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Total synthesis of synargentolide B

Udugu Ramulu, Singanaboina Rajaram, Dasari Ramesh, Katragadda Suresh Babu *

Natural Products Chemistry Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India

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ABSTRACT

A simple and efficient stereoselective synthesis of synargentolide B was achieved by using ethyl (*S*)-2-hydroxypropanoate as a readily available starting material. The key steps involved in the synthesis are Horner–Wadsworth–Emmons olefination, Sharpless asymmetric dihydroxylation, zinc allylation, and Hoveyda–Grubbs IInd generation catalyzed ring closing metathesis.

1. Introduction

Over the past two decades, naturally occurring polyacetoxy side chain containing α,β-unsaturated δ-lactones[1] are a growing class of natural products isolated from a wide variety of sources. In particular, α,β-unsaturated δ-lactones exhibit cytotoxicity against human tumor cells, antifungal and antimicrobial properties.[2] In addition they inhibit HIV protease,[3] induce apoptosis,[4] and antileukemic[5] along with other immunosuppressive properties.[6] Due to these biological activities and structural features, δ-lactones have attracted the wide attention of a number of synthetic organic chemists.

Synargentolides A–E **1**–**5** are α,β-unsaturated δ-lactones (Fig. 1), which possess a polyacetoxy side chain skeleton isolated by Rivett and Davies-Coleman et al.[7] from the South African plant *Syncolostemon argenteus*, in 1998. The structures of five α-pyrones have been established based on spectroscopic, chiroptical, and chemical evidences. In 1990, Pereda-Miranda et al. reported (6*R*)-[(5*R*,6*S*)-diacetyloxy-(1*S*,2*R*)-dihydroxy-3*E*-heptenyl]-5,6-dihydro-2*H*-pyran-2-one **1** from the leaves of Mexican plant *Hyptis oblongifolia*.[8] Recently, Prasad et al.[9] and Sabitha et al.[10] established the structure of **1** by the total synthesis of four diastereomers, individually. The absolute stereochemistry was confirmed by X-ray crystal structure analysis of the corresponding tetraacetate of **1** by Prasad

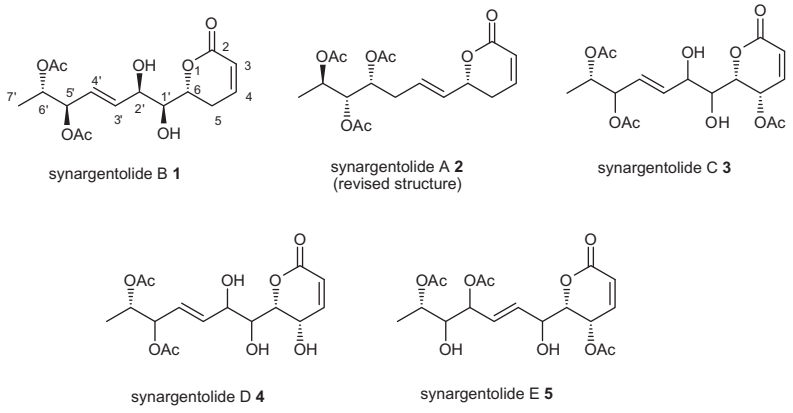

Figure 1. Structures of synargentolides A–E **1**–**5**.

* Corresponding author. Tel.: +91 40 27191881; fax: +91 40 27160512.
E-mail address: suresh@iict.res.in (K. Suresh Babu).

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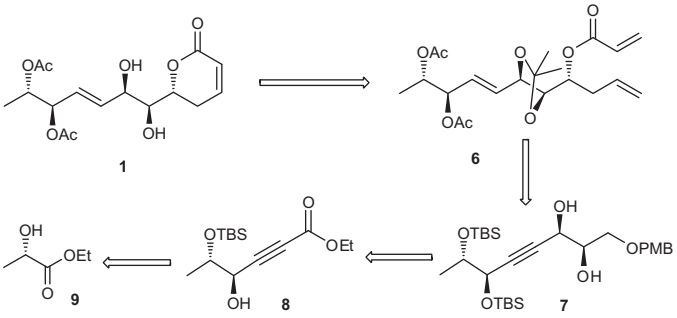
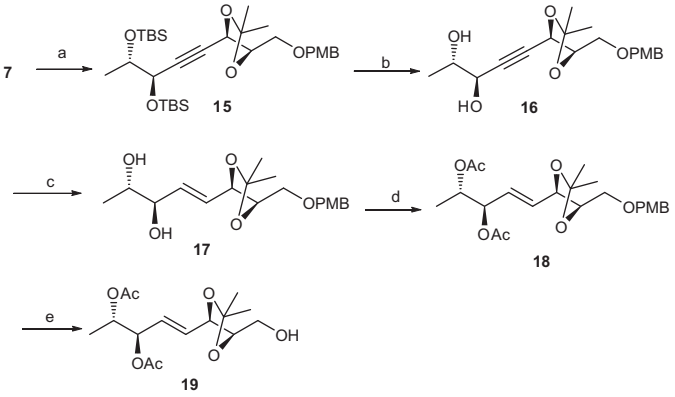


Scheme 1. Retrosynthetic analysis of **1**.



Scheme 3. Reagents and conditions: (a) 2,2 dimethoxypropane, PTSA, CH_2Cl_2, 0 °C–rt, 2 h, 92%; (b) TBAF, THF, 0 °C–rt, 4 h, 92%; (c) Red-Al, dry THF, 0 °C–rt, 8 h, 80%; (d) Ac_2O, triethylamine, CH_2Cl_2, DMAP (cat) 0 °C–rt, 6 h, 93%; (e) DDQ, CH_2Cl_2/H_2O (9:1), rt, 2 h, 93%.

et al. In 2014, Akkewar et al.[11] also reported its total synthesis by using D-ribose and L-ascorbic acid as starting materials.

As part of our ongoing research program on the total synthesis of biologically active δ-lactone containing natural products, the structural features of synargentolide B **1** prompted us to attempt the synthesis of this molecule. Recently we have accomplished the synthesis of pectinolides A–C,[12a] clonostachydiol,[12b] pectinolide H,[12d] etc.[12] Herein, we report a simple and efficient approach for the stereoselective total synthesis of synargentolide B **1** in a concise manner from the inexpensive and readily available starting material ethyl (*S*)-2-hydroxypropanoate **9**.

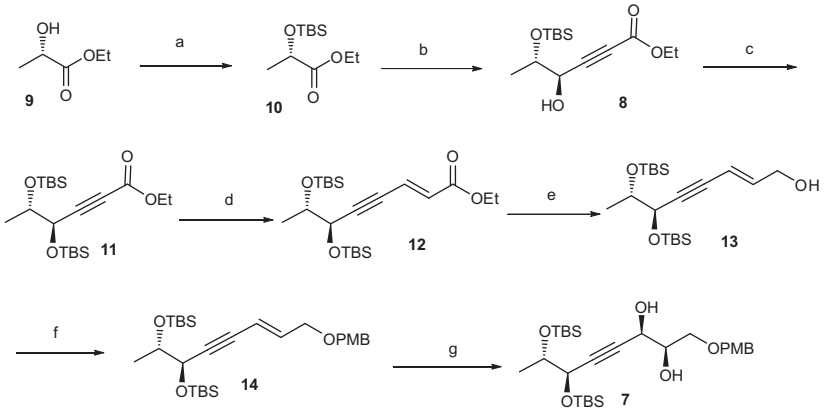
2. Results and discussion

According to the retrosynthetic analysis as shown in Scheme 1, the target synargentolide B **1** can be synthesized by ring closing metathesis of compound **6**, which in turn could be obtained from the compound **7** by zinc allylation, followed by acryloylation. Intermediate **7** could in turn be prepared from hydroxy ester **8** by Witting–Horner olefination, Sharpless asymmetric dihydroxylation, followed by other transformation reactions. Compound **8** could be synthesized starting from ethyl (*S*)-2-hydroxypropanoate **9**.

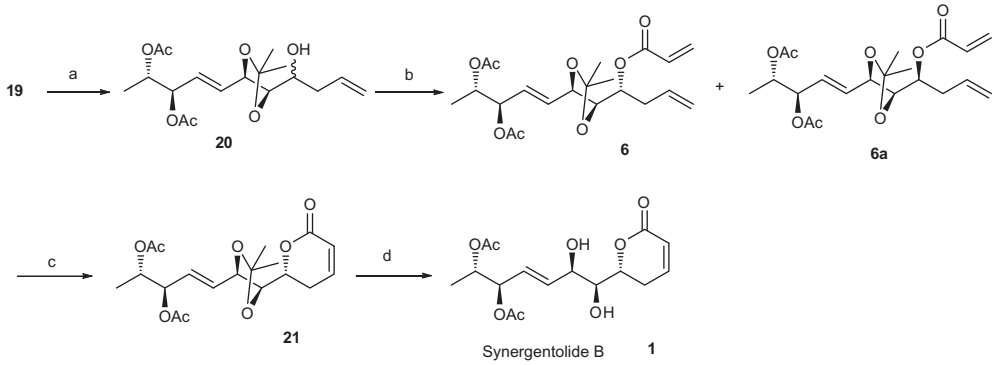
As shown in Scheme 2, the commercially available alcoholic ester **9** was initially protected as its silyl ether **10** $[\alpha]_D^{25} = -25.1$ (*c* 2.5, $CHCl_3$) [Lit[13b] = −21.7 (*c* 1.17, $CHCl_3$)] in 93% yield with TBSCl and imidazole. The silyl ester **10** was reduced with DIBAL-H −78 °C to give the aldehyde in 84% yield. The thus obtained aldehyde was treated with ethyl propiolate and LiHMDS in dry THF to give hydroxy ester **8** $[\alpha]_D^{25} = +3.4$ (*c* 2.5, $CHCl_3$) [Lit[13a] = +0.8 (*c* 4.3, $CHCl_3$)] in 76% yield (dr 97:3).[13a] The newly generated hydroxy group was protected with TBSCl using imidazole to give disilyl ether **11** in 88% yield. Reduction of ester **11** using DIBAL-H at −78 °C gave the corresponding aldehyde in 90% yield. The resultant aldehyde underwent a Wittig reaction with triethylphosphonoacetate, and sodium hydride in dry THF to give **12** in 89% yield (Scheme 2). Ester **12** was reduced with DIBAL-H at 0 °C to give alcohol **13** in 96% yield. Allylic alcohol **13** was protected with PMB imidate derived from *p*-methoxybenzyl alcohol to provide PMB-ether **14** in 84% yield. Compound **14** was subjected to Sharpless asymmetric dihydroxylation reaction using AD-mix-β at 0 °C to furnish diol **7** in 90% yield (dr 97.5:2.5).[14]

Diol **7** was protected with 2,2-dimethoxy propane in the presence of *p*-toluene sulfonic acid to give acetonide protected compound **15** in 92% yield. Next, the di-TBS ethers in **15** were removed using TBAF in THF to give diol **16** in 92% yield. The triple bond in **16** was selectively converted into *trans*-double bond to give **17** with Red-Al[15] in dry THF in 80% yield. The secondary diol in **17** was acetylated with acetic anhydride in the presence of triethylamine, and DMAP (cat) in dry dichloromethane to afford diacetyl compound **18** in 93% yield (Scheme 3).

The deprotection of the PMB group in **18** with DDQ/H_2O (9:1) provided primary alcohol **19** in 93% yield. The primary alcohol **19** was oxidized with IBX[16] in EtOAc at reflux to afford the corresponding aldehyde, which was further subjected to zinc allylation[17] by allylbromide, saturated NH_4Cl in THF to give an inseparable mixture of **20** in 82% yield (88:12 determined by chiral HPLC), which was separated by conversion into its acryloylester **6**



Scheme 2. Reagents and conditions: (a) imidazole, TBSCl, CH_2Cl_2, rt, 8 h, 93%; (b) (i) DIBAL-H, CH_2Cl_2, −78 °C, 0.5 h, 84%; (ii) ethyl propiolate, LIHMDS, dry THF, −78 °C to rt, 3 h, 76%; (c) imidazole, TBSCl, CH_2Cl_2, rt, 8 h, 88%; (d) (i) DIBAL-H, CH_2Cl_2, −78 °C, 0.5 h, 90%; (ii) NaH, triethylphosphonoacetate 0 °C, 2 h, 89%; (e) DIBAL-H, CH_2Cl_2, −78 °C to 0 °C, 0.5 h, 96%; (f) PMB imidate, PTSA (cat), dry CH_2Cl_2, 0 °C–rt, 8 h, 84%; (h) AD-mix-β, $MeSO_2NH_2$, *t*-BuOH/H_2O (1:1), 0 °C, 36 h, 90%.



Scheme 4. Reagents and conditions: (a) (i) IBX, EtOAc, reflux, 4 h, 87%; (ii) Zn, allylbromide, saturated NH_4Cl 0 °C–rt, 9 h, 82%; (b) TEA, acryloylchloride, DCM, 0 °C, 10 min, 66%; (c) Hoveyda–Grubbs-II, toluene, 80 °C, 1 h, 92%; (d) PPTS, MeOH, reflux, 6 h, 70%.

and **6a** in 66% and 9% yields, respectively. The major compound **6** was subjected to a ring closing metathesis protocol with Hoveyda Grubbs-IInd catalyst[18] (10 mol %) in toluene at 80 °C to give compound **21** $[\alpha]_D^{25}$ = +42.2 (*c* 0.2, $CHCl_3$) {Lit[10] = +45.5 (*c* 0.46, $CHCl_3$)} in 92% yield. Finally, the deprotection of acetonide group in **21** using PPTS in methanol gave the target molecule synargentolide B **1** in 70% yield (Scheme 4). The physical and spectroscopic properties of these compounds were identical to those reported earlier (Tables 1–3).

3. Conclusion

In conclusion, we have reported a simple and efficient approach for the synthesis of synargentolide B **1** in a stereoselective manner. The crucial steps involved in the synthesis are the Sharpless asymmetric dihydroxylation, zinc allylation and ring closing metathesis for the synthesis of this plant derived natural product.

4. Experimental

4.1. General

Reactions were conducted under N_2 in anhydrous solvents such as DCM, THF, DMSO, CH_3CN, Et_2O, toluene, and EtOAc. All reactions were monitored by TLC (silica-coated plates and visualizing under UV light). Yields refer to after chromatography and spectroscopically (^1H, ^{13}C NMR) homogeneous material. Air-sensitive reagents were transferred by syringe or double-ended needle. Evaporation of solvents was performed at reduced pressure on a Buchi rotary evaporator. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on a Varian Gemini 200 and BruckerAvance 300

Table 2
^{13}C NMR data of synargentolide B **1**

Position-C	Lit[9]	Lit[10]	Lit[11]	Our synthesis	Natural product[7]
C-2	166.4	166.3	163.73	166.4	166.3
C-3	121.1	121.1	120.93	121.1	121.2
C-4	148.6	148.6	145.80	148.7	148.6
C-5	26.4	26.3	25.52	26.4	26.4
C-6	78.9	78.9	76.83	78.9	79.0
C-1′	75.7	75.6	74.26	75.8	75.8
C-2′	71.4	71.3	69.50	71.5	71.5
C-3′	136.5	136.4	134.17	136.6	136.6
C-4′	126.6	126.6	126.66	126.6	126.7
C-5′	76.2	76.1	74.97	76.3	76.3
C-6′	72.1	72.0	70.05	72.1	72.2
C-7′	15.1	15.2	15.08	15.1	15.2
Ac-CO	172.2	172.1	170.45	172.2	172.2
Ac-CO	171.9	171.8	170.29	171.9	171.8
Ac-Me	20.9	21.1	21.13	20.9	21.0
Ac-Me	21.0	21.2	20.46	21.0	21.1

Table 1
^1H NMR data of synargentolide B **1**

Position-H	Lit[9]	Lit[10]	Lit[11]	Our synthesis	Natural product[7]
3	6.01 (d, 9.6, 1H)	6.02 (dt, 9.8, 1.5, 1H)	6.03 (dt, 9.8, 1.5, 1H)	6.03 (dt, 9.7, 1.2, 1H)	5.97 (m, 9.7, 1H)
4	6.95 (dt, 9.4, 4.9, 1H)	6.95 (ddd, 9.8, 5.2, 3.5, 1H)	6.95 (ddd, 9.8, 5.3, 3.3, 1H)	6.95 (ddd, 9.6, 5.8, 3.0, 1H)	7.06 (m, 1H)
5	2.62–2.49 (m, 2H)	2.57 (m, 2H)	2.58 (m, 2H)	2.57 (m, 2H)	2.56 (m, 2H)
6	4.57–4.50 (m, 1H)	4.53 (m, 1H)	4.52 (m, 1H)	4.52 (m, 1H)	4.53 (td, 6.5, 3.2, 1H)
1′	3.76–3.64 (m, 1H)	3.70 (m, 1H)	3.71 (dd, 6.8, 2.7, 1H)	3.70 (m, 1H)	3.65 (m, 1H)
2′	4.49–4.41 (m, 1H)	4.48 (m, 1H)	4.48 (m, 1H)	4.49 (m, 1H)	4.31 (m, 1H)
3′	5.88 (dd, 15.7, 5.2, 1H)	5.88 (dd, 15.6, 5.0, 1H)	5.89 (dd, 15.8, 5.3, 1H)	5.88 (dd, 15.7, 5.2, 1H)	5.94 (ddd, 15.7, 5.8, 0.9, 1H)
4′	5.79 (dd, 15.6, 6.6, 1H)	5.79 (dd, 15.6, 6.0, 1H)	5.81 (dd, 15.8, 6.8, 1H)	5.79 (dd, 15.6, 6.0, 1H)	5.79 (ddd, 15.7, 6.8, 1.2, 1H)
5′	5.31 (dt, 9.9, 3.6, 1H)	5.31 (dd, 6.0, 3.8, 1H)	5.33 (dd, 6.4, 3.8, 1H)	5.32 (m, 1H)	5.40 (dd, 6.8, 3.5, 1H)
6′	5.05 (dq, 10.2, 3.7, 1H)	5.05 (dq, 6.6, 3.8, 1H)	5.07 (dq, 6.4, 3.8, 1H)	5.07 (m, 1H)	5.04 (m, 1H)
7′	1.19 (d, 6.5, 3H)	1.20 (d, 6.6, 3H)	1.21 (d, 6.4, 3H)	1.21 (d, 6.5, 3H)	1.20 (d, 6.6, 3H)
Ac-Me	2.07 (s, 3H)	2.08 (s, 3H)	2.09 (s, 3H)	2.08 (s, 3H)	2.05 (s, 3H)
Ac-Me	2.03 (s, 3H)	2.04 (s, 3H)	2.05 (s, 3H)	2.04 (s, 3H)	2.01 (s, 3H)
1′-OH	3.05 (br s, 1H)	—	—	—	—
2′-OH	2.95 (br s, 1H)	—	—	—	—

Table 3
Comparison of specific rotations of synargentolide B **1**

Lit[9]	Lit[10]	Lit[11]	Our synthesis	Natural product[7]
+26.3 (*c* 0.2, $CHCl_3$)	+25.6 (*c* 0.7, $CHCl_3$)	+27.1 (*c* 0.2, CH_2Cl_2)	+24.8 (*c* 0.4, $CHCl_3$)	+28.8 (*c* 0.18, $CHCl_3$)

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spectrometers. Chemical shifts (δ) are reported relative to TMS ($\delta = 0.0$) as an internal standard. Mass spectra were obtained on MS-EI, MS-ESI, HRMS mass spectrometers of Agilent Technologies 1100 Series. Column chromatography was performed on silica gel (60–120 mesh) supplied by Acme Chemical Co., India. TLC was performed on Merck 60 F-254 silica gel plates. IR (FT-IR) spectra were recorded either on KBr pellets or neat as thin film or in $CHCl_3$. Optical rotations were recorded on JASCO DIP-360 digital polarimeter at 25 °C.

4.1.1. (*S*)-Ethyl 2-(*tert*-butyldimethylsilyloxy)propanoate 10

To a solution of ethyl (*S*)-2 hydroxypropanoate (**9**) (6 g, 50.84 mmol) in dry DCM (125 mL) was added imidazole (5.18 g, 76.27 mmol), and the mixture was stirred for 10 min at 0 °C. To this solution *tert*-butyldimethylsilyl chloride (9.19 g, 61.01 mmol) was added at 0 °C, and the mixture was stirred at room temperature for 8 h. After completion of the reaction, the mixture was diluted with ice-water and extracted into DCM (3 × 125 mL). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography using hexane/ethyl acetate (98:2) to give pure compound **10** (10.97 g, 93%) as a colorless liquid. $[\alpha]_D^{25} = -25.1$ (*c* 2.5, $CHCl_3$) [Lit[13b] = −21.7 (*c* 1.17, $CHCl_3$)]; IR (neat, cm^{-1}): ν_{max} 2955, 2932, 2897, 2859, 1736, 1373, 1257, 1146, 1061, 833, 778; ^1H NMR (300 MHz, $CDCl_3$): δ 4.30 (q, $J = 6.4$ Hz, 1H), 4.23–4.12 (m, 2H), 1.39 (d, $J = 7.1$ Hz, 3H), 1.27 (t, $J = 6.4$ Hz, 3H), 0.90 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.9, 68.4, 60.6, 25.6, 21.2, 18.2, 14.1, −5.0, −5.4; ESI/MS (*m*/*z*): 255 $(M+Na)^+$.

4.1.2. (4*R*,5*S*)-Ethyl 5-(*tert*-butyldimethylsilyloxy)-4-hydroxyhex-2-ynoate 8

To a cooled (−78 °C) stirred solution of compound **10** (9.0 g, 38.80 mmol) in dry DCM (150 mL) was added DIBAL-H (1.0 M, in toluene, 38.8 mL, 38.8 mmol) and the reaction mixture was stirred for 0.5 h. After completion of the reaction, the reaction was quenched with saturated sodium potassium tartrate (50 mL) and stirred for 0.5 h. The reaction mixture was extracted into DCM (3 × 125 mL). The combined organic phase was washed with brine, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The crude residue was purified by column chromatography using (hexane/ethyl acetate 95:5) to give the pure aldehyde (6.12 g, 84%) as a colorless liquid.

To a stirred solution of ethyl propiolate (4.38 g, 44.68 mmol) in dry THF (30 ml) was added LiHMDS (1.0 M, in hexane, 38.3 ml, 38.3 mmol) at −78 °C and the reaction mixture was stirred at −78 °C for 30 min. The aldehyde (6.0 g, 31.90 mmol) dissolved in THF (50 ml) was added dropwise to the reaction mixture over 1 h. Stirring was continued for 2 h. After completion of the reaction, the mixture was quenched with saturated NH_4Cl (40 mL) and stirred for 0.5 h, then diluted with water. The reaction mixture was extracted into ethyl acetate (3 × 125 mL). The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The crude residue was purified by column chromatography using (hexane/ethyl acetate) (85:15) to give pure compound **8** (6.93 g, 76%) as a brown liquid. The de was determined by chiral HPLC column: (ATLANTIS C18: 150 × 4.6 mm, 5 μ) mobile phase: 80% ACN in WATER, Flow rate: 1.0 ml/min, detection: 210 nm, 94% de). $[\alpha]_D^{25} = +3.4$ (*c* 2.5, $CHCl_3$) [Lit[13a] = +0.8 (*c* 4.3, $CHCl_3$)]; IR (neat, cm^{-1}): ν_{max} 3446, 2957, 2932, 2896, 2859, 2240, 1716, 1472, 1464, 1368, 1251, 1093, 837, 778; ^1H NMR (300 MHz, $CDCl_3$): δ 4.37–4.32 (m, 1H), 4.24 (q, $J = 7.1$, Hz, 2H), 4.03–3.94 (m, 1H), 2.50 (br s, 1H), 1.31 (t, $J = 7.1$ Hz, 3H), 1.26 (d, $J = 6.2$ Hz, 3H), 0.91 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.2, 85.5, 77.3, 70.6, 66.9, 61.9, 25.6, 18.8, 17.9, 13.8, −4.6, −5.0; ESI/MS (*m*/*z*): 309 $(M+Na)^+$.

4.1.3. (4*R*,5*S*)-Ethyl 4,5-bis(*tert*-butyldimethylsilyloxy)hex-2-ynoate 11

To a solution of the ethyl ester compound **8** (5.2 g, 18.18 mmol) in dry CH_2Cl_2 (100 mL) was added imidazole (1.85 g, 27.3 mmol) and the reaction mixture was stirred for 10 min at 0 °C. To this solution *tert*-butyldimethylsilyl chloride (3.28 g, 21.8 mmol) was added at 0 °C, and the mixture was stirred at room temperature for 8 h. After completion of the reaction, the mixture was diluted with ice-water and extracted into CH_2Cl_2 (3 × 100 mL). The combined extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography using (hexane/ethylacetate) (96:4) to give pure compound **11** (6.33 g, 88%) as a colorless liquid. $[\alpha]_D^{25} = -9.1$ (*c* 2.3, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 2957, 2931, 2888, 2859, 1739, 2241, 1718, 1473, 1364, 1251, 1116, 837, 779; ^1H NMR (300 MHz, $CDCl_3$): δ 4.22 (q, $J = 7.5$ Hz, 2H), 4.17 (d, $J = 6.0$ Hz, 1H), 3.89–3.79 (m, 1H), 1.30 (t, $J = 7.5$ Hz, 3H), 1.20 (d, $J = 6.0$ Hz, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.16 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.4, 87.7, 76.7, 71.7, 68.4, 61.7, 25.8, 25.7, 19.9, 18.1, 18.0, 14.0, −4.5, −4.6, −4.8, −5.1; ESI/MS (*m*/*z*): 423 (M+Na).

4.1.4. (6*R*,7*S*,*E*)-Ethyl 6,7-bis(*tert*-butyldimethylsilyloxy)oct-2-en-4-ynoate 12

To a cooled (−78 °C) solution of ester compound **11** (5.1 g, 12.75 mmol) in dry CH_2Cl_2 (75 ml) was added DIBAL-H (1.0 M in toluene, 12.8 mL, 12.75 mmol) and the reaction was stirred for 0.5 h. After completion of the reaction, the reaction was quenched with saturated sodium potassium tartrate (30 mL) and stirred for 0.5 h. The reaction mixture was extracted into CH_2Cl_2 (3 × 75 mL). The combined organic phase was washed with brine, and dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (hexane/ethylacetate, 93:7) to give the aldehyde (4.08 g, 90%) as a colorless oil.

To a cooled solution (0 °C) of triethylphosphonoacetate (3.58 g, 16.01 mmol) in dry THF (30 mL), was slowly added NaH (60%) (0.55 g, 13.87 mmol) and the reaction mixture was stirred for 30 min at the same temperature. A solution of the aldehyde (3.8 g, 10.67 mmol) obtained above in THF (20 mL) was added dropwise and stirred for 1 h. After completion of the reaction, it was quenched with saturated NH_4Cl, and extracted into ethylacetate (3 × 100 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography using (hexane/ethylacetate 94:6) to give the product **12** (4.04 g, 89% yield) as a colorless liquid. $[\alpha]_D^{25} = -11.7$ (*c* 3.0, $CHCl_3$). IR (neat): 2957, 2931, 2887, 2858, 2213, 1720, 1621, 1472, 1363, 1301, 1258, 1154, 1114, 835, 777 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.77$ (dd, $J = 15.8$, 1.5 Hz, 1H), 6.18 (d, $J = 15.8$ Hz, 1H), 4.25–4.18 (m, 3H), 3.84–3.78 (m, 1H), 1.30 (t, $J = 7.1$ Hz, 3H), 1.19 (d, $J = 6.0$ Hz, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.8$, 130.1, 125.0, 100.0, 81.5, 71.9, 69.0, 60.7, 25.7, 20.1, 18.1, 18.0, 14.1, −4.6, −4.7, −5.1; ESI/MS (*m*/*z*): 449 (M+Na).

4.1.5. (6*R*,7*S*,*E*)-6,7-Bis(*tert*-butyldimethylsilyloxy)oct-2-en-4-yn-1-ol 13 dot alcohol 13

To a cooled (0 °C) stirred solution of compound **12** (3.9 g, 9.15 mmol) in dry CH_2Cl_2 (75 mL) was added DIBAL-H (1.0 M in toluene, 18.3 mL, 18.30 mmol) and the reaction mixture was stirred for 0.5 h. After completion of the reaction, the reaction was quenched with saturated sodium potassium tartrate (30 mL) and

stirred for 0.5 h. The reaction mixture was extracted into CH_2Cl_2 (3 × 75 mL). The combined organic phase was washed with brine, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, the residue was purified by column chromatography using (hexane/ethylacetate 80:20) to give the alcohol **13** (3.374 g, 96% yield) as a colorless liquid. $[\alpha]_D^{25} = -14.2$ (*c* 3.2, $CHCl_3$). IR (neat): 3422, 2956, 2931, 2887, 2858, 2213, 1472, 1463, 1362, 1256, 1115, 1042, 836, 777 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.20 (dt, *J* = 15.4, 5.5 Hz, 1H), 5.75 (d, *J* = 14.4 Hz, 1H), 4.24–4.16 (m, 3H), 3.81–3.76 (m, 1H), 1.19 (d, *J* = 6.6 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.1, 110.4, 91.2, 82.4, 72.2, 68.9, 62.9, 25.8, 25.7, 19.9, 18.2, 18.1, −4.4, −4.5, −5.0; ESI/MS (*m*/*z*): 407 (M+Na).

4.1.6. (5*R*,6*S*)-5-((*E*)-5-(4-Methoxybenzyloxy)pent-3-en-1-ynyl)-2,2,3,3,6,8,8,9,9-nonamethyl-4,7-dioxa-3,8-disiladecane 14

To a cooled (0 °C) solution of alcohol compound **13** (3.5 g, 9.11 mmol) in dry CH_2Cl_2 (60 mL) was added PMB imidate (3.86 g, 13.67 mmol) followed by PTSA (catalytic amount) and the reaction was stirred at room temperature for 8 h. After completion of the reaction, it was quenched with triethylamine and diluted with water (60 mL), and extracted with DCM (3 × 75 mL). The combined organic layers was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (hexane/ethylacetate, 88:12) to give compound **14** (3.85 g, 84%) as a brown color liquid. $[\alpha]_D^{25} = -10.5$ (*c* 3.4, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 2956, 2931, 2858, 1614, 1515, 1463, 1251, 1112, 1039, 832, 775; ^1H NMR (300 MHz, $CDCl_3$): δ 7.28–7.23 (m, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.14 (dt, *J* = 15.8, 5.9 Hz, 1H), 5.74 (d, *J* = 14.8 Hz, 1H), 4.44 (s, 2H), 4.18 (d, *J* = 5.9 Hz, 1H), 4.02 (d, *J* = 6.8 Hz, 1H), 3.80 (s, 3H), 1.19 (d, *J* = 6.0 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.2, 139.0, 130.0, 129.3, 113.8, 111.7, 91.0, 82.6, 72.2, 71.9, 69.5, 68.9, 55.2, 25.8, 25.7, 19.9, 18.2, 18.1, −4.5, −4.6, −5.0. ESI/MS (*m*/*z*): 527 (M+Na).

4.1.7. (2*R*,3*R*,6*R*,7*S*)-6,7-Bis(*tert*-butyldimethylsilyloxy)-1-(4-methoxybenzyloxy)oct-4-yne-2,3-diol 7

To a solution of AD-mix-β (6.11 g, 6.11 mmol) in *t*-BuOH/H_2O (1:1) (40 mL) was added methanesulfonamide (0.425 g, 4.36 mmol) at room temperature and stirred for 10 min. The solution was then cooled to 0 °C, olefin **14** (2.2 g, 4.36 mmol) added, and the entire reaction mixture was stirred vigorously at this temperature for 36 h. After completion of the reaction (as noticed by TLC), the reaction was quenched with sodium sulfite (6.5 g) and stirring was continued for another 0.5 h after which the reaction mixture was brought to room temperature. The product was extracted into EtOAc (3 × 75 mL), and the combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography using (hexane/ethylacetate) (77:23) as eluent to obtain diol **7** (2.11 g, 90% yield, 95% de) as a colorless viscous liquid. The de was determined by chiral HPLC column: (XDB C18: 250 × 4.6 mm, 5 μ) mobile phase: 90% ACN in WATER, Flow rate: 1.0 ml/min, detection: 210 nm, 96% de). $[\alpha]_D^{25} = -19.4$ (*c* 3.4, $CHCl_3$). IR (neat): 3437, 2929, 2856, 1587, 1463, 1282, 1250, 1128, 831, 777 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.23 (m, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.49 (s, 2H), 4.43 (dd, *J* = 6.1, 1.2 Hz, 1H), 4.14 (dd, *J* = 5.0, 1.4 Hz, 1H), 3.83–3.77 (m, 5H), 3.68 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.59 (dd, *J* = 9.6, 5.6 Hz, 1H), 1.16 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 129.7, 129.4, 113.8, 86.9, 82.3, 73.3, 72.1, 70.2, 68.4, 63.8, 55.2, 25.8, 25.7, 19.5, 18.2, 18.1, −4.5, −4.6 ESI/MS (*m*/*z*): 561 (M+Na).

4.1.8. (5*R*,6*S*)-5-((*E*)-5-(((4*R*,5*R*)-5-((4-Methoxybenzyloxy)methyl)-2,2-dimethyl 1,3 dioxolan-4-yl)ethynyl)-2,2,3,3,6,8,8,9,9-nonamethyl-4,7-dioxa-3,8-disiladecane 15

To a cooled (0 °C) solution of diol compound **7** (2.0 g, 3.717 mmol) in dry CH_2Cl_2 (40 mL) was added 2,2-dimethoxypropane (2.3 ml, 18.60 mmol) and a catalytic amount of PTSA. The resulting mixture was bought to room temperature and stirred for 2 h. After completion of the reaction, the mixture was quenched with saturated $NaHCO_3$ solution, and extracted into DCM (3 × 50 mL). The combined extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography using (hexane/ethylacetate) (90:10) to give pure compound **15** (1.97 g, 92%) as a colorless oil. $[\alpha]_D^{25} = +18.2$ (*c* 1.4, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 2955, 2931, 2888, 2858, 1614, 1514, 1463, 1380, 1250, 1111, 1037, 833, 777; ^1H NMR (300 MHz, $CDCl_3$): δ 7.30–7.22 (m, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 4.53 (s, 2H), 4.49 (dd, *J* = 7.5, 1.5 Hz, 1H), 4.26–4.18 (m, 1H), 4.15–4.09 (m, 1H), 3.88–3.73 (m, 4H), 3.64–3.49 (m, 2H), 1.47 (s, 3H), 1.42 (s, 3H), 1.16 (s, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.2, 129.9, 129.3, 113.7, 110.5, 87.1, 81.4, 80.9, 73.2, 72.0, 68.9, 68.4, 67.4, 55.2, 27.0, 26.2, 25.8, 25.7, 19.5, 18.2, 18.0, −4.5, −5.0; ESI/MS (*m*/*z*): 601 (M+Na).

4.1.9. (2*S*,3*R*)-5-((4*R*,5*R*)-5-((4-Methoxybenzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-yne-2,3-diol 16

To a cooled (0 °C) solution of acetonide protected compound **15** (1.8 g, 3.11 mmol) in dry THF (15 mL) was added TBAF (9.3 ml, 1 M in THF, 9.34 mmol) and stirred for 4 h at room temperature. After completion of the reaction, the reaction was diluted with water and extracted into EtOAc (3 × 50 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuum. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 40:60) to give pure compound **16** (1.0 g, 92%) as a colorless liquid. $[\alpha]_D^{25} = +32.9$ (*c* 1.7, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3446, 3073, 3029, 2977, 2928, 2871, 1637, 1452, 1078, 928, 741, 669; ^1H NMR (300 MHz, $CDCl_3$): δ 7.29–7.24 (m, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 4.56–4.52 (m, 3H), 4.31 (dd, *J* = 3.6, 1.6 Hz, 1H), 4.23–4.19 (m, 1H), 3.86 (dd, *J* = 6.4, 3.6 Hz, 1H), 3.81 (s, 3H), 3.60 (d, *J* = 4.3 Hz, 2H), 1.48 (s, 3H), 1.42 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.2, 129.6, 129.4, 113.8, 110.7, 84.1, 83.3, 80.7, 73.2, 70.1, 68.7, 67.5, 67.0, 55.2, 26.8, 26.2, 18.2; ESI/MS (*m*/*z*): 373 (M+Na).

4.1.10. (2*S*,3*R*,*E*)-5-((4*R*,5*R*)-5-((4-Methoxybenzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-ene-2,3-diol 17

To a cooled (0 °C) solution of **16** (0.8 g, 2.285 mmol) in dry THF (10 mL) was added Red-Al (2.2 ml, 11.428 mmol) and stirred at room temperature for 12 h. After completion of the reaction, the mixture was quenched with saturated $NaHCO_3$ solution and extracted into EtOAC (3 × 50 mL). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography using (hexane/ethyl) acetate (45:55) to give pure **17** (0.643 g, 80%) as a colorless gummy liquid. $[\alpha]_D^{25} = +9.5$ (*c* 1.1, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 3445, 2984, 2931, 1611, 1514, 1458, 1382, 1302, 1248, 1171, 1079, 1032, 848, 819; ^1H NMR (30 0 MHz, $CDCl_3$): δ 7.28–7.23 (m, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.83–5.72 (m, 2H), 4.51 (s, 2H), 4.26–4.22 (m, 1H), 4.07–4.02 (m, 1H), 3.91–3.85 (m, 1H), 3.84–3.76 (m, 4H), 3.61–3.51 (m, 2H), 1.43 (s, 6H), 1.08 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.3, 132.5, 130.4, 129.8, 129.4, 113.7, 109.5, 79.9, 78.8, 75.6, 73.2, 69.9, 68.9, 55.2, 26.9, 17.7; ESI/MS (*m*/*z*): 375 (M+Na).

4.1.11. (2*S*,3*R*,*E*)-5-((4*R*,5*R*)-5-((4-methoxybenzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-ene-2,3-diyl diacetate 18

To a cooled (0 °C) solution of diol **17** (520 mg, 1.47 mmol) in CH_2Cl_2 (15 mL) were added triethylamine (0.83 ml, 5.9 mmol), acetic anhydride (0.42 mL, 4.43 mmol), and a catalytic amount of DMAP and stirred at room temperature for 6 h. After completion of the reaction, the reaction was diluted with aqueous $NaHCO_3$ (5 mL) and extracted into DCM (2 × 30 mL). The combined organic phase was washed with brine, and dried over Na_2SO_4. After evaporation of the solvent, the crude residue was purified by column chromatography using (hexane/ethylacetate) (75:25) as eluent to afford the desired product **18** (596 mg, 93% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +3.2 (*c* 1.3, $CHCl_3$). IR (neat): 2987, 2937, 1741, 1612, 1513, 1458, 1371, 1301, 1246, 1172, 1087, 1032, 820, 760 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.28–7.23 (m, 2H), 6.88 (d, *J* = 6.5 Hz, 2H), 5.83–5.65 (m, 2H), 5.38 (dd, *J* = 6.2, 3.5 Hz, 1H), 5.05–4.97 (m, 1H), 4.52 (s, 2H), 4.25 (dd, *J* = 8.2, 6.1 Hz, 1H), 3.88–3.83 (m, 1H), 3.80 (s, 3H), 3.56–3.51 (m, 2H), 2.07 (s, 3H), 2.02 (s, 3H), 1.43 (s, 3H), 1.42 (s, 3H), 1.14 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 169.8, 159.2, 132.2, 129.8, 129.3, 127.4, 113.7, 109.6, 79.9, 78.2, 74.2, 73.2, 70.4, 68.8, 55.2, 26.9, 26.8, 21.1, 21.0, 14.9. ESI/MS (*m*/*z*): 459 (M+Na).

4.1.12. (2*S*,3*R*,*E*)-5-((4*R*,5*R*)-5-(Hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-ene-2,3-diyl diacetate 19

To a cooled (0 °C) solution of **18** (550 mg, 1.267 mmol) in CH_2Cl_2 (18 mL) and water (2 mL) was added DDQ (575 mg, 2.534 mmol) and stirred at room temperature for 2 h. After completion of the reaction, saturated $NaHCO_3$ (15 ml) solution was added, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography using (hexane/ethylacetate) (70:30) to give compound **19** (370 mg, 93% yield) as a colorless liquid. $[\alpha]_D^{25}$ = +13.2 (*c* = 0.3, $CHCl_3$). IR (neat): 3445, 2987, 2936, 1740, 1633, 1372, 1229, 1167, 1053, 975, 856, 608 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.87–5.71 (m, 2H), 5.42–5.32 (m, 1H), 5.11–5.00 (m, 1H), 4.41–4.32 (m, 1H), 3.89–3.74 (m, 2H), 3.65–3.52 (m, 1H), 2.08 (s, 3H), 2.05 (s, 3H), 1.44 (s, 6H), 1.19 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 169.8, 131.9, 128.0, 109.5, 81.0, 80.9, 74.3, 70.3, 60.5, 26.9, 26.8, 21.1, 20.9, 15.0; ESI/MS (*m*/*z*): 339 (M+Na).

4.1.13. (2*S*,3*R*,*E*)-5-((4*R*,5*R*)-5-(1-Hydroxybut-3-enyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-ene-2,3-diyl diacetate 20

To a solution of **19** (330 mg, 1.05 mmol) in EtOAc (10 mL) was added IBX (882 mg, 3.15 mmol) at room temperature and then refluxed for 4 h. After completion of the reaction, the reaction was filtered through a shot pad of Celite and the Celite pad was washed with EtOAc (2 × 20 mL). The organic layer was washed with saturated $NaHSO_3$ solution (2 × 20 mL), brine (1 × 50 mL), dried over anhydrous Na_2SO_4, and concentrated. The crude residue was purified by column chromatography using hexane/ethylacetate (75:25) as eluent to obtain pure aldehyde (285 mg, 87% yield) as a colorless liquid.

To a cooled (0 °C) solution of the aldehyde (250 mg, 0.796 mmol) in THF (4 mL) was added allyl bromide (0.2 ml, 2.388 mmol) and zinc (207 mg, 3.18 mmol). Saturated NH_4Cl (1 ml) was then added dropwise to the reaction mixture over 10 min and stirred at the same temperature for 1 h. The reaction mixture was then stirred at room temperature for 8 h. After completion of the reaction, the reaction was diluted with saturated NH_4Cl (5 ml), poured into water (5 ml), and extracted with ethylacetate (3 × 25). The combined organic layer was washed with brine (1 × 25 mL), and dried over anhydrous Na_2SO_4, and concentrated. The crude residue was purified by column chromatography using (hexane/ethylacetate) (80:20) as eluent to obtain pure compound **20** (232 mg, 82%) as a colorless liquid. IR (neat, cm^{-1}): ν_{max} 3456, 2987, 2923, 1740, 1633, 1372, 1228, 1168, 1059, 978, 878, 765: ^1H NMR (300 MHz, $CDCl_3$): δ 5.93–5.73 (m, 3H), 5.43–5.29 (m, 1H), 5.20–5.01 (m, 3H), 4.53–4.44 (m, 1H), 3.89–3.80 (m, 1H), 3.73–3.62 (m, 1H), 2.38–2.15 (m, 2H), 2.08 (s, 3H), 2.04 (s, 3H), 1.44 (s, 3H), 1.42 (s, 3H), 1.20 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 169.9, 133.9, 133.5, 127.2, 118.3, 109.1, 82.5, 77.0, 74.4, 70.5, 37.5, 26.9, 26.8, 21.1, 21.0, 15.0; ESI/MS (*m*/*z*): 379 (M+Na).

4.1.14. (2*S*,3*R*,*E*)-5-((4*R*,5*R*)-5-((*R*)-1-(Acryloyloxy)but-3-enyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-ene-2,3-diyl diacetate 6

To a cooled (0 °C) solution of alcohol **20** (165 mg, 0.463 mmol) in dry CH_2Cl_2 (5 mL) was added triethylamine (0.16 mL, 1.158 mmol) and acryloyl chloride (0.1 mL, 1.02 mmol) and stirred at the same temperature for 10 min. After completion, the reaction was quenched with saturated sodium bicarbonate (5 ml) and extracted into CH_2Cl_2 (3 × 15 mL). The combined organic phase was washed with brine, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the crude residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 90:10) to give acryl ester compound **6** (125 mg, 66%) as a colorless liquid. $[\alpha]_D^{25}$ = +18.3 (*c* 0.8, $CHCl_3$); IR (neat, cm^{-1}): ν_{max} 2921, 2851, 1743, 1619, 1383, 1227, 1067, 770; ^1H NMR (300 MHz, $CDCl_3$): δ 6.42 (d, *J* = 17.4 Hz, 1H), 6.10 (dd, *J* = 17.2, 10.4 Hz, 1H), 5.92–5.69 (m, 4H), 5.42–5.39 (m, 1H), 5.22–4.98 (m, 4H), 4.40–4.36 (m, 1H), 3.85–3.79 (m, 1H), 2.56–2.30 (m, 2H), 2.09 (s, 3H), 2.04 (s, 3H), 1.42 (s, 3H), 1.41 (s, 3H), 1.18 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 169.8, 165.3, 132.7, 132.2, 131.5, 128.1, 127.7, 118.4, 109.7, 80.7, 78.7, 74.0, 72.6, 70.5, 35.6, 26.9, 26.8, 21.1, 20.1, 14.8; ESI/MS (*m*/*z*): 431 (M+Na).

4.1.15. (2*S*,3*R*,*E*)-5-((4*R*,5*R*)-2,2-Dimethyl-5-((*R*)-6-oxo-3,6-dihydro-2*H*-pyran-2-yl)-1,3-dioxolan-4-yl)pent-4-ene-2,3-diyl diacetate 21

A solution of compound **6** (30 mg, 0.0735 mmol) in dry toluene (15 mL) was first bubbled with nitrogen flow, after which Hoveyda Grubbs II generation catalyst (4.6 mg, 0.007 mmol) was added at once and the resulting mixture was heated under nitrogen at 80 °C for 1 h. After completion of the reaction, the mixture was cooled to room temperature and the solvent was evaporated in vacuo. The crude residue was purified by column chromatography on silica gel (hexane/ethylacetate, 42:58) to give compound **21** (25.8 mg, 92%) as a colorless liquid. $[\alpha]_D^{25}$ = +42.2 (*c* 0.2, $CHCl_3$) [Lit[10] = +45.5 (*c* 0.46, $CHCl_3$)]; IR (neat, cm^{-1}): ν_{max} 2924, 2853, 1739, 1609, 1374, 1243, 1067, 977, 816; ^1H NMR (300 MHz, $CDCl_3$): δ 6.92 (ddd, *J* = 8.4, 4.7, 3.8 Hz, 1H), 6.04 (dt, *J* = 9.9, 1.9 Hz, 1H), 5.92–5.82 (m, 2H), 5.41 (dd, *J* = 5.3, 3.5 Hz, 1H), 5.10–5.01 (m, 1H), 4.51–4.41 (m, 2H), 3.89 (t, *J* = 7.1 Hz, 1H), 2.56–2.52 (m, 2H), 2.09 (s, 3H), 2.05 (s, 3H), 1.43 (s, 3H), 1.42 (s, 3H), 1.22 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 169.9, 162.6, 144.6, 132.4, 127.3, 121.4, 110.3, 80.8, 79.1, 78.0, 74.5, 70.6, 26.9, 26.2, 21.1, 21.0, 15.0; ESI/MS (*m*/*z*): 405 (M+Na).

4.1.16. (2*S*,3*R*,6*R*,7*S*,*E*)-6,7-Dihydroxy-7-((*R*)-6-oxo-3,6-dyhydro-2*H*-pyran-2-yl)hept-4-ene-2,3-diyl diacetate 1

To a cooled (0 °C) solution of compound **21** (15 mg, 0.039 mmol) in MeOH (4 mL) was added PPTS (29 mg, 0.117 mmol) and the resulting mixture was refluxed for 6 h. After completion of the reaction, the MeOH was evaporated under vacuum and diluted with ethylacetate (10 ml). Solid $NaHCO_3$ was added to the reaction mixture which was stirred for an additional 10 min. The reaction mixture was then filtered through a shot pad

of Celite, and the Celite pad was washed with EtOAC (3 × 5 ml). The combined organic phase was washed with brine, and dried over Na_2SO_4. After evaporation of the solvent, the crude residue was purified by column chromatography using (hexane/ethylacetate) (10:90) as eluent to afford the desired product **1** (9.4 mg, 70% yield) as colorless liquid. $[\alpha]_D^{25}$ = +24.8 (*c* 0.4, $CHCl_3$), [Lit.[7] = +28.8 (*c* 0.18, $CHCl_3$)]. IR (neat, cm^{-1}): ν_{max} 3435, 2924, 2853, 1738, 1610, 1383, 1244, 772; ^1H NMR (300 MHz, $CDCl_3$): δ 6.95 (ddd, *J* = 9.6, 5.8, 3.0 Hz, 1H), 6.03 (dt, *J* = 9.7, 1.2 Hz, 1H), 5.88 (dd, *J* = 15.7, 5.2 Hz, 1H), 5.79 (dd, *J* = 15.6, 6.0 Hz, 1H), 5.32 (m, 1H), 5.07 (m, 1H), 4.52 (m, 1H), 4.49 (m, 1H), 3.70 (m, 1H), 2.57 (m, 2H), 2.41 (br s, 1H), 2.08 (s, 3H), 2.04 (s, 3H), 1.21 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, MeOH-d_4): δ 172.2, 171.9, 166.4, 148.7, 136.6, 126.6, 121.1, 78.9, 76.3, 75.8, 72.1, 71.5, 26.4, 21.0, 20.9, 15.1; ESI/MS (*m*/*z*): 365 $(M+Na)^+$.

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