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# Synthesis of Murisolin, (15*R*, 16*R*, 19*R*, 20*S*)-Murisolin A, and (15*R*, 16*R*, 19*S*, 20*S*)-16,19-*cis*-Murisolin and Their Inhibitory Action with Bovine Heart Mitochondrial Complex I

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**Abstract:** The asymmetric total synthesis of murisolin, (15*R*, 16*R*, 19*R*, 20*S*)-murisolin A, and (15*R*, 16*R*, 19*S*, 20*S*)-16,19-*cis*-murisolin was performed by using an epoxy alcohol as a versatile chiral building block for synthesizing the stereoisomers of mono-THF annonaceous acetogenins. The inhibitory activity of these murisolin compounds was examined with bovine heart mitochondrial complex I, and they showed almost the same activity.

**Keywords:** annonaceous acetogenins · antitumor agents · mitochondrial complex I · natural products · total synthesis

## Introduction

Annonaceous acetogenins, which are present in a number of tropical or subtropical plants of the *Annonaceae* family, have attracted much attention as they exhibit a wide variety of biological activities, for example, cytotoxic, antitumoral, antimalarial, antibiotic, antiparasitic, and antifeedant. So far, more than 400 compounds have been isolated. Most of them contain one or more tetrahydrofuran (THF) rings, together with an α,β-unsaturated γ-lactone on a chain 35 or 37 carbon atoms long. The mode of action is assumed to be based on inhibitory activity against NADH–ubiquinone oxidoreductase of mitochondrial complex I.[1]

Murisolin (**1**) is a mono-THF annonaceous acetogenin[2] isolated from the seed of *Annona muricata* by Cortes and co-workers in 1990.[3] Five years later, it and its diastereomers, murisolin A (**2a** or **2b**) and 16,19-*cis*-murisolin (**3a**), were isolated from the seed of *Asimina triloba* by McLaughlin and co-workers.[4] The structures assigned by these two groups are shown in Scheme 1. In 2004 and 2005, the total synthesis of **1**, **3a**, and **3b** was reported by Tanaka and co-workers.[5] At the same time, Curran and co-workers reported the synthesis of a stereoisomer library of murisolin and 15 of its isomers, including **1**, **2a**, **2b**, **3a**, and **3b**.[6] Quite recently, Curran et al. also reported the synthesis of a 28-member stereoisomer library of murisolins.[7]

## Results and Discussion

We previously reported a method for constructing the THF moiety for acetogenins that have *threo-trans-threo* or *erythro-trans-threo* relationships from chiral epoxy alcohol **4**. We applied the synthesis to mono-THF acetogenins (10*R*)- and

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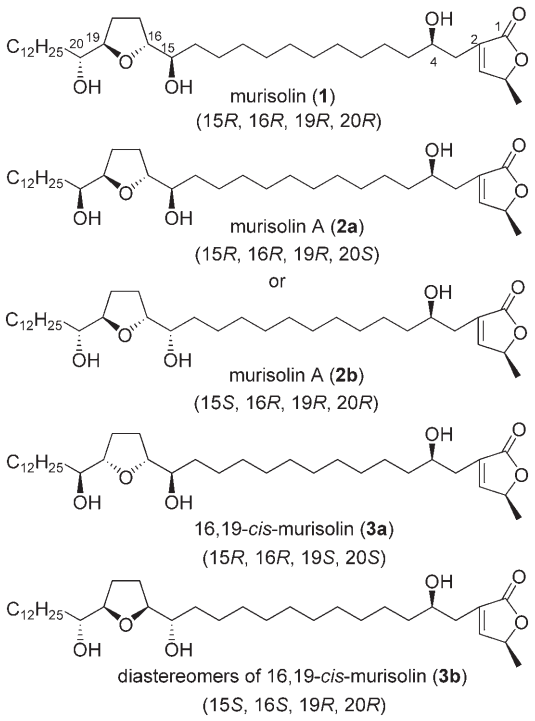
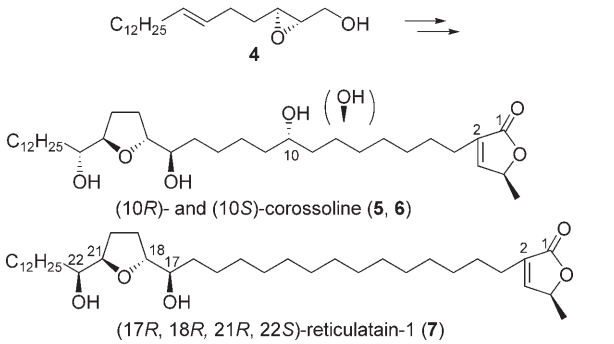



Scheme 1. Proposed structures of murisolin (**1**), murisolin A (**2a**, **2b**), and 16,19-*cis*-murisolin (**3a**).

(10*S*)-corossoline (**5**, **6**),[8] and (17*R*, 18*R*, 21*R*, 22*S*)-reticulatain-1 (**7**) (Scheme 2).[9] Herein, we describe a systematic and stereoselective construction of the mono-THF moieties of annonaceous acetogenins from chiral epoxy alcohol **4**. We focused on the synthesis of murisolin **1**, **2a**, and **3a**, and the evaluation of their biological activity.

The synthetic strategy of **1**, **2a**, and **3a** is shown in Scheme 3. The mono-THF moieties were synthesized from epoxy alcohol **4** by using Sharpless AD mix β (AD = asymmetric dihydroxylation) for *threo-trans-threo* THF moiety **8**, a combination of AD mix β with the Mitsunobu reaction for *erythro-trans-threo* THF moiety **9**, and AD mix α for *threo-cis-threo* THF moiety **10** (Scheme 3).




Scheme 2. Synthesis of (10*R*)- and (10*S*)-corossoline (**5**, **6**) and (17*R*, 18*R*, 21*R*, 22*S*)-reticulatain-1 (**7**) from chiral epoxy alcohol **4**.

As shown in Scheme 4, the THF part of **1** was constructed by a multistep process starting from acrolein and laurylmagnesium bromide. Grignard reaction of acrolein with laurylmagnesium bromide gave allylic alcohol **12**. Johnson–Claisen rearrangement with 1,1,1-triethoxyethane and a catalytic amount of propionic acid gave ester **13**. The conversion of compound **13** into **8** via chiral building block **4** was performed by using the Sharpless epoxidation with L-(+)-diethyl tartrate and dihydroxylation with AD mix β as the key steps, according to our previously published method (Scheme 4).[8]

Scheme 5 shows the synthesis of the THF part of **2a**. Compound **14** was subjected to the Mitsunobu reaction.[10] In this reaction, the product yields are highly dependent on the p$K_a$ values of the acid, perhaps due to the steric hindrance of the acetonide group.[11] *p*-Nitrobenzoic acid gave a good result. On the other hand, acetic or benzoic acid afforded the product in low yield as previously reported.[9] Hydrolysis of *p*-nitrobenzoate **15** with methanolic NaOH gave **16**. The inverted secondary hydroxy group of **16** was protected as the MOM ether to afford **17**. Selective deprotection of the acetonide group of **17** with 60% AcOH gave diol **18**. Silylation of the primary hydroxy group of **18** with TBDMSCl, $Et_3N$, and DMAP afforded **19**. Successive treatment with MsCl and TBAF furnished terminal epoxide **20**. Alkynylation with lithium acetylide–ethylene diamine complex afforded alkyne **21**. Protection of the secondary hydroxy group as the MOM ether gave the THF moiety **9** (Scheme 5).

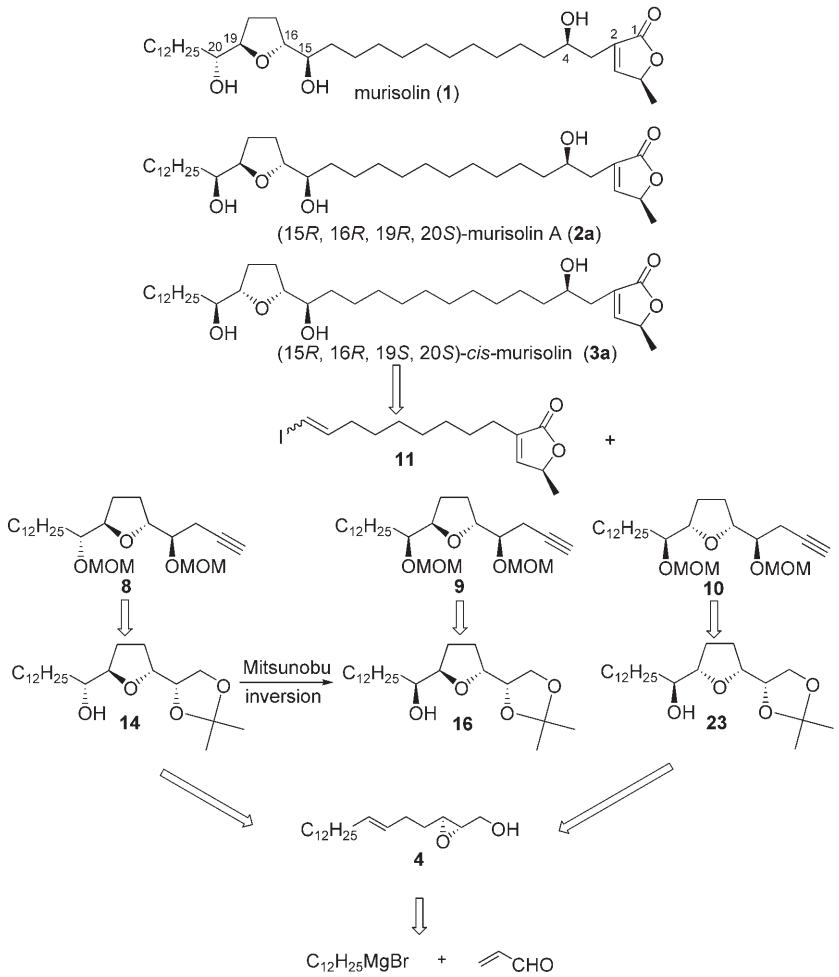
Scheme 6 shows the synthesis of the THF part of **3a**. Asymmetric dihydroxylation of **4** with AD mix α and subsequent acid-catalyzed cyclization with *p*-TsOH resulted in **22**. *Threo-cis-threo* THF moiety **10** was obtained by a multistep process from **22**, which is the same procedure as that shown in Scheme 5.

The α,β-unsaturated γ-lactone segment was synthesized as shown in Scheme 7. Initially, we selected vinyl iodide **30** as the coupling partner of **29**. We examined the direct alkyla-

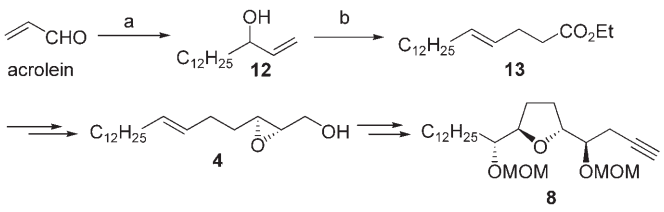
**Abstract in Japanese:**

熱帯・亜熱帯産のバンレイシ科植物より単離されたバンレイシ科アセトゲニンは抗腫瘍などの広範な生物活性を有し，活性発現メカニズムはミトコンドリア電子伝達系の complex I の阻害である。我々はこの化合物の優れた生物活性と特異な構造に着目して合成研究を行ってきた。今回はキラルなエポキシアルコール 4 を合成中間体として murisolin (1), (15*R*, 16*R*, 19*R*, 20*S*)-murisolin-A (2a), (15*R*, 16*R*, 19*S*, 20*S*)-16, 19-cis-murisolin (3a)の系統的な不斉全合成を行った。また化合物 1, 2a, 3a のミトコンドリア complex I 阻害活性試験を行ったところ $IC_{50}$ はほぼ同じ値であり，THF 環部分の立体化学は活性に影響が無いことを確認した。




Scheme 3. Synthetic strategy of **1**, **2a**, and **3a**.




Scheme 4. Synthesis of the THF moiety of **1**. a) $C_{12}H_{25}MgBr$, $Et_2O$, 92%; b) $CH_3C(OEt)_3$, propionic acid, reflux, 86%. See reference [8] for the conversion of **13** into **8**.

tion of γ-lactone **29** (prepared by the method of White et al.[12]) with iodide **30** by using LDA, KHMDS, or NaHMDS (HMDS = 1,1,1,3,3,3-hexamethyldisilazane, LDA = lithium diisopropylamide). All cases, however, resulted in poor yields of the product. We then chose the method of Keinan and co-workers with some modification to prepare **11** (Scheme 7).[13] Sharpless asymmetric dihydroxylation of 1,8-nonadiene with $(DHQD)_2AQN$ as a ligand[14] gave diol **31** with 93% *ee* based on $^1H$ NMR spectroscopic analysis of the corresponding Mosher ester derivative. The primary hydroxy group was selectively converted into the corresponding tosylate, and secondary hydroxy group was protected in the form of silyl ether **32** by using TBDMSCl. The tosyl group was converted to iodide **33** by using NaI in the presence of sodium bicarbonate under reflux in acetone. Lactone **29** was alkylated with iodide **33** with LDA in THF/HMPA to afford **34**, which was oxidized with *m*CPBA following thermal elimination of sulfoxide to afford **35**. Selective dihydroxylation of the monosubstituted double bond followed by oxidative cleavage with $NaIO_4$ produced aldehyde **36**. Finally, olefination with iodoform and chromium dichloride afforded the desired vinyl iodide **11** in the form of a mixture of *E/Z* (3:1) isomers.[15]

The THF moiety **8** and γ-lactone **11** were coupled by the Sonogashira cross-coupling reaction[16] to furnish **37** in 76% yield (Scheme 8). Diimide reduction[17] with *p*-$TsNHNH_2$ and NaOAc in ethylene glycol/diethyl ether under reflux afforded saturated product **38**. Finally, deprotection of the MOM-protected ethers and TBDMS ether with $BF_3{\cdot}Et_2O$ afforded **1** (Scheme 8).[13]

The spectroscopic and physical data ($^1H$ NMR, $^{13}C$ NMR, IR, and MS spectra and melting point) of synthetic **1** are in good agreement with those reported.[3,5] The specific rotation of synthetic **1** is consistent with the highest values reported by Tanaka and co-workers.[5]

The synthesis of **2a** was carried out as described for **1** (Scheme 9). The spectroscopic and physical data ($^1H$ NMR, $^{13}C$ NMR, IR, and MS spectra and melting point) of synthetic **2** are in good agreement with those reported. The specific rotation of synthetic **2** is consistent with that reported by Curran and co-workers, although it is little lower than that reported for natural **2**.[4,6]

McLaughlin and co-workers reported the $^1H$ NMR spectra of tris-(*R*)- and -(*S*)-MTPA esters (MTPA = α-methoxy-α-(trifluoromethyl)phenylacetyl) of natural **2**.[4] As shown in Table 1, the $^1H$ NMR chemical shifts of the carbinol centers of the corresponding tris-(*R*)-MTPA ester of synthetic **2a** are identical to those reported for natural **2**. Recently, Curran et al. published a very important report about the stereochemistry of murisolin isomers.[18] They reported that

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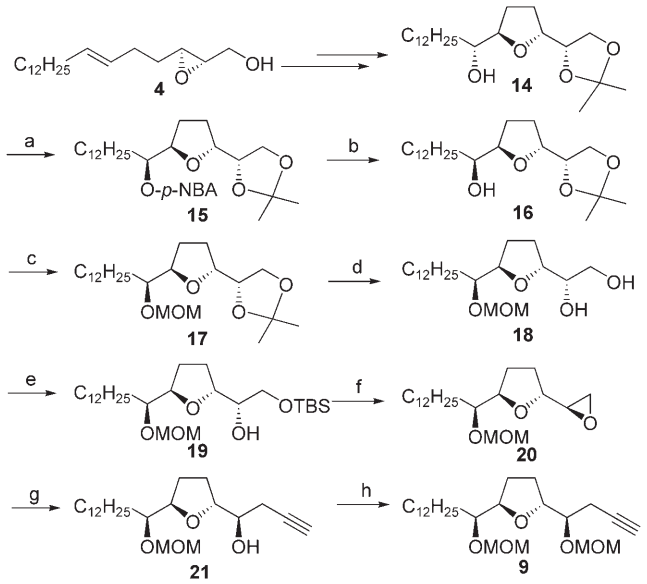
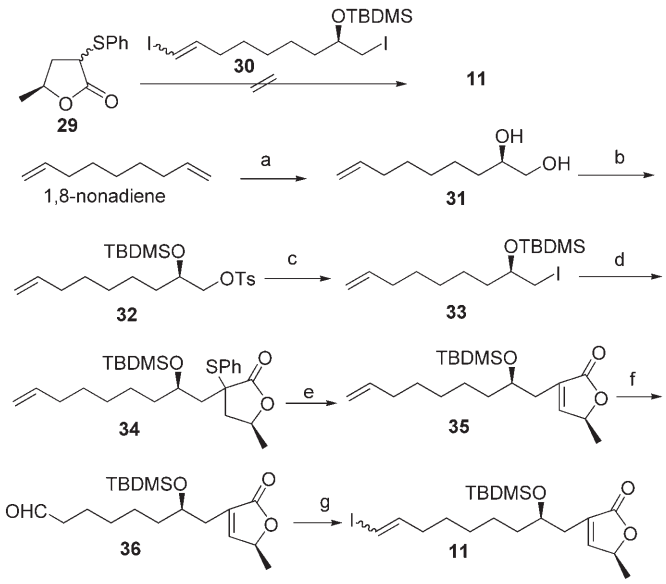
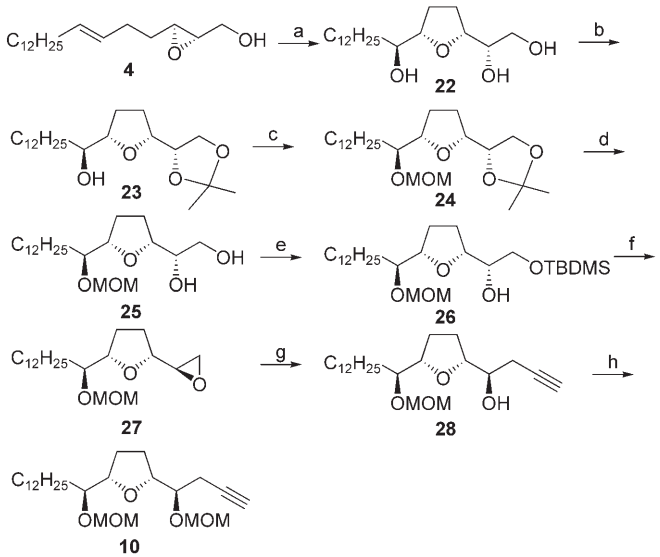


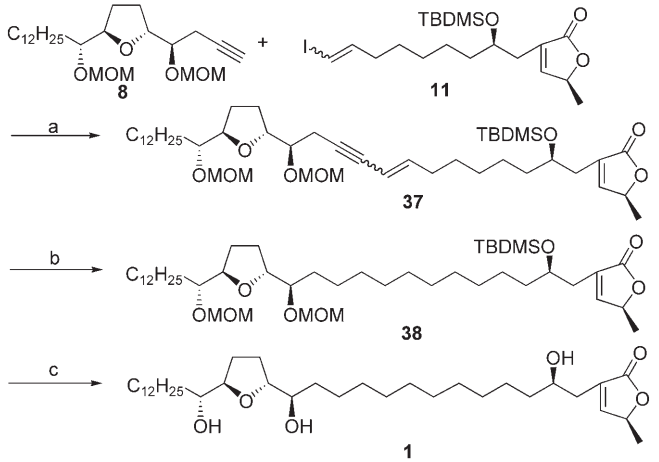
Scheme 5. Synthesis of the THF moiety of **2a**. a) *p*-Nitrobenzoic acid, DEAD, $PPh_3$, THF, 85%; b) NaOH, MeOH, 91%; c) MOMCl, *i*$Pr_2$NEt, $CH_2Cl_2$, 92%; d) 60% AcOH, 60°C, 96%; e) TBDMSCl, $Et_3N$, DMAP, $CH_2Cl_2$, 95%; f) i) MsCl, $Et_3N$, $CH_2Cl_2$; ii) TBAF, THF, 85%; g) lithium acetylide–ethylenediamine complex, DMSO, 83%); h) MOMCl, *i*$Pr_2$NEt, $CH_2Cl_2$, 93%. See reference [8] for the conversion of **4** into **14**. DEAD = diethyl azodicarboxylate, DMAP = 4-dimethylaminopyridine, DMSO = dimethyl sulfoxide, MOM = methoxymethyl, Ms = methanesulfonyl, *p*-NBA = OC-$C_6H_4$-*p*-$NO_2$, TBAF = tetrabutylammonium fluoride, TBDMS = *tert*-butyldimethylsilyl.



Scheme 7. Synthesis of γ-lactone moiety **11**. a) $K_3[Fe(CN)_6]$, $(DHQD)_2AQN$, $K_2CO_3$, $K_2OsO_2(OH)_4$, $CH_3SO_2NH_2$, *t*BuOH/$H_2O$, 66%; b) i) *p*-TsCl, pyridine; ii) TBDMSCl, imidazole, DMF, 99%; c) NaI, $NaHCO_3$, acetone, reflux, 97%; d) LDA, THF/HMPA, 43%; e) i) *m*CPBA, $CH_2Cl_2$; ii) toluene, reflux, 81%; f) i) $K_3[Fe(CN)_6]$, $K_2CO_3$, $K_2OsO_2(OH)_4$, $CH_3SO_2NH_2$, *t*BuOH/$H_2O$; ii) $NaIO_4$, THF/$H_2O$, 85%; g) $CHI_3$, $CrCl_2$, THF, 50%. AQN = anthraquinone, DHQH = dihydroquinidine, DMF = *N*,*N*-dimethylformamide, HMPA = hexamethylphosphoramide, *m*CPBA = *m*-chloroperbenzoic acid.



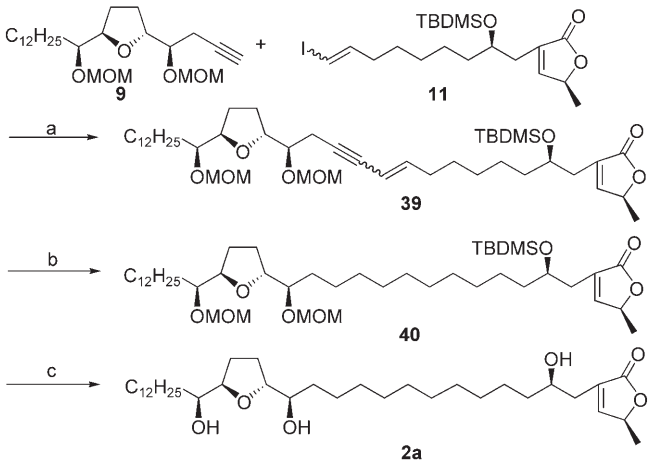
Scheme 6. Synthesis of the THF moiety of **3a**. a) i) AD mix α, $CH_3SO_2NH_2$, *t*BuOH/$H_2O$; ii) *p*-TsOH, $CH_2Cl_2$, 79%); b) DMP, *p*-TsOH, quant.; c) MOMCl, *i*$Pr_2$NEt, $CH_2Cl_2$, quant.; d) 60% AcOH, 60°C, 96%; e) TBDMSCl, $Et_3N$, DMAP, $CH_2Cl_2$, 99%; f) i) MsCl, $Et_3N$, $CH_2Cl_2$; ii) TBAF, THF, 87%; g) lithium acetylide–ethylenediamine complex, DMSO, 83%; h) MOMCl, *i*$Pr_2$NEt, $CH_2Cl_2$, 96%. DMP = 2,2-dimethoxypropane, *p*-Ts = tosyl.



Scheme 8. Synthesis of **1**. a) $[Cl_2Pd(PPh_3)_2]$ (5 mol%), CuI (10 mol%), $Et_3N$, 76%; b) *p*-TsNHNH2, NaOAc, diethoxyethane, 79%; c) $BF_3{\cdot}Et_2O$, $Me_2S$, 84%.

the tris-MTPA ester of **2a** and **2b** could not be distinguished by $^1$H NMR spectroscopy. Thus, it is impossible to determine the absolute configuration of the THF moiety by the advanced Mosher method.[18,19] They suggested that the absolute configuration of natural murisolin A is that of **2b**, that is, (15*S* 16*R*, 19*R*, 20*R*), by comparing the melting points of synthetic **2a** (74–75°C) and **2b** (83–84°C) with that reported for the natural compound (83–84°C).[4,18] Our synthetic sample **2a** (m.p.: 75–76°C) seems to be a diastereomer of natural **2**, as Curran et al. suggested.[18]



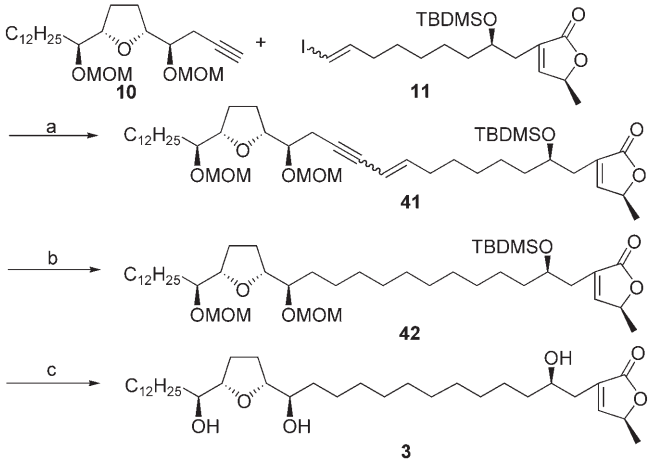

Scheme 9. Synthesis of **2a**. a) $[Cl_2Pd(PPh_3)_2]$ (5 mol%), CuI (10 mol%), $Et_3N$, 91%; b) *p*-$TsNHNH_2$, NaOAc, diethoxyethane, 76%; c) $BF_3{\cdot}Et_2O$, $Me_2S$, 75%.

Table 1. $^1$H NMR chemical shifts of the tris-(*R*)-MTPA esters of synthetic **2a** and those reported for natural **2**.[4]

| MTPA ester | 4-H | 15-H | 16-H | 19-H | 20-H |
|---|---|---|---|---|---|
| (*R*)-MTPA–**2a** | 5.38 | 4.98 | 3.76 | 3.98 | 5.26 |
| (*R*)-MTPA–natural **2** | 5.38 | 4.97 | 3.75 | 3.99 | 5.27 |

The synthesis of **3a** was carried out as described above (Scheme 10). The spectroscopic and physical data ($^1$H NMR, $^{13}$C NMR, IR, and MS spectra, optical rotation, and melting point) of synthetic **3a** were in good agreement with those reported.[4,5] On the other hand, the melting point of **3a** (75.5–76.5 °C) is much higher than that reported for the natural compound (67–68 °C).[5] Tanaka and co-workers also reported the same result.[5b] The absolute configuration of **3a** was reported to be (15*R*, 16*R*, 19*S*, 20*S*) by McLaughlin and co-workers.[4] They made the tris-(*R*)- and -(*S*)-Mosher esters from the natural product and deduced the structure. However, Curran and co-workers suggested that this is not a meaningful analysis because they proved that tris-(*R*)- and -(*S*)-Mosher esters of **3a** and **3b** could not be differentiated by $^1$H NMR spectroscopy.[18] They suggested that the absolute configuration of natural **3** is **3b** by comparing the melting points of synthetic **3a** (63–64 °C) and **3b** (72–73 °C) with that reported for the natural compound (67–68 °C).[4,18,20]

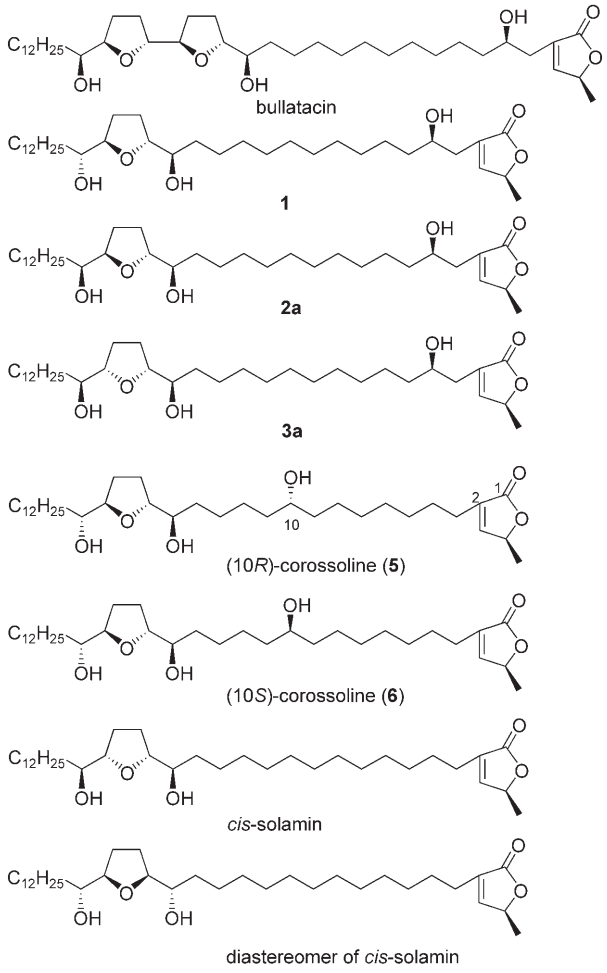
Curran et al. prepared all the murisolin isomers and separated each compound by chiral HPLC.[7,18] Thus, when a natural sample and all candidate isomers are available, the absolute configuration of murisolin A and 16,19-*cis*-murisolin can be assigned by HPLC co-injections.




Scheme 10. Synthesis of **3a**. a) $[Cl_2Pd(PPh_3)_2]$ (5 mol%), CuI (10 mol%), $Et_3N$, 88%; b) *p*-$TsNHNH_2$, NaOAc, diethoxyethane, 78%; c) $BF_3{\cdot}Et_2O$, $Me_2S$, 82%.

Table 2. Inhibitory activity of various acetogenins on mitochondrial complex I.

| Sample | $IC_{50}$ [nM] | Sample | $IC_{50}$ [nM] |
|---|---|---|---|
| bullatacin | 0.8 | *cis*-solamin | 2.6 |
| **1** | 1.8 | diastereomer of *cis*-solamin | 2.5 |
| **2a** | 1.3 | (10*R*)-corossoline | 1.5 |
| **3a** | 1.4 | (10*S*)-corossoline | 2.0 |




Scheme 11. Structures of the biological compounds tested.

Compounds **1**, **2a**, and **3a** were tested as inhibitors of bovine heart mitochondrial complex I. Bullatacin, one of the most potent natural acetogenins, was used as a control; the $IC_{50}$ value used, a measure of inhibitory potency, was ($0.8\pm0.06$) nM. Under the same conditions, **1**, **2a**, and **3a** exhibited almost the same activity (**1**: $IC_{50}=(1.8\pm0.1)$ nM, **2a**: $IC_{50}=(1.3\pm0.1)$ nM, **3a**: $IC_{50}=(1.4\pm0.2)$ nM). The potencies were almost identical to those of corossoline and *cis*-solamin, which were synthesized by us (Table 2 and Scheme 11).[21] This observation is in agreement with the results reported by Miyoshi and co-workers, who found that the stereochemistry around the THF ring(s) and the presence of hydroxy groups in the spacer region are of minor importance for the activity.[22–24]

## Conclusions

We have performed the total synthesis of murisolin (**1**), (15*R*, 16*R*, 19*R*, 20*S*)-murisolin A (**2a**), and (15*R*, 16*R*, 19*S*, 20*S*)-16,19-*cis*-murisolin (**3a**) from chiral epoxy alcohol **4**. These compounds elicited almost the same activity with bovine heart mitochondrial complex I.

## Experimental Section

*General*

All melting points are uncorrected. $^1$H (500 MHz) and $^{13}$C NMR (125 MHz) spectra were recorded on a Bruker DRX 500 FT-NMR spectrometer in $CDCl_3$ with residual $CHCl_3$ as the standard. The coupling constants are given in Hz. Mass spectra were obtained on JEOL JMS-HX211 A and JMS-HX110 A mass spectrometers. IR spectra were recorded on a JASCO FT/IR-480 Plus infrared spectrometer. Optical rotations were determined with a JASCO DIP-1000 polarimeter.

*Syntheses*

**12**: A solution of 1-bromododecane (28.8 mL, 120 mmol) in $Et_2O$ (120 mL) was added dropwise to a suspension of magnesium (3.5 g, 14.1 mmol), a small amount of iodine, and one drop of 1,2-dibromoethane in $Et_2O$ (100 mL) at 23 °C. After the mixture was stirred for 2 h, a solution of distilled acrolein (7.4 mL, 100 mmol) in $Et_2O$ (20 mL) was added at 0 °C, and the mixture was stirred for 2 h at 23 °C. The reaction was quenched with saturated $NH_4Cl$ solution, and the mixture was extracted with $Et_2O$ ($3\times100$ mL). The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified with silica-gel column chromatography (hexane/EtOAc = 7:1) to give **12** (20.8 g, 92%) as a colorless oil. IR (film): $\tilde{\nu}=3342$, 3079, 2924, 2854, 1466, 990, 920; $^1$H NMR (500 MHz, $CDCl_3$): $\delta=0.88$ (t, $J=6.7$ Hz, 3H), 1.26–1.30 (m, 22H), 1.43 (d, $J=4.2$ Hz, 1H), 4.09 (m, 1H), 5.10 (dd, $J=10.4$, 1.1 Hz, 1H), 5.22 (dd, $J=17.2$, 1.2 Hz, 1H), 5.87 ppm (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta=14.1$, 22.7, 25.4, 29.4, 29.6, 29.6, 29.7, 29.7, 32.0, 37.1, 73.3, 114.5, 141.4 ppm; elemental analysis: calcd (%) for $C_{15}H_{30}O$: C 79.58, H 13.36; found: C 79.29, H 13.31.

**13**: Compound **12** (22.6 g, 119 mmol) was dissolved in 1,1,1-triethoxyethane (36.6 mL, 200 mmol), and a catalytic amount of propionic acid was added to the mixture. The mixture was heated under reflux for 16 h. The reaction was quenched with saturated $NaHCO_3$ solution (30 mL), and the mixture was extracted with $Et_2O$ ($4\times30$ mL). The organic phase was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified with silica-gel column chromatography (hexane/EtOAc = 20:1) to give **13** (30.3 g, 86%) as a colorless oil. IR (film): $\tilde{\nu}=2920$, 2854, 1743, 1465, 1437, 1247, 1168, 968 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta=0.88$ (t, $J=6.7$ Hz, 3H), 1.20–1.30 (m, 23H), 1.96 (m, 2H), 2.30–2.36 (m, 4H), 4.13 (q, $J=7.1$ Hz, 2H), 5.42 ppm (m, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta=14.1$, 14.3, 22.7, 28.0, 29.2, 29.4, 29.5, 29.5, 29.7, 29.7, 29.7, 32.0, 32.5, 34.5, 60.2, 127.9, 131.9, 173.3 ppm; elemental analysis: calcd (%) for $C_{19}H_{36}O_2$: C 76.97, H 12.24; found: C 76.71, H 12.18.

**15**: DEAD (40% in toluene, 4.0 mL, 9.16 mmol) was added dropwise to a solution of **14** (846 mg, 2.3 mmol), *p*-nitrobenzoic acid (1.54 g, 9.16 mmol), and $PPh_3$ (2.40 g, 9.16 mmol) in THF (20 mL) at 0 °C. After being stirred for 19 h at room temperature, the reaction mixture was concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 50:1) to afford **15** (1.00 g, 85%) as a colorless oil. $[\alpha]_D^{24}=-1.73$ ($c=1.00$ in $CHCl_3$); IR (film): $\tilde{\nu}=3111$, 3079, 2924, 3055, 2854, 1726, 1608, 1530, 1465, 1370, 1347, 1319, 1272, 1213, 1154, 1102, 1067, 1014, 945, 873, 846, 783, 720 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta=0.88$ (t, $J=6.8$ Hz, 3H), 1.22–1.26 (m, 20H), 1.33 (s, 3H), 1.37 (s, 3H), 1.68–1.73 (m, 2H), 1.82–1.93 (m, 2H), 2.05–2.13 (m, 2H), 3.77 (m, 1H), 3.86 (m, 1H), 3.98 (m, 1H), 4.06 (m, 1H), 4.16 (m, 1H), 5.23 (m, 1H), 8.19–8.30 ppm (m, 4H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta=14.1$, 22.7, 25.2, 25.4, 26.6, 27.3, 28.3, 29.4, 29.4, 29.5, 29.5, 29.6, 29.6, 29.7, 31.0, 31.9, 67.4, 76.8, 77.7, 80.4, 80.6, 109.4, 123.6, 130.7, 135.9, 150.6, 164.3 ppm; MS (FAB): $m/z=519$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{29}H_{45}O_7N$: 519.3196 $[M+H]^+$; found: 519.3193.

**16**: Ester **15** (441 mg, 0.85 mmol) was dissolved in MeOH (5 mL) and treated with NaOH (250 mg, 6.3 mmol) at room temperature. After being stirred for 20 h, the reaction mixture was concentrated and extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 5:1) to afford **16** (286 mg, 91%) as a waxy solid. M.p.: 29–30 °C; $[\alpha]_D^{21}=+2.1$ ($c=0.46$ in $CHCl_3$); IR (film):$\tilde{\nu}=3413$, 2981, 2914, 2847, 1465, 1370, 1254, 1214, 1155, 1066, 947, 851 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta=0.88$ (t, $J=7.0$ Hz, 3H), 1.24–1.28 (m, 20H), 1.36 (s, 3H), 1.38–1.40 (m, 2H), 1.42 (s, 3H), 1.78–1.94 (m, 4H), 2.09 −2.14 (m, 1H), 3.75 (m, 1H), 3.82 (m, 1H), 3.90 (m, 1H), 3.96 (m, 1H), 4.02 (m, 1H), 4.09 ppm (m, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta=14.1$, 22.7, 24.8, 25.3, 26.0, 26.7, 29.0, 29.4, 29.6, 29.6, 29.7, 29.7, 31.9, 32.6, 67.3, 71.8, 78.1, 80.3, 82.8, 109.4 ppm; MS (FAB): $m/z=371$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{22}H_{43}O_4$: 371.3161 $[M+H]^+$; found: 371.3168.

**17**: MOMCl (caution! 0.12 mL, 1.5 mmol) was added to a solution of **16** (285 mg, 0.77 mmol) and $i$Pr$_2$NEt (0.34 mL, 1.9 mmol) in $CH_2Cl_2$ (6 mL) at 0 °C. After the mixture was stirred for 20 h, the reaction was quenched with saturated $NH_4Cl$ (3 mL) and extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 4:1) to afford **17** (296 mg, 92%) as a colorless oil. $[\alpha]_D^{20}=-12.7$ ($c=0.46$ in $CHCl_3$); IR (film): $\tilde{\nu}=2984$, 2925, 2854, 1465, 1370, 1254, 1213, 1151, 1067, 1041, 919, 850 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta=0.88$ (t, $J=6.8$ Hz, 3H), 1.26–1.31 (m, 20H), 1.35 (s, 3H), 1.40 (s, 3H), 1.75–1.81 (m, 1H), 1.85–1.96 (m, 2H), 2.10 (m, 1H), 3.39 (s, 3H), 3.64 (m, 1H), 3.81 (m, 1H), 3.87 (m, 1H), 3.98 (m, 1H), 4.07 (m, 1H), 4.64 (d, $J=6.6$ Hz, 1H), 4.75 ppm (d, $J=6.6$ Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta=14.1$, 22.7, 25.3, 25.7, 26.2, 26.7, 29.0, 29.4, 29.6, 29.6, 29.7, 29.7, 29.7, 29.8, 31.8, 31.9, 55.7, 67.6, 78.1, 78.6, 80.3, 81.9, 96.8, 109.3 ppm; MS (FAB): $m/z=437$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{24}H_{46}O_5Na$: 437.3243 $[M+Na]^+$; found: 437.3248.

**18**: Compound **17** (291 mg, 0.70 mmol) was treated with acetic acid (60%, 5 mL) at 60 °C. After being stirred for 2 h at the same temperature, the reaction mixture was concentrated, and the residue was subjected to chromatography over silica gel (hexane/EtOAc = 1:1) to afford **18** (251 mg, 96%) as a colorless oil. $[\alpha]_D^{19}=+4.96$ ($c=2.07$, in $CHCl_3$); IR (film): $\tilde{\nu}=3410$, 2925, 2854, 1466, 1378, 1304, 1214, 1150, 1038, 919, 721 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta=0.88$ (t, $J=6.8$ Hz, 3H), 1.26–1.30 (m, 20H), 1.40–1.51 (m, 2H), 1.77–2.00 (m, 4H), 2.40 (brs, 2H, OH), 3.39 (s, 3H), 3.64 (m, 2H), 3.73 (m, 2H), 3.93 (m, 1H), 4.00 (m, 1H), 4.65 (d, $J=6.6$ Hz, 1H), 4.75 ppm (d, $J=6.6$ Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta=14.1$, 22.7, 25.7, 26.4, 27.7, 29.4, 29.6, 29.6, 29.7, 29.7, 29.7, 29.8, 31.6, 31.9, 55.7, 64.1, 73.2, 78.8, 80.5, 81.8, 96.7 ppm; MS

(FAB): $m/z = 374$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{21}H_{43}O_5$: 375.3110 $[M+H]^+$; found: 374.3116.

**19**: TBDMSCl (150 mg, 0.67 mmo), $Et_3N$ (0.093 mL, 0.67 mmol), and DMAP (8.2 mg, 0.067 mmol) were added to a solution of **18** (250 mg, 0.67 mmol) in $CH_2Cl_2$ (10 mL). After the mixture was stirred for 22 h, the reaction was quenched with saturated $NH_4Cl$ (10 mL), and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 5:1) to afford **19** (310 mg, 95%) as a colorless oil. $[\alpha]_D^{18} = -11.3$ ($c = 2.66$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3479$, 2926, 2855, 1465, 1361, 1254, 1149, 1107, 1040, 920, 837, 778 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.07$ (s, 6H), 0.87 (t, $J = 6.8$ Hz, 3H), 0.88 (s, 9H), 1.26–1.30 (m, 18H), 1.43–1.50 (m, 4H), 1.87 (m, 4H), 2.03 (m, 1H), 2.42 (d, $J = 4.4$ Hz, 1H, OH), 3.39 (s, 3H), 3.56 (m, 1H), 3.63 (m, 1H), 3.73 (m, 2H), 3.86 (m, 1H), 3.97 (m, 1H), 4.65 (d, $J = 6.6$ Hz, 1H), 4.75 ppm (d, $J = 6.6$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = -5.4$, 0.0, 14.1, 18.3, 22.7, 25.6, 25.9, 26.5, 28.1, 29.4, 29.6, 29.7, 29.7, 29.8, 31.8, 31.9, 55.7, 64.4, 73.4, 78.8, 79.3, 81.8, 96.7 ppm; MS (FAB): $m/z = 511$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{27}H_{56}O_5SiNa$: 511.3795 $[M+Na]^+$; found: 511.3802.

**20**: MsCl (0.12 mL, 1.50 mmol) was added to a solution of **19** (640 mg, 1.3 mmol) and $Et_3N$ (0.36 mL, 2.60 mmol) in $CH_2Cl_2$ (10 mL) at −5 °C. After the mixture was stirred for 10 min at the same temperature, the reaction was quenched with saturated $NH_4Cl$ (3 mL), and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was dissolved in THF (5 mL), and TBAF (1.0 M in THF, 5.2 mL, 5.2 mmol) was added to this solution at 0 °C. After being stirred for 12 h at room temperature, the mixture was extracted with diethyl ether. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 5:1) to afford **20** (398 mg, 85%) as a colorless oil. $[\alpha]_D^{20} = -10.8$ ($c = 1.66$ in $CHCl_3$); IR (film): $\tilde{\nu} = 2925$, 2854, 1466, 1377, 1302, 1255, 1214, 1149, 1104, 1039, 919, 891 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta =$ 0.88 (t, $J = 6.8$ Hz, 3H), 1.26–1.30 (m, 20H), 1.40–1.51 (m, 2H), 1.82–1.98 (m, 3H), 2.08 (m, 1H), 2.68 (m, 1H), 2.75 (m, 1H), 3.38 (s, 3H), 3.67 (m, 1H), 3.88 (m, 1H), 4.00 (m, 1H), 4.65 (d, $J = 6.6$ Hz, 1H), 4.75 ppm (d, $J = 6.6$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = 14.1$, 22.7, 25.6, 26.1, 29.0, 29.4, 29.6, 29.6, 29.6, 29.7, 29.7, 29.8, 31.9, 44.2, 54.2, 55.7, 78.6, 82.2, 96.8 ppm; MS (FAB): $m/z = 379$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{21}H_{40}O_4Na$: 379.2825 $[M+Na]^+$; found: 379.2820.

**21**: A solution of **20** 192 mg, 0.53 mmol) in DMSO (2 mL) was added to a suspension of lithium acetylide ethylenediamine complex (220 mg, 2.1 mmol) in DMSO (2 mL). After the mixture was stirred for 24 h at room temperature, the reaction was quenched with saturated $NH_4Cl$ (5 mL) at 0 °C, and the mixture was extracted with diethyl ether. The organic phase was washed with water then brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 4:1) to afford **21** (167 mg, 83%) as a colorless oil. $[\alpha]_D^{29} = +1.69$ ($c = 0.32$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3458$, 3312, 2925, 2854, 2120, 1466, 1377, 1302, 1215, 1149, 1104, 1038, 919 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.88$ (t, $J = 6.8$ Hz, 3H), 1.24–1.30 (m, 20H), 1.42 (m, 2H), 1.47 (m, 1H), 1.75 (m, 1H), 1.95 (m, 2H), 2.01 (t, $J = 2.7$ Hz, 1H), 2.42 (m, 2H), 2.48 (d, $J = 5.3$ Hz, 1H, OH), 3.39 (s, 3H), 3.60 (m, 1H), 3.70 (m, 1H), 3.99 (m, 2H), 4.66 (d, $J = 6.6$ Hz, 1H), 4.77 ppm (d, $J = 6.6$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = 14.1$, 22.7, 24.0, 25.7, 26.7, 28.4, 29.4, 29.6, 29.6, 29.7, 29.7, 29.7, 29.8, 31.8, 31.9, 55.7, 70.2, 71.9, 77.3, 78.4, 80.6, 81.0, 81.9, 96.8 ppm; MS (FAB): $m/z = 383$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{23}H_{43}O_4$: 383.3161 $[M+H]^+$; found: 383.3156.

**9**: MOMCl (caution! 0.11 mL, 1.5 mmol) was added to a solution of **21** (287 mg, 0.75 mmol) and $i$Pr$_2$NEt (0.33 mL, 1.9 mmol) in $CH_2Cl_2$ (6 mL) at 0 °C. After the mixture was stirred for 23 h at room temperature, the reaction was quenched with saturated $NH_4Cl$ (5 mL), and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 5:1) to afford **9** (300 mg, 93%) as a colorless oil. $[\alpha]_D^{15} = -22.7$ ($c = 0.57$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3312$, 2925, 2854, 2121, 1466, 1215, 1150, 1104, 1039, 918 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.88$ (t, $J = 6.8$ Hz, 3H), 1.24–1.30 (m, 21H), 1.37–1.50 (m, 3H), 1.73 (m, 1H), 1.92 (m, 2H), 1.99 (t, $J = 2.6$ Hz, 1H), 2.42 (dt, $J = 6.2$, 2.6 Hz, 2H), 2.48 (d, $J = 5.3$ Hz, 1H), 3.39 (s, 3H), 3.59 (m, 1H), 3.65 (m, 1H), 3.70 (m, 1H), 3.99 (m, 2H), 4.14 (m, 1H), 4.66 (d, $J = 6.6$ Hz, 1H), 4.79 ppm (d, $J = 6.6$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = 14.1$, 21.8, 22.7, 25.6, 26.5, 28.3, 29.4, 29.6, 29.6 (3C), 29.7, 29.7, 29.7, 29.8, 31.9, 31.9, 55.7, 55.8, 69.8, 77.3, 78.6, 80.3, 81.0, 81.7, 96.6, 96.9 ppm; MS (FAB): $m/z = 427$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{25}H_{47}O_5$: 427.3423 $[M+H]^+$; found: 427.3420.

**22**: A solution of **4** (516 mg, 1.74 mmol) in $t$BuOH/$H_2O$ (1:1, 5 mL) and methanesulfonamide (166 mg, 1.74 mmol) were added to a suspension of AD mix α (1.40 g, 1 mmol) in $t$BuOH/$H_2O$ (1:1, 10 mL) at 0 °C. After the mixture was stirred for 11 h at this temperature, the reaction was quenched with saturated aqueous $Na_2SO_3$ (10 mL), and the mixture was extracted with EtOAc. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was dissolved in $CH_2Cl_2$ (10 mL), and a catalytic amount of $p$-TsOH was added to this solution at 0 °C. After vigorous stirring for 30 min, the reaction mixture was diluted with diethyl ether, filtered, and concentrated. The crude solid was recrystallized (EtOAc) to afford **22** (456 mg, 79%) as a colorless solid. M.p.: 68–69 °C; $[\alpha]_D^{21} = +1.07$ ($c = 1.04$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3417$, 2921, 2849, 1463, 1379, 1227, 1137, 1058, 877 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.88$ (t, $J = 6.6$ Hz, 3H), 1.24–1.40 (m, 20H), 1.46 (m, 3H), 1.78 (m, 1H), 1.82–1.94 (m, 3H), 2.20–2.70 (br s, 3H, OH), 3.43 (m, 1H), 3.62 (m, 1H), 3.72 (m, 1H), 3.81 (m, 2H), 3.96 ppm (m, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = 14.1$, 22.7, 25.7, 26.5, 28.1, 29.4, 29.6, 29.7, 29.6, 29.6, 29.7, 31.9, 34.2, 63.9, 73.3, 74.3, 80.4, 82.4 ppm; MS (FAB): $m/z =$ 331 $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{19}H_{39}O_4$: 331.2848 $[M+H]^+$; found: 331.2856.

**23**: Compound **22** (456 mg, 1.38 mmol) was treated with 2,2-dimethoxypropane (4.6 mL) and a catalytic amount of $p$-TsOH at room temperature. After being stirred for 6 h, the reaction mixture was diluted with diethyl ether. The organic phase was washed with saturated aqueous $NaHCO_3$ (10 mL) then brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 5:1) to afford **23** (511 mg, quant.) as a colorless oil. $[\alpha]_D^{22} =$ −3.50 ($c = 0.16$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3491$, 2983, 2925, 2854, 1466, 1370, 1254, 1213, 1155, 1067, 946, 849 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.88$ (t, $J = 6.7$ Hz, 3H), 1.26–1.55 (m, 21H), 1.35 (s, 3H), 1.42 (s, 3H), 1.75 (m, 1H), 1.85–1.95 (m, 2H), 1.96–2.02 (m, 1H), 2.41 (d, $J = 4.2$ Hz, 1H), 3.37 (m, 1H), 3.80 (m, 2H), 3.92 (m, 1H), 4.07 ppm (m, 2H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = 14.1$, 22.7, 25.2, 25.7, 26.4, 27.6, 27.7, 29.3, 29.6, 29.7, 29.7, 29.7, 31.9, 34.1, 67.1, 74.4, 77.7, 80.2, 83.0, 109.5 ppm; MS (FAB): $m/z = 371$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{22}H_{43}O_4$: 371.3161 $[M+H]^+$; found: 371.3155.

**24**: MOMCl (caution! 0.30 mL, 4.1 mmol) was added to a solution of **23** (511 mg, 1.38 mmol) and $i$Pr$_2$NEt (0.60 mL, 3.5 mmol) in $CH_2Cl_2$ (5 mL) at 0 °C. After the mixture was stirred for 13 h, the reaction was quenched with saturated $NH_4Cl$ (3 mL), and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 5:1) to afford **24** (572 mg, quant.) as a colorless oil. $[\alpha]_D^{20} = -25.4$ ($c = 1.01$ in $CHCl_3$); IR (film): $\tilde{\nu} = 2984$, 2925, 2854, 1466, 1369, 1254, 1213, 1150, 1041, 919, 850 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.88$ (t, $J = 6.4$ Hz, 3H), 1.26–1.50 (m, 20H), 1.34 (s, 3H), 1.41 (s, 3H), 1.59–1.67 (m, 1H), 1.80–1.89 (m, 2H), 1.99–2.04 (m, 1H), 3.39 (s, 3H), 3.45 (m, 1H), 3.84–3.92 (m, 4H), 4.07 (m, 1H), 4.67 (d, $J =$ 6.6 Hz, 1H), 4.78 ppm (d, $J = 6.6$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = 14.1$, 22.7, 25.3, 25.4, 26.7, 27.4, 28.5, 29.3, 29.6, 29.6, 29.6, 29.7, 29.7, 29.8, 31.4, 31.9, 55.7, 67.6, 78.0, 79.9, 80.2, 82.5, 96.6, 109.2 ppm; MS (FAB): $m/z = 437$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{24}H_{46}O_5Na$: 437.3243 $[M+Na]^+$; found: 437.3251.

**25**: Compound **24** (572 mg, 1.38 mmol) was treated with acetic acid (60%, 11 mL) at 60 °C. After being stirred for 2 h at the same temperature, the reaction mixture was concentrated, and the residue was subjected to chromatography over silica gel (hexane/EtOAc = 1:1) to afford **25** (494 mg, 96%) as a colorless oil. M.p.: 51.5–52.5 °C; $[\alpha]_D^{18} = +25.7$ ($c =$

1.04 in $CHCl_3$); IR (film): $\tilde{\nu}$ = 3422, 2917, 2848, 1463, 1376, 1346, 1310, 1264, 1218, 1150, 1103, 1037, 917, 728 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ = 0.87 (t, $J$ = 7.0 Hz, 3H), 1.26–1.60 (m, 22H), 1.71–1.98 (m, 5H), 2.59 (br s, 1H, OH), 3.39 (s, 3H), 3.42 (m, 1H), 3.56–3.69 (m, 3H), 3.83–3.87 (m, 1H), 3.96–4.02 (m, 2H), 4.69 (d, $J$ = 6.9 Hz, 1H), 4.71 ppm (d, $J$ = 6.9 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ = 14.1, 22.7, 25.4, 25.7, 28.2, 29.3, 29.6, 29.6, 29.6, 29.8, 31.9, 31.9, 55.9, 63.7, 73.0, 80.2, 80.6, 80.9, 96.3 ppm; MS (FAB): $m/z$ = 375 $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{21}H_{43}O_5$: 375.3110 $[M+H]^+$; found: 375.3118.

**26**: TBDMSCl (298 mg, 1.98 mmo), $Et_3N$ (0.18 mL, 1.32 mmol), and DMAP (15.9 mg, 0.13 mmol) were added to a solution of **25** (494 mg, 1.32 mmol) in $CH_2Cl_2$ (13 mL). After the mixture was stirred for 24 h, the reaction was quenched with saturated $NH_4Cl$ (10 mL), and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 3:1) to afford **26** (640 mg, 99%) as a colorless oil. $[\alpha]_D^{16} = +1.18$ ($c$ = 1.10 in $CHCl_3$); IR (film): $\tilde{\nu}$ = 3460, 2925, 2855, 1464, 1362, 1254, 1218, 1106, 1039, 919, 837, 778 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ = 0.06 (s, 6H), 0.88 (t, $J$ = 7.0 Hz, 3H), 0.90 (s, 9H), 1.26–1.70 (m, 23H), 1.91–1.98 (m, 3H), 2.98 (d, $J$ = 2.9 Hz, 1H, OH), 3.39 (s, 3H), 3.45 (m, 1H), 3.67 (m, 3H), 3.95 (m, 2H), 4.68 (d, $J$ = 6.7 Hz, 1H), 4.75 ppm (d, $J$ = 6.7 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ = −5.44, −5.4, 14.1, 18.3, 22.7, 25.4, 25.9, 26.1, 27.9, 29.3, 29.6, 29.6, 29.6, 29.7, 29.8, 31.7, 31.9, 55.8, 64.4, 73.2, 79.8, 80.1, 81.4, 96.4 ppm; MS (FAB): $m/z$ = 511 $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{27}H_{56}O_5SiNa$: 511.3795 $[M+Na]^+$; found: 511.3791.

**27**: MsCl (0.12 mL, 1.50 mmol) was added to a solution of **26** (640 mg, 1.3 mmol) and $Et_3N$ (0.36 mL, 2.60 mmol) in $CH_2Cl_2$ (10 mL) at −5 °C. After the mixture was stirred for 10 min at the same temperature, the reaction was quenched with saturated $NH_4Cl$ (3 mL), and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was dissolved in THF (5 mL), and TBAF (1.0 M in THF, 5.2 mL, 5.2 mmol) was added to this solution at 0 °C. After the mixture was stirred for 3 h at room temperature, the organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 5:1) to afford **27** (406 mg, 87%) as a colorless oil. $[\alpha]_D^{16} = -27.3$ ($c$ = 1.06 in $CHCl_3$); IR (film): $\tilde{\nu}$ = 2925, 2854, 1467, 1361, 1254, 1216, 1149, 1102, 1042, 918, 893 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ = 0.88 (t, $J$ = 6.8 Hz, 3H), 1.22–1.31 (m, 16H), 1.36–1.46 (m, 4H), 1.49–1.53 (m, 2H), 1.67–1.70 (m, 1H), 1.84–1.90 (m, 2H), 1.99–2.03 (m, 1H), 2.67 (m, 2H), 2.97 (m, 1H), 3.40 (s, 3H), 3.50 (m, 1H), 3.85 (m, 1H), 3.93 (m, 1H), 4.69 (d, $J$ = 6.7 Hz, 1H), 4.83 ppm (d, $J$ = 6.7 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ = 14.1, 22.7, 25.3, 27.7, 28.6, 29.4, 29.6, 29.6, 29.7, 29.7, 29.8, 31.3, 31.9, 43.8, 54.1, 55.7, 78.4, 79.8, 82.7, 96.7 ppm; MS (FAB): $m/z$ = 379 $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{21}H_{40}O_4Na$: 379.2824 $[M+Na]^+$; found: 379.2828.

**28**: A solution of **27** (406 mg, 1.14 mmol) in DMSO (0.9 mL) was added to a suspension of lithium acetylide ethylenediamine complex (583 mg, 5.7 mmol) in DMSO (2 mL). After the mixture was stirred for 22 h at room temperature, the reaction was quenched with saturated $NH_4Cl$ (5 mL) at 0 °C, and the mixture was extracted with diethyl ether. The organic phase was washed with water then brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 4:1) to afford **28** (365 mg, 83%) as a colorless oil. $[\alpha]_D^{29} = +5.79$ ($c$ = 1.02 in $CHCl_3$); IR (film): $\tilde{\nu}$ = 3444, 3313, 2925, 2853, 2119, 1466, 1376, 1300, 1216, 1150, 1103, 1036, 919 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ = 0.88 (t, $J$ = 6.9 Hz, 3H), 1.25–1.40 (m, 20H), 1.52–1.63 (m, 2H), 1.86 (m, 1H), 1.92–2.01 (m, 3H), 2.00 (t, $J$ = 2.6 Hz, 1H), 2.46 (dd, $J$ = 6.7, 2.6 Hz, 2H), 3.40 (s, 3H), 3.46 (m, 1H), 3.50 (m, 1H), 3.59 (m, 1H), 4.04 (m, 1H), 4.12 (m, 1H), 4.69 (d, $J$ = 7.2 Hz, 1H), 4.70 ppm (d, $J$ = 7.2 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ = 14.1, 22.7, 24.9, 25.4, 28.1, 28.2, 29.3, 29.6, 29.6, 29.7, 29.8, 31.9, 31.9, 55.9, 69.8, 72.4, 80.2, 80.3, 81.0, 81.4, 96.3 ppm; MS (FAB): $m/z$ = 383 $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{23}H_{43}O_4$: 383.3161 $[M+H]^+$; found: 383.3161.

**10**: MOMCl (caution! 0.14 mL, 1.90 mmol) was added to a solution of **28** (365 mg, 0.95 mmol) and $i$Pr$_2$NEt (0.41 mL, 2.4 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C. After the mixture was stirred for 23 h at room temperature, the reaction was quenched with saturated $NH_4Cl$ (5 mL), and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 5:1) to afford **10** (389 mg, 96%) as a colorless oil. $[\alpha]_D^{23} = -29.0$ ($c$ = 0.57 in $CHCl_3$); IR (film): $\tilde{\nu}$ = 3312, 2925, 2853, 2822, 2121, 1467, 1215, 1150, 1103, 1041, 918 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ = 0.87 (t, $J$ = 6.8 Hz, 3H), 1.25–1.50 (m, 21H), 1.57–1.72 (m, 2H), 1.86–1.92 (m, 2H), 1.96 (t, $J$ = 2.7 Hz, 1H), 2.40 (ddd, $J$ = 16.8, 6.1, 2.7 Hz, 1H), 2.55 (ddd, $J$ = 16.8, 5.5, 2.7 Hz, 1H), 3.38 (s, 3H), 3.40 (s, 3H), 3.50 (m, 1H), 3.69 (m, 1H), 3.92 (m, 1H), 4.08 (m, 1H), 4.66 (d, $J$ = 6.6 Hz, 1H), 4.77 (s, 2H), 4.81 ppm (d, $J$ = 6.7 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ = 14.1, 21.5, 22.7, 25.4, 27.4, 27.7, 29.3, 29.6, 29.6, 29.6, 29.6, 29.6, 29.8, 31.2, 31.9, 55.7, 55.7, 69.7, 77.5, 79.8, 80.4, 81.1, 82.0, 96.6, 96.7 ppm; MS (FAB): $m/z$ = 449 $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{25}H_{46}O_5Na$: 449.3243 $[M+Na]^+$; found: 449.3235.

**31**: 1,8-Nonadiene (2.9 g, 23 mmol) in $t$BuOH/$H_2O$ (1:1, 67 mL) was added to a suspension of AQN(DHQD)$_2$ (200 mg, 0.23 mmol), $K_2OsO_4{\cdot}2H_2O$ (34 mg, 0.093 mmol), $K_3[Fe(CN)_6]$ (23 g, 70 mmol), $K_2CO_3$ (9.64 g, 70 mmol), and $CH_3SO_2NH_2$ (2.21 g, 23 mmol) in $t$BuOH/$H_2O$ (1:1, 70 mL) at 0 °C. After the mixture was stirred for 20 min at this temperature, the reaction was quenched with saturated aqueous $Na_2SO_3$ (50 mL), and the mixture was extracted with EtOAc. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 1:1) to afford **31** (2.43 g, 66%) as a colorless oil. $[\alpha]_D^{18} = +0.25$ ($c$ = 1.08 in $CHCl_3$); IR (film): $\tilde{\nu}$ = 3366, 3037, 2977, 2857, 1641, 1463, 1227, 1066, 993 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ = 1.34–1.45 (m, 8H), 1.80 (br s, 1H, OH), 1.96 (br s, 1H, OH), 2.05 (m, 2H), 3.45 (m, 1H), 3.67 (m, 2H), 4.95 (m, 2H), 5.80 ppm (m, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ = 25.4, 28.8, 29.1, 33.7, 66.9, 72.3, 114.3, 139.0 ppm; MS (CI): $m/z$ = 159 $[M+H]^+$; HRMS (CI): $m/z$ calcd for $C_9H_{19}O_2$: 159.1385 $[M+H]^+$; found: 159.1387.

**32**: $p$-TsCl (2.48 g, 13 mmol) was added to a solution of **31** (1.47 g, 9.3 mmol) in pyridine (19 mL) at 0 °C. After the mixture was stirred for 1 h at room temperature, the reaction was quenched with $H_2O$, and the mixture was extracted with diethyl ether. The organic phase was washed with saturated $NH_4Cl$ then brine, dried over $MgSO_4$, filtered, and concentrated. The residue was dissolved in DMF (7 mL), and imidazole (1.88 g, 28 mmol) and TBDMSCl (2.0 g, 13.8 mmol) were added to the mixture. After the mixture was stirred for 5 h, the reaction was quenched with saturated aqueous $NH_4Cl$, and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 20:1) to afford **32** (2.91 g, 99%) as a colorless oil. $[\alpha]_D^{18} = +4.13$ ($c$ = 1.10 in $CHCl_3$); IR (film): $\tilde{\nu}$ = 3075, 2929, 2857, 1640, 1599, 1496, 1463, 1365, 1307, 1291, 1255, 1211, 1189, 1178, 1098, 1049, 1020, 979, 910, 813, 777, 666 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ = 0.02 (s, 6H), 0.84 (s, 9H), 1.25–1.41 (m, 8H), 2.02 (m, 2H), 2.45 (s, 3H), 3.84 (m, 3H), 4.92–5.00 (m, 2H), 5.80 (m, 1H), 7.34 (d, $J$ = 8.1 Hz, 2H), 7.79 ppm (d, $J$ = 7.8 Hz, 2H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ = −4.8, −4.6, 18.0, 21.6, 24.6, 25.7 (3C), 28.7, 29.1, 33.6, 70.0, 73.1, 114.3, 128.0 (2C), 133.1, 138.9, 144.7 ppm.

**33**: $NaHCO_3$ (3.44 g, 40 mmol) and NaI (5.1 g, 34 mmol) were added to a solution of **32** (2.15 g, 6.9 mmol) in acetone (23 mL). After the mixture was heated under reflux for 22 h, the reaction was quenched with $H_2O$, and the mixture was extracted with diethyl ether. The organic phase was washed with saturated aqueous $Na_2S_2O_3$ then brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 10:1) to afford **33** (2.42 g, 93%) as a colorless oil. $[\alpha]_D^{20} = +8.54$ ($c$ = 1.10 in $CHCl_3$); IR (film): $\tilde{\nu}$ = 3077, 2928, 2856, 1641, 1599, 1471, 1463, 1433, 1389, 1307, 1183, 1084, 1039, 1006, 938, 910 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ = 0.07 (s, 3H), 0.09 (s, 3H), 0.90 (s, 9H), 1.26–1.63 (m, 8H), 2.06 (m, 2H), 3.18 (d, $J$ = 5.2 Hz, 2H), 3.53 (m, 1H), 4.92–5.02 (m, 2H), 5.76–5.85 ppm (m, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ = −4.6, −4.4, 14.1, 18.1, 24.8, 25.8, 28.8, 29.0, 33.7,

36.8, 71.4, 114.3, 139.0 ppm; MS (CI): $m/z = 383$ $[M+H]^+$; HRMS (CI): $m/z$ calcd for $C_{15}H_{32}OSiI$: 383.1269 $[M+H]^+$; found: 383.1264.

**34**: Lactone **29** (1.32 g, 6.3 mmol) was added dropwise to a solution of LDA (prepared from *n*BuLi (6.96 mmol, 2.6 M in hexane) and diisopropylamine (1.06 mL, 7.6 mmol) in THF (10 mL)) at −20 °C. After the mixture was stirred for 30 min at this temperature, a solution of **33** (2.42 g, 6.3 mmol) in HMPA (3.1 mL, 17.7 mmol) and THF (6.1 mL) were added dropwise, and the reaction mixture was allowed to warm to room temperature. The reaction was quenched with saturated $NH_4Cl$, and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography over silica gel (hexane/EtOAc = 10:1) to afford **34** (1.26 g, 43 %) as a colorless oil. IR (film): $\tilde{\nu} = 3076$, 2929, 2856, 1766, 1640, 1583, 1472, 1463, 1440, 1383, 1342, 1184, 1118, 1052, 1026, 1005, 938, 908, 836, 809, 775, 750, 692 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta =$ 0.02 (s, 0.6 H), 0.03 (s, 0.6 H), 0.12 (s, 2.4 H), 0.16 (s, 2.4 H), 0.86 (s, 1.8 H), 0.90 (s, 7.2 H), 1.23 (d, $J = 6.3$ Hz, 2.4 H), 1.38 (d, $J = 6.2$ Hz, 0.6 H), 1.44–1.49 (m, 2 H), 1.83–1.91 (m, 2 H), 1.98–2.09 (m, 3 H), 2.33 (dd, $J = 14.3$, 5.3 Hz, 0.2 H), 2.43 (dd, $J = 14.3$, 10.3 Hz, 0.2 H), 2.95 (m, 0.2 H), 3.04 (dd, $J = 14.3$, 7.6 Hz, 0.8 H), 3.85 (m, 0.2 H), 4.23–4.28 (m, 0.8 H), 4.51 (m, 0.8 H), 4.63 (m, 0.2 H), 4.92–5.01 (m, 2 H), 5.76–5.84 (m, 1 H), 7.32–7.38 (m, 3 H), 7.54–7.58 ppm (m, 2 H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = -4.2$, −3.9, 18.0, 20.4, 21.3, 24.2, 24.2, 25.9, 25.9, 26.0, 28.8, 29.1, 29.2, 33.6, 37.9, 38.4, 39.4, 41.1, 41.6, 42.4, 55.0, 55.4, 69.4, 70.2, 73.3, 73.6, 114.2, 114.3, 128.9, 129.0, 129.0, 129.5, 129.6, 130.3, 136.7, 137.0, 137.0, 138.9, 139.0, 175.1, 177.6 ppm; MS (FAB): $m/z = 463$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{26}H_{43}O_3SiS$: 463.2702 $[M+H]^+$; found: 463.2695.

**35**: *m*CPBA (65 %, 722 mg, 2.72 mmol) was added to a solution of **34** (1.26 g, 2.72 mmol) in $CH_2Cl_2$ (50 mL) at 0 °C. After the mixture was stirred for 10 min, saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$ (1:1, 20 mL) were added. The mixture was stirred for 1 h and extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was dissolved in toluene (25 mL) and heated under reflux for 1.5 h. After being cooled to room temperature, the mixture was concentrated, and the residue was subjected to chromatography over silica gel (hexane/EtOAc = 10:1) to afford **35** (777 mg, 81 %) as a colorless oil. $[\alpha]_D^{24} = +20.8$ ($c = 0.51$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3077$, 2930, 2857, 1758, 1641, 1472, 1463, 1319, 1255, 1077, 1029, 837, 775 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.03$ (s, 3 H), 0.06 (s, 3 H), 0.88 (s, 9 H), 1.26–1.47 (m, 8 H), 1.45 (d, $J = 6.7$ Hz, 3 H), 2.04 (m, 2 H), 2.43(d, $J = 5.8$ Hz, 1 H), 3.96 (m, 1 H), 4.92–5.01 (m, 3 H), 5.79 (m, 1 H), 7.17 ppm (d, $J = 1.2$ Hz, 1 H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta =$ −4.5, 18.0, 19.0, 25.0, 25.9, 28.8, 29.2, 32.7, 33.7, 36.9, 70.1, 77.5, 114.2, 130.8, 139.1, 151.6, 174.1 ppm; MS (FAB): $m/z = 353$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{20}H_{37}O_3Si$: 353.2512 $[M+H]^+$; found: 353.2509.

**36**: A solution of **35** (374 mg, 1.06 mmol) in *t*BuOH/$H_2O$ (1:1, 2.2 mL) was added to a suspension of $K_2OsO_4 \cdot 2H_2O$ (1.6 mg, 0.0042 mmol), $K_3[Fe(CN)_6]$ (1.05 g, 3.18 mmmol), $K_2CO_3$ (439 mg, 3.18 mmol), and $CH_3SO_2NH_2$ (101 mg, 1.06 mmol) in *t*BuOH/$H_2O$ (1:1, 4.0 mL) at 0 °C. After the mixture was stirred for 25 h at this temperature, the reaction was quenched with saturated $Na_2SO_3$, and the mixture was extracted with EtOAc. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was dissolved in THF/$H_2O$ (4:1, 20 mL), and $NaIO_4$ (1.13 g, 5.3 mmol) was added to the solution at 0 °C. After being stirred for 30 min at this temperature, the mixture was diluted with $H_2O$ (25 mL) and extracted with diethyl ether (2 × 20 mL). The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography with silica gel (hexane/EtOAc = 4:1) to afford **36** (308 mg, 82 %) as a colorless oil. This compound was used for the next step without further purification. $[\alpha]_D^{22} = +20.6$ ($c = 0.50$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3080$, 2931, 2857, 2715, 1755, 1655, 1471, 1463, 1319, 1255, 1072, 1028, 836, 775 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.03$ (s, 3 H), 0.05 (s, 3 H), 0.88 (s, 9 H), 1.25–1.49 (m, 6 H), 1.41 (d, $J = 6.8$ Hz, 3 H), 1.63 (m, 2 H), 2.40–2.44 (m, 4 H), 3.96 (m, 1 H), 5.00 (qd, $J = 6.8$, 1.3 Hz, 1 H), 7.11 (1 H, d, $J = 1.3$ Hz), 9.76 ppm (t, $J = 1.5$ Hz, 1 H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = -4.5$, −4.4, 18.1, 19.0, 22.0, 24.9, 25.9, 29.2, 32.8, 36.7, 43.8, 70.1, 77.5, 130.8, 151.6, 174.0, 202.6 ppm.

**11**: A solution of **36** (308 mg, 0.87 mmol) and iodoform (1.03 g, 2.61 mmol) in THF (10 mL) was added dropwise to a suspension of $CrCl_2$ (900 mg, 7.0 mmol) in THF (12 mL) at 0 °C. After the mixture was stirred for 8 h, the reaction was quenched with $H_2O$, and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography with silica gel (hexane/EtOAc = 5:1) to afford **11** (209 mg, 50 %) as a colorless oil. IR (film): $\tilde{\nu} = 3051$, 2929, 2856, 1756, 1654, 1605, 1471, 1462, 1361, 1254, 1095, 1067, 1028, 941, 836, 775 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta = 0.03$ (s, 3 H), 0.05 (s, 3 H), 0.88 (s, 9 H), 1.25–1.49 (m, 8 H), 1.38 (d, $J = 6.8$ Hz, 3 H), 2.02–2.07 (m, 1.5 H), 2.11–2.15 (m, 0.5 H), 2.43 (dd, $J = 5.5$, 1.1 Hz, 2 H), 3.95 (m, 1 H), 5.02 (q, $J =$ 6.8, Hz, 1 H), 5.97 (dt, $J = 14.3$, 1.4 Hz, 0.75 H), 6.17 (m, 0.5 H), 6.50 (dt, $J = 14.3$, 7.2 Hz, 0.75 H), 7.11 ppm (s, 1 H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = -4.4$, 18.1, 19.0, 24.9, 25.0, 25.9, 25.9, 27.9, 28.3, 29.0, 29.2, 32.8, 34.6, 35.9, 36.8, 36.8, 70.1, 74.4, 77.4, 82.2, 130.8, 141.3, 146.6, 151.5, 174.0 ppm; MS (FAB): $m/z = 479$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{20}H_{36}O_3SiI$: 479.1480 $[M+H]^+$; found: 479.1481.

**37**: $[Cl_2Pd(PPh_3)_2]$ (3.75 mg, 0.0053 mmol) was added to a solution of **11** (51 mg, 0.11 mmol) in $Et_3N$ (0.2 mL). After the solution was stirred for 30 min, a solution of **8** (45 mg, 0.11 mmol) in $Et_3N$ (0.2 mL) and CuI (2.0 mg, 0.011 mmol) were added. After the mixture was stirred for 12 h, the reaction was quenched with saturated $NH_4Cl$ (5 mL), and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography with silica gel (hexane/EtOAc = 5:1) to afford **37** (62 mg, 76 %) as a colorless oil. IR (film): $\tilde{\nu} = 2926$, 2854, 1759, 1654, 1465, 1374, 1318, 1254, 1206, 1150, 1101, 1038, 945, 837, 775 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.01$ (s, 3 H), 0.05 (s, 3 H), 0.88 (s, 9 H), 0.88 (t, $J = 6.8$ Hz, 3 H), 1.14–1.47 (m, 32 H), 1.42 (d, $J = 6.5$ Hz, 3 H), 1.62–1.74 (m, 3 H), 1.90–1.99 (m, 2 H), 2.02–2.06 (m, 1.5 H), 2.24 (m, 0.5 H), 2.40–2.62 (m, 4 H), 3.37 (s, 3 H), 3.39 (s, 3 H), 3.44 (m, 1 H), 3.63 (m, 1 H), 3.93 (m, 1 H), 3.99 (m, 1 H), 4.12 (m, 1 H), 4.65 (d, $J = 6.7$ Hz, 1 H), 4.75 (s, 2 H), 4.81 (d, $J = 6.7$ Hz, 1 H), 4.99 (q, $J = 6.5$ Hz, 1 H), 5.40 (d, $J = 15.9$ Hz, 0.75 H), 5.77 (m, 0.5 H), 6.01 (dt, $J = 15.8$, 7.1 Hz, 0.75 H), 7.09 ppm (s, 1 H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = -4.5$, 14.0, 18.0, 18.9, 22.6, 24.9, 25.5, 25.8, 28.1, 28.4, 28.7, 29.1, 29.6, 29.6, 29.6, 29.6, 29.8, 31.2, 31.9, 32.7, 32.8, 36.8, 55.6, 55.7, 69.9, 70.1, 77.4, 77.5, 77.8, 77.8, 78.7, 79.6, 80.1, 80.3, 80.3, 80.5, 81.7, 81.8, 84.9, 90.6, 93.1, 96.4, 96.5, 96.5, 96.7, 109.2, 109.8, 130.8, 142.8, 143.6, 151.4, 151.6, 173.9 ppm; MS (FAB): $m/z = 800$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{45}H_{80}O_8SiNa$: 799.5520 $[M+Na]^+$; found: 799.5502.

**38**: A solution of sodium acetate (556 mg, 6.78 mmol) in $H_2O$ (16 mL) was added to a refluxing solution of **37** (31 mg, 0.04 mmol) and *p*-toluenesulfonylhydrazide (1.1 g, 5.6 mmol) in diethoxyethane (12 mL) over 4 h. After being cooled to room temperature, the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography with silica gel (hexane/EtOAc = 4:1) to afford **38** (24.7 mg, 79 %) as a colorless oil. $[\alpha]_D^{23} = +29.5$ ($c = 0.24$ in $CHCl_3$); IR (film): $\tilde{\nu} =$ 2926, 2854, 1760, 1654, 1464, 1374, 1318, 1254, 1149, 1100, 1033, 919, 836, 775 $cm^{-1}$;. $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.02$ (s, 3 H), 0.06 (s, 3 H), 0.88 (s, 9 H), 0.88 (t, $J = 6.8$ Hz, 3 H), 1.25–1.48 (m, 41 H), 1.41 (d, $J =$ 6.8 Hz, 3 H), 1.63–1.69 (m, 3 H), 1.92 (m, 2 H), 2.42 (d, $J = 5.6$ Hz, 2 H), 3.39 (s, 6 H), 3.46 (m, 2 H), 3.94–3.99 (m, 3 H), 4.66 (d, $J = 6.7$ Hz, 2 H), 4.83 (d, $J = 6.7$ Hz, 2 H), 5.00 (q, $J = 6.8$ Hz, 1 H), 7.11 ppm (s, 1 H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = -4.5$, 14.1, 18.0, 19.0, 22.7, 25.1, 25.5, 25.9, 28.4, 29.3, 29.6, 29.6, 29.7, 29.7, 29.7, 29.8, 31.3, 31.9, 32.8, 37.0, 55.7, 70.2, 77.4, 79.7, 81.5, 96.7, 130.9, 151.4, 174.0 ppm; MS (FAB): $m/z = 806$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{45}H_{86}O_8SiNa$: 805.5989 $[M+Na]^+$; found: 805.5973.

**1**: $BF_3 \cdot Et_2O$ (0.19 mL) was added to a solution of **38** (20 mg, 0.26 mmol) in dimethyl sulfide (1.5 mL) at 0 °C. After the mixture was stirred for 1 h at this temperature, the reaction was quenched with saturated $NaHCO_3$ (5 mL), and the mixture was extracted with diethyl ether. The organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was subjected to chromatography with silica gel (hexane/EtOAc = 1:2) to afford **1** (12.5 mg, 84 %) as a colorless waxy solid. M.p.:

72–73 °C; $[\alpha]_D^{23} = +20.6$ ($c = 0.42$ in $CHCl_3$), +20.4 ($c = 0.40$ in MeOH); IR (KBr): $\tilde{\nu} = 3444, 2919, 2851, 1747, 1652, 1465, 1319, 1202, 1074, 1028, 737\ cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.88$ (t, $J = 6.9$ Hz, 3H), 1.25–1.57 (m, 42H), 1.43 (d, $J = 6.8$ Hz, 3H), 1.63–1.71 (m, 2H), 1.94–2.01 (m, 2H), 2.41 (dd, $J = 15.3$, 8.2 Hz, 1H), 2.51 (dd, $J = 15.3$, 1.6 Hz, 1H), 2.20–2.40 (brs, 3H, OH), 3.40 (m, 1H), 3.77–3.85 (m, 3H), 5.05 (qd, $J = 6.8$, 1.2 Hz, 1H), 7.18 ppm (d, $J = 1.2$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = 14.1, 19.1, 22.7, 25.6, 25.6, 28.7, 29.3, 29.5, 29.6, 29.6, 29.6, 29.7, 29.7, 31.9, 33.4, 33.5, 37.4, 70.0, 74.0, 74.1, 77.9, 82.6, 82.6, 131.2, 151.7, 174.6$ ppm; MS (FAB): $m/z = 581$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{35}H_{65}O_6$: 581.4781 $[M+H]^+$; found: 581.4774.

**39**: The procedure was the same as that used for the preparation of **37**. Compound **39** (32 mg, 91%) was prepared from **9** (22 mg, 0.044 mmol) and **11** (21 mg, 0.044 mmol) as a yellow oil. IR (film): $\tilde{\nu} = 2926, 2854, 1759, 1654, 1464, 1374, 1318, 1255, 1206, 1149, 1100, 1039, 954, 837, 775\ cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.02$ (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 0.87 (t, $J = 6.8$ Hz, 3H), 1.14–1.47 (m, 30H), 1.40 (d, $J = 6.9$ Hz, 3H), 1.71–1.75 (m, 1H), 1.87–2.01 (m, 3H), 2.02–2.07(m, 1.6H), 2.24 (m, 0.4H), 2.41 (d, $J = 5.7$ Hz, 2H), 2.50–2.64 (m, 2H), 3.38 (s, 3H), 3.40 (s, 3H), 3.61–3.68 (m, 2H), 3.93–4.00 (m, 2H), 4.09–4.13 (m, 1H), 4.65 (d, $J = 6.7$ Hz, 1H), 4.73–4.78 (m, 3H), 4.99 (qd, $J = 6.8$, 1.1 Hz, 1H), 5.41 (d, $J = 15.9$ Hz, 0.8H), 5.77 (m, 0.4H), 6.01 (dt, $J = 15.9$, 7.1 Hz, 0.8H), 7.10 ppm (s, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = -4.5, 14.1, 18.0, 18.9, 22.6, 24.9, 25.6, 25.9, 26.5, 28.3, 28.7, 29.2, 29.3, 29.6, 29.6, 29.6, 29.6, 29.6, 29.8, 31.9, 31.9, 32.8, 32.8, 36.8, 55.6, 55.7, 55.8, 70.2, 77.4, 77.6, 77.7, 78.6, 78.7, 78.8, 80.3, 80.4, 80.6, 81.6, 81.7, 84.8, 96.4, 96.5, 96.5, 96.8, 109.2, 109.8, 130.8, 142.8, 143.6, 151.4, 151.6, 173.9$ ppm; MS (FAB): $m/z = 800$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{45}H_{80}O_8SiNa$: 799.5520 $[M+Na]^+$; found: 799.5514.

**40**: The procedure was the same as the diimide reduction used for the preparation of **38**. Compound **40** (12 mg, 76%) was prepared from **39** (16 mg, 0.020 mmol) as a colorless oil. $[\alpha]_D^{23} = +10.3$ ($c$ 0.18 in $CHCl_3$); IR (film): $\tilde{\nu} = 2928, 2854, 1759, 1655, 1464, 1374, 1318, 1255, 1206, 1149, 1100, 1036, 919, 836, 775\ cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.02$ (s, 3H), 0.04 (s, 3H), 0.88 (s, 9H), 0.88 (t, $J = 6.8$ Hz, 3H), 1.25–1.48 (m, 41H), 1.41 (d, $J = 6.8$ Hz, 3H), 1.50–1.64 (m, 2H), 1.80–1.92 (m, 3H), 2.42 (d, $J = 5.6$ Hz, 2H), 3.39 (s, 3H), 3.40 (s, 3H), 3.46 (m, 1H), 3.68 (m, 1H), 3.95 (m, 3H), 4.66 (d, $J = 6.7$ Hz, 2H), 4.78 (d, $J = 6.7$ Hz, 2H), 4.83 (d, $J = 6.7$ Hz, 1H), 5.00 (dq, $J = 6.8$ 1.3 Hz, 1H), 7.11 ppm (d, $J = 1.3$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = -4.5, 14.1, 18.0, 19.0, 22.7, 25.2, 25.5, 25.9, 26.6, 28.6, 29.4, 29.6, 29.6, 29.7, 29.7, 29.8, 29.8, 31.3, 31.9, 32.7, 37.0, 55.7, 70.2, 77.5, 78.7, 79.6, 81.4, 81.7, 96.6, 96.7, 130.8, 151.5, 174.1$ ppm; MS (FAB): $m/z = 806$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{45}H_{86}O_8SiNa$: 805.5989 $[M+Na]^+$; found: 805.5999.

**2a**: The procedure was the same as that used for the preparation of **1**. Compound **2** (9.5 mg, 75%) was prepared from **40** (17 mg, 0.022 mmol) as a colorless waxy solid. M.p.: 74–75 °C; $[\alpha]_D^{23} = +13.9$ ($c$ 0.19 in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3437, 2919, 2850, 1747, 1653, 1468, 1320, 1203, 1074, 1028\ cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.88$ (t, $J = 6.9$ Hz, 3H), 1.23–1.53 (m, 42H), 1.43 (d, $J = 6.8$ Hz, 3H), 1.56–1.66 (m, 1H), 1.85–1.91 (m, 2H), 1.98 (brs, 1H, OH), 2.00 (m, 1H), 2.19 (brs, 1H, OH), 2.30 (brs, 1H, OH), 2.40 (dd, $J = 15.3$, 8.3 Hz, 1H), 2.52 (dd, $J = 15.3$, 1.7 Hz, 1H), 3.39 (m, 1H), 3.80–3.90 (m, 4H), 5.05 (qd, $J = 6.8$, 1.3 Hz, 1H), 7.17 ppm (d, $J = 1.3$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = 14.1, 19.1, 22.7, 25.2, 25.6, 26.0, 28.6, 29.4, 29.5, 29.5, 29.6, 29.6, 29.6, 29.7, 31.9, 32.5, 33.2, 33.3, 37.4, 70.0, 71.5, 74.4, 78.0, 82.1, 83.2, 131.2, 151.8, 174.7$ ppm; MS (FAB): $m/z = 581$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{35}H_{65}O_6$: 581.4781 $[M+H]^+$; found: 581.4779.

Tris-(*R*)-MTPA esters of **2a**: A mixture of DMAP (1.2 mg, 0.01 mmol) and one drop of $Et_3N$ in $CH_2Cl_2$ (0.1 mL) was treated with **2a** (5.8 mg, 0.01 mmol). Immediately, one drop of neat MTPA chloride was added. After the reaction was completed, the mixture was purified with preparative TLC (hexane/EtOAc = 3:1) to give the tris-(*R*)-MTPA esters of **2a**. $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.88$ (t, $J = 7.0$ Hz, 3H), 1.22–1.50 (m, 42H), 1.43 (d, $J = 6.8$ Hz, 3H), 1.71–1.78 (m, 2H), 1.90–1.97 (m, 2H), 2.61 (dd, $J = 15.3$, 8.3 Hz, 1H), 2.66 (dd, $J = 15.3$, 1.6 Hz, 1H), 3.50 (s, 3H), 3.53 (s, 3H), 3.60 (s, 3H), 3.76(m, 1H), 3.98 (m, 1H), 4.90 (qd, $J = 6.8$, 1.3 Hz, 1H), 4.98 (m, 1H), 5.26 (m, 1H), 5.38 (m, 1H), 6.97 (d, $J = 1.3$ Hz, 1H), 7.33–7.61 (m, 5H).

**41**: The procedure was the same as that used for the preparation of **37**. Compound **41** (34 mg, 88%) was prepared from **10** (22 mg, 0.05 mmol) and **11** (24 mg, 0.05 mmol) as a yellow oil. IR (film): $\tilde{\nu} = 2926, 2854, 1759, 1654, 1465, 1373, 1318, 1254, 1206, 1150, 1101, 1042, 954, 837, 775\ cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.01$ (s, 3H), 0.04 (s, 3H), 0.86 (s, 9H), 0.87 (t, $J = 6.8$ Hz, 3H), 1.14–1.47 (m, 28H), 1.41 (d, $J = 6.8$ Hz, 3H), 1.63–1.71 (m, 3H), 1.84–1.91 (m, 3H), 2.02–2.07(m, 1.6H), 2.24 (m, 0.4H), 2.41 (d, $J = 5.7$ Hz, 2H), 2.40–2.62 (m, 2H), 3.37 (s, 3H), 3.39 (s, 3H), 3.48 (m, 1H), 3.65 (m, 1H), 3.88–3.96 (m, 2H), 4.02–4.07 (m, 1H), 4.65 (d, $J = 6.7$ Hz, 1H), 4.73 (d, $J = 6.7$ Hz, 1H), 4.75 (d, $J = 6.7$ Hz, 1H), 4.81 (d, $J = 6.7$ Hz, 1H), 4.99 (q, $J = 6.8$ Hz, 1H), 5.40 (d, $J = 15.9$ Hz, 0.8H), 5.77 (m, 0.4H), 6.01 (dt, $J = 15.8$, 7.1 Hz, 0.8H), 7.10 ppm ( s, 1H); $^{13}C$ NMR ($CDCl_3$, 500 MHz): $\delta = -4.6, -4.5, 14.0, 18.0, 18.9, 22.6, 24.9, 25.4, 25.8, 27.5, 27.7, 28.7, 29.1, 29.6, 29.6, 29.8, 31.2, 31.9, 32.7, 36.8, 55.6, 55.6, 55.7, 66.7, 70.1, 74.1, 77.4, 77.5, 77.9, 79.7, 79.8, 80.4, 80.5, 80.6, 82.0, 84.9, 96.4, 96.5, 96.7, 96.7, 109.8, 130.8, 142.8, 143.5, 151.4, 151.6, 173.9$ ppm; MS (FAB): $m/z = 800$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{45}H_{80}O_8SiNa$: 799.5520 $[M+Na]^+$; found: 799.5538.

**42**: The procedure was the same as the diimide reduction used for the preparation of **38**. Compound **42** (19 mg, 78%) was prepared from **41** (25 mg, 0.032 mmol) as a colorless oil. $[\alpha]_D^{23} = -1.01$ ($c = 0.12$ in $CHCl_3$); IR (film): $\tilde{\nu} = 2926, 2854, 1760, 1654, 1464, 1374, 1318, 1254, 1149, 1100, 1033, 919, 836, 775\ cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.02$ (s, 3H), 0.05 (s, 3H), 0.87 (s, 9H), 0.88 (t, $J = 6.8$ Hz, 3H), 1.25–1.50 (m, 41H), 1.41 (d, $J = 6.8$ Hz, 3H), 1.60 (m, 3H), 1.85 (m, 2H), 2.42 (d, $J = 5.6$ Hz, 2H), 3.39 (s, 6H), 3.51 (m, 2H), 3.88 (m, 2H), 3.95 (m, 1H), 4.66 (d, $J = 6.7$ Hz, 2H), 4.82 (d, $J = 6.7$ Hz, 2H), 5.00 (q, $J = 6.8$ Hz, 1H), 7.11 ppm (s, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = -4.5, 14.1, 18.0, 19.0, 22.7, 25.2, 25.5, 25.9, 27.6, 29.3, 29.6, 29.7, 29.7, 29.8, 31.3, 31.3, 31.9, 32.8, 37.0, 55.7, 70.2, 77.4, 79.9, 81.9, 96.7, 130.9, 151.4, 174.0$ ppm; MS (FAB): $m/z = 806$ $[M+Na]^+$; HRMS (FAB): $m/z$ calcd for $C_{45}H_{86}O_8SiNa$: 805.5989 $[M+Na]^+$; found: 805.5970.

**3a**: The procedure was the same as that used for the preparation of **1**. Compound **3** (8.8 mg, 82%) was prepared from **42** (14 mg, 0.018 mmol) as a colorless waxy solid. M.p.: 75.5–76.5 °C; $[\alpha]_D^{23} = +11.2$ ($c = 0.21$ in $CH_2Cl_2$); IR (KBr): $\tilde{\nu} = 3400, 2921, 2851, 1748, 1652, 1468, 1318, 1203, 1075, 1028\ cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta = 0.88$ (t, $J = 7.0$ Hz, 3H), 1.22–1.50 (m, 42H), 1.43 (d, $J = 6.8$ Hz, 3H), 1.71–1.78 (m, 2H), 1.90–1.97 (m, 2H), 2.22 (brs, 1H, OH), 2.35 (brs, 2H, OH), 2.41 (dd, $J = 15.3$, 8.3 Hz, 1H), 2.52 (dd, $J = 15.3$, 1.6 Hz, 1H), 3.42 (m, 2H), 3.80–3.86 (m, 3H), 5.05 (qd, $J = 6.8$, 1.4 Hz, 1H), 7.18 ppm (d, $J = 1.4$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta = 14.1, 19.1, 22.7, 25.5, 25.7, 25.7, 28.1, 29.3, 29.4, 29.5, 29.5, 29.5, 29.6, 29.6, 29.6, 29.7, 29.7, 29.7, 31.9, 33.4, 34.1, 37.4, 70.0, 74.4, 77.9, 82.7, 131.2, 151.7, 174.6$ ppm; MS (FAB): $m/z = 581$ $[M+H]^+$; HRMS (FAB): $m/z$ calcd for $C_{35}H_{65}O_6$: 581.4781 $[M+H]^+$; found: 581.4791.

## Acknowledgements

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