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A carbohydrate approach for the synthesis of tetrahydropyran containing C16–C29 fragment of sorangicin A

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ABSTRACT

A carbohydrate derived synthesis of C16–C29 fragment of sorangicin A is described utilizing regioselective epoxide opening, segment-coupled Prins cyclization reaction and cross metathesis as the key steps.

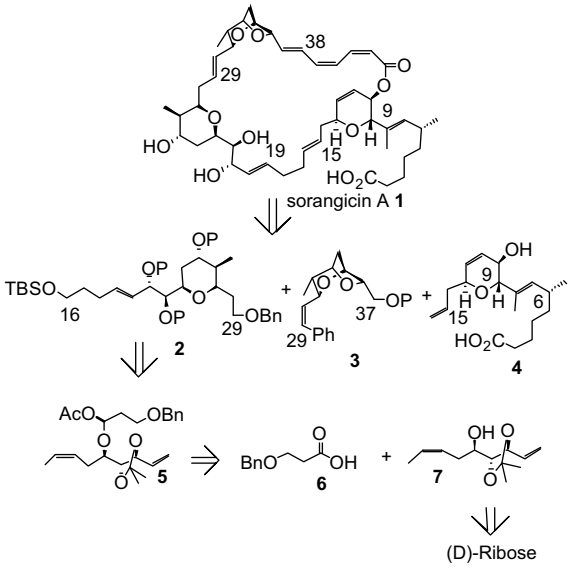
1. Introduction

The increasing multi-resistance in bacteria has been a major demand for the discovery of new and novel antibiotic compounds. The polyether and polyene macrolides, sorangicins are potent antibiotic compounds which were isolated from gliding bacteria *Sorangium cellulosum*[1] in 1985 and their structures were determined by Hofle and Reichenbach in 1989.[2] Sorangicin A was found to exhibit extraordinary antibiotic activity against both Gram-positive (MIC $<0.01\sim2$ μg/mL) and Gram-negative bacteria (MIC 2 $\sim>32$ μg/mL).[3] Mechanistic studies revealed that the sorangicins inhibit DNA dependent RNA polymerase in both *Escherichia coli* and *Staphylococcus aureus* similar to rifampicin. Albeit the chemical structures of both rifampicin and sorangicin are different, the similarity in behaviour was expected due to the conformational flexibility of sorangicin molecule which can undergo amino acid modifications within the binding pocket of the subunit.[4]

The novel architecture of sorangicin, with a 31-membered macrolide ring, dioxabicyclo[3.2.1]octane moiety, the *cis,cis,trans*-trienoate, dihydropyran and tetrahydropyran units combined together with the significant biological activity has featured sorangicin A as an challenging target for the synthetic organic chemists. Even though there are no reports for the total synthesis, significant efforts from Amos Smith III et al.[5] and other groups[6] have resulted in the synthesis of advanced key intermediate fragments of sorangicin A. In continuation to the synthesis of biologically active natural products targeting macrolides[7] with potent antibiotic and anti tumor activities, we herein describe an efficient synthesis of C16 to C29 fragment of sorangicin A starting from the readily available chiral substrate D-ribose.

2. Results and discussion

Our retrosynthetic analysis revealed three key intermediate fragments **2**, **3** and **4** (Scheme 1). Our initial focus was on the synthesis of fragment **2** with 6 chiral centers and a tetrahydropyran ring. We envisioned that the fragment **2** could be achieved by segment coupled Prins cyclization of the compound **5** followed by selective manipulations and cross metathesis reaction. Compound **5** in turn could be obtained by coupling homoallyl alcohol **7** and 3-benzyloxy propionic acid **6** followed by two step manipulations. The homoallyl alcohol **7** can be easily synthesized from D-ribose in 6 steps.



Scheme 1. Retrosynthesis.

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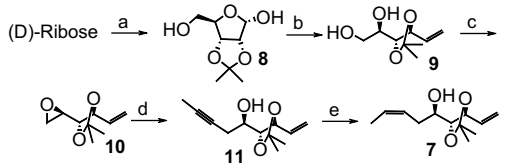
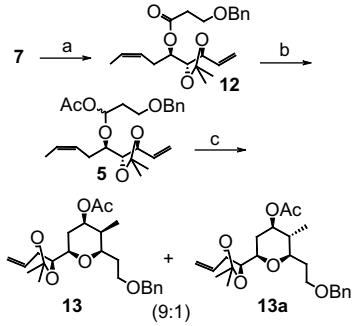
The synthesis began with isopropylidination of D-ribose with acetone in presence of catalytic amount of concd H_2SO_4 to get compound **8**.[8] 1C-Wittig reaction of lactol **8** with methyltriphenylphosphonium bromide in the presence of potassium *tert* butoxide yielded olefin **9**.[9] Selective mono tosylation of diol **9** followed by treatment with NaH provided epoxide **10**. Regioselective epoxide opening[10] with lithiated propyne afforded homo propargylic alcohol **11**, which was partially reduced to homo allylic alcohol **7** under Lindlar's condition (Scheme 2) in 98% yield.



Scheme 2. Synthesis of homoallyl alcohol **7**. Reagents and conditions: (a) cat. H_2SO_4, acetone, rt, 2.5 h, 93%. (b) Ph_3PCH_3Br, KO^{t}Bu, THF, 0 °C–rt, 13 h. (c) (i) Et_3N, Bu_2SnO, TsCl, 0 °C–rt, 5 h, (ii) NaH, THF, 0 °C–rt, 4 h, overall yield for 3 steps 61%. (d) CH_3CCH, *n*-BuLi, HMPA, −78 °C to 0 °C, 18 h, 99%. (e) Pd/$CaCO_3$, MeOH, 10 min rt, 98%.

Initially, with the homoallyl alcohol **7** in hand, we investigated the Prins cyclization with 3-benzyloxy propionaldehyde. Several attempts with Prins cyclization produced no fruitful results.[11] This prompted us to alter our strategy for the segment coupled Prins cyclization. The alcohol **7** was esterified with 3-benzyloxy propanoic acid **6** employing DCC, DMAP to get the ester **12** in 95% yield. The ester on treatment with DIBAL-H gave lactol, which was further masked as acetate **5** upon treatment with acetic anhydride and pyridine in 98% overall yield. The substrate **5** was subjected to the segment-coupled Prins cyclization[12] employing $BF_3\cdot Et_2O$, AcOH at −20 °C to get the mixtures of easily separable tetrahydropyran acetates **13** and **13a** in 9:1 ratio (Scheme 3 and Fig. 1).



Scheme 3. Synthesis of **13**. Reagents and conditions: (a) **6**, DCC, DMAP, DCM, 0 °C to rt, 5 h, 95%. (b) (i) DIBAL-H, DCM, −78 °C, (ii) Ac_2O, pyridine, DMAP, 15 h, overall yield 98%. (c) $BF_3\cdot Et_2O$, AcOH, hexane, 30 min 70%.

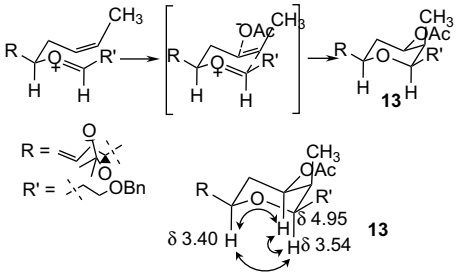
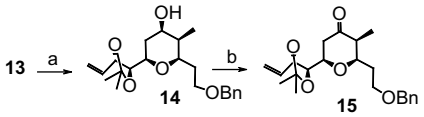


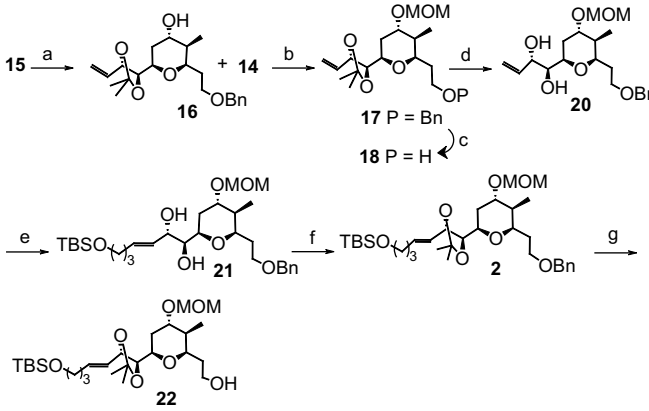
Figure 1. Chair like transition state for segment coupled Prins cyclization and significant NOE correlations observed confirming 2,4,6-*syn* substitution for compound **13**.

The compound **13** was treated with sodium methoxide in methanol to get the alcohol **14**. Inversion of C25 hydroxyl under Mitsunobu conditions did not succeed to our expectations.[13] Thus the only option left for us was to proceed further by the regular oxidation and stereoselective reduction. PCC oxidation of compound **14** afforded ketone **15** (Scheme 4) which was subjected to stereoselective reduction. Several reducing agents such as $NaCNBH_3$, $NaBH(OAc)_3$, $Zn(BH_4)_2$, Red Al, $NaBH_4$ and $LialH_4$ were investigated and found to result in undesired product **14** (>90% yields),[14] whereas, reduction with N-Selectride and K-Selectride gave 30% of the desired product **16**.



Scheme 4. Synthesis of ketone **15**. Reagents and conditions: NaOMe, MeOH, rt, 2 h, 89%. (b) PCC, Celite, DCM, 0 °C to rt, 2 h, 96%.

Finally, the transformation turned out to be the best with DIBAL-H[5c] (46% yield) which gave desired alcohol **16**. Thus after reduction with DIBAL-H, the alcohol **16** was protected with chloromethylmethyl ether to afford the MOM-ether **17**. Selective debenzylation of **17** with lithium napthalenide yielded **18**. With the C19–C29 fragment **17** in hand it remained to effect cross metathesis to extend the chain from C16 to C19. Thus, a cross metathesis reaction between compound **17** and TBS protected 4-pentene-1-ol **19** employing Grubbs' 2nd generation catalyst was attempted. The reaction did not succeed to our expectations and resulted in an unidentified by product[15] which may be attributed to the presence of acetonide moiety. Hence the metathesis reaction was attempted once again with the free diol. Thus, isopropylidene group in **17** was unmasked using 70% AcOH to get the free diol **20** in 90% yield. Gratifyingly, cross metathesis reaction of diol **20** and TBS protected 4-pentene-1-ol **19** gave the desired product **21** as the only product in 65% yield.[16] The diol was reprotected as acetonide **2** and then treated with lithium napthanelide to yield the known fragment[5c] **22** (Scheme 5) which can be utilized further for the total synthesis of sorangicin A.



Scheme 5. Synthesis of **22**. Reagents and conditions: (a) DIBAL-H, DCM, −78 °C, 1.5 h, 46% for **16**, 50% for **14**. (b) MOMCl, 2,6-lutidine, CH_3CN, rt, 12 h, 98%, (c) Li napthalene, THF, 96%. (d) 70% AcOH, 45 °C, 4 h, 90%. (e) **19**, 2nd generation Grubbs catalyst, DCM, rt, 12 h, 65%. (f) 2,2-DMP, DCM, rt, 1 h, 98%. (g) Li, napthalene, THF, −20 °C, 97%.

3. Conclusions

In conclusion, we have synthesized a key intermediate, C16–C29 fragment required for the total synthesis of sorangicin A utilizing, segment-coupled Prins reaction, regioselective epoxide opening reaction as the key steps starting from the chiral precursor D-ribose in total of 17 steps with an overall yield of 7.7%. Studies towards the synthesis of other key intermediate fragments and the total synthesis of sorangicin A are currently being investigated.

4. Experimental section

4.1. General information

All the reagents employed were obtained commercially from M/s. Aldrich and used without further purifications unless otherwise stated. For anhydrous reactions, solvents were dried following known literature and removal of solvent was performed under reduced pressure using a rotary evaporator. All reactions requiring anhydrous conditions were carried out in oven-dried glassware under a nitrogen atmosphere. The ^{1}H NMR spectra were recorded at 300 or 400 MHz, and the ^{13}C NMR spectra were recorded at 75 MHz/100 MHz at ambient temperature. Chemical shifts of the ^{1}H NMR spectra are expressed in ppm relative to the solvent residual signal 7.26 in $CDCl_3$ or to tetramethylsilane (δ=0.00). Chemical shifts of the ^{13}C NMR spectra are expressed in ppm relative to the solvent signal 77.00 in $CDCl_3$ unless otherwise noted. One or more of the following methods were used for visualization: UV absorption by fluorescence quenching; iodine staining; anisaldehyde stain (ethanol (135 mL)/H_2SO_4 (5 mL)/AcOH (1.5 mL)/*p*-anisaldehyde 3.7 mL). Column chromatography was performed using 60–120 mesh silica gel. Ethyl acetate and hexane were the common eluents used unless specified.

4.1.1. 2,3-O-Isopropylidene-D-ribose **8**

To a stirred suspension of D-ribose (20.0 g, 133.3 mmol) in acetone (200 mL) was added drop wise concd H_2SO_4 (0.6 mL) at room temperature and the reaction mixture was stirred at room temperature for 2.5 h. The mixture was neutralized with solid $NaHCO_3$, filtered and evaporated under reduced pressure to give colorless syrup. The residue was purified by silica gel column chromatography (50% EtOAc/hexane) to afford **8** as a colorless syrup (23.5 g, 93%). R_f (50% EtOAc/hexane) 0.40; IR (neat) ν_{max}: 3400, 2986, 2941, 1376, 1211, 1068 cm^{-1}; $[\alpha]_D^{34}$ −37.4 (*c* 1.1, acetone); Lit.[8] $[\alpha]_D^{25}$ −37 (*c* 53, acetone); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.39 (s, 1H), 4.81 (d, *J*=6.0 Hz, 1H), 4.56 (d, *J*=6.0 Hz, 1H), 4.39 (br t, *J*=2.6 Hz, 1H), 3.71 (t, *J*=2.6 Hz, 2H), 1.47 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (75 MHz, CD_3OD): δ 113.1, 103.9, 88.5, 87.9, 83.4, 64.3, 26.7, 24.9; MS (ES): *m*/*z* 213 (M^++Na); HRMS (ESI) *m*/*z* calcd for $C_8H_{14}O_5Na$ 213.0738, found 213.0736.

4.1.2. (R)-1-((4S,5S)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)-ethane-1,2-diol **9**

To a stirred suspension of methyl triphenylphosphonium bromide (65.7 g, 184 mmol) in THF (200 mL) was added potassium *tert*-butoxide (17.7 g, 157 mmol) at 0 °C and the reaction mixture was stirred for 20 min at same temperature and then at room temperature for 1 h. After the mixture was cooled to 0 °C, a solution of **8** (10 g, 52.6 mmol) in THF (60 mL) was added and the reaction mixture was stirred at room temperature for 12 h and poured into water carefully. The mixture was extracted with ethyl acetate and the organic layer was dried over anhydrous sodium sulphate, filtered, and evaporated. The resulting syrup was purified by silica gel column chromatography (60% EtOAc/hexane) to give diol **9** as a colorless liquid with a little contamination of triphenylphosphine oxide. Analytical sample of diol was obtained by preparative TLC. R_f (50% EtOAc/hexane) 0.40; IR (neat) ν_{max}: 3415, 2987, 2928, 2856, 1646, 1377, 1217, 1059 cm^{-1}; $[\alpha]_D^{29}$ +5.3 (*c* 5.40, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.99 (ddd, *J*=17.6, 10.4, 6.8 Hz, 1H), 5.45 (td, *J*=17.6, 1.6 Hz, 1H), 5.32 (td, *J*=10.4, 1.2 Hz, 1H), 4.69 (tt, *J*=6.4, 1.3 Hz, 1H), 4.09 (dd, *J*=8.4, 6.4 Hz, 1H), 3.83–3.59 (m, 3H), 2.88 (br s, 2H), 1.45 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.5, 117.8, 108.7, 78.3, 77.5, 69.8, 64.0, 27.5, 25.1; MS (ES): *m*/*z* 188 (M+H^+); HRMS (ESI) *m*/*z* calcd for $C_9H_{16}O_4Na$ 211.0946, found 211.0938.

4.1.3. (4R,5S)-2,2-Dimethyl-4-((R)-oxiran-2-yl)-5-vinyl-1,3-dioxolane **10**

A stirred solution of the diol (9.9 g, 52.6 mmol) and dibutyltin oxide (2.6 g, 10.5 mmol) in anhydrous dichloromethane (100 mL) was added dropwise tryethylamine (11 mL, 79 mmol) at 0 °C, then the reaction mixture was allowed to warm to room temperature. After 15 min at room temperature, the reaction mixture was cooled to 0 °C then *p*-toluenesulfonylchloride (10.3 g, 52.6 mmol) was added portion wise and stirred at rt for 5 h. The reaction was monitered by TLC and filtered through sintered funnel on Celite bed; the organic layer was dried over anhydrous sodium sulphate, filtered, and evaporated. The resulting colorless oil was directly used for the next reaction without any further purification. To the suspension of NaH (1.9 g, 78.9 mmol) in dry THF (70 mL) was cooled to 0 °C and added monotosylate compound (18.0 g, 52.6 mmol) in THF (100 mL) in a drop wise manner. The reaction was left to room temperature and stirred for 4 h, quenched at 0 °C using saturated aqueous NH_4Cl solution (20 mL). Then diethyl ether (150 mL) and water (100 mL) were added, the organic layer was separated and the aqueous layer was extracted with diethyl ether (3×100 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulphate and concentrated at reduced pressure. Column chromatography of crude product afforded **10** (5.4 g, 61% over three steps) as a colourless oil. R_f (50% Et_2O/hexane) 0.70; IR (neat) ν_{max}: 2990, 2925, 2854, 1459, 1378, 1216 cm^{-1}; $[\alpha]_D^{28}$ +16.1 (*c* 0.75, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.96 (ddd, *J*=16.6, 10.6, 6.8 Hz, 1H), 5.46 (td, *J*=17.3, 1.5 Hz, 1H), 5.32 (td, *J*=10.6, 1.5 Hz, 1H), 4.69 (tt, *J*=6.0, 1.5 Hz, 1H), 3.63 (dd, *J*=7.5, 6.8 Hz, 1H), 2.90–2.85 (m, 1H), 2.78 (dt, *J*=3.8, 1.5 Hz, 1H), 2.60 (dd, *J*=5.3, 2.3 Hz, 1H), 1.50 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.4, 118.6, 109.0, 78.8, 78.5, 49.7, 45.5, 27.5, 25.0; MS (ES): *m*/*z* 171 (M+H^+); HRMS (ESI): *m*/*z* calcd for $C_9H_{14}O_3Na$ 193.0840, found 193.0838.

4.1.4. (R)-1-((4S,5S)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)pent-3-yn-1-ol **11**

A solution of *n*-butyl lithium in hexane (18.7 mL, 30 mmol, 1.6 M solution in hexane) was added to a solution of propyne (2.27 g, 40 mmol) in THF (40 mL) at −78 °C and the mixture was stirred for 15 min under nitrogen atmosphere. The reaction mixture was warmed to −10 °C over 30 min and then cooled to −78 °C. Dry HMPA (10 mL) was added, followed by dropwise addition, over 15 min, of epoxide (3.4 g, 20 mmol) in HMPA (15 mL). The reaction was stirred at −20 °C for 30 min, warmed to 20 °C over 4 h, and stirred for an additional 12 h. The mixture was then poured into ice water (100 mL) and extracted with ether (3×100 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulphate and concentrated at reduced pressure. The resulting syrup was purified by silica gel column chromatography (15% EtOAc/hexane) to give pale yellow color alcohol **11** (4.15 g, 99%). R_f (10% EtOAc/hexane) 0.20; IR (neat) ν_{max}: 3458, 2987, 2923, 1376, 1216, 1167, 1058 cm^{-1}; $[\alpha]_D^{28}$ −2.2 (*c* 1.40, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.99 (ddd, *J*=17.3, 10.6, 6.0 Hz, 1H), 5.40 (td, *J*=17.3, 1.5 Hz, 1H), 5.23 (tt, *J*=10.6, 1.5 Hz, 1H), 4.65 (tt, *J*=6.8, 1.5 Hz, 1H), 3.96 (dd, *J*=9.0, 6.8 Hz, 1H), 3.80–3.58 (m, 1H), 2.61–2.48 (m, 1H), 2.43–2.29 (m, 1H), 1.83–1.78 (m, 3H), 1.44 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.9, 117.8, 108.6, 79.3, 78.7, 78.5, 74.4, 68.1, 27.6, 25.3, 24.5, 3.5; MS (ESI) *m*/*z* 233 (M^++Na); HRMS (ESI): *m*/*z* calcd for $C_{12}H_{18}O_3Na$ 233.1153, found 233.1148.

4.1.5. (R,Z)-1-((4S,5S)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)-pent-3-en-1-ol **7**

To a solution of **11** (0.5 g, 2 mmol) in 5 mL of methanol/quinoline (10:0.3) was added Lindlar's catalyst (10 mg). The reaction mixture was stirred for 10 min under atmosphere of H_2 at room temperature and filtered through a Celite pad. The filtrate was

concentrated, and the residue was purified by silica gel column chromatography using (10% EtOAc/hexane) to give olefin **7** (0.49 g, 98%) as a colorless liquid. R_f (10% EtOAc/hexane) 0.30; IR (neat) ν_{max}: 3448, 2986, 2927, 1375, 1217, 1057 cm^{-1}; $[\alpha]_D^{27}$ −2.3 (*c* 0.90, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 6.02 (ddd, *J*=17.3, 10.5, 6.8 Hz, 1H), 5.76–5.60 (m, 1H), 5.51–5.36 (m, 2H), 5.27 (d, *J*=10.6 Hz, 1H), 4.61 (t, *J*=6.8 Hz, 1H), 3.94 (dd, *J*=9.0, 6.8 Hz, 1H), 3.70–3.54 (m, 1H), 2.49–2.35 (m, 1H), 2.33–2.19 (m, 1H), 1.66 (d, *J*=6.8 Hz, 3H), 1.46 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.5, 127.7, 125.3, 118.0, 108.6, 80.1, 78.8, 69.5, 31.3, 27.7, 25.3, 12.9; MS (ES): *m*/*z* 235 (M^++Na); HRMS (ESI) *m*/*z* calcd for $C_{12}H_{20}O_3Na$ 235.1310, found 235.1304.

4.1.6. *(R,Z)-1-((4S,5S)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)-pent-3-enyl 3-(benzyloxy)propanoate* ***12***

A solution of 3-*O*-benzyl propionic acid-**6** (3.05 g, 16.9 mmol) in 30 mL dichloromethane was cooled to 0 °C. A sample of DCC (4.3 g, 20 mmol) was added in several portions and a white precipitate formed quickly. After 15 min stirring, alcohol **7** (3.0 g, 14.1 mmol) was added as a solution in 15 mL dichloromethane along with a small amount of DMAP. The cooling bath was removed and stirring was continued for 5 h. The solution was filtered and the solvent was removed under reduced pressure. The resulting oil purified by column chromatography (5% EtOAc/hexane) to obtain **12** (4.97 g, 95%) as colorless oil. R_f (10% EtOAc/hexane) 0.40; IR (neat) ν_{max}: 2925, 2857, 1741, 1455, 1374, 1177, 1069 cm^{-1}; $[\alpha]_D^{27}$ −4.1 (*c* 2.05, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.35–7.18 (m, 5H), 5.75 (ddd, *J*=17.3, 9.8, 6.8 Hz, 1H), 5.61–5.46 (m, 1H), 5.42–5.23 (m, 2H), 5.14 (d, *J*=9.8 Hz, 1H), 4.95–4.85 (m, 1H), 4.55 (t, *J*=6.8 Hz, 1H), 4.50 (s, 2H), 4.16 (dd, *J*=8.3, 6.8 Hz, 1H), 3.67 (t, *J*=6.0 Hz, 2H), 2.57–2.33 (m, 4H), 1.58 (d, *J*=6.8 Hz, 3H), 1.47 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 138.0, 135.7, 133.1, 128.3, 127.6, 127.0, 124.3, 118.3, 108.7, 78.7, 77.6, 73.0, 71.6, 65.5, 35.2, 28.5, 27.6, 25.2, 12.8; MS (ES): *m*/*z* 397 (M^++Na); HRMS (ESI): *m*/*z* calcd for $C_{22}H_{30}O_5Na$ 397.1990, found 397.1999.

4.1.7. *3-(Benzyloxy)-1-((R,Z)-1-((4S,5S)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)pent-3-enyloxy)propyl acetate* ***5***

A sample of ester **12** (4.97 g, 13.2 mmol) was dissolved in 50 mL dichloromethane and cooled to −78 °C. Then 1.0 M solution of DIBAL-H in toluene (18.87 mL, 26.5 mmol) were added dropwise and stirring was continued for 45 min. TLC (9:1 hexane/ethyl acetate) analysis indicated that all the starting material **12** was consumed at this time. Then pyridine (3.2 mL, 39 mmol), DMAP (4.86 g, 39 mmol) and acetic anhydride (7.53 mL, 80 mmol) were added and stirring was continued at −78 °C for 14 h. The solution was allowed to warmed 0 °C and stirred for an additional hour. The reaction was quenched with 20 mL satd aq NH_4Cl solution and 20 mL saturated aq sodium potassium tartrate solution and the solution was warmed to 23 °C. The mixture was diluted with dichloromethane and stirred vigorously for 1 h. After extraction with dichloromethane (4×70 mL), the combined organic extracts were washed with ice-cooled 1 M potassium bisulfate (2×20 mL), saturated aq sodium bicarbonate (3×20 mL) and brine. After drying over anhydrous sodium sulphate, the solvent was evaporated and the residue was purified by silica gel column chromatography (10% ethylacetate/hexane) to afford product **5** (5.4 g, 98%) as a colorless oil. R_f (10% ethyl acetate/hexanes, TLC plate developed twice) 0.5; IR (neat) ν_{max}: 2928, 2859, 1739, 1374, 1240, 1109, 759 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.40–7.21 (m, 5H), 6.17 (t, *J*=6.0 Hz, 1H), 6.02–5.88 (m, 1H), 5.64–5.50 (m, 1H), 5.51–5.39 (m, 1H), 5.38–5.28 (m, 1H), 5.22–5.13 (m, 1H), 4.58 (t, 1H), 4.51–4.43 (m, 2H), 4.07 (dd, *J*=7.5, 1.51 Hz, 1H), 3.78–3.71 (m, 1H), 3.59–3.41 (m, 2H), 2.62–2.31 (m, 2H), 2.01 (s, 3H), 1.94 (m, 2H), 1.64 (d, *J*=6.8 Hz, 3H), 1.47 (s, 3H), 1.34 (s, 3H); MS (ES): *m*/*z* 441 (M^++Na); HRMS (ESI): *m*/*z* calcd for $C_{24}H_{34}O_6Na$ 441.2253, found 441.2242.

4.1.8. *(2R,3S,4R,6R)-2-(2-(Benzyloxy)ethyl)-6-((4R,5R)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)-3-methyltetrahydro-2H-pyran-4-yl acetate* ***13***

A premixed solution of $BF_3{\cdot}OEt_2$ (1.82 mL, 31.5 mmol) and AcOH (2.6 mL, 20 mmol) in hexane (15 mL) was added the solution of α-acetoxy ether **5** (4.4 g, 10 mmol) in hexane (40 mL) by cannula at −20 °C. The reaction mixture was stirred for 30 min at −20 °C and then warmed to 0 °C, whereupon saturated aqueous $NaHCO_3$ (20 mL) was added. The reaction mixture was diluted with hexane (30 mL), washed with brine (20 mL), filtered, dried over anhydrous sodium sulphate and concentrated in vacuum. The resulting orange oil was purified by flash chromatography on silica gel (10% EtOAc/hexane) to afford more polar tetrahydropyran **13** (3.07 g, 70%) as a major diastereomer. R_f (10% EtOAc/hexane) 0.4; IR (neat) ν_{max}: 2983, 2929, 2861, 1740, 1373, 1241, 1103 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.39–7.19 (m, 5H), 5.82 (ddd, *J*=17.4, 10.5, 6.8 Hz, 1H), 5.30 (d, *J*=17.4 Hz, 1H), 5.10 (d, *J*=10.6 Hz, 1H), 5.02–4.89 (m, 1H), 4.61 (t, *J*=6.8 Hz, 1H), 4.47 (d, *J*=3.0 Hz, 2H), 3.95 (d, *J*=8.3, 6.0 Hz, 1H), 3.54 (td, *J*=9.0, 2.2 Hz, 1H), 3.48 (dt, *J*=6.8, 1.5 Hz, 2H), 3.38 (dt, *J*=10.6, 1.5 Hz, 1H), 2.04 (s, 3H), 2.02–1.85 (m, 2H), 1.84–1.71 (m, 1H), 1.67–1.51 (m, 2H), 1.46 (s, 3H), 1.36 (s, 3H), 0.91 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.2, 138.4, 136.4, 133.7, 128.4, 127.6, 117.3, 108.6, 79.4, 78.7, 75.1, 74.1, 73.0, 72.9, 67.1, 35.8, 33.1, 28.8, 27.7, 25.3, 21.1, 5.8; MS (ES): *m*/*z* 441 (M^++Na); HRMS (ESI) *m*/*z* calcd for $C_{24}H_{34}O_6Na$ 441.2253, found 441.2235.

4.1.9. *(2R,3R,4R,6R)-2-(2-(Benzyloxy)ethyl)-6-((4R,5R)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)-3-methyltetrahydro-2H-pyran-4-ol* ***14***

To stirred solution of compound **13** (2.7 g, 6.0 mmol) in methanol (30 mL) at 0 °C was added sodium methoxide (1.0 g, 18.0 mmol) and stirred at room temperature for 2 h. The methanol was then removed under reduced pressure and water (30 mL) was added. The mixture was extracted with dichloromethane (3×30 mL) and the combined organic layer was dried over anhydrous sodium sulphate and the solvent was removed under reduced pressure. Column chromatography (30% EtOAc/hexane) of the crude mixture afforded pure **14** (2.0 g, 89%) as a colorless oil. R_f (30% EtOAc/hexane) 0.35; IR (neat) ν_{max}: 2926, 2825, 1655, 1457, 1382 cm^{-1}; $[\alpha]_D^{28}$ +28.2 (*c* 1.15, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.38–7.30 (m, 5H), 5.92–5.80 (m, 1H), 5.37–5.30 (d, *J*=16.6 Hz, 1H), 5.14–5.10 (d, *J*=10.5 Hz, 1H), 4.64 (t, *J*=6.4 Hz, 1H), 4.50 (d, *J*=3.8 Hz, 2H), 3.95 (dd, *J*=8.3, 6.0 Hz, 1H), 3.93–3.85 (m, 1H), 3.54–3.41 (m, 3H), 3.38–3.27 (m, 1H), 1.93–1.75 (m, 3H), 1.70–1.55 (m, 1H), 1.43 (s, 3H), 1.48–1.36 (m, 1H), 1.34 (s, 3H), 0.9 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.4, 136.4, 133.8, 128.3, 127.6, 117.2, 108.5, 79.5, 78.7, 75.3, 74.2, 73.0, 70.6, 67.2, 38.5, 33.2, 32.2, 27.7, 25.3, 4.9; MS (ES): *m*/*z* 399 (M^++Na); HRMS (ESI): *m*/*z* calcd for $C_{22}H_{32}O_5Na$ 399.2147, found 399.2129.

4.1.10. *(2R,3S,6R)-2-(2-(Benzyloxy)ethyl)-6-((4R,5R)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)-3-methyldihydro-2H-pyran-4(3H)-one* ***15***

To stirred solution of alcohol **14** (2.0 g, 5.31 mmol) in dichloromethane (60 mL) at 0 °C was added pyridinium chlorochromate (2.85 g, 13.2 mmol) and Celite (2.85 g) and stirred at room temperature for 2 h. Diethyl ether (100 mL) was added and the reaction mixture was filtered through a small pad of Celite and silica gel. The filtered cake was washed thoroughly with ether (2×30 mL) and the filtrate was concentrated under reduced pressure. After flash chromatography (20% EtOAc/hexane), the residue afforded the ketone **15** (1.90 g, 96%) as a colorless liquid. R_f (30% EtOAc/hexane) 0.70; IR (neat) ν_{max}: 2928, 2859, 1716, 1378, 1102 cm^{-1}; $[\alpha]_D^{27}$ +56.2 (*c* 1.75, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.40–7.20 (m, 5H), 5.84 (ddd, *J*=17.3, 10.6, 6.8 Hz, 1H), 5.36 (td, *J*=17.3, 1.5 Hz, 1H), 5.14 (td, *J*=10.5, 1.5 Hz, 1H), 4.68 (t, *J*=6.8 Hz, 1H), 4.49 (d, *J*=1.5 Hz, 2H), 4.08

(dt, J=6.8, 1.5 Hz, 1H), 3.77 (td, J=9.0, 3.0 Hz, 1H), 3.63–3.48 (m, 3H), 2.62–2.24 (m, 3H), 1.88 (ddd, J=18.9, 9.0, 4.5 Hz, 1H), 1.74–1.57 (m, 1H), 1.45 (s, 3H), 1.37 (s, 3H), 1.44 (d, J=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 210.6, 138.2, 133.0, 128.4, 127.6, 127.5, 117.7, 108.8, 79.5, 78.4, 75.7, 75.2, 73.0, 66.6, 49.2, 40.8, 32.2, 27.5, 25.2, 10.8; MS (ES) m/z 397 (M^++Na); HRMS (ESI): m/z calcd for $C_{22}H_{30}O_5Na$ 397.1990, found 397.2000.

4.1.11. (2R,3R,4S,6R)-2-(2-(Benzyloxy)ethyl)-6-((4R,5R)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)-3-methyltetrahydro-2H-pyran-4-ol **16**

To a stirring solution of (+)-**15** (3.0 g, 8.0 mmol) in dichloromethane (35 mL) at −78 °C was added DIBAL (16.0 mL, 16 mmol, 1.0 M solution in toluene). The reaction was maintained at −78 °C until complete consumption of starting material occurred (judged by TLC analysis) for 1.5 h. The reaction was quenched by the addition of a 1:2 mixture of Celite to $Na_2SO_4\cdot10H_2O$ and then allowed to warm to rt. Filtration and washing of the filter cake with 2×50 mL dichloromethane was followed by concentration to yield mixture of alcohols **16**/**14** (48:52 by HPLC) in 96% yield. This mixture was separated using column chromatography (20% EtOAc/Hexane) to yield the desired alcohol **16** (1.38 g, 46% yield) as a yellow liquid and **14** (1.5 g, 50% yield) as a colorless oil. R_f (30% EtOAc/hexane) 0.35; IR (neat) ν_{max}: 3455, 2926, 2857, 1455, 1376 cm^{-1}; $[\alpha]_D^{27}$ +11.7 (c 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.27 (m, 5H), 5.95–5.82 (m, 1H), 5.32 (td, J=13, 17.18 Hz, 1H), 5.19–5.11 (m, 1H), 4.64 (t, J=6.4 Hz, 1H), 4.50 (d, J=5.0 Hz, 2H), 4.03–3.90 (m, 3H), 3.86–3.72 (m, 1H), 3.60–3.45 (m, 2H), 1.88–1.49 (m, 5H), 1.45 (s, 3H), 1.35 (s, 3H), 0.90 (d, J=7.17 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.5, 134.0, 128.4, 127.6, 127.5, 117.3, 108.5, 79.9, 78.9, 73.0, 70.7, 70.6, 70.3, 67.6, 38.8, 33.2, 31.2, 27.3, 25.4, 11.0; MS (ES): m/z 399 (M^++Na); HRMS (ESI): m/z calcd for $C_{22}H_{32}O_5Na$ 399.2147, found 399.2142.

4.1.12. (2R,3S,4S,6R)-2-(2-(Benzyloxy)ethyl)-6-((4R,5R)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)-4-(methoxymethoxy)-3-methyltetrahydro-2H-pyran **17**

To a solution of alcohol (+)-**16** (0.2 g, 0.53 mmol) in acetonitrile (3.0 mL) was added 2,6-lutidine (0.24 mL, 2.12 mmol) followed by MOMCl (0.12 mL, 1.60 mmol). The resulting reaction mixture was then allowed to stir overnight at room temperature at which point it was quenched by the addition of 5 mL of satd $NaHCO_3$ and 30 mL of EtOAc. The organic phase was then separated and the aqueous phase was washed with EtOAc (2×30 mL). The combined organic layer was dried over anhydrous sodium sulphate, filtered and concentrated to yield a crude oil. Purification was accomplished by column chromatography (10% EtOAc/hexane) to provide (+)-**17** (0.218 g, 98% yield) as a clear, colorless oil. R_f (10% EtOAc/hexane) 0.40; IR (neat) ν_{max}: 2925, 2857, 1376, 1215, 1068, 1037, 759 cm^{-1}; $[\alpha]_D^{27}$ +19.7 (c 0.85, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39–7.22 (m, 5H), 5.87 (ddd, J=16.6, 10.6, 6.8 Hz, 1H), 5.32 (td, J=16.6, 1.5 Hz, 1H), 5.12 (td, J=10.6, 1.5 Hz, 1H), 4.66 (s, 2H), 4.62 (t, J=6.8 Hz, 1H), 4.50 (d, J=3.8 Hz, 2H), 3.98–3.85 (m, 2H), 3.78–3.64 (m, 2H), 3.57–3.45 (m, 2H), 3.34 (s, 3H), 1.85–1.48 (m, 5H), 1.44 (s, 3H), 1.35 (s, 3H), 0.92 (d, J=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.5, 134.0, 128.3, 127.6, 127.5, 117.2, 108.5, 94.8, 79.9, 78.9, 75.1, 73.0, 71.3, 71.1, 67.6, 55.3, 36.3, 33.2, 28.8, 27.7, 25.4, 11.0; MS (ES): m/z 443 (M^++Na); HRMS (ESI): m/z calcd for $C_{24}H_{36}O_6Na$ 443.2409, found 443.2396.

4.1.13. 2-((2R,3S,4S,6R)-6-((4R,5R)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)-4-(methoxymethoxy)-3-methyltetrahydro-2H-pyran-2-yl)ethanol **18**

To a stirred solution of naphthalene (0.24 g, 1.9 mmol) in THF (4 mL), were added lithium metal (0.01 g, 1.4 mmol) in small pieces. The reaction mixture was stirred at room temperature under an argon atmosphere until lithium metal was completely dissolved (3–4 h). The resulting dark green solution of lithium naphthalenide was then cooled to −25 °C, followed by addition of a solution of compound **17** (0.10 g, 0.23 mmol) in THF (0.5 mL) dropwise over 5 min. The resulting mixture was stirred at −25 °C for 30 min. saturated aqueous ammonium chloride (1 mL) and water (1 mL) were then added. The resulting solution was extracted with ether (3×10 mL). The combined extracts were washed with water and brine, dried over anhydrous sodium sulphate and concentrated in vacuum The crude product was purified by column chromatography (40% EtOAc/hexane) to afford **18** (0.073 g, 96%) as a yellow liquid. R_f (40% EtOAc/hexane) 0.30; IR (neat) ν_{max}: 3445, 2927, 1601, 1460, 1378, 1100, 1065, 1038 cm^{-1}; $[\alpha]_D^{27}$ +15.6 (c 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.95 (ddd, J=17.4, 10.0, 7.0 Hz, 1H), 5.40 (td, J=17.0, 1.3 Hz, 1H), 5.28 (d, J=10.7 Hz, 1H), 4.68 (s, 2H), 4.63 (dt, J=6.3, 0.7 Hz, 1H), 4.02–3.92 (m, 2H), 3.88–3.65 (m, 4H), 3.37 (s, 3H), 1.90–1.74 (m, 2H), 1.74–1.55 (m, 3H), 1.46 (s, 3H), 1.36 (s, 3H), 0.95 (d, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.7, 118.2, 108.5, 94.8, 79.7, 79.0, 75.0, 74.0, 71.2, 61.4, 55.4, 36.5, 35.1, 28.4, 27.7, 25.4, 11.2; MS (ES): m/z 353 (M+Na)$^+$; HRMS (ESI): m/z calcd for $C_{17}H_{30}O_6Na$ 353.1940, found 353.1956.

4.1.14. (1S,2S)-1-((2R,4S,5S,6R)-6-(2-(Benzyloxy)ethyl)-4-(methoxymethoxy)-5-methyltetrahydro-2H-pyran-2-yl)but-3-ene-1,2-diol **20**

Compound **17** (0.5 g, 1.20 mmol) was taken in 70% acetic acid (10 mL) and stirred for 4 h at 45 °C. After completion of reaction (TLC), the acidic solution was concentrated under reduced pressure to give a crude product which was purified by column chromatography (40% EtOAc/Hexane) to yield compound **20** (0.41 g, 90%) as a colorless oil. R_f (50% EtOAc/hexane) 0.3; IR (neat) ν_{max}: 3442, 2887, 1453, 1101, 1037 cm^{-1}; $[\alpha]_D^{30}$ +20.9 (c 1.10, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39–7.27 (m, 5H), 5.94 (ddd, J=17.2, 10.7, 6.6 Hz, 1H), 5.42–5.25 (m, 2H), 4.67 (s, 2H), 4.50 (s, 2H), 4.24 (br t, J=5.8 Hz, 1H), 4.03 (td, J=9.4, 2.4 Hz, 1H), 3.84–3.71 (m, 2H), 3.59–3.44 (m, 3H), 3.36 (s, 3H), 3.03 (d, J=3.0 Hz, 1H), 2.07 (d, J=4.1 Hz, 1H), 1.92–1.53 (m, 5H), 0.92 (d, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 136.8, 128.3, 127.6, 127.5, 117.6, 94.8, 75.2, 75.1, 75.0, 74.6, 73.0, 72.0, 67.3, 55.4, 36.2, 33.0, 28.0, 10.9; MS (ES): m/z 381 (M^++1); HRMS (ESI): m/z calcd for $C_{21}H_{32}O_6Na$ 403.2096, found 403.2089.

4.1.15. (1S,2S,E)-1-((2R,4S,5S,6R)-6-(2-(Benzyloxy)ethyl)-4-(methoxymethoxy)-5-methyltetrahydro-2H-pyran-2-yl)-7-(tert-butyldimethylsilyloxy)hept-3-ene-1,2-diol **21**

Diol **20** (0.2 g, 0.52 mmol) and TBS protected 4-pentene-1-ol **19** (0.63 g, 3.15 mmol) were added via syringe to a stirring solution of Grubbs 2nd generation catalyst (0.05 mmol, 5.0 mol %) in dichloromethane (2.5 mL). The flask was capped with a rubber septum, flushed with dry nitrogen and stirred under nitrogen for 12 h at rt. The reaction mixture was then reduced in volume to 0.5 mL and purified directly by silica gel column chromatography (30% EtOAc/hexane) to provide (+)-**21** (0.177 g, 65% yield) as a brown color oil. R_f (50% EtOAc in hexane) 0.40; IR (neat) ν_{max}: 3445, 2926, 2856, 1736, 1460, 1255, 1101, 1038 cm^{-1}; $[\alpha]_D^{28}$ +17.5 (c 0.83, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.27 (m, 5H), 5.79 (td, J=15.5, 6.8 Hz, 1H), 5.53 (dd, J=15.5, 7.4 Hz, 1H), 4.67 (s, 2H), 4.50 (s, 2H), 4.15 (t, J=6.8 Hz, 1H), 4.09–3.98 (m, 1H), 3.83–3.70 (m, 2H), 3.61 (t, J=6.4 Hz, 2H), 3.53 (t, J=6.4 Hz, 2H), 3.45–3.37 (m, 1H), 3.36 (s, 3H), 2.13 (q, J=6.8 Hz, 1H), 2.04 (br s, 1H), 1.94–1.52 (m, 7H), 0.92 (d, J=7.2 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.4, 135.0, 128.7, 128.3, 127.6, 127.5, 94.8, 75.5, 75.2, 75.1, 75.0, 73.0, 72.1, 67.4, 62.5, 55.4, 36.2, 33.0, 32.2, 28.8, 28.1, 25.9, 18.3, 10.9, −5.3; MS (ES): m/z 553 (M^++H); HRMS (ESI): m/z calcd for $C_{30}H_{52}O_7SiNa$ 575.3375, found 575.3399.

*4.1.16. ((E)-5-((4R,5R)-5-((2R,4S,5S,6R)-6-(2-(Benzyloxy)ethyl)-4-(methoxymethoxy)-5-methyltetrahydro-2H-pyran-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-enyloxy)(tert-butyl)-dimethylsilane **2***

To a solution of diol **21** (0.12 g, 0.23 mmol) in dry dichloromethane (3 mL) was added 2,2-dimethoxy propane (0.08 mL, 0.69 mmol) and a catalytic amount of pyridinium *p*-toluenesulfonate. The homogeneous solution was stirred for 1 h. Dichloromethane (10 mL) and saturated $NaHCO_3$ (100 mL) were added and the mixture was extracted with dichloromethane (2×20 mL). The combined organic layers was dried over anhydrous sodium sulphate and evaporated. Purification by silica gel column chromatography (10% EtOAc/hexane) yielded white color acetal **2** (0.13 g, 98%). R_f (10% EtOAc/hexane) 0.6; IR (neat) ν_{max}: 2929, 2858, 1374, 1251, 1099, 838 cm^{-1}; $[\alpha]_D^{25}$ +15.0 (*c* 0.75, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.38–7.27 (m, 5H), 5.87–5.65 (m, 1H), 5.52 (dd, *J*=15.5, 7.7.1 Hz, 1H), 4.67 (s, 2H), 4.58 (t, *J*=6.8 Hz, 1H), 4.50 (s, 2H), 3.97–3.82 (m, 2H), 3.79–3.67 (m, 2H), 3.58 (t, *J*=6.2 Hz, 2H), 3.56–3.44 (m, 2H), 3.35 (s, 3H), 2.17–1.96 (m, 2H), 1.89–1.49 (m, 7H), 1.43 (s, 3H), 1.34 (s, 3H), 0.92 (d, *J*=7.2 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.5, 134.5, 128.3, 127.5, 125.6, 125.0, 108.1, 94.6, 79.9, 78.9, 75.0, 72.8, 71.5, 71.3, 67.8, 62.6, 55.3, 36.2, 33.1, 32.3, 28.8, 28.5, 27.7, 25.9, 25.4, 18.3, 11.0, −5.3; MS (ES): *m*/*z* 615 (M^++Na); HRMS (ESI): *m*/*z* calcd for $C_{33}H_{56}O_7SiNa$ 615.3688, found 615.3693.

*4.1.17. 2-((2R,3S,4S,6R)-6-((4R,5R)-5-((E)-5-(tert-Butyldimethylsilyloxy)pent-1-enyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-(methoxymethoxy)-3-methyltetrahydro-2H-pyran-2-yl)-ethanol **22***

To a stirred solution of naphthalene (0.038 g, 0.304 mmol) in THF (2 mL), was added lithium metal (0.0014 g, 0.20 mmol). The reaction mixture was stirred at room temperature under an argon atmosphere until lithium metal was completely dissolved (3–4 h). The resulting dark green solution of lithium naphthalenide was then cooled to −25 °C, followed by addition of a solution of compound **2** (0.015 g, 0.025 mmol) in THF (0.5 mL) dropwise over 5 min. The resulting mixture was stirred at −25 °C for 30 min saturated aqueous ammonium chloride (1 mL) and water (1 mL) were then added. The resulting solution was extracted with diethyl ether (3×10 mL). The combined extracts were washed with water and brine, dried over anhydrous sodium sulphate and concentrated in vacuum. The crude product was purified by column chromatography (40% EtOAc/hexane) to afford **22** (0.012 g, 97%) as a yellow liquid. R_f (40% EtOAc/hexane) 0.35; IR (neat) ν_{max}: 3448, 2925, 2855, 1736, 1463, 1377, 1251, 1216, 1092, 1040 cm^{-1}; $[\alpha]_D^{27}$ +9.5 (*c* 0.6, $CHCl_3$); Lit.[5c] $[\alpha]_D^{20}$ +8.8 (*c* 0.35, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 5.90–5.78 (m, 1H), 5.56 (dd, *J*=15.2, 8.0 Hz, 1H), 4.68 (br s, 2H), 4.59 (dd, *J*=8.0, 6.3 Hz, 1H), 4.04–3.89 (m, 2H), 3.89–3.78 (m, 1H), 3.78–3.68 (m, 3H), 3.64 (t, *J*=6.2 Hz, 2H), 3.37 (s, 3H), 2.21–2.10 (m, 2H), 1.84–1.73 (m, 2H), 1.72–1.55 (m, 5H), 1.44 (s, 3H), 1.44–1.43 (m, 1H), 1.34 (s, 3H), 0.94 (d, *J*=7.1 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.3, 125.3, 108.0, 94.7, 79.7, 79.0, 74.9, 73.9, 71.2, 62.8, 61.1, 55.0, 36.5, 35.1, 31.9, 28.8, 28.3, 27.7, 25.9, 25.3, 18.3, 11.2, −5.3; MS (ES): *m*/*z* 502 ($M+H)^+$; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{50}O_7Si$ 502.3325, found 502.3347.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.06.035.

References and notes

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