First enantioselective total synthesis of (8*S*, 12*R*, 15*S*) prostaglandin J₂

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Despite the stability and potential hazard of hydroxyiodinane oxide **20** have not been reported, it is well known that members of iodine oxides are quite thermally unstable. Caution must be paid in all manipulation involving iodine **20**

Experimental section

(3a*R*,4*R*,5*R*,6a*S*)-Benzoic acid 2-oxo-4-[(1*E*)-3-oxo-oct-1-enyl]-hexahydro-cyclopenta[*b*]furan-5-yl ester (**10**)

To a stirred mixture of NaH (60% dispersion in mineral oil, 38 mg, 0.952 mmol, 1.02 equiv) in dry THF (7.5 mL) under an argon atmosphere and cooled in an ice bath was added portionwise via cannula a solution of dimethyl (2-oxoheptyl)phosphonate (224 mg, 1.008 mmol, 1.08 equiv) in dry THF (12 mL). The cooling bath was removed and the mixture was stirred at rt for 1 h and then cooled to 0°C. A thick white precipitate was formed within 30 min at r.t. A solution of aldehyde **7** (255 mg, 0.933 mmol, 1.0 equiv) in dry THF (3 mL) was added dropwise via cannula to the cold phosphonate mixture. The resulting brown yellow mixture was stirred for 90 min at r.t.. After dropwise addition of acetic acid (81 μ L), the mixture was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (45 mL); the solution was washed twice with water (2x75 mL) and then with brine (2x15 mL). The aqueous phase was backwashed twice with EtOAc. The combined organic layers were dried on Na₂SO₄, filtered, and evaporated in vacuo to give a yellow oil (678 mg) that was purified by chromatography on silica gel (21 g). Elution with hexanes-EtOAc, 7:3, gave the desired enone **10** (276 mg, 80%) as a colourless oil. The ¹H NMR data are in complete agreement with the values tabulated in the literature¹⁰

¹H-NMR (300 MHz, CDCl₃) δ : 8.01-7.96 (m, 2H), 7.62-7.55 (m, 1H), 7.48-7.42 (m, 2H), 6.69 (dd, J = 7.4, 15.7 Hz, 1H), 6.24 (d, J = 15.7 Hz, 1H), 5.38-5.30 and 5.16-5.09 (2m, 1H), 2.96-2.85

and 2.70-2.46 (2m, 3H and 4H respectively), 2.32 (ddd, $J = 1.9, 4.7, 15.5$ Hz, 1H), 1.60 (quintuplet, $J = 7.4$ Hz, 2H), 1.36-1.21 (m, 4H), 0.88 (t, $J = 6.8$ Hz).

(3*aR*,4*R*,5*R*,6*aS*)-Benzoic acid 4-[(1*E*,3*S*)-3-hydroxy-oct-1-enyl]-2-oxo-hexahydro-cyclopenta[*b*]furan-5-yl ester (**11**)

A Schlenk flask equipped with a rubber septum was flame-dried and placed under an argon atmosphere. LiAlH₄ (1M in THF, 5.91 mL, 5.91 mmol, 3.5 equiv) was introduced via syringe at room temperature, then a solution of super dry EtOH (273 mg, 5.91 mmol, 3.5 equiv) in dry THF (6 mL) was added dropwise via cannula over a period of *ca.* 10 min with stirring. Subsequently a THF solution of (*S*)-BINOL (1.69 g, 5.91 mmol, 3.5 equiv in 9.9 mL of dry THF) was added dropwise, and the resulting mixture was stirred for an additional 30 min at rt and used for the asymmetric reduction. The (*S*)-BINAL-H reagent thus formed in THF was a homogeneous, milky mixture, which did not separate any precipitate; this mixture was cooled to -100°C and a solution of enone **10** (624 mg, 1.689 mmol, 1.0 equiv) in dry THF (21.3 mL) was added dropwise via cannula. After stirring for 1 h at the same temperature, the asymmetric reduction was completed. Excess BINAL-H was destroyed by addition of methanol (645 μL) at -78°C and the mixture was warmed to r.t.. Water (3 mL) and Et₂O (210 mL) were added; the resulting solution was stirred for *ca.* 1 h, then dried on MgSO₄, filtered, and concentrated under reduced pressure to give 2.25 g of a crude product. Column chromatography of this residue (silica gel, hexanes-Et₂O, 6:4 $\rightarrow$ 100% Et₂O) gave crystalline binaphthol (1.44 g) and allylic alcohol **11** (495 mg, 80%) as a colourless oil. HPLC analysis (10:1 hexanes-2-propanol as eluent, flow rate 2 mL/min) indicated the ratio of **11** (*t_R* 24.5 min) to the 15*R* isomer (*t_R* 18.3 min) to be 97:3. $[\alpha]_{\text{D}}^{20} = -74.7$ ($c = 0.55$, CH₂Cl₂); IR (liquid film) 3463, 2934, 2846, 1767, 1714, 1450, 1269, 1172, 1111, 965, 710 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃)

δ : 8.03-7.99 (m, 2H), 7.61-7.54 (m, 1H), 7.49-7.41 (m, 2H), 5.71-5.56 (m, 2H), 5.30-5.22 and 5.10-5.04 (2m, 1H), 4.14-4.06 (m, 1H), 2.94-2.46 (m, 5H), 2.24 (ddd, 1H, $J = 1.7, 5.2, 15.2$ Hz), 1.70 (br s, 1H), 1.56-1.42 and 1.36-1.17 (2m, 2H and 6H), 0.87 (t, $J = 6.7$ Hz, 3H); ^{13}C -NMR (75 MHz, CDCl_3) δ : 176.3 (0), 166.0 (0), 136.3 (1), 133.2 (1), 129.5 (2x1), 128.4 (2x1), 128.2 (1), 129.4 (0), 83.2 (1), 78.9 (1), 72.1 (1), 53.8 (1), 42.6 (1), 37.4 (2), 37.1 (2), 34.8 (2), 31.6 (2), 24.9 (2), 22.4 (2), 13.9 (3); ESI-MS (positive ions) m/z 395 (36) $[\text{M} + \text{Na}]^+$, 390 (100) $[\text{M} + \text{H}_2\text{O}]^+$, 354 (96) $[\text{M} - \text{H}_2\text{O}]^+$. Anal. Calcd. for $\text{C}_{22}\text{H}_{28}\text{O}_5$: C, 71.33; H, 7.07; O, 21.60. Found C, 71.37; H, 7.10.

(3a*R*,4*R*,5*R*,6a*S*)-Benzoic acid 4-[(1*E*,3*S*)-3-(*tert*-butyl-dimethyl-silanyloxy)-oct-1-enyl]-2-oxo-hexahydro-cyclopenta[*b*]furan-5-yl ester (**12**)

Imidazole (381 mg, 5.622 mmol, 2.4 equiv) and DMAP (87 mg, 0.702 mmol, 0.3 equiv) were added to a stirred solution of allylic alcohol **11** (870 mg, 2.343 mmol, 1.0 equiv) in dry DCM (21.6 mL) under an argon atmosphere. The resulting mixture was cooled in an ice bath and a solution of TBDMSCl (423 mg, 2.919 mmol, 1.2 equiv) in dry DCM (3.3 mL) was added dropwise via cannula. The cooling bath was removed and stirring was continued for 90 min at r.t.. More imidazole (159 mg, 2.343 mmol, 1.0 equiv) and TBDMSCl (105 mg, 0.702 mmol, 0.3 equiv) were added to force the reaction to completion. After stirring for an additional 4 h, the excess silylating agent was destroyed by addition of water and then of a saturated solution of NaHCO_3 . The mixture was then diluted with Et_2O and the two phases were separated. The aqueous solution was backwashed with ether, the combined organic layers were dried on MgSO_4 , filtered, and evaporated

in vacuo. The crude product was purified by column chromatography on silica gel; elution with hexanes-EtOAc, 9:1, gave the desired silyl ether **12** (1.08 g, 95%) as colourless needles, mp = 64-65°C; $[\alpha]_{\text{D}}^{20} = -81.4$ ($c = 0.88$, CH_2Cl_2); IR (liquid film) 2925, 2855, 1771, 1714, 1454, 1265, 1172, 1111, 1071, 961, 833, 772, 710 cm^{-1} ; $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 8.03-7.99 (m, 2H), 7.62-7.54 (m, 1H), 7.48-7.43 (m, 2H), 5.63 (dd, $J = 5.7, 15.5$ Hz, 1H), 5.50 (dd, $J = 6.1, 15.5$ Hz, 1H), 5.27-5.19 and 5.10-5.04 (2m, 2x1H), 4.08 (q, $J = 6.1$ Hz, 1H), 2.93-2.47 (m, 5H), 2.21 (ddd, $J = 2.1, 5.6, 15.5$ Hz, 1H), 1.55-1.35, 1.35-1.17 (2m, 2H and 6H), 0.85 (overlapped s and t, 12H), 0.02-0.04 (2s, 2x3H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 176.3 (0), 165.8 (0), 137.1 (1), 133.1 (1), 129.5 (2x1), 128.3 (2x1), 126.8 (1), 129.4 (0), 83.0 (1), 78.8 (1), 72.7 (1), 53.4 (1), 42.4 (1), 38.0 (2), 37.4 (2), 34.5 (2), 31.6 (2), 24.7 (2), 22.4 (2), (3x3), 18.0 (0), 13.8 (3), -4.5 (3), -5.0 (3); ESI-MS (positive ions) m/z 511 (84) $[\text{M} + \text{Na} + \text{H}]^+$, 506 (100) $[\text{M} + \text{H}_2\text{O} + \text{H}]^+$, 355 (35) $[\text{M} - \text{TBSOH}]^+$. Anal. Calcd. for $\text{C}_{28}\text{H}_{42}\text{O}_5\text{Si}$: C, 69.10; H, 8.70; O, 16.44; Si, 5.77. Found C, 69.14; H, 8.68.

(3*aR*,4*R*,5*R*,6*aS*)-4-[(1*E*,3*S*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-oct-1-enyl]-5-hydroxy-hexahydro-cyclopenta[*b*]furan-2-one (**13**)

A catalytic amount of potassium carbonate was added to a stirred solution of benzoate **12** (120 mg, 0.247 mmol, 1.0 equiv) in methanol (3.6 mL). The mixture was stirred at room temperature for 36 h, then diluted with DCM and filtered on a short pad of Celite to remove the inorganic base. After washing Celite exhaustively with DCM, the organic solution was concentrated under reduced pressure. Column chromatography of the residue (silica gel, hexanes-EtOAc, 9:1 → 8:2) afforded the desired alcohol-lactone **13** (90 mg, 98%) as a colourless oil, $[\alpha]_D^{20} = -16$ ($c = 0.73$, CH_2Cl_2); IR (liquid film) 3392, 2925, 2846, 1758, 1172, 1080, 1031, 965 cm^{-1} ; $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 5.61 (dd, $J = 5.7, 15.3$ Hz, 1H), 5.42 (dd, $J = 9.0, 15.3$ Hz, 1H), 4.99-4.89 (m, 1H), 4.15-3.97 (m, 2H), 2.85-2.30 (m, 5H), 2.01 (ddd, $J = 2.8, 6.9, 15.0$ Hz, 1H), 1.56-1.40 and 1.38-1.19 (2m, 2H and 6H), 0.91 (overlapped s and t, 9H and 3H), 0.06, 0.03 (s and s, 3H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 176.7 (0), 137.7 (1), 127.5 (1), 82.6 (1), 76.9 (1), 72.3 (1), 56.0 (1), 42.6 (1), 39.9 (2), 38.2 (2), 34.3 (2), 31.6 (2), 24.9 (2), 22.5 (2), 25.8 (3x3), 18.2 (0), 13.9 (3), -4.4 (3), -4.8 (3); ESI-MS (positive ions) m/z 401 (100) $[\text{M} + \text{H}_2\text{O}]^+$. Anal. Calcd. for $\text{C}_{21}\text{H}_{38}\text{O}_4\text{Si}$: C, 65.92; H, 10.01; O, 16.73; Si, 7.34. Found C, 65.88; H, 10.03.

(3a*R*,4*R*,6a*S*)-4-[(1*E*,3*S*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-oct-1-enyl]-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (**14**)

To a stirred solution of the alcohol-lactone **13** (300 mg, 0.786 mmol, 1.0 equiv) in dry THF (1.75 mL) under an argon atmosphere was added solid triphenylphosphine (228 mg, 0.873 mmol, 1.11 equiv), followed by diethylazodicarboxylate (152 mg, 0.873 mmol, 1.11 equiv) dropwise over five minutes. A slight exothermic reaction was noticed. After stirring the mixture for 2 h at r.t., further Ph_3P (129 mg, 0.471 mmol, 0.6 equiv) and DEAD (82 mg, 0.471 mmol, 0.6 equiv) were added to force the reaction to completion. Stirring was continued for an additional 5 h, then the reaction mixture was concentrated in vacuo. Column chromatography of the residue (silica gel, hexanes-EtOAc, 98:2 $\rightarrow$ 97:3) afforded the expected olefin **14** (222 mg, 76%), $[\alpha]_{\text{D}}^{20} = +203.5$ ($c = 1.0$, CH_2Cl_2); IR (liquid film) 2943, 2855, 1771, 1463, 1353, 1252, 1159, 1071, 1023, 965, 833, 776 cm^{-1} ; ^1H -NMR (300 MHz, CDCl_3) δ : 6.04-5.97 and 5.97-5.91 (m and m, 1H), 5.58-5.51 (m, 1H), 5.50-5.43 (m, 2H), 4.10-4.01 (m, 1H), 3.28-3.21 (m, 1H), 2.93-2.75 (m, 2H), 2.47-2.35 (m, 1H), 1.57-1.41, 1.41-1.23 (m and m, 2H and 6H), 0.90 (overlapped s and t, 9H and 3H), 0.05 and 0.02 (s and s, 3H each); ^{13}C -NMR (75 MHz, CDCl_3) δ : 176.7 (0); 140.2 (1), 134.9 (1), 129.8 (1), 129.1 (1), 89.4 (1), 73.4 (1), 55.1 (1), 42.8 (1), 38.1 (2), 34.9 (2), 31.6 (2), 24.8 (2), 22.5 (2), 25.8 (3x3), 18.2 (0), 13.9 (3), -4.3 (3), -4.8 (3); EIMS (70 eV) m/z 365 (4) $[\text{M} + \text{H}]^+$, 293 (37), 233 (8), 207 (10), 187 (28), 161 (10), 131 (18), 117 (27), 105 (10), 91 (17), 75 (100), 57 (18), 41 (45). Anal. Calcd. for $\text{C}_{21}\text{H}_{36}\text{O}_3\text{Si}$: C, 69.18; H, 9.95; O, 13.16; Si, 7.70. Found C, 69.21; H, 10.00.

(3a*R*,4*S*,6a*S*)-4-[(1*E*,3*S*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-oct-1-enyl]-3,3a,4,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-ol (**14a**)

DIBAL-H (1M in hexanes, 693 μ L, 0.693 mmol, 1.2 equiv) was added dropwise via syringe to a stirred solution of lactone **14** (210 mg, 0.576 mmol, 1.0 equiv) in dry DCM (4 mL) precooled to -78°C under an argon atmosphere. After stirring for 30 min at the same temperature, more DIBAL-H (1M in hexanes, 180 μ L, 0.171 mmol, 0.3 equiv) was added to force the reaction to completion. Stirring was continued for an additional 15 min and then the excess reducing agent was destroyed by addition of a saturated solution of NH_4Cl at -78°C . The mixture was gradually warmed to room temperature and diluted with DCM, followed by addition of a saturated solution of sodium and potassium tartrate (6 mL). The two phases were separated and the aqueous one was backwashed with DCM; the combined organic layers were dried on MgSO_4 , filtered, and evaporated in vacuo to give the expected lactol **14a** (203 mg, 96%) as a pure product, that was employed in the following step without further purification.

(5*Z*)-7-[(1*R*,2*R*,5*S*)-2-[(1*E*,3*S*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-oct-1-enyl]-5-hydroxy-cyclopent-3-enyl]-hept-5-enoic acid (**15**)

Freshly sublimed potassium *tert*-butoxide (1.1 g, 9.84 mmol, 8.0 eq) was added portionwise to a suspension of (4-carboxybutyl)-triphenylphosphonium bromide (2.18 g, 4.917 mmol, 4.0 equiv) in dry THF (15.6 mL) under an argon atmosphere at r.t.. After having been stirred for 30 min, the solution became orange and a THF solution (12 mL) of lactol **14a** (450 mg, 1.23 mmol, 1.0 equiv) was added dropwise via cannula at r.t.. Stirring was continued for an additional 1 h and then the reaction was quenched by adding a saturated solution of NH₄Cl (51 mL) and acetic acid (600 μ L, 1.05 equiv with respect to *t*BuOK); Et₂O was added to the mixture and the organic layer was separated whereas the aqueous phase was extracted with an additional Et₂O. The organic phases were combined, dried on MgSO₄, filtered, and concentrated at reduced pressure. The crude acid (712 mg) was purified on silica gel. Elution with hexanes-EtOAc, 9:1 $\rightarrow$ 7:3, afforded hydroxy acid **15** (810 mg, 84%) as a pale yellow oil, $[\alpha]_D^{20} = +105$ ($c = 1.04$, CH₂Cl₂); IR (liquid film) 3600-3100 (*OH* and *COOH*), 2960, 2933, 2855, 1709, 1458, 1405, 1362, 1251, 1075, 1027, 1005, 965, 868, 833, 776, 736 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ : 5.99-5.93 and 5.93-5.89 (m and m, 1H each), 5.62-5.35 (m, 4H), 4.67 (dt, $J = 6.0, 1.7$ Hz, 1H), 4.07 (br q, $J = 6.2$ Hz, 1H), 3.05 (td, $J = 7.6, 1.9$ Hz, 1H), 2.38 (t, $J = 7.4$ Hz, 2H), 2.35-2.11 (m, 4H), 1.82-1.66 (m, 3H), 1.58-1.41 (m, 2H), 1.30 (br s, 6H), 0.90 (overlapped s and t, 9H and 3H), 0.06, 0.04 (s and s, 3H each); ¹³C-NMR (75 MHz, CDCl₃) δ : 178.3 (0), 139.6 (1), 134.6 (1), 132.7 (1), 131.2 (1), 129.8 (1), 129.2 (1), 76.5 (1),

73.4 (1), 52.1 (1), 50.0 (1), 38.2 (2), 33.1 (2), 31.7 (2), 26.4 (2), 25.2 (2), 25.0 (2), 24.4 (2), 22.5 (2), 25.8 (3x3), 18.2 (0), 13.9 (3), -4.3 (3), -4.8 (3); ESI-MS (APCI) m/z 450 (9) $[M]^+$, 317 (100) $[M - TBSOH]^+$. Anal. Calcd. for $C_{26}H_{46}O_4Si$: C, 69.28; H, 10.29; O, 14.20; Si, 6.23. Found C, 69.22; H, 10.27.

(5Z)-7-[(1R,2R,5S)-2-[(1E,3S)-3-(*tert*-Butyl-dimethyl-silanyloxy)-oct-1-enyl]-5-hydroxy-cyclopent-3-enyl]-hept-5-enoic acid methyl ester (**9**)

A stirred solution of hydroxy acid **15** (747 mg, 1.656 mmol) in Et_2O (16.5 mL) was cooled in an ice bath and an ethereal solution of CH_2N_2 was added in excess. Evaporation of the volatiles left a residue (699 mg) that was purified by flash chromatography (silica gel; hexanes- $EtOAc$, 97:3 $\rightarrow$ 9:1) to give the expected methyl ester **9** (693 mg, 90%) as a pale yellow oil; $[\alpha]_D^{20} = +105.5$ ($c = 1.025$, CH_2Cl_2); IR (liquid film) 3422, 2929, 1742, 1462, 1251, 1078, 968, 836, 775 cm^{-1} ; 1H -NMR (300 MHz, $CDCl_3$) δ : 5.99-5.93 and 5.93-5.86 (m and m, 1H each), 5.63-5.33 (m, 4H), 4.66 (dt, $J = 6.2, 1.7$ Hz, 1H), 4.04 (br q, $J = 6.0$ Hz, 1H), 3.68 (s, 3H), 3.04 (td, $J = 1.7, 7.6$ Hz, 1H), 2.40-2.09 (2m, 2H each), 2.34 (t, $J = 7.6$ Hz, 2H), 1.83-1.67 (m, 3H), 1.55-1.39 (m, 2H), 1.30 (br s, 6H), 0.99 (overlapped s and t, 9H and 3H), 0.06 and 0.03 (s and s, 3H each); ^{13}C -NMR (75 MHz, $CDCl_3$) δ : 174.0 (0), 139.4 (1), 134.6 (1), 132.7 (1), 131.2 (1), 129.6 (1), 129.3 (1), 76.4 (1), 73.3 (1), 52.1 (1), 51.3 (3), 50.0 (1), 38.2 (2), 33.3 (2), 31.6 (2), 26.5 (2), 25.2 (2), 24.9 (2), 24.6 (2), 22.5 (2), 25.8 (3x3), 18.1 (0i), 13.9 (3), -4.3 (3), -4.9 (3); EIMS (70 eV) m/z 447 (2) $[M - H_2O]^+$; 407 (22), 389 (10), 375 (21), 357 (8), 315 (19), 305 (8), 283 (12), 265 (10), 241 (18), 215 (10), 199 (15), 169 (12),

157 (10), 143 (11), 129 (21), 117 (27), 105 (19), 91 (16), 75 (100), 55 (27), 41 (49). Anal. Calcd. for $C_{27}H_{48}O_4Si$: C, 69.78; H, 10.41; O, 13.77; Si, 6.04. Found C, 69.81; H, 10.44.

(5*Z*)-7-[(1*R*,2*S*,5*R*)-2-[(1*E*,3*S*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-oct-1-enyl]-5-(2-nitrophenylselenanyl)-cyclopent-3-enyl]-hept-5-enoic acid methyl ester (**16**)

To a stirred solution of methyl ester **9** (585 mg, 1.26 mmol) in dry THF (15.6 mL) at r.t under an argon atmosphere was added solid, freshly sublimed (*o*-nitrophenyl) selenocyanate (432 mg, 1.89 mmol, 1.5 equiv), followed by *n*Bu₃P (410 mg, 2.028 mmol, 1.61 equiv) dropwise via a syringe. Stirring was continued for an additional 90 min; the reaction mixture was then diluted with EtOAc and the organic layer was washed with a saturated solution of NaHCO₃ and with brine, dried on MgSO₄, filtered, and concentrated in vacuo. Flash column chromatography (silica gel, hexanes-EtOAc, 98:2 → 95:5) of the residue gave selenide **16** (654 mg, 80%) as a brown yellow oil. $[\alpha]_D^{20} = -74.5$ ($c = 0.55$, CH₂Cl₂); IR (liquid film) 2930, 2856, 1738, 1591, 1567, 1516, 1462, 1332, 1304, 1250, 1096, 970, 837, 776, 730 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ : 8.28 (dd, $J = 1.4, 8.3$ Hz, 1H), 7.67 (dd, $J = 1.0, 8.1$ Hz, 1H), 7.53 (td, $J = 8.1, 1.4$ Hz, 1H), 7.34 (td, $J = 8.3, 1.4$ Hz, 1H), 5.94-5.88 and 5.77-5.73 (m and m, 1H each), 5.58-5.40 (m, 4H), 4.14-4.10 (m, 1H), 4.04 (br q, $J = 6.0$ Hz, 1H), 3.68 (s, 3H), 3.16-3.08 (m, 1H), 2.31 (t, $J = 7.5$ Hz, 2H), 2.36-2.27 and 2.16-2.02 (m and m, 2H each), 2.23-2.14 (m, 1H), 1.70 (quintuplet, $J = 7.5$ Hz, 2H), 1.54-1.37 (m, 2H), 1.29 (br s,

6H), 0.90 (s, 9H), 0.89 (t, 3H), 0.06 and 0.04 (s and s, 3H each); ^{13}C -NMR (75 MHz, CDCl_3) δ : 174.7 (0), 147.7 (0), 135.5 (0); 136.7 (1), 135.2 (1), 134.2 (1), 132.4 (1), 131.6 (1), 130.9 (1), 130.7 (1), 128.4 (1), 127.2 (1), 126.2 (1), 74.0 (1), 54.7 (1), 52.2 (3), 51.5 (1), 51.2 (1), 39.1 (2), 34.2 (2), 32.5 (2), 27.5 (2), 25.8 (2), 25.5 (2), 23.4 (2), 26.7 (3x3), 19.0 (0), 14.8 (3), -3.3 (3), -4.0 (0); ESI-MS (positive ions) m/z 674 (57) $[\text{M} + \text{Na} + 2\text{H}]^+$, 672 (100) $[\text{M} + \text{Na}]^+$, 670 (52) $[\text{M} + \text{Na} - 2\text{H}]^+$. Anal. Calcd. for $\text{C}_{33}\text{H}_{51}\text{NO}_5\text{SeSi}$: C, 61.09; H, 7.92; N, 2.16; O, 12.33; Se, 12.17; Si, 4.33. Found C, 61.12; H, 7.94.

(5Z)-7-[(1S,4S,5R)-5-[(1E,3S)-3-(*tert*-Butyl-dimethyl-silanyloxy)-oct-1-enyl]-4-hydroxy-cyclopent-2-enyl]-hept-5-enoic acid methyl ester (**8**)

To a stirred solution of selenide **16** (600 mg, 0.924 mmol) in dry THF (23.1 mL) under an argon atmosphere was added pyridine (300 μL) via a syringe at r.t.. The mixture was cooled to -20°C and 30% v/v hydrogen peroxide (1.3 mL, 12.93 mmol, 14 equiv) was added dropwise. Stirring was continued at the same temperature for an additional 48 h. The reaction was then quenched by adding water and diluted with EtOAc; the aqueous phase was extracted with EtOAc and the combined organic layers were washed with a saturated solution of NaHCO_3 and brine, dried on MgSO_4 , filtered, and evaporated in vacuo. Flash column chromatography (silica gel; hexanes-EtOAc, 9:1) of the residue afforded the desired transposed allylic alcohol **8** (240 mg), contaminated by an unidentified product, and a mixture of chromatographically inseparable olefins **19** (63 mg, 15%). Alcohol **8**: IR (liquid film) 3454, 2934, 2846, 1745, 1520, 1458, 1436, 1366, 1331, 1252,

1150, 1080, 970, 838, 772 cm^{-1} ; ^1H -NMR (300 MHz, CDCl_3) δ : 6.0-5.97 and 5.93-5.88 (m and m, 1H each), 5.72 and 5.59 (dd and dd, $J = 8.6, 15.8$ Hz and $J = 6.0, 15.8$ Hz, respectively, 1H each), 5.48-5.35 (m, 2H), 4.68-4.61 (m, 1H), 4.19-4.09 (m, 1H), 3.68 (s, 3H), 2.75-2.64 (m, 1H), 2.40-2.0 (m, 5H), 2.32 (t, $J = 7.6$ Hz, 2H), 1.70 (quintuplet, $J = 7.6$ Hz, 2H), 1.56-1.43 (m, 2H), 1.30 (br s, 6H), 0.91 (s, 9H), 0.90 (t, $J = 6.9$ Hz, 3H), 0.08 and 0.05 (s and s, 3H each); ^{13}C -NMR (75 MHz, CDCl_3) δ : 173.8 (0), 139.4 (1), 137.1 (1), 132.1 (1), 129.8 (1), 128.1 (1), 127.3 (1), 78.0 (1), 73.4 (1), 52.1 (1), 51.3 (3), 48.6 (1), 38.3 (2), 33.3 (2), 31.6 (2), 30.1 (2), 26.4 (2), 25.0 (2), 24.6 (2), 22.5 (2), 25.7 (3x3), 18.1 (0), 14.0 (3), -4.4 (3), -4.9 (3); EIMS (70 eV) m/z 447 (3) $[\text{M} - \text{H}_2\text{O}]^+$, 407 (20), 389 (4), 375 (11), 357 (4), 333 (2), 315 (28), 305 (7), 265 (9), 241 (10), 215 (11), 187 (20), 169 (10), 145 (11), 131 (22), 105 (21), 91 (28), 75 (100), 55 (34), 41 (52). Anal. Calcd. for $\text{C}_{27}\text{H}_{48}\text{O}_4\text{Si}$: C, 69.78; H, 10.41; O, 13.77; Si, 6.04. Found C, 69.82; H, 10.39.

Olefins **19**: IR (liquid film) 2954, 2929, 2857, 1742, 1462, 1436, 1361, 1250, 1150, 1078, 967, 873, 836, 775 cm^{-1} ; ^1H -NMR (300 MHz, CDCl_3) δ : 6.28 and 6.09 (dd and dd, $J = 7.9, 15.2$ Hz and $J = 6.4, 15.4$ Hz, 0.5H each), 5.60-5.21 (m, 5H), 4.09 (br q, $J = 5.7$ Hz, 1H), 3.66 and 3.65 (s and s, 1.5H each), 3.22-3.11 and 2.88-2.59 (m and m, 2H each), 2.37-2.21, 2.16-2.06 and 2.04-1.93 (m, m, and m, 2H), 1.77-1.61 (m, 2H), 1.55-1.43 (m, 2H), 1.27 (br s, 6H), 0.88 (overlapped s and q, 10H), 0.06, 0.03, 0.006, and -0.01 (s, s, s, and s, totally 6H); ^{13}C -NMR (75 MHz, CDCl_3) δ : 173.9 (0), 149.0 (0), 139.7 (0), 133.9 (1), 133.6 (1), 130.3 (1), 129.8 (1), 129.0 (1), 128.9 (1), 128.0 (1), 127.9 (1), 127.5 (1), 126.0 (1), 125.7 (1), 123.0 (1), 74.2 (1), 73.8 (1), 51.3 (3), 38.5 (2), 34.8 (2), 33.3 (2), 31.7 (2), 26.6 (2), 26.3 (2), 25.0 (2), 24.9 (2), 22.6 (2), 22.5 (2), 25.8 (3x3), 18.1 (0), 13.9 (3), -4.3 (3), -4.8 (3).

(5*Z*)-7-[(1*S*, 4*S*, 5*R*)-5-[(1*E*,3*S*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-oct-1-enyl]-4-hydroxy-cyclopent-2-enyl]-hept-5-enoic acid (**17**)

Methyl ester **8** (240 mg, 0.516 mmol, 1.0 equiv) was dissolved in MeOH (6.9 mL) and solid Ba(OH)₂·8H₂O (465 mg, 1.473 mmol, 4.0 equiv) was added in a single portion. Stirring was continued for 24 at room temperature, the reaction mixture was then diluted with brine and acidified with glacial acetic acid. EtOAc was added, the two phases were separated and the aqueous one was extracted with EtOAc. The combined organic layers were washed twice with brine, dried on MgSO₄, filtered, and concentrated in vacuo. Flash column chromatography of the residue (silica gel; hexanes-EtOAc, 9:1 → 6:4) afforded the desired hydroxy acid **17** (216 mg, 52% over two steps) as a pale yellow oil; $[\alpha]_D^{20} = +93$ ($c = 1.56$, CH₂Cl₂); IR (liquid film) 3600-3200 (*OH* and *COOH*), 2929, 2857, 1713, 1462, 1265, 1082, 973, 837, 741, 705 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ : 6.01-5.96 and 5.94-5.89 (m and m, 1H), 5.71 and 5.58 (dd and dd, $J = 8.1, 15.6$ Hz and $J = 6.2, 15.6$ Hz, respectively, 1H), 5.48-5.36 (m, 2H), 4.65 (dt, $J = 6.2, 1.9$ Hz, 1H), 4.12 (br q, $J = 6.2$ Hz, 1H), 2.76-2.64 (m, 1H), 2.42-1.96 (m, 5H), 2.36 (t, $J = 7.4$ Hz, 2H), 1.71 (quintuplet, $J = 7.4$ Hz, 2H), 1.60-1.43 (m, 2H), 1.30 (br s, 6H), 0.91 (overlapped s and t, 9H and 3H respectively), 0.08 and 0.07 (s and s, 3H); ¹³C-NMR (75 MHz, CDCl₃) δ : 178.7 (0), 139.4 (1), 137.0 (1), 132.1 (1), 129.7 (1), 128.3 (1), 127.3 (1), 78.0 (1), 73.6 (1), 52.1 (1), 48.6 (1), 38.3 (2), 33.2 (2), 31.6 (2), 30.2 (2), 26.4 (2), 25.0 (2), 24.4 (2), 22.5 (2), 25.8 (3x3), 18.2 (0), 13.9 (3), -4.3 (3), -4.8 (3); ESI-MS (positive ions) m/z 473 (37) [M + Na]⁺, 470 (65) [M + H₂O + 2H]⁺, 468 (100) [M + H₂O]⁺. Anal. Calcd. for C₂₆H₄₆O₄Si: C, 69.28; H, 10.29; O, 14.20; Si, 6.23. Found C, 69.33; H, 10.27.

(5*Z*)-7-[(1*S*,5*R*)-5-[(1*E*,3*S*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-oct-1-enyl]-4-oxo-cyclopent-2-enyl]-hept-5-enoic acid (**18**)

To a stirred solution of hydroxy acid **17** (93 mg, 0.206 mmol, 1.0 equiv) in dry DCM (21 mL) was added glacial acetic acid (15 mg, 0.248 mmol, 1.2 equiv) and solid periodinane **20** (90 mg, 0.227 mmol, 1.1 equiv) in a single portion. Stirring was continued for an additional 30 min until reaction completion. The mixture was then diluted with Et₂O, filtered on a short pad of silica gel-Celite, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel; hexanes-EtOAc, 9:1 → 100% EtOAc) afforded the desired cyclopentenone **18** (75 mg, 80%) as a pale yellow oil; $[\alpha]_D^{20} = +84.3$ ($c = 0.72$, CH₂Cl₂); IR (liquid film) 3600-3100 (*COOH*), 2930, 2857, 1713, 1589, 1463, 1360, 1257, 1197, 1140, 1111, 1083, 1005, 969, 836, 810, 776, 732, 670 cm⁻¹; ¹H-NMR (300 MHz, CD₂Cl₂) δ : 7.61 (dd, $J = 2.3, 5.7$ Hz, 1H), 6.14 (dd, $J = 1.9, 5.7$ Hz, 1H), 5.67-5.42 (m, 4H), 4.13 (br q, $J = 5.8$ Hz, 1H), 2.90-2.78 and 2.64 (m and dd, respectively, $J_{dd} = 2.8, 6.4$ Hz, 1H), 2.43-2.28 and 2.21-2.06 (m and m, 4H and 2H), 1.73 (quintuplet, $J = 7.3$ Hz, 2H), 1.56-1.42 (m, 2H), 1.31 (br s, 6H), 0.92 (s, 9H), 0.89 (t, 3H), 0.09 and 0.08 (s and s, 3H); ¹³C-NMR (75 MHz, CD₂Cl₂) δ : 209.1 (0), 178.7 (0), 166.6 (1), 137.7 (1), 133.5 (1), 132.0 (1), 127.6 (1), 126.3 (1), 74.0 (1), 55.2 (1), 48.8 (1), 39.0 (2), 33.8 (2), 32.6 (2), 31.7 (2), 27.3 (2), 25.7 (2), 25.3 (2), 23.4 (2), 26.4 (3x3), 23.4 (0), 14.6 (3), -3.7 (3), -4.3 (3); ESI-MS (positive ions) m/z 472 (35) [M + Na + H]⁺, 471 (50) [M + Na]⁺, 466 (41) [M + H₂O]⁺, 317 (100) [M – TBSOH]⁺. HRMS calcd. for C₂₆H₄₄O₄Si 448.3009, found 448.3007.

(5*Z*)-7-[(1*S*,5*R*)-5-((1*E*,3*S*)-3-Hydroxy-oct-1-enyl)-4-oxo-cyclopent-2-enyl]-hept-5-enoic acid (**1**)

Cyclopentenone **18** (36 mg, 80.22 μmol) was dissolved in CH_3CN (5.4 mL) in a Teflon test tube; the solution was cooled to $-20\text{ }^\circ\text{C}$ and 48% aq HF (150 μL) was added dropwise. The mixture was stirred for 4 h at the same temperature, then diluted with THF (7.8 mL, so that the ratio THF: CH_3CN was about 1.5:1) and quenched by addition of a pH $\approx$ 6.96 phosphate buffer (3 mL). The mixture was gradually warmed to r.t. and diluted with DCM. The aqueous phase was extracted with DCM (3 x 9 mL) and the combined organic layers were washed with water (2 x 9 mL) and with brine (2 x 9 mL), dried on MgSO_4 , filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (reverse phase RP-18; $\text{MeOH-H}_2\text{O}$, 55:45) yielded the desired PGJ₂ **1** (27 mg, 88%) as colourless oil $[\alpha]_{\text{D}}^{20} = +177$ ($c = 1$, CH_2Cl_2); IR (liquid film) 3600-3100 (*OH* and *COOH*), 2928, 1705, 1582, 1195, 734 cm^{-1} ; $^1\text{H-NMR}$ (300 MHz, CD_2Cl_2) δ : 7.66 (d, $J = 5.2$ Hz, 1H), 6.15 (d, $J = 5.2$ Hz, 1H), 5.73-5.60 and 5.60-5.44 (m and m, 2H), 4.13 (q, $J = 7.2$ Hz, 1H), 2.91-2.81 (br s, 1H) 2.71-2.63 (br s, 1H), 2.38 (t, $J = 7.2$ Hz, 2H), 2.45-2.31 and 2.21-2.07 (m and m, 2H), 1.72 (quintuplet, $J = 7.2$ Hz, 2H), 1.63-1.45 (m, 2H), 1.33 (br s, 6H), 0.92 (br t, 3H); $^{13}\text{C-NMR}$ (75 MHz, CD_2Cl_2) δ : 209.1 (0), 177.5 (0), 166.7 (1), 137.1 (1), 133.5 (1), 132.3 (1), 127.6 (1), 127.2 (1), 73.5 (1), 55.2 (1), 48.9 (1), 37.8 (2), 33.7 (2), 32.5 (2), 31.4 (2), 27.2 (2), 25.8 (2), 25.3 (2), 23.4 (2), 14.6 (3); ESI-MS (APCI) m/z 317 (100) $[\text{M} - \text{OH}]^+$. HRMS calcd. for $\text{C}_{20}\text{H}_{30}\text{O}_4$ 334.2144, found 334.2141.

(3a*R*,4*R*,5*R*,6a*S*)-Benzoic acid 4-formyl-2-oxo-hexahydro-cyclopenta[*b*]furan-5-yl ester (**ent-7**)

(3a*R*,4*S*,5*R*,6a*S*)-Benzoic acid 4-hydroxymethyl-2-oxo-hexahydro-cyclopenta[*b*]furan-5-yl ester **7a** (585 mg, 2.124 mmol) in dry dichloromethane (4.5 mL) was added *via* a cannula to a solution of Dess-Martin periodinane (1.06 g, 2.55 mmol, 1.2 eq) in dry dichloromethane (9 mL) at 0 °C under argon. The reaction was allowed to warm to room temperature for 1 h, after which a white precipitate had formed. Ether (20 mL) was added and the mixture was cooled to 0 °C. Sodium thiosulfate (4.2 g) and saturated aqueous sodium hydrogen carbonate (18 mL) were added and the mixture warmed to room temperature and stirred for a further 10 min after which the precipitate had gone. The mixture was extracted with ether (3 x 10 mL) and the organic layers combined, washed with saturated aqueous sodium hydrogen carbonate (5 mL) and brine (5 mL), dried on Na₂SO₄ and concentrated under reduced pressure to give the desired aldehyde **ent-7** (534 mg, 92%) which was used immediately without further purification.

The ¹H NMR data are in complete agreement with the values tabulated in the literature (Fleming, I.; Winter, S. B. D. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2687)

¹H-NMR (300 MHz, CDCl₃) δ 9.83 (s, 1H, CH=O), 7.99 (br d, *J* = 7.1 Hz, 2H), 7.57 (br t, *J* = 7.4 Hz, 1H), 7.45 (br t, *J* = 7.4 Hz, 2H), 5.75 (br d, *J* = 5.5 Hz, 1H), 5.14 (br t, *J* = 6.2 Hz, 1H), 3.57-3.46 (m, 1H), 3.20 (br s, 1H), 2.98 (dd, *J* = 10.9, 18.6 Hz, 1H), 2.53-2.45 (m, 1H), 2.47 (m, 1H), 2.08 (dt, *J* = 16.0, 5.7 Hz, 1H).