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Tetrahedron
Tetrahedron 60 (2004) 2531–2538

Synthesis of $\Delta^{12,14}$-15-deoxy-PG-J_1 methyl ester and *epi*-Δ^{12}-15-deoxy-PG-J_1

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Received 22 October 2003; revised 22 December 2003; accepted 15 January 2004

Abstract—The synthesis of racemic $\Delta^{12,14}$-15-deoxy-PG-J_1 is readily achieved in six steps employing as the key transformation a one-pot conjugate addition–Peterson olefination sequence using *exo*-2-trimethylsilyl-3a,4,7,7a-tetrahydro-4,7-methanoinden-1-one. Additionally a Noyori-type three-component coupling approach is employed for the synthesis of enantioenriched *epi*-Δ^{12}-15-deoxy-PG-J_1 from 4(*S*)-*tert*-butyldimethylsilyloxycyclopent-2-enone.

1. Introduction

The prostaglandin family of arachidonic acid-derived C-20 natural products, for example PG-D_2 **1**, control a myriad of complex, seemingly diverse biological functions.[1] More recently it has been demonstrated that the cyclopentenone prostanoids, for example PG-J_2 **2**, putative end products of the arachidonic acid-cyclooxygenase cascade, possess distinct and important activities.[2] Interestingly, these activities sometimes counter those of the earlier products of the cascade, suggesting the intriguing possibility of a regulatory-feedback system. For example PG-$F_{2\alpha}$ has been shown to cause the contraction of smooth muscle, whereas, PG-A_1 is a smooth muscle relaxant.[2b] Amongst the cyclopentenone prostanoids and related compounds those possessing the so-called cross-conjugated dienone structural motif **3**–**6** appear to demonstrate the most interesting and potent biological activities (Fig. 1).

Currently the complex mechanisms by which these compounds confer their biological activities are not entirely clear. However, it was recently reported that $\Delta^{12,14}$-15-deoxy-PG-J_2 **3** was a potent inhibitor of influenza A viral replication, a property linked to the induction of cytoprotective, heat shock protein synthesis.[3] Additionally, $\Delta^{12,14}$-15-deoxy-PG-J_2 **3** was found to be a high affinity ligand for the PPAR-γ nuclear receptor.[2,4] In a series of papers Noyori, Suzuki and co-workers have reported structure-activity optimisation studies of cross-conjugated cyclopentenone prostaglandin analogues, aimed at identifying a clinical candidate for the treatment of cancer. These efforts culminated in the development of **4**.[5] The possibility that

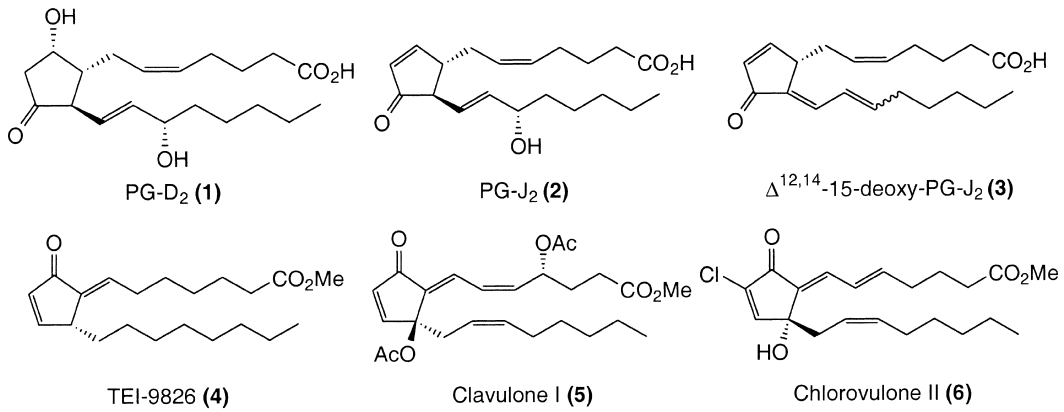

Figure 1.

Keywords: $\Delta^{12,14}$-15-Deoxy-PG-J_1 methyl ester; Conjugate addition–Peterson olefination; *epi*-Δ^{12}-15-Deoxy-PG-J_1; Cross-conjugated cyclopenteone.
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0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2004.01.048

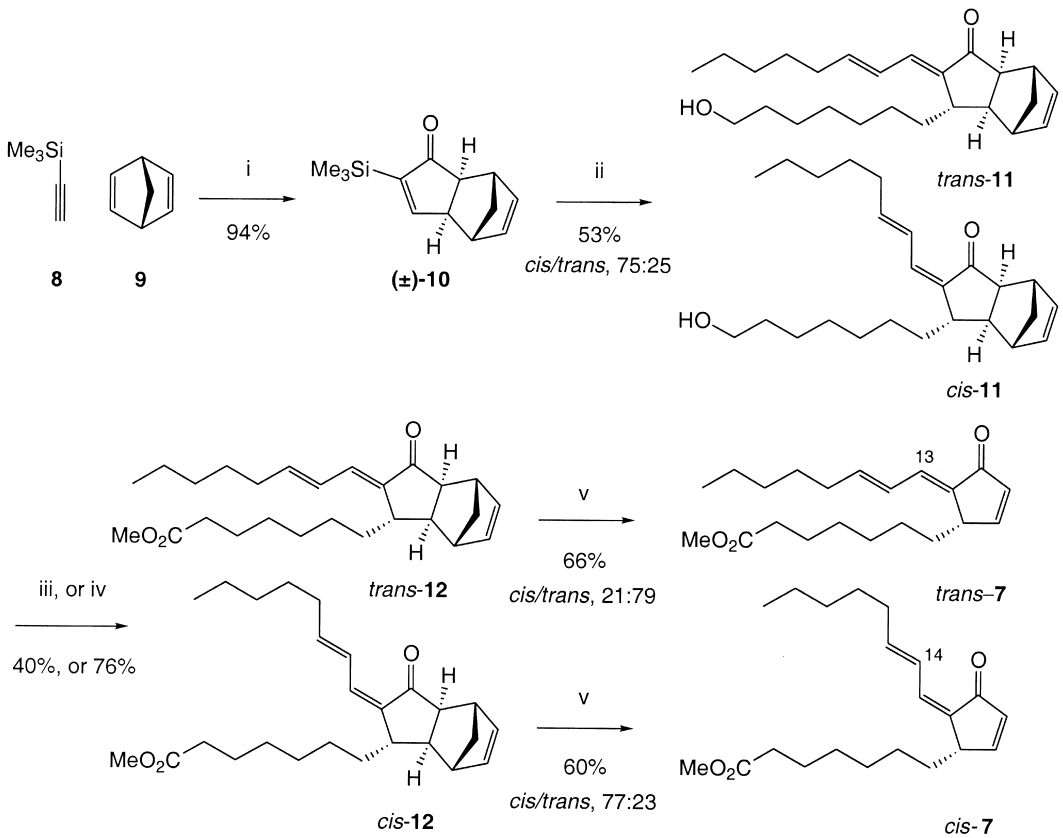
$\Delta^{12,14}$-15-deoxy-PG-J_2 **3** is formed from PG-D_2 **1** post extraction has been speculated upon, since **2** has been detected only rarely in vivo.[6] Apparently part of the reason for this may be the reactive nature of the prostanoid, undergoing conjugation rapidly with cellular nucleophilic species such as glutathione, and consequently removing these compounds from circulation as water soluble metabolites.[6,7]

2. Results and discussion

The PG-D_1 and PG-J_1 series of prostaglandins, lacking unsaturation in the α-side-chain, have yet to be discovered from a natural source, unlike PG-E_1 and A_1.[1,2] Although there has been one previous synthesis of optically active PG-J_1[8] to the best of our knowledge the preparation of $\Delta^{12,14}$-15-deoxy-PG-J_1 has not been reported.

The three-component coupling protocol developed by Noyori has emerged as the most efficient means for the synthesis of cyclopentenone prostanoids.[9] We have recently reported a variation of this method, namely the conjugate addition–Peterson olefination reaction, for the construction of cross-conjugated compounds and have employed this method for the preparation of (±)-TEI-9826 **4**.[10] Now we report that, using a similar protocol, the synthesis of both *cis*- and *trans*-$\Delta^{12,14}$-15-deoxy-PG-J_1 **7** has been achieved (see Scheme 1). The availability of both stereoisomers is potentially of interest, since recently it was reported that *cis*-$\Delta^{12,14}$-15-deoxy-PG-J_2 **3** was a more potent PPAR-γ ligand than its *trans*- counterpart.[11]

The masked cyclopentenone building block **10** was readily available following the Pauson–Khand cycloaddition between trimethysilylacetylene **8** and norbornadiene **9**. Optimum yields for this transformation were achieved under thermal microwave promoted conditions, with one equivalent of $Co_2(CO)_8$.[12] One-pot conjugate addition of the silyl protected Grignard reagent, under copper(I) catalysis, followed by addition of *trans*-oct-2-enal gave an isomeric mixture of the corresponding adducts (*cis*/*trans*, 75:25 by ^{1}H NMR spectroscopy). Separation of the crude reaction mixture proved problematic, consequently direct removal of the silicon protecting group under proteolysis was necessary. This gave a separable mixture of *cis*-**11** and *trans*-**11** in a combined yield of 53% for the three steps. However, during this deprotection some isomerisation of the dienone was observed (*cis*/*trans*, 60:40). Functional group interconversion of the hydroxyl group into the methyl ester moiety was achieved in two ways. Initially an unseparated mixture of alkene geometrical isomers (*cis*/*trans*, 60:40) was directly oxidised into the carboxylic acid using Jones reagent. The crude acid, following aqueous work-up, was then converted into the *cis*- and *trans*-methyl esters **12** on treatment with (trimethylsilyl)diazomethane in 40% combined yield. More efficient conversion was achieved using a three-step protocol in which *trans*-**11**



Scheme 1. Synthesis of *trans*-$\Delta^{12,14}$-15-deoxy-PG-J_1 and *cis*-$\Delta^{12,14}$-15-deoxy-PG-J_1. Reagents and conditions: (i) $Co_2(CO)_8$, DCE, μ-wave, 90 °C, 20 min; (ii) (a) $BrMg(CH_2)_7OTBS$, CuI (13 mol%), Et_2O, −78 to −20 °C, 1 h; (b) oct-2-enal, −20 °C to rt, 15 h; (c) AcOH/H_2O/THF (6:3:4), rt, 15 h; (iii) (a) CrO_3–H_2SO_4, acetone, 0 °C, 1 h; (b) $Me_3SiCH_2N_2$, PhH, MeOH, rt, 0.5 h; (iv) (a) Dess–Martin Periodinane, DCM, rt, 3 h; (b) $NaClO_2$, NaH_2PO_4, ^{t}BuOH, Me_2CCMe_2, rt, 15 h; (c) Me_3SiCHN_2, PhH, MeOH, rt, 1.5 h; (v) $MeAlCl_2$, maleic anhydride (10 equiv.), DCM, μ-wave, 100 °C, 200 s.

was oxidised, initially with the Dess–Martin periodinane, then sodium chlorite and finally the acid was converted without purification into the *trans*-methyl ester **12** in 76% overall yield. Isomer separation, by flash column chromatography, and subsequent Lewis acid mediated *retro*-Diels–Alder reaction,[13] in the presence of maleic anhydride (MA), afforded both geometrical isomeric cross-conjugated cyclopentenones. Optimum results for this thermal process were obtained following short bursts of microwave irradiation.[14] Interestingly, in contrast to the longer periods under standard conductive heating,[10] these short-intense reaction periods gave only limited double bond isomerisation. Thus, *cis*-**12** gave mainly *cis*-**7** in 60% yield (*cis*/*trans*, 77:23) and similarly *trans*-**12** gave *trans*-**7** in 66% yield (*cis*/*trans*, 21:79). These isomeric mixtures proved readily separable by flash column chromatography.

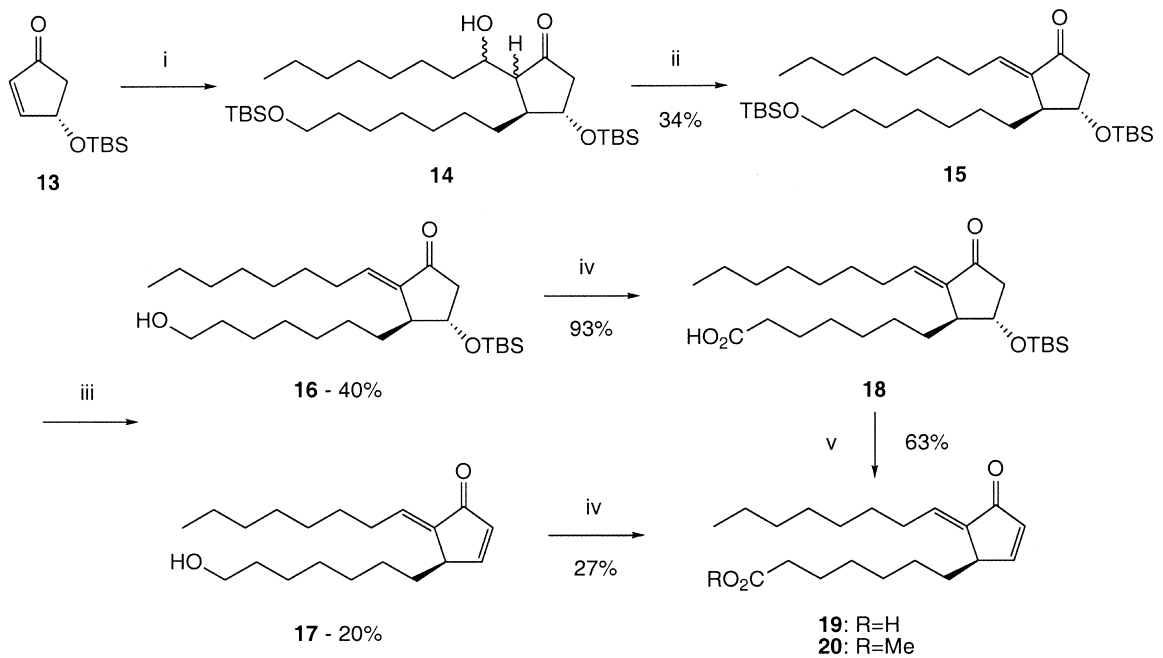
Generally proton NMR spectroscopy proved to be important as a diagnostic tool, enabling the conformation of the exocyclic-alkylidene double bond to be determined, since significant anisotropic effects are observed when either proton in the 13- or 14-position is *syn*-orientated to the carbonyl moiety. For example, *cis*-**7**: 6.37 ppm (13-H), 7.69 ppm (14-H); *trans*-**7**: 6.93 ppm (13-H), 6.17–6.32 ppm (14-H).[15]

In view of the current interest in Δ^{12}-15-deoxy-PG-J's,[2,11] we adopted a second strategy, based on the traditional three-component coupling methodology of Noyori[9] (as used in the synthesis of Δ^{7}-PGA-type systems), for the production of some other novel cross-conjugated compounds. Although this sequence is a less efficient method for accessing the cross-conjugated cyclopentenone system than the conjugate addition–Peterson olefination sequence described, it enables homochiral material to be prepared more efficiently. Studies indicate that compounds possessing the natural PG stereochemistry at the single stereocentre are recognised by metabolic enzymes more readily than the corresponding epimeric compounds. For example, Noyori has shown that *epi*-PG-A analogues of this type exhibit considerably longer half-lives in rat serum than their naturally configured counterparts.[6a] Hence we targeted the preparation of an 8-*epi*-PG-J_1 analogue in order to explore the synthetic strategy.

Thus, 4(*S*)-*tert*-butyldimethylsilyloxycyclopent-2-enone **13**[16] reacted with the Grignard reagent derived from 1-*tert*-butyldimethylsilyloxy-7-bromoheptane in ether containing copper(I) iodide at −78 °C for 30 min. Octanal was then added and the reaction was stirred at low temperature (−78 °C) overnight. Work-up furnished the crude alcohol **14** as a mixture of diastereoisomers, which was immediately converted into the corresponding mesylate and treated with *N*,*N*-dimethylaminopyridine to afford the unsaturated ketone **15** in 34% yield over the two steps (Scheme 2).

Deprotection of the bis-silylated compound **15** was effected using aqueous acetic acid to give a readily separated mixture of the alcohol **16** (40%) and the dienone **17** (20%). The former compound was readily converted into acid **18** (93% yield) which on treatment initially with (trimethylsilyl)-diazomethane, then aqueous base gave 8(*R*)-Δ^{12}-15-deoxy-PG-J_1 methyl ester **20** (63% yield). The more sensitive dienone **17** gave the carboxylic acid **19** in a lower-yielding two-step procedure.

In conclusion, we have developed an efficient method for the synthesis of both geometrical stereoisomers of racemic $\Delta^{12,14}$-15-deoxy-PG-J_1. Significantly the conjugate addition reaction proceeds with very high diastereoselectivity; consequently in order to generate enantioenriched, or homochiral material the corresponding enantioenriched, or



Scheme 2. Synthesis of *epi*-8(*R*)- Δ^{12}-15-deoxy-PG-J_1. Reagents and conditions: (i) (a) $BrMg(CH_2)_7OTBS$, CuI (10 mol%), Et_2O, −78 °C to −20 °C, 1 h; (b) octanal, −78 °C, 16 h; (ii) MsCl, DMAP, DCM, rt, 16 h; (iii) AcOH/H_2O/THF (3:1:1), rt, 4 days; (iv) (a) Dess–Martin Periodinane, DCM, rt, 3 h; (b) $NaClO_2$, NaH_2PO_4, ^{t}BuOH, Me_2CCMe_2, rt, 15 h; (v) (a) Me_3SiCHN_2, PhH, MeOH, rt, 1.5 h; (b) Na_2CO_3, MeOH, 0 °C to rt, 2 h.

homochiral Pauson–Khand adduct could be employed.[17] A related three-component coupling method enabled the enantioselective synthesis of *epi*-Δ^{12}-15-deoxy-PG-J_1.

3. Experimental

3.1. General

Starting materials were purchased from commercial sources and were used without further purification. Anhydrous Et_2O was distilled under nitrogen from the sodium-benzophenone ketyl radical, DCM was distilled from CaH_2. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded using a Bruker AMX400 spectrometer. Infrared spectroscopy was performed on a Perkin–Elmer Paragon 1000 FTIR spectrometer. Optical rotation measurements were recorded using a Optical Activity, Polaar 2001 polarimeter at 589 nm and are quoted in units of 10^{-1}deg cm^2g^{-1}. Flash column chromatography, under moderate pressure was performed using silica gel-ICN 32-63, 60 Å. Focused microwave irradiation used in this study was generated by a Coherent Synthesis-Smith Workstation package (Personal Chemistry AB, Sweden).

3.1.1. 1-*tert*-Butyldimethylsilyloxy-7-bromoheptane.[18] A solution of 7-bromoheptanol (3.48 g, 17.8 mmol, 1 equiv.) in DCM (50 cm^3) was cooled to 0 °C and treated with TBSCl (2.96 g, 19.6 mmol, 1.1 equiv.) and TEA (3.1 cm^3, 22.2 mmol, 1.25 equiv.). A catalytic amount of DMAP (ca.10 mg) was added and stirring was continued for 15 h during which period room temperature was reached. The solvent was removed in vacuo before Et_2O (50 cm^3) and H_2O (50 cm^3) were added. The resultant aqueous phase was further extracted with Et_2O (3×50 cm^3) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal under reduced pressure and purification by flash column chromatography (Hex–Et_2O; 19:1) gave 1-*tert*-butyldimethylsilyloxy-7-bromoheptane (4.30 g, 78%) as a colourless liquid. R_f=0.6 (Hex–Et_2O; 19:1); *m/z* (CI) 311 (MH^+, 100%, ^{81}Br), 309 (MH^+, 100%, ^{79}Br); δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, CH_3), 0.90 (9H, s, CH_3), 1.28–1.37 (4H, m, CH_2), 1.39–1.45 (2H, m, CH_2), 1.46–1.55 (2H, m, CH_2), 1.85 (2H, pent, J=7.5 Hz, CH_2), 3.41 (2H, t, J=7.0 Hz, CH_2), 3.62 (2H, t, J=6.5 Hz, CH_2); δ_C (100 MHz, $CDCl_3$) −5.3, 18.4, 25.6, 26.0, 28.2, 28.6, 32.8, 34.0, 63.1.

3.1.2. *exo*-2-Trimethylsilyl-3a,4,7,7a-tetrahydro-4,7-methanoinden-1-one 10.[12] At room temperature $Co_2(CO)_8$ (352 mg, 1.03 mmol, 1 equiv.) was added to a solution of trimethylsilylacetylene **8** (0.15 cm^3, 1.06 mmol, 1 equiv.) in DCE (4 cm^3). Stirring was continued for 1 h. Norbornadiene **9** (0.55 cm^3, 5.0 mmol, 5 equiv.) was added and the mixture was heated in the microwave (Smith Creator, 300 W) at 90 °C for 20 min. Silica (ca. 2 g) was added to the crude reaction mixture and the solvent was removed under reduced pressure. Purification by flash column chromatography (Hex→Hex–EtOAc; 9:1) afforded the title compound **10** (218 mg, 94%) as a colourless solid, mp 94–95 °C (Hex). R_f *exo*-**10**=0.25 [*endo*-**10**=0.2] (Hex–EtOAc; 9:1); ν_{max} ($CDCl_3$/cm^{-1}) 3062, 2972, 1689, 1570, 1247; *m/z* (CI) 219 (MH^+, 100%); found 219.12086, $C_{13}H_{18}OSi{\cdot}H$ requires 219.12053 (+1.5 ppm); δ_H (400 MHz, $CDCl_3$) −0.17 (9H, s, CH_3), 1.05 (1H, d, J=11.25 Hz, CH_2), 1.22 (1H, d, J=11.25 Hz, CH_2), 2.01 (1H, d, J=6.25 Hz, CH), 2.52 (1H, s, CH), 2.72–2.74 (1H, m, CH), 2.80 (1H, s, CH), 6.21–6.30 (2H, m, 2×CH), 7.65 (1H, d, J=2.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) −2.1, 41.1, 42.8, 43.7, 51.9, 53.2, 137.2, 138.1, 152.0, 172.7, 213.0; Found C, 71.50; H, 8.31%, $C_{13}H_{18}OSi$ requires C, 71.60; H, 8.30%.

3.1.3. (±)-3-(7-Hydroxylheptyl)-2-[*trans*-oct-2-en-*cis*/*trans*-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one 11. Under N_2, at room temperature 1-*tert*-butyldimethylsilyloxy-8-bromoheptane (580 mg, 1.88 mmol, 1.3 equiv.) was added dropwise over 0.25 h to a rapidly stirred mixture of magnesium (200 mg, 8.23 mmol, 5.9 equiv.) and a catalytic amount of iodine (ca. 5 mg) in THF (10 cm^3). The resultant Grignard reagent was stirred at room temperature for 2 h before TLC analysis (Hex–Et_2O; 19:1) indicated consumption of starting material. This reagent was added via cannula to a slurry of CuI (36 mg, 0.19 mmol, 0.13 equiv.) in Et_2O (10 cm^3) at −50 °C [washed with Et_2O (5 cm^3)]. The mixture was stirred for 0.25 h before cooling to −78 °C and addition of enone **10** (307 mg, 1.41 mmol, 1 equiv.) in Et_2O (10 m^3) [washed with Et_2O (5 cm^3)]. Stirring was continued for 1 h during which period the temperature was raised to −20 °C. With stirring freshly distilled *trans*-oct-2-enal (0.4 cm^3, 2.81 mmol, 2 equiv.) was added and the reaction mixture was allowed to reach room temperature over a 15 h period. A saturated solution of NH_4Cl (50 cm^3) was added and the mixture was extracted with Et_2O (3×50 cm^3). The combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal afforded the crude products of the conjugate addition–Peterson olefination process. This mixture was dissolved in THF (4 cm^3) and at room temperature a solution of acetic acid (12 cm^3) in H_2O (6 cm^3) was added dropwise. The mixture was stirred at room temperature for 15 h before EtOAc (50 cm^3) and a saturated solution of $NaHCO_3$ (100 cm^3) were added. The resultant aqueous layer was further extracted with EtOAc (3×50 cm^3) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by addition of silica (ca. 15 g), solvent removal in vacuo and purification by flash column chromatography (Hex–EtOAc; 9:1→3:1) afforded initially *cis*-**11** (130 mg, 25%) as a viscous yellow oil. R_f=0.15 (Hex–EtOAc; 3:1); ν_{max} (neat/cm^{-1}) 3404, 3059, 2928, 2855, 1731, 1708, 1623, 1590, 1459; *m/z* (ES) 409 (MK^+, 100%), 393 (MNa^+, 50%); found 393.2774, $C_{25}H_{38}O_2{\cdot}Na$ requires 393.2770 (+1.1 ppm); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, J=7.0 Hz, CH_3), 1.25–1.48 (17H, m, CH_2), 1.48–1.60 (3H, m, CH_2), 1.84 (1H, d, J=8.0 Hz, CH), 2.18 (2H, q, J=7.25 Hz, CH_2), 2.32 (1H, d, J=8.0 Hz, CH), 2.33–2.40 (1H, m, CH), 2.70 (1H, s, CH), 3.06 (1H, s, CH), 3.63 (2H, t, J=7.0 Hz, CH_2), 6.02 (1H, dt, J=7.25, 15.25 Hz, CH), 6.16–6.22 (2H, m, CH), 6.24 (1H, dd, J=1.0, 11.25 Hz, CH), 7.53 (1H, ddt, J=1.25, 11.25, 15.25 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.5, 25.8, 26.4, 28.7, 29.4, 29.8, 31.5, 32.8, 33.0, 38.7, 43.4, 45.8, 46.1, 47.9, 49.4, 55.8, 63.0, 127.0, 137.6, 137.8, 138.6, 140.6, 145.4, 208.8. Further elution gave *trans*-**11** (148 mg, 28%) as a pale yellow oil. R_f=0.1 (Hex–EtOAc; 3:1); *m/z* (ES) 393 (MNa^+, 100%); found 393.2787, $C_{25}H_{38}O_2{\cdot}Na$ requires 393.2770 (+4.4 ppm); ν_{max} (neat/cm^{-1}) 3429, 3059, 2927, 2855, 1700, 1624, 1623, 1598, 1460; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t,

J=7.0 Hz, CH_3), 1.24–1.50 (17H, m, CH_2), 1.54–1.60 (3H, m, CH_2), 1.91 (1H, d, J=7.5 Hz, CH), 2.19 (2H, q, J=7.0 Hz, CH_2), 2.39 (1H, d, J=7.5 Hz, CH), 2.65–2.69 (1H, m, CH), 2.73 (1H, s, CH), 3.02 (1H, s, CH), 3.64 (2H, t, J=6.5 Hz, CH_2), 6.16–6.24 (4H, m, CH), 6.84–6.88 (1H, m, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.5, 25.7, 26.5, 28.4, 29.4, 29.8, 31.4, 32.8, 33.5, 37.5, 43.2, 43.3, 46.4, 48.1, 49.6, 54.6, 63.0, 126.3, 133.4, 137.6, 138.8, 142.6, 146.9, 208.8.

3.1.4. (±)-7-{2-[*trans*-Oct-2-en-*cis*/*trans*-ylidene]-3-oxo-2,3,3a,4,7,7a-hexahydro-1H-4,7-methanoinden-1-yl}heptanoic acid methyl ester 12. At 0 °C a mixture of *cis*-**11** and *trans*-**11** (1.636 g, 4.42 mmol, 1 equiv.) [*cis*/*trans*; 60:40] in acetone (30 cm^3) was treated with a 1.28 mol dm^{-3} solution of chromic acid (7.3 cm^3, 9.34 mmol, 2.1 equiv.) in a dropwise fashion. Stirring was continued for 1 h at room temperature. Et_2O (50 cm^3) and H_2O (50 cm^3) were added and the resultant aqueous phase was further extracted with Et_2O (3×50 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. At room temperature the crude mixture of the isomeric carboxylic acids was dissolved in benzene (20 cm^3) and methanol (5 cm^3). A 2.0 mol dm^{-3} solution of (trimethylsilyl)diazomethane in hexane (3.0 cm^3, 5.94 mmol, 1.3 equiv.) was added and stirring was continued for 0.5 h. Silica (ca. 10 g) was added and the solvents were removed in vacuo. The crude mixture was then purified by flash column chromatography (Hex–EtOAc; 19:1→9:1) affording *cis*-**12** (425 mg, 24%) as a yellow oil. R_f=0.35 (Hex–EtOAc; 9:1); ν_{max} (neat/cm^{-1}) 2930, 2857, 1731, 1685, 1622, 1588, 1460; *m*/*z* (ES) 421 (MNa^+, 100%); found 421.2721, $C_{26}H_{38}O_3$·Na requires 421.2791 (+0.6 ppm); δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, J=7.0 Hz, CH_3), 1.25–1.36 (11H, m, CH_2), 1.37–1.46 (4H, m, CH_2), 1.47–1.57 (1H, m, CH_2), 1.58–1.77 (2H, m, CH_2), 1.83 (1H, d, J=8.0 Hz, CH), 2.18 (2H, q, J=7.25 Hz, CH_2), 2.31 (2H, t, J=7.5 Hz, CH_2), 2.33 (1H, d, J=8.0 Hz, CH), 2.33–2.38 (1H, m, CH), 2.70 (1H, s, CH), 3.07 (1H, s, CH), 3.66 (3H, s, CH_3), 6.02 (1H, dt, J=7.25, 15.0 Hz, CH), 6.15–6.21 (2H, m, CH), 6.24 (1H, dd, J=1.0, 11.25 Hz, CH), 7.52 (1H, ddt, J=1.25, 11.25, 15.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.5, 24.9, 26.3, 28.6, 29.1, 29.4, 31.5, 33.0, 34.0, 38.6, 43.3, 45.8, 46.1, 47.9, 49.4, 51.4, 55.8, 126.9, 137.6, 137.8, 138.5, 140.5, 145.4, 174.1, 208.8. Further elution afforded *trans*-**12** (283 mg, 16%) as a pale yellow oil. R_f=0.25 (Hex–EtOAc; 9:1); ν_{max} (neat/cm^{-1}) 2931, 2857, 1730, 1691, 1624, 1598, 1460, 1437; *m*/*z* (ES) 437 (MK^+, 100%), 421 (MNa^+, 10%); found 421.2709, $C_{26}H_{38}O_3$·Na requires 421.2719 (−2.3 ppm); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, J=7.0 Hz, CH_3), 1.23–1.38 (11H, m, CH_2), 1.40–1.48 (2H, m, CH_2), 1.53–1.66 (3H, m, CH_2), 1.91 (1H, d, J=7.5 Hz, CH), 2.21 (2H, q, J=7.0 Hz, CH_2), 2.29 (2H, t, J=7.5 Hz, CH_2), 2.37 (1H, d, J=7.5 Hz, CH), 2.64–2.68 (1H, m, CH), 2.74 (1H, s, CH), 3.05 (1H, s, CH), 3.68 (3H, s, CH_3), 6.17–6.24 (4H, m, CH), 6.84–6.88 (1H, m, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.4, 24.9, 26.3, 28.4, 29.1, 29.4, 31.4, 33.5, 34.0, 37.5, 43.2, 43.3, 46.3, 48.1, 49.6, 51.4, 54.6, 126.3, 133.4, 137.5, 138.7, 142.5, 146.9, 174.1, 208.8.

3.1.5. (±)-7-{2-[*trans*-Oct-2-en-*trans*-ylidene]-3-oxo-2,3,3a,4,7,7a-hexahydro-1H-4,7-methano inden-1-yl} heptanoic acid methyl ester 12. At room temperature, alcohol **11** (100 mg, 0.27 mmol, 1 equiv.) in DCM (6 cm^3) was treated with Dess–Martin's periodinane (149 mg, 0.35 mmol, 1.3 equiv.) and stirring was continued for 3 h. Et_2O (20 cm^3), saturated $NaHCO_3$ (10 cm^3) and Na_2SO_3 (10 cm^3) were added and the resultant aqueous layer was further extracted with Et_2O (4×10 cm^3). The combined extracts were dried over $MgSO_4$ and filtration, solvent removal under reduced pressure gave the aldehyde [R_f=0.45 (Hex–EtOAc; 3:1)]. At room temperature the crude aldehyde (ca. 0.27 mmol, 1 equiv.) was dissolved in a mixture of ^{t}BuOH (6 cm^3) and 2,3-dimethylbut-2-ene (4.0 cm^3) and a solution of $NaClO_2$ (450 mg, 4.98 mmol, 18 equiv.) and NaH_2PO_4 (450 mg, 3.75 mmol, 14 equiv.) in H_2O (5 cm^3) was added dropwise. Stirring was continued for 1.5 h before the volatile materials were removed under reduced pressure and the residue was dissolved in Et_2O (5 cm^3) and H_2O (5 cm^3). This mixture was acidified with 1.0 M HCl solution (ca. p*H* 3) and the resultant aqueous layer was further extracted with Et_2O (5×10 cm^3). The combined extracts were dried over $MgSO_4$. Filtration and solvent removal in vacuo gave the crude acid (ca.0.27 mmol, 1 equiv.), which was dissolved in PhH (18 cm^3) and MeOH (5 cm^3). A 2.0 M solution of (trimethylsilyl)diazomethane in hexane (0.14 cm^3, 0.28 mmol, 1.05 equiv.) was added. After stirring at room temperature for 1.5 h the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (Hex–EtOAc; 19:1→9:1). Thus, *trans*-**12** (82 mg, 76%) was isolated as a pale yellow oil, whose data corresponded with that described above.

3.1.6. 7-{5-[(*trans*)-Oct-2-en-(*cis*)-ylidene]-4-oxocyclopen-2-enyl}heptanoic acid methyl ester [*cis*-$\Delta^{12,14}$-15-deoxy-PG-J_1] 7. Under N_2 a solution of *cis*-**12** (277 mg, 0.696 mmol, 1 equiv.) and maleic anhydride (682 mg, 6.96 mmol, 10 equiv.) in DCM (8 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (0.7 cm^3, 0.7 mmol, 1 equiv.). The solution was then split into two dry microwavable vials under a nitrogen atmosphere. Each vial was irradiated (Smith Creator, 300 W) at 110 °C for two bursts of 100 s. The reaction mixture was then poured into a rapidly stirred saturated solution of $NaHCO_3$ (25 cm^3) and Et_2O (25 cm^3). This mixture was partitioned for 1 h before extraction and subsequent re-extraction of the aqueous phase with Et_2O (5×25 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed in vacuo. Purification by flash column chromatography (Hex–EtOAc; 9:1→3:1) gave *cis*-**7** (107 mg, 46%) as a viscous pale yellow oil. Further elution afforded *trans*-**7** (32 mg, 14%). R_f=0.3 (Hex–EtOAc; 4:1); ν_{max} (neat/cm^{-1}) 3054, 2930, 2858, 1732, 1682, 1630, 1608, 1582, 1436, 1370; *m*/*z* (ES) 355 (MNa^+, 100%); found 355.2252, $C_{21}H_{32}O_3$·Na requires 355.2249 (+0.8 ppm); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, J=7.0 Hz, CH_3), 1.26–1.37 (10H, m, CH_2), 1.42–1.53 (3H, m, CH_2), 1.57–1.66 (2H, m, CH_2), 1.68–1.77 (1H, m, CH_2), 2.22 (2H, dq, J=1.25, 7.0 Hz, CH_2), 2.30 (2H, t, J=7.5 Hz, CH_2), 3.28–3.35 (1H, m, CH), 3.67 (3H, s, CH_3), 6.06 (1H, dt, J=7.0, 15.25 Hz, CH), 6.28 (1H, dd, J=2.0, 6.0 Hz, CH), 6.37 (1H, d, J=11.0 Hz, CH), 7.43 (1H, dd, J=2.5, 6.0 Hz, CH), 7.69 (1H, ddt, J=1.25, 11.0, 15.25, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.5, 24.8, 26.1, 28.7, 28.9, 29.4, 31.5, 33.0, 33.3, 34.0, 45.6, 51.4, 126.3, 134.2, 135.8, 136.5, 145.6, 159.7, 174.1, 197.5.

3.1.7. 7-{5-[(*trans*)-Oct-2-en-(*trans*)-ylidene]-4-oxocyclopen-2-enyl}heptanoic acid methyl ester [*trans*-$\Delta^{12,14}$-15-deoxy-PG-J_1] 7. Following the procedure outlined above: under N_2, a solution of *trans*-**12** (252 mg, 0.633 mmol, 1 equiv.) in DCM (8 cm^3) was initially treated with a 1.0 M solution of $MeAlCl_2$ in hexane (0.65 cm^3, 0.65 mmol, 1 equiv.) then split into two dry microwavable vials. Each vial was irradiated (Smith Creator, 300 W) at 110 °C for two bursts of 100 s. The reaction mixture was then poured into a rapidly stirred saturated solution of $NaHCO_3$ (25 cm^3) and Et_2O (25 cm^3). This mixture was partitioned for 0.5 h before extraction and subsequent re-extraction of the aqueous phase with Et_2O (5×25 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed in vacuo. Purification by flash column chromatography (Hex–EtOAc; 9:1→3:1) gave initially *cis*-**7** (30 mg, 14%), then *trans*-**7** (110 mg, 52%) as viscous yellow oils. R_f=0.2 (Hex–EtOAc; 4:1); ν_{max} (neat/cm^{-1}) 3054, 2931, 2858, 1734, 1690, 1631, 1579, 1437; *m/z* (CI) 333 (MH^+, 25%), 265 (100%); found 333.24347, $C_{21}H_{32}O_3$·H requires 333.24298 (+1.6 ppm); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, *J*=7.0 Hz, CH_3), 1.27–1.36 (10H, m, CH_2), 1.45 (2H, pent, *J*=7.0 Hz, CH_2), 1.53–1.65 (3H, m, CH_2), 1.81–1.92 (1H, m, CH_2), 2.22 (2H, q, *J*=7.0 Hz, CH_2), 2.29 (2H, t, *J*=7.5 Hz, CH_2), 3.51–3.57 (1H, m, CH), 3.65 (3H, s, CH_3), 6.17–6.32 (2H, m, CH), 6.35 (1H, dd, *J*=2.0, 6.0 Hz, CH), 6.93 (1H, d, *J*=11.0 Hz, CH), 7.52 (1H, ddd, *J*=1.0, 2.5, 6.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.5, 24.8, 25.8, 28.5, 29.0, 29.4, 31.4, 32.9, 33.4, 34.0, 43.5, 51.4, 125.7, 131.3, 135.2, 135.6, 146.5, 160.9, 174.1, 197.5.

3.1.8. (3*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-[7-(*tert*-butyldimethylsilyloxy)heptyl]-2-[*trans*-octylidene]cyclopentanone 15. Under N_2, a stirred mixture of magnesium turnings (372 mg, 15.31 mmol, 2.2 equiv.) and a spatula tip of I_2 in Et_2O (15 cm^3) was treated dropwise with 1-*tert*-butyldimethylsilyloxy-7-bromoheptane (2.36 g, 7.62 mmol, 1.08 equiv.) at room temperature. The resultant mixture was stirred at room temperature for 3 h. The resultant Grignard reagent was transferred to a pre-cooled mixture of CuI (116 mg, 0.61 mmol, 0.1 equiv.) in Et_2O (8 cm^3) at −78 °C and this mixture was allowed to warm gradually to 0 °C over 1 h. The resultant mixture was then re-cooled to −78 °C, and a solution of **13**[16] (1.58 g, 7.06 mmol, 1 equiv.) in Et_2O (6 cm^3) was added dropwise. After stirring at −78 °C for 30 min, neat octanal (1.10 g, 8.47 mmol, 1.2 equiv.) was introduced and the mixture was stirred at −78 °C overnight. The reaction was quenched with addition of a 1:4 mixture of conc. ammonia to sat. ammonium chloride (20 cm^3) and stirred until the organic phase had clearly separated. The organic layer was separated and the aqueous layer was extracted using EtOAc (3×50 cm^3). The combined organic extracts were washed with sat. NaCl solution, dried over $MgSO_4$ and concentrated to affording the crude alcohol **14** (4.29 g), which was used in the next reaction directly. To a stirred mixture of the alcohol **14** (4.29 g, 7.06 mmol, 1 equiv.) and *N*,*N*-dimethylaminopyridine (4.31 g, 35.3 mmol, 5 equiv.) in dichloromethane (30 cm^3) was added slowly methanesulfonyl chloride (0.90 g, 7.77 mmol, 1.1 equiv.) at room temperature. The reaction mixture was stirred overnight before dilution with Et_2O (50 cm^3) and 2 M dilute HCl (20 cm^3). The organic layer was separated and the aqueous layer was extracted using ether (3×50 cm^3). The combined organic layers were washed with saturated NaCl solution, dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash column chromatography (Hex–Et_2O 19:1→9:1) to yield the ketone **15** (1.35 g, 34%) as a viscous oil. $[\alpha]_D$=−31.8 (*c*=4.4, $CHCl_3$); ν_{max} (neat/cm^{-1}) 2927, 2855, 1726, 1651, 1471, 1255, 1098, 1071; *m/z* (ES) 575 (MNa^+, 100%), 379 (50%), 291 (38%); found 575.4301, $C_{32}H_{64}O_3Si_2$·Na requires 575.4292 (+1.6 ppm); δ_H (400 MHz, $CDCl_3$) 0.06 (12H, s, CH_3), 0.84 (9H, s, CH_3), 0.89–0.92 (12H, m, CH_3), 1.60–1.26 (22H, m, CH_2), 2.12–2.16 (2H, m, CH_2), 2.20 (1H, d, *J*=18.0 Hz, 5-CH_2), 2.55 (1H, dd, *J*=5.0, 18.0 Hz, 5-CH_2), 2.78 (1H, m, 3-CH), 3.60 (2H, t, *J*=6.5 Hz, CH_2), 4.24 (1H, d, *J*=5.0 Hz, 4-CH), 6.60 (1H, dt, *J*=1.5, 8.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) −5.0, −4.95, −4.4, −4.35, 14.3, 18.1, 18.6, 22.9, 25.95, 26.0, 26.05, 26.1, 26.25, 26.3, 26.35, 27.9, 29.0, 29.4, 29.6, 29.65, 29.7, 30.0, 31.9, 33.1, 33.5, 46.6, 49.5, 63.5, 72.0, 138.0, 140.6, 216.6.

3.1.9. (3*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-(7-hydroxyheptyl)-2-[*trans*-octylidene] cyclopentanone 16 and (4*R*)-4-(7-hydroxyheptyl)-5-[*trans*-octylidene]cyclopent-2-enone 17. To a stirred mixture of the ketone **15** (218 mg, 0.394 mmol) in THF (0.5 cm^3) was added H_2O (0.5 cm^3) and then AcOH (1.5 cm^3) at room temperature. The resultant mixture was stirred at rt for 4 days until TLC analysis indicated that the reaction was complete. The reaction was quenched on addition of sat. $NaHCO_3$ solution (15 cm^3) and the resulting mixture was extracted with EtOAc (3×15 cm^3). The combined organic layers were washed with brine (15 cm^3), dried over $MgSO_4$ and concentrated in vacuo, whereupon the residue was purified by column chromatography (Hex–Et_2O; 9:1→1:1) thus yielding the hydroxyketone **16** (70 mg, 40%) as a colourless oil. $[\alpha]_D$=−30.9 (*c*=6.9, $CHCl_3$); ν_{max} (neat/cm^{-1}) 3443, 2926, 2854, 1724, 1650; *m/z* (ES) 461 (MNa^+, 100%); found 461.3431, $C_{26}H_{50}O_3Si$·Na requires 461.3427 (+0.9 ppm); δ_H (400 MHz, $CDCl_3$) 0.06 (3H, s, CH_3), 0.07 (3H, s, CH_3), 0.85 (9H, s, CH_3), 0.89 (3H, t, *J*=7.0 Hz, CH_3), 1.60–1.20 (23H, m, OH, CH_2), 2.12–2.18 (2H, m, CH_2), 2.26 (1H, d, *J*=18.0 Hz, 5-CH_2), 2.56 (1H, dd, *J*=5.0, 18.0 Hz, 5-CH_2), 2.70–2.78 (1H, m, 3-CH), 3.65 (2H, t, *J*=6.5 Hz, CH_2), 4.24 (1H, d, *J*=5.0 Hz, 4-CH), 6.61 (1H, dt, *J*=1.5, 7.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) −4.45, −4.4, 14.2, 18.1, 22.8, 25.75, 25.8, 25.85, 25.9, 27.8, 28.9, 29.3, 29.5, 29.55, 29.6, 29.9, 31.9, 32.9, 33.2, 46.5, 49.4, 63.1, 74.9, 138.0, 140.4, 205.8. Further elution gave **17** (24 mg, 20%) as a colourless oil. $[\alpha]_D$=−145 (*c*=4.15, $CHCl_3$); ν_{max} (neat/cm^{-1}) 3429, 2926, 2855, 1696, 1650; *m/z* (CI) 307 (MH^+, 100%); found 307.2642, $C_{20}H_{35}O_2$ requires 307.2637 (+2.0 ppm); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, *J*=7.0 Hz, CH_3), 1.47 (1H, s, OH), 1.20–1.90 (22H, m, CH_2), 2.18–2.30 (2H, m, CH_2), 3.44–3.50 (1H, m, 4-CH), 3.63 (2H, t, *J*=7.0 Hz, CH_2), 6.32 (1H, dd, *J*=2.0, 6.0 Hz, 2-CH), 6.55 (1H, t, *J*=7.5 Hz, CH), 7.52 (1H, dd, *J*=2.5, 6.0 Hz, 3-CH); δ_C (100 MHz, $CDCl_3$) 22.8, 25.7, 25.8, 28.7, 29.1, 29.2, 29.3, 29.5, 29.8, 30.4, 31.7, 32.5, 32.8, 43.5, 63.1, 135.0, 136.0, 138.0, 162.0, 197.2.

3.1.10. (3*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-(6-carboxyhexyl)-2-[*trans*-octylidene] cyclopentanone 18. To a solution of the alcohol **16** (102 mg, 0.23 mmol, 1 equiv.) in

dichloromethane (2.5 cm^3) was added Dess–Martin's periodinane (128 mg, 0.30 mmol, 1.3 equiv.) at room temperature. The resulting mixture was stirred for 1 h. Saturated aqueous solutions of Na_2CO_3 (3 cm^3) and Na_2SO_3 (3 cm^3) were added to quench the reaction, and the resultant mixture was extracted with Et_2O (3×10 cm^3); the combined organic layers were dried over $MgSO_4$, filtered and concentrated to yield the crude aldehyde which was used directly in the next step without further purification. To a mixture of the aldehyde (ca. 0.23 mmol, 1 equiv.), *tert*-butyl alcohol (5.0 cm^3) and 2,3-dimethylbut-2-ene (3.1 cm^3), H_2O (3.0 cm^3), NaH_2PO_4 (388 mg, 3.2 mmol, 14 equiv.) and $NaClO_2$ (388 mg, 4.3 mmol, 19 equiv.) were added sequentially. The resulting mixture was stirred at room temperature for 16 h. Aqueous 2 M HCl was added to acidify the mixture, followed by extraction with Et_2O (30 cm^3). The extract was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (Hex–Et_2O–AcOH; 3:1:0.01) to yield the carboxylic acid **18** (97 mg, 93%) as a pale oil. $[\alpha]_D$=−25.4 (c=4.25, $CHCl_3$); ν_{max} (neat/cm^{-1}) 3000, 2927, 2856, 1710, 1647; *m/z* (ES) 453 (MH^+, 100%), 371 (22%), 321 (32%); found 453.3402, $C_{26}H_{49}O_4Si$ requires 453.3400 (+0.4 ppm); δ_H (400 MHz, $CDCl_3$) 0.05 (3H, s, CH_3), 0.06 (3H, s, CH_3), 0.84 (9H, s, CH_3), 0.88 (3H, t, J=7.5 Hz, CH_3), 1.19–1.88 (20H, m, CH_2), 2.09–2.15 (2H, m, CH_2), 2.24 (1H, d, J=18.5 Hz, 5-CH_2), 2.34 (2H, t, J=7.5 Hz, CH_2), 2.55 (1H, dd, J=5.0, 18.5 Hz, 5-CH_2), 2.77–2.81 (1H, m, 3-CH), 4.24 (1H, d, J=5.0 Hz, 4-CH), 6.61 (1H, dt, J=1.5, 7.0 Hz, CH), 6.80–7.01 (1H, s(br), CO_2H); δ_C (100 MHz, $CDCl_3$) −4.45, −4.4, 14.8, 18.6, 22.9, 25.0, 25.95, 26.0, 26.05, 27.8, 29.0, 29.4, 29.5, 29.6, 29.7, 29.8, 32.0, 33.4, 34.5, 46.6, 49.5, 72.0, 138.2, 140.5, 179.3, 206.0.

3.1.11. (4*R*)-4-(6-Carboxyhexyl)-5-[*trans*-octylidene]-cyclopent-2-enone [*epi*-8*R*-Δ^{12}-15-deoxy-PG-J_1] 19. To a solution of the alcohol **17** (99 mg, 0.32 mmol, 1 equiv.) in DCM (2.2 cm^3) was added Dess–Martin's periodinane (178 mg, 0.42 mmol, 1.3 equiv.) at room temperature. The resulting mixture was stirred until TLC analysis indicated that the reaction was complete. Then sat. aqueous Na_2CO_3 (3 cm^3) and sat. aqueous Na_2SO_3 (3 cm^3) were added and the resultant mixture was extracted with Et_2O (3×10 cm^3). The combined organic solutions were dried over $MgSO_4$, filtered and concentrated to yield the crude aldehyde, which was used directly in the next step without further purification. To a mixture of the aldehyde (0.75 mmol, 1 equiv.), *tert*-butyl alcohol (6.8 cm^3) and 2,3-dimethylbut-2-ene (4.3 cm^3) was added sequentially H_2O (4.0 cm^3), NaH_2PO_4 (533 mg, 4.4 mmol, 14 equiv.) and $NaClO_2$ (533 mg, 5.9 mmol, 18 equiv.) at room temperature. The resulting mixture was stirred for 16 h. Work-up as described above gave the crude product, which was purified by flash column chromatography (Hex–Et_2O–AcOH; 3:1:0.01) to yield the carboxylic acid **19** (27 mg, 27%) as a pale oil. $[\alpha]_D$=−96.8 (c=2.2, $CHCl_3$); ν_{max} (neat/cm^{-1}) 3000, 2927, 2885, 1720, 1709, 1647; *m/z* (ES) 343 (MNa^+, 63%); found 343.2234, $C_{20}H_{32}O_3Na$ requires 343.2249 (−4.4 ppm); δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, J=7.0 Hz, CH_3), 1.10–1.85 (20H, m, CH_2), 2.24 (2H, t, J=7.5 Hz, CH_2), 2.34 (2H, t, J=7.5 Hz, CH_2), 3.45–3.52 (1H, m, 4-CH), 6.34 (1H, dd, J=2.0, 6.0 Hz, 2-CH), 6.56 (1H, t, J=7.5 Hz, CH), 7.50–7.56 (1H, m, 3-CH); δ_C (100 MHz, $CDCl_3$) 14.3, 22.9, 24.8, 25.9, 28.9, 29.2, 29.3, 29.4, 29.45, 29.7, 32.0, 32.6, 34.1, 43.6, 135.1, 136.3, 138.1, 162.1, 179.3, 197.3.

3.1.12. (4*R*)-4-(6-Carboxyhexyl)-5-[*trans*-octylidene]-cyclopent-2-enone methyl ester [*epi*-8*R*-Δ^{12}-15-deoxy-PG-J_1 methyl ester] 20. At room temperature a solution of **18** (60 mg, 0.13 mmol, 1 equiv.) in a mixture of benzene (10 cm^3) and MeOH (3 cm^3) was treated with a 2.0 M solution of (trimethylsilyl)diazomethane in hexane (0.1 cm^3, 0.2 mmol, 1.5 equiv.). Stirring was continued for 0.5 h before the solvent was removed under reduced pressure. Purification by flash column chromatography (Hex–Et_2O; 9:1) gave the methyl ester (50.5 mg, 81%) as a colourless oil. At 0 °C a solution of the methyl ester (16 mg, 0.03 mmol) in MeOH (2.5 cm^3) was treated with a 10% solution of Na_2CO_3 (2.5 cm^3). The reaction was warmed to room temperature over 2 h before a 1 M aqueous solution of HCl (2 cm^3) and water (5 cm^3) were added. The resultant solution was extracted with Et_2O (4×10 cm^3) and the combined organic extracts were dried over $MgSO_4$. Filtration, solvent removal in vacuo and purification by flash column chromatography (Hex–EtOAc; 4:1) gave **20** (9 mg, 78%) as a pale yellow oil. $[\alpha]_D$=−110 (c=0.9, $CDCl_3$); ν_{max} (neat/cm^{-1}) 2926, 2855, 1740, 1701, 1654; *m/z* (CI) 352 (MNH_4^+, 10%), 335 (MH^+, 100%); found 335.25857, $C_{21}H_{34}O_3{\cdot}H$ requires 335.25861 (−0.1 ppm); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, J=7.0 Hz, CH_3), 1.20–1.85 (14H, m, CH_2), 1.42–1.65 (5H, m, CH_2), 1.75–1.87 (1H, m, CH_2), 2.26 (2H, pent, J=7.5 Hz, CH_2), 2.29 (2H, t, J=7.5 Hz, CH_2), 3.44–3.52 (1H, m, 4-CH), 3.66 (3H, s, CH_3), 6.32 (1H, dd, J=1.75, 6.0 Hz, 2-CH), 6.56 (1H, t, J=7.5 Hz, CH), 7.52 (1H, ddd, J=0.75, 2.5, 6.0 Hz, 3-CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.6, 24.8, 25.7, 28.7, 29.0, 29.1, 29.15, 29.4, 29.45, 31.7, 32.4, 34.0, 43.3, 51.4, 134.9, 135.8, 137.8, 161.7, 174.1, 196.9.

Acknowledgements

Charterhouse Therapeutics, Oxford are gratefully acknowledged for the provision of a lectureship (P. E.). The Ministry of Science and Technology and NIBGE, Pakistan are thanked for a PhD scholarship awarded to M. I. Professor Stan Roberts, University of Liverpool is thanked for helpful advice and discussions.

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