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Asymmetric synthesis of cytospolides C and D through successful exploration of stereoselective Julia–Kocienski olefination and Suzuki reaction followed by macrolactonization

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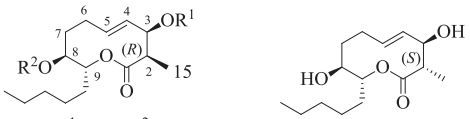
ABSTRACT

Asymmetric total synthesis of two naturally occurring nonenolides cytospolides C (**3**) and D (**4**) was accomplished through successful exploration of stereoselective Julia–Kocienski (JK) olefination reaction for the construction of the required *E*-olefinic geometry (C_4–C_5) present in the target molecule. In an alternative approach Suzuki cross coupling reaction of an *E*-vinylic bromide and an alkylborane species was also efficiently applied to access the macrolactonization precursor. Late stage lactonization through Mitsunobu cyclization afforded the target molecules in good yield.

1. Introduction

The genus *Cytospora sp.* is found to be a rich source of biologically active secondary metabolites such as antibiotic grahamimycins,[1] antibacterial compound cytoskyrins[2] and cytotoxic material such as cytosporinols.[3] In 2011 five new nonanolides cytospolides A–E (**1**–**5**)[4b] have been isolated from endophytic fungus *Cytospora* sp. isolated from *Ilex canariensis* Poir (Aquifoliaceae, Aquifoliales), an evergreen shrub found mainly in the island of Gomera, Spain. cytospolides A–E (Fig. 1) have ten-membered ring lactone (nonanolide) as its core structural unit and the carbon skeleton contains 15 carbon atoms with a unique C-2 methyl substitution (Fig. 1). In general nonanolides are categorized into two structural families: (i) with a C-9 methyl substitution and (ii) having higher alkyl substitution at C-9. Cytospolides,[4] herbarumins,[5] pinolidoxin,[6] seimatopolides A and B[7] and achaetolide[8] are few representative examples belong to the second family of nonanolides. The structure of cytospolide-A (**1**) has been established by spectroscopic techniques and the absolute configuration was confirmed by single crystal X-ray analysis. The most likely absolute configuration of cytospolide-A is suggested to be (2*R*,3*R*,8*S*,9*R*) and is further confirmed by solid state CD/TD-DFT analysis. In the same year cytospolides F–Q[4a] (out of which 10 compounds are nonanolide) and decytospolides A and B (having δ-lactone moiety) was isolated from the same source and also structurally characterized.



1, R^1 = Ac, R^2 = H
2, R^2 =H, R^2 =Ac
3, R^1=R^2= Ac
4, R^1=R^2= H

5

Fig. 1. Cytospolides A–E (**1**–**5**).

It was noteworthy that inversion of the absolute configuration at C-2 from (2*R*) of **4** to (2*S*) of **5** leads to a surprising increase in cytotoxic activity. In a cytotoxic in vitro bioassay **1**, **3**, and **4** showed no activity against the A-549 cell line at 50.0 μg/mL, whereas **2** and **5** displayed strong cytotoxic activity with IC_{50} values of 5.15 and 7.09 μg/mL, respectively. Thus it is evident that the 8-*O*-monoacetate and the absolute configuration on C-2 clearly play important roles in the growth inhibition of the tumor line.[4b]

The first asymmetric synthesis of cytospolide-E (*Z*-isomer) was reported by Yadav et al.[9] by applying a late stage ring closing metathesis (RCM) reaction. Later on asymmetric synthesis of the

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cytospolide-E was reported from our group[10] and by Kamal's group[11] by adopting the same late stage RCM strategy, and in both the cases *Z*-cytospolide-E was obtained. The formation of exclusive '*Z*' geometry in all the three reports has been confirmed by extensive ^{1}H NMR analysis. Though the reason for formation of exclusive '*Z*' isomer remains elusive, we can conclude that by adopting a RCM strategy at late stage with the properly substituted terminal olefins '*E*'-cytospolide will be difficult to synthesize. Hence an alternative strategy is very much needed for the total synthesis of the macrolactones belonging to the Cytospolide family.

Recently Kamal's group[11] was successful in achieving the first total synthesis of naturally occurring cytospolide D (**4**), by adopting a stereoselective cross metathesis (CM) reaction (which fixes the required '*E*'-geometry) followed by Yamaguchi macrolactonization method. Recently we have also explored the similar strategy (*E*-selective CM followed by macrolactonization) for the total synthesis of structurally related xyolide and seimatopolide A and B.[12]

The general synthetic strategy to construct the internal olefinic unsaturation in such nonenolides (C_4–C_5 in cytospolides A–E) is mainly centered on successful exploration of RCM/CM as documented in the earlier literature. Among the alternative approaches (without exploration of metathesis) a properly substituted furun surrogate can serve as excellent precursor for such olefinic species as reported by Prasad et al. in their synthesis of seimatopolide A.[13] Where as a disubstituted acetylenic compound also can serve as a potential precursor of such species as evident from the total synthesis of seimatopolide A.[14] The stereoselective cross-metathesis reaction has proven to be an efficient process for the construction of internal *E*-olefins, however its success is often dependant on optimization of coupling partners and judicious catalyst selection. We also argued in the similar line that stereoselective JK-olefination or Suzuki coupling reaction might serve as an excellent alternative for constructing the internal *E*-olefinic unsaturation in cytosploides C and D.

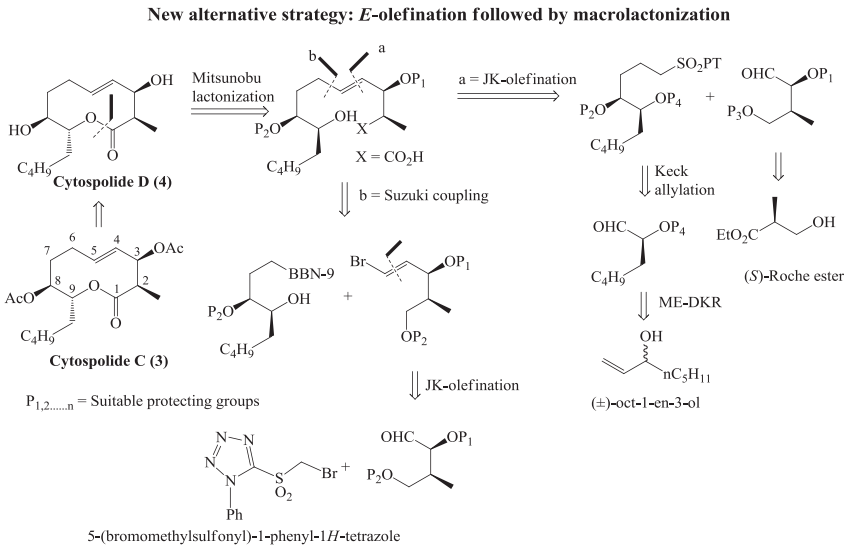
2. Results and discussion

The retrosynthetic disconnection for cytospolide C (**3**) and D (**4**) is outlined below (Scheme 1). We envisioned that as Julia–Kocienski (JK) olefination is known to be very efficient in generating *E*-alkene selectively, the internal double bond between C_4–C_5 can be constructed using a JK-olefination reaction. The crucial ester linkage between C_1–C_9 was planned to be accessed by intramolecular Mitsunobu lactonization (–OH activation through S_N2 inversion) reaction. The sulfone fragment required in JK-olefination was accessed by ME-DKR (metal enzyme combined dynamic kinetic resolution; fixes the C_9 stereocenter) and stereoselective Keck allylation reaction (fixes the C_8 stereocenter) starting from (±)-oct-1-en-3-ol (Scheme 1). Whereas the aldehyde fragment was constructed from CBS mediated stereoselective carbonyl reduction of vinyl ketone, which in turn can be easily accessed from commercially available (*S*)-Roche ester (fixes the C_2–Me stereocenter of the cytospolides).

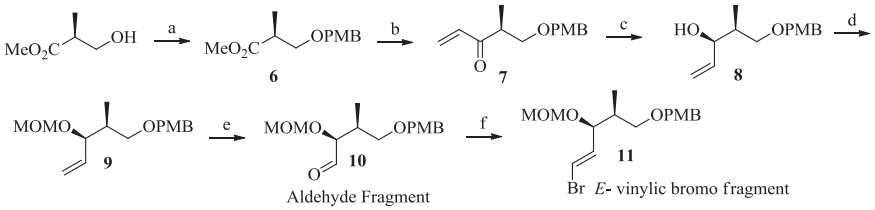
We also propose an alternative approach, which involves successful exploration of Suzuki cross coupling reaction of the properly functionalized (*E*)-vinylic bromide and alkylborane compound for the synthesis of final lactonization precursor (C_5–C_6 bond, Scheme 1). The (*E*)-vinylic bromide was synthesized by adopting a stereoselective JK-olefination reaction from 5-(bromomethylsulfonyl)-1-phenyl-1*H*-tetrazole ($PTSO_2$-CH_2Br). The alkylborane compound, which will be used in the Suzuki coupling reaction, was planned to be synthesized from the same intermediate required to access the sulfone fragment in the previous route.

2.1. Synthesis of the aldehyde 10 and *E*-vinylic bromide fragment 11

The synthetic sequence was initiated from commercially available (*S*)-Roche ester as a chiral pool starting material. Protection of the free hydroxyl group with PMB-imidate afforded compound **6** in 95% yield. The vinyl ketone **7** was synthesized from compound **6** in two steps (formation of the respective Weinreb amide[15] and then coupling with vinylmagnesium bromide) with an overall 88% yield. Compound **7** on CBS reduction[16] afforded compound **8** in 82% yield (dr=12:1). Prior to the CBS reduction, we had also attempted to reduce the crabonyl group in compound **7** by using some achiral hydride sources ($LiAlH_4$, $NaBH_4$ and DIBAL-H) through a substrate controlled approach. But the unusual low selectivity compelled us to adopt the use of a chiral reducing agent. The secondary hydroxy group in **8** was protected as its MOM (methoxymethyl) ether by treatment with diisopropylethylamine (DIPEA) and MOM-Cl (methoxymethyl chloride) affording compound **9** in 90% yield. Lemieux–Johnson oxidative cleavage[17] of compound **9** with OsO_4, NMO followed by treatment with $NaIO_4$ afforded the desired aldehyde **10** in 90% yield (Scheme 2). The aldehyde **10** was next subjected to JK-olefination with 5-(bromomethylsulfonyl)-1-



Scheme 1. Proposed retrosynthetic analysis of cytospolide C and D.



Scheme 2. Synthesis of aldehyde and *E*-vinylic iodide fragment; Reagents and conditions: (a) PMBO(C=NH)CCl_3, CSA, DCM: cyclohexane (1:2), rt, 6 h, 95%; (b) (i) Me–NH(OMe)·HCl, $AlMe_3$, benzene, reflux, 3 h; (ii) CH_2=CHMgBr, THF, −78 °C, 2 h, 88% (overall two steps); (c) (*S*)-CBS (10 mol %), BH_3·DMS, THF, −78 °C to rt, 82%; (d) MOM-Cl, DIPEA, DCM, rt, 4 h, 90%; (e) OsO_4, NMO, THF:water (3:1), $NaIO_4$, rt, 12 h, 90%; (f) KHMDS, PT-SO_2CH_2Br, $MgBr_2$·Et_2O, THF, −78 °C to rt, 1 h, 82%.

phenyl-1*H*-tetrazole (PTSO$_2$-CH_2Br)[18b] in presence of KHMDS at −78 °C using $MgBr_2$·Et_2O as an additive[18a] to afford the (*E*)-vinylic bromide **11** in 82% yield as a major product (*E*:*Z*=12:1). The presence of special additive ($MgBr_2$·Et_2O) is essential to obtain the high '*E*'-selectivity in the compound **11**. It was observed that when aldehyde **10** and PTSO$_2$CH$_2$Br was subjected to JK-olefination reaction without this additive, the compound **11** was obtained with poor selectivity (*E*:*Z*∼1:1). This procedure for synthesizing *E*-vinylic bromide through JK-olefination is very unique and can serve as an alternative for the well explored Takai[19] and Stork–Zhao olefination[20] for the synthesis of stereochemically pure *E*-vinylic halides (Scheme 2) from the corresponding aldehydes.

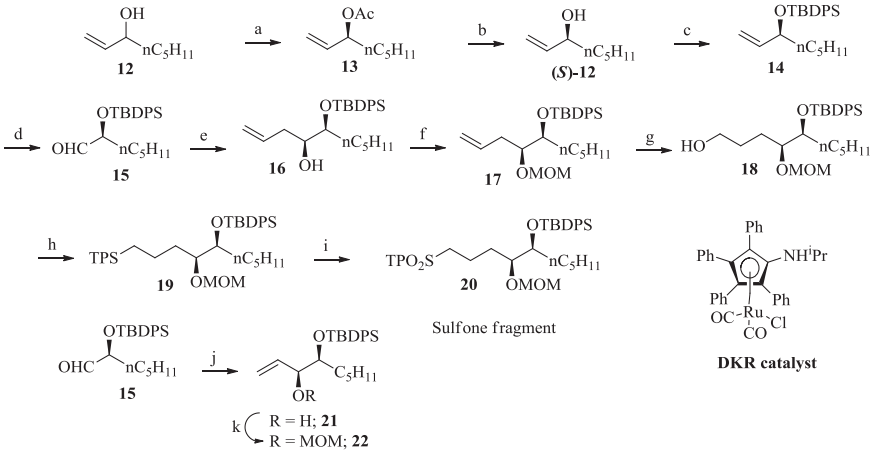
2.2. Synthesis of the sulfone fragment 20

The synthesis starts from commercially available (±)-oct-1-en-3-ol (**12**). ME-DKR (metal enzyme combined dynamic kinetic resolution) of secondary alcohol functionality in compound (±)-**12** was achieved by coupling enzyme catalyzed transesterification reaction with metal catalyzed (ruthenium based catalyst shown in Scheme 3) racemization method.[21] Isopropenyl acetate was used as an acyl donor in the DKR reaction. The ME-DKR reaction is highly efficient for compound **12** as it yields the corresponding acetate (*S*)-**13** in 94% yield with excellent enantioselection (ee=98%; The enantioselectivity was determined by chiral HPLC analysis, [CHIRALPAK AD-H, 254 nm] by deprotecting the acetate group and converting the free alcohol group into its benzoate ester). The acetate functionality in compound **13** was removed by treatment with K_2CO_3 in MeOH to yield optically pure (*S*)-**12** in 95% yield. The free hydroxyl group in alcohol (*S*)-**12** was protected as its TBDPS (*tert*-butyldiphenyl silyl) ether by treatment with imidazole and TBDPS-Cl to afford the compound **14** in 92% yield. Oxidative cleavage of **14** under Lemieux–Johnson condition furnished the aldehyde **15** in 85% yield. Asymmetric Keck allylation of the aldehyde with allyltributyltin and (*S*)-BINOL afforded the desired homoallylic alcohol **16** in 76% yield with excellent diastereoselection (19:1).[22] The secondary hydroxy functionality in compound **16** was protected as its MOM (methoxymethyl) ether by treatment with DIPEA and MOM-Cl in refluxing condition afforded compound **17** in 94% yield. Hydroboration of the corresponding MOM protected compound with BH_3·SMe_2 afforded the alcohol **18** in 82% yield. The free hydroxyl group in compound **18**, was transformed into the corresponding 1-phenyl-1*H*-tetrazol-5-yl sulfide **19** through a Mitsunobu reaction, and subsequent Mo(IV)-catalyzed oxidation of **19**[23] furnish the desired sulfone **20** in 92% yield (Scheme 3).

The alkylborane component required for Suzuki cross coupling reaction with the *E*-vinylic bromide **11** was synthesized from aldehyde **15** as described in the following section. The aldehyde upon reaction with CH_2=CHMgBr at −78 °C furnished compound **21** as a major diastereomer (7:3 ratio). The absolute configuration of compound **21** was confirmed by comparing its spectral and optical data with that of known compound.[24] The secondary alcohol group in compound **21** was protected as its MOM (methoxymethyl) ether by treatment with DIPEA and MOM-Cl in 94% yield.

2.3. JK-olefination/Suzuki cross coupling reaction followed by macrolactonization for the synthesis of cytospolide C and D

After successful completion of both the required fragments **20** and **10**, stereoselective JK-olefination reaction was attempted with the two compounds. JK-olefination of compound **20** and **10** in



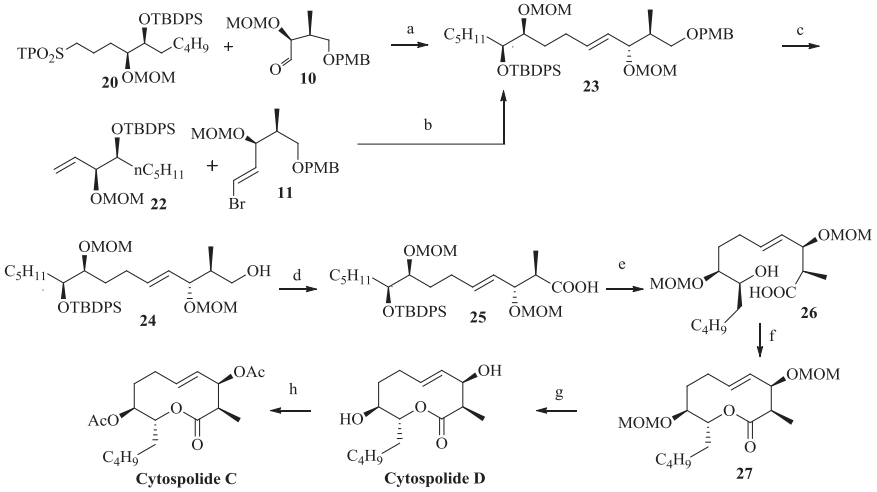
Scheme 3. Synthesis of the sulfone fragment; Reagents and Conditions: (a) CAL-B, isopropenylacetate, chlorodicarbonyl[1-(isopropylamino)-2,3,4,5-tetraphenylcyclopentadienyl] ruthenium(II), K_2CO_3, KO^{t}Bu, toluene, 25 °C, 94%, ee=98%; (b) K_2CO_3, MeOH, rt, 2 h, 95%; (c) Imidazole, TBDPS-Cl, DCM, rt, 6 h, 92%; (d) (i) OsO_4, NMO, THF/H_2O (3:1), 12 h, rt, (ii) $NaIO_4$, rt, 1 h, 85% (in two steps); (e) (*S*)-BINOL, Ti(OPr)$_4$, allyltributyltin, DCM, −78 °C then −20 °C, 72 h, 76%, *dr* (19:1); (f) MOM-Cl, DIPEA, NaI, DCM, 12 h, reflux, 94%; (g) BH_3·SMe_2, THF, 3.5 h, rt, 82%; (h) PTSH, Ph_3P, DIAD, THF, −20 °C to 0 °C, 4 h, 94%; (i) $(NH_4)_6Mo_7O_{24}$·$4H_2O$, H_2O_2, EtOH, rt, 12 h, 92%. (j) CH_2=CHMgBr, THF, −78 °C, 1 h, 93%; (l) MOM-Cl, DIPEA, DCM, rt, 2 h, 94%.

presence of KHMDS as a base at −78 °C, afforded the desired olefin **23** in 72% yield (*E*/*Z*=9:1).[25] Compound **23**, was also synthesized by Suzuki cross coupling reaction[26] of *E*-vinylic bromide **11** and organo borane derivative prepared from compound **22** with 9-BBN. Initially compound **22** was subjected to hydroboration reaction with 9-BBN, which furnished the corresponding alkylborane derivative. The Suzuki cross coupling reaction of *E*-vinylic bromide **11** and alkylborane derived from **22** proceeded smoothly in presence of $Pd(dppf)_2Cl_2$ to furnish compound **23** in 84% yield with excellent diastereocontrol (exclusive formation of *E*-isomer).[27] Compound **23** upon treatment with DDQ furnished the alcohol **24** in 90% yield.[28] Next the alcohol **24** was then subjected to oxidation in presence of BAIB and TEMPO to afford the desired acid **25** in 88% yield.[29] Compound **25** upon treatment with TBAF afforded the desired seco-acid **26** in 82% yield. Macrolactonization of the compound **26** under Mitsunobu lactonization condition (in high dilution *c*=0.05 M) furnished the desired ring closing lactone **27** in 75% yield.[30] Finally deprotection of the MOM functionalities in 2(N) HCl[31] afforded the cytospolide D in 90% yield (Scheme 4; overall yield=10.1% by Suzuki route and 7.2% by JK route from *S*-Roche ester). Cytospolide D on treatment with Ac_2O in presence of Et_3N and DMAP (catalytic) afforded cytospolide C in 90% yield. The spectral (^1H and ^{13}C NMR) characteristic of our synthesized cytospolide C/D matches perfectly with the naturally occurring and synthetic compounds.[11]

3. Experimental section

3.1. General experimental methods

All oxygen and/or moisture-sensitive reactions were carried out under N_2 atmosphere in glassware that had been flame-dried under a vacuum (~0.5 mmHg) and purged with N_2 prior to use. Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates with UV light, ethanolic anisaldehyde, and phosphomolybdic acid/heat as developing agents. Silica gel 230–400 mesh was used for column chromatography. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated. ^1H and ^{13}C NMR spectra were recorded on a 200 and 400 MHz NMR instrument, and are reported relative to internal $CHCl_3$ (^1H, δ=7.26), and $CDCl_3$ (^{13}C, δ=77.0; center peak of most downfield signal). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad, ov=overlapping, app=apparent. Mass spectrometric analysis was performed in the CRF, IIT-Kharagpur (TOF analyzer). Optical rotations were measured on a digital polarimeter using a 100 mm path-length cell at 589 nm. Chiral HPLC



	Overall yield	No of steps
i) This work	7.2%,	18 steps, using JK route, cytospolide-D (*E*-isomer)
	10.1%,	16 steps, using Suzuki route
ii) Yadav's work	10.5%	12 steps, cytospolide-E (*Z*-isomer)[9]
iii) Kamal's work	2.5%	16 steps, cytospolide-D (*Z*-isomer)[11]
	1.2%	16 steps, cytospolide-D (*E*-isomer)
iv) our previous work	7.5%	16 steps, cytospolide-D (*Z*-isomer)[10]

Scheme 4. Fragment coupling and completion of the synthesis; Reagents and Conditions: (a) KHMDS, THF, −78 °C to rt, 2 h, 72% (*dr*=9:1); (b) (i) 9-BBN; THF, rt, 16 h; (ii) aq NaOH, **11**,$Pd(dppf)_2Cl_2 \cdot CH_2Cl_2$ (10 mol %; [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane]), 84%; (c) DDQ, DCM:Phosphate buffer (9:1), rt, 2 h, 90%; (d) BAIB, TEMPO, 4 h, DCM:H_2O (1:1), 88%; (e) TBAF, THF, rt, 4 h, 82%; (f) DIAD, Ph_3P, toluene, 12 h, 75%; (g) 2 N HCl, THF, rt, 12 h, 90%; (h) Ac_2O, Et_3N, DCM, rt, 6 h, 90%.

In conclusion we have successfully synthesized cytospolides C and D by applying a short, reliable and flexible synthetic strategy. The main highlight of our synthetic venture involves successful exploration of JK-olefination or Suzuki cross coupling reaction for the construction of the required *E*-olefinic unsaturation present in the target molecule. Finally Mitsunobu lactonization reaction enables us to complete the total synthesis of the target molecules cytospolides C and D. The adapted strategy can serve as an excellent alternative way enroute to such small ring macrolides over the traditional ring closing metathesis route.

was measured with AD-H column in a Shimadzu Prominence system attached with UV–vis detector.

3.2. (*S*)-Methyl 3-(4-methoxybenzyloxy)-2-methylpropanoate (6)

A solution of 4-methoxybenzyl alcohol (1.98 g, 15.0 mmol) in 30 mL of ether was added to a suspension of 60% NaH (0.078 g, 1.95 mmol) in 10 mL of ether at room temperature. The resulting mixture was stirred at room temperature for 30 min and cooled to

0 °C. Trichloroacetonitrile (TCA, 2.0 mL, 15.0 mmol) was added to it and the reaction mixture was allowed to warm slowly to room temperature over 6 h. The solution was then concentrated to an orange syrup, which was dissolved in anhydrous hexane (15 mL) containing few drops of MeOH. This suspension was shaken vigorously and filtered through Celite, and the filtrate was concentrated to afford the crude imidate. The crude imidate was taken in cyclohexane (60 mL) and a solution of commercially available (*S*)-Roche ester (1.77 g, 15.0 mmol) in 30 mL of DCM was added. The resulting solution was cooled to 0 °C and CSA (0.35 g, 1.5 mmol) was added to it. The reaction mixture was stirred for 6 h at room temperature, slowly developing a white precipitate of trichloroacetamide. The solution was then filtered off and washed with DCM. The filtrate was washed with $NaHCO_3$ solution, water and brine. The organic solvent was dried over $MgSO_4$ and purified by means of silica gel column chromatography (EtOAc–hexane, 1:20) yielded compound **6** as a colorless oil (3.39 g, 95%).

R_f=0.4 (EtOAc/hexane=1:5).

$[\alpha]_D^{28}$=+8.1 (*c*=1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (2H, d, *J*=8.4 Hz, Ar*H*), 6.85 (2H, d, *J*=8.4 Hz, Ar*H*), 4.43 (2H, s, $-OCH_2$), 3.81 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 3.65–3.60 (1H, m, $-OCH_2$), 3.47–3.42 (1H, m, $-OCH_2$), 2.79–2.72 (1H, m, C*H*), 1.15 (3H, d, *J*=7.2 Hz, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$) δ 175.4, 159.2, 130.3, 129.2, 113.8, 72.8, 71.7, 55.3, 51.7, 40.2, 14.0.

HRESIMS (*m*/*z*) found 261.1104 $[M+Na]^+$ (calcd for $C_{13}H_{18}O_4Na$, 261.1102).

3.3. (*S*)-5-(4-Methoxybenzyloxy)-4-methylpent-1-en-3-one (7)

To a solution of *N*,*O*-dimethylhydroxylamine (0.3 g, 5.0 mmol) in 6 mL of benzene was added a solution of Me_3Al (2.5 mL, 5.0 mmol) in 6 mL of benzene via cannula at 0 °C. The resulting mixture was stirred at room temperature for 1 h. To the reaction mixture was added compound **6** (0.47 g, 2.0 mmol) in 2 mL of benzene and the reaction mixture was heated to reflux for 3 h. The reaction mixture was then cooled to 0 °C and quenched carefully with 5 mL of 1 (M) HCl. The layer was separated and the aqueous phase was extracted with 50 mL of DCM. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo to afford the crude amide as yellow oil. R_f=0.4 (EtOAc/hexane, 1:2).

A 1.0 M solution of vinylmagnesium bromide in THF (8.0 mL, 8.0 mmol) was added to a stirred solution crude amide in anhydrous THF (10 mL) at −78 °C under N_2. The mixture was stirred at −78 °C for 3 h and then it was quenched with saturated aq NH_4Cl (5 mL) solution. The organic solution was extracted with EtOAc (3×20 mL). The combined organic extracts were washed with brine (1×30 mL), and then dried over $MgSO_4$. The organic solution was filtered and concentrated to afford the crude product. The residue was then purified by column chromatography (EtOAc/hexane, 1:4), to furnish the title compound **7** (0.43 g, 1.84 mmol, 88% in overall three steps) as a colorless oil.

R_f=0.4 (EtOAc/hexane, 1:4).

$[\alpha]_D^{28}$=+1.8 (*c*=0.75, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.20 (2H, m, Ar*H*), 6.87–6.85 (2H, m, Ar*H*), 6.43 (1H, dd, *J*=17.2, 10.8 Hz, =CH), 6.27 (1H, d, *J*=17.2 Hz, $=CH_2$), 5.77 (1H, d, *J*=10.8 Hz, $=CH_2$), 4.43, 4.39 (2H, ABq, *J*=11.6 Hz, $-OCH_2$), 3.78 (3H, s, OCH_3), 3.66 (1H, t, *J*=8.4 Hz, CH_2), 3.46–3.42 (1H, m, CH_2), 3.18–3.13(1H, m, C*H*), 0.87 (3H, d, *J*=7.2 Hz, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 159.1, 135.4, 130.1, 129.2, 128.3, 113.7, 72.8, 71.8, 55.2, 43.6, 13.8.

HRESIMS (*m*/*z*) found 257.1160 $[M+Na]^+$ (calcd for $C_{14}H_{18}O_3Na$, 257.1153).

3.4. (3*R*,4*S*)-5-(4-Methoxybenzyloxy)-4-methylpent-1-en-3-ol (8)

To a stirred solution of (*S*)-2-methyl-CBS-oxazaborolidine (1.0 M in toluene, 0.2 mL, 0.2 mmol) in THF (0.6 mL) at −78 °C and under N_2, was added BH_3·DMS complex (2.0 M in THF, 1 mL, 2.0 mmol) followed by a solution of **7** (0.446 g, 2.0 mmol) in THF (5 mL). After 6 h, H_2O (5 mL) was added and the mixture was warmed to room temperature. Et_2O was added and the mixture was washed with 5% aq HCl. The aqueous phase was extracted with Et_2O (25 mL), and the combined organic phases were washed with H_2O and brine and then dried with $MgSO_4$. The organic solvent was then evaporated under vacuum to afford the crude alcohol, which was further purified by column chromatography (EtOAc/hexane, 1:3) to furnish **8** (0.386 g, 82%) as a colorless oil.

R_f=0.3 (EtOAc/hexane, 1:3).

$[\alpha]_D^{28}$=−2.1 (*c*=1.3 $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.25–7.21 (2H, m, Ar*H*), 6.88–6.84 (2H, m, Ar*H*), 5.90–5.73 (1H, m, =C*H*), 5.27–5.09 (2H, m, $=CH_2$), 4.42 (2H, s, $-OCH_2$), 3.99 (1H, t, *J*=6.8 Hz, OC*H*), 3.76 (3H, s, OCH_3), 3.57–3.38 (2H, m, OCH_2), 1.91–1.81 (1H, m, C*H*), 0.89 (3H, d, *J*=6.8 Hz, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$) δ 159.3, 139.5, 130.0, 129.4, 115.7, 113.9, 77.2, 74.1, 73.1, 55.3, 38.6, 13.7.

HRESIMS (*m*/*z*) found 259.1306 $[M+Na]^+$ (calcd for $C_{14}H_{20}O_3Na$, 259.1309).

3.5. 1-Methoxy-4-(((2*S*,3*R*)-3-(methoxymethoxy)-2-methylpent-4-enyloxy)methyl)benzene (9)

To a solution of alcohol **8** (0.5 g, 2.14 mmol) in dry DCM (10 mL), DIPEA (0.6 mL, 3.21 mmol) was added at 0 °C and the mixture was stirred for 15 min at the same temperature. MOM-Cl (0.2 mL, 2.56 mmol) and TBAI (catalytic) were then added and the reaction mixture was stirred for an additional 4 h at room temperature. Water was then added and the mixture was extracted with DCM, and washed with water and brine. The organic extracts were dried with $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc/hexane, 1:10) to furnish compound **9** (0.54 g, 90%) as a colorless oil.

R_f=0.7 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=−5.6 (*c*=1.3, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.32–7.28 (2H, m, Ar*H*), 6.94–6.89 (2H, m, Ar*H*), 5.85–5.67 (1H, m, =C*H*), 5.30–5.21 (2H, m, $=CH_2$), 4.73 (1H, d, *J*=6.6 Hz, OCH_2O), 4.57 (1H, d, *J*=6.6 Hz, OCH_2O), 4.46 (2H, s, $-OCH_2$), 4.16 (1H, t, *J*=5.9 Hz, $-OCH$), 3.82 (3H, s, OCH_3), 3.59–3.51 (1H, m, $-OCH_2$), 3.39 (4H, m, $-OCH_2$, OCH_3), 2.07–1.89 (1H, m, C*H*), 1.04 (3H, d, *J*=6.8 Hz, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$) δ 159.1, 136.1, 130.7, 129.1, 118.4, 113.6, 93.7, 78.6, 72.6, 71.8, 55.3, 55.1, 38.0, 13.1.

HRESIMS (*m*/*z*) found 303.1585 $[M+Na]^+$ (calcd for $C_{16}H_{24}O_4Na$, 303.1572).

3.6. (2*S*,3*S*)-4-(4-Methoxybenzyloxy)-2-(methoxymethoxy)-3-methylbutanal (10)

To a stirred solution of the olefin **9** (0.56 g, 2.0 mmol) in THF/H_2O (3:1) at room temperature, NMO (0.35 g, 3.0 mmol), 0.05 M solution of OsO_4 in toluene (4.0 mL, 0.2 mmol) and $NaIO_4$ (0.64 g, 3.0 mmol) were sequentially added. The mixture was stirred vigorously at room temperature for 12 h, then quenched by the addition of saturated aqueous Na_2SO_3 solution and extracted with EtOAc. The combined organic layers were washed with aqueous $NaHCO_3$ solution, dried over $MgSO_4$ and concentrated under reduced pressure. Purification was accomplished by flash column chromatography by

eluting with EtOAc/hexane (1:7) to afford the aldehyde **10** (0.5 g, 90%).

R_f=0.45 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=−3.2 (*c*=1.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.69 (1H, d, *J*=1.6 Hz, C*H*O), 7.23 (2H, d, *J*=8.4 Hz, Ar*H*), 6.86 (2H, d, *J*=8.4 Hz, Ar*H*), 4.70 (2H, dd, *J*=19.6, 6.8 Hz, OCH_2O), 4.40 (2H, d, *J*=3.6 Hz, OCH_2), 4.08–4.06 (1H, m, OC*H*), 3.81 (3H, s, OCH_3), 3.41–3.36 (5H, ov, OCH_2, OCH_3), 2.39–2.31 (1H, m, C*H*), 1.01 (3H, d, *J*=7.0 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz) δ 202.9, 159.1, 130.2, 129.1, 113.7, 97.2, 84.2, 72.5, 70.2, 56.0, 55.3, 36.8, 13.6.

HRESIMS (*m*/*z*) found 305.1361 $[M+Na]^+$ (calcd for $C_{15}H_{22}O_5Na$, 305.1364).

3.7. 1-(((2*S*,3*S*,*E*)-5-Bromo-3-(methoxymethoxy)-2-methylpent-4-enyloxy)methyl)-4-methoxybenzene (11)

To a solution of 5-(bromomethylsulfonyl)-1-phenyl-1*H*-tetrazole ($PTSO_2$-CH_2Br, 0.3 g, 1.0 mmol) in THF (4 mL) at −78 °C was added $MgBr_2\cdot Et_2O$ (2.0 mL, 2.0 mmol, 2 equiv), and KHMDS (2.0 mL, 2.0 mmol, 2 equiv) followed by aldehyde **10** (282 mg, 1.0 mmol, 1 equiv) in 2 mL of THF. The reaction solution was stirred at −78 °C for 1 h and then quenched by the addition of saturated solution of NH_4Cl and then it was extracted with EtOAc. The combined organic layers were washed with brine solution, dried over $MgSO_4$ and concentrated under reduced pressure. Purification was accomplished by flash column chromatography eluting with EtOAc/hexane (1:7) afforded the vinylic bromide **11** (0.35 g, 82%) as a colorless oil.

R_f=0.45 (EtOAc/hexane, 1:3).

$[\alpha]_D^{28}$=−10.2 (*c*=1.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.25 (2H, d, *J*=8.4 Hz, Ar*H*), 6.88 (2H, d, *J*=8.4 Hz, Ar*H*), 6.25 (1H, d, *J*=13.6 Hz, =C*H*Br), 6.10 (1H, dd, *J*=13.6, 8.0 Hz, =C*H*), 4.65 (1H, d, *J*=6.8 Hz, −OCH_2O), 4.51 (1H, d, *J*=6.8 Hz, −OCH_2O), 4.43 (1H, d, *J*=11.6 Hz, OCH_2), 4.37 (1H, d, *J*=11.6 Hz, OCH_2), 4.10 (1H, q, *J*=7.6, 5.6 Hz, OC*H*), 3.80 (3H, s, OCH_3), 3.45–3.41 (1H, m, OCH_2), 3.36 (3H, s, OCH_3), 3.34–3.29 (1H, m, OCH_2), 1.95–1.88 (1H, m, C*H*), 0.87 (3H, d, *J*=6.8 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.3, 136.7, 130.6, 129.4, 113.9, 108.5, 94.4, 73.0, 71.8, 55.8, 55.4, 38.5, 12.5.

HRESIMS (*m*/*z*) found: 381.0680 $[M+Na]^+$ (calcd for $C_{16}H_{23}^{79}BrO_4Na$, 381.0677).

3.8. (*S*)-Oct-1-en-3-yl acetate (13)

In a 50 mL round bottom flask attached with a grease free high vacuum stopcock, chlorodicarbonyl(1-(isopropylamino)-2,3,4,5-tetraphenylcyclopentadienyl) ruthenium (II) [DKR catalyst, 0.084 g, 0.136 mmol] was taken. The flask was successively charged with alcohol **12** (0.430 g, 3.4 mmol) in 10 mL dry toluene, Na_2CO_3 (0.36 g, 3.4 mmol), CAL-B (0.025 g) and KO^{t}Bu (0.019 g, 0.17 mmol) followed by isopropenyl acetate (0.55 mL, 5 mmol). The reaction mixture was stirred at room temperature under argon atmosphere for almost 8 h. After completion of the reaction the mixture was filtered off and the solvent was evaporated to afford the crude acetate, which was subsequently purified by silica gel column chromatography (EtOAc/hexane, 1:10) to afford the pure acetate **13** in 94% (0.54 g, 3.2 mmol) yield.

R_f=0.6 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=−2.73 (*c*=1.0, $CHCl_3$).

3.9. (*S*)-Oct-1-en-3-ol [(*S*)-12]

The acetate group in compound **13** (2.04 g, 12.0 mmol) was deprotected by adding K_2CO_3 (0.55 g, 4.0 mmol) in MeOH (30 mL) solvent. After 2 h MeOH was evaporated under reduced pressure. The residue was taken in Et_2O, and washed successively with water and brine. The organic layer was dried with $MgSO_4$ and evaporated under reduced pressure. The product was purified by flash chromatography (EtOAc/hexane, 1:5) to afford compound (*S*)-**12** in 95% yield (1.45 g) as a liquid.

R_f=0.4 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=−7.5 (*c*=1.0, $CHCl_3$).

3.10. (*S*)-*tert*-Butyl(oct-1-en-3-yloxy)diphenylsilane (14)

Alcohol (*S*)-**12** (3.5 g, 27.1 mmol) was taken in anhydrous DCM (50 mL) and cooled to 0 °C. Imidazole (2.76 g, 40.7 mmol) and DMAP (catalytic) were added to the solution followed by TBDPSCl (8.50 mL, 32.6 mmol). The reaction mixture was then stirred at room temperature for 6 h. After that water was added to the reaction solution and the organic layer was washed with brine and dried with $MgSO_4$. Evaporation and purification by silica gel column chromatography (EtOAc/hexane, 1:20) gave the TBDPS-protected alcohol **14** (9.13 g, 92%) as a colorless oil.

R_f=0.35 (EtOAc/hexane, 1:20).

$[\alpha]_D^{28}$=−19.3 (*c*=0.7, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75–7.67 (4H, m, Ar*H*), 7.43–7.37 (6H, m, Ar*H*), 5.91–5.74 (1H, m, =C*H*), 5.05–4.95 (2H, m, =CH_2), 4.21–4.12 (1H, m, C*H*), 1.43–1.27 (2H, m, CH_2), 1.3–1.1 (6H, m, CH_2), 1.1 (9H, s, Si(CH_3)$_3$), 0.84 (3H, t, *J*=6.2 Hz, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$) δ 141.0, 136.0, 135.9, 134.6, 134.4, 129.5, 129.4, 127.5, 127.4, 114.1, 74.7, 37.6, 31.8, 27.1, 24.2, 22.6, 19.4, 14.1.

HRESIMS (*m*/*z*) found 389.2271 $[M+Na]^+$ (calcd for $C_{24}H_{34}OSiNa$, 389.2277).

3.11. (*S*)-2-(*tert*-Butyldiphenylsilyloxy)heptanal (15)

TBDPS-protected alcohol **14** (6.0 g, 16.3 mmol) was taken in THF/H_2O (3:1, 56 mL), OsO_4 (0.05 M in toluene, 32 mL) and NMO (3.82 g, 32.7 mmol) were then added at room temperature and the mixture was stirred for 12 h. A saturated solution of $NaHSO_3$ was added and the solution was further stirred for 1 h. The organic layer was extracted with ethyl acetate and washed with water and brine. The organic solvent was dried with $MgSO_4$ and the solvents were evaporated to dryness to afford the diol. The crude diol was then taken in THF (30 mL) and water (20 mL), followed by addition of $NaIO_4$ (3.48 g, 16.33 mmol). The mixture was then stirred for 1 h and the reaction was followed by TLC analysis to verify cleavage of the glycol was complete. Water (25 mL) was then added and the reaction mixture was extracted with ethyl acetate, washed with brine, and dried with $MgSO_4$. The organic layer was concentrated in a rotary evaporator to yield the crude residue, which was then purified by silica gel column chromatography (EtOAc/hexane, 1:20) to afford aldehyde **15** (5.1 g, 85%).

R_f=0.4 (EtOAc/hexane, 1:20).

$[\alpha]_D^{28}$=+6.3 (*c*=1.6, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ 9.61 (1H, d, *J*=1.8 Hz, C*H*O), 7.70–7.64 (4H, m, Ar*H*), 7.46–7.35 (6H, m, Ar*H*), 4.06 (1H, td, *J*=5.8, 1.6 Hz, C*H*), 1.65–1.59 (2H, m, CH_2), 1.46–1.30 (6H, m, CH_2), 1.14 (9H, s, Si(CH_3)$_3$), 0.86 (3H, t, *J*=6.2 Hz, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$) δ 204.1, 135.9, 135.8, 133.3, 133.2, 130.1, 127.9, 127.8, 78.1, 32.9, 31.7, 27.0, 23.8, 22.4, 19.4, 13.9.

HRESIMS (*m*/*z*) found 391.2068 $[M+Na]^+$ (calcd for $C_{23}H_{32}O_2SiNa$, 391.2070).

3.12. (4*S*,5*S*)-5-(*tert*-Butyldiphenylsilyloxy)dec-1-en-4-ol (16)

A mixture of (*S*)-BINOL (0.11 g, 0.4 mmol), 1 M Ti(O^{i}Pr)$_4$ in DCM (0.4 mL, 0.4 mmol), and oven-dried powdered 4 Å sieves (0.8 g) in DCM (8 mL) was heated at reflux for 1 h. The red-brown mixture

was then cooled to room temperature and aldehyde **15** (1.44 g, 3.94 mmol) was added. After being stirred for 10 min, the contents were cooled to −78 °C, and allyltri-*n*-butylstannane (1.45 g, 4.38 mmol) was added. The reaction mixture was stirred for 10 min and then placed in a −20 °C freezer for 72 h. Saturated $NaHCO_3$ (1 mL) was then added to it, and the contents were stirred for 1 h and then poured over Na_2SO_4 and filtered through a plug of Celite. The crude material was purified by flash chromatography, eluting with EtOAc/hexane (1:20) to furnish the (*S*)-allylic alcohol **16** (1.49 g, 76%).

R_f=0.3 (EtOAc/hexane, 1:20).

$[\alpha]_D^{28}$=+8.6 (*c*=0.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.74–7.70 (4H, m, Ar*H*), 7.48–7.30 (6H, m, Ar*H*), 5.89–5.75 (1H, m, =C*H*), 5.08–5.01 (2H, m, =CH_2), 3.69–3.55 (2H, m, C*H*), 2.28 (2H, t, *J*=6.6 Hz, =CH–CH_2), 1.59–1.53 (2H, m, CH_2), 1.40–1.37 (1H, m, CH_2), 1.33–1.19 (5H, m, CH_2), 1.14 (9H, s, Si(CH_3)$_3$), 0.83 (3H, t, *J*=6.2 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz): δ 136.1, 135.4, 134.2, 133.6, 130.0, 129.8, 127.9, 127.7, 117.2, 75.8, 72.4, 38.6, 33.4, 31.8, 29.9, 27.3, 24.8, 22.6, 19.7, 14.1.

HRESIMS (*m*/*z*) found 433.2529 $[M+Na]^+$ (calcd for $C_{26}H_{38}O_2SiNa$, 433.2538).

3.13. (5*S*,6*S*)-5-Allyl-9,9-dimethyl-6-pentyl-8,8-diphenyl-2,4,7-trioxa-8-siladecane (17)

NaI (4.85 g, 32.2 mmol) and MOM-Cl (2.05 mL, 26.8 mmol) in 25 mL DCM was stirred for 10 min at room temperature. Then a solution of alcohol **16** (1.1 g, 2.68 mmol) and DIPEA (7.47 mL, 42.9 mmol) in 25 mL DCM was added and stirred for 1 h then for an additional 12 h under refluxing condition. Water was added to the reaction mixture and the contents were extracted with DCM. The organic extracts were washed with water and brine. The organic extracts were dried over $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc/hexane, 1:30) to afford the desired product **17** (1.14 g) in 94% yield.

R_f=0.5 (EtOAc/hexane, 1:20).

$[\alpha]_D^{28}$=+2.6 (*c*=0.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.77–7.70 (4H, m, Ar*H*), 7.50–7.38 (6H, m, Ar*H*), 5.85–5.80 (1H, m, =C*H*), 5.17–5.09 (2H, m, =CH_2), 4.42 (2H, s, OCH_2O), 3.84–3.76 (1H, m, C*H*), 3.55–3.48 (1H, m, C*H*), 3.22 (3H, s, OCH_3), 2.61–2.58 (1H, m, =CH–CH_2), 2.30–2.22 (1H, m, =CH–CH_2), 1.57–1.39 (3H, m, CH_2), 1.36–1.19 (5H, m, CH_2), 1.14 (9H, s, Si(CH_3)$_3$), 0.88 (3H, t, *J*=6.2 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz) δ 136.4, 136.2, 134.3, 134.2, 129.8, 129.7, 128.5, 127.7, 127.6, 116.3, 96.6, 80.5, 74.2, 55.5, 34.0, 32.0, 31.3, 27.3, 25.9, 22.6, 19.6, 14.1.

HRESIMS (*m*/*z*) found 477.2816 $[M+Na]^+$ (calcd for $C_{28}H_{42}O_3SiNa$, 477.2800).

3.14. (4*S*,5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-4-(methoxymethoxy)decan-1-ol (18)

To a cooled (0 °C), stirred solution of **17** (1.3 g, 2.86 mmol) in THF (6 mL) was added $BH_3{\cdot}SMe_2$ (1.5 mL, 2.0 M in THF, 3 mmol). The mixture was stirred for an additional 2 h and then quenched with EtOAc followed by the addition of 3 M aqueous NaOH (4 mL) and 30% H_2O_2 (4 mL). The mixture was stirred vigorously for 3.5 h. It was then extracted with EtOAc and washed with brine. The organic solvent was dried ($MgSO_4$), concentrated and purified by silica gel column chromatography (EtOAc/hexane, 1:5) to provide the alcohol **18** (1.1 g, 2.34 mmol) with 82% yield.

R_f=0.3 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=+3.6 (*c*=0.3, $CHCl_3$).

^{1}H NMR($CDCl_3$, 400 MHz): δ 7.69–7.65 (4H, m, Ar*H*), 7.44–7.23 (6H, m, Ar*H*), 4.33 (2H, s, OCH_2O), 3.89–3.80 (1H, m, C*H*), 3.63–3.60 (2H, m, CH_2), 3.49–3.40 (1H, m, C*H*), 3.28 (3H, s, OCH_3), 1.85–1.82 (1H, m, CH_2), 1.60–1.50 (2H, m, CH_2), 1.49–1.46 (3H, m, CH_2), 1.20–1.10 (6H, m, CH_2), 1.10–1.05 (9H, s, Si(CH_3)$_3$), 0.88 (3H, t, *J*=6.2 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz) δ 136.1, 134.3, 129.8, 129.7, 127.7, 127.6, 96.8, 81.4, 74.1, 63.1, 55.6, 32.0, 31.2, 29.7, 27.2, 25.9, 25.3, 22.6, 19.6, 14.3.

HRESIMS (*m*/*z*) found 495.2918 $[M+Na]^+$ (cacld for $C_{28}H_{44}O_4SiNa$, 495.2906).

3.15. 5-((4*S*,5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-4-(methoxymethoxy)decylthio)-1-phenyl-1*H*-tetrazole (19)

DIAD (0.42 mL, 2.1 mmol) was added to a solution of alcohol **18** (0.6 g, 1.27 mmol), Ph_3P (triphenyl phosphine, 0.5 g, 1.91 mmol) and 1-phenyl-5-mercapto-1*H*-tetrazole [PT-SH] (0.36 g, 2.0 mmol) in THF (10 mL) at −10 °C. The solution was stirred at 0 °C for 4 h, the reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ solution and brine, dried with anhydrous $MgSO_4$ and concentrated in vacuum to give the crude sulphide, which was then purified by silica gel column chromatography (EtOAc/hexane, 1:8) to provide the sulphide **19** (0.74 g, 1.20 mmol) with 94% yield.

R_f=0.6 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=+11.2 (*c*=0.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67–7.62 (4H, m, Ar*H*), 7.59–7.52 (5H, m, Ar*H*), 7.43–7.31 (6H, m, Ar*H*), 4.28 (2H, s, OCH_2O), 3.75 (1H, t, *J*=4 Hz, C*H*), 3.41–3.37 (2H, m, CH_2), 3.31–3.29 (1H, m, C*H*), 3.17 (3H, s, OCH_3), 1.93–1.90 (2H, m, CH_2), 1.58–1.50 (1H, m, CH_2), 1.43–1.38 (2H, m, CH_2), 1.30–1.27 (2H, m, CH_2), 1.25–1.14 (5H, m, CH_2), 1.04 (9H, s, Si(CH_3)$_3$), 0.79 (3H, t, *J*=6.2 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz) δ 154.5, 136.1, 136.0, 134.2, 130.2, 129.9, 129.7, 127.7, 127.6, 124.0, 96.8, 80.7, 74.0, 55.6, 33.6, 32.0, 31.2, 29.8, 27.9, 27.2, 26.1, 26.0, 22.6, 19.5, 14.1.

HRESIMS (*m*/*z*) found 655.3104 $[M+Na]^+$ (calcd for $C_{35}H_{48}N_4O_3SsiNa$, 655.3113).

3.16. 5-((4*S*,5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-4-(methoxymethoxy)decylsulfonyl)-1-phenyl-1*H*-tetrazole (20)

To the solution of sulphide **19** (0.74 g, 1.20 mmol) in ethanol (15 mL) was added the mixture of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (0.44 g, 0.36 mmol) and 30% H_2O_2 solution (4.0 mL) at 0 °C. The mixture was stirred at room temperature for 12 h and then the reaction mixture was poured into 10% $Na_2S_2O_3$ solution and extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ solution and brine, dried with anhydrous $MgSO_4$ and concentrated in vacuo. The residue was purified over silica gel column chromatography by eluting with EtOAc/hexane (1:10) gave sulfone **20** (0.73 g, 1.10 mmol) as colorless gummy oil in 92% yield.

R_f=0.7 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=+1.6 (*c*=0.2, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69–7.59 (9H, m, Ar*H*), 7.42–7.35 (6H, m, Ar*H*), 4.26 (2H, s, OCH_2O), 3.78–3.70 (1H, m, C*H*), 3.68–3.61 (2H, m, CH_2), 3.27–3.20 (1H, m, C*H*), 3.17 (3H, s, OCH_3), 2.02–1.97 (1H, m, CH_2), 1.89–1.87 (1H, m, CH_2), 1.60–1.40 (3H, m, CH_2), 1.32–1.15 (7H, m, CH_2), 1.00 (9H, s, Si(CH_3)$_3$), 0.86 (3H, t, *J*=6.2 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz) δ 153.6, 136.1, 136.0, 134.2, 134.0, 133.2, 131.6, 130.0, 129.8, 127.8, 127.7, 125.2, 96.8, 80.3, 73.9, 56.0, 55.8, 32.0, 31.1, 29.8, 28.4, 27.2, 26.0,22.6, 19.5, 19.2, 14.1.

HRESIMS (*m*/*z*) found 687.3025 $[M+Na]^+$ (calcd for $C_{35}H_{48}N_4O_5SsiNa$, 687.3012).

3.17. (3*S*,4*S*)-4-(*tert*-Butyldiphenylsilyloxy)non-1-en-3-ol (21)

Aldehyde **15** (1.84 g, 5.0 mmol) was taken in 20 mL of anhydrous THF. Freshly generated solution of vinylmagnesium bromide (1 M, 6.0 mmol) was added to it at −78 °C. The reaction mixture was then kept at the room temperature for 1 h, after that saturated NH_4Cl solution was added to it. The solution was extracted with EtOAc, and the organic layer was washed with water and brine. The organic layer was dried ($MgSO_4$) and evaporated. Purification by silica gel column chromatography (EtOAc/hexane, 1:15) afforded the alcohol **21** (1.28 g, 3.25 mmol, as a major diastereomer in 7:3 ratio) in overall 93% yield.

R_f=0.4 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=+1.6 (*c*=0.2, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.72–7.69 (4H, m, Ar*H*), 7.44–7.37 (6H, m, Ar*H*), 5.85 (1H, ddd, *J*=5.2, 10.4, 17.2 Hz, =C*H*), 5.32 (1H, d, *J*=17.2 Hz, =CH_2), 5.16 (1H, d, *J*=10.4 Hz, =CH_2), 4.07–4.05 (1H, m, C*H*), 3.70–3.66 (1H, m, C*H*), 1.59–1.53 (1H, m, CH_2), 1.38–1.20 (7H, m, CH_2), 1.02 (9H, s, Si(CH_3)$_3$), 0.77 (3H, t, *J*=6.2 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz): δ 138.7, 136.1, 134.2, 129.9, 127.8, 127.7, 116.2, 76.8, 74.5, 33.4, 31.8, 27.3, 24.7, 22.5, 19.7, 14.1.

HRESIMS (*m*/*z*) found 419.2384 [M+Na]$^+$ (calcd for $C_{25}H_{36}O_2SiNa$, 419.2382).

3.18. (5*S*,6*S*)-9,9-Dimethyl-6-pentyl-8,8-diphenyl-5-vinyl-2,4,7-trioxa-8-siladecane (22)

To a solution of alcohol **21** (0.84 g, 2.14 mmol) in dry DCM (10 mL), DIPEA (0.6 mL, 3.21 mmol) was added at 0 °C and the mixture was stirred for 15 min at the same temperature. MOM-Cl (0.2 mL, 2.56 mmol) and TBAI (catalytic) were then added and the reaction mixture was stirred for an additional 2 h at room temperature. Water was added and the mixture was extracted with DCM, and washed with water and brine. The organic extracts were dried with $MgSO_4$, concentrated and purified by silica gel column chromatography (EtOAc/hexane, 1:10) to furnish **22** (0.88 g, 94%) as a colorless oil.

R_f=0.7 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=−5.6 (*c*=1.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75–7.73 (4H, m, Ar*H*), 7.44–7.37 (6H, m, Ar*H*), 5.92 (1H, ddd, *J*=5.2, 10.4, 17.2 Hz, =C*H*), 5.28 (2H, t, *J*=9.6 Hz, =CH_2), 4.54 (1H, d, *J*=6.4 Hz, OCH_2O), 4.45 (1H, d, *J*=6.4 Hz, OCH_2O), 4.04 (1H, t, *J*=5.2 Hz, C*H*), 3.85–3.82 (1H, m, C*H*), 3.23 (3H, s, OCH_3), 1.54–1.51 (1H, m, CH_2), 1.42–1.28 (7H, m, CH_2), 1.04 (9H, s, Si(CH_3)$_3$), 0.79 (3H, t, *J*=6.2 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.3, 135.1, 134.6, 134.3, 129.7, 127.7, 127.6, 117.8, 94.8, 79.9, 75.3, 55.5, 32.5, 32.1, 27.3, 27.2, 25.2, 22.6, 19.7, 14.1.

HRESIMS (*m*/*z*) found 463.2649 [M+Na]$^+$ (calcd for $C_{27}H_{40}O_3SiNa$, 463.2644).

3.19. (5*R*,10*S*,11*S*,*E*)-5-((*S*)-1-(4-Methoxybenzyloxy)propan-2-yl)-10-(methoxymethoxy)-14,14-dimethyl-11-pentyl-13,13-diphenyl-2,4,12-trioxa-13-silapentadec-6-ene (23)

3.19.1. JK-olefination reaction procedure. To a solution of sulfone **20** (0.6 g, 0.94 mmol) in THF (6 mL) was added 0.5 M solution of KHMDS in toluene (2.06 mL, 1.03 mmol) at −78 °C. The reaction mixture was stirred at −78 °C for 15 min then a solution of aldehyde **10** (294 mg, 1.04 mmol) in THF (3 mL) was added into this mixture. The reaction mixture was then allowed to warm to room temperature during 2 h and poured into saturated NH_4Cl solution. This mixture was then extracted with ethyl acetate and the organic layer was washed with saturated $NaHCO_3$ solution and brine. After drying with anhydrous $MgSO_4$, solvent was removed in vacuo and the residue was purified by silica gel column chromatography (EtOAc/hexane, 1:10) to afford olefin **23** (0.48 g, 0.67 mmol) in 72% yield.

3.19.2. Suzuki cross coupling reaction procedure. To a stirred solution of compound **22** (0.44 g, 1 mmol) in THF (5 mL) was added a solution of 9-BBN (2 mL, 0.5 M in THF, 1.0 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred at that temperature for 16 h. The resulting mixture was cooled to 0 °C before aq NaOH (1 mL, 3.0 M), Pd(dppf)$Cl_2\cdot CH_2Cl_2$ (0.08 g, 0.1 mmol), and bromide **11** (0.36 g, 1 mmol) were sequentially added. The mixture so obtained was warmed to room temperature and stirred at that temperature for 16 h before it was quenched with saturated aqueous NH_4Cl (2 mL). The resultant mixture was extracted with EtOAc (3×10 mL), and the combined organic phases were washed with brine (5 mL) and dried over anhydrous $MgSO_4$. After filtration and evaporation of the solvent under vacuum, the residue was subjected to flash column chromatography using EtOAc/hexane (1:10) as eluent to furnish the coupling product **23** (0.60 g, 0.84 mmol) as a pale yellow oil.

R_f=0.5 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=+5.3 (*c*=0.5, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69–7.61 (4H, m, Ar*H*), 7.42–7.36 (6H, m, Ar*H*), 7.24 (2H, d, *J*=8.4 Hz, Ar*H*), 6.87 (2H, d, *J*=8.4 Hz, Ar*H*), 5.70 (1H, td, *J*=15.4, 7.2 Hz, =C*H*–CH), 5.33 (1H, dd, *J*=15.4, 7.0 Hz, =C*H*–CH_2), 4.72 (1H, d, *J*=7.2 Hz, OCH_2O), 4.47 (1H, d, *J*=7.2 Hz, OCH_2O), 4.46–4.43 (2H, m, OCH_2O), 4.32 (2H, s, OCH_2), 4.02 (1H, dd, *J*=8.0, 5.2 Hz, C*H*), 3.80 (3H, s, OCH_3), 3.76–3.74 (1H, m, C*H*), 3.50 (1H, dd, *J*=8.8, 5.6 Hz, C*H*), 3.36 (3H, s, OCH_3), 3.32 (3H, s, OCH_3), 3.32–3.28 (2H, m, OCH_2), 2.19–2.17 (1H, m, CH_2), 1.98–1.89 (3H, m, CH_2), 1.50–1.32 (6H, m, CH_2), 1.18–1.13 (3H, m, CH_2), 1.11 (9H, s, Si(CH_3)$_3$), 1.06 (3H, d, *J*=7.1 Hz, CH_3), 0.90 (3H, t, *J*=6.8 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz) δ 159.2, 136.1, 134.9, 134.3, 134.2, 130.9, 129.7, 129.6, 128.5, 127.6, 127.5, 113.8, 96.7, 93.6, 80.9, 77.6, 74.1, 72.8, 72.5, 55.5, 55.3, 38.9, 31.9, 31.3, 29.4, 28.8, 27.2, 25.9, 22.6, 19.5, 14.1.

HRESIMS (*m*/*z*) found 743.4307 M+Na]$^+$ (calcd for $C_{43}H_{64}O_7SiNa$, 743.4318).

3.20. (2*S*,3*R*,8*S*,9*S*,*E*)-9-(*tert*-Butyldiphenylsilyloxy)-3,8-bis(methoxymethoxy)-2-methyltetradec-4-en-1-ol (24)

Compound **23** (0.34 g, 0.47 mmol) was taken in 5 mL of DCM:phosphate buffer (9:1). DDQ (0.14 g, 0.6 mmol) was added to it in one portion. The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was then filtered off, and the filtrate was washed with 5% $NaHCO_3$ solution, water and brine. The organic layer was dried with $MgSO_4$ and evaporated in vacuo. Purification of the crude product by silica gel column chromatography (EtOAc/hexane, 1:3) afforded the desired product **24** (0.253 g, 0.42 mmol) in 90% yield.

R_f=0.2 (EtOAc/hexane, 1:3).

$[\alpha]_D^{28}$=−7.8 (*c*=0.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69–7.65 (4H, m, Ar*H*), 7.41–7.34 (6H, m, Ar*H*), 5.65 (1H, td, *J*=15.2, 7.0 Hz, =C*H*–CH), 5.33 (1H, dd, *J*=15.2, 7.0 Hz, =C*H*–CH_2), 4.69 (1H, d, *J*=6.8 Hz, OCH_2O), 4.51 (1H, d, *J*=6.8 Hz, OCH_2O), 4.33 (2H, s, OCH_2O), 4.11–4.06 (1H, m, C*H*), 3.76–3.73 (1H, m, C*H*), 3.68–3.65 (1H, m, C*H*), 3.52–3.49 (1H, m, CH_2), 3.43–3.40 (1H, m, CH_2), 3.36 (3H, s, OCH_3), 3.20 (3H, s, OCH_3), 2.17–2.10 (1H, m, OCH_2), 1.95–1.88 (3H, m, OCH_2), 1.50–1.30 (6H, m, OCH_2), 1.18–1.13 (3H, m, OCH_2), 1.05 (9H, s, Si(CH_3)$_3$), 0.91 (3H, d, *J*=7.2 Hz, CH_3), 0.75 (3H, t, *J*=6.8 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.2, 136.1, 135.7, 134.2, 129.8, 127.7, 127.6, 127.2, 96.7, 93.6, 80.8, 79.5, 74.1, 65.6, 55.7, 55.5, 40.0, 31.9, 31.3, 29.4, 28.7, 27.2, 26.0, 22.6, 19.5, 14.1, 12.3.

HRESIMS (*m*/*z*) found 623.3823 [M+Na]$^+$ (calcd for $C_{35}H_{56}O_6SiNa$, 623.3846).

3.21. (2*R*,3*R*,8*S*,9*S*,*E*)-9-(*tert*-Butyldiphenylsilyloxy)-3,8-bis(methoxymethoxy)-2-methyltetradec-4-enoic acid (25)

To a solution of above alcohol **24** (0.25 g, 0.42 mmol) in DCM:H_2O (1:1, 8 mL) were added TEMPO (0.024 g, 0.16 mmol) and BAIB (0.53 g, 1.67 mmol). After stirring at room temperature for 4 h, the reaction mixture was diluted with DCM (10 mL) and then washed with saturated aqueous $Na_2S_2O_3$ (10 mL). The organic layer was dried over $MgSO_4$, filtered, and the filtrate was concentrated under reduced pressure to give the crude carboxylic acid, which was further purified by flash column chromatography (EtOAc/hexane=1:2) gave acid **25** (0.23 g, 88%) as a colorless oil.

R_f=0.3 (EtOAc/hexane, 1:1).

$[\alpha]_D^{28}$=−20.6 (*c*=0.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69–7.66 (4H, m, Ar*H*), 7.43–7.35 (6H, m, Ar*H*), 5.70 (1H, td, *J*=15.6, 7.0 Hz, =C*H*–CH), 5.33–5.30 (1H, m, =C*H*–CH_2), 4.72 (1H, d, *J*=6.8 Hz, OCH_2O), 4.51 (1H, d, *J*=6.8 Hz, OCH_2O), 4.33 (2H, s, OCH_2O), 4.31–4.26 (1H, m, C*H*), 3.86–3.80 (1H, m, C*H*), 3.36–3.30 (4H, m, C*H*, CH_3), 3.20 (3H, s, CH_3), 2.65 (1H, t, *J*=6.4 Hz, CH_2), 2.25–2.21 (1H, m, OCH_2), 2.01–1.90 (3H, m, OCH_2), 1.50–1.36 (3H, m, OCH_2), 1.30–1.20 (6H, m, OCH_2), 1.09 (3H, d, *J*=7.1 Hz, CH_3), 1.05 (9H, s, Si(CH_3)$_3$), 0.80 (3H, t, *J*=6.8 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz) δ 178.9, 136.6, 136.1, 134.2, 129.7, 129.6, 127.5, 126.8, 96.5, 93.5, 80.5, 77.5, 74.0, 55.9, 55.3, 44.9, 31.9, 31.3, 29.2, 25.9, 22.5, 21.1, 19.5, 14.3, 12.0.

HRESIMS (*m*/*z*) found 637.3543 $[M+Na]^+$ (calcd for $C_{35}H_{54}O_7SiNa$, 637.3536).

3.22. (2*R*,3*R*,8*S*,9*S*,*E*)-9-Hydroxy-3,8-bis(methoxymethoxy)-2-methyltetradec-4-enoic acid (26)

To a solution of **25** (0.16 g, 0.27 mmol) in dry THF (2 mL) was added TBAF (1.0 M in THF, 0.5 mmol, 0.5 mL) at room temperature and stirring was continued for 4 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (10 mL) solution, the layers were separated and the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were washed with water, brine and then it was dried over $MgSO_4$. The organic solvent was concentrated and purified by silica gel column chromatography (EtOAc/hexane, 1:2) to afford the carboxylic acid **26** (0.83 g, 0.22 mmol) in 82% yield.

R_f=0.2 (EtOAc/hexane, 1:1).

$[\alpha]_D^{28}$=−10.6 (*c*=0.4, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.70 (1H, td, *J*=15.2, 7.0 Hz, =C*H*–CH), 5.30 (1H, dd, *J*=15.2, 6.8 Hz, =C*H*–CH_2), 4.70–4.51 (3H, m, OCH_2O), 4.49 (1H, d, *J*=7.2 Hz, OCH_2O), 4.16 (1H, t, *J*=7.2 Hz, C*H*), 3.51–3.49 (1H, brs, C*H*), 3.40 (3H, s, CH_3), 3.34 (3H, s, CH_3), 2.62 (1H, t, *J*=6.8 Hz, C*H*), 2.15–2.03 (2H, m, CH_2), 1.79–1.69 (1H, m, OCH_2), 1.59–1.43 (3H, m, OCH_2), 1.38–1.29 (6H, m, OCH_2), 1.10 (3H, d, *J*=7.0 Hz, CH_3), 0.88 (3H, t, *J*=6.8 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 50 MHz): δ 178.3, 136.1, 127.9, 96.7, 93.6, 81.5, 78.1, 72.7, 55.9, 55.7, 45.3, 32.0, 30.2, 28.0, 27.9, 27.2, 25.9, 22.8, 14.2, 12.9.

HRESIMS (*m*/*z*) found 399.2352 $[M+Na]^+$ (calcd for $C_{19}H_{36}O_7Na$, 399.2358).

3.23. (3*R*,4*R*,9*S*,10*R*,*E*)-4,9-Bis(methoxymethoxy)-3-methyl-10-pentyl-3,4,7,8,9,10-hexahydro-2*H*-oxecin-2-one (27)

To a solution of Ph_3P (0.2 g, 0.8 mmol) and DIAD (157 μl, 0.8 mmol) in 50 mL toluene under N_2 atmosphere at 0 °C was added a solution of seco-acid **26** (0.05 g, 0.13 mmol) in 50 mL of toluene via syringe pump over 1 h. The resulting mixture was then slowly allowed to attain room temperature. After 12 h starting material was disappeared as indicated by TLC, the reaction mixture was then concentrated and the crude material was purified by flash chromatography on silica gel with EtOAc/hexane (1:10) to afforded the macrolactone **27** (0.035 g, 0.1 mmol) in 75% yield.

R_f=0.5 (EtOAc/hexane, 1:3).

$[\alpha]_D^{28}$=−20.8 (*c*=0.3, $CHCl_3$).

^{1}H NMR($CDCl_3$, 400 MHz) δ 5.60 (1H, td, *J*=15.6, 4.0 Hz, =C*H*–CH), 5.44 (1H, dd, *J*=15.4, 2.0 Hz, =C*H*–CH_2), 4.99 (1H, dd, *J*=10.0, 5.6 Hz, C*H*), 4.79 (1H, dt, *J*=10.8, 2.4 Hz, C*H*), 4.68 (2H, dd, *J*=6.4, 2.0 Hz, OCH_2O), 4.61 (2H, dd, *J*=10.4, 6.8 Hz, OCH_2O), 3.67 (1H, dt, *J*=11.6, 3.6 Hz, C*H*), 3.41 (3H, s, CH_3), 3.37 (3H, s, CH_3), 3.06–2.99 (1H, m, C*H*), 2.69 (1H, qd, *J*=15.2, 3.6 Hz, C*H*), 2.00–1.89 (1H, m, CH_2), 1.87–1.77 (1H, m, CH_2), 1.70–1.56 (3H, m, CH_2), 1.52–1.47 (1H, m, CH_2), 1.36–1.27 (6H, m, CH_2), 1.20–1.18 (3H, m, CH_2), 0.92 (3H, t, *J*=6.6 Hz, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ=172.7, 134.1, 126.9, 96.3, 94.5, 75.9, 72.8, 70.4, 55.8, 55.7, 45.0, 34.7, 31.1, 28.8, 26.0, 24.3, 22.7, 14.2, 12.9.

HRESIMS (*m*/*z*) found 381.2254 $[M+Na]^+$ (calcd for $C_{19}H_{34}O_6Na$, 381.2252).

3.24. (3*R*,4*R*,9*S*,10*R*,*E*)-4,9-Dihydroxy-3-methyl-10-pentyl-3,4,7,8,9,10-hexahydro-2*H*-oxecin-2-one (cytospolide D)

To a solution of ring closing compound **27** (0.03 g, 0.08 mmol) in THF (2 mL) was added HCl (1 mL, 2 M) at room temperature and stirred for 12 h. Water was added to the reaction mixture and it was extracted with ethyl acetate. The organic layer was washed with $NaHCO_3$ and brine. It was then dried over $MgSO_4$, concentrated in a rotary evaporator and purified by silica gel column chromatography (EtOAc/hexane, 1:1) to afford the target molecule cytospolide D (0.02 g, 0.067 mmol) in 90% yield as a white amorphous solid.

R_f=0.4 (EtOAc/hexane, 2:1).

$[\alpha]_D^{28}$=−78.6 (*c*=0.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.61 (2H, ov, =C*H*–CH, =C*H*–CH_2), 4.77 (1H, td, *J*=7.5, 4.0 Hz, C*H*), 4.30–4.28 (1H, m, C*H*), 3.65 (1H, t, *J*=7.0 Hz, C*H*), 2.69 (1H, qd, *J*=6.8, 3.2 Hz, C*H*), 2.35–2.32 (1H, m, CH_2), 2.15–2.13 (1H, m, CH_2), 2.00–1.85 (2H, m, CH_2), 1.72–1.68 (1H, m, CH_2), 1.53–1.50 (1H, m, CH_2), 1.28–1.20 (9H, m, CH_2), 0.88 (3H, t, *J*=6.6 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.4, 133.1, 127.6, 77.8, 73.9, 71.9, 46.7, 38.1, 32.1, 31.7, 28.3, 24.3, 22.5, 14.0, 12.4.

HRESIMS (*m*/*z*) found 293.1730 $[M+Na]^+$ (calcd for $C_{15}H_{26}O_4Na$, 293.1728).

3.25. (2*R*,3*S*,8*R*,9*R*,*E*)-9-Methyl-10-oxo-2-pentyl-3,4,5,8,9,10-hexahydro-2*H*-oxecine-3,8-diyl diacetate (cytospolide C)

To the solution of cytospolide D (0.011 g, 0.04 mmol) in Et_3N (2 mL) Ac_2O (1 mL) was added at room temperature and stirred for 6 h. The reaction mixture was then concentrated and the crude material was purified by flash chromatography on silica gel with EtOAc/hexane (1:10) to afford cytospolide C (0.012 g, 0.036 mmol) in 90% yield.

R_f=0.4 (EtOAc/hexane, 1:5).

$[\alpha]_D^{28}$=−52.0 (*c*=0.3, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.64 (1H, dd, *J*=16.2, 2.8 Hz, =C*H*–CH), 5.55 (1H, ddd, *J*=16.2, 9.6, 5.0 Hz, =C*H*–CH_2), 5.35 (1H, brs, C*H*), 4.94 (1H, td, *J*=7.3, 4.0 Hz, C*H*), 4.75 (1H, td, *J*=7.2, 1.0 Hz, C*H*), 2.74 (1H, qd, *J*=6.8, 3.0 Hz, C*H*), 2.25–2.18 (2H, m, CH_2), 2.14 (3H, s, CH_3), 2.04 (3H, s, CH_3), 1.90–1.84 (2H, m, CH_2), 1.63–1.60 (1H, m, CH_2), 1.40–1.20 (10H, m, CH_2), 0.88 (3H, t, *J*=6.6 Hz, CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.7, 170.3, 169.9, 129.2, 129.0, 75.6, 75.1, 72.6, 45.0, 35.3, 32.0, 31.7, 24.1, 22.5, 21.2, 20.9, 14.0, 12.3.

HRESIMS (m/z) found: 355.2112 for $C_{19}H_{31}O_6$ $[M+H]^+$, calculated: 355.2112.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.04.014.

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