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Enantioselective total synthesis of *iso*-cladospolide B, cladospolide C and cladospolide B from tartaric acid

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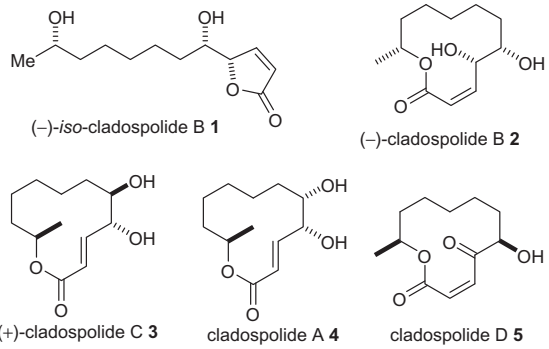
ABSTRACT

The enantioselective synthesis of the natural products cladospolide B, cladospolide C, and *iso*-cladospolide B has been accomplished from tartaric acid. Key reactions in the synthetic sequence include the elaboration of a γ-hydroxy amide derived from tartaric acid via alkene cross metathesis, Yamaguchi lactonization, and ring closing metathesis.

1. Introduction

Cladospolides A–D **1**–**5** are 12-membered lactones isolated from the fermented broth of cultures derived either from marine fungi or from soil fungus.[1] One of the exceptions to this macrolactone class is *iso*-cladospolide B **1**, isolated from Red Sea sponge *Cladosporium* sp. and also from fermentation of the marine fungal species I96S215 which is a butenolide.[2] A few syntheses of individual cladospolides[3] either from chiral pool precursors or by asymmetric synthesis are reported in the literature. Herein, we report our efforts in the synthesis of cladospolides B, C, and *iso*-cladospolide B from D-tartaric acid.



(–)-*iso*-cladospolide B **1**

(–)-cladospolide B **2**

(+)-cladospolide C **3**

cladospolide A **4**

cladospolide D **5**

2. Results and discussion

Our approach for the synthesis of cladospolides **1**–**3** is based on the elaboration of the aldehyde obtained from ozonolysis of the olefin in **6**, with selective *E*- or *Z*-Wittig olefination and subsequent lactonization leading to the title compounds. Allylic alcohol **6** can be obtained from iodide **7** involving a Boord type fragmentation. Elaboration of the γ-hydroxy amide **8** via cross metathesis with penten-2-ol was used for the synthesis of **7**. The synthesis of γ-hydroxy amide **8** from the *bis*-Weinreb amide of tartaric acid **9** is a procedure already well established in our laboratory[5] (Scheme 1).

2.1. Synthesis of (−)-*iso*-cladspolide B 1

At first, γ-hydroxyamide **8** was synthesized from the bis-Weinreb amide **9** as described earlier[6] involving a controlled Grignard reagent addition followed by a stereoselective reduction. The secondary hydroxy group in **8** was transformed into the silyl ether **10** involving standard reaction conditions. Olefin cross-metathesis of **10** with (*S*)-and (*R*)-penten-2-ol in the presence of Grubb's second generation catalyst afforded the cross-metathesis product **11a** and **11b** in 69% and 64% yield, respectively.[7] Protection of the free hydroxy group in **11a** and **11b** as the TBS ether followed by hydrogenation afforded the saturated amide **12a** and **12b** in almost quantitative yield. Reaction of the amide **12a** and **12b** with $NaBH_4$ resulted in the primary alcohol, which was transformed into the iodide **13a** and **13b** in good yield. Treatment of the iodide **13a** and **13b** with zinc dust in refluxing ethanol furnished the pivotal allylic alcohol **14a** and **14b** in 99% yield (Scheme 2).[8] Allylic alcohols **14a** and **14b** served as the precursor for the synthesis of (−)-*iso*-caldospolide B **1** and (−)-cladospolide C *ent*-**3**.

Thus, the reaction of **14a** with acryloyl chloride in the presence of Et_3N yielded acryloyl ester **15** in 62% yield. Exposure of **15** to Grubbs' second generation catalyst in toluene produced butenolide **16** in 86% yield. Treatment of **16** with methanolic HCl cleanly furnished (−)-*iso*-cladospolide B **1** in 79% yield (Scheme 3).

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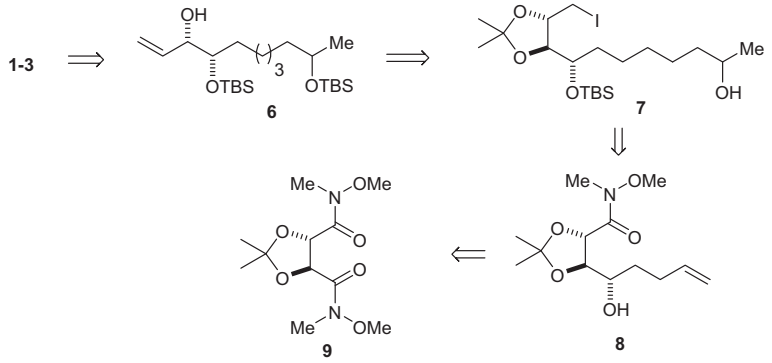
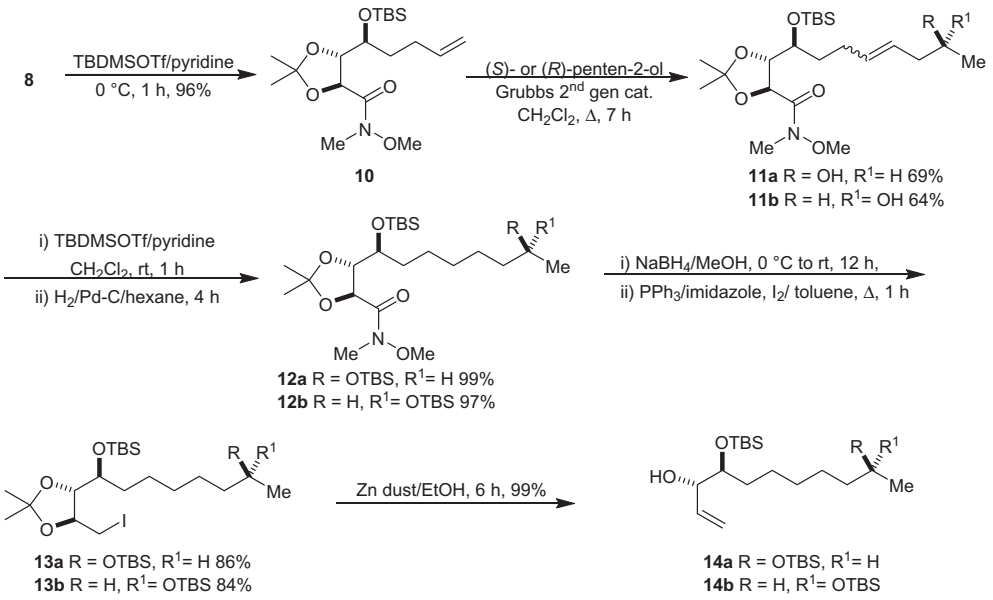
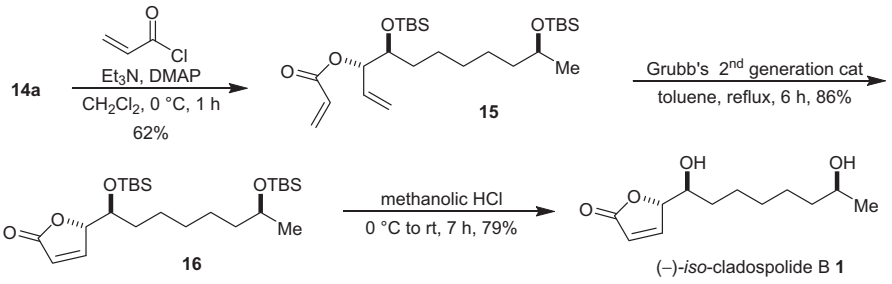


Scheme 1. Retrosynthesis for the synthesis of cladospolides **1**–**3**.



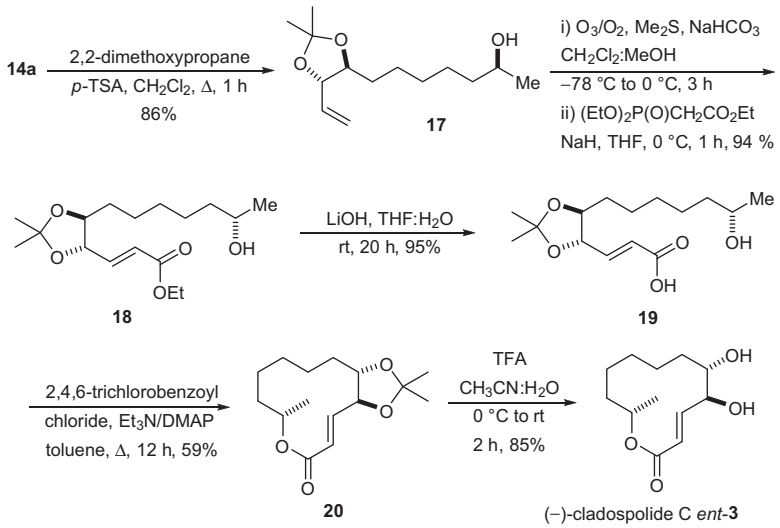
Scheme 2. Synthesis of key allylic alcohol unit **14a** and **14b**.



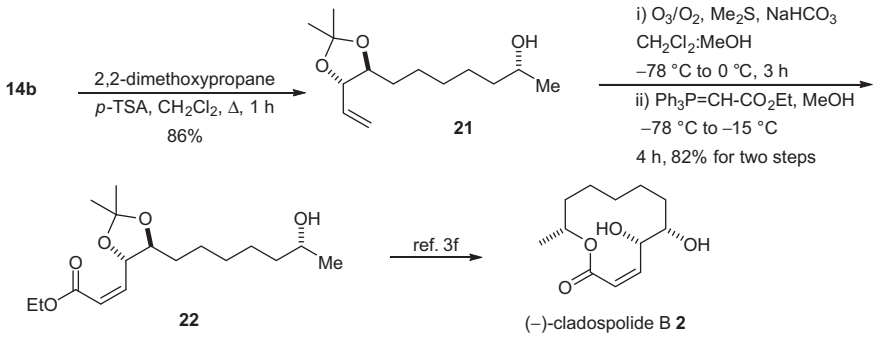
Scheme 3. Total synthesis of (−)-*iso*-cladospolide B **1**.

2.2. Synthesis of (−)-cladospolide C *ent*-3

For the synthesis of (−)-cladospolide C *ent*-**3**, allylic alcohol **14a** was reacted with 2,2-dimethoxy propane in the presence of *p*-TSA resulting in deprotection of the bis-silyl ether with the concomitant protection of the vicinal diol to yield acetonide **17** in 86% yield. Ozonolysis of the olefin in **17** furnished the aldehyde, which upon Wittig reaction with triethyl phosphonoacetate afforded the *E*-ester **18** in 94% yield. Saponification of **18** with LiOH provided the hydroxy acid **19** in 95% yield. Macrolactonization under Yamaguchi lactonization conditions smoothly furnished lactone **20** in 59% yield. Deprotection of the acetonide in **20** afforded (−)-cladospolide C *ent*-**3** in 85% yield; the spectroscopic data are in complete agreement with those reported in the literature (Scheme 4).[4c]



Scheme 4. Total synthesis of (−)-cladospolide C *ent*-**3**.



Scheme 5. Formal total synthesis of (−)-cladospolide B **2**.

2.3. Synthesis of (−)-cladospolide B 2

For the synthesis of (−)-cladospolide B **2**, alcohol **14b** was treated with 2,2-dimethoxy propane in the presence of *p*-TSA to furnish acetonide **21** in 86% yield. Ozonolysis of the olefin in **21** gave an aldehyde, which was subjected to a Wittig reaction to yield the *Z*-ester **22** as the major product in 82% yield.[9] Since the conversion of **22** to (−)-cladospolide B **2** is already reported in the literature,[3f] the present sequence constitutes a formal total synthesis of cladospolide B **2** (Scheme 5).

3. Conclusion

In conclusion, an enantiodivergent total synthesis of *iso*-cladospolide B and cladospolide C and a formal approach to the total synthesis of cladospolide B from D-tartaric acid have been reported. Key reactions en route to the target compounds include olefin cross metathesis, Yamaguchi lactonization, and ring closing metathesis.

4. Experimental

4.1. General

Column chromatography was performed on silica gel, Acme grade 100–200 mesh. TLC plates were visualized either with UV in an iodine chamber, or with phosphomolybdic acid spray, unless noted otherwise. Unless stated otherwise, all reagents were purchased from commercial sources and used without additional purification. THF was freshly distilled over Na-benzophenone ketyl. Melting points are uncorrected. Unless stated otherwise, all the reactions were performed under an inert atmosphere. Unless stated otherwise, all NMR spectra were recorded in $CDCl_3$.

4.2. Preparation of (4*S*,5*S*)-*N*-methoxy-5-((*S*)-1-(*tert*-butyldimethyl-silanyloxy)pent-4-enyl)-*N*,2,2-trimethyl-1,3-dioxolane-4-carboxamide 10

To a stirred ice-cooled solution of **8** (1 g, 3.7 mmol) in dry dichloromethane (10 mL) was added pyridine (0.6 mL, 7.4 mmol) at 0 °C. After 10 min, TBDMSOTf (1 mL, 4.4 mmol) was introduced dropwise to the reaction mixture at 0 °C. The progress of the reaction was monitored by TLC and after the reaction was complete (~1 h), it was poured into ice-cooled water (10 mL) and extracted with EtOAc (2 × 20 mL). The combined EtOAc extracts were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of the solvent and silica gel column chromatography of the residue using petroleum ether/EtOAc (4:1) as an eluent yielded **10** (1.38 g, 96%) as a colorless oil. $[\alpha]_D$ = +9.1 (*c* 0.8, $CHCl_3$). IR (neat) 2955, 1674, 1457, 1257, 776 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.81 (ddt, *J* = 16.8, 10.3, 6.5 Hz, 1H), 5.02 (d, *J* = 17.0 Hz, 1H), 4.95 (d, *J* = 10.2 Hz, 1H), 4.72 (s, 1H), 4.57 (s, 1H), 3.84 (dt, *J* = 9.0, 4.8 Hz, 1H), 3.75 (s, 3H), 3.21 (s, 3H), 2.26–1.76 (m, 2H), 1.75–1.46 (m, 2H), 1.45 (s, 3H), 1.43 (s, 3H), 0.87 (s, 9H), 0.07(s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4 (Cq), 138.4 (CH), 114.6 (CH_2), 111.0 (Cq), 80.0 (CH), 72.3 (CH), 71.5 (CH), 61.8 (CH_3), 32.2 (CH_3), 32.0 (CH_2), 29.8 (CH_2), 27.0 (CH_3), 26.2 (CH_3), 25.8 (CH_3, 3C), 18.1 (Cq), −4.48 (CH_3), −4.54 (CH_3). HRMS: *m*/*z* for $C_{19}H_{37}NO_5Si$+Na, calcd: 410.2339; found: 410.2333.

4.3. Preparation of (4*S*,5*S*)-5-((1*S*,7*S*)-7-hydroxy-1-(*tert*-butyldimethyl-silanyloxy)oct-4-enyl)-*N*-methoxy-*N*,2,2-trimethyl-1,3-dioxolane-4-carboxamide 11a

To a solution of **10** (0.5 g, 1.28 mmol) and (*S*)-(+)-4-penten-2-ol (0.17 g, 1.93 mmol) in dry CH_2Cl_2 (128 mL) was added Grubbs' 2nd generation catalyst (0.06 g, 0.07 mmol) under a nitrogen atmosphere. The reaction mixture was refluxed for 7 h under a nitrogen atmosphere. Evaporation of the solvent and purification of the resulting residue by silica gel column chromatography using petroleum ether/EtOAc (6:4) as eluent afforded **11a** (0.4 g, 69%) as a light brown oil. $[\alpha]_D$ = +10.3 (*c* 1.8, $CHCl_3$); IR (neat) 3464, 2956, 1671, 1473, 837 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) for a mixture of *E*/*Z* isomers: δ 5.54 (td, *J* = 15.5, 6.4 Hz, 1H), 5.47 (td, *J* = 12.5, 6.1 Hz, 1H), 4.71 (s, 1H), 4.56 (s, 1H), 3.87–3.76 (m, 2H), 3.75 (s, 3H), 3.21 (s, 3H), 2.35–1.89 (m, 4H), 1.85 (br s, 1H), 1.75–1.51 (m, 2H), 1.43 (s, 3H), 1.42 (s, 3H), 1.18 (d, *J* = 6.2 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) for a mixture of *E*/*Z* isomers: δ 170.4 (Cq), 133.8 (CH), 132.4 (CH), 126.6 (CH), 125.7 (CH), 111.0 (Cq), 79.8 (CH), 72.4 (CH), 71.4 (CH), 67.6 (CH), 67.1 (CH), 61.9 (CH), 42.6 (CH_2), 37.1 (CH_2), 32.6 (CH_2), 32.3 (CH_3), 28.9 (CH_3), 27.0 (CH_3), 26.2 (CH_3), 25.8 (3C, CH_3), 23.7 (CH_2), 22.7 (CH_3), 18.1 (Cq), −4.5 (CH_3, 2C). HRMS: *m*/*z* for $C_{22}H_{43}NO_6Si$+Na, calcd: 468.2757; found: 468.2754.

Performing the reaction with (*R*)-pentene-2-ol furnished **11b** in 64% yield: $[\alpha]_D$ = +4.2 (*c* 3.5, $CHCl_3$). IR (neat): ν_{max} 3403, 2931, 1665, 1256, 776 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.75–5.25 (m, 2H), 4.76 (s, 1H), 4.62 (s, 1H), 3.98–3.62 (m, 5H), 3.26 (s, 3H), 2.49–2.15 (m, 4H), 1.91 (br s, 1H), 1.79–1.35 (m, 8H), 1.23 (d, *J* = 6.2 Hz, 3H), 0.92 (s, 9H), 0.10 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5 (Cq), 133.8 (CH), 126.6 (CH), 111.0 (Cq), 79.9 (CH), 72.4 (CH), 71.5 (CH), 67.3 (CH), 62.0 (CH_3), 42.6 (CH_2), 32.6 (CH_2), 32.3 (CH_3), 28.9 (CH_2), 27.1 (CH_3), 26.3 (CH_3), 25.9 (CH_3, 3C), 22.7 (CH_3), 18.2 (Cq), −4.4 (CH_3, 2C). HRMS: *m*/*z* for $C_{22}H_{43}NO_6Si$+Na, calcd 468.2757; found 468.2735.

4.4. Preparation of (4*S*,5*S*)-5-((1*S*,7*S*)-1,7-bis(*tert*-butyldimethyl-silanyloxy)octyl)-*N*-methoxy-*N*,2,2-trimethyl-1,3-dioxolane-4-carboxamide 12a

To a pre-cooled solution of **11a** (0.35 g, 0.78 mmol) in dry CH_2Cl_2 (5 mL) was added pyridine (0.13 mL, 1.6 mmol) at 0 °C. After 10 min, TBDMSOTf (0.21 mL, 0.94 mmol) was introduced dropwise to the reaction mixture at 0 °C. The progress of the reaction was monitored by TLC and after the reaction was complete (~1 h), it was poured into ice-cold water (10 mL) and extracted with EtOAc (2 × 10 mL). The combined EtOAc extracts were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of the solvent and silica gel column chromatography of the resulting residue using petroleum ether/EtOAc (9:1) as eluent yielded TBDMS ether (0.41 g, 93%) as a colorless oil.

To a solution of the TBDMS ether (0.35 g, 0.62 mmol) (obtained above) in hexane (4 mL) was added 10% palladium on activated charcoal (60 mg) under an argon atmosphere. The reaction mixture was stirred for 4 h under a hydrogen atmosphere. It was then filtered through a short pad of Celite and the Celite pad was washed with ether (10 mL). Evaporation of the solvent followed by silica gel column chromatography of the residue using petroleum ether/EtOAc (9:1) as eluent furnished **12a** (0.35 g, 99%) as a colorless oil. $[\alpha]_D$ = +9.6 (*c* 1.8, $CHCl_3$); IR (neat) 2928, 2856, 1677, 1463, 775 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 4.73 (s, 1H), 4.56 (s, 1H), 3.92–3.65 (m, 5H), 3.22 (s, 3H), 1.65–1.16 (m, 16H), 1.11 (d, *J* = 6.0 Hz, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.07 (s, 6H), 0.05 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4 (Cq), 110.9 (Cq), 80.1 (CH), 72.3 (CH), 72.1 (CH), 68.5 (CH), 61.7 (CH_3), 39.6 (CH_2), 32.7 (CH_2), 32.2 (CH_3), 29.8 (CH_2), 29.7 (CH_2), 26.9 (CH_3), 26.1 (CH_3), 25.8 (CH_3, 3C), 25.7 (CH_3, 3C), 25.6 (CH_2), 23.7 (CH_3), 18.0 (Cq, 2C), −4.5 (CH_3), −4.6 (CH_3, 2C), −4.8(CH_3). HRMS: *m*/*z* for $C_{28}H_{59}NO_6Si_2$+Na calcd: 584.3779; found: 584.3770.

Performing the reaction with **11b** yielded **12b** in 97% yield: $[\alpha]_D$ = +3.7 (*c* 1.8, $CHCl_3$). IR (neat) 2930, 1676, 1380, 1072, 775 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.74–5.26 (m, 2H), 4.78 (s, 1H), 4.63 (s, 1H), 4.15–3.55 (m, 5H), 3.27 (s, 3H), 2.62–1.81 (m, 4H), 1.77–1.55 (m, 2H), 1.51 (s, 3H), 1.49 (s, 3H), 1.17 (d, *J* = 6.0 Hz, 3H), 0.94 (s, 9H), 0.93 (s, 9H), 0.11 (s, 6H), 0.10 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5 (Cq), 131.9 (CH), 127.3 (CH), 111.0 (Cq), 80.1 (CH), 72.3 (CH), 71.7 (CH), 68.8 (CH), 61.8 (CH_3), 43.0 (CH_2), 37.5 (CH_2), 32.6 (CH_2), 32.3 (CH_3), 28.8 (CH_2), 27.0 (CH_3), 26.2 (CH_3), 25.8 (CH_3, 6C), 23.4 (CH_3), 18.1 (Cq, 2C), −4.5 (CH_3, 2C), −4.7 (CH_3, 2C). HRMS: *m*/*z* for $C_{28}H_{57}NO_6Si_2$+Na, calcd: 584.3779; found: 584.3774.

4.5. Preparation of (4*R*,5*S*)-4-((1*S*,7*S*)-1,7-bis(*tert*-butyldimethyl-silanyloxy)octyl)-5-(iodomethyl)-2,2-dimethyl-1,3-dioxolane 13a

In a single necked round bottomed flask equipped with a magnetic stirrer bar and a guard tube was placed a solution of amide **12a** (0.32 g, 0.56 mmol) in MeOH (6 mL). Next, $NaBH_4$ (0.11 g, 3 mmol) was introduced into the reaction mixture portion wise at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred overnight at the same temperature. After the reaction was complete (TLC), most of the methanol was removed under reduced pressure; water (10 mL) was added to the reaction mixture and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (5 mL), and dried over Na_2SO_4. Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (9:1) as eluent gave the alcohol (0.28 g, 96%) as a colorless oil. $[\alpha]_D$ = −4.3 (*c* 1.9, $CHCl_3$); IR (neat) 3477, 2933, 1464, 1254, 835, 775 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 4.22–3.99 (m, 1H), 3.97–3.59 (m, 5H), 2.55–2.38 (m, 1H), 1.76–1.25 (m, 16H), 1.17 (d, *J* = 6.0 Hz, 3H), 0.97 (s, 9H), 0.95 (s, 9H), 0.14 (s, 6H), 0.11 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.6 (Cq), 80.7 (CH), 77.0 (CH), 72.0 (CH), 68.6 (CH), 62.9 (CH_2), 39.7 (CH_2), 32.5 (CH_2), 29.8 (CH_2), 27.1 (CH_3), 27.0 (CH_3), 26.2 (CH_2), 25.9 (CH_3, 6C), 25.7 (CH_2), 23.8 (CH_3), 18.2 (Cq), −4.2 (CH_3), −4.4 (CH_3), −4.7 (CH_3), −4.7 (CH_3). HRMS: *m*/*z* for $C_{26}H_{56}O_5Si_2$+Na calcd: 527.3564; found: 527.3563.

To a solution of the alcohol obtained above (0.25 g, 0.49 mmol) in dry toluene (6 mL) were added PPh_3 (0.39 g, 1.47 mmol), imidazole (0.1 g, 1.47 mmol), and iodine (0.19 g, 0.74 mmol), under an argon atmosphere at room temperature. The reaction mixture was then stirred at reflux for 1 h. After the reaction was complete (TLC), it was cooled to room temperature and poured into water (10 mL) and extracted with ether (3 × 10 mL). The combined ether layers were washed with brine (5 mL), a saturated solution of sodium thiosulfate (5 mL), water (5 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/ether (95:5) as eluent afforded **13a** (0.25 g, 84%) as a colorless oil. $[\alpha]_D$ = +10.3 (*c* 0.6, $CHCl_3$). IR (neat): ν_{max} 2929, 1471, 1254, 1067, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.98–3.87 (m, 1H), 3.85–3.63 (m, 3H), 3.42 (dd, *J* = 10.6, 4.2 Hz, 1H), 3.25 (dd, *J* = 10.6, 5.8 Hz, 1H), 1.74–1.56 (m, 2H), 1.54–1.22 (m, 14H), 1.11 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.05 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 109.2 (Cq), 82.9 (CH), 75.7 (CH), 71.9 (CH), 68.6 (CH), 39.7 (CH_2), 33.0 (CH_2), 29.8 (CH_2), 27.6 (CH_3), 27.3 (CH_3), 26.0 (CH_2), 25.93 (CH_3, 3C), 25.92 (CH_3, 3C), 25.7 (CH_2), 23.8 (CH_3), 18.2 (Cq), 18.1 (Cq, 2C), 7.7 (CH_2), −4.0 (CH_3), −4.4 (CH_3), −4.6 (CH_3), −4.7 (CH_3). HRMS: *m*/*z* for $C_{26}H_{55}IO_4Si_2$+Na, calcd: 637.2581; found: 637.2580.

Performing the reaction with **12b** afforded **13b** in 86% yield. $[\alpha]_D = -11.6$ (*c* 1.3, $CHCl_3$). IR (neat): 2954, 1372, 1255, 1067, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.90 (dd, *J* = 11.6, 5.8 Hz, 1H), 3.84–3.65 (m, 3H), 3.42 (dd, *J* = 10.6, 4.2 Hz, 1H), 3.26 (dd, *J* = 10.6, 5.8 Hz, 1H), 1.74–1.51 (m, 2H), 1.49–1.16 (m, 14H), 1.11 (d, *J* = 6.0 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.05 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 109.1 (Cq), 82.9 (CH), 75.6 (CH), 71.8 (CH), 68.6 (CH), 39.6 (CH_2), 32.9 (CH_2), 29.8 (CH_2), 27.6 (CH_3), 27.3 (CH_3), 25.9 (CH_3, 6C), 25.7 (CH_2), 23.8 (CH_3), 18.1 (Cq, 2C), 7.7 (CH_2), −4.0 (CH_3), −4.4 (CH_3), −4.6 (CH_3), −4.7 (CH_3). HRMS: *m*/*z* for $C_{26}H_{55}IO_4Si_2$+Na, calcd: 637.2581; found: 637.2587.

4.6. Preparation of (3*S*,4*S*,10*S*)-4,10-bis(*tert*-butyl-dimethylsilanyloxy)undec-1-en-3-ol 14a

To a solution of the iodide **13a** (0.22 g, 0.35 mmol) in absolute ethanol was added activated zinc dust (0.19 g, 2.9 mmol) (6 mL) at room temperature and stirred at reflux. The progress of the reaction was followed by TLC. After completion of the reaction (~1 h), it was filtered through a short pad of Celite and the Celite pad was washed with ether (2 × 10 mL). Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (9:1) as eluent furnished **14a** (0.16 g, 100%) as a colorless oil. $[\alpha]_D = +2.5$ (*c* 1.2, $CHCl_3$). IR (neat): ν_{max} 3473, 2931, 1463, 1255, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.90 (ddd, *J* = 16.8, 10.5, 5.7 Hz, 1H), 5.37 (d, *J* = 17.4 Hz, 1H), 5.24 (d, *J* = 10.5 Hz, 1H), 4.12–3.91 (m, 1H), 3.89–3.65 (m, 1H), 3.63 (dd, *J* = 10.8, 5.0 Hz, 1H), 2.40 (d, *J* = 6.2 Hz, 1H), 1.65–1.27 (m, 10H), 1.17 (d, *J* = 6.0 Hz, 3H), 0.97 (s, 9H), 0.95 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.9 (CH), 116.2 (CH_2), 75.6 (CH), 74.5 (CH), 68.8 (CH), 39.9 (CH_2), 33.9 (CH_2), 30.2 (CH_2), 26.2 (CH_3, 3C), 26.1 (CH_3, 3C), 26.0 (CH_2), 25.3 (CH_2), 24.1 (CH_3), 18.2 (Cq, 2C) −4.0 (CH_3), −4.2 (CH_3), −4.3 (CH_3), −4.5 (CH_3). HRMS: *m*/*z* for $C_{23}H_{50}O_3Si_2$+Na, calcd: 453.3196; found: 453.3193.

Performing the reaction with **13b** afforded **14b** in 99% yield. $[\alpha]_D = -10.4$ (*c* 1.8, $CHCl_3$). IR (neat) 3462, 2898, 1472, 1067, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.84 (ddd, *J* = 16.5, 10.5, 5.7 Hz, 1H), 5.31 (d, *J* = 17.2 Hz, 1H), 5.17 (d, *J* = 10.5 Hz, 1H), 4.05–3.87 (m, 1H), 3.82–3.73 (m, 1H), 3.57 (dd, *J* = 10.5, 4.6 Hz, 1H), 2.35 (d, *J* = 6.0 Hz, 1H), 1.67–1.19 (m, 10H), 1.11 (d, *J* = 6.0 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.04 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6 (CH), 115.9 (CH_2), 75.3 (CH), 74.2 (CH), 68.5 (CH), 39.6 (CH_2), 33.6 (CH_2), 29.9 (CH_2), 25.9 (CH_3, 6C), 25.7 (CH_2), 25.0 (CH_2), 23.8 (CH_3), 18.1 (Cq, 2C), −4.3 (CH_3), −4.4 (CH_3), −4.5 (CH_3), −4.8 (CH_3). HRMS: *m*/*z* for $C_{23}H_{50}O_3Si_2$+Na, calcd: 453.3196; found: 453.3193.

4.7. Preparation of (3*S*,4*S*,10*S*)-4,10-bis(*tert*-butyl-dimethylsilanyloxy)undec-1-en-3-yl acrylate 15

To an ice-cold solution of **14a** (0.10 g, 0.23 mmol) in CH_2Cl_2 (4 mL) was added DMAP (0.03 g, 0.23 mmol) and Et_3N (0.1 mL, 0.69 mmol) and stirred for 15 min at 0 °C. Acryloyl chloride (0.06 mL, 0.69 mmol) was introduced into the reaction mixture dropwise at 0 °C and stirred at the same temperature for 0.5 h. After the reaction was complete (TLC), it was poured into water (5 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with saturated sodium bicarbonate solution (5 mL), brine (5 mL) and dried (Na_2SO_4). Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/ether (95:5) as eluent resulted in the acryloyl ester **15** (0.07 g, 62%) as a colorless oil. $[\alpha]_D = -16.3$ (*c* 0.8, $CHCl_3$). IR (neat): ν_{max} 3080, 2932, 1728, 1529, 1273, 720 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 6.39 (d, *J* = 17.4 Hz, 1H), 6.11 (dd, *J* = 17.1 Hz, 10.2 Hz, 1H), 5.96–5.72 (m, 2H), 5.41–5.10 (m, 3H), 3.85–3.61 (m, 2H), 1.49–1.13 (m, 10H), 1.10 (d, *J* = 6.0 Hz, 3H), 0.84 (s, 18H), 0.05 (s, 3H), 0.03 (s, 3H), 0.00 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2 (Cq), 133.0 (CH), 130.8 (CH), 128.7 (CH_2), 117.6 (CH_2), 77.0 (CH), 72.7 (CH), 68.6 (CH), 39.7 (CH_2), 32.6 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 25.9 (CH_3, 3C), 25.8 (CH_3, 2C), 25.7 (CH_3), 25.0 (CH_2), 23.8 (CH_3), 18.1 (Cq), 18.0 (Cq), −4.4 (CH_3, 2C), −4.6 (CH_3), −4.7 (CH_3). HRMS: *m*/*z* for $C_{26}H_{52}O_4Si_2$+Na, calcd: 507.3302; found: 507.3300.

4.8. Preparation of (*S*)-5-((1*S*,7*S*)-1,7-bis(*tert*-butyl-dimethylsilanyloxy)octyl)furan-2(5*H*)-one 16

To a solution of the acryloyl ester **15** (0.05 g, 0.1 mmol) in 2 mL toluene was added Grubbs' 2nd generation catalyst (0.008 g, 0.01 mmol) in 2 mL of toluene and stirred under reflux for 6 h. It was then cooled to room temperature and most of the toluene was evaporated off. Column chromatography of the resultant residue using petroleum ether/EtOAc (9:1) as eluent afforded **16** in 86% (0.04 g) yield. $[\alpha]_D = -80.7$ (*c* 0.8, $CHCl_3$). IR (neat): ν_{max} 2930, 1789, 1760, 1255, 1074, 774 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.41 (dd, *J* = 5.7, 1.5 Hz, 1H), 6.11 (dd, *J* = 5.7, 2.1 Hz, 1H), 4.94 (td, *J* = 3.6, 1.8 Hz, 1H), 4.05–3.81 (m, 1H), 3.79–3.65 (m, 1H), 1.51–1.24 (m, 10H), 1.10 (d, *J* = 6.0 Hz, 3H), 0.85 (s, 9H), 0.84 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H), 0.00 (s, 3H), −0.01 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.9 (Cq), 154.1 (CH), 122.6 (CH_2), 85.4 (CH), 72.0 (CH), 68.5 (CH), 39.6 (CH_2), 32.4 (CH_2), 29.7 (CH_2), 25.9 (CH_3, 3C), 25.7 (CH_3, 3C), 25.61 (CH_2), 25.55 (CH_2), 23.8 (CH_3), 18.1 (Cq), 18.0 (Cq), −4.4 (CH_3), −4.5 (CH_3), −4.6 (CH_3), −4.7 (CH_3). HRMS: *m*/*z* for $C_{24}H_{48}O_4Si_2$+Na, calcd: 479.2989; found: 479.2983.

4.9. Preparation of (−)-*iso*-cladospolide B 1

To an ice-cold solution of lactone **16** (27 mg, 0.6 mmol) in methanol (1.5 mL) was added methanolic HCl (4 mL) at 0 °C. The reaction mixture was slowly allowed to return to room temperature and stirred at the same temperature. Progress of the reaction was monitored by TLC. After the reaction was complete (~7 h), the solvent was evaporated off. Silica gel column chromatography of the resulting residue using EtOAc as eluent furnished (−)-*iso*-cladospolide B **1** (10 mg, 79%) as a colorless oil. $[\alpha]_D = -63.3$ (*c* 1, MeOH); Lit.[3c] $[\alpha]_D = -61.6$ (*c* 0.5, MeOH). IR (neat): ν_{max} 3402, 2857, 1747, 1600, 1463, 828 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 5.8, 1H), 6.18 (dd, *J* = 6.0, 1.4 Hz, 1H), 5.15–4.91 (m, 1H), 3.87–3.69 (m, 2H), 2.32–1.89 (br s, 2H), 1.75–1.21 (m, 10H), 1.80 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9 (Cq), 153.8 (CH), 122.5 (CH), 86.1 (CH), 71.5 (CH), 67.9 (CH), 39.0 (CH_2), 32.9 (CH_2), 29.2 (CH_2), 25.4 (CH_2), 25.3 (CH_2), 23.4 (CH_3). HRMS: *m*/*z* for $C_{12}H_{20}O_4$+Na, calcd: 251.1259; found 251.1265.

4.10. Preparation of (*S*)-7-((4*S*,5*S*)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)heptan-2-ol 17

To a solution of **14a** (0.2 g, 0.46 mmol) in dry CH_2Cl_2 (4 mL) was added *p*-TSA (0.13 g, 0.7 mmol) and 2,2-dimethoxy propane (0.11 mL, 0.92 mmol) under argon atmosphere and refluxed for 3.5 h. After the reaction was complete (TLC), it was cooled to room temperature. Solid K_2CO_3 (0.09 g) was introduced and stirred for 15 min at room temperature. The reaction mixture was filtered through a short pad of Celite and the Celite pad was washed with EtOAc (2 × 10 mL). Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (6:4) as eluent yielded **17** (0.09 g, 86%) as a pale yellow oil. $[\alpha]_D = +4.6$ (*c* 2.0, $CHCl_3$). IR (neat): ν_{max} 3418, 2861, 1371, 1017, 874 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.79 (ddd,

J = 17.4, 10.2, 7.4 Hz, 1H), 5.35 (d, J = 17.1 Hz, 1H), 5.23 (d, J = 10.2 Hz, 1H), 3.96 (t, J = 8.0 Hz, 1H), 3.77 (dd, J = 11.5, 5.8 Hz, 1H), 3.66 (td, J = 8.2, 6.0 Hz, 1H), 1.73–1.26 (m, 17H), 1.16 (d, J = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.4 (CH), 118.8 (CH), 108.5 (Cq), 82.7 (CH), 80.6 (CH), 68.0 (CH), 39.2 (CH_2), 31.7 (CH_2), 29.6 (CH_2), 27.2 (CH_3), 26.9 (CH_3), 26.0 (CH_2), 25.5 (CH_2), 23.4 (CH_3). HRMS: m/z for $C_{14}H_{26}O_3$+Na, calcd: 265.1780; found: 265.1782.

4.11. Preparation of (*E*)-ethyl 3-((4*S*,5*S*)-5-((*S*)-6-hydroxyheptyl)-2,2-dimethyl-1,3-dioxolan-4-yl)acrylate 18

Ozone was bubbled through a pre cooled (−78 °C) solution of **17** (40 mg, 0.16 mmol) in a mixture of CH_2Cl_2/MeOH (4:1, 5 mL) containing solid $NaHCO_3$ (15 mg) until the pale blue color persisted. Excess ozone was flushed off with oxygen and Me_2S (0.2 mL) was added. The reaction mixture was warmed up to 0 °C and stirred at the same temperature for 3 h. It was then concentrated under reduced pressure and filtered through a short pad of Celite and the Celite pad was washed with EtOAc (10 mL). Evaporation of the solvent yielded the crude aldehyde, which was subjected to the next reaction without further purification.

To an ice cold suspension of NaH (16 mg, 0.41 mmol) in THF (1 mL) was added triethyl phosphonoacetate (0.08 mL, 0.41 mmol) in THF (2 mL) dropwise at 0 °C and stirred for 0.5 h at the same temperature. The solution of the crude aldehyde (50 mg, 0.16 mmol) (obtained above) in THF (2 mL) was slowly introduced at 0 °C and the reaction mixture was stirred for 0.5 h at the same temperature. After completion of the reaction, it was quenched with saturated NH_4Cl (5 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine (5 mL), and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (6:4) as eluent afforded **18** (0.46 mg, 94%) as a colorless oil. $[\alpha]_D$ = −7.1 (c 1.2, CH_2Cl_2). IR (neat): ν_{max} 3437, 2984, 1722, 1371, 1036 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.83 (dd, J = 15.6, 5.8 Hz, 1H), 6.08 (d, J = 15.6 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 4.14–4.06 (m, 1H), 3.88–3.55 (m, 2H), 1.76–1.64 (m, 4H), 1.50–1.20 (m, 16H), 1.15 (d, J = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9 (Cq), 144.0 (CH), 122.6 (CH), 109.3 (Cq), 80.5 (CH), 80.1 (CH), 67.9 (CH), 60.5 (CH_2), 39.1 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 27.2 (CH_3), 26.5 (CH_3), 25.8 (CH_2), 25.4 (CH_2), 23.4 (CH_3), 14.1 (CH_3). HRMS: m/z for $C_{17}H_{30}O_5$+Na, calcd: 337.1991; found: 337.1992.

4.12. Preparation of (*E*)-3-((4*S*,5*S*)-5-((*S*)-6-hydroxyheptyl)-2,2-dimethyl-1,3-dioxolan-4-yl) acrylic acid 19

To a solution of the hydroxy ester **18** (0.08 g, 0.25 mmol) in THF/H_2O (4:1, 4 mL) was added LiOH (0.05 g, 1.3 mmol) at room temperature and stirred for 20 h at the same temperature. The progress of the reaction was monitored by TLC and after reaction was complete, it was diluted with water (5 mL), neutralized with dil HCl (pH 3) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (5 mL), and dried (Na_2SO_4). Most of the solvent was removed under reduced pressure and silica gel column chromatography of the resulting residue using EtOAc as eluent afforded **19** (0.07 g, 95%) as a colorless oil. $[\alpha]_D$ = −14.8 (c 1.1, $CHCl_3$). IR (neat) 3437, 2934, 1704, 1373, 980 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93 (dd, J = 15.5, 5.6 Hz, 1H), 6.12 (d, J = 15.5 Hz, 1H), 5.61 (br s, 2H), 4.20–4.02 (m, 1H), 3.95–3.55 (m, 2H), 1.74–1.26 (m, 16H), 1.17 (d, J = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1 (Cq), 146.2 (CH), 122.1 (CH), 109.5 (Cq), 80.5 (CH), 80.1 (CH), 68.2 (CH), 38.9 (CH_2), 31.9 (CH_2), 29.5 (CH_2), 27.2 (CH_3), 26.6 (CH_3), 25.8 (CH_2), 25.4 (CH_2), 23.2 (CH_3). HRMS: m/z for $C_{15}H_{26}O_5$+Na, calcd: 309.1678; found: 309.1677.

4.13. Preparation of (3a*S*,8*S*,13a*S*,*E*)-2,2,8-trimethyl-9,10,11,12,13,13a-hexahydro-3a*H*-[1,3]dioxolo[4,5-*e*][1]oxacyclododecin-6(8*H*)-one 20

To a solution of acid **19** (52 mg, 0.18 mmol) and Et_3N (0.03 mL, 0.22 mmol) in dry THF (0.9 mL) was added 2,4,6-trichlorobenzoyl chloride (0.03 mL, 0.2 mmol) dropwise under an argon atmosphere at room temperature. The reaction mixture was stirred at room temperature for 2 h, followed by dilution with dry toluene (22 mL) and was then added dropwise to a refluxing solution of DMAP (710 mg, 5.8 mmol) in dry toluene (54 mL). After the addition, the mixture was refluxed for 10 h, and then concentrated in vacuum. The residue was dissolved in EtOAc (30 mL) and washed with 1 M HCl (20 mL), saturated $NaHCO_3$ (5 mL) and brine (5 mL), dried over Na_2SO_4. Evaporation of the solvent followed by silica gel column chromatography of the resulting residue using petroleum ether/ether (9:1) as eluent furnished macrolactone **20** (30 mg, 59%). $[\alpha]_D$ = −6.3 (c 1.5, MeOH). IR (neat) 2984, 1723, 1381, 1163, 858 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.79 (dd, J = 15.8, 9.6 Hz, 1H), 6.24 (d, J = 15.7 Hz, 1H), 5.29–4.78 (m, 1H), 4.05 (t, J = 9.0 Hz, 1H), 3.92 (ddd, J = 11.3, 8.6, 4.2 Hz, 1H), 2.15–1.76 (m, 1H), 1.75–1.55 (m, 4H), 1.54–0.98 (m, 14H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6 (Cq), 143.8 (CH), 125.9 (CH), 109.2 (Cq), 80.3 (CH), 80.0 (CH), 75.4 (CH), 35.3 (CH_2), 29.4 (CH_2), 27.8 (CH_2), 27.1 (CH_3), 26.8 (CH_3), 25.1 (CH_2), 24.9 (CH_2), 20.6 (CH_3). HRMS: m/z for $C_{15}H_{24}O_4$+Na, calcd: 291.1572; found: 291.1577.

4.14. Preparation of cladospolide C *ent*-3

To an ice-cold solution of macrolactone **20** (20 mg, 0.07 mmol) in CH_3CN/H_2O (2:1, 1.5 mL) was added TFA (0.1 mL) dropwise at 0 °C. The reaction mixture was slowly warmed to room temperature and stirred for 2 h at the same temperature. Solid $NaHCO_3$ was added and stirred for 10 min at room temperature. It was filtered through a short pad of Celite and the Celite pad was washed with EtOAc (10 mL). The combined organic layers were washed with brine (1 × 3 mL), dried over Na_2SO_4. Evaporation of the solvent followed by silica gel column chromatography of the resulting residue using EtOAc as eluent afforded *ent*-**3** (13 mg, 85%) as a colorless solid. Mp: 91–92 °C. $[\alpha]_D$ = −58.7 (c 0.5, MeOH); lit.[4c] $[\alpha]_D$ = +58.2 (c 0.5, MeOH for the enantiomer). IR (KBr) 3401, 2932, 1718, 1260, 1033 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.82 (dd, J = 15.7, 9.4 Hz, 1H), 6.05 (d, J = 15.8 Hz, 1H), 4.96 (dqd, J = 12.6, 6.2, 3.9 Hz, 1H), 3.98 (t, J = 8.0 Hz, 1H), 3.69–3.25 (m, 1H), 2.54 (br s, 2H), 1.85–1.12 (m, 10H), 1.30 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8 (Cq), 145.4 (CH), 124.4 (CH), 77.5 (CH), 76.5 (CH), 74.4 (CH), 33.9 (CH_2), 32.1 (CH_2), 27.3 (CH_2), 24.5 (CH_2), 24.0 (CH_2), 20.8 (CH_3).

4.15. Preparation of (*R*)-7-((4*S*,5*S*)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)heptan-2-ol 21

To a solution of **14b** (0.18 g, 0.42 mmol) in dry CH_2Cl_2 (4 mL) was added p-TSA (0.12 g, 0.63 mmol) and 2,2-dimethoxy propane (0.1 mL, 0.84 mmol) under an argon atmosphere and refluxed for 3.5 h. After the reaction was complete (TLC), it was cooled to room temperature. Solid K_2CO_3 (0.09 g), was introduced and stirred for 15 min at room temperature. The reaction mixture was filtered through a short pad of Celite and the Celite pad was washed with EtOAc (2 × 10 mL). Evaporation of the solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (6:4) as eluent yielded **21** (0.09 g, 89%) as a pale yellow oil. $[\alpha]_D$ = −8.7 (c 0.7, $CHCl_3$). IR (neat) 3420, 2861, 1371, 1018, 874 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80 (ddd, J = 17.4, 10.2, 7.2 Hz, 1H), 5.35 (d, J = 17.1 Hz, 1H), 5.23 (d, J = 10.2 Hz, 1H), 3.97 (t, J = 7.9 Hz, 1H), 3.77 (td, J = 12.6, 6.3 Hz, 1H), 3.72–3.50 (m, 1H),

1.75–1.23 (m, 16H), 1.17 (d, J = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.5 (CH), 118.7 (CH_2), 108.4 (Cq), 82.7 (CH), 80.6 (CH), 68.0 (CH), 39.2 (CH_2), 31.7 (CH_2), 29.6 (CH_2), 27.3 (CH_3), 26.9 (CH_3), 26.0 (CH_2), 25.6 (CH_2), 23.5 (CH_3). HRMS: m/z for $C_{14}H_{26}O_3$+Na calcd 265.1780; found 265.1777.

4.16. Preparation of (*Z*)-ethyl 3-((4*S*,5*S*)-5-((*R*)-6-hydroxyheptyl)-2,2-dimethyl-1,3-dioxolan-4-yl)acrylate 22

Ozone was bubbled through a pre cooled (−78 °C) solution of **21** (0.05 g, 0.2 mmol) in a mixture of CH_2Cl_2/MeOH (4:1, 5 mL) containing solid $NaHCO_3$ (15 mg) until the pale blue color persisted. Excess ozone was flushed off with oxygen and Me_2S (0.2 mL) was added. The reaction mixture was warmed up to 0 °C and stirred at the same temperature for 3 h. It was then concentrated under reduced pressure, filtered through a short pad of Celite, and the Celite pad was washed with EtOAc (10 mL). Evaporation of the solvent yielded the crude aldehyde which was subjected to the next reaction without further purification.

To a solution of the crude aldehyde (obtained above) (0.07 g, 0.2 mmol) in dry MeOH (3 mL) was added (carbethoxymethylene)triphenyl phosphorane (0.17 g, 0.5 mmol) at −78 °C under a nitrogen atmosphere. The reaction mixture was slowly warmed up to −15 °C and stirred for 4 h at the same temperature. The p of the reaction was followed by TLC. After completion of the reaction (~3 h), most of the solvent was removed under reduced pressure. Silica gel column chromatography of the resulting residue using petroleum ether/EtOAc (6:4) as eluent afforded **22** (0.052 g, 82%) as a colorless oil. $[\alpha]_D$ = +31.4 (c 1.1, $CHCl_3$). IR (neat) 3420, 2860, 1723, 1193, 875 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.16 (dd, J = 11.8, 8.8 Hz, 1H), 5.97 (d, J = 11.7 Hz, 1H), 5.30 (t, J = 8.2 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.95–3.52 (m, 2H), 1.85–1.23 (m, 19H), 1.21 (d, J = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5 (Cq), 145.5 (CH), 123.1 (CH_2), 109.2 (Cq), 81.0 (CH), 76.1 (CH), 68.1 (CH), 60.5 (CH_2), 39.2 (CH_2), 32.0 (CH_2), 29.6 (CH_2), 27.4 (CH_3), 27.1 (CH_3), 25.9 (CH_2), 25.6 (CH_2), 23.5 (CH_3), 14.2 (CH_3). HRMS: m/z for $C_{17}H_{30}O_5$+Na, calcd: 337.1991; found: 337.1995.

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