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Synthetic studies on cytotoxic macrolides cruentarens A and B: stereoselective synthesis of the C_8–C_{19} segment of cruentarens A and B

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ABSTRACT

A stereoselective synthesis of the C_8–C_{19} segment of cruentarens A and B, cytotoxic natural products, has been accomplished. The key steps involve a stereoselective radical cyclization, stereospecific methylation of a γ, δ-epoxy acrylate, nucleophilic epoxide ring opening and a *cis*-Wittig olefination.

1. Introduction

Cruentarens A and B are cytotoxic macrolides isolated from myxobacterium, *Byssovorax cruenta*[1,2] (Fig. 1). While cruentaren A shows strong cytotoxicity against the L929 cell line with an IC_{50} value of 1.2 ngm L^{-1}, cruentaren B showed only marginal cytotoxicity and no antifungal activity.[2] Structurally, cruentaren A resembles the benzlactones apicularen A[3] and salicylihalimide A.[4] Considering their novel structures and the biological activities[5] of cruentarens, many groups focussed their attention towards the synthesis of these targets. Synthesis of cruentaren A has been achieved by Maier et al.[6] and also by Fürstner et al.[7] Chakraborthy et al.[8] reported a convergent total synthesis of cruentaren B. Recently Maier et al.[9] reported the synthesis of some cruentaren A analogues. The unique structural features of cruentarens coupled with their activity attracted our interest in their synthesis. Herein, we report the synthesis of the C_8–C_{19} segment of cruentarens A and B in which the key steps involve radical cyclization, epoxide opening with trimethyl aluminium, methyl lithium and a *cis*-Wittig olefination.

2. Results and discussion

As shown in Scheme 1, our synthetic strategy involves macrolactonization between the C_1-carboxylic acid and C_{15}-hydroxy group (cruentaren A) and C_9-hydroxy group (cruentaren B) of segment **1** which involves the assembly of three fragments, aryl boronic acid **2**, bromo compound **3** and propargyl amide **4**. The fragment **3** could in turn be obtained from a *cis*-Wittig olefination of phosphonium salt **6** and aldehyde **7**. The target molecules could be achieved from the common intermediate **5**.

As summarized in Scheme 2, the synthesis of phosphonium salt **6** commenced with known allyl alcohol **8**.[10] Treatment of alcohol **8** with *N*-bromosuccinimide and ethyl vinyl ether[11] in dichloromethane resulted in the formation of bromo acetal **9**[12] as an inseparable 1:1 diastereomeric mixture in 93% yield, which stereoselective radical cyclization in refluxing benzene using *n*-tributyl tin hydride and AIBN[13] furnished the lactol ether **10**[12] (96:4 *trans*–*cis* ratio). The preferential *trans* geometry[13] of the resulting new stereogenic centre was set from earlier studies and also according to one of the Beckwith guidelines, which states that 2- or 4-substituted radicals give mainly *trans*-disubstituted cyclopentyl derivatives, we proceeded further. The hydrolysis of lactol ether **10** using 80% acetic acid under reflux conditions afforded the lactol **11**[12] which was converted into diol **12**[14] with $NaBH_4/CH_3OH$. The primary hydroxyl group of the diol **12** was protected as its TBS ether **13** by using TBS chloride and imidazole and later the secondary group was protected with TBDPS chloride to give the disilyl ether **14**. Selective deprotection of the TBS with catalytic CSA in a 1:1 mixture of DCM and CH_3OH furnished primary alcohol **15** which was subjected to iodination using triphenyl phosphine (TPP), imidazole and iodine to give the iodo compound **16**. The phosphonium salt **6** was obtained by refluxing a 1:1.1 mixture of iodo compound **16** and TPP in benzene for 48 h.

Synthesis of aldehyde **7** began with the known *cis* epoxy alcohol **17**[15] (Scheme 3). The hydroxyl group was oxidized using Swern conditions[16] to afford an aldehyde which on Wittig olefination[17] with the stable ylide carboethoxymethylenetriphenylphosphorane produced γ, δ-epoxy acrylate **18**[18] in 92% yield over two steps. Upon treatment of **18** with excess of trimethyl aluminium in the presence of water in dichloromethane at −40 °C,[19] methylation took place at the γ-position with complete regio- and stereoselectivity to afford the *syn* alcohol **19**[18] as the sole product in 92% isolated yield. The hydroxyl group of **19** was protected as the TBS ether followed by treatment with DIBAL reduction provided the allyl alcohol **21**, which set the platform for introducing two more stereogenic centres via Sharpless asymmetric epoxidation.[20]Thus the

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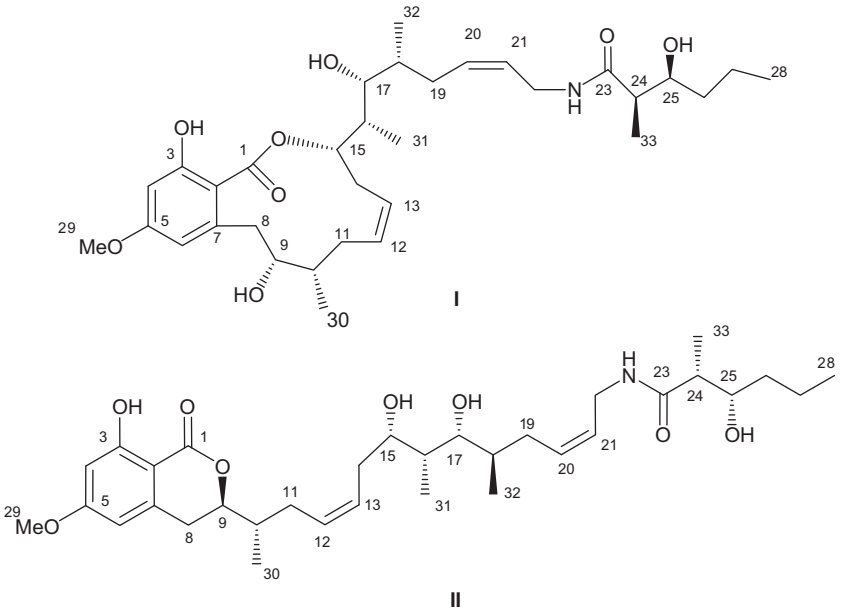


Figure 1. Structures of cruentarens A **I** and B **II**.

allyl alcohol **21** on treatment with L-(+)-DIPT, Ti(O^iPr)$_4$ and TBHP yielded epoxy alcohol **22** which was regioselectively opened with the Gillmann cuprate[21] generated from MeLi and CuI at −40 °C to furnish the diol **23**. Further, the diol was protected as acetonide **24** with 2,2-dimethoxy propane and PPTS in dry DCM in 93% yield. Cleavage of the benzyl ether in the acetonide with lithium in liquid ammonia[22] at −33 °C afforded the primary alcohol **25**, which on subsequent oxidation with TEMPO/BIAB[23] gave the aldehyde **7** in 77% yield (two steps).

With the phosphonium salt **6** and aldehyde **7** in hand, we explored the possibilities for the synthesis of the C_8–C_{19} fragment by employing a *cis*-Wittig olefination procedure. The *Z* olefin, within the C_8–C_{19} fragment, was formed by a Wittig reaction[8] between the phosphonium salt **6** and aldehyde **7** using substoichiometric amount of *n*-BuLi as the base and THF as solvent at −78 °C for 12 h in 75% yield with *Z*/*E* = 10:1 selectivity. The *Z* configuration of the double bond was confirmed by the coupling constant (*J* = 11.1 Hz) of the two olefinic protons. An excess of this base or use of other bases and variation in temperature resulted in lower selectivity and elimination products.

3. Conclusion

In conclusion, we succeeded in accomplishing the stereoselective synthesis of the C_8–C_{19} fragment of cuentarens A and B. Key features of the synthesis of our target include radical cyclization, regioselective methylation of a γ, δ-epoxy acrylate and a *cis*-Wittig olefination. Research towards the total synthesis of cruentarens A and B is in progress in our laboratory. This approach is readily applicable for the synthesis of cruentarens A and B as well as additional analogues.

4. Experimental section

4.1. General remarks

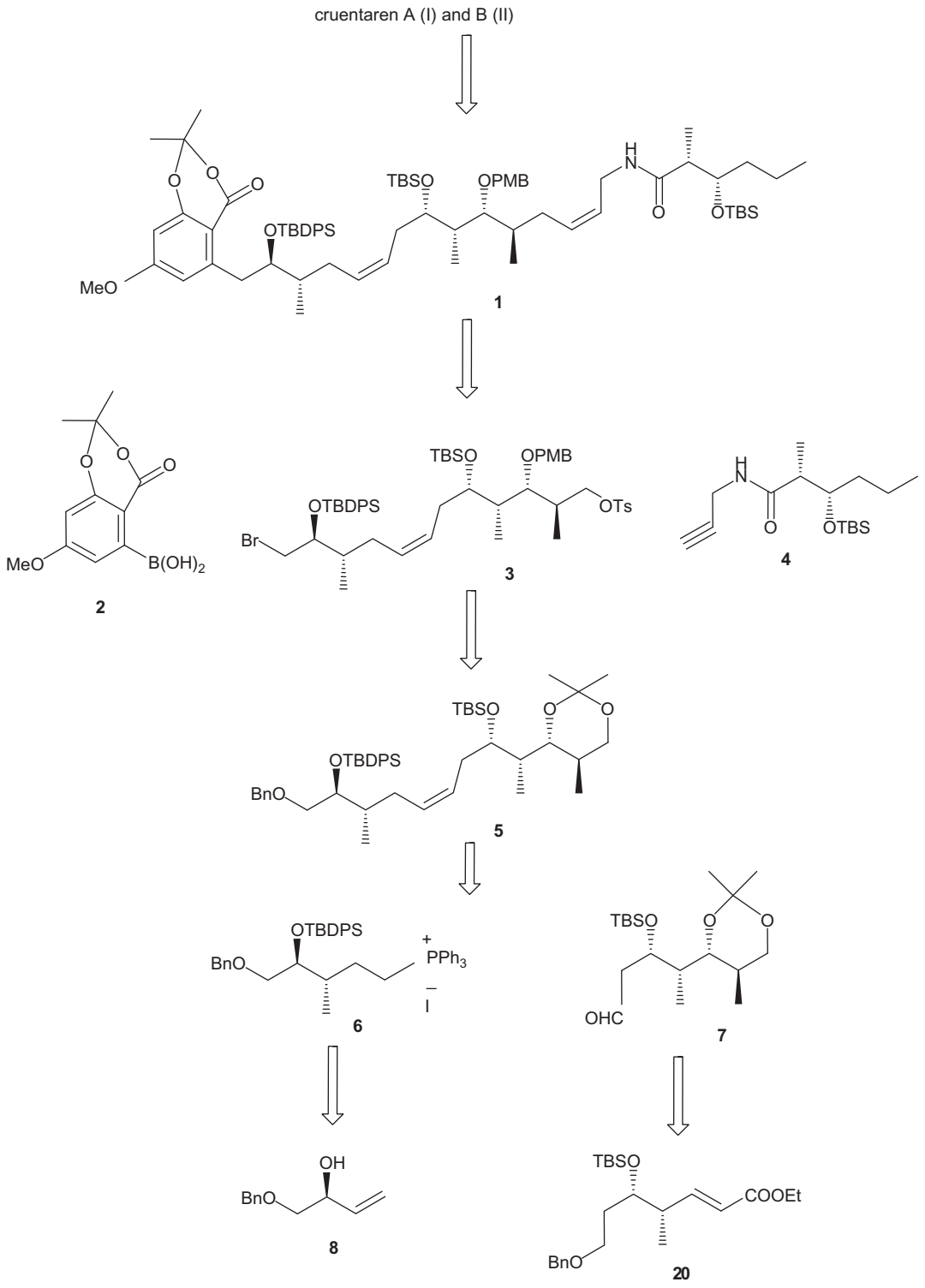
All air- or moisture-sensitive reactions were carried out under a nitrogen atmosphere. Solvents were distilled over Na/benzophenone for THF, over P_2O_5 followed by CaH_2 for DCM, DMF and over P_2O_5 for benzene. Commercially available reagents were used without purification except NBS which was freshly recrystallized from hot water before use. The progress of all the reactions was monitored by thin-layer chromatography (TLC) using glass plates precoated with Silica Gel 60 F254 to a thickness of 0.5 mm (Merck). Column chromatography was carried out using silica gel (60–120 mesh). Optical rotation values were measured with JASCO DIP-360 digital polarimeter at 25 °C and IR spectra were recorded with a Perkin–Elmer FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with Varian Gemini 200 MHz, Bruker Avance 300 MHz, Varian Unity 400 MHz or Varian Inova 500 MHz spectrometer using trimethylsilane as an internal standard in $CDCl_3$.

4.1.1. (*S*)-((2-(2-Bromo-1-ethoxyethoxy)but-3-enyloxy)-methyl)benzene 9

Ethyl vinyl ether (5.71 mL, 59.65 mmol) was added to a stirred solution of alcohol **8** (4.45 g, 25 mmol) and NBS (5.34 g, 29.99 mmol) in dry CH_2Cl_2 (187 mL) under a nitrogen atmosphere at 0 °C. The reaction mixture was then brought to room temperature and stirred for 3 h. Solvent was removed at reduced pressure and residue was chromatographed on silica gel column as quickly as possible to give the pure bromo acetal **9** (7.4 g, 90%) as a colourless oil. R_f = 0.6 (10% EtOAc/hexane). IR (neat): *ν* 2976, 2922, 2865, 1421, 1364, 1108, 1058, 1027, 730 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): *δ* 7.35–7.22 (m, 5H), 5.9–5.7 (m, 1H), 5.40–5.19 (m, 2H), 4.9–4.7 (m, 1H), 4.55–4.5 (m, 2H), 4.3–4.2 (m, 1H), 3.79–3.4 (m, 4H) 3.4–3.29 (m, 2H), 1.25–1.1 (m, 3H); MS (ESI): *m*/*z* 353 [M+Na]$^+$; HRMS (ESI): [M+Na]$^+$ calcd for $C_{15}H_{21}O_3NaBr$: 351.0570; found: 351.0564.

4.1.2. (2*S*,3*S*)-2-(Benzyloxymethyl)-5-ethoxy-3-methyl tetrahydrofuran 10

Tri *n*-butyl-tin hydride (7.22 mL, 26.86 mmol) was added dropwise to a refluxing solution of bromo acetal **9** (5.89 g, 17.91 mmol) in dry benzene (72 mL) with catalytic AIBN under a nitrogen atmosphere. The reduction completed within 30 min as indicated by TLC analysis. Benzene was stripped-off; the crude residue was charged on silica gel column and eluted first with petroleum ether to remove excess tri-*n*-butyl-tin hydride and *n*-Bu_3SnBr formed in the reaction. Then the product was eluted with 3% ethyl acetate/

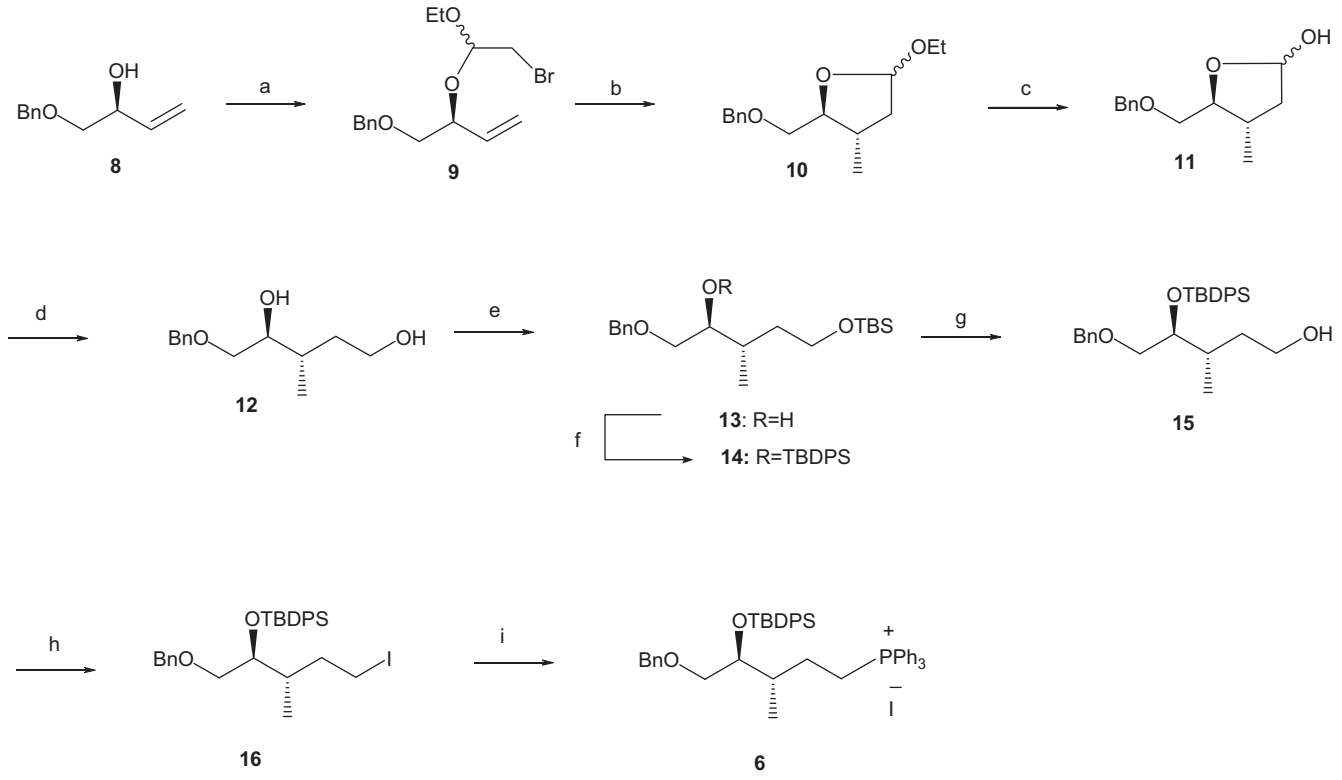


Scheme 1.

hexane after complete removal of tin impurities to give the pure lactol ether **10** (4.16 g, 93%) as a colourless liquid. R_f = 0.5 (10% EtOAc/hexane). IR (neat): ν 2971, 2929, 2902, 2872, 1452, 1372, 1110, 991, 739 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.38–7.2 (m, 5H), 5.1–5.0 (m, 1H), 4.57–4.55 (m, 2H), 3.8–3.3 (m, 5H), 2.4–2.0 (m, 2H), 1.6–1.44 (m, 1H), 1.17 (t, J = 6.7 Hz, 3H), 1.06 (d, J = 6.7 Hz, 3H); MS (ESI): m/z 273 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{15}H_{22}O_3Na$: 273.1466; found: 273.1472.

4.1.3. (4*S*,5*S*)-5-(Benzyloxymethyl)-4-methyltetrahydro furan-2-ol 11

The solution of lactol ether **10** (3.35 g, 13.43 mmol) in 80% aq AcOH (60 mL) solution was refluxed for 4 h. The mixture was cooled to 0 °C, neutralized by solid $NaHCO_3$ and extracted with ethyl acetate (2 × 100 mL). The organic extracts were washed with water (2 × 50 mL) followed by brine (1 × 50 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation of the solvent



Scheme 2. Reagents and conditions: (a) NBS, ethyl vinyl ether, CH_2Cl_2, 0 °C to rt, 3 h, 90%; (b) *n*-Bu_3SnH, AIBN, benzene, reflux, 30 min, 93%; (c) 80% AcOH, reflux, 4 h, 90%; (d) $NaBH_4$, CH_3OH, 0 °C to rt, 2.5 h, 90%; (e) TBSCl, imidazole, CH_2Cl_2, 0 °C to rt, 30 min, 95%; (f) TBDPSCl, imidazole, cat DMAP, DMF, 0 °C to rt 6 h, 98%; (g) CSA, CH_3OH/CH_2Cl_2 (1:1), 0 °C to rt, 1.5 h, 90%; (h) TPP, I_2, imidazole, THF, 0 °C to rt, 1 h, 89%; (i) TPP, benzene, reflux, 48 h, 92%.

followed by purification (column chromatography) afforded pure lactol **11** (2.68 g, 90% yield) as a colourless oil. R_f = 0.3 (30% EtOAc/hexane). IR (neat): *ν* 3418, 2927, 2866, 1453, 1092, 981, 739 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 7.35–7.22 (m, 5H), 5.5–5.35 (m, 1H), 4.6–4.5 (m, 2H), 3.77–3.4 (m, 3H), 2.4 (m, 1H), 1.65–1.45 (m, 2H), 1.14–1.05 (m, 3H); MS (ESI): *m*/*z* 245 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{13}H_{18}O_3Na$: 245.1153; found: 245.1163.

4.1.4. (3*S*,4*S*)-5-(Benzyloxy)-3-methylpentane-1,4-diol 12

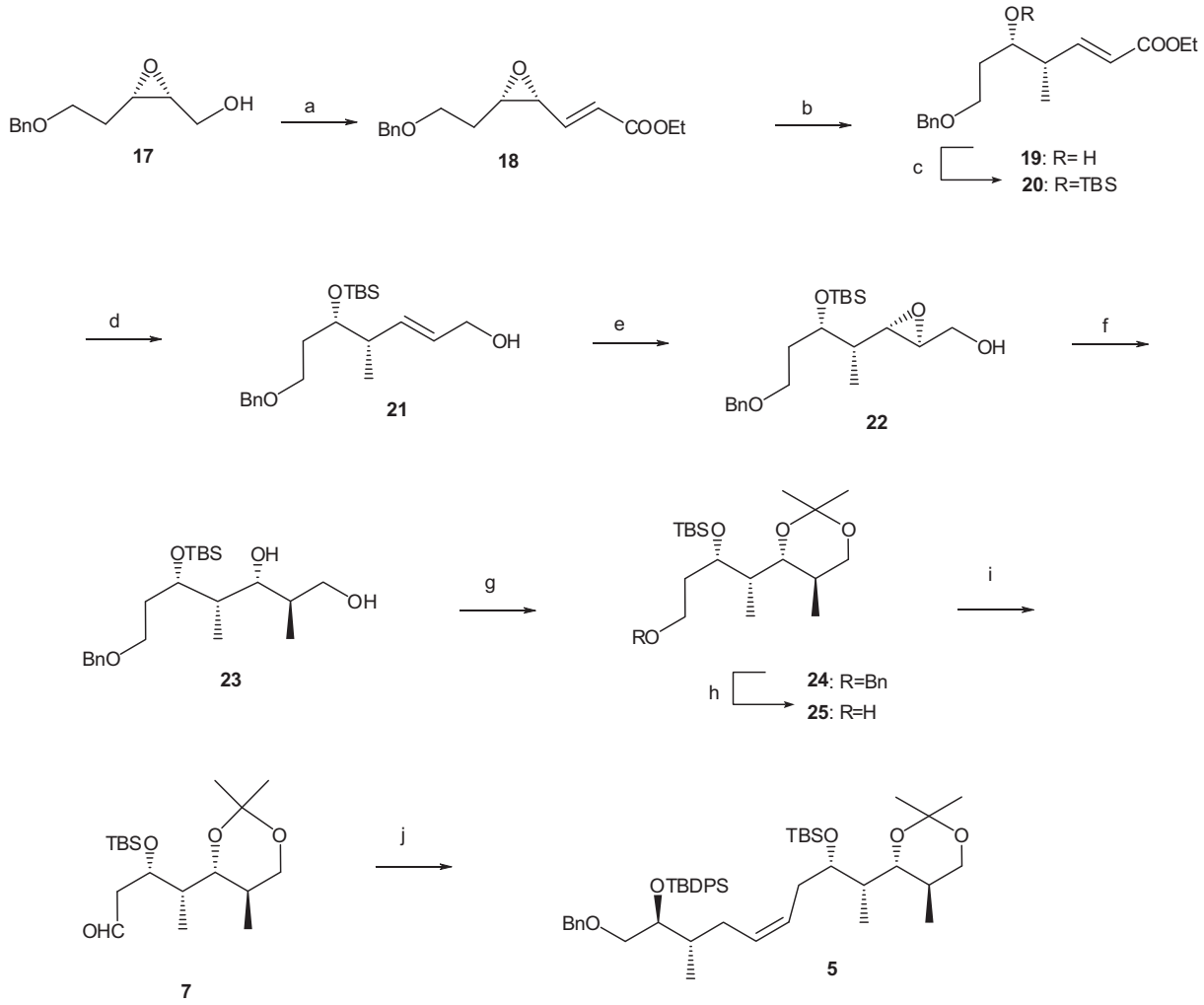
Treatment of a solution of lactol **11** (2.47 g, 11.15 mmol) in CH_2Cl_2/EtOH (1:1, 6 mL) with $NaBH_4$ (932 mg, 24.53 mmol) at 0 °C for 30 min and stirring at room temperature for 2 h and after workup in the usual manner yielded the diol **12** (2.24 g, 90%) as a colourless oil. R_f = 0.3 (50% EtOAc/hexane). $[\alpha]_D^{25} = +2.2$ (*c* 1.0, $CHCl_3$); IR (neat): *ν* 3385, 2922, 2871, 1454, 1100, 1065, 742 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 7.35–7.15 (m, 5H), 4.55 (s, 2H), 3.8–3.35 (m, 5H), 1.85–1.5 (m, 3H), 0.91 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 300 MHz): *δ* 137.8, 128.4, 127.7, 74.3, 73.5, 72.7, 60.5, 36.3, 33.8, 16.4; MS (ESI): *m*/*z* 247 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{13}H_{20}O_3Na$: 247.1310; found: 247.1315.

4.1.5. (2*S*,3*S*)-1-(Benzyloxy)-5-(*tert*-butyldimethylsilyloxy)-3-methylpentan-2-ol 13

Diol **12** (2.0 g, 8.92 mmol) was added into a round-bottomed flask followed by CH_2Cl_2 (36 mL) and cooled to 0 °C. Imidazole (1.33 g, 18.04 mmol) was added and allowed to stir for 5 min. TBSCl (1.47 g, 9.8 mmol) was added in one portion and continued the stirring for 30 min. The reaction was quenched with 20 mL of water. Organic layer was separated and dried over anhydrous Na_2SO_4. Concentration in vacuo and purification by flash column chromatography gave silyl ether **13** (2.86 g, 95%) as a pale yellow oil. R_f = 0.6 (10% EtOAc/hexane). $[\alpha]_D^{25} = +1.0$ (*c* 1.0, $CHCl_3$); IR (neat): *ν* 3453, 2954, 2929, 2858, 1252, 1093, 834, 774 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 7.35–7.24 (m, 5H), 4.55 (s, 2H), 3.75–3.35 (m, 5H), 1.85–1.65 (m, 2H), 1.5–1.42 (m, 1H), 0.91 (d, *J* = 6.7 hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz): *δ* 138.09, 128.28, 127.59, 74.23, 73.26, 72.55, 61.06, 35.23, 33.21, 25.85, 18.2, 16.0, −5.45; MS (ESI): *m*/*z* 339 $[M+H]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{19}H_{34}O_3NaSi$: 361.2174; found: 361.2189.

4.1.6. (5*S*,6*S*)-5-(Benzyloxymethyl)-2,2,6,10,10,11,11-heptamethyl-3,3-diphenyl-4,9-dioxa-3,10-disiladodecane 14

Alcohol **13** (2.7 g, 8.02 mmol) was combined with imidazole (1.09 g, 16.04 mmol), 4-(dimethylamino)pyridine (97.8 mg, 0.8 mmol) and DMF (10 mL). The solution was cooled to 0 °C and treated with TBDPSCl (2.746 g, 10.02 mmol). The reaction mixture was stirred at room temperature for 6 h and the reaction was quenched with satd aq $NaHCO_3$ (50 mL). The aqueous phase was extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with water (2 × 50 mL), brine, dried over $MgSO_4$, filtered and concentrated. Purification of the crude product by flash column chromatography afforded disilyl ether **14** (4.527 g, 98%) as a colourless viscous liquid. R_f = 0.7 (5% EtOAc/hexane). $[\alpha]_D^{25} = -5.1$ (*c* 1.0, $CHCl_3$); IR (neat): *ν* 2955, 2931, 2858, 1466, 1103, 1046, 834, 701 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 7.7–7.63 (m, 4H), 7.41–7.2 (m, 9H), 7.07–7.03 (m, 2H), 4.21–4.15 (m, 2H), 3.82–3.78 (m, 1H), 3.6–3.47 (m, 2H), 3.39 (d, *J* = 5.2 Hz, 2H), 1.9–1.8 (m, 1H), 1.72–1.62 (m, 1H), 1.4–1.3 (m, 1H), 1.05 (s, 9H),0.95 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR



Scheme 3. Reagents and conditions: (a) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C; (ii) Ph_3PCHCO_2Et, benzene, reflux, 4 h, 92% (for two steps).; (b) Me_3Al, CH_2Cl_2,H_2O, −40 °C, 1.5 h, 92%; (c) TBSCl, Et_3N, DMAP, CH_2Cl_2, rt, 24 h, 95%; (d) DIBAL-H, Et_2O, −78 °C to −20 °C, 1 h, 90%; (e) L-(+)-DIPT, $Ti(O^iPr)_4$,TBHP, CH_2Cl_2, −20 °C, 8 h, 89%; (f) CH_3Li, CuI, Et_2O, −40 °C, 2 h, 80%; (g) PPTS, CH_2Cl_2, 1 h, 93%; (h) Li, liq. NH_3, THF, −33 °C, 1 h, 91%; (i) TEMPO, BAIB, CH_2Cl_2, 0 °C to rt, 2 h, 85%; (j) **6**, *n*-BuLi, THF, −78 °C to 23 °C, 12 h, 75% (*Z*/*E* = 10:1).

($CDCl_3$, 300 MHz): δ 138.30, 136.06, 135.88, 134.81, 133.94, 129.43, 129.24, 128.07, 127.53, 127.4, 127.22, 76.19, 72.86, 72.26, 61.65, 34.84, 33.68, 27.07, 25.96, 19.54, 18.29, 15.53, -5.29; MS (ESI): *m*/*z* 599 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{35}H_{52}O_3NaSi2$: 599.3352; found: 599.3351.

4.1.7. (3*S*,4*S*)-5-(Benzyloxy)-4-(*tert*-butyldiphenylsilyloxy)-3-methylpentan-1-ol 15

Camphorsulfonic acid (491 mg, 2.11 mmol) was added to a stirred 0 °C solution of the disilyl ether **14** (3.69 g, 6.42 mmol) in 25 mL of dichloromethane and 25 mL of methanol. After 1.5 h the reaction was quenched with satd $NaHCO_3$, extracted three times with dichloromethane and dried over Na_2SO_4. Concentration in vacuo and purification by flash column chromatography yielded alcohol **15** (2.67 g, 90%) as a colourless viscous oil. R_f = 0.4 (20% EtOAc/hexane). $[\alpha]_D^{25} = -8.5$ (*c* 1.0, $CHCl_3$); IR (neat): ν 3423, 2929, 2857, 1460, 1107, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.65–7.6 (m, 4H), 7.4–7.2 (m, 9H), 7.05–7.04 (m, 2H), 4.2 (s, 2H), 3.85–3.75 (m, 1H), 3.60–3.38 (m, 4H), 1.84–1.75 (m, 1H) 1.62–1.59 (m, 1H), 1.45–1.4 (m, 1H), 1.05 (s, 9H), 0.94 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ 138.06, 136.07, 135.83, 134.44, 133.61, 129.58, 129.38, 128.13, 127.61, 127.46, 127.35, 127.28, 75.76, 72.92, 72.03, 60.78, 34.43, 33.47, 27.06, 19.49, 15.79; MS (ESI): *m*/*z* 485 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{29}H_{38}O_3NaSi$: 485.2487; found: 485.2487.

4.1.8. ((2*S*,3*S*)-1-(Benzyloxy)-5-iodo-3-methylpentan-2-yloxy)(*tert*-butyl)diphenylsilane 16

To a stirred solution of alcohol **15** (2.52 g, 5.46 mmol) in dry THF (22 mL) was added triphenyl phosphine (1.71 g, 6.55 mmol), imidazole (928 mg, 13.65 mmol) and iodine (1.795 g, 7.09 mmol) at 0 °C under nitrogen atmosphere. After 1 h the reaction mixture was diluted with diethyl ether (10 mL), washed with 10% $Na_2S_2O_3$, brine and dried over anhydrous Na_2SO_4. Concentration in vacuo and column chromatography through a short pad of silica gel afforded iodo compound **16** (2.78 g, 89%) as a pale yellow liquid. R_f = 0.7 (5% EtOAc/hexane). $[\alpha]_D^{25} = -6.0$ (*c* 1.0, $CHCl_3$); IR (neat): ν 2959, 2931, 2858, 1427, 1109, 739, 701 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.65–7.6 (m, 4H), 7.4–7.2 (m, 9H), 7.06–7.02 (m, 2H), 4.2 (d, *J* = 3.7 Hz, 2H), 3.75–3.7 (m, 1H), 3.36–3.32 (m, 2H), 3.2–3.1 (m, 1H), 3.04–2.94 (m, 1H), 2.05–1.95 (m, 1H), 1.82–1.63 (m, 2H), 1.05 (s, 9H), 0.9 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ 138.01, 135.98, 135.77, 134.46, 133.48, 129.55, 129.35, 128.1, 127.53, 127.5, 127.28, 75.25, 72.88, 71.87, 37.83, 35.80, 27.05, 19.46, 14.8, 5.5; MS (ESI): *m*/*z* 595 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{29}H_{37}O_2NaSiI$: 595.1505; found: 595.1520.

4.1.9. Preparation of phosphonium salt 6

To a solution of iodo compound **16** (2.5 g, 4.37 mmol) in 5 mL of benzene was added triphenylphosphine (1.26 g, 4.8 mmol) in 1 mL of benzene under argon atmosphere and stirred for 48 h. During this time the solution forms a thick precipitate. The reaction mixture was cooled to 0 °C and diluted with ether (10 mL). The precipitate was collected by filtration and washed with hexane. The solid was dried under reduced pressure to give the phosphonium salt **6** (3.3 g, 92%) as a pale yellow solid.

4.1.10. (*E*)-Ethyl 3-((2*R*,3*S*)-3-(2-(benzyloxy)ethyl)oxiran-2-yl)acrylate 18

To oxalyl chloride (3.848 mL, 44.82 mmol) in CH_2Cl_2 (144 mL) at −78 °C was added dimethyl sulfoxide (6.78 mL, 95.63 mmol) over 15 min. The reaction mixture was stirred for an additional 15 min before epoxy alcohol **17** (6.22 g, 29.88 mmol) dissolved in CH_2Cl_2 (28 mL) was added via a cannula. The mixture was stirred for 30 min before triethylamine (20.77 mL, 150 mmol) was added dropwise. The reaction mixture was allowed to warm up to room temperature for 30 min and water (172 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (2 × 160 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The resulting aldehyde obtained after concentration was used immediately for the next step without further purification.

To a stirred solution of the aldehyde in 144 mL of benzene was added Ph_3PCHCO_2Et (10.92 g, 31.2 mmol) in one portion. The reaction mixture was concentrated in vacuo after stirring at 80 °C for 4 h. Purification by flash column chromatography gave epoxy acrylate **18** 6.61 g (92%) as a colourless liquid. R_f = 0.7 (30% EtOAc/hexane). $[\alpha]_D^{25} = -7.2$ (*c* 1.0, $CHCl_3$); IR (neat): *ν* 2924, 2856, 1718, 1306, 1265, 1183, 1100, 1033, 977 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 7.37–7.20 (m, 5H), 6.77 (dd, *J* = 15.6, 6.3 Hz, 1H), 6.06 (d, *J* = 15.6 Hz, 1H), 4.50 (s, 2H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.65–3.55 (m, 2H), 3.54–3.47 (m, 1H), 3.38–3.29 (m, 1H), 1.88–1.76 (m, 2H), 1.30 (t, *J* = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 200 MHz): *δ* 165.28, 141.60, 138.04, 128.22, 127.45, 127.39, 125.12, 72.89, 66.98, 60.40, 57.16, 54.87, 28.17, 14.04; MS (ESI): *m*/*z* 299 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{16}H_{20}O_4Na$: 299.1259; found: 299.1254.

4.1.11. (4*S*,5*S*,*E*)-Ethyl 7-(benzyloxy)-5-hydroxy-4-methylhept-2-enoate 19

Epoxy acrylate **18** (5.79 g, 21 mmol) was added into a round-bottomed flask followed by CH_2Cl_2 (210 mL) and cooled to −40 °C. Me_3Al (2 M in toluene, 105 mL, 210 mmol) was added and allowed to stir for 5 min. Then H_2O (2.25 mL, 125.9 mmol) was added and continued the reaction at same temperature for 1.5 h before it was quenched with satd aq NH_4Cl solution. Organic layer was separated and dried over anhydrous Na_2SO_4. Concentration in vacuo and purification by flash column chromatography gave the hydroxyl ester **19** (5.64 g, 92%) as a colourless liquid. R_f = 0.3 (20% EtOAc/hexane). $[\alpha]_D^{25} = -14.4$ (*c* 1.0, $CHCl_3$); IR (neat): *ν* 3480, 2973, 2868, 1716, 1454, 1368, 1271, 1182, 1096, 1033, 987 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 7.36–7.22 (m, 5H), 6.88 (dd, *J* = 15.9, 8.3 Hz, 1H), 5.79 (dd, *J* = 15.9, 1.5 Hz, 1H), 4.50 (s, 2H), 4.16 (q, *J* = 6.8 Hz, 2H), 3.75–3.67 (m, 2H), 3.61 (dt, *J* = 9.0, 6.8 Hz, 1H), 3.03 (d, *J* = 2.3 Hz, 1H), 2.45–2.31 (m, 1H), 1.74–1.66 (m, 2H), 1.29 (t, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 200 MHz): *δ* 166.52, 150.75, 137.69, 128.40, 127.77, 127.62, 121.52, 74.21, 73.37, 69.30, 60.15, 42.59, 33.56, 14.57, 14.18; MS (ESI): *m*/*z* 315 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{17}H_{24}O_4Na$: 315.1572; found: 315.1562.

4.1.12. (4*S*,5*S*,*E*)-Ethyl-7-(benzyloxy)-5-(*tert*-butyldimethyl silyloxy)-4-methylhept-2-enoate 20

To a solution of hydroxyl ester **19** (4.29 g, 14.7 mmol) in CH_2Cl_2 (58 mL) were added Et_3N (4.09 mL, 29.4), dimethylaminopyridine (179 mg, 1.47 mmol) and TBSCl (2.64 g, 17.64 mmol). This solution was stirred for 24 h and then the reaction was quenched with satd aq sodium bicarbonate. The layers were separated and the aqueous layer was extracted with ether (3 × 60 mL). The combined organic layers were washed with brine (60 mL) and dried over anhydrous sodium sulfate. After removal of the solvent in vacuo, flash chromatography on silica gel afforded the ester **20** (5.67 g, 95%) as a pale yellow oil. R_f = 0.6 (10% EtOAc/hexane). $[\alpha]_D^{25} = -34.5$ (*c* 1.0, $CHCl_3$); IR (neat): *ν* 2955, 2857, 1720, 1651, 1257, 1096, 1033, 837, 775 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 7.35–7.20 (m, 5H), 6.99 (dd, *J* = 15.8 Hz, 7.5 Hz, 1H), 5.76 (dd, *J* = 15.8 Hz, 1.5 Hz, 1H), 4.45 (m, 2H), 4.15 (q, *J* = 6.7 Hz, 2H), 3.84 (dt, *J* = 7.5 Hz, 4.5 Hz, 1H), 3.52–3.42 (m, 2H), 2.44–2.36 (m, 1H), 1.8–1.6 (m, 2H), 1.3 (t, *J* = 6.7 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.03 (d, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz): *δ* 166.6, 151.3, 138.3, 128.3, 127.6, 127.5, 121.0, 72.9, 72.2, 66.7, 60.0, 41.9, 33.7, 25.8, 18.0, 14.2, 13.9, −4.4, −4.6; MS (ESI): *m*/*z* 407 $[M+H]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{23}H_{38}O_4NaSi$: 429.2437; found: 429.2436.

4.1.13. (4*S*,5*S*,*E*)-7-(Benzyloxy)-5-(tert-butyldimethylsilyloxy)-4-methylhept-2-en-1-ol 21

To a −78 °C solution of ester **20** (5.37 g, 13.23 mmol) in Et_2O (78 mL) was added DIBAL-H (33.07 mL of a 1.0 M solution in hexanes, 33.07 mmol) dropwise. The mixture was allowed to warm up to −20 °C for 1 h and then the reaction was quenched with satd aq sodium potassium tartrate (Rochelle's salt, 70 mL) and diluted with Et_2O. The mixture was stirred at room temperature for 12 h. The aqueous phase was extracted with Et_2O (3 × 40 mL), dried over anhydrous $MgSO_4$, filtered and concentrated to provide pure allyl alcohol **21** (4.33 g, 90%) as a colourless oil. R_f = 0.5 (30% EtOAc/hexane). $[\alpha]_D^{25} = -26.5$ (*c* 1.0, $CHCl_3$); IR (neat): *ν* 3415, 2955, 2929, 2856, 1461, 1253, 1097, 837, 773 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 7.39−7.2 (m, 5H), 5.75–5.55 (m, 2H), 4.5–4.39 (m, 2H), 4.1–4.05 (m, 2H), 3.8–3.7 (m, 1H), 3.5–3.42 (m, 2H), 2.34–2.25 (m, 1H), 1.8–1.6 (m, 2H), 0.97 (d, *J* = 7.5 Hz, 3H), 0.88 (s, 9H), 0.01 (s, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz): *δ* 138.1, 135.6, 128.3, 128.2, 127.7, 127.5, 73.4, 72.9, 66.5, 58.2, 37.6, 34.0, 25.8, 18.0, 17.1, −4.4, −4.5; MS (ESI): *m*/*z* 387 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{21}H_{36}O_3NaSi$: 387.2331; found: 387.2337.

4.1.14. ((2*S*,3*S*)-3-((2*S*,3*S*)-5-(Benzyloxy)-3-(*tert*-butyldimethylsilyloxy)pentan-2-yl)oxiran-2-yl)methanol 22

Dry CH_2Cl_2 (77 mL) was added to 2.2 g of 4 Å powdered activated molecular sieves and the suspension mixture was cooled to −20 °C under nitrogen atmosphere. L-(+)-DIPT (0.26 mL, 1.26 mmol) and $Ti(O^iPr)_4$ (0.3 mL, 1.05 mmol) were added subsequently with stirring and the resulting mixture was stirred for 30 min at −20 °C. The allyl alcohol **21** (3.84 g, 10.55 mmol) in dry CH_2Cl_2 (20 mL) was added and the resulting mixture was stirred for another 30 min at −20 °C. TBHP (9.89 mL, 3.2 M in toluene, 31.65 mmol) was then added and the resulting mixture was stirred at the same temperature for 8 h. It was then warmed to 0 °C, the reaction was quenched with 10 mL of water and the reaction mixture was stirred for 2 h at room temperature. 30% aq NaOH solution saturated with NaCl (15 mL) was then added and the resulting mixture was stirred vigorously for another 30 min at room temperature. The resulting mixture was filtered through Celite pad and the filter cake was washed well with CH_2Cl_2. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). Combined organic phases were washed with brine and dried over Na_2SO_4. Removal of solvent under reduced pressure and purification afforded epoxy alcohol **22** (3.56 g, 89%) as a pale yellow liquid. R_f = 0.3 (30% EtOAc/hexane). $[\alpha]_D^{25} = -24.5$ (*c* 1.0, $CHCl_3$); IR (neat): *ν* 3346, 2954, 2930, 2857, 1463, 1253, 1091, 1024, 836, 773 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): *δ* 7.38–7.22 (m, 5H), 4.45–4.35 (m, 2H), 3.89–3.8 (m, 2H), 3.61–3.54 (m,

1H), 3.45–3.38 (m, 2H), 2.95–2.8 (m, 2H), 1.8–1.7 (m, 1H), 1.66–1.6 (m, 1H) 1.5–1.4 (m, 1H), 0.98 (d, J = 7.3 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ 138.2, 128.2, 127.6, 127.5, 72.9, 72.0, 66.78, 61.72, 58.0, 57.8, 41.0, 33.6, 25.7, 21.6, 17.9, −4.5, −4.6; MS (ESI): m/z 403 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{21}H_{36}0_4NaSi$: 403.2280; found: 403.2292.

4.1.15. (2*R*,3*R*,4*S*,5*S*)-7-(Benzyloxy)-5-(*tert*-butyldimethylsilyloxy)-2,4-dimethylheptane-1,3-diol 23

To a cold (−23 °C) suspension of copper(I) iodide (6.58 g, 34.56 mmol) in dry ether (20 mL), MeLi (34.56 mL, 69.12 mmol, 2.0 M) in ether was added dropwise until it become a clear solution. After 30 min. at this temperature the solution was cooled to −40 °C and then epoxy alcohol **22** (3.14 g, 8.64 mmol) in ether (50 mL) was added dropwise. After being stirred for 2 h at −40 °C and then for 30 min at −23 °C, the mixture was poured into satd aq NH_4Cl (30 mL) and the blue aqueous layer was thoroughly extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The contamination of the 1,2-diol was eliminated by exposing the crude reaction mixture to aq $NaIO_4$ followed by silica gel column chromatography using petroleum ether/EtOAc to give pure 1,3-diol **23** (2.73 g, 80%) as a colourless syrup. R_f = 0.3 (40% EtOAc/hexane). $[\alpha]_D^{25} = -14.5$ (c 1.0, $CHCl_3$); IR (neat): ν 3413, 2931, 2858, 1462, 1254, 1090, 1026, 976, 836, 774 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.3–7.22 (m, 5H), 4.5–4.4 (m, 2H), 4.1–4.0 (m, 1H), 3.65–3.5 (m, 3H) 3.5–3.39 (m, 3H), 1.9–1.8 (m, 3H), 1.7–1.6 (m, 1H), 0.90 (s, 9H), 0.88 (d, J = 5.2 Hz, 3H), 0.71 (d, J = 6.7 Hz, 3H), 0.1 (d, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ 138.1, 128.3, 127.6, 127.5, 81.0, 75.4, 73.0, 68.6, 66.7, 37.5, 37.4, 34.6, 25.7, 17.8, 13.5, 5.9, −3.8, −4.6; MS (ESI): m/z 397 $[M+H]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{22}H_{40}O_4NaSi$: 419.2593; found: 419.2591.

4.1.16. ((3*S*,4*S*)-1-(Benzyloxy)-4-((4*R*,5*R*)-2,2,5-trimethyl-1,3-dioxan-4-yl)pentan-3-yloxy)(tert-butyl)dimethylsilane 24

To a solution of diol **23** (2.39 g, 6.04 mmol) in dry CH_2Cl_2 (30 mL), 2,2-dimethoxy propane (3.69 mL, 30.2 mmol) and PPTS (770 mg) were added. The mixture was stirred at the same temperature for 1 h. Sodium bicarbonate was added to neutralize PPTS and filtered. Removal of solvent and purification by silica gel column chromatography afforded the acetonide **24** (2.44 g, 93%) as a colourless syrup. R_f = 0.6 (5% EtOAc/hexane). $[\alpha]_D^{25} = -23.5$ (c 1.0, $CHCl_3$); (neat): ν 2932, 2856, 1461, 1378, 1254, 1111, 1005, 835, 772 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.3–7.24 (m, 5H), 4.45 (m, 2H), 3.8–3.7 (m, 2H), 3.6–3.58 (m, 1H), 3.5–3.4 (m, 2H), 1.9–1.7 (m, 4H), 1.4 (s, 3H) 1.3 (s, 3H), 0.9 (s, 9H), 0.83 (d, J = 5.8 Hz, 3H), 0.62 (d, J = 6.8 Hz, 3H), 0.02 (s, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ 138.6, 128.2, 127.6, 127.4, 97.6, 72.7, 72.6, 72.0, 67.0, 66.5, 38.7, 32.9, 30.7, 29.7, 25.9, 19.0, 17.9, 12.5, 9.9, −4.2, −4.7 MS (ESI): m/z 459 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{25}H_{44}O_4$ NaSi: 459.2906; found: 459.2896.

4.1.17. (3*S*,4*S*)-3-(*tert*-Butyldimethylsilyloxy)-4-((4*R*,5*R*)-2,2,5-trimethyl-1,3-dioxan-4-yl)pentan-1-ol 25

To a solution of lithium (0.167 g, 23.8 mmol) in liquid NH_3 (28 mL) was added compound **24** (2.09 g, 4.8 mmol) in dry THF (2 mL) at −33 °C. The reaction mixture was stirred for 1 h at the same temperature and the reaction was quenched with solid NH_4Cl till blue colour disappears. Ammonia was allowed to evaporate and the residual mixture was taken in ethyl acetate (10 mL), washed with water (2 × 5 mL) and brine (1 × 3 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification of the residue by silica gel column chromatography afforded alcohol **25** (1.51 g, 91%) as a pale yellow syrup. R_f = 0.3 (20% EtOAc/hexane). $[\alpha]_D^{25} = -30.5$ (c 1.0, $CHCl_3$); IR (neat): ν 3444, 2955, 2933, 2857, 1464,, 1381, 1256, 1064, 1006, 835, 772 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.8–3.6 (m, 5H), 3.5–3.4 (m, 1H), 1.9–1.7 (m, 4H), 1.4 (s, 3H), 1.3 (s, 3H), 0.92 (s, 9H), 0.9 (d, J = 4.1 Hz, 3H), 0.7 (d, J = 6.6 Hz, 3H), 0.1 (s, 3H), 0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ 97.9, 73.8, 72.8, 66.4, 60.4, 38.2, 34.5, 30.7, 29.6, 25.8, 25.4, 18.9, 12.5, 9.8, −4.4, −4.6; MS (ESI): m/z 369 $[M+Na]^+$; HRMS (ESI): $[M+Na]^+$ calcd for $C_{18}H_{38}0_4NaSi$: 369.2437; found: 369.2442.

4.1.18. (3*S*,4*S*)-3-(*tert*-Butyldimethylsilyloxy)-4-((4*R*,5*R*)-2,2,5-trimethyl-1,3-dioxan-4-yl)pentanal 7

To a stirred solution of **25** (830 mg, 2.4 mmol) in CH_2Cl_2 (24 mL) was added TEMPO (113 mg, 0.72 mmol) followed by iodobenzene diacetate (2.3 g, 7.2 mmol). After stirring for 2 h at rt, the reaction mixture was treated with 5% aq $Na_2S_2O_3$ solution (3 mL) and satd aq $NaHCO_3$ solution (3 mL). After 15 min, the organic phase was separated and the aqueous phase was extracted with Et_2O (3 × 8 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to get the corresponding aldehyde (701 mg, 85%) as viscous colourless oil, which was immediately used for the olefination reaction.

4.1.19. (5*S*,10*S*,11*S*,*Z*)-11-(Benzyloxymethyl)-2,2,3,3,10,14,14-heptamethyl-13,13-diphenyl-5-((*S*)-1-((4*R*,5*R*)-2,2,5-trimethyl-1,3-dioxan-4-yl)ethyl)-4,12-dioxa-3,13 disilapentadec-7-ene 5

In a flame-dried 10-mL flask, phosphonium salt **6** (242 mg, 0.29 mmol) was dried under high vacuum for 1 h. Under argon, it was dissolved in fresh, dry THF (1 mL) and n-BuLi (0.11 mL of a 2.4 M solution in hexane, 0.29 mmol) was added dropwise. After stirring for 1 h at 23 °C, the flask containing the deep-red suspension was cooled to −78 °C and a precooled (−78 °C) solution of freshly prepared aldehyde **7** (99.6 mg, 0.29 mmol) in THF (1.9 mL) was added dropwise. After stirring for an additional 12 h, the reaction mixture was allowed to slowly warm to 23 °C overnight. The reaction was quenched with satd aq NH_4Cl and some H_2O and the reaction mixture was extracted (1 × Et_2O, 2 × CH_2Cl_2). The combined organic phase was dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography to give pure olefin (168 mg, 75%, Z/E=10:1) as a yellow liquid. R_f = 0.8 (2% EtOAc/hexane). $[\alpha]_D^{25} = -15.5$ (c 1.0, $CHCl_3$); IR (neat): ν 3303, 2920, 2850, 1689, 1563, 1508, 1343, 1209, 747 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.68–7.62 (m, 4H), 7.34–7.2 (m, 11H), 5.61 (dt, J = 11.1, 6.0 Hz, 1H), 5.48 (ddd, J = 11.1, 10.0, 7.2 Hz, 1H), 4.2 (d, J = 6.7 Hz, 2H), 3.9–3.8 (m, 2H), 3.6–3.38 (m, 5H), 2.4–2.3 (m, 4H), 2.2–2.1 (m, 1H), 2.0–1.75 (m, 2H), 1.34 (s, 3H), 1.3 (s, 3H), 1.08 (d, J = 6.7 Hz, 3H), 1.02 (s, 9H), 0.9 (s, 9H), 0.78 (d, J = 7.5 Hz, 3H), 0.6 (d, J = 6.7 Hz, 3H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ 139.4, 135.8, 135.7, 133.9, 131.6, 129.5, 128.4, 128.2, 127.6, 127.1, 126.8, 126.6, 126.0, 97.9, 76.1, 73.5, 72.9, 66.3, 63.1, 59.5, 38.2, 37.0, 30.3, 29.9, 28.3, 27.0, 26.9, 26.1, 22.6, 19.6, 19.2, 16.0, 12.4, 9.9, −5.0, −5.2; MS (ESI): m/z 796 $[M+Na]^+$.

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References

1. Kunze, B.; Steinmetz, H.; Höfle, G.; Huss, M.; Wieczorek, H.; Reichenbach, H. *J. Antibiot.* **2006**, *59*, 664–668.
2. Jundt, L.; Steinmetz, H.; Luger, P.; Weber, M.; Kunze, B.; Reichenbach, H.; Höfle, G. *Eur. J. Org. Chem.* **2006**, 5036–5044.
3. (a) Kunze, B.; Jansen, R.; Sasse, F.; Höfle, G.; Reichenbach, H. *J. Antibiot.* **1998**, *51*, 1075–1080; (b) Jansen, R.; Kunze, B.; Reichenbach, H.; Höfle, G. *Eur. J. Org. Chem.* **2000**, 913–919.
4. (a) Erickson, K. L.; Beutler, J. A.; Cardellina, J. H., II; Boyd, M. R. *J. Org. Chem.* **1997**, *62*, 8188–8192; (b) Wu, Y.; Esser, L.; De Brabander, J. K. *Angew. Chem.* **2000**, *112*, 4478–4480. *Angew. Chem., Int. Ed.* **2000**, *39*, 4308–4310; For a review, see: (c) Yet, L. *Chem. Rev.* **2003**, *103*, 4283–4306.

5. Kunze, B.; Sasse, F.; Wieczorek, H.; Huss, M. *FEBS Lett.* **2007**, *581*, 3523–3527.
6. (a) Vintonyak, V. V.; Maier, M. E. *Org. Lett.* **2007**, *9*, 655–658; (b) Vintonyak, V. V.; Maier, M. E. *Angew. Chem., Int. Ed.* **2007**, *46*, 5209–5211; (c) Maier, M. E.; Ritschel, J. *Arkivoc* **2008**, 314–329.
7. Fürstner, A.; Bindl, M.; Jean, L. *Angew. Chem., Int. Ed.* **2007**, *46*, 9275–9278.
8. Chakraborthy, T. K.; Chattopadhyay, A. K. *J. Org. Chem.* **2007**, *73*, 3578–3581.
9. Vintonyak, V. V.; Cala, M.; Lay, F.; Kunze, B.; Sasse, F.; Maier, M. E. *Chem. Eur. J.* **2008**, *14*, 3709–3720.
10. Fujii, N.; Habashita, H.; Akaji, M.; Nakai, H.; Ibuka, T.; Fujiwara, M.; Tamamura, H.; Yamamoto, Y. *J. Chem. Soc., Perkin Trans. 1* **1996**, 866–867.
11. (a) Ueno, Y.; Moriya, O.; Chino, K.; Watanabe, M.; Okawara, M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1351–1356; (b) Stork, G.; Mook, R., Jr.; Biller, S. A.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1983**, *105*, 3741–3742.
12. RamaRao, A. V.; Gurjar, M. K.; Bose, D. S.; Devi, R. R. *J. Org. Chem.* **1991**, *56*, 1320–1321 (Isomer).
13. (a) Yadav, J. S.; Gadgil, V. R. *J. Chem. Soc., Chem. Commun.* **1989**, 1824–1825; (b) Beckwith, A. L. J.; Easton, C. J.; Serelis, A. K. *J. Chem. Soc., Chem. Commun.* **1980**, 482–483; (c) Beckwith, A. L. J.; Lawrence, T.; Serelis, A. K. *J. Chem. Soc., Chem. Commun.* **1980**, 484–485; (d) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734–736.
14. Oikawa, M.; Oikawa, H.; Ichihara, A. *Tetrahedron* **1995**, 6237–6254.
15. Schomaker, J. M.; Pulgam, V. R.; Borhan, B. *J. Am. Chem. Soc.* **2004**, *126*, 13600–13601.
16. (a) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660; (b) Mancuso, A. J.; Huang, S. L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480–2482; (c) Mancuso, A. J.; Brownfain, D. S.; Swern, D. *J. Org. Chem.* **1979**, *44*, 4148–4150.
17. (a) Isler, V. O.; Gutmann, H.; Montavon, M.; Ruegg, R.; Ryser, G.; Zeller, P. *Helv. Chem. Acta.* **1957**, *40*, 1242–1249; (b) Ireland, R. E.; Norbeck, D. W. *J. Org. Chem.* **1985**, *50*, 2198–2200.
18. Yadav, J. S.; Chetia, L. *Org. Lett*. **2007**, 9, 22, 4587–4589.
19. Miyashita, M.; Hoshino, M.; Yoshikoshi, A. *J. Org. Chem.* **1991**, *56*, 6483–6485.
20. (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974–5976; (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780.
21. Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873–3888.
22. Yadav, J. S.; Reddy, K. B.; Prasad, A. R.; Rehmann, H. U. *Tetrahedron* **2008**, 2063–2070.
23. De Mico, A.; Margarita, R.; Parlanti, L.; Vescovi, A.; Piancatelli, G. *J. Org. Chem.* **1997**, *62*, 6974–6977.