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Enantiodivergent total synthesis of microcarpalide from L-tartaric acid

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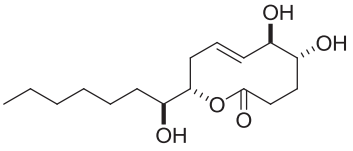
ABSTRACT

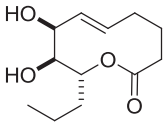
Stereoselective approach for the synthesis of both enantiomers of bio-active decanolactone microcarpalide is described from L-tartaric acid. The synthesis of the key intermediates en route to the natural product is achieved from L-tartaric acid involving the elaboration of γ-hydroxy amide derived from tartaric acid and ring opening of an epoxide derived from tartaric acid.

1. Introduction

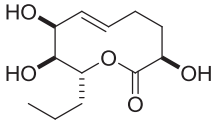
Microcarpalide is a 10-membered lactone isolated from the fermentation broths of unidentified endophytic fungi by Hemscheidt's group.[1] Microcarpalide is structurally similar to other decanolides herbarumin I (**2**), herbarumin II (**3**), and lethaloxin (**4**). It was found to be weakly cytotoxic to mammalian cells and acts as a microfilament disrupting agent. Since the isolation of microcarpalide, a handful of total syntheses of **1** were reported,[2,3] majority of which involve ring closing metathesis (RCM) of a suitably protected diene ester to install the required *E*-alkene. We earlier in 2007 reported a formal total synthesis of microcarpalide[4] and herein we report in detail our efforts concerning the synthesis of both enantiomers of microcarpalide from L-tartaric acid.



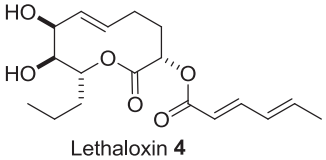
Microcarpalide **1**



Herbarumin **I 2**

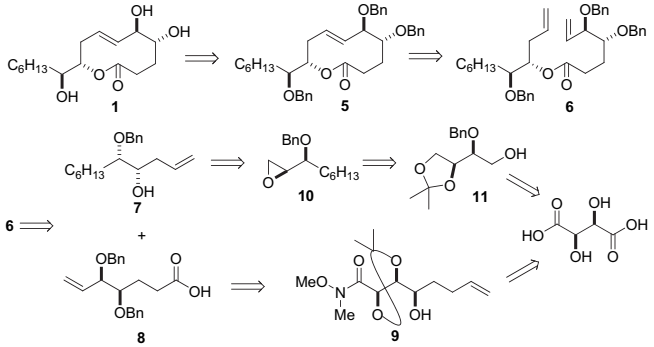


Herbarumin **II 3**



Lethaloxin **4**

Our approach for the synthesis of natural (−)-microcarpalide **1** is based on the ring closing metathesis (RCM) of the known diene ester **6** to yield the macrolactone. Synthesis of the acid fragment **8** required for the formation of the diene ester is anticipated by elaboration of the γ-hydroxy amide **9**[5] derived from tartaric acid while the alcohol fragment **7** is envisaged by extrapolation of the epoxide **10** also derived from L-tartaric acid (Scheme 1).



Scheme 1. Retrosynthesis for microcarpalide.

The synthetic sequence commenced with synthesis of the γ-hydroxy amide **9** derived from tartaric acid using a procedure established in our laboratory involving controlled addition of Grignard reagent followed by stereoselective reduction.[5] Treatment of **9** with benzyl bromide in presence of Ag_2O afforded the benzyl ether **12** in 71% yield. Ozonolysis of the olefin in **12** to the aldehyde followed by reduction with $NaBH_4$ resulted in the primary alcohol **13** in 58% yield accompanied with the formation of the diol **14** in 16% yield. Protection of the primary hydroxy group in **13** as the silyl ether **15** and

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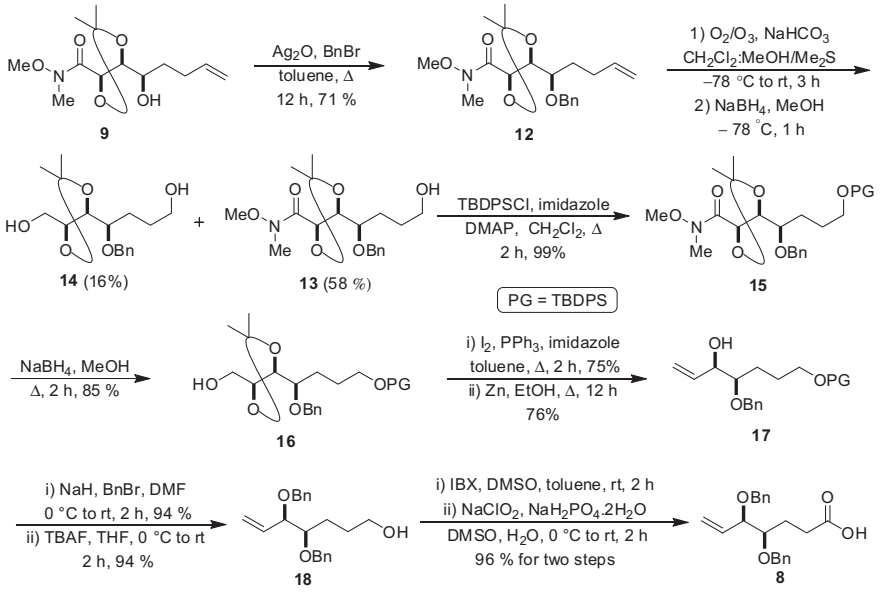
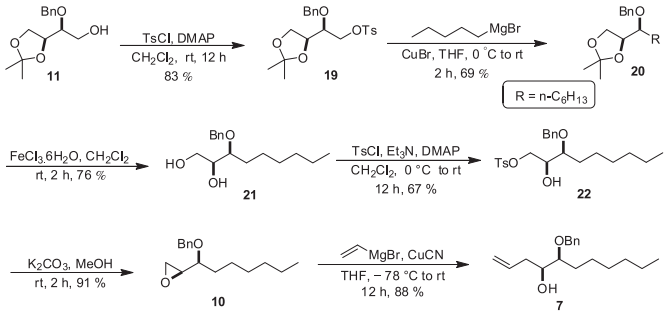
further reduction of the amide with $NaBH_4$ furnished the alcohol **16** in 85% yield. Conversion of the primary alcohol to the iodide (75% yield) followed by reaction with zinc dust in refluxing ethanol produced the allylic alcohol **17** in 76% yield.[6] Protection of the free hydroxy group in **17** as the benzyl ether and deprotection of the silyl ether afforded the known primary alcohol **18**[3j] in 94% yield. Oxidation of the alcohol **18** to the aldehyde and further oxidation to the alcohol furnished the acid **8** in 96% yield for two steps (Scheme 2).

Accordingly, alcohol **11** was transformed into the diol **28** using a procedure reported by us.[8] $NaIO_4$ mediated cleavage of the diol **28** afforded the aldehyde, which on reduction with $NaBH_4$ furnished the primary alcohol **29** in 80% yield for two steps. Elaboration of the primary alcohol **29** involving the displacement of the corresponding tosylate afforded **30**, which on deprotection of the MOM ether resulted in *ent*-**7** in quantitative yield (Scheme 6).



Scheme 2. Synthesis of the acid fragment **8**.

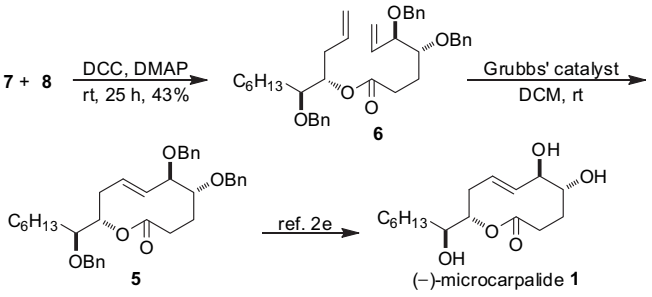
For the synthesis of the homoallylic alcohol fragment **7**, the known alcohol **11**[7] was converted to the tosylate **19**, which on reaction with *n*-pentylmagnesium bromide afforded **20** in 69% yield. $FeCl_3$ mediated deprotection of the acetonide in **20** furnished the diol **21** in 76% yield (88% based on starting material recovery). Following a procedure described by Sharma et.al.[3l] diol **21** was transformed into the epoxide **10** using standard conditions. Opening of the epoxide **10** with vinylmagnesium bromide afforded the required homoallylic alcohol **7** in 88% yield (Scheme 3).



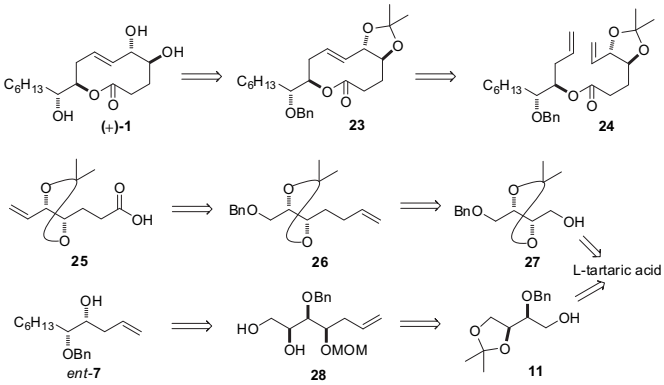
Scheme 3. Synthesis of the alcohol fragment **7**.

DCC mediated coupling of alcohol **7** and acid **8** resulted in the ester **6**. Conversion of the ester to the macrolactone **5** by RCM reaction and further deprotection of the benzyl ether is already reported in literature,[3g] hence, the present sequence constitutes a formal synthesis of (−)-microcarpalide (Scheme 4).

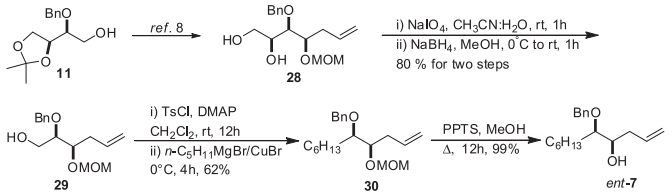
For the synthesis of (+)-microcarpalide **1**, RCM of the diene ester **24** is anticipated to construct the decanolactone. Synthesis of the required acid fragment **25** is envisaged by extension of the primary alcohol **27** while elaboration of the diol **28** is planned for the synthesis of required alcohol fragment *ent*-**7** as depicted in Scheme 5.



Scheme 4. Formal synthesis of (−)-microcarpalide.



Scheme 5. Retrosynthesis for (+)-microcarpalide.



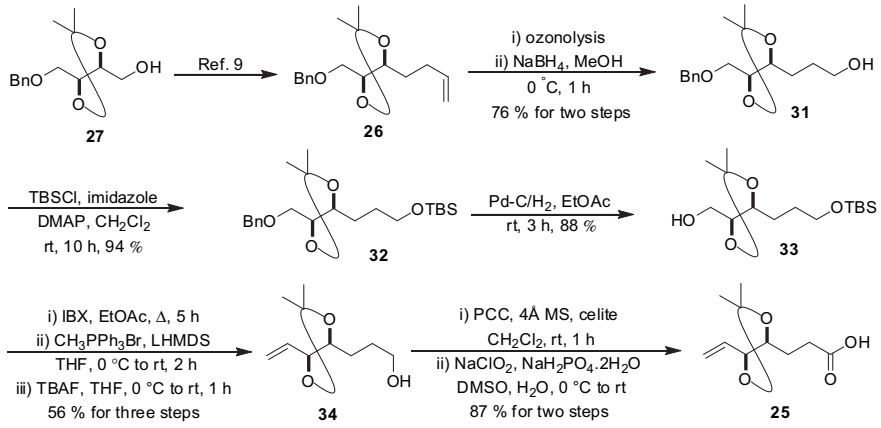
Scheme 6. Synthesis of *ent*-**7**.

For the synthesis of the acid fragment **25**, benzyloxy alcohol **27** was elaborated to the alkene **26** using a known procedure.[9] Ozonolysis of **26** resulted in the aldehyde, which on reduction with $NaBH_4$ afforded the primary alcohol **31** in 76% yield for two steps. Protection of the primary alcohol in **31** as the TBS ether followed by deprotection of the benzyl ether afforded **33** in 88% yield. IBX oxidation of **33** produced the aldehyde which on Wittig olefination followed by TBS deprotection with TBAF furnished the alkenol **34** in 56% yield for three steps. Primary alcohol in **34** was transformed into the acid using standard conditions to yield the required acid fragment in 87% yield for two steps (Scheme 7).

2. Experimental

2.1. (4*R*,5*S*)-5-((*R*)-1-(Benzyloxy)pent-4-en-1-yl)-*N*-methoxy-*N*,2,2-trimethyl-1,3-dioxolane-4-carboxamide (12)

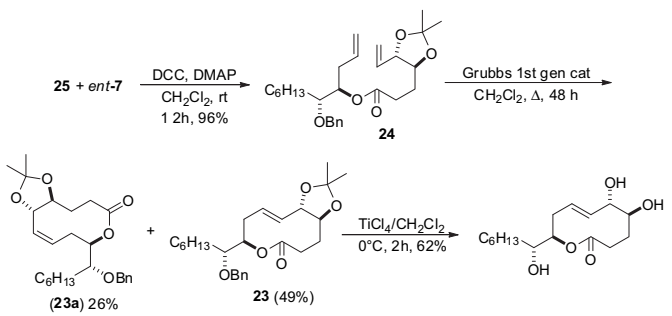
To a stirred solution of **9** (0.231 g, 0.84 mmol) in toluene (3 mL) was added Ag_2O (0.589 g, 2.53 mmol) at room temperature and stirred for 1 h. Benzyl bromide (0.12 mL, 1.01 mmol) was added to the reaction mixture at same temperature and refluxed for 12 h. After completion of the reaction (TLC), it was filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2 (15 mL). The residue obtained after concentration of the solvent was purified by column chromatography furnish the benzyl ether **12** (0.217 g) in 71% yield as a colorless oil. R_f 0.6 (petroleum ether/EtOAc 1:1); $[\alpha]_D^{24}$ +11.8 (*c* 0.8, $CHCl_3$); IR (neat) 2985, 2935, 1667, 1449, 1384, 1070 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.19 (m, 5H), 5.79 (ddt, *J*=16.9, 10.1, 6.7 Hz, 1H), 4.99 (dd, *J*=18.9, 10.3 Hz, 2H), 4.75 (br s, 2H), 4.65, 4.58 (ABq, *J*=11.3 Hz, 2H), 3.64 (br s, 4H), 3.18 (br s, 3H), 2.32–2.04 (m, 2H), 1.68 (q, *J*=7.4 Hz, 2H), 1.48 (s, 3H), 1.47(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.2 (Cq), 138.4 (Cq), 138.2 (CH), 128.2 (CH), 127.9 (CH), 127.5 (CH), 114.9 (CH_2), 111.1 (Cq), 78.9 (CH), 77.2 (CH), 72.5 (CH), 72.3 (CH_2), 61.7 (CH_3), 32.2 (CH_3), 29.8 (CH_2), 29.3 (CH_2), 27.0 (CH_3), 26.1 (CH_3); HRMS M^++Na found 386.1934; $C_{20}H_{29}NO_5$+Na requires 386.1943.



Scheme 7. Synthesis of the acid fragment **25**.

DCC mediated coupling of *ent*-**7** and acid **25** produced the known ester **24** in 96% yield. Ring closing metathesis of **24** with Grubbs first generation catalyst produced the *Z* and *E* lactones **23a** and **23** in 26% and 49% yield after chromatography.[10] (*E*)-Lactone **23** was treated with $TiCl_4$ to afford microcarpalide in 62% yield (Scheme 8).

In conclusion, facile synthesis of microcarpalide in both enantiomeric forms has been accomplished starting from L-tartaric acid. Main feature of the synthesis include the elaboration of γ-hydroxy amide and L-threotol derivatives derived from tartaric acid and ring closing metathesis to construct the 10-membered lactone ring.



Scheme 8. Synthesis of (+)-microcarpalide.

2.2. (4*R*,5*S*)-5-((*R*)-1-(Benzyloxy)-4-hydroxybutyl)-*N*-methoxy-*N*,2,2-trimethyl-1,3-sdioxolane-4-carboxamide (13)

Ozone was bubbled through a pre-cooled (−78 °C) solution of **12** (0.173 g, 0.47 mmol) in a mixture of CH_2Cl_2/MeOH (4:1, 10 mL), containing solid $NaHCO_3$ (0.010 g) until the pale blue color persisted. Excess ozone was flushed off with oxygen and Me_2S (0.5 mL) was added. The reaction mixture was warmed to 0 °C and stirred for 3 h. The reaction mixture was concentrated under reduced pressure and filtered through a short pad of Celite. The Celite pad was washed with ether (20 mL). Evaporation of the solvent yielded the crude aldehyde, which was subjected to the next reaction without further purification.

To a pre-cooled solution (−78 °C) of the aldehyde prepared above in MeOH (3 mL) was added $NaBH_4$ (0.036 g, 0.95 mmol) portion wise. The reaction mixture was stirred at same temperature for 1 h. After the reaction was completed (TLC), it was quenched by addition of cold water at −78 °C. The reaction mixture was extracted with EtOAc (2×15 mL) and the combined EtOAc extracts were washed with brine (5 mL) and dried over Na_2SO_4. Residue obtained after evaporation of solvent was purified by column

chromatography to obtain **13** (0.101 g) in 58% overall yield for two steps as a colorless oil. R_f 0.4 (EtOAc); $[\alpha]_D^{24}$ +12.2 (*c* 1.7, $CHCl_3$); IR (neat) 3445, 2987, 2936, 2873, 1663, 1451, 1385, 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51–7.20 (m, 5H), 4.74 (br s, 2H),4.66, 4.58 (ABq, *J*=11.4 Hz, 2H), 3.64 (s, 3H), 3.78–3.54 (m, 3H), 3.17 (br s, 3H), 2.02 (br s, 1H), 1.76–1.52 (m, 4H), 1.47 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.1 (Cq), 138.2 (Cq), 128.2 (CH), 128.0 (CH), 127.6 (CH), 111.1 (Cq), 78.9 (CH), 77.8 (CH), 72.6 (CH), 72.2 (CH_2), 62.5 (CH_2), 61.7 (CH_3), 32.2 (CH_3), 28.8 (CH_2), 27.0 (CH_3), 26.4 (CH_2), 26.1 (CH_3); HRMS M^++Na found 390.1892; $C_{20}H_{29}NO_5$+Na requires 390.1893.

2.3. (*R*)-4-(Benzyloxy)-4-((4*S*,5*S*)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)butan-1-ol (14)

Diol **14** (0.024 g) yield 16%. R_f 0.3 (EtOAc); $[\alpha]_D^{24}$ +14.7 (*c* 2.4, $CHCl_3$); IR (neat) 3417, 2934, 2874, 1454, 1372, 1250, 1214, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.21 (m, 5H), 4.68, 4.61 (ABq, *J*=11.4 Hz, 2H), 4.01 (dt, *J*=12.4, 8.4 Hz, 2H), 3.80 (dd, *J*=8.4, 3.1 Hz, 1H), 3.70–3.55 (m, 4H), 2.28 (br s, 2H), 1.79–1.53 (m, 4H), 1.42 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 137.8 (Cq), 128.4 (CH), 128.1 (CH), 127.9 (CH), 108.9 (Cq), 78.5 (CH), 78.0 (CH), 77.3 (CH), 72.9 (CH_2), 62.6 (CH_2), 62.5 (CH_2), 28.9 (CH_2), 27.0 6 (CH_3), 27.01 (CH_3), 26.6 (CH_2); HRMS M^++Na found 333.1682; $C_{20}H_{29}NO_5$+Na requires 333.1678.

2.4. (4*R*,5*S*)-5-((*R*)-1-(Benzyloxy)-4-((*tert*-butyldiphenylsilyl) oxy)butyl)-*N*-methoxy-*N*,2,2-trimethyl-1,3-dioxolane-4-carboxamide (15)

To a stirred solution of the alcohol **13** (0.101 g, 0.27 mmol), imidazole (0.037 g, 0.55 mmol), and DMAP (0.007 g, 0.055 mmol) in CH_2Cl_2 (3 mL) was added TBDPSCl (0.08 mL, 0.33 mmol), at room temperature and refluxed for 2 h. After completion of the reaction (TLC), it was poured into water (5 mL) and extracted with diethyl ether (2×10 mL). The combined organic extracts were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography of the resulting residue yielded **15** (0.164 g) in quantitative yield as a colorless oil. R_f 0.5 (petroleum ether/EtOAc 7:3); $[\alpha]_D^{24}$+8.7 (*c* 0.8, $CHCl_3$); IR (neat) 2933, 2858, 1669, 1109, 1020, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J*=6.8 Hz, 4H), 7.46–7.20 (m, 11H), 4.75 (br s, 2H), 4.62, 4.55 (ABq, *J*=11.4 Hz, 2H), 3.70–3.56 (m, 3H), 3.61 (s, 3H), 3.16 (br s, 3H), 1.81–1.70 (m, 2H), 1.69–1.56 (m, 2H), 1.48 (s, 3H), 1.46 (s, 3H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.2 (Cq), 138.4 (Cq), 135.5 (CH), 134.8 (CH), 133.9 (Cq), 129.5 (CH), 128.2 (CH), 127.9 (CH), 127.6 (CH), 111.1 (Cq), 79.0 (CH), 77.8 (CH), 72.51 (CH), 72.16 (CH_2), 63.7 (CH_2), 61.6 (CH_3), 32.2 (CH_3), 28.8 (CH_2), 27.05 (CH_3), 26.8 (CH_3), 26.4 (CH_2), 26.1 (CH_3), 19.2 (Cq); HRMS M^++Na found 628.3069; $C_{20}H_{29}NO_5$+Na requires 628.3070.

2.5. ((4*S*,5*S*)-5-((*R*)-1-(Benzyloxy)-4-((*tert*-butyldiphenylsilyl) oxy)butyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (16)

To a pre-cooled solution (0 °C) of the Weinreb amide **15** (0.164 g, 0.27 mmol) prepared above in MeOH (3 mL) was added $NaBH_4$ (0.031 g, 0.81 mmol) portion wise. The reaction mixture was slowly allowed to warm up to room temperature and refluxed for 2 h. After the reaction was completed (TLC), it was quenched by addition of cold water at 0 °C. The reaction mixture was extracted with EtOAc (2×15 mL) and the combined EtOAc extracts were washed with brine (5 mL) and dried over Na_2SO_4. Residue obtained after evaporation of solvent was purified by column chromatography to obtain **16** (0.126 g) in 85% yield as a colorless oil. R_f 0.3 (petroleum ether/EtOAc 7:3); $[\alpha]_D^{24}$ +4.8 (*c* 1.2, $CHCl_3$); IR (neat) 3447, 2931, 2858, 1109, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J*=7.7, 1.3 Hz, 4H), 7.48–7.22 (m, 11H), 4.62, 4.57 (ABq, *J*=11.4 Hz, 2H), 4.0 (t, *J*=3.3 Hz, 2H), 3.74–3.51 (m, 5H), 2.32 (br s, 1H), 1.88–1.51 (m, 4H), 1.41 (s, 6H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 139.4 (Cq), 137.0 (CH), 135.3 (Cq), 131.0 (CH), 129.8 (CH), 129.5 (CH), 129.3 (CH), 129.0 (CH), 110.2 (Cq), 80.0 (CH), 79.4 (CH), 76.6 (CH), 74.3 (CH_2), 65.0 (CH_2), 64.1 (CH_2), 30.4 (CH_2), 28.53 (CH_3), 28.46 (CH_3), 28.3 (CH_3), 27.9 (CH_2), 20.6 (Cq); HRMS M^++Na found 571.2859; $C_{20}H_{29}NO_5$+Na requires 571.2856.

2.6. (3*R*,4*R*)-4-(Benzyloxy)-7-((*tert*-butyldiphenylsilyl)oxy) hept-1-en-3-ol (17)

To a solution of **16** (0.115 g, 0.2 mmol) in dry toluene (3 mL) were added triphenylphosphine (0.165 g, 0.62 mmol), imidazole (0.043 g, 0.62 mmol), and iodine (0.106 g, 0.41 mmol) at room temperature and the reaction mixture was stirred under reflux for 2 h. After the reaction was completed (TLC), it was cooled to room temperature and poured into water (10 mL). It was then extracted with ether (3×20 mL) and the combined organic layers were washed with brine (30 mL), satd sodium thiosulfate (5 mL), and dried over Na_2SO_4. Silica gel column chromatography of the residue obtained after evaporation of the solvent, gave the iodide (0.081 g, 75%) as a colorless oil. R_f 0.6 (petroleum ether/ether 9:1); $[\alpha]_D^{24}$ −15.9 (*c* 0.6, $CHCl_3$); IR (neat) 2931, 2858, 1109, 1020, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J*=7.6, 1.2 Hz, 4H), 7.46–7.23 (m, 11H), 4.62, 4.57 (ABq, *J*=11.4 Hz, 2H), 3.91 (dd, *J*=7.5, 4.4 Hz, 1H), 3.87–3.74 (m, 1H), 3.67 (t, *J*=5.6 Hz, 2H), 3.54 (dt, *J*=7.3, 3.1 Hz, 1H), 3.32 (dd, *J*=10.7, 4.1 Hz, 1H), 3.20 (dd, *J*=10.7, 5.2 Hz, 1H), 1.83–1.69 (m, 2H), 1.67–1.55 (m, 2H), 1.46 (s, 3H), 1.41 (s, 3H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.2 (Cq), 135.6 (CH), 133.9 (Cq), 129.6 (CH), 128.4 (CH), 128.07 (CH), 127.8 (CH), 127.6 (CH), 109.3 (Cq), 81.8 (CH), 77.7 (CH), 75.5 (CH), 72.7 (CH_2), 63.6 (CH_2), 28.8 (CH_2), 27.5 (CH_3), 27.3 (CH_3), 26.9 (CH_3), 26.6 (CH_2), 19.2 (Cq), 7.5 (CH_2); HRMS M^++Na found 681.1878; $C_{20}H_{29}NO_5$+Na requires 681.1873.

To a solution of the iodide (0.081 g, 0.15 mmol) prepared above in absolute ethanol (2 mL) was added zinc dust (0.78 g, 1.20 mmol) at room temperature and refluxed for 5 h. Progress of the reaction was followed by TLC. After the reaction was completed it was filtered through a short pad of Celite and the Celite pad was washed with ether (2×10 mL). Silica gel column chromatography of the residue obtained after evaporation of the solvent, furnished the allylic alcohol **17** (0.054 g, 76%) as a colorless oil. R_f 0.5 (petroleum ether/EtOAc 9:1); $[\alpha]_D^{24}$ −5.5 (*c* 1.2, $CHCl_3$); IR (neat) 3456, 3071, 2932, 2859, 1111, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J*=7.6, 1.1 Hz, 4H), 7.47–7.21 (m, 11H), 5.88 (ddd, *J*=17.0, 10.4, 6.3 Hz, 1H), 5.37 (d, *J*=16.6 Hz, 1H), 5.23 (d, *J*=10.5 Hz, 1H), 4.63, 4.53 (ABq, *J*=11.3 Hz, 2H), 4.10 (t, *J*=6.3 Hz, 1H), 3.68 (t, *J*=5.8 Hz, 2H), 3.47–3.33 (m, 1H), 1.87–1.56 (m, 4H), 1.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.1 (Cq), 137.4 (CH), 135.5 (CH), 133.9 (Cq), 129.6 (CH), 128.4 (CH), 127.85 (CH), 127.81 (CH), 127.6 (CH), 117.0 (CH_2), 81.9 (CH), 74.4 (CH), 72.3 (CH_2), 63.8 (CH_2), 27.8 (CH_2), 26.8 (CH_3), 26.4 (CH_2), 19.2 (Cq); HRMS M^++Na found 497.2473; $C_{20}H_{29}NO_5$+Na requires 497.2488.

2.7. (4*R*,5*R*)-4,5-Bis(benzyloxy)hept-6-en-1-ol (18)

To a stirred solution of the allylic alcohol **17** (0.103 g, 0.21 mmol) in DMF (2 mL) was added NaH (0.013 g, 0.32 mmol) portion wise at 0 °C and stirred it for 45 min at the same temperature. Benzyl bromide (0.038 mL, 0.32 mmol) was added to the reaction mixture at 0 °C and stirred at room temperature for 2 h. After the reaction was completed (TLC), it was cooled to room temperature and poured into water (10 mL). It was then extracted with ether (2×15 mL) and the combined organic layers were washed with brine (5 mL), and dried over Na_2SO_4. Silica gel column

chromatography of the residue obtained after evaporation of the solvent, gave the bis benzyl ether (0.113 g), 94% as a colorless oil. R_f 0.6 (petroleum ether/EtOAc 9:1); $[\alpha]_D^{24}$+3.07 (*c* 1.3, $CHCl_3$); IR (neat) 3069, 2929, 2857, 1641, 1111, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.64 (dd, *J*=8.1, 1.8 Hz, 4H), 7.45–7.17 (m, 16H), 5.83 (ddd, *J*=18.6, 10.8, 7.5 Hz, 1H), 5.28 (dd, *J*=18.0, 10.4 Hz, 2H), 4.71, 4.52 (ABq, *J*=11.1 Hz, 2H), 4.63, 4.39 (ABq, *J*=11.7 Hz, 2H), 3.87 (t, *J*=6.6 Hz, 1H), 3.62 (t, *J*=5.7 Hz, 2H), 3.47 (ddd, *J*=8.1, 4.8, 3.3 Hz, 1H), 1.79–1.64 (m, 2H), 1.62–1.41 (m, 2H), 1.03 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) 138.8 (Cq), 138.6 (Cq), 135.5 (CH), 135.4 (CH), 134.0 (Cq), 129.5 (CH), 128.26 (CH), 128.21 (CH), 127.9 (CH), 127.7 (CH), 127.5 (CH), 127.42 (CH), 127.40 (CH), 118.6 (CH_2), 82.8 (CH), 81.1 (CH), 73.1 (CH_2), 70.5 (CH_2), 63.8 (CH_2), 28.6 (CH_2), 27.1 (CH_2), 26.8 (CH_3), 19.2 (Cq); HRMS M^++Na found 587.2951; $C_{20}H_{29}NO_5$+Na requires 587.2957.

To a pre-cooled (0 °C) solution of the bis benzyl ether (prepared above) (0.176 g, 0.31 mmol) in THF (3 mL) was added TBAF (0.5 mL, 0.46 mmol) and stirred at room temperature and stirred for 2 h. After the reaction was completed (TLC), it was poured into cold water (15 mL) and extracted with EtOAc. The organic layer was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification of the resulting residue by column chromatography furnished the alcohol **18** (0.095 g) in 94% yield as a colorless oil. R_f 0.3 (petroleum ether/EtOAc 7:3); $[\alpha]_D^{24}$ +7.08 (*c* 1.23, $CHCl_3$); lit.[3j] $[\alpha]_D^{24}$ +10.4 (*c* 1.3, $CHCl_3$); IR (neat) 3405, 2925, 2867, 1088, 1063, 736, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.21 (m, 10H), 5.83 (ddd, *J*=17.5, 10.4, 7.5 Hz, 1H), 5.33 (dd, *J*=17.4, 10.0 Hz, 2H), 4.77, 4.57 (ABq, *J*=11.4 Hz, 2H), 4.66, 4.42 (ABq=11.9 Hz, 2H), 3.96 (t, *J*=6.7 Hz, 1H), 3.57 (t, *J*=5.8 Hz, 2H), 3.45–3.55 (m, 1H), 1.92 (br s, 1H), 1.81–1.63 (m, 2H), 1.62–1.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.5 (2×Cq), 135.2 (CH), 128.4 (2×CH), 128.1 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 119.0 (CH_2), 82.4 (CH), 81.0 (CH), 73.2 (CH_2), 70.6 (CH_2), 62.8 (CH_2), 29.0 (CH_2), 27.2 (CH_2); HRMS M^++Na found 349.1792; $C_{20}H_{29}NO_5$+Na requires 349.1780.

2.8. (4*R*,5*R*)-4,5-Bis(benzyloxy)hept-6-enoic acid (8)

To a stirred solution of the alcohol **18** (0.037 g, 0.11 mmol) in DMSO/toluene (1:0.5 mL) was added IBX (0.095 g, 0.34 mmol) at room temperature and stirred for 2 h. After the reaction was completed (TLC), water (0.2 mL) was added. Reaction mixture was filtered through a short pad of Celite and the Celite pad was washed with ether (2×5 mL). The organic layer was diluted with ether (20 mL) and washed with water (10 mL).Combined ethereal extracts were washed with brine and dried over Na_2SO_4. Evaporation of the solvent yielded the crude aldehyde, which was subjected to the next reaction without further purification.

To a pre-cooled solution (0 °C) of the aldehyde prepared above in DMSO/H_2O (0.5:0.5 mL) was added $NaH_2PO_4{\cdot}2H_2O$ (0.177 g, 1.13 mmol) at room temperature and stirred it for 5 min $NaClO_2$ (0.051 g, 0.56 mmol) was added at 0 °C and stirred at room temperature for 2 h. After the reaction was completed (TLC), water (10 mL) was added and extracted with EtOAc (2×15 mL). Combined EtOAc extracts were washed with brine (5 mL) and dried over Na_2SO_4. Residue obtained after evaporation of solvent was purified by column chromatography to obtain **8** (0.034 g) in 96% overall yield in two steps as a colorless oil. R_f 0.4 (petroleum ether/EtOAc 1:1); $[\alpha]_D^{24}$ +15.5 (*c* 0.71, $CHCl_3$); lit.[3j] $[\alpha]_D^{24}$ +16.8 (*c* 0.7, $CHCl_3$); IR (neat) 3420, 3030, 2921, 2871, 1710, 1071, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.24 (m, 10H), 5.88 (ddt, *J*=17.5, 10.5, 7.6 Hz, 1H), 5.40 (dd, *J*=14.1, 4.9 Hz, 2H), 4.82, 4.59 (ABq, *J*=11.4 Hz, 2H), 4.71, 4.46 (ABq, *J*=11.9 Hz, 2H), 3.98 (t, *J*=6.5 Hz, 1H), 3.61 (ddd, *J*=9.3, 5.7, 3.6 Hz, 1H), 2.59–2.45 (m, 2H), 2.06–1.91 (m, 1H), 1.87–1.73 (m, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) 179.8 (Cq), 138.4 (2×Cq), 134.9 (CH), 128.4 (CH), 128.1 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 119.3 (CH_2), 82.5 (CH), 79.8 (CH), 73.4 (CH_2), 70.6 (CH_2), 30.3 (CH_2), 25.9 (CH_2); HRMS M^++Na found 379.1308; $C_{20}H_{29}NO_5$+Na requires 379.1312.

2.9. (*S*)-2-(Benzyloxy)-2-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl) ethyl 4-methylbenzenesulfonate (19)

To a stirred solution of alcohol **11** (0.5 g, 1. 98 mmol) in CH_2Cl_2 (4 mL) was added DMAP (0.726 g, 5.95 mmol), followed by *p*-TsCl (0.754 g, 3.96 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred for 12 h at the same temperature. After completion of the reaction (TLC), it was poured into water (15 mL) and extracted with diethyl ether (2×20 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography of the resulting residue yielded **19** (0.666 g) in 83% yield as colorless oil. R_f 0.8 (petroleum ether/EtOAc 1:1); $[\alpha]_D^{24}$+13.1 (*c* 1.0, $CHCl_3$); IR (neat) 2936, 2866, 1686, 1542, 1365, 1177 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J*=8.2 Hz, 2H), 7.20–7.36 (m, 7H), 4.66, 4.58 (ABq, *J*=11.8 Hz, 2H), 4.23–4.12 (m, 2H), 4.08 (dd, *J*=10.5, 6.2 Hz, 1H), 3.91 (dd, *J*=8.4, 6.8 Hz, 1H), 3.73 (dd, *J*=8.3, 6.6 Hz, 1H), 3.67 (dt, *J*=10.5, 5.2 Hz, 1H), 2.42 (s, 3H), 1.33 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 145.0 (Cq), 137.6 (Cq), 132.6 (Cq), 129.9 (CH), 128.4 (CH), 128.0 (CH), 127.9 (CH), 109.5 (Cq), 76.3 (CH), 75.2 (CH), 73.2 (CH_2), 69.4 (CH_2), 65.1 (CH_2), 26.1 (CH_3), 25.1 (CH_3), 21.6 (CH_3); HRMS M^++Na found 429.1349; $C_{20}H_{29}NO_5$+Na requires 429.1348.

3. (*S*)-4-((*S*)-1-(Benzyloxy)heptyl)-2,2-dimethyl-1,3-dioxolane (20)

To a stirred solution of CuBr (0.351 g, 2.43 mmol) in THF (2 mL) was added *n*-pentylmagnesiun bromide (10 mL, 8.0 mmol 0.8 M solution in THF) at 0 °C and stirred for 15 min. A solution of the tosylate **19** (0.66 g, 1.62 mmol) was added to the reaction mixture at 0 °C. The reaction mixture was slowly warmed to room temperature and stirred for 2 h. After completion of the reaction (TLC), it was poured into satd NH_4Cl solution (15 mL) and extracted with diethyl ether (2×20 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography of the resulting residue yielded **20** (0.344 g) in 69% yield as colorless oil. R_f 0.7 (petroleum ether/EtOAc 95:5); $[\alpha]_D^{24}$ −39.5 (*c* 1.4, $CHCl_3$); IR (neat) 2931, 2863, 1651, 1545, 1069 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.19 (m, 5H), 4.75, 4.60 (ABq, *J*=11.6 Hz, 2H), 4.19 (dt, *J*=17.4, 6.7 Hz, 1H), 3.96 (t, *J*=6.6 Hz, 1H), 3.66 (t, *J*=7.7 Hz, 1H), 3.48–3.33 (m, 1H), 1.43 (s, 3H), 1.36 (s, 3H), 1.48–1.18 (m, 10H), 0.86 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.8 (Cq), 128.2 (CH), 127.9 (CH), 127.5 (CH), 109.2 (Cq), 79.7 (CH), 78.5 (CH), 72.8 (CH_2), 66.0 (CH_2), 31.7 (CH_2), 30.7 (CH_2) 29.3 (CH_2), 26.5 (CH_3), 25.5 (CH_2), 25.4 (CH_3), 22.6 (CH_2), 14.0 (CH_3); HRMS M^++Na found 329.2090; $C_{20}H_{29}NO_5$+Na requires 329.2093.

3.1. (2*S*,3*S*)-3-(Benzyloxy)nonane-1,2-diol (21)

To a stirred solution of **20** (0.15 g, 0.49 mmol) in CH_2Cl_2 (2 mL) was added $FeCl_3.6H_2O$ (0.397 g, 1.47 mmol) at room temperature and stirred for 2 h. After completion of the reaction (TLC), the reaction mixture was diluted with CH_2Cl_2 (5 mL) and solid $NaHCO_3$ (0.5 g) and water (0.1 mL) were added and stirred it for 15 min. The reaction mixture was filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2 (30 mL). The residue obtained after concentration of the solvent was purified by column chromatoghaphy to furnish the diol **21** (0.099 g) in 76% yield as a colorless oil. R_f 0.4 (petroleum ether/EtOAc 1:1); $[\alpha]_D^{24}$ +34.1 (*c* 1.0, $CHCl_3$); IR (neat) 3370, 2930, 2863, 1653, 1545, 1085, 1046 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.20 (m, 5H), 4.65, 4.46 (ABq, *J*=11.3 Hz, 2H), 3.70–3.52 (m, 3H), 3.45 (dt, *J*=10.8, 5.5 Hz, 1H), 2.64

(br s, 1H), 2.28 (br s, 1H), 1.65–1.49 (m, 2H), 1.43–1.25 (m, 8H), 0.87 (t, J=7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.0 (Cq) 128.5 (CH), 127.9 (CH×2), 79.7 (CH), 72.7 (CH), 72.1 (CH_2), 64.0 (CH_2), 31.7 (CH_2), 30.0 (CH_2), 29.5 (CH_2) 25.0 (CH_2), 22.6 (CH_2), 14.0 (CH_3); HRMS M^++Na found 289.1779; $C_{20}H_{29}NO_5$+Na requires 289.1780.

3.2. (2*S*,3*S*)-3-(Benzyloxy)-2-hydroxynonyl 4-methylbenzenesulfonate (22)

To a stirred solution of the diol **21** (0.06 g, 0.22 mmol) in CH_2Cl_2 (1 mL) was added Et_3N (0.1 mL, 0.67 mmol), followed by *p*-TsCl (0.086 g, 0.45 mmol) at 0 °C under argon atmosphere. The reaction mixture was stirred for 12 h at room temperature. After completion of the reaction (TLC), it was poured into water (5 mL) and extracted with diethyl ether (2×5 mL). The combined organic extracts were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography of the resulting residue yielded **22** (0.062 g) in 67% yield as a colorless oil. R_f 0.5 (petroleum ether/EtOAc 4:1); $[\alpha]_D^{24}$ +3.3 (*c* 1.0, $CHCl_3$); IR (neat) 3422, 2927, 2858, 1598, 1362, 1176, 1097, 975, 814 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J=8.0 Hz, 2H), 7.38–7.18 (m, 7H), 4.57, 4.39 (ABq, J=11.3 Hz, 2H), 4.03 (qd, J=10.0, 5.4 Hz, 2H), 3.79 (td, J=9.6, 6.7 Hz, 1H), 3.46 (td, J=9.5, 5.8 Hz, 1H), 2.42 (s, 3H), 2.33 (d, J=7.1 Hz, 1H), 1.65–1.46 (m, 2H), 1.38–1.20 (br m, 8H), 0.87 (t, J=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 145 (Cq), 137.8 (Cq), 132.6 (Cq), 129.9 (CH), 128.4 (CH), 128.0 (CH), 127.9 (CH), 77.9 (CH), 72.4 (CH_2), 70.5 (CH_2), 70.1 (CH), 31.7 (CH_2), 29.9 (CH_2), 29.3 (CH_2), 25.2 (CH_2), 22.5 (CH_2), 21.6 (CH_3), 14.0 (CH_3); HRMS M^++Na found 443.2038; $C_{20}H_{29}NO_5$+Na requires 443.1868.

3.3. (*S*)-2-((*S*)-1-(Benzyloxy)heptyl)oxirane (10)

To a stirred solution of **22** (0.085 g, 0.20 mmol) in MeOH (1.5 mL) was added K_2CO_3 (0.056 g, 0.40 mmol) at room temperature and stirred for 2 h. After completion of the reaction (TLC), it was filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2 (15 mL). The residue obtained after concentration of the solvent was purified by column chromatography to furnish epoxide **10** (0.045 g) in 91% yield as a colorless oil. R_f 0.5 (petroleum ether/EtOAc 9:1); $[\alpha]_D^{24}$ −30.2 (*c* 1.0, $CHCl_3$); IR (neat) 2927, 2857, 1608, 1093, 737 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.19 (m, 5H), 4.82, 4.57 (ABq, J=11.8 Hz, 2H), 3.10–2.94 (m, 2H), 2.77 (t, J=4.1 Hz, 1H), 2.48 (dd, J=4.6, 0.8 Hz, 1H), 1.74–1.60 (m, 1H), 1.59–1.40 (m, 2H), 1.39–1.20 (m, 7H), 0.87 (t, J=6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.6 (Cq), 128.2 (CH), 127.8 (CH), 127.4 (CH), 80.5 (CH), 71.6 (CH_2), 55.1 (CH), 43.1 (CH_2), 32.3 (CH_2), 31.7 (CH_2), 29.2 (CH_2), 25.4 (CH_2), 22.6 (CH_2), 14.0 (CH_3); HRMS M^++Na found 271.1673; $C_{20}H_{29}NO_5$+Na requires 271.1674.

3.4. (4*S*,5*S*)-5-(Benzyloxy)undec-1-en-4-ol (7)

To a stirred solution of CuCN (0.006 g, 0.058 mmol) in THF (0.5 mL) was added vinylmagnesium bromide (0.7 mL, 0.70 mmol 1 M solution in THF) at −78 °C and stirred for 15 min. A solution of the epoxide **10** (0.036 g, 0.14 mmol) in THF (1 mL) was added to the reaction mixture at −78 °C. The reaction mixture was slowly warmed up to room temperature and stirred overnight. After completion of the reaction (TLC), it was poured into satd NH_4Cl solution (5 mL) and extracted with diethyl ether (2×10 mL). The combined organic extracts were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography of the resulting residue yielded **7** (0.034 g) in 88% yield as colorless oil. R_f 0.4 (petroleum ether/EtOAc 9:1); $[\alpha]_D^{24}$ +19.3 (*c* 1.5, $CHCl_3$); lit.[3g] $[\alpha]_D^{24}$ +17.4 (*c* 1.5, $CHCl_3$); IR (neat) 3450, 2930, 2860, 1591, 1444, 1093, 1071 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.22 (m, 5H), 5.86 (ddt, J=17.3, 10.6, 7.0 Hz, 1H), 5.11 (dd, J=16.8, 6.3 Hz, 2H), 4.64, 4.50 (ABq, J=11.3 Hz, 2H), 3.63 (td, J=9.8, 4.9 Hz, 1H), 3.32 (q, J=5.5 Hz, 1H), 2.41–2.17 (m, 3H), 1.72–1.49 (m, 2H), 1.43–1.23 (br m, 8H), 0.89 (t, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.4 (Cq), 135.0 (CH), 128.4 (CH), 127.8 (CH), 127.7 (CH), 117.2 (CH_2), 81.4 (CH), 72.3 (CH_2), 78.0 (CH), 38.1 (CH_2), 31.8 (CH_2), 30.1 (CH_2), 29.5 (CH_2), 25.1 (CH_2), 22.6 (CH_2), 14.1 (CH_3); HRMS M^++Na found 299.1987; $C_{20}H_{29}NO_5$+Na requires 299.1987.

3.5. (4*R*,5*R*)-(4*S*,5*S*)-5-(Benzyloxy)undec-1-en-4-yl 4,5-bis(benzyloxy)hept-6-enoate (6)

To a stirred solution of acid **8** (0.016 g, 0.047 mmol), in CH_2Cl_2 (0.5 mL) were added alcohol **7** (0.011 g, 0.039 mmol, in 0.5 mL CH_2Cl_2), DCC (0.017 g, 0.079 mmol), and DMAP (0.002 g, 0.0079 mmol), at room temperature and stirred for 25 h. After completion of the reaction (TLC), it was filtered through a short pad of silica gel and the silica gel pad was washed with diethyl ether (20 mL). Evaporation of the solvent and purification of the resulting residue by column chromatography furnished the ester **6** (0.013 g) in 43% yield as a colorless oil. R_f 0.7 (petroleum ether/ether 4:1); $[\alpha]_D^{24}$+2.0 (*c* 1.5, $CHCl_3$); lit.[3g] $[\alpha]_D^{24}$+1.9 (*c* 1.4, $CHCl_3$); IR (neat) 2928, 2858, 1732, 1071, 734, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.20 (m, 15H), 5.87–5.63 (m, 2H), 5.30 (dd, J=17.4, 9.6 Hz, 2H), 5.15–5.05 (m, 2H), 5.03–4.93 (m, 1H), 4.72, 4.51 (ABq, J=11.4 Hz, 2H), 4.62, 4.38 (ABq, J=11.7 Hz, 2H), 4.56 (s, 2H), 3.88 (t, J=6.3 Hz, 1H), 3.51 (ddd, J=9.0, 5.7, 3.6 Hz, 1H), 3.42 (dt, J=7.2, 4.2 Hz, 1H), 2.54–2.37 (m, 2H), 2.36–2.18 (m, 2H), 2.03–1.83 (m, 1H), 1.81–1.61 (m, 1H), 1.55–1.32 (br m, 2H), 1.23 (br m, 8H), 0.86 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 173.1 (Cq), 138.5 (CH), 138.4 (CH), 135.0 (CH), 134.1 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 119.1 (CH_2), 117.5 (CH_2), 82.5 (CH), 80.1 (CH), 78.9 (CH), 73.4 (CH_2), 73.2 (CH), 72.3 (CH_2), 70.5 (CH_2), 34.3 (CH_2), 31.7 (CH_2), 30.6 (CH_2), 29.9 (CH_2), 29.3 (CH_2), 26.2 (CH_2), 25.6 (CH_2), 22.6 (CH_2), 14.1 (CH_3); HRMS M^++Na found 621.3556; $C_{20}H_{29}NO_5$+Na requires 621.3556.

3.6. (2*R*,3*R*)-2-(Benzyloxy)-3-(methoxymethoxy)hex-5-en-1-ol (29)

To a stirred solution of **28** (0.218 g, 0.73 mmol) in CH_3CN/H_2O (3:1 mL) was added $NaIO_4$ (0.315 g, 1.47 mmol) at room temperature and stirred for 1 h. After completion of the reaction (TLC), it was filtered through a short pad of Celite and the Celite pad was washed with EtOAc (15 mL). The EtOAc layer was washed with water (10 mL) followed by brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent yielded the crude aldehyde, which was subjected to the next reaction without further purification.

To a pre-cooled solution (0 °C) of the aldehyde prepared above in MeOH (3 mL) was added $NaBH_4$ (0.055 g, 0.73 mmol) portion wise. The reaction mixture was slowly allowed to warm to room temperature and stirred for 1 h. After the reaction was completed (TLC), it was quenched by addition of cold water at 0 °C. The reaction mixture was extracted with EtOAc (2×15 mL) and the combined EtOAc extracts were washed with brine (5 mL) and dried over Na_2SO_4. Residue obtained after evaporation of solvent was purified by column chromatography to obtain **29** (0.155 g) in 80% overall yield in two steps as a colorless oil. R_f 0.5 (petroleum ether/EtOAc 6:4); $[\alpha]_D^{24}$ −21.5 (*c* 1.5, $CHCl_3$); IR (neat) 3454, 2933, 2890, 1099, 1035, 915 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.23 (m, 5H), 5.80 (ddt, J=17.1, 10.1, 7.1 Hz, 1H), 5.08 (dd, J=16.9, 9.3 Hz, 2H), 4.68 (s, 2H), 4.64 (s, 2H), 3.89–3.72 (m, 2H), 3.68 (dd, J=11.5, 5.8 Hz, 1H), 3.58 (dd, J=10.0, 5.3 Hz, 1H), 3.39 (s, 3H), 2.54–2.25 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.2 (Cq), 134.6 (CH), 128.4 (CH), 127.9 (CH), 127.8 (CH), 117.5 (CH_2), 96.9 (CH_2), 79.9 (CH), 77.3 (CH), 72.9 (CH_2), 61.2 (CH_2), 55.9 (CH_3), 35.2 (CH_2); HRMS M^++Na found 389.1416; $C_{20}H_{29}NO_5$+Na requires 389.1418.

3.7. ((((4*R*,5*R*)-4-(Methoxymethoxy)undec-1-en-5-yl)oxy) methyl)benzene (30)

To a stirred solution of alcohol **29** (0.12 g, 0.45 mmol) in CH_2Cl_2 (2 mL) was added DMAP (0.165 g, 1.35 mmol), followed by *p*-TsCl (0.171 g, 0.90 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred for 12 h at the same temperature. After completion of the reaction (TLC), it was poured into water (15 mL) and extracted with diethyl ether (2×20 mL). The combined organic extracts were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent yielded the crude tosylate, which was subjected to the next reaction without further purification.

To a stirred solution of CuBr (0.097 g, 0.65 mmol) in THF (1 mL) was added *n*-pentylmagnesiun bromide (2.8 mL, 2.2 mmol 0.8 M solution in THF) at 0 °C and stirred for 15 min. A solution of the tosylate (prepared above) was dissolved in THF (2 mL) and was added to the reaction mixture at 0 °C. The reaction mixture was slowly warmed to room temperature and stirred for 4 h. After completion of the reaction (TLC), it was poured into satd NH_4Cl solution (15 mL) and extracted with diethyl ether (2×20 mL). The combined organic extracts were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography of the resulting residue yielded **30** (0.089 g) in 62% overall yield for two steps as a colorless oil. R_f 0.5 (petroleum ether/Ether 9:1); $[\alpha]_D^{24}$+4.0 (*c* 1.5, $CHCl_3$); IR (neat) 2928, 2858, 1100, 1041, 915 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.20 (m, 5H), 5.82 (ddt, *J*=17.1, 10.1, 7.0 Hz, 1H), 5.06 (dd, *J*=17.0, 9.6 Hz, 2H), 4.68 (s, 2H), 4.60, 4.56 (ABq, *J*=11.5 Hz, 2H), 3.70 (dt, *J*=8.6, 4.4 Hz, 1H), 3.44 (dt, *J*=7.5, 3.4 Hz, 1H), 3.37 (s, 3H), 2.53–2.36 (m, 1H), 2.33–2.16 (m, 1H), 1.66–1.54 (m, 1H), 1.53–1.36 (m, 2H), 1.27 (br s, 7H), 0.88 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.6 (Cq), 135.3 (CH), 128.2 (CH), 127.9 (CH), 127.5 (CH), 116.8 (CH_2), 96.5 (CH_2), 80.1 (CH), 78.0 (CH), 72.5 (CH_2), 55.6 (CH_3), 34.8 (CH_2), 31.7 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 25.8 (CH_2), 22.5 (CH_2), 14.01 (CH_2); HRMS M^++Na found 343.2249; $C_{20}H_{29}NO_5$+Na requires 343.2249.

3.8. Preparation of (4*R*,5*R*)-5-(benzyloxy)undec-1-en-4-ol (*ent*-7)

To a stirred solution of **30** (0.089 g, 0.27 mmol) in MeOH (2 mL) was added PPTS (0.070 g, 0.27 mmol) at room temperature and refluxed for 12 h. After completion of the reaction (TLC), solid $NaHCO_3$ (0.1 g) was added and stirred for 10 min. Reaction mixture was filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2 (15 mL). The residue obtained after concentration of the solvent was purified by column chromatography to furnish the homoallylic alcohol *ent*-**7** (0.075 g) in quantitative yield as a colorless oil. R_f 0.4 (petroleum ether/EtOAc 9:1); $[\alpha]_D^{24}$ −19.0 (*c* 1.1, $CHCl_3$); lit.[3g] $[\alpha]_D^{24}$ +17.4 (*c* 1.5, $CHCl_3$ for the enantiomer); IR (neat) 3460, 2927, 2857, 1606, 1450, 1090, 1070, 912 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43–7.25 (m, 5H), 5.86 (ddt, *J*=17.4, 10.5, 7.0 Hz, 1H), 5.10 (dd, *J*=16.6, 5.98 Hz, 2H), 4.66, 4.51 (ABq, *J*=11.3 Hz, 2H), 3.64 (dt, *J*=9.9, 5.0 Hz, 1H), 3.33 (q, *J*=5.5 Hz, 1H), 2.39–2.19 (m, 3H), 1.69–1.51(m, 2H), 1.44–1.21 (br m, 8H), 0.87 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.4 (Cq), 135.0 (CH), 128.4 (CH), 127.8 (CH), 127.7 (CH), 117.2 (CH_2), 81.4 (CH), 72.3 (CH_2), 72.0 (CH), 38.0 (CH_2), 31.7 (CH_2), 30.1 (CH_2), 29.5 (CH_2), 25.1 (CH_2), 22.6 (CH_2), 14.0 (CH_3); HRMS M^++Na found 299.1988; $C_{20}H_{29}NO_5$+Na requires 299.1987.

3.9. 3-((4*S*,5*S*)-5-((Benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)propan-1-ol (31)

Ozone was bubbled through a pre-cooled (−78 °C) solution of **26** (0.724 g, 2.62 mmol) in a mixture of CH_2Cl_2/MeOH (4:1, 20 mL), containing solid $NaHCO_3$ (20 mg) until the pale blue color persisted. Excess ozone was flushed off with oxygen and Me_2S (1 mL) was added. The reaction mixture was warmed to 0 °C and stirred for 3 h. The reaction mixture was concentrated under reduced pressure and filtered through a short pad of Celite. The Celite pad was washed with ether (20 mL). Evaporation of the solvent yielded the crude aldehyde, which was subjected to the next reaction without further purification.

To a pre-cooled solution (0 °C) of the aldehyde prepared above in MeOH (4 mL) was added $NaBH_4$ (0.2 g, 5.24 mmol) portion wise. The reaction mixture was slowly allowed to warm up to room temperature and stirred for 1 h. After the reaction was completed (TLC), it was quenched by addition of cold water at 0 °C. The reaction mixture was extracted with EtOAc (2×20 mL) and the combined EtOAc extracts were washed with brine (5 mL) and dried over Na_2SO_4. Residue obtained after evaporation of the solvent was purified by column chromatography to obtain **31** (0.559 g) in 76% overall yield for two steps as a colorless oil. R_f 0.4 (petroleum ether/EtOAc 7:3); $[\alpha]_D^{24}$ −9.9 (*c* 1.8, $CHCl_3$); IR (neat) 3450, 2986, 2935, 2868, 1376, 1245, 1216, 1088, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.20 (m, 5H), 4.59, 4.56 (ABq, *J*=12.8 Hz, 2H), 3.83 (br, d, *J*=3.6 Hz, 2H), 3.64 (br s, 2H), 3.57 (ddd, *J*=14.3, 10.4, 3.8 Hz, 2H), 2.20 (br s, 1H), 1.81–1.91 (m, 4H), 1.41 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 137.8 (Cq), 128.3 (CH), 127.64 (CH), 127.61 (CH), 108.8 (Cq), 79.9 (CH), 78.3 (CH), 73.5 (CH_2), 70.3 (CH_2), 62.5 (CH_2), 29.7 (CH_2), 29.3 (CH_2), 27.2 (CH_3), 26.9 (CH_3); HRMS M^++Na found 303.1572; $C_{20}H_{29}NO_5$+Na requires 303.1572.

4. (3-((4*S*,5*S*)-5-((Benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)propoxy)(*tert*-butyl)dimethylsilane (32)

To a pre-cooled (0 °C) solution of **31** (0.082 g, 0.29 mmol) in CH_2Cl_2 (2 mL) were added DMAP (0.007 g, 0.058 mmol) and imidazole (0.039 g, 0.58 mmol) followed by TBSCl (0.065 g, 0.43 mmol) under argon atmosphere. The reaction mixture was stirred at room temperature for 12 h. After the reaction is complete (TLC), it was poured into cold water (5 mL) and extracted with diethyl ether (2×10 mL). The ethereal layer was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification of the resulting residue by column chromatography furnished the TBS ether (0.108 g) in 94% yield as colorless oil. R_f 0.6 (petroleum ether/ether 9:1); $[\alpha]_D^{24}$ −11.3 (*c* 1.0, $CHCl_3$); IR (neat) 2930, 2858, 1253, 1094, 834, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.21 (m, 5H), 4.59, 4.55 (ABq, *J*=12.2 Hz, 2H), 3.91–3.74 (m, 2H), 3.68–3.58 (m, 2H), 3.55 (d, *J*=4.2 Hz, 2H), 1.76–1.51 (m, 4H), 1.40 (s, 3H), 1.38 (s, 3H), 0.87 (s, 9H), 0.026 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.0 (Cq), 128.3 (CH), 127.6 (2×CH), 108.7 (Cq), 80.1 (CH), 78.1 (CH), 73.5 (CH_2), 70.6 (CH_2), 62.8 (CH_2), 29.5 (CH_2), 29.1 (CH_2), 27.3 (CH_3), 27.0 (CH_3), 25.9 (CH_3), 18.1 (Cq), −5.3 (CH_3); HRMS M^++Na found 417.2436; $C_{20}H_{29}NO_5$+Na requires 417.2437.

4.1. ((4*S*,5*S*)-5-(3-((*tert*-Butyldimethylsilyl)oxy)propyl)-2,2-dimethyl-1,3-dioxolan-4 yl)methanol (33)

TBS protected benzyl ether **32** (0.050 g, 0.12 mmol) was dissolved in MeOH (2 mL) and degassed. Pd/C (0.01 g) was added to the reaction mixture and stirred under hydrogen atmosphere (balloon) for 3 h. After completion of the reaction (TLC), it was filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2 (15 mL). The residue obtained after concentration of the solvent was purified by column chromatography to furnish the alcohol **33** (0.032 g) in 88% yield as a colorless oil. R_f 0.5 (petroleum ether/EtOAc 7:3); $[\alpha]_D^{24}$ −11.3 (*c* 1.0, $CHCl_3$); IR (neat) 3448, 2932, 2859, 1254, 1097, 834, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.95–3.80 (m, 1H), 3.79–3.67 (m, 2H), 3.66–3.50 (m, 3H), 2.22 (br s, 1H), 1.76–1.50 (m, 4H), 1.38 (s, 3H), 1.37 (s, 3H), 0.85 (s, 9H), 0.016

(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 108.6 (Cq), 81.5 (CH), 76.7 (CH), 62.8 (CH_2), 62.0 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 27.3 (CH_3), 27.0 (CH_3), 25.9 (CH_3), 18.3 (Cq), −5.3 (CH_3); HRMS M^++Na found 327.1966; $C_{20}H_{29}NO_5$+Na requires 327.1968.

4.2. 3-((4*S*,5*S*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl) propan-1-ol (34)

To a stirred solution of **33** (0.454 g, 1.49 mmol) in EtOAc (7 mL) was added IBX (1.463 g 5.22 mmol) and refluxed for 5 h. After the reaction is complete (TLC), it was filtered through a short pad of Celite and the Celite pad was washed with EtOAc (30 mL). The organic layer was washed with water (10 mL), brine (10 mL), and dried over Na_2SO_4. The residue obtained after evaporation of the solvent afforded the crude aldehyde, which was used in the next step without further purification.

To a stirred solution of methyl triphenyl phosphonium bromide (2.127 g, 5.96 mmol) in THF (3 mL) was added LiHMDS (4.5 mL, 4.47 mmol, 1.0 M solution in THF) at 0 °C and stirred for 45 min. Aldehyde (prepared above) was dissolved in THF (3 mL) and added to the reaction mixture at 0 °C. Reaction mixture was warmed to room temperature and stirred for 2 h. After completion of the reaction (TLC), it was poured into cold water (15 mL) and extracted with diethyl ether (2×20 mL). The ethereal layer was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by purification of the resulting residue by column chromatography using petroleum ether/EtOAc (95:5) as eluent furnished the alkene, which was subjected to next step without further purification.

To a pre-cooled (0 °C) solution of alkene (prepared above) in THF (2 mL) was added TBAF (2.2 mL, 2.23 mmol). Reaction mixture was allowed to room temperature and stirred for 1 h. After the reaction is complete (TLC), it was poured in to cold water (15 mL) and extracted with EtOAc (2×10 mL). The organic layer was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification of the resulting residue by column chromatography furnished the alcohol **34** (0.156 g) in 56% overall yield for three steps as a colorless oil. R_f 0.5 (petroleum ether/EtOAc 1:1); $[\alpha]_D^{24}$ +3.0 (*c* 2.0, $CHCl_3$); lit.[11] $[\alpha]_D^{24}$+2.48 (*c* 1.61 in $CHCl_3$); IR (neat) 3432, 2986, 2936, 2871, 1372, 1241, 1050 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (ddd, *J*=17.3, 10.2, 7.4 Hz, 1H), 5.33 (d, *J*=17.1 Hz, 1H), 5.22 (d, *J*=10.3 Hz, 1H), 3.97 (t, *J*=7.9 Hz, 1H), 3.73–3.57 (m, 3H), 2.34 (br s, 1H), 1.78–1.34 (m, 4H), 1.38 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 135.0 (CH), 119.1 (CH_2), 108.7 (Cq), 82.7 (CH_2), 80.5 (CH_2), 62.5 (CH_2), 29.4 (CH_2), 28.3 (CH_3), 27.2 (CH_3), 26.9 (CH_3); HRMS M^++Na found 209.1157; $C_{20}H_{29}NO_5$+Na requires 209.1154.

4.3. 3-((4*S*,5*S*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl) propanoic acid (25)

To a stirred suspension of PCC (0.9 g, 4.19 mmol), in dichloromethane (3 mL) was added a solution of the alcohol 34 (0.156 g, 0.83mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred at room temperature for 1 h. After completion of the reaction (TLC), it was filtered through a short pad of silica gel and the silica gel pad was washed with diethyl ether (30 mL). Evaporation of the solvent and the resulting crude aldehyde was subjected to next step without further purification.

To a pre-cooled (0 °C) solution of the aldehyde (prepared above) in DMSO/H_2O (2:2 mL) was added $NaH_2PO_4{\cdot}2H_2O$ (1.308 g, 8.4 mmol), and stirred it for 5 min. $NaClO_2$ (0.38 g, 4.19 mmol) was added to the reaction at the same temperature warmed to room temperature and stirred for 2 h. After the reaction was completed (TLC), it was poured in to cold water (15 mL) and extracted with EtOAc (2×10 mL). The organic layer was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification of the resulting residue by column chromatography furnished the acid **25** (0.145 g) in 87% overall yield for two steps as a colorless oil. R_f 0.4 (petroleum ether/EtOAc 1:1); $[\alpha]_D^{24}$ −6.3 (*c* 0.7, $CHCl_3$); lit.[12] $[\alpha]_D^{24}$ +6.8 (*c* 0.59, $CHCl_3$ for the enantiomer); IR (neat) 3457, 3225, 2987, 2933, 1712, 1376, 1241, 1067 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (ddd, *J*=17.3, 10.2, 7.6 Hz, 1H), 5.36 (d, *J*=17.1 Hz, 1H), 5.25 (d, *J*=10.2 Hz, 1H), 4.0 (t, *J*=7.8 Hz, 1H), 3.69 (dt, *J*=8.2, 3.4 Hz, 1H), 2.64–2.37 (m, 2H), 2.0–1.89 (m, 1H), 1.87–1.73 (m, 1H), 1.39 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 178.5 (Cq), 134.8 (CH), 119.3 (CH_2), 108.9 (Cq), 84.4 (CH_2), 79.3 (CH), 30.3 (CH_2), 27.1 (CH_3), 26.9 (CH_3), 26.4 (CH_2); HRMS M^++Na found 223.0945; $C_{20}H_{29}NO_5$+Na requires 223.0946.

4.4. (4*R*,5*R*)-5-(Benzyloxy)undec-1-en-4-yl 3-((4*S*,5*S*)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)propanoate (24)

To a stirred solution of acid **25** (0.067 g, 0.33 mmol), in CH_2Cl_2 (0.5 mL) were added alcohol *ent*-**7** (0.062 g, 0.22 mmol, in 0.5 mL CH_2Cl_2), DCC (0.031 g, 0.15 mmol), and DMAP (0.002 g, 0.015 mmol), at room temperature and stirred for 12 h. After completion of the reaction (TLC), it was filtered through a short pad of silica gel and the silica gel pad was washed with diethyl ether (20 mL). Evaporation of the solvent and purification of the resulting residue by column chromatography furnished the ester **24** (0.030 g) in 96% yield as a colorless oil. R_f 0.6 (petroleum ether/EtOAc 9:1); $[\alpha]_D^{24}$ +2.3 (*c* 3.0, $CHCl_3$); lit.[3l] $[\alpha]_D^{24}$ −1.9 (*c* 4.2, $CHCl_3$) for the enantiomer; IR (neat) 2931, 2860, 1736, 1370, 1243, 1070, 926 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.19 (m, 5H), 5.82–5.64 (m,2H), 5.35 (d, *J*=17.0 Hz, 1H), 5.24 (d, *J*=10.2 Hz, 1H), 5.15–4.95 (m, 3H), 4.57 (s, 2H), 3.97 (t, *J*=7.8 Hz, 1H), 3.66 (dt, *J*=8.2, 3.6 Hz, 1H), 3.43 (dt, *J*=7.5, 4.5 Hz, 1H), 2.55–2.23 (m, 4H), 1.97–1.72 (m, 2H), 1.44–1.30 (m, 3H), 1.39 (s, 3H), 1.37 (s, 3H), 1.23 (br s, 7H), 0.86 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.7 (Cq), 138.4 (Cq), 135.0 (CH), 134.0 (CH), 128.3 (CH), 127.8 (CH), 127.6 (CH), 119.2 (CH_2), 117.6 (CH_2), 108.8 (Cq), 82.4 (CH), 79.4 (CH), 78.9 (CH), 73.4 (CH), 72.3 (CH_2), 34.4 (CH_2), 31.7 (CH_2), 30.7 (CH_2), 29.8 (CH_2), 29.3 (CH_2), 27.2 (CH_3), 26.9 (CH_3), 26.8 (CH_2), 25.5 (CH_2), 22.5 (CH_2), 14.0 (CH_3); HRMS M^++Na found 481.2930; $C_{20}H_{29}NO_5$+Na requires 481.2930.

4.5. (3a*S*,8*R*,11a*S*,*E*)-8-((*R*)-1-(Benzyloxy)heptyl)-2,2-dimethyl-4,5,8,9-tetrahydro-3a*H*-[1,3]dioxolo[4,5-*e*]oxecin-6(11a*H*)-one (23)

To a stirred solution of the diene ester **24** (0.081 g, 0.17 mmol) in CH_2Cl_2 (176 mL) was added Grubbs' first generation catalyst (0.029 g, 0.035 mmol) and refluxed for 2 days. After completion of the reaction (TLC), it was filtered through a short pad of silica gel and the silica gel pad was washed with diethyl ether (20 mL). Evaporation of the solvent and purification of the resulting residue by column chromatography furnished 2:1 ratio of the *E* and *Z*-lactones **23** and **23a** in (0.036 g) 49% and (0.019 g) 26% yield as a brown colorless oil. R_f 0.5 (petroleum ether/EtOAc 7:3); $[\alpha]_D^{24}$ +45.0 (*c* 2.8, $CHCl_3$); lit.[3i] $[\alpha]_D^{24}$ −37.9 (*c* 3.0, $CHCl_3$) for enantiomer; IR (neat) 2929, 2859, 1730, 1235, 1064 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 5.83 (ddd, 1H, minor), 5.72 (ddd, *J*=15.7, 11.3, 4.5 Hz, 1H), 5.65 (dd, *J*=11.8, 5.3 Hz, 1H, minor), 5.26 (dd, *J*=15.5, 9.0 Hz, 1H), 5.05 (br d, *J*=11.1 Hz, 1H, minor), 4.98–4.92 (br m, 1H, minor), 4.90–4.85 (br m, 1H), 4.59, 4.50 (ABq, *J*=11.6 Hz, 2H), 4.52 (d, *J*=6.2 Hz, 1H, minor), 3.86 (t, *J*=8.6 Hz, 1H), 3.80 (t, *J*=6.3 Hz, 1H, minor), 3.70 (td, *J*=10.8, 4.1 Hz, 1H, minor), 3.58 (t, *J*=7.7 Hz, 1H), 3.46–3.32 (m, 1H), 2.64–2.39 (m, 2H), 2.36–2.15 (m, 2H), 2.06–1.89 (m, 2H), 1.62–1.45 (m, 2H), 1.35 (s, 6H), 1.23 (br envelope, 8H), 0.84 (br t, *J*=6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 173.4 (Cq, minor), 171.9 (Cq), 138.2 (Cq), 132.8 (Cq, minor), 130.4 (CH), 130.3 (CH, minor), 129.7 (CH, minor), 129.3 (CH, minor), 129.1 (CH), 128.5 (CH, minor), 128.4 (CH), 128.04 (CH, minor), 127.97 (CH), 127.8 (CH),

108.8 (Cq), 108.4 (Cq, minor), 84.4 (CH), 82.1 (CH, minor), 80.4 (CH), 79. 8 (CH), 79.4 (CH, minor), 76.0 (CH, minor), 73.3 (CH), 72.7 (CH_2, minor), 72.5 (CH_2), 35.3 (CH_2, minor), 34.3 (CH_2), 31.7 (CH_2), 31.6 (CH_2, minor), 31.0 (CH_2, minor), 30.9 (CH_2), 30.6 (CH_2, minor), 30.0 (CH_2), 29.4 (CH_2), 29.1 (CH_2, minor), 27.1 (CH_3), 27.0 (CH_3, minor), 26.9 (CH_3), 25.6 (CH_2), 25.3 (CH_2), 24.5 (CH_2, minor), 22.6 (CH_2), 14.1 (CH_3); HRMS M^++Na found 453.2620; $C_{20}H_{29}NO_5$+Na requires 453.2617.

4.6. (3a*S*,8*R*,11a*S*,*Z*)-8-((*R*)-1-(Benzyloxy)heptyl)-2,2-dimethyl-4,5,8,9-tetrahydro-3a*H*-[1,3]dioxolo[4,5-*e*]oxecin-6(11a*H*)-one (23a)

Z-Lactone **23a** (0.019 g) 26% yield. R_f 0.3 (petroleum ether/EtOAc 7:3); $[\alpha]_D^{24}$ −3.1 (*c* 1.6, $CHCl_3$); lit.[3l] $[\alpha]_D^{24}$ +4.5 (*c* 1.6, $CHCl_3$) for the enantiomer; IR (neat) 2930, 2860, 1734, 1241, 1056, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.21 (m, 5H), 5.73 (dt, *J*=10.2, 6.6, Hz, 1H), 5.49 (t, *J*=10.2 Hz, 1H), 5.09 (dt, *J*=11.9, 1.8 Hz, 1H), 4.64, 4.57 (ABq, *J*=11.6 Hz, 2H), 4.64–4.43 (m, 1H), 3.65 (t, *J*=8.5 Hz, 1H), 3.48 (dt, *J*=8.9, 4.7 Hz, 1H), 2.77–2.54 (m, 2H), 2.42–1.95 (m,4H), 1.58–1.37 (m, 3H), 1.42 (s, 3H), 1.39 (s, 3H), 1.36–1.22 (br m, 7H), 0.88 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.8 (Cq), 138.3 (Cq), 130.8 (CH), 130.4 (CH), 128.4 (CH), 127.7 (2×CH), 107.6 (Cq), 81.5 (CH), 79.6 (CH), 77.0 (CH), 72.8 (CH), 72.6 (CH_2), 32.1 (CH_2), 31.7 (CH_2), 30.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.2 (CH_2), 27.0 (CH_3), 26.9 (CH_3), 25.4 (CH_2), 22.6 (CH_2), 14.1 (CH_3); HRMS M^++Na found 453.2610; $C_{20}H_{29}NO_5$+Na requires 453.2617.

4.7. Microcarpalide (+)-1

To a pre-cooled (0 °C) solution of **23** (0.037 g, 0.086 mmol) in CH_2Cl_2 (1 mL) was added $TiCl_4$ (0.28 mL, 0.25 mmol, 0.9 M solution in CH_2Cl_2). Reaction mixture was stirred at same temperature for 2 h. After the reaction is complete (TLC), cold water (1 mL) was added and it was filtered through a short pad of Celite and Celite pad was washed with ethylacetate (5 mL). Filtrate was washed with satd $NaHCO_3$ (5 mL) and the aqueous layer was extracted with EtOAc (2×5 mL). Combined EtOAc layer was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by purification of the resulting residue by column chromatography furnished (+)-**1** (0.016 g) in 62% yield as a colorless oil. R_f 0.5 EtOAc; $[\alpha]_D^{24}$ +26.3 (*c* 0.65, MeOH); lit.[3l] $[\alpha]_D^{24}$ −22.0 (*c* 0.67, MeOH) for enantiomer; lit.[3m] $[\alpha]_D^{24}$ −27.28 (*c* 0.83, MeOH) for the enantiomer; IR (neat) 3417, 2928, 2857, 1713, 1436, 1224, 1156, 1064, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$; mixture of conformers) δ 5.70 (dd, *J*=15.8, 2.1 Hz, 1H, H-6), 5.72–5.60 (m, 1H, H-7, minor), 5.50 (dddd, *J*=15.5, 10.0, 5.1, 1.9 Hz, 1H, H-7), 5.06 (dd, *J*=15.5, 9.2 Hz, 1H, H-6, minor), 4.82 (dt, *J*=11.3, 4.5 Hz, 1H, H-9), 4.61 (ddd, *J*=8.0, 4.3, 2.6 Hz, 1H, H-9, minor), 4.11 (br m, 1H, H-5), 3.78 (br m, 1H, H-4), 3.64–3.57 (m, 1H, H-5, minor), 3.55 (br m, 1H, H-10), 3.37–3.28 (m, 1H, H-4, minor), 3.13 (d, *J*=3.8 Hz, 1H, 4-OH), 2.90 (d, *J*=6.5 Hz, 1H, 5-OH, minor), 2.87 (d, *J*=5.3 Hz, 2H, 5, 10-OH), 2.57–2.50 (br m, 2H, H-2, minor), 2.52–2.42 (br m, 1H, H-2), 2.32–2.24 (br m, 1H, H-8), 2.32–2.24 (br m, 1H, H-8, minor), 2.20–2.05 (br m, 3H, H-2, 3, 8), 2.20–2.05 (br m, 1H, H-2, minor), 2.01–1.93 (br m, 1H, H-3, minor), 1.77 (br ddd, 1H, H-3), 1.76–1.72 (m, 1H, H-3, minor), 1.45–1.38 (br m, 2H, H-11), 1.45–1.38 (br m, 2H, H-11, minor), 1.36–1.20 (br envelope, 8H, H-12, 13, 14, 15), 1.36–1.20 (br envelope, 8H, H-12, 13, 14, 15, minor), 0.88 (t, *J*=6.8 Hz, 3H, H-16); ^{13}C NMR (100 MHz, $CDCl_3$) 176.3 (Cq-1), 173.5 (Cq-1, minor), 134.5 (CH-6), 133.7 (CH-6, minor), 129.9 (CH-7, minor), 126.6 (CH-7), 79.6 (CH-9), 79.5 (CH-5, minor), 76.9 (CH-4, minor), 76.4 (CH-9, minor), 73.7 (CH-10, minor), 73.3 (CH-4), 72.8 (CH-10), 72.4 (CH-5), 36.6 (CH_2-8), 35.9 (CH_2-2, minor), 34.1 (CH_2-11), 33.8 (CH_2-11, minor), 32.5 (CH_2-14), 32.2 (CH_2-14, minor), 32.1 (CH_2-8, minor), 29.9 (CH_2-13), 29.0 (CH_2-2), 26.4 (CH_2-3), 26.1 (CH_2-12), 23.3 (CH_2-15), 14.3 (CH_3-16); HRMS M^++Na found 323.1835; $C_{20}H_{29}NO_5$+Na requires 323.1834.

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