### **Electronic Supplementary Information (ESI)**

# A short route towards merosesquiterpenes with a benzoxanthene skeleton

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#### **General procedures**

All reaction was carried out under argon atmosphere. Dichloromethane (DCM) was dried over calcium hydride. Tetrahydrofuran, benzene and toluene were dried over sodium-benzophenone.

Thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching and phosphomolybdic acid solution staining.

Flash chromatography was performed on silica gel 60 (230-400 mesh). Chromatography separations were carried out by conventional column on silica gel 60 (230-400 Mesh), using Hexanes-MeOtBu (H-E) mixtures of increasing polarity.

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded at 600 MHz, 500 MHz or 400 MHz and 150 MHz, 125 MHz or 100 MHz, respectively. CDCl<sub>3</sub> was treated with  $K_2CO_3$ . Chemical shifts ( $\delta$ H) are quoted in parts per million (ppm) referenced to the appropriate residual solvent peak and tetramethylsilane.

Data for <sup>1</sup>H NMR spectra are reported as follows: chemical shift ( $\delta$  ppm) (multiplicity, coupling constant (Hz), integration), with the abbreviations s, br s, d, br d, t, q, and m denoting singlet, broad singlet, doublet, broad doublet, triplet, and multiplet respectively. J = coupling constant in Hertz (Hz)

Data for <sup>13</sup>C NMR spectra are reported in terms of chemical shift relative to Me<sub>4</sub>Si ( $\delta$  0.0) and the signals were assigned utilizing DEPT experiments and on the basis of heteronuclear correlations.

Infrared spectra (IR) were recorded as thin films or as solids on a FTIR spectrophotometer with samples between sodium chloride plates or as potassium bromide pellets and are reported in frequency of absorption ( $cm^{-1}$ ). Only selected absorbances (v max) are reported.

 $[\alpha]^{D}$  measurements were carried out in a polarimeter, utilizing a 1 dm length cell and CHCl<sub>3</sub> as a solvent. Concentration is expressed in mg/mL.

Mass spectra: HRMS were recorded on a TOF spectrometer, utilizing the ES or APcI ionization techniques.

#### **Experimental Procedures**

1-((4aR,6aS,10aS,10bR)-4a,7,7,10a-tetramethyl-4a,5,6,6a,7,8,9,10,10a,10bdecahydro-1H-benzo[f]chromen-2-yl)ethanone (10)



60% Sodium hydride dispersion in mineral oil (1.6 g, 40.5 mmol) was added to a solution of **11** (5 g, 16.2 mmol) in benzene (100 mL) at 0 °C under an argon atmosphere. After 5 min, the reaction mixture was stirred under reflux for 24 h. The reaction was poured into ice and concentrated in vacuo to give a crude product, which was dissolved in ether (150 mL) and washed with brine (2 x 50 mL). The organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated to give a crude product which was purified by flash chromatography on silica gel (15% ether/hexanes), affording 2.96 g of **10** (63%), as a white solid.

 $[\alpha]_D^{25} = +110.3$  (c 9.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.46 (s, 1H), 2.36 (dd, J = 16.8, 4.6 Hz, 1H), 2.20 (s, 3H), 2.03 (dt, J = 12.5, 3.2 Hz, 1H), 1.89 (dd, J = 12.9, 1.7 Hz, 1H), 1.85 (dd, J = 12.9, 1.7 Hz, 1H), 1.73 (m, 1H), 1.59 (m, 1H), 1.48 – 1.35 (m, 2H), 1.35 – 1.24 (m, 3H), 1.16 (s, 3H), 1.12 (dd, J = 13.4, 4.0 Hz, 1H), 0.95 (dd, J = 12.3, 2.2 Hz, 1H), 0.91 (m, 1H), 0.88 (s, 3H), 0.84 (s, 3H), 0.81 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$ : 196.9 (C), 155.8 (CH), 117.0 (C), 80.2 (C), 56.3 (CH), 51.7 (CH), 41.9 (CH<sub>2</sub>), 40.6 (CH<sub>2</sub>), 39.3 (CH<sub>2</sub>), 37.2 (C), 33.5 (CH<sub>3</sub>), 33.3 (C), 24.8 (CH<sub>3</sub>), 21.7 (CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 19.8 (CH<sub>2</sub>), 18.6 (CH<sub>2</sub>), 16.8 (CH<sub>2</sub>), 15.2 (CH<sub>3</sub>). IR (KBr): 1622, 1458,

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1388, 1215, 1190, 1124 cm<sup>-1</sup>. HRMS (ES+/TOF) m/z: calcd for C<sub>19</sub>H<sub>31</sub>O<sub>2</sub> (M+H<sup>+</sup>) 291.2324, found: 291.2311.

(4aS,6aR,12aR,12bS)-4,4,6a,12b-tetramethyl-2,3,4,4a,5,6,6a,12,12a,12b-decahydro-1H-benzo[a]xanthen-11-yl acetate (16)



*trans*-1,2-Bis(phenylsulfonyl)ethylene (2.46 g, 8.00 mmol) and *p*-toluenesulphonic acid (15 mg) was added to a solution of  $\alpha$ , $\beta$ -enone **10** (2.1 g, 7.28 mmol) in isopropenyl acetate (6 mL), and the mixture was heated at 160 °C for 5 h in a sealed tube. At this time, TLC showed no remaining starting material. The reaction was allowed to cool to room temperature and the crude product was purified by flash chromatography on silica gel (75% ether/hexanes), affording a mixture of two adducts **13a-b** (ratio 1.2 : 1) (4.3 g, 93%), as a white solid. Then, Na-Hg (10-15 molar equiv based on Na) was added to a solution of the mixture of adducts and NaH<sub>2</sub>PO<sub>4</sub> (517 mg, 4.31 mmol) in methanol (50 mL) at room temperature, and the slurry was stirred for 3 h. At this time, TLC showed no remaining starting material. Then, the resulting mixture was filtered through a silica gel pad and the solvent was evaporated in vacuo. The residue was dissolved in ether (50 mL), washed with water (2 x 15 mL) and brine water (1 x 15 mL). The organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to give an unresolvable mixture of epimers **14a-b** (ratio 1.2 : 1) (930 mg, 90%), which was dissolved directly in 1,4-

dioxane (20 mL) and 2,3-dichloro-5,6- dicyano-1,4-benzoquinone (620 mg, 2,74 mmol) was added. The reaction mixture was stirred at room temperature for 1 h. Then the solvent was evaporated in vacuo, and the residue was dissolved in ether (50 mL), washed with water (5 x 15 mL) and brine (15 mL). The organic phase was dried over anhydrous  $Na_2SO_4$  and concentrated to give a crude product which was chromatographed on silica gel (5 % ether/hexanes) to give 865 mg of pure **16** (94%) as a colourless syrup.

[α]<sub>D</sub><sup>25</sup> = +50.1 (c 4.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.07 (t, J = 8.2 Hz, 1H), 6.67 (d, J = 8.2 Hz, 1H), 6.58 (d, J = 7.9 Hz, 1H), 2.51 (dd, J = 16.7, 5.1 Hz, 1H), 2.32 (s, 3H), 2.27 (dd, J = 17.0, 3.6 Hz, 1H), 2.07 (dt, J = 12.5, 3.1 Hz, 1H), 1.76 (m, 1H), 1.68 (dt, J = 14.5, 7.3 Hz, 3H), 1.63 – 1.54 (m, 2H), 1.51 – 1.31 (m, 2H), 1.28 (m, 1H), 1.18 (s, 3H), 1.03 (dd, J = 12.2, 1.9 Hz, 1H), 0.96 (m, 1H), 0.91 (s, 3H), 0.89 (s, 3H), 0.85 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 169.2 (C), 154.5 (C), 149.7 (C), 127.1 (CH), 115.8 (C), 114.9 (CH), 113.0 (CH), 77.2 (C), 56.3 (CH), 51.5 (CH), 41.9 (CH<sub>2</sub>), 41.1 (CH<sub>2</sub>), 39.3 (CH<sub>2</sub>), 37.0 (C), 33.6 (CH<sub>3</sub>), 33.3 (C), 21.7 (CH<sub>3</sub>), 21.0 (CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 19.9 (CH<sub>2</sub>), 18.6 (CH<sub>2</sub>), 17.4 (CH<sub>2</sub>), 15.0 (CH<sub>3</sub>). IR (film): 1763, 1584, 1459, 1366, 1262, 1210, 1038, 802 cm<sup>-1</sup>. HRMS (ES+/TOF) *m*/*z*: calcd for C<sub>23</sub>H<sub>33</sub>O<sub>3</sub> (M+H<sup>+</sup>) 357.2430, found: 357.2426. (4aS,6aR,7aR,8S,9S,12aR,12bS)- and (4aS,6aR,7aS,8S,9S,12aR,12bS)- 4,4,6a,12btetramethyl-8,9-bis(phenylsulfonyl)-2,3,4,4a,5,6,6a,7a,8,9,10,12,12a,12btetradecahydro-1H-benzo[a]xanthen-11-yl acetate (13a-b)



250 mg of the mixture of tetracyclic bis sulphone adducts **13a-b** was purified by flash chromatography (70% ether/hexanes) to give 80 mg of a white solid, consisting of a pure stereoisomer (**13a**), 45 mg of a white solid, consisting of a pure stereoisomer (**13b**) and 100 mg of a mixture of adducts **13a** and **13b**.

Compound **13a** (pure stereoisomer):  $[\alpha]_D^{25} = +22.1$  (c 8.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.03 (d, J = 7.5 Hz, 2H), 7.91 (d, J = 7.6 Hz, 2H), 7.71 (t, J = 7.4 Hz, 1H), 7.65 – 7.57 (m, 3H), 7.51 (t, J = 7.7 Hz, 2H), 4.96 (br s, 1H), 4.52 – 4.40 (m, 2H), 2.80 (m, 1H), 2.62 (br d, J = 18.6 Hz, 1H), 2.55 (dd, J = 15.3, 3.6 Hz, 1H), 2.16 (s, 3H), 1.83 (dd, J = 16.1, 12.6 Hz, 1H), 1.66 – 1.51 (m, 3H), 1.49 – 1.36 (m, 3H), 1.34 – 1.24 (m, 3H), 1.23 – 1.13 (m, 3H), 1.10 (s, 3H), 0.95 (dd, J = 17.0, 9.0 Hz, 1H), 0.87 – 0.82 (m, 2H), 0.78 (s, 3H), 0.71 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  168.6 (C), 142.5 (C), 137.2 (C), 136.6 (C), 134.5 (CH), 133.2 (CH), 129.6 (2CH), 129.4 (2CH), 128.8 (2CH), 128.6 (2CH), 120.4 (C), 75.1 (C), 65.3 (CH), 59.9 (CH), 56.9 (CH), 56.4 (CH), 53.6 (CH), 42.1 (CH<sub>2</sub>), 40.5 (CH<sub>2</sub>), 38.6 (CH<sub>2</sub>), 36.9 (C), 33.5 (C), 33.4 (CH<sub>3</sub>), 24.2 (CH<sub>2</sub>), 21.5 (CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 19.8 (CH<sub>2</sub>), 19.3 (CH<sub>3</sub>), 18.6 (CH<sub>2</sub>), 18.6 (CH<sub>2</sub>), 15.0 (CH<sub>3</sub>). IR (KBr): 1759, 1447, 1308, 1145, 1081, 753, 744, 688, 564, 541 cm<sup>-1</sup>. HRMS (APcI) *m/z*: calcd for C<sub>35</sub>H<sub>44</sub>O<sub>7</sub>S<sub>2</sub>Na (M+Na<sup>+</sup>) 663.2426, found: 663.2435.

Compound **13b** (pure stereoisomer):  $[\alpha]_D^{25} = +32.4$  (c 10.7, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.85 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 8.0 Hz, 2H), 7.76 – 7.62 (m, 2H), 7.61 – 7.50 (m, 4H), 4.94 (br s, 1H), 4.10-3.95 (m, 2H), 2.84 (m, 1H), 2.55 (d, J = 17.7 Hz, 1H), 2.19 (s, 3H),2.10 – 2.30 (m, 2H), 1.75 – 0.70 (m, 12H), 0.97 (s, 3H), 0.91 – 0.84 (m, 3H), 0.83 (s, 3H), 0.75 (s, 6H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  168.6 (C), 139.3 (C), 138.6 (C), 137.4 (C), 134.2 (CH), 134.0 (CH), 129.5 (2CH), 129.2 (2CH), 129.1 (2CH), 129.0 (2CH), 119.7 (C), 76.3 (C), 64.9 (CH), 64.7 (CH), 56.1 (CH), 55.7 (CH), 50.8 (CH), 41.8 (CH<sub>2</sub>), 39.1 (CH<sub>2</sub>), 36.9 (C), 33.4 (CH<sub>3</sub>), 33.2 (CH<sub>2</sub>), 27.1 (C), 25.4 (CH<sub>2</sub>), 22.9 (CH<sub>3</sub>), 21.6 (CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 19.8 (CH<sub>2</sub>), 18.9 (CH<sub>2</sub>), 18.5 (CH<sub>2</sub>), 14.9 (CH<sub>3</sub>). IR (KBr): 1763, 1441, 1302, 1152, 1080, 757, 740, 679, 546 cm<sup>-1</sup>. HRMS (APcI) *m/z*: calcd for C<sub>35</sub>H<sub>44</sub>O<sub>7</sub>S<sub>2</sub>Na (M+Na<sup>+</sup>) 663.2426, found: 663.2443.

(4aS,6aR,7aS,12aR,12bS)- and (4aS,6aR,7aR,12aR,12bS)-4,4,6a,12b-tetramethyl-2,3,4,4a,5,6,6a,7a,10,12,12a,12b-dodecahydro-1H-benzo[a]xanthen-11-yl acetate (14a-b)



Mixture of epimers: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 5.85 – 5.79 (m, 1H), 5.75 (d, *J* = 2.3 Hz, 1H), 5.66 (dd, *J* = 10.1, 2.5 Hz, 1H), 4.95 (t, *J* = 6.8 Hz, 1H), 4.81 (t, *J* = 7.0 Hz, 1H), 2.83 – 2.76 (m, 3H), 2.44 (dd, *J* = 13.7, 3.1 Hz, 1H), 2.19 (s, 3H), 2.17 (s, 3H), 1.35 (s, 3H), 1.12 (s, 3H), 0.88 (s, 3H), 0.85 (s, 3H), 0.84 (s, 3H), 0.81 (s, 3H), 0.80 (s,

3H), 0.78 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 169.0 (C), 168.7 (C), 141.4 (C), 139.2 (C), 126.3 (CH), 126.0 (CH), 125.1 (C), 123.6 (CH), 122.6 (CH), 121.2 (C), 76.0 (C), 75.9 (C), 65.7 (CH), 65.4 (CH), 57.7 (CH), 56.3 (CH), 51.3 (2C), 43.0 (CH<sub>2</sub>), 42.1 (CH<sub>2</sub>), 42.0 (CH<sub>2</sub>), 41.6 (CH<sub>2</sub>), 39.4 (CH<sub>2</sub>), 38.8 (CH<sub>2</sub>), 37.3 (C), 37.1 (C), 33.6 (CH<sub>3</sub>), 33.5 (CH<sub>3</sub>), 33.4 (CH), 33.3 (CH), 28.9 (CH<sub>2</sub>), 28.9 (CH<sub>2</sub>), 24.9 (CH<sub>2</sub>), 24.9 (CH<sub>2</sub>), 21.7 (CH<sub>3</sub>), 21.5 (CH<sub>3</sub>), 20.9 (CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 20.3 (CH<sub>3</sub>), 20.2 (CH<sub>3</sub>), 20.0 (CH<sub>2</sub>), 19.5 (CH<sub>2</sub>), 18.7 (CH<sub>2</sub>), 18.6 (CH<sub>2</sub>), 15.4 (CH<sub>3</sub>), 15.2 (CH<sub>3</sub>). HRMS (ES+/TOF) *m*/*z*: calcd for C<sub>23</sub>H<sub>35</sub>O<sub>3</sub> (M+H<sup>+</sup>) 359.2586, found: 359.2593.

# 2-(((1R,2R,4aS,8aS)-2-hydroxy-2,5,5,8a-tetramethyl-decahydronaphthalen-1yl)methyl)phenyl acetate (15)



Hydrochloric acid (1 drop) was added to a stirred solution of **14a-b** (25 mg, 0.07 mmol) in chloroform (5 mL). After completion of the reaction (5 min, monitored by TLC) the solvent was evaporated in vacuo to give 25 mg of **15** (quantitative yield) as a colourless syrup.

 $[\alpha]_D^{25} = +10.4$  (c 10.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.43 – 7.35 (m, 1H), 7.20 – 7.13 (m, 2H), 6.97 (m, 1H), 2.69 (dd, J = 15.0, 6.0 Hz, 1H), 2.60 (dd, J = 15.0, 4.9 Hz, 1H), 2.35 (s, 3H), 1.85 (dt, J = 12.4, 3.1 Hz, 1H), 1.73 – 1.61 (m, 3H), 1.61 – 1.51 (m, 2H), 1.46 (dd, J = 12.8, 3.9 Hz, 1H), 1.43 – 1.30 (m, 3H), 1.27 (s, 3H), 1.16 – 1.06 (m, 1H), 0.96 (dd, J = 12.1, 2.1 Hz, 1H), 0.90 (s, 3H), 0.87 (s, 3H), 0.81 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ : 169.7 (C), 148.5 (C), 136.3 (C), 130.9 (CH), 126.7 (CH), 126.3 (CH), 122.5 (CH), 74.0 (C), 62.2 (CH), 56.3 (CH), 44.2 (CH<sub>2</sub>), 41.9 (CH<sub>2</sub>), 40.4 (CH<sub>2</sub>), 39.3 (C), 33.6 (CH<sub>3</sub>), 33.5 (C), 24.8 (CH<sub>2</sub>), 24.6 (CH<sub>3</sub>), 21.7 (CH<sub>3</sub>), 21.3 (CH<sub>3</sub>), 20.4 (CH<sub>2</sub>), 18.7 (CH<sub>2</sub>), 15.5 (CH<sub>3</sub>). IR (film): 3510, 1764, 1489, 1458, 1367, 1208, 1172, 1095, 748 cm<sup>-1</sup>. HRMS (APcI) m/z: calcd for C<sub>23</sub>H<sub>34</sub>O<sub>3</sub>Na (M+Na<sup>+</sup>) 381.2406, found: 381.2407.

# (4aS,6aR,12aR,12bS)-4,4,6a,12b-tetramethyl-2,3,4,4a,5,6,6a,12,12a,12b-decahydro-1H-benzo[a]xanthen-11-ol (17)



Conc. hydrochloric acid (1 mL) was added to a stirred solution of **16** (520 mg, 1.46 mmol) in MeOH (10 mL) and the reaction mixture was refluxed for 15 min, at which time TLC showed no starting material remaining. Then, the solvent was removed in vacuum and ether - water (30 : 10 mL) was added. Phases were shaken and separated. The organic phase was washed with water (10 mL) and brine (10 mL), and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under vacuum afforded a crude product which was directly purified by flash chromatography (35 % ether/hexanes) to yield 436 mg of **17** (95 %) as a yellow solid.

[α]<sub>D</sub><sup>25</sup> = +68.5 (c 1.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 6.94 (t, J = 8.0 Hz, 1H), 6.39 (d, J = 8.2 Hz, 1H), 6.32 (d, J = 7.9 Hz, 1H), 2.65 (dd, J = 16.4, 5.2 Hz, 1H), 2.34 (dd, J = 16.4, 13.1 Hz, 1H), 2.07 (dt, J = 12.6, 3.2 Hz, 1H), 1.77 (d, J = 12.7 Hz, 2H), 1.73 – 1.59 (m, 3H), 1.53 – 1.33 (m, 3H), 1.20 (s, 3H), 1.16 (dd, J = 13.4, 4.0 Hz, 1H), 1.04 (dd, J = 12.2, 2.0 Hz, 1H), 0.97 (td, J = 13.0, 3.7 Hz, 1H), 0.92 (s, 3H), 0.91 (s, 3H), 0.85 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 154.0 (C), 153.8 (C), 126.7 (CH), 109.5 (C), 109.4 (CH), 105.8 (CH), 55.9 (CH), 51.4 (CH), 41.6 (CH<sub>2</sub>), 40.8 (CH<sub>2</sub>), 39.0 (CH<sub>2</sub>), 36.7 (C), 33.2 (CH<sub>3</sub>), 33.0 (C), 29.4 (CH<sub>2</sub>), 21.4 (CH<sub>3</sub>), 20.4 (CH<sub>3</sub>), 19.5 (CH<sub>2</sub>), 18.3 (CH<sub>2</sub>), 16.6 (CH<sub>2</sub>), 14.6 (CH<sub>3</sub>). IR (KBr): 3401, 1459, 1286, 1127, 771 cm<sup>-1</sup>. HRMS (ES+/TOF) *m/z*: calcd for C<sub>21</sub>H<sub>31</sub>O<sub>2</sub> (M+H<sup>+</sup>) 315.2324, found: 315.2329.

#### (4aS,6aR,12aR,12bS)-8,10-dibromo-4,4,6a,12b-tetramethyl-

2,3,4,4a,5,6,6a,12,12a,12b-decahydro-1H-benzo[a]xanthen-11-ol (18)



To an ice cold solution of **17** (300 mg, 0.95 mmol) in  $CH_2Cl_2$  (10 mL), bromine (384 mg, 2.4 mmol) was added dropwise over 5 min. After stirring for 10 min at the same temperature, NaHSO<sub>3</sub> (5 mL) was added, and then ether (20 mL). The organic phase was washed with brine (2 x 10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated to give 419 mg (93%) of **18**, as a yellow solid.

[α]<sub>D</sub><sup>25</sup> = +46.8 (c 20.8, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 7.43 (s, 1H), 5.47 (br s, 1H) 2.73 (dd, J = 17.2, 5.2 Hz, 1H), 2.41 (dd, J = 17.1, 13.2 Hz, 1H), 2.14 (m, 1H), 1.84 – 1.72 (m, 3H), 1.64 (dt, J = 13.7, 3.5 Hz, 1H), 1.59 (dd, J = 13.2, 5.1 Hz, 1H), 1.52 – 1.34 (m, 4H), 1.18 (s, 3H), 1.04 (dd, J = 12.3, 2.0 Hz, 1H), 0.96 (td, J = 13.0, 3.6 Hz, 1H) 0.91 (s, 6H), 0.85 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ: 150.6 (C), 149.8 (C), 131.4 (CH), 112.6 (C), 102.5 (C), 99.6 (C), 78.7 (C), 56.2 (CH), 51.3 (CH), 41.9 (CH<sub>2</sub>), 40.7 (CH<sub>2</sub>), 39.3 (CH<sub>2</sub>), 37.0 (C), 33.6 (CH<sub>3</sub>), 33.3 (C), 21.7 (CH<sub>3</sub>), 20.9 (CH<sub>3</sub>), 19.9 (CH<sub>2</sub>), 18.6 (CH<sub>2</sub>), 18.6 (CH<sub>2</sub>), 14.9 (CH<sub>3</sub>). IR (KBr): 3517, 1445, 1317, 1226, 1126, 924, 717 cm<sup>-1</sup>. HRMS (ES+/TOF) *m/z*: calcd for C<sub>21</sub>H<sub>29</sub>O<sub>2</sub>Br<sub>2</sub> (M+H<sup>+</sup>) 471.0534, found: 471.0533.

## (4aS,6aR,12aR,12bS)-10-bromo-4,4,6a,12b-tetramethyl-1,2,3,4,4a,5,6,6a,12,12adecahydro-12bH-benzo[a]xanthene-8,11-dione (19)



To a solution of **18** (320 mg, 0.68 mmol) in acetic acid anhydride (10 mL) and MeCN (5 mL) was added a solution of  $CrO_3$  (75 mg, 0.75 mmol) in H<sub>2</sub>O (5 mL), upon which the solution turned black. The reaction mixture was heated at 60 °C for 1.5 h. After cooling to room temperature the mixture was diluted with H<sub>2</sub>O (15 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 20 mL). The combined organic phases were washed with brine (2 ×

20 mL), dried over anhydrous  $Na_2SO_4$  and concentrated to obtain 260 mg (94%) of compound **19** as an orange solid.

[α]<sub>D</sub><sup>25</sup> = +39.1 (c 3.9, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 7.13 (s, 1H), 2.56 (dd, J = 18.5, 4.7 Hz, 1H), 2.22 (m, 1H), 2.14 (dd, J = 18.5, 12.9 Hz, 1H), 1.84 – 1.66 (m, 2H), 1.61 (tt, J = 13.4, 3.4 Hz, 1H), 1.52 – 1.23 (m, 3H), 1.22 (s, 3H), 1.20 – 1.09 (m, 3H), 0.98 (dd, J = 12.3, 2.0 Hz, 1H), 0.90 (s, 3H), 0.89 (m, 1H), 0.88 (s, 3H), 0.83 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 179.7 (C), 178.9 (C), 152.2 (C), 138.7 (C), 135.3 (CH), 118.5 (C), 82.0 (C), 55.9 (CH), 51.1 (CH), 41.6 (CH<sub>2</sub>), 40.0 (CH<sub>2</sub>), 39.2 (CH<sub>2</sub>), 37.1 (C), 33.3 (CH<sub>3</sub>), 33.2 (C), 21.5 (CH<sub>3</sub>), 20.5 (CH<sub>3</sub>), 19.7 (CH<sub>2</sub>), 18.4 (CH<sub>2</sub>), 17.4 (CH<sub>2</sub>), 15.0 (CH<sub>3</sub>). IR (KBr): 1635, 1662, 1481, 1103, 775, 666 cm<sup>-1</sup>. HRMS (ES+/TOF) *m/z*: calcd for C<sub>21</sub>H<sub>28</sub>O<sub>3</sub>Br (M+H<sup>+</sup>) 407.1222, found: 407.1225.

Cyclospongiaquinone-1 (5)



To a stirred solution of **19** (210 mg, 0.52 mmol) in THF (20 mL) and  $H_2O$  (1.5 mL) was added NaN<sub>3</sub> (51 mg, 0.78 mmol) at room temperature and the resulting mixture was stirred for 1 h. The mixture was extracted with EtOAc (2 x 20 mL) and the combined organic layers were washed with  $H_2O$  (2 x 15 mL) and brine (15 mL). Then, the organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The residue was

directly used in the next reaction without purification. To a stirred solution of this residue in toluene (15 mL) and MeOH (1 mL) was added  $CsCO_3$  (254 mg, 0.78 mmol) at room temperature and the resulting mixture was stirred for 30 min. The mixture was diluted with ether (20 mL) and washed with H<sub>2</sub>O (2 x 10 mL) and brine (10 mL) and the organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under vacuum afforded a mixture which was directly purified by flash chromatography (25 % ether/hexanes) to yield 131 mg of **5** (71%) as yellow solid.

 $[\alpha]_D^{25} = +87.9$  (c 3.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$ : 5.75 (s, 1H), 3.80 (s, 3H), 2.50 (dd, J = 18.1, 4.7 Hz, 1H), 2.26 – 2.18 (m, 1H), 2.08 (dd, J = 18.1, 12.9 Hz, 1H), 1.83 – 1.68 (m, 3H), 1.61 (tdd, J = 13.7, 8.6, 5.1 Hz, 1H), 1.43 (dd, J = 12.8, 4.6 Hz, 2H), 1.40 – 1.31 (m, 2H), 1.21 (s, 3H), 1.15 (m, 1H), 1.01 – 0.91 (m, 2H), 0.89 (s, 3H), 0.86 (s, 3H), 0.82 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$ : 182.3 (C), 181.5 (C), 159.5 (C), 152.7 (C), 116.5 (C), 104.8 (CH), 81.9 (C), 56.5 (CH<sub>3</sub>), 56.1 (CH), 51.3 (CH), 41.8 (CH<sub>2</sub>), 40.2 (CH<sub>2</sub>), 39.3 (CH<sub>2</sub>), 37.2 (C), 33.5 (CH<sub>3</sub>), 33.3 (C), 21.6 (CH<sub>3</sub>), 20.6 (CH<sub>3</sub>), 19.8 (CH<sub>2</sub>), 18.5 (CH<sub>2</sub>), 16.4 (CH<sub>2</sub>), 15.1 (CH<sub>3</sub>). IR (KBr): 1655, 1605, 1458, 1245, 1126, 1122, 1054 cm<sup>-1</sup>. HRMS (ES+/TOF) *m*/*z*: calcd for C<sub>22</sub>H<sub>31</sub>O<sub>4</sub> (M+H<sup>+</sup>) 359.2222, found: 359.2214. (4aS,6aR,12aR,12bS)-9-methoxy-4,4,6a,12b-tetramethyl-1,2,3,4,4a,5,6,6a,12,12adecahydro-12bH-benzo[a]xanthene-8,11-dione (21)



To a solution of **19** (175 mg, 0.43 mmol) in dried methanol (10 mL) was added sodium methoxide (93 mg, 1.72 mmol) and the solution was stirred at room temperature for 15 min, at which time TLC showed no **19**. Then, the solvent was removed, and ether (25 mL) and water (6 mL) were added to the crude product and the organic phase was washed with water (10 mL), brine (10 mL) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under vacuum afforded a mixture which was directly purified by flash chromatography (25 % ether/hexanes) to yield 76 mg of **21** and 76 mg of **5** (99%) as yellow solids.

Compound **21**:  $[\alpha]_D^{25} = +60.1$  (c 2.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$ : 5.78 (s, 1H), 3.78 (s, 3H), 2.50 (dd, J = 18.8, 4.7 Hz, 1H), 2.20 (dt, J = 6.4, 2.9 Hz, 1H), 2.09 (dd, J = 18.8, 12.8 Hz, 1H), 1.81 – 1.68 (m, 3H), 1.67 – 1.55 (m, 2H), 1.43 (dd, J = 12.8, 4.7 Hz, 1H), 1.33 (m, 1H), 1.20 (s, 3H), 1.19 – 1.11 (m, 2H), 0.98 (m, 1H), 0.94 (dd, J = 13.0, 3.8 Hz, 1H), 0.89 (s, 3H), 0.86 (s, 3H), 0.82 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$ : 187.1 (C), 177.1 (C), 157.1 (C), 150.8 (C), 118.8 (C), 106.9 (CH), 81.4 (C), 56.3 (CH<sub>3</sub>), 56.1 (CH), 51.2 (CH), 41.8 (CH<sub>2</sub>), 40.3 (CH<sub>2</sub>), 39.4 (CH<sub>2</sub>), 37.2 (C), 33.5 (CH<sub>3</sub>), 33.3 (C), 21.6 (CH<sub>3</sub>), 20.6 (CH<sub>3</sub>), 19.8 (CH<sub>2</sub>), 18.5 (CH<sub>2</sub>), 16.7 (CH<sub>2</sub>), 15.1

(CH<sub>3</sub>). IR (KBr): 1690, 1647, 1628, 1601, 1458, 1379, 1239, 1123, 1042 cm<sup>-1</sup>. HRMS (ES+/TOF) m/z: calcd for C<sub>22</sub>H<sub>31</sub>O<sub>4</sub> (M+H<sup>+</sup>) 359.2222, found: 359.2211.

#### (4aS,6aR,12aR,12bS)-11-hydroxy-4,4,6a,12b-tetramethyl-

2,3,4,4a,5,6,6a,12,12a,12b-decahydro-1H-benzo[a]xanthene-10-carboxyaldehyde (22)



To a stirred solution of phenol **17** (315 mg, 1.00 mmol) in freshly distilled THF (15 mL) was added anhydrous magnesium chloride (145 mg, 1.50 mmol), paraformaldehyde (400mg) and triethylamine (406 mg, 4.00 mmol) at room temperature. The reaction mixture was stirred at reflux for 12 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and quenched with 1M aqueous HCl solution. The solvent was removed in vacuum and ether – water (25-10 mL) was added. The organic phase was washed with water (10 mL) and brine (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under vacuum afforded a crude product which was directly purified by flash chromatography (20 % ether/hexanes) to yield 318 mg of **22** (93 %) as a yellow solid.

 $[\alpha]_D^{25} = +126.7$  (c 29.6, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$ : 11.80 (s, 1H), 9.64 (s, 1H), 7.24 (d, J = 8.6 Hz, 1H), 6.40 (d, J = 8.6 Hz, 1H), 2.73 (dd, J = 17.0, 5.0 Hz, 1H),

2.33 (dd, J = 17.0, 13.2 Hz, 1H), 2.09 (dt, J = 12.5, 3.2 Hz, 1H), 1.84 – 1.75 (m, 2H), 1.73 – 1.58 (m, 2H), 1.55 (dd, J = 13.2, 5.0 Hz, 1H), 1.52 – 1.24 (m, 3H), 1.21 (s, 3H), 1.21 – 1.13 (m, 2H), 1.03 (dd, J = 12.2, 2.2 Hz, 1H), 0.92 (s, 3H), 0.91 (s, 3H), 0.88 (m, 1H), 0.85 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$ : 194.4 (CH), 162.1 (C), 161.0 (C), 132.5 (CH), 114.1 (C), 110.2 (CH), 110.2 (C), 79.2 (C), 56.2 (CH), 51.3 (CH), 41.9 (CH<sub>2</sub>), 40.9 (CH<sub>2</sub>), 39.3 (CH<sub>2</sub>), 37.1 (C), 33.5 (CH<sub>3</sub>), 33.3 (C), 21.7 (CH<sub>3</sub>), 20.9 (CH<sub>3</sub>), 19.8 (CH<sub>2</sub>), 18.6 (CH<sub>2</sub>), 16.3 (CH<sub>2</sub>), 15.0 (CH<sub>3</sub>). IR (KBr): 1625, 1488, 1379, 1232, 1085, 802, 759, 640 cm<sup>-1</sup>. HRMS (ES+/TOF) *m/z*: calcd for C<sub>22</sub>H<sub>31</sub>O<sub>3</sub> (M+H<sup>+</sup>) 343.2273, found: 343.2266.

# (4aS,6aR,12aR,12bS)-10-formyl-4,4,6a,12b-tetramethyl-2,3,4,4a,5,6,6a,12,12a,12bdecahydro-1H-benzo[a]xanthen-11-yl acetate (23)



To a stirred solution of **22** (285 mg, 0.83 mmol) in pyridine (2 mL) was added acetic anhydride (1 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 3 h, at which time TLC showed no starting material. Then, water (3 mL) was added at 0 °C to quench the reaction, and the reaction mixture was stirred for an additional 10 min. Then, ether (30 mL) was added, and the phases were shaken and separated. The organic phase was washed with 2 N HCl solution (4 x 10 mL), water (10 mL), saturated aq NaHCO<sub>3</sub> (4 x 10 mL), and brine (10 mL) and dried over anhydrous Na<sub>2</sub>SO<sub>4.</sub> Then, the solvent was removed in vacuum to obtain 307 mg (96 %) of compound **23** as a colourless syrup.

[α]<sub>D</sub><sup>25</sup> = +118.0 (c 6.0, CHCl<sub>3</sub>).<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 9.84 (s, 1H), 7.58 (d, J = 8.6 Hz, 1H), 6.77 (d, J = 8.6 Hz, 1H), 2.56 (dd, J = 16.7, 4.9 Hz, 1H), 2.41 (s, 3H), 2.30 (m, 1H), 2.10 (ddd, J = 12.5, 3.2, 1H), 1.79 (ddd, J = 13.7, 5.8, 3.6 Hz, 1H), 1.75 – 1.64 (m, 3H), 1.59 (dd, J = 13.3, 5.0 Hz, 1H), 1.48 (ddd, J = 13.6, 6.6, 3.2 Hz, 1H), 1.43 (m, 1H), 1.36 (m, 1H), 1.20 (s, 3H), 1.16 (dt, J = 13.8, 6.8 Hz, 1H), 1.03 (dd, J = 12.2, 2.1 Hz, 1H), 0.97 (m, 1H), 0.91 (s, 3H), 0.90 (s, 3H), 0.85 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 188.2 (CH), 169.0 (C), 160.0 (C), 151.1 (C), 131.5 (CH), 120.8 (C), 116.9 (C), 115.34 (CH), 79.0 (C), 56.2 (CH), 51.1 (CH), 41.8 (CH<sub>2</sub>), 40.8 (CH<sub>2</sub>), 39.2 (CH<sub>2</sub>), 37.1 (C), 33.5 (CH<sub>3</sub>), 33.3 (C), 21.7 (CH<sub>3</sub>), 21.0 (CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 19.8 (CH<sub>2</sub>), 18.6 (CH<sub>2</sub>), 17.0 (CH<sub>2</sub>), 15.0 (CH<sub>3</sub>). IR (film): 1769, 1693, 1603, 1272, 1185, 1077, 905, 821 cm<sup>-1</sup>. HRMS (ES+/TOF) *m*/*z*: calcd for C<sub>24</sub>H<sub>33</sub>O<sub>4</sub> (M+H<sup>+</sup>) 385.2379, found: 385.2387.

(4aS,6aR,12aR,12bS)-11-acetoxy-4,4,6a,12b-tetramethyl-2,3,4,4a,5,6,6a,12,12a,12bdecahydro-1H-benzo[a]xanthene-10-carboxylic acid (24)



To a solution of **23** (250 mg, 0.65 mmol) and NaH<sub>2</sub>PO<sub>4</sub> (195 mg, 1.63 mmol) in *tert*butanol (5 mL), 1-hexene (1.5 mL) and water (4 mL) at 0 °C, was slowly added a solution of NaClO<sub>2</sub> (80%, 187 mg, 2.60 mmol) in H<sub>2</sub>O (1 mL). The mixture was stirred at room temperature for 24 h, and then an aqueous sodium hydroxide solution (5%, 5 mL) was added. The mixture was extracted with ether (10 mL). The aqueous phase was acidified to pH = 3 by adding concentrated HCl, and then was extracted with ether (2 x 15 mL). The combined organic phases were washed with water (2 x 10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to give a crude product which was purified by flash chromatography (60% ether/hexanes) to give 221 mg (85%) of **24** as a yellow solid.

[α]<sub>D</sub><sup>25</sup> = +158.4 (c 0.8, CHCl<sub>3</sub>).<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.87 (d, J = 8.8 Hz, 1H), 6.71 (d, J = 8.8 Hz, 1H), 2.57 (br d, J = 14.8 Hz, 1H), 2.36 (s, 3H), 2.31 (dd, J = 15.5 Hz, 1H), 2.10 (ddd, J = 12.4, 3.0 Hz, 2H), 1.78 (br d, J = 12.4 Hz, 1H), 1.74 – 1.64 (m, 2H), 1.60 (m, 1H), 1.53 – 1.30 (m, 3H), 1.20 (s, 3H), 1.15 (dd, J = 13.5, 3.9 Hz, 1H), 1.03 (dd, J = 12.2, 1.8 Hz, 1H), 0.97 (ddd, J = 13.2, 3.7 Hz, 1H), 0.91 (s, 3H), 0.89 (s, 3H), 0.85 (s, 3H).<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.1 (C), 169.3 (C), 159.4 (C), 151.4 (C), 131.2 (CH), 117.2 (C), 114.9 (CH), 113.1 (C), 78.6 (C), 56.2 (CH), 51.2 (CH), 41.9 (CH<sub>2</sub>), 40.9 (CH<sub>2</sub>), 39.2 (CH<sub>2</sub>), 37.0 (C), 33.5 (C), 33.4 (CH<sub>3</sub>), 21.7 (CH<sub>3</sub>), 21.1 (CH<sub>3</sub>), 21.0 (CH<sub>3</sub>), 19.8 (CH<sub>2</sub>), 18.6 (CH<sub>2</sub>), 17.3 (CH<sub>2</sub>), 15.0 (CH<sub>3</sub>). IR (film): 1772, 1683, 1608, 1266, 1190, 1125, 1059 cm<sup>-1</sup>. HRMS (MALDI+/TOF) *m/z*: calcd for C<sub>24</sub>H<sub>32</sub>O<sub>5</sub>Na (M+Na<sup>+</sup>) 423.2147, found: 423.2142.

#### Hongoquercin A (6)



A tube containing a stir bar was charged with 1,4-benzoquinone (0.8 mg, 0.008 mmol),  $Pd(OAc)_2$  (3.6 mg, 0.016 mmol), Boc-Phe-OH (8 mg, 0.032 mmol),  $Li_2CO_3$  (24 mg, 0.32 mmol), carboxylic acid **24** (65 mg, 0.16 mmol), MeBF<sub>3</sub>K (58 mg, 0.48 mmol), Ag<sub>2</sub>CO<sub>3</sub> (88 mg, 0.32mmol) and *t*-BuOH (2 mL). Then, the tube was sealed in an argon atmosphere and the resulting mixture was stirred vigorously at room temperature for 10 min before being placed in an oil bath at 90 °C and stirred at this temperature for 20 h. The mixture was then cooled to room temperature, quenched with 2 N aqueous HCl (4 mL) and extracted with Et<sub>2</sub>O (3 x 10 mL). The combined organic extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to give a crude product which was purified by flash chromatography (60% ether/hexanes) to give 50 mg (83%) of **6** as a white solid.

[α]<sub>D</sub><sup>25</sup> = + 139.1 (c 0.56, MeOH).<sup>1</sup>H NMR (600 MHz, CD<sub>3</sub>OD) δ 6.10 (s, 1H), 2.64 (dd, J = 16.8, 5.0 Hz, 1H), 2.45 (s, 3H), 2.27 (dd, J = 16.8, 13.2 Hz, 1H), 2.04 (dt, J = 12.3,3.1 Hz, 1H), 1.78 (br d, J = 12.6 Hz, 2H), 1.74 – 1.61 (m, 2H), 1.56 – 1.46 (m, 2H), 1.46 – 1.38 (m, 2H), 1.27 – 1.18 (m, 1H), 1.18 (s, 3H), 1.07 (dd, J = 12.3, 2.1 Hz, 1H), 1.01 (td, J = 13.1, 3.9 Hz, 1H), 0.95 (s, 3H), 0.92 (s, 3H), 0.88 (s, 3H). <sup>13</sup>C NMR (150 MHz, CD<sub>3</sub>OD) δ 175.6 (C), 164.5 (C), 158.9 (C), 141.7 (C), 112.8 (CH), 108.8 (C), 105.0 (C), 78.9 (C), 57.5 (CH), 53.2 (CH), 43.0 (CH<sub>2</sub>), 42.1 (CH<sub>2</sub>), 40.5 (CH<sub>2</sub>), 38.1 (C), 34.2 (C), 33.9 (CH<sub>3</sub>), 24.2 (CH<sub>3</sub>), 22.0 (CH<sub>3</sub>), 21.1 (CH<sub>3</sub>), 20.8 (CH<sub>2</sub>), 19.6 (CH<sub>2</sub>), S19 17.7 (CH<sub>2</sub>), 15.4 (CH<sub>3</sub>). IR (KBr): 1621, 1585, 1457, 1370, 1259, 1118, 1082, 850 cm<sup>-1</sup>. HRMS (MALDI+/TOF) *m/z*: calcd for C<sub>23</sub>H<sub>32</sub>O<sub>4</sub>Na (M+Na<sup>+</sup>) 395.2198, found: 395.2186.



















































S34



