



Supporting Information

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The total synthesis of the fungal metabolite diversinol

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Experimental

Materials and methods. Flash column chromatography was performed using silica gel 60 (230–400 mesh) provided by Macherey-Nagel. TLC was performed using silica gel 60 F₂₅₄ coated aluminium sheets provided by Merck. NMR spectras were measured on a Bruker AM400 and a DRX500, respectively, with the solvent as an internal standard. Mass spectras were measured on a Finnigan MAT90 (EI-MS, HRMS). Elemental analyses were recorded on a Heraeus CHN-O-Rapid. IR spectras were measured as KBr wafers on a FT-IR Bruker IFS 88. Melting points were recorded on a MelTempII apparatus provided by Laboratory Devices Inc. and are uncorrected. All reagents are commercially available (Acros, Aldrich, Fluka, Lancaster, Merck) and were used without any further purification unless

otherwise mentioned. The employed solvents were distilled prior to use.

Orcinoldimethylether was prepared according to: R. N. Mirrington, G. I. Feutrill, *Org. Synth.* **1973**, *53*, 90-93.

4-Methyl-2,6-dimethoxybenzaldehyde:

To a solution of 8.06 g (52.9 mmol) orcinoldimethylether in 100 ml diethylether were added 11.9 g (79.5 mmol) tetramethylethylenediamine (TMEDA). The solution was cooled to 0 °C and 49.7 ml (79.5 mmol, 1.6 M) *n*-butyllithium were slowly added. The reaction mixture was stirred for 2h at room temperature followed by the addition of 11.6 g (159 mmol) *N,N*-dimethylformamide under ice cooling. After stirring for 4h at room temperature and the addition of brine, the mixture was extracted three times with 200 ml portions of diethylether. After drying over sodium sulfate and evaporation of the solvent, the crude product was purified by column chromatography (ethylacetate/cyclohexane 1/2, v/v), giving

8.51 g (89%) 4-methyl-2,6-dimethoxybenzaldehyde as a yellow solid.

Mp.: 91 °C. - R_f : 0.29 (EE/CH 1/2, v/v). - IR (KBr): 2788 (w), 1670 (m, ν C=O), 1470 (m), 1407 (m), 1241 (m) cm^{-1} . - ^1H NMR (500 MHz, CDCl_3): δ = 2.37 (s, 3 H, CH_3), 3.88 (s, 6 H, OCH_3), 6.38 (s, 2 H, H_{ar}), 10.44 (s, 1 H, CHO). - ^{13}C NMR (125 MHz, CDCl_3): δ = 23.0 (+, CH_3), 56.0 (+, OCH_3), 104.7 (+, CH_{ar}), 112.1 ($\text{C}_{\text{quart.}}$), 147.7 ($\text{C}_{\text{quart.}}$), 162.3 ($\text{C}_{\text{quart.}}$), 189.1 (+, CHO). - EI-MS: m/z (%) = 180 (100) [M^+]. - HR-EIMS: calc. 180.0786, found 180.0783. - $\text{C}_{10}\text{H}_{12}\text{O}_3$ (180.2 g/mol): calc. C 66.65, H 6.71; found C 66.97, H 6.61.

4-Methyl-6-methoxy-salicylic aldehyde (3): To a solution of 25.2 g (140 mmol) 2,6-dimethoxy-4-methylbenzaldehyde in 300 ml acetonitrile and 150 ml dichloromethane were slowly added 47.0 g (0.350 mol) aluminium chloride as well as 52.5 g (0.350 mol) sodium iodide under ice cooling. After stirring for 1h at room temperature water was slowly added under ice cooling and the mixture was extracted with three 200 ml portions of dichloromethane. After drying over sodium sulfate and evaporation of the solvent the crude product was purified by column chromatography (ethylacetate/cyclohexane 1/5, v/v) giving 18.6 g (80%) **6** as a yellow solid.

Mp.: 81 °C. - R_f : 0.46 (EE/CH 1/5, v/v). - IR (KBr): 2984 (m), 2982 (m), 1650 (m, ν C=O), 1353 (m), 1234 (m), 1121 (m) cm^{-1} . - ^1H NMR (500 MHz, CDCl_3): δ = 3.32 (s, 3 H, CH_3), 3.87 (s, 3 H,

OCH₃), 6.18 (s, 1 H, H_{ar}), 6.34 (s, 1 H, H_{ar}), 10.24 (s, 1 H, CHO), 11.99 (s, 1 H, OH). – ¹³C NMR (125 MHz, CDCl₃): δ = 23.3 (+, CH₃), 56.0 (+, OCH₃), 102.5 (+, CH_{ar}), 109.3 (C_{quart.}), 110.5 (+, CH_{ar}), 150.9 (C_{quart.}), 162.6 (C_{quart.}), 164.0 (C_{quart.}), 193.9 (+, CHO). – EI-MS: m/z (%) = 166 (100) [M⁺], 148 (26) [M⁺ – H₂O]. – HR-EIMS: calc. 166.0629, found 166.0628. – C₉H₁₀O₃ (166.2 g/mol): calc. C 65.05, H 6.07; found C 65.45, H 6.11.

4-hydroxycyclohexen-1-one (**4**) was prepared according to a four step literature procedure starting from benzoquinone and cyclopentadiene.^[11] The yield of the last step could be improved significantly.

4-Hydroxycyclohexen-1-one (4): 7.85 g (44.0 mmol) 1,4,4a,6,7,8a-Hexahydro-8-hydroxy-1,4-methanonaphthalen-5-one^[11] were pyrolyzed for 30 min at 250 °C and 300 mbar in a bulb to bulb distillation apparatus. The whole distillate was subjected to column chromatography (ethylacetate/cyclohexane 1/1, v/v) to give 3.22 g (65%) **7** as a colorless oil.

R_f: 0.14 (EE/CH 1/1, v/v). – IR (KBr): 3397 (s, ? OH), 2955 (m), 2873 (m), 1677 (s, ? C=O). – ¹H NMR (400 MHz, CDCl₃): δ = 1.88-1.99 (m, 1 H, 5-CH₂), 2.24-2.37 (m, 2 H, 5-CH₂, 6-CH₂), 2.48-2.55 (m, 1 H, 6-CH₂), 2.77 (d, ³J_{HH} = 6.1 Hz, 1 H, OH), 4.48-4.56 (m, 1 H, 4-H), 5.90 (ddd, ³J_{HH} = 10.2 Hz, ⁴J_{HH} = 2.0 Hz, ⁴J_{HH} = 1.1 Hz, 1 H, 2-H), 6.89 (ddd, ³J_{HH} = 10.2 Hz, ³J_{HH} = 2.3 Hz, ⁴J_{HH} = 1.7 Hz, 1 H, 3-H). – ¹³C NMR (100 MHz, CDCl₃): δ

= 32.4 (-, C-5), 35.3 (-, C-6), 66.2 (+, C-4), 129.1 (+, C-2), 153.1 (+, C-3), 199.1 ($C_{\text{quart.}}$, C-1). - EI-MS: m/z (%) = 112 (46) [M^+], 84 (100) [$M^+ - C_2H_4$]. - HR-EIMS: calc. 112.0524, found 112.0527.

4-Hydroxy-8-methoxy-6-methyl-2,3,4,4a-tetrahydroxanthen-1-one (5):

A suspension of 6.63 g (39.9 mmol) 4-methyl-6-methoxysalicylic aldehyde (**3**), 8.87 g (79.1 mmol) 4-hydroxycyclohexen-1-one (**4**) and 1.36 g (19.9 mmol) imidazole in 60 mL water/dioxane (v/v, 2/1) was sonified for 7 d. The mixture was extracted three times with 150 mL portions of ethyl acetate, dried over sodium sulfate and purified by column chromatography (ethyl acetate/cyclohexane 1/2, v/v) giving 6.34 g (61%) **5** as a separable mixture of two diastereomers (cis/trans = 1.5/1).

Cis-5: (Mp.: 130–132 °C). - R_f : 0.11 (EE/CH 1/2, v/v). - IR (KBr): 3417 (m, ν OH), 2929 (m), 1674 (m, ν C=O), 1594 (m), 1054 (m) cm^{-1} . - ^1H NMR (500 MHz, CDCl_3): δ = 1.81–1.89 (m, 1 H, CH_2), 2.17–2.21 (m, 1 H, CH_2), 2.31 (s, 3 H, $\text{CH}_{3\text{ar}}$), 2.45–2.52 (m, 1 H, CH_2), 2.59–2.65 (m, 1 H, CH_2), 2.80 (s, 1 H, OH), 3.82 (s, 3 H, OCH_3), 4.27 (m, 1 H, 4-H), 4.72 (dd, $^3J_{\text{HH}} = 8.8$ Hz, $^4J_{\text{HH}} = 2.2$ Hz, 1 H, 4a-H), 6.29 (s, 1 H, H_{ar}), 6.38 (s, 1 H, H_{ar}), 7.81 (d, $^4J(\text{H},\text{H}) = 1.9$ Hz, 1 H, H-9). - ^{13}C NMR (125 MHz, CDCl_3): δ = 22.8 (+, $\text{CH}_{3\text{ar}}$), 26.3 (-, CH_2), 37.0 (-, CH_2), 56.0

(+, OCH₃), 71.6 (+, C-4), 80.3 (+, C-4a), 105.5 (+, CH_{ar}), 109.5 (+, CH_{ar}), 109.7 (C_{quart.}), 124.2 (C_{quart.}), 129.7 (+, C-9), 144.8 (C_{quart.}), 156.2 (C_{quart.}), 158.4 (C_{quart.}), 195.7 (C-1). – EI-MS: m/z (%) = 260 (3) [M⁺], 43 (100) [C₂H₃O⁺]. – HR-EIMS: calc. 260.1048, found 260.1046.

Trans-5: (Mp.: 126–128 °C). – R_f: 0.21 (EE/CH 1/2, v/v). – IR (KBr): 3491 (m, ν OH), 2898 (m), 1672 (m, ν C=O), 1597 (m), 1170 (m) cm⁻¹. – ¹H NMR (500 MHz, CDCl₃): δ = 1.82–1.89 (m, 1 H, CH₂), 2.29–2.41 (m, 5 H, CH_{3ar}, CH₂), 2.61 (s, 1H, OH), 2.79–2.87 (m, 1 H, CH₂), 3.86 (s, 3 H, OCH₃), 4.45 (m, 1 H, 4-H), 4.94 (dd, ³J_{HH} = 2.8 Hz, ³J_{HH} = 2.5 Hz, 1 H, 4a-H), 6.29 (s, 1 H, H_{ar}), 6.35 (s, 1 H, H_{ar}), 7.84 (d, ⁴J_{HH} = 2.2 Hz, 1 H, 9-H). – ¹³C NMR (125 MHz, CDCl₃): δ = 22.7 (+, CH_{3ar}), 24.0 (-, CH₂), 32.5 (-, CH₂), 56.0 (+, OCH₃), 65.4 (+, C-4), 77.4 (+, C-4a), 105.6 (+, CH_{ar}), 109.6 (+, CH_{ar}), 109.6 (C_{quart.}), 124.6 (C_{quart.}), 129.0 (+, C-9), 144.3 (C_{quart.}), 155.9 (C_{quart.}), 158.2 (C_{quart.}), 197.0 (C-1). – EI-MS: m/z (%) = 260 (8) [M⁺], 43 (100) [C₂H₃O⁺]. – HR-EIMS: calc. 260.1048, found 260.1056. – C₁₅H₁₆O₄ (260.2 g/mol): calc. C 69.22, H 6.20; found C 68.87, H 6.33.

8-Methoxy-4-(2-methoxy-ethoxymethoxy)-6-methyl-2,3,4,4a-tetrahydroxanthen-1-one (6):

To a solution of 2.74 g (10.5 mmol) cis/trans-4-hydroxy-8-methoxy-6-methyl-2,3,4,4a-tetrahydroxanthen-1-one (5) in 35 ml of dichloromethane were added 2.04 g (15.8 mmol) *N,N*-diisopropylethylamine followed by 1.97 g (15.8 mmol) 1-

chloromethoxy-2-methoxyethane (MEM-chloride). The reaction mixture was stirred for 3h at room temperature. After the addition of water, the mixture was extracted three times with 100 ml portions of dichloromethane. After drying over sodium sulfate and evaporation of the solvent the residue was purified by column chromatography (ethylacetate/cyclohexane 1/2, v/v) yielding 2.47 g (75%) **6** as a brown oil and an inseparable mixture of two diastereomers (cis/trans = 3/1).

R_f : 0.20 (EE/CH 1/2, v/v). - IR (KBr): 2947 (w), 1676 (m, ν C=O), 1596 (w) cm^{-1} . - ^1H NMR (500 MHz, CDCl_3): d = 2.24-2.30 (m, 9 H, $\text{CH}_{3\text{ar}}$, CH_2), 2.38-2.50 (m, 2 H, CH_2), 2.58-2.63 (m, 2 H, CH_2), 2.69-2.77 (m, 1 H, CH_2), 3.41 (s, 6 H, OCH_3), 3.55-3.63 (m, 4 H, $\text{O-CH}_2\text{-CH}_2\text{-O}$), 3.77-3.88 (m, 10 H, $\text{O-CH}_2\text{-CH}_2\text{-O}$, OCH_3), 4.23-4.28 (m, 1 H, cis 4-H), 4.46-4.48 (m, 1 H, trans 4-H), 4.77-4.79 (m, 1 H, cis 4a-H), 4.88-4.89 (m, 1 H, trans 4a-H), 4.95 (d, $^2J_{\text{HH}} = 7.1$ Hz, 1 H, $\text{O-CH}_2\text{-O}$), 5.01 (d, $^2J_{\text{HH}} = 7.1$ Hz, 1 H, $\text{O-CH}_2\text{-O}$), 6.24 (s, 1 H, H_{ar}), 6.28 (s, 1 H, H_{ar}), 6.29 (s, 1 H, H_{ar}), 6.36 (s, 1 H, H_{ar}), 7.80-7.84 (m, 2 H, 9-H). - ^{13}C NMR (125 MHz, CDCl_3): d = 22.5 (+, CH_3), 22.5 (+, CH_3), 23.1 (-, CH_2), 24.9 (-, CH_2), 32.9 (-, CH_2), 36.7 (-, CH_2), 55.7 (+, $2 \times \text{OCH}_3$), 59.1 (+, $2 \times \text{OCH}_3$), 67.1 (-, $\text{O-CH}_2\text{-CH}_2\text{-O}$), 67.2 (-, $\text{O-CH}_2\text{-CH}_2\text{-O}$), 71.8 (-, $2 \times \text{O-CH}_2\text{-CH}_2\text{-O}$), 75.6 (+, $2 \times \text{C-4}$), 78.6 (+, $2 \times \text{C-4a}$), 94.8 (-, $\text{O-CH}_2\text{-O}$), 95.0 (-, $\text{O-CH}_2\text{-O}$), 104.9 (+, CH_{ar}), 105.0 (+, CH_{ar}), 109.0 ($\text{C}_{\text{quart.}}$), 109.3 ($\text{C}_{\text{quart.}}$), 109.4 (+, CH_{ar}), 109.6 (+, CH_{ar}), 123.9 ($\text{C}_{\text{quart.}}$), 124.7 ($\text{C}_{\text{quart.}}$), 128.4 (+, C-9), 129.7 (+, C-9), 144.0 ($\text{C}_{\text{quart.}}$), 144.5 ($\text{C}_{\text{quart.}}$), 156.1

(C_{quart.}), 156.4 (C_{quart.}), 157.9 (C_{quart.}), 158.1 (C_{quart.}), 195.4 (C-1), 196.4 (C-1). - EI-MS: m/z (%) = 348 (1) [M⁺], 89 (100) [C₄H₉O₂⁺]. - HR-EIMS: calc. 348.1572, found 348.1567.

(9R*, 9aR*, 4S*)-7, 9a-Dibromo-9-hydroxy-8-methoxy-4-(2-methoxy-ethoxymethoxy-)-6-methyl-2,3,4,4a,9,9a-hexahydroxanthren-1-one (7):

To a solution of 2.98 g (8.55 mmol) cis/trans-8-methoxy-4-(2-methoxy-ethoxymethoxy-)-6-methyl-2,3,4,4a-tetrahydroxanthren-1-one (**6**) in 50 ml THF/H₂O (1/1, v/v) were added 8.23 g (17.1 mmol) tetrabutylammonium tribromide at room temperature. The mixture was stirred at room temperature for 5h followed by the addition of water. The mixture was extracted with three 100 ml portions of diethylether and the combined organic phases dried over sodium sulfate. After evaporation of the solvent, the residue was purified by column chromatography (ethylacetate/cyclohexane 1/2, v/v) giving 2.34 g (52%) **7** as a yellow oil and an inseparable mixture of two distereomers (cis/trans > 9/1).

*R*_f: 0.25 (EE/CH 1/2, v/v). - IR (KBr): 3410 (w, v OH), 2938 (w), 1723 (w, v C=O), 1607 (w), 1461 (w) cm⁻¹. - ¹H NMR (500 MHz, CDCl₃): δ = 1.73-1.82 (m, 1 H, CH₂), 2.27-2.41 (m, 5 H, CH_{3ar}, CH₂), 2.48-2.57 (m, 1 H, CH₂), 2.83 (s, 1H, OH), 3.38-3.43 (m, 5 H, OCH₃, O-CH₂-CH₂-O), 3.60-3.64 (m, 2 H, O-CH₂-CH₂-O), 3.85 (s, 3 H, OCH₃), 3.87-3.92 (m, 1 H, 4-H), 4.51-4.56 (m, 1 H, 4a-H), 4.98 (d, ²J_{HH} = 7.1 Hz, 1 H, O-CH₂-O), 5.36 (d, ²J_{HH}

= 7.1 Hz, 1 H, O-CH₂-O), 6.47 (s, 1 H, H_{ar}). - ¹³C NMR (125 MHz, CDCl₃): δ = 24.0 (+, CH₃), 26.8 (-, CH₂), 34.9 (-, CH₂), 56.2 (+, OCH₃), 59.4 (+, OCH₃), 62.8 (+, C-4), 67.5 (-, O-CH₂-CH₂-O), 72.2 (-, O-CH₂-CH₂-O), 76.4 (+, C-4a), 95.9 (-, O-CH₂-O), 104.4 (C_{quart.}), 106.2 (+, CH_{ar}), 106.5 (C_{quart.}), 108.8 (C_{quart.}), 140.8 (C_{quart.}), 150.0 (C_{quart.}), 157.6 (C_{quart.}), 201.9 (C-1). - EI-MS: m/z (%) = 522/524/526 (9/18/9) [M⁺], 434/436/438 (50/100/50) [M⁺-C₄H₈O₂]. - HR-EIMS: calc. 521.9888, found 521.9888.

(9R*,4S*)-7-Bromo-9-hydroxy-8-methoxy-4-(2-methoxy-ethoxymethoxy)-6-methyl-2,3,4,9-tetrahydroxanthren-1-one (8):

To a solution of 5.67 g (10.8 mmol) 7,9a-dibromo-9-hydroxy-8-methoxy-4-(2-methoxy-ethoxymethoxy)-6-methyl-2,3,4,4a,9,9a-hexahydroxanthren-1-one (7) in 100 ml dioxane were added 3.64 g (32.4 mmol) DABCO at room temperature and the mixture was stirred for 16h. After the addition of water, the mixture was extracted with three 100 ml portions of diethylether. After drying over sodium sulfate and evaporation of the solvent the crude product was purified by column chromatography (ethylacetate/cyclohexane 1/1 + 5% triethylamine, v/v) giving 2.52 g (53%) **8** as a brown oil.

R_f: 0.10 (EE/CH 1/2 + 5% triethylamine, v/v). - IR (KBr): 3421 (m, ν OH), 2943 (m), 2893 (m), 1661 (m, ν C=O), 1462 (m) cm⁻¹. - ¹H NMR (500 MHz, CDCl₃): δ = 2.24-2.27 (m, 2 H, CH₂), 2.38-2.48 (m, 4 H, CH₃, CH₂), 2.78-2.84 (m, 1 H, CH₂), 3.03 (s, 1 H, OH), 3.38 (s, 3 H, OCH₃), 3.56-3.64 (m, 2 H, O-CH₂-CH₂-O), 3.80-3.88

(m, 2 H, O-CH₂-CH₂-O), 3.89 (s, 3 H, OCH₃), 4.68 (dd, ³J_{HH} = 5.34, 5.02 Hz, 1 H, 4-H), 4.97 (d, ²J_{HH} = 7.1 Hz, 1 H, O-CH₂-O), 5.18 (d, ²J_{HH} = 7.1 Hz, 1 H, O-CH₂-O), 5.95 (s, 1 H, 9-H), 6.63 (s, 1 H, H_{ar}). - ¹³C NMR (125 MHz, CDCl₃): δ = 23.9 (+, CH₃), 27.9 (-, CH₂), 33.8 (-, CH₂), 54.5 (+, C-9), 56.4 (+, OCH₃), 59.4 (+, OCH₃), 67.7 (-, O-CH₂-CH₂-O), 69.4 (+, C-4), 72.1 (-, O-CH₂-CH₂-O), 95.5 (-, O-CH₂-O), 104.2 (C_{quart.}), 109.1 (+, CH_{ar}), 111.3 (C_{quart.}), 114.2 (C_{quart.}), 140.2 (C_{quart.}), 147.3 (C_{quart.}), 157.3 (C_{quart.}), 164.9 (C_{quart.}), 197.9 (C_{quart.}, C-1). - EI-MS: m/z (%) = 442/444 (2/2) [M⁺], 335/337 (67/73) [M⁺-C₄H₁₁O₃], 45 (100) [C₂H₅O⁺]. - HR-EIMS: calc. 442.0627, found 442.0632.

7-Bromo-8-methoxy-4-(2-methoxy-ethoxymethoxy)-6-methyl-3,4-dihydro-2H-xanthene-1,9-dione (9):

To a solution of 0.657 g (1.48 mmol) 7-bromo-9-hydroxy-8-methoxy-4-(2-methoxy-ethoxymethoxy)-6-methyl-2,3,4,9-tetrahydroxanthene-1-one (**8**) in 50 ml dichloromethane and 10 ml acetonitrile were added 1.00 g molecular sieves as well as 0.600 g (4.44 mmol) *N*-methylmorpholine-*N*-oxide under an argon atmosphere. After stirring for 15 minutes 0.052 g (10 mol%) tetrapropylammoniumperruthenate (TPAP) were added and the mixture was sonified for 6 h. After evaporation of the solvent the crude reaction mixture was directly subjected to column chromatography (acetone/chloroform 1/5, v/v) yielding 0.249 g (40%) **9** as a red-brown oil.

R_f : 0.21 (CHCl_3 /acetone 5/1, v/v). - IR (KBr): 2890 (w), 1701 (m), 1615 (w), 1402 (w), 1111 (w) cm^{-1} . - ^1H NMR (400 MHz, CDCl_3): d = 2.22-2.37 (m, 2 H, CH_2), 2.48-2.56 (m, 4 H, CH_3 , CH), 2.78-2.85 (m, 1 H, CH), 3.38 (s, 3 H, OCH_3), 3.56-3.60 (m, 2 H, $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$), 3.80-3.84 (m, 2 H, $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$), 3.91 (s, 3 H, OCH_3), 4.88 (dd, $^3J_{\text{HH}} = 5.0$, 4.8 Hz, 1 H, 4-H), 4.97 (d, $^2J_{\text{HH}} = 7.3$ Hz, 1 H, $\text{O}-\text{CH}_2-\text{O}$), 5.20 (d, $^2J_{\text{HH}} = 7.3$ Hz, 1 H, $\text{O}-\text{CH}_2-\text{O}$), 6.74 (s, 1 H, H_{ar}). - ^{13}C NMR (100 MHz, CDCl_3): d = 24.3 (+, CH_3), 27.1 (-, CH_2), 34.9 (-, CH_2), 56.8 (+, OCH_3), 59.4 (+, OCH_3), 67.9 (-, $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$), 69.9 (+, C-4), 71.9 (-, $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$), 95.6 (-, $\text{O}-\text{CH}_2-\text{O}$), 104.0 ($\text{C}_{\text{quart.}}$), 110.3 (+, CH_{ar}), 115.2 ($\text{C}_{\text{quart.}}$), 117.0 ($\text{C}_{\text{quart.}}$), 145.8 ($\text{C}_{\text{quart.}}$), 153.1 ($\text{C}_{\text{quart.}}$), 158.9 ($\text{C}_{\text{quart.}}$), 161.2 ($\text{C}_{\text{quart.}}$), 172.5 ($\text{C}_{\text{quart.}}$, C-9), 192.9 ($\text{C}_{\text{quart.}}$, C-1). - EI-MS: m/z (%) = 440/442 (1/1) [M^+], 351/353 (52/52) [$\text{M}^+ - \text{C}_4\text{H}_9\text{O}_2$], 45 (100) [$\text{C}_2\text{H}_5\text{O}^+$]. - HR-EIMS: calc. 440.0470, found 440.0473.

(4S*,4aR*)-7-Bromo-1-hydroxy-8-methoxy-4-(2-methoxy-ethoxy-methoxy)-4a,6-dimethyl-2,3,4,4a-tetrahydroxanthene-9-one (10):

To a suspension of 0.223 g (2.49 mmol) coppercyanide in 5 ml diethylether were slowly added 1.56 ml methyllithium (2.49 mmol; 1.6 M diethylether) at $-50\text{ }^\circ\text{C}$ under an argon atmosphere. After the copper cyanide had dissolved the solution was stirred for 30 min at $-78\text{ }^\circ\text{C}$. In a second flask 0.220 g (498 μmol) 7-bromo-8-methoxy-4-(2-methoxy-ethoxymethoxy)-6-methyl-3,4-dihydro-2H-xanthene-1,9-dione (**9**) were dissolved in

5 ml THF and cooled to -78 °C. After addition of the cuprate the resulting deep red solution was stirred at -78 °C for 5 h. After the addition of 5 ml 10% hydrochloric acid the mixture was filtered and the residue was washed thoroughly with ethylacetate. The organic phase was separated and dried over sodium sulfate. After evaporation of the solvent the product was purified by column chromatography (ethylacetate/cyclohexane 1/2, v/v) yielding 0.117 g (52%) **10** as a yellow oil.

R_f : 0.24 (ethylacetate/cyclohexane 1/2, v/v). - IR (KBr): 2927 (w), 1597 (w), 1468 (vw), 1118 (vw) cm^{-1} . - ^1H NMR (400 MHz, CDCl_3): d = 1.45 (s, 3 H, CH_3), 1.91-1.99 (m, 1 H, CH_2), 2.11-2.22 (m, 1 H, CH), 2.29-2.43 (m, 4 H, CH_3 , CH), 2.69-2.79 (m, 1 H, CH_2), 3.41 (s, 3H, OCH_3), 3.55-3.64 (m, 2 H, $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$), 3.79-3.84 (m, 2 H, $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$), 3.92 (s, 3 H, OCH_3), 4.23 (dd, $^3J_{\text{HH}} = 1.8, 1.5$ Hz, 1 H, 4-H), 4.86 (d, $^2J_{\text{HH}} = 7.1$ Hz, 1 H, $\text{O}-\text{CH}_2-\text{O}$), 5.15 (d, $^2J_{\text{HH}} = 7.1$ Hz, 1 H, $\text{O}-\text{CH}_2-\text{O}$), 6.47 (s, 1 H, H_{ar}), 15.97 (s, 1 H, 1-OH). - ^{13}C NMR (100 MHz, CDCl_3): d = 23.4 (-, CH_2), 24.7 (+, CH_3), 26.3 (+, CH_3), 26.5 (-, CH_2), 56.6 (+, OCH_3), 59.4 (+, OCH_3), 67.4 (-, $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$), 72.2 (-, $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$), 74.1 (+, C-4), 81.6 ($\text{C}_{\text{quart.}}$, C-4a), 95.6 (-, $\text{O}-\text{CH}_2-\text{O}$), 106.0 ($\text{C}_{\text{quart.}}$), 106.3 ($\text{C}_{\text{quart.}}$), 107.0 (+, $\text{CH}_{\text{ar.}}$), 109.1 ($\text{C}_{\text{quart.}}$), 146.6 ($\text{C}_{\text{quart.}}$), 156.2 ($\text{C}_{\text{quart.}}$), 159.5 ($\text{C}_{\text{quart.}}$), 181.2 ($\text{C}_{\text{quart.}}$, C-9), 182.3 ($\text{C}_{\text{quart.}}$, C-1). - EI-MS: m/z (%) = 456/458 (1/1) [M^+], 256 (75) [$\text{M}^+ - \text{C}_5\text{H}_{13}\text{BrO}_3$]. - HR-EIMS: calc. 456.0783, found 456.0788.

(4S*,4aR*)-1-Hydroxy-8-methoxy-4-(2-methoxy-ethoxymethoxy)-4a,6-dimethyl-2,3,4,4a-tetrahydroxanthren-9-one (11):

To a solution of 0.117 g (260 μmol) 7-bromo-1-hydroxy-8-methoxy-4-(2-methoxy-ethoxymethoxy)-4a,6-dimethyl-2,3,4,4a-tetrahydroxanthren-9-one (**10**) in 5 ml of tetrahydrofuran were slowly added 0.550 ml *tert*-butyllithium (820 μmol ; 1.5 M in pentane) at -78 °C under an atmosphere of argon. The resulting yellow solution was stirred for 3 h at -78 °C. After the addition of saturated NaHCO_3 -solution the mixture was extracted with three 50 ml portions of diethylether. The combined organic phases were dried over sodium sulfate and after evaporation of the solvent the product was purified by column chromatography (ethylacetate/cyclohexane 1/2, v/v) giving 0.091 g (93%) **11** as a yellow oil.

R_f : 0.19 (ethylacetate/cyclohexane 1/2, v/v). - IR (KBr): 2920 (w), 1592 (w), 1475 (vw), 1121 (vw) cm^{-1} . - ^1H NMR (400 MHz, CDCl_3): d = 1.43 (s, 3 H, CH_3), 1.89-1.98 (m, 1 H, CH_2), 2.09-2.15 (m, 1 H, CH), 2.27-2.33 (m, 4 H, CH_3 , CH), 2.66-2.75 (m, 1 H, CH_2), 3.41 (s, 3H, OCH_3), 3.57-3.61 (m, 2 H, $\text{O-CH}_2\text{-CH}_2\text{-O}$), 3.77-3.80 (m, 2 H, $\text{O-CH}_2\text{-CH}_2\text{-O}$), 3.91 (s, 3 H, OCH_3), 4.08 (dd, $^3J_{\text{HH}} = 4.0, 1.5$ Hz, 1 H, 4-H), 4.85 (d, $^2J_{\text{HH}} = 7.1$ Hz, 1 H, $\text{O-CH}_2\text{-O}$), 4.97 (d, $^2J_{\text{HH}} = 7.1$ Hz, 1 H, $\text{O-CH}_2\text{-O}$), 6.31 (m, 2 H, H_{ar}), 16.16 (s, 1 H, 1-OH). - ^{13}C NMR (100 MHz, CDCl_3): d = 22.7 (+, CH_3), 23.4 (-, CH_2), 26.3 (+, CH_3), 26.5 (-, CH_2), 56.5 (+, OCH_3), 59.4 (+, OCH_3), 67.4 (-, $\text{O-CH}_2\text{-CH}_2\text{-O}$), 72.1 (-, $\text{O-CH}_2\text{-}$

CH_2-O), 75.2 (+, C-4), 80.2 ($C_{quart.}$, C-4a), 95.5 (-, O- CH_2-O), 105.7 (+, CH_{ar}), 106.2 ($C_{quart.}$), 107.8 ($C_{quart.}$), 111.6 (+, CH_{ar}), 147.5 ($C_{quart.}$), 160.2 ($C_{quart.}$), 160.9 ($C_{quart.}$), 181.5 ($C_{quart.}$), 181.6 ($C_{quart.}$). - EI-MS: m/z (%) = 378 (35) [M^+], 289 (45) [$M^+ - C_4H_9O_2$]. - HR-EIMS: calc. 378.1678, found 378.1676.

(4S*,4aS*,9aS*)-9a-hydroxy-8-methoxy-4-(2-methoxy-ethoxymethoxy)-4a,6-dimethyl-3,4,4a,9a-tetrahydro-2H-xanthene-1,9-dione (12):

To a solution of 34 mg (0.089 mmol) 1-hydroxy-8-methoxy-4-(2-methoxy-ethoxymethoxy)-4a,6-dimethyl-2,3,4,4a-tetrahydro-xanthene-9-one (**11**) in 5 ml ethanol were added 28 mg magnesium monoperoxophthalate (49 μ mol; 80%) at room temperature. The solution was stirred for 5 h and after evaporation of the solvent the residue was subjected to column chromatography (ethylacetate/cyclohexane 1/1, v/v) to give 20 mg (57%) **12** as a pale yellow oil.

R_f : 0.06 (ethylacetate/cyclohexane 1/1, v/v). - IR (KBr): 3416 (m, ν OH), 2944 (w), 1742 (w), 1615 (m, ν C=O), 1113 (w) cm^{-1} . - 1H NMR (400 MHz, $CDCl_3$): δ = 1.27 (s, 3 H, CH_3), 1.92-2.01 (m, 1 H, CH_2), 2.20-2.32 (m, 6 H, CH_3 , CH_2), 3.42 (s, 3H, OCH_3), 3.60-3.63 (m, 2 H, O- CH_2-CH_2-O), 3.83-3.86 (m, 5 H, OCH_3 , O- CH_2-CH_2-O), 3.89 (s, 1 H, OH), 4.25 (dd, $^3J_{HH}$ = 2.8, 2.3 Hz, 1 H, 4-H), 4.94 (d, $^2J_{HH}$ = 7.1 Hz, 1 H, O- CH_2-O), 5.09 (d, $^2J_{HH}$ = 7.1 Hz, 1 H, O- CH_2-O), 6.36 (m, 2 H, H_{ar}). - ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.8 (+, CH_3), 22.7 (+, CH_3), 27.3 (-, CH_2), 33.3 (-, CH_2), 56.4 (+, OCH_3), 59.4 (+, OCH_3), 68.2 (-, O- CH_2-CH_2-O), 71.9 (-, O-

CH₂-CH₂-O), 78.4 (C_{quart.}), 79.4 (+, C-4), 82.9 (C_{quart.}), 96.4 (-, O-CH₂-O), 106.3 (+, CH_{ar}), 108.2 (C_{quart.}), 110.6 (+, CH_{ar}), 147.6 (C_{quart.}), 158.6 (C_{quart.}), 162.1 (C_{quart.}), 183.2 (C_{quart.}), 204.9 (C-1). - EI-MS: m/z (%) = 394 (4) [M⁺], 165 (100) [C₉H₉O₃⁺]. - HR-EIMS: calc. 394.1627, found 394.1631.

(4S*,4aS*,9aS*)-4,8,9a-Zrihydroxy-4a,6-dimethyl-3,4,4a,9a-tetrahydro-2H-xanthene-1,9-dione (13):

To a solution of 22 mg (56 μmol) 9a-hydroxy-8-methoxy-4-(2-methoxy-ethoxymethoxy)-4a,6-dimethyl-3,4,4a,9a-tetrahydro-2H-xanthene-1,9-dione (**12**) in 5 ml dichloromethane were added 0.56 ml borontribromide (0.56 mmol; 1M in dichloromethane) at room temperature. The resulting deep red solution was stirred for 7 h. After the addition of water the mixture was extracted with three 10 ml portions of dichloromethane. The combined organic phases were dried over sodium sulfate and after evaporation of the solvent the crude product was purified by column chromatography (ethylacetate/cyclohexane 1/1, v/v) giving 6.0 mg (40%) **13** as a yellow solid.

*R*_f: 0.21 (ethylacetate/cyclohexane 1/1, v/v). - IR (KBr): 3408 (m, ν OH), 2948 (w), 1632 (w, ν C=O), 1432 (m), 1372 (w) cm⁻¹. - ¹H NMR (400 MHz, CDCl₃): δ = 1.36 (s, 3 H, CH₃), 2.29-2.46 (m, 5 H, CH₃, CH₂), 3.07-3.22 (m, 1H, CH₂), 3.59-3.64 (m, 1 H, CH₂), 4.40 (dd, ³J_{HH} = 2.8, 2.3 Hz, 1 H, 4-H), 6.28 (s, 1 H, H_{ar}), 6.30 (s, 1H, H_{ar}), 6.37 (s, 1H, OH), 6.82 (s, 1H, OH), 11.37 (s, 1H, OH). - ¹³C NMR (100 MHz, CDCl₃): δ = 16.7 (+, CH₃), 22.4 (+, CH₃), 27.7 (-, CH₂), 32.1 (-, CH₂), 73.4 (+, C-4), 74.7

(C_{quart.}), 80.5 (C_{quart.}), 109.0 (+, CH_{ar}), 108.4 (C_{quart.}), 111.3 (+, CH_{ar}), 151.5 (C_{quart.}), 156.6 (C_{quart.}), 163.0 (C_{quart.}), 187.1 (C-9), 201.6 (C-1). - EI-MS: m/z (%) = 292 (41) [M⁺], 152 (100) [C₈H₈O₃⁺]. - HR-EIMS: calc. 292.0938, found 292.0940.

Diversonol (2, (4S*,4aS*,9aS*)-1,4,8,9a-Tetrahydro-4a,6-dimethyl-1,2,3,4,4a,9a-hexahydro-xanthen-9-one):

To a solution of 6.0 mg (20 μmol) 4,8,9a-trihydroxy-4a,6-dimethyl-3,4,4a,9a-tetrahydro-2H-xanthene-1,9-dione (**13**) in 1.5 ml dichloromethane/methanol (1/2, v/v) were added portion wise 0.8 mg sodium borohydride (20 μmol) at -78 °C under an atmosphere of argon. The conversion was controlled by TLC (ca. 20 min). After evaporation of the solvent the reaction mixture was directly subjected to column chromatography (ethylacetate/cyclohexane 1/1, v/v) giving 4.0 mg (66%) Diversonol (**2**) as a pale yellow solid.

R_f: 0.37 (ethylacetate/cyclohexane 1/1, v/v). - ¹H NMR (600 MHz, CDCl₃): d = 1.38 (s, 3 H, CH₃), 1.43-1.46 (m, 1 H, CH₂), 1.65-1.68 (m, 1H, CH₂), 1.93-1.97 (m, 1 H, CH₂), 2.13-2.18 (m, 1 H, CH₂), 2.24 (s, 3 H, CH_{3ar}), 3.99 (dd, ³J_{HH} = 3.2, 2.9 Hz, 1 H, 1-H), 4.28 (dd, ³J_{HH} = 3.0, 2.9 Hz, 1 H, 4-H), 5.01 (d, ³J_{HH} = 4.6 Hz, 1 H, OH), 6.29 (s, 1 H, OH), 6.31 (s, 2H, H_{ar}), 6.72 (s, 1H, OH), 11.30 (s, 1H, OH). - ¹³C NMR (125 MHz, CDCl₃): d = 19.4 (+, CH₃), 21.9 (+, CH_{3ar}), 22.7 (-, CH₂), 24.9 (-, CH₂), 66.2 (+, C-4), 73.4 (C-1.), 75.6 (C-4a), 81.2 (C-9a), 104.5 (C-8a), 108.7 (+, CH_{ar}), 109.0 (+, CH_{ar}), 149.5 (C_{quart.}), 158.5 (C_{quart.}),

161.7 ($C_{\text{quart.}}$), 194.3 (C-9). - EI-MS: m/z (%) = 294 (1) [M^+], 84 (100). - HR-EIMS: calc. 294.1103, found 294.1109.