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Total Synthesis of (+)-Goniodenin

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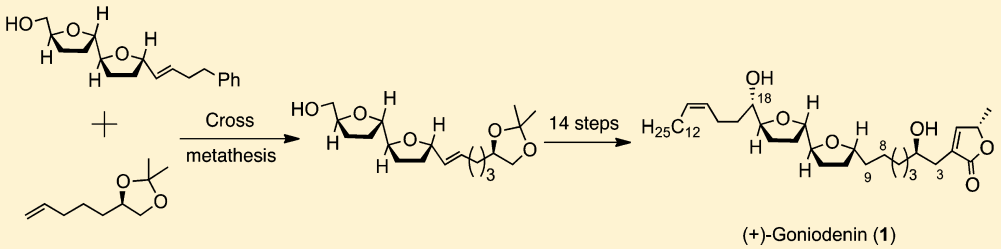
Supporting Information



ABSTRACT: Goniodenin is a lipophilic polyketide originating from plant sources and which possesses a potent cytotoxic activity against cancer cell lines. The first total synthesis of (+)-goniodenin has been achieved in 23 steps from (*R*)-glycidol. The synthetic sequence featured a cross metathesis for the formation of the C_8−C_9 bond and installation of the terminal γ-butenolactone ring unit by the alkylation of α-phenylthio-γ-butyrolactone with the corresponding C_3-*O*-triflate. The stereogenic center at C_{18} carbon was created by Hiyama−Fujita reduction of the corresponding ketone with high diastereoselectivity.

INTRODUCTION

Annonaceous acetogenins are waxy substances consisting of a long chain fatty acid with a 2-propanol unit at the C_2 position that forms a γ-butenolactone unit. They are found commonly in the Annonaceae plant family.[1] Their complex structures and diverse biological activities including anticancer, immunosuppressive, pesticidal, and other properties have attracted synthetic chemists[2] and medical scientists.[3] Goniodenin (**1**) is an acetogenin isolated from the bark of *Goniothalamus giganteus* (Annonaceae) in 1995 by McLaughlin et al.[4] It consists of a linear C-34 unbranched fatty acid with a *trans-threo-trans*-bis-THF ring unit in the central part and a methyl-substituted γ-butenolactone unit at the right terminus. This natural product is the only acetogenin that possesses an alkenyl unit on the linear carbon chain (Figure 1). Additionally, goniocin (**2**) is a related acetogenin that has been isolated from the same plant together with **1** in 1994 by the same group.[5] Although **1** and **2** possess the same methyl-substituted γ-butenolactone unit with an *S*-stereogenic carbon center, the remaining parts of the molecule including the contiguous THF ring and the adjacent hydroxy group for **1** and those for **2** are displayed as mirror images. The total synthesis of **2** was reported by Sinha and Keinan et al. in 1998[6] and recently by our group in 2016.[7]

Several Annonaceous acetogenins possessing a *trans-threo-trans*-bis-THF ring unit on the C_{10} to C_{17} carbon chain and an additional hydroxy group adjacent to the ring at C_{18} are shown in Figure 2. They consist of two pairs of the enantiomeric isomers (**I** and *ent*-**I** and also **II** and *ent*-**II**). Each of the isomers is as a mirror image in *trans-threo-trans*-bis-THF ring and the adjacent C_{18} *threo*-hydroxy group. Goniodenin belongs to an *ent*-**I** type structure having 18*S*,17*S*,14*S*,13*S*,10*R* stereogeic centers on the carbon chain. The production of such diverse structures in nature is quite interesting.[8]

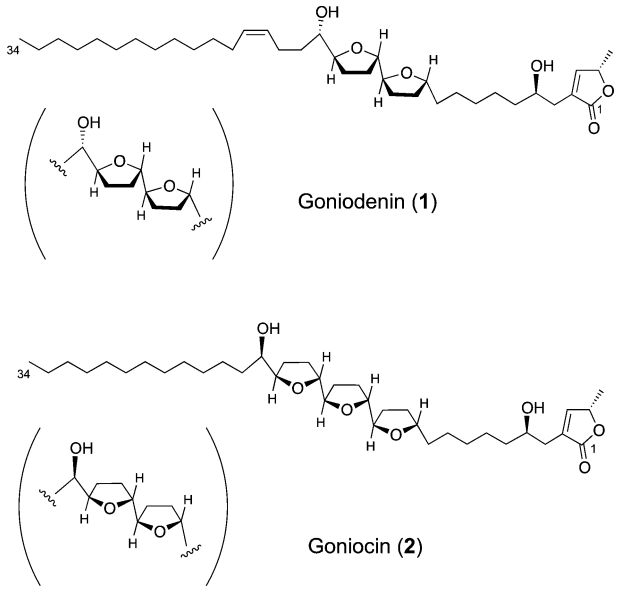


Figure 1. Goniodenin and goniocin.

A general biosynthetic hypothesis of acetogenins was proposed by McLaughlin et al. in 1996,[9] and for **1** and **2** specifically by Sinha and Keinan et al. in 1998.[6] A ring-opening of *cis*-epoxides would undergo a cyclization to construct a contiguous THF ring unit in a cascade sequence triggered by the nucleophilic attack of the internal hydroxy group or an external water molecule.[10,11] The absolute structure of **1**[12] was determined by the Mosher analysis of the C_4 and C_{18} secondary

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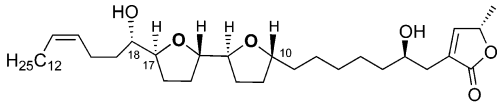


Goniodenin (**1**)

Acetogenins with trans-threo-trans-bis-THF ring

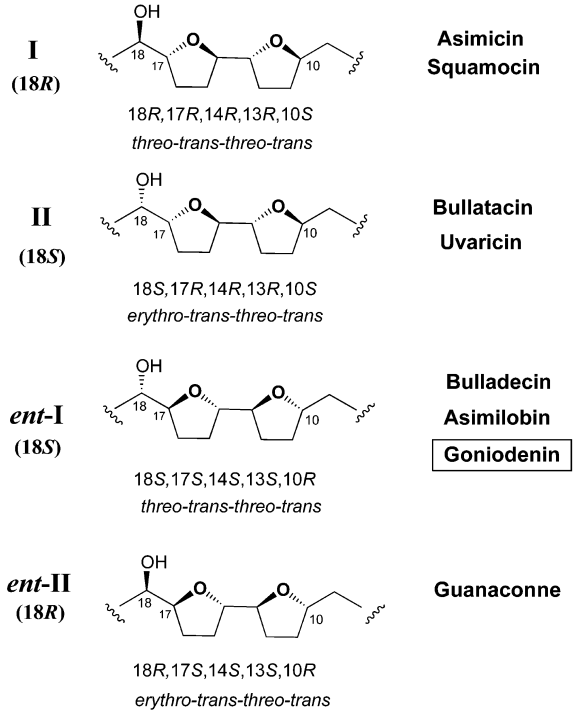


Figure 2. Several acetogenins that have a *trans-threo-trans*-bis-THF ring unit.

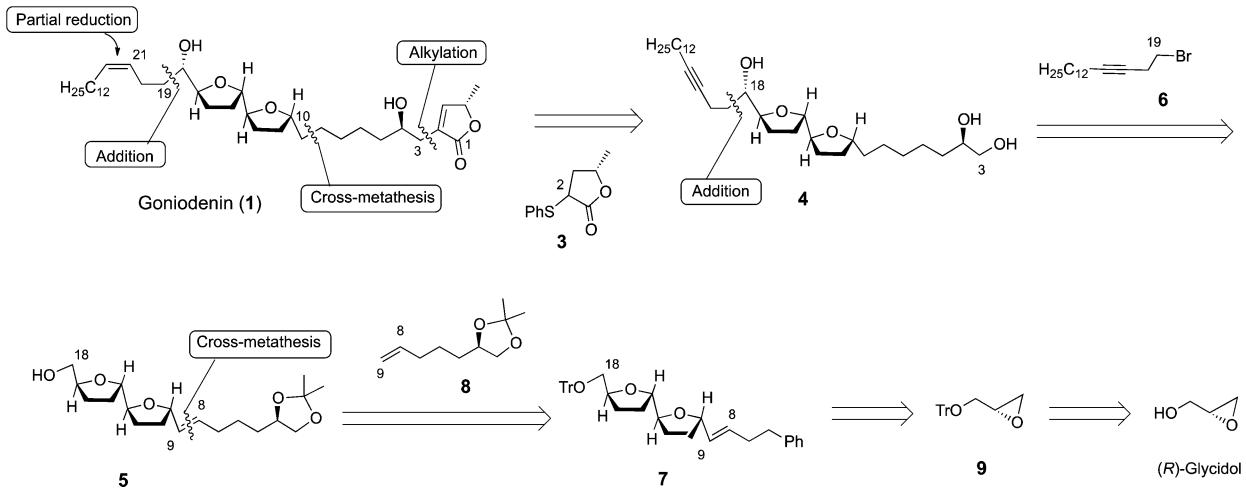
hydroxyl-carbon centers. Asymmetric synthesis would be necessary to confirm the molecular structure of **1**. Beyond the synthetic challenge of these unique structures in comparison with **2**, goniodenin has a great intrinsic value with its highly potent cytotoxic activity in growth inhibition of cancer cells.[13] In this paper, we report the first total synthesis of goniodenin.

RESULTS AND DISCUSSION

The retrosynthesis of **1** is outlined in Scheme 1. We analyzed synthetic route and envisaged the following points: i, because goniodenin possesses a *Z*-alkene in the carbon chain, reduction of the C_8−C_9 double bond should be performed before an introduction of the alkynyl carbon chain unit; ii, due to the instability of the γ-butenolactone unit under basic conditions,[14] the Grignard addition at the C_{18} carbonyl group must be executed in the absence of the γ-butenolactone unit; iii, the five stereogenic centers between C_{10} to C_{18} consisting of 10*R*,13*S*,14*S*,17*S*,18*S* chiral carbons could be synthesized by the same method reported in the previous synthesis of goniocin.[7] Because the γ-butenolactone unit **3**[15] must be introduced at a late stage for the synthesis, we therefore set compound **4** as a requisite precursor for the introduction of the lactone unit. Compound **4** could be formed by the coupling of **5** with **6**. The cross-metathesis of **7** with the known alkene **8**[16] would afford **5**. Because the corresponding enantiomer of *ent*-**7** has been prepared from (*R*)-*O*-tritylglycidol, the compound **7** would be prepared by the same procedure from (*R*)-glycidol via (*S*)-*O*-tritylglycidol **9**.[17]

The preparation of C3 to C34 carbon chain unit is shown in Scheme 2. The synthesis commenced with the *O*-tritylation of (*R*)-glycidol with trityl chloride to afford (*S*)-*O*-tritylglycidol **9** in 90% yield. The intermediate **7** was prepared from **9** in 28% overall yield by the same seven-step sequence developed for the synthesis of *ent*-**7**.[7] Acid-catalyzed deprotection of the *O*-trityl group of **7** gave **10** in quantitative yield. Cross-metathesis of **10** with **8** in the presence of Grubbs's (II) catalyst gave **5** in 58% yield. Reduction of the double bond was carried out by PtO_2-catalyzed hydrogenation in 90% yield to give **11**. Swern oxidation of the primary alcohol resulted in the quantitative formation of aldehyde **12**. Addition of an excess of hexadec-3-ynylmagnesium bromide to aldehyde **12** in THF gave a mixture of desired isomer (*S*)-**13** and undesired isomer (*R*)-**13** in 55% yield (71% yield based on the 23% recovery of **12**) with a ratio of 64:36. Chemical yield and stereoselectivity did not increase, even when other solvents or the $MgBr_2$ complex of the aldehyde[7] were used. The isomers were inseparable by chromatography at this stage, and they were separated later after the conversion to silyl ethers.

Scheme 1. Retrosynthesis for Goniodenin (1)



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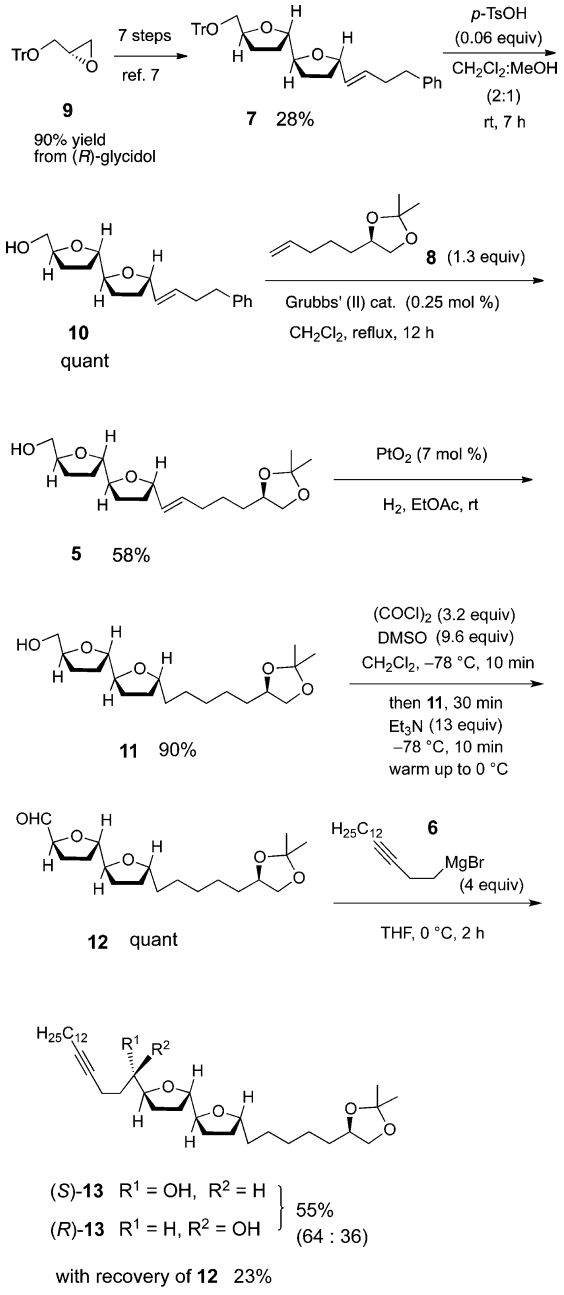
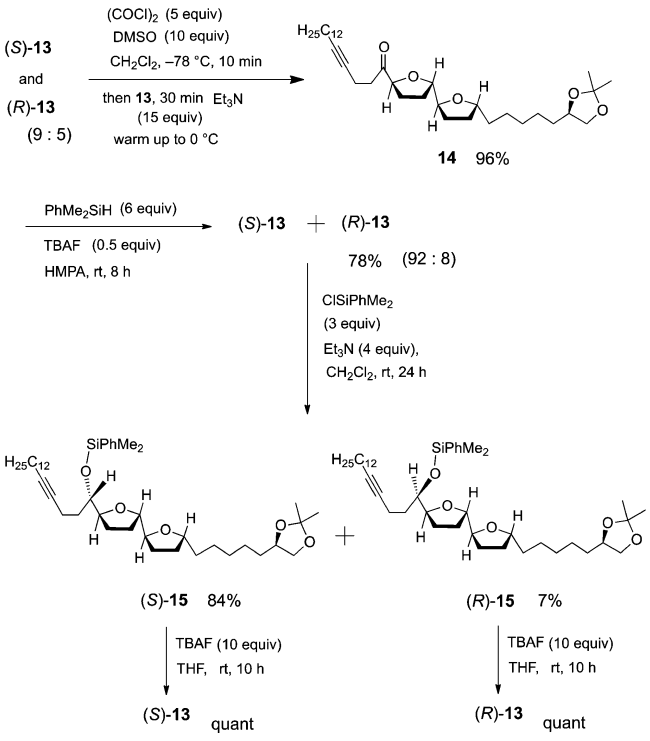
Scheme 2. Synthesis of C3 to C34 Carbon Chain Unit



Scheme 3. Stereoselective Construction of the C_{18} Carbon Center



Because Mitsunobu inversion of (*R*)-**13** did not give satisfactory results, we examined the diastereoselective reduction of the corresponding ketone (Scheme 3). Swern oxidation of **13** gave ketone **14** in 96% yield. Although we have examined several reducing reagents including $LiBH_4$, $LiAl(O\text{-}tBu)_3H$, L-selectride, and other hydride reagents in appropriate solvents, they gave unfavorable selectivity. However, we found that Fujita−Hiyama reduction using $HSiMe_2Ph$ with catalytic TBAF[18] improved its selectivity with a ratio of 92:8 in 78% yield. Diastereomeric mixtures were separated after the transformation to phenyl(dimethyl)silyl ethers **15**. Silylation of the mixture with phenyl(dimethyl)silyl chloride provided (*S*)-**15** in 84% yield and (*R*)-**15** in 7% yield. Desilylation of each isomer with TBAF gave pure isomers (*S*)-**13** and (*R*)-**13**, in quantitative yield.

The stereochemistry of the C_{18}-carbon center in (*S*)-**13** and (*R*)-**13** was determined by the Mosher method as shown in Scheme 4. The isomer (*S*)-**13** was subjected to the ester formation with (*R*)-(−)-MTPACl, {α-methoxy-α-(trifluoromethyl)phenylacetyl} chloride and (*S*)-(+)-MTPACl to afford **16** and **16′**, respectively. A difference of chemical shift values in ^1H NMR near the stereogenic center for **16** and **16′** were listed. Negative values on the left carbons and positive values on the right carbons confirmed an *S*-stereogenic center on the C_{18} carbon.

With the C_4 to C_{34} carbon unit in hand, we next needed to introduce a γ-butenolactone unit (Scheme 5). First, removal of the acetonide and silyl ether of (*S*)-**15** under acidic conditions gave 1,2-diol **4** in 82% yield. Selective trifluoromethanesulfonation of the primary hydroxy group with triflic anhydride followed by silylation of the two secondary hydroxy groups with TBSOTf afforded the intermediate for the next alkylation. Thus, the alkylation of a lithium salt of phenylthiolactone **3**[15] with the *O*-triflate at −20 °C in a mixture of THF and HMPA gave **17** in 65% yield. Oxidation of the phenylsulfenyl group with 1 equiv of *m*CPBA and heating of the resulting phenylsulfinyl compound at 100 °C in toluene gave γ-butenolactone **18** in 93% yield. Partial hydrogenation of the alkynyl bond in **18** in the presence of Lindlar's catalyst gave *Z*-alkene **19** in 90% yield. Finally, deprotection of the two silyl ethers with hydrogen fluoride furnished the synthesis of goniodenin **1** in 77% yield. The spectroscopic data including ^{13}C NMR[19] fully matched those reported for the natural product. Specific rotation values was recorded to be +6.6 (*c* 0.3, CH_2Cl_2) in accord with that of the natural product.

We have accomplished the total synthesis of (+)-goniodenin in 23 steps and also (+)-goniocin in the preceding paper. The question about the two natural acetogenins arises as to how their bis-THF rings could be formed within the same plant. If

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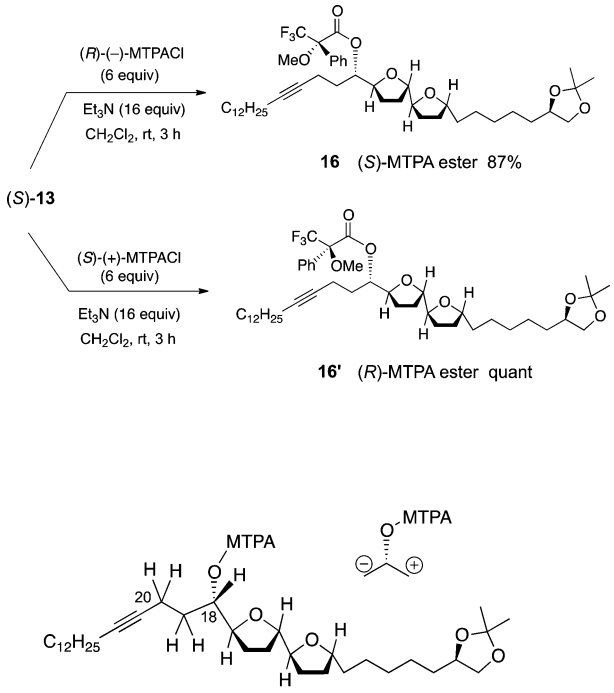
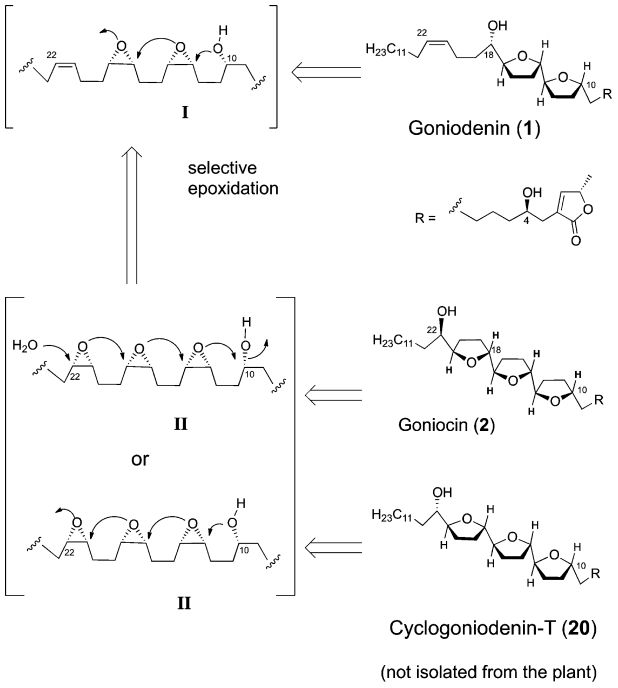
Scheme 4. Stereochemistry of the C18 Carbon Center



position	(*S*)-MTPA ester	(*R*)-MTPA ester	**16** – **16'** (*S*) – (*R*)
20	1.947	2.206	–0.259
19	1.712	1.850	–0.138
18	5.248	5.238	+0.010
17	4.101	4.115	–0.014
16α	2.048	1.927	+0.121
16β	1.634	1.550	+0.084

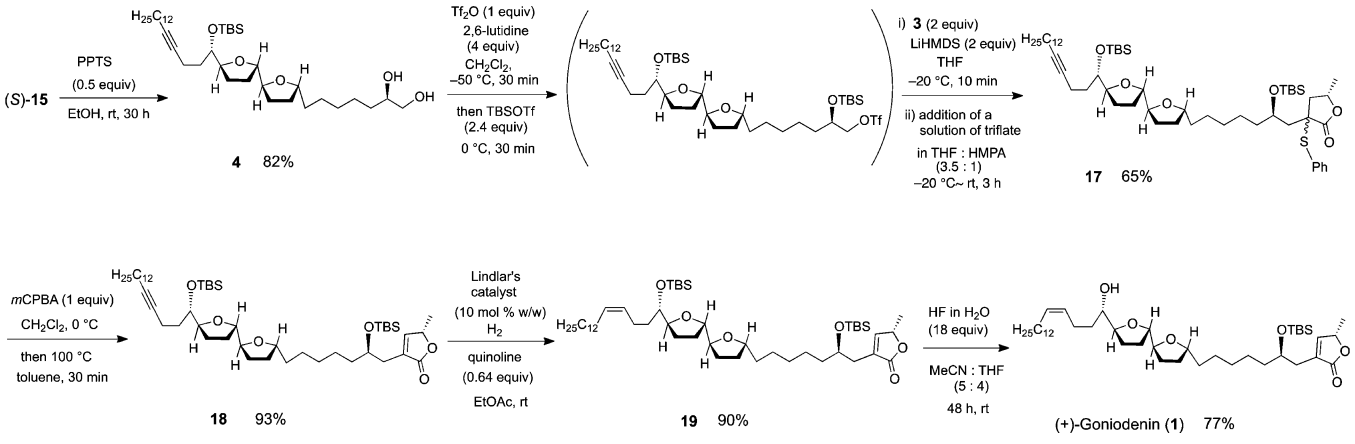
both materials were produced from the same intermediate according to the hypothesis proposed by Sinha and Keinan et al., goniodenin **1** could be produced from C_{14}–C_{15} and C_{18}–C_{19} di-*cis*-epoxy-C_{21}-alkene **I** in Scheme 6. A cascade process might be initiated by the nucleophilic attack of the C_{10} hydroxy group and thus forming the bis-THF rings and C_{18} hydroxy group in the domino process. The C_{21}–C_{22} alkenyl bond remains in this process. On the other hand, goniocin **2** may be formed from tri-*cis*-epoxide **II** which could be produced by selective epoxidation from **I**. Nucleophilic attack by an external

Scheme 6. Biosynthesis of Goniodenin and Goniocin



hydroxide source (perhaps a water molecule) at the terminal epoxide at C_{22} and successive ring-openings of the epoxides could proceed one after the other, ending with the elimination of the hydroxy group at C_{10} ultimately to give **2**. However, a question arises as to why the cascade reaction in the case of **II** does not proceed in the opposite way, from right to left in Scheme 6, in a pathway similar to goniodenin. Such a pathway could produce cyclogoniodenin-T (**20**), which was synthesized from natural goniodenin in two chemical steps.[4] Although a total of 15 Annonaceous acetogenins were isolated form the bark of the tree with **1**, this material has never been isolated only from *Goniothalamus giganteus,* or any other Annonaceous plants. However, even if compound **20** exists in the extract of the plant, it is anticipated that its separation from goniocin would be quite difficult due to the similarity of the structures. If **20** is present as a minor component in the mixture, it could be difficult to identify. Considering the biosynthesis of goniodenin and goniocin, the presence or the absence of cyclogoniodenin-T in nature would be quite interesting from the viewpoint of

Scheme 5. Total Synthesis of Goniodenin



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the biosynthesis of acetogenins, particularly in the formation of the contiguous THF rings by epoxide ring-opening in a cascade process.[20]

CONCLUSION

In summary, we have achieved the stereocontrolled total synthesis of **1** in 23 steps with 2% overall yield from (*R*)-glycidol. The C_{18} stereogenic center was constructed by Fujita–Hiyama reduction with high selectivity. This enantiomerically pure (+)-goniodenin has matched with the stereochemistry of natural (+)-goniodenin. To clarify the biosynthesis of **1**, **2**, and other related natural acetogenins, further research of a component in the natural plant source involving *Goniothalamus giganteus* will be necessary.

EXPERIMENTAL SECTION

General Information. The ^{1}H NMR and ^{13}C NMR spectra were recorded on 400 or 500 MHz spectrometers. ^{1}H NMR chemical shifts were internally referenced to the residual proton signals in $CDCl_3$ (δ 7.26), and ^{13}C NMR chemical shifts were internally referenced to the carbon signal of $CDCl_3$ (δ 77.00). THF was dried over sodium benzophenone ketyl. CH_2Cl_2 was dried over P_4O_{10}. These solvents were distilled freshly before use. Low and high resolution mass spectra were obtained on a double-focusing high resolution magnetic-sector mass-analyzed instrument, operating in a fast atom bombardment (FAB) mode or electron (EI) mode.

*Preparation of **7**.* Compound **7** was prepared from **9** exactly by the same procedure reported for the preparation of its enantiomeric isomer.[7] The specific rotation of **7** was $[\alpha]^D_{22}$ −23.4 (*c* 1.6, $CHCl_3$).

*(E)-5-(Hydroxymethyl)-5′-(4-phenylbut-1-en-1-yl)octahydro-2,2′-bifuran (**10**).* A solution of **7** (7.3 g, 13.4 mmol) and *p*-toluenesulfonic acid monohydrate (152 mg, 0.8 mmol) in a mixture of CH_2Cl_2 (32 mL) and MeOH (16 mL) was stirred for 7 h at room temperature. After an addition of triethylamine (0.22 mL, 160 mg, 1.58 mmol), the whole mixture was condensed and the crude product was purified directly by column chromatography on silica gel eluted with 50% EtOAc in hexane to give alcohol **10** (4.05 g) in quantitative yield. Colorless oil. R_f = 0.22 (40% EtOAc in hexane); $[\alpha]^D_{23}$ +2.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.24 (2H, m), 7.19–7.15 (3H, m), 5.69 (1H, dt, *J* = 16.0, 5.9 Hz), 5.48 (1H, ddt, *J* = 16.0, 7.3, 1.3 Hz), 4.37 (1H, dt, *J* = 6.8, 6.4 Hz), 4.13 (1H m), 3.91 (2H, m), 3.69 (1H, dd, *J* = 11.9, 3.2 Hz), 3.49 (1H, dd, *J* = 11.9, 5.4 Hz), 2.74–2.62 (2H, m), 2.40–2.26 (2H, m), 2.09–1.92 (6H, m), 1.78–1.56 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 131.7, 131.2, 128.4, 128.2, 125.7, 82.2, 81.7, 80.4, 79.8, 64.5, 35.4, 34.0, 32.8, 28.7, 28.7, 27.4; LRMS (FAB) *m*/*z*: $[M + Na]^+$ 325; HRMS (FAB) *m*/*z*: $[M + Na]^+$ calcd for $C_{19}H_{26}O_3Na$ 325.1780; found 325.1777.

*5-(Hydoxymethyl)-5′-((E)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-pent-1-en-1-yl)octahydro-2,2′-bifuran (**5**). Cross-metathesis of **10** with **8**.* To a solution of **10** (3.8 g, 12.6 mmol) and acetonide **8** (2.8 g, 16.8 mmol) in CH_2Cl_2 (25 mL) was added Grubbs second catalyst (26 mg, 0.25 mol %), and the reaction mixture was refluxed for 12 h. After cooling, the mixture was condensed and residual product was purified by column chromatography on silica gel eluted with EtOAc to give alkene **5** (1.9 g) in 45% yield. The rest of the polar and less polar fractions were combined and the mixture (ca. 4.1 g) was subjected to the second metathesis reaction in CH_2Cl_2 (25 mL) in the presence of Grubbs second catalyst (26 mg, 0.03 mmol). Purification gave an additional amount of **5** (575 mg) in 14% yield. Totally, 2.47 g of **5** was obtained in 58% yield. Colorless oil. R_f = 0.44 (80% EtOAc in hexane); $[\alpha]^D_{24}$ −5.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (1H, dt, *J* = 15.1, 6.8 Hz), 5.43 (1H, dd, *J* = 15.1, 6.8 Hz), 4.35 (1H, q, *J* = 6.8 Hz), 4.11 (1H, m), 4.06–3.98 (2H, m), 3.94–3.86 (2H, m), 3.68 (1H, m), 3.50–3.44 (2H, m), 2.14 (1H, t, *J* = 5.9 Hz), 2.10–1.89 (6H, m), 1.77–1.57 (5H, m), 1.54–1.29 (3H, m), 1.38 (3H, s), 1.33 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.0, 131.1, 108.6, 82.3, 81.7, 80.5, 79.8, 75.9, 69.4, 64.5, 33.0, 32.9, 32.0, 28.7, 28.6, 27.4, 26.9, 25.7, 25.1; LRMS (FAB) *m*/*z*: $[M + Na]^+$ 363; HRMS (FAB) *m*/*z*: $[M + Na]^+$ calcd for $C_{19}H_{32}O_5Na$ 363.2147; found 363.2151.

*5-(Hydoxymethyl)-5′-((E)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-pentyl)octahydro-2,2′-bifuran (**11**).* To a solution of alkene **5** (575 mg, 1.69 mmol) in EtOAc (17 mL) was added platinum oxide (57 mg, 7 mol %). The mixture was evacuated and backfilled with hydrogen three times. The reaction mixture was stirred for 12 h under hydrogen atmosphere, and the slurry was filtered through a Celite pad. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel eluted with 80% EtOAc in hexane to give **11** (518 mg) in 90% yield. Colorless oil. R_f = 0.44 (80% EtOAc in hexane); $[\alpha]^D_{21}$ −8.0 (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (1H, m), 4.06–3.99 (2H, m), 3.93 (1H, m), 3.88–3.82 (2H, m), 3.68 (1H, m), 3.50–3.43 (2H, m), 2.16 (1H, t, *J* = 5.9 Hz), 2.03–1.90 (4H, m), 1.77–1.52 (6H, m), 1.50–1.22 (7H, m), 1.38 (3H, s), 1.33 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.5, 82.4, 81.5, 79.83, 79.78, 76.1, 69.46, 64.51, 35.6, 33.5, 32.0, 29.7, 28.73, 28.65, 27.4, 26.9, 25.9, 25.71, 25.66; LRMS (FAB) *m*/*z*: $[M + Na]^+$ 365; HRMS (FAB) *m*/*z*: $[M + Na]^+$ calcd for $C_{19}H_{34}O_5Na$ 365.2304; found 365.2307.

*5-Formyl-5′-((E)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)pentyl)-octahydro-2,2′-bifuran (**12**).* To a solution of oxalyl chloride (0.2 mL, 305 mg, 2.4 mmol) in dry CH_2Cl_2 (2.3 mL) was added a solution of dimethyl sulfoxide (0.51 mL, 560 mg, 7.2 mmol) in dry CH_2Cl_2 (2.3 mL) at −78 °C dropwise. After the mixture was stirred for 10 min, a solution of alcohol **11** (280 mg, 0.82 mmol) in CH_2Cl_2 (4.4 mL) was dropped into the mixture at the same temperature. The reaction was continued for 30 min. Then triethylamine (990 mg, 9.8 mmol, 1.4 mL) was added at −78 °C. The mixture was stirred for 15 min at the same temperature and allowed to warm to 0 °C. It was quenched with water and extracted with EtOAc for three times. The combined extract was washed with water, brine and dried over $MgSO_4$. Solvent was removed, and the crude product was purified by silica gel column chromatography eluted with 80% EtOAc in hexane to give aldehyde **12** (278 mg) quantitatively. Colorless oil. R_f = 0.5 (80% EtOAc in hexane); $[\alpha]^D_{24}$ −30.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (1H, d, *J* = 2.2 Hz), 4.34 (1H, dt, *J* = 7.3, 2.2 Hz), 4.09–4.00 (3H, m), 3.97–3.89 (2H, m), 3.49 (1H, t, *J* = 7.3 Hz), 2.21 (1H, m), 2.06–1.89 (4H, m), 1.76–1.59 (4H, m), 1.53–1.25 (9H, m), 1.40 (3H, s), 1.35 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 108.5, 83.5, 83.2, 80.8, 79.9, 76.0, 69.4, 35.5, 33.5, 32.0, 29.7, 28.6, 27.9, 27.4, 26.9, 25.9, 25.7, 25.6; LRMS (FAB) *m*/*z*: $[M + Na]^+$ 363; HRMS (FAB) *m*/*z*: $[M + Na]^+$ calcd for $C_{19}H_{32}O_5Na$ 363.2147; found 363.2143.

*5-((S)-1-Hydroxyheptadec-4-yn-1-yl)-5′-((E)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)pentan-1-yl)octahydro-2,2′-bifuran (S)-**13** and 5-((R)-1-Hydroxyheptadec-4-yn-1-yl)-5′-((E)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)pentan-1-yl)octahydro-2,2′-bifuran (R)-**13**.* Flakes of Mg (94 mg, 3.86 mmol) and I_2 (1 grain) were placed in THF (3.3 mL) to which hexadec-3-ynyl bromide (988 mg, 3.28 mmol) in THF (3.3 mL) was added dropwise at room temperature. Then the mixture was refluxed for 30 min to form hexadec-3-ynylmagnesium bromide. A solution of aldehyde **12** (278 mg, 0.82 mmol) in THF (7 mL) was added dropwise to the Grignard reagent at 0 °C. The mixture was stirred for 30 min at the same temperature and stirred for an additional 90 min. It was quenched by the addition of saturated aqueous ammonium chloride. The resultant mixture was extracted with EtOAc three times, and the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated. Purification by column chromatography on silica gel eluted with 25% EtOAc in hexane afforded **13** (252 mg) in 55% yield as a mixture of diastereomeric alcohols (64:36) with 23% recovery of **12** (64 mg). Colorless oil. R_f = 0.2 (20% EtOAc in hexane). The isomers were not separable by chromatographic methods. However, they could be separated after the silylation in the following step.

*5-(Heptadec-4-ynoyl)-5′-((E)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)pentan-1-yl)octahydro-2,2′-bifuran (**14**). Oxidation of a Diastereomixture of (S)-**13** and (R)-**13**.* To a solution of oxalyl chloride (28 μL, 38 mg, 0.3 mmol) in dry CH_2Cl_2 (0.5 mL) was added a solution of dimethyl sulfoxide (42 μL, 46 mg, 0.6 mmol) in dry CH_2Cl_2 (0.5 mL) at −78 °C dropwise. The mixture was stirred for 10 min, and a solution of alcohol **13** (34 mg, 0.06 mmol) in CH_2Cl_2 (1.0 mL) was

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dropped into the mixture at the same temperature. After 30 min, triethylamine (125 μL, 91 mg, 0.9 mmol) was added to the mixture and the whole mixture was stirred for an additional 15 min at −78 °C. Then the mixture was allowed to warm to 0 °C, quenched with water, and extracted with EtOAc three times, and the combined extract was washed with water, brine, and dried over $MgSO_4$. Solvent was removed, and the residual oil was purified by silica gel column chromatography eluted with 15% EtOAc in hexane to give ketone **14** (32 mg) in 96% yield. Colorless oil. R_f = 0.41 (20% EtOAc in hexane); $[\alpha]^D_{23}$ −32.9 (*c* 0.45, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (1H, t, *J* = 7.3 Hz), 4.09−4.00 (3H, m), 3.95−3.87 (2H, m), 3.48 (1H, t, *J* = 7.3 Hz), 2.82 (1H, dt, *J* = 18.2, 7.3 Hz), 2.74 (1H, dt, *J* = 18.2, 7.3 Hz) 2.46−2.35 (2H, m), 2.22 (1H. m), 2.09 (2H, tt, *J* = 6.8, 2.2 Hz), 2.05−1.84 (4H, m), 1.76−1.54 (2H, m), 1.51−1.25 (31H, m), 1.39 (3H, s), 1.34 (3H, s), 0.87 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.0, 108.5, 83.8, 83.2, 80.8, 80.7, 79.9, 78.6, 76.1, 69.4, 37.7, 35.6, 33.5, 32.0, 31.9, 29.7, 29.66, 29.63(2C), 29.5, 29.3, 29.1(2C), 29.0, 28.9, 28.6, 28.0, 26.9, 26.0, 25.73, 25.59, 22.6, 18.7, 14.1, 12.8; LRMS (FAB) *m*/*z*: $[M + Na]^+$ 583; HRMS (FAB) *m*/*z*: $[M + Na]^+$ calcd for $C_{35}H_{60}O_5Na$ 583.4338; found 583.4340.

*Stereoselective Reduction of **14**.* Commercial THF solution of tetrabutylammonium fluoride (TBAF) was neutralized with dil HCl, and solvent was evaporated. The residue was dried under vacuum in the presence of P_2O_5 overnight. The solid was dissolved in dry THF and its concentration was adjusted to 0.5 M. The TBAF solution (0.08 mL, 0.04 mmol) was added to a HMPA (0.3 mL) solution of **14** (45 mg, 0.08 mmol) and $PhMe_2SiH$ (73 μL, 65 mg, 0.48 mmmol). The mixture was stirred for 8 h at room temperature, diluted with water, and extracted with ether. The extract was washed with brine and dried over $MgSO_4$. The crude product was purified by silica gel column chromatography eluted with 30% EtOAc in hexane to give (*S*)-**13** (35 mg) in 78% yield. The ratio of (*S*)-**13** and (*R*)-**13** (92:8) was determined by ^{1}H NMR.

*Preparation of (S)-**15** and (R)-**15**.* To a solution of secondary alcohol **13** (200 mg, 0.355 mol) in CH_2Cl_2 (10 mL) were added triethylamine (198 μL, 138 mg, 1.42 mmol) and chloro(dimethyl)-phenylsilane (181 mg, 1.06 mmol). The reaction mixture was stirred at room temperature for 24 h. EtOAc and sat. aq $NaHCO_3$ solution were added. The resulting mixture was extracted with EtOAc three times, and then the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated. Purification by flash column chromatography on silica gel eluted with 10% *tert*-butyl methyl ether in hexane gave (*S*)-**15** (208 mg) in 84% yield and (*R*)-**15** (17 mg) in 7% yield. (*S*)-**15**; colorless oil. R_f = 0.5 (20% *tert*-butyl methyl ether in hexane); $[\alpha]^D_{24}$ −30.0 (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.60 (2H, m), 7.38−7.31 (3H, m), 4.09−3.99 (2H, m), 3.92−3.80 (4H, m), 3.75 (1H, m), 3.48 (1H, t, *J* = 7.3 Hz), 2.28−2.10 (4H, m), 1.99−1.77 (4H, m), 1.74−1.25 (36H, m), 1.39 (3H, s), 1.34 (3H, s), 0.87 (3H, t, *J* = 6.8 Hz), 0.41 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 133.7, 129.2, 127.6, 108.5, 82.3, 81.7, 80.9, 80.7, 79.7, 79.6, 76.1, 74.2, 69.5, 35.7, 33.5, 32.2, 31.9 (2C), 29.8, 29.67, 29.66, 29.64, 29.6, 29.4, 29.2, 29.1, 28.9, 28.5, 28.4, 27.8, 26.9, 26.1, 25.8, 25.7, 22.7, 18.8, 15.3, 14.1, −0.9, −1.0; LRMS (FAB) *m*/*z*: $[M + Na]^+$ 719; HRMS (FAB) *m*/*z*: $[M + Na]^+$ calcd for $C_{43}H_{72}O_5SiNa$ 719.5047; found 719.5049. (*R*)-**15**; colorless oil. R_f = 0.45 (20% *tert*-butyl methyl ether in hexane); $[\alpha]^D_{24}$ + 3.6 (*c* 0.45, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.59 (2H, m), 7.35−7.33 (3H, m), 4.09−3.99 (3H, m), 3.88−3.80 (3H, m), 3.68 (1H, m), 3.48 (1H, t, *J* = 7.3 Hz), 2.25−2.08 (4H, m), 1.99−1.77 (5H, m), 1.67−1.25 (35H, m), 1.40 (3H, s), 1.35 (3H, s), 0.87 (3H, t, *J* = 6.8 Hz), 0.41 (3H, s), 0.40 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.9, 134.5, 130.2, 128.6, 109.5, 83.4, 82.7, 82.0, 81.7, 80.5, 80.4, 77.1, 73.8, 70.5, 36.6, 34.48, 34.45, 33.1, 32.9, 30.7, 30.64, 30.61 (2C), 30.5, 30.3, 30.2, 30.1, 29.9, 29.4, 29.3, 27.9, 27.1, 26.9, 26.7 (2C), 23.7, 19.7, 16.3, 15.1, 0.2, 0.0; LRMS (FAB) *m*/*z*: $[M + Na]^+$ 719; HRMS (FAB) *m*/*z*: $[M + Na]^+$ calcd for $C_{43}H_{72}O_5SiNa$ 719.5047; found 719.5044.

*Desilylation of (S)-**15** and (R)-**15**.* To a solution of (*S*)-**15** (14 mg, 20 μmol) in THF (100 μL) was added tetrabutylammonium fluoride (100 μL, 1 M in THF). The reaction mixture was stirred at room temperature for 10 min and then concentrated. Purification by column chromatography on silica gel eluted with 30% EtOAc in hexane afforded (*S*)-**13** (17.1 mg) quantitatively. (*S*)-**13**; colorless oil. R_f = 0.3 (30% EtOAc in hexane); $[\alpha]^D_{24}$ −21.9 (*c* 1.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.08−4.00 (2H, m), 3.95−3.83 (4H, m), 3.53 (1H, m), 3.48 (1H, t, *J* = 7.3 Hz), 2.50 (1H, brs), 2.37−2.27 (2H, m), 2.14−2.10 (2H, m), 2.03−1.92 (4H, m), 1.70−1.54 (7H, m), 1.52−1.25 (29H, m), 1.40 (3H, s), 1.34 (3H, s), 0.87 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.6, 82.7, 82.2, 81.2, 80.6, 79.9, 79.6, 76.1, 72.8, 69.5, 35.7, 33.5, 32.9, 32.0, 31.9, 29.7, 29.67, 29.65 (2C), 29.6, 29.4, 29.2, 29.1, 28.9, 28.8, 28.7, 28.3, 27.0, 26.0, 25.8, 25.7, 22.7, 18.8, 15.2, 14.1. LRMS (FAB) *m*/*z* 585 $(M + Na)^+$; HRMS (FAB) calcd for $C_{35}H_{62}NaO_5$ *m*/*z* 585.4495, found 585.4490. The other isomer (*R*)-**13** (6.4 mg) was obtained as a colorless oil from (*R*)-**15** (8 mg). (*R*)-**13**; colorless oil. R_f = 0.3 (30% EtOAc in hexane); $[\alpha]^D_{24}$ −2.7 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.09−4.00 (3H, m), 3.98−3.90 (2H, m), 3.89−3.82 (2H, m), 3.48 (1H, t, *J* = 7.3 Hz), 2.35−2.23 (3H, m), 2.13−2.08 (2H, m), 2.03−1.91 (3H, m), 1.89−1.77 (2H, m), 1.67−1.25 (35H, m), 1.40 (s, 3 H), 1.35 (s, 3 H), 0.87 (3H, t, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.56, 82.77, 82.35, 81.68, 80.91, 79.82, 79.35, 76.10, 73.51, 70.46, 35.64, 33.48, 31.92, 31.76, 30.08, 29.79, 29.76, 29.73, 29.67, 29.65, 29.54, 29.35, 29.17, 29.10, 28.92, 28.76, 28.61, 26.90, 25.86, 25.71, 24.84, 22.69, 18.74, 15.62, 14.13. LRMS (FAB) *m*/*z*: $[M + Na]^+$ 585; HRMS (FAB) *m*/*z*: $[M + Na]^+$ calcd for $C_{35}H_{62}O_5Na$ 585.4495; found 585.4489.

*Preparation of (S)-MTPA Ester (**16**).* To a solution of alcohol (*S*)-**13** (2.5 mg, 4.44 μmol) in CH_2Cl_2 (0.5 mL) were added triethylamine (7.3 mg, 72 μmol, 10 μL) and (*R*)-(−)-α-methoxy-α-trifluoromethyl-phenylacetyl chloride (5 μL, 6.7 mg, 26.5 μmol). The reaction mixture was stirred at room temperature for 3 h. Saturated aq $NaHCO_3$ solution was added. The resulting mixture was extracted with EtOAc three times, and then the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated. Purification by column chromatography on silica gel eluted with 15% EtOAc in hexane afforded (*S*)-MTPA ester (3 mg) in 87% yield as a colorless oil. R_f = 0.7 (20% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.62 (2 H, m), 7.39−7.38 (3H, m), 5.25 (1H, dt, *J* = 12.8, 7.3 Hz), 4.10−4.00 (3H, m), 3.94−3.79 (3H, m), 3.63 (3H, s), 3.48 (1H, t, *J* = 7.3 Hz), 2.14−2.01 (4H, m), 1.99−1.86 (4H, m), 1.83−1.53 (7H, m), 1.50−1.25 (29H, m), 1.40 (3H, s), 1.35 (3H, s), 0.87 (3H, t, *J* = 6.8 Hz); LRMS (FAB) *m*/*z* 801 $(M+Na)^+$; HRMS (FAB) calcd for $C_{45}H_{69}F_3NaO_7$ *m*/*z* 801.4893, found, 801.4901. LRMS (FAB) *m*/*z*: $[M + Na]^+$ 801; HRMS (FAB) *m*/*z*: $[M + Na]^+$ calcd for $C_{45}H_{69}F_3O_7Na$ 801.4893; found 801.4901.

*Preparation of (R)-MTPA Ester (**16′**).* (*R*)-MTPA ester **16′** (3.4 mg) was obtained in quantitative yield from (*S*)-**13** (2.5 mg, 4.4 μmol) in CH_2Cl_2 (0.5 mL) under the same reaction conditions for the formation of **16** except for the use of (*S*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride instead of (*R*)-(−)-α-methoxy-α-trifluoromethylphenylacetyl chloride. A colorless oil. R_f = 0.7 (20% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61−7.59 (2H, m), 7.40−7.38 (3H, m), 5.23 (1H, dt, *J* = 13.7, 5.4 Hz), 4.11−3.99 (3H, m), 3.86−3.79 (3H, m), 3.56 (3H, s), 3.47 (1H, t, *J* = 7.3 Hz), 2.28−2.10 (4H, m), 1.96−1.76 (6H, m), 1.69−1.51 (6H, m), 1.49−1.25 (28H, m), 1.39 (3 H, s), 1.34 (3 H, s), 0.87 (3 H, t, *J* = 6.8 Hz).

*Preparation of (2R)-7-(5′-((S)-1-Hydroxyheptadec-4-yn-1-yl)-octahydro-[2,2′-bifuran]-5-yl)heptane-1,2-diol (**4**).* To a solution of (*S*)-**15** (52 mg, 75 μmol) in EtOH (4 mL) was added pyridinium *p*-toluenesulfonate (10 mg, 40 μmol) at room temperature. The mixture was stirred for 30 h and concentrated. The crude mixture was purified by silica gel column chromatography eluted with 5% MeOH in $CHCl_3$ to give **4** (32 mg) in 82% yield. Amorphous solid. R_f = 0.26 (5% MeOH in $CHCl_3$); mp 50−51 °C; $[\alpha]^D_{24}$ −15.3 (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 (1H, m), 3.89−3.78 (3H, m), 3.69 (1H, m), 3.60 (1H, m), 3.53 (1H, q, *J* = 6.8 Hz), 3.41 (1H, m), 3.30 (1H, brs), 2.98 (1H, brs), 2.85 (1H, brs), 2.38−2.24 (2H, m), 2.13−2.09 (2H, m), 2.03−1.90 (4H, m), 1.66−1.24 (36H, m), 0.87 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.9, 82.0, 81.4, 80.6, 80.0, 79.7, 72.8, 72.2, 66.9, 35.4, 32.8, 32.6, 32.0, 31.9, 29.7, 29.62 (2C), 29.56, 29.49, 29.3, 29.2, 29.1, 28.91, 28.88, 28.7, 28.3, 25.9, 25.4, 22.7, 18.7, 15.1, 14.1; LRMS (FAB) *m*/*z*: $[M + Na]^+$ 545; HRMS (FAB)

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m/z: [M + Na]$^+$ calcd for $C_{32}H_{58}O_5Na$ 545.4182; found 545.4188. Anal. Calcd for $C_{32}H_{58}O_5 \cdot 0.17H_2O$; C, 73.01; H, 11.18. Found: C, 73.02; H, 11.10.

Preparation of ***17***. To a solution of triol **4** (200 mg, 0.38 mmol) and 2,6-lutidine (0.18 mL, 166 mg, 1.55 mmol) in CH_2Cl_2 (1.9 mL) was added trifluoromethanesulfonic anhydride (64 μL, 108 mg, 0.38 mmol) at −78 °C. The mixture was warmed up to −50 °C during 30 min. Successively, *tert*-butyldimethylsilyl trifluoromethanesulfonate (211 μL, 242 mg, 0.92 mmol) was added to the mixture at the same temperature, and the reaction mixture was allowed to warm to 0 °C during 30 min. Saturated $NaHCO_3$ solution was added to the mixture, and the mixture was extracted with diethyl ether three times. The combined extract was washed with brine, dried over $MgSO_4$, and concentrated. Purification of the crude product provided the corresponding *O*-triflate by column chromatography on silica gel eluted with 5% EtOAc in hexane. This material is not stable enough to store and should be used for the next reaction subsequently. This material was dried by vacuum pumping for 1 h and used for the next step. The lithium salt of lactone **3** was prepared as follows: lithium bis(trimethylsilyl)amide (24% THF solution, 0.58 mL, 0.76 mmol) was added to a solution of lactone **3** (158 mg, 0.76 mmol) in dry THF (1 mL) at −20 °C, and the mixture was stirred for 10 min at the same temperature. To this solution were added the above triflate dissolved in THF (2 mL) and HMPA (0.1 mL, 0.57 mmol) at −20 °C successively. The resulting mixture was stirred at −15 °C for 15 min and at 0 °C for 15 min. The reaction was continued for additional 2 h at room temperature and quenched with sat. NH_4Cl solution. The mixture was extracted with EtOAc three times, and the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated. The crude oil was purified by column chromatography on silica gel eluted with 10% EtOAc in hexane to give **17** (233 mg) in 65% yield. Colorless oil. R_f = 0.4 (10% EtOAc in hexane); ^{1}H NMR (500 MHz, $CDCl_3$, a 85:15 ratio of diastereomeric mixtures) δ 7.56−7.53 (2H, m), 7.40−7.31 (3H, m), 4.60 (0.15H, m), 4.51 (0.85H, d *J* = 6.7 Hz), 4.24 (0.85H, m), 3.95 (0.85H, dt, *J* = 7.0, 6.4 Hz), 3.91−3.84 (3.3H, m), 3.76 (1H, m), 3.03 (0.85H, dd, *J* = 14.0, 7.6 Hz), 2.46−2.10 (4.15H, m), 2.01−1.81 (7H, m), 1.71−1.63 (4H, m), 1.58−1.24 (32H, m), 1.22 (3H, d, *J* = 6.1 Hz), 0.89−0.86 (21H, m), 0.15 (2.55H, s), 0.11 (2.55H, s), 0.07 (3H, s), 0.07 (3H, s), 0.03 (0.45H, s), 0.01 (0.45H, s); ^{13}C NMR (125 MHz, $CDCl_3$, a 85:15 ratio of diastereomeric mixtures; the following data are listed for the major isomer only) δ 177.5, 136.7, 130.4, 129.6, 129.0, 82.0, 81.9, 80.9, 80.6, 79.9, 79.6, 73.5, 73.3, 69.5, 55.4, 41.2, 39.5, 38.5, 35.7, 32.1, 31.9, 31.7, 29.9, 29.67, 29.65, 29.63, 29.57, 29.3, 29.20, 29.16, 28.9, 28.43, 28.41, 27.3, 26.1, 26.00, 25.98, 24.5, 22.7, 21.3, 18.8, 18.2, 18.0, 15.3, 14.1, −3.80, −3.82, −4.3, −4.7; LRMS (FAB) *m/z*: [M + Na]$^+$ 963; HRMS (FAB) *m/z*: [M + Na]$^+$ calcd for $C_{55}H_{96}O_6SSi_2Na$ 963.6364; found 963.6358.

Preparation of ***18***. To a solution of **17** (130 mg, 0.138 mmol) in CH_2Cl_2 (2.4 mL) was added *m*-chloroperbenzoic acid (43 mg containing with 25% water, 0.138 mmol) at 0 °C, and the mixture was stirred for 30 min. Saturated aq. $NaHCO_3$ was added, the mixture was extracted with EtOAc three times, and then the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated. The residue was dissolved in toluene (4 mL), and the mixture was heated at 100 °C for 30 min and concentrated after cooling. Purification of the residual oil afforded **18** (107 mg) in 93% yield by column chromatography on silica gel eluted with 20% EtOAc in hexane. Colorless oil. R_f = 0.5 (20% EtOAc in hexane); $[\alpha]^D_{22}$ −6.5 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (1H, d, *J* = 1.3 Hz), 4.99 (1H, dq, *J* = 6.8, 1.3 Hz), 3.98−3.85 (5H, m), 3.76 (1H, m), 2.42−2.40 (2H, m), 2.31−2.10 (4H, m), 2.02−1.85 (4H, m), 1.74−1.59 (4H, m), 1.52−1.25 (32H, m), 1.41 (3H, d, *J* = 6.8 Hz), 0.87 (9H, s), 0.87 (3H, overlapped with two *tert*-Bu groups), 0.865 (9H, s), 0.07 (3H, s), 0.06 (3H, s), 0.04 (3H, s), 0.01 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 151.5, 130.8, 81.95, 81.92, 81.0, 80.6, 79.9, 79.7, 77.5, 73.4, 70.1, 36.9, 35.7, 32.7, 32.1, 31.9, 31.6, 29.9, 29.67, 29.65(2C), 29.6, 29.4, 29.2, 29.1, 28.9, 28.4, 27.2, 26.2, 26.0(2C), 25.86, 25.1, 22.7, 19.0, 18.8, 18.2, 18.0, 15.3, 14.1, −4.3, −4.4, −4.5, −4.8; LRMS (FAB) *m/z*: [M + Na]$^+$ 853; HRMS (FAB) *m/z*: [M + Na]$^+$ calcd for $C_{49}H_{90}O_6Si_2Na$ 853.6174; found 853.6179.

Preparation of ***19***. A mixture of **18** (60 mg, 0.072 mmol), Lindlar's catalyst (poisoned with Pb, 6 mg), and quinoline (6 mg, 0.046 mmol) in EtOAc (0.7 mL) was evacuated and backfilled with hydrogen three times. After the reaction mixture was stirred for 40 min under hydrogen atmosphere at room temperature, the catalyst was filtered off through Celite pad and the filtrate was concentrated. The residue was purified by column chromatography on silica gel eluted with 10% EtOAc in hexane to give **19** (54 mg) in 90% yield. Colorless oil. R_f = 0.5 (20% EtOAc in hexane); $[\alpha]^D_{24}$ −1.1 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (1H, d, *J* = 0.9 Hz), 5.39−5.30 (2H, m), 5.00 (1H, dq, *J* = 6.8, 0.9 Hz), 3.93 (1H, m), 3.89−3.81 (4H, m), 3.67 (1H, m), 2.42−2.40 (2H, m), 2.22 (1H, m), 2.01−1.86 (7H, m), 1.72−1.50 (4H, m), 1.48−1.25 (32H, m), 1.41 (3H, d, *J* = 6.8 Hz), 0.88 (9H, s), 0.87 (3H, t, *J* = 6.8 Hz), 0.86 (9H, s), 0.06 (3H, s), 0.05 (3H, s), 0.04 (3H, s), 0.01 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 151.6, 130.8, 130.1, 129.7, 82.1, 81.9, 81.0, 79.7, 77.6, 74.4, 70.1, 36.9, 35.7, 32.7, 32.4, 32.1, 31.9, 29.9, 29.8, 29.7(4C), 29.6, 29.4, 28.4(2C), 27.3, 27.0, 26.1, 26.0, 25.9, 25.1, 23.9, 22.7, 19.0, 18.9, 18.2, 18.0, 14.1, −4.2, −4.4, −4.5, −4.7; LRMS (FAB) *m/z*: [M + Na]$^+$ 855; HRMS (FAB) *m/z*: [M + Na]$^+$ calcd for $C_{49}H_{92}O_6Si_2Na$ 855.6330; found 855.6332.

*Synthesis of Goniodenin (****1****)*. A plastic test tube was charged with **19** (54 mg, 0.06 mmol) in acetonitrile (2 mL) and THF (1.6 mL). Hydrofluoric acid (55% in H_2O, 40 μL) was added, and then the mixture was stirred at room temperature for 48 h. The reaction was quenched with cold sat. aq NaHCO3 carefully and extracted with CH_2Cl_2 three times, and then the combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated. Purification by column chromatography on silica gel eluted with 80% EtOAc in hexane gave **1** (30 mg) in 77% yield. Colorless oil. R_f = 0.5 (80% EtOAc in hexane); $[\alpha]^D_{22}$ + 6.6 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (1H, d, *J* = 1.5 Hz), 5.35−5.30 (2H, m), 5.05 (1H, dq, *J* = 6.7, 1.5 Hz), 3.93 (1H, m), 3.89−3.81 (4H, m), 3.40 (1H, m), 2.58 (1H, brs), 2.51 (1H, d of quint, *J* = 15.2, 1.5 Hz), 2.41−2.36 (2H, m), 2.26−2.11 (2H, m), 2.04−1.91 (6H, m), 1.66 (1H, brs), 1.64−1.57 (6H, m), 1.51−1.24 (29H, m), 1.42 (3H, d, *J* = 7.0 Hz), 0.87 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 151.8, 131.1, 130.6, 129.1, 83.0, 82.1, 81.2, 79.9, 78.0, 73.6, 69.9, 37.3, 35.7, 33.34, 33.30, 32.0, 31.9, 29.7, 29.66(2C), 29.64 (2C), 29.58, 29.56, 29.35, 29.32, 28.9, 28.7, 28.4, 27.2, 26.0, 25.5, 23.4, 22.7, 19.1, 14.1; LRMS (FAB) *m/z*: [M + Na]$^+$ 627; HRMS (FAB) *m/z*: [M + Na]$^+$ calcd for $C_{37}H_{64}O_6Na$ 627.4601; found 627.4607.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02432.

^{1}H and ^{13}C NMR spectra for all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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