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Synthesis of 2′-dealkylmumbaistatin

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Dedicated to Professor Henning Hopf on the occasion of his 65th birthday

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Abstract—The sterically congested 1,2,3-substituted 3′-dealkyl mumbaistatin derivatives **16**, **20**, and **21** were prepared for the first time by base-catalyzed cyclization of the 2,3-bis-substituted naphthoquinone precursor **11** followed by bromine mediated photooxidation and methyl ether cleavage.

1. Introduction

Mumbaistatin (**1**), a novel glucose-6-phosphate translocase inhibitor produced by the *Streptomyces* sp. DSM 11641 was isolated in 2001 by Laszlo et al.[1] Its structure is composed of a 3,8-dihydroxyanthraquinone, acylated at C-1 with a sterically congested 2′,6′-disubstituted benzoic acid. Moreover, a carboxylic group at C-2 adds to the steric

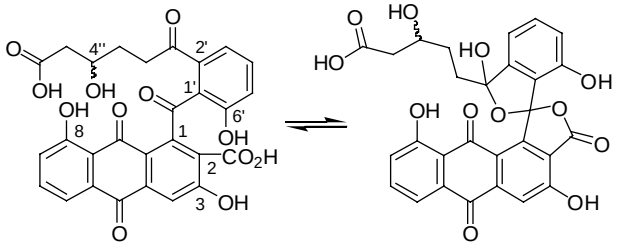

Chart 1. Structure of the open chain (**1a**) and cyclic hemiacetal form (**1b**) of mumbaistatin.[1]

demand. The open chain form **1a** is in equilibrium with the hemiacetal form **1b** (Chart 1).

Mumbaistatin (**1**) was found to be the strongest naturally occurring inhibitor of glucose-6-phosphate translocase (G6P-T1) known today.[1] Inhibitors of G6Pase are of interest for the regulation of blood glucose and for the treatment of the non-insulin-dependent type II diabetes mellitus (NIDDM). The compound may therefore be a lead structure in the design of new antidiabetic drugs. Because of this potential biological importance, the group of Schmalz has published two synthetic approaches to prepare mumbaistatin (**1**) synthetically.[2,3] The anthraquinone skeleton was either constructed by the Hauser phthalide annulation method[2,4] or by a Diels–Alder reaction involving aryne intermediates, as pioneered by Suzuki et al.[3,5] In both cases, the substituted benzoyl residue was subsequently attached using an organometallic reaction of a 1-formyl anthracene, followed by oxidation. However, both approaches failed to introduce the carboxyl group at C-2 of the anthraquinone. We now present a solution to this specific problem, disclosing the synthesis of 2′-dealkylmumbaistatin derivatives **16**, **20**, and **21**.

In this work, we used an entirely different approach in the construction of the anthraquinone skeleton in which the steric congestion of the highly substituted ring A is overcome by an intramolecular anionic reaction. We recently investigated the reaction of the highly electron-deficient 2-acetyl-1,4-naphthoquinone (**2a**, $R^1=H$, $R^2=Me$) with the diene **3**.[6] Due to its fixed transoid configuration, this diene is not capable of Diels–Alder type cycloadditions.[7] However, the inherent silyl-ketene acetal functionality of **3** allows Lewis acid-catalyzed nucleophilic additions, in particular of the sterically less hindered methylene group. The highly electron-deficient 2-acetyl-1,4-naphthoquinones (**2a** and **2b**) are particularly good acceptors and no catalyst at all was required for the Michael addition of **3** to afford the 2,3-bissubstituted naphthoquinone (**4a**) after oxidation of the intermediate adduct with cerium ammonium nitrate (CAN) as shown in Scheme 1.[6]

Keywords: 3′-Dealkyl mumbaistatin; Anthraquinone synthesis; Base-catalyzed aldol cyclization; Photooxidation.
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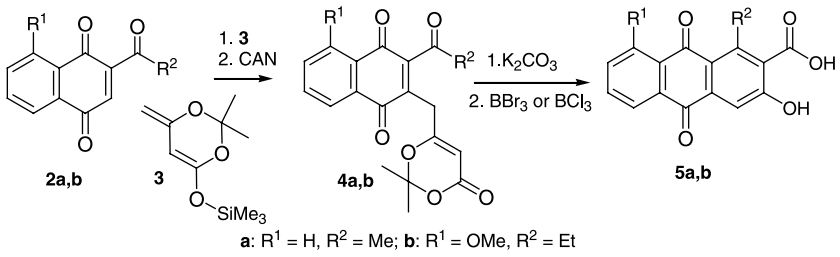


Scheme 1. Construction of contiguously 1,2,3-substituted anthraquinones **5a**[6] and **5b**.[8]

Base treatment of **4a** then furnished the 1-methyl-9, 10-anthraquinone **5a** in 73% yield. This procedure was used by Uno et al. to prepare the bioactive 1-ethylanthraquinone aloesaponarin I and K1115A (**5b**; R^1=OMe, R^2=Et) via the intermediates **2b** and **4b**.[8] The strategy of the present work was to replace the acetyl or propionyl residue on the naphthoquinone core by a phenylacetyl residue (R^2=CH_2Ph) followed by oxidation of the resulting benzylic methylene group at C-1 of the anthraquinone **5** (R^2=CH_2Ph) (see Schemes 3 and 4).

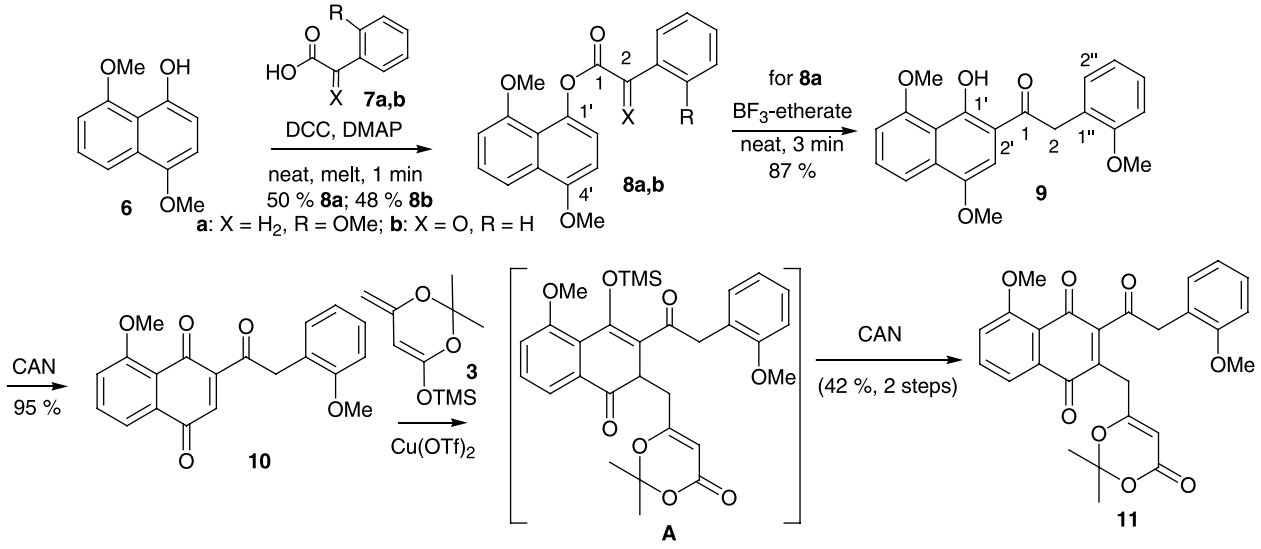
2. Results and discussion

2.1. Construction of the 2,3-dialylated naphthoquinone 11

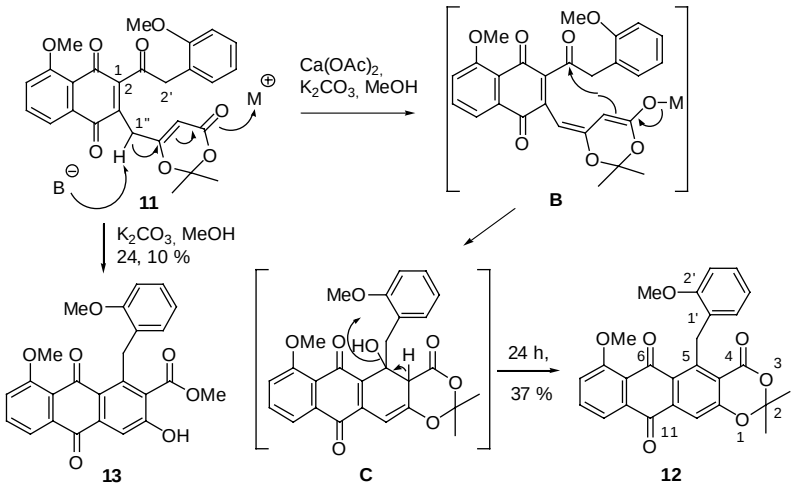
Based on this concept, the synthesis of the 2,3-disubstituted naphthoquinone **11** was tackled first (Scheme 2). The tight hydrogen bond and thus low nucleophilicity of 4, 8-dimethoxynaphthol (**6**), was a problem using normal acylation conditions in the reaction with 2-methoxyphenylacetic acid (**7a**) or 2-oxo-2-phenylacetic acid (**7b**). However, employing modified Steglich[9] neat conditions, with a melt of the reaction components **6** and **7a** or **7b** together with the usual amounts of dicyclohexyl carbodiimide (DCC) and dimethylaminopyridine (DMAP) gave the desired esters **8a** and **8b** in 50 and 48% yield, respectively. Next, the Fries rearrangement was tried on both the phenylacetic ester **8a** and the phenylglyoxylic esters **8b**. The expected 2-acylation product **9** was isolated in the reaction of ester **8a** with boron trifluoride etherate in 87% yield, but no Fries rearrangement products could be detected from the reaction of the phenylglyoxylic ester **8b** under a variety of conditions. Thus, the missing oxygen atom at C-2 had to be introduced in a later step. However, we were confident that this step would be possible photochemically, based on the experience of photooxidation in the angucyclinone antibiotics series.[10,11] Oxidation of the hydroquinone monomethyl ether **9** with cerium ammonium nitrate (CAN) was possible on a multigram scale in 95% yield to afford the acylated naphthoquinone **10**. The transoid fixed diene **3**, prepared from the parent dioxin by deprotonation with LDA and silylation of the enolate with trimethylsilyl chloride,[7] was used to introduce the 'bottom' part side chain at C-3 of the naphthoquinone. The best yields in this reaction were attained using equimolar amounts of cuprous triflate as a mild Lewis-acid catalyst. The presumable silylated Michael addition intermediate **A** was not isolated but immediately oxidized to the 2,3-bis-substituted naphthoquinone **11** (42% over the two steps).

2.2. Base-catalyzed cyclization of 11 to the 1,3-dioxanaphthacene-4,6,11-trione 12

In their K1115A synthesis, Uno et al.[8] showed that two different cyclization modes can be adopted depending on the strength of the base used, initiated by deprotonation at



Scheme 2. Construction of the 2,3-bis-substituted naphthoquinone **11**.

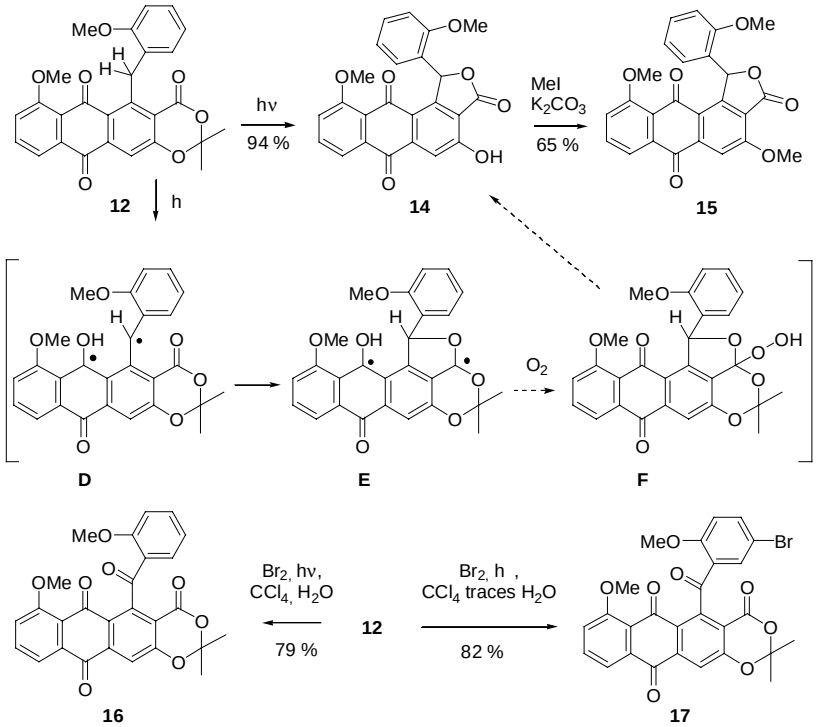


Scheme 3. Cyclization of the disubstituted naphthoquinone **11** to the 1,3-dioxanaphthacene-4,6,11-trione **12** and the methyl ester **13**.

either 2′ or 1″-C in compound **11**. In fact, the choice of the suitable base was crucial to induce the desired cyclization and after some experimentation a mixture of potassium carbonate buffered by addition of calcium acetate gave the best results in the multistep aldol-type condensation proceeding via the enolate **B** and the alcohol **C**. A simultaneous transesterification using the stronger base potassium carbonate gave the anthraquinone methyl ester **13**, however in only 10% yield because these conditions were appropriate for transesterification but not optimal to induce the desired cyclization.

2.3. Oxidation of the benzylic position at C-5

With the 1-benzyl-anthraquinone **12** in hand, the oxidation of the benzylic position was studied next (Scheme 4). In connection with the angucyclinone antibiotics series, we observed the facile photooxidation of the benzylic position of the angularly condensed benzo[*a*]anthraquinone system.[11] Therefore, anthraquinone **12** was subjected to irradiation with sunlight in dichloromethane solution as in the previous experiments with angucyclinones. However, not the expected carbonyl oxidation product **16** but rather the 10-hydroxy-4-methoxy-1-(2-methoxyphenyl)anthra[2,1-*c*]furan-3,6,11(1*H*)-trione (**14**) was isolated. In line with earlier evidence, we suggest that the biradical **D**, formed upon light induced excitation of the anthraquinone **12**, cyclizes with the proximate lactone carbonyl to yield an anthra[2,1-*c*]furan intermediate **E**. In fact, proximity seems to be a decisive factor for this reaction since the ester **13** with more rotational flexibility did not undergo similar photochemical cyclization reactions. The intermediate **E** may then further react with molecular oxygen in a multistep fashion to yield the stable anthra[2,1-*c*]furan lactone **14**, as



Scheme 4. Photooxidation of 1,3-dioxanaphthacene-4,6,11-trione **12** to the anthra[2,1-*c*]furan **15** and bromination of **12** to the ketones **16** and **17**.

observed in the angucyclinone series.[11] Chemically, the first oxidation step was performed in the photooxidation and further oxidative transformation of **14** was certainly possible.

However, we were looking for a shorter pathway to study a direct conversion of **12** to the carbonyl compound **16**. Thus, the light induced radical bromination of **12** was investigated, again leading to a surprising result. By accident, we used tetrachloromethane solvent of different quality, for example, water content, obtaining mixtures of the desired carbonyl compound **16** in addition to various amounts of the monobrominated compound **17**. Later it was found that water saturated tetrachloromethane solutions of **12** afforded the carbonyl compound **16** in 79%, whereas, on a small scale, solutions with only traces of water gave the bromo compound **17** in 82% yield. The reaction can be rationalized assuming a displacement reaction of the bromine with the hydroxyl compound to yield an intermediate alcohol, which is further oxidized to the ketone **16** with excess of bromine, or possibly by photochemical oxidation.[10] With a comparatively high content of water, this reaction may be faster than bromination of the aromatic nucleus. The electron deficient aromatic **16** does not undergo further bromination.

2.4. Methyl ether and acetonide cleavage

Finally, the cleavage of the acetonide group in **11** as a model compound and of the two methyl ether groups in anthraquinone **12** was studied. The dioxolane ring was easily cleaved by base-catalyzed transesterification as demonstrated in the conversion of **11** to the methyl ester **13** using K_2CO_3 in methanol (see Scheme 3). As expected, acetonide cleavage was also possible under mild acidic conditions but simultaneous reduction of the acylated naphthoquinone **11** by the methanol present was observed to yield the hydroquinone **18** in 94% yield. Oxidation of **18** with CAN gave the naphthoquinone **19** in good yield (91%). These experiments demonstrate the easy cleavage of the acetonide that may be of importance in the late steps of mumbaistatin synthesis.

Both methyl ethers were activated towards Lewis-acid-mediated cleavage by neighboring aromatic carbonyl groups, the methoxy group of the side chain even by three carbonyls. In fact, the C-2′ methoxyl group was cleaved first upon boron tribromide treatment and the monophenol **20** was isolated in 95% yield. Prolonged reaction also affected the dioxolane protecting group and the bisphenol **21** was isolated in only 20% yield (Scheme 5).

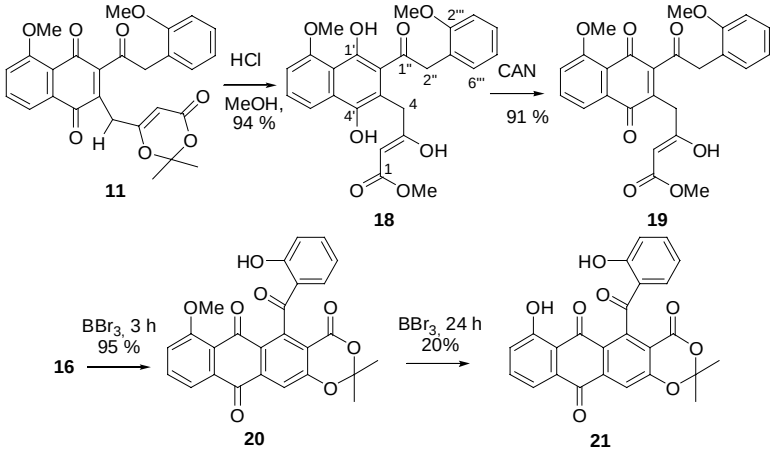
In summary, the 1,2,3-contiguously substituted 3′-dealkyl mumbaistatin derivatives **16**, **20**, and **21** were prepared for the first time, employing an intramolecular base-catalyzed condensation reaction of a 2,3-bisalkylated naphthoquinone precursor **11** followed by photooxidation and methyl ether cleavage. The attachment of the side chain, present in mubaistatin (**1**), can be effected at a late stage by a palladium mediated coupling reaction starting from an appropriate 6′′′ brominated precursor **18**.

3. Experimental

3.1. General

For general methods and instrumentation see Ref.[12]

3.1.1. 4,8-Dimethoxynaphthalen-1-yl-2-(2-methoxyphenyl)acetate (8a). A mixture of finely ground 4,8-dimethoxynaphthol (**6**) (prepared from 1,5-dihydroxynaphthalene by formylation and Bayer–Villiger oxidation[13]) (8.07 g, 39.6 mmol), 2-methoxyphenylacetic acid (**7a**) (9.85 g, 59.3 mmol), dicyclohexyl carbodiimide (DCC, 12.24 g, 59.3 mmol) and dimethylaminopyridine (DMAP, 7.26 g, 59.3 mmol) was heated in a flask to ca. 120 °C. The mixture was maintained at this temperature for 1 min after the entire solid was molten. The cooled mixture was then dissolved in CH_2Cl_2 (800 ml) and left in the refrigerator at −20 °C overnight. The precipitated urea was filtered off, the solvent removed under reduced pressure and the residue purified by silica gel column chromatography using a gradient of CH_2Cl_2 to CH_2Cl_2/MeOH 98:2 to afford the ester **8a** as white needles (6.71 g, 50%, mp 109 °C): IR (KBr) 3001 (CH), 2956 (CH), 2937 (CH), 2837 (OCH_3), 1761 (C═O), 1601 (CH), 1514 (CH), 1412, 1271, 1250, 1228, 1147, 1068 cm^{-1}; UV (methanol) λ_{max} (log ε) 270 nm (4.78), 331



Scheme 5. Methyl ester and methyl ether cleavage of **11** and **16** using HCl/MeOH or boron tribromide.

(4.01), 344 (3.92); ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.94 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 4.03 (s, 2H, 2-H), 6.80 (d, ^3J=8.3 Hz, 1H, 3′-H), 6.90–7.05 (m, 4H, 4′-H, 5′-H, 6′-H, 7″-H), 7.34–7.45 (m, 3H, 2″-H, 3″-H, 6″-H), 7.91 (d, ^3J=8.5 Hz, 1H, 5″-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.89 (d, C-2), 55.98/56.16/56.38 (3×s, 3×OCH_3), 104.19 (d, C-3″), 107.21 (d, C-7″), 111.06 (d, C-5″), 115.24 (d, C-3′), 119.12 (d, C-2″), 120.14 (s, C-8a″), 121.00 (d, C-5′), 123.28 (s, C-1′), 126.21 (d, C-6″), 128.68 (s, C-4a″), 128.98 (d, C-4′), 131.50 (d, C-6′), 140.36 (s, C-1″), 153.64 (s, C-8″), 155.64 (s, C-4″), 158.09 (s, C-2′), 171.64 (s, C-1); MS (EI, 70 eV) *m/z* (%) 352 (12) [M^+], 204 (100) [$C_{10}H_5(OCH_3)_2OH^+$], 189 (44) [$C_{10}H_5(OCH_3)_2OH^+$–CH_3], 121 (19) [$C_7H_6OCH_3^+$], 91 (28) [$C_7H_7^+$], 57 (57) [$C_3H_5O^+$], 28 (75) [CO^+]; HR EIMS calculated for $C_{21}H_{20}O_5$: 352.13107, Found: 352.13101±2 ppm. Anal. Calcd for $C_{21}H_{20}O_5$: C, 71.58; H, 5.72. Found: C, 71.40; H, 5.60.

3.1.2. 4,8-Dimethoxynaphthalen-1-yl 2-(2-methoxyphenyl)-2-oxoacetate (8b). 4,8-Dimethoxynaphthol (**6**) (3.00 g, 14.7 mmol) was reacted according to the procedure described for **8a** using phenylglyoxylic acid (**7b**) (3.31 g, 22.1 mmol), DCC (12.24 g, 59.3 mmol) and DMAP (7.26 g, 59.3 mmol) to afford ester **8b** (2.37 g, 48%, mp 150 °C, decomp.) as a red-brown solid: IR (KBr) 2935 (CH), 2852 (OCH_3), 1759 (C=O), 1705 (C=O), 1608, 1448, 1408, 1377, 1068 cm^{-1}; UV (methanol) λ_{max} (log ε) 333 nm (3.15), 348 (3.23); ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.74 (s, 3H, 4″-OCH_3), 4.08 (s, 3H, 8″-OCH_3), 6.90 (d, ^3J=7.4 Hz, 1H, 2″-H), 7.36–7.45 (m, 5H, 3′-H, 5′-H, 3″-H, 6″-H, 7″-H), 7.60–7.68 (m, 3H, 2′-H, 4′-H, 6′-H), 7.85 (dd, ^3J=8.5 Hz, ^4J=0.9 Hz, 1H, 5″-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 55.69 (q, 4″-OCH_3), 56.22 (q, 8″-OCH_3), 105.59 (d, C-2″), 108.98 (d, C-3″), 115.22 (d, C-7″), 115.83 (d, C-5″), 116.01 (s, C-8a″), 126.36 (d, C-6″), 126.57 (s, C-4a″), 128.23 (d, C-3′, C-5′), 128.58 (d, C-2′, C-6′), 138.12 (d, C-4′), 143.50 (s, C-1′), 147.31 (s, C-1″), 148.08 (s, C-8″), 156.40 (s, C-1), 174.36 (C-2); MS (EI, 70 eV) *m/z* (%) 334 (9) [M^+−H], 307 (8), 279 (18), 205 (20), 167 (46), 149 (89) [$C_7H_5O_3^+$], 105 (89), 57 (99), 44 (100) [CO_2^+]. Anal. Calcd for $C_{21}H_{20}O_5$: C, 71.42; H, 4.79. Found: C, 70.98; H, 4.31.

3.1.3. 1-(1-Hydroxy-4,8-dimethoxynaphthalen-2-yl)-2-(2-methoxyphenyl)-ethanone (9).[14] A melt of esters **8a** (ca. 110 °C, 8.84 g, 25.1 mmol) was treated rapidly under nitrogen with BF_3–etherate (3.76 ml, 29.9 mmol). The reaction was terminated after 3 min resulting in a solid. After cooling, the product was dissolved in CH_2Cl_2 (200 ml) and washed with water. The aqueous phase was extracted with another charge of CH_2Cl_2 (100 ml), the combined organic phase was dried (Na_2SO_4), the solvent was evaporated at reduced pressure, and the residue purified by column chromatography on silica gel (CH_2Cl_2) to afford naphthol **9** (7.69 g, 87%, mp 139 °C) as yellow needles: UV (methanol) λ_{max} (log ε) 269 nm (4.76), 395 (3.91); IR (KBr) 3097 (OH), 2947 (CH), 2929 (CH), 2831 (OCH_3), 1626 (C=O), 1574, 1379, 1273, 1242, 1072, 891, 754 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.86 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 4.07 (s, 3H, OCH_3), 4.40 (s, 2H, 2-H), 6.93–7.02 (m, 3H, 3″-H, 5″-H, 7′-H), 7.15 (s, 1H, 3′-H), 7.27–7.30 (m, 2H, 4″-H, 6″-H), 7.56 (dd, ^3J=8.2, 8.0 Hz, 1H, 6′-H), 7.84 (dd, ^3J=8.3 Hz, ^4J=1.0 Hz, 1H, 5′-H), 13.91 (s, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 41.59 (t, C-2), 55.92/56.08/56.76 (3×q, 3×OCH_3), 103.19 (d, C-3′), 107.68 (d, C-7′), 111.07 (d, C-5′), 113.04 (s, C-2′), 115.00 (d, C-3″), 117.20 (s, C-8a′), 121.22 (d, C-5″), 124.29 (s, C-1″), 128.89 (d, C-6′), 130.42 (d, C-4″), 131.30 (d, C-6″), 132.92 (s, C-4a′), 147.13 (s, C-1′), 157.39 (s, C-4′), 159.11 (s, C-8′), 159.75 (s, C-2″), 203.04 (s, C-1); MS (EI, 70 eV) *m/z* (%) 352 (27) [M^+], 231 (100) [$M^+-C_7H_7OCH_3$], 204 (41) [$C_{10}H_5(OCH_3)_2OH^+$], 189 (54) [$C_{10}H_5(OCH_3)_2OH^+$–CH_3], 174 (12) [$C_{10}H_5(OCH_3)_2OH^+$–2×CH_3], 121 (20) [$C_7H_6OCH_3^+$], 91 (13) [$C_7H_7^+$]; HR EIM calculated for $C_{21}H_{20}O_5$ 352.13107. Found: 352.1310±2 ppm. Anal. Calcd for $C_{21}H_{20}O_5$: C, 71.20; H, 5.53. Found: C, 71.58; H, 5.72.

3.1.4. 8-Methoxy-2-[2-(2-methoxyphenyl)-acetyl]-[1,4]naphthoquinone (10). A solution of the hydroquinone derivative **9** (7.42 g, 21.0 mmol) in acetonitrile (150 ml) was reacted with a 1 M aqueous solution of cerium ammonium nitrate (CAN, 42.00 ml, 42.0 mmol) and stirred for 15 min. The mixture was diluted by addition of water (300 ml) and extracted three times with CH_2Cl_2 (3× 200 ml). The combined organic phase was dried (Na_2SO_4), the solvent evaporated at reduced pressure, and the residue purified by column chromatography on silica gel to afford the pure quinone **10** as red-brown crystals (6.68 g, 95%), mp 118 °C after recrystallization from EtOAc/petroleum ether (50–70 °C): UV (methanol) λ_{max} (log ε) 269 nm (4.78), 399 (3.62); IR (KBr) 3039 (CH), 3006 (CH), 2943 (CH), 2841 (OCH_3), 1716 (C=O), 1651 (C=O), 1585, 1495, 1469, 1296, 1250, 1047 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.77 (s, 3H, 2″-OCH_3), 4.07 (s, 3H, 8-OCH_3), 4.17 (s, 2H, 2′-H), 6.83 (d, ^3J=8.2 Hz, 1H, 3″-H), 6.87 (s, 1H, 3-H), 6.89–6.97 (m, 2H, 5″-H, 6″-H), 7.24 (d, ^3J=7.2 Hz, 1H, 7-H), 7.37 (dd, $^3J_1$=$^3J_2$=4.8 Hz, 1H, 4″-H), 7.72–7.78 (m, 2H, 5-H, 6-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 45.77 (t, C-2′), 55.61/56.97 (2×s, 2×OCH_3), 110.76 (d, C-3″), 118.84 (d, C-7), 119.43 (d, C-5″), 121.17 (s, C-5), 122.82 (s, C-1″), 129.33 (s, C-8a), 132.20 (d, C-4″), 133.75 (d, C-6″), 134.30 (d, C-6), 135.77 (s, C-4a), 149.57 (d, C-3), 157.73 (s, C-2), 160.34/160.46 (2×s, C-2″, C-8), 185.44 (s, C-1′); MS (EI, 70 eV) *m/z* (%) 336 (13) [M^+], 308 (3) [M^+−CO], 121 (100) [$C_7H_6OCH_3^+$], 91 (62) [$C_7H_7^+$]; HR MS calculated for $C_{20}H_{16}O_5$: 336.09977. Found: 336.09958±2 ppm. Anal. Calcd for $C_{20}H_{16}O_5$: C, 71.42; H, 4.79. Found: C, 71.09; H, 4.68.

3.1.5. 2-(2,2-Dimethyl-6-oxo-6*H*-[1,3]dioxin-4-ylmethyl)-5-methoxy-3-[2-(2-methoxyphenyl)-acetyl]-[1,4]naphthoquinone (11). A solution of diene **3**[7] (3.892 g, 17.84 mmol) in dry CH_2Cl_2 (20 ml) was stirred for 20 min under nitrogen at −20 °C with Cu(II)–triflate (2.156 g, 5.95 mmol). The solution was cooled to −60 °C and naphthoquinone **10** (2.000 g, 5.95 mmol) was added in one portion. The mixture was stirred for 6 h at −20 °C and the reaction was then quenched by addition of 2 N HCl (30 ml). The phases were separated and the aqueous phase extracted twice with CH_2Cl_2 (2×30 ml). The solvent was removed under reduced pressure and the crude product dissolved in acetonitrile (40 ml) and treated with a solution of CAN (6.527 g, 11.90 mmol) in water (10 ml). After stirring for 15 min the mixture was diluted with CH_2Cl_2 (150 ml) and water (150 ml). The phases were separated and the organic

phase was extracted twice with CH_2Cl_2 (2×100 ml). The combined organic phase was dried (Na_2SO_4), the solvent was evaporated at reduced pressure, and the residue purified by column chromatography on silica gel (CH_2Cl_2/MeOH 99:1) to afford the bisalkylated naphthoquinone **11** (1.170 g, 42%, mp 57 °C) as orange needles: UV (methanol) λ_{max} (log ε) 269 nm (4.88), 400 (3.62); IR (KBr) $\tilde{\nu}$ (cm^{-1}) 2997 (CH), 2925 (CH), 2844 (OCH_3), 1732 (C=O), 1662 (C=O), 1635, 1392, 1263, 1203, 1014, 756; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.64 (s, 6H, 2×CH_3), 3.32 (s, 2H, 3-CH_2), 3.71 (s, 3H, 2‴-OCH_3), 4.05 (s, 3H, 5-OCH_3), 4.11 (s, 2H, 2″-CH), 5.11 (s, 1H, 5′-H), 6.84 (d, ^3J=8.2 Hz, 1H, 3‴-H), 6.91–6.94 (m, 1H, 5‴-H), 7.21 (d, ^3J=7.2 Hz, 1H, 6‴-H), 7.24–7.29 (m, 1H, 4‴-H), 7.37 (dd, ^3J=6.9 Hz, ^4J=2.3 Hz, 1H, 6-H), 7.70–7.74 (m, 2H, 7-H, 8-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.32 (q, 2′-CH_3), 31.22 (t, 3-CH_2), 46.54 (t, C-2″), 55.55/57.05 (2×OCH_3), 94.62 (d, C-5′), 107.39 (s, C-2′), 110.85 (d, C-3‴), 118.94 (d, C-6), 119.45 (s, C-1‴), 119.94 (d, C-5‴), 121.38 (d, C-8), 121.47 (s, C-4a), 129.66 (d, C-4‴), 132.23 (d, C-6‴), 133.77 (s, C-8a), 136.11 (d, C-7), 137.34 (s, C-3), 149.60 (s, C-2), 157.74 (s, C-2‴), 160.28 (s, C-5), 161.20 (s, C-6′), 168.00 (s, C-4′), 182.75/184.40 (2×s, C-1, C-4), 200.60 (s, C-1″); MS (EI, 70 eV) *m/z* (%) 376 (20) [$M^+-C_4H_6O_3+2H$], 255 (100) [$M^+-C_4H_6O_3-C_7H_6OCH_3+2H$], 240 (19) [$M^+-C_4H_6O_3-C_7H_6OCH_3-CH_3+2H$], 121 (12) [$C_7H_6OCH_3^+$], 91 (23) [$C_7H_7^+$], 44 (10) [$CO_2^+$]. Anal. Calcd for $C_{27}H_{24}O_8$: C, 68.06; H, 5.08. Found: C, 67.64; H, 5.02.

3.1.6. 7-Methoxy-5-(2-methoxybenzyl)-2,2-dimethyl-1,3-dioxanaphthacene-4,6,11-trione (12). A solution of naphthoquinone **11** (1.000 g, 2.10 mmol) in methanol (20 ml) was treated with dry $CaCl_2$ (1.000 g, 6.33 mmol) and subsequently with dry K_2CO_3 (145 mg, 1.05 mmol) and the mixture was stirred for 24 h at 20 °C. The reaction was quenched by addition of 1 M HCl (20 ml), the mixture extracted with CH_2Cl_2 (2×30 ml), and the combined organic phase was dried (Na_2SO_4), the solvent evaporated at reduced pressure, and the residue purified by column chromatography on silica gel (CH_2Cl_2/MeOH 99:1) to afford the cyclization product **12** (352 mg, 37%, mp 177 °C) as orange crystals: UV (methanol) λ_{max} (log ε) 269 nm (5.02), 375 (3.80); IR (KBr) $\tilde{\nu}$ (cm^{-1}) 3072 (CH), 3001 (CH), 2925 (CH), 2839 (OCH_3), 1741 (C=O), 1672 (C=O), 1595, 1323, 1275, 1248, 1014, 750; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.70 (s, 6H, 2×2-CH_3), 3.83 (s, 3H, 2′-OCH_3), 3.98 (s, 3H, 7-OCH_3), 5.27 (s, 2H, CH_2), 6.70–6.78 (m, 2H, 5′-H, 6′-H), 6.83 (d, ^3J=8.6 Hz, 1H, 3′-H), 7.07–7.16 (m, 1H, 4′-H), 7.32 (dd, ^3J=8.3 Hz, ^4J=1.1 Hz, 1H, 8-H), 7.68 (dd, ^3J=8.3, 7.7 Hz, 1H, 9-H), 7.74 (s, 1H, 12-H), 7.81 (dd, ^3J=7.7 Hz, ^4J=1.1 Hz, 1H, 10-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.44/25.99 (2×q, 2×2-CH_3), 30.16 (t, 5-CH_2), 55.94 (q, 2′-OCH_3), 57.00 (q, 7-OCH_3), 106.13 (s, C-2), 110.74 (d, C-12), 114.56 (d, C-8), 118.89 (d, C-10), 119.35 (d, C-3′), 120.52 (d, C-4′), 125.54 (s, C-6a), 127.27 (d, C-5′), 129.08 (d, C-9), 130.57 (s, C-5a), 132.54 (s, C-1′), 134.41 (d, C-6′), 134.97 (s, C-10a), 139.08 (s, C-4a), 150.15 (s, C-11a), 158.01 (s, C-5), 158.86 (s, C-12a), 159.57 (s, C-2′), 169.05 (s, C-4), 183.40 (s, C-11), 184.63 (s, C-6); MS (EI, 70 eV) *m/z* (%) 458 (38) [M^+], 400 (100) [$M^+-C_3H_6O$], 385 (76) [$M^+-C_3H_6O-CH_3$], 279 (16) [$M^+-C_3H_6O-C_7H_6OCH_3$], 121 (34) [$C_7H_6OCH_3^+$], 91 (24) [$C_7H_7^+$], 28 (49) [CO^+]; HR MS calculated for $C_{27}H_{22}O_7$: 458.13655. Found: 458.13623. Anal. Calcd for $C_{27}H_{22}O_7$: C, 70.73; H, 4.84. Found: C, 70.51; H, 4.49.

3.1.7. Methyl 3-hydroxy-8-methoxy-1-(2-methoxybenzyl)-9,10-dioxo-9,10-dihydroanthracene-2-carboxylate (13). A solution of naphthoquinone **11** (200 mg, 0.42 mmol) in methanol (3 ml) was treated with dry K_2CO_3 (70 mg, 0.51 mmol) and stirred for 24 h at 20°. The reaction was quenched by addition of 0.1 M HCl (10 ml), extracted with CH_2Cl_2 (2×10 ml), the combined organic phase was dried (Na_2SO_4), the solvent evaporated at reduced pressure, and the residue purified by column chromatography on silica gel (CH_2Cl_2/MeOH 99:1) to afford the methyl ester **13** (18 mg, 10%, mp 198 °C) as orange-red needles: UV (methanol) λ_{max} (log ε) 269 nm (5.00), 420 (4.08); IR (KBr) $\tilde{\nu}$ (cm^{-1}) 3002 (CH), 2952 (CH), 2918 (CH), 2848 (OCH_3), 1741 (C=O), 1670 (C=O), 1631, 1583, 1282, 1242, 1173, 1020, 754; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.57 (d, ^4J=1.9 Hz, 2H, 1-CH_2), 3.64 (s, 3H, 2′-OCH_3), 3.78 (s, 3H, CO_2CH_3), 4.10 (s, 3H, 8-OCH_3), 7.07 (d, ^3J=8.3 Hz, 1H, 3′-H), 7.13 (d, ^3J=7.4 Hz, 1H, 5′-H), 7.22 (dd, ^3J=7.4 Hz, ^4J=1.9 Hz, 1H, 6′-H), 7.39–7.47 (m, 2H, 7-H, 4′-H), 7.79 (dd, ^3J=8.4, 7.7 Hz, 1H, 6-H), 7.84 (s, 1H, 4-H), 8.03 (dd, ^3J=7.7 Hz, ^4J=1.0=Hz, 1H, 5-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 39.84 (t, 1-CH_2), 52.47 (q, CO_2CH_3), 55.95 (q, 2′-OCH_3), 57.12 (q, 8-OCH_3), 111.57 (d, C-4), 116.21 (s, C-8a), 118.60 (d, C-3′), 120.54 (d, C-7), 120.84 (d, C-5), 121.13 (d, C-5′), 121.37 (s, C-9a), 123.41 (s, C-2), 130.49 (d, C-6), 131.71 (s, C-10a), 131.86 (s, C-1), 135.31 (s, C-1′), 136.12 (s, C-6′), 136.14 (s, C-4a), 142.40 (s, C-8), 157.03 (s, C-3), 161.31 (s, C-2′), 171.16 (s, CO_2CH_3), 183.04 (s, C-10), 189.09 (s, C-9); MS (EI, 70 eV) *m/z* (%) 432 (59) [M^+], 401 (100) [M^+-OCH_3], 359 (42) [$M^+-C_3H_5O_2$], 327 (17) [$M^+-OCH_3-C_3H_6O_2$], 296 (19), 186 (20), 149 (20), 57 (66) [$C_3H_5O^+$], 43 (54) [CH_3CO^+]; HR MS calculated for $C_{25}H_{20}O_7$: 432.12090. Found: 432.12209.

3.1.8. 4-Hydroxy-10-methoxy-1-(2-methoxyphenyl)-anthra[1,2-*c*]furan-3,6,11(1*H*)-trione (14). The benzoylanthraquinone **12** (20 mg, 0.04 mmol) was dissolved in CH_2Cl_2 (ca. 25 ml), the solution placed in 10 NMR tubes and irradiated for 1 day in the sunlight. The solvent was removed under reduced pressure to afford the lactone **14** (17 mg, 94%, mp 238 °C) as yellow needles from diethyl ether: UV (methanol) λ_{max} (log ε) 270 nm (4.79), 358 (4.02); IR (KBr) $\tilde{\nu}$ (cm^{-1}) 3086 (CH), 2951 (CH), 2922 (CH), 2850 (OCH_3), 1745 (C=O), 1653 (C=O), 1585, 1331, 1261, 1014, 756; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 3.91 (s, 3H, 2′-OCH_3), 3.94 (s, 3H, 10-OCH_3), 6.88 (dd, ^3J=7.4, 7.0 Hz, 1H, 5′-H), 6.96 (br s, 1H, 6′-H), 7.03 (d, ^3J=8.2 Hz, 1H, 3′-H), 7.37–7.42 (m, 3H, 1-H, 9-H, 4′-H), 7.76 (dd, ^3J=7.8, 7.3 Hz, 1H, 8-H), 7.86 (s, 1H, 5-H), 7.96 (dd, ^3J=7.8 Hz, ^4J=1.1 Hz, 1H, 7-H), 8.69 (br s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.78 (q, 2′-OCH_3), 56.49 (q, 10-OCH_3), 83.18 (d, C-1), 111.40 (d, C-6′), 114.15 (d, C-5), 117.72 (s, C-3a), 118.81 (d, C-9), 119.92 (d, C-7), 120.86 (s, C-10a), 123.58 (s, C-11a), 123.70 (s, C-1′), 128.71 (d, C-3′), 130.73 (d, C-4′), 135.14 (d, C-8), 135.26 (s, C-6a), 139.78 (s, C-5a), 151.33 (s, C-11b), 158.06 (s, C-2′), 159.21 (s, C-4), 160.52 (s, C-10), 171.00 (s, C-3), 179.74 (s, C-11), 182.52 (s, C-6); MS (EI, 70 eV) *m/z* (%) 416 (100) [M^+], 385 (12) [M^+-OCH_3], 372 (37) [M^+-CO_2], 357 (33)

$[M^+ - CO_2 - CH_3]$, 327 (11) $[M^+ - CO_2 - CH_3 - CH_2O]$, 91 (29) $[C_7H_7^+]$, 57 (33) $[C_3H_5O^+]$, 41 (29) $[C_3H_5^+]$, 29 (13) $[CHO^+]$; HR MS calculated for $C_{24}H_{16}O_7$: 416.08960. Found: 416.08960. Anal. Calcd for $C_{24}H_{16}O_7$: C, 69.23; H 3.87. Found: C, 69.34; H 4.30.

3.1.9. 4,10-Dimethoxy-1-(2-methoxyphenyl)anthra[2,1-*c*]furan-3,6,11(1*H*)-trione (15). A solution of lactone **14** (9 mg, 0.02 mmol) at 0 °C in Et_2O (2 ml) was treated at 0 °C with an ethereal solution of diazomethane (0.4 M, 0.15 ml). The mixture was kept for 12 h at room temperature and the solvent was removed under reduced pressure. The crude product was purified by preparative layer chromatography on silica gel (1 mm, CH_2Cl_2/MeOH 98:2) to afford the trimethyl ether **15** (6 mg, 65%, mp 244 °C) as yellow needles: UV (methanol) λ_{max} (log ε) 271 nm (3.77); IR (KBr) $\tilde{\nu}$ (cm^{-1}) 3086 (CH), 3012 (CH), 2937 (CH), 2837 (OCH_3), 1763 (C═O), 1674 (C═O), 1603, 1468, 1335, 1254, 1207, 1074, 1011, 968, 754; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84 (s, 3H, 2′-OCH_3), 3.90 (s, 3H, 10-OCH_3), 4.23 (s, 3H, 4′-OCH_3), 6.70–6.73 (m, 2H, 5′-H, 6′-H), 6.90 (d, ^3J=8.3 Hz, 1H, 3′-H), 7.18 (s, 1H, 1-H), 7.22–7.26 (m, 2H, 9-H, 4′-H), 7.62 (dd, ^3J=8.2, 7.9 Hz, 1H, 8-H), 7.77 (s, 1H, 5-H), 7.82 (dd, ^3J=7.6 Hz, ^4J=1.0 Hz, 1H, 7-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.78 (q, 2′-OCH_3), 56.71 (q, 10-OCH_3), 57.03 (q, 4-OCH_3), 80.48 (d, C-1), 108.85 (d, C-5), 111.40 (d, C-3′), 118.99 (d, C-9), 120.04 (d, C-7), 120.25 (d, C-5′), 120.61 (s, C-3a), 121.28 (s, C-10a), 123.31 (s, C-11a), 124.15 (s, C-1′), 128.95 (d, C-6′), 130.32 (d, C-4′), 134.98 (d, C-8), 135.00 (s, C-6a), 138.95 (s, C-5a), 154.01 (s, C-11b), 158.20 (s, C-2′), 160.42 (s, C-4), 161.02 (s, C-10), 166.98 (s, C-3), 179.98 (s, C-11), 182.99 (s, C-6); MS (EI, 70 eV) *m/z* (%) 430 (67) $[M^+]$, 371 (20) $[M^+ - CO_2 - CH_3]$, 366 (16) $[M^+ - CO_2 - CH_3 - CH_3]$, 326 (15), 279 (14), 233 (18), 160 (42), 149 (42), 135 (67), 57 (70) $[C_3H_5O^+]$, 44 (73) $[CO_2^+]$ 43 (100) $[CH_3CO^+]$; HR MS calculated for $C_{25}H_{18}O_7$: 430.10525. Found: 430.10520. Anal. Calcd for $C_{25}H_{18}O_7$: C, 69.76; H, 4.22. Found: C, 69.87; H, 4.01.

3.1.10. 7-Methoxy-5-(2-methoxybenzoyl)-2,2-dimethyl-4*H*-anthra[2,3-*d*][1,3]dioxin-4,6,11-trione (16). A solution of the benzylanthraquinone **12** (20.0 mg, 0.044 mmol) in CCl_4 (1 ml) was treated with elemental bromine (6.7 µl 0.132 mmol) and two drops of water and the mixture was irradiated with a 100 W tungsten lamp. The mixture was diluted with CH_2Cl_2 (10 ml) and washed with saturated aqueous $NaHCO_3$ solution (10 ml) and water (10 ml). The organic phase was dried (Na_2SO_4), the solvent evaporated at reduced pressure, and the residue purified by column chromatography on silica gel (CH_2Cl_2/MeOH 99:1) to yield the benzoylanthraquinone **16** (18 mg, 88%, mp 249 °C) as pale yellow crystals: UV (methanol) λ_{max} (log ε) 270 nm (4.54), 391 (3.95); IR (KBr) $\tilde{\nu}$ (cm^{-1}) 3093 (CH), 3001 (CH), 2927 (CH), 2841 (OCH_3), 1743 (C═O), 1670 (C═O), 1595, 1446, 1344, 1282, 1232, 1016, 962, 856, 752; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 1.80 (s, 3H, 2-CH_3), 1.82 (s, 3H, 2-CH_3), 3.45 (s, 3H, 2′-OCH_3), 3.97 (s, 3H, 7-OCH_3), 6.94 (d, ^3J=8.2 Hz, 1H, 3′-H), 7.24 (ddd, $^3J_1$=$^3J_2$=7.5 Hz, ^4J=0.8 Hz, 1H, 5′-H), 7.41 (dd, ^3J=8.4 Hz, ^4J=0.8 Hz, 1H, 8-H), 7.59 (ddd, ^3J=8.2, 7.5 Hz, ^4J=1.8 Hz, 1H, 4′-H), 7.78 (dd, ^3J=8.4, 7.9 Hz, 1H, 9-H), 7.87 (s, 1H, 12-H), 7.95 (dd, ^3J=7.9 Hz, ^4J=1.1 Hz, 1H, 10-H), 8.30 (d, ^3J=7.5 Hz, 1H, 6′-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.49/25.57 (2×q, 2×2-CH_3), 55.57 (q, 2′-OCH_3), 56.42 (q, 7-OCH_3), 106.97 (s, C-2), 111.86 (d, C-3′), 114.63 (d, C-12), 115.02 (s, C-4a), 118.87 (d, C-8), 119.52 (d, C-10), 121.03 (d, C-5′), 126.58 (s, C-1′), 128.03 (s, C-11a), 129.81 (d, C-6′), 134.03 (d, C-4′), 134.18 (s, C-6a), 134.89 (s, C-5a), 135.27 (d, C-9), 135.38 (s, C-10a), 138.61 (s, C-5), 158.17 (s, C-4), 158.98/159.01 (2×s, C-12a, C-2′), 160.71 (s, C-7), 180.15 (s, C-6), 182.21 (s, C-11), 191.64 (s, 5-CO); MS (EI, 70 eV) *m/z* (%) 472 (16) $[M^+]$, 414 (13) $[M^+ - C_3H_6O]$, 383 (100) $[M^+ - C_3H_6O - OCH_3]$, 352 (12) $[M^+ - C_3H_6O - OCH_3 - OCH_3]$, 294 (12), 279 (6) $[M^+ - C_3H_6O - C_8H_7O_2]$, 149 (16), 135 (16) $[C_8H_7O_2^+]$, 57 (11) $[C_3H_5O^+]$, 43 (7) $[CH_3CO^+]$; HR MS calculated for $C_{27}H_{20}O_8$: 472.11582. Found: 472.11420. Anal. Calcd for $C_{27}H_{20}O_8$: C, 68.64; H, 4.27. Found: C, 68.14; H, 4.17.

3.1.11. 5-(5-Bromo-2-methoxybenzoyl)-7-methoxy-2,2-dimethyl-4*H*-anthra[2,3-*d*][1,3]dioxin-4,6,11-trione (17). A solution of the benzylanthraquinone **12** (55 mg, 0.12 mmol) was irradiated in the presence of bromine (56 mg, 0.35 mmol) as described for **16**, however, without addition of water. The brominated benzoylanthraquinone **17** was obtained (55 mg, 86%, mp 241 °C) as a yellow solid: UV (methanol) λ_{max} (log ε) 272 nm (4.51), 389 (3.92); IR (KBr) $\tilde{\nu}$ (cm^{-1}) 2999 (CH), 2937 (CH), 2843 (OCH_3), 1743 (C═O), 1668 (C═O), 1593, 1481, 1448, 1340, 1282, 1271, 1230, 1030 (C–Br), 964; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.79 (s, 6H, 2×2-CH_3), 3.41 (s, 3H, 2′-OCH_3), 3.93 (s, 3H, 7-OCH_3), 6.73 (d, ^3J=8.8 Hz, 1H, 3′-H), 7.35 (dd, ^3J=8.5 Hz, ^4J=0.8 Hz, 1H, 8-H), 7.55 (dd, ^3J=8.8 Hz, ^4J=2.6 Hz, 1H, 4′-H), 7.73 (dd, ^3J=8.4, 7.7 Hz, 1H, 9-H), 7.85 (s, 1H, 12-H), 7.92 (dd, ^3J=7.7 Hz, ^4J=1.1 Hz, 1H, 10-H), 8.47 (br s, 1H, 6′-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.65/25.86 (2×q, 2×2-CH_3), 55.96 (q, 2′-OCH_3), 56.66 (q, 7-OCH_3), 107.01 (s, C-2), 113.85 (d, C-3′), 114.91 (d, C-12), 115.13 (s, C-4a), 118.87 (d, C-8), 119.76 (d, C-10), 121.06 (s, C-5′), 128.05 (s, C-1′), 128.30 (s, C-11a), 132.94 (d, C-9), 134.78 (s, C-6a), 135.33 (d, C-6′), 136.38 (d, C-4′), 136.54 (s, C-10a), 138.49 (s, C-5a), 149.78 (s, C-5), 157.91 (s, C-4), 158.15 (s, C-12a), 158.86 (s, C-2′), 160.65 (s, C-7), 180.17 (s, C-6), 182.25 (C-11), 190.89 (s, 5-CO); MS (EI, 70 eV) *m/z* (%) 552 (12) $[M^+(^{81}Br)]$, 550 $[M^+(^{79}Br)]$, 463 (70) $[M^+(^{81}Br) - C_3H_6O - OCH_3]$, 461 (68) $[M^+(^{79}Br) - C_3H_6O - OCH_3]$, 401 (31), 352 (27), 326 (30), 283 (57), 173 (43), 157 (41), 135 (24) $[C_8H_7O_2^+]$, 111 (100), 57 (35) $[C_3H_5O^+]$, 43 (65) $[CH_3CO^+]$; HR MS calculated for $C_{27}H_{19}BrO_8$: 550.02633 (^{79}Br). Found: 550.02655 (^{79}Br). Anal. Calcd for $C_{27}H_{19}BrO_8$: C, 58.82; H, 3.47. Found: C, 58.91; H, 3.39.

3.1.12. Methyl 4-{1,4-dihydroxy-5-methoxy-3-[2-(2-methoxyphenyl)-acetyl]-naphthalen-2-yl}-3-hydroxy-but-2-enoate (18). A solution of naphthoquinone **11** (40 mg, 0.08 mmol) in 1 M HCl/MeOH (3 ml) was stirred at room temperature for 1 h. The solvent was evaporated at reduced pressure to afford the hydroquinone methyl ester **18** (36 mg, 94%) as a polar red-brown oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.80 (br s, 6H, 1-OCH_3, 2‴OCH_3), 3.94 (s, 2H, 4-H), 4.12 (s, 3H, 5′-OCH_3), 4.50 (s, 2H, 2″-H), 6.89–6.99 (m, 3H, 6′-H, 3‴-H, 5‴-H), 7.14 (s, 1H, 2-H), 7.22–7.36 (m,

2H, 4‴-H, 6‴-H), 7.59 (dd, ^3J=8.1, 8.0 Hz, 1H, 7′-H), 7.84 (dd, ^3J=8.1 Hz, ^4J=0.8 Hz, 1H, 8′-H), 12.99 (s, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.98 (t, C-4), 45.49 (t, C-2″), 52.88 (q, 1-OCH_3), 55.81/56.82 (2×q, 5′-OCH_3, 2‴-OCH_3), 106.06 (d, C-2), 108.12 (d, C-6′), 110.83 (d, C-8′), 111.14 (s, C-2′), 113.52 (s, C-4a′), 113.70 (d, C-3‴), 120.97 (d, C-5‴), 122.97 (s, C-3′), 124.70 (s, C-1‴), 126.80 (s, C-8a′), 128.74 (d, C-4‴), 130.70 (d, C-7′), 131.64 (d, C-6‴), 144.64 (s, C-4′), 151.02 (s, C-1′), 157.97 (s, C-5′), 159.35 (s, C-2‴), 159.66 (s, C-1), 169.74 (s, C-3), 201.69 (s, CO).

3.1.13. Methyl 3-hydroxy-4-{5-methoxy-3-[2-(2-methoxyphenyl)-acetyl]-1,4-dioxo-1,4-dihydronaphthalen-2-yl}-but-2-enoate (19). A solution of the hydroquinone **18** (60 mg, 0.13 mmol) in acetonitrile (3 ml) was treated with a solution of CAN (145 mg, 0.27 mmol) in water (1 ml) and the mixture was stirred for 15 min at 20 °C. The reaction was quenched by addition of CH_2Cl_2 (25 ml) and water (25 ml) and the aqueous phase was extracted with CH_2Cl_2 (2×25 ml). The combined organic phase was dried (Na_2SO_4), the solvent evaporated at reduced pressure, and the residue purified by column chromatography on silica gel (CH_2Cl_2/MeOH 99:1) to afford the naphthoquinone **19** (54 mg, 91%) as orange needles: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.53 (s, 3H, 1-OCH_3), 3.72 (s, 2‴OCH_3), 3.79–3.90 (m, 4H, 4-H, 2″-H), 3.97 (s, 5′-OCH_3), 4.62 (s, 1H, 2-H), 6.76–6.86 (m, 2H, 3‴-H, 5‴-H), 7.13–7.40 (m, 3H, 6″-H, 7″-H, 8″-H), 7.69 (dd, ^3J=8.1, 7.9 Hz, 1H, 4‴-H), 7.93 (d, ^3J=6.6 Hz, 1H, 6‴-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 32.73 (t, C-4), 46.01 (t, C-2″), 52.27 (q, 1-OCH_3), 56.01/56.13 (2×q, 5′-OCH_3, 2‴-OCH_3), 102.07 (d, C-2), 113.76 (d, C-3‴), 119.57 (s, C-1‴), 120.07 (d, C-5‴), 121.42 (d, C-8′), 121.74 (d C-4a′), 129.57 (d, C-4‴), 132.17 (d, C-6‴), 133.98 (s, C-8a′), 135.95 (d, C-7′), 137.59 (s, C-2′), 148.72 (s, C-3′), 150.38 (s, C-1), 170.43 (s, C-3), 183.23/184.27 (2×s, C-1′, C-4′), 200.34 (s, C-1″).

3.1.14. 5-(2-Hydroxybenzoyl)-7-methoxy-2,2-dimethyl-4*H*-anthra[2,3-*d*][1,3]dioxin-4,6,11-trione (20). A solution of the dimethoxyanthraquinone **16** (18 mg, 0.04 mmol) in dry CH_2Cl_2 (3 ml) was treated with a solution of boron tribromide (1.0 M in CH_2Cl_2, 114 µl, 0.12 mmol). After stirring for 3 h at room temperature, 1 M HCl (5 ml) was added and the mixture was extracted with CH_2Cl_2 (2× 10 ml). The combined organic phase was dried (Na_2SO_4), the solvent evaporated at reduced pressure, and the residue purified by column chromatography on silica gel (CH_2Cl_2) to yield the monomethoxyanthraquinone **20** (16 mg, 95%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.81 (s, 6H, 2×2-CH_3), 3.95 (s, 3H, 7-OCH_3), 6.70 (ddd, ^3J=7.9, 7.7 Hz, ^4J=0.6 Hz, 1H, 5′-H), 6.98 (dd, ^3J=7.9 Hz, ^4J=1.6 Hz, 1H, 6′-H), 7.12 (d, ^3J=8.3 Hz, 1H, 8-H), 7.37 (d, ^3J=8.4 Hz, 1H, 3′-H), 7.42 (ddd, ^3J=8.4, 7.7 Hz, ^4J=1.6 Hz, 1H, 4′-H), 7.76 (dd, ^3J=8.3, 7.8 Hz, 1H, 9-H), 7.96 (d, ^3J=7.8 Hz, 1H, 10-H), 8.00 (s, 1H, 12-H), 11.61 (s, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.79/26.05 (2×q, 2×2-CH_3), 56.68 (q, 7-OCH_3), 107.24 (s, C-2), 116.20 (s, C-1′), 116.91 (d, C-12), 118.41 (d, C-8), 118.75 (d, C-10), 119.03 (d, C-3′), 119.86 (d, C-5′), 120.96 (s, C-4a), 121.34 (s, C-6a), 128.77 (s, C-10a), 129.55 (d, C-4′), 134.66 (s, C-11a), 135.21 (d, C-9), 135.55 (d, C-6′), 138.87 (s, C-5a), 143.65 (s, C-5), 157.28 (s, C-7), 159.39 (s, C-4), 160.86 (s, C-12a), 161.49 (s, C-2′), 179.40 (s, C-6), 181.79 (s, C-11), 199.85 (s, 5-CO); MS (EI, 70 eV) *m/z* (%) 458 (100) [M^+], 400 (78) [$M^+-C_3H_6O$], 383 (52) [$M^+-C_3H_6O$–OH], 372 (81) [$M^+-C_3H_6O$–CO], 355 (55) [$M^+-C_3H_6$-O–CO–OH], 121 (49) [$C_7H_6OCH_3^+$], 57 (38) [$C_3H_5O^+$], 43 (37) [CH_3CO^+]; HR MS calculated for $C_{26}H_{18}O_8$: 458.10017. Found: 458.10015.

3.1.15. 7-Hydroxy-5-(2-hydroxybenzoyl)-2,2-dimethyl-4*H*-anthra[2,3-*d*][1,3]dioxin-4,6,11-trione (21). A solution of the monomethoxyanthraquinone **20** (16 mg, 0.035 mmol) was treated by portion-wise addition of 5 equiv of boron tribromide. The reaction was monitored by TLC and worked up as described above before the entire amount of starting material was consumed. The crude product was purified by preparative TLC on silica gel (1 mm) to yield the bisphenol **21** (3 mg, 20%, mp 94 °C) as an orange-red solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.84 (s, 6H, 2×2-CH_3), 6.73 (dd, ^3J=8.0, 7.6 Hz, 1H, 5′-H), 6.97 (d, ^3J=8.0 Hz, 1H, 6′-H), 7.15 (d, ^3J=8.5 Hz, 1H, 8-H), 7.34 (d, ^3J=8.4 Hz, 1H, 3′-H), 7.48 (dd, ^3J=8.4, 7.6 Hz, 1H, 4′-H), 7.75 (d, ^3J=8.5, 8.2 Hz, 1H, 9-H), 8.01 (d, ^3J=8.2 Hz, 1H, 10-H), 8.08 (s, 1H, 12-H), 11.94 (s, 1H, 2′-OH), 12.61 (s, 1H, 7-OH); MS (EI, 70 eV) *m/z* (%) 444 (14) [M^+], 386 (9) [$M^+-C_3H_6O$], 358 (19) [$M^+-C_3H_6O$–CO], 330 (7) [$M^+-C_3H_6O$–CO–CO], 257 (8), 236 (8), 149 (17), 97 (41), 69 (58), 57 (84) [$C_3H_5O^+$], 43 (100) [CH_3CO^+]; HR MS calculated for $C_{25}H_{16}O_8$: 444.08452 Found: 444.08427.

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