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The First Stereoselective Total Synthesis of (–)-Synrotolide

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The first stereoselective total synthesis of (–)-synrotolide has been realized by two different approaches, both starting from (*S*)-ethyl lactate. Both strategies used stereo- and regioselective epoxide opening with a nucleophile, aldehyde alkyne coupling and ring-closing metathesis as key steps. Judicious choice of reagents ($CeCl_3 \cdot 7H_2O$ and H_2SiF_6) for the chemoselective removal of protecting groups delivered the target molecule.

Introduction

Natural products possessing the 5,6-dihydro-2*H*-pyran-2-one (α,β-unsaturated δ-lactone) structural motif are well-known for their broad range of biological properties such as insect growth inhibition, antitumor, antibacterial, antifungal, and immunosuppressive properties.[1] Synrotolide (**1**)[2] belongs to this α,β-unsaturated δ-lactone class and was isolated from the leaves of *Syncolostemon rotundifolius*. Spectroscopic as well as X-ray analysis was used to determine the absolute stereochemistry of synrotolide as 6*R*-[3*R*,6*S*-(diacetyloxy)-4*R*,5*S*-(dihydroxy)-1-heptenyl]-5,6-dihydro-2*H*-pyran-2-one. Other related members isolated from different species include spicigerolide (**2**),[3] hyptolide (**3**),[4] anamarine (**4**),[5] synargentolide A (**5**),[6] and synparvolide (**6**)[7] (Figure 1), which possess an array of properties ranging from cytotoxicity against human tumor cells to antibacterial and/or antifungal activity.[8] To the best of our knowledge, the total synthesis of synrotolide (**1**) has not been reported to date. However, two syntheses[9] on a synthetic derivative of synrotolide, synrotolide diacetate have been reported. In a continuation of our efforts toward the synthesis of δ-lactone-containing natural products,[10] in this communication, we wish to report the first stereoselective synthesis of synrotolide (**1**) by using two novel strategies, both starting from commercially available (*S*)-ethyl lactate.

The retrosynthetic analysis for synrotolide **1** by two approaches is depicted in Scheme 1. Synrotolide **1** synthesis was envisioned by chemoselective deprotection of protecting groups in lactones **7a** and **7b**. These two lactones could be generated from homoallylic alcohols **8a** and **8b** by acrylo-

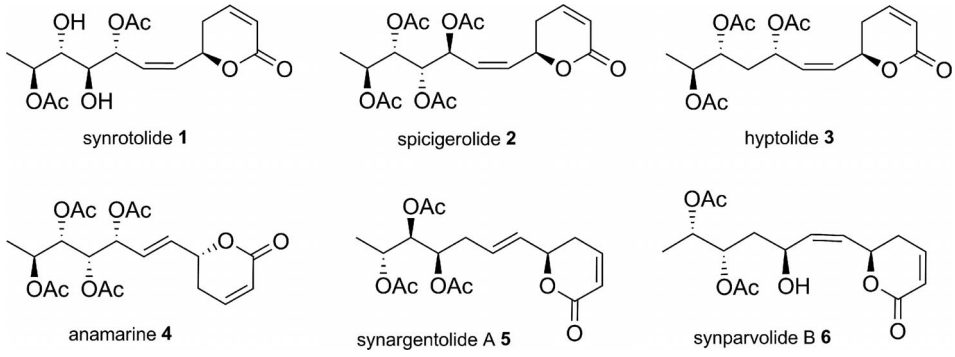

Figure 1. Synrotolide type pyranone polyacetates.

ylation followed by ring-closing metathesis (RCM) reaction. The key intermediates **8a** and **8b** could be obtained by two synthetic strategies involving an aldehyde and alkyne coupling reaction. Aldehydes **9** and **11** were prepared from (*S*)-ethyl lactate.

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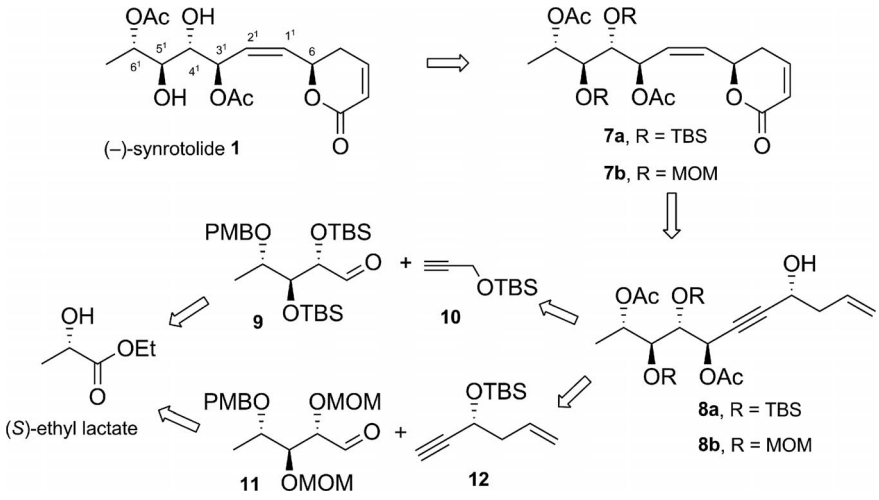
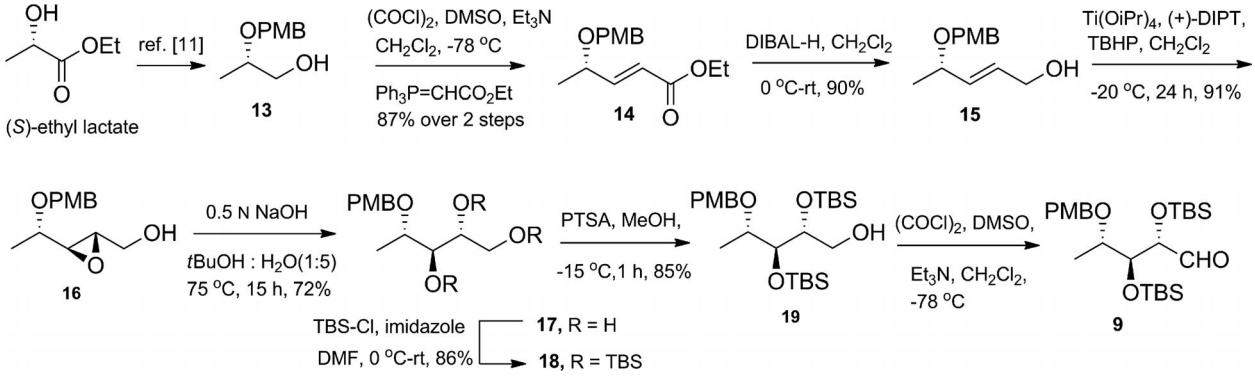


Scheme 1. Retrosynthetic analysis.

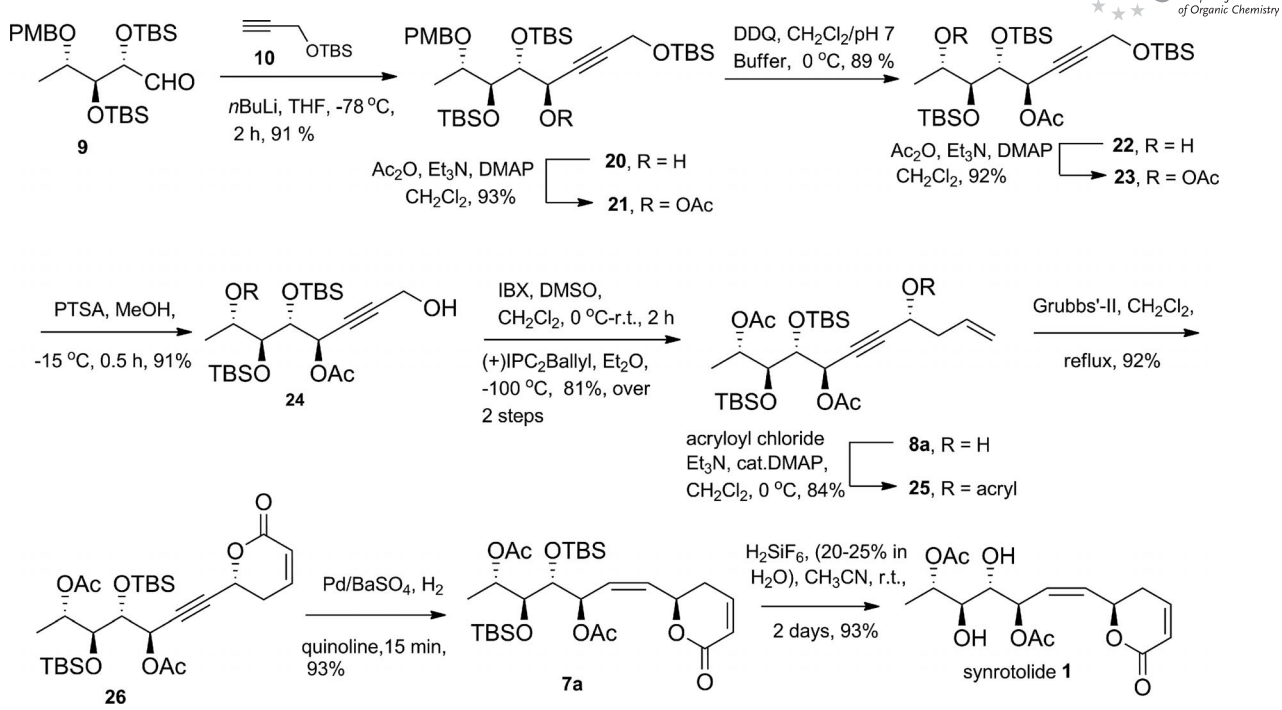
Results and Discussion

The first approach for the synthesis of synrotolide **1** started from PMB-protected alcohol **13**, which was prepared from (*S*)-ethyl lactate by following a reported procedure (Scheme 2).[11] Oxidation of alcohol **13** provided the aldehyde, which was then subjected to Wittig olefination for the homologation of the chain by using a stabilized ylide, $Ph_3P{=}CHCOOEt$ to give α,β-unsaturated ester **14**. The ester group was reduced with diisobutylaluminum hydride (DIBAL-H) in CH_2Cl_2 to give alcohol **15**. The Sharpless epoxidation[12] of allyl alcohol **15** with L-(+)-DIPT and TBHP afforded epoxy alcohol **16** (97:3 *dr*).[13] To generate the chiral center at C4′, nucleophilic epoxide ring opening was conducted with hydroxide ions. The stereo- and regioselective epoxide ring opening of 2,3-epoxy alcohol **16** by using 0.5 N NaOH in H_2O/*t*BuOH (5:1)[12] at 70 °C for 15 h thus provided PMB-protected tetrol **17** (94:6 *dr*).[14] Here, the selection of protecting groups would play a crucial role, because reported attempts[9] to deprotect the acetonide group in the presence of two OAc groups under different conditions were not fruitful at the last stage. To this end, we chose silyl and MOM protecting groups in the first and second approach, respectively, assuming that they could be removed by using tetrabutylammonium fluoride (TBAF), HF-Py, trifluoroacetic acid (TFA) and $TiCl_4$. Thus, the free triols in **17** were silylated by using TBSCl (3 equiv.) to afford fully protected tetrol compound **18**. The selective deprotection of the primary silicon protecting group was achieved by using *p*-toluenesulfonic acid (PTSA) in MeOH at –15 °C to provide free alcohol **19** in 85% yield. Oxidation of the alcohol afforded aldehyde **9**, which was used for the next reaction without further purification.

As expected, 1-*tert*-butyldimethylsilyloxy-2-propyne (**10**) reacted with crude aldehyde **9** to afford *anti*-**20** as the major isomer (93:7 *dr*) (Scheme 3).[15] The newly generated hydroxyl group was acetylated to give monoacetate compound **21**. Oxidative removal of the PMB group delivered free hydroxy compound **22**, which was acetylated to give **23**. Deprotection of the primary TBS group was accomplished by using PTSA in MeOH at –15 °C for 30 min to provide propargylic alcohol **24**. 2-Iodoxybenzoic acid (IBX) mediated oxidation of the alcohol produced the aldehyde, which was subjected to stereoselective allylation with $(+)$-$(Ipc)_2$B-allyl[16] to provide the expected homoallylic alcohol **8a** (*dr* 97:3)[17] in good yield (81%). Acrylation of alcohol **8a** with acryloyl chloride followed by RCM[18] in the presence of the second-generation Grubbs' ruthenium



Scheme 2. Synthesis of aldehyde **9**.



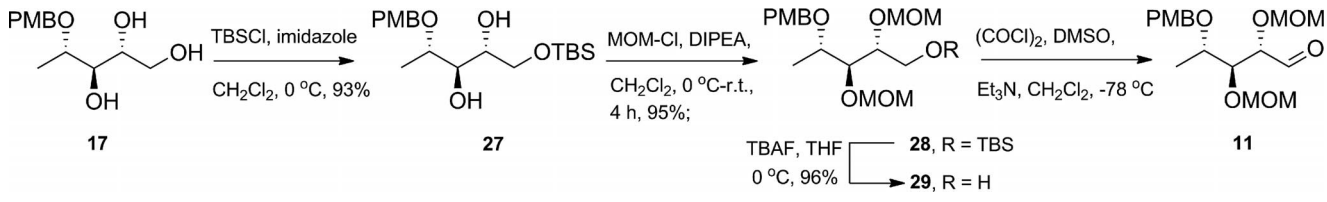
Scheme 3. Synthesis of synrotolide **1** (approach 1).

catalyst (10 mol-%) afforded lactone **26**. Partial hydrogenation of the triple bond to the *Z*-olefin with Lindlar's catalyst afforded **7a** in 93% yield. Attempts to deprotect the TBS groups by using TBAF and HF-Py in tetrahydrofuran (THF) failed to give the expected molecule **1**. However, we were successful in selective removal of the TBS groups in the presence of two OAc groups. The desilylation was achieved by the action of H_2SiF_6 (20–25% in H_2O)[19] in acetonitrile (CH_3CN) to give synrotolide **1** in 93% yield, the spectroscopic data of which were identical to those of the natural product.

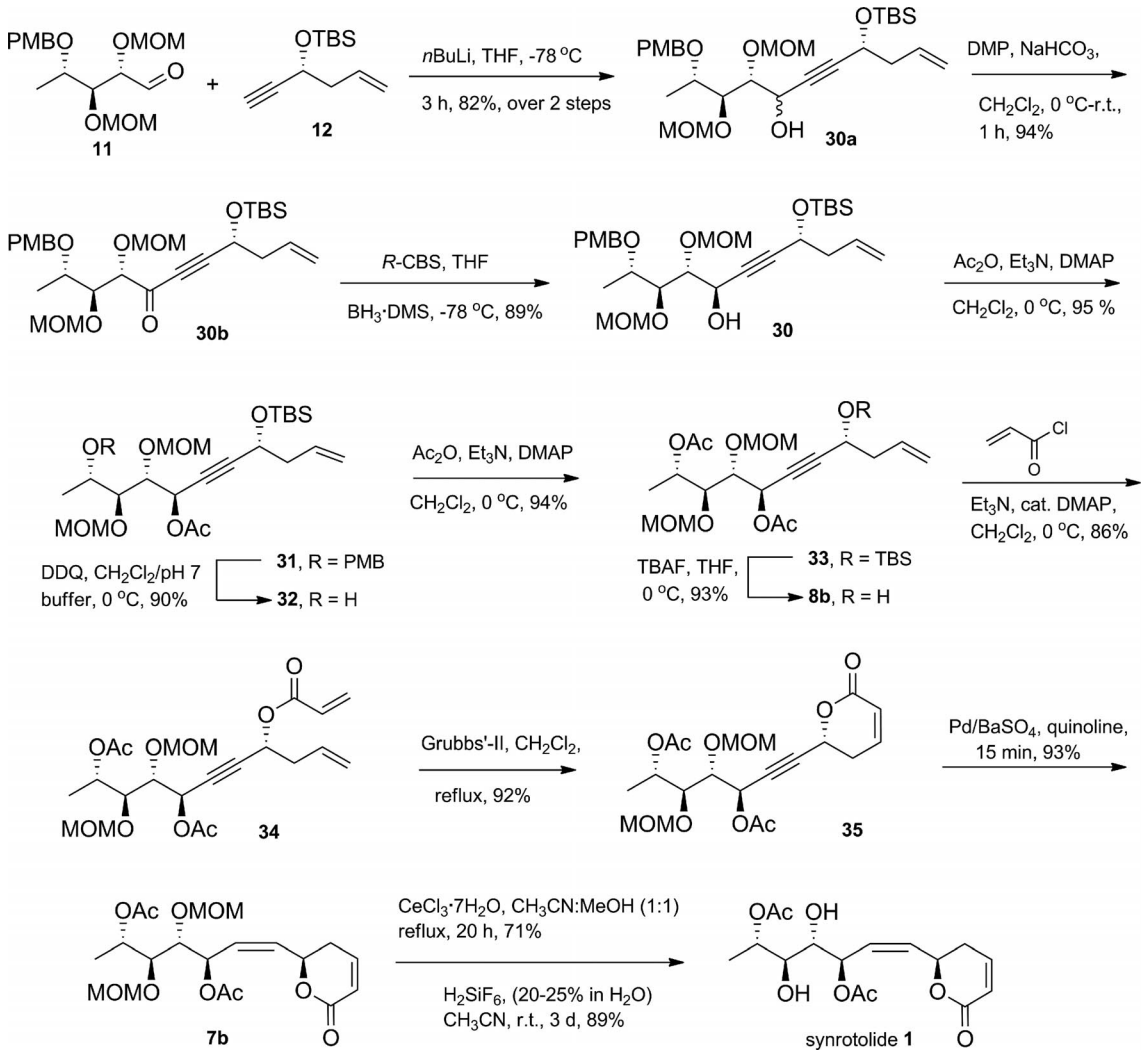
The second approach to the target compound was based on selective removal of MOM protecting groups. Therefore, we planned to synthesize bis-MOM protected aldehyde **11** (Scheme 4).

PMB-protected tetrol compound **17**, which was prepared from (*S*)-ethyl lactate (see Scheme 2), was used as the precursor. Tetrol **17**, on treatment with TBSCl and imidazole, was monosilylated to afford **27** in 93% yield. Further reaction with chloromethyl methyl ether (MOMCl) and *N*,*N*-diisopropylethylamine (DIPEA) in dichloromethane, provided the fully protected compound **28**, desilylation of which afforded the free alcohol **29**. This free alcohol was oxidized to aldehyde **11**, which was used for the next reaction without further purification.

With aldehyde **11** in hand, coupling with alkyne unit **12** was planned. The coupling partner, alkyne fragment **12** was prepared from 3-butyn-1-ol by following the procedure reported recently by us.[20] Lithiated alkyne **12** reacted with aldehyde **11** to afford alcohol **30a** as a mixture of diastereomers (80:20 *dr*),[21] which, without separation, was converted in 94% yield into keto compound **30b** by using Dess–Martin periodinane (DMP) in CH_2Cl_2. Ketone **30b** was stereoselectively reduced to the chiral propargyl alcohol **30** in 89% yield by using (*R*)-2-methyl-CBS-oxazaborolidine with the required stereoselectivity (9:1 *dr*)[21] (Scheme 5). The newly generated hydroxy group was acetylated with acetic anhydride to form monoacetate **31**. Removal of the PMB group and subsequent acetylation of the resulting alcohol **32** provided **33** as described in the first approach. Cleavage of the silicon protecting group with TBAF resulted in the formation of homoallylic alcohol **8b** as reported in Scheme 3. We then assembled the pyranone ring to give **35** by acryloylation of **8b** followed by RCM reaction. Partial hydrogenation of the triple bond to the *Z*-olefin with Lindlar's catalyst afforded **7b** in 93% yield. The final



Scheme 4. Synthesis of aldehyde **11**.



Scheme 5. Synthesis of synrotolide **1** (approach 2).

stage of the synthesis required selective deprotection of MOM groups, which proved to be challenging. Use of Lewis acids such as TFA or $TiCl_4$ for deprotection of the MOM groups in the presence of two OAc groups resulted in decomposition of the starting material. Fortunately, the use of $CeCl_3 \cdot 7H_2O$ in refluxing CH_3CN/MeOH (1:1)[22] delivered the desired target molecule, synrotolide **1** in 71% yield. Deprotection of the MOM groups was also successful, as reported in the first approach, by the action of H_2SiF_6 in CH_3CN to give synrotolide **1** in 89% yield. Spectroscopic data for synthetic **1** matched the reported data for the natural product in all regards.

Conclusions

We have successfully achieved the first total synthesis of natural product (–)-synrotolide (**1**) by two different approaches. The main feature of the synthesis is the chemoselective removal of TBS and MOM protecting groups in the last stage by using $CeCl_3 \cdot 7H_2O$ and H_2SiF_6. Both strategies used stereo- and regioselective epoxide opening with a nucleophile, aldehyde alkyne coupling and RCM reactions as the key steps.

Experimental Section

General: All reactions were performed under an inert atmosphere. All glassware used for reactions were oven/flame-dried. Anhydrous solvents were distilled prior to use: THF from Na and benzophenone; CH_2Cl_2 from CaH_2; MeOH from Mg cake. Commercial reagents were used without purification. Column chromatography was carried out by using silica gel (60–120 mesh). Analytical thin-layer chromatography (TLC) was run on silica gel 60 F254 precoated plates (250 μm thickness). Optical rotations $[a]_D^{25}$ were measured with an Anton Paar MCP-200 polarimeter and the concentration *c* is given in g/100 mL. Infrared spectra were recorded in $CHCl_3$/KBr (as mentioned) with a Thermo Nicolet Nexus 670 spectrometer and are reported in wave numbers (cm^{-1}). Mass spectroscopic data were obtained with MS (EI) ESI, HRMS mass spectrometers Quattro Micro Waters. High-resolution mass spectra (HRMS) [ESI^+] were obtained with either a TOF or a double focusing spectrometer Orbitrap Exactive (Thermo Scientific, Ger-

many). ^{1}H NMR spectra were recorded at 300, 400, 500 and ^{13}C NMR spectra at 75, 125 MHz with Avance-300, Avance-500, and Inova-400 spectrometers in $CDCl_3$ solution unless otherwise mentioned; chemical shifts are given in ppm downfield from tetramethylsilane and coupling constants (*J*) are reported in Hertz [Hz]. The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. The diastereomeric purity was determined by HPLC analysis.

(*S*,*E*)-Ethyl 4-[(4-Methoxybenzyl)oxy]pent-2-enoate (14): A solution of oxalyl chloride (4.30 mL, 51.02 mmol) in freshly distilled CH_2Cl_2 (80 mL) was cooled to –78 °C, and anhydrous DMSO (7.04 mL, 102.04 mmol) in CH_2Cl_2 (20 mL) was added dropwise. The mixture was stirred for 15 min at –78 °C, then alcohol **13** (5 g, 25.51 mmol) in CH_2Cl_2 (20 mL) was added dropwise. The reaction was stirred for 30 min at –78 °C then triethylamine (neat, 21.1 mL, 153.04 mmol) was added dropwise. The mixture was stirred for 30 min at –78 °C, then ethoxycarbonylmethylene triphenylphosphorane (13.27 g, 38.26 mmol) was added at same temperature, and the reaction mixture was stirred for 4 h (until room temp.); then it was transferred to a separatory funnel and washed with H_2O (50 mL), 1 N HCl (50 mL), saturated sodium hydrogen carbonate (50 mL), then brine (50 mL). Each wash was back-extracted with CH_2Cl_2 (2× 50 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (hexane/EtOAc, 9:1) to afford **14** (5.85 g, 87% yield from two steps) as a colorless oil. $[\alpha]_D^{25}$ = –40.0 (*c* = 0.90, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.3 Hz, 2 H), 6.93–6.84 (m, 1 H), 6.88 (d, *J* = 8.3 Hz, 2 H), 6.01 (dd, *J* = 15.8, 1.5 Hz, 1 H), 4.51 (d, *J* = 12.0 Hz, 1 H), 4.36 (d, *J* = 12.0 Hz, 1 H), 4.22 (q, *J* = 6.7 Hz, 2 H), 4.17–4.05 (m, 1 H), 3.81 (s, 3 H), 1.34–1.28 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 166.2, 159.1, 149.2, 130.0, 129.1, 121.1, 113.7, 73.4, 70.2, 60.3, 55.1, 20.5, 14.1 ppm. IR (neat): $\tilde{\nu}$ = 2979.1, 1718.7, 1611.8, 1513.4, 1299.0, 1250.0, 1177.2, 1034.7, 823.5, 771.8 cm^{-1}. MS (ESI): *m*/*z* = 287 [M + Na]$^+$.

(*S*,*E*)-4-[(4-Methoxybenzyl)oxy]pent-2-en-1-ol (15): DIBAL-H (34.70 mL, 41.66 mmol) was added to a stirred solution of ester **14** (5.50 g, 20.83 mmol) in CH_2Cl_2 (85 mL) at 0 °C and the mixture was stirred at the same temperature for 1 h. After monitoring with TLC, the reaction was quenched with aq. MeOH (5 mL) at 0 °C. Then a saturated solution of sodium potassium tartrate (35 mL) was added, and the mixture was extracted with CH_2Cl_2 (3× 50 mL). The organic layer was washed with brine (2× 40 mL) and H_2O (2× 40 mL) and the combined organic layer was dried with anhydrous Na_2SO_4, concentrated under vacuum and the crude alcohol was purified by column chromatography (hexane/EtOAc, 7:3) to afford **15** (4.16 g, 90% yield) as a colorless oil. $[\alpha]_D^{25}$ = –27.8 (*c* = 0.90, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.19 (d, *J* = 7.9 Hz, 2 H), 6.81 (d, *J* = 7.9 Hz, 2 H), 5.80–5.73 (m, 1 H), 5.62 (dd, *J* = 15.8, 7.9 Hz, 1 H), 4.45 (d, *J* = 11.8 Hz, 2 H), 4.29 (d, *J* = 11.8 Hz, 2 H), 4.12 (dd, *J* = 4.9, 0.9 Hz, 2 H), 3.94–3.87 (m, 1 H), 3.78 (s, 3 H), 1.25 (d, *J* = 5.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.9, 134.2, 133.3, 130.8, 129.1, 113.6, 74.7, 69.6, 62.8, 55.2, 21.3 ppm. IR (neat): $\tilde{\nu}$ = 3426.4, 2971.9, 1612.1, 1512.8, 1460.5, 1247.2, 1075.6, 1032.6, 820.5 cm^{-1}. MS (ESI): *m*/*z* = 241 [M + NH_3]$^+$.

((2*S*,3*S*)-3-{(*S*)-1-[(4-Methoxybenzyl)oxy]ethyl}oxiran-2-yl)methanol (16): To a freshly flame-dried double-necked round-bottomed flask equipped with activated molecular sieves (4 Å, ca. 7 g) and anhydrous CH_2Cl_2 (80 mL) at –20 °C were added $Ti(OiPr)_4$ (5.34 mL, 18.24 mmol) and L-(+)-diisopropyl tartrate (4.69 g, 20.06 mmol), and the mixture was stirred for 30 min. To this reaction mixture, allyl alcohol **15** (4.05 g, 18.24 mmol) followed, after an interval of 30 min, by TBHP (5 M in toluene, 18.24 mL, 91.20 mmol) were added and stirring was continued until completion of the reaction (8 h). The reaction mixture was warmed to 0 °C, filtered through Celite, and the filtrate was quenched with water (20 mL), and 15% aqueous NaOH solution (8 mL), and stirred vigorously for 1 h. The biphasic solution was separated and the aqueous layer was extracted with CH_2Cl_2 (2× 50 mL). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated under vacuum. The crude residue was purified by column chromatography (hexane/EtOAc, 7:3) to afford pure epoxide **16** (3.95 g, 91%) as a colorless oil. $[\alpha]_D^{25}$ = –16.8 (*c* = 1.2, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 4.51 (s, 2 H), 3.87 (dd, *J* = 12.6, 2.7 Hz, 1 H), 3.80 (s, 3 H), 3.59 (dd, *J* = 12.6, 4.4 Hz, 1 H), 3.49–3.44 (m, 1 H), 3.12–3.09 (m, 1 H), 2.95 (dd, *J* = 5.1, 2.2 Hz, 1 H), 1.27 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.0, 130.2, 129.0, 113.6, 73.7, 70.9, 61.3, 57.7, 55.1, 17.4 ppm. IR (neat): $\tilde{\nu}$ = 3445.3, 2976.3, 2928.9, 1611.8, 1513.0, 1461.6, 1247.9, 1087.8, 1033.7, 821.7, 768.9 cm^{-1}. MS (ESI): *m*/*z* = 261 [M + Na]$^+$.

(2*R*,3*R*,4*S*)-4-[(4-Methoxybenzyl)oxy]pentane-1,2,3-triol (17): A solution of epoxy alcohol **16** (3.75 g, 15.75 mmol) in a mixture of 0.5 N NaOH in H_2O/*t*BuOH (5:1) (75 mL) was stirred for 15 h at 70 °C. Upon completion of the reaction (indicated by TLC), the mixture was extracted with EtOAc (4× 30 mL), and the organic extracts were washed with brine (20 mL) and dried with anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography (3:7, hexane/EtOAc) to furnish triol **17** (2.90 g, 72%) as a colorless liquid. $[\alpha]_D^{25}$ = + 41.14 (*c* = 0.70, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.6 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 4.60 (d, *J* = 11.1 Hz, 1 H), 4.40 (d, *J* = 11.1 Hz, 1 H), 3.81 (s, 3 H), 3.81–3.66 (m, 5 H), 2.97 (d, *J* = 2.6 Hz, 1 H), 2.53 (d, *J* = 3.3 Hz, 1 H), 1.30 (d, *J* = 5.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.3, 129.8, 129.4, 113.9, 76.2, 74.0, 72.2, 70.4, 63.8, 55.2, 14.8 ppm. IR (neat): $\tilde{\nu}$ = 3405.8, 2934.1, 1612.4, 1513.4, 1460.7, 1248.1, 1072.2, 1033.6, 823.5 cm^{-1}. MS (ESI): *m*/*z* = 279 [M + Na]$^+$. HRMS (ESI): *m*/*z* calcd. for $C_{13}H_{20}O_5Na$ [M + Na]$^+$ 279.12029; found 279.11944.

(5*S*,6*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-5-{(*S*)-1-[(4-methoxybenzyl)oxy]ethyl}-2,2,3,3,9,9,10,10-octamethyl-4,8-dioxa-3,9-disilaundecane (18): To an ice-bath cooled solution of triol **17** (0.90 g, 3.51 mmol) and imidazole (1.43 g, 21.09 mmol) in a mixture of anhydrous CH_2Cl_2 (10 mL) and DMF (10 mL) was added a solution of TBSCl (1.69 g, 3.83 mmol) in anhydrous CH_2Cl_2 (3 mL). The mixture was stirred at room temp. for 24 h, then diluted with water (20 mL) and extracted with diethyl ether (3× 20 mL). The combined organic phases were washed with brine (20 mL) and dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/EtOAc, 3:97) to give **18** (1.80 g, 86%) as a colorless oil. $[\alpha]_D^{25}$ = + 16.8 (*c* = 0.20, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.6 Hz, 2 H), 6.85 (d, *J* = 8.6 Hz, 2 H), 4.43 (ABq, *J* = 20.2, 11.1 Hz, 2 H), 3.80 (s, 3 H), 3.81–3.61 (m, 4 H), 3.50 (dd, *J* = 11.7, 7.7 Hz, 1 H), 1.15 (d, *J* = 5.8 Hz, 3 H), 0.89 (s, 18 H), 0.85 (s, 9 H), 0.09–0.01 (m, 18 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.8, 131.0, 129.1, 113.5, 76.8, 75.9, 75.1, 70.4, 65.4, 55.2, 26.1, 26.0, 18.4, 18.3, 18.2, 15.4, –4.1, –4.2, –4.4, –4.7, –5.2, –5.3 ppm. IR (neat): $\tilde{\nu}$ = 2954.3, 2930.4, 2856.8, 1249.6, 1093.0, 1038.0, 832.3, 744.0 cm^{-1}. MS (ESI): *m*/*z* = 621 [M + Na]$^+$. HRMS (ESI): *m*/*z* calcd. for $C_{31}H_{63}O_5NaSi_3$ [M + Na]$^+$ 599.39778; found 599.39658.

(2*R*,3*S*,4*S*)-2,3-Bis[(*tert*-butyldimethylsilyl)oxy]-4-[(4-methoxybenzyl)oxy]pentan-1-ol (19): To an ice-salt bath cooled solution of

tri-TBS ether **18** (1.75 g, 2.92 mmol) in MeOH (20 mL), was added PTSA (0.27 g, 1.46 mmol) as a solid. The reaction mixture was stirred at –15 °C for 30 min, then the reaction was quenched with solid $NaHCO_3$ (2 g) and filtered. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography (hexane/EtOAc, 85:15) to afford primary alcohol **19** (1.2 g, 85%) as a colorless oil. $[\alpha]_D^{25}$ = +24.8 (*c* = 0.20, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 4.50 (d, *J* = 11.4 Hz, 1 H), 4.44 (d, *J* = 11.4 Hz, 1 H), 3.80 (s, 3 H), 3.82–3.78 (m, 1 H), 3.75–3.71 (m, 1 H), 3.68–3.62 (m, 3 H), 1.16 (d, *J* = 6.4 Hz, 3 H), 0.90 (s, 9 H), 0.87 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H), 0.08 (s, 3 H), 0.04 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.9, 130.5, 129.1, 113.6, 76.9, 75.4, 73.4, 70.6, 63.4, 55.1, 25.9, 25.8, 18.2, 18.0, 14.7, –4.3, –4.5, –4.6, –4.7 ppm. IR (neat): $\tilde{\nu}$ = 3449.8, 2954.8, 2930.9, 2856.9, 1513.3, 1465.8, 1250.3, 1091.3, 1037.5, 834.0, 775.7 cm^{-1}. MS (ESI): *m*/*z* = 485 $[M + H]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{49}O_5Si_2$ $[M + H]^+$ 485.31130; found 485.31062.

(5*S*,6*R*,7*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-5-{(*S*)-1-[(4-methoxybenzyl)oxy]ethyl}-2,2,3,3,12,12,13,13-octamethyl-4,11-dioxa-3,12-disilatetradec-8-yn-7-ol (20): A solution of oxalyl chloride (0.31 mL, 3.71 mmol) in freshly distilled CH_2Cl_2 (10 mL) was cooled to –78 °C, and anhydrous DMSO (0.58 mL, 7.43 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The mixture was stirred for 15 min at –78 °C, then alcohol **19** (0.90 g, 1.85 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The reaction was stirred for 1.5 h at –78 °C then triethylamine (neat, 1.54 mL, 11.15 mmol) was added dropwise. The mixture was stirred for 30 min at –78 °C then 30 min at 0 °C, then transferred to a separatory funnel and washed with H_2O (10 mL), 1 N HCl (10 mL), saturated sodium hydrogen carbonate (10 mL), then brine (10 mL). Each wash was back-extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was passed through a short silica plug with 100% CH_2Cl_2, concentrated under reduced pressure, and then crude aldehyde **9** (0.86 g, 96%, yellow oil) was immediately subjected to the next reaction without further purification.

*n*BuLi (2.5 M in hexanes, 1.06 mL, 2.67 mmol) was added to a solution of alkyne **10** (0.454 g, 2.67 mmol) in THF (10 mL) at –78 °C. After stirring for 5 min, the reaction mixture was warmed to –20 °C and stirred for 30 min. The mixture was cooled back to –78 °C and a solution of crude aldehyde **9** (0.86 g, 1.784 mmol) in THF (5 mL) was added dropwise. The resulting mixture was stirred for 2 h at –78 °C, then the mixture was poured onto saturated aqueous NH_4Cl solution (20 mL) and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (90:10, hexane/EtOAc) to afford **20** (1.10 g, 91% yield over 2 steps) as almost completely a single diastereomer (93:7 *dr*) as a colorless liquid. $[\alpha]_D^{25}$ = –11.5 (*c* = 0.50, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.6 Hz, 2 H), 6.85 (d, *J* = 8.6 Hz, 2 H), 4.56–4.39 (m, 3 H), 4.38–4.28 (m, 2 H), 3.91–3.83 (m, 1 H), 3.79 (s, 3 H), 3.76 (t, *J* = 6.1 Hz, 1 H), 3.43 (d, *J* = 6.1 Hz, 1 H), 1.18 (d, *J* = 6.2 Hz, 3 H), 0.90 (s, 9 H), 0.89 (s, 18 H), 0.13 (s, 3 H), 0.12 (s, 3 H), 0.10 (s, 3 H), 0.09 (s, 3 H), 0.08 (s, 3 H), 0.06 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 159.1, 130.0, 129.5, 113.6, 84.5, 84.1, 77.7, 76.8, 74.9, 70.7, 65.1, 55.1, 51.7, 26.0, 25.9, 25.8, 18.2, 18.1, 15.3, –4.4, –5.1, –5.2 ppm; IR (neat): $\tilde{\nu}$ = 3448.4, 2930.9, 2857.4, 1513.5, 1250.8, 1088.7, 835.6, 773.2 cm^{-1}. MS (ESI): *m*/*z* = 670 $[M + Na]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{34}H_{68}O6NaSi_3$ $[M + Na]^+$ 670.43489; found 670.43418.

(5*S*,6*R*,7*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-5-{(*S*)-1-[(4-methoxybenzyl)oxy]ethyl}-2,2,3,3,12,12,13,13-octamethyl-4,11-dioxa-3,12-disilatetradec-8-yn-7-yl Acetate (21): Anhydrous Et_3N (0.63 mL, 4.60 mmol), Ac_2O (0.236 mL, 2.30 mmol), and DMAP (5 mg) were added to a solution of alcohol **20** (1.0 g, 1.533 mmol) in anhydrous CH_2Cl_2 (20 mL) at room temp. under a nitrogen atmosphere. The mixture was stirred at room temp. for 30 min, then the reaction was quenched with saturated $NaHCO_3$ (10 mL). The organic layer was extracted with CH_2Cl_2 (2 × 10 mL) and the combined organic layers were dried with Na_2SO_4. The solvent was removed under reduced pressure, and the mixture was purified by column chromatography (hexane/EtOAc, 90:10) to afford **21** (0.987 g, 93%) as a colorless liquid. $[\alpha]_D^{25}$ = –13.2 (*c* = 0.76, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.4 Hz, 2 H), 6.86 (d, *J* = 8.4 Hz, 2 H), 5.79–5.75 (m, 1 H), 4.54–4.27 (m, 5 H), 3.91 (dd, *J* = 7.7, 2.2 Hz, 1 H), 3.80 (s, 3 H), 3.68–3.60 (m, 1 H), 2.06 (s, 3 H), 1.08 (d, *J* = 6.4 Hz, 3 H), 0.91 (s, 9 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.15–0.07 (m, 18 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.1, 158.8, 129.5, 129.1, 113.5, 79.8, 79.2, 75.0, 74.9, 74.2, 70.0, 66.8, 55.2, 51.6, 26.1, 25.9, 25.7, 21.0, 18.3, 18.2, 12.9, –3.7, –4.0, –4.7, –5.0, –5.1, –5.2 ppm. IR (neat): $\tilde{\nu}$ = 2954.9, 2931.1, 2857.4, 1768.0, 1513.4, 1466.2, 1251.1, 1224.8, 1093.0, 1032.0, 836.7, 775.6 cm^{-1}. MS (ESI): *m*/*z* = 712 $[M + Na]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{36}H_{70}O_7NaSi_3$ $[M + Na]^+$ 712.44546; found 712.44514.

(5*S*,6*R*,7*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-5-[(*S*)-1-hydroxyethyl]-2,2,3,3,12,12,13,13-octamethyl-4,11-dioxa-3,12-disilatetradec-8-yn-7-yl Acetate (22): To an ice-bath cooled solution of **21** (0.95 g, 1.36 mmol) in aq. CH_2Cl_2 (20 mL; CH_2Cl_2/buffer (pH 7), 9:1), DDQ (0.34 g, 1.50 mmol) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction mixture was washed with 5% aq. $NaHCO_3$ solution (15 mL), the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with water, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (hexane/EtOAc, 90:10) to afford alcohol **22** (0.695 g, 89%) as a liquid. $[\alpha]_D^{25}$ = –29.50 (*c* = 0.68, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.69–5.67 (m, 1 H), 4.34 (d, *J* = 1.6 Hz, 2 H), 4.06–3.99 (m, 1 H), 3.76–3.72 (m, 2 H), 2.09 (s, 3 H), 1.16 (d, *J* = 6.4 Hz, 3 H), 0.92 (s, 18 H), 0.89 (s, 9 H), 0.19 (s, 3 H), 0.16 (s, 3 H), 0.13 (s, 3 H), 0.10 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.1, 85.9, 79.3, 76.9, 76.2, 66.7, 51.6, 26.0, 25.9, 25.7, 20.9, 18.3, 18.2, 17.3, –4.0, –4.2, –4.3, –4.5, –5.2 ppm. IR (neat): $\tilde{\nu}$ = 3455.1, 2955.4, 2931.5, 2858.0, 1748, 1466.7, 1367.6, 1253.7, 1092.4, 1022.1, 836.0, 776.3 cm^{-1}. MS (ESI): *m*/*z* = 592 $[M + Na]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{28}H_{62}O6NaSi_3$ $[M + Na]^+$ 592.38794; found 592.38680.

(2*S*,3*S*,4*R*,5*R*)-3,4,8-Tris[(*tert*-butyldimethylsilyl)oxy]oct-6-yne-2,5-diyl Diacetate (23): Anhydrous Et_3N (0.47 mL, 3.39 mmol), Ac_2O (0.173 mL, 1.69 mmol), and DMAP (5 mg) were added to a solution of alcohol **22** (0.65 g, 1.13 mmol) in anhydrous CH_2Cl_2 (20 mL) at room temp. under a nitrogen atmosphere. The mixture was stirred at room temp. for 30 min. The reaction was quenched with saturated $NaHCO_3$ (10 mL) and the organic layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried with Na_2SO_4, the solvent was removed under reduced pressure, and the mixture was purified by column chromatography (hexane/EtOAc, 95:5) to afford **23** (0.64 g, 92%) as a colorless liquid. $[\alpha]_D^{25}$ = –24.4 (*c* = 0.50, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.73 (d, *J* = 1.8 Hz, 1 H), 5.27 (qd, *J* = 6.4, 1.8 Hz, 1 H), 4.34 (d, *J* = 1.5 Hz, 2 H), 3.86 (dd, *J* = 8.1, 1.7 Hz, 1 H), 3.63 (dd, *J* = 8.1, 2.4 Hz, 1 H), 2.09 (s, 3 H), 2.04 (s, 3 H), 1.16 (d, *J* = 6.4 Hz, 3 H), 0.93 (s, 18 H), 0.88 (s, 9 H), 0.17 (s, 3 H), 0.15 (s, 3 H), 0.14 (s, 3 H), 0.11 (s, 3 H), 0.09 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$,

75 MHz): δ = 169.8, 169.1, 86.0, 78.7, 74.9, 74.8, 71.0, 66.6, 51.6, 26.0, 25.9, 25.7, 21.3, 20.9, 18.3, 18.2, 12.8, –4.0, –4.1, –4.7, –4.8, –5.2, –5.3 ppm. IR (neat): ṽ = 2955.4, 2931.8, 2858.2, 1746.3, 1467.3, 1369.1, 1253.0, 1224.7, 1156.6, 1089.5, 1027.9, 835.8, 777.8 cm^{-1}. MS (ESI): *m*/*z* = 634 [M + Na]$^+$. HRMS (ESI): *m*/*z* calcd. for $C_{30}H_{64}O_7NaSi_3$ [M + Na]$^+$ 634.39851; found 634.39795.

(2*S*,3*S*,4*R*,5*R*)-3,4-Bis[(*tert*-butyldimethylsilyl)oxy]-8-hydroxyoct-6-yne-2,5-diyl Diacetate (24): To an ice-bath cooled solution of the tri-TBS ether **23** (0.60 g, 0.974 mmol) in MeOH (10 mL) was added PTSA (0.089 g, 0.487 mmol) as a solid. The reaction mixture was stirred at –15 °C for 30 min, then the reaction was quenched with solid $NaHCO_3$ (1 g) and filtered. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography (hexane/EtOAc, 85:15) to afford primary alcohol **24** (0.44 g, 91%) as a colorless oil. $[\alpha]_D^{25}$ = –21.7 (*c* = 0.60, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.71–5.69 (m, 1 H), 5.28 (qd, *J* = 6.2, 2.1 Hz, 1 H), 4.33–4.26 (m, 2 H), 3.87 (dd, *J* = 7.9, 2.1 Hz, 1 H), 3.68 (dd, *J* = 7.7, 2.5 Hz, 1 H), 2.01 (s, 3 H), 2.06 (s, 3 H), 1.18 (d, *J* = 6.4 Hz, 3 H), 0.94 (s, 9 H), 0.93 (s, 9 H), 0.17 (s, 3 H), 0.15 (s, 3 H), 0.14 (s, 3 H), 0.12 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 170.0, 169.3, 85.7, 80.0, 74.9, 74.8, 71.1, 66.5, 50.9, 25.9, 25.8, 21.3, 20.9, 18.3, 12.9, –4.1, –4.2, –4.6, –4.8 ppm. IR (neat): ṽ = 3453.7, 2932.7, 2858.5, 1745.7, 1370.0, 1253.4, 1225.2, 1155.4, 1116.5, 1028.5, 834.4, 774.9 cm^{-1}. MS (ESI): *m*/*z* = 520 [M + Na]$^+$. HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{50}O_7NaSi_2$ [M + Na]$^+$ 520.31203; found 520.31014.

(2*S*,3*S*,4*R*,5*R*,8*R*)-3,4-Bis[(*tert*-butyldimethylsilyl)oxy]-8-hydroxyundec-10-en-6-yne-2,5-diyl Diacetate (8a): To an ice-cooled solution of IBX (0.34 g, 1.195 mmol) in DMSO (0.27 mL, 3.98 mmol) and CH_2Cl_2 (5 mL), was added a solution of alcohol **24** (0.40 g, 0.79 mmol) in CH_2Cl_2 (5 mL). The mixture was stirred at room temp. for 2 h and then filtered through a Celite pad and washed with Et_2O (30 mL). The combined organic filtrates were washed with H_2O (2× 10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude aldehyde (0.358 g, 90%, yellow oil) was immediately subjected to the next reaction without further purification.

To a solution of (+)-IPC_2B(allyl) (1.0 M in pentane, 0.86 mL, 0.860 mmol) in Et_2O (10 mL) at –100 °C, a solution of the above crude aldehyde (0.358, 0.717 mmol) in Et_2O (5 mL) was added slowly. The mixture was stirred at –100 °C for 2 h and then warmed to 0 °C. The reaction was quenched by dropwise addition of H_2O (15 mL), then the mixture was diluted with Et_2O (20 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2× 10 mL) and the combined organic layers were washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated. The crude reaction mixture was further purified by column chromatography (hexane/EtOAc, 95:5) to give homoallyl alcohol **8a** (0.345 g, 81% over 2 steps) as a clear liquid. $[\alpha]_D^{25}$ = –18.6 (*c* = 0.90, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.95–5.79 (m, 1 H), 5.74–5.70 (m, 1 H), 5.29 (qd, *J* = 6.6, 1.8 Hz, 1 H), 5.22–5.12 (m, 2 H), 4.49–4.40 (m, 1 H), 3.86 (dd, *J* = 8.3, 1.8 Hz, 1 H), 3.64 (dd, *J* = 8.3, 2.2 Hz, 1 H), 2.42–2.32 (m, 2 H), 2.10 (s, 3 H), 2.06 (s, 3 H), 1.13 (d, *J* = 7.3 Hz, 3 H), 0.93 (s, 9 H), 0.92 (s, 9 H), 0.17 (s, 3 H), 0.16 (s, 3 H), 0.15 (s, 3 H), 0.12 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.0, 169.3, 132.9, 118.8, 88.0, 79.2, 74.8, 74.7, 71.0, 66.6, 61.4, 41.8, 25.9, 25.8, 21.4, 21.0, 18.3, 12.6, –4.0, –4.1, –4.7, –4.9 ppm. IR (neat): ṽ = 3430.8, 2932.4, 2858.7, 1744.9, 1341.4, 1253.4, 1225.3, 1155.9, 1118.6, 1031.8, 834.2, 776.4 cm^{-1}. MS (ESI): *m*/*z* = 496 [M + Na]$^+$.

(2*S*,3*S*,4*R*,5*R*,8*R*)-8-(Acryloyloxy)-3,4-bis[(*tert*-butyldimethylsilyl)oxy]undec-10-en-6-yne-2,5-diyl Diacetate (25): Acryloyl chloride (0.073 mL, 0.830 mmol) was added dropwise under N_2 to a solution of alcohol **8a** (0.30 g, 0.553 mmol) and Et_3N (0.220 mL, 1.66 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at 0 °C for 1 h. Upon completion, the mixture was poured into brine (2 mL) and extracted with CH_2Cl_2 (2× 10 mL). The organic phase was washed with 1M aq. HCl, dried with anhydrous Na_2SO_4, and concentrated. The crude product was purified by column chromatography (hexane/EtOAc, 95:5) to afford the corresponding acrylic ester **25** (0.275 g, 84%) as a colorless oil. $[\alpha]_D^{25}$ = –35.0 (*c* = 0.72, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.41 (dd, *J* = 17.1, 1.1 Hz, 1 H), 6.09 (dd, *J* = 17.3, 10.3 Hz, 1 H), 5.89–5.74 (m, 3 H), 5.60–5.52 (m, 1 H), 5.27 (qd, *J* = 6.4, 1.7 Hz, 1 H), 5.20–5.07 (m, 2 H), 3.83 (dd, *J* = 8.4, 1.7 Hz, 1 H), 3.62 (dd, *J* = 8.6, 2.0 Hz, 1 H), 2.60–2.51 (m, 2 H), 2.09 (s, 3 H), 2.05 (s, 3 H), 1.15 (d, *J* = 6.4 Hz, 3 H), 0.92 (s, 18 H), 0.15 (s, 3 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.10 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.8, 169.1, 164.7, 132.0, 131.3, 127.9, 118.7, 84.3, 80.1, 74.7, 70.9, 66.4, 63.0, 39.0, 25.9, 25.8, 21.3, 21.0, 18.3, 12.5, –4.0, –4.8, –4.9 ppm. IR (neat): ṽ = 2987.5, 2934.5, 1736.6, 1374.8, 1231.6, 1180.4, 1064.2, 1023.4, 983.1 cm^{-1}. MS (ESI): *m*/*z* = 614 [M + Na]$^+$. HRMS (ESI): *m*/*z* calcd. for $C_{30}H_{64}O_8NaSi_2$ [M + Na]$^+$ 614.35390; found 614.35304.

(2*S*,3*S*,4*R*,5*R*)-3,4-Bis[(*tert*-butyldimethylsilyl)oxy]-7-[(*R*)-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]hept-6-yne-2,5-diyl Diacetate (26): A solution of Grubbs' second-generation catalyst (G-II; 0.033 g, 0.0419 mmol, 10 mol-%) in CH_2Cl_2 (10 mL) was added dropwise to a solution of acrylic ester **25** (0.250 g, 0.419 mmol) in CH_2Cl_2 (60 mL) at room temp., and stirring was continued for 5 h while heating to reflux. The solvent was evaporated and the crude product was purified by column chromatography (hexane/EtOAc, 75:25) to give lactone **26** (0.219 g, 92%) as a pale-yellow oil. $[\alpha]_D^{25}$ = –19.50 (*c* = 0.70, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.86 (dt, *J* = 9.9, 4.4 Hz, 1 H), 6.07 (dt, *J* = 9.9, 1.8 Hz, 1 H), 5.75 (dd, *J* = 2.2, 1.6 Hz, 1 H), 5.28–5.22 (m, 2 H), 3.81 (dd, *J* = 8.3, 1.9 Hz, 1 H), 3.65 (dd, *J* = 8.3, 2.2 Hz, 1 H), 2.72–2.58 (m, 2 H), 2.10 (s, 3 H), 2.06 (s, 3 H), 1.16 (d, *J* = 6.5 Hz, 3 H), 0.94 (s, 9 H), 0.93 (s, 9 H), 0.15 (s, 3 H), 0.14 (s, 6 H), 0.11 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.7, 169.2, 161.9, 143.6, 121.2, 82.4, 80.7, 77.9, 74.7, 68.2, 66.5, 62.2, 29.6, 25.9, 25.8, 20.9, 20.5, 17.5, 18.3, –4.1, –4.2, –4.6, –4.8 ppm. IR (neat): ṽ = 2988.3, 2937.4, 1736.8, 1376.0, 1244.1, 1058.1, 863.8 cm^{-1}. MS (ESI): *m*/*z* = 586 [M + Na]$^+$. HRMS (ESI): *m*/*z* calcd. for $C_{28}H_{52}O_8NaSi_2$ [M + Na]$^+$ 586.32260; found 586.32146.

(2*S*,3*S*,4*R*,5*R*,*Z*)-3,4-Bis[(*tert*-butyldimethylsilyl)oxy]-7-(6-oxo-3,6-dihydro-2*H*-pyran-2-yl)hept-6-ene-2,5-diyl Diacetate (7a): To a solution of **26** (0.20 g, 0.352 mmol) in EtOAc (5 mL), one drop of quinoline and Lindlar's catalyst (Pd/$BaSO_4$) (0.0035 g, 0.0352 mmol, 10 mol-%) were added and the mixture was stirred at room temp. under H_2 for 15 min. After completion of the reaction, the reaction mixture was filtered and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (hexane/EtOAc, 75:25) to afford **26** (0.186 g, 93%) as a colorless liquid. $[\alpha]_D^{25}$ = –20.10 (*c* = 0.80, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.94–6.85 (m, 1 H), 6.09–6.03 (m, 1 H), 5.86 (ddd, *J* = 8.8, 8.0, 0.6 Hz, 1 H), 5.63 (ddd, *J* = 10.4, 9.3, 0.9 Hz, 1 H), 5.50–5.38 (m, 2 H), 4.49–4.85 (m, 1 H), 4.33–4.16 (m, 2 H), 2.45–2.40 (m, 2 H), 2.09 (s, 3 H), 2.06 (s, 3 H), 1.35 (d, *J* = 6.1 Hz, 3 H), 0.94 (s, 18 H), 0.14 (s, 3 H), 0.13 (s, 6 H), 0.11 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.2, 169.5, 165.1, 143.8, 132.4, 128.4, 122.3, 77.8, 75.1, 71.3, 66.8, 30.0, 26.3, 26.2, 21.8, 21.4, 18.7, 17.1, –3.6, –4.3, –4.5 ppm. IR (neat): ṽ = 1737.4, 1376.8, 1244.8, 1058.4, 817.1 cm^{-1}. MS (ESI): *m*/*z* = 588

$[M + Na]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{28}H_{54}O_8NaSi_2$ $[M + Na]^+$ 588.32362; found 588.32446.

(2*S*,3*R*,4*S*,5*R*,*Z*)-3,4-Dihydroxy-7-(6-oxo-3,6-dihydro-2*H*-pyran-2-yl)hept-6-ene-2,5-diyl Diacetate (1): To a solution of **7a** (4.0 mg, 0.0047 mmol) in MeCN (1 mL) was added fluorosilicic acid (H_2SiF_6; 20–25 wt.-% in water, 0.1 mL). After 2 d stirring at room temp., the mixture was filtered through a Celite pad and concentrated under reduced pressure. Purification by column chromatography gave synrotolide **1** (2.0 mg, 90%). $[\alpha]_D^{25}$ = –24.8 (*c* = 0.20, MeOH). ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 7.10–7.02 (m, 1 H), 6.00–5.95 (m, 1 H), 5.82 (dd, *J* = 11.1, 8.8 Hz, 1 H), 5.72 (dd, *J* = 10.8, 10.5 Hz, 1 H), 5.64–5.58 (m, 1 H), 5.38 (d, *J* = 5.9 Hz, 1 H), 5.34–5.26 (m, 1 H), 5.04 (d, *J* = 5.9 Hz, 1 H), 5.05–5.00 (m, 1 H), 3.54–3.46 (m, 1 H), 3.35–3.29 (m, 1 H), 2.45–2.34 (m, 2 H), 2.01 (s, 3 H), 1.99 (s, 3 H), 1.09 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 125 MHz): δ = 169.8, 169.5, 163.3, 147.1, 131.9, 126.8, 120.1, 73.9, 71.3, 71.1, 71.0, 70.0, 29.5, 21.1, 20.7, 12.8 ppm. IR (neat): $\tilde{\nu}$ = 3449.4, 2921.7, 1739.3, 1642.9, 1377.7, 1258.8, 1022.4 cm^{-1}. MS (ESI): *m*/*z* = 365 $[M + Na]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{22}O_8Na$ $[M + Na]^+$ 365.12069; found 365.12034.

(2*R*,3*R*,4*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-4-[(4-methoxybenzyl)-oxy]pentane-2,3-diol (27): To a stirred solution of triol **17** (1.25 g, 4.88 mmol) in CH_2Cl_2 (30 mL), imidazole (0.66 g, 9.84 mmol) was added at 0 °C and the mixture was stirred for 15 min. *tert*-Butyl dimethyl silyl chloride (0.73 g, 4.88 mmol) was added at 0 °C and the mixture was stirred for 1 h. Upon completion of the reaction (indicated by TLC), the reaction mixture was concentrated under reduced pressure and purified by chromatography (hexane/EtOAc, 8:2) to give **27** (1.68, 93%) as a colorless liquid. $[\alpha]_D^{25}$ = +22.0 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.6 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 4.57 (d, *J* = 11.1 Hz, 1 H), 4.41 (d, *J* = 11.1 Hz, 1 H), 3.80 (s, 3 H), 3.81–3.62 (m, 5 H), 1.28 (d, *J* = 6.1 Hz, 3 H), 0.90 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.3, 129.8, 129.4, 113.9, 76.2, 74.0, 72.2, 70.4, 63.8, 55.2, 14.8 ppm. IR (neat): $\tilde{\nu}$ = 3452.1, 2931.3, 2858.0, 1612.8, 1513.6, 1465.1, 1250.6, 1078.9, 1037.9, 836.1, 778.3 cm^{-1}. MS (ESI): *m*/*z* = 393 $[M + Na]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{34}O_5NaSi$ $[M + Na]^+$ 393.20677; found 393.20516.

(5*S*,6*R*)-5-{(*S*)-1-[(4-Methoxybenzyl)oxy]ethyl}-6-(methoxymethoxy)-9,9,10,10-tetramethyl-2,4,8-trioxa-9-silaundecane (28): To diol **27** (1.65 g, 4.45 mmol) in anhydrous CH_2Cl_2 (30 mL) at 0 °C, were successively added DIPEA (3.81 mL, 22.29 mmol), catalytic DMAP and MOMCl (1.10 mL, 13.35 mmol). The mixture was stirred for 4 h at room temp., then the reaction was quenched by adding water (20 mL) and the mixture was extracted with CH_2Cl_2 (2 × 25 mL). The organic extracts were washed with brine (20 mL), dried with anhydrous Na_2SO_4, and concentrated under vacuo to remove the solvent. The crude material was purified by column chromatography (hexane/EtOAc, 9:1) to afford the pure product **28** (1.94 g, 95%) as an oil. $[\alpha]_D^{25}$ = –13.00 (*c* = 0.40, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 9.0 Hz, 2 H), 6.86 (d, *J* = 9.0 Hz, 2 H), 4.82–4.65 (m, 4 H), 4.48 (ABq, *J* = 11.3, 4.3 Hz, 2 H), 3.88–3.69 (m, 5 H), 3.80 (s, 3 H), 3.39 (s, 3 H), 3.35 (s, 3 H), 1.25 (d, *J* = 6.0 Hz, 3 H), 0.89 (s, 9 H), 0.04 (s, 6 H), 0.07 ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 158.9, 130.7, 129.0, 113.6, 96.9, 96.5, 78.3, 78.1, 74.6, 70.2, 63.5, 55.9, 55.6, 55.1, 25.8, 18.2, 15.3, –5.3, –5.4 ppm. IR (neat): $\tilde{\nu}$ = 2930.7, 2856.3, 1613.2, 1513.4, 1465.8, 1249.8, 1101.9, 1033.5, 836.6, 774.4 cm^{-1}. MS (ESI): *m*/*z* = 481 $[M + Na]^+$.

(2*R*,3*S*,4*S*)-4-[(4-Methoxybenzyl)oxy]-2,3-bis(methoxymethoxy)pentan-1-ol (29): To a solution of **28** (1.90 g, 4.14 mmol) in anhydrous THF (20 mL) was added TBAF (1M in THF, 4.56 mL, 4.56 mmol) dropwise at 0 °C, and the mixture was stirred for 30 min. H_2O (5 mL) was added, and the mixture was extracted with EtOAc. The organic extracts were washed with brine and dried with anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography (hexane/EtOAc, 7:3) to furnish alcohol **29** (1.35 g, 95%) as a colorless liquid. $[\alpha]_D^{25}$ = +29.40 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 9.0 Hz, 2 H), 6.87 (d, *J* = 9.0 Hz, 2 H), 4.80 (d, *J* = 6.7 Hz, 1 H), 4.74 (d, *J* = 6.0 Hz, 1 H), 4.73 (d, *J* = 6.0 Hz, 1 H), 4.65 (d, *J* = 6.7 Hz, 1 H), 4.50 (ABq, *J* = 11.3, 2.3 Hz, 2 H), 3.88–3.83 (m, 1 H), 3.80 (s, 3 H), 3.81–3.66 (m, 4 H), 3.41 (s, 3 H), 3.39 (s, 3 H), 1.24 (d, *J* = 6.7 Hz, 3 H), ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 159.1, 130.3, 129.1, 113.7, 97.4, 96.5, 79.7, 78.9, 74.6, 70.5, 62.0, 56.1, 55.7, 55.2, 15.0 ppm. IR (neat): $\tilde{\nu}$ = 3453.6, 2933.5, 1611.6, 1513.3, 1248.3, 1202.4, 1030.7, 917.8, 822.7 cm^{-1}. MS (ESI): *m*/*z* = 367 $[M + Na]^+$. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{28}O_7Na$ $[M + Na]^+$ 367.17272; found 367.17140.

(5*S*,6*S*,10*R*)-10-Allyl-5-{(*S*)-1-[(4-methoxybenzyl)oxy]ethyl}-6-(methoxymethoxy)-12,12,13,13-tetramethyl-2,4,11-trioxa-12-silatetradec-8-yn-7-one (30b): A solution of oxalyl chloride (0.44 mL, 5.23 mmol) in freshly distilled CH_2Cl_2 (10 mL) was cooled to –78 °C, and anhydrous DMSO (0.74 mL, 10.40 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The mixture was stirred for 15 min at –78 °C, then alcohol **29** (0.90 g, 2.61 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The reaction was stirred for 1.5 h at –78 °C, then triethylamine (neat, 2.17 mL, 15.69 mmol) was added dropwise. The mixture was stirred for 30 min at –78 °C then for 30 min at 0 °C, then transferred to a separatory funnel and washed with H_2O (10 mL), 1 N HCl (10 mL), saturated sodium hydrogen carbonate (10 mL), then brine (10 mL). Each wash was back-extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was passed through a short silica plug with 100% CH_2Cl_2, concentrated under reduced pressure, and then crude aldehyde **11** (0.89 g, 95%, yellow oil) was immediately subjected to the next reaction without further purification.

*n*BuLi (2.5 M in hexanes, 1.36 mL, 3.4 mmol) was added to a solution of alkyne **12** (0.65 g, 3.10 mmol) in THF (10 mL) at –78 °C. After stirring for 1 h at –78 °C, a solution of aldehyde **11** (0.89 g, 2.58 mmol) in THF (8 mL) was added dropwise. The resulting mixture was stirred for 2 h at –78 °C, then poured onto saturated aqueous NH_4Cl solution (20 mL) and extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine (20 mL), dried with Na_2SO_4, and concentrated under reduced pressure to afford the crude product **30a** (1.08 g, 82% over 2 steps) as a mixture of non-separable diastereoisomers (80:20 *dr*) as an oil. The crude aldehyde **30a** was immediately subjected to the next reaction without further purification.

Dess–Martin periodinane (0.88 g, 2.09 mmol) and $NaHCO_3$ (0.20 g, 2.28 mmol) were added to alcohol **30a** (1.05 g, 1.90 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After stirring for 30 min, the reaction was warmed to 25 °C for 1 h. After 30 min, the reaction was diluted with hexanes and filtered through Celite. The filtrate was concentrated in vacuo and the residue was purified by silica gel chromatography (hexane/EtOAc, 9:1) to afford ketone **30b** (0.98 g, 94%) as a colorless liquid. $[\alpha]_D^{25}$ = –19.8 (*c* = 0.50, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 8.6 Hz, 2 H), 6.85 (d, *J* = 8.6 Hz, 2 H), 5.85–5.76 (m, 1 H), 5.15–5.08 (m, 2 H), 4.79 (d, *J* = 6.7 Hz, 1 H), 4.74 (ABq, *J* = 8.2, 6.7 Hz, 2 H), 4.70 (d, *J* = 6.7 Hz, 1 H), 4.48–4.36 (m, 4 H), 4.13 (dd, *J* = 7.4, 3.3 Hz, 1 H), 3.79 (s, 3 H), 3.78–3.72 (m, 1 H), 3.40 (s, 3 H), 3.39 (s, 3 H), 2.43–

2.39 (m, 2 H), 1.21 (d, J = 6.2 Hz, 3 H), 0.89 (s, 9 H), 0.12 (s, 3 H), 0.08 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 184.7, 158.8, 132.9, 130.5, 129.2, 118.3, 113.4, 96.3, 96.2, 82.1, 81.2, 80.0, 73.2, 70.5, 62.6, 56.1, 55.9, 55.1, 42.2, 25.6, 18.0, 16.3 ppm. IR (neat): $\tilde{\nu}$ = 2933.4, 2895.5, 1683.4, 1613.2, 1513.7, 1250.1, 1149.7, 1100.0, 1034.1, 918.8, 836.1, 778.9 cm^{-1}. MS (ESI): m/z = 573 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{29}H_{46}O_8NaSi$ [M + Na]$^+$ 573.28542; found 573.28269.

(5*S*,6*R*,7*R*,10*R*)-10-Allyl-5-{(*S*)-1-[(4-methoxybenzyl)oxy]ethyl}-6-(methoxymethoxy)-12,12,13,13-tetramethyl-2,4,11-trioxa-12-silatetradec-8-yn-7-ol (30): To a stirred solution of *R*-CBS catalyst (1M in toluene, 0.17 mL, 0.17 mmol) in THF (5 mL), BH_3·DMS (2M in THF, 0.97 mL, 1.95 mmol) was added at 0 °C and the mixture was stirred for 0.5 h. The mixture was cooled to –78 °C, then a concentrated solution of keto compound **30b** (0.98 g, 1.77 mmol) in THF (0.5 mL) was added, and the mixture was stirred for 8 h at –78 °C. The mixture was quenched with MeOH (1 mL) at –78 °C and warmed to room temp., then the solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/EtOAc, 9:1) to afford the pure product **30** (0.87 g, 89%) as an oil. $[\alpha]_D^{25}$ = +5.5 (c = 0.40, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 5.95–5.78 (m, 1 H), 5.16–5.04 (m, 2 H), 4.89 (d, J = 6.7 Hz, 1 H), 4.83 (d, J = 6.2 Hz, 1 H), 4.78 (d, J = 6.2 Hz, 1 H), 4.74–4.67 (m, 1 H), 4.69 (d, J = 6.7 Hz, 1 H), 4.49 (s, 3 H), 4.47–4.39 (m, 1 H), 4.04 (dd, J = 6.9, 3.2 Hz, 1 H), 3.87–3.76 (m, 1 H), 3.80 (s, 3 H), 3.67 (dd, J = 6.9, 3.2 Hz, 1 H), 3.52 (d, J = 7.3 Hz, 1 H), 3.42 (s, 3 H), 3.34 (s, 3 H), 2.46–2.39 (m, 2 H), 1.24 (d, J = 6.2 Hz, 3 H), 0.89 (s, 9 H), 0.13 (s, 3 H), 0.10 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.0, 133.8, 130.5, 129.0, 117.7, 113.6, 97.8, 97.6, 86.9, 82.9, 79.9, 78.4, 74.4, 70.2, 62.7, 62.5, 56.4, 56.1, 55.2, 43.0, 25.6, 18.1, 14.4, –4.5, –5.1 ppm. IR (neat): $\tilde{\nu}$ = 3451.5, 2932.5, 1513.4, 1249.2, 1149.5, 1098.2, 1032.0, 834.0, 774.9 cm^{-1}. MS (ESI): m/z = 575 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{29}H_{48}O8NaSi$ [M + Na]$^+$ 575.30107; found 575.29788.

(5*S*,6*R*,7*R*,10*R*)-10-Allyl-5-{(*S*)-1-[(4-methoxybenzyl)oxy]ethyl}-6-(methoxymethoxy)-12,12,13,13-tetramethyl-2,4,11-trioxa-12-silatetradec-8-yn-7-yl Acetate (31): Anhydrous Et_3N (0.47 mL, 3.44 mmol), Ac_2O (0.21 mL, 2.06 mmol), and DMAP (5 mg) were added to a solution of alcohol **30** (0.76 g, 1.37 mmol) in anhydrous CH_2Cl_2 (20 mL) at room temp. under a nitrogen atmosphere and the mixture was stirred at room temp. for 30 min. The reaction mixture was quenched with saturated $NaHCO_3$, the organic layer was extracted with CH_2Cl_2 (2 × 20 mL), and the combined organic layers were dried with Na_2SO_4. The solvent was removed under reduced pressure, and the mixture was purified by column chromatography (hexane/EtOAc, 9:1) to afford pure product **31** (0.77 g, 95%) as an oil. $[\alpha]_D^{25}$ = +20.6 (c = 0.50, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 5.86–5.76 (m, 1 H), 5.67 (dd, J = 5.6, 1.8 Hz, 1 H), 5.12–5.05 (m, 2 H), 4.87 (d, J = 6.7 Hz, 1 H), 4.76–4.71 (m, 3 H), 4.49 (s, 2 H), 4.38 (td, J = 6.4, 1.6 Hz, 1 H), 3.98–3.95 (m, 1 H), 3.92–3.88 (m, 1 H), 3.88–3.83 (m, 1 H), 3.80 (s, 3 H), 3.37 (s, 3 H), 3.35 (s, 3 H), 2.41–2.37 (m, 2 H), 2.10 (s, 3 H), 1.25 (d, J = 6.2 Hz, 3 H), 0.88 (s, 9 H), 0.10 (s, 3 H), 0.07 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.5, 158.9, 133.6, 130.6, 129.1, 117.7, 113.6, 97.6, 97.0, 88.1, 79.9, 78.5, 78.0, 74.2, 70.3, 64.1, 62.6, 56.2, 56.0, 55.2, 42.8, 25.6, 18.1, 15.1, –4.5, –5.1 ppm. IR (neat): $\tilde{\nu}$ = 2933.1, 2857.2, 1748.2, 1616.1, 1513.7, 1247.8, 1247.3, 1094.4, 1030.1, 835.2, 774.4 cm^{-1}. MS (ESI): m/z = 617 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{31}H_{50}O_9NaSi$ [M + Na]$^+$ 617.31163; found 617.30869.

(5*S*,6*R*,7*R*,10*R*)-10-Allyl-5-[(*S*)-1-hydroxyethyl]-6-(methoxymethoxy)-12,12,13,13-tetramethyl-2,4,11-trioxa-12-silatetradec-8-yn-7-yl Acetate (32): To an ice-bath cooled solution of **31** (0.75 g, 1.26 mmol) in aq. CH_2Cl_2 (20 mL; CH_2Cl_2/buffer (pH 7), 9:1), DDQ (0.31 g, 1.38 mmol) was added and the reaction mixture was stirred for 1 h at 0 °C. The reaction mixture was washed with 5% aq. $NaHCO_3$ solution (10 mL), the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with water, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (hexane/EtOAc, 80:20) to afford alcohol **32** (0.53 g, 90%) as a liquid. $[\alpha]_D^{25}$ = –8.6 (c = 0.50, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.87–5.77 (m, 1 H), 5.75 (dd, J = 3.9, 1.8 Hz, 1 H), 5.14–5.07 (m, 2 H), 4.98 (d, J = 6.8 Hz, 1 H), 4.73 (d, J = 6.8 Hz, 1 H), 4.67 (d, J = 6.8 Hz, 1 H), 4.60 (d, J = 6.8 Hz, 1 H), 4.40 (td, J = 6.4, 1.6 Hz, 1 H), 4.07–4.00 (m, 1 H), 3.81 (dd, J = 7.0, 4.1 Hz, 1 H), 3.68 (dd, J = 7.0, 3.5 Hz, 1 H), 3.44 (s, 3 H), 3.42 (s, 3 H), 2.84 (br. s, 1 H), 2.43–2.39 (m, 2 H), 2.11 (s, 3 H), 1.25 (d, J = 6.5 Hz, 3 H), 0.89 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.6, 133.5, 117.9, 98.3, 97.9, 88.3, 83.8, 79.6, 78.5, 66.5, 63.5, 62.6, 56.4, 56.2, 42.7, 25.6, 20.8, 18.1, 17.5, –4.6, –5.1 ppm. IR (neat): $\tilde{\nu}$ = 3445.5, 2931.6, 1594.8, 1458.7, 1420.6, 1119.3, 1033.5, 768.7 cm^{-1}. MS (ESI): m/z = 497 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{23}H_{42}O_8NaSi$ [M + Na]$^+$ 497.25412; found 497.25057.

(2*S*,3*S*,4*R*,5*R*,8*R*)-8-[(*tert*-Butyldimethylsilyl)oxy]-3,4-bis(methoxymethoxy)undec-10-en-6-yne-2,5-diyl Diacetate (33): Anhydrous Et_3N (0.43 mL, 3.16 mmol), Ac_2O (0.16 mL, 1.58 mmol), and DMAP (5 mg) were added to a solution of alcohol **32** (0.5 g, 1.05 mmol) in anhydrous CH_2Cl_2 (20 mL) at room temp. under a nitrogen atmosphere. The mixture was stirred at room temp. for 30 min, then the reaction was quenched with saturated $NaHCO_3$ (15 mL). The organic layer was extracted with CH_2Cl_2 (2 × 10 mL) and the combined organic layers were dried with Na_2SO_4. The solvent was removed under reduced pressure and the mixture was purified by column chromatography (hexane/EtOAc, 90:10) to afford **33** (0.51 g, 94%) as a liquid. $[\alpha]_D^{25}$ = +13.7 (c = 0.70, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.88–5.78 (m, 1 H), 5.62 (dd, J = 5.6, 1.6 Hz, 1 H), 5.25–5.20 (m, 1 H), 5.14–5.07 (m, 2 H), 4.89 (d, J = 6.8 Hz, 1 H), 4.73 (d, J = 6.8 Hz, 1 H), 4.71 (d, J = 6.7 Hz, 1 H), 4.68 (d, J = 6.7 Hz, 1 H), 4.41 (td, J = 6.4, 1.6 Hz, 1 H), 3.94 (t, J = 4.8 Hz, 1 H), 3.87–3.83 (m, 1 H), 3.42 (s, 3 H), 3.39 (s, 3 H), 2.44–2.40 (m, 2 H), 2.09 (s, 3 H), 2.07 (s, 3 H), 1.30 (d, J = 6.4 Hz, 3 H), 0.89 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.8, 169.4, 133.6, 117.7, 97.6, 96.8, 88.5, 80.9, 78.1, 78.0, 70.1, 63.8, 62.6, 56.2, 42.7, 25.7, 21.2, 20.8, 15.1, –4.6, –5.1 ppm. IR (neat): $\tilde{\nu}$ = 2934.5, 2896.8, 1746.9, 1468.2, 1372.4, 1236.0, 1152.8, 1082.0, 1032.0, 921.4, 838.6, 779.4 cm^{-1}. MS (ESI): m/z = 539 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{25}H_{44}O_9NaSi$ [M + Na]$^+$ 539.26468; found 539.26129.

(2*S*,3*S*,4*R*,5*R*,8*R*)-8-Hydroxy-3,4-bis(methoxymethoxy)undec-10-en-6-yne-2,5-diyl Diacetate (8b): To a solution of **33** (0.5 g, 0.96 mmol) in anhydrous THF (10 mL), was added TBAF (1M in THF, 1.06 mL, 1.06 mmol) dropwise at 0 °C, and the mixture was stirred for 30 min. H_2O (2 mL) was added, and the mixture was extracted with EtOAc. The organic extracts were washed with brine and dried with anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography (hexane/EtOAc, 7:3) to furnish alcohol **8b** (0.36 g, 93%) as a colorless liquid. $[\alpha]_D^{25}$ = +18.7 (c = 0.80, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.95–5.78 (m, 1 H), 5.62 (dd, J = 7.1, 1.7 Hz, 1 H), 5.33–5.11 (m, 3 H), 4.80 (d, J = 6.7 Hz, 1 H), 4.75–4.65 (m, 2 H), 4.49–4.39 (m, 1 H), 4.04–3.98 (m, 1 H), 3.96–3.89 (m, 1 H), 3.42

(s, 3 H), 3.41 (s, 3 H), 3.06–3.01 (m, 1 H), 2.49–2.41 (m, 2 H), 2.11 (s, 3 H), 2.08 (s, 3 H), 1.32 (d, J = 6.4 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.3, 169.5, 132.9, 118.5, 97.3, 96.2, 88.3, 80.1, 78.1, 77.8, 70.2, 63.7, 61.4, 56.4, 56.1, 41.6, 21.3, 20.9, 15.9 ppm. IR (neat): $\tilde{\nu}$ = 3450.4, 2938.0, 1742.2, 1640.0, 1372.8, 1232.4, 1150.7, 1027.0, 919.3, 760.3 cm^{-1}. MS (ESI): m/z = 425 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{19}H_{30}O_9Na$ [M + Na]$^+$ 425.17820; found 425.17538.

(2*S*,3*S*,4*R*,5*R*,8*R*)-8-(Acryloyloxy)-3,4-bis(methoxymethoxy)undec-10-en-6-yne-2,5-diyl Diacetate (34): Acryloyl chloride (0.08 mL, 3.17 mmol) was added dropwise under N_2 to a solution of **8b** (0.30 g, 0.76 mmol) and Et_3N (0.31 mL, 2.23 mmol) in CH_2Cl_2 (10 mL) at 0 °C, and the mixture was stirred at 0 °C for 1 h. Upon completion of reaction, the mixture was poured into brine (2 mL) and extracted with CH_2Cl_2 (2× 10 mL). The organic phase was dried with anhydrous Na_2SO_4, and concentrated. The crude product was purified by column chromatography (EtOAc/hexane, 10%) to afford the corresponding acrylic ester **34** (0.29 g, 86%) as a colorless oil. $[\alpha]_D^{25}$ = +56.3 (c = 0.60, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.44 (dd, J = 17.1, 1.3 Hz, 1 H), 6.12 (dd, J = 17.1, 10.3 Hz, 1 H), 5.87 (dd, J = 10.3, 1.3 Hz, 1 H), 5.84–5.73 (m, 1 H), 5.63 (dd, J = 5.2, 1.5 Hz, 1 H), 5.51 (td, J = 6.2, 1.3 Hz, 1 H), 5.29–5.10 (m, 3 H), 4.86 (d, J = 6.7 Hz, 1 H), 4.76–4.65 (m, 3 H), 3.96–3.83 (m, 2 H), 3.42 (s, 3 H), 3.38 (s, 3 H), 2.61–2.51 (m, 2 H), 2.11 (s, 3 H), 2.07 (s, 3 H), 1.30 (d, J = 6.4 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.9, 169.4, 164.7, 131.8, 131.5, 127.8, 118.9, 97.6, 96.9, 84.0, 81.1, 78.1, 77.9, 70.1, 63.5, 63.1, 56.3, 38.7, 21.2, 20.9, 14.9 ppm. IR (neat): $\tilde{\nu}$ = 2936.5, 1730.9, 1609.7, 1513.5, 1250.0, 1151.8, 1106.7, 1032.5, 920.5, 825.7 cm^{-1}. MS (ESI): m/z = 479 [M + Na]$^+$.

(2*S*,3*S*,4*R*,5*R*)-3,4-Bis(methoxymethoxy)-7-[(*R*)-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]hept-6-yne-2,5-diyl Diacetate (35): A solution of Grubbs' second-generation catalyst (G-II; 0.021 g, 0.027 mmol, 10 mol-%) in CH_2Cl_2 (10 mL) was added dropwise to a solution of **34** (0.25 g, 0.548 mmol) in CH_2Cl_2 (60 mL) at room temp., and stirring was continued for 5 h with heating to reflux. The solvent was evaporated and the crude product was purified by silica gel column chromatography (hexane/EtOAc, 7:3) to give lactone **35** (0.216 g, 91%) as a pale-yellow oil. $[\alpha]_D^{25}$ = +45.7 (c = 0.70, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.89 (dt, J = 10.0, 4.3 Hz, 1 H), 6.08 (dt, J = 9.8, 1.7 Hz, 1 H), 5.64 (dd, J = 5.6, 1.5 Hz, 1 H), 5.27–5.18 (m, 2 H), 4.84 (d, J = 6.9 Hz, 1 H), 4.73 (d, J = 6.9 Hz, 1 H), 4.72 (d, J = 6.7 Hz, 1 H), 4.69 (d, J = 6.7 Hz, 1 H), 3.93–3.86 (m, 2 H), 3.42 (s, 3 H), 3.40 (s, 3 H), 2.72–2.65 (m, 2 H), 2.12 (s, 3 H), 2.08 (s, 3 H), 1.30 (d, J = 6.4 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.1, 169.5, 162.4, 144.1, 122.5, 97.5, 96.9, 82.7, 81.9, 77.9, 77.8, 70.2, 66.8, 63.2, 56.3, 29.7, 21.3, 20.8, 15.2 ppm. IR (neat): $\tilde{\nu}$ = 2987.3, 1737.8, 1406.4, 1373.8, 1232.71181.3, 1063.9, 1023.3, 983.4 cm^{-1}. MS (ESI): m/z = 451 [M + Na]$^+$.

(2*S*,3*S*,4*R*,5*R*,*Z*)-3,4-Bis(methoxymethoxy)-7-[(*R*)-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]hept-6-ene-2,5-diyl Diacetate (7b): To a solution of **35** (0.20 g, 0.465 mmol) in EtOAc (5 mL), two drops of quinoline and Lindlar's catalyst (Pd/$BaSO_4$) (0.005 g, 0.046 mmol, 10 mol-%) were added and the mixture was stirred at room temp. under H_2 for 30 min. After completion of the reaction, the mixture was filtered and the solvent was removed under reduced pressure. The crude product was purified on silica gel column chromatography (hexane/EtOAc, 7:4) to afford **7b** (0.186 g, 93%) as a colorless liquid. $[\alpha]_D^{25}$ = +21.6 (c = 0.90, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.92–6.86 (m, 1 H), 6.09 (dt, J = 9.6, 1.6 Hz, 1 H), 5.92–5.84 (m, 1 H), 5.62 (dd, J = 4.8, 1.3 Hz, 1 H), 5.51–5.39 (m, 1 H), 5.30–5.18 (m, 2 H), 4.86 (d, J = 6.8 Hz, 1 H), 4.73 (d, J = 6.9 Hz, 1 H), 4.72 (d, J = 6.8 Hz, 1 H), 4.70 (d, J = 6.9 Hz, 1 H), 3.92–3.85 (m, 2 H), 3.42 (s, 3 H), 3.40 (s, 3 H), 2.70–2.65 (m, 2 H), 2.13 (s, 3 H), 2.09 (s, 3 H), 1.29 (d, J = 6.4 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.9, 169.3, 162.2, 143.8, 132.6, 127.8, 122.3, 97.3, 96.6, 77.6, 77.5, 69.9, 66.5, 63.0, 56.0, 29.4, 21.0, 20.6, 15.0 ppm. MS (ESI): m/z = 453 [M + Na]$^+$. IR (neat): $\tilde{\nu}$ = 2988.3, 1737.4, 1376.8, 1244.8, 1058.4, 864.2, 817.1 cm^{-1}. MS (ESI): m/z = 453 [M + Na]$^+$.

(2*S*,3*R*,4*S*,5*R*,*Z*)-3,4-Dihydroxy-7-[(*R*)-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]hept-6-ene-2,5-diyl Diacetate (1): To a stirred solution of **7b** (0.020 g, 0.046 mmol) in a mixture of MeOH (5 mL) and MeCN (5 mL) was added $CeCl_3{\cdot}7H_2O$ (0.173 g, 0.465 mmol). After stirring for 24 h at reflux temperature (reaction followed by TLC), the mixture was filtered through Celite and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (hexane/EtOAc, 2:8) to afford synrotolide **1** (0.011 g, 71%) as a colorless viscous oil. To a solution of **7b** (0.02 g, 0.046 mmol) in MeCN (2 mL) was added fluorosilicic acid (H_2SiF_6; 20–25 wt.-% in water, 0.2 mL) and the mixture was stirred at room temp. for 3 d. After completion of the reaction, the mixture was filtered through Celite and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (hexane/EtOAc, 2:8) to afford synrotolide **1** (0.014 g, 89%) as a colorless viscous oil. $[\alpha]_D^{25}$ = –24.8 (c = 0.20, MeOH). ^{1}H NMR (500 MHz, [D_6]DMSO): δ = 7.10–7.02 (m, 1 H), 6.00–5.95 (m, 1 H), 5.82 (dd, J = 11.1, 8.8 Hz, 1 H), 5.72 (dd, J = 10.8, 10.5 Hz, 1 H), 5.64–5.58 (m, 1 H), 5.38 (d, J = 5.9 Hz, 1 H), 5.34–5.26 (m, 1 H), 5.04 (d, J = 5.9 Hz, 1 H), 5.05–5.00 (m, 1 H), 3.54–3.46 (m, 1 H), 3.35–3.29 (m, 1 H), 2.45–2.34 (m, 2 H), 2.01 (s, 3 H), 1.99 (s, 3 H), 1.09 (d, J = 6.4 Hz, 3 H) ppm. ^{13}C NMR ([D_6]DMSO, 125 MHz): δ = 169.8, 169.5, 163.3, 147.1, 131.9, 126.8, 120.1, 73.9, 71.3, 71.1, 71.0, 70.0, 29.5, 21.1, 20.7, 12.8 ppm. IR (neat): $\tilde{\nu}$ = 3449.4, 2921.7, 1739.3, 1642.9, 1377.7, 1258.8, 1022.4 cm^{-1}. MS (ESI): m/z = 365 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{16}H_{22}O_8Na$ [M + Na]$^+$ 365.12069; found 365.12034.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of all compounds.

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