Tetrahedron: *Asymmetry* xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Stereoselective synthesis of dendrodolide-L

Sheshurao Bujaranipalli, Saibal Das *

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

ARTICLE INFO

Article history:
Received 23 January 2016
Accepted 16 February 2016
Available online xxxx

ABSTRACT

An efficient stereoselective total synthesis of 12-membered macrolide dendrodolide L has been achieved. The key reactions involved are Keck asymmetric allylation, Jacobsen's hydrolytic kinetic resolution, Sharpless asymmetric epoxidation, Mitsunobu reaction and ring-closing metathesis reaction.

1. Introduction

Marine fungi, a potential source of biologically active secondary metabolites, are a topic of growing interest. Dendrodolide L is a secondary metabolite, which was isolated by Zhang et al. from dendrochium sp.,[1] (a fungus associated with the sea cucumber *Holothuria nobilis Selenka*, which was collected from the South China Sea) along with twelve other dendrodolides (Fig. 1). The structure of dendrodolide L **12** was elucidated by means of a detailed spectroscopic analysis and X-ray single crystal diffraction studies. Furthermore, it was shown to exhibit in vitro cytotoxicity against the tumour cell line HCT-116 with an IC_{50} value of 26.5 μg/mL. Over last two years, the synthesis of a few dendrodolides has been reported using various protocols.[2] In continuation of our interests in the synthesis of bioactive natural products,[3] we herein report the stereoselective total synthesis of dendrodolide L **12** using Keck asymmetric allylation, Jacobsen's hydrolytic kinetic resolution, Sharpless asymmetric epoxidation, Mitsunobu reaction and ring closing metathesis (RCM) reaction as the key steps.

2. Results and discussion

As outlined below, the retrosynthetic approach (Scheme 1) suggests that the construction of the 12-membered macrolide could be obtained using an RCM approach of compound **14**. Compound **14** was envisaged from esterification of compound **15** and **16**, which may possibly be prepared from easily available butane-1,4-diol **17** (route 1)/5-hexene-1-ol **18** (route 2) and propane-1,3-diol **19**, respectively.

To begin the synthesis, the proposed acid subunit **16** was produced (Scheme 2) from propane-1,3-diol **19**, which was selectively mono-protected as its PMB ether using a literature procedure.[4]

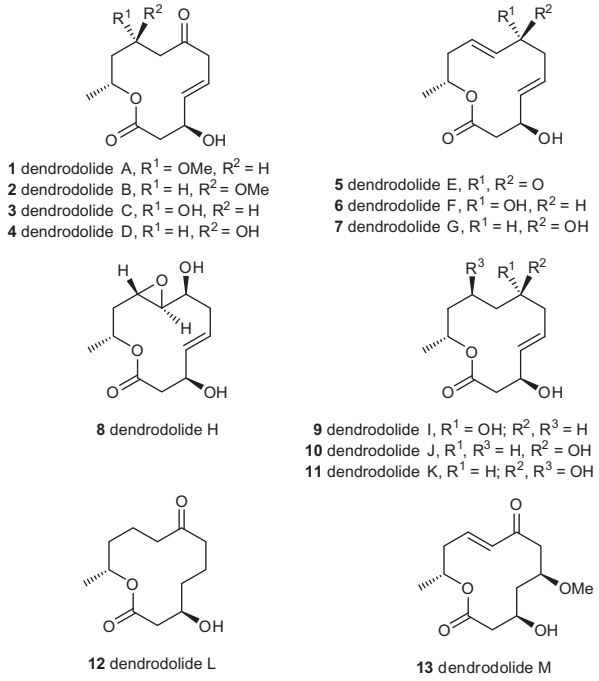


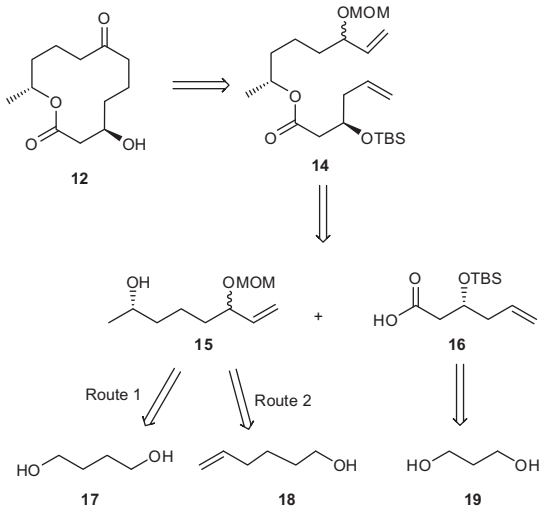
Figure 1. Structures of dendrodolides A–M.

Oxidation of the free hydroxyl group of **20** under PCC oxidation conditions afforded the desired aldehyde, which was then subjected to Keck asymmetric allylation[5] conditions [(*R*)-BINOL, $Ti(O^iPr_4)$, allyl tributyltin, 4 Å MS, dry CH_2Cl_2, −78 °C to −20 °C] to produce homoallylic alcohol 21 in 84% yield and with good enantioselectivity (>96% ee, by HPLC).

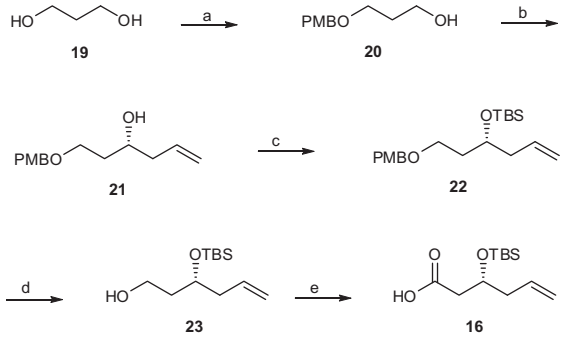
The chiral secondary alcohol functionality in alcohol **21** was protected as its TBS ether by treatment with imidazole/TBSCl in

* Corresponding author. Tel.: +91 40 2719 1887; fax: +91 40 2716 0512.
E-mail address: saibal@iict.res.in (S. Das).

http://dx.doi.org/10.1016/j.tetasy.2016.02.007
0957-4166/



Scheme 1. Retrosynthetic analysis of dendrodolide **12**.

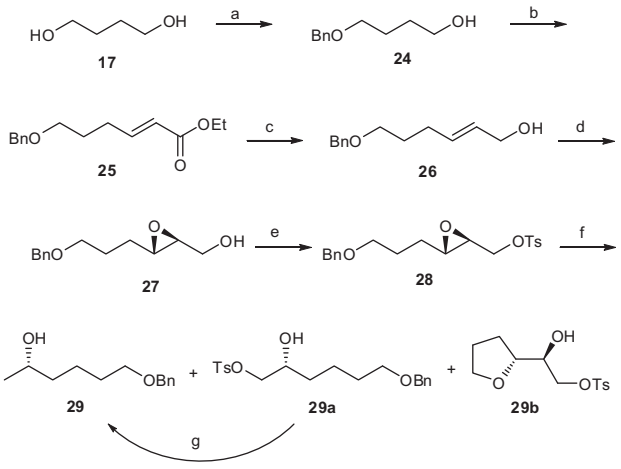


Scheme 2. Reagents and conditions: (a) PMBOH, Amberlyst-15 (cat.), CH_2Cl_2, 6 h, 75%; (b) (1) PCC, Celite, CH_2Cl_2, 0 °C–rt, 1 h; (2) (*R*)-BINOL, Ti(O^iPr_4), 4 Å molecular sieves, allyl tributyltin, CH_2Cl_2, −78 °C then −20 °C, 6 h, 77% from two steps; (c) TBSCl, imidazole, CH_2Cl_2, 0 °C–rt, 3 h, 96%; (d) DDQ, CH_2Cl_2: pH 7 buffer (9:1), 0 °C–rt, 30 min, 82%; (e) TEMPO, BAIB, CH_2Cl_2/H_2O (1:1), 0 °C–rt, 1 h, 76%.

dichloromethane to give compound **22** in 96% yield. Removal of the PMB group in compound **22** was successfully achieved using DDQ in CH_2Cl_2/pH 7 buffer (9:1) to provide compound **23** in 82% yield. The primary alcohol **23** was then oxidized to its acid under BAIB/TEMPO in CH_2Cl_2/H_2O (1:1) conditions to yield the expected acid **16** in 76% yield.

Alcohol fragment **15** was synthesised via two different approaches. In route 1 (Scheme 3), the butane-1,4-diol **17** was selectively mono-protected as its benzyl ether using BnBr and NaH in THF to afford **24** in 80% yield. Oxidation of the alcohol was achieved under Swern oxidation conditions [$(COCl)_2$, DMSO, TEA, CH_2Cl_2, −78 °C] to afford the corresponding aldehyde, which was further treated with (ethoxycarbonylmethylene)triphenylphosphorane for two carbon homologation in benzene under reflux conditions to provide (*E*)-allyl ester **25** in 91% yield over two steps. The *E*-geometry of the double bond was confirmed by the coupling constant between the respective olefin protons (J = 15.6 Hz).

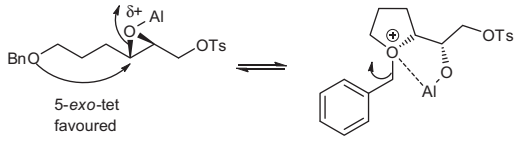
Compound **25** was then treated with DIBAL-H in CH_2Cl_2 to provide allyl alcohol **26** in 92% yield. Exposure of compound **26** to Sharpless asymmetric epoxidation conditions[6] [(+)-DET, cumene hydroperoxide, Ti(O^iPr)$_4$, CH_2Cl_2] afforded the desired epoxyalcohol **27** in 89% yield. The epoxy alcohol was then converted into its corresponding, 2,3-epoxytosylate **28** in 94% yield using TsCl,



Scheme 3. Reagents and conditions: (a) NaH, BnBr, THF, 0 °C–rt, 1 h, 80.%, (b) (1) $(COCl)_2$, DMSO, TEA, CH_2Cl_2, −78 °C (2) Ph_3P = $CHCO_2Et$, benzene, reflux, 4 h, 91% from two steps; (c) DIBAL-H, CH_2Cl_2, 0 °C–rt, 1 h, 92%; (d) (+)-DET, Ti(O^iPr)$_4$, Cumene hydroperoxide, 4 Å MS, CH_2Cl_2, −20 °C, 12 h, 89%; (e) TsCl, TEA, CH_2Cl_2, 0 °C–rt, 3 h, 94%; (f) see Table 1; (g) $LiAlH_4$, THF, 0 °C–rt, 30 min, 86%.

TEA in CH_2Cl_2. Regioselective reduction of epoxide **28** using DIBAL-H[7] in CH_2Cl_2 at −20 °C to room temperature gave a mixture of fully reduced compound **29** in 22% yield, partially reduced compound **29a** in 16% yield and the undesired substituted tetrahydrofuran (THF) derivative **29b** in 40% yield instead of giving **23** as reported. Compound **29a** was then further reduced with $LiAlH_4$ in THF to obtain **29** in 86% yield.

The formation of the undesired furan compound **29b** can be attributed to the chelation of the aluminium, thus leading to the thermodynamically more stable and more favored 5-*exo*-tet cyclization which resulted in the cleavage of the benzyl ether after forming the THF ring (Scheme 4). The cleavage of the epoxide can be explained by Baldwin rules,[8] in which 5-*exo*-tet is favored where as 6-*endo*-tet is disfavored. Several attempts were made to minimize the formation of compound **29b** and to improve the yield of the compound **29**/**29a** (Table 1).



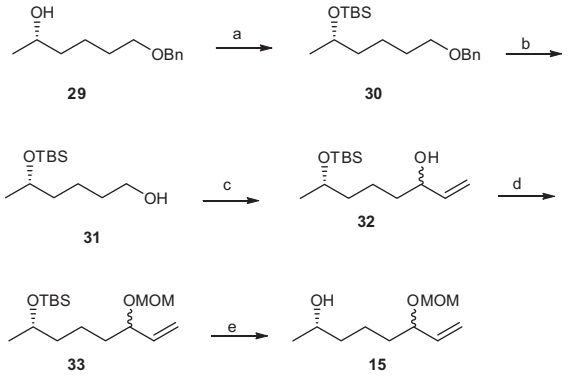
Scheme 4. Proposed mechanism for tetrahydrofuran derivative formation.

When the reaction was carried out at 0 °C–rt in hexane, only 16% of **29** was formed, whereas **29b** was formed in 73% (entry 1, Table 1) but when the reaction was carried out at lower temperatures, only trace amounts of **29a** and **29b** were formed (entries 2 and 3) thus indicating the role of temperature. In THF, when the reaction was carried out at 0 °C–rt, almost exclusive formation of undesired **29b** was observed (entry 4) whereas at lower temperatures, only trace amounts of **29a** and **29b** were formed (entries 5 and 6). In CH_2Cl_2, at 0 °C–rt under a longer reaction time, 18% of desired **29** and 77% of undesired **29b** were obtained (entry 7). At a lower temperature, a partially reduced compound **29a** and the undesired tetrahydrofuran compound **29b** were formed in 68% and 12% yields respectively (entry 8). However, when less equivalents of DIBAL-H were used, a mixture of **29a** and **29b** was formed. Increasing the equivalents of DIBALH from 1 to 2, an improvement in the yield for the desired compound **29a** was observed (entries 9 and 10).

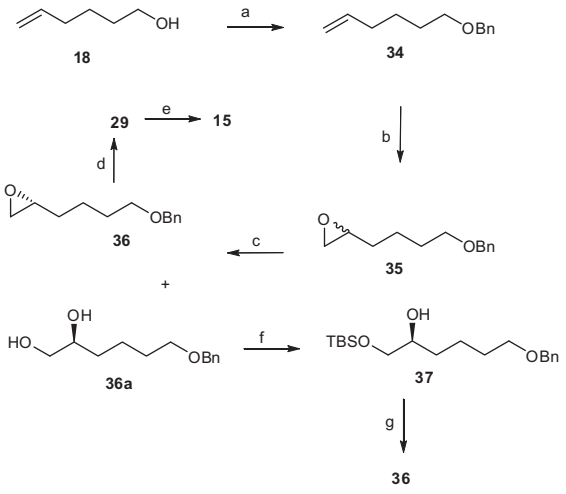
Table 1

Entry	Solvent	DIBAL-H[a]	Temp (°C)	Time (h)	Yield, **29** (%)[b]	Yield, **29a** (%)[b]	Yield, **29b** (%)[b]
1	Hexane	3	0–rt	4	16	Trace	73
2	Hexane	3	−20	4	—	Trace	Trace
3	Hexane	3	−78	4	—	Trace	Trace
4	THF	3	0–rt	4	—	Trace	86
5	THF	3	−20	4	—	—	Trace
6	THF	3	−78	4	—	—	Trace
7	CH_2Cl_2	3	0–rt	12	18	Trace	77
8	CH_2Cl_2	3	−78	1.5	—	68	12
9	CH_2Cl_2	1	−20	4	—	43	26
10	CH_2Cl_2	2	−20	4	—	76	18
11	CH_2Cl_2	3	−20–rt	12	22	16	40

[a] Molar equivalents of DIBAL-H used relative to **28**.
[b] Isolated yields after column chromatography.



Scheme 5. Reagents and conditions: (a) TBSCl, imidazole, CH_2Cl_2, 0 °C–rt, 3 h, 97%; (b) H_2, 10% Pd/C, EtOAc, 4 h, 94%; (c) (1) $(COCl)_2$, DMSO, TEA, CH_2Cl_2, −78 °C; (2) vinyl magnesium bromide, THF, 0 °C–rt, 30 min, 79% over two steps; (d) MOMCl, DIPEA, CH_2Cl_2, 0 °C–rt, 10 h, 89%; (e) TBAF, THF, 0 °C–rt, 3 h, 90%.

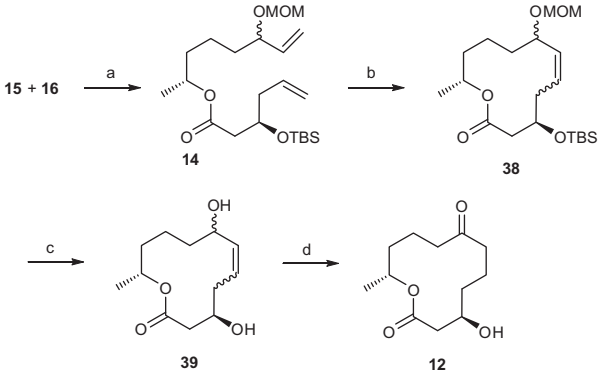


Scheme 6. Reagents and conditions: (a) NaH, BnBr, THF, 0 °C–rt, 3 h, 95.%; (b) *m*-CPBA, CH_2Cl_2, 0 °C–rt, 1 h, 96%; (c) (*R*,*R*)-Salen-Co^{III}OAc (0.5 mol %), dist. H_2O (0.55 equiv), 0 °C–rt, 14 h, 43% for **36**, 47% for **36a**; (d) $LiAlH_4$, THF, 0 °C–rt, 3 h, 89%; (e) see Scheme 5; (f) TBSCl, imidazole, CH_2Cl_2, 0 °C–rt, 3 h, 91%; (g) (1) TsCl, TEA, CH_2Cl_2, 0 °C–rt, 10 h; (2) TBAF, THF, 0 °C–rt, 6 h, 72% over two steps.

At this stage, alcohol **29** was protected as its TBS ether using TBSCl/imidazole in CH_2Cl_2 to afford compound **30** in 97% yield. The benzyl group was deprotected using Pd/C in EtOAc in the presence of hydrogen to afford primary alcohol **31** in 94% yield (Scheme 5). This alcohol was oxidized under Swern conditions to afford the corresponding aldehyde, which was subjected to Grignard reaction with vinyl magnesium bromide to furnish the desired diastereomeric alcohol **32** in 79% yield over two steps. Compound **32** would be converted into keto functionality in a later stage. The secondary alcohol present in olefinic compound **32** was then protected as its MOM ether using MOMCl (50% in methyl acetate)[9] in the presence of Hunig's base in CH_2Cl_2 to provide compound **33** in 89% yield and subsequent removal of the silyl ether with TBAF afforded the secondary alcohol **15** in 90% yield.

Another route was explored for the synthesis of intermediate **15** (Scheme 6). Compound 5-hexene-1-ol **18** was protected as its benzyl ether using BnBr, NaH in THF to afford **34** in 95% yield. It was then subjected to epoxidation using *m*-CPBA in CH_2Cl_2 to furnish epoxide **35** in 96% yield. Racemic epoxide **35** was resolved using (*R*,*R*)-Salen-Co^{III}OAc catalyst to provide the enantioenriched (>96% ee, based on HPLC) epoxide **36**[10] in 43% yield along with diol **36a** in 47%. Diol **36a** was then converted into the required epoxide **36** in 3 steps by regioselective protection of the primary alcohol in **36a** as its TBS ether using TBSCl/imidazole in CH_2Cl_2 followed by conversion of the secondary alcohol to its tosyl derivative and finally desilylation using TBAF to furnish the desired epoxide **36** in 78% over two steps. Reductive opening of epoxide **36** using $LiAlH_4$ in THF furnished the secondary alcohol **29** in 89% yield.[11] Target compound **15** was prepared from compound **29** as discussed earlier in Scheme 5.

With both fragments **15** and **16** in hand, the coupling was achieved using classical Mitsunobu conditions[12] to obtain the corresponding desired ester **14** in 82% yield (Scheme 7). Treatment of the ester with Grubbs second generation catalyst (5 mol %) under dilute conditions in degassed CH_2Cl_2 under reflux conditions



Scheme 7. Reagents and conditions: (a) TPP, DIAD, toluene, 30 min, 82%; (b) Grubbs II generation catalyst (5 mol %), CH_2Cl_2, reflux, 4 h, 79%; (c) 4 M HCl/THF (1:1), 5 h, 78%; (d) (1) MnO_2, CH_2Cl_2, rt, 3 h; (2) Pd/C, H_2, EtOAc, 1 h, 76% over two steps.

furnished the desired lactone **38** in 79% yield as a mixture of diastereomers. Acid catalyzed removal of MOM as well as TBS groups using 4 M HCl in THF afforded **39** in 78% yield. The secondary allylic alcohol in compound **39** was then oxidized to a ketone with MnO_2 in CH_2Cl_2, which was then subjected to hydrogenation with Pd/C in the presence of hydrogen in EtOAc to furnish the target molecule dendrodolide L in 76% over two steps. The spectroscopic and analytical data of the synthesized target compound were in agreement with the natural product. The specific rotation of compound **12** $[\alpha]_D^{27}$ = +8.6 (*c* 0.2, $CHCl_3$) was in agreement with the reported value $[\alpha]_D^{27}$ = +10.7 (*c* 0.065, $CHCl_3$).[1]

3. Conclusion

In conclusion, we have accomplished the stereoselective total synthesis of dendrodolide L **12** by employing Keck asymmetric allylation, Jacobsen's hydrolytic kinetic resolution, Sharpless asymmetric epoxidation, Mitsunobu reaction and RCM reaction as the key steps with an overall yield of 19.7% starting from enantiopure epoxide **36**.

4. Experimental

4.1. General

Reactions were conducted under N_2 in anhydrous solvents such as CH_2Cl_2, DMSO, and THF. Evaporation of the solvents was performed at a reduced pressure on a Buchi rotary evaporator. ^1H and ^{13}C NMR spectra of samples in $CDCl_3$ were recorded on Varian FT-400 MHz, Varian FT-500 MHz and Bruker UXNMR FT-300 MHz (Avance) spectrometers at ambient temperature. Chemical shifts δ are reported relative to TMS (δ = 0.0) as an internal standard. FTIR spectra were recorded on a Perkin–Elmer 683 infrared spectrometer; neat or as thin films in KBr. Optical rotations were measured on an Anton Paar MLP 200 modular circular digital polarimeter using a 2 mL cell with a path length of 1 dm. Mass spectra were recorded EI conditions at 70 eV on ES-MSD (Agilent technologies) spectrometers. Column chromatography was performed on silica gel (60–120 mesh) packed in glass columns.

4.1.1. (*R*)-1-((4-Methoxybenzyl)oxy)hex-5-en-3-ol 21

To a mixture of **20** (3 g, 15.31 mmol) and Celite in CH_2Cl_2 (40 mL) was added pyridinium chlorochromate (4.45 g, 22.96 mmol) portionwise at 0 °C and after being stirred for 1 h, the crude reaction mixture was filtered through a small plug of silica and the residue was washed with CH_2Cl_2. The filtrate was concentrated under reduced pressure to afford the aldehyde (2.73 g) which was used directly in the next step.

A dry two neck round bottomed flask was charged with (*R*)-BINOL (0.4 g, 1.4 mmol) and vacuum-flame-dried powdered molecular sieves (4 Å). One neck was fitted with a reflux condenser and the other was closed with a rubber septum. Dry CH_2Cl_2 (10 mL) was added followed by titanium (IV) isopropoxide (0.29 mL, 1.4 mmol) by syringe, resulting in an immediate colour change to deep red, then refluxed for approximately 1 h. The reaction mixture was cooled to room temperature and then the aldehyde (2.73 g, 14.07 mmol) in CH_2Cl_2 (30 mL) was added dropwise and stirred for 5 min. The reaction mixture was then cooled to −78 °C, and allyltributylstannane (4.75 mL, 15.48 mmol) was added by syringe. The resulting mixture was stirred for 30 min and then transferred to a freezer at −20 °C and allowed to stand for 6 h. The reaction mixture was filtered over a small pad of Celite and concentrated. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to give **21** as a light yellow oil (2.79 g, 77% over two steps). $[\alpha]_D^{27}$ = +3.6 (*c* 1.6, $CHCl_3$), lit.[5b] $[\alpha]_D^{27}$ = +4.6 (*c* 0.60, $CHCl_3$; IR (neat): 3439, 3075, 2927, 1613, 1513, 1248, 1089, 1034, 819, 793 cm^{-1}; (^1H, 500 MHz): δ 7.24 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.87–5.78 (m, 1H), 5.12–5.07 (m, 2H), 4.45 (s, 2H), 3.88–3.82 (m, 1H), 3.80 (s, 3H), 3.71–3.66 (m, 1H), 3.63–3.58 (m, 1H), 2.89 (br s, 1H), 2.25–2.21 (m, 2H), 1.76–1.72 (m, 2H); (^{13}C, 100 MHz): δ 158.9, 134.6, 129.0, 117.2, 113.5, 72.6, 69.9, 68.1, 54.9, 41.6, 35.5; MS (ESI): *m*/*z* = 259 $(M+Na)^+$; HRMS (ESI): calcd for $C_{14}H_{20}O_3Na$ $(M+Na)^+$, 259.1304, found 259.1300.

4.1.2. (*R*)-*tert*-Butyl((1-((4-methoxybenzyl)oxy)hex-5-en-3-yl)oxy)dimethylsilane 22

To a solution of homoallylic compound **21** (1.27 g, 5.38 mmol) in CH_2Cl_2 (15 mL) was added imidazole (1.1 g, 16.14 mmol) followed by TBSCl (0.89 g, 5.91 mmol) at 0 °C and the reaction mixture was stirred for 3 h. After completion of the reaction, it was diluted with CH_2Cl_2, washed with H_2O (20 mL), brine (20 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to give **22** as a colourless liquid (1.8 g, 96%). $[\alpha]_D^{27}$ = −17.4 (*c* 1.9, $CHCl_3$); IR (neat): 2953, 2931, 2857, 1613, 1513, 1465, 1363, 1249, 1094, 1040, 912, 836, 774 cm^{-1}; (^1H, 500 MHz): δ 7.27–7.24 (m, 2H), 6.89–6.86 (m, 2H), 5.85–5.75 (m, 1H), 5.05–5.00 (m, 2H), 4.44 (d, *J* = 11.4 Hz, 1H), 4.38 (d, *J* = 11.4 Hz, 1H), 3.91–3.86 (m, 1H), 3.80 (s, 3H), 3.51 (t, *J* = 6.7 Hz, 2H), 2.27–2.18 (m, 2H), 1.81–1.74 (m, 1H), 1.72–1.65 (m, 1H), 1.60–1.57 (m, 1H), 0.88 (s, 9H), 0.04 (d, *J* = 5.4 Hz, 6H); (^{13}C, 100 MHz): δ 159.0, 134.9, 130.6, 129.2, 116.9, 113.7, 72.5, 68.9, 66.7, 55.2, 42.2, 36.6, 25.8, 18.0, −4.3, −4.7; MS (ESI): *m*/*z* = 373 $(M+Na)^+$. HRMS (ESI): calcd for $C_{20}H_{34}O_3NaSi$ $(M+Na)^+$, 373.2169, found 373.2168.

4.1.3. (*R*)-3-((*tert*-Butyldimethylsilyl)oxy)hex-5-en-1-ol 23

Compound **22** (1.67 g, 4.77 mmol) was taken up in CH_2Cl_2 after which pH 7 buffer (20 mL, 9:1) was added. Next, DDQ (1.3 g, 5.72 mmol) was added in one portion at 0 °C. After being stirred for 30 min at room temperature, the reaction mixture was quenched with solid $NaHCO_3$ and stirring was continued for 30 min and then filtered. The filtrate was washed with H_2O (10 mL), brine (10 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to give **23** as a colourless liquid (0.9 g, 82%). $[\alpha]_D^{27}$ = −28.8 (*c* 1.24, $CHCl_3$); IR (neat): 3356, 2932, 2858, 1469, 1363, 1255, 1074, 912, 836, 775 cm^{-1}; (^1H, 500 MHz): δ 5.82–5.72 (m, 1H), 5.11–5.04 (m, 2H), 4.00–3.95 (m, 1H), 3.86–3.80 (m, 1H), 3.75–3.69 (m, 1H), 2.34 (br s, 1H), 2.32–2.29 (m, 2H), 1.85–1.78 (m, 1H), 1.70–1.63 (m, 1H), 0.9 (s, 9H), 0.1 (d, *J* = 4.7 Hz, 6H); (^{13}C, 100 MHz): δ 134.4, 117.2, 71.1, 60.0, 41.6, 37.6, 25.7, 17.9, −4.4, −4.8; MS (ESI): *m*/*z* = 253 $(M+Na)^+$, 231 $(M+H)^+$; HRMS (ESI): calcd for $C_{12}H_{27}O_2Si$ $(M+H)^+$, 231.1774, found 231.1772.

4.1.4. (*R*)-3-((*tert*-Butyldimethylsilyl)oxy)hex-5-enoic acid 16

Compound **23** (0.76 g, 3.3 mmol) was taken up in CH_2Cl_2/H_2O (8 mL, 1:1) and the reaction mixture was cooled to 0 °C, then TEMPO (144 mg, 0.92 mmol), BAIB (3.19 g, 9.91 mmol) was added sequentially. After being stirred for 1 h, the reaction mixture was diluted with CH_2Cl_2, and quenched with a saturated solution of hypo. The mixture was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were washed with H_2O (10 mL), brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to give **16** as a colourless oil (0.61 g, 76%). $[\alpha]_D^{27}$ = −23.4 (*c* 2.0, $CHCl_3$); IR (neat): 2928, 2876, 1713, 1460, 1255, 1092, 835, 773 cm^{-1}; (^1H, 400 MHz): δ 5.87–5.73 (m, 1H), 5.13–5.05 (m, 2H), 4.23–4.16 (m, 1H), 2.55–2.43 (m, 2H),

2.32–2.28 (m, 2H), 0.88 (s, 9H), 0.08 (d, J = 8.3 Hz, 6H); (^{13}C, 100 MHz): δ 177.3, 133.6, 117.9, 68.7, 41.8, 41.7, 25.6, 17.8, −4.6, −5.0; MS (ESI): m/z = 267 (M+Na)$^+$; HRMS (ESI): calcd for $C_{12}H_{24}O_3NaSi$ (M+Na)$^+$, 267.1386, found 267.1381.

4.1.5. ((2*S*,3*S*)-3-(3-(Benzyloxy)propyl)oxiran-2-yl) methanol 27

To a suspension of flame dried 4 Å molecular sieves in dry CH_2Cl_2 (50 mL) at −20 °C, was added (+)-DET (1.26 mL, 6.79 mmol) followed by Ti(O^iPr)$_4$ (1.21 mL, 4.07 mmol). After stirring for 30 min, cumene hydroperoxide (9.68 mL, 80% solution, 50.97 mmol) was added dropwise. The reaction mixture was stirred for a further 30 min at the same temperature before the addition of **26** (7.0 g, 33.98 mmol) in CH_2Cl_2 (50 mL). The reaction mixture was stirred at −20 °C for 12 h, then warmed up to 0 °C, and quenched with an aq. basic solution (0.695 g of NaOH in 6.95 mL of brine). The reaction mixture was stirred for 1 h before being filtered through a small bed of Celite and washed with CH_2Cl_2. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography to afford **27** (6.71 g, 89%) as a light yellow liquid. $[\alpha]_D^{27}$ = −27.0 (c 1.8, $CHCl_3$), lit.[6b] [α]$_D$ = −29, $CHCl_3$; IR (neat): 3330, 2961, 2857, 1470, 1427, 1378, 1219, 1107, 1007, 703 cm^{-1}; (^{1}H, 500 MHz): δ 7.37–7.26 (m, 5H), 4.50 (s, 2H), 3.85 (dd, J = 12.5, 2.7 Hz, 1H), 3.59 (dd, J = 12.5, 4.4 Hz, 1H), 3.54–3.48 (m, 2H), 2.98–2.95 (m, 1H), 2.92–2.89 (m, 1H), 1.81–1.61 (m, 4H); (^{13}C, 125 MHz): δ 138.2, 128.3, 127.6, 127.5, 72.8, 69.5, 61.6, 58.4, 55.6, 28.3, 26.0; MS (ESI): m/z = 245 (M+Na)$^+$; HRMS (ESI): calcd for $C_{13}H_{18}O_3Na$ (M+Na)$^+$, 245.1148, found 245.1159.

4.1.6. ((2*S*,3*S*)-3-(3-(Benzyloxy)propyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate 28

To a solution of compound **27** (3 g, 13.51 mmol) in anhydrous CH_2Cl_2 (30 mL) was added Et_3N (5.6 mL, 40.54 mmol) at 0 °C followed by tosyl chloride (2.83 g, 14.86 mmol). After the solution had been stirred for 3 h at room temperature, volatiles were removed under vacuo. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to give **28** (4.77 g, 94%) as a light yellow liquid. $[\alpha]_D^{27}$ = −23.8 (c 1.3, $CHCl_3$); IR (neat): 2931, 1598, 1453, 1364, 1177, 1098, 962, 817, 772 cm^{-1}; (^{1}H, 500 MHz): δ 7.81–7.77 (m, 2H), 7.36–7.28 (m, 7H), 4.48 (s, 2H), 4.15 (dd, J = 11.4, 3.8 Hz, 1H), 3.95 (dd, J = 11.4, 5.4 Hz, 1H), 3.52–3.40 (m, 2H), 2.98–2.93 (m, 1H), 2.83–2.80 (m, 1H), 2.44 (s, 3H), 1.76–1.60 (m, 4H); (^{13}C, 100 MHz): δ 145.0, 138.2, 132.6, 129.8, 128.3, 127.8, 127.5, 72.8, 70.0, 69.3, 56.4, 54.5, 28.1, 25.9, 21.6; MS (ESI): m/z = 399 (M+Na)$^+$; HRMS (ESI): calcd for $C_{20}H_{24}O_5S$ (M+H)$^+$, 377.1417, found 377.1408.

4.1.7. (*S*)-6-(Benzyloxy)hexan-2-ol 29

To a solution of compound **28** (2.61 g, 6.94 mmol) in anhydrous CH_2Cl_2 (25 mL) was added DIBAL-H (25% in toluene, 11.8 mL, 20.84 mmol) dropwise at −20 °C. After the solution had been stirred for 12 h at room temperature, it was cooled to 0 °C, and then treated with a saturated solution of sodium potassium tartarate and allowed to stir for 2 h. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to afford **29** (317 mg, 22%), **29a** (410 mg, 16%), **29b** (800 mg, 40%). $[\alpha]_D^{27}$ = +7.9 (c 2.0, $CHCl_3$); IR (neat): 3356, 2940, 1657, 1466, 1416, 1375, 1300 cm^{-1}; (^{1}H, 500 MHz): δ 7.39–7.27 (m, 5H), 4.51 (s, 2H), 3.83–3.77 (m, 1H), 3.48 (t, J = 6.5 Hz, 2H), 1.68–1.58 (m, 2H), 1.52–1.40 (m, 4H), 1.18 (d, J = 6.2 Hz, 3H); (^{13}C, 100 MHz): δ 138.4, 128.2, 127.5, 127.4, 72.8, 70.1, 67.7, 38.9, 29.5, 23.3, 22.3; MS (ESI): m/z = 231 (M+Na)$^+$; HRMS (ESI): calcd for $C_{13}H_{21}O_2$ (M+H)$^+$, 209.1536, found 209.1533.

4.1.8. (*R*)-6-(Benzyloxy)-2-hydroxyhexyl 4-methylbenzene sulfonate 29a

$[\alpha]_D^{27}$ = +9.5 (c 0.64, $CHCl_3$); IR (neat): 3421, 2923, 2854, 1727, 1598, 1456, 1358, 1175, 1091, 973, 772 cm^{-1}; (^{1}H, 500 MHz): δ 7.72 (d, J = 8.3 Hz, 2H), 7.31–7.20 (m, 7H), 4.41 (s, 2H), 3.95 (dd, J = 9.5, 2.6 Hz, 1H), 3.83–3.78 (m, 1H), 3.77–3.70 (m, 1H), 3.38 (t, J = 6.2 Hz, 2H), 2.38 (s, 3H), 1.57–1.49 (m, 3H), 1.40–1.34 (m, 3H); (^{13}C, 100 MHz): δ 145.0, 138.4, 132.6, 129.9, 128.3, 127.9, 127.6, 127.5, 73.8, 72.9, 69.9, 69.3, 32.3, 31.9, 22.6, 21.6; MS (ESI): m/z = 401 (M+Na)$^+$; HRMS (ESI): calcd for $C_{20}H_{27}O_5S$ (M+H)$^+$, 379.1574, found 379.1580.

4.1.9. (*S*)-2-Hydroxy-2-((*R*)-tetrahydrofuran-2-yl)ethyl 4-methylbenzenesulfonate 29b

$[\alpha]_D^{27}$ = −12.1 (c 1.4, $CHCl_3$); IR (neat): 3446, 2924, 1633, 1357, 1302, 1174, 1082, 772 cm^{-1}; (^{1}H, 500 MHz): δ 7.80 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 4.20 (dd, J = 10.3, 3.0 Hz, 1H), 4.02 (dd, J = 10.3, 6.7 Hz, 1H), 3.83–3.75 (m, 3H), 3.74–3.68 (m, 1H), 2.45 (s, 3H), 1.98–1.78 (m, 4H); (^{13}C, 100 MHz): δ 144.9, 132.5, 129.8, 127.9, 78.4, 71.7, 71.1, 68.5, 27.1, 25.5, 21.6; MS (ESI): m/z = 309 (M+Na)$^+$, 304 (M+NH$_4$)$^+$; HRMS (ESI): calcd for $C_{13}H_{18}O_5SNa$ (M+Na)$^+$, 309.0751, found 309.0767.

4.1.10. (7*S*)-7-((*tert*-Butyldimethylsilyl)oxy)oct-1-en-3-ol 32

At first, DMSO (1.04 mL, 14.65 mmol) was added at −78 °C to a solution of oxalyl chloride (0.96 mL, 10.99 mmol) in CH_2Cl_2 (20 mL), and the resulting solution was stirred for 15 min. A solution of the alcohol **31** (1.7 g, 7.32 mmol) in CH_2Cl_2 (15 mL), was then added dropwise at −78 °C over 15 min. After the solution had been stirred for an additional 30 min, Et_3N (6.12 mL, 43.96 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 1 h. The reaction mixture was poured into ice cooled water and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give a crude aldehyde (1.52 g) which was directly used for next step without further purification.

To a solution of the aldehyde (1.52 g, 6.6 mmol) in anhydrous THF (10 mL) was added vinyl magnesium bromide (0.7 M in THF, 10.35 mL, 7.27 mmol) at 0 °C. The reaction mixture was stirred for 30 min at room temperature, then quenched with saturated solution of NH_4Cl at 0 °C and extracted with EtOAc (2 × 15 mL). The combined organic extracts were washed with brine and dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to give **32** as a slightly yellow colour liquid (1.49 g, 79% over two steps). $[\alpha]_D^{27}$ = +6.5 (c 1.5, $CHCl_3$); IR (neat): 3419, 2936, 2880, 1461, 1378, 1248, 1039 cm^{-1}; (^{1}H, 500 MHz): δ 5.90–5.82 (m, 1H), 5.22 (dt, J = 17.2, 1.3 Hz, 1H), 5.10 (dt, J = 10.5, 1.2 Hz, 1H), 4.13–4.07 (m, 1H), 3.82–3.75 (m, 1H), 1.59–1.30 (m, 6H), 1.12 (d, J = 5.9 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); (^{13}C, 100 MHz): δ 141.1, 114.6, 114.5, 73.2, 73.1, 68.5, 68.4, 39.5, 39.4, 37.0, 36.9, 25.8, 23.7, 21.6, 21.4, 18.1, −4.4, −4.7; MS (ESI): m/z = 281 (M+Na)$^+$, 259 (M+H)$^+$; HRMS (ESI): calcd for $C_{14}H_{31}O_2Si$ (M+H)$^+$, 259.2087, found 233.2083.

4.1.11. (9*S*)-9,11,11,12,12-Pentamethyl-5-vinyl-2,4,10-trioxa-11-silatridecane 33

To a stirred solution of **32** (0.9 g, 3.48 mmol) in anhydrous CH_2Cl_2 (10 mL) was added diisopropylethylamine (3.0 mL, 17.44 mmol) at 0 °C followed by MOMCl (50% solution in methyl acetate, 0.61 mL, 3.83 mmol). Stirring was continued for 10 h at room temperature, and then quenched with water (5 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo.

The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to afford **33** (0.93 g, 89%) as a colourless liquid. $[\alpha]_D^{27}$ = +8.9 (*c* 1.0, $CHCl_3$); IR (neat): 2932, 2858, 1466, 1375, 1254, 1152, 1099, 1039, 922, 835, 774 cm^{-1}; (^1H, 300 MHz): δ 5.73–5.59 (m, 1H), 5.23–5.15 (m, 2H), 4.71 (d, *J* = 6.7 Hz, 1H), 4.53 (dd, *J* = 6.7, 1.1 Hz, 1H), 4.02–3.93 (m, 1H), 3.83–3.72 (m, 1H), 3.38 (s, 3H), 1.60–1.36 (m, 6H), 1.12 (d, *J* = 6.0 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H); (^{13}C, 100 MHz): δ 138.3, 117.1, 117.0, 96.3, 93.6, 93.5, 68.4, 55.3, 39.5, 35.45, 35.43, 29.7, 29.6, 25.8, 23.8, 21.8, 21.7, 18.1, −4.4, −4.7; MS (ESI): *m*/*z* = 325 $(M+Na)^+$; HRMS (ESI): calcd for $C_{16}H_{35}O_3Si$ Na $(M+Na)^+$, 325.2169, found 325.2162.

4.1.12. (2*S*)-6-(Methoxymethoxy)oct-7-en-2-ol 15

To a stirred solution of **33** (0.8 g, 2.64 mmol) in THF (10 mL) was added TBAF (2.91 mL, 1 M in THF, 2.91 mmol) and stirred for 3 h at room temperature. It was then quenched with water (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to afford **15** (0.44 g, 90%) as a colourless liquid. $[\alpha]_D^{27}$ = +4.6 (*c* 0.4, $CHCl_3$); IR (neat): 3424, 2937, 1218, 1152, 1099, 1036, 924, 772 cm^{-1}; (^1H, 300 MHz): δ 5.74–5.60 (m, 1H), 5.25–5.16 (m, 2H), 4.71 (d, *J* = 6.7 Hz, 1H), 4.54 (d, *J* = 6.7 Hz, 1H), 4.04–3.95 (m, 1H), 3.85–3.76 (m, 1H), 3.38 (s, 3H), 1.66–1.38 (m, 6H), 1.19 (d, *J* = 6.0 Hz, 3H); (^{13}C, 100 MHz): δ 138.2, 117.1, 93.6, 77.2, 67.8, 55.3, 39.0, 35.2, 23.4, 21.4; MS (ESI): *m*/*z* = 211 $(M+Na)^+$; HRMS (ESI): calcd for $C_{10}H_{20}O_3Na$ $(M+Na)^+$, 211.1304, found 211.1301.

4.1.13. (3*R*)-(2*R*)-6-(Methoxymethoxy)oct-7-en-2-yl 3-((*tert*-butyldimethylsilyl)oxy)hex-5-enoate 14

Triphenyl phosphine (0.28 g, 4.24 mmol) and DIAD (0.84 mL, 4.24 mmol) were added sequentially to a stirred solution of acid **16** (0.52 g, 2.12 mmol) and alcohol **15** (0.4 g, 2.12 mmol) in dry toluene (5 mL). After 30 min, EtOAc (5 mL) and H_2O (5 mL) were added. The layers were separated and the aqueous phase extracted with EtOAc (. 10 mL). The combined organic portions were washed with brine solution (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to afford diene compound **14** (0.72 g, 82%) as a light yellow liquid. $[\alpha]_D^{27}$ = −20.1 (*c* 0.74, $CHCl_3$); IR (neat): 2933, 2858, 1733, 1464, 1379, 1254, 1175, 1096, 1040, 920, 836, 776 cm^{-1}; (^1H, 500 MHz): δ 5.86–5.75 (m, 1H), 5.71–5.60 (m, 1H), 5.22–5.16 (m, 2H), 5.09–5.04 (m, 2H), 4.91–4.84 (m, 1H), 4.7 (d, *J* = 6.7 Hz, 1H), 4.53 (d, *J* = 6.5 Hz, 1H), 4.22–4.16 (m, 1H), 4.00–3.94 (m, 1H), 3.37 (s, 2H), 2.45–2.40 (m, 2H), 2.32–2.24 (m, 2H), 1.64–1.58 (m, 2H), 1.54–1.36 (m, 4H), 1.21 (d, *J* = 6.1 Hz, 3H), 0.87 (s, 9H), 0.06 (d, *J* = 11.4 Hz, 6H); (^{13}C, 75 MHz): δ 171.2, 138.1, 134.2, 117.5, 117.2, 93.6, 70.8, 68.7, 55.3, 42.3, 41.9, 35.6, 35.1, 25.7, 21.1, 19.7, 17.9, −4.5, −4.8; MS (ESI): *m*/*z* = 437 $(M+Na)^+$; HRMS (ESI): calcd for $C_{22}H_{43}O_5Si$ $(M+H)^+$, 415.2874, found 415.2858.

4.1.14. (4*R*,12*R*)-4-((*tert*-Butyldimethylsilyl)oxy)-8-(methoxymethoxy)-12-methyloxacyclododec-6-en-2-one 38

A solution of compound **14** (100 mg, 0.24 mmol) in degassed CH_2Cl_2 (81 mL) was treated with 5% mol of Grubbs 2nd generation catalyst and stirred at reflux for 4 h. The reaction mixture was filtered through a pad of SiO_2, washed with CH_2Cl_2 and concentrated under reduced pressure. Purification by silica gel column chromatography (Hexanes/EtOAc) gave **38** (73 mg, 79%). $[\alpha]_D^{27}$ = −1.3 (*c* 0.48, $CHCl_3$); (^1H, 500 MHz): δ 5.64 −5.53 (m, 1H), 5.31–5.18 (m, 1H), 5.08–4.84 (m, 1H), 4.71–4.63 (m, 1H), 4.53–4.45 (m, 1H), 4.16–3.94 (m, 2H), 3.35–3.31 (m, 3H), 2.68–2.55 (m, 1H), 2.50–2.33 (m, 3H), 1.58–1.27 (m, 6H), 1.23–1.14 (m, 3H), 0.91–0.87 (m, 9H), 0.11–0.05 (m, 6H); (^{13}C, 100 MHz): δ 170.2, 170.1, 133.5, 131.6, 130.5, 129.7, 93.8, 93.58, 93.51, 76.4, 75.7, 72.3, 70.6, 69.9, 68.7, 55.2, 45.7, 42.7, 42.6, 32.8, 30.9, 30.8, 29.1, 25.77, 25.73, 20.2, 19.4, 18.1, 18.0, 17.2, 16.8, −4.7, −4.8, −4.9.; MS (ESI): *m*/*z* = 409 $(M+Na)^+$; HRMS (ESI): calcd for $C_{20}H_{39}O_5Si$ $(M+H)^+$, 387.2561, found 387.2545.

4.1.15. (4*R*,12*R*)-4,8-Dihydroxy-12-methyloxacyclododec-6-en-2-one 39

A solution of compound **38** (100 mg, 0.259 mmol) in THF (5 mL) was treated with 4 M HCl (5 mL) and allowed to stir for 5 h, after which EtOAc (5 mL) and H_2O (5 mL) were added. The layers were separated and the aqueous phase was extracted with EtOAc (2 × 5 mL). The combined organic portion was washed with saturated sodium bicarbonate solution (10 mL) followed by brine solution (10 mL), dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hexanes/EtOAc) to give **39** (46 mg, 78%) as a colourless liquid. $[\alpha]_D^{27}$ = −8.2 (*c* 0.96, $CHCl_3$); IR (neat): 3400, 2925, 2853, 1722, 1451, 1377, 1268, 1038, 722 cm^{-1}; (^1H, 500 MHz): δ 5.78–5.60 (m, 1H), 5.56–5.38 (m, 1H), 5.08–4.86 (m, 1H), 4.21–4.01 (m, 2H), 2.63–2.15 (m, 4H), 1.78–1.37 (m, 6H), 1.16–1.10 (m, 1H); (^{13}C, 125 MHz): δ 172.9, 172.3, 172.2, 135.7, 135.1, 134.6, 128.3, 127.7, 127.2, 126.9, 126.3, 126.0, 78.0, 73.7, 72.0, 71.8, 70.9, 70.2, 69.7, 68.7, 68.5, 65.3, 61.8, 42.4, 41.4, 41.0, 34.6, 34.8, 33.7, 32.9, 31.8, 31.2, 30.9, 23.3, 22.5, 22.0, 19.4, 18.2, 17.8, 17.5, 17.4, 16.6, 15.2, 14.0; MS (ESI): *m*/*z* = 229 $(M+H)^+$; HRMS (ESI): calcd for $C_{12}H_{21}O_4$ $(M+H)^+$, 229.1199, found 229.1197.

4.1.16. Dendrodolide L 12

At first, MnO_2 (76 mg, 0.877 mmol) was added to a stirred solution of **39** (40 mg, 0.17 mmol) in CH_2Cl_2 at room temperature. After the mixture had been stirred for 3 h, the solvent was evaporated and the crude reaction mixture was filtered through a small pad of silica gel and concentrated to give a keto compound (33 mg) as a pale yellow liquid, which was used for the next step without further characterization.

To a stirred solution of ketone (33 mg, 0.146 mmol) in EtOAc (2 mL) was added a catalytic amount of 10% Pd/C and the reaction mixture was stirred for 1 h under a hydrogen atmosphere. The reaction mixture was filtered through a small plug of Celite and washed with EtOAc (2 × 5 mL). The combined organic layers were concentrated under reduced pressure and the residue was purified by silica gel column chromatography (Hexanes/EtOAc) to give the title compound dendrodolide L (**12**) (30 mg, 76% over two steps). $[\alpha]_D^{27}$ = +8.6 (*c* 0.2, $CHCl_3$); IR (KBr): 3380, 2952, 2872, 1716, 1251, 1169, 1062, 980 cm^{-1}; (^1H, 500 MHz): δ 5.23–5.17 (m, 1H), 4.04–3.98 (m, 1H), 2.90 (ddd, *J* = 16.1, 8.8, 3.5 Hz, 1H), 2.78 (ddd, *J* = 12.8, 9.1, 3.3 Hz, 1H), 2.73 (dd, *J* = 14.0, 3.5 Hz, 1H), 2.49 (dd, *J* = 14.0, 7.4 Hz, 1H), 2.25–2.18 (m, 2H), 1.95–1.86 (m, 2H), 1.81–1.75 (m, 1H), 1.73–1.51 (m, 4H), 1.33–1.27 (m, 1H), 1.23 (d, *J* = 6.5 Hz, 3H); (^{13}C, 125 MHz): δ 211.3, 170.5, 70.9, 67.3, 41.9, 40.5, 39.8, 34.1, 31.4, 29.6, 20.1, 18.1, 17.5; MS (ESI): *m*/*z* = 251 $(M+Na)^+$; HRMS (ESI): calcd for $C_{12}H_{20}O_4Na$ $(M+Na)^+$, 251.1254, found 251.1247.

Acknowledgements

S.B. thanks UGC, New Delhi for the award of fellowship. All the authors thank CSIR, New Delhi, India for financial support as part of XII Five Year plan programme under title ORIGIN (CSC-0108).

References

1. Sun, P.; Xu, D.-X.; Mandi, A.; Kurtan, T.; Li, T.-J.; Schulz, B.; Zhang, W. *J. Org. Chem.* **2013**, *78*, 7030–7047.
2. (a) Mohapatra, D. K.; Prabhakarreddy, D.; Srinivas, G.; Karthik, P.; Yadav, J. S. *Asian J. Org. Chem.* **2015**, *5*, 452–461; (b) Mohapatra, D. K.; Karthik, P.; Eswar, B.; Prabhakarreddy, D.; Yadav, J. S. *Asian J. Org. Chem.* **2014**, *11*, 1210–1216; (c) Mohapatra, D. K.; Karthik, P.; Srinivas, G.; Yadav, J. S. *Tetrahedron Lett.* **2015**, *56*, 6377–6380; (d) Venkanna, A.; Siva, B.; Poornima, B.; babu, K. S.; Rao, J. M. *Tetrahedron Lett.* **2014**, *55*, 403–406.
3. (a) Bujaranipalli, S.; Eppa, G. C.; Das, S. *Synlett* **2013**, 1117–1120; (b) Dachavaram, S. S.; Kalyankar, K. B.; Das, S. *Tetrahedron Lett.* **2014**, *55*, 5629–5631; (c) Bujaranipalli, S.; Das, S. *Tetrahedron Lett.* **2015**, *56*, 3747–3749.
4. Chavan, S. P.; Harale, K. R. *Tetrahedron Lett.* **2012**, *53*, 4683–4686.
5. (a) Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467–8468; (b) Schleicher, K. D.; Jamison, T. F. *Beilstein J. Org. Chem.* **2013**, *9*, 1533–1550
(c) HPLC method: CHIRAL PAK IC 250 × 4.6 mm 5μ (column), 5% IPA in hexane (mobile phase), flow rate 1 mL/min, t_R: 13.1 min (major enantiomer) and 11.4 min (minor enantiomer).
6. (a) Gao, Y.; Klunder, J. M.; Hanson, R. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780; (b) Kermadec, D.; Prudhomme, M. *Tetrahedron Lett.* **1993**, *34*, 2757–2758.
7. (a) Chong, J. M. *Tetrahedron Lett.* **1992**, *33*, 33–36; (b) Johannsen, J.; Chong, J. M. *Tetrahedron Lett.* **1994**, *35*, 7197–7200.
8. Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734–736.
9. Berliner, M. A.; Belecki, K. *J. Org. Chem.* **2005**, *70*, 9618–9621.
10. (a) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307–1315; (b) Sabitha, G.; Gopal, P.; Yadav, J. S. *Tetrahedron: Asymmetry* **2009**, *20*, 1493–1499; (c) Yadav, J. S.; Reddy, U. V. S.; Reddy, B. V. S. *Tetrahedron Lett.* **2009**, *50*, 5984–5986
(d) HPLC Method: CHIRAL PAK IC 250 × 4.6 mm 5 μ (column), 3% IPA in hexane (mobile phase), flow rate 1 mL/min, t_R: 10.0 min (major enantiomer) and 10.6 min (minor enantiomer).
11. Dey, S.; Sudalai, A. *Tetrahedron: Asymmetry* **2015**, *26*, 344–349.
12. Mitsunobu, O.; Yamada, Y. *Bull. Chem. Soc. Jpn.* **1967**, *10*, 2380–2382.