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ORIGINAL PAPER

Stereoselective total synthesis of verbalactone

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Abstract A simple and efficient route for the stereoselective total synthesis of verbalactone from commercially available inexpensive starting material D-mannitol using Barbier allylation, α-aminoxylation, and Yamaguchi macrolactonization as key steps is reported.

Keywords D-Mannitol · Barbier allylation · α-Aminoxylation · Yamaguchi macrolactonization · Verbalactone

Introduction

A 12-membered C_2 symmetric dilactone, verbalactone (**1**), is the first example for which a 1,7-dioxacyclododecane moiety was reported as the ring system of a natural product. Verbalactone (**1**) was isolated from the roots of *Verbascum undulatum Lam*., a biennial plant of the genus *Verbascum* that belongs to the family Scrophulariaceae by Mitaku et al. [1], and exhibits antibacterial activity against various Gram-positive (MIC 62.5 mg/cm^3) and Gram-negative bacteria (MIC 125 mg/cm^3) [2]. The absolute stereochemistry of verbalactone structure, 4*R*,6*R*,10*R*,12*R*, were determined by spectroscopic methods, chemical correlation and is similar to the NMR profile of (3*R*,5*R*)-dihydroxydecanoic acid [3–6].

The interesting biologically active nature and stereochemical complexity of verbalactone attracted scientists from worldwide toward the total synthesis of this lactone. The first total synthesis of verbalactone was reported by Barua and co-workers in 2004 using Barbier–Grignard and Sharpless asymmetric dihydroxylation reactions as key steps [7]. Further Sharma and Reddy reported another route from L-malic acid [8]. Subsequently, Allais and Louvel reported a different strategy for the synthesis of verbalactone with commercially available hexanal as a starting material using highly diastereo- and enantioselective allylmetalations and Yamaguchi macrolactonization [9]. Meanwhile, several scientists reported with either chiral pool starting material or stereoselective methods to install stereogenic centers and consequent Yamaguchi macrolactonization to construct the lactone [10–14] (Fig. 1).

The reported synthetic routes to verbalactone mainly associated with the long reaction sequences, lower yields, and dependence on the chiral pool resources are some of the disadvantages in the earlier reported methods. To overcome the problems associated with the earlier approaches, herein, we reported an alternative route for the synthesis of verbalactone. In this context, we would like to report an efficient and high-yielding enantioselective synthesis of verbalactone employing an entirely different approach. This strategy involves a concise divergent synthesis of the target molecule **1** from inexpensive starting material, i.e., D-mannitol, and subsequent Yamaguchi macrolactonization to achieve the cyclic ring.

Results and discussion

The retrosynthesis route for the synthesis of verbalactone is outlined in Scheme 1. The target molecule **1** could be

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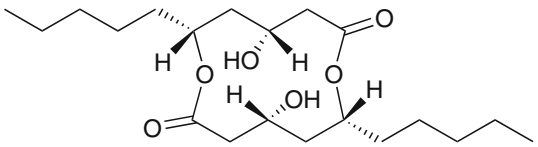
synthesized through Yamaguchi's macrolactonization of a hydroxyl acid **2** which in turn could be obtained from ester **3**. The ester **3** could be prepared from the chiral aldehyde **4**, which in turn is derived from commercially available D-mannitol.

The total synthesis of **1** was initiated with the known chiral aldehyde **4** as illustrated in Scheme 2. Accordingly, **4** [15] on zinc-mediated Barbier allylation gave the allylic alcohol **5**. Here *anti* selectivity in Barbier allylation can be explained by the Felkin–Anh chelation model as shown in Fig. 2. Due to chelation of ZnBr to the aldehyde carbonyl, the nucleophile approaches from less-hindered side, thus resulting in the formation of *anti* isomer predominantly.

The treatment of alcohol **5** with BnBr and sodium hydride in dry THF at 25 to 30 °C for 6 h yielded **6**, which on hydrolysis with 70 % aq. acetic acid gave diol **7**. Oxidative cleavage of **7** followed by Wittig olefination of the resultant aldehyde afforded the ester **3**. The reduction of **3** with LAH in dichloromethane at −78 °C for 2 h gave alcohol **8** (88 %). Oxidation of **8** under Swern condition gave the corresponding aldehyde **8a**. This aldehyde was subjected to α-aminoxylation [16–18] catalyzed by L-proline, followed by in situ reduction using $NaBH_4$ to furnish the required α-amino-substituted diol **8b**. The reductive hydrogenation of α-amino-substituted diol using 10 % Pd–C in methanol afforded the chiral diol **9** in 72 % yield (>97 % de). Selective mono-tosylation of diol **9** in the presence of Bu_2SnO and Et_3N in CH_2Cl_2 furnished **9a**. Nucleophilic cyclization of the tosylate **9a** in the presence of K_2CO_3 in MeOH afforded epoxide **10**. Opening of epoxide **10** with CuI and *n*-BuLi gave secondary alcohol **11** (72 %) and subsequent silylation of the secondary alcohol **11** with TBSCl and imidazole in CH_2Cl_2 gave **12** in 70 % yield. Silyl ether **12** was oxidized with $RuCl_3/NaIO_4$ in $CCl_4/MeCN/H_2O$ to furnish acid **13** in 72 % yield. Acid **13** was subjected to esterification under Yamaguchi reaction conditions [19] to give lactone **14** in 77 % yield. Finally, since deprotection of the benzyl groups in **14** has already been reported in the literature [8], the synthesis of **14** formally constitutes the synthesis of verbalactone **1**. The optical rotation value, IR, mass, ^1H and ^{13}C NMR data of the synthetic **14** were in good agreement with the data reported by Sharma et al. [8].



Verbalactone (**1**)

Fig. 1 Structure of verbalactone (**1**)

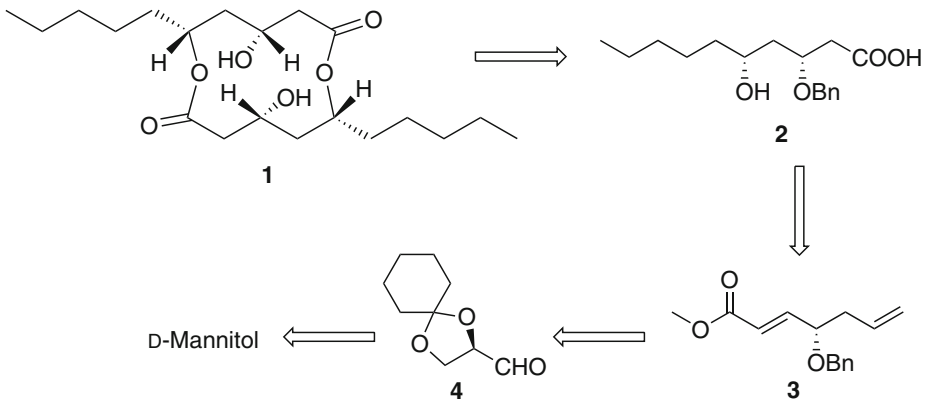
Conclusion

In conclusion, a simple and efficient route for the stereoselective total synthesis of verbalactone (**1**) is reported utilizing Barbier allylation, α-aminoxylation, and Yamaguchi macrolactonization as key steps.

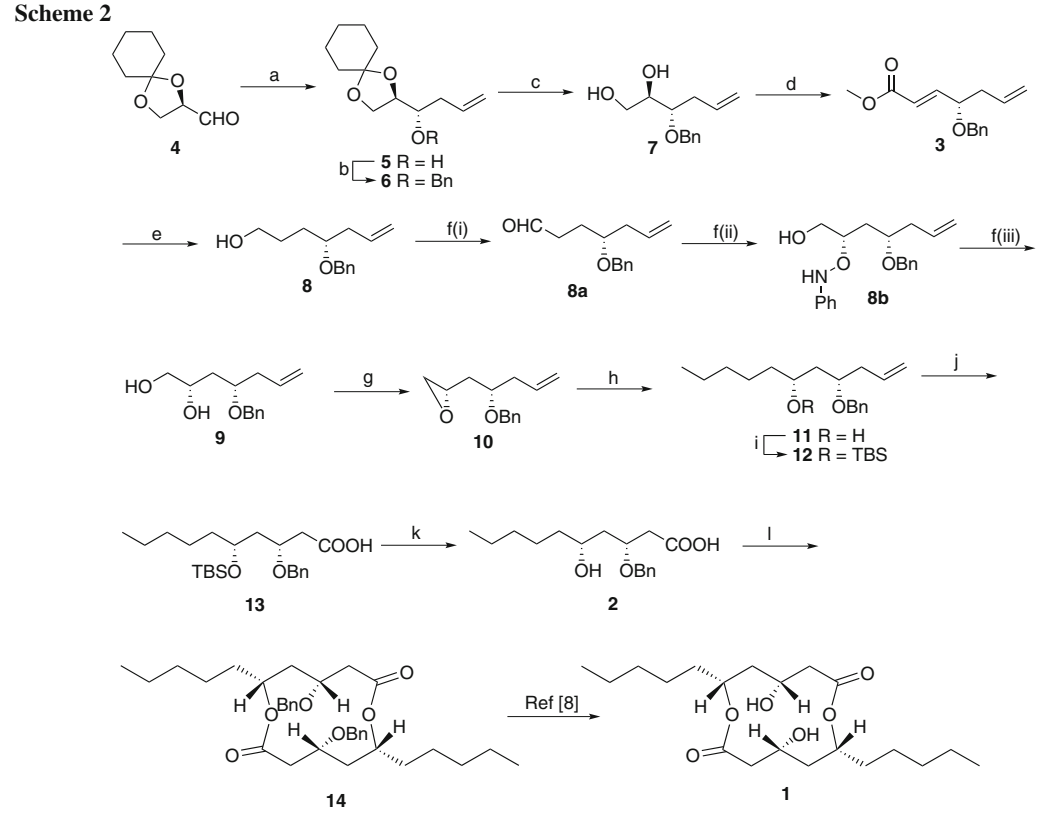
Experimental

All chemicals and solvents were purchased from Sigma–Aldrich and Merck and used without further purification. All reactions were monitored by thin-layer chromatography (TLC) on silica Merck 60 F254 precoated aluminum plates. ^1H and ^{13}C NMR spectra were recorded with 500, 300, 150, and 75 MHz Bruker spectrometer. Chemical shifts are reported in δ units (ppm) with tetramethylsilane

Scheme 1



Scheme 2



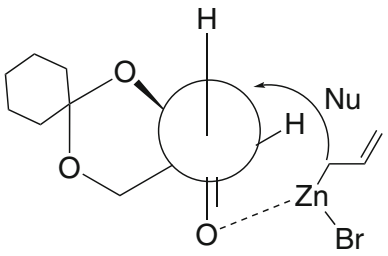


Fig. 2 Barbier allylation by the Felkin–Anh chelation model

(TMS) as a reference. All coupling constants (*J*) are reported in Hertz. Multiplicity is indicated as s (singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), m (multiplet). FT-IR spectra were taken on IR spectrophotometer using NaCl optics. Mass spectra were performed on direct inlet system or LC by MSD trap SL. Optical rotation values are recorded on digital polarimeter at 25 °C.

*(S)-1-((R)-1,4-Dioxaspiro[4.5]decan-2-yl)but-3-en-1-ol (**5**) [20]*

Allyl bromide (10.7 cm^3, 126.30 mmol, 1.2 equiv) was added over 15 min to a mixture of 18 g aldehyde **4** (105.26 mmol, 1 equiv) and 13.7 g dry zinc (210.50 mmol, 2 equiv) in 100 cm^3 THF at 0 °C followed by the addition of 72 cm^3 sat. NH_4Cl solution. After 6 h, the reaction mixture was diluted with 50 cm^3 sat. NH_4Cl solution and extracted with ethyl acetate (2 × 100 cm^3). The organic layers were washed with water (2 × 50 cm^3) and 50 cm^3 brine, dried over Na_2SO_4, concentrated under reduced pressure and the residue was purified by column chromatography (silica gel 60–120 mesh, 5 % EtOAc in pet. ether) to furnish **5** (17.5 g, 78 %) as a yellow liquid. $[\alpha]_D = +1.7$ ($c = 2.5$, $CHCl_3$).

*(R)-2-((S)-1-(Benzyloxy)but-3-enyl)-1,4-dioxaspiro[4.5]decane (**6**) [21]*

NaH (2.41 g, 103.7 mmol, 2 equiv) was added to a cooled (0 °C) solution of 11.0 g **5** (51.8 mmol, 1 equiv) in 50 cm^3 dry THF, stirred for 30 min, and treated with 6.9 cm^3 BnBr (57.1 mmol, 1.1 equiv). After stirring at room temperature for 6 h, the reaction mixture was quenched with 8 cm^3 sat. NH_4Cl solution and extracted with ethyl acetate (2 × 40 cm^3). The organic layers were washed with water (2 × 10 cm^3), 30 cm^3 brine, dried (Na_2SO_4), evaporated under reduced pressure; the residue was purified by column chromatography (silica gel 60-120 mesh, 3 % EtOAc in pet. ether) to furnish **6** (12 g, 83 %) as a yellow liquid. $[\alpha]_D = +41.7$ ($c = 1.5$, $CHCl_3$).

*(2R,3S)-3-(Benzyloxy)hex-5-ene-1,2-diol (**7**) [22]*
A solution of 11.6 g **6** (38.41 mmol, 1 equiv) in 120 cm^3 70 % aq. acetic acid was stirred at room temperature for 12 h. After the completion of reaction, it was quenched with $NaHCO_3$ and adjusted its pH to 2–3. The reaction mixture was extracted with ethyl acetate (3 × 100 cm^3) and dried over Na_2SO_4 followed by the evaporation of solvent under reduced pressure. Further purification of the residue was done by column chromatography (silica gel 60–120 mesh, 40 % EtOAc in pet. ether) furnishing **7** (6.2 g, 73 %) as a yellow liquid. $[\alpha]_D = +41.9$ ($c = 1.0$, $CHCl_3$).

(S,E)-Methyl 4-(benzyloxy)hepta-2,6-dienoate (**3**, $C_{15}H_{18}O_3$)
$NaIO_4$ (8.6 g, 40.54 mmol, 1.5 equiv) was added to a cooled (0 °C) solution of 6 g **7** (27.02 mmol, 1 equiv) in 60 cm^3 CH_2Cl_2, followed by the addition of 4 cm^3 sat. $NaHCO_3$ and stirred at room temperature for 5 h. Further the reaction mixture was dried over Na_2SO_4, filtered and evaporated the solvent under reduced pressure gave the corresponding aldehyde, which was used directly for the next step.

(Methoxycarbonylmethylene)triphenylphosphorane (13.5 g, 40.54 mmol, 1.5 equiv) was added to the above-obtained aldehyde which was already dissolved in 80 cm^3 benzene and the reaction mixture was allowed for reflux. After 2 h, solvent was evaporated and the residue was purified by column chromatography (silica gel 60–120 mesh, 10 % EtOAc in pet. ether) furnishing **3** (6.04 g, 91 %) as a yellow liquid. *E* isomer: $[\alpha]_D = +74.6$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.36$–7.24 (m, 5H, $-C_6H_5$), 6.59 (dd, 1H, $J = 6.6$, 15.8 Hz, olefinic), 5.89 (d, 1H, $J = 15.8$ Hz, olefinic), 5.79–5.61 (m, 1H, olefinic), 4.99–4.91 (m, 2H olefinic), 4.54 (s, 2H, benzylic), 3.73 (s, 3H, $-OCH_3$), 3.57–3.49 (m, 1H, –OCH), 2.48–2.31 (m, 2H, allylic) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 166.8$, 147.1, 139.8, 134.1, 129.2, 128.9, 128.6, 119.2, 113.4, 82.3, 70.8, 52.2, 39.6 ppm; IR (neat):$\bar{\nu} = 3{,}390$, 2,902, 1,722, 1,612, 1,512, 1,448, 1,386, 1,164, 1,037 cm^{-1}; MS (ESI): $m/z = 247$ ($[M + H]^+$).

(R)-4-(Benzyloxy)hept-6-en-1-ol (**8**, $C_{14}H_{20}O_2$)
DIBAL-H (30.0 cm^3, 42.27 mmol, 20 mol% in toluene, 2 equiv) was added to a stirred solution of 5.2 g ester **3** (21.13 mmol, 1 equiv) in 30 cm^3 dry CH_2Cl_2 at −78 °C and the reaction mixture was stirred at the same temperature for 2 h. Further the reaction mixture was quenched with few drops of MeOH and 5 cm^3 aq. sodium potassium tartrate, and filtered through Celite. It was dried over Na_2SO_4 followed by the evaporation of solvent under reduced pressure. Finally, the residue was purified by column chromatography (silica gel 60–120 mesh, 30 % EtOAc in pet. ether) gave **8** (4.04 g, 88 %) as a colorless liquid. $[\alpha]_D = -30.6$ ($c = 1.07$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.44$–7.28 (m, 5H, $-C_6H_5$), 5.79–5.67 (m, 1H, olefinic), 5.07–4.94 (m, 2H olefinic), 4.51 (d, 1H, $J = 10.8$ Hz, benzylic), 4.41 (d, 1H, $J = 10.8$ Hz, benzylic), 3.76 (t, 2H, $J = 5.8$ Hz, $-OCH_3$), 3.48–3.38 (m, 1H, –OCH), 2.32–2.11 (m, 2H, allylic), 1.92 (br.s, 1H, –OH), 1.59–1.22 (m, 4H, 2 × $-CH_2$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 139.6$, 133.9, 129.1, 128.8, 128.5, 116.3, 78.4, 72.2, 63.4, 36.2, 31.3, 28.4 ppm; IR: $\bar{\nu} = 3{,}363$, 2,926, 2,856, 1,496, 1,443 cm^{-1}; MS (ESI): $m/z = 243$ ($[M + Na]^+$), 221 ($[M + H]^+$).

*(2S,4S)-4-(Benzyloxy)hept-6-ene-1,2-diol (**9**) [23]*
Dry DMSO (2.7 cm^3, 36.36 mmol, 2 equiv) was added dropwise to a solution of 2.2 cm^3 oxalyl chloride (25.45 mmol, 1.5 equiv) in 15 cm^3 dry CH_2Cl_2 at −78 °C and stirred the reaction mixture for 20 min. Now a solution of 4.0 g **8** (18.18 mmol, 1 equiv) in 15 cm^3 dry CH_2Cl_2 was added to the above reaction mixture and stirred for 2 h at −78 °C. Then it was quenched with 12 cm^3 Et_3N (90.90 mmol, 5 equiv) and diluted with 50 cm^3 CH_2Cl_2. Further, the reaction mixture was washed with 50 cm^3 water, 50 cm^3 brine, dried over Na_2SO_4 followed by solvent evaporation. The obtained residue was purified by column chromatography (silica gel 60–120 mesh, 10 % EtOAc in pet. ether) to furnish the corresponding aldehyde **8a** as a yellow liquid.

One portion of 0.42 g L-proline (3.63 mmol, 20 mol%, 0.2 equiv) was added to a stirred solution of 3.9 g aldehyde (18.12 mmol, 1 equiv) and 1.94 g nitrosobenzene (18.12 mmol, 1 equiv) in 20 cm^3 DMSO at 25 °C. After 24 h, the temperature was lowered to 0 °C, followed by dilution with 30 cm^3 anhydrous MeOH and the careful addition of excess $NaBH_4$ (1.45 g, 36.33 mmol, 2 equiv). Now the reaction mixture was quenched after 10 min by pouring the reaction mixture into a vigorously stirred biphasic solution of Et_2O and aqueous HCl (1 M). Then the organic layer was separated and the aqueous phase was extracted with EtOAc (3 × 30 cm^3). Further, the combined organic phase was dried over anhydrous Na_2SO_4, concentrated, and purified by column chromatography over silica gel using EtOAc/pet. ether (40:60) as eluent, which gave the pure aminoxy alcohol **8b** as a pure diastereomer. At this time, 4.9 g aminoxy alcohol (14.98 mmol, 1 equiv) was dissolved in 30 cm^3 EtOAc and 0.25 g 10 % Pd/C was added to this solution. Now the reaction mixture was allowed for stirring at 1 bar hydrogen pressure for 12 h. After completion of the reaction (monitored by TLC), it was filtered through Celite pad. Further, the filtrate was dried over Na_2SO_4, concentrated, and the residue was purified by column chromatography using 40 % EtOAc in

pet. ether as eluent to give the pure diol **9** (2.9 g, 69 %) as a yellow liquid. $[\alpha]_D^{25} = +6.8$ ($c = 0.5$, $CHCl_3$).

*(S)-2-((S)-2-(Benzyloxy)pent-4-enyl)oxirane (**10**) [23]*
p-TsCl (2.2 g, 11.86 mmol, 1 equiv) was added portion wise at 0 °C to a cooled (0 °C) stirred solution of 2.8 g diol **9** (11.86 mmol, 1 equiv), DMAP (cat.), and 3.3 cm^3 Et_3N (23.72 mmol, 2 equiv) in 20 cm^3 CH_2Cl_2 and the reaction mixture was stirred at room temperature for 14 h. Work-up as described for **15** and purification by column chromatography (silica gel 60–120 mesh, 10 % EtOAc in pet. ether) gave mono-tosylate **9a** (4.2 g, 88 %) as a yellow syrup.

A solution of 4.2 g of the above crude tosylate **9a** (11.5 mmol, 1 equiv) in 25 cm^3 MeOH was treated with 4.0 g K_2CO_3 (28.84 mmol, 2.5 equiv) and stirred at room temperature for 1 h. After, the reaction mixture was treated with 10 cm^3 aq. NH_4Cl solution and MeOH was evaporated below 40 °C under reduced pressure. Further the residue was extracted with ether (3 × 25 cm^3) and combined organic layers were washed with 25 cm^3 water, 25 cm^3 brine, dried over Na_2SO_4 followed by evaporation. Finally, the residue was purified by column chromatography (silica gel 60–120 mesh, 10 % EtOAc in pet. ether) to afford **10** (1.7 g, 68 %) as a colorless liquid. $[\alpha]_D^{25} = +23.1$ ($c = 3.1$, $CHCl_3$).

(4S,6R)-4-(Benzyloxy)undec-1-en-6-ol (**11**, $C_{18}H_{28}O_2$)
n-Butyllithium (14 cm^3, 29.35 mmol, 2 M solution in *n*-hexane, 4 equiv) was added at −20 °C to a stirred mixture of 2.7 g copper(I) iodide (14.67 mmol, 2 equiv) in 20 cm^3 dry ether and stirred for 0.5 h. A solution of 1.6 g **10** (7.33 mmol, 1 equiv) in 10 cm^3 dry ether was added to the above mixture and stirred for 1 h. The reaction mixture was quenched with 10 cm^3 aq. NH_4Cl solution and allowed to stir for 15 min. Organic layer was separated and the aqueous layer was washed with ethyl acetate (2 × 20 cm^3). The combined organic layers were washed with water (2 × 10 cm^3), 10 cm^3 brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel 60–120 mesh, 12 % EtOAc in pet. ether) to give **11** (1.56 g, 78 %) as a colorless liquid. $[\alpha]_D = +31.6$ ($c = 0.7$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.37–7.22 (m, 5H, $–C_6H_5$), 5.83–5.69 (m, 1H, olefinic), 5.06–4.97 (m, 2H olefinic), 4.61 (d, 1H, J = 10.9 Hz, benzylic), 4.39 (d, 1H, J = 10.9 Hz, benzylic), 3.82–3.76 (m, 1H, –OCH), 3.648–3.57 (m, 1H, –OCH), 2.32–2.22 (m, 2H, allylic), 2.06 (br s, 1H, –OH), 1.57 (t, 2H, J = 8.1 Hz, $–CH_2$), 1.46–1.07 (m, 8H, 4 × $–CH_2$), 0.93 (t, 3H, J = 7.6 Hz, $–CH_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.8, 136.3, 128.9, 128.5, 128.2, 114.1, 75.9, 72.2, 70.1, 44.4, 38.6, 36.5, 33.2, 24.2, 23.8, 14.6 ppm; IR (neat): $\bar{\nu}$ = 3,351, 3,052, 2,931, 2,855, 1,732, 1,611, 1,509, 1,461, 1,247, 1,106, 1,036, 823, 701 cm^{-1}; MS (ESI): m/z = 299 ($[M + Na]^+$).

((4S,6R)-4-(Benzyloxy)undec-1-en-6-yloxy)(tert.-butyl)-dimethylsilane (**12**, $C_{24}H_{42}O_2Si$)
The stirred solution of alcohol 1.5 g **11** (5.43 mmol, 1 equiv) and 1.1 g imidazole (16.30 mmol, 3 equiv) in 20 cm^3 dry CH_2Cl_2 was treated with 0.91 g TBSCl (5.93 mmol, 1.1 equiv) at 0 °C under nitrogen atmosphere and stirred at room temperature for 4 h. The reaction mixture was quenched with 10 cm^3 aq. NH_4Cl solution and extracted with CH_2Cl_2 (2 × 50 cm^3). The combined extracts were washed with 30 cm^3 water, 30 cm^3 brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (silica gel 60–120 mesh, 5 % EtOAc in pet. ether) to furnish **12** (2.0 g, 91 %) as a colorless liquid. $[\alpha]_D = +57.4$ ($c = 0.76$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.34–7.22 (m, 5H, $–C_6H_5$), 5.82–5.69 (m, 1H, olefinic), 5.08–4.97 (m, 2H olefinic), 4.61 (q, 2H, J = 11.1 Hz, benzylic), 3.61 (m, 1H, –OCH), 3.49 (p, 1H, J = 6.1, 9.2 Hz, –OCH), 2.39–2.12 (m, 2H, allylic), 1.56 (t, 2H, J = 8.1 Hz, $–CH_2$), 1.40–1.11 (m, 8H, 4 × $–CH_2$), 1.02 (s, 9H, *t*-butyl), 0.91 (t, 3H, J = 7.5 Hz, $–CH_3$), 0.21 (s, 6H, 2 × $–CH_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.6, 136.8, 128.8, 128.5, 128.3, 116.4, 76.9, 74.2, 73.1, 44.6, 38.3, 34.3, 26.8, 26.1, 23.2, 19.1, 13.8, −4.9 ppm; IR (neat): $\bar{\nu}$ = 2,959, 2,854, 1,477, 1,368, 1,264, 1,128, 1,049, 996 cm^{-1}; MS (ESI): m/z = 413 ($[M + Na]^+$), 391 ($[M + H]^+$).

(3R,5R)-3-(Benzyloxy)-5-(tert.-butyldimethylsilyloxy)-decanoic acid (**13**, $C_{23}H_{40}O_4Si$)
$NaIO_4$ (3.95 g, 18.46 mmol, 4 equiv) was added to a solution of 1.8 g olefin **12** (4.61 mmol, 1 equiv) in a mixture of 6 cm^3 CCl_4, 6 cm^3 CH_3CN, and 9 cm^3 H_2O followed by the addition of 0.02 g $RuCl_3$ (0.09 mmol, 0.05 equiv) and the entire mixture was stirred vigorously for 2 h at room temperature. The reaction mixture was diluted with 5 cm^3 CH_2Cl_2 and the upper aqueous phase was extracted with CH_2Cl_2 (2 × 10 cm^3). The combined organic layers were dried over Na_2SO_4 and concentrated. The obtained crude residue was purified by column chromatography (silica gel 60–120 mesh, 25 % EtOAc in pet. ether) to afford **13** (1.6 g, 85 %) as a liquid. $[\alpha]_D = +22.24$ ($c = 0.42$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.34–7.24 (m, 5H, $–C_6H_5$), 4.49 (d, 1H, J = 11.8 Hz, benzylic), 4.39 (d, 1H, J = 11.8 Hz, benzylic), 3.57 (m, 1H, –OCH), 3.48–3.39 (m, 1H, –OCH), 2.61 (d, 2H, J = 6.3 Hz, $–CH_2$), 1.54 (m, 2H, $–CH_2$), 1.46–1.17 (m, 8H, 4 × $–CH_2$), 0.98 (s, 9H, *t*-butyl), 0.84 (t, 3H, J = 7.5 Hz, $–CH_3$), 0.33 (s, 6H, 2 × $–CH_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.8, 138.4, 129.3, 128.5, 128.3, 75.8, 74.7, 72.8, 45.3, 40.1, 33.8, 32.3, 28.8, 26.8,

23.2, 18.8, 13.8, −4.4, −4.1 ppm; IR (neat): $\bar{\nu}$ = 3,581, 3,033, 2,953, 1,713, 1,606 cm^{-1}. MS (ESI): *m/z* = 431 ($[M + Na]^+$), 409 ($[M + H]^+$).

(3R,5R)-3-(Benzyloxy)-5-hydroxydecanoic acid (**2**, $C_{17}H_{26}O_4$)

TBAF (1.1 cm^3, 4.11 mmol, 1.2 equiv) was added to a cooled (0 °C) solution of 1.4 g **13** (3.43 mmol, 1 equiv) in 10 cm^3 dry THF under nitrogen atmosphere and stirred for 3 h. After completion of reaction, the reaction mixture was diluted with 5 cm^3 water and extracted with ethyl acetate (2 × 50 cm^3). The combined organic layers were washed with water (2 × 10 cm^3), 10 cm^3 brine, dried over Na_2SO_4, evaporated, and the residue was purified by column chromatography (silica gel 60–120 mesh, 55 % EtOAc in pet. ether) to give **2** (0.86 g, 86 %) as a liquid. $[\alpha]_D$ = +32.6 (*c* = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.37–7.25 (m, 5H, $–C_6H_5$), 4.43 (d, 1H, *J* = 11.7 Hz, benzylic), 4.39 (d, 1H, *J* = 11.7 Hz, benzylic), 3.87–3.78 (m, 1H, –OCH), 3.51–3.43 (m, 1H, –OCH), 2.58 (d, 2H, *J* = 6.5 Hz, $–CH_2$), 1.54 (m, 2H, $–CH_2$), 1.46–1.27 (m, 8H, 4 × $–CH_2$), 0.94 (t, 3H, *J* = 7.3 Hz, $–CH_3$) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 175.6, 138.5, 129.2, 128.4, 128.2, 74.6, 72.3, 71.2, 44.2, 40.8, 38.4, 32.2, 25.8, 22.4, 14.3 ppm; IR (neat): $\bar{\nu}$ = 3,481, 2,939, 2,851, 2,112, 1,723, 1,614, 1,512, 1,362, 1,041, 778 cm^{-1}; MS (ESI): *m/z* = 317 ($[M + Na]^+$), 295 ($[M + H]^+$).

*(3R,5R,9R,11R)-3,9-Bis(benzyloxy)-5,11-dipentylcyclododecane-1,7-dione (**14**) [8]*

A solution of 0.4 cm^3 2,4,6-trichlorobenzoyl chloride (2.55 mmol, 2 equiv) in 2 cm^3 dry THF was added to a stirred solution of 0.5 g **2** (1.7 mmol, 1 equiv) and 0.7 cm^3 Et_3N (5.1 mmol, 4 equiv) in 3 cm^3 dry THF. The resulting mixture was stirred for 2 h at room temperature under nitrogen atmosphere and evaporated to afford the mixed anhydride. Now, it was diluted with 10 cm^3 toluene and filtered quickly through Celite. The filtrate was added dropwise to a stirred solution of 0.06 g DMAP (0.51 mmol, 0.3 equiv) in 490 cm^3 toluene (total volume used for this operation was 500 cm^3) at 90 °C over a period of 8 h. After the complete addition, the reaction mixture was stirred at 100 °C for 2 h. Further, it was cooled, washed with 40 cm^3 7 % aq $NaHCO_3$, 40 cm^3 2 M aqueous HCl, 40 cm^3 brine, and dried over Na_2SO_4. The separated organic layer was evaporated under reduced pressure and the obtained residue was purified by column chromatography (silica gel 60–120 mesh, 15 % EtOAc in pet. ether) to give **14** (0.48 g, 52 %) as a syrup. $[\alpha]_D$ = +12.3 (*c* = 0.8, $CHCl_3$).

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References

1. Magiatis P, Spanakis D, Mitaku S, Tsitsa E, Mentis A, Harvala C (2001) J Nat Prod 64:1093
2. Doshida J, Hasegawa H, Onuki H, Shimidzu N (1996) J Antibiot 49:1105
3. Takano S, Seton M, Ogasawara K (1992) Tetrahedron Asymm 3:533
4. Bennett F, Knight D, Fenton G (1991) J Chem Soc Perkin Trans 1:1543
5. Bennett F, Knight D, Fenton G (1989) Heterocycles 29:639
6. Yang YL, Falck JR (1982) Tetrahedron Lett 23:4305
7. Gogoi S, Barua NC, Kalita B (2004) Tetrahedron Lett 45:5577
8. Sharma GVM, Reddy ChG (2004) Tetrahedron Lett 45:7483
9. Allais F, Louvel MC, Cossy J (2007) Synlett 18:451
10. Salunke GB, Shivakumar I, Gurjar MK (2009) Tetrahedron Lett 50:2048
11. Garg A, Singh VK (2009) Tetrahedron 65:8677
12. Das B, Laxmminarayana K, Krishnaiah M, Nandan Kumar D (2009) Helv Chim Acta 92:1840
13. Sabitha G, Bhaskar V, Yadav JS (2008) Synth Commun 38:3129
14. Wu JZ, Gao J, Ren GB, Zhen ZB, Zhang YH, Wu YK (2009) Tetrahedron 65:289
15. Chatopadyay A, Mamdapur VR (1995) J Org Chem 60:585
16. Hayashi Y, Yamaguchi J, Hibino K, Shoji M (2003) Tetrahedron Lett 44:8293
17. List B (2002) Tetrahedron 58:5573
18. Hayashi Y, Yamaguchi J, Sumiya T, Shoji M (2004) Angew Chem Int Ed 43:1112
19. Inanaga J, Hirata K, Saeki H, Katsuki T, Yamaguchi M (1979) Bull Chem Soc Jpn 52:1989
20. Vilanova C, Sánchez-Péris M, Roldán S, Dhotare B, Carda M, Chattopadhyay A (2013) Tetrahedron Lett 54:6562
21. Chandrasekhar S, Sreelakshmi L (2012) Tetrahedron Lett 53:3233
22. Bujaranipalli S, Eppa G, Das S (2013) Synlett 24:1117
23. Kamal A, Reddy PV, Prabhakar S, Balakrishna M (2009) Tetrahedron Asymm 20:2861