

SUPPLEMENTARY MATERIAL

The Stille Reaction in the Synthesis of Carotenoid

Butenolides: Synthesis of 6'-*epi*-Peridinin

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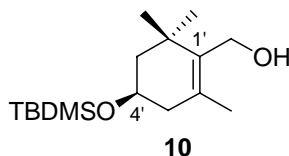
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General Procedures

General. All reactions were carried out under an atmosphere of argon, and those not involving aqueous reagents were carried out in oven-dried glassware. Tetrahydrofuran was distilled over sodium/benzophenone; dichloromethane was distilled over calcium hydride. Flash column chromatography was carried out using Merck Kieselgel 60 (230-400 mesh) under pressure. High performance liquid chromatography was performed using a Waters machine using a dualwave detector (254 and 390 nm). Analytical thin layer chromatography (TLC) was performed on aluminium plates with Merck Kieselgel 60F254 and visualised by UV irradiation (254 nm) or by staining with solution of phosphomolibdic acid. UV/Vis spectra were recorded on a HP5989A spectrophotometer. Infrared spectra were obtained on MIDAC Prospect FTIR spectrophotometer, from a thin film deposited into a NaCl glass. Mass spectra were obtained on a Hewlett-Packard HP59970 instrument operating at 70 eV by electron ionisation. High Resolution mass spectra were taken on a VG Autospec instrument. ¹H NMR spectra were recorded in CDCl₃, C₆D₆ and (CD₃)₂CO, at ambient temperature on Bruker AMX-400, ARX-600 and Varian Inova-750 spectrometers at 400, 600 and 750 MHz, respectively, with residual protic solvent as the internal reference

(CHCl₃, δ_{H} = 7.23; C₆D₆, δ_{H} = 7.26; (CD₃)₂CO, δ_{H} = 2.09 ppm); chemical shifts (δ) are given in parts per million (ppm), and coupling constants (J) are given in Hertz (Hz). The proton spectra are reported as follows: δ (multiplicity, coupling constant J , number of protons, assignment). ¹³C NMR spectra were recorded in CDCl₃ at ambient temperature on the same spectrometers with the central peak of CHCl₃ (δ_{C} = 77.0 ppm), C₆H₆ (δ_{C} = 128.0 ppm) or (CD₃)₂CO (δ_{C} = 20.51 ppm) as the internal reference. DEPT135 are used to aid in the assignment of signal in the ¹³C NMR spectra; difference NOE experiments were also performed in certain cases.

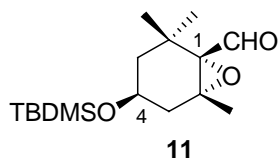
[(*R*)-4-(*tert*-Butyldimethylsilyloxy)-2,6,6-trimethylcyclohex-1-enyl]-methanol **10**



To a solution of (*R*)-*tert*-butyldimethylsilyl-4-iodo-3,5,5-trimethylcyclohex-3-en-1-yl ether **9** (1.0 g, 2.63 mmol) in THF (3 mL) at -78°C was added dropwise *t*BuLi (3.25 mL, 1.7 M in pentane, 5.52 mmol) and then, via cannula, a suspension of paraformaldehyde (0.12 g, 3.94 mmol) in THF (2 mL). The reaction mixture was stirred for 1 h at -78°C and for 15 h at 25°C . Brine was then added and the mixture was extracted with *t*BuOMe (3x). The combined organic extracts were dried (Na₂SO₄) and the solvent was removed. The residue was purified by chromatography (silicagel, 80:20 hexane/EtOAc), to afford 1.59 g (71%) of **10** as a white solid. **M.p.**: $69-71^{\circ}\text{C}$ (hexane/EtOAc). $[\alpha]_{\text{D}}^{25} -109.2$ (c 0.03, CHCl₃). **¹H-NMR** (400 MHz, CDCl₃): δ 4.11 (d, J = 11.4 Hz, 1H, H₁), 4.03 (d, J = 11.4 Hz, 1H, H₁), 3.88 (m, 1H, H_{4'}), 2.11 (m, 1H, H_{3'}), 2.00 (dd, J = 17.0, 9.4 Hz, 1H, H_{3'}), 1.71 (s, 3H, C₃-CH₃), 1.59 (ddd, J = 12.3, 3.3, 2.0 Hz, 1H, H_{5'}), 1.43 (t, J = 12.1 Hz, 1H, H_{5'}), 1.05 (s, 3H, C₆-CH₃), 1.01 (s, 3H, C₆-CH₃), 0.85 (s, 9H, SiC(CH₃)₃), 0.03 (s, 6H, Si(CH₃)₂) ppm. **¹³C-NMR** (100 MHz, CDCl₃): δ 137.1 (s, C_{1'}), 131.2 (s, C_{2'}), 65.5 (d, C_{4'}), 58.2 (t, C₁), 48.4 (t, C_{5'}), 42.6 (t, C_{3'}), 36.6 (s, C_{6'}), 29.3 (q, C₆-CH₃), 28.4 (q, C₆-CH₃), 25.8 (q, 3x, SiC(CH₃)₃), 19.4 (q, C₂-CH₃), 18.1 (s, SiC(CH₃)₃), -4.7 (q, 2x, Si(CH₃)₂) ppm. **MS (EI⁺)**: m/z (%) 209

(23), 135 (45), 119 (59), 109 (19), 107 (27), 105 (15), 93 (27), 91 (42), 77 (17), 75 (100), 73 (57), 67 (19). **HRMS (EI⁺)**: Calcd. for C₁₆H₃₀OSi, 266.2066; Found, 266.2065. **FTIR** (NaCl): ν 3600-3100 (br, OH), 2926 (s, C-H), 2857 (s, C-H), 1465 (m), 1382 (m), 1253 (s), 1087 (s) cm⁻¹. **Elemental Analysis**: Calcd for C₁₆H₃₂O₂Si: C, 67.54; H, 11.34. Found: C, 67.54; H, 11.52.

(1*S*,4*S*,6*R*)-4-(*tert*-Butyldimethylsilyloxy)-2,2,6-trimethyl-7-oxa-bicyclo[4.1.0]heptane-1-carboxaldehyde **11**

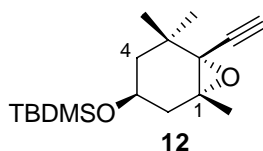


To a solution of (–)-*D*-DET (0.79 mL, 4.61 mmol) in CH₂Cl₂ (7 mL) and 4 Å molecular Sieves, was added, at –20 °C, Ti(O^{*i*}Pr)₄ (1.13 mL, 3.84 mmol) and, after 10 min stirring, a solution of TBHP (1.64 mL, 4.69 M in *iso*-octane, 7.68 mmol). After stirring for 30 min at –20 °C, a solution of alcohol **10** (1.09 g, 3.84 mmol) in CH₂Cl₂ (7 mL) was added, and the resulting mixture was stirred for an additional 12 h. Then ^{*t*}BuOMe (5 mL), a 30% aqueous NaOH solution (0.2 mL) and brine (0.2 mL) were added, and the mixture was allowed to reach ambient temperature. Solid Na₂SO₄ and Celite[®] were added, and the mixture was filtered, washing thoroughly with ^{*t*}BuOMe. The filtrate was dried (Na₂SO₄) and the solvent was removed. The residue was purified by chromatography (silicagel, gradient 85:15 → 80:20 hexane/EtOAc), to afford 1.13 g (98%) of [(1*R*,4*S*,6*R*)-4-(*tert*-butyldimethylsilyloxy)-2,2,6-trimethyl-7-oxa bicyclo[4.1.0]heptan-1-yl]methanol as a colorless oil.

DMSO (0.64 mL, 9.04 mmol) was added to a cooled (–60 °C) solution of oxalyl chloride (0.46 mL, 5.27 mmol) in CH₂Cl₂ (12 mL). After stirring for 5 min, a solution of the epoxyalcohol obtained above (1.13 g, 3.77 mmol) in CH₂Cl₂ (12 mL) was added and stirring was maintained for 15 min. At the same temperature, Et₃N (3.5 mL, 24.86 mmol) was added and, after 10 min stirring, the mixture was allowed to reach ambient temperature. It was then poured over H₂O and extracted with CH₂Cl₂ (3x). The combined organic layers were dried (Na₂SO₄) and the solvent was removed. The residue was purified by chromatography (silicagel, 95:5 hexane/EtOAc) to afford 1.02 g (91%) of **11** as

a colorless oil. $[\alpha]_D^{29}$ -97.2 (c 0.04, CHCl_3). **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 9.76 (s, 1H, CHO), 3.9-3.8 (m, 1H, H_4), 2.20 (dd, $J = 14.8, 5.1$ Hz, 1H, H_5), 1.67 (dd, $J = 14.8, 7.4$ Hz, 1H, H_5), 1.45 (dd, $J = 13.3, 3.0$ Hz, 1H, H_3), 1.34 (s, 3H, $\text{C}_6\text{-CH}_3$), 1.3-1.2 (m, 1H, H_3), 1.24 (s, 3H, $\text{C}_2\text{-CH}_3$), 1.03 (s, 3H, $\text{C}_2\text{-CH}_3$), 0.84 (s, 9H, $\text{SiC}(\text{CH}_3)_3$), 0.01 (s, 6H, $\text{Si}(\text{CH}_3)_2$) ppm. **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 200.3 (d, CHO), 72.2 (s, C_1), 66.1 (s, C_6), 64.1 (d, C_4), 46.2 (t, C_3), 40.7 (t, C_5), 33.5 (s, C_2), 27.9 (q, $\text{C}_6\text{-CH}_3$), 26.1 (q, $\text{C}_2\text{-CH}_3$), 25.7 (q, 3x, $\text{SiC}(\text{CH}_3)_3$), 20.5 (q, $\text{C}_2\text{-CH}_3$), 17.9 (s, $\text{SiC}(\text{CH}_3)_3$), -4.9 (q, 2x, $\text{Si}(\text{CH}_3)_2$) ppm. **MS (EI^+)**: m/z (%) 225 (9), 171 (9), 169 (16), 157 (29), 155 (12), 143 (9), 123 (10), 121 (14), 109 (16), 101 (12), 93 (11), 91 (10), 75 (100), 73 (28). **HRMS (EI^+)**: Calcd. for $\text{C}_{12}\text{H}_{21}\text{O}_3\text{Si}$ [$\text{M}^+ - t\text{Bu}$], 241.1260; Found, 241.1245. **FTIR** (NaCl): ν 2931 (s, C-H), 2857 (s, C-H), 1728 (s, C=O), 1469 (m), 1386 (m), 1255 (s), 1089 (s) cm^{-1} .

tert*-Butyldimethylsilyl (1*R*,3*S*,6*R*)-6-Ethynyl-1,5,5-trimethyl-7-oxa-bicyclo[4.1.0]heptan-3-yl Ether **12*

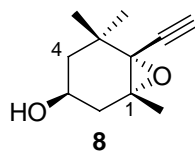


*n*BuLi (11.8 mL, 1.54 M in hexane, 15.9 mmol) was added dropwise to a solution of diisopropylamine (2.23 mL, 15.9 mmol) in THF (90 mL) at 0 °C, and the solution was stirred for 30 min. After cooling down to -78 °C, trimethylsilyldiazomethane (8.0 mL, 2.0 M in THF, 15.9 mmol) was added and the resulting mixture was stirred for 30 min. A solution of **11** (3.38 g, 11.34 mmol) in THF (28 mL) was added and stirring was maintained for 1 h at -78 °C and, after removing the acetone/ CO_2 bath, for 2 h at 25 °C. The reaction mixture was added to ice-cooled water, and extracted with Et_2O (3x). The combined organic extracts were dried (Na_2SO_4) and the solvent was removed. The residue was purified by chromatography (silicagel, gradient hexane \rightarrow 99:1 hexane/ EtOAc) to afford 3.10 g (92%) of **12** as a yellow oil. $[\alpha]_D^{29}$ -114.1 (c 0.01, CHCl_3). **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 3.8-3.7 (m, 1H, H_4), 2.32 (s, 1H, H_2), 2.02 (ddd, $J = 14.8, 7.1, 1.5$ Hz, 1H, H_2), 1.77 (dd, $J = 14.8, 9.7$ Hz, 1H, H_2), 1.44 (s, 3H, $\text{C}_1\text{-CH}_3$), 1.4-1.3 (m, 1H, H_4), 1.2-1.1 (m, 1H, H_4), 1.16 (s, 3H, $\text{C}_5\text{-CH}_3$), 1.13 (s, 3H, $\text{C}_5\text{-CH}_3$), 0.83 (s, 9H, $\text{SiC}(\text{CH}_3)_3$), 0.00 (s, 6H, $\text{Si}(\text{CH}_3)_2$)

ppm. **¹³C-NMR** (100 MHz, CDCl₃): δ 80.6 (s, C_{1'}), 73.7 (d, C_{2'}), 64.2 (s, C₆), 63.7 (d, C₃), 63.5 (s, C₁), 42.0 (t, C₄), 38.9 (t, C₂), 34.8 (s, C₅), 26.7 (q, C₅-CH₃), 25.8 (q, SiC(CH₃)₃), 24.6 (q, C₅-CH₃), 23.0 (q, C₁-CH₃), 18.1 (s, SiC(CH₃)₃), -4.7 (q, Si(CH₃)₂) ppm. **MS (EI⁺)**: *m/z* (%) 237 (M⁺-*t*Bu, 20), 208 (10), 181 (21), 179 (11), 144 (12), 143 (100), 136 (17), 121 (50), 115 (43), 93 (25), 77 (11), 75 (51), 73 (41). **HRMS (EI⁺)**: Calcd. for C₁₇H₃₀O₂Si, 294.2015; Found, 294.2003. **FTIR** (NaCl): ν 3311 (m, C≡C-H), 2957 (s, C-H), 2930 (s, C-H), 2857 (m, C-H), 1472 (m), 1385 (m), 1364 (m), 1253 (s), 1098 (s) cm⁻¹.

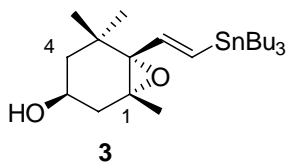
(1*R*,3*S*,6*R*)-6-Ethynyl-1,5,5-trimethyl-7-oxabicyclo[4.1.0]heptan-3-ol

8



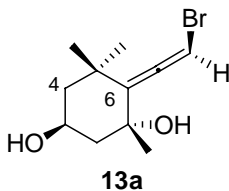
A solution of silylether **12** (1.62 g, 5.49 mmol) in THF (10 mL) was treated with *n*Bu₄NF (10.97 mL, 1M in THF, 10.97 mmol) and the mixture was stirred for 2 h at 25 °C. It was then poured over an aqueous saturated NaHCO₃ solution and extracted with *t*BuOMe (3x). The organic extracts were dried (Na₂SO₄) and the residue was purified by chromatography (silicagel, 85:15 hexane/EtOAc), to afford 0.84 g (85%) of **8** as a white solid. **M.p.**: 70-73 °C (hexane/EtOAc). **[α]_D²⁴** -76.0 (c 0.05, CHCl₃). **¹H-NMR** (400 MHz, CDCl₃): δ 3.78 (dddd, *J* = 10.2, 8.6, 5.0, 3.5 Hz, 1H, H₃), 2.37 (s, 1H, H_{2'}), 2.32 (dd, *J* = 14.3, 5.1 Hz, 1H, H₂), 1.59 (dd, *J* = 14.3, 8.6 Hz, 1H, H₂), 1.55 (ddd, *J* = 13.1, 3.4, 1.8 Hz, 1H, H₄), 1.48 (s, 3H, C₁-CH₃), 1.24 (s, 3H, C₅-CH₃), 1.19 (ddd, *J* = 13.3, 10.4, 2.9 Hz, 1H, H₄), 1.09 (s, 3H, C₅-CH₃) ppm. **¹³C-NMR** (100 MHz, CDCl₃): δ 80.4 (s, C_{1'}), 74.0 (d, C_{2'}), 66.4 (s, C₁), 63.6 (d, C₃), 62.9 (s, C₆), 45.6 (t, C₄), 39.6 (t, C₂), 33.9 (s, C₅), 29.6 (q, C₅-CH₃), 25.3 (q, C₅-CH₃), 21.3 (q, C₁-CH₃). **MS (EI⁺)**: *m/z* (%) 180 (M⁺, 8), 179 (M⁺-1, 10), 136 (28), 122 (15), 121 (100), 119 (17), 107 (17), 96 (40), 95 (17), 94 (16), 93 (65), 91 (26), 80 (19), 79 (63), 77 (37), 69 (16). **HRMS (FAB⁺)**: Calcd. for C₁₁H₁₆O₂, 180.1150; Found, 180.1158. **FTIR** (NaCl): ν 3600-3100 (br, OH), 3292 (s, C≡C-H), 2963 (s, C-H), 2930 (s, C-H), 2100 (w, C≡C), 1461 (m), 1108 (s), 1051 (s) cm⁻¹. **Elemental Analysis**: Calcd for C₁₁H₁₆O₂: C, 73.30; H, 8.95. Found: C, 73.28; H, 9.12.

(1*R*,3*S*,6*S*)-6-[(*E*)-2-(tributylstannyl)ethenyl]-1,5,5-trimethyl-7-oxa-bicyclo[4.1.0]heptan-3-ol **3**



To a solution of alkyne **8** (0.20 g, 1.13 mmol) in THF (6 mL) were sequentially added $\text{PdCl}_2(\text{PPh}_3)_2$ (0.015 g, 0.02 mmol) and Bu_3SnH (0.36 mL, 1.35 mmol) dropwise. After stirring for 10 min at 25 °C, the solvent was removed, and the residue was purified by reversed-phase chromatography (C-18 silicagel, CH_3CN), to afford 0.36 g (68%) of **3** as a colorless oil. $[\alpha]_D^{26} -83.9$ (c 0.05, CHCl_3). **$^1\text{H-NMR}$** (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 6.29 (d, $J = 19.1$ Hz, 1H, $\text{H}_{1'}$ or $\text{H}_{2'}$), 6.19 (d, $J = 19.1$ Hz, 1H, $\text{H}_{2'}$ or $\text{H}_{1'}$), 3.71 (m, 1H, H_3), 3.43 (d, $J = 4.6$ Hz, 1H, OH), 2.21 (ddd, $J = 14.2, 5.0, 1.7$ Hz, 1H, H_2), 1.6-1.5 (m, 8H, $\text{H}_2+\text{H}_4+\text{Sn-}n\text{Bu}_3$), 1.4-1.3 (m, 6H, $\text{Sn-}n\text{Bu}_3$), 1.20 (m, 1H, H_4), 1.13 (s, 6H, $\text{C}_1\text{-CH}_3+\text{C}_5\text{-CH}_3$), 1.0-0.8 (m, 15H, $\text{Sn-}n\text{Bu}_3$), 0.88 (s, 3H, $\text{C}_5\text{-CH}_3$) ppm. **$^{13}\text{C-NMR}$** (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 146.0 (d, $\text{C}_{1'}$), 132.4 (d, $\text{C}_{2'}$), 73.3 (s, C_6), 67.4 (s, C_1), 64.8 (d, C_3), 49.0 (t, C_4), 42.8 (t, C_2), 36.3 (s, C_5), 30.9 (q, $\text{C}_5\text{-CH}_3$), 30.7 (t, $\text{Sn-}n\text{Bu}_3$), 28.9 (t, $\text{Sn-}n\text{Bu}_3$), 26.3 (q, $\text{C}_5\text{-CH}_3$), 21.4 (q, $\text{C}_1\text{-CH}_3$), 15.0 (q, $\text{Sn-}n\text{Bu}_3$), 11.1 (t, $\text{Sn-}n\text{Bu}_3$) ppm. **MS (FAB $^+$)**: m/z (%) 419 (15), 417 (15), 416 (19), 415 (100), 414 (40), 413 (78), 412 (32), 411 (43), 357 (18), 291 (33), 289 (26), 179 (45), 177 (57), 176 (18), 175 (39). **HRMS (FAB $^+$)**: Calcd. for $\text{C}_{23}\text{H}_{43}\text{O}_2^{118}\text{Sn}$, 469.2279; Found, 469.2279. **FTIR** (NaCl): ν 3600-3100 (br, OH), 2957 (s, C-H), 2924 (s, C-H), 2852 (m, C-H), 1594 (w), 1160 (m), 1325 (m), 1049 (m) cm^{-1} .

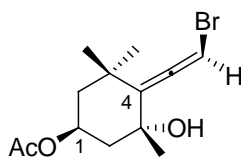
(1*R*,3*S*,6*aR*)-6-(2-Bromovinilidene)-1,5,5-trimethylcyclohexane-1,3-diol **13a**



To a cooled (-10 °C) solution of **8** (0.20 g, 1.11 mmol) in Et_2O (5 mL) were sequentially added CuBr (0.16 g, 1.11 mmol), NH_4Br (0.06 g, 0.56 mmol) and HBr (aqueous 48%, 0.20 mL, 1.78 mmol), and the mixture was stirred for 2.5 h

at -10 °C. After addition of $\text{NH}_4\text{Cl}/\text{NH}_3$ (1:1, 10 mL), the layers were separated and the aqueous layer was extracted with Et_2O (3x). The combined organic layers were washed with brine (2x), dried (Na_2SO_4) and the solvent was removed. The residue was purified by chromatography (silicagel, gradient 60:40 \rightarrow 40:60 hexane/ EtOAc), to afford 0.25 g (85%) of **13a** as a white solid. **M.p.**: 134-135 °C (hexane/ EtOAc). $[\alpha]_D^{24}$ -59.0 (c 0.02, CHCl_3). **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 5.95 (s, 1H, H_2), 4.25 (tt, $J = 11.4, 4.1$ Hz, 1H, H_3), 2.20 (ddd, $J = 13.4, 4.1, 2.4$ Hz, 1H, H_2), 1.88 (ddd, $J = 12.5, 4.1, 2.4$ Hz, 1H, H_4), 1.39 (t, $J = 11.6$ Hz, 1H, H_2), 1.39 (s, 3H, $\text{C}_1\text{-CH}_3$), 1.31 (t, $J = 11.9$ Hz, 1H, H_4), 1.29 (s, 3H, $\text{C}_5\text{-CH}_3$), 1.12 (s, 3H, $\text{C}_5\text{-CH}_3$) ppm. **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 198.4 (s, C_1), 124.2 (s, C_6), 74.2 (d, C_2), 72.3 (s, C_1), 63.8 (d, C_3), 48.7 (t, C_4), 48.4 (t, C_2), 35.9 (s, C_5), 31.3 (q, $\text{C}_5\text{-CH}_3$), 30.6 (q, $\text{C}_1\text{-CH}_3$), 29.4 (q, $\text{C}_5\text{-CH}_3$) ppm. **MS (EI^+)**: m/z (%) 182 (13), 181 (100), 163 (36), 160 (76), 158 (69), 139 (12), 125 (17), 123 (83), 122 (12), 121 (35), 107 (24), 105 (35), 95 (18), 91 (14), 87 (22), 85 (11), 83 (29), 81 (20), 80 (11), 79 (42), 77 (43). **HRMS (EI^+)**: Calcd. for $\text{C}_{11}\text{H}_{17}^{79}\text{BrO}_2$, 260.0412; Found, 260.0418. **FTIR** (NaCl): ν 3600-3100 (br, OH), 2927 (s, C-H), 1950 (w, C=C=C), 1458 (m), 1152 (s), 1041 (s) cm^{-1} . **Elemental Analysis**: Calcd for $\text{C}_{11}\text{H}_{17}\text{BrO}_2$: C, 50.59; H, 6.56. Found: C, 50.86; H, 6.63.

(1*S*,3*R*,4*aR*)-4-(2-Bromovinylidene)-3-hydroxy-3,5,5-trimethylcyclohex-1-yl Acetate 7a



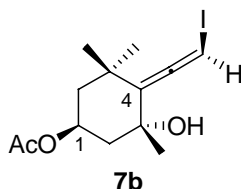
7a

Acetic anhydride (2.10 mL, 22.37 mmol) was added to a solution of **13** (1.16 g, 4.47 mmol), in pyridine (14 mL). After stirring for 16 h at ambient temperature, $t\text{BuOMe}$ was added and the mixture was washed with a saturated solution of CuSO_4 (2x), dried (Na_2SO_4) and the solvent was removed. The residue was purified by chromatography (silicagel, gradient 90:10 \rightarrow 80:20 hexane/ EtOAc), to afford 1.15 g (85%) of (1*S*,3*R*,4*aR*)-**7** and 0.06 g (4%) of (1*S*,3*R*,4*aS*)-**7**, both as white solids.

(1*S*,3*R*,4*aR*)-**7a**. **M.p.**: 94-96 °C (hexane/EtOAc). $[\alpha]_D^{24}$ -35.7 (*c* 0.03, CHCl₃). **¹H-NMR** (400 MHz, CDCl₃): δ 5.95 (s, 1H, H_{2'}), 5.28 (m, 1H, H₁), 2.20 (ddd, *J* = 13.0, 4.1, 2.3 Hz, 1H, H₂), 1.98 (s, 3H, CO-CH₃), 1.90 (ddd, *J* = 12.4, 4.1, 2.3 Hz, 1H, H₆), 1.5-1.3 (m, 2H, H₂ + H₆), 1.38 (s, 3H, C₃-CH₃), 1.32 (s, 3H, C₅-CH₃), 1.11 (s, 3H, C₅-CH₃) ppm. **¹³C-NMR** (100 MHz, CDCl₃): δ 198.3 (s, C_{1'}), 170.4 (s, C=O), 123.7 (s, C₄), 74.2 (d, C_{2'}), 71.8 (s, C₃), 67.4 (d, C₁), 44.6 (t, 2x, C₂ + C₆), 35.7 (s, C₅), 31.1 (q, C₅-CH₃), 30.3 (q, C₃-CH₃), 29.0 (q, C₅-CH₃), 21.2 (q, CO-CH₃). **MS (EI⁺)**: *m/z* (%) 304 (M⁺, 4), 302 (M⁺, 3), 186 (17), 163 (100), 160 (50), 158 (40), 121 (32), 107 (21), 105 (46), 91 (16), 84 (38), 81 (15), 79 (24), 77 (27), 69 (18). **HRMS (EI⁺)**: Calcd. for C₁₃H₁₉⁷⁹BrO₃, 302.0518; Found, 302.0528. Calcd. for C₁₃H₁₉⁸¹BrO₃, 304.0497; Found, 304.0498. **FTIR** (NaCl): ν 3600-3100 (br, OH), 3058 (w, C-H), 2966 (s, C-H), 2927 (s, C-H), 2859 (m, C-H), 1949 (w, C=C=C), 1720 (s, C=O), 1366 (s), 1267 (s, C-O), 1031 (s) cm⁻¹. **Elemental Analysis**: Calcd for C₁₃H₁₉BrO₃: C, 51.50; H, 6.32. Found: C, 51.32; H, 6.35.

(1*S*,3*R*,4*aS*)-**7a**. **M.p.**: 75-76 °C (hexane/EtOAc). $[\alpha]_D^{23}$ -71.3 (*c* 0.03, CHCl₃). **¹H-NMR** (400 MHz, CDCl₃): δ 6.12 (s, 1H, H_{2'}), 5.31 (m, 1H, H₁), 2.22 (ddd, *J* = 12.7, 4.3, 2.3 Hz, 1H, H₂), 1.99 (s, 3H, CO-CH₃), 1.92 (ddd, *J* = 12.5, 4.3, 2.3 Hz, 1H, H₆), 1.5-1.3 (m, 2H, H₂ + H₆), 1.40 (s, 3H, C₃-CH₃), 1.37 (s, 3H, C₅-CH₃), 1.09 (s, 3H, C₅-CH₃) ppm. **¹³C-NMR** (100 MHz, CDCl₃): δ 197.5 (s, C_{1'}), 170.4 (s, C=O), 123.8 (s, C₄), 75.3 (d, C_{2'}), 71.7 (s, C₃), 67.5 (d, C₁), 44.7 (t, C₆), 44.5 (t, C₂), 35.4 (s, C₅), 31.8 (q, C₅-CH₃), 30.6 (q, C₃-CH₃), 28.9 (q, C₅-CH₃), 21.3 (q, CO-CH₃). **MS (EI⁺)**: *m/z* (%) 304 (M⁺, 2), 302 (M⁺, 2), 163 (100), 160 (46), 158 (46), 121 (26), 107 (18), 105 (47), 84 (53), 79 (19), 77 (20). **HRMS (EI⁺)**: Calcd. for C₁₃H₁₉⁷⁹BrO₃, 302.0518; Found, 302.0522. Calcd. for C₁₃H₁₉⁸¹BrO₃, 304.0497; Found, 304.0508. **FTIR** (NaCl): ν 3450 (br, OH), 3058 (w, C-H), 2966 (s, C-H), 2926 (s, C-H), 2853 (m, C-H), 1947 (w, C=C=C), 1730 (s, C=O), 1366 (s), 1264 (s, C-O), 1032 (m) cm⁻¹. **Elemental Analysis**: Calcd for C₁₃H₁₉BrO₃: C, 51.50; H, 6.32. Found: C, 51.43; H, 6.23.

(1*S*,3*R*,4*aR*)-3-Hydroxy-6-(2-iodovinylidene)-1,5,5-trimethylcyclohex-1-yl Acetate **7b**



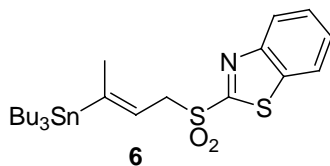
Following the same procedure, **8** (0.46 g, 2.51 mmol) in Et₂O (10 mL) was treated with CuI (0.478 g, 2.51 mmol), NH₄I (0.182 g, 1.25 mmol) and HI (aqueous 57%, 0.60 mL, 4.01 mmol) for 1.5 h, and provided after chromatography (silicagel, hexane/EtOAc 60:40), to afford 0.63 g (81%) of **13b** as a white solid, which was used in the next step.

The reaction of **13b** (0.57 g, 1.84 mmol) and Ac₂O (0.863 mL, 9.22 mmol) in pyridine (5.7 mL) during 8 h afforded, after purification by chromatography (silicagel, hexane/EtOAc 90:10 → 80:20), 0.59 g (91%) of (1*S*,3*R*,4*aR*)-**7b** as a white solid [m.p. 103-106 °C (hexane/EtOAc)], and 0.05 g (8%) of (1*S*,3*R*,4*aS*)-**7b** as a white solid [m.p. 105-107 °C (hexane/EtOAc)].

(1*S*,3*R*,4*aR*)-**7b**: ¹H-NMR (400 MHz, CDCl₃): δ 5.72 (s, 1H, H_{2'}), 5.25 (m, 1H, H₁), 2.17 (dd, *J* = 12.9, 4.1 Hz, 1H, H₂), 1.97 (s, 3H, CO-CH₃), 1.87 (dd, *J* = 12.4, 4.0 Hz, 1H, H₆), 1.44 (t, *J* = 11.5 Hz, 1H, H₂), 1.4-1.3 (m, 1H, H₆), 1.36 (s, 3H, C₃-CH₃), 1.30 (s, 3H, C₅-CH₃), 1.10 (s, 3H, C₅-CH₃) ppm. ¹³C-NMR (100 MHz, CDCl₃): δ 201.6 (s, C_{1'}), 170.4 (s, C=O), 119.0 (s, C₄), 71.5 (s, C₃), 67.5 (d, C₁), 44.5 (t, 2x, C₂ + C₆), 38.3 (d, C_{2'}), 35.0 (s, C₅), 30.8 (q, C₅-CH₃), 30.4 (q, C₃-CH₃), 29.4 (q, C₅-CH₃), 21.2 (q, CO-CH₃). **Elemental Analysis:** Calcd for C₁₃H₁₉IO₃: C, 44.59; H, 5.47. Found: C, 44.62; H, 5.44.

(1*S*,3*R*,4*aS*)-**7b**: ¹H-NMR (400 MHz, CDCl₃): δ 5.84 (s, 1H, H_{2'}), 5.28 (m, 1H, H₁), 2.19 (ddd, *J* = 12.7, 4.3, 2.3 Hz, 1H, H₂), 1.98 (s, 3H, CO-CH₃), 1.89 (ddd, *J* = 12.5, 4.3, 2.3 Hz, 1H, H₆), 1.4-1.3 (m, 2H, H₂ + H₆), 1.37 (s, 3H, C₃-CH₃), 1.32 (s, 3H, C₅-CH₃), 1.08 (s, 3H, C₅-CH₃) ppm. ¹³C-NMR (100 MHz, CDCl₃): δ 200.7 (s, C_{1'}), 170.2 (s, C=O), 118.9 (s, C₄), 71.2 (s, C₃), 67.5 (d, C₁), 44.7 (t, C₂), 44.5 (t, C₆), 38.7 (d, C_{2'}), 34.7 (s, C₅), 31.9 (q, C₅-CH₃), 30.6 (q, C₃-CH₃), 28.1 (q, C₅-CH₃), 21.2 (q, CO-CH₃).

(*E*)-1-(Benzothiazol-2-yl)sulphonyl-3-(tri-*n*-butylstannyl)-3-methylprop-2-ene **6**

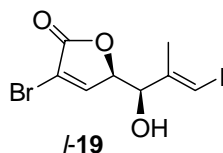


A solution of (*E*)-3-tri-*n*-butylstannyl-but-2-en-1-ol **14** (4.37g, 12.12 mmol), 2-mercaptobenzothiazol (3.04 g, 18.19 mmol) and PPh₃ (5.08 g, 19.40 mmol), in anhydrous THF (65 mL) was stirred at 0 °C for 5 min. A solution of diisopropyl azodicarboxylate (DIAD, 3.52 mL, 18.19 mmol) in THF (22 mL) was then added dropwise. The cool bath was removed and, after stirring for 30 min at 25 °C, the solvent was evaporated and the residue was purified by chromatography (silicagel, 96:2:2 hexane/EtOAc/Et₃N), to afford 6.07 g (98%) of (*E*)-1-(benzothiazol-2-yl)sulphonyl-3-(tri-*n*-butylstannyl)-3-methylprop-2-ene. **¹H-NMR** (400 MHz, C₆D₆): δ 7.90 (d, *J* = 8.2 Hz, 1H, ArH), 7.23 (d, *J* = 8.0 Hz, 1H, ArH), 7.08 (t, *J* = 8.2 Hz, 1H, ArH), 6.89 (t, *J* = 8.2 Hz, 1H, ArH), 5.95 (t, *J* = 7.2 Hz, 1H, H₂), 4.04 (d, *J* = 7.2 Hz, 2H, 2H₁), 1.94 (s, ³*J*_{SnH} = 64.4 Hz, 3H, C₃-CH₃), 1.8-1.6 (m, 6H, Sn-*n*Bu₃), 1.6-1.5 (m, 6H, Sn-*n*Bu₃), 1.1-1.0 (m, 15H, Sn-*n*Bu₃) ppm. **¹³C-NMR** (100 MHz, C₆D₆): δ 166.7 (s), 154.0 (s), 145.4 (s), 135.9 (s), 133.8 (d), 126.1 (d), 124.3 (d), 121.8 (d), 121.1 (d), 30.7 (t), 29.6 (t, ³*J*_{SnC} = 19.3 Hz), 27.7 (t, ²*J*_{SnC} = 53.9 Hz), 19.3 (q), 13.9 (q), 9.5 (t, ¹*J*_{SnC} = 323.5 Hz). **MS (FAB⁺)**: *m/z* (%) 513 (M⁺+3, 10), 512 (M⁺+2, 35), 511 (M⁺+1, 16), 510 (M⁺, 28), 509 (12), 508 (15), 458 (18), 456 (26), 455 (25), 454 (100), 453 (41), 452 (M⁺-Bu, 74), 451 (29), 450 (39), 400 (23), 399 (10), 398 (18), 396 (12), 291 (21), 289 (20), 287 (13), 286 (31), 285 (11), 284 (23), 282 (13), 235 (20), 233 (18), 231 (12), 220 (16), 188 (15). **HRMS (FAB⁺)**: Calcd. for C₂₃H₃₈NS₂¹¹⁸Sn, 510.1462; Found, 510.1450. **FTIR** (NaCl): ν 2954 (s, C-H), 2923 (s, C-H), 2850 (m, C-H), 1458 (m), 1427 (m), 994 (m) cm⁻¹.

To a stirred solution of (*E*)-1-(benzothiazol-2-yl)sulphonyl-3-(tri-*n*-butylstannyl)-3-methylprop-2-ene (2.5 g, 4.90 mmol) in EtOH (250 mL), was dropwise added, at 25 °C, a solution of (NH₄)₆Mo₇O₂₄·4H₂O (1.21 g, 0.98 mmol) in aqueous hydrogen peroxide (35%, 6.32 mL, 73.54 mmol). After stirring for 2.5 h, a 20% aqueous solution of Na₂S₂O₅ (150 mL) was added. The mixture was extracted with Et₂O (3x), and the combined organic layers were washed with brine (2x),

dried (Na₂SO₄) and the solvent was removed. The residue was purified by chromatography (silicagel, 85:12:3 hexane/EtOAc/Et₃N) and crystallization to afford 2.97 g (56%) of **6** as white crystals. **M.p.**: 78-79 °C (Et₂O/hexane) **¹H-NMR** (400 MHz, C₆D₆): δ 7.93 (d, *J* = 8.2 Hz, 1H, ArH), 7.12 (d, *J* = 8.5 Hz, 1H, ArH), 7.04 (t, *J* = 8.1 Hz, 1H, ArH), 6.91 (t, *J* = 8.0 Hz, 1H, ArH), 5.70 (tq, *J* = 7.4, 1.8 Hz, ³*J*_{Sn-H} = 63 Hz, 1H, H₂), 4.12 (dd, *J* = 7.4, 3.8 Hz, 2H, 2H₁), 1.69 (d, *J* = 1.5 Hz, ³*J*_{SnH} = 62.4 Hz, 3H, C₃-CH₃), 1.4-1.3 (m, 6H, Sn-*n*Bu₃), 1.3-1.2 (m, 6H, Sn-*n*Bu₃), 0.9-0.8 (m, 15H, Sn-*n*Bu₃) ppm. **¹³C-NMR** (100 MHz, C₆D₆): δ 167.6 (s), 153.2 (s), 153.1 (s), 137.1 (s), 128.3 (d), 127.4 (d), 125.1 (d), 123.6 (d), 122.3 (d), 53.4 (t), 29.3 (t, ³*J*_{SnC} = 20.1 Hz), 27.6 (t, ²*J*_{SnC} = 55.4 Hz), 19.7 (q), 13.8 (q), 9.5 (t, ¹*J*_{SnC} = 325.2 Hz). **MS (FAB⁺)**: *m/z* (%) 544 (M⁺+1, 7), 486 (21), 422 (25), 420 (20), 416 (17), 368 (28), 366 (22), 302 (27), 300 (20), 291 (23), 289 (20), 287 (17), 256 (22), 254 (53), 253 (20), 252 (38), 250 (18), 235 (37), 233 (32), 231 (24), 200 (18), 181 (17), 179 (77), 178 (22), 177 (100), 176 (32), 175 (79), 174 (18), 173 (37), 159 (17), 157 (16), 155 (15), 154 (17). **HRMS (FAB⁺)**: Calcd. for C₂₃H₃₈N O₂S₂¹²⁰Sn, 544.1366; Found, 544.1350. **FTIR** (NaCl): ν 2956 (s, C-H), 2926 (s, C-H), 1472 (m), 1318 (s), 1139 (m) cm⁻¹. **UV** (MeOH): λ_{max} 238, 274 nm. **Elemental Analysis**: Calcd. for C₂₃H₃₇NO₂S₂Sn: C, 50.93; H, 6.88. Found: C, 51.05; H, 6.93.

(5*R*^{*})-3-Bromo-5-[(1*R*^{*},2*E*)-1-hydroxy-3-iodo-2-methylpropenyl]-5*H*-furan-2-one **19**



Recently distilled (2x) chlorotrimethylsilane (1.79 mL, 14.07 mmol) and Et₃N (3.92 mL, 28.14 mmol) were added dropwise to a solution of 3-bromo-5*H*-furan-2-one **16** (1.35 g, 8.28 mmol) in CH₂Cl₂ (100 mL) and the mixture was stirred for 1 h at 25 °C. Removal of the solvent provided a residue which was used in the next step without purification.

To a cooled (−78 °C) solution of (*E*)-3-iodo-2-methylprop-2-enal **18** (1.62 g, 8.28 mmol) in CH₂Cl₂ (15 mL) was added recently distilled (2x) BF₃·OEt₂ (1.02 mL, 8.28 mmol), followed by a solution of the silyloxyfuran **17** obtained above in

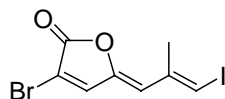
CH₂Cl₂ (12 mL). After stirring for 1.5 h at –78 °C a phosphate buffer solution in H₂O pH 7.2 solution (20 mL) was added and the mixture was extracted with CH₂Cl₂ (3x). The combined organic layers were dried (Na₂SO₄) and the solvent was removed. The residue was purified by chromatography (silicagel, 80:20:10 hexane/EtOAc/CH₂Cl₂) to provide 2.34 g (78%) of *l*-**19** and 0.24 g (8%) of *ul*-**19**.

(*R**,*R**)-**19**: **M.p.**: 98-100 °C (hexane/EtOAc). **¹H-NMR** (400 MHz, CDCl₃): δ 7.38 (d, *J* = 1.7 Hz, 1H, H₄), 6.49 (s, 1H, H₃'), 5.01 (dd, *J* = 5.9, 1.7 Hz, 1H, H₅), 4.29 (d, *J* = 5.9 Hz, 1H, H₁'), 2.62 (broad s, 1H, OH), 1.88 (s, 3H, CH₃) ppm. **¹³C-NMR** (100 MHz, CDCl₃): δ 167.7 (s, C=O), 149.1 (d, C₄), 144.2 (s, C₂'), 114.5 (s, C₃), 83.6 (d, C₅), 82.7 (d, C₃'), 76.3 (d, C₁'), 20.7 (q, C₂'-CH₃) ppm. **MS (FAB⁺)**: *m/z* (%) 360 (M⁺, 7), 359 (M⁺, 7), 308 (10), 307 (41), 290 (7), 289 (21), 282 (6), 219 (6), 197 (13). **HRMS (FAB⁺)**: Calcd. for C₈H₉⁷⁹Br¹²⁷IO₃, 358.8780; Found, 358.8788. **FTIR** (NaCl): ν 3600-3200 (br, OH), 3091 (w), 2919 (w), 1765 (s, C=O), 1608 (w), 1157 (w) cm⁻¹. **Elemental Analysis**: Calcd for C₈H₈BrIO₃: C, 26.77; H, 2.25. Found: C, 26.80; H, 2.23.

(*S**,*R**)-**19**: **¹H-NMR** (400 MHz, CDCl₃): δ 7.50 (d, *J* = 1.7 Hz, 1H, H₄), 6.51 (s, 1H, H₃'), 4.99 (dd, *J* = 5.0, 1.7 Hz, 1H, H₅), 4.41 (d, *J* = 5.0 Hz, 1H, H₁'), 3.24 (broad s, 1H, OH), 1.88 (s, 3H, CH₃) ppm. **¹³C-NMR** (100 MHz, CDCl₃): δ 168.6 (s, C=O), 150.1 (d, C₄), 144.0 (s, C₂'), 113.9 (s, C₃), 82.8 (d, C₅), 82.2 (d, C₃'), 74.8 (d, C₁'), 21.1 (q, C₂'-CH₃) ppm. **MS (EI⁺)**: *m/z* (%) 360 (M⁺, 1), 358 (M⁺, 1), 198 (4), 197 (100), 162 (6). **HRMS (EI⁺)**: Calcd. for C₈H₈⁷⁹Br¹²⁷IO₃, 357.8702; Found, 357.8704. Calcd. for C₈H₈⁸¹Br¹²⁷IO₃, 359.8681; Found, 359.8666. **FTIR** (NaCl): ν 3600-3200 (br, OH), 3092 (w, C-H), 2957 (w, C-H), 1775 (s, C=O), 1606 (w), 1057 (m), 1021 (m), 987 (m) cm⁻¹.

(5*Z*)-3-Bromo-5-[(*E*)-3-iodo-2-methylpropenylidene]-5*H*-furan-2-one

2



Z-2

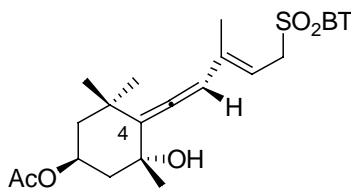
A solution of DIAD (1.10 mL, 5.44 mmol) was added dropwise to a cooled (–50 °C) solution of (5*S**)-3-bromo-5-[(1*S**,2*E*)-1-hydroxy-3-iodo-2-methylpropenyl]-5*H*-furan-2-one (*R**,*R**)-**19** (0.65 g, 1.81 mmol) and PPh₃ (1.43 g, 5.44 mmol) in

THF (17 mL). The reaction mixture was slowly warmed up to ambient temperature with stirring for 3.5 h. After addition of H₂O the mixture was extracted with CH₂Cl₂ (3x). The combined organic layers were dried (Na₂SO₄) and the solvent was removed. The residue was purified by chromatography (silicagel, 90:10 hexane/EtOAc) to afford **Z-2** (0.35 g, 57%) and **E-2** (0.05 g, 8%) in 7:1 ratio as yellow solids.

(5Z,2'E)-2: M.p.: 87-88 °C (CH₂Cl₂/Et₂O). **¹H-NMR** (400 MHz, CDCl₃): δ 7.42 (s, 1H, H₄), 6.97 (s, 1H, H₃), 5.73 (s, 1H, H₁), 2.21 (s, 3H, CH₃) ppm. **¹³C-NMR** (100 MHz, CDCl₃): δ 165.1 (s, C=O), 144.9 (s, C₅), 142.5 (d, C₄), 142.0 (s, C₂'), 114.5 (d, C₁'), 111.6 (s, C₃), 93.1 (d, C₃'), 22.9 (q, C₂'-CH₃) ppm. **MS (FAB⁺):** *m/z* (%), 343 (M⁺, 2), 342 (2), 341 (M⁺, 2), 340 (1), 292 (3), 274 (2), 258 (1), 257 (2). **HRMS (FAB⁺):** Calcd. for C₈H₇⁸¹BrIO₂, 342.8654; Found, 342.8658. **FTIR** (NaCl): ν 3053 (w, C-H), 2924 (w, C-H), 2854 (w, C-H), 1780 (s, C=O), 975 (m) cm⁻¹. **UV** (MeOH): λ_{max} 343 nm. **Elemental Analysis:** Calcd for C₈H₆BrIO₂: C, 28.18; H, 1.77. Found: C, 28.00; H, 1.73.

(5E,2'E)-2: M.p.: 107-108 °C (CH₂Cl₂/Et₂O). **¹H-NMR** (400 MHz, CDCl₃): δ 7.82 (s, 1H, H₄), 6.80 (d, *J* = 0.9 Hz, 1H, H₃), 6.36 (s, 1H, H₁'), 2.10 (d, *J* = 0.9 Hz, 3H, CH₃) ppm. **¹³C-NMR** (100 MHz, CDCl₃): δ 164.4 (s, C=O), 146.9 (s, C₅), 141.0 (s, C₂'), 138.2 (d, C₄), 117.0 (d, C₁'), 114.8 (s, C₃), 91.4 (d, C₃'), 23.0 (q, C₂'-CH₃) ppm. **MS (FAB⁺):** *m/z* (%) 323 (30), 322 (100), 282 (42), 279 (16), 251 (16), 250 (34), 210 (18), 193 (17), 191 (18), 167 (60), 165 (27). **HRMS (FAB⁺):** Calcd. for C₈H₇⁷⁹BrIO₂, 340.8674; Found, 340.8689. **FTIR** (NaCl): ν 2922 (w, C-H), 2853 (w, C-H), 1749 (s, C=O) cm⁻¹. **UV** (MeOH): λ_{max} 346 nm. **Elemental Analysis:** Calcd for C₈H₆BrIO₂: C, 28.18; H, 1.77. Found: C, 28.61; H, 1.77.

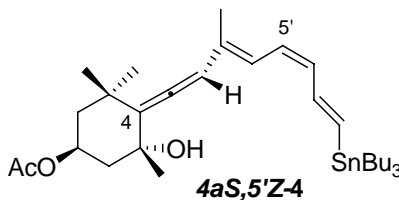
(1S,3R,4aS)-4-[(3E)-5-(Benzothiazol-2-yl)sulphonyl]-3-methylpenta-1,3-dienylidene]-3-hydroxy-3,5,5-trimethylcyclohex-1-yl Acetate
4aS-5



4aS-5

$\text{PdCl}_2(\text{PhCN})_2$ (0.013 g, 0.033 mmol) was added to a solution of **4aR-7a** (0.050 g, 0.165 mmol) in DMF (2 mL) and, after 5 min at 25 °C, a solution of **6** (0.134 g, 0.248 mmol) in THF (1.6 mL) was added. At this point the reaction mixture was thoroughly degassed using freeze-thaw cycles (3x) before the addition of $(i\text{Pr})_2\text{NEt}$ (0.043 mL, 0.248 mmol). After heating to 40 °C for 1.5 h, an aqueous saturated KF solution was added, the layers were separated and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were washed with brine (3x), dried (Na_2SO_4) and the solvent was removed. The residue was purified by chromatography (silicagel, gradient 70:30 \rightarrow 60:40 hexane/EtOAc), to afford 0.050 g (64%) of **4aS-5** as an orange foam. **M.p.**: 133-134 °C (hexane/EtOAc). $[\alpha]_{\text{D}}^{24}$ -30.4 (c 0.05, CHCl_3). **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 8.18 (d, J = 7.7 Hz, 1H, ArH), 7.95 (d, J = 7.5 Hz, 1H, ArH), 7.6-7.5 (m, 2H, ArH), 6.00 (s, 1H, H_2), 5.42 (t, J = 8.1 Hz, 1H, H_4), 5.26 (m, 1H, H_1), 4.31 (d, J = 8.1 Hz, 2H, 2H_5), 2.14 (ddd, J = 12.8, 4.1, 2.1 Hz, 1H, H_2), 1.98 (s, 3H, CO- CH_3), 1.85 (ddd, J = 12.3, 4.0, 2.0 Hz, 1H, H_6), 1.50 (s, 3H, C_3 - CH_3), 1.5-1.2 (m, 2H, H_2 and H_6), 1.21 (s, 3H, C_5 - CH_3), 1.16 (s, 3H, C_3 - CH_3), 0.88 (s, 3H, C_5 - CH_3) ppm. **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 201.7 (s, C_1), 170.3 (s, C=O), 165.5 (s, C_{Ar}), 152.5 (s, C_{Ar}), 141.3 (s, C_3), 137.0 (s, C_{Ar}), 127.9 (d, C_{Ar}), 127.6 (d, C_{Ar}), 125.3 (d, C_{Ar}), 122.2 (d, C_{Ar}), 117.7 (s, C_4), 111.1 (d, C_4), 101.7 (d, C_2), 72.2 (s, C_3), 67.7 (d, C_1), 55.2 (t, C_5), 44.8 (t, 2x, C_2 + C_6), 35.2 (s, C_5), 31.8 (q, C_5 - CH_3), 30.9 (q, C_3 - CH_3), 29.2 (q, C_5 - CH_3), 21.2 (q, CO- CH_3), 14.1 (q, C_3 - CH_3) ppm. **MS (EI $^+$)**: m/z (%) 475 (M^+ , 8), 411 (22), 385 (20), 382 (43), 277 (89), 276 (36), 268 (27), 217 (99), 216 (24), 214 (27), 201 (41), 200 (30), 199 (29), 189 (68), 187 (22), 173 (41), 163 (41), 161 (30), 159 (100), 158 (22), 157 (21), 145 (22), 143 (26), 136 (68), 135 (77), 133 (67), 131 (27), 121 (24), 119 (35), 117 (21), 108 (25), 107 (22), 105 (43), 95 (23), 91 (36). **HRMS (EI $^+$)**: Calcd. for $\text{C}_{24}\text{H}_{29}\text{NO}_5\text{S}_2$, 475.1487; Found, 475.1487. **FTIR** (NaCl): ν 3600-3100 (br, OH), 2962 (s, C-H), 2924 (s, C-H), 2852 (w, CH), 1939 (w, C=C=C), 1726 (s, C=O), 1250 (s, C-O), 1186 (s) cm^{-1} . **Elemental Analysis**: Calcd for $\text{C}_{24}\text{H}_{29}\text{NO}_5\text{S}_2$: C, 60.61; H, 6.15; N, 2.94; S, 13.48. Found: C, 60.44; H, 6.15; N, 2.92; S, 13.25.

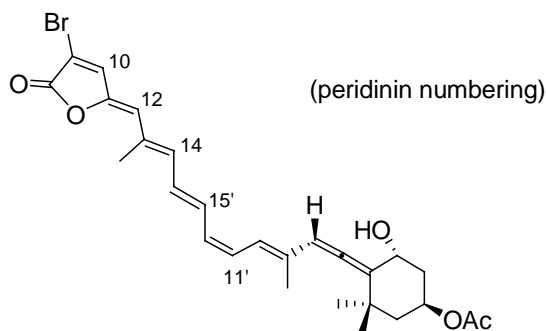
**(1*S*,3*R*,4*aS*)-4-[(3*E*,5*Z*,7*E*)-3-hydroxy-3-methyl-8-(tributylstannyl)-
octa-1,3,5,7-tetraenylidene]-3,5,5-trimethylcyclohexyl
Acetate 4*aS*,5'*Z*-4**



To a cooled (-78 °C) solution of sulphone **4aS-5** (0.23 g, 0.47 mmol) in anhydrous THF (22 mL) was added NaHMDS (1.42 mL, 1 M in THF, 1.42 mmol) dropwise and the resulting mixture was stirred for 30 min. Then, a solution of **15** (0.24 g, 0.71 mmol) in anhydrous THF (11 mL) was slowly added, and the mixture was stirred for a further 2 h at the same temperature. H₂O was slowly added, and the reaction mixture was allowed to reach ambient temperature. It was then diluted with Et₂O and the separated aqueous layer was further extracted with Et₂O (3x). The combined organic layers were dried (Na₂SO₄) and the solvent was removed. The residue was purified by chromatography (silicagel, 90:10:2 hexane/EtOAc/Et₃N), to afford **4aS,5'Z-4** (149 mg, 52%) as an oil, and **4aS,5'E-4** (51.6 mg, 12%) as an oil, which rapidly decomposed. $[\alpha]_D^{22}$ -59.9 (c 0.04, CHCl₃). **¹H-NMR** (400 MHz, C₆D₆): δ 7.43 (dd, *J* = 18.5, 10.4 Hz, 1H, H₇), 6.75 (d, *J* = 11.6 Hz, 1H, H_{4'}), 6.55 (d, *J* = 18.5 Hz, 1H, H₈), 6.25 (t, *J* = 11.0 Hz, 1H, H_{5'} or H₆), 6.20 (t, *J* = 10.5 Hz, 1H, H₆ or H₅), 6.03 (s, 1H, H₂), 5.66 (ddd, *J* = 11.5, 7.3, 4.2 Hz, 1H, H₁), 2.23 (ddd, *J* = 12.6, 4.1, 2.1 Hz, 1H, H₂ or H₆), 2.00 (ddd, *J* = 12.2, 4.0, 2.0 Hz, 1H, H₆ or H₂), 1.72 (s, 3H, CO-CH₃), 1.71 (s, 3H, C₃-CH₃), 1.6-1.5 (m, 6H, SnBu₃), 1.44 (s, 3H, C₅-CH₃), 1.4-1.3 (m, 8H, SnBu₃ + H₂ + H₆), 1.15 (s, 3H, C₃-CH₃), 1.1-1.0 (m, 6H, SnBu₃), 1.03 (s, 3H, C₅-CH₃), 1.0-0.9 (m, 9H, SnBu₃) ppm. **¹³C-NMR** (100 MHz, C₆D₆): δ 202.2 (s, C_{1'}), 169.3 (s, C=O), 142.3 (d, C_{8'}), 136.0 (d, C_{6'}), 133.4 (s, C_{3'}), 131.7 (d, C_{7'}), 124.4 (d, C_{5'}), 123.3 (d, C_{4'}), 117.4 (s, C₄), 103.5 (d, C_{2'}), 72.1 (s, C₃), 67.7 (d, C₁), 45.2 (t, 2x, C₆ + C₂), 35.3 (s, C₅), 32.0 (q, C₅-CH₃), 30.8 (q, C₃-CH₃), 29.2 (q, C₅-CH₃), 29.2 (t, SnBu₃), 27.3 (t, SnBu₃), 20.6 (q, CO-CH₃), 13.7 (q, C₃-CH₃), 13.6 (q, SnBu₃), 9.6 (t, SnBu₃) ppm. **MS (FAB⁺):** *m/z* (%) 549 (M⁺-Bu, 4), 547 (3), 545 (2), 531 (13), 530 (6), 529 (12), 473 (10), 471 (20), 469 (13), 297 (13), 295 (19), 293 (81), 292 (31), 291 (96), 290 (35),

289 (70), 288 (18), 287 (25), 239 (18), 237 (24), 235 (41), 234 (14), 233 (32), 232 (12), 231 (20), 183 (19), 181 (21), 179 (100), 178 (30), 177 (99), 176 (33), 175 (66), 174 (10), 173 (18). **HRMS (FAB⁺)**: Calcd. for C₂₈H₄₅O₃¹¹⁶Sn, 545.2386; Found, 545.2388. Calcd. for C₂₈H₄₅O₃¹²⁰Sn, 549.2391; Found, 549.2385. **FTIR** (NaCl): ν 3359 (m), 3194 (m), 2959 (s, C-H), 2924 (s, C-H), 2852 (s, C-H), 1932 (w, C=C=C), 1721 (m, C=O), 1660 (s), 1632 (s), 1466 (m), 1262 (s, C-O) cm⁻¹. **UV** (MeOH): λ_{max} 306, 319, 332 nm.

Bromide **Z-20**



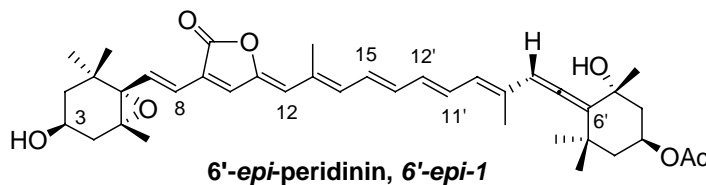
Z-20

AsPh₃ (0.005 g, 0.005 mmol) was added to a solution of Pd₂(dba)₃·CHCl₃ (0.003 g, 0.003 mmol) in THF (3.5 mL). After 5 min stirring at 25 °C, **2** (0.127 g, 0.372 mmol) was added and stirring was kept at 25 °C for 10 min. Then, a solution of **Z-4** (0.169 g, 0.279 mmol) in THF (1.5 mL) was added followed by Ph₂PO₂NBu₄ (0.107 g, 0.232 mmol) in one portion and BHT (trace). At this point, the reaction mixture was thoroughly degassed using freeze/thaw cycles (3x). The resulting dark red reaction mixture was stirred for 5.5 h at 25 °C, brine was added, and the mixture was extracted with 90:10 EtOAc/CH₂Cl₂ (3x). The combined organic layers were dried (Na₂SO₄) and the solvent was removed. The residue was purified by chromatography (silicagel, gradient 80:20 → 70:30 hexane/EtOAc) to afford 84.0 mg (68%) of **Z-20** as a red solid, and 17.0 mg of unstable **E-20**.

Z-20. ¹H-NMR (600 MHz, CDCl₃): δ 7.43 (s, 1H, H₁₀), 6.95 (t, J = 12.3 Hz, 1H, H_{15'}), 6.59 (t, J = 12.6 Hz, 1H, H₁₅), 6.55 (d, J = 12.3 Hz, 1H, H₁₄), 6.52 (d, J = 12.3 Hz, 1H, H_{10'}), 6.41 (t, J = 11.7 Hz, 1H, H_{11'}), 6.18 (s, 1H, H₈), 6.14 (t, J = 11.5 Hz, 1H, H_{12'}), 5.77 (s, 1H, H₁₂), 5.35 (m, 1H, H₃), 2.3-2.2 (m, 1H, H₄), 2.20 (s, 3H, C₁₃-CH₃), 2.01 (s, 3H, CO-CH₃), 1.94 (d, J = 10.6 Hz, 1H, H₂), 1.83 (s,

3H, C₉-CH₃), 1.5-1.4 (m, 1H, H_{4'}), 1.40 (s, 3H, C_{1'}-CH₃), 1.4-1.3 (m, 1H, H₂), 1.33 (s, 3H, C_{5'}-CH₃), 1.05 (s, 3H, C_{1'}-CH₃) ppm. **¹³C-NMR** (150 MHz, CDCl₃): δ 202.8 (s, C₇'), 170.4 (s, CH₃C=O), 165.7 (s, C=O), 146.1 (s, C₁₁'), 142.2 (d, C₁₀'), 139.5 (d, C₁₄'), 135.1 (s, C₉'), 133.4 (s, C₁₃'), 132.8 (d, C₁₅'), 129.5 (d, C₁₅'), 128.8 (d, C₁₂'), 128.0 (d, C₁₁'), 123.2 (d, C₁₀'), 120.2 (d, C₁₂'), 117.7 (s, C₆'), 109.1 (s, C₉'), 103.8 (d, C₈'), 72.6 (s, C₅'), 67.9 (d, C₃'), 45.0 (t, C₂' or C₄'), 44.9 (t, C₄' or C₂'), 35.5 (s, C₁'), 32.0 (q, C₁'-CH₃), 31.2 (q, C₅'-CH₃), 29.4 (q, C₁'-CH₃), 21.3 (q, CO-CH₃), 15.3 (q, C₁₃'-CH₃), 14.1 (q, C₉'-CH₃). **MS (FAB⁺)**: *m/z* (%) 531 (13), 530 (M⁺, 55), 529 (13), 528 (M⁺, 47), 453 (32), 451 (29). **HRMS (EI⁺)**: Calcd. for C₂₈H₃₃⁷⁹BrO₅, 528.1511; Found, 528.1530. Calcd. for C₂₈H₃₃⁸¹BrO₅, 530.1491; Found, 530.1481. **FTIR** (NaCl): ν 3600-3100 (br, OH), 2961 (w, C-H), 2924 (w, C-H), 2853 (w, C-H), 1929 (w, C=C=C), 1755 (s, C=O), 1554 (m), 1260 (m), 976 (m) cm⁻¹. **UV** (MeOH): λ_{max} 244, 289, 456 nm.

6'-*epi*-Peridinidin, 6'-*epi*-1



AsPh₃ (0.002 g, 0.002 mmol) was added to a solution of Pd₂(dba)₃·CHCl₃ (0.001 g, 0.001 mmol) in THF (1.0 mL). After 5 min at 25 °C, bromide (11'*Z*)-**20** (0.019 g, 0.035 mmol) was added and the mixture was stirred an additional 10 min. Then, a solution of stannane **3** (0.020 g, 0.043 mmol) in THF (1.5 mL) was added via cannula followed by Ph₂PO₂NBu₄ (0.016 g, 0.035 mmol) in one portion and BHT (trace). At this point, the reaction mixture was thoroughly degassed using freeze/thaw cycles (3x). After 31 h at 55 °C, brine was added, and the mixture was extracted with EtOAc/CH₂Cl₂ (90:10) (3x). The combined organic layers were dried (Na₂SO₄) and the solvent was removed. Purification of the residue by chromatography (silicagel, gradient 70:30 to 0:100 hexane/EtOAc) afforded 15.9 mg (72%) of 6'-*epi*-**1** as a red solid. **¹H-NMR** (750 MHz, (CD₃)₂CO): δ 7.57 (s, 1H, H₁₀), 7.22 (d, *J* = 15.2 Hz, 1H, H₇), 6.82 (dd, *J* = 14.2, 11.2 Hz, 1H, H_{11'}), 6.80 (dd, *J* = 14.0, 11.2 Hz, 1H, H₁₅), 6.68 (dd, *J* = 14.0, 11.8 Hz, 1H, H₁₅'), 6.62 (d, *J* = 11.2 Hz, 1H, H₁₄), 6.52 (dd, *J* = 14.2, 11.2 Hz, 1H, H_{12'}), 6.42 (d, *J* = 15.4 Hz, 1H, H₈), 6.26 (s, 1H, H₈'), 6.23 (d, *J* = 11.0

Hz, 1H, H_{10'}), 6.09 (s, 1H, H₁₂), 5.40 (m, 1H, H_{3'}), 4.23 (s, 1H, C_{5'}-OH), 3.86 (s, 1H, C₃-OH), 3.77 (m, 1H, H₃), 2.30 (dd, $J = 14.4, 3.2$ Hz, 1H, H₄), 2.21 (s, 3H, C₁₃-CH₃), 2.17 (d, $J = 12.0$ Hz, 1H, H_{4'}), 2.01 (s, 3H, CO-CH₃), 1.93 (m, 1H, H_{2'}), 1.91 (s, 3H, C₉-CH₃), 1.68 (dd, $J = 14.3, 9.3$ Hz, 1H, H₄), 1.57 (d, $J = 12.7$ Hz, 1H, H₂), 1.46 (s, 3H, C_{1'}-CH₃), 1.44 (d, $J = 12.1$ Hz, 1H, H_{4'}), 1.4-1.3 (m, 1H, H_{2'}), 1.35 (s, 3H, C_{5'}-CH₃), 1.29 (t, $J = 12.0$ Hz, 1H, H₂), 1.19 (s, 3H, C₁-CH₃), 1.17 (s, 3H, C₅-CH₃), 1.06 (s, 3H, C_{1'}-CH₃), 0.94 (s, 3H, C₁-CH₃). **¹³C-NMR** (100.6 MHz, (CD₃)₂CO): δ 204.4 (s, C₇), 171.4 (s, CO-CH₃), 170.2 (s, C=O), 149.0 (s, C₁₁), 140.0 (d, C₁₄), 139.5 (d, C_{15'}), 138.8 (d, C₁₀), 137.0 (s, C_{9'}), 135.6 (d, C₇), 135.3 (s, C₁₃), 134.7 (d, C_{12'}), 133.7 (d, C_{11'}), 130.7 (d, C₁₅), 130.0 (d, C_{10'}), 126.4 (s, C₉), 123.6 (d, C₈), 120.7 (d, C₁₂), 119.5 (s, C_{6'}), 104.9 (d, C_{8'}), 73.4 (s, C₅), 71.8 (s, C₆), 69.5 (d, C_{3'}), 69.0 (s, C₅), 64.7 (d, C₃), 48.9 (t, C₂), 47.5 (t, C_{4'}), 47.2 (t, C_{2'}), 42.8 (t, C₄), 37.2 (s, C_{1'}), 36.8 (s, C₁), 33.7 (q, C_{1'}-CH₃), 32.2 (q, C_{5'}-CH₃), 31-30 (q, 2x, C_{1'}-CH₃, C₁-CH₃), 26.4 (q, C₁-CH₃), 22.2 (q, CO-CH₃), 21.2 (q, C₅-CH₃), 16.4 (q, C₁₃-CH₃), 15.5 (q, C₉-CH₃). **MS (FAB⁺):** m/z (%), 631 (M⁺+1, 6), 630 (M⁺, 12), 252 (20), 241 (22), 239 (34), 228 (23), 227 (22), 226 (22), 215 (21), 204 (23), 202 (30), 191 (26), 190 (23), 189 (30), 181 (24), 180 (32), 179 (23), 178 (41), 176 (28), 168 (20), 167 (40), 166 (30), 165 (74). **HRMS (EI⁺):** Calcd for C₃₉H₅₀O₇, 630.3557; found, 630.3550. Calcd for C₃₉H₅₁O₇, 631.3635; found, 631.3637. **FTIR** (NaCl): ν 3500-3300 (br, OH), 3359 (s), 3000-2850 (s, C-H), 1926 (w, C=C=C), 1750 (s, C=O) cm⁻¹.