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An Efficient Synthesis of (–)-Posticlure: The Sex Pheromone of *Orgyia postica*

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An efficient multigram synthesis of (–)-posticlure, the first *trans*-epoxide sex pheromone found in *Orgyia postica*, from diethyl L-tartrate is described. The synthesis was completed in seven steps and 27 % overall yield. The synthetic strategy features double-Wittig olefination and a stereoselective one-pot conversion of diol to epoxide as the key steps.

Introduction

Orgyia postica is a tussock moth and a known pest to mango and litchi in Okinawa, Japan.[1] Wakamura et al. in 2001 isolated the first *trans*-epoxide pheromone from *Orgyia postica* and identified it as (6*Z*,9*Z*,11*S*,12*S*)-*trans*-11,12-epoxyhenicosa-6,9-diene.[2] It was named "posticlure" (**1**, Figure 1) in reference to the species name.[3] The coupling constant of J = 2.2 Hz between the epoxide protons confirmed the *trans*-oxirane structure. In the same report, Wakamura described a short synthesis of natural posticlure and its optical antipode employing the Sharpless asymmetric epoxidation reaction with 59% *ee*. The optically pure samples were obtained by preparative HPLC for field study. Enantioselective synthesis of both (–)- and (+)-posticlure employing the Sharpless asymmetric dihydroxylation procedure has also been reported.[4,5] No chiral pool synthesis, which could give highly optically pure material, has been reported. Herein a short, multigram stereoselective synthesis of (–)-posticlure (**1**) starting from diethyl L-tartrate is described. The keys steps are double-Wittig olefination and a stereoselective one-pot conversion of diol to epoxide.

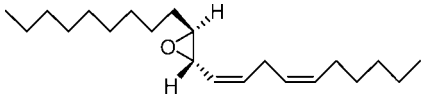
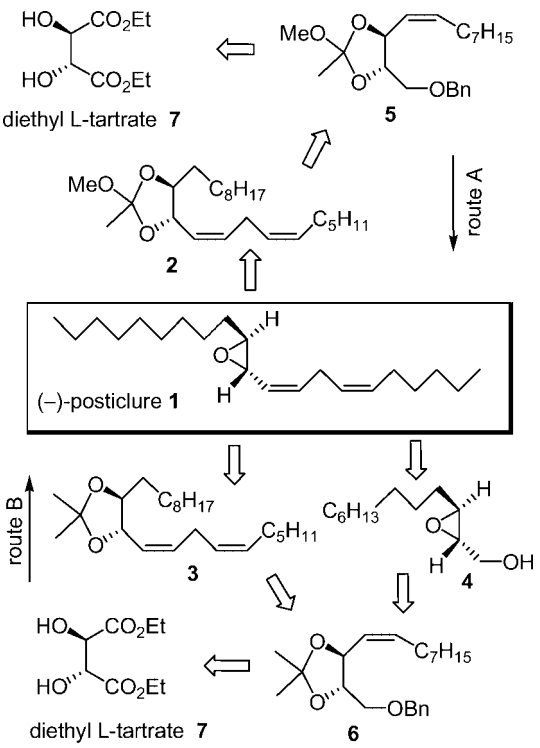


Figure 1. (–)-Posticlure (**1**), the first *trans*-epoxide pheromone.

Results and Discussion

The various strategic considerations for the synthesis of (–)-posticlure (**1**) from diethyl L-tartrate (**7**) are shown in Scheme 1. The target compound can be envisioned to be easily derived from a cyclic orthoacetate **2**, which, via the acetoxonium ion, can be opened with bromide to give the acetoxy bromide intermediate which upon hydrolysis would produce the epoxide stereoselectively.[6] Compound **2** can be derived from a vicinal diol. Hence the inherent chirality of diethyl L-tartrate (**7**) can be envisioned in compounds **2** and **5** and these can be derived (from diethyl L-tartrate) by successively attaching the corresponding side-chains by Wittig olefination (route A). We planned to protect the diethyl L-tartrate hydroxy groups as a cyclic orthoacetate al-



Scheme 1. Strategic considerations for the synthesis of (–)-posticlure (**1**).

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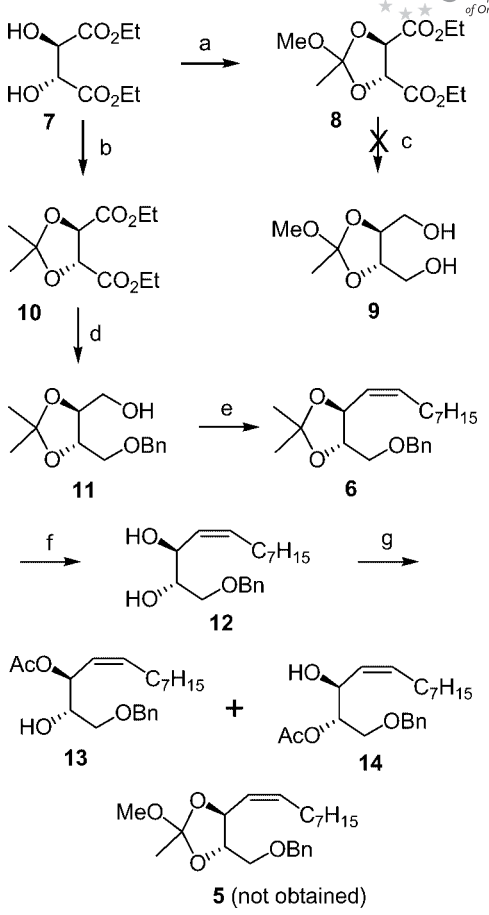
though the stability of this cyclic orthoacetate was of much concern. An alternative route would be to use the acetonide which is more stable (route B, Scheme 1). Thus, compound **2** could also be derived from **3** (although this involves an additional step of acetonide deprotection and orthoacetate formation). Further, **3** can be obtained (via **6**) from diethyl L-tartrate (**7**) by acetonide protection.[7] While this strategy involves first attaching the diene side-chain and then installing the epoxide in the final step, an alternative strategy could be to first install the epoxide **4** from **6** and then attach the diene side-chain in the final step.

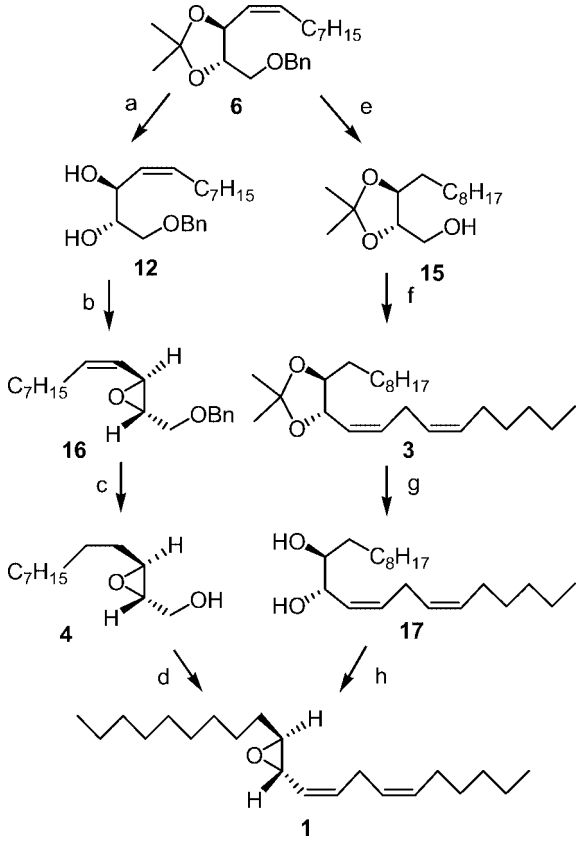
At the onset, the reaction of diethyl L-tartrate (**7**) with trimethyl orthoacetate and catalytic *p*TsOH gave compound **8**[8] in quantitative yield (Scheme 2). The $LiAlH_4$ reduction of **8** was a messy reaction. Even reverse addition, when $LiAlH_4$ was added in portions to the solution of **8** in dry THF at 0 °C, failed to give **9**.[9] Changing the reducing agent to DIBAl-H also failed to deliver **9**. This could be due to the poor stability of the cyclic orthoacetate, which is probably hydrolyzed or decomposes during the reaction or work up. Hence we planned to synthesize first compound **5** (Scheme 2) by acetonide protection so that we could probe the stability of the cyclic orthoacetate towards subsequent reaction conditions. Acetonide protection of diethyl L-tartrate with 2,2-dimethoxypropane and catalytic *p*TsOH gave **10**.[10] $LiAlH_4$ reduction of **10** and further monohydroxy protection with benzyl bromide afforded **11** in 82% yield.[11] Swern oxidation of **11** and subsequent Wittig reaction with *n*-$C_7H_{15}CH{=}PPh_3$ afforded the *Z* isomer **6** (^{1}H NMR indicated a 97:3 *Z*/*E* mixture, however this is of no consequence since this double bond needs to be saturated at a later stage) in 80% yield. Further deprotection of the acetonide in **6** gave the corresponding diol **12** which, when treated with trimethyl orthoacetate and catalytic *p*TsOH, failed to deliver the cyclic orthoacetate **5**. However, a mixture of regioisomeric monoacetoxy diols **13** and **14** was obtained in 78% yield.[12] Thus, the cyclic orthoacetate could not be prepared and we opted to complete the synthesis of the target by acetonide protection.[13]



Scheme 2. Attempted synthesis of cyclic orthoacetate **5**. Reagents and conditions: (a) $CH_3C(OCH_3)_3$ (1.5 equiv.), *p*TsOH (cat.), CH_2Cl_2, room temp., 12 h, quant.; (b) $(CH_3)_2C(OCH_3)_2$ (1.5 equiv.), *p*TsOH (cat.), benzene, reflux, 8 h, quant.; (c) $LiAlH_4$ (2.5 equiv.), THF, 0 °C, 12 h; (d) i. $LiAlH_4$ (2.5 equiv.), THF, reflux, 4 h; ii. NaH (1.1 equiv.), DMF, –15 °C, 30 min, BnBr (1 equiv.), 1 h, room temp., 1 h, 82% from **10**; (e) i. $(COCl)_2$ (1.5 equiv.), DMSO (3.0 equiv.), –78 °C, 20 min, **11**, 45 min, Et_3N (5 equiv.), –78 °C, 30 min, to room temperature, 1 h; ii. *n*-$C_7H_{15}CH_2P^+Ph_3Br^-$ (1.1 equiv.), *n*BuLi (1.1 equiv.), room temp., 30 min, –80 °C, aldehyde (from **11**), 2 h, room temp., overnight, 80% from **11**; (f) 4 N HCl, MeOH, room temp., 8 h, 93%; (g) $CH_3C(OCH_3)_3$ (1.2 equiv.), *p*TsOH (cat.), CH_2Cl_2, 0 °C, 1.5 h, 78% (**13**+**14**).

The synthesis of (–)-posticlure (**1**) from **6** was completed as shown in Scheme 3. We had two different strategies available from **6** to the target molecule **1**: 1) to install the epoxide stereoselectively first and then to attach the *cis*,*cis*-diene side-chain and 2) to attach the *cis*,*cis*-diene side-chain first followed by installation of the *trans*-epoxide. Both strategies involve the same number of steps to the target molecule and were executed as follows. The diol **12** was easily transformed into the epoxide using the Sharpless one-pot method.[6] Thus, the treatment of diol **12** with trimethyl orthoacetate and catalytic *p*TsOH at room temperature followed by removal of volatiles afforded the intermediate cyclic orthoacetate which, without isolation, was immediately treated with acetyl bromide to afford the regioisomeric halohydrin acetates.[14] Treatment of these with K_2CO_3 in MeOH resulted in hydrolysis of the acetate and subsequent oxirane formation affording stereoselectively the epoxide **16** in 90% yield from **12**. Subsequent hydrogenation of the double bond and debenzylation with Pearlman's catalyst [$Pd(OH)_2$/C (20%)][15] gave the epoxy alcohol **4**[16] in 94% yield. Further oxidation of the alcohol with PCC under buffered conditions with $NaHCO_3$ followed by condensation of the aldehyde with (*Z*)-*n*-$C_5H_{11}CH{=}CHCH_2$-$CH{=}PPh_3$ at –80 °C afforded (–)-posticlure (**1**) in 77% yield, $[a]_D^{20}$ = –11.2 (*c* = 0.4, $CHCl_3$) {ref.[5] $[a]_D^{20}$ = –10.8 (*c* = 1.07, $CHCl_3$); ref.[4] $[a]_D^{20}$ = –11.1 (*c* = 1, $CHCl_3$)}. The spectroscopic and analytical data of **1** matched well with those reported.[4,5] The overall yield for this seven-step strategy was 27%.

Alternatively, hydrogenation of the double bond and debenzylation of **6** with Pearlman's catalyst [$Pd(OH)_2$/C (20%)] afforded the acetonide alcohol **15** in an excellent yield of 95%. Further Swern oxidation of **15** and subsequent Wittig reaction following a similar approach to that described in the literature[4] with (*Z*)-*n*-$C_5H_{11}CH{=}CHCH_2$-



Scheme 3. Synthesis of (–)-posticlure (**1**) from **6**. Reagents and conditions: (a) 4 N HCl, MeOH, room temp., 8 h, 93%; (b) i. $CH_3C(OCH_3)_3$ (1.2 equiv.), *p*TsOH (cat.), CH_2Cl_2, room temp., 30 min; ii. CH_3COBr (1.24 equiv.), CH_2Cl_2, room temp., 1.5 h; iii. K_2CO_3 (1.5 equiv.), MeOH, room temp., 2.5 h, 90% overall; (c) $Pd(OH)_2$/C (20%), H_2 (80 psi), MeOH/EtOAc (1:5), room temp., 12 h, 94%; (d) i. PCC (1.5 equiv.), $NaHCO_3$ (1.5 equiv.), CH_2Cl_2, 0 °C, 4 h; ii. (*Z*)-*n*-$C_5H_{11}CH{=}CHCH_2CH_2P^+Ph_3I^-$ (1.1 equiv.), *n*BuLi (1.1 equiv.), room temp., 30 min, –80 °C, aldehyde (from **4**), 1 h, room temp., overnight, 77%; (e) $Pd(OH)_2$/C (20%), H_2 (80 psi), MeOH/EtOAc (1:5), room temp., 12 h, 95%; (f) i. $(COCl)_2$ (1.5 equiv.), DMSO (3 equiv.), –78 °C, 20 min, **15**, 45 min, Et_3N (5 equiv.), –78 °C, 30 min, to room temperature, 1 h; ii. (*Z*)-*n*-$C_5H_{11}CH{=}CHCH_2CH_2P^+Ph_3I^-$ (1.1 equiv.), *n*BuLi (1.1 equiv.), room temp., 30 min, –80 °C, aldehyde (from **15**), 1 h, room temp., overnight, 79%; (g) 4 N HCl, MeOH, room temp., 8 h, 92%; (h) i. $CH_3C(OCH_3)_3$ (1.2 equiv.), *p*TsOH (cat.), CH_2Cl_2, room temp., 20 min; ii. CH_3COBr (1.2 equiv.), CH_2Cl_2, room temp., 1.5 h; iii. K_2CO_3 (1.5 equiv.), MeOH, room temp., 2.5 h, 89% overall.

$CH{=}PPh_3$ at –80 °C afforded the *Z* isomer **3**[4] (^{1}H NMR indicated a 97:3 *Z*/*E* ratio at the newly formed double bond at C-9) in 79% yield. Deprotection of the acetonide was achieved using 4 N HCl in MeOH to give the diol **17** in 92% yield. The diol **17** was easily transformed into the epoxide by employing the one-pot procedure described for the synthesis of **16** to afford stereoselectively the *trans*-epoxide (–)-posticlure (**1**) in 89% yield, $[\alpha]_D^{20} = -11.3$ (*c* = 0.48, $CHCl_3$). The overall yield for this alternative strategy was also 27%.

Conclusions

In summary a highly efficient and stereoselective multigram synthesis of (–)-posticlure has been achieved starting from chiral pool material, diethyl L-tartrate, in seven steps and 27% overall yield. The inherent chirality of diethyl L-tartrate is realized in the target pheromone and the required side-chains were easily attached through successive Wittig olefination reactions. The required *trans*-oxirane structure was installed through a one-pot stereoselective conversion of diol to epoxide. The synthesis of the unnatural antipode (+)-posticlure can also be visualized by employing diethyl D-tartrate. This alternative route will provide an easy excess to both (–)- and (+)-posticlure in multigram quantities for field study and pest control.

Experimental Section

Solvents were purified and dried by standard procedures before use. Commercially available reagents were used as procured. Melting points are uncorrected. Optical rotations were measured using the sodium D line at 589 nm with a Perkin–Elmer Model 343 polarimeter at 20 °C. IR spectra were recorded with a Bruker TENSOR 27 spectrometer as neat thin films or $CHCl_3$ solution for solids. ^{1}H and ^{13}C NMR were recorded with an Eclipse 300 MHz JEOL, a Bruker Avance 300 MHz or a Gemini 200 MHz spectrometer with TMS (δ = 0.00 ppm) and $CHCl_3$ (δ = 77.00 ppm) as internal standards for ^{1}H and ^{13}C NMR, respectively. Mass spectra were recorded with a JEOL AX505HA spectrometer. The Wittig salts were prepared by refluxing an equimolar mixture of the corresponding alkyl halide and PPh_3 in CH_3CN solvent with a pinch of $NaHCO_3$ for 18 h. The solvent was removed by rotary evaporation and the white sticky solids were dried under high vacuum and handled under argon.

Diethyl (4*R*,5*R*)-2-Methoxy-2-methyl-1,3-dioxolane-4,5-dicarboxylate (8): Trimethyl orthoacetate (1.75 g, 14.56 mmol, 1.5 equiv.) was added to a solution of diethyl L-tartrate (**7**, 2 g, 9.7 mmol) and *p*TsOH (25 mg) in dry CH_2Cl_2 (30 mL) and the mixture stirred for 12 h at room temperature. After adding a pinch of $NaHCO_3$, the reaction mixture was stirred for 15 min and water (50 mL) was added. The organic layer was separated and washed with water, brine, dried (Na_2SO_4) and concentrated to give virtually pure **8** (2.53 g, quantitative) as a colourless oil. $[\alpha]_D^{20} = -22.8$ (*c* = 1.12, $CHCl_3$) {ref.[8] –22.19 (*c* = 0.96, $CHCl_3$)}. IR (neat): $\tilde{\nu}$ = 2986, 2948, 2840, 1754, 1467, 1384, 1274, 1218, 1160, 1101, 1052, 892, 861 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ = 1.32 (t, *J* = 6.9 Hz, 3 H, CH_3CH_2O), 1.33 (t, *J* = 6.9 Hz, 3 H, CH_3CH_2O), 1.67 (s, 3 H, C-CH_3), 3.33 (s, 3 H, OCH_3), 4.27 (q, *J* = 6.9 Hz, 2 H, CH_3CH_2O), 4.26–4.33 (m, 2 H, CH_3CH_2O), 4.73 (d, *J* = 5.4 Hz, 1 H, CH-O), 4.97 (d, *J* = 5.4 Hz, 1 H, CH-O) ppm. ^{13}C NMR (75 MHz, $CDCl_3$/$CHCl_3$): δ = 13.93 (2 C), 20.99, 50.35, 61.82, 61.84, 76.23, 76.63, 124.53, 168.75, 168.91 ppm. MS (EI): *m*/*z* (%) = 247 (5.1) $[M - 15]^+$, 231 (24.2), 217 (5.7), 189 (100), 115 (9.3), 75 (8.1), 59 (4.3), 43 (26.6).

Diethyl (2*R*,3*R*)-2,3-*O*-Isopropylidenetartrate (10): 2,2-Dimethoxypropane (18.94 g, 22.4 mL, 181.9 mmol, 1.5 equiv.) was added to a solution of diethyl L-tartrate (**7**, 25 g, 121.25 mmol) and *p*TsOH (250 mg) in dry benzene (300 mL) and the reaction mixture refluxed for 8 h with Dean–Stark removal of MeOH. After cooling to room temperature, $NaHCO_3$ (3 g) was added and the mixture was stirred for 15 min. Water (200 mL) was added and the organic layer separated. The aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated to give **10** (29.8 g, quantitative) as a pale yellow oil. IR (neat): $\tilde{\nu}$ = 2989, 2943, 1752, 1445,

1378, 1259, 1213, 1162, 1112, 1023, 858, 703 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$/TMS): δ = 1.32 (t, J = 7.2 Hz, 6 H, CH_3CH_2O), 1.50 (s, 6 H, C-CH_3), 4.30 (q, J = 7.2 Hz, 4 H, CH_3CH_2O), 4.76–4.83 (m, 2 H, CH-O) ppm. MS (EI): m/z (%) = 246 (1.8) $[M]^+$, 231 (77.2), 217 (100), 203 (40.2), 173 (39.8), 159 (32.6), 104 (23.3), 76 (14.8), 59 (28.1), 43 (68.9). An ester exchange was observed with approximately 25% mixed ester formed [in the ^1H NMR with a peak at δ = 3.83 (s, 3 H) ppm, corresponding to an OMe group].[10] However this is of no consequence as the compound will be reduced in the next step.

(2*S*,3*S*)-4-Benzyloxy-2,3-(isopropylidenedioxy)butan-1-ol (11): A suspension of $LiAlH_4$ (11.56 g, 304.6 mmol, 2.5 equiv.) in dry THF (400 mL) was cooled with ice/water and a solution of **10** (30 g, 121.82 mmol) in dry THF (50 mL) was added dropwise over 15 min. The reaction mixture was refluxed for 4 h. It was then cooled to 0 °C and quenched with 10% aq. NaOH (30 mL), water (10 mL) and EtOAc (100 mL). The white precipitate was filtered through a pad of silica gel and washed with a mixture of MeOH/EtOAc (1:3, 400 mL). The filtrate was concentrated to give the corresponding acetonide diol as a colourless syrup (18.9 g). IR (neat): $\tilde{\nu}$ = 3410, 2988, 2935, 2881, 1457, 1377, 1251, 1219, 1166, 1109, 1054, 986, 907, 845, 733, 681 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$/TMS): δ = 1.43 (s, 6 H, C-CH_3), 2.91 (br. s, 2 H, OH), 3.67–3.83 (m, 4 H, CH_2OH), 3.97–4.01 (m, 2 H, CH-O) ppm.

Oil-free NaH (3.22 g, 134.1 mmol, 1.1 equiv.) was added in portions over 20 min to a solution of the above acetonide diol in dry DMF (200 mL) at –15 °C. The reaction mixture was stirred at –15 °C for 30 min and BnBr (20.83 g, 121.8 mmol, 1 equiv.) in dry DMF (20 mL) was added. After 1 h the reaction mixture was warmed to room temperature and stirred for another 1 h. It was quenched with ice/water and the aqueous layer extracted with EtOAc (4 × 50 mL). The combined organic layers were washed with water (2 × 50 mL), brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography using hexane/EtOAc (7:3) as eluent to afford **11** (25.18 g, 82% from **10**) as a colourless oil. $[\alpha]_D^{20}$ = +9.1 (c = 1, $CHCl_3$) {ref.[11b] +9.0 (c = 0.99, $CHCl_3$)}. IR (neat): $\tilde{\nu}$ = 3464, 3031, 2987, 2932, 2872, 1496, 1454, 1375, 1251, 1215, 1166, 1082, 991, 907, 847, 741, 700, 608 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$/TMS): δ = 1.40 (s, 3 H, C-CH_3), 1.41 (s, 3 H, C-CH_3), 2.62 (s, 1 H, OH), 3.55 (dd, J = 10.2, 5.4 Hz, 1 H, 4-H), 3.62–3.68 (m, 2 H, 1-H), 3.75 (dd, J = 11.9, 4.1 Hz, 1 H, 4′-H), 3.90–3.96 (m, 1 H, 2-H), 4.04 (dt, J = 8.4, 5.4 Hz, 1 H, 3-H), 4.57 (s, 2 H, CH_2Ph), 7.29–7.36 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$/$CHCl_3$): δ = 26.85, 26.88, 62.38, 70.38, 73.56, 76.52, 79.57, 109.23, 127.59 (2 C), 127.67, 128.31 (2 C), 137.59 ppm. MS (EI): m/z (%) = 252 (1.8) $[M]^+$, 251 (6.2) $[M – 1]^+$, 237, (24.8), 194 (16.2), 176 (12.3), 131 (37.1), 105 (14.8), 91 (100), 59 (52.9), 43 (14.1). HRMS: calcd. for $C_{14}H_{19}O_4$ [M – H] 251.1283; found 251.1288.

(2*S*,3*S*,4*Z*)-1-Benzyloxy-2,3-(isopropylidenedioxy)dodeca-4-ene (6): Dimethyl sulfoxide (6.51 g, 6.0 mL, 83.32 mmol, 3 equiv.) in CH_2Cl_2 (15 mL), was added to a solution of $(COCl)_2$ (5.28 g, 3.5 mL, 41.6 mmol, 1.5 equiv.) in CH_2Cl_2 (100 mL) at –78 °C. After 20 min, a solution of **11** (7 g, 27.74 mmol) in CH_2Cl_2 (15 mL) was added and the mixture stirred for 45 min. Et_3N (14.04 g, 19.4 mL, 138.7 mmol, 5 equiv.) in CH_2Cl_2 (15 mL) was added and the resulting mixture was stirred for another 30 min and then warmed to room temperature over 1 h. It was then quenched with water and extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated to give the corresponding aldehyde, which was used directly in the next reaction.

To a solution of octyltriphenylphosphonium bromide (13.89 g, 30.50 mmol, 1.1 equiv.) in dry THF (150 mL) was added *n*BuLi (12.2 mL, 2.5 M in hexane, 30.5 mmol, 1.1 equiv.) at room temperature. After stirring for 30 min, the mixture was cooled to –80 °C and a solution of the above aldehyde in THF (15 mL) was added. The mixture was stirred for another 2 h and then at room temperature overnight. It was then quenched with a saturated aq. NH_4Cl solution and THF removed on a rotavapor at low pressure. Water (100 mL) was added and the mixture extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography using hexane/EtOAc (95:5) as eluent to afford **6** (7.68 g, 80% from **11**) as a colourless oil (^1H NMR indicated 97:3 Z/E mixture). $[\alpha]_D^{20}$ = +1.9 (c = 6, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3057, 2985, 2927, 2856, 1716, 1587, 1457, 1435, 1374, 1242, 1215, 1167, 1086, 1027, 912, 861, 743, 697 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$/TMS): δ = 0.88 (t, J = 6.7 Hz, 3 H, 12-H), 1.22–1.39 (m, 10 H, 11-, 10-, 9-, 8-, 7-H), 1.44 (s, 6 H, C-CH_3), 1.94–2.15 (m, 2 H, 6-H), 3.51–3.62 (m, 2 H, 1-H), 3.83–3.88 (m, 1 H, 2-H), 4.59 (s, 2 H, CH_2Ph), 4.56–4.67 (m, 1 H, 3-H), 5.38 (ddt, J = 10.8, 9.8, 1.5 Hz, 1 H, 4-H), 5.68 (dt, J = 10.8, 7.6 Hz, 1 H, 5-H), 7.28–7.34 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$/$CHCl_3$): δ = 14.04, 22.59, 26.94, 27.14, 27.69, 29.08, 29.13, 29.54, 31.74, 69.19, 73.40, 73.51, 80.40, 109.11, 127.55, 128.26, 128.41, 128.51, 128.78, 133.55, 133.81, 136.39 ppm. MS (EI): m/z (%) = 346 (4.1) $[M]^+$, 331 (7.2), 277 (67.8), 262 (76.2), 196 (27.3), 183 (46.1), 97 (48.3), 91 (100), 83 (18.1), 69 (14.9), 43 (17.1). HRMS: calcd. for $C_{22}H_{34}O_3$ [M] 346.2509; found 346.2513.

(2*S*,3*S*,4*Z*)-1-Benzyloxydodec-4-ene-2,3-diol (12): A 4 N solution of HCl (25 mL) was added to a solution of **6** (8 g, 23.08 mmol) in MeOH (150 mL) and the mixture stirred at room temperature for 8 h. Solid $NaHCO_3$ (6 g) was added and stirred for 15 min. MeOH was partly removed on a rotavapor under reduced pressure, water (150 mL) was added and the mixture extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography using hexane/EtOAc (3:2) as eluent to give **12** (6.58 g, 93%) as a colourless oil. $[\alpha]_D^{20}$ = +4.5 (c = 2, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3400, 3064, 3029, 3010, 2955, 2925, 2856, 1722, 1659, 1495, 1455, 1363, 1307, 1276, 1208, 1116, 1033, 912, 738, 698 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$/TMS): δ = 0.88 (t, J = 6.8 Hz, 3 H, 12-H), 1.2–1.38 (m, 10 H, 11-, 10-, 9-, 8-, 7-H), 1.94–2.18 (m, 2 H, 6-H), 2.88 (br. s, 2 H, OH), 3.46 (dd, J = 9.6, 6.0 Hz, 1 H, 2-H), 3.54–3.65 (m, 2 H, 1-H), 4.42 (ddd, J = 8.9, 6.5, 1.0 Hz, 1 H, 3-H), 4.52 (s, 2 H, CH_2Ph), 5.39 (ddt, J = 10.9, 9.0, 1.5 Hz, 1 H, 4-H), 5.60 (ddt, J = 10.8, 7.6, 0.9 Hz, 1 H, 5-H), 7.28–7.35 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$/$CHCl_3$): δ = 14.00, 22.56, 27.86, 29.08, 29.20, 29.48, 31.73, 68.21, 71.25, 73.51, 73.63, 127.69 (2 C), 127.76, 127.83, 128.38 (2 C), 134.91, 137.64 ppm. MS (EI): m/z (%) = 289 (1.8) $[M – 17]^+$, 277 (1.5), 263 (1.7), 245 (6.3), 197 (1.9), 181 (5.4), 155 (17.4), 107 (15.5), 95 (16.4), 91 (100), 81 (16.8), 57 (27.9), 43 (13.1), 41 (14.2). HRMS: calcd. for $C_{19}H_{31}O_3$ [M + H] 307.2274; found 307.2279.

(2*S*,3*S*,4*Z*)-1-Benzyloxy-3-(acetoxy)dodec-4-en-2-ol (13) and (2*S*,3*S*,4*Z*)-1-Benzyloxy-2-(acetoxy)dodec-4-en-3-ol (14): Trimethyl orthoacetate (0.377 g, 3.13 mmol, 1.2 equiv.) was added to a solution of **12** (0.8 g, 2.61 mmol) in CH_2Cl_2 (25 mL) and *p*TsOH (10 mg) at 0 °C and the mixture was stirred for 1.5 h (TLC showed consumption of polar material). $NaHCO_3$ (500 mg) was added and the mixture stirred for 5 min followed by the addition of water (50 mL). The organic layer was separated, washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography using hexane/EtOAc (3:2) as eluent to give a mixture of **13** and **14** (0.709 g, 78%) as a colourless oil (^1H NMR analysis indicated a 1:3 mixture of regioisomers). $[\alpha]_D^{20}$ = +5.6 (c =

1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3462, 3064, 3028, 2955, 2926, 2856, 1740, 1659, 1496, 1455, 1370, 1238, 1180, 1108, 1026, 911, 817, 740, 700, 606 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$/TMS) major isomer:* δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.2–1.38 (m, 10 H), 2.04 (s, 3 H), 2.01–2.22 (m, 2 H), 2.5 (br. s, 1 H), 3.48 (dd, J = 9.8, 5.8 Hz, 1 H), 3.57 (dd, J = 9.9, 3.7 Hz, 1 H), 3.77–3.85 (m, 1 H), 4.52 (s, 2 H), 5.31–5.40 (m, 1 H), 5.62–5.71 (m, 2 H), 7.25–7.36 (m, 5 H) ppm; characteristic peaks for the minor isomer: δ = 3.62 (dd, J = 10.5, 5.1 Hz, 1 H), 3.68 (dd, J = 10.6, 4.1 Hz, 1 H), 4.54 (s, 2 H), 4.65–4.70 (m, 1 H), 4.95–5.00 (m, 1 H), 5.31–5.36 (m, 1 H), 5.55–5.63 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$/$CHCl_3$) major isomer: δ = 14.02, 21.10, 22.55, 28.00, 29.07, 29.19, 29.32, 31.73, 70.65, 70.78, 72.20, 73.47, 123.86, 127.64 (2 C), 128.35 (2 C), 135.09, 136.73, 137.64, 170.23. MS (EI): m/z (%) = 349 (1.4) $[M + 1]^+$, 331 (18.1) $[M^+ – 17]^+$, 289 (10.5), 271 (8.2), 241 (10.3), 197 (17.3), 155 (33.4), 107 (19.5), 91 (100), 81 (17.8), 57 (17.9), 43 (69.1), 41 (18.5). HRMS: calcd. for $C_{21}H_{33}O_4$ [M + H] 349.2379; found 349.2386. *Individual peaks are not assigned as we did not investigate which is major and minor.

(2*S*,3*S*,4*Z*)-1-Benzyloxy-2,3-epoxydodec-4-ene (16): *p*TsOH (25 mg) followed by trimethyl orthoacetate (1.89 g, 15.7 mmol, 1.2 equiv.) was added to a solution of diol **12** (4 g, 13.05 mmol) in dry CH_2Cl_2 (50 mL) and the mixture stirred at room temperature for 30 min. The solvent was evaporated and the residual methanol was removed under high vacuum. CH_2Cl_2 (50 mL) and CH_3COBr (1.99 g, 1.2 mL, 16.2 mmol, 1.24 equiv.) was added to the residue and the mixture stirred for 1.5 h at room temperature. It was then concentrated and the residue diluted with MeOH (80 mL) and treated with K_2CO_3 (2.71 g, 19.59 mmol, 1.5 equiv.). The mixture was stirred for 2.5 h at room temperature and then poured into water (100 mL) and extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography using hexane/EtOAc (9:1) as eluent to give **16** (3.39 g, 90%) as a colourless oil. $[\alpha]_D^{20}$ = –13.4 (c = 4, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3063, 3027, 2955, 2926, 2855, 1718, 1665, 1496, 1456, 1382, 1359, 1308, 1245, 1206, 1103, 1058, 1027, 966, 902, 874, 738, 699 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$/TMS): δ = 0.88 (t, J = 6.8 Hz, 3 H, 12-H), 1.2–1.32 (m, 8 H, 11-, 10-, 9-, 8-H), 1.33–1.43 (m, 2 H, 7-H), 2.10–2.29 (m, 2 H, 6-H), 3.06–3.11 (m, 1 H, 2-H), 3.48–3.56 (m, 2 H, 1-H), 3.77 (dd, J = 11.4, 3.0 Hz, 1 H, 3-H), 4.58 (d, J = 2.7 Hz, 2 H, CH_2Ph), 5.06 (ddt, J = 10.4, 9.3, 1.2 Hz, 1 H, 4-H), 5.74 (dt, J = 10.8, 7.5 Hz, 1 H, 5-H), 7.26–7.35 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$/$CHCl_3$): δ = 14.00, 22.55, 27.67, 29.06 (2 C), 29.47, 31.75, 51.59, 58.40, 69.90, 73.20, 126.02, 127.64 (3 C), 128.33 (2 C), 137.26, 137.84 ppm. MS (EI): m/z (%) = 288 (2.1) $[M]^+$, 287 (2.2) $[M – 1]^+$, 271 (3.8), 253 (4.2), 241 (4.3), 197 (4.5), 181 (8.2), 167 (5.1), 133 (15.1), 107 (18.8), 104 (38.1), 91 (100), 83 (10.2), 55 (12.3), 43 (11.3), 41 (18.0). HRMS: calcd. for $C_{19}H_{28}O_2$ [M] 288.2090; found 288.2093.

(2*S*,3*S*)-2,3-Epoxydodecan-1-ol (4): $Pd(OH)_2$/C (20%, 500 mg) was added to a solution of **16** (2 g, 6.93 mmol) in MeOH/EtOAc (1:5, 50 mL). The mixture was pressurized to 80 psi of H_2 in an autoclave and stirred at room temperature for 12 h. The catalyst was filtered through a pad of silica gel and washed with EtOAc (50 mL). The filtrate was concentrated and the residue purified by flash chromatography using hexane/EtOAc (4:1) as eluent to afford **4** (1.302 g, 94%) as a white solid. M.p. 59–60 °C (ref.[16] 62.5–63 °C). $[\alpha]_D^{20}$ = –31.9 (c = 3, $CHCl_3$) {ref.[16] –29.4 (c = 6.8, $CHCl_3$)}. IR ($CHCl_3$): $\tilde{\nu}$ = 3480, 2985, 2927, 2854, 1450, 1305, 1245, 1103, 1090, 903, 840, 710, 685 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$/TMS): δ = 0.88 (t, J = 6.7 Hz, 3 H, 12-H), 1.21–1.38 (m, 12 H, 11-, 10-, 9-, 8-, 7-, 6-H), 1.41–1.45 (m, 2 H, 5-H), 1.56–1.58 (m, 2 H, 4-H), 1.84 (br. s, 1 H, OH), 2.94–2.96 (m, 2 H, 1-H), 3.63 (ddd, J = 12.6, 7.2, 4.1 Hz, 1 H, 3-H), 3.93 (ddd, J = 12.6, 5.2, 2.1 Hz, 1 H, 2-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$/$CHCl_3$): δ = 14.10, 22.60, 25.91, 29.33, 29.41, 29.55 (2 C), 31.61, 31.92, 56.20, 58.72, 61.91 ppm. MS (EI): m/z (%) = 169 (10.8) $[M – 31]^+$, 157 (2.2), 109 (22.7), 97 (100), 95 (45.8), 83 (73.1), 81 (28.9), 71 (55.6), 69 (89.8), 57 (73), 43 (36.6), 41 (12.4). HRMS: calcd. for $C_{12}H_{23}O_2$ [M – H] 199.1698; found 199.1699.

(2*S*,3*S*)-2,3-(Isopropylidenedioxy)dodecan-1-ol (15): $Pd(OH)_2$/C (20%, 400 mg) was added to a solution of **6** (2 g, 5.77 mmol) in MeOH/EtOAc (1:5, 30 mL). The mixture was pressurized to 80 psi of H_2 in an autoclave and stirred at room temperature for 12 h. The catalyst was filtered through a pad of silica gel and washed with EtOAc (50 mL). The filtrate was concentrated and the residue purified by flash chromatography using hexane/EtOAc (4:1) as eluent to afford **15** (1.42 g, 95%) as a colourless oil. $[\alpha]_D^{20}$ = –23.3 (c = 0.38, $CHCl_3$) {ref.[4] –21.6 (c = 1, $CHCl_3$)}. IR (neat): $\tilde{\nu}$ = 3466, 2986, 2927, 2856, 1462, 1375, 1246, 1219, 1168, 1103, 1051, 903, 854, 722 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$/TMS): δ = 0.88 (t, J = 6.6 Hz, 3 H, 12-H), 1.22–1.38 (m, 14 H, 11-, 10-, 9-, 8-, 7-, 6-, 5-H), 1.40 (s, 3 H, C-CH_3), 1.41 (s, 3 H, C-CH_3), 1.44–1.61 (m, 2 H, 4-H), 2.44 (s, 1 H, OH), 3.60 (dd, J = 11.2, 4.0 Hz, 1 H, 3-H), 3.70–3.81 (m, 2 H, 1-H), 3.82–3.89 (m, 1 H, 2-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$/$CHCl_3$): δ = 14.00, 22.58, 25.89, 26.95, 27.27, 29.21, 29.42 (2 C), 29.62, 31.79, 33.04, 62.08, 76.92, 81.56, 108.48 ppm. MS (EI): m/z (%) = 243 (100) $[M – 15]^+$, 227 (22.2), 165 (3.8), 123 (9.2), 109 (22.3), 95 (39.1), 81 (23.1), 59 (68.9), 55 (19.8), 43 (36.2). HRMS: calcd. for $C_{15}H_{29}O_3$ [M – H] 257.2117; found 257.2121.

(6*Z*,9*Z*,11*S*,12*S*)-11,12-(Isopropylidenedioxy)henicosa-6,9-diene (3): Dimethyl sulfoxide (3.63 g, 3.3 mL, 46.45 mmol, 3 equiv.) in CH_2Cl_2 (10 mL), was added to a solution of $(COCl)_2$ (2.95 g, 2 mL, 23.21 mmol, 1.5 equiv.) in CH_2Cl_2 (80 mL) at –78 °C. After 20 min, a solution of **15** (4 g, 15.48 mmol) in CH_2Cl_2 (10 mL) was added and the mixture stirred for 45 min. Et_3N (7.83 g, 10.8 mL, 77.36 mmol, 5 equiv.) in CH_2Cl_2 (10 mL) was added and the resulting mixture stirred for another 30 min and then warmed to room temperature over 1 h. The reaction mixture was quenched with water and extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated to give the corresponding aldehyde which was used directly for the next reaction.

*n*BuLi (6.9 mL, 2.5 M in hexane, 17.2 mmol, 1.1 equiv.) was added to a solution of (*Z*)-(non-3-enyl)triphenylphosphonium iodide (8.76 g, 17.02 mmol, 1.1 equiv.) in dry THF (100 mL) at room temperature. After stirring for 30 min, the mixture was cooled to –80 °C and a solution of the above aldehyde in THF (10 mL) was added. The mixture was stirred for another 1 h and then at room temperature overnight. It was quenched with saturated aq. NH_4Cl and THF was removed on a rotavapor at low pressure. Water (75 mL) was added and the mixture extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography using hexane/EtOAc (9:1) as eluent to afford **3** (4.46 g, 79% from **15**) as a colourless oil (^1H NMR indicated 97:3 *Z*/*E* mixture). $[\alpha]_D^{20}$ = +1.5 (c = 4, $CHCl_3$).[17] IR (neat): $\tilde{\nu}$ = 3013, 2985, 2957, 2927, 2850, 1712, 1462, 1373, 1338, 1170, 1103, 1051, 914, 882, 725 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$/TMS): δ = 0.85–0.91 (m, 6 H, 1-, 21-H), 1.23–1.38 (m, 20 H, 20-, 19-, 18-, 17-, 16-, 15-, 14-, 4-, 3-, 2-H), 1.41 (s, 3 H, C-CH_3), 1.42 (s, 3 H, C-CH_3), 1.47–1.58 (m, 2 H, 13-H), 2.05 (br. dd, J = 13.8, 7.2 Hz, 2 H, 5-H), 2.89 (dt, J = 7.2, 1.2 Hz, 2 H, 8-H), 3.6–3.67 (m, 1 H,

12-H), 4.38 (t, J = 8.7 Hz, 1 H, 11-H), 5.26–5.47 (m, 3 H, olefin-H), 5.66 (ddt, J = 10.8, 7.4, 0.9 Hz, 1 H, olefin-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3/CHCl_3$): δ = 14.02, 14.07, 22.53, 22.65, 26.02, 26.19, 27.09, 27.25, 27.28, 29.23, 29.28, 29.49, 29.51, 29.74, 31.49, 31.81, 31.87, 76.67, 80.91, 108.26, 126.67 (2 C), 131.04, 134.18 ppm. MS (EI): m/z (%) = 349 (4.8) $[M – 15]^+$, 289 (6.2), 208, (11.8), 155 (16.1), 97 (88.3), 83 (9.3), 69 (34.9), 55 (100), 43 (7.1). HRMS: calcd. for $C_{24}H_{43}O_2$ [M – H] 363.3264; found 363.3271.

(6*Z*,9*Z*,11*S*,12*S*)-11,12-Dihydroxyhenicosa-6,9-diene (17): A 4 N solution of HCl (12 mL) was added to a solution of **3** (4 g, 10.97 mmol) in MeOH (100 mL) and the mixture stirred at room temperature for 8 h. Solid $NaHCO_3$ (4 g) was added and the mixture stirred for 15 min. MeOH was partly removed on a rotavapor, the mixture diluted with water (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography using hexane/EtOAc (3:2) as eluent to give **17** (3.28 g, 92%) as a colourless oil. $[\alpha]_D^{20}$ = +2.5 (c = 5, $CHCl_3$).[17] IR (neat): $\tilde{\nu}$ = 3370, 3011, 2956, 2925, 2855, 1712, 1462, 1377, 1274, 1230, 1045, 1027, 723 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ = 0.84–0.92 (m, 6 H, 1-, 21-H), 1.2–1.38 (m, 20 H, 20-, 19-, 18-, 17-, 16-, 15-, 14-, 4-, 3-, 2-H), 1.41–1.52 (m, 2 H, 13-H), 2.0–2.1 (m, 2 H, 5-H), 2.53 (br. s, 2 H, OH), 2.81–2.92 (m, 2 H, 8-H), 3.39–3.5 (m, 1 H, 12-H), 4.22 (dt, J = 8.0, 0.9 Hz, 1 H, 11-H), 5.28–5.36 (m, 1 H, olefin-H), 5.37–5.47 (m, 2 H, olefin-H), 5.60 (ddt, J = 10.8, 7.5, 0.9 Hz, 1 H, olefin-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3/CHCl_3$): δ = 14.00, 14.04, 22.52, 22.64, 25.71, 26.34, 27.24, 29.21, 29.28, 29.54 (2 C), 29.63, 31.47, 31.85, 32.78, 71.06, 74.99, 126.60, 128.77, 131.09, 132.98 ppm. MS (EI): m/z (%) = 324 (1.3) $[M]^+$, 307 (36.2) $[M – 17]^+$, 306 (13.8), 289 (11.2), 213 (32.3), 157 (54.1), 112 (39.4), 97 (38.3), 83 (89.5), 69 (65.1), 57 (100), 55 (96.4), 43 (59.4), 41 (79.2). HRMS: calcd. for $C_{21}H_{40}O_2$ [M] 324.3030; found 324.3034.

(11*S*,12*S*)-(–)-Posticlure (1) from 4: Epoxy alcohol **4** (1 g, 5 mmol) in CH_2Cl_2 (5 mL) was added to a stirred slurry of PCC (1.62 g, 7.5 mmol, 1.5 equiv.) and $NaHCO_3$ (0.63 g, 7.5 mmol, 1.5 equiv.) in dry CH_2Cl_2 (50 mL) at 0 °C and the mixture stirred for 4 h. It was then warmed to room temperature, filtered through a pad of silica gel and washed with CH_2Cl_2 (75 mL). The filtrate was concentrated to give the corresponding aldehyde which was used directly in the next reaction.

*n*BuLi (2.2 mL, 2.5 M in hexane, 5.5 mmol, 1.1 equiv.) was added to a solution of (*Z*)-(non-3-enyl)triphenylphosphonium iodide (2.83 g, 5.5 mmol, 1.1 equiv.) in dry THF (50 mL) at room temperature. After stirring for 30 min, the mixture was cooled to –80 °C and a solution of the above aldehyde in THF (5 mL) was added. The mixture was stirred for another 1 h and then at room temperature overnight. It was quenched with saturated aq. NH_4Cl and THF was removed on a rotavapor at low pressure. Water (50 mL) was added and the mixture extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography using hexane/diethyl ether (9:1) as eluent to afford **1** (1.18 g, 77% from **4**) as a colourless oil. $[\alpha]_D^{20}$ = –11.2 (c = 0.4, $CHCl_3$) {ref.[5] –10.8 (c = 1.07, $CHCl_3$); ref.[4] –11.1 (c = 1, $CHCl_3$)}. IR ($CHCl_3$): $\tilde{\nu}$ = 3013, 2957, 2926, 2855, 1718, 1462, 1376, 1312, 1273, 1241, 1102, 1042, 968, 912, 878, 732 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ = 0.88 (m, 6 H, 1-, 21-H), 1.2–1.32 (m, 18 H, 20-, 19-, 18-, 17-, 16-, 15-, 14-, 3-, 2-H), 1.33–1.39 (m, 2 H, 4-H), 1.48–1.62 (m, 2 H, 13-H), 2.07 (dt, J = 7.2, 7.0 Hz, 2 H, 5-H), 2.82 (dt, J = 5.8, 2.2 Hz, 1 H, 12-H), 2.96 (dd, J = 7.5, 7.4 Hz, 2 H, 8-H), 3.37 (ddd, J = 8.9, 2.2, 0.9 Hz, 1 H, 11-H), 5.06 (ddt, J = 10.8, 8.7, 1.5 Hz, 1 H, 10-H), 5.37 (dtt, J = 10.8, 7.2, 1.5 Hz, 1 H, 7-H), 5.44 (dtt, J = 10.8, 7.2, 1.5 Hz, 1 H, 6-H), 5.67 (ddt, J = 10.8, 7.5, 0.9 Hz, 1 H, 9-H) ppm.[18] ^{13}C NMR (75 MHz, $CDCl_3/CHCl_3$): δ = 14.00, 14.05, 22.53, 22.63, 25.90, 26.04, 27.20, 29.21, 29.26, 29.43, 29.49, 29.52, 31.47, 31.86, 32.04, 54.27, 60.10, 126.75, 127.31, 131.07, 134.24 ppm. MS (EI): m/z (%) = 306 (3.1) $[M]^+$, 289 (2.4), 249 (2.1), 235 (3.2), 209 (3.3), 195 (34.4), 179 (8.7), 155 (15.3), 136 (8.8), 109 (18.1), 95 (28.3), 93 (28.4), 79 (88.5), 67 (53.9), 55 (70.1), 43 (73.3), 41 (100). HRMS: calcd. for $C_{21}H_{38}O$ 306.2924; found 306.2927.

(11*S*,12*S*)-(–)-Posticlure (1) from 17: *p*TsOH (12 mg) followed by trimethyl orthoacetate (0.888 g, 7.39 mmol, 1.2 equiv.) was added to a solution of diol **17** (2 g, 6.16 mmol) in dry CH_2Cl_2 (10 mL) and the mixture stirred at room temperature for 20 min. The solvent was evaporated and the residual methanol was removed under high vacuum. CH_2Cl_2 (10 mL) and CH_3COBr (0.910 g, 0.550 mL, 7.4 mmol, 1.2 equiv.) was added to the residue and the mixture stirred for 1.5 h at room temperature. It was then concentrated, the residue diluted with MeOH (15 mL) and treated with K_2CO_3 (1.28 g, 9.24 mmol, 1.5 equiv.). The mixture was stirred for 2.5 h at room temperature, then poured into water (50 mL) and extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography using hexane/diethyl ether (9:1) as eluent to give **1** (1.68 g, 89%) as a colourless oil. $[\alpha]_D^{20}$ = –11.3 (c = 0.48, $CHCl_3$).

Supporting Information (see also the footnote on the first page of this article): Spectra of relevant compounds.

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[7] If diethyl L-tartrate is protected as a cyclic orthoacetate and carried forward (**7** → **5** → **2**, route A) then compound **2** can be converted directly into **1**. However, by acetonide protection (**7** → **6** → **3**, route B), the conversion of compound **3** into **1** has to proceed via the orthoacetate **2**, which is the intermediate in the diol-to-epoxide conversion. This means one extra step of acetonide deprotection. Similarly the conversion of **7** into **4** proceeds via compound **6**.
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[9] The reduction of compound **8** to **9** is not known in the literature. For an example of cyclic orthoformate reduction with $LiAlH_4$, see: K. C. Nicolaou, D. P. Papahatjis, D. A. Claremon, R. L. Magolda, R. E. Dolle, *J. Org. Chem.* **1985**, *50*, 1440–1456.

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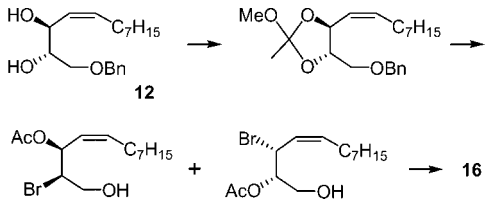
[11] Compounds **10** and **11** were synthesized following literature procedures, see: a) Z.-J. Yao, Y.-L. Wu, *J. Org. Chem.* **1995**, *60*, 1170–1176. In this reference there is a discrepancy in the sign of the optical rotation. The enantiomer of **11**, prepared from D-tartaric acid, is reported to have $[\alpha]_D^{20}$ = +9.0 (*c* = 4.1, $CHCl_3$). The same compound is reported to have $[\alpha]_D^{20}$ = –9.0 (*c* = 1.6, EtOAc) in D. T. Fox, C. D. Poulter, *J. Org. Chem.* **2005**, *70*, 1978–1985 and $[\alpha]_D^{20}$ = –8.0 (*c* = 0.975, $CHCl_3$) in b) E. Hungerbuhler, D. Seebach, *Helv. Chim. Acta* **1981**, *64*, 687–702.
[12] The diol **12** was treated with trimethyl orthoacetate and catalytic *p*-TsOH in dry CH_2Cl_2 at 0 °C. After complete consumption of the starting material (TLC, 1.5 h) a fast-moving spot was detected on a TLC sheet which we believed could be cyclic orthoacetate **5**. Also a polar spot corresponding to **13** and **14** was noticed. After aqueous work-up and column chromatography **13** and **14** were isolated as a mixture. The integration of the allylic proton (C-3) and also the acetyl (CH_3) group indicated that **13** and **14** were present in a 1:3 ratio. However, we did not investigate which is the major isomer. Even avoiding aqueous work-up, that is, quenching the reaction with solid $NaHCO_3$, filtration, concentration and column chromatography, afforded the mixture in the same ratio. For a similar conversion of vicinal diols to monoacetoxy products using trimethyl orthoacetate, see: M. Ikejiri, K. Miyashita, T. Tsunemi, T. Imanishi, *Tetrahedron Lett.* **2004**, *45*, 1243–1246.
[13] If the cyclic orthoacetate was stable to multistep reactions we could save one step in the synthetic strategy, that is, route A vs. route B (see Scheme 1).
[14] The intermediates are shown below. The cyclic orthoacetate is formed as exemplified by this conversion, though probably it is not stable to isolation.



[15] For an example of debenzylation with Pearlman's catalyst in the presence of an epoxide, see: D.-G. Liu, B. Wang, G.-Q. Lin, *J. Org. Chem.* **2000**, *65*, 9114–9119.
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[17] The optical rotation value for this compound did not match with that reported in ref.[4]
[18] Individual peaks are assigned in analogy with ref.[5]

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