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Stereoselective total synthesis of decarestrictine-J via Ring Closing Metathesis (RCM)

J.S. Yadav *, K. Anantha Lakshmi, N. Mallikarjuna Reddy, Attaluri R. Prasad, Basi V. Subba Reddy

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500007, India

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ABSTRACT

Stereoselective total synthesis of decarestrictine-J, a polyketide natural product is described. The synthesis involves the Prins cyclisation and Ring Closing Metathesis (RCM) as key steps.

1. Introduction

Decanolides[1a,b] have attracted special attention over the last few years. Of these, decarestrictine family is one of the most important classes of compounds (Fig. 1). The decarestrictines[2] are secondary metabolites that were isolated from various penicillium strains and identified as bioactive compounds by chemical screening.[3] Several members of the decarestrictine family have been shown to inhibit the biosynthesis of cholesterol. Hence, these compounds are used for developing cholesterol lowering drugs.[4]

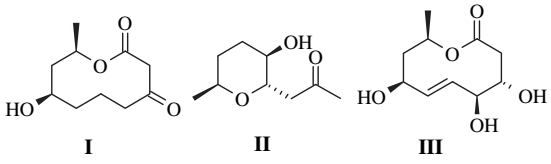

Figure 1. Decarestrictine-J (**I**), decarestrictine L (**II**), decarestrictine D (**III**).

Consequently, there have been some reports on the total synthesis of decarestrictines.[5] The Prins cyclisation has emerged as a powerful synthetic tool for the construction of six-membered ring. It has been utilized in the synthesis of several natural products.[6] However, there are no reports on the use of Prins cyclisation to generate and conserve the stereocenters of **7** in decarestrictine-J. Recently, we have explored the utility of Prins cyclisation in the synthesis of some natural products.[7] As a part of this ongoing program, we have attempted the total synthesis of decarestrictine-J utilizing the Prins cyclisation as a key step.

2. Results and discussions

In our retrosynthetic analysis (Scheme 1), we envisioned that the target molecule **I** could be achieved from 13 through Ring Closing Metathesis (RCM). The compound **13** could in turn be obtained via esterification of compound **7** with relevant acid **12**. The required 1,3-diol **7** was proposed to obtain from homoallylic alcohol **1** by Prins cyclisation with acetaldehyde.

The total synthesis of decarestrictine-J is described in Scheme 2 with 7.4% overall yield. Accordingly, regioselective ring opening of (*R*)-benzyl glycidal ether with vinyl magnesium bromide using copper cyanide gave the homoallylic alcohol **1**.[8a] The Prins cyclisation of **1** with acetaldehyde in presence of TFA followed by hydrolysis of the resulting trifloroacetate afforded tetrahydropyran **2** in 52% yield.[8b] TBS protection of **2** with TBSCl, DMAP and imidazole provided the corresponding TBS ether **3** in 87% yield. The secondary hydroxyl group of **3** was protected as its benzyl ether using NaH, BnBr in THF to afford compound **4**. Deprotection of TBS ether gave the pyranyl methanol **5** in 81% yield. The primary hydroxyl group of **5** was subjected to iodination using Ph_3P,

* Corresponding author. Tel.: +91 40 27193030; fax: +91 40 27160512.
E-mail address: yadavpub@iict.res.in (J.S. Yadav).

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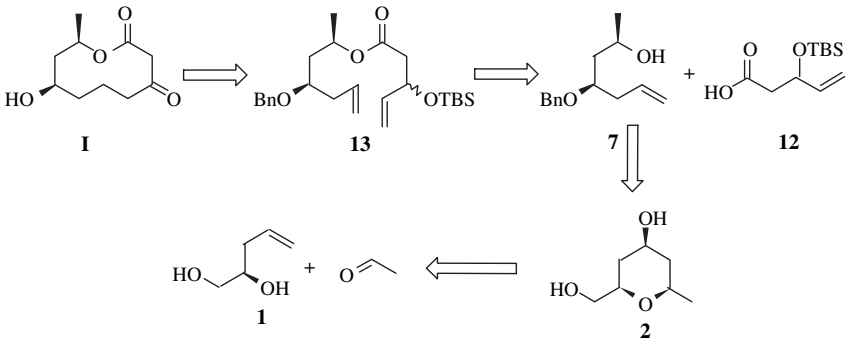
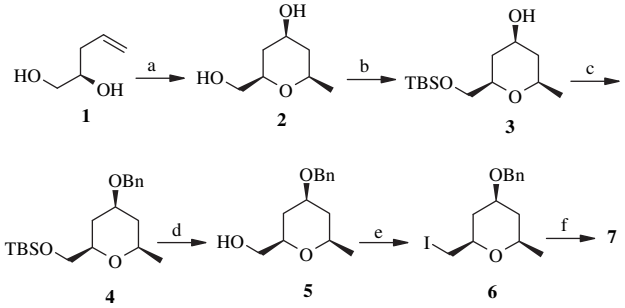
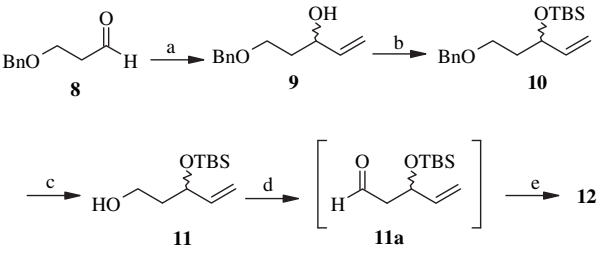


Scheme 1. Retrosynthetic analysis of decarestrictine-J.



Scheme 2. Reagents and conditions: (a) Acetaldehyde, TFA, DCM then K_2CO_3, MeOH rt, 3 h, 52%; (b) TBSCl, Imidazole, DMAP, DCM, 0 °C-rt, 3 h, 87%; (c) NaH, BnBr, dry THF, rt, 6 h, 90%; (d) CSA, MeOH, 0 °C, 10 min, (e) Ph_3P, imidazole, I_2, THF, 0 °C-rt, 2 h, 92%; (f) Zn, EtOH, reflux, 1 h, 88%.

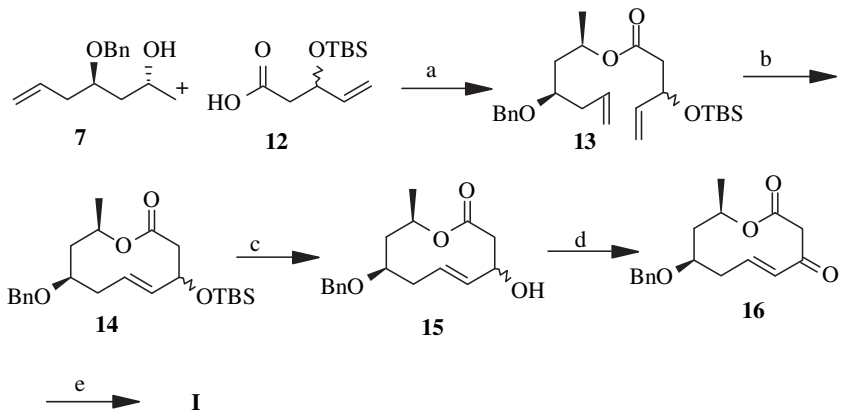


Scheme 3. Reagents and conditions: (a) vinyl magnesium bromide, CuCN, THF, 0 °C-rt, 4 h, 80%; (b) TBSCl, imidazole, DMAP, DCM, 0 °C-rt, 3 h, 94%; (c) Na, liq. NH_3, THF, −78 °C, 30 min (d) IBX, DMSO, DCM, 0 °C-rt, 2 h, 72%; (e) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, *t*-BuOH, 6 h, 83%.

imidazole and iodine to give **6** in 92%, which upon reductive opening using Zn in ethanol furnished the homoallyl alcohol **7** in 88%.[9]

Next, the synthesis of fragment **12** was achieved as described in Scheme 2. Accordingly, aldehyde **8** was treated with vinyl magnesium bromide and CuCN in THF gave the corresponding alcohol **9** in 80% yield. Protection of free OH group using TBSCl, DMAP, and imidazole gave the corresponding TBS ether **10** in 92% yield. Debenzylation of **10** using sodium in liq. ammonia gave the corresponding alcohol **11**, which was subsequently oxidized with IBX in DMSO/DCM system to yield the corresponding aldehyde **11a** in 68% yield. Oxidation of **11a** with $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene in *t*-BuOH/H_2O afforded the acid fragment **12** in 83% yield (Scheme 3).[10]

Finally, we have attempted the coupling of two fragments **12** and **7**. Thus, esterification of the free OH group of **7** with acid **12** in the presence of DCC[11] and a catalytic amount of DMAP gave the diene **13** as depicted in Scheme 3 and set a stage for macrocyclisation by Ring Closing Metathesis.[12] The diene upon treatment with 5 mol% Grubb's II catalyst under high dilution conditions (0.001 M in DCM) afforded the cyclic ester **14** in 64% yield. Deprotection of TBS ether in **14** using TBAF in dry THF provided the corresponding alcohol **15** in 92% yield. Treatment of compound **15** with IBX in DMSO yielded the corresponding ketone **16** in 85% yield. Upon treatment of **16** with Pd/C[13] in EtOAc under hydrogen atmosphere afforded the target molecule, decarestrictine-J (**I**) in 81% yield. The spectral data of thus synthesized decarestrictine-J (**I**) were identical with the natural product (Scheme 4).[4]



Scheme 4. Reagents and conditions: (a) DCC, DMAP, DCM, 83% (b) Grubb's II catalyst, DCM, reflux, 16 h, 64%; (c) TBAF, THF, 0 °C-rt, 4 h, 92%; (d) IBX, DMSO, DCM, 0 °C-rt, 2 h, 85%; (e) Pd/C, EtOH, 6 h, 81%.

3. Conclusion

In summary, the stereoselective total synthesis of decarestrictine-J has been achieved for the first time via the Prins cyclisation. Further applications of the Prins cylisation in the synthesis of natural products are in progress and will be disclosed in due course.

4. Experimental section

4.1. General

Commercial reagents were used without further purification, all solvents were purified by standard techniques and Infrared spectra were recorded on Perkin–Elmer 683 spectrometer. Optical rotations were obtained on Jasco Dip 360 digital polarimeter. NMR spectra were recorded in $CDCl_3$ solvent on Varian Gemini 200, Brucker 300 and Varian Unity 400 NMR spectrometers. Chemical shifts (δ) are quoted in parts per million and are referenced to tetramethylsilane (TMS) as an internal standard. Coupling constants (J) are quoted in Hertz. Column chromatographic separations were carried out on silica gel (60–120 mesh) and flash chromatographic separations were carried out using 230–400 mesh, silica gel. Mass spectra were recorded on Micromass VG-7070H for EI and VG Autospec M for FABMS.

*4.1.1. (2R,4S,6R)-Tetrahydro-2-(hydroxymethyl)-6-methyl-2H-pyran-4-ol (**2**).* Trifluoroacetic acid (95 mL) was added slowly to a solution of the homoallylic alcohol **1** (5 g, 49.01 mmol) and acetaldehyde (5.4 g, 122 mmol) in CH_2Cl_2 (150 mL) at 25 °C under nitrogen atmosphere. The reaction mixture was stirred for 3.0 h and then quenched with saturated sodium hydrogen carbonate solution (300 mL) and the pH was adjusted to >7 by addition of triethylamine. The mixture was extracted with CH_2Cl_2 (4×100 mL) and the combined organic layers were concentrated under reduced pressure. The resulting trifluoroacetate was directly used in the next reaction without purification. The residue was dissolved in methanol (75 mL) and treated with potassium carbonate (17.9 g) for 0.5 h. The solvent was removed under reduced pressure and then diluted with water (40 mL). The resulting mixture was extracted with CH_2Cl_2 (3×50 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. Purification of the crude by column chromatography on silica gel gave the product **2** (3.718 g, 52%) as a colourless liquid. R_f=0.3 (60% EtOAc/Hexane). $[\alpha]_D^{20}$=−13.3 (*c* 0.5, $CHCl_3$); IR (neat): υ 3398, 2925, 2856, 1722, 1452, 1363, 1178, 1030, 976 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.25 (3H, d, J=6.1 Hz, CH_3), 1.81–1.87 (2H, dd, J=3.7, 2.2 Hz, $2CH_a$), 1.92–1.98 (2H, dd, J=3.9, 2.4 Hz, $2CH_e$), 3.45–3.65 (4H, m, OCH), 3.78–3.87 (1H, m, OCH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 36.5, 42.3, 65.8, 67.3, 71.6, 76.05; LC-MS: *m*/*z*: 169 (100, M+Na^+), 102 (68), 79 (20); HRMS (ESI): *m*/*z* [M+Na]$^+$ calcd for $C_7H_{14}O_3Na$: 169.0840; found: 169.0839.

*4.1.2. [(2R,4S,6R)-2-(tert-Butyldimethylsilyloxy)methyl]-6-methyltetrahydro-2H-pyran-4-ol (**3**).* To a solution of **2** (3.7 g, 25.34 mmol) in dry CH_2Cl_2 (40 mL) were added catalytic amount of DMAP (15 mg) and imidazole (3.10 g, 45.6 mmol) in one portion followed by TBSCl (3.8 g, 25.3 mmol) in three portions at 0 °C. The resulting mixture was stirred for 4 h and slowly warmed to room temperature. Then, the mixture was quenched by addition of water (15 mL), diluted with CH_2Cl_2 (3×40 mL), washed with brine (20 mL), and dried over anhydrous Na_2SO_4 and concentrated in vacuo. Purification of the crude by column chromatography (SiO_2, 10% EtOAc in hexane) afforded TBS ether **3** (5.7 g, 87%) as a colourless oil. R_f=0.7 (20% EtOAc/Hexane). $[\alpha]_D^{20}$=−4.5 (*c* 0.55, $CHCl_3$); IR (neat): υ 3379, 2932, 2858, 1464, 1372, 1129, 1033, 837 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.04 (6H, s, Me_2Si), 0.86 (9H, s, terbutyl), 1.21 (3H, d, J=6.1 Hz, CH_3), 1.89–1.96 (2H, dd, J=3.77, 2.26 Hz, $2CH_a$), 2.01–2.07 (2H, dd, J=3.21, 2.45 Hz, $2CH_e$) 3.35–3.54 (3H, m, OCH), 3.69–3.86 (2H, m, OCH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ −5.5, −3.6, 18.2, 21.5, 25.7, 37.6, 42.9, 66.3, 68, 71.6, 76.1; LC-MS: *m*/*z*: 283 (60, M+Na^+), 129(35), 111(40), 92(53); HRMS (ESI): *m*/*z* 283 [M+Na]$^+$ calcd for $C_7H_{14}O_3Na$: 283.1705; found: 283.1708.

*4.1.3. {[(2R,4S,6R)-4-(Benzyloxy)-6-methyl-tetrahydro-2H-pyran-2-yl]methoxy}(tert-butyl)dimethylsilane (**4**).* To a stirred solution of alcohol **3** (4 g, 15.38 mmol) in THF (40 ml), NaH (0.92 g, 38.3 mmol) was added at 0 °C and stirred for 30 min at the same temperature. Then, benzyl bromide (2.63 mL, 15.38 mmol) was added and stirred for 2 h. After completion of the reaction as indicated by TLC, the mixture was quenched with aq NH_4Cl (40 mL) and the extracted with EtOAc (3×40 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude residue was purified by column chromatography (silica gel, 60–120 mesh, EtOAc: hexane, 1:9) to afford **4** (4.84 g, 90%) as a light yellow syrup.

R_f=0.8 (10% EtOAc/Hexane). $[\alpha]_D^{20}$=+2 (*c* 0.5, $CHCl_3$); IR (neat): υ 3030, 2931, 2857, 1460, 1253, 1122, 1073, 837 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.05 (6H, s, Me_2Si), 0.89 (9H, s, terbutyl), 1.21 (3H, d, J=6.1 Hz, CH_3), 1.95–2.01 (2H, dd, J=7.5, 2.2 Hz, $2CH_a$), 2.04–2.1 (2H, dd, J=8.3, 2.2 Hz, $2CH_e$), 3.28–3.55 (4H, m, 2×OCH and OCH_2), 3.65–3.7 (1H, m, OCH), 4.54 (2H, s, OCH_2Ph), 7.21–7.30 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ −5.2, −5.3, 18.3, 21.7, 25.9, 34.6, 39.9, 66.4, 69.5, 71.7, 74.6, 76.24, 127.5, 128.3, 138.6; LC-MS: *m*/*z* 373 (100, M+Na^+), 368 (55), 351 (40); HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{20}H_{35}O_3Si$: 351.2277; found: 351.2361.

*4.1.4. [(2R,4S,6R)-4-(Benzyloxy)-6-methyl-tetrahydro-2H-pyran-2yl]methanol (**5**).* To a stirred solution of compound **4** (4.84 g, 13.82 mmol) in MeOH (40 mL), was added a catalytic amount of CSA at 0 °C and stirred for 10 min at the same temperature. Upon completion, the mixture was quenched with $NaHCO_3$, extracted with EtOAc (2×50 mL) and concentrated under reduced pressure. The resulting crude residue was purified by column chromatography to afford the alcohol **5** (3.92 g, 81%) as colourless oil R_f=0.3 (20% EtOAc/Hexane). $[\alpha]_D^{20}$=−10.7 (*c* 0.5, $CHCl_3$); IR (neat): υ 3446, 3030, 2934, 2861, 1452, 1365, 1115, 1072, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.24 (3H, d, J=6.1 Hz, CH_3), 1.84–2.0 (4H, m, 2×CH_2), 3.35–3.55 (5H, m, 3×OCH and CH_2), 4.5 (2H, s, OCH_2Ph), 7.18–7.27 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 33.5, 39.8, 66, 69.5, 71.8, 74.3, 76, 127.5, 128.3, 138.5; LC-MS: *m*/*z* 291 (100, M+Na^+); HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{14}H_{21}O_3$: 236.1416; found: 237.1489.

*4.1.5. (2R,4S,6R)-4-(Benzyloxy)-tetrahydro-2-(iodomethyl)-6-methyl-2H-pyran (**6**).* To a stirred solution of alcohol **5** (3.5 g, 14.83 mmol) in dry THF (35 mL) were added imidazole (2.42 g, 35.5 mmol) and triphenylphosphine (4.66 g, 17.79 mmol) and I_2 (4.57 g, 17.796 mmol) successively at 0 °C. The resulting reaction mixture was stirred for 2 h at room temperature and then quenched by adding water (15 mL), and extracted with DCM (3×30 mL). The organic layers were washed with brine (15 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. Purification of the crude residue by column chromatography gave the pure product **6** (4.97 g, 92%) as a pale yellow liquid. R_f=0.7 (SiO_2, 30% EtOAc in hexane). $[\alpha]_D^{28}$=−14.9 (*c* 0.5, $CHCl_3$); IR (neat): υ 3029, 2939, 2856, 1451, 1660, 1362, 1159, 1081, 739 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.24 (3H d, J=5.8 Hz, CH_3), 1.93–1.98 (2H, m, CH_2), 2.25–2.29 (2H, m, CH_2), 3.11–3.21 (2H, m, ICH_2), 3.28–3.35(1H, m, OCH), 3.42–3.57 (2H, m, 2×OCH), 4.54 (2H, s, OCH_2Ph), 7.24–7.3 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.8, 21.6, 37.5, 39.4, 69.6, 72.1, 74.1, 75, 127.5, 128.4, 138.4; LC-MS: *m*/*z* 369 (25, M+Na^+), 301

(20), 263(20), 249 (35); HRMS (ESI): m/z $[M+NH_4]^+$ calcd for $C_{14}H_{23}INO_2$: 364.0768; found: 364.0769.

*4.1.6. (2R,4R)-4-(Benzyloxy)hept-6-en-2-ol (**7**).* To the iodide **6** (3 g, 8.287 mmol) in ethanol (80 mL), zinc dust (10.93 g, 165.6 mmol) was added. The resulting mixture was refluxed for 1 h and then cooled to 25 °C. Addition of solid ammonium chloride (10 g) and ether (200 mL) followed by stirring for 5 min gave a grey suspension which was filtered through Celite. The filtrate was concentrated in vacuo and purified by flash chromatography to give compound **7** (1.62 g, 88%) as a pale yellow liquid. R_f=0.4 (10% EtOAc/Hexane). $[\alpha]_D^{20}=-21.8$ (c 0.5, $CHCl_3$); IR (neat): υ 3427, 3070, 3031, 2967, 2930, 1640, 1453, 1093, 1066, 914, 739 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.18 (3H, d, J=6.4 Hz, CH_3), 1.51–1.56 (2H, t, J=5.5 Hz, CH_2), 2.07 (1H, br s, OH), 2.20–2.41 (2H, m, allylic CH_2) 3.65–3.71 (1H, m, OCH), 3.99–4.05 (1H, m, OCH), 4.36–4.65 (2H, m, OCH_2Ph), 4.99–5.06 (2H, m, olefin), 5.66–5.8 (1H, m, olefin), 7.17–7.28 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.6, 37.9, 41.7, 64.5, 71.2, 76.2, 117.4, 127.7, 128.4, 134.4, 138.8; LC-MS: m/z 243 (30, $M+Na^+$); HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{14}H_{21}O_2$: 221.1536; found: 221.1525.

*4.1.7. 5-(Benzyloxy)pent-1-en-3-ol (**9**).* To a solution of compound **8** (7 g, 42.68 mmol) in dry THF (100 mL) was added a commercially available vinyl magnesium bromide (6.658 g, 51.21 mmol) in THF at 0 °C. The mixture was warmed to 40 °C and then allowed to stir for 4 h at 40 °C. Upon completion, saturated NH_4Cl solution (100 mL) was added and the mixture was extracted with EtOAc (3×30 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography afforded the pure product **9** (6.47 g, 80%) as a pale yellow liquid. R_f=0.45 (10% EtOAc/hexane). IR (neat): υ 3420, 3030, 2922, 2862, 1640, 1452, 1098, 740, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.73–1.8 (2H, m, CH_2), 3.53–3.68 (2H, m, OCH_2), 4.27 (1H, m, OCH), 4.46 (2H, s, OCH_2Ph), 5.03 (1H, d, J=10.5 Hz, olefin), 5.2 (1H, d, J=17.3 Hz, olefin), 5.74–5.85 (2H, m, olefin), 7.2–7.27 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 36.2, 68.2, 71.8, 73.2, 114.3, 127.6, 128.5, 137.8, 140.5; LC-MS: m/z 215 (90, $M+Na^+$), 157 (20), 129 (35), 91 (100); HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{12}H_{16}NaO_2$: 215.1043; found: 215.1041.

*4.1.8. 5-(Benzyloxy)pent-1-en-3-yloxy(tert-butyl)dimethylsilane (**10**).* To a solution of **9** (2.10 g, 13.4 mmol) in dry CH_2Cl_2 (30 mL) were added a catalytic DMAP (10 mg) and imidazole (1.37 g, 20.0 mmol) in one portion followed by TBSCl (2.43 mg, 16.0 mmol) in three portions at 0 °C. The reaction mixture was stirred for 4 h and slowly warmed to room temperature. Upon completion, the mixture was quenched by the addition of saturated NH_4Cl solution (15 mL), diluted with CH_2Cl_2 (30 mL), washed with brine (15 mL), dried over Na_2SO_4 and concentrated in vacuo. Purification of the crude by column chromatography afforded TBS ether **10** (3.34 g, 92%) as a colourless oil. R_f=0.7 (10% EtOAc/Hexane). IR (neat): υ 3030, 2953, 2857, 16.43, 14.64, 1361, 1253, 1092, 837, 776 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.03 (3H, s, MeSi), 0.05 (3H, s, MeSi), 0.82 (9H, s, terbutyl), 1.75–1.81 (2H, m, CH_2), 3.4–3.62 (2H, m, OCH_2), 4.27–4.33 (1H, m, OCH), 4.43–4.54 (2H, s, OCH_2Ph), 4.99–5.04 (1H, dt, J=7.5, 1.3 Hz, olefin), 5.11–5.18 (1H, dt, J=17.1, 1.5 Hz, olefin), 5.75–5.86 (1H, m, olefin), 7.27–7.35 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ −4.9, −4.3, 18.2, 25.8, 38.1, 66.7, 70.8, 73, 113.6, 127.6, 128.3, 138.5, 141.5; LC-MS: m/z 329 (60, $M+Na^+$); HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{31}O_2Si$: 307.2088; found: 307.2082.

*4.1.9. 3-(tert-Butyldimethylsilyloxy)pent-4-en-1-ol (**11**).* To a stirred solution of compound **10** (5.91 g, 19.31 mmol) in THF (20 mL) were added liq. NH_3 (40 mL), and Na metal (0.72 g, 31.3 mmol) and the reaction mixture was stirred for 30 min at −78 °C. On completion, the mixture was quenched with NH_4Cl (10 g) and then extracted with DCM (2×30 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude residue was purified by column chromatography to afford alcohol **11** (3.12 g, 68%) as a pale yellow liquid. R_f=0.35 (10% EtOAc/Hexane). IR (neat): υ 3371, 3080, 2954, 2931, 2889, 2858, 1467, 1254, 1085, 1023, 922, 837, 776 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.05 (3H, s, MeSi), 0.08 (3H, s, MeSi), 0.9 (9H, s, terbutyl), 1.66–1.90 (2H, m, CH_2), 2.39 (1H, br s, OH), 3.67–3.85 (2H, m, OCH_2), 4.38–4.43 (1H, m, OCH), 5.07–5.24 (2H, m, olefin), 5.8–5.9 (1H, m, olefin); ^{13}C NMR ($CDCl_3$, 75 MHz): δ −5.3, −5.1, 18.1, 25.8, 39.2, 60, 73.1, 114.3, 140.6; LC-MS: m/z 239 (100, $M+Na^+$); HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{11}H_{25}O_2Si$: 217.1618; found: 217.1609.

*4.1.10. 3-(tert-Butyldimethylsilyloxy)pent-4-enoic acid (**12**).* To a stirred solution of IBX (8.283 g, 29.58 mmol) in DMSO (30 mL) was added compound **11** (2.13 g, 9.86 mmol) in CH_2Cl_2 (10 mL) at 0 °C. After complete conversion, the reaction mixture was filtered through Celite pad, washed with water (30 mL) and extracted with ether (3×40 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo and purified by flash column chromatography to afford aldehyde **11a**.

To a stirred solution of aldehyde **11a** (1.3 g, 6.07 mmol) in *t*-BuOH (10 mL) were added solutions of 2-methyl-2-butene (10 mL), $NaClO_2$ (0.829 g, 9.11 mmol) and NaH_2PO_4 (1.09, 9.112 mmol) in water (5 mL) and stirred over 6 h at room temperature. The solvent was removed under reduced pressure and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude residue was purified by column chromatography to afford acid **12** (1.162 mg, 83%) as a light yellow liquid. R_f=0.2 (10% EtOAc/Hexane). IR (neat): υ 2956, 2858, 1714, 1467, 1254, 1088, 835, 777 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 0.07 (3H, s, MeSi), 0.08 (3H, s, MeSi), 0.89 (9H, s, terbutyl), 2.56 (2H, d, J=6.0 Hz, CH_2), 4.55–4.61 (1H, q, J=6.1 Hz, OCH), 5.11–5.3 (2H, m, olefin), 5.79–5.9 (1H, m, olefin); ^{13}C NMR ($CDCl_3$, 75 MHz): δ −5.2, −4.4, 18.1, 25.6, 42.8, 70.5, 115.4, 139.2, 174.7; LC-MS: m/z 253 (52, $M+Na^+$); HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{11}H_{23}O_3Si$: 231.1411; found: 231.1416.

*4.1.11. (3R)-(2R,4R)-4-(Benzyloxy)hept-6-en-2yl-3-hydroxypent-4-enoate (**13**).* To a stirred solution of alcohol **7** (0.4 g, 1.81 mmol) in CH_2Cl_2 (10 mL) were added compound **12** (0.5 g, 2.18 mmol) followed by DCC (0.74 g, 3.63 mmol) and DMAP (0.44 g, 3.63 mmol) at room temperature and allowed to stir for 15 h. After completion, the mixture was filtered and the resulting filtrate was evaporated in vacuo. The crude residue was purified by column chromatography to afford ester **13** (567 mg, 81%) as colourless oil. R_f=0.2 (20% EtOAc/Hexane). IR (neat): υ 3073, 2930, 2857, 1734, 1641, 1463, 1369, 1254, 1088, 835, 778 cm^{-1}; $[\alpha]_D^{20}=-30.8$ (c 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 0.04 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.84 (9H, s, terbutyl), 1.21 (3H, d, J=6.2 Hz, CH_3), 1.59–1.75 (2H, m, CH_2), 2.2–2.47 (4H, m, 2×CH_2), 3.38–3.49 (1H, m, OCH), 4.34–4.44 (1H, m, OCH), 4.47–4.55 (2H, m, OCH_2Ph), 4.98–5.20 (5H, m, OCHMe and olefin), 5.7–5.8 (2H, m, olefin), 7.18–7.3 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ −4.9, −4.5, 18.1, 20.8, 25.8, 38.3, 41.1, 43.8, 68.3, 70.6, 71.4, 74.8, 114.6, 117.4, 127.6, 128, 128.3, 134.1, 140.2, 170.5; LC-MS: m/z 455 (100, $M+Na^+$); HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{25}H_{40}O_4SiNa$: 455.2593; found: 455.2579.

*4.1.12. (8R,10R,E)-8-(Benzyloxy)-4-(tert-butyldimethylsilyloxy)-10-methyl-3,4,7,8,9,10-hexahydrooxecin-2-one (**14**).* Grubbs' II catalyst (0.88 mg, 5 mol %) was dissolved in CH_2Cl_2 (10 mL) and was added drop wise to a solution of the acrylic ester **15** (0.2 g, 0.462 mmol) in 700 mL of CH_2Cl_2. The reaction mixture was stirred under reflux at 45 °C for 12 h by which time all of the starting material was consumed (TLC). The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography to

obtain **14** (120 mg, 64%) as colourless oil. R_f=0.6 (10% EtOAc/Hexane). $[\alpha]_D^{28}$=−2.0 (*c* 1, $CHCl_3$); IR (neat): *υ* 2927, 2856, 1735, 1460, 1365, 1253, 1074, 836, 778 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 0.05 (3H, s, MeSi), 0.07 (3H, s, MeSi), 0.87 (9H, s, terbutyl), 1.40 (3H, d, *J*=6.4 Hz), 1.85–1.99 (2H, m, CH_2), 2.22–2.47 (2H, m, CH_2), 2.71–2.85 (2H, m, CH_2), 4.42–4.57 (2H, m, OCH2Ph), 4.92 (1H, m, OCHMe), 5.22–5.56 (2H, m, olefin), 7.21–7.31 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): *δ* −4.9, −4.5, 18.2, 20.3, 25.7, 34.8, 39.8, 44.3, 65.4, 69.8, 70.6, 78.3, 127.2, 127.4, 127.5, 128.4, 133.1, 138.4, 169.3; LC-MS: *m*/*z* 427 (45, M+Na^+); HRMS (ESI): *m*/*z* $[M+Na]^+$ calcd for $C_{23}H_{36}O_4SiNa$: 427.228; found: 427.2289.

*4.1.13. (8R,10R,E)-8-(Benzyloxy)-4-hydroxy-10-methyl-3,4,7,8,9,10-hexahydrooxecin-2-one (**15**).* A solution of compound **14** (120 mg, 0.297 mmol) in THF (10 mL) was treated with a 1.1 M solution of TBAF in THF (3.5 mL, 0.35 mmol) at room temperature for 1 h. The solvent was removed and then diluted with EtOAc (20 mL) and water (20 mL). The mixture was saturated with sodium chloride and extracted with EtOAc (4×20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography to afford pure compound **15** (79 mg, 92%). R_f=0.3 (30% EtOAc/Hexane). $[\alpha]_D^{28}$=+15.2 (*c* 0.85, $CHCl_3$); IR (neat): *υ* 2927, 2856, 1735, 1460, 1365, 1253, 1074, 836, 778 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 1.32 (3H, d, *J*=6.5 Hz, CH_3), 1.81–1.88 (2H, m, CH_2), 2.2–2.33 (2H, m, CH_2), 2.79–2.93 (2H, m, CH_2), 3.38–3.43 (1H, m, OCH), 4.39–4.53 (2H, m, OCH_2Ph), 4.93–4.99 (1H, m, OCHMe), 5.29–5.46 (2H, m, olefin), 7.17–7.26 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): *δ* 20.3, 34.9, 37.4, 43.3, 64.7, 69.9, 70.7, 78.3, 127.3, 127.6, 128.4, 129, 132.2, 138.4, 168.8; LC-MS: 329 (100, M+K^+), 308 (35, M+NH_4^+); HRMS (ESI): *m*/*z* $[M+Na]^+$ calcd for $C_{17}H_{22}O_4Na$: 313.1415; found: 313.1427.

*4.1.14. (E,8R,10R)-8-(Benzyloxy)-7,8,9,10-tetrahydro-10-methyl-3H-oxecine-2,4-dione (**16**).* To a stirred solution of IBX (0.202 g, 0.72 mmol) in DMSO (10 mL) was added compound **15** (70 mg) in CH_2Cl_2 (2 mL) at 0 °C. After completion of the reaction as indicated by TLC, the reaction mixture was filtered through a small Celite pad and washed with water (10 mL) and then extracted with ether (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo and then purified by column chromatography to afford compound **16** (1.44 g, 72%). R_f=0.6 (30% EtOAc/Hexane). $[\alpha]_D^{28}$=−76 (*c* 0.15, $CHCl_3$); IR (neat): *υ* 3443, 2979, 2924, 2856, 1742, 1705, 1451, 1262, 1174, 1094, 969, 741 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 1.30 (3H, d, *J*=6.1 Hz, CH_3), 1.85–1.88 (2H, m, CH_2), 1.97–2.04 (1H, m, CH), 2.32–2.38 (1H, m, CH), 2.48–2.53 (1H, m, CH), 2.67–2.75 (1H, m, CH), 3.48–3.52(1H, m, OCH), 4.42–4.53 (2H, m, OCH_2Ph), 4.91–4.95 (1H, m, OCHMe), 5.79–6.14 (2H, m, olefin), 7.22–7.33 (5H, m, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): *δ* 20.6, 34.6, 38.3, 51, 68.8, 70.6, 71.3, 127.4, 127.7, 128.4, 130.4, 135.3, 138.1, 166.1, 196.5; LC-MS: *m*/*z* 311 (80, M+Na^+) HRMS (ESI): *m*/*z* $[M+Na]^+$ calcd for $C_{17}H_2{}_0O_4Na$: 311.1259; found: 311.1255.

*4.1.15. (8R,10R)-8-Hydroxy-10-methyl oxecane-2,4-dione (**1**).* To a solution of **16** (40 mg, 0.138 mmol) in EtOAc (2 ml), was added 10% Pd/C (catalytic) and stirred under hydrogen atmosphere for 6 h. Then, the reaction mixture was filtered through a small Celite pad and concentrated in vacuo. The crude residue thus obtained was purified by column chromatography (SiO_2, 30% EtOAc/Hexane) to afford decarestrictine-*J*=(I) (33 mg, 81%). R_f=0.15 (30% EtOAc/Hexane). Its melting point was 51–54 °C; (lit.: [5g] 54–55 °C) and $[\alpha]_D^{28}$=−141 (*c* 0.15, MeOH); (lit.: [5g] −154 (*c* 0.1, MeOH)).The ^1H NMR, ^{13}C NMR and mass spectral data were in good agreement with those of reported natural decarestrictine-*J*=(**1**).[4] IR (neat): *υ* 3422, 2924, 2854, 1738, 1706, 1448, 1259, 1074, 966 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): *δ* 1.30 (3H, d, *J*=6.2 Hz, CH_3), 1.51–1.74 (3H, m, $6H_b$, $7H_a$, $7H_b$), 1.83–1.92 (2H, m, $9H_a$, $9H_b$), 2.0–2.08 (1H, m, $6H_a$), 2.25–2.34 (1H, m, $5H_b$), 2.66–2.76 (1H, m, $5H_a$), 3.38 (2H, d, *J*=2.8 Hz, $2H_a$, $2H_b$), 3.65–3.72 (1H, m, OCH), 5.15–5.22 (1H, m, OCHMe); ^{13}C NMR ($CDCl_3$, 75 MHz): 20.8, 21.4, 37, 39.3, 44.2, 51.8, 69.4, 71.6, 166.6, 202.9; LC-MS: *m*/*z* 223 (43, M+Na^+), 153 (100), 102 (72); HRMS (ESI): *m*/*z* $[M+Na]^+$ calcd for $C_{10}H_{16}O_4Na$: 223.0946; found: 223.0942.

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Appendix. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2009.10.100.

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