 (×4), 134.1, 134.0, 131.1, 131.0, 129.47, 129.46, 129.3 (×2), 128.7, 128.6 (×6), 127.9 (×6), 127.6 (×4), 127.1 (×3), 113.7 (×2), 86.8, 84.3, 74.6, 70.0, 68.4, 66.8, 62.5, 55.2, 38.7, 38.4, 31.6, 28.2, 26.8 (×3), 19.1, 13.9, 10.3; HRMS (ESI) calcd for $C_{56}H_{66}O_6SiNa$ [$(M+Na)^+$] 885.4521, found 885.4543.

*4.1.32. Primary alcohol **48**.* To a solution of trityl ether **47** (71.9 mg, 83.3 μmol) and 2,6-lutidine (49.0 μL, 421 μmol) in CH_2Cl_2 (1 mL) at 0 °C was added TBSOTf (46.0 μL, 201 μmol). The resultant solution was allowed to warm to room temperature and stirred for 1 h before it was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with $CHCl_3$, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/80 to 1/40) gave a bis-TBS ether (82.9 mg, 91%) as a colorless oil: $[\alpha]_D^{26}$ +21.6 (*c* 1.0, $CHCl_3$); IR (film) 2955, 2929, 2885, 2856, 1514, 1249, 1111, 1087, 834, 775, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67–7.62 (m, 4H), 7.47–7.41 (m, 6H), 7.40–7.31 (m, 6H), 7.30–7.24 (m, 6H), 7.24–7.18 (m, 5H), 6.80–6.76 (m, 2H), 5.62 (dd, *J*=9.0, 9.0 Hz, 1H), 5.49 (ddd, *J*=11.5, 9.0, 6.0 Hz, 1H), 4.90 (d, *J*=10.5 Hz, 1H), 4.62 (br d, *J*=9.5 Hz, 1H), 4.41 (d, *J*=10.5 Hz, 1H), 3.79 (m, 1H), 3.75 (s, 3H), 3.70–3.57 (m, 2H), 3.28 (dd, *J*=9.5, 1.3 Hz, 1H), 3.07 (dd, *J*=8.5, 5.0 Hz, 1H), 2.98 (dd, *J*=8.5, 6.0 Hz, 1H), 2.60 (m, 1H), 2.16–2.06 (m, 2H), 1.52–1.38 (m, 3H), 1.01 (s, 9H), 0.89 (s, 9H), 0.83 (s, 9H), 0.74 (d, *J*=7.0 Hz, 3H), 0.64 (d, *J*=6.5 Hz, 3H), 0.07 (s, 3H), 0.03 (s, 3H), −0.01 (s, 3H), −0.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 144.1 (×3), 135.5 (×4), 134.14, 134.11, 131.7, 130.8, 129.42, 129.40, 129.3 (×2), 128.7 (×6), 127.7 (×6), 127.55 (×2), 127.54 (×2), 127.0, 126.9 (×3), 113.5 (×2), 86.5, 86.4, 74.3, 71.6, 70.9, 67.8, 62.9, 55.2, 38.6, 38.3, 34.1, 28.1, 26.9 (×3), 25.9 (×3), 25.8 (×3), 19.1, 18.1, 18.0, 13.4, 10.9, −4.1, −4.4, −4.6, −4.8; HRMS (ESI) calcd for $C_{68}H_{94}O_6Si_3Na$ [$(M+Na)^+$] 1113.6250, found 1113.6277.

To a solution of the above bis-TBS ether (80.7 mg, 73.9 μmol) in CH_2Cl_2/MeOH (3/1, v/v, 400 μL) at 0 °C was added $ZnBr_2$ (167 mg, 742 μmol). The resultant solution was stirred at 0 °C for 1 h. An additional portion of $ZnBr_2$ (83.0 mg, 369 μmol) was added, and the mixture was stirred at 0 °C for 3 h before it was quenched with saturated aqueous $NaHCO_3$ solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/40 to 1/20) gave primary alcohol **48** (59.2 mg, 94%) as a colorless oil: $[\alpha]_D^{26}$ +5.1 (*c* 1.0, $CHCl_3$); IR (film) 3472, 2955, 2929, 2885, 2857, 1514, 1250, 1110, 1091, 1038, 836, 776, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67–7.62 (m, 4H), 7.42–7.38 (m, 2H), 7.38–7.33 (m, 4H), 7.25–7.22 (m, 2H), 6.82–6.78 (m, 2H), 5.65 (dd, *J*=11.0, 9.5 Hz, 1H), 5.49 (ddd, *J*=11.0, 7.0, 7.0 Hz, 1H), 4.82 (d, *J*=11.5 Hz, 1H), 4.58 (dd, *J*=9.5, 3.3 Hz, 1H), 4.43 (d, *J*=11.5 Hz, 1H), 3.76 (s, 3H), 3.74 (m, 1H), 3.70–3.59 (m, 2H), 3.44 (ddd, *J*=11.5, 6.0, 6.0 Hz, 1H), 3.36 (ddd, *J*=11.5, 6.0, 6.0 Hz, 1H), 3.27 (dd, *J*=8.5, 3.3 Hz, 1H), 2.34–2.23 (m, 2H), 2.10 (m, 1H), 2.04 (br dd, *J*=6.0, 6.0 Hz, 1H), 1.56–1.40 (m, 3H), 1.02 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.77 (d, *J*=7.0 Hz, 3H), 0.71 (d, *J*=6.5 Hz, 3H), 0.06 (s, 3H), 0.06 (s, 6H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 135.5 (×4), 134.12, 134.09, 132.1, 131.3, 129.42, 129.41, 129.35 (×2), 127.9, 127.55 (×2), 127.53 (×2), 113.5 (×2), 86.4, 74.4, 72.3, 70.4, 65.6, 62.9, 55.2, 38.7, 38.4, 32.7, 28.2, 26.9 (×3), 25.9 (×3), 25.8 (×3), 19.1, 18.04, 18.02, 13.8, 11.1, −4.1, −4.5, −4.6, −4.7; HRMS (ESI) calcd for $C_{49}H_{80}O_6Si_3Na$ [$(M+Na)^+$] 871.5155, found 871.5172.

*4.1.33. Thioester **42**.* To a solution of primary alcohol **48** (60.1 mg, 70.8 μmol) in DMSO (700 μL) at room temperature was added IBX (50.6 mg, 177 μmol). The resultant solution was stirred at room temperature for 3 h 20 min before THF (350 μL) was added. The mixture was stirred for further 1 h. The reaction was quenched with a 1/1 mixture of saturated aqueous $NaHCO_3$ solution and saturated aqueous $Na_2S_2O_3$ solution. The mixture was extracted with diethyl ether, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/40 to 1/20) gave an aldehyde (54.3 mg, 91%) as a colorless oil, which was immediately used in the next reaction without further purification.

To a solution of the above aldehyde (54.3 mg, 64.1 μmol), 2-methyl-2-butene (68.0 μL, 643 μmol), and NaH_2PO_4 (15.4 mg, 128 μmol) in *t*-BuOH/H_2O (5/1, v/v, 1.28 mL) at 0 °C was added $NaClO_2$ (17.4 mg, 193 μmol). The resultant mixture was stirred at 0 °C for 1 h before it was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude acid was azeotropically dried with benzene and immediately used in the next reaction without purification.

To a solution of the above crude acid, *i*-Pr_2NEt (16.7 μL, 96.1 μmol), and *p*-toluenethiol (9.6 mg, 77 μmol) in CH_2Cl_2 (1 mL) at 0 °C was added PyBOP® (40.0 mg, 76.9 μmol). The resultant solution was allowed to warm to room temperature and stirred for 10 h. The reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with EtOAc, and the combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/80 to 1/40) gave thioester **42** (48.0 mg, 77% for the two steps) as a colorless oil: $[\alpha]_D^{26}$ +59.5 (*c* 1.0, $CHCl_3$); IR (film) 2955, 2929, 2894, 2857, 1700, 1514, 1250, 1111, 835, 777, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67–7.62 (m, 4H), 7.42–7.36 (m, 2H), 7.36–7.31 (m, 4H), 7.26–7.20 (m, 4H), 7.20–7.16 (m, 2H), 6.81–6.76 (m, 2H), 5.73 (dd, *J*=11.0, 9.5 Hz, 1H), 5.61 (m, 1H), 4.88 (d, *J*=11.5 Hz, 1H), 4.57 (dd, *J*=9.0, 1.5 Hz, 1H), 4.40 (d, *J*=11.5 Hz, 1H), 4.26 (dd, *J*=7.5, 4.5 Hz, 1H), 3.75 (s, 3H), 3.69–3.59 (m, 2H), 3.25 (dd, *J*=9.0, 1.5 Hz, 1H), 2.57 (m, 1H), 2.45 (m, 1H), 2.33 (s, 3H), 2.11 (m, 1H), 1.52–1.37 (m, 3H), 1.01 (s, 9H), 0.98 (s, 9H), 0.88 (s, 9H), 0.71 (d, *J*=8.0 Hz, 3H), 0.67 (d, *J*=7.0 Hz, 3H), 0.18 (s, 3H), 0.11 (s, 3H), 0.04 (s. 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.0, 158.8, 139.4, 135.6 (×4), 134.6 (×2), 134.15, 134.11, 132.2, 131.6, 123.0 (×2), 129.43, 129.41, 129.3 (×2), 127.6 (×4), 124.6, 124.3, 113.5 (×2), 86.2, 78.2, 74.3, 70.7, 62.9, 55.2, 38.5, 38.3, 34.6, 28.1, 26.9 (×3), 25.9 (×3), 25.8 (×3), 21.3, 19.1, 18.2, 18.0, 13.5, 10.9, −4.2, −4.6, −4.80, −4.82; HRMS (ESI) calcd for $C_{56}H_{84}O_6SSi_3Na$ [$(M+Na)^+$] 991.5189, found 991.5217.

*4.1.34. Alcohol **49**.* To a solution of propargylic alcohol **45** (27.6 mg, 39.0 μmol) in CH_2Cl_2 (450 μL) were added triethylamine (25.3 μL, 351 μmol), acetic anhydride (12.8 μL, 135 μmol), and DMAP (1.2 mg, 9.8 μmol). The resultant solution was stirred at room temperature for 30 min before it was diluted with EtOAc. The mixture was washed with 1 M HCl solution, saturated aqueous $NaHCO_3$ solution, and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude acetate (26.6 mg) was used for the next reaction without purification.

To a solution of the above acetate (26.6 mg) in EtOH (700 μL) at room temperature was added pyridinium *p*-toluenesulfonate (2.7 mg, 11 μmol). The resultant solution was stirred at room temperature for 18 h before it was quenched with triethylamine. The mixture was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=1/1 to 2/1) to give diol (21.4 mg, 83% for the two steps) as a colorless oil: $[\alpha]_D^{28}$ +52.0 (*c* 1.0, $CHCl_3$); IR (film) 3420, 2955, 2931, 2860, 1739, 1612, 1514, 1467, 1247, 1089, 1034,

704 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.68–7.62 (m, 4H), 7.42–7.32 (m, 6H), 7.27–7.22 (m, 2H), 6.82–6.78 (m, 2H), 5.56 (dd, *J*=4.1, 2.0 Hz, 1H), 4.75 (d, *J*=11.0 Hz, 1H), 4.48 (d, *J*=11.0 Hz, 1H), 3.76 (s, 3H), 3.74 (m, 1H), 3.70–3.61 (m, 2H), 3.58 (dd, *J*=11.3, 3.8 Hz, 1H), 3.46 (dd, *J*=11.3, 6.2 Hz, 1H), 3.41 (dd, *J*=9.6, 2.0 Hz, 1H), 2.40–2.74 (m, 2H), 2.13 (m, 1H), 2.08 (s, 3H), 1.75 (dddd, *J*=13.7, 7.2, 6.9, 2.5 Hz, 1H), 1.52 (m, 1H), 1.44 (m, 1H), 1.01 (s, 9H), 0.76 (d, *J*=6.9 Hz, 3H), 0.71 (d, *J*=6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.0, 159.2, 135.5 (×4), 134.04, 134.01, 130.3, 129.6 (×2), 129.51, 129.48, 127.6 (×4), 113.7 (×2), 84.1, 81.8, 77.5, 73.8, 69.9, 67.9, 65.3, 62.6, 55.2, 39.1, 38.2, 28.2, 26.8 (×3), 24.1, 21.2, 19.1, 13.5, 10.2; HRMS (ESI) calcd for $C_{39}H_{52}O_7SiNa$ [$(M+Na)^+$] 683.3375, found 683.3360.

To a solution of the above diol (19.0 mg, 28.7 μmol) and 2,6-lutidine (16.7 μL, 143 μmol) in CH_2Cl_2 (500 μL) at 0 °C was added TBSOTf (16.5 μL, 71.8 μmol). The resultant solution was stirred at 0 °C for 45 min before it was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was washed with 1 M HCl solution, saturated aqueous $NaHCO_3$ solution, and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude bis-TBS ether (26.0 mg) was used for the next reaction without purification.

To a solution of the above bis-TBS ether (26.0 mg) in CH_2Cl_2 (1 mL) at −78 °C was added DIBALH (1.04 M solution in hexanes, 69.0 μL, 71.8 μmol). The resultant solution was stirred at −78 °C for 40 min before it was quenched with MeOH. Saturated aqueous potassium sodium tartrate solution was added, and the mixture was diluted with EtOAc and vigorously stirred at room temperature until the layers became clear. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography (silica gel, EtOAc/hexanes=1/15 to 10/1) gave alcohol **49** (22.7 mg, 93% for the two steps) as a colorless oil: ^1H NMR (600 MHz, $CDCl_3$) δ 7.67–7.63 (m, 4H), 7.42–7.32 (m, 6H), 7.27–7.21 (m, 2H), 6.82–6.78 (m, 2H), 4.67 (d, *J*=11.3 Hz, 1H), 4.55 (d, *J*=11.3 Hz, 1H), 4.45 (m, 1H), 3.77 (m, 1H), 3.76 (s, 3H), 3.74–3.63 (m, 2H), 3.54 (dd, *J*=10.0, 5.5 Hz, 1H), 3.52 (dd, *J*=10.0, 5.5 Hz, 1H), 3.37 (dd, *J*=9.3, 3.5 Hz, 1H), 2.45 (ddd, *J*=16.8, 5.9, 2.1 Hz, 1H), 2.33 (ddd, *J*=16.8, 5.5, 1.7 Hz, 1H), 2.18 (d, *J*=8.2 Hz, 1H), 2.15 (m, 1H), 1.84 (m, 1H), 1.58 (m, 1H), 1.46 (m, 1H), 1.03 (s, 9H), 0.87 (s, 9H), 0.86 (s, 9H), 0.734 (d, *J*=7.3 Hz, 3H), 0.728 (d, *J*=6.9 Hz, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H).

*4.1.35. Enone **41**.* To a suspension of thioester **42** (19.4 mg, 20.0 μmol), copper(I) diphenylphosphinate (11.2 mg, 39.9 μmol), and $Pd_2(dba)_3$ (1.80 mg, 1.97 μmol) in hexanes (100 μL, degassed) and THF (22 μL, degassed) at room temperature was added a portion (28 μL, 8.16 μmol) of a stock solution of triethylphosphite (48 μL) in THF (0.95 mL, degassed). After stirring for 25 min, a solution of vinylstannane **27** (10.2 mg, 22.0 μmol) in THF/hexanes (1/2, v/v, 600 μL+250 μL rinse, degassed) was added, and the resultant brown suspension was stirred at room temperature for 6 h. The mixture was diluted with hexane and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=1/40 to 1/20 to 1/10 to 1/5) to give enone **41** (17.0 mg, 74%) as a pale yellow oil, along with unreacted thioester **42** (4.3 mg, 22%) and homo-coupling product **38** (1.7 mg, ca. 14%, contaminated with some impurities. Data for **41**: $[\alpha]_D^{27}$ +8.7 (*c* 1.0, $CHCl_3$); IR (film) 3032, 2954, 2929, 2893, 2856, 1683, 1514, 1471, 1250, 1091, 1038, 836, 777, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.66–7.61 (m, 4H), 7.41–7.36 (m, 2H), 7.36–7.29 (m, 8H), 7.28–7.24 (m, 1H), 7.23–7.19 (m, 2H), 6.80–6.76 (m, 2H), 6.20 (s, 1H), 6.12 (s, 1H), 5.87 (m, 1H), 5.79 (br d, *J*=10.0 Hz, 1H), 5.67 (dd, *J*=11.5, 9.5 Hz, 1H), 5.49 (ddd, *J*=11.5, 7.5, 7.5 Hz, 1H), 4.86 (d, *J*=11.0 Hz, 1H), 4.81 (dd, *J*=6.7, 6.7 Hz, 1H), 4.60 (d, *J*=12.5 Hz, 1H), 4.58 (m, 1H), 4.57 (d, *J*=12.5 Hz, 1H), 4.53 (d, *J*=10.5 Hz, 1H), 4.39 (d, *J*=11.0 Hz, 1H), 4.13 (br s, 1H), 4.01 (dd, *J*=13.0, 6.5 Hz, 1H), 3.81 (m, 1H), 3.74 (s, 3H), 3.66–3.55 (m, 2H), 3.56 (dd, *J*=10.5, 6.0 Hz, 1H), 3.47 (dd, *J*=10.5, 4.5 Hz, 1H), 3.25 (dd, *J*=9.0, 1.5 Hz, 1H), 2.49 (m, 1H), 2.38 (m, 1H), 2.30 (m, 1H), 2.12–2.01 (m, 2H), 2.01–1.88 (m, 3H), 1.52–1.36 (m, 4H), 1.00 (s, 9H), 0.87 (s, 9H), 0.86 (s, 9H), 0.69 (d, *J*=7.0 Hz, 3H), 0.65 (d, *J*=7.0 Hz, 3H), 0.04 (s, 3H), 0.01 (s, 3H), −0.01 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 158.8, 147.5, 138.4, 135.5 (×4), 134.14, 134.11, 131.9, 131.6, 129.42, 129.41, 129.2 (×2), 128.3 (×2), 127.6 (×2), 127.55 (×2), 127.54 (×3), 127.4, 125.6, 125.3, 123.7, 113.5 (×2), 86.2, 81.4, 77.5, 76.8, 75.6, 74.3, 73.4, 73.04, 73.01, 70.8, 62.9, 55.2, 38.5, 38.4, 34.5, 32.6, 28.1, 27.9, 27.2, 26.9 (×3), 25.9 (×3), 25.8 (×3), 19.1, 18.2, 18.0, 13.4, 10.9, −4.1, −4.57, −4.58, −5.0; HRMS (ESI) calcd for $C_{68}H_{100}O_9Si_3Na$ [$(M+Na)^+$] 1167.6567, found 1167.6544.

*4.1.36. C15–C36 segment **2**.* To a solution of enone **41** (17.3 mg, 15.1 μmol) in EtOH (755 μL) was added $CeCl_3\cdot 7H_2O$ (8.4 mg, 23 μmol). The resultant solution was stirred at room temperature for 20 min. The solution was cooled to −40 °C and treated with $NaBH_4$ (0.68 mg, 18 μmol). The resultant mixture was stirred at −40 °C for 45 min before it was quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, EtOAc/hexanes=1/10 to 1/7) gave alcohol **2** (15.8 mg, 91%) as a colorless oil: $[\alpha]_D^{28}$ +10.4 (*c* 0.3, $CHCl_3$); IR (film) 3478, 3066, 3039, 2954, 2928, 2985, 2856, 1249, 1090, 836, 776, 702 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.66–7.61 (m, 4H), 7.40–7.35 (m, 2H), 7.35–7.29 (m, 8H), 7.28–7.24 (m, 1H), 7.23–7.20 (m, 2H), 6.80–6.76 (m, 2H), 5.85 (dddd, *J*=10.0, 5.5, 2.1, 2.0 Hz, 1H), 5.80 (m, 1H), 5.66 (dddd, *J*=11.3, 9.2, 1.7, 1.7 Hz, 1H), 5.42 (ddd, *J*=11.3, 8.6, 4.8 Hz, 1H), 5.20 (s, 1H), 5.08 (d, *J*=1.0 Hz, 1H), 4.87 (d, *J*=11.0 Hz, 1H), 4.60 (dd, *J*=8.9, 1.1 Hz, 1H), 4.59 (d, *J*=12.1 Hz, 1H), 4.56 (d, *J*=12.1 Hz, 1H), 4.43 (dd, *J*=6.9, 6.9 Hz, 1H), 4.40 (d, *J*=11.0 Hz, 1H), 4.07 (m, 1H), 3.93 (dd, *J*=13.4, 6.5 Hz, 1H), 3.89 (br s, 1H), 3.82–3.77 (m, 2H), 3.74 (s, 3H), 3.67–3.59 (m, 2H), 3.55 (dd, *J*=10.6, 6.2 Hz, 1H), 3.46 (dd, *J*=10.6, 4.4 Hz, 1H), 3.25 (dd, *J*=9.2, 2.0 Hz, 1H), 2.75 (m, 1H), 2.52 (m, 1H), 2.16–1.98 (m, 5H), 1.98–1.86 (m, 2H), 1.71 (dddd, *J*=11.7, 8.3, 7.9, 7.6 Hz, 1H), 1.52–1.38 (m, 3H), 1.00 (s, 9H), 0.87 (s, 9H), 0.86 (s, 9H), 0.73 (d, *J*=6.8 Hz, 3H), 0.66 (d, *J*=6.9 Hz, 3H), 0.06 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.8, 149.5, 138.4, 135.5 (×4), 134.17, 134.13, 132.6, 131.6, 129.4 (×2), 129.2 (×2), 128.3 (×2), 127.8, 127.57 (×2), 127.54 (×5), 125.8, 125.0, 113.6 (×2), 110.2, 86.6, 81.0, 79.6, 77.2, 74.1, 73.42, 73.37, 73.29, 73.07, 73.05, 70.9, 62.9, 55.2, 38.6, 38.3, 33.3, 31.5, 28.1, 27.9, 27.5, 26.9 (×3), 25.92 (×3), 25.87 (×3), 19.1, 18.2, 18.0, 13.4, 10.9, −4.3 (×2), −4.4, −4.7; HRMS (ESI) calcd for $C_{68}H_{102}O_9Si_3Na$ [$(M+Na)^+$] 1169.6724, found 1169.6726.

*4.1.37. Acetonide **50**.* To a solution of alcohol **2** (6.3 mg, 5.5 μmol) in THF (600 μL) at room temperature was added TBAF (1.0 M solution in THF, 27 μL, 27 μmol). The resultant solution was allowed to warm to 50 °C. After being stirred at 50 °C for 25 h, the solution was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=2/1 to 1/0) to give a tetraol (4.7 mg) contaminated with some impurities, which was used in the next reaction without further purification: ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.31 (m, 4H), 7.29–7.24 (m, 3H), 7.86–7.82 (m, 2H), 5.92–5.85 (m, 2H), 5.79 (br d, *J*=10.0 Hz, 1H), 5.63 (ddd, *J*=10.5, 10.5, 6.0 Hz, 1H), 5.19 (s, 1H), 5.19 (s, 1H), 4.72 (d, *J*=11.0 Hz, 1H), 4.61–4.51 (m, 5H), 4.17 (br s, 1H), 4.06–3.99 (m, 2H), 3.85–3.77 (m, 2H), 3.77 (s, 3H), 3.66 (ddd, *J*=11.0, 6.5, 6.5 Hz, 1H), 3.59 (ddd, *J*=11.0, 6.5, 6.5 Hz, 1H), 3.54 (dd, *J*=10.0, 6.0 Hz, 1H), 3.49–3.44 (m, 2H), 2.56 (ddd, *J*=14.0, 10.0, 4.0 Hz, 1H), 2.23 (ddd, *J*=14.0, 12.5, 6.0 Hz, 1H), 2.16–2.08 (m, 2H), 2.06–1.99 (m, 2H), 1.99–1.83 (m, 3H), 1.59 (m, 1H), 1.57 (br s, 4H), 1.47–1.42 (m, 2H), 0.79 (d, *J*=6.5 Hz, 3H), 0.73 (d, *J*=7.5 Hz, 3H).

To a solution of the above tetraol (4.7 mg) in CH_2Cl_2 (1.0 mL) at 0 °C were added 2,2-dimethoxypropane (6.7 μL, 55 μmol) and CSA (0.13 mg, 0.56 μmol). The resultant solution was stirred at room temperature for 1.5 h before it was quenched with saturated aqueous $NaHCO_3$ solution. The mixture was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude acetonide was contaminated with the corresponding 2-methoxy-2-propyl ether, and thus used in the next reaction without purification.

To a solution of the above mixture in EtOH (500 μL) at 0 °C was added a portion (40 μL, 0.56 μmol) of stock solution of pyridinium *p*-toluenesulfonate (3.5 mg) in EtOH (1 mL). The resultant solution was stirred at room temperature for 25 min before it was quenched with triethylamine (excess). The mixture was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, EtOAc/hexanes=3/2) to give acetonide **50** (3.6 mg, 91% for the three steps) as a colorless oil: $[\alpha]_D^{28}$ +4.9 (*c* 0.1, $CHCl_3$); IR (film) 3446, 2955, 2922, 2855, 1514, 1456, 1377, 1248, 1059 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.33–7.31 (m, 4H), 7.28–7.24 (m, 3H), 6.86–6.82 (m, 2H), 5.91 (dd, *J*=11.0, 8.6 Hz, 1H), 5.86 (dddd, *J*=10.0, 5.5, 2.4, 2.0 Hz, 1H), 5.76 (m, 1H), 5.68 (ddd, *J*=11.0, 8.2, 7.9 Hz, 1H), 5.31 (s, 1H), 5.25 (s, 1H), 4.73 (d, *J*=11.0 Hz, 1H), 4.59 (d, *J*=12.4 Hz, 1H), 4.55 (d, *J*=12.4 Hz, 1H), 4.54 (d, *J*=11.0 Hz, 1H), 4.52–4.47 (m, 2H), 4.14 (m, 1H), 4.10 (d, *J*=8.6 Hz, 1H), 4.00 (dd, *J*=12.7, 6.5 Hz, 1H), 3.93 (ddd, *J*=8.6, 6.2, 3.8 Hz, 1H), 3.80 (m, 1H), 3.77 (s, 3H), 3.65 (ddd, *J*=10.7, 6.9, 4.3 Hz, 1H), 3.58 (ddd, *J*=10.7, 6.5, 6.2 Hz, 1H), 3.55 (dd, *J*=10.3, 6.2 Hz, 1H), 3.46 (dd, *J*=10.3, 4.1 Hz, 1H), 3.45 (m, 1H), 2.73 (br s, 2H), 2.62 (dddd, *J*=14.8, 8.6, 3.4, 1.0 Hz, 1H), 2.35 (ddd, *J*=14.8, 7.6, 6.2 Hz, 1H), 2.18–2.08 (m, 2H), 2.08–1.90 (m, 4H), 1.78 (dddd, *J*=12.0, 8.3, 8.2, 7.6 Hz, 1H), 1.59 (m, 1H), 1.47–1.43 (m, 2H), 1.40 (s, 3H), 1.37 (s, 3H), 0.79 (d, *J*=6.9 Hz, 3H), 0.74 (d, *J*=7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.1, 146.5, 138.4, 131.9, 131.2, 129.4 (×2), 128.45, 128.36 (×2), 127.60 (×2), 127.56, 127.4, 125.3, 113.7 (×2), 112.2, 108.4, 84.5, 81.2, 80.3, 80.2, 79.6, 76.9, 74.7, 73.4, 73.05, 72.99, 68.4, 61.1, 55.3, 38.3, 37.6, 32.0, 29.4, 27.8 (×2), 27.14, 27.09, 26.9, 14.6, 10.6; HRMS (ESI) calcd for $C_{43}H_{60}O_9Na$ [$(M+Na)^+$] 743.4130, found 743.4149.

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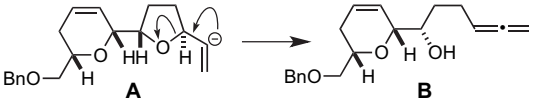

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