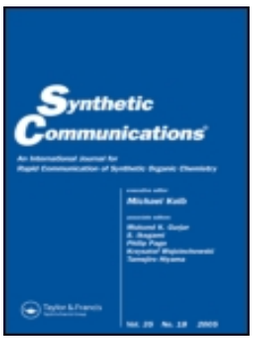

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Stereoselective total synthesis of sporiolide B and attempted synthesis of sporiolide A

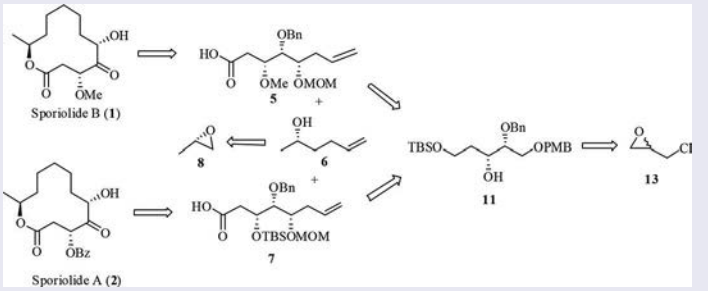
Gattu Sridhar and Gangavaram V. M. Sharma

Organic and Biomolecular Chemistry Division, CSIR Indian Institute of Chemical Technology, Hyderabad, India

ABSTRACT

A simple and efficient stereoselective total synthesis of sporiolide B and attempted synthesis of sporiolide A, from epichlorohydrin, using asymmetric synthetic approach is reported. The key reactions involved are Sharpless epoxidation, Jacobsen reaction, *syn*-allylation, Yamaguchi esterification, and Grubbs ring-closing metatheses reaction to result in the macrocyclic ring system.

GRAPHICAL ABSTRACT



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KEYWORDS
Ring-closing metathesis; *syn*-allylation; sporiolide A; sporiolide B; Yamaguchi esterification

Introduction

Over the past few years, natural products have continued to be of interest on account of their diverse biological properties. Synthesis of biologically important natural products has always fascinated organic chemists. Because of their continuous efforts, tremendous development in the synthesis of complex natural products such as macrolides, steroids, terpenes, and alkaloids has been possible. Natural products containing a medium ring lactone framework are found in plants, insects (pheromones), and bacteria (antibiotics), and they can have a terrestrial or a marine origin.

Sporiolide B (**1**) and sporiolide A (**2**) are 12-membered macrolides isolated by Shigemori et al.[1] from a marine-derived fungus *Cladosporium* sp., which was separated from an Okinawan marine brown alga *Actinotrichia fragilis*. Macrolides **1** and **2** were found to exhibit cytotoxicity against murine lymphoma L1210 cell line with IC_{50} values of 0.13 and 0.81 μg/mL, respectively. Further assays revealed that sporiolide A (**2**) shows moderate antifungal activity against *Candida albicans* (MIC 16.7 μg/mL), *Cryptococcus neoformans*

CONTACT Gattu Sridhar sridhar1org@yahoo.com Organic and Biomolecular Chemistry Division, CSIR Indian Institute of Chemical Technology, Hyderabad, 500107, India.
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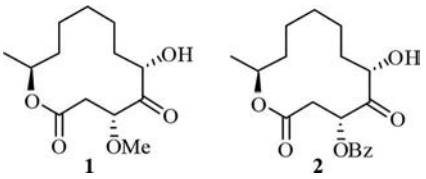


Figure 1. Structures of sporiolide B (**1**) and sporiolide A (**2**).

(MIC 8.4 μg/mL), *Aspergillus niger* (MIC 16.7 μg/mL), and *N. crassa* (MIC 8.4 μg/mL) respectively.

In 2006 the first synthesis of sporiolide B was reported[2] from D-xylose in 15 linear steps and 3.5% of overall yield. In 2007, Du et al.[3] again reported synthesis of sporiolide B from D-glucal in 17 steps with 4.8% overall yield, and in 2006[4] reported the first total synthesis of sporiolide A from D-glucal in 16 steps with 6.1% of overall yield. In 2010 Venkateswarlu et al.[5] reported stereoselective total synthesis of cytotoxic sporiolide A from D-mannital in 13% steps with 7% of overall yield.

In this study our main aim is to synthesize both the macrolides sporiolide B (**1**) and sporiolide A (**2**) (Fig. 1). Sporiolide B (**1**) was successfully achieved and met with failure to give sporiolide A (**2**).

Results and discussion

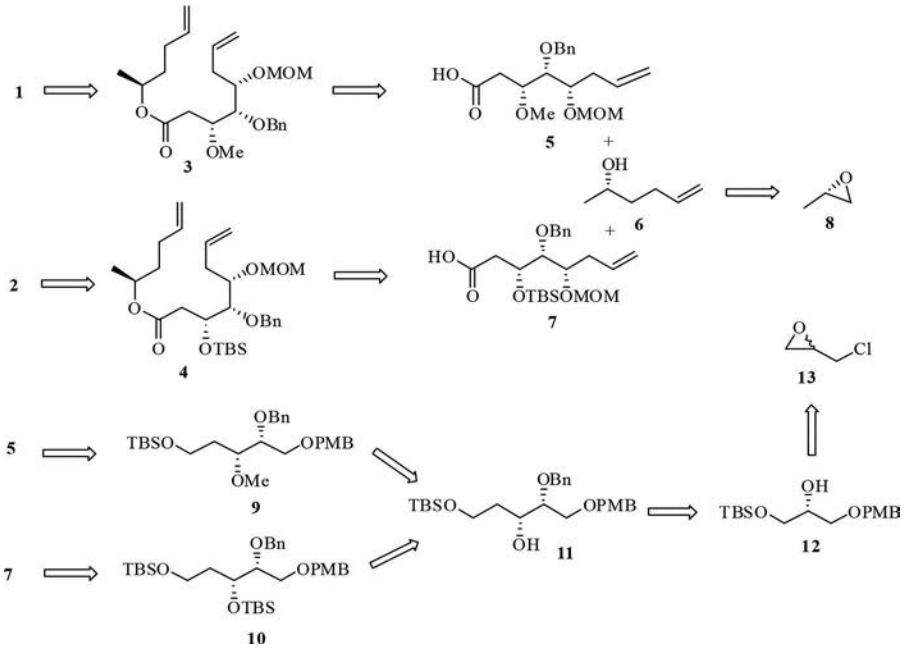
As shown in Scheme 1 the retrosynthetic analysis of macrolactone **1** revealed that it could be obtained from *bis*-olefin **3**, while macrolactone **2** could be obtained from *bis*-olefin **4**, by ring-closing metathesis (RCM) protocol. *Bis*-olefin **3** in turn could be realized by esterfication of acid **5** with alcohol **6** and *bis*-olefin **4** from acid **7** and alcohol **6**. The alcohol **6** could be realized from propylene epoxide **8**.

Acids **5** and **7** could be derived from **9** and **10** respectively, while both the **9** and **10** could be made from **11**. Alcohol **11** could be realized from the known alcohol **12**, which can be derived from epichlorohydrin **13**.

Accordingly, reaction of the known alcohol **12**[6] (prepared from **13**), with BnBr and NaH in tetrahydrofuran (THF) at 0 °C to 35 °C for 6 h afforded the benzyl ether **14** in 85% yield (Scheme 2). Desilylation of **14** with tetrabutylammonium fluoride (TBAF) in THF for 1 h gave **15** in 85% yield. Swern oxidation of **15** and subsequent Wittig olefination of **15a** afforded the ester **16** in 87% yield.

Diisobutylaluminium hydride (DIBAL-H) reduction of **16** in CH_2Cl_2 at 0 °C for 2 h furnished the allylic alcohol **17** (86%), which on Sharpless epoxidation[7] with (+)-diisopropyl tartrate (DIPT), $Ti(O^iPr)_4$, and cumene hydroperoxide in CH_2Cl_2 afforded **18** (85%). Epoxide **18** on opening with Red-Al in dry THF for 3 h afforded **19** (85%), which on treatment with TBSCl and imidazole in CH_2Cl_2 for 2 h gave TBS ether **11** in 90% yield, a common intermediate for **1** and **2**.

For the synthesis of sporiolide B (**1**), **11** was subjected to reaction with methyl iodide and NaH in THF at 0 °C to 35 °C for 4 h to afford **9** in 85% yield. Oxidative deprotection of paramethoxybenzyl (PMB) ether in **9** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in aqueous CH_2Cl_2 at 0 °C to 35 °C for 1 h gave **20** (87%), which on Swern oxidation followed by 1,2-*syn* allylation[8] of aldehyde **20a** with allyltributyltin and $MgBr_2 \cdot Et_2O$ in CH_2Cl_2 at − 78 °C for 4 h furnished the allylic alcohol **21** in 79% yield. Reaction of **21** with MOMCl

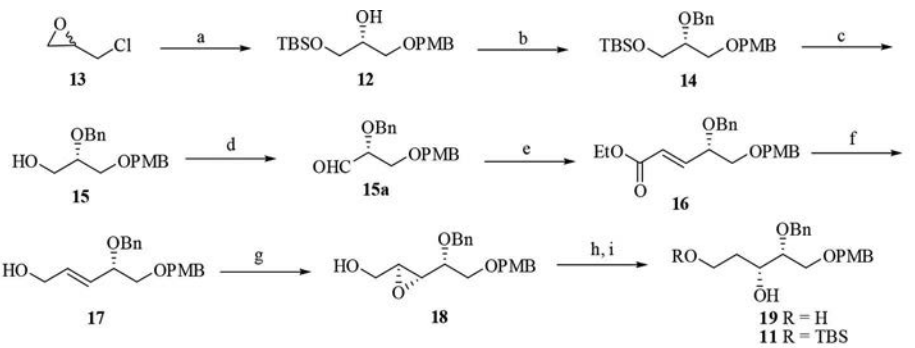


Scheme 1. Retroanalysis of sporiolide B (**1**) and sporiolide A (**2**).

and DIPEA in CH_2Cl_2 at 0 °C to 35 °C for 6 h furnished the methoxy methyl (MOM) ether **22** in 86% yield. Desilylation of **22** with TBAF in THF at 0 °C to 35 °C for 1 h gave **23** (89%), which on oxidation with 2,2,6,6-tetramethyl piperidine-1-oxyl (TEMPO) and bis(acetoxy) iodobenzene (BAIB) in CH_2Cl_2/H_2O (1:1) furnished the acid **5** in 81% yield.

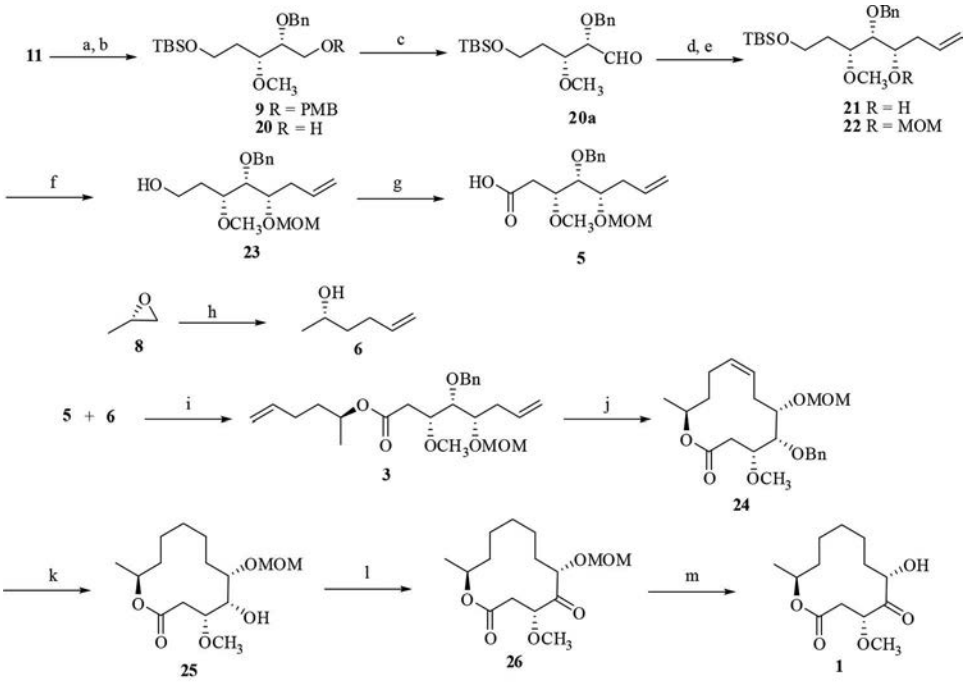
Likewise, alcohol **6** was prepared from the known epoxide **8**.[9] Accordingly, treatment of **8** with allylmagnesium chloride in ether at − 78 °C gave alcohol **6**.

Esterification of acid **5** and alcohol **6** under Yamaguchi conditions[10] in the presence of 2,4,6-trichlorobenzoyl chloride and Et_3N followed by DMAP in toluene for 1 h afforded *bis*- olefin **3** in 87% yield. RCM reaction of ester **3** with Grubb's[11] second-generation



Reagents and conditions: a) ref. 2; b) Benzyl bromide, NaH, THF, 0 °C to 35 °C, 6 h; c) TBAF, THF, 0 °C to 35 °C, 1 h; d) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78 °C, 2 h; e) Ph_3P=CHCOOEt, Benzene, reflux, 2 h; f) DIBAL-H, CH_2Cl_2, 0 °C to 35 °C, 2 h; g) (+)-DIPT, $Ti(OiPr)_4$, Cumene hydroperoxide, CH_2Cl_2, -20 °C, 5 h; h) Red-Al, dry THF, 0 °C to 35 °C, 3 h; i) TBS-Cl, Imidazole, *n*-Bu_2SnO, CH_2Cl_2, 0 °C to 35 °C, 2 h.

Scheme 2. Synthesis of fragment **11**.

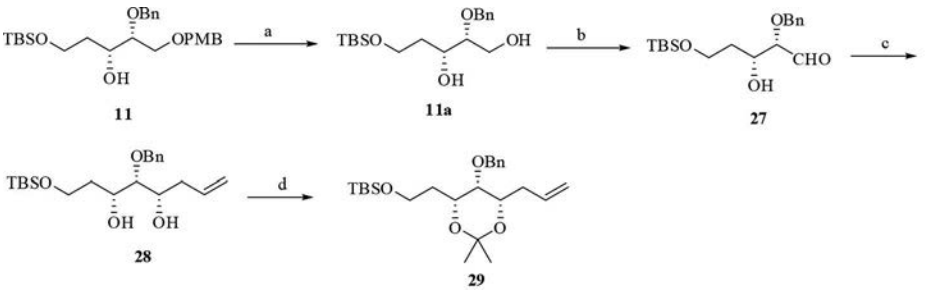


Reagents and conditions: a) CH_3I, NaH, THF, 0 °C-35 °C, 4 h; b) DDQ, aq. CH_2Cl_2, 1 h; c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78 °C, 2 h; d) Allyltributyltin, $MgBr_2$. Et_2O, THF, -78 °C, 4h; e) MOM-Cl, DIPEA, CH_2Cl_2, 0 °C-35 °C, 6 h; f) TBAF, THF, 0 °C-35 °C, 1 h; g) TEMPO, BAIB, CH_2Cl_2 : H_2O (1:1), 0 °C-35 °C, 2 h; h) Mg, allyl chloride, di ethyl ether, -78 °C, 2 h; i) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, DMAP, toluene, 35 °C, 1 h; j) Grubb's second generation catalyst, CH_2Cl_2, reflux, 6 h; k) H_2, 10% Pd-C, MeOH, 35 °C, 12 h; l) Dess Martin periodinane, CH_2Cl_2, 0 °C-35 °C, 4 h; m) 10% aq. HCl, THF, 0 °C- 35 °C, 5 h.

Scheme 3. Synthesis of sporiolide B (**1**).

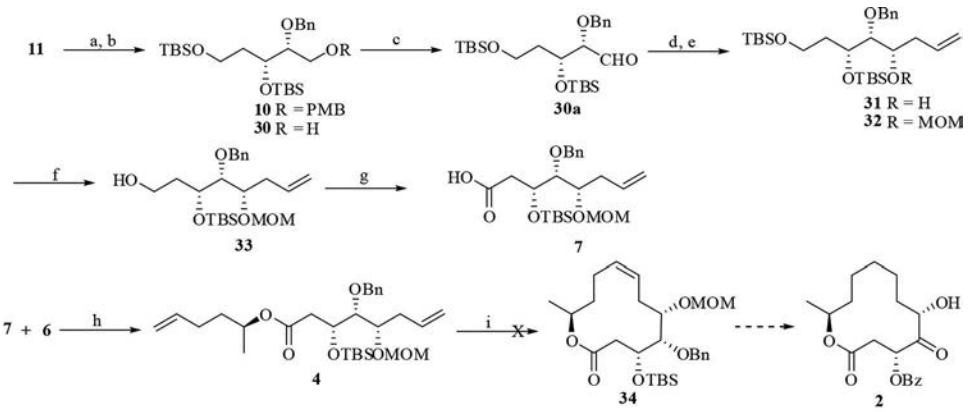
catalyst in CH_2Cl_2 at reflux for 6 h furnished lactone **24** in 76% yield. Hydrogenation of **24** with 10% Pd-C in MeOH for 12 h afforded **25** in 77% yield, by concomitant debenzylation followed by double-bond reduction.

Oxidation of **25** with Dess–Martin periodinane[12] in anhydrous CH_2Cl_2 at 0 °C to 35 °C for 4 h furnished ketone **26** in 80% yield. Finally, deprotection of MOM ether with 10% HCl in THF for 5 h afforded sporiolide B **1** in 84% yield, whose spectral and optical rotation data were comparable with the data reported in literature.[1]



Reagents and conditions: a) DDQ, aq. CH_2Cl_2, 1 h; b) TEMPO, tetrabutylammonium chloride, NCS, CH_2Cl_2, P^H 8.6 buffer, 0 °C–35 °C, 1 h; c) Allyltributyltin, $MgBr_2$. Et_2O, THF, -78 °C, 4 h; d) $Me_2C(OMe)_2$, *p*-TsOH, CH_2Cl_2, 0 °C–35 °C, 1 h.

Scheme 4. Synthesis of fragment **29**.



Reagents and conditions: a) TBS-Cl, Imidazole, CH_2Cl_2, 0 °C to 35 °C, 2 h; b) DDQ, aq. CH_2Cl_2, 1 h; c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78 °C, 2 h; d) Allyltributyltin, $MgBr_2$. Et_2O, THF, -78 °C, 4h; e) MOM-Cl, DIPEA, CH_2Cl_2, 0 °C to 35 °C, 6 h; f) PPTS, MeOH, 0 °C to 35 °C, 1 h; g) TEMPO, BAIB, CH_2Cl_2 : H_2O (1:1), 0 °C to 35 °C, 2 h; h) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, DMAP, toluene, 35 °C, 1 h; i) Grubb's second generation catalyst, CH_2Cl_2, reflux, 6 h.

Scheme 5. Attempted synthesis of sporiolide A (2).

To ascertain the absolute stereochemistry in **21, 11** was subjected oxidative deprotection of PMB ether with DDQ in aqueous CH_2Cl_2 at 0 °C to 35 °C for 1 h to give **11a**. Selective oxidation of primary alcohol with TEMPO, TBACl, and NCS and buffer in CH_2Cl_2 for 1 h furnished aldehyde **27**, which on *syn*-allylation[8] with allyltributyltin and $MgBr_2 \cdot Et_2O$ in CH_2Cl_2 at − 78 °C for 4 h gave the corresponding allylic alcohol **28** in 79% yield.

Reaction of **28** with 2,2-dimethoxy propane and *p*-TsOH (cat.) in CH_2Cl_2 at 0 °C to 35 °C for 1 h furnished acetonide **29** (73%), whose ^{13}C NMR confirmed the *syn*-1,3-diol[13] in **29**.

For the synthesis of **2**, alcohol **11** was subjected to reaction with TBSCl in the presence of imidazole in CH_2Cl_2 to give TBS ether **10** in 84% yield. Oxidative deprotection of PMB ether **10** with DDQ in aqueous CH_2Cl_2 at 0 °C to 35 °C for 1 h gave **30** in 79% yield. Swern oxidation of **30** in CH_2Cl_2 for 2 h furnished the aldehyde **30a**, which on *syn*-allylation[8] with allyltributyltin and $MgBr_2 \cdot Et_2O$ in CH_2Cl_2 at − 78 °C for 4 h gave the corresponding allylic alcohol **31** in 76% yield.

Reaction of **31** with MOMCl and DIPEA in CH_2Cl_2 at 0 °C to 35 °C for 6 h furnished the MOM ether **32** in 76% yield. Desilylation of **32** with PPTS in MeOH at 0 °C to 35 °C for 1 h gave **33** in 78% yield, which on oxidation with TEMPO and BAIB in aqueous CH_2Cl_2 (1:1) furnished the acid **7** in 72% yield.

Acid **7** on esterification with alcohol **6** under Yamaguchi conditions[10] afforded *bis*-olefin **4** in 70% yield. Ester **4** was subjected to RCM reaction with Grubb's[11] second-generation catalyst under different reaction conditions, which, however, met with failure to give macrolactone **34**.

Experimental

*(4S,5R,6R)-5-(Benzyloxy)-8-(*tert*-butyldimethylsilyloxy)-6-methoxyoct-1-en-4-ol (21)*

To a solution of oxalyl chloride (0.9 mL, 10.54 mmol) in dry CH_2Cl_2 (15 mL) at − 78 °C, dry DMSO (2.8 mL, 21.18 mmol) was added dropwise and stirred for 20 min. A solution of **20** (2.5 g, 7.06 mmol) in dry CH_2Cl_2 (20 mL) was added and stirred for 2 h at − 78 °C. Workup as described for **15a** furnished the corresponding aldehyde **20a**.

To a solution of the aldehyde **20a** (2.5 g, 7.1 mmol) in dry CH_2Cl_2 (25 mL), $MgBr_2 \cdot OEt_2$ (3.66 g, 14.20 mmol) was added at − 78 °C. The reaction mixture was stirred at − 78 °C for 45 min. Allyltributyltin (3.26 mL, 10.63 mmol) was added to the reaction mixture dropwise and stirred for 4 h at − 78 °C. It was quenched by the addition of saturated NH_4Cl solution (15 mL), allowed to warm to room temperature, and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). Solvent was evaporated and the residue was purified by column chromatography (60- to 120-mesh silica gel, 9% EtOAc in petroleum ether) to furnish **21** (2.2 g, 79%) as a yellow syrup. The dr of *syn* and *anti* alcohol is 97:3. $[\alpha]_D^{25} = +73.7$ (*c* 0.5, $CHCl_3$); IR (neat): 3425, 3070, 2929, 1719, 1642, 1452, 1376, 1316, 1273, 1176, 1099, 1026, 919, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.39–7.28 (m, 5H, ArH-Bn), 5.98–5.79 (m, 1H, olefinic), 5.20–5.08 (m, 2H, olefinic), 4.90 (d, 2H, *J* = 6.9 Hz, benzylic), 4.27–4.18 (m, 1H, -OCH), 3.90–3.68 (m, 3H, $-OCH_2$,-OCH), 3.55 (s, 3H, $-OCH_3$), 3.47–3.38 (m, 1H, -OCH), 2.59–2.48 (m, 2H, $-CH_2$), 1.99–1.78 (m, 2H, $-CH_2$), 0.93 (s, 9H, 3 × $-CH_3$), 0.14 (s, 6H, 2 × $-CH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.8, 134.6, 128.4, 128.3, 128.1, 128.0, 127.9, 117.4, 104.9, 80.3, 73.9, 70.5, 60.1, 58.7, 39.1, 38.3, 25.6, 17.9, −3.6; HRMS (ESI): *m/z* calculated for $C_{22}H_{38}O_4NaSi$ $[M+Na]^+$ 417.1659, found 417.1665.

(3R,4S,5S)-((S)-Hex-5-en-2-yl)4-(benzyloxy)-3-methoxy-5-(methoxymethoxy)oct-7-enoate (3)

To a solution of acid **5** (0.7 g, 2.07 mmol) and Et_3N (0.5 mL, 4.13 mmol) in dry THF (15 mL) at 0 °C, 2,4,6-trichlorobenzoyl chloride (0.32 mL, 2.07 mmol) in dry THF (5 mL) was added and stirred the reaction mixture at 35 °C temperature for 2 h under a nitrogen atmosphere. It was filtered and the filtrate evaporated. The resulting anhydride was dissolved in toluene (10 mL) and treated with alcohol **6** (0.2 g, 2.07 mmol) in toluene (2 mL), and catalytic amount of DMAP in dry toluene (10 mL) was added to the reaction mixture and stirred for 1 h at 35 °C temperature. It was filtered through celite and washed with toluene (2 × 25 mL). Solvent was evaporated and purified the residue by column chromatography (60- to 120-mesh silica gel, 6% EtOAc in petroleum ether) to afford **3** (0.75 g, 87%) as a yellow syrup with 100% diastereoselectivity. $[\alpha]_D^{25} = +97.6$ (*c* 0.5, $CHCl_3$); IR (neat): 3448, 3073, 2930, 1731, 1639, 1453, 1376, 1274, 1161, 1103, 1035, 916, 748, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.36–7.27 (m, 5H, ArH-Bn), 5.93–5.73 (m, 2H, olefinic), 5.15–5.04 (m, 4H, olefinic), 4.99–4.93 (m, 2H, benzylic), 4.67 (s, 2H, $-OCH_2$), 3.95–3.88 (m, 2H, 2 × -OCH), 3.80–3.76 (m, 1H, -OCH), 3.68–3.63 (m, 1H, -OCH), 3.39 (s, 6H, 2 × $-OCH_3$), 2.70–2.61 (m, 2H, $-CH_2$), 2.49–2.43 (m, 2H, $-CH_2$), 2.15–2.04 (m, 2H, $-CH_2$), 1.77–1.62 (m, 2H, $-CH_2$), 1.20 (d, 3H, *J* = 6.2 Hz, $-CH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.7, 138.4, 137.8, 134.8, 128.2, 127.8, 127.5, 117.4, 114.8, 96.0, 79.8, 78.4, 73.4, 70.4, 57.8, 55.9, 36.4, 35.3, 35.1, 29.6, 19.8; HRMS (ESI): *m/z* calculated for $C_{24}H_{36}O_6Na$ $[M+Na]^+$ 443.1469, found 443.1477.

(4R,5R,6S,12S)-5-(Benzyloxy)-4-methoxy-6-(methoxymethoxy)-12-methyloxacyclododec-8-en-2-one (24)

To a stirred solution of **3** (0.5 g, 1.19 mmol) in dry CH_2Cl_2 (1 mg/1 mL, 500 mL), Grubbs' second-generation catalyst (10 mol%) was added and stirred at reflux for 6 h and then at 35 °C in the open air for an additional 1 h. The reaction mixture was filtered through celite

and concentrated, and the residue was purified by column chromatography (60- to 120-mesh silica gel, 8% EtOAc in petroleum ether) to afford **24** (0.35 g, 76%) as a yellow syrup with 100% diastereoselectivity. $[\alpha]_D^{25} = +61.8$ (*c* 0.5, $CHCl_3$); IR (neat): 3449, 2925, 2852, 1731, 1633, 1456, 1372, 1247, 1149, 1099, 1032, 958, 917, 749, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.49–7.29 (m, 5H, ArH-Bn), 5.40–5.25 (m, 2H, olefinic), 4.69 (m, 4H, benzylic, -OCH_2), 4.07–3.83 (m, 2H, 2 × -OCH), 3.74–3.48 (m, 1H, -OCH), 3.38 (s, 6H, 2 × -OCH_3), 3.37–3.31 (m, 1H, -OCH), 2.71–2.56 (m, 1H, -CH), 2.35–2.11 (m, 1H, -CH), 2.35–2.11 (m, 1H, allylic -CH), 2.04–1.84 (m, 1H, allylic -CH), 1.34–1.24 (m, 2H, allylic -CH_2), 1.22 (d, 3H, $J = 6.3$ Hz, -CH_3), 0.98–0.81 (m, 2H, -CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.0, 138.8, 133.8, 128.6, 128.1, 127.6, 97.4, 79.6, 74.2, 74.6, 67.3, 67.6, 56.5, 56.2, 38.7, 38.4, 26.8, 28.6, 24.4; HRMS (ESI): *m/z* calculated for $C_{22}H_{32}O_6Na$ $[M+Na]^+$ 415.1132, found 415.1126.

(4R,6S,12S)-6-Hydroxy-4-methoxy-12-methyloxacyclododecane-2,5-dione (1)

A stirred solution of **26** (0.03 g, 0.09 mmol) in THF (20 mL) was cooled to 0 °C, treated with 10% aqueous HCl (1 mL), and stirred at 35 °C for 5 h. The reaction mixture was quenched with saturated $NaHCO_3$ solution (5 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with water (2 × 15 mL) and brine (15 mL), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by column chromatography (60- to 120-mesh silica gel, 20% EtOAc in petroleum ether) to give **1** (21 mg, 84%) as a colorless amorphous solid with 100% diastereoselectivity. $[\alpha]_D^{25} = -29.1$ (*c* 0.5, $CHCl_3$); IR (neat): 3429, 2934, 1710, 1646, 1220, 1170, 1106, 763, 713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.83–4.81 (m, 1H, -OCH), 4.44 (d, 1H, $J = 8.7$ Hz, -OCH), 4.30 (d, 1H, $J = 5.7$ Hz, -OCH), 3.53 (s, 3H, -OCH_3), 3.43 (t, 1H, $J = 12.6$ Hz, -CH), 2.60 (dd, 1H, $J = 8.8$ Hz, 13.9 Hz, -CH), 2.06–2.04 (m, 1H, -CH), 1.69–1.58 (m, 2H, 2 × -CH), 1.57–1.48 (m, 2H, 2 × -CH), 1.47–1.38 (m, 2H, 2 × -CH), 1.36–1.25 (m, 2H, 2 × -CH), 1.23 (d, 3H, $J = 6.4$ Hz, -CH_3), 1.09–1.07 (m, 1H, -CH); ^{13}C NMR (75 MHz, $CHCl_3$): δ 208.8, 170.6, 76.1, 74.4, 73.3, 58.4, 41.3, 33.4, 29.9, 26.5, 23.8, 22.1, 20.8; HRMS (ESI): *m/z* calculated for $C_{13}H_{22}O_5Na$ $[M+Na]^+$ 281.1367, found 281.1369.

*(3R,4R,5S)-((S)-Hex-5-en-2-yl)4-(benzyloxy)-3-(*tert*-butyldimethylsilyloxy)-5-(methoxymethoxy)oct-7-enoate (4)*

To a solution of acid **5** (0.3 g, 0.68 mmol) and Et_3N (0.2 mL, 1.36 mmol) in dry THF (10 mL) at 0 °C, 2,4,6-trichlorobenzoyl chloride (0.1 mL, 0.68 mmol) in dry THF (3 mL) was added and stirred at 35 °C for 2 h under a nitrogen atmosphere. It was filtered, and the filtrate evaporated. The resulting anhydride was dissolved in toluene (3 mL) and treated with alcohol **6** (0.11 g, 0.68 mmol) in toluene (7 mL), and a catalytic amount of DMAP in dry toluene (5 mL) was added to the reaction mixture and stirred for 1 h at 35 °C. It was filtered through celite and washed with toluene (2 × 15 mL). The solvent was evaporated and the residue was purified by column chromatography (60- to 120-mesh silica gel, 7% EtOAc in petroleum ether) to afford **3** (0.25 g, 70%) as a yellow syrup with 100% diastereoselectivity. $[\alpha]_D^{25} = +31.7$ (*c* 0.5, $CHCl_3$); IR (neat): 2932, 2857, 1740, 1643, 1462, 1239, 1096, 919, 776, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.37–7.27 (m, 5H, ArH-Bn), 5.93–5.74 (m, 2H, olefinic), 5.13–5.06 (m, 2H, olefinic), 5.04–4.94 (m, 2H, olefinic),

4.92–4.87 (m, 1H, benzylic), 4.82 (m, 1H, $J = 11.4$ Hz, benzylic), 4.72–4.63 (m, 3H, -OCH, -OCH_2), 4.45–4.40 (m, 1H, -OCH), 3.80–3.77 (m, 1H, -OCH), 3.61–3.57 (m, 1H, -OCH), 3.39 (s, 3H, -OCH_3), 2.67-2.61 (m, 2H, -CH_2), 2.47–2.43 (m, 2H, -CH_2), 2.31–1.72 (m, 4H, 2 × -CH_2), 1.20 (d, 3H, $J = 6.25$ Hz, -CH_3), 0.88 (s, 9H, 3 × -CH_3), 0.09 (d, 6H, $J = 6.6$ Hz, 2 × -CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.4, 138.6, 137.7, 134.9, 128.2, 127.6, 127.4, 117.2, 114.8, 95.9, 83.2, 73.6, 70.5, 69.8, 68.7, 55.9, 39.1, 35.0, 29.5, 25.8, 19.7, 17.9, 16.5, −4.4, −4.8; HRMS (ESI): *m/z* calculated for $C_{29}H_{48}O_6NaSi$ $[M+Na]^+$ 543.3112, found 543.3101.

Conclusion

Thus, in summary an efficient stereoselective total synthesis of sporiolide B (**1**) has been achieved in 22 steps with a 4.35% overall yield, while the attempted synthesis of sporiolide A (**2**) from epichlorohydrin failed to give macrolactone at the macrocyclization stage.

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