Tetrahedron: *Asymmetry* 21 (2010) 2524–2529

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Towards the total synthesis of etnangien: synthesis of C32–C42 fragment by using a desymmetrization strategy

Gowravaram Sabitha *, Kurra Yadagiri, Martha Bhikshapathi, Gajangi Chandrashekhar, Jhillu Singh Yadav

Organic Division I, Indian Institute of Chemical Technology, Hyderabad 500 007, India

ARTICLE INFO

Article history:
Received 6 September 2010
Accepted 4 October 2010
Available online 8 November 2010

ABSTRACT

The construction of the C32–C42 fragment of etnangien is described using a desymmetrization strategy generating five stereogenic centers from a bicyclic lactone. Another notable feature includes the use of the Sharpless asymmetric epoxidation to generate a stereogenic center at C40.

1. Introduction

The genus *Sorangium* has been found to produce interesting structures,[1] such as the antifungal soraphens,[2] the antibacterial sorangicins[3], and thuggacins,[4] as well as the anticancer epothilones.[5] Recently, a new macrolactone etnangien **1** was isolated by Hofle et al. from the myxobacterium *Sorangium cellulosum*,[6] and it displays potent antibiotic activity against a range of Gram-positive bacteria, by inhibition of RNA-polymerase, in vitro and in vivo. Importantly, it retains activity against retroviral DNA polymerase, and shows no cross-resistance to rifampicine, the only clinically used RNA-polymerase inhibitor so far. It was also found to show low cytotoxicity against mammalian cell cultures. Moreover, etnangien displays a number of salient motifs comprising of a 22-membered macrolactone with a polyunsaturated side chain and includes 12 stereogenic centers. Due to its biological importance, and its structural challenge, the synthesis of etnangien **1** has attracted our attention to take-up its synthesis. So far, only one report has appeared on the total synthesis of etnangien.[7] Herein, we report the synthesis of the C32–C42 fragment using a desymmetrization strategy.

2. Results and discussion

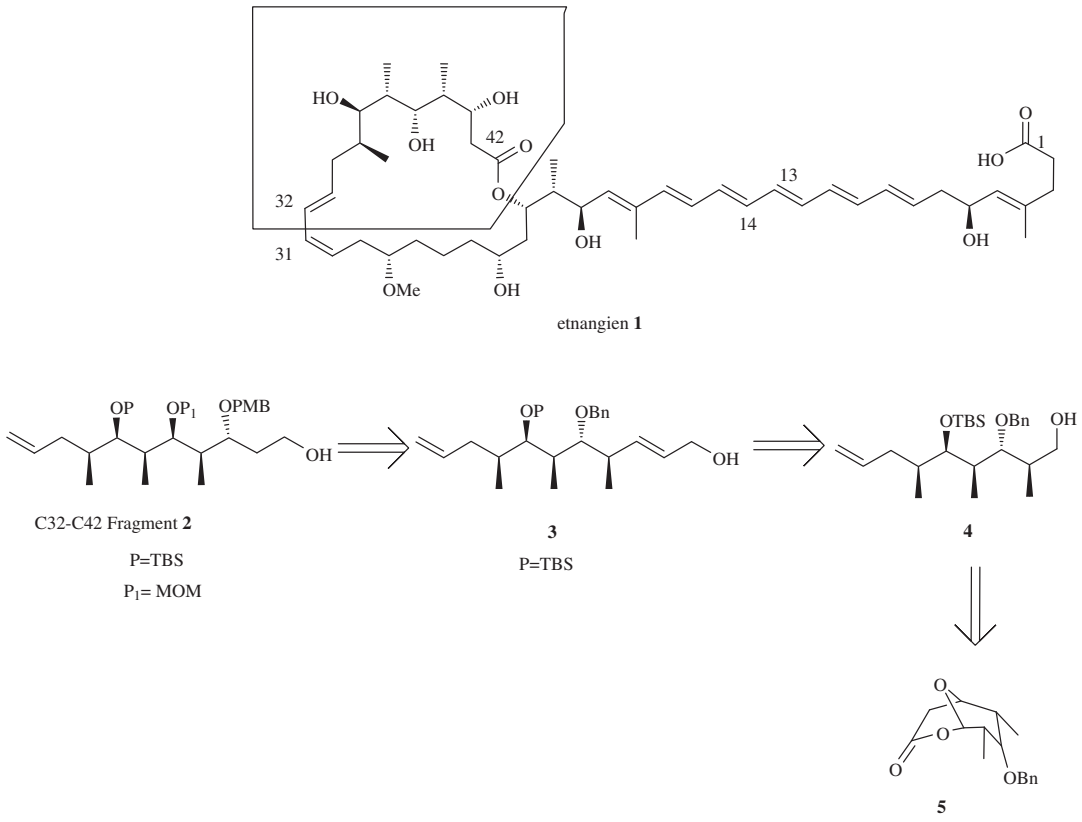
The retrosynthetic analysis is represented in Scheme 1. The intermediate **4** with five stereogenic centers could be obtained from a known bicyclic lactone **5** employing LAH mediated reduction. Unit **3** could be made by Wittig homologation and the final fragment **2** could be obtained by utilizing a Sharpless asymmetric epoxidation reaction to generate the stereogenic center at C40.

2.1. Synthesis of the C32–C42 fragment of etnangien

The synthesis of the C32–C42 fragment of etnangien started from the known bicyclic lactone **5**,[8] which was prepared using a desymmetrization strategy.[9] Lactone **5**, upon allylation with allyl bromide using NaHMDS afforded allylic lactone **6**, which was reduced using LAH to furnish triol **7** in 85% yield (Scheme 2). The 1,3-diol moiety was protected as the acetonide **8** and the primary hydroxyl functionality was converted to its corresponding pivolylate **9** using pivolyl chloride in the presence of NEt_3 in DCM in 92% yield. The acetonide group of **9** was hydrolyzed with PTSA in MeOH to afford diol **10** in 75% yield. The primary hydroxyl group in compound **10** was selectively tosylated with TsCl in the presence of NEt_3 and Bu_3SnO in DCM to afford tosylate **11** in 87% yield. The secondary hydroxyl group was protected as a TBS ether using TBSTf in presence of 2,6-lutidine in DCM to afford **12** in 92% yield. The $-CH_2OTs$ group of compound **12** was transformed into a methyl group and simultaneous deprotection of the pivaloyl group was achieved by using LAH in refluxing THF to give **4** in 86% yield. Compound **4**, upon oxidation using IBX in DMSO and DCM, furnished the aldehyde, which upon Wittig homologation with $PPh_3{=}CHCO_2Et$ in benzene at room temperature afforded α,β-unsaturated ester **13** in 73% yield. The ester group of compound **13** was reduced to allylic alcohol **3** using DIBAL-H at −78 °C in CH_2Cl_2 in 72% yield. Allylic alcohol **3** upon Sharpless asymmetric epoxidation furnished epoxy alcohol **14** in 80% yield, which on treating with Red-Al yielded 1,3-diol **15** in 82% yield. Deprotection of the benzyl ether in compound **15** was achieved using lithium naphthalide in dry THF to afford triol **16** in 76% yield. The 1,3-dihydroxy groups of triol **16** were protected as its PMB acetal **17** using anisaldehyde dimethyl acetal, and a catalytic amount of PPTS in CH_2Cl_2 in 84% yield. Inversion of the hydroxyl functionality in compound **17** was achieved using Mitsunobu conditions[10] to afford **18**, which was protected as its MOM ether **19** by treatment with Hunig's base and MOMCl in 78% yield. Compound **19** upon treatment with Dibal-H[11] resulted in the C32–C42 fragment **2** of etnangien. The structure of **2** was characterized by spectroscopic and analytical data.

* Corresponding author. Tel.: +91 40 27191629; fax: +91 40 27160512.
E-mail address: gowravaramsr@yahoo.com (G. Sabitha).

0957-4166/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2010.10.003



Scheme 1. The retrosynthetic analysis of etnangien.

3. Conclusion

In conclusion, the synthesis of the C32–C42 fragment of etnangien has been achieved using a desymmetrization strategy.

4. Experimental

4.1. General

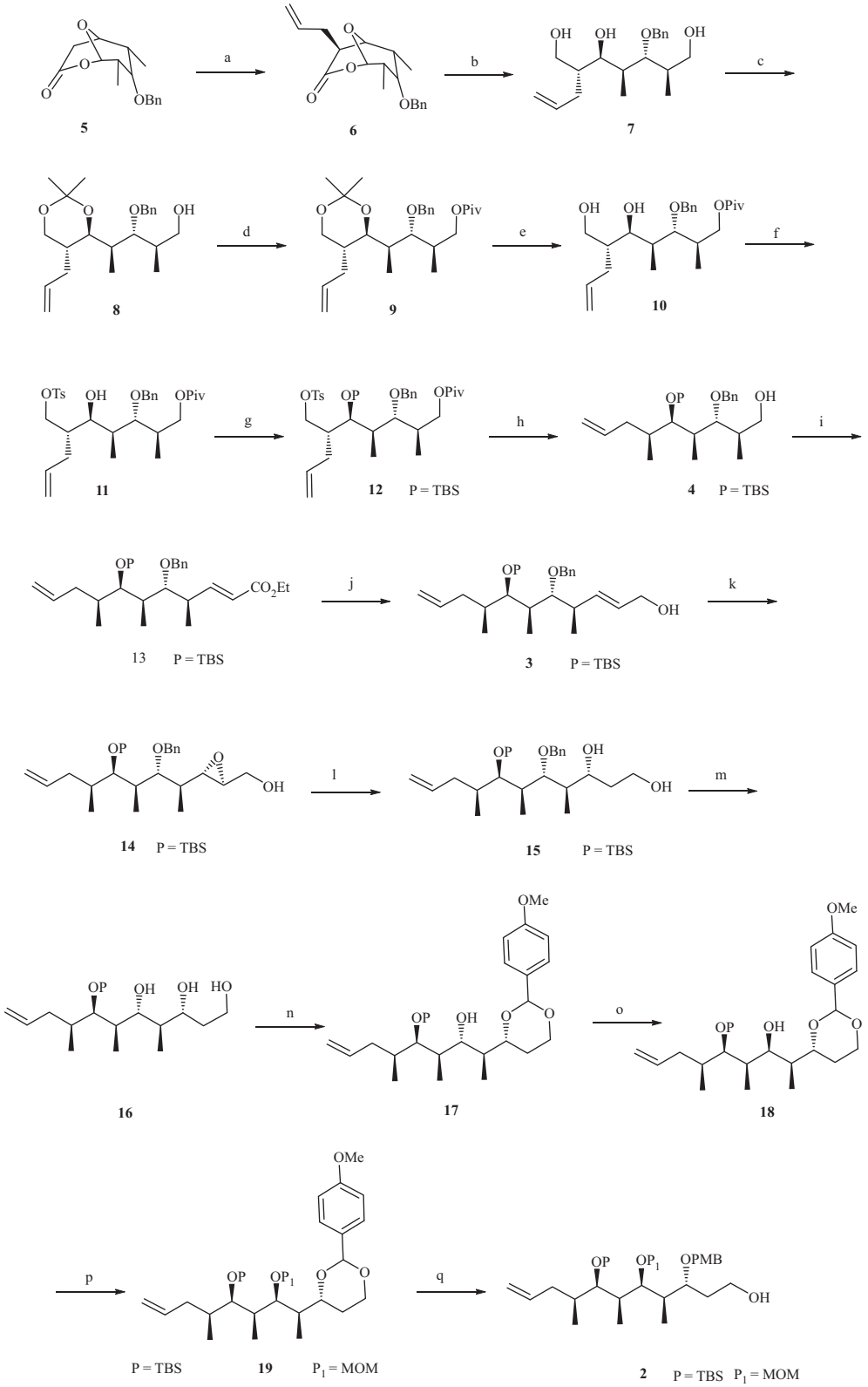
Reactions were conducted under N_2 in anhydrous solvents, such as CH_2Cl_2, THF, and EtOAc. All reactions were monitored by TLC (silica-coated plates and visualizing under UV light). Petroleum ether (bp 60–80 °C) was used. Yields refer to chromatographically and spectroscopically (^{1}H and ^{13}C NMR) homogeneous material. Air sensitive reagents were transferred by syringe or double-ended needle. Evaporation of solvents was performed at reduced pressure on a Buchi rotary evaporator. ^{1}H and ^{13}C NMR spectra of samples in $CDCl_3$ were recorded on Varian FT-200 MHz (Gemini) and Bruker UXNMR FT-300 MHz (Avance) spectrometers. Chemical shifts δ are reported relative to TMS (δ = 0.0) as an internal standard. Mass spectra were recorded E1 conditions at 70 eV on LC-MSD (Agilent technologies) spectrometers. Column chromatography was performed on silica gel (60–120 mesh) supplied by Acme Chemical Co., India. TLC was performed on Merck 60 F-254 silica gel plates. Optical rotations were measured with a JASCO DIP-370 Polarimeter.

4.2. (4*R*)-7-(Benzyloxy)-4-allyl-6,8-dimethyl-2,9-dioxabicyclo[3.3.1]nonan-3-one (6)

To a stirred solution of lactone **5** (30 g, 108 mmol) in anhydrous THF (150 mL) at −78 °C under a nitrogen atmosphere, was added LHMDS (141 mL, 141.30 mmol, 1.0 M) dropwise. After 1-h stirring at −78 °C, allylbromide (neat 27.9 mL, 326 mmol) was added dropwise. The reaction mixture was stirred for 3 h at the same temperature and quenched with a saturated aqueous NH_4Cl solution (30 mL) and extracted with ether (3 × 150 mL). The organic extracts were washed with water and brine, and dried over anhydrous Na_2SO_4 (2 g), concentrated in vacuo, and purified by column chromatography on silica gel to give the allylated lactone **6** (27.47 g, 80%) as a viscous liquid. $[\alpha]_D^{25} = -34.6$ (*c* 1, $CHCl_3$); IR (neat) ν_{max} 2926, 1725 1638, 1452, 1058 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34–7.23 (m, 5H), 5.79–5.65 (m, 1H), 5.36 (d, 1H, *J* = 3.1 Hz), 5.14–5.07 (m, 2H), 4.57 (ABq, 2H, *J* = 11.3 Hz), 3.83 (dd, 1H, *J* = 6.7 Hz), 3.55 (t, 1H, *J* = 3.2 Hz), 2.66–2.57 (m, 2H), 2.52–2.38 (m, 1H), 2.25–2.16 (m, 1H), 2.07–1.97 (m, 1H), 1.15 (d, 3H, *J* = 7.5 Hz), 0.89 (d, 3H, *J* = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.5, 129.8, 122.4, 121.7, 120.7, 114.4, 111.4, 68.6, 58.0, 56.0, 53.4, 46.6, 29.5, 26.7, 24.1, 23.0; ESIMS: 317 (M^++1).

4.3. (2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-5-(benzyloxy)-4,6 dimethylheptane-1,3,7-triol (7)

To a stirred suspension of $LiAlH_4$ (4.77 g, 125.41 mmol) in dry THF (30 mL) at 0 °C, a solution of lactone **6** (27 g, 83.85 mmol) in dry THF (60 mL) was added dropwise. The reaction mixture was refluxed for 3 h. It was then cooled to 0 °C, diluted with ether, and quenched by the dropwise addition of saturated aqueous Na_2SO_4. The solid material was filtered and washed thoroughly with hot ethyl acetate several times. The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by silica gel column chromatography to afford compound **7** (23.37 g, 85%) as a viscous liquid. $[\alpha]_D^{25} = +1.3$ (*c* 1, $CHCl_3$); IR (neat) ν_{max} 3408, 2926, 1638, 1452, 1058 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33–7.25 (m, 5H), 5.79–5.65 (m, 1H), 5.05–4.97 (m, 2H), 4.67 (s, 2H), 3.98–3.89 (m, 1H), 3.81–3.71 (m, 2H), 3.69–3.59 (m, 2H), 3.52 (d, 1H, *J* = 3.1, 9.1 Hz), 2.01–1.85 (m, 3H), 1.84–1.76 (m, 2H), 1.15 (d, 3H, *J* = 6.7 Hz), 0.97 (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ



Scheme 2. Reagents and conditions: (a) NaHMDS allylbromide; dry THF, −78 °C 4 h, 80%; (b) LAH, dry THF, 0 °C to rt, 3 h, 85%; (c) **2**, 2 DMP, *p*PTS, 0 °C to rt, dry CH_2Cl_2, 12 h, 90%; (d) pivolyl chloride, Et_3N, 0 °C to rt, 12 h, 92%; (e) *p*TSA, MeOH, 0 °C to rt, 12 h, 75%; (f) TsCl, Bu_3SnO, Et_3N, dry CH_2Cl_2, 0 °C to rt, 10 h, 87%; (g) TBS-Tf., 2.6 lutidine, dry CH_2Cl_2, 0 °C to rt, 2 h, 92%; (h) LAH, dry THF, 0 °C to rt, 3 h, 86%; (i) (i) dry DMSO, dry CH_2Cl_2, $(COCl)_2$, Et_3N, −78 °C; (ii) PPh_3=$CHCO_2Et$, dry benzene, rt, 15 h, 73%; (j) DIBAL, dry CH_2Cl_2 −78 °C, 2 h, 72%; (k) (+) DET, $Ti(O^iPr)_4$, cummene hydroperoxide dry CH_2Cl_2, −23 °C, 6 h, 80%; (l) Red-Al, dry THF, 0 °C to rt, 2 h, 82%; (m) Li, naphthalene, dry THF, 0 °C to rt, 1.5 h, 76%; (n) MeO–Ph–$CH(OMe)_2$, dry CH_2Cl_2, PPTS, 0 °C to rt, 2 h, 84%; (o) DEAD, TPP, *p*-$C_6H_4(NO_2)COOH$, dry THF, 0 °C to rt, then K_2CO_3, MeOH, 4 h, 65%; (p) MOMCl, *i*-Pr_2EtN, dry CH_2Cl_2, 0 °C rt, 4 h, 78%; (q) DIBAL-H, dry CH_2Cl_2, −78 °C, 1 h, 80%.

137.4, 135.7, 128.6, 128.2, 127.9, 116.7, 88.7, 76.4, 74.7, 65.8, 41.9, 37.9, 35.4, 32.8, 14.7, 11.8; ESIMS: 323 (M^++1).

4.4. (2*R*,3*R*,4*R*)-4-[(4*R*,5*R*)-5-Allyl-2,2-dimethyl-1,3-dioxan-4-yl]-3-(benzyloxy)-2-methylpentan-1-ol 8

To a solution of triol **7** (23 g, 71.42 mmol) in dry DCM (40 mL), 2,2-dimethoxy propane (10.6 mL, 85.67 mmol) and PTSA (1.1 g, 7.14 mmol) were added. The mixture was stirred at ambient temperature for 12 h. Sodium bicarbonate was added to neutralize PTSA and filtered. Removal of the solvent and purification by silica gel column chromatography afforded the mono acetonide **8** (23.22 g, 90%) as a white solid. $[\alpha]_D^{25} = -19.9$ (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35–7.25 (m, 5H), 5.75–5.62 (m, 1H), 5.06–4.97 (m, 2H), 4.64 (ABq, 2H, *J* = 11.3 Hz), 3.98 (dd, 1H, *J* = 1.5, 10.5 Hz), 3.84 (dd, 2H, *J* = 3.0, 11.3 Hz), 3.73 (dd, 1H, *J* = 4.5, 11.3 Hz), 3.52–3.43 (m, 3H), 2.61–2.56 (br s, 1H), 2.12–2.01 (m, 2H), 1.94–1.76 (m, 2H), 1.33 (s, 6H), 1.21 (d, 3H, *J* = 6.7 Hz), 0.88 (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.3, 134.9, 128.4, 127.6, 126.9, 116.9, 97.8, 85.6, 75.4, 71.5, 64.2, 64, 37.3, 35.9, 34.6, 32.5, 29.5, 19.7, 16.3, 9.9; ESIMS: 363 (M^++1).

4.5. (2*R*,3*R*,4*R*)-4-[(4*R*,5*R*)-5-Allyl-2,2-dimethyl-1,3-ioxan-4-yl]-3-(benzyloxy)-2-methylpentyl pivalate 9

To a stirred and cooled solution of alcohol **8** (23 g, 63.53 mmol) and triethylamine (35.9 mL, 253 mmol) in dry DCM (40 mL), trimethyl acetyl chloride (23.5 ml, 190.60 mmol) was slowly added. The mixture was stirred overnight at room temperature. The reaction mixture was diluted with CH_2Cl_2 and washed with aqueous copper sulfate solution, water, and brine solution, and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by silica gel column chromatography to afford compound **9** (26.03 g, 92%) as a solid. $[\alpha]_D^{25} = -18.4$ (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.31–7.21 (m, 5H), 5.73–5.59 (m, 1H), 5.03–4.96 (m, 2H), 4.61 (ABq, 2H, *J* = 12 Hz), 4.28 (dd, 1H, *J* = 5.2, 10.5 Hz), 3.92–3.87 (m, 2H), 3.71 (dd, 1H, *J* = 4.5, 11.3 Hz), 3.48 (dd, 1H, *J* = 9.8, 11.3 Hz), 3.88 (dd, 1H, *J* = 2.2, 9.8 Hz), 2.19–1.95 (m, 3H), 1.87–1.69 (m, 2H), 1.31 (d, 6H, *J* = 7.5 Hz), 1.19 (s, 9H), 1.11 (d, 3H, *J* = 6.7 Hz), 0.92 (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.7, 139.1, 134.9, 128.2, 127.2, 126.6, 116.8, 97.8, 82.7, 74.8, 71.4, 65.7, 64, 37.0, 34.9, 34.7, 32.4, 29.5, 27.2, 19.7, 16.2, 9.8. ESIMS: 447 (M^++1).

4.6. (2*R*,3*R*,4*S*,5*R*,6*R*)-3-(Benzyloxy)-5-hydroxy-6-(hydroxymethyl)-2,4-dimethyl-8-nonenyl pivalate 10

To a stirred solution of compound **9** (25.5 g 54.72 mmol) in methanol (50 mL) was added a catalytic amount of PTSA. The reaction mixture was stirred overnight at room temperature. Sodium bicarbonate was added to neutralize the PTSA and filtered. The filtrate was concentrated under reduced pressure and purification by silica gel column chromatography afforded **10** (17.40 g, 75%) as a pure liquid. $[\alpha]_D^{25} = +9.8$ (*c* 0.5, $CHCl_3$); IR (neat): ν_{max} 3447, 2971, 2928, 1727, 1640, 1459, 1285, 1158, 1092, 1061 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37–7.24 (m, 5H), 5.79–5.66 (m, 1H), 5.05–4.97 (m, 2H), 4.57 (ABq, 2H, *J* = 10.5 Hz), 4.26 (dd, 1H, *J* = 3.7, 10.5 Hz), 4.17–4.08 (m, 1H), 3.92 (d, 1H, *J* = 9 1 Hz), 3.72–3.58 (m, 2H), 3.42 (dd, 1H, *J* = 2.2, 9.8 Hz), 2.26–2.15 (m, 1H), 1.99–1.89 (m, 2H), 1.87–1.73 (m, 2H), 1.23 (s, 9H), 1.15 (d, 3H, *J* = 6.7 Hz), 0.97 (d, 3H, *J* = 6.7 Hz); ESIMS: 407 (M^++1).

4.7. (2*R*,3*R*,4*S*,5*R*,6*R*)-3-(Benzyloxy)-5-hydroxy-2,4-dimethyl-6-([(4-methylphenyl)sulfonyl]oxymethyl)-8-nonenyl pivalate 11

A solution of **10** (17 g, 41.87 mmol) in dry DCM (30 mL), containing triethylamine (17.79 ml, 125.6 mmol), was cooled to 0 °C and treated with *p*-toluenesulphonyl chloride (8.839 g, 46.52 mmol) and a catalytic amount of Bu_2SnO. The reaction mixture was stirred at room temperature for 10 h, after which it was diluted with water and extracted with DCM. The organic layer was washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure and purification by silica gel column chromatography afforded **11** (2.72 g, 87%) as a viscous liquid. $[\alpha]_D^{25} = +10.9$ (*c* 1, $CHCl_3$); IR (KBr): 3489, 2927, 1725, 1458, 1359, 1176, 1092 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, 2H, *J* = 8.3 Hz), 7.33–7.23 (m, 7H), 5.72–5.57 (m, 1H), 5.06–4.97 (m, 2H), 4.57 (ABq, 2H, *J* = 10.5 Hz), 4.27–4.17 (m, 2H), 4.14–4.05 (m, 2H), 3.79–3.69 (m, 1H), 3.39 (dd, 1H, *J* = 3.2, 8.4 Hz), 3.11 (br s 1H), 2.40 (s, 3H), 2.15–1.99 (m, 2H), 1.93–1.86 (m, 1H), 1.93–1.86 (m, 1H), 1.78–1.69 (m, 1H), 1.23 (s, 9H), 1.03 (d, 3H, *J* = 6.7 Hz), 0.97 (d, 3H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.3, 144.4, 137.2, 134.5, 129.6, 128.6, 128.1, 128.0, 127.9, 117.8, 87.0, 76.3, 69.2, 68.4, 65.9, 40.9, 35.7, 34.3, 31.0, 27.2, 21.5, 14.6, 11.3; ESIMS: 561 (M^++1).

4.8. (2*R*,3*R*,4*R*,5*R*,6*R*)-3-(Benzyloxy)-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-2,4-dimethyl-6-([(4-methylphenyl)sulfonyl]oxymethyl)-8-nonenyl pivalate 12

tert-Butyldimethylsilyl triflouoromethanesulphonate (8.3 g, 35.55 mmol) was added to an ice-cold solution of compound **11** (20 g, 29.62 mmol) in dry DCM (50 mL) followed by the slow addition of 2,6-lutidine (10.31 g, 88.8 mmol). The reaction mixture was stirred for 2 h at 0 °C before being diluted with DCM and washed with saturated aqueous NH_4Cl and brine solution. The organic phase was dried over Na_2SO_4, and concentrated. Purification by column chromatography afforded the pure compound **12** (22.17 g, 92%). $[\alpha]_D^{25} = +3.7$ (*c* 0.5, $CHCl_3$); IR(KBr): ν_{max} 2958, 1726, 1640, 1461, 1365, 1177, 1061, 835, 774 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.69 (d, 2H, *J* = 8.3 Hz), 7.32–7.26 (m, 7H), 5.62–5.48 (m, 1H), 4.93–4.84 (m, 2H), 4.56 (s, 2H), 4.21 (dd, 1H, *J* = 5.2, 11.3 Hz), 4.05 (dd, 1H, *J* = 5.2, 9.8 Hz), 3.98–3.88 (m, 4H), 3.27 (dd, 1H, *J* = 3.7, 8.3 Hz), 2.42 (s, 3H), 2.21–2.08 (m, 2H), 2.02–1.88 (m, 2H), 1.19 (s, 9H), 1.07 (d, 3H, *J* = 7.5 Hz), 0.88 (d, 3H, *J* = 6.7 Hz), 0.85 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.5, 144.5, 138.4, 135.6, 133, 129.7, 128.3, 127.9, 127.4, 127.3, 117.2, 84.2, 74.2, 71.8, 70.1, 65.9, 44.0, 39.5, 34.8, 32.2, 27.2, 26.0, 21.5, 18.4, 15.9, 12.0, −3.2, −4.0; ESIMS: 693 (M^++NH_4^+).

4.9. (2*R*,3*R*,4*R*,5*R*,6*S*)-3-(Benzyloxy)-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-2,4,6-trimethyl-8-nonen-1-ol 4

To a stirred suspension of $LiAlH_4$ (1.56 g, 44.11 mmol) in dry THF (20 mL) at 0 °C was added dropwise a solution of compound **12** (18.5 g, 27.40 mmol) in dry THF (30 mL). The reaction mixture was refluxed for 3 h. It was then cooled to 0 °C, diluted with ether, and quenched by the dropwise addition of saturated aqueous Na_2SO_4. The solid material was filtered and washed thoroughly with hot ethyl acetate for several times. The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by silica gel column chromatography to afford compound **4** (9.8 g, 86%) as a viscous liquid. $[\alpha]_D^{25} = -25.3$ (*c* 0.5, $CHCl_3$); IR(KBr): ν_{max} 3353, 2928, 2264, 1713, 1536, 1222, 1044 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.33–7.26 (m, 5H), 5.71–5.63 (m, 1H), 4.98–4.92 (m, 2H), 4.63 (ABq, 2H, *J* = 11.7 Hz), 3.81–3.78 (m, 2H), 3.55–3.51 (m, 1H), 3.32 (dd, 1H, *J* = 2.9, 7.8 Hz), 2.49–2.44 (br s, 1H), 2.31–2.24 (m, 1H), 2.03–1.98 (m, 1H), 1.94–1.89 (m, 1H), 1.81–1.73 (m, 1H), 1.66–1.61 (m, 1H), 1.15 (d, 3H, *J* = 6.8 Hz), 0.92 (s, 9H), 0.90 (d, 3H, *J* = 6.8 Hz), 0.85 (d, 3H, *J* = 5.8 Hz), 0.06 (d, 6H, *J* = 4.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.9, 128.4, 127.8, 127.5, 115.6, 88.1,

75.2, 75.0, 65.1, 39.7, 38.8, 37.4, 36.0, 26.1, 18.5, 16.6, 14.6, 12.4, −3.5, −3.6; ESIMS: 443 (M^++Na).

4.10. Ethyl (2*E*,4*R*,5*R*,6*R*,7*R*,8*S*)-5-(benzyloxy)-7-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-4,6,8-trimethyl-2,10-undecadienoate 13

In an oven-dried flask under an N_2 atmosphere, DMSO (6.41 mL, 90.41 mmol) was dissolved in dry DCM (35 mL). The solution was cooled to −78 °C, and $(COCl)_2$ (5.69 g, 45.53 mmol) was added dropwise. After 5 min, alcohol **4** (9.5 g, 22.61 mmol) in dry DCM (20 mL) was added drop wise. The white slurry was stirred for 10 min at −78 °C, before Et_3N (13.70 g, 135.66 mmol) was added drop wise. The solution was allowed to warm to ambient temperature before being diluted in Et_2O (20 mL) and washed with aqueous NH_4Cl (20 mL), $NaHCO_3$ (15 mL), and brine (20 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo to give crude aldehyde **13** (8.82 g, 80%), which was used directly for the next reaction.

The mixture of the above prepared aldehyde (8.82 g, 21.11 mmol) and PPh_3=$CHCO_2Et$ (14.68 g, 42.20 mmol) in dry DCM (25 mL) was stirred for 15 h. at rt. The reaction mixture was concentrated and the resultant residue was purified by column chromatography to give α,β-unsaturated ester **13** (7.51 g, 73%) as a viscous liquid. $[\alpha]_D^{25} = -7.5$ (*c* 1, $CHCl_3$); IR(KBr): ν_{max} 2957, 2929, 1720, 1691, 1642, 1460, 1253, 1095, 1064, 835, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33–7.28 (m, 5H), 7.06 (dd, 1H, *J* = 8.3, 15.8 Hz), 5.78 (dd, 1H, *J* = 1.5, 15.8 Hz), 5.74–5.58 (m, 1H), 5.02–4.89 (m, 2H), 4.61 (ABq, 2H, *J* = 11.3 Hz), 4.18 (q, 2H, *J* = 6.7, 14.3 Hz), 3.82–3.79 (m, 1H), 3.26 (dd, 1H, *J* = 2.2, 9.0 Hz), 2.73–2.63 (m, 1H), 2.29–2.19 (m, 1H), 1.86–1.68 (m, 2H), 1.63–1.54 (m, 1H), 1.31 (t, 3H, *J* = 7.5 Hz), 1.2 (d, 3H, *J* = 7.5 Hz), 0.91 (s, 9H), 0.81 (d, 3H, *J* = 5.2 Hz), 0.8 (d, 3H, *J* = 4.5 Hz), 0.03 (d, 6H, *J* = 5.2 Hz); ESIMS: 489 (M^++1).

4.11. (2*E*,4*R*,5*R*,6*R*,7*R*,8*S*)-5-(Benzyloxy)-7-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-4,6,8-trimethyl-2,10-undecadien-1-ol 3

At −78 °C, 1.4 M solution of DIBAL-H (17.83 mL, 30.32 mmol) was slowly added to a solution of α,β-unsaturated ester **13** (7.4 g, 15.16 mmol) in dry DCM (15 mL). The solution was stirred for 2 h at −78 °C before being quenched with EtOAc (5 mL). The mixture was allowed to warm to ambient temperature before an aqueous solution of Rochelle's salt was added (30 mL) and stirred for 1 h. The aqueous phase was extracted with DCM and the combined organic extracts were dried over anhydrous Na_2SO_4, concentrated, and purified by column chromatography on silica gel to afford the desired allylic alcohol **3** (4.86 g, 72%) as a pale yellow oil. $[\alpha]_D^{25} = +1.4$ (*c* 1, $CHCl_3$); IR (KBr): ν_{max} 2956, 1720, 1459, 1254, 1093, 835, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.31–7.23 (m, 5H), 5.82–5.58 (m, 3H), 4.99–4.88 (m, 2H), 4.61 (ABq, 2H, *J* = 11.1 Hz), 4.11–4.03 (m, 2H), 3.85–3.81 (m,1H), 3.18 (dd, 1H, *J* = 2.2, 8.8 Hz) 2.52–2.47 (m, 1H), 2.31–2.22 (m, 1H), 1.83–1.68 (m, 2H), 1.63–1.53 (m, 1H), 1.15 (d, 3H, *J* = 6.9 Hz), 0.91 (s, 9H), 0.83 (d, 3H, *J* = 3.3 Hz), 0.8 (d, 3H, *J* = 3.7 Hz), 0.04 (d, 6H, *J* = 5.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.1, 138.0, 134.6, 130.4, 128.7, 128.5, 128.2, 115.4, 79.4, 75.0, 74.9, 68.1, 38.8, 38.6, 37.3, 36.3, 26.1, 17.7, 14.8, 13.9, 11.9, −3.5, −3.6; ESIMS: 479 (M^++Na).

4.12. [(2*S*,3*S*)-3-((1*S*,2*R*,3*R*,4*R*,5*S*)-2-(Benzyloxy)-4-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-1,3,5-trimethyl-7-octenyl)oxiran-2-yl]methanol 14

In a 250 mL two neck round bottomed flask, 50 mL of dry DCM was added to 4 Å powdered activated molecular sieves and the suspension mixture was cooled to −20 °C, after which $Ti(O^iPr)_4$ (0.573 g, 2.01 mmol) and L-(+)-DET (0.415 g, 2.01 mmol) in dry DCM (5 mL) were added with stirring and the resulting mixture was stirred for 30 min at −25 °C. Compound **3** (4.5 g, 10.08 mmol) in dry DCM (15 mL) was then added and the resulting mixture was stirred for another 30 min at −25 °C followed by the addition of cumene hydroperoxide (1.78 mL, 12.10 mmol). The resulting mixture was stirred at the same temperature for 6 h, after which it was warmed to 0 °C, quenched with 10 mL of water, and stirred for 1 h at room temperature. After that 30% aqueous NaOH solution saturated with NaCl (10 mL) was then added and the reaction mixture was stirred vigorously for another 30 min at room temperature. The resulting mixture was then filtered through Celite rinsing with DCM. The organic phase was separated and the aqueous phase was extracted with DCM. Combined organic phases were washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and purified by silica gel column chromatography to afford **14** (3.41 g, 75%) as a viscous liquid. $[\alpha]_D^{25} = -12.8$ (*c* 0.5, $CHCl_3$); IR (KBr): ν_{max} 3422, 2931, 1718, 1460, 1256, 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.28 (m, 5H), 5.76–5.61 (m, 1H), 5.01–4.89 (m, 2H), 4.61 (ABq, 2H, *J* = 6.7 Hz), 3.89–3.78 (m, 2H), 3.62–3.51 (m, 1H), 3.27 (dd, 1H, *J* = 1.5, 9.0 Hz), 3.07 (dd, 1H, *J* = 2.2, 6.7 Hz), 2.87–2.83 (m, 1H), 2.33–2.22 (m, 1H), 2.11–2.02 (m, 1H), 1.81–1.73 (m, 1H), 1.64–1.42 (m, 2H), 1.07 (d, 3H, *J* = 7.5 Hz), 0.91 (s, 9H), 0.9 (d, 3H, *J* = 7.5 Hz), 0.86 (d, 3H, *J* = 6.1 Hz), 0.06 (d, 6H, *J* = 7.5 Hz); ESIMS: 463 (M^++1).

4.13. (3*R*,4*R*,5*R*,6*R*,7*R*,8*S*)-5-(Benzyloxy)-7-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-4,6,8-trimethyl-10-undecene-1,3-diol 15

A solution of compound **14** (3.2 g, 4.92 mmol) in dry DCM (10 mL) was cooled to 0 °C and Red-Al (2.8 ml, 20% solution in hexane, 9.00 mmol) was added to it over a period of 2 h. The mixture was quenched with NH_4Cl. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and purified by column chromatography to give the required alcohol **15** (2.63 g 82%) as a viscous liquid. $[\alpha]_D^{25} = +1.6$ (*c* 1, $CHCl_3$); IR (KBr): ν_{max} 3423, 2926, 2360, 1721, 1543, 1219, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.34–7.27 (m, 5H), 5.73–5.59 (m, 1H), 4.65 (ABq, 2H, *J* = 6.7 Hz), 3.86–3.66 (m, 3H), 3.51–3.45 (m, 1H), 3.29 (dd, 1H, *J* = 4.5, 6.7 Hz), 2.90–2.75 (m, 1H), 2.34–2.25 (m, 1H), 2.03–1.75 (m, 4H), 1.68–1.57 (m, 2H), 0.97 (d, 3H, *J* = 7.5 Hz), 0.91 (s, 9H), 0.92 (d, 3H, *J* = 4.5 Hz), 0.84 (d, 3H, *J* = 6.7 Hz), 0.04 (d, 6H, *J* = 3.1 Hz); ESIMS: 465 (M^++1).

4.14. (3*R*,4*R*,5*R*,6*R*,7*R*,8*S*)-7-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-4,6,8-trimethyl-10-undecene-1,3,5-triol 16

To solution of naphthalene (5.51 g, 43.10 mmol) in dry THF (15 mL) in a round bottom flask, lithium metal (0.362 g, 51.72 mmol) was added to it in fractions at 0 °C and the resulting gray colored suspension was stirred for 30 min. To this was added compound **15** (2 g, 4.31 mmol) in dry THF (10 mL) over a period of 10 min. The reaction mixture was then stirred for another 1 h at 0 °C and quenched by the addition of solid ammonium chloride. The ammonia was then allowed to evaporate. The residue left was partitioned between water and ether and the aqueous phase extracted with ether. The organic layers were combined, washed once with water, brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford pure **16** (0.56 g, 76%) as a clear colorless liquid. $[\alpha]_D^{25} = -14.6$ (*c* 1, $CHCl_3$); IR (KBr): ν_{max} 3421, 2926, 1633, 1383, 1219, 1051, 772 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.72–5.62 (m, 1H), 5.03–4.98 (m, 2H), 3.94–3.84 (m, 2H), 3.85–3.76 (m, 2H), 3.52–3.48 (m, 1H), 2.23–2.15 (m, 1H), 2.08–2.01 (m, 1H), 1.91–1.76 (m, 3H), 1.75–1.76 (m, 2H), 0.97 (d, 3H, *J* = 7.8 Hz), 0.95–0.91 (m, 12H), 0.85 (d, 3H,

J = 6.8 Hz), 0.13 (d, 6H, J = 10.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.5, 116.2, 82.2, 80.3, 76.4, 62.2, 41.0, 38.8, 38.3, 36.4, 35.8, 29.7, 25.8, 16, 14.8, 14.0, −3.7, −4.3; ESIMS: 375 (M^++1).

4.15. (2*S*,3*R*,4*R*,5*R*,6*S*)-5-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-2-[(4*R*)-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]-4,6-dimethyl-8-nonen-3-ol 17

A solution of triol compound **16** (1 g, 2.67 mmol) in dry DCM (10 mL) was cooled to 0 °C and catalytic amount of PPTS followed by PMB acetal (0.583 g, 20% solution in hexane, 3.20 mmol) was added to it over a period of 2 h. The mixture was then quenched with sodium bicarbonate. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and purified by column chromatography to give the required alcohol **17** (1.10 g 84%) as a viscous liquid. $[\alpha]_D^{25} = -9.4$ (c 1, $CHCl_3$); IR (KBr): ν_{max} 3486, 1740, 1615, 1517, 1463, 1248, 1103, 1037, 831, 772 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.55 (d, 2H, J = 8.6 Hz), 7.02 (d, 2H, J = 8.4 Hz), 5.92–5.82 (m, 1H), 5.62 (s, 1H), 5.17–5.1 (m, 2H), 4.43 (dd, 1H, J = 3.3, 10.9 Hz), 4.21–4.06 (m, 1H), 4.02–3.94 (m, 2H), 3.97 (s, 3H), 3.64–3.53 (m, 1H), 2.53–2.43 (m, 1H), 2.33–2.24 (m, 2H), 2.21–1.88 (m, 4H), 1.18 (d, 3H, J = 7.1 Hz), 1.10–0.99 (m, 6H), 1.05 (s, 9H), 0.22 (s, 3H), 0.16 (s, 3H); ESIMS: 493 (M^++1).

4.16. (2*S*,3*S*,4*R*,5*R*,6*S*)-5-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-2-[(4*R*)-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]-4,6-dimethyl-8-nonen-3-ol 18

At 0 °C, a solution of compound **17** (0.60 g, 1.21 mmol) in THF (10 ml) was treated with TPP (0.41 g, 1.58 mmol) and DEAD (0.27 mL, 1.58 mmol) followed by *para*-nitro benzoic acid (0.26 g, 1.58 mmol) and stirring was continued for 2 h. The mixture was concentrated and the resulting crude product was purified by silica gel column chromatography.

At 0 °C, a solution of the above benzoate in dry methanol (15 mL) was treated with Na (0.056 g, 2.43 mmol) and the resulting reaction mixture was stirred at rt (monitored by TLC). After 2 h, the reaction mixture was neutralized with AcOH at 0 °C, evaporated, and purified by column chromatography to obtain inverted alcohol **18** (0.24 g, 78%). $[\alpha]_D^{25} = -11.5$ (c 0.5, $CHCl_3$); IR (KBr): ν_{max} 3486, 1740, 1615, 1517, 1463, 1248, 1103, 1037, 831, 772 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 (d, 2H, J = 8.6 Hz), 6.81 (d, 2H, J = 8.6 Hz), 5.72–5.58 (m, 1H), 5.39 (s, 1H), 4.95 (m, 2H), 4.23 (dd, 1H, J = 3.5, 10.9 Hz), 4.14–4.06 (m, 1H), 3.92 (dt, 1H, J = 1.8, 11.3 Hz), 3.79 (s, 3H), 3.73 (t, 3H, J = 2.4 Hz), 3.51 (d, 1H, J = 9 4 Hz), 2.19–2.04 (m, 2H), 1.96–1.79 (m, 4H), 1.78–1.68 (m, 2H), 0.99 (d, 3H, J = 7.1 Hz), 0.95 (d, 3H, J = 6.7 Hz), 0.9 (s, 9H), 0.84 (d, 3H, J = 6.9 Hz), 0.02 (d, 6H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.2, 137.6, 127.5, 127.3, 116.0, 113.4, 101.0, 78.8, 78.3, 67.3, 55.2, 40.5, 40.0, 39.9, 39.6, 34.7, 28.9, 25.9, 16.0, 14.2, 14.0, 13.8, −4.2, −4.3; ESIMS: 493 (M^++1).

4.17. *tert*-Butyl[((1*R*,2*S*)-1-(1*R*,2*S*,3*S*)-2-(methoxymethoxy)-3-[(4*R*)-2-(4-methoxyphenyl)-1,3-dioxan-4-yl]-1-methylbutyl-2-methyl-4-pentenyl)oxy]dimethylsilane 19

To a stirred solution of compound **18** (0.3 g, 0.60 mmol) in anhydrous dichloromethane (15 mL) at 0 °C under nitrogen, ^{i}Pr$_2$NEt (0.23 g, 1.82 mmol) was added followed by the dropwise addition of MOMCl (0.09 mL, 1.12 mmol). After stirring for 4 h at room temperature, the reaction mixture was diluted with water, saturated aqueous NH_4Cl, and brine solution, and then dried over anhydrous Na_2SO_4. The residue was concentrated in vacuo and purified by silica gel column chromatography to afford pure compound **19** (0.24 g, 75%) as a clear colorless liquid. $[\alpha]_D^{25} = -3.3$ (c 0.5, $CHCl_3$); IR(KBr): ν_{max} 2926, 2854, 1735, 1621, 1458, 1248, 1100, 1033, 831, 772 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.37 (d, 2H, J = 8.6 Hz), 6.84 (d, 2H, J = 8.4 Hz), 5.72–5.62 (m, 1H), 5.44 (s, 1H), 4.99–4.91 (m, 2H), 4.65 (ABq, 2H, J = 6.4 Hz), 4.24 (dd, 1H, J = 4.1, 11.7 Hz), 4.02–3.88 (m, 2H), 3.79 (s, 3H), 3.46–3.33 (m, 2H), 3.39 (s, 3H), 2.36–2.22 (m, 1H), 2.14–1.93 (m, 2H), 1.84–1.64 (m, 2H), 1.62–1.46 (m, 2H), 1.00 (d, 3H, J = 7.1 Hz), 0.91–0.81 (m, 6H), 0.87 (s, 9H), 0.04 (s, 3H), −0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.7, 138.2, 131.5, 127.3, 115.4, 113.4, 101.1, 98.1, 84.7, 77.7, 74.7, 67.1, 55.9, 55.2, 40.0, 39.8, 38.5, 37.6, 29.6, 28.5, 26.1, 18.4, 14.7, 12.5, 12.4, −3.6, −3.9; ESIMS: 559 (M^++Na).

4.18. (3*R*,4*R*,5*S*,6*R*,7*R*,8*S*)-7-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-3-[(4-methoxybenzyl)oxy]-5-(methoxymethoxy)-4,6,8-trimethyl-10-undecen-1-ol 2

A cold (−78 °C) solution of PMB acetal **19** (0.2 g, 0.40 mmol) in DCM (10 mL) was treated with diisobutylaluminum hydride (0.26 mL, 0.44 mmol). The reaction mixture was allowed to warm to 0 °C for 1 h. Excess hydride was quenched by the dropwise addition of saturated aqueous sodium potassium tartrate (caution vigorous evolution of H_2, may result) and the mixture was allowed to warm to rt. After vigorous stirring for 1 h, the organic solution was washed with brine. The aqueous layer was extracted with Et_2O and the combined organic phases were washed with brine and dried over anhydrous Na_2SO_4. Filtration and concentration followed by flash chromatography provided alcohol **2** (0.16 g, 80%) as a clear colorless liquid. $[\alpha]_D^{25} = +11.7$ (c 0.5, $CHCl_3$); IR (KBr): ν_{max} 3449, 2928, 2855, 1724, 1614, 1513, 1463, 1249, 1034, 834, 772 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.22 (d, 2H, J = 8.1 Hz), 6.82 (d, 2H, J = 8.3 Hz), 5.77–5.63 (m, 1H), 5.02–4.93 (m, 2H), 4.60 (s, 2H), 4.4 (ABq, 2H, J = 11.1 Hz), 3.89 (dd, 1H, J = 3.2, 7.9 Hz), 3.79 (s, 3H), 3.72–3.65 (m, 2H), 3.39–3.34 (m, 1H), 3.33 (s, 3H), 3.24 (t, 1H, J = 5.6 Hz), 2.33–2.14 (m, 2H), 1.82–1.72 (m, 3H), 1.69–1.55 (m, 2H), 0.96–0.81 (m, 9H), 0.91 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.6, 138, 129.4, 115.6, 113.8, 98.3, 85.5, 78.6, 74.4, 70.5, 61.5, 55.9, 55.2, 39.4, 38.8, 37.8, 35.6, 31.9, 29.6, 26.1, 14.1, 13.0, 11.6, −3.5, −3.6; ESIMS: 561 (M^++Na).

Acknowledgments

K.Y. and G.C. thank UGC, and M.B. thanks CSIR, New Delhi for the award of fellowships.

References

1. Gerth, K.; Pradella, S.; Perlowa, O.; Beyer, S.; Muller, R. *J. Biotechnol.* **2003**, *106*, 233.
2. (a) Bedorf, N.; Schomburg, D.; Gerth, K.; Reichenbach, H.; Hofle, G. *Annalen* **1993**, 1017; (b) Gerth, K.; Bedorf, N.; Irschik, H.; Hofle, G.; Reichenbach, H. *J. Antibiot.* **1994**, *47*, 23.
3. (a) Jansen, R.; Wray, V.; Irschik, H.; Reichenbach, H.; Hofle, G. *Tetrahedron Lett.* **1985**, *26*, 6031; (b) Irschik, H.; Jansen, R.; Gerth, K.; Hofle, G.; Reichenbach, H. *J. Antibiot.* **1987**, *40*, 7; (c) Jansen, R.; Irschik, H.; Reichenbach, H.; Schomburg, D.; Wray, V.; Hofle, G. *Annalen* **1989**, 111; (d) Jansen, R.; Irschik, H.; Reichenbach, H.; Wray, V.; Hofle, G. *Annalen* **1989**, 213.
4. Jansen, R.; Hofle, G.; Kunze, B.; Reichenbach, H.; Steinmetz, H.; Irschik, H. *Chem. Eur. J.* **2007**, *13*, 5822.
5. (a) Hoefle, G.; Bedorf, N.; Steinmetz, H.; Schomburg, D.; Gerth, K.; Reichenbach, H. *Angew. Chem., Int. Ed.* **1996**, *35*, 1567; (b) Gerth, K.; Bedorf, N.; Hofle, G.; Irschik, H.; Reichenbach, H. *J. Antibiot.* **1996**, *49*, 560; (c) Hofle, G.; Reichenbach, H. In *Anticancer Agents from Natural Products*; Cragg, G. M., Kingston, D. G. I., Newman, D. J., Eds.; CRC Press, Taylor & Francis Group: Boca Raton, FL, 2005; p 413.
6. (a) Hofle, G.; Reichenbach, H.; Irschik, H.; Schummer, D. German Patent DE 196 30 980 A1: 1–7 (5.2. 1998).; (b) Irschik, H.; Schummer, D.; Hofle, G.; Reichenbach, H.; Steinmetz, H.; Jansen, R. *J. Nat. Prod.* **2007**, *70*, 1060.
7. Li, P.; Li, J.; Arikan, F.; Ahlbrecht, W.; Dieckmann, M.; Menche, D. *J. Am. Chem. Soc.* **2009**, *131*, 11678.
8. Yadav, J. S.; Reddy, K. B.; Sabitha, G. *Tetrahedron Lett.* **2004**, *45*, 6475.
9. (a) Yadav, J. S.; Padmavani, B.; Venugopal, Ch. *Tetrahedron Lett.* **2009**, *50*, 3772; (b) Yadav, J. S.; Samad Hossain, S. K.; Mohapatra, D. K. *Tetrahedron Lett.* **2010**, *51*, 4179.
10. Mitsunobu, O. *Synthesis* **1981**, 1–28.
11. Marshall, J. A.; Johns, B. A. *J. Org. Chem.* **1998**, *63*, 7885.