Tetrahedron 65 (2009) 3545–3552

Contents lists available at ScienceDirect

Tetrahedron

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

Total synthesis of (−)-baconipyrone C

J.S. Yadav *, K. Sathaiah, R. Srinivas

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

ARTICLE INFO

Article history:
Received 19 September 2008
Received in revised form 11 December 2008
Accepted 12 December 2008
Available online 24 December 2008

Keywords:
(−)-Baconipyrone C
Desymmetrization
Enzymatic resolution
Sharpless epoxidation
Gilmans' reaction

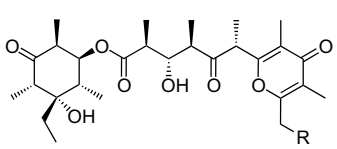
ABSTRACT

A highly stereoselective asymmetric total synthesis of marine polypropionate (−)-baconipyrone C has been achieved. Utilization of desymmetrization technique to create five stereogenic centres, Sharpless epoxidation, Gilman's reaction and resolution of methyl group using enzyme PS-C is the highlight of the synthesis.

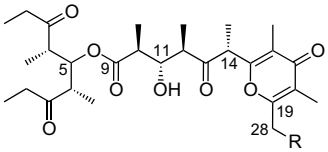
1. Introduction

Natural products derived from marine molluscs gained interest for their variety of bioactive secondary metabolities, unusual structures and concomitant biological activities (antimicrobial activities and cytotoxicities).[1] The original role of these bioactive substances has been considered to be a defensive function from predators, prevention of fouling, inhibition of overgrowth and the protection from ultraviolet radiation.[2]

Baconipyrones A–D (**1**–**4**) were isolated in 1989 by Faulkner et al. from *Siphonaria baconi* collected from intertidal rock platforms near Melbourne, Australia.[3]



Baconipyrone A **1**, R = Me
Baconipyrone, B **2**, R = H



Baconipyrone C **3**, R = Me
Baconipyrone D **4**, R = H

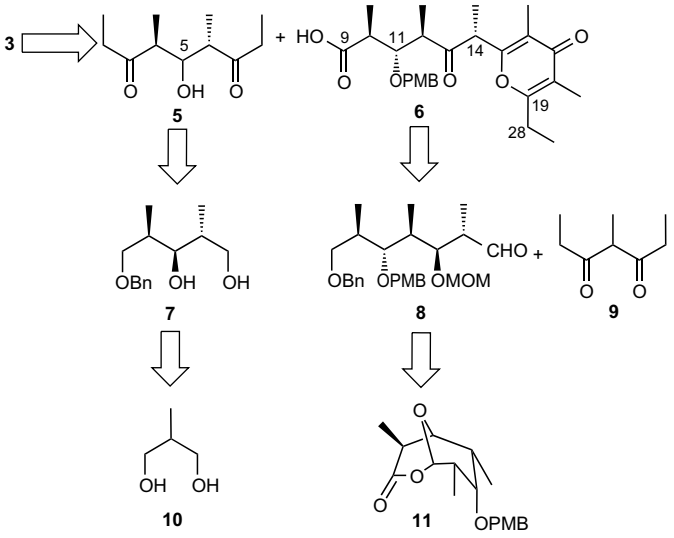
Marine pulmonates of the genus *siphonaria* are the sources of diverse range of polyketides,[4] macrolides[1c] and polyether antibiotics.[5] The baconipyrones all contain a tetrasubstituted γ-pyrone with a polypropionate side chain lacking normal polypropionic skeleton with noncontiguous, ester-type backbone.[6,7] In baconipyrone A and B γ-pyrone moiety is connected through an ester linkage to a highly substituted β-hydroxy cyclohexanone, whereas in baconipyrone C and D, through an acyclic β-hydroxy 1,5-diketone. The first total synthesis of (−)-baconipyrone C was reported by Paterson et al. in 2000.[8] The full absolute stereochemistry of baconipyrone C and D and structural revision of baconipyrone A and B were reported by Vogel et al. via C–C bond forming reaction based on the sulfurdioxide induced condensation of 1,3-dioxy-1,3-dienes to enoxysilanes, by synthesizing (−)-(4*S*,6*S*)-4,6-dimethyl-5-hydroxynonan-3,7-dione and (+)-(2*S*,3*S*,4*S*,5*S*,6*S*)-3-ethyl-3,5-dihydroxy-2,4,6-trimethyl cyclohexanone derivatives.[9] A baconipyrone type ester has been reported from siphonarins on chromatographic purification lending support to the baconipyrone may be isolation artifacts.[1b]

2. Results and discussion

As part of our studies in the synthesis of marine polypropionates,[10] we now report on the second total synthesis of (−)-baconipyrone C. Our retrosynthetic analysis envisions that **3** could be obtained from coupling of alcohol **5** and γ-pyrone carboxylic acid **6** via Yonemitsu–Yamaguchi esterification (Scheme 1). Enzymatic resolution, functional group transformations and Gilman's opening of chiral epoxide obtained from 2-methyl 1,3-propane diol result in the C_2-symmetric alcohol **5** and **6** in turn obtained from lactone **11** where we employed desymmetrization technique to create five consecutive stereogenic centres and

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

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.12.049



Scheme 1. Retrosynthetic analysis of (−)-baconipyrone C.

explore the synthesis of rifamycin S,[11] discodermolide,[12] scytophycin C,[13] membrenone C,[10a] prelactone B[14] and bafilomycin A1.[15]

2.1. Synthesis of the C1–C8 fragment (5)

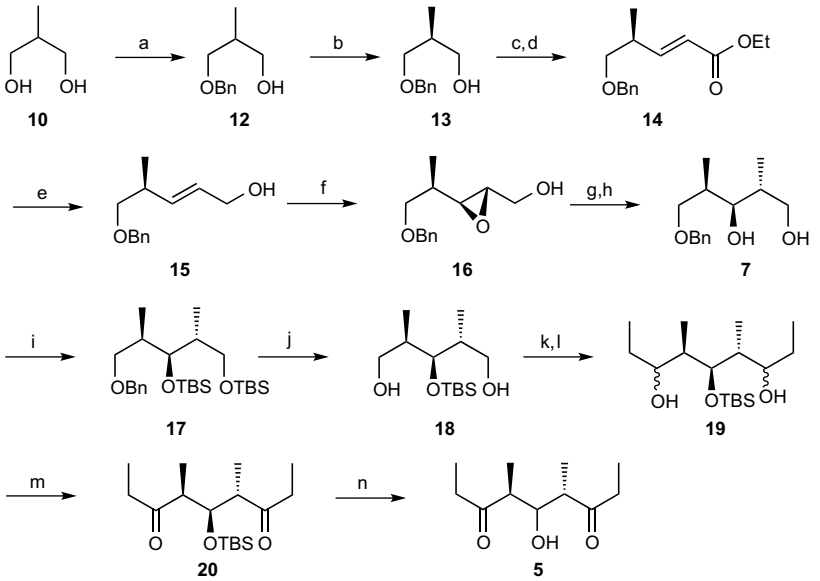
The synthesis of intermediate **5** commenced with compound **10**, which we protected as its monobenzyl ether using NaH and BnBr in THF to furnish **12** in 78% yield (Scheme 2). Enzymatic resolution of methyl group **12** with PS-C enzyme resulted in compound **13** in 35% yield.[16,17] Swern oxidation of primary alcohol and reaction with stable ylide (ethoxycarbonylmethylene) triphenyl phosphorane furnished trans-α,β-unsaturated ester **14** in 90% (*E*/*Z*, 95:5) yield. The DIBAL-H reduction of **14** in CH_2Cl_2 furnished **15** in high yield. Sharpless[18] asymmetric epoxidation of **15** using (+)-DIPT, Ti(O^iPr)$_4$ and TBHP in CH_2Cl_2 gave the chiral epoxy alcohol **16** in 89% yield. Opening of epoxide **16** with Gilman's[19] reagent (Me_2CuLi) followed by the $NaIO_4$ chopping in THF/H_2O (4:1) gave the pure diol **7** in 65% yield (from **16**).

The protection of diol **7** as its di-*tert*-butyl dimethylsilyl ether was achieved by using *tert*-butyl dimethylsilyl [trifluoromethanesulfonate] and 2,6-lutidine in CH_2Cl_2, which results in the di TBS ether **17** in high yield. Hydrogenolysis of benzyl and primary TBS ethers **17** using Pd/C in methanol gave 1,5-diol **18** in 76% yield. Swern oxidation of compound **18**, followed by the immediate addition of EtMgBr at 0 °C in dry THF furnished a diastereomeric mixture **19** in 60% yield. The dialdehyde was not purified, the diastereomers were not separated and were used as crude in subsequent steps. Swern oxidation of **19**, followed by TBS ether deprotection of **20** with HF/pyridine in THF gave compound **5** in 84% yield.

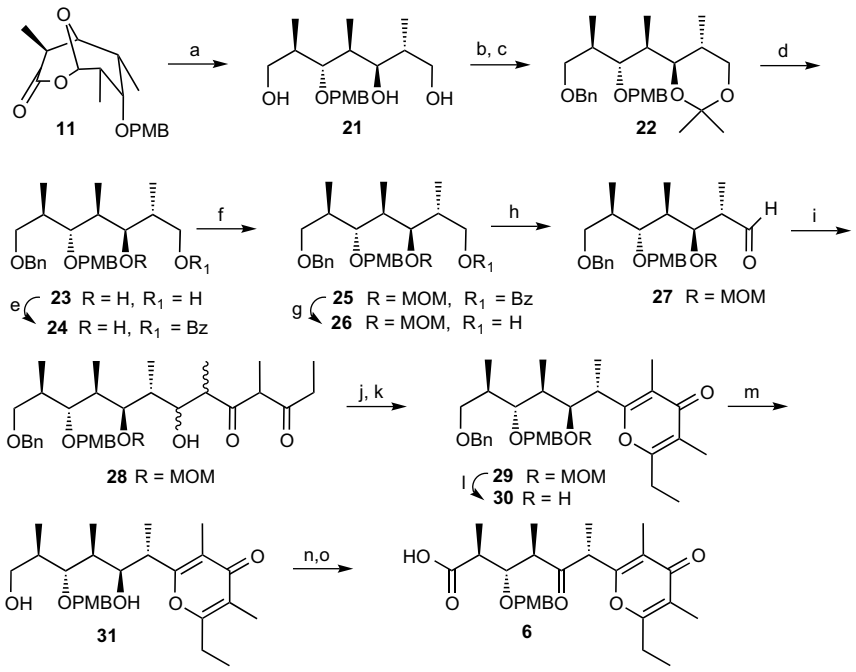
2.2. Synthesis of the C9–C19 fragment (6)

The synthesis of fragment **6** started with lactone **11**[10] by a desymmetrization technique where we used to create five stereogenic centres at once. Reductive opening of methylated lactone **11** with $LiAlH_4$ in dry THF furnished triol **21** in 90% yield (Scheme 3). The 1,3-diol group of **21** was protected as an acetonide employing 2,2-dimethoxy propane and CSA in CH_2Cl_2/Et_2O (9:1) and the free primary hydroxy group was protected as its benzyl ether using NaH and BnBr to furnish **22**. Benzyl ether **22** was treated with aq 2 N HCl to furnish **23** and selective protection of the primary hydroxy group as its benzoyl ester **24** was achieved in 90% yield under standard conditions (C_6H_5COCl/Et_3N/DMAP). The secondary hydroxyl group **24** was protected as its MOM-ether **25** using MOMCl, DIPEA and DMAP in CH_2Cl_2 and the subsequent removal of benzoyl group furnished **26** in 90% yield after treating with aq 3 N KOH in THF/MeOH (1:1:1). Oxidation of primary alcohol **26** with IBX-DMSO gave the corresponding aldehyde **27** in 90% yield.

Aldehyde **27** was added to the lithium enolate of **9**[20] generated by the addition of LDA at −78 °C, resulted compound **28**, which was subjected to Dess–Martin periodinane[21] oxidation followed by Ph_3P/CCl_4 cyclization[22] in THF to give the desired γ-pyrone **29** in 45% yield over three steps. γ-Pyrone **29** formed via cyclization/elimination process was confirmed by the presence of two singlets for two vinylic methyl groups at δ 1.94 and δ 1.90, a triplet for one methyl group at δ 1.07 and a quartet for two allylic protons at δ 2.49 corresponding to γ-pyrone moiety.



Scheme 2. Reagents and conditions: (a) NaH, BnBr, TBAI, THF, 0 °C to rt, 12 h, 78%; (b) PS-C, OAC, $^iPr_2O$, 30 °C, 7 h, 35%; (c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C to 0 °C, 2 h; (d) Ph_3PCHCO_2Et, CH_2Cl_2, rt, 12 h, 90%; (e) DIBAL-H, CH_2Cl_2, 0 °C, 2 h, 90%; (f) (+) DIPT, Ti(O^iPr)$_4$, TBHP, CH_2Cl_2, −30 °C, 89%, 8 h; (g) Me_2CuLi, Et_2O, −30 °C, 6 h; (h) $NaIO_4$, THF/H_2O (4:1), rt, 2 h, 65%; (i) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C to rt, 2 h, 86%; (j) Pd/C, H_2, MeOH, 12 h, 76%; (k) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C to −30 °C, 3 h; (l) EtMgBr, 0 °C to rt, 1 h; (m) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C to −30 °C, 3 h, 79%; (n) HF/pyridine, THF, 0 °C, 2 h, 84%.

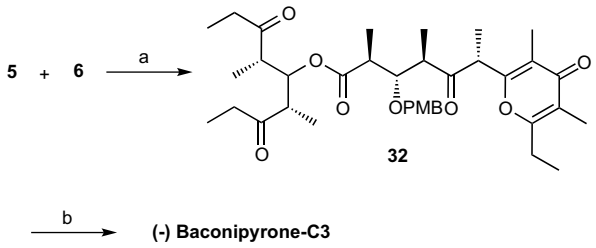


Scheme 3. Reagents and conditions: (a) $LiAlH_4$, THF, 0 °C to rt, 4 h, 90%; (b) 2,2-DMP, CSA, CH_2Cl_2: Et_2O (9:1), 0 °C to rt, 1 h, 92%; (c) NaH, BnBr, THF, reflux, 5 h, 95%; (d) aq 2 N HCl, THF, 25 °C, 5 h, 89%; (e) C_6H_5COCl, Et_3N, DMAP, CH_2Cl_2, 0 °C to rt, 5 h, 94%; (f) MOMCl, DIPEA, DMAP, CH_2Cl_2, 0 °C to rt, 20 h, 80%; (g) aq 3 N KOH, MeOH, THF (1:1), rt, 5 h, 90%; (h) IBX/DMSO, CH_2Cl_2, rt, 1 h, 90%; (i) **9**, LDA, THF, −78 °C, 2 h; (j) Dess–Martin periodinane, CH_2Cl_2, 0 °C to rt, 1 h; (k) TPP/CCl_4, THF, 36 h, 45%; (l) TMSBr, CH_2Cl_2, −10 °C, 14 h, 76%; (m) Raney-Ni, H_2, rt, 5 h, 90%; (n) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C to −30 °C, 3 h; (o) $NaClO_2$, $NaH_2PO_4{\cdot}2H_2O$, DMSO, H_2O, 2 h, 80%.

2.3. Coupling of fragments 5 and 6 to obtain 3

After successful synthesis of γ-pyrone moiety, now we focused on the deprotection of MOM-ether **29** in the presence of PMB ether. It was achieved by using TMSBr[23] in CH_2Cl_2 at −10 °C conditions to furnish **30** and its benzyl ether was deprotected with Raney-Ni in ethanol, which resulted in compound **31**.[24] Swern oxidation of **31** followed by further oxidation of aldehyde with $NaClO_2$, $NaH_2PO_4{\cdot}2H_2O$ in DMSO resulted in compound **6** in 80% yield over two steps.

The esterification carried out between fragments **5** and **6** resulted in compound **32** in 35% yield by modified Yonemitsu–Yamaguchi protocol as previously reported by Paterson et al.[8] (Scheme 4). Finally oxidative removal of the PMB ether with DDQ in buffered CH_2Cl_2 gave (−)-baconipyrone C **3** as a colourless oil. The spectroscopic (^1H NMR, ^{13}C NMR, IR, mass) and physical data of (−)-baconipyrone C **3** were in good agreement with the reported data.[8]



Scheme 4. Reagents and conditions: (a) 2,4,6-trichlorobenzoyl chloride, Et_3N, DMAP, toluene, −78 °C to −20 °C, 1 h, 35%; (b) DDQ, CH_2Cl_2/pH 7 buffer (9:1), 1 h, 70%.

3. Conclusion

In conclusion, the total synthesis of (−)-baconipyrone C has been achieved in stereocontrolled manner by the creation of five consecutive stereogenic centres via desymmetrization and the synthesis of (2*S*)-3-(benzyloxy)-2-methylpropan-1-ol by using PS-C from readily available starting materials.

4. Experimental

4.1. General

Commercial reagents were used without further purification. All solvents were purified by standard techniques. All reactions were monitored by TLC (silica-coated plates and visualizing under UV light). Ethylacetate and hexane were used as eluent. Air sensitive reagents were transferred by syringe or double-ended needle. Evaporation of solvents was performed at reduced pressure on a Buchi rotary evaporator. Infrared (IR) spectra were recorded on a Perkin–Elmer 683 spectrometer. Optical rotations were obtained on a Jasco Dip 360 digital polarimeter at 25 °C. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on varian Gemini 200, Bruker 300, varian unity 400 and 500 NMR spectrometers. Chemical shifts (δ) are quoted in parts per million and referenced to tetramethylsilane (TMS) as internal standard. Coupling constants (J) are quoted in hertz. Mass spectra were recorded in E1 conditions at 70 eV on an LC-MSD (Agilent technologies) spectrometers. All high resolution spectra were recorded on QSTAR XL hybrid MS/MS system equipped with an ESI source (IICT, Hyderabad). Column chromatographic separations were performed on silica gel (60–120 and 100–200 mesh) supplied by Acme Chemical Co., India.

*4.1.1. Ethyl (E,4S)-5-(benzyloxy)-4-methyl-2-pentenoate (**14**)*

To a stirred solution of oxalyl chloride (10.58 g, 83.33 mmol) in dry CH_2Cl_2 (120 mL) at −78 °C, dry DMSO (7.81 g, 99.99 mmol) was added drop wise. After 30 min, alcohol **13** (10.00 g, 55.55 mmol) in CH_2Cl_2 (30 mL) was added over 10 min. After stirring for 2 h at −78 °C, Et_3N (46.46 mL, 333.33 mmol) was added and stirred for 30 min, at −78 °C, warmed to −30 °C over 1 h and then to 0 °C for 15 min. To this reaction mixture (ethoxycarbonylmethylene)

triphenyl phosphorane (29.00 g, 83.33 mmol) in 100 mL CH_2Cl_2 was added and stirred for 12 h at room temperature and then quenched by the addition of water and extracted with CH_2Cl_2 (3×100 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated. The crude was purified by silica gel column chromatography (1:9 EtOAc/hexane) to give yellow oil **14** in 85% (11.71 g) yield. R_f (1:9 EtOAc/hexane) 0.62; $[\alpha]_D^{25}$ −6.4 (*c* 1.88, $CHCl_3$); IR (KBr): 3030, 2974, 1718, 1653, 1184, 1096, 741, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.27 (5H, m, Ar–H), 6.90 (1H, dd, *J*=15.6, 7.4 Hz, olefin), 5.8 (1H, dd, *J*=15.6, 1.5 Hz, olefin), 4.49 (2H, s, benzylic CH_2), 4.17 (2H, q, *J*=7.4 Hz, OCH_2CH_3), 3.45–3.28 (2H, m, CH_2OBn), 2.73–2.52 (1H, m, $CHCH_3$), 1.30 (3H, t, *J*=7.4 Hz, OCH_2CH_3), 1.10 (3H, d, *J*=6.7 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.4, 150.9, 128.4, 128.2, 127.5, 127.4, 120.8, 73.7, 73.0, 59.9, 36.6, 15.8, 14.1; ESI-MS: *m*/*z* 249 $[MH]^+$. HRMS (ESI): $[MNa]^+$, found 271.1297. $C_{15}H_{20}O_3Na$ requires 271.1310.

4.1.2. (E,4S)-5-(Benzyloxy)-4-methyl-2-penten-1-ol (**15**)

To a cooled (0 °C) solution of **14** (11.00 g, 44.35 mmol) in dry CH_2Cl_2 (120 mL), DIBAL-H (63.36 mL, 88.66 mmol, 20% solution in toluene) was added slowly for 15 min and stirred for 2 h at 0 °C, before being quenched with methanol (3 mL) and sodium potassium tartarate solution (100 mL). The reaction mixture was passed through a short pad of Celite. The filtrate was concentrated and purified the residue by column chromatography (1:4, EtOAc/hexane) to furnish allylic alcohol **15** (8.72 g, 95%) as a colourless liquid. R_f (1:4, EtOAc/hexane) 0.48; $[\alpha]_D^{25}$ −4.85 (*c* 2.13, $CHCl_3$); IR (Neat): 3444, 2925, 2856, 1637, 1094, 756, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.30 (5H, m, Ar–H), 6.69 (2H, m, olefin), 4.56 (2H, s, benzylic CH_2), 4.38–4.27 (2H, m, CH_2OBn), 4.08 (2H, d, *J*=3.8 Hz, CH=$CHCH_2$), 2.52 (1H, m, $CHCH_3$), 1.6 (1H, br s, OH), 1.08 (3H, d, *J*=6.8 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.1, 134.3, 128.8, 128.0, 127.3, 127.2, 74.8, 72.6, 63.0, 36.2, 16.7; ESI-MS: *m*/*z* 229 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 229.1198. $C_{13}H_{18}O_2Na$ requires 229.1204.

4.1.3. (2S,3S)-3-[(1R)-2-(Benzyloxy)-1-methylethyl]oxiran-2-ylmethanol (**16**)

To a solution of (+) DIPT (1.93 g, 8.25 mmol) in dry CH_2Cl_2 (100 mL) at −30 °C containing 4 Å MS (3.50 g), sequentially $Ti(O^iPr)_4$ (2.11 g, 7.43 mmol) and TBHP (8.18 g, 90.78 mmol) were added and stirred for 30 min. A solution of alcohol **15** (8.50 g, 41.26 mmol) in CH_2Cl_2 (30 mL) was added and stirred for 10 h at −30 °C. It was then quenched with 45 mL of water and 30% aqueous NaOH solution, saturated with NaCl (20 mL) and the resulting mixture stirred vigorously for another 30 min at room temperature. The resulting mixture was vacuum filtered through Celite 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 (3×100 mL). Combined organic phases were washed with brine and dried over Na_2SO_4. Removal of solvent under reduced pressure and purification by column chromatography (3:7, EtOAc/hexane) afforded **16** (8.20 g, 89%) as a viscous liquid. R_f (3:7, EtOAc/hexane) 0.42; $[\alpha]_D^{25}$ −26.12 (*c* 1.25, $CHCl_3$);[1] IR (Neat): 3442, 1638, 1455, 1365, 1092, 741, 699 cm^{-1}; H NMR (200 MHz, $CDCl_3$): δ 7.29 (5H, m, Ar–H), 4.50 (2H, s, benzylic CH_2), 3.84 (1H, m, CHOH), 3.57 (1H, dd, *J*=12.4, 3.8 Hz, CHOH), 3.44 (1H, dd, *J*=5.2, 1.5 Hz, epoxide), 3.39 (1H, dd, *J*=7.8, 3.7 Hz, epoxide), 2.93 (2H, m, CH_2OBn), 1.84–1.61(1H, m, $CHCH_3$), 1.60 (1H, br s, OH), 1.0 (3H, d, *J*=6.8 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.2, 128.3, 127.5, 127.4, 73.0, 72.6, 61.8, 58.6, 58.0, 35.8, 13.4; ESI-MS: *m*/*z* 245 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 245.1148. $C_{13}H_{18}O_3Na$ requires 245.1153.

4.1.4. (2R,3R,4R)-5-(Benzyloxy)-2,4-dimethylpentane-1,3-diol (**7**)

To a cold (0 °C) suspension of copper(I) iodide (27.45 g, 144.12 mmol) in dry ether (100 mL), MeLi (144.14 mL, 288.24 mmol, 2.0 M) in ether was added drop wise until it become a clear solution. After 30 min at this temperature, the solution was cooled to −30 °C and epoxy alcohol **16** (8.00 g, 36.03 mmol) in ether 40 mL was added drop wise. After being stirred for 2 h at −30 °C, and then 4 h at −20 °C, the mixture was poured into saturated aqueous NH_4Cl and the blue aqueous layer was thoroughly extracted with CH_2Cl_2 (3×100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The contamination of the 1,2-diol was eliminated by exposing the crude reaction mixture to $NaIO_4$ followed by silica gel column chromatography (2:3, EtOAc/hexane) to give pure 1,3-diol **7** (5.57 g, 65%). R_f (2:3, EtOAc/hexane) 0.38; $[\alpha]_D^{25}$ −4.2 (*c* 1.22, $CHCl_3$); IR (Neat): 3431, 3030, 2966, 2875, 1638, 1456, 1095, 1027, 739, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.36–7.24 (5H, m, Ar-H), 4.50 (2H, s, benzylic CH_2), 3.72 (1H, dd, *J*=9.4, 1.7 Hz, CHOH), 3.65–3.49 (4H, m, CH_2OBn, CH_2OH), 3.36 (2H, br s, OH), 1.92–1.75 (2H, m, 2×$CHCH_3$), 1.01 (3H, d, *J*=6.8 Hz, $CHCH_3$), 0.75 (3H, d, *J*=6.8 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.8, 128.4, 127.7, 127.5, 79.9, 75.6, 73.5, 68.9, 37.3, 35.2, 13.4, 9.4; ESI-MS: *m*/*z* 239 $[MH]^+$. HRMS (ESI): $[MNa]^+$, found 261.1465. $C_{14}H_{22}O_3Na$ requires 261.1466.

4.1.5. [((2R,3S,4R)-5-(Benzyloxy)-3-[1-(tert-butyl)-1,1-dimethylsilyl]oxy-2,4-dimethylpentyl)oxy](tert-butyl)dimethylsilane (**17**)

2,6-Lutidine (14.66 mL, 126.06 mmol) was added drop wise to a cooled solution (0 °C) of alcohol **7** (5.00 g, 21.01 mmol) in dry CH_2Cl_2 (30 mL). After 10 min, *tert*-butyldimethylsilyltrifluoromethane sulfonate (TBSOTf, 14.47 mL, 63.03 mmol) was added drop wise and stirring was continued for 2 h at 0 °C. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with 5% aq H_2SO_4, $NaHCO_3$, water and brine. The organic layer was dried and concentrated in vacuo. The residue was purified by column chromatography (1:19, EtOAc/hexane) to give di TBS ether **17** as a colourless oil (8.41 g, 86%). R_f (1:19, EtOAc/hexane) 0.58; $[\alpha]_D^{25}$ +7.93 (*c* 0.91, $CHCl_3$); IR (Neat): 2956, 2837, 1466, 1253, 1177, 1092, 836 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.28 (5H, m, Ar–H), 4.45 (2H, ABq, *J*=12.0 Hz, benzylic CH_2), 3.76 (1H, dd, *J*=7.17, 1.8 Hz, CHOTBS), 3.63 (1H, dd, *J*=9.8, 4.9 Hz, 1H, CH_2OBn), 3.40–3.30 (2H, m, CH_2OTBS), 3.20 (1H, dd, *J*=8.7, 6.8 Hz, CH_2OBn), 2.01–1.89 (1H, m, $CHCH_3$), 1.81–1.69 (1H, m, $CHCH_3$), 0.94–0.84 (24H, m, 2×$(CH_3)_3$, 2×$CHCH_3$), 0.04 (6H, s, $(CH_3)_2Si$), 0.02 (6H, s, $(CH_3)_2Si$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.8, 128.3, 127.5, 127.4, 74.0, 73.3, 72.7, 65.5, 40.6, 36.0, 26.1, 26.0, 18.4, 18.3, 14.1, 11.2, –4.0, –4.2, −5.3, −5.4; ESI-MS: *m*/*z* 467 $[MH]^+$. HRMS (ESI): $[MH]^+$, found 467.3371. $C_{26}H_{51}O_3Si_2$ requires 467.3376.

4.1.6. (2R,4R)-3-[1-(tert-Butyl)-1,1-dimethylsilyl]oxy-2,4-dimethylpentane-1,5-diol (**18**)

To a solution of di TBS ether **17** (8.00 g, 17.16 mmol) in methanol (30 mL) was added 10% Pd/C (1.70 g) and the reaction mixture was stirred under hydrogen atmosphere for 12 h at room temperature. After completion of the reaction, mixture was filtered through Celite pad to remove the catalyst. Concentrated in vacuo and purified by column chromatography (2:3, EtOAc/hexane) to give 1,5-diol **18** as a viscous liquid (3.41 g, 76%). R_f (2:3, EtOAc/hexane) 0.35; $[\alpha]_D^{25}$ −1.2 (*c* 0.91, $CHCl_3$); IR (Neat): 3457, 2956, 1466, 1177, 1092 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.82 (1H, dd, *J*=5.3, 3.0 Hz, CHOTBS), 3.62–3.50 (5H, m, 2×CH_2OH, OH), 2.03 (1H, br s, OH), 2.01–1.89 (1H, m, $CHCH_3$), 1.88–1.82 (1H, m, $CHCH_3$), 0.99 (3H, d, *J*=7.2 Hz, $CHCH_3$), 0.92 (9H, s, $(CH_3)_3$), 0.90 (3H, d, *J*=7.5 Hz, $CHCH_3$), 0.12 (3H, s, CH_3Si), 0.10 (3H, s, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): δ 76.2, 65.7, 65.5, 39.5, 39.0, 26.0, 18.3, 15.0, 12.1, −4.3, −4.4; ESI-MS: *m*/*z* 263 $[MH]^+$. HRMS (ESI): $[MNa]^+$, found 285.1850. $C_{13}H_{30}O_3Si$ Na requires 285.1861.

*4.1.7. (4R,6R)-5-[1-(tert-Butyl)-1,1-dimethylsilyl]oxy-4,6-dimethylnonane-3,7-diol (**19**)*

To a solution of oxalyl chloride (5.81 g, 45.80 mmol) in dry CH_2Cl_2 (30 mL) at −78 °C, dry DMSO (7.15 g, 91.60 mmol) was added drop wise. After 30 min, alcohol **18** (3.0 g, 11.45 mmol) in CH_2Cl_2 (10 mL) was added over 10 min. After stirring for 2 h at −78 °C, Et_3N (13.90 g, 137.40 mmol) was added slowly and stirred for 30 min, and then warmed to −30 °C and stirred further for 30 min. Hexane/toluene (3:1, 400 mL) was added to the reaction mixture at −30 °C, the resulting suspension was filtered through Celite and concentrated in vacuo to give the dialdehyde.

Freshly prepared EtMgBr (prepared in situ from 1.37 g (57.25 mmol) of Mg and 6.24 g (57.25 mmol) of ethyl bromide in 20 mL of dry THF) was added drop wise to a stirred solution of the above dialdehyde in dry THF (10 mL) at 0 °C. After addition was complete, the reaction mixture was stirred for 1 h before being quenched with saturated aqueous NH_4Cl, extracted with EtOAc (3×50 mL), washed with brine and concentrated in vacuo. Column chromatography using (1:5, EtOAc/hexane) afforded **19** (2.18 g, 60%) as mixture of diastereomers. R_f (1:5, EtOAc/hexane) 0.45; IR (Neat): 3437, 2928, 2855, 1712 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.89–3.82 (1H, m, J=8.7, 6.2 Hz, CHOTBS), 3.7 (1H, dd, J=6.8, 2.6 Hz, CHOH), 3.55–3.48 (1H, dd, J=5.9, 3.0 Hz, CHOH), 3.08 (1H, br s, OH), 1.88–1.81 (1H, m, $CHCH_3$), 1.77–1.70 (1H, m, $CHCH_3$), 1.55–1.45 (2H, m, CH_2CH_3), 1.33 (2H, m, CH_2CH_3), 0.99 (3H, d, J=7.5 Hz, $CHCH_3$), 0.93 (6H, m, 2×CH_2CH_3), 0.92 (9H, s, $(CH_3)_3$), 0.91 (3H, d, J=7.5 Hz, $CHCH_3$), 0.14 (3H, s, CH_3Si), 0.11 (3H, s, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): δ 80.9, 74.0, 72.5, 40.9, 37.8, 29.7, 28.6, 27.6, 26.2, 11.7, 10.6, 9.7, −3.3, −3.9; ESI-MS: m/z 341 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 341.2488. $C_{17}H_{38}O_3$ SiNa requires 341.2487.

*4.1.8. (4S,6S)-5-[1-(tert-Butyl)-1,1-dimethylsilyl]oxy-4,6-dimethylnonane-3,7-dione (**20**)*

To a stirred solution of oxalyl chloride (4.00 g, 31.45 mmol) in dry CH_2Cl_2 (20 mL) at −78 °C was added dry DMSO (4.92 g, 63.00 mmol) drop wise. After 30 min, alcohol **19** (2.00 g, 6.30 mmol) in CH_2Cl_2 (10 mL) was added over 10 min. After stirring for 2 h at −78 °C, Et_3N (9.54 g, 94.35 mmol) was added slowly and stirred for 30 min, and then warmed to −30 °C and stirred further for 30 min. Hexane/toluene (3:1, 300 mL) was added to the reaction mixture at −30 °C, the resulting suspension was filtered through Celite, concentrated in vacuo and purification by column chromatography (1:19, EtOAc/hexane) afforded diketo compound **20** (1.57 g, 79%) as a colourless oil. R_f (1:19, EtOAc/hexane) 0.50; $[\alpha]_D^{25}$ +35.93 (c 2.51, $CHCl_3$); IR (Neat): 2928, 2855, 1712 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.37 (1H, dd, J=14.4, 6.2 Hz, CHOTBS), 2.74–2.61 (2H, m, $CHCH_3$), 2.56–2.35 (4H, m, CH_2CH_3), 1.05 (3H, d, J=7.0 Hz, CH_3CH), 1.03 (3H, t, J=7.0 Hz, 3H, CH_2CH_3), 1.01 (3H, t, J=7.0 Hz, CH_2CH_3), 0.94 (3H, d, J=7.0 Hz, CH_3CH), 0.86 (9H, s, $(CH_3)_3$), 0.04 (6H, s, $(CH_3)_2Si$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.2, 212.9, 74.7, 73.4, 51.3, 50.6, 36.1, 35.9, 18.0, 12.0, 11.4, 7.4, 7.3, −4.6, −4.9; ESI-MS: m/z 315 $[MH]^+$. HRMS (ESI): $[MNa]^+$, found 337.2170. $C_{17}H_{34}O_3SiNa$ requires 337.2174.

*4.1.9. (4S,6S)-5-Hydroxy-4,6-dimethylnonane-3,7-dione (**5**)*

To the above diketone **20** (0.50 g, 1.60 mmol) in THF (5 mL) was added pyridinium hydrogen fluoride (2 mL) at 0 °C and the reaction mixture was stirred at 0 °C for 2 h before being quenched with saturated aqueous $NaHCO_3$ until no further effervescence and neutral pH was obtained. The reaction mixture was extracted with EtOAc (3×30 mL), washed with saturated $CuSO_4$, brine, dried (Na_2SO_4) and concentrated in vacuo, and purification by column chromatography (3:7, EtOAc/hexane) afforded the pure alcohol **5** (0.26 g, 84%) as a colourless oil. R_f (3:7, EtOAc/hexane) 0.22; $[\alpha]_D^{25}$ −15.60 (c 2.0, $CHCl_3$) (lit.[8] $[\alpha]_D^{20}$ −16.4 (c 1.1, $CHCl_3$)); IR (Neat): 3495, 2927, 2854, 1711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.94 (1H, ddd, J=11.7, 7.8, 3.9 Hz, CHOH), 3.20 (1H, d, J=4.9 Hz, OH), 2.70–2.57 (2H, m, 2×$CHCH_3$,), 2.56–2.35 (4H, m, 2×CH_2CH_3), 1.14 (3H, d, J=7.2 Hz, $CHCH_3$), 1.05 (3H, t, J=7.2 Hz, CH_2CH_3), 1.04 (3H, d, J=7.2 Hz, $CHCH_3$), 1.03 (3H, t, J=7.2 Hz, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 215.6, 215.5, 73.4, 47.6, 47.3, 36.2, 34.7, 13.8, 10.0, 7.5, 7.30; ESI-MS: m/z 223 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 223.1308. $C_{11}H_{20}O_3Na$ requires 223.1310.

*4.1.10. (2R,3R,4S,5R,6R)-5-[(4-Methoxybenzyl)oxy]-2,4,6-trimethyl heptane-1,3,7-triol (**21**)*

To a stirred suspension of $LiAlH_4$ (4.66 g, 124.60 mmol) in dry THF (150 mL) at 0 °C was added drop wise a solution of methyl lactone **11** (16.00 g, 49.84 mmol) in dry THF (30 mL). The reaction mixture was allowed to warm to 25 °C and stirred for 4 h. Reaction mixture was then cooled to 0 °C and quenched with drop wise addition of saturated aqueous NH_4Cl. The precipitate formed was filtered and washed with ethylacetate. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure, and the crude was purified by silica gel column chromatography (3:2, EtOAc/hexane) to afford the pure product **21** (14.66 g, 90%) as a viscous liquid. R_f (3:2, EtOAc/hexane) 0.34; $[\alpha]_D^{25}$ +1.8 (c 2.51, $CHCl_3$); IR (Neat): 3445, 1032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.22 (2H, d, J=8.7 Hz, Ar–H), 6.84 (2H, d, J=8.5 Hz, Ar–H), 4.60 (2H, ABq, J=10.4 Hz, benzylic CH_2), 3.77 (4H, m, Ar–OCH_3,), 3.75 (1H, dd, J=10.5, 3.8 Hz, CHOPMB), 3.65 (1H, dd, J=10.7, 4.2 Hz, CHOH), 3.58 (2H, m, CHOH, CHOH), 3.50 (1H, dd, J=9.2, 2.5 Hz, CHOH), 2.01 (1H, m, $CHCH_3$), 1.90–1.78 (2H, m, 2H, $CHCH_3$), 1.42 (3H, br s, OH), 1.14 (3H, d, J=6.7 Hz, $CHCH_3$), 0.94 (3H, d, J=6.7 Hz, $CHCH_3$), 0.72 (3H, d, J=6.7 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.8, 129.7, 129.4, 114.2, 88.0, 76.4, 76.0, 68.6, 65.0, 55.1, 37.8, 37.0, 35.4, 14.6, 13.1, 11.4; ESI-MS: m/z 349 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 349.2006. $C_{18}H_{30}O_5Na$ requires 349.1990.

4.1.11. 3-(4-Methoxybenzyloxy)-2-methyl-4-[2,2,5-trimethyl-(4S,5S)-1,3-dioxan-4-yl]-(2R,3R,4R)-pentan-1-ol

2,2-Dimethoxypropane (22.40 mL, 184 mmol) and CSA (1.68 g, 36.80 mmol) were added successively to a solution of triol **21** (12.00 g, 36.80 mmol) in 120 mL mixture of CH_2Cl_2/Et_2O (9:1). The solution was stirred for 1 h at room temperature and then quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with ether (4×100 mL). The organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The crude compound was purified on column chromatography (2:3, EtOAc/hexane) to afford the monoacetonide (12.36 g, 92%) as a white crystalline solid. R_f (2:3, EtOAc/hexane) 0.65; mp: 92–93 °C; $[\alpha]_D^{25}$ −39.5 (c 3.41, $CHCl_3$); IR (Neat): 3475 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$): δ 7.19 (2H, d, J=8.8 Hz, Ar–H), 6.83 (2H, d, J=8.5 Hz, Ar–H), 4.55 (2H, ABq, J=10.4 Hz, benzylic CH_2), 3.91–3.80 (2H, m, 2H, CH_2OH), 3.79 (3H, s, Ar–OCH_3), 3.67 (1H, dd, J=11.7, 5.8 Hz, $OCHCHCH_3$), 3.56–3.41 (3H, m, CH_3CH_2O and CH), 2.77–2.59 (1H, br s, OH), 2.01–1.79 (3H, m, 3×$CHCH_3$), 1.39 (3H, s, CH_3), 1.35 (3H, s, CH_3), 1.20 (3H, d, J=7.2 Hz, $CHCH_3$), 0.86 (3H, d, J=7.2 Hz, $CHCH_3$), 0.73 (3H, d, J=7.2 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.0, 130.5, 128.5, 113,7, 97.8, 85.1, 75.0, 73.2, 66.0, 64.0, 55.2, 37.3, 36.0, 30.2, 29.7, 19.5, 16.3, 12.4, 9.8; ESI-MS: m/z 389 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 389.2309. $C_{21}H_{34}O_5Na$ requires 389.2303.

*4.1.12. (4R,5R)-4-{(1R,2R,3R)-4-(Benzyloxy)-2-[(4-methoxybenzyl)oxy]-1,3-dimethylbutyl}-2,2,5-trimethyl-1,3-dioxane (**22**)*

To a stirred suspension of NaH (2.04 g, 42.60 mmol) in dry THF (120 mL) under nitrogen atmosphere was added monoacetonide (10.40 g, 28.40 mmol) in dry THF (40 mL) drop wise at 0 °C. The reaction mixture was allowed to warm to 25 °C and then heated under reflux for 1 h. It was then cooled to 25 °C and benzyl bromide (3.72 mL, 31.24 mmol) was added drop wise. Refluxed for 3 h and cooled to 0 °C, and then quenched with ice and extracted with

ether (3×100 mL). The combined extracts were washed with brine, dried over Na_2SO_4 and purified by column chromatography (1:5, EtOAc/hexane) to afford **22** (12.28 g, 95%) as a colourless oil. R_f (1:5, EtOAc/hexane) 0.55; $[\alpha]_D^{25}$ −27.1 (*c* 5.64, $CHCl_3$); IR(Neat): 1083, 1036 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$): δ 7.30–7.21 (5H, m, Ar–H), 7.16 (2H, d, *J*=8.3 Hz, Ar–H), 6.80 (2H, d, *J*=8.3 Hz, Ar–H), 4.51 (2H, ABq, *J*=11.3 Hz, benzylic CH_2), 4.45 (2H, s, benzylic CH_2), 3.83 (1H, d, *J*=10.5 Hz, CHOH), 3.79 (3H, s, OCH_3), 3.65 (1H, d, *J*=5.2 Hz, CHOBn), 3.61 (1H, d, *J*=4.5 Hz, CHOBn), 3.44 (1H, t, *J*=11.3 Hz, CHOPMB), 3.37–3.28 (2H, m, CH_2O), 2.14 (1H, m, $CHCH_3$), 1.96–1.75 (2H, m, $CHCH_3$), 1.36 (3H, s, CH_3), 1.34 (3H, s, CH_3), 1.11 (3H, d, *J*=6.7 Hz, $CHCH_3$), 0.86 (3H, d, *J*=6.7 Hz, $CHCH_3$), 0.66 (3H, d, *J*=6.5 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.8, 138.8, 129.4, 128.4, 128.2, 127.3, 127.3, 113.6, 97.9, 82.8, 74.4, 73.4, 73.0, 72.0, 66.3, 55.2, 36.9, 36.0, 30.3, 29.8, 19.5, 16.7, 12.4, 9.8; ESI-MS: *m*/*z* 479 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 479.2760. $C_{28}H_{40}O_5Na$ requires 479.2773.

*4.1.13. 7-Benzyloxy-5-(4-methoxybenzyloxy)-2,4,6-trimethyl-(2R,3R,4S,5R,6R)-heptane-1,3-diol (**23**)*

To a solution of **22** (11.60 g, 25.44 mmol) in THF (80 mL) was added aqueous 2 N HCl (63.60 mL, 127.2 mmol) and the resulting reaction mixture was stirred for 5 h at 25 °C. It was diluted with ethylacetate and extracted the aqueous layer twice with ethylacetate (2×100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, evaporated the solvent under reduced pressure and purified by column chromatography (4:6, EtOAc/hexane) to afford diol **23** (9.40 g, 89%) as a viscous liquid. R_f (2:3, EtOAc/hexane) 0.45; $[\alpha]_D^{25}$ +50.2 (*c* 1.38, $CHCl_3$); IR(Neat): 3446 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ 7.34–7.24 (5H, m, Ar–H), 7.09 (2H, d, *J*=8.4 Hz, Ar–H), 6.80 (2H, d, *J*=8.4 Hz, Ar–H), 4.49 (2H, s, benzylic CH_2), 4.45 (2H, ABq, *J*=10.7 Hz, benzylic CH_2), 4.00 (1H, br s, OH), 3.79 (3H, s, Ar–OCH_3), 3.77 (1H, br s, OH), 3.67 (1H, dd, *J*=8.4, 3.8 Hz, CHOH), 3.60–3.43 (5H, m, CH_2OH, CH_2OBn, CHOPMB), 2.13–2.04 (1H, m, $CHCH_3$), 1.88–1.78 (2H, m, 2×$CHCH_3$), 1.11 (3H, d, *J*=6.9 Hz, $CHCH_3$), 0.98 (3H, d, *J*=6.9 Hz, $CHCH_3$), 0.70 (3H, d, *J*=6.9 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.3, 138.4, 130.0, 129.3, 128.3, 127.6, 127.5, 113.8, 86.8, 76.7, 75.6, 73.1, 72.1, 69.0, 55.2, 37.2, 36.7, 34.6, 14.8, 13.2, 11.6; ESI-MS: *m*/*z* 439 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 439.2454. $C_{25}H_{36}O_5Na$ requires 439.2460.

*4.1.14. 1-[1-[2-Benzyloxy-1-methyl-(1R)-ethyl]-3-hydroxy-2,4-dimethyl-5-phenylcarbonyloxy-(1R,2S,3R,4R)-pentyloxymethyl]-4-methoxybenzene (**24**)*

To a solution of diol **23** (9.03 g, 21.67 mmol) in dry CH_2Cl_2 (80 mL) at 0 °C were added Et_3N (9.03 mL, 65.01 mmol), benzoyl chloride (3.01 mL, 26.01 mmol) and catalytic amount of DMAP. It was allowed to stir at room temperature for 3 h. The reaction mixture was diluted with DCM and washed with 10% $NaHCO_3$ solution, water and brine successively. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo, the crude obtained was purified through column chromatography (1:4, EtOAc/hexane) to get **24** as a pale yellow liquid in 94% (10.61 g) yield. R_f (1:4, EtOAc/hexane) 0.38; $[\alpha]_D^{25}$ +40.4 (*c* 2.35, $CHCl_3$); IR (Neat): 3479, 1717, 1611, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (2H, d, *J*=6.5 Hz, Ar–H), 7.51 (1H, t, *J*=7.8 Hz, Ar–H), 7.40 (2H, t, *J*=7.8 Hz, Ar–H), 7.29 (5H, m, Ar–H), 7.09 (2H, d, *J*=9.1 Hz, Ar–H), 6.75 (2H, d, *J*=9.1 Hz, Ar–H), 4.52–4.43 (5H, m, benzylic CH_2, CHOBz), 4.38–4.32 (1H, m, CHOBz), 3.77 (4H, s, Ar–OCH_3, CHOH), 3.63 (1H, m, CHOPMB), 3.58 (1H, br s, OH), 3.54 (1H, d, *J*=7.8 Hz, CHOBn), 3.47 (1H, d, *J*=7.8 Hz, CHOBn), 2.11 (1H, m, $CHCH_3$), 1.99 (1H, m, $CHCH_3$), 1.90 (1H, m, $CHCH_3$), 1.08 (3H, d, *J*=6.5 Hz, $CHCH_3$), 1.03 (3H, d, *J*=7.8 Hz, $CHCH_3$), 0.93 (3H, d, *J*=6.5 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.9, 159.3, 138.4, 132.6, 130.6, 130.2, 129.5, 129.4, 128.3, 128.2, 127.6, 127.5, 113.9, 86.5, 75.6, 73.2, 72.2, 70.9, 67.4, 55.3, 36.8, 36.3, 34.4, 15.0, 13.6, 11.1; ESI-MS: *m*/*z* 543 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 543.2715. $C_{32}H_{40}O_6Na$ requires 543.2722.

*4.1.15. 1-[1-[2-Benzyloxy-1-methyl-(1R)-ethyl]-3-methoxymethoxy-2,4-dimethyl-5-phenylcarbonyloxy-(1R,2R,3R,4R)-pentyloxymethyl]-4-methoxybenzene (**25**)*

DIPEA (25.52 mL, 147.52 mmol) was added drop wise to a stirred and cooled (0 °C) solution of alcohol **24** (9.60 g, 18.44 mmol) in CH_2Cl_2 (100 mL). After 15 min, methoxymethylene chloride (MOMCl) (4.20 mL, 73.76 mmol) followed by DMAP (2.24 g, 18.44 mmol) was added drop wise over a period of 10 min and stirring was continued for 1 h. The cold bath was removed and stirring was continued for 20 h. The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were washed with brine, dried and evaporated. The residue was purified by silica gel column chromatography (1:5, EtOAc/hexane) to give MOM-ether **25** (8.32 g, 80%) as a pale yellow oil. R_f (1:5, EtOAc/hexane) 0.58; $[\alpha]_D^{25}$ −9.1 (*c* 2.76, $CHCl_3$); IR (Neat): 1719, 1610, 1034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.94 (2H, d, *J*=6.8 Hz, Ar–H), 7.50 (1H, t, *J*=7.5 Hz, Ar–H), 7.34 (2H, t, *J*=7.5 Hz, Ar–H), 7.28 (5H, m, Ar–H), 7.16 (2H, d, *J*=8.3 Hz, Ar–H), 6.74 (2H, d, *J*=9.0 Hz, Ar–H), 4.63 (2H, s, benzylic CH_2), 4.56 (2H, ABq, *J*=11.3 Hz, benzylic CH_2), 4.47 (2H, s, CH_2OBz), 4.39 (1H, dd, *J*=10.5, 3.7 Hz, $CHOCH_3$), 4.22 (1H, dd, *J*=10.5, 6.0 Hz, $CHOCH_3$), 3.81 (1H, d, *J*=8.3 Hz, CHOH), 3.76 (3H, s, Ar–OCH_3), 3.60 (1H, dd, *J*=9.0, 5.2 Hz, CHOPMB), 3.43 (2H, m, CH_2OBn), 3.35 (3H, s, CH_2OCH_3), 2.19 (1H, m, $CHCH_3$), 2.06 (1H, m, $CHCH_3$), 1.95 (1H, m, $CHCH_3$), 1.14 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.00 (3H, d, *J*=7.5 Hz, $CHCH_3$), 0.92 (3H, d, *J*=6.7 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.5, 158.8, 138.7, 132.7, 131.3, 130.4, 129.4, 128.6, 128.3, 128.2, 127.4, 127.3, 113.6, 98.3, 83.7, 81.0, 73.7, 73.04, 72.3, 76.2, 55.7, 55.2, 38.0, 36.7, 36.0, 16.2, 14.8, 11.0; ESI-MS: *m*/*z* 587 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 587.2962. $C_{34}H_{44}O_7Na$ requires 587.2984.

*4.1.16. 7-Benzyloxy-5-(4-methoxybenzyloxy)-3-methoxymethoxy-2,4,6-trimethyl-(2R,3R,4R,5R,6R)-heptane-1-ol (**26**)*

To a solution of benzoate ester **25** (7.60 g, 13.44 mmol), aqueous 3 N KOH solution (67.20 mL, 201.6 mmol), methanol (67.20 mL) and THF (67.20 mL) were added in 1:1:1 ratio. The reaction mixture was stirred for 5 h at 25 °C. Removed the solvent under reduced pressure, diluted with ethylacetate and extracted the aqueous layer twice with ethylacetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in vacuo, and the crude product obtained was purified by column chromatography (1:3, EtOAc/hexane) to get **26** (5.56 g, 90%) as a colourless viscous liquid. R_f (1:3, EtOAc/hexane) 0.55; $[\alpha]_D^{25}$ +12.2 (*c* 3.08, $CHCl_3$); IR (Neat): 3466, 1034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.31–7.22 (5H, m, Ar–H), 7.16 (2H, d, *J*=9.0 Hz, Ar–H), 6.79 (2H, d, *J*=8.3 Hz, Ar–H), 4.62 (1H, d, *J*=6.8 Hz, benzylic CH), 4.55 (1H, d, *J*=10.5 Hz, benzylic CH), 4.51–4.43 (4H, m, benzylic CH_2, CH_2OCH_3), 3.78 (3H, s, OCH_3), 3.71 (1H, d, *J*=8.3 Hz, CHOMOM), 3.64 (1H, m, CHOBn), 3.54 (1H, dd, *J*=9.0, 5.2 Hz, CHOPMB), 3.48–3.38 (2H, m, CHOBn, CHOH), 3.35 (3H, s, CH_2OCH_3), 3.31 (1H, m, CHOH), 2.72 (1H, br s, OH), 2.13 (1H, m, $CHCH_3$), 1.86 (1H, m, $CHCH_3$), 1.75 (1H, m, $CHCH_3$), 1.08 (3H, d, *J*=6.8 Hz, $CHCH_3$), 0.94 (3H, d, *J*=6.8 Hz, $CHCH_3$), 0.87 (3H, d, *J*=6.8 Hz, 3H, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.0, 138.7, 131.0, 129.0, 128.3, 127.5, 127.5, 113.7, 98.3, 84.5, 81.4, 74.2, 73.1, 72.3, 65.4, 55.9, 55.2, 39.0, 37.6, 36.3, 15.9, 14.5, 11.9; ESI-MS: *m*/*z* 483 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 483.2710. $C_{27}H_{40}O_6Na$ requires 483.2722.

*4.1.17. 7-Benzyloxy-5-(4-methoxybenzyloxy)-3-methoxymethoxy-2,4,6-trimethyl-(2S,3S,4R,5R,6R)-heptanal (**27**)*

To a clear solution of IBX (4.92 g, 17.52 mmol) in DMSO (17.40 mL, 1 M) at 25 °C was added drop wise a solution of alcohol **26** (5.40 g, 11.7 mmol) in dry DCM. The resulting mixture was

stirred for 1 h at 25 °C. Diluted with ether and the solid was filtered through Celite pad. The filtrate was washed twice with saturated aqueous $NaHCO_3$ solution, water and brine, and purified by flash column chromatography (1:4, EtOAc/hexane) afforded aldehyde **27** (4.83 g, 90%) as viscous liquid. R_f (1:4, EtOAc/hexane) 0.52; $[\alpha]_D^{25}$ +9.1 (*c* 2.45, $CHCl_3$); IR (Neat): 1724, 1032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 9.60 (1H, d, *J*=2.9 Hz, CHO), 7.30–7.26 (5H, m, Ar–H), 7.16 (2H, d, *J*=8.8 Hz, Ar–H), 6.80 (2H, d, *J*=8.8 Hz, Ar–H), 4.60 (1H, d, *J*=6.5 Hz, benzylic CH), 4.56 (1H, d, *J*=8.0 Hz, benzylic CH), 4.45 (4H, m, benzylic CH_2, CH_2OBn), 4.02 (1H, dd, *J*=8.0, 2.1 Hz, CHOMOM), 3.79 (3H, s, Ar–OCH_3), 3.55 (1H, dd, *J*=8.7, 5.1 Hz, $CHOCH_3$), 3.41 (1H, dd, *J*=8.7, 6.5 Hz, $CHOCH_3$), 3.37 (1H, dd, *J*=8.0, 4.3 Hz, CHOPMB), 3.29 (3H, s, CH_2OCH_3), 2.55 (1H, dqd, *J*=7.3, 6.5, 2.9 Hz, CH_3CHCHO), 2.15 (1H, m, $CHCH_3$), 1.87 (1H, m, $CHCH_3$), 1.09 (3H, d, *J*=7.3 Hz, $CHCH_3$), 0.97 (3H, d, *J*=6.5 Hz, $CHCH_3$), 0.93 (3H, d, *J*=7.3 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.1, 159.0, 138.6, 131.0, 128.9, 128.2, 127.6, 127.4, 113.7, 97.8, 83.7, 79.6, 73.9, 73.0, 72.2, 55.7, 55.1, 50.4, 38.3, 36.2, 15.9, 11.6, 11.4; ESI-MS: *m*/*z* 481 $[MNa]^+$. HRMS (ESI): $[MNa]^+$, found 481.2548. $C_{27}H_{38}O_6Na$ requires 481.2566.

4.1.18. 13-Benzyloxy-7-hydroxy-11-(4-methoxybenzyloxy)-9-methoxymethoxy-4,6,8,10,12-pentamethyl-(8R,9R,10R,11R,12R)-tridecane-3,5-dione (**29**)

A solution of LDA in THF was prepared by adding *n*-BuLi (2.5 M in *n*-hexane, 8.73 mL, 21.82 mmol) to a solution of $(^iPr)_2NH$ (3.30 mL, 23.52 mmol) in dry THF (20 mL) at 0 °C with stirring under argon. After 20 min, it was cooled to −78 °C and diketone **9** (1.24 g, 8.73 mmol) in THF (4 mL+4 mL) was added drop wise to the stirred solution. HMPA (8 mL) was added and the mixture was stirred for 15 min at −78 °C then gradually brought to 0 °C over a period of 1 h. Again the mixture was cooled to −78 °C, then aldehyde **25** (4.00 g, 8.73 mmol) in THF (8 mL+8 mL) was added drop wise to the mixture and then stirring was continued for 1 h at −78 °C. The reaction was quenched with saturated NH_4Cl solution at −78 °C and gradually brought to room temperature. It was diluted with ether and the aqueous layer extracted twice with ether. The combined organic phases were successively washed with water and brine, and dried over Na_2SO_4. The solvent was removed in vacuo to afford the diastereomeric mixture of aldol products **28** as viscous liquid.

To the above crude mixture (5.3 g, 8.83 mmol) in dry CH_2Cl_2 (20 mL) under argon atmosphere was added Dess–Martin periodinane (7.50 g, 17.68 mmol) at 0 °C. The reaction mixture was stirred for 1 h at 25 °C and diluted with ether. The solid was filtered, the combined organic layers washed with saturated aqueous $NaHCO_3$ and dried. Solvent was evaporated under reduced pressure to afford the triketone.

The crude triketone (~5.3 g, 8.86 mmol) in dry THF (20 mL) was added to the stirred solution of TPP (11.62 g, 44.3 mmol) and CCl_4 (8.55 mL, 88.6 mmol) in THF (50 mL) under an atmosphere of argon and the reaction mixture was allowed to stir at room temperature for 36 h. The reaction mixture was diluted with ether and filtered through Celite pad. The combined organic layers were washed with $NaHCO_3$ solution, brine and dried over Na_2SO_4. The solvent was removed in vacuo and purified by flash column chromatography (1:3, EtOAc/hexane) to afford γ-pyrone **29** (2.27 g, 45% over three steps) as viscous liquid. R_f (1:3, EtOAc/hexane) 0.28; $[\alpha]_D^{25}$ −39.6 (*c* 1.92, $CHCl_3$); IR (Neat): 1656, 1611 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.28 (5H, m, Ar–H), 7.17 (2H, d, *J*=8.9 Hz, Ar–H), 6.79 (2H, d, *J*=8.9 Hz, Ar–H), 4.63 (1H, d, *J*=10.4 Hz, benzylic CH_2), 4.51 (1H, d, *J*=11.8 Hz, benzylic CH_2), 4.48 (2H, s, benzylic CH_2), 4.31 (1H, d, *J*=5.9 Hz, OCH–OCH_3), 4.17 (1H, d, *J*=5.9 Hz, OCH–OCH_3), 4.02 (1H, d, *J*=8.9 Hz, CHOMOM), 3.78 (3H, s, Ar–OCH_3), 3.62 (1H, dd, *J*=5.9, 8.9 Hz, CH–OBn), 3.43–3.37 (2H, m, CH–OBn, CH–OPMB), 3.16 (3H, s, OCH_2–OCH_3), 3.12 (1H, m, C=$CCHCH_3$), 2.50 (2H, q, *J*=7.4 Hz, C=CCH_2CH_3), 2.27–2.17 (1H, m, $CHCH_3$), 1.97 (1H, m, $CHCH_3$), 1.94 (3H, s, CCH_3), 1.90 (3H, s, CCH_3), 1.13 (6H, d, *J*=7.4 Hz, $CHCH_3$, $CHCH_3$), 1.08 (3H, t, *J*=7.4 Hz, CH_2CH_3), 0.93 (3H, d, *J*=7.4 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.8, 164.9, 164.0, 158.8, 138.7, 131.6, 128.7, 128.2, 127.4, 119.2, 117.8, 113.6, 97.8, 83.5, 81.5, 73.8, 73.1, 72.2, 55.6, 55.2, 39.2, 38.0, 36.1, 29.6, 24.8, 16.3, 15.0, 11.2, 10.3, 9.5, 9.4; ESI-MS: *m*/*z* 581 $[MH]^+$. HRMS (ESI): $[MH]^+$, found. 581.3470. $C_{35}H_{49}O_7$ requires 581.3478.

4.1.19. 2-(1S,2S,3S,4R,5R)-6-(Benzyloxy)-2-hydroxy-4-[(4-methoxybenzyl)oxy]-1,3,5-trimethylhexyl-6-ethyl-3,5-dimethyl-4H-4-pyranone (**30**)

Bu_4NBr (1.67 g, 5.16 mmol) was added to the solution of TMSCl (0.67 mL, 5.16 mmol) in dry CH_2Cl_2 at 0 °C. After stirring for 1 h, a solution of compound **29** (1.00 g, 1.72 mmol) in CH_2Cl_2 was introduced and the mixture was stirred at −10 °C for 14 h. The mixture was quenched with saturated aqueous $NaHCO_3$, the aqueous layer was extracted with CH_2Cl_2, the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated. Purification of the residue by column chromatography (2:3, EtOAc/hexane) afforded a secondary free hydroxy compound **30** (0.70 g, 76%) as a colourless liquid. R_f (2:3, EtOAc/hexane) 0.45; $[\alpha]_D^{25}$ +12.21 (*c* 1.5, $CHCl_3$); IR (Neat): 3447, 1653, 1592, 1513, 1457, 1037, 758 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.37–7.28 (5H, m, Ar–H), 7.14 (2H, d, *J*=9.0 Hz, Ar–H), 6.81 (2H, d, *J*=8.3 Hz, Ar–H), 4.52 (2H, s, benzylic CH_2), 4.51 (2H, ABq, *J*=10.6 Hz, benzylic CH_2), 4.18 (1H, d, *J*=9.8 Hz, 1H, CHOH), 3.78 (3H, s, Ar–OCH_3), 3.66 (1H, dd, *J*=5.3 Hz, CHOBn), 3.60–3.50 (3H, m, 3H, CH–OBn, CH–OPMB, CH=$CHCHCH_3$), 3.13–3.02 (1H, m, $CHCH_3$), 2.62 (2H, q, *J*=7.6 Hz, CH_2CH_3), 2.20–2.08 (1H, m, $CHCH_3$), 2.00 (4H, m, CCH_3, $CHCH_3$), 1.94 (3H, s, CCH_3), 1.88 (3H, s, CCH_3), 1.20 (3H, t, *J*=7.5 Hz, CH_2CH_3), 1.16 (3H, d, *J*=7.5 Hz, $CHCH_3$), 1.08 (6H, d, *J*=6.0 Hz, $CHCH_3$, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.8, 164.8, 163.8, 159.3, 138.4, 130.0, 129.3, 128.3, 127.63, 127.6, 119.2, 117.2, 113.8, 86.5, 75.6, 73.2, 72.2, 71.9, 55.2, 38.6, 36.8, 34.2, 24.7, 15.03, 15.0, 14.4, 11.1, 9.6, 9.5; ESI-MS: *m*/*z* 559 $[MNa]^+$. HRMS (ESI): $[MNa]^+$ found 559.3043. $C_{33}H_{44}O_6Na$ requires 559.3035.

4.1.20. 2-(1S,2S,3S,4R,5R)-2,6-Dihydroxy-4-[(4-methoxybenzyl)oxy]-1,3,5-trimethylhexyl-6-ethyl-3,5-dimethyl-4H-4-pyranone (**31**)

To a stirred suspension of Raney-Ni (1.20 g) in ethanol was added alcohol **30** (0.60 g, 1.12 mmol) in ethanol under hydrogen atmosphere at room temperature. The reaction mixture was stirred for 5 h at room temperature. The reaction mass was filtered through Celite, concentrated in vacuo and purified by column chromatography (3:2, EtOAc/hexane) to afford product **31** (0.45 g, 90%) as a viscous liquid. R_f (3:2, EtOAc/hexane) 0.22; $[\alpha]_D^{25}$ −9.8 (*c* 0.91, $CHCl_3$); IR (Neat): 3447, 2969, 2930, 1653, 1592, 1037, 758 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.21 (2H, d, *J*=8.7 Hz, Ar–H), 6.81 (2H, d, *J*=8.3 Hz, Ar–H), 4.61 (2H, s, benzylic CH_2), 4.17 (1H, d, *J*=9.8 Hz, CHOH), 3.81 (1H, m, CH=$CHCHCH_3$), 3.77 (3H, s, OCH_3), 3.66 (1H, dd, *J*=10.5, 3.8 Hz, CHOH), 3.57 (1H, dd, *J*=4.6, 3.0 Hz, CHOPMB), 3.37 (1H, br s, OH), 3.08 (1H, td, *J*=13.6, 7.5 Hz, CHOH), 2.58 (2H, q, *J*=7.5 Hz, CH_2CH_3), 2.04–1.92 (2H, m, $CHCH_3$), 1.95 (3H, s, CCH_3), 1.87 (3H, s, CCH_3), 1.19 (3H, t, *J*=7.5 Hz, CH_2CH_3), 1.14–1.04 (9H, m, 3×$CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.6, 164.8, 163.8, 159.4, 129.8, 129.3, 117.7, 113.9, 96.1, 87.5, 75.9, 71.8, 64.9, 55.1, 38.8, 37.7, 35.3, 24.7, 15.0, 14.4, 11.2, 10.8, 9.7, 9.5; ESI-MS: *m*/*z* 447 $[MH]^+$. HRMS (ESI): $[MH]^+$, found 447.2753. $C_{26}H_{38}O_6$ requires 447.2746.

4.1.21. (2S,3S,4R,6R)-6-(6-Ethyl-3,5-dimethyl-4-oxo-4H-2-pyranyl)-3-[(4-methoxybenzyl)oxy]-2,4-dimethyl-5-oxoheptanoic acid (**6**)

To a stirred solution of oxalyl chloride (0.51 g, 4.02 mmol) in dry CH_2Cl_2 (3 mL) at −78 °C, dry DMSO (0.63 g, 8.04 mmol) was added

drop wise. After 30 min, diol **31** (0.30 g, 0.67 mmol) in CH_2Cl_2 (2 mL) was added over 10 min. After stirring for 2 h at −78 °C, Et_3N (1.7 mL, 12.06 mmol) was added slowly and stirred for 30 min, and then warmed to −30 °C and stirred further for 30 min. Hexane/toluene (3:1, 300 mL) was added to the reaction mixture at −30 °C, the resulting suspension was filtered through Celite and concentrated in vacuo to give the keto aldehyde.

To a solution of crude keto aldehyde (~0.30 g, 0.67 mmol) in DMSO (2 mL) was added sodium dihydrogen phosphate (0.10 g, 0.64 mmol) solution at 0 °C. To this well stirred mixture at 0 °C was added saturated sodium chlorite (0.092 g, 1.01 mmol) solution and allowed it to stir at room temperature over 2 h before being poured into brine solution and extracted with diethyl ether (6×20 mL). The combined organic layers were dried and concentrated in vacuo. Silica gel column chromatography (1:3, acetone/hexane) gave a pure keto acid **6** (0.25 g, 80%) as a viscous liquid. R_f (1:3, acetone/hexane) 0.45; $[\alpha]_D^{25}$ −94.2 (*c* 0.75, $CHCl_3$) (lit.[8] $[\alpha]_D^{20}$ −96.5 (*c* 0.4, $CHCl_3$)); IR (Neat): 3440–2700, 1730, 1651, 1585, 1177, 1037, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.16 (2H, d, *J*=8.3 Hz, Ar–H), 6.85 (2H, d, *J*=8.3 Hz, Ar–H), 4.55 (1H, d, *J*=10.6 Hz, benzylic CH), 4.26 (1H, d, *J*=10.6 Hz, benzylic CH), 3.92 (1H, q, *J*=6.8 Hz, C=CCHCH$_3$), 3.85 (1H, d, *J*=7.6, 2.3 Hz, CHOPMB), 3.79 (3H, s, OCH_3), 3.06 (1H, dq, *J*=9.8, 6.7 Hz, $CHCH_3$), 2.82 (1H, qd, *J*=7.2, 2.6 Hz, $CHCH_3$), 2.54 (2H, q, *J*=7.6 Hz, CH_2CH_3), 1.95 (3H, s, CCH_3), 1.93 (3H, s, CCH_3), 1.25 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.24 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.14 (3H, t, *J*=7.5 Hz, CH_2CH_3), 0.87 (3H, d, *J*=6.7 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 209.6, 180.0, 176.4, 165.0, 160.0, 159.3, 129.8, 129.5, 120.4, 118.4, 113.7, 84.7, 74.0, 55.2, 51.0, 46.3, 41.2, 24.8, 13.5, 12.7, 12.5, 11.2, 9.9, 9.5; ESI-MS: *m*/*z* 459 $[MH]^+$. HRMS (ESI): $[MH]^+$, found 459.2377. $C_{26}H_{35}O_7$ requires 459.2382.

4.1.22. *p*-Methoxybenzyl baconipyrone C (**32**)

2,4,6-Trichlorobenzoyl chloride (0.71 mL, 4.62 mmol) was added to a stirred solution of **6** (0.10 g, 0.22 mmol) and Et_3N (0.7 mL, 5.06 mmol) in toluene (10 mL) at −78 °C. After stirring for 20 min, compound **5** (0.065 g, 0.33 mmol) and DMAP (1.33 g, 11.00 mmol) in toluene were added to the above compound, and the reaction mixture was warmed to −20 °C and the resulted white slurry was stirred at −20 °C for 30 min, before being quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with ethylacetate (4×20 mL), dried over Na_2SO_4 and concentrated in vacuo. Silica gel column chromatography (1:4, acetone/hexane) gave **32** (0.048 g, 35%) as a colourless oil. R_f (1:4, acetone/hexane) 0.54; $[\alpha]_D^{25}$ −29.20 (*c* 1.2, $CHCl_3$); IR (Neat): 2929, 2855, 1719, 1653, 1612, 1459, 1249, 1177, 1037 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.15 (2H, d, *J*=8.5 Hz, Ar–H), 6.86 (2H, d, *J*=8.5 Hz, Ar–H), 5.50 (1H, dd, *J*=7.7, 5.2 Hz, CHO(C=O)), 4.46 (1H, d, *J*=10.7 Hz, benzylic CH), 4.21(1H, d, *J*=10.7 Hz, benzylic CH), 3.94 (1H, q, *J*=6.8 Hz, C=CCHCH$_3$), 3.83–3.78 (1H, m, CHOPMB), 3.80 (3H, s, OCH_3), 2.92 (1H, dq, *J*=9.8, 6.8 Hz, CHaCHbCH$_3$, CHaCHbCH$_3$), 2.87 (1H, dq, *J*=15.0, 7.2 Hz, CHaCHbCH$_3$), 2.77–2.67 (2H, m, $CHCH_3$, $CHCH_3$), 2.54 (2H, q, *J*=7.6 Hz, CH_2CH_3), 2.54 (1H, m, $CHCH_3$), 2.47 (1H, m, CHaCHbCH$_3$), 2.38 (1H, dq, *J*=7.2, 18.0 Hz, CHaCHbCH$_3$), 1.98 (3H, s, CCH_3), 1.93 (3H, s, CCH_3), 1.25 (3H, d, *J*=7.2 Hz, $CHCH_3$), 1.22 (3H, d, *J*=7.3 Hz, $CHCH_3$), 1.14 (3H, t, *J*=7.2 Hz, 3H, CH_2CH_3), 1.11 (3H, d, *J*=7.2 Hz, $CHCH_3$), 1.07 (3H, d, *J*=7.2 Hz, 3H, $CHCH_3$), 1.03–0.96 (9H, m, $CHCH_3$, CH_2CH_3, CH_2CH_3), 0.75 (3H, d, *J*=6.8 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 211.5, 209.4, 179.6, 172.3, 164.7, 160.6, 159.3, 130.0, 129.4, 120.2, 118.3, 113.7, 83.3, 74.4, 73.1, 55.3, 50.6, 47.5, 46.2, 46.3, 41.2, 35.4, 34.9, 24.7, 13.2, 13.1, 12.9, 11.5, 11.3, 10.8, 9.8, 9.8, 7.7, 7.6; ESI-MS: *m*/*z* 641.3 $[MH]^+$. HRMS (ESI): $[MH]^+$, found 641.3710. $C_{37}H_{52}O_9$ requires 641.3690.

4.1.23. Baconipyrone C (**3**)

To a stirred solution of **26** (0.03 g, 0.047 mmol) in 2 mL mixture of CH_2Cl_2/pH 7 buffer (9:1), DDQ (0.021 g, 0.094 mmol) was added at 0 °C. The reaction mixture was stirred for 1 h at room temperature before being quenched with $NaHCO_3$. The product was purified by flash column chromatography (7:3, EtOAc/hexane) to afford **3** (0.017 g, 70%) as colourless oil. R_f (7:3, EtOAc/hexane) 0.28; $[\alpha]_D^{25}$ −70.20 (*c* 0.4, MeOH) (lit.[8] $[\alpha]^{20}{}_D$ −73.3 (*c* 0.77, MeOH)); IR (Neat): 3443, 1718, 1652, 1596 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.47 (1H, dd, *J*=9.2, 3.7 Hz, CHO(C=O)), 4.14 (1H, q, *J*=6.9 Hz, C=CCHCH$_3$), 3.55 (1H, t, *J*=7.3 Hz, CHOH), 3.39 (1H, br s, OH), 2.86 (1H, dq, *J*=8.7, 7.3 Hz, $CHCH_3$), 2.83 (2H, m, $CHCH_3$), 2.75 (1H, dq, *J*=18.3, 7.3 Hz, CHaCHbCH$_3$), 2.55 (2H, q, *J*=7.3 Hz, CH_2CH_3), 2.54 (1H, m, $CHCH_3$), 2.51 (1H, dq, *J*=18.3, 7.3 Hz, CHaCHbCH$_3$), 2.40 (1H, dq, *J*=18.3, 7.3 Hz, CHaCHbCH$_3$), 2.34 (1H, dq, *J*=18.3, 7.3 Hz, CHaCHbCH$_3$), 2.09 (3H, s, CCH_3), 1.93 (3H, s, CCH_3), 1.39 (3H, d, *J*=7.3 Hz, $CHCH_3$), 1.22 (3H, d, *J*=7.3 Hz, $CHCH_3$), 1.16 (3H, t, *J*=7.3 Hz, CH_2CH_3), 1.09 (3H, d, *J*=7.3 Hz, $CHCH_3$), 1.02 (3H, d, *J*=7.3 Hz, $CHCH_3$), 1.01 (3H, t, *J*=7.3 Hz, CH_2CH_3), 0.91 (3H, t, *J*=7.3 Hz, CH_2CH_3), 0.86 (3H, d, *J*=6.6 Hz, $CHCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 211.9, 210.8, 210.4, 179.7, 174.1, 164.6, 160.6, 120.4, 118.30, 77.50, 73.8, 51.0, 48.6, 47.3, 45.8, 41.1, 35.1, 24.7, 15.1, 14.1, 13.4, 13.1, 11.3, 9.9, 9.7, 9.5, 7.7, 7.3; ESI-MS: *m*/*z* 521.3 $[MH]^+$. HRMS (ESI): $[MNa]^+$, found 543.2932. $C_{29}H_{44}O_8$ requires 543.2933.

Acknowledgements

K.S. thanks UGC, India for the award of research fellowship.

References and notes

1. (a) Review: Faulkner, D. J. *Nat. Prod. Rep.* **1996**, *13*, 75; (b) Davies-Coleman, M. T.; Garson, M. *J. Nat. Prod. Rep.* **1998**, *15*, 477; (c) Norcross, R. D.; Paterson, I. *Chem. Rev. (Washington, D.C.)* **1995**, *95*, 2041.
2. Pawlik, R. *Chem. Rev.* **1993**, *93*, 1911.
3. Manker, C. D.; Faulkner, D. J.; Stout, J. T.; Clardy, J. *J. Org. Chem.* **1989**, *54*, 5371.
4. (a) O' Hagan, D. *Nat. Prod. Rep.* **1989**, *6*, 205; (b) O' Hagan, D. *The Polyketide Metabolites*; Horwood: Chichester, UK, 1991; (c) O' Hagan, D. *J. Nat. Prod. Rep.* **1995**, *12*, 1.
5. (a) Garson, M. J. *Chem. Rev.* **1993**, *93*, 1699; (b) Garson, M. J.; Jones, D. D.; Small, C. J.; Liang, J.; Clardy, J. *Tetrahedron Lett.* **1994**, *35*, 6921; (c) Garson, M. J.; Goodman, J. M.; Paterson, I. *Tetrahedron Lett.* **1994**, *35*, 6929.
6. Brecknell, D. J.; Collett, L. A.; Davies-Coleman, M. T.; Garson, M. J.; Jones, D. D. *Tetrahedron* **2000**, *56*, 2497.
7. Gillingham, D. G.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 3860.
8. Paterson, I.; Chen, D. Y.-K.; Acena, J. L.; Franklin, A. S. *Org. Lett.* **2000**, *2*, 1513.
9. Turks, M.; Murcia, M. C.; Scopelliti, R.; Vogel, P. *Org. Lett.* **2004**, *6*, 3031.
10. (a) Yadav, J. S.; Srinivas, R.; Sathaiah, K. *Tetrahedron Lett.* **2006**, *47*, 1603; (b) Yadav, J. S.; Ravindar, K.; Reddy, B. V. S. *Synlett* **2007**, 1957.
11. Yadav, J. S.; Rao, C. S.; Chandrasekhar, S.; Ramarao, A. V. *Tetrahedron Lett.* **1995**, *36*, 7717.
12. Yadav, J. S.; Abraham, S.; Reddy, M. M.; Sabitha, G.; Sankar, A. R.; Kunwar, A. C. *Tetrahedron Lett.* **2002**, *43*, 3453.
13. Yadav, J. S.; Md. Ahmed, M. *Tetrahedron Lett.* **2002**, *43*, 7147.
14. Yadav, J. S.; Reddy, K. B.; Sabitha, G. *Tetrahedron Lett.* **2004**, *45*, 6475.
15. Yadav, J. S.; Reddy, K. B.; Sabitha, G. *Tetrahedron* **2008**, *64*, 1971.
16. Grisenti, P.; Ferraboschi, P.; Manzocchi, A.; Santaniello, E. *Tetrahedron* **1992**, *48*, 3827.
17. White, J. D.; Kawasaki, M. *J. Org. Chem.* **1992**, *57*, 5292.
18. Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.
19. Komatsu, K.; Tanino, K.; Miyashita, M. *Angew. Chem.* **2004**, *116*, 4441.
20. Kalaitzakis, D.; Rozzell, J. D.; Kambourakis, S.; Smonou, I. *Eur. J. Org. Chem.* **2006**, 2309.
21. Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.
22. (a) Yamamura, S.; Nishiyama, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2025; (b) Arimoto, H.; Nishiyama, S.; Yamamura, S. *Tetrahedron Lett.* **1990**, *31*, 5491; (c) Arimoto, H.; Nishiyama, S.; Yamamura, S. *Tetrahedron Lett.* **1990**, *31*, 5619; (d) Paterson, I.; Franklin, A. S. *Tetrahedron Lett.* **1994**, *35*, 6925.
23. Aissa, C.; Riveiros, R.; Ragot, J.; Furstner, A. *J. Am. Chem. Soc.* **2003**, *125*, 15512.
24. Paterson, I.; Norcross, R. D.; Ward, R. A.; Romea, P.; Anne Lister, M. *J. Am. Chem. Soc.* **1994**, *116*, 11287.