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Asymmetric synthetic study of macrolactin analogues

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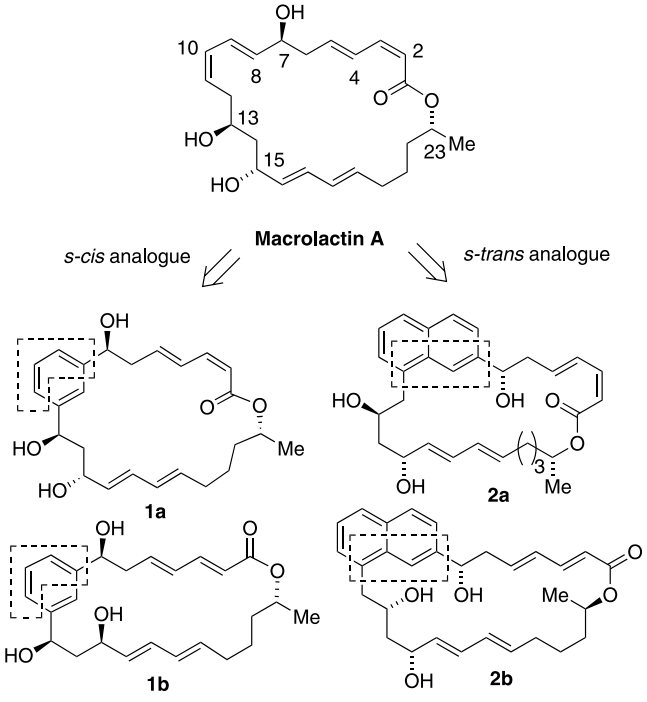
Abstract—We designed two aromatic analogues **1a** and **1b** of macrolactin A with expectation of enhancing biological activity and metabolical stability. As a result of retrosynthetic analysis of these compounds **1a–b**, two synthetic strategies have been examined. The first strategy includes the enantioselective addition of nonadienyl anion, derived from **3**, to aldehyde **4** as a key step. The second one includes epimerization of ynone **7** to (*E*,*E*)-conjugated dienone **31** and subsequent diastereoselective hydride-reduction of **31**. Although the former route furnished no desired target, the latter one was revealed to work well for the synthesis of **1**. Unfortunately, the aimed (2*Z*,4*E*)-analogue **1a** could not be synthesized due to an epimerization of the (2*Z*)-olefin into the (2*E*)-olefin. However, these methods could be applied to the total asymmetric synthesis of the (2*E*,4*E*)-analogue **1b**. Overall, control of all of the four stereocenters was achieved by means of asymmetric and diastereoselective reactions without using any chiral natural sources.

1. Introduction

Macrolactins A–M, which were isolated in 1989[1] and 2001[2] are a family of 24-membered polyene macrolides produced by a deep sea marine bacterium. Though structurally quite diverse, these macrolactins are distinguished by biological activities against various viruses and cancer cell lines. Among them, macrolactin A exhibits a broad spectrum of activity with significant antiviral and cancer cell cytotoxic properties including inhibition of B16–F10 murine melanoma cell replication.[1,2] In addition, this compound features three sets of conjugated dienes and four stereogenic centers in the molecule. Because of its unreliable supply from cell culture as well as its structural characteristics and broad therapeutic potential, macrolactin A has been an attractive target for asymmetric synthesis. Thus far, three total synthesis[3] and novel synthetic studies[4] have been developed, but there are still problems to be solved for therapeutic applications. With an aim of increasing the metabolical stability and identifying requisite substructure of macrolactin A to exhibit biological activity, we planed to replace the (2*Z*,4*E*)- and (8*E*,10*Z*)-dienic moieties by the (2*E*,4*E*)-dienoate and more stable aromatic ring, respectively (Scheme 1). From the point of view that the (8*E*,10*Z*)-dienic moiety should adopt a *s-cis* or *s-trans* form as a major configuration, we designed 1,3-disubstituted benzenes **1a–b** and 1,7-disubstituted naphthalenes **2a–b**,



Scheme 1. Macrolactin A analogues.

Keywords: Macrolactin A; Antibiotics; Antivirus; Asymmetric synthesis; Ynone; Isomerization; (*E*,*E*)-Conjugated dienone.
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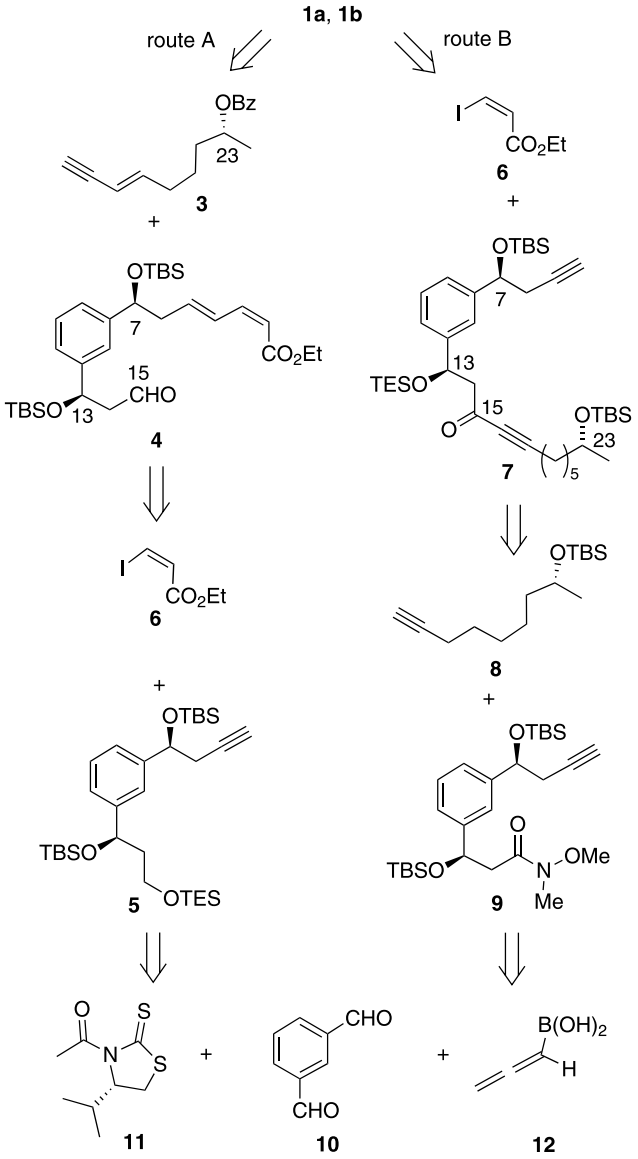
respectively. We first targeted the benzene analogues **1a** and **1b**. While, in both analogues **1a** and **1b**, a rigid phenyl group was introduced instead of the (8*E*,10*Z*)-dienic moiety, only **1b** was replaced the (2*Z*,4*E*)-dienic moiety to the (2*E*,4*E*)-dienic moiety.[5] We have already reported the synthetic studies on macrolactin A and its analogues.[6] Then we describe here the details of an asymmetric total synthesis of a macrolactin analogue **1b** by means of enantioselective and diastereoselective reactions without using any chiral natural sources.

2. Results and discussion

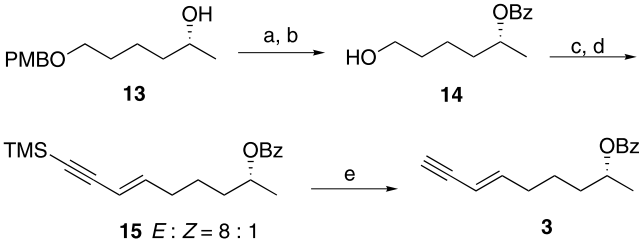
Retrosynthetic analysis. Our retrosynthetic analysis of the macrolactin analogues **1a** and **1b** was described in Scheme 2. This strategy relies on several asymmetric reactions to construct three chiral carbon centers (C7, C13, and C23). In addition, the key step of the strategy is a introduction of the (16*E*,18*E*)-dienyl segment with concurrent formation of the C15 stereogenic center. To investigate the key reaction, we examined two synthetic routes; (1) the asymmetric addition of alkenylzirconocene derived from **3** to aldehyde **4** and (2) the addition of alkynyl anion of **8** to Winreb amide **9** and subsequent epimerization and hydride-reduction of the resulting dienone **7**. Fortunately, these starting materials could be prepared from the same compounds **10**, **11**, and **12**.



Scheme 2. Retrosynthetic analysis of macrolactin analogue **1a**.

2.1. Investigation of the route A using asymmetric addition of alkenylzirconocene to aldehyde 4

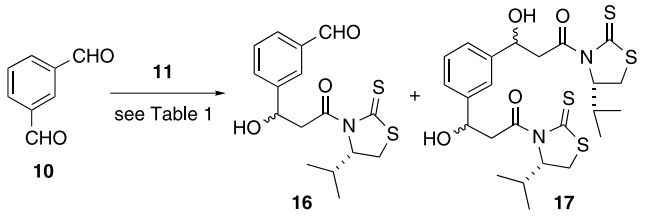
The asymmetric synthesis of **3** and **4**, which were required to examine the enantioselective addition, was conducted as follows. We have already reported the asymmetric synthesis of nonracemic alcohol **13**,[6a] which was obtained in 99% yield with 95%ee according to the Seebach's procedure[7] (Scheme 3). The benzoylation and deprotection of the PMB-group of **13** gave rise to alcohol **14** in 86% yield. The subjection of **14** to oxidation with IBX[8] (2-iodoxybenzoic acid) and subsequent Wittig olefination[9] afforded enyne **15**, which was converted to the desired product **3** by removal of the TMS group. The *E*-configuration of enynes **3** was determined by the coupling constant ($J=14.4$ Hz) between olefinic protons of **3**.



Scheme 3. (a) BzCl, Et_3N, DMAP, CH_2Cl_2, 0 °C, quant; (b) DDQ, CH_2Cl_2–H_2O, 86%; (c) IBX, DMSO–THF, 93%; (d) $Ph_3P^+CH_2CCTMSBr^-$, *n*-BuLi, THF, −25 °C, 91%; (e) TBAF, THF, 86%.

Having the requisite enyne **3** with high enantioselectivity, our attention was directed to the asymmetric synthesis of aldehyde **4**. The synthesis of **4** commenced from the diastereoselective aldol reaction of (*S*)-3-acetyl-4-isopropyl-1,3-thiazolidine-2-thione **11**[10] with dialdehyde **10**. The representative results were shown in Table 1. Although we examined several reaction conditions, the aldol adducts **16** were obtained with moderate diastereoselectivity (53–68% de). The two diastereomers **16** could be separated by column chromatography, but we did not determine the stereochemistry of these adducts. In addition, the side-products **17** were produced as an inseparable mixture of four diastereomers via double aldol reaction together with **16**. Then, we next investigated the aldol reaction of mono-aldehyde **18**, which was prepared in two steps from **10** (Scheme 4). The $TiCl_4$-mediated aldol reaction of **11** with **18** in the presence of *i*-Pr_2NEt proceeded with good diastereoselectivity (88% de) to provide **19** in 80% yield. The relative configuration of **19** was determined to be *R* based on the literature results[10] and the modified MTPA-method.[11] After protection of the hydroxy group of **19**, subjection of the resulting TBS-ether to methanolysis and oxidation gave rise to aldehyde **20**, which was converted to TBS ether **21** stereoselectively by the diastereoselective

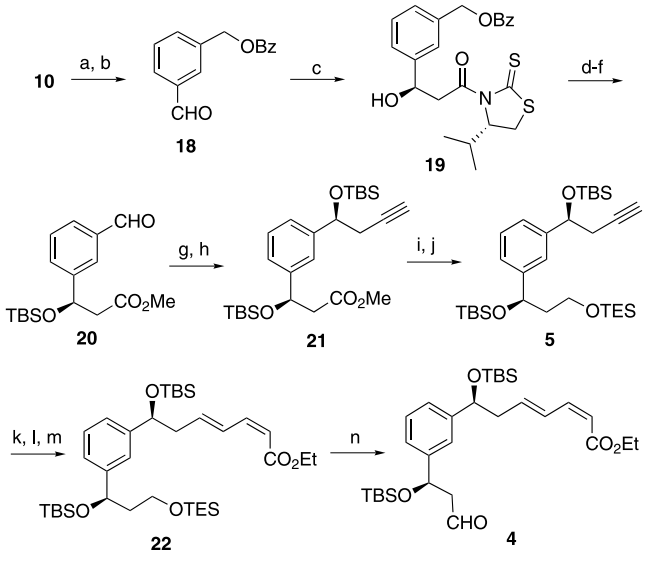
Table 1. Diastereoselective aldol reaction of **10** with **11**



Entry	Reaction conditions	Yield (%)		de of **16** (%)
		16	**17**	
1	$Yb(OTf)_3$, $(i\text{-}Pr)_2NEt$	0	0	—
2	$Sn(OTf)_2$, *N*-ethylpiperazine	23	35	53
3	$TiCl_4$, $(i\text{-}Pr)_2NEt$	39	19	68
4	$TiCl_4$, *N*-ethylpiperazine	42	22	64

propargylation with allenylboronic acid **12** according to the Yamamoto's protocol[12] and TBS protection of the resultant alcohol. The propargylation proceeded with good stereoselectivity (*R*:*S*=10:90) by using (+)-diisopropyl tartrate as a chiral source. After transformation of **21** into TES ether **5** by the reduction and protection, (*Z*,*E*)-dienoester **22** was derived from **5** in moderate yield by the standard three-step sequence: bromination, hydrostanylation,[13] and Stille cross-coupling.[14] The reaction of TES ether **22** with IBX directly gave rise to the desired product **4** in 66% yield.[15]

We examined the final coupling reaction of aldehyde **4** and enyne **3** using the Wipf's protocol[16] (Scheme 5). Although the hydrozirconation of **3** with $Cp_2Zr(H)Cl$ proceeded cleanly, no desired product **23** was obtained by the Me_2Zn-mediated nucleophilic addition of the corresponding alkenylzirconocene with **4**, even in the presence of chiral



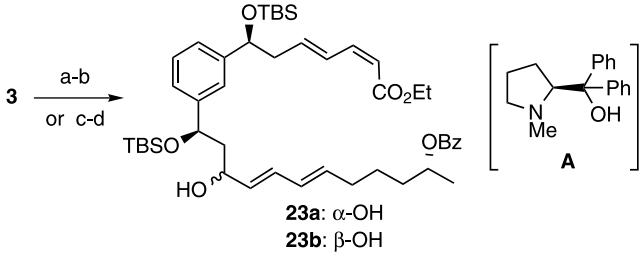
Scheme 4. (a) $NaBH_4$, MeOH, 0 °C, 64%; (b) BzCl, Et_3N, CH_2Cl_2, 0 °C, quant; (c) *N*-acetyl-(*S*)-4-IPTT **11**, $TiCl_4$, $i\text{-}Pr_2NEt$, CH_2Cl_2, −78 °C, 80%, 88%de; (d) TBSOTf, 2,6-lutidine, CH_2Cl_2, 84%; (e) K_2CO_3, MeOH; (f) IBX, DMSO–THF, 84% (2 steps); (g) $CH_2{=}C{=}CHB(OH)_2$ **12**, (+)-diisopropyl tartrate, MS 4A, toluene, −78 °C, 88%, 80%de; (h) TBSCl, imidazole, DMF, quant; (i) DIBAL, CH_2Cl_2, −78 °C then $NaBH_4$, MeOH, 0 °C 86%; (j) TESCI, imidazole, DMF, quant; (k) BrCN, *n*-BuLi, THF, −78 to −40 °C, 93%; (l) $PdCl_2(PPh_3)_2$, Bu_3SnH, benzene; (m) $Pd_2(dba)_2$, ethyl (*Z*)-3-iodopropenoate **6**, $i\text{-}Pr_2NEt$, DMF, 33% (2 steps); (n) IBX, DMSO–H_2O, 66%.

amino alcohol **A** as a promoter. Then, we next investigated the $CrCl_2/NiCl_2$-mediated cross-coupling[17] of **4** with the alkadienyl iodide, which was easily prepared from **3** via the corresponding alkenylzirconocene. Whereas the cross-coupling reaction successfully occurred, the desired product **23a** was obtained in 28% yield together with the diastereomer **23b** (**23a**:**23b**=1:1). Since we could not improve the stereoselectivity, we turned our attention to the second strategy.

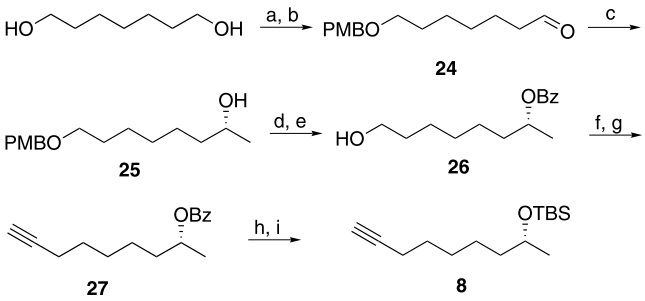
2.2. Investigation of the route B using the addition of alkyne 8 to Winreb amide 9

The strategy involves assembly of three fragments **6**, **8**, and **9** as shown in Scheme 2. Alkyne **8** bearing a stereogenic center (C23), plays a central role in our strategy, serving not only as an ideal nucleophile for joining with the amide **9**, but also as a latent functional group of the (16*E*,18*E*)-conjugated dienone moiety of **1**.

We anticipated that these compounds **8** and **9** could be prepared from **24** and **18** by the same reactions such as asymmetric methylation, asymmetric propargylation of **12**,[6] and diastereoselective aldol condensation of **11**.[7] We commenced from an efficient enantioselective preparation of alkyne **8** (Scheme 6). Synthesis of **8** began with PMB aldehyde **24** derived from 1,7-heptanediol in two steps. This aldehyde **24** was first subjected to the reported asymmetric methylation using Me_2Zn and $Ti(O\text{-}i\text{-}Pr)_4$ in the presence of (+)-TADDOL[7] (20 mol%) to give the desired secondary alcohol **25** in 90% yield with high enantioselectivity (95%ee). The enantioselectivity and absolute configuration were determined by a modified method of the Mosher



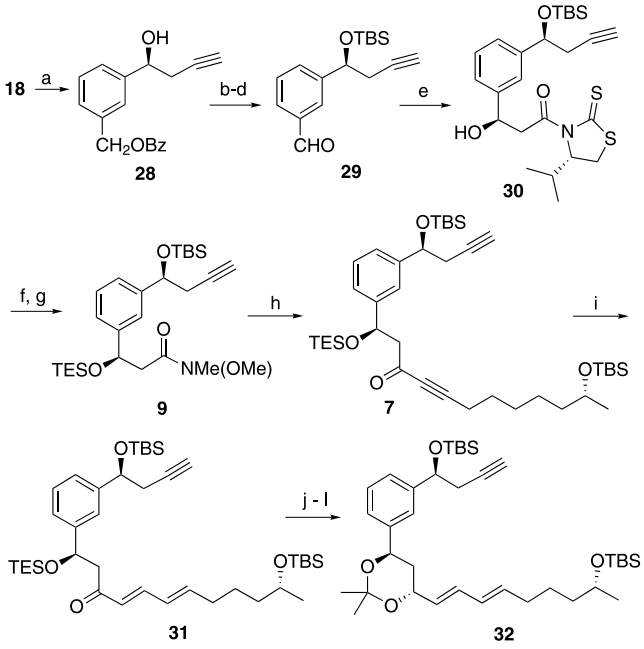
Scheme 5. (a) $Cp_2Zr(H)Cl$, CH_2Cl_2; (b) Me_2Zn, chiral ligand A, **4**, toluene, 25 °C–rt; (c) $Cp_2Zr(H)Cl$, CH_2Cl_2 then NIS, 0 °C, 77%; (d) $CrCl_2$, $NiCl_2$, **4**, DMSO, 56%.



Scheme 6. (a) PMBCI, NAH, THF, 0 °C; (b) IBX, DMSO, THF, 48% (2 steps); (c) Me_2Zn, (+)-TADDOL, Ti(O-*i*-Pr)$_4$, toluene, −25 °C, 90%, 95%ee; (d) BzCl, Et_3N, DMAP, CH_2Cl_2, 0 °C, quant; (e) DDQ, CH_2Cl_2, H_2O, 80%; (f) IBX, DMSO, THF, 95%; (g) $(MeO)_2P(O)CHN_2$, *t*-BuOK, THF, −78 °C→rt, 85%; (h) 3 N KOH/MeOH (1:1), 87%; (i) TBSCl, imidazole, DMF, quant.

protocol.[11] The resulting alcohol **25** was protected as a benzoate before removal of the terminal PMB ether to furnish primary alcohol **26**. Oxidation of **26** to an aldehyde, followed by exposure to the Seyferth–Gilbert reagent,[18] produced alkyne **27** which finally replaced the protecting group from benzoate to *tert*-butyldimethysilyl (TBS) ether to give the desired product **8**.

Having established the synthesis of the C16–C24 fragment **8**, we next sought the construction of **9** from aldehyde **18**. Propargylation of **18** with allenylboronic acid **12** under the same conditions[12] as that of **20** gave chiral alcohol **28** as the single product with moderate enantioselectivity (85% yield, 80%ee) (Scheme 7). Fortunately, the optically pure alcohol **28** (>95%ee) was easily obtained by recrystallization of **28**



Scheme 7. (a) CH_2=C=CHB(OH)$_2$ **12**, (+)-diisopropyl tartrate, MS 4A, toluene, −78 °C, 85%, 80%ee; (b) TBSCl, imidazole, DMF, quant; (c) K_2CO_3, MeOH, 95%; (d) IBX, DMSO, THF, 90%; (e) **11**, $TiCl_4$, *i*-Pr_2NEt, CH_2Cl_2, −78 °C, 80%, 92%de; (f) MeONHMe·HCl, Et_3N, CH_2Cl_2 91%; (g) TESCI, pyridine, quant; (h) EtMgBr, **8**, THF, 70%; (i) dppb, toluene, THF; (j) AcOH/THF/H_2O (8:8:1), 40% (2 steps); (k) $Me_4NBH(OAc)_3$, AcOH, MeCN, 89%; (l) 2,2-dimethoxypropane, PPTS, CH_2Cl_2, 83%.

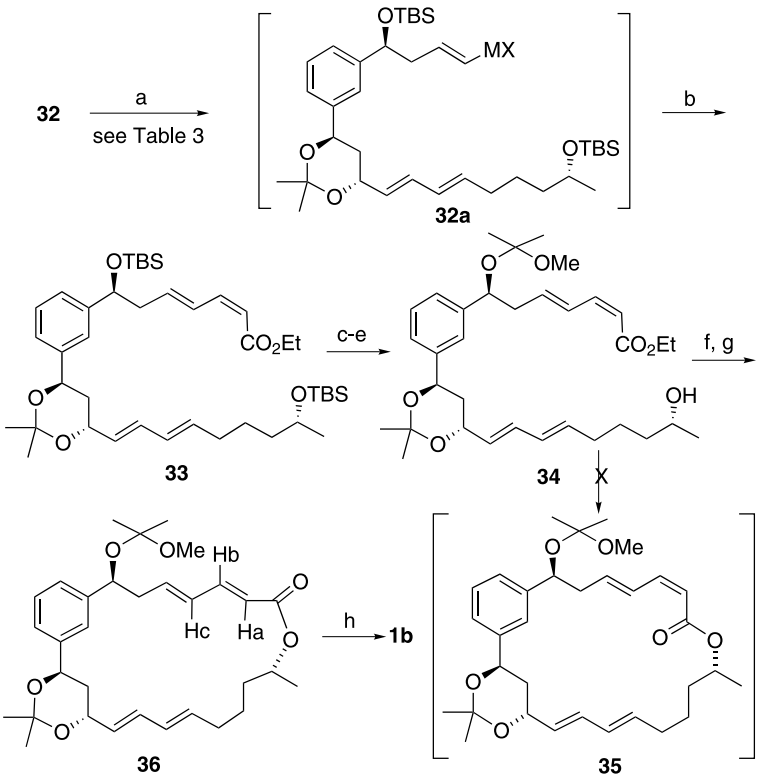
(80%ee) from a mixture of AcOEt and hexane. The enantioselectivity and absolute configuration were determined by a modified method of the Mosher protocol.[11] After protection of the alcohol **28**, hydrolysis of the benzoate afforded the primary alcohol (K_2CO_3, MeOH), which was oxidized with IBX[8] to provide the desired aldehyde **29**. Condensation of **29** with **11** in the presence of $TiCl_4$ (1.1 equiv) and *i*-Pr_2NEt (1.1 equiv) afforded aldol product **30**[10] along with a small amount of its diastereomer (80% yield, 92% de). These products were separated by column chromatography, and major product **30** was treated with *N*-methoxymethylamine, followed by TESCl to yield Weinreb amide **9** in good yield. With the two chiral building blocks now accessible, we investigated the key steps of this strategy, that is, their coupling reaction and stereoselective construction of the (*E*,*E*)-conjugated dienone unit. The coupling reaction of **8** and **9** proceeded smoothly using ethylmagnesium bromide as a base[19] to afforded the desired ynone **7** in good yield. Although the triphenylphosphine-catalyzed isomerization of an ynone to a conjugated dienone has been reported,[20] the desired product could not be obtained in reasonable yield under the standard conditions (Table 2, entry 1). After many experiments as shown in Table 2, use of bis(diphenylphosphino)butane (dppb) in a mixture of toluene and THF (1:1) at room temperature led to the best result to give **31** in 49% yield (entry 5).

Table 2. Phosphine-catalyzed epimerization of ynone **7** to dienone **31**

Entry	Reaction conditions	Yield (%)
1	PPh_3, toluene, 110 °C	31
2	*n*-Bu_3P, toluene, rt	20
3	*n*-Bu_3P, toluene/THF, rt	28
4	dppb, toluene, rt	30
5	dppb, toluene/THF, rt	49

After removal of the TES protecting group, subsequent construction of the fourth stereogenic center was carried out by hydroxyl-directed reduction.[21] Reduction of the resulting alcohol derived from **31** with $Me_4NBH(OAc)_3$ provided the corresponding 1,3-*anti*-diol in 89% yield and 93:7 diastereoselectivity. This 1,3-*anti*-diol was protected as acetonide under the standard conditions to afford **32** as a single isomer. The relative configuration of **32** was determined by the inspection of the ^{13}C chemical shifts of the acetonide methyl groups of **32**,[1b] that is, both signals of two methyl groups appeared at 25 ppm (δ: 25.1 and 25.5). This phenomena strongly indicates that acetonide **32** possesses the 1,3-*anti* configuration.

We finally examined the cross-coupling reaction of acetonide **32** and iodide **6** (Scheme 8 and Table 3). At first, the Pd-mediated cross-coupling was examined in the same manner[13,14] as that of **5**, but the desired product **33** was obtained only in a miserable yield (entry 1). Therefore, we undertook the exploration of other cross-coupling reactions. Whereas the desired product **33** was obtained under neither Negishi[22] nor Denmark[23] reaction conditions, the Cu-catalyzed reaction of **32a** (MX=Bu_3Sn) with **6** proceeded smoothly to give **33** in 58% yield from **32** (entries 2–4).[24] Although the reaction of **33** under acidic conditions gave a mixture of mono-TBS adducts, the C7 TBS group of **33**



Scheme 8. (a) Conditions A; (b) conditions B; (c) TBAF, THF, 0 °C, 92%; (d) CH_2=CMe(OMe), PPTS, CH_2Cl_2, −40 °C, 82%; (e) TBAF, AcOH (1:1), THF, 89%; (f) 3 N KOH, THF, EtOH, 60 °C; (g) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, then DMAP, toluene, 40% (3 steps); (h) PPTS; MeOH, 61%.

Table 3. Transition metal-catalyzed cross-coupling reaction of **32** and **6a**,**b**

Entry	Conditions A	Conditions B	Yield (%)
1	BrCN, BuLi; Bu_3SnH, $PdCl_2(PPh)_3$	**6**, $Pd(dba)_2$	32
2	$Cp_2Zr(H)Cl$; $ZnCl_2$	**6**, $PdCl_2(PPh_3)_2$, DIBAL	0
3	$(HMe_2Si)_2O$, *t*-Bu_3P-Pt(DVDS)	**6**, TBAF, $Pd(dba)_2$	0
4	BrCN, BuLi; Bu_3SnH, $PdCl_2(PPh)_3$	**6**, CuTC	58

could be removed regioselectively with TBAF, which was followed by protection/deprotection manipulation to furnish the desired alcohol **34** as the single isomer. After hydrolysis of **34**, lactonization of the resulting (2*Z*,4*E*)-carboxylic acid (J_{Ha-Hb}=11.3 Hz) by a modified Yamaguchi's method[25] did not provide the desired (2*Z*,4*E*)-lactone **35** at all, and gave unexpected (2*E*,4*E*)-lactone **36** as the single isomer (J_{Ha-Hb}=15.3 Hz).[26] From the fact that McClure et al.[3c] succeeded in a total synthesis of macrolactin A by the same procedure, the replacement of the (8*E*,10*Z*)-dienic moiety to the aromatic ring seems to prohibit the macrocyclization into the (2*Z*,4*E*)-lactone. Finally, global deprotection of the methoxyisopropylidene acetal and acetonide of **36** afforded the macrolactin A analogue **1b** in 61% yield.

3. Conclusion

The synthesis of **1b** was thus completed in 23 steps in the longest linear sequence, while another aimed compound **1a** could not be synthesized. This strategy features the following reactions: (1) three asymmetric reactions to generate the chiral centers, (2) isomerization of ynone to (*E*,*E*)-conjugated dienone, (3) the Cu-catalyzed cross-coupling reaction to construct the (*Z*,*E*)-conjugated dienoate. The biological activities of the synthetic intermediates and **1b**, prepared in this study, are now investigated in order to establish structure–activity relationship of macrolactin A. These results will be reported in the future.

4. Experimental

4.1. General information

Melting points are uncorrected. IR spectra were obtained using a JASCO FTIR-410 spectrometer. ^1H NMR (500 MHz) and ^{13}C NMR (125.7 MHz) spectra were obtained using a JEOL JNM-LA-500 spectrometer using TMS as an internal standard. Optical rotations were measured with a JASCO DIP-360 polarimeter. Nominal (MS) and high resolution mass spectra (HRMS) were measured with a JEOL JMS-01SG-2 or JMS-HX/HX 110A mass spectrometer. Column chromatography was carried out using Merck Kieselgel 60. Dry solvents purchased from Kanto Chemicals were used in all reactions.

4.1.1. (2*R*)-6-Hydroxyhexan-2-yl Benzoate (14). To a solution of (2*R*)-6-(4-methoxybenzyloxy)-2-hexanol **13**[6a] (2.80 g, 11.7 mmol), triethylamine (3.28 mL, 23.5 mmol), and DMAP (72.0 mg, 0.580 mmol) in CH_2Cl_2 (40 mL) was added benzoyl chloride (1.78 mL, 15.3 mmol) at 0 °C. The whole mixture was stirred at ambient temperature for 1 h, before quenching with a saturated sodium bicarbonate solution. The organic layer was extracted with ether three times. The combined extracts were washed with water and brine, dried over magnesium sulfate, and then concentrated under reduced pressure. The crude mixture was purified on silica gel (elution: 5:1 hexane/ethyl acetate) to give the benzoate (3.52 g, 85%) as a colorless oil. To a mixture of the benzoate (3.52 g, 10.5 mmol), CH_2Cl_2 (36 mL), and H_2O (2 mL) was added DDQ (3.04 g, 13.4 mmol) at 0 °C and the resulting mixture was stirred at room temperature for 2 h, before quenching with a saturated sodium bicarbonate solution. The mixture was diluted with ether and then filtered through a pad of Celite. The combined filtrates were condensed and purified by column chromatography on silica gel (elution: 2:1 hexane/ethyl acetate) to furnish **14** (1.90 g, 81%) as a colorless oil. $[\alpha]_D^{26}=28.1$ ($c=1.25$, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 8.04 (d, 2H, $J=7.6$ Hz), 7.54 (dd, 1H, $J=7.6$, 7.6 Hz), 7.43 (dd, 2H, $J=7.6$, 7.6 Hz), 5.17 (m, 1H), 3.63 (m, 2H), 1.77 (m, 1H), 1.63 (m, 4H), 1.47 (m, 2H), 1.34 (d, 3H, $J=6.4$ Hz); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 166.3, 132.7, 130.7, 129.5, 128.3, 71.5, 62.5, 35.7, 32.4, 21.6, 19.9; IR ($CHCl_3$): 3515, 3020, 1708, 1280 cm^{-1}; MS (EI) *m/z* (relative intensity) 222 (M^+, 82), 91 (100); HRMS (EI^+) calcd for $C_{13}H_{18}O_3$ (M^+) 222.1256, found 222.1252.

4.1.2. (2*R*,6*E*)-9-(Trimethylsilyl)non-6-en-8-yn-2-yl benzoate (15). To a solution of **14** (1.00 g, 4.50 mmol) in a 2:1 mixture of DMSO and THF (45 mL) was added IBX (1.89 g, 6.75 mmol), and the mixture was stirred at room temperature for 30 min. After being quenched with a saturated sodium bicarbonate solution, the aqueous layer was extracted with diethyl ether and the combined organic extracts were washed with brine, dried, and then concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to give the aldehyde (893 mg, 90%) as a colorless oil. A magnetically stirred slurry of (3-(trimethylsilyl)prop-2-ynyl)triphenylphosphinium bromide (2.07 g, 4.55 mmol) in dry THF (10 mL) was cooled to −78 °C under an argon atmosphere. A 1.58 M solution of *n*-butyllithium (3.10 mL, 4.55 mmol) in *n*-hexane was added dropwise over a 1 min period, and this mixture was stirred at −78 °C for 5 min. During this time, the color of the reaction mixture changed from pale yellow to brown. Subsequently, a solution of the prepared aldehyde (836 mg, 3.80 mmol) in THF (10 mL) was added to the mixture over a 1 min period. The resulting mixture was stirred at −78 °C for 12 h and then allowed to warm to ambient temperature. Stirring was continued for an additional 2 h, and then the reaction mixture was quenched with water. Extraction of the mixture with dichloromethane, washing of the combined extracts with brine, drying, and removal of solvents afforded the crude product, which was purified by SiO_2 column chromatography (elution: 15:1 hexane/ethyl acetate) to furnish **15** (532 mg, 44%). $[\alpha]_D^{23}=22.1$ ($c=1.04$, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.85 (d, 2H, $J=7.9$ Hz), 7.36 (dd, 1H, $J=7.9$, 7.9 Hz), 7.25 (dd, 2H, $J=7.9$, 7.9 Hz), 6.00 (dt, 1H, $J=15.9$, 7.0 Hz), 5.34 (d, 1H, $J=15.9$ Hz), 4.98 (m, 1H), 1.96 (m, 2H), 1.58–1.29 (m, 4H), 1.15 (d, 3H, $J=6.1$ Hz), 0.00 (s, 9H); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 166.1, 145.3, 132.8, 130.8, 129.5, 128.3, 110.2, 103.9, 92.9, 71.3, 35.5, 32.8, 24.5, 20.1, 0.0; IR ($CHCl_3$): 2957, 2139, 1710 cm^{-1}; MS (CI) *m/z* (relative intensity) 314 (M^+, 6), 242 (56), 91 (100); HRMS (CI^+) calcd for $C_{19}H_{26}O_2Si$ (M^+) 314.1702, found 314.1706.

4.1.3. (2*R*,6*E*)-Nona-6-en-8-yn-2-yl benzoate (3). To a solution of **15** (504 mg, 1.60 mmol) in THF (12 mL) was added a 1.0 M solution of tetra-*n*-butylammonium fluoride (3.20 mL, 3.20 mmol) in THF at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, before being diluted with diethyl ether. The reaction mixture was quenched with a saturated ammonium chloride solution and then the whole was poured into a saturated sodium bicarbonate solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with brine, dried, concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 10:1 hexane/ethyl acetate) to give **3** as a colorless oil (321 mg, 64%) $[\alpha]_D^{24}=24.3$ ($c=1.47$, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.90 (d, 1H, $J=7.6$ Hz), 7.41 (dd, 1H, $J=7.6$, 7.6 Hz), 7.30 (dd, 2H, $J=7.9$, 7.9 Hz), 6.09 (dt, 1H, $J=15.3$, 7.0 Hz), 5.34 (d, 1H, $J=15.3$ Hz), 5.03 (m, 1H), 2.66 (s, 1H), 2.01 (m, 2H), 1.64–1.30 (m, 4H), 1.20 (d, 3H, $J=6.4$ Hz); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 166.0, 145.9, 132.7, 130.7, 129.4, 128.2, 109.0, 82.3, 75.9, 71.2, 35.3, 32.6, 24.3, 20.0; IR ($CHCl_3$): 3021, 1709, 1279 cm^{-1}; MS (CI) *m/z* (relative intensity) 242 (M^+, 36), 91 (100); HRMS (CI^+) calcd for $C_{16}H_{18}O_2$ (M^+) 242.1307, found 242.1309.

4.1.4. 3-[1-Hydroxy-3-((4*S*)-4-isopropyl-2-thioxothiazolidin-3-yl)-3-oxopropyl]benzaldehyde (16). (Table 1, entry 2): To a fleshly dried tin(II) triflate (451 mg, 1.08 mmol) were successively added a solution of **11** (200 mg, 0.983 mmol) in CH_2Cl_2 (2.5 mL) and *N*-ethylpiperazine (0.148 mL, 1.08 mmol) at −40 °C under an argon atmosphere. After the mixture was stirred for 4 h, a solution of **10** (132 mg, 0.938 mmol) in CH_2Cl_2 (2.5 mL) was added to the mixture at −78 °C, and the whole was stirred for 2 h. The mixture was poured into a mixture of a phosphate buffer solution (pH 7.0, 200 mL) and ethyl acetate with vigorous stirring. The organic layer was washed with brine, dried, concentrated in vacuo. The crude products were purified by SiO_2 column chromatography (elution: 2:1 hexane/ethyl acetate) to give two diastereomers of **16** (60.0 mg, 18% and 18.0 mg, 5.4%) and **17** (190 mg, 35%). (Entry 3): To a solution of **11** (275 mg, 1.34 mmol) in CH_2Cl_2 (7 mL) were successively added titanium(IV) chloride (0.162 mL, 1.48 mmol) and diisopropylethylamine (0.256 mL, 1.48 mmol) at −40 °C under an argon atmosphere. After the mixture was stirred at this temperature for 2 h, a solution of **10** (181 mg, 1.34 mmol) in dry CH_2Cl_2 (7 mL) was added to the mixture at −78 °C, and the mixture was stirred at −78 °C for 30 min. The mixture was poured into a mixture of aqueous phosphate buffer solution (pH 7.0, 200 mL) and ethyl acetate with vigorous stirring. The organic layer was washed with brine, dried, concentrated in vacuo. The crude products were purified by SiO_2 column chromatography (elution: 2:1 hexane/ethyl acetate) to give two diastereomers of **16**

(139 mg, 33% and 26.0 mg, 6.2%) and **17** (136 mg, 19%). (Entry 4): To a solution of **11** (100 mg, 0.492 mmol) in CH_2Cl_2 (2.5 mL) were successively added titanium(IV) chloride (0.059 mL, 0.54 mmol) and *N*-ethylpiperazine (0.074 mL, 0.54 mmol) at −40 °C under an argon atmosphere. The same procedure described above gave two diastereomers of **16** (57.1 mg, 34% and 12.5 mg, 7.5%) and **17** (58.4 mg, 22%). Less polar isomer of **16**; $[\alpha]_D^{23}=+315$ ($c=1.09$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.6 (s, 1H), 7.93 (s, 1H), 7.82 (d, 1H, $J=7.6$ Hz), 7.69 (d, 1H, $J=7.6$ Hz), 7.54 (dd, 1H, $J=7.6$, 7.6 Hz), 5.35 (d, 1H, $J=8.9$ Hz), 5.16 (t, 1H, $J=7.1$ Hz), 3.90 (dd, 1H, $J=17.4$, 2.7 Hz), 3.55–3.49 (m, 2H), 3.38 (br, 1H), 3.05 (d, 1H, $J=11.6$ Hz), 2.38 (m, 1H), 1.07 (d, 3H, $J=6.7$ Hz), 1.00 (d, 3H, $J=6.7$ Hz); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 203.0, 192.2, 172.2, 143.6, 136.6, 131.8, 129.2, 128.9, 127.1, 71.4, 69.5, 46.9, 30.8, 30.7, 19.0, 17.8; IR ($CHCl_3$): 3575, 1698, 1604, 1361, 1311 cm^{-1}; MS (FAB) *m/z* (relative intensity) 338 (MH^+, 30), 162 (88), 154 (100), 136 (77); HRMS (FAB^+) calcd for $C_{16}H_{20}NO_3S_2$ (MH^+) 338.0885, found 338.0894. Polar isomer of **16**; $[\alpha]_D^{24}=+208$ ($c=1.93$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 10.0 (s, 1H), 7.92 (s, 1H), 7.82 (d, 1H, $J=7.6$ Hz), 7.69 (d, 1H, $J=7.6$ Hz), 7.54 (dd, 1H, $J=7.6$, 7.6 Hz), 5.22 (m, 2H), 3.84 (m, 2H), 3.57 (m, 2H), 3.07 (d, 1H, $J=11.6$ Hz), 2.38 (m, 1H), 1.08 (d, 3H, $J=6.7$ Hz), 1.00 (d, 3H, $J=6.7$ Hz); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 203.2, 192.3, 172.8, 143.7, 136.7, 132.0, 129.3, 129.1, 127.3, 71.3, 70.0, 46.7, 30.7, 30.6, 19.0, 17.8; IR ($CHCl_3$): 3549, 1699 cm^{-1}; MS (FAB) *m/z* (relative intensity) 338 (MH^+, 17), 162 (100); HRMS (FAB^+) calcd for $C_{16}H_{20}NO_3S_2$ (MH^+) 338.0885, found 338.0888.

4.1.5. 3-Formylbenzyl benzoate (18). To a solution of **10** (19.0 g, 0.142 mol) in ethanol (420 mL) was added sodium borohydride (1.33 g, 35.4 mmol) at 0 °C and the mixture was stirred at room temperature for 1 h. After the solvent was removed, ethyl acetate and water were added to the residue. The combined extracts were washed with brine, dried, and then concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 1:1 hexane/ethyl acetate) to furnish the desired aldehyde (12.1 g, 63%) as a colorless oil along with diol (5.97 g, 30%). To a solution of the aldehyde (1.00 g, 7.34 mmol) in CH_2Cl_2 (25 mL) were successively added triethylamine (2.04 mL, 14.7 mmol) and benzoyl chloride (1.11 mL, 9.55 mmol) at 0 °C. After being stirred at ambient temperature for 1 h, the mixture was quenched with a saturated sodium bicarbonate solution, and the resultant mixture was extracted with ether. The combined extracts were washed with water and brine, dried, concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to give **18** (1.54 g, 87%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ:9.97 (s, 1H), 8.04 (d, 2H, $J=7.0$ Hz), 7.92 (s, 1H), 7.79 (d, 1H, $J=7.6$ Hz), 7.66 (d, 1H, $J=7.6$ Hz), 7.49 (m, 1H), 7.37 (t, 2H, $J=7.8$ Hz), 5.37 (s, 2H); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 192.0, 166.2, 137.4, 136.7, 133.9, 133.3, 129.8, 129.7, 129.5, 129.4, 129.0, 128.5, 65.7; IR ($CHCl_3$): 1693, 1605, 1451, 1372 cm^{-1}; MS (EI) *m/z* (relative intensity) 240 (M^+, 1), 105 (100); HRMS (EI^+) calcd for $C_{15}H_{12}O_3$ (M^+) 240.0786, found 240.0788.

4.1.6. 3-((1*R*)-1-Hydroxy-3-((4*S*)-isopropyl-2-thioxothiazolidin-3-yl)-3-oxopropyl)benzyl benzoate (19). To a solution of **11** (100 mg, 0.492 mmol) in CH_2Cl_2 (2.5 mL) were successively added titanium(IV) chloride (0.059 mL, 0.54 mmol) and diisopropylethylamine (0.092 mL, 0.54 mmol) at −40 °C under an argon atmosphere. After the mixture was stirred at −40 °C for 2 h, a solution of **18** (107 mg, 0.447 mmol) in CH_2Cl_2 (2.5 mL) was added to this mixture at −78 °C, and the whole was stirred for 30 min. The same work-up procedure described for **16** gave the desired product **19** (150 mg, 76%) along with the minor diastereomer (9.0 mg, 4.5%). **19**: $[\alpha]_D^{23}=+210$ ($c=1.20$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.07 (d, 2H, $J=7.6$ Hz), 7.55 (t, 1H, $J=7.3$ Hz), 7.48 (s, 1H), 7.43 (t, 2H, $J=7.6$ Hz), 7.37 (m, 3H), 5.36 (s, 2H), 5.29 (d, 1H, $J=8.6$ Hz), 5.11 (t, 1H, $J=7.0$ Hz), 3.80 (dd, 1H, $J=17.4$, 2.44 Hz), 3.60 (dd, 1H, $J=17.6$, 9.3 Hz), 3.45 (dd, 1H, $J=11.3$, 7.9 Hz), 3.34 (s, 1H), 2.99 (d, 1H, $J=11.6$ Hz), 2.35 (m, 1H), 1.04 (d, 3H, $J=6.7$ Hz), 0.97 (d, 3H, $J=6.7$ Hz); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 203.1, 172.4, 166.4, 142.9, 136.3, 133.0, 130.0, 129.7, 128.8, 128.4, 127.4, 125.7, 125.5, 71.4, 69.9, 66.5, 46.7, 30.7, 30.6, 18.9, 17.6; IR ($CHCl_3$): 1713, 1274 cm^{-1}; MS (EI) *m/z* (relative intensity) 443 (M^+, 0.3), 105 (100); HRMS (EI^+) calcd for $C_{23}H_{25}NO_4S_2$ (M^+) 443.1225, found 443.1222.

4.1.7. Methyl (3*R*)-3-(3-formylphenyl)-3-(*tert*-butyldimethylsillyloxy)propanoate (20). To a solution of **19** (57.0 mg, 0.128 mmol) in CH_2Cl_2 (1.3 mL) were added 2,6-lutidine (0.045 mL, 0.39 mmol) and TBSOTf (0.044 mL, 0.19 mmol) at 0 °C, and the whole mixture was stirred at room temperature for 30 min. After being quenched with a saturated sodium bicarbonate solution, the mixture was extracted with ether. The combined extracts were washed with brine, dried, and then concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to give TBS ether as a colorless oil (60.0 mg, 84%). To a solution of the obtained TBS ether (60.0 mg, 0.107 mmol) in methanol (4.3 mL) was added K_2CO_3 (32.6 mg, 0.236 mmol) at room temperature, and the whole was stirred at room temperature for 2 h. After the solvent was removed, ethyl acetate and water were added to the residue, and the separated organic extract was concentrated in vacuo. To a solution of the obtained residue in a 2/1 mixture of DMSO and THF (1.2 mL) was added IBX (58.0 mg, 0.207 mmol), and the whole was stirred at room temperature for 30 min. After being quenched with a saturated sodium bicarbonate solution, the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with brine, dried, and then concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to give aldehyde (28.0 mg, 84% in 2 steps) as a colorless oil. $[\alpha]_D^{23}=+61.6$ ($c=1.09$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ:10.0 (s, 1H), 7.87 (s, 1H), 7.79 (d, 1H, $J=7.6$ Hz), 7.64 (d, 1H, $J=7.6$ Hz), 7.51 (dd, 1H, $J=7.6$, 7.6 Hz), 5.24 (dd, 1H, $J=4.2$, 9.2 Hz), 3.67 (s, 3H), 2.75 (dd, 1H, $J=14.7$, 9.2 Hz), 2.58 (dd, 1H, $J=14.7$, 4.2 Hz), 0.85 (s, 9H), 0.04 (sm, 3H), −0.16 (s, 3H); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 192.2, 171.1, 145.3, 136.6, 131.9, 129.1, 129.0, 127.0, 71.6, 51.7, 46.0, 25.6, 18.0, −4.7, −5.3; IR ($CHCl_3$): 2254, 1734, 1700 cm^{-1}; MS (FAB) *m/z* (relative

intensity) 323 (MH^+, 15), 265 (100); HRMS (FAB^+) calcd for $C_{17}H_{27}O_4Si$ (MH^+) 323.1679, found 323.1659.

4.1.8. Methyl (3*R*)-3-(*tert*-butyldimethylsillyloxy)-3-[3-((1*S*)-1-(*tert*-butyldimethylsillyloxy)-3-butynyl)phenyl]-propanoate (21). To a solution of the chiral boron reagent, prepared from **12** (0.148 mmol) according to the literature procedure,[12] was added **20** (24.0 mg, 0.0744 mmol) at −78 °C, and the mixture was allowed to stand at −78 °C for 20 h. After being quenched with a 1.0 M hydrochloric acid solution, the mixture was extracted with ether two times. The combined extracts were washed with water and brine, dried, and then concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 3:1 hexane/ether) to give alcohol (23.3 mg, 88%, 80% de) as a colorless oil. $[\alpha]_D^{28}=+32.7$ ($c=1.09$, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.38–7.25 (m, 4H), 5.14 (dd, 1H, $J=3.4$, 9.5 Hz), 4.86 (m, 1H), 3.67 (s, 3H), 2.71 (dd, 1H, $J=14.7$, 9.5 Hz), 2.62 (m, 1H), 2.54 (dd, 1H, $J=14.7$, 3.4 Hz), 2.42 (m, 1H), 2.04 (s, 1H), 0.83 (s, 9H), 0.00 (s, 3H), −0.21 (s, 3H); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 171.5, 144.3, 142.6, 128.5, 125.4, 124.9, 123.2, 80.5, 72.3, 72.2, 71.0, 51.6, 46.2, 29.5, 25.6, 18.0, −4.7, −5.3; IR ($CHCl_3$): 3307, 1733 cm^{-1}; MS (FAB) *m/z* (relative intensity) 363 (MH^+, 9), 305 (100); HRMS (FAB^+) calcd for $C_{20}H_{31}O_4Si$ (MH^+) 363.1992, found 363.1976. To a solution of the obtained alcohol (1.04 g, 2.88 mmol) in DMF (28 mL) were added imidazole (587 mg, 8.63 mmol) and TBSCl (867 mg, 5.75 mmol) at room temperature, and the whole was stirred at room temperature for 4 h. After being quenched with a saturated sodium bicarbonate solution, the mixture was extracted with ether. The extract was washed with water and brine, dried, and then concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 10:1 hexane/ethyl acetate) to give **21** (1.28 g, quantitative yield) as a colorless oil. $[\alpha]_D^{28}=+23.0$ ($c=1.09$, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.27–7.20 (m, 4H), 5.12 (m, 1H), 4.78 (m, 1H), 3.66 (s, 3H), 2.71 (m, 1H), 2.59–2.43 (m, 3H), 1.90 (s, 1H), 0.86 (s, 9H), 0.82 (s, 9H), 0.05 (s, 3H), 0.00 (s, 3H), −0.10 (s, 3H), −0.20 (s, 3H); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 171.5, 144.1, 143.9, 128.1, 125.1, 123.6, 123.4, 81.5, 73.8, 72.2, 69.9, 51.5, 46.2, 30.9, 25.7, 25.6, 18.2, 18.0, −4.6, −4.7, −4.9, −5.3; IR ($CHCl_3$): 2955, 2857, 1734 cm^{-1}; MS (EI) *m/z* (relative intensity) 476 (M^+, 0.3), 419 (100); HRMS (EI^+) calcd for $C_{26}H_{44}O_4Si_2$ (M^+) 476.2778, found 476.2780.

4.1.9. 1-((1*S*)-1-(*tert*-Butyldimethylsillyloxy)-3-butynyl)-3-[(1*R*)-1-(*tert*-butyldimethylsillyloxy)-3-(triethylsillyl-oxy)propyl]benzene (5). To a stirred solution of **21** (1.28 g, 2.68 mmol) in CH_2Cl_2 (15 mL) was added a 0.93 M solution of DIBAL (11.5 mL, 10.7 mmol) in *n*-hexane at −78 °C under an argon atmosphere, and this mixture was stirred for 1 h. After being quenched with water, the mixture was extracted with three portions of dichloromethane. The combined extracts were washed with brine, drying, and concentrated in vacuo. The crude product was then dissolved in methanol (27 mL), and sodium borohydride (405 mg, 107 mmol) was added to the mixture. After the whole was stirred at ambient temperature for 1 h, the solvent was removed and ethyl acetate and water were added to the residue. The organic layer was washed with water and brine, dried, and then concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to give alcohol (1.03 g, 86%). $[\alpha]_D^{27}=+26.2$ ($c=1.09$, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.43–7.25 (m, 4H), 5.03 (m, 1H), 4.88 (m, 1H), 3.78 (m, 2H), 2.70–2.51 (m, 3H), 2.01 (m, 3H), 0.96 (s, 9H), 0.95 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H), 0.00 (s, 3H), −0.08 (s, 3H); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 144.2, 143.9, 128.0, 125.0, 124.8, 123.5, 81.5, 74.6, 73.8, 69.9, 60.3, 42.0, 30.9, 25.8, 25.7, 18.2, 18.1, −4.6, −4.7, −4.9, −5.2; IR ($CHCl_3$): 3308, 2955, 2932 cm^{-1}; MS (FAB) *m/z* (relative intensity) 449 (MH^+, 2), 317 (25), 73 (100); HRMS (FAB^+) calcd for $C_{25}H_{45}O_3Si_2$ (MH^+) 449.2907, found 449.2858. To a solution of the obtained alcohol (200 mg, 0.446 mmol) in DMF (4.5 mL) were added imidazole (91.0 mg, 1.33 mmol) and TESCl (0.150 mL, 0.891 mmol) at room temperature, and the mixture was stirred at room temperature for 5 h. After being quenched with a saturated sodium bicarbonate solution, the mixture was extracted with ether. The extract was washed with water and brine, dried, and then concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 15:1 hexane/ethyl acetate) to give **5** (250 mg, quantitative yield) as a colorless oil. $[\alpha]_D^{27}=+9.7$ ($c=0.97$, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.43–7.25 (m, 4H), 4.75 (m, 2H), 3.63 (m, 1H), 3.52 (m, 1H), 2.50 (m, 1H), 2.40 (m, 1H), 1.85 (m, 2H), 1.73 (m, 1H), 0.90 (t, 9H, $J=7.9$ Hz), 0.81 (s, 9H), 0.80 (s, 9H), 0.51 (q, 6H, $J=7.9$ Hz), −0.03 (s, 3H), −0.05 (s, 3H), −0.16 (s, 3H), −0.24 (s, 3H); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 145.4, 143.8, 127.9, 125.1, 124.5, 123.6, 81.7, 73.9, 71.9, 69.8, 59.4, 44.0, 30.9, 25.9, 25.8, 18.3, 18.2, 6.8, 4.5, −4.6, −4.7, −5.0, −5.1; IR ($CHCl_3$): 2955, 2879 cm^{-1}; MS (EI) *m/z* (relative intensity) 562 (M^+, 1.5), 505 (70), 477 (78), 75 (100); HRMS (EI^+) calcd for $C_{31}H_{58}O_3Si_3$ (M^+) 562.3694, found 562.3687.

4.1.10. Ethyl (7*S*,2*Z*,4*E*)-7-(*tert*-butyldimethylsillyloxy)-7-[3-((1*R*)-1-(*tert*-butyldimethylsillyloxy)-3-triethylsillyl-oxypropyl)phenyl]hepta-2,4-dienoate (22). To a solution of **5** (882 mg, 1.57 mmol) in THF (15.6 mL) was added a 1.58 M solution of *n*-butyllithium (1.49 mL, 2.35 mmol) in *n*-hexane. After the solution was stirred at −78 °C for 1 h, a 1 M solution of cyanogen bromide (3.10 mL, 3.10 mmol) in THF was added to the mixture. The reaction mixture was stirred at −78 °C for an additional hour, before warming to −40 °C. The mixture was then poured into a 1 M solution of sodium hydroxide and the mixture was extracted with diethyl ether. The combined organic extracts were filtered through a pad of Celite. The filtrate was concentrated in vacuo and the crude product was purified by SiO_2 column chromatography (elution: 40:1 hexane/ethyl acetate) to give bromoalkyne (939 mg, 93%) as a colorless oil. To a benzene solution (14.6 mL) of the obtained bromoalkyne (939 mg, 1.46 mmol) was added bis(triphenylphosphine)palladium(II)-chloride (51.3 mg, 0.5 mol%), which was followed by the slow addition of tri-*n*-butyltinhydride (0.620 mL, 3.21 mmol) over a 5 min period. The resulting mixture was stirred at room temperature for 30 min. After the solvent was removed, the crude vinyl stannane was dissolved in DMF (11 mL) and to the solution were successively added (*Z*)-3-iodopropenoate (372 mg, 1.64 mmol), $Pd_2(dba)_2$ (626 mg, 0.109 mmol), and diisopropylethylamine (0.284 mL, 1.65 mmol). The whole was

stirred at room temperature for 1 h before being quenched with a saturated sodium bicarbonate solution. The mixture was extracted with ether, and the extract was washed with water and brine, dried, and then concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 10:1 hexane/ethyl acetate) to give the desired product **22** (315 mg, 33% in 2 steps) as a colorless oil. $[\alpha]_D^{34}=+14$ ($c=0.97$, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ:7.34 (dd, 1H, $J=11.3$, 14.7 Hz), 7.28–7.11 (m, 4H), 6.48 (dd, 1H, $J=11.3$, 11.3 Hz), 5.98 (dt, 1H, $J=14.7$, 7.9 Hz), 5.55 (d, 1H, $J=11.3$ Hz), 4.78 (dd, 1H, $J=7.9$, 4.3 Hz), 4.68 (m, 1H), 4.16 (q, 2H, $J=7.0$ Hz), 3.70 (m, 1H), 3.56 (m, 1H), 2.57 (m, 1H), 2.50 (m, 1H), 1.89 (m, 1H), 1.78 (m, 1H), 1.27 (t, 3H, $J=7.0$ Hz), 0.90 (t, 9H, $J=$ 7.9 Hz), 0.81 (s, 9H), 0.80 (s, 9H), 0.51 (q, 6H, $J=7.9$ Hz), −0.03 (s, 3H), −0.05 (s, 3H), −0.16 (s, 3H), −0.19 (s, 3H); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 166.3, 145.5, 144.9, 144.5, 141.4, 128.9, 127.9, 124.9, 124.5, 123.5, 116.0, 74.9, 71.8, 59.7, 59.3, 44.4, 44.0, 25.8, 25.7, 18.2, 18.1, 14.2, 6.8, 4.5, −4.6, −4.7, −5.0, −5.1; IR ($CHCl_3$): 2955, 2360 cm^{-1}; MS (CI) *m/z* (relative intensity) 663 (MH^+, 4), 605 (10), 399 (72), 133 (100); HRMS (CI^+) calcd for $C_{36}H_{67}O_5Si_3$ (MH^+) 663.4296, found 663.4283.

4.1.11. Ethyl (7*S*,2*Z*,4*E*)-7-*tert*-Butyldimethylsillyloxy-7-[3-((1*R*)-1-*tert*-butyldimethylsillyloxy-2-formylethyl)-phenyl]hepta-2,4-dienoate (4). To a solution of **22** (250 mg, 0.377 mmol) in a mixture of DMSO, THF, and H_2O (2.6/1.3/0.02 mL) was added IBX (232 mg, 0.829 mmol), and the mixture was stirred at room temperature for 1 h before being quenched with a saturated sodium bicarbonate solution. The mixture was extracted with diethyl ether, and the combined extracts were washed with brine, dried, and concentrated in vacuo. The crude product was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to give **4** as a colorless oil (136 mg, 66%). $[\alpha]_D^{28}=+26$ ($c=0.97$, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ:9.77 (s, 1H), 7.36 (dd, 1H, $J=11.3$, 14.5 Hz), 7.30–7.17 (m, 4H), 6.50 (dd, 1H, $J=11.3$, 11.3 Hz), 5.99 (m, 1H), 5.56 (d, 1H, $J=11.3$ Hz), 5.20 (m, 1H), 4.73 (m, 1H), 4.17 (q, 2H, $J=6.7$ Hz), 2.85 (m, 1H), 2.62–2.41 (m, 3H), 1.28 (t, 3H, $J=6.7$ Hz), 0.86 (s, 18H), 0.04 (s, 3H), 0.01 (s, 3H), −0.26 (s, 3H), −0.27 (s, 3H); ^{13}C NMR ($J=126$ Hz, $CDCl_3$) δ: 201.1, 166.3, 144.9, 144.7, 143.5, 140.9, 129.1, 128.4, 125.1, 124.6, 123.2, 116.1, 74.6, 70.8, 59.8, 53.8, 44.3, 25.7, 25.6, 18.1, 18.0, 14.2, −4.6, −4.7, −5.0, −5.2; IR ($CHCl_3$): 2955, 2931, 2857, 1717, 1638 cm^{-1}; MS (CI) *m/z* (relative intensity) 547 (MH^+, 12), 489 (20), 283 (100); HRMS (CI^+) calcd for $C_{30}H_{51}O_5Si_2$ (MH^+) 547.3275, found 547.3284.

4.1.12. 7-(4-Methoxyphenylmethoxy)heptanal (24). To a suspension of sodium hydride (1.80 g, 75.6 mmol) in DMF (200 mL) was added 1,7-heptanediol (10.0 g, 75.6 mmol) at 0 °C under an argon atmosphere, and the mixture was stirred at room temperature for 30 min. To the resulting solution was slowly added 4-methoxybenzyl chloride (10.3 mL, 75.6 mmol) at −20 °C, and the whole was stirred overnight at 0 °C. After being quenched with water, the mixture was extracted with ether. The extract was washed with brine, dried, and then concentrated in vacuo. The crude residue was purified by SiO_2 column chromatography (elution: 2:1 hexane/ethyl acetate) to give PMB alcohol (9.37 g, 50%) as a colorless oil; ^1H NMR ($CDCl_3$) δ: 7.26 (d, 2H, $J=8.2$ Hz), 6.87 (d, 2H, $J=8.2$ Hz), 4.43 (s, 2H), 3.80 (s, 3H), 3.63 (m, 2H), 3.43 (t, 2H, $J=6.4$ Hz), 1.63–1.53 (m, 4H), 1.40–1.30 (m, 6H), 1.20 (br, 1H); ^{13}C NMR ($CDCl_3$) δ: 159.0, 130.6, 129.1, 113.6, 72.4, 70.0, 62.8, 55.1, 32.6, 29.6, 29.1, 26.1, 25.6; IR ($CHCl_3$): 3623, 3443, 3008, 2963, 2860, 1612, 1513, 1462, 1248, 1090, 1035, 777 cm^{-1}; MS (EI) *m/z* (relative intensity) 252 (M^+,10), 137 (97), 121 (100), 107 (16), 91 (14); HRMS (EI^+) calcd for $C_{15}H_{24}O_3$ (M^+) 252.1725, found 252.1719. To a solution of oxalyl chloride (4.05 mL, 46.4 mmol) in CH_2Cl_2 (40 mL) were successively added a solution of DMSO (3.8 mL, 54 mmol) in CH_2Cl_2 (50 mL) at −50 °C and a solution of the obtained alcohol (9.00 g, 35.6 mmol) in CH_2Cl_2 (30 mL) at −78 °C. After being stirred for 1.5 h, the mixture was quenched with triethylamine (15 mL) at −78 °C, and the whole mixture was allowed to warm to 0 °C. The mixture was then quenched with water at 0 °C, and the mixture was extracted with ethyl acetate. The extract was washed with water and brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to give **24** (8.32 g, 93%) as a colorless oil; ^1H NMR ($CDCl_3$) δ: 9.76 (s, 1H), 7.25 (d, 2H, $J=$ 8.5 Hz), 6.88 (d, 2H, $J=8.5$ Hz), 4.43 (s, 2H), 3.80 (s, 3H), 3.43 (t, 2H, $J=6.6$ Hz), 2.42 (t, 2H, $J=7.4$ Hz), 1.67–1.56 (m, 4H), 1.43–1.29 (m, 4H); ^{13} C NMR ($CDCl_3$) δ: 202.6, 158.9, 130.6, 129.1, 113.6, 72.4, 69.8, 55.1, 43.7, 29.4, 28.8, 25.9, 21.9; IR ($CHCl_3$): 3007, 2938, 2860, 1722, 1612, 1247, 1224, 1091, 1035 cm^{-1}; MS (EI) *m/z* (relative intensity) 250 (M^+,3.2), 137 (30), 121 (100), 91 (10); HRMS (EI^+) calcd for $C_{15}H_{22}O_3$ (M^+) 250.1569, found 250.1564.

4.1.13. (2*R*)-8-(4-Methoxyphenylmethoxy)octan-2-ol (25). (+)-TADDOL (1.01 g, 2.16 mmol) was placed in a dry Schlenk tube under an argon atmosphere. To this, Ti(O-*i*-Pr)$_4$ (0.764 mL, 2.59 mmol) and toluene (16 mL) were successively added, and the mixture was stirred at room temperature for 5 h. After toluene and 2-propanol were removed in vacuo, toluene (32 mL) and Ti(O-*i*-Pr)$_4$ (5.57 mL, 21.6 mmol) were added to the yellow residue at room temperature. After being cooled to −25 °C, to the resulting mixture were added a solution of **24** (2.40 g, 10.8 mmol) in toluene (24 mL) and then a 1.0 M solution of Me_2Zn (21.6 mL, 21.6 mmol) in *n*-hexane, and the mixture was stirred at the same temperature for 12 h. After being quenched with an ammonium chloride solution, the mixture was filtrated through a pad of Celite. The filtrate was washed with brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 2:1 hexane/ethyl acetate) to furnish **25** (2.58 g, 90%, 95%ee) as a colorless oil; $[\alpha]_D^{22}=3.60$ ($c=1.05$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 7.26 (d, 2H, $J=8.2$ Hz), 6.88 (d, 2H, $J=8.2$ Hz), 4.43 (s, 2H), 3.81 (s, 3H), 3.78 (m, 1H), 3.43 (t, 2H, $J=6.7$ Hz), 1.64–1.55 (m, 2H), 1.50–1.25 (m, 8H), 1.18 (d, 3H, $J=6.1$ Hz); ^{13}C NMR ($CDCl_3$) δ: 159.0, 130.7, 129.2, 113.7, 72.5, 70.1, 68.0, 52.2, 39.2, 29.6, 29.4, 26.1, 25.7, 23.4; IR ($CHCl_3$): 3454, 3009, 2934, 2860, 1513, 1462, 1248, 1232, 1093 cm^{-1}; MS (EI) *m/z* (relative intensity) 266 (M^+,3.0), 137 (45), 121 (100), 91 (10); HRMS (EI^+) calcd for $C_{16}H_{26}O_3$ (M^+) 266.1882, found 266.1892. The enantiomeric excess of **25** was determined by HPLC analysis. Chiral column; eluent; flow rate; retention

times for each compounds are as follows: Daicel Chiralcel OD, 3% 2-propanol in hexane, 1.2 mL/min, (*R*) (major) 20.5 min, (*S*) (minor) 21.7 min.

4.1.14. Determination of the absolute configuration of 25. The absolute configuration of **25** was determined by ^{1}H NMR methods previously described by Kusumi et al.[11] The ^{1}H NMR chemical shifts of (+) and (−)-MTPA esters of **25** are as follows: (+)-MTPA ester; ^{1}H NMR ($CDCl_3$) δ: 7.53 (m, 2H), 7.37 (m, 3H), 7.23 (d, 2H, J=8.5 Hz), 6.87 (d, 2H, J=8.5 Hz), 5.14 (m, 1H), 4.40 (s, 2H), 3.80 (s, 3H), 3.56 (s, 3H), 3.35 (t, 2H, J=6.4 Hz), 1.67–1.48 (m, 10H), 1.32 (d, 3H, J=6.1 Hz), (−)-MTPA ester; ^{1}H NMR ($CDCl_3$) δ: 7.53 (m, 2H), 7.37 (m, 3H), 7.23 (d, 2H, J=8.5 Hz), 6.87 (d, 2H, J=8.5 Hz), 5.14 (m, 1H), 4.41 (s, 2H), 3.80 (s, 3H), 3.42 (t, 2H, J=6.4 Hz), 1.48–1.33 (m, 10H), 1.24 (d, 3H, J=6.1 Hz).

4.1.15. (7*R*)-7-Benzoyloxyoctanol (26). To a solution of **25** (3.29 g, 12.2 mmol) in CH_2Cl_2 (20 mL) were successively added triethylamine (3.67 mL, 24.4 mmol), DMAP (74.5 mg, 0.610 mmol), and benzoyl chloride at 0 °C. The whole mixture was stirred at ambient temperature for 20 h. After being quenched with a saturated sodium bicarbonate solution, the mixture was extracted with ether. The organic layer was washed with water and brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 10:1 hexane/ethyl acetate) to give benzoate (3.98 g, quantitative yield) as a pale yellow oil; $[\alpha]_D^{22}$=19.0 (c=1.01, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.04 (d, 2H, J=7.4 Hz), 7.55 (dd, 1H, J=7.4, 7.4 Hz), 7.43 (dd, 2H, J=7.4, 7.4 Hz), 7.25 (d, 2H, J=8.2 Hz), 6.87 (d, 2H, J=8.2 Hz), 5.15 (m, 1H), 4.41 (s, 2H), 3.80 (s, 3H), 3.42 (t, 2H, J=6.7 Hz), 1.74–1.70 (m, 1H), 1.65–1.55 (m, 3H), 1.40–1.30 (m, 6H), 1.33 (d, 3H, J=6.1 Hz); ^{13}C NMR ($CDCl_3$) δ: 166.1, 158.9, 132.6, 130.8, 129.4, 129.1, 128.2, 113.6, 72.4, 71.5, 69.9, 55.1, 35.9, 29.6, 29.2, 26.0, 25.3, 19.9; IR ($CHCl_3$): 3007, 2937, 2860, 1708, 1512, 1280, 1248, 1108 cm^{-1}; MS (CI) *m*/*z* (relative intensity) 371 (MH^+,5.0), 241 (11), 121 (100); HRMS (CI^+) calcd for $C_{23}H_{31}O_4$ (MH^+) 371.2222, found 371.2210. To a solution of the obtained benzoate (1.24 g, 3.35 mmol) in a mixture of CH_2Cl_2 and H_2O (34 mL and 2 mL) was added DDQ (850 mg, 3.74 mmol) at 0 °C and the mixture was stirred at room temperature for 1 h. After being quenched with a saturated sodium bicarbonate solution, the reaction mixture was diluted with ether and filtered through a pad of Celite. The combined filtrates were concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to furnish **26** (790 mg, 80%) as a colorless oil; $[\alpha]_D^{22}$=26.4 (c=0.97, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.04 (d, 2H, J=7.4 Hz), 7.55 (dd, 1H, J=7.4, 7.4 Hz), 7.43 (dd, 2H, J=7.4, 7.4 Hz), 5.15 (dt, 1H, J=6.4, 8.9 Hz), 3.62 (t, 2H, J=6.4 Hz), 1.80–1.70 (m, 1H), 1.65–1.60 (m, 1H), 1.60–1.53 (m, 2H), 1.45–1.35 (m, 6H), 1.33 (d, 3H, J=6.4 Hz); ^{13}C NMR ($CDCl_3$) δ: 166.2, 132.6, 130.7, 129.3, 128.2, 71.5, 62.6, 35.8, 32.5, 29.1, 25.5, 25.3, 19.9; IR ($CHCl_3$): 3481, 2936, 2861, 1708, 1281, 1117 cm^{-1}; MS (CI) *m*/*z* (relative intensity) 251 (MH^+,75), 123 (4.0); HRMS (CI^+) calcd for $C_{15}H_{23}O_3$ (MH^+) 251.1647, found 251.1658.

4.1.16. (8*R*)-8-Benzoyloxy-1-nonyne (27). To a solution of **26** (4.70 g, 18.8 mmol) in a 2/1 mixture of DMSO and THF (180 mL) was added IBX (7.90 g, 28.1 mmol), and the mixture was stirred at room temperature for 30 min. After being poured into a saturated sodium bicarbonate solution, the whole was extracted with ether. The combined extracts were washed, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to give aldehyde (4.40 g, 95%) as a colorless oil; $[\alpha]_D^{18}$=29.6 (c=0.960, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 9.73 (s, 1H), 8.04 (d, 2H, J=7.4 Hz), 7.55 (dd, 1H, J=7.4, 7.4 Hz), 7.43 (dd, 2H, J=7.4, 7.4 Hz), 5.15 (m, 1H), 2.40 (m, 2H), 1.80–1.70 (m, 1H), 1.66–1.58 (m, 3H), 1.45–1.35 (m, 4H), 1.33 (d, 3H, J=6.4 Hz); ^{13}C NMR ($CDCl_3$) δ: 202.3, 165.9, 132.5, 130.6, 129.2, 128.0, 71.2, 43.5, 35.6, 28.7, 25.0, 21.7, 19.8; IR ($CHCl_3$): 3028, 2939, 2863, 1715, 1453, 1281, 1116 cm^{-1}; MS (CI) *m*/*z* (relative intensity) 249 (MH^+, 100), 127 (45), 123 (40), 109 (27); HRMS (EI^+) calcd for $C_{15}H_{21}O_3$ (MH^+) 249.1491, found 249.1497. A magnetically stirred slurry of potassium *tert*-butoxide (3.97 g, 35.4 mmol) in THF (40 mL) was cooled to −78 °C under an argon atmosphere. To this mixture was added a solution of dimethyl (diazomethyl)phosphonate (6.31 g, 35.4 mmol) in THF (50 mL) dropwise over a 1 min period, and the resulting mixture was stirred for 5 min. During this time, the color of the reaction mixture changed from pale yellow to brown. Subsequently, to the mixture was added a solution of the obtained aldehyde (4.40 g, 17.7 mmol) in THF (40 mL) over a 1 min period. The resulting solution was stirred at −78 °C for 24 h and then allowed to warm to ambient temperature. Stirring was continued for an additional 4 h, and then the reaction mixture was quenched with water. The mixture was extracted with three portions of dichloromethane, and the combined extracts were washing with brine, drying, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 10:1 hexane/ethyl acetate) to furnish **27** (3.70 g, 85%). $[\alpha]_D^{23}$=34.4 (c=1.17, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.03 (d, 2H, J=7.4 Hz), 7.55 (dd, 1H, J=7.4, 7.4 Hz), 7.44 (dd, 2H, J=7.4, 7.4 Hz), 5.15 (m, 1H), 2.18 (m, 2H), 1.93 (s, 1H), 1.80–1.70 (m, 1H), 1.66–1.58 (m, 1H), 1.58–1.49 (m, 2H), 1.50–1.35 (m, 4H), 1.34 (d, 3H, J=6.4 Hz); ^{13}C NMR ($CDCl_3$) δ: 166.2, 132.7, 130.8, 129.5, 128.3, 84.5, 71.5, 68.2, 35.9, 28.5, 28.3, 24.9, 20.1, 18.3; IR ($CDCl_3$): 3307, 2940, 2963, 1709, 1453, 1281, 1120 cm^{-1}; MS (CI) *m*/*z* (relative intensity) 245 (MH^+, 100), 227 (16), 123 (73), 105 (67); HRMS (EI^+) calcd for $C_{16}H_{21}O_2$ (MH^+) 245.1542, found 245.1535.

4.1.17. (8*R*)-8-(*tert*-Butyldimethylsilyloxy)-1-nonyne (8). To a solution of **27** (3.00 g, 12.3 mmol) in methanol (80 mL) was added a 3 N potassium hydroxide solution (80 mL) and the whole was stirred at room temperature for 3 h. After being concentrated in vacuo, the mixture was extracted with ether. The extracts were washed with water and brine, drying, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 2:1 hexane/ether) to give alcohol (1.43 g, 87%) as a colorless oil; $[\alpha]_D^{19}$=7.9 (c=0.96, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 3.80 (m, 1H), 2.20 (m, 2H), 1.97 (s, 1H), 1.66 (br, 1H), 1.60–1.50 (m, 2H), 1.50–1.38 (m, 5H), 1.38–1.28 (m, 1H), 1.19 (d, 3H, J=6.4 Hz); ^{13}C NMR ($CDCl_3$) δ: 84.5, 68.2, 67.9, 39.1, 28.7, 28.4, 25.2, 23.5, 18.3; IR

($CHCl_3$): 3610, 3306, 3008, 2936, 2861 cm^{-1}; MS (EI) *m/z* (relative intensity) 140 (M^+, 100), 96 (17); HRMS (EI^+) calcd for $C_9H_{17}O$ (M^+) 140.1201, found 140.1212. To a solution of the obtained alcohol (700 mg, 4.99 mmol) in DMF (50 mL) were added imidazole (1.02 g, 14.9 mmol) and TBSCl (1.50 g, 9.98 mmol) at room temperature. The whole was stirred at room temperature for 2 h. After being quenched with a saturated sodium bicarbonate solution, the mixture was extracted with ether. The combined extracts were washed with water and brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 20:1 hexane/ethyl acetate) to give the desired product **8** (1.26 g, quantitative yield) as a colorless oil; $[\alpha]_D^{19}=11.2$ ($c=1.04$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 3.73 (m, 1H), 2.13 (m, 2H), 1.88 (s, 1H), 1.54–1.44 (m, 2H), 1.44–1.28 (m, 5H), 1.28–1.18 (m, 1H), 1.07 (d, 3H, $J=6.4$ Hz), 0.84 (s, 9H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 84.6, 77.2, 76.9, 76.7, 68.5, 68.1, 39.5, 28.8, 28.5, 25.9, 25.2, 23.8, 18.3, 18.1, −4.4, −4.7; IR ($CHCl_3$):3306, 2933, 2858 cm^{-1}; MS (CI) *m/z* (relative intensity) 255 (MH^+, 100), 140 (11), 96 (17); HRMS (CI^+) calcd for $C_{15}H_{31}OSi$ (MH^+) 255.2144, found 255.2149.

4.1.18. (1*S*)-1-(3-Benzoyloxymethylphenyl)-3-butyn-1-ol (28). By using the same procedure described for **21**, the aldehyde **18** (7.00 g, 29.1 mmol) was transformed into the crude product **28**, which was purified by SiO_2 column chromatography (elution: 3:1 hexane/ether) to give a recovered starting material (2.10 g, 29%) and **28** (4.75 g, 56%, 80%ee) as colorless crystals. The enantiomeric excess of the product was improved from 80 to 99%ee by recrystallization from hexane/ethyl acetate. The ee was determined by ^1H NMR analysis of (+)- and (−)-MTPA esters of **28**; mp 70–72 °C; $[\alpha]_D^{23}=30.9$ ($c=1.11$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ:8.05 (d, 2H, $J=7.3$ Hz), 7.54 (dd, 1H, $J=7.3$, 7.3 Hz), 7.49–7.32 (m, 6H), 5.33 (s, 2H), 4.87 (m, 1H), 2.79 (m, 1H), 2.63 (m, 2H), 2.04 (s, 1H); ^{13}C NMR ($CDCl_3$) δ: 166.4, 143.0, 136.2, 133.0, 129.9, 129.6, 128.7, 128.3, 127.6, 125.7, 125.5, 80.5, 72.0, 71.0, 66.5, 29.3; IR ($CHCl_3$): 3595, 3306, 3023, 2360, 1715, 1603, 1452, 1376, 1274 cm^{-1}; MS (EI) *m/z* (relative intensity) 280 (M^+, 37), 231 (35), 129 (20), 73 (100); Anal. calcd for $C_{15}H_{21}O_3$: C, 77.12; H, 5.75. found: C, 77.36; H, 5.90.

4.1.19. Determination of the absolute configuration of 28. The absolute configuration was determined by ^1H NMR analysis of (+)- and (−)-MTPA esters of **28**: (+)-MTPA ester; ^1H NMR ($CDCl_3$) δ: 8.06 (d, 2H, $J=7.6$ Hz), 7.58 (dd, 1H, $J=7.3$ Hz), 7.46–7.20 (m, 11H), 6.09 (dd, 1H, $J=8.1$, 5.0 Hz), 5.28 (m, 1H), 3.62 (s, 3H), 2.85 (ddd, 1H, $J=16.9$, 8.2, 2.4 Hz), 2.74 (ddd, 1H, $J=17.2$, 5.0, 2.6 Hz), 2.02 (t, 1H, $J=2.4$ Hz), (−)-MTPA ester; ^1H NMR ($CDCl_3$) δ: 8.06 (d, 2H, $J=7.3$ Hz), 7.57 (dd, 1H, $J=7.3$ Hz), 7.47–7.30 (m, 11H), 6.14 (t, 1H, $J=6.6$ Hz), 5.36 (m, 1H), 3.46 (s, 3H), 2.82 (ddd, 1H, $J=17.2$, 7.3, 2.3 Hz), 2.73 (ddd, 1H, $J=16.9$, 6.0, 2.8 Hz), 1.90 (t, 1H, $J=2.4$ Hz).

4.1.20. 3-[(1*S*)-1-(*tert*-Butyldimethylsilyloxy)but-3-ynyl]-benzaldehyde (29). To a solution of **28** (4.80 g, 17.0 mmol) in DMF (170 mL) were added imidazole (2.30 mg, 34.0 mmol) and TBSCl (3.80 g, 25.0 mmol) at room temperature, and the whole was stirred at room temperature for 2 h. After the usual workup, the obtained crude product was purified by SiO_2 column chromatography (elution: 20:1 hexane/ethyl acetate) to give TBS ether (6.07 g, quantitative yield) as a colorless oil; $[\alpha]_D^{26}=17.0$ ($c=1.48$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ:8.08 (d, 2H, $J=7.3$ Hz), 7.56 (dd, 1H, $J=7.3$, 7.3 Hz), 7.47–7.41 (m, 3H), 7.37–7.30 (m, 3H), 5.37 (m, 2H), 4.84 (t, 1H, $J=6.4$ Hz), 2.59 (ddd, 1H, $J=16.5$, 6.4, 2.3 Hz), 2.49 (ddd, 1H, $J=16.5$, 6.4, 2.3 Hz), 1.94 (t, 1H, $J=2.3$ Hz), 0.87 (s, 9H), 0.08 (s, 3H), −0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 166.5, 144.5, 135.9, 133.1, 130.2, 129.8, 128.4, 128.3, 127.2, 125.8, 125.6, 81.4, 73.5, 70.1, 66.6, 30.9, 25.7, 18.2, −4.9, −5.0; IR ($CHCl_3$); 3308, 2931, 2857, 1715, 1603, 1455, 1274, 1199, 1110 cm^{-1}; MS (FAB) *m/z* (relative intensity) 395 (MH^+, 14), 231 (35), 73 (100); HRMS (FAB^+) calcd for $C_{24}H_{31}O_3Si$ (MH^+) 395.2042, found 395.2049. To a solution of the obtained TBS ether (6.07 g, 15.3 mmol) in methanol (150 mL) was added potassium carbonate (20.0 g, 153 mmol) at room temperature, and the mixture was stirred for 1 h. After evaporation and washing with water of the reaction mixture, the obtained product was dissolved in a 2/1 mixture of DMSO and THF (120 mL) and to this mixture was added IBX (4.40 g, 15.7 mmol). The crude product obtained by the usual workup was purified by SiO_2 column chromatography (elution: 5:1 hexane/ethyl acetate) to give aldehyde **29** (3.44 g, 86% in two steps) as a colorless oil; $[\alpha]_D^{20}=33.5$ ($c=1.08$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 10.0 (s, 1H), 7.87 (s, 1H), 7.77 (d, 1H, $J=7.6$ Hz), 7.65 (d, 1H, $J=7.6$ Hz), 7.50 (dd, 1H, $J=7.6$, 7.6 Hz), 4.89 (t, 1H, $J=6.4$ Hz), 2.59 (ddd, 1H, $J=16.5$, 6.4, 2.3 Hz), 2.49 (ddd, 1H, $J=16.5$, 6.4, 2.3 Hz), 1.95 (t, 1H, $J=2.3$ Hz), 0.88 (s, 9H), 0.08 (s, 3H), −0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 192.1, 144.9, 136.3, 131.9, 128.9, 128.8, 127.1, 80.7, 73.0, 70.5, 30.7, 25.7, 18.1, −4.9, −5.0; IR ($CHCl_3$):3307, 2955, 2932, 2889, 2858, 1698, 1215, 1103 cm^{-1}; MS (FAB) *m/z* (relative intensity) 289 (MH^+, 12), 249 (55), 231 (45), 97 (32), 73 (100); HRMS (FAB^+) calcd for $C_{17}H_{25}O_2Si$ (MH^+) 289.1624, found 289.1622.

4.1.21. (4*S*)-*N*-[(3*R*)-3-[3-((1*S*)-1-*tert*-Butyldimethylsilyloxy-3-butynyl)phenyl]-3-hydroxypropanoyl]-4-isopropyl-1,3-thiazolidine-2-thione (30). According to the procedure described for **16**, the same reaction of aldehyde **29** (2.68 g, 9.33 mmol), **11** (2.09 g, 10.3 mmol), titanium(IV) chloride (1.23 mL, 11.2 mmol), and diisopropylethylamine (1.93 mL, 11.2 mmol) provided the desired product **30** (3.45 g, 74%) along with the minor diastereomer (142 mg, 3.1%) after purification by SiO_2 column chromatography (elution: 3:1 hexane/ethyl acetate); **30**: $[\alpha]_D^{17}=+213$ ($c=1.09$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ:7.31 (m, 4H), 5.27 (m, 1H), 5.14 (t, 1H, $J=7.0$ Hz), 4.82 (t, 1H, $J=6.4$ Hz), 3.80 (m, 1H), 3.52 (m, 2H), 3.14–3.00 (m, 1H), 2.58 (ddd, 1H, $J=16.6$, 6.4, 2.6 Hz), 2.48 (ddd, 1H, $J=16.6$, 6.4, 2.6 Hz), 2.38 (m, 1H), 1.96 (t, 1H, $J=2.6$ Hz), 1.07 (d, 1H, $J=6.7$ Hz), 1.00 (d, 1H, $J=7.0$ Hz), 0.88 (s, 9H), 0.07 (s, 3H), −0.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 203.0, 172.6, 144.3, 142.3, 128.4, 125.3, 124.8, 123.5, 81.6, 73.6, 71.4, 70.1, 47.0, 30.9, 30.8, 30.7, 25.8, 19.0, 18.2, 17.8, −4.8, −5.0; IR ($CHCl_3$): 3570, 3307, 2959, 2857, 1681, 1468, 1362, 1311, 1256, 1167, 1093 cm^{-1}; MS (FAB) *m/z* (relative intensity) 492 (MH^+, 1.2), 162 (83), 73 (100); HRMS (FAB^+) calcd for $C_{25}H_{38}O_3NSiS_2$ (MH^+) 492.2062, found 492.2047.

4.1.22. Determination of the absolute configuration of 30. The absolute configuration of **30** was determined by ^{1}H NMR analysis of (+)- and (−)-MTPA esters derived from **30** in 4 steps: (+)-MTPA ester; ^{1}H NMR ($CDCl_3$) δ: 7.39–7.28 (m, 9H), 6.18 (dd, 1H, J=8.9, 4.9 Hz), 4.80 (t, 1H, J=6.3 Hz), 3.51 (m, 2H), 3.42 (s, 3H), 2.57 (ddd, 1H, J=16.5, 7.0, 2.8 Hz), 2.46 (ddd, 1H, J=16.6, 5.9, 2.6 Hz), 2.19 (m, 1H), 1.96 (m, 1H), 1.92 (t, 1H, J=2.6 Hz), 0.89 (s, 9H), 0.86 (s, 9H), 0.06 (s, 3H), 0.01 (s, 6H), −0.11 (s, 3H), (−)-MTPA ester; ^{1}H NMR ($CDCl_3$) δ: 7.37–7.12 (m, 9H), 6.11 (dd, 1H, J=8.7, 5.3 Hz), 4.77 (dd, 1H, J=7.0, 5.8 Hz), 3.68 (m, 1H), 3.58 (m, 1H), 3.50 (s, 3H), 2.55 (ddd, 1H, J=16.5, 7.0, 2.8 Hz), 2.43 (ddd, 1H, J=16.6, 5.9, 2.6 Hz), 2.21 (m, 1H), 2.00 (m, 1H), 1.93 (t, 1H, J=2.6 Hz), 0.90 (s, 9H), 0.87 (s, 9H), 0.06 (s, 3H), 0.03 (s, 6H), −0.11 (s, 3H).

4.1.23. (3*R*)-3-[3-[(1*S*)-1-(*tert*-Butyldimethylsilyloxy)-3-butynyl]phenyl]-*N*-methoxy-*N*-methyl-3-triethylsilyloxypropionamide (9). A mixture of *N*,*O*-dimethylhydroxylamine hydrochloride (7.01 g, 72.7 mmol) and triethylamine (9.69 mL, 72.7 mmol) in CH_2Cl_2 (70 mL) was stirred at room temperature for 1 h. The reaction mixture was added to a solution of **30** in CH_2Cl_2 (18 mL) at room temperature and the whole mixture was stirred for 21 h. After being poured into a 5% hydrochloric acid solution at 0 °C, the mixture was extracted with ethyl acetate. The extracts were washed with brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 1:1 to 1:2 hexane/ethyl acetate) to furnish Weinreb amide (2.30 g, 91%) as a colorless oil; $[\alpha]_D^{17}$=+22 (c=0.95, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.42–7.24 (m, 4H), 5.15 (m, 1H), 4.83 (t, 1H, J=6.4 Hz), 4.30 (br, 1H), 3.61 (s, 3H), 3.20 (s, 3H), 2.90–2.70 (m, 2H), 2.58 (ddd, 1H, J=16.6, 6.4, 2.6 Hz), 2.48 (ddd, 1H, J=16.6, 6.4, 2.6 Hz), 1.95 (t, 1H, J=2.6 Hz), 0.89 (s, 9H), 0.08 (s, 3H), −0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 173.1, 144.0, 142.9, 128.1, 124.9, 124.6, 123.2, 81.6, 73.6, 70.1, 70.0, 69.9, 61.1, 40.3, 31.8, 30.9, 25.7, 18.1, −4.8, −5.0; IR ($CHCl_3$): 3480, 3307, 3008, 2933, 2889, 2858, 1640, 1468, 1422, 1390, 1255, 1105 cm^{-1}; MS (FAB) m/z (relative intensity) 392 (MH^+, 18), 374 (100), 332 (33), 73 (68); HRMS (FAB^+) calcd for $C_{21}H_{34}O_4NSi$ (MH^+) 392.2257, found 392.2264. To a solution of the Weinreb amide in pyridine (20 mL) was added triethylsilylchloride (1.08 mL, 6.46 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with toluene (20 mL) and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 10:1 hexane/ethyl acetate) to give **9** (2.90 g, quantitative yield) as a colorless oil; $[\alpha]_D^{18}$=+25.8 (c=1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.42–7.24 (m, 4H), 5.26 (dd, 1H, J=8.6, 4.6 Hz), 4.81 (t, 1H, J=6.3 Hz), 3.61 (s, 3H), 3.16 (s, 3H), 3.04 (m, 1H), 2.61–2.43 (m, 3H), 1.93 (t, 1H, J=2.1 Hz), 0.88 (s, 9H), 0.84 (t, 9H, J=8.1 Hz), 0.52 (q, 6H, J=8.1 Hz), 0.08 (s, 3H), −0.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 171.6, 144.7, 143.9, 128.0, 125.0, 124.8, 123.4, 81.4, 73.7, 71.7, 69.8, 61.1, 43.0, 31.7, 30.7, 25.6, 18.1, 6.5, 4.5, −4.9, −5.2; IR ($CHCl_3$): 3308, 3003, 2956, 2879, 2360, 1649, 1466, 1388, 1254, 1079 cm^{-1}; MS (FAB) m/z (relative intensity) 506 (MH^+, 6.5), 476 (58), 374 (73), 115 (42), 73 (100); HRMS (FAB^+) calcd for $C_{27}H_{48}O_4NSi_2$ (MH^+) 506.3122, found 506.3107.

4.1.24. (1*R*,11*R*)-11-(*tert*-Butyldimethylsilyloxy)-1-[3-[(1*S*)-1-(*tert*-butyldimethylsilyloxy)-3-butynyl]phenyl]-1-triethylsilyloxy-4-dodecyn-3-one (7). To a solution of alkyne **8** (172 mg, 0.676 mmol) in THF (1.5 mL) was added a 1.0 M solution of ethylmagnesium bromide (0.66 mL, 0.66 mmol) in THF at 0 °C and the mixture was stirred at room temperature for 30 min. To this mixture was added a solution of **17** (260 mg, 0.442 mmol) in THF (2.0 mL) over a 5 min period, and the whole mixture was stirred at room temperature for 2 h. After being quenched with water, the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 20:1–5:1 hexane/ethyl acetate) to furnish **7** (240 mg, 70%) as a colorless oil; $[\alpha]_D^{22}$=+3.10 (c=1.08, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.34–7.23 (m, 4H), 5.27 (dd, 1H, J=8.9, 4.3 Hz), 4.80 (t, 1H, J=6.4 Hz), 3.77 (m, 1H), 3.02 (dd, 1H, J=8.9, 14.9 Hz), 2.70 (dd, J=4.3, 14.9 Hz), 2.57 (ddd, 1H, J=16.6, 6.4, 2.4 Hz), 2.47 (ddd, 1H, J=16.6, 6.4, 2.4 Hz), 2.36 (t, 2H, J=7.0 Hz), 1.94 (t, 1H, J=2.4 Hz), 1.45–1.33 (m, 5H), 1.34–1.22 (m, 3H), 1.12 (d, 3H, J=6.1 Hz), 0.88 (s, 9H), 0.88 (s, 9H), 0.83 (t, 9H, J=7.9 Hz), 0.51 (q, 6H, J=7.9 Hz), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), −0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 185.5, 144.1, 144.0, 128.2, 125.1, 125.0, 123.5, 94.7, 81.4, 81.3, 73.7, 71.3, 69.9, 68.4, 56.4, 39.4, 30.8, 28.9, 27.6, 25.8, 25.7, 25.1, 23.7, 18.9, 18.1, 18.0, 6.6, 4.6, −4.5, −4.8, −4.9, −5.1; IR ($CHCl_3$): 3308, 2955, 2933, 2881, 2858, 2213, 1668, 1466, 1255, 1217, 1100, 1080, 837 cm^{-1}; MS (FAB) m/z (relative intensity) 697 (MH^-, 20), 565 (32), 153 (64), 131 (100); HRMS (FAB^-) calcd for $C_{40}H_{69}O_4Si_3$ (MH^-) 697.4504, found 697.4517.

4.1.25. (1*R*,4*E*,6*E*,11*R*)-11-(*tert*-Butyldimethylsilyloxy)-1-[3-[(1*S*)-1-(*tert*-butyldimethylsilyloxy)-3-butynyl]-phenyl]-1-triethylsilyloxy-4,6-dodecadien-3-one (31). (Entry 1): To a solution of ynone **7** (46.0 mg, 0.658 mmol) in toluene (0.3 mL) was added triphenylphosphine (17.2 mg, 0.0658 mmol) and the mixture was stirred at 100 °C for 6 h. After removal of solvent under reduced pressure, purification on silica gel (elution: 30:1 hexane/ethyl acetate) furnished **31** as a colorless oil (14.5 mg, 31%). (Entry 2): To a solution of ynone **7** (50.0 mg, 0.0715 mmol) in toluene (0.35 mL) was added tri-*n*-butylphosphine (0.018 mL, 0.072 mmol) and the mixture was stirred at room temperature for 1 h. The same work-up described above furnished **31** as a colorless oil (10.0 mg, 20%). (Entry 3): To a solution of ynone **7** (80.0 mg, 0.114 mmol) in THF–toluene (0.25–0.25 mL) was added tri-*n*-butylphosphine (0.0030 mL, 0.011 mmol) and the mixture was stirred at room temperature for 5 h. The same work-up described above furnished **31** as a colorless oil (22.6 mg, 28%). (Entry 4): To a solution of ynone **7** (34.0 mg, 0.0486 mmol) in toluene (0.24 mL) was added 1,4-bis(diphenylphosphino)butane (41.5 mg, 0.097 mmol) and the mixture was stirred at room temperature for 1 h. The same work-up described above furnished **31** as a colorless oil (10.5 mg, 30%). (Entry 5): To a solution of ynone **7** (570 mg, 0.815 mmol) in a 1/1 mixture of THF and toluene (4 mL) was added 1,4-bis(diphenylphosphino)butane (69.5 mg, 0.163 mmol), and the mixture was stirred at room temperature for 6 h. The same work-up described above furnished **31** as a colorless oil (280 mg, 49%) along

with the recovered starting material **7** (170 mg, 30%). $[\alpha]_D^{22}=+35.5$ ($c=1.09$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 7.44–7.18 (m, 4H), 7.11 (dd, 1H, $J=15.6$, 9.8 Hz), 6.16 (m, 2H), 6.06 (d, 1H, $J=15.6$ Hz), 5.21 (dd, 1H, $J=8.4$, 4.1 Hz), 4.80 (t, 1H, $J=6.3$ Hz), 3.78 (m, 1H), 3.10 (dd, 1H, $J=8.4$, 14.7 Hz), 2.70 (dd, $J=4.1$, 14.7 Hz), 2.57 (ddd, 1H, $J=16.7$, 6.3, 2.6 Hz), 2.47 (ddd, 1H, $J=16.7$, 6.4, 2.6 Hz), 2.18 (m, 2H), 1.93 (t, 1H, $J=2.6$ Hz), 1.62–1.46 (m, 1H), 1.47–1.35 (m, 3H), 1.12 (d, 3H, $J=6.1$ Hz), 0.89 (s, 9H), 0.88 (s, 9H), 0.81 (t, 9H, $J=7.9$ Hz), 0.48 (q, 6H, $J=7.9$ Hz), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), −0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 198.8, 145.7, 144.8, 144.0, 143.8, 129.1, 128.1, 125.0, 124.9, 123.5, 81.6, 73.8, 71.2, 69.8, 68.3, 51.2, 39.0, 33.1, 30.8, 25.8, 25.7, 24.8, 23.8, 18.2, 18.0, 6.6, 4.6, −4.5, −4.8, −5.1; IR ($CHCl_3$): 3307, 2956, 2932, 2880, 2858, 1633, 1592, 1467, 1364, 1255, 1101, 1004, 939, 909, 837 cm^{-1}; MS (FAB) *m/z* (relative intensity) 697 (MH^-, 6.5), 565 (13), 153 (100), 131 (93); HRMS (FAB^-) calcd for $C_{40}H_{69}O_4Si_3$ (MH^-) 697.4504, found 697.4512.

4.1.26. (4*R*,6*R*)-4-[3-[(1*S*)-1-(*tert*-Butyldimethylsilyloxy)-3-butynyl]phenyl]-6-[(1*E*,3*E*,8*R*)-8-(*tert*-butyldimethylsilyloxy)nona-1,3-dienyl]-2,2-dimethyl-1,3-dioxane (32). Dienone **31** (630 mg, 0.901 mmol) was dissolved in a mixture of AcOH/THF/H_2O (8:8:1, 10 mL), and the solution was stirred at room temperature for 24 h. After being quenched with a saturated sodium bicarbonate solution, the mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 3:1 hexane/ethyl acetate) to give alcohol (440 mg, 83%) as a colorless oil; $[\alpha]_D^{20}=+12$ ($c=0.96$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 7.34–7.19 (m, 4H), 7.11 (dd, 1H, $J=15.6$, 9.8 Hz), 6.15 (m, 2H), 6.03 (d, 1H, $J=15.6$ Hz), 5.16 (m, 1H), 4.79 (t, 1H, $J=6.4$ Hz), 3.73 (m, 1H), 2.90 (m, 2H), 2.53 (ddd, 1H, $J=16.7$, 6.3, 2.6 Hz), 2.43 (ddd, 1H, $J=16.7$, 6.4, 2.6 Hz), 2.15 (m, 2H), 1.91 (t, 1H, $J=2.6$ Hz), 1.62–1.46 (m, 1H), 1.47–1.35 (m, 3H), 1.08 (d, 3H, $J=6.1$ Hz), 0.89 (s, 9H), 0.88 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), −0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 200.6, 146.7, 144.5, 144.2, 142.9, 128.8, 128.3, 127.9, 125.0, 124.7, 123.2, 81.6, 73.6, 70.0, 69.9, 68.2, 48.4, 39.0, 33.1, 30.9, 25.8, 25.7, 24.7, 23.7, 18.1, 18.0, −4.5, −4.9, −5.0; IR ($CHCl_3$): 3672, 3510, 3307, 2955, 2932, 2858, 1633, 1593, 1467, 1362, 1255, 1105, 1002, 937, 909, 837 cm^{-1}; MS (FAB) *m/z* (relative intensity) 607 ($M+Na^+$, 28), 73 (100); HRMS (FAB^+) calcd for $C_{34}H_{56}NaO_4Si_2$ ($M+Na^+$) 607.3615, found 607.3621. To a solution of tetramethylammonium triacetoxyborohydride (1.42 g, 6.01 mmol) in acetonitrile (3 mL) was added acetic acid (3 mL), and the mixture was stirred at room temperature for 30 min. To the cooled mixture at −40 °C was added a solution of the obtained alcohol (440 mg, 0.752 mmol) in acetonitrile (2.2 mL) via cannula. After being stirred at −40 °C for 18 h, the mixture was quenched with a 0.5 N sodium potassium tartrate solution and then diluted with chloroform. The aqueous layer was extracted with chloroform and the combined extracts were washed with a saturated sodium bicarbonate solution and brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 2:1 hexane/ethyl acetate) to give alcohols as a diastereomixture (374 mg, 85%); $[\alpha]_D^{22}=22.1$ ($c=1.00$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 7.43–7.19 (m, 4H), 6.19 (dd, 1H, $J=15.3$, 10.4 Hz), 6.03 (dd, 1H, $J=14.8$, 10.4 Hz), 5.66 (m, 2H), 5.03 (m, 1H), 4.82 (t, 1H, $J=6.1$ Hz), 4.37 (m, 1H), 3.78 (m, 1H), 3.14 (br, 1H), 2.62 (br, 1H), 2.58 (ddd, 1H, $J=16.6$, 6.1, 2.6 Hz), 2.47 (ddd, 1H, $J=16.6$, 6.1, 2.6 Hz), 2.07 (m, 2H), 2.00–1.90 (m, 2H), 1.94 (t, 1H, $J=2.6$ Hz), 1.52–1.32 (m, 4H), 1.11 (d, 3H, $J=6.1$ Hz), 0.89 (s, 9H), 0.88 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), −0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 144.2, 144.1, 135.6, 132.6, 130.9, 129.4, 128.3, 124.9, 124.7, 123.2, 81.6, 73.7, 71.7, 70.1, 70.0, 68.4, 44.5, 39.1, 32.6, 30.9, 25.8, 25.7, 25.3, 23.7, 18.2, 18.1, −4.5, −4.8, −4.9, −5.0; IR ($CHCl_3$): 3601, 3503, 3307, 2931, 2858, 1467, 1378, 1255, 1105, 992, 909, 837 cm^{-1}; MS (FAB) *m/z* (relative intensity) 609 ($M+Na^+$, 18), 249 (8), 73 (100); HRMS (FAB^+) calcd for $C_{34}H_{58}NaO_4Si_2$ ($M+Na^+$) 609.3771, found 609.3766. To a solution of the obtained diol (370 mg, 0.640 mmol) in dichloromethane (6.0 mL) were successively added 2,2-dimethoxypropane (0.784 mL, 6.40 mmol) and a catalytic amount of pyridinium *p*-toluenesulfonate at 0 °C and the reaction mixture was stirred for 1 h. After being poured into a saturated sodium bicarbonate solution, the aqueous layer was extracted with diethyl ether. The combined extracts were washed with brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 20:1 hexane/ethyl acetate) to furnish a major diastereomer **32** (288 mg, 74%) as a colorless oil along with a minor diastereomer (21.4 mg, 5.6%). **32**; $[\alpha]_D^{21}=3.0$ ($c=0.70$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 7.43–7.19 (m, 4H), 6.22 (dd, 1H, $J=15.3$, 10.4 Hz), 6.04 (dd, 1H, $J=14.8$, 10.4 Hz), 5.68 (m, 2H), 4.93 (m, 1H), 4.83 (t, 1H, $J=6.1$ Hz), 4.52 (m, 1H), 3.77 (m, 1H), 2.57 (ddd, 1H, $J=16.6$, 6.1, 2.6 Hz), 2.47 (ddd, 1H, $J=16.6$, 6.1, 2.6 Hz), 2.10–2.00 (m, 4H), 1.96 (t, 1H, $J=2.6$ Hz), 1.52–1.32 (m, 4H), 1.47 (s, 3H), 1.46 (s, 3H), 1.11 (d, 3H, $J=6.1$ Hz), 0.89 (s, 9H), 0.88 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), −0.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 144.1, 142.4, 135.6, 131.4, 130.7, 129.6, 128.1, 124.9, 124.8, 123.4, 100.7, 81.8, 73.6, 69.9, 68.4, 68.3, 67.7, 39.3, 39.2, 32.6, 31.0, 25.9, 25.8, 25.6, 25.4, 25.1, 23.9, 18.2, 18.1, −4.3, −4.7, −4.8, −4.9; IR ($CHCl_3$): 3307, 2931, 2858, 1467, 1378, 1255, 1105, 992, 909, 837 cm^{-1}; MS (FAB) *m/z* (relative intensity) 649 ($M+Na^+$, 3.0), 587 (4.0), 176 (8.2), 73 (100); HRMS (FAB^+) calcd for $C_{37}H_{62}NaO_4Si_2$ ($M+Na^+$) 649.4084, found 649.4077.

4.1.27. (2*Z*,4*E*,7*S*)-7-*tert*-Butyldimethylsilyloxy-7-[3-[(4*R*,6*R*)-6-[(1*E*,3*E*,8*R*)-8-(*tert*-butyldimethylsilyloxy)nona-1,3-dienyl]-2,2-dimethyl-1,3-dioxan-4-yl]]phenylhepta-2,4-dienoic acid ethyl ester (33). (Entry 1): To a cooled solution of alkyne **32** (100 mg, 0.159 mmol) in THF (1.9 mL) was added a 1.58 M solution *n*-butyllithium in *n*-hexane (0.190 mmol, 0.120 mL). The solution was stirred at −78 °C for 1 h, before being quenched with a solution of cyanogen bromide in THF (0.190 mmol, 0.190 mL). The reaction mixture was stirred at −78 °C for an additional hour and then allowed to warm to −40 °C. The reaction mixture was then poured into a sodium hydroxide solution (1 M) and extracted with diethyl ether. The combined organic layers were dried and filtered through a pad of Celite. After concentration in vacuo, the crude bromoalkyne (87.0 mg, 0.123 mmol) was dissolved in benzene (1.4 mL).

The addition of bis(triphenylphosphine)palladium(II)-chloride (5.4 mg, 0.5 mol%) to the solution was followed by a slow addition of tri-*n*-butyltinhydride (0.066 mL, 0.34 mmol) over 5 min. The solution was stirred at room temperature for 30 min before removal of the solvent under reduced pressure. The crude vinyl stannane was dissolved in DMF (0.43 mL) and to the solution were added (*Z*)-3-iodopropenoate (15.0 mg, 0.0664 mmol), $Pd_2(dba)_2$ (3.1 mg, 0.0039 mmol), and diisopropylethylamine (0.011 mL, 0.064 mmol). The whole was stirred at room temperature for 1 h before being quenched with a saturated sodium bicarbonate solution. The organic layer was extracted with ether. The extract was washed with water and brine, dried, condensed in vacuo. The residue was purified by SiO_2 column chromatography (elution: 10:1 hexane/ethyl acetate) to give **33** as a colorless oil (15.6 mg, 32% in 3 steps). (Entry 4): To a cooled solution of alkyne **32** (110 mg, 0.159 mmol) in THF (1.7 mL) was added a 1.58 M solution of *n*-butyllithium (0.190 mmol, 0.120 mL) in *n*-hexane, and the mixture was stirred at −78 °C for 1 h. After a 1 M solution of cyanogen bromide (0.190 mmol, 0.190 mL) in THF was added to the mixture, the reaction mixture was stirred at −78 °C for 1 h and then allowed to warm to −40 °C over a 10 min period. The mixture was poured into a 1 M sodium hydroxide solution and the resulting mixture was extracted with diethyl ether. The combined extracts were washed with brine, dried, and filtered through a pad of Celite. The solvent was removed under reduced pressure to provide a crude product, which was dissolved in benzene (1.4 mL). To the mixture was added bis(triphenylphosphine)palladium(II)chloride (6.1 mg, 0.5 mol%), which was followed by a slow addition of tri-*n*-butyltinhydride (0.060 mL, 0.31 mmol) over a 5 min period. After the mixture was stirred at room temperature for 30 min and concentrated in vacuo, the obtained vinylstannane was dissolved in NMP (1.4 mL). To the mixture were successively added (*Z*)-3-iodopropenoate (38.4 mg, 0.170 mmol) and copper (I) 2-thiophenecarboxylate (40.5 mg, 0.212 mmol) at 0 °C. The reaction mixture was then diluted with ether and filtered through a plug of alumina to remove copper salts and tri-*n*-butyltin thiophene-2-carboxylate. The combined filtrates were washed with brine, dried, and the concentrated in vacuo. Several drops of triethylamine were added to the residue before purification by SiO_2 column chromatography (elution: 100:1:0.5 to 100:20:0.5 hexane/ethyl acetate/triethylamine) to give **33** as a colorless oil (72.6 mg, 58%). $[\alpha]_D^{23}=1.50$ ($c=1.75$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 7.38 (dd, 1H, $J=11.3$, 11.3 Hz), 7.33–7.10 (m, 4H), 6.51 (dd, 1H, $J=11.3$, 11.3 Hz), 6.21 (dd, 1H, $J=15.1$, 10.5 Hz), 6.03 (m, 2H), 5.68 (m, 2H), 5.57 (d, 1H, $J=11.3$ Hz), 4.91 (m, 1H), 4.72 (m, 1H), 4.52 (m, 1H), 4.17 (q, 2H, $J=7.0$ Hz), 3.76 (m, 1H), 2.53 (m, 2H), 2.03 (m, 4H), 1.48 (s, 3H), 1.46 (s, 3H), 1.44–1.31 (m, 4H), 1.28 (t, 3H, $J=7.0$ Hz), 1.10 (d, 3H, $J=6.1$ Hz), 0.87 (s, 9H), 0.86 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H), −0.01 (s, 3H), −0.15 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 166.5, 145.1, 145.0, 142.6, 141.7, 135.7, 131.4, 130.8, 129.7, 129.0, 128.3, 124.7, 124.6, 123.4, 116.1, 100.7, 74.7, 68.4, 68.3, 67.8, 59.8, 44.5, 39.4, 39.2, 32.6, 25.9, 25.7, 25.6, 25.4, 25.1, 23.8, 18.1, 18.0, 14.2, −4.5, −4.7, −4.8, −5.0; IR ($CHCl_3$): 2955, 2931, 2857, 1706, 1638, 1602, 1467, 1378, 1255, 1231, 1074, 996, 904, 836 cm^{-1}; MS (FAB) *m/z* (relative intensity) 749 ($M+Na^+$, 5.0), 587 (10), 247 (9.2), 73 (100); HRMS (FAB^+) calcd for $C_{42}H_{70}NaO_6Si_2$ ($M+Na^+$) 749.4609, found 749.4615.

4.1.28. (2*Z*,4*E*,7*S*)-7-[3-[(4*R*,6*R*)-6-[(1*E*,3*E*,8*R*)-8-Hydroxynona-1,3-dienyl]-2,2-dimethyl-1,3-dioxan-4-yl]]-phenyl-7-(1-methoxy-1-methylethoxy)hepta-2,4-dienoic acid ethyl ester (34). To a solution of **33** (76.0 mg, 105 μmol) in THF (1.0 mL) was added a 1 M solution of tetra-*n*-butylammonium fluoride (0.21 mL, 0.21 mmol) in THF at 0 °C, and the reaction mixture was stirred for 1 h. The reaction mixture was quenched with a mixture of ether and a saturated ammonium chloride solution and then the resulting mixture was poured into a saturated sodium bicarbonate solution. The mixture was extracted with diethyl ether several times. The combined extracts were washed with brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 4:1 hexane/ethyl acetate) to give alcohol (58.9 mg, 92%) as a colorless oil; $[\alpha]_D^{26}=+8.60$ ($c=1.01$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ:7.48 (dd, 1H, $J=11.3$, 11.3 Hz), 7.41–7.21 (m, 4H), 6.54 (dd, 1H, $J=11.3$, 11.3 Hz), 6.22 (dd, 1H, $J=15.3$, 10.4 Hz), 6.05 (m, 2H), 5.69 (m, 2H), 5.60 (d, 1H, $J=11.3$ Hz), 4.93 (m, 1H), 4.79 (m, 1H), 4.53 (m, 1H), 4.17 (q, 2H, $J=7.3$ Hz), 3.78 (m, 1H), 2.65 (m, 2H), 2.14 (br, 1H), 2.06 (m, 4H), 1.48 (s, 6H), 1.45–1.32 (m, 4H), 1.29 (t, 3H, $J=7.3$ Hz), 1.11 (d, 3H, $J=5.8$ Hz), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$) δ: 166.5, 144.5, 144.1, 142.9, 140.3, 135.7, 131.5, 130.6, 129.6, 129.5, 128.7, 125.5, 124.9, 123.4, 116.7, 100.8, 73.6, 68.4, 68.3, 67.8, 59.9, 42.6, 39.4, 39.1, 32.6, 25.8, 25.5, 25.3, 25.0, 23.8, 18.0, 14.2, −4.5, −4.8; IR ($CHCl_3$): 3686, 3026, 2993, 2932, 2858, 1705, 1603, 1466, 1377, 1193, 994 cm^{-1}; MS (FAB) *m/z* (relative intensity) 635 ($M+Na^+$, 64), 211 (11), 176 (12), 91 (12), 73 (100); HRMS (FAB^+) calcd for $C_{36}H_{56}NaO_6Si$ ($M+Na^+$) 635.3744, found 635.3738. To a cooled solution of the obtained alcohol (58.9 mg, 96.2 μmol) in dichloromethane (1.0 mL) were added 2-methoxypropene (18.4 μL, 193 μmol) and a catalytic amount of pyridinium *p*-toluenesulfonate at 0 °C and the mixture was stirred for 1 h. After being poured into a saturated sodium bicarbonate solution, the mixture was extracted with diethyl ether. The combined extracts were washed with brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 85:15:0.5 hexane/ethyl acetate/triethylamine) to furnish ether (53.2 mg, 82%) as a colorless oil; $[\alpha]_D^{31}=+7.3$ ($c=0.74$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ:7.36 (dd, 1H, $J=11.3$, 11.3 Hz), 7.30–7.11 (m, 4H), 6.48 (dd, 1H, $J=11.3$, 11.3 Hz), 6.22 (dd, 1H, $J=15.1$, 10.5 Hz), 6.04 (dd, 1H, $J=15.0$, 10.5 Hz), 5.94 (m, 1H), 5.69 (m, 2H), 5.56 (d, 1H, $J=11.3$ Hz), 4.92 (m, 1H), 4.76 (t, 1H, $J=6.6$ Hz), 4.52 (m, 1H), 4.17 (q, 2H, $J=7.2$ Hz), 3.78 (m, 1H), 3.08 (s, 3H), 2.66 (ddd, 1H, $J=14.2$, 7.3, 7.2 Hz), 2.55 (ddd, 1H, $J=14.2$, 6.9, 6.6 Hz), 2.04 (m, 4H), 1.48 (s, 3H), 1.47 (s, 3H), 1.44–1.31 (m, 4H), 1.38 (s, 3H), 1.28 (t, 3H, $J=7.2$ Hz), 1.12 (s, 3H), 1.11 (d, 3H, $J=6.1$ Hz), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$) δ: 166.5, 144.8, 144.5, 142.6, 141.1, 135.7, 131.4, 130.7, 129.6, 129.0, 128.4, 125.3, 124.6, 124.0, 116.2, 101.1, 100.7, 72.8, 68.4, 68.3, 67.7, 59.8, 49.3, 42.6, 39.4, 39.1, 32.6, 26.0, 25.8, 25.5, 25.3, 25.1, 25.0, 23.8, 18.1, 14.2, −4.5, −4.8; IR ($CHCl_3$): 2994, 2933, 2850, 1707, 1634, 1603, 1459, 1378, 1233, 1217, 1199, 1073, 1014, 995 cm^{-1}; MS (FAB) *m/z* (relative

intensity) 707 ($M+Na^+$, 28), 176 (13), 173 (8.0), 73 (100); HRMS (FAB^+) calcd for $C_{40}H_{64}NaO_7Si$ ($M+Na^+$) 707.4319, found 707.4311. To a solution of the obtained ether (53.2 mg, 78.6 μmol) in THF (0.8 mL) was added a 1/1 mixture of tetra-*n*-butylammonium fluoride and acetic acid (1.2 mL) at room temperature. After being stirred for 24 h and poured into a saturated sodium bicarbonate solution, the mixture was extracted with diethyl ether. The combined extracts were washed with brine, dried, and then concentrated in vacuo. The residue was purified by SiO_2 column chromatography (elution: 80:20:0.5 hexane/ethyl acetate/triethylamine) to give **34** (40.0 mg, 89%) as a colorless oil; $[\alpha]_D^{31}=+11$ ($c=0.74$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ:7.35 (dd, 1H, $J=11.3$, 11.3 Hz), 7.30–7.11 (m, 4H), 6.48 (dd, 1H, $J=11.3$, 11.3 Hz), 6.22 (dd, 1H, $J=15.3$, 10.4 Hz), 6.05 (dd, 1H, $J=15.3$, 10.4 Hz), 5.94 (m, 1H), 5.69 (m, 2H), 5.56 (d, 1H, $J=11.3$ Hz), 4.92 (m, 1H), 4.76 (t, 1H, $J=6.4$ Hz), 4.52 (m, 1H), 4.17 (q, 2H, $J=7.2$ Hz), 3.79 (m, 1H), 3.08 (s, 3H), 2.66 (ddd, 1H, $J=14.1$, 7.1, 7.1 Hz), 2.55 (ddd, 1H, $J=14.1$, 6.9, 6.7 Hz), 2.06 (m, 4H), 1.49 (s, 3H), 1.49 (s, 3H), 1.44–1.31 (m, 4H), 1.40 (s, 3H), 1.28 (t, 3H, $J=7.2$ Hz), 1.19 (d, 3H, $J=6.1$ Hz), 1.12 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 166.5, 144.8, 144.5, 142.6, 141.1, 135.3, 131.3, 130.9, 129.9, 129.0, 128.4, 125.3, 124.6, 124.0, 116.2, 101.2, 100.7, 72.8, 68.3, 68.0, 67.7, 59.8, 49.3, 42.6, 39.4, 38.7, 32.5, 26.0, 25.5, 25.3, 25.1, 25.0, 23.5, 14.2; IR ($CHCl_3$): 3700, 2995, 2935, 2354, 1708, 1641, 1603, 1378, 1187, 1066, 1034, 994, 908 cm^{-1}; MS (FAB) *m/z* (relative intensity) 593 ($M+Na^+$, 33), 176 (14), 173 (6.2), 73 (100); HRMS (FAB^+) calcd for $C_{34}H_{50}NaO_7$ ($M+Na^+$) 593.3454, found 593.3449.

4.1.29. (2*R*,4*R*,5*E*,7*E*,12*R*,15*E*,17*E*,20*S*)-2,4-Dihydroxy-20-(1-methoxy-1-methylethoxy)-13-oxabicyclo[19.3.1]-pentacosa-1(25),5,7,15,17,21,23-heptaen-14-one dimethylacetal (36). A solution of ester **34** (35.0 mg, 61.3 μmol) in a 1/1/1 mixture of THF, ethanol, and 3 N KOH (0.6 mL) was heated to 60 °C for 2 h. After the solvent was evaporated under reduced pressure, diethyl ether and a saturated ammonium chloride solution were added to the residue. The resulting mixture was extracted with diethyl ether. The combined extracts were dried and filtered through a pad of Celite. Triethylamine was added to the filtrates before evaporation of the solvents. To a solution of the triethylamine salt in THF (0.6 mL) was added 2,4,6-trichlorobenzoyl chloride (30.0 mg, 122 μmol) at 0 °C, and the reaction mixture was stirred at room temperature for 4 h. After removal of the solvents, DMAP (45.0 mg, 368 μmol) was added to a solution of the obtained residue in toluene (6.0 mL) at room temperature. The mixture was stirred for 1 h. After the solvent was removed under reduced pressure, the residue was purified by SiO_2 column chromatography (elution: 85:15:0.5 hexane/ethyl acetate/triethylamine) to give **36** (14.0 mg, 44% in 3 steps); $[\alpha]_D^{31}=+63$ ($c=0.90$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 7.44–7.28 (m, 3H), 7.05 (dd, 1H, $J=11.1$, 11.1 Hz), 6.84 (s, 1H), 6.22–5.91 (m, 3H), 5.74 (d, 1H, $J=15.9$ Hz), 5.70 (m, 1H), 5.70 (m, 1H), 5.60 (m, 1H), 5.51 (m, 1H), 4.90 (m, 2H), 4.66 (dd, 1H, $J=9.8$, 4.0 Hz), 4.53 (m, 1H), 3.15 (s, 3H), 2.55 (m, 2H), 2.11 (m, 2H), 1.93 (t, 2H, $J=7.2$ Hz), 1.48 (s, 6H), 1.44–1.31 (m, 4H), 1.40 (s, 3H), 1.20 (d, 3H, $J=6.4$ Hz), 1.12 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 166.5, 144.1, 143.4, 142.2, 139.5, 134.6, 131.3, 131.2, 130.7, 130.0, 129.2, 124.4, 124.3, 124.0, 120.5, 101.2, 100.5, 73.0, 70.4, 67.9, 67.8, 49.2, 41.9, 39.5, 34.1, 31.3, 26.4, 26.1, 25.7, 24.9, 23.5, 19.6; IR ($CHCl_3$): 3002, 2935, 2870, 2366, 2340, 1701, 1640, 1615, 1445, 1379, 1249, 1201, 1151, 1111, 1074, 1034, 996, 908, 739 cm^{-1}; MS (FAB) *m/z* (relative intensity) 547 ($M+Na^+$, 38), 176 (10), 73 (100); HRMS (FAB^+) calcd for $C_{32}H_{44}NaO_6$ ($M+Na^+$) 547.3036, found 547.3032.

4.1.30. (2*R*,4*R*,5*E*,7*E*,12*R*,15*E*,17*E*,20*S*)-2,4,20-Trihydroxy-13-oxabicyclo[19.3.1]pentacosa-1(25),5,7,15,17,21,23-heptaen-14-one (1b). The lactone **36** (9.0 mg, 17 μmol) was dissolved in wet methanol (0.3 mL) and the mixture was treated with a catalytic amount of PPTS. After being stirred at room temperature for 1 h, the mixture was concentrated in vacuo and the resulting residue was purified by SiO_2 column chromatography (elution: 1:2 hexane/ethyl acetate) to give **1b** (4.3 mg, 61%) as a white amorphous; $[\alpha]_D^{23}=93$ ($c=0.40$, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 7.45–7.30 (m, 2H), 7.19 (m, 2H), 7.08 (dd, 1H, $J=15.3$, 11.0 Hz), 6.15 (m, 2H), 6.02 (m, 1H), 5.93 (m, 1H), 5.72 (d, 1H, $J=15.3$ Hz), 5.61 (m, 2H), 5.03 (m, 1H), 4.97 (m, 1H), 4.92 (dd, 1H, $J=6.7$, 2.4 Hz), 4.41 (m, 1H), 3.56 (br, 1H), 2.79 (m, 1H), 2.69 (br, 1H), 2.62 (m, 1H), 2.21 (br, 1H), 2.09 (m, 2H), 1.98 (m, 2H), 1.55–1.37 (m, 4H), 1.22 (d, 3H, $J=6.4$ Hz); ^{13}C NMR ($CDCl_3$) δ: 166.7, 143.9, 137.7, 134.6, 132.6, 131.7, 130.7, 130.3, 129.2, 129.0, 128.4, 124.9, 124.8, 123.7, 121.1, 73.4, 71.7, 70.5, 70.4, 44.1, 41.8, 34.4, 31.5, 24.1, 19.9; IR ($CHCl_3$): 3559, 3156, 2254, 1794, 1697, 1642, 1466, 1381, 1096, 991 cm^{-1}; MS (FAB) *m/z* (relative intensity) 435 ($M+Na^+$, 10), 281 (10), 207 (10), 176 (19), 147 (32), 73 (93), 55 (100); HRMS (FAB^+) calcd for $C_{25}H_{32}NaO_5$ ($M+Na^+$) 435.2147, found 435.2154.

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