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PAPER

A flexible and unified strategy for syntheses of cladospolides A, B, C, and *iso*-cladospolide B†‡

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A simple, efficient and flexible strategy for the syntheses of cladospolides A–C and *iso*-cladospolide B is reported here. This strategy involves Julia–Kocienski olefination and Yamaguchi macrolactonization as key steps, starting from either D-ribose or suitable tartaric acid esters. Although our initial efforts towards cladospolide A involving a ring closing metathetic approach were not successful, changing the mode of ring closure and the use of Julia–Kocienski olefination for the construction of the key intermediate solved this issue and paved the way for the completion of total syntheses of this class of natural products.

Introduction

Marine fungi, being a potential source of new biologically active secondary metabolites, are a topic of growing interest. Cladospolides (A–D) (Fig. 1) are such secondary metabolites, responsible for the host plant's growth, and were isolated[1–4] from different *Cladosporium sp.* Structurally this class of natural products differ in the position, number and stereochemistry of hydroxyl groups as well as the double bond and these trivial differences in functionality affect their biological profiles significantly. The first two members, cladospolides A[1] and B[2] were first isolated from the culture filtrate of *Cladosporium cladosporioides* FI-113 in 1985 by Isogai and co-workers. Later in 2000, Ireland and co-workers isolated cladospolide B as well as γ-butenolide *iso*-cladospolide B from the sponge-derived fungus *Cladosporium herbarum* and marine fungal species I962S215 respectively,[3b] whereas, cladospolide C was isolated from the metabolites of the soil fungus *Cladosporium tenuissimum* by Fukuda and co-workers in 1995.[3a] Although isolated from the same species, (−)-cladospolide A **1** is found to inhibit root growth of lettuce seedlings, while cladospolide B **2** promotes the growth. Likewise, cladospolide C **4** was also found to inhibit shoot elongation of rice seedlings.[2] Unlike other congeners, cladospolide D **5**, the recently isolated species from *Cladosporium sp.* FT-0012 by Omura and co-workers, shows antimicrobial activity with IC_{50} values of 0.1 and 29 μg mL^{-1} against *Mucor racemosus* and *Pyricularia oryzae* respectively.[4]

The promising biological profiles of the cladospolide family of natural products have attracted the interest of the synthetic community since their isolation and they have been the subject of total synthesis by various groups.[5–9] As a part of our ongoing research program on the synthesis of biologically active natural and unnatural products using a metathetic approach,[10] we became interested in developing a general strategy for syntheses of this class of natural products. As an outcome of our synthetic voyage, we had earlier reported an expedient route to the total synthesis of (−)-cladospolide A **1**.[5b] Herein, we discuss in detail our cumulative efforts to the total synthesis of (−)-cladospolide A and other family members.

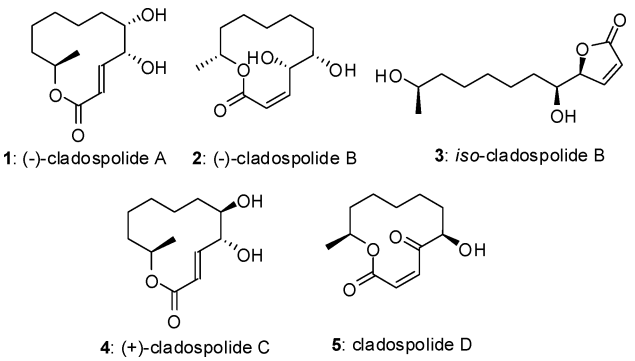

Fig. 1 Cladospolide family.

Results and discussion

First generation strategy: (−)-cladospolide A

According to our first strategy a ring closing metathesis was planned as the key step for the synthesis of cladospolide A (Fig. 2). We envisaged that **1** could be derived from **6** in a couple of steps involving selective hydrogenation and removal of the protecting group. The diene lactone **6** could be obtained from **7** *via* a regioselective RCM. The RCM precursor **7** could be synthesized from alcohol **8** and acid **9**. The carboxylic acid **9** could be traced

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‡ Dedicated to my colleague, Professor V. K. Singh, on the occasion of his 60th birthday.

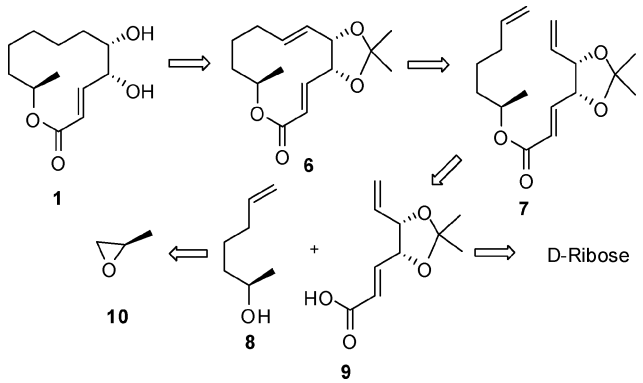
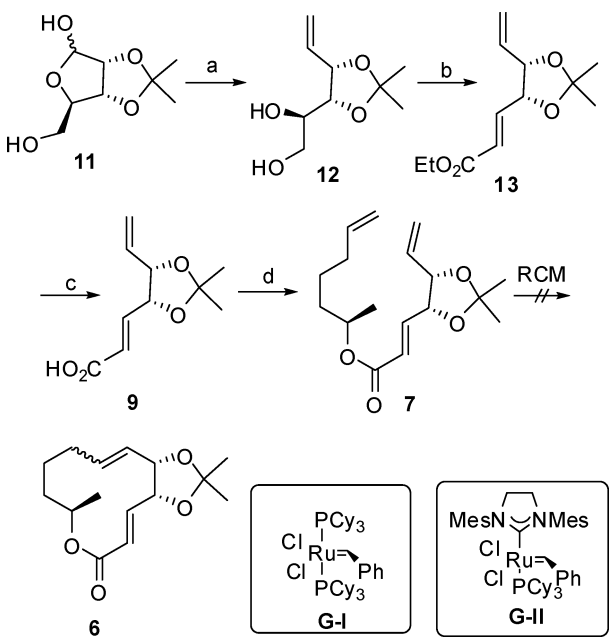


Fig. 2 Retrosynthetic analysis.

to D-ribose and the known alcohol **8** could be derived from chiral epoxide **10** in good quantity.

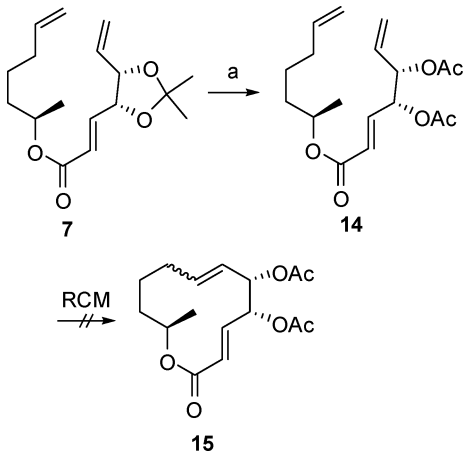
So, our initial synthetic journey towards cladospolide A began with the synthesis of acid **9** involving Wittig reaction of ribose monoacetonide **11** using triphenylphosphonium methylidene to afford diol **12**[11] (Scheme 1). The diol was then oxidatively cleaved with silica supported $NaIO_4$[12] and the resultant aldehyde was subjected to Horner–Wadsworth–Emmons reaction[13] to afford the (*E*)-α,β-unsaturated ester **13** in 87% yield. The other coupling partner, alcohol **8** was obtained by the ring opening of enantiomerically pure *R*-propylene oxide **10**, derived from the racemic counterpart through Jacobsen's hydrolytic kinetic resolution,[14] with 4-butenylmagnesium bromide in the presence of Li_2CuCl_4.[15] Exposure of ester **13** to an aqueous solution of lithium hydroxide provided the acid **9**, which under Yamaguchi conditions[16] was coupled with alcohol **8** to provide the ring closing metathesis precursor **7** in moderate yield.



Scheme 1 *Reagents and conditions*: (a) Ph_3PCH_3Br, KO^{t}Bu, THF, 0 °C, 80%; (b) i) silica supp. $NaIO_4$, CH_2Cl_2; ii) $(OEt)_2P(O)CH_2CO_2Et$, NaH, THF, 0 °C, 87% (for two steps); (c) LiOH, THF/MeOH/H_2O; (d) **8**, 2,4,6-trichlorobenzoyl chloride, Et_3N, toluene, DMAP, 46% (for two steps).

After the successful synthesis of RCM precursor **7** the stage was set for the key ring closing metathesis reaction[17] but, to our dismay, all our attempts to carry out the ring closing metathesis reaction of triene **7** failed to provide the required product **6**. Various substrate concentrations in refluxing CH_2Cl_2 or toluene were examined, however, only unidentified products and unreacted starting material were isolated in all the cases. Our observed results were found to be in accordance with the results observed later by Hou and co-workers in their total synthesis of (+)-cladospolide C,[8d] where a similar ring closing metathesis reaction provided the desired product only in nominal yield.

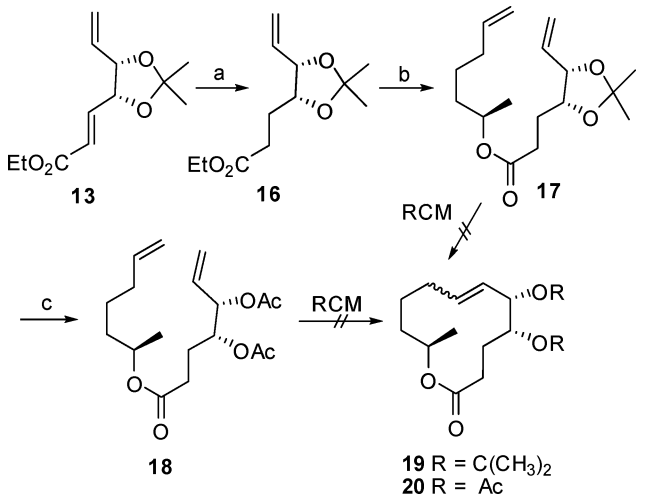
On the basis of our earlier experience in our laboratory,[10m] we anticipated that the presence of acetonide in the vicinity of the RCM site might hinder the progress of the reaction. Accordingly, the acetonide group was deprotected under mild conditions[18] using $CuCl_2$ to afford a trienediol which was further acetylated to provide the diacetate **14** (Scheme 2). Yet again, the diacetate **14** also failed to undergo the ring closing metathesis reaction and similar results were observed under a variety of conditions.



Scheme 2 *Reagents and conditions*: (a) i) $CuCl_2{\cdot}2H_2O$, CH_3CN; ii) Ac_2O, Py, DMAP, 79% (for two steps).

This unexpected failure of the ring closing metathesis reaction forced us to think that the presence of an extra double bond in the form of the α,β-unsaturated ester could perhaps increase the complicacy during the ring closing metathesis reaction. Hence, attempts were initiated to synthesize ring closing metathesis precursor **17** lacking the conjugated double bond. Thus, regioselective reduction of the conjugated double bond in ester **13** was achieved by a mixture of $NaBH_4$ and Cu_2Cl_2 (Scheme 3).[19] Saponification of **16** followed by esterification of the resultant acid with alcohol **8** provided the diene **17**. This whole process also didn't solve the problem, as the diene **17** failed to undergo RCM. Moving a step further, compound **17** was converted into diacetate **18** using a two step sequence, removal of acetonide and formation of diacetate, and then subjected to the ring closing metathesis reaction, but all our efforts once again failed to produce the required cyclised product.

We had observed that during the RCM reaction, the sterically less hindered olefin reacts with Grubbs' catalyst much faster and further rearranges to afford undesired products (Fig. 3). In order to succeed in our ring closing metathesis approach, we felt that it was



Scheme 3 *Reagents and conditions*: (a) $NaBH_4$, Cu_2Cl_2, THF–EtOH, –20 °C, 94%; (b) i) LiOH, THF–MeOH–H_2O; ii) **8**, DCC, DMAP, CH_2Cl_2, 42% (for two steps); (c) i) $CuCl_2{\cdot}2H_2O$, CH_3CN; ii) Ac_2O, Py, 78% (for two steps).

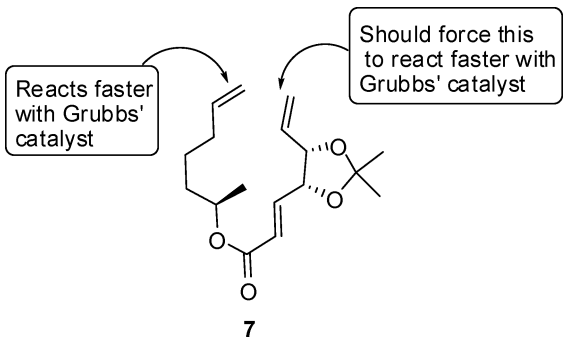


Fig. 3 Relay ring closing metathesis approach.

imperative to force the other alkene to react with the ruthenium catalyst faster.

Therefore, a relay approach was planned, wherein an allyl ether could be tethered to the less reactive alkene, which should then generate the Ru-carbene on the required side selectively and the key relay RCM reaction[17c,20] could be carried out on substrate **21** (Fig. 4). The relay RCM precursor **21** could be synthesized from acid **22** which in turn could be achieved starting from the commercially available D-ribose.

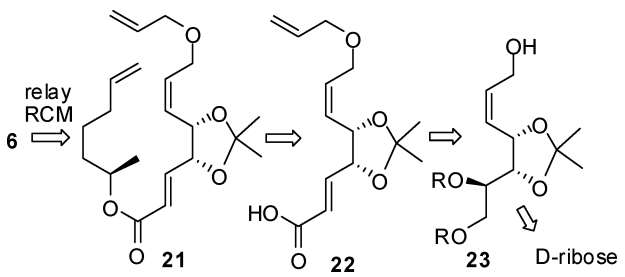
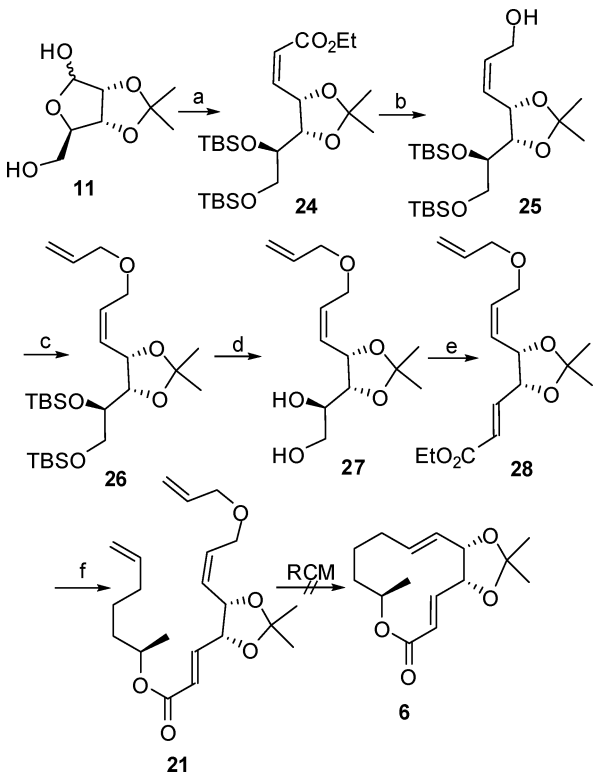


Fig. 4 Retrosynthetic analysis.

Accordingly, our revised synthetic expedition towards cladospolide A commenced with the synthesis of α,β-unsaturated ester **24** from ribose monoacetonide **11** in a two step sequence, first Wittig reaction with ethyl(triphenylphosphoranylidene) acetate, and then protection of the diol as a bis-silyl ether (Scheme 4). DIBAL-H reduction of ester **24** provided alcohol **25** which on allylation gave the diene **26** in 89% yield. Removal of vicinal silyl ether was accomplished with tetrabutyl ammonium fluoride in THF to give the diol **27** which on oxidative cleavage with silica supp. $NaIO_4$ followed by Horner–Wadsworth–Emmons reaction afforded the α,β-unsaturated ester **28** in good yield. Hydrolysis of ester **28** and subsequent esterification with alcohol **8** furnished the relay RCM precursor **21** in moderate yield. Nonetheless, the tetraene **21** also failed to undergo RCM reaction in the presence of either Grubbs' first (**G-I**) or second generation (**G-II**) catalyst under various substrate concentrations (0.002–0.02 M).



Scheme 4 *Reagents and conditions*: (a) i) $Ph_3P{=}CHCO_2Et$, PhCOOH, CH_2Cl_2, rt; ii) TBSCl, DMF, rt, 2 h, 76% (for two steps); (b) DIBAL-H, CH_2Cl_2, 0 °C, 70%; (c) NaH, allylbromide, THF, rt, 12 h, 89%; (d) TBAF, THF, rt, 96%; (e) i) silica supp. $NaIO_4$, CH_2Cl_2; ii) NaH, $(OEt)_2P(O)CH_2CO_2Et$, THF, rt, 63% (for two steps); (f) i) LiOH, THF–MeOH–H_2O; ii) **8**, DCC, DMAP, CH_2Cl_2, 35% (for two steps).

Second generation strategy: (–)-cladospolide A

After spending much of our time in troubleshooting RCM and relay RCM reactions toward cladospolide A, we modified our strategy and planned a variation on the site of macrolide closure. A Yamaguchi macrolactonization was planned to construct the macrolide and we envisioned that the macrolide **1** could be easily synthesised from the precursor **29**, which in turn could be constructed from hydroxy acid **30** through macrolactonization (Fig. 5). We chose alkene **32** to be a good substrate to convert to the hydroxy acid **30** in a sequence of steps. The alkene **32** could, in turn, be assembled through a cross-metathetic route between

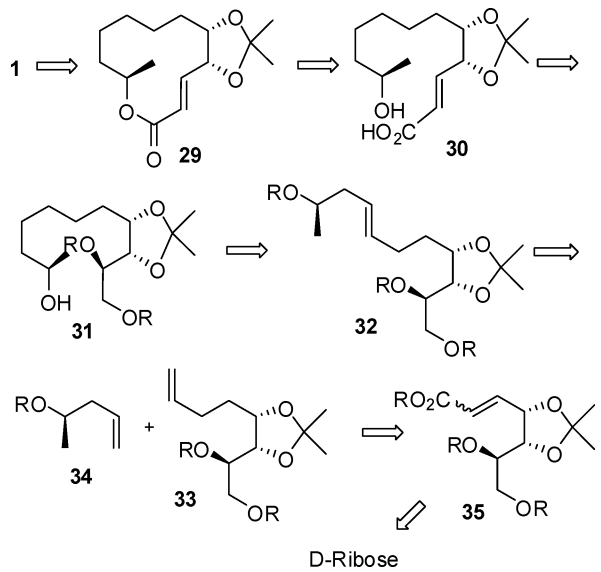
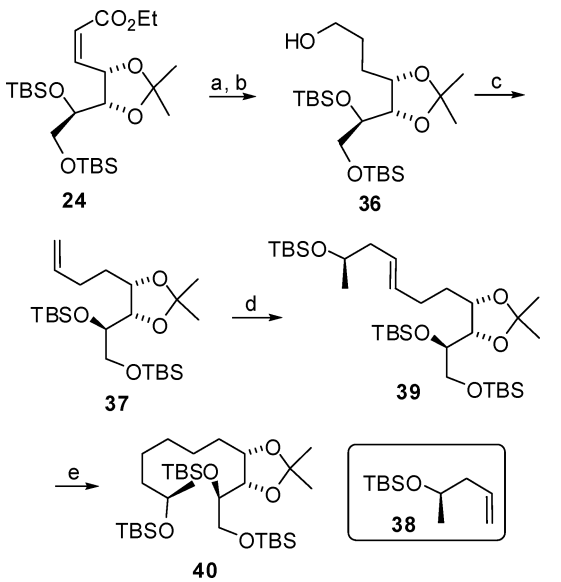


Fig. 5 Retrosynthetic analysis of cladospolide A.

alkenes **33** and **34** and the alkene **33** might well be obtained from commercially available D-ribose-derived ester **35** in a few steps.

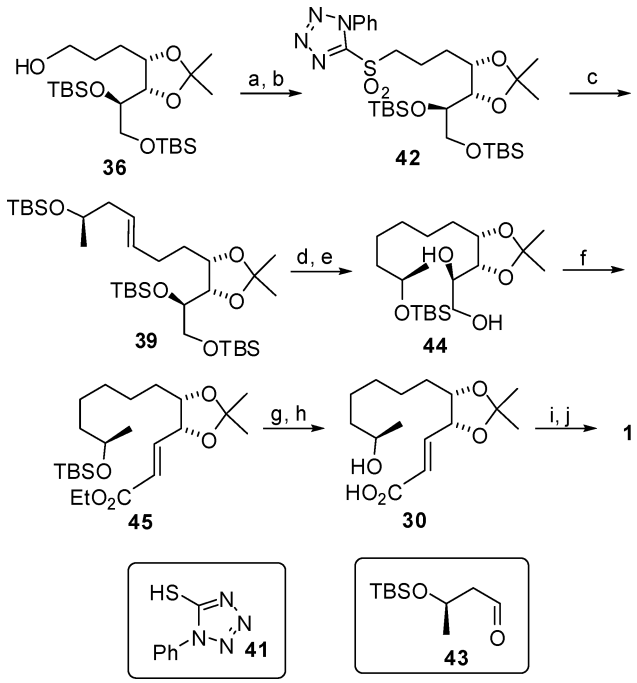
Thus, the revised synthesis of cladospolide A commenced with the hydrogenation of α,β-unsaturated ester **24** and subsequent reduction with LAH afforded the alcohol **36** in good yield (Scheme 5). The primary alcohol **36** was then oxidized and subjected to Wittig reaction to furnish one of the cross-metathesis precursors **37** in excellent yield. Delightfully, exposure of the alkene **37** to the key cross-metathesis reaction with known alkene partner **38**[21] in the presence of Grubbs' second generation catalyst (**G-II**) delivered our desired intermediate **39** as the major isomer along with some undesired dimerised product. Hydrogenation of intermediate **39** gave the saturated intermediate



Scheme 5 *Reagents and conditions*: (a) H_2, Pd/C, EtOH, rt, 2 h, 89%; (b) $LiAlH_4$, Et_2O, 0 °C, 15 min, 82%; (c) i) PCC, CH_3COONa, 4 Å MS, CH_2Cl_2, 0 °C; ii) Ph_3PCH_3Br, KO^{t}Bu, THF, 0 °C, 78% (for two steps); (d) **38**, **G-II** 5 mol%, toluene, 110 °C, 6 h; (e) H_2, Pd/C, EtOH, rt, 2 h, 42% (for two steps).

40 in overall 42% yield from alkene **37**. The low yield in the cross-metathesis reaction made us think about an alternative strategy to increase the efficiency of the coupling step. Our prior experience in applying Julia–Kocienski olefination[22] in the formal total synthesis of palmerolide A[10b] came in handy to be utilized in the construction of the key intermediate **39**.

Thus, the alcohol **36** was converted into the sulfone **42**, required for the key Julia–Kocienski olefination, in a couple of steps using a Mitsunobu reaction with 1-phenyl-1*H*-tetrazole-5-thiol[23] **41**, followed by oxidation of the resultant sulfide (Scheme 6). We were delighted to see the smooth proceeding of the Julia–Kocienski olefination between sulfone **42** and the known aldehyde **43**[24] to furnish the key intermediate **39** in high yield. Having the alkene **39** in appreciable quantity, we then looked at the hydrogenation and lactonization. Hydrogenation and selective removal of vicinal silyl ethers proceeded to afford the diol **44**, which on oxidative cleavage in the presence of silica supported $NaIO_4$ followed by Horner–Wadsworth–Emmons reaction furnished the *trans* α,β-unsaturated ester **45** in 64% yield along with the minor *cis*-isomer. The *trans* α,β-unsaturated ester **45**, on hydrolysis as well as removal of the secondary silyl ether with tetrabutyl ammonium fluoride at elevated temperature, provided the hydroxy acid **30** thereby setting the stage for the key lactonisation step. The lactonisation of the hydroxy acid **30** was accomplished efficiently utilizing the Yamaguchi protocol to afford the macrolactone, which upon cleavage of the acetonide with trifluoroacetic acid[6f] furnished (–)-cladospolide A **1**. The spectral data of synthetic (–)-cladospolide A **1** matched with



Scheme 6 *Reagents and conditions*: (a) **41**, DIAD, PPh_3, THF, –20 °C, 92%; (b) $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$, 30% H_2O_2, EtOH, rt, 88%; (c) **43**, LiHMDS, THF, –78 °C, 83%; (d) H_2, Pd/C, EtOH, rt, 2 h, 84%; (e) TBAF (1 M sol^n in THF), THF, 0 °C, 2 h, 80%; (f) i) silica supp. $NaIO_4$, CH_2Cl_2, 0 °C, 1 h; ii) $(OEt)_2P(O)CH_2COOEt$, LiCl, DIPEA, THF, 6 h, 64% (for two steps); (g) LiOH, THF–MeOH–H_2O, 4 h, 93%; (h) TBAF (1 M sol^n in THF), THF, 55 °C, 81%; (i) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, 2 h, then DMAP, toluene, reflux, 8 h, 71%; (j) TFA, CH_3CN–H_2O, 0 °C, 1 h, 65%.

that of the natural isomer in all aspects and thus a total synthesis of (–)-cladospolide A **1** has been successfully accomplished.

Synthesis of (–)-cladospolide B and *iso*-cladospolide B

After the successful synthesis of (–)-cladospolide A **1**, we planned to synthesize other members of this family and decided to implement this general strategy for the syntheses of this class of natural products. Therefore, taking the different stereochemical aspects of the congeners of this family into consideration, we anticipated that cladospolide B **2** could be synthesized utilizing a similar strategy involving Julia–Kocienski olefination and macrolactonization as pivotal reactions starting from commercially available L-(+)-tartrate. As per our retrosynthetic analysis, the macrolide **2** could be easily obtained from the hydroxy acid **46** through Yamaguchi macrolactonization (Fig. 6). The seco acid **46** could be traced back to compound **47** involving Wittig reaction and compound **47** is expected to be obtained from the intermediate **48**. Here, we visualized that the key intermediate **48** could be constructed by Julia–Kocienski olefination between sulfone **49** and aldehyde **50**. Sulfone **49** could be easily derived from commercially accessible L-(+)-tartaric acid ester in a few steps.

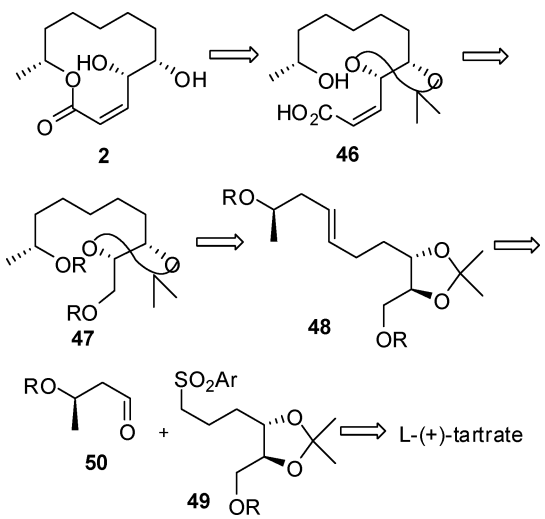
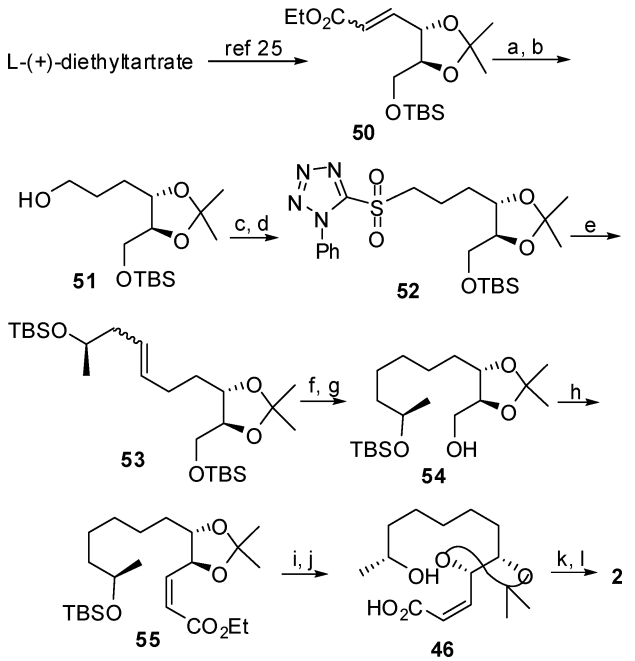


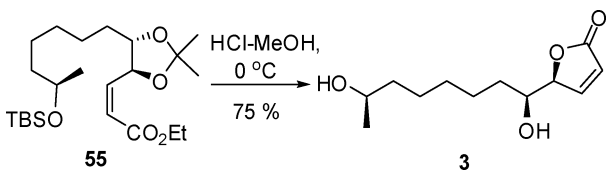
Fig. 6 Retrosynthetic analysis of cladospolide B.

Our journey for the synthesis of (–)-cladospolide B began with the conversion of L-(+)-diethyltartrate to the known α,β-unsaturated ester **50** in a sequence of steps (Scheme 7).[25] Ester **50**, upon catalytic hydrogenation and LAH reduction, afforded alcohol **51** in good yield. Subsequently, alcohol **51** was converted into the sulfone **52** in a couple of steps using Mitsunobu reaction with 1-phenyl-1*H*-tetrazole-5-thiol **41**, followed by oxidation of the resultant sulfide. The pivotal Julia–Kocienski olefination between sulfone **52** and the aldehyde **43** in the presence of LiHMDS proceeded smoothly to provide **53** as an inseparable mixture of *E* and *Z* isomers in the ratio of 2.7 : 1 in 84% yield. However, the mixture of alkenes **53** was easily transformed into alcohol **54** as a single isomer, by catalytic hydrogenation and selective removal of the primary silyl ether with TBAF at 0 °C. Oxidation of the alcohol **54** followed by Wittig reaction with ethyl(triphenylphosphoranylidene) acetate at lower tempetature[6f] furnished the desired *cis* α,β-unsaturated ester **55** as the major



Scheme 7 *Reagents and conditions*: (a) H_2/Pd-C, EtOH, 95%; (b) $LiAlH_4$, Et_2O, 0 °C, 88%; (c) **41**, PPh_3, DIAD, THF, –20 °C, 95%; (d) $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$, 30% H_2O_2, EtOH, rt, 72%; (e) **43**, LiHMDS, THF, –78 °C, 84%; (f) H_2/Pd-C, EtOH, 93%; (g) TBAF, THF, 0 °C, 94%; (h) i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, –78 °C; ii) $Ph_3PCHCOOEt$, MeOH, –78 °C, 65% (for two steps); (i) LiOH, THF–MeOH–H_2O, 75%; (j) TBAF, THF, 55 °C, 83%; (k) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, then DMAP, toluene, reflux, 60%; (l) TFA, CH_3CN–H_2O, 62%.

isomer in 65% yield. The saponification of the *cis* ester **55** with LiOH afforded the free acid, which upon deprotection of the secondary TBS ether resulted in the key hydroxy acid **46** in moderate yield. The seco acid **46** was successfully cyclised using Yamaguchi protocol to lactone, which upon deprotection afforded cladospolide B **2** in 62% yield. The spectral data of synthetic **2** matched with that reported earlier,[6b] thus confirming the completion of a total synthesis of cladospolide B. Accomplishment of total synthesis of *iso*-cladospolide B **3** was achieved in one step from *cis* α,β-unsaturated ester **55**, by acidic treatment (Scheme 8).



Scheme 8 Synthesis of *iso*-cladospolide B.

Synthesis of (+)-cladospolide C

Successful exploitation of our designed strategy to the total synthesis of cladospolide B **2** and *iso*-cladospolide B **3**, took us to extending the same strategy toward the synthesis of cladospolide C **4** as well. Hence, following our unified strategy, we anticipated that the twelve membered macrolide cladospolide C **4** could be obtained from open precursor **56** by involving Yamaguchi's protocol (Fig. 7). The hydroxy acid **56** could in turn be synthesised

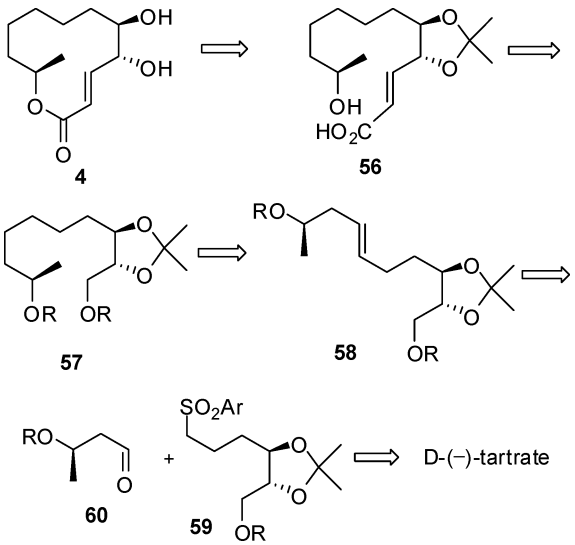


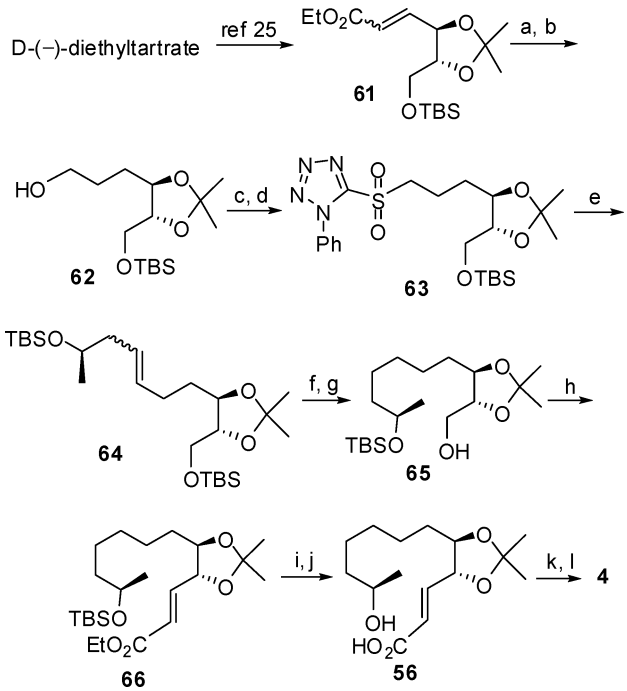
Fig. 7 Retrosynthetic analysis of cladospolide C.

from compound **57** by involving Horner–Wadsworth–Emmons reaction and accordingly, intermediate **58** was expected to deliver compound **57** in a few steps. The key intermediate **58** was thought to be constructed by Julia–Kocienski olefination between sulfone **59** derived from commercially available D-(−)-tartrate and known aldehyde **60**.

So, for the total synthesis of cladospolide C, we embarked on the construction of the required sulfone from D-(−)-diethyltartrate, which in a few steps was converted into α,β-unsaturated ester **61** following the known protocol (Scheme 9).[25] Ester **61**, on hydrogenation followed by reduction with LAH, furnished alcohol **62** which was subsequently transformed into the corresponding sulfone **63** utilizing the well established two step sequence. Exposure of the sulfone **63** to the known aldehyde **43** in the presence of LiHMDS resulted in the formation of the key intermediate **64** in 72% yield as an inseparable mixture of *E* and *Z* isomers favoring *E* in a 2.5 : 1 ratio. Pleasingly, the mixture of alkenes **64**, on hydrogenation followed by deprotection of the primary TBS ether, afforded the alcohol **65** as a single isomer. Oxidation of alcohol **65** under Swern conditions followed by Horner–Wadsworth–Emmons reaction resulted in the *trans* α,β-unsaturated ester **66** in 54% yield along with a small amount of its *cis* isomer. Saponification of the ester **66** and the cleavage of the secondary TBS ether went efficiently to furnish the seco acid **56** in excellent yield. The acid **56** was pleasingly cyclised under Yamaguchi conditions to the desired lactone, which upon deprotection under TFA conditions afforded cladospolide C **4** in 67% yield.

Conclusions

In conclusion, we have successfully achieved the total syntheses of cladospolides A, B, C and *iso*-cladospolide B utilising a unified and efficient strategy. The strategy involves a Julia–Kocienski olefination between either a sugar or a tartaric acid ester-derived sulfone and a siloxy aldehyde to construct the pivotal alkene intermediate and a Yamaguchi lactonization to make the twelve-membered cycle.



Scheme 9 *Reagents and conditions*: (a) H_2/Pd–C, EtOH, 82%; (b) $LiAlH_4$, Et_2O, 0 °C, 95%; (c) **41**, PPh_3, DIAD, THF, –20 °C, 92%; (d) $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$, 30% H_2O_2, EtOH, rt, 76%; (e) **43**, LiHMDS, THF, –78 °C, 72%; (f) H_2/Pd–C, EtOH, 90%; (g) TBAF, THF, 0 °C, 94%; (h) i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, –78 °C; ii) $(OEt)_2P(O)CH_2COOEt$, LiCl, DIPEA, THF, 54% (for two steps); (i) LiOH, THF–MeOH–H_2O, 79%; (j) TBAF, THF, 55 °C, 83%; (k) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, then DMAP, toluene, reflux, 63%; (l) TFA, CH_3CN–H_2O, 67%.

Experimental

General experimental section is provided in the ESI.†

Experimental procedures and spectral data for selected compounds

(*E*)-((*R*)-Hept-6-en-2-yl) 3-((4*R*,5*S*)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)acrylate (7). To a stirred solution of ester **13** (0.2 g, 0.88 mmol) in a mixture of THF (12 mL), MeOH (3 mL) and water (3 mL) was added 1 M solution of lithium hydroxide (1.8 mL). The reaction mixture was stirred for 1 h at rt. The aqueous phase was washed with Et_2O, acidified with 10% aq. citric acid and extracted with EtOAc (3 × 10 mL). The combined organic phase was washed with brine solution, dried over Na_2SO_4 and concentrated in *vacuo*. The crude acid was used for the next step without further purification.

To a stirred solution of crude acid **9** (0.140 g, 0.71 mmol) in toluene (5 mL) was added DMAP (0.097 g, 0.78 mmol), (*R*)-hept-6-en-ol **8** (0.097 g, 0.85 mmol) and Et_3N (0.12 mL, 0.852 mmol). Then 2,4,6-trichloroacetylchloride (0.173 g, 0.71 mmol) was added at 0 °C and the resulting mixture was stirred at room temperature for 1 h. The mixture was filtered through a pad of Celite, the insoluble residue was carefully washed with Et_2O, the combined organic parts were concentrated and purified by flash column chromatography (3% ethyl acetate in hexanes) to afford the triene ester **7** (0.12 g, 46% for two steps). R_f 0.7 (3% ethyl acetate in hexanes); $[\alpha]_D^{20}$ +20.7 (*c* 0.30, $CHCl_3$); IR (neat): 3080, 2984, 2936, 1719, 1378, 1216, 1050, 987, 862 cm^{-1}; ^1H NMR

(400 MHz, $CDCl_3$): δ 6.76 (dd, J = 15.5, 5.8 Hz, 1H), 6.04 (dd, J = 15.5, 1.5 Hz, 1H), 5.88–5.62 (m, 2H), 5.36 (d, J = 17.4, 1H), 5.27 (d, J = 10.7, 1H), 5.14–4.9 (m, 3H), 4.76–4.70 (m, 2H), 2.06 (q, J = 7.3, 2H), 1.56 (s, 3H), 1.42 (s, 3H), 1.24 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 143.3, 138.6, 133.6, 123.4, 119.4, 114.9, 109.7, 79.9, 77.7, 71.2, 35.5, 33.6, 27.9, 25.5, 24.8, 20.1; HRMS (ESI) calcd. for $C_{17}H_{26}O_4SiNa$ m/z 317.1729, found m/z 317.1730

(3*S*,4*R*,*E*)-7-((*R*)-Hept-6-en-2-yloxy)-7-oxohepta-1,5-diene-3,4-diyl diacetate (14). A solution of triene ester **7** (0.02 g, 0.068 mmol) in CH_3CN (5 mL) was treated with cupric chloride (0.023 g, 0.136 mmol). After stirring for 3 h at rt, the reaction mixture was diluted with water and extracted with ethyl acetate (3 × 20 mL). The organic layer was separated, dried over anhydrous Na_2SO_4, concentrated and without further purification was carried through to the next step.

To a stirred solution of the trienediol **7a** (0.045 g, 0.18 mmol) in pyridine (1 mL) was added acetic anhydride (0.05 g, 0.53 mmol) and a catalytic amount of DMAP. After 2 h, the solvent was evaporated *in vacuo* and was purified to afford (1% ethyl acetate in hexanes) trienediacetate **14** as a colorless liquid (0.48 g, 79%). R_f 0.5 (6% ethyl acetate in hexanes); $[\alpha]_D^{20}$ +24.0 (c 0.25, $CHCl_3$); IR (neat): 3026, 2936, 1747, 1716, 1374, 1221, 1126, 1031, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.82 (dd, J = 15.9, 5.5 Hz, 1H), 6.01 (dd, J = 15.9, 1.8 Hz, 1H), 5.84–5.74 (m, 2H), 5.61–5.89 (m, 1H), 5.50–5.46 (m, 1H), 5.39–5.32 (m, 2H), 5.04–4.95 (m, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.09–2.04 (m, 2H), 1.69–1.37 (m, 2H), 1.25 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 169.9, 165.4, 140.1, 138.5, 131.2, 124.7, 120.2, 114.4, 74.4, 72.8, 71.6, 35.5, 33.6, 24.8, 21.1, 21.0, 20.1; HRMS (ESI) calcd. for $C_{18}H_{26}O_6SiNa$ m/z 361.1627, found m/z 361.1605.

(*R*)-Hept-6-en-2-yl 3-((4*R*,5*S*)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)propanoate (17). To a stirred solution of ester **16** (0.2 g, 0.884 mmol) in a mixture of THF (12 mL), MeOH (3 mL) and water (3 mL) was added 1 M solution of lithium hydroxide (1.8 mL). The reaction mixture was stirred for 1 h at rt. The aqueous phase was washed with Et_2O, acidified with 10% aq. citric acid and extracted with EtOAc (3 × 15 mL). The combined organic phase was washed with brine solution, dried over Na_2SO_4 and concentrated in *vacuo*. The crude acid was used for the next step without further purification.

To a stirred solution of the above crude acid (0.11 g) in CH_2Cl_2 (10 mL) was added DMAP (0.216 g, 1.77 mmol), (*R*)-hept-6-en-ol **8** (0.101 g, 0.884 mmol). Then DCC (0.273 g, 1.33 mmol) was added at rt and the resulting mixture was stirred at room temperature for 3 h. The mixture was filtered through a Celite pad, the insoluble residue was carefully washed with CH_2Cl_2, the combined organic washings were concentrated and purified by flash column chromatography (5% ethyl acetate in hexanes) to afford diene ester **45** (0.11 g, 42% for two steps). R_f 0.5 (6% ethyl acetate in hexanes); $[\alpha]_D^{20}$ +11.7 (c 0.41, $CHCl_3$); IR (neat): 2984, 2938, 1724, 1380, 1251, 1176, 1059, 925, 867 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.86–5.79 (m, 2H), 5.35–5.27 (m, 2H), 5.29–4.89 (m, 3H), 4.52 (t, J = 7.2 Hz, 1H), 4.21–4.12 (m, 1H), 2.65–2.33 (m, 2H), 2.05 (q, J = 6.3 Hz, 2H), 1.78–1.58 (m, 6H), 1.48 (s, 3H), 1.36 (s, 3H), 1.20 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 138.3, 133.9, 118.5, 114.7, 108.3, 79.5, 77.1, 70.8, 35.2, 33.4, 31.1, 28.1, 26.0, 25.5, 24.6, 19.9; HRMS (ESI) calcd. for $C_{17}H_{28}O_4Si$ Na m/z 319.1885, found m/z 319.1899.

(3*S*,4*R*)-7-((*R*)-Hept-6-en-2-yloxy)-7-oxohept-1-ene-3,4-diyl diacetate (18). To a solution of diene ester **17** (0.1 g, 0.34 mmol) in CH_3CN (10 mL) was added cupric chloride (0.58 g, 0.68 mmol). After stirring for 2 h at RT, the reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was separated, dried over anhydrous Na_2SO_4, concentrated and used for the next step without further purification.

A solution of crude trienediol in pyridine (1 mL) was treated with acetic anhydride (0.122 g, 1.33 mmol) and a catalytic amount of DMAP. After 2 h the reaction mixture was evaporated to make a slurry and it was purified (3% ethyl acetate in hexanes) to afford the diacetate **18** (78% for two steps). R_f 0.2 (10% ethyl acetate in hexanes); $[\alpha]_D^{20}$ +5.2 (c 0.50, $CHCl_3$); IR (neat): 2928, 2256, 1736, 1641, 1446, 1229, 1050, 911, 735, 649 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.84–5.74 (m, 2H), 5.42–5.30 (m, 3H), 5.07–4.87 (m, 4H), 2.39–2.23 (m, 2H), 2.08 (s, 3H), 2.06 (s, 3H) 2.12–2.03 (m, 1H), 1.64–1.35 (m, 2H), 1.20 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 170.5, 170.0, 138.4, 131.8, 119.6, 114.8, 74.9, 73.0, 71.2, 35.3, 33.5, 30.6, 29.7, 24.7, 24.5, 21.1, 21.0, 20.0; HRMS (ESI) calcd. for $C_{18}H_{28}O_6Si$ Na m/z 363.1784, found m/z 363.1794.

(*E*)-((*R*)-Hept-6-en-2-yl) 3-((4*R*,5*S*)-5-((*Z*)-3-(allyloxy)prop-1-enyl)-2,2-dimethyl-1,3-dioxolan-4-yl)acrylate (21). To a stirred solution of α,β-unsaturated ester **28** (0.5 g, 1.7 mmol) in a mixture of THF (34 mL), MeOH (8.5 mL) and water (8.5 mL) was added 1 M solution of lithium hydroxide (3.5 mL). The reaction mixture was stirred for 1 h at room temperature. The aqueous phase was washed with Et_2O, acidified with 10% aq. citric acid and extracted with EtOAc (3 × 20 mL). The combined organic phase was washed with brine solution, dried over Na_2SO_4 and concentrated in *vacuo*. The crude acid was used for the next step without further purification.

To the mixture of above crude acid (1.7 mmol), (*R*)-hept-6-en-ol **8** (0.194 g, 1.7 mmol) and DMAP (0.207 g, 1.7 mmol) in CH_2Cl_2 (15 mL) was added a solution of DCC (0.421 g, 1.2 mmol) in CH_2Cl_2 (5 mL) at room temperature. The resulting mixture was stirred for 5 h. The mixture was filtered through a pad of Celite, the insoluble residue was carefully washed with CH_2Cl_2, the combined organic washings were concentrated and purified by flash column chromatography (5% ethyl acetate in hexanes) to afford ester **21** (0.180 g, 35% for two steps). R_f 0.5 (5% ethyl acetate in hexanes); $[\alpha]_D^{20}$ +38.2 (c 0.57, $CHCl_3$); IR (neat): 2926, 1718, 1380,1164, 916 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.76 (dd, J = 15.9, 6.1 Hz, 1H), 6.23 (dd, J = 15.8, 1.2 Hz, 1H), 5.96–5.86 (m, 1H), 5.84–5.74 (m, 2H), 5.54–5.48 (m, 1H), 5.32–5.19 (m, 2H), 5.08–5.04 (m, 1H), 5.04–4.93 (m, 3H), 4.75–4.71 (m, 1H), 4.07–4.06 (m, 2H), 3.99–3.96 (m, 2H), 2.60 (q, J = 7.3 Hz, 2H), 1.68–1.48 (m, 2H), 1.46–1.37 (m, 2H), 1.55 (s, 3H), 1.41 (s, 3H), 1.23 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 143.4, 138.6, 134.6, 128.4, 123.5, 117.5, 114.9, 109.7, 77.8, 74.7, 71.4, 71.2, 66.0, 35.5, 33.6, 28.0, 25.5, 24.8, 20.1; HRMS (ESI) calcd. for $C_{21}H_{32}O_5Na$ m/z 387.2147, found m/z 387.2126.

General procedure for Julia–Kocienski olefination reaction

To a solution of sulfone (1 mmol) and aldehyde (1.4 mmol) in anhydrous THF (13 mL) was added a 0.5 M solution of freshly prepared LiHMDS (3 mmol) [prepared by adding 1.6 M solution of *n*-BuLi (3 mmol) in hexane dropwise over a period of 5 min to a pre cooled solution of HMDS (3.1 mmol) in THF at –20 °C and then stirring at –10 °C for 30 min] dropwise at –78 °C. After stirring for 20 min at the same temp., the reaction was quenched with water and the aqueous part was extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude residue was purified by silica gel column chromatography.

General procedure for hydrogenation of alkene

To a solution of alkene (1 mmol) in EtOH (11 mL) was added 5% Pd–C (30 mg) and the resulting mixture was stirred for 2 h. The reaction mixture was filtered through a pad of celite, the filtrate was concentrated in *vacuo* and was purified by silica gel column chromatography.

General procedure for the removal of TBS protection

To a solution of TBS ether (1 mmol) in THF (30 mL) at 0 °C was added tetrabutyl ammonium fluoride (2 mmol, 1 M sol^n in THF) and the mixture was stirred at the same temperature for 2 h. The solvent was evaporated, the residue was adsorbed into silica gel and purified by column chromatography.

(*R*)-5-((4*S*,5*S*)-5-((*R*,*E*)-6-(*tert*-Butyldimethylsilyloxy)hept-3-enyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecane (39). Following the general procedure for the Julia–Kocienski olefination, to a solution of sulfone **42** (100 mg, 0.15 mmol) and aldehyde **43** (44 mg, 0.21 mmol) in anhydrous THF (2 mL) was added a 0.5 M solution of freshly prepared LiHMDS (0.81 mL, 0.45 mmol) dropwise at –78 °C. The crude residue was purified by silica gel column chromatography (1% ethyl acetate in hexanes) to afford compound **39** (80 mg, 83%) as a colourless oil. R_f 0.28 (2% ethyl acetate in hexanes); $[\alpha]_D^{20}$ –27.6 (*c* 0.50, $CHCl_3$); IR (neat): 3020, 2931, 1657, 1045 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.45–5.42 (m, 2H), 4.09–4.05 (m, 3H), 3.80–3.74 (m, 1H), 3.66 (dd, *J* = 11.3, 4.8 Hz, 1H), 2.13–2.03 (m, 4H), 1.63–1.53 (m, 2H), 1.40 (s, 3H), 1.31 (s, 3H), 1.10 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.86 (s, 9H), 0.11(s, 3H), 0.08 (s, 3H), 0.06 (s, 6H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.0, 127.2, 107.8, 77.4, 76.4, 72.6, 68.8, 65.3, 43.0, 30.1, 29.1, 28.4, 26.0, 25.96, 25.90, 23.3, 18.4, 18.1, –3.5, –4.5, –4.6, –4.7, –5.3, –5.4.

(*R*)-5-((4*S*,5*S*)-5-((*R*)-6-(*tert*-Butyldimethylsilyloxy)heptyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecane (40). Following the general procedure for hydrogenation of alkene, a solution of compound **39** (2.25 g, 3.64 mmol) in EtOH (60 mL) was treated with 5% Pd–C (110 mg). The crude material was purified by silica gel column chromatography (2% ethyl acetate in hexanes) resulting in saturated compound **40** (1.90 g, 84%) as a colourless oil. R_f 0.26 (2% ethyl acetate in hexanes); $[\alpha]_D^{20}$ –29.7 (*c* 0.66, $CHCl_3$); IR (neat): 3021, 2930, 2858, 2640, 1380, 1044 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.08–4.04 (m, 2H), 3.79–3.73 (m, 3H), 3.68–3.64 (m, 1H), 1.65–1.24 (complex m, 10H), 1.39 (s, 3H), 1.30 (s, 3H), 1.09 (d, *J* = 6.1 Hz, 3H), 0.90 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), 0.05 (s, 6H), 0.037 (s, 3H), 0.033(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 107.7, 76.6, 72.6, 68.5, 65.3, 39.6, 30.0, 29.8, 28.4, 26.1, 26.0, 25.96, 25.90, 23.8, 18.4, 18.2, 18.1, –3.5, –4.4, –4.7, –4.8, –5.3,–5.4; HRMS (ESI): calcd for $C_{32}H_{70}O_5Si_3Na$ *m*/*z* 641.4429, found *m*/*z* 641.4412.

(*R*)-1-((4*R*,5*S*)-5-((*R*)-6-(*tert*-Butyldimethylsilyloxy)heptyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethane-1,2-diol (44). Following the general procedure for the removal of TBS protection, a solution of compound **40** (300 mg, 0.48 mmol) in THF (15 mL) at 0 °C was treated with tetrabutyl ammonium fluoride (1.9 mL, 1 M sol^n in THF). Silica gel column chromatography (35% ethyl acetate in hexanes) afforded the diol **44** (153 mg, 80%) as a thick liquid. R_f 0.32 (50% ethyl acetate in hexanes); $[\alpha]_D^{20}$ –9.4 (*c* 0.50, $CHCl_3$); IR (neat): 3431, 2931, 1461, 1374, 1256, 1047, 911 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.20–4.15 (m, 1H), 3.94 (dd, *J* = 8.2, 5.8 Hz, 1H), 3.83–3.68 (m, 4H), 2.69 (bs, 2H), 1.69–1.65 (m, 1H), 1.59–1.42 (m, 1H), 1.39 (s, 3H), 1.32 (s, 3H), 1.37–1.24 (complex m, 8H), 1.09 (d, *J* = 6.1 Hz, 3H), 0.86 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.2, 78.1, 77.9, 69.7, 68.8, 64.8, 39.8, 29.9, 29.5, 28.2, 26.8, 26.0, 25.9, 25.7, 23.9, 18.3, –4.2, –4.5; HRMS (ESI): calcd for $C_{20}H_{42}O_5SiNa$ *m*/*z* 413.2699, found *m*/*z* 413.2714.

***tert*-Butyl(((4*S*,5*S*)-5-((*R*)-6-(*tert*-butyldimethylsilyloxy)-heptyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)dimethylsilane (53a).** Following the general procedure for the Julia–Kocienski olefination, to a solution of sulfone **52** (2.4 g, 4.90 mmol) and aldehyde **43** (1.6 g, 8.33 mmol) in anhydrous THF (50 mL) was added a 0.5 M solution of freshly prepared LiHMDS (25.5 mL, 12.74 mmol) dropwise at –78 °C. The crude material was purified by silica gel column chromatography (1% ethyl acetate in hexanes) to afford compound **53** (1.9 g, 84%) as a colourless oil as an inseparable mixture of *E* and *Z* isomers in a 2.7 : 1 ratio. R_f 0.28 (2% ethyl acetate in hexanes); IR (neat): 2985, 1742, 1374, 1242, 1047 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.44–5.40 (m, 2H), 3.91–3.86 (m, 1H), 3.82–3.72 (m, 2H), 3.69–3.65 (m, 2H), 2.21–2.04 (m, 4H), 1.69–1.63 (m, 2H), 1.39 (s, 3H), 1.36 (s, 3H), 1.09 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H), 0.036 (s, 6H), 0.034 (s, 3H).

Following the general procedure for hydrogenation of alkene, a solution of compound **53** (170 mg, 0.35 mmol) in EtOH (10 mL) was treated with 10% Pd–C (10 mg). Purification by silica gel column chromatography (2% ethyl acetate in hexanes) resulted in compound **53a** (160 mg, 93%) as a colourless oil. R_f 0.26 (2% ethyl acetate in hexanes); $[\alpha]_D^{20}$ –21.1 (*c* 0.66, $CHCl_3$); IR (neat): 2932, 2859, 2640, 1378, 1255, 1086 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.90–3.85 (m, 1H), 3.76–3.72 (m, 2H), 3.70–3.64 (m, 2H), 1.54–1.22 (complex m, 10H), 1.40 (s, 3H), 1.37 (s, 3H), 1.10 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.06 (s, 6H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.2, 81.1, 78.7, 68.6, 63.7, 39.6, 33.4, 29.8, 27.3, 26.9, 26.0, 25.8, 25.6, 23.7, 18.3, 18.1, –4.4, –4.7, –5.40, –5.46; HRMS (ESI): calcd for $C_{25}H_{54}O_4Si_2Na$ *m*/*z* 497.3458, found *m*/*z* 497.3466.

((4*S*,5*S*)-5-((*R*)-6-(*tert*-Butyldimethylsilyloxy)heptyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (54). Following the general procedure for removal of TBS protection, a solution of compound

53a (150 mg, 0.31 mmol) in THF (5 mL) at 0 °C was treated with TBAF (0.28 mL, 1 M sol^{n} in THF). Purification by silica gel column chromatography (30% ethyl acetate in hexanes) provided alcohol **54** (110 mg, 94%) as a thick liquid. R_f 0.32 (50% ethyl acetate in hexanes); $[\alpha]_D^{20}$ –22.0 (*c* 0.83, $CHCl_3$); IR (neat): 3435, 3019, 2934, 2862, 1216, 1020 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.89–3.84 (m, 2H), 3.81–3.71 (m, 2H), 3.61–3.57 (m, 1H), 1.97 (t, 1H), 1.58–1.25 (complex m, 10H), 1.59–1.42 (m, 1H), 1.41 (s, 3H), 1.41 (s, 3H), 1.10 (d, J = 6.1 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.5, 81.4, 77.3, 68.5, 62.0, 39.5, 33.0, 29.7, 27.3, 26.9, 25.9, 25.8, 25.6, 23.7, 18.1, –4.4, –4.7; HRMS (ESI): calcd for $C_{19}H_{41}O_4Si$ m/z 361.2774, found m/z 361.2780.

***tert*-Butyl(((4*R*,5*R*)-5-((*R*)-6-(*tert*-butyldimethylsilyloxy)-heptyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)dimethylsilane (64a).** Following the general procedure for the Julia–Kocienski olefination, to a solution of sulfone **63** (520 mg, 1.04 mmol) and aldehyde **43** (356 mg, 1.76 mmol) in anhydrous THF (11 mL) was added a 0.5 M solution of freshly prepared LiHMDS (5.4 mL, 2.70 mmol) dropwise at –78 °C. The crude residue was purified by silica gel column chromatography (1% ethyl acetate in hexanes) to afford compound **64** (350 mg, 72%) as a colourless oil as an inseparable mixture of *E* and *Z* isomers in a 2.5 : 1 ratio. R_f 0.28 (2% ethyl acetate in hexanes); IR (neat): 2930, 2858, 1737, 1378, 1256, 1125 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.44–5.40 (m, 2H), 3.88 (dt, J = 7.3, 4.0 Hz, 1H), 3.83–3.72 (m, 2H), 3.69–3.65 (m, 2H), 2.20–2.03 (m, 4H), 1.68–1.61 (m, 2H), 1.40 (s, 3H), 1.36 (s, 3H), 1.10 (d, J = 5.8 Hz, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H), 0.037 (s, 6H), 0.034 (s, 3H).

Following the general procedure for hydrogenation of alkene, a solution of compound **64** (350 mg, 0.74 mmol) in EtOH (20 mL) was treated 10% Pd–C (53 mg). The crude material was purified by silica gel column chromatography (2% ethyl acetate in hexanes) resulting in compound **64a** (320 mg, 90%) as a colourless oil. R_f 0.26 (2% ethyl acetate in hexanes); $[\alpha]_D^{20}$ –17.0 (*c* 0.88, $CHCl_3$); IR (neat): 2931, 2858, 1472, 1377, 1255, 1085 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.87 (dt, J = 7.5, 2.9 Hz, 1H), 3.76–3.72 (m, 2H), 3.70–3.65 (m, 2H), 1.59–1.26 (complex m, 10H), 1.40 (s, 3H), 1.37 (s, 3H), 1.10 (d, J = 5.8 Hz, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.06 (s, 6H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.2, 81.1, 78.7, 68.5, 63.7, 39.6, 33.5, 29.8, 27.3, 26.9, 26.1, 25.8, 25.7, 23.7, 18.3, 18.1, –4.4, –4.7, –5.40, –5.46; HRMS (ESI): calcd for $C_{25}H_{54}O_4Si_2Na$ m/z 497.3458, found m/z 497.3474.

((4*R*,5*R*)-5-((*R*)-6-(*tert*-Butyldimethylsilyloxy)heptyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (65). Following the general procedure for removal of TBS protection, to a solution of compound **64a** (320 mg, 0.67 mmol) in THF (11 mL) at 0 °C was added tetrabutyl ammonium fluoride (0.60 mL, 1 M sol^{n} in THF). The crude material was purified by column chromatography (35% ethyl acetate in hexanes) to provide alcohol **65** (230 mg, 94%) as a thick liquid. R_f 0.32 (50% ethyl acetate in hexanes); $[\alpha]_D^{20}$ 10.4 (*c* 0.83, $CHCl_3$); IR (neat): 3403, 3018, 2932, 2857, 1216, 1020 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.88 (dt, J = 7.9, 3.9 Hz, 1H), 3.80 (ddd, J = 5.1, 3.0 Hz, 1H), 3.76–3.70 (m, 2H), 3.61–3.55 (m, 1H) 1.88 (dd, J = 5.1, 5.1 Hz, 1H), 1.57–1.25 (complex m, 10H), 1.41 (s, 3H), 1.40 (s, 3H), 1.10 (d, J = 6.1 Hz, 3H), 0.87 (s, 9H), 0.039 (s, 3H), 0.035 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.5, 81.5, 77.3, 68.5, 61.9, 39.5, 33.0, 29.7, 27.3, 26.9, 25.9, 25.8, 25.6, 23.7, 18.0, –4.4, –4.7; HRMS (ESI): calcd for $C_{19}H_{41}O_4Si$ m/z 361.2774, found m/z 361.2779.

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