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Enantiospecific Formal Total Synthesis of Iriomoteolide 3a

S. Mothish Kumar and Kavirayani R. Prasad*[a]

Abstract: A formal total synthesis of the marine macrolide iriomoteolide 3a is described. Salient features of the synthesis include the elaboration of a β-keto phosphonate derived from D-(−)-tartaric acid and the extension of a chiral butyrolactone derived from L-glutamic acid. Ring-closing metathesis is employed to construct the macrolactone core of the natural product.

Keywords: iriomoteolide 3a · lactones · macrocycles · natural products · total synthesis

Introduction

Iriomoteolide 3a (**1**, Figure 1) is a 15-membered marine macrolide isolated by Tsuda's group from the *Amphidinium* strain HYA024 off the Iriomote island of Japan.[1] Iriomoteolide 3a (**1**) consists of a sensitive epoxide, a 3,4-dihydroxy-1,5-hexadiene unit, and a 1,4-pentadiene side chain.

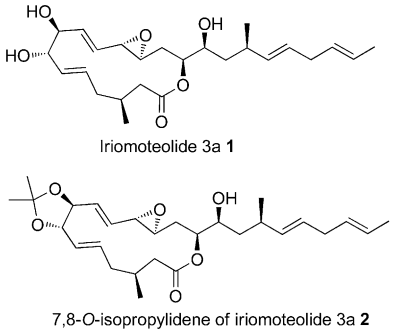

Figure 1. Iriomoteolide 3a (**1**) and 7,8-*O*-isopropylidene **2**.

Compound **1** and its isopropylidene derivative **2** were shown to exhibit impressive cytotoxic activity against the lymphoma cell line DG-75 [half-maximal inhibitory concentration (IC_{50}) = 0.08 and 0.02 μg mL^{-1}] and Raji cells (IC_{50} = 0.05 and 0.02 μg mL^{-1}). Interestingly, deprotection of the acetonide in **2** to parent macrolide **1** is problematic, and hence, protection of the vicinal diol present in the macrolide with other protecting groups is essential in the total synthesis. A solitary total synthesis of **1** was reported by the Nevado group,[2] whereas the synthesis of a macrocyclic core structurally similar to that of **2** was reported by Reddy's group.[3]

[a] S. M. Kumar, Prof. Dr. K. R. Prasad
Department of Organic Chemistry
Indian Institute of Science
Bangalore 560 012 (India)
Fax: (+91) 8023600529
E-mail: prasad@orgchem.iisc.ernet.in

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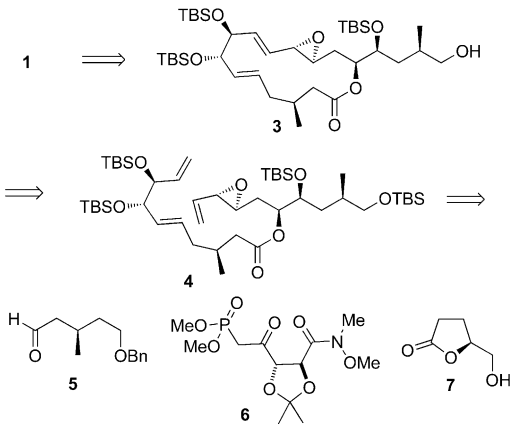
The synthesis of the isopropylidene derivative of iriomoteolide 3a, that is, **2**, has also surfaced in the literature.[4a] In continuation of our efforts in the total synthesis of macrolactone-containing natural products,[5] herein, we report a formal approach to the synthesis of **1**.

Results and Discussion

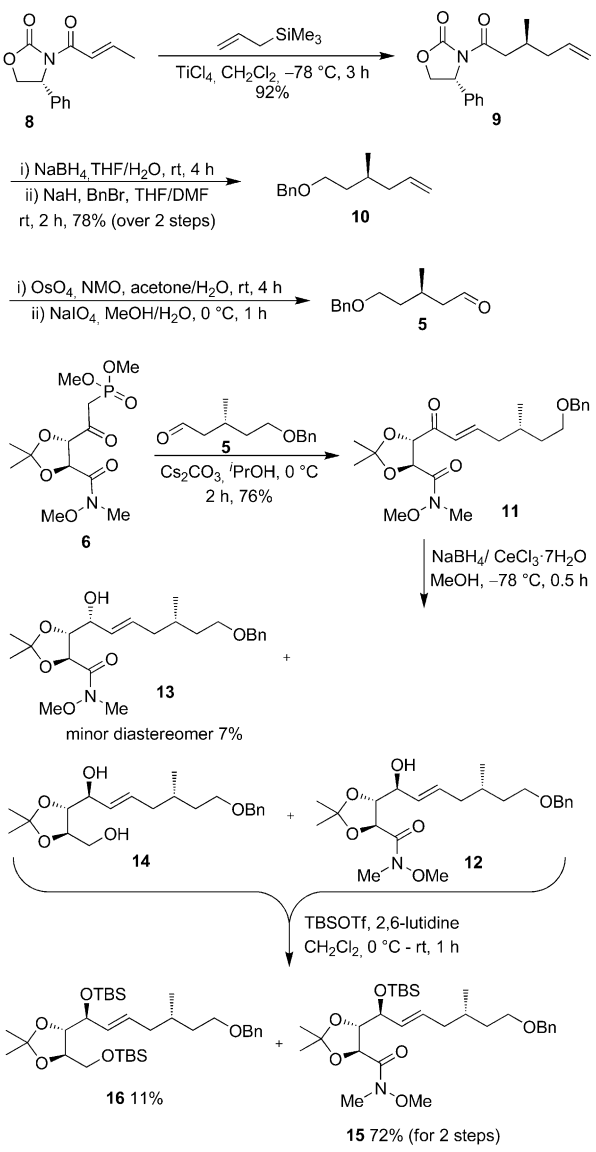
Our approach for the synthesis of **1** was based on elaboration of known Nevado's intermediate **3**, the synthesis of which was anticipated by ring-closing metathesis of ester **4**. Synthesis of the alcohol unit possessing the epoxy alkene was envisaged from elaboration of hydroxy butyrolactone **7** (obtained from L-glutamic acid), whereas synthesis of the acid fragment was planned by elaboration of β-keto phosphonate **6** derived from D-(−)-tartaric acid[6] and aldehyde **5** (Scheme 1).



Scheme 1. Retrosynthesis of iriomoteolide 3a (**1**). TBS = *tert*-butyldimethyl silyl; Bn = benzyl.

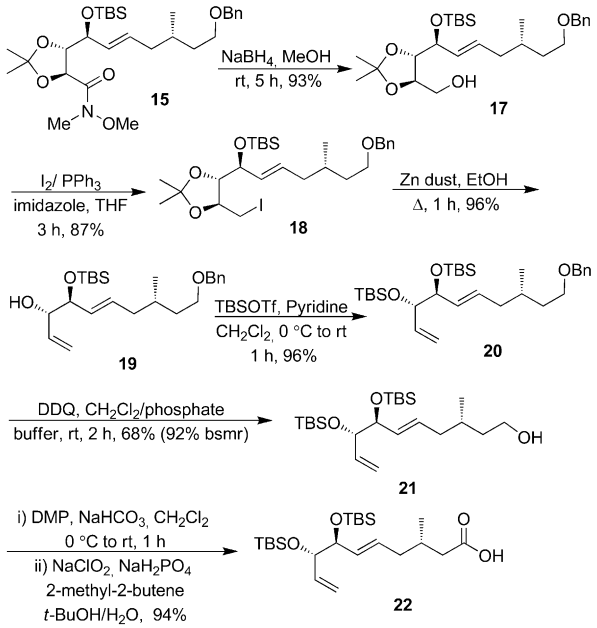
Accordingly, the synthetic sequence commenced with the known Hosomi–Sakurai allylation of α,β-unsaturated-*N*-acyloxazolidinone **8** to furnish **9**[7] possessing the requisite methyl chiral center in 92% yield. The oxazolidinone in **9**

was reduced with $NaBH_4$ to yield the alcohol, which was transformed into benzyl (Bn) ether **10** in 78% yield over two steps. Treatment of the olefin in **10** with a catalytic amount of OsO_4 and *N*-methylmorpholine-*N*-oxide (NMO) furnished the corresponding diol, which upon oxidative cleavage with $NaIO_4$ afforded crude aldehyde **5**. Horner–Wadsworth–Emmons olefination of aldehyde **5** with β-keto phosphonate **6** derived from D-(−)-tartaric acid afforded (*E*)-α,β-unsaturated ketone **11** in 76% yield. Reduction of the ketone in **11** under Luche conditions afforded minor *erythro* diastereomer **13**[8] along with an inseparable mixture of major *threo* diastereomer **12** and diol **14** resulting from competing reduction of the Weinreb amide. Major diastereomer **12** was isolated in pure form as *tert*-butyldimethylsilyl (TBS) ether **15** in 72% yield over two steps (Scheme 2).



Scheme 2. Synthesis of Weinreb amide **15**. TBS = *tert*-butyldimethyl silyl; NMO = *N*-methylmorpholine-*N*-oxide.

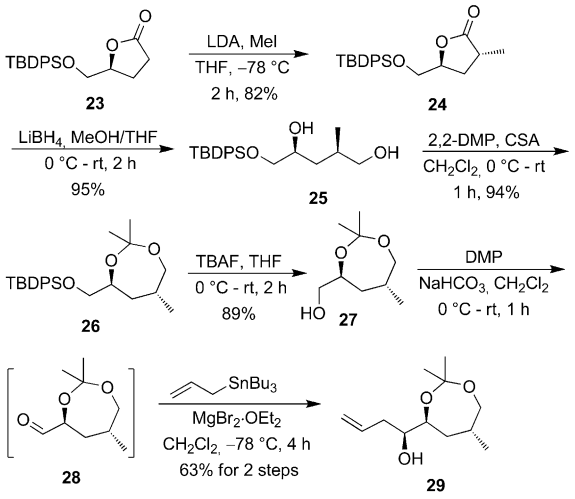
Reduction of the Weinreb amide in **15** with $NaBH_4$ gave alcohol **17** in 93% yield, which was transformed into iodide **18** in 87% yield. Treatment of **18** with freshly activated zinc dust in refluxing ethanol furnished allyl alcohol **19** in excellent yield. Protection of the free alcohol in **19** as TBS ether **20** under standard reaction conditions followed by deprotection of the primary benzyl group by using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) at room temperature furnished corresponding alcohol **21** in 68% yield (92% based on recovered starting material).[9] Neither a longer reaction time nor an increase in the temperature improved the yield of product alcohol **21** in the debenzylation of **20** with DDQ. Dess–Martin periodinane oxidation of alcohol **21** afforded the aldehyde, which was further oxidized under Pinnick conditions[10] to give acid fragment **22** in 94% yield (Scheme 3).



Scheme 3. Synthesis of acid fragment **22**. DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; DMP = Dess–Martin periodinane.

Synthesis of the alcohol fragment in ester **4** commenced with the known stereoselective methylation of butyrolactone **23** derived from L-glutamic acid (Scheme 4).[11] By using a strategy that was described earlier,[12] lactone **24** was transformed into known alcohol **27** involving a sequence of reduction with $LiBH_4$, protection of the formed 1,4-diol with 2,2-dimethoxypropane, and deprotection of the *tert*-butyldiphenylsilyl (TBDPS) group. Oxidation of **27** with Dess–Martin periodinane furnished aldehyde **28**, which upon Keck allylation[13] by employing allyltributyltin in the presence of $MgBr_2 \cdot OEt_2$ gave *threo* allylic alcohol **29** as a single diastereomer in 63% yield.

The hydroxy group in **29** was protected as its *p*-methoxybenzyl (PMB) ether by using NaH and PMBCl, which upon subsequent treatment with silica gel led to the deprotection

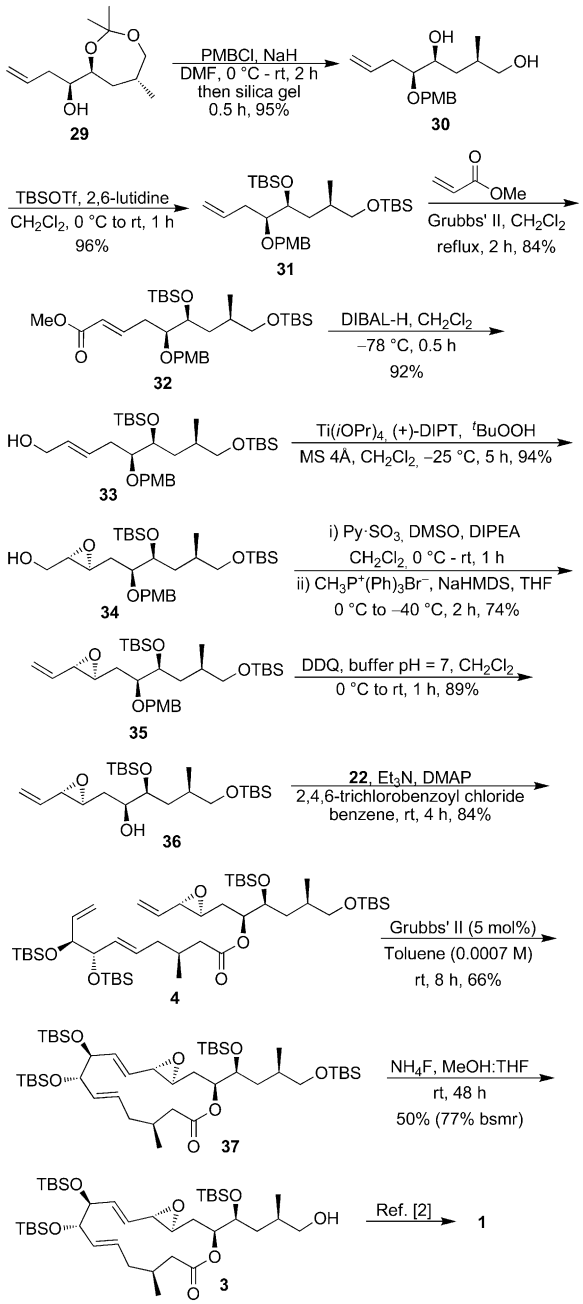


Scheme 4. Synthesis of alcohol **29**. TBDPS = *tert*-butyldiphenylsilyl; 2,2-DMP = 2,2-dimethoxypropane; CSA = camphorsulfonic acid; TBAF = *tetra*-butylammonium fluoride; DMP = Dess–Martin periodinane.

of the acetonide[14] to afford 1,4-diol **30** in 95% yield (Scheme 5). Diol **30** was reprotected as bis-TBS ether **31**, which upon olefin cross-metathesis with methyl acrylate by using Grubbs second-generation catalyst afforded unsaturated ester **32** in 84% yield. Reduction of the ester in **32** with diisobutylaluminum hydride (DIBAL-H) furnished allyl alcohol **33** in 92% yield. Sharpless asymmetric epoxidation of allyl alcohol **33** afforded epoxide **34** in 94% yield. Oxidation of the alcohol in **34** by using SO_3·Py (Py = pyridine) gave the aldehyde, which under Wittig olefination conditions produced olefin **35** in 74% yield. Finally, the PMB group was cleanly deprotected with DDQ to give known alcohol **36**[15] in 89% yield. Esterification of alcohol **36** and acid fragment **22** under Yamaguchi conditions[16] furnished ester **4** in 84% yield. Ring-closing metathesis of **4** with Grubbs second-generation catalyst afforded macrolactone **37** in 66% yield. The primary TBS group in **37** was selectively deprotected by using NH_4F in MeOH to give known Nevado's key intermediate **3** in 50% yield (77% based on recovered starting material). The spectral and physical data of **3** were in agreement with those reported by Nevado's group.[2] Given that the conversion of **3** into iriomoteolide 3a (**1**) was reported by Nevado's group, the present sequence constitutes a formal total synthesis of **1**.

Conclusions

In conclusion, a formal approach to iriomoteolide 3a is presented from the β-ketophosphonate derived from D-(−)-tartaric acid. Salient features of the synthesis include Hosomi–Sakurai allylation, Keck allylation, Horner–Wadsworth–Emmons olefination, olefin cross-metathesis, and ring-closing metathesis reactions.



Scheme 5. Formal total synthesis of iriomoteolide 3a (**1**). PMB = *p*-methoxybenzyl; TBS = *tert*-butyldimethylsilyl; DIBAL-H = diisobutylaluminum hydride; DIPT = diisopropyl tartrate; DIPEA = diisopropylethylamine; NaHMDS = sodium hexamethyldisilazide; DMAP = *N*,*N*-dimethylaminopyridine.

Experimental Section

General methods

Column chromatography was performed on Acme's silica gel, 100–200 mesh. TLC plates were visualized either with UV, in an iodine chamber, or with phosphomolybdic acid spray. Unless stated otherwise, all reagents were purchased from commercial sources and were used without additional purification. Dichloromethane was freshly distilled with calcium hydride before use. THF was freshly distilled with Na-benzophenone

ketyl. Petroleum ether refers to the fraction boiling at 60–80 °C. Optical rotations were recorded at 24 °C. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded with a 400 MHz machine in $CDCl_3$ as solvent, and the chemical shifts are reported in ppm from the residual solvent as an internal standard. HRMS was obtained by using a Micromass-Q-TOF machine, operating in the electrospray ionization (ESI) mode. Unless stated otherwise, all reactions were performed under an inert atmosphere.

Syntheses

9: $TiCl_4$ (1.0 mL, 8.65 mmol) was added dropwise to a precooled (−78 °C) solution of oxazolidinone **8** (1.0 g, 4.33 mmol) in CH_2Cl_2 (45 mL), and the mixture was stirred at the same temperature for 20 min. Allyltrimethylsilane (1.8 mL, 10.83 mmol) was introduced into the mixture, which was stirred at −78 °C for another 2 h. Upon completion of the reaction (monitored by TLC), it was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (30 mL), and the mixture was extracted with EtOAc (2×20 mL). The combined organic extract was washed with brine (20 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave the crude residue, which was purified by silica gel column chromatography (petroleum ether/EtOAc = 3:7) to furnish **9** (1.09 g, 92 %) as a colorless oil. $[\alpha]_D^{24} = +29.1$ ($c = 1.5$, $CHCl_3$); IR (neat): $\tilde{\nu} = 3071$, 2962, 1782, 1706, 1384, 1198 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.39$–7.26 (m, 5H), 5.78–5.68 (m, 1H), 5.42 (dd, $J = 8.8$, 3.6 Hz, 1H), 5.00–4.96 (m, 2H), 4.66 (t, $J = 8.8$ Hz, 1H), 4.25 (dd, $J = 8.8$, 3.6 Hz, 1H), 3.00–2.66 (m, 2H), 2.13–2.02 (m, 2H), 1.97–1.90 (m, 1H), 0.89 ppm (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 172.2$, 153.7, 139.2, 136.5, 129.2 (2C), 128.7, 125.9 (2C), 116.5, 69.8, 57.6, 41.7, 40.8, 29.5, 19.6 ppm; HRMS (ESI): m/z: calcd for $C_{16}H_{19}NO_3 + Na^+$: 296.1263; found: 296.1263.

10: $NaBH_4$ (0.84 g, 22.0 mmol) was added at 0 °C to a solution of oxazolidinone **9** (1.2 g, 4.4 mmol) in THF/H_2O (5:1, 25 mL), and the mixture was stirred at room temperature. Upon completion of the reaction, it was quenched with aqueous 2 N HCl (4 mL) and extracted with diethyl ether (2×20 mL). The combined organic layer was washed with brine (10 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave the crude residue, which was used as such in the next step without further purification.

NaH (60 % dispersion in mineral oil, 0.26 g, 6.6 mmol) was added to a precooled (0 °C) solution of the crude alcohol obtained above in THF/DMF (4:1, 6 mL), and the mixture was stirred for 0.5 h. Benzyl bromide (0.68 mL, 5.72 mmol) was introduced into the mixture, which was stirred at room temperature for another 2 h. Upon completion of the reaction (TLC), it was quenched with ice cold water (5 mL), and the mixture was extracted with diethyl ether (2×20 mL). The combined organic layer was washed with brine (10 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave a crude residue, which upon purification by silica gel column chromatography (petroleum ether/Et_2O = 9:1) gave benzyl ether **10** (0.69 g, 78 % over 2 steps) as a colorless oil. $[\alpha]_D^{24} = +5.0$ ($c = 0.4$, $CHCl_3$); IR (neat): $\tilde{\nu} = 3067$, 2932, 2863, 1600 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.33$–7.23 (m, 5H), 5.85–5.74 (m, 1H), 5.02–4.96 (m, 2H), 4.48 (s, 2H), 3.57–3.43 (m, 2H), 2.15–2.00 (m, 1H), 1.98–1.82 (m, 1H), 1.74–1.61 (m, 2H), 1.50–1.35 (m, 1H), 0.88 ppm (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 138.6$, 137.2, 128.3 (2C), 127.6 (2C), 127.4, 115.8, 72.8, 68.5, 41.4, 36.2, 29.7, 19.4 ppm; HRMS (ESI): m/z: calcd for $C_{14}H_{20}O + Na^+$: 227.1412; found: 227.1413.

11: OsO_4 (0.004 g, 0.02 mmol) and NMO (0.57 g, 4.9 mmol) were added at room temperature to a solution of benzyl ether **10** (0.4 g, 1.96 mmol) in acetone/H_2O (10 mL, 4:1), and the mixture was stirred for 4 h at the same temperature. Upon completion of the reaction (monitored by TLC), a saturated aqueous solution of Na_2SO_3 (10 mL) was added, and the mixture was stirred for 0.5 h. The mixture was extracted with EtOAc (2×10 mL), and the combined organic layer was washed with brine (10 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave the crude residue, which was used as such in the next reaction without further purification.

$NaIO_4$ (0.63 g, 2.94 mmol) was added to a precooled (0 °C) solution of the diol obtained above in MeOH/H_2O (9:1, 8 mL), and the mixture was stirred at the same temperature for 1 h. Upon completion of the reaction (monitored by TLC), the mixture was filtered through a short pad of Celite, and the Celite pad was washed with CH_2Cl_2 (20 mL). Evaporation of the solvent gave crude aldehyde **5**, which was used as such in the next reaction without further purification.

Cs_2CO_3 (0.81 g, 2.47 mmol) was added to a solution of β-keto phosphonate **6** (0.56 g, 1.65 mmol) in *i*PrOH (10 mL), and the mixture was stirred at room temperature for 45 min. The mixture was then cooled to 0 °C and a freshly prepared solution of aldehyde **5** (obtained above) in *i*PrOH (5 mL) was added dropwise. The mixture was then stirred at the same temperature for 1 h. Upon completion of the reaction (monitored by TLC), 10 % citric acid solution (20 mL) was added, and the mixture was extracted with EtOAc (2×20 mL). The combined organic layer was washed with brine (10 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave a crude residue, which upon purification by silica gel column chromatography (petroleum ether/EtOAc = 3:2) furnished ketone **11** (0.55 g, 76 %) as a colorless oil. $[\alpha]_D^{24} = +4.3$ ($c = 1.2$, $CHCl_3$); IR (neat): $\tilde{\nu} = 2936$, 2872, 1720, 1672, 1090 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.40$–7.20 (m, 5H), 7.04 (dt, $J = 15.6$, 7.2 Hz, 1H), 6.45 (d, $J = 15.6$ Hz, 1H), 5.13 (br s, 1H), 4.97 (br d, $J = 4.4$ Hz, 1H), 4.48 (s, 2H), 3.69 (s, 3H), 3.73–3.40 (m, 2H), 3.21 (s, 3H), 2.34–2.21 (m, 1H), 2.17–2.03 (m, 1H), 1.23–1.78 (m, 1H), 1.63 (dt, $J = 13.6$, 6.8 Hz, 1H), 1.51 (s, 3H), 1.51–1.44 (m, 1H), 1.26 (s, 3H), 0.91 ppm (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 196.0$, 170.0, 149.3, 138.4, 128.4 (2C), 127.62 (2C), 127.60, 127.3, 112.9, 81.4, 74.3, 72.9, 68.1, 61.6, 40.2, 36.4, 32.5, 29.6, 26.7, 26.4, 19.5 ppm; HRMS (ESI): m/z: calcd for $C_{23}H_{33}NO_6 + Na^+$: 442.2206; found: 442.2203.

12: $CeCl_3 \cdot 7H_2O$ (0.71 g, 1.9 mmol) was added to a solution of **11** (0.55 g, 1.27 mmol) in MeOH (15 mL), and the mixture was stirred at room temperature for 45 min. The mixture was then cooled to −78 °C and $NaBH_4$ (0.073 g, 1.9 mmol) was added portionwise. The resulting mixture was then stirred at the same temperature for 1 h. Upon completion of the reaction (monitored by TLC), it was quenched by the addition of water (1 mL) at −78 °C, and the mixture was slowly warmed up to room temperature. The mixture was then poured into water (10 mL) and extracted with EtOAc (2×5 mL). The combined organic layer was washed with brine (5 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave the crude residue, which was purified by silica gel column chromatography (petroleum ether/EtOAc = 1:1) to furnish minor diastereomer **13** (0.04 g, 7 %) as a colorless oil and a nonseparable mixture of **12** and **14** (0.47 g).

Minor diastereomer **13**: $[\alpha]_D^{24} = -4.5$ ($c = 1.0$, $CHCl_3$); IR (neat): $\tilde{\nu} = 3470$, 2935, 1719, 1667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.34$–7.26 (m, 5H), 5.78 (dt, $J = 15.2$, 7.2 Hz, 1H), 5.43 (dd, $J = 15.2$, 5.2 Hz, 1H), 4.74 (br s, 1H), 4.60 (br s, 1H), 4.49 (s, 2H), 4.42–4.32 (m, 1H), 3.72 (s, 3H), 3.55–3.43 (m, 2H), 3.12 (s, 3H), 2.37 (s, 1H), 2.09–2.03 (m, 1H), 1.92–1.81 (m, 1H), 1.70–1.63 (m, 2H), 1.48 (s, 3H), 1.45 (s, 3H), 1.45–1.38 (m, 1H), 0.85 ppm (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 170.2, 138.5, 132.9, 128.3 (3C), 127.6 (2C), 127.5, 111.0, 80.3, 72.9, 72.0, 70.9, 68.4, 61.8, 39.8, 36.2, 32.3, 29.8, 26.9, 26.0, 19.3 ppm; HRMS (ESI): m/z: calcd for $C_{23}H_{35}NO_6 + Na^+$: 444.2362; found: 444.2360.

15: 2,6-Lutidine (0.27 mL, 2.23 mmol) and *tert*-butyldimethylsilyl triflate (0.3 mL, 1.34 mmol) were added to a precooled (0 °C) solution of **12/14** (0.47 g, obtained above) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for 1 h. Upon completion of the reaction (TLC), the mixture was diluted with EtOAc (2×10 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (10 mL). The combined organic extract was dried with anhydrous Na_2SO_4. Evaporation of the solvent under reduced pressure gave the crude residue, which upon purification by silica gel column chromatography (petroleum ether/EtOAc = 7:3) furnished **15** (0.49 g, 72 % for 2 steps) as a colorless oil. $[\alpha]_D^{24} = +7.7$ ($c = 2.2$, $CHCl_3$); IR (neat): $\tilde{\nu} = 2931$, 2858, 1673, 1381, 1097 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.34$–7.26 (m, 5H), 5.69 (dt, $J = 15.2$, 7.2 Hz, 1H), 5.55 (dd, $J = 15.2$, 5.6 Hz, 1H), 4.72 (br s, 1H), 4.61–4.51 (m, 1H), 4.49 (s, 2H), 4.35 (t, $J = 5.2$ Hz, 1H), 3.71 (s, 3H), 3.55–3.46 (m, 2H), 3.19 (s, 3H), 2.17–2.02 (m, 1H), 1.99–1.84 (m, 1H), 1.76–1.60 (m, 2H), 1.48–1.40 (m, 1H), 1.45 (s, 3H), 1.43 (s, 3H), 0.89 (d, $J = 3.6$ Hz, 3H), 0.86 (s, 9H), 0.05 (s, 3H), 0.04 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.4$, 138.6,

131.3, 129.8, 128.3 (2C), 127.6 (2C), 127.5, 111.4, 80.8, 72.9, 72.6, 72.3, 68.5, 61.8, 39.7, 36.3, 32.2, 30.0, 27.0, 26.3, 25.7 (3C), 19.3, 18.2, −4.5, −4.9 ppm; HRMS (ESI): *m/z*: calcd for $C_{29}H_{49}NO_6Si+Na^+$: 558.3227; found: 558.3229.

16: Colorless oil (0.08 g, 11%). $[\alpha]_D^{24}=+3.87$ ($c=0.8$, $CHCl_3$); IR (neat): $\tilde{\nu}=2955$, 2931, 2858, 1465, 1254 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=$ 7.33–7.25 (m, 5H), 5.70–5.63 (m, 1H), 5.55 (dd, $J=15.2$, 6.0 Hz, 1H), 4.51 (s, 2H), 4.31 (t, $J=5.2$ Hz, 1H), 4.06–3.98 (m, 1H), 3.90 (dd, $J=7.6$, 4.4 Hz, 1H), 3.81 (dd, $J=11.2$, 3.2 Hz, 1H), 3.69 (dd, $J=11.2$, 4.4 Hz, 1H), 3.55–3.45 (m, 2H), 2.19–2.07 (m, 1H), 1.92 (quint., $J=6.8$ Hz, 1H), 1.74–1.62 (m, 2H), 1.51–1.45 (m, 1H), 1.41 (s, 3H), 1.39 (s, 3H), 0.92 (s, 21H), 0.06 (s, 9H), 0.04 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 138.6, 131.1, 130.4, 128.3 (2C), 127.5 (2C), 127.4, 109.0, 80.0, 77.9, 73.3, 72.8, 68.5, 64.2, 39.7, 36.3, 30.0, 27.3, 27.2, 26.0 (3C), 25.9 (3C), 19.4, 18.4, 18.2 −4.4, −4.8, −5.2, −5.3 ppm; HRMS (ESI): *m/z*: calcd for $C_{33}H_{60}O_5Si_2+Na^+$: 615.3877; found: 615.3875.

17: $NaBH_4$ (0.57 g, 14.9 mmol) was added portionwise to a precooled (0°C) solution of Weinreb amide **15** (0.41 g, 0.75 mmol) in MeOH (10 mL), and the mixture was stirred at room temperature for 2 h. Upon completion of the reaction (monitored by TLC), it was quenched by the addition of water (10 mL), and the mixture was extracted with EtOAc (2×20 mL). The combined organic extract was washed with brine (10 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave the crude residue, which was purified by silica gel column chromatography (petroleum ether/EtOAc=2:3) to furnish **17** (0.33 g, 93%) as a colorless oil. $[\alpha]_D^{24}=-10.9$ ($c=2.0$, $CHCl_3$); IR (neat): $\tilde{\nu}=3479$, 2931, 2858, 1457, 1103 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.33$–7.26 (m, 5H), 5.68 (dt, $J=15.6$, 7.6 Hz, 1H), 5.51 (dd, $J=15.6$, 5.6 Hz, 1H), 4.49 (s, 2H), 4.37 (t, $J=5.2$ Hz, 1H), 4.09–3.93 (m, 1H), 3.80 (dd, $J=8.0$, 4.8 Hz, 1H), 3.74–3.62 (m, 2H), 3.57–3.44 (m, 2H), 2.60 (dd, $J=7.2$, 5.6 Hz, 1H), 2.18–2.05 (m, 1H), 1.92 (quint., $J=6.8$ Hz, 1H), 1.72–1.39 (m, 2H), 1.43–1.30 (m, 1H), 1.40 (s, 3H), 1.36 (s, 3H), 0.95–0.83 (s, 12H), 0.09 (s, 3H), 0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$138.5, 131.9, 129.2, 128.3 (2C), 127.6 (2C), 127.5, 108.9, 81.1, 77.3 (2C), 72.8, 68.4, 63.2, 39.7, 36.2, 30.1, 27.1, 26.9, 25.7 (3C), 19.5, 18.2, −4.6, −5.0 ppm; HRMS (ESI): *m/z*: calcd for $C_{27}H_{46}O_5Si+Na^+$: 501.3012; found: 501.3016.

18: Triphenylphosphine (0.26 g, 1.0 mmol), imidazole (0.09 g, 1.34 mmol), and iodine (0.26 g, 1.0 mmol) were added at room temperature to a solution of **17** (0.32 g, 0.67 mmol) in dry THF (4 mL), and the mixture was stirred at the same temperature for 3 h. Upon completion of the reaction (TLC), the mixture was poured into water (10 mL) and extracted with EtOAc (2×20 mL). The combined organic layer was washed with saturated sodium thiosulfate solution (10 mL) and brine (10 mL) and dried with anhydrous Na_2SO_4. Silica gel column chromatography (petroleum ether/EtOAc=9:1) of the residue obtained after evaporation of the solvent gave iodide **18** (0.34 g, 87%) as a colorless oil. $[\alpha]_D^{24}=+10.6$ ($c=1.6$, $CHCl_3$); IR (neat): $\tilde{\nu}=2956$, 2930, 2858, 1459, 1370, 1073 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.38$–7.20 (m, 5H), 5.68 (dt, $J=15.2$, 7.2 Hz, 1H), 5.50 (dd, $J=15.2$, 6.0 Hz, 1H), 4.49 (s, 2H), 4.33 (br s, 1H), 3.81–3.68 (m, 2H), 3.56–3.45 (m, 2H), 3.43 (dd, $J=8.8$, 2.4 Hz, 1H), 3.27 (dd, $J=10.4$, 4.0 Hz, 1H), 2.19–2.04 (m, 1H), 1.20–1.84 (m, 1H), 1.79–1.61 (m, 2H), 1.45 (s, 3H), 1.45–1.31 (m, 1H), 1.36 (s, 3H), 0.95–0.85 (s, 12H), 0.09 (s, 3H), 0.05 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$138.6, 131.8, 129.6, 128.3 (2C), 127.6 (2C), 127.5, 109.3, 83.4, 75.7, 72.8, 72.7, 68.4, 39.7, 36.3, 30.0, 27.6, 27.3, 25.8 (3C), 19.5, 18.2, 8.3, −4.6, −4.8 ppm; HRMS (ESI): *m/z*: calcd for $C_{27}H_{45}IO_4Si+Na^+$: 611.2030; found: 611.2029.

19: Zinc dust (0.74 g, 11.2 mmol) was added at room temperature to a solution of iodide **18** (0.33 g, 0.56 mmol) in absolute ethanol (4 mL), and the mixture was heated at reflux for 1 h. Upon completion of the reaction (TLC), the mixture was filtered through a short pad of Celite, and the Celite pad was washed with CH_2Cl_2 (20 mL). Silica gel column chromatography (petroleum ether/EtOAc) of the residue obtained after evaporation of the solvent furnished alcohol **19** (0.218 g, 96%) as a colorless oil. $[\alpha]_D^{24}=+1.6$ ($c=1.5$, $CHCl_3$); IR (neat): $\tilde{\nu}=3478$, 2930, 2859, 1461, 1101 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.35$–7.22 (m, 5H), 5.84 (ddd, $J=17.2$, 10.8, 6.4 Hz, 1H), 5.62 (dt, $J=15.2$, 7.2 Hz, 1H), 5.41 (dd, $J=$ 15.2, 5.6 Hz, 1H), 5.32 (d, $J=17.2$ Hz, 1H), 5.18 (d, $J=10.8$ Hz, 1H), 4.51 (s, 2H), 3.99–3.86 (m, 2H), 3.60–3.42 (m, 2H), 3.63 (d, $J=2.4$ Hz, 1H), 2.17–2.02 (m, 1H), 1.97–1.81 (m, 1H), 1.82–1.59 (m, 2H), 1.52–1.37 (m, 1H), 0.91 (s, 9H), 0.89 (d, $J=6.4$ Hz, 3H), 0.09 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.6$, 136.9, 132.3, 131.0, 128.3 (2C), 127.6 (2C), 127.5, 116.4, 77.4, 75.9, 72.8, 68.4, 39.6, 36.4, 29.9, 25.9 (3C), 19.4, 18.1, −3.9, −4.8 ppm; HRMS (ESI): *m/z*: calcd for $C_{24}H_{40}O_3Si+Na^+$: 427.2644; found: 427.2646.

20: 2,6-Lutidine (0.16 mL, 1.29 mmol) and *tert*-butyldimethylsilyl triflate (0.18 mL, 0.78 mmol) were added at 0°C to a solution of alcohol **19** (0.21 g, 0.52 mmol) in CH_2Cl_2 (4 mL). The mixture was stirred at room temperature for 1 h. Upon completion of the reaction, the mixture was diluted with EtOAc (2×10 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (10 mL). The combined organic extract was dried with anhydrous Na_2SO_4. Evaporation of the solvent under reduced pressure gave the crude residue, which upon purification by silica gel column chromatography (petroleum ether) furnished **20** (0.26 g, 96%) as a colorless oil. $[\alpha]_D^{24}=-34.9$ ($c=2.4$, $CHCl_3$); IR (neat): $\tilde{\nu}=2930$, 2858, 1461, 1363, 1098 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.36$–7.26 (m, 5H), 5.91 (ddd, $J=17.2$, 10.8, 4.4 Hz, 1H), 5.55 (dt, $J=15.2$, 6.8 Hz, 1H), 5.44 (dd, $J=$ 15.2, 6.0 Hz, 1H), 5.21 (d, $J=17.2$ Hz, 1H), 5.12 (d, $J=10.8$ Hz, 1H), 4.52 (s, 2H), 4.15–4.00 (m, 2H), 3.58–3.46 (m, 2H), 2.17–2.02 (m, 1H), 1.94–1.80 (m, 1H), 1.77–1.61 (m, 2H), 1.53–1.38 (m, 1H), 0.93–0.89 (m, 21H), 0.09 (s, 6H), 0.07 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 138.7, 137.5, 130.5, 130.2, 128.3 (2C), 127.5 (2C), 127.4, 115.0, 76.3, 76.2, 72.9, 68.6, 39.7, 36.3, 29.9, 25.9 (6C), 19.4, 18.2 (2C), −4.4, −4.6, −4.7, −4.8 ppm; HRMS (ESI): *m/z*: calcd for $C_{30}H_{54}O_3Si_2+Na^+$: 541.3509; found: 541.3504.

21: DDQ (0.088 g, 0.39 mmol) was added to a solution of **20** (0.1 g, 0.19 mmol) in CH_2Cl_2/phosphate buffer (4 mL, 19:1), and the resulting mixture was stirred at room temperature for 2 h. Progress of the reaction was monitored by TLC, and after 2 h, the mixture was diluted with a saturated aqueous solution of $NaHCO_3$ (5 mL) and extracted with EtOAc (2×10 mL). (Partial conversion of the starting material into the product was observed by TLC; petroleum ether/EtOAc=9:1, $R_f=0.3$; stirring for a longer time led to decomposition). The combined organic layer was dried with anhydrous Na_2SO_4, and the residue obtained after evaporation of the solvent was purified by silica gel column chromatography (petroleum ether) to give recovered starting material **20** (0.026 g, 26%) and alcohol **21** (0.056 g, 68%, 92% based on recovered starting material) as a colorless oil. $[\alpha]_D^{24}=-47.9$ ($c=2.0$, $CHCl_3$); IR (neat): $\tilde{\nu}=3405$, 2931, 2858, 1461, 1116 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.90$ (ddd, $J=17.2$, 10.8, 4.8 Hz, 1H), 5.52 (dt, $J=15.6$, 7.2 Hz, 1H), 5.41 (dd, $J=15.6$, 5.2 Hz, 1H), 5.18 (d, $J=17.6$ Hz, 1H), 5.10 (d, $J=10.4$ Hz, 1H), 4.13–4.00 (m, 2H), 3.74–3.61 (m, 2H), 2.14–2.00 (m, 1H), 1.98–1.81 (m, 1H), 1.70–1.53 (m, 2H), 1.46–1.33 (m, 1H), 1.20 (s, 1H), 0.96–0.84 (m, 21H), 0.074 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.046 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=137.4$, 130.6, 130.0, 114.9, 76.2, 76.1, 61.1, 39.7, 39.4, 29.6, 25.8 (6C), 19.4, 18.2, 18.1, −4.5, −4.68, −4.74, −4.8 ppm; HRMS (ESI): *m/z*: calcd for $C_{23}H_{48}O_3Si_2+Na^+$: 451.3040; found: 451.3037.

22: $NaHCO_3$ (0.053 g, 0.63 mmol) and Dess–Martin periodinane (0.13 g, 0.32 mmol) were added at 0°C to a stirred solution of alcohol **21** (0.09 g, 0.21 mmol) in dry CH_2Cl_2 (4 mL). The mixture was warmed to room temperature and stirred for 2 h at the same temperature. Upon completion of the reaction (TLC), it was quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL) and $Na_2S_2O_3$ (5 mL), and the mixture was diluted with Et_2O (10 mL). The aqueous phase was extracted with Et_2O (2× 10 mL). The combined organic layer was washed with brine (10 mL), dried with anhydrous Na_2SO_4, and concentrated. The crude aldehyde thus obtained as a yellow oil was used as such in the next step without further purification.

Phosphate buffer (1 mL, pH≈3.6) and 2-methyl-2-butene (0.07 mL, 0.63 mmol) were added at room temperature to a stirred solution of the aldehyde obtained above in *t*BuOH (2 mL). A solution of $NaClO_2$ (0.057 g, 0.63 mmol) in H_2O (1 mL) was added to the mixture, which was stirred at room temperature for 3 h. Upon completion of the reaction (TLC), the mixture was acidified with 1 N HCl to pH 4. Most of the sol-

vent was evaporated off, and the mixture was diluted with EtOAc (5 mL) and brine (5 mL). The organic layer was separated off, and the aqueous layer was extracted with EtOAc (2×10 mL). The combined organic extract was dried with anhydrous Na_2SO_4, and the residue thus obtained after evaporation of the solvent was purified by silica gel column chromatography (petroleum ether/EtOAc=4:1) to afford **22** (0.088 g, 94%) as a colorless oil. $[\alpha]_D^{24}=-43.8$ ($c=1.5$, $CHCl_3$); IR (neat): $\tilde{\nu}=3432$, 2932, 2860, 1713, 1078 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.89$ (ddd, $J=17.2$, 10.8, 4.4 Hz, 1H), 5.53 (dt, $J=15.2$, 6.8 Hz, 1H), 5.45 (dd, $J=15.2$, 5.2 Hz, 1H), 5.19 (d, $J=17.2$ Hz, 1H), 5.11 (d, $J=10.8$ Hz, 1H), 4.16–4.01 (m, 2H), 2.41 (dd, $J=15.2$, 5.2 Hz, 1H), 2.19–1.91 (m, 4H), 0.97 (d, $J=6.0$ Hz, 3H), 0.92 (s, 9H), 0.91 (s, 9H), 0.07 (s, 6H), 0.053 (s, 3H), 0.048 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=179.5$, 137.3, 131.5, 128.9, 115.1, 76.2, 75.9, 40.7, 39.3, 30.1, 25.8 (6C), 19.4, 18.2, 18.1, −4.5, −4.67, −4.75, −4.8 ppm; HRMS (ESI): m/z: calcd for $C_{23}H_{46}O_4Si_2+Na^+$: 465.2832; found: 465.2839.

24: *n*BuLi (4.9 mL, 7.26 mmol) was added dropwise at 0°C to a solution of diisopropylamine (1.02 mL, 7.26 mmol) in THF (10 mL), and the mixture was stirred at the same temperature for 0.5 h. The mixture was cooled to −78°C, and a solution of lactone **23**[9] (2.3 g, 6.50 mmol) in THF (15 mL) was added dropwise; the mixture was then stirred for another 30 min. MeI (0.61 mL, 9.9 mmol) was introduced into the mixture, which was stirred for another 30 min at the same temperature. Upon completion of the reaction (indicated by TLC), it was quenched with a saturated aqueous solution of NH_4Cl (20 mL). The mixture was extracted with EtOAc (2×30 mL) and washed with brine (20 mL). The combined organic extract was dried with anhydrous Na_2SO_4, and the residue thus obtained after evaporation of the solvent was purified by silica gel column chromatography (petroleum ether/EtOAc=9:1) to afford **25** (1.99 g, 82%) as a white solid. M.p. 75–77°C (Ref. [9c] m.p. 76–77°C). $[\alpha]_D^{24}=+34.1$ ($c=1.0$, $CHCl_3$) {Ref. [9c] $[\alpha]_D^{25}=+35.0$ ($c=2.0$, $CHCl_3$)}; IR (neat): $\tilde{\nu}=2934$, 2860, 1773, 1201, 1112 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.67$ (d, $J=7.6$ Hz, 4H), 7.52–7.35 (m, 6H), 4.56 (dd, $J=8.4$, 3.2 Hz, 1H), 3.87 (dd, $J=11.2$, 3.2 Hz, 1H), 3.68 (dd, $J=11.2$, 3.2 Hz, 1H), 2.97–2.73 (m, 1H), 2.59 (ddd, $J=12.8$, 9.6, 2.8 Hz, 1H), 1.98 (ddd, $J=12.8$, 9.6, 9.2 Hz, 1H), 1.30 (d, $J=7.2$ Hz, 3H), 1.07 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=180.3$, 135.6 (2C), 135.5 (2C), 132.9, 132.5, 129.9 (2C), 127.8 (4C), 77.5, 65.5, 34.2, 32.2, 26.7 (3C), 19.2, 16.4 ppm; HRMS (ESI): m/z: calcd for $C_{22}H_{28}O_3Si+Na^+$: 391.1705; found: 391.1704.

25: MeOH (0.21 mL, 7.25 mmol) and $LiBH_4$ (2.0 M in THF, 7.3 mL, 14.51 mmol) were added to a precooled (0°C) solution of lactone **24** (2.67 g, 7.25 mmol) in THF (30 mL), and the mixture was stirred at room temperature for 1 h. Upon completion of the reaction (TLC), it was quenched with a saturated aqueous solution of NH_4Cl (20 mL), and the mixture was extracted with EtOAc (2×30 mL). The combined organic extract was dried with anhydrous Na_2SO_4, and the residue thus obtained after evaporation of the solvent was purified by silica gel column chromatography (petroleum ether/EtOAc=2:3) to afford **25** (2.56 g, 95%) as a colorless oil. $[\alpha]_D^{24}=+2.9$ ($c=1.7$, $CHCl_3$); IR (neat): $\tilde{\nu}=3366$, 2931, 2860, 1462, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.65$ (d, $J=7.6$ Hz, 4H), 7.51–7.34 (m, 6H), 3.95–3.81 (m, 1H), 3.61 (dd, $J=10.0$, 3.6 Hz, 1H), 3.58–3.38 (m, 3H), 2.85 (br s, 2H), 1.92–1.77 (m, 1H), 1.51–1.35 (m, 2H), 1.07 (s, 9H), 0.90 ppm (d, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=135.50$ (2C), 135.49 (2C), 133.1, 133.0, 129.8 (2C), 127.8 (4C), 69.3, 68.0, 67.6, 36.4, 32.3, 26.8 (3C), 19.2, 16.9 ppm; HRMS (ESI): m/z: calcd for $C_{22}H_{32}O_3Si+Na^+$: 395.2018; found: 395.2017.

26: 2,2-Dimethoxypropane (1.9 mL, 15.0 mmol) and camphorsulfonic acid (0.035 g, 0.15 mmol) were added at 0°C to a solution of diol **25** (2.8 g, 7.53 mmol) in CH_2Cl_2 (15 mL), and the mixture was stirred at room temperature for 1 h. Upon completion of the reaction (TLC), it was quenched with a saturated aqueous solution of $NaHCO_3$ (15 mL), and the mixture was extracted with EtOAc (2×20 mL). The combined organic extract was washed with brine (20 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent followed by silica gel column chromatography (petroleum ether/EtOAc=9:1) of the crude residue furnished **26** (2.9 g, 94%) as a colorless oil. $[\alpha]_D^{24}=-13.86$ ($c=1.5$, $CHCl_3$); IR (neat): $\tilde{\nu}=2936$, 2862, 1383, 1219, 1080 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.78$–7.64 (m, 4H), 7.50–7.32 (m, 6H), 3.97–3.85 (m, 2H), 3.66 (dd, $J=10.4$, 6.8 Hz, 1H), 3.50 (dd, $J=10.4$, 6.0 Hz, 1H), 3.38 (d, $J=12.0$ Hz, 1H), 1.95–1.80 (m, 1H), 1.60–1.47 (m, 1H), 1.54–1.35 (m, 1H), 1.34 (s, 3H), 1.28 (s, 3H), 1.07 (s, 9H), 1.06 ppm (d, $J=8.0$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=135.7$ (2C), 135.6 (2C), 133.7 (2C), 129.6 (2C), 127.6 (4C), 100.6, 68.8, 67.2, 65.9, 37.5, 31.0, 26.8 (3C), 25.01, 25.00, 19.2, 17.1 ppm; HRMS (ESI): m/z: calcd for $C_{25}H_{36}O_3Si+Na^+$: 435.2331; found: 435.2332.

27: *tetra*-Butylammonium fluoride (1.0 M in THF, 6.8 mL, 6.8 mmol) was added at 0°C to a solution of **26** (2.34 g, 5.70 mmol) in THF (15 mL), and the mixture was stirred at room temperature for 2 h. Upon completion of the reaction (TLC), it was diluted with cold water, and the mixture was extracted with EtOAc (2×20 mL). The combined organic extract was washed with brine (20 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent followed by silica gel column chromatography (petroleum ether/EtOAc=3:2) of the crude residue furnished **27** (0.84 g, 89%) as a colorless oil. $[\alpha]_D^{24}=+13.27$ ($c=1.1$, $CHCl_3$); IR (neat): $\tilde{\nu}=3451$, 2937, 1380, 1221, 1064, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=4.05$–3.90 (m, 1H), 3.89 (d, $J=12.0$ Hz, 1H), 3.51–3.36 (m, 2H), 3.38 (d, $J=12.0$ Hz, 1H), 2.13 (br s, 1H), 1.90–1.80 (m, 1H), 1.58–1.40 (m, 1H), 1.35 (s, 6H), 1.29 (d, $J=14.0$ Hz, 1H) 1.06 ppm (d, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=101.0$, 68.9, 66.0, 65.9, 37.1, 30.8, 25.3, 24.9, 17.0 ppm; HRMS (ESI): m/z: calcd for $C_9H_{18}O_3+Na^+$: 197.1154; found: 197.1155.

29: $NaHCO_3$ (1.02 g, 12.2 mmol) and Dess–Martin periodinane (2.58 g, 6.10 mmol) were added at 0°C to a solution of alcohol **27** (0.7 g, 4.07 mmol) in dry CH_2Cl_2 (20 mL). The mixture was warmed to room temperature and stirred for 1 h. Upon completion of the reaction (TLC), it was quenched with a saturated aqueous solution of $NaHCO_3$ (10 mL) and $Na_2S_2O_3$ (10 mL), and the mixture was diluted with diethyl ether (30 mL). The aqueous phase was extracted with Et_2O (2×20 mL). The combined organic layer was washed with water (20 mL) and brine (20 mL) and dried with anhydrous Na_2SO_4. Evaporation of solvent gave crude aldehyde **28** as a yellow oil, which was used as such in the next step without further purification.

$MgBr_2{\cdot}OEt_2$ (2.98 g, 11.5 mmol) was added at −78°C to a solution of aldehyde **28** obtained above in CH_2Cl_2 (30 mL), and the mixture was stirred for 45 min. Allyltributyltin (3.8 mL, 12.3 mmol) was introduced dropwise into the mixture, which was stirred for another 2 h at the same temperature. Upon completion of the reaction (TLC), it was quenched with a saturated aqueous solution of NH_4Cl (20 mL), and the mixture was extracted with EtOAc (2×20 mL). The combined organic layer was washed with brine (20 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave the crude residue, which upon purification by silica gel column chromatography (petroleum ether/EtOAc=7:3) afforded **29** (0.543 g, 66%) as a colorless oil. $[\alpha]_D^{24}=-2.13$ ($c=0.8$, $CHCl_3$); IR (neat): $\tilde{\nu}=3480$, 2939, 1383, 1220, 1164, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=5.89$ (ddd, $J=17.2$, 10.4, 3.2 Hz, 1H), 5.18–5.03 (m, 2H), 3.89 (d, $J=12.0$ Hz, 1H), 3.73 (dd, $J=10.8$, 6.0 Hz, 1H), 3.48–3.44 (m, 1H), 3.38 (d, $J=12.0$ Hz, 1H), 2.36 (d, $J=4.0$ Hz, 1H), 2.31 (dd, $J=8.8$, 4.0 Hz, 1H), 2.27–2.13 (m, 1H), 1.92–1.80 (m, 1H), 1.69–1.61 (m, 1H), 1.41 (d, $J=14.0$ Hz, 1H), 1.36 (s, 3H), 1.33 (s, 3H), 1.03 ppm (d, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=134.7$, 117.2, 100.9, 73.3, 70.6, 66.0, 38.2, 37.5, 30.9, 25.4, 24.8, 17.0 ppm; HRMS (ESI): m/z: calcd for $C_{12}H_{22}O_3+Na^+$: 237.1467; found: 237.1469.

30: NaH (60% dispersion in mineral oil, 0.30 g, 7.57 mmol) was added at 0°C to a solution of alcohol **29** (0.81 g, 3.78 mmol) in dry DMF (15 mL), and the mixture was stirred at the same temperature for 1 h. *p*-Methoxybenzyl chloride (1.0 mL, 7.57 mmol) was then introduced into the mixture, which was stirred at room temperature for another 1 h. Upon completion of the reaction (TLC), it was quenched with water (10 mL), and the mixture was extracted with diethyl ether (3×20 mL). The combined organic extract was stirred with silica gel (2.0 g) for 0.5 h. Evaporation of solvent gave the crude residue, which upon purification by silica gel column chromatography (petroleum ether/EtOAc=1:9) gave **30** (1.06 g, 95%) as a colorless oil. $[\alpha]_D^{24}=+33.3$ ($c=1.0$, $CHCl_3$); IR (neat): $\tilde{\nu}=3410$, 2934, 1612, 1514, 1038 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta=7.25$

(d, J=8.8 Hz, 2H), 6.87 (d, J=8.4 Hz, 2H), 5.94–5.76 (m, 1H), 5.20–5.03 (m, 2H), 4.63 (d, J=10.8 Hz, 1H), 4.41 (d, J=10.8 Hz, 1H), 3.79 (s, 3H), 3.69 (dd, J=11.6, 6.4 Hz, 1H), 3.54–3.37 (m, 2H), 3.35 (q, J=5.6 Hz, 1H), 2.92 (brs, 2H), 2.55–2.38 (m, 1H), 2.36–2.21 (m, 1H), 1.89 (sext., J=6.0 Hz, 1H), 1.58–1.45 (m, 2H), 0.92 ppm (d, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.3, 133.9, 130.1, 129.5 (2C), 117.5, 113.9 (2C), 81.2, 71.9, 69.9, 67.3, 55.2, 36.8, 34.6, 32.3, 17.3 ppm; HRMS (ESI): m/z: calcd for $C_{17}H_{26}O_4+Na^+$: 317.1729; found: 317.1731.

31: 2,6-Lutidine (2.5 mL, 20.8 mmol) and *tert*-butyldimethylsilyl triflate (2.4 mL, 10.4 mmol) were added successively to a precooled (0 °C) solution of alcohol **30** (1.02 g, 3.47 mmol) in CH_2Cl_2 (20 mL), and the mixture was stirred at room temperature for 1 h. Upon completion of the reaction (TLC), it was diluted with diethyl ether (20 mL), and the mixture was washed with a saturated aqueous solution of $NaHCO_3$ (20 mL). The combined organic extract was dried with anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure to give a crude residue, which upon purification by silica gel column chromatography (petroleum ether/EtOAc=9:1) furnished **31** (1.74 g, 96%) as a colorless oil. $[\alpha]_D^{24}=-21.33$ (c=1.2, $CHCl_3$); IR (neat): $\tilde{\nu}$=2955, 2859, 1613, 1514, 1258 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.24 (d, J=7.6 Hz, 2H), 6.86 (d, J=8.4 Hz, 2H), 5.89–5.82 (m, 1H), 5.08 (d, J=17.2 Hz, 1H), 5.01 (dd, J=10.0, 1.2 Hz, 1H), 4.51 and 4.47 (ABq, J=12.4 Hz, 2H), 3.89 (dd, J=8.4, 4.0 Hz, 1H), 3.80 (s, 3H), 3.48 (dd, J=9.6, 4.8 Hz, 1H), 3.43–3.26 (m, 2H), 2.48–2.35 (m, 1H), 2.28–2.10 (m, 1H), 1.22–1.62 (m, 2H), 1.23–1.12 (m, 1H), 0.93 (d, J=6.4 Hz, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.044 (s, 3H), 0.040 (s, 3H), 0.03 (s, 3H), 0.0 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.1, 136.7, 130.9, 129.2 (2C), 116.1, 113.6 (2C), 81.5, 71.7, 70.5, 67.8, 55.2, 35.0, 33.4, 32.2, 26.0 (3C), 25.9 (3C), 18.4, 18.3, 18.0, −4.2, −4.5, −5.4 ppm (2C); HRMS (ESI): m/z: calcd for $C_{29}H_{54}O_4Si_2+Na^+$: 545.3458; found: 545.3460.

32: Methyl acrylate (2.4 mL, 26.8 mmol) and Grubbs second-generation catalyst (57 mg, 0.067 mmol) were added to a solution of olefin **31** (0.7 g, 1.34 mmol) in CH_2Cl_2 (13 mL), and the mixture was heated at reflux for 2 h. Upon completion of the reaction (TLC), the solvent was evaporated off, and the crude residue thus obtained was purified by silica gel column chromatography (petroleum ether/EtOAc=9:1) to afford **32** (0.65 mg, 84%) as a colorless oil. $[\alpha]_D^{24}=-23.42$ (c=1.2, $CHCl_3$); IR (neat): $\tilde{\nu}$=2955, 2859, 1726, 1254, 836 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.23 (d, J=8.8 Hz, 2H), 7.05–6.89 (m, 1H), 6.87 (dd, J=6.8, 2.0 Hz, 2H), 5.86 (d, J=15.6 Hz, 1H), 4.50 and 4.44 (ABq, J=11.6 Hz, 2H), 3.99–3.85 (m, 1H), 3.81 (s, 3H), 3.74 (s, 3H), 3.45 (dd, J=9.6, 4.8 Hz, 1H), 3.42 (dt, J=7.2, 3.6 Hz, 1H), 3.36 (dd, J=9.6, 6.0 Hz, 1H), 2.56–2.50 (m, 1H), 2.41–2.25 (m, 1H), 1.85–1.58 (m, 2H), 1.24–1.07 (m, 1H), 0.93 (d, J=6.4 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.05 (s, 3H), 0.049 (s, 3H), 0.04 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=166.9, 159.2, 147.6, 130.4, 129.3 (2C), 122.3, 113.7 (2C), 80.5, 71.8, 70.1, 67.7, 55.2, 51.4, 34.8, 32.1, 32.0, 25.9 (3C), 25.8 (3C), 18.4, 18.3, 17.9, −4.2, −4.6, −5.3, −5.4 ppm; HRMS (ESI): m/z: calcd for $C_{31}H_{56}O_6Si_2+Na^+$: 603.3513; found: 603.3516.

33: DIBAL-H (1.7 mL, 1.7 mmol) was added at −78 °C to a solution of ester **32** (0.49 g, 0.85 mmol) in CH_2Cl_2 (10 mL), and the mixture was stirred at the same temperature for 10 min. Upon completion of the reaction (TLC), it was quenched with an aqueous saturated solution of sodium potassium tartrate (10 mL), and the mixture was stirred at room temperature for 0.5 h. The mixture was then extracted with EtOAc (2× 20 mL), and the combined organic extract was washed with brine (10 mL) and dried with anhydrous Na_2SO_4. Evaporation of solvent gave the crude residue, which upon purification by silica gel column chromatography (petroleum ether/EtOAc=4:1) gave **33** (0.43 g, 92%) as a colorless oil. $[\alpha]_D^{24}=-24.12$ (c=1.6, $CHCl_3$); IR (neat): $\tilde{\nu}$=3443, 2955, 2859, 1513, 1252, 1080, 836 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.24 (d, J=8.8 Hz, 2H), 6.88 (dd, J=6.4, 2.0 Hz, 2H), 5.74–5.61 (m, 2H), 4.52 and 4.43 (ABq, J=11.6 Hz, 2H), 4.06 (brs, 2H), 3.97–3.83 (m, 1H), 3.81 (s, 3H), 3.49 (dd, J=9.6, 4.8 Hz, 1H), 3.43–3.39 (m, 2H), 2.46–2.32 (m, 1H), 2.26–2.09 (m, 1H), 1.85–1.61 (m, 2H), 1.31–1.19 (m, 2H), 0.94 (d, J=4.0 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.05 (s, 9H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.1, 130.9, 130.8, 130.6, 129.4 (2C), 113.6 (2C), 81.4, 71.6, 70.4, 67.8, 63.8, 55.3, 35.0, 32.2, 31.7, 25.9 (3C), 25.8 (3C), 18.4, 18.3, 18.0, −4.2, −4.5, −5.3, −5.4 ppm; HRMS (ESI): m/z: calcd for $C_{30}H_{56}O_5Si_2+Na^+$: 575.3564; found: 575.3561.

34: L-(+)-Diisopropyl tartrate (0.02 g, 0.06 mmol), Ti(O*i*Pr)$_4$ (0.02 mL, 0.06 mmol), and *tert*-butylhydroperoxide (5 M in decane, 0.08 mL, 0.4 mmol) were added sequentially at −23 °C to a stirred suspension of powdered 4 Å molecular sieves (0.3 g) in dry CH_2Cl_2 (2 mL). The mixture was stirred at the same temperature for 45 min, and a solution of allyl alcohol **33** (0.10 g, 0.18 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise; the mixture was stirred for 12 h. Upon completion of the reaction (TLC), it was quenched with H_2O (4 mL), and 10% NaOH/saturated aqueous NaCl solution (1:1, 2.0 mL) was added to the mixture, which was stirred vigorously at room temperature for 1 h. The mixture was then filtered through a short pad of Celite, and the Celite pad was washed with CH_2Cl_2 (10 mL). The solvent was evaporated off, and the crude residue thus obtained was purified by silica gel column chromatography (petroleum ether/EtOAc=4:1) to afford epoxy alcohol **34** (0.096 g, 94%) as a colorless oil. $[\alpha]_D^{24}=-37.92$ (c=2.6, $CHCl_3$); IR (neat): $\tilde{\nu}$=3456, 2956, 2932, 1464, 1252, 836 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.24 (d, J=8.4 Hz, 2H), 6.86 (dd, J=8.4, 2.0 Hz, 2H), 4.56 and 4.46 (ABq, J=11.2 Hz, 2H), 4.00–3.96 (m, 1H), 3.85 (d, J=12.4 Hz, 1H), 3.79 (s, 3H), 3.63–3.49 (m, 2H), 3.46 (dd, J=9.6, 4.8 Hz, 1H), 3.35 (dd, J=9.6, 6.4 Hz, 1H), 3.04 (ddd, J=6.8, 4.8, 2.0 Hz, 1H), 2.95 (dt, J=4.4, 2.4 Hz, 1H), 1.90–1.85 (m, 3H), 1.85–1.60 (m, 2H), 1.15–1.05 (m, 1H), 0.91 (d, J=6.4 Hz, 3H), 0.88 (s, 9H), 0.85 (s, 9H), 0.034 (s, 6H), 0.029 (s, 3H), 0.018 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.2, 130.6, 129.3 (2C), 113.8 (2C), 79.0, 71.9, 69.7, 67.7, 61.6, 59.2, 55.2, 54.1, 34.7, 32.1, 31.2, 25.9 (3C), 25.8 (3C), 18.5, 18.3, 17.9, −4.2, −4.6, −5.38, −5.40 ppm; HRMS (ESI): m/z: calcd for $C_{30}H_{56}O_6Si_2+Na^+$: 591.3513; found: 591.3510.

35: DMSO (1.0 mL), diisopropylethylamine (1.0 mL, 5.80 mmol), and SO_3·Py (0.46 g, 2.9 mmol) were added at 0 °C to a solution of alcohol **34** (0.33 g, 0.58 mmol) in CH_2Cl_2 (10 mL), and the mixture was stirred at room temperature for 1 h. Upon completion of the reaction (indicated by TLC), the mixture was diluted with water (10 mL) and extracted with Et_2O (2×10 mL). The combined organic extract was washed with brine (10 mL) and dried with anhydrous Na_2SO_4. Evaporation of solvent gave the crude aldehyde, which was used as such in the next reaction without further purification.

Sodium hexamethyldisilazane (2.0 M in THF, 1.5 mL, 2.9 mmol) was added to a precooled (0 °C) solution of $CH_3P^+(PPh)_3Br^-$ (1.2 g, 3.5 mmol) in THF (4 mL), and the mixture was stirred for 0.5 h. The mixture was then cooled to −40 °C, and a solution of the aldehyde obtained above in THF (4 mL) was added dropwise; the mixture was then stirred for another 2 h. Upon completion of the reaction (TLC), it was quenched with H_2O (5 mL), and the mixture was extracted with EtOAc (2× 10 mL). The combined organic layer was washed with brine (10 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave the crude residue, which upon purification by silica gel column chromatography (petroleum ether/Et_2O=9:1) afforded **35** (0.24 g, 74%) as a colorless oil. $[\alpha]_D^{24}=-26.3$ (c=1.0, $CHCl_3$); IR (neat): $\tilde{\nu}$=3437, 2931, 2858, 1612, 1083 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26 (d, J=8.8 Hz, 2H), 6.87 (d, J=11.2 Hz, 2H), 5.59 (ddd, J=17.4, 10.0, 7.6 Hz, 1H), 5.45 (d, J=17.4 Hz, 1H), 5.27 (d, J=10.0 Hz, 1H), 4.56 and 4.49 (ABq, J=11.2 Hz, 2H), 3.94 (dt, J=8.0, 3.6 Hz, 1H), 3.82 (s, 3H), 3.65–3.51 (m, 1H), 3.48 (dd, J=9.6, 4.8 Hz, 1H), 3.37 (dd, J=9.6, 6.4 Hz, 1H), 3.15 (dd, J=7.2, 1.6 Hz, 1H), 3.01–2.88 (m, 1H), 1.90–1.75 (m, 2H), 1.75–1.60 (m, 2H), 1.13 (ddd, J=13.6, 8.8, 5.2 Hz, 1H), 0.94 (d, J=6.8 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.057 (s, 3H), 0.054 (s, 3H), 0.046 (s, 3H), 0.03 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.2, 135.9, 130.7 (2C), 129.3, 119.0, 113.7 (2C), 78.9, 71.9, 69.8, 67.7, 59.6, 58.6, 55.3, 34.7, 32.2, 31.7, 25.9 (3C), 25.8 (3C), 18.5, 18.4, 18.0, −4.2, −4.6, −5.36, −5.38 ppm; HRMS (ESI): m/z: calcd for $C_{31}H_{56}O_5Si_2+Na^+$: 587.3564; found: 587.3565.

36: DDQ (0.14 g, 0.6 mmol) was added to a solution of **35** (0.17 g, 0.3 mmol) in CH_2Cl_2/phosphate buffer pH 7 (19:1, 10 mL), and the resulting mixture was stirred at room temperature for 1 h. Upon completion of the reaction (TLC), it was diluted with a saturated aqueous solution of $NaHCO_3$ (10 mL), and the mixture was extracted with EtOAc (2× 20 mL). The combined organic layer was dried with anhydrous Na_2SO_4,

and the residue obtained after evaporation of the solvent was purified by silica gel column chromatography (petroleum ether/EtOAc = 4:1) to afford **36** (0.12 g, 89%) as a colorless oil. $[\alpha]_D^{24} = -4.9$ ($c = 1.0$, $CHCl_3$) {Ref. [4a] $[\alpha]_D^{20} = -26.0$ ($c = 1.0$, $CHCl_3$)}; IR (neat): $\tilde{\nu} = 3473$, 2956, 2859, 1463, 1255 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.60$ (ddd, $J = 17.2$, 10.0, 7.6 Hz, 1H), 5.48 (dd, $J = 17.2$, 1.2 Hz, 1H), 5.28 (d, $J = 10.0$ Hz, 1H), 3.78–3.62 (m, 2H), 3.47 (dd, $J = 9.6$, 5.2 Hz, 1H), 3.38 (dd, $J = 9.6$, 6.4 Hz, 1H), 3.15 (dd, $J = 7.6$, 2.0 Hz, 1H), 3.12–3.00 (m, 1H), 2.29 (d, $J = 8.4$ Hz, 1H), 1.90 (ddd, $J = 14.0$, 9.6, 4.0 Hz, 1H), 1.81 (ddd, $J = 14.0$, 8.8, 4.4 Hz, 1H), 1.73–1.62 (m, 1H), 1.47 (ddd, $J = 14.0$, 7.6, 3.6 Hz, 1H), 1.19 (ddd, $J = 14.0$, 8.8, 4.4 Hz, 1H), 0.92–0.90 (m, 21H), 0.10 (s, 3H), 0.08 (s, 3H), 0.04 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 135.6$, 119.2, 73.2, 69.9, 68.4, 58.8, 58.2, 37.3, 37.2, 32.2, 25.9 (3C), 25.8 (3C), 18.3, 18.0, 17.1, −4.1, −4.5, −5.4 ppm (2C); HRMS (ESI): m/z: calcd for $C_{23}H_{48}O_4Si_2 + Na^+$: 467.2989; found: 467.2989.

4: Et_3N (0.04 mL, 0.24 mmol) and 2,4,6-trichlorobenzoyl chloride (0.03 mL, 0.19 mmol) were added at room temperature to a solution of acid **22** (0.072 g, 0.16 mmol) in benzene (2 mL). After stirring the mixture for 1 h, a solution of alcohol **36** (0.06 g, 0.135 mmol) and DMAP (0.02 g, 0.135 mmol) in benzene (2 mL) was added to the mixture at room temperature, which was stirred for 4 h. Upon completion of the reaction (TLC), it was quenched with a saturated solution of NH_4Cl (5 mL), and the mixture was extracted with Et_2O (2 × 20 mL). The combined organic extract was washed with brine (10 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave the crude residue, which upon purification by silica gel column chromatography (petroleum ether) afforded **4** (0.098 g, 84%) as a colorless oil. $[\alpha]_D^{24} = -36.1$ ($c = 2.4$, $CHCl_3$); IR (neat): $\tilde{\nu} = 2956$, 2932, 2859, 1739, 1076 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.88$ (ddd, $J = 17.2$, 10.4, 4.4 Hz, 1H), 5.59–5.35 (m, 4H), 5.25 (dd, $J = 10.4$, 1.2 Hz, 1H), 5.18 (d, $J = 17.6$ Hz, 1H), 5.10 (d, $J = 10.4$ Hz, 1H), 5.08–4.96 (m, 1H), 4.14–4.01 (m, 2H), 3.91–3.81 (m, 1H), 3.42 (dd, $J = 9.6$, 5.2 Hz, 1H), 3.32 (dd, $J = 9.6$, 6.0 Hz, 1H), 3.09 (d, $J = 7.6$ Hz, 1H), 2.92–2.80 (m, 1H), 2.34 (dd, $J = 14.8$, 4.8 Hz, 1H), 2.15–1.93 (m, 4H), 2.00–1.83 (m, 1H), 1.82–1.63 (m, 2H), 1.64–1.54 (m, 1H), 0.96–0.84 (m, 43H), 0.13 (s, 3H), 0.09 (s, 3H), 0.07 (s, 6H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 172.5$, 137.3, 135.5, 131.3, 129.0, 119.3, 115.1, 76.1, 75.9, 72.7, 70.0, 67.7, 59.1, 57.7, 41.2, 39.5, 35.5, 31.9, 31.6, 30.1, 25.9 (6C), 25.8 (6C), 19.3, 18.3, 18.2, 18.1, 18.0, 17.9, −4.3, −4.5, −4.64, −4.67, −4.7, −4.8, −5.41, −5.44 ppm; HRMS (ESI): m/z: calcd for $C_{46}H_{92}O_7Si_4 + Na^+$: 891.5818; found: 891.5817.

37: Grubbs second-generation catalyst (2.0 mg, 0.0025 mmol) was added to a solution of **4** (0.046 g, 0.053 mmol) in toluene (75 mL), and the mixture was stirred at room temperature for 8 h. Upon completion of the reaction (TLC), the solvent was evaporated off, and the crude residue thus obtained was purified by silica gel column chromatography (petroleum ether/EtOAc = 9:1) to afford macrolactone **37** (0.029 g, 66%) as a colorless oil. $[\alpha]_D^{24} = +5.75$ ($c = 1.2$, $CHCl_3$); IR (neat): $\tilde{\nu} = 2956$, 2859, 1739, 1652, 1255, 1076 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.66$ (dd, $J = 15.6$, 7.6 Hz, 1H), 5.49 (dt, $J = 15.6$, 6.4 Hz, 1H), 5.38 (dd, $J = 15.6$, 5.2 Hz, 1H), 5.12 (dd, $J = 15.6$, 8.8 Hz, 1H), 5.01 (dd, $J = 11.6$, 2.4 Hz, 1H), 4.08–3.95 (m, 2H), 3.84 (dt, $J = 8.4$, 4.4 Hz, 1H), 3.39 (d, $J = 5.2$ Hz, 2H), 3.00 (dd, $J = 8.8$, 1.2 Hz, 1H), 2.78 (d, $J = 10.0$ Hz, 1H), 2.45–2.27 (m, 3H), 2.23–2.13 (m, 1H), 1.97 (dd, $J = 18.0$, 6.0 Hz, 1H), 1.91–1.74 (m, 1H), 1.80–1.65 (m, 1H), 1.63–1.47 (m, 1H), 1.35–1.16 (m, 1H), 1.22–1.05 (m, 1H), 0.99 (d, $J = 6.8$ Hz, 3H), 0.93–0.83 (m, 39H), 0.14 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.03 (s, 6H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 172.5$, 137.0, 132.2, 129.3, 129.2, 77.7, 77.3, 72.2, 70.1, 67.4, 59.4, 57.7, 38.0, 37.6, 35.2, 31.8, 31.6, 28.1, 25.9 (12C), 21.1, 18.3, 18.2, 18.1, 18.0, 17.9, −4.2 (2C), −4.3 (3C), −4.6, −5.4, −5.5 ppm; HRMS (ESI): m/z: calcd for $C_{44}H_{88}O_7Si_4 + Na^+$: 863.5505; found: 863.5510.

3: NH_4F (0.02 g, 0.56 mmol) was added to a solution of **37** (0.046 g, 0.055 mmol) in MeOH/THF (10:1, 2 mL), and the mixture was stirred at room temperature for 48 h. The mixture was then diluted with brine (5 mL) and extracted with EtOAc (2 × 10 mL). The organic layer was dried with anhydrous Na_2SO_4, and evaporation of the solvent under reduced pressure gave the crude residue, which upon purification by silica gel column chromatography (petroleum ether/EtOAc = 9:1) gave recovered starting material **37** (0.016 g); further elution gave required alcohol **3** (0.02 g, 50%, 77% based on recovered starting material) as a colorless oil. $[\alpha]_D^{24} = +9.4$ ($c = 1.0$, $CHCl_3$) {Ref. [2] $[\alpha]_D^{20} = +6.7$ ($c = 1.0$, $CHCl_3$)}; IR (neat): $\tilde{\nu} = 3424$, 2932, 2859, 1737, 1459, 1254 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.65$ (dd, $J = 15.6$, 7.2 Hz, 1H), 5.47 (dt, $J = 15.6$, 6.4 Hz, 1H), 5.35 (dd, $J = 15.6$, 5.2 Hz, 1H), 5.14–5.08 (m, 2H), 4.05–3.92 (m, 2H), 3.81 (dd, $J = 10.8$, 5.2 Hz, 1H), 3.50–3.32 (m, 2H), 2.99 (dd, $J = 8.8$, 1.2 Hz, 1H), 2.79 (d, $J = 10.0$ Hz, 1H), 2.40 (dd, $J = 18.0$, 5.6 Hz, 1H), 2.36–2.24 (m, 2H), 2.19–2.09 (m, 1H), 2.03–1.97 (m, 1H), 1.95 (dd, $J = 18.0$, 6.4 Hz, 1H), 1.83–1.75 (m, 2H), 1.58–1.51 (m, 1H), 1.31–1.20 (m, 2H), 0.97 (d, $J = 6.8$ Hz, 3H), 0.91 (d, $J = 6.8$ Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.042 (s, 3H), 0.039 (s, 3H), 0.02 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 172.7$, 137.2, 132.2, 129.4, 129.1, 77.6 (2C), 71.7, 70.8, 67.8, 59.4, 57.5, 38.1, 37.6, 36.6, 32.7, 32.0, 28.3, 26.0 (3C), 25.9 (3C), 25.7 (3C), 21.2, 18.2, 18.1, 18.0, 17.9, −4.2 (2C), −4.3, −4.4, −4.5, −4.6 ppm; HRMS (ESI): m/z: calcd for $C_{38}H_{74}O_7Si_3 + Na^+$: 749.4640; found: 749.4642.

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[14] Efforts to isolate the PMB ether of **29** were futile. We observed consistently deprotection of the acetonide group in the silica gel purification of the PMB ether of **29**. Given that deprotection of the acetonide is the next step, we treated the mixture with silica gel to get 1,4-diol **30** cleanly.

[15] A similar reaction sequence was employed for the conversion of **34** into **36** by Zhang et al. in their synthesis of **2**, which is the isopropylidene derivative of iriomoteolide 3a.

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