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Stereoselective total synthesis of (+)-strictifolione and (6*R*)-6-[(4*R*,6*R*)-4,6-dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one by Prins reaction and olefin cross-metathesis

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ABSTRACT

Prins and olefin cross-metathesis reactions were used as the key steps for the stereoselective total synthesis of (+)-strictifolione and (6*R*)-6-[(4*R*,6*R*)-4,6-dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one. Removal of MOM protecting groups under neutral conditions using $CeCl_3{\cdot}7H_2O$ is an attractive addition to the present strategy.

1. Introduction

α-Pyrone derivatives (5,6-dihydro-2*H*-pyran-2-ones), isolated from natural sources,[1] have attracted much attention over the last decade due to their medicinal potential[2] as antiviral, antifungal, antibacterial, antimalarial and antitumor compounds, as well as plant growth inhibition. Strictifolione **1**,[3] a 6-substituted 5,6-dihydro-α-pyrone, has been isolated by Aimi et al. from the stem bark of *Cryptocarya strictifolia* that grows in Indonesia, and has been shown to display antifungal activity. Its structure was proposed based on spectroscopic analysis. The absolute configuration of strictifolione was confirmed by accomplishing its first total synthesis as being (6*R*,4′*S*,6′*S*).[4]

Later, two more asymmetric syntheses[5] and a formal synthesis were reported.[6] (6*R*)-6-[(4*R*,6*R*)-4,6-Dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one **2**[7] is also one such natural product, isolated from *Ravensara crassifolia* by Hostetmann et al. along with a structurally similar compound **3**.[8] The absolute configuration of these 6-alkylated α-pyrones from *R. crassifolia* was determined by LC-NMR.[9] To the best of our knowledge, only one report has appeared with regard to the synthesis of **2**.[10] (see Fig. 1).

Within our recently initiated program on synthesis of bioactive lactones where Prins and ring-closing metathesis (RCM) reactions are used as one of the key steps,[11] we decided to undertake a stereoselective synthesis of **1** and **2** using Prins, olefin cross-metathesis reactions and MOM deprotection as key steps. Retrosynthetic analysis revealed that target compound **1** could be obtained from **4** and **5** by olefin cross-metathesis using Grubbs' catalyst. Compound **4**, could in turn be obtained from **6**, was prepared via a Prins route from **7**. Vinyl lactone **5** could in turn be prepared from known allylic alcohol **8** (Scheme 1).

However, the retrosynthesis for target molecule **2** reveals that it could be obtained by olefin cross-metathesis reaction of **9** and **8** followed by simple manipulations. Similarly **9**, could in turn be obtained from **10**, was prepared via Prins route from **7**.

2. Results and discussion

The synthesis starts from the known homoallylic alcohol **7**.[11] The classical TFA-mediated Prins reaction between the known homoallylic alcohol **7** and benzaldehyde **11**, followed by hydrolysis of the resulting trifluoroacetate yielded the desired trisubstituted pyran. MOM protection of the resulting alcohol with MOMCl in the presence of Hunig's base afforded **6** in 90% yield. The tetrahydropyran ring was opened in a different manner using Li in liquid NH_3 to furnish the key open chain compound **12**. The primary alcohol was protected as tosyl derivative **13** and exposure to a base afforded epoxide **14**. Opening of the epoxide with vinyl magnesium bromide was unsuccessful, but we were successful in opening of the epoxide with the Li acetylide to provide the homopropargylic alcohol **15** in 80% yield. Partial reduction of the terminal triple bond using Lindlar's catalyst gave the required homoallylic alcohol **16**. MOM deprotection under neutral conditions[12] using $CeCl_3{\cdot}7H_2O$ in CH_3CN/MeOH (1:1) afforded diol **4** (Scheme 2).

The other key intermediate **5** was synthesized starting from homoallylic alcohol **8**.[13] Accordingly, the secondary hydroxyl was protected as the silyl ether **17** with TBDMSCl and imidazole and the primary THP ether was cleaved to furnish a free alcohol. Oxidation using IBX in DMSO/CH_2Cl_2 furnished the aldehyde, which was subjected directly to a homologation using Still–Gennari conditions to give *Z*-unsaturated ester. Compound **18** was lactonized using methanol in the presence of PTSA to afford vinyl lactone **5** in very good yield (Scheme 3).

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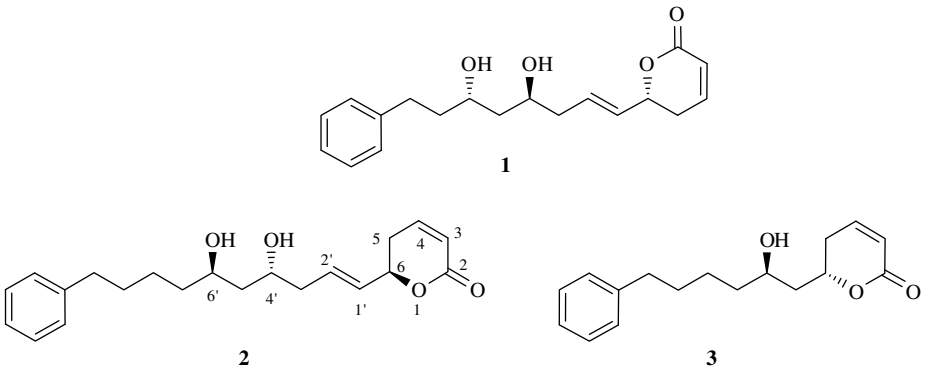
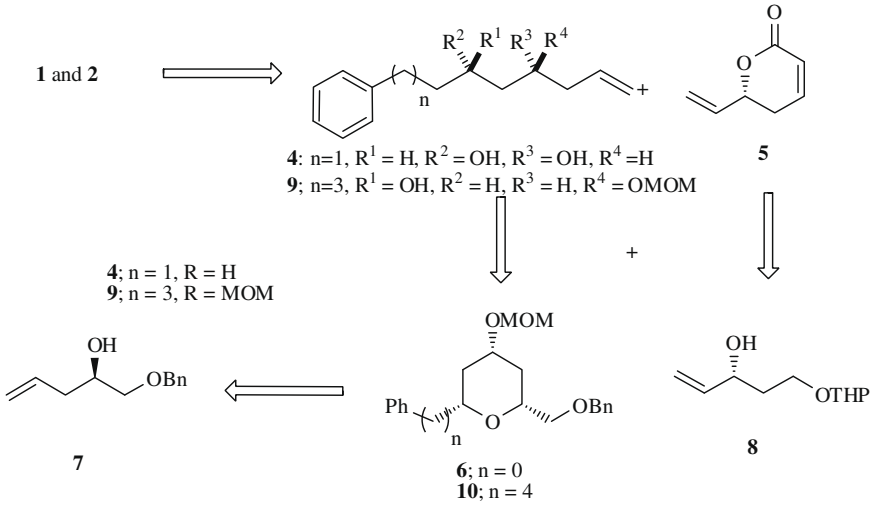


Figure 1.



Scheme 1. Retrosynthetic analysis for **1** and **2**.

With the two key fragments **4** and **5** in hand, the next concern was to couple them by olefin cross-metathesis reaction.[14] Thus, cross-coupling reaction of **4** and **5** using Grubbs' second generation catalyst in dichloromethane at 50 °C led to a target molecule **1** directly as a single cross-coupled product in 63% yield (Scheme 4). The spectroscopic data of synthetic **1** are in good agreement with that reported in the literature.

Having achieved a synthesis of the target **1**, we now undertook the synthesis of **2**, which also relies on the use of Prins, olefin cross-metathesis reactions and MOM deprotection as key steps. The synthesis of **2** commenced from the known homoallylic alcohol **7**.[11]

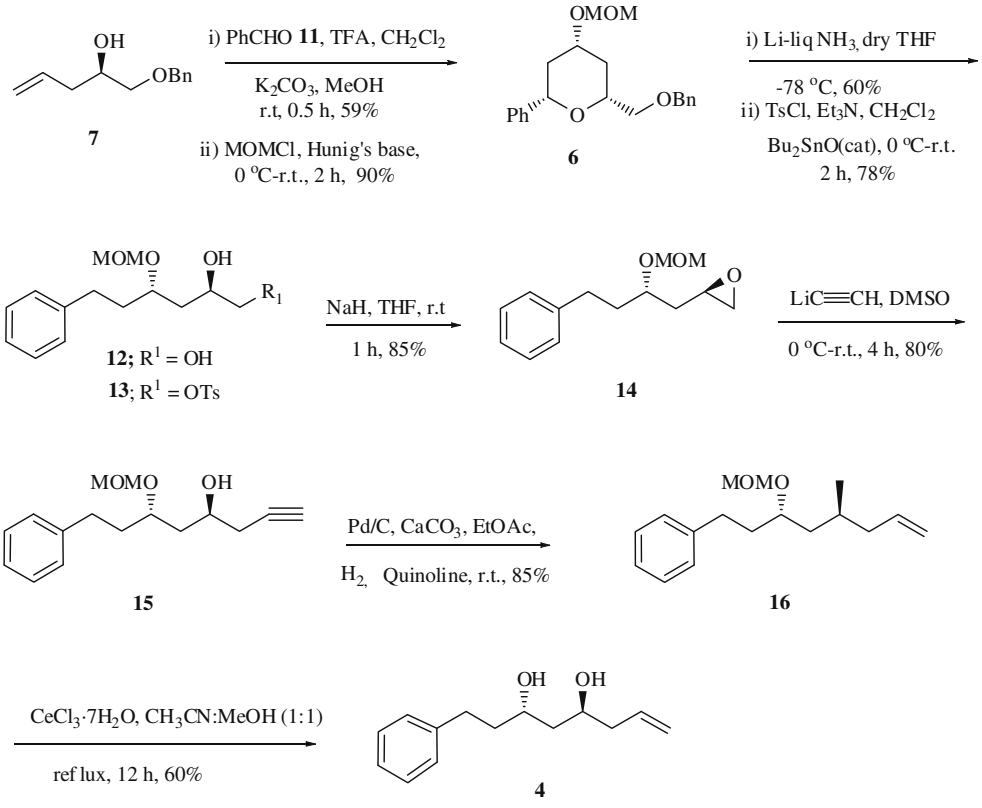
Prins cyclization of **7** with 5-phenyl-1-pentanal **19** in the presence of TFA followed by hydrolysis of the resulting trifluoroacetate yielded the desired trisubstituted pyran **20** (Scheme 5). The secondary hydroxyl group in **20** was protected as MOM ether **9** using MOMCl and Hunig's base in 95% yield. Compound **9**, on debenzylation using Li in liquid NH_3, gave primary alcohol **21**. Alcohol **21** on exposure to TPP, iodine, and imidazole in refluxing ethanol was converted into the corresponding iodide **22** in 3 h, which on treatment with Zn dust in Et_2O/CH_3CN (3:1) at 0 °C to rt, furnished the key ring-opened homoallylic alcohol **23** with the required *anti*-1,3-diol system. The *anti* relative stereochemistry of the 1,3-diol was established by its conversion to the corresponding acetonide (PPTS, 2,2-dimethoxypropane, dry DCM, rt, 2 h, 95% yield). The *anti* relative configuration of the hydroxyl groups was confirmed by analysis of the ^{13}C NMR spectra (δ = 25.08 and 24.85 ppm for the methyl groups and 100.02 ppm for the quaternary center).[15]

Next, the olefin cross-metathesis reaction[14] of homoallyl alcohol **10** with the allyl alcohol **8**[13] in the presence of Grubbs' second generation catalyst (10 mol %) in dichloromethane at room temperature afforded a cross-coupling product **23** in 70% yield and with excellent stereoselectivity (*E*/*Z* ratio of 20:1) as observed by ^1H NMR spectroscopy. In this reaction, the formation of the homo dimer of **10** was observed in very low yield as a by-product. The two hydroxyl groups in **23** were protected as MOM ethers **24**, and subsequent removal of the THP group using PPTS methanol gave primary alcohol **25**. Oxidation using iodoxybenzoic acid (IBX) in DMSO/DCM[16] at room temperature, followed by chain elongation using Still–Gennari Wittig reaction ($(F_3CCH_2O)_2POCH_2$-COOMe, NaH, THF, −78 °C), afforded the α,β-unsaturated ester **26** predominantly as the *Z*-isomer, established by ^1H NMR spectroscopy.

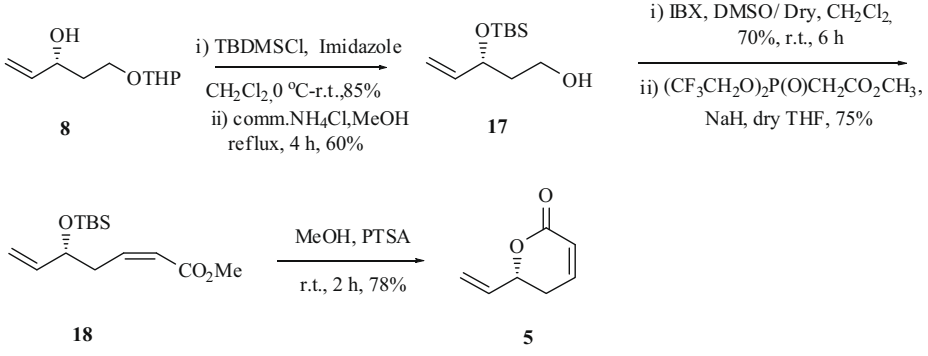
Finally, removal of the MOM protecting group and lactonization were realized in a one-pot manner in the presence of $CeCl_3 \cdot 7H_2O$ in $MeOH/CH_3CN$ (1:1)[12] to furnish target molecule in 73% isolated yield. Synthetic **1** was completely identical in all respects (mp, ^1H, ^{13}C NMR, and $[\alpha]_D^{25}$) with the natural one.

3. Conclusions

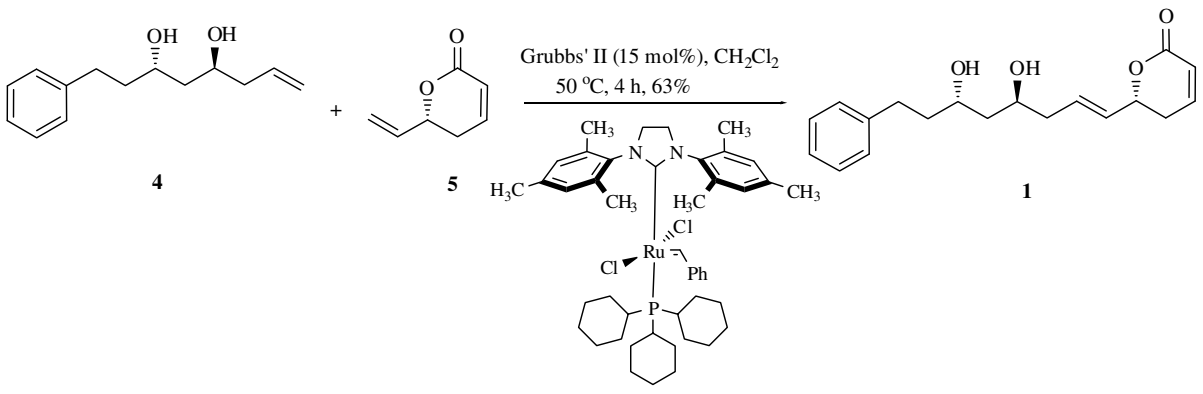
In conclusion, the total stereoselective synthesis of target molecules **1** and **2** has been accomplished. The highlights of the synthesis are the successful utilization of the Prins reaction to introduce the stereogenic centers at C4′ and C6′ and a cross-



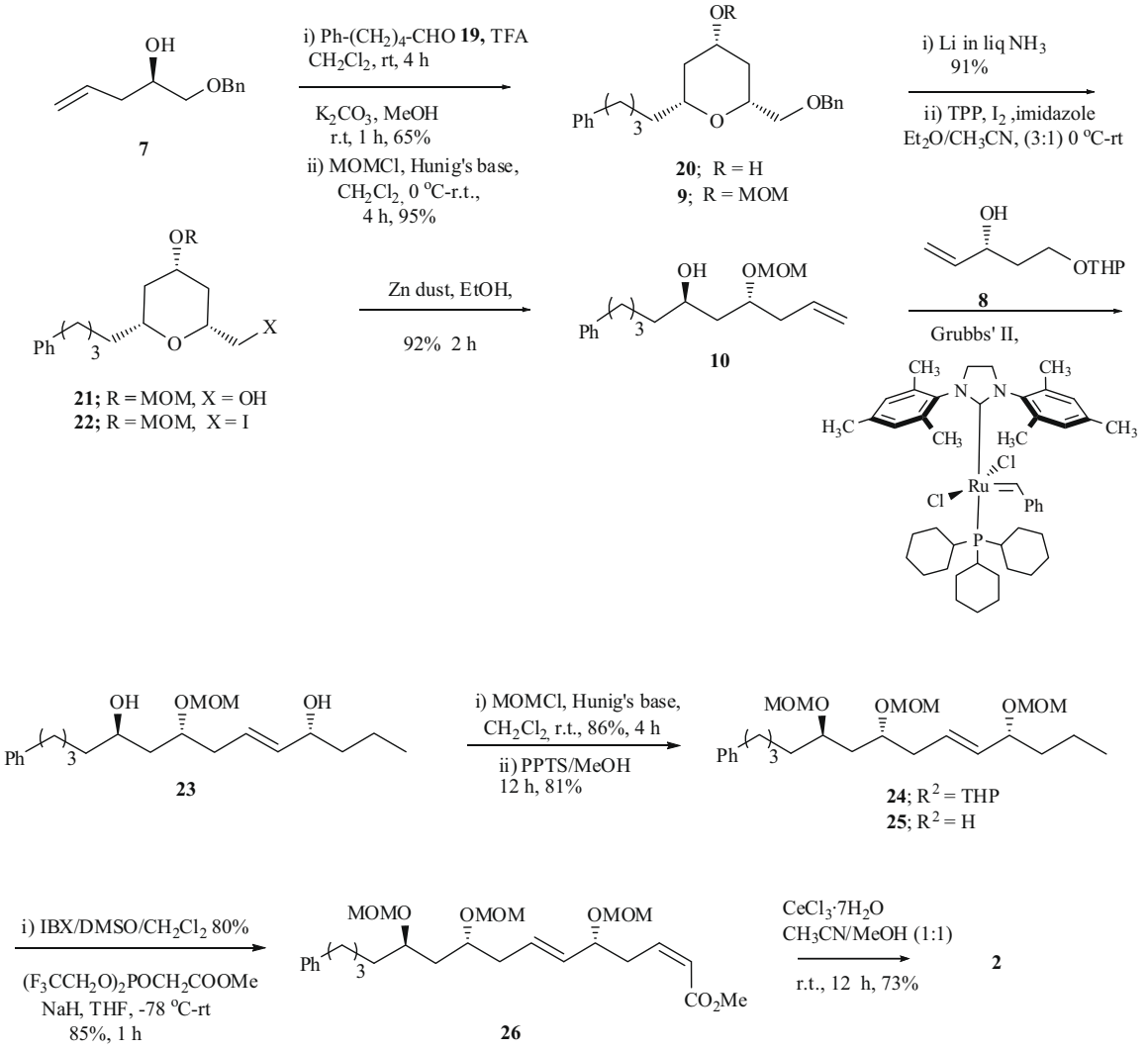
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

metathesis (CM) reaction to control the (*E*)-double bond at C1′–C2′ and removal of MOM protecting groups under neutral conditions. Further studies on the utility of the vinyl lactone for other molecules are currently in progress and will be reported in due course.

4. Experimental

4.1. General

Reactions were conducted under N_2 in anhydrous solvents such as CH_2Cl_2, THF, and EtOAc. All reactions were monitored by TLC (silica-coated plates and visualizing under UV light). Light petroleum ether (bp 60–80 °C) was used. Yields refer to chromatographically 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 of samples in $CDCl_3$ were recorded on Varian FT-200 MHz (Gemini) and Bruker UXNMR FT-300 MHz (Avance) spectrometers. Chemical shifts (δ) are reported relative to TMS (δ = 0.0) as an internal standard. Mass spectra were recorded in E1 conditions at 70 eV on an LC-MSD (Agilent technologies) spectrometers. All high resolution spectra were recorded on QSTAR XL hybrid ms/ms system (Applied Biosystems/MDS sciex, foster city, USA), equipped with an ESI source (IICT, Hyderabad). 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. Optical rotations were measured with JASCO DIP-370 Polarimeter at 25 °C.

4.1.1. (3*S*)-5-(Tetrahydro-2*H*-2-pyranyloxy)-1-penten-3-ol 8

A mixture of epoxy iodo compound (7.0 g, 22.4 mmol), NaI (8.35 g, 56.08 mmol) and activated Zn dust (4.39 g, 67.73 mmol) in methanol (30 mL) was refluxed under N_2 atm for 3 h. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography to afford the **8** as a yellow liquid (9.6 g, 80%). $[\alpha]_D^{25} = -9.6$ (*c* 3.75, $CHCl_3$) ^1H NMR ($CDCl_3$, 300 MHz): δ 5.92–5.80 (m, 1H), 5.31–5.06 (m, 2H), 4.60–4.55 (m, 1H), 4.36–4.26 (m, 1H), 4.00H–4.34 (m, 4H), 2.74 (s, OH, 1H), 1.91–1.47 (m, 8H). ^{13}C NMR ($CDCl_3$, 50 MHz): 140.4, 114.2, 98.8, 71.9, 65.6, 62.1, 36.2, 30.4, 25.2, 19.3. ESIMS: 209 (M+Na).

4.1.2. (3*S*)-3-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-4-penten-1-ol 17

To the THP ether (2.5 g, 7.81 mmol) in methanol (20 mL), commercial NH_4Cl (0.49 g, 9.36 mmol) was added and heated at reflux for 4 h. Methanol was removed, diluted with water (15 mL), and extracted with ether (3 × 25 mL). The combined ether extracts were dried over Na_2SO_4. Evaporation of solvent, followed by

column chromatography (ethylacetate/pet ether, 4:6) furnished THP cleaved product (1.01 g, 60% yield). $[\alpha]_D^{25} = +1.9$ (*c* 1.2, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.90–5.77 (m, 1H), 5.24–5.05 (m, 2H), 4.43–4.35 (m, 1H), 3.84–3.64 (m, 2H), 2.13 (br s, OH, 1H), 1.88–1.62 (m, 2H), 0.92 (s, 9H), 0.06 (s, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 140.6, 114.3, 73.1, 60.1, 39.1, 25.8, 18.1, −4.4. ESIMS: 239 (M+Na).

4.1.3. Methyl(2*Z*,5*S*)-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-2,6-heptadienoate 18

To a stirred suspension of NaH (1.06 g, 46.4 mmol) in dry THF (40 mL) at 0 °C under nitrogen was added bis-(2,2,2-trifluoroethyl) (methoxy-carbonylmethyl) phosphonate (8.09 g, 25.07 mmol) in dry THF (20 mL). After the mixture was stirred for 30 min at 0 °C, the reaction mixture was cooled to −78 °C, and then a solution of aldehyde (5 g, 23.3 mmol) in dry THF (20 mL) was added dropwise. After stirring for 1 h, the reaction mixture was diluted with 5 mL of Et_2O and quenched by the slow addition of 4 mL of H_2O. The layers were separated, and the aqueous phase was extracted with two 10 mL portions of Et_2O. The organic extract was washed with brine solution, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel to give α,β-unsaturated ester **18** (4.7 g, 75%) as a viscous liquid. $[\alpha]_D^{25} = -8.1$ (*c* 0.5, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 6.30 (dt, *J* = 4.5, 6.7 Hz, 1H), 5.86–5.73 (m, 2H), 5.23–5.03 (qt, *J* = 2.2, 1.5 Hz, 2H), 4.27 (q, 1H), 3.69 (s, 3H), 2.86 (dt, *J* = 2.2, 1.5 Hz, 2H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 158.8, 146.3, 120.5, 72.4, 51.0, 37.0, 29.6, 25.7, −4.7.

4.1.4. (6*R*)-6-Vinyl-5,6-dihydro-2*H*-2-pyranone 5

To a stirred solution of compound **18** (0.5 g, 1.96 mmol) in MeOH was added a catalytic amount of PTSA under an N_2 atmosphere. After stirring for 3 h at room temperature, the reaction mixture was quenched with solid $NaHCO_3$ and filtered off, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography to afford compound **5** as a yellow liquid (019 g, 80%). ^1H NMR ($CDCl_3$, 300 MHz): δ 6.87–6.80 (m, 1H), 6.06–5.87 (m, 2H), 5.45–5.37 (t, 1H, *J* = 1.1 Hz), 5.32–5.26 (t, 1H), 4.95–4.86 (m, 1H), 2.47–2.41 (m, 2H): ^{13}C NMR ($CDCl_3$, 50 MHz): δ 163.7, 144.3, 134.8, 121.6, 117.8, 77.7, 29.3; HRMS: calcd 147.0429 (M+Na); found 147.0421 (M+Na). $[\alpha]_D^{25} = +95.2$ (*c* 0.85, $CHCl_3$).

4.1.5. (2*R*,4*R*,6*S*)-2-[(Benzyloxy)methyl]-4-(methoxymethoxy)-6-phenyltetrahydro-2*H*-pyran 6

To a solution of hydroxyl compound (2.5 g, 8.38 mmol) in anhydrous DCM (10 mL) at 0 °C under nitrogen was added $^iPr_2NEt$ (6.54 g, 50.28 mmol) dropwise and after 5 min MOMCl (3.08 mL, 41.9 mmol) was added dropwise. After stirring for 2 h at room temperature, the reaction mixture was diluted with water, saturated aqueous NH_4Cl, and brine solution, then dried over anhydrous Na_2SO_4. The residue was purified on silica gel column chromatography to afford pure **6** as a clear colorless liquid (2.57 g, 90%). $[\alpha]_D^{25} = -13$ (*c* 0.3, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.33–7.21 (m, 10H), 4.66 (s, 2H), 4.57 (s, 2H), 4.37 (m, 1H), 3.93–3.80 (m, 1H), 3.77–3.67 (m, 1H), 3.66–3.47 (m, 2H), 3.34 (s, 3H), 2.23–2.08 (tq, *J* = 2.6 Hz, 2H), 1.56–1.28 (m, 2H).^{13}C NMR ($CDCl_3$, 50 MHz): δ 141.9, 137.5, 128.3, 128.2, 127.6, 127.5, 127.4, 125.9, 94.4, 77.8, 75.5, 73.4, 73.1, 73.0, 55.3, 40.5, 35.2. ESIMS: 365 (M+Na).

4.1.6. (2*S*,4*S*)-4-(Ethylperoxy)-6-phenylhexane-1,2-diol 12

To a solution of lithium (0.13 g, 43.8 mmol) in liquid NH_3 (25 mL) was added compound **6** (2.5 g, 7.3 mmol) in dry THF (8 mL). The mixture was stirred for 2–3 h and quenched with solid NH_4Cl (1.36 g). Ammonia was allowed to evaporate and the residual mixture was taken in ether (35 mL) and washed with water (2 × 10 mL), brine (1 × 10 mL), and dried over Na_2SO_4. Removal of the solvent and purification by column chromatography of the crude product afforded alcohol **12** (1.1 g, 60%) as a colorless liquid. R_f = 0.5 (SiO_2, 20% EtOAc in hexane). $[\alpha]_D^{25} = +41$ (*c* 2.4, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.31–7.13 (m, 5H), 4.69 (s, 2H), 4.02–3.80 (m, 2H), 3.65–3.55 (m, 1H), 3.48–3.38 (m, 4H), 3.24 (s, OH, 1H), 2.77–2.59 (td, 2H, *J* = 3.0, 6.0 Hz), 2.00–1.50 (m, 4H): ^{13}C NMR ($CDCl_3$, 50 MHz): δ: 141.76, 128.42, 128.23, 125.92, 96.50, 75.75, 68.51, 66.84, 55.97, 37.37, 36.81, 31.64 HRMS: calcd 277.1415 (M+Na), found 147.1423 (M+Na).

4.1.7. (2*R*)-2-[(2*S*)-2-(Methoxymethoxy)-4-phenylbutyl] oxetane 14

To a stirred suspension of freshly activated sodium hydride (0.32 g, 14.1 mmol) in dry THF (30 mL) at 0 °C, compound **13** (4 g, 9.45 mmol) in dry THF (10 mL) was added dropwise. After completion of the reaction (3 h), the reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc. The organic layer was washed with brine solution, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure, purification by silica-gel column chromatography afforded **14** (1.9 g, 85%) as a viscous liquid. $[\alpha]_D^{25} = +12.3$ (*c* 2.1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.30–7.19 (m, 5H), 4.71 (s, 2H), 3.87–3.75 (tt, *J* = 6.04, 12.08, 15.10 Hz, 1H), 3.43 (s, 3H), 3.05–2.97 (m, 1H), 2.81–2.60 (m, 2H), 2.50–2.46 (m, 1H), 1.98–1.57 (m, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 141.86, 128.31, 128.2, 125.76, 95.7, 75.18, 55.59, 49.42, 47.29, 37.86, 36.7, 31.38. HRMS calcd 259.1310 (M+Na), found 259.1320 (M+Na).

4.1.8. (4*R*,6*S*)-6-(Methoxymethoxy)-8-phenyl-1-octyn-4-ol 15

A lithium acetylide-EDA complex (0.33 g 19.4 mmol) was added to a solution of epoxide **14** (2 g, 8.47 mmol) in dry DMSO (22 mL), and the mixture was stirred overnight at room temperature. After quenching with ice, 0.5 M H_2SO_4 was used to neutralize the basic solution to pH 7. The solution was extracted with diethyl ether (3 × 50 mL), dried over $MgSO_4$, and concentrated in vacuo to give **15** (1.77 g, 80%) as a colorless oil. $[\alpha]_D^{25} = +40.7$ (*c* 1.95, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.27–7.10 (m, 5H), 4.65 (s, 2H), 4.07–3.96 (m, 1H), 3.90–3.80 (m, 1H), 3.41 (s, 3H), 2.92 (br s, 1H, OH), 2.70–2.61 (td, *J* = 2.83, 3.77 Hz, 2H), 2.40–2.33 (m, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.94–1.66 (m, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 141.6, 128.3, 128.1, 125.1, 96.4, 80.9, 75.6, 70.5, 66.4, 55.8, 40.2, 36.6, 31.6, 27.2. HRMS: calcd 285.1466 (M+Na), found 285.1478 (M+Na).

4.1.9. (4*R*,6*S*)-6-(Ethylperoxy)-8-phenyl-1-octen-4ol 16

To solution of alkyne **15** (10 g, 38.02 mmol) in EtOAc, 3 drops of quinoline and Lindlar's catalyst ($Pd/BaSO_4$) were added and stirred at room temperature under an H_2 atm for 12 h. After completion of the reaction, the reaction mixture was filtered and the solvent was removed under reduced pressure. The crude product was purified on silica gel column chromatography to afford compound **16** as a yellow liquid (8.46 g, 85%). $[\alpha]_D^{25} = +35.5$ (*c* 1.6, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.28–7.08 (m, 5H), 5.94–5.70 (m, 1H), 5.14–5.03 (dt, 2H, *J* = 5.8, 11.7 Hz), 4.64 (s, 2H), 3.86 (td, 2H, *J* = 5.8, 11.7 Hz), 3.40 (s, 3H), 2.70–2.59 (m, 2H), 2.20 (td, 2H, *J* = 7.3, 5.8, 1.4 Hz), 1.99–1.55 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 141.8, 134.8, 128.4, 128.2, 125.8, 117.5, 96.4, 75.7, 67.1, 55.8, 42.0, 40.8, 36.7, 31.6; HRMS: calcd 287.1623 (M+Na), found 287.1615 (M+Na).

4.1.10. (3*S*,5*R*)-1-Phenyl-7-octene-3,5-diol 4

To a stirred solution of compound **16** (0.3 g, 1.13 mmol) in a mixture of MeOH (5 mL) and CH_3CN (5 mL) was added $CeCl_3{\cdot}7H_2O$ (cat.) under N_2,[12] then the mixture was stirred at rt for 12 h. The mixture was quenched with solid $NaHCO_3$ (0.5 g) and filtered,

the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (8:13 EtOAc/hexane) to afford compound **4** as a yellow liquid (0.15 g, 60% yield), ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.28–7.9 (m, 5H), 5.85–5.70 (m, 1H), 5.16–5.08 (m, 2H), 4.02–3.88 (m, 2H), 2.85–2.59 (m, 2H), 2.28–2.19 (m, 2H), 1.92–1.59 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 141.9, 134.5, 128.3, 125.8, 118.2, 68.6, 68.1, 41.9, 39.0, 32.1; HRMS: calcd 243.1360 (M+Na), found 243.1371 (M+Na).

4.1.11. (6*R*)-6-[(*E*,4*S*,6*S*)-4,6-Dihydroxy-8-phenyl-1-octenyl]-5,6-dihydro-2*H*-2-pyranone 1

A solution of compound **4** (0.152 g, 0.69 mmol) and compound **5** (0.438 g, 3.45 mmol) in dichloromethane (100 mL) was first bubbled with nitrogen flow, after which Grubbs type **II** catalyst (0.089 g, 0.103 mmol) was added at once and the resulting mixture heated under nitrogen at 50 °C for 4 h. After cooling and concentration, the solvent was removed and the crude mixture was purified by flash chromatography (AcOEt/hexanes: 20/80) to give lactone **1** (0.119 g, 63%) as a white solid. mp: 109–114 °C: $[\alpha]_D^{37} = +37.8$ (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.29–7.07 (m, 5 H), 6.84 (ddd, 1H, *J* = 9.5, 4.4, 3.6 Hz), 6.00 (dt, 1H, *J* = 9.5, 2.2 Hz), 5.86 (ddt, 1H, *J* = 15.4, 7.3, 1.4 Hz), 5.6 (dd, 1H, *J* = 15.5, 6.5 Hz), 4.86 (m, 1H), 3.95 (m, 2H), 2.87–2.57 (m, 2H), 2.42–2.40 (m, 2H), 2.28–2.23 (m, 2H), 1.90–1.71 (m, 2H), 1.62 (t, 2H, *J* = 5.5 Hz) ^{13}C NMR ($CDCl_3$, 50 MHz): δ 163.8, 144.7, 141.8, 131.1, 129.9, 128.4, 128.3, 125.8, 121.5, 77.7, 68.7, 68.2, 42.1, 40.3, 38.9, 38.1, 29.7; HRMS: calcd 339.1572 (M+Na), found 339.1573 (M+Na).

4.1.12. (2*R*,4*R*,6*R*)-2-[(benzyloxy)methyl]-6-(4-phenylbutyl) tetrahydro-2*H*-4-pyranol 20

Trifluoroacetic acid (80.2 mL, 1041.6 mmol) was added slowly to a solution of homoallylic alcohol **7** (10.0 g, 52.0 mmol) and 5-phenyl-1-pentanal **19** (25.3 g, 156.0 mmol) in CH_2Cl_2 (200 mL) at room temperature under a nitrogen atmosphere. The reaction mixture was stirred for 4 h and then saturated aqueous sodium hydrogen carbonate solution (200 mL) was added and the pH adjusted to >7 by the addition of triethylamine. The layers were then separated and the aqueous layer was extracted with CH_2Cl_2 (4 × 60 mL). The organic layers were combined, dried over anhydrous Na_2SO_4 (3 g), and the solvent was removed under reduced pressure. The residue was dissolved in methanol (75 mL) and stirred with potassium carbonate (14.4 g, 104 mmol) for 1 h. After removing MeOH under reduced pressure, water (50 mL) was added. The mixture was extracted with dichloromethane (3 × 50 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 (3 g) and the solvent was removed under reduced pressure. Column chromatography (1:4 EtOAc/hexane) afforded pure product **20** (11.9 g, 65% yield) as a colorless liquid. R_f = 0.4 (SiO_2, 20% EtOAc in hexane); $[\alpha]_D^{25} = +10.0$ (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.33–7.07 (m, 10H), 4.54 (q, *J* = 12.2, 15.2 Hz, 2H), 3.79–3.68 (m, 1H), 3.54–3.36 (m, 3H), 3.31–3.21 (m, 1H), 2.59 (t, *J* = 7.3 Hz, 2H), 1.98–1.83 (m, 2H), 1.68–1.04 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 142.5, 138.2, 128.3, 128.2, 127.6, 127.5, 125.5, 75.6, 74.9, 73.3, 73.1, 68.0, 40.9, 37.8, 35.8, 35.7, 31.4, 25.2; IR (neat): 3408, 2933, 2856, 1602, 1496, 1452, 1367, 1323, 1105, 1032, 741, 698 cm^{-1}; HRMS(ESI.): [M+Na]$^+$ *m/z* calcd for $C_{23}H_{30}O_3Na$: 377.2092; found 377.2106; (+3.5396 ppm error).

4.1.13. (2*R*,4*R*,6*R*)-2-[(Benzyloxy)methyl]-4-(methoxymethoxy) -6-(4-phenylbutyl)tetrahydro-2*H*-pyran 9

To alcohol **20** (9.5 g, 26.8 mmol) in anhydrous CH_2Cl_2 (50 mL) at 0 °C were added diisopropyl ethylamine (10.38 g, 80.5 mmol), catalytic DMAP (10 mg) and MOMCl (4.2 g, 53.6 mmol) successively and the mixture was stirred for 4 h at room temperature, quenched by adding water (20 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The organic extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4 (2 g), and concentrated under vacuum to remove the solvent and the crude residue was purified by column chromatography (2:23 EtOAc/hexane) to afford the MOM ether **9** (10.2 g, 95% yield) as a colorless oil. R_f = 0.4 (SiO_2, 15% EtOAc in hexane); $[\alpha]_D^{25} = +5.7$ (*c* 1.02, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) = 7.32–7.02 (m, 10H), 4.62 (s, 2H), 4.54 (q, *J* = 11.0, 13.2 Hz, 2H), 3.75–3.57 (m, 1H), 3.55–3.19 (m, 7H), 2.60 (t, *J* = 7.3 Hz, 2H), 2.03–1.84 (m, 2H), 1.73–1.05 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 142.4, 138.2, 128.2, 128.1, 127.5, 127.4, 125.4, 94.2, 75.7, 74.9, 73.3, 73.1, 72.8, 55.2, 38.4, 35.9, 35.8, 35.3, 31.4, 25.2; IR (neat): 2927, 2857, 1602, 1494, 1452, 1369, 1102, 1038, 741, 699 cm^{-1}; HRMS(ESI): [M+Na]$^+$ *m/z* calcd for $C_{25}H_{34}O_4Na$: 421.2354; found: 421.2341 (−3.2751 ppm error).

4.1.14. [(2*R*,4*R*,6*R*)-4-(Methoxymethoxy)-6-(4-phenylbutyl) tetrahydro-2*H*-2-pyranyl]methanol 21

Lithium metal (500 mg, 71.6 mmol) was added to a stirred solution of freshly distilled ammonia (10 mL) and compound **9** (9.5 g, 23.8 mmol) in dry THF (50 mL) in a 250 mL two necked round bottomed flask fitted with a cold finger condenser at −33 °C. The reaction mixture was then stirred for another 10 min at −33 °C and quenched by the addition of solid ammonium chloride (5 g) and the ammonia was then allowed to evaporate. The residue left was partitioned between water (5 mL) and ether (10 mL) and the aqueous phase was extracted with ether. The combined organic layers were washed with water (2 mL), brine (2 mL), dried over anhydrous Na_2SO_4 (3 g), and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 EtOAc/hexane) to afford pure **21** (6.69 g, 91% yield) as a clear colorless liquid. R_f = 0.4 (SiO_2, 40% EtOAc in hexane); $[\alpha]_D^{25} = +3.0$ (*c* 0.32, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) = 7.30–7.02 (m, 5H), 4.63 (s, 2H), 3.78–3.23 (m, 8H), 2.60 (t, *J* = 7.2 Hz, 2H), 1.99–1.76 (m, 2H), 1.73–1.08 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 142.4, 128.3, 128.1, 125.6, 94.3, 75.9, 75.5, 72.8, 65.9, 55.2, 38.4, 35.8, 35.7, 34.2, 31.3, 25.0; IR (neat): 3462, 2930, 2856, 1603, 1494, 1453, 1374, 1101, 1037, 748, 700 cm^{-1}; HRMS (ESI): [M+Na]$^+$ *m/z* calcd for $C_{18}H_{28}O_4Na$: 331.1885, found: 331.1882 (-0.9945 ppm error).

4.1.15. (2*R*,4*R*,6*R*)-2-(Iodomethyl)-4-(methoxymethoxy)-6-(4-phenylbutyl)tetrahydro-2*H*-pyran 22

To a stirred solution of **21** (6.0 g, 19.4 mmol) in a mixture of 45 mL of dry ether and 15 mL of dry CH_3CN was added TPP (7.6 g, 29.2 mmol), imidazole (3.31 g, 48.7 mmol), and iodine (5.91 g, 23.3 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 20 min, after which the solids were filtered and washed with ether (15 mL). The filtrate was extracted with ether (2 × 10 mL), washed with 10% aqueous $Na_2S_2O_3$ solution (10 mL), water (5 mL), brine (5 mL) solution, and dried over anhydrous Na_2SO_4 (2 g). The residue was concentrated under reduced pressure. Column chromatography (2:23 EtOAc/hexane) afforded pure product **22** (7.49 g, 92% yield) as a colorless liquid. R_f = 0.4 (SiO_2, 10% EtOAc in hexane); ^{1}H NMR (200 MHz, $CDCl_3$): δ (ppm) = 7.29–7.02 (m, 5H), 4.62 (s, 2H), 3.77–3.57 (m, 1H), 3.39–3.08 (m, 7H), 2.60 (t, *J* = 6.8, 2H), 2.24–2.10 (m, 1H), 1.94–1.78 (m, 1H), 1.74–1.04 (m, 8H); IR (neat): 3024, 2935, 2854, 1602, 1495, 1452, 1369, 1147, 1099, 1039, 746, 700 cm^{-1}; ESI-MS: *m/z* 441 [M+Na]$^+$.

4.1.16. (5*R*,7*R*)-7-(Methoxymethoxy)-1-phenyl-9-decen-5-ol 10

A solution of compound **22** (6.0 g, 14.3 mmol) in ethanol (50 mL) was added to zinc dust (18.6 g, 287.0 mmol) in a 250 mL round bottomed flask. The reaction mixture was stirred at reflux for 2 h and then Et_2O (10 mL) and NH_4Cl (3 g) were added to the reaction mixture at 0 °C. The mixture was allowed to stir at room temperature for 1 h and then filtered through Buckner funnel-flask setup and the filtrate was concentrated under reduced pressure.

Column chromatography (3:22 EtOAc/hexane) afforded pure product **10** (3.8 g, 92% yield) as a colorless liquid. R_f = 0.4 (SiO_2, 10% EtOAc in hexane); $[\alpha]_D^{25} = -30.5$ (*c* 1.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.23–7.02 (m, 5H), 5.82–5.66 (m, 1H), 5.11–5.01 (m, 2H), 4.66 (d, *J* = 6.7 Hz, 1H), 4.59 (d, *J* = 6.7 Hz, 1H), 3.89–3.75 (m, 2H), 3.38 (s, 3H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.40–2.19 (m, 2H), 1.76–1.20 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 142.5, 134.2, 128.2, 128.1, 125.5, 117.4, 96.1, 75.1, 67.5, 55.6, 41.2, 39.3, 37.8, 35.8, 31.4, 25.3; IR (neat): 3462, 3025, 2933, 2856, 1641, 1602, 1494, 1449, 1372, 1213, 1149, 1098, 1036, 915, 750, 699 cm^{-1}; HRMS (ESI): $[M+Na]^+$ *m/z* calcd for $C_{18}H_{28}O_3Na$: 315.1936, found: 315.1932; (−1.3158 ppm error).

4.1.17. (3*R*,4*E*,7*R*,9*R*)-7-(Methoxymethoxy)-13-phenyl-1-(tetrahydro-2*H*-2-pyranyloxy)-4-tridecene-3,9-diol 23

Grubbs' second generation catalyst (0.145 g, 0.17 mmol, 10 mol %) was dissolved in 10 mL of CH_2Cl_2 and was added dropwise to a solution of compound **10** (1.0 g, 3.4 mmol) and compound **8** (1.2 g, 6.8 mmol) in 100 mL of CH_2Cl_2 at 0 °C. After completion of addition, reaction mixture was allowed to stir for 1 h. The solvent was removed under reduced pressure and the crude product was purified by silica gel column chromatography (11:9 EtOAc/hexane) to afford the pure product **23** (1.04 g, 68% yield) as a colorless liquid. R_f = 0.2 (SiO_2, 50% EtOAc in hexane); $[\alpha]_D^{25} = -18.0$ (*c* 1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ (ppm) = 7.28–7.02 (m, 5H), 5.72–5.45 (m, 2H), 4.76–4.52 (m, 3H), 4.32–4.21 (m, 1H), 4.0–3.71 (m, 4H), 3.63–3.42 (m, 2H), 3.38 (s, 3H), 2.61 (t, *J* = 6.8 Hz, 2H), 2.42–2.14 (m, 2H), 1.88–1.24 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 142.6, 135.5, 128.3, 128.1, 126.4, 125.5, 98.8, 96.2, 75.4, 70.8, 67.6, 65.5, 62.1, 55.7, 41.2, 37.7, 37.3, 36.6, 35.9, 31.5, 30.4, 25.4, 25.2, 19.3; IR (neat): 3435, 2932, 1733, 1641, 1604, 1447, 1031, 910, 810, 754, 699 cm^{-1}; HRMS (ESI): $[M+Na]^+$ *m/z* calcd for $C_{26}H_{42}O_6Na$: 473.2879; found: 473.2883 $[M+Na]^+$ (+0.8256 ppm error).

4.1.18. 2-[(3*R*,4*E*,7*R*,9*R*)-3,7,9-Tri(methoxymethoxy)-13-phenyl-4-tridecenyl]oxytetrahydro-2*H*-pyran 24

To the diol **23** (0.785 g, 1.74 mmol) in anhydrous CH_2Cl_2 (15 mL) at 0 °C were added diisopropylethylamine (0.56 g, 6.1 mmol), a catalytic amount of DMAP (5 mg), and MOMCl (0.4 g, 5.23 mmol) successively and the mixture was stirred for 4 h at room temperature, quenched by adding water (10 mL), and extracted with CH_2Cl_2 (3 × 10 mL). The organic extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4 (2 g), and concentrated under vacuum to remove the solvent. The crude residue was purified by column chromatography (1:4 EtOAc/hexane) to afford compound **24** (0.8 g, 86% yield) as a colorless oil. R_f = 0.3 (SiO_2, 20% EtOAc in hexane); $[\alpha]_D^{25} = +9.3$ (*c* 1.2, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ (ppm) = 7.33–7.02 (m, 5H), 5.74–5.54 (m, 1H), 5.41–5.26 (m, 1H), 4.78–4.51 (m, 6H), 4.49–4.41 (m, 1H), 4.19–4.04 (m, 1H), 3.90–3.56 (m, 4H), 3.52–3.30 (m, 11H), 2.60 (t, *J* = 7.3 Hz, 2H), 2.35–2.24 (m, 2H), 1.95–1.22 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 142.4, 132.6, 129.6, 128.2, 128.1, 125.5, 98.8, 96.0, 93.3, 75.0, 74.5, 73.9, 73.5, 63.9, 63.8, 62.1, 55.5, 55.2, 40.1, 38.1, 35.8, 35.0, 31.6, 30.6, 25.4, 24.5, 19.5; IR (neat): 2930, 1448, 1374, 1209, 980, 917, 751,700 cm^{-1}; HRMS (ESI): $[M+Na]^+$ *m/z* calcd for $C_{30}H_{50}O_8Na$: 561.3403; found: 561.3408 (+0.8215 ppm error).

4.1.19. (3*R*,4*E*,7*R*,9*R*)-3,7,9-Tri(methoxymethoxy)-13-phenyl-4-tridecen-1-ol 25

To a stirred solution of compound **24** (0.750 g, 1.39 mmol) in MeOH (15 mL) was added a catalytic amount of pyridinium *p*-toluenesulfonate under a nitrogen atmosphere. After stirring for 12 h at room temperature, the reaction mixture was quenched with solid $NaHCO_3$ (1 g) and filtered off, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography to afford compound **25** as a pale yellow liquid (0.512 g, 81% yield). R_f = 0.3 (SiO_2, 50% EtOAc in hexane); $[\alpha]_D^{25} = +18.5$ (*c* 1.3, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ (ppm) = 7.28–7.02 (m, 5H), 5.75–5.58 (m, 1H), 5.44–5.29 (m, 1H), 4.74–4.54 (m, 6H), 4.49–4.42 (m, 1H), 4.27–4.13 (m, 1H), 3.79–3.58 (m, 4H), 3.39–3.30 (m, 9H), 2.60 (t, *J* = 8.0 Hz, 2H), 2.35–2.23 (m, 2H), 1.86–1.22 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 142.4, 132.2, 129.9, 128.2, 128.1, 125.5, 96.0, 95.8, 93.3, 75.4, 75.1, 74.6, 59.8, 55.5, 55.4, 40.1, 38.0, 37.8, 35.8, 34.9, 31.5, 24.5; IR (neat): 3477, 2928, 2854, 1448, 1376, 1213, 1035, 917, 750, 699 cm^{-1}; HRMS (ESI): $[M+Na]^+$ *m/z* calcd for $C_{25}H_{42}O_7Na$: 477.2828; found: 477.2834 (+1.2071 ppm error).

4.1.20. Methyl (2*Z*,5*R*,6*E*,9*R*,11*R*)-5,9,11-tri(methoxymethoxy)-15-phenyl-2,6-pentadecadienoate 26

To an ice-cooled solution of 2-iodoxybenzoic acid (0.446 g, 1.65 mmol) in dry DMSO (4.5 mL, 63.22 mmol) was added a solution of alcohol **25** (0.5 g, 1.10 mmol) in dry CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for 2 h and then filtered through a Celite pad and washed with Et_2O (15 mL). The combined organic filtrates were washed with H_2O (2 × 5 mL) and brine (5 mL), dried over anhydrous Na_2SO_4 (2 g), and concentrated in vacuo. The unstable crude aldehyde product was used for further reaction. In a 50 mL round bottomed flask, NaH (0.0318 g, 1.32 mmol) was taken and to it 4 mL of dry THF was added under an N_2 atmosphere. After 5 min, bis-(2,2,2-trifluoroethyl)(methoxycarbonyl methyl)] phosphonate (0.281 g, 0.884 mmol) in 2 mL of dry THF was added at 0 °C. It was allowed to stir for 30 min. The reaction mixture was cooled to −78 °C and the above crude aldehyde (0.4 g, 0.884 mmol) in dry THF (2 mL) was added over a period of 10 min after which the resulting mixture was stirred for 1 h at −78 °C. The reaction mixture was quenched with saturated NH_4Cl (5 mL) and the product was extracted into ether (2 × 10 mL). The organic layer was dried over anhydrous Na_2SO_4 (2 g) and evaporated in vacuo (water bath temperature should not exceed 35 °C) and the product was purified using silica gel column chromatography (3:17 EtOAc/hexane) to afford (*Z*)-olefin ester **26** as light yellow liquid (0.382 g, 85% yield). R_f = 0.3 (SiO_2, 20% EtOAc in hexane); $[\alpha]_D^{25} = +15.0$ (*c* 1.05, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.24–7.02 (m, 5H), 6.34–6.23 (m, 1H), 5.81 (d, *J* = 11.5 Hz, 1H), 5.72–5.59 (m, 1H), 5.42–5.29 (m, 1H), 4.69–4.52 (m, 6H), 4.51–4.41 (m, 1H), 4.14–4.04 (m, 1H), 3.76–3.58 (m, 4H), 3.35–3.29 (m, 9H), 2.95–2.86 (m, 2H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.33–2.25 (m, 2H), 1.68–1.22 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 166.6, 145.9, 142.5, 132.0, 130.1, 128.3, 128.2, 125.6, 120.7, 96.1, 96.0, 93.5, 75.7, 75.2, 74.6, 55.6, 55.4, 51.0, 40.3, 38.2, 35.9, 35.1, 34.9, 31.6, 24.6; IR (neat): 2929, 1723, 1645, 1440, 1097, 1036, 917, 820, 749, 699 cm^{-1}; HRMS (ESI): $[M+Na]^+$ *m/z* calcd for $C_{28}H_{44}O_8Na$: 531.2933; found: 531.2942 (+1.5272 ppm error).

4.1.21. (6*R*)-6-[(*E*,4*R*,6*R*)-4,6-Dihydroxy-10-phenyl-1-decenyl]-5,6-dihydro-2*H*-2-pyranone 2

To a stirred solution of compound **14** (0.3 g, 0.59 mmol) in a mixture of MeOH (5 mL) and CH_3CN (5 mL) was added $CeCl_3 \cdot 7H_2O$ (cat.) under N_2,[12] then the mixture was stirred at rt for 12 h. The mixture was quenched with solid $NaHCO_3$ (0.5 g) and filtered. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (7:13 EtOAc/hexane) to afford compound **2** as a white solid (0.148 g, 73% yield), mp: 64–66 °C. R_f = 0.2 (SiO_2, 70% EtOAc in hexane); $[\alpha]_D^{25} = +52.5$ (*c* 0.25, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ (ppm) = 7.27–7.01 (m, 5H), 6.88–6.78 (m, 1H), 6.01 (d, *J* = 9.8 Hz, 1H), 5.85 (ddd, *J* = 7.5, 7.5, 15.1 Hz, 1H), 5.64 (dd, *J* = 6.0, 15.1 Hz, 1H), 4.86 (q, *J* = 7.5, 14.3 Hz, 1H), 4.05–3.78 (m, 2H), 3.0 (br s, 2-OH), 2.60 (t,

J = 7.5 Hz, 2H), 2.45–2.36 (m, 2H), 2.29–2.18 (m, 2H), 1.68–1.58 (m, 2H), 1.54–1.39 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 164.1, 144.7, 142.4, 131.4, 129.7, 128.3, 128.2, 125.6, 121.4, 77.8, 69.2, 68.2, 42.0, 40.3, 37.3, 35.8, 31.3, 29.7, 25.4; IR (neat): 3404, 2925, 2854, 1706, 1492, 1455, 1383, 1257, 1204, 1139, 1021, 971, 817, 749, 700 cm^{-1}; HRMS (ESI): $[M+Na]^+$ m/z calcd for $C_{21}H_{28}O_4Na$: 367.1909; found: 367.1925 (+4.2630 ppm error).

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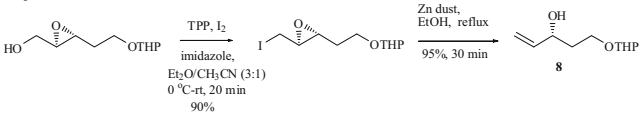
References

1. (a) Rychnovsky, S. D. *Chem. Rev.* **1995**, *95*, 2021–2040; (b) Kobayashi, M.; Higuchi, K.; Murakami, N.; Tajima, H.; Aoki, S. *Tetrahedron Lett.* **1997**, *38*, 2859–2862.
2. (a) Jodynis-Licbert, J.; Murias, M.; Bloszyik, E. *Planta Med.* **2000**, *66*, 199–205; (b) Drewes, S. E.; Schlapelo, B. M.; Horn, M. M.; Scott-Shaw, R.; Sander, O. *Phytochemistry* **1995**, *38*, 1427–1430.
3. Juliawaty, L. D.; Kitajima, M.; Takayama, H.; Achmad, S. A.; Aimi, N. *Phytochemistry* **2000**, *54*, 989–993.
4. Juliawaty, L. D.; Watanabe, Y.; Kitajima, M.; Takayama, H.; Achmad, S. A.; Takayama, H.; Aimi, N. *Tetrahedron Lett.* **2002**, *43*, 8657–8660.
5. (a) Bouz, B. S.; Cossy, J. *Org. Lett.* **2003**, *5*, 1995–1997; (b) Enders, D.; Lenzen, A.; Muller, M. *Synthesis* **2004**, 1486–1496.
6. Tosaki, S.-Y.; Nemoto, T.; Ohshima, T.; Shibaski, M. *Org. Lett.* **2003**, *5*, 495–498.
7. Raoelison, G. E.; Terreaux, C.; Queiroz, E. F.; Zsila, F.; Simonyi, M.; Antus, S.; Randriantsova, A.; Hostettmann, K. *Helv. Chim. Acta* **2001**, *84*, 3470–3476.
8. Sabitha, G.; Srinivas, Ch.; Sudhakar, K.; Rajkumar, M.; Maruthi, C.; Yadav, J. S. *Synthesis* **2007**, *24*, 3886–3890.
9. Queiroz, E.-F.; Wolfender, J.-L.; Raoelison, G.; Hostettmann, K. *Phytochem-Anal.* **2003**, *14*, 34–39.
10. Krishna, P. R.; Srinivas, R. *Tetrahedron Lett.* **2007**, *48*, 2013–2015.
11. Sabitha, G.; Narjis, F.; Reddy, E. V.; Yadav, J. S. *Tetrahedron Lett* **2008**, *48*, 6087–6089.
12. Sabitha, G.; Babu, R. S.; Gopal, P.; Yadav, J. S. in preparation.
13. (a) Garegg, P. J.; Samuelson, B. *J. Chem. Soc., Chem. Commun.* **1979**, 978; (b) Kang, S.-K.; Kim, S.-G.; Cho, D.-G.; Jeon, J.-H. *Synth. Commun.* **1993**, *23*, 681. The known epoxy alcohol was converted into the corresponding iodide,[13a] which on reductive elimination with Zn dust in refluxing ethanol[13b] afforded chiral allylic alcohol **8**.



14. (a) BouzBouz, S.; Simmons, R.; Cossy, J. *Org. Lett.* **2004**, *6*, 3465–3467; (b) Comin, M. J.; Parrish, D. A.; Deschamps, J. R.; Victor E. Marquez, V. E. *Org. Lett.* **2006**, *8*, 705–708; (c) Connon, S. J.; Blechert, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1900; (d) Hoveyda, A. H.; Gillingham, D. G.; Van Veldhuizen, J. J.; Kataoka, O.; Garber, S. B.; Kingsbury, J. S.; Harrity, J. P. A. *Org. Biomol. Chem.* **2004**, *2*, 8; (e) Marsh, G. P.; Parsons, P. J.; McCarthy, C.; Corniquet, X. G. *Org. Lett.* **2007**, *9*, 2613–2616; (f) Moura-Letts, G.; Curran, D. P. *Org. Lett.* **2007**, *9*, 5–8; (g) Bieniek, M.; Bujok, R.; Cabaj, M.; Lugan, N.; Lavigne, G.; Arlt, D.; Grela, K. *J. Am. Chem. Soc.* **2006**, *128*, 13652–13653.
15. Rychnovsky, S. D.; Rogers, B. N.; Richardson, R. I. *Acc. Chem. Res.* **1998**, *31*, 9.
16. Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35*, 8019.